universität wien

DISSERTATION

Titel der Dissertation

"Total Syntheses of (-)–Kendomycin and

(+)–Echinopine A and B"

Verfasser

Mag. Thomas Magauer

angestrebter akademischer Grad

Doktor der Naturwissenschaften (Dr.rer.nat.)

Wien, Oktober 2009

Studienkennzahl lt. Studienblatt:	A 091 419
Dissertationsgebiet lt. Studienblatt:	Chemie
Betreuerin / Betreuer:	Univ.–Prof. Dr. Johann Mulzer

Für meine Eltern Karl und Irmgard

und für Nadine

DIE GEFÄHRLICHSTE WELTANSCHAUUNG IST DIE WELTANSCHAUUNG

DERJENIGEN, DIE DIE WELT NICHT ANGESCHAUT HABEN

(Alexander von Humboldt)

Danksagung

Auch wenn ein paar Zeilen dafür nicht ausreichend sind, möchte ich mich an dieser Stelle bei all jenen Personen bedanken, die mich während meiner Studienzeit, insbesonders bei der zwischen November 2007 und November 2009 durchgeführten Dissertation, begleiteten und unterstützten. Die letzten Jahre am Institut für Organische Chemie waren sicher einer der lehrreichsten, interessantesten und anspruchsvollsten Abschnitte meines bisherigen Lebens. Auch wenn der Weg in der Naturstoffsynthese oft steinig und beschwerlich ist, man mit vielen Misserfolgen und Enttäuschungen konfrontiert wird, so lassen die umso schöneren Erfolgsmomente all die Anstrengungen schnell vergessen.

Genau diese Anstrengungen und schönen Momente konnte ich Dank folgender Personen bewältigen und genießen:

An erster Stelle möchte ich mich bei **Prof. Johann Mulzer** bedanken, der mir die Durchführung meiner Dissertation in seiner hervorragenden Arbeitsgruppe ermöglichte. Ihm verdanke ich vor allem mein (stetig gewachsenes) Interesse für das Gebiet der organischen Chemie, das er bereits während meines Grundstudiums mit spannenden und aufregenden Vorlesungen wecken konnte. Ganz besonders möchte ich mich bei ihm für die vielen motivierenden und lehrreichen Gespräche bedanken. Letztere trugen ganz wesentlich und positiv zu meiner wissenschaftlichen und persönlichen Entwicklung bei. Weiters möchte ich ihm für die Möglichkeit der unabhängigen und eigenständigen Arbeitsweise und der Würdigung meiner Arbeit danken.

Meinen Laborkolleginnen Kathrin Höferl–Prantz und Tanja „Muhmu“ Gaich, die mich bereits während meiner Diplomarbeit betreuten, motivierten und unterstützen, möchte ich ein ganz großes Dankeschön aussprechen. Die vielen gemeinsamen und lustigen Stunden, sei es im Labor, beim gemeinsamen Mittagessen oder bei einem Glas Bier, vermisse ich jetzt schon.

Ein besonderer Dank geht an Konrad Tiefenbacher (Echinopine–Team) und Harry J. Martin (Kendomycin–Team), welche meine Projekte anhand zahlreicher Diskussionen, unermüdlicher Unterstützung und diverser Ratschläge zügig vorantrieben.

Für das nette Arbeitsklima und die schöne Zeit in der Mulzer-Gruppe möchte ich mich bei meinen Kollegen bedanken: Alexey Gromov, Wolfgang Felzmann, Valentin Enev, Fritz Hammerschmidt, Roland Barth, Neil Sheddan, Stefan Marchart, Jürgen Ramharter, Harald Weinstabl, Andreas Gollner, Martin

Himmelbauer, Katja Jantos, Marion Kögl – die leider nicht mehr unter uns ist, Peter Siengalewicz und bei der Rinner Arbeitsgruppe (Uwe Rinner, Christoph Lentsch, Christoph Aichinger, Rita Fürst).

Ohne einer funktionierenden und gut organisierten NMR–, HPLC– und MS–Abteilung hat es ein Organiker schwer. Danke für die hervorragende Arbeit des NMR–Teams: Hanspeter Kählig, Lothar Brecker und Susanne Felsinger. Danke für die super Unterstützung des HPLC–Teams: Sabine Schneider, Michael Zinke und Fikret Nasufi. Danke für die raschen und verlässlichen Messungen des MS–Teams: Peter Unteregger und Josef Plangger.

Bei Martina Drescher, Jale Karolyi–Özgür und Sabine Brkovic möchte ich mich für die gute Zusammenarbeit und deren ständige Hilfsbereitschaft bedanken.

Ohne meine besten Freunde Pauli, Berni, Dosi und Gunther hätte der Weg durch mein Studium nicht so viel Spaß gemacht. Bei Nadine, einer der großartigsten Menschen, die ich in meinem Leben kennengelernt habe möchte ich mich einfach nur kurz bedanken. Ihr gewaltiges Entgegenkommen und die unermessliche Unterstützung in vielen Bereichen meines Lebens lassen sich kaum in Worte fassen.

Zuletzt möchte ich meinen Eltern für ihre immense Unterstützung, die vielen großartigen Gespräche und die positive Denkweise, die Sie mir in die Wiege gelegt haben, bedanken.

Publications, Conference Contributions and Awards Resulting from this Thesis

Publications

Peer–Reviewed

"Total Synthesis of the Antibiotic Kendomycin by Macrocyclization via Photo–Fries Rearrangement and Ring Closing Metathesis (RCM)", T. Magauer, H. J. Martin, J. Mulzer, *Angew. Chem., Int. Ed.* **2009**, *48*, 6032–6036.

"Ring Closing Metathesis and Photo–Fries Reaction for the Construction of the Ansamycin Antibiotic Kendomycin. Development of a Protecting Group Free Oxidative Endgame", T. Magauer, H. J. Martin, J. Mulzer, *Chem. Eur. J.* **2009***, Accepted*.

"Total Synthesis of (+)–Echinopine A and B: Determination of Absolute Stereochemistry", T. Magauer, J. Mulzer, K. Tiefenbacher, *Org. Lett.* **2009**, *ASAP*.

Press–Releases

Radio

„Neuartiges Antibiotikum gegen resistente Keime", E. Schütz, *Dimensionen-Magazin*, Österreich 1 (Ö1), 11.09.2009.

Journals

"Neue Leitstrukturen für Antibiotikum entwickelt", A. Geipel-Kern, *PROCESS PharmaTEC*, Vogel Business Media, Würzburg **2009**, *5*, 14.

Online

„Neuartiges Antibiotikum gegen resistente Keime", W. Weitlaner, Pressetext Austria, http://pressetext.at, www.derstandard.at, www.wien-heute.at (08.09.2009); V. Schallhart, Universität Wien, http://public.univie.ac.at (08.09.2009); R. Müller, Portal für Organische Chemie, www.organische-chemie.ch (09.09.2009), M. Mössmer, Österreich Journal, www.oesterreichjournal.at Ausgabe *76*, 60 (07.10.2009).

„Neue Hoffnung gegen resistente Bakterien: Wiener Chemiker synthetisieren Wirkstoff“, Austria Presse Agentur, www.news.at, www.oe24.at, www.springermedizin.at (08.09.2009).

Conference Contributions

Posters

Poster presented at the “**Gordon Research Conference – Natural Products**”. Title of presented poster: “Total Synthesis of the *ansa*–Polyketide Kendomycin via Photo–Fries Rearrangement & Ring Closing Metathesis”, Tilton, NH, USA (26–31 July 2009).

Poster presented at the “**10th Tetrahedron Symposium**”. Title of presented poster: “Total Synthesis of the *ansa*–Polyketide Kendomycin via Photo–Fries Rearrangement & Ring Closing Metathesis”, Paris, France (13–26 June 2009).

Poster presented at the “**Synthesefest of the Ludwig–Maximilian University**”. Title of presented poster: “Total Synthesis of Kendomycin”, Munich, Germany (17–18 March 2009).

Poster presented at the “**21. Irseer Naturstofftage der DECHEMA e.V.**”. Title of presented poster: “Total Synthesis of Kendomycin”, Irsee, Germany (25–27 February 2009).

Poster presented at the “**IASOC 2008 – Ischia Advanced School of Organic Chemistry**”. Title of presented poster: “Towards the Total Synthesis of Kendomycin”, Ischia, Italy (27 September–02 October 2008).

Poster presented at the “**BOSS XI – 11th Belgium Organic Synthesis Symposium**”. Title of presented poster: “Towards the Total Synthesis of the *ansa*–Macrocycle Kendomycin”, Ghent, Belgium (13–18 July 2008).

Oral Presentations

Invited oral presentation at the “**38. Doktorandenworkshop Naturstoffe: Chemie, Biologie und Ökologie Leibniz–Institut für Pflanzenbiochemie**”. Title of presentation: “Neue Projekte aus der Wiener Naturstoffsynthese”, Halle (Saale), Germany (16 October 2009).

Short oral presentation at the “**21. Irseer Naturstofftage der DECHEMA e.V.**”. Title of presentation: “Total Synthesis of the *ansa*–Compound Kendomycin”, Irsee, Germany (25–27 February 2009).

Invited oral presentation at the "**Symposium of Organic Chemistry at ESPCI**". Title of presentation: "Total Synthesis of Kendomycin", Paris, France (6 February 2009).

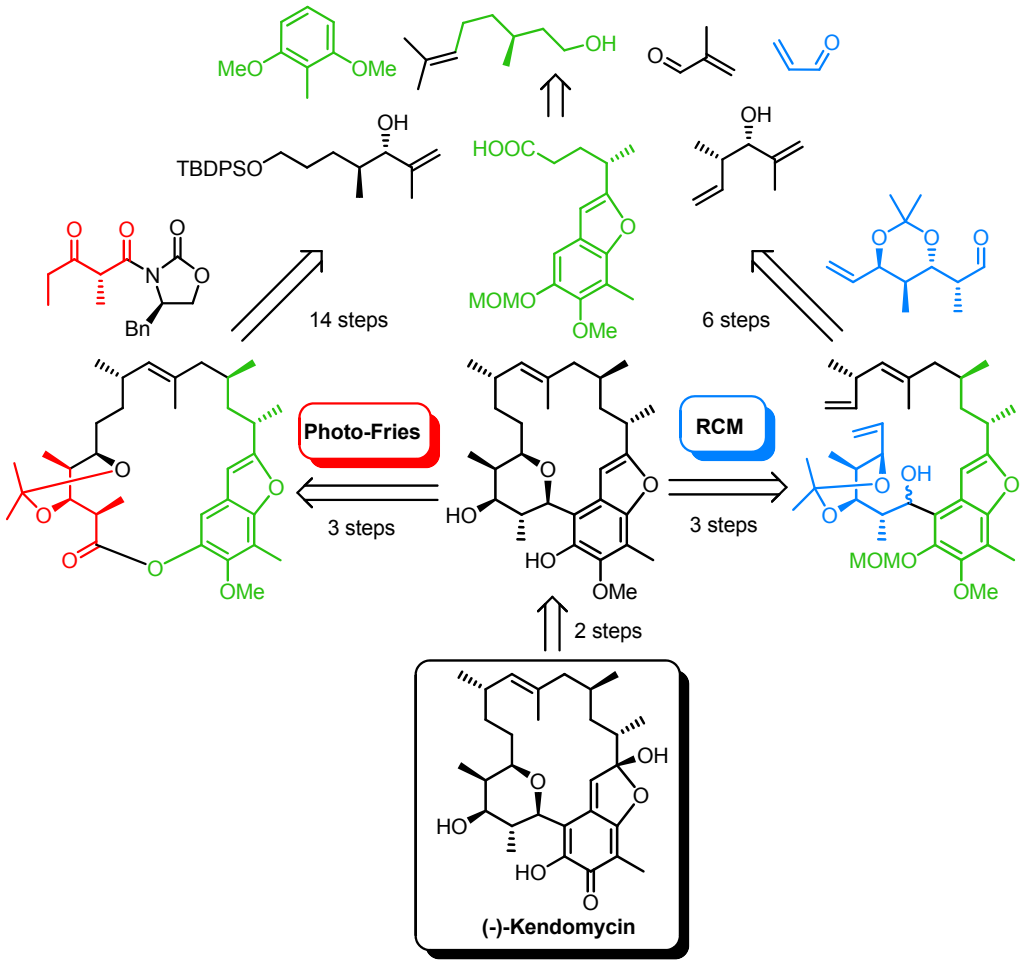
Awards

Thieme Chemistry – SYNFACTS Poster Prize at the "Synthesefest of the Ludwig–Maximilian University". Title of presented poster: "Total Synthesis of Kendomycin", Munich, Germany (17–18 March 2009).

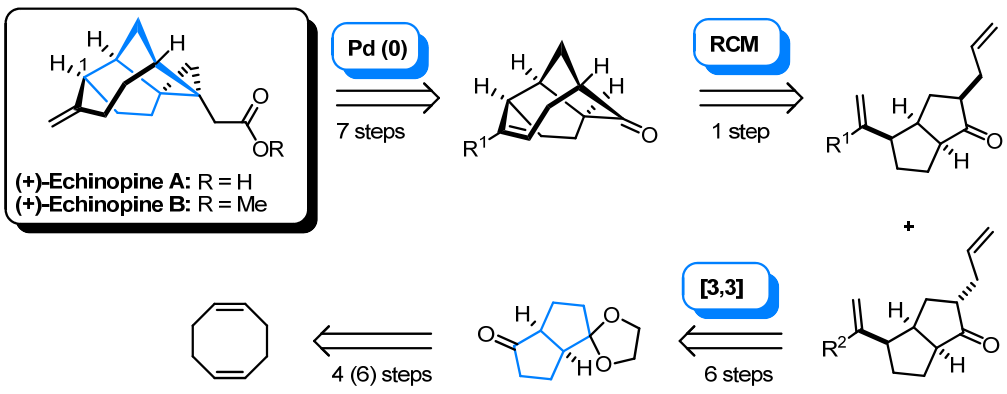
The "kendomycin–family": T. Magauer, A. B. Smith III and C. Lee at the Gordon Natural Products Research Conference 2009 (Tilton, NH, USA).

A. Graphical Abstract

Total Synthesis of (-)-Kendomycin



Total Syntheses of (+)-Echinopine A and B: Determination of Absolute Stereochemistry



B. Abstract

This Ph.D. thesis describes the first total syntheses of (+)–echinopine A and B and two total syntheses of the antibiotic (-)–kendomycin.

Kendomycin, an unprecedented *ansa*–polyketide was first isolated in 1996 (in 1999 re–isolation from *Streptomyces violaceoruber*) and has been fascinating (bio)chemists due to its promising biological activity (endothelin receptor antagonist, antiosteoporotic and antibacterial activity, cytotoxic activity comparable to cisplatin) and remarkable complex molecular framework (fully carbogenic *ansa*–chain, nine stereocenters, pentasubstituted tetrahydropyran ring, unique *p*–quinone methide chromophore).

The total syntheses focused on two convergent strategies, whereas both took advantage of diastereoselective Claisen–Ireland rearrangements of unusual complexity to construct the north–east domain. Formation of the fully substituted carbon skeleton was either accomplished via a highly efficient photo–Fries rearrangement or ring closing metathesis (RCM) reaction. Apart from the application of the powerful RCM reaction, the so far underestimated photo–Fries rearrangement was extended to the construction of macrocycles. The final steps to install the quinone–methide–lactol unit could be performed by a chemoselective oxidation–hydrolysis sequence, thus avoiding additional protective groups manipulations.

Echinopine A and **B**, novel tetracyclic sesquiterpenoids from *Echinops spinosus* were isolated in 2007 and have attracted great interest because of their unique 3,5,5,7–membered ring skeleton. Limitation of material and scarcity of sample source prevented proper biological testing and determination of the absolute stereochemistry. These limitations, the complex and novel molecular architecture render the title compounds ideal targets for total synthesis.

The concise total syntheses are characterized by (1) 1,5–cyclooctadiene as an inexpensive, easily available starting material, (2) the extension of Myers' [3,3]–sigmatropic protocol to the stereoselective installation of vinyl and isopropenyl units, (3) RCM as an efficient tool to close the strained seven–membered ring and (4) the extension of an unusual Pd(0)–C_2–homologation of phenyltriflates to vinyltriflates. In addition, the proposed structures were validated and the absolute stereochemistry could be determined.

C. Zusammenfassung

Die vorliegende Dissertation beschreibt die Totalsynthesen von (+)–Echinopine A und B, sowie zwei Totalsynthesen des Antibiotikums (-)–Kendomycin.

Kendomycin, ein neuratiges *ansa*–Polyketid, wurde 1996 erstmals isoliert (Reisolierung 1999 aus *Streptomyces violaceoruber)* und hat seitdem (Bio)Chemiker aufgrund der vielversprechenden biologischen Aktivtät (Endothelin–Rezeptor–Antagonist, antiosteoporotische/antibakterielle Aktivität, zytotoxische Aktivität vergleichbar mit Cisplatin) und der komplexen molekularen Struktur (vollständig kohlenstoffhältige *ansa*–Kette, neun Stereozentren, fünffach substituierter Tetrahydropyran Ring, einzigartiger *p*–chinoider Chromophor) fasziniert.

Die Totalsynthesen stützten sich auf zwei konvergente Strategien, wobei beide auf einer ungewöhnlich komplexen, diastereoselektiven Claisen–Ireland Umlagerung für den Aufbau der nordöstlichen Domäne basierten. Die Bildung des vollständig substituierten Kohlenstoffskelettes wurde einerseits durch eine äußerst effiziente Photo–Fries Reaktion beziehungsweise durch ringschließende Metathese (RCM) erreicht. Abgesehen von der effizienten RCM Reaktion, wurde die bis jetzt unterschätzte Photo–Fries Reaktion für den Aufbau von Makrozyklen erweitert. Der Aufbau der Chinon–Laktol Einheit konnte mit Hilfe einer chemoselektiven Oxidations–Hydrolyse Sequenz, ohne Hinzunahme von Schutzgruppen, bewältigt werden.

Echinopine A und **B**, neuartige tetrazyklische Sesquiterpene, wurden 2007 aus *Echinops spinosus* isoliert und lenkten aufgrund ihres einzigartigen 3,5,5,7– Ringgerüstes die Aufmerksamkeit auf sich. Aufgrund der geringen Verfügbarkeit der Naturstoffe und der Probenquelle konnten weder angemessene biologische Tests, noch eine Bestimmung der Absolutkonfiguration durchgeführt werden. Diese Einschränkungen und die komplexe molekulare Architektur machen die Titelverbindungen zu idealen Zielstrukturen für die Totalsynthese.

Die Totalsynthesen bestechen durch (1) die Verwendung von 1,5–Cyclooktadien als billiges, leicht zugängliches Startmaterial, (2) die Erweiterung von Myers‘ [3,3]–sigmatropen Umlagerungsprotokolls für die stereoselektive Anlegung von Vinyl– und Isopropenyleinheiten, (3) eine RCM um den gespannten sieben–gliedrigen Ring aufzubauen und (4) die Erweiterung einer ungewöhnlichen Pd(0)–C_2–Verlängerung von Phenyltriflaten auf Vinyltriflate. Zusätzlich konnten die ursprünglich vorgeschlagenen Strukturen validiert und die absolute Stereochemie bestimmt werden.

Table of Contents

PART A: Total Synthesis of (-)–Kendomycin

1. Introduction and Background

1.1. Isolation and Biological Activity

The novel *ansa*–macrolide kendomycin (**1**) was originally isolated by Funahashi[1] from *Streptomyces sp.* AL–71389 as (-)–TAN 2162 and in 2000, Zeeck's group from Göttingen disclosed the re–isolation of **1** from *Streptomyces violaceoruber*.[2]

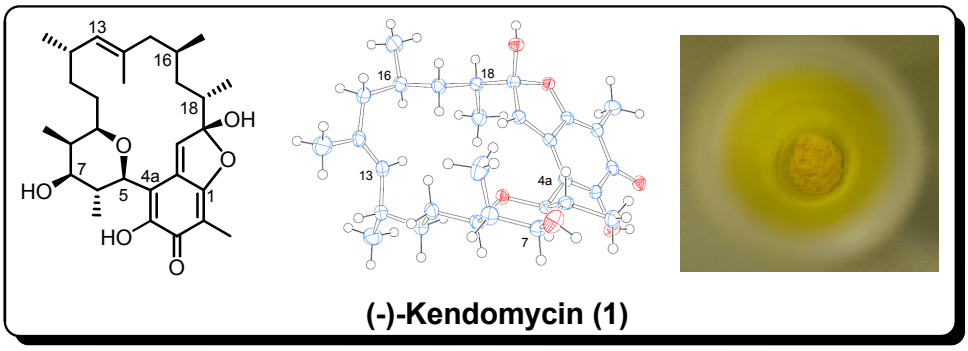


Figure 1. 2D–view and X–ray structure of kendomycin (**1**). Re–crystallization from dichloromethane provided yellow crystals suitable for X–ray analysis.

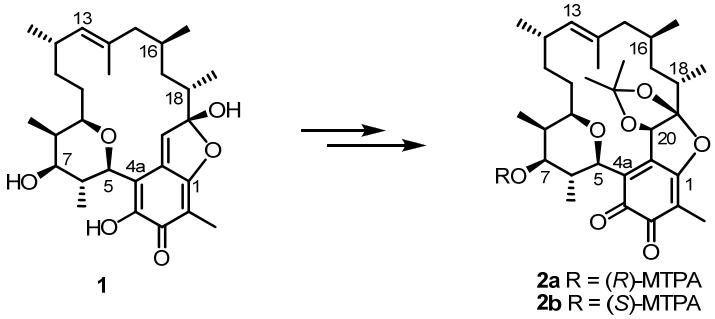
The patent literature describes compound **1** as a highly active endothelin receptor antagonist with promising antiosteoporotic activity.[1,3] *In vitro* assays by Zeeck and co–workers revealed that **1** and **2** (see Scheme 1) also efficiently act against different human tumor cell lines (HMO2, HEP–G2 and MCF7). The cytotoxic activity is comparable to the established drugs cisplatin and doxorubicin, whereas the mode of action is mainly attributed to proteasome inhibition.[4] In addition, kendomycin exhibits a remarkable antibiotic activity against Gram–positive and Gram–negative bacteria, including multidrug–resistant *Staphylococcus aureus* (MRSA) strains. In 2008, Boyce reported that kendomycin and several

[1] (a) Y. Funahashi, N. Kawamura, T. Ishimaru, *Jap. Pat.* 08 231 551 [A2 960 910], **1996**; *Chem. Abstr.* **1997**, *126*, 6553; (b) Y. Funahashi, T. Ishimaru, N. Kawamura, *Jap. Pat.* 08 231 552 [A2 960910], **1996**; *Chem. Abstr.* **1996**, *125*, 326518.
[2] (a) H. B. Bode, A. Zeeck, *J. Chem. Soc., Perkin Trans. I* **1999**, 323–328; (b) H. B. Bode, A. Zeeck, *J. Chem. Soc., Perkin Trans. I* **2000**, 2665–2670.
[3] M. H. Su, M. I. Hosken, B. J. Hotovec, T. L. Johnston, *US Pat.* 5728727 [A980317], **1998**; *Chem. Abstr.* **1998**, *128*, 239489.
[4] Y. A. Elnakady, M. Rohde, F. Sasse, C. Backes, A. Keller, H.–P. Lenhof, K. J. Weissman, R. Mueller, *ChemBioChem* **2007**, *8*, 1261–1272.

analogues inhibit the Bcl–xl–Bak interaction, which plays a significant role in apoptosis.[5] These salient qualities render compound **1** an interesting and promising agent for further drug development.

1.2. Structure Elucidation and Molecular Framework

Based on careful 2D–NMR experiments (HMBC, COSY), HRMS and X–ray analysis, Zeeck's group was able to unambiguously assign the relative stereochemistry of **1**.[2] Determination of the absolute stereochemistry was achieved by means of advanced Mosher's ester analysis of stable ketal **2**, which was obtained from **1** by oxidation with $FeCl_3$ in acetone and subsequent derivatization (Scheme 1).



Scheme 1. Determination of the absolute stereochemistry of (-)–**1** via Mosher's advanced ester methodology. The C7-stereocenter was designated to be (*S*)-configured.

The outstanding and unprecedented molecular structure of **1** is manifested in nine stereocenters, a fully carbogenic *ansa*–chain, a highly substituted tetrahydropyran ring and a unique *p*–quinone methide chromophor. The latter, which is susceptible to nucleophilic 1,6–addition at the C20 position, seems to be responsible for the instability of compound **1** in aqueous DMSO and methanol.[5] Figure 2 emphasizes the synthetically most challenging domains of kendomycin.

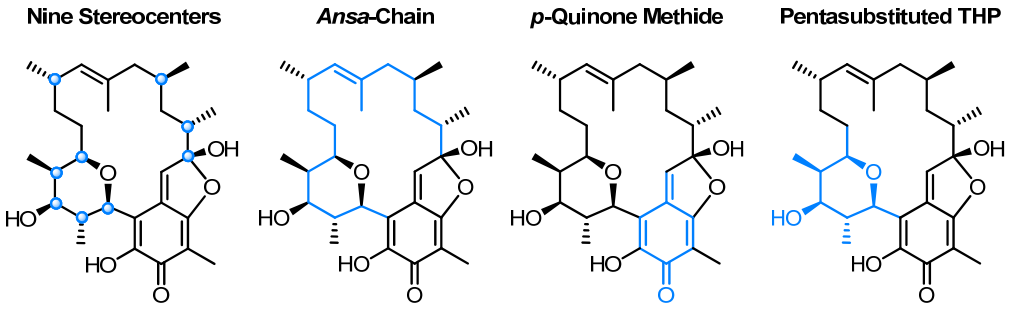


Figure 2. Structural features of **1**.

[5] C. O. Janssen, S. Lim, E. P. Lo, K. F. Wan, V. C. Yu, M. A. Lee, S. B. Ng, M. J. Everett, A. D. Buss, D. P. Lane, R. S. Boyce, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5771-5773.

1.3. Biosynthesis

The general biosynthesis of polyketides starts with the polyketide synthase (PKS; classified into type I, II and III) catalyzed linkage of short–chain activated fatty acids such as acetyl CoA, propionyl CoA, (methyl)malonyl CoA and butyryl CoA.[6] Several Claisen–type reactions for chain elongation followed by additional transformations provide a great variety of polyketides (secondary metabolites).

The introductorily mentioned PKS, responsible for the assemblage of the acyl CoA components, is a massive multienzyme complex and consists of several enzyme domains. The latter are grouped into modules, each responsible for an individual chain propagation step.[7] The acyl transferase (AT) domain, which selects the acyl CoA extender unit, an acyl carrier protein (ACP) for binding and further reaction and the ketoacyl synthase (KS), which catalyzes the decarboxylative Claisen condensation are the minimum requirements of one extension module. In addition to the essential domains of the loading module ("load" in Figure 3), further modifications are realized in the extension modules (modules 1 to 8) by β–ketoacyl reductase (KR), β–hydroxyacyl dehydratase (DH), enoyl reductase (ER) and methyl transferase (MT) domains. The thioesterase (TE) domain (termination module) is located in the last module and catalyzes the release of the nascent polyketide chain from the enzyme complex with concomitant macrocyclization.

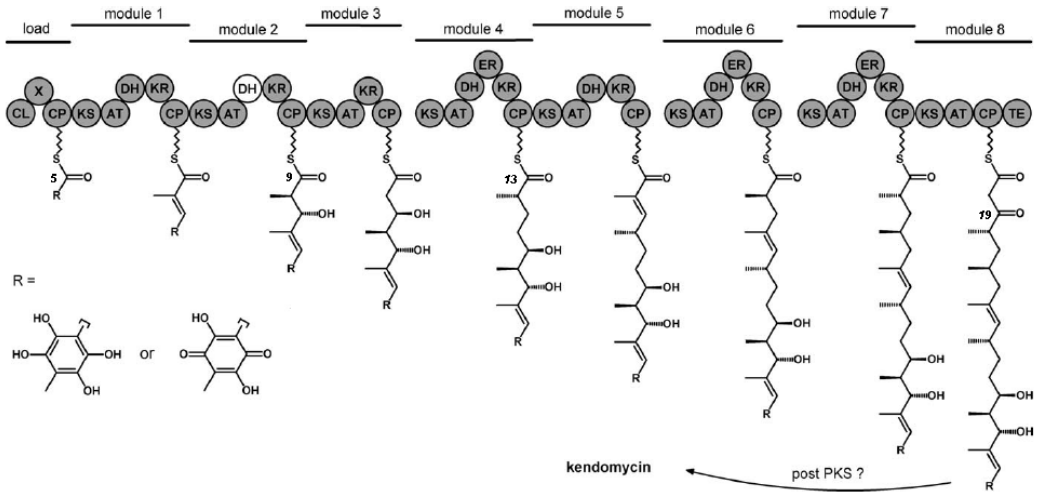
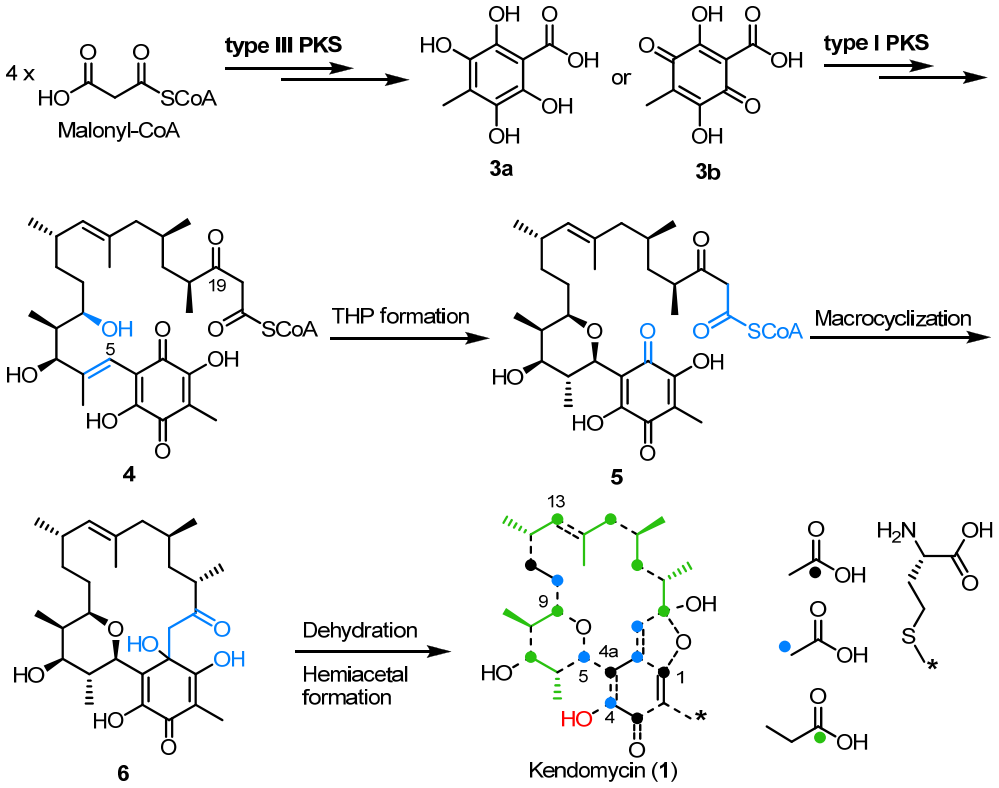


Figure 3. Type I PKS mediated biosynthesis of kendomycin (**1**) in a clockwise manner from C5 to C19. The unusual starter unit R (shown on the left) is provided from the type III PKS depended pathway shown on page 4 (reproduced with minor alterations from ref. 8). CL = CoA ligase, X = so far unknown quinone formation domain.

[6] F. J. Leeper, J. C. Vederas, Eds., Biosynthesis: Aromatic Polyketides, Isoprenoids, Alkaloids (Topics in Current Chemistry), Springer, 1st edition **2000**, 1–53.
[7] J. E. McMurry, T. P. Begley, The Organic Chemistry of Biological Pathways, Roberts & Company Publishers, **2005**, 369–378.

In contrast to other polyketides, an unusual loading unit and a biochemically unknown termination step are involved in the biosynthesis of **1**. Both, kendomycin type I PKS and type III PKS, act as a hybrid system during the biosynthesis.[8] The biosynthesis of the benzoic acid starter unit **3**, which in turn is processed by a type I PKS, is addressed to the ACP independent type III PKS ("chalcon synthase").



Scheme 2. Biosynthesis and labeling pattern of **1**.

Condensation of four molecules of malonyl CoA (Scheme 2), incorporation of molecular oxygen to install the C4–OH functionality and further modifications give **3a** or/and **3b**, which in turn are activated by a CoA ligase (CL) domain and linked to the ACP domain of the type I PKS. After incorporation of eight extender units (six molecules of methylmalonyl CoA and two of malonyl CoA) the stage is set for termination. Pyran ring formation between the benzylic C5 carbon atom and the C9 hydroxyl group in **4** probably initiates the final steps. Compared to the usual macrolactonization step, a decarboxylative thioesterase (TE) mediates an aldol–like condensation to give the fully carbogenic *ansa*–macrocycle **6**. Finally, spontaneous dehydration and hemiacetal formation completes the biosynthesis of **1**, even

[8] S. C. Wenzel, H. B. Bode, I. Kochems, R. Mueller, *ChemBioChem* **2008**, *9*, 2711–2721.

though the detailed biochemical mechanisms of the latter steps are not fully understood. Detailed labelling studies disclosed the origin of all oxygen and carbon atoms.[2]

2. Previous Synthetic Work

The pioneering work of the Mulzer group strongly influenced all syntheses and fragment preparations developed so far. Several synthetic strategies, which were directed by their preliminary results, in particularly with regard to the observed atropisomerism, will be covered in the following chapters.

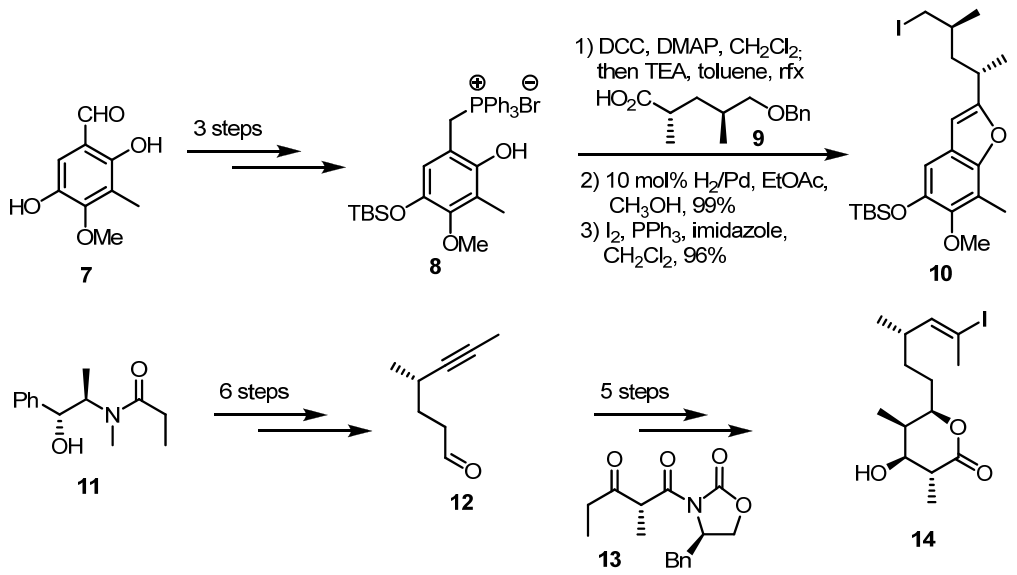
2.1. Reported Total Syntheses of Kendomycin

2.1.1. Lee's Total Synthesis of Kendomycin

Strategy: Macro–C–Glycosidation: Avoiding the problem of atropisomerism.

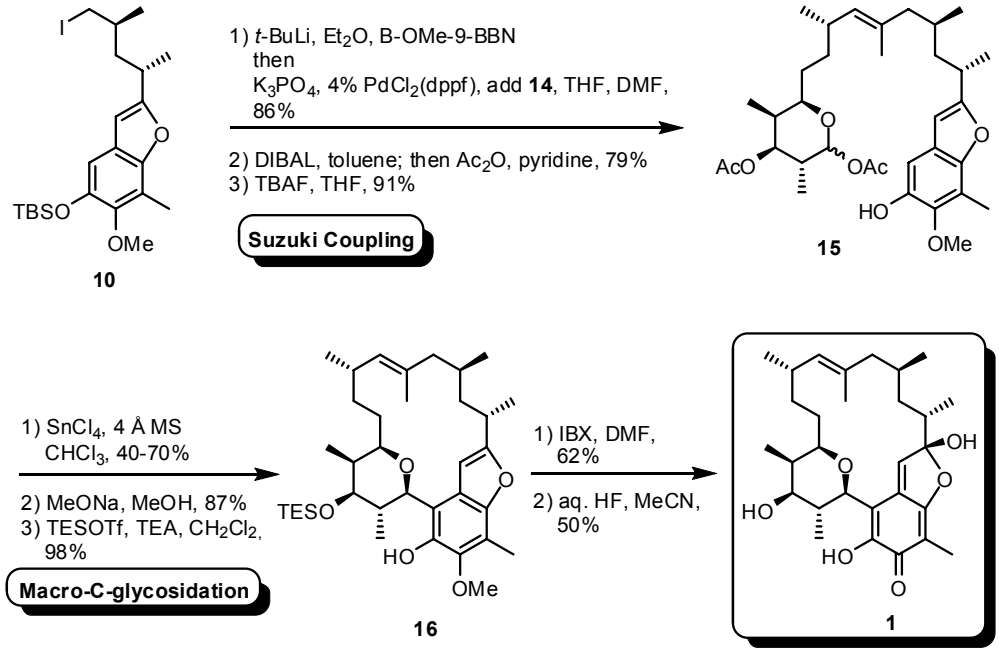
In 2004, the first total synthesis of kendomycin was reported by Lee and co–workers.[9] Their elegant and elaborated strategy focused on the Suzuki–Miyaura coupling partners **10** and **14** (Scheme 3), and furthermore key–intermediate **15** (Scheme 4), the macroglycosidation precursor. Installation of benzofuran **10** was accomplished by one pot esterification of phosphonium salt **8** with acid **9** and Wittig reaction, followed by hydrogenolysis and Appel reaction. Preparation of vinyl iodide **14** started with Myers' asymmetric alkylation of **11** to give, after five steps, aldehyde **12**. Elongation with Evans extended auxiliary **13** and further functional group manipulations afforded lactone **14** in eleven steps from compound **11**.

[9] Y. Yu, H. Men, C. Lee, *J. Am. Chem. Soc.* **2004**, *126*, 14720–14721.



Scheme 3. Lee's syntheses of the eastern and western portion of **1**.

A high yielding three steps sequence, including the Suzuki–Miyuara coupling of **10** and **14** gave rapid access to phenol **15** (Scheme 4). Formation of an intermediate O–glycoside and subsequent rearrangement to the C–glycoside with $SnCl_4$ provided, after exchange of the secondary acetate, sufficient amounts of macrocycle **16**. All efforts to close the macrocycle by Friedel–Crafts acylation with the corresponding TBS protected phenol failed.



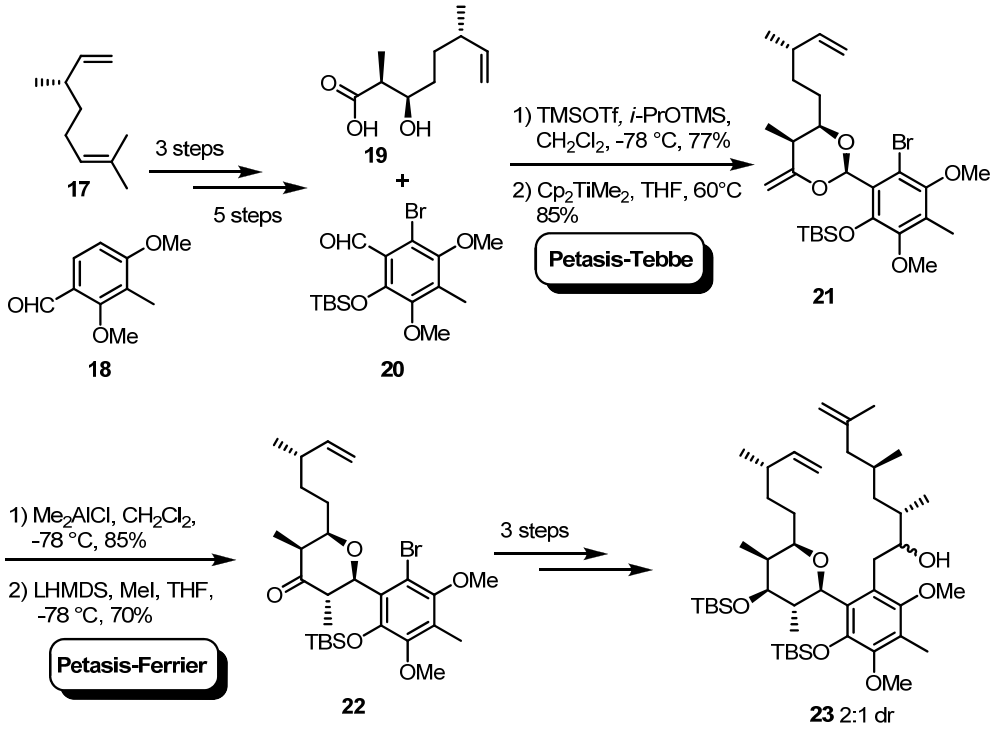
Scheme 4. The key–steps of Lee's synthesis.

Formation of the unstable *o*–quinone chromophor with IBX, followed by one pot deprotection and hydrolysis with aqueous HF gave **1** in 20 linear steps.

2.1.2. Smith's Total Synthesis of Kendomycin

Strategy: Petasis–Ferrier rearrangement and RCM: The hunt for the (*E*)–double bond geometry.

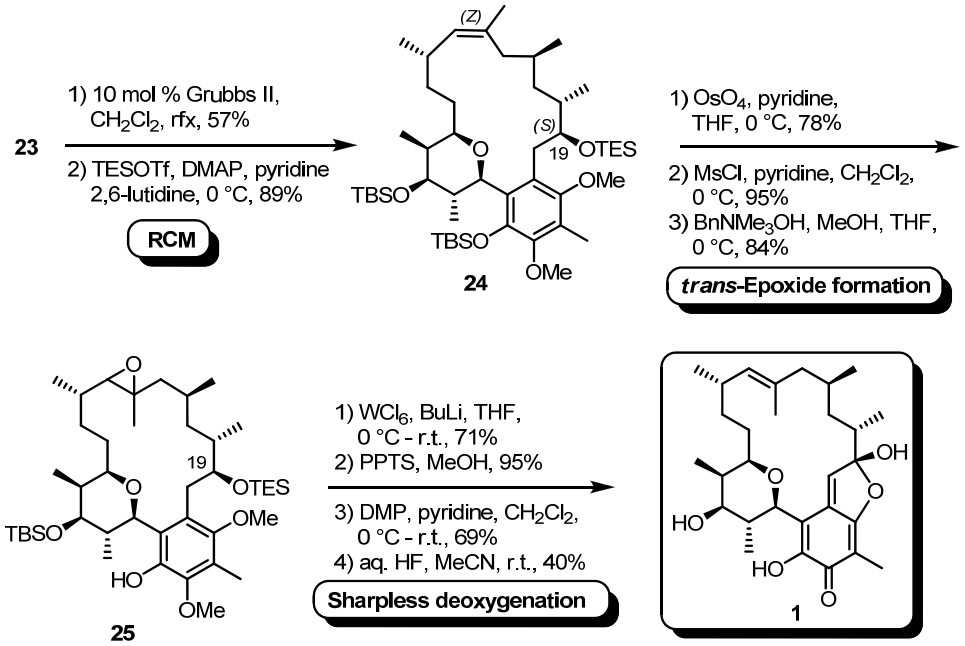
The second total synthesis of (-)–**1**, relying on a more conventional approach, was achieved by Smith and co–workers in 2005.[10] The synthetic plan focused on a Petasis–Ferrier rearrangement to construct the tetrahydropyran unit and a RCM reaction to build up the macrocyclic skeleton. Despite the negative RCM results from the Mulzer group (see page 16) they were convinced, that TBS protected phenol **23** would be a superior and more productive RCM precursor (Scheme 5). Preparation of enol acetal **21** started with the condensation of β–hydroxy acid **19** and benzaldehyde **20.** The so obtained dioxanone intermediate was converted to **21** via Petasis–Tebbe methylenation. Lewis acid induced Petasis–Ferrier rearrangement followed by diastereoselective methylation, presumably via a skewed–boat–like transition state (TS), generated tetrahydropyran **22**. After three more steps the stage was set for the envisaged RCM reaction.



Scheme 5. Smith's approach to RCM precursor **23**.

[10] A. B. III Smith, E. F. Mesaros, E. Meyer, *J. Am. Chem. Soc.* **2005**, *127*, 6948–6949.

Careful experimentation showed, that on treatment of the 2:1 diastereomeric mixture **23** with Grubbs second generation catalyst, only the major (*S*)–alcohol participated in the RCM reaction (Scheme 6). The unexpected and undesired formation of the (*Z*)–olefin geometry required a rather laborious, four steps isomerization sequence of macrocycle **24**, relying on formation of *trans*–epoxide **25** and Sharpless deoxygenation with tungsten(IV).



Scheme 6. Smith's final steps towards **1**: Macrocyclization and double bond isomerization.

Selective desilylation and Dess–Martin oxidation of the secondary C19 alcohol as well as the phenol gave an intermediate *o*–quinone, which was hydrolyzed to **1**. The second total synthesis of **1** was accomplished with a longest linear sequence of 21 steps and with an overall yield of 0.49%.

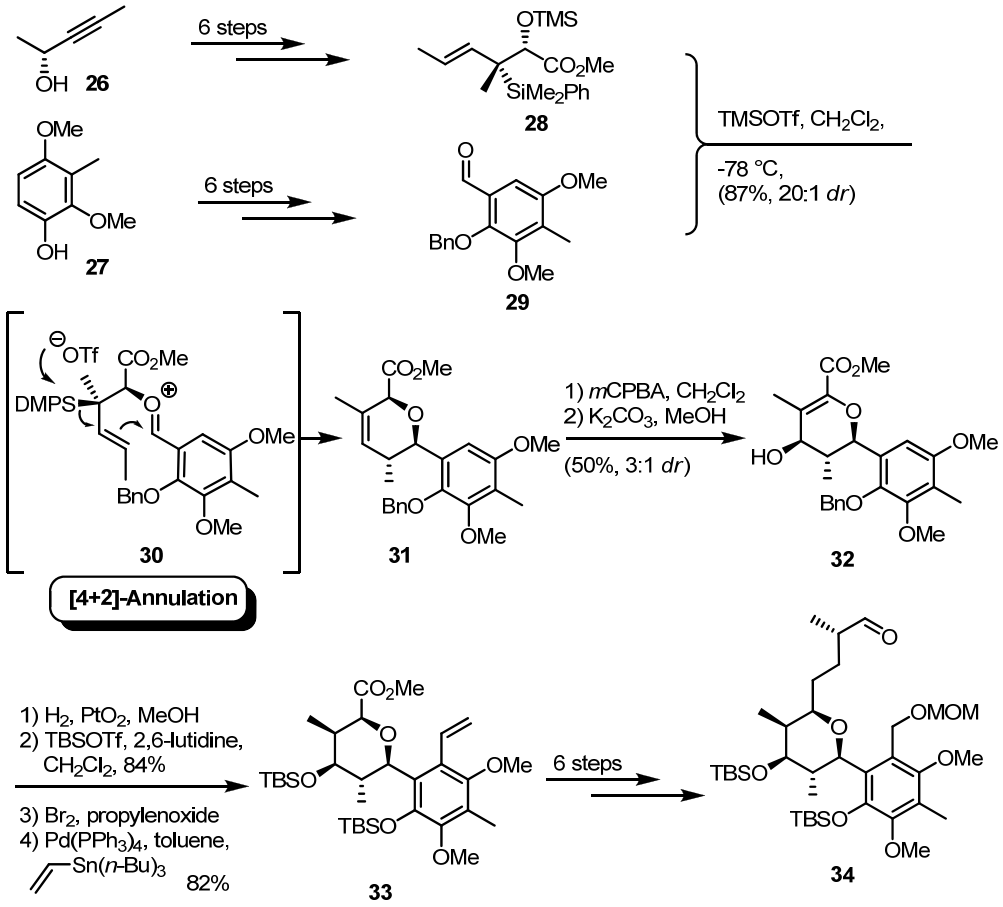
2.1.3. Panek's Total Synthesis of Kendomycin

Strategy: [4+2]–Annulation and intramolecular Barbier–type reaction: A linear approach.

Panek's stereocontrolled [4+2]–annulation strategy[11] in combination with an intramolecular Barbier–type cyclization culminated in the third total synthesis of kendomycin (Scheme 7).[12] *Syn*–selective [4+2]–annulation of (*E*)–vinyl silane **28** with benzaldehyde **29** gave the desired dihydropyran **31** in good yield and diastereoselectivity. Epoxidation and regioselective base induced epoxide opening delivered

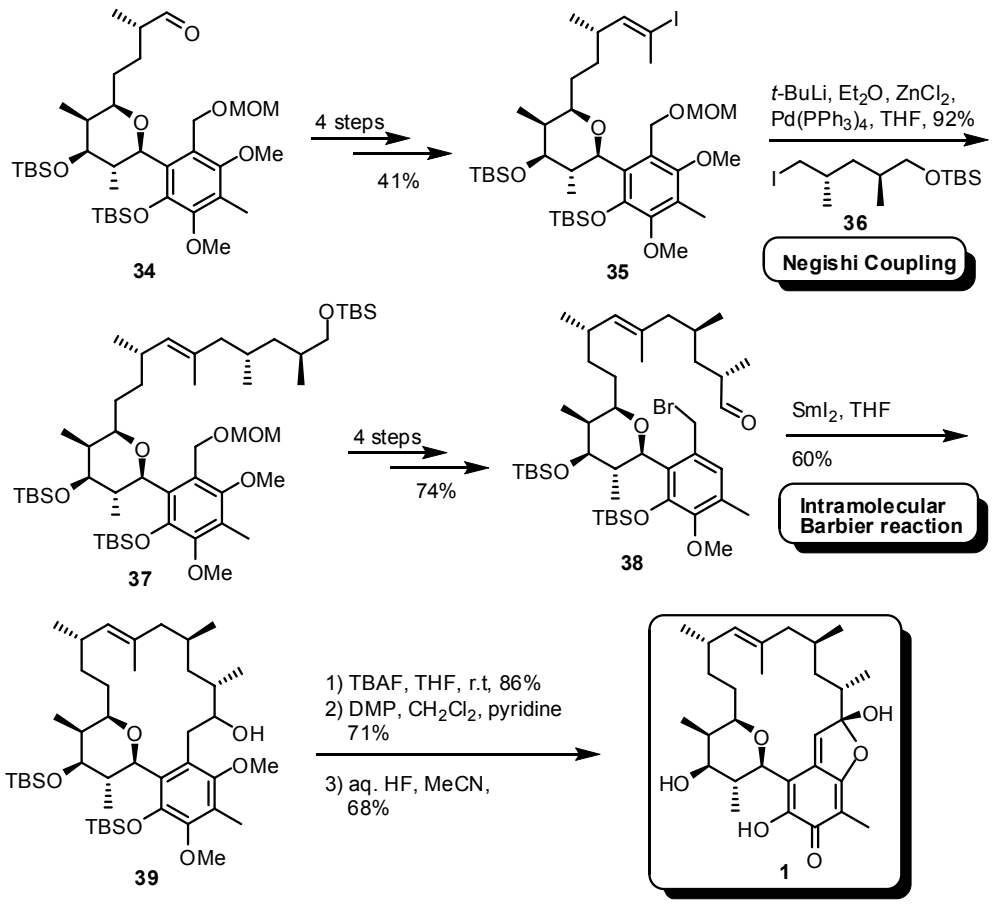
[11] J. T. Lowe, J. S. Panek, *Org. Lett*. **2005**, *7*, 1529–1532.
[12] J. T. Lowe, J. S. Panek, *Org. Lett*. **2008**, *10*, 3813–3816.

intermediate **32**. Further functional group manipulations and introduction of the styrene unit by a Stille coupling gave the fully substituted arene–THP fragment **33**. Aldehyde **34** was obtained after additional six steps.



Scheme 7. Panek's [4+2]–annulation strategy.

Negishi type coupling of vinyliodide **35**, easily obtained from **34** in four steps, and alkyliodide **36** provided the complete kendomycin carbon scaffold **37** (Scheme 8). Release of the aldehyde and the benzylbromide function within four steps paved the way for the final sequence.



Scheme 8. Completion of Panek's total synthesis.

Intramolecular SmI_2–mediated Barbier macrocyclization of **38** produced secondary alcohol **39** in good yield. Selective cleavage of the phenolic TBS protecting group, oxidation and subsequent treatment with aqueous HF resulted in complete deprotection with simultaneous formation of **1**.

A major drawback is the high linearity of the synthesis, which proceeds in 32 steps (1.1% overall yield) from alcohol **26**.

2.2. Reported Formal Syntheses of Kendomycin

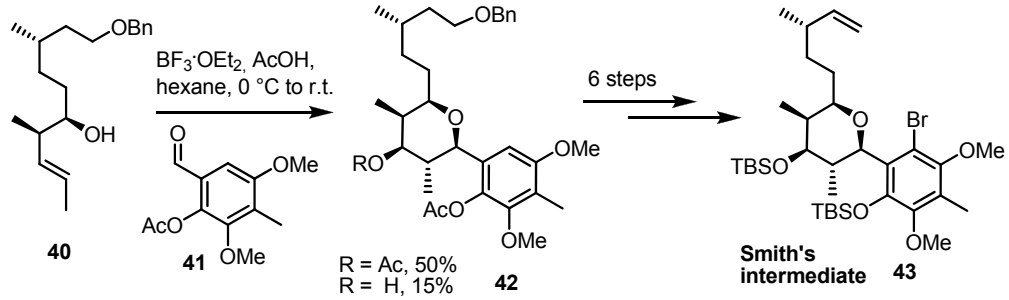
2.2.1. Rychnovsky's Formal Syntheses of Kendomycin

Strategy: Intramolecular–Prins cyclization: Low selectivity for the desired macrocycle.

The key steps of Rychnovsky's formal syntheses of kendomycin (**1**), published in 2006[13] and 2008[14], were both based on Prins–reactions. The desired Lewis acid (BF_3-OEt_2) promoted intermolecular cyclization of

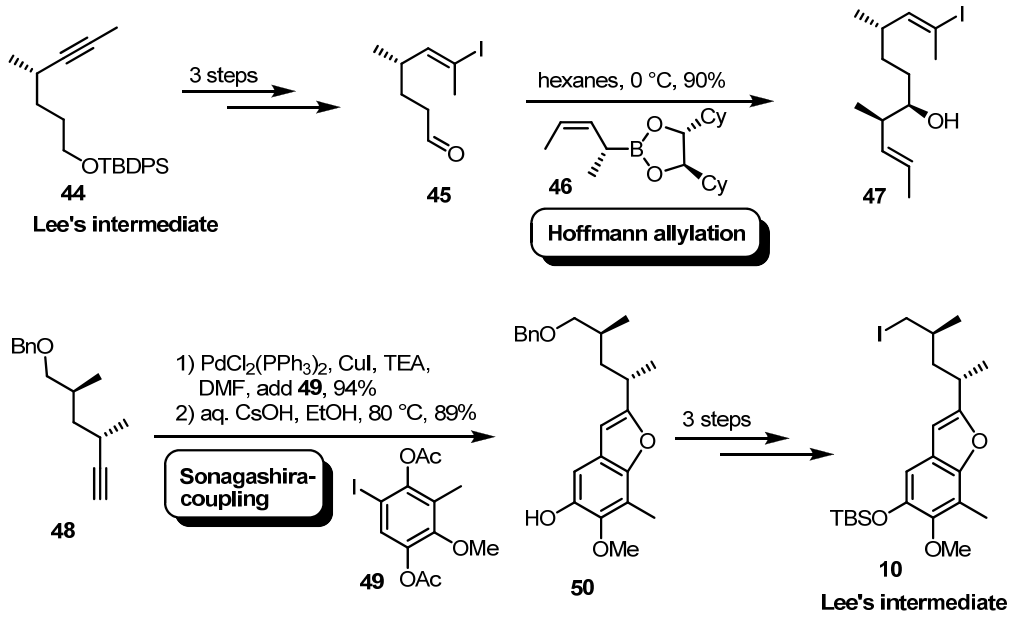
[13] K. B. Bahnck, S. D. Rychnovsky, *Chem. Commun.* **2006**, 2388–2390.

homoallylic alcohol **40** with benzaldehyde **41** was achieved after some optimization (Scheme 9). THP fragment **42** was obtained in moderate yield and transformed to bromide **43** within six steps, a fragment of Smith's total synthesis.



Scheme 9. Rychnovsky's first formal synthesis.

In 2008, they revisited the Prins–cyclization and extended it to an intramolecular version (Scheme 10). Homoallylic alcohol **47** was obtained in four steps from known compound **44** via Hoffmann's allylation of vinyl iodide **45**. The modified synthesis of Lee's intermediate **10** started from alkyne **48** by Sonagashira coupling with iodide **49** and subsequent base induced 5–*endo*–dig cyclization to benzofuran **50**. A three step procedure was then necessary to complete the synthesis of **10**.

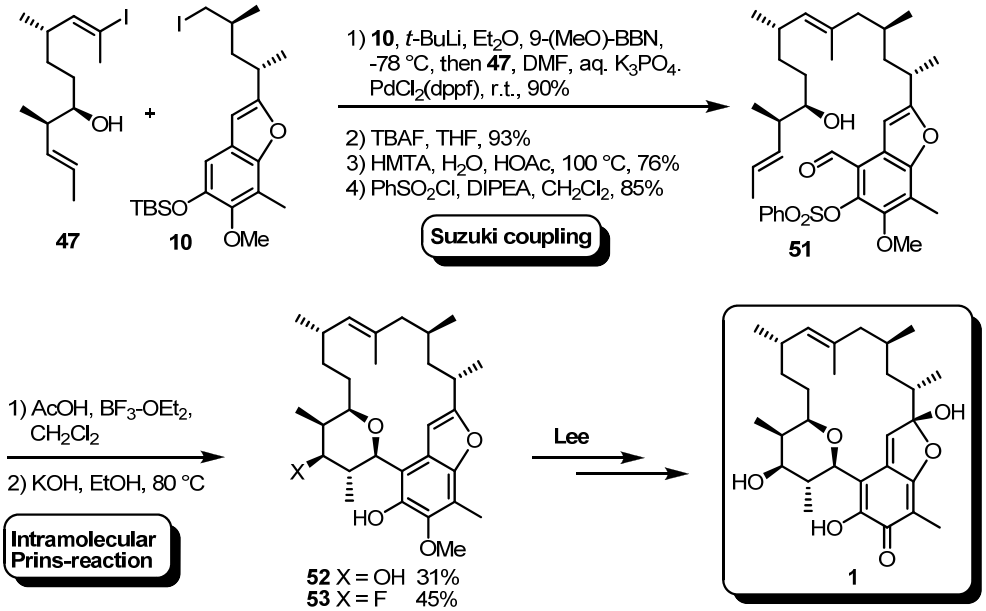


Scheme 10. Alternative synthesis of Lee's right–hand portion of **1**.

[14] K. B. Bahnck, S. D. Rychnovsky, *J. Am. Chem. Soc.* **2008**, *130*, 13177–13181.

Linkage of **47** and **10** was achieved via Lee's established Suzuki Miyuara coupling sequence (Scheme 11). Desilylation, Duff formylation and installation of an electron withdrawing benzenesulfonyl protecting group, essential for efficient cyclization, provided the desired Prins precursor **51**.

Acid induced intramolecular cyclization under high dilution conditions followed by saponification gave a mixture of Lee's intermediate **52** and the corresponding fluorine derivative **53**. However, due to the unfavorable ratio of **52** and **53**, the synthetic practicability seems to be rather restricted. Efforts to reproduce Lee's final steps failed.



Scheme 11. Rychnovsky's formal synthesis via intramolecular Prins–cyclization.

A chronological summary of all total and formal syntheses reported so far is given in the following table. Lee's elegant synthesis is outstanding and the most efficient one published so far. Our second synthesis is just four steps longer and features a higher overall yield compared to Smith's synthesis. Panek's synthesis from 2008 features interesting chemistry but a major drawback is the lack of convergence. Rychnovsky's first formal synthesis, reported in 2006, describes only a very basic building block from Smith's synthesis.

		Total Syntheses		Formal Syntheses	
	Year	**LLS**	**Yield**	**LLS**	**Yield**
Lee	2004	20	1.3%		
Smith	2005	21	0.5%		
Panek	2008	32	1.1%		
Rychnovsky	2008	(20)	(2.6%)	17	8.8%
Rychnovsky	2006	(22)	(0.5%)	12	13.5%
Own Work	2009	32	0.4%		
Own Work	2009	24	1.0%		

Table 1. Overview about the reported total and formal syntheses of (-)–kendomycin. The number of steps and quoted yields were determined by starting from commercially available starting materials. LLS = Longest linear sequence.

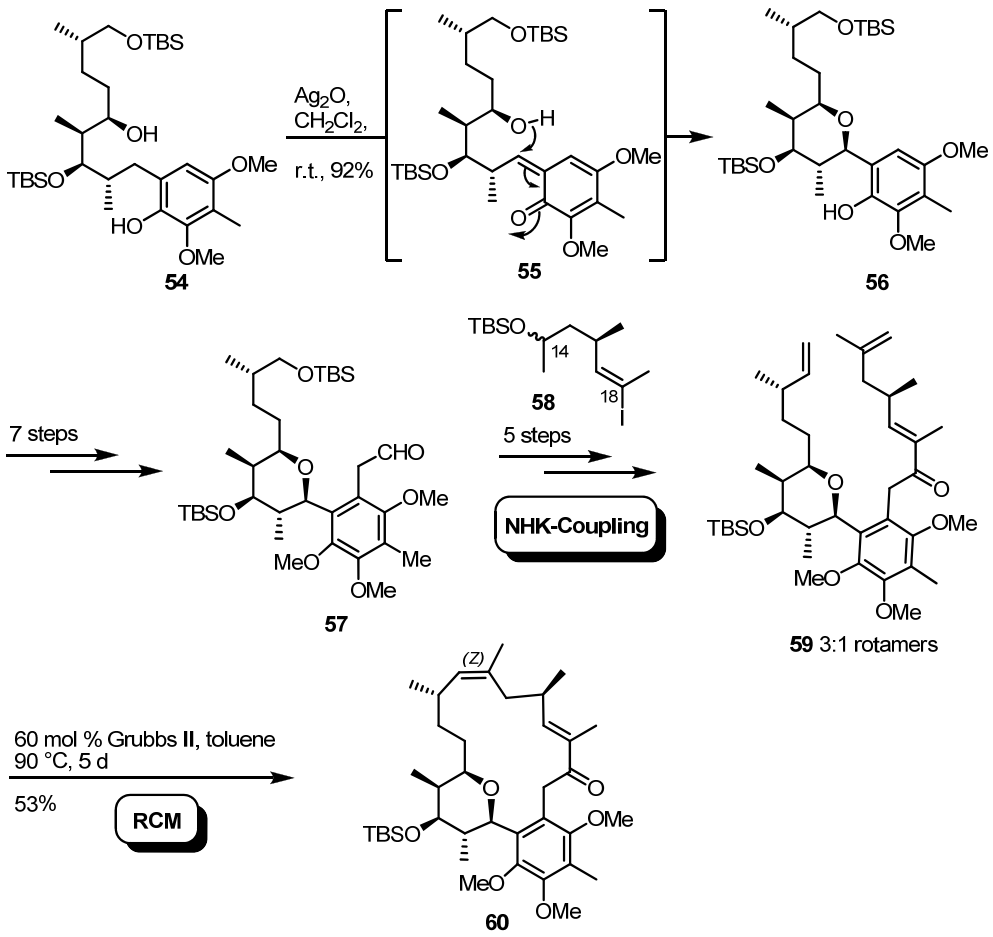
2.3. Fragment Preparations of Kendomycin

2.3.1. Arimoto's Approach to the Macrocyclic Core of Kendomycin

Strategy: RCM: Problems similar to Smith and Mulzer.

Arimoto's synthesis of the south–western domain of kendomycin was already described in 2004 (Scheme 12).[15] Preparation of intermediate **54** was accomplished in 18 linear steps via standard chemistry. A silver(I) promoted oxidative cyclization of **54**, presumably involving *o*–quinone methide **55**, delivered the desired THP moiety in excellent yield. Transformation of homobenzylic aldehyde **57** to pentasubstituted arene **56** was realized in another seven steps.

[15] T. Sengoku, H. Arimoto, D. Uemura, *Chem. Commun*. **2004**, *10*, 1220–1221.



Scheme 12. Arimoto's synthesis of a major portion of **1**.

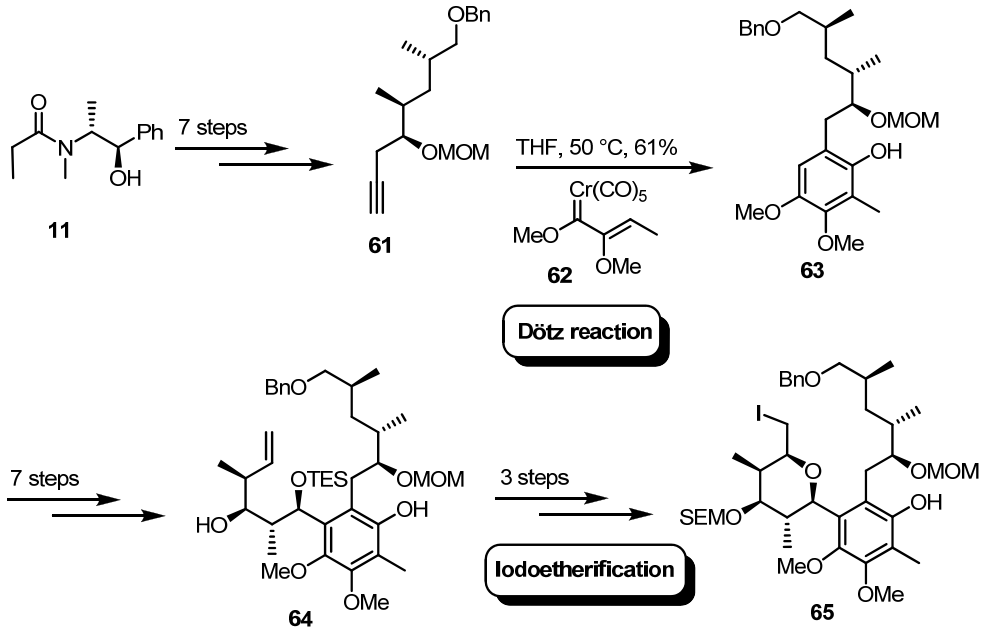
Linkage of the eastern C14–C18 domain, which was described in 2007, consumed additional five synthetic operations, whereas the key–step consisted of a Nozaki–Hiyama–Kishi reaction between **57** and **58**.[16] Subjecting the 3:1 rotameric mixture (the kendomycin like rotamer proved to be favored) of **59** to a variety of RCM conditions was disappointing. A substoichiometric amount of Grubbs' second generation catalayst (60 mol %) and long reaction times were necessary to construct the undesired (*Z*)–configured macrocycle **60**. Apart from this drawback, a 35 steps sequence to **60** would not necessarily facilitate the synthesis of **1**.

2.3.2. White's Approach to Kendomycin

Strategy: Dötz–annulation reaction: *De novo* synthesis of the aromatic core.

[16] T. Sengoku, D. Uemura, H. Arimoto, *Chem. Lett.* **2007**, *36*, 726–727.

White's group reported the *de novo* synthesis of kendomycin's arene core via the Dötz annulation reaction in 2005 (Scheme 13).[17] A high yielding seven steps sequence, starting from Myers' *N*–propionylpseudoephedrine **11**, lead to alkyne **61**. Preparation of the Fischer–type alkenylchromium carbenoid **62** was realized in three steps from 1-methoxyprop-1-yne. Highly regioselective Dötz annulation, followed by oxidative workup provided intermediate **63** in good yield. Transformation of **63** to **64**, which possesses the fully functionalized arene core, was achieved by seven synthetic operations and paved the way for the owing THP formation. The three remaining steps were realized by initial protecting group manipulations and final iodocyclization to give **65**.



Scheme 13. White's Dötz annulations strategy.

2.3.3. Williams' Synthesis of Kendomycin's *Ansa*–Chain

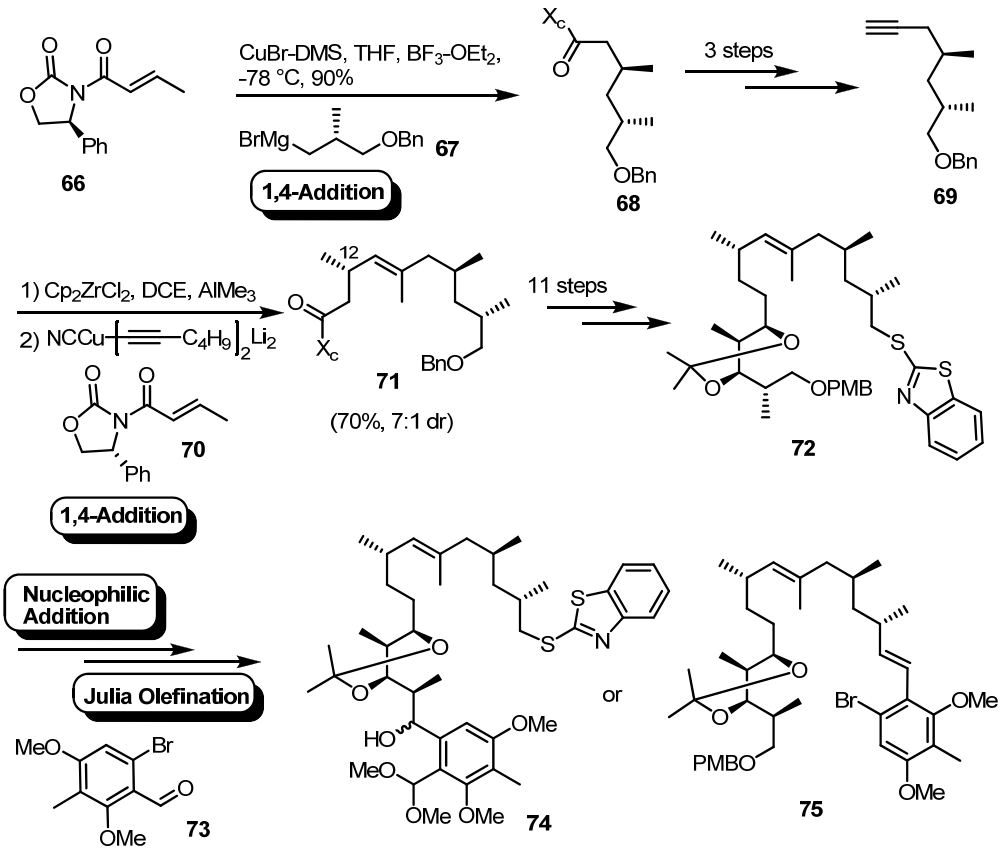
Strategy: Asymmetric conjugate addition: Linear construction of the *ansa*–chain.

An auxiliary based approach of the *ansa*–chain was disclosed by Williams in 2005 (Scheme 14).[18] Conjugate addition of **67** to *N*–enoyl oxazolidine **66** gave the 1,3–*anti*–fragment **68**. Negishi's *syn*–carboalumination protocol followed by *in situ* transmetallation with an higher–order cuprate set the stage for the second 1,4–addition. The application of **70** secured the diastereoselective installation of

[17] J. D. White, H. Smits, *Org. Lett*. **2005**, *7*, 235–238.
[18] D. Williams, K. Shamim, *Org. Lett.* **2005**, *7*, 4161–4164.

the C12 methyl group. Additional eleven steps from **71** were necessary to create the fully substituted *ansa*–chain **72**.

Connection to the aromatic moiety was accomplished via two pathways. First, nucleophilic addition of lithiated arene **73**, which was protected as its dimethoxyacetale prior to halogen–metal exchange, delivered **74** in three steps from **72**. Second, (*E*)–selective Julia olefination of benzaldehyde **73** with **72** derived sulfone provided **75** in two steps and excellent yield.



Scheme 14. Williams' approach of the fully substituted *ansa*–chain.

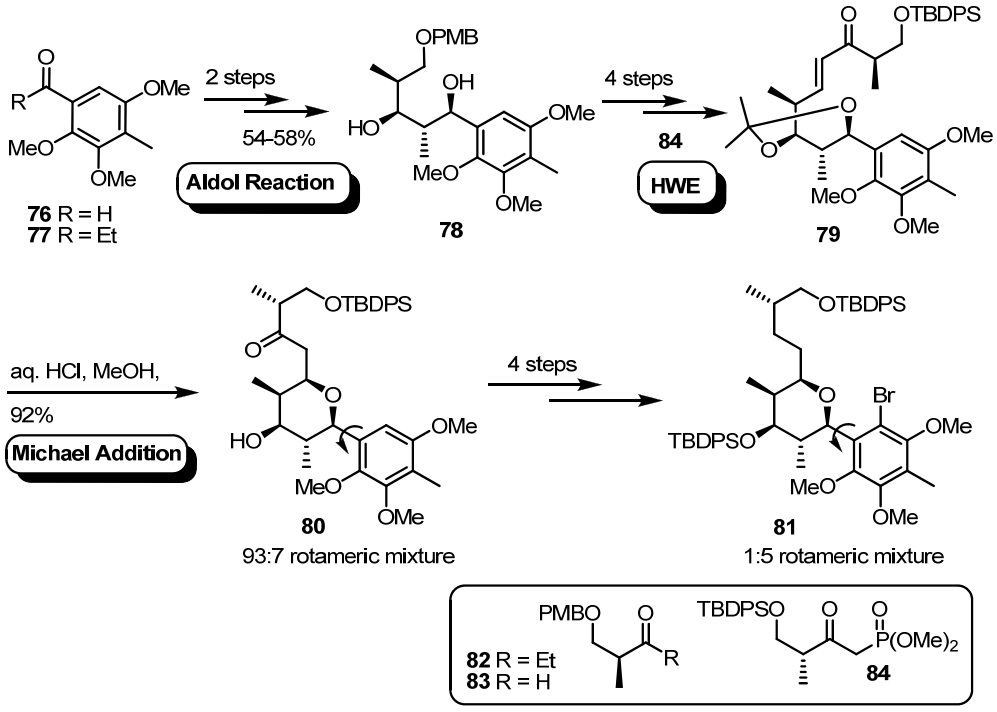
2.4. Mulzer's Approaches to Kendomycin

2.4.1. 1st Generation Approach: Michael–Addition for the Preparation of the THP Ring

The first generation approach culminated in the synthesis of the south–west domain of kendomycin (**1**).[19] The preparation of diol **78** was either achieved via *anti*–selective Peterson (**76** and **82**, Cy_2BCl) or

[19] H. J. Martin, M. Drescher, H. Kählig, S. Schneider, J. Mulzer, *Angew. Chem., Int. Ed*. **2001**, *40*, 3186–3188.

syn–selective titanium enolate aldol reaction (**77** and **83**, Ti(O*i*Pr)$_3$Cl) and subsequent stereoselective Evans–Carreira 1,3–*anti* reduction (Scheme 15). Four additional steps delivered α,β–unsaturated ketone **79**, which upon treatment with HCl cyclized to the desired tetrahydropyran **80**. Careful 2D–NMR experiments with **80** and **81** disclosed the first aryl–C–glycoside atropisomerism, which was depended on the degree of arene substitution. NOE experiments confirmed the preferred kendomycin–like orientation of **80** and revealed that in **81** the opposite rotamer is predominant. The latter resulted in great steric hindrance of the bromide function and all efforts to install the western side chain failed.



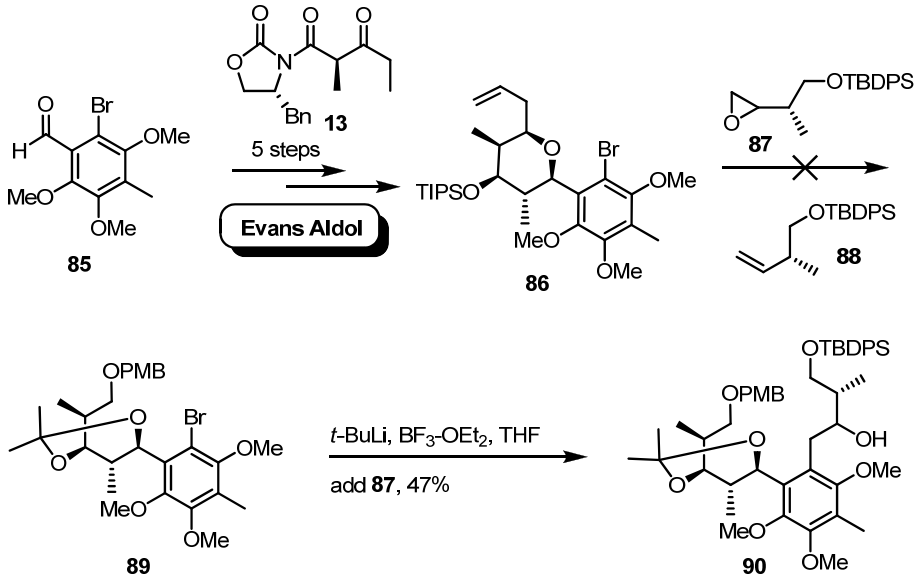
Scheme 15. Mulzer's 1st generation approach.

2.4.2. 2nd Generation Approach: Preparation of the *hexa*–Substituted Arene Core & Improvement of Tetrahydropyran Formation

Installation of the fully substituted arene **85** prior to THP formation revealed the Peterson *anti*–aldol chemistry to be low diastereoselective.[20] This problem could be solved by the well established extended Evans' aldol methodology. In that manner, the preparation of the fully substituted tetrahydropyran **86** was achieved in 5 steps from **85** with excellent diastereoselectivity (Scheme 16). Albeit all attempts to connect the side chains **87** and **88**, either via epoxide opening or via Heck coupling, to the rotameric mixture **86** failed, a moderate yield of the hexasubstituted arene **90** could be obtain with metallated **89**.

[20] M. M. B. Marques, S. Pichlmair, H. J. Martin, J. Mulzer, *Synthesis* **2002,** 2766–2770.

The former results and additional experiments strongly suggested the installation of the eastern domain prior to the western side chain.

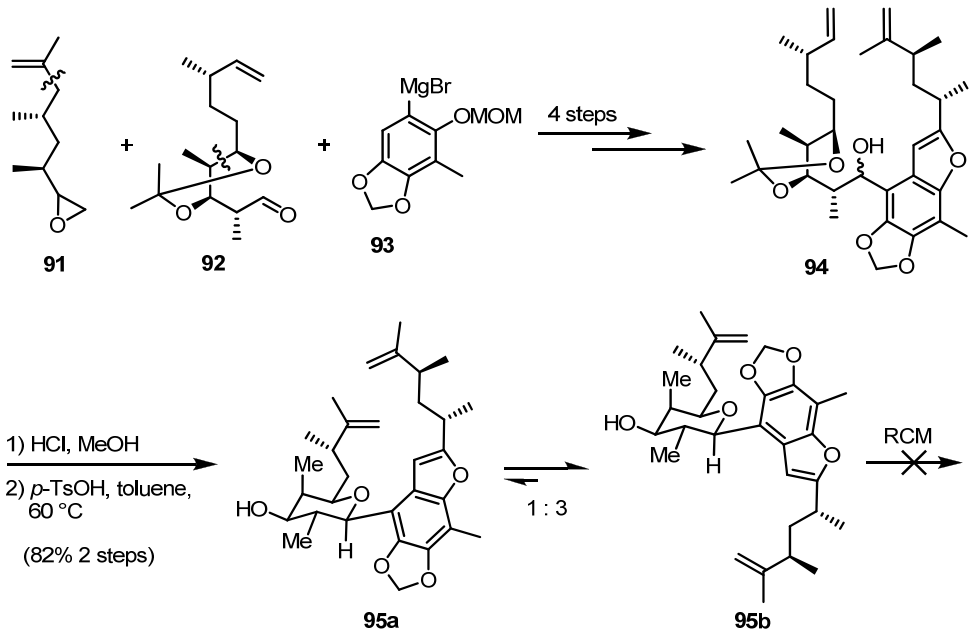


Scheme 16. Mulzer's 2nd generation approach.

2.4.3. 3rd Generation Approach: Preparation of the Full Carbon Skeleton and Attempted RCM

In 2003, a revised and superior strategy particularly with regard to prior benzofuran formation lead to highly advanced precursor **94** (Scheme 17).[21] The convergent and concise synthesis focused on well elaborated building blocks **91**, **92** and **93**. Epoxide **91**, which was easily prepared via auxiliary chemistry and Schlosser–Fouquet coupling to introduce the isopropenyl functionality, and Grignard **93** served for the right hand portion of kendomycin. Aldehyde **92** was built up by Evans *syn*–aldol methodology and chiral pool building block β–(+)–citronellene. Linkage of **91** to **93**, followed by benzofuran formation and connection of aldehyde **92** via an *o*–lithiation – nucleophilc addition sequence, provided benzylic alcohol **94** in four steps. Deprotection and S_N1–cyclization afforded a 1:3 rotameric mixture of **95a** and **95b**, whereas the disadvantageous rotamer **95b** prevailed. Not surprisingly, intermediate **95** did not undergo the desired RCM reaction.

[21] S. Pichlmair, M. M. B. Marques, M. P. Green, H. J. Martin, J. Mulzer, *Org. Lett.* **2003**, *5*, 4657–4659.



Scheme 17. The 3rd generation approach.

In order to circumvent the unfavorable atropisomerism, which seemed to be the major hindrance for successful cyclization, several analogs were designed and tested for the RCM reaction (Figure 4). Intermediates **96** to **98** were prepared in an analogous manner to that of **94** (for **98** compare **101**). The desired RCM reaction was never observed, albeit the conformation of **98** (R = MOM) was fixed in a kendomycin–like orientation.[22]

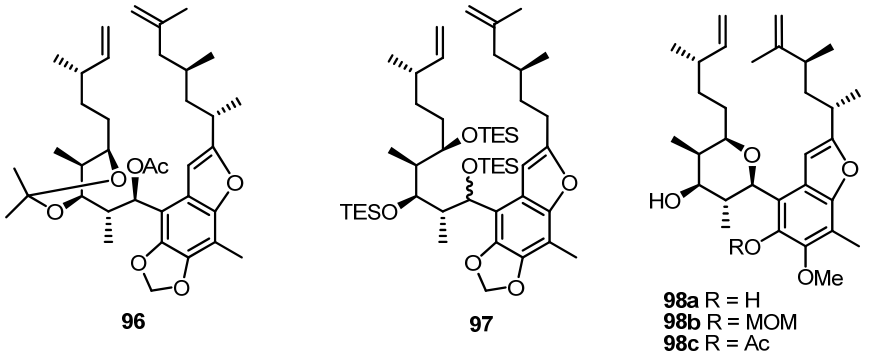
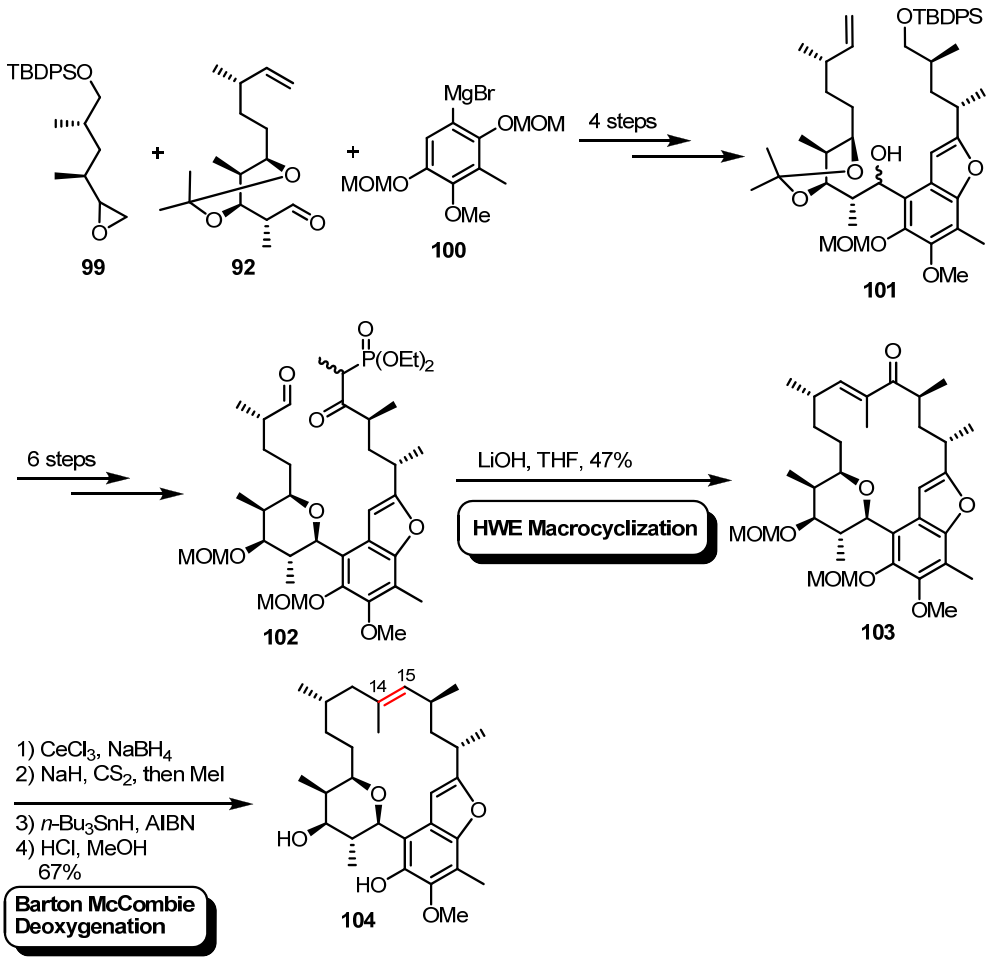


Figure 4. Alternative RCM precursors.

[22]J. Mulzer, S. Pichlmair, M. P. Green, M. M. B. Marques, H. J. Martin, *Proc. Nat. Acad. Sci*. **2004**, *101*, 11980–11985.

2.4.4. 4th Generation Approach: Macrocyclisation via Horner–Wadsworth–Emmons Reaction

Since RCM macrocyclization proved to be impossible for several benzofuran analogs, it was time for a new cyclization strategy.[22] The construction of more versatile intermediate **101** was executed in a similar manner to that of **94** (Scheme 18). Finally, the reliable intramolecular Horner–Wadsworth–Emmons (HWE) reaction showed to be the method of choice and preparation of β–keto phosphonate **102** could be performed straight forward from **101**. Indeed, on treatment with LiOH, **102** smoothly cyclized to ketone **103**.



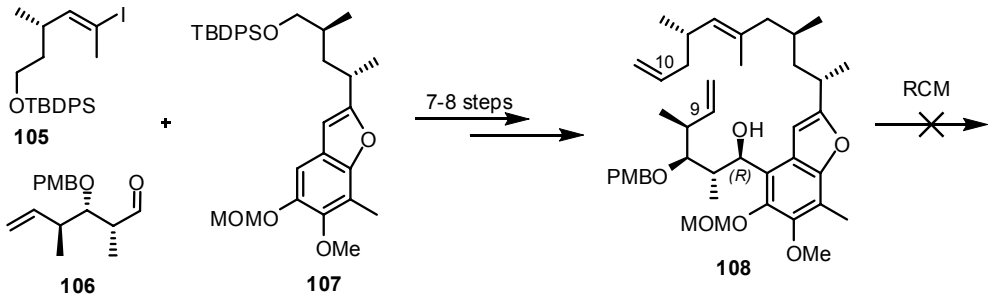
Scheme 18. The 4th generation approach: Successful macrocyclization.

After numerous unsuccessful attempts to remove the undesired ketone function in **103**, deoxygenation was achieved with Barton McCombie's protocol. Unfortunately, extensive 2D–NMR studies of **104** showed that the double bond entirely migrated to the C14–C15 position. Having arrived at the most

disappointing stage of the synthesis they decided to give up the ring closure between C13 and C14 completely.

2.4.5. 5th Generation Approach: RCM – Etherification Approach

Disconnection of the C9–C10 bond was the key strategy of the fifth generation approach, which is described in more detail in the appended full paper.[23]



Scheme 19. The 5th generation approach. Attempted RCM between C9 and C10.

[23] (a) T. Magauer, H. J. Martin, J. Mulzer, *Chem. Eur. J.* **2009***, Accepted*; (b) T. Magauer, *Towards the Total Synthesis of the ansa–Macrocycle Kendomycin*, Diploma Thesis, University of Vienna, **2007**.

3. Results

3.1. Total Synthesis of the Antibiotic Kendomycin by Macrocyclization via Photo–Fries Rearrangement and Ring Closing Metathesis (RCM)

T. Magauer, H. J. Martin, J. Mulzer, *Angew. Chem., Int. Ed.* ***2009***, *48*, 6032–6036.

The supporting information was omitted in order to avoid redundancy. For detailed experimental procedures and NMR data see SI of the full paper (section 3.2).

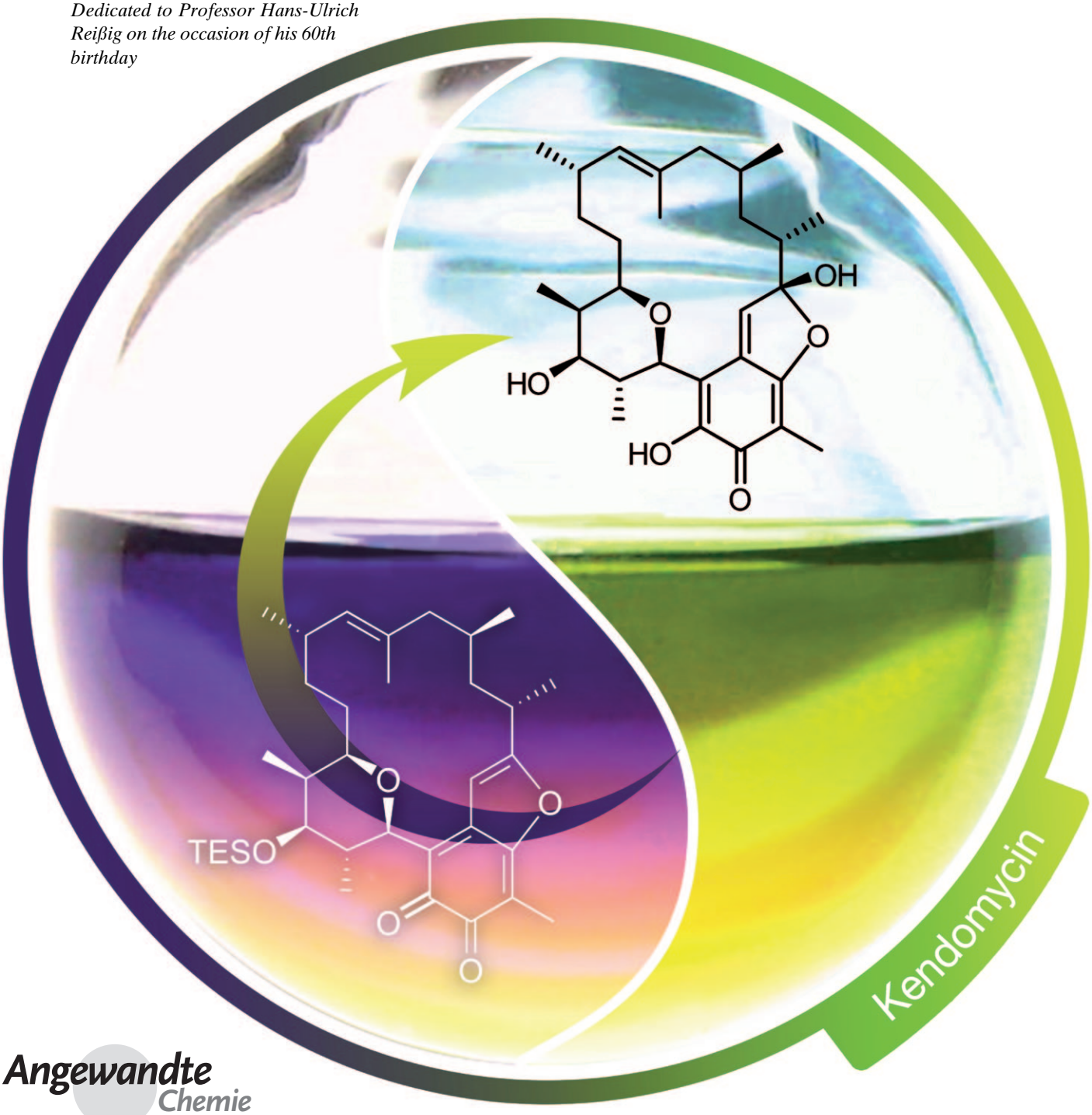
Natural Product Synthesis

DOI: 10.1002/anie.200900522

Total Synthesis of the Antibiotic Kendomycin by Macrocyclization using Photo-Fries Rearrangement and Ring-Closing Metathesis**

*Thomas Magauer, Harry J. Martin, and Johann Mulzer**

Dedicated to Professor Hans-Ulrich Reißig on the occasion of his 60th birthday

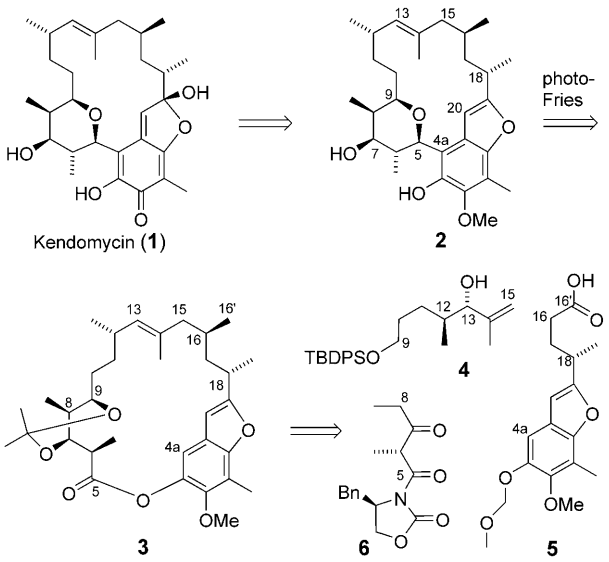


Kendomycin [**1**, (−)-TAN2162], an ansamycin isolated from different *Streptomyces* species, has been shown in studies over the last decade to be a potent endothelin receptor antagonist and antiosteoperotic compound with remarkable antibacterial and cytostatic activity.[1] The challenging structure and diverse pharmacological profile of kendomycin[1,2] has motivated us[3] and, sometime later a number of other groups,[4–6] to carry out studies towards its synthesis. To date, three total syntheses[4] and one formal synthesis[5] have been reported, along with a number of fragment preparations.[6] The main problem for all the approaches has been the formation of the strained macrocyclic *ansa*-ring. For example, macrocyclizations were performed using C-glycosidation,[4a] Barbier-type organometallic addition,[4d] Prins reaction,[5] and Horner–Wadsworth–Emmons olefination.[6e] Most strikingly, all attempts to achieve 13,14-macrocyclization by ring-closing metathesis (RCM)[4b,6a,e] were plagued by low yields and formation of the undesired 13,14-*Z*-olefin. We tested alternative locations for RCM connections; however to our disappointment, both the 9,10- and the 19,20-positions proved to be unsuited.[7] Nonetheless, we were still convinced that RCM should be a highly serviceable tool for ring closure.

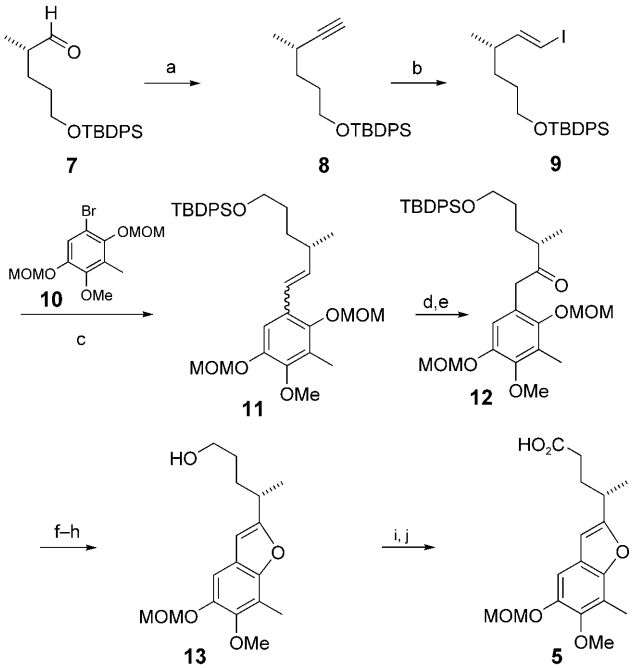
As we have demonstrated in previous studies,[3,6e] hindered rotation around the C4a/C5 bond connecting the tetrahydropyran ring and the aromatic system makes ring closure difficult. Therefore, we decided to postpone tetrahydropyran formation until after macrocyclization, and consequently, we report herein two novel ring closures: the first by a photo-Fries ring contraction[8] connecting C4a/C5, and the second by a RCM to form a 10,11-olefin. Both routes would lead to the known benzofuran intermediate **2**.[4a]

The photo-Fries route (Scheme 1) centers around macrolactone **3** as a key intermediate, which was assembled from building blocks **4**, **5**, and **6** by a Claisen–Ireland rearrangement (C15/C16 connection) and Evans aldolization (C8/C9-connection).

The synthesis of the benzofuran fragment **5** (Scheme 2) started with known aldehyde **7**,[4a] which is easily available from citronellene (see the Supporting Information). A Colvin C_1 chain elongation[9] furnished alkyne **8**, which was converted into vinyl iodide **9**. Negishi coupling[10] with aryl bromide **10**[6e] led to styrene **11**, which after epoxidation was subjected to palladium(0)-mediated rearrangement[11] to ketone **12**. Acid-catalyzed formation of the furan ring concomitantly removed the 3-OMOM group, which was reinstalled. Desilylation delivered alcohol **13**, which was oxidized to carboxylic acid **5**.



Scheme 1. Retrosynthesis of **1**: Photo-Fries approach. TBDPS = *tert*-butyldiphenylsilyl, Bn = benzyl.



Scheme 2. Synthesis of carboxylic acid **5**. a) $TMSCHN_2$, *n*BuLi, THF, −78 °C to RT, 83 %; b) $[Cp_2ZrHCl]$, benzene, 50 °C; I_2, 0 °C, 76 %; c) $[Pd(PPh_3)_4]$, *t*BuLi, $ZnCl_2$, Et_2O/THF, 0 °C, 67 %; d) DMDO, acetone, RT, 99 % (d.r. 1.1:1); e) $Pd(OAc)_2$, PBu_3, *t*BuOH, reflux, 81 % (2 steps); f) TfOH, toluene/EtOH (4:1), molecular sieves 4 Å, 80 °C, 5 min; g) MOMCl, NaH, DMF, 0 °C, 90 % (2 steps); h) TBAF, THF, RT, 89 %; i) IBX, DMSO, RT, 97 %; j) $NaClO_2$/NaH_2PO_4, 2,3-dimethylbut-2-ene, *t*BuOH/H_2O, 99 %. MOM = methoxymethyl, TMS = trimethylsilyl, Cp = cyclopentadienyl, DMDO = dimethyldioxirane, Tf = trifluoromethanesulfonyl, DMF = dimethylformamide, TBAF = tetra-*n*-butylammonium fluoride, THF = tetrahydrofuran, IBX = *o*-iodoxybenzoic acid, DMSO = dimethylsulfoxide.

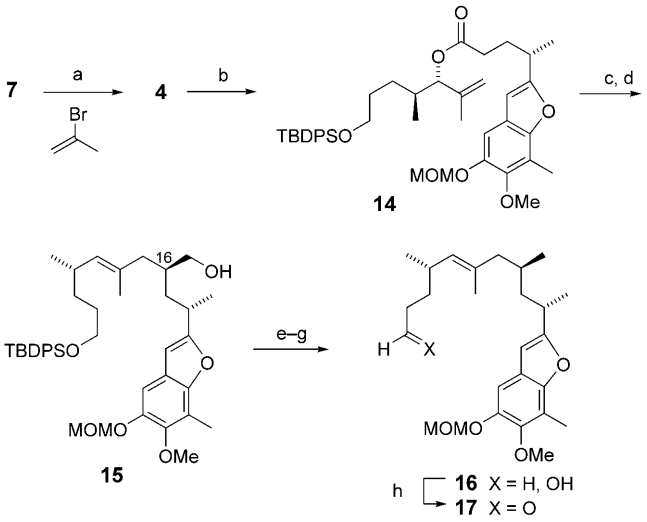
Allylic alcohol **4**,[12] which was available from aldehyde **7** by Nozaki–Hiyama–Kishi addition[13] of isopropenyl bromide

[*] Mag. T. Magauer, Dr. H. J. Martin, Prof. J. Mulzer
Institute of Organic Chemistry, University of Vienna
Währingerstrasse 38, 1090 Vienna (Austria)
Fax: (+43) 1-4277-52189
E-mail: johann.mulzer@univie.ac.at
Homepage: http://www.univie.ac.at/rg_mulzer/

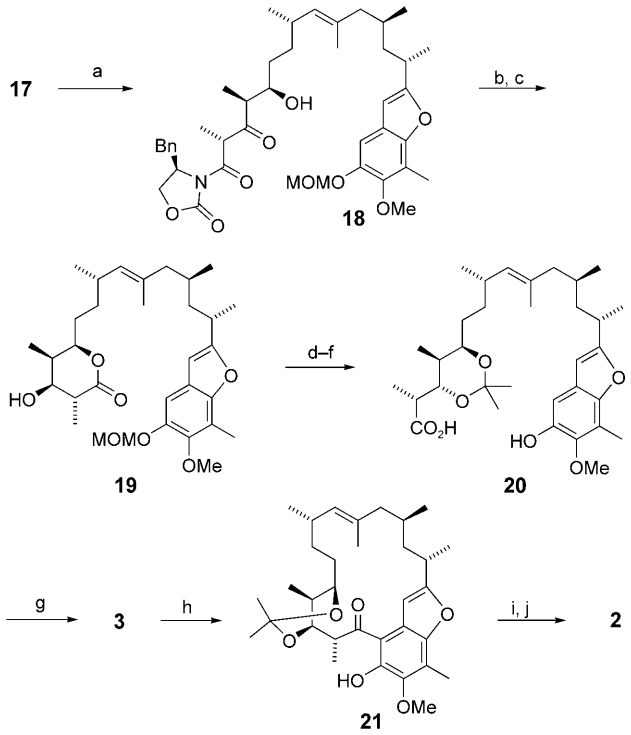
[**] We thank Dr. Lothar Brecker and Susanne Felsinger for NMR spectra, and Prof. A. Zeeck for an authentic sample of **1**.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.200900522.

(Scheme 3), was connected with carboxylic acid **5** to furnish ester **14** as the substrate of an Claisen–Ireland rearrangement, which, after reduction, led to primary alcohol **15** as an easily separable 4:1 diastereomeric mixture at C16.[14] Reduction and desilylation gave alcohol **16**, which was oxidized to aldehyde **17**.



Scheme 3. Synthesis of aldehyde **17**. a) $CrCl_2$ (4 equiv), $NiCl_2$ (0.04 equiv), DMF, 0 °C to RT, 86% (d.r. 1.4:1); b) EDCI, DMAP, **5**, CH_2Cl_2, 85%; c) LHMDS, HMPA, TBSCl, −78 °C to reflux; d) $LiAlH_4$, Et_2O, 0 °C, 84% (d.r. 4:1, 2 steps); e) MsCl, Et_3N, CH_2Cl_2, 0 °C; f) $LiAlH_4$, Et_2O, 0 °C, 94% (2 steps); g) TBAF, THF, RT, 93%; h) IBX, DMSO, RT, 93%. EDCI = 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, DMAP = 4-(dimethylamino)pyridine, HMDS = hexamethyldisilazane, HMPA = hexamethylphosphoramide, TBS = *tert*-butyldimethylsilyl, Ms = methanesulfonyl.

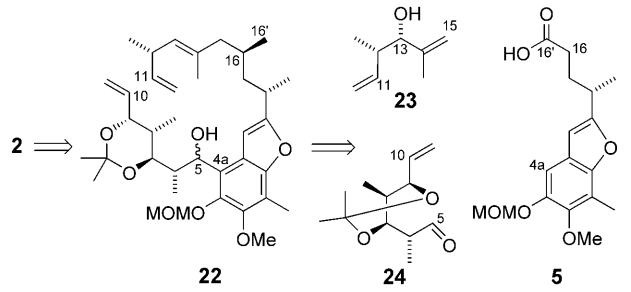


Scheme 4. Synthesis of benzofuran **2**. a) **6**, $Sn(OTf)_2$, CH_2Cl_2, Et_3N, −20 °C, then −78 °C, then **17**, 87% (d.r. 6:1); b) $Me_4NBH(OAc)_3$, CH_3CN/AcOH (2:1), −32 °C to 0 °C, 72% (d.r. 20:1); c) LiOH, H_2O_2, THF/H_2O (3:1), 96%; d) 3 M HCl, dioxane, 50 °C; e) $(CH_3)_2C(OMe)_2$, CSA, RT, 85% (2 steps); f) LiOH, THF/MeOH/H_2O (2:1:1), 12 h, RT, 84%; g) EDCI, DMAP, DMAP·HCl, $CHCl_3$, reflux, 20 h, 55%; h) *hν* (254 nm), cyclohexane, 50 min, 75%; i) $NaBH_4$, MeOH, RT, then 0.5 M HCl; j) TsOH, toluene, 60 °C, 71% (2 steps). CSA = camphorsulfonic acid, Ts = 4-toluenesulfonyl.

Aldol addition with the Evans ketoimide **6**[15] furnished intermediate **18**, which has the full carbon skeleton of kendomycin. Reduction[16] of the ketone and hydrolytic removal of the auxiliary led to lactone **19**, which was converted into *seco*-acid **20** by formation of the acetonide-protected methylester. Macrolactonization under modified Boden–Keck conditions[17] gave monomer **3** in 55% yield, which underwent clean photo-Fries rearrangement to give ketone **21**. Reduction to the secondary alcohol, followed by removal of the acetonide and S_N1 cyclization, furnished key intermediate **2** (Scheme 4).

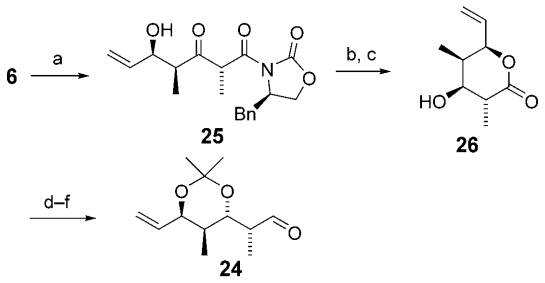
Our second route is outlined in Scheme 5. In contrast to earlier RCM attempts, RCM of triene **22** should not meet with major ring strain and thus proceed smoothly, as two monosubstituted olefins are connected. The tetrahydropyran ring is formed later, such that the above-mentioned atropisomerism cannot impede the macrocyclization. Triene **22** was to be constructed from building blocks **23**, **24**, and **5**.

Aldehyde **24** was obtained by Evans aldolization from ketoimide **6** and acrolein (Scheme 6) to give adduct **25** with good diastereoselectivity, which was converted into lactone **26** by reduction and removal of the auxiliary. For the conversion of **26** into aldehyde **24**, an analogous sequence was used as for the preparation of **20** from **19**.

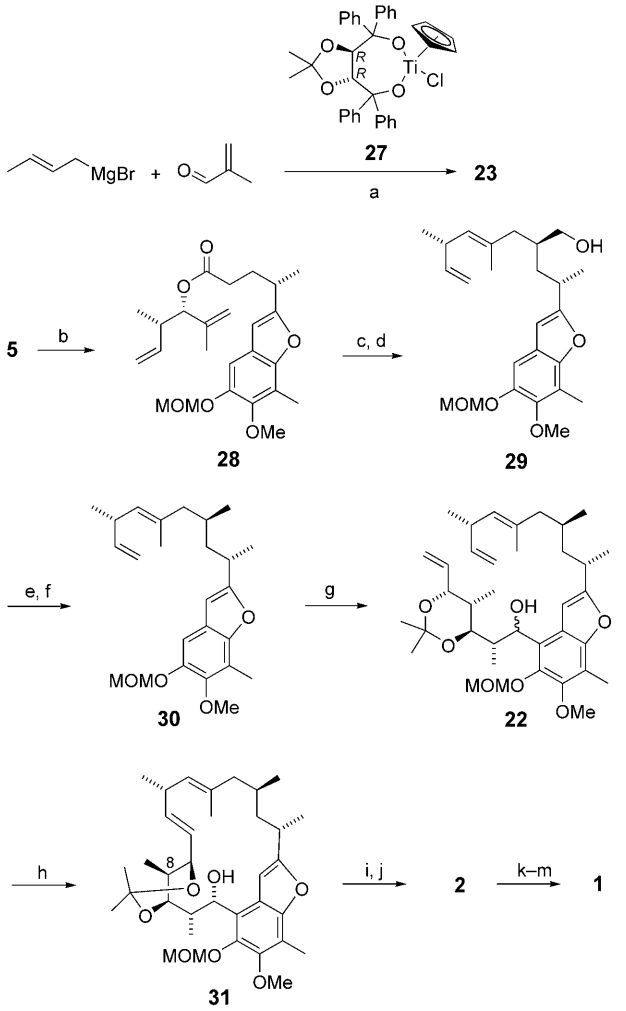


Scheme 5. Retrosynthesis of **2**: RCM route.

For the preparation of allylic alcohol **23**, a Duthaler–Hafner crotylation[18] of methacrolein with titanate **27** was the method of choice (Scheme 7). Esterification of acid **5** with alcohol **23** paved the way for the Claisen–Ireland rearrangement, by which ester **28** was smoothly converted into the acid, and after reduction, into alcohol **29**. Deoxygenation furnished diene **30**. Subsequent *ortho*-directed metalation and addition of aldehyde **24** gave alcohol **22** as a mixture of diastereomers. RCM with second-generation Grubbs catalyst[19] induced smooth ring closure to form the 10,11-*E*-olefin **31** exclusively. The extremely broad ^1H NMR signal of the 8-CH_3 group, which sharpens to a doublet on raising the temperature to



Scheme 6. Synthesis of aldehyde **24**. a) $Sn(OTf)_2$, CH_2Cl_2, Et_3N, −20 °C, −78 °C, then acrolein, 91% (d.r. 5:1); b) $Me_4NBH(OAc)_3$, CH_3CN/AcOH (2:1), −32 °C to 0 °C, 70% (d.r. 6:1); c) LiOH, H_2O_2, THF/H_2O (2:1), RT, 72%; d) $(CH_3)_2C(OMe)_2$, CSA, RT, 91%; e) $LiAlH_4$, Et_2O, 0 °C, 96%; f) pyridine·SO_3, Et_3N, CH_2Cl_2/DMSO, −5 °C, 99%.



Scheme 7. RCM and synthesis of **1**. a) Reaction of but-2-enyl-MgBr with **27**, then methacrolein, Et_2O, −78 °C, 52% (d.r. 50:1, 86% *ee*); b) DMAP, EDCI, CH_2Cl_2, RT, then **23**, 81%; c) LHMDS (4 equiv), HMPA, THF, then **28** dissolved in TBSCl, −78 °C to RT, then DMF, microwave irradiation (10 min, 180 °C); d) $LiAlH_4$, Et_2O, 0 °C, 89% (d.r. 4:1, 2 steps); e) MsCl, CH_2Cl_2, 0 °C; f) $LiAlH_4$, Et_2O, 0 °C, 89% (2 steps); g) *n*BuLi, TMEDA, THF, then **24**, −78 °C to −30 °C, 90% (d.r. 3.2:1); h) Grubbs II catalyst, 20 mol%, CH_2Cl_2, reflux, 16 h, 62% (*E* only); i) $N_2(COOK)_2$, AcOH, CH_2Cl_2, 40 h, reflux, 60%; j) 3 M HCl, MeOH, RT, 96%; k) TESOTf, Et_3N, CH_2Cl_2, 0 °C, 82%; l) IBX, DMF, RT, 24 h; m) 0.1 M HF, MeCN, RT, 30% (2 steps). TMEDA = tetramethylethylendiamine, TES = triethylsilyl.

350 K (see Supporting Information), indicates that the conformational mobility in **31** is significantly restricted. Selective reduction of the double bond with diimide,[20] followed by acid-catalyzed formation of the tetrahydropyran ring and removal of the OMOM group, led to intermediate **2**, which was oxidized to **1**.[4a] The analytical data of the synthetic material were in full agreement with those of an authentic sample kindly provided by Professor Zeeck.

In conclusion, we have presented two novel approaches to the antibiotic kendomycin (RCM route: 23 linear steps, photo-Fries route: 29 linear steps). Apart from Claisen–Ireland rearrangements of unusual complexity, this work not only demonstrates the hitherto unrecognized capability of the photo-Fries ring contraction for the formation of macrocycles, but also reemphasizes the unparalleled potential of RCM for connecting monosubstituted olefin residues.

Received: January 28, 2009
Published online: April 6, 2009

Keywords: aldol reactions · antibiotics · benzofurans · Claisen–Ireland rearrangement · total synthesis

[1] a) H. B. Bode, A. Zeeck, *J. Chem. Soc. Perkin Trans. 1* **2000**, 323; b) H. B. Bode, A. Zeeck, *J. Chem. Soc. Perkin Trans. 1* **2000**, 2665.
[2] a) S. C. Wenzel, H. B. Bode, I. Kochems, R. Müller, *ChemBioChem* **2008**, *9*, 2711; b) C. O. Janssen, S. Lim, E. P. Lo, K. F. Wan, V. C. Yu, M. A. Lee, S. B. Ng, M. J. Everett, A. D. Buss, D. P. Lane, R. S. Boyce, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5771.
[3] H. J. Martin, M. Drescher, H. Kählig, S. Schneider, J. Mulzer, *Angew. Chem.* **2001**, *113*, 3287; *Angew. Chem. Int. Ed.* **2001**, *40*, 3186.
[4] a) Y. Yu, H. Men, C. Lee, *J. Am. Chem. Soc.* **2004**, *126*, 14720; b) A. B. Smith III, E. F. Mesaros, E. Meyer, *J. Am. Chem. Soc.* **2006**, *128*, 5292; c) A. B. Smith III, E. F. Mesaros, E. Meyer, *J. Am. Chem. Soc.* **2005**, *127*, 6948; d) J. T. Lowe, J. S. Panek, *Org. Lett.* **2008**, *10*, 3813.
[5] K. B. Bahnck, S. D. Rychnovsky, *J. Am. Chem. Soc.* **2008**, *130*, 13177.
[6] a) T. Sengoku, D. Uemura, H. Arimoto, *Chem. Lett.* **2007**, *36*, 726; b) T. Sengoku, H. Arimoto, D. Uemura, *Chem. Commun.* **2004**, *10*, 1220; c) J. D. White, H. Smits, *Org. Lett.* **2005**, *7*, 235; d) D. Williams, K. Shamim, *Org. Lett.* **2005**, *7*, 4161; e) J. Mulzer, S. Pichlmair, M. P. Green, M. M. B. Marques, H. J. Martin, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 11980.
[7] T. Magauer, *Towards the Total Synthesis of the ansa-Macrocycle Kendomycin*, Diploma Thesis, University of Vienna, **2007**.
[8] P. Magnus, C. Lescop, *Tetrahedron Lett.* **2001**, *41*, 7193.
[9] E. W. Colvin, B. J. Hamill, *J. Chem. Soc. Chem. Commun.* **1973**, 151.
[10] a) E. Negishi, C. Kotora, C. Xu, *J. Org. Chem.* **1997**, *62*, 8957; b) Review: E. Negishi, Q. Hu, Z. Huang, M. Qian, G. Wang, *Aldrichimica Acta* **2005**, *38*, 71.
[11] S. Kulasegaram, R. J. Kulawiec, *J. Org. Chem.* **1997**, *62*, 6547.
[12] Compound **4** and its C13 epimer were obtained as an easily separable 1.4:1 mixture. The epimer was recycled by oxidation to the ketone and reduction with $NaBH_4$ (d.r. 2:1).
[13] a) Y. Okude, S. Hirano, T. Hiyama, H. Nozaki, *J. Am. Chem. Soc.* **1976**, *98*, 3179; b) A. Fürstner, N. Shi, *J. Am. Chem. Soc.* **1996**, *118*, 12349.
[14] Claisen–Ireland rearrangements of this dimension are rare in the literature; we are aware of three examples of similar complexity:

a) C. E. Stivala, A. Zakarian, *J. Am. Chem. Soc.* **2008**, *130*, 3774; b) M. J. Fisher, C. D. Myers, J. Joglar, S. H. Chen, S. J. Danishefsky, *J. Org. Chem.* **1991**, *56*, 5826; c) R. E. Ireland, D. Häbich, D. W. Norbeck, *J. Am. Chem. Soc.* **1985**, *107*, 3271.

