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A Straightforward Lithiation Strategy for a Densely Functionalized Trifluoromethylated Motif

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Maryse Schladebach BSc

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ABSTRACT

Carbenoids are a unique class of organometallic compounds that exhibit both nucleophilic and electrophilic reactivity. In particular, lithium carbenoids play a crucial role in organic synthesis, especially in homologation reactions. Despite their versatility, their limited stability represents a challenge, which can be addressed through carefully controlled reaction conditions, appropriate solvents, and stabilization strategies. This study investigates the synthesis and reactivity of lithium carbenoids and their application in organofluorine chemistry. A particular focus is placed on the C-3- homologation of aldehydes using 3,3,3-trifluoropropenyl lithium carbenoids obtained *via* halogen-lithium exchange of 2-bromo-3,3,3-trifluoropropene (BTP) in the presence of a MeLi-LiBr solution. The products were characterized using NMR spectroscopy, and the results demonstrate that both aromatic and aliphatic aldehydes can be efficiently homologated.

Carbenoide sind eine besondere Klasse von Organometallverbindungen, die sowohl nukleophile als auch elektrophile Reaktivität zeigen. Insbesondere Lithium-Carbenoide spielen eine zentrale Rolle in der organischen Synthese, vor allem bei Homologierungsreaktionen. Trotz ihrer Vielseitigkeit ist ihre begrenzte Stabilität eine Herausforderung, die durch gezielte Reaktionsbedingungen, geeignete Lösungsmittel und Stabilisierungsstrategien überwunden werden kann.
Diese Arbeit untersucht die Synthese und Reaktivität von Lithium-Carbenoiden und deren Anwendung in der organischen Fluorchemie. Ein besonderer Fokus liegt auf der C-3-Homologierung mittels 3,3,3-Trifluoropropenyllithiumcarbenoiden, welche *via* Halogen-Lithium-Austausch von 2-Brom-3,3,3-trifluorpropen (BTP) in Gegenwart einer MeLi-LiBr-Lösung hergestellt wurden. Die Methode wurde optimiert, um hohe Selektivität und Ausbeute zu erzielen. Die Produkte wurden mittels NMR-Spektroskopie charakterisiert, und die Ergebnisse zeigen, dass sowohl

aromatische als auch aliphatische Aldehyde effizient trifluormethyliert werden können.

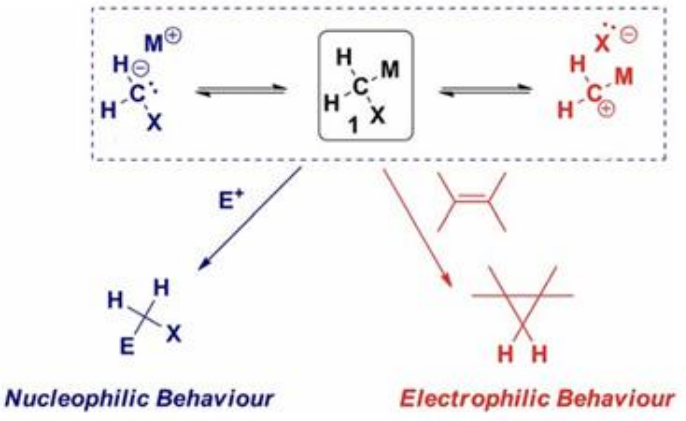
1. INTRODUCTION

1.1. CARBENOIDS

Carbenoids are a special class of organometallic compounds introduced for the first time in 1964 by Closs and Moss.[2]

They consist of a metal atom, typically lithium or magnesium, bonded to a carbon atom that is also attached to an electronegative element, such as a halogen.[2]

Carbenoids are chemically similar to carbenes, exhibiting both nucleophilic and electrophilic reactivity, but they do not share the same properties. While carbenes are highly reactive species with a divalent carbon atom, carbenoids maintain a more stable electronic structure, making them less reactive.[5]



Scheme 1. Ambiphilicity and reactivity profile of carbenoids

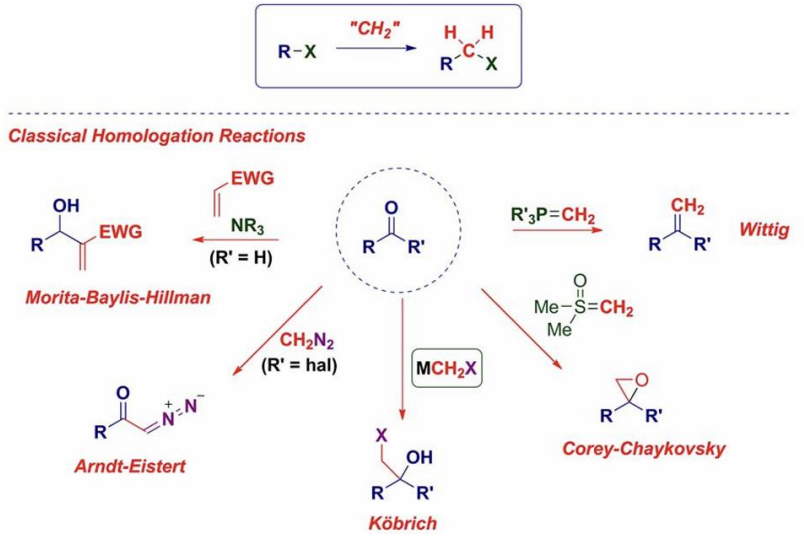
Carbenoids are distinguished by their ambiphilic reactivity, allowing them to act as both nucleophiles and electrophiles, which greatly enhances their versatility. This dual reactivity arises from the simultaneous presence of an

electron-withdrawing and an electron-donating group at the carbon center (Scheme 1). [3]

The ability to react in both ways enables carbenoids to be used in a wide range of chemical processes, from nucleophilic additions to cyclopropanation reactions. One example of such an application is the Simmons-Smith reaction, in which olefins are converted into three-membered rings (cyclopropanes). [2]

A significant advancement in the field originated from the work of Gert Köbrich and coworkers in the 1960s and has since proven to be highly valuable in organic synthesis, particularly in homologation reactions. These reactions allow the introduction of a single carbon unit into a molecule, thereby extending its structure.[2]

A well-known method for homologation is the Arndt-Eistert reaction, where carboxylic acids react with diazomethane to form alpha-diazoketones. However, diazomethane is not only highly toxic but also explosive, which has led to the development of safer alternatives. Over time, several other homologation techniques have been introduced that are less dangerous and offer broader applications. These include the Wittig reaction, the Corey-Chaykovsky reaction, the Morita-Baylis-Hillman reaction, and the Köbrich reaction (Scheme 2).[3]



Scheme 2. General context of homologation in synthetic medicinal chemistry

The reactivity of carbenoids is primarily influenced by the reaction conditions. At low temperatures and in the presence of more electropositive metals, they tend to be nucleophilic because the carbon atom carries a negative charge, similar to a carbanion. As the temperature rises, in the presence of less electropositive metals, their reactivity shifts, and the carbon atom becomes electrophilic, allowing it to accept electrons. This change in reactivity can be attributed to the two possible ionic states of the carbon atom.[2]

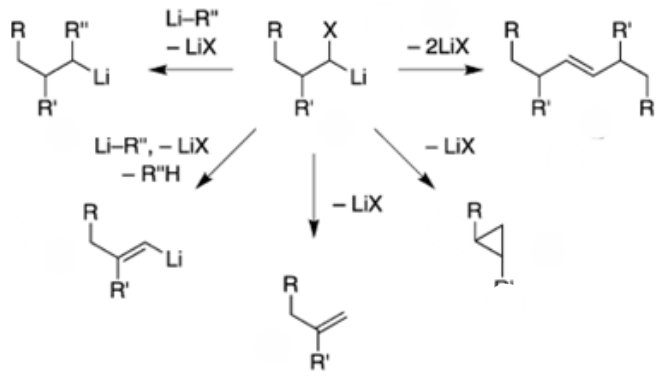
Another crucial factor is the metal attached to the carbenoid. Lithium and magnesium carbenoids are especially strong nucleophiles, while zinc and rhodium carbenoids tend to react electrophilically. [1]

A significant advantage of carbenoid-based homologation methods over traditional ones, like the Matteson homologation, is their simplicity. While conventional methods often involve multiple steps and extra modifications, the carbenoid-based methodologies enable the direct incorporation of the desired carbon unit in a single step.[1]

1.2. LITHIUM CARBENOIDS

Lithium carbenoids are organometallic compounds consisting of a lithium atom and at least one electronegative atom, typically a halogen linked at the same carbon center. These compounds are part of the carbenoid family and are commonly referred to as halogenated carbenoids. They are widely used in homologation reactions.

These compounds are highly versatile and can be applied in a variety of reactions, provided their high reactivity is carefully controlled. Without proper management, however, they may undergo undesirable side reactions, including bimolecular decomposition, nucleophilic substitutions, or elimination reactions. Lithium carbenoids can also experience intramolecular shifts, potentially leading to the formation of unintended products (Scheme 3).[5]

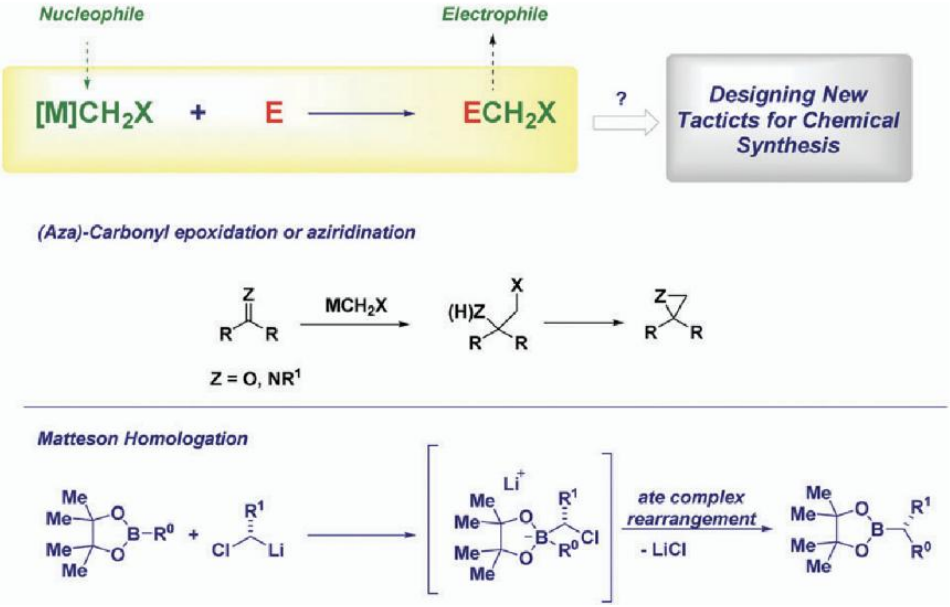


Scheme 3. A selection of potentially deleterious reactivity pathwaysavailable to α-haloalkyllithiums (X=Cl, Br)

Despite their tendency to undergo side reactions, lithium carbenoids are extremely valuable in organic synthesis, particularly in homologation reactions. They allow for the nucleophilic introduction of a CH_2X-unit (i.e. $LiCH_2X$) into a molecule, which can later react electrophilically.[4]

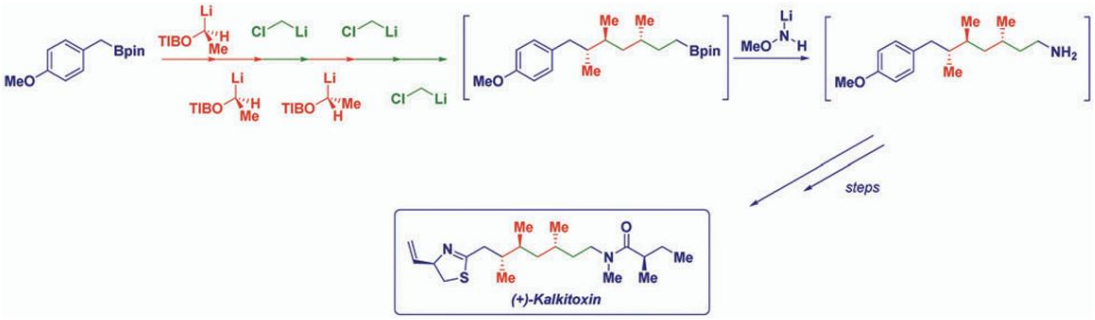
The ability to achieve the desired final product in a single synthetic step offers a significant advantage over other methods that require multiple steps and additional transformations. A typical example of these strategies include the epoxidation or aziridination of carbonyls and imines, as well as

the Matteson homologation of boronic esters with (possibly) chiral carbenoids. In the first case, the intermediate alkoxide (or amide) attacks the electrophilic halomethyl group, forming a three-membered cycle. On the other hand, the ate complex rearrangement leads to the expulsion of the halide, resulting in the homologated structure. (Scheme 4). However, these reactions often require additional adjustments to achieve the desired outcomes. In contrast, lithium carbenoids can perform the homologation in a single, efficient step.[4]



Scheme 4. Exploiting the introduction of a CH2X fragment: general considerations

In the area of stereochemistry, lithium-borylation has become a key method for controlling the arrangement of atoms along a carbon chain and for creating multiple stereocenters with high stereoselectivity. Aggarwal and coworkers developed an efficient approach for synthesizing (+)-kalkitoxin and (+)-hydroxyphthioceranic acid using boronic acid esters in homologation reactions. By the iterative homologation, carried out with chiral lithiated benzoate esters and chloromethyllithium, they successfully introduced the required CH_2 units and made the process more efficient by eliminating the need for purification between reactions (Scheme 5).[4]



Scheme 5. Aggarwal´s assembly-line synthesis of (+)-kalkitoxin

1.3. THE LIMITED STABILITY OF LITHIUM CARBENOIDS

Lithium carbenoids are highly reactive compounds widely used as reagents for C-C bond formation in organic chemistry. A major challenge in their application is their instability, as they are very sensitive to temperature and can decompose easily under unfavourable conditions.[3]

This instability is further promoted by the Kirmse α-elimination, where the compound breaks down due to the strong interaction between the lithium atom and the halogen atom in the carbenoid. These interactions make the carbenoids ineffective unless they are properly stabilized.[6]

To address this instability, several strategies have been developed. The employment of stabilizing-groups which required additional removal steps that could degrees the chemoselectivity of the process,[4] or in contrast external stabilization. In particular, the employment of ethereal solvents, which coordinate the metal atom (Scheme 6, path b), proved to be effective in reducing the interactions between the lithium and the halogen, and thus preventing the α-elimination. Solvents like THF and hexamethylphosphoramide (HMPA) can stabilize di- and trihalogenated carbenoids while also increasing their reactivity. However, caution must be exercised with HMPA, as it can, in some cases, enhance α-elimination, especially with monohalogenated carbenoids (Scheme 6, path c).[3]

In addition, the presence of lithium halides such as LiBr, which coordinate the halogen atom of the carbenoid, helps to prevent the undesired decomposition (Scheme 6, path a).[3, 7]

Scheme 6. Degradation pathway of a carbenoid and possible points of interaction to suppress it

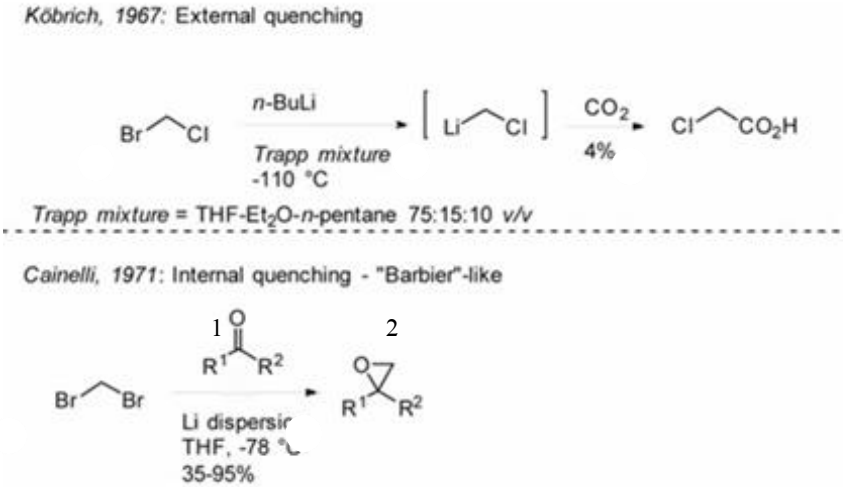
The importance of the reaction conditions for generating these highly reactive species is crucial.[2] Using Barbier-type conditions, in which the electrophile is already present in the reaction mixture when the lithium carbenoids is formed, is considered the best way to do batch reactions with these compounds. [3]

Lithium carbenoids can be generated through the typical methods reported for organometallic compounds, including lithium-halogen exchange, lithium-hydrogen exchange, lithium-sulfinyl exchange, and lithium-tin exchange. These protocols are essential for obtaining stable carbenoids in adequate quantities.[3]

Pioneers like Köbrich and Cainelli played a key role in developing stable reaction conditions by making discoveries that allowed for the synthesis and controlled use of carbenoids. For example, Köbrich discovered that bromochloromethane reacts with n-butyllithium at low temperatures to form chloromethyllithium, although the yield was only 4% (Scheme 7).[3]

Despite these early advances, decomposition remained a persistent challenge. Cainelli discovered that using Barbier-like reaction conditions,

where the carbenoid is generated in the presence of an electrophile, prevents decomposition and enables efficient reactions. This allows it to convert carbonyl compound **1** into epoxide **2** (Scheme 7). [3]



Scheme 7. Initial considerations on lithium carbenoid generation

To ensure the stability of the carbenoids very low temperatures must be employed. Typically, lithium carbenoids are formed between -78 °C and -110°C, as these temperatures prevent decomposition via α-elimination ensuring sufficient reactivity. At higher temperatures, the decomposition rates rise significantly, leading to undesirable side reactions.[3]
The stability of lithium carbenoids is largely determined by the choice of solvents, stabilizing agents, and reaction conditions. Only with careful control over these factors lithium carbenoids can be successfully applied in organic synthesis.

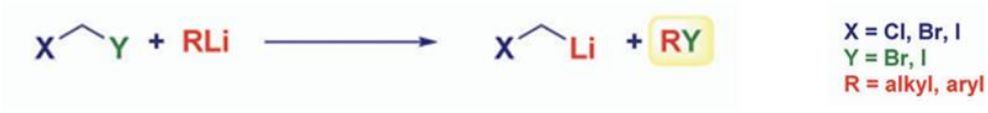
1.4. THE GENERATION OF LITHIUM CARBENOIDS

The typical methods reported for the generation of lithium carbenoids include: lithium-halogen exchange, lithium-hydrogen exchange, lithium-sulfinyl exchange, and lithium-tin exchange.[3]

The lithium-halogen exchange could be considered as an oxidative addition of lithium to the dihalomethanes, precursors of the desired halocarbenoids (Scheme 8).[4] This method is particularly popular and utilizes widely

available starting materials.[3] The halogen-lithium exchange occurs extremely rapidly, preventing unwanted side reactions and it occurs only on the heavier halogen leaving untouched the other one.[4]

Thus, heavier halogens such as iodine-containing compounds are particularly ideal, however, for industrial applications, the more economical bromochloromethane is commonly employed.[3,4]



Scheme 8. Preparation of monohalolithium and dihalolithium carbenoids via halogen-Li-exchange

Based on the understanding that LiBr is playing a crucial role for stabilizing halolithium carbenoids, ensuring a successful transformation, the group of Prof. V. Pace demonstrated that the employment of MeLi-LiBr complex in ethereal solvents at -78°C provides an even more efficient method for generating chloromethyllithium from chloroiodomethane.[7] This optimization, builds on previous work by D. S. Matteson showed as lithium bromide not only stabilizes the carbenoid through its coordinative effect but also prevents MeLi from reacting with the electrophilic substrate present in the reaction medium under Barbier conditions. The process mainly involves generating the carbenoid directly in situ, followed by its immediate reaction with the electrophile. Additionally, lithium bromide acts as a mild Lewis acid, which helps the carbenoid attack the electrophilic partner more easily. [3]

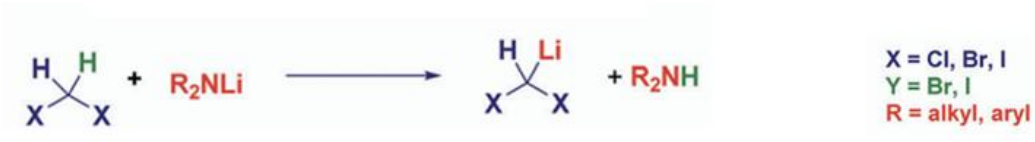
A stoichiometric ratio of 1:1 between dihalomethane and the organolithium reagent is usually sufficient, but a slight excess of dihalomethane (0.2–0.4 equivalents) helps minimize side reactions and the slow addition of the alkyllithium over 10–30 minutes, ensure a controlled reaction.[3]

Another method for accessing halogenated lithium carbenoids is the lithium–hydrogen exchange. Because of the high efficiency and rapid nature

of the lithium–halogen exchange, deprotonation has not been the preferred method for generating monohalolithium carbenoids. This is also because at very low temperatures (–115 °C), the strongly basic s-BuLi favours the halogen exchange over the deprotonation of a dihalomethane. [3]

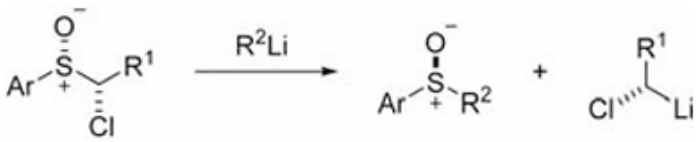
Because of the acidity of dihalomethanes conferred by the electron-withdrawing halogens, their proton can be easily removed by treatment with a lithium amide base such as LDA and LTMP (Scheme 9). [4, 3]

Deprotonation has emerged as the preferred technique for the synthesis of dihalomethylcarbenoids (e.g., $LiCHCl_2$, $LiCHBr_2$, and $LiCHI_2$) from their respective dihalomethane precursors. [3]



Scheme 9. Preparation of monohalolithium and dihalolithium carbenoids via proton-Li exchange

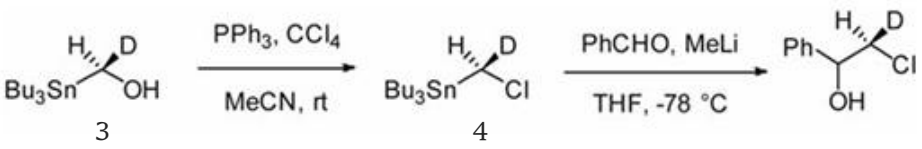
Furthermore, the investigation on the chiral stability of halolithium carbenoids prompted at first Hoffmann and then Blakemore to report a suitable method for the preparation and employment of chiral halogenated lithium carbenoids. This approach permitted the access to configurationally stable lithium carbenoids derived from halogenated aryl sulfoxides upon lithium-sulfinyl exchange. The reaction proceeds with inversion of configuration at sulfur and high stereofidelity (Scheme 10). Since α-halosulfoxides are not commercially available, they must be synthesized. [3]



Scheme 10. Lithium carbenoids from halogenated arylsulfoxides

Similarly, the lithium–tin exchange allows the synthesis of stereochemically stable chloromethyllithium compounds. These were generated by treating a

chiral stannane with MeLi. The key precursor, enantiopure chloromethylstannane-[D1], was obtained from homochiral tributylstannyl-[D1]-methanol (3) (Scheme 11). [3]



Scheme 11. Preparation of chiral chloromethyllithium via tin-lithium exchange

To summarize, the lithium–halogen exchange continues to be the method of choice for preparing monohalogenated lithium carbenoids due to its efficiency. However, alternatives like the lithium-sulfinyl or tin exchange offer distinct advantages when more stable intermediates or precise stereochemical control are needed.[3]

1.5. FLUORINATION

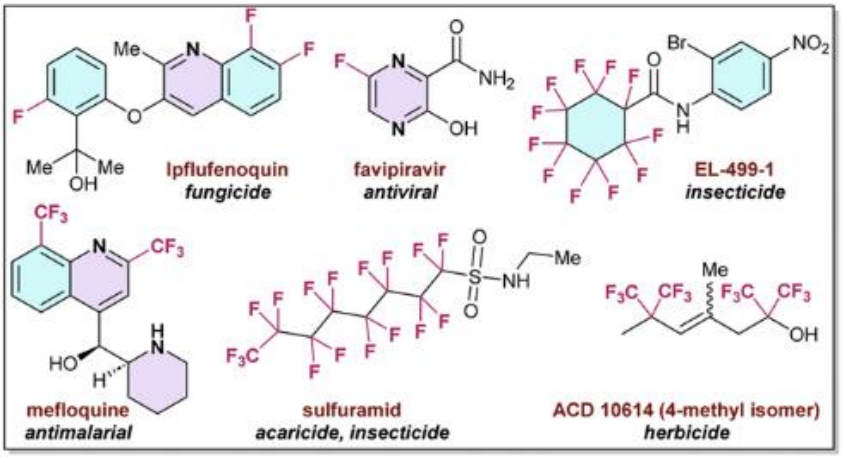
Fluorine is an extraordinary element that profoundly affects the chemical and physical properties of organic molecules due to its high electronegativity, small size, and exceptional bond strength. [19]
Fluorine can replace hydrogen or oxygen in molecules, often exhibiting similar or even enhanced biological activity. [8,19]

Adding a trifluoromethyl group (CF_3) to organic molecules enhances their lipophilicity and alters their electron density. A difluoromethyl group (CF_2H) has the ability to donate hydrogen bonds without being nucleophilic, while also being highly lipophilic, making it a unique mimic of a hydroxy group. A difluoromethylene group (CF_2=) serves as a reactive site for nucleophiles and can act as a potential isostere of carbonyl groups. [12]

Fluorine-containing groups enhance lipophilicity, allowing fluorinated compounds to more readily penetrate cell membranes, improve absorption, and often delay metabolism, due to the strength of C–F bonds compared to C–H bonds, in pharmaceutical agents. [8, 19]

Due to these unique properties, organofluorine chemistry has attracted significant interest in agrochemicals, the pharmaceutical industry, and materials science in recent decades. More than 20% of pharmaceutical products and 30% of agrochemical products contain fluorine compounds, as these greatly influence their biological activity, metabolic stability, and physicochemical properties.