[15] a) J. S. Clark, R. Metternich, V. J. Novack, G. S. Sheppard, D. A. Evans, *J. Am. Chem. Soc.* **1990**, *112*, 866; b) D. A. Evans, J. S. Clark, D. L. Rieger, *Tetrahedron* **1992**, *48*, 2127.

[16] D. A. Evans, K. T. Chapman, E. M. Carreira, *J. Am. Chem. Soc.* **1988**, *110*, 3578.

[17] E. P. Boden, G. E. Keck, *J. Org. Chem.* **1985**, *50*, 2394.

[18] a) A. Hafner, R. O. Duthaler, R. Marti, G. Rihs, P. Rothe-Streit, F. Schwarzenbach, *J. Am. Chem. Soc.* **1992**, *114*, 2321; b) Review: A. Hafner, R. O. Duthaler, *Chem. Rev.* **1992**, *92*, 807.

[19] a) M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953; b) B. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100.

[20] D. J. Pasto, R. T. Taylor, *Org. React.* **1991**, *40*, 91 – 155.

3.2. Ring Closing Metathesis and Photo–Fries Reaction for the Construction of the Ansamycin Antibiotic Kendomycin. Development of a Protecting Group Free Oxidative Endgame

T. Magauer, H. J. Martin, J. Mulzer, *Chem. Eur. J.* **2009***, Accepted*.

CHEMISTRY
A EUROPEAN JOURNAL

FULL PAPER

DOI: 10.1002/chem.200((will be filled in by the editorial staff))

Ring Closing Metathesis and Photo-Fries Reaction for the Construction of the Ansamycin Antibiotic Kendomycin. Development of a Protecting Group Free Oxidative Endgame.

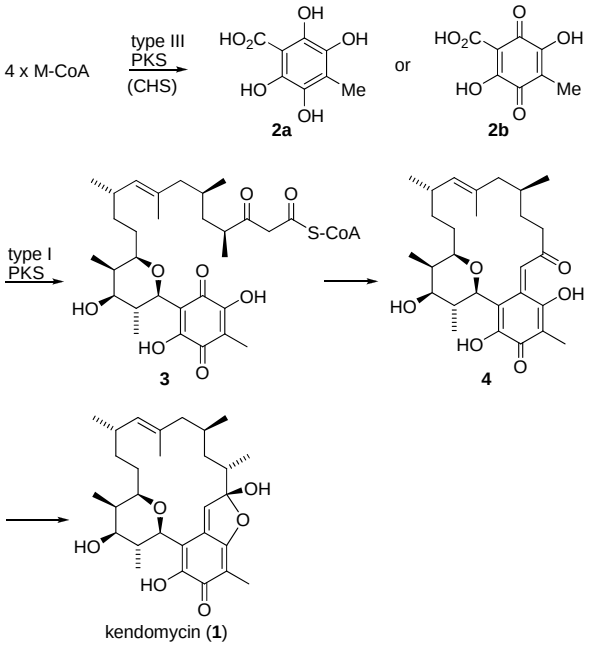
Thomas Magauer, Harry J. Martin, Johann Mulzer*[a]

Abstract: Two convergent total syntheses of the *ansa*-polyketide (-)-Kendomycin **1** are described. The syntheses benefit from the use of readily available and cheap starting materials. Highly complex diastereoselective Claisen-Ireland rearrangements were used to introduce the (*E*)-double bond and the C16-Me group. The ring closure of the strained *ansa* macrocycle was achieved by RCM and a highly efficient combination of macrolactonization and photo-Fries reaction. A protecting group free endgame *via* an unstable *o*-quinone is presented. Additionally some unsuccessful synthetic efforts towards the total synthesis of **1** are described.

Keywords: RCM • photo-Fries • Claisen-Ireland rearrangement • polyketides • *ansa*-compound

Introduction

Kendomycin [(-)-TAN 2162] (**1**) was first reported in 1996,[1] and re-isolated in 2000 by Zeeck and Bode during their screening program for new metabolites from *Actinomycetes*.[2] Biological testing revealed **1** to be a potent endothelin receptor antagonist and antiosteoperotic compound with remarkable antibacterial and cytostatic activity,[2,3] most likely through proteasome inhibition.[3a] Beside the diverse pharmacological qualities, which have attracted (bio)-chemists in the last years, Kendomycin discloses an unique molecular architecture with a fully carbogenic *ansa*-polyketide chain, nine stereogenic centers, a pentasubstituted tetrahydropyran ring and a remarkable *p*-quinone-methide chromophore. The biosynthesis (Scheme 1)[2b, 4] implies the formation of benzoic acid **2a** or the corresponding quinoid nucleus **2b** from malonate subunits under the mediation of chalcone synthase (CHS). This core unit is then loaded onto the type I polyketide synthase (PKS) to form keto acid **3** which undergoes cyclization to ketone **4** under decarboxylation. Ketalization leads to **1** eventually.



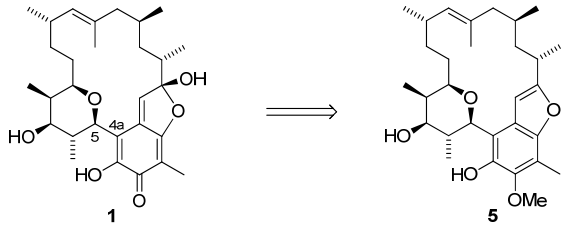
Scheme 1. Biosynthesis of kendomycin.

The challenging framework and the promising pharmacological profile of (**1**) has motivated us[5] and sometime later, a number of other groups[6-8] to carry out studies towards its synthesis. So far four total syntheses[6] and one formal one[7] have been reported, along with a number of fragment preparations.[8] All these approaches loosely follow the biogenetic pathway by starting with an aromatic polyphenol subunit, attaching a polyketide chain and then aiming for cyclization. The main challenge has thus been the

formation of the strained macrocyclic *ansa*-ring and the late stage generation of the quinone and lactol units. So far, macrocyclizations have been performed *via* RCM[6b], C-glycosidation,[6a] Barbier-type organometal addition,[6d] Prins reaction[7] and Horner Wadsworth Emmons olefination.[8e] In continuation of earlier reports[5] we now want to disclose our recent efforts, which have culminated in two successful syntheses.[6e]

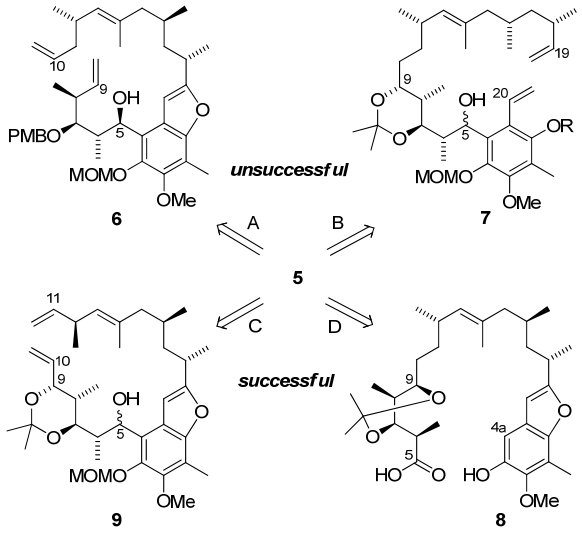
Results and Discussion

It is obvious that the formation of the quinone methide chromophore should be deferred to the end of the synthesis, *via* the oxidation of known[6a] benzofuran **5** (Scheme 2). A further general consideration concerns the tetrahydropyran ring which preferably should be installed after the macrocyclization - mainly because of restricted rotation around the C4a-C5 bond[5d] which might be disadvantageous for subsequent ring closures.



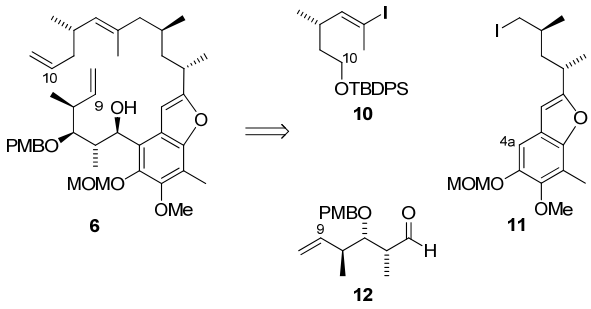
Scheme 2. Benzofuran precursor of kendomycin.

In this report we present four general approaches toward the synthesis of the common precursor **5** (Scheme 3). Three of them address the ring closing metathesis (RCM) at different sites as key steps. In the first approach (A), we intended to combine olefinic carbons C9 and C10 of compound **6** *via* RCM, followed by an addition of C5-OH to C9 for tetrahydropyran ring formation. In approaches B and C using compounds **7** and **9**, respectively as RCM precursors, the tetrahydropran ring should be generated by diastereoselctive S_N1-reaction of the C9-OH with an in situ generated benzylic cation at C5.[9] The final approach (D) focuses on the macrolactonization of compound **8** followed by a photo-Fries reaction, and the tetrahydropyran should be formed by C5-carbonyl reduction and S_N1 cyclization. It should be noted at this point, that only approaches C and D have been successful, in contrast to route A where the RCM did not work and B, where the RCM precursor **7** could not be made at all.



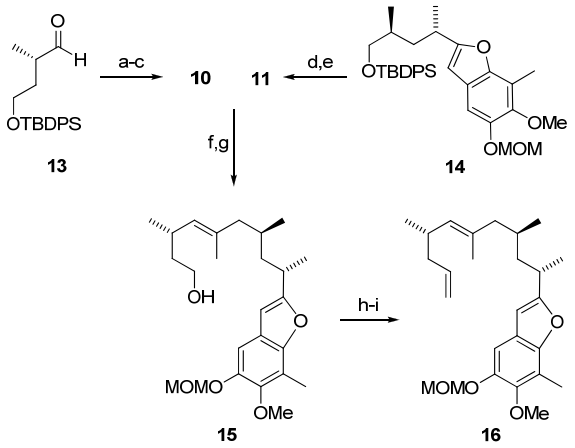
Scheme 3. Precursors for macrocyclizations..

RCM and trans-etherification (Route A): Retrosynthetically, the RCM precursor **6** was disconnected into vinyl iodide **10**, alkyl iodide **11** and aldehyde **12** (Scheme 4). The synthesis of the northern diene portion should be achieved by a Negishi cross coupling of iodides **10** and **11,** followed by chain elongation to the 10-olefin. *Ortho*-directed lithiation of C4a and addition to aldehyde **12** should set the stage for the envisaged RCM reaction.



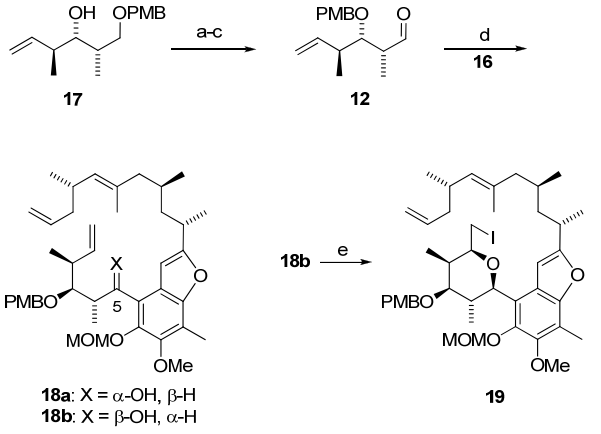
Scheme 4. Retrosynthetic disconnections for route A.

Vinyliodide **10** was easily available from known aldehyde **13**.[10] Colvin's one carbon chain elongation[11] afforded the corresponding alkyne, which was alkylated with MeI and converted to **10** by hydrozirconation/iodination. Iodide **11** was prepared from known[9] compound **14** via a two step standard procedure. Pd(0) assisted Negishi coupling[12] of iodides **10** and **11**, followed by deprotection gave (*E*)-olefin **15** which was converted to 1,4-diene **16** *via* IBX-oxidation and Wittig methylenation (Scheme 5).



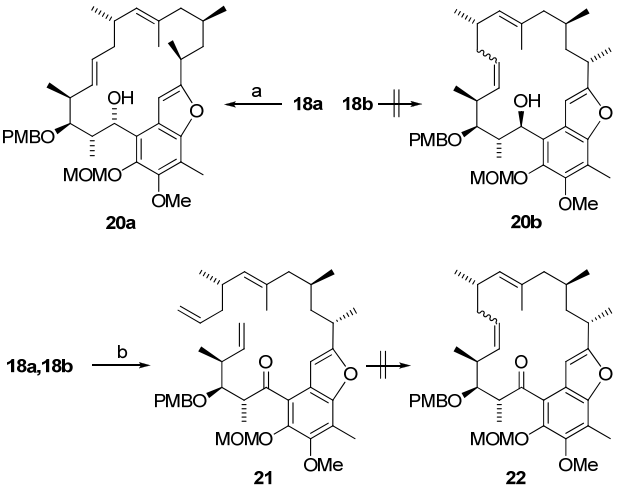
Scheme 5. Synthesis of compound **16**. a) $TMSCHN_2$, LDA, THF, -78 °C to r.t., 82%; b) BuLi, MeI, THF, -78 °C to r.t. 95%; c) Cp_2ZrClH, benzene, THF, I_2, 83% ; d) TBAF, THF, 94%, e) I_2, PPh_3, CH_2Cl_2, 88%; f) **11**, *t*BuLi, $ZnCl_2$, Et_2O/THF, 5 mol% $Pd(PPh_3)_4$, -78 °C - r.t. add **10** in THF; g) TBAF, THF, 67% 2 steps; h) IBX, DMSO, r.t., 97%; i) $MePPh_3Br$, *t*BuOK, THF, 0°C, 90%.

Aldehyde **12** was available from known alcohol **17**[13] *via* 1,3 shift of the PMB protecting group and oxidation of the primary alcohol with IBX (Scheme 6). MOM-directed *ortho*-lithiation of **16** followed by nucleophilic addition to aldehyde **12** afforded benzylic alcohols **18a** and **18b** as a 1.5:1 diastereomeric mixture. The configuration at the benzylic carbon C5 was assigned by converting compound **18b** into cyclic iodoether **19.** 2D NMR experiments (NOESY) revealed that **19** and hence **18b** have the desired *R*-configuration at C5.



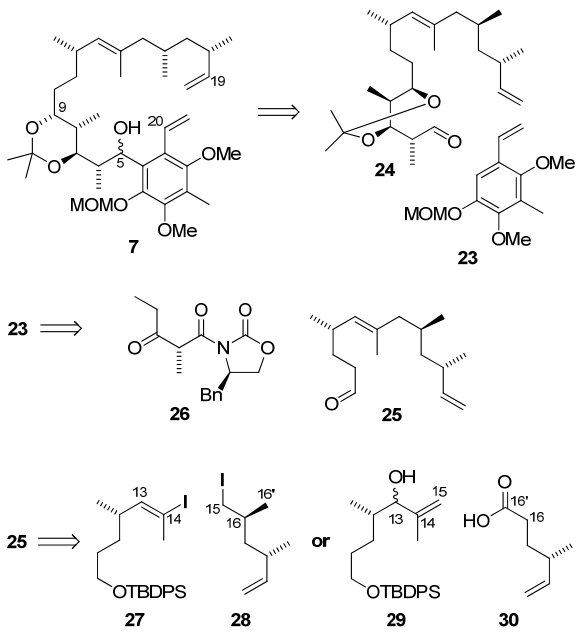
Scheme 6. a) DDQ, CH_2Cl_2, 3Å MS, 0 °C, 74%; b) DIBAL, CH_2Cl_2, -78 °C to -10 °C, 93%; c) CH_2Cl_2, DMSO, $(COCl)_2$, NEt_3, -78 °C, 99%; d) **16**, *n*BuLi, TMEDA, THF, -40 °C then **12**, -78 °C to -25 °C, 75% (dr = 1.5:1); e) *t*butyl-4-methylpyridine, I_2, CH_2Cl_2, -78 °C to -10 °C, 50%.

Subjecting **18b** to Grubbs' II catalyst[14] did not result in the desired cyclization to **20b**, but only decomposition of starting material was observed (Scheme 7). In contrast, **18a** underwent the cyclization and afforded macrocyle **20a** which was used for testing purposes. Unfortunately all attempts to form the tetrahydropyran by iodination, oxymercuration or selenocyclization failed. Additionally, as RCM of ketone **21** was not successful, we abandoned approach A at this point[15] and turned to route B.



Scheme 7. a) Grubbs' II catalyst, 15 mol%, CH_2Cl_2, reflux, 16 h, 46%; b) IBX, DMSO, r.t., 96%.

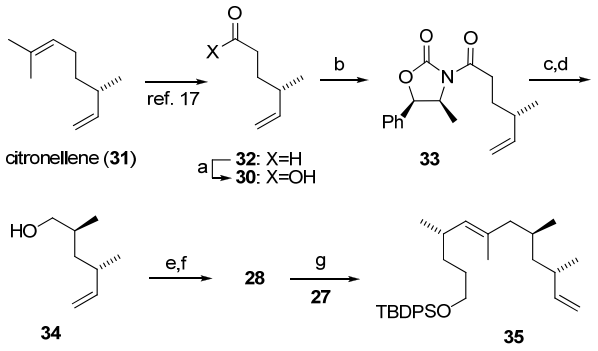
RCM reaction at C19/C20 (Route B): Installation of the 13,14-(*E*)-double bond *via* Negishi coupling and C4/5 conection *via* an *o*-lithiation aldehyde addition sequence have proven reliable and efficient. Additionally, we envisaged the Ireland-Claisen rearrangement[16] as an appropriate tool for generating the 13,14-(*E*)-olefin along with the C-16 methyl group. Thus *seco* compound **7** should be available from styrene **23** and aldehyde **24**, which could be formed by an Evans aldol addition of aldehyde **25** and ketoimide **26** (Scheme 8). The installation of the C14/C15 double bond should then be achieved by either Negishi coupling of iodides **27**[7] and **28** or by esterification of acid **30** with alcohol **29** followed by an Ireland-Claisen rearrangement.



Scheme 8. Retrosynthetic disconnections for route B.

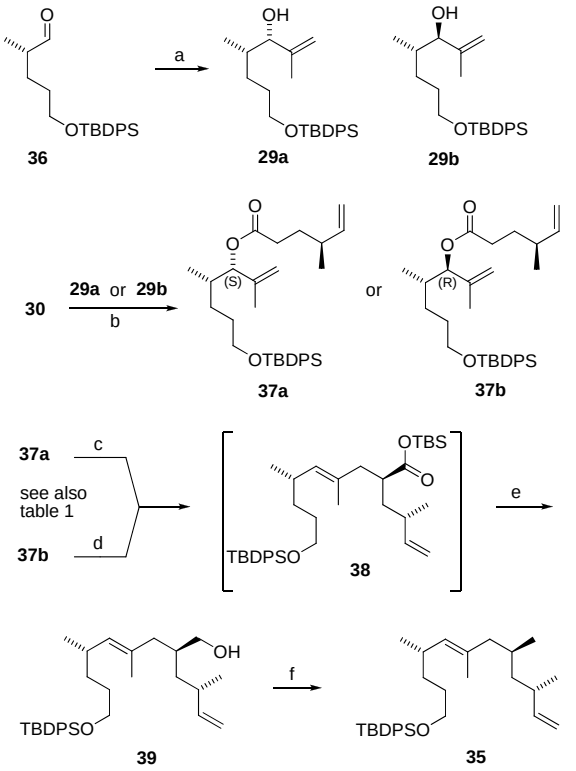
The synthesis started with known[6a] aldehyde **32**, easily available from citronellene **31** in 2 steps.[17] Pinnick oxidation[18] to

the corresponding acid **30** followed by amidation afforded oxazolidinone **33** in good yield (Scheme 9). The second methyl group was introduced *via* diastereoselective alkylation with methyl iodide, and reductive removal of the auxiliary afforded primary alcohol **34.** Subsequent Finkelstein reaction delivered gram quantities of alkyl iodide **28** in excellent yield. Coupling of known vinyl iodide **27** with **28** smoothly afforded diene **35** as a key fragment.



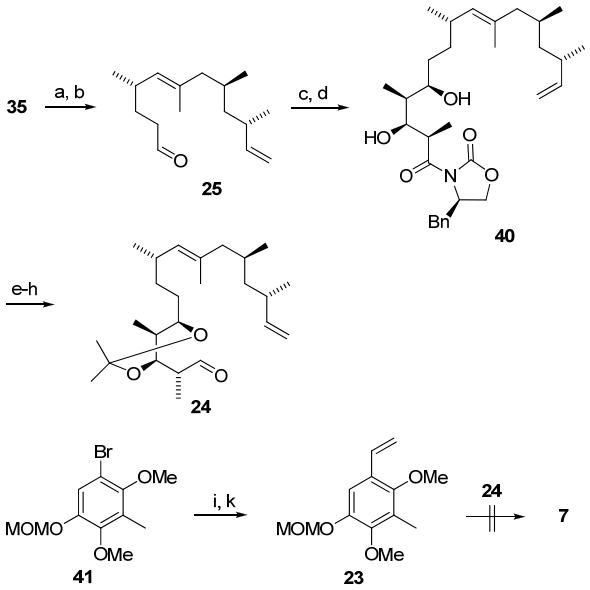
Scheme 9. a) $NaClO_2$, NaH_2PO_4, *t*BuOH, H_2O, 73% from **31**; b) DIC, DMAP, Evans' oxazolidinone, CH_2Cl_2, 82%; c) LHMDS, MeI, THF, -78 °C to r.t., 74% (dr = 10:1); d) $LiAlH_4$, Et_2O, 0 °C, 80%; e) MsCl, NEt_3, CH_2Cl_2, 0 °C; f) NaI, acetone, r.t., 86% from **34**; g) 2.2 equiv. *t*BuLi, $ZnCl_2$, -78 °C to 0 °C, then **27**, Et_2O/THF, 5 mol% $Pd(PPh_3)_4$, 0 °C, 95%.

In another approach (Scheme 10) for the synthesis of **35** we decided to use an Ireland-Claisen reaction. This should give access to the trisubstituted (*E*)-olefin and generate the stereocenter at C16 with the desired configuration. For this purpose, known aldehyde **36** [6a] was treated with isopropenyl bromide in a Hiyama-Kishi reaction to give a 1.4:1 mixture of allylic alcohols **29**.[19] The alcohols were separated and esterified with carboxylic acid **30** to afford compounds **37a** and **37b**, respectively. Treatment of **37a** with LDA in THF/HMPA afforded a (*Z*)-silyl ketene acetal, which was rearranged to the corresponding silyl ester **38** in good yield and acceptable diastereoselectivity (see also table 1).[20] Reaction with potassium fluoride and subsequent reduction with $LiAlH_4$ furnished alcohol **30** which was reduced to give the C16-methyl group in **35**. Since the ester enolate geometry strongly depends on the solvents, treatment of **37b** with LDA in THF should give the corresponding (*Z*)-enolate, and thus, the rearrangement should likewise provide compound **39** after desilylation and reduction. Disappointingly, all attempts to rearrange the (*Z*)-enolate of **37b** proved to be low yielding.



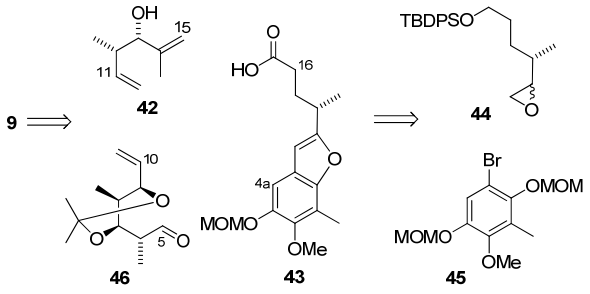
Scheme 10. a) $CrCl_2$ (4 equiv.), $NiCl_2$ (0.04 equiv.), DMF, 0 °C to r.t., 86% (dr = 1.4:1); b) DIC, DMAP, CH_2Cl_2, then **29a** or **29b**, 92%; c) LDA, THF-HMPA (23%) then TBSCl, -78 °C to reflux; d) LDA, THF, then TBSCl-HMPA, -78 °C to reflux; e) i. HMPA, $KHCO_3$, KF, MeI, 0 °C, ii. $LiAlH_4$, Et_2O, 0 °C, 63% from **37a** (dr = 5:1), 8% from **37b**; f) i. MsCl, NEt_3, CH_2Cl_2, 0 °C, ii. $LiAlH_4$, THF, 0 °C to r.t., 90%.

Nevertheless, the rearrangement of **37a** had provided us with gram quantities of diene **35** and so we focused on the elongation sequence (Scheme 11). Deprotection and IBX oxidation furnished aldehyde **25** in 77% yield over two steps. Extended Evans aldol methodology[21] followed by 1,3 reduction[22] afforded stereotetrad (C6 to C9) **40** in good yield and high diastereoselectivity. Base induced hydrolysis to remove the auxiliary and treatment with camphorsulfonic acid in 2,2-dimethoxypropane and methanol afforded the methyl ester. Reduction with $LiAlH_4$ and oxidation of the resulting primary alcohol to aldehyde **24** paved the way for testing the final key steps. Thus, known aryl bromide **41**[23] was formylated and then converted to styrene **23** *via* Wittig methylenation. To obtain the desired RCM precursor **7**, **23** and **24** had to be coupled as before, but unfortunately, addition of *n*BuLi to **23** did not give the expected *ortho*-lithiated[24] product but led to polymerization of the styrene unit. So, with a heavy heart after so much experimentation, we abandoned route B.



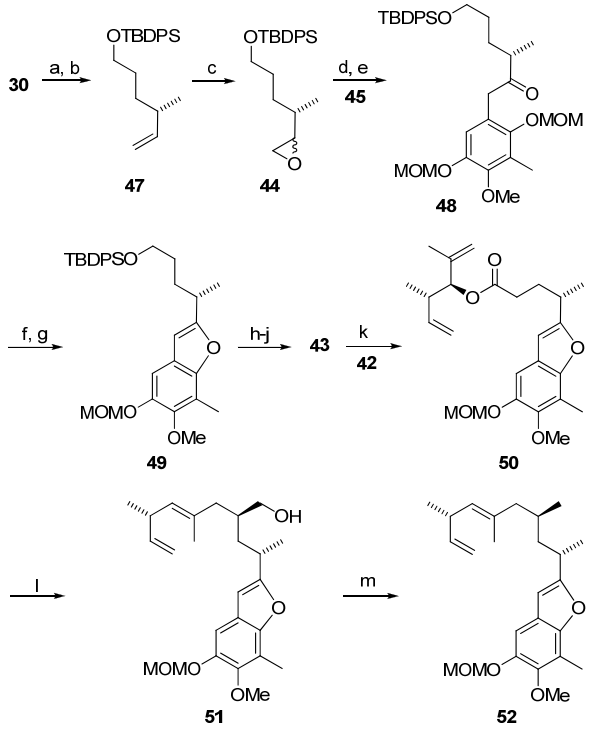
Scheme 11. a) TBAF, THF, r.t., 87%; b) IBX, DMSO, r.t., 95%; c) **26**, $Sn(OTf)_2$, CH_2Cl_2, NEt_3, -35 °C, then -78 °C, then add **25**, 76% (dr = 10:1); d) $Me_4NBH(OAc)_3$, CH_3CN:AcOH (1.9:1), -32 °C, 76% (dr = 20:1); e) LiOH, H_2O_2, THF/H_2O (3:1), 92%; f) 2,2-dimethoxypropane, CSA, 16 h, r.t., 90%; g) $LiAlH_4$, Et_2O, 0 °C, 99%; h) IBX, DMSO, r.t., 99%; i) *t*BuLi, DMF, 1N HCl, -78 °C to r.t., 83%; k) $MePPh_3Br$, *t*BuOK, THF, 0 °C , 98%.

RCM reaction at C10/C11 (Route C): In our final RCM approach we aimed for the generation of a C10/C11 olefin which has subsequently to be reduced in presence of the 13,14-olefin. For the formation of the 13,14-tri-substituted double bond we wanted to reapply the Ireland-Claisen approach using the known allylic alcohol **42**[25] and carboxylic acid **43** as simple precursors. Carboxylic acid **43** should be assembled from epoxide **44** and known aryl bromide **45**.[8e] The missing tetrahydropyran side chain should be introduced in the usual way by *ortho*-lithiation of the C4a position and addition of aldehyde **46** (Scheme 12).



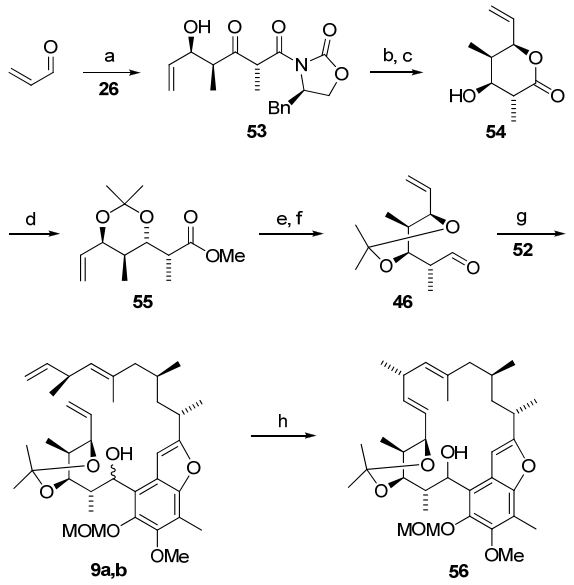
Scheme 12. Retrosynthetic disconnections for route C.

For the enantioselective preparation of allylic alcohol **42**, a Duthaler-Hafner crotylation[26] of methacrolein proved to be the method of choice, as the asymmetric crotylation protocols by Roush [27] or Brown[28] lacked enantio- or diastereoselectivity in this case. The synthesis of acid **43** started from aldehyde **32** (available from citronellene **31** in two steps, see supporting information)**,** which was reduced to the corresponding alcohol and converted into silylether **47** (Scheme 13) and then into epoxide **44**. Treatment of **44** with a cuprate reagent derived from bromide **45** gave the corresponding alcohol as a mixture of diastereomers (ca. 1:1). Oxidation led to ketone **48**, which after treatment with triflic acid and reprotection with MOMCl furnished benzofuran **49** in good yield. Desilylation and two-step oxidation of the primary alcohol afforded carboxylic acid **43** which was esterificated with alcohol **42** to provide the rearrangement precursor **50**. To our dismay, the Ireland-Claisen conditions we had used for Route B did not work out as expected. In our first tries, we had to struggle with moderate yields and very low diasteroselectivities. Fortunately, after a lot of optimization (see table 1), yield and diasteroselectivity were improved considerably. Subsequent reduction of the 16'-OH finished the synthesis of 1,3-diolefin **52**.



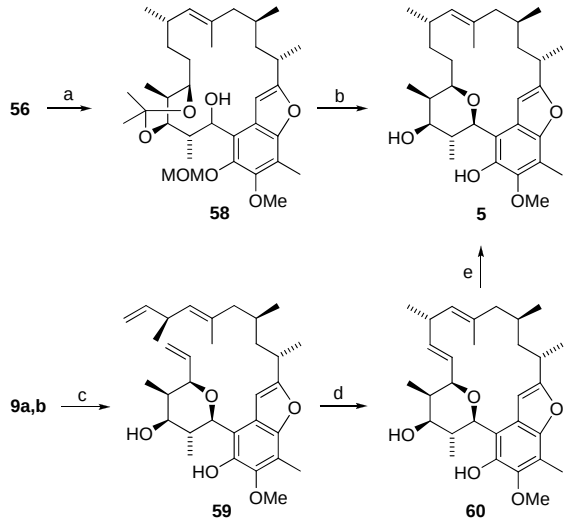
Scheme 13. a) $LiAlH_4$, Et_2O, 0 °C, 77% from citronellene **31**; b) TBDPSCl,imidazole, THF, r.t., 90%; c) *m*CPBA, CH_2Cl_2, 0 °C, 96%; d) **45**, Mg, THF, reflux 2h, - 40 °C, CuI, then **44**, -40 °C to 0 °C, 4h, 87%; e) DMSO, $(COCl)_2$, NEt_3, CH_2Cl_2, -78 °C, 95%; f) TfOH, toluene, 80 °C; g) MOMCl, NaH, DMF, 95% from **47**; h) TBAF, THF, r.t., 89%; i) IBX, DMSO, r.t., 97%; j) $NaClO_2$, NaH_2PO_4, *t*BuOH, H_2O, 99 %; k) DMAP, EDCI-HCl, CH_2Cl_2, r.t., 86%; l) i. LHMDS (4 equiv.), HMPA, THF, then **50** dissolved in THF/TBSCl, -78 °C to r.t., then DMF, microwave, 15 min, 180 °C, ii. $LiAlH_4$, Et_2O, 0 °C, 89% (dr = 4:1); m) i. MsCl, CH_2Cl_2, 0 °C, ii. $LiAlH_4$, Et_2O, 0 °C, 89%.

Aldehyde **46** was obtained *via* Evans aldol addition of ketoimide **26** and acrolein (Scheme 14) to give adduct **53** in good yield and diastereoselectivity. Lactonization to **54** was performed *via* stereoselective carbonyl reduction and subsequent removal of the auxiliary. Treatment with camphorsulfonic acid in dimethoxypropane furnished ester **55** which was converted into aldehyde **46** by a reduction-oxidation sequence. *Ortho*-directed lithiation of **52** and addition of aldehyde **46** gave tri-olefin **9** as a 3.5:1 mixture of diastereomers **9a**/**9b**, which was separated by chromatography. RCM of the major diastereomer (**9a**) with Grubbs' second generation catalyst induced smooth ring closure to 10,11-(*E*)-olefin **56** exclusively.



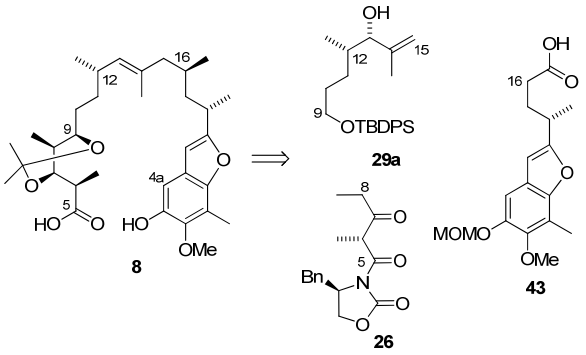
Scheme 14. . a) $Sn(OTf)_2$, CH_2Cl_2, Et_3N, -20 °C, -78 °C, then acrolein, 91% (dr = 5:1); b) $Me_4NBH(OAc)_3$, CH_3CN/AcOH (2:1), -32 °C to 0 °C, 70% (dr = 6:1); c) LiOH, H_2O_2, THF/H_2O (2:1), r.t., 72%; d) $(CH_3)_2C(OMe)_2$, CSA, r.t., 91%; e) $LiAlH_4$, Et_2O, 0 °C, 96%; f) Pyridine·SO_3, NEt_3, CH_2Cl_2/DMSO, -5 °C, 99%.; g) *n*BuLi, TMEDA, THF, then **52**, -78 °C to -30 °C, 90% (dr = 3.5:1); h) Grubbs' II catalyst, 20 mol%, CH_2Cl_2, reflux, 16 h, 62% ((*E*) only).

Site selective reduction of the 10,11-olefin with diimide,[29] followed by acid induced formation of the tetrahydropyran ring and concomitant removal of the MOM-group led to key intermediate **5**. Since the minor diastereomer **9b** did not undergo the RCM reaction and the S_N1 tetrahydropyran formation is independent of the configuration at C5 we concluded that it might be advantageous to change the order of the cyclization reactions (Scheme 15). Treatment of the **9a,b**-mixture with HCl resulted in clean formation of tetrahydropyran **59**, which, not surprisingly showed the typical atropismerism (1.5:1) of those compounds. Pleasingly, the subsequent RCM afforded the desired macrocyle in excellent yield and almost exclusively as the (*E*)-isomer **60** (15:1).[30] The success of this RCM came totally unexpected, as we had anticipated major problems from the tetrahydropyran ring. Diolefin **59** was reduced with high site selectivity to compound **5** with diimide.



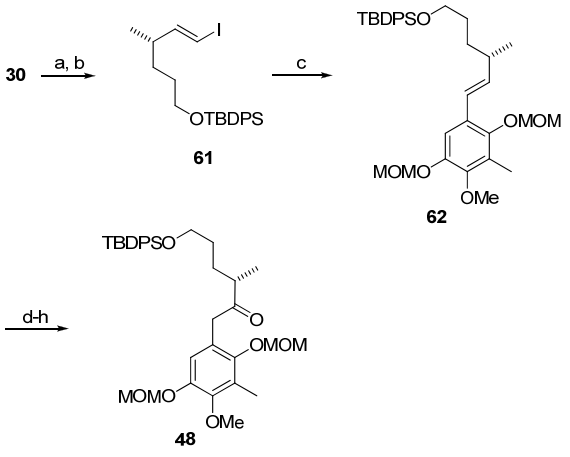
Scheme 15. Synthesis of benzofuran **5** *via* RCM. a) $N_2(COOK)_2$, AcOH, CH_2Cl_2, 40h, reflux, 58%; b) 3N HCl, MeOH, r.t., 96%; c) 3N HCl, MeOH, r.t., 71%; d) Grubbs' II catalyst, 20 mol%, CH_2Cl_2, reflux, 16 h, 83% (*E*:*Z* = 15:1); e) $N_2(COOK)_2$, AcOH, CH_2Cl_2, 5h, reflux, 71%.

Macrolactonization and photo-Fries reaction to close the C4a/C5 bond (route D): This approach (Scheme 16) was centered around *seco* acid **8** as a key intermediate. The carbon skeleton should be assembled from the established building blocks **43** and **29a** which would give the (*E*)-13,14-olefinic unit *via* Claisen–Ireland rearrangement. Evans aldol addition of a C9-aldehyde with ketoimide **26** should be used for the C8-C5-chain elongation.



Scheme 16. Retrosynthesis for route D.

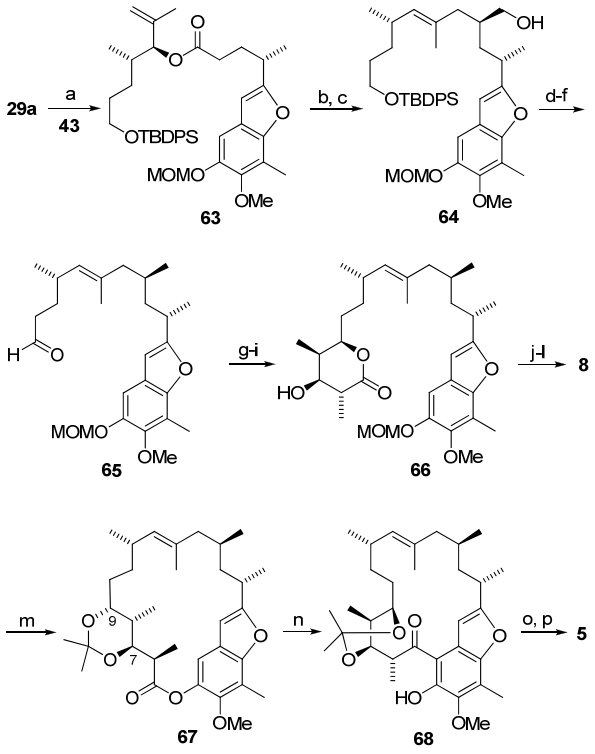
For ketone **48**, which serves as the precursor of acid **43**, we developed a new route (Scheme 17). Starting with aldehyde **30**, Colvin's chain elongation furnished the corresponding alkyne which was converted into vinyl iodide **61**. Negishi coupling with aryl bromide **45** furnished styrene **62**, which, after epoxidation was subjected to a Pd(0)-mediated rearrangement[31] to ketone **48**.



Scheme 17. Synthesis of compound **48**. a) $TMSCHN_2$, *n*BuLi, THF, -78 °C to r.t., 83%; b) Cp_2ZrHCl, benzene, 50 °C; I_2, 0 °C, 76%; c) **45**, *t*BuLi, $ZnCl_2$, Et_2O/THF, -78 °C to 0 °C, $Pd(PPh_3)_4$, then add **61**, 67%; d) DMDO, acetone, r.t., 99%; e) $Pd(OAc)_2$, PBu_3, *t*BuOH, reflux, 81%.

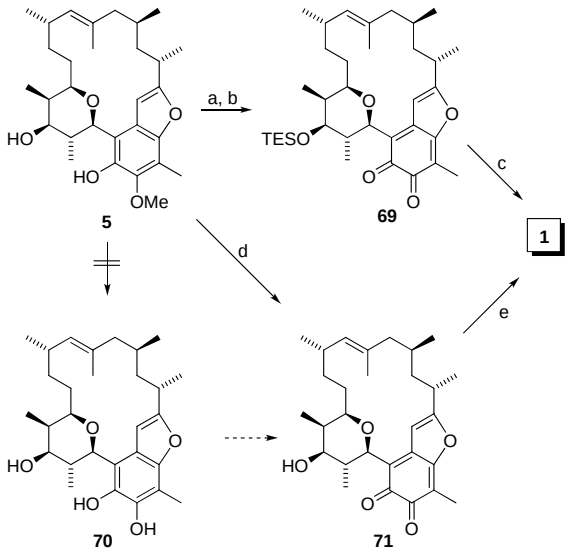
Allylic alcohol **29a** was connected with acid **43** to furnish ester **63** as the substrate of an Ireland-Claisen rearrangement (Scheme 18). Treatment with excess LHMDS and reductive work-up led to

primary alcohol **64** as an easily separable 4:1 diastereomeric mixture. Subsequent reduction of the carboxyl to the methyl group followed by desilylation and oxidation gave aldehyde **65** which was subjected to an aldol addition with ketoimide **26**. Diastereoselective 1,3-reduction followed by acid catalyzed lactonization furnished lactone **66** which was converted into *seco* acid **8** *via* the 7,9-acetonide protected methyl ester. Macrolactonization of **8** under modified Boden-Keck conditions[32] worked nicely to give 55% of monomer **67**, which underwent clean photo-Fries rearrangement to ketone **68**. Reduction of the ketone to the alcohol (diastereomeric mixture) followed by removal of the acetonide and S_N1-cyclization furnished key intermediate **5**.



Scheme 18. Synthesis of benzofuran **5** *via* photo-Fries rearrangement. a) EDCI, DMAP, **43**, CH_2Cl_2, 85%; b) LHMDS, HMPA, TBSCl, -78 °C to reflux; c) $LiAlH_4$, Et_2O, 0 °C, 84% from **63** (dr = 4:1); d) i. MsCl, Et_3N, CH_2Cl_2, 0 °C, ii. $LiAlH_4$, Et_2O, 0 °C, 94% (2 steps); e) TBAF, THF, r.t., 93%; f) IBX, DMSO, r.t., 93%; g) **26**, $Sn(OTf)_2$, CH_2Cl_2, Et_3N, -20 °C, then -78 °C, then **65**, 87% (dr = 6:1); h) $Me_4NBH(OAc)_3$, CH_3CN/AcOH (2:1), -32 °C to 0 °C, 72% (dr = 20:1); i) LiOH, H_2O_2, THF/H_2O (3:1), 96%; j) 3N HCl, dioxane, 50 °C; k) $(CH_3)_2C(OMe)_2$, CSA, r.t., 85% 2 steps; l) LiOH, THF/MeOH/H_2O (2:1:1), 12 h, r.t., 84%; m) EDCI, DMAP, DMAP·HCl, $CHCl_3$, reflux, 20 h, 55%; n) *hv*, 254 nm, cyclohexane, 50 min, 75%; o) $NaBH_4$, MeOH, r.t., then 0.5N HCl; p) TsOH, toluene, 60 °C, 71% from **68**.

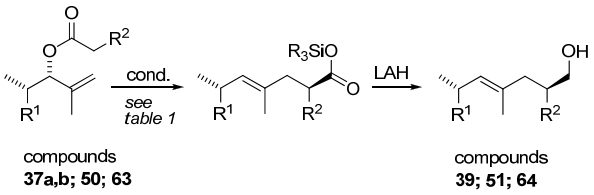
Completion of the total synthesis: With two succesful approaches for benzofuran intermediate **5** in hands, we focused on the crucial oxidative endgame (Scheme 19). Firstly, we reproduced Lee's endgame[6a] by starting with protection of the C7-OH to give the corresponding TES ether which was then oxidized with IBX to provide the unstable yet isolable *o*-quinone **69**. On treatment of **69** with aqueous HF, the silyl group was removed and 1,6 conjugate addition of water occurred to furnish the target molecule (**1**). In an alternative approach we tried to avoid the OTES protecting group. For this purpose we envisaged a biomimetic pathway, by first converting **5** into catechol **70**, followed by oxidation to quinone **71** and spontaneous addition of water. Unfortunately we could not remove the phenolic methyl ether even under a variety of conditions. Still convinced that it should be possible to work out a protecting group free endgame we tried the direct oxidation of **5** with different oxidants, for instance Fremy's salt ($(KSO_3)_2NO$), CAN, Ag_2O, PIDA, $NaIO_4$ and IBX. These experiments all failed, but finally we discovered that DDQ in CH_2Cl_2/H_2O cleanly oxidized **5** to *o*-quinone **71**, which was immediately hydrolyzed to kendomycin (**1**) on treatment with diluted hydrochloric acid.



Scheme 19. Oxidation of **5**. a) TESOTf, Et_3N, CH_2Cl_2, 0 °C, 82%; b) IBX, DMF, r.t., 24 h c) 0.1 M HF, MeCN, r.t., 30 % (2 steps); d) DDQ, CH_2Cl_2/H_2O =10:1, r.t., 52% e) aq. HCl (1%), MeCN, 50%.

Conclusion

In conclusion we have presented four synthetic approaches, two of which resulted in convergent total syntheses of kendomycin (**1**). For the stereoselective installation of the (*E*)-13,14-olefin we investigated the experimental conditions for three Ireland-Claisen reactions of unusual complexity, summarized in Scheme 20 and Table 1, respectively.



Scheme 20. Ireland-Claisen rearrangements.

Table 1. Reaction conditions for Ireland-Claisen rearrangements.

compound	Base (equiv.) /SiR_3X (equiv.)[a]	reaction conditions[b]	product	yield[c]	dr[d]
37a	**LDA (1.2) / TBSCl (1.1)**	**THF/HMPA, 2h**	**39**	**63 %**	**5:1**
37b	LDA (1.2) / TBSCl (1.1)	THF, 2h	39	traces	n.d.
50	LDA (1.25) / TBSCl (1.1)	THF/HMPA, 3h	51	20%	n.d.
50	LDA (1.25) / TBSOTf (1.1)	THF/HMPA, 15h	51	35%	5:1
50	LDA (3.0) / TMSCl (3.0)	THF/HMPA, 14h r.t	51	17%	n.d.
50	LDA (3.0) / TBSCl (10.0)	THF/HMPA/toluene[e], 1h	51	59%	1.1:1
50	LDA (3.2) / TBSCl (5.5)	THF, 2h	51	19%	4:1
50	LDA (5.0) / TBSCl (7.0)	THF/HMPA, 3h	51	46%	10:1
50	LHMDS (1.25) / TBSCl (1.2)	THF/HMPA, 3h[f]	51	traces	n.d.
50	LHMDS (4.0) / TBSCl (6.0)	THF/HMPA, 3h	51	64	1:1
50	**LHMDS (4.0) / TBSCl (6.0)**	**THF/HMPA, 3h[f]**	**51**	**84%**	**4:1**
63	LDA (1.25) / TBSCl (6.0)	THF/DMPU, 2h[f]	64	n.d.	n.d.
63	LDA (5.0) / TBSCl (5.5)	THF/DMPU, 2h	64	n.d.	n.d.
63	LHMDS (4.0) / TBSCl (6.0)	THF/HMPA, 3h[f]	64	47%	2:1
63	LHMDS (5.0) / TBSCl (6.0)	THF/HMPA, 4h[f]	64	63%	2:1
63	LHMDS (6.0) / TBSCl (7.0)	THF/HMPA, 2h[f]	64	58%	2:1
63	**LHMDS (4.0) / TBSCl (6.0)**	**THF/HMPA; DMF[f],[g]**	**64**	**89%**	**4:1**

[a] Enolization and silyl ketene acetal formation were performed at -78 °C. [b] The reactions were refluxed, unless otherwise stated. All rearrangement products were treated with $LiAlH_4$ after workup. [c] Yields were determined after reductive workup [d] The diastereomeric ratio (dr) was determined by ^{1}H-NMR. [e] Internal quench conditions. [f] The silyl-ketene acetal was isolated before rearrangement.[g] The starting material was added as a solution in THF/TBSCl. The rearrangement was performed under microwave irradiation at 180 °C.

For the formation of the tetrahydopyran ring a remarkably efficient S_N1 cyclization was used either before or after the macrocyclization. Regarding the crucial issue of ring closure, our work not only demonstrates the so far unrecognized capability of the photo-Fries ring contraction for the formation of macrocycles, but also reemphasizes the unparalleled potential of RCM for connecting monosubstituted olefin residues. Additionally a protecting group free endgame for converting **5** into **1** was developed, which saves another synthetic step.

Experimental Section

All solvents were distilled prior to use, except THF, which was purchased from Acros Organics (99.85%, H_2O < 50 ppm) and used without further purification. Et_2O, toluene and benzene were distilled from sodium. CH_2Cl_2 and $CHCl_3$ were passed through an Al_2O_3-$MgSO_4$ column or distilled over P_2O_5. Acetone was distilled over P_2O_5. DMF, DMSO, NEt_3, *i*Pr_2NH, *i*Pr_2NEt, TMEDA, HMPA and 2,6-lutidine were distilled from CaH_2. TBSCl was dissolved in hexane or THF (3 M), treated with Et_3N (3%) and transferred *via* a syringe filter to the reaction mixture. CpZrHCl was prepared according to the Negishi procedure[33]. Solvent degassing was achieved by repeated (at least 4 cycles) freeze-pump-thaw (FPT) cycles. All non-aqueous reactions were performed under an atmosphere of argon using oven-dried or flame-dried glassware and standard syringe/septa techniques. ^{1}H- and ^{13}C-NMR spectra were measured in $CDCl_3$ on a Bruker Avance DRX-400 or DRX-600 at 400.13 MHz (100.61 MHz) or 600.13 MHz (150.90 MHz), respectively. Chemical shifts are given in ppm and were referenced to residual $CHCl_3$ (^{1}H, δ = 7.26 ppm, ^{13}C, δ =77.00 ppm) or toluene (^{1}H, δ = 7.09, 7.00, 6.98 ppm, ^{13}C, δ =137.9, 129.2, 128.3, 125.5, 20.4 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in Hz, integration. Assignments of proton resonances were confirmed by correlated spectroscopy. IR spectra were recorded as thin films on a silicon plate on a Perkin-Elmer 1600 FT-IR spectrometer. Mass spectra were measured on a Micro mass, trio 200 Fisions Instruments. High-resolution mass spectra (HRMS) were performed with a Finnigan MAT 8230 with a resolution of 10000. Optical rotations were measured on a Perkin-Elmer 351 polarimeter at 20 °C (reported as follows: concentration (*c* in g/100mL), solvent). The reaction progress was monitored on precoated TLC plates (Merck Kieselgel 60 F254). Spots were visualized under UV light (254nm) and/or were stained with ceric ammonium molybdate (CAM), *p*-anisaldehyde or potassium permanganate stain. Column chromatography was performed with Merck silica gel 60 (230-400 mesh). Analytical HPLC was performed on a Jasco System (PU-980 pump, UV 975 and RI 930) using a Nucleosil 50 column (5 µm, Ø 4 mm x 241 mm) at ambient temperature. Preparative HPLC was performed on a Dynamix Model SD-1 equipped with a Model UV-1 absorbance detector using a Supershere (60 Å pore size, 4 µm particle size, Ø 25 mm x 250 mm) at ambient temperature. Yields refer to chromatographically purified compounds, unless otherwise stated.

***S*)-*tert*-Butyl(4-methylhex-5-enyloxy)diphenylsilane (47).** β-(-)-Citronellene (20.3 g, 147 mmol, 1.0 equiv.) and sodium acetate (12.6 g, 154 mmol, 1.05 equiv.) were dissolved in CH_2Cl_2 (490 mL) and cooled to -20 °C. *m*-CPBA (75 %, 35.4 g, 154 mmol, 1.05 equiv.) was added in small portions and stirring was continued for 1.5 h, allowing the suspension to warm to 0 °C. The reaction was quenched by careful addition of saturated aqueous $NaHCO_3$ (200 mL) and extracted with CH_2Cl_2 (3 x 70 mL). The combined organic fractions were washed with 1 N NaOH (100 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was dissolved in Et_2O (245 mL), cooled to 0 °C and H_5IO_6 (50 g, 220 mmol, 1.5 equiv.) in THF (220 mL) was added within 45 min. Stirring was continued until TLC analysis showed complete consumption of the starting material. The mixture was diluted with Et_2O (500 mL), H_2O (300 mL) was added and the phases were separated. The organic layer was washed twice with brine, dried over $MgSO_4$ and filtered. This solution was recooled to 0 °C and $LiAlH_4$ (4 M in Et_2O, 44 mL, 176 mmol, 1.2 equiv.) was added *via* a dropping funnel over 2 h. The solution was slowly quenched with ethylacetate (10 mL), 1 N $KHSO_4$ (200 mL) was carefully added and the aqueous layer was extracted with Et_2O (3 x 100 mL). The organic fraction was dried over $MgSO_4$, filtered and evaporated to dryness. Purification of the residue by flash chromatography (pentane : diethylether = 5 : 1) afforded the alcohol as a colorless oil (13.0 g, 77% over 3 steps). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 5.69 (ddd, J = 17.4, 10.2, 7.4 Hz, 1H), 4.99-4.90 (m, 1H), 3.63 (t, J = 6.3 Hz, 2 H), 2.20-2.07 (m, 1H), 1.62-1.51 (m, 2H), 1.40-1.32 (m, 2H), 1.31-1.25 (br, OH), 1.00 (d, J = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 144.4, 112.8, 63.1, 37.6, 32.6, 30.5, 20.2; IR (film): 3331, 3077, 2935, 1640, 1455, 1419, 1374, 1058 cm^{-1}; HRMS (ESI) (*m/z*): $[M-H_2O]^+$ calcd for C_7H_{12}, 96.0939, found, 96.0919; $[\alpha]_D^{20}$ +18.8 (*c* 1.25, CH_2Cl_2).

Above prepared alcohol (3.30 g, 28.8 mmol, 1.0 equiv.) in DMF (29 mL) was cooled to 0 °C and imidazole (3.92 g, 57.6 mmol, 2 equiv.) was added. After 5 min TBDPSCl (7.4

mL, 28.8 mmol, 1.0 equiv.) was transferred to the solution *via* cannula and stirring was continued for 1 h at ambient temperature. The reaction mixture was diluted with Et_2O (200 mL), quenched with NH_4Cl (100 mL) and the phases were separated. The aqueous layer was extracted with Et_2O (3 x 50 mL), the organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (hexane : ethylacetate = 10 : 1) afforded compound **47** as a colorless oil (9.10 g, 90%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.71-7.64 (m, 4H), 7.45-7.33 (m, 6H), 5.68 (ddd, J = 17.3, 10.1, 7.3 Hz, 1H), 4.96-4.88 (m, 1H), 3.65 (t, J = 6.6 Hz, 2 H), 2.16-2.04 (m, 1H), 1.62-1.52 (m, 2H), 1.39-1.32 (m, 2H), 1.05 (s, 9H), 0.98 (d, J = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 144.7, 135.6, 134.2, 129.5, 127.6, 112.5, 64.1, 37.4, 32.7, 30.2, 26.9, 20.2, 19.2; IR (film): 2932, 1639, 1589, 1473, 1427, 1389, 1361, 1112 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{19}H_{23}OSi$, 295.1518, found, 295.1522; $[\alpha]_D^{20}$ +6.7 (*c* 1.10, CH_2Cl_2).

(*S*)-*tert*-Butyl(4-(oxiran-2-yl)pentyloxy)diphenylsilane (44). Alkene **47** (5.91 g, 16.74 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (57 mL) and cooled to 0 °C. *m*-CPBA (75%, 9.3 g, 40.17 mmol, 2.4 equiv.) was added in small portions and stirring was continued for 3 h. The reaction was filtered over Celite, quenched by the careful addition of saturated aqueous $NaHCO_3$ (70 mL) and extracted with CH_2Cl_2 (3 x 70 mL). The combined organic fractions were dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the residue by flash chromatography (hexane : ethylacetate from 10 : 1 to 5 : 1) afforded epoxide **44** as a colorless oil (mixture of diastereomers) (5.91 g, 96%). ^{1}H-NMR (The asterisk denotes the minor diastereomer, 400MHz, $CDCl_3$): δ = 7.69-7.65 (m, 4H), 7.45-7.35 (m, 6H), 3.70-3.63 (m, 2H), 2.75-2.64 (m, 2H), 2.51-2.47(m, 1H), 2.47-2.44* (m, 1H), 1.72-1.55 (m, 2H), 1.52-1.40 (m, 1H), 1.40-1.19 (m, 2H), 1.06 (s, 9H), 1.02 (d, J = 6.6 Hz, 3H), 0.92* (d, J = 6.8, 3H); ^{13}C-NMR (The asterisk denotes the minor diastereomer, 100MHz, $CDCl_3$): δ = 135.6, 134.1*, 134.0, 129.6, 129.5*, 127.6, 64.1*, 64.0, 57.0, 56.9*, 46.9, 45.6*, 36.0, 35.8*, 30.7*, 30.1, 29.9*, 29.7, 26.9, 19.2, 17.1, 15.6*; IR (film): 3071, 3048, 2932, 1590, 1472, 1428, 1390, 1361, 1268, 1189, 1112 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{21}H_{25}O_2Si$, 311.1467, found, 311.1464.

(*S*)-6-(*tert*-Butyldiphenylsilyloxy)-1-(4-methoxy-2,5-bis(methoxymethoxy)-3-methylphenyl)-3-methylhexan-2-one (48). Bromide **45** (11.3 g, 35.18 mmol, 3 equiv.) was dissolved in THF (50 mL). Mg (855 mg, 35.18 mmol, 3 equiv.), a crump of iodine and 2 drops of dibromoethane were added and the mixture was heated to reflux until the Mg has been completely consumed (1.5 h). The reaction was allowed to cool to room temperature and transferred to a solution of CuI (223 mg, 1.17 mmol, 0.1 equiv.) in THF (12 mL) at -50 °C. The resulting grey suspension was stirred for 30 min at -30 °C and then cooled to -45 °C. Epoxide **44** (4.3 g, 11.7 mmol, 1 equiv.) in THF (23 mL) was added dropwise and the temperature was raised to 0 °C within 4 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (100 mL) and the phases were separated. The aqueous layer was extracted with Et_2O (4 x 50 mL), the combined organic phases were dried over $MgSO_4$, filtered and concentrated. Purification by flash chromatography (hexane : ethylacetate from 10 : 1 to 3:1) gave 6.2 g (87%) of a diastereomeric mixture of the alcohols.

Oxalylchloride (1.72 mL, 20.30 mmol, 2 equiv.) was dissolved in CH_2Cl_2 (50 mL), cooled to -78 °C and DMSO (2.88 mL, 40.60 mmol, 4 equiv.) was added dropwise. After 40 min, above alcohol (6.2 g, 10.15 mmol, 1 equiv.) in CH_2Cl_2 (20 mL) was added *via* syringe and stirring was continued for additional 45 min. DIPEA (10.6 mL, 60.90 mmol, 6 equiv.) was added and the solution was warmed to 0 °C. The reaction was hydrolyzed with saturated aqueous NH_4Cl (100 mL), extracted with CH_2Cl_2 (3 x 50 mL), washed with brine, dried over $MgSO_4$ and filtered. Purification by column chromatography (hexane : ethylacetate from 5 :1 to 3 : 1) afforded 5.8 g (95%) of ketone **48**. ^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.68-7.63 (m, 4H), 7.45-7.34 (m, 6H), 6.74 (s, 1H), 5.14 (s, 2H), 4.83 (s, 2H), 3.80 (s, 3H), 3.73 (d, J = 3.8 Hz, 2H), 3.63 (t, J = 6.2 Hz, 2H), 3.51 (s, 3H), 3.48 (s, 3H), 2.68-2.58 (m, 1H), 2.20 (s, 3H), 1.80-1.70 (m, 1H), 1.56-1.47 (m, 2H), 1.48-1.39 (m, 1H), 1.09 (d, J = 6.8 Hz, 3H), 1.04 (s, 9H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 211.8, 150.0, 148.0, 146.9, 135.5, 134.0, 129.5, 127.6, 125.8, 123.5, 116.2, 99.7, 95.5, 63.7, 60.4, 57.4, 56.2, 45.0, 43.3, 30.1, 29.1, 26.8, 19.2, 16.5, 10.4; IR (film): 2933, 1710, 1559, 1481, 1237, 1155, 1112, 967 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{35}H_{48}O_7Si$, 608.3169, found, 608.3186; $[\alpha]_D^{20}$ +9.1 (*c* 0.95, CH_2Cl_2).

(*S*)-*tert*-Butyl(4-(6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)pentyloxy)diphenylsilane (49). Ketone **48** (15.8 g, 25.95 mmol, 1.0 equiv.) and 15.8 g of molecular sieves (4Å) in 500 mL of toluene : EtOH = 4 : 1 were heated to 80 °C. After the addition of TfOH (689 µl, 7.79 mmol, 0.3 equiv.) stirring was continued at 80 °C for 5 min and then the mixture was rapidly cooled to 0°C. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (300 mL), filtered over Celite and the mixture was extracted with Et_2O (3 x 100 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was removed *in vacuo* affording crude furan (13 g, 100%), which was used without further purification in the next step. A small sample was purified by column chromatography (hexane : ethylacetate from 5 : 1 to 3 : 1) to obtain an analytically pure sample. ^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.70-7.65 (m, 4H), 7.45-7.33 (m, 6H), 6.90 (s, 1H), 6.23 (d, J = 0.5 Hz, 1H), 5.52 (s, 1H), 3.84 (s, 3H), 3.69 (t, J = 6.3 Hz, 2H), 2.96-2.86 (m, 1H), 2.45 (s, 3H), 1.93-1.82 (m, 1H), 1.74-1.63 (m, 1H), 1.67-1.57 (m, 2H), 1.31 (d, J = 6.8 Hz, 3H), 1.07 (s, 9H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 164.0, 147.9, 145.1, 142.4, 135.6, 134.0, 129.5, 127.6, 124.1, 113.8, 102.0, 100.7, 63.8, 61.4, 33.3, 31.6, 30.0, 26.9, 19.2, 19.1, 9.3; IR (film): 3529, 2933, 2858, 1607, 1459, 1427, 1360, 1111, 864 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{31}H_{38}O_4Si$, 502.2539, found, 502.2537; $[\alpha]_D^{20}$ +12.1 (*c* 2.45, CH_2Cl_2).

Crude furan (13 g, 25.95 mmol, 1.0 equiv.) in DMF (130 mL) was cooled to 0 °C. Then NaH (1.5 g, 38.85 mmol, 1.5 equiv.) was added in small portions, followed by the careful addition of neat MOMCl (2.75 mL, 36.26 mmol, 1.4 equiv.). The dark-brown solution was stirred for 1 h, diluted with Et_2O (200 mL) and quenched with saturated aqueous NH_4Cl (150 mL). The product was extracted with Et_2O : hexane = 1 : 1 (3 x 50 mL), washed with brine and dried over anhydrous $MgSO_4$. The solvent was evaporated and the pale yellow oil was purified by column chromatography (hexane : ethylacetate = 3 : 1) to furnish furan **49** (13.4 g, 95%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.68-7.62 (m, 4H), 7.44-7.31 (m, 6H), 7.07 (s, 1H), 6.22 (s, 1H), 5.21 (s, 2H), 3.84 (s, 3H), 3.67 (t, J = 6.2 Hz, 2H), 3.55 (s, 3H), 2.93-2.86 (m, 1H), 2.40 (s, 3H), 1.90-1.80 (m, 1H), 1.71-1.59 (m, 1H), 1.63-1.54 (m, 2H), 1.29 (d, J = 7.1 Hz, 3H), 1.04 (s, 9H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 164.0, 149.2, 146.9, 145.5, 135.5, 134.0, 129.5, 127.6, 123.4, 115.3, 105.0, 100.8, 96.2, 63.8, 61.0, 56.1, 33.3, 31.6, 30.0, 26.8, 19.2, 19.1, 9.1; IR (film): 2932, 1684, 1653, 1559, 1473, 1427, 1260, 1153, 1112, 1044 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{33}H_{42}O_5Si$, 546.2802, found, 546.2792; $[\alpha]_D^{20}$ +12.6 (*c* 1.40, CH_2Cl_2).

(*S*)-4-(6-Methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)pentanoic acid (43). A solution of benzofuran **49** (7.63 g, 13.93 mmol, 1.0 equiv.) in THF (280 mL) was treated with TBAF (1 M in THF, 15.33 mL, 15.33 mmol, 1.1 equiv.) and stirred overnight at room temperature. Finally the reaction was quenched with NH_4Cl (150 mL) and the aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated to dryness. Purification by column chromatography using gradient elution (hexane : ethylacetate from 3: 1 to 1 : 1) furnished the alcohol as a pale yellow oil (3.84 g, 89%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.07 (s, 1H), 6.27 (s, 1H), 5.21 (s, 2H), 3.84 (s, 3H), 3.64 (t, J = 6.3 Hz, 2H), 3.54 (s, 3H), 2.99-2.89 (m, 1H), 2.42 (s, 3H), 1.88-1.77 (m, 1H), 1.73-1.63 (m, 1H), 1.65-1.54 (m, 2H), 1.32 (d, J = 7.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 163.7, 149.2, 146.9, 145.6, 123.4, 115.3, 105.0, 101.0, 96.2, 62.9, 61.0, 56.1, 33.5, 31.6, 30.3, 19.1, 9.1; IR (film): 3854, 3676, 2935, 1653, 1559, 1457, 1153, 1043 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{17}H_{24}O_5$, 308.1624, found, 308.1620; $[\alpha]_D^{20}$ +13.4 (*c* 1.60, CH_2Cl_2).

A 100 mL Schlenk flask was charged with above alcohol (3.57 g, 11.58 mmol, 1.0 equiv.) and DMSO (60 mL, 0.2 M). IBX (8.1 g, 28.94 mmol, 2.5 equiv.) was added over a period of 20 min and stirring was continued for 2 h at ambient temperature. The solution was diluted with Et_2O : hexane = 1 : 1 (100 mL) and H_2O (100 mL). The mixture was filtered over Celite, the layers were separated and the aqueous layer was extracted with Et_2O : hexane = 1 : 1 (3 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was filtered over a plug of silica to give pure aldehyde as a pale orange oil (3.43 g, 97%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 9.74 (t, J = 1.4 Hz, 1H), 7.08 (s, 1H), 6.28 (s, 1H), 5.21 (s, 2H), 3.84 (s, 3H), 3.54 (s, 3H), 3.03-2.93 (m, 1H), 2.47 (dt, J = 7.5, 1.4 Hz, 2H), 2.41 (s, 3H), 2.10-1.93 (m, 2H), 1.34 (d, J = 7.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 202.0, 162.3, 149.3, 147.1, 145.8, 123.2, 115.4, 105.1, 101.6, 96.1, 61.0, 56.1, 41.6, 33.0, 27.7, 19.0, 9.1; IR (film): 2932, 1723, 1653, 1559, 1457, 1340, 1219, 1153, 1119, 1090, 1042 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{17}H_{22}O_5$, 306.1467, found, 306.1464; $[\alpha]_D^{20}$ +17.2 (*c* 0.75, CH_2Cl_2).

Above aldehyde (3.43 g, 11.19 mmol, 1.0 equiv.) was dissolved in 75 mL *t*-BuOH (0.15 M), treated with 2-methyl-2-butene (1 mL / mmol, 11.2 mL), and cooled to 5 °C. $NaClO_2$ (18.9 g, 167.85 mmol, 15 equiv.) and 18.9 g NaH_2PO_4 were dissolved in H_2O (110 mL, 1.5 M), transferred to a 250 mL dropping funnel, and added over a period of 20 min. After 50 min at r.t. TLC analysis showed complete consumption and the reaction mixture was partitioned between CH_2Cl_2 (150 mL) and brine (100 mL). The aqueous layer was extracted with three portions of CH_2Cl_2 (50 mL) and the combined organic extracts were dried over $MgSO_4$. Evaporation of the solvent gave crude acid, which was purified by flash chromatography (hexane : ethylacetate from 3 : 1 to 1 : 1) to give acid **43** as an orange-viscous oil (3.60 g, 99%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.08 (s, 1H), 6.29 (s, 1H), 5.21 (s, 2H), 3.85 (s, 3H), 3.54 (s, 3H), 3.04-2.94 (m, 1H), 2.42-2.35 (m, 2H), 2.41 (s, 3H), 2.12-1.92 (m, 2H), 1.34 (d, J = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 177.7, 162.4, 149.3, 147.0, 145.7, 123.2, 115.4, 105.1, 101.6, 96.2, 61.0, 56.1, 33.0, 31.4, 30.2, 19.0, 9.1; IR (film): 3629, 2933, 1707, 1653, 1607, 1559, 1457, 1420, 1261, 1153, 1117, 1043 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{17}H_{22}O_6$, 322.1416, found, 322.1421; $[\alpha]_D^{20}$ +35.5 (*c* 0.65, CH_2Cl_2).

(*S*)-((3*S*,4*S*)-2,4-Dimethylhexa-1,5-dien-3-yl) 4-(6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)pentanoate (50). A mixture of acid **43** (2.55 g, 7.91 mmol, 1.0 equiv.), alcohol **42** (1.20 g, 9.51 mmol, 1.2 equiv.), EDCI·HCl (1.97 g, 10.28 mmol, 1.3 equiv.) and DMAP (1.26 g, 10.31 mmol, 1.3 equiv.) in CH_2Cl_2 (30 mL) was stirred at room temperature for 1.5 h. The reaction was diluted with CH_2Cl_2 (100 mL), quenched with 1% HCl (20 mL) and washed with brine (2 x 50 mL). The organic layer was dried over $MgSO_4$, concentrated *in vacuo* and the residue was purified by flash chromatography (hexane : ethylacetate from 15 :1 to 5 :1) to give ester **50** (2.75 g, 81%).

^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.07 (s, 1H), 6.27 (s, 1H), 5.70 (ddd, *J* = 17.2, 10.2, 8.0 Hz, 1H), 5.21 (s, 2H), 5.06-4.98 (m, 2H), 5.05 (d, *J* = 7.8 Hz, 1H), 4.96-4.91 (m, 2H), 3.84 (s, 3H), 3.54 (s, 3H), 3.02-2.91 (m, 1H), 2.52-2.43 (m, 1H), 2.41 (s, 3H), 2.36-2.30 (m, 2H), 2.10-1.99 (m, 1H), 1.99-1.89 (m, 1H), 1.72 (s, 3H), 1.32 (d, *J* = 7.1 Hz, 3H), 0.96 (d, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 172.5, 162.7, 149.3, 147.0, 145.7, 141.8, 139.8, 123.3, 115.2, 114.4, 113.4, 105.1, 101.4, 96.2, 80.3, 61.0, 56.1, 40.0, 33.0, 32.1, 30.5, 18.9, 18.2, 16.6, 9.1; IR (film): 2967, 1734, 1700, 1684, 1653, 1559, 1457, 1152, 1117 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{25}H_{34}O_6Na$, 453.2253, found, 453.2269; $[\alpha]_D^{20}$ +26.8 (*c* 1.30, CH_2Cl_2).

(2*S*,6*S*,*E*)-2-((*S*)-2-(6-Methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)propyl)-4,6-dimethylocta-4,7-dien-1-ol (51). LHMDS (1 M in THF, 11.1 mL, 12.08 mmol, 4 equiv.) was diluted with THF (12 mL), cooled to -78 °C and freshly distilled HMPA (7.5 mL) was slowly added *via* cannula. After 5 min ester **50** (2.3 g, 3.28 mmol, 1.0 equiv.) in THF (2.1 mL, 0.5 mL rinse) was transferred to a freshly prepared TBSCl-solution (3 M in THF, 6.56 mL, 19.68 mmol, 6 equiv.) and added dropwise to the above LHMDS / HMPA mixture. The reaction mixture was stirred for 40 min at -78 °C, allowed to warm to 0 °C over 15 min, stirred for additional 5 min at room temperature and partitioned between H_2O (100 mL) and Et_2O (3 x 70 mL). The combined organic fractions were washed with brine, dried over $MgSO_4$ and evaporated to dryness. The crude ketene silyl acetal was dissolved in DMF (12 mL) and heated under microwave irradiation at 180 °C for 15 min. The mixture was partitioned between H_2O (100 mL) and Et_2O (100 mL), extracted with Et_2O (3 x 50 mL), washed with brine (50 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude ester was dissolved in Et_2O (30 mL), transferred to an ice-bath and $LiAlH_4$ (4 M in Et_2O, 1.51 mL, 6.04 mmol, 2 equiv.) was added carefully *via* cannula. After 30 min at room temperature TLC analysis showed complete consumption of the starting material and the reaction mixture was quenched at 0 °C by slow addition of ethylacetate, diluted with Et_2O (100 mL) and washed with 1% HCl (100 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL), and the combined organic fractions were washed with brine (50 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by column chromatography (hexane : ethylacetate from 10 : 1 to 5 : 1) afforded alcohol **51** as a colorless oil (1.11 g, 89%, dr = 4 : 1 as determined by ^{1}H-NMR). *S*-**51:** ^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.07 (s, 1H), 6.28 (s, 1H), 5.74 (ddd, *J* = 17.1, 10.5, 6.4 Hz, 1H), 5.21 (s, 2H), 5.05 (d, *J* = 8.8 Hz, 1H), 4.95 (dt, *J* = 17.2, 1.6 Hz, 1H), 4.89 (dt, *J* = 10.2, 1.5 Hz, 1H), 3.84 (s, 3H), 3.54 (s, 3H), 3.49 (d, *J* = 5.1 Hz, 2H), 3.12-2.97 (m, 2H), 2.41 (s, 3H), 2.13-1.99 (m, 2H), 1.88-1.78 (m, 1H), 1.78-1.69 (m, 1H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.49-1.41 (m, 1H), 1.42-1.36 (br, OH), 1.31 (d, *J* = 7.1 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 163.9, 149.2, 146.9, 145.6, 142.9, 133.3, 130.7, 123.4, 115.3, 112.0, 105.0, 100.9, 96.2, 66.1, 61.0, 56.1, 42.8, 37.7, 36.4, 36.2, 31.5, 20.5, 20.1, 16.2, 9.1; IR (film): 3451, 2927, 1559, 1449, 1340, 1219, 1154, 1116, 1091, 1044 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{25}H_{36}O_5$, 416.2563, found, 416.2569; $[\alpha]_D^{20}$ +9.5 (*c* 1.95, CH_2Cl_2). *R*-**51:** ^{1}H-NMR (400MHz, $CDCl_3$): δ δ = 7.07 (s, 1H), 6.26 (s, 1H), 5.75 (ddd, *J* = 17.0, 10.4, 6.4 Hz, 1H), 5.21 (s, 2H), 5.04 (dd, *J* = 8.8, 1.0 Hz, 1H), 4.98 (dt, *J* = 17.2, 1.6 Hz, 1H), 4.91 (dt, *J* = 10.1, 1.5 Hz, 1H), 3.84 (s, 3H), 3.57-3.52 (m, 2H), 3.54 (s, 3H), 3.11-3.00 (m, 2H), 2.41 (s, 3H), 2.05 (dd, *J* = 14.4, 6.8 Hz, 2H), 1.97 (dd, *J* =13.5, 6.4, 1H), 1.79-1.69 (m, 2H), 1.62-1.51 (m, 1H), 1.55 (d, *J* = 1.3 Hz, 3H), 1.30 (d, *J* = 6.8 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 163.8, 149.2, 147.0, 145.6, 142.9, 133.2, 130.7, 123.4, 115.3, 112.0, 105.0, 101.0, 96.2, 65.7, 61.0, 56.1, 42.7, 36.9, 36.3, 36.0, 31.4, 20.6, 20.3, 16.1, 9.1; IR (film): 3451, 2928, 1606, 1451, 1340, 1219, 1154, 1117, 1090, 1044 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{25}H_{36}O_5$, 416.2563, found, 416.2565; $[\alpha]_D^{20}$ -18.4 (*c* 1.10, CH_2Cl_2).

6-Methoxy-5-(methoxymethoxy)-7-methyl-2-((2*S*,4*S*,8*S*,*E*)-4,6,8-trimethyldeca-6,9-dien-2-yl)benzofuran (52). Alcohol **51** (370 mg, 0.89 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (5 mL), cooled to 0 °C and treated with Et_3N (150 µL, 1.06 mmol, 1.2 equiv.). After 5 min MsCl (80 µl, 1.06 mmol, 1.2 equiv.) was added and stirring was continued for 30 min. The solution was poured onto H_2O (20 mL), extracted with CH_2Cl_2 (3 x 10 mL), washed with brine and dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the crude mesylate was immediately redissolved in Et_2O (9 mL). $LiAlH_4$ (4 M in Et_2O, 670 µL, 2.67 mmol, 3 equiv.) was carefully added to the ice cooled solution and the cloudy mixture was allowed to warm to room temperature over 30 min. After 2 h the reaction mixture was quenched at 0 °C by slow addition of ethylacetate, diluted with Et_2O (40 mL) and washed with 1% HCl (10 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL), and the combined organic fractions were washed with brine (10 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by flash chromatography (hexane : ethylacetate = 5 : 1) afforded diolefin **52** as a an oil (310 mg, 89%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.07 (s, 1H), 6.24 (s, 1H), 5.76 (ddd, *J* = 17.2, 10.4, 6.1 Hz, 1H), 5.21 (s, 2H), 4.99-4.94, m 1H), 4.96 (dt, *J* = 17.3, 1.7 Hz, 1H), 4.88 (dt, *J* = 10.4, 1.6 Hz, 1H), 3.84 (s, 3H), 3.54 (s, 3H), 3.11-2.95 (m, 2H), 2.42 (s, 3H), 2.07 (dd, *J* = 13.3, 5.2 Hz, 1H), 1.79 (dd, *J* = 12.6, 8.1 Hz, 1H), 1.74-1.64 (m, 1H), 1.59-1.44 (m, 2H), 1.57 (d, *J* = 1.3 Hz, 3H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 164.7, 149.1, 146.8, 145.8, 142.9, 133.3, 130.1, 123.5, 115.3, 111.7, 105.0, 100.4, 96.2, 61.0, 56.1, 48.0, 43.0, 36.3, 31.3, 28.3, 20.6, 19.5, 19.1, 16.1, 9.1; IR (film): 2926, 1684, 1653, 1559, 1507, 1458, 1153, 1117, 1044 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{25}H_{36}O_4$, 400.2614, found, 400.2607; $[\alpha]_D^{20}$ +3.0 (*c* 1.35, CH_2Cl_2).

2*R*,4*S*,5*R*)-1-((*R*)-4-Benzyl-2-oxooxazolidin-3-yl)-5-hydroxy-2,4-dimethylhept-6-ene-1,3-dione (53). A 250 mL Schlenk flask was charged with acid-free $Sn(OTf)_2$ (5.3 g, 12.71 mmol, 1.1 equiv.) and CH_2Cl_2 (42 mL, 0.3 M). The white suspension was treated at -20 °C with Et_3N (1.76 mL, 12.71 mmol, 1.1 equiv.) whereupon the mixture turned pale yellow. After 5 min β-keto imide **26** (3.34 g, 11.54 mmol, 1.0 equiv.) in CH_2Cl_2 (19 mL, 0.6 M) was added dropwise and the clear solution was stirred for 1 h at -20°C. Freshly distilled acrolein (2.31 mL, 34.62 mmol, 3 equiv.) was dissolved in CH_2Cl_2 (35 mL, 1 M) and slowly added at -78 °C. After 30 min at -78 °C, the yellow-orange solution was poured onto a cooled (0 °C) and vigorously stirred mixture of CH_2Cl_2 : 1 M $NaHSO_4$ (150 mL, 1 : 1). After 20 min at room temperature the aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL), the organic phase was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and concentrated. Purification of the residue by gradient flash chromatography (hexane : ethylacetate from 3 : 1 to 1 : 1) yielded **53** as a viscous oil (3.64 g, 91%, dr = 5 : 1 as determined by HPLC and ^{1}H-NMR). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 7.37-7.27 (m, 3H), 7.23-7.17 (m, 2H), 5.82 (ddd, *J* = 16.9, 10.7, 5.9 Hz, 1H), 5.31 (d, *J* = 17.2 Hz, 1H), 5.20 (d, *J* = 10.6 Hz, 1H), 4.87 (q, *J* = 7.2 Hz, 1H), 4.80-4.72 (m, 1H), 4.49-4.43 (br, 1H), 4.30-4.24 (m, 1H), 4.19 (dd, *J* = 9.1, 3.0 Hz, 1H), 3.30 (dd, *J* = 13.5, 3.2 Hz, 1H), 2.93-2.84 (m, 1H), 2.78 (dd, *J* =13.5, 9.6 Hz, 1H), 2.46(d, *J* = 3.3 Hz, OH), 1.48 (d, *J* = 7.3 Hz, 3H), 1.24 (d, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 210.8, 170.4, 153.3, 137.5, 135.0, 129.3, 129.0, 127.4, 116.3, 72.7, 66.5, 55.3, 52.0, 48.9, 38.0, 12.8, 10.9; IR (film): 3629, 3510, 2984, 1773, 1684, 1653, 1559, 1456, 1362, 1214, 1121 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{19}H_{23}O_5NNa$, 368.1473, found, 368.1477; $[\alpha]_D^{20}$ -115.3 (*c* 1.6, CH_2Cl_2).

(3*R*,4*S*,5*R*,6*R*)-4-Hydroxy-3,5-dimethyl-6-vinyltetrahydro-2*H*-pyran-2-one (54). $Me_4NBH(OAc)_3$ (2.85 g, 10.85 mmol, 5 equiv.) was dissolved in 360 mL MeCN : AcOH = 1.9 : 1, cooled to -32 °C and aldol product **53** (750 mg, 2.17 mmol, 1.0 equiv.) in MeCN (6 mL) was added dropwise. The reaction was stirred for 3 h at -32 °C, allowed to warm to 0 °C overnight, diluted with CH_2Cl_2 (100 mL) and quenched by the addition of saturated aqueous Rochelle's salt (150 mL). Saturated aqueous $NaHCO_3$ was carefully added to the vigorously stirred solution over 20 min. After 1 h no more gas evolution was observed and the two-phase mixture was partitioned between CH_2Cl_2 (400 mL) and H_2O (100 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL), and the combined organic fractions were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (hexane : ethylacetate = 3 : 1) afforded the diol as a viscous oil (527 mg, 70%, dr ≥ 6 : 1 as determined by ^{1}H-NMR). ^{1}H-NMR (600MHz, $CDCl_3$): δ = 7.36-7.31 (m, 2H), 7.30-7.27 (m, 1H), 7.22-7.18 (m, 2H), 5.97 (ddd, *J* = 16.9, 10.9, 5.8 Hz, 1H), 5.32 (d, *J* = 17.4 Hz, 1H), 5.21 (d, *J* = 10.6 Hz, 1H), 4.73-4.68 (m, 1H), 4.34-4.30 (br, 1H), 4.27-4.22 (m, 1H), 4.20 (dd, *J* = 8.7, 2.6 Hz, 1H), 3.98 (d, *J* = 9.8 Hz, 1H), 3.84 (dq, *J* =7.1, 1.9 Hz, 1H), 3.80-3.76 (br, OH), 3.41-3.34 (br, OH), 3.24 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.80 (dd, *J* =13.5, 9.3 Hz, 1H), 2.03-1.96 (m, 1H), 1.28 (d, *J* = 7.2 Hz, 3H), 0.84 (d, *J* = 7.2 Hz, 3H); ^{13}C-NMR (150MHz, $CDCl_3$): δ = 178.0, 152.8, 137.9, 134.9, 129.4, 129.0, 127.5, 115.7, 75.7, 73.4, 66.2, 55.0, 39.3, 39.2, 37.8, 12.1, 9.7; IR (film): 3448, 2976, 1780, 1700, 1559, 1456, 1388, 1211 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{19}H_{25}O_5NNa$, 370.1630, found, 370.1644; $[\alpha]_D^{20}$ -30.5 (*c* 0.80, CH_2Cl_2).

A solution of the diol (1.98 g, 5.71 mmol, 1.0 equiv.) in THF-H_2O (80 mL, 3 : 1) was treated at 0°C with H_2O_2 (30% in H_2O, 2.3 mL). LiOH (383 mg, 9,14 mmol, 1.6 equiv.) was added and stirring was continued for 1 h at ambient temperature. The reaction was acidified by the addition of 1 N HCl (20 mL) and stirred for further 5 min. The biphasic mixture was diluted with H_2O (100 mL), extracted with Et_2O (3 x 70 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (hexane : ethylacetate from 3 : 1 to 1 : 1) gave lactone **54** (700 mg, 72%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 5.85 (ddd, *J* = 17.2, 11.0, 5.7 Hz, 1H), 5.40 (d, *J* = 17.2 Hz, 1H), 5.3 (d, *J* = 10.6 Hz, 1H), 4.80-4.74 (m, 1H), 3.88 (dd, *J* = 9.6, 4.0 Hz, 1H), 2.57-2.48 (m, 1H), 2.27-2.19 (m, 1H), 2.09-2.01 (br, OH), 1.41 (d, *J* = 7.1 Hz, 3H), 0.97 (d, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 173.2, 133.6, 117.4, 79.9, 73.7, 60.4, 40.1, 37.9, 21.0, 14.4, 14.2, 5.5; IR (film): 3446, 2977, 1718, 1700, 1653, 1559, 1507, 1458, 1213, 1094 cm^{-1}; HRMS (ESI) (*m/z*): [M-H_2O]$^+$ calcd for $C_9H_{12}O_2$, 152.0837, found, 152.0844; $[\alpha]_D^{20}$+103.8 (*c* 0.60, CH_2Cl_2).

(*R*)-Methyl 2-((4*S*,5*S*,6*R*)-2,2,5-trimethyl-6-vinyl-1,3-dioxan-4-yl)propanoate (55). Lactone **54** (700 mg, 4.11 mmol, 1.0 equiv.) was dissolved in 2,2-dimethoxypropane (40 mL), treated with camphorsulfonic acid (96 mg, 0.41 mmol, 0.1 equiv.) and stirred overnight at room temperature. The solution was diluted with Et_2O (100 mL), neutralized with saturated aqueous $NaHCO_3$ (50 mL), extracted with Et_2O (3 x 50 mL), washed with brine (70 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by flash chromatography (hexane : ethylacetate = 10 : 1) to yield ester **55** (903 mg, 91%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 5.79 (ddd, *J* = 17.1, 10.7, 6.1 Hz, 1H), 5.25 (dt, *J* = 17.3, 1.7 Hz, 1H), 5.16 (dt, *J* = 10.5, 1.6 Hz, 1H), 4.39-4.35 (m, 1H), 3.71-3.66 (m, 1H), 3.69 (s, 3H), 2.59 (dq, *J* = 6.99, 4.99 Hz, 1H), 2.00-1.90 (m, 1H), 1.34 (s, 3H), 1.33 (s, 3H), 1.21 (d, *J* = 7.1 Hz, 3H), 0.83 (d, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 174.8, 134.7, 115.7, 100.7, 75.1, 70.8, 51.7, 42.9, 37.4, 25.2, 23.7, 12.8, 11.4; IR (film): 2988, 1740, 1700, 1653, 1559, 1458, 1301, 1226, 1176, 1025, 1001 cm^{-1}; HRMS (ESI) (*m/z*): [M-Me]$^+$ calcd for $C_{12}H_{19}O_4$, 227.1283, found, 227.1289; $[\alpha]_D^{20}$ -20.3 (*c* 1.05, CH_2Cl_2).

(*R*)-2-((4*S*,5*S*,6*R*)-2,2,5-Trimethyl-6-vinyl-1,3-dioxan-4-yl)propanal (46). Ester **55** (900 mg, 3.71 mmol, 1.0 equiv.) in Et_2O (40 mL) was cooled to 0 °C and $LiAlH_4$ (4 M in Et_2O, 1.49 mL, 5.57 mmol, 1.5 equiv.) was carefully added *via* cannula. After 30 min at 0 °C TLC analysis showed complete consumption of the starting material and the reaction mixture was quenched by slow addition of ethylacetate, diluted with Et_2O (80 mL) and washed with 1% HCl (100 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL), and the combined organic fractions were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (hexane : ethylacetate = 3 : 1) afforded the alcohol as a colorless oil (761 mg, 96%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 5.80 (ddd, *J* = 17.1, 10.1, 6.2 Hz, 1H), 5.26(dt, *J* = 17.3, 1.6 Hz, 1H), 5.16 (dt, *J* = 10.8, 1.6 Hz, 1H), 4.39-4.34 (m, 1H), 3.70-3.65 (m, 2H), 3.57 (dd, *J* = 8.1, 2.7 Hz, 1H), 2.36 (t, *J* = 5.4 Hz, OH), 2.01-1.92 (m, 1H), 1.90-1.81 (m, 1H), 1.38 (s, 3H), 1.35 (s, 3H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 135.7, 115.7, 100.6, 76.8, 71.1, 67.1, 37.2, 36.5, 25.4, 23.8, 13.0, 10.6; IR (film): 3423, 2987, 1684, 1653, 1559, 1507, 1457, 1380, 1226, 1180, 1027 cm^{-1}; HRMS (ESI) (*m/z*): [M-Me]$^+$ calcd for $C_{11}H_{19}O_3$, 199.1334, found, 199.1332; $[\alpha]_D^{20}$ +11.8 (*c* 0.80, CH_2Cl_2).

A solution of the above prepared alcohol (23 mg, 0.107 mmol, 1.0 equiv.) in CH_2Cl_2 (0.5 mL, 0.2 M) was cooled to -5 °C. Et_3N (45 µL, 0.321 mmol, 3 equiv.) and subsequently SO_3·Pyr (51 mg, 0.321 mmol, 3 equiv.) in DMSO (0.5 mL, 0.6 M) were added dropwise. The mixture was stirred for 1.5 h at -5 °C and quenched with aqueous 1 M $KHSO_4$ solution (0.5 mL). The phases were partitioned between brine and Et_2O (1 : 1, 40 mL) and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic fractions were concentrated to 5 mL under reduced pressure, filtered over a plug of silica and excess solvent was removed *in vacuo* to afford aldehyde **46** (23 mg, 99%). ^{1}H-NMR (400MHz, $CDCl_3$): δ = 9.71 (d, *J* = 1.0 Hz, 1H), 5.80 (ddd, *J* = 17.1, 10.7, 6.2 Hz, 1H), 5.27(dt, *J* = 17.3, 1.7 Hz, 1H), 5.18 (dt, *J* = 10.6, 1.6 Hz, 1H), 4.40-4.35 (m, 1H), 3.84 (dd, *J* = 8.1, 3.3 Hz, 1H), 2.44 (ddq, *J* = 7.0, 3.2, 0.9 Hz, 1H), 2.04-1.94 (m, 1H), 1.36 (s, 3H), 1.33 (s, 3H), 1.17 (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 204.2, 135.4, 115.9, 100.8, 73.2, 70.9, 48.6, 36.7, 25.1, 23.8, 12.7, 7.8; IR (film): 2986, 1734, 1684, 1653, 1559, 1507, 1458, 1380, 1225 cm^{-1}; HRMS (ESI) (*m/z*): [M-Me]$^+$ calcd for $C_{11}H_{17}O_3$, 197.1178, found, 197.1171; $[\alpha]_D^{20}$ -39.0 (*c* 0.70, CH_2Cl_2).

(*S*)-1-(6-Methoxy-5-(methoxymethoxy)-7-methyl-2-((2*S*,4*S*,8*S*,*E*)-4,6,8-trimethyldeca-6,9-dien-2-yl)benzofuran-4-yl)-2-((4*R*,5*S*,6*R*)-2,2,5-trimethyl-6-vinyl-1,3-dioxan-4-yl)propan-1-ol (9a,b). To a solution of benzofuran **52** (100 mg, 0.250 mmol, 1.4 equiv.) in THF (0.6 mL) freshly distilled TMEDA (80 µL, 0.535 mmol, 3 equiv.) was added at ambient temperature. The solution was cooled to –78 °C and *n*-BuLi (156 µL, 0.250 mmol, 1.4 equiv.) was added dropwise. After 1.5 h at –30 °C the orange solution was recooled to –78°C and aldehyde **46** (38 mg, 0.178 mmol, 1.0 equiv.) in THF (0.5 mL) was added *via* cannula. The reaction mixture was warmed to –25 °C over 2 h, diluted with Et_2O (40 mL) and finally quenched with saturated aqueous NH_4Cl solution (10 mL). The reaction mixture was extracted with diethyl ether (3 x 10 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. The residue was purified by column chromatography (hexane : ethylacetate from 20 : 1 to 5 : 1) to furnish 97 mg (90%, dr = 4 : 1 as determined by ^{1}H-NMR) of alcohols **9a** and **9b**. Separation of the diastereomers for analytical purpose was done by HPLC, yielding diastereomer **9a** and **9b** as light orange, viscous oils. **9a:** ^{1}H-NMR (600MHz, $CDCl_3$): δ = 6.63 (s, 1H), 5.79-5.72 (m, 2H), 5.21 (dt, *J* = 17.0, 1.7 Hz, 1H), 5.17 (dd, *J* = 6.0, 4.9 Hz, 1H), 5.13 (dt, *J* = 10.6, 1.7 Hz, 1H), 5.10 (d, *J* = 5.7 Hz, 1H), 5.09 (d, *J* = 5.7 Hz, 1H), 4.98-4.95 (m, 1H), 4.95 (dt, *J* = 17.4, 1.7 Hz, 1H), 4.88 (dt, *J* = 10.2, 1.5 Hz, 1H), 4.33 (t, *J* = 5.7 Hz, 1H), 3.77 (s, 3H), 3.56 (s, 3H), 3.44 (d, *J* = 4.5 Hz, OH), 3.32 (d, *J* = 8.5, 1.3 Hz, 1H), 3.09-3.03 (m, 1H), 3.03-2.96 (m, 1H), 2.39 (s, 3H), 2.35-2.29 (m, 1H), 2.09 (dd, *J* = 12.8, 5.7 Hz, 1H), 1.98-1.91 (m, 1H), 1.78 (dd, *J* = 13.2, 7.9 Hz, 1H), 1.72-1.65 (m, 1H), 1.61-1.54 (m, 1H), 1.58 (d, *J* = 1.1 Hz, 3H), 1.50-1.44 (m, 1H), 1.33 (s, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H), 1.11 (s, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H), 0.72 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (150MHz, $CDCl_3$): δ = 164.0, 150.1, 147.0, 144.0, 143.3, 135.8, 133.3, 130.1, 125.1, 123.0, 115.5, 114.2, 111.7, 101.3, 100.5, 99.9, 76.8, 74.2, 71.7, 60.6, 57.4, 47.9, 43.0, 40.7, 37.1, 36.3, 31.2, 28.3, 25.3, 23.7, 20.6, 19.5, 19.1, 16.0, 12.4, 9.1, 8.8; IR (film): 3497, 2965, 2930, 1844, 1636, 1458, 1381, 1224, 1159, 1116, 1054 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{37}H_{56}O_7Na$, 635.3924, found, 635.3919; $[\alpha]_D^{20}$ -3.9 (*c* 0.95, CH_2Cl_2). **9b:** ^{1}H-NMR (600MHz, $CDCl_3$): δ = 6.51(s, 1H), 5.85 (ddd, *J* = 17.1, 10.7, 6.3 Hz, 1H), 5.76 (ddd, *J* = 17.2, 10.4, 6.0 Hz, 1H), 5.27 (dt, *J* = 17.4, 1.7 Hz, 1H), 5.17 (dd, *J* = 10.8, 1.6 Hz, 1H), 5.13-5.08 (m, 3H), 4.98-4.95 (m, 1H), 4.96 (dt, *J* = 17.4, 1.7 Hz, 1H), 4.88 (dt, *J* = 10.2, 1.7 Hz, 1H), 4.40 (t, *J* = 5.5 Hz, 1H), 3.97 (dd, *J* = 7.9, 1.5 Hz, 1H), 3.79 (s, 3H), 3.60 (s, 3H), 3.24-3.10 (br, OH), 3.10-3.03 (m, 1H), 3.03-2.97 (m, 1H), 2.40 (s, 3H), 2.35-2.29 (m, 1H), 2.07 (dd, *J* = 13.0, 5.9 Hz, 1H), 2.03-1.97 (m, 1H), 1.79 (dd, *J* = 12.8, 8.3 Hz, 1H), 1.73-1.67 (m, 1H), 1.58-1.54 (m, 1H), 1.57 (d, *J* = 1.5 Hz, 3H), 1.53-1.49 (m, 1H), 1.44 (s, 3H), 1.39 (s, 3H), 1.28 (d, *J* = 6.8 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.4 Hz, 3H), 0.72 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (150MHz, $CDCl_3$): δ = 164.2, 150.1, 147.5, 144.4, 143.3, 136.1, 133.3, 130.1, 125.5, 123.0, 115.6, 114.4, 111.7, 100.6, 100.4, 100.2, 73.5, 71.4, 70.7, 60.7, 57.7, 48.0, 42.8, 41.0, 36.8, 36.3, 31.2, 28.2, 25.6, 24.1, 20.6, 19.4, 18.9, 16.0, 12.9, 10.7, 9.1; IR (film): 3469, 2965, 2930, 1457, 1380, 1340, 1226, 1160, 1116, 1023 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{37}H_{56}O_7Na$, 635.3924, found, 635.3915; $[\alpha]_D^{20}$ -13.1 (*c* 0.90, CH_2Cl_2).

Macrocycle 56. Compound **9a** (80 mg, 0.131 mmol, 1.0 equiv.) was dissolved in degassed CH_2Cl_2 (130 mL) and heated to reflux. Grubbs' II catalyst (22 mg, 0.026 mmol, 0.2 equiv.) in degassed CH_2Cl_2 (15 mL) was added *via* syringe pump within 16 h. After completion of the addition the mixture was stirred for another 30 min. The temperature was lowered to room temperature and air was bubbled through the solution to destroy excess catalyst. The solvent was evaporated and purification by column chromatography (hexane : ethylacetate from 10 : 1 to 5 : 1) afforded 47 mg (62%) of macrocycle **56** (rotamers) as a white foam. ^{1}H-NMR (600MHz, $CDCl_3$): δ = 6.42 (s, 1H), 5.78 (dd, *J* = 15.5, 4.2 Hz, 1H), 5.31 (dd, *J* = 15.5, 9.1 Hz, 1H), 5.10 (dd, *J* = 9.3, 4.7 Hz, 1H), 5.09 (d, *J* = 5.7 Hz, 1H), 5.03-4.95 (br, 1H), 4.82 (d, *J* = 8.7 Hz, 1H), 4.16 (dd, *J* = 8.7, 6.0 Hz, 1H), 3.78 (s, 3H), 3.58 (s, 3H), 3.54 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.11-3.04 (m, 1H), 3.04-2.98 (m, 1H), 2.46-2.37 (m, 1H), 2.42 (s, 3H), 2.21 (d, *J* = 14.7 Hz, 1H), 2.11-2.03 (br, 1H), 2.02-1.92 (br, 1H), 1.72-1.58 (br, 2H), 1.51 (s, 3H), 1.48-1.41 (m, 1H), 1.29-1.18 (m, 12H), 1.01-0.95 (m, 6H), 0.72-0.53 (br, 3H); ^{1}H-NMR (400MHz, C_7D_8, 350 K): δ = 6.44 (s, 1H), 5.65 (ddd, *J* = 15.5, 4.9 Hz, 1H), 5.44 (ddd, *J* = 15.5, 8.2, 1.7 Hz, 1H), 5.32 (d, *J* = 8.2 Hz, 1H), 5.03 (d, *J* = 5.6 Hz, 1H), 4.99 (d, *J* = 5.6 Hz, 1H), 4.88 (d, *J* = 8.8 Hz, 1H), 4.23 (dd, *J* = 8.0, 6.1 Hz, 1H), 3.69 (dd, *J* = 8.8, 4.5 Hz, 1H), 3.66 (s, 3H), 3.33 (s, 3H), 2.99-2.89 (m, 2H), 2.72-2.63 (br, OH), 2.59-2.49 (m, 1H), 2.40 (s, 3H), 2.16-2.07 (m, 2H), 1.94 (ddd, *J* = 13.7, 8.9, 5.4 Hz, 1H), 1.80-1.70 (m, 1H), 1.70-1.60 (m, 1H), 1.52-1.41 (m, 1H), 1.50 (s, 3H), 1.47 (d, *J* = 6.6 Hz, 3H), 1.34 (s, 3H), 1.26 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 3H), 0.70 (d, *J* = 7.0 Hz, 3H); ^{13}C-NMR (100MHz, C_7D_8, 350 K): δ = 163.6, 149.0, 146.6, 139.5, 137.9, 133.4, 128.6, 127.9, 127.2, 122.8, 114.9, 102.5, 100.9, 99.1, 75.2, 71.9, 60.6, 57.5, 45.4, 43.4, 40.4, 35.4, 34.8, 32.6, 30.0, 29.2, 26.1, 21.4, 21.2, 21.0, 19.3, 17.0, 13.2, 11.8, 9.5; IR (film): 3440, 2960, 1683, 1652, 1557, 1455, 1378, 1163, 1113 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{35}H_{52}O_7Na$, 607.3612, found, 607.3616; $[\alpha]_D^{20}$ +53.9 (*c* 1.20, CH_2Cl_2).

4-((2*R*,3*R*,4*S*,5*R*,6*R*)-4-Hydroxy-3,5-dimethyl-6-vinyltetrahydro-2*H*-pyran-2-yl)-6-methoxy-7-methyl-2-((2*S*,4*S*,8*S*,*E*)-4,6,8-trimethyldeca-6,9-dien-2-yl)benzofuran-5-ol (59). A mixture of **9a,b** (200 mg, 0.326 mmol) was dissolved in MeOH (7 mL) and treated with 3 drops of 3 N HCl. The reaction mixture was stirred at room temperature overnight, diluted with H_2O (50 mL) and extracted with CH_2Cl_2 (4 x 20 mL). The organic extracts were dried over $MgSO_4$, concentrated *in vacuo* and purified by flash chromatography (hexane : ethylacetate from 5 : 1 to 3 : 1) to afford tetrahydropyran **59** (120 mg, 72%, 1.5 : 1 rotamers) as a white foam. ^{1}H-NMR (Rotamers, 600MHz, $CDCl_3$): δ = 7.67 (br, 0.5OH)+5.60 (br, 0.5OH), 6.55(br, 0.5H)+6.18(br, 0.5H), 5.88-5.79 (m, 1H), 5.76 (ddd, *J* = 17.4, 10.2, 6.0 Hz, 1H), 5.27 (d, *J* = 16.6 Hz, 1H), 5.17 (br, 1H), 4.98-4.93 (m, 2H), 4.90-4.87 (m, 1H), 4.75 (br, 0.5H)+4.49 (br, 0.5H), 4.23 (dd, *J* = 4.0, 1.7 Hz, 1H), 3.84 (br, 3H), 3.70 (br, 1H), 3.10-3.02 (m, 1H), 3.02-2.96 (m, 1H), 2.42 (s, 3H), 2.25-1.95 (br, 1H), 2.16-2.11 (br, 1H), 2.08 (dd, *J* = 13.0, 5.5 Hz, 1H), 1.78 (dd, *J* = 12.3, 8.5 Hz, 1H), 1.73-1.65 (m, 1H+OH), 1.63-1.55 (m, 1H), 1.57 (s, 3H), 1.51-1.45 (m, 1H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.09 (br, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (The asterisk denotes signals not apparent in the ^{13}C-spectrum, 150MHz, $CDCl_3$): δ = 163.7, 146.9*, 143.3, 136.4*, 133.3, 130.1, 115.2*, 114.3*, 111.7, 98.9*, 82.8*, 80.2*,76.8*, 61.3*, 48.1*, 47.9, 42.9, 39.1, 37.7*, 36.3, 31.3, 28.3, 20.6, 19.5, 19.2, 16.0, 13.6*, 9.2, 6.6*; IR (film): 3391, 2964, 2927, 1636, 1604, 1455, 1405, 1384, 1284, 1114, 1048 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{32}H_{46}O_5$, 510.3345, found, 510.3331; $[\alpha]_D^{20}$ +87.2 (*c* 1.75, CH_2Cl_2).

Diolefin 60. Compound **59** (50 mg, 0.098 mmol, 1.0 equiv.) was dissolved in degassed CH_2Cl_2 (100 mL) and heated to reflux (45 °C outside temperature). Grubbs' II catalyst (16.6 mg, 0.020 mmol, 0.2 equiv.) in degassed CH_2Cl_2 (13 mL) was added *via* syringe pump within 16 h. After completion of the addition the mixture was stirred for another 30 min. The temperature was lowered to room temperature and air was bubbled through the solution to destroy excess catalyst. The solvent was evaporated and purification by column chromatography (hexane : ethylacetate from 5 : 1 to 3 : 1) afforded 39 mg (83%, 15 : 1 = *E* : *Z*) of macrocycle **60**. The mixture was used in the next step without further purification. ^{1}H-NMR (400MHz, $CDCl_3$): δ = 6.66 (s, 1H), 5.59 (ddd, *J* = 15.6, 8.7, 2.0 Hz, 1H), 5.54 (s, OH), 5.33 (dd, *J* = 15.5, 2.1 Hz, 1H), 4.92 (d, *J* = 9.1 Hz, 1H), 4.74 (d, *J* = 10.1 Hz, 1H), 4.27 (dd, *J* = 4.4, 2.1 Hz, 1H), 3.81 (s, 3H), 3.76-3.69 (m, 1H), 3.17-3.04 (m, 1H), 3.04-2.93 (m, 1H), 2.44 (s, 3H), 2.12-2.04 (m, 1H), 1.95 (dd, *J* = 12.8, 4.9 Hz, 2H), 1.87-1.79 (m, 1H), 1.79-1.71 (m, 1H), 1.69 (s, 3H), 1.66-1.45 (m, 2H), 1.55 (br, OH), 1.33 (d, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 7.1 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H) 0.95 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 162.0, 148.3, 141.8, 136.8, 133.0, 130.2, 125.2, 122.4, 115.5, 112.9, 104.6, 76.7, 75.7, 61.4, 44.4, 43.4, 38.9, 38.4, 35.8, 31.0, 28.8, 22.1, 21.3, 19.2, 18.1, 12.8, 9.4, 7.0; IR (film): 3450, 2967, 1683, 1653, 1456, 1404, 1380, 1321, 1109 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{30}H_{42}O_5$, 482.3032, found, 482.3023;

Tetrahydropyran 5. To a vigorously stirred refluxing solution of **60** (37 mg, 0.076 mmol, 1.0 equiv.) and AcOH (11 µL, 0.192 mmol, 2.5 equiv.) in CH_2Cl_2 (7 mL) was added dipotassium azodicarboxylate (89 mg, 0.460 mmol, 6 equiv.) over a period of 6 h. The mixture was cooled to room temperature, filtered over Celite and concentrated *in vacuo*. The crude product was purified by HPLC (hexane : ethylacetate = 4 : 1) to give **5** as a white foam (28 mg, 76%). All analytical data matched with those reported by Lee[6a] and Rychnovsky.[7] ^{1}H-NMR (600MHz, $CDCl_3$): δ = 6.55 (s, 1H), 5.53 (s, 1H), 4.60 (d, *J* = 9.5 Hz, 1H), 4.54 (d, *J* = 10.2 Hz, 1H), 3.83 (s, 3H), 3.67-3.62 (m, 1H), 3.44 (ddd, *J* = 11.0, 2.3, 1.1 Hz, 1H), 3.11-3.04 (m, 1H), 2.47-2.41 (m, 1H), 2.45 (s, 3H),

2.26-2.19 (m, 1H), 1.93-1.88 (m, 1H), 1.84-1.77 (m, 1H), 1.62 (s, 3H), 1.61-1.54 (m, 1H), 1.53-1.49 (br, OH), 1.48-1.41 (m, 2H), 1.38 (d, J =6.8 Hz, 3H), 1.35-1.18 (m, 5H), 1.04 (d, J =7.0 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H), 0.81 (d, J = 6.4 Hz, 3H), 0.76 (d, J =6.4 Hz, 3H); ^{13}C-NMR (150MHz, $CDCl_3$): δ = 159.7, 148.2, 141.6, 141.5, 131.5, 129.0, 122.1, 115.7, 112.5, 104.7, 77.8, 77.3 (2xCH), 61.4, 43.8, 41.8, 39.6, 38.6, 33.7, 32.5, 31.5, 31.1, 27.5, 21.8, 21.0, 19.6, 18.7, 12.8, 9.4, 6.6; IR (film): 3463, 2924, 2854, 1457, 1375, 1325, 1109, 1001 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{30}H_{44}O_5Na$, 507.3086, found, 507.3082; $[\alpha]_D^{20}$ +19.4 (*c* 0.17, $CHCl_3$)

***O*-quinone 71.** Macrocycle **5** (6 mg, 0.012 mmol, 1 equiv.) was dissolved in 1 mL CH_2Cl_2 / H_2O (10 : 1) and treated with DDQ (4.2 mg, 0.019 mmol, 1.5 equiv.) at room temperature. The color of the solution turned dark purple within 15 min, whereas TLC analysis showed complete consumption of the starting material. The mixture was directly loaded onto a silica column and eluted (hexane : ethylacetate from 3 : 1 to 2 : 1), to collect purple-blue fractions. The solvent was carefully evaporated to afford labile *o*-quinone **71** (3 mg, 52%) as a violet-blue compound. ^{1}H-NMR (400MHz, $CDCl_3$): δ = 6.11 (s, 1H), 4.72 (d, J = 9.8 Hz, 1H), 4.17 (d, J = 10.0 Hz, 1H), 3.55-3.48 (m, 1H), 3.32-3.26 (m, 1H), 2.97-2.87 (m, 1H), 2.34-2.27 (m, 1H), 2.27-2.21 (m, 1H), 1.90 (s, 3H), 1.88-1.80 (m, 1H), 1.81-1.73 (m, 1H), 1.68-1.54 (m, 3H), 1.62 (s, 3H), 1.47-1.37 (m, 1H), 1.44-1.31 (m, 1H), 1.36-1.24 (m, 2H), 1.19-1.09 (m, 1H), 1.25 (d, J =6.8 Hz, 3H), 0.91 (d, J =6.1 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.5 Hz, 3H), 0.80 (d, J =6.5 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ = 177.2, 173.7, 164.3, 147.4, 131.3, 129.1, 125.4, 113.7, 105.3, 78.3, 76.4, 75.8, 42.1, 41.7, 39.4, 38.2, 33.8, 32.5, 32.1, 29.7, 27.7, 21.8, 21.0, 19.6, 17.9, 17.0, 13.0, 8.2, 6.4; IR (film): 3625, 2924, 2359, 17.32, 1699, 1652, 1584, 1455, 1377, 1326, 1094 cm^{-1}; HRMS (ESI) (*m/z*): [M+MeCN+Na]$^+$ calcd for $C_{31}H_{43}O_5NNa$, 532.3039, found, 532.3058.

Kendomycin 1. *O*-quinone **71** (2 mg, 0.0043 mmol) was dissolved in MeCN (2 mL) and treated with one drop of 1% HCl. The initial blue solution turned yellow within 15 min and the reaction mixture was partitioned between etyhlacetate (50 mL) and brine (15 mL). The aqueous phase was extracted with ethylacetate (3 x 10 mL), the organic layer was dried over $MgSO_4$ and concentrated *in vacuo.* Purification by flash chromatography (hexane : ethylacetate from 3 : 1 to 2 : 1) gave kendomycin **1** (1 mg, 50%) as a yellow solid. m.p. 226-227 °C (authentic sample: 235-236 °C); $[\alpha]_D^{20}$ -76.4 (*c* 0.11, MeOH), (lit. $[\alpha]_D^{20}$ -80 (*c* 2.71, MeOH)[2], $[\alpha]_D^{20}$ -79.3 (*c* 0.135, MeOH),[2b-d] $[\alpha]_D^{20}$ -82.4 (*c* 0.514, MeOH)[2a]), ^{1}H-NMR (600MHz, CD_3COCD_3): δ = 8.10 (s, 1H), 7.19 (s, 1H), 6.54 (s, 1H), 4.64 (d, J = 10.0 Hz, 1H), 4.36 (d, J = 10.3 Hz, 1H), 3.95 (d, J = 4.5 Hz, 1H), 3.56 (m, 1H), 3.53 (ddd, J = 11.0, 2.3, 1.1 Hz, 1H), 2.42 (m, 1H), 2.36 (m, 1H), 2.12 (br d, J = 17.0 Hz, 1H), 1.96 (m, 1H), 1.88 (m, 1H), 1.84 (s, 3H), 1.71 (m, 1H), 1.67 (m, 1H), 1.64 (m, 1H), 1.61 (s, 3H), 1.57 (m, 1H (10-H^a)[34]), 1.45 (ddd, J = 12.9, 11.4, 2.9 Hz, 1H), 1.33 (m, 2H (11-H_2)), 1.25 (m, 10-H^b), 0.95 (d, J =7.0 Hz, 3H), 0.94 (d, J = 6.5 Hz, 3H), 0.89 (d, J = 6.5 Hz, 3H), 0.87 (d, J =6.5 Hz, 3H), 0.71 (d, J = 7.0 Hz, 3H); ^{13}C-NMR (150MHz, CD_3COCD_3): δ = 182.1, 168.6, 146.8, 141.3, 132.1, 130.2, 129,9, 119.1, 111.0, 104.2, 78.7, 77.8, 76.2, 46.1, 41.4, 40.8, 39.8, 38.1, 35.9, 33.6, 33.5, 26.5, 22.7, 19.9, 19.7, 13.3, 12.7, 7.6, 7.2; IR (film): 3322, 2926, 1670, 1614, 1585, 1329, 1098 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{29}H_{42}O_6$, 486.2981, found, 486.2975.