Examples of fluorinated drugs with various medical activities (such as anticancer agents, antibiotics, antidepressants, anticonvulsants, antipsychotics, and antiemetics) are shown in Scheme 12. [13]

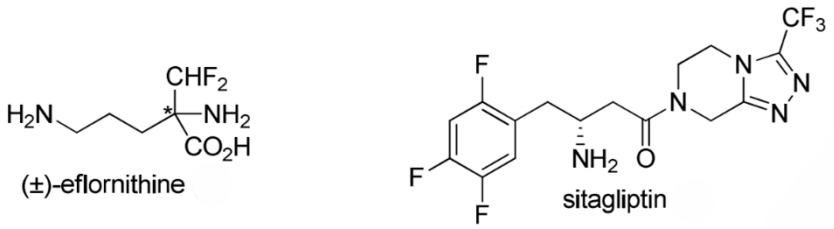


Scheme 12. Selected examples of CF3-embaded pharmaceuticals and agrochemicals

Against this background, it is not surprising that fluorine-containing derivatives of amino acids are attracting growing research interest. Derivatives of unnatural amino alcohols and their corresponding amino acids play a crucial role as key components of bioactive peptides, enzyme inhibitors, therapeutic agents, and chiral ligands.[10] Incorporating unnatural amino acids into peptide frameworks can help restrict structural flexibility, thereby strengthening their ability to bind biological targets. [9]

Fluorinated amino acid can often be incorporated into proteins without structural changes allowing scientists to study protein structures using ^{19}F NMR or spectrofluorimetry and to study enzyme mechanisms. In drug research, fluorination can help to create specific structures or side-chain shapes. The successful development of fluorinated amino acid drugs, such

as (±)-Eflornithine (used for trypanosomiasis and facial hirsutism) and Sitagliptin (an antidiabetic drug), demonstrates the importance of these compounds in pharmaceutical chemistry (Scheme 13).[8]



Scheme 13. Some fluorinated amino acid drugs

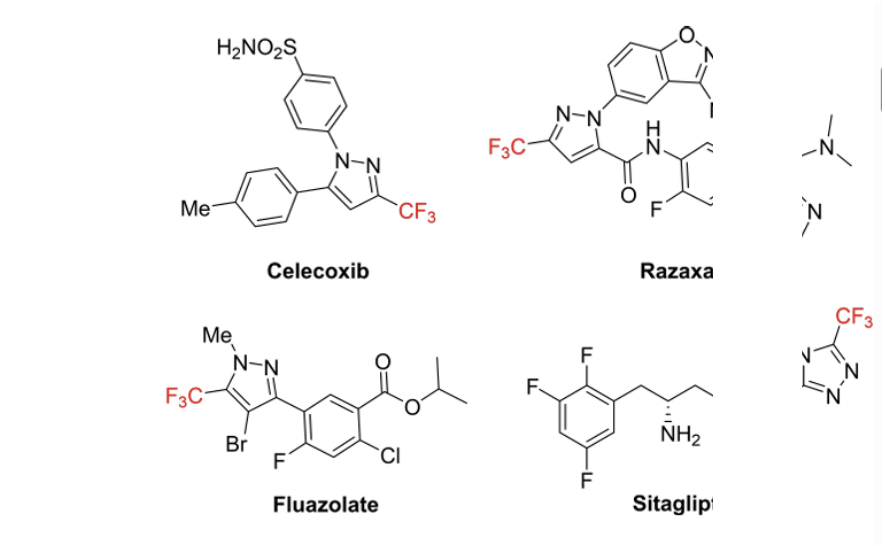
Moreover, fluorination can significantly shift enzyme selectivity by modifying electronic dynamics, steric factors, and substrate interactions, thereby increasing the selectivity of certain enzymes for specific enantiomers. [11]

1.5.1. FLUORINATION TECHNIQUES

The synthesis of fluorinated molecules presents a significant challenge due to the unique chemical behaviour of fluorine-containing compounds. One common approach involves incorporating fluorinated building blocks through multi-step synthesis to achieve complex target structures. Alternatively, fluorine atoms can be introduced later in the synthesis via ionic or radical reactions. In recent years, the development of more practical and efficient fluorination reagents has made it easier to selectively add a single fluorine atom, sparking growing interest in this area of research. [14]

1.6. TRIFLUOROMETHYLATION

Trifluoromethyl-containing compounds are an important group of fluorinated molecules with many biological effects. They are widely used in medicine and agriculture, with examples like Celecoxib (a COX-2 inhibitor), Razaxaban (a blood thinner), Fluazolate (an herbicide), and Sitagliptin (a DPP-4 inhibitor) (Scheme 14). [15]



Scheme 14. Representative examples of biologically active trifluoromethylated compounds

Because of their importance, researchers have worked hard to find better ways to add CF_3-groups to organic molecules.
One of the most promising reagents for this is 2-Bromo-3,3,3-trifluoropropene (BTP). It is highly reactive and can be used in many different chemical reactions. [15]

1.6.1. 2-BROM-3,3,3-TRIFLUORPROPEN (BTP)

BTP is an environmentally friendly, readily available, and useful raw material in synthetic chemistry. It can be produced by dehydrobromination from the dibromo adduct of trifluoropropene.

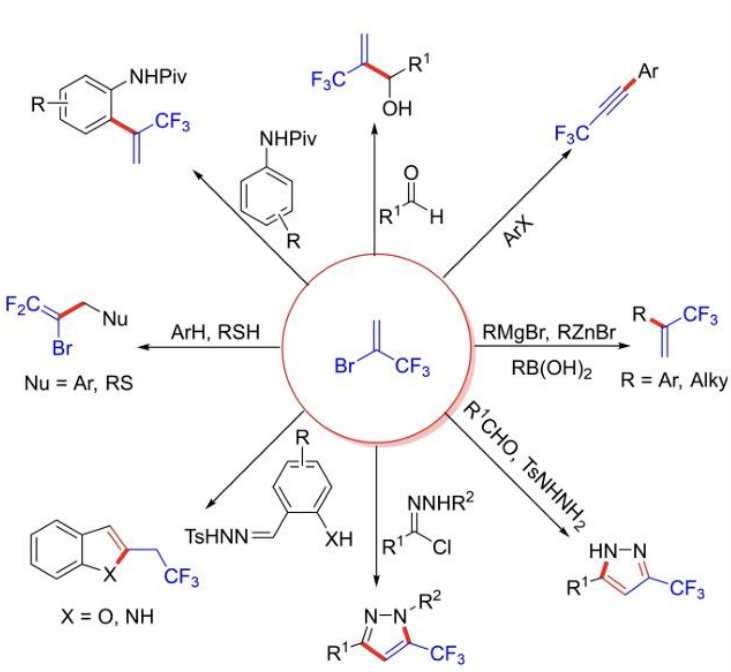
In early studies, the typical lithium-halogen exchange reaction of BTP occurred in the presence of a lithium reagent. This reaction then proceeded with ketones, aldehydes, or epoxides, leading to the formation of alcohols containing a trifluoromethyl group. [15, 16]

Under strong base conditions, BTP could also generate a 3,3,3-trifluoropropynyl anion, which reacted with various electrophiles. [15]

Over the past decades, BTP has been widely used in classical cross-coupling reactions, either directly or after conversion into organometallic species such as boron, zinc, tin, silicon, or lithium. [15, 17]

BTP has also been explored as a coupling partner in carbon-carbon bond formation. In addition, H-bond functionalization has proven to be valuable for the synthesis of trifluoromethylated compounds. [15]

Due to its unique structure, BTP has recently been utilized as a C-2 synthon in cycloaddition reactions, enabling the construction of trifluoromethyl-containing (hetero)cyclic compounds such as cyclopropane. Other reactions have also been reported, though less frequently, including SN2'-type reactions and intermolecular Stetter reactions (Scheme 15). [15]



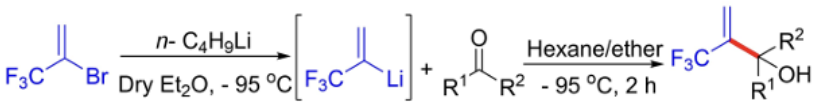
Scheme 15. Various reactions of BTP

1.6.2. THE ADDITION REACTION OF ORGANOMETALLIC REAGENTS WITH CARBONYL COMPOUNDS

The versatile reactivity of BTP enables a wide range of chemical transformations, including addition, coupling, and cycloaddition reactions. Particularly significant is the direct reaction of BTP with carbonyl compounds, as it provides an efficient method for introducing the trifluoromethyl group into organic molecules.[15]

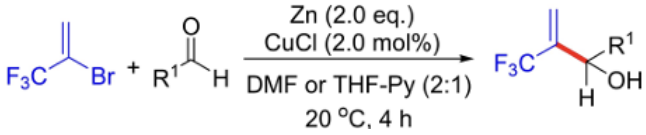
A well-established approach involves the addition of organometallic reagents to carbonyl compounds. This method is one of the fundamental transformations in organic chemistry, allowing for the targeted synthesis of trifluoromethylated alcohols. The reactivity of BTP in such reactions largely depends on the reaction conditions as well as the choice of metal or catalyst used.[15]

An early approach employs lithium-halogen exchange with n-butyllithium (n-BuLi) at extremely low temperatures (-100 °C). This generates a reactive intermediate that reacts with carbonyl compounds (Scheme 16). However, this method is challenging due to the thermal instability of the intermediate and the potential for side reactions. [15,16]



Scheme 16. Addition reactions of BTP with carbonyl compounds in the presence of n-C4H9Li

A milder alternative approach is the zinc-mediated Barbier reaction, in which zinc dust activates BTP, allowing it to react with aldehydes at room temperature (Scheme 17). This method offers high yields, mild reaction conditions, and good tolerance toward functional groups. [15, 18]

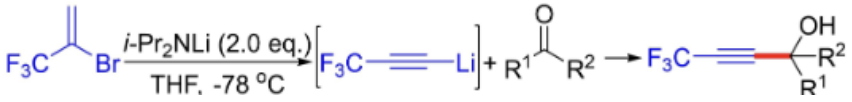


Scheme 17. Zinc-promoted Barbier-type reaction of BTP with aldehydes

Another approach is the BF_3-catalyzed ring opening of epoxides, where $BF_3{\cdot}OEt_2$ reduces the ring strain of the epoxide, facilitating an electrophilic attack by BTP.

Scheme 18. BF3-promoted ring-opening reactions of BTP with oxiranes

Finally, an LDA-mediated method uses lithium diisopropylamide (LDA) to convert BTP into a trifluoromethyl-substituted alkyne. This alkyne can then react with aldehydes or ketones to form trifluoromethylated propargyl alcohols. [15]



Scheme 19. Addition reactions of BTP with carbonyl compounds in the presence of LDA

2. WORK PROJECT

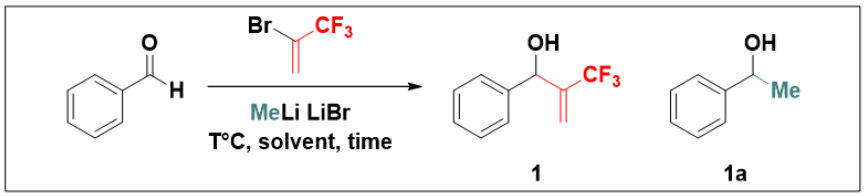
Based on the high interest and successful employment of various halogenated Lithium carbenoids on a broad range of electrophiles in the Prof. Pace´s group, coupled with the increasing interest for the development of methodologies aiming the selective introduction of the fluorine atom into an organic array, during my thesis internship we focused the attention on the C-3 homologation process via the employment of the versatile 2-bromo-3,3,3-trifluoropropene (BTP).

While the C-1 homologation operated via halogenated lithium carbenoids is wide explored, giving access to a vast gamma of homologated products, the insertion of a 3 carbon Sinton in a single step remain still a challenging operation. Considering the high potential of the already reported procedures, we envision the possible employment of BTP as lithium carbenoid precursor under milder condition, such as more convenient temperatures, to expand the scope and thus the chemoselectivity of the methodology. Due to the efficient employment of MeLi complexed with LiBr for the lithium-halogen exchange process to access mono-halogenated lithium carbenoids at low temperature (usually -78°C) under Barbier type condition, in ethereal solvents such as THF or Et_2O, able to reduce the possible alpha elimination process and thus increase the synthetic applicability of these type of carbenoids, we rationalised the possible access *in situ* of the 3,3,3-trifluoroisopropenyllithium by reacting BTP with MeLi-LiBr under Barbier type condition.

Despite the thermal instability of the corresponding reactive lithium species already at temperature > 105 °C and the possible non selective direct addition of the organolithium to the reactive electrophiles, giving as side product the corresponding alcohol, we investigated the halogen-lithium exchange on BTP in the presence of benzaldehyde with MeLi complexed with LiBr solution in THF (Table 1).

The reaction proved to be feasible at -78°C giving the corresponding product in 60 % yields and 40 % of the side product in 2 h (entry 1). Due to the fast halogen-lithium exchange occurring while using MeLi LiBr and the promising results obtained, we decide to further investigate the process with the aim to reduce the non-selective addition of the lithiated species und thus increasing the yield of the desired product. Reducing the load of MeLi LiBr (2 equivalent) and the rate of addition (slow addition within 20 min), 80% of the desired product was isolated, proving that at our condition the halogen-lithium exchange, and thus the addition to the electrophile, proceed faster than the direct attack of MeLi (entry 2). Reducing the temperature < -78°C did not particularly increase the yield, as well employing a mixture 1:1 of THF: Et_2O as solvent (entry 3-5). Finally, with the aim of reducing the time of the reaction and investigate the possible stability of the C-3 lithium carbenoid at higher temperature, the reaction with 2 equivalents of MeLi LiBr in dry THF, slowly added over a period of 20 min at 0°C, proved to be convenient, giving access to the desired homologated products in 97% of yield within 1h (entry 6).

Table 1. optimization



	RLi	equiv	solvent	Temperature(°C)	Time	Yield (1:1a)
Entry 1	MeLi LiBr	3	THF	-78	2h	60:40
Entry 2	MeLi LiBr	2	THF	-78	2h	80:20
Entry 3	MeLi LiBr	2	THF	-100	2h	70:30
Entry 4	MeLi LiBr	2	THF:Et_2O (1:1)	-78	2h	75:25
Entry 5	MeLi LiBr	2	Et_2O	-78	2h	79:21
Entry 6	MeLi LiBr	2	THF	0	1h	97:3

With the optimized condition in hand we focus on the scope of the reaction employing a *vast* gamma of substituted aromatic and aliphatic aldehydes.

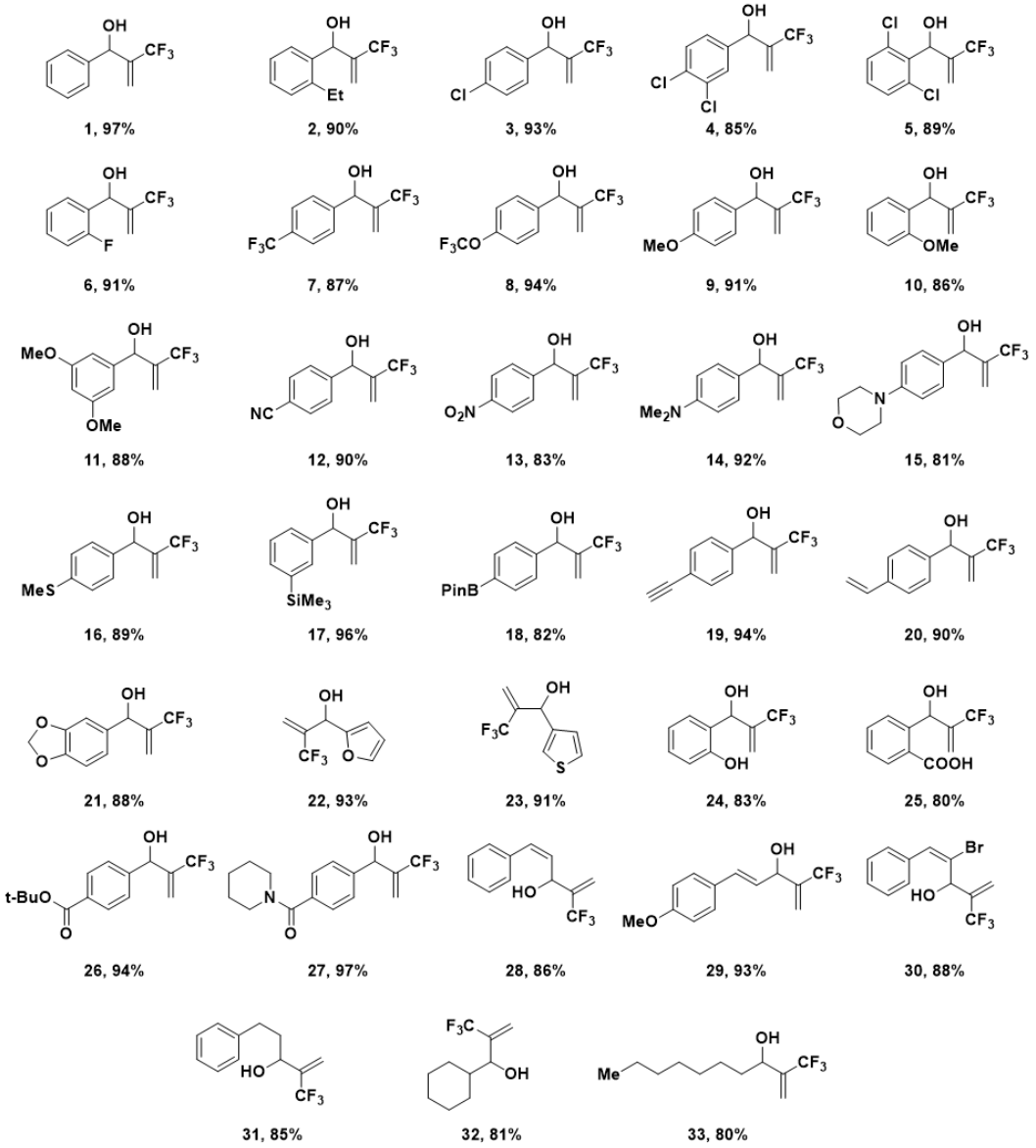
Electron-withdrawing groups such as cyano (CN), nitro (NO_2), trifluoromethoxy (OCF_3), halogens (Cl, Br, F), and boronic ester (Bpin) were well tolerated under the reaction conditions. Similarly, electron-donating groups such as methoxy (MeO), methylthio (MeS), dimethylamino (NMe_2), ethynyl, and vinyl substituents also proved to be compatible with the process.

Notably, the reaction proceeded efficiently even in the presence of sensitive functional groups, including amide, ester, hydroxyl (OH), carboxyl (COOH), boronic ester (Bpin) and silyl ($SiMe_3$); heterocyclic structures such as furan, thiophene and piperononyl substrates were successfully employed. Additionally, sterically hindered and aliphatic aldehydes, linear or cyclic systems, underwent the transformation without significant side reactions.

Moreover, the reaction proved to be adaptable to substrates with substituents in various positions, including para, meta, and ortho. The method resulted in high yields and demonstrated good selectivity, as the desired C-3 homologation of aldehydes proceeded with minimal competing side reactions.

The isolated and characterized products, with the related yields, are reported in Table 2. These results highlight the broad applicability and functional group tolerance of this approach, making it a promising synthetic tool for introducing 3,3,3-trifluoropropenyl group into diverse aldehydes.

Table 2. isolated products



3. CONCLUSION

Our study confirmed that a broad range of aldehydes undergo efficient C-3 trifluoro-homologation under the optimized conditions, leading to the targeted products in high yields with good selectivity. The reaction consistently achieved complete conversion of the starting materials, and purification effectively removed any minor side products. Aldehydes bearing both electron-donating and electron-withdrawing groups reacted smoothly, with no noticeable impact from sensitive functional groups. Moreover, the reaction proved to be adaptable to substrates with substituents in various positions, including para, meta, and ortho, as well for aliphatic linear or cyclic substrates. This methodology demonstrated broad applicability, successfully extending to both aromatic and aliphatic aldehydes.

4. EXPERIMENTAL SECTION

4.1. MATERIALS AND METHODS

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded at 297 K on a Bruker Avance III 400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, 40 MHz for ^{15}N, 376 MHz for ^{19}F) equipped with a directly detecting broadband observe (BBFO) probe, with a Bruker Avance III 500 spectrometer (500 MHz for ^{1}H, 125 MHz for ^{13}C) using a Prodigy cryoprobe, and with a Bruker DRX 200 spectrometer (200 MHz for ^{1}H, 50 MHz for ^{13}C) with a ^{1}H/ ^{13}C dual probe.

The centre of the solvent signal was used as an internal standard which was related to TMS with δ 7.26 ppm (^{1}H in $CDCl_3$), δ 7.16 ppm (^{1}H in C_6D_6), δ 77.00 ppm (^{13}C in $CDCl_3$) and δ 128.06 ppm (^{13}C in C_6D_6). Absolute referencing via Ξ ratio was used for the ^{19}F NMR spectra. Spin-spin coupling constants (J) are given in Hz.

In nearly all cases, full and unambiguous assignment of all resonances was performed by combined application of standard NMR

techniques, such as APT, HSQC, HMBC, HSQC-TOCSY, COSY and NOESY experiments.

All the reactions were carried out under inert atmosphere of argon.

THF was distilled over Na/benzophenone.

Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar and TCI Europe. Solutions were evaporated under reduced pressure with a rotary evaporator. TLC was carried out on aluminium sheets precoated with silica gel 60F254 (Merchery-Nagel, Merk); the spots were visualised under UV light (λ = 254 nm).

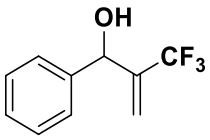
4.2. GENERAL PROCEDURE

4.2.1. GENERAL PROCEDURE

To a solution of aldehyde (1.0 equiv) in dry THF (3 mL) cooled at 0 °C, the BTP carbenoids precursor was added (2 equiv) under Argon atmosphere. After 10 min, MeLi-LiBr 1.5 M solution in diethyl ether (2 equiv) was added dropwise during a period of 20 min and, then the stirring was continued for additional 1h. The mixture was quenched with saturated (aq.) NH_4Cl (3 mL) and extracted with ethyl acetate. The organic layer was washed with saturated (aq.) NaCl (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure (bath: rt for aliphatic compounds) to give the crude compound eventually purified as indicated below.

4.3. SPECTRAL AND CHARACTERIZATION DATA

1-phenyl-2-(trifluoromethyl)prop-2-en-1-ol (1) [1]



By following the General Procedure, starting from Benzaldehyde (200 mg, 1.9 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.4 mL, 3.8 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl

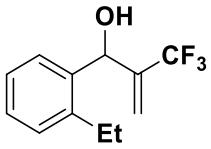
ether (0.5 mL, 3.8 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 97 % yield (373 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38 (m, 5H, Ph H-2,3,4,5,6), 5.93 (s, 1H, H-3), 5.81 (s, 1H, H-1), 5.44 (s, 1H, H-3), 2.34 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.0 (q, *J*=28.2 Hz, C-2), 140.4 (Ph C-1), 128.8 (2C, Ph C-3,5), 128.7 (Ph C-4), 127.0 (2C, Ph C-2,6), 123.1 (q, *J*=208.5 Hz, CF_3), 120.0 (q, *J*=5.5 Hz, C-3), 71.5 (1H, OH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(2-ethylphenyl)-2-(trifluoromethyl)prop-2-en-1-ol (2)



By following the General Procedure, starting from 2-Ethylbenzaldehyde (200 mg, 1.5 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 3.0 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.0 mL, 3.0 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 90% yield (311 mg) as colourless oil without any further purification.

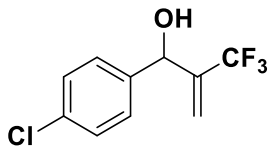
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44 (dd, *J*=7.4, 1.8 Hz, 1H, Ph H-6), 7.30 (m, 3H, Ph H-3,4,5), 5.97 (s, 1H, H-3), 5.75 (s, 1H, H-1), 5.68 (s, 1H, H-3), 2.69 (m, 2H, CH_2), 2.12 (s, 1H, OH), 1.26 (t, *J*=7.6 Hz, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.9 (Ph C-1), 141.0 (q, *J*=25.4 Hz, C-2), 137.4 (Ph C-2), 129.1 (Ph C-3), 128.8 (Ph C-4), 126.8 (Ph C-6), 126.4 (Ph C-5),

124.9 (q, *J*=272.8 Hz, CF_3), 120.7 (q, *J*=5.2 Hz, C-3), 67.4 (C-1), 25.2 (CH_2), 15.5 (CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.3 (s, F-1, CF_3).

1-(4-chlorophenyl)-2-(trifluoromethyl)prop-2-en-1-ol (3)



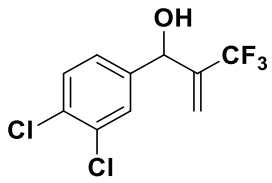
By following the General Procedure, starting from 4-Chlorobenzaldehyde (200 mg, 1.4 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 2.9 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.9 mL, 2.9 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 93% yield (308 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35 (d, *J*=8.6 Hz, 2H, Ph C-3,5), 7.31 (d, *J*=8.6 Hz, 2H, Ph C-2,6), 5.94 (s, 1H, H-3), 5.80 (s, 1H, C-1), 5.42 (s, 1H, H-3), 2.21 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.7 (q, *J*=26.1, C-2), 138.9 (Ph C-1), 134.5 (Ph C-4), 129.0 (2C, Ph C-3,5), 128.4 (2C, Ph C-2,6), 123.1 (q, *J*=261,6, CF_3), 120.3 (q, *J*=5.4 Hz, C-3), 70.8 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(3,4-dichlorophenyl)-2-(trifluoromethyl)prop-2-en-1-ol (4)



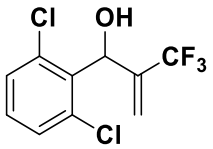
By following the General Procedure, starting from 3,4-Dichlorobenzaldehyde (200 mg, 1.1 mmol, 1 equiv), 2-bromo-3,3,3-trifluoropropen (0.3 mL, 2.3 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.5 mL, 2.3 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 85% yield (253 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47 (s, 1H, Ph H-2), 7.44 (d, *J*=8.3 Hz, 1H, Ph H-2), 7.19 (dd, *J*=8.3, 2.1 Hz, 1H, Ph H-6), 5.96 (s, 1H, H-3), 5.78 (s, 1H, H-1), 5.38 (s, 1H, H-3), 2.46 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.5 (Ph C-1), 140.4 (q, *J*=28.4 Hz, C-2), 133.0 (Ph C-4), 132.7 (Ph C-3), 130.8 (Ph C-5), 128.9 (Ph C-2), 126.3 (Ph C-6), 123.1 (q, *J*=272.4 Hz, CF_3), 120.9 (q, *J*=5.3 Hz, C-3), 70.3 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(2,6-dichlorophenyl)-2-(trifluoromethyl)prop-2-en-1-ol (5)



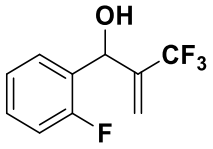
By following the General Procedure, starting from 2,6-Dichlorobenzaldehyde (200 mg, 1.1 mmol, 1 equiv), 2-bromo-3,3,3-trifluoropropen (0.2 mL, 2.3 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.5 mL, 2.3 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 89 % yield (265 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34 (m, 2H, Ph H-3,5), 7.23 (m, 1H, Ph H-4), 6.23 (dq, *J*=10.5, 1.0 Hz, 1H, H-3), 5.97 (t, *J*=1.6 Hz, 1H, H-1), 5.55 (t, *J*=1.8 Hz, 1H, H-3), 3.25 (d, *J*=10.5 Hz, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.5 (q, *J*=28.2 Hz, C-2), 135.4 (Ph C-1), 134.3 (Ph C-4), 130.2 (2C, Ph C-2,6), 129.6 (2C, Ph C-3,5), 123.1 (q, *J*=272.4 Hz, CF_3), 120.6 (q, *J*=5.6 Hz, C-3), 69.2 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.0 (s, F-1, CF_3).

1-(2-fluorophenyl)-2-(trifluoromethyl)prop-2-en-1-ol (6)



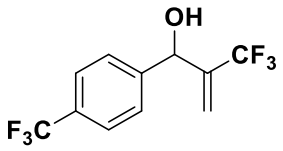
By following the General Procedure, starting from 2-Fluorobenzaldehyde (200 mg, 1.6 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 3.2 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.7 mL, 3.2 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 91% yield (321 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44 (m, 1H, Ph H-4), 7.32 (m, 1H, Ph H-3), 7.18 (m, Ph H-6), 7.06 (m, Ph H-5), 5.94 (s, 1H, H-3), 5.75 (d, *J*=4.9 Hz, 1H, H-1), 5.73 (t, *J*=1.5 Hz, 1H, H-3), 2.54 (d, *J*=5.0 Hz, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.2 (d, *J*=247.8 Hz, Ph C-2), 139.9 (q, *J*=28.3 Hz, C-2), 130.3 (d, *J*=8.4 Hz, Ph C-1), 128.4 (d, *J*=3.6 Hz, Ph C-4), 127.4 (d, *J*=13.1 Hz, Ph C-6), 124.5 (d, *J*=3.6 Hz, Ph C-5), 123.2 (q, *J*=272.3, CF_3), 120.5 (q, *J*=5.3 Hz, C-3), 115.7 (d, *J*=21.8 Hz, Ph C-3), 65.3 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -118.8 (m, F-2, F), -65.5 (s, F-1, CF_3).

2-(trifluoromethyl)-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-ol (7) [1]



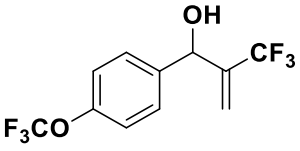
By following the General Procedure, starting from 4-(Trifluoromethyl)benzaldehyde (200 mg, 1.2 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.2 mL, 2.3 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.5 mL, 2.3 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 87% yield (282 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (d, *J*=8.2 Hz, 2H, Ph H-3,5), 7.50 (d, *J*=8.3 Hz, 2H, Ph H-2,6), 5.96 (s, 1H, H-3), 5.78 (s, 1H, H-1), 5.50 (s, 1H, H-3), 2.84 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.3 (Ph C-1), 140.7 (q, *J*=28.3 Hz, C-2), 130.8 (q, *J*=32.6 Hz, Ph C-4), 127.3 (2C, Ph C-3,5), 125.8 (q, *J*=3.8 Hz, 2C, Ph C-2,6), 126.3 (q, *J*=155.8 Hz, CF_3), 123.6 (q, *J*=176.9 Hz, CF_3), 120.8 (q, *J*=5.4 Hz, C-3), 70.9 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -62.7 (s, F-2, CF3), -65.3 (s, F-1, CF_3).

1-(4-(trifluoromethoxy)phenyl)-2-(trifluoromethyl)prop-2-en-1-ol (8)



By following the General Procedure, starting from 4-(Trifluoromethoxy)benzaldehyde (200 mg, 1.2 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.2 mL, 2.3 mmol, 2 equiv), Methyllithium lithium

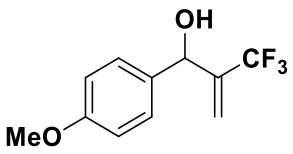
bromide complex solution 1.5 M in diethyl ether (1.5 mL, 2.3 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 94% yield (323 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (d, *J*=8.1 Hz, 2H, Ph H-2,6), 7.51 (d, *J*=8.1 Hz, 2H, Ph H-3,5), 5.97 (q, *J*=1.5 Hz, H-3), 5.79 (s, 1H, H-1), 5.50 (s, 1H, H-3), 2.29 (d, *J*=4.0 Hz, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.2 (Ph C-4), 140.7 (q, *J*=23.1 Hz, C-2), 130.9 (q, *J*=33.4 Hz, Ph C-1), 127.3 (2C, Ph C-3,5), 125.8 (q, *J*=3.6 Hz, 2C, Ph C-2,6), 124.1 (q, *J*=272.1 Hz, CF_3), 123.2 (q, *J*=273.9 Hz, OCF_3), 120.8 (q, *J*=5.4 Hz, C-3), 70.9 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.3 (s, F-1, CF_3), -62.7 (s, F-1, OCF_3).

1-(4-methoxyphenyl)-2-(trifluoromethyl)prop-2-en-1-ol (9)



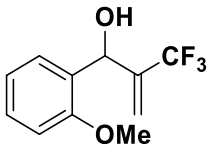
By following the General Procedure, starting from 4-Methoxybenzaldehyde (200 mg, 1.5 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 2.9 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.0 mL, 2.9 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 91% yield (316 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.22 (d, *J*=8.0 Hz, 2H, Ph H-2,6), 6.84 (d, *J*=8.4 Hz, 2H, Ph H-3,5), 5.86 (s, 1H, H-3), 5.77 (s, 1H, H-1), 5.28 (s, 1H, H-3), 3.75 (s, 3H, CH_3), 2.67 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.7 (Ph C-4), 141.1 (q, *J*=27.8 Hz, C-2), 132.6 (Ph C-1), 128.3 (Ph C-2,6), 123.3 (q, *J*=273.9 Hz, CF_3), 119.2 (q, *J*=5.4 Hz, C-3), 114.2 (Ph C-2), 114.1 (2C, Ph C-3,5), 70.8 (C-1), 55.2 (CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.1 (s, F-1, CF_3).

1-(2-methoxyphenyl)-2-(trifluoromethyl)prop-2-en-1-ol (10)



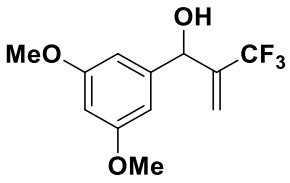
By following the General Procedure, starting from 2-Methoxybenzaldehyde (200 mg, 1.5 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 2.9 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.0 mL, 2.9 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 86% yield (299 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32 (m, 2H, Ph H-5,6), 6.99 (t, *J*=7.5 Hz, 1H, Ph H-3), 6.91 (d, *J*=8.6 Hz, 1H, Ph H-4), 5.89 (s, 1H, H-3), 5.66 (s, 1H, H-1), 5.62 (s, 1H, H-3), 3.85 (s, 3H, CH_3), 2.91 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.0 (Ph C-2), 140.5 (q, *J*=19.9 Hz, C-2), 129.7 (Ph C-4), 128.4 (Ph C-6), 128.3 (Ph C-1), 123.7 (q, *J*=105.8 Hz, CF_3), 121.0 (Ph C-5), 119.8 (q, *J*=5.4 Hz, C-3), 111.0 (Ph C-3), 67.9 (CH_3), 55.6 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.3 (s, F-1, CF_3).

1-(3,5-dimethoxyphenyl)-2-(trifluoromethyl)prop-2-en-1-ol (11)



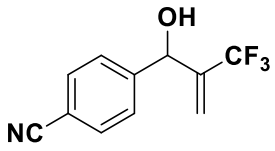
By following the General Procedure, starting from 3,5-Dimethoxybenzaldehyde (200 mg, 1.2 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 2.4 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.6 mL, 2.4 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 88% yield (277 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.90 (s, 1H, Ph H-4), 6.81 (s, 2H, Ph H-2,6), 5.86 (s, 1H, H-3), 5.62 (s, 1H, H-1), 5.59 (s, 1H, H-3), 3.75 (d, *J*=7.8 Hz, 6H, CH_3), 3.26 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.8 (Ph C-3), 151.0 (Ph C-5), 140.4 (q, *J*=28.3 Hz, C-2), 129.5 (Ph C-1), 123.4 (q, *J*=274.3 Hz, CF_3), 119.8 (q, *J*=5.4 Hz, C-3), 114.2 (Ph C-2), 113.8 (Ph C-6), 112.0 (Ph C-4), 67.4 (OH), 56.0 (CH_3), 55.7 (CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

4-(1-hydroxy-2-(trifluoromethyl)allyl)benzonitrile (12)



By following the General Procedure, starting from 4-Formylbenzonitrile (200 mg, 1.5 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 3.0 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl

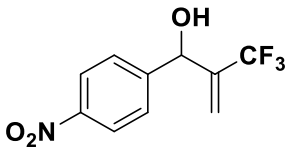
ether (2.0 mL, 3.0 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 90% yield (307 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, *J*=8.1 Hz, 2H, Ph H-3,5), 7.51 (d, *J*=8.0 Hz, 2H, Ph H-2,6), 5.98 (s, 1H, H-3), 5.80 (s, 1H, H-1), 5.50 (s, 1H, H-3), 2.43 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.6 (Ph C-1), 140.5 (q, *J*=31.6 Hz, C-2), 132.5 (2C, Ph C-3,5), 127.7 (2C, Ph C-2,6), 122.9 (q, *J*=269.2 Hz, CF_3), 121.1 (q, *J*=5.4 Hz, C-3), 118.6 (CN), 112,3 (Ph C-4), 70.7 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(4-nitrophenyl)-2-(trifluoromethyl)prop-2-en-1-ol (13)



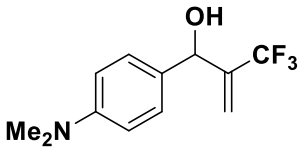
By following the General Procedure, starting from 4-Nitrobenzaldehyde (200 mg, 1.3 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 2.6 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.8 mL, 2.6 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 83% yield (267 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23 (d, *J*=8.8 Hz, 2H, Ph H-3,5), 7.57 (d, *J*=8.8 Hz, 2H, Ph H-2,6), 6.00 (s, 1H, H-3), 5.82 (s, 1H, H-1), 5.57 (d, *J*=3.5 Hz, 1H, H-3), 2.41 (d, *J*=4.0 Hz, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.0 (Ph C-1), 147.3 (Ph C-4), 140.5 (q, *J*=28.5 Hz, C-2), 127.8 (2C, Ph C-2,6), 124.0 (2C, Ph C-3,5), 123.1 (q, *J*=268.3 Hz, CF_3), 121.3 (q, *J*=5.4 Hz, C-3), 70.6 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(4-(dimethylamino)phenyl)-2-(trifluoromethyl)prop-2-en-1-ol (14)

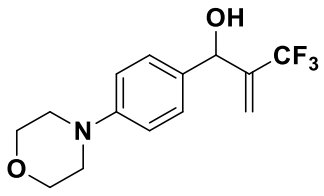


By following the General Procedure, starting from 4-(Dimethylamino)benzaldehyde (200 mg, 1.3 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 2.7 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.8 mL, 2.7 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 92% yield (293 mg) as colourless oil without any further purification.
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.21 (d, *J*=8.3 Hz, 2H, Ph H-2,6), 6.72 (d, *J*=8.5 Hz, 2H, Ph H-3,5), 5.90 (s, 1H, H-3), 5.85 (s, 1H, H-1), 5.31 (s, 1H, H-3), 2.96 (s, 6H, CH_3), 2.31 (m, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 150.8 (Ph C-4), 141.2 (q, *J*=28.0 Hz, C-2), 128.2 (Ph C-1), 128.1 (2C, Ph C-2,6), 123.4 (q, *J*=279.9 Hz, CF_3), 118.9 (q, *J*=5.3 Hz, C-3), 112.6 (2C, Ph C-3,5), 71.2 (C-1), 40.6 (CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.1 (s, F-1, CF_3).

1-(4-morpholinophenyl)-2-(trifluoromethyl)prop-2-en-1-ol (15)



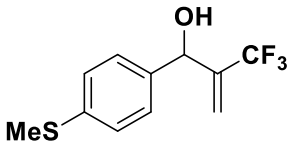
By following the General Procedure, starting from 4-Morpholinobenzaldehyde (120 mg, 1.0 mmol, 1 equiv), 2-bromo-3,3,3-trifluoropropen (0.2 mL, 2.0 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.3 mL, 2.0 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 81% yield (232 mg) as colourless oil without any further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.24 (d, *J*=8.8 Hz, 2H, Ph H-2,6), 6.87 (d, *J*=8.9 Hz, 2H, Ph H-3,5), 5.88 (s, 1H, H-3), 5.81 (s, 1H, H-1), 5.31 (s, 1H, H-3), 3.81 (s, 4H, CH_2), 3.12 (s, 4H, CH_2).

^{13}C NMR (150 MHz, $CDCl_3$) δ: 151.3 (Ph C-4), 141.2 (q, *J*=27.9 Hz, C-2), 131.9 (Ph C-1), 128.0 (2C, Ph C-2,6), 123.3 (q, *J*=274.2 Hz, CF_3), 119.2 (q, *J*=5.1 Hz, C-3), 115.5 (2C, Ph C-3,5), 70.8 (C-1), 66.8 (2C, Morpholin C-3,5), 49.1 (2C, Morpholin C-2,6).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(4-(methylthio)phenyl)-2-(trifluoromethyl)prop-2-en-1-ol (16)



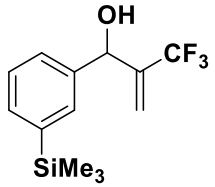
By following the General Procedure, starting from 4-(Methylthio)benzaldehyde (200 mg, 1.3 mmol, 1 equiv), 2-bromo-3,3,3-trifluoropropen (0.3 mL, 2.6 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.8 mL, 2.6 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 89% yield (287 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.27 (m, *J*=8.5 Hz, 4H, Ph H-2,3,5,6), 5.93 (s, 1H, H-3), 5.82 (s, 1H, H-1), 5.40 (s, 1H, H-3), 2.49 (s, 3H, CH_3), 2.13 (d, *J*=3.8 Hz, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.9 (q, *J*=28.0 Hz, C-2), 139.2 (Ph C-4), 137.2 (Ph C-1), 127.5 (2C, Ph C-3,5), 126.6 (2C, Ph C-2,6), 123.2 (q, *J*=274.3 Hz, CF_3), 119.9 (q, *J* = 5.4 Hz, C-3), 71.0 (C-1), 15.7 (CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

2-(trifluoromethyl)-1-(3-(trimethylsilyl)phenyl)prop-2-en-1-ol (17)



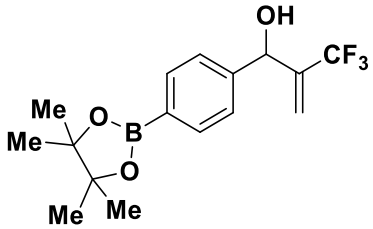
By following the General Procedure, starting from 3-(Trimethylsilyl)benzaldehyde (155 mg, 1.2 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.2 mL, 2.2 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.6 mL, 2.2 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 96% yield (316 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (tt, *J*=3.7, 1.3 Hz, 2H, Ph H-2,4), 7.28 (s, 1H, Ph H-5), 7.26 (d, *J*=2.4 Hz, 1H, Ph H-6), 5.84 (s, 1H, H-3), 5.70 (s, 1H, H-1), 5.34 (d, *J*=3.6 Hz, 1H, H-3), 2.14 (dd, *J*=4.2, 1.5 Hz, 1H, OH), 0.19 (s, 9H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.4 (Ph C-1), 141.1 (q, *J*=27.8 Hz, C-2), 139.6 (Ph C-3), 133.7 (Ph C-5), 131.9 (Ph C-2), 128.2 (Ph C-4), 127.4 Ph C-6), 123.3 (q, *J*=272.3 Hz, CF_3), 119.97 (q, *J*=5.3 Hz, C-3), 71.7 (C-1), -1.1 (3C, CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-2-(trifluoromethyl)prop-2-en-1-ol (18)



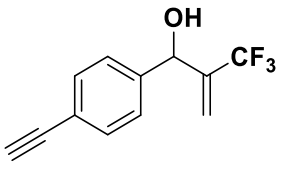
By following the General Procedure, starting from 4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (200 mg, 0.9 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.2 mL, 1.7 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.2 mL, 1.7 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 82% yield (242 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (dd, *J*=7.7, 5.7 Hz, 2H, Ph H-3,5), 7.36 (d, *J*=7.8 Hz, 2H, Ph H-2,6), 5.92 (d, *J*=4.1 Hz, 1H, H-3), 5.76 (d, *J*=2.9 Hz, 1H, H-1), 5.42 (s, 1H, H-3), 2.57 (s, 1H, OH), 1.34 (s, 12H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.4 (Ph C-1), 140.9 (q, *J*=27.9 Hz, C-2), 135.2 (2C, Ph C-3,5), 126.3 (2C, Ph C-2,6), 124.8 (Ph C-4), 123.3 (q, *J*=268.1 Hz, CF_3), 120.2 (q, *J*=5.4 Hz, C-3), 84.1 (2C, C-4,5), 71.3 (C-1), 25.0 (4C, CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(4-ethynylphenyl)-2-(trifluoromethyl)prop-2-en-1-ol (19)



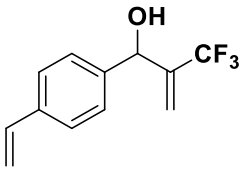
By following the General Procedure, starting from 4-Ethynylbenzaldehyde (200mg, 1.5 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 3.0 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.0 mL, 3.0 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 94% yield (319 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 (d, *J*=8.3 Hz, 2H, Ph H-3,5), 7.33 (d, *J*=8.1 Hz, 2H, Ph H-2,6), 5.93 (s, 1H, H-3), 5.77 (s, 1H, H-1), 5.42 (s, 1H, H-3), 3.09 (s, 1H, CH), 2.27 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.0 (Ph C-1), 140.8 (q, *J*=28.2 Hz, C-2), 132.6 (2C, Ph C-3,5), 126.9 (2C, Ph C-2,6), 123,2 (q, *J*=272.4 Hz, CF_3), 122.5 (Ph C-4), 120.41 (q, *J*=5.3 Hz, C-3), 83.3 (CC), 77.9 (CH), 71.1 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

2-(trifluoromethyl)-1-(4-vinylphenyl)prop-2-en-1-ol (20)



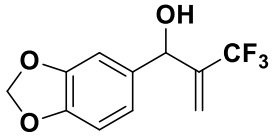
By following the General Procedure, starting from 4-Vinylbenzaldehyde (200 mg, 1.5 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 3.0 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.0 mL, 3.0 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 90% yield (308 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42 (d, *J*=8.1 Hz, 2H, Ph H-3,5), 7.32 (d, *J*=8.2 Hz, 2H, Ph H-2,6), 6.72 (dd, *J*=17.6, 10.9 Hz, 1H, $CHCH_2$), 5.93 (m, 1H, H-3), 5.80 (m, 2H, H-3), 5.77 (d, *J*=18.3 Hz, 1H, H-3), 5.42 (s, 1H, C-2), 5.28 (d, *J*=10.9 Hz, 1H, $CHCH_2$), 2.25 (d, *J*=3.7 Hz, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 103.3 (q, *J*=22.6 Hz, C-2), 102.4 (Ph C-1), 100.6 (Ph C-4), 98.9 ($CHCH_2$), 89.7 (2C, Ph C-3,5), 89.2 (2C, Ph C-2,6), 85.8 (q, *J*=272.6 Hz, CF_3), 82.5 (q, *J*=5.4 Hz, C-3), 77.2 ($CHCH_2$), 33.7 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(benzo[d][1,3]dioxol-5-yl)-2-(trifluoromethyl)prop-2-en-1-ol (21)



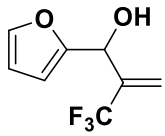
By following the General Procedure, starting from Benzo[d][1,3]dioxole-5-carbaldehyde (200 mg, 1.3 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 2.7 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.8 mL, 2.7 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 88% yield (281 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.78 (m, 3H, Ph H-2,3,6), 5.92 (m, 2H, Dioxolan CH_2), 5.89 (s, 1H, H-3), 5.79 (s, 1H, H-1), 5.27 (s, 1H, H-3), 2.78 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.1 (Ph C-5), 153.9 (Ph C-4), 147.07 (q, *J*=28.2 Hz, C-2), 140.5 (Ph C-1), 129.4 (q, *J*=272.3 Hz, CF_3), 127.0 (Ph C-2), 125.6 (q, *J*=5.4 Hz, C-3), 114.4 (Ph C-3), 113.4 (Ph C-6), 107.4 (Dioxalan CH_2), 77.2 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

1-(furan-2-yl)-2-(trifluoromethyl)prop-2-en-1-ol (22) [1]



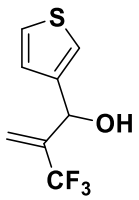
By following the General Procedure, starting from Furan-2-carbaldehyde (200 mg, 2.1 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.4 mL, 4.2 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.8 mL, 4.2 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 93% yield (375 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (m, 1H, Ar H-5), 6.36 (dd, *J*=3.3, 1.8 Hz, 1H, Ar H-3), 6.33 (d, *J*=3.3 Hz, 1H, Ar H-4), 5.99 (s, 1H, H-3), 5.90 (s, 1H, H-1), 5.46 (d, *J*=4.9 Hz, 1H, H-3), 2.40 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.7 (Ar C-2), 143.2 (Ar C-5), 138.7 (q, *J*=29.1 Hz, C-2), 123.0 (q, *J*=280.9 Hz, CF_3), 120.9 (q, *J*=5.4 Hz, C-3), 110.7 (Ar C-4), 108.5 (Ar C-3), 64.9 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.9 (s, F-1, CF_3).