Acknowledgements

We thank Prof. Zeeck, University of Göttingen, for authentic samples of **1** and Dr. Lothar Brecker, Dr. Hanspeter Kählig and Susanne Felsinger, all University of Vienna, for NMR measurements.

[1] a) Y. Funahashi, N. Kawamura, T. Ishimaru, JP Patent 08231551[A2960910] 1996 [Chem. Abstr. 1997, 126, 6553]; b) Y. Funahashi, N. Kawamura, JP Patent 08231552 [A2960910] 1996 [Chem. Abstr. 1996, 125, 326518]; c) M. H. Su, M. I. Hosken, B. J. Hotovec, T. L. Johnston, US Patent 5728727 [A980317] 1998 [Chem. Abstr. 1998, 128, 239489].

[2] a) H. B. Bode, A. Zeeck, *J. Chem. Soc., Perkin Trans. 1* **2000**, 323; b) H. B. Bode, A. Zeeck , *J. Chem. Soc., Perkin Trans. 1* **2000**, 2665.

[3] a) Y. A. Elnakady, M. Rohde, F. Sasse, C. Backes, A. Keller, H.-P. Lenhof, K. J. Weissman, R.Müller, *Chem. Bio. Chem.* **2007**, *8*, 1261. b) C. O. Janssen, S. Lim, E. P. Lo, K. F. Wan, V. C. Yu, M. A. Lee, S. B. Ng, M. J. Everett, A. D. Buss, D. P. Lane, R. S. Boyce*, Bioorg. Med. Chem. Lett.* **2008**, *18*, 5771.

[4] S.C. Wenzel, H. B. Bode, I. Kochems, R. Mueller, *Chem. Bio. Chem.* **2008**, *9*, 2711.

[5] a) M. P. Green, S. Pichlmair, M. M. B. Marques, H. J. Martin, O. Diwald, T. Berger, J. Mulzer, *Org. Lett.* **2004** *6*, 3131; b) M. M. B. Marques, S. Pichlmair, H. J. Martin, J. Mulzer, *Synthesis* **2002,** 2766; c) H. J. Martin, M. Drescher, H. Kählig, S. Schneider, J. Mulzer. *Angew. Chem. Int. Ed*. **2001**, *40*, 3186.

[6] a) Y. Yu; H. Men, C. Lee, *J. Am. Chem. Soc.* **2004**, *126*, 14720; b) A. B. III Smith, E. F. Mesaros, E. Meyer, *J. Am. Chem. Soc.* **2006**, *128*, 5292; c) A. B. III Smith, E. F. Mesaros, E. Meyer, *J. Am. Chem. Soc.* **2005**, *127*, 6948; d) J. T. Lowe, J. S. Panek, *Org. Lett*. **2008**, *10*, 3813. e) Magauer, T.; Martin, H. J.; Mulzer, J. *Angew. Chem. Int. Ed.* ***2009***, *48*, 6032.

[7] K. B. Bahnck, S. D. Rychnovsky, *J. Am. Chem. Soc.* **2008**, *130*, 13177.

[8] a) T. Sengoku, D. Uemura, H. Arimoto, *Chem. Lett.* **2007**, *36*, 726; b) T. Sengoku, H. Arimoto, D. Uemura, *Chem. Commun*. **2004**, *10*, 1220; c) J. D. White, H. Smits, *Org. Lett*. **2005**, *7*, 235; d) D. Williams, K. Shamim, *Org. Lett.* **2005**, *7*, 4161; e) J. Mulzer, S. Pichlmair, M. P. Green, M. M. B. Marques, H. J. Martin, *Proc. Nat. Acad. Sci*. **2004**, *101*, 11980.

[9] S. Pichlmair, M. M. B. Marques, M. P. Green, H. J. Martin, J. Mulzer, *Org. Lett.* **2003**, *5*, 4657.

[10] J. Uenishi, R. Kawahama, O. J. Yonemitsu, *J. Org. Chem.*, **1997**, *62*, 1691.

[11] E. W. Colvin, B. J. Hamill, *J.Chem. Soc., Chem. Commun*. **1973**, 151.

[12] a) E. Negishi, C. Kotora, C. Xu, *J. Org. Chem*. **1997**, *62*, 8957; b) Review: E. Negishi, Q. Hu, Z. Huang, M. Qian, G. Wang*, Aldrichim. Acta* **2005**, *38*, 71.

[13] W-H. Jung, C. Harrison, Y. Shin, J-H. Fournier, R. Balachandran, B.S. Raccor, R. P. Sikorski, A. Vogt, D. P. Curran, B.W. Day, *J. Med. Chem.*, **2007**, *50*, 2951.

[14] (a) M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *6,* 953; (b) B. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc*. **1996,** *118*, 100.

[15] at that time we became aware that the White group had unsuccessfully pursued a related approach for the tetrahydropyran formation: H. Smits, *Studies Towards the Total Synthesis of (-)-Kendomycin,* Dissertation, Oregon State University, 2007.

[16] (a) R. E. Ireland, D. Habich, D. W. Norbeck, *J. Am. Chem. Soc.* **1985**, *107*, 3271; (b) R. E. Ireland, P. Wipf, J. D. Armstrong *J. Org. Chem.* **1990**, *56*, 650; (c) R. E. Ireland, R. H. Mueller, A. K. Willard, *J. Am. Chem. Soc.* **1976**, *98*, 2868; (d) A. M. M. Castro, *Chem. Rev*. **2004**, *104*, 2939.

[17] (a) K. Mori, *Tetrahedron* **2008**, *64*, 4060; (b) A. G. M. Barrett, R. A. E. Carr, S. V. Attwood, G. Richardson, N. D. A. Walshe, *J. Org. Chem.* **1986**, *51*, 4840.

[18] B. S. Bal, W. E. Childers, H.W. Pinnick, *Tetrahedron* **1981**, 37, 2091.

[19] (a) Y. Okude, S. Hirano, T. Hiyama, H. Nozaki, *J. Am. Chem. Soc.* **1976**, *98*, 3179; (b) A. Fürstner, N. Shi, *J. Am. Chem. Soc.* **1996**, *118*, 12349; (c) **29a** and **29b** were obtained as an easily separable 1.4:1-mixture. **29b** was recycled by oxidation to the ketone and reduction with $NaBH_4$ (dr = 2:1).

[20] Claisen-Ireland rearrangements of this dimension are rare in the literature; we are aware of three examples of similar complexity: a) C. E. Stivala, A. Zakarian, *J. Am. Chem. Soc.* **2008**, *130*, 3774; b) M. J. Fisher, C. D. Myers, J. Joglar, S. H. Chen, S. J. Danishefsky, *J. Org. Chem.* **1991**, *56*, 5826; c) R. E. Ireland, D. Habich, D. W. Norbeck, *J. Am. Chem. Soc*. **1985**, *107*, 3271.

[21] a) J. S. Clark, R. Metternich, V. J. Novack, G. S. Sheppard, D. A. Evans *, J. Am. Chem. Soc.* **1990**, *112*, 866; b) D. A. Evans, J. S. Clark, D. L. Rieger, *Tetrahedron* **1992**, *48*, 2127.

[22] D. A. Evans, K. T. Chapman, E. M. Carreira*, J. Am. Chem. Soc.* **1988**, *110*, 3578.

[23] S. Pichlmair, *Stereoselective Synthesis of the Carbon Skeleton of Kendomycin*, Dissertation, University of Vienna, 2004.

[24] (a) M.R. Winkle, R.C. Ronald, *J. Org. Chem*. **1982**, *47*, 2101; (b) V. Snieckus, *Chem. Rev*. **1990**, *90*, 879.

[25] E. Merifield and E. J. Thomas, *J. Chem. Soc*., *Perkin Trans. 1*, **1999**, 3269.

[26] a) A. Hafner, R. O. Duthaler, R. Marti, G. Rihs, P. Rothe-Streit, F. Schwarzenbach, *J. Am. Chem. Soc.* **1992**, *114*, 2321; b) Review: A. Hafner, R.O. Duthaler, *Chem. Rev.* **1992**, *92*, 807.

[27] (a) W. R. Roush, K. Ando, D. B. Powers, A. D. Palkowitz, R. L. Halterman, *J. Am. Chem. Soc.* **1990**, *112*, 6339; (b) W. R. Roush, R. L. Halterman, *J. Am. Chem. Soc.* **1986**, *108*, 294.

[28] H. C. Brown, S. K. Bhat, *J. Am. Chem. Soc.* **1986**, *108*, 5919.

[29] D. J. Pasto, R. T. Taylor, in *Org. React.* **1991**, *40*, (L. A. Paquette, editor), John Wiley & Sons, New York, pp. 91-155.

[30] Replacement of CH_2Cl_2 with benzene gave a E:Z = 2.5:1 mixture in 80% yield.

[31] S. Kulasegaram, R. J. Kulawiec, *J. Org. Chem.* **1997**, *62*, 6547.

[32] E. P. Boden, G. E. Keck, *J. Org. Chem.* **1985**, *50*, 2394.

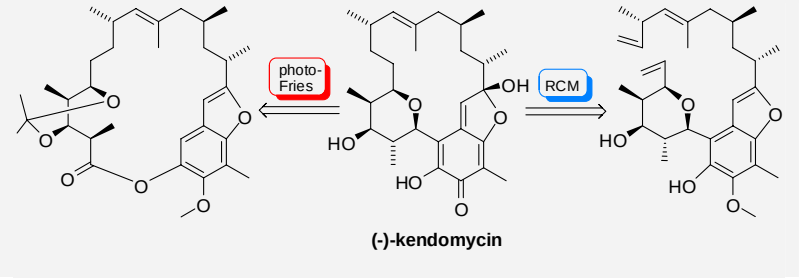
[33] Z. Huang, E. Negishi, *Org. Lett.* **2006**, *8*, 3675.

[34] 2D-NMR experiments with natural and synthetic Kendomycin showed that protons 10-H_2 and 11-H_2 have been misassigned (compare ref.[2,6a-d])

Received: ((will be filled in by the editorial staff))
Revised: ((will be filled in by the editorial staff))
Published online: ((will be filled in by the editorial staff))

*Thomas Magauer, Harry J. Martin, and Johann Mulzer**……..…
Page – Page

Ring Closing Metathesis and Photo-Fries Reaction for the Construction of the Ansamycin Antibiotic Kendomycin. Development of a Protecting Group Free Oxidative Endgame.



(-)-kendomycin

The so far underestimated photo-Fries reaction serves as an efficient tool for the total synthesis of (-)-kendomycin. A powerful RCM is the basis of the second total synthesis.

The installation of the lactol unit was performed by a chemoselective oxidation-hydrolysis sequence, thus avoiding additional protecting groups.

Ring Closing Metathesis and Photo-Fries Reaction for the Construction of the Ansamycin Antibiotic Kendomycin. Development of a Protecting Group Free Oxidative Endgame.

SUPPORTING INFORMATION

Thomas Magauer, Harry J. Martin and Johann Mulzer*

Institute of Organic Chemistry, University of Vienna

Währingerstraße 38

1090 Vienna

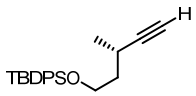
Austria

General Methods

All solvents were distilled prior to use, except THF, which was purchased from Acros Organics (99.85%, H_2O < 50 ppm) and used without further purification. Et_2O, toluene and benzene were distilled from sodium. CH_2Cl_2 and $CHCl_3$ were passed through an Al_2O_3-$MgSO_4$ column or distilled over P_2O_5. Acetone was distilled over P_2O_5. DMF, DMSO, NEt_3, *i*Pr_2NH, *i*Pr_2NEt, TMEDA, HMPA and 2,6-lutidine were distilled from CaH_2. TBSCl was dissolved in hexane or THF (3 M), treated with Et_3N (3%) and transferred *via* a syringe filter to the reaction mixture. CpZrHCl was prepared according to the Negishi procedure[1]. Solvent degassing was achieved by repeated (at least 4 cycles) freeze-pump-thaw (FPT) cycles. All non-aqueous reactions were performed under an atmosphere of argon using oven-dried or flame-dried glassware and standard syringe/septa techniques. ^{1}H- and ^{13}C-NMR spectra were measured in $CDCl_3$ on a Bruker Avance DRX-400 or DRX-600 at 400.13 MHz (100.61 MHz) or 600.13 MHz (150.90 MHz), respectively. Chemical shifts are given in ppm and were referenced to residual $CHCl_3$ (^{1}H, δ = 7.26 ppm, ^{13}C, δ =77.00 ppm) or toluene (^{1}H, δ = 7.09, 7.00, 6.98 ppm, ^{13}C, δ =137.9, 129.2, 128.3, 125.5, 20.4 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in Hz, integration. Assignments of proton resonances were confirmed by correlated spectroscopy. IR spectra were recorded as thin films on a silicon plate on a Perkin-Elmer 1600 FT-IR spectrometer. Mass spectra were measured on a Micro mass, trio 200 Fisions Instruments. High-resolution mass spectra (HRMS) were performed with a Finnigan MAT 8230 with a resolution of 10000. Optical rotations were measured on a Perkin-Elmer 351 polarimeter at 20 °C (reported as follows: concentration (*c* in g/100mL), solvent). The reaction progress was monitored on precoated TLC plates (Merck Kieselgel 60 F254). Spots were visualized under UV light (254nm) and/or were stained with ceric ammonium molybdate (CAM), *p*-anisaldehyde or potassium permanganate stain. Column chromatography was performed with Merck silica gel 60 (230-400 mesh). Analytical HPLC was performed on a Jasco System (PU-980 pump, UV 975 and RI 930) using a Nucleosil 50 column (5 µm, Ø 4 mm x 241 mm) at ambient temperature. Preparative HPLC was performed on a Dynamix Model SD-1 equipped with a Model UV-1 absorbance detector using a Supershere (60 Å pore size, 4 µm

[1] Huang, Z.; Negishi, E. *Org. Lett.* **2006**, *8*, 3675.

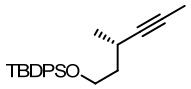
particle size, Ø 25 mm x 250 mm) at ambient temperature. Yields refer to chromatographically purified compounds, unless otherwise stated.



(*S*)-*tert*-Butyl(3-methylpent-4-ynyloxy)diphenylsilane (72).

DIPA (1.23 mL, 8.81 mmol, 1.15 equiv.) was dissolved in THF (7 mL), cooled to -78 °C and *n*-BuLi (2.5 M in hexane, 3.52 mL, 8.81 mmol, 1.15 equiv.) was added. The resulting solution was stirred for 10 min at 0 °C, recooled to -78 °C and subsequently treated with $TMSCHN_2$ (4.4 mL, 8.81 mmol, 1.15 equiv.). The temperature was kept for 0.5 h, after which aldehyde **13** (2.61 g, 7.66 mmol, 1 equiv.) in THF (1 M) was added *via* syringe. Stirring was continued for 1 h at -78 °C, and 2 h at room temperature. The reaction was quenched by the addition of NH_4Cl (20 mL) and extracted with Et_2O (3 x 10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (hexane : ethylacetate = 10 : 1) affording 2.10 g (82%) of pure **72**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.70–7.63 (m, 4H), 7.45–7.34 (m, 6H), 3.87–3.73 (m, 2H), 2.79–2.68 (m, 1H), 1.99 (d, *J* = 2.5 Hz, 1H), 1.72–1.66 (m, 2H), 1.19 (d, *J* = 7.1 Hz, 3H), 1.05 (s, 9H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 135.6, 129.5, 127.6, 68.3, 69.5, 39.5, 26.8, 22.2, 20.9, 19.2; HRMS (ESI) (m/z): $[M\text{-}t\text{Bu}]^+$ calcd for $C_{18}H_{19}OSi$, 279.1205, found, 279.1201; IR (film): 2932, 1700, 1653, 1472, 1428, 1112 cm^{-1}; $[\alpha]_D^{20}$ +4.5 (c 1.11, CH_2Cl_2).

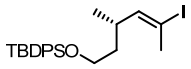


(*S*)-*tert*-Butyl(3-methylhex-4-ynyloxy)diphenylsilane (73).

A solution of alkyne **72** (2.10 g, 6.23 mmol, 1 equiv.) in THF (20 mL) was cooled to -78 °C and treated with *n*-BuLi (2.5 M in hexane, 5.49 mL, 13.72 mmol, 2.2 equiv.). After 20 min MeI (1.01 mL, 16.22 mmol, 2.6 equiv.) was added and the temperature was raised to room temperature over night. The solution was treated with NH_4Cl (20 mL), extracted with Et_2O (3 x 10 mL), dried

over $MgSO_4$, filtered and the solvent was evaporated. Purification by flash chromatography (hexane : ethylacetate = 50 : 1) yielded 2.08 g (95%) **73**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.71–7.64 (m, 4H), 7.45–7.34 (m, 6H), 3.86–3.72 (m, 2H), 1.75 (d, *J* = 2.8 Hz, 3H), 1.72–1.57 (m, 2H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.05 (s, 9H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 135.6, 134.1, 134.0, 129.5, 127.6, 127.5, 83.5, 61.9, 40.0, 26.8, 22.4, 21.4, 19.2, 3.5; HRMS (ESI) (m/z): [M-*t*Bu]$^+$ calcd for $C_{19}H_{21}OSi$, 293.1362, found, 293.1360; IR (film): 3071, 2932, 2363, 1700, 1653, 1428, 1112 cm^{-1}; $[\alpha]_D^{20}$ +5.9 (c 0.88, CH_2Cl_2).

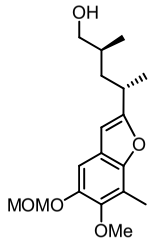


(*S,E*)-*tert*-Butyl(5-iodo-3-methylhex-4-enyloxy)diphenylsilane (10).

A 250 mL Schlenk flask was charged with Cp_2ZrCl_2 (5.53 g, 18.92 mmol, 2.8 equiv.) and THF (50 mL). The solution was cooled to 0 °C and DIBAL-H (1 M in heptane, 18.93 mL, 18.93 mmol, 2.8 equiv.) was slowly added *via* cannula. The white precipitate was stirred for 1.5 h at room temperature, after which the supernatant was carefully removed. Alkyne **73** (2.37 g, 6.76 mmol, 1 equiv.) in benzene (15 mL) was added and the resulting suspension was heated to 40 °C for 3.5 h. The mixture was cooled to 0 °C and I_2 (4.80 g, 18.92 mmol, 2.8 equiv.) in benzene (40 mL) was slowly transferred to the solution.

The reaction was quenched after 5 min by the addition of 1 M $Na_2S_2O_3$ solution. Stirring was continued until both layers became colorless. The aqueous phase was extracted with Et_2O (4 x 20 mL), the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated to dryness. Subsequent flash chromatography (hexane : ethylacetate = 50 : 1) yielded 2.67 g (83%) of vinyl iodide **10**.

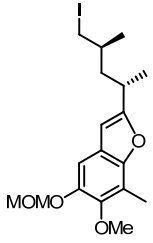
^{1}H-NMR (400MHz, $CDCl_3$): δ 7.71–7.65 (m, 4H), 7.48–7.37 (m, 6H), 5.95 (dq, *J* = 9.2, 1.2 Hz, 1H), 3.66 (dd, *J* = 6.8, 5.6 Hz, 2H), 2.79–2.67 (m, 1H), 2.40 (d, *J* = 1.5 Hz, 3H), 1.63–1.52 (m, 1H), 1.51–1.41 (m, 1H), 1.07 (s, 9H), 0.97 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 146.8, 135.5, 134.0, 129.6, 127.6, 93.1, 61.6, 39.5, 32.0, 27.8, 26.9, 20.3, 19.2; HRMS (ESI) (m/z): [M-*t*Bu]$^+$ calcd for $C_{19}H_{22}IOSi$, 421.0485, found, 421.0470; IR (film): 3071, 2958, 1634, 1589, 1471, 1428, 1389, 1360 cm^{-1}; $[\alpha]_D^{20}$ +19.3 (c 0.81, CH_2Cl_2).



(2*S*,4*S*)-4-(6-Methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-2-methylpentan-1-ol (74).

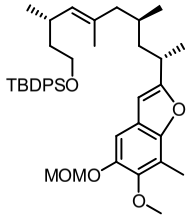
Compound **14** (4.96 g, 8.85 mmol, 1 equiv.) was dissolved in THF (180 mL) and TBAF (1 M in THF, 10.62 mL, 10.62 mmol, 1.2 equiv.) was added at ambient temperature. The mixture was stirred overnight, finally quenched with 200 mL of H_2O and the aqueous layer was extracted with Et_2O (3 x 70 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was evaporated. Purification by column chromatography (hexane : ethylacetate from 5 : 1 to 3 : 1) furnished 2.68 g (94%) of **74**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.07 (s, 1H), 6.26 (s, 1H), 5.20 (s, 2H), 3.83 (s, 3H), 3.54 (s, 3H), 3.56–3.47 (m, 2H), 3.03 (m, 1H), 2.41 (s, 3H), 1.79–1.69 (m, 1H), 1.67–1.59 (m, 2H), 1.30 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 164.2, 123.4, 115.3, 105.0, 100.7, 96.2, 68.2, 61.0, 56.1, 39.0, 33.4, 31.2, 19.3, 16.7, 9.1; HRMS (ESI) (m/z): [M]$^+$ calcd for $C_{18}H_{26}O_5$, 322.1780, found, 322.1786; IR (film): 3745, 3676, 2932, 1684, 1653, 1560, 1457, 1043 cm^{-1}; $[\alpha]_D^{20}$ +0.9 (c 0.78, CH_2Cl_2).



2-((2*S*,4*S*)-5-Iodo-4-methylpentan-2-yl)-6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran (11).

To a solution of alcohol **74** (700 mg, 2.17 mmol, 1 equiv.) in CH_2Cl_2 (14 mL) was added imidazole (192 mg, 2.82 mmol, 1.3 equiv.) and triphenylphosphine (740 mg, 2.82 mmol, 1.3 equiv.) at 0 °C. After 5 min iodine (716 mg, 2.82 mmol, 1.3 equiv.) was added in three portions. Stirring was continued for 1 h at room temperature. The reaction was diluted with CH_2Cl_2, quenched with NH_4Cl (60 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated. The crude residue was purified by flash chromatography (hexane : ethylacetate = 15 : 1) to obtain 822 mg (88%) of pure iodine **11**. ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.08 (s, 1H), 6.28 (s, 1H), 5.21 (s, 2H), 3.84 (s, 3H), 3.54 (s, 3H), 3.27 (d, *J* = 4.8 Hz, 2H), 2.97 (m, 1H), 2.43 (s, 3H), 1.73–1.56 (m, 2H), 1.50–1.40 (m, 1H), 1.32 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 163.3, 149.2, 146.9, 145.7, 123.3, 115.3, 105.0, 100.9, 96.1, 60.9, 56.1, 42.5, 31.9, 31.2, 27.9, 19.6, 17.9, 9.1; HRMS (EI, 70eV, 70 °C) (m/z): $[M]^+$ calcd for $C_{18}H_{25}IO_4$, 432.0798, found, 432.0802; IR (film): 2962, 1605, 1455, 1422, 1338, 1311, 1260, 1218, 1152 cm^{-1}; $[\alpha]_D^{20}$ +8.4 (c 0.65, CH_2Cl_2).

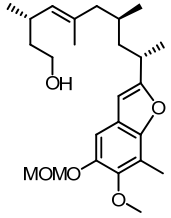


***tert*-Butyl((3*S*,7*S*,9*S*,*E*)-9-(6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-3,5,7-trimethyldec-4-enyloxy)diphenylsilane (75).**

To flame-dried $ZnCl_2$ (126 mg, 0.925 mmol, 1.5 equiv.) was added alkyl iodide **11** (400 mg, 0.925 mmol, 1.5 equiv.) in degassed Et_2O (5 mL). The suspension was cooled to -78 °C and *t*-BuLi (1.7 M in pentane, 1.63 mL, 2.776 mmol, 4.5 equiv.) was rapidly added. The pale yellow solution was stirred for 5 min at -78 °C and 1.5 h at 0 °C. Then $Pd(PPh_3)_4$ (36 mg, 0.033 mmol, 0.05 equiv.) and vinyl iodide **10** (295 mg, 0.617 mmol, 1 equiv.) in degassed THF (3 mL) were added at 0 °C. The yellow mixture was stirred for 2.5 h at 0 °C and allowed to warm to room temperature

overnight. The reaction was diluted with Et_2O (10 mL) and quenched by the addition of NH_4Cl (20 mL). The phases were separated, extracted with Et_2O (4 x 10 mL), washed with brine, dried over $MgSO_4$, filtered and evaporated to dryness. The crude product (405 mg, 100%) was directly used in the next step. A small amount was purified by HPLC (hexane : ethylacteate = 20 : 1) to furnish pure **75**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69–7.62 (m, 4H), 7.43–7.31 (m, 6H), 7.08 (s, 1H), 6.24 (s, 1H), 5.21 (s, 2H), 4.84 (d, *J* = 9.3 Hz, 1H), 3.84 (s, 3H), 3.66–3.60 (m, 2H), 3.55 (s, 3H), 3.05–2.94 (m, 1H), 2.65–2.53 (m, 1H), 2.43 (s, 3H), 2.04 (dd, *J* = 12.5, 5.1 Hz, 1H), 1.72 (dd, *J* = 11.5, 8.5 Hz, 1H), 1.68–1.56 (m, 2H), 1.54 (s, 3H), 1.53–1.38 (m, 3H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 9H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.75 (d, *J* = 6.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 164.8, 149.2, 146.9, 145.5, 135.6, 135.5, 134.2, 137.7, 1322.6, 129.4, 127.5, 123.5, 115.3, 105.0, 100.4, 96.2, 62.3, 61.0, 56.1, 48.0, 43.0, 40.5, 31.3, 28.8, 28.2, 26.9, 21.3, 19.5, 19.2, 16.0, 9.11; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{41}H_{56}O_5Si$, 656.3897, found, 656.3877; IR (film): 2928, 1589, 1455, 1428, 1339, 1218, 1153, 1112, 1044 cm^{-1}; $[\alpha]_D^{20}$ +3.3 (c 1.32, CH_2Cl_2).

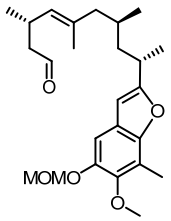


(3*S*,7*S*,9*S*,*E*)-9-(6-Methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-3,5,7-trimethyldec-4-en-1-ol (15).

Crude product **75** (405 mg, 0.616 mmol, 1 equiv.) was dissolved in THF (20 mL) and TBAF was added at room temperature. The solution was stirred for 24 h and quenched by the addition of H_2O (20 mL). The layers were separated, extracted with Et_2O (3 x 15 mL), dried over $MgSO_4$ and concentrated. Purification by flash column chromatography (hexane : ethylacetate = 3 : 1) afforded 173 mg (67% over 2 steps) of primary alcohol **15**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.08 (s, 1H), 6.25 (s, 1H), 5.21 (s, 2H), 4.91 (d, *J* = 9.3 Hz, 1H), 3.84 (s, 3H), 3.67–3.56 (m, 2H), 3.54 (s, 3H), 3.06–2.95 (m, 2H), 2.59–2.46 (m, 1H), 2.42 (s, 3H), 2.07

(dd, *J* = 12.6, 5.3 Hz, 1H), 1.77 (dd, *J* = 12.6, 8.3 Hz, 1H), 1.73–1.59 (m, 2H), 1.58 (d, *J* = 1.3 Hz, 3H), 1.57–1.41 (m, 3H), 1.27 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 164.7, 149.1, 146.9, 145.5, 133.0, 132.4, 123.5, 115.2, 105.0, 100.4, 96.2, 61.6, 61.0, 56.1, 48.0, 43.0, 40.5, 31.3, 29.3, 28.2, 21.4, 19.5, 19.1, 16.0, 9.1; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{25}H_{38}O_5$, 418.2719, found, 418.2726; IR (film): 3442, 2926, 1700, 1653, 1604, 1452, 1340, 1219, 1153, 1117, 1090, 1045 cm^{-1}; $[\alpha]_D^{20}$ +14.5(c 1.80, CH_2Cl_2).



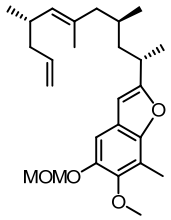
(3*S*,7*S*,9*S*,*E*)-9-(6-Methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-3,5,7-trimethyldec-4-enal (76).

A 50 mL flask was charged with alcohol **15** (560 mg, 1.34 mmol, 1 equiv.) in DMSO (7 mL). After the addition of IBX (1.39 g, 4.96 mmol, 3.6 equiv.) the solution was stirred for 30 min at ambient temperature.

The solution was diluted with Et_2O : hexane = 1 : 1 (15 mL) and 15 mL of H_2O to precipitate remaining IBX. The mixture was filtered over Celite, the phases were separated and the aqueous layer was extracted with Et_2O : hexane = 1 : 1 (3 x 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered over a plug of silica and evaporated to dryness. Crude aldehyde **76** (541 mg, 97%) was used in the next step without further purification.

^{1}H-NMR (400MHz, $CDCl_3$): δ 9.69 (t, *J* = 2.4 Hz, 1H), 7.08 (s, 1H), 6.24 (s, 1H), 5.21 (s, 2H), 4.95 (d, *J* = 9.7 Hz, 1H), 3.84 (s, 3H), 3.54 (s, 3H), 3.04–2.91 (m, 2H), 2.42 (s, 3H), 2.37–2.32 (m, 2H), 2.06 (dd, *J* = 12.5, 5.4 Hz, 1H), 1.75 (dd, *J* = 12.5, 8.5 Hz, 1H), 1.71–1.62 (m, 1H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.59–1.52 (m, 1H), 1.50–1.42 (m, 1H), 1.27 (d, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.31 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 202.7, 164.6, 149.2, 146.9, 133.9, 130.6, 123.5, 115.3, 105.0, 100.4, 96.2, 61.0, 56.1, 51.2, 47.8, 43.0, 31.3, 28.2, 27.9, 21.2, 19.5, 19.2,

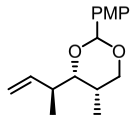
16.2, 9.1; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{25}H_{36}O_5$, 416.2563, found, 416.2556; IR (film): 2959, 1725, 1653, 1605, 1455, 1419, 1379, 1219, 1153 cm^{-1}; $[\alpha]_D^{20}$ +36.9 (c 1.05, CH_2Cl_2).



6-Methoxy-5-(methoxymethoxy)-7-methyl-2-((2*S*,4*S*,8*S*,*E*)-4,6,8-trimethylundeca-6,10-dien-2-yl)benzofuran (16).

$MePPh_3Br$ (189 mg, 0.52 mmol, 2 equiv.) was suspended in THF (2 mL) and placed on an ice bath. Subsequently *t*-BuOK (59 mg, 0.52 mmol, 2 equiv.) was added and the yellow suspension was stirred for 1.5 h at room temperature. The orange solution was cooled to 0 °C and aldehyde **76** (110 mg, 0.26 mmol, 1 equiv.) in THF (0.8 mL) was added dropwise. After 1 h the reaction was quenched by the addition of saturated aqueous NH_4Cl (20 mL) and the aqueous phase was extracted with Et_2O : hexane = 1 : 1 (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash chromatography (hexane : ethylacetate = 3 : 1) gave 99 mg (90%) of diene **16**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.09 (s, 1H), 6.25 (s, 1H), 5.77 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.22 (s, 3H), 5.03–4.91 (m, 2H), 3.85 (s, 3H), 3.55 (s, 3H), 3.07–2.96 (m, 1H), 2.50–2.40 (m, 1H), 2.43 (s, 3H), 2.08 (dd, *J* = 12.6, 5.3 Hz, 1H), 2.05–1.99 (m, 2H), 1.77 (dd, *J* = 12.6, 8.3 Hz, 1H), 1.74–1.64 (m, 1H), 1.64–1.44 (m, 2H), 1.57 (d, *J* = 1.3 Hz, 3H), 1.28 (d, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 164.8, 149.2, 146.9, 145.5, 137.6, 132.5, 132.3, 123.5, 115.3, 105.0, 100.4, 96.2, 61.0, 56.1, 48.0, 43.0, 42.0, 32.5, 31.3, 28.2, 20.8, 19.5, 19.2, 16.2, 9.1; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{26}H_{38}O_4$, 414.2770, found, 414.2761; IR (film): 2958, 1700, 1653, 1606, 1452, 1379, 1219, 1153, 1044 cm^{-1}; $[\alpha]_D^{20}$ +16.8 (c 2.50, CH_2Cl_2).

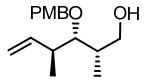


(4*S*,5*S*)-4-((*S*)-But-3-en-2-yl)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxane (77).

Alcohol **17** (950 mg, 3.59 mmol, 1 equiv.) and 1 g of powered molecular sieve 3Å in CH_2Cl_2 (32 mL) was cooled to 0 °C and DDQ (978 mg, 4.3 mmol, 1.2 equiv.) was added in three portions over a period of 5 min. The resulting green-black solution was stirred for 1.5 h, allowing the reaction to warm to ambient temperature.

After the addition of Et_2O (80 mL), the reaction was quenched with saturated $Na_2S_2O_3$ (30 mL) and $NaHCO_3$ (30 mL). The aqueous layer was extracted with Et_2O (3 x 20 mL), washed with brine and dried over $MgSO_4$, filtrated and evaporated to dryness. Purification by flash chromatography (hexane : ethylacetate = 10 : 1) afforded 700 mg (74%, 85% BORSM) **77** as a colorless oil.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.41 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.98 (ddd, *J* = 17.2, 10.5, 6.6 Hz, 1H), 5.43 (s, 1H), 5.10–5.00 (m, 2H), 4.04 (dd, *J* = 4.0, 3.0 Hz, 2H), 3.79 (s, 3H), 3.56 (dd, J = 9.9, 2.2 Hz, 1H), 2.44–2.34 (m, 1H), 1.72–1.64 (m, 1H), 1.19 (d, *J* = 7.1, 3H), 0.97 (d, *J* = 7.1, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 159.7, 141.6, 131.6, 130.8, 127.2, 113.8, 113.5, 101.4, 83.6, 55.3, 45.1, 38.5, 30.1, 17.2, 14.3, 10.9; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{16}H_{22}O_3$, 262.1569, found, 262.1557; IR (film): 3077, 2966, 2838, 1677, 1615, 1517, 1463, 1395, 1302, 1248 cm^{-1}; $[\alpha]_D^{20}$ -30.5 (c 1.98, CH_2Cl_2).

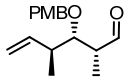


(2*S*,3*S*,4*S*)-3-(4-Methoxybenzyloxy)-2,4-dimethylhex-5-en-1-ol (78).

Acetal **77** (690 mg, 2.63 mmol, 1 equiv.) in CH_2Cl_2 (7 mL) was cooled to -78 °C. DIBAL-H (1.5 M in toluene 5.3 mL, 8.00 mmol, 3 equiv.) was added *via* a dropping funnel over 15 min. The reaction mixture was warmed to -10 °C within 5 h, diluted with CH_2Cl_2 (7 mL) and finally quenched with Na-K-tartrate (15 mL). The resulting suspension was stirred until precise phase separation was achieved (2 h). The mixture was extracted with CH_2Cl_2 (3 x 5 mL), washed with brine (15 mL),

dried over $MgSO_4$ and concentrated. Flash chromatography (hexane : ethylacetate = 3 : 1) of the residual oil yielded 650 mg (93%) of **78**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.1 Hz, 2H), 6.87 (d, *J* = 8.1 Hz, 2H), 5.96 (ddd, *J* = 18.1, 9.3, 8.2, 1H), 5.13–5.01 (m, 2H), 4.58 (d, *J* = 10.7, 1H), 4.44 (d, *J* = 10.7, 1H), 3.79 (s, 3H), 3.64–3.51 (m, 2H), 3.38 (dd, *J* = 3.8 Hz, 1H), 2.52 (m, 1H), 1.99–1.89 (m, 1H), 1.75 (t, *J* = 5.1 Hz, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 7.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 159.2, 141.8, 130.9, 129.4, 114.5, 113.8, 83.9, 73.7, 66.2, 55.3, 40.8, 37.6, 17.4, 11.2; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{16}H_{24}O_3$, 264.1725, found, 264.1719; IR (film): 3417, 3074, 2964, 1613, 1586, 1514, 1462, 1301, 1248, 1173 cm^{-1}; $[\alpha]_D^{20}$ +3.6 (c 1.96, CH_2Cl_2).



(2*R*,3*S*,4*S*)-3-(4-Methoxybenzyloxy)-2,4-dimethylhex-5-enal (12).

Method A:

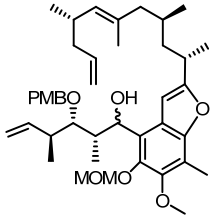
To alcohol **78** (112 mg, 0.42 mmol, 1 equiv.) in CH_2Cl_2 (2 mL) $NaHCO_3$ (125 mg, 1.48 mmol, 3.5 equiv.) and Dess-Martin periodinate (467 mg, 1.10 mmol, 2.6 equiv.) were added. The reaction mixture was stirred for 0.5 h at 0 °C, followed by 2 h at room temperature. Then a mixture of saturated aqueous $Na_2S_2O_3$ (5 mL) and saturated $NaHCO_3$ (5 mL) was added and stirred until the solution was clear. The mixture was extracted with Et_2O (3 x 10 mL), dried over $MgSO_4$, filtered and evaporated to dryness, obtaining 98 mg (89%) of a colorless oil, which was directly used in the next step.

Method B:

A 25 ml Schlenk flask was charged with oxalychloride (295 µL, 3.48 mmol, 2 equiv.) and CH_2Cl_2 (3.4 mL) and the resulting solution was cooled to -78 °C. Then DMSO (494 µL, 6.96 mmol, 4 equiv.) was added dropwise (gas outlet!). After the reaction was stirred for 1 h, alcohol **78** (0.3 M in CH_2Cl_2, 5.8 mL, 1.74 mmol, 1 equiv.) was slowly added and stirring was continued for additional 45 min. After the addition of DIPEA (1.45 mL, 10.44 mmol, 6 equiv.) a white slurry was formed and the reaction was warmed to 0 °C, hydrolyzed with saturated aqueous NH_4Cl (15 mL), extracted with CH_2Cl_2 (3 x 20), washed with brine, dried over $MgSO_4$ and filtered. The

solvent was carefully removed under reduced pressure and the residue was rapidly filtered over a small pad of silica to give 455 mg (99%) of **12**.

^{1}H-NMR (600MHz, $CDCl_3$): δ 9.62 (d, *J* = 1.4 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 2 H), 6.76 (d, *J* = 8.8 Hz, 2H), 5.76 (ddd, *J* = 17.1, 10.4, 8.2 Hz, 1H), 4.99–4.95 (m, 2H), 4.38 (d, *J* = 10.8 Hz, 1H), 4.33 (d, *J* = 10.8 Hz, 1H), 3.70 (s, 3H), 3.61 (dd, *J* = 5.7, 4.5 Hz, 1H), 2.49 (ddq, *J* = 7.2, 2.3, 1.1 Hz, 1H), 2.43–2.37 (m, 1H), 1.07 (d, *J* = 7.2 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (150MHz, $CDCl_3$): δ 204.4, 159.2, 140.3, 130.3, 129.3, 115.7, 113.7, 81.6, 73.3, 55.2, 49.2, 41.1, 17.1, 8.9; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{16}H_{22}O_3$, 262.1569, found, 262.1560; IR (film): 2971, 1722, 1613, 1586, 1514, 1462, 1345, 1302, 1248, 1174 cm^{-1}; $[\alpha]_D^{20}$ -20.9 (c 2.31, CH_2Cl_2).



(1*S*,2*S*,3*S*,4*S*)-1-(6-methoxy-5-(methoxymethoxy)-7-methyl-2-((2*S*,4*S*,8*S*,*E*)-4,6,8-trimethylundeca-6,10-dien-2-yl)benzofuran-4-yl)-3-(4-methoxybenzyloxy)-2,4-dimethylhex-5-en-1-ol (18a) and (1*R*,2*S*,3*S*,4*S*)-1-(6-Methoxy-5-(methoxymethoxy)-7-methyl-2-((2*S*,4*S*,8*S*,*E*)-4,6,8-trimethylundeca-6,10-dien-2-yl)benzofuran-4-yl)-3-(4-methoxybenzyloxy)-2,4-dimethylhex-5-en-1-ol (18b).

Method A:

Diene **16** (170 mg, 0.410 mmol, 1 equiv.) was dissolved in THF (1.5 mL, 0.3 M). After the addition of TMEDA (148 µL, 0.98 mmol, 2.4 equiv.) the solution was cooled to -40 °C and *n*-BuLi (2.5 M in hexane, 197 µL, 0.49 mmol, 1.2 equiv.) was slowly added *via* cannula. The temperature was raised to -30 °C and stirring was continued at this temperature for 1 h. The reaction mixture was cooled to -78 °C and aldehyde **12** in THF (0.5 mL) was added *via* cannula. Stirring was continued for 2 h allowing the reaction to warm to -25 °C.

The reaction was taken up in Et_2O and quenched by the addition of saturated NH_4Cl. Extraction was done by Et_2O (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification by HPLC (hexane : ethylacetate = 20 : 1) afforded 127 mg of pure **18a** and 81 mg of pure **18b**, (208 mg, 75%, **18a** : **18b** = 1.5 : 1).

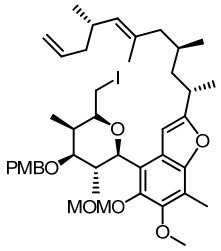
Method B:

$NaBH_4$ (125 mg, 3.33 mmol, 15 equiv.) was added to dry MeOH (2 mL) at 0 °C. Ketone **21** (150 mg, 0.22 mmol, 1 equiv.) in MeOH (0.5 mL) was added *via* syringe. The reaction was allowed to warm to ambient temperature and stirred for 6 h. TLC analysis showed complete consumption of the starting material and the reaction was taken up in Et_2O (40 mL). HCl (0.5 N, 10 mL) was added and stirring was continued for 10 min. The mixture was neutralized by adding saturated $NaHCO_3$ and the phases were separated. The aqueous layer was extracted with Et_2O (3 x 10 mL), the organic phases were dried over $MgSO_4$ and concentrated. Purification by column chromatography (hexane : ethylacetate = 20 : 1) afforded 92 mg (61%, **18a** : **18b** = 1 :3).

18b: ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.34 (br, 1H), 6.04 (ddd, *J* = 17.5, 10.0, 7.6 Hz, 1H), 5.75 (ddt, *J* = 17.1, 10.1, 7.0 Hz, 1H), 5.18–4.84 (m, 8H), 4.73 (d, *J* = 11.0 Hz, 1H), 4.67 (d, *J* = 11.0 Hz, 1H), 3.91 (dd, *J* = 8.5, 1.6 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.52 (s, 3H), 3.04–2.93 (m, 1H), 2.60–2.50 (m, 1H), 2.50–2.49 (m, 1H), 2.39 (s, 3H), 2.07 (dd, *J* = 12.5, 4.8 Hz, 1H), 2.03–1.97 (m, 2H), 1.72 (dd, *J* = 12.5, 8.7 Hz, 1H), 1.69–1.61 (m, 1H), 1.61–1.42 (m, 4H), 1.53 (d, *J* = 1.2 Hz, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.1 Hz, 3H), 0.64 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 164.3, 159.0, 147.5, 144.5, 142.7, 137.6, 132.5, 132.3, 131.7, 129.2, 115.3, 114.4, 114.0, 113.7, 100.1, 100.0, 82.5, 74.1, 60.7, 57.6, 55.2, 47.9, 43.1, 42.0, 41.3, 40.9, 32.5, 31.3, 28.2, 20.8, 19.3, 19.0, 17.1, 16.1, 10.3, 9.1; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{42}H_{60}O_7$, 676.4339, found, 676.4341; IR (film): 3490, 2959, 1640, 1613 , 1455, 1393, 1301, 1247, 1113 cm^{-1}; $[\alpha]_D^{20}$ +5.7 (c 1.62, CH_2Cl_2).

18a: ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.56 (s, 1H), 5.85 (ddd, *J* = 18.2, 9.3, 8.2 Hz, 1H), 5.75 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.27 (dd, *J* = 6.3, 4.6 Hz, 1H), 5.10 (s, 2H), 5.10–4.89 (m, 5H), 4.51 (d, *J* = 10.5 Hz, 1H), 4.28 (d, *J* = 10.5 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.56 (s, 3H), 3.42 (d, *J* = 4.29 Hz, 1H), 3.22 (dd, *J* = 7.7, 2.7 Hz, 1H), 3.01–2.90

(m, 1H), 2.59–2.48 (m, 1H), 2.48–2.37 (m, 2H), 2.40 (s, 3H), 2.07–1.97 (m, 3H), 1.74 (dd, *J* = 12.7, 8.3 Hz, 1H), 1.69–1.59 (m, 1H), 1.55 (s, 3H), 1.54–1.39 (m, 2H), 1.23 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 7.1 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 164.2, 159.0, 150.2, 147.5, 144.0, 142.0, 137.6, 132.5, 132.3, 131.1, 129.2, 125.5, 122.6, 115.3, 114.3, 113.7, 101.1, 99.9, 85.4, 73.3, 60.7, 57.6, 55.3, 48.0, 42.9, 42.0, 41.4, 41.1, 32.5, 31.2, 28.2, 20.8, 19.3, 18.9, 16.8, 26.1, 9.3, 9.1; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{42}H_{60}O_7$, 676.4339, found, 676.4344; IR (film): 3490, 2959, 1640, 1613, 1514, 1455, 1393, 1301, 1247, 1113 cm^{-1}; $[\alpha]_D^{20}$ +41.3 (c 1.27, CH_2Cl_2).

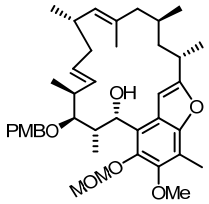


4-((2*R*,3*R*,4*R*,5*R*,6*R*)-6-(Iodomethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydro-2H-pyran-2-yl)-6-methoxy-5-(methoxymethoxy)-2-((3*S*,7*S*,*E*)-3,5,7-trimethyldeca-5,9-dienyl)benzofuran (19).

A solution of **18b** (5 mg, 0.007 mmol, 1 equiv.) in CH_2Cl_2 (1 mL) was cooled to -78 °C. 2,6-Di-*tert*-butyl-4-methylpyridine (2 mg, 0.012 mmol, 1.6 equiv.) was added, followed by I_2 (3 mg, 0.011 mmol, 1.5 equiv.). The temperature was raised to -10°C over 4 h and the reaction mixture was diluted with Et_2O (30 mL) and hydrolyzed with $NaHCO_3$ / $Na_2S_2O_3$ (10 mL). The phases were separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure. Flash chromatography (hexane : ethylacetate = 5 : 1) gave 3 mg (50%) of **19**.

^{1}H- NMR (600MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 0.89 (d, *J* = 7.2 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H), 0.72 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (150MHz, $CDCl_3$): δ 164.2, 159.3, 150.6, 147.3, 144.2, 137.6, 132.5, 132.3, 130.3, 129.6, 121.7, 121.6, 115.3, 113.8, 100.6, 83.5, 79.5, 78.8, 70.0, 60.8, 57.9, 55.3, 48.1, 42.9, 42.7, 42.0, 35.4, 33.4, 32.5, 31.6, 31.1, 28.1, 22.6,

20.8, 19.4, 18.8, 16.2, 14.1, 13.1, 9.1, 5.4, 5.2; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{42}H_{59}O_7I$, 802.3305, found, 802,3301; IR (film): 2924, 1640, 1613, 1513, 1455, 1372, 1247, 1112 cm^{-1}; $[\alpha]_D^{20}$ +16.7 (c 0.30, CH_2Cl_2).



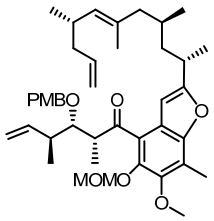
Macrocycle 20a.

Compound **18a** (57 mg, 0.083 mmol, 1 equiv.) was dissolved in degassed CH_2Cl_2 (30 mL, 3 mM) in a 250 mL Schlenk flask. The solution was heated to reflux (45°C) and Grubbs' II catalyst (11 mg, 0.012 mmol, 0.15 equiv.) was added in degassed CH_2Cl_2 (14 mL, 1 mM) over 16 h *via* syringe pump.

After completion of addition the mixture was stirred for another 2 h. The temperature was lowered to room temperature and air was bubbled through the solution in order to destroy excess catalyst. The solvent was evaporated and purification by column chromatography (hexane : ethylacetate = 10 : 1) afforded 25 mg (46%) of macrocycle **20a**.

^{1}H-NMR (600MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.43 (s, 1H), 5.45 (dd, *J* = 15.5, 8.1 Hz, 1H), 5.34–5.27 (m, 1H), 5.19–5.15 (br, 1H), 5.15 (s, 2H), 4.90 (d, *J* = 9.5 Hz, 1H), 4.45 (d, *J* = 10.8 Hz, 1H), 4.33 (d, *J* = 10.8 Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 3.60 (s, 3H), 3.54–3.49 (br, 1H), 3.29 (dd, *J* = 4.72 Hz, 1H), 3.05–2.96 (m, 1H), 2.55–2.46 (br, 1H), 2.41 (s, 3H), 2.31–2.42 (m, 1H), 2.16–2.10 (m, 1H), 2.09–2.03 (m, 1H), 1.98 (dd, *J* = 14.7, 4.3 Hz, 1H), 1.88 (dd, *J* = 14.7, 6.3 Hz, 1H), 1.86–1.81 (m, 1H), 1.73–1.63 (m, 2H), 1.62 (s, 3H), 1.58–1.49 (m, 1H), 1.28 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (150MHz,$CDCl_3$): δ 163.8, 158.9, 150.2, 147.5, 144.8, 133.8, 132.2, 131.5, 130.9, 129.3, 127.8, 124.6, 121.6, 114.7, 113.6, 101.2, 100.3, 83.6, 74.4, 73.0, 60.7, 57.8, 55.2, 45.8, 42.5, 42.0, 41.3, 40.4, 32.0, 31.6, 29.4, 20.8, 20.3, 19.5, 19.1, 19.0, 10.9,

9.1; HRMS (ESI) (m/z): $[M]^+$ calcd for $C_{40}H_{56}O_7$, 648.4026, found, 648.4051; IR (film): 3676, 2926, 1700, 1653, 1612, 1514, 1456, 1301, 1248, 1160, 1113 cm^{-1}; $[\alpha]_D^{20}$ +0.6 (c 0.85, CH_2Cl_2).



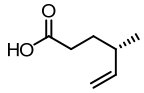
(2*R*,3*S*,4*S*)-1-(6-Methoxy-5-(methoxymethoxy)-7-methyl-2-((2*S*,4*S*,8*S*,*E*)-4,6,8-trimethylundeca-6,10-dien-2-yl)benzofuran-4-yl)-3-(4-methoxybenzyloxy)-2,4-dimethylhex-5-en-1-one (21).

A mixture of alcohols **18a** and **18b** (160 mg, 0.23 mmol, 1 equiv.) was dissolved in DMSO (1 mL), IBX (193 mg, 0.69 mmol, 2.9 equiv.) was slowly added and the resulting clear solution was stirred for 50 min.

Dilution with Et_2O : hexane = 1 : 1 (50 mL) and H_2O (15 mL) caused precipitation of remaining IBX, which was removed by filtration over a small plug of Celite. The aqueous phase was extracted with Et_2O (3 x 10 mL), the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (hexane : ethylacetate from 20 : 1 to 10 : 1) afforded 152 mg (96%) of pure ketone **21**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.18 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.52 (s, 1H), 5.82 (ddd, *J* = 17.6, 10.1, 6.9 Hz, 1H), 5.77–5.68 (m, 1H), 5.13 (d, *J* = 5.3 Hz, 1H), 5.06 (d, *J* = 5.3 Hz, 1H), 5.02–4.84 (m, 4H), 4.76 (d, *J* = 17.2 Hz, 1H), 4.32 (d, *J* = 10.6 Hz, 1H), 4.28 (d, *J* = 10.6 Hz, 1H), 3.96–3.88 (m, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.63 (dd, *J* = 5.5, 5.0 Hz, 1H), 3.41 (s, 3H), 3.02–2.91 (m, 1H), 2.45 (s, 3H), 2.44–2.33 (m, 2H), 2.05–1.96 (m, 3H), 1.72 (dd, *J* = 12.8, 8.5 Hz, 1H), 1.68–1.59 (m, 1H), 1.53 (s, 3H), 1.51–1.44 (m, 2H), 1.31 (d, *J* = 6.8 Hz, 3H), 1.23 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 7.1 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.77 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 205.9, 166.6, 158.9, 150.1, 147.7, 144.9, 141.2, 137.6, 132.5, 132.2, 131.0, 128.9, 123.8, 123.1, 115.3, 114.4, 113.6, 101.0, 100.4, 84.2, 73.8, 61.0, 58.0, 55.2, 49.4, 48.0, 42.8,

42.1, 42.0, 32.5, 31.3, 29.7, 28.2, 20.8, 19.2, 18.9, 17.6, 16.1, 10.8, 9.5; HRMS (ESI) (m/z): $[M+Na]^+$ calcd for $C_{42}H_{58}O_7$, 697.4080, found, 697.4089; IR (film): 2956, 1673, 1588, 1513, 1454, 1413, 1384, 1337, 1302, 1247, 1161, 1032 cm^{-1}; $[\alpha]_D^{20}$ +42.0 (c 1.64, CH_2Cl_2).



(*S*)-4-Methylhex-5-enoic acid (30).

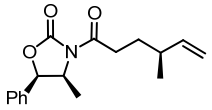
β-(-)-Citronellene (3.8 g, 27.48 mmol, 1.0 equiv.) and sodium acetate (2.4 g, 28.85 mmol, 1.05 equiv.) were dissolved in CH_2Cl_2 (80 mL) and cooled to -20 °C. *m*-CPBA (75%, 6.64 g, 28.85 mmol, 1.05 equiv.) was added in small portions and stirring was continued for 1.5 h, allowing the suspension to warm to 0 °C. The reaction was quenched by careful addition of saturated aqueous $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic fractions were washed with 1 N NaOH (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*.

The crude epoxide was dissolved in Et_2O (70 mL), cooled to 0 °C and H_5IO_6 (6.26 g, 27.48 mmol, 1.0 equiv.) in THF (30 mL) was added within 25 min. Stirring was continued until TLC analysis showed complete consumption of the starting material. The mixture was diluted with Et_2O (500 mL), H_2O (300 mL) was added and the phases were separated. The organic layer was washed twice with brine, dried over $MgSO_4$ and evaporated to dryness.

The crude aldehyde was dissolved in 180 mL *t*-BuOH (0.15 M), treated with 2-methyl-2-butene (1 mL / mmol, 27 mL), and cooled to 10 °C. $NaClO_2$ (46.5 g, 412.20 mmol, 15 equiv.) and 46.5 g NaH_2PO_4 were dissolved in H_2O (270 mL, 1.5 M), transferred to a 500 mL dropping funnel, and added over a period of 30 min. After 1.5 h at 0 °C TLC analysis showed complete consumption and the reaction mixture was diluted with Et_2O (400 mL). The organic layer was extracted with 1N NaOH (3 x 70 mL), washed with Et_2O (3 x 30 mL) and acidified with 1 N HCl. The aqueous phase was extracted with CH_2Cl_2 (4 x 50 mL), the combined organic extracts were washed with brine (60 mL) and dried over $MgSO_4$. Evaporation of the solvent gave pure acid **30** (2.56 g, 73% 3 steps).

^{1}H-NMR (400MHz, $CDCl_3$): δ 5.64 (ddd, *J* = 17.4, 9.9, 7.7 Hz, 1H), 5.02-5.94 (m, 2H), 2.35 (dt, *J* = 8.7, 6.5 Hz, 2 H), 2.21-2.12 (m, 1H), 1.73-1.55 (m, 2H), 1.02 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR

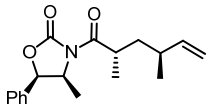
(100MHz, $CDCl_3$): δ 180.1, 143.2, 113.8, 37.4, 31.9, 31.1, 20.1; IR (film): 3853-2932, 2966, 1711, 1641, 1456, 1420, 1376, 1280, 1217, 1110 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_7H_{12}O_2$, 128.0837, found, 128.0839; $[\alpha]_D^{20}$+11.5 (*c* 1.00, CH_2Cl_2).



(4*S*,5*R*)-4-Methyl-3-((S)-4-methylhex-5-enoyl)-5-phenyloxazolidin-2-one (33).

A mixture of acid **30** (200 mg, 1.56 mmol, 1.0 equiv.), (4*S*, 5*R*)-4-methyl-5-phenyloxazolidin-2-one (304 mg, 1.72 mmol, 1.1 equiv.), DIC (151 µL, 1.72 mmol, 1.1 equiv.) and DMAP (190 mg, 1.56 mmol, 1.0 equiv.) in CH_2Cl_2 (8 mL) was stirred at ambient temperature overnight. The reaction was diluted with EE (100 mL), quenched with 1% HCl (2 mL) and washed with brine (20 mL). The organic layer was dried over $MgSO_4$, concentrated and the residue was purified by flash chromatography (hexane : ethylacetate = 5 :1) to furnish **33** (367 mg, 82%) as a white solid.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.45-7.34 (m, 3H), 7.33-7.28 (m, 2H), 5.69 (ddd, *J* = 17.9, 10.6, 7.5 Hz, 1H), 5.65 (d, *J* =7.3 Hz, 1H), 5.05-4.94 (m, 2H), 4.80-4.71 (m, 1H), 3.04-2.85 (m, 2H), 2.28-2.16 (m, 1H), 1.74-1.65 (m, 2H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 173.2, 153.0, 143.6, 133.4, 128.7, 125.6, 113.6, 78.9, 54.7, 37.4, 33.5, 30.8, 20.2, 14.5; IR (film): 3070, 2962, 1783, 1699, 1640, 1347, 1197, 1122, 1090, 1067, 1040 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{17}H_{21}O_3N$, 287.1521, found, 287.1519; $[\alpha]_D^{20}$-27.6 (*c* 0.95, CH_2Cl_2).

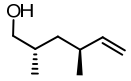


(4*S*,5*R*)-3-((2*S*,4*S*)-2,4-Dimethylhex-5-enoyl)-4-methyl-5-phenyloxazolidin-2-one (79).

A solution of compound **33** (60 mg, 0.208 mmol, 1.0 equiv.) in THF (1.4 mL) was cooled to -78 °C and treated with LHMDS (1 M in THF, 229 µL, 0.229 mmol, 1.1 equiv.). After 1 h at -78 °C, MeI

(40 µL, 0.626 mmol, 3 equiv.) was added and the solution was allowed to warm to room temperature overnight. The solution was quenched by the addition of saturated aqueous NH_4Cl (0.2 mL), diluted with CH_2Cl_2 (50 mL) and washed with brine (10 mL). The organic extracts were dried over $MgSO_4$, concentrated *in vacuo* and purified by flash chromatography (hexane : ethylacetate from 10 : 1 to 5 : 1) to afford 46 mg (74%, dr = 10:1 as determined by ^{1}H-NMR) of **79** as an oil.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.44-7.34 (m, 3H), 7.33-7.28 (m, 2H), 5.69 (ddd, *J* = 17.9, 9.7, 8.0 Hz, 1H), 5.63 (d, *J* =7.3 Hz, 1H), 4.98-4.91 (m, 2H), 4.79-4.71 (m, 1H), 3.83-3.73 (m, 1H), 2.23-2.12 (m, 1H), 1.84 (ddd, *J* = 13.6, 8.7, 6.0 Hz, 1H), 1.37 (ddd, *J* = 13.8, 8.3, 5.6 Hz, 1H), 1.19 (d, *J* = 6.8 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 176.9, 152.5, 144.1, 133.4, 128.7, 125.6, 113.1, 78.8, 54.9, 40.0, 36.1, 35.7, 20.3, 17.8, 14.4; IR (film): 2967, 1783, 1701, 1456, 1343, 1247, 1196, 1121, 1068 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{18}H_{23}O_3N$, 301.1678, found, 301.1680; $[\alpha]_D^{20}$+5.7 (*c* 1.20, CH_2Cl_2).

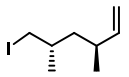


(2*S*,4*S*)-2,4-Dimethylhex-5-en-1-ol (34).

Oxazolidinone **79** (70 mg, 0.232 mmol, 1.0 equiv.) in THF (2.5 mL) was treated with LAH (18 mg, 0.487 mmol, 2.1 equiv.) at 0 °C. The reaction mixture was quenched after 1 h by slow addition of ethylacetate, diluted with Et_2O (50 mL) and washed with 1% HCl (10 mL). The aqueous layer was extracted with Et_2O (3 x 10 mL), and the combined organic fractions were washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (pentane : diethylether = 3 : 1) afforded alcohol **34** as a colorless oil (23 mg, 80%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 5.71 (ddd, *J* = 17.4, 10.1, 7.5 Hz, 1H), 5.01-4.89 (m, 2H), 3.69-3.57-3.50 (m, 1H), 3.45-3.38 (m, 1H), 2.30-2.19 (m, 1H), 1.76-1.66 (m, 1H), 1.25 (t, *J* = 5.4 Hz, OH), 1.32 (ddd, *J* = 13.8, 7.0, 6.6 Hz, 1H), 1.19-1.11 (m, 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 145.0, 112.4, 68.2, 40.2, 35.2, 33.2, 20.1, 16.9; IR (film): 3356,

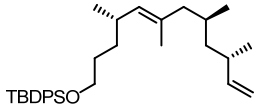
2959, 2925, 2361, 1458 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_8H_{16}O$, 128.1201, found, 128.1203; $[\alpha]_D^{20}$+1.1 (*c* 1.00, CH_2Cl_2).



(3*S*,5*S*)-6-Iodo-3,5-dimethylhex-1-ene (28).

Alcohol **34** (4.50 g, 35.09 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (115 mL), cooled to 0 °C and treated with Et_3N (7.29 mL, 52.62 mmol, 1.5 equiv.). After 5 min MsCl (8.3 ml, 49.13 mmol, 1.4 equiv.) was added and stirring was continued for 30 min. The solution was poured onto H_2O (100 mL), extracted with CH_2Cl_2 (3 x 50 mL), washed with brine and dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the crude mesylate was immediately dissolved in acetone (170 mL). NaI (36.8 g, 245 mmol, 7 equiv.) was added and the solution was refluxed for 4 h. The mixture was cooled to room temperature, filtered over Celite and saturated aqueous $Na_2S_2O_3$ (40 mL) was added. The solution was diluted with H_2O (200 mL) and the aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were dried over $MgSO_4$, filtered and evaporated to dryness. Purification of the crude product by column chromatography (pentane : diethylether = 10 : 1) yielded 7.2 g (86%) of pure iodide **28**.

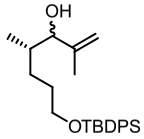
^{1}H-NMR (400MHz, $CDCl_3$): δ 5.66 (ddd, *J* = 17.5, 10.0, 7.6 Hz, 1H), 5.01-4.91 (m, 2H), 3.25 (dd, *J* = 9.7, 4.2 Hz, 1H), 3.18 (dd, *J* = 9.9, 5.8 Hz, 1H), 2.24-2.12 (m, 1H), 1.50-1.41 (m, 1H), 1.35-1.27 (m, 1H), 1.24-1.16 (m, 1H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.96 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 144.2, 113.0, 43.3, 35.4, 31.9, 21.1, 20.5, 18.2; IR (film): 2959, 2925, 2361, 1456, 1377, 1192, 1120 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_8H_{15}I$, 238.0218, found, 238.0223; $[\alpha]_D^{20}$+10.1 (*c* 1.20, CH_2Cl_2).



***tert*-Butyldiphenyl((4*S*,8*S*,10*S*,*E*)-4,6,8,10-tetramethyldodeca-5,11-dienyloxy)silane (35).**

A mixture of flame-dried $ZnCl_2$ (51 mg, 0.38 mmol, 1.87 equiv.) and alkyliodide **28** (90 mg, 0.38 mmol, 1.87 equiv.) in degassed Et_2O (3 mL) was cooled to -78 °C and *t*-BuLi (1.7 M in pentane, 443 µL, 0.75 mmol, 3.74 equiv.) was added *via* syringe in one portion. The solution was placed on an ice-bath and stirred for 1 h. To this white suspension, vinyliodide **27** (99 mg, 0.201 mmol, 1.0 equiv.) and $Pd(PPh_3)_4$ (12 mg, 0.010 mmol, 0.05 equiv.) in degassed THF (2 mL) were added dropwise *via* cannula. The suspension cleared within 2 h at 0 °C, whereas TLC analysis showed complete consumption of the vinyliodide. The mixture was treated with saturated aqueous NH_4Cl, extracted with Et_2O and the organic layer was washed with brine. Purification by column chromatography (hexane : ethylacetate = 50 : 1) gave alkene **35** (90 mg, 95%) as an oil.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.70-7.64 (m, 4H), 7.44-7.34 (m, 6H), 5.70 (ddd, *J* = 17.3, 10.0, 7.5 Hz, 1H), 4.99-4.87 (m, 2H), 4.85 (d, *J* = 9.3 Hz, 1H), 3.63 (t, *J* = 6.4 Hz, 2H), 2.36-2.26 (m, 1H), 2.27-2.19 (m, 1H), 2.06-1.97 (m, 1H), 1.68-1.60 (m, 2H), 1.60-1.46 (m, 2H), 1.51 (d, *J* = 1.1 Hz, 3H), 1.42-1.32 (m, 1H), 1.28-1.19 (m, 1H), 1.18-1.09 (m, 2H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 145.4, 135.6, 134.2, 133.0, 132.4, 129.4, 127.5, 112.0, 64.2, 47.8, 44.2, 35.3, 33.9, 32.1, 30.7, 28.1, 26.9, 21.4, 20.1, 19.7, 19.2, 16.0; IR (film): 2957, 2861, 1456, 1428, 138, 1112 cm^{-1}; HRMS (ESI) (*m/z*): $[M\text{-}t\text{Bu}]^+$ calcd for $C_{28}H_{39}OSi$, 419.2770, found, 419.2772; $[\alpha]_D^{20}$+8.2 (*c* 1.30, CH_2Cl_2.



(4*S*)-7-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethylhept-1-en-3-ol (29a) and (3*R*,4*S*)-7-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethylhept-1-en-3-ol (29)

Method A:

A Schlenk flask was charged with anhydrous $CrCl_2$ (108 mg, 0.879 mmol, 4 equiv.) and $NiCl_2$ (1 mg, 0.009 mmol, 0.04 equiv.) and cooled to 0 °C. To this mixture degassed DMF (3.3 mL) was added and stirring was continued for 10 min at 0 °C. The dark-green solution was warmed to ambient temperature and aldehyde **36** (78 mg, 0.219 mmol, 1.0 equiv.) in 0.5 mL of degassed DMF, followed by 2-bromopropene (38 µL, 0.439 mmol, 2 equiv.) was added. The reaction

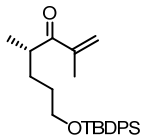
mixture was stirred for 3 h until TLC analysis revealed full consumption of the starting material. Finally the reaction was quenched by the addition of diethylether (5 ml) and water (5 mL). The aqueous phase was extracted with Et_2O (3 x 10 mL). The combined organic fractions were dried over $MgSO_4$ and the solvent was removed in *vacuo*. Purification of the residue by HPLC (hexane : ethylacetate = 10 : 1) afforded 40 mg of alcohol **29a** and 34 mg of alcohol **29b** (74 mg, dr = 1.4 : 1, 86% for both diastereomers).

Method B:

Ketone **80** (250 mg, 0.63 mmol, 1 equiv.) in MeOH (10 mL) was treated with $CeCl_3$ (710 mg, 1.90 mmol, 3 equiv.) and $NaBH_4$ (70 mg, 1.90 mmol, 3 equiv.) at 0 °C. The reaction was quenched after 5 min by the addition of 1% HCl (1 mL), diluted with H_2O (50 mL) and extracted with Et_2O (4 x 20 mL). The combined organic fractions were washed with brine (20 mL), dried over $MgSO_4$ and concentrated. The diastereomeric alcohols (250 mg, **29a** : **29b** = 2 : 1 , 99% for both diastereomers) were separated as described above.

29a: ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.70-7.65 (m, 4H), 7.45-7.35 (m, 6H), 4.92-4.85 (m, 2H), 3.76 (dd, *J* = 7.3, 3.3 Hz, 1 H), 3.67 (t, *J* = 6.3 Hz, 2H), 1.72-1.66 (m, 1H), 1.71-1.66 (m, 1H), 1.70 (s, 3H), 1.68-1.56 (m, 1H),1.56-1.44 (m, 1H), 1.18-1.09 (m, 1H), 1.05 (s, 9H), 0.82 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 146.6, 135.6, 134.1, 129.5, 127.6, 112.3, 80.8, 64.3, 35.6, 30.1, 27.7, 26.9, 19.2, 17.5, 16.2; IR (film): 3446, 3070, 2930, 2858, 1652, 1558, 1472, 1428, 1387, 1112, 900 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{21}H_{27}O_2Si$, 339.1780, found, 339.1778; $[\alpha]_D^{20}$-5.0 (*c* 1.2, CH_2Cl_2).

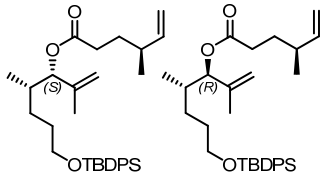
29b: ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69-7.64 (m, 4H), 7.45-7.35 (m, 6H), 4.95-4.86 (m, 2H), 3.86-3.81 (br, 1H), 3.65 (t, *J* = 6.3 Hz, 2H), 1.68(s, 3H), 1.67-1.52 (m, 2H), 1.64-1.57 (m, 1H), 1.51-1.42 (m, 1H),1.23-1.10 (m, 1H), 1.05 (s, 9H), 0.88 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 146.6, 135.6, 134.1, 129.5, 127.6, 112.3, 80.8, 64.3, 35.6, 30.1, 27.7, 26.9, 19.2, 17.5, 16.2; IR (film): 3442, 3071, 2932, 2858, 1653, 1559, 1472, 1428, 1389, 1361, 1112, 900 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{21}H_{27}O_2Si$, 339.1780, found, 339.1778; $[\alpha]_D^{20}$-6.6 (*c* 1.2, CH_2Cl_2).



(*S*)-7-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethylhept-1-en-3-one (80).

A solution of alcohol **29b** (335 mg, 0.85 mmol, 1.0 equiv.) in CH_2Cl_2 (4 mL) was cooled to -5 °C. Et_3N (351 µL, 2.53 mmol, 3 equiv.), followed by SO_3·Pyr (403 mg, 2.53 mmol, 3 equiv.) in DMSO (4 mL) were added dropwise. The mixture was stirred for 1.5 h at -5°C and quenched with aqueous 1 M $KHSO_4$ solution (1 mL). The phases were partitioned between brine and Et_2O (1 : 1, 60 mL) and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic fractions were concentrated to 5 mL under reduced pressure, filtered over a plug of silica and excess solvent was removed *in vacuo* to afford ketone **80** (331 mg, 99%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69-7.62 (m, 4H), 7.45-7.34 (m, 6H), 5.89 (br, 1H), 5.73 (br, 1H), 3.63 (t, *J* = 6.2 Hz, 2H), 3.26-3.15 (m, 1H), 1.87 (s, 3H), 1.78-1.68 (m, 1H), 1.56-1.40 (m, 3H), 1.06 (d, *J* = 7.1 Hz, 3H), 1.04 (s, 9H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 206.1, 144.1, 135.6, 134.0, 129.5, 127.6, 123.9, 63.7, 39.2, 30.2, 30.1, 26.9, 19.2, 18.0, 17.5; IR (film): 3071, 2931, 2858, 1675, 1629, 1589, 1461, 1428, 1378, 1189, 1112 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{21}H_{25}O_2Si$, 337.1624, found, 337.1617; $[\alpha]_D^{20}$+8.3 (*c* 1.15, CH_2Cl_2).



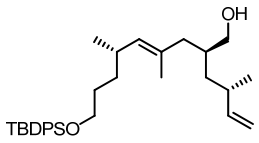
(*S*)-((3*S*,4*S*)-7-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethylhept-1-en-3-yl) 4-methylhex-5-enoate (37a) and (*S*)-((3*R*,4*S*)-7-(*tert*-butyldiphenylsilyloxy)-2,4-dimethylhept-1-en-3-yl) 4-methylhex-5-enoate (37b).

A mixture of acid **30** (65 mg, 0.507 mmol, 1.0 equiv.), alcohol **29** (221 mg, 0.557 mmol, 1.1 equiv.), DIC (49 µL, 0.557 mmol, 1.1 equiv.) and DMAP (62 mg, 0.507 mmol, 1.0 equiv.) in CH_2Cl_2 (4 mL) was stirred at ambient temperature overnight. The reaction was diluted with CH_2Cl_2 (70

mL), quenched with 1% HCl (10 mL) and washed with brine (20 mL). The organic layer was dried over $MgSO_4$, concentrated and the residue was purified by flash chromatography (hexane : ethylacetate = 50 : 1) to furnish ester **37a** or **37b** (236 mg, 92%).

37a: ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69-7.64 (m, 4H), 7.45-7.35 (m, 6H), 5.62 (ddd, *J* = 17.3, 10.0, 7.6 Hz, 1H), 4.98-4.90 (m, 4H), 4.95 (d, *J* = 7.1 Hz, 1H), 3.64 (dt, *J* = 6.0, 1.9 Hz, 2H), 2.36-2.22 (m, 2H), 2.18-2.06 (m, 1H), 1.81-1.72 (m, 1H), 1.69 (s, 3H), 1.68-1.55 (m, 4H), 1.53-1.42 (m, 1H), 1.15-1.06 (m, 1H), 1.05 (s, 9H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 173.1, 143.5, 142.2, 135.6, 134.1, 129.5, 127.6, 113.9, 113.6, 81.4, 64.1, 37.5, 34.2, 32.3, 31.4, 30.0, 27.9, 26.9, 20.1, 19.2, 18.4, 15.8; IR (film): 3072, 2931, 2859, 1737, 1653, 1462, 1428, 1378, 1254, 1178, 1111 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{28}H_{37}O_3Si$, 449.2512, found, 449.2519; $[\alpha]_D^{20}$-0.6 (*c* 0.90, CH_2Cl_2).

37b: ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.68-7.63 (m, 4H), 7.45-7.34 (m, 6H), 5.64 (ddd, *J* = 17.4, 10.1, 7.6 Hz, 1H), 5.02 (d, *J* = 6.3 Hz, 1H), 5.00-4.92 (m, 2H), 4.91-4.86 (m, 2H), 3.64 (t, *J* = 6.3 Hz, 2H), 2.31 (ddd, *J* = 7.0, 8.7, 3.3 Hz, 2H), 2.20-2.08 (m, 1H), 1.80-1.70 (m, 1H), 1.69 (s, 3H), 1.69-1.57 (m, 2H), 1.57-1.48 (m, 2H), 1.47-1.37 (m, 1H), 1.20-1.10 (m, 1H), 1.04 (s, 9H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 173.0, 143.5, 142.3, 135.6, 134.0, 129.5, 127.6, 113.6, 113.1, 80.3, 63.9, 37.5, 34.3, 32.3, 31.4, 30.0, 29.2, 26.8, 20.1, 19.2, 18.7, 14.5; IR (film): 3072, 2933, 2858, 1736, 1428, 1379, 1176, 1112 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{28}H_{37}O_3Si$, 449.2512, found, 449.2517; $[\alpha]_D^{20}$+4.0 (*c* 1.05, CH_2Cl_2).



(2*S*,6*S*,*E*)-9-(*tert*-Butyldiphenylsilyloxy)-4,6-dimethyl-2-((*S*)-2-methylbut-3-enyl)non-4-en-1-ol (39).

Freshly prepared LDA (1 M in THF, 0.49 mL, 0.49 mmol, 1.25 equiv.) was cooled to -78 °C and freshly distilled HMPA (120 µL) was added *via* syringe. After 5 min ester **37a** (190 mg, 0.374 mmol, 1.0 equiv.) was added as a solution in THF (1 mL). After 20 min TBSCl (4 M in THF, 103 µL, 0.41 mmol, 1.1 equiv.) was added to the reaction mixture and stirring was continued for 20 min

at -78 °C. The solution was allowed to warm to ambient temperature and refluxed for 2 h. The reaction mixture was diluted at room temperature by the addition of pentane : Et_2O (1 : 1, 70 mL) and washed with brine (30 mL). The aqueous layer was extracted with Et_2O (3 x 15 mL), the combined organic fractions were dried over $MgSO_4$ and the solvent was removed *in vacuo*.

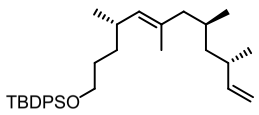
The crude TBS-ester was dissolved in HMPA (1 mL) followed by the addition of $KHCO_3$ (56 mg, 0.562 mmol, 1.5 equiv.) and KF·H_2O (33 mg, 0.562 mmol, 1.5 equiv.). After 30 min MeI (47 µL, 0.749 mmol, 2.0 equiv.) was added and stirring was continued over night. The reaction mixture was partitioned between Et_2O (50 mL) and H_2O (20 mL), the aqueous layer was extracted with Et_2O (2 x 10 mL) and the organic fraction was dried over $MgSO_4$. The mixture was filtered and concentrated to about 5 mL.

The flask was transferred to an ice-bath and LAH (30 mg, 0.785 mmol, 2.1 equiv.) was added. After 30 min at 0 °C the reaction mixture was quenched by the slow addition of ethylacetate, diluted with Et_2O (50 mL) and washed with 1% HCl (20 mL). The aqueous layer was extracted with Et_2O (3 x 20 mL), the combined organic fractions were washed with brine (30 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by column chromatography (hexane : ethylacetate from 10 : 1 to 5 : 1) afforded alcohol **39** as a colorless oil (138 mg, 63%, dr = 5 : 1 as determined by ^{1}H-NMR).

***S*-39:** ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69-7.64 (m, 4H), 7.44-7.35 (m, 6H), 5.66 (ddd, *J* = 17.2, 10.1, 8.1 Hz, 1H), 5.01-4.86 (m, 2H), 4.93 (d, *J* = 10.3 Hz, 1H), 3.63 (t, *J* = 6.4 Hz, 2H), 3.50-3.45 (m, 2H), 2.37-2.27 (m, 1H), 2.27-2.17 (m, 1H), 2.01 (dd, *J* = 13.3, 8.7, 1H), 1.92 (dd, *J* = 13.5, 8.7 Hz, 1H), 1.76-1.66 (m, 1H), 1.56 (d, *J* = 1.3 Hz, 3H), 1.56-1.46 (m, 2H), 1.41-1.34 (m, 1H), 1.39-1.30 (m, 1H), 1.26-1.20 (m, 1H), 1.20-1.12 (m, 1H), 1.05 (s, 9H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 144.7, 135.6, 134.2, 133.5, 132.4, 129.5, 127.6, 112.8, 66.3, 64.1, 42.4, 38.5, 35.9, 35.7, 33.7, 32.2, 30.6, 26.9, 21.1, 21.0, 19.2, 16.2; IR (film): 3394, 3072, 2930, 1639, 1590, 1453, 1387, 1112 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{28}H_{39}O_2Si$, 435.2719, found, 435.2722; $[\alpha]_D^{20}$+7.9 (*c* 1.00, CH_2Cl_2).

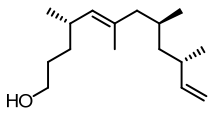
***R*-39:** ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69-7.64 (m, 4H), 7.45-7.35 (m, 6H), 5.63 (ddd, *J* = 17.4, 10.0, 7.7 Hz, 1H), 5.01-4.88 (m, 3H), 3.63 (t, *J* = 6.4 Hz, 2H), 3.59-3.45 (m, 2H), 2.38-2.28 (m, 1H), 2.31-2.19 (m, 1H), 2.02 (dd, *J* = 13.4, 8.1, 1H), 1.93 (dd, *J* = 13.4, 6.6 Hz, 1H), 1.79-1.69 (m, 1H), 1.59-

1.56 (m, 2H), 1.57 (s, 3H), 1.43-1.33 (m, 1H), 1.30-1.18 (m, 3H), 1.05 (s, 9H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 144.7, 135.6, 134.2, 133.5, 132.6, 129.5, 127.6, 112.9, 65.9, 64.1, 43.2, 38.1, 35.7, 35.6, 33.7, 32.1, 30.6, 26.9, 21.3, 21.1, 19.2, 16.2; IR (film): 3356, 3072, 2930, 2859, 1640, 1590, 1472, 1428, 1388, 1112 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{28}H_{39}O_2Si$, 435.2719, found, 435.2716; $[\alpha]_D^{20}$+8.8 (*c* 0.90, CH_2Cl_2).



***tert*-Butyldiphenyl((4*S*,8*S*,10*S*,*E*)-4,6,8,10-tetramethyldodeca-5,11-dienyloxy)silane (35).**

Alcohol **39** (100 mg, 0.20 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (5 mL), cooled to 0 °C and treated with Et_3N (34 μL, 0.24 mmol, 1.2 equiv.). After 5 min MsCl (19 μl, 0.24 mmol, 1.2 equiv.) was added and stirring was continued for 30 min. The solution was poured onto H_2O (10 mL), extracted with CH_2Cl_2 (3 x 5 mL), washed with brine and dried over $MgSO_4$. Evaporation of the solvent gave the crude mesylate, which was immediately dissolved in Et_2O (2 mL). LAH (11 mg, 0.30 mmol, 1.5 equiv.) was carefully added to the ice cooled solution and the cloudy mixture was allowed to warm to room temperature over 30 min. After 2 h the reaction mixture was quenched at 0 °C by slow addition of ethylacetate, diluted with Et_2O (20 mL) and washed with 1% HCl (10 mL). The aqueous layer was extracted with Et_2O (3 x 5 mL), and the combined organic fractions were washed with brine, dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by flash chromatography (hexane : ethylacetate = 50 : 1) afforded alkene **35** as an oil (86 mg, 90%). Analytical data matched those reported on pp. 16.

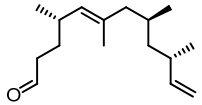


(4*S*,8*S*,10*S*,*E*)-4,6,8,10-Tetramethyldodeca-5,11-dien-1-ol (81).

A solution of alkene **35** (1.70 g, 3.57 mmol, 1.0 equiv.) in THF (70 mL) was treated with TBAF (1 M in THF, 4.27 mL, 4.28 mmol, 1.2 equiv.) and stirred overnight at room temperature. Finally

the reaction was quenched with 50 mL of NH_4Cl and the aqueous layer was extracted with Et_2O (3 x 30 mL). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated to dryness. Purification by column chromatography using gradient elution (hexane : ethylacetate from 10 : 1 to 5 : 1) furnished alcohol **81** as a yellow oil (739 mg, 87%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 5.69 (ddd, *J* = 17.4, 10.2, 7.4 Hz, 1H), 4.99-4.86 (m, 2H), 4.85 (d, *J* = 9.6 Hz, 1H), 3.61 (q, *J* = 6.1 Hz, 2H), 2.40-2.30 (m, 1H), 2.27-2.18 (m, 1H), 2.07-1.97 (m, 1H), 1.70-1.62 (m, 2H), 1.58-1.48 (m, 2H), 1.55 (d, *J* = 1.3 Hz, 3H), 1.43-1.33 (m, 1H), 1.28-1.18 (m, 1H), 1.19-1.09 (m, 2H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 145.4, 132.7, 132.6, 112.0, 63.3, 47.8, 44.2, 35.3, 33.8, 32.2, 30.9, 28.1, 21.4, 20.1, 19.8, 16.1; IR (film): 3331, 2951, 2360, 1458, 1375, 1060 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{16}H_{30}O$, 238.2297, found, 238.2296; $[\alpha]_D^{20}$+17.9 (*c* 1.55, CH_2Cl_2).

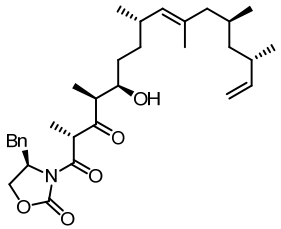


(4*S*,8*S*,10*S*,*E*)-4,6,8,10-tetramethyldodeca-5,11-dienal (25).

A 50 mL flask was charged with alcohol **81** (925 mg, 3.88 mmol, 1.0 equiv.) and DMSO (19 mL, 0.2 M). IBX (3.8 g, 13.58 mmol, 3.5 equiv.) was added and stirring was continued for 2 h at ambient temperature. The solution was diluted with Et_2O : hexane = 1 : 1 (50 mL) and H_2O (30 mL) to precipitate unreacted IBX. The mixture was filtered over Celite, the layers were separated and the aqueous layer was extracted with Et_2O : hexane = 1 : 1 (3 x 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was filtered over a plug of silica to give 870 mg (95%) of aldehyde **25**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 9.75 (t, *J* = 1.8 Hz, 1H), 5.69 (ddd, *J* = 17.4, 10.0, 7.5 Hz, 1H), 4.99-4.87 (m, 2H), 4.82 (d, *J* = 9.6 Hz, 1H), 2.42-2.30 (m, 3H), 2.29-2.18 (m, 1H), 2.07-1.98 (m, 1H), 1.73-1.62 (m, 3H), 1.53 (s, 3H), 1.52-1.41 (m, 1H), 1.19-1.09 (m, 2H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 202.9, 145.3, 134.0, 131.5, 112.0, 47.8, 44.1, 42.3, 35.3, 32.0, 29.8, 28.0, 21.3, 20.1, 19.8, 16.1; IR (film): 2957, 2924,

2869, 2714, 1728, 1640, 1456, 1375, 1112 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{16}H_{28}O$, 236.2140, found, 236.2135; $[\alpha]_D^{20}$+16.1 (*c* 1.20, CH_2Cl_2).

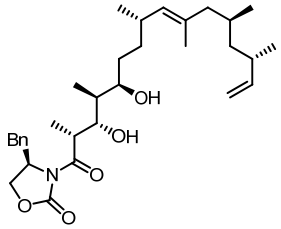


(2*R*,4*S*,5*R*,8*S*,12*S*,14*S*,*E*)-1-((*R*)-4-Benzyl-2-oxooxazolidin-3-yl)-5-hydroxy-2,4,8,10,12,14-hexamethylhexadeca-9,15-diene-1,3-dione (82).

A 100 mL Schlenk flask was charged with acid free $Sn(OTf)_2$ (3.77 g, 9.05 mmol, 2.2 equiv.) and CH_2Cl_2 (30 mL, 0.3 M). The white suspension was treated at -20 °C with Et_3N (1.19 mL, 8.67 mmol, 2.1 equiv.) whereupon the mixture turned pale yellow. After 5 min β-keto imide **26** (1.82 g, 6.29 mmol, 1.5 equiv.) in CH_2Cl_2 (9 mL, 0.7 M) was added dropwise and the clear solution was stirred for 1 h at -20 °C. Aldehyde **25** (960 mg, 4.06 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (6.5 mL, 0.6 M) and slowly added at -78 °C. After 1 h at -78 °C TLC analysis showed complete consumption of the starting material and the yellow-orange solution was poured onto a cooled and vigorously stirred mixture of CH_2Cl_2 and 1 M $NaHSO_4$ (100 mL, 1 : 1). After 20 min at room temperature the aqueous phase was extracted with CH_2Cl_2 (3 x 25 mL), the organic phase was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the residue by gradient flash chromatography (hexane : ethylacetate from 5 : 1 to 1 : 1) yielded **82** as a viscous oil (1.61 g, 76%, dr = 10 : 1 as determined by ^{1}H-NMR).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.37-7.27 (m, 3H), 7.22-7.17 (m, 2H), 5.69 (ddd, *J* = 17.4, 10.0, 7.0 Hz, 1H), 4.99-4.92 (m, 1H), 4.92-4.85 (m, 2H), 4.85-4.81 (m, 1H), 4.79-4.71 (m, 1H), 4.29-4.23 (m, 1H), 4.21-4.16 (m, 1H), 3.93-3.85 (br, 1H), 3.31 (dd, *J* = 13.3, 2.4 Hz, 1H), 2.82-2.73 (m, 2H), 2.44 (br, OH), 2.41-2.29 (m, 1H), 2.28-2.18 (m, 1H), 2.07-1.97 (m, 1H), 1.71-1.59 (m, 2H), 1.57-1.49 (m, 1H), 1.54 (d, *J* = 1.3 Hz, 3H), 1.47 (d, *J* = 7.1 Hz, 3H), 1.37-1.29 (m, 2H), 1.29-1.23 (m, 1H), 1.21 (d, *J* = 7.1 Hz, 3H), 1.19-1.11 (m, 2H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H),

0.79 (d, *J* = 6.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 169.7, 152.9, 145.4, 135.0, 132.8, 132.5, 129.4, 129.0, 127.4, 112.0, 71.2, 66.5, 55.3, 51.9, 48.4, 47.8, 44.2, 38.0 (2xCH), 35.3, 34.0, 32.2, 32.0, 28.1, 21.4, 20.1, 19.8, 16.1, 12.9, 9.9; IR (film): 3536, 2955, 1782, 1715, 1455, 1360, 1215, 1122 cm^{-1}; HRMS (ESI) (*m/z*): $[M+Na]^+$ calcd for $C_{32}H_{47}O_5NNa$, 548.3352, found, 548.3346; $[\alpha]_D^{20}$-54.9 (*c* 1.00, CH_2Cl_2).

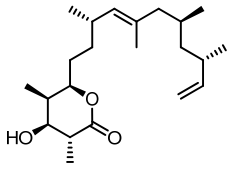


(*R*)-4-Benzyl-3-((2*R*,3*S*,4*S*,5*R*,8*S*,12*S*,14*S*,*E*)-3,5-dihydroxy-2,4,8,10,12,14-hexamethylhexadeca-9,15-dienoyl)oxazolidin-2-one (40).

$Me_4NBH(OAc)_3$ (3.74 g, 14.25 mmol, 5 equiv.) was dissolved in 400 mL MeCN : AcOH = 1.9 : 1, cooled to -32 °C and aldol product **82** (1.5 g, 2.85 mmol, 1.0 equiv.) in MeCN (3 mL) was added dropwise. The reaction was stirred for 3 h at -32 °C, allowed to warm to 0 °C overnight, diluted with CH_2Cl_2 (70 mL) and quenched by the addition of saturated aqueous Rochelle's salt (40 mL). Saturated aqueous $NaHCO_3$ (50 mL) was carefully added to the vigorously stirred solution over 20 min. After 1 h no more gas evolution was observed, the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL), and the combined organic fractions were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (hexane : ethylacetate from 3 : 1 to 2 : 1) afforded diol **40** as a viscous oil (1.14 g, 76%, dr ≥ 20 : 1 as determined by ^{1}H-NMR).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.37-7.27 (m, 3H), 7.23-7.18 (m, 2H), 5.69 (ddd, *J* = 17.4, 10.2, 7.4 Hz, 1H), 4.99-4.87 (m, 2H), 4.87 (d, *J* = 8.8 Hz, 1H), 4.73-4.66 (m, 1H), 4.26-4.17 (m, 2H), 3.96 (dd, *J* = 9.0, 2.4 Hz, 1H), 3.88 (dq, *J* = 7.0, 2.5 Hz, 1H), 3.80 (dt, *J* = 9.3, 2.3 Hz, 1H), 3.25 (dd, *J* = 13.4, 9.3 Hz, 1H), 2.79 (dd, *J* = 13.4, 9.3 Hz, 1H), 2.42-2.30 (m, 1H), 2.29-2.17 (m, 1H), 2.07-1.98 (m, 1H), 1.87-1.77 (m, 1H), 1.71-1.59 (m, 2H), 1.55-1.45 (m, 1H), 1.54 (d, *J* = 1.1 Hz, 3H), 1.45-1.29 (m, 2H), 1.41-1.30 (m, 1H), 1.27 (d, *J* = 7.1 Hz, 3H), 1.19-1.09 (m, 2H), 0.95 (d, *J* = 6.6 Hz,

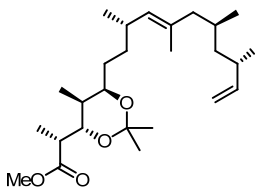
3H), 0.93 (d, *J* = 6.1 Hz, 3H), 0.83 (d, *J* = 7.1 Hz, 3H), 0.79 (d, *J* = 6.1 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 178.0, 152.8, 145.4, 134.9, 132.8, 132.6, 129.4, 129.0, 127.5, 112.0, 73.6 (2xCH), 66.2, 55.1, 47.8, 44.2, 39.6, 39.2, 37.8, 35.3, 34.5, 32.3, 31.0, 28.1, 21.4, 20.1, 19.7, 16.1, 11.5, 10.1; IR (film): 3475, 2956, 1783, 1700, 1455, 1387, 1211, 1107, cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{32}H_{49}O_5N$, 527.3611, found, 527.3615; $[\alpha]_D^{20}$-23.9 (*c* 0.90, CH_2Cl_2).



(3*R*,4*S*,5*R*,6*R*)-4-Hydroxy-3,5-dimethyl-6-((3*S*,7*S*,9*S*,*E*)-3,5,7,9-tetramethylundeca-4,10-dienyl)tetrahydro-2*H*-pyran-2-one (83).

A solution of diol **40** (1.14 g, 2.16 mmol, 1.0 equiv.) in THF/H_2O = 3 : 1 (22 mL 0.1 M) was treated at 0 °C with H_2O_2 (30% in H_2O, 864 µL). LiOH (145 mg, 3.46 mmol, 1.6 equiv.) was added in one portion and stirring was continued for 1 h at ambient temperature. The reaction was acidified with 1 N HCl and stirred for further 5 min. The mixture was diluted with H_2O (50 mL), extracted with Et_2O (4 x 30 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (hexane : ethylacetate from 5 : 1 to 3 : 1) gave lactone **83** (700 mg, 92%) as an oil.

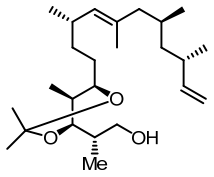
^{1}H-NMR (400MHz, $CDCl_3$): δ 5.68 (ddd, *J* = 17.4, 10.0, 7.5 Hz, 1H), 4.98-4.86 (m, 2H), 4.85 (d, *J* = 9.4 Hz, 1H), 4.16 (ddd, *J* = 8.2, 5.4, 2.5 Hz, 1H), 3.79 (dd, *J* = 10.2, 4.2 Hz, 1H), 2.44 (dq, *J* = 10.4, 7.1 Hz, 1H), 2.39-2.30 (m, 1H), 2.27-2.17 (m, 1H), 2.14-2.05 (m, 1H), 2.07-1.98 (m, 1H), 1.83-1.72 (m, 1H), 1.71-1.57 (m, 2H), 1.53 (d, *J* = 1.2 Hz, 3H), 1.48-1.35 (m, 1H), 1.42-1.29 (m, 2H), 1.38 (d, *J* = 7.1 Hz, 3H), 1.17-1.09 (m, 2H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 6H), 0.77 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 173.7, 145.3, 133.2, 132.1, 112.0, 78.0, 73.9, 47.7, 44.2, 39.8, 37.3, 35.3, 33.2, 32.1, 30.2, 28.0, 21.3, 20.1, 19.7, 16.1, 14.3, 4.4; IR (film): 3448, 2956, 2915, 1714, 1629, 1456, 1375, 1293, 1215, 1103, 1038 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{22}H_{38}O_3$, 350.2821, found, 350.2832; $[\alpha]_D^{20}$+44.7 (*c* 1.50, CH_2Cl_2).



(*R*)-Methyl 2-((4*S*,5*S*,6*R*)-2,2,5-trimethyl-6-((3*S*,7*S*,9*S*,*E*)-3,5,7,9-tetramethylundeca-4,10-dienyl)-1,3-dioxan-4-yl)propanoate (84).

Lactone **83 (**700 mg, 1.99 mmol, 1.0 equiv.) was dissolved in 2,2-dimethoxypropane (20 mL), treated with camphorsulfonic acid (46 mg, 0.19 mmol, 0.1 equiv.) and stirred overnight at room temperature. The solution was diluted with Et_2O (100 mL), neutralized with saturated aqueous $NaHCO_3$ (40 mL), extracted with Et_2O (3 x 30 mL), washed with brine (50 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by flash chromatography (hexane : ethylacetate = 10 : 1) to yield ester **84** (757 mg, 90%).

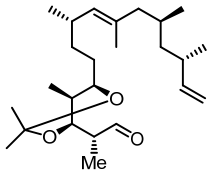
^{1}H-NMR (400MHz, $CDCl_3$): δ 5.69 (ddd, *J* = 17.4, 10.1, 7.5 Hz, 1H), 4.99-4.87 (m, 2H), 4.86 (d, *J* = 9.4 Hz, 1H), 3.72 (dd, *J* = 9.1, 4.3 Hz, 1H), 3.68 (s, 3H), 3.61 (dd, *J* = 7.7, 4.9 Hz, 1H), 2.60-2.52 (m, 1H), 2.41-2.29 (m, 1H), 2.27-2.17 (m, 1H), 2.07-1.97 (m, 1H), 1.84-1.74 (m, 1H), 1.71-1.60 (m, 2H), 1.54 (d, *J* = 1.0 Hz, 3H), 1.45-1.37 (m, 1H), 1.33-1.20 (m, 2H), 1.30 (s, 3H), 1.29 (s, 3H), 1.28-1.21 (m, 1H), 1.22-1.07 (m, 2H), 1.19 (d, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 174.9, 145.4, 132.7, 132.5, 112.0, 100.5, 75.4, 69.3, 51.6, 47.8, 44.2, 43.0, 36.8, 35.3, 33.8, 32.3, 28.5, 28.1, 25.0, 23.7, 21.3, 20.1, 19.7, 16.1, 11.9, 11.4; IR (film): 2926, 1743, 1494, 1455, 1380, 1227, 1112, 1050 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{26}H_{46}O_4$, 422.3396, found, 422.3394; $[\alpha]_D^{20}$-12.8 (*c* 1.00, CH_2Cl_2).



(*S*)-2-((4*S*,5*S*,6*R*)-2,2,5-Trimethyl-6-((3*S*,7*S*,9*S*,*E*)-3,5,7,9-tetramethylundeca-4,10-dienyl)-1,3-dioxan-4-yl)propan-1-ol (85).

Ester **84** (730 mg, 1.73 mmol, 1.0 equiv.) in Et_2O (17 mL) was cooled in an ice-bath and LAH (138 mg, 3.63 mmol, 2.1 equiv.) was added carefully in small portions. After 30 min at 0 °C TLC analysis showed complete consumption of the starting material and the reaction mixture was quenched by slow addition of ethylacetate, diluted with Et_2O (80 mL) and washed with 1% HCl (100 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL), and the combined organic fractions were washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (hexane : ethylacetate = 2 : 1) afforded alcohol **85** as a colorless oil (677 mg, 99%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 5.69 (ddd, *J* = 17.3, 10.0, 7.5 Hz, 1H), 4.98-4.87 (m, 2H), 4.87 (d, *J* = 8.1 Hz, 1H), 3.72 (dd, *J* = 8.8, 4.3 Hz, 1H), 3.69-3.63 (m, 2H), 3.50 (dd, *J* = 7.8, 2.8 Hz, 1H), 2.43 (t, *J* = 4.9 Hz, 1H), 2.40-2.30 (m, 1H), 2.29-2.17 (m, 1H), 2.07-1.98 (m, 1H), 1.89-1.75 (m, 2H), 1.71-1.60 (m, 2H), 1.55 (d, *J* = 1.2 Hz, 3H), 1.47-1.38 (m, 1H), 1.34 (s, 3H), 1.32-1.23 (m, 2H), 1.31 (s, 3H), 1.31-1.23 (m, 1H), 1.20-1.07 (m, 2H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 145.4, 132.7, 132.5, 112.0, 100.4, 77.7, 69.6, 67.3, 47.8, 44.2, 37.4, 35.8, 35.3, 33.8, 32.2, 28.4, 28.1, 25.2, 23.7, 21.3, 20.1, 19.7, 16.1, 12.2, 10.6; IR (film): 3424, 3074, 2958, 1639, 1457, 1380, 1226, 1167, 1019 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{25}H_{46}O_3$, 394.3447, found, 394.3445; $[\alpha]_D^{20}$+1.9 (*c* 1.05, CH_2Cl_2).

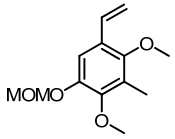


(*R*)-2-((4*R*,5*S*,6*R*)-2,2,5-Trimethyl-6-((3*S*,7*S*,9*S*,*E*)-3,5,7,9-tetramethylundeca-4,10-dienyl)-1,3-dioxan-4-yl)propanal (24).

To a solution of alcohol **85** (110 mg, 0.28 mmol, 1.0 equiv.) in DMSO (2 mL), IBX (273 mg, 0.98 mmol, 3.5 equiv.) was added over a period of 20 min and stirring was continued for 1.5 h at

ambient temperature. The solution was diluted with Et_2O : hexane = 1 : 1 (60 mL) and H_2O (20 mL) to precipitate unreacted IBX. The mixture was filtered over Celite, the layers were separated and the aqueous layer was extracted with Et_2O : hexane = 1 : 1 (3 x 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was filtered over a plug of silica to give aldehyde **24** as an oil (108 mg, 99%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 9.70 (s, 1H), 5.69 (ddd, *J* = 17.4, 10.2, 7.4, 1H), 4.99-4.86 (m, 2H), 4.86 (d, *J* = 9.3 Hz, 1H), 3.76 (dd, *J* = 8.0, 3.2 Hz, 1H), 3.74-3.69 (m, 1H), 2.41 (dq, *J* = 7.0, 3.2 Hz, 1H), 2.38-2.29 (m, 1H), 2.29-2.16 (m, 1H), 2.07-1.97 (m, 1H), 1.88-1.76 (m, 1H), 1.71-1.60 (m, 2H), 1.54 (d, *J* = 1.3 Hz, 3H), 1.49-1.40 (m, 1H), 1.32 (s, 3H), 1.32-1.20 (m, 2H), 1.30-1.24 (m, 1H), 1.29 (s, 3H), 1.20-1.08 (m, 2H), 1.14 (d, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 204.4, 145.4, 132.6, 112.0, 100.6, 73.7, 69.4, 48.8, 47.8, 44.2, 36.2, 35.3, 33.8, 32.2, 28.4, 28.1, 24.8, 23.6, 21.3, 20.1, 19.7, 16.1, 12.0, 7.8; IR (film): 2957, 2362, 1734, 1639, 1457, 1381, 1225, 1165, 1019 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{25}H_{44}O_3$, 392.3290, found, 392.3298; $[\alpha]_D^{20}$-26.0 (*c* 1.50, CH_2Cl_2).



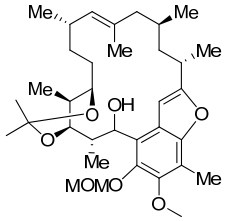
2,4-Dimethoxy-1-(methoxymethoxy)-3-methyl-5-vinylbenzene (23).

Bromide **41** (1 g, 3.43 mmol, 1.0 equiv.) was dissolved in Et_2O (34 mL, 0.1 M), cooled to –78 °C and *t*-BuLi (4 mL, 6.86 mmol, 2 equiv.) was added dropwise *via* syringe. The white suspension was stirred for 20 min at –78 °C, 15 min at 0 °C and subsequently treated with DMF (534 µL, 6.86 mmol, 2 equiv.). The solution was allowed to warm to ambient temperature over 1 h, diluted with Et_2O (70 mL) and quenched with saturated aqueous NH_4Cl (20 mL). The organic extracts were dried over $MgSO_4$, concentrated and purified by flash chromatography (hexane : ethylacetate from 10 : 1 to 5 : 1) to give pure aldehyde (687 mg, 83%).

To (methyl)triphenylphosphonium bromide (654 mg, 1.83 mmol, 2.2 equiv.) in THF (3.7 mL) *t*-BuOK (196 mg, 1.75 mmol, 2.1 equiv.) was added in 3 portions at 0 °C. The cloudy-orange

suspension was stirred for 45 min at room temperature, recooled to 0 °C and the above aldehyde (200 mg, 0.83 mmol, 1.0 equiv.) was added as a solution in THF (2.7 mL). The mixture was warmed to ambient temperature within 30 min, whereupon TLC analysis showed complete consumption of the starting material. The solution was diluted with 50 mL Et_2O / hexane (1 : 1), washed with saturated aqueous NH_4Cl (10 mL) and extracted with diethyl ether (3 x 10 mL). The organic layer was dried over $MgSO_4$ and the solvent was removed *in vacuo*. The residue was purified by column chromatography (hexane : ethylacetate from 5 : 1 to 3 : 1) to furnish arene **23** (194 mg, 98%) as an oil.

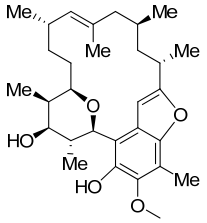
^{1}H-NMR (400MHz, $CDCl_3$): δ 7.14 (s, 1H), 6.94 (dd, *J* = 17.7, 11.1 Hz, 1H), 5.67 (dd, *J* = 17.7, 1.3 Hz, 1H), 5.25 (dd, *J* = 11.0, 1.3 Hz, 1H), 5.20 (s, 2H), 3.82 (s, 3H), 3.68 (s, 3H), 3.53 (s, 3H), 2.21 (s, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 151.5, 148.9, 146.9, 131.2, 126.4, 125.6, 114.0, 111.2, 95.6, 61.0, 60.4, 56.1, 9.3; IR (film): 2934, 2361, 1482, 1396, 1322, 1241, 1154, 1121, 1093, 1061, 1040 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{13}H_{18}O_4$, 238.1205, found, 238.1203.



Olefin 58.

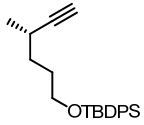
To a stirred refluxing solution of **56** (35 mg, 0.059 mmol, 1.0 equiv.) in CH_2Cl_2 (5 mL) was added portionwise dipotassium azodicarboxylate (58 mg, 0.299 mmol, 5 equiv.), followed by AcOH (9 µL, 0.150 mmol, 2.5 equiv.) in CH_2Cl_2 (1 mL). After 36 h the mixture was cooled to room temperature, filtered through silica and the filtrate was concentrated *in vacuo*. The crude product was purified by flash chromatography (hexane : ethylacetate = 10 : 1) to give **58** as a white foam (21 mg, 60%). ^{1}H-NMR (600MHz, $CDCl_3$): δ 6.27 (s, 1H), 5.16 (d, *J* = 5.7 Hz, 1H), 5.10-5.05 (m, 1H), 5.10(d, *J* = 5.7 Hz, 1H), 4.85 (d, *J* = 5.7 Hz, 1H), 4.85 (d, *J* = 9.1 Hz, 1H), 3.81-3.74 (m, 1H+OH), 3.78 (s, 3H), 3.59 (s, 3H), 3.55-3.50 (m, 1H), 3.04-2.95 (m, 1H), 2.43-2.33 (m, 1H),

2.40 (s, 3H), 2.20-2.12 (br, 1H), 2.12-2.04 (br, 1H), 2.01-1.95 (m, 1H), 1.97-1.91 (br, 1H), 1.84-1.77 (br, 1H). 1.69-1.62 (m, 1H), 1.61 (s, 3H), 1.55-1.47 (br, 1H), 1.41-1.33 (m, 1H), 1.31-1.22 (m, 1H), 1.28 (d, *J* =6.8 Hz, 3H), 1.27-1.19 (m, 1H), 1.20 (s, 3H), 1.14 (d, *J* =6.4 Hz, 3H), 1.07-1.01 (br, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.91-0.84 (br, 3H); ^{13}C-NMR (150MHz, $CDCl_3$): δ 164.6, 149.9, 147.6, 145.2, 132.2, 131.3, 124.6, 121.4, 119.4, 114.3, 100.3, 99.4, 98.7, 71.6, 73.0, 71.2, 60.5, 57.7, 45.9, 42.6, 40.7, 34.7, 34.1, 32.4, 31.1, 28.3, 27.8, 24.3, 20.3, 19.1, 18.8, 12.1, 10.5, 9.1; IR (film): 3435, 2930, 1654, 1559, 1490, 1458, 1378, 1248, 1158, 1109, 1001 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{35}H_{54}O_7Na$, 609.3767, found, 609.3781; $[\alpha]_D^{20}$ -9.8 (*c* 1.0, CH_2Cl_2).



Tetrahydropyran 5.

Compound **58** (20 mg, 0.034 mmol) was dissolved in MeOH (1 mL) and treated with a drop of 3N HCl. The reaction mixture was stirred for 4 h at room temperature, diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (4 x 10 mL). The organic extracts were dried over $MgSO_4$, concentrated *in vacuo* and purified by flash chromatography (hexane : ethyl acetate from 2 : 1 to 1 : 1) to afford tetrahydropyran **5** (16 mg, 96%) as a white foam. All analytical data matched with those of the material described previously (confer conversion of **60** to **5**).

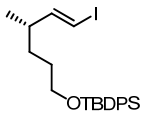


(*S*)-*tert*-Butyl(4-methylhex-5-ynyloxy)diphenylsilane (86).

A solution of trimethylsilyl diazomethane (2 M in Et_2O, 6.73 mL, 13.45 mmol, 1.2 equiv.) was diluted with THF (33 mL) and cooled to -78 °C. *n*-BuLi (2.5 M in hexane, 5.38 mL, 13.45 mmol, 1.2 equiv.) was added dropwise and stirring was continued for 45 min. A solution of aldehyde **36** (3.97 g, 11.21 mmol, 1.0 equiv.) in THF (11 mL) was added over a period of 20 min. After 1 h at -78 °C the reaction mixture was stirred for 30 min at 0 °C and for 1 h at ambient temperature. As TLC analysis showed complete consumption of the starting material, the mixture was partitioned between saturated aqueous NH_4Cl (100 mL) and Et_2O (100 mL). The aqueous layer was extracted with Et_2O (100 mL), the organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (hexane : ethylacetate = 50 : 1) afforded 3.24 g (83%) of alkyne **86**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69-7.65 (m, 4H), 7.45-7.35 (m, 6H), 3.69 (t, *J* = 6.2 Hz, 2H), 2.48-2.38 (m, 1H), 2.02 (d, *J* = 2.3 Hz, 1H), 1.81-1.62 (m, 2H), 1.60-1.46 (m, 2H), 1.18 (d, *J* = 6.8 Hz, 3H), 1.05 (s, 9H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 135.6, 134.1, 129.5, 127.6, 89.0, 68.2, 63.6, 33.0, 30.2, 26.9, 25.4, 21.0, 19.2; IR (film): 2934, 2856, 1427, 1111, 889 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{19}H_{21}OSi$, 293.1362, found, 293.1355; $[\alpha]_D^{20}$+12.3 (*c* 1.1, CH_2Cl_2).

61

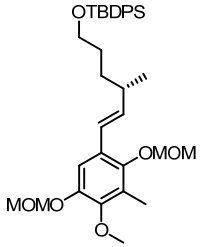


(*S*,*E*)-*tert*-Butyl(6-iodo-4-methylhex-5-enyloxy)diphenylsilane (87).

A 25 mL Schlenk flask was charged with Cp_2ZrHCl (207 mg, 0.804 mmol, 1.2 equiv.) followed by 2.7 mL THF (0.35 M). The white suspension was cooled in an ice bath and alkyne **86** (235 mg, 0.670 mmol) in THF (0.7 mL) was added slowly *via* cannula. The mixture was stirred for 1 h until a clear, slightly yellow solution has formed. The reaction mixture was cooled in a dry-ice-acetone bath and iodine (238 mg, 0.938 mmol, 1.4 equiv.) in THF (1 mL) was added slowly until the violet color persisted. The reaction was quenched by the addition of 1 M $Na_2S_2O_3$ solution. Stirring was continued until both layers became colorless. The aqueous phase was extracted with Et_2O (4 x 20 mL), the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated to dryness. Chromatography (hexane) yielded 243 mg (76%) of vinyl

iodide **87**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69-7.64 (m, 4H), 7.46-7.36 (m, 6H), 6.38 (dd, *J* = 14.4, 8.1 Hz, 1H), 5.91 (dd, *J* = 14.4, 0.8 Hz, 1H), 3.64 (t, *J* = 6.3 Hz, 2H), 2.20-2.08 (m, 1H), 1.59-1.46 (m, 2H), 1.40-1.32 (m, 2H), 1.05 (s, 9H), 0.98 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 152.1, 135.6, 134.0, 129.5, 127.6, 73.4, 63.8, 40.4, 32.2, 30.0, 26.9, 19.7, 19.2; IR (film): 2931, 2857, 1684, 1653, 1559, 1507, 1472, 1428, 1112 cm^{-1}; HRMS (ESI) (*m/z*): [M-*t*Bu]$^+$ calcd for $C_{19}H_{22}IOSi$, 421.0485, found, 421.0482; $[\alpha]_D^{20}$+25.6 (*c* 1.4, CH_2Cl_2).

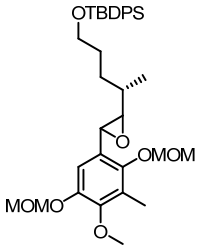


(*S*,*E*)-*tert*-Butyl(6-(4-methoxy-2,5-bis(methoxymethoxy)-3-methylphenyl)-4-methylhex-5-enyloxy)diphenylsilane (62).

To flame-dried anhydrous $ZnCl_2$ (128 mg, 0.940 mmol, 1.8 equiv.) aryl bromide **45** (302 mg, 0.940 mmol, 1.8 equiv.) in degassed Et_2O (9 mL) was added. The suspension was cooled to -78°C and *t*-BuLi (1.7 M in pentane, 1.1 mL, 1.88 mmol, 3.6 equiv.) was added rapidly. The pale yellow solution was stirred for 30 min at -78 °C and 1 h at 0°C. To this white suspension vinyl iodide **9** (250 mg, 0.522 mmol, 1.0 equiv.) along with $Pd(PPh_3)_4$ (30 mg, 0.026 mmol, 0.05 equiv.) in degassed THF (3 mL) was added slowly. The clear orange solution was stirred for 2 h at 0 °C, diluted with Et_2O (10 mL) and quenched by the addition of NH_4Cl (10 mL). The phases were separated, the organic phase was extracted with a 1 : 1 mixture of Et_2O-hexane (4 x 10 mL), washed with brine, dried over $MgSO_4$ and evaporated to dryness.

Purification by flash chromatography (hexane : ethylacteate = 20 : 1) afforded 270 mg **62** (208 mg, 67%, determined by ^{1}H-NMR) along with dehalogenated **45**. This mixture was used in the next step without further purification. A small sample was purified by HPLC to furnish analytically pure **62**.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69-7.64 (m, 4H), 7.44-7.33 (m, 6H), 7.06 (s, 1H), 6.53 (d, *J* = 15.9 Hz, 1H), 5.96 (dd, *J* = 15.9, 8.1 Hz, 1H), 5.19 (s, 2H), 4.88 (s, 2H), 3.80 (s, 3H), 3.66 (t, *J* = 6.3 Hz, 2H), 3.57 (s, 3H), 3.53 (s, 3H), 2.33-2.22 (m, 1H), 2.23 (s, 3H), 1.64-1.52 (m, 2H), 1.49-1.39 (m, 2H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.05 (s, 9H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 148.4, 148.0, 147.1, 137.3, 135.6, 134.1, 129.5, 127.6, 127.0, 126.0, 123.0, 111.3, 99.7, 95.6, 64.0, 60.5, 57.6, 56.3, 37.3, 33.1, 30.5, 26.7, 20.7, 19.2, 10.2; IR (film): 2933, 1653, 1559, 1481, 1428, 1394, 1156, 1112, 1050, 971 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{35}H_{48}O_6Si$, 592.3220, found, 592.3226; $[\alpha]_D^{20}$+24.9 (*c* 1.0, CH_2Cl_2).