1-(thiophen-3-yl)-2-(trifluoromethyl)prop-2-en-1-ol (23)



By following the General Procedure, starting from Thiophene-3-carbaldehyde (200 mg, 1.8 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.4 mL, 3.6 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.4 mL, 3.6 mmol, 2.0 equiv) and dry THF (5

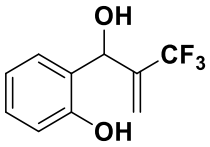
mL), the desired compound was obtained in 91% yield (341 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31 (s, 1H, Ar H-2), 7.29 (s, 1H, Ar H-4), 7.04 (dd, *J*=5.0, 1.4 Hz, 1H, Ar H-5), 5.93 (dt, *J*=2.7, 1.4 Hz, 1H, H-3), 5.79 (m, 1H, H-1), 5.52 (d, *J*=4.0 Hz, 1H, H-3), 2.33 (d, *J*=4.1 Hz, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.8 (Ar C-3), 140.9 (q, *J*=22.8 Hz, C-2), 126.7 (Ar C-5), 126.1 (Ar C-4), 123,3 (q, *J*=267.0 Hz, CF_3), 123.1 (Ar C-2), 120.1 (q, *J*=5.4 Hz, C-3), 67.4 (C-1).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.4 (s, F-1, CF_3).

2-(1-hydroxy-2-(trifluoromethyl)allyl)phenol (24)



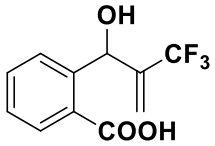
By following the General Procedure, starting from 2-Hydroxybenzaldehyde (200 mg, 1.6 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 3.3 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.2 mL, 3.3 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 83% yield (289 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.29 (bs, OH), 7.23 (m, 1H, Ph H-6), 7.03 (dd, *J*=7.6, 1.7 Hz, 1H, Ph H-4), 6.88 (m, 2H, Ph 3,5), 5.93 (s, 1H, H-3), 5.62 (s, 1H, H-1), 5.56 (s, 1H, H-3), 3.41 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.3 (Ph C-2), 139.0 (q, *J*=28.3 Hz, C-2), 130.1 (Ph C-1), 128.5 (Ph C-4), 123.9 (Ph C-6), 123.3 (q, *J*=272.8 Hz, CF_3), 121.6 (q, *J*=5.5 Hz, C-3), 120.6 (Ph C-5), 117.3 (Ph C-3), 71.5 (C-1.)

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.1 (s, F-1, CF_3).

2-(1-hydroxy-2-(trifluoromethyl)allyl)benzoic acid (25)



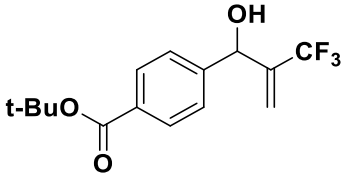
By following the General Procedure, starting from 2-Formylbenzoic acid (200 mg, 1.3 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 2.7 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.8 mL, 2.6 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 80% yield (256 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J*=7.6 Hz, 1H, Ph H-3), 7.73 (td, *J*=7.5, 1.1 Hz, 1H, Ph H-5), 7.60 (t, *J*=7.5 Hz, 1H, Ph H-6), 7.48 (d, *J*=7.8 Hz, 1H, Ph H-4), 6.05 (s, 2H, CH_2 H-3), 5.73 (s, 1H, H-1).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.6 (COOH), 146.8 (Ph C-1), 135.3 (q, *J*=36.8 Hz, C-2), 134.7 (Ph C-5), 130.1 (Ph C-3), 126.2 (Ph C-2), 125.8 (Ph C-4), 124.3 (q, *J*=5.3 Hz, C-3), 123.0 (Ph C-6), 122.5 (q, *J*=287.1 Hz, CF_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

tert-butyl 4-(1-hydroxy-2-(trifluoromethyl)allyl)benzoate (26)



By following the General Procedure, starting from Tert-butyl 4-formylbenzoate (200 mg, 1.0 mmol, 1 equiv), 2-bromo-3,3,3-tri-

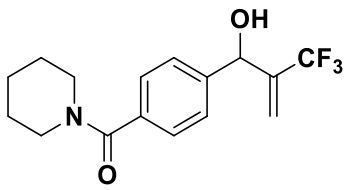
fluoropropen (0.2 mL, 1.9 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.3 mL, 1.9 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 94% yield (284 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (ddd, *J*=8.4, 3.7, 1.8 Hz, 2H, Ph C-3,5), 7.39 (dd, *J*=8.5, 2.3 Hz, 2H, Ph C-2,6), 5.91 (s, 1H, H-3), 5.77 (s, 1H, H-1), 5.44 (s, 1H, H-3), 1.58 (s, 9H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.7 (C=O), 144.9 (m, C-2), 140.9 (q, *J*=28.1 Hz, Ph C-1), 132.1 (Ph C-4), 129.8 (2C, Ph C-3,5), 127.2 (2C, Ph C-2,6), 123.2 (q, *J*=273.9 Hz, CF_3), 120.4 (m, C-3), 81.5 ($C(CH_3)_3$), 71.0 (C-1), 28.3 (CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.2 (s, F-1, CF_3).

(4-(1-hydroxy-2-(trifluoromethyl)allyl)phenyl)(piperidin-1-yl)methanone (27)



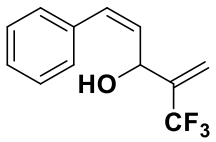
By following the General Procedure, starting from 4-(Piperidine-1-carbonyl)benzaldehyde (200 mg, 0.9 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.2 mL, 1.8 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.2 mL, 1.8 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 97% yield (273 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31 (d, *J*=8.3 Hz, 2H, Ph H-3,5), 7.27 (d, *J*=7.8 Hz, 2H, Ph H-2,6), 5.88 (d, *J*=1.7 Hz, 1H, H-3), 5.78 (t, *J*=1.4 Hz, 1H, H-1), 5.36 (s, 1H, H-3), 3.66 (s, 2H, Piperidin CH-2).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.3 (CO), 142.4 (Ph C-1), 141.1 (q, *J*=28.0 Hz, C-2), 135.9 (Ph C-4), 127.0 (2C, Ph C-3,5), 127.0 (2C, Ph C-2,6), 123.3 (q, *J*=257.6 Hz, CF_3), 120.0 (q, *J*=5.4 Hz, C-3), 70.7 (C-1), 48.9 (Piperidin C-2), 43.3 (Piperidin C-6), 26.6 (Piperidin C-3), 25.5 (Piperidin C-5), 24.6 (Piperidin C-4).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.1 (s, F-1, CF_3).

(Z)-1-phenyl-4-(trifluoromethyl)penta-1,4-dien-3-ol (28) [1]



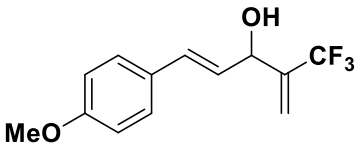
By following the General Procedure, starting from (Z)-3-Phenylacrylaldehyde (200 mg, 1.5 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 3.0 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.0 mL, 3.0 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 86% yield (294 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36 (d, *J*=7.1 Hz, 2H, Ph H-2,6), 7.30 (t, *J*=7.4 Hz, 2H, Ph H-3,5), 7.24 (s, 1H, Ph H-4), 6.66 (d, *J*=15.9, 1H, H-1), 6.17 (dd, *J*=15.8 Hz, 6.9 Hz, 1H, H-2), 5.86 (s, 1H, H-5), 5.80 (s, 1H, H-5), 4.98 (d, *J*=7.0 Hz, 1H, H-3), 2.37 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.5 (C-1), 140.4 (q, *J*=28.3 Hz, C-4), 136.2 (Ph C-1), 132.7 (C-2), 128.8 (2C, Ph C-2,6), 128.3 (2C, Ph C-3,5), 126.8 (Ph C-4), 123.3 (q, *J*=273.3 Hz, CF_3), 119.8 (q, *J*=5.4 Hz, C-5), 70.1 (C-3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.3 (s, F-1, CF_3).

(E)-1-(4-methoxyphenyl)-4-(trifluoromethyl)penta-1,4-dien-3-ol (29)



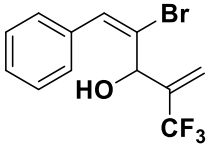
By following the General Procedure, starting from (E)-3-(4-Methoxyphenyl)acrylaldehyde (200 mg, 1.2 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 2.4 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (1.6 mL, 2.4 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 93% yield (288 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33 (d, *J*=8.7 Hz, 2H, Ph H-2,6), 6.87 (d, *J*=8.7 Hz, 2H, Ph H-3,5), 6.65 (d, *J*=15.8 Hz, 1H, H-1), 6.07 (dd, *J*=15.8, 7.1 Hz, 1H, H-2), 5.89 (d, *J*=1.6 Hz, 1H, H-5), 5.84 (t, *J*=1.4 Hz, 1H, H-3), 5.01 (d, *J*=7.0 Hz, 1H, H-5), 3.81 (s, 3H, CH_3), 1.92 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.7 (Ph C-4), 140.7 (q, *J*=28.5 Hz, C-4), 132.5 (C-1), 128.9 (Ph C-1), 128.1 (2C, Ph C-2,6), 126.2 (Ph C-2), 123.4 (q, *J*=172.9 Hz, CF_3), 119.6 (q, *J*=5.5 Hz, C-5), 114.2 (2C, Ph C-3,5), 70.4 (C-3), 55.5 (CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.4 (s, F-1, CF_3).

(E)-2-bromo-1-phenyl-4-(trifluoromethyl)penta-1,4-dien-3-ol (30)



By following the General Procedure, starting from (E)-2-Bromo-3-phenylacrylaldehyde (200 mg, 1.0 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.2 mL, 1.9 mmol, 2.0 equiv), Methyllithium lithium bromide

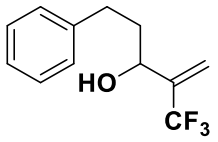
complex solution 1.5 M in diethyl ether (1.3 mL, 1.9 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 88% yield (270 mg) as colourless oil after column chromatography on silica gel (petroleum ether/ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (m, 2H, Ph H-2,6), 7.41 (m, 3H, Ph H-3,4,5), 6.09 (s, 1H, H-5), 5.99 (s,1H, H-5), 5.13 (s, 1H, H-3), 2.58 (d, *J*=5.5 Hz, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.8 (q, *J*=28.5 Hz, C-4), 134.7 (Ph C-1), 131.4 (C-1), 129.3 (2C, Ph C-3,5), 128.8 (Ph C-4), 128.4 (2C, Ph C-2,6), 125.2 (C-2), 124.8 (q, *J*=229.3 Hz, CF_3), 122.0 (q, *J*=5.4 Hz, C-5), 74.3 (C-3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.4 (s, F-1, CF_3).

5-phenyl-2-(trifluoromethyl)pent-1-en-3-ol (31) [1]



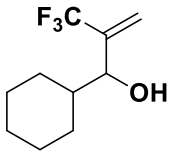
By following the General Procedure, starting from 3-Phenylpropanal (200 mg, 1.5 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 3.0 mmol, 2.0 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.0 mL, 3.0 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 85% yield (293 mg) as colourless oil without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.27 (m, 5H, Ph H-2,3,4,5), 5.86 (s, 1H, CH_2 H-1), 5.77 (s, 1H, H-3), 4.39 (d, *J*=8.6, 27.7 Hz 1H, CH_2 H-1), 2.78 (m, 2H, H-5), 2.01 (m, 2H, H-4), 1.78 (s, 1H, OH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.8 (q, *J*=27.7 Hz, C-2), 141.4 (Ph C-1), 128.7 (2C, Ph C-3,5), 128.6 (2C, Ph C-2,6), 126.2 (Ph C-4), 123.5 (q, *J*=272.1 Hz, CF_3), 119.3 (q, *J*=5.8 Hz, C-1), 68.7 (C-3), 37.9 (C-4), 31.7 (C-5).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.6 (s, F-1, CF_3).

1-cyclohexyl-2-(trifluoromethyl)prop-2-en-1-ol (32)



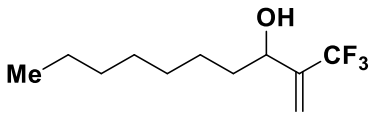
By following the General Procedure, starting from Cyclohexanecarbaldehyde (200 mg, 1.8 mmol, 1 equiv), 2-bromo-3,3,3-trifluoropropen (0.4 mL, 3.6 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.3 mL, 3.6 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 81% yield (304 mg) as colourless oil after column chromatography on silica gel (petroleum ether).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.80 (s, 1H, H-3), 5.63 (s, 1H, H-1), 5.26 (s, 1H, H-3), 4.06 (t, *J*=5.1 Hz, 1H, OH), 2.42 (d, *J*=4.9 Hz, CH), 1.73-1.56 (m, 5H), 1.11 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.4 (q, *J*=26.1, C-2), 123.6 (q, *J*=270.7 Hz, CF_3), 119.9 (q, *J*=5.8 Hz, C-3), 73.6 (C-1), 41.8 (CH), 30.1 (2C, CH_2), 26.3 (3C, CH_2).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.6 (s, F-1, CF_3).

2-(trifluoromethyl)dec-1-en-3-ol (33)



By following the General Procedure, starting from Octanal (200 mg, 1.5 mmol, 1 equiv), 2-bromo-3,3,3-tri-fluoropropen (0.3 mL, 3.1 mmol, 2 equiv), Methyllithium lithium bromide complex solution 1.5 M in diethyl ether (2.0 mL, 3.1 mmol, 2.0 equiv) and dry THF (5 mL), the desired compound was obtained in 80% yield (269 mg) as colourless oil after column chromatography on silica gel (petroleum ether).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.82 (m,1H, H-1), 5.73 (m, 1H, H-1), 4.35 (t, *J*=6.1 Hz, 1H, H-3), 1.71 (dt, *J*=10.4, 4.8 Hz, 2H, H-4), 1.44 (m, 10H, H-5,6,7,8,9), 0.88 (m, 3H, CH_3).

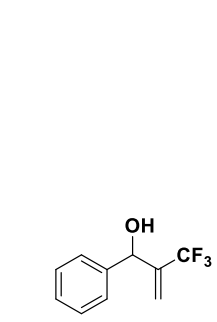
^{13}C NMR (100 MHz, $CDCl_3$) δ: 142. 1 (q, *J*=25.5 Hz, C-2), 123.6 (q, *J*=276,9 Hz, CF_3), 118.9 (q, *J*=5.8 Hz, C-1), 69.3 (C-3), 36.4 (C-4), 31.9 (C-8), 29.4 (C-6), 29.3 (C-7), 25.5 (C-5), 22.8 (C-9), 14.2 (CH_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -65.7 (s, F-1, CF_3).

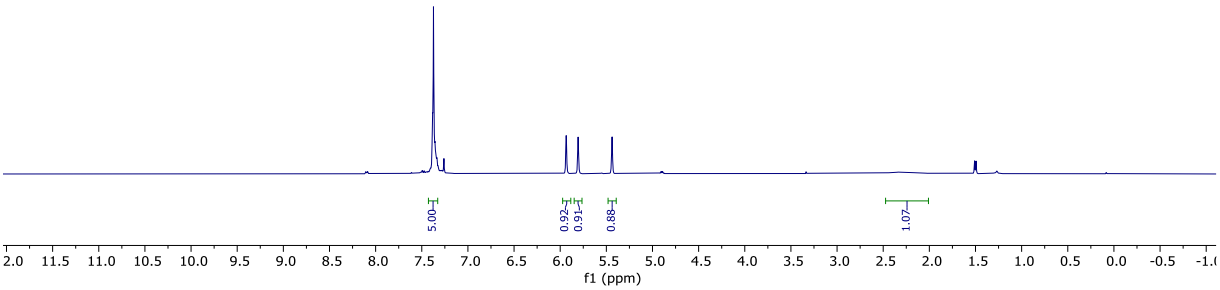
(1) Nadano, R., Fuchibe, K., Ikeda, M., Takahashi, H., & Ichikawa, J. (2010). Rapid and Slow Generation of 1-Trifluoromethylvinyllithium: Syntheses and Applications of CF3-Containing Allylic Alcohols, Allylic Amines, and Vinyl Ketones. *Chemistry, an Asian Journal*, *5*(8), 1875–1883. https://doi.org/10.1002/asia.201000139

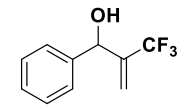
4.4. 1H-, 13C- AND 19F-NMR SPECTRA FOR ALL THE COMPOUNDS

Compound 1

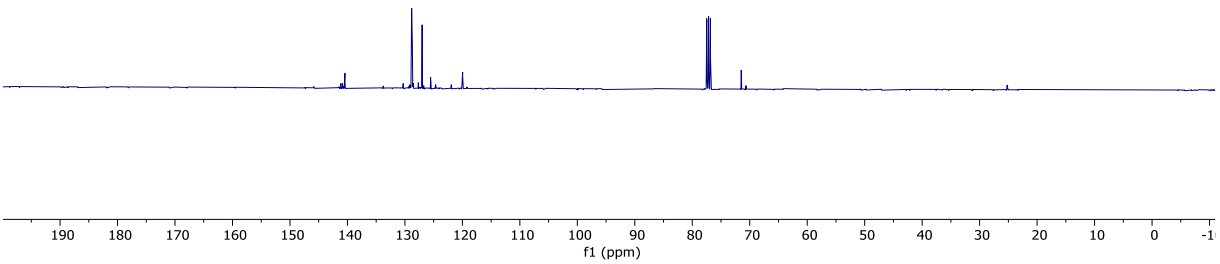


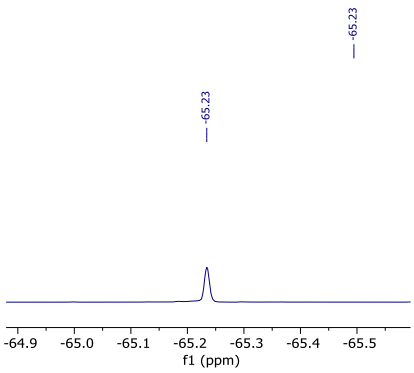
^{1}H NMR, 400 MHz, $CDCl_3$

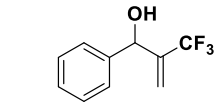




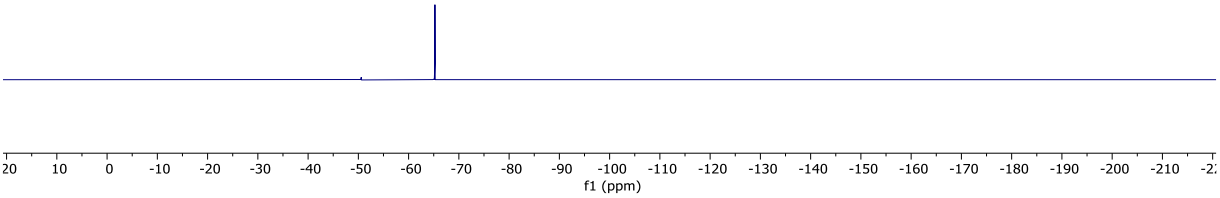
^{13}C NMR, 100 MHz, $CDCl_3$



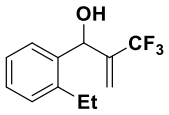




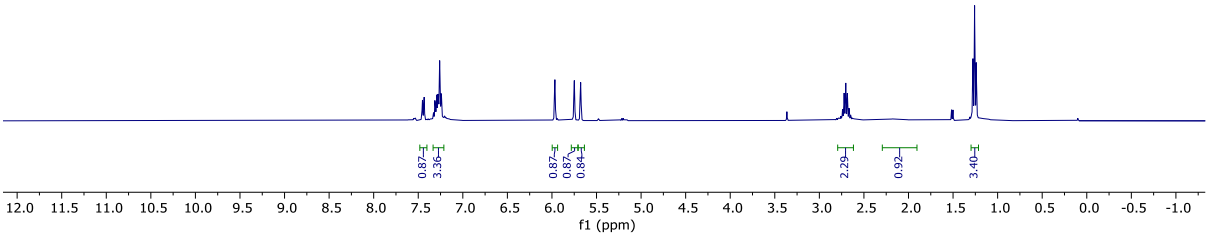
^{19}F NMR, 376 MHz, $CDCl_3$

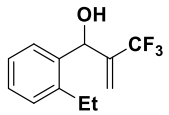


Compound 2

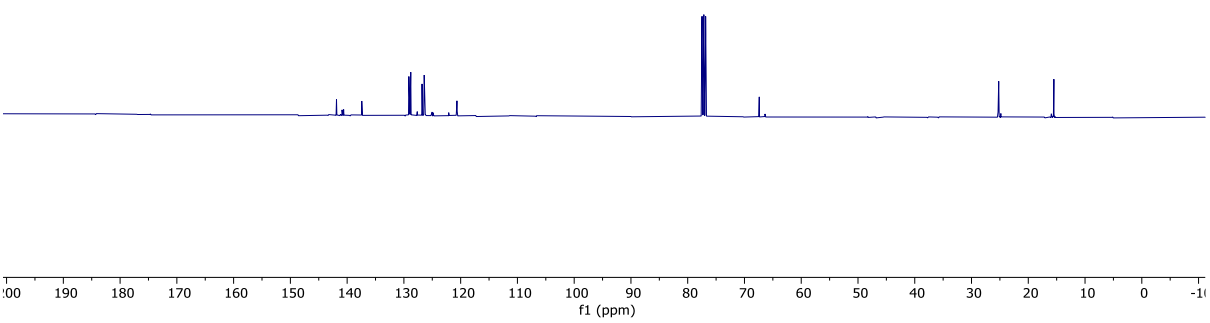


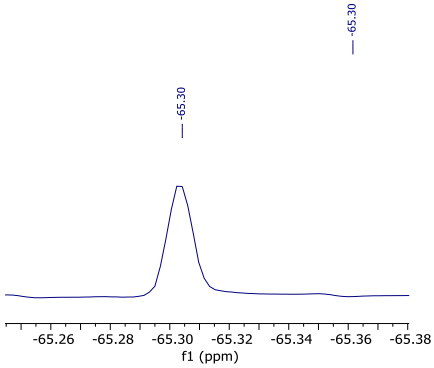
^{1}H NMR, 400 MHz, $CDCl_3$

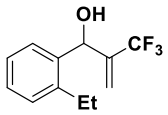




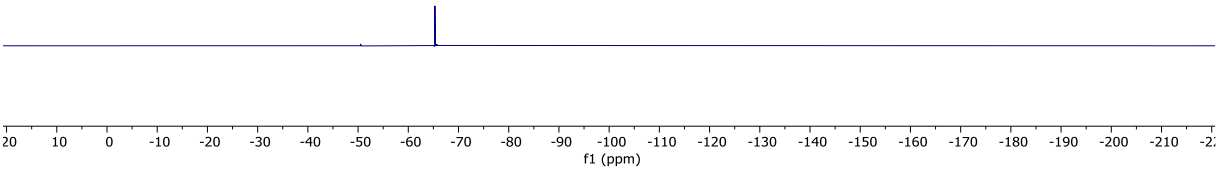
^{13}C NMR, 100 MHz, $CDCl_3$



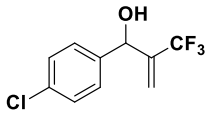




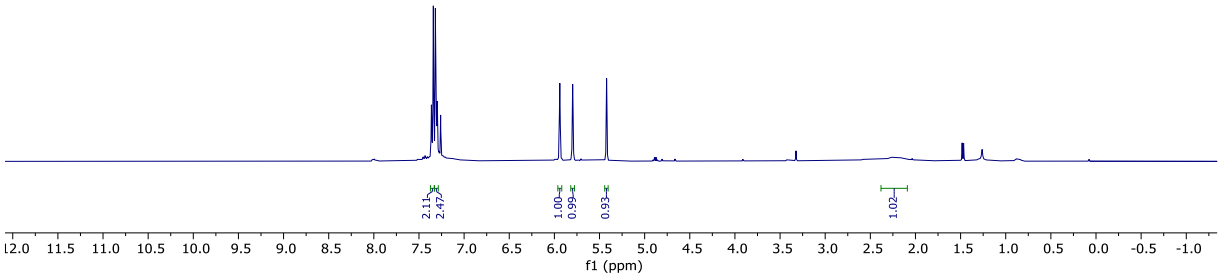
^{19}F NMR, 376 MHz, $CDCl_3$

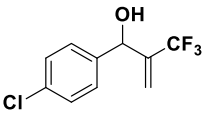


Compound 3

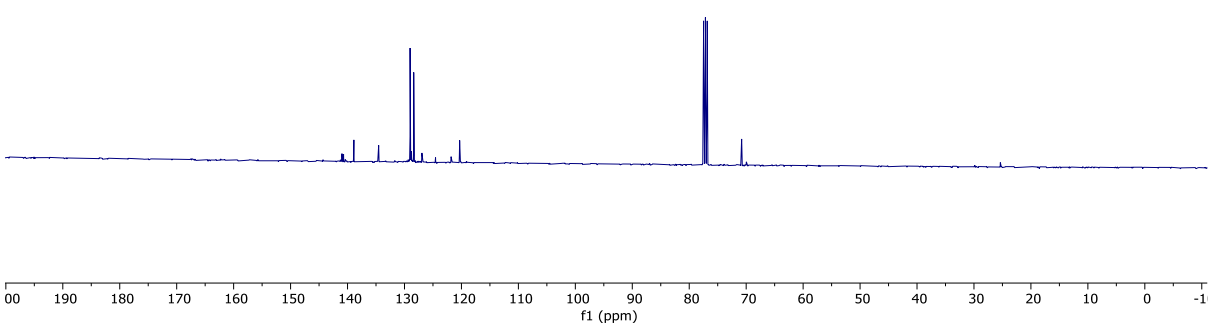


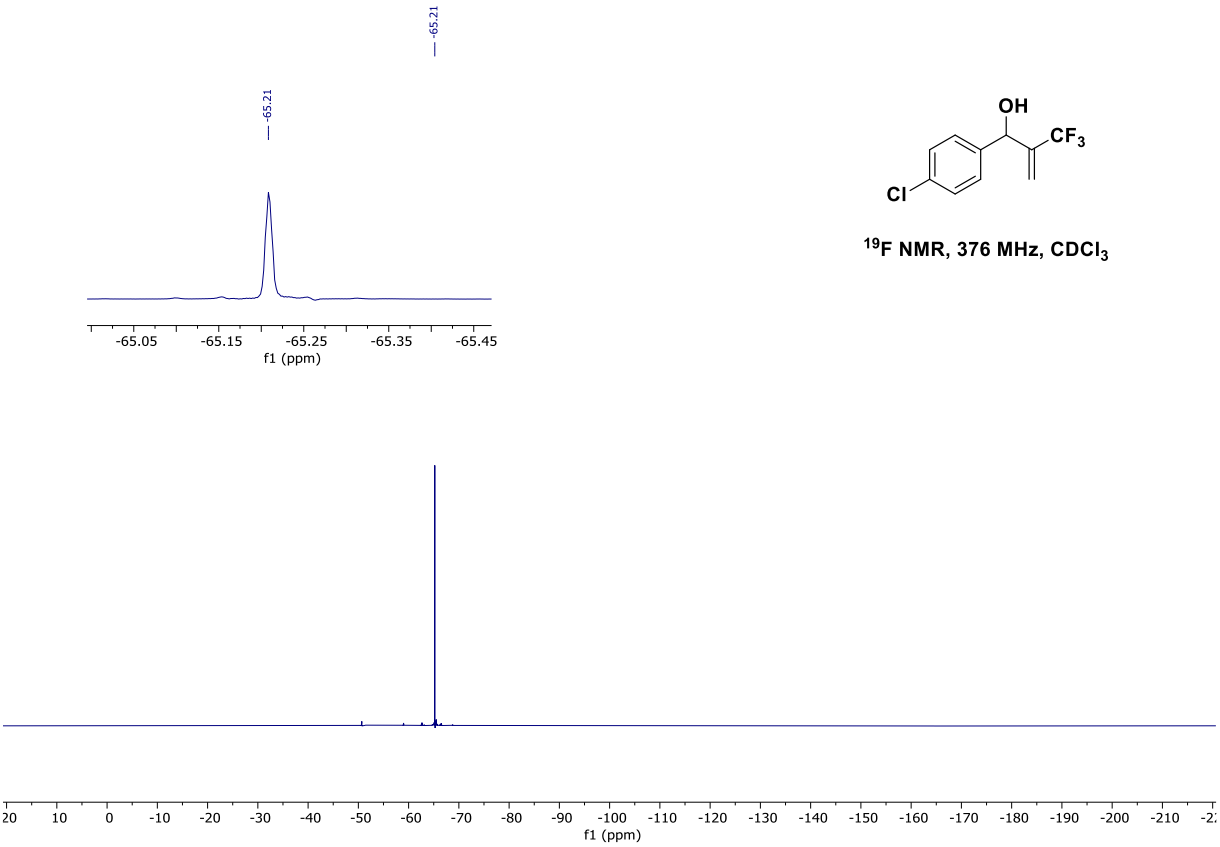
^{1}H NMR, 400 MHz, $CDCl_3$





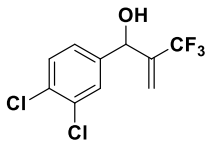
^{13}C NMR, 100 MHz, $CDCl_3$



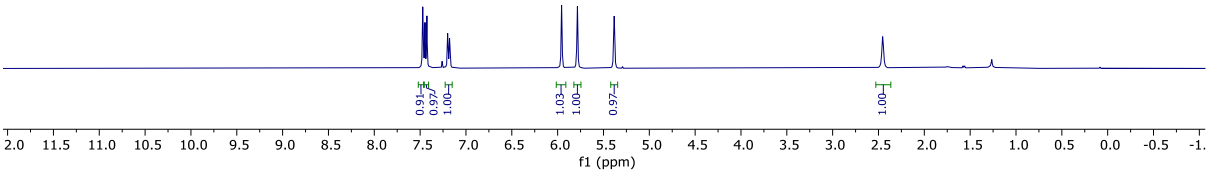


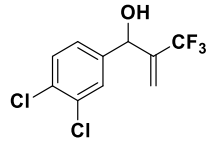
^{19}F NMR, 376 MHz, $CDCl_3$

Compound 4

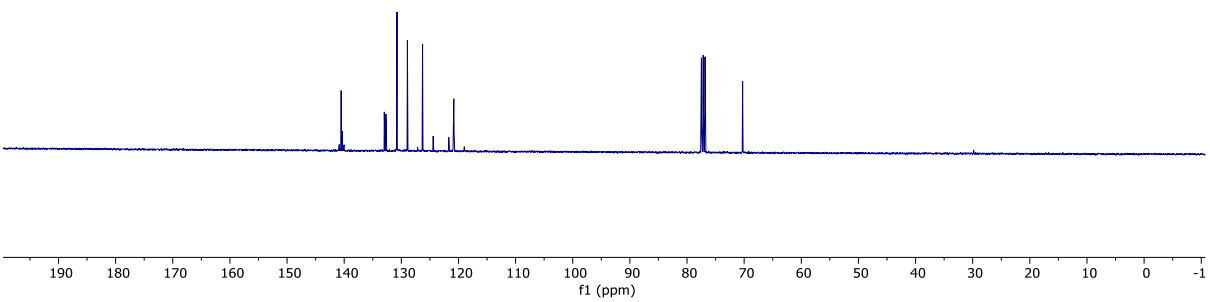


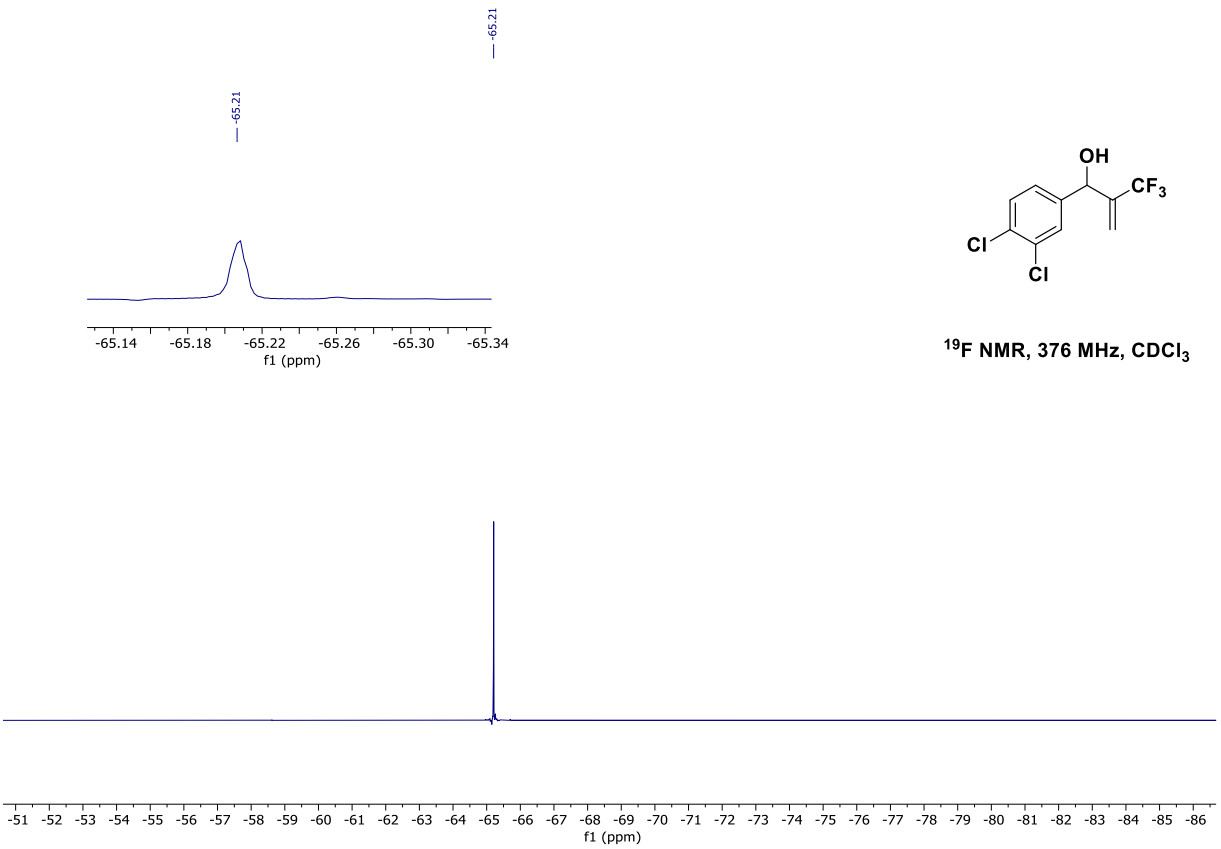
^{1}H NMR, 400 MHz, $CDCl_3$





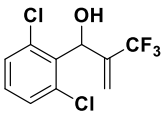
^{13}C NMR, 100 MHz, $CDCl_3$



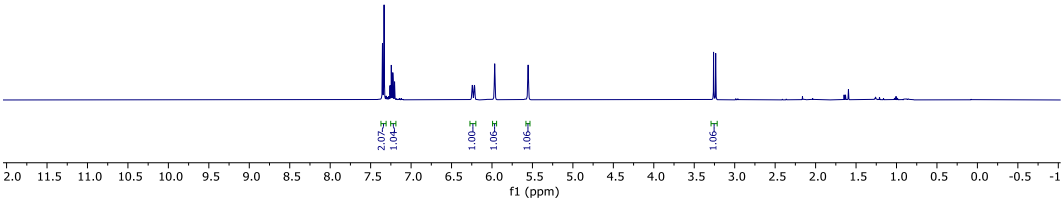


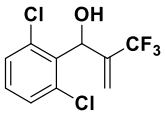
^{19}F NMR, 376 MHz, $CDCl_3$

Compound 5

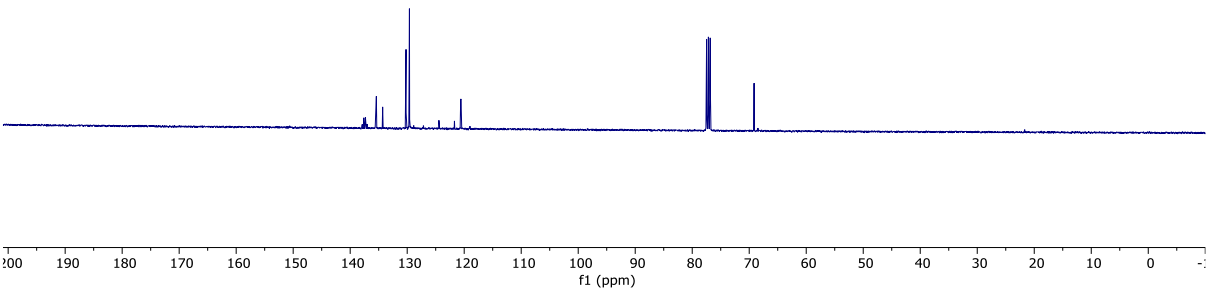