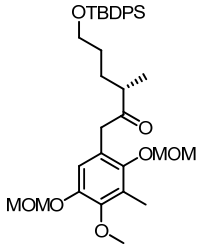


***tert*-Butyl((4*S*)-4-(3-(4-methoxy-2,5-bis(methoxymethoxy)-3-methylphenyl)oxiran-2-yl)pentyloxy)diphenylsilane (88).**

Alkene **62** (50 mg, 0.084 mmol, 1.0 equiv.) was dissolved in acetone (1 mL) and treated with DMDO (0.07 M - 0.09 M in acetone, 4 mL, 0.032 mmol, 3.8 equiv.) at ambient temperature. After stirring for 15 min, the reaction mixture was concentrated and loaded directly onto a column of silica. Flash chromatography (hexane : ethylacetate = 3 : 1) gave epoxide **88** as a pale oil (50 mg, 99%, 1.1 : 1 mixture of diastereomers).

^{1}H-NMR (The asterisk denotes the minor diastereomer, 400MHz, $CDCl_3$): δ 7.70-7.63 (m, 4H), 7.45-7.32 (m, 6H), 6.72 (s, 1H), 5.19-5.12 (m, 2H), 4.99-4.91 (m, 2H), 3.96 (d, *J* = 2.27 Hz, 1H), 3.91* (d, *J* = 2.27 Hz, 1H), 3.81 (s, 3H), 3.71-3.63 (m, 2H), 3.57* (s, 3H), 3.52 (s, 3H), 3.50 (s, 3H), 2.70-2.65 (m, 1H), 2.23* (s, 3H), 2.22 (s, 3H), 1.73-1.59 (m, 2H), 1.57-1.48 (m, 1H), 1.55-1.34 (m, 2H), 1.06* (d, *J* = 6.6 Hz, 3H), 1.05* (s, 9H), 1.04 (s, 9H), 1.00 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (The asterisk denotes the minor diastereomer, 100MHz, $CDCl_3$): δ 149.5, 148.5, 147.3, 135.6*, 135.5, 134.1*,134.0, 129.5, 127.6, 126.7, 126.6*, 125.8, 110.5, 100.1, 95.5, 67.2, 67.1*, 64.1, 64.0*,

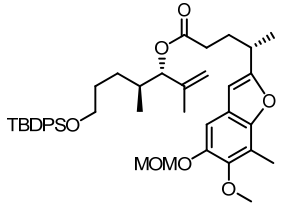
60.4, 57.5, 56.3, 54.0, 53.1*, 35.9, 35.7*, 30.5*, 30.1, 29.9, 26.9, 19.2, 16.6, 15.8*, 10.2, 10.1*; IR (film): 2933, 1734, 1559, 1486, 1429, 1394, 1360, 1238, 1156, 1112, 1050 cm^{-1}; HRMS (ESI) (*m/z*): [M+Na]$^+$ calcd for $C_{35}H_{48}O_7SiNa$, 631.3076, found, 631.3069.



(*S*)-6-(*tert*-Butyldiphenylsilyloxy)-1-(4-methoxy-2,5-bis(methoxymethoxy)-3-methylphenyl)-3-methylhexan-2-one (48).

In a 5 mL Schlenk flask, $Pd(OAc)_2$ (9 mg, 0.038 mmol, 0.1 equiv.) was added to degassed *t*-BuOH (1.5 mL) followed by the addition of PBu_3 (28 µL, 0.113 mmol, 0.3 equiv.). After 5 min epoxide **88** (230 mg, 0.377 mmol, 1.0 equiv.) was added to the reaction mixture and the solution was refluxed for 1.5 h. The mixture was allowed to cool to room temperature, at which point excess *t*-BuOH was evaporated. The crude product was purified by flash chromatography (hexane : ethylacetate from 10 : 1 to 3 :1) to yield ketone **48** as a yellow oil (185 mg, 81%).

All analytical data matched with those of the material described previously (confer conversion of **44**/**45** to **48**).

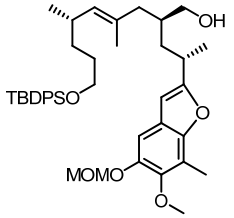


(*S*)-((3*S*,4*S*)-7-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethylhept-1-en-3-yl) 4-(6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)pentanoate (63).

A mixture of acid **43** (1.39 g, 4.30 mmol, 1.1 equiv.), alcohol **29a** (1.55 g, 3.91 mmol, 1.0 equiv.), EDCI·HCl (1.19 g, 6.25 mmol, 1.6 equiv.) and DMAP (954 mg, 7.82 mmol, 2 equiv.) in CH_2Cl_2 (8 mL) was stirred at ambient temperature for 2 h. The reaction was diluted with CH_2Cl_2 (70 mL), quenched with 1% HCl (10 mL) and washed with brine (50 mL). The organic layer was dried over $MgSO_4$, concentrated and the residue was purified by flash chromatography (hexane : ethylacetate from 15 :1 to 5 :1) to give ester **63** (2.35 g, 86%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.68-7.62 (m, 4H), 7.43-7.33 (m, 6H), 7.07 (s, 1H), 6.25 (s, 1H), 5.20 (s, 2H), 4.96 (d, *J* = 7.6 Hz, 1H), 4.92 (s, 2H), 3.83 (s, 3H), 3.63 (dt, *J* = 6.1, 1.9 Hz, 2H), 3.54 (s, 3H), 2.99-2.89 (m, 1H), 2.40 (s, 3H), 2.36-2.29 (m, 2H), 2.09-1.99 (m, 1H), 1.99-1.89 (m, 1H), 1.80-1.72 (m, 1H), 1.69-1.60 (m, 1H), 1.68 (s, 3H), 1.64-1.57 (m, 1H), 1.52-1.42 (m, 1H), 1.30 (d, *J* = 7.1 Hz, 3H), 1.14-1.05 (m, 1H), 1.02 (s, 9H), 0.82 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 172.7, 162.7, 149.3, 147.0, 145.7, 142.2, 135.5, 134.1, 129.5, 127.6, 123.3, 115.4, 114.0, 105.1, 101.4, 96.2, 81.6, 64.0, 61.0, 56.1, 34.2, 33.1, 32.1, 30.5, 29.9, 27.9, 26.8, 19.2, 18.9, 18.4, 15.8, 9.1; IR (film): 2932, 1734, 1559, 1457, 1153, 1113, 1044 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{42}H_{56}O_7Si$, 700.3795, found, 700.3814; $[\alpha]_D^{20}$+13.9 (*c* 0.90, CH_2Cl_2).

63



(2*S*,6*S*,*E*)-9-(*tert*-Butyldiphenylsilyloxy)-2-((*S*)-2-(6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)propyl)-4,6-dimethylnon-4-en-1-ol (64).

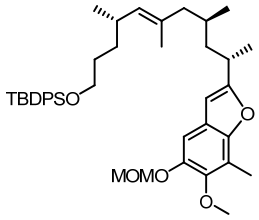
LHMDS (1 M in THF, 13.1 mL, 13.12 mmol, 4 equiv.) was cooled to -78 °C and freshly distilled HMPA (3 mL) was slowly added *via* cannula. After 5 min ester **63** (2.3 g, 3.28 mmol, 1.0 equiv.) was added as a solution in THF : HMPA = 4 : 1 (10 mL), whereupon the cloudy orange solution turned clear. After 45 min a freshly prepared TBSCl-solution (3 M in THF, 6.56 mL, 19.68 mmol, 6 equiv.) was added to the reaction mixture and stirring was continued for 20 min at -78 °C. The

solution was allowed to warm to 0 °C over 15 min, stirred for additional 5 min at ambient temperature and partitioned between H_2O (100 mL) and Et_2O (3 x 70 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated to dryness. The crude ketene silyl acetal was dissolved in THF (15 mL) and refluxed for 3 h. The mixture was allowed to cool to 40 °C, concentrated under reduced pressure and Et_2O (33 mL) was added. The flask was immersed in an ice-bath and LAH (4 M in Et_2O, 1.64 mL, 6.56 mmol, 2 equiv.) was added carefully *via* cannula. After 30 min at room temperature TLC analysis showed complete consumption of the starting material and the reaction mixture was quenched at 0°C by slow addition of ethylacetate, diluted with Et_2O (50 mL) and washed with 1% HCl (100 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL), the combined organic fractions were washed with brine (50 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by column chromatography (hexane : ethylacetate from 10 : 1 to 3 : 1) afforded alcohol **64** as a colorless oil (1.89 g, 84%, dr = 4 : 1 as determined by ^{1}H-NMR).

***S*-64:** ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.70-7.62 (m, 4H), 7.44-7.33 (m, 6H), 7.08 (s, 1H), 6.28 (s, 1H), 5.21 (s, 2H), 4.95 (d, *J* = 9.1 Hz, 1H), 3.84 (s, 3H), 3.63 (t, *J* = 6.4 Hz, 2H), 3.54 (s, 3H), 3.47 (d, *J* = 5.1 Hz, 2H), 3.08-2.97 (m, 1H), 2.42 (s, 3H), 2.37-2.25 (m, 1H), 2.09-1.99 (m, 2H), 1.84 (ddd, *J* = 13.8, 8.0, 6.0 Hz, 1H), 1.76-1.66 (m, 1H), 1.57-1.43 (m, 2H), 1.55 (s, 3H), 1.49-1.40 (m, 1H), 1.42-1.33 (m, 1H), 1.31 (d, *J* = 6.8 Hz, 3H), 1.28-1.18 (m, 1H), 1.04 (s, 9H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 164.0, 149.2, 146.9, 145.6, 135.6, 134.1, 133.7, 132.1, 129.5, 127.5, 123.4, 115.3, 105.1, 100.9, 96.2, 66.0, 64.1, 61.0, 56.1, 42.6, 37.7, 36.1, 33.7, 32.2, 31.6, 30.6, 26.9, 21.2, 20.2, 19.2, 16.2, 9.1; IR (film): 3675, 3629, 2932, 1653, 1457, 1153, 1112, 1044 cm^{-1}; HRMS (ESI) (*m/z*): [M]$^+$ calcd for $C_{42}H_{58}O_6Si$, 686.4003, found, 686.3982; $[\alpha]_D^{20}$+15.8 (*c* 1.25, CH_2Cl_2).

***R*-64:** ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.70-7.63 (m, 4H), 7.44-7.33 (m, 6H), 7.06 (s, 1H), 6.25 (s, 1H), 5.20 (s, 2H), 4.94 (d, *J* = 9.1 Hz, 1H), 3.83 (s, 3H), 3.63 (t, *J* = 6.4 Hz, 2H), 3.57-3.51(br, 2H), 3.54 (s, 3H), 3.11-3.00 (m, 1H), 2.40 (s, 3H), 2.36-2.26 (m, 1H), 2.06-1.93 (m, 2H), 1.78-1.66 (m, 2H), 1.61-1.51 (m, 1H), 1.58-1.46 (m, 2H), 1.50 (s, 3H), 1.41-1.33 (m, 1H), 1.29 (d, *J* = 7.07 Hz, 3H), 1.26-1.20 (m, 1H), 1.04 (s, 9H), 0.89 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 163.8, 149.1, 147.0, 145.6, 135.6, 134.2, 133.7, 132.3, 129.5, 127.5, 123.4, 115.3, 105.1, 101.0, 96.2,

65.8, 64.1, 61.0, 56.1, 42.8, 37.0, 35.9, 33.7, 32.2, 31.3, 30.7, 26.9, 21.3, 20.2, 19.2, 16.0, 9.1; IR (film): 3448, 2931, 1653, 1458, 1153, 1112, 1043 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{42}H_{58}O_6SiNa$, 709.3900, found, 709.3915; $[\alpha]_D^{20}$-1.2 (*c* 0.55, CH_2Cl_2).

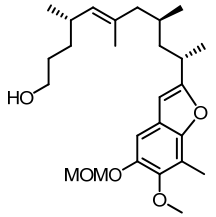


***tert*-Butyl((4*S*,8*S*,10*S*,*E*)-10-(6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-4,6,8-trimethylundec-5-enyloxy)diphenylsilane (89).**

Alcohol (*S*)-**64** (1.69 g, 2.46 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (12 mL, 0.2 M), cooled to 0 °C and treated with Et_3N (410 µL, 2.96 mmol, 1.2 equiv.). After 5 min MsCl (229 µl, 2.96 mmol, 1.2 equiv.) was added and stirring was continued for 30 min. The solution was poured onto H_2O (50 mL), extracted with CH_2Cl_2 (3 x 20 mL), washed with brine and dried over $MgSO_4$. Evaporation of the solvent gave the crude mesylate, which was immediately dissolved in Et_2O (25 mL). LAH (4 M in Et_2O, 1.85 mL, 7.38 mmol, 3 equiv.) was carefully added to the ice cooled solution and the cloudy mixture was allowed to warm to room temperature over 30 min. After 2 h the reaction mixture was quenched at 0 °C by the slow addition of ethylacetate, diluted with Et_2O (50 mL) and washed with 1% HCl (100 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL), and the combined organic fractions were washed with brine, dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by flash chromatography (hexane : ethylacetate = 5 : 1) afforded alkene **89** as an oil (1.55 g, 94%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.69-7.63 (m, 4H), 7.43-7.33 (m, 6H), 7.07 (s, 1H), 6.24 (s, 1H), 5.21 (s, 2H), 4.87 (d, *J* = 9.1 Hz, 1H), 3.84 (s, 3H), 3.62 (t, *J* = 6.4 Hz, 2H), 3.54 (s, 3H), 3.07-2.95 (m, 1H), 2.42 (s, 3H), 2.37-2.24 (m, 1H), 2.06 (dd, *J* = 12.7, 4.8 Hz, 1H), 1.74 (dd, *J* = 12.7, 8.3 Hz, 1H), 1.71-1.61 (m, 1H), 1.61-1.45 (m, 2H), 1.57-1.45 (m, 2H), 1.51 (s, 3H), 1.41-1.34 (m, 1H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.26-1.17 (m, 1H), 1.04 (s, 9H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.3 Hz, 3H); ^{13}C-

NMR (100MHz, $CDCl_3$): δ 164.8, 149.2, 146.9, 145.5, 135.6, 134.2, 133.2, 132.2, 129.4, 127.5, 123.5, 115.3, 105.0, 100.4, 96.2, 64.1, 61.0, 56.1, 48.1, 43.1, 33.9, 32.1, 31.3, 30.7, 28.3, 26.9, 21.4, 19.5, 19.2 (C_q+CH_3), 16.1, 9.1; IR (film): 2928, 1653, 1559, 1458, 1153, 1112, 1044 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{42}H_{58}O_5Si$, 670.4054, found, 670.4067; $[\alpha]_D^{20}$+14.0 (*c* 1.25, CH_2Cl_2).

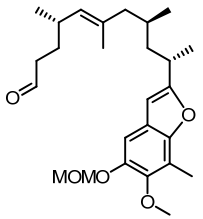


(4*S*,8*S*,10*S*,*E*)-10-(6-Methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-4,6,8-trimethylundec-5-en-1-ol (90).

A solution of **89** (50 mg, 0.075 mmol, 1.0 equiv.) in THF (1.5 mL) was treated with TBAF (1 M in THF, 82 µL, 0.082 mmol, 1.1 equiv.) and stirred for 2 h at room temperature. The reaction was diluted with Et_2O (20 mL), quenched with saturated aqueous NH_4Cl (10 mL) and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated to dryness. Purification by flash chromatography using gradient elution (hexane : ethylacetate from 3: 1 to 2 : 1) furnished alcohol **90** as a pale yellow oil (29 mg, 93%).

^{1}H-NMR (600MHz, $CDCl_3$): δ 7.07 (s, 1H), 6.24 (d, *J* = 0.8 Hz, 1H), 5.21 (s, 2H), 4.88 (dd, *J* = 9.1, 1.1 Hz, 1H), 3.84 (s, 3H), 3.63-3.59 (m, 2H), 3.54 (s, 3H), 3.03-2.97 (m, 1H), 2.42 (s, 3H), 2.39-2.32 (m, 1H), 2.06 (dd, *J* = 13.2, 5.7 Hz, 1H), 1.76 (ddd, *J* = 13.2, 8.4, 0.6 Hz, 1H), 1.72-1.64 (m, 1H), 1.59-1.53 (m, 1H), 1.58-1.45 (m, 2H), 1.55 (d, *J* =1.1 Hz, 3H), 1.52-1.45 (m, 1H), 1.41-1.34 (m, 1H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.26-1.18 (m, 1H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (150MHz, $CDCl_3$): δ 164.8, 149.1, 146.9, 145.5, 133.9, 132.7, 123.5, 115.3, 105.0, 100.4, 96.2, 63.3, 61.0, 56.1, 48.0, 43.0, 33.8, 32.2, 31.3, 30.9, 28.2, 21.4, 19.6, 19.2, 16.1, 9.1;

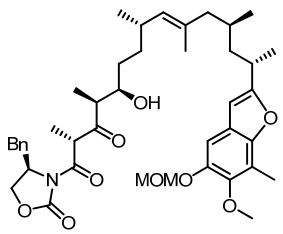
IR (film): 3629,3422, 2928, 1654, 1606, 1458, 1340, 1219, 1153, 1116, 1044 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{26}H_{40}O_5$, 432.2876, found, 432.2862; $[\alpha]_D^{20}$+19.8 (*c* 1.0, CH_2Cl_2).



(4*S*,8*S*,10*S*,*E*)-10-(6-Methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-4,6,8-trimethylundec-5-enal (65).

Alcohol **90** (265 mg, 0.61 mmol, 1.0 equiv.) was dissolved in DMSO (3 mL, 0.2 M) and IBX (429 mg, 1.53 mmol, 2.5 equiv.) was added over a period of 20 min. After stirring for 2 h at room temperature the solution was diluted with Et_2O : hexane = 1 : 1 (30 mL) and H_2O (30 mL) to precipitate unreacted IBX. The mixture was filtered over Celite, the layers were separated and the aqueous layer was extracted with Et_2O : hexane = 1 : 1 (3 x 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was filtered over a plug of silica to give aldehyde **65** as a colorless oil (245 mg, 93%).

^{1}H-NMR (600MHz, $CDCl_3$): δ 9.74 (t, *J* = 1.7 Hz, 1H), 7.07 (s, 1H), 6.24 (d, *J* = 0.8 Hz, 1H), 5.21 (s, 2H), 4.84 (dd, *J* = 9.7, 1.0 Hz, 1H), 3.84 (s, 3H), 3.54 (s, 3H), 3.03-2.96 (m, 1H), 2.42 (s, 3H), 2.42-2.34 (m, 3H), 2.07 (dd, *J* = 12.9, 5.9 Hz, 1H), 1.76 (dd, *J* = 13.4, 8.7, 1H), 1.72-1.64 (m, 2H), 1.60-1.55 (m, 1H), 1.54 (d, *J* =1.1 Hz, 3H), 1.50-1.43 (m, 2H), 1.27 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR (150MHz, $CDCl_3$): δ 202.9, 164.7, 149.1, 146.9, 145.4, 133.7, 131.7, 123.5, 115.3, 104.9, 100.4, 96.1, 61.0, 56.1, 48.0, 43.0, 42.3, 32.0, 31.3, 29.7, 28.2, 21.3, 19.6, 19.2, 16.1, 9.1; IR (film): 2924, 1718, 1684, 1653, 1559, 1457, 1116 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{26}H_{38}O_5$, 430.2719, found, 430.2705; $[\alpha]_D^{20}$+16.4 (*c* 0.75, CH_2Cl_2).

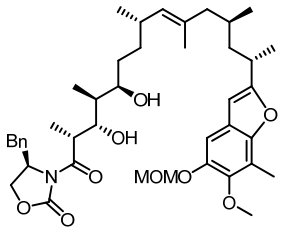


(2*R*,4*S*,5*R*,8*S*,12*S*,14*S*,*E*)-1-((*R*)-4-Benzyl-2-oxooxazolidin-3-yl)-5-hydroxy-14-(6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-2,4,8,10,12-pentamethylpentadec-9-ene-1,3-dione (91).

A 25 mL Schlenk flask was charged with acid free $Sn(OTf)_2$ (502 mg, 1.21 mmol, 1.7 equiv.) and CH_2Cl_2 (4 mL, 0.3 M). The white suspension was treated at -20 °C with Et_3N (167 µL, 1.21 mmol, 1.7 equiv.) whereupon the mixture turned pale yellow. After 5 min β-keto imide 2**6** (338 mg, 1.17 mmol, 1.6 equiv.) in CH_2Cl_2 (2 mL, 0.6 M) was added dropwise and the clear solution was stirred for 1 h at -20 °C. Aldehyde **65** (308 mg, 0.72 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (1.2 mL, 0.6 M) and added slowly at -78 °C. After 45 min at -78°C TLC analysis showed complete consumption of the starting material and the yellow-orange solution was poured onto a cooled and vigorously stirred mixture of CH_2Cl_2 and 1 M $NaHSO_4$ (50 mL, 1 : 1). After 20 min at room temperature the aqueous phase was extracted with CH_2Cl_2 (3 x 15 mL), the organic phase was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the residue by gradient flash chromatography (hexane : ethylacetate from 3 : 1 to 1 : 1) yielded **91** as a viscous oil (448 mg, 87%, dr = 6 : 1 as determined by HPLC and ^{1}H-NMR).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.36-7.27 (m, 3H), 7.22-7.17 (m, 2H), 7.07 (s, 1H), 6.24 (s, 1H), 5.21 (s, 2H), 4.88 (d, *J* = 8.8 Hz, 1H), 4.85 (q, *J* = 7.2 Hz, 1H), 4.78-4.70 (m, 1H), 4.28-4.21 (m, 1H), 4.17 (dd, *J* = 9.1, 3.0 Hz, 1H), 3.92-3.85 (m, 1H), 3.84 (s, 3H), 3.54 (s, 3H), 3.30 (dd, *J* = 13.3, 3.2 Hz, 1H), 3.05-2.94 (m, 1H), 2.81-2.72 (m, 2H), 2.45 (d, *J* = 3.0 Hz, OH), 2.42 (s, 3H), 2.40-2.29 (m, 1H), 2.07 (dd, *J* = 12.4, 5.1 Hz, 1H), 1.78 (dd, *J* = 12.4, 8.2 Hz, 1H), 1.71-1.63 (m, 1H), 1.60-1.44 (m, 2H), 1.54 (d, *J* = 1.3 Hz, 3H), 1.54-1.41 (m, 2H), 1.46 (d, *J* = 7.3 Hz, 3H), 1.37-1.26 (m, 2H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.20 (d, *J* = 7.3 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 212.2, 170.3, 164.8, 153.6, 149.2, 146.9, 145.5, 135.0, 132.8,

132.6, 129.4, 129.0, 127.4, 123.5, 115.3, 105.0, 100.4, 96.2, 71.2, 66.5, 61.0, 56.1, 55.3, 51.9, 48.4, 48.1, 43.0, 38.0, 34.0, 32.3, 32.0, 31.3, 28.2, 21.4, 19.5, 19.2, 16.1, 12.9, 9.9, 9.1; IR (film): 3567, 2956, 1773, 1701, 1685, 1653, 1648, 1559, 1458, 1358, 1217, 1116 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{42}H_{57}O_9NNa$, 742.3831, found, 742.3948; $[\alpha]_D^{20}$-41.4 (*c* 1.0, CH_2Cl_2).

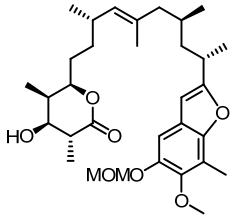


(R)-4-Benzyl-3-((2R,3S,4S,5R,8S,12S,14S,E)-3,5-dihydroxy-14-(6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-2,4,8,10,12-pentamethylpentadec-9-enoyl)oxazolidin-2-one (92).

$Me_4NBH(OAc)_3$ (73 mg, 0.278 mmol, 5 equiv.) was dissolved in 9 mL MeCN : AcOH = 1.9 : 1, cooled to -32 °C and aldol product **91** (main diastereomer, 40 mg, 0.056 mmol, 1.0 equiv.) in MeCN (1 mL) was added dropwise. The reaction was stirred for 3 h at -32 °C, allowed to warm to 0 °C overnight, diluted with CH_2Cl_2 (20 mL) and quenched with a saturated aqueous solution of Rochelle's salt (10 mL). Saturated aqueous $NaHCO_3$ was carefully added to the vigorously stirred solution over 20 min. After 1 h no more gas evolution was observed and the two-phase mixture was partitioned between CH_2Cl_2 (20 mL) and H_2O (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL), and the combined organic fractions were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash chromatography (hexane : ethylacetate from 3 : 1 to 2 : 1) afforded diol **92** as a viscous oil (29 mg, 72%,dr $\geq$ 20 : 1 as determined by ^{1}H-NMR).

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.37-7.27 (m, 3H), 7.22-7.17 (m, 2H), 7.07 (s, 1H), 6.24 (s, 1H), 5.20 (s, 2H), 4.89 (d, *J* = 9.3 Hz, 1H), 4.72-4.65 (m, 1H), 4.25-4.16 (m, 2H), 3.98-3.93 (m, 1H), 3.87 (dq, *J* = 7.24, 2.4 Hz, 1H), 3.83 (s, 3H), 3.82-3.75 (br, 1H), 3.59 (d, *J* = 2.5 Hz, OH), 3.54 (s, 3H), 3.24 (dd, *J* = 13.4, 3.3 Hz, 1H), 3.05-2.94 (m, 1H), 2.79 (dd, *J* = 13.4, 9.3 Hz, 1H), 2.55 (d, *J* = 6.3 Hz,

OH), 2.41 (s, 3H), 2.40-2.31 (m, 1H), 2.08 (dd, *J* = 12.3, 5.2 Hz, 1H), 1.87-1.78 (m, 1H), 1.75 (dd, *J* =12.6, 8.3 Hz, 1H), 1.71-1.62 (m, 1H), 1.62-1.44 (m, 2H), 1.58-1.45 (m, 2H), 1.55 (d, *J* = 1.3 Hz, 3H), 1.49-1.29 (m, 2H), 1.27 (d, *J* = 6.8 Hz, 6H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 6H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 178.1, 164.8, 152.8, 149.2, 146.9, 145.2, 134.9, 133.1, 132.4, 129.4, 129.0, 127.5, 123.5, 115.3, 105.0, 100.4, 96.2, 73.7, 73.6, 66.2, 61.0, 56.1, 55.0, 48.1, 43.1, 39.6, 39.2, 37.8, 34.5, 32.3, 31.3, 31.0, 28.2, 21.4, 19.5, 19.2, 16.1, 11.5, 10.1, 9.1; IR (film): 3678, 3452, 2925, 1783, 1700, 1559, 1455, 1386, 1217, 1153, 1116, 1043 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{42}H_{59}O_9NNa$, 744.4088, found, 744.4098; $[\alpha]_D^{20}$-8.4 (*c* 1.05, CH_2Cl_2).

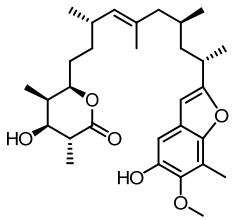


(3*R*,4*S*,5*R*,6*R*)-4-Hydroxy-6-((3*S*,7*S*,9*S*,*E*)-9-(6-methoxy-5-(methoxymethoxy)-7-methylbenzofuran-2-yl)-3,5,7-trimethyldec-4-enyl)-3,5-dimethyltetrahydro-2H-pyran-2-one (66).

A solution of diol **92** (635 mg, 0.88 mmol, 1.0 equiv.) in THF / H_2O = 3 : 1 (9 mL 0.1 M) was treated at 0 °C with H_2O_2 (30% in H_2O, 352 µL). LiOH (59 mg, 1.41 mmol, 1.6 equiv.) was added in one portion and stirring was continued for 1 h at ambient temperature. The mixture was acidified with 1 N HCl (5 mL), stirred for further 5 min and then diluted with H_2O (30 mL), extracted with Et_2O (3 x 20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (hexane : ethylacetate from 3 : 1 to 1 : 1) gave lactone **66** (458 mg, 96%) as an oil.

^{1}H-NMR (400MHz, $CDCl_3$): δ 7.07 (s, 1H), 6.24 (s, 1H), 5.21 (s, 2H), 4.87 (d, *J* = 9.1 Hz, 1H), 4.14 (ddd, *J* = 8.1, 5.4, 2.3 Hz, 1H), 3.84 (s, 3H), 3.77 (dd, *J* = 10.2, 4.2 Hz, 1H), 3.54 (s, 3H), 3.06-2.95 (m, 1H), 2.48-2.40 (m, 1H), 2.42 (s, 3H), 2.40-2.31 (m, 1H), 2.11-2.02 (m, 2H), 1.94-1.84 (m, OH), 1.82-1.69 (m, 2H), 1.73-1.62 (m, 1H), 1.62-1.52 (m, 1H), 1.54 (d, *J* = 1.3 Hz, 3H), 1.52-1.43 (m,

1H), 1.46-1.35 (m, 1H), 1.42-1.29 (m, 2H), 1.38 (d, *J* = 7.1 Hz, 3H), 1.27 (d, *J* = 7.1 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 173.6, 164.7, 149.2, 146.8, 145.5, 132.9, 132.3, 123.5, 115.3, 105.0, 100.4, 96.2, 79.9, 73.9, 61.0, 56.1, 47.9, 43.0, 39.8, 37.3, 33.1, 32.1, 31.3, 30.2, 28.2, 21.3, 19.6, 19.2, 16.2, 14.2, 9.1, 4.4; IR (film): 3454, 2927, 1733, 1700, 1559, 1456, 1219, 1153, 1115, 1043 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{32}H_{48}O_7Na$, 567.3298, found, 567.3310; $[\alpha]_D^{20}$+50.7 (*c* 0.55, CH_2Cl_2).

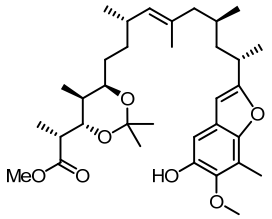


(3*R*,4*S*,5*R*,6*R*)-4-Hydroxy-6-((3*S*,7*S*,9*S*,*E*)-9-(5-hydroxy-6-methoxy-7-methylbenzofuran-2-yl)-3,5,7-trimethyldec-4-enyl)-3,5-dimethyltetrahydro-2*H*-pyran-2-one (93).

Lactone **66** (93 mg, 0.170 mmol, 1.0 equiv.) in dioxane (2 mL) was heated to 50 °C and 2 drops of 3 N HCl were added. After stirring for 2 h the reaction mixture was poured onto H_2O (10 mL), extracted with Et_2O (4 x 20 mL), washed with brine (15 mL), dried over $MgSO_4$ and concentrated. For analytical purposes a small sample of crude phenol **93** was purified by flash chromatography (hexane : ethylacetate = 3 : 1).

^{1}H-NMR (400MHz, $CDCl_3$): δ 6.86 (s, 1H), 6.23 (s, 1H), 5.46 (s, OH), 4.87 (d, *J* = 9.1 Hz, 1H), 4.15 (ddd, *J* = 8.4, 5.4, 2.6 Hz, 1H), 3.83 (s, 3H), 3.82-3.75 (m, 1H), 3.04-2.94 (m, 1H), 2.47-2.40 (m, 1H), 2.45 (s, 3H), 2.40-2.30 (m, 1H), 2.11-2.02 (m, 2H), 1.81-1.70 (m, 2H+OH), 1.70-1.62 (m, 1H), 1.62-1.53 (m, 1H), 1.54 (d, *J* = 1.3 Hz, 3H), 1.51-1.42 (m, 1H), 1.47-1.36 (m, 1H), 1.42-1.29 (m, 2H), 1.39 (d, *J* = 7.3 Hz, 3H), 1.27 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.3 Hz, 3H), 0.93 (d, *J* = 7.1 Hz, 3H), 0.82 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 173.6, 164.7, 147.8, 145.1, 142.8, 133.0, 132.3, 123.7, 113.7, 101.9, 100.3, 79.9, 74.0, 61.5, 47.9, 43.0, 39.8, 37.3, 33.2, 32.2, 31.3, 30.3, 28.2, 21.3, 19.5, 19.1, 16.1, 14.2, 9.4, 4.4; IR (film): 3443, 2925, 1718, 1653, 1609, 1559, 1507, 1457, 1380, 1217, 1111 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{30}H_{44}O_6Na$, 523.3036,

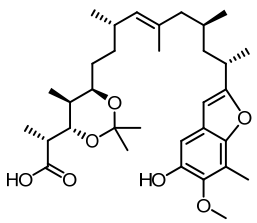
found, 523.3030; $[\alpha]_D^{20}$+55.1 (*c* 1.40, CH_2Cl_2).



(*R*)-Methyl 2-((4*S*,5*S*,6*R*)-6-((3*S*,7*S*,9*S*,*E*)-9-(5-hydroxy-6-methoxy-7-methylbenzofuran-2-yl)-3,5,7-trimethyldec-4-enyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propanoate (94).

Phenol **93** was dissolved in 2,2-dimethoxypropane (2 mL), treated with camphorsulfonic acid (4 mg, 0.017 mmol, 0.1 equiv.) and stirred overnight at room temperature. The solution was diluted with Et_2O (10 mL), neutralized with saturated aqueous $NaHCO_3$ (10 mL), extracted with Et_2O (3 x 10 mL), washed with brine (10 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by flash chromatography (hexane : ethylacetate = 5 : 1) to yield ester **94** (82 mg, 85% over 2 steps).

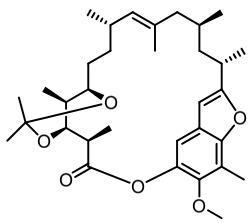
^{1}H-NMR (400MHz, $CDCl_3$): δ 6.87 (s, 1H), 6.23 (s, 1H), 5.43 (s, OH), 4.89 (d, *J* = 9.3 Hz, 1H), 3.83 (s, 3H), 3.75-3.68 (m, 1H), 3.68 (s, 3H), 3.61 (dd, *J* = 7.6, 5.1 Hz, 1H), 3.04-2.94 (m, 1H), 2.60-2.51 (m, 1H), 2.45 (s, 3H), 2.41-2.27 (m, 1H), 2.06 (dd, *J* = 12.5, 4.9 Hz, 1H), 1.82-1.75 (m, 1H), 1.81-1.73 (m, 1H), 1.72-1.64 (m, 1H), 1.61-1.44 (m, 2H), 1.55 (d, *J* = 1.3 Hz, 3H), 1.48-1.36 (m, 1H), 1.33-1.21 (m, 2H), 1.30 (s, 3H), 1.29 (s, 3H), 1.27 (d, *J* = 7.1 Hz, 3H), 1.26-1.19 (m, 1H), 1.18 (d, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.3 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 174.9, 164.8, 147.5, 145.1, 142.5, 133.0, 132.3, 124.2, 113.8, 101.9, 100.5, 100.3, 75.4, 69.3, 61.5, 51.6, 48.1, 43.0 (2C), 36.8, 33.8, 32.2, 31.3, 28.5, 28.2, 25.0, 23.7, 21.3, 19.5, 19.1, 16.1, 11.9, 11.4, 9.4; IR (film): 3445, 2954, 1738, 1609, 1456, 1380, 1225, 1111, 1021 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{34}H_{52}O_7Na$, 595.3611 found, 595.3607; $[\alpha]_D^{20}$-3.0 (*c* 0.50, CH_2Cl_2).



(*R*)-2-((4*S*,5*S*,6*R*)-6-((3*S*,7*S*,9*S*,*E*)-9-(5-Hydroxy-6-methoxy-7-methylbenzofuran-2-yl)-3,5,7-trimethyldec-4-enyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propanoic acid (95).

Ester **94** (69 mg, 0.12 mmol, 1.0 equiv.) was dissolved in THF-MeOH-H_2O (1 mL, 2 : 2 : 1), treated with LiOH (51 mg, 1.21 mmol, 10 equiv.) and stirred for 16 h at room temperature. The mixture was diluted with H_2O (10 mL), acidified to pH 5 with 1% HCl, extracted with CH_2Cl_2 (4 x 10 mL) and dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the crude material was purified by flash chromatography (hexane : ethylacetate from 2 : 1 to 1 : 1) to afford *seco*-acid **95** (58 mg, 84%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 6.87 (s, 1H), 6.23 (s, 1H), 4.87 (d, *J* = 9.3 Hz, 1H), 3.83 (s, 3H), 3.74-3.68 (m, 1H), 3.64 (dd, *J* = 7.6, 3.8 Hz, 1H), 3.04-2.94 (m, 1H), 2.68 (dq, *J* = 7.2, 3.9 Hz, 1H), 2.45 (s, 3H), 2.40-2.29 (m, 1H), 2.06 (dd, *J* = 12.4, 5.6 Hz, 1H), 1.80-1.72 (m, 2H), 1.72-1.63 (m, 1H), 1.61-1.44 (m, 2H), 1.54 (d, *J* = 1.0 Hz, 3H), 1.46-1.38 (m, 1H), 1.36-1.19 (m, 2H), 1.36 (s, 6H), 1.30-1.21 (m, 1H), 1.27 (d, *J* = 7.3 Hz, 3H), 1.21 (d, *J* = 7.3 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.3 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 175.6, 164.8, 147.8, 145.1, 142.4, 132.8, 132.4, 124.2, 113.8, 102.0, 101.2, 100.3, 75.3, 69.6, 61.4, 48.0, 43.0 42.7, 36.4, 33.7, 32.3, 31.3, 28.3, 28.2, 25.0, 23.8, 21.3, 19.5, 19.1, 16.1, 12.4, 11.2, 9.4; IR (film): 3312, 2976, 2931, 1709, 1653, 1608, 1457, 1419, 1381, 1225, 1111, 1020 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{33}H_{50}O_7Na$, 581.3454 found, 581.3451; $[\alpha]_D^{20}$-6.3 (*c* 1.00, CH_2Cl_2).



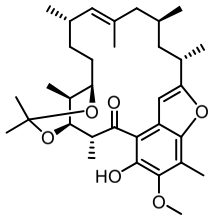
Macrolactone 67.

A 50 mL Schlenk flask was charged with EDCI·HCl (14 mg, 0.072 mmol, 2 equiv.), DMAP (13 mg, 0.107 mmol, 3 equiv.), and DMAP·HCl (11 mg, 0.072 mmol, 2 equiv.). Ethanol-free $CHCl_3$ (25 mL) was added, the mixture was heated to reflux and *seco*-acid **95** (20 mg, 0.036 mmol, 1.0 equiv.) in $CHCl_3$ (4 mL) was added *via* syringe pump over 20 h. The reaction was cooled to room temperature and quenched with saturated aqueous NH_4Cl (40 mL). The layers were separated, the aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL), and the combined organic extracts were dried over $MgSO_4$, filtered through a short pad of silica gel, and concentrated *in vacuo*. Flash column chromatography (hexane : ethylacetate from 20 : 1 to 10 : 1) provided macrolactone **67** along with dimer **67'** as yellow viscous oils (14 mg, 73%, 3 : 1).

67: ^{1}H-NMR (400MHz, $CDCl_3$): δ 7.04 (s, 1H), 6.20 (s, 1H), 4.42 (d, *J* = 8.8 Hz, 1H), 3.80 (s, 3H), 3.80-3.74 (m, 1H), 3.56 (t, *J* = 4.9 Hz, 1H), 3.17-3.07 (m, 1H), 3.05 (dq, *J* = 7.1, 4.5 Hz, 1H), 2.45 (s, 3H), 2.30-2.17 (m, 1H), 1.97 (d, *J* = 14.7 Hz, 1H), 1.94-1.86 (m, 1H), 1.63-1.54 (m, 1H), 1.52-1.42 (m, 1H), 1.51 (s, 3H), 1.49-1.23 (m, 2H), 1.44 (s, 3H), 1.41 (s, 3H), 1.41-1.30 (m, 1H), 1.38 (d, *J* = 6.8 Hz, 3H), 1.37-1.21 (m, 1H), 1.33 (d, *J* =7.3 Hz, 3H), 1.02-0.80 (m, 2H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.3 Hz, 3H), 0.79 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 172.6, 162.8, 151.4, 146.7, 140.2, 131.4, 129.2, 123.5, 115.5, 110.0, 102.7, 100.6, 78.2, 69.6, 61.5, 43.9, 42.7, 42.4, 33.7, 33.5, 32.0, 31.4, 28.1, 27.9, 26.8, 24.3, 21.5, 20.1, 19.1, 18.9, 14.2, 12.9, 9.2; IR (film): 2930, 1760, 1604, 1456, 1418, 1379, 1226, 1195, 1111, 1024, 1001 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{33}H_{48}O_6Na$, 563.3349 found, 563.3352; $[\alpha]_D^{20}$-41.7 (*c* 0.35, CH_2Cl_2).

67' ^{1}H-NMR (400MHz, $CDCl_3$): δ 6.92 (s, 1H), 6.25 (s, 1H), 4.88 (d, *J* = 9.3 Hz, 1H), 3.84-3.78 (m, 1H), 3.74 (s, 3H), 3.68 (t, *J* = 6.7 Hz, 1H), 3.04-2.94 (m, 1H), 2.93-2.85 (m, 1H), 2.43 (s, 3H), 2.41-2.30 (m, 1H), 2.05 (dd, *J* = 13.1, 5.6 Hz, 1H), 1.98-1.89 (m, 1H), 1.76 (dd, *J* = 13.3, 8.0 Hz, 1H),

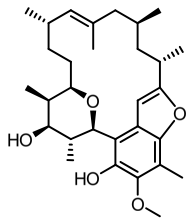
1.69-1.60 (m, 1H), 1.61-1.45 (m, 2H). 1.53 (d, *J* = 1.0 Hz, 3H), 1.51-1.21 (m, 2H), 1.37 (s, 3H), 1.36 (d, *J* = 6.8 Hz, 3H), 1.33 (s, 3H), 1.33-1.23 (m, 2H), 1.26 (d, *J* =6.8 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 173.2, 165.3, 151.4, 146.4, 140.0, 132.8, 132.2, 130.1 123.8, 115.5, 110.4, 100.4, 76.1, 69.1, 61.4, 47.5, 44.2, 42.9, 36.9, 33.7, 32.4, 31.4, 28.6 (2C), 25.5, 24.2, 21.4, 20.0, 19.8, 16.6, 13.1, 12.5, 9.3; IR (film): 2930, 1762, 1601, 1457, 1418, 1379, 1226, 1195, 1111, 1024, 1001 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{66}H_{96}O_{12}Na$, 1103.6800 found, 1103.6770; $[\alpha]_D^{20}$-36.6 (*c* 0.50, CH_2Cl_2).



Ketone 68.

Macrolactone **67** (4.0 mg, 7.4 μmol) in cyclohexane (10 mL) was irradiated with a Hannovia 700W medium pressure mercury lamp with a quartz filter at room temperatur for 50 min. The intensely yellow solution was concentrated and the crude residue was subjected to flash column chromatography (hexane : ethylacetate = 10 : 1) to furnish ketone **68** as a yellow oil (3.1 mg, 75%).

^{1}H-NMR (400MHz, $CDCl_3$): δ 13.73 (s, 1H), 6.77 (s, 1H), 4.67 (d, *J* = 9.1 Hz, 1H), 3.91 (s, 3H), 3.90-3.81 (m, 2H), 3.60 (dd, *J* = 8.5, 6.7 Hz, 1H), 3.14-3.04(m, 1H), 2.54-2.44 (m, 1H), 2.50 (s, 3H), 2.30 (d, *J* = 14.4 Hz, 1H), 1.86-1.77 (m, 1H), 1.70 (d, *J* = 1.0 Hz, 3H), 1.64-1.56 (m, 1H), 1.50-1.42 (m, 1H), 1.49 (dd, *J* = 9.3, 5.6 HZ, 1H), 1.49-1.21 (m, 1H), 1.44-1.34 (m, 1H), 1.39-1.17 (m, 2H), 1.37 (s, 3H), 1.36 (d, *J* = 6.3 Hz, 3H), 1.35 (s, 3H), 1.34 (d, *J* =6.3 Hz, 3H), 1.17-1.07 (m, 1H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.1 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): δ 208.1, 163.7, 156.3, 147.2, 143.6, 132.5, 129.2, 125.3, 121.9, 110.6, 103.8, 100.3, 78.2, 68.4, 60.6, 47.3, 43.8, 43.6, 37.0, 32.1, 31.7, 31.3, 30.3, 26.9, 25.9, 24.4, 21.5, 20.9, 20.0, 19.5, 15.8, 12.5, 9.9; IR (film): 2930, 1613, 1455, 1379, 1313, 1265, 1162, 1124, 1083 cm^{-1}; HRMS (ESI) (*m/z*): $[M+Na]^+$ calcd for $C_{33}H_{48}O_6Na$, 563.3349 found, 563.3355; $[\alpha]_D^{20}$-58.7 (*c* 0.30, CH_2Cl_2).

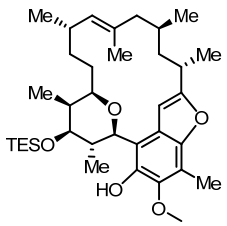


Tetrahydropyran 5.

Ketone **68** (3.0 mg, 5.5 μmol, 1.0 equiv.) was dissolved in MeOH (1 mL) and $NaBH_4$ (0.8 mg, 22.2 μmol, 4 equiv.) was added in one portion, whereupon the yellow solution immediately turned colorless. After 10 min, the reaction was quenched by the dropwise addition of 0.5 N HCl (200 μL) and stirring was continued at room temperature for 30 min. H_2O (10 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (4 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated to dryness. The residue was dried by azeotropic distillation with toluene (2 x 5 mL) and used without further purification.

The crude product was dissolved in toluene (1 mL) and a catalytical amount of *p*-toluenesulfonic acid was added. The flask was capped and the solution was heated to 60 °C for 30 min. The mixture was allowed to cool to room temperature and was directly loaded onto a silica column and purified by flash chromatography (hexane : ethylacetate from 2 : 1 to 1 : 1) gave tetrahydropyran **5** (1.9 mg, 71%) as a white foam. All analytical data matched with those of the material described previously (confer conversion of **60** to **5**).[2]

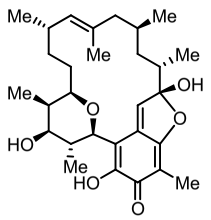
[2] Y. Yu, H. Men, C. Lee, *J. Am.Chem. Soc.* **2004**, *126*, 14720.



TES Ether 96.

Tetrahydropyran **5** (18 mg, 0.037 mmol, 1.0 equiv.) in CH_2Cl_2 (4 mL) was cooled to 0 °C and Et_3N (36 µL, 0.260, 7 equiv.) was added. After 5 min TESOTf (10 µL, 0.045 mmol, 1.2 equiv.) in CH_2Cl_2 (1 mL) was added to the solution *via* cannula. The mixture was allowed to warm to room temperature overnight, and was quenched with aqueous saturated $NaHCO_3$ (20 µL) and concentrated under reduced pressure. Purification by flash chromatography (hexane : ethylacetate from 20 : 1 to 10 :1) afforded pure TES-ether **96** (18mg, 82%). The analytical data matched those reported by Lee.[2]

^{1}H-NMR (600MHz, $CDCl_3$): δ 6.55 (s, 1H), 5.51 (s, 1H), 4.60 (d, *J* = 9.4 Hz, 1H), 4.52 (d, *J* = 10.2 Hz, 1H), 3.82 (s, 3H), 3.62 (d, *J* = 10.0, 4.7 Hz, 1H), 3.40 (d, *J* = 11.0, 1H), 3.10-3.02 (m, 1H), 2.48-2.40 (m, 1H), 2.45 (s, 3H), 2.26-2.18 (m, 1H), 1.87-1.79 (m, 1H), 1.78-1.73 (m, 1H), 1.62 (s, 3H), 1.61-1.54 (m, 1H), 1.47-1.39 (m, 2H), 1.37 (d, *J* =6.8 Hz, 3H), 1.36-1.17 (m, 5H), 1.03 (d, *J* =6.8 Hz, 3H), 0.98 (t, *J* = 7.9 Hz, 9H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* =6.7 Hz, 3H), 0.76 (d, *J* = 6.5 Hz, 3H), 0.63 (q, *J* = 7.9 Hz, 6H); ^{13}C-NMR (150MHz, $CDCl_3$): δ 159.6, 148.2, 141.6, 141.4, 131.5, 129.0, 122.2, 116.2, 112.3, 104.9, 77.9, 77.7, 77.5, 61.4, 43.8, 41.8, 40.8, 38.7, 33.7, 32.6, 31.5, 31.3, 27.5, 21.8, 21.0, 19.6, 18.7, 13.3, 9.4, 7.0, 6.9, 5.1; IR (film): 2954, 1456, 1404, 1383, 1325, 1107, 1081 cm^{-1}; HRMS (ESI) (*m/z*): $[M]^+$ calcd for $C_{36}H_{58}O_5SiNa$, 621.3951, found, 621.3943; $[\alpha]_D^{23}$+37.2 (*c* 1.00, $CHCl_3$).



Kendomycin (1).

TES-ether **96** (17mg, 0.028 mmol, 1.0 equiv.) was dissolved in degassed DMF (3 mL), and IBX (24 mg, 0.085 mmol, 3 equiv.) was added at room temperature, whereupon the solution turned orange. After stirred for 24 h in the dark, TLC analysis showed complete consumption of the starting material. The purple solution was directly loaded onto a silica column and eluted (hexane : ethylacetate = 10 : 1) to afford the o-quinone as a purple-blue oil, which was dissolved in MeCN (3 mL) and treated with aqueous HF (0.1 M, 369 µL, 0.037 mmol, 1.3 equiv.). The initial blue solution turned yellow within 4 h and the reaction mixture was partitioned between etyhlacetate (50 mL) and saturated aqueous $NaHCO_3$ (10 mL). The aqueous phase was extracted with ethylacetate (3 x 10 mL), and the organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (hexane : ethylacetate = 2 : 1) gave kendomycin **1** (4 mg, 29% over 2 steps) as a yellow solid.

All analytical data matched with those of the material described previously (confer conversion of **71** to **1**).

Comparison of the ^{1}H- and ^{13}C-NMR Data of Natural and Synthetic (-)-Kendomycin **1**.

^{1}H-NMR (600 MHz, CD_3COCD_3)		^{13}C-NMR (600 MHz, CD_3COCD_3)	
Natural	Synthetic	Natural	Synthetic
8.10 (s, 4-OH)	8.10 (s, 4-OH)	182.1 (C-3)	182.1 (C-3)
7.19 (s, 20-H)	7.19 (s, 20-H)	168.6 (C-1)	168.6 (C-1)
6.54 (s, 19-OH)	6.54 (s, 19-OH)	146.8 (C-4)	146.8 (C-4)
4.64 (d, *J* = 10.2 Hz, 13-H)	4.64 (d, *J* = 10.0 Hz, 13-H)	141.3 (C-20)	141.3 (C-20)
4.36 (d, *J* = 10.4 Hz, 5-H)	4.35 (d, *J* = 10.3 Hz, 5-H)	132.1 (C-14)	132.1 (C-14)
3.95 (d, *J* = 4.5 Hz, 7-OH)	3.95 (d, *J* = 4.5 Hz, 7-OH)	130.2 (C-20a)	130.2 (C-20a)
3.56 (m, 7-H)	3.56 (m, 7-H)	129.9 (C-13)	129.9 (C-13)
3.53 (ddd, *J* = 10.8, 2.5, 1.1 Hz, 9-H)	3.53 (ddd, *J* = 11.0, 2.3, 1.1 Hz, 9-H)	119.1 (C-19)	119.1 (C-19)
2.41 (m, 18-H)	2.42 (m, 18-H)	111.0 (C-4a)	111.0 (C-4a)
2.36 (m, 12-H)	2.36 (m, 12-H)	104.2 (C-2)	104.2 (C-2)
2.12 (br d, *J* = 17.1 Hz, 15-H^{a})	2.12 (br d, *J* = 17.0 Hz, 15-H^{a})	78.7 (C-9)	78.7 (C-9)
1.96 (m, 16-H)	1.96 (m, 16-H)	77.7 (C-5)	77.8 (C-5)
1.88 (m, 8-H)	1.88 (m, 8-H)	76.2 (C-7)	76.2 (C-7)
1.84 (s, 2-CH_3)	1.84 (s, 2-CH_3)	46.1 (C-15)	46.1 (C-15)
1.70 (m, 6-H)	1.71 (m, 6-H)	41.4 (C-18)	41.4 (C-18)
1.68 (m, 15-H^{b})	1.67 (m, 15-H^{b})	40.8 (C-8)	40.8 (C-8)
1.63 (m, 17-H^{a})	1.64 (m, 17-H^{a})	39.7 (C-17)	39.8 (C-17)
1.61 (s, 14-CH_3)	1.61 (s, 14-CH_3)	38.1 (C-6)	38.1 (C-6)
1.57 (m, 10-H^{a})	1.57 (m, 10-H^{a})	35.8 (C-11)	35.9 (C-11)
1.45 (ddd, *J* = 13.1, 11.2, 3.0 Hz, 17-H^{b})	1.45 (ddd, *J* = 12.9, 11.4, 2.9 Hz, 17-H^{b})	33.4 (C-12)	33.6 (C-12)
1.32 (m, 11-H_2)	1.32 (m, 11-H_2)	33.5 (C-10)	33.5 (C-10)
1.25 (m, 10-H^{b})	1.25 (m, 10-H^{b})	26.5 (C-16)	26.5 (C-16)
0.95 (d, *J* = 7.0 Hz, 8-CH_3)	0.95 (d, *J* = 7.0 Hz, 8-CH_3)	22.7 (C-12)	22.7 (C-12)
0.94 (d, *J* = 6.5 Hz, 16-CH_3)	0.94 (d, *J* = 6.5 Hz, 16-CH_3)	19.9 (14-CH_3)	19.9 (14-CH_3)
0.89 (d, *J* = 6.5 Hz, 6-CH_3)	0.89 (d, *J* = 6.5 Hz, 6-CH_3)	19.7 (16-CH_3)	19.7 (16-CH_3)
0.87 (d, *J* = 6.5 Hz, 12-CH_3)	0.87 (d, *J* = 6.5 Hz, 12-CH_3)	13.3 (6-CH_3)	13.3 (6-CH_3)
0.71 (d, *J* = 7.0 Hz, 18-CH_3)	0.71 (d, *J* = 7.0 Hz, 18-CH_3)	12.6 (18-CH_3)	12.7 (18-CH_3)
		7.6 (2-CH_3)	7.6 (2-CH_3)
		7.2 (8-CH_3)	7.2 (8-CH_3)

Ring Closing Metathesis and Photo-Fries Reaction for the Construction of the Ansamycin Antibiotic Kendomycin. Development of a Protecting Group Free Oxidative Endgame.

SUPPORTING INFORMATION (^{1}H and ^{13}C NMR)

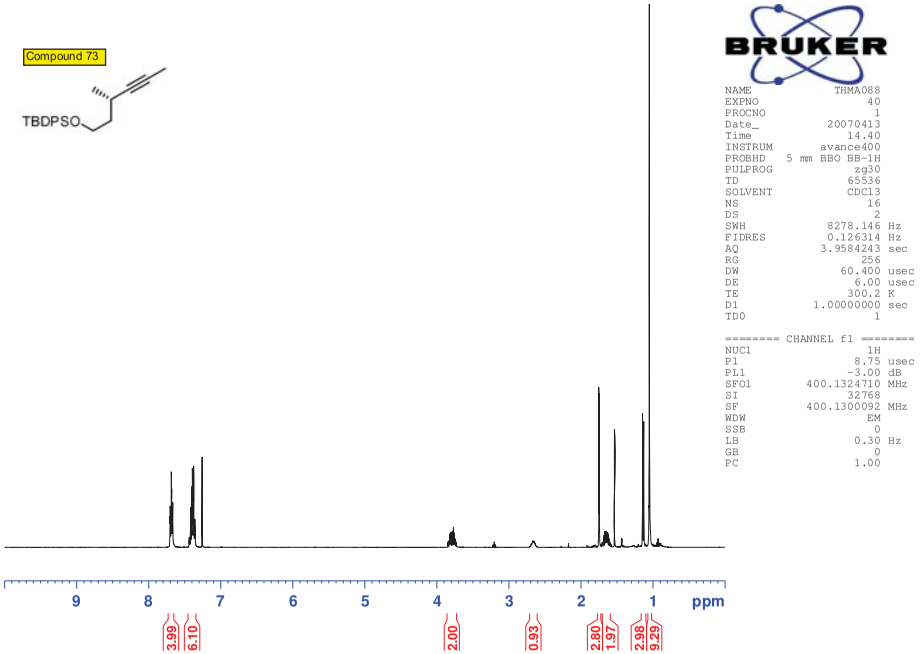
Thomas Magauer, Harry J. Martin and Johann Mulzer*

Institute of Organic Chemistry, University of Vienna

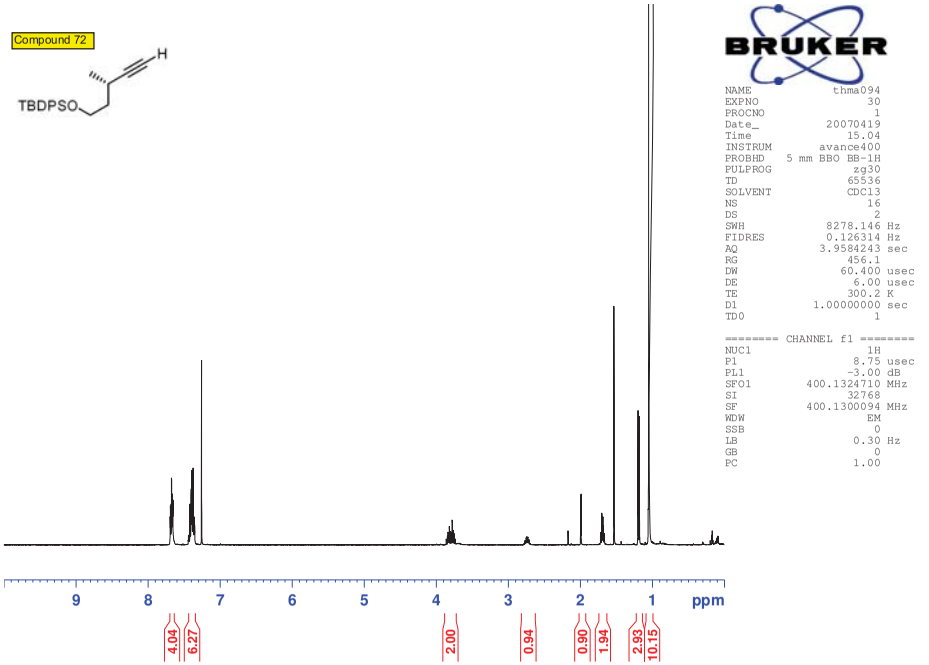
Währingerstraße 38

1090 Vienna

Austria

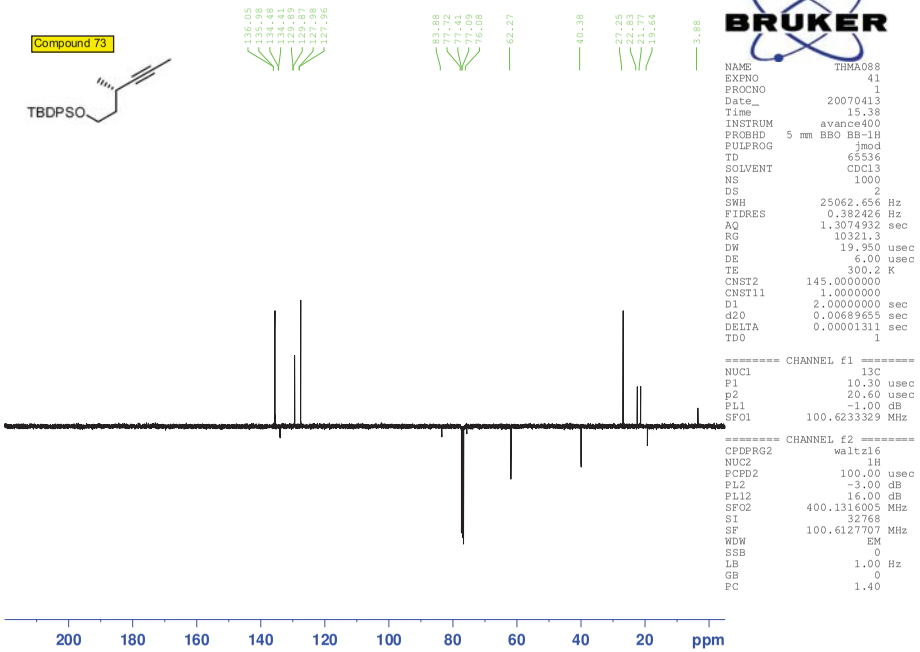



```
NAME                THMA088
EXPNO                    40
PROCNO                    1
Date_              20070413
Time                  14.40
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                     256
DW                  60.400 usec
DE                   6.00 usec
TE                  300.2 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1           400.1324710 MHz
SI                   32768
SF             400.1300092 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```

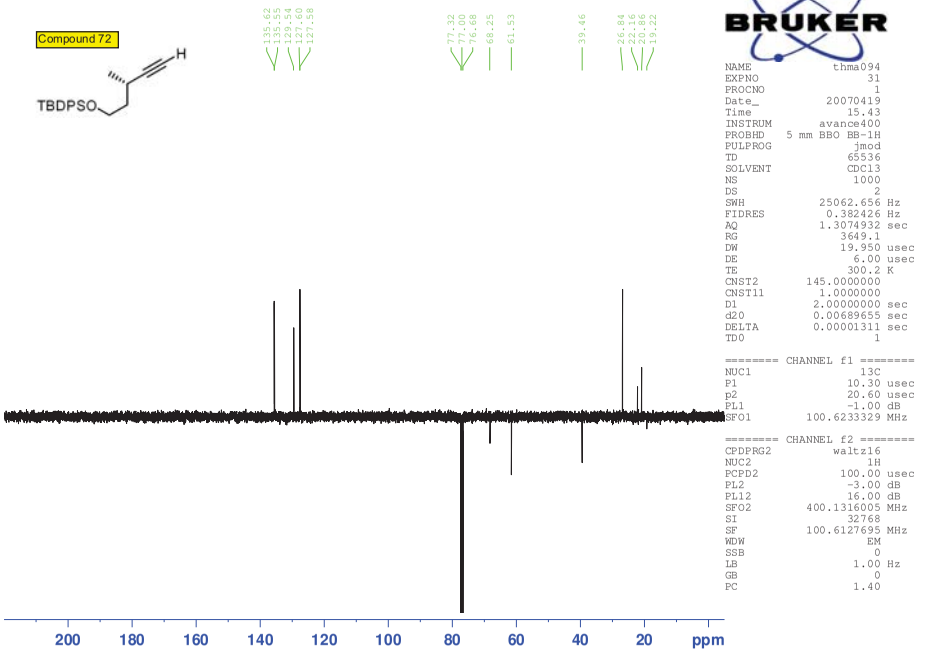



```
NAME                thma094
EXPNO                    30
PROCNO                    1
Date_              20070419
Time                  15.04
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                   456.1
DW                  60.400 usec
DE                   6.00 usec
TE                  300.2 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1           400.1324710 MHz
SI                   32768
SF             400.1300094 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```

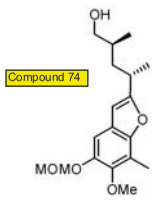
73



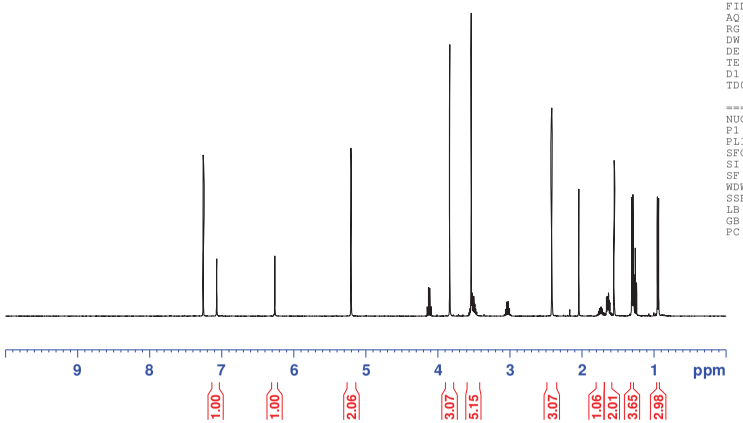

```
NAME                THMA088
EXPNO                    41
PROCNO                    1
Date_              20070413
Time                  15.38
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1000
DS                       2
SWH              25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                10321.3
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2           400.1316005 MHz
SI                   32768
SF             100.6127707 MHz
WDW                     EM
SSB                      0
LB                  1.00 Hz
GB                       0
PC                    1.40
```




```
NAME                thma094
EXPNO                    31
PROCNO                    1
Date_              20070419
Time                  15.43
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1000
DS                       2
SWH              25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                3649.1
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2           400.1316005 MHz
SI                   32768
SF             100.6127695 MHz
WDW                     EM
SSB                      0
LB                  1.00 Hz
GB                       0
PC                    1.40
```

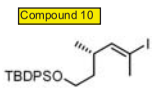


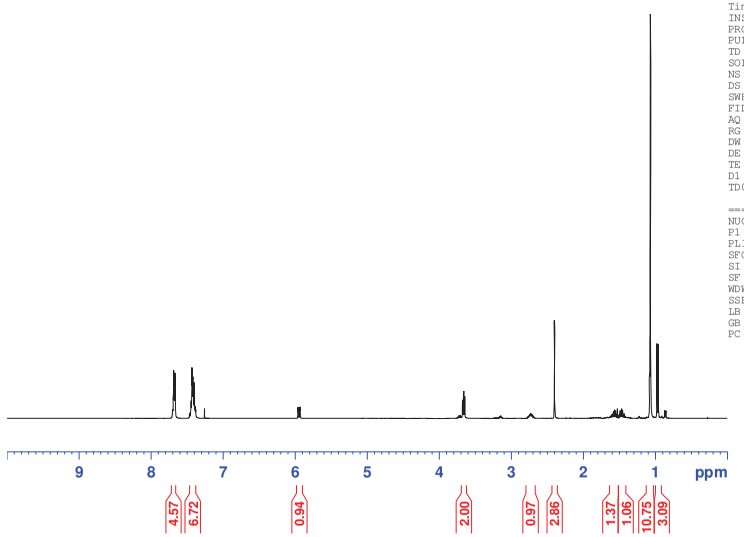
Compound 74




```
NAME                THMA 084
EXPNO                     70
PROCNO                     1
Date_               20070412
Time                   22.21
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                8278.146 Hz
FIDRES                0.126314 Hz
AQ                 3.9584243 sec
RG                       512
DW                    60.400 usec
DE                     6.00 usec
TE                     300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                     32768
SF             400.1300095 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                      1.00
```

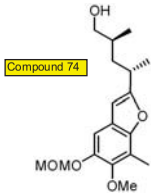
Compound 10



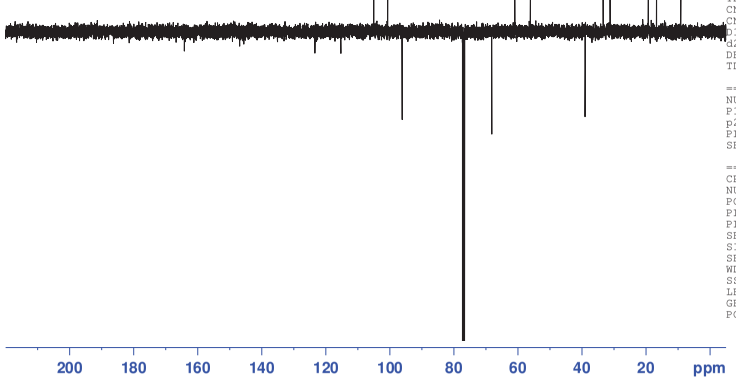



```
NAME                thma100
EXPNO                    10
PROCNO                    1
Date_               20070424
Time                   7.57
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                8278.146 Hz
FIDRES                0.126314 Hz
AQ                 3.9584243 sec
RG                        64
DW                    60.400 usec
DE                     6.00 usec
TE                     300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                     32768
SF             400.1300093 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                      1.00
```

74

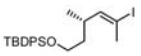


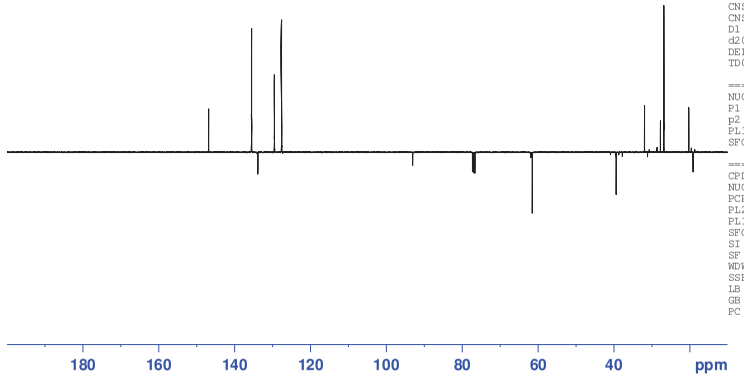
Compound 74



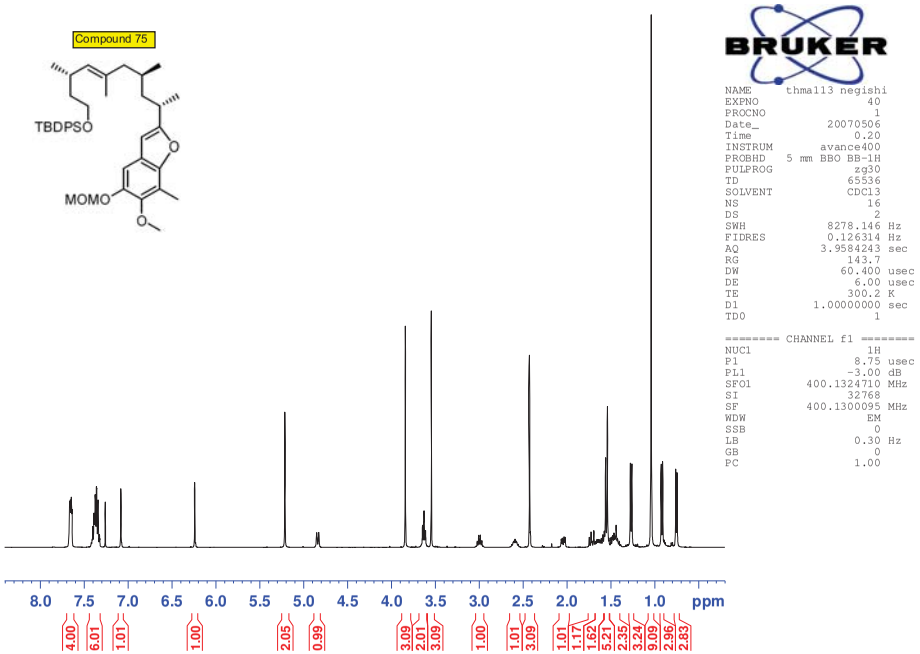

```
NAME                THMA 084
EXPNO                     71
PROCNO                     1
Date_               20070412
Time                   23.18
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1000
DS                         2
SWH               25062.656 Hz
FIDRES                0.382426 Hz
AQ                 1.3074932 sec
RG                    4597.6
DW                    19.950 usec
DE                     6.00 usec
TE                     300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                  2.00000000 sec
D20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                     32768
SF             100.6127694 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                      1.00
```

Compound 10

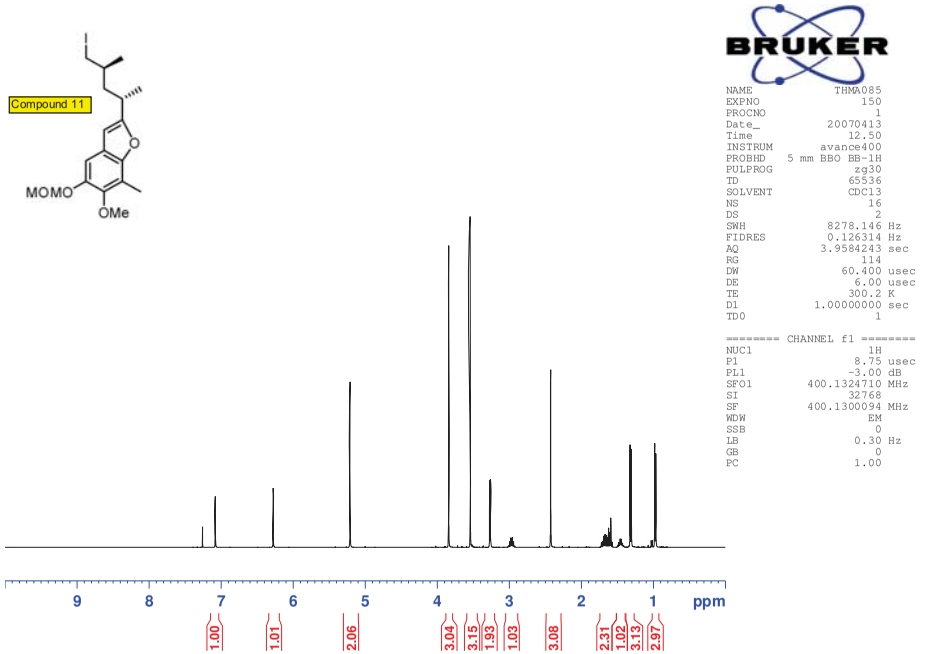





```
NAME                thma100
EXPNO                    11
PROCNO                    1
Date_               20070424
Time                   8.54
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1000
DS                         2
SWH               25062.656 Hz
FIDRES                0.382426 Hz
AQ                 1.3074932 sec
RG                    5792.6
DW                    19.950 usec
DE                     6.00 usec
TE                     300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                  2.00000000 sec
D20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                     32768
SF             100.6127736 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                     18.00
```

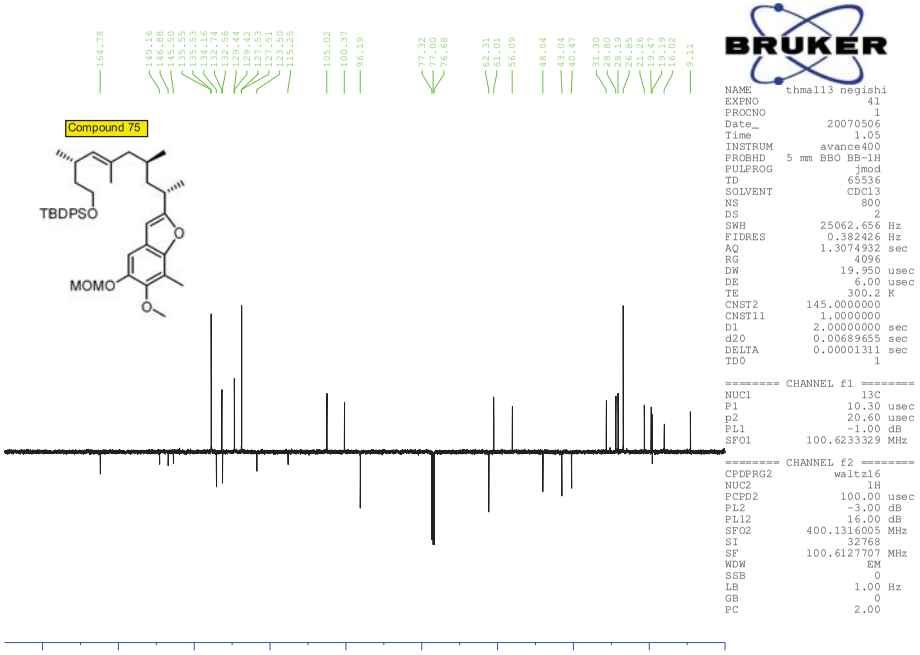



```
NAME          thma113 negishi
EXPNO                      40
PROCNO                      1
Date_               20070506
Time                    0.20
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     143.7
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                     32768
SF             400.1300095 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

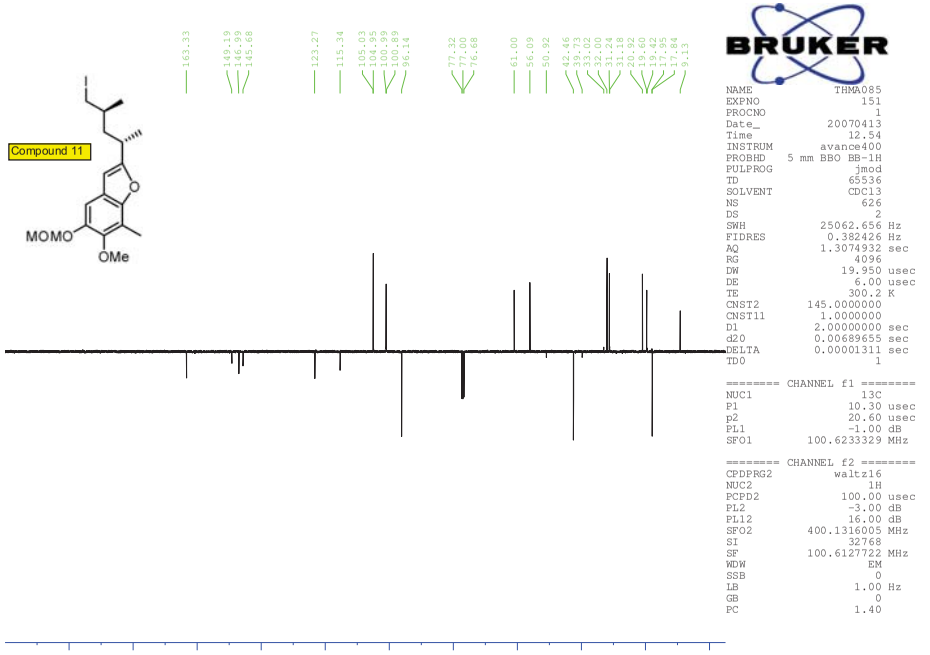



```
NAME             THMA085
EXPNO                150
PROCNO                 1
Date_           20070413
Time                12.50
INSTRUM       avance400
PROBHD    5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            8278.146 Hz
FIDRES         0.126314 Hz
AQ             3.9584243 sec
RG                   114
DW                60.400 usec
DE                 6.00 usec
TE                300.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 8.75 usec
PL1               -3.00 dB
SFO1       400.1324710 MHz
SI                 32768
SF         400.1300094 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

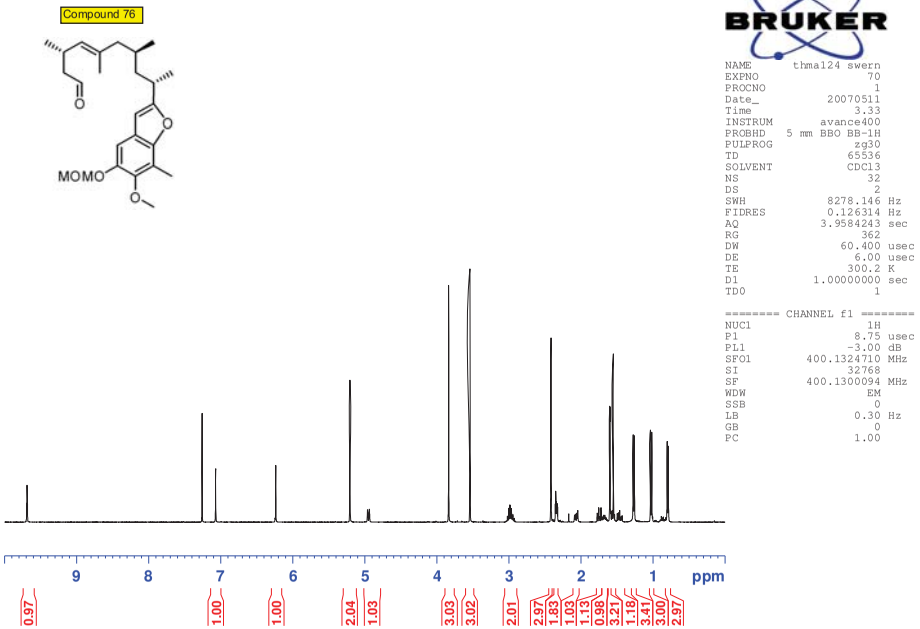
75



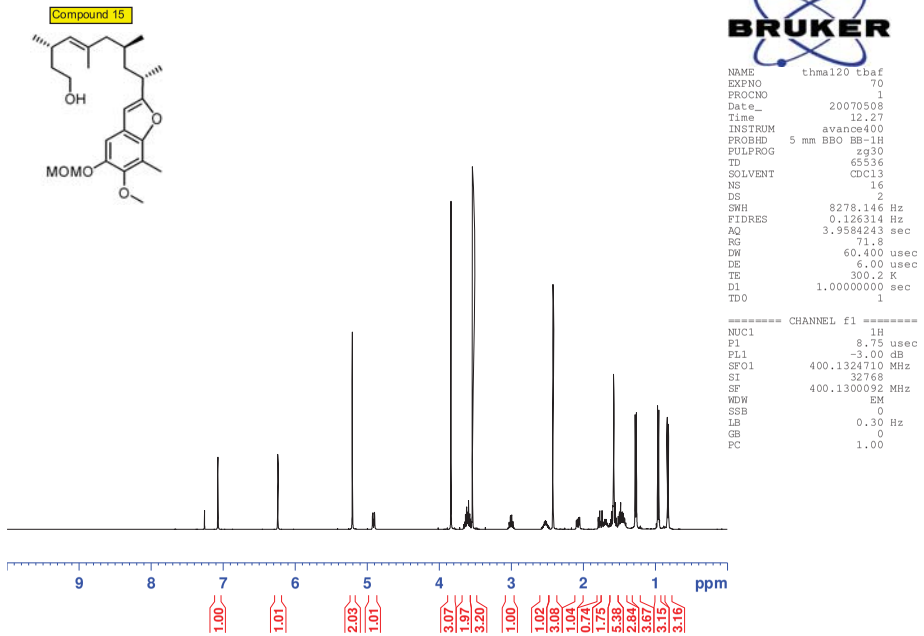

```
NAME          thma113 negishi
EXPNO                      41
PROCNO                      1
Date_               20070506
Time                    1.05
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                       800
DS                         2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                      4096
DW                   19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                  2.00000000 sec
d20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2          400.1316005 MHz
SI                     32768
SF            100.6127707 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      2.00
```




```
NAME             THMA085
EXPNO                151
PROCNO                 1
Date_           20070413
Time                12.54
INSTRUM       avance400
PROBHD    5 mm BBO BB-1H
PULPROG             jmod
TD                 65536
SOLVENT            CDCl3
NS                   626
DS                     2
SWH           25062.656 Hz
FIDRES         0.382426 Hz
AQ             1.3074932 sec
RG                  4096
DW                19.950 usec
DE                 6.00 usec
TE                300.2 K
CNST2         145.0000000
CNST11          1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                10.30 usec
p2                20.60 usec
PL1               -1.00 dB
SFO1      100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2            100.00 usec
PL2               -3.00 dB
PL12              16.00 dB
SFO2      400.1316005 MHz
SI                 32768
SF        100.6127722 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

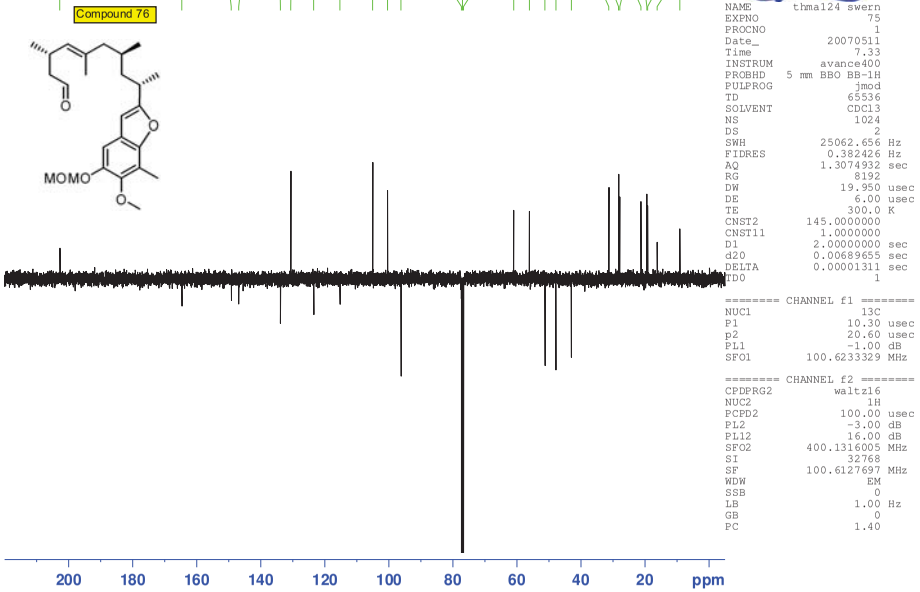



```
NAME          thma124 swern
EXPNO                    70
PROCNO                    1
Date_              20070511
Time                   3.33
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      32
DS                       2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                     362
DW                60.400 usec
DE                 6.00 usec
TE                 300.2 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                  8.75 usec
PL1                -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300094 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.00
```

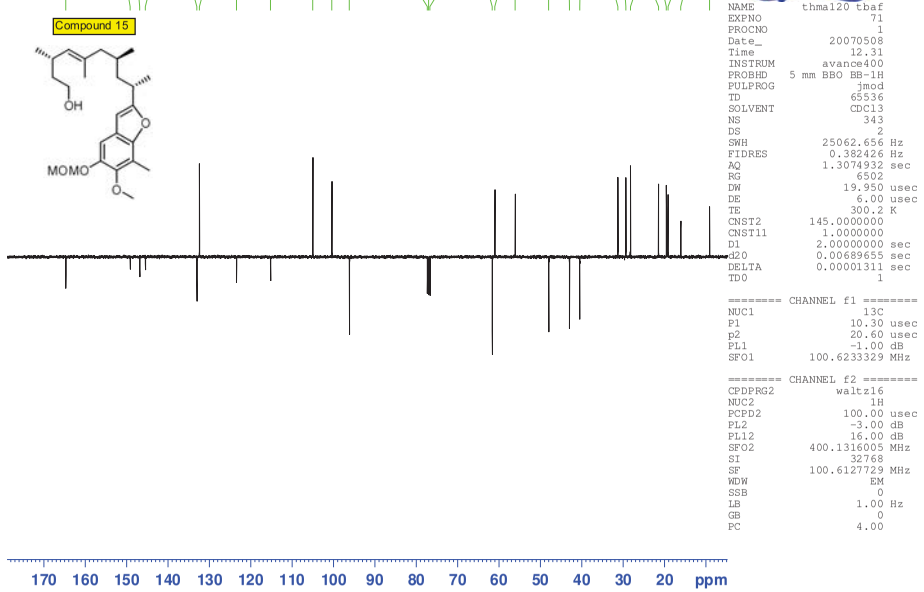



```
NAME          thma120 tbaf
EXPNO                    70
PROCNO                    1
Date_              20070508
Time                  12.27
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                    71.8
DW                60.400 usec
DE                 6.00 usec
TE                 300.2 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                  8.75 usec
PL1                -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300092 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.00
```

76

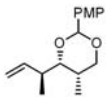



```
NAME          thma124 swern
EXPNO                    75
PROCNO                    1
Date_              20070511
Time                   7.33
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1024
DS                       2
SWH             25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                    8192
DW                19.950 usec
DE                 6.00 usec
TE                 300.0 K
CNST2          145.0000000
CNST11           1.0000000
D1             2.00000000 sec
d20            0.00689655 sec
DELTA          0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.30 usec
p2                 20.60 usec
PL1                -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2             100.00 usec
PL2                -3.00 dB
PL12               16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127697 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                   1.40
```



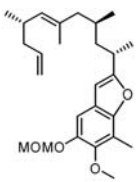

```
NAME          thma120 tbaf
EXPNO                    71
PROCNO                    1
Date_              20070508
Time                  12.31
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                      343
DS                       2
SWH             25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                    6502
DW                19.950 usec
DE                 6.00 usec
TE                 300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1             2.00000000 sec
d20            0.00689655 sec
DELTA          0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.30 usec
p2                 20.60 usec
PL1                -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2             100.00 usec
PL2                -3.00 dB
PL12               16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127729 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                   4.00
```

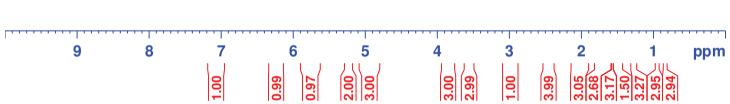
Compound 77




```
NAME                thma201
EXPNO                     1
PROCNO                    1
Date_              20070706
Time                  15.05
INSTRUM               spect
PROBHD   5 mm DUL 13C-1
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                        8
DS                        0
SWH                3742.515 Hz
FIDRES            0.114212 Hz
AQ                4.3778548 sec
RG                    645.1
DW                  133.600 usec
DE                    6.00 usec
TE                   300.0 K
D1                0.50000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    11.00 usec
PL1                   -3.00 dB
SFO1           250.1316258 MHz
SI                    32768
SF             250.1300073 MHz
WDW                      no
SSB                       0
LB                    0.00 Hz
GB                        0
PC                    1.00
```

Compound 16

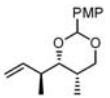





```
NAME           THMA127 Wittig
EXPNO                      60
PROCNO                      1
Date_               20070511
Time                   18.55
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                        57
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                       1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1            400.1324710 MHz
SI                     32768
SF              400.1300093 MHz
WDW                       EM
SSB                        0
LB                     0.30 Hz
GB                         0
PC                     1.00
```

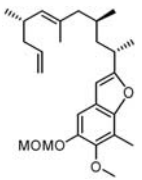
77

Compound 77



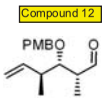

```
NAME                thma201
EXPNO                    51
PROCNO                    1
Date_              20070707
Time                   4.41
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     2000
DS                        2
SWH               25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                    16384
DW                  19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127703 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                    3.00
```

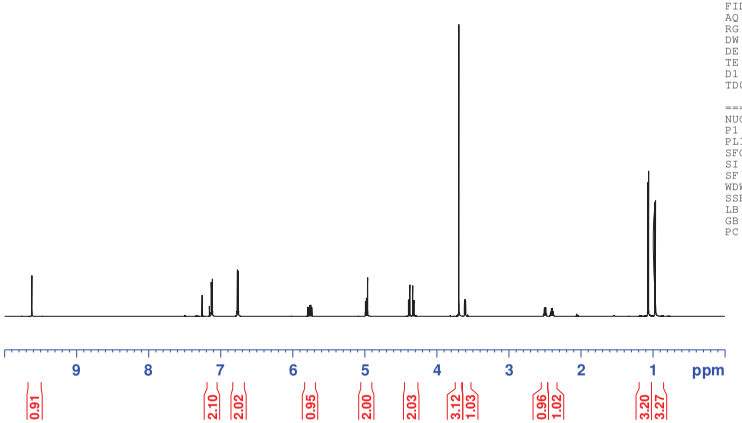
Compound 16




```
NAME           THMA127 Wittig
EXPNO                      61
PROCNO                      1
Date_               20070511
Time                   19.52
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                      1000
DS                         2
SWH               25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                    9195.2
DW                  19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127722 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                    1.40
```

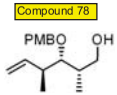
Compound 12

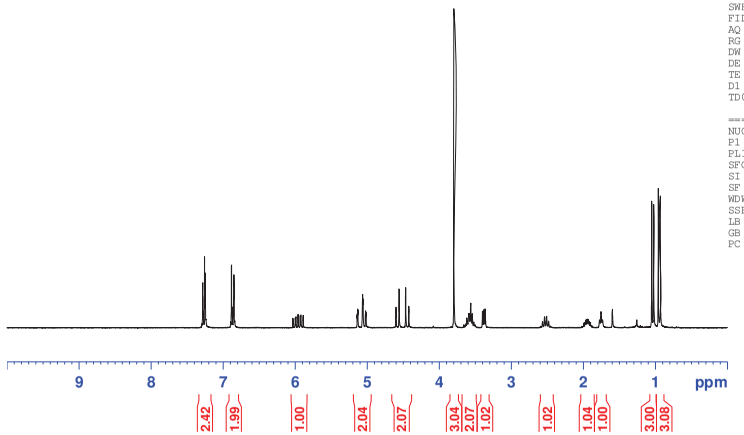





```
NAME                thma073
EXPNO                    30
PROCNO                    1
Date_              20070706
Time                   2.53
INSTRUM             avance600
PROBHD    5 mm PAQNP Swi
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       32
DS                        2
SWH               12376.237 Hz
FIDRES                0.188846 Hz
AQ                    2.6477449 sec
RG                         80.6
DW                       40.400 usec
DE                        6.00 usec
TE                       298.1 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.85 usec
PL1                    -6.00 dB
SFO1             600.1337060 MHz
SI                      32768
SF               600.1300783 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```

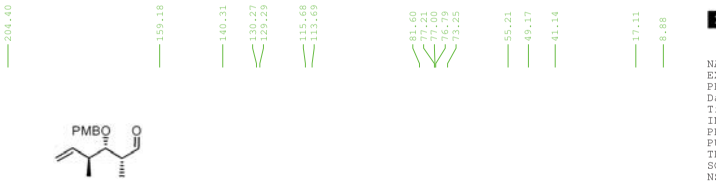
Compound 78

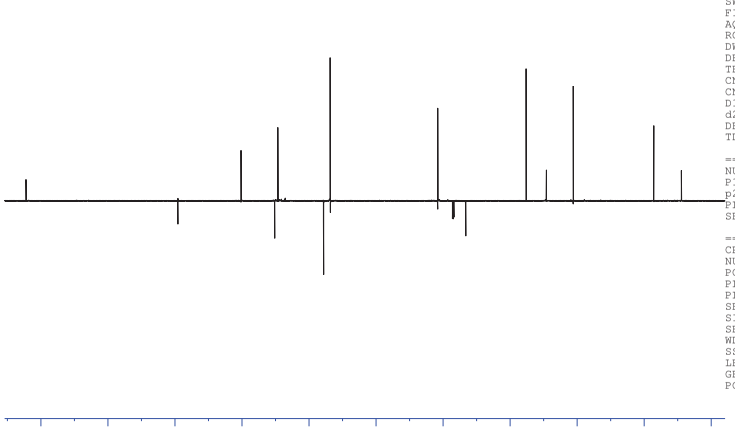





```
NAME                thma202
EXPNO                     1
PROCNO                    1
Date_              20070710
Time                  10.06
INSTRUM               spect
PROBHD    5 mm DUL 13C-1
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                        8
DS                        0
SWH                3742.515 Hz
FIDRES                0.114212 Hz
AQ                    4.3778548 sec
RG                          512
DW                      133.600 usec
DE                        6.00 usec
TE                       300.0 K
D1                0.50000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     11.00 usec
PL1                    -3.00 dB
SFO1             250.1316258 MHz
SI                      32768
SF               250.1300074 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```

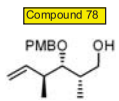
78



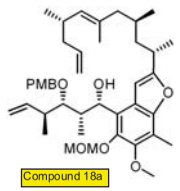



```
NAME                thma073
EXPNO                    33
PROCNO                    1
Date_              20070706
Time                   5.08
INSTRUM             avance600
PROBHD    5 mm PAQNP Swi
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1000
DS                        4
SWH               35971.223 Hz
FIDRES                0.548877 Hz
AQ                    0.9110143 sec
RG                       4597.6
DW                       13.900 usec
DE                        6.00 usec
TE                       298.1 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001019 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      13C
P1                     8.00 usec
p2                    16.00 usec
PL1                    0.00 dB
SFO1             150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                 80.00 usec
PL2                    -6.00 dB
PL12                   12.20 dB
SFO2             600.1324005 MHz
SI                      32768
SF               150.9028193 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     5.00
```

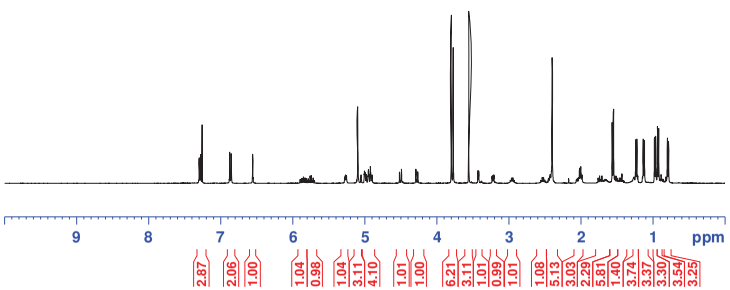
Compound 78

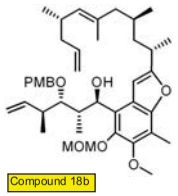



```
NAME                thma202
EXPNO                    81
PROCNO                    1
Date_              20070710
Time                  15.02
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1000
DS                        2
SWH               25062.656 Hz
FIDRES                0.382426 Hz
AQ                    1.3074932 sec
RG                        6502
DW                       19.950 usec
DE                        6.00 usec
TE                       300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2             400.1316005 MHz
SI                      32768
SF               100.6127707 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     2.00
```

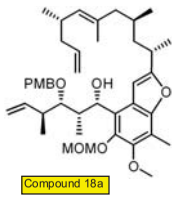


Compound 18a

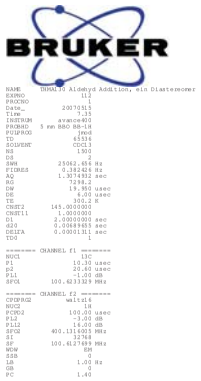


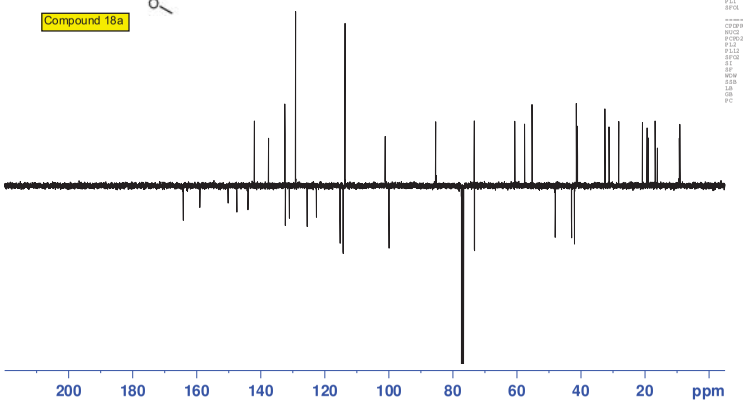


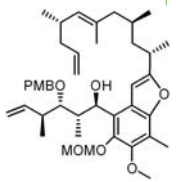
Compound 18b



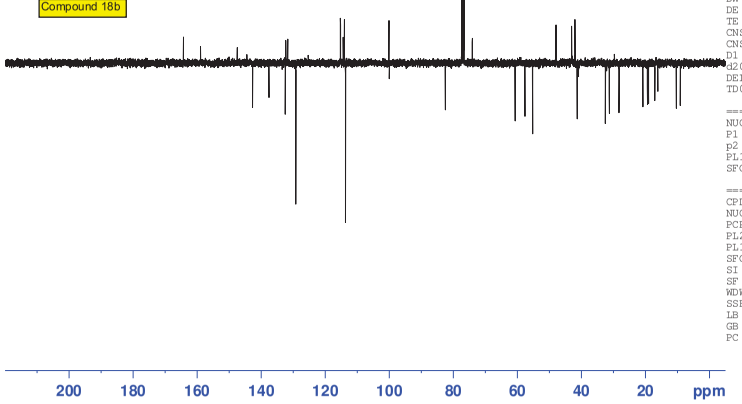
Compound 18a

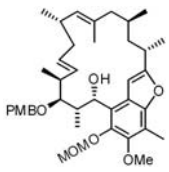




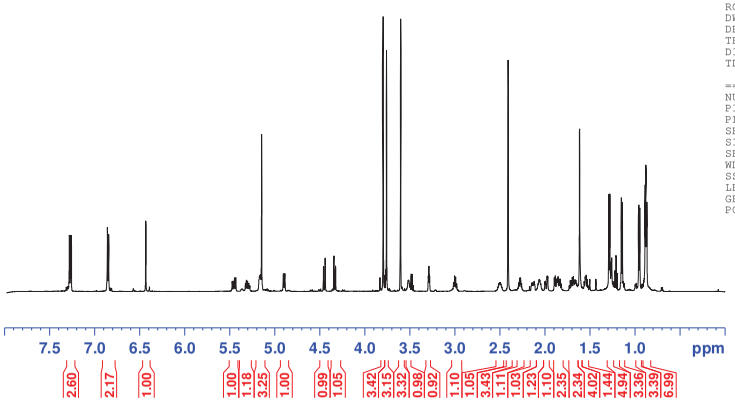


Compound 18b





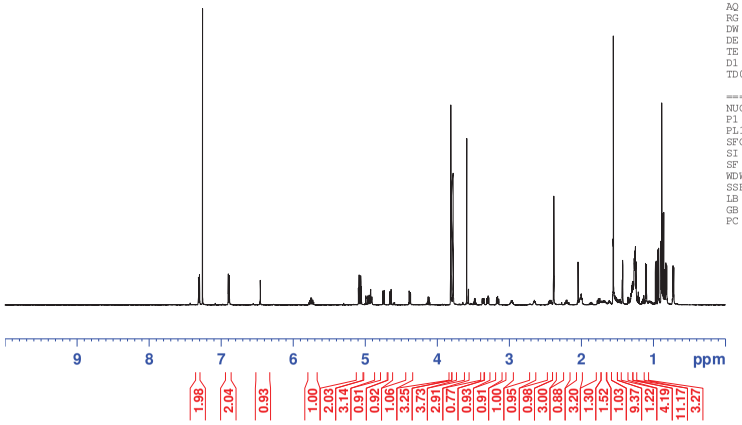
Compound 20a



BRUKER

```
NAME                 THMA 132
EXPNO                       1
PROCNO                      1
Date_             20070516
Time                   19.45
INSTRUM            avance600
PROBHD    5 mm TBI 1H/13
PULPROG                 zg30
TD                     16384
SOLVENT                CDCl3
NS                        32
DS                         2
SWH                4807.692 Hz
FIDRES                0.293438 Hz
AQ                 1.7040900 sec
RG                      90.5
DW                   104.000 usec
DE                     6.00 usec
TE                    297.1 K
D1                 1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.50 usec
PL1                    -2.00 dB
SFO1           600.1324005 MHz
SI                      65536
SF             600.1300170 MHz
WDW                        no
SSB                         0
LB                      0.00 Hz
GB                          0
PC                      1.00
```

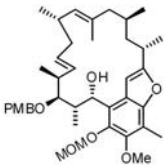

Compound 19



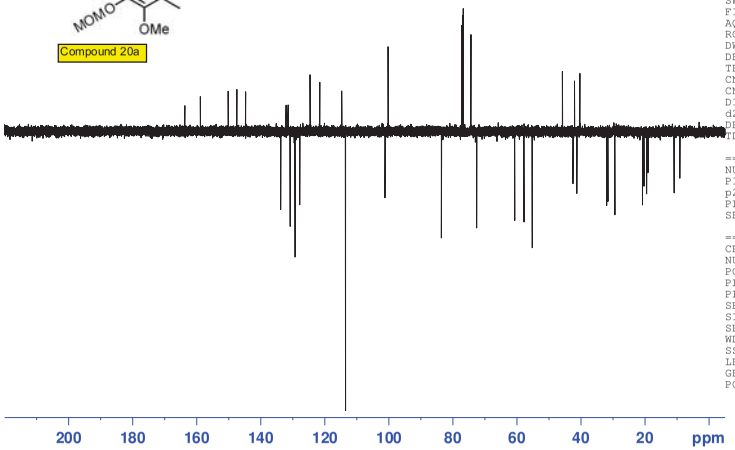
BRUKER

```
NAME                 thma149
EXPNO                     10
PROCNO                     1
Date_             20070530
Time                   17.18
INSTRUM            avance600
PROBHD    5 mm PAQNP Swi
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        32
DS                         2
SWH               12376.237 Hz
FIDRES                0.188846 Hz
AQ                 2.6477449 sec
RG                       362
DW                    40.400 usec
DE                     6.00 usec
TE                    298.1 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                       1H
P1                     13.85 usec
PL1                    -6.00 dB
SFO1           600.1337060 MHz
SI                      32768
SF             600.1300174 MHz
WDW                        no
SSB                         0
LB                      0.00 Hz
GB                          0
PC                      1.00
```

80

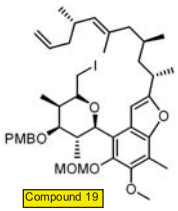


Compound 20a

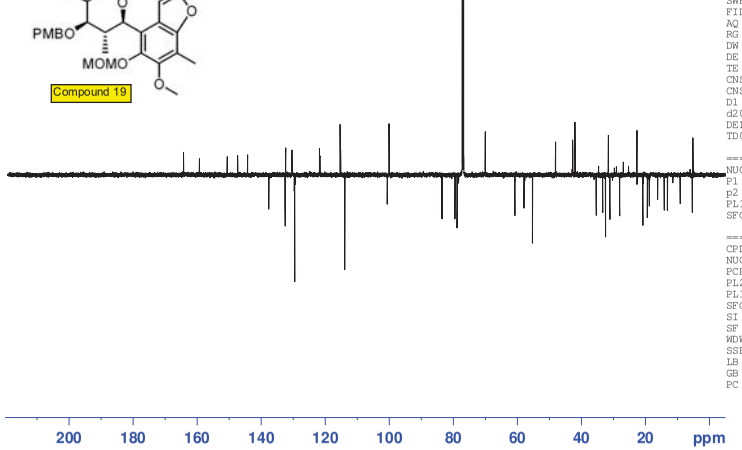


BRUKER

```
NAME                 THMA 132
EXPNO                       7
PROCNO                      1
Date_             20070517
Time                    5.51
INSTRUM            avance600
PROBHD    5 mm TBI 1H/13
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                       3072
DS                         4
SWH               36231.883 Hz
FIDRES                0.552855 Hz
AQ                 0.9044606 sec
RG                      4096
DW                    13.800 usec
DE                     6.00 usec
TE                    297.1 K
CNST2             145.0000000
CNST11              1.0000000
D1                  1.00000000 sec
d20                 0.00689655 sec
DELTA               0.00001592 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     12.50 usec
p2                     25.00 usec
PL1                    -5.00 dB
SFO1           150.9185938 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  80.00 usec
PL2                    -2.00 dB
PL12                   17.00 dB
SFO2           600.1324005 MHz
SI                      32768
SF             150.9028138 MHz
WDW                        no
SSB                         0
LB                      0.00 Hz
GB                          0
PC                      1.40
```

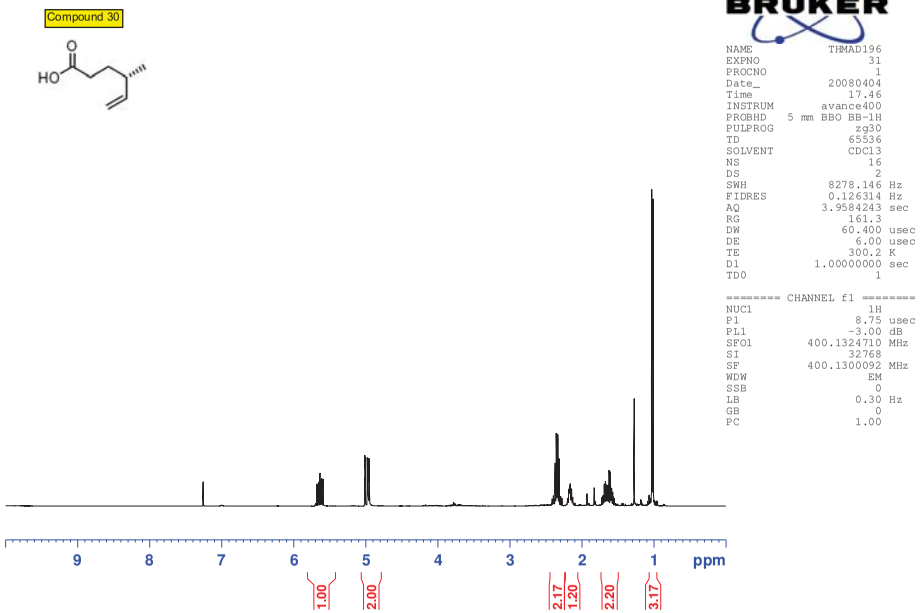


Compound 19

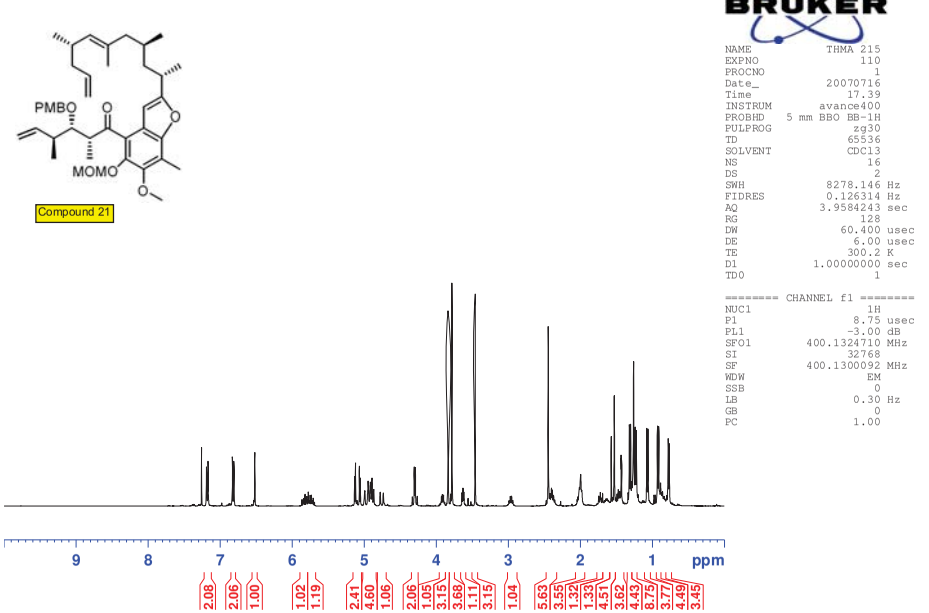


BRUKER

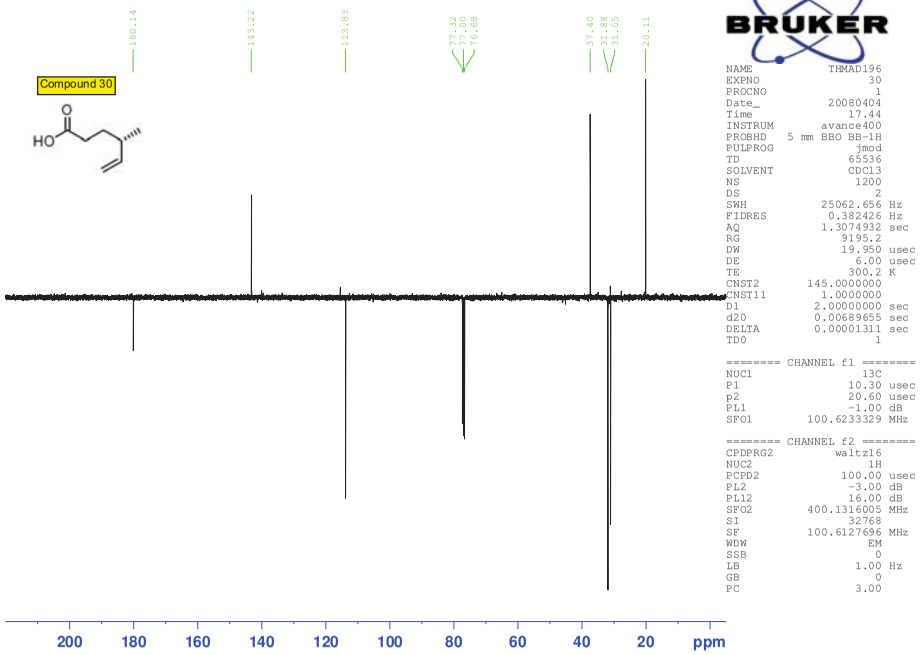
```
NAME                 thma149
EXPNO                     16
PROCNO                     1
Date_             20070531
Time                    8.14
INSTRUM            avance600
PROBHD    5 mm PAQNP Swi
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                       8280
DS                         4
SWH               35971.223 Hz
FIDRES                0.548877 Hz
AQ                 0.9110143 sec
RG                      4597.6
DW                    13.900 usec
DE                     6.00 usec
TE                    298.1 K
CNST2             145.0000000
CNST11              1.0000000
D1                  2.00000000 sec
d20                 0.00689655 sec
DELTA               0.00001019 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                      8.00 usec
p2                     16.00 usec
PL1                     0.00 dB
SFO1           150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  80.00 usec
PL2                    -6.00 dB
PL12                   12.20 dB
SFO2           600.1324005 MHz
SI                      32768
SF             150.9028132 MHz
WDW                        EM
SSB                         0
LB                      1.00 Hz
GB                          0
PC                      4.00
```



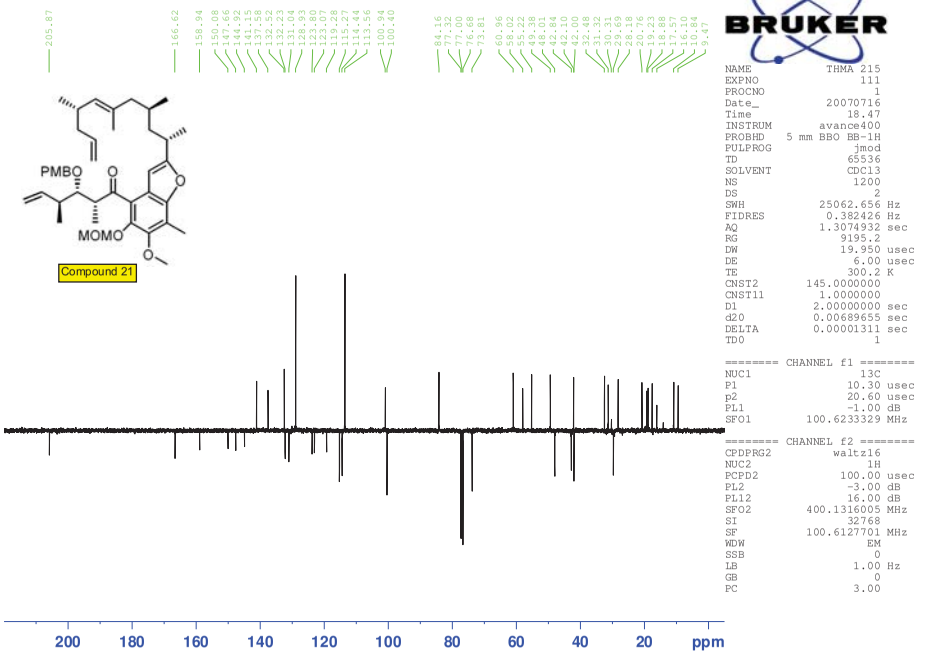

```
NAME                THMAD196
EXPNO                     31
PROCNO                     1
Date_               20080404
Time                   17.46
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     161.3
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                     32768
SF             400.1300092 MHz
WDW                       EM
SSB                        0
LB                     0.30 Hz
GB                         0
PC                      1.00
```




```
NAME                THMA 215
EXPNO                    110
PROCNO                     1
Date_               20070716
Time                   17.39
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                       128
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                     32768
SF             400.1300092 MHz
WDW                       EM
SSB                        0
LB                     0.30 Hz
GB                         0
PC                      1.00
```

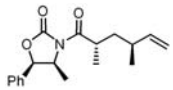