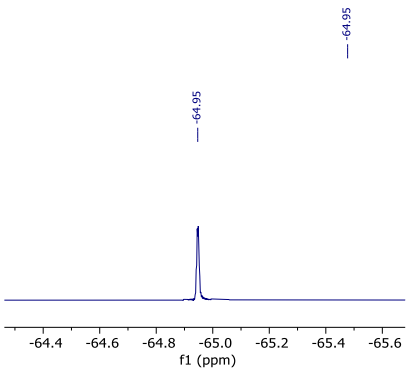
^{1}H NMR, 400 MHz, $CDCl_3$

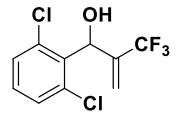




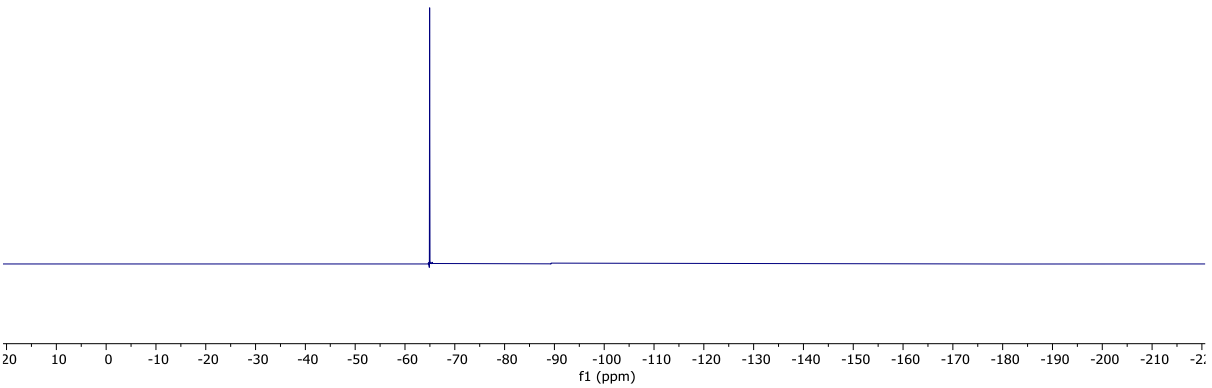
^{13}C NMR, 100 MHz, $CDCl_3$



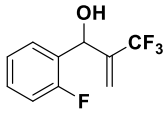




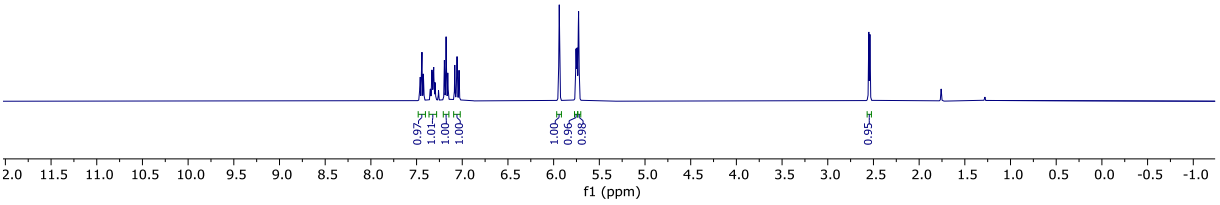
^{19}F NMR, 376 MHz, $CDCl_3$

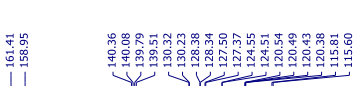


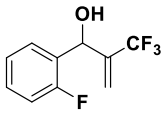
Compound 6



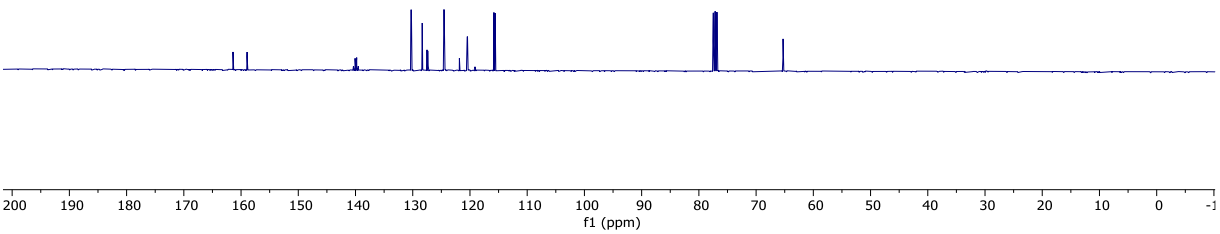
^{1}H NMR, 400 MHz, $CDCl_3$

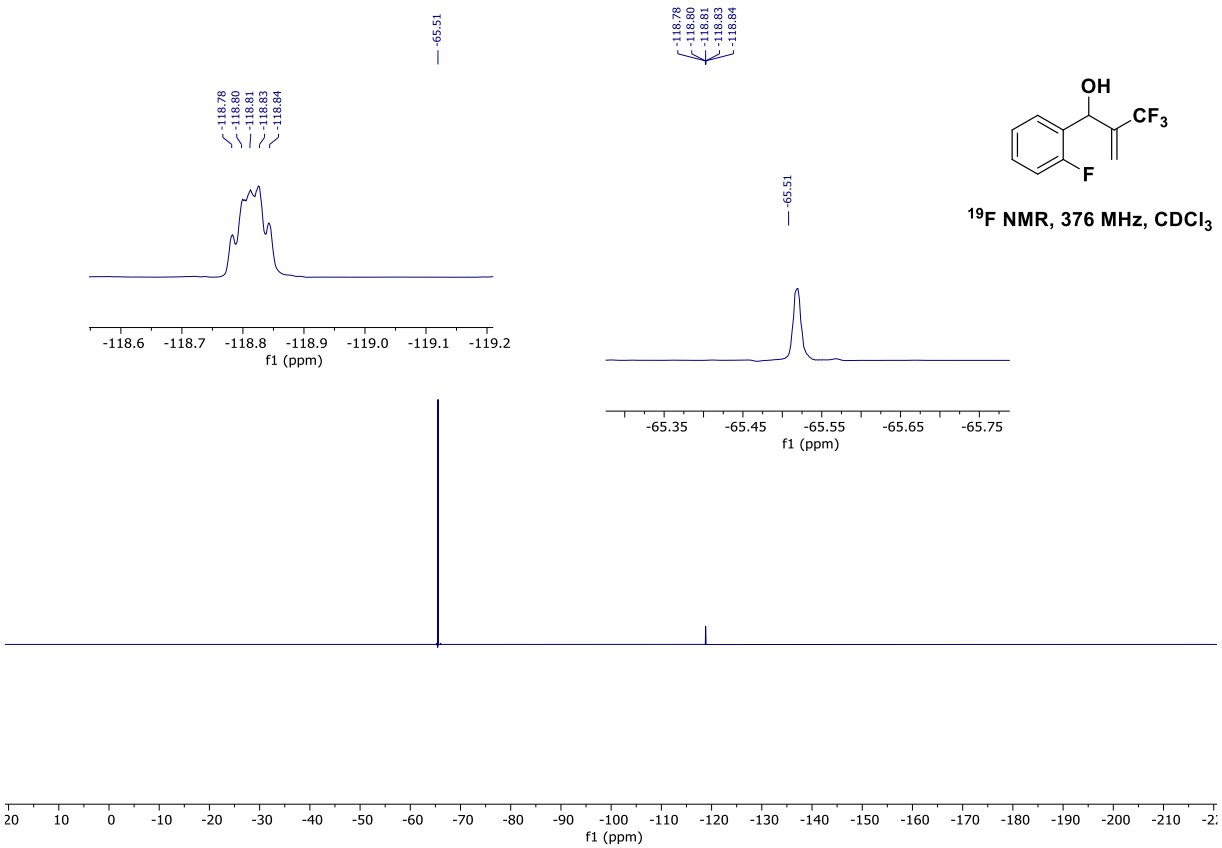






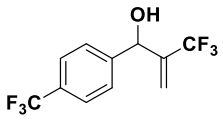
^{13}C NMR, 100 MHz, $CDCl_3$



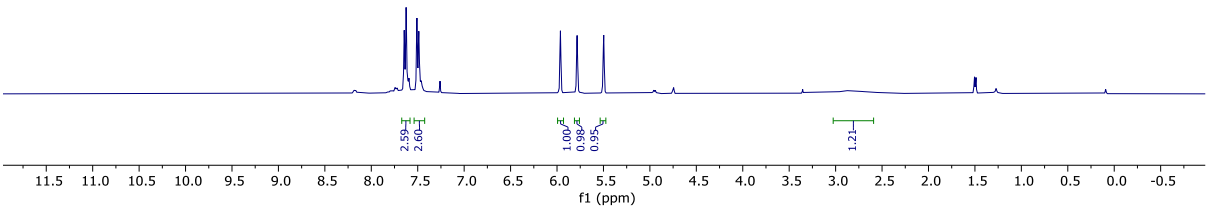


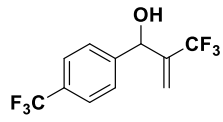
^{19}F NMR, 376 MHz, $CDCl_3$

Compound 7

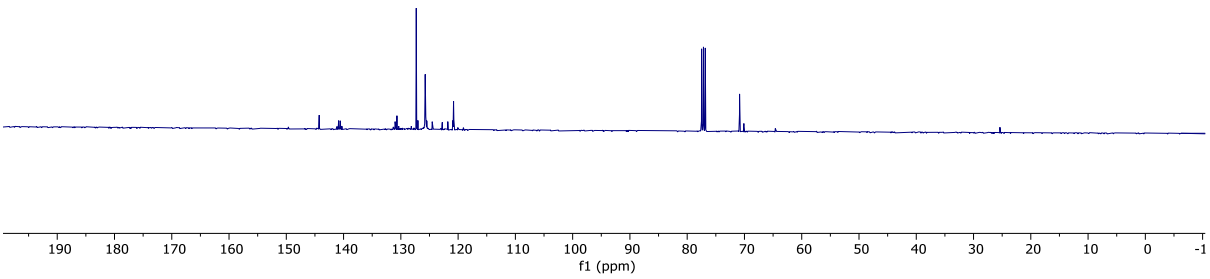


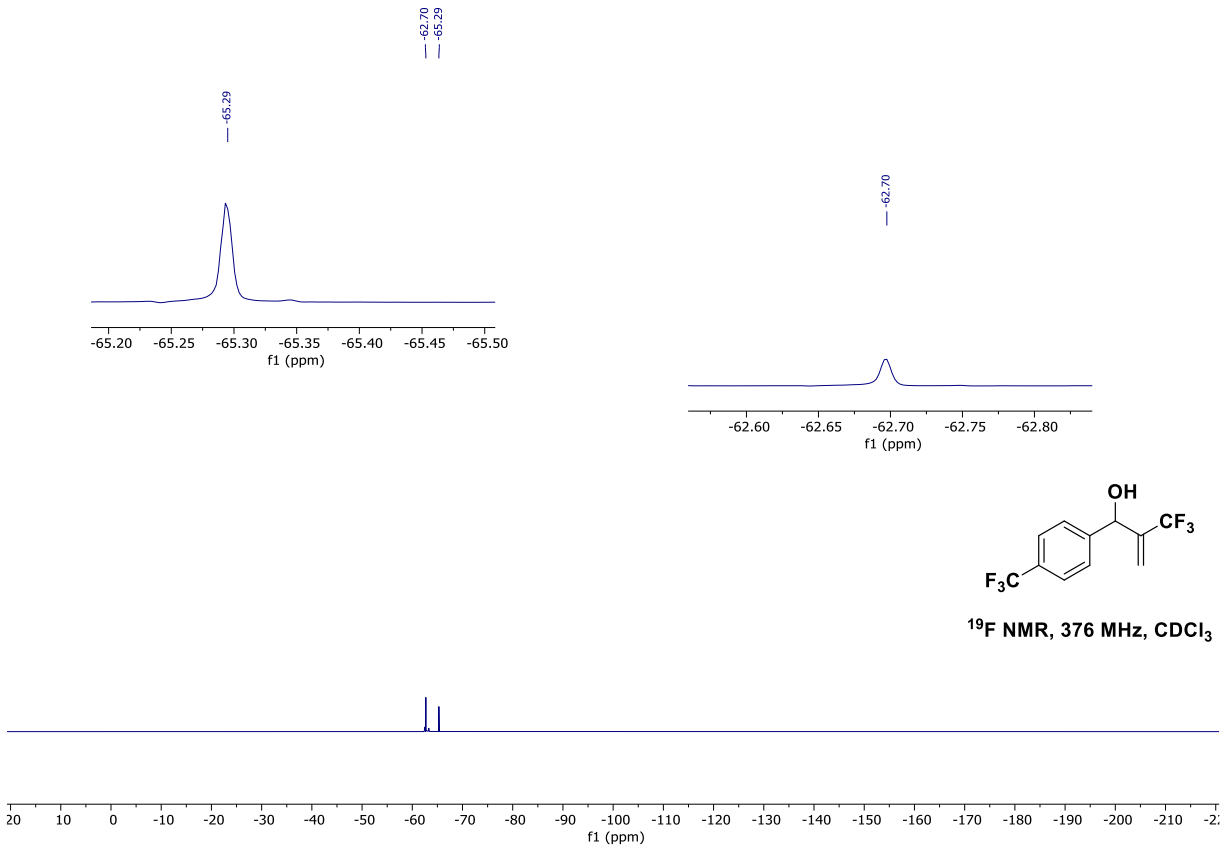
^{1}H NMR, 400 MHz, $CDCl_3$





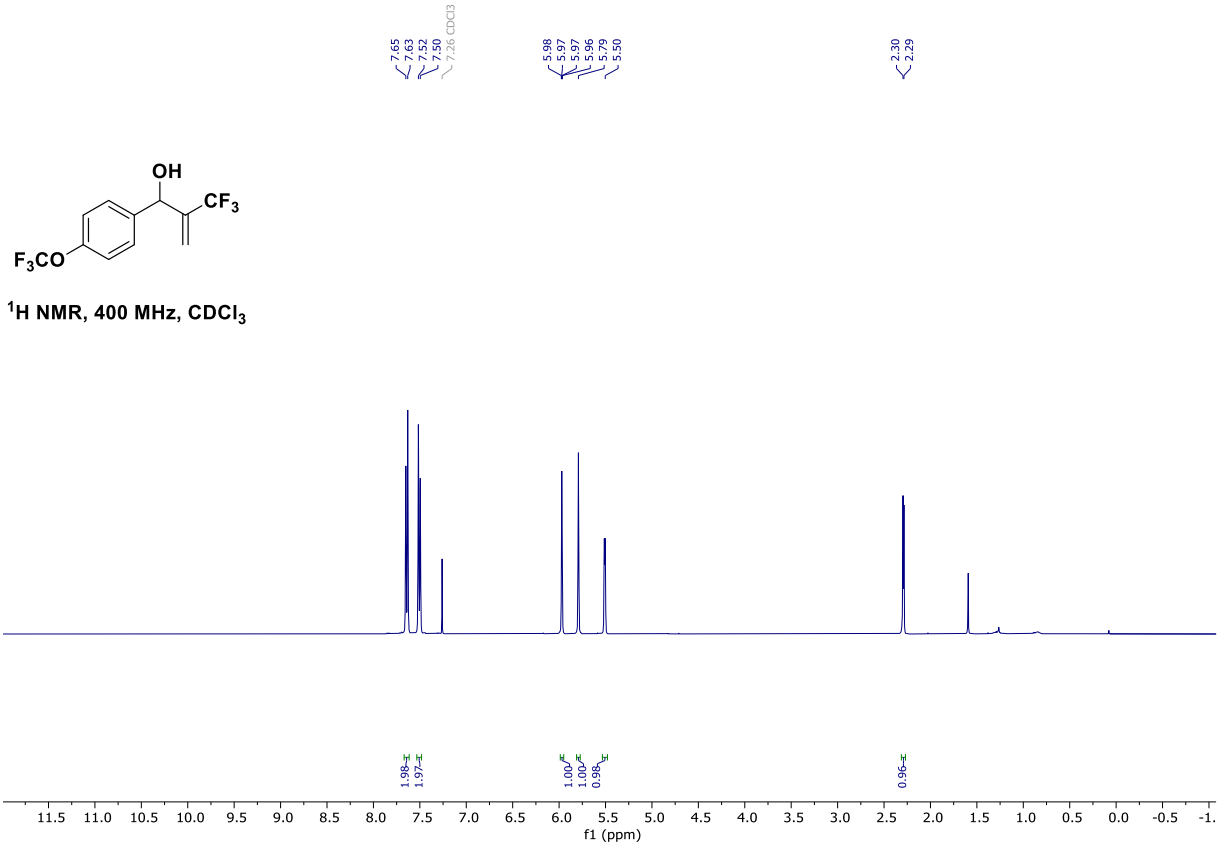
^{13}C NMR, 100 MHz, $CDCl_3$

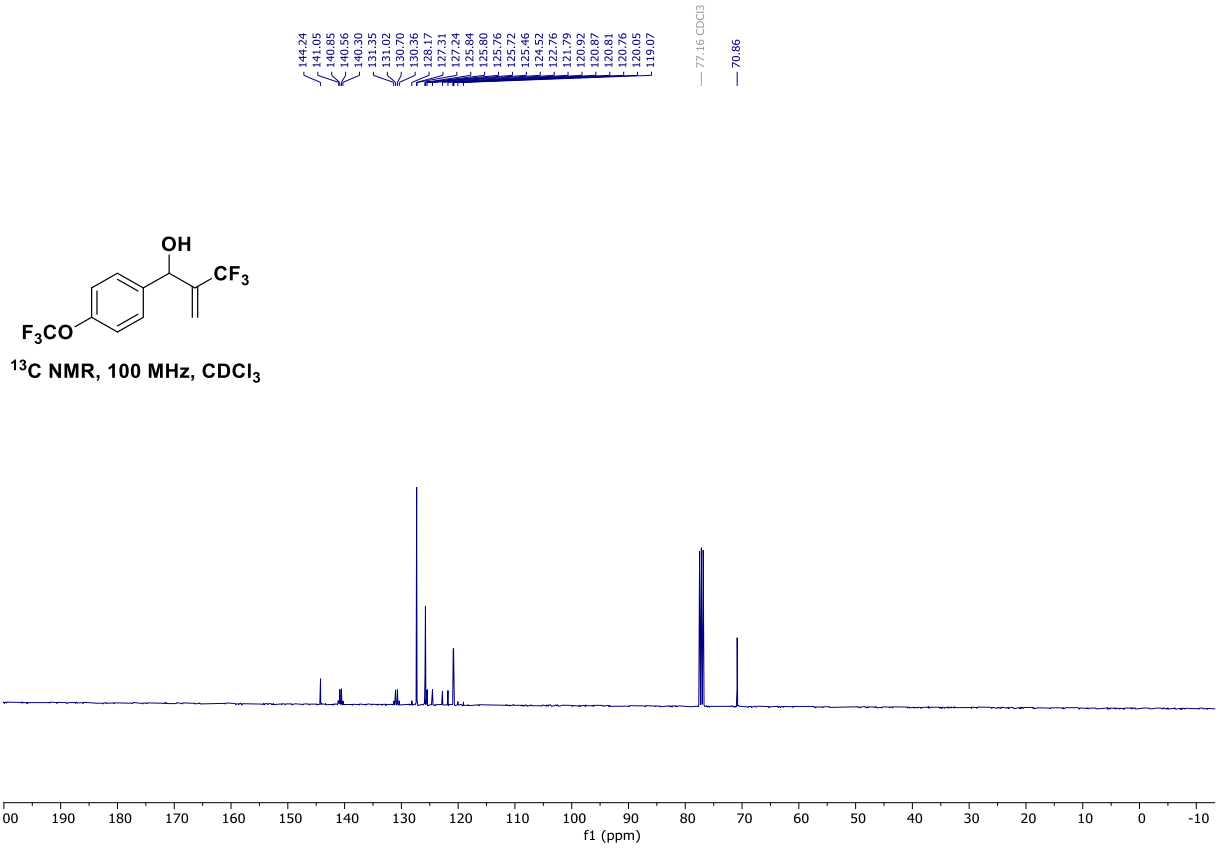


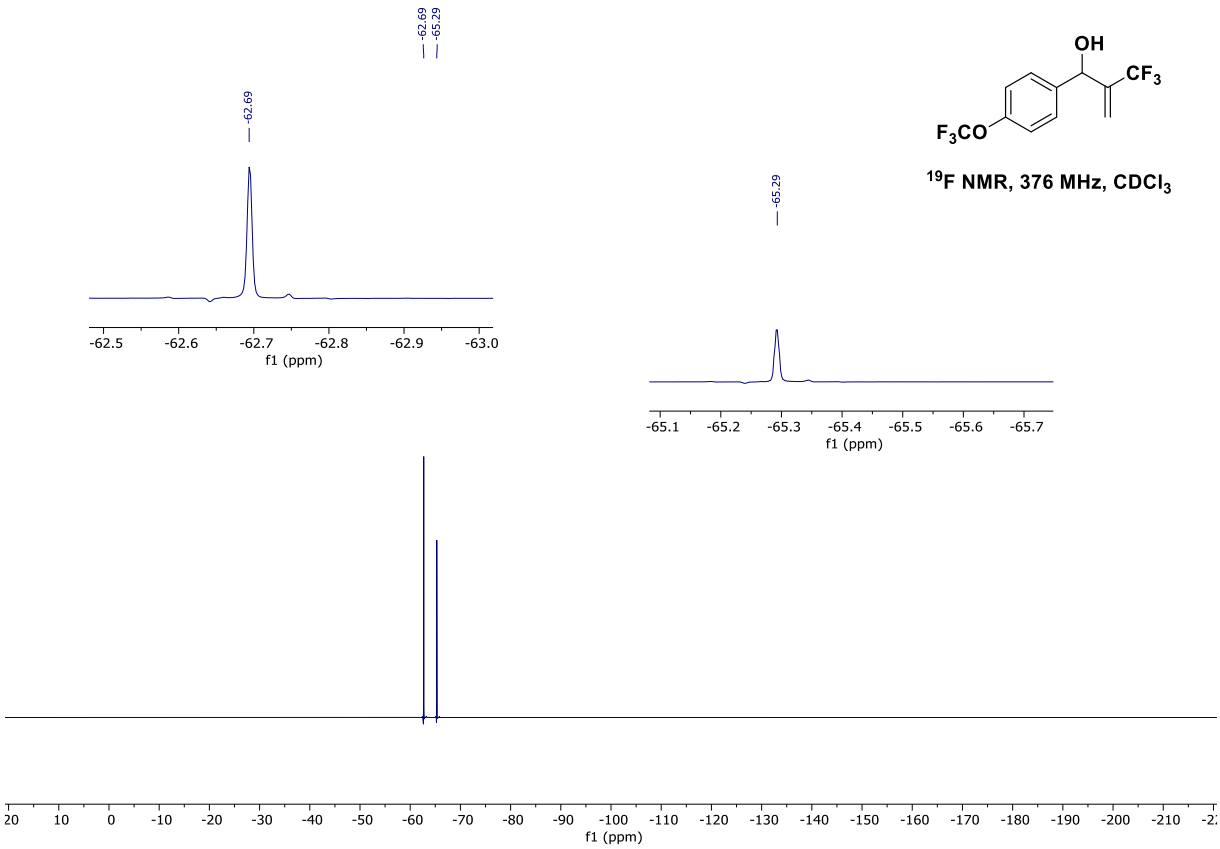


^{19}F NMR, 376 MHz, $CDCl_3$

Compound 8

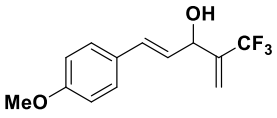

7.65
7.63
7.52
7.50
7.26 CDCl3
5.98
5.97
5.97
5.96
5.79
5.50
2.30
2.29
OH
CF3
F3CO
1H NMR, 400 MHz, CDCl3
1.98
1.97
1.00
1.00
0.98
0.96
f1 (ppm)


144.24
141.05
140.85
140.56
140.30
131.35
131.02
130.70
130.36
128.17
127.31
127.24
125.84
125.80
125.76
125.72
125.46
124.52
122.76
121.79
120.92
120.87
120.81
120.76
120.05
119.07
77.16 CDCl3
70.86
OH
CF3
F3CO
13C NMR, 100 MHz, CDCl3
f1 (ppm)