```
NAME                THMAD196
EXPNO                     30
PROCNO                     1
Date_               20080404
Time                   17.44
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1200
DS                         2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                    9195.2
DW                   19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1             2.00000000 sec
d20            0.00689655 sec
DELTA          0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                     32768
SF             100.6127696 MHz
WDW                       EM
SSB                        0
LB                     1.00 Hz
GB                         0
PC                      3.00
```

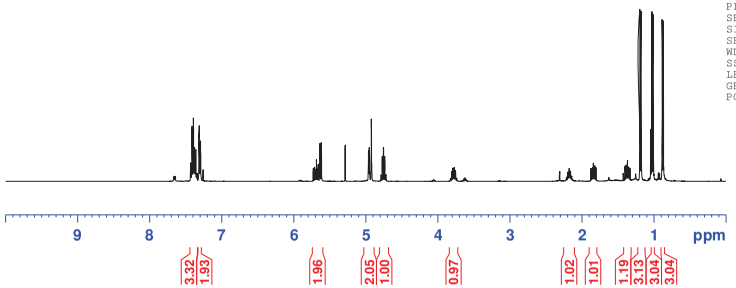



```
NAME                THMA 215
EXPNO                    111
PROCNO                     1
Date_               20070716
Time                   18.47
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1200
DS                         2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                    9195.2
DW                   19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1             2.00000000 sec
d20            0.00689655 sec
DELTA          0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                     32768
SF             100.6127701 MHz
WDW                       EM
SSB                        0
LB                     1.00 Hz
GB                         0
PC                      3.00
```

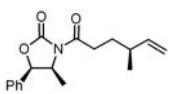
Compound 79



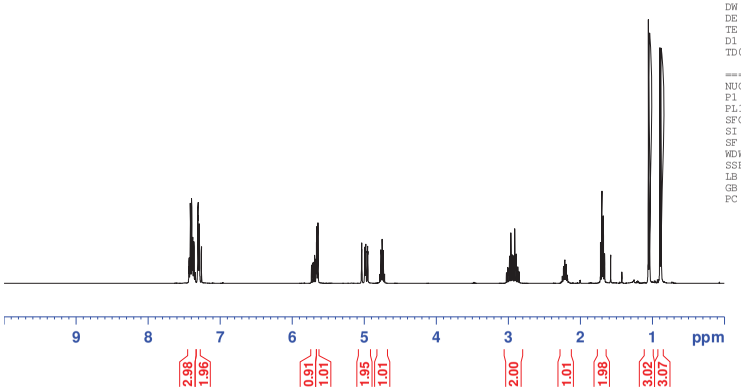
```
NAME                thmad203
EXPNO                     40
PROCNO                     1
Date_               20080409
Time                   11.04
INSTRUM              avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       80.6
DW                    60.400 usec
DE                     6.00 usec
TE                     300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1            400.1324710 MHz
SI                       32768
SF              400.1300093 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```



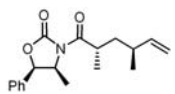
Compound 33



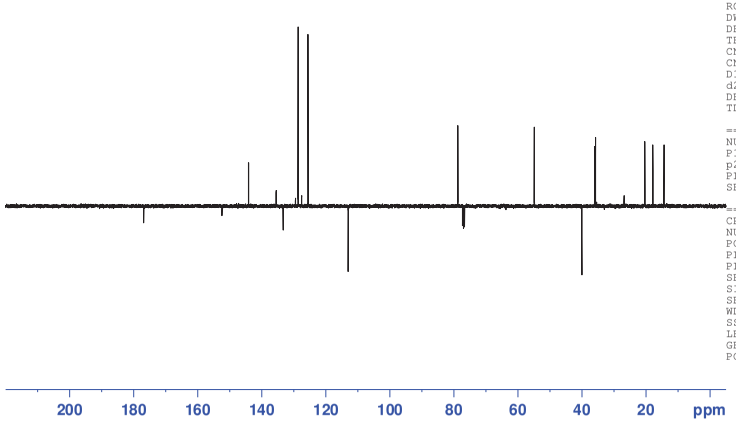
```
NAME                THMAD199
EXPNO                     60
PROCNO                     1
Date_               20080407
Time                   21.34
INSTRUM              avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       143.7
DW                    60.400 usec
DE                     6.00 usec
TE                     300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1            400.1324710 MHz
SI                       32768
SF              400.1300093 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```



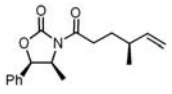
Compound 79



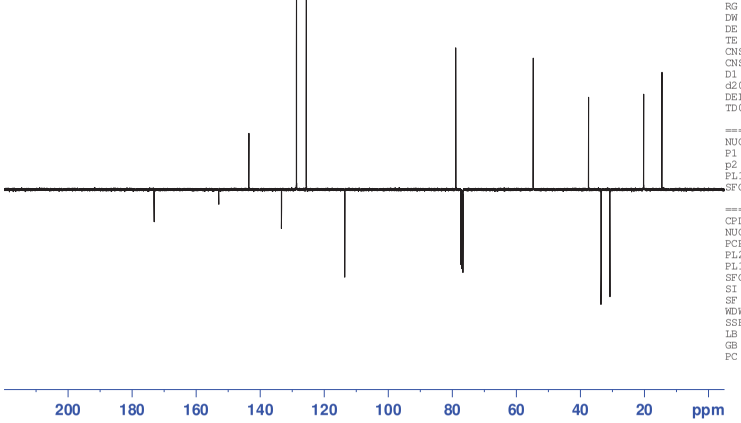

```
NAME                thmad203
EXPNO                     41
PROCNO                     1
Date_               20080409
Time                   11.10
INSTRUM              avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                       100
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                    10321.3
DW                    19.950 usec
DE                     6.00 usec
TE                     300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                  2.00000000 sec
d20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1            100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2            400.1316005 MHz
SI                       32768
SF              100.6127728 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      6.50
```



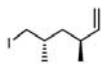
Compound 33

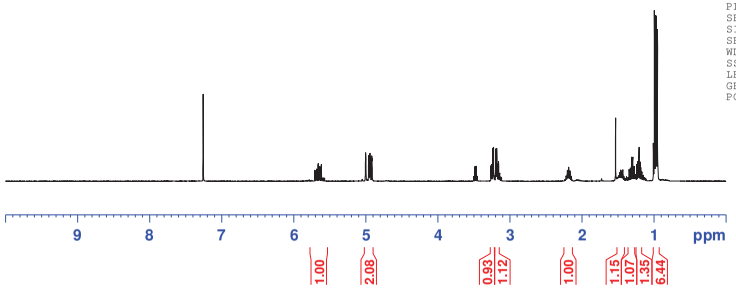



```
NAME                THMAD199
EXPNO                     61
PROCNO                     1
Date_               20080407
Time                   22.58
INSTRUM              avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                       1500
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                    5792.6
DW                    19.950 usec
DE                     6.00 usec
TE                     300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                  2.00000000 sec
d20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1            100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2            400.1316005 MHz
SI                       32768
SF              100.6127715 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```



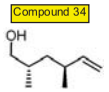
Compound 28

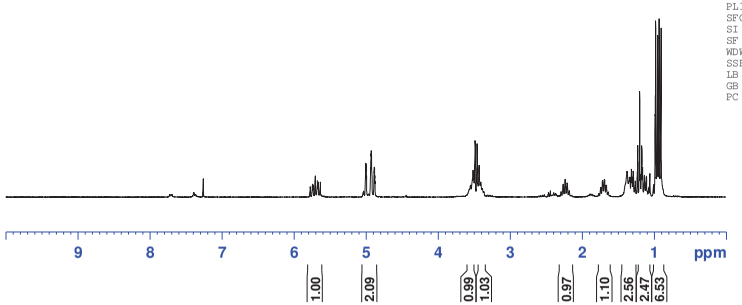





```
NAME                thmad098
EXPNO                     30
PROCNO                     1
Date_               20080131
Time                   11.34
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES                0.126314 Hz
AQ                  3.9584243 sec
RG                      322.5
DW                     60.400 usec
DE                      6.00 usec
TE                     300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1             400.1324710 MHz
SI                       32768
SF               400.1300095 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

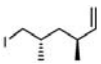
Compound 34





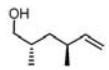

```
NAME                thmad194
EXPNO                      1
PROCNO                     1
Date_               20080403
Time                   16.11
INSTRUM                spect
PROBHD    5 mm DUL 13C-1
PULPROG                 zg30
TD                     32768
SOLVENT                CDCl3
NS                         8
DS                         0
SWH                 3742.515 Hz
FIDRES                0.114212 Hz
AQ                  4.3778548 sec
RG                      287.4
DW                    133.600 usec
DE                      6.00 usec
TE                     294.4 K
D1                 0.50000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                       1H
P1                     11.00 usec
PL1                    -3.00 dB
SFO1             250.1316258 MHz
SI                       32768
SF               250.1300070 MHz
WDW                       EM
SSB                        0
LB                      0.10 Hz
GB                         0
PC                      1.00
```

Compound 28

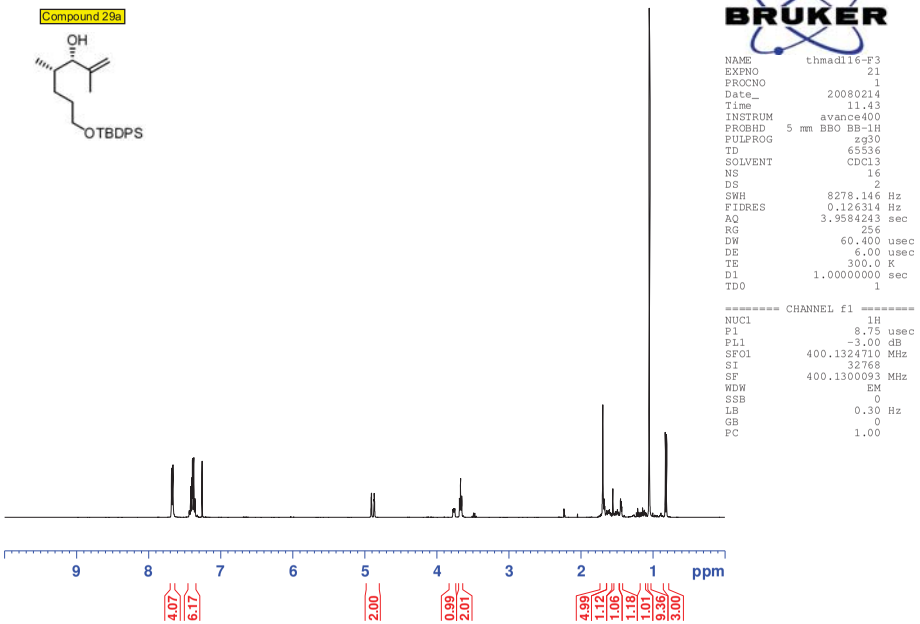



```
NAME                thmad098
EXPNO                     31
PROCNO                     1
Date_               20080131
Time                   12.59
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1500
DS                         2
SWH                25062.656 Hz
FIDRES                0.382426 Hz
AQ                  1.3074932 sec
RG                      6502
DW                    19.950 usec
DE                      6.00 usec
TE                     300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
D20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2             400.1316005 MHz
SI                       32768
SF               100.6127696 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      5.00
```

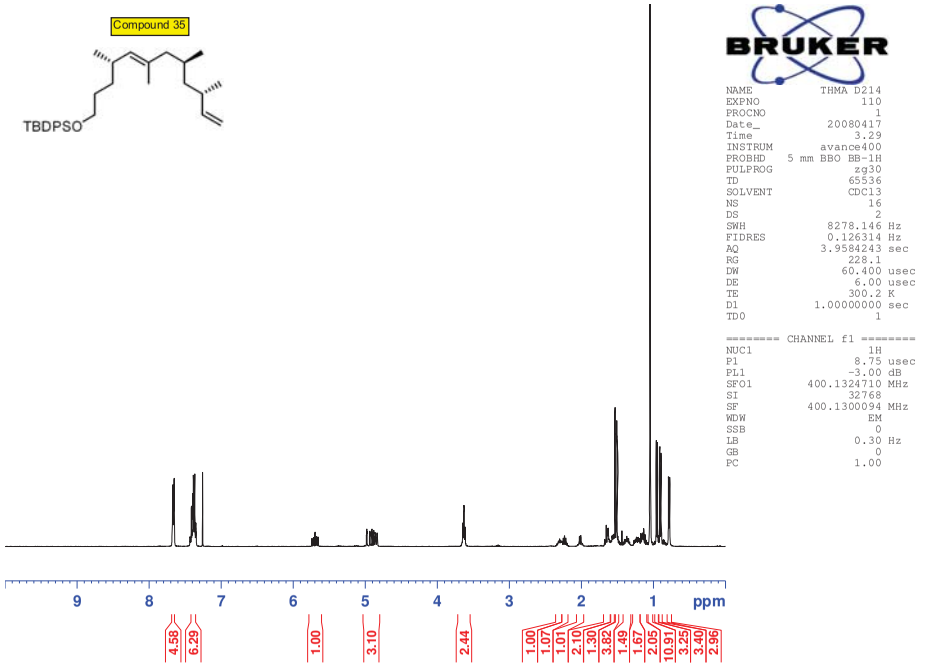
Compound 34



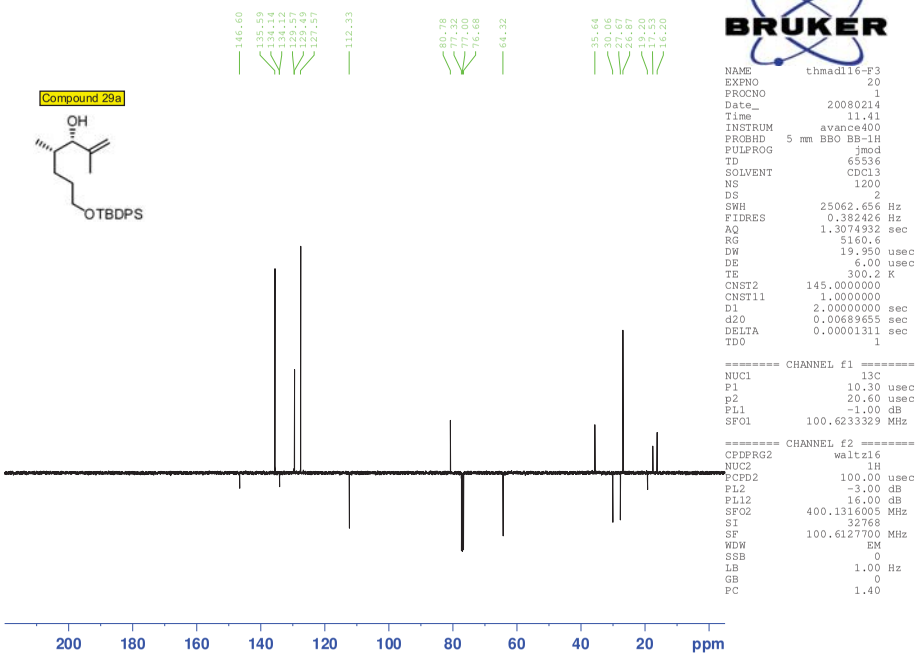

```
NAME                thma d095
EXPNO                     11
PROCNO                     1
Date_               20080130
Time                   10.46
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1779
DS                         2
SWH                25062.656 Hz
FIDRES                0.382426 Hz
AQ                  1.3074932 sec
RG                    7298.2
DW                    19.950 usec
DE                      6.00 usec
TE                     300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
D20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2             400.1316005 MHz
SI                       32768
SF               100.6127697 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      3.50
```



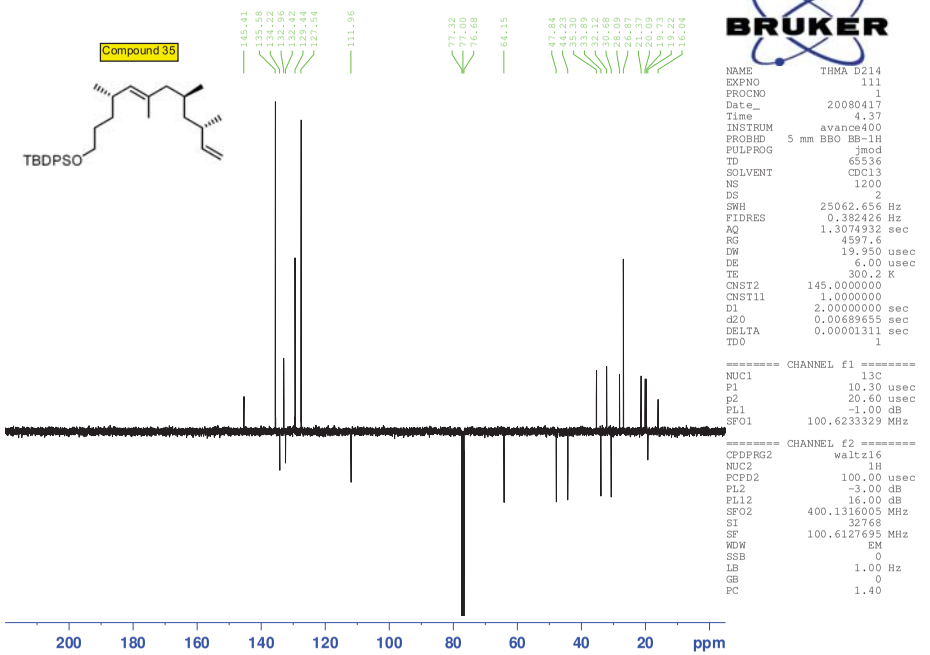

```
NAME            thmadl16-F3
EXPNO                    21
PROCNO                    1
Date_             20080214
Time                 11.43
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES               0.126314 Hz
AQ                3.9584243 sec
RG                     256
DW                  60.400 usec
DE                   6.00 usec
TE                  300.0 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1           400.1324710 MHz
SI                   32768
SF             400.1300093 MHz
WDW                     EM
SSB                      0
LB                   0.30 Hz
GB                       0
PC                    1.00
```



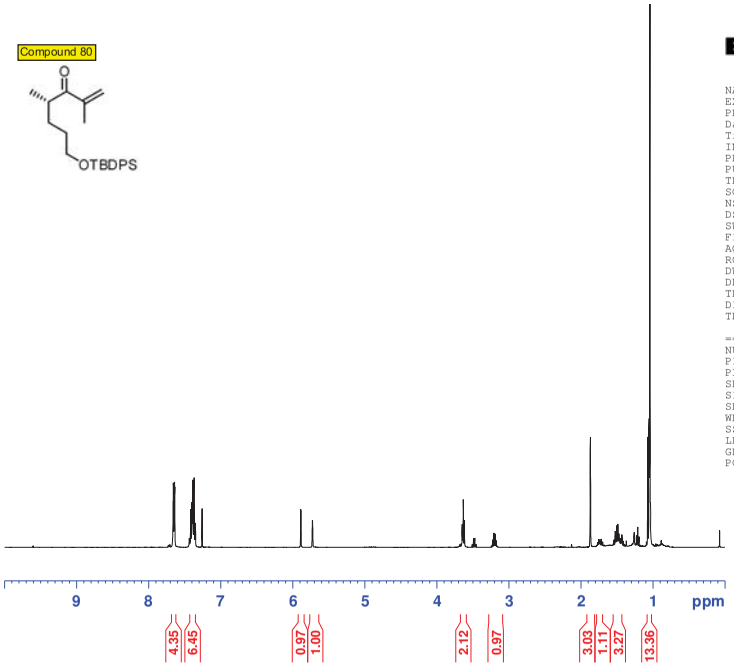

```
NAME            THMA D214
EXPNO                  110
PROCNO                   1
Date_             20080417
Time                 3.29
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES               0.126314 Hz
AQ                3.9584243 sec
RG                   228.1
DW                  60.400 usec
DE                   6.00 usec
TE                  300.2 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1           400.1324710 MHz
SI                   32768
SF             400.1300094 MHz
WDW                     EM
SSB                      0
LB                   0.30 Hz
GB                       0
PC                    1.00
```

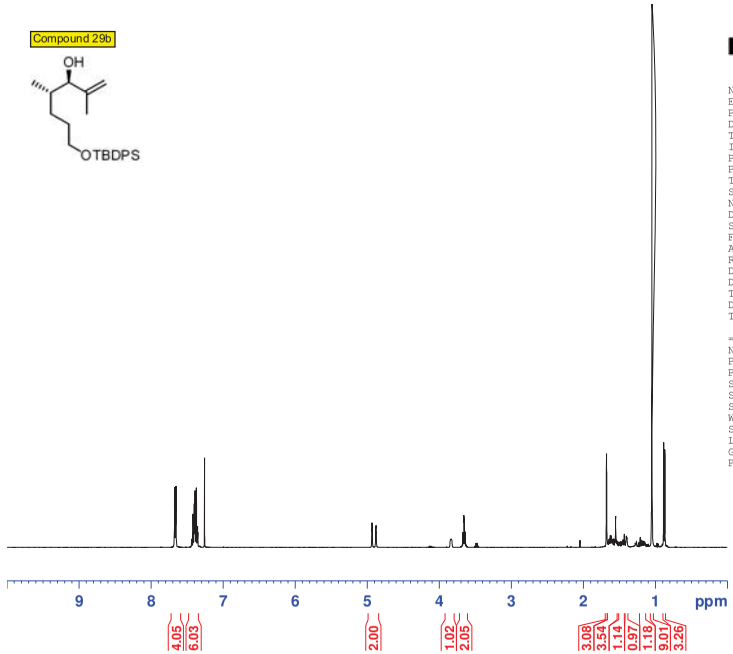

```
NAME            thmadl16-F3
EXPNO                    20
PROCNO                    1
Date_             20080214
Time                 11.41
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1200
DS                       2
SWH              25062.656 Hz
FIDRES               0.382426 Hz
AQ                1.3074932 sec
RG                   5160.6
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2           400.1316005 MHz
SI                   32768
SF             100.6127700 MHz
WDW                     EM
SSB                      0
LB                   1.00 Hz
GB                       0
PC                    1.40
```




```
NAME            THMA D214
EXPNO                  111
PROCNO                   1
Date_             20080417
Time                 4.37
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1200
DS                       2
SWH              25062.656 Hz
FIDRES               0.382426 Hz
AQ                1.3074932 sec
RG                   4597.6
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2           400.1316005 MHz
SI                   32768
SF             100.6127695 MHz
WDW                     EM
SSB                      0
LB                   1.00 Hz
GB                       0
PC                    1.40
```

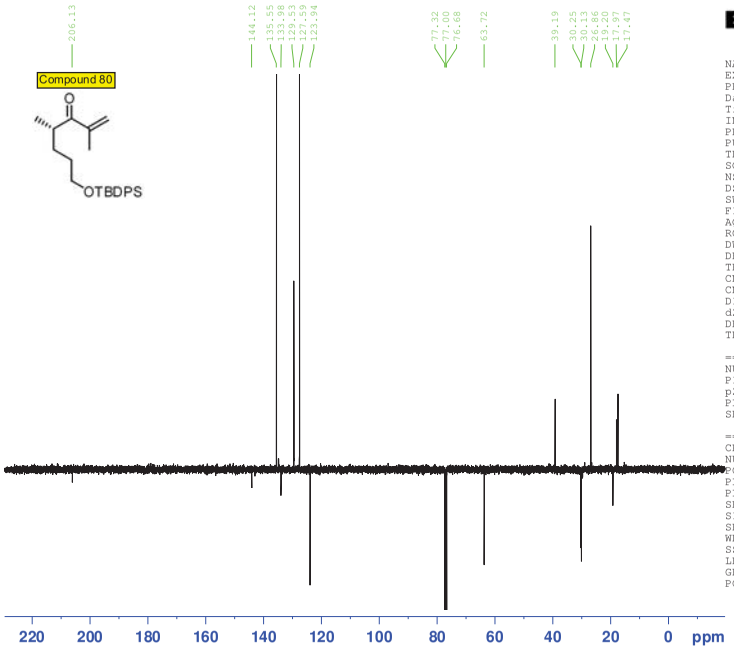



```
NAME            THMA_D281
EXPNO                 120
PROCNO                  1
Date_            20080515
Time                21.20
INSTRUM          avance400
PROBHD   5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                     181
DW                  60.400 usec
DE                   6.00 usec
TE                  300.2 K
D1               1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  8.75 usec
PL1                -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300092 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

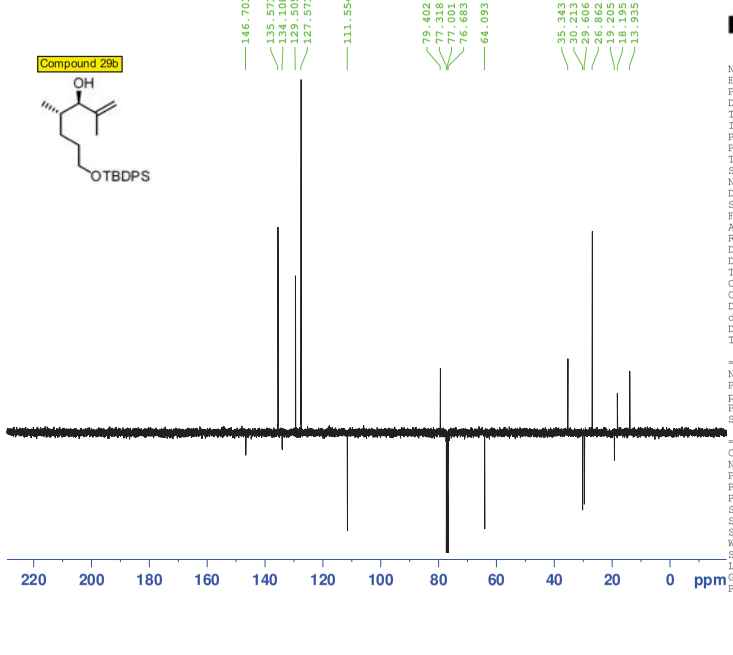



```
NAME            thmad116-F4
EXPNO                  11
PROCNO                  1
Date_            20080214
Time                 9.35
INSTRUM          avance400
PROBHD   5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                   322.5
DW                  60.400 usec
DE                   6.00 usec
TE                  300.2 K
D1               1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  8.75 usec
PL1                -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300093 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

85

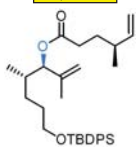


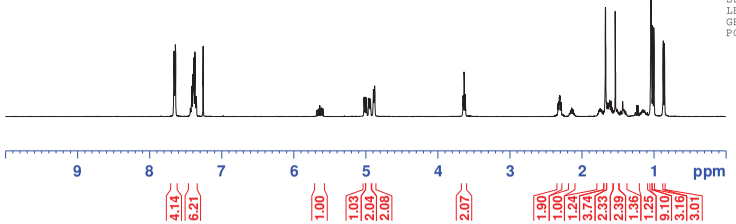

```
NAME            THMA_D281
EXPNO                 121
PROCNO                  1
Date_            20080515
Time                22.17
INSTRUM          avance400
PROBHD   5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1000
DS                       2
SWH             25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                 14596.5
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.30 usec
p2                  20.60 usec
PL1                -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2             100.00 usec
PL2                -3.00 dB
PL12               16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127698 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```




```
NAME            thmad116-F4
EXPNO                  10
PROCNO                  1
Date_            20080214
Time                 9.32
INSTRUM          avance400
PROBHD   5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                     572
DS                       2
SWH             25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                  2896.3
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.30 usec
p2                  20.60 usec
PL1                -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2             100.00 usec
PL2                -3.00 dB
PL12               16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127696 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

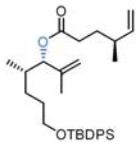
Compound 37b

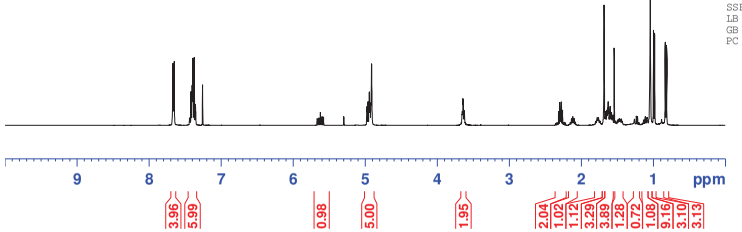





```
NAME                THMAD197
EXPNO                     70
PROCNO                     1
Date_               20080405
Time                   1.42
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                      287.4
DW                   60.400 usec
DE                    6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1              400.1324710 MHz
SI                       32768
SF                400.1300093 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                      1.00
```

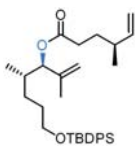
Compound 37a





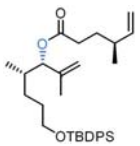

```
NAME                THMA D224
EXPNO                     20
PROCNO                     1
Date_               20080421
Time                  13.36
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                      203.2
DW                   60.400 usec
DE                    6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1              400.1324710 MHz
SI                       32768
SF                400.1300094 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                      1.00
```

Compound 37b

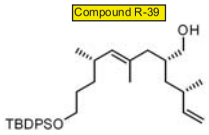


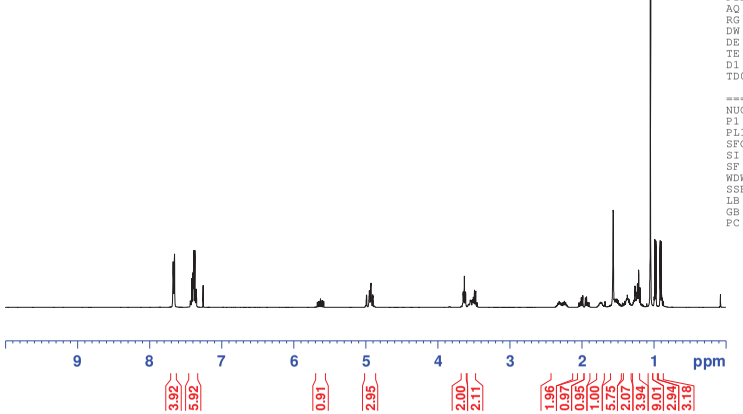

```
NAME                THMAD197
EXPNO                     71
PROCNO                     1
Date_               20080405
Time                   2.50
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1200
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                     9195.2
DW                   19.950 usec
DE                    6.00 usec
TE                    300.0 K
CNST2             145.0000000
CNST11              1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1              100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2              400.1316005 MHz
SI                       32768
SF                100.6127694 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                      1.40
```

Compound 37a

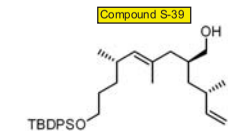


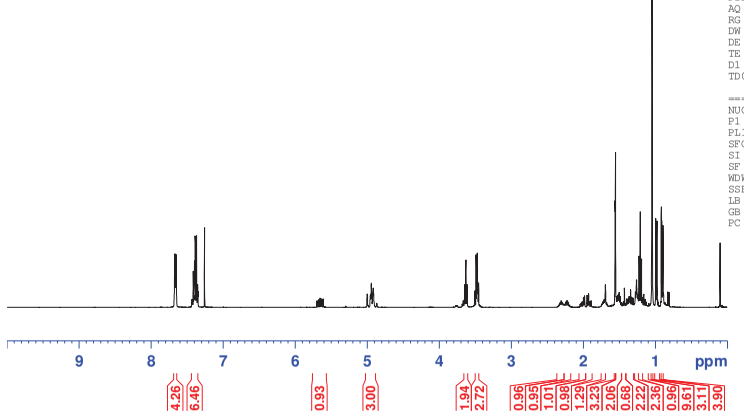

```
NAME                THMA D224
EXPNO                     21
PROCNO                     1
Date_               20080421
Time                  14.15
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                       689
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                      6502
DW                   19.950 usec
DE                    6.00 usec
TE                    300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1              100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2              400.1316005 MHz
SI                       32768
SF                100.6127698 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                      1.40
```





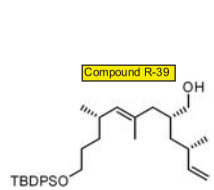

```
NAME                THMAD210
EXPNO                     50
PROCNO                     1
Date_               20080411
Time                   16.16
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       128
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                     32768
SF                400.1300092 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                      1.00
```



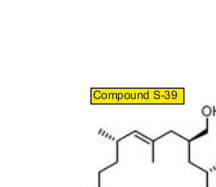



```
NAME                THMA D227
EXPNO                     90
PROCNO                     1
Date_               20080423
Time                   2.23
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                     322.5
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                     32768
SF                400.1300093 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                      1.00
```

87

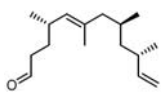


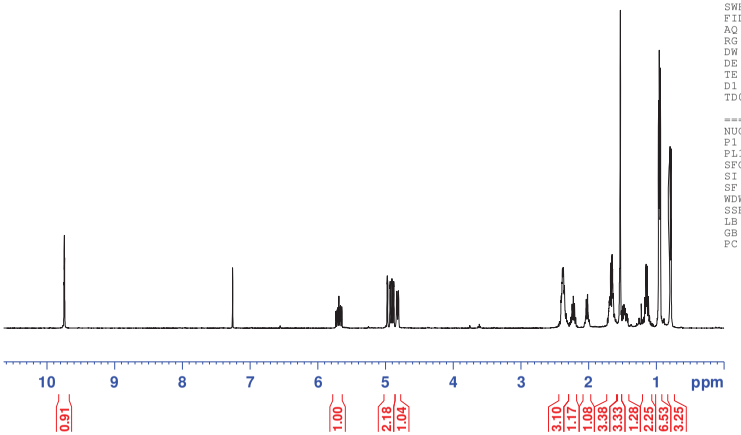

```
NAME                THMAD210
EXPNO                     51
PROCNO                     1
Date_               20080411
Time                   17.24
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1200
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                   10321.3
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                     32768
SF             100.6127701 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                      4.00
```




```
NAME                THMA D227
EXPNO                     91
PROCNO                     1
Date_               20080423
Time                   3.32
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1200
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                      8192
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                     32768
SF             100.6127698 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                      3.00
```

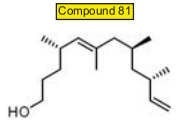
Compound 25

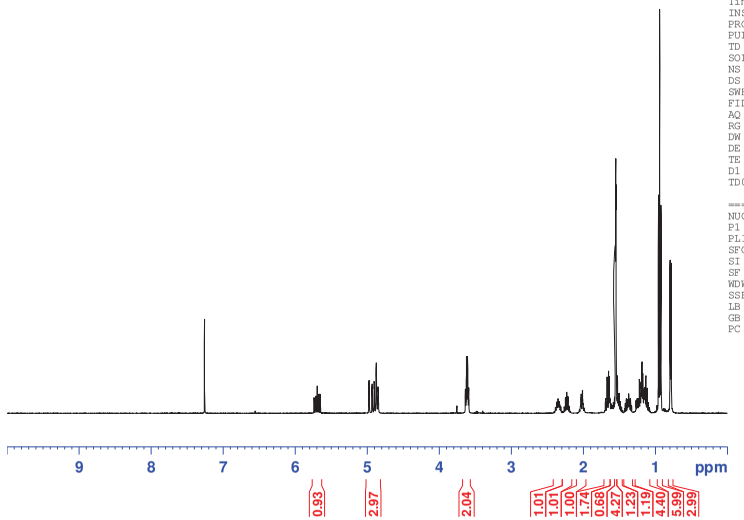





```
NAME                THMA D220
EXPNO                     120
PROCNO                      1
Date_                20080418
Time                    13.04
INSTRUM               avance400
PROBHD     5 mm BBO BB-1H
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                   3.9584243 sec
RG                        181
DW                     60.400 usec
DE                      6.00 usec
TE                      300.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1           400.1324710 MHz
SI                      32768
SF             400.1300095 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                      1.00
```

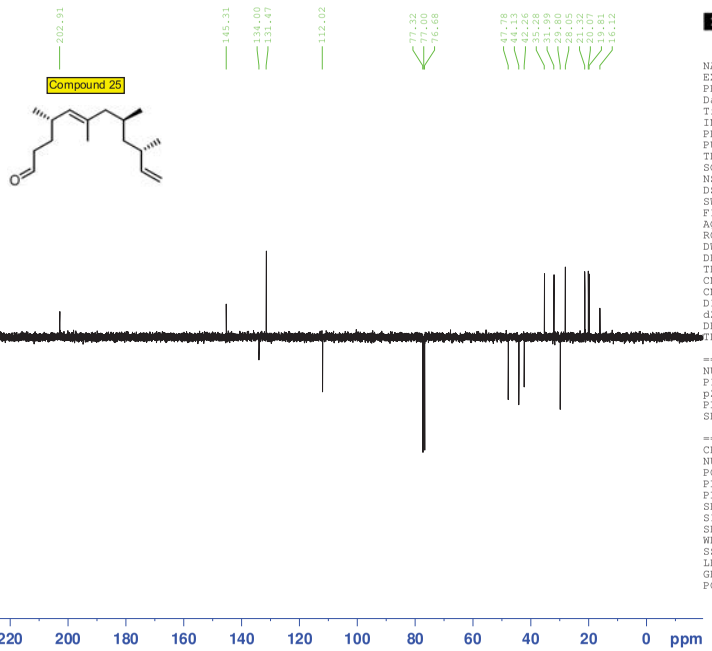
Compound 81






```
NAME                THMA D218
EXPNO                     100
PROCNO                      1
Date_                20080417
Time                    1.14
INSTRUM               avance400
PROBHD     5 mm BBO BB-1H
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES               0.126314 Hz
AQ                   3.9584243 sec
RG                        362
DW                     60.400 usec
DE                      6.00 usec
TE                      300.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1           400.1324710 MHz
SI                      32768
SF             400.1300093 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                      1.00
```

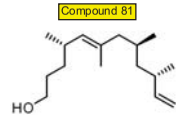
88



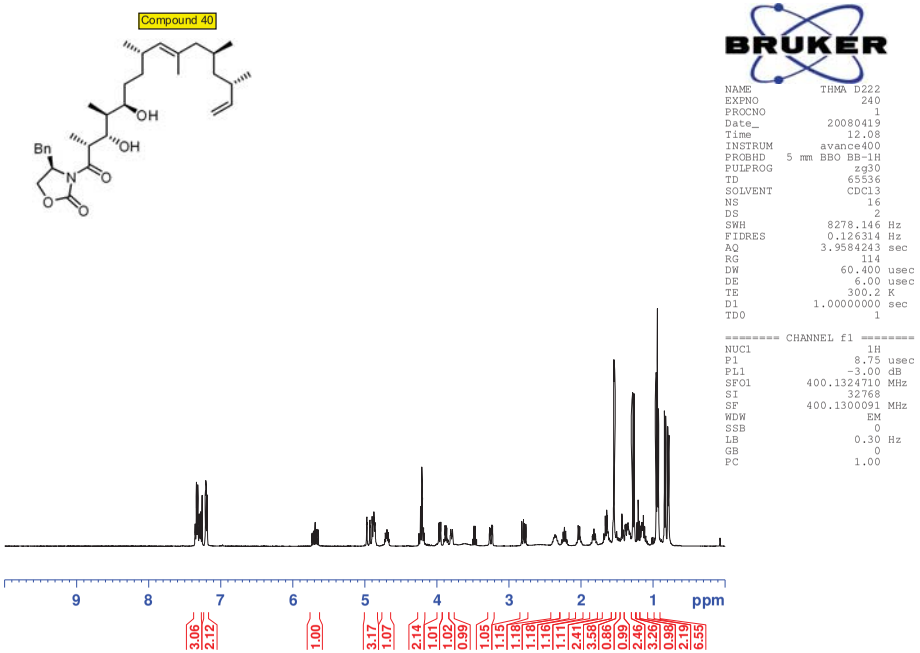
Compound 25


```
NAME                THMA D220
EXPNO                     121
PROCNO                      1
Date_                20080418
Time                    13.19
INSTRUM               avance400
PROBHD     5 mm BBO BB-1H
PULPROG                 jmod
TD                      65536
SOLVENT                 CDCl3
NS                        282
DS                          2
SWH                 25062.656 Hz
FIDRES               0.382426 Hz
AQ                   1.3074932 sec
RG                       8192
DW                     19.950 usec
DE                      6.00 usec
TE                      300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2           400.1316005 MHz
SI                      32768
SF             100.6127695 MHz
WDW                        EM
SSB                         0
LB                     1.00 Hz
GB                          0
PC                      1.40
```

Compound 81

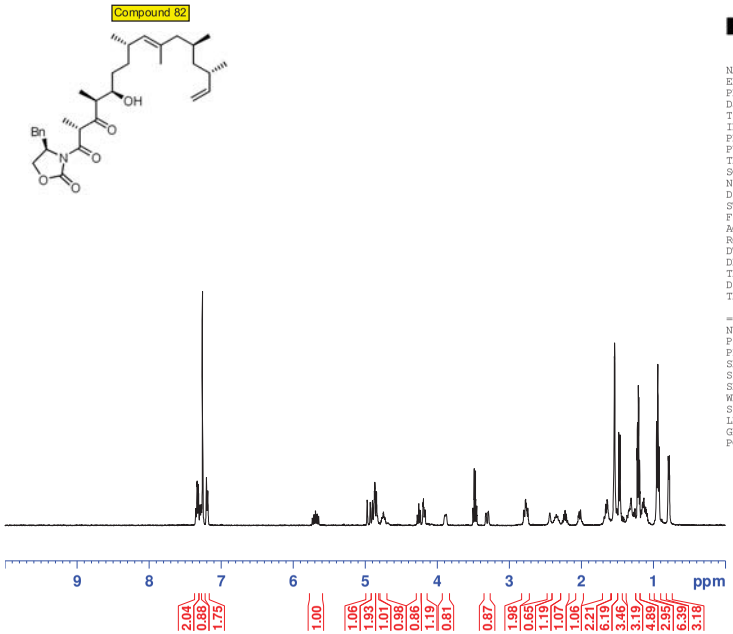



```
NAME                THMA D218
EXPNO                     101
PROCNO                      1
Date_                20080417
Time                    2.22
INSTRUM               avance400
PROBHD     5 mm BBO BB-1H
PULPROG                 jmod
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                 25062.656 Hz
FIDRES               0.382426 Hz
AQ                   1.3074932 sec
RG                       4096
DW                     19.950 usec
DE                      6.00 usec
TE                      300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2           400.1316005 MHz
SI                      32768
SF             100.6127692 MHz
WDW                        EM
SSB                         0
LB                     1.00 Hz
GB                          0
PC                      1.40
```



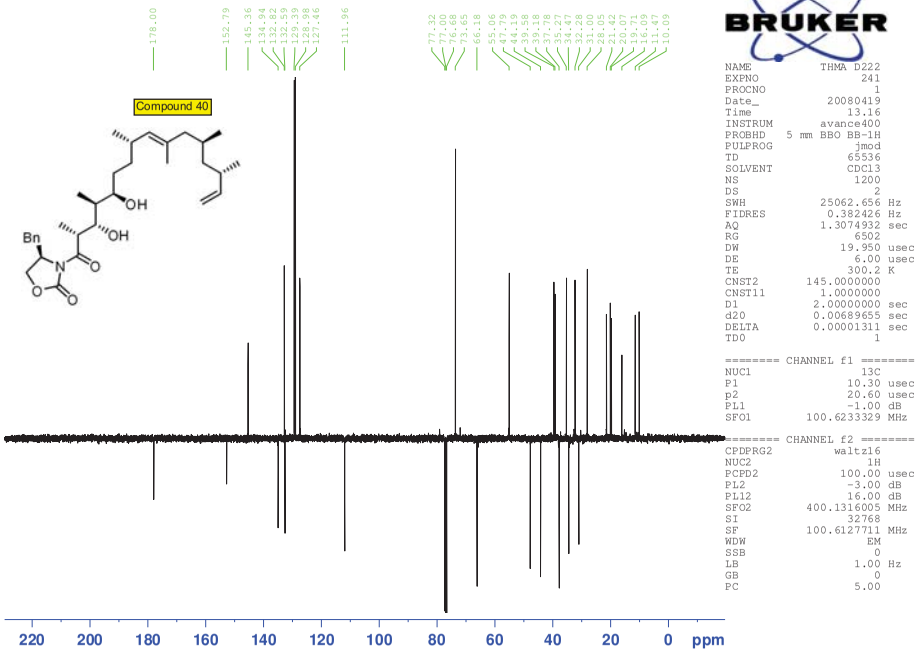
BRUKER

```
NAME                THMA D222
EXPNO                    240
PROCNO                     1
Date_               20080419
Time                   12.08
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                       114
DW                  60.400 usec
DE                   6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                       32768
SF             400.1300091 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```



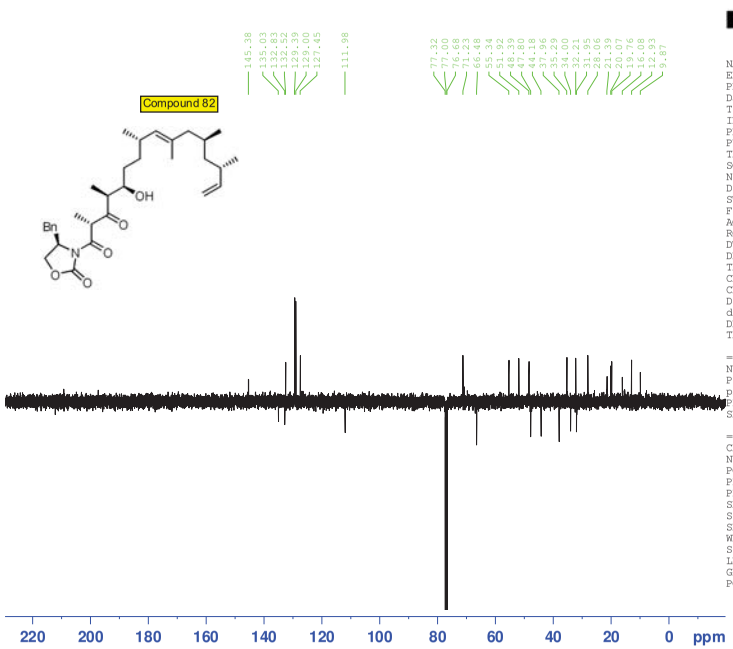
BRUKER

```
NAME              THMA D221D2
EXPNO                    50
PROCNO                    1
Date_               20080417
Time                   21.05
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                       362
DW                  60.400 usec
DE                   6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                       32768
SF             400.1300096 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

BRUKER

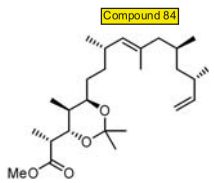
```
NAME                THMA D222
EXPNO                    241
PROCNO                     1
Date_               20080419
Time                   13.16
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                      6502
DW                  19.950 usec
DE                   6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                       32768
SF             100.6127711 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     5.00
```

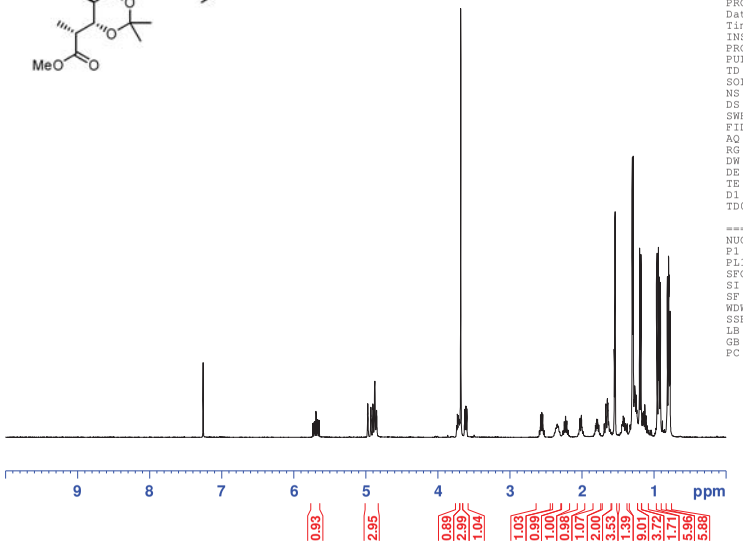


BRUKER

```
NAME              THMA D221D2
EXPNO                    51
PROCNO                    1
Date_               20080417
Time                   22.13
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                    5160.6
DW                  19.950 usec
DE                   6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                       32768
SF             100.6127693 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

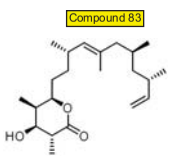
Compound 84

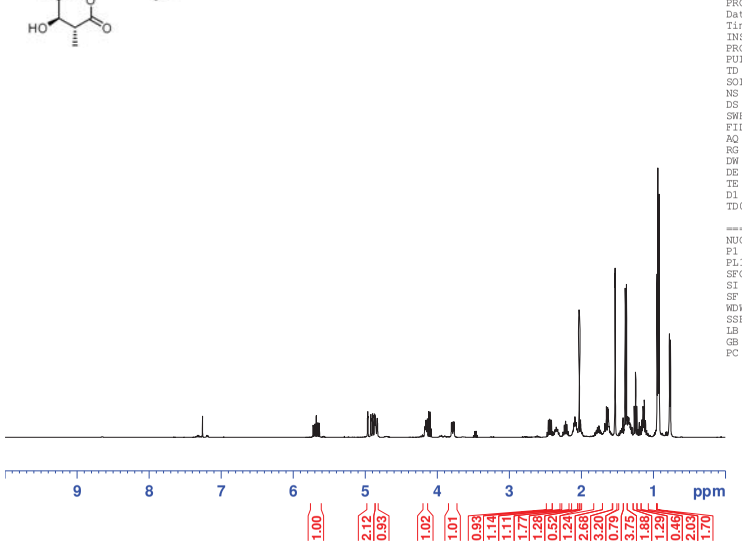




```
NAME                THMA D238
EXPNO                    30
PROCNO                    1
Date_              20080429
Time                  11.08
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     143.7
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1          400.1324710 MHz
SI                    32768
SF            400.1300094 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Compound 83

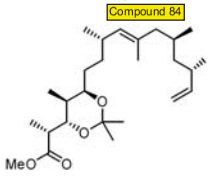




```
NAME                THMA D225
EXPNO                    30
PROCNO                    1
Date_              20080422
Time                  18.16
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      80.6
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1          400.1324710 MHz
SI                    32768
SF            400.1300091 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

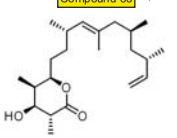
90

Compound 84



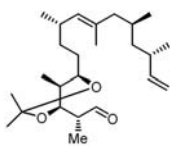

```
NAME                THMA D238
EXPNO                    31
PROCNO                    1
Date_              20080429
Time                  12.16
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                    5792.6
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2         145.0000000
CNST11          1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2          400.1316005 MHz
SI                    32768
SF            100.6127693 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

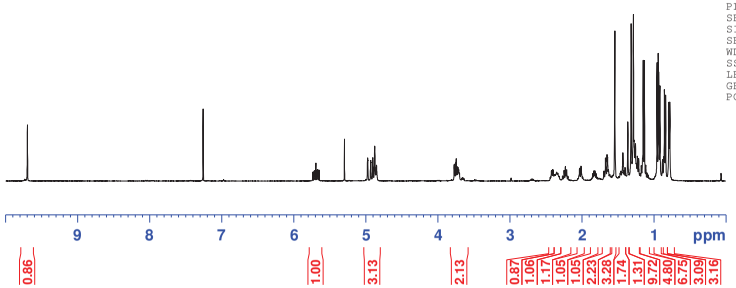
Compound 83




```
NAME                THMA D225
EXPNO                    31
PROCNO                    1
Date_              20080422
Time                  18.14
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                    3649.1
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2         145.0000000
CNST11          1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2          400.1316005 MHz
SI                    32768
SF            100.6127712 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     5.00
```

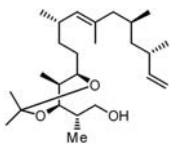
Compound 24

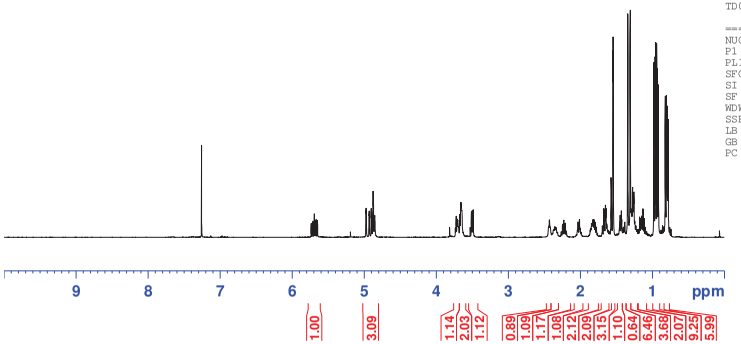





```
NAME                THMA D243
EXPNO                     100
PROCNO                      1
Date_              20080430
Time                   11.05
INSTRUM              avance400
PROBHD     5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                      287.4
DW                     60.400 usec
DE                      6.00 usec
TE                     300.2 K
D1                  1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1             400.1324710 MHz
SI                      32768
SF               400.1300095 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

Compound 85

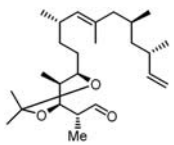


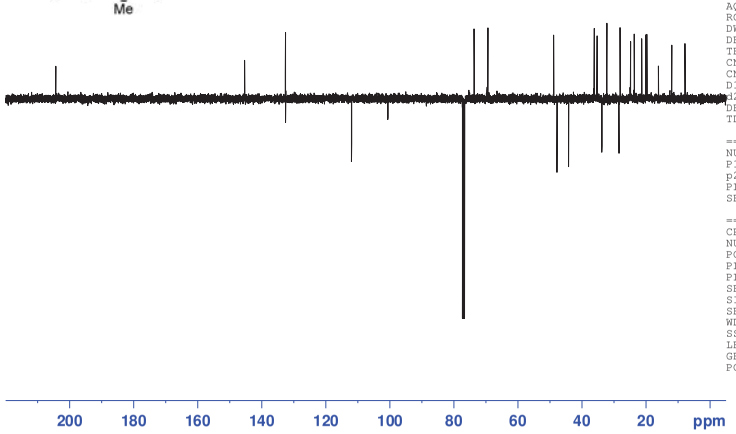



```
NAME                THMA D234
EXPNO                      40
PROCNO                      1
Date_              20080425
Time                   15.09
INSTRUM              avance400
PROBHD     5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        32
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                      181
DW                     60.400 usec
DE                      6.00 usec
TE                     300.2 K
D1                  1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1             400.1324710 MHz
SI                      32768
SF               400.1300093 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

91

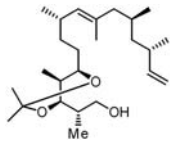
Compound 24

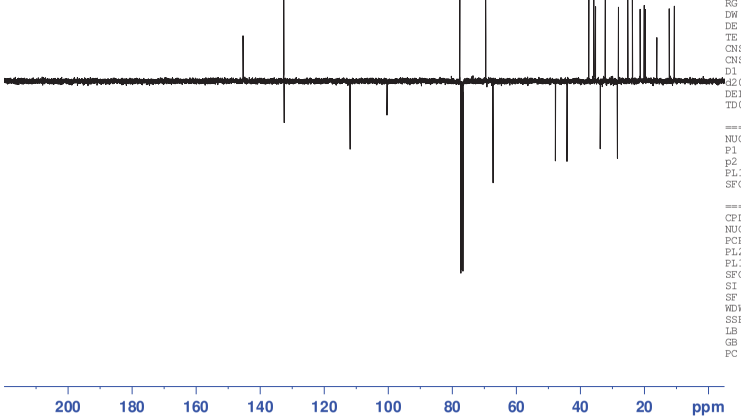




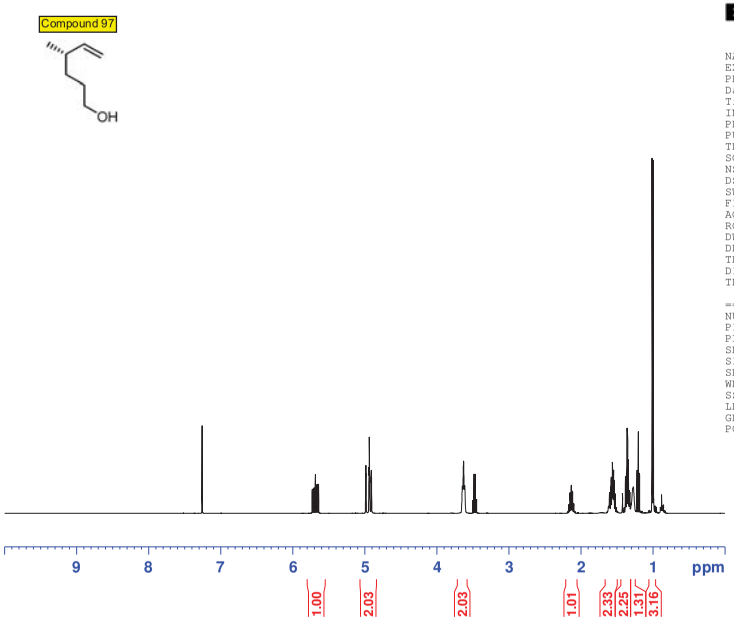

```
NAME                THMA D243
EXPNO                     101
PROCNO                      1
Date_              20080430
Time                   11.27
INSTRUM              avance400
PROBHD     5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1200
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                     7298.2
DW                     19.950 usec
DE                      6.00 usec
TE                     300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                  2.00000000 sec
D20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2             400.1316005 MHz
SI                      32768
SF               100.6127695 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       2.00
```

Compound 85

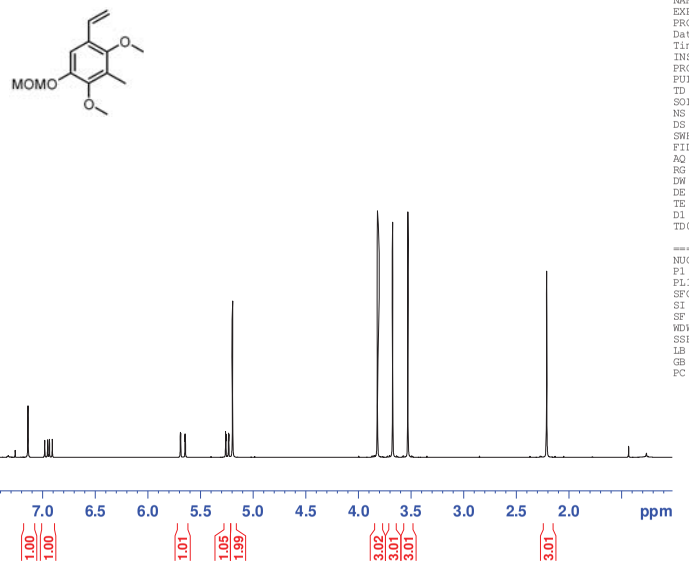





```
NAME                THMA D234
EXPNO                      41
PROCNO                      1
Date_              20080425
Time                   16.02
INSTRUM              avance400
PROBHD     5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      2000
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                    10321.3
DW                     19.950 usec
DE                      6.00 usec
TE                     300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                  2.00000000 sec
D20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2             400.1316005 MHz
SI                      32768
SF               100.6127697 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       4.00
```

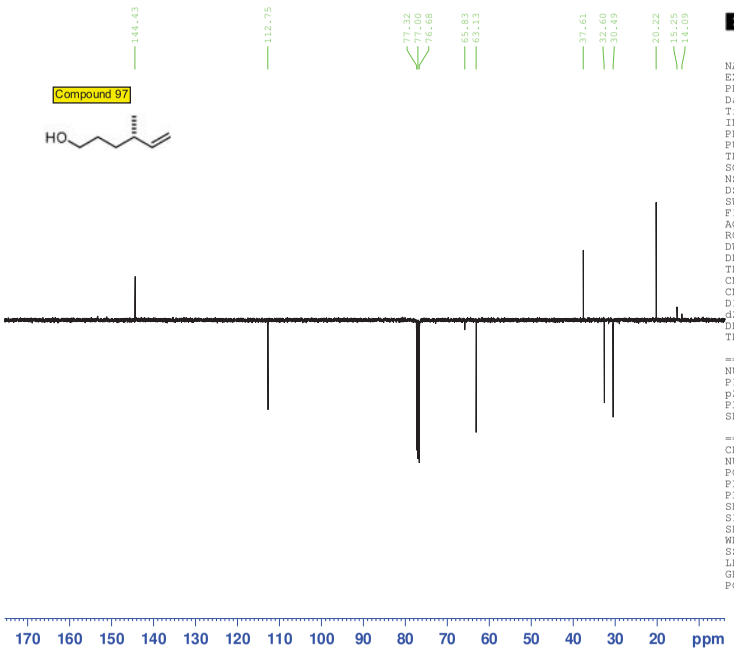



```
NAME                thmad129
EXPNO                    101
PROCNO                     1
Date_               20080220
Time                   0.27
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    287.4
DW                   60.400 usec
DE                    6.00 usec
TE                   300.0 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                     32768
SF             400.1300092 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                     1.00
```

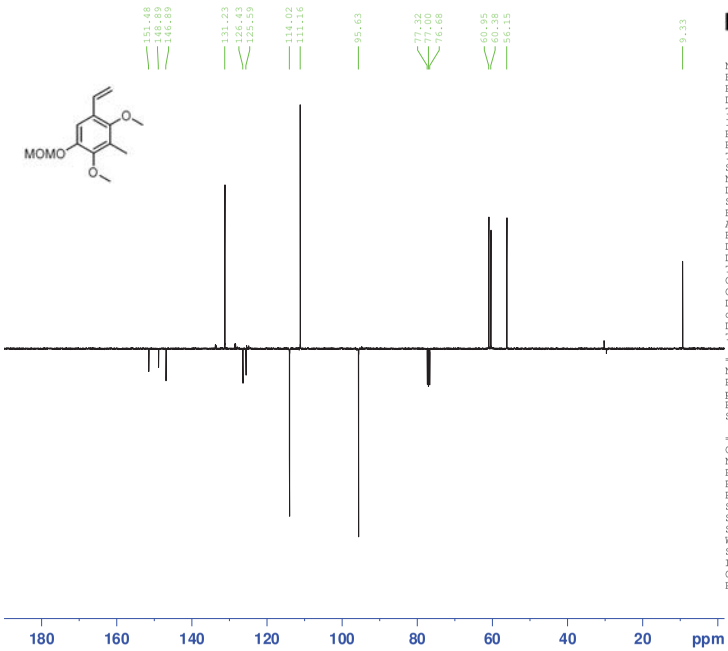



```
NAME                THMA D276
EXPNO                    30
PROCNO                    1
Date_               20090209
Time                  16.22
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                     50.8
DW                   60.400 usec
DE                    6.00 usec
TE                   300.0 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                     32768
SF             400.1300091 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                     1.00
```

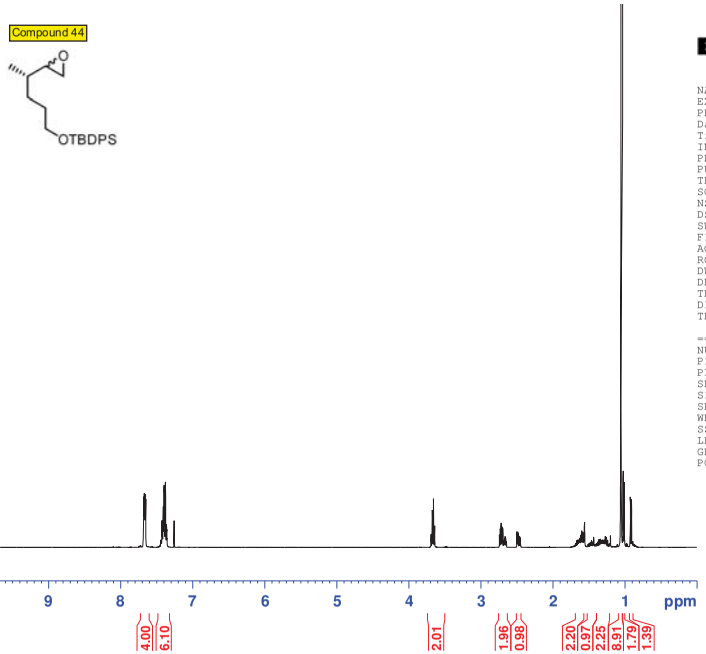
92



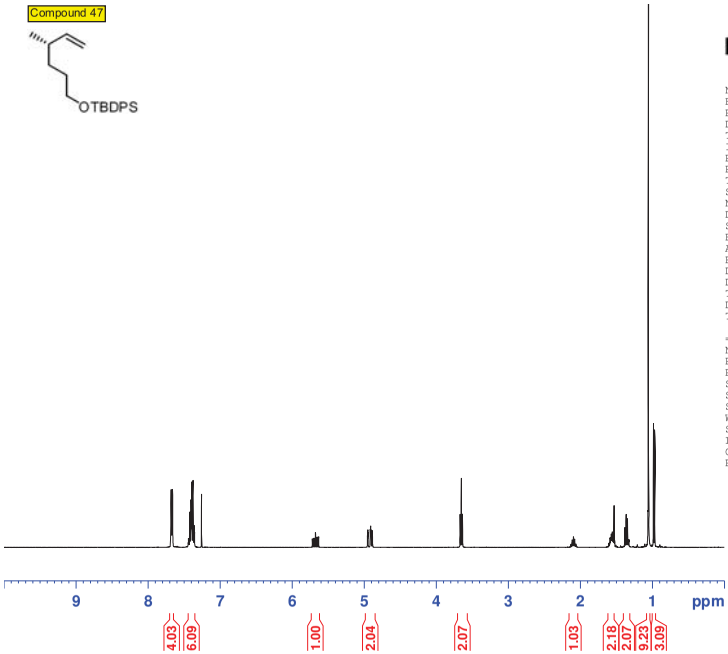

```
NAME                thmad129
EXPNO                    100
PROCNO                     1
Date_               20080220
Time                   0.25
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     2000
DS                        2
SWH               25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                   10321.3
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                     32768
SF             100.6127699 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                     1.40
```



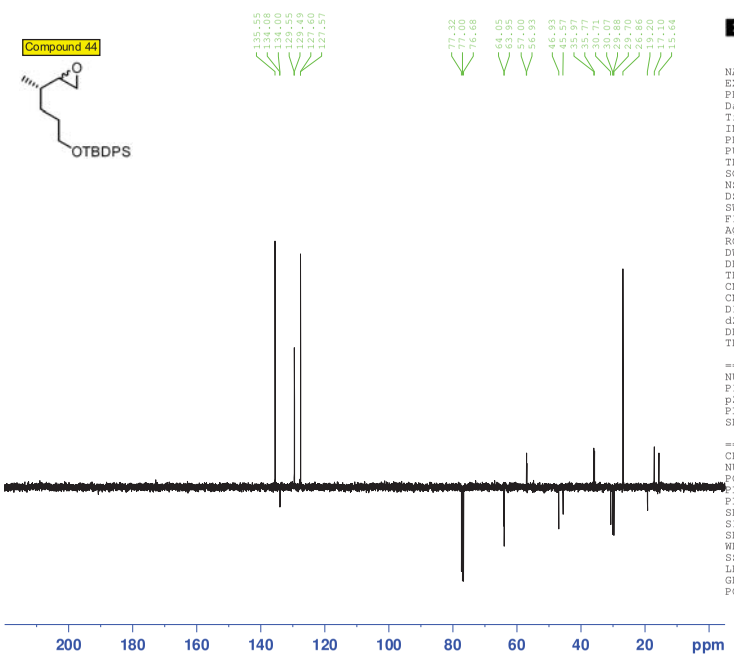

```
NAME                THMA D276
EXPNO                    31
PROCNO                    1
Date_               20090209
Time                  17.30
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                   4597.6
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                     32768
SF             100.6127745 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                     8.00
```



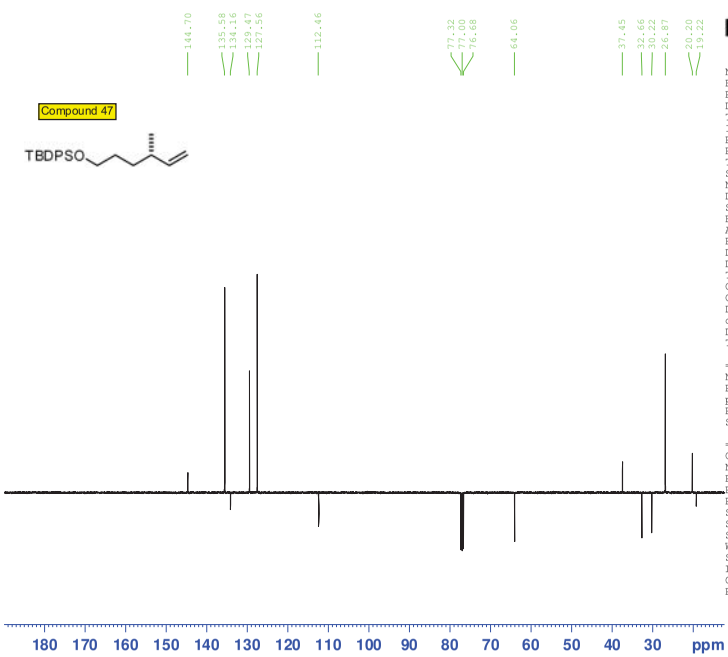

```
NAME                THMAD313
EXPNO                   10
PROCNO                   1
Date_             20080527
Time                 13.22
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    143.7
DW                 60.400 usec
DE                  6.00 usec
TE                  300.2 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300093 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```



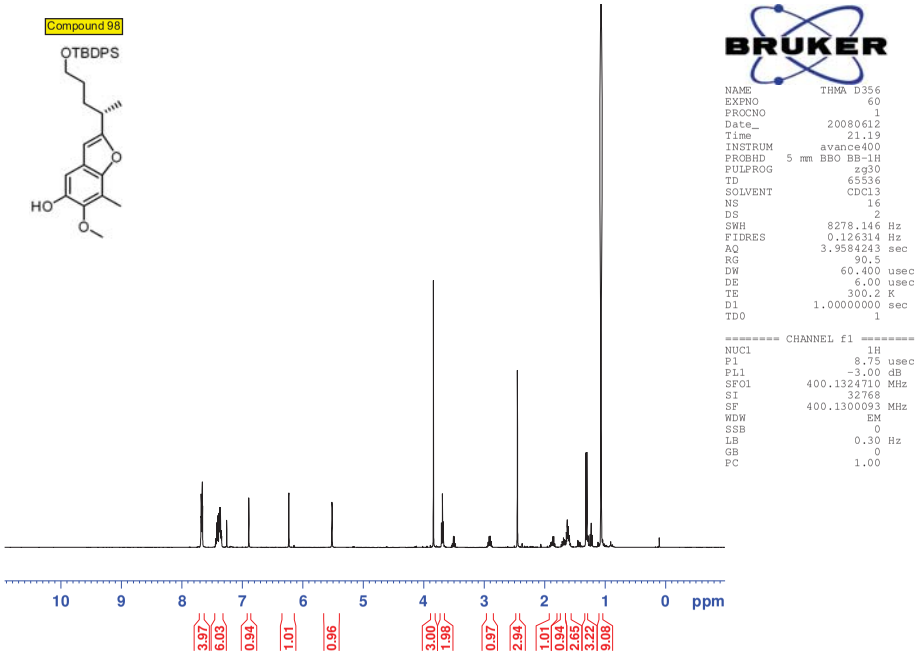

```
NAME                thmad130
EXPNO                   51
PROCNO                   1
Date_             20080220
Time                 21.50
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    181
DW                 60.400 usec
DE                  6.00 usec
TE                  300.2 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300095 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

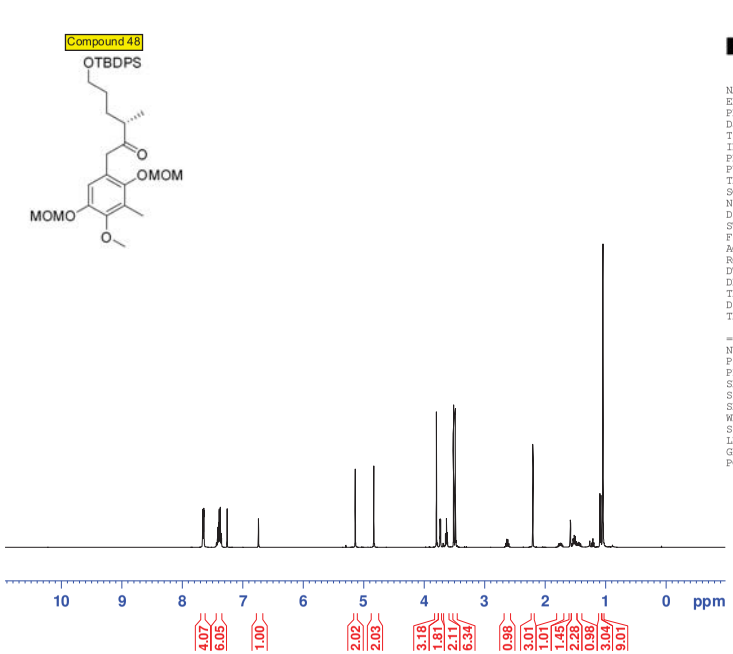

```
NAME                THMAD313
EXPNO                   11
PROCNO                   1
Date_             20080527
Time                 13.24
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                      230
DS                        2
SWH               25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                   9195.2
DW                 19.950 usec
DE                  6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127707 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```



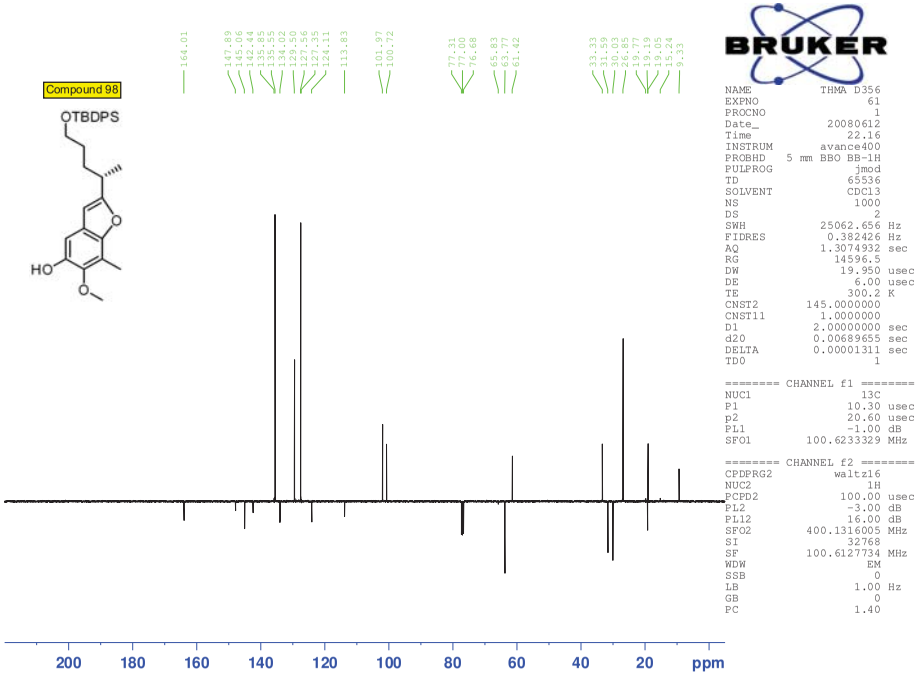

```
NAME                thmad130
EXPNO                   50
PROCNO                   1
Date_             20080220
Time                 21.48
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                      1500
DS                        2
SWH               25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                   5792.6
DW                 19.950 usec
DE                  6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127700 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```



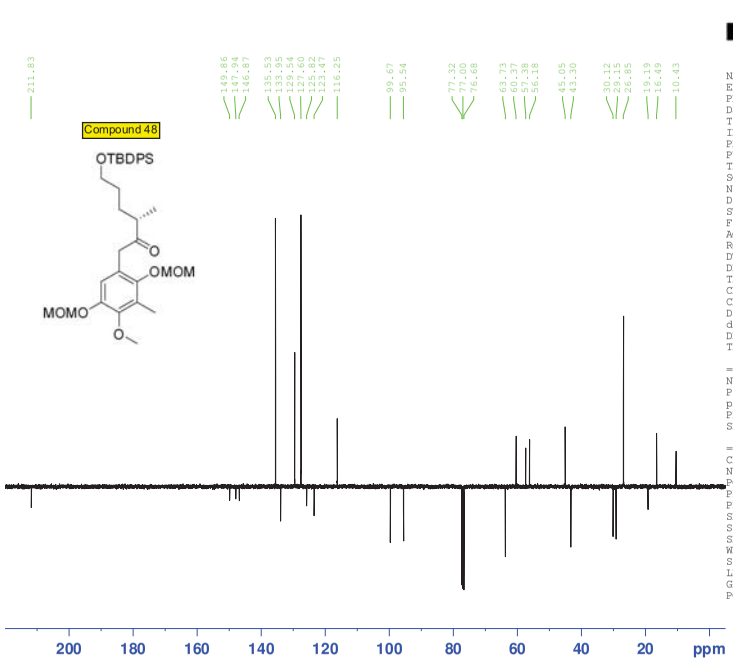

```
NAME                THMA D356
EXPNO                    60
PROCNO                    1
Date_              20080612
Time                 21.19
INSTRUM            avance400
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES                0.126314 Hz
AQ                 3.9584243 sec
RG                      90.5
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300093 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```



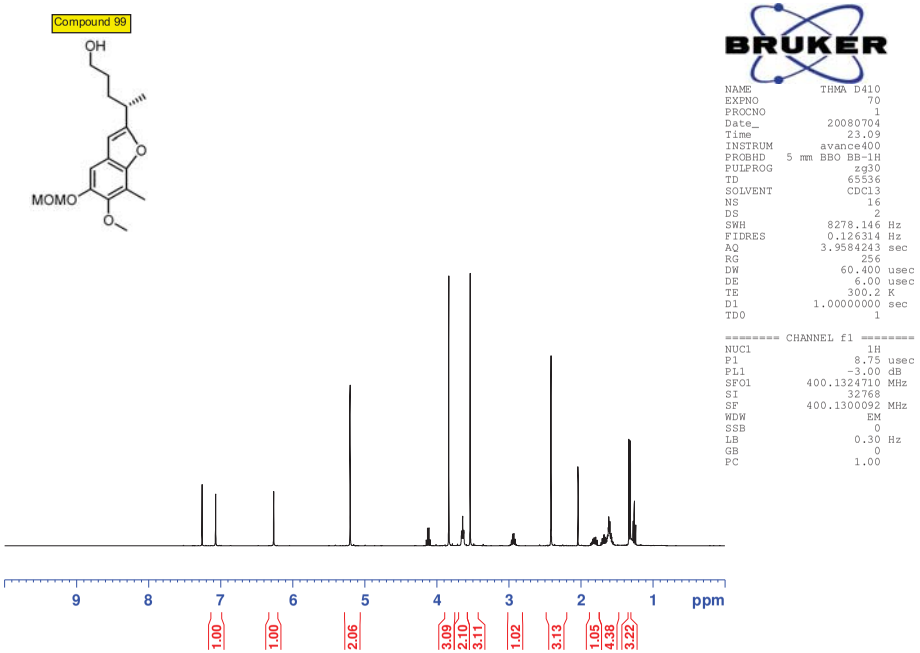

```
NAME                THMA D413
EXPNO                    20
PROCNO                    1
Date_              20080707
Time                 10.10
INSTRUM            avance400
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES                0.126314 Hz
AQ                 3.9584243 sec
RG                     203.2
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300091 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

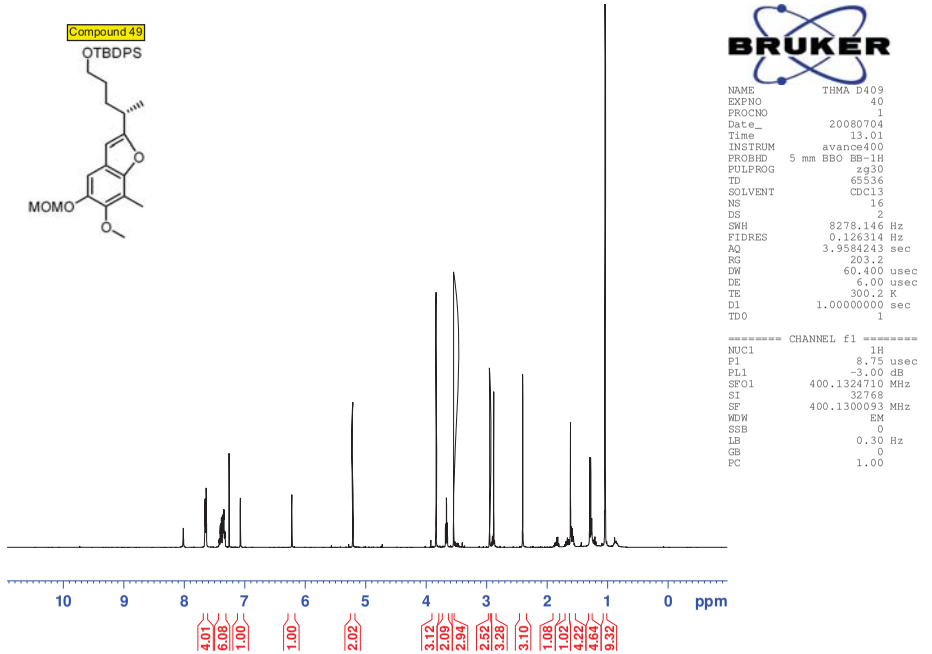

```
NAME                THMA D356
EXPNO                    61
PROCNO                    1
Date_              20080612
Time                 22.16
INSTRUM            avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1000
DS                        2
SWH               25062.656 Hz
FIDRES                0.382426 Hz
AQ                 1.3074932 sec
RG                   14596.5
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127734 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```



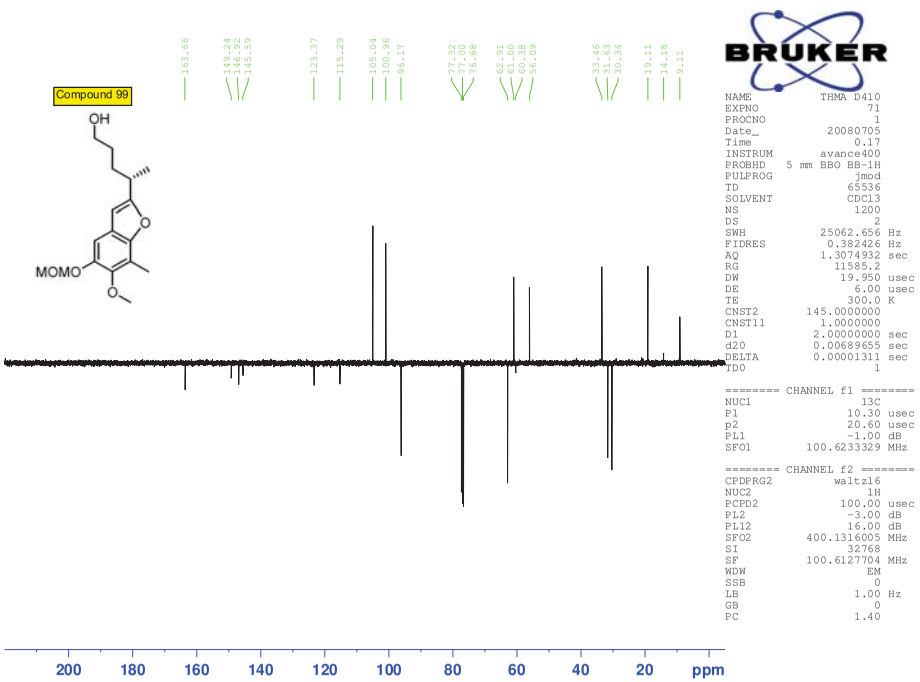

```
NAME                THMA D413
EXPNO                    21
PROCNO                    1
Date_              20080707
Time                 11.19
INSTRUM            avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES                0.382426 Hz
AQ                 1.3074932 sec
RG                     8192
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127708 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```



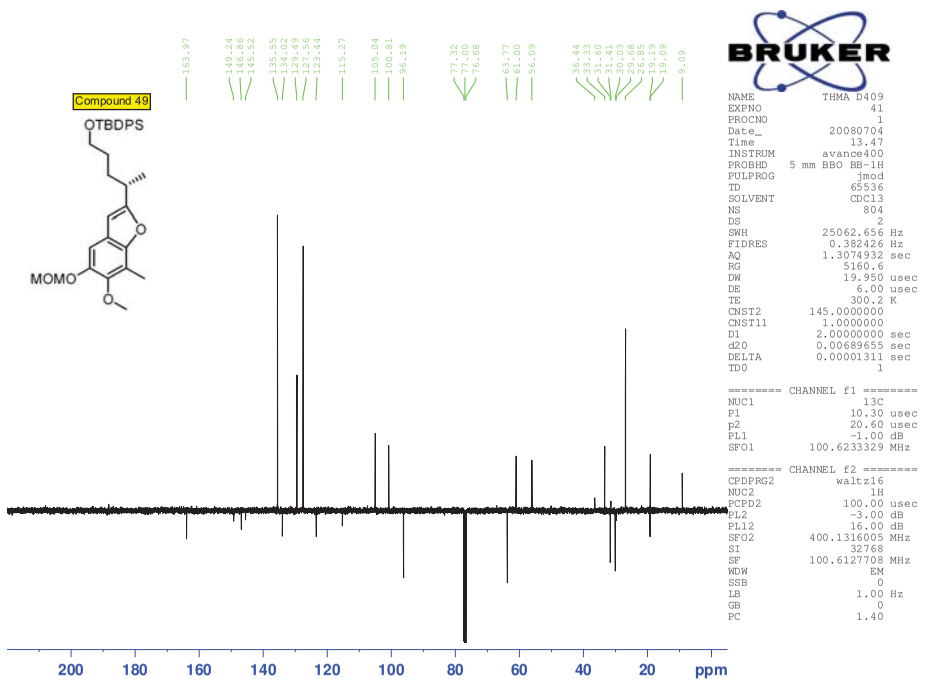

```
NAME                THMA D410
EXPNO                    70
PROCNO                    1
Date_              20080704
Time                  23.09
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      256
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300092 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.00
```




```
NAME                THMA D409
EXPNO                    40
PROCNO                    1
Date_              20080704
Time                  13.01
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                    203.2
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300093 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.00
```

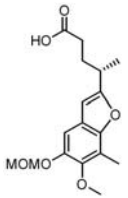



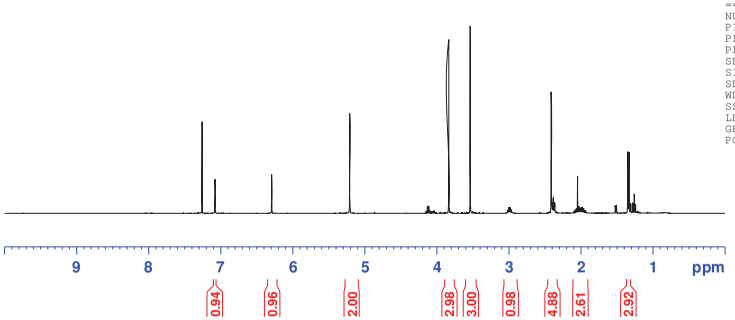

```
NAME                THMA D410
EXPNO                    71
PROCNO                    1
Date_              20080705
Time                   0.17
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                   11585.2
DW                   19.950 usec
DE                    6.00 usec
TE                   300.0 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
D20              0.00689655 sec
DELTA            0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127704 MHz
WDW                      EM
SSB                       0
LB                    1.00 Hz
GB                        0
PC                    1.40
```




```
NAME                THMA D409
EXPNO                    41
PROCNO                    1
Date_              20080704
Time                  13.47
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                      804
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                    5160.6
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
D20              0.00689655 sec
DELTA            0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127708 MHz
WDW                      EM
SSB                       0
LB                    1.00 Hz
GB                        0
PC                    1.40
```

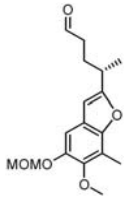
Compound 43

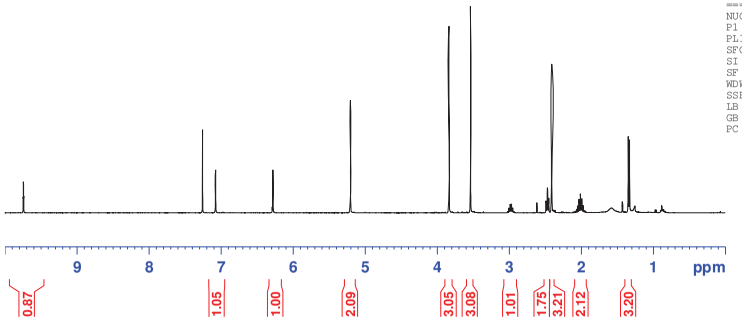





```
NAME                THMA D738
EXPNO                      10
PROCNO                      1
Date_                20081215
Time                     8.37
INSTRUM                AVIII400
PROBHD   5 mm PABBO BB-
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                 8223.685 Hz
FIDRES              0.125483 Hz
AQ                  3.9846387 sec
RG                        512
DW                   60.800 usec
DE                    6.50 usec
TE                   292.3 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                    13.50 usec
PL1                   -1.80 dB
PL1W             15.28361320 W
SFO1             400.2724718 MHz
SI                      32768
SF               400.2700105 MHz
WDW                        EM
SSB                         0
LB                    0.30 Hz
GB                          0
PC                    1.00
```

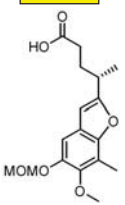
Compound 100





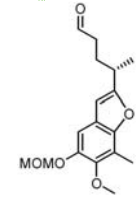

```
NAME                THMA D411
EXPNO                     100
PROCNO                      1
Date_                20080705
Time                     7.51
INSTRUM              avance400
PROBHD   5 mm BBO BB-1H
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                        362
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                    8.75 usec
PL1                   -3.00 dB
SFO1             400.1324710 MHz
SI                      32768
SF               400.1300093 MHz
WDW                        EM
SSB                         0
LB                    0.30 Hz
GB                          0
PC                    1.00
```

Compound 43

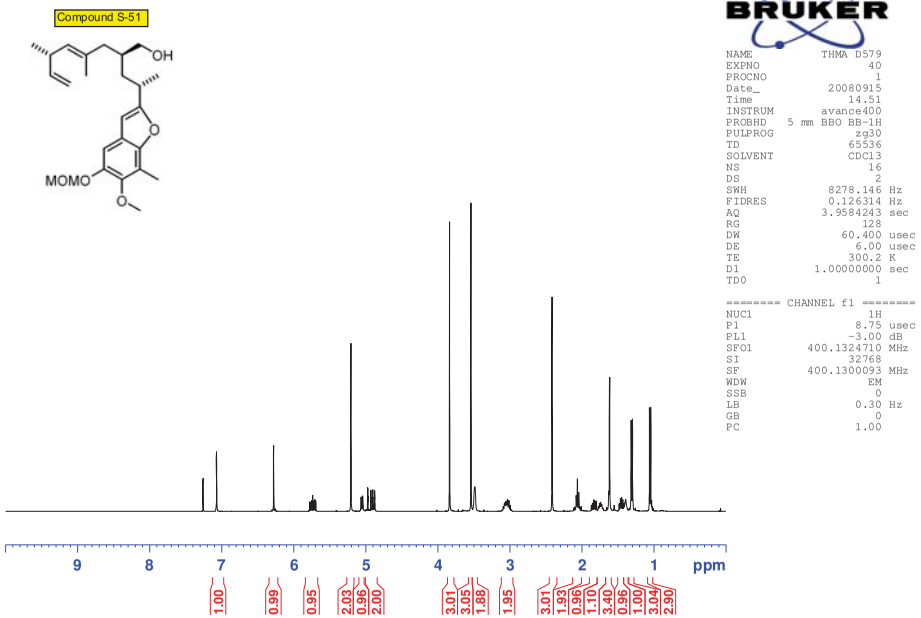



```
NAME                THMA D412
EXPNO                      91
PROCNO                      1
Date_                20080705
Time                     5.09
INSTRUM              avance400
PROBHD   5 mm BBO BB-1H
PULPROG                  jmod
TD                      65536
SOLVENT                 CDCl3
NS                       1200
DS                          2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                      16384
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                   10.30 usec
p2                   20.60 usec
PL1                   -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                       1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2             400.1316005 MHz
SI                      32768
SF               100.6127696 MHz
WDW                        EM
SSB                         0
LB                    1.00 Hz
GB                          0
PC                    1.40
```

Compound 100

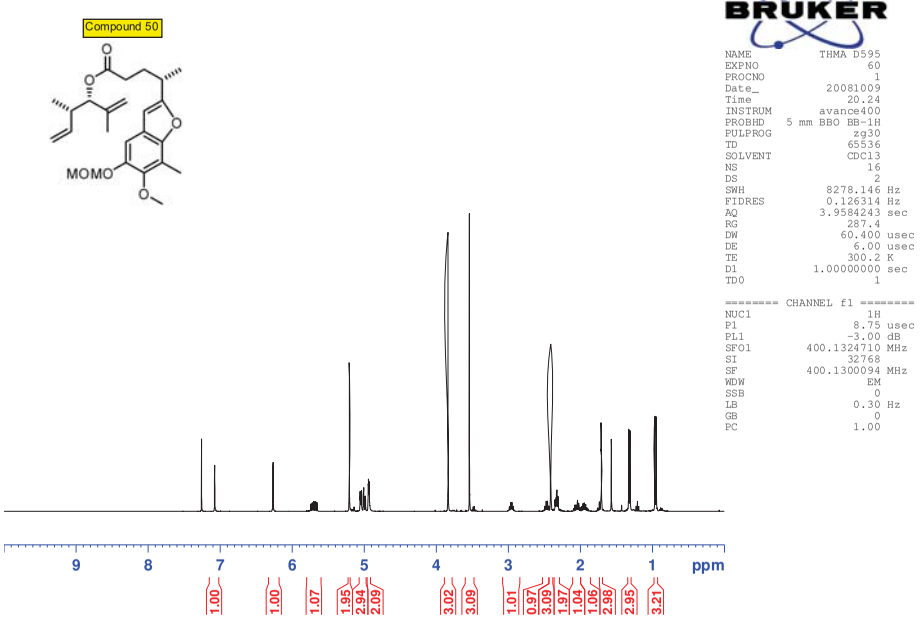



```
NAME                THMA D411
EXPNO                     101
PROCNO                      1
Date_                20080705
Time                     8.59
INSTRUM              avance400
PROBHD   5 mm BBO BB-1H
PULPROG                  jmod
TD                      65536
SOLVENT                 CDCl3
NS                       1200
DS                          2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                    9195.2
DW                   19.950 usec
DE                    6.00 usec
TE                   300.0 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                   10.30 usec
p2                   20.60 usec
PL1                   -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                       1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2             400.1316005 MHz
SI                      32768
SF               100.6127699 MHz
WDW                        EM
SSB                         0
LB                    1.00 Hz
GB                          0
PC                    1.40
```



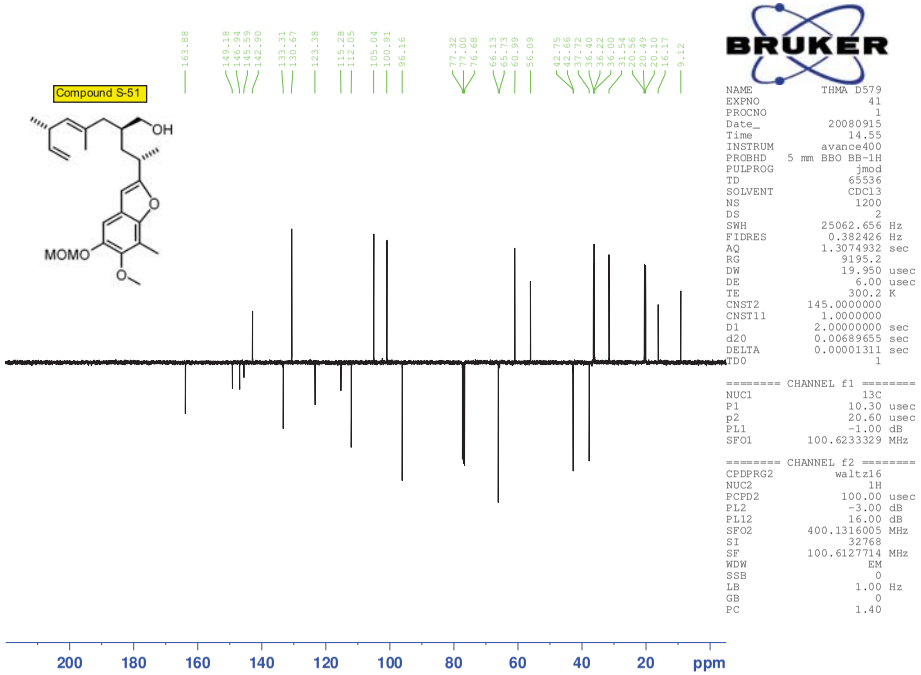
BRUKER

```
NAME                THMA D579
EXPNO                    40
PROCNO                    1
Date_              20080915
Time                  14.51
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      128
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300093 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```



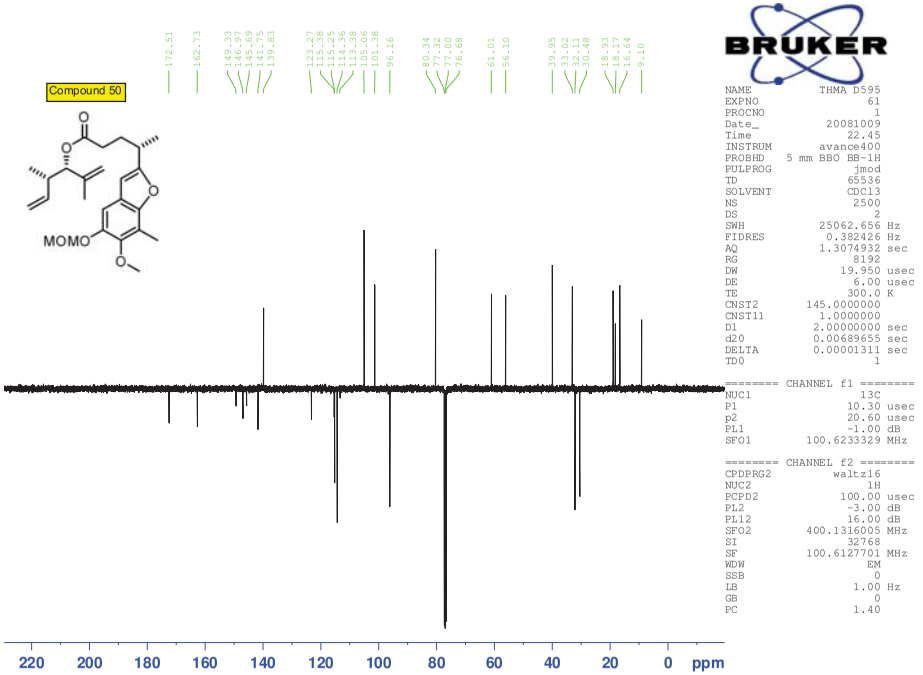
BRUKER

```
NAME                THMA D595
EXPNO                    60
PROCNO                    1
Date_              20081009
Time                  20.24
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                    287.4
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300094 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

BRUKER

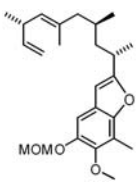
```
NAME                THMA D579
EXPNO                    41
PROCNO                    1
Date_              20080915
Time                  14.55
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                    9195.2
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127714 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

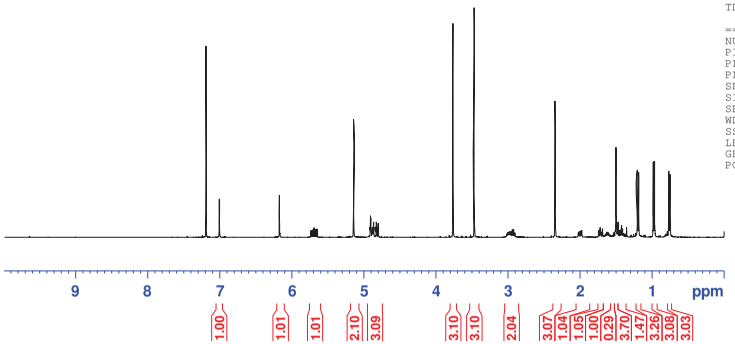


BRUKER

```
NAME                THMA D595
EXPNO                    61
PROCNO                    1
Date_              20081009
Time                  22.45
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     2500
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                     8192
DW                   19.950 usec
DE                    6.00 usec
TE                   300.0 K
CNST2             145.0000000
CNST11              1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127701 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

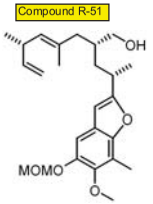
Compound 52

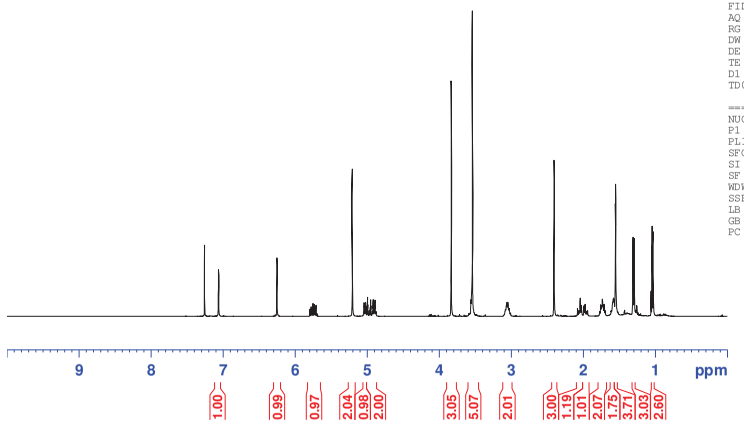





```
NAME                THMA D748
EXPNO                    60
PROCNO                    1
Date_              20090102
Time                  17.49
INSTRUM             AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8223.685 Hz
FIDRES             0.125483 Hz
AQ                 3.9846387 sec
RG                      575
DW                   60.800 usec
DE                    6.50 usec
TE                   292.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    13.50 usec
PL1                   -1.80 dB
PL1W           15.28361320 W
SFO1           400.2724718 MHz
SI                    32768
SF             400.2700385 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

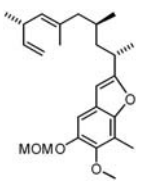
Compound R-51





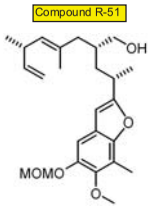

```
NAME                THMA D598
EXPNO                    40
PROCNO                    1
Date_              20081014
Time                  21.04
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     228.1
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300094 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Compound 52

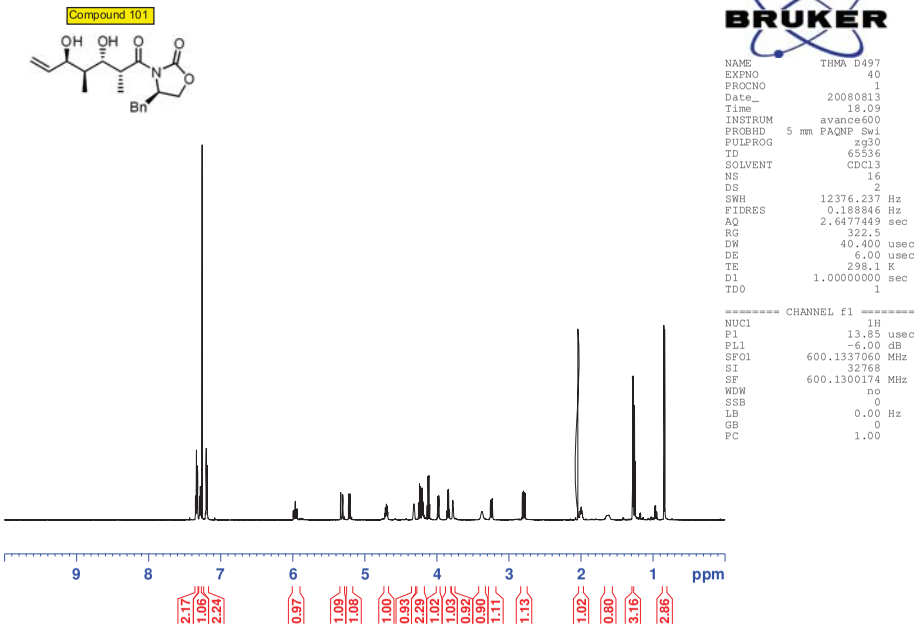



```
NAME                THMA D603
EXPNO                    21
PROCNO                    1
Date_              20081015
Time                  11.59
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                     4096
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127693 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.10
```

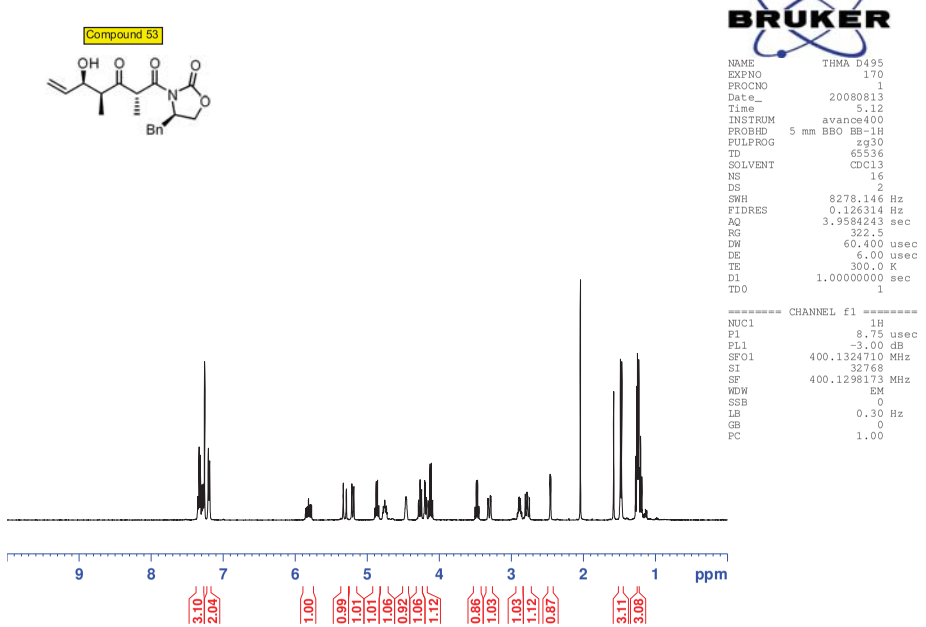
Compound R-51




```
NAME                THMA D598
EXPNO                    41
PROCNO                    1
Date_              20081014
Time                  22.12
INSTRUM             avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                   5160.6
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127703 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

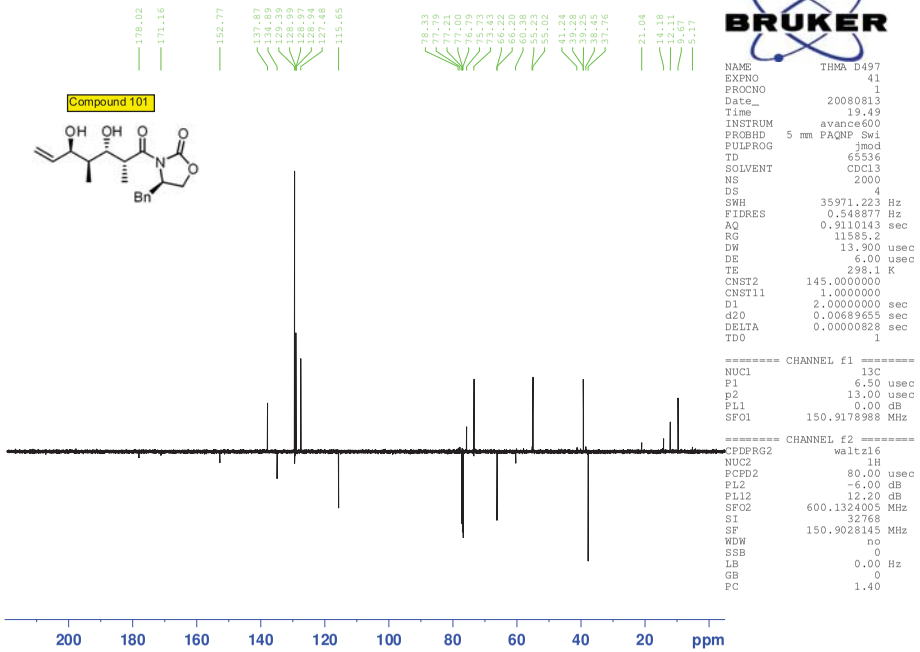



```
NAME                THMA D497
EXPNO                     40
PROCNO                     1
Date_               20080813
Time                   18.09
INSTRUM             avance600
PROBHD   5 mm PAQNP Swi
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                12376.237 Hz
FIDRES             0.188846 Hz
AQ                 2.6477449 sec
RG                     322.5
DW                    40.400 usec
DE                     6.00 usec
TE                    298.1 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     13.85 usec
PL1                    -6.00 dB
SFO1              600.1337060 MHz
SI                       32768
SF                600.1300174 MHz
WDW                       no
SSB                        0
LB                      0.00 Hz
GB                         0
PC                      1.00
```

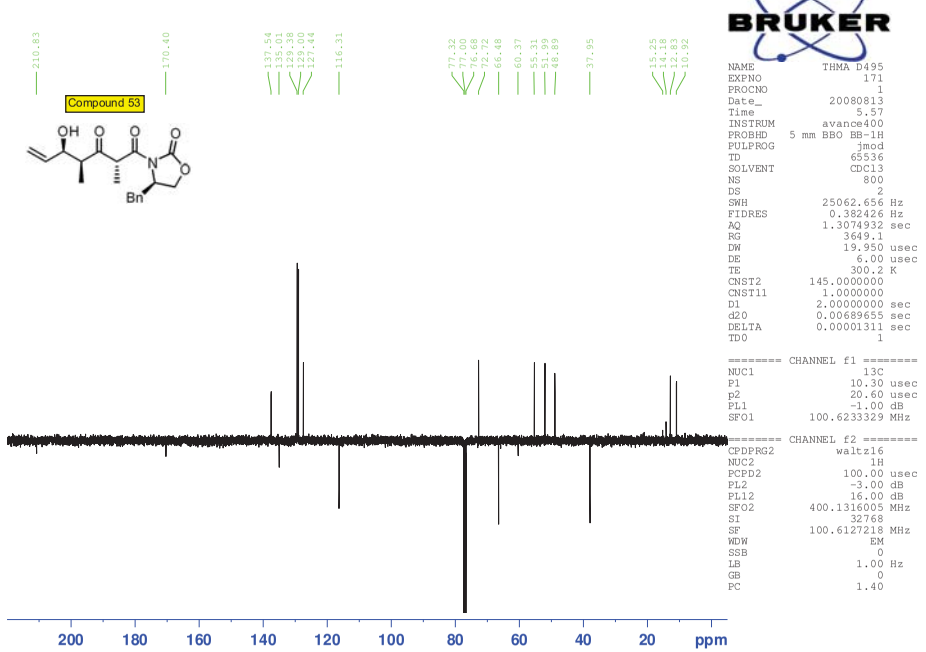



```
NAME                THMA D495
EXPNO                    170
PROCNO                     1
Date_               20080813
Time                    5.12
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                 3.9584243 sec
RG                     322.5
DW                    60.400 usec
DE                     6.00 usec
TE                    300.0 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                    -3.00 dB
SFO1              400.1324710 MHz
SI                       32768
SF                400.1298173 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

99

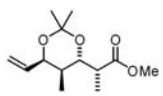


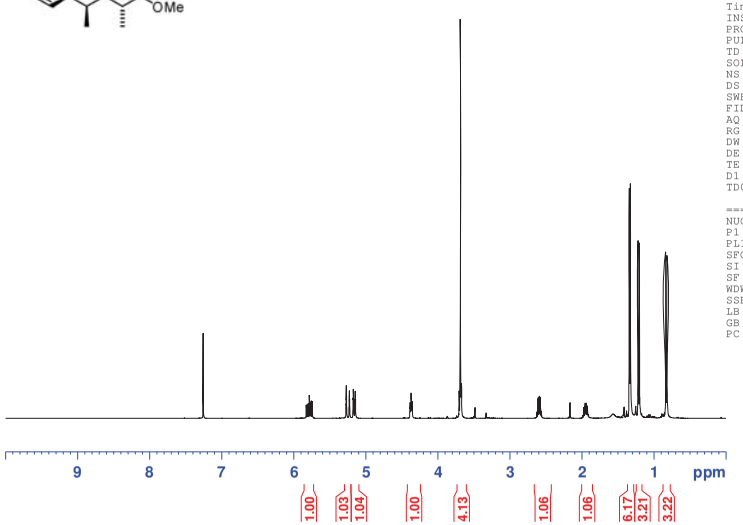

```
NAME                THMA D497
EXPNO                     41
PROCNO                     1
Date_               20080813
Time                   19.49
INSTRUM             avance600
PROBHD   5 mm PAQNP Swi
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                       2000
DS                         4
SWH                35971.223 Hz
FIDRES              0.548877 Hz
AQ                 0.9110143 sec
RG                   11585.2
DW                    13.900 usec
DE                     6.00 usec
TE                    298.1 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00000828 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                     6.50 usec
p2                    13.00 usec
PL1                    0.00 dB
SFO1              150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2               waltz16
NUC2                      1H
PCPD2                 80.00 usec
PL2                    -6.00 dB
PL12                   12.20 dB
SFO2              600.1324005 MHz
SI                       32768
SF                150.9028145 MHz
WDW                       no
SSB                        0
LB                      0.00 Hz
GB                         0
PC                      1.40
```




```
NAME                THMA D495
EXPNO                    171
PROCNO                     1
Date_               20080813
Time                    5.57
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                       800
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                 1.3074932 sec
RG                    3649.1
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1              100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2               waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2              400.1316005 MHz
SI                       32768
SF                100.6127218 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

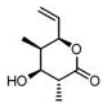
Compound 55

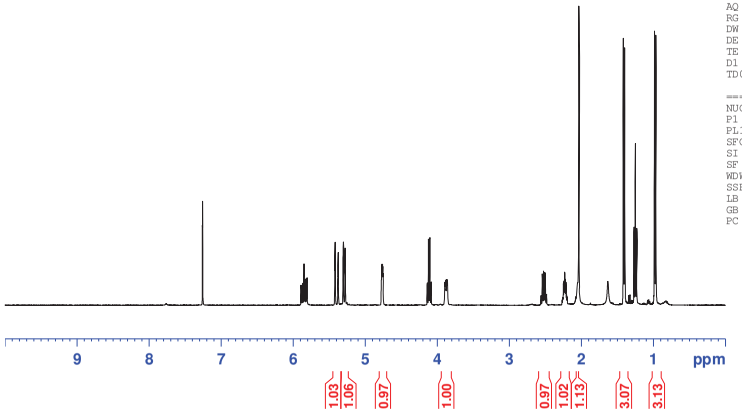





```
NAME                THMA D500
EXPNO                     80
PROCNO                     1
Date_               20080818
Time                   19.54
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       256
DW                    60.400 usec
DE                     6.00 usec
TE                     300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1            400.1324710 MHz
SI                       32768
SF              400.1300093 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

Compound 54

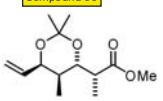





```
NAME                THMA D499
EXPNO                    231
PROCNO                     1
Date_               20080815
Time                    8.21
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       256
DW                    60.400 usec
DE                     6.00 usec
TE                     300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1            400.1324710 MHz
SI                       32768
SF              400.1300094 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