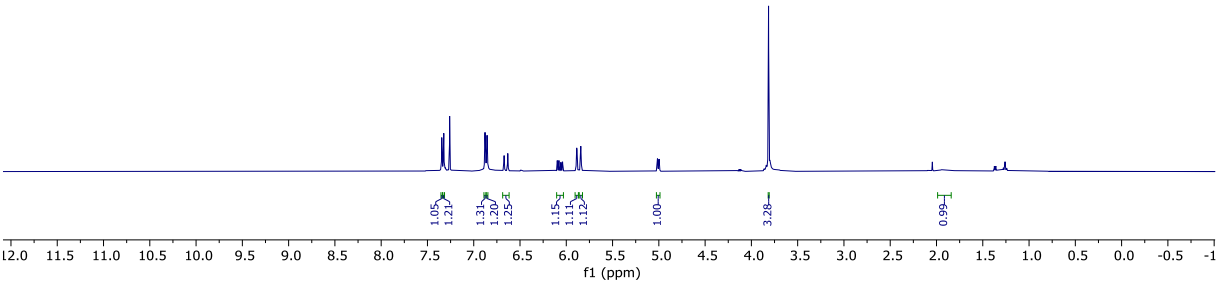


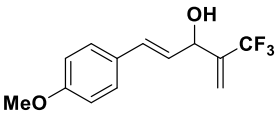
^{19}F NMR, 376 MHz, $CDCl_3$

Compound 9

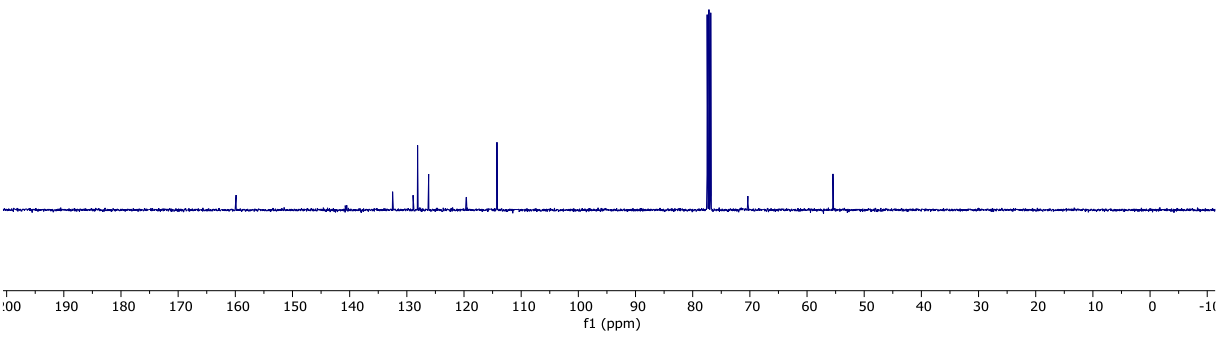


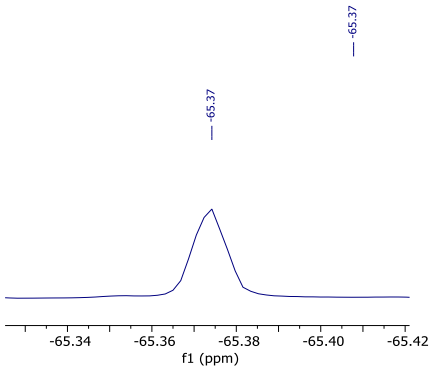
^{1}H NMR, 400 MHz, $CDCl_3$

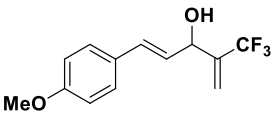




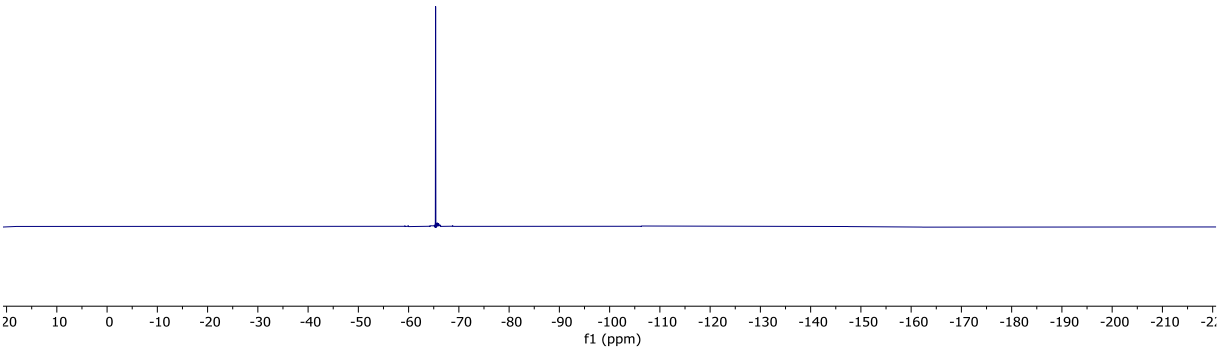
^{13}C NMR, 100 MHz, $CDCl_3$



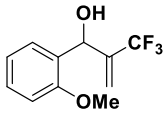




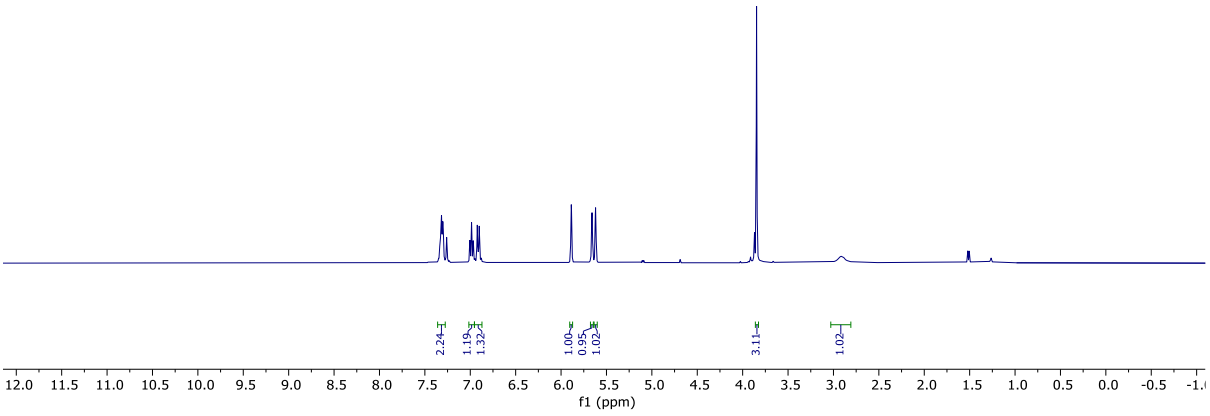
^{19}F NMR, 376 MHz, $CDCl_3$

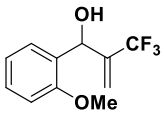


Compound 10

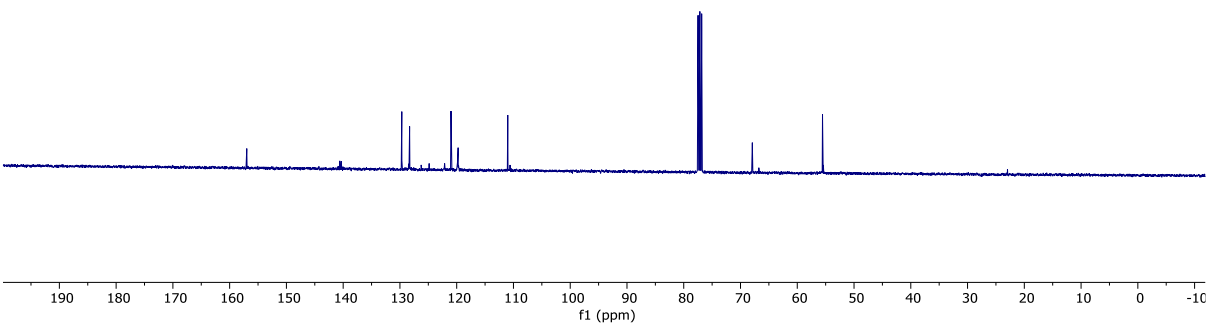


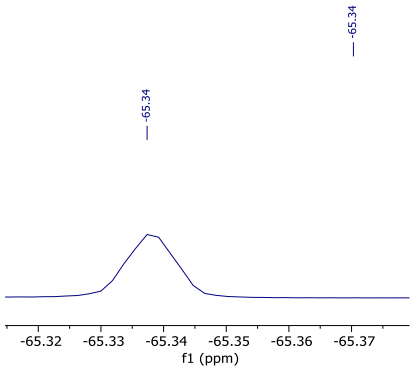
^{1}H NMR, 400 MHz, $CDCl_3$

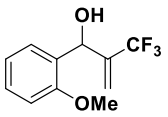




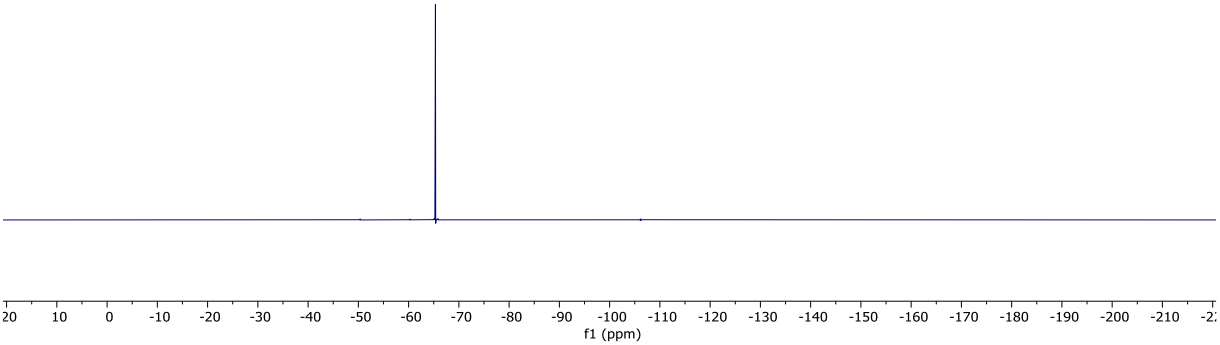
^{13}C NMR, 100 MHz, $CDCl_3$



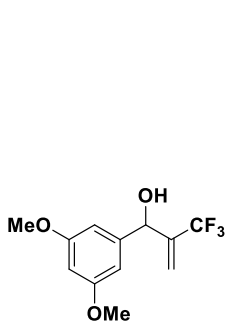




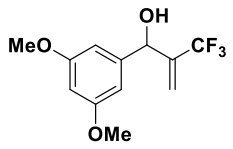
^{19}F NMR, 376 MHz, $CDCl_3$



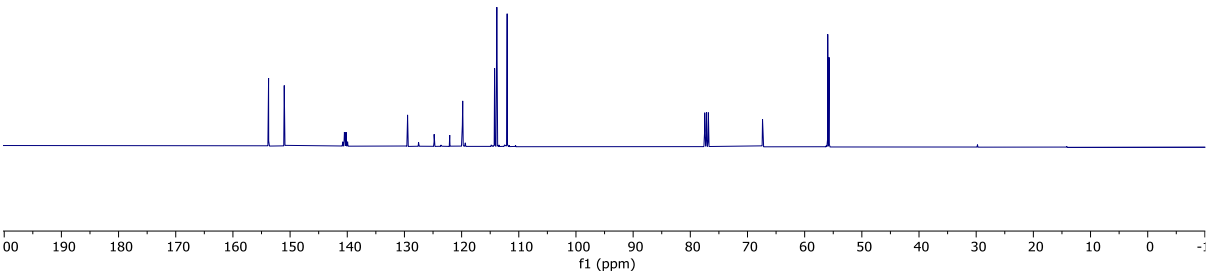
Compound 11

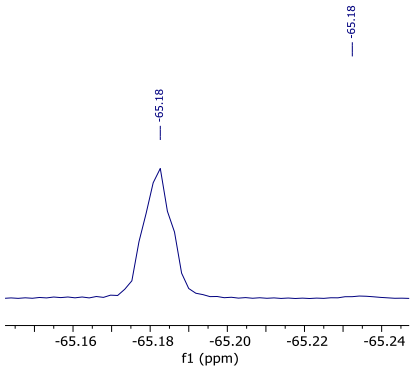


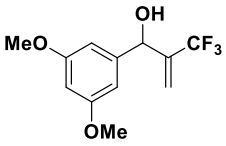
^{1}H NMR, 400 MHz, $CDCl_3$



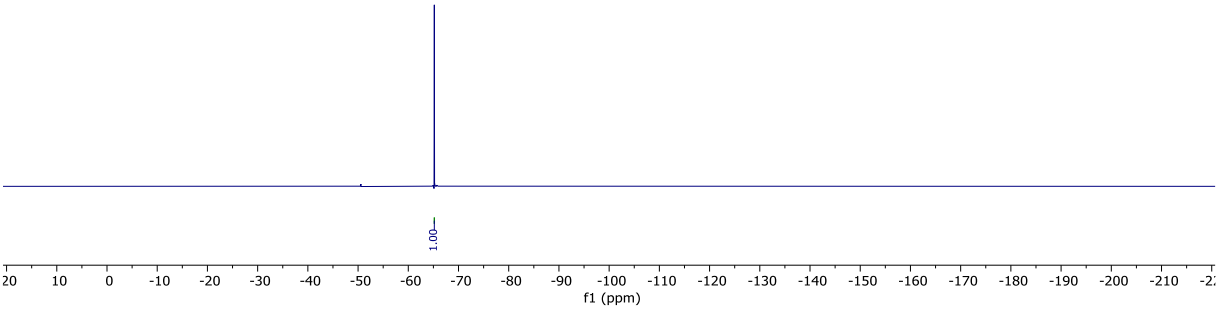
^{13}C NMR, 100 MHz, $CDCl_3$



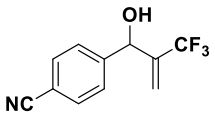




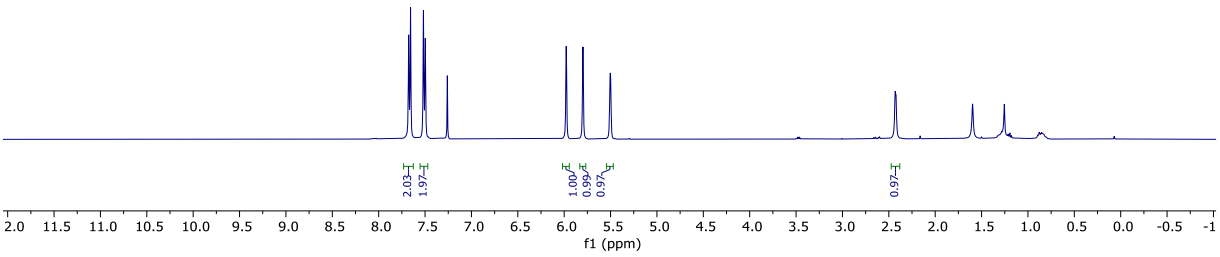
^{19}F NMR, 376 MHz, $CDCl_3$

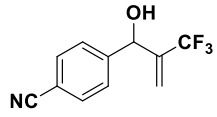


Compound 12

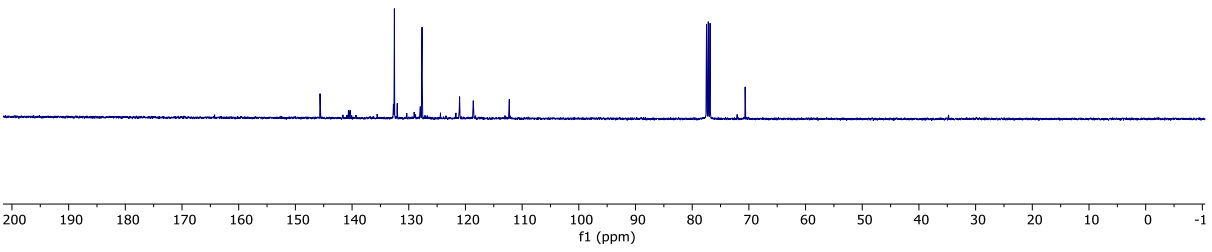


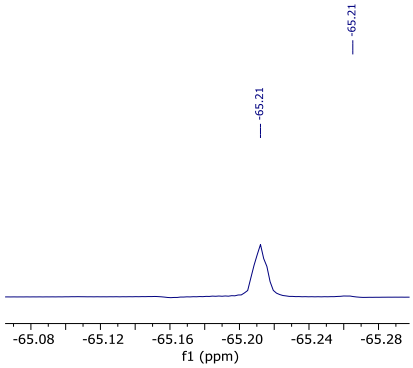
^{1}H NMR, 400 MHz, $CDCl_3$

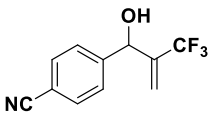




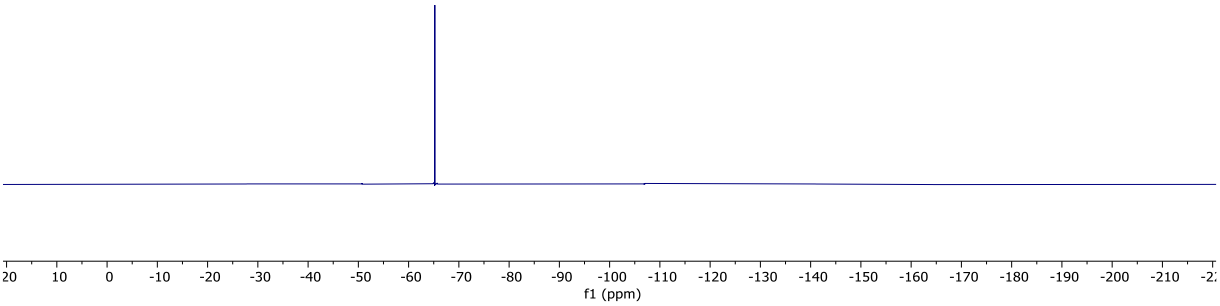
^{13}C NMR, 100 MHz, $CDCl_3$



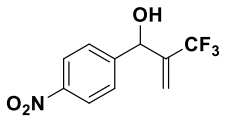




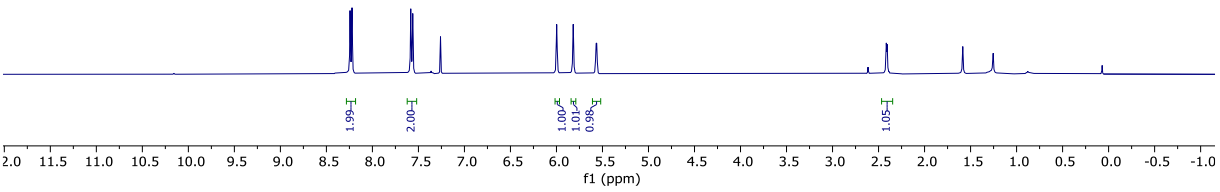
^{19}F NMR, 376 MHz, $CDCl_3$

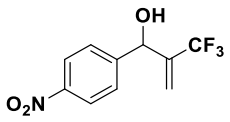


Compound 13

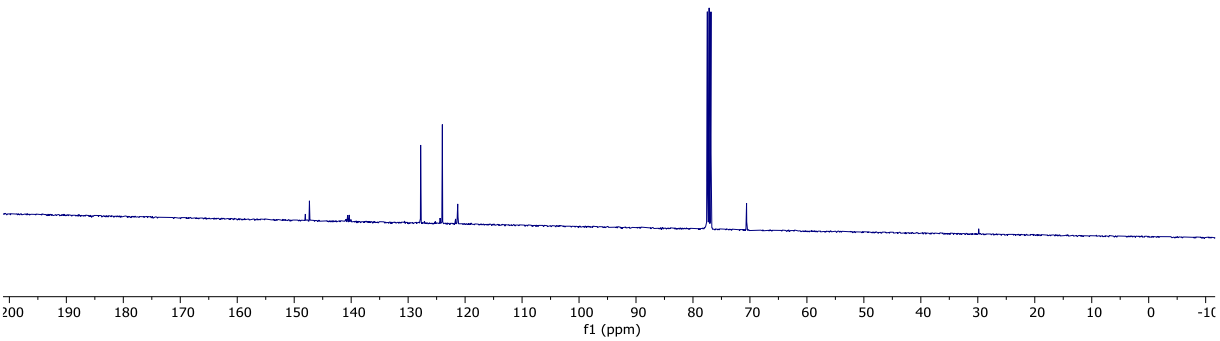


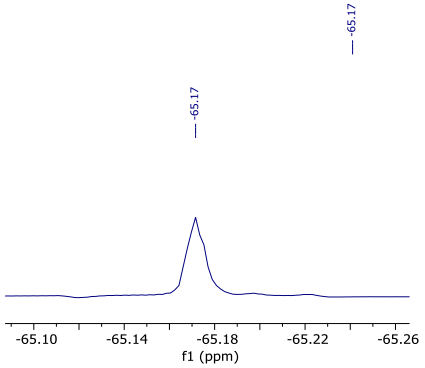
^{1}H NMR, 400 MHz, $CDCl_3$