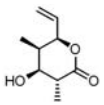
100

Compound 55



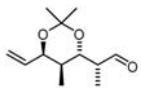

```
NAME                THMA D500
EXPNO                     81
PROCNO                     1
Date_               20080818
Time                   20.51
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1000
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                      4096
DW                    19.950 usec
DE                     6.00 usec
TE                     300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1            100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2               waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2            400.1316005 MHz
SI                       32768
SF              100.6127698 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

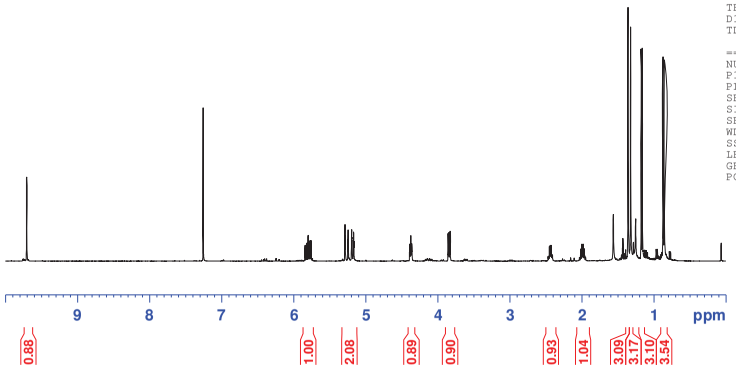
Compound 54




```
NAME                THMA D499
EXPNO                    230
PROCNO                     1
Date_               20080815
Time                    8.19
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                     65536
SOLVENT                CDCl3
NS                      1500
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                    7298.2
DW                    19.950 usec
DE                     6.00 usec
TE                     300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1            100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2               waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2            400.1316005 MHz
SI                       32768
SF              100.6127706 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

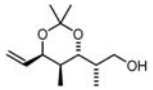
Compound 46

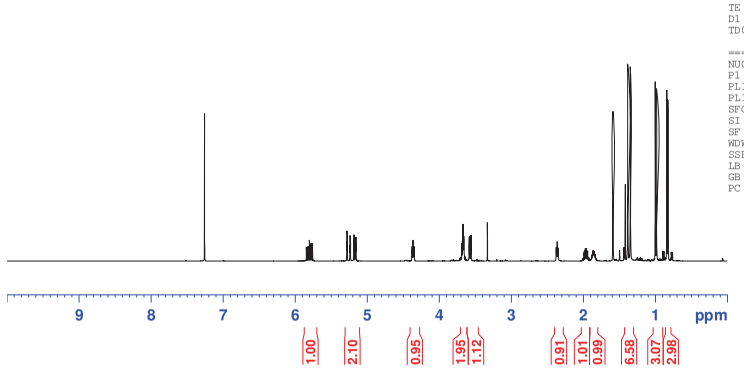





```
NAME                THMA D504
EXPNO                      90
PROCNO                      1
Date_                20080818
Time                    22.15
INSTRUM               avance400
PROBHD   5 mm BBO BB-1H
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8278.146 Hz
FIDRES                0.126314 Hz
AQ                   3.9584243 sec
RG                        256
DW                     60.400 usec
DE                      6.00 usec
TE                     300.2 K
D1                  1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1          400.1324710 MHz
SI                      32768
SF            400.1300093 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                      1.00
```

Compound 102

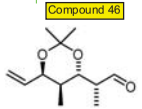





```
NAME                THMA D503
EXPNO                     160
PROCNO                      1
Date_                20080910
Time                    13.16
INSTRUM               AVIII400
PROBHD   5 mm PABBO BB-
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8223.685 Hz
FIDRES                0.125483 Hz
AQ                   3.9846387 sec
RG                        322
DW                     60.800 usec
DE                      6.50 usec
TE                     292.7 K
D1                  1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      13.50 usec
PL1                    -1.80 dB
PL1W          15.28361320 W
SFO1          400.2724718 MHz
SI                      32768
SF            400.2700054 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                      1.00
```

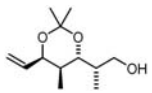
101

Compound 46

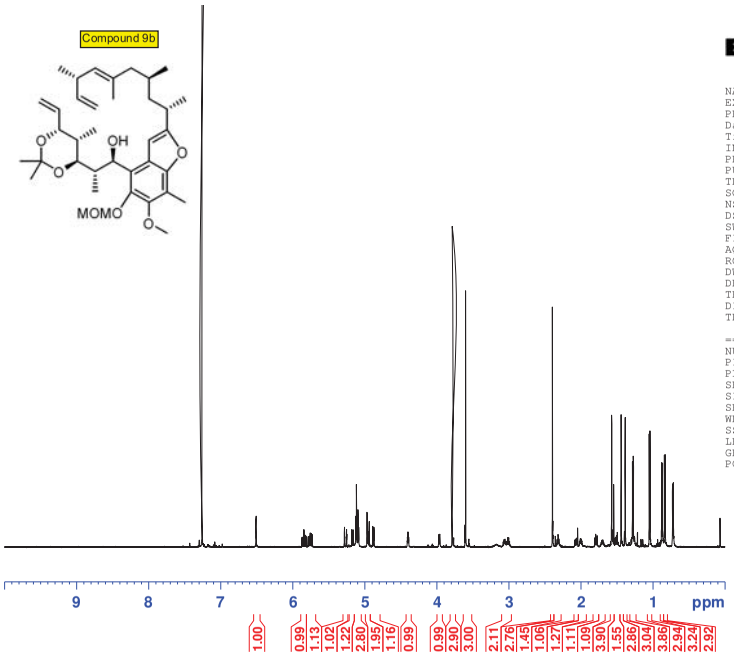



```
NAME                THMA D504
EXPNO                      91
PROCNO                      1
Date_                20080818
Time                    23.11
INSTRUM               avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 jmod
TD                      65536
SOLVENT                 CDCl3
NS                       1000
DS                          2
SWH                 25062.656 Hz
FIDRES                0.382426 Hz
AQ                   1.3074932 sec
RG                       4597.6
DW                     19.950 usec
DE                      6.00 usec
TE                     300.2 K
CNST2         145.0000000
CNST11          1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       13C
P1                      10.30 usec
p2                      20.60 usec
PL1                    -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2          400.1316005 MHz
SI                      32768
SF            100.6127696 MHz
WDW                        EM
SSB                         0
LB                     1.00 Hz
GB                          0
PC                      1.40
```

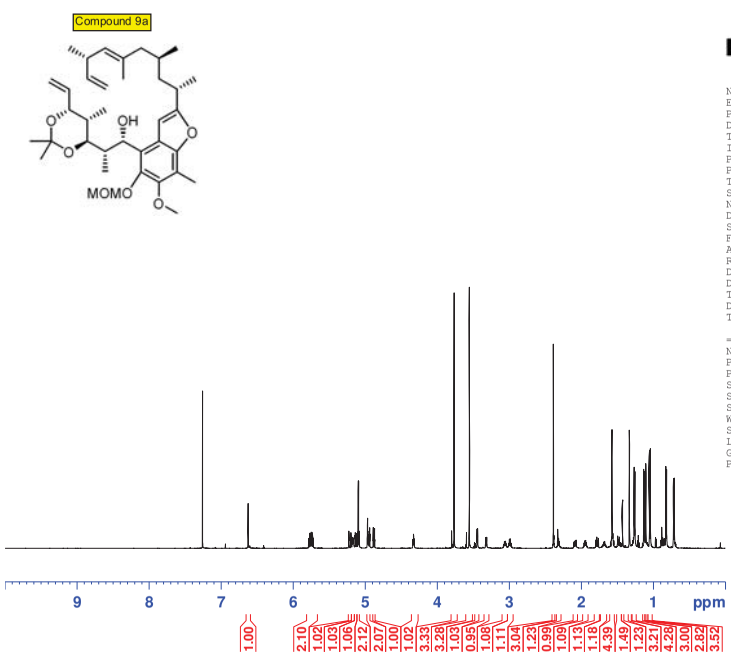
Compound 102



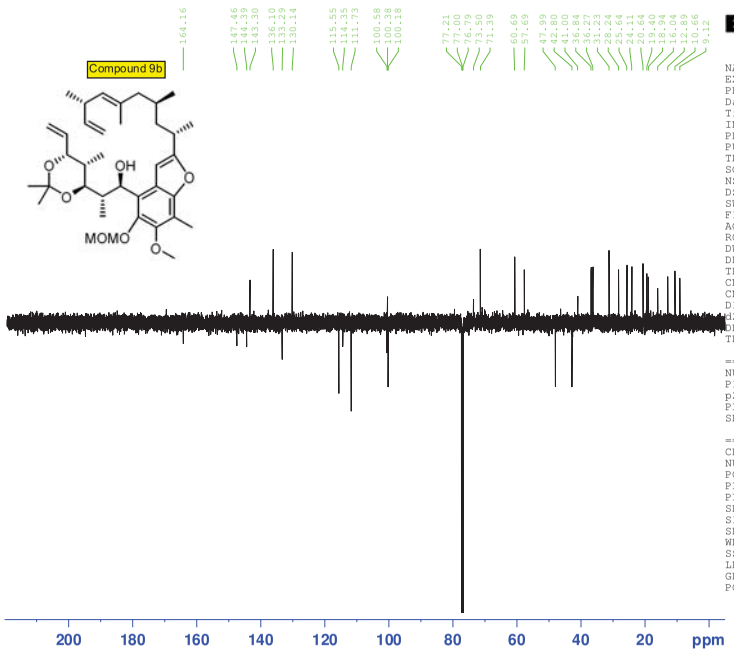

```
NAME                THMA D503
EXPNO                     101
PROCNO                      1
Date_                20080819
Time                     2.29
INSTRUM               avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 jmod
TD                      65536
SOLVENT                 CDCl3
NS                       2000
DS                          2
SWH                 25062.656 Hz
FIDRES                0.382426 Hz
AQ                   1.3074932 sec
RG                       2896.3
DW                     19.950 usec
DE                      6.00 usec
TE                     300.2 K
CNST2         145.0000000
CNST11          1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       13C
P1                      10.30 usec
p2                      20.60 usec
PL1                    -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2          400.1316005 MHz
SI                      32768
SF            100.6127700 MHz
WDW                        EM
SSB                         0
LB                     1.00 Hz
GB                          0
PC                      4.00
```



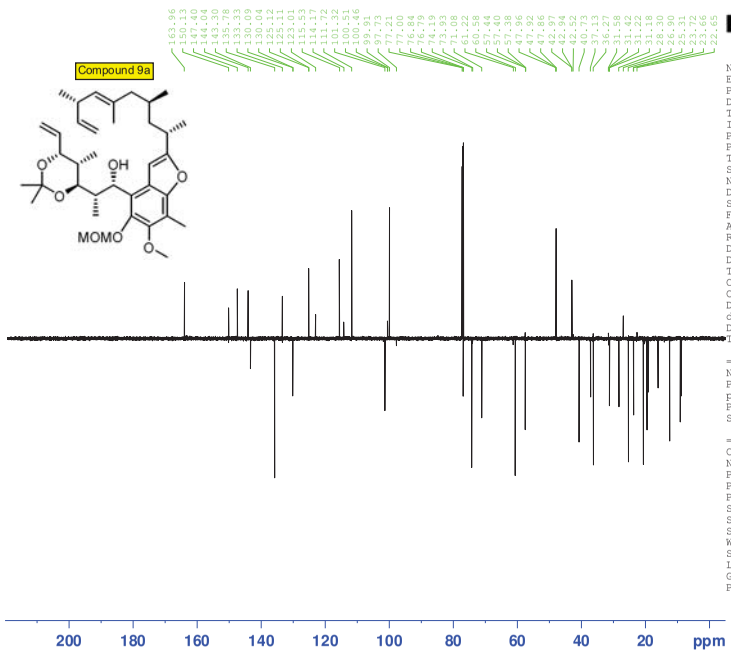

```
NAME                THMA D750
EXPNO                    20
PROCNO                    1
Date_              20090108
Time                  20.10
INSTRUM          avance600
PROBHD    5 mm PAQNP Swi
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH              12376.237 Hz
FIDRES            0.188846 Hz
AQ               2.6477449 sec
RG                   724.1
DW                  40.400 usec
DE                   6.00 usec
TE                  298.1 K
D1               1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   13.85 usec
PL1                  -6.00 dB
SFO1          600.1337060 MHz
SI                    32768
SF            600.1300174 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```




```
NAME                THMAD750
EXPNO                    10
PROCNO                    1
Date_              20090102
Time                  19.50
INSTRUM          avance600
PROBHD    5 mm PAQNP Swi
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       64
DS                        2
SWH              12376.237 Hz
FIDRES            0.188846 Hz
AQ               2.6477449 sec
RG                   228.1
DW                  40.400 usec
DE                   6.00 usec
TE                  298.1 K
D1               1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   13.85 usec
PL1                  -6.00 dB
SFO1          600.1337060 MHz
SI                    32768
SF            600.1300174 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```

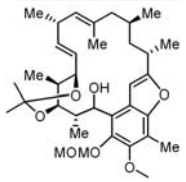



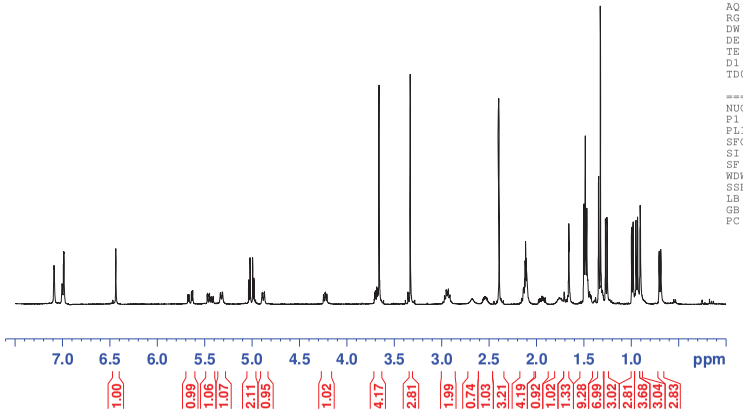

```
NAME                THMA D750
EXPNO                    26
PROCNO                    1
Date_              20090109
Time                  0.22
INSTRUM          avance600
PROBHD    5 mm PAQNP Swi
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        4
SWH              35971.223 Hz
FIDRES            0.548877 Hz
AQ               0.9110143 sec
RG                    8192
DW                  13.900 usec
DE                   6.00 usec
TE                  298.1 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
D20               0.00689655 sec
DELTA             0.00000828 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   6.50 usec
p2                  13.00 usec
PL1                  0.00 dB
SFO1          150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                80.00 usec
PL2                  -6.00 dB
PL12                 12.20 dB
SFO2          600.1324005 MHz
SI                    32768
SF            150.9028126 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```




```
NAME                THMAD750
EXPNO                    16
PROCNO                    1
Date_              20090103
Time                  7.46
INSTRUM          avance600
PROBHD    5 mm PAQNP Swi
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     7000
DS                        4
SWH              35971.223 Hz
FIDRES            0.548877 Hz
AQ               0.9110143 sec
RG                    8192
DW                  13.900 usec
DE                   6.00 usec
TE                  298.1 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
D20               0.00689655 sec
DELTA             0.00000828 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   6.50 usec
p2                  13.00 usec
PL1                  0.00 dB
SFO1          150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                80.00 usec
PL2                  -6.00 dB
PL12                 12.20 dB
SFO2          600.1324005 MHz
SI                    32768
SF            150.9028128 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
```

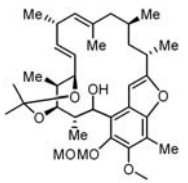
Compound 56 - C7D8 350.2K





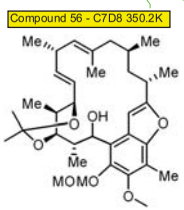
```
NAME          THMA D753 Temp
EXPNO                     6
PROCNO                    1
Date_              20090108
Time                  9.34
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   16024
SOLVENT                Tol
NS                       8
DS                       2
SWH               3205.128 Hz
FIDRES               0.200020 Hz
AQ                2.4997940 sec
RG                     181
DW                 156.000 usec
DE                   6.00 usec
TE                  350.2 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1          400.1314000 MHz
SI                   32768
SF            400.1300043 MHz
WDW                     EM
SSB                      0
LB                    0.10 Hz
GB                       0
PC                    1.00
```

Compound 56 - CDCl3 298.1K



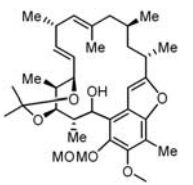

```
NAME          THMA D753
EXPNO                    10
PROCNO                    1
Date_              20090107
Time                  9.53
INSTRUM          avance600
PROBHD    5 mm PAQNP Swi
PULPROG               zg30
TD                   65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH              12376.237 Hz
FIDRES               0.188846 Hz
AQ                2.6477449 sec
RG                     128
DW                  40.400 usec
DE                   6.00 usec
TE                  298.1 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                     1H
P1                   13.85 usec
PL1                  -6.00 dB
SFO1          600.1337060 MHz
SI                   32768
SF            600.1300171 MHz
WDW                     no
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.00
```

Compound 56 - C7D8 350.2K



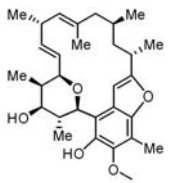

```
NAME          THMA D753 Temp
EXPNO                    15
PROCNO                    1
Date_              20090108
Time                 13.05
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG              jmod
TD                   65536
SOLVENT                Tol
NS                    1200
DS                       2
SWH              25062.656 Hz
FIDRES               0.382426 Hz
AQ                1.3074932 sec
RG                    8192
DW                  19.950 usec
DE                   6.00 usec
TE                  350.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6126818 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

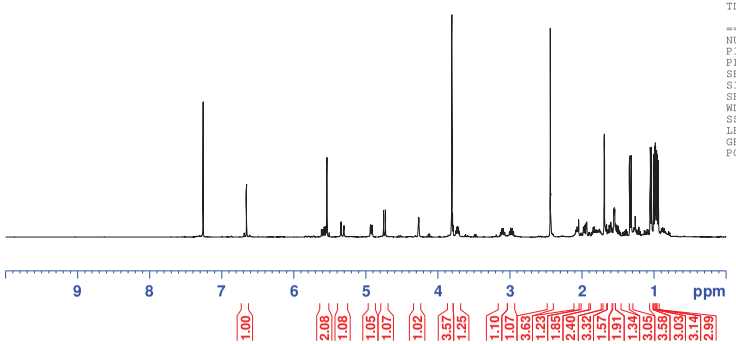
Compound 56 - CDCl3 298.1K




```
NAME          THMA D753
EXPNO                    16
PROCNO                    1
Date_              20090107
Time                 13.33
INSTRUM          avance600
PROBHD    5 mm PAQNP Swi
PULPROG              jmod
TD                   65536
SOLVENT               CDCl3
NS                    1200
DS                       4
SWH              35971.223 Hz
FIDRES               0.548877 Hz
AQ                0.9110143 sec
RG                    1824.6
DW                  13.900 usec
DE                   6.00 usec
TE                  298.1 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00000828 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                    6.50 usec
p2                   13.00 usec
PL1                   0.00 dB
SFO1          150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                80.00 usec
PL2                  -6.00 dB
PL12                 12.20 dB
SFO2          600.1324005 MHz
SI                   32768
SF            150.9028143 MHz
WDW                     no
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.40
```

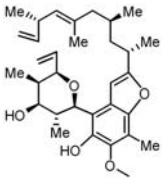
Compound 60

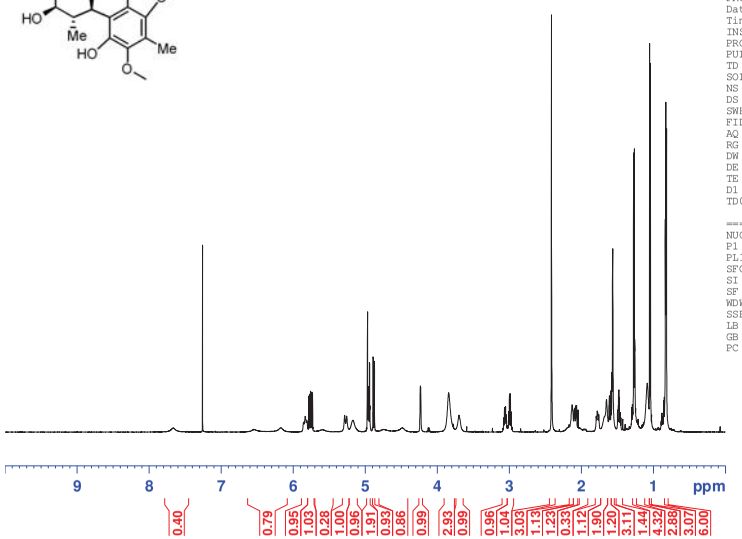




```
NAME                THMA D780
EXPNO                      61
PROCNO                      1
Date_                20090203
Time                     0.16
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                8278.146 Hz
FIDRES                0.126314 Hz
AQ                 3.9584243 sec
RG                     322.5
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1          400.1324710 MHz
SI                     32768
SF            400.1300092 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                      1.00
```

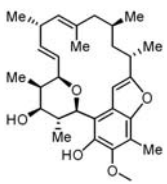
Compound 59





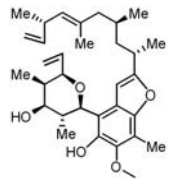
```
NAME                THMA D770
EXPNO                      10
PROCNO                      1
Date_                20090126
Time                    10.52
INSTRUM             avance600
PROBHD   5 mm PAQNP Swi
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH               12376.237 Hz
FIDRES                0.188846 Hz
AQ                 2.6477449 sec
RG                       114
DW                   40.400 usec
DE                     6.00 usec
TE                    298.1 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                    13.85 usec
PL1                   -6.00 dB
SFO1          600.1337060 MHz
SI                     32768
SF            600.1300174 MHz
WDW                       no
SSB                        0
LB                    0.00 Hz
GB                         0
PC                      1.00
```

Compound 60



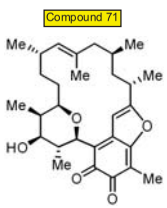

```
NAME                THMA D780
EXPNO                      60
PROCNO                      1
Date_                20090203
Time                     0.14
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                       1000
DS                         2
SWH               25062.656 Hz
FIDRES                0.382426 Hz
AQ                 1.3074932 sec
RG                      8192
DW                   19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2          400.1316005 MHz
SI                     32768
SF            100.6127698 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                      1.40
```

Compound 59



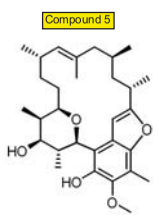

```
NAME                THMA D770
EXPNO                      11
PROCNO                      1
Date_                20090126
Time                    11.52
INSTRUM             avance600
PROBHD   5 mm PAQNP Swi
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                       1190
DS                         4
SWH               35971.223 Hz
FIDRES                0.548877 Hz
AQ                 0.9110143 sec
RG                     4597.6
DW                   13.900 usec
DE                     6.00 usec
TE                    298.1 K
CNST2             145.0000000
CNST11              1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00000828 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                     6.50 usec
p2                    13.00 usec
PL1                    0.00 dB
SFO1          150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                 80.00 usec
PL2                   -6.00 dB
PL12                  12.20 dB
SFO2          600.1324005 MHz
SI                     32768
SF            150.9028149 MHz
WDW                       no
SSB                        0
LB                    0.00 Hz
GB                         0
PC                      1.40
```

Compound 71



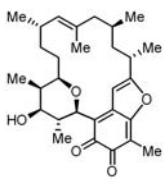

```
NAME                THMA D781
EXPNO                    260
PROCNO                     1
Date_               20090202
Time                   15.07
INSTRUM              AVIII400
PROBHD     5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                        4
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9846387 sec
RG                      724
DW                  60.800 usec
DE                   6.50 usec
TE                  292.4 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                    13.50 usec
PL1                   -1.80 dB
PL1W             15.28361320 W
SFO1             400.2724718 MHz
SI                      32768
SF               400.2700105 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                     1.00
```

Compound 5



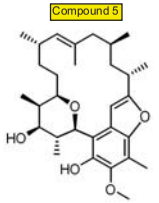

```
NAME                THMA D725
EXPNO                     10
PROCNO                     1
Date_               20081209
Time                    9.13
INSTRUM             avance600
PROBHD     5 mm PAQNP Swi
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               12376.237 Hz
FIDRES            0.188846 Hz
AQ                2.6477449 sec
RG                      362
DW                  40.400 usec
DE                   6.00 usec
TE                  298.1 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                    13.85 usec
PL1                   -6.00 dB
SFO1             600.1337060 MHz
SI                      32768
SF               600.1300174 MHz
WDW                       no
SSB                         0
LB                     0.00 Hz
GB                          0
PC                     1.00
```

Compound 71



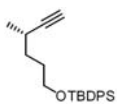

```
NAME                THMA D778
EXPNO                    106
PROCNO                     1
Date_               20090130
Time                    3.35
INSTRUM             avance400
PROBHD     5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                      5000
DS                        2
SWH               25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                    7298.2
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2            145.0000000
CNST11             1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2             400.1316005 MHz
SI                      32768
SF               100.6127691 MHz
WDW                        EM
SSB                         0
LB                     1.00 Hz
GB                          0
PC                     1.10
```

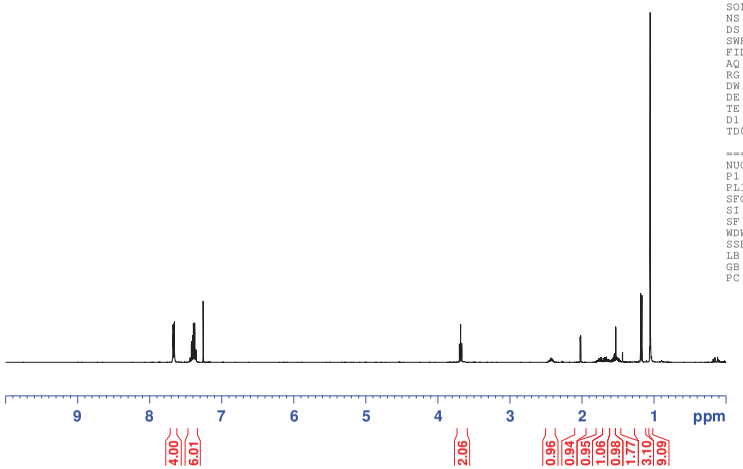
Compound 5




```
NAME                THMA D725
EXPNO                     11
PROCNO                     1
Date_               20081209
Time                    9.19
INSTRUM             avance600
PROBHD     5 mm PAQNP Swi
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                      2000
DS                        4
SWH               35971.223 Hz
FIDRES            0.548877 Hz
AQ                0.9110143 sec
RG                    9195.2
DW                  13.900 usec
DE                   6.00 usec
TE                  298.1 K
CNST2            145.0000000
CNST11             1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00000828 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                     6.50 usec
p2                    13.00 usec
PL1                    0.00 dB
SFO1             150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                 80.00 usec
PL2                   -6.00 dB
PL12                  12.20 dB
SFO2             600.1324005 MHz
SI                      32768
SF               150.9028133 MHz
WDW                       no
SSB                         0
LB                     0.00 Hz
GB                          0
PC                     1.40
```

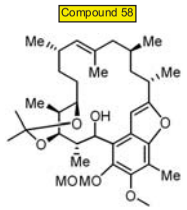
Compound 86

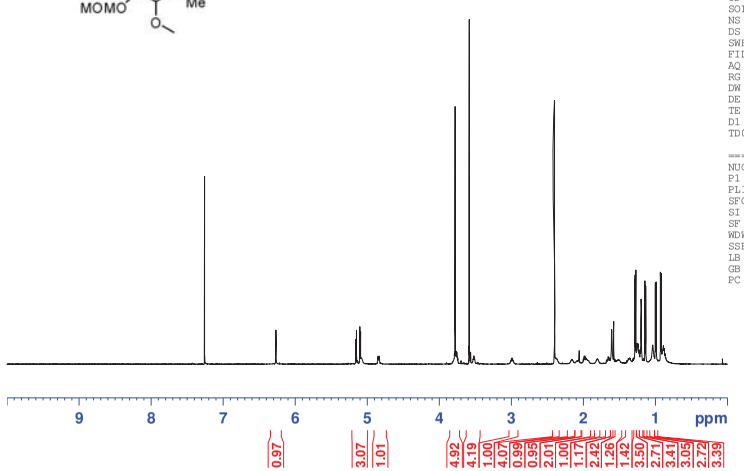





```
NAME                THMA D121
EXPNO                    10
PROCNO                    1
Date_              20080217
Time                  19.23
INSTRUM           avance400
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES                0.126314 Hz
AQ                 3.9584243 sec
RG                      256
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300095 MHz
WDW                      no
SSB                       0
LB                    0.00 Hz
GB                        0
PC                    1.00
```

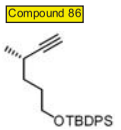
Compound 58





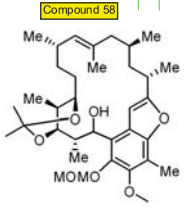

```
NAME                THMA D722
EXPNO                    10
PROCNO                    1
Date_              20081203
Time                  11.05
INSTRUM           avance600
PROBHD   5 mm PAQNP Swi
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               12376.237 Hz
FIDRES                0.188846 Hz
AQ                 2.6477449 sec
RG                    228.1
DW                   40.400 usec
DE                    6.00 usec
TE                   298.1 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   13.85 usec
PL1                  -6.00 dB
SFO1           600.1337060 MHz
SI                    32768
SF             600.1300174 MHz
WDW                      no
SSB                       0
LB                    0.00 Hz
GB                        0
PC                    1.00
```

Compound 86



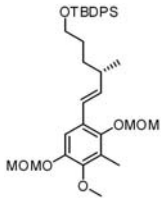

```
NAME                THMA D121
EXPNO                    11
PROCNO                    1
Date_              20080217
Time                  21.16
INSTRUM           avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     2000
DS                        2
SWH               25062.656 Hz
FIDRES                0.382426 Hz
AQ                 1.3074932 sec
RG                    11585.2
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                     1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127699 MHz
WDW                      no
SSB                       0
LB                    0.00 Hz
GB                        0
PC                    1.40
```

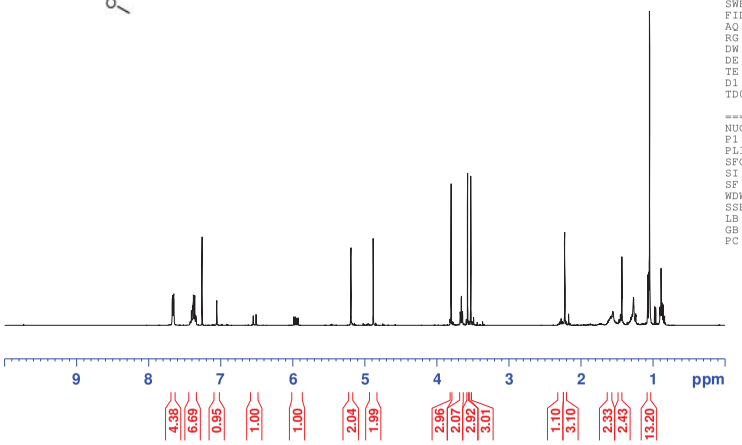
Compound 58




```
NAME                THMA D722
EXPNO                    16
PROCNO                    1
Date_              20081203
Time                  16.27
INSTRUM           avance600
PROBHD   5 mm PAQNP Swi
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1600
DS                        4
SWH               35971.223 Hz
FIDRES                0.548877 Hz
AQ                 0.9110143 sec
RG                    5792.6
DW                   13.900 usec
DE                    6.00 usec
TE                   298.1 K
CNST2             145.0000000
CNST11              1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00000828 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    6.50 usec
p2                   13.00 usec
PL1                   0.00 dB
SFO1           150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                     1H
PCPD2                 80.00 usec
PL2                   -6.00 dB
PL12                  12.20 dB
SFO2           600.1324005 MHz
SI                    32768
SF             150.9028131 MHz
WDW                      no
SSB                       0
LB                    0.00 Hz
GB                        0
PC                    1.00
```

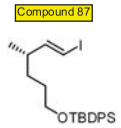
Compound 62





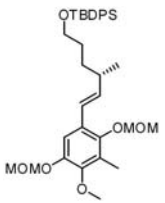

```
NAME                THMA D370
EXPNO                    10
PROCNO                    1
Date_              20080620
Time                  13.44
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     228.1
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300093 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Compound 87



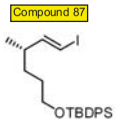

```
NAME                THMA D436
EXPNO                   110
PROCNO                    1
Date_              20080722
Time                  19.47
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     228.1
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300092 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Compound 62



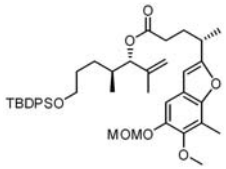

```
NAME                THMA D370
EXPNO                    11
PROCNO                    1
Date_              20080620
Time                  14.00
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                    3649.1
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                  2.00000000 sec
d20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127699 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

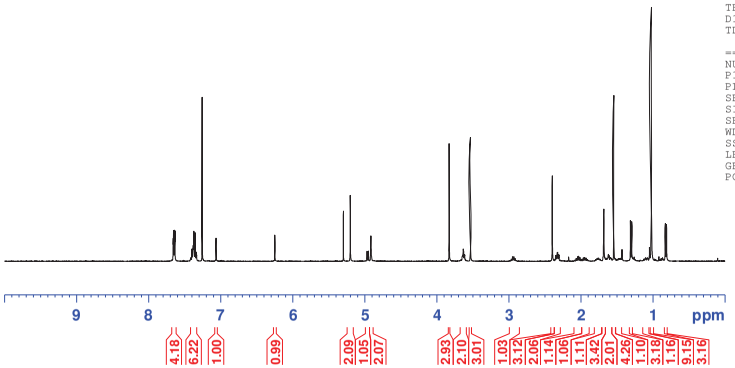
Compound 87




```
NAME                THMA D436
EXPNO                   111
PROCNO                    1
Date_              20080722
Time                  20.55
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                    13004
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2             145.0000000
CNST11              1.0000000
D1                  2.00000000 sec
d20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127698 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

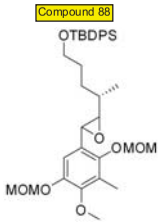
Compound 63

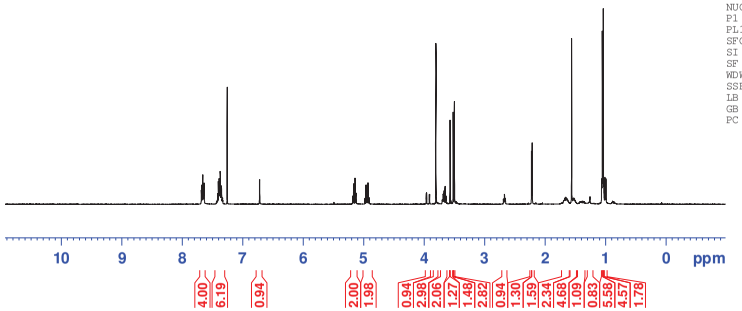





```
NAME                THMA D414
EXPNO                    50
PROCNO                    1
Date_              20080821
Time                  10.28
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                      362
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300093 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

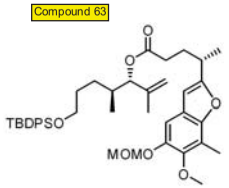
Compound 88





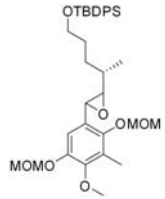

```
NAME                THMA D377-7
EXPNO                    40
PROCNO                    1
Date_              20080625
Time                  12.44
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                    322.5
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300093 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Compound 63



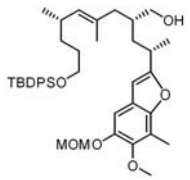

```
NAME                THMA D414
EXPNO                    31
PROCNO                    1
Date_              20080707
Time                  13.23
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                   10321.3
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2            145.0000000
CNST11             1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127699 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

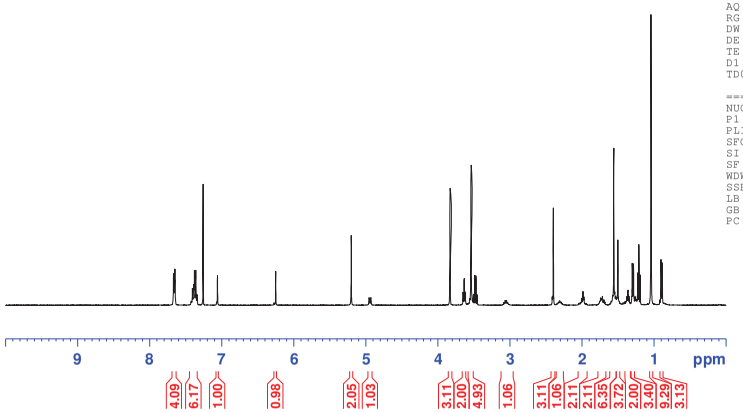
Compound 88




```
NAME                THMA D377-7
EXPNO                    41
PROCNO                    1
Date_              20080625
Time                  13.11
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                   14596.5
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2            145.0000000
CNST11             1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127699 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

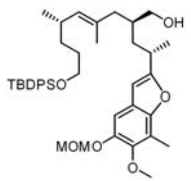
Compound R-64

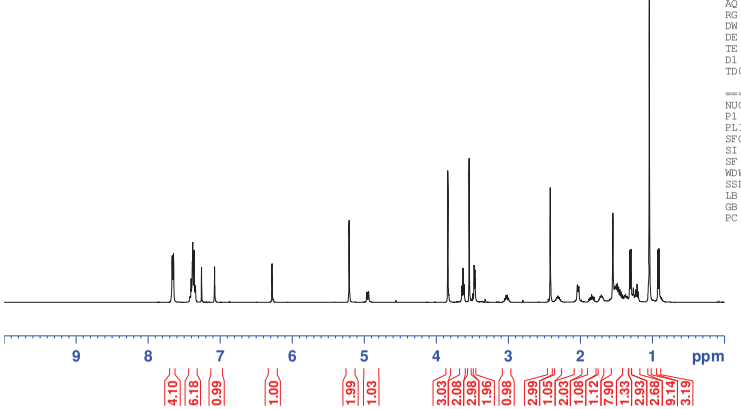





```
NAME                THMAD_509b
EXPNO                       70
PROCNO                       1
Date_                 20080822
Time                     11.00
INSTRUM                avance400
PROBHD    5 mm BBO BB-1H
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                   8278.146 Hz
FIDRES                0.126314 Hz
AQ                    3.9584243 sec
RG                       322.5
DW                      60.400 usec
DE                       6.00 usec
TE                      300.2 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       8.75 usec
PL1                     -3.00 dB
SFO1                400.1324710 MHz
SI                        32768
SF                  400.1300093 MHz
WDW                          EM
SSB                           0
LB                         0.30 Hz
GB                            0
PC                         1.00
```

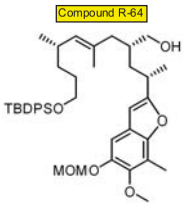
Compound S-64

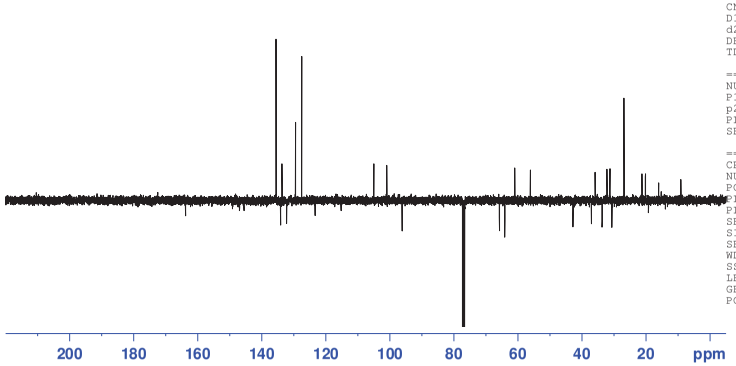





```
NAME                THMA_D415
EXPNO                       40
PROCNO                       1
Date_                 20080707
Time                     17.12
INSTRUM                avance400
PROBHD    5 mm BBO BB-1H
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                   8278.146 Hz
FIDRES                0.126314 Hz
AQ                    3.9584243 sec
RG                       161.3
DW                      60.400 usec
DE                       6.00 usec
TE                      300.2 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       8.75 usec
PL1                     -3.00 dB
SFO1                400.1324710 MHz
SI                        32768
SF                  400.1300094 MHz
WDW                          EM
SSB                           0
LB                         0.30 Hz
GB                            0
PC                         1.00
```

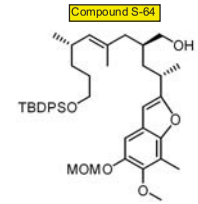
Compound R-64

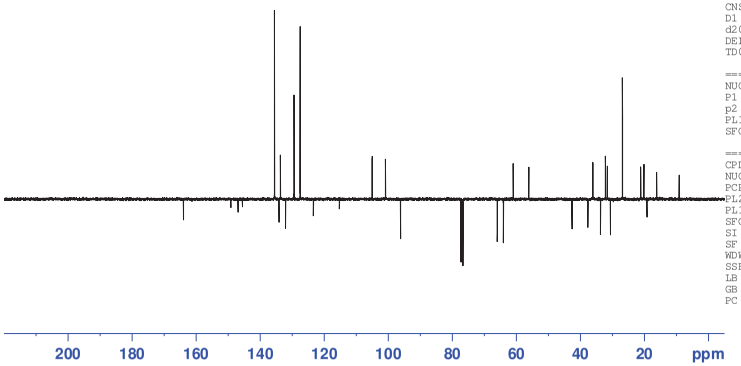





```
NAME                THMAD_509b
EXPNO                       71
PROCNO                       1
Date_                 20080822
Time                     11.16
INSTRUM                avance400
PROBHD    5 mm BBO BB-1H
PULPROG                  jmod
TD                       65536
SOLVENT                  CDCl3
NS                         774
DS                           2
SWH                  25062.656 Hz
FIDRES                0.382426 Hz
AQ                    1.3074932 sec
RG                        3251
DW                      19.950 usec
DE                       6.00 usec
TE                      300.2 K
CNST2                145.0000000
CNST11                 1.0000000
D1                    2.00000000 sec
d20                   0.00689655 sec
DELTA                 0.00001311 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                      10.30 usec
p2                      20.60 usec
PL1                     -1.00 dB
SFO1                100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                  100.00 usec
PL2                     -3.00 dB
PL12                    16.00 dB
SFO2                400.1316005 MHz
SI                        32768
SF                  100.6127699 MHz
WDW                          EM
SSB                           0
LB                         1.00 Hz
GB                            0
PC                         1.40
```

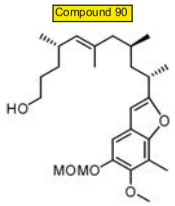
Compound S-64

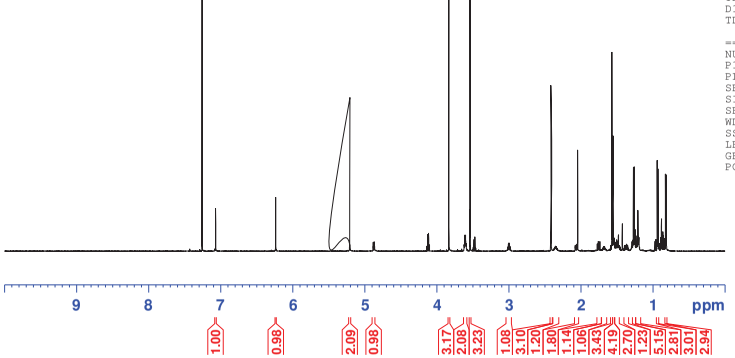





```
NAME                THMA_D415
EXPNO                       41
PROCNO                       1
Date_                 20080707
Time                     18.21
INSTRUM                avance400
PROBHD    5 mm BBO BB-1H
PULPROG                  jmod
TD                       65536
SOLVENT                  CDCl3
NS                        1200
DS                           2
SWH                  25062.656 Hz
FIDRES                0.382426 Hz
AQ                    1.3074932 sec
RG                        8192
DW                      19.950 usec
DE                       6.00 usec
TE                      300.2 K
CNST2                145.0000000
CNST11                 1.0000000
D1                    2.00000000 sec
d20                   0.00689655 sec
DELTA                 0.00001311 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                      10.30 usec
p2                      20.60 usec
PL1                     -1.00 dB
SFO1                100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                  100.00 usec
PL2                     -3.00 dB
PL12                    16.00 dB
SFO2                400.1316005 MHz
SI                        32768
SF                  100.6127711 MHz
WDW                          EM
SSB                           0
LB                         1.00 Hz
GB                            0
PC                         1.40
```

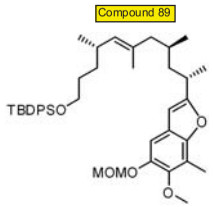
Compound 90

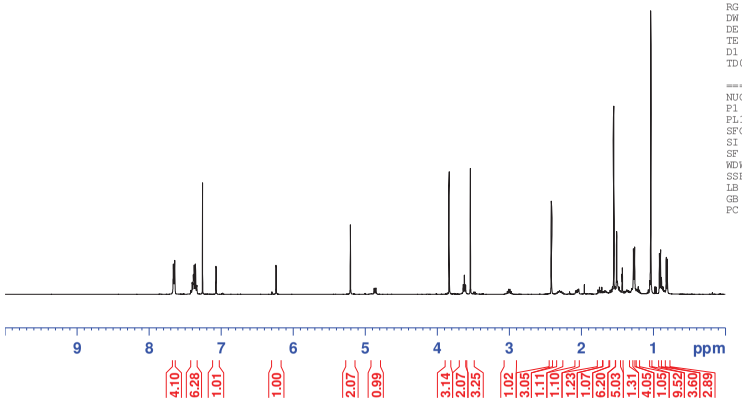





```
NAME              THMA D491
EXPNO                    50
PROCNO                    1
Date_              20080812
Time                  12.03
INSTRUM          avance600
PROBHD   5 mm PAQNP Swi
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH              12376.237 Hz
FIDRES               0.188846 Hz
AQ                2.6477449 sec
RG                    456.1
DW                   40.400 usec
DE                    6.00 usec
TE                   298.1 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    13.85 usec
PL1                   -6.00 dB
SFO1           600.1337060 MHz
SI                    32768
SF             600.1300174 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```

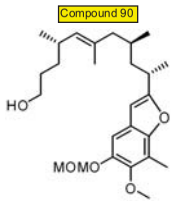
Compound 89





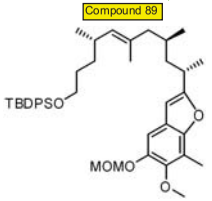

```
NAME              THMA D419
EXPNO                    20
PROCNO                    1
Date_              20080708
Time                  17.21
INSTRUM          avance400
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES               0.126314 Hz
AQ                3.9584243 sec
RG                    322.5
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300093 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Compound 90



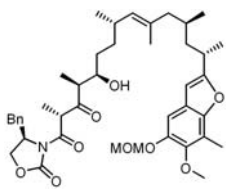

```
NAME              THMA D491
EXPNO                    51
PROCNO                    1
Date_              20080812
Time                  13.03
INSTRUM          avance600
PROBHD   5 mm PAQNP Swi
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        4
SWH              35971.223 Hz
FIDRES               0.548877 Hz
AQ                0.9110143 sec
RG                    2298.8
DW                   13.900 usec
DE                    6.00 usec
TE                   298.1 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00000828 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    6.50 usec
p2                   13.00 usec
PL1                   0.00 dB
SFO1           150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                80.00 usec
PL2                  -6.00 dB
PL12                 12.20 dB
SFO2           600.1324005 MHz
SI                    32768
SF             150.9028131 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
```

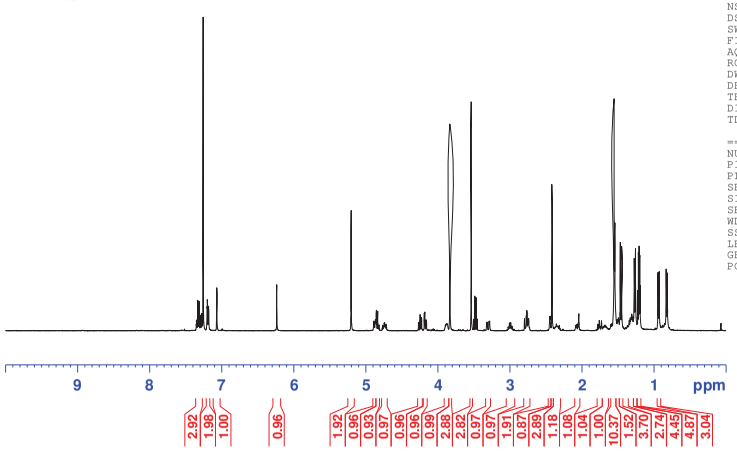
Compound 89




```
NAME              THMA D419
EXPNO                    21
PROCNO                    1
Date_              20080708
Time                  18.29
INSTRUM          avance400
PROBHD   5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1200
DS                        2
SWH              25062.656 Hz
FIDRES               0.382426 Hz
AQ                1.3074932 sec
RG                   11585.2
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127696 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

Compound 91

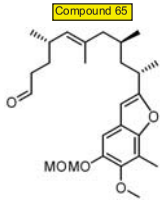


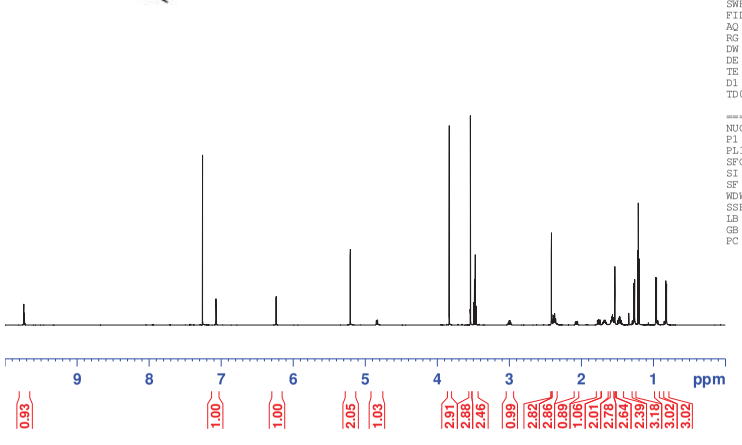


BRUKER

```
NAME          THMA D588 HPLC
EXPNO                    20
PROCNO                    1
Date_              20081008
Time                  17.23
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    406.4
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1          400.1324710 MHz
SI                    32768
SF            400.1300095 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Compound 65

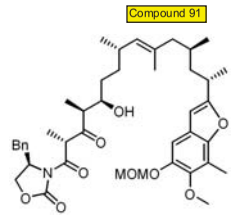




BRUKER

```
NAME          THMA D493
EXPNO                    60
PROCNO                    1
Date_              20080812
Time                  15.48
INSTRUM          avance600
PROBHD    5 mm PAQNP Swi
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               12376.237 Hz
FIDRES            0.188846 Hz
AQ                2.6477449 sec
RG                      512
DW                   40.400 usec
DE                    6.00 usec
TE                   298.1 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   13.85 usec
PL1                  -6.00 dB
SFO1          600.1337060 MHz
SI                    32768
SF            600.1300174 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```

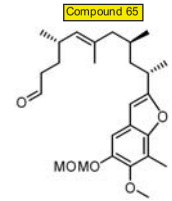
Compound 91



BRUKER

```
NAME          THMA D588 HPLC
EXPNO                    21
PROCNO                    1
Date_              20081008
Time                  19.05
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1800
DS                        2
SWH               25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                   5792.6
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2          400.1316005 MHz
SI                    32768
SF            100.6127696 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.10
```

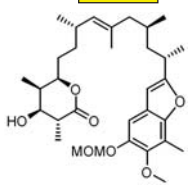
Compound 65

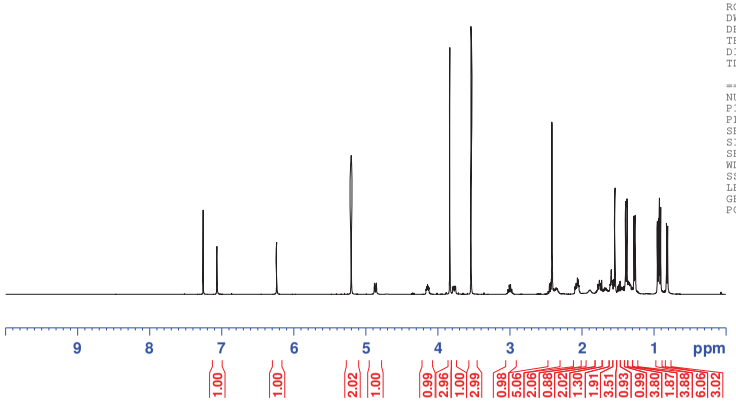


BRUKER

```
NAME          THMA D493
EXPNO                    61
PROCNO                    1
Date_              20080812
Time                  16.19
INSTRUM          avance600
PROBHD    5 mm PAQNP Swi
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                      605
DS                        4
SWH               35971.223 Hz
FIDRES            0.548877 Hz
AQ                0.9110143 sec
RG                     6502
DW                   13.900 usec
DE                    6.00 usec
TE                   298.1 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00685965 sec
DELTA            0.00000828 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    6.50 usec
p2                   13.00 usec
PL1                   0.00 dB
SFO1          150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                80.00 usec
PL2                  -6.00 dB
PL12                 12.20 dB
SFO2          600.1324005 MHz
SI                    32768
SF            150.9028131 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
```

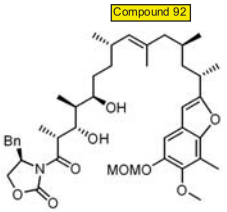
Compound 66

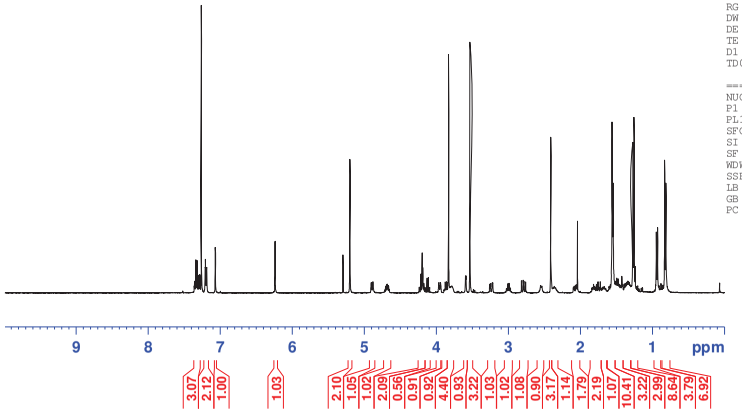




```
NAME                THMA D597
EXPNO                      31
PROCNO                      1
Date_            20081010
Time                    12.45
INSTRUM            avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                         32
DS                          2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     228.1
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1            400.1324710 MHz
SI                       32768
SF              400.1300093 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

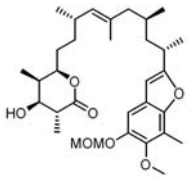
Compound 92

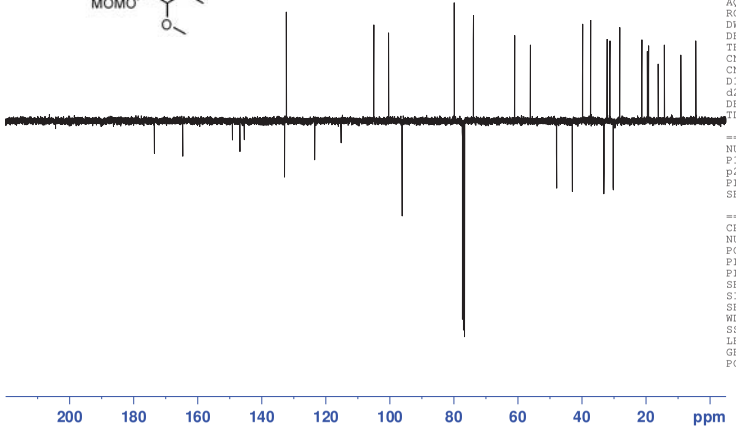




```
NAME                THMA D593
EXPNO                      10
PROCNO                      1
Date_            20081009
Time                    10.43
INSTRUM            avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                         16
DS                          2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                       362
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                 1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                      8.75 usec
PL1                    -3.00 dB
SFO1            400.1324710 MHz
SI                       32768
SF              400.1300095 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

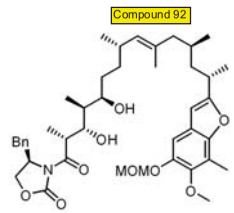
Compound 66

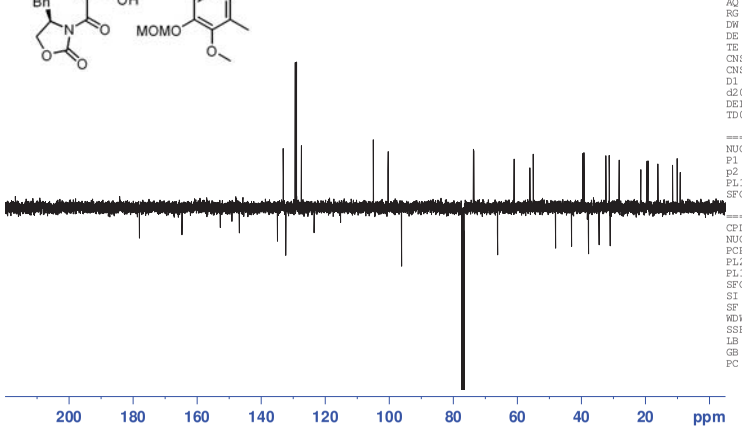




```
NAME                THMA D597
EXPNO                      30
PROCNO                      1
Date_            20081010
Time                    12.42
INSTRUM            avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                       1493
DS                          2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                     13004
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1            100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2            400.1316005 MHz
SI                       32768
SF              100.6127706 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.40
```

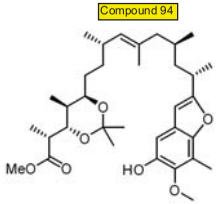
Compound 92

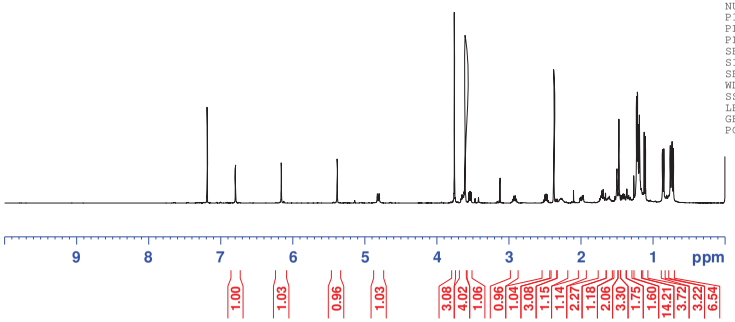




```
NAME                THMA D593
EXPNO                      11
PROCNO                      1
Date_            20081009
Time                    11.49
INSTRUM            avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                       2155
DS                          2
SWH               25062.656 Hz
FIDRES             0.382426 Hz
AQ                 1.3074932 sec
RG                      7298.2
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     10.30 usec
p2                     20.60 usec
PL1                    -1.00 dB
SFO1            100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                 100.00 usec
PL2                    -3.00 dB
PL12                   16.00 dB
SFO2            400.1316005 MHz
SI                       32768
SF              100.6127699 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.40
```

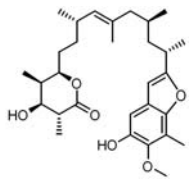
Compound 94

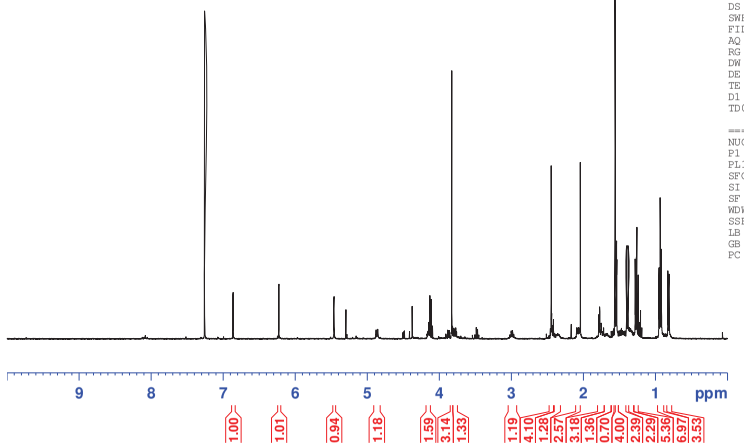




```
NAME                THMA_D611
EXPNO                     180
PROCNO                      1
Date_            20081016
Time                    15.39
INSTRUM              AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8223.685 Hz
FIDRES              0.125483 Hz
AQ                  3.9846387 sec
RG                        256
DW                   60.800 usec
DE                    6.50 usec
TE                   292.4 K
D1                  1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                    13.50 usec
PL1                   -1.80 dB
PL1W             15.28361320 W
SFO1             400.2724718 MHz
SI                      32768
SF               400.2700325 MHz
WDW                        EM
SSB                         0
LB                   0.30 Hz
GB                          0
PC                       1.00
```

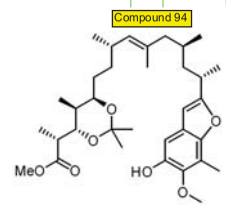
Compound 93





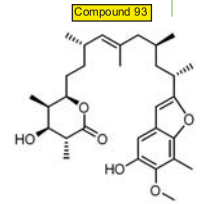
```
NAME                THMA_D600
EXPNO                      50
PROCNO                      1
Date_            20081015
Time                     1.09
INSTRUM              avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                        362
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                  1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                    8.75 usec
PL1                   -3.00 dB
SFO1             400.1324710 MHz
SI                      32768
SF               400.1300094 MHz
WDW                        no
SSB                         0
LB                   0.00 Hz
GB                          0
PC                       1.00
```

Compound 94

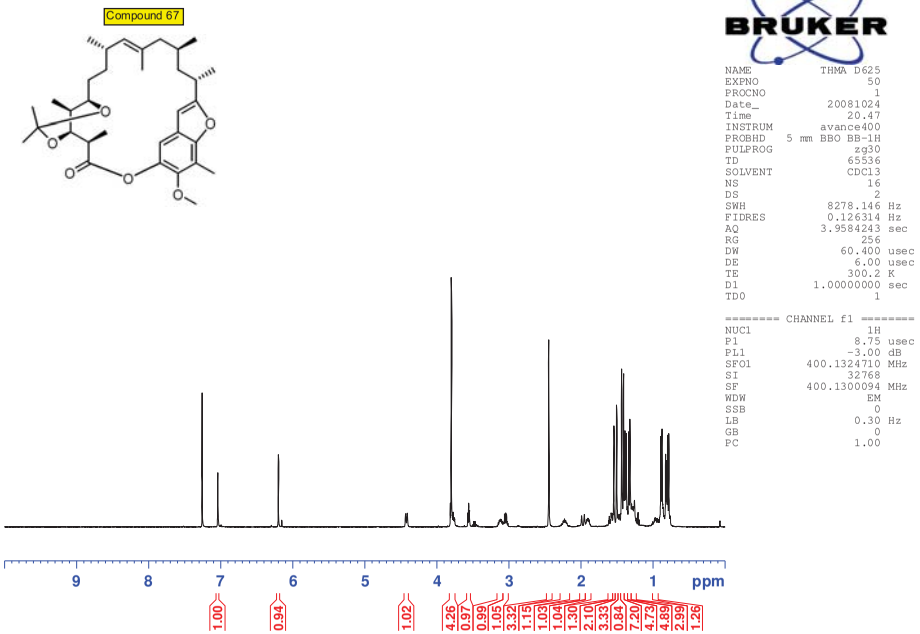



```
NAME                THMA_D609
EXPNO                      31
PROCNO                      1
Date_            20081016
Time                    18.05
INSTRUM              avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                        1800
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                       7298.2
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                  2.00000000 sec
d20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2             400.1316005 MHz
SI                      32768
SF               100.6127691 MHz
WDW                        EM
SSB                         0
LB                   1.00 Hz
GB                          0
PC                       1.30
```

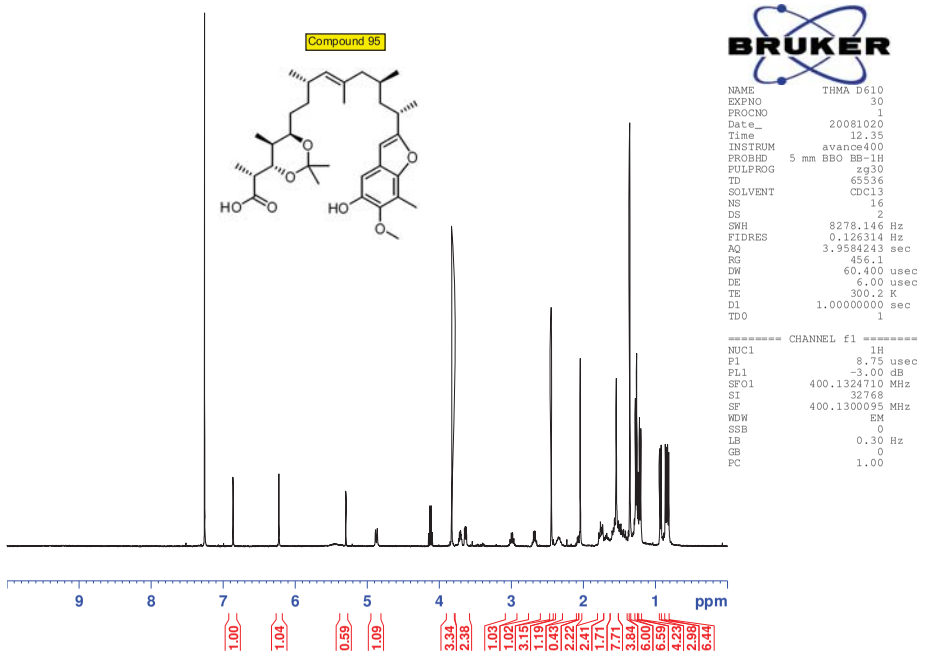
Compound 93



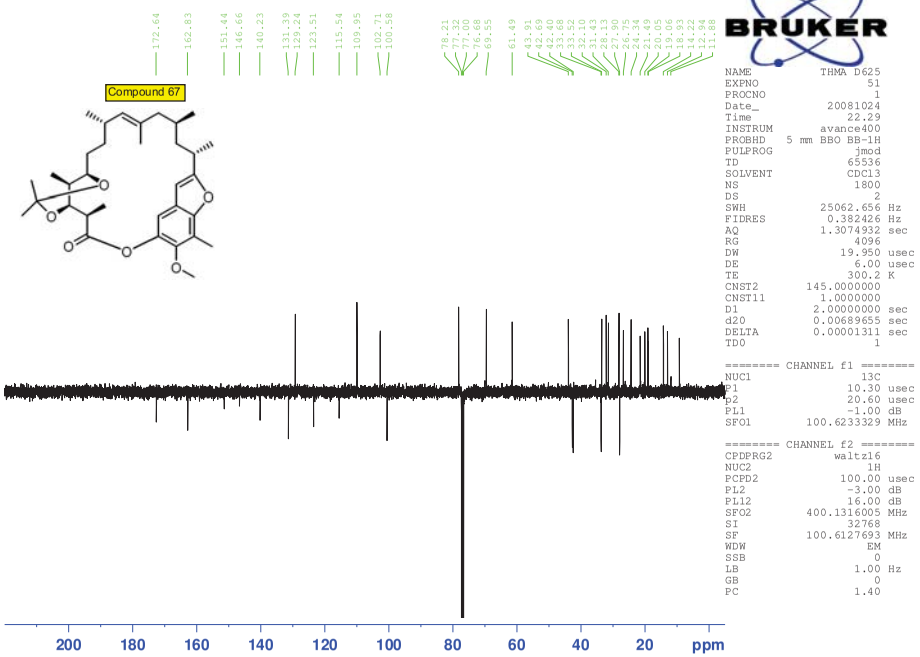

```
NAME                THMA_D600
EXPNO                      51
PROCNO                      1
Date_            20081015
Time                     2.17
INSTRUM              avance400
PROBHD    5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                        1200
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                       7298.2
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                  2.00000000 sec
d20                 0.00689655 sec
DELTA               0.00001311 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2             400.1316005 MHz
SI                      32768
SF               100.6127697 MHz
WDW                        no
SSB                         0
LB                   0.00 Hz
GB                          0
PC                       1.10
```



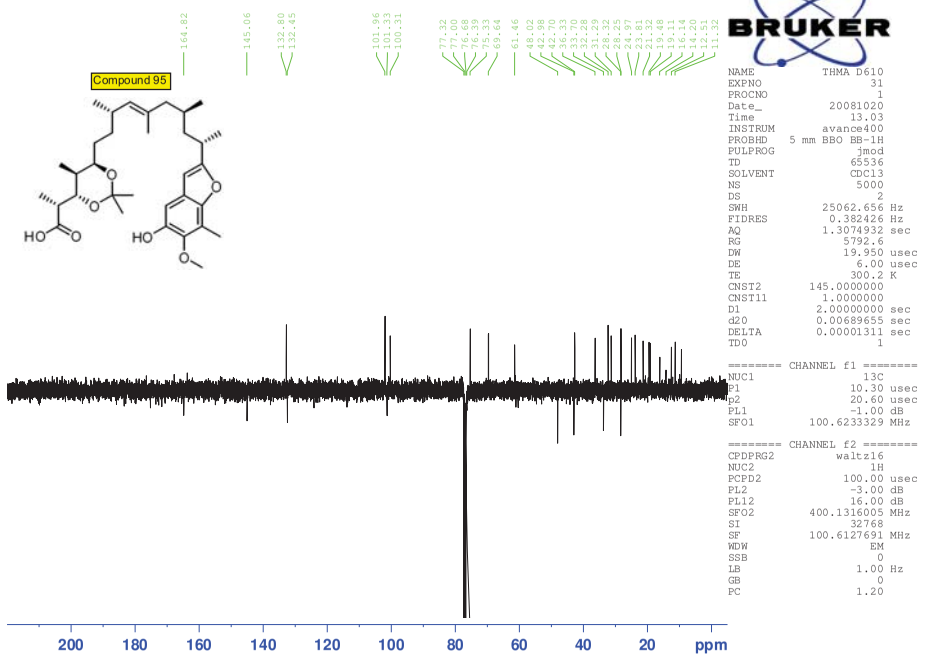

```
NAME                THMA D625
EXPNO                    50
PROCNO                    1
Date_              20081024
Time                  20.47
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                      256
DW                 60.400 usec
DE                  6.00 usec
TE                  300.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1          400.1324710 MHz
SI                    32768
SF            400.1300094 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```




```
NAME                THMA D610
EXPNO                    30
PROCNO                    1
Date_              20081020
Time                  12.35
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    456.1
DW                 60.400 usec
DE                  6.00 usec
TE                  300.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1          400.1324710 MHz
SI                    32768
SF            400.1300095 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```

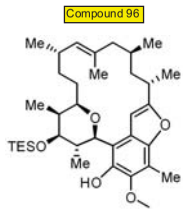




```
NAME                THMA D625
EXPNO                    51
PROCNO                    1
Date_              20081024
Time                  22.29
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1800
DS                        2
SWH              25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                     4096
DW                 19.950 usec
DE                  6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.30 usec
P2                  20.60 usec
PL1                 -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2          400.1316005 MHz
SI                    32768
SF            100.6127693 MHz
WDW                     EM
SSB                      0
LB                  1.00 Hz
GB                       0
PC                    1.40
```



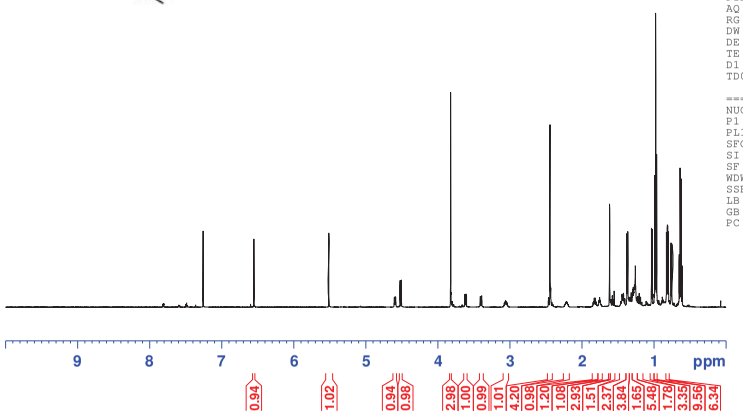

```
NAME                THMA D610
EXPNO                    31
PROCNO                    1
Date_              20081020
Time                  13.03
INSTRUM           avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     5000
DS                        2
SWH              25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                   5792.6
DW                 19.950 usec
DE                  6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.30 usec
P2                  20.60 usec
PL1                 -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2          400.1316005 MHz
SI                    32768
SF            100.6127691 MHz
WDW                     EM
SSB                      0
LB                  1.00 Hz
GB                       0
PC                    1.20
```

Compound 96

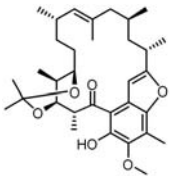


BRUKER

```
NAME                THMA D757
EXPNO                    10
PROCNO                    1
Date_              20090109
Time                  12.17
INSTRUM           avance600
PROBHD     5 mm PAQNP Swi
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               12376.237 Hz
FIDRES                0.188846 Hz
AQ                2.6477449 sec
RG                    161.3
DW                   40.400 usec
DE                    6.00 usec
TE                   298.1 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    13.85 usec
PL1                   -6.00 dB
SFO1             600.1337060 MHz
SI                      32768
SF               600.1300174 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```

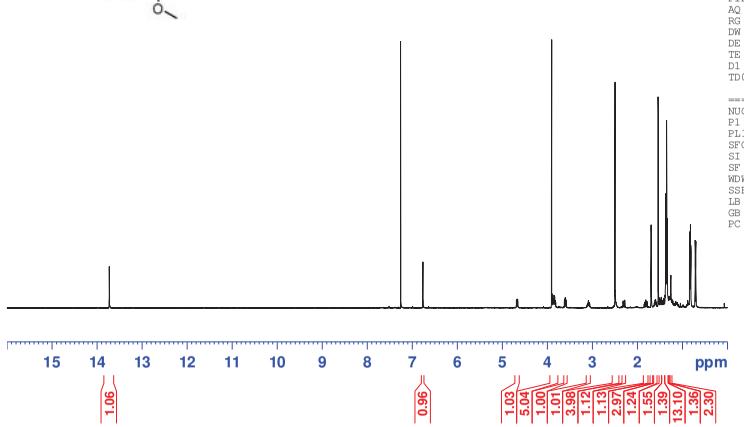


Compound 68

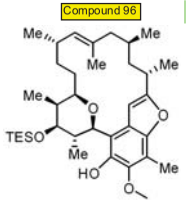


BRUKER

```
NAME                THMA D638
EXPNO                    20
PROCNO                    1
Date_              20081031
Time                  11.52
INSTRUM           avance400
PROBHD     5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       64
DS                        2
SWH                8278.146 Hz
FIDRES                0.126314 Hz
AQ                3.9584243 sec
RG                    406.4
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    8.75 usec
PL1                   -3.00 dB
SFO1             400.1324710 MHz
SI                      32768
SF               400.1300094 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```



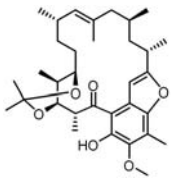
Compound 96



BRUKER

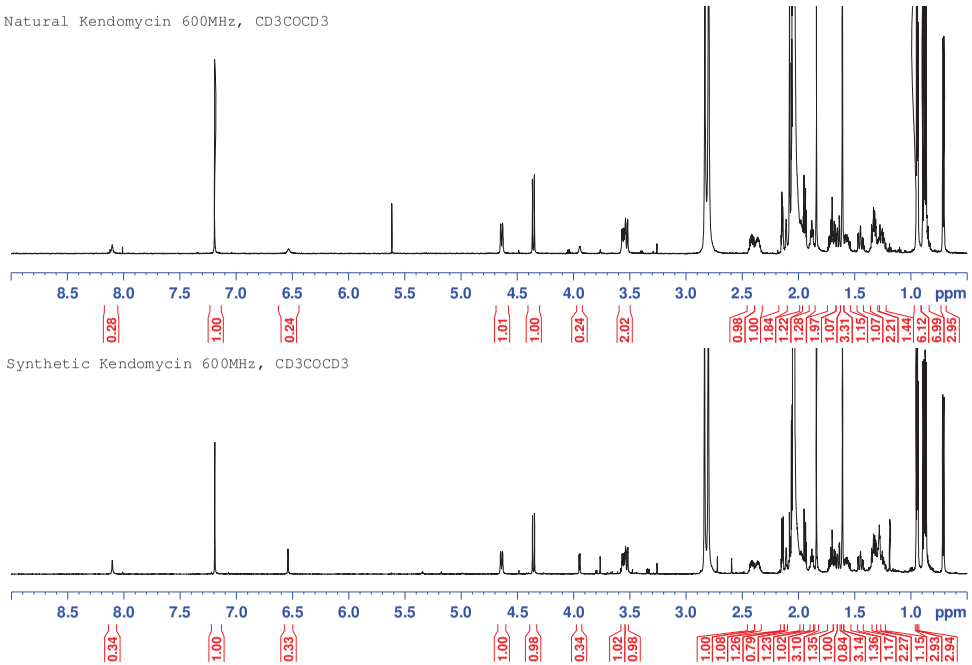
```
NAME                THMA D757
EXPNO                    11
PROCNO                    1
Date_              20090109
Time                  13.06
INSTRUM           avance600
PROBHD     5 mm PAQNP Swi
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     1000
DS                        4
SWH               35971.223 Hz
FIDRES                0.548877 Hz
AQ                0.9110143 sec
RG                    10321.3
DW                   13.900 usec
DE                    6.00 usec
TE                   298.1 K
CNST2            145.0000000
CNST11             1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00000828 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                    6.50 usec
p2                   13.00 usec
PL1                   0.00 dB
SFO1             150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                80.00 usec
PL2                   -6.00 dB
PL12                  12.20 dB
SFO2             600.1324005 MHz
SI                      32768
SF               150.9028127 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
```

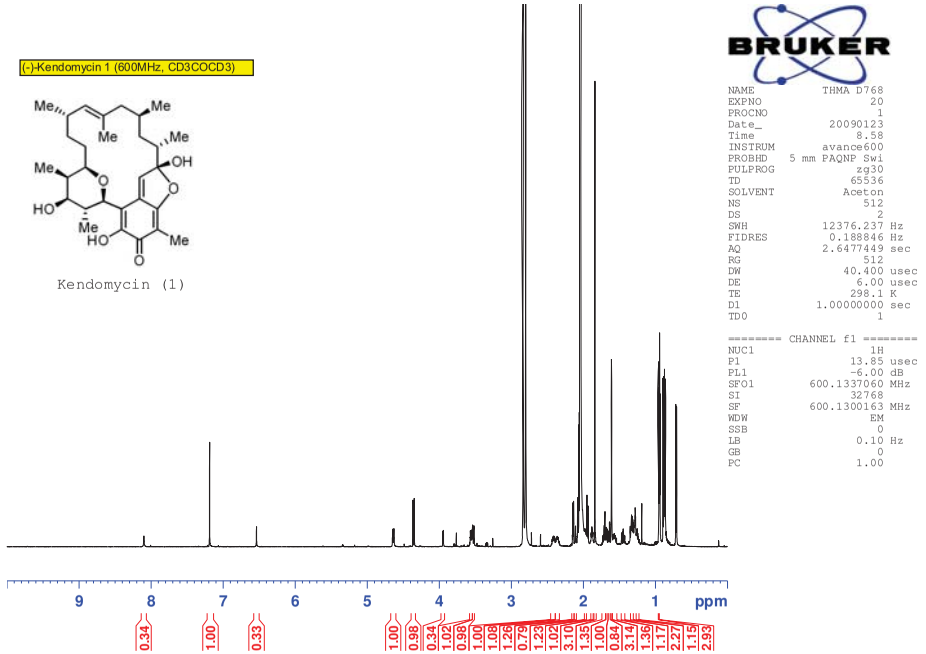

Compound 68

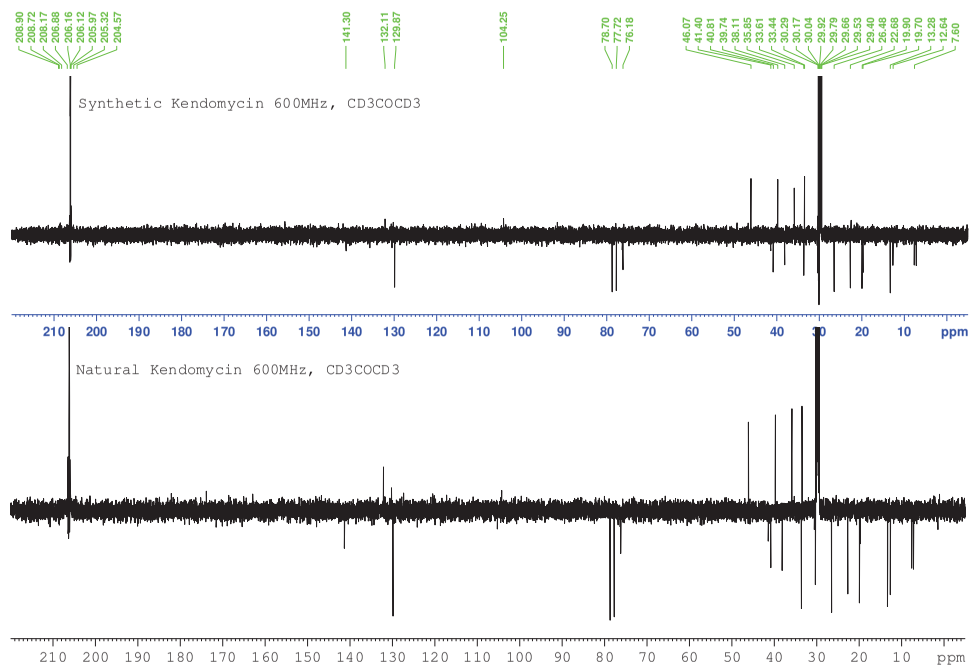


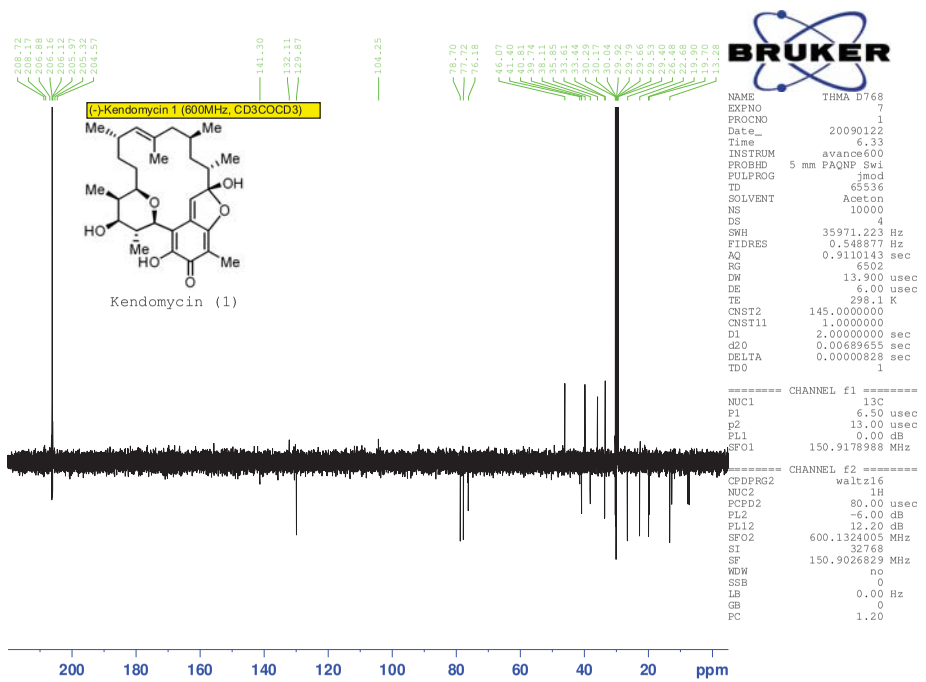
BRUKER

```
NAME                THMA D638
EXPNO                    26
PROCNO                    1
Date_              20081031
Time                  20.01
INSTRUM           avance400
PROBHD     5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     4500
DS                        2
SWH               25062.656 Hz
FIDRES                0.382426 Hz
AQ                1.3074932 sec
RG                    6502
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2            145.0000000
CNST11             1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1             100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2               100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2             400.1316005 MHz
SI                      32768
SF               100.6127691 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
```


Natural Kendomycin 600MHz, CD3COCD3
Synthetic Kendomycin 600MHz, CD3COCD3
ppm


(-)-Kendomycin 1 (600MHz, CD3COCD3)
Kendomycin (1)
BRUKER
NAME THMA D768
EXPNO 20
PROCNO 1
Date_ 20090123
Time 8.58
INSTRUM avance600
PROBHD 5 mm PAQNP Swi
PULPROG zg30
TD 65536
SOLVENT Aceton
NS 512
DS 2
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6477449 sec
RG 512
DW 40.400 usec
DE 6.00 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 13.85 usec
PL1 -6.00 dB
SFO1 600.1337060 MHz
SI 32768
SF 600.1300163 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00
ppm


Synthetic Kendomycin 600MHz, CD3COCD3
Natural Kendomycin 600MHz, CD3COCD3
ppm


(-)-Kendomycin 1 (600MHz, CD3COCD3)
Kendomycin (1)
BRUKER
NAME THMA D768
EXPNO 7
PROCNO 1
Date_ 20090122
Time 6.33
INSTRUM avance600
PROBHD 5 mm PAQNP Swi
PULPROG jmod
TD 65536
SOLVENT Aceton
NS 10000
DS 4
SWH 35971.223 Hz
FIDRES 0.548877 Hz
AQ 0.9110143 sec
RG 6502
DW 13.900 usec
DE 6.00 usec
TE 298.1 K
CNST2 145.0000000
CNST11 1.0000000
D1 2.00000000 sec
d20 0.00689655 sec
DELTA 0.00000828 sec
TD0 1
CHANNEL f1
NUC1 13C
P1 6.50 usec
p2 13.00 usec
PL1 0.00 dB
SFO1 150.9178988 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -6.00 dB
PL12 12.20 dB
SFO2 600.1324005 MHz
SI 32768
SF 150.9026829 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.20
ppm

4. Summary

In summary, we have accomplished two convergent enantioselective syntheses of the *ansa*–macrolide kendomycin. The routes developed during this dissertation start from common and inexpensive starting materials such as β–(+)–citronellene, 2,6–dimethoxytoluene and (meth)acrolein. The outstanding key step for both, the photo–Fries and the RCM approach, are the highly complex Ireland–Claisen rearrangements. High efficiency and diastereoselectivity were achieved after some optimization work. In this manner, the installation of the north–eastern domain, with concomitant formation of the (*E*)–double bond, and the desired C16 stereocenter was achieved in one step. For the preparation of the eastern benzofuran moiety two successful strategies, a Pd(0)–mediated Negishi coupling and an epoxide opening reaction, were pursued. The incorporation of the underestimated photo–Fries reaction in total synthesis demonstrates its power and efficiency. The drawback of the latter approach is the high number of linear steps (32 steps from 2,6–dimethoxytoluene) and an overall yield of 0.4%, which is, however, comparable to that of Smith's total synthesis (0.5%).

In order to overcome the above drawbacks we focused on an alternative synthesis in parallel. Primarily efforts to close the macrocycle at various positions via RCM were meager. The finally developed RCM–approach, which aims at the C10–C11 disconnection, diminishes the number of steps to 24 and increases the overall yield to 1.0%. This optimized sequence also would allow for a rapid and modular synthesis of well–designed derivatives.

In contrast to Rychnovsky, we were able to reproduce Lee's final steps and disclosed the fourth total synthesis of kendomycin. The development of a protecting group free endgame for the preparation of the quinone–lactol unit saved another two steps.

PART B: Total Syntheses of (+)–Echinopine A and B

5. Introduction and Background

5.1. Overview

Terpenes belong to the most abundant natural products and contain more than 20.000 members of great diversity.[24] The word "terpene", which was originally applied to hydrocarbons found in turpentine is often used in place of "terpenoid (isoprenoid)". In a strict sense, the term "terpenoids" also include the rearranged and oxidized compounds. Terpenoids are important constitutes in perfume (e.g. patchoulol, cineol) and flavouring (e.g. menthol) industry and medicine (e.g. paclitaxel).[25] Apart from that, terpenoids frequently serve as excellent chiral building blocks for organic synthesis[26] and are used for the design of catalyst ligands.

In 1959, Ruzicka[27] reemphasized the famous isoprene rule, which was already proposed by Wallach in 1887: All terpenoids are built up by multiple isoprenoid (2–methyl–1,3–butadiene) units. According to this, the primary classification of terpenoids is done by the number of isoprene units: C_5 hemiterpenes, C_{10} monoterpnes, C_{15} sesquiterpenes, C_{20} diterpenes, C_{25} sesterpenes, C_{30} triterpenes, C_{40} tetraterpenes and $(C_5)_n$ polyterpenes. Further classification, for instance, is done with regard to the terpenoid family, which is often named after the first or most common member (e.g. guaiane-type terpenoids).

Figure 5 shows a personal selection of terpenoids, whereas the most versatile and complex natural products are derived from the C_{15}– to C_{30}–members.

[24] C. S. Sell, A Fragrant Introduction to Terpenoid Chemistry (Kindle Edition), Royal Society of Chemistry, 1st edition **2003**.
[25] E. Breitmaier, Terpenes: Flavors, Fragrances, Pharmaca, Pheromones, Wiley–VCH **2006**.
[26] a) T.–L. Ho, Enantioselective Synthesis: Natural Products from Chiral Terpenes, John Wiley & Sons, Inc., New York **1992**; b) D. J. Ager, Handbook of Chiral Chemicals, Taylor & Francis Group, LLC, 2nd edition **2006**, 59–72.
[27] L. Ruzicka, *Proc. Chem. Soc.* (London) **1959**, 341.

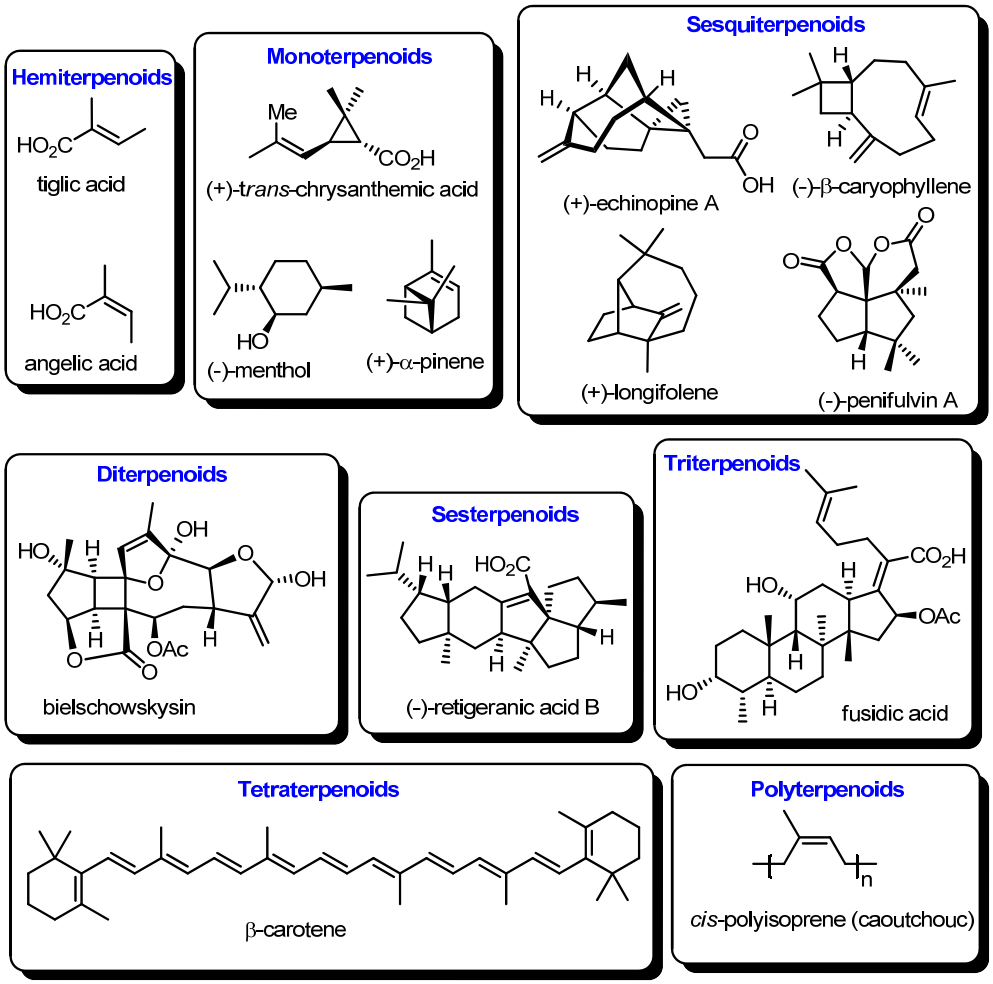


Figure 5. A selection of naturally occurring terpenoids.

5.2. Isolation, Biological Activity and Structure of Echinopine A and B

(+)–Echinopine A (**109**) and B (**110**), two novel tetracyclic sesquiterpenoids were isolated in 2008 from the roots of *Echinops spinosus* (Morocco).[28] Repeated solvent extraction (MeOH, CH_2Cl_2 and EtOAc), column chromatography and separation with RP–HPLC afforded 2 mg of (+)–**109** and 1.6 mg of (+)–**110** respectively. Because of the scarcity of natural product source, determination of the relative stereochemistry could only be performed by 2D–NMR and HRMS.

The X–ray structure of synthetic **109** is shown in Figure 6 and represents (-)–**109**, since structural refinements, complicated due to low intensity of reflections, were more accurate.

[28] M. Dong, B. Cong, S. H. Yu, F. Sauriol, C.–H. Huo, Q.–W. Shi, Y.–C. Gu, L. O. Zamir, H. Kiyota, *Org. Lett.*, **2008**, *10*, 701–704.

The densily packed 3,5,5,7–tetracycle features two vicinal quaternary centers, 5 stereocenters in total, a 1,1–disubstituted olefin unit and a carboxyl functionality.

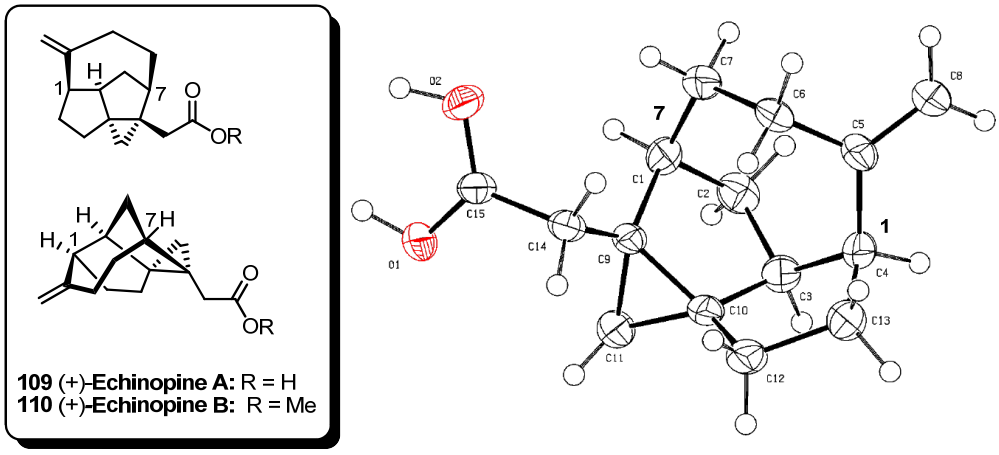


Figure 6. 2D–Views of (+)–echinopine A (**109**) and B (**110**). Confirmation of the relative structure by X–ray structure analysis of synthetic **109**.

Due to the low amounts of isolated echinopine A and B, only an *in vitro* biological test against the human breast cancer MCF–7 line could be performed, whereas both proved to be inactive. However, proper biological screening assays of the title compounds are currently pursued at the University of Hannover in corporation with Prof. Kalesse.

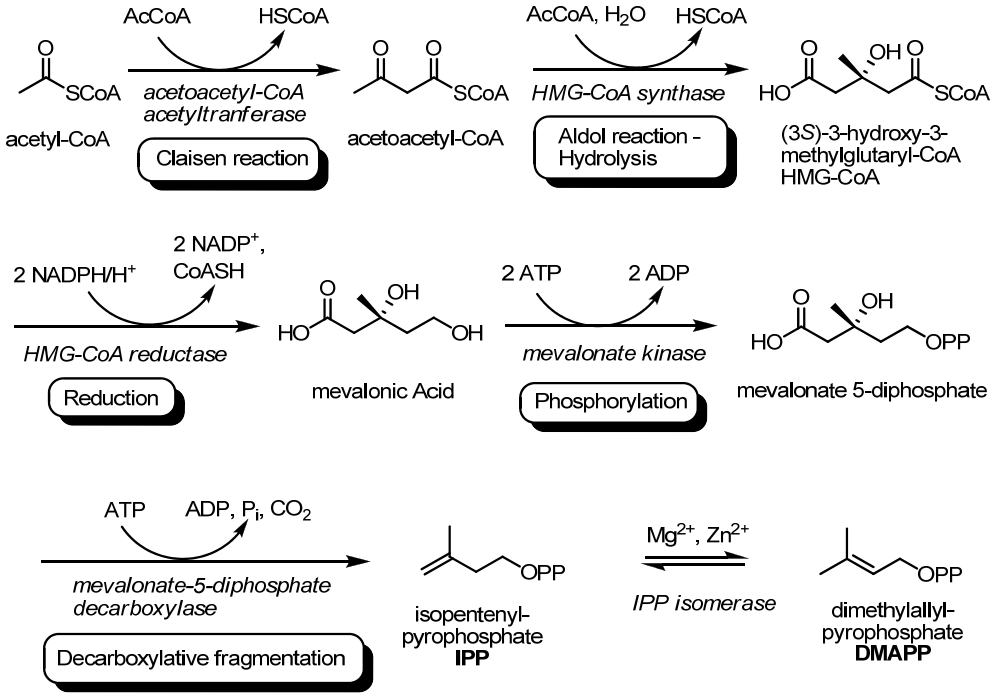
5.3. Biosynthesis

5.3.1. Biosynthesis of Terpenes

The biosynthetic origin of all terpenes is isopentenyl diphosphate (IPP), which, after isomerization to dimethylallyl diphosphate (DMAPP), is sequentially elongated by prenyltransferases to geranyl diphosphate (GPP, C_{10}), farnesyl diphosphate (FPP, C_{15}), and geranyl–geranyl diphosphate (GGP, C_{20}).[29] For the biosynthesis of IPP two different pathways are considered: The mevalonate (MVA)[30] and the Rohmer (1–deoxyxylose–5–phosphate, DXP)[31] pathway. The former is considered for the synthesis of sesquiterpenes and triterpenes in animals and plants, the latter for monoterpenes, diterpenes, and tetraterpenes. Both pathways work in bacteria.

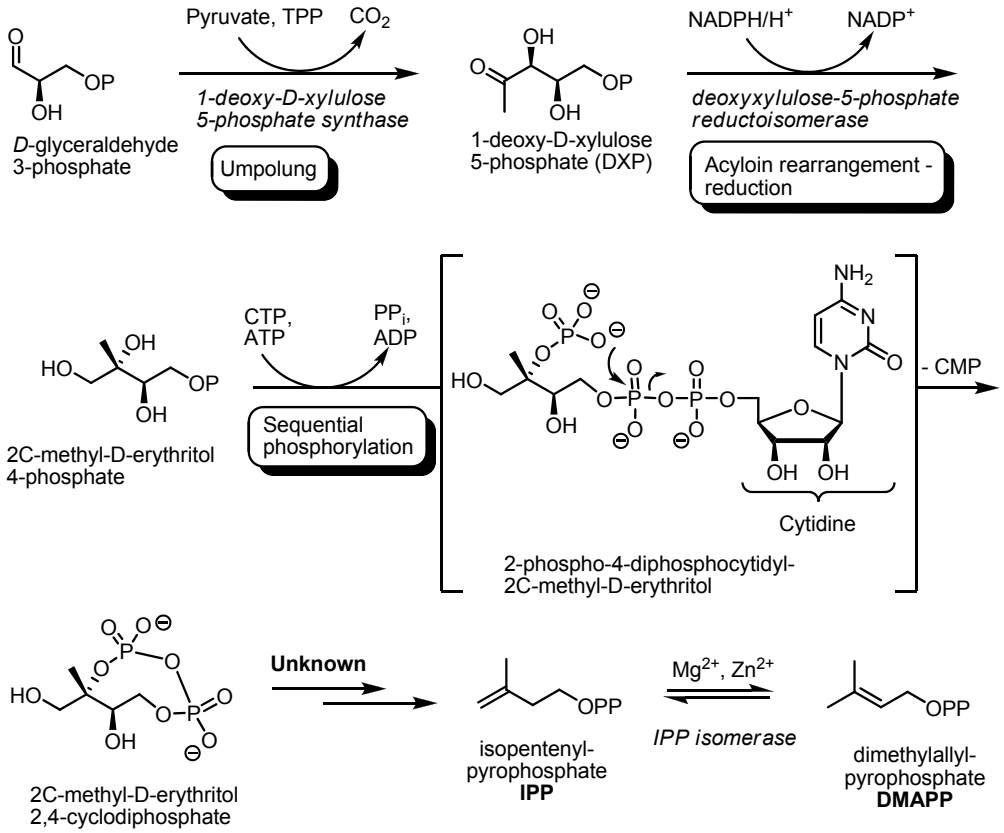
[29] F. J. Leeper, J. C. Vederas, Eds., Biosynthesis: Aromatic Polyketides, Isoprenoids, Alkaloids (Topics in Current Chemistry), Springer, 1st edition **2000**, 54–92.
[30] W. R. Nes, M. L. McKean, Biochemistry of steroids and other isopentanoids, University Park Press, Baltimore **1977**.
[31] a) M. Rohmer *Nat. Prod. Rep.* **1999**, *16*, 565–574; b) M. Rohmer, M. Knani, P. Simonin, B. Sutter, H. Sahm, *Biochem J.* **1993**, *295*, 517–524.

The mevalonic pathway: The MVA pathway (Scheme 20) starts with the condensation of three molecules of acetyl CoA, first to give acetoacetyl CoA via a Claisen condensation and second to afford HMG–CoA via an aldol–like reaction. The six–carbon thioester intermediate is reduced to mevalonic acid (MVA) by NADPH/H^+, which in turn is phosphorylated with the consumption of three molecules of ATP and converted to IPP by decarboxylative fragmentation. The next step, before elongation can take place, is the isomerization of IPP to DMAPP by IPP isomerase.



Scheme 20. The mevalonate (MVA) pathway.

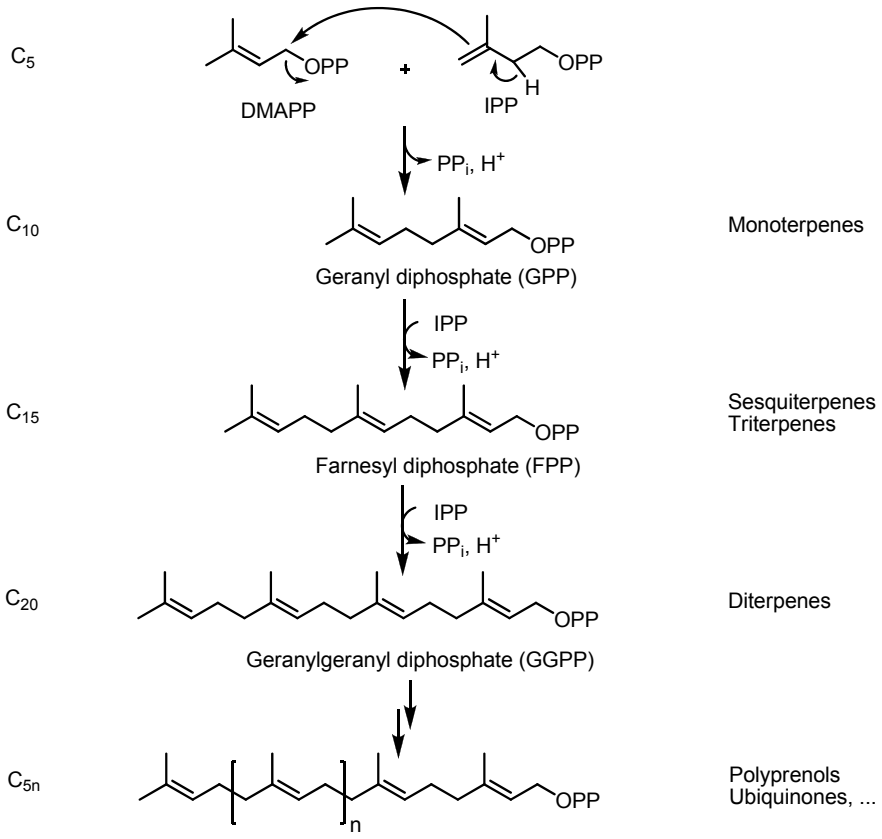
The Rohmer – DXP pathway: The DXP pathway (Scheme 21), which was discovered in 1993, is still not fully understood. The synthesis of IPP is initiated by a thiamin catalyzed "Umpolungs"–reaction of pyruvate, which then attacks glyceraldehydes 3–phosphate with concomitant loss of CO_2. The so produced DXP is converted to 2C–methyl–*D*–erythritol 4–phosphate by an acyloin type rearrangement, to give an intermediate aldehyde, which is reduced by one equivalent of NADPH/H^+. Sequential phosphorylation by CTP (cytidine triphosphate) and ATP results in the formation of 2C–methyl–*D*–erythritol 2,4–cyclodiphosphate. Little is known about the further conversion to IPP.



Scheme 21. The Rhomer – deoxyxylulose (DXP) pathway.

Scheme 22 shows the biosynthesis of higher terpenoids. After isomerization of IPP to DMAPP, Mg (II) mediated head–to–tail condensation of IPP with DMAPP gives geranyl diphosphate (GPP, C_{10}). Nucleophilic Alder–ene–type attack[32] of IPP at the primary position of GPP creates the C_{15} terpenoid farnesyl diphosphate (FPP).

[32] K. Alder, F. Pascher, A. Schmitz, *Chem. Ber*. **1943**, *76*, 27–53.



Scheme 22. Biosynthesis of higher terpenoids.

Tail–to–tail dimerization of FPP gives triterpenes and reductive coupling of two FPP units affords squalene, the biosynthetic precursor of steroids. Geranylgeranyl diphosphate (GGPP) and higher terpenes are derived from FPP by sequential addition of IPP molecules.

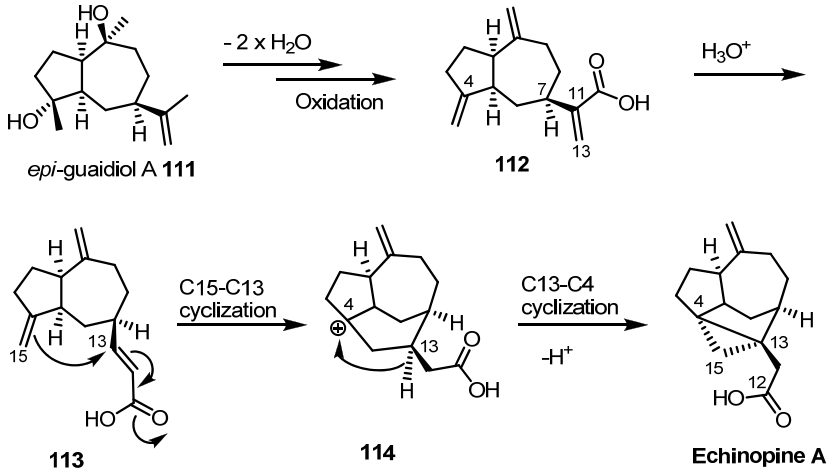
The great diversity of natural occurring terpenoids, in turn, arises from enzymatic catalyzed (terpene cyclases) cascade reactions such as cyclization of carbocation intermediates, Wagner–Meerwein rearrangements, hydride shifts, attack of nucleophiles (H_2O) and deprotonation.

5.3.2. Proposed Biosynthesis of Echinopine A and B

Kiyota and Shi[28] also speculated about the possible biosynthetic origin of echinopine A (**109**) and B (**110**). Although their biosynthesis is plausible and reasonable, there is no evidence for this kind of pathway (Scheme 23). However, proposed **112** could be derived from recently isolated *epi*–guaidiol A **111**.[33] Hydration of the C11–C13 double bond, followed by acid induced migration of the C7–C11 bond gives α,β–unsaturated acid **113**. Attack of the C14-C15 *exo*–methylene group at the C13 double bond of **113**

[33] Y. Xu, H.–W. Zhang, X.–C. Wan, Z.–M. Zou, *Magn. Reson. Chem*. **2009**, *47*, 527–531.

and additional cyclization of **114** with loss of a proton leads to echinopine A. Subsequent esterification affords echinopine B.



Scheme 23. Proposed biosynthesis of echinopine A.

6. Total Syntheses of Selected Terpenoids

The following total syntheses of sesquiterpenoids were chosen particularly with regard to echinopine A and B structurally related natural products. The ambition was to find structurally closely related targets such as 5,5–, 5,7– and 3,5,7– membered compounds. Natural products possessing a *cis*–5,7–membered scaffold are not as omnipresent as the thermodynamically favored *cis*–fused 5,5–analogs. The low occurrence of 3,5,7–membered frameworks in nature is reflected in that examples of terpenoids with an inherent cyclopropane–cyclopentane bicycle are limited (e.g. shizukaol, chloranthalactone). The presented publications should provide an insight into (modern) strategies for the synthesis of the relevant structural motifs.

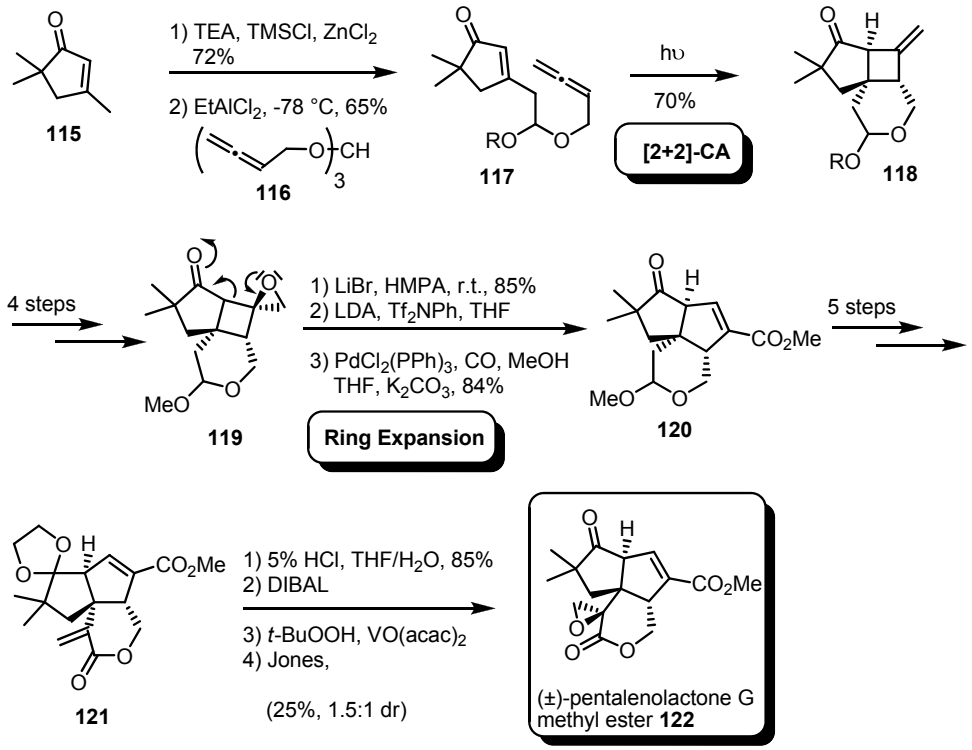
6.1. 5,5–Membered Ring Systems

6.1.1. Pirrung's Total Synthesis of (±)–Pentalenolactone G Methyl Ester

Strategy: Intramolecular [2+2]–cycloaddition – ring expansion.

In 1988, a total synthesis of (±)–pentalenolactone G methyl ester **112** (Scheme 24), bearing a 5,5–fused framework was reported by Pirrung.[34] Conversion of **115** to the corresponding dienylsilylether and treatment with tris((allenyl)methyl)orthoformate **116** gave cyclization precursor **117**. Irradiation induced the desired [2+2]–cycloaddition and provided *cis*–fused tricycle **118** in good yield. After four steps, rearrangement of epoxide **119**, presumably initiated by a LiBr induced retro aldol–type reaction, afforded the desired 5,5–membered ring skeleton. Palladium mediated carbonylative coupling of the vinyltriflate afforded α,β–unsaturated methylester **120**, which was converted to **121** in five steps. The remaining steps of the total synthesis were accomplished relying on Danishefsky's procedure and provided **122** in 0.5% overall yield.

[34] M. C. Pirrung, S. A. Thomson, *J. Org. Chem.* **1988**, *53*, 227–230.



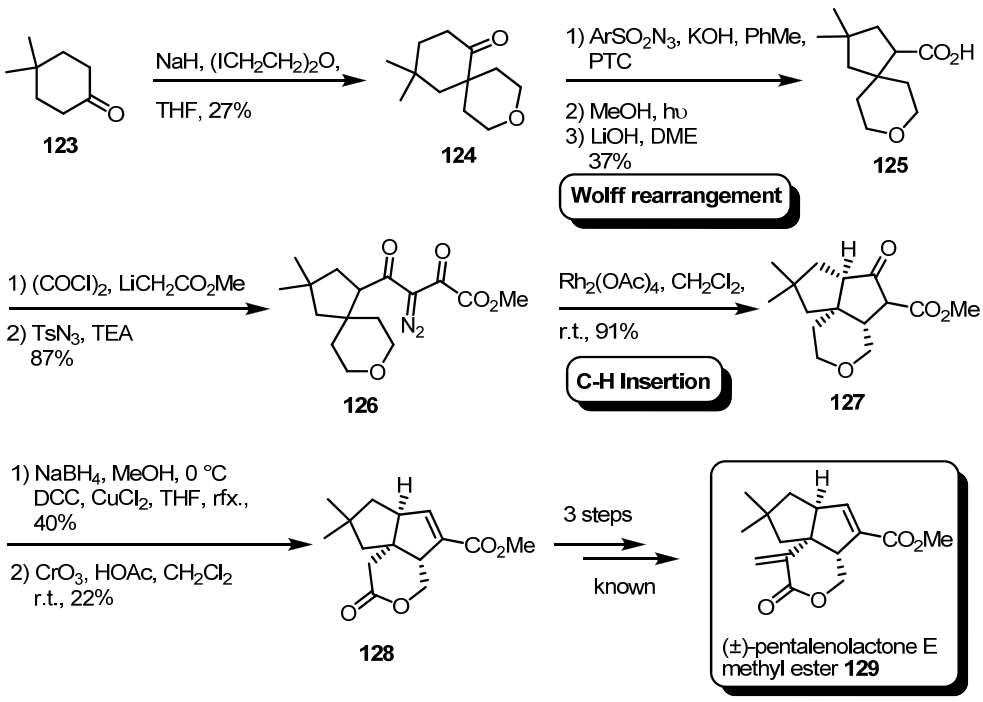
Scheme 24. Pirrung's [2+2]–cycloaddition – ring expansion strategy.

6.1.2. Taber's Formal Synthesis of (±)–Pentalenolactone E

Strategy: Rh(II) catalyzed C–H insertion.

Taber's formal synthesis of (±)–pentalenolactone E, published in 1985[35] and 1987[36], was accomplished via a Rh(II) catalyzed C–H insertion as the key step (Scheme 25). Conversion of the C_2–symmetric ketone **123** to *spiro*–compound **124** followed by a Wolff ring contraction creates the left–hand five–membered ring. Regitz' diazo transfer reaction with **125** provided intermediate **126**, which on treatment with $Rh_2(OAc)_4$ gave the complete skeleton of the target compound.

[35] D. F. Taber, J. L. Schuchardt, *J. Am. Chem. Soc.* **1985**, *107*, 5289–5290.
[36] D. F. Taber, J. L. Schuchardt, *Tetrahedron* **1987**, *43*, 5677.



Scheme 25. Taber's Rhodium(II) catalyzed C–H insertion strategy.

Deoxygenation and installation of the six–membered lactone afforded **128**. The completion of the synthesis could be realized by three literature known steps.

6.2. 5,7–Membered Ring Systems

The most difficult task arises from the preparation of *cis*–fused bicycles, which feature a ketone or double bond functionality next to the ring junction. The ketone intermediates are prone to *cis*–*trans* isomerization and acidic induced migration of 1,1–disubstituted double bonds[37] complicates the installation of *exo*–methylene groups. A practical method for the late stage installation of the latter was recently published by Vanderwal.[38]

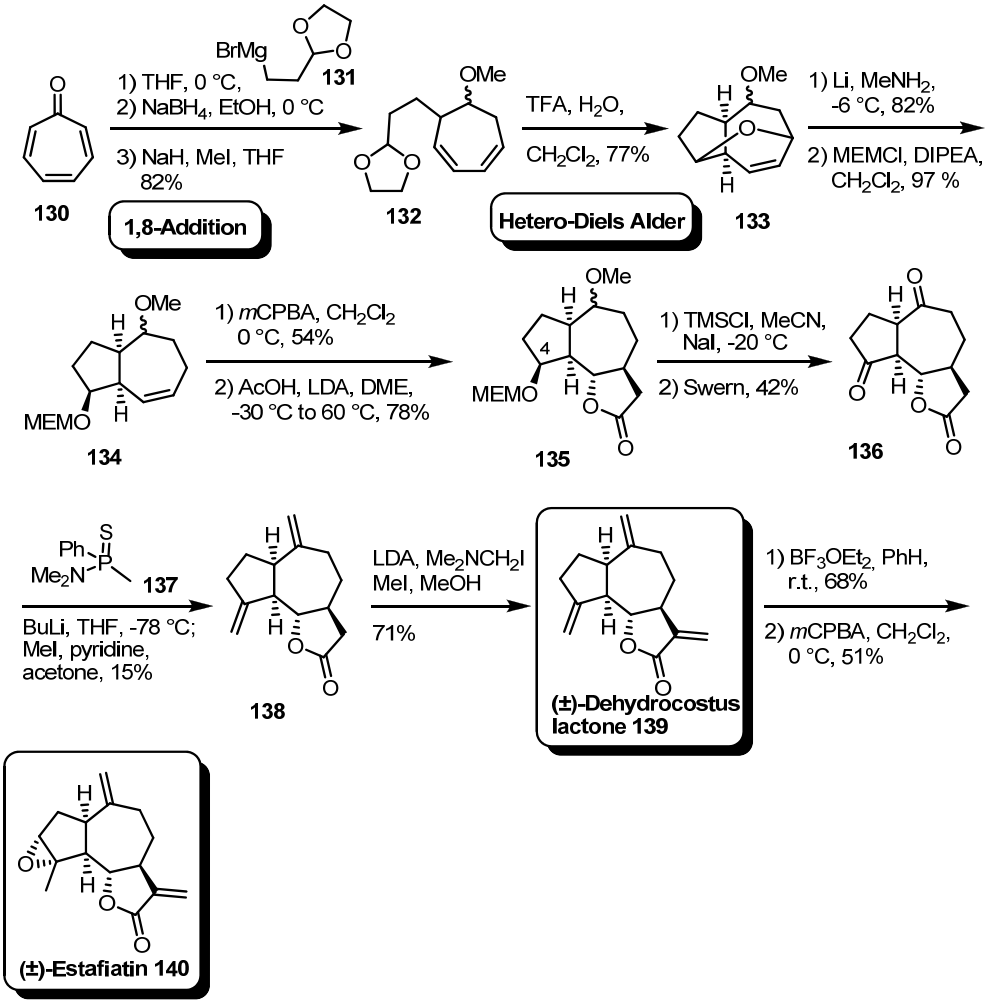
6.2.1. Rigby's Total Synthesis of (±)–Dehydrocostus Lactone & (±)–Estafiatin

Strategy: Intramolecular hetero Diels–Alder reaction.

The first total syntheses of the guainolide sesquiterpenes (±)–dehydrocostus lactone **139** and (±)–estafiatin **140** were reported by Rigby (Scheme 26).[39] The key step was an intramolecular Diels–Alder

[37] G. L. Lange, C. Gottardo, *J. Org. Chem.* **1995**, *60*, 2183–2187.
[38] M. S. Dowling, C. D. Vanderwal, *J. Am. Chem. Soc.* **2009**, *ASAP*.
[39] J. H. Rigby, J. Z. Wilson, *J. Am. Chem. Soc.* **1984**, *106*, 8217–8224.

reaction with tropone **130**. Nucleophilic 1,8–addition of Grignard **131** to **130** followed by immediate reduction, in order to prevent [1,5]–H shifts mediated double bond isomerization, and protection gave diene **132**. One pot cleavage of the acetale and intramolecular hetero Diels–Alder reaction afforded tricyclic allyl ether **133**. Birch reduction of the allylic C–O bond and protection gave *cis*–hydroazulene **134**. Introduction of the appended lactone ring was performed via stereoselective epoxidation and subsequent epoxide opening with dilithioacetate to give **135**.



Scheme 26. Preparation of a *cis*–annulated 5,7–bicycle via a hetero Diels–Alder reaction.

After double deprotection and Swern oxidation, introduction of the exocyclic methylene groups was achieved with olefination reagent **137**, albeit in low yield. Attempts to introduce the double bonds by different methods only resulted in *cis*–*trans* epimerization, although it was known, that hydroazulenes with an appended butyrolactone often favor the *cis*–annulation. Since all efforts to cleave the methoxy

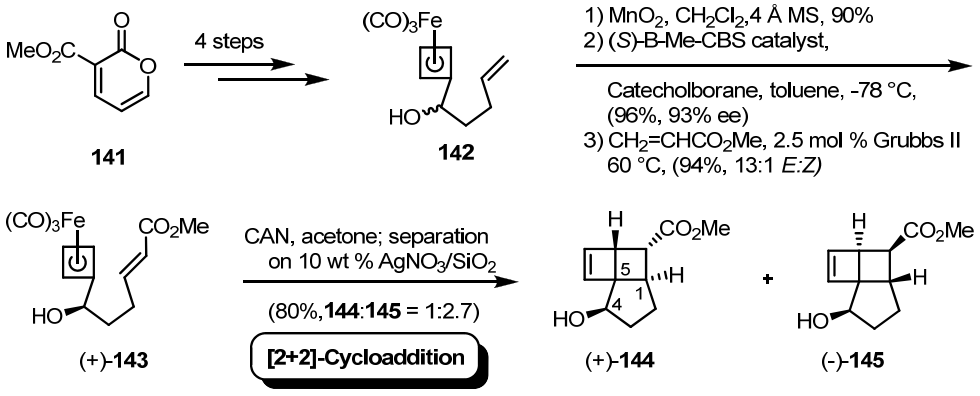
group after *mono*–olefination of **135** (C4 position) resulted in double bond migration, the simultaneous installation of the double bonds was essential.

Eschenmoser methylenation of **138** gave (±)–dehydrocostus lactone **139** in 1% overall yield. Conversion to (±)–estafiatin **140** was performed via double bond isomerization and epoxidation.

6.2.2. Snapper's Total Synthesis of *ent*–(+)–Pleocarpenene and *ent*–(-)–Pleocarpenone

Strategy: [2+2]–Cycloaddition – cyclopropanation – rearrangement.

In 2007, Snapper from Boston College reported the intramolecular cycloaddition–cyclopropanation–thermal rearrangement strategy for the total synthesis of the guaiane type sesquiterpenes pleocarpenene **148** and pleocarpenone **149**.[40] The synthesis started with α–pyrone **141**, which was converted to iron protected cyclobutadiene **142** in four steps (Scheme 27). The enantioselective route was realized by allylic MnO_2 oxidation of **142**, followed by (*S*)–B–Me–CBS reduction and final cross–metathesis to give the C_1–elongated ester (+)–**143**. Treatment of (+)–**143** with CAN initiated the liberation of the cyclobutadiene moiety and afforded, after formal [2+2]–cycloaddition, enantioenriched diastereomers (+)–**144** and (-)–**145** as a 1:2.7 ratio in good yield.

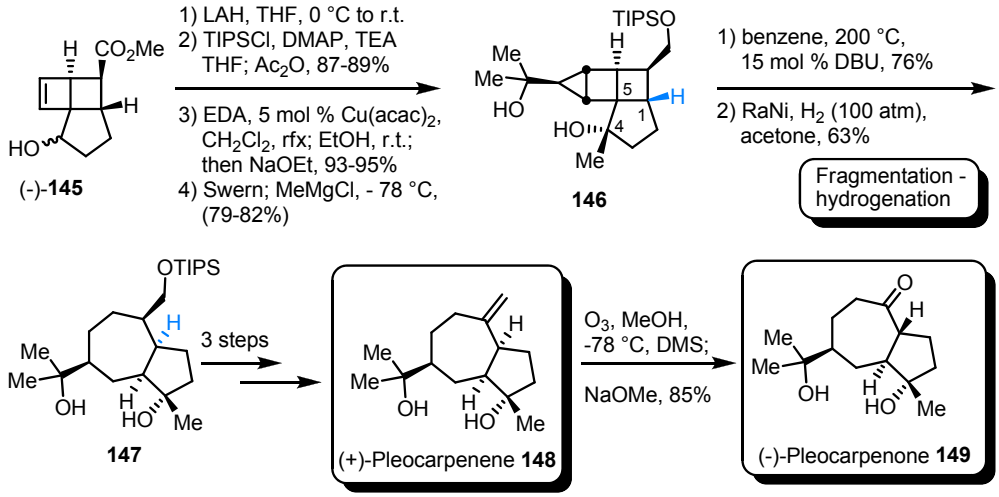


Scheme 27. Snapper's [2+2]–cycloaddition – cyclopropanation – fragmentation strategy.

Next they focused on the preparation of **146**, whereas, in principle, both diastereomers (concerning the hydroxyl group at C4) of one enantiomeric series could be used for this transformation (Scheme 28). The sequence started with reduction of (-)–**145** and sequential protection of the primary and secondary alcohol. Cu(II) mediated cyclopropanation with ethyl diazoacetate (EDA) from the less congested convex

[40] M. J. Williams, H. L. Deak, M. L. Snapper, *J. Am. Chem. Soc.* **2007**, *129,* 486–487.

face with *in situ* cleavage of the acetate, followed by oxidation and nucleophilic attack of excess MeMgCl gave diol **146**. Heating the strained tetracycle **146** to 200 °C, in the presence of catalytic amounts of DBU, caused the desired rearrangement with simultaneous inversion of stereochemistry at C1. Their mechanistic model, already published in 2001,[41] suggests a stepwise fragmentation–recombination sequence. Hydrogenation provided the desired *cis*–annulation in **147**. A high yielding three step sequence was used for the conversion of **147** to pleocarpenene **148**. Ozonolysis of the *exo*–methylene group and *cis*–*trans* isomerization of the ring junction finally afforded pleocarpenone **149** in 18 steps from α–pyrone **141**.



Scheme 28. Completion of the synthesis.

The major drawback is the use of highly complex intermediates such as **146**, which are degraded to a much simpler 5,7–membered ring system in the course of the synthesis.

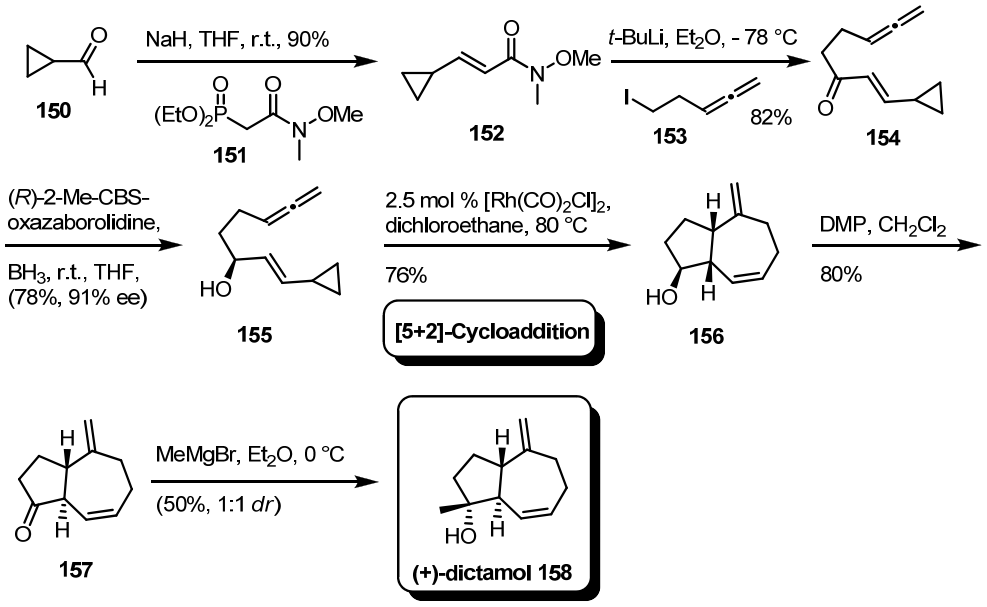
6.2.3. Wender's Total Synthesis of (+)–Dictamol

Strategy: [5+2]–Cycloaddition.

The Rh(I) catalyzed [5+2]–cycloaddition was used as the key step in Wender's nine steps total synthesis of (+)–dictamol **158**.[42] The synthesis of the allene–cyclopropane cyclization precursor **155** started with a Horner–Wadsworth–Emmons reaction of **151** with commercially available **150** (Scheme 29). Addition of lithiated 1–iodo–3,4–butadiene **153** to **152** and subsequent CBS reduction of **154** provided (*R*)–**155**. Treatment with catalytic amounts of Rh(I) such as $Rh(PPh_3)_3Cl$ or $[Rh(CO)_2Cl]_2$ delivered the desired

[41] H. L. Deak, S. S. Stokes, M. L. Snapper, *J. Am. Chem. Soc.* **2001**, *123*, 5152–5153.
[42] P. A. Wender, M. Fuji, C. O. Husfeld, J. A. Love, *Org. Lett.* **1999**, *1*, 137–139.

[5+2]–cycloadduct **156** in good yields and high diastereoselectivity. The remaining steps towards **158** were achieved via Dess–Martin oxidation, silica gel chromatography with concomitant *cis–trans* epimerization and methylation.



Scheme 29. Wender's total synthesis of (+)–Dictamol.

6.3. 3,5,7–Membered Ring Systems

The major challenge is again the preparation of the 5,7–membered framework, as the cyclopropane moiety is most often obtained either from chiral pool starting material or introduced at last.

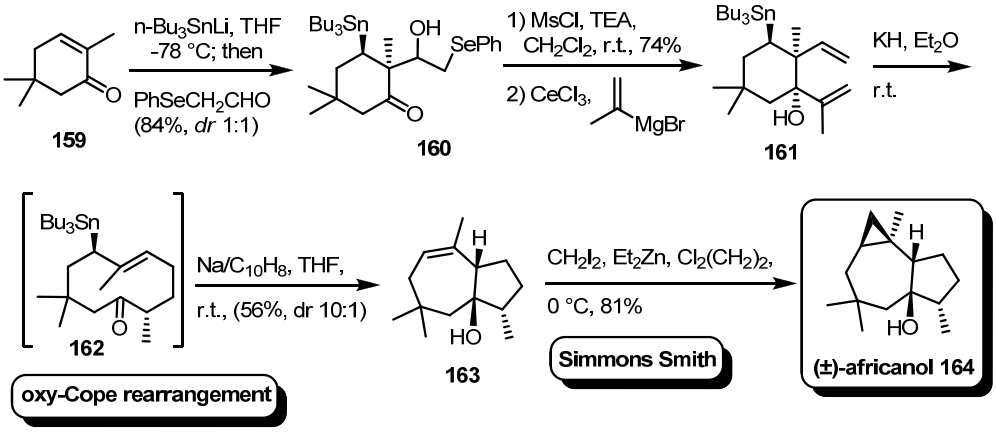
6.3.1. White's Total Synthesis of (±)–Africanol

Strategy: Anionic oxy–Cope rearrangement – cyclization.

Several total syntheses of the tricyclic sesquiterpenoid africanol **164** have been reported.[43] White's six steps synthesis[44] starts with a conjugate addition–enolate trapping sequence to α,β–unsaturated ketone **159** (Scheme 30). After separation of the 1:1 diastereomeric mixture of **160**, the vinyl moiety was installed via elimination and the isopropenyl group via equatorial Grignard addition.

[43] a) H. Shirahama, K. Hayana, Y. Kanemoto, S. Misumi, T. Ohtsuka, N. Hashiba, A. Furusaki, S. Murata, R. Noyori, T. Matsumoto, *Tetrahedron Lett.* **1980**, *21*, 4835–4838; b) L. A. Paquette, W. H. Ham, *Tetrahedron. Lett.* **1986**, *27*, 2341–2343; c) L. A. Paquette, W. H. Ham, *J. Am. Chem. Soc.* **1987**, *109*, 3025–3036.
[44] W. Fan, J. B. White, *J. Org. Chem.* **1993**, *58,* 3557–3562.

Anionic oxy–Cope rearrangement of **161** gave the unstable 5–cyclodecenone **162**, which, upon *in situ* treatment with sodium naphtalenide, cyclized to **163** via an intermediate ketyl radical. Careful experimentation showed that the diastereoselectivity of the cyclization step depends on the reaction conditions (TBAF, $SnCl_4$, SmI_2) as well as on the stereochemical relationships of the substituents in the ten–membered intermediate **162** (*cis* vs. *trans*). A mechanistic model for this transformation is still missing. Simmons–Smith cyclopropanation from the less hindered convex face afforded (±)–africanol **164** in an overall yield of 11%.



Scheme 30. White's oxy–Cope rearrangement approach to (±)–africanol.

6.3.2. Wijnberg's & Groot's Total Synthesis of (±)–Alloaromadendrane–4α, 10α–diol

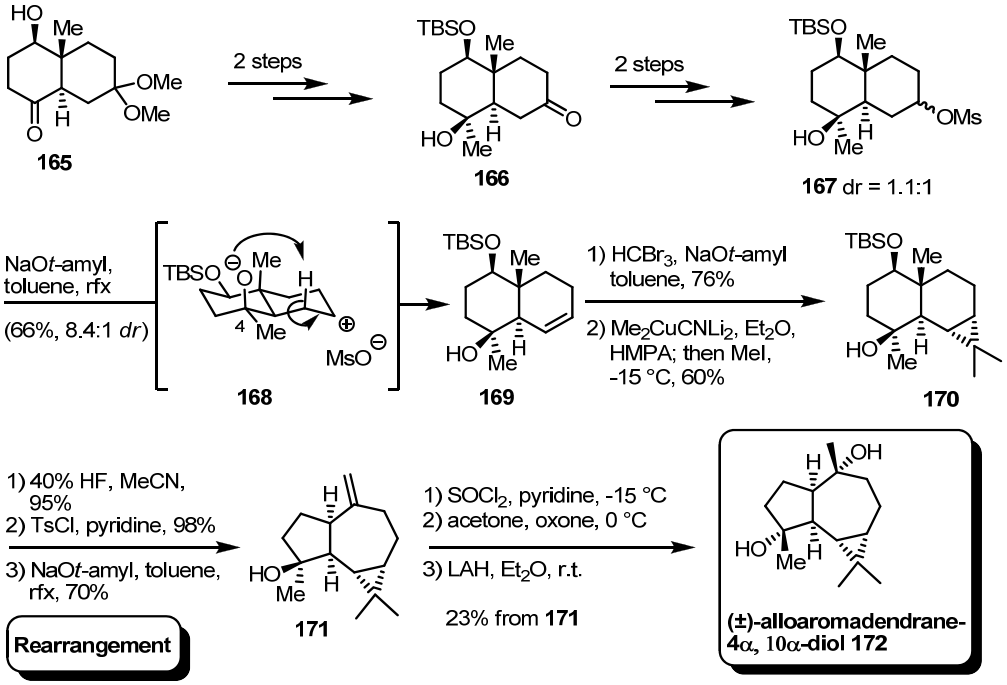
Strategy: Fragmentative rearrangement.

A total synthesis of (±)–alloaromadendrane–4α, 10α–diol **172**, bearing a *cis*–fused 5,7–membered aromadendrane skeleton, was reported from Wijnberg and Groot.[45] Starting from known **165** they constructed fragment **167** in four steps (Scheme 31). Treatment of mesylate **167** (1.1:1 diastereomeric mixture) with base in refluxing toluene predominantly afforded the desired elimination product **169**, probably via internal 1,3–diaxial deprotonation of dipolar intermediate **168**. The suggested intermediate was supported by additional experiments. Rerun of the sequence gave almost the same yield and regioselectivity for the axial α–mesylate as well as the equatorial β–mesylate within two minutes. Compounds lacking the oxygen substituent at C4 did not show any elimination or fragmentation.

The installation of the *gem*–dimethylcyclopropane moiety was realized by dibromocarbene addition to **169** and subsequent methylation. Deprotection of **170** followed by selective tosylation paved the way

[45] L. H. D. Jenniskens, J. B. P. A. Wijnberg, A. deGroot, *J. Org. Chem.* **1991**, *56*, 6585–6591.

for the key reaction. Heating a solution of the tosylate and excess sodium *t*–amylate afforded almost exclusively the rearranged 5,7–membered framework **171** in good yield. Again, internal deprotonation by the preformed axial alkoxide substituent probably favored the formation of the *exo*–double bond. The total synthesis was finished via elimination, double epoxidation with *in situ* generated DMDO and a final reduction step.



Scheme 31. Wijnberg's & Groot's total synthesis of (±)–alloaromadendrane–4α, 10α–diol.

7. Results

7.1. Total Synthesis of (+)–Echinopine A and B: Determination of Absolute Stereochemistry

T. Magauer, J. Mulzer, K. Tiefenbacher, *Org. Lett.* **2009**, *ASAP*.

ORGANIC LETTERS

XXXX
Vol. xx, No. x

Total Syntheses of (+)-Echinopine A and B: Determination of Absolute Stereochemistry

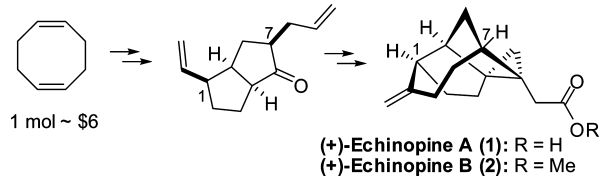
Thomas Magauer,* Johann Mulzer, and Konrad Tiefenbacher*

University of Vienna, Institute of Organic Chemistry, Währingerstrasse 38, 1090 Vienna, Austria

thomas.magauer@univie.ac.at; konrad.tiefenbacher@univie.ac.at

Received September 30, 2009

ABSTRACT



The first total syntheses of the novel 3,5,5,7-sesquiterpenoids (+)-Echinopine A (1) and B (2) were achieved. Thereby the proposed structures were confirmed, and the absolute stereochemistry was determined. The key features are (1) the stereoselective installation of the vinyl-moiety on the concave side of the bicyclo[3.3.0]octane core via Myers' [3,3]-sigmatropic rearrangement, (2) the finding that the substituent on the C7 position next to the ketone can be epimerized to the desired concave face under basic conditions, (3) the closure of the highly strained seven-membered ring via RCM, and (4) the unusual C2-homologation of a vinyltriflate with a ketene silyl acetal.

Echinopine A (**1**) and B (**2**) were isolated in 2007 by Shi and Kiyota during their screening for biologically active compounds from *Echinops spinosus*.[1] The structures of these novel, unprecedented sesquiterpenoids were elucidated by ^{1}H, ^{13}C, 2D-NMR and HRMS. Their molecular framework consists of a unique 3,5,5,7-membered ring skeleton (Figure 1), which is believed to arise from a guaiane-type precursor

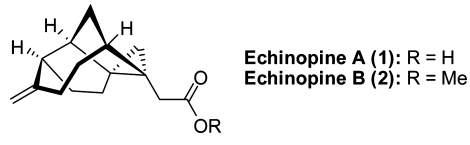


Figure 1. Structures of Echinopine A and B.

via skeletal rearrangement. The complex tetracyclic architecture features five contiguous stereocenters, two of which are quaternary.

Because of the scarcity of the natural product source, the biological activity has not satisfactorily been uncovered so far. Additionally no X-ray crystallographic analysis or chemical derivatization could be performed.[1] The absolute configuration is unknown, and the assignment of the relative stereochemistry is solely based on ^{1}H NMR spectroscopy.

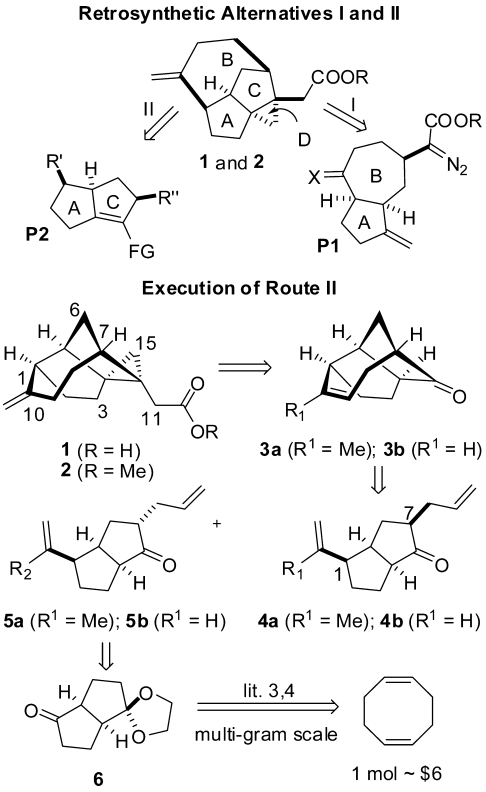
The unprecedented structure and the unknown biological profile motivated us to embark on the total synthesis of **1** and **2**.

For a retrosynthetic analysis (Scheme 1) we considered two alternatives (I and II), leading to bicyclic precursors **P1** and **P2**, respectively. **P1** is a *cis*-fused AB-guaianolide system in which both rings C and D might be generated in a one-step cyclopropanation. However, this approach would be jeopardized by a potential *cis-trans*-isomerization, if for instance X = O. Alternatively, for X = CH_2 there would be a regio problem in the cyclopropanation as well as a high risk of double bond migration. Therefore we preferred route II, which goes back to a diquinane AC precursor **P2** with two *cis*-appendages R′ and R″, suitable for closing the seven-membered ring C via RCM.

(1) Dong, M.; Cong, B.; Yu, S.-H.; Sauriol, F.; Huo, C.-H.; Shi, Q.-W.; Gu, Y.-C.; Zamir, L. O.; Kiyota, H. *Org. Lett.* **2008**, *10*, 701–704.

10.1021/ol902263k CCC: $40.75

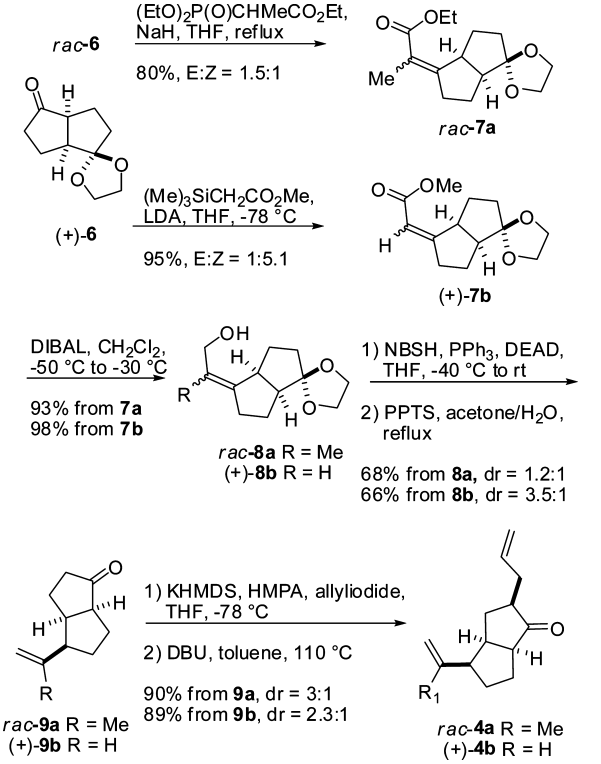
Scheme 1. Retrosynthetic Analysis of **1** and **2**



Thus, the *exo*-methylene group at C10 was retrosynthetically shifted to the *endo*-position. The cyclopropane and the acetic acid side chain were to be grafted on ketone **3**, which in turn should be elaborated from bis-alkene **4**. The synthesis of **4** was not trivial as both the vinyl/isopropenyl group at C1 (numbering identical to the final compounds) and the allyl group at C7 are located on the sterically encumbered concave face of the bicyclo[3.3.0]octane core. We therefore decided to explore a DRCM (dynamic ring closing metathesis), which has been described only once so far.[2] Equilibration of the kinetically allylated ketone **5** to RCM precursor **4** and in situ RCM should therefore deliver tricycle **3**. Ketone **5** in turn should be accessible from known racemic[3] or optically active[4] bicycle **6**, which can be easily prepared in multigram quantities from inexpensive 1,5-cyclooctadiene.

The synthesis of the RCM precursors (Scheme 2) *rac*-**4a** and (+)-**4b** started by converting ketone **6** to unsaturated

Scheme 2. Preparation of RCM Precursors **4a/4b**



esters **7a** and **7b** via Horner−Wadsworth−Emmons[5] and Peterson[6] olefination. Initial efforts to force the C1 side chain on the more hindered concave face by hydrogenating either the unsaturated esters or allylic alcohols resulted in 1:1 diastereomeric mixtures. Careful experimentation, however, revealed that the allylic alcohols **8a** and **8b** could be converted to the desired vinyl appendages by Myers' [3,3]-sigmatropic rearrangement protocol.[7] The stereochemical outcome can be rationalized by steric interactions with the adjacent cyclopentane ring (Figure 2), which is larger for the (*Z*)- than for the (*E*)-isomer. In fact, after separating the **8a** *Z*/*E* mixture, (*Z*)-**8a** afforded after deketalization a 10:1 ratio in favor of diastereomer **9a**, whereas the ratio dropped to 1.2:1 for (*E*)-**8a**. For compound **8b** (*Z*/*E* 5.1:1), the effect was less pronounced, giving **9b** as an easily separable 3.4:1 diastereomeric mixture.

Having secured gram quantities of both **9a** and **9b**, we finished the preparation of the RCM precursors. Allylation with KHMDS (only 1.05 equiv, otherwise bisallylation was observed) and excess allyliodide gave **5a** and **5b** in excellent yield and as single diastereomers.

The envisaged DRCM strategy was investigated under a variety of RCM catalysts, bases, Lewis acids, and solvents (Grubbs II, Grubbs Hoveyda II, "Grubbs III",[8] DBU, Schwesinger's *t*-Bu-P$_4$-base, $ZnCl_2$, $AlCl_3$,[9] toluene, CH_2Cl_2). After extensive experimentation, we realized that DRCM was

(2) Wang, J.; Lee, V.; Sintim, H. O. *Chem.—Eur. J.* **2009**, *15*, 2747–2750.
(3) (a) Perard-Viret, J.; Rassat, A. *Tetrahedron: Asymmetry* **1994**, *5*, 1–4. (b) Zhong, Y.-W.; Lei, X.-S.; Lin, G.-Q. *Tetrahedron: Asymmetry* **2002**, *13*, 2251–2255.
(4) Lemke, K.; Ballschuh, S.; Kunath, A.; Theilm, F. *Tetrahedron: Asymmetry* **1997**, *8*, 2051–2055.
(5) Wadsworth, W. S., Jr.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733–1738.
(6) (a) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780–784. (b) Shimoji, K.; Taguchi, H.; Oshima, K.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 1620–1621.
(7) (a) Myers, A. G.; Zheng, B. *Tetrahedron Lett.* **1996**, *37*, 4841–4844. (b) Myers, A. G.; Zheng, B.; Movassaghi, M. *J. Org. Chem.* **1997**, *62*, 7507–7507.
(8) Stewart, I. C.; Ung, T.; Pletnev, A. A.; Berlin, J. M.; Grubbs, R. H.; Schrodi, Y. *Org. Lett.* **2007**, *9*, 1589–1592.
(9) Bentz, D.; Laschat, S. *Synthesis* **2000**, *12*, 1766–1773.

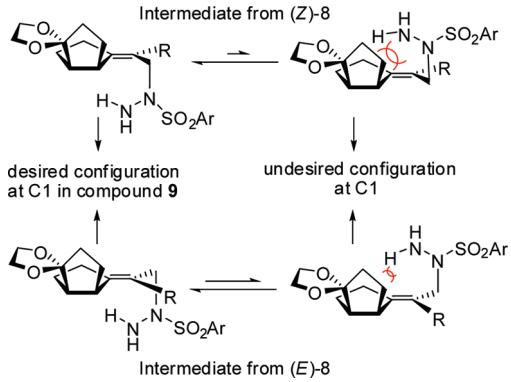


Figure 2. Models for the stereoselective [3,3]-sigmatropic rearrangement.

ineffective. However the DRCM experiments revealed that DBU (toluene, 110 °C) efficiently epimerized both **5a** and **5b** to mixtures of **4a/5a** (dr = 3:1) and **4b/5b** (dr = 2.3:1) with the desired *cis*-diastereomers in excess. The undesired diastereomers could be easily separated by HPLC and recycled.

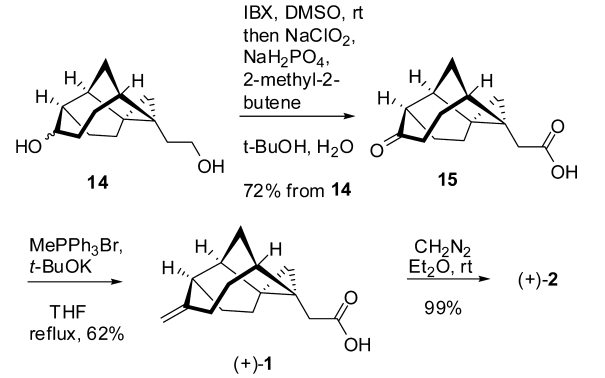
Next RCM was applied to **4a** and **4b**. To our surprise all attempts to close the seven-membered ring from **4a** failed, under a variety of reaction conditions (Grubbs II, Grubbs Hoveyda II, "Grubbs III", CH_2Cl_2, toluene, 2,6-dichlorobenzoquinone[10]). Only homodimers across the allylic units were observed. Gratifyingly the less hindered **4b** was smoothly converted to the desired core framework **3b** when exposed to Grubbs II catalyst (5 mol %) in refluxing CH_2Cl_2 (Scheme 3). As **5b** gave only polymers under these conditions, we streamlined our synthesis by submitting the **4b/5b** mixture to the RCM reaction, from which **3b** was readily isolated as the only monomeric product. In principle, the material can be carried through from **7b** to **3b** without separation as **4b** is the only diastereomer capable of RCM.

With **3b** in hand we started the installation of the remaining functionalities. We envisioned the introduction of the C2 side chain stepwise (path A) or directly (path B). In either case, the procedure commenced with the formation of the vinyltriflate with KHMDS/$PhNTf_2$ and a Pd(0)-mediated coupling reaction. As one-step formylation[11] failed, path A was focused on the well-established C1 elongation protocol with CO/MeOH in DMF,[12] which afforded the α,β-unsaturated methyl ester in excellent yield. Stereoselective Corey−Chaykovsky cyclopropanation[13] furnished ester **10**, and primary alcohol **12** was obtained after C1 elongation. Functionalization of the disubstituted double bound of **12** was accomplished by epoxidation with DMDO (which gave higher yields than *m*CPBA) and regioselective epoxide opening with LAH at elevated temperature to give **14** as a 16:1 diastereoisomeric mixture. Efforts to introduce appropriate functionality at C-10 in **12** via ene reactions with singlet oxygen[14] or formaldehyde[15] resulted only in the recovery of starting material.

In a more direct access to **14** (path B) we extended related methodology of Musco and Santi[16] to the vinyltriflate derived from ketone **3a**. Indeed, reaction with (1-methoxyvinyloxy)trimethylsilane and $Pd(PPh_3)_4$ furnished methyl ester **11** in 54% yield (not optimized). Regioselective cyclopropanation with modified Furukawa−Simmons−Smith's reagent[17] afforded the tetracyclic intermediate **13** in excellent yield. Epoxidation and LAH reduction gave **14** as before.

Oxidation of **14** (Scheme 4) first with IBX and then with $NaClO_2$[18] furnished ketoacid **15**, whose Wittig methylenation

Scheme 4. Completion of the Syntheses

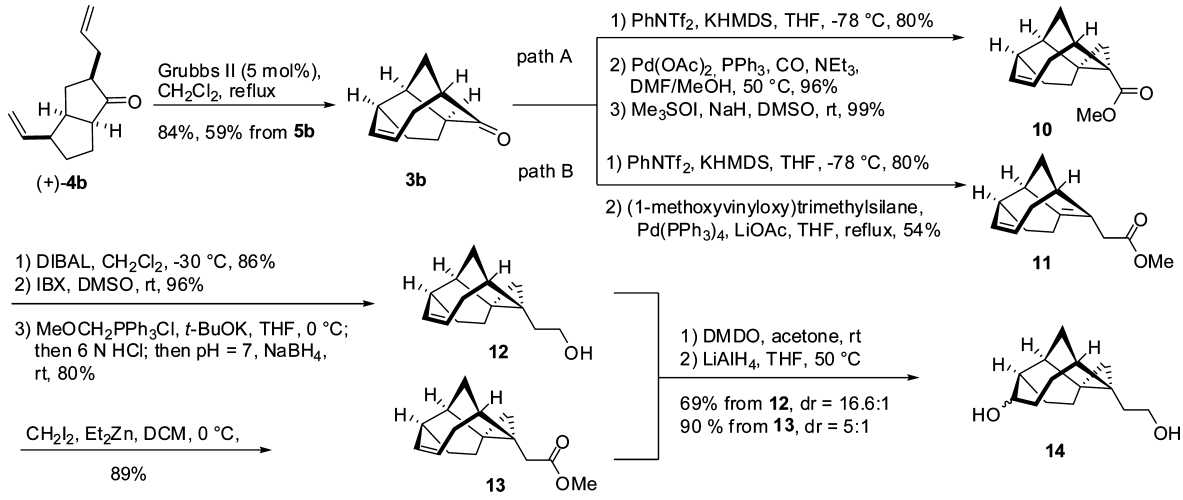


in refluxing THF led to (+)−**1** ($[\alpha]^{22}_D$ = +26 (*c* 0.70, $CHCl_3$), lit.[1] $[\alpha]^{22}_D$ = +23 (*c* 0.11, $CHCl_3$)). The acid was converted to (+)-**2** ($[\alpha]^{22}_D$ = +22 (*c* 0.60, $CHCl_3$), lit.[1] $[\alpha]^{22}_D$ = +21 (*c* 0.14, $CHCl_3$)) with diazomethane. The analytical data for **1** and **2** (HRMS, ^1H and ^{13}C NMR, $[\alpha]^{22}_D$) matched those reported by Shi and Kiyota in all respects. The relative configuration of **1** was also confirmed by single crystal analysis, whereas the absolute configuration of **1** and **2** follows unambiguously from the synthesis.

In summary, the first total synthesis of Echinopine A (**1**) and B (**2**) was achieved in optically active form in 15 steps from known ketone **6** in 7% overall yield. The sequence is easy to perform and scaleable and starts from

(10) Hong, S. H.; Sanders, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160–17161.
(11) (a) Behenna, D. C.; Stockdill, J. L.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 4077–4080. (b) Bosanac, T.; Basu, K.; Smith, A. B., III *J. Am. Chem. Soc.* **2009**, *131*, 2348–2358.
(12) (a) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4630–4632. (b) Cacchi, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1986**, *26*, 1109–1112.
(13) Chaykovsky, M.; Corey, E. J. *J. Am. Chem. Soc.* **1965**, *87*, 1353–1364.
(14) Maras, A.; Seçen, H.; Sütbevaz, Y.; Balci, M. *J. Org. Chem.* **1998**, *63*, 2039–2041.
(15) Maruoka, K.; Concepcion, A. B.; Murase, N.; Oishi, M.; Hirayama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 3943–3949.
(16) Carfagna, C.; Musco, A.; Sallese, G.; Santi, R.; Fiorani, T. *J. Org. Chem.* **1991**, *56*, 261–263. (b) Mallinger, A.; Le Gall, T.; Mioskowski, A *J. Org. Chem.* **2009**, *74*, 1124–1129.
(17) (a) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1966**, *7*, 3353–3354. (b) Simmons, H. E., Jr.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323–5324. (c) Simmons, H. E., Jr.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256–4264.
(18) Bal, B. S.; Childers, W. E.; Pinnick, H. W. *Tetrahedron* **1981**, *37*, 2091–2096.

Scheme 3. Construction of the Polycyclic [3,5,5,7] Skeleton



inexpensive material. Notable chemical features of the synthesis are (1) the stereoselective installation of the vinyl moiety on the concave side of the bicyclo[3.3.0]octane core via Myers' [3,3]-sigmatropic rearrangement, (2) the finding that the C7-substituent next to the ketone (see **4** and **5** in Scheme 1) can be epimerized to the desired concave face under basic conditions, (3) the closure of the highly strained seven-membered ring via RCM, and (4) the unusual C2-homologation of a vinyltriflate with a ketene silyl acetal.

Acknowledgment. The authors thank A. Roller and Prof. V. Arion (University of Vienna) for the crystal structure analysis of **1** and Prof. A. Fürstner (MPI Mülheim) for helpful discussions.

Supporting Information Available: Experimental procedures and analytical data for all new compounds and crystal data of **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL902263K

Total Syntheses of (+)-Echinopine A and B: Determination of Absolute Stereochemistry

SUPPORTING INFORMATION

Thomas Magauer*, Johann Mulzer and Konrad Tiefenbacher*

Institute of Organic Chemistry, University of Vienna
Währingerstraße 38
1090 Vienna
Austria

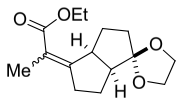
E-mail: thomas.magauer@univie.ac.at, konrad.tiefenbacher@univie.ac.at

Experimental part

General

All reactions were carried out in oven-dried glassware under an argon atmosphere using standard syringe/septa techniques, unless otherwise stated. Anhydrous toluene was distilled from sodium/benzophenone under argon. Anhydrous CH_2Cl_2, DMF (*N,N*-dimethylformamide) and HMPA (hexamethylphosphoramide) were distilled from CaH_2 under argon or reduced pressure, respectively. Anhydrous THF (tetrahydrofurane) was purchased from Acros (99.85%, water < 50 ppm). All other solvents were HPLC grade. Solvent degassing was achieved by repeated (at least 4 cycles) freeze-pump-thaw (FPT) cycles. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with E. Merck silica gel 60-F254 plates. Flash column chromatography was performed with Merck silica gel (0.04-0.063mm, 240-400 mesh) under pressure. Preparative HPLC was performed on a Dynamix Model SD-1 equipped with a Model UV-1 absorbance detector using a Supershere (60 Å pore size, 4 µm particle size, Ø 25 mm x 250 mm) at ambient temperature. Spots were visualized under UV light (254nm) and/or were stained with ceric ammonium molybdate (CAM), *p*-anisaldehyde or potassium permanganate stain. Yields refer to chromatographically and spectroscopically pure compounds, unless stated otherwise. NMR spectra were recorded on either Bruker Avance DRX-400 or DRX-600 at 400.13 MHz (100.61 MHz) or 600.13 MHz (150.90 MHz) spectrometer. Unless stated otherwise, all NMR spectra were measured in $CDCl_3$ solutions and referenced to the residual $CHCl_3$ signal (^{1}H, δ = 7.26 ppm; ^{13}C, δ =77.00 ppm). All ^{1}H and ^{13}C shifts are given in ppm (s = singlet; d = dublet; t = triplet; q = quadruplet; qu = quintet, m = multiplet; b = broad signal). Assignments of proton resonances were confirmed, when possible, by correlated spectroscopy. IR spectra were recorded as thin films on a silicon plate on a Perkin-Elmer 1600 FT-IR spectrometer. Optical rotations were measured on a P 341 Perkin- Elmer polarimeter at 589 nm with a 100 mm path length cell at 20°C, unless otherwise stated (reported as follows: concentration (*c* in g/100mL), solvent). Mass spectra were measured on a Micro mass, trio 200 Fisions Instruments. High resolution mass spectra (HRMS) were performed with a Finnigan MAT 8230 with a resolution of 10000.

Procedures



Ester *rac*-**7a.** NaH (60%, 524 mg, 13.16 mmol, 1.7 equiv.) was washed with pentane (3 x 10 mL), suspended in THF (4 mL) and cooled to 0 °C. Triethyl-2-phosphonoacetate (2.86 mL, 13.16 mmol, 1.7 equiv.) was added dropwise *via* syringe and stirring was continued for 40 min at room temperature. Ketone rac-**6** in THF (8 mL) was added and finally the solution was heated to reflux for 2 h. The reaction was cooled to ambient temperature, diluted with Et_2O (50 mL) and brine (50 mL) was added. The layers were separated, the aqueous layer was extracted with Et_2O (3 x 20 mL), the combined organic fractions were dried ($MgSO_4$), filtered and the solvent was evaporated. Purification of the crude residue by flash chromatography (hexane : ethylacetate = 20 : 1 to 5 : 1) yielded ester *rac*-**7a** (1.63 g, 80% for both diastereomers, *E*:*Z* = 1.5:1) as a colorless oil. Separation of the diastereomers was performed by HPLC.

***(E)*-7a: ^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.16 (q, *J* = 7.1 Hz, 2H), 3.94-3.89 (m, 4H), 3.30-3.20 (m, 1H), 2.87-2.73 (m, 2H), 2.46 (q, *J* = 7.8 Hz, 1H), 2.20-2.08 (m, 1H), 1.91-1.82 (m, 4H), 1.81-1.72 (m, 3H), 1.53-1.43 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.7 (C), 163.9 (C), 119.0 (C), 118.8 (C), 64.9 (CH_2), 64.0 (CH_2), 59.9 (CH_2), 50.0 (CH), 47.6 (CH), 34.5 (CH_2), 33.9 (CH_2), 28.2 (CH_2), 27.1 (CH_2), 16.2 (CH_3), 14.4 (CH_3).

IR [cm^{-1}]: 2957, 1706, 1269, 1185, 1095.

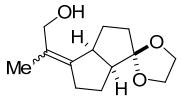
HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{15}H_{22}O_4$: 266.1518, found: 266.1512.

***(Z)*-7a: ^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.17 (q, *J* = 7.1 Hz, 2H), 3.94-3.89 (m, 4H), 3.77-3.68 (m, 1H), 2.57-2.35 (m, 3H), 2.33-2.22 (m, 1H), 1.88-1.80 (m, 4H), 1.79-1.69 (m, 3H), 1.45-1.35 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.1 (C), 163.4 (C), 119.0 (C), 118.6 (C), 64.9 (CH_2), 64.0 (CH_2), 59.9 (CH_2), 51.3 (CH), 47.1 (CH), 34.8 (CH_2), 33.8 (CH_2), 29.8 (CH_2), 25.4 (CH_2), 16.4 (CH_3), 14.3 (CH_3).

IR [cm^{-1}]: 2959, 1709, 1269, 1206, 1106, 1087.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{15}H_{22}O_4$: 266.1518, found: 266.1511.



Allylalcohol *rac*-**8a.** Ester rac-**7a** (1.5 g, 5.63 mmol, 1 equiv.) was dissolved in CH_2Cl_2 (19 mL) and cooled to -50 °C. DIBAL-H (1.5 M in toluene, 7.5 mL, 11.26 mmol, 2.0 equiv.) was added *via* syringe and the solution was warmed to -30 °C within 2 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL), quenched by the addition of Na-K-tartrate (70 mL) and stirred over night. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL), dried over $MgSO_4$ and concentrated. Purification by flash chromatography (hexane : ethylacetate = 3 : 1 to 1 : 1) gave allylalcohol **9** (1.10 g, 93%) as a colorless oil. Purification by HPLC gave pure *rac-(E)*-**8a** and *rac-(Z)*-**8a**.

***(E)*-8a: ^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.11 (d, *J* = 11.4 Hz, 1H), 4.05 (d, *J* = 11.4 Hz, 1H), 3.95-3.88 (m, 4H), 3.13 (bq, *J* = 7.8 Hz, 1H), 2.46 (dt, *J* = 8.5, 6.2 Hz, 1H), 2.40-2.32 (m, 2H), 2.12-2.01 (m, 1H), 1.85-1.63 (m, 4H), 1.74 (s, 3H), 1.49-1.39 (m, 1H), 1.24 (bs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.2 (C), 124.9 (C), 118.9 (C), 65.2 (CH_2), 64.9 (CH_2), 64.0 (CH_2), 50.4 (CH), 45.0 (CH), 34.9 (CH_2), 30.1 (CH_2), 29.0 (CH_2), 27.0 (CH_2), 16.7 (CH_3).

IR [cm^{-1}]: 3426 (b), 2955, 1034, 947.

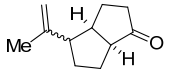
HRMS (EI) (m/z): $[M-H_2O]^+$ calcd. for $C_{13}H_{18}O_2$: 206.1307, found: 206.1303.

***(Z)*-8a: ^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.15 (d, *J* = 11.3 Hz, 1H), 4.08 (d, *J* = 11.4 Hz, 1H), 3.94-3.89 (m, 4H), 3.21 (bq, *J* = 7.9 Hz, 1H), 2.47 (q, *J* = 7.9 Hz, 1H), 2.42-2.23 (m, 2H), 2.10-2.00 (m, 1H), 1.90-1.82 (m, 1H), 1.78-1.66 (m, 6H), 1.45-1.36 (m, 1H), 1.26 (bs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.4 (C), 124.8 (C), 118.9 (C), 65.0 (CH_2), 64.9 (CH_2), 64.0 (CH_2), 51.1 (CH), 44.3 (CH), 35.0 (CH_2), 31.1 (CH_2), 30.6 (CH_2), 26.4 (CH_2), 16.9 (CH_3).

IR [cm^{-1}]: 3393 (b), 2931, 1455, 1119.

HRMS (EI) (m/z): $[M-H_2O]^+$ calcd. for $C_{13}H_{18}O_2$: 206.1307, found: 206.1304.



Ketone *rac*-**9a.** To a solution of PPh_3 (935 mg, 3.55 mmol, 1.6 equiv.) in 9 mL THF (0.4 M) was slowly added DEAD (620 mg, 3.55 mmol, 1.6 equiv.) at -15 °C. The orange mixture was stirred

for 15 min at -15 °C, cooled to -40 °C and allylalcohol *rac-(E)*-**8a** (500 mg, 2.25 mmol, 1 equiv.) was added *via* syringe (0.4 M in THF). After 5 min *o*-nitrobenzenesulfonylhydrazide (NBSH, 680 mg, 3.10 mmol, 1.4 equiv.) in THF (0.4 M) was added to the white suspension and the temperature was raised to –15 °C within 1 h. Stirring was continued at this temperature for 1 h and finally warmed to ambient temperature over night. TLC analysis showed complete consumption of the starting material and the reaction mixture was concentrated to about 10 mL. The residue was passed through a plug of silica twice, concentrated and dissolved in acetone/H_2O (23 mL, 2.4:1). PPTS (170 mg, 0.70 mmol, 0.3 equiv.) was added and the mixture was refluxed for 50 min. The solvent was evaporated and the crude product was directly loaded onto a silica column. Purification by flash chromatography (hexane : ethylacetate = 50 : 1 to 10 : 1) afforded a 1.2:1 mixture[1] of *rac*-**9a** and its C1-diastereomer (330 mg, 68 % 2 steps), which was easily separated by HPLC.

9a: **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.86-4.83 (m, 1H), 4.70 (s, 1H), 2.95 (qu, *J* = 8.4 Hz, 1H), 2.67 (t, *J* = 10.1 Hz, 1H), 2.57 (qu, *J* = 6.3 Hz, 1H), 2.33-2.13 (m, 2H), 1.97-1.75 (m, 3H), 1.79 (s, 3H), 1.65 (qu, *J* = 6.2 Hz, 1H), 1.48-1.32 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 222.8 (C), 144.6 (C), 110.3 (CH_2), 51.1 (CH), 50.8 (CH), 41.7 (CH), 39.4 (CH_2), 28.8 (CH_2), 27.2 (CH_2), 23.3 (CH_3), 21.6 (CH_2).

IR [cm^{-1}]: 2956, 1738, 1647, 1458, 1092.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{11}H_{16}O$: 164.1201, found: 164.1198

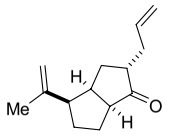
C1-diastereomer of **9a:** **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.79-4.75 (m, 1H), 4.75-4.71 (m, 1H), 2.68-2.57 (m, 2H), 2.35-2.26 (m, 2H), 2.15-1.99 (m, 3H), 1.88- 1.65 (m, 3H), 1.73 (s, 3H), 1.60-1.49 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 223.4 (C), 146.1 (C), 110.4 (CH_2), 53.0 (CH), 52.2 (CH), 45.2 (CH), 36.2 (CH_2), 32.4 (CH_2), 27.6 (CH_2), 23.7 (CH_2), 20.3 (CH_3).

IR [cm^{-1}]: 2954, 1738, 1644, 1456, 1410, 1135.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{11}H_{16}O$: 164.1201, found: 164.1198.

[1] *rac-(Z)*-**8a** afforded similarly high yield but a 10:1 ratio in favor of *rac*-**9a**.



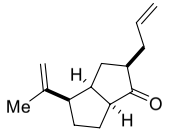
Ketone *rac*-**5a.** KHMDS (0.5 M in toluene, 2.0 mL, 1.02 mmol, 1.05 equiv.) was diluted with THF (6.4 mL) and cooled to -78 °C. Ketone *rac*-**9a** (160 mg, 0.97 mmol, 1 equiv.) in 2 mL THF (0.5 M) was added dropwise over a period of 5 min. After an additional 40 min at -78 °C HMPA (2 mL) was added, followed by the rapid addition of allyliodide (713 µL, 7.79 mmol, 8 equiv.). The reaction mixture was quenched after 30 min at -78 °C with saturated aqueous $NaHCO_3$ solution (10 mL) and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic fractions were washed with brine, dried ($MgSO_4$) and evaporated to give an oil, which was purified by gradient flash chromatography (hexane : ethylacetate = 20 : 1 to 15 : 1) to afford *rac*-**5a** (179 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.73 (ddt, *J* = 17.0, 12.1, 6.0 Hz, 1H), 5.07-4.98 (m, 2H), 4.87-4.85 (m, 1H), 4.71 (s, 1H), 2.96-2.86 (m, 1H), 2.74-2.67 (m, 1H), 2.58 (qu, *J* = 6.5 Hz, 1H), 2.44-2.35 (m, 1H), 2.22-2.14 (m, 1H), 2.09-2.00 (m, 1H), 1.96-1.78 (m, 2H), 1.78 (s, 3H), 1.73-1.64 (m, 2H), 1.61-1.53 (m, 1H), 1.41 (dq, *J* = 12.5, 7.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 223.9 (C), 144.9 (C), 135.7 (CH), 116.5 (CH_2), 110.3 (CH_2), 51.2 (CH), 51.2 (CH), 49.0 (CH), 38.9 (CH), 35.1 (CH_2), 29.9 (CH_2), 27.9 (CH_2), 27.6 (CH_2), 23.4 (CH_3).

IR [cm^{-1}]: 2950, 2869, 1733, 1642, 1451.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{14}H_{20}O$: 204.1514, found: 204.1509.



Ketone *rac*-**4a.** A solution of *rac*-**5a** (50 mg. 0.24 mmol, 1 equiv.) was dissolved in toluene (10 mL) and heated to 80 °C. DBU (29 µL, 0.20 mmol, 0.8 equiv.) was added and stirring was continued for 48 h. The solution was cooled to ambient temperature, the solvent was evaporated under reduced pressure and the crude residue was passed through a plug of silica (hexane :

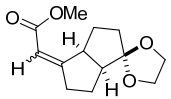
ethylacetate = 10 : 1) to afford 50 mg (99%, dr = 3:1*)* of *rac*-**4a** and *rac*-**5a**. For analytical purposes a small amount of *rac*-**4a** was purified by HPLC (hexane : ethylacetate = 15 : 1).

^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.75 (ddt, *J* = 17.2, 12.1, 5.9 Hz, 1H), 5.05-5.01 (m, 1H), 5.00-4.96 (m, 1H), 4.83-4.81 (m, 1H), 4.67 (s, 1H), 2.85 (qu, *J* = 8.6 Hz, 1H), 2.75 (t, *J* = 9.8 Hz, 1H), 2.54 (qu, *J* = 6.1 Hz, 1H), 2.52-2.47 (m, 1H), 2.39-2.32 (m, 1H), 1.98-1.91 (m, 3H), 1.84-1.76 (m, 1H), 1.79 (s, 3H), 1.61 (qu, *J* = 6.1 Hz, 1H), 1.34 (dq, *J* = 12.5, 7.6 Hz, 1H), 0.97 (dt, *J* = 13.4, 10.4 Hz, 1H).

^{13}C NMR (600 MHz, $CDCl_3$) δ = 223.9 (C), 144.4 (C), 136.1 (CH), 116.1 (CH_2), 110.2 (CH_2), 50.8 (CH), 50.6 (CH), 49.4 (CH), 39.2 (CH), 32.9 (CH_2), 28.2 (CH_2), 28.0 (CH_2), 26.9 (CH_2), 23.3 (CH_3).

IR [cm^{-1}]: 2950, 2869, 1733, 1642, 1451.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{14}H_{20}O$: 204.1514, found: 204.1507.



Ester (+)-**7b.** A solution of DIPA (6.3 mL, 45.0 mmol, 2 equiv.) in THF (110 mL) was cooled to -78 °C and treated with BuLi (2.5 M in hexane, 18.0 mL, 45.0 mmol, 2 equiv.). After 15 min methyl trimethylsilylacetate (7.4 mL, 45.0 mmol, 2 equiv.) in THF (45 mL) was added dropwise and the resulting yellow-orange mixture was stirred for 20 min at -78 °C. Ketone (+)-**6** (4.1 g, 22.50 mmol, 1 equiv.) in THF (40 mL) was transferred to the solution *via* syringe and warmed to –15 °C within 1.5 h. As TLC analysis showed complete consumption of the starting material, the mixture was partitioned between saturated aqueous NH_4Cl (150 mL) and Et_2O (100 mL). The aqueous layer was extracted with Et_2O (3 x 80 mL), the combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated. Flash chromatography (hexane : ethylacetate = 5 : 1) afforded 5.07 g (95%, *Z:E* = 5.1:1) of unsaturated methylester (+)-**7b**, which was used without further purification in the next step. For analytical purposes a small amount of (+)-**7b** was purified by HPLC (hexane : ethylacetate = 3 : 1).

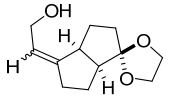
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.72-5.70 (m, 1H), 3.95-3.90 (m, 4H), 3.83-3.74 (m, 1H), 3.68 (s, 3H), 2.66-2.55 (m, 2H), 2.41-2.31 (m, 2H), 1.85-1.73 (m, 3H), 1.70-1.62 (m, 1H), 1.47-1.37 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.1 (C), 166.7 (C), 118.7 (C), 110.7 (CH), 64.9 (CH_2), 64.1 (CH_2), 50.8 (CH_3), 50.6 (CH), 45.7 (CH), 35.9 (CH_2), 35.3 (CH_2), 29.6 (CH_2), 25.1 (CH_2).

IR [cm^{-1}]: 2951, 1717, 1654, 1213, 1137.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{13}H_{18}O_4$: 238,1205, found: 238,1201.

$[\alpha]_D^{20}$ = +208.6 (*c* = 0.95, $CHCl_3$)



Allylalcohol (+)-**8b**. Methylester (+)-**7b** (4.9 g, 20.56 mmol, 1 equiv., 5.1:1 *Z*/*E*-mixture) was dissolved CH_2Cl_2 (51 mL) and cooled to -50 °C. DIBAL-H (1.5 M in toluene, 34.3 mL, 51.41 mmol, 2.5 equiv.) was added *via* syringe and the solution was warmed to -30 °C within 1 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and finally quenched with saturated aqueous Na-K-tartrate solution (100 mL). The resulting suspension was stirred until a clear phase separation was achieved (3 h). The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL), dried over $MgSO_4$ and concentrated. The residue was filtered over a small plug of silica (hexane : ethylacetate = 3 : 1 to 1 : 1) to afford 4.24 g (98%) of (+)-**8b** as an oil. The crude product was used in the next step without further purification.

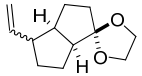
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.48-5.40 (m, 1H), 4.22-4.07 (m, 2H), 3.96-3.86 (m, 4H), 3.22-3.13 (m, 1H), 2.52 (dt, *J* = 8.5, 5.1 Hz, 2H), 2.29-2.18 (m, 1H), 2.10-1.98 (m, 1H), 1.84-1.57 (m, 4H), 1.41 (m, 1H), 1.21 (bs, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.8 (C), 119.0 (CH), 118.6 (C), 64.9 (CH_2), 64.0 (CH_2), 60.7 (CH_2), 50.7 (CH), 43.1 (CH), 35.4 (CH_2), 34.2 (CH_2), 30.4 (CH_2), 26.2 (CH_2).

IR [cm^{-1}]: 3416 (b), 2954, 2879, 1080, 1006.

HRMS (EI) (m/z): $[M-H_2O]^+$ calcd. for $C_{12}H_{16}O_2$ 192.1150, found: 192.1155.

$[\alpha]_D^{20}$ = +155.0 (*c* = 0.40, $CHCl_3$)



Ketal (+)-**16.** To a solution of PPh_3 (8.46 g, 32.26 mmol, 1.6 equiv.) in 81 mL THF (0.4 M) was slowly added DEAD (5.62 g, 32.26 mmol, 1.6 equiv.) at -15 °C. The orange mixture was stirred

for 15 min at -15 °C, cooled to -40 °C and allylalcohol (+)-**8b** (4.24 g, 20.16 mmol, 1 equiv.) was added via syringe (0.4 M in THF). After 5 min NBSH (6.13 g, 28.23 mmol, 1.4 equiv.) in THF (0.4 M) was added to the white suspension and the temperature was raised to –15 °C within 1 h. Stirring was continued at this temperature for 1 h and finally warmed to ambient temperature over night. TLC analysis showed complete consumption of the starting material and the reaction mixture was concentrated to 50 mL. The residue was passed through a plug of silica twice (pentane : Et_2O = 5 : 1), the solvent was evaporated and purification by column chromatography and HPLC (hexane : ethylacetate = 15 : 1) afforded 2.14 g (+)-**16** and 0.61 g of its C1-diastereomer (70% for both diastereomers).

(+)-**16:** **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 5.88 (ddd, *J* = 17.1, 10.5, 6.7 Hz, 1H), 5.06-4.98 (m, 2H), 3.94-3.85 (m, 4H), 2.61 (qu, *J* = 7.8 Hz, 1H), 2.56-2.44 (m, 1H), 1.83-1.76 (m, 1H), 1.72-1.65 (m, 1H), 1.65-1.49 (m, 5H), 1.49-1.41 (m, 1H), 1.41-1.32 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 139.6 (CH), 118.9 (C), 114.4 (CH_2), 64.9 (CH_2), 64.1 (CH_2), 49.8 (CH), 47.9 (CH), 45.5 (CH), 35.9 (CH_2), 30.2 (CH_2), 26.4 (CH_2), 24.0 (CH_2).

IR [cm^{-1}]: 2953, 2360, 1558, 1094, 1040 .

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{12}H_{18}O_2$: 194.1307, found: 194.1302.

$[\alpha]_D^{20}$ = +82.0 (*c* = 1.00, $CHCl_3$)

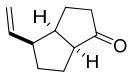
C1-diastereomer of (+)-**16:** **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 5.76 (ddd, *J* = 17.3, 10.0, 7.4 Hz, 1H), 4.99 (ddd, *J* = 17.2, 1.9, 1.2 Hz, 1H), 4.90 (ddd, *J* = 10.2, 2.0, 0.9 Hz, 1H), 3.94-3.83 (m, 4H), 2.40 (q, *J* = 9.0 Hz, 1H), 2.28-2.19 (m, 1H), 2.12-2.03 (m, 1H), 1.86-1.74 (m, 1H), 1.72-1.66 (m, 5H), 1.59-1.49 (m, 1H), 1.43-1.27 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.2 (CH), 118.7 (C), 113.1 (CH_2), 64.7 (CH_2), 63.7 (CH_2), 52.2 (CH), 49.8 (CH), 47.7 (CH), 34.4 (CH_2), 33.5 (CH_2), 27.8 (CH_2), 26.8 (CH_2).

IR [cm^{-1}]: 2950, 2873, 1638, 1284, 1074.

HRMS (EI) (m/z): $[M\text{-}H^+]^-$ calcd. for $C_{12}H_{17}O_2$: 193.1229, found: 193.1226.

$[\alpha]_D^{20}$ = +61.3 (*c* = 1.05, $CHCl_3$)



Ketone (+)-**9b.** To a solution of (+)-**16** (1.7 g, 8.75 mmol, 1 equiv.) in acetone/H_2O (2.4 : 1, 88 mL) was added PPTS (660 mg, 2.62 mmol, 0.3 equiv.). The mixture was heated to reflux for 40 min, cooled to ambient temperature and diluted with H_2O (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL), the combined organic fractions were washed with brine (30 mL), dried ($MgSO_4$) and concentrated. Purification by flash chromatography (pentane : Et_2O = 10 : 1 to 5 : 1) furnished volatile ketone (+)-**9b** (1.23 g, 94%) as a colorless oil.

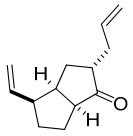
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.87 (ddd, *J* = 17.1, 10.5, 6.8 Hz, 1H), 5.11-5.04 (m, 2H), 2.85 (qu, *J* = 8.2 Hz, 1H), 2.76-2.61 (m, 2H), 2.32-2.14 (m, 2H), 1.96-1.81 (m, 3H), 1.72 (dqu, *J* = 6.4, 2.7 Hz, 1H), 1.60-1.48 (m, 1H), 1.47-1.35 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 222.7 (C), 138.1 (CH), 115.3 (CH_2), 51.3 (CH), 48.0 (CH), 44.5 (CH), 39.4 (CH_2), 29.5 (CH_2), 28.6 (CH_2), 22.3 (CH_2).

IR [cm^{-1}]: 2955, 2874, 1738, 1654, 1521, 1360.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{10}H_{14}O$: 150.1045, found: 150.1042.

$[\alpha]_D^{20}$ = +151.9 (*c* = 1.00, $CHCl_3$)



Ketone (+)-**5b.** KHMDS (0.5 M in toluene, 16.8 mL, 8.39 mmol, 1.05 equiv.) was diluted with THF (65 mL) and cooled to -78 °C. Ketone (+)-**9b** (1.2 g, 7.99 mmol, 1 equiv.) in 16 mL THF (0.5 M) was added dropwise over a period of 10 min. After stirred for an additional 1 h at -78 °C, HMPA (4 mL) was added, followed by the rapid addition of allyliodide (5.84 mL, 63.90 mmol, 8 equiv.). The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution after 10 min and the aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic fractions were washed with brine, dried ($MgSO_4$) and evaporated to give an oil, which was purified by gradient flash chromatography (hexane : ethylacetate = 20 : 1 to 10 : 1) to afford pure ketone (+)-**5b** (1.36 g, 89%).

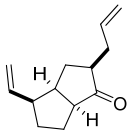
^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.89-5.82 (m, 1H), 5.76-5.69 (m, 1H), 5.09-5.00 (m, 4H), 2.83 (dq, *J* = 8.5, 5.5 Hz, 1H), 2.76-2.70 (m, 1H), 2.67 (dt, *J* = 9.3, 2.6 Hz, 1H), 2.43-2.38 (m, 1H), 2.17 (dq, *J* = 8.3, 5.3 Hz, 1H), 2.07-2.01 (m, 1H), 1.94-1.83 (m, 3H), 1.74 (dqu, *J* = 6.4, 2.4 Hz, 1H), 1.66-1.60 (m, 1H), 1.37 (dq, *J* = 11.7, 7.6 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ = 223.8 (C), 138.4 (CH), 135.7 (CH), 116.6 (CH_2), 115.3 (CH_2), 51.9 (CH), 48.9 (CH), 47.7 (CH), 41.5 (CH), 34.9 (CH_2), 30.3 (CH_2), 29.6 (CH_2), 28.2 (CH_2).

IR [cm^{-1}]: 2951, 2871, 1733, 1640, 1116.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{13}H_{18}O$: 190.1358, found: 190.1353.

$[\alpha]_D^{20}$ = +209.8 (*c* = 1.10, $CHCl_3$)



Ketone (+)-**4b.** A solution of ketone (+)-**5b** (1.24 g, 5.78 mmol, 1 equiv.) was dissolved in toluene (65 mL) and heated to 110 °C. DBU (777 µL, 5.20 mmol, 0.8 equiv.) was added and stirring was continued over night. The solution was cooled to ambient temperature, the solvent was evaporated under reduced pressure and the crude residue was purified by a short silica column (hexane : ethylacetate = 20 : 1) to afford 1.24 g (99%, dr = 2.3:1*)* of ketone (+)-**4b** and (+)-**5b**, which could be used in the next step without further purification. For analytical purposes a small amount was separated by HPLC (hexane : ethylacetate = 30 : 1).

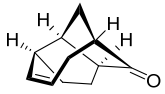
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.89 (ddd, *J* = 17.1, 10.4, 6.6 Hz, 1H), 5.76 (ddt, *J* = 17.1, 12.1, 5.9 Hz, 1H), 5.11-4.97 (m, 4H), 2.80-2.71 (m, 2H), 2.71-2.63 (m, 1H), 2.55-2.46 (m, 1H), 2.40-2.30 (m, 1H), 2.10-2.00 (m, 1H), 2.03-1.93 (m, 1H), 1.93-1.77 (m, 2H), 1.67 (qu, *J* = 6.3 Hz, 1H), 1.33 (dq, *J* = 11.5, 9.3 Hz, 1H), 1.08 (dt, *J* = 13.3, 9.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 221.0 (C), 138.0 (CH), 136.1 (CH), 116.1 (CH_2), 115.3 (CH_2), 51.0 (CH), 49.6 (CH), 48.0 (CH), 42.0 (CH), 32.9 (CH_2), 28.9 (CH_2), 28.8 (CH_2), 28.2 (CH_2).

IR [cm^{-1}]: 2954, 2872, 1733, 1641, 1455.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{13}H_{18}O$: 190.1358, found: 190.1354.

$[\alpha]_D^{20}$ = +40.0 (*c* = 0.40, $CHCl_3$)



Tricyclic ketone (+)-**3b**. The 2.3:1 mixture of (+)-**4b** and (+)-**5b** (1.1 g, 5.78 mmol, 1 equiv.) was dissolved in degassed CH_2Cl_2 (1.2 L, 4.5 mM) and heated to reflux. Grubbs II catalyst (245 mg, 0.289 mmol, 0.05 equiv.) in degassed CH_2Cl_2 (20 mL) was added *via* syringe pump within 16 h. After 18 h air was bubbled through the solution for 30 min and the mixture was concentrated. Purification of the dark brown oil by gradient column chromatography (hexane : ethylacetate = 50 : 1 to 15 : 1) yielded tricyclic ketone (+)-**3b** as a pale-red oil (549 mg, 59%, 84% based on pure diastereomer (+)-**4b**).

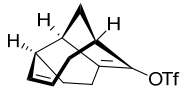
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.35-5.22 (m, 2H), 2.85 (qu, *J* = 7.7 Hz, 1H), 2.84-2.77 (bs, 1H), 2.65-2.47 (m, 3H), 2.41-2.31 (m, 1H), 2.32-2.23 (m, 1H), 2.05-1.95 (m, 2H), 1.05-1.74 (m, 1H), 1.71-1.60 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 228.0 (C), 131.6 (CH), 124.8 (CH), 52.1 (CH), 46.4 (CH), 45.0 (2 x CH), 36.2 (CH_2), 34.9 (CH_2), 28.8 (CH_2), 26.2 (CH_2).

IR [cm^{-1}]: 2938, 2358, 1733, 1426, 1102.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{11}H_{14}O$: 162.1045, found: 162.1043.

$[\alpha]_D^{20}$ = +81.7 (*c* = 1.00, $CHCl_3$)



Vinyltriflate (+)-**17.** To a solution of $PhNTf_2$ (2.29 g, 6.41 mmol, 2 equiv.) and tricyclic ketone (+)-**3b** (520 mg, 3.21 mmol, 1 equiv.) in THF (65 mL) was added KHMDS (0.5 M in toluene, 12.8 mL, 6.41 mmol, 2 equiv.) at -78 °C. The mixture was stirred for 1 h at -78 °C and 0.5 h at -30 °C. TLC analysis showed complete conversion of the starting material and the reaction mixture was quenched by the addition of NH_4Cl (50 mL). The phases were separated, extracted with a 1 : 1 mixture of Et_2O-hexane (3 x 30 mL), washed with brine, dried over $MgSO_4$ and evaporated to dryness. The residual oil was diluted with a small amount of hexane and purification by flash chromatography (hexane : ethylacetate = 50 : 1) afforded 753 mg (80%) of vinyltriflate (+)-**17** as a colorless oil.

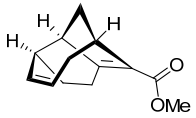
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.21-5.08 (m, 2H), 3.12-3.06 (bs, 1H), 2.95 (t, *J* = 7.0 Hz, 1H), 2.76-2.69 (b, 1H), 2.59 (bd, *J* = 18.8 Hz, 1H), 2.47-2.39 (m, 1H), 2.35-2.25 (m, 1H), 2.29-2.19 (m, 1H), 2.24-2.12 (m, 1H), 2.19-2.07 (m, 1H), 1.79 (d, *J* = 12.8 Hz, 1H), 1.78-1.71 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.9 (C), 139.1 (C), 131.0 (CH), 122.5 (CH), 117.1 (C), 49.2 (CH), 44.5 (CH), 42.8 (CH), 37.5 (CH_2), 32.9 (CH_2), 27.3 (CH_2), 20.7 (CH_2).

IR [cm^{-1}]: 2941, 1420, 1246, 1209, 1142, 1036.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{12}H_{13}O_3F_3S$: 294.0538, found: 294.0529.

$[\alpha]_D^{20}$ = +62.1 (*c* = 0.63, $CHCl_3$)



Ester (+)-**18.** $Pd(OAc)_2$ (7.8 mg, 0.035 mmol, 0.03 equiv.), PPh_3 (18 mg, 0.069 mmol, 0.06 equiv.) and NEt_3 (229 µl, 2.31 mmol, 2 equiv.) was sequentially added to a solution of vinyltriflate **20** (340 mg, 1.16 mmol, 1 equiv.) in DMF (14 mL) and MeOH (14 mL). CO was bubbled through the orange solution for 10 min. The flask was sealed under 1 atm of CO and heated to 50 °C for 1 h. The solution was cooled to ambient temperature, diluted with Et_2O (100 mL) and washed with brine (2 x 50 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated. The crude residue was purified by flash chromatography (hexane : ethylacetate = 50 : 1 to 20 : 1) to yield α,β-unsaturated ester (+)-**18** (227 mg, 96%) as a colorless oil.

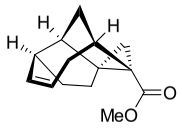
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.18-5.11 (m, 1H), 5.09-5.02 (m, 1H), 3.71 (s, 3H), 3.36-3.30 (bs, 1H), 3.09 (t, *J* = 7.6 Hz, 1H), 2.83 (ddd, *J* = 14.7, 9.0, 5.5 Hz, 1H), 2.73-2.61 (m, 2H), 2.42-2.30 (m, 1H), 2.35-2.21 (m, 2H), 2.10-2.01 (m, 1H), 1.78-1.70 (m, 1H), 1.70 (d, *J* = 12.9 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.5 (C), 165.9 (C), 130.5 (CH), 126.9 (C), 123.8 (CH), 54.4 (CH), 50.9 (CH_3), 46.4 (CH), 41.2 (CH), 39.7 (CH_2), 33.5 (CH_2), 28.5 (CH_2), 23.8 (CH_2).

IR [cm^{-1}]: 2936, 1706, 1436, 1293, 1109.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{13}H_{16}O_2$: 204.1150, found: 204.1146.

$[\alpha]_D^{20}$ = -52.5 (*c* = 1.1, $CHCl_3$)



Tetracyclic Ester (+)-**10.** To an ice-cooled mixture of NaH (60%, 49 mg, 1.23 mmol, 1.2 equiv.) and trimethylsulfoxonium iodide (272 mg, 1.23 mmol, 1.2 equiv.) was added DMSO (1.8 mL) dropwise over 5 min. After stirred for 10 min at 10 °C, methylester (+)-**18** (210 mg, 1.03 mmol, 1 equiv.) in DMSO (1 mL, 2 x 0.4 mL rinse) was added *via* syringe. The mixture was stirred for 40 min at ambient temperature, diluted with Et_2O (50 mL), quenched by the addition of saturated aqueous NH_4Cl (50 mL) and extracted with Et_2O/hexane = 1 : 1 (3 x 20 mL). The organic phase was washed with brine (20 mL), the solvent was evaporated and the crude product was filtered over a small plug of silica (hexane : ethylacetate = 20 : 1) to afford tetracyclic ester (+)-**10** (222 mg, 99%) as a colorless oil.

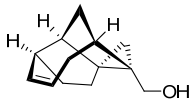
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.32-5.21 (m, 2H), 3.62 (s, 3H), 3.02 (bd, *J* = 17.4 Hz, 1H), 2.67-2.60 (b, 1H), 2.60-2.54 (bs, 1H), 2.32 (t, *J* = 6.4 Hz, 1H), 2.15 (dt, *J* = 13.6, 9.0 Hz, 1H), 2.01-1.93 (m, 2H), 1.89-1.81 (m, 1H), 1.79-1.72 (m, 1H), 1.66-1.54 (m, 2H), 1.35 (d, *J* = 4.5 Hz, 1H), 1.06 (d, *J* = 4.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.8 (C), 132.0 (CH), 124.4 (CH), 50.9 (CH_3), 48.9 (CH), 45.3 (CH), 44.2 (C), 39.2 (CH), 35.9 (C), 34.5 (CH_2), 33.6 (CH_2), 30.5 (CH_2), 24.0 (CH_2), 22.2 (CH_2).

IR [cm^{-1}]: 2946, 1717, 1433, 1338, 1156, 1132.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{14}H_{18}O_2$: 218.1307, found: 218.1304.

$[\alpha]_D^{20}$ = +120.4 (*c* = 0.45, $CHCl_3$)



Alcohol (+)-**19**. Ester (+)-**10** (213 mg, 0.98 mmol, 1 equiv.) in CH_2Cl_2 (5 mL) was cooled to -30 °C and treated with DIBAL (1.5 M in toluene, 1.43 mL, 2.15 mmol, 2.2 equiv.). After 20 min TLC analysis showed complete consumption of the starting material and the temperature was raised to 0 °C. The reaction was diluted with CH_2Cl_2 (50 mL) and quenched by the careful addition of saturated aqueous Na/K-Tartrate (20 mL) solution. Stirring was continued for 2 h and the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL), the combined organic fractions were dried ($MgSO_4$), filtered and the solvent was evaporated to yield

pure primary alcohol (+)-**19** (160 mg, 86%) as a white solid. The crude product was used in the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.37-5.23 (m, 2H), 3.76 (dd, *J* = 11.4, 5.4 Hz, 1H), 3.14 (dd, *J* = 11.4, 2.4 Hz, 1H), 2.64-2.57 (bs, 1H), 2.56-2.43 (m, 2H), 2.33-2.28 (bt, *J* = 6.8 Hz, 1H), 2.10-1.93 (m, 2H), 1.79-1.67 (m, 2H), 1.59-1.47 (m, 2H), 1.21-1.15 (bs, 1H), 0.66 (dd, *J* = 4.8, 1.5 Hz, 1H), 0.57 (d, *J* = 5.0 Hz, 1H).

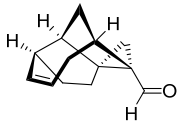
^{13}C NMR (100 MHz, $CDCl_3$) δ = 133.0 (CH), 124.0 (CH), 65.4 (CH_2), 49.3 (CH), 45.4 (CH), 39.7 (CH), 38.5 (C), 33.8 (CH_2), 33.1 (CH_2), 33.0 (C), 30.3 (CH_2), 23.7 (CH_2), 16.3 (CH_2).

IR [cm^{-1}]: 3333, 2933, 2335, 1023.

HRMS (EI) (m/z): $[M-H_2O]^+$ calcd. for $C_{13}H_{16}$: 172.1252, found: 172.1248.

$[\alpha]_D^{20}$ = +88.7 (*c* = 0.55, $CHCl_3$)

mp 85-89 °C



Aldehyde (+)-**20.** Alcohol (+)-**19** (150 mg, 0.79 mmol, 1equiv.) was dissolved in DMSO (3 mL) and treated with IBX (662 mg, 2.37 mmol, 3 equiv.). After 1 h at room temperature, the reaction mixture was directly loaded onto a silica column. Elution of the product (hexane : ethylacetate = 10 : 1 to 3 : 1) afforded (+)-**20** as a white solid (145 mg, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.28 (s, 1H), 5.35-5.22 (m, 2H), 3.07 (bd, *J* = 18.4 Hz, 1H), 2.71-2.63 (m, 2H), 2.39 (t, *J* = 6.4 Hz, 1H), 2.12 (bd, *J* = 18.4 Hz, 1H), 2.03-1.93 (m, 1H), 1.93-1.80 (m, 2H), 1.80-1.71 (m, 1H), 1.72-1.66 (m, 2H), 1.65 (d, *J* = 5.2 Hz, 1H), 1.20 (d, *J* = 5.2 Hz, 1H).

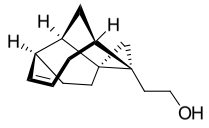
^{13}C NMR (100 MHz, $CDCl_3$) δ = 200.9 (C), 132.5 (CH), 123.6 (CH), 48.4 (CH), 45.4 (CH), 43.1 (C), 38.1 (CH), 33.4 (CH_2), 33.3 (CH_2), 31.4 (CH_2), 24.2 (CH_2), 21.2(CH_2).

IR [cm^{-1}]: 2945, 1705, 1675, 1306, 1157, 1036.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{13}H_{16}O$: 188.1201, found: 188.1200.

$[\alpha]_D^{20}$ = +287.6 (*c* = 0.55, $CHCl_3$)

mp 125-128 °C



Alcohol (+)-**12.** $MeOCH_2PPh_3Cl$ (528 mg, 1.54 mmol, 2 equiv.) was dissolved in 5.1 mL THF and cooled to 0 °C. *t*-BuOK (173 mg, 1.54 mmol, 2 equiv.) was added in one portion and the resulting red-orange suspension was stirred for 1 h at 0 °C. Aldehyde (+)-**20** (145 mg, 0.77 mmol, 1 equiv.) in 1.5 mL THF was added *via* syringe, whereas the solution turned pale-orange. After stirring for 20 min at ambient temperature, the reaction was quenched by slow addition of 6 N HCl (4 mL). As TLC analysis showed complete hydrolysis of the enol ether (1.5 h), the mixture was carefully adjusted to pH = 7 with solid $NaHCO_3$. $NaBH_4$ (146 mg, 3.85 mmol, 5 equiv.) was added in 5 portions, stirring was continued for further 10 min and the reaction was finally quenched by 1% HCl. The layers were separated, the aqueous phase was extracted with Et_2O (4 x 5 mL), the combined organic fractions were dried ($MgSO_4$) and concentrated. Purification by column chromatography (hexane : ethylacetate = 5 : 1 to 2 : 1) yielded solid alcohol (+)-**12** (125 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.33-5.20 (m, 2H), 3.86-3.71 (m 2H), 2.61-2.54 (bs, 1H), 2.36-2.24 (b, 3H), 2.05-1.91 (m, 2H), 1.81-1.67 (m, 2H), 1.68-1.59 (m, 1H), 1.58-1.51 (m, 2H), 1.55-1.47 (m, 1H), 1.39 (bs, OH), 0.87 (dt, *J* = 14.8, 7.4 Hz, 1H), 0.58 (d, *J* = 4.8 Hz, 1H), 0.34 (d, *J* = 4.8 Hz, 1H).

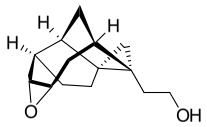
^{13}C NMR (100 MHz, $CDCl_3$) δ = 132.8 (CH), 123.6 (CH), 62.4 (CH_2), 49.0 (CH), 45.3 (CH), 40.2 (CH), 37.2 (C), 33.8 (CH_2), 33.4 (CH_2), 33.1 (CH_2), 30.4 (CH_2), 28.2 (C), 23.2 (CH_2), 16.2 (CH_2).

IR [cm^{-1}]: 3309, 2936, 1637, 1456.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{14}H_{20}O$: 204.1514, found: 204.1515.

$[\alpha]_D^{20}$ = +92.9 (*c* = 1.00, $CHCl_3$)

mp 63-69 °C



Epoxide (+)-**21**. Primary alcohol (+)-**12** (115 mg, 0.56 mmol, 1 equiv.) in acetone (1 mL) was treated with DMDO (0.07 M in acetone, 24 mL, 1.69 mmol, 3.0 equiv.) at room temperature for 30 min. The solvent was evaporated to give pure epoxide (+)-**21** (118 mg, 95%, dr = 16.6:1) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.87-3.71 (m, 2H), 3.15 (t, *J* = 4.5 Hz, 1H), 2.90 (dt, *J* = 3.8, 1.3 Hz, 1H), 2.71 (t, *J* = 7.4 Hz, 1H), 2.24-2.08 (m, 5H), 1.94-1.85 (m, 1H), 1.83-1.71 (m, 3H), 1.58-1.48 (m, 1H), 1.39 (b, OH), 1.30-1.20 (m, 1H), 0.99 (ddd, *J* = 13.8, 8.6, 6.8 Hz, 1H), 0.57 (dd, *J* = 5.0, 1.8 Hz, 1H), 0.38 (d, *J* = 5.0 Hz, 1H).

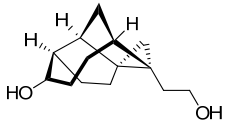
^{13}C NMR (100 MHz, $CDCl_3$) δ = 63.9 (CH), 62.2 (CH_2), 58.2 (CH), 47.5 (CH), 40.3 (CH), 39.8 (CH), 38.8 (C), 33.3 (CH_2), 30.9 (CH_2), 29.8 (C), 29.4 (CH_2), 27.0 (CH_2), 23.8 (CH_2), 16.4 (CH_2).

IR [cm^{-1}]: 3418, 2914, 1718, 1448, 1269.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{14}H_{20}O_2$: 220.1463, found: 220.1465.

$[\alpha]_D^{20}$ = +43.6 (*c* = 1.00, $CHCl_3$)

mp 93-95 °C



Diol (+)-**14.** To an ice-cold solution of epoxide (+)-**21** (80 mg, 0.36 mmol, 1 equiv.) in THF (7 mL) was added LAH (4M in Et_2O, 454 µL, 1.82 mmol, 5 equiv.) *via* syringe. The solution was warmed to room temperature within 5 min and heated to 50 °C for 2 h. The mixture was cooled to ambient temperature, quenched by careful addition of 1% HCl and the aqueous layer was extracted with CH_2Cl_2 (4 x 10 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated. Purification by column chromatography (hexane : ethylacetate = 3 : 1 to 1 : 2) gave diol (+)-**14** (58 mg, 73%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.87-3.70 (m, 3H), 2.27-2.16 (m, 3H), 2.11-2.00 (m, 1H), 2.00-1.91 (m, 2H), 1.81 (dt, *J* = 12.1, 4.6 Hz, 1H), 1.77-1.23 (m, 9H), 0.97 (ddd, *J* = 13.7, 8.4, 6.7 Hz, 1H), 0.60 (dd, *J* = 4.8, 1.8 Hz, 1H), 0.27 (d, *J* = 4.8 Hz, 1H).

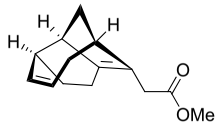
^{13}C NMR (100 MHz, $CDCl_3$) δ = 76.2 (CH), 62.8 (CH_2), 47.8 (CH), 47.1 (CH), 40.0 (CH), 39.5 (C), 32.9 (CH_2), 30.2 (C), 29.6 (CH_2), 29.0 (CH_2), 27.6 (CH_2), 25.0 (CH_2), 24.3 (CH_2), 15.9 (CH_2).

IR [cm^{-1}]: 3390, 2935, 1648, 1549, 1091.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{14}H_{22}O_2$: 222.1620, found: 222.1621.

$[\alpha]_D^{20}$ = +43.8 (*c* = 1.10, $CHCl_3$)

mp 131-133 °C



Ester (+)-**11.** Flame dried LiOAc (138 mg, 2.10 mmol. 2.5 equiv.), $Pd(PPh_3)_4$ (97 mg, 0.08 mmol, 0.1 equiv.) and (1-methoxyvinyloxy)trimethylsilane[2] (246 mg, 1.68 mmol, 2 equiv.) were sequentially added to a solution of vinyltriflate (+)-**17** (250 mg, 0.84 mmol, 1 equiv.) in degassed THF (8 mL). The mixture was refluxed for 3 h, cooled to ambient temperature and finally H_2O (20 mL) was added. The aqueous layer was extracted with Et_2O (3 x 20 mL), the combined organic fractions were dried and concentrated in *vacuo*. Purification by column chromatography (hexane : ethylacetate = 30 : 1) gave methylester (+)-**11** (98 mg, 54%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.14-5.06 (m, 1H), 5.03-4.95 (m, 1H), 3.67 (s, 3H), 3.06 (d, *J* = 15.2 Hz, 1H), 3.06-3.01 (b, 1H), 2.92 (d, *J* = 15.6 Hz, 1H), 2.88 (bt, *J* = 7.7 Hz, 1H), 2.61-2.54 (m, 1H), 2.38 (bd, *J* = 18.7 Hz, 1H), 2.28-2.04 (m, 5H), 1.70 (d, *J* = 12.6 Hz, 1H), 1.68-1.63 (m, 1H).

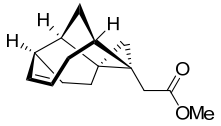
^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.4 (C), 146.7 (C), 132.1 (CH), 127.8 (C), 122.3 (C), 52.7 (CH), 51.8 (CH_3), 47.9 (CH), 42.2 (CH), 38.3 (CH_2), 33.4 (CH_2), 32.8 (CH_2), 29.4 (CH_2), 21.4 (CH_2).

IR [cm^{-1}]: 2931, 1739, 1436, 1271, 1131.

[2] Oisaki, K.; Suto, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.*, **2003**, *125*, 5644–5645.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{14}H_{18}O_2$: 218.1307, found: 218.1303.

$[\alpha]_D^{20}$ = +46.6 (*c* = 0.49, $CHCl_3$)



Tetracyclic ester (+)-**13.** To a solution of methylester (+)-**11** (86 mg, 0.39 mmol, 1 equiv.) in CH_2Cl_2 (7 mL) at 0 °C was added CH_2I_2 (44 µL, 0.55 mmol, 1.4 equiv.), followed by Et_2Zn (1.1 M in toluene, 890 µL, 0.98 mmol, 2.5 equiv.). After stirring for 1.5 h at 0 °C TLC analysis showed complete consumption of the starting material and the reaction was quenched by the addition of saturated aqueous NH_4Cl (2 mL) solution. After stirring for 30 min with saturated aqueous Na/K-Tartrate solution (5 mL), the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were dried over $MgSO_4$ and filtered. Evaporation of the solvent and purification by flash chromatography (hexane : ethylacetate = 30 : 1) afforded tetracyclic ester (+)-**13** (80 mg, 89%) as a colorless oil.

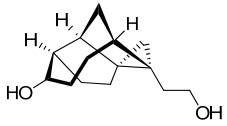
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.34-5.20 (m, 2H), 3.68 (s, 3H), 2.62-2.55 (b, 1H), 2.46 (dd, *J* = 15.4, 1.5 Hz, 1H), 2.46-2.43 (b, 1H), 2.37 (bd, *J* = 17.9 Hz, 1H), 2.29 (t, *J* = 6.2 Hz, 1H), 2.03-1.93 (m, 2H), 1.74-1.64 (m, 2H), 1.59 (d, *J* = 15.7 Hz, 1H), 1.58-1.53 (m, 2H), 1.39 (dt, *J* = 13.1, 9.0 Hz, 1H), 0.71 (dd, *J* = 5.3, 1.5 Hz, 1H), 0.49 (d, *J* = 5.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.1 (C), 133.0 (CH), 123.6 (CH), 51.4 (CH_3), 49.1 (CH), 45.4 (CH), 40.4 (CH), 38.1 (C), 35.6 (C), 33.9 (CH_2), 33.5 (CH_2), 30.3 (CH_2), 28.5 (CH_2), 23.5 (CH_2), 16.6 (CH_2).

IR [cm^{-1}]: 2943, 1743, 1435, 1281, 1160.

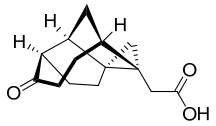
HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{15}H_{20}O_2$: 232.1463, found: 232.1457.

$[\alpha]_D^{20}$ = +90.3 (*c* = 0.88, $CHCl_3$)



Diol (+)-**14.** Tetracyclic ester (+)-**13** (40 mg, 0.17 mmol, 1 equiv.) was treated with DMDO (0.07 M in acetone, 3 mL, 0.21 mmol, 1.2 equiv.) at room temperature for 30 min. The solvent was evaporated to give crude epoxide (dr = 5:1), which was directly used in the next step.

To an ice-cold solution of the epoxide in THF (7 mL) was added LAH (4 M in Et_2O, 344 µL, 1.38 mmol, 8 equiv.) dropwise. The solution was warmed to room temperature within 5 min and heated to 50 °C for 2.5 h. The mixture was cooled to 0 °C, quenched by careful addition of 1% HCl and the aqueous layer was extracted with CH_2Cl_2 (4 x 10 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated. Purification by column chromatography (hexane : ethylacetate = 3 : 1 to 1 : 2) gave diol (+)-**14** (34 mg, 90%, dr = 5:1). Analytical data matched those reported on pp. S17-S18.



Ketoacid (+)-**15**. Diol (+)-**14** (55 mg, 0.25 mmol, 1 equiv.) and IBX (346 mg, 1.24 mmol, 5 equiv.) in DMSO (2 mL) were stirred for 1 h at ambient temperature. The reaction mixture was diluted with Et_2O (50 mL), washed with H_2O (3 x 10 mL) and the aqueous layer was extracted with Et_2O/hexane (1:1, 3 x 10 mL). The combined organic fractions were dried ($MgSO_4$), filtered over a small plug of silica and concentrated.

The crude product was dissolved in *t*-BuOH (2.5 mL), treated with 2-methyl-2-butene (1 mL / mmol, 0.25 mL), and cooled to 5 °C. $NaClO_2$ (419 mg, 3.71 mmol, 15 equiv.) and 419 mg NaH_2PO_4 were dissolved in H_2O (2.5 mL, 1.5 M) and added over a period of 5 min. After 15 min at room temperature TLC analysis showed complete consumption and the reaction mixture was separated between CH_2Cl_2 (50 mL) and brine (20 mL). The aqueous layer was extracted with three portions of CH_2Cl_2 (15 mL) and the combined organic extracts were dried over $MgSO_4$. Evaporation of the solvent gave crude ketoacid, which was purified by flash chromatography (hexane : ethylacetate from 2 : 1 to 1 : 2) to give 41 mg (72 %) of (+)-**15** as a white solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ = 10.5 (b, OH), 2.93 (t, *J* = 8.5 Hz, 1H), 2.63 (dd, *J* = 15.3, 1.7 Hz, 1H), 2.55 (dt, *J* = 7.2, 3.6 Hz, 1H), 2.47-2.42 (m, 1H), 2.40 (t, *J* = 8.1 Hz, 1H), 2.22-2.17 (m,

1H), 2.15-1.96 (m, 4H), 1.82 (d, J = 15.5 Hz, 1H), 1.70-1.63 (m, 2H), 1.59-1.52 (m, 1H), 1.39 (d, J = 14.4 Hz, 1H), 0.84 (dd, J = 5.7, 1.5 Hz, 1H), 0.63 (d, J = 6.0 Hz, 1H).

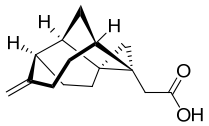
^{13}C NMR (150 MHz, $CDCl_3$) δ = 214.7 (C), 177.5 (C), 55.5 (CH), 46.6 (CH), 39.7 (CH), 35.9 (CH_2), 35.1 (CH_2), 30.5 (CH_2), 30.2 (C), 28.8 (CH_2), 27.8 (CH_2), 25.3 (CH_2), 16.2 (CH_2).

IR [cm^{-1}]: 2943, 1701, 1697, 1459, 1220, 1063.

HRMS (ESI) (m/z): $[M\text{-}H^+]^-$ calcd. for $C_{14}H_{17}O_3$: 233.1178, found: 233.1175.

$[\alpha]_D^{20}$ = +43.8 (c = 1.10, $CHCl_3$)

mp 131-133 °C



Echinopine A (1). To a solution of $MePPh_3Br$ (290 mg, 0.811 mmol, 5 equiv.) in THF (2.7 mL) was added *t*-BuOK at room temperature. After 30 min ketoacid (+)-**15** (38 mg, 0.162 mmol, 1 equiv.) in THF (1 mL, 2 x 0.3 mL rinse) was transferred to the yellow-orange solution *via* syringe. The mixture was refluxed for 45 min, cooled to ambient temperature, diluted with Et_2O (50 mL) and quenched by the addition of 0.1% HCl (10 mL). The phases were separated, the aqueous layer was extracted with Et_2O (4 x 10 mL), the combined organic fractions were dried and concentrated. Purification by column chromatography (hexane : ethylacetate = 3 : 1 to 1 : 1) afforded Echinopine A (**1**) (23 mg, 62%) as a white solid. Crystallization from hexane at ambient temperature afforded crystals suitable for X-ray analysis.

^{1}H NMR (600 MHz, $CDCl_3$) δ = 10.81 (b, OH), 4.64 (d, J = 2.6 Hz, 1H), 4.61 (d, J = 2.6 Hz, 1H), 2.81 (dt, J = 9.3, 2.4 Hz, 1H), 2.67 (dd, J = 15.3, 1.7 Hz, 1H), 2.44 (m, 1H), 2.27 (t, J = 8.1 Hz, 1H), 2.17 (m, 1H), 2.13 (dt, J = 13.2, 4.2 Hz, 1H), 1.96 (m, 1H), 1.94 (m, 1H), 1.83 (dt, J = 13.2, 4.2 Hz, 1H), 1.76 (d, J = 15.5 Hz, 1H), 1.66 (dddd, J = 14.0, 9.7, 6.8, 2.8 Hz, 1H), 1.53 (ddd, J = 13.7, 9.7, 4.1 Hz, 1H), 1.45 (dtd, J = 13.8, 7.6, 1.5 Hz, 1H), 1.37 (d, J = 13.6 Hz, 1H), 1.28 (ddt, J = 13.5, 4.2, 2.6 Hz, 1H), 0.74 (dd, J = 5.3, 1.5 Hz, 1H), 0.51 (d, J = 5.3 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ = 178.6 (C), 154.3 (C), 112.1 (CH_2), 48.7 (CH), 48.5 (CH), 41.4 (C), 40.5 (CH), 35.2 (CH_2), 32.7 (CH_2), 31.0 (CH_2), 30.5 (CH_2), 29.9 (C), 29.4 (CH_2), 25.7 (CH_2), 16.1 (CH_2).

IR [cm^{-1}]: 3064, 2930, 2877, 1702, 1699, 1455, 1306 1131.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{15}H_{20}O_2$: 232.1463, found: 232.1464.

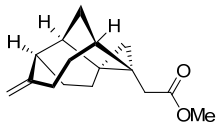
$[\alpha]_D^{22}$ = +26.1 (c = 0.70, $CHCl_3$), lit.[3] **$[\alpha]_D^{22}$** = +23 (c = 0.11, $CHCl_3$)

mp 99-102 °C

[3] Dong, M.; Cong, B.; Yu, S.-H.; Sauriol, F.; Huo, C.-H.; Shi, Q.-W.; Gu, Y.-C.; Zamir, L. O.; Kiyota, H. *Org. Lett.*, **2008**, *10*, 701-704.

Comparison of the NMR Spectral Data of Natural and Synthetic Echinopine A

	Natural ^{1}H-NMR (500 MHz, $CHCl_3$)	Synthetic ^{1}H-NMR (600 MHz, $CHCl_3$)	Natural ^{13}C-NMR (500 MHz, $CHCl_3$)	Synthetic ^{13}C-NMR (600 MHz, $CHCl_3$)
1	2.81 (dt, *J* = 9.1, 2.1 Hz)	2.81 (dt, *J* = 9.3, 2.4 Hz)	48.7	48.7
2a	2.16 (m)	2.17 (m)	31.1	31.0
2b	1.66 (dddd, *J* = 14.0, 9.7, 6.7, 2.6 Hz)	1.66 (dddd, *J* = 14.0, 9.7, 6.8, 2.8 Hz)		
3a	1.95 (m)	1.96 (m)	25.8	25.7
3b	1.52 (ddd, *J* = 13.5, 9.7, 4.9 Hz)	1.53 (ddd, *J* = 13.7, 9.7, 4.1 Hz)		
4			41.5	41.4
5	2.26 (t, *J* = 8.0 Hz)	2.27 (t, *J* = 8.1 Hz)	48.6	48.5
6a	1.44 (dtd, *J* = 13.7, 7.4, 0.9 Hz)	1.45 (dtd, *J* = 13.8, 7.6, 1.5 Hz)	30.5	30.5
6b	1.36 (d, *J* = 13.7 Hz)	1.37 (d, *J* = 13.6 Hz)		
7	2.43 (m)	2.44 (m)	40.6	40.5
8a	1.93 (m)	1.94 (m)	32.8	32.7
8b	1.27 (ddt, J = 13.6, 4.0, 3.0 Hz)	1.28 (ddt, J = 13.5, 4.2, 2.6 Hz)		
9a	2.12 (dt, *J* = 13.3, 4.7 Hz)	2.13 (dt, *J* = 13.2, 4.2 Hz)	29.4	29.9
9b	1.82 (dt, *J* = 13.3, 4.2 Hz)	1.83 (dt, *J* = 13.2, 4.2 Hz)		
10			154.3	154.3
11a	2.66 (dd, *J* = 15.3, 1.3 Hz)	2.67 (dd, *J* = 15.3, 1.7 Hz)	35.2	35.2
11b	1.75 (d, *J* = 15.3 Hz)	1.76 (d, *J* = 15.5 Hz)		
12			178.2	178.6
13			30.0	29.9
14a	4.63 (d, *J* = 2.6 Hz)	4.64 (d, *J* = 2.6 Hz)	112.1	112.1
14b	4.60 (d, *J* = 2.6 Hz)	4.61 (d, *J* = 2.6 Hz)		
15a	0.73 (dd, *J* = 5.3, 1.3 Hz)	0.74 (dd, *J* = 5.3, 1.5 Hz)	16.1	16.1
15b	0.50 (d, *J* = 5.3 Hz)	0.51 (d, *J* = 5.3 Hz)		
OH	10.53 (b)	10.81 (b)		



Echinopine B (2). A solution CH_2N_2 (1 M in Et_2O, 130 µL, 0.13 mmol, 5 equiv.) was added dropwise to Echinopine A (6 mg, 0.026 mmol, 1 equiv.) in Et_2O (1 mL). After 30 min excess CH_2N_2 and solvent was removed under reduced pressure to afford 6 mg (95%) of pure Echinopine B **2** as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ = 4.63 (d, *J* = 2.6 Hz, 1H), 4.61 (d, *J* = 2.6 Hz, 1H), 3.68 (s, 3H), 2.81 (dt, *J* = 9.1, 1.9 Hz, 1H), 2.63 (dd, *J* = 15.0, 1.4 Hz, 1H), 2.39 (m, 1H), 2.26 (t, *J* = 8.1 Hz, 1H), 2.15 (m, 1H), 2.12 (m, 1H), 1.94 (m, 1H), 1.93 (m, 1H), 1.83 (dt, *J* = 13.2, 4.2 Hz, 1H), 1.73 (d, *J* = 15.1 Hz, 1H), 1.65 (dddd, *J* = 14.0, 9.7, 6.7, 2.8 Hz, 1H), 1.53 (ddd, *J* = 13.5, 9.7, 3.9 Hz, 1H), 1.44 (dtd, *J* = 14.0, 7.4, 1.1 Hz, 1H), 1.35 (d, *J* = 13.6 Hz, 1H), 1.26 (ddt, J = 13.5, 4.0, 3.1 Hz, 1H), 0.69 (dd, *J* = 5.3, 1.3 Hz, 1H), 0.47 (d, *J* = 5.3 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ = 173.7 (C), 154.4 (C), 112.0 (CH_2), 51.5 (CH_3), 48.7 (CH), 48.6 (CH), 41.4 (C), 40.6 (CH), 35.3 (CH_2), 32.8 (CH_2), 31.1 (CH_2), 30.5 (CH_2), 30.1 (C), 29.5 (CH_2), 25.7 (CH_2), 16.0 (CH_2).

IR [cm^{-1}]: 2931, 1745, 1636, 1434, 1272, 1166.

HRMS (EI) (m/z): $[M]^+$ calcd. for $C_{16}H_{22}O_2$: 246.1620, found: 246.1611.

$[\alpha]_D^{22}$ = +21.6 (*c* = 0.60, $CHCl_3$), lit.[3] **$[\alpha]_D^{22}$** = +21 (*c* = 0.14, $CHCl_3$)

Comparison of the NMR Spectral Data of Natural and Synthetic Echinopine B

	Natural ^{1}H-NMR (500 MHz, $CHCl_3$)	Synthetic ^{1}H-NMR (600 MHz, $CHCl_3$)	Natural ^{13}C-NMR (500 MHz, $CHCl_3$)	Synthetic ^{13}C-NMR (600 MHz, $CHCl_3$)
1	2.80 (bt, *J* = 10 Hz)	2.81 (dt, *J* = 9.3, 2.4 Hz)	48.5	48.7
2a	2.14 (m)	2.15 (m)	30.9	31.1
2b	1.65 (m)	1.65 (dddd, *J* = 14.0, 9.7, 6.7, 2.8 Hz)		
3a	1.93 (m)	1.93 (m)	25.4	25.7
3b	1.51 (m)	1.53 (ddd, *J* = 13.5, 9.7, 3.9 Hz)		
4			29.8	30.1
5	2.25 (t, *J* = 9 Hz)	2.26 (t, *J* = 8.1 Hz)	48.4	48.6
6a	1.44 (m)	1.45 (dtd, *J* = 14.0, 7.4, 1.1 Hz)	30.3	30.5
6b	1.35 (d, *J* = 13.8 Hz)	1.35 (d, *J* = 13.6 Hz)		
7	2.39 (m)	2.39 (m)	40.4	40.6
8a	1.93 (m)	1.94 (m)	32.5	32.8
8b	1.26 (m)	1.26 (ddt, J = 13.5, 4.0, 3.1 Hz)		
9a	2.11 (m)	2.12 (m)	29.3	29.5
9b	1.82 (dt, *J* = 13.2, 4.0 Hz)	1.83 (dt, *J* = 13.2, 4.2 Hz)		
10			154.3	154.4
11a	2.65 (dd, *J* = 15.1, 1.3 Hz)	2.63 (dd, *J* = 15.0, 1.4 Hz)	35.1	35.3
11b	1.72 (d, *J* = 15.1 Hz)	1.73 (d, *J* = 15.2 Hz)		
12			173.7	173.7
13			41.0	41.3
14a	4.63 (d, *J* = 2.6 Hz)	4.63 (d, *J* = 2.6 Hz)	111.9	112.0
14b	4.60 (d, *J* = 2.6 Hz)	4.61 (d, *J* = 2.6 Hz)		
15a	0.69 (dd, *J* = 5.1, 1.3 Hz)	0.69 (dd, *J* = 5.3, 1.3 Hz)	15.7	16.0
15b	0.47 (d, *J* = 5.1 Hz)	0.47 (d, *J* = 5.3 Hz)		
OMe	3.68 (s)	3.68 (s)	51.3	51.5

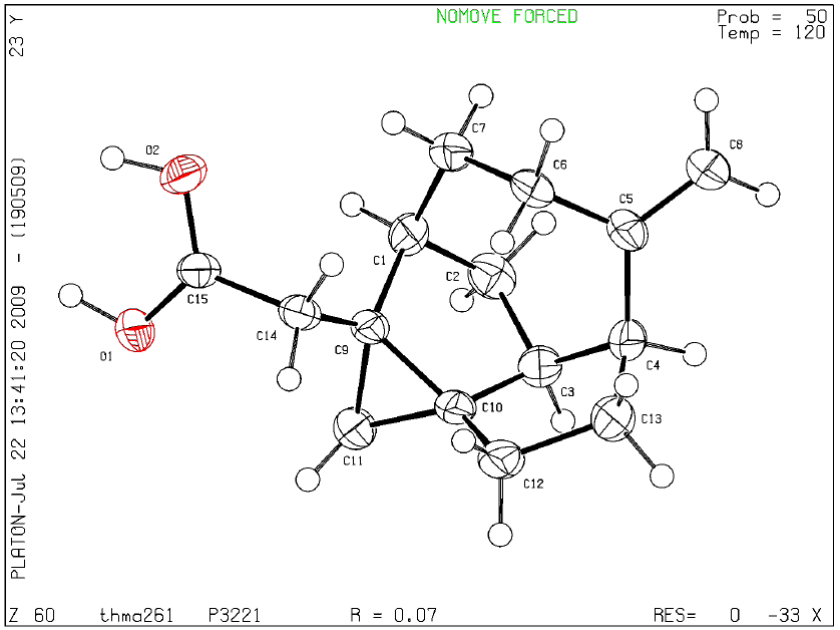
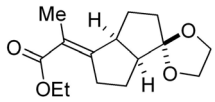
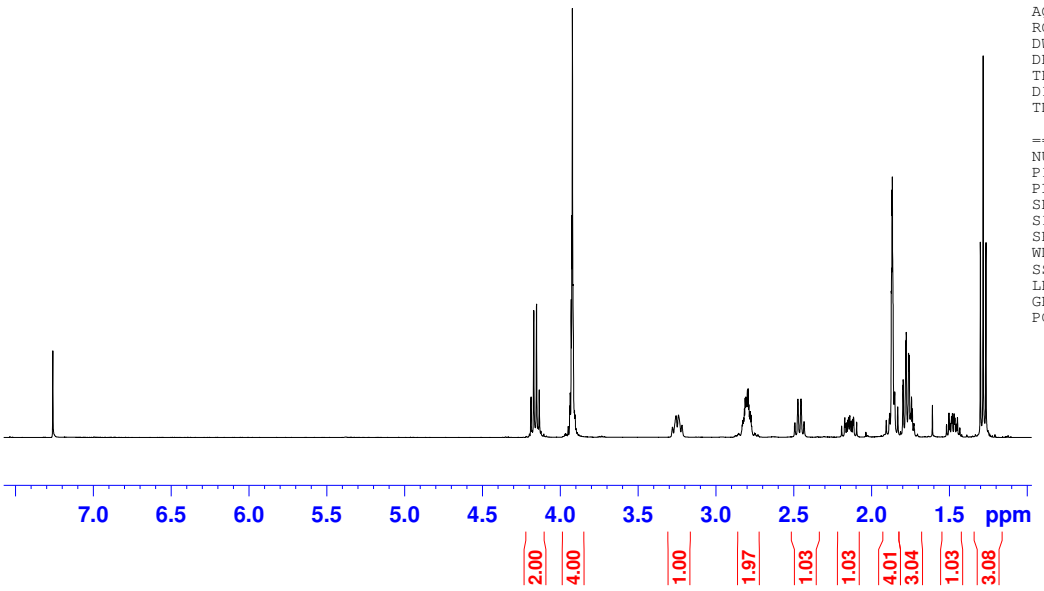


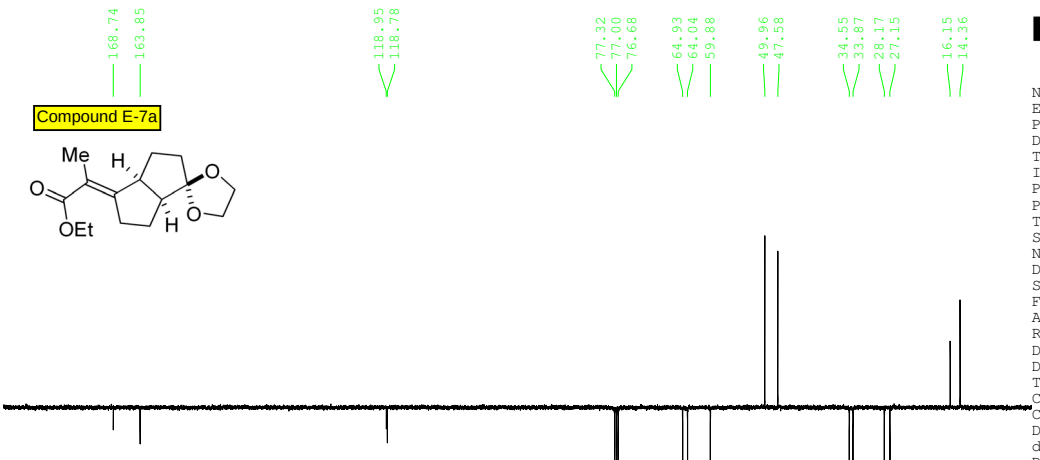
Figure 1: ORTEP view of Echinopine A with labeling scheme. The thermal ellipsoids are drawn at 50% probability level.

Compound E-7a





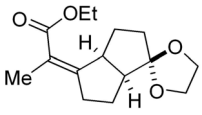

```
NAME            THMA E067
EXPNO                  10
PROCNO                  1
Date_            20090403
Time                14.17
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9584243 sec
RG                  161.3
DW                 60.400 usec
DE                  6.00 usec
TE                 300.2 K
D1            1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300094 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

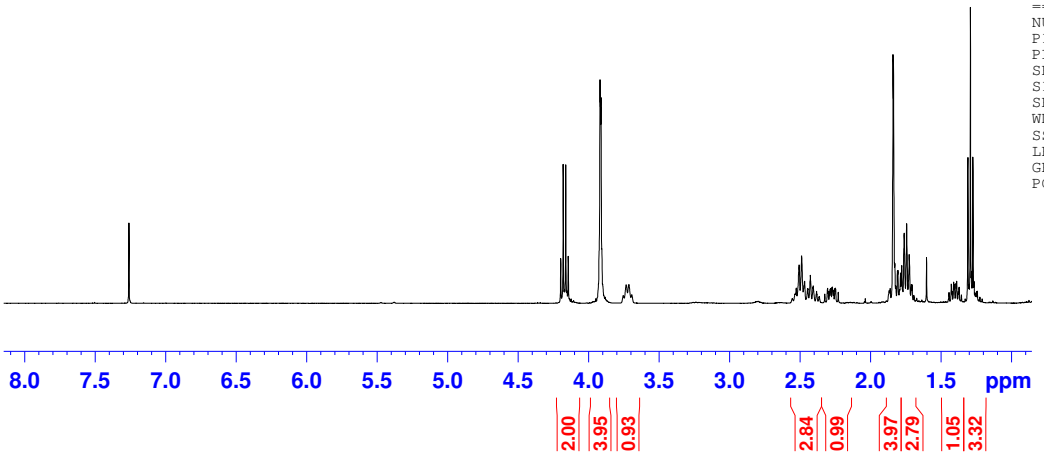


Compound E-7a


```
NAME            THMA E067
EXPNO                  11
PROCNO                  1
Date_            20090403
Time                15.26
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1200
DS                       2
SWH            25062.656 Hz
FIDRES          0.382426 Hz
AQ              1.3074932 sec
RG                 5160.6
DW                 19.950 usec
DE                  6.00 usec
TE                 300.2 K
CNST2         145.0000000
CNST11          1.0000000
D1            2.00000000 sec
d20           0.00689655 sec
DELTA         0.00001311 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127704 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

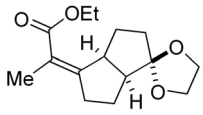
Compound Z-7a





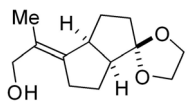

```
NAME            THMA E067
EXPNO                  20
PROCNO                  1
Date_            20090404
Time                2.39
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                    181
DW                 60.400 usec
DE                  6.00 usec
TE                 300.2 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1          400.1324710 MHz
SI                  32768
SF            400.1300092 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

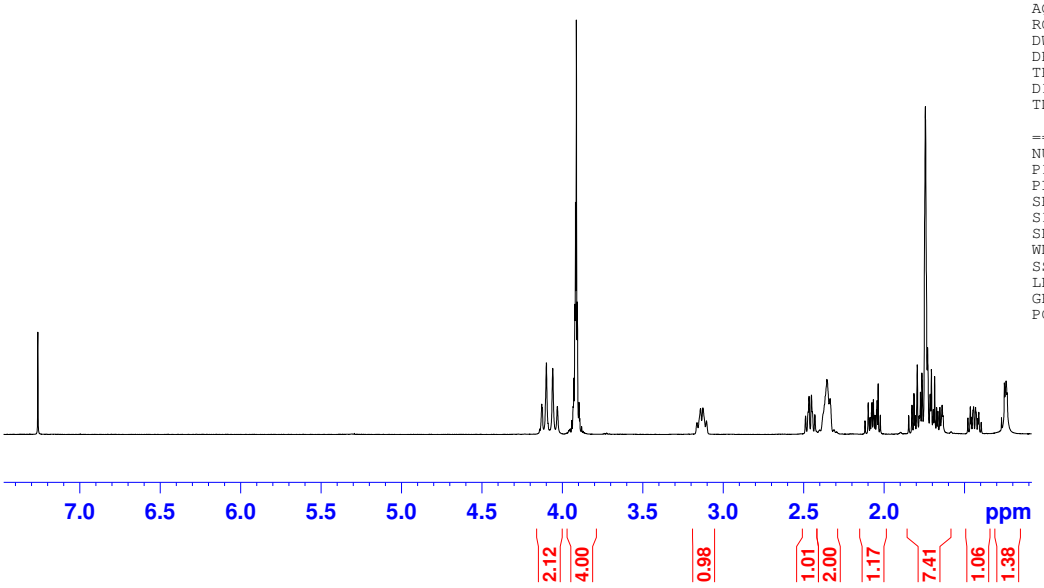
Compound Z-7a




```
NAME            THMA E067
EXPNO                  21
PROCNO                  1
Date_            20090404
Time                3.46
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG              jmod
TD                  65536
SOLVENT             CDCl3
NS                   1200
DS                      2
SWH              25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                   4096
DW                 19.950 usec
DE                  6.00 usec
TE                 300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                   1H
PCPD2             100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2          400.1316005 MHz
SI                  32768
SF            100.6127701 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   3.00
```

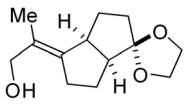
Compound E-8a





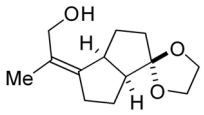

```
NAME            THMA E079
EXPNO                  30
PROCNO                  1
Date_            20090404
Time                5.47
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                   161.3
DW                60.400 usec
DE                 6.00 usec
TE                 300.2 K
D1            1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  8.75 usec
PL1                -3.00 dB
SFO1         400.1324710 MHz
SI                  32768
SF           400.1300092 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.00
```

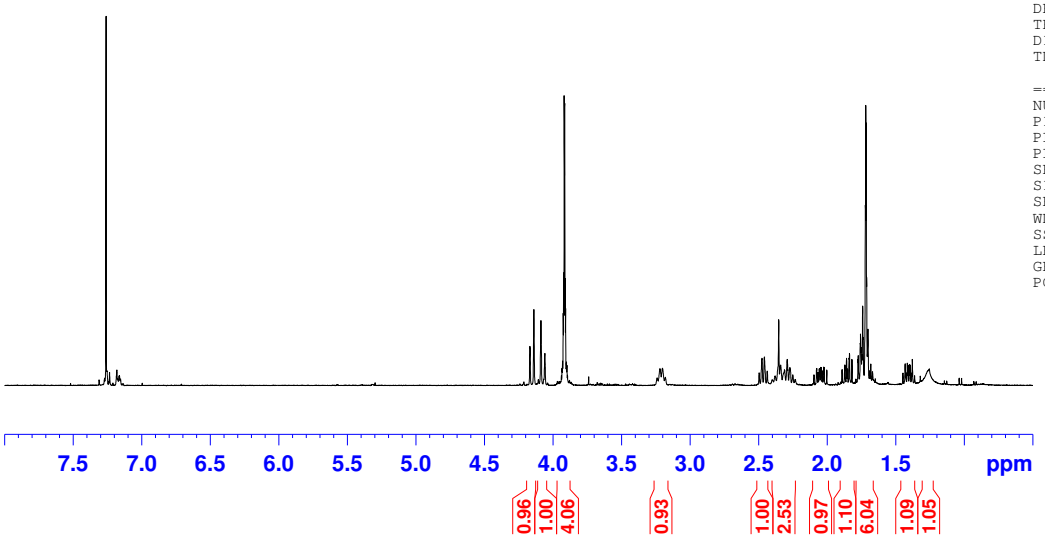
Compound E-8a




```
NAME            THMA E079
EXPNO                  31
PROCNO                  1
Date_            20090404
Time                6.55
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG             jmod
TD                  65536
SOLVENT             CDCl3
NS                   1200
DS                      2
SWH             25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                   3251
DW                19.950 usec
DE                 6.00 usec
TE                 300.2 K
CNST2         145.0000000
CNST11          1.0000000
D1            2.00000000 sec
d20           0.00689655 sec
DELTA         0.00001311 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 10.30 usec
p2                 20.60 usec
PL1                -1.00 dB
SFO1         100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                   1H
PCPD2             100.00 usec
PL2                -3.00 dB
PL12               16.00 dB
SFO2         400.1316005 MHz
SI                  32768
SF           100.6127706 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                   3.00
```

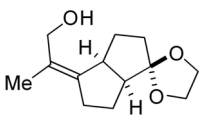
Compound Z-8a





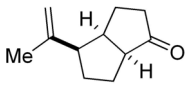

```
NAME            THMAE KTE7
EXPNO                340
PROCNO                 1
Date_           20090407
Time               17.21
INSTRUM         AVIII400
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                      4
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                    575
DW                 60.800 usec
DE                  6.50 usec
TE                 298.2 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  13.50 usec
PL1                 -1.80 dB
PL1W           15.28361320 W
SFO1           400.2724718 MHz
SI                  32768
SF             400.2700104 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

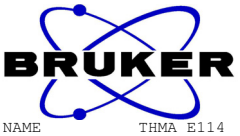
Compound Z-8a



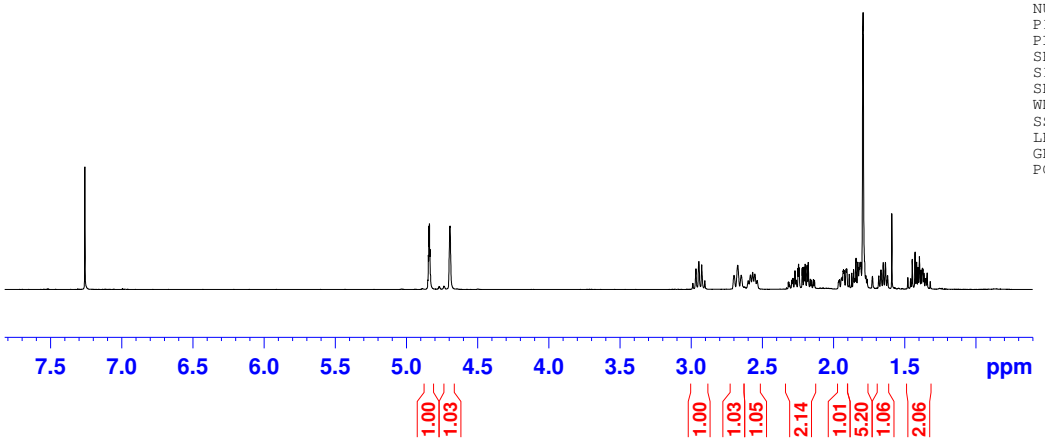

```
NAME            THMAE KTE7
EXPNO                171
PROCNO                 1
Date_           20090721
Time                3.11
INSTRUM         AVIII400
PROBHD   5 mm PABBO BB-
PULPROG             jmod
TD                  65536
SOLVENT             CDCl3
NS                   7000
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                   2050
DW                 20.800 usec
DE                  6.50 usec
TE                 298.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
D20              0.00689655 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.00 usec
P2                  20.00 usec
PL1                 -1.50 dB
PL1W           47.89980698 W
SFO1           100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                 -1.80 dB
PL12                14.70 dB
PL2W           15.28361320 W
PL12W           0.34215751 W
SFO2           400.2716011 MHz
SI                  32768
SF             100.6479720 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

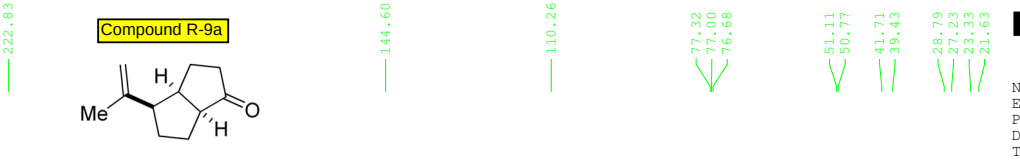
Compound R-9a





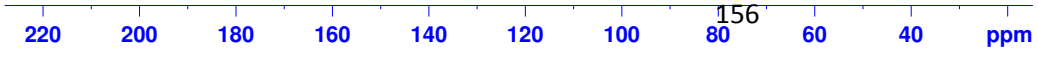
```
NAME            THMA E114
EXPNO                20
PROCNO                1
Date_          20090430
Time              21.47
INSTRUM        avance400
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9584243 sec
RG                   181
DW                60.400 usec
DE                 6.00 usec
TE                300.2 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                 8.75 usec
PL1               -3.00 dB
SFO1         400.1324710 MHz
SI                32768
SF           400.1300094 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



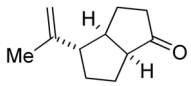


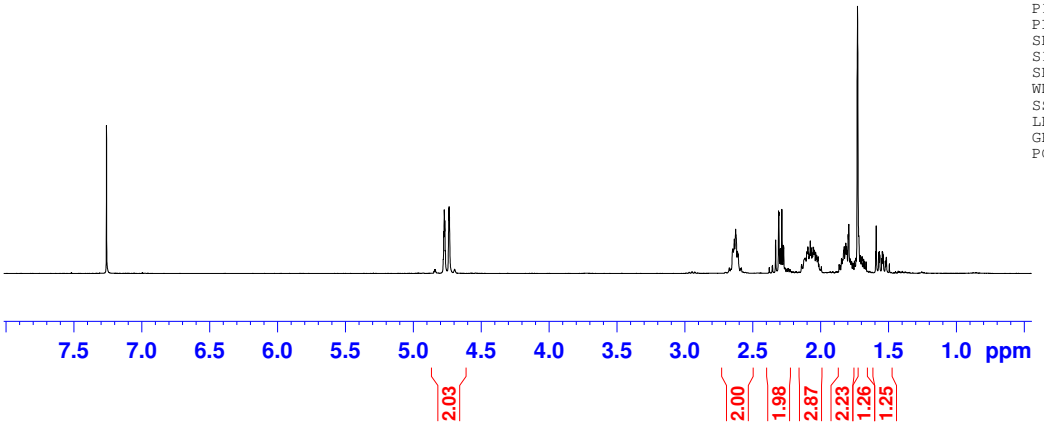
Compound R-9a

```
NAME            THMA E114
EXPNO                21
PROCNO                1
Date_          20090430
Time              22.44
INSTRUM        avance400
PROBHD   5 mm BBO BB-1H
PULPROG             jmod
TD                 65536
SOLVENT            CDCl3
NS                  1000
DS                     2
SWH            25062.656 Hz
FIDRES          0.382426 Hz
AQ              1.3074932 sec
RG                  8192
DW                19.950 usec
DE                 6.00 usec
TE                300.2 K
CNST2        145.0000000
CNST11         1.0000000
D1           2.00000000 sec
d20          0.00689655 sec
DELTA        0.00001311 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                10.30 usec
p2                20.60 usec
PL1               -1.00 dB
SFO1         100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             100.00 usec
PL2                -3.00 dB
PL12               16.00 dB
SFO2         400.1316005 MHz
SI                32768
SF           100.6127702 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.80
```



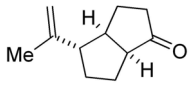
Compound S-9a





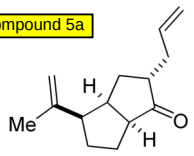

```
NAME            THMA E114
EXPNO                  30
PROCNO                  1
Date_            20090501
Time                0.44
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                   203.2
DW                  60.400 usec
DE                   6.00 usec
TE                  300.2 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1          400.1324710 MHz
SI                  32768
SF            400.1300094 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

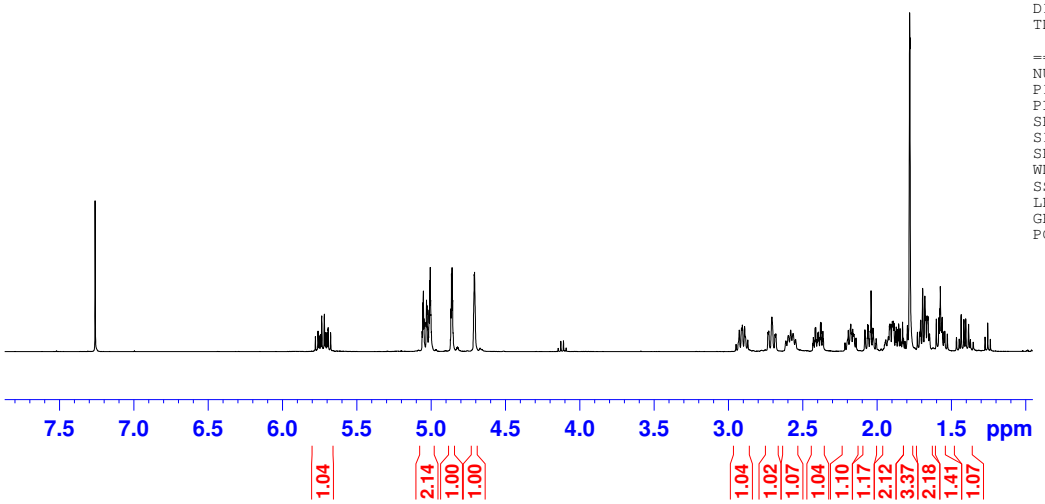
Compound S-9a




```
NAME            THMA E114
EXPNO                  31
PROCNO                  1
Date_            20090501
Time                1.41
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG              jmod
TD                  65536
SOLVENT             CDCl3
NS                   1000
DS                      2
SWH              25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                 14596.5
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2          400.1316005 MHz
SI                  32768
SF            100.6127701 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00
```

Compound 5a



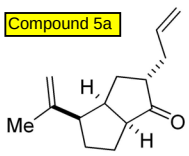


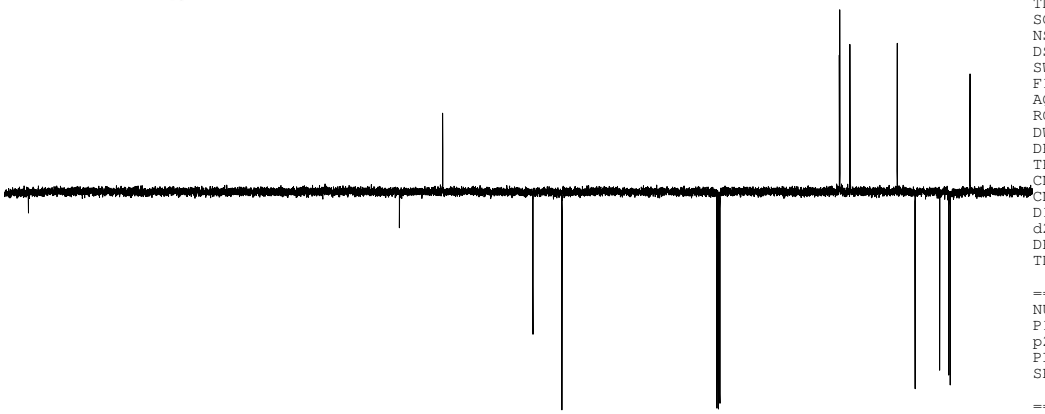
BRUKER

```
NAME                KTE 10F3
EXPNO                     80
PROCNO                     1
Date_               20090418
Time                    5.22
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8278.146 Hz
FIDRES              0.126314 Hz
AQ                  3.9584243 sec
RG                       181
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1              400.1324710 MHz
SI                     32768
SF                400.1300094 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

223.92
144.90
135.68
116.52
110.33
77.32
77.00
76.68
51.24
51.15
48.99
38.91
35.11
29.86
27.95
27.63
23.42

Compound 5a

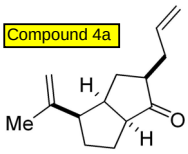


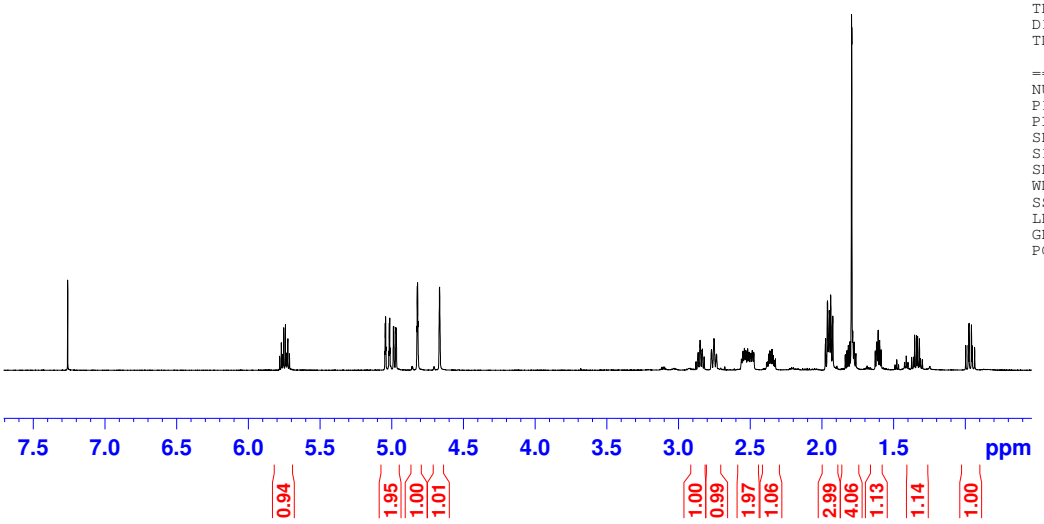


BRUKER

```
NAME                KTE 10F3
EXPNO                     81
PROCNO                     1
Date_               20090418
Time                    6.19
INSTRUM             avance400
PROBHD   5 mm BBO BB-1H
PULPROG                 jmod
TD                     65536
SOLVENT                CDCl3
NS                      1000
DS                         2
SWH                25062.656 Hz
FIDRES              0.382426 Hz
AQ                  1.3074932 sec
RG                    9195.2
DW                    19.950 usec
DE                     6.00 usec
TE                    300.2 K
CNST2              145.0000000
CNST11               1.0000000
D1                 2.00000000 sec
d20                0.00689655 sec
DELTA              0.00001311 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                    10.30 usec
p2                    20.60 usec
PL1                   -1.00 dB
SFO1              100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                100.00 usec
PL2                   -3.00 dB
PL12                  16.00 dB
SFO2              400.1316005 MHz
SI                     32768
SF                100.6127698 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

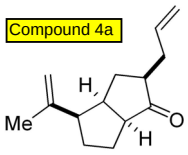
Compound 4a





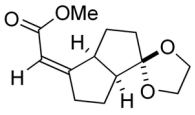

```
NAME            THMA E098
EXPNO                  10
PROCNO                  1
Date_            20090423
Time                14.05
INSTRUM         avance600
PROBHD   5 mm PAQNP Swi
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH             12376.237 Hz
FIDRES          0.188846 Hz
AQ              2.6477449 sec
RG                    181
DW                 40.400 usec
DE                  6.00 usec
TE                 298.1 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  13.85 usec
PL1                 -6.00 dB
SFO1          600.1337060 MHz
SI                  32768
SF            600.1300174 MHz
WDW                    no
SSB                     0
LB                   0.00 Hz
GB                      0
PC                   1.00
```

Compound 4a



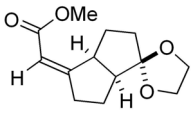

```
NAME            THMA E098
EXPNO                  11
PROCNO                  1
Date_            20090423
Time                16.10
INSTRUM         avance600
PROBHD   5 mm PAQNP Swi
PULPROG              jmod
TD                  65536
SOLVENT             CDCl3
NS                   2500
DS                      4
SWH             35971.223 Hz
FIDRES          0.548877 Hz
AQ              0.9110143 sec
RG                 2298.8
DW                 13.900 usec
DE                  6.00 usec
TE                 298.1 K
CNST2         145.0000000
CNST11          1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00000828 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                   6.50 usec
p2                  13.00 usec
PL1                  0.00 dB
SFO1          150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                 -6.00 dB
PL12                12.20 dB
SFO2          600.1324005 MHz
SI                  32768
SF            150.9028143 MHz
WDW                    no
SSB                     0
LB                   0.00 Hz
GB                      0
PC                   6.00
```

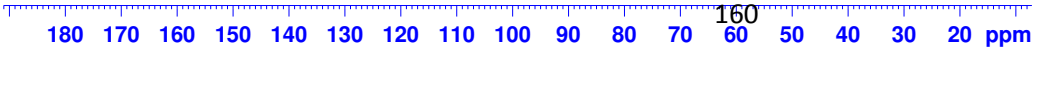
Compound 7b




```
NAME          THMA E236-F1
EXPNO                   20
PROCNO                   1
Date_             20090717
Time                 11.06
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    143.7
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300092 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

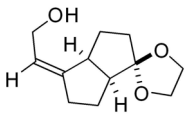
Compound 7b





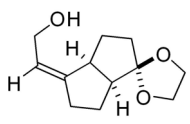

```
NAME          THMA E236-F1
EXPNO                   21
PROCNO                   1
Date_             20090717
Time                 11.58
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                     931
DS                       2
SWH              25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                   9195.2
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1             2.00000000 sec
d20            0.00689655 sec
DELTA          0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127702 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    3.00
```

Compound 8b



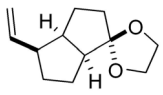

```
NAME            THMA E263
EXPNO                 270
PROCNO                  1
Date_            20090717
Time                14.33
INSTRUM          AVIII400
PROBHD   5 mm PABBO BB-
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                     575
DW                60.800 usec
DE                 6.50 usec
TE                298.2 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  13.50 usec
PL1                 -1.80 dB
PL1W           15.28361320 W
SFO1           400.2724718 MHz
SI                   32768
SF             400.2700105 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

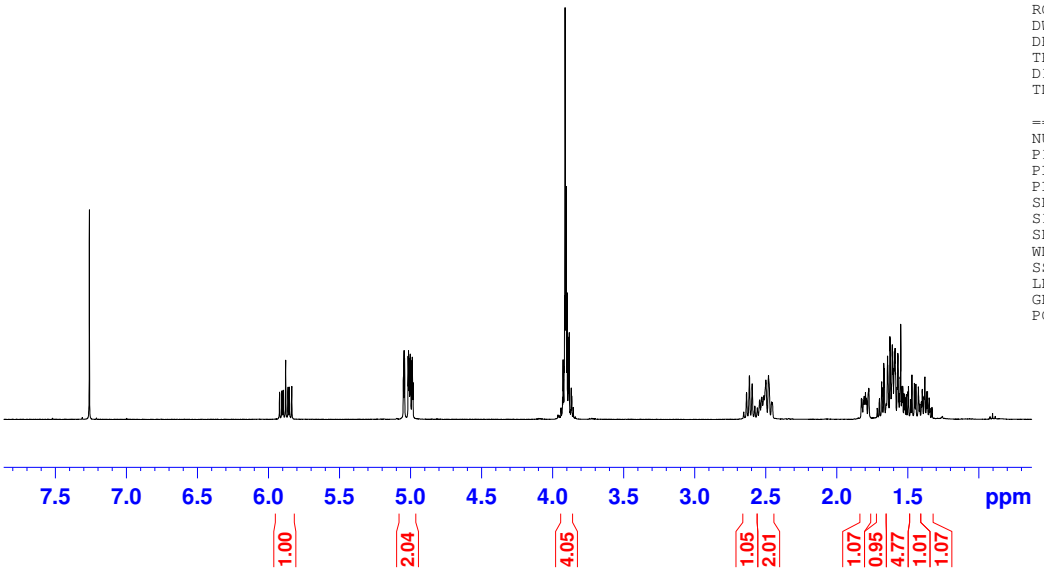
Compound 8b




```
NAME            THMA E263
EXPNO                 271
PROCNO                  1
Date_            20090718
Time                 2.14
INSTRUM          AVIII400
PROBHD   5 mm PABBO BB-
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    6000
DS                       4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    2050
DW                20.800 usec
DE                 6.50 usec
TE                298.2 K
CNST2          145.0000000
CNST11           1.0000000
D1             2.00000000 sec
D20            0.00689655 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.00 usec
P2                  20.00 usec
PL1                 -1.50 dB
PL1W           47.89980698 W
SFO1           100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                 -1.80 dB
PL12                14.70 dB
PL2W           15.28361320 W
PL12W           0.34215751 W
SFO2           400.2716011 MHz
SI                   32768
SF             100.6479720 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   2.00
```

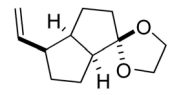
Compound S-16





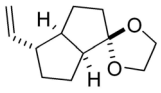

```
NAME          THMA E242AB
EXPNO             210
PROCNO              1
Date_        20090702
Time            15.22
INSTRUM       AVIII400
PROBHD   5 mm PABBO BB-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.125483 Hz
AQ           3.9846387 sec
RG                 406
DW              60.800 usec
DE               6.50 usec
TE              298.2 K
D1           1.00000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1                1H
P1               13.50 usec
PL1              -1.80 dB
PL1W        15.28361320 W
SFO1       400.2724718 MHz
SI               32768
SF         400.2700105 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```

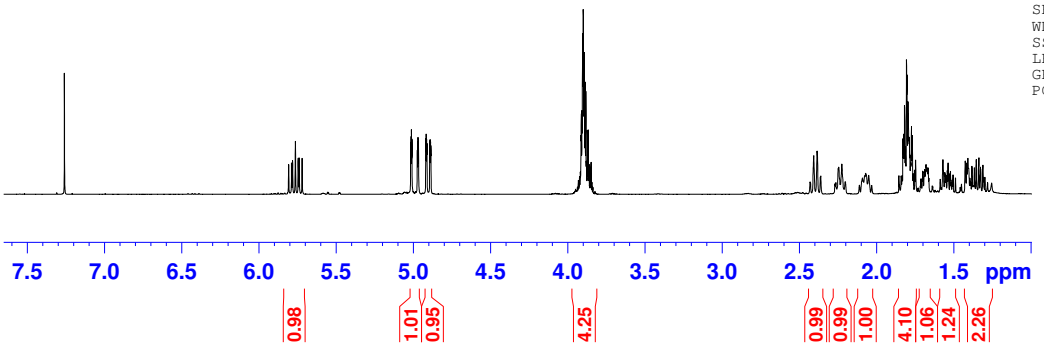
Compound S-16




```
NAME          THMA E242AB
EXPNO             211
PROCNO              1
Date_        20090703
Time            0.01
INSTRUM       AVIII400
PROBHD   5 mm PABBO BB-
PULPROG           jmod
TD               65536
SOLVENT          CDCl3
NS                3000
DS                   4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ           1.3631988 sec
RG                2050
DW              20.800 usec
DE               6.50 usec
TE              298.2 K
CNST2       145.0000000
CNST11        1.0000000
D1           2.00000000 sec
D20          0.00689655 sec
TD0                 1

======== CHANNEL f1 ========
NUC1                13C
P1               10.00 usec
P2               20.00 usec
PL1              -1.50 dB
PL1W        47.89980698 W
SFO1       100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                1H
PCPD2           100.00 usec
PL2              -1.80 dB
PL12             14.70 dB
PL2W        15.28361320 W
PL12W        0.34215751 W
SFO2       400.2716011 MHz
SI               32768
SF         100.6479720 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

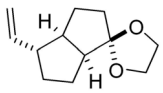
Compound R-16





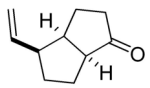

```
NAME            THMA E242AB
EXPNO                   220
PROCNO                    1
Date_            20090702
Time                 15.27
INSTRUM          AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               8223.685 Hz
FIDRES            0.125483 Hz
AQ               3.9846387 sec
RG                      181
DW                 60.800 usec
DE                  6.50 usec
TE                 298.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.50 usec
PL1                  -1.80 dB
PL1W           15.28361320 W
SFO1           400.2724718 MHz
SI                    32768
SF             400.2700107 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

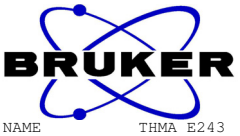
Compound R-16



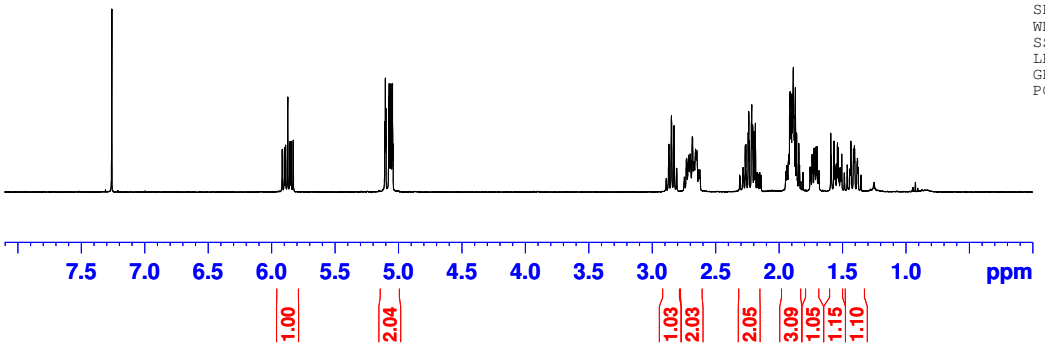

```
NAME            THMA E242AB
EXPNO                   222
PROCNO                    1
Date_            20090703
Time                  2.55
INSTRUM          AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     3000
DS                        4
SWH              24038.461 Hz
FIDRES            0.366798 Hz
AQ               1.3631988 sec
RG                     2050
DW                 20.800 usec
DE                  6.50 usec
TE                 298.2 K
CNST2          145.0000000
CNST11           1.0000000
D1              2.00000000 sec
D20             0.00689655 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.00 usec
P2                   20.00 usec
PL1                  -1.50 dB
PL1W           47.89980698 W
SFO1           100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                  -1.80 dB
PL12                 14.70 dB
PL2W           15.28361320 W
PL12W           0.34215751 W
SFO2           400.2716011 MHz
SI                    32768
SF             100.6479720 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    5.00
```

Compound 9b

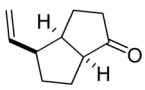




```
NAME              THMA E243
EXPNO                   280
PROCNO                    1
Date_              20090702
Time                  19.06
INSTRUM           AVIII400
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                        1
DS                        2
SWH                8223.685 Hz
FIDRES             0.125483 Hz
AQ                 3.9846387 sec
RG                      322
DW                   60.800 usec
DE                    6.50 usec
TE                   298.3 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    13.50 usec
PL1                   -1.80 dB
PL1W             15.28361320 W
SFO1             400.2724718 MHz
SI                      32768
SF               400.2700107 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

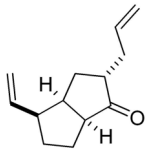


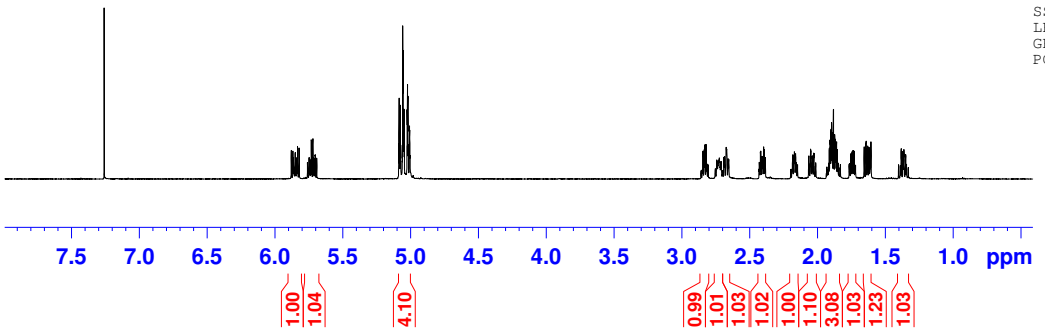
Compound 9b



```
NAME              THMA E243
EXPNO                   281
PROCNO                    1
Date_              20090703
Time                  4.52
INSTRUM           AVIII400
PROBHD   5 mm PABBO BB-
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     2000
DS                        4
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                     2050
DW                   20.800 usec
DE                    6.50 usec
TE                   298.2 K
CNST2            145.0000000
CNST11             1.0000000
D1                 2.00000000 sec
D20                0.00689655 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    10.00 usec
P2                    20.00 usec
PL1                   -1.50 dB
PL1W             47.89980698 W
SFO1             100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                100.00 usec
PL2                   -1.80 dB
PL12                  14.70 dB
PL2W             15.28361320 W
PL12W             0.34215751 W
SFO2             400.2716011 MHz
SI                      32768
SF               100.6479732 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     4.00
```

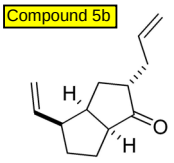
Compound 5b





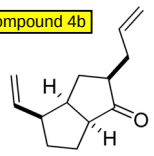

```
NAME            THMA E152
EXPNO                20
PROCNO                1
Date_          20090519
Time               1.34
INSTRUM       avance600
PROBHD   5 mm PAQNP Swi
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH           12376.237 Hz
FIDRES         0.188846 Hz
AQ            2.6477449 sec
RG                   181
DW                40.400 usec
DE                 6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 13.85 usec
PL1                -6.00 dB
SFO1         600.1337060 MHz
SI                 32768
SF           600.1300174 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00
```

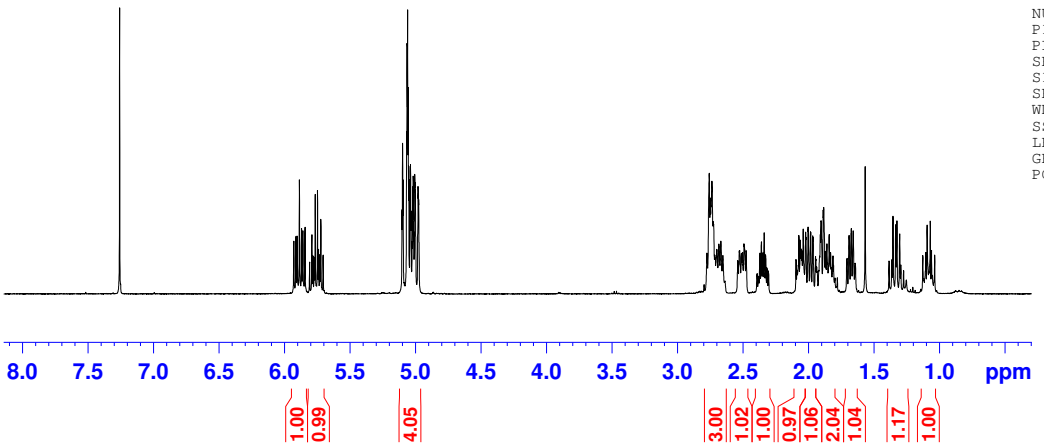
Compound 5b




```
NAME            THMA E152
EXPNO                25
PROCNO                1
Date_          20090519
Time               4.35
INSTRUM       avance600
PROBHD   5 mm PAQNP Swi
PULPROG             jmod
TD                 65536
SOLVENT            CDCl3
NS                  1200
DS                     4
SWH           35971.223 Hz
FIDRES         0.548877 Hz
AQ            0.9110143 sec
RG                  2048
DW                13.900 usec
DE                 6.00 usec
TE                298.1 K
CNST2        145.0000000
CNST11         1.0000000
D1           2.00000000 sec
d20          0.00689655 sec
DELTA        0.00000828 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                 6.50 usec
p2                13.00 usec
PL1                0.00 dB
SFO1         150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                -6.00 dB
PL12               12.20 dB
SFO2         600.1324005 MHz
SI                 32768
SF           150.9028144 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  3.00
```

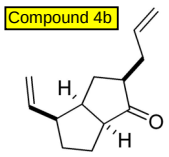
Compound 4b

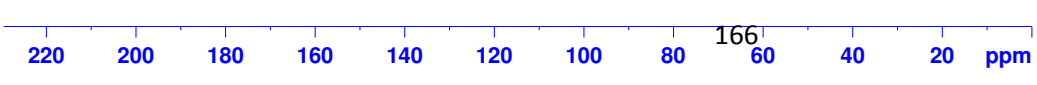





```
NAME          THMA E245-F1
EXPNO                   20
PROCNO                   1
Date_             20090710
Time                 12.59
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                    287.4
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1           400.1324710 MHz
SI                   32768
SF             400.1300093 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

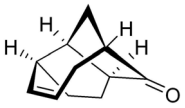
Compound 4b

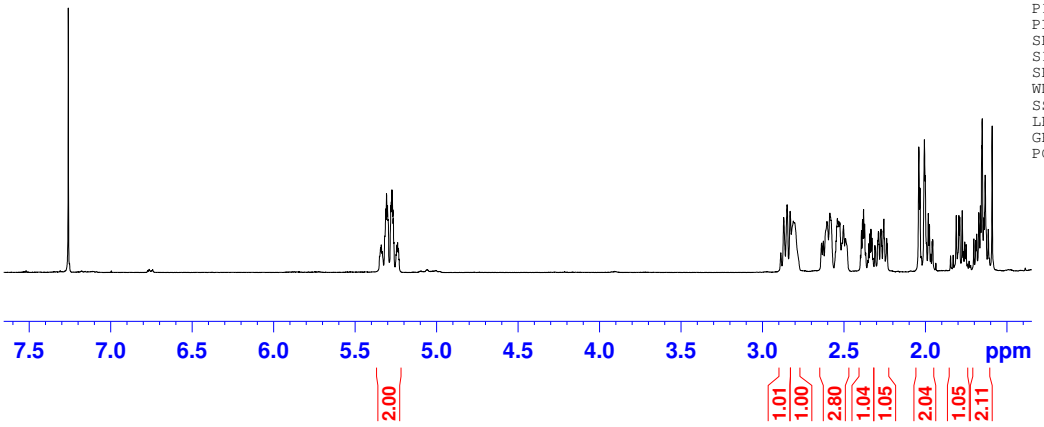





```
NAME          THMA E245-F1
EXPNO                   21
PROCNO                   1
Date_             20090710
Time                 13.02
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1000
DS                       2
SWH              25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                    8192
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1           100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                    1H
PCPD2                100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2           400.1316005 MHz
SI                   32768
SF             100.6127699 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    3.00
```

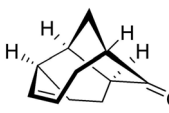
Compound 3b





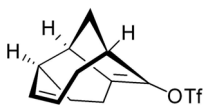

```
NAME            THMA E163
EXPNO                  20
PROCNO                  1
Date_            20090527
Time                10.24
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                   203.2
DW                  60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300093 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

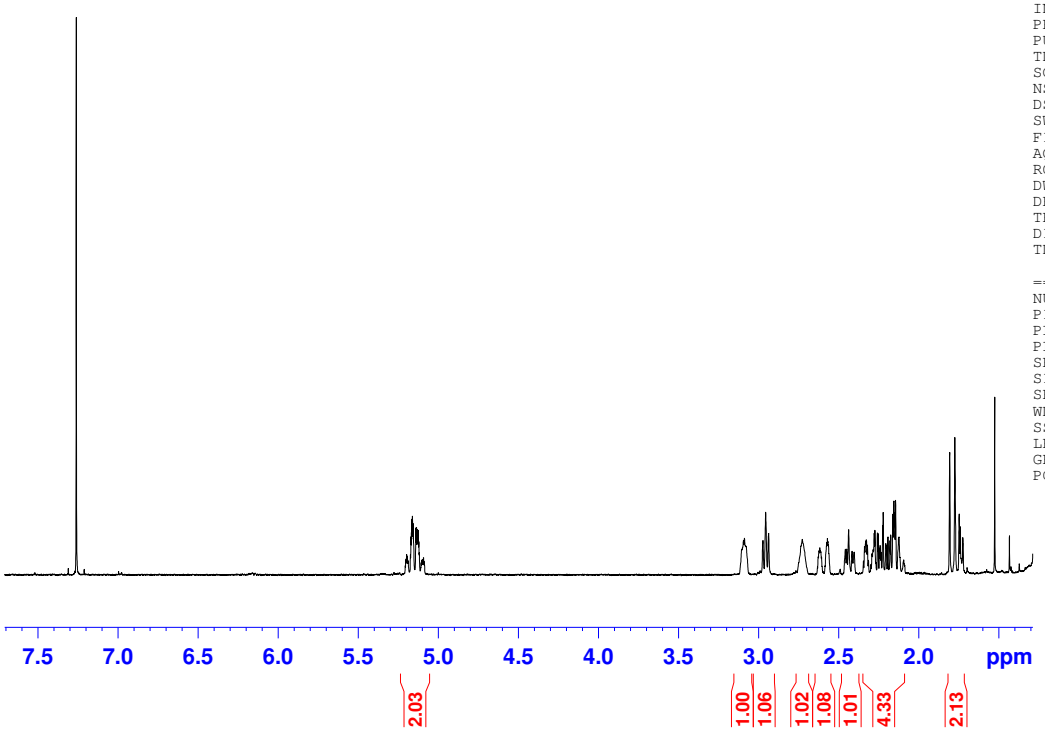
Compound 3b




```
NAME            THMA E163
EXPNO                  21
PROCNO                  1
Date_            20090527
Time                10.43
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1600
DS                       2
SWH             25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                  9195.2
DW                  19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1             2.00000000 sec
d20            0.00689655 sec
DELTA          0.00001311 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127707 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   8.00
```

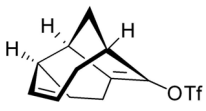
Compound 17





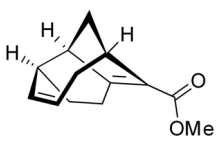

```
NAME            THMA E251
EXPNO                 220
PROCNO                  1
Date_            20090707
Time                14.57
INSTRUM          AVIII400
PROBHD   5 mm PABBO BB-
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       1
DS                       2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                     575
DW                60.800 usec
DE                 6.50 usec
TE                298.2 K
D1            1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.50 usec
PL1                  -1.80 dB
PL1W          15.28361320 W
SFO1          400.2724718 MHz
SI                   32768
SF            400.2700105 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

Compound 17



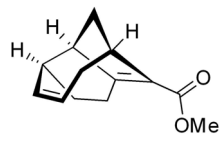

```
NAME            THMA E251
EXPNO                 221
PROCNO                  1
Date_            20090708
Time                4.11
INSTRUM          AVIII400
PROBHD   5 mm PABBO BB-
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    4000
DS                       4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    2050
DW                20.800 usec
DE                 6.50 usec
TE                298.2 K
CNST2         145.0000000
CNST11          1.0000000
D1            2.00000000 sec
D20           0.00689655 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.00 usec
P2                   20.00 usec
PL1                  -1.50 dB
PL1W          47.89980698 W
SFO1          100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                  -1.80 dB
PL12                 14.70 dB
PL2W          15.28361320 W
PL12W          0.34215751 W
SFO2          400.2716011 MHz
SI                   32768
SF            100.6479720 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   3.40
```

Compound 18



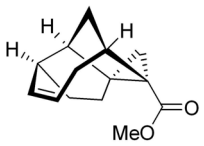

```
NAME              THMA E175
EXPNO                   430
PROCNO                    1
Date_              20090530
Time                  18.43
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                      256
DS                        2
SWH                8278.146 Hz
FIDRES             0.126314 Hz
AQ                 3.9584243 sec
RG                     456.1
DW                    60.400 usec
DE                     6.00 usec
TE                    300.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           400.1324710 MHz
SI                    32768
SF             400.1300094 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Compound 18



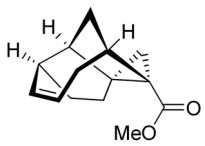

```
NAME              THMA E252
EXPNO                   431
PROCNO                    1
Date_              20090708
Time                   7.05
INSTRUM          AVIII400
PROBHD    5 mm PABBO BB-
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     3000
DS                        4
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                     2050
DW                    20.800 usec
DE                     6.50 usec
TE                    298.2 K
CNST2          145.0000000
CNST11           1.0000000
D1              2.00000000 sec
D20             0.00689655 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    10.00 usec
P2                    20.00 usec
PL1                   -1.50 dB
PL1W           47.89980698 W
SFO1           100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                100.00 usec
PL2                   -1.80 dB
PL12                  14.70 dB
PL2W           15.28361320 W
PL12W           0.34215751 W
SFO2           400.2716011 MHz
SI                    32768
SF             100.6479720 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.60
```

Compound 10

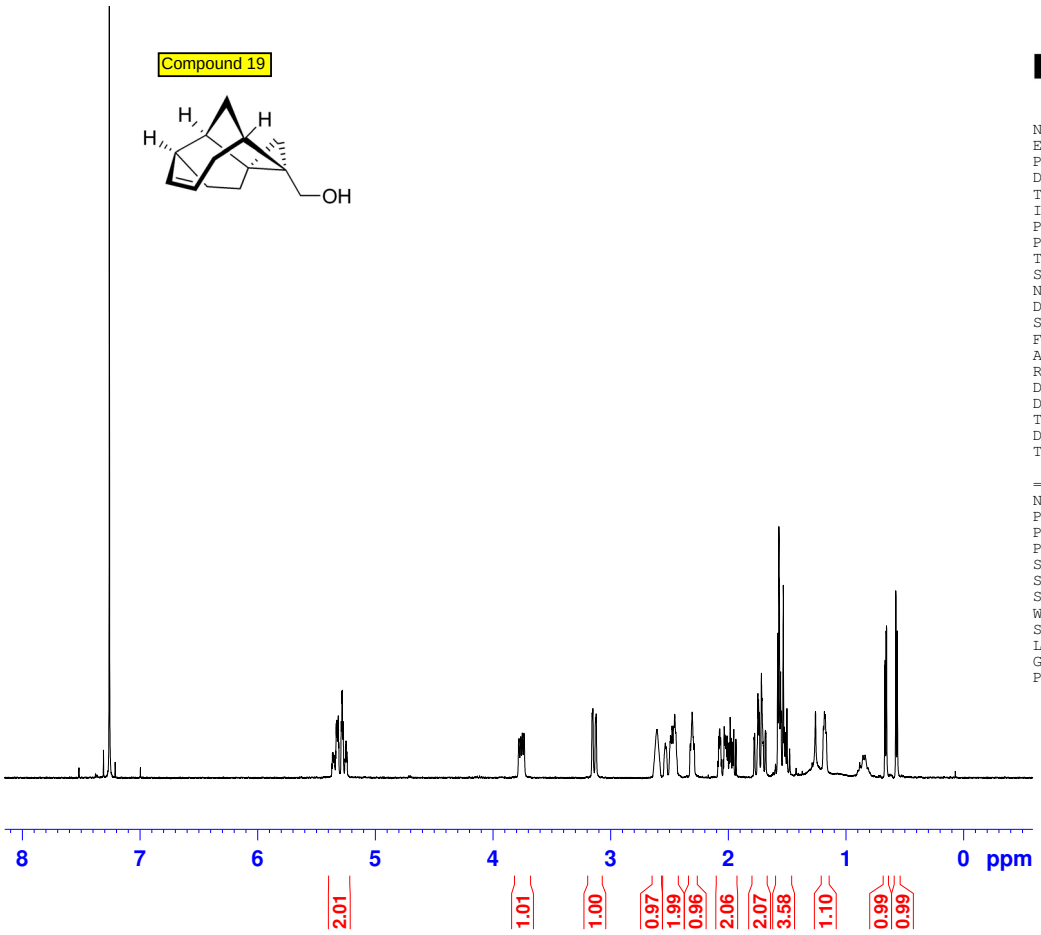



```
NAME          THMA EK784HF
EXPNO                   20
PROCNO                   1
Date_             20090603
Time                 14.01
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                   287.4
DW                  60.400 usec
DE                   6.00 usec
TE                  300.2 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1          400.1324710 MHz
SI                  32768
SF            400.1300095 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

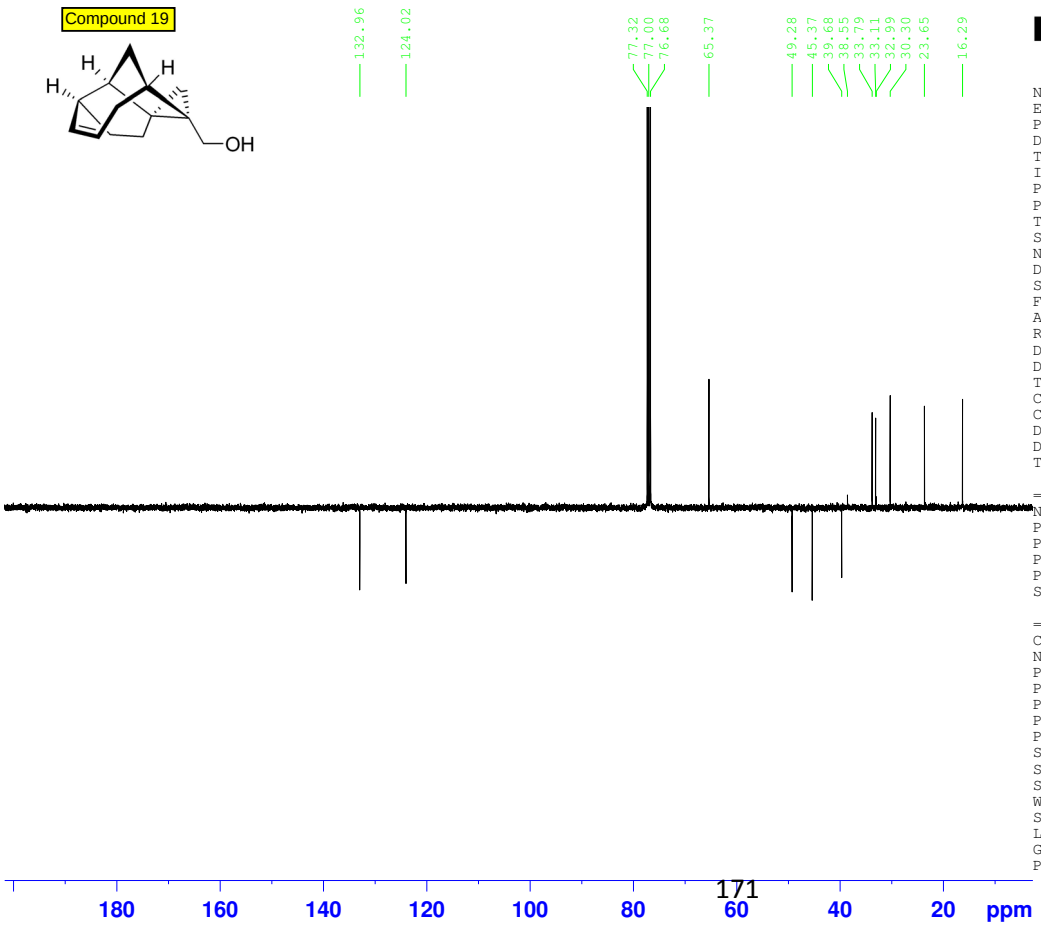
Compound 10




```
NAME          THMA EK784HF
EXPNO                   21
PROCNO                   1
Date_             20090603
Time                 15.09
INSTRUM          avance400
PROBHD    5 mm BBO BB-1H
PULPROG              jmod
TD                  65536
SOLVENT             CDCl3
NS                   2500
DS                      2
SWH             25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                  5160.6
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2               100.00 usec
PL2                 -3.00 dB
PL12                16.00 dB
SFO2          400.1316005 MHz
SI                  32768
SF            100.6127697 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

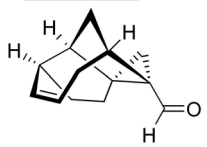


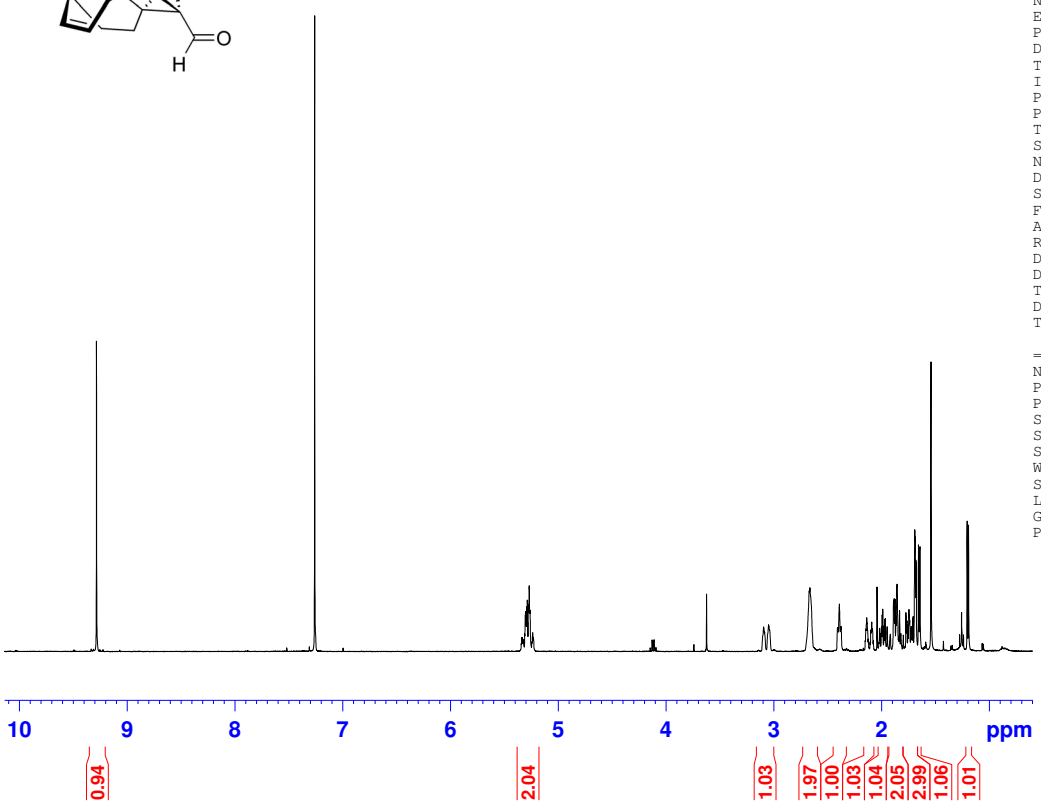

```
NAME            THMA E254
EXPNO                  20
PROCNO                  1
Date_           20090708
Time                9.54
INSTRUM         AVIII400
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                    912
DW                 60.800 usec
DE                  6.50 usec
TE                 298.2 K
D1            1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  13.50 usec
PL1                 -1.80 dB
PL1W         15.28361320 W
SFO1         400.2724718 MHz
SI                  32768
SF           400.2700107 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```




```
NAME            THMA E254
EXPNO                  21
PROCNO                  1
Date_           20090709
Time                3.43
INSTRUM         AVIII400
PROBHD   5 mm PABBO BB-
PULPROG              jmod
TD                  65536
SOLVENT             CDCl3
NS                   4500
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                   2050
DW                 20.800 usec
DE                  6.50 usec
TE                 298.2 K
CNST2        145.0000000
CNST11         1.0000000
D1             2.00000000 sec
D20            0.00689655 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.00 usec
P2                  20.00 usec
PL1                 -1.50 dB
PL1W         47.89980698 W
SFO1         100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                 -1.80 dB
PL12                14.70 dB
PL2W         15.28361320 W
PL12W         0.34215751 W
SFO2         400.2716011 MHz
SI                  32768
SF           100.6479720 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

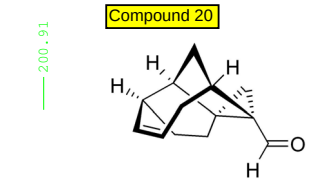
Compound 20





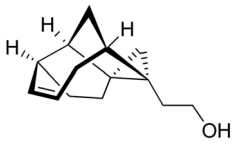

```
NAME            THMA E206
EXPNO                  60
PROCNO                  1
Date_            20090613
Time                0.49
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      32
DS                       2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9584243 sec
RG                   645.1
DW                  60.400 usec
DE                    6.00 usec
TE                   300.0 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   8.75 usec
PL1                 -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300094 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

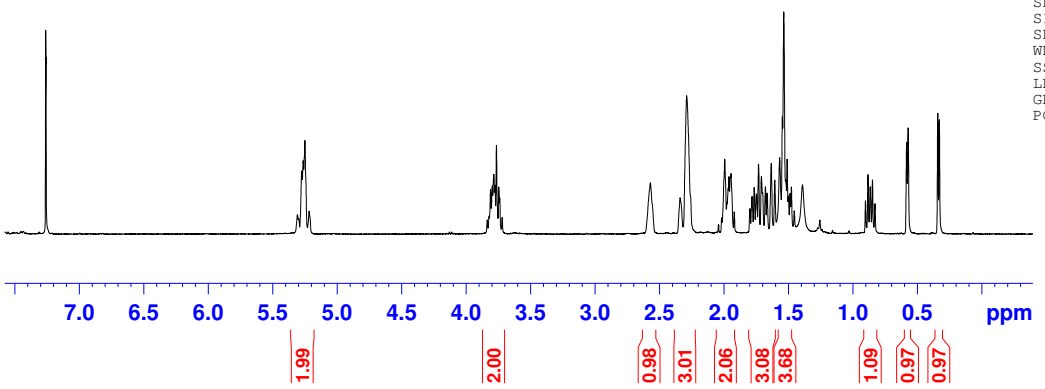
Compound 20




```
NAME            THMA E206
EXPNO                  61
PROCNO                  1
Date_            20090613
Time                2.42
INSTRUM         avance400
PROBHD   5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    2000
DS                       2
SWH             25062.656 Hz
FIDRES           0.382426 Hz
AQ               1.3074932 sec
RG                  7298.2
DW                  19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1             2.00000000 sec
d20            0.00689655 sec
DELTA          0.00001311 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  10.30 usec
p2                  20.60 usec
PL1                 -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127694 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

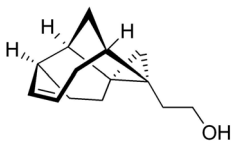
Compound 12





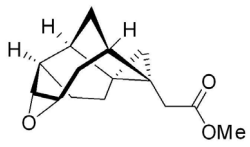

```
NAME              K 795 HF
EXPNO                   30
PROCNO                   1
Date_             20090615
Time                 15.35
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                     256
DW                  60.400 usec
DE                   6.00 usec
TE                  300.2 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300095 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

Compound 12



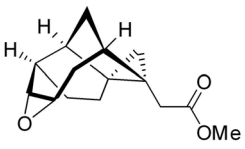

```
NAME              K 795 HF
EXPNO                   31
PROCNO                   1
Date_             20090615
Time                 15.54
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    1200
DS                       2
SWH              25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                  7298.2
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1             2.00000000 sec
d20            0.00689655 sec
DELTA          0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                    1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127697 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

Compound 21

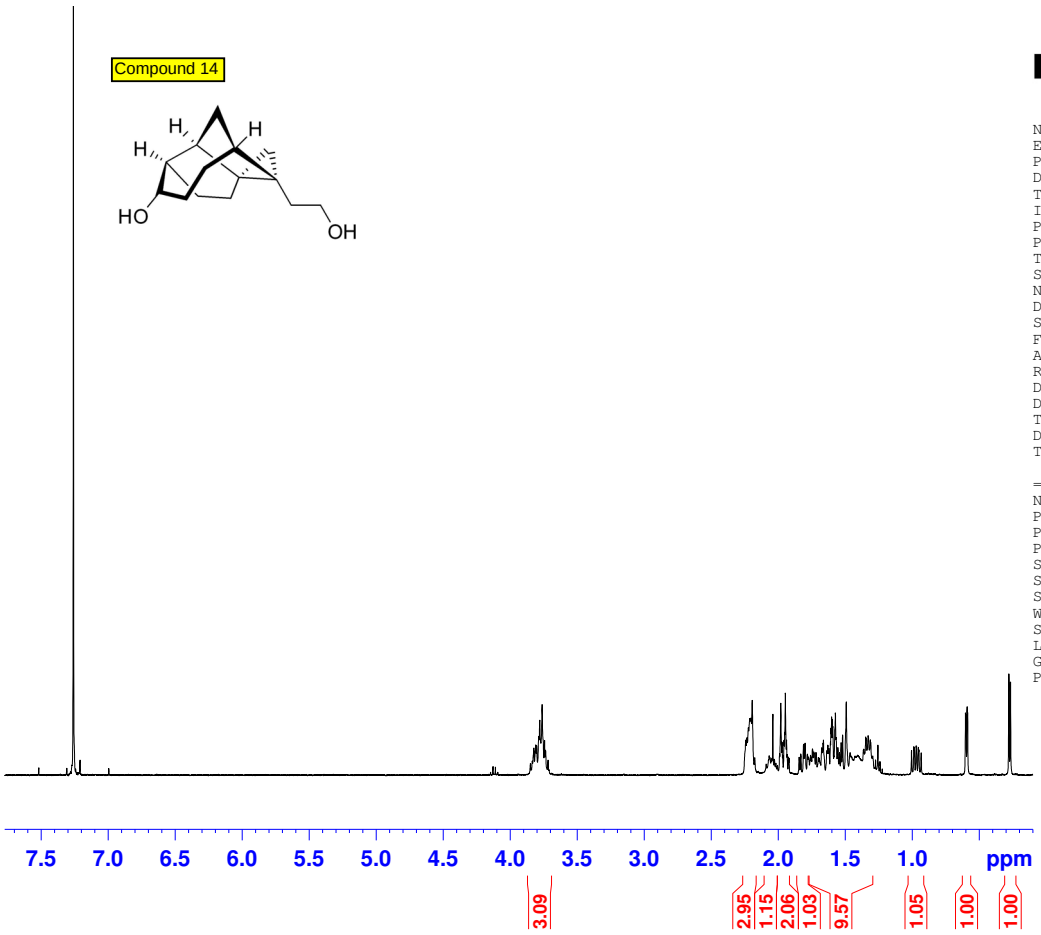



```
NAME            THMA E257
EXPNO                370
PROCNO                 1
Date_           20090708
Time               19.18
INSTRUM          AVIII400
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                      1
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                    645
DW                 60.800 usec
DE                  6.50 usec
TE                 298.3 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  13.50 usec
PL1                 -1.80 dB
PL1W           15.28361320 W
SFO1           400.2724718 MHz
SI                  32768
SF             400.2700105 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

Compound 21

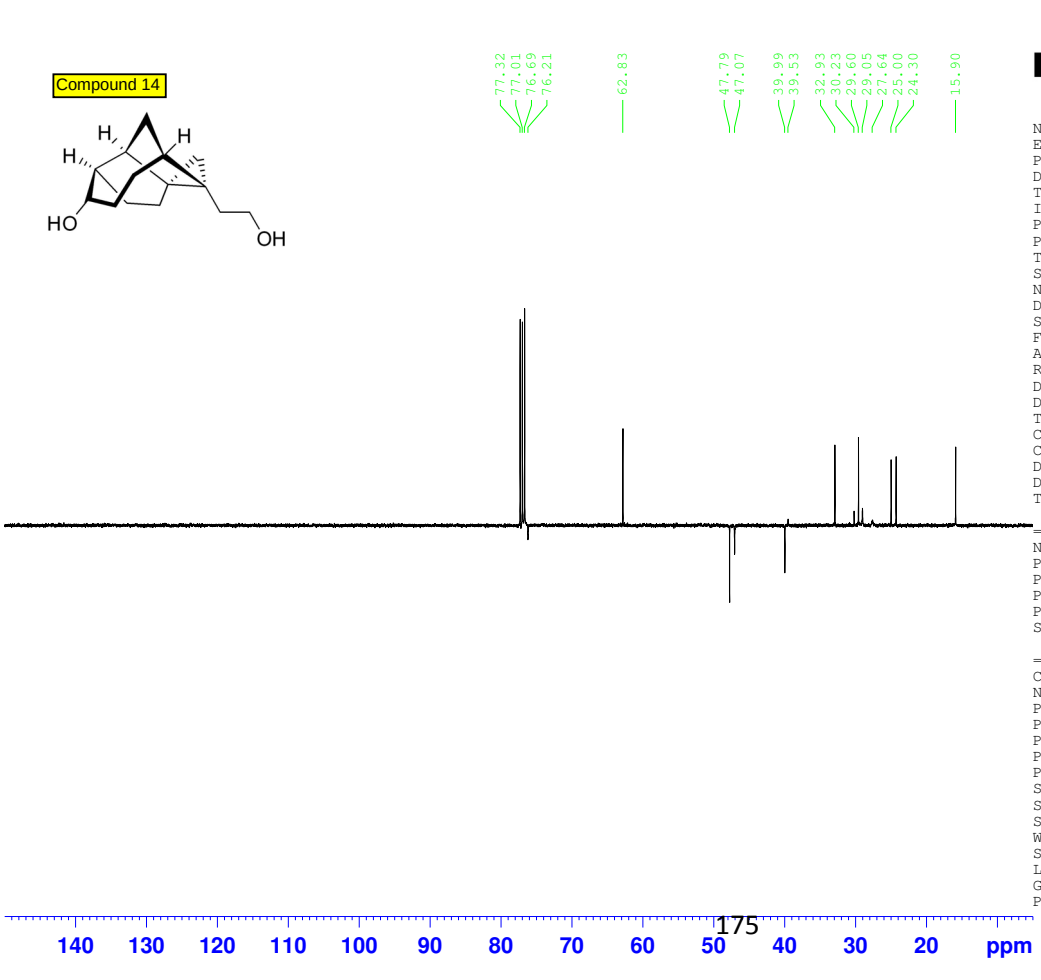



```
NAME            THMA E257
EXPNO                371
PROCNO                 1
Date_           20090709
Time                6.37
INSTRUM          AVIII400
PROBHD   5 mm PABBO BB-
PULPROG             jmod
TD                  65536
SOLVENT             CDCl3
NS                   3000
DS                      4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                   2050
DW                 20.800 usec
DE                  6.50 usec
TE                 298.1 K
CNST2          145.0000000
CNST11           1.0000000
D1              2.00000000 sec
D20             0.00689655 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                  10.00 usec
P2                  20.00 usec
PL1                 -1.50 dB
PL1W           47.89980698 W
SFO1           100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2              100.00 usec
PL2                 -1.80 dB
PL12                14.70 dB
PL2W           15.28361320 W
PL12W           0.34215751 W
SFO2           400.2716011 MHz
SI                  32768
SF             100.6479720 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   3.00
```



BRUKER

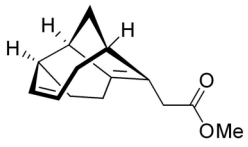
```
NAME            THMA E258
EXPNO                  60
PROCNO                  1
Date_            20090709
Time                12.15
INSTRUM          AVIII400
PROBHD   5 mm PABBO BB-
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       1
DS                       2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9846387 sec
RG                     456
DW                60.800 usec
DE                 6.50 usec
TE                298.2 K
D1            1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.50 usec
PL1                  -1.80 dB
PL1W          15.28361320 W
SFO1          400.2724718 MHz
SI                   32768
SF            400.2700105 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```



BRUKER

```
NAME            THMA E258
EXPNO                  61
PROCNO                  1
Date_            20090710
Time                0.21
INSTRUM          AVIII400
PROBHD   5 mm PABBO BB-
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    4000
DS                       4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    2050
DW                20.800 usec
DE                 6.50 usec
TE                298.2 K
CNST2         145.0000000
CNST11          1.0000000
D1            2.00000000 sec
D20           0.00689655 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.00 usec
P2                   20.00 usec
PL1                  -1.50 dB
PL1W          47.89980698 W
SFO1          100.6580364 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                  -1.80 dB
PL12                 14.70 dB
PL2W          15.28361320 W
PL12W          0.34215751 W
SFO2          400.2716011 MHz
SI                   32768
SF            100.6479720 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    2.00
```

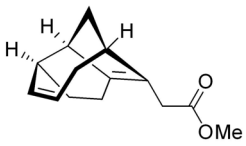
Compound 11



BRUKER

```
NAME              K 801 HF
EXPNO                   10
PROCNO                   1
Date_             20090626
Time                 15.18
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      32
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                   574.7
DW                  60.400 usec
DE                   6.00 usec
TE                  300.2 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1          400.1324710 MHz
SI                   32768
SF            400.1300094 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

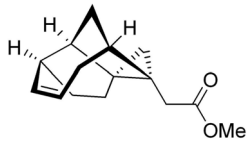
Compound 11



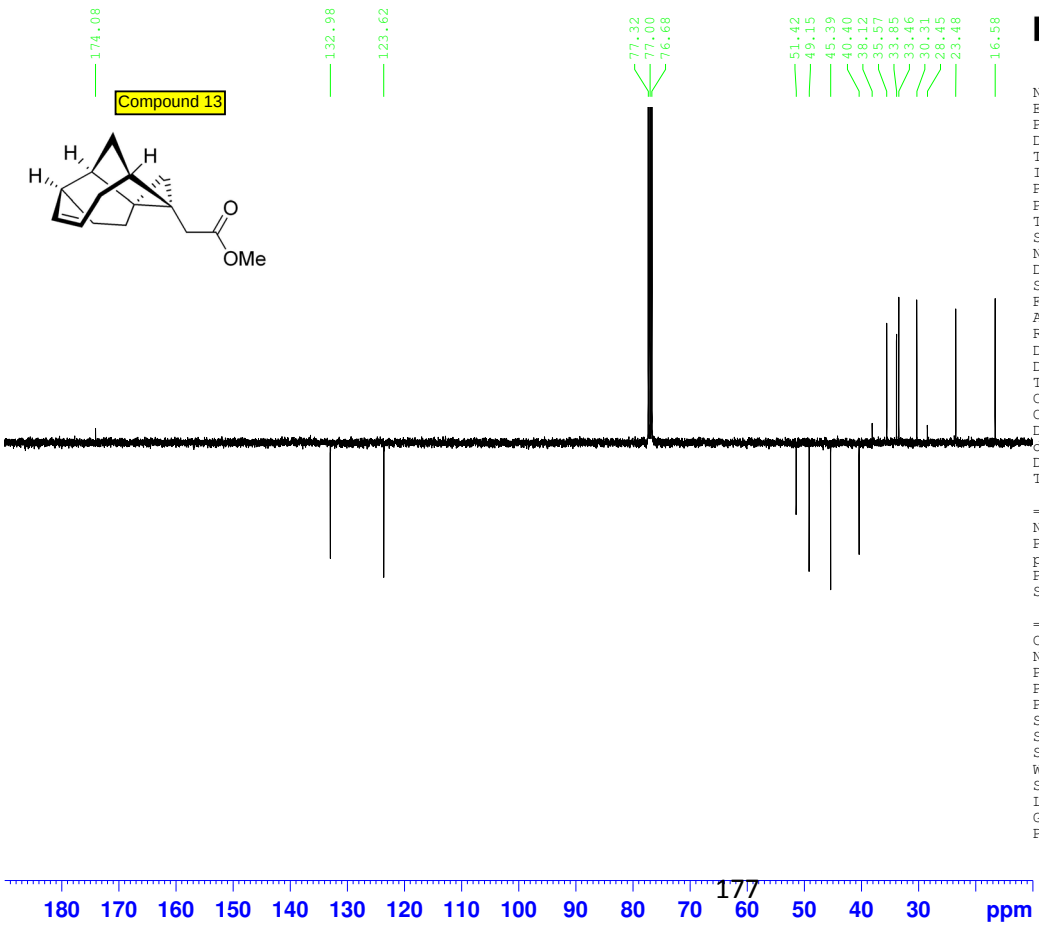
BRUKER

```
NAME              K 801 HF
EXPNO                   15
PROCNO                   1
Date_             20090627
Time                  0.07
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG               jmod
TD                   65536
SOLVENT              CDCl3
NS                    5000
DS                       2
SWH              25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                   5792.6
DW                  19.950 usec
DE                   6.00 usec
TE                  300.2 K
CNST2          145.0000000
CNST11           1.0000000
D1               2.00000000 sec
d20              0.00689655 sec
DELTA            0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                    1H
PCPD2              100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127695 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

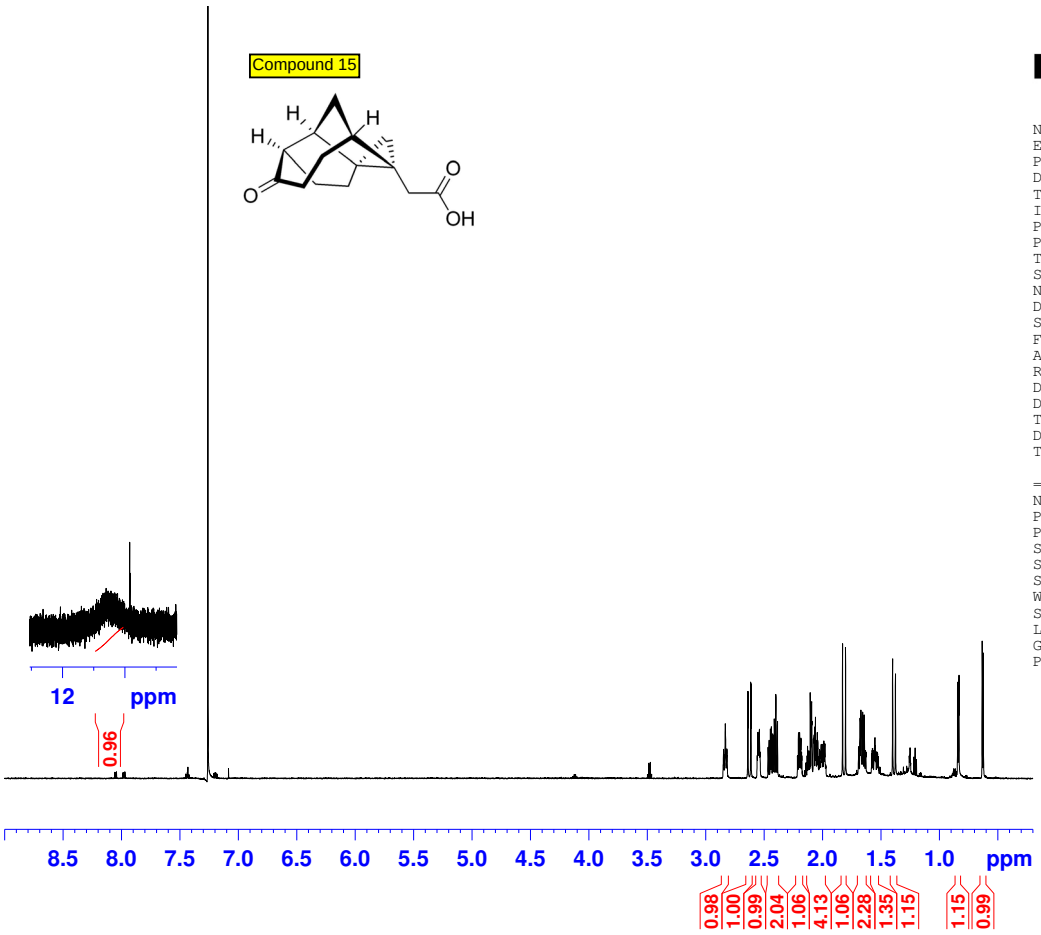
Compound 13



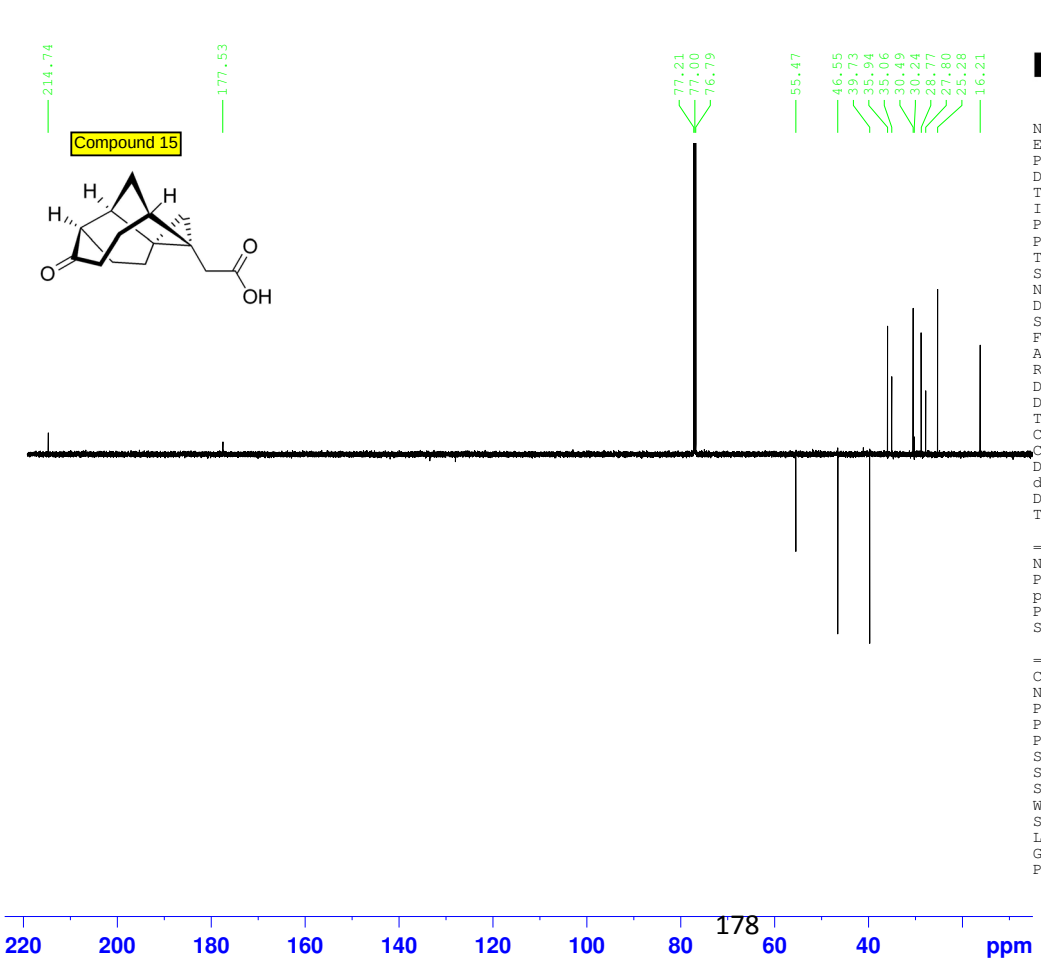

```
NAME              K 807 HF
EXPNO                   40
PROCNO                   1
Date_             20090709
Time                 13.42
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       32
DS                        2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9584243 sec
RG                      512
DW                   60.400 usec
DE                    6.00 usec
TE                   300.2 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                    8.75 usec
PL1                  -3.00 dB
SFO1          400.1324710 MHz
SI                    32768
SF            400.1300093 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```



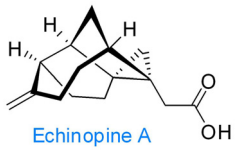

```
NAME              K 807 HF
EXPNO                   41
PROCNO                   1
Date_             20090709
Time                 14.06
INSTRUM         avance400
PROBHD    5 mm BBO BB-1H
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     6000
DS                        2
SWH              25062.656 Hz
FIDRES            0.382426 Hz
AQ                1.3074932 sec
RG                  14596.5
DW                   19.950 usec
DE                    6.00 usec
TE                   300.2 K
CNST2           145.0000000
CNST11            1.0000000
D1              2.00000000 sec
d20             0.00689655 sec
DELTA           0.00001311 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   10.30 usec
p2                   20.60 usec
PL1                  -1.00 dB
SFO1          100.6233329 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                    1H
PCPD2               100.00 usec
PL2                  -3.00 dB
PL12                 16.00 dB
SFO2          400.1316005 MHz
SI                    32768
SF            100.6127692 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```



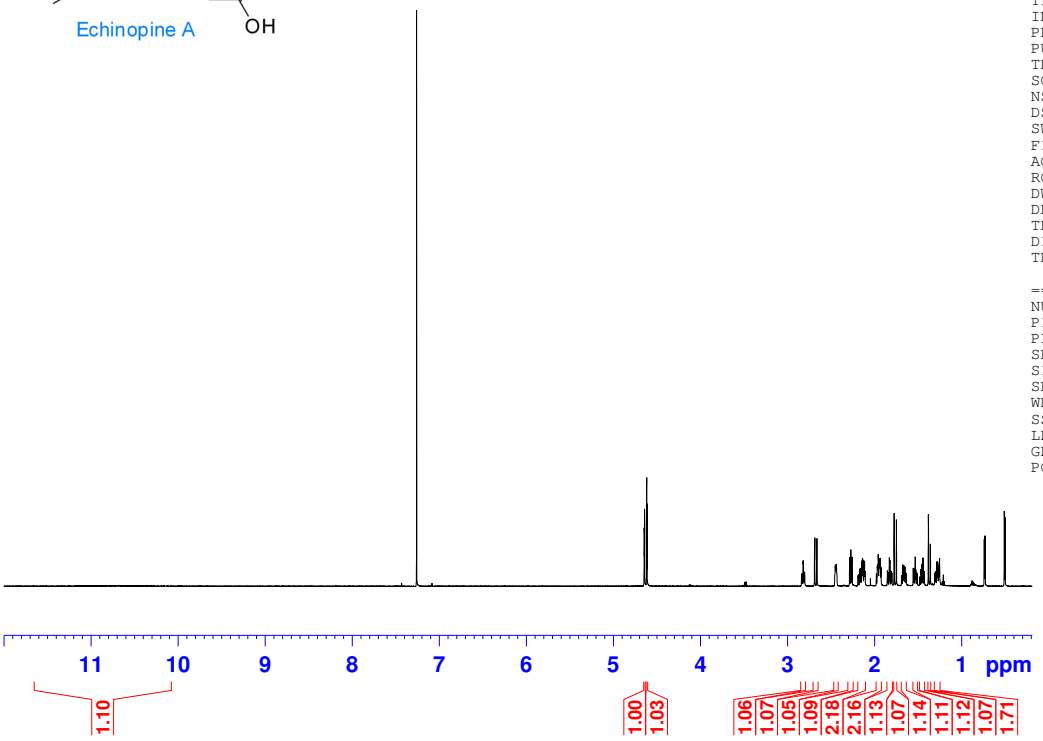

```
NAME            THMA E260
EXPNO                20
PROCNO                1
Date_          20090710
Time              20.29
INSTRUM        avance600
PROBHD   5 mm PAQNP Swi
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    64
DS                     2
SWH           12376.237 Hz
FIDRES         0.188846 Hz
AQ            2.6477449 sec
RG                724.1
DW               40.400 usec
DE                6.00 usec
TE                298.1 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                13.85 usec
PL1               -6.00 dB
SFO1         600.1337060 MHz
SI                 32768
SF           600.1300174 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00
```



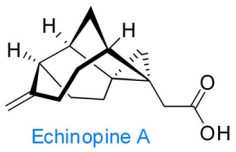

```
NAME            THMA E260
EXPNO                26
PROCNO                1
Date_          20090711
Time              10.38
INSTRUM        avance600
PROBHD   5 mm PAQNP Swi
PULPROG              jmod
TD                 65536
SOLVENT            CDCl3
NS                  8000
DS                     4
SWH           35971.223 Hz
FIDRES         0.548877 Hz
AQ            0.9110143 sec
RG               9195.2
DW               13.900 usec
DE                6.00 usec
TE                298.1 K
CNST2        145.0000000
CNST11         1.0000000
D1           2.00000000 sec
d20          0.00689655 sec
DELTA        0.00000828 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 6.50 usec
p2                13.00 usec
PL1                0.00 dB
SFO1         150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             80.00 usec
PL2               -6.00 dB
PL12              12.20 dB
SFO2         600.1324005 MHz
SI                 32768
SF           150.9028132 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  2.00
```



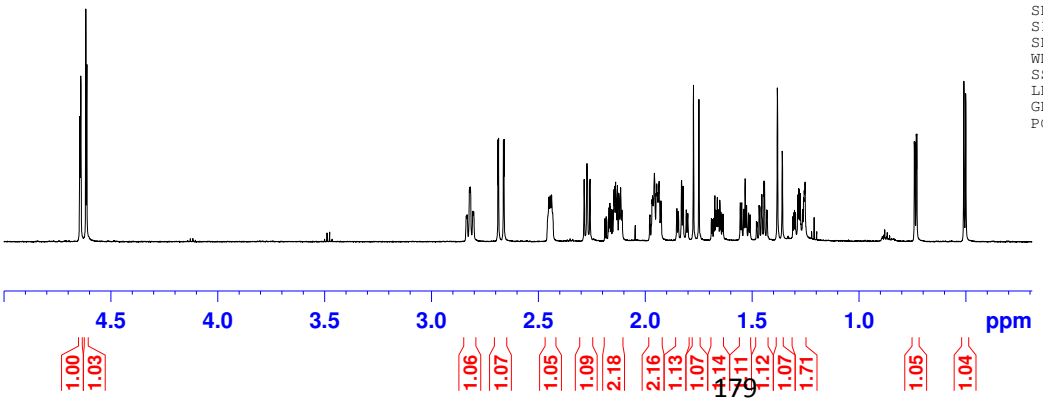
Echinopine A



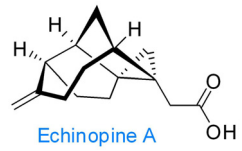

```
NAME      THMA Echinopine A
EXPNO                   10
PROCNO                   1
Date_             20090710
Time                 14.09
INSTRUM         avance600
PROBHD   5 mm PAQNP Swi
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      32
DS                       2
SWH              12376.237 Hz
FIDRES            0.188846 Hz
AQ                2.6477449 sec
RG                    406.4
DW                   40.400 usec
DE                    6.00 usec
TE                   298.1 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.85 usec
PL1                  -6.00 dB
SFO1           600.1337060 MHz
SI                   32768
SF             600.1300174 MHz
WDW                     no
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.00
```



Echinopine A

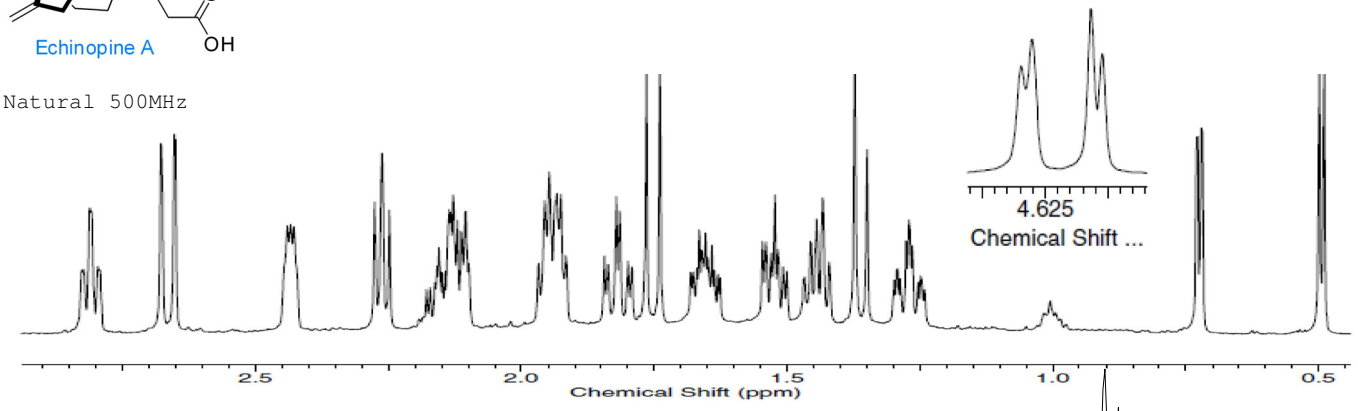



```
NAME      THMA Echinopine A
EXPNO                   10
PROCNO                   1
Date_             20090710
Time                 14.09
INSTRUM         avance600
PROBHD   5 mm PAQNP Swi
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      32
DS                       2
SWH              12376.237 Hz
FIDRES            0.188846 Hz
AQ                2.6477449 sec
RG                    406.4
DW                   40.400 usec
DE                    6.00 usec
TE                   298.1 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   13.85 usec
PL1                  -6.00 dB
SFO1           600.1337060 MHz
SI                   32768
SF             600.1300174 MHz
WDW                     no
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.00
```

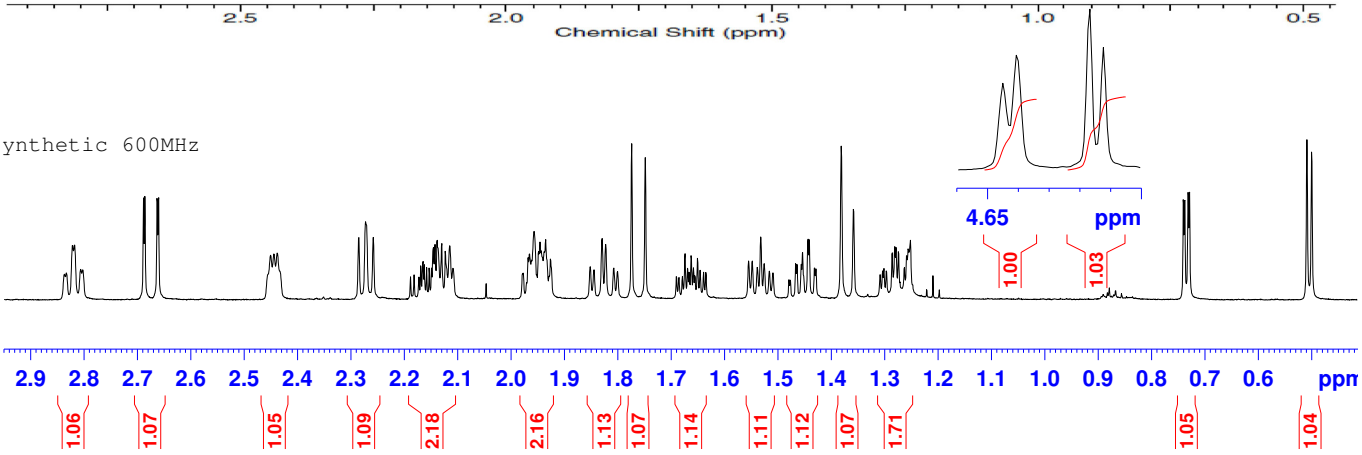


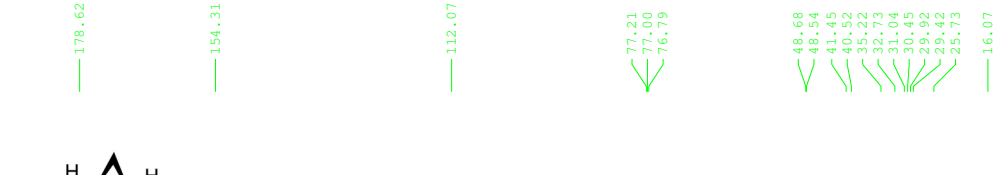
Echinopine A

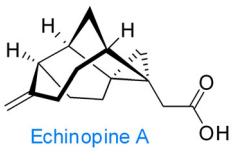
Natural 500MHz



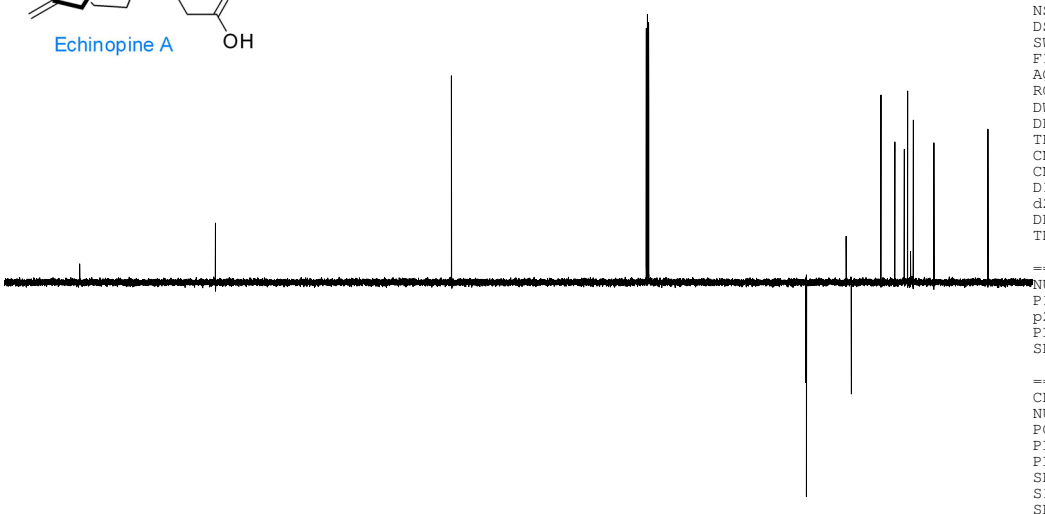
Synthetic 600MHz

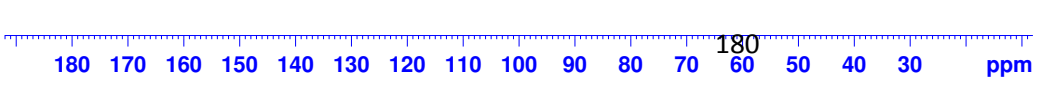






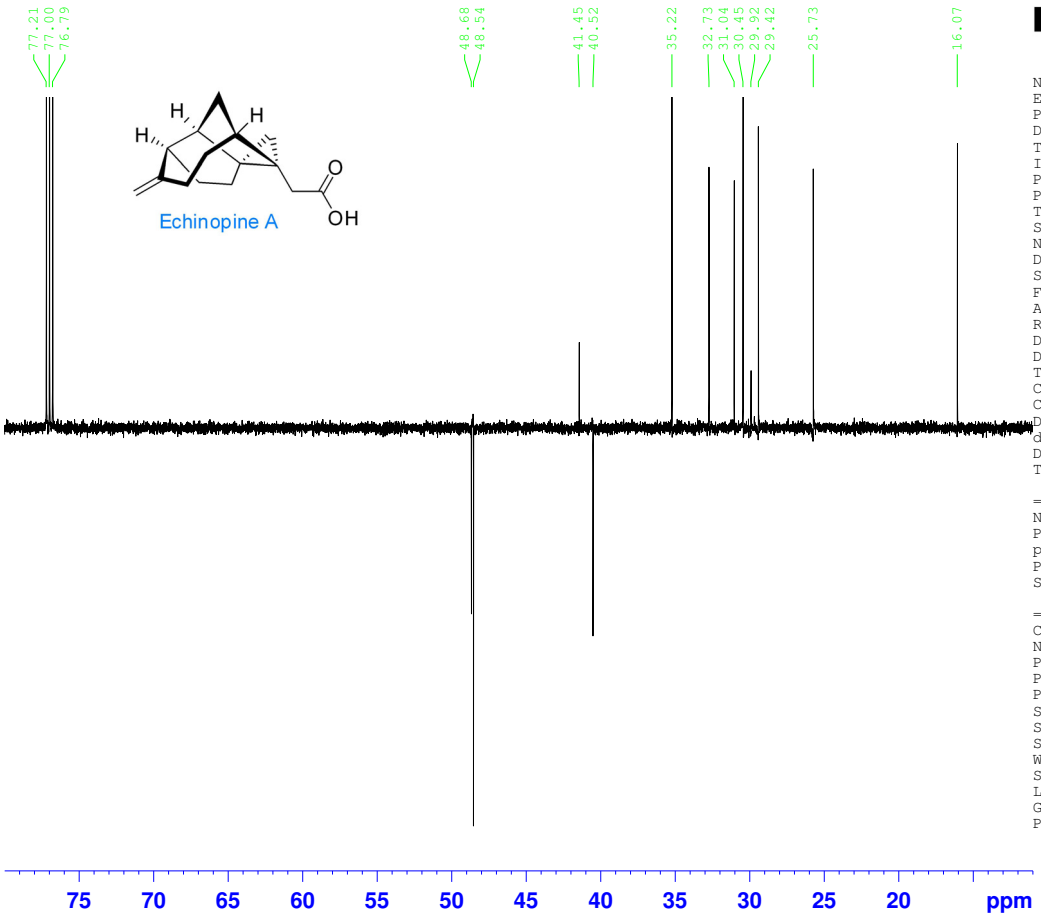
Echinopine A





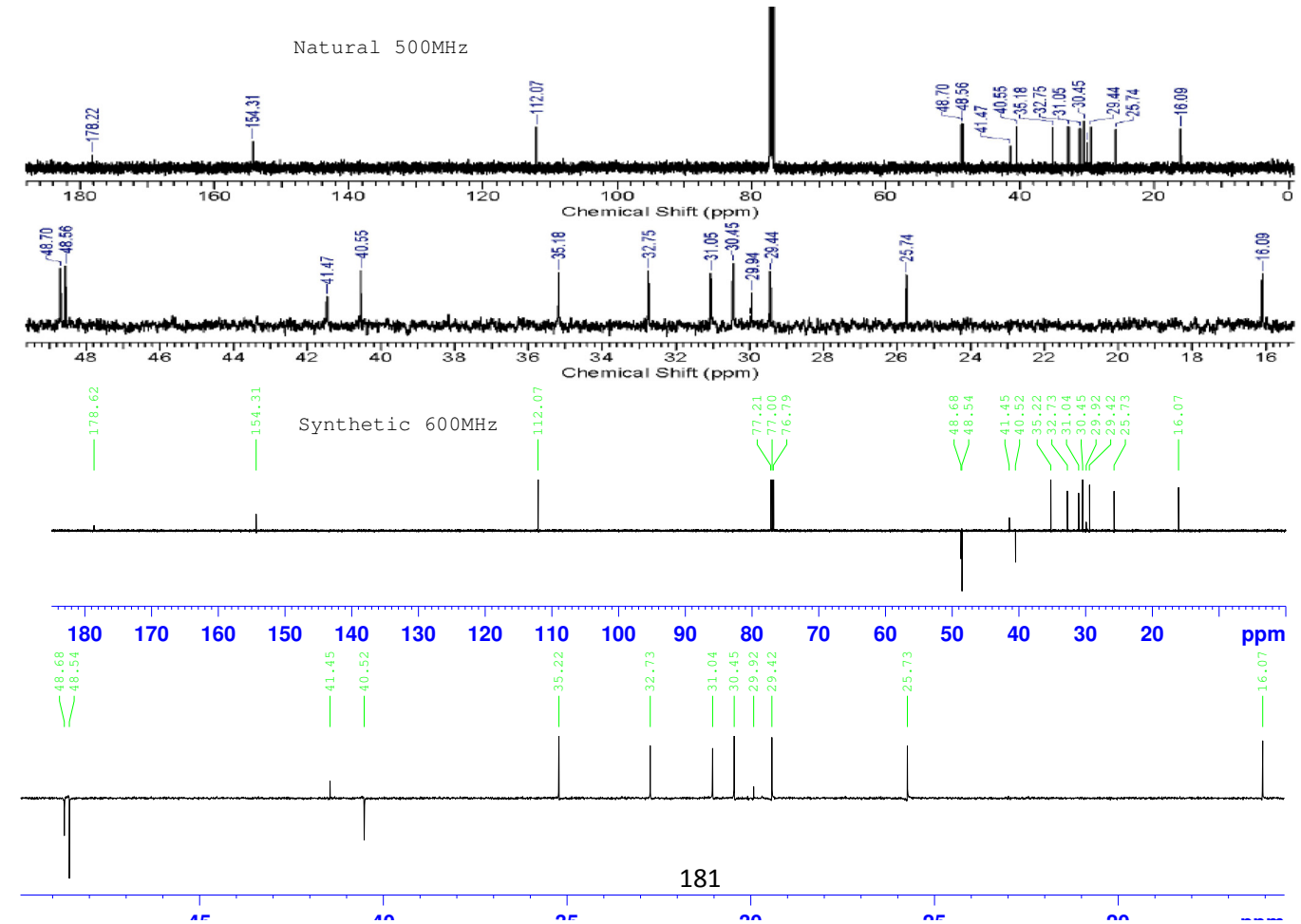
BRUKER

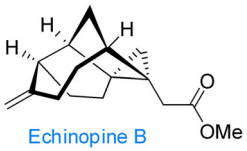
```
NAME          THMA Echinopine A
EXPNO                        16
PROCNO                        1
Date_                  20090710
Time                      20.21
INSTRUM                avance600
PROBHD    5 mm PAQNP Swi
PULPROG                    jmod
TD                        65536
SOLVENT                   CDCl3
NS                         3000
DS                            4
SWH                  35971.223 Hz
FIDRES                0.548877 Hz
AQ                    0.9110143 sec
RG                      10321.3
DW                       13.900 usec
DE                        6.00 usec
TE                       298.1 K
CNST2                145.0000000
CNST11                 1.0000000
D1                    2.00000000 sec
d20                   0.00689655 sec
DELTA                 0.00000828 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                        13C
P1                         6.50 usec
p2                        13.00 usec
PL1                        0.00 dB
SFO1                150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                         1H
PCPD2                     80.00 usec
PL2                       -6.00 dB
PL12                      12.20 dB
SFO2                600.1324005 MHz
SI                        32768
SF                  150.9028132 MHz
WDW                          no
SSB                           0
LB                         0.00 Hz
GB                            0
PC                         3.00
```



BRUKER

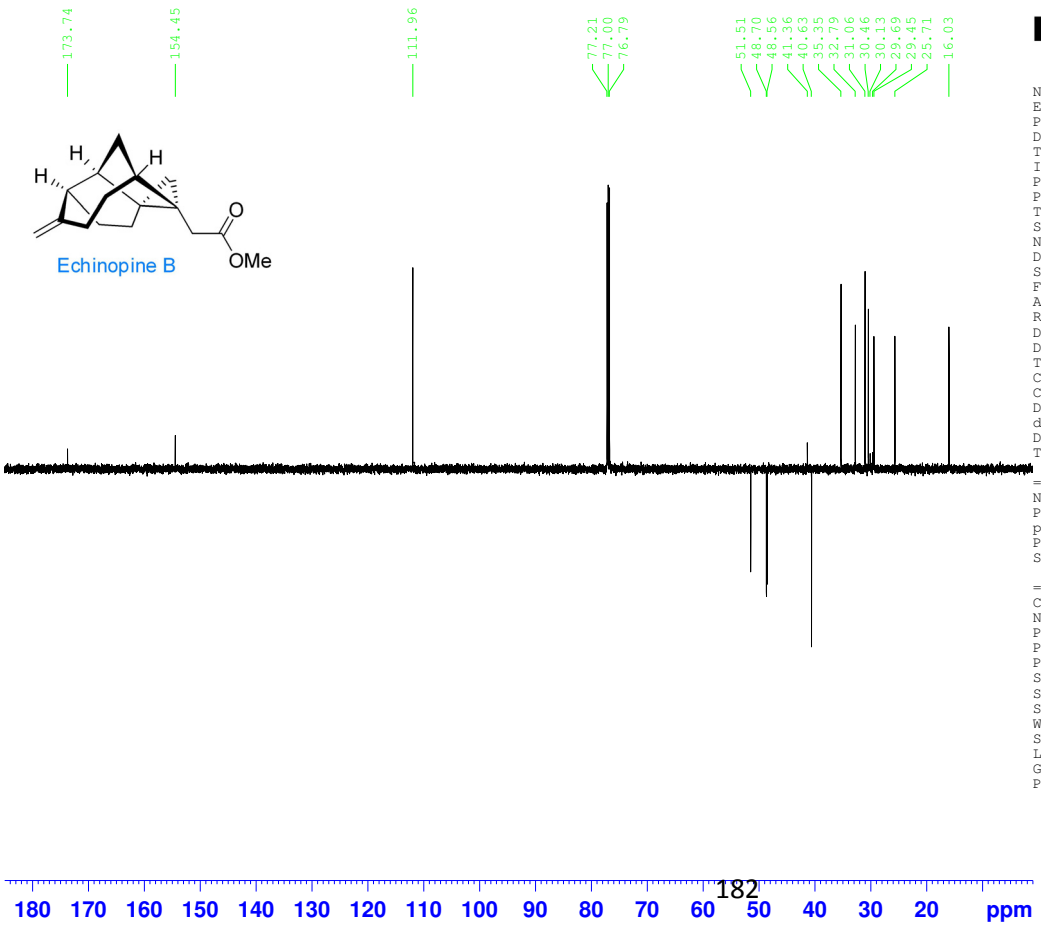
```
NAME        THMA Echinopine A
EXPNO                    16
PROCNO                    1
Date_              20090710
Time                  20.21
INSTRUM          avance600
PROBHD    5 mm PAQNP Swi
PULPROG                jmod
TD                    65536
SOLVENT               CDCl3
NS                     3000
DS                        4
SWH               35971.223 Hz
FIDRES             0.548877 Hz
AQ                0.9110143 sec
RG                  10321.3
DW                   13.900 usec
DE                    6.00 usec
TE                   298.1 K
CNST2           145.0000000
CNST11            1.0000000
D1                2.00000000 sec
d20               0.00689655 sec
DELTA             0.00000828 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                     6.50 usec
p2                    13.00 usec
PL1                    0.00 dB
SFO1           150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                  -6.00 dB
PL12                 12.20 dB
SFO2           600.1324005 MHz
SI                    32768
SF             150.9028132 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     3.00
```





Echinopine B


```
NAME        THMA Echinopine B opt
EXPNO                       10
PROCNO                       1
Date_                 20090713
Time                     14.56
INSTRUM              avance600
PROBHD    5 mm PAQNP Swi
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                 12376.237 Hz
FIDRES                0.188846 Hz
AQ                    2.6477449 sec
RG                        287.4
DW                       40.400 usec
DE                        6.00 usec
TE                       298.1 K
D1                  1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       13.85 usec
PL1                      -6.00 dB
SFO1                600.1337060 MHz
SI                        32768
SF                  600.1300174 MHz
WDW                          EM
SSB                           0
LB                         0.30 Hz
GB                            0
PC                         1.00
```



Echinopine B

```
NAME        THMA Echinopine B opt
EXPNO                       11
PROCNO                       1
Date_                 20090713
Time                     15.08
INSTRUM              avance600
PROBHD    5 mm PAQNP Swi
PULPROG                  jmod
TD                      65536
SOLVENT                 CDCl3
NS                       1158
DS                          4
SWH                 35971.223 Hz
FIDRES                0.548877 Hz
AQ                    0.9110143 sec
RG                       5792.6
DW                       13.900 usec
DE                        6.00 usec
TE                       298.1 K
CNST2               145.0000000
CNST11                1.0000000
D1                    2.00000000 sec
d20                   0.00689655 sec
DELTA                 0.00000828 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                        6.50 usec
p2                       13.00 usec
PL1                       0.00 dB
SFO1                150.9178988 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                    80.00 usec
PL2                      -6.00 dB
PL12                     12.20 dB
SFO2                600.1324005 MHz
SI                        32768
SF                  150.9028128 MHz
WDW                          EM
SSB                           0
LB                         1.00 Hz
GB                            0
PC                         2.00
```

8. Summary

In conclusion, we have accomplished the first total syntheses of the sesquiterpenoids (+)–echinopine A and B and the determination of their absolute stereochemistry.

The key features are: (1) The stereoselective installation of the vinyl–moiety on the hindered concave side of the RCM precursor via Myers' [3,3]–sigmatropic rearrangement. (2) The successful equilibration of the C7–substituent to the desired concave face under basic conditions. (3) The installation of the highly strained 7–membered ring via RCM. (4) The extension of the unusual Pd(0)–mediated C2–homologation of aryltriflates with a ketene silyl acetal. (5) 1,5–cyclooctadiene as an inexpensive, readily available starting material. The efficient syntheses, (14)15 linear steps from known enantiopure and easily accessible starting material allows for diversification and the preparation of sufficient material for proper biological testing. In addition, we were able to grow crystals suitable for crystal structure analysis. The X-ray structure of synthetic echinopine A confirmed the proposed structure.

Unfortunately we were not able to realize the originally planned dynamic RCM, which would have saved an additional step, under a variety of conditions. All efforts to install the 7-membered ring bearing a trisubstituted double bond via RCM failed, probably due to the high ring strain.

9. Abbreviations

Ac	acetyl
ACP	acyl carrier protein
ADP	adenosinediphosphate
AIBN	azobisisobutyronitrile
AT	acyl transferase
ATP	adenosinetriphosphate
9–BBN	9–borabicyclo[3.3.1]nonane
Bn	benzyl
CAN	ceric ammonium nitrate
CBS	Corey–Bakshi–Shibata reduction
CL	CoA–ligase
COSY	correlated spectroscopy
CSA	camphersulfonic acid
CTP	cytidine triphosphate
Cy	cyclohexyl
DBU	1,8–diaza–bicyclo[5.4.0]–7–undecene
DIBAL	diisobutylaluminium hydride
DCC	*N,N'*–dicyclohexylcarbodiimide
DIPEA	diisopropylethylamine (Huenig's base)
DH	β–hydroxyacyl dehydratase
DMF	*N,N'*–dimethylformamide
DMAP	4–dimethylaminopyridine

DMAPP	dimethylallyl diphosphate
DME	dimethoxyethane
DMP	Dess–Martin periodinane
DMPS	dimethylphenylsilyl
DMSO	dimethyl sulfoxide
DXP	1–deoxyxylose–5–phosphate
Ee	enantiomeric excess
EDA	ethyl diazo acetate
ER	enoyl reductase
GGP	geranyl–geranyl diphosphate
GPP	geranyl diphosphate
HMBC	*hetero*–nuclear multiple bond correlation
HMG	3–hydroxy–3–methylglutaryl
HMPA	hexamethylphosphoramide
HMTA	hexamethylentetramine
HRMS	high resolution mass spectrometry
IBX	2–iodoxybenzoic acid
IPP	isopentenyl diphosphate
KR	β–ketoacyl reductase
KS	ketoacyl synthase
LDA	lithium diisopropylamide
LAH	lithium aluminiumhydride
LHMDS	lithium bis(trimethylsilyl)amide
L–selectride	lithium *tri–sec*–butylborohydride
*m*CPBA	*meta*–chloroperoxybenzoic acid

MEM	methoxyethyl
MOM	methoxymethyl
MRSA	multi–resistant *Staphylococcus Aureus*
Ms	methanesulfonyl (mesyl)
MS	molecular sieve
MT	methyl transferase
MTPA	methoxy trifluoromethyl phenylacetic acid
MVA	mevalonic acid
NADPH	nicotinamide adenine dinucleotide phosphate
NIS	*N*–iodosuccinimide
NOE	nuclear Overhauser enhancement
PKS	polyketide synthase
PMB	*para*–methoxybenzyl
PPTS	pyridinium *para*–toluenesulfonate
PTC	phase transfer catalyst
RCM	ring closing metathesis
rfx	reflux
r.t.	room temperature
TBAF	tetrabutylammonium fluoride
TBS	*tert*–butyldimethylsilyl
TBDPS	*tert*–butyldiphenylsilyl
TE	thioesterase
TEA	triethylamine
TES	triethylsilyl
Tf	trifluoromethanesulfonyl

TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	tetrahydropyran
TIPS	triisopropylsilyl
TMS	trimethylsilyl
TPP	thiamine pyrophosphate
Ts	*para*–toluenesulfonyl
TS	transition state

D. Curriculum Vitae

Personal Data

Name	Thomas Magauer
Date of Birth	21.03.1983
Place of Birth	Linz, Austria
Citizenship	Austria
Marital Status	Single
Address	Thurngasse 15/10, A-1090 Vienna
Degree	*Mag. rer. nat.*
Telephone	+43 699 171 149 72
Email-Address	thomas.magauer@univie.ac.at magauerthomas@gmx.at

Education

Since November 2007	University of Vienna – Ph.D. research: *"Total Syntheses of (-)–Kendomycin and (+)–Echinopine A and*" in the group of Prof. Dr. Johann Mulzer
23.10.2007	University of Vienna – Graduation in minimum time (10 terms) and with distinction (*Magister rer. nat.,* comparable to M.Sc.*)*
Feb. 2007-Oct. 2007	University of Vienna - Diploma thesis: "*Towards the Synthesis of the ansa-Macrocycle Kendomycin"* in the research group of Prof. Dr. Johann Mulzer
2002-2007	University of Vienna – Study of Chemistry, specialized in Organic Chemistry, Spectroscopy and Analytical Chemistry
2002	Military service at HUAK Enns.
1993-2001	Gymnasium Werndlpark, Leopold-Werndl Straße 5, 4400 Steyr, focusing on math and science.
1989-1993	Primary school Karl-Punzer-Straße 73-75, 4400 Steyr

Internships

Summer 1999	Plumber Schlossgangl, trainee
Autumn 2001	BMW Automobiles, trainee for 3 months
Summer 2003	Company SLR-Gusswerk II, casting trainee
Summer 2004	Company Naintsch-Luzenac, R & D laboratory
Summer 2005	Company MAN Steyrer Werke, Dept. of environment
Summer 2005	BMW Automobiles, R & D laboratory
Summer term 2007	University of Vienna, tutor of undergraduate students in the organic chemistry lab
February to October 2007	University of Vienna, Research assistant.
Since November 2007	University of Vienna, Assistant position. Teaching, supervision, tutoring and grading students in organic chemistry

Awards

2005	Leistungsstipendium (University of Vienna)
2008	Gesellschaft Österreichischer Chemiker (GÖCH) Diploma Thesis Prize (Best Diploma Thesis)
2009	Thieme Chemistry - SYNFACTS Poster Prize at the “Synthesefest of the Ludwig-Maximilian University”.

Language and other skills

Languages	▪ German – mother language ▪ English – spoken - excellent, written - excellent, comprehension - excellent ▪ French – spoken – basic, written – basic, comprehension – basic
Technical	▪ Skilled operator of NMR, IR and HPLC instruments and software (Topspin) ▪ Extensive knowledge of office tools and operating systems (MacOS X Snow Leopard, Windows, Ms Office) ▪ Experienced with a variety of chemistry software (Beilstein, CS ChemOffice, IsisBase, IsisDraw, SciFinder)

Social/Teamwork Interests

Sports	Rock Climbing, Hiking, Snowboarding, Beach Volleyball, Soccer, Swimming, Basketball, Gym, Cycling
Other	Camping, Music, Cooking