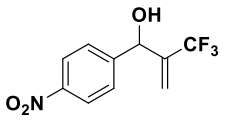




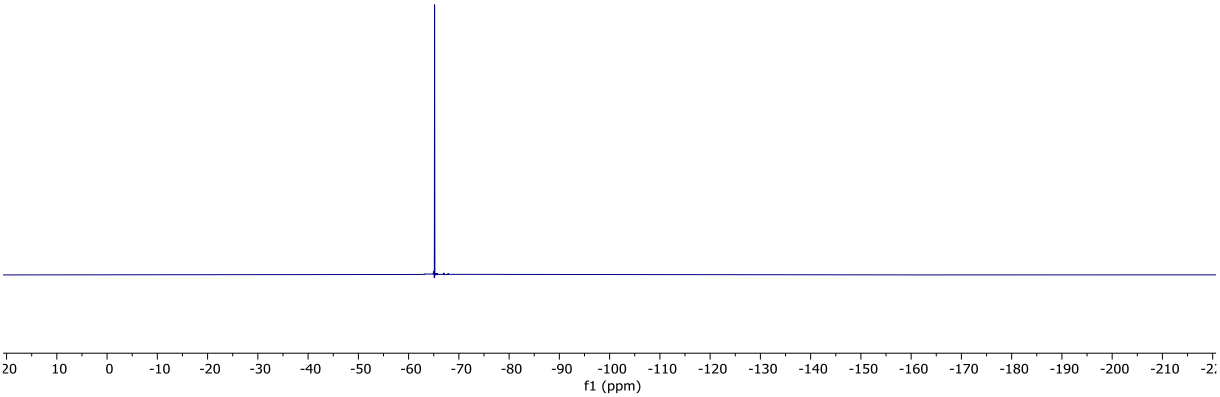
^{13}C NMR, 100 MHz, $CDCl_3$



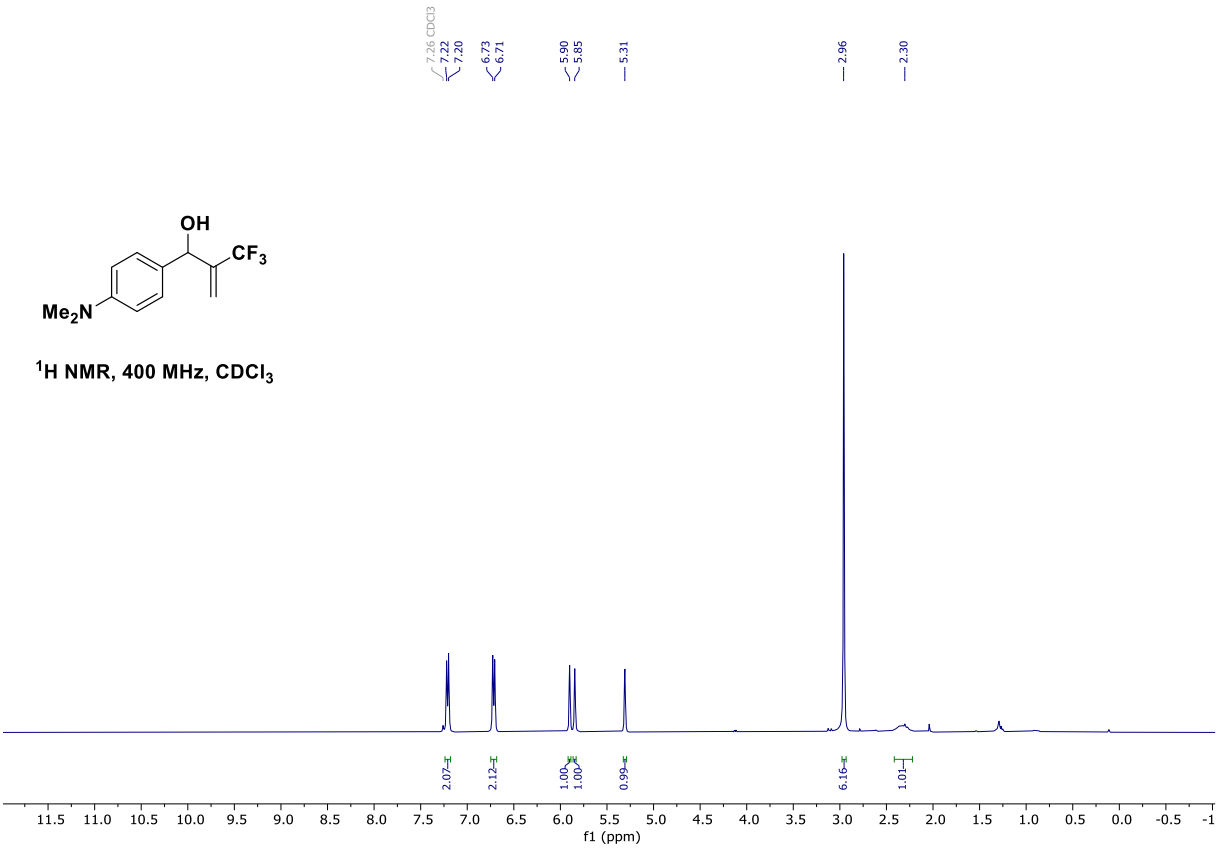




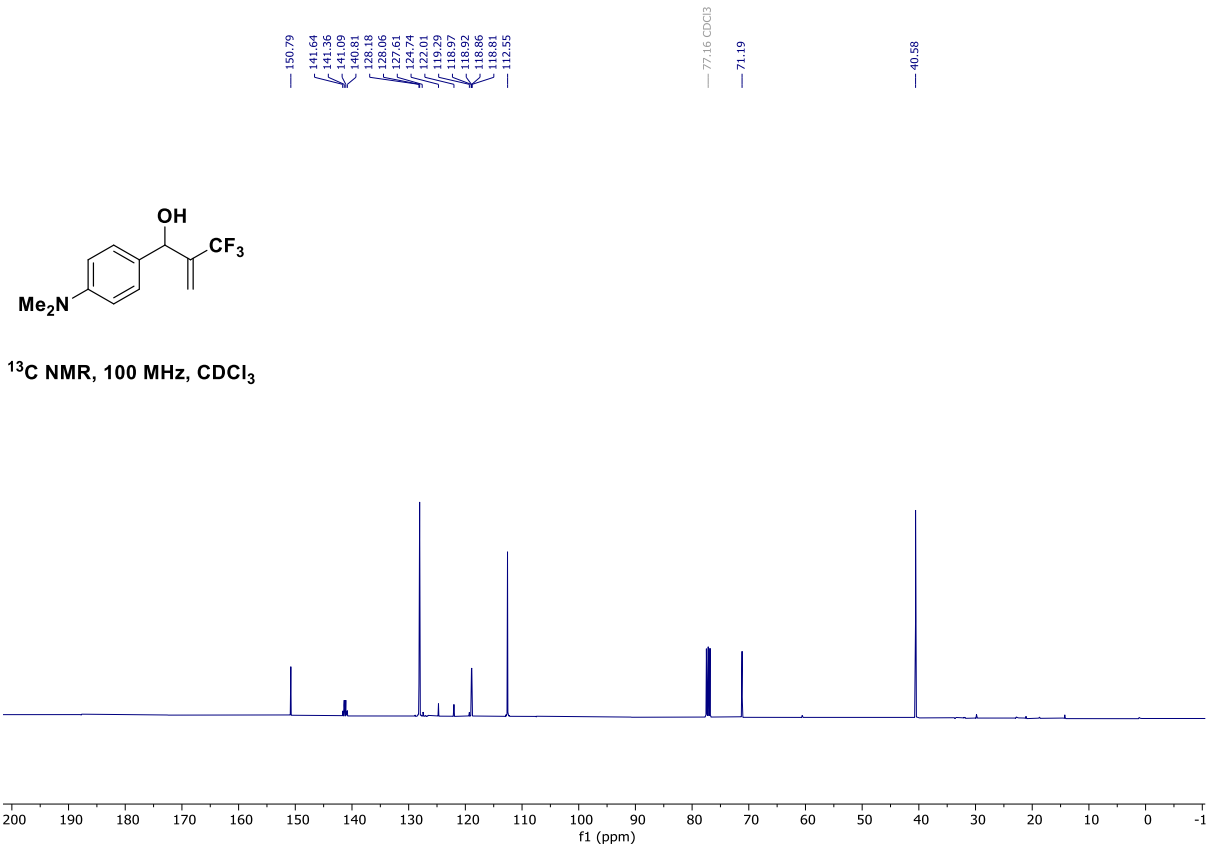
^{19}F NMR, 376 MHz, $CDCl_3$



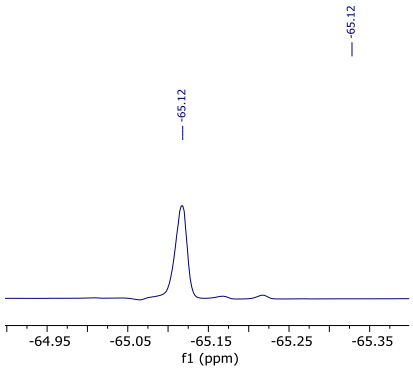
Compound 14

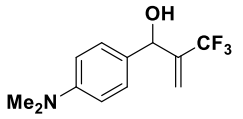


^{1}H NMR, 400 MHz, $CDCl_3$

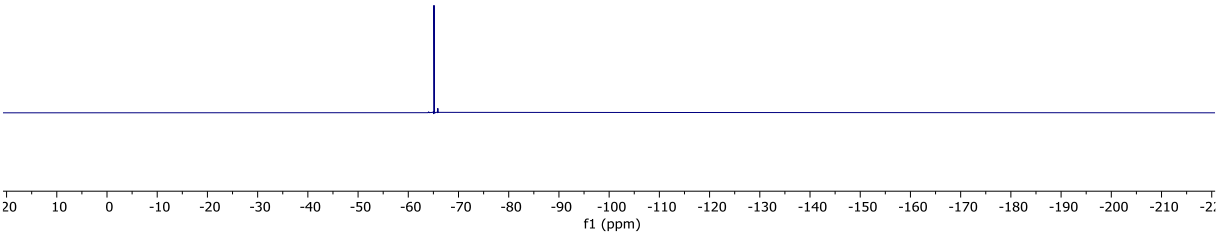


^{13}C NMR, 100 MHz, $CDCl_3$

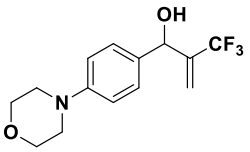




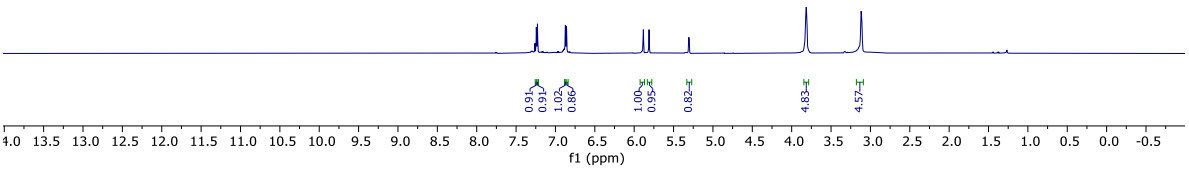
^{19}F NMR, 376 MHz, $CDCl_3$

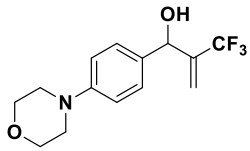


Compound 15

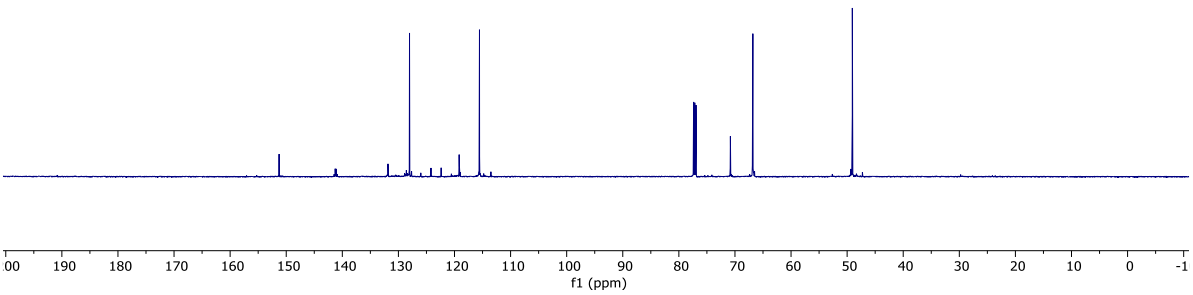


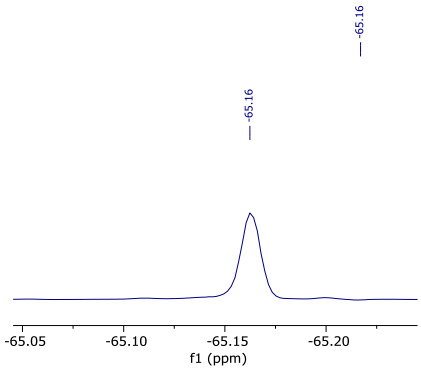
^{1}H NMR, 600 MHz, $CDCl_3$

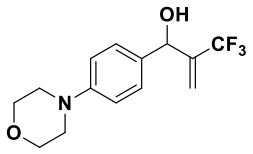




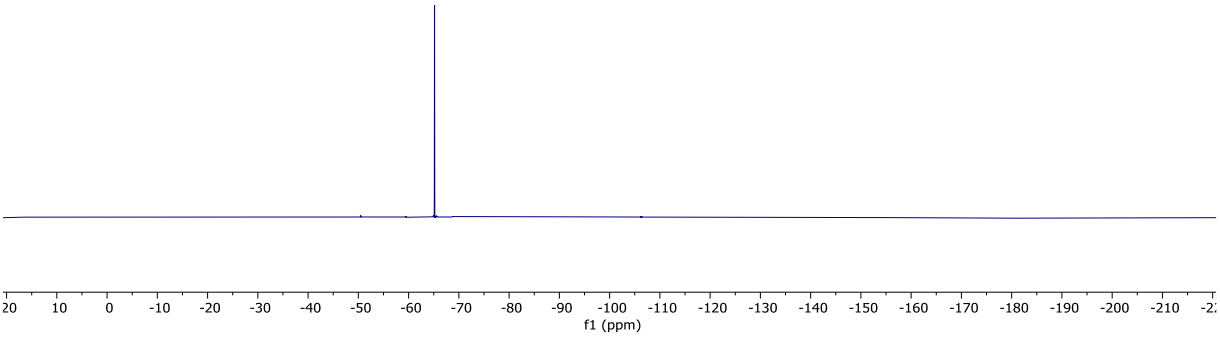
^{13}C NMR, 150 MHz, $CDCl_3$



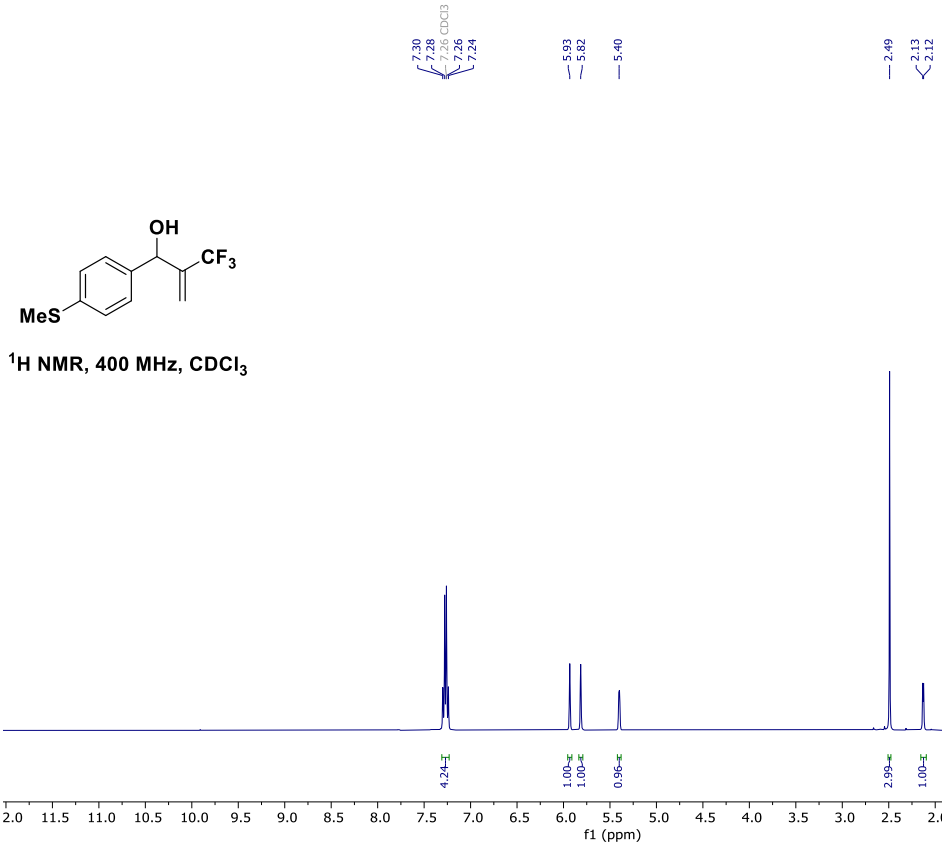




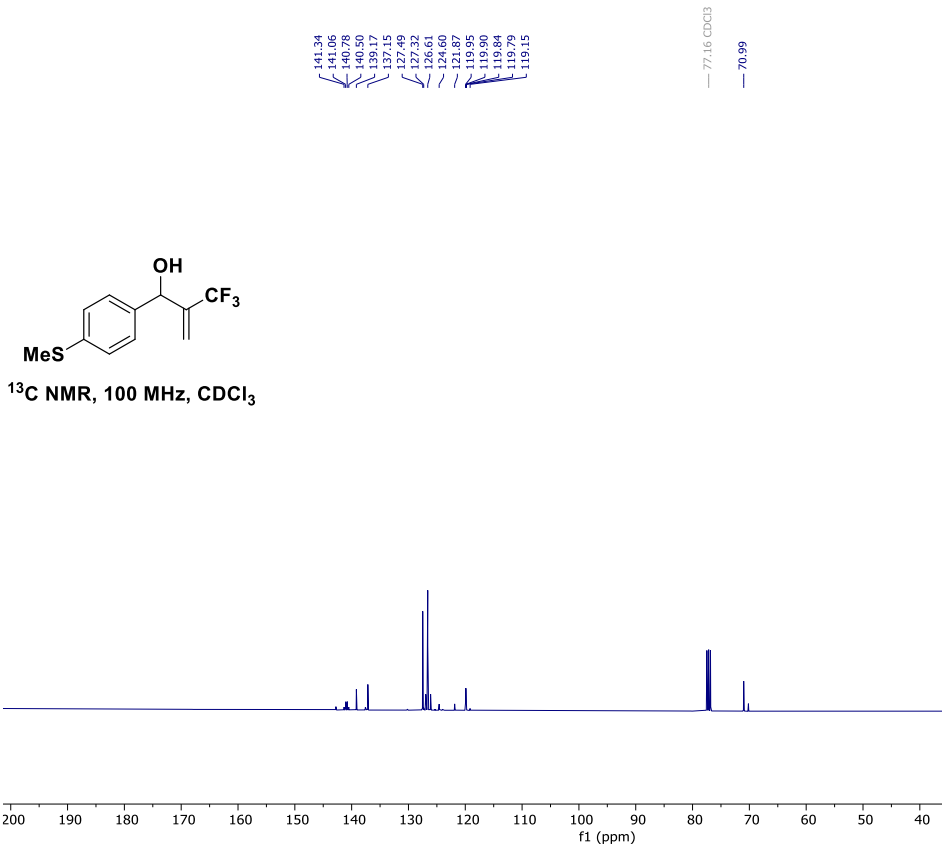
^{19}F NMR, 376 MHz, $CDCl_3$



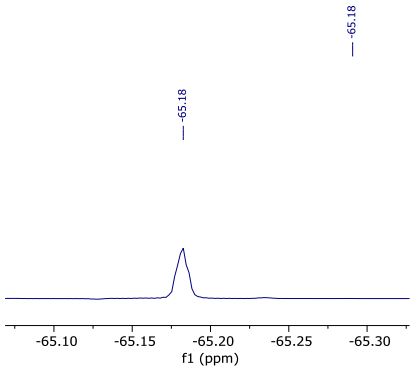
Compound 16

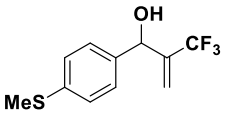


^{1}H NMR, 400 MHz, $CDCl_3$

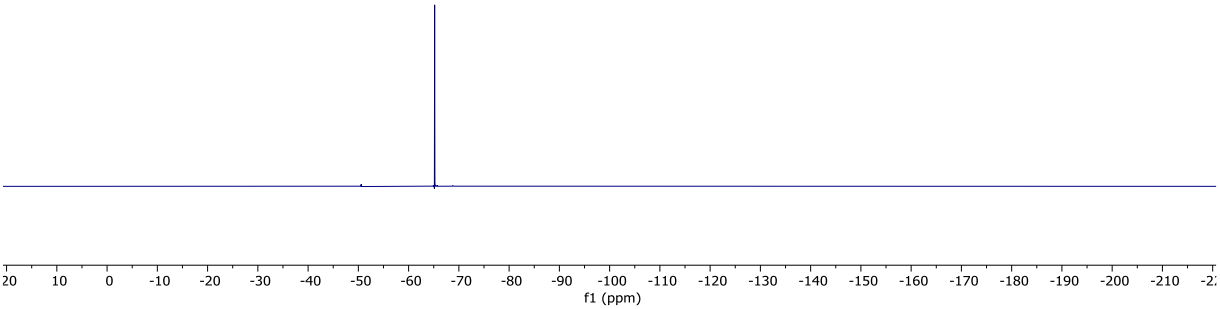


^{13}C NMR, 100 MHz, $CDCl_3$

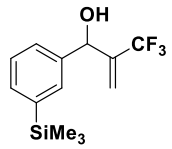




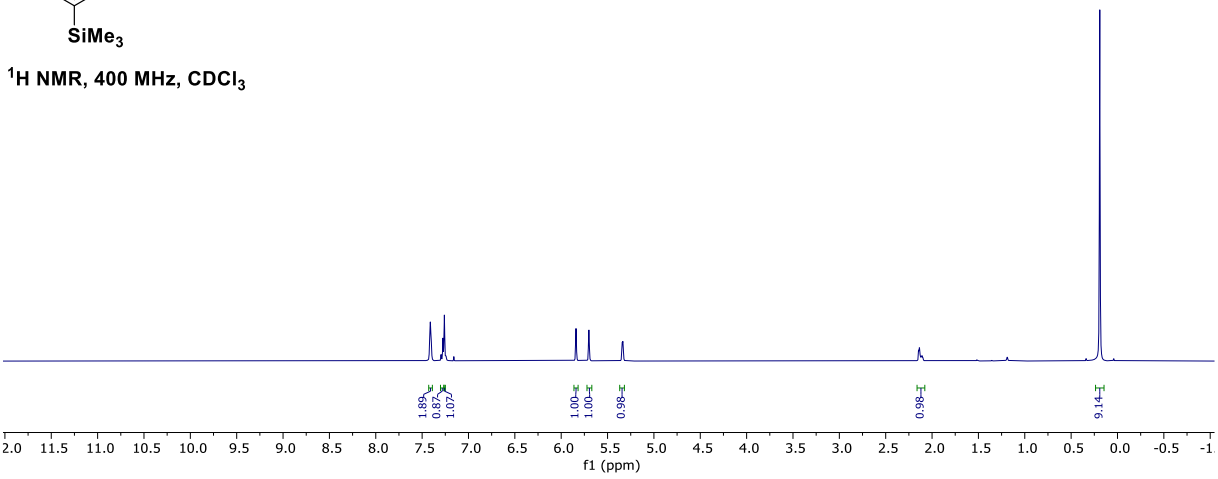
^{19}F NMR, 376 MHz, $CDCl_3$

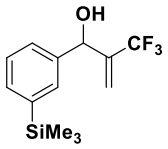


Compound 17

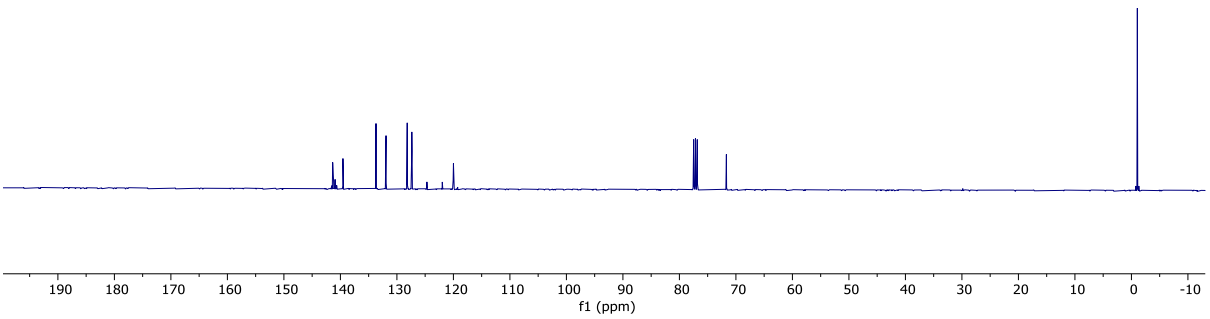


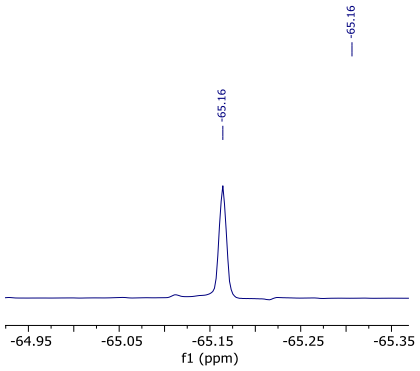
^{1}H NMR, 400 MHz, $CDCl_3$

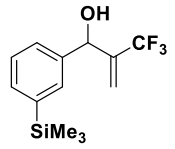




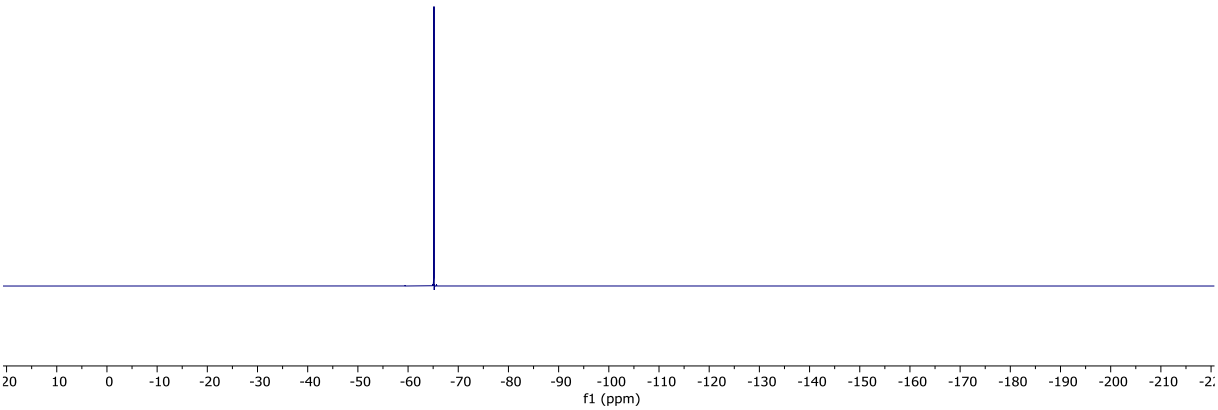
^{13}C NMR, 100 MHz, $CDCl_3$



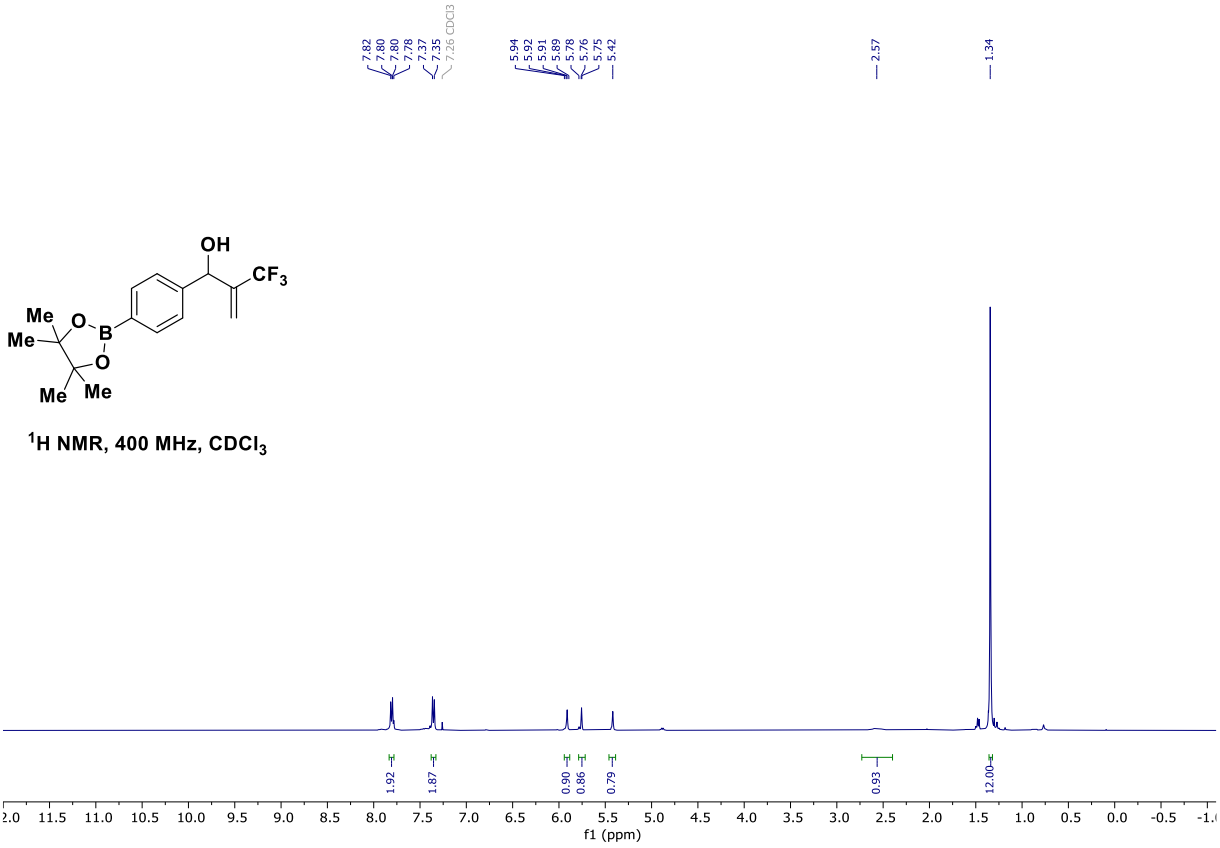




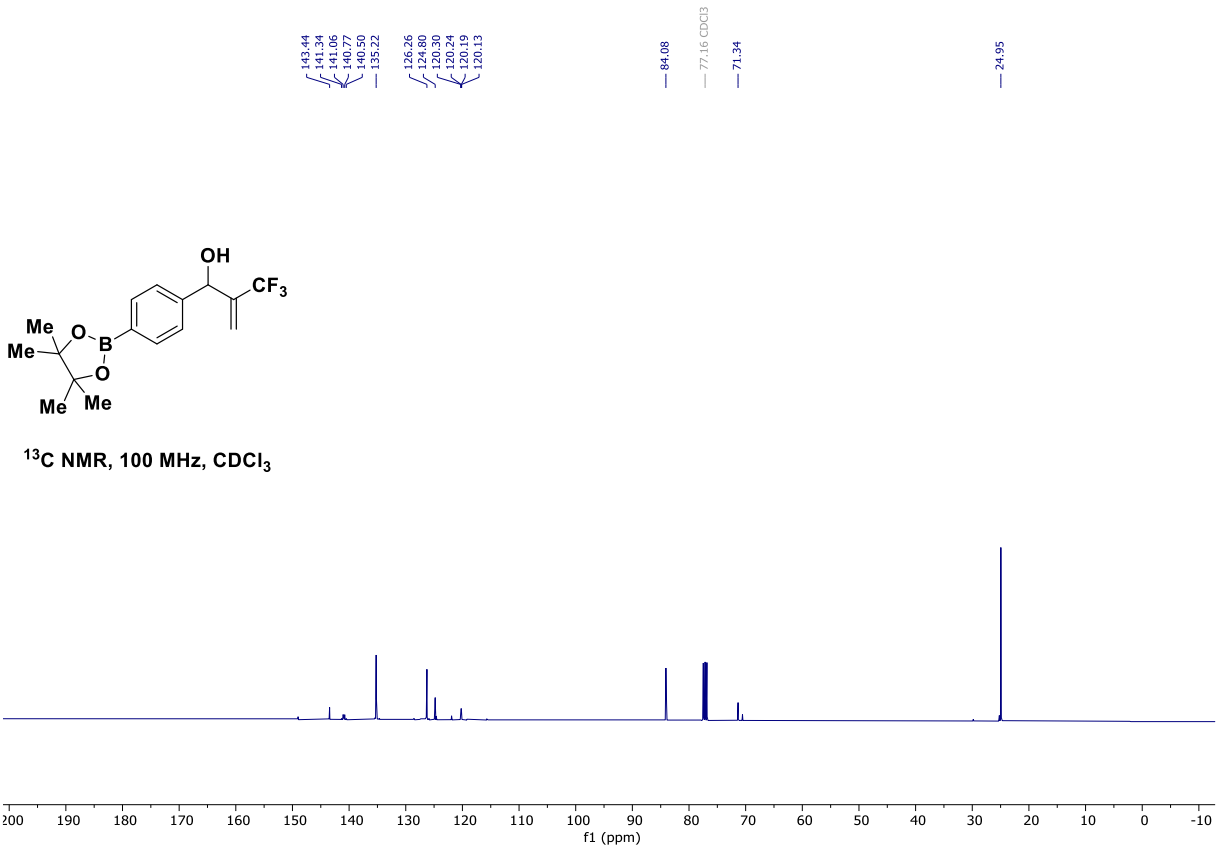
^{19}F NMR, 376 MHz, $CDCl_3$



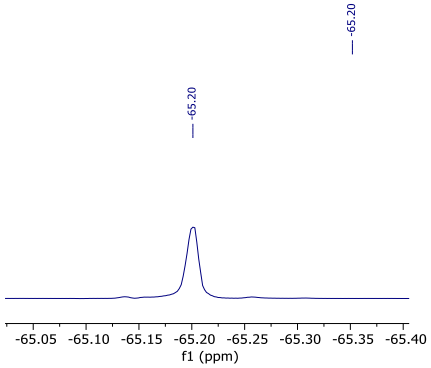
Compound 18

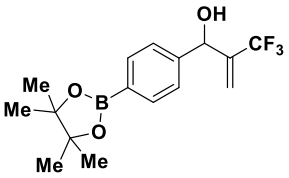


^{1}H NMR, 400 MHz, $CDCl_3$

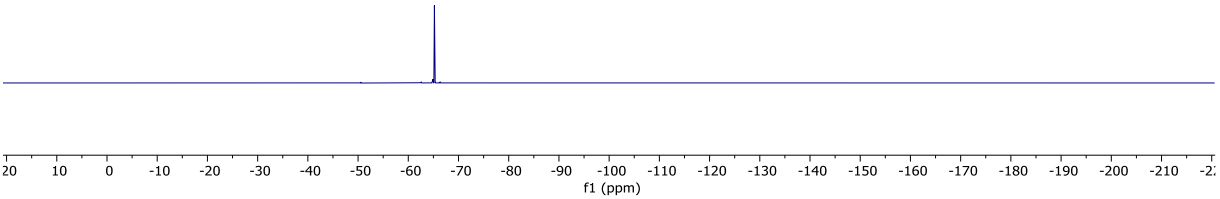


^{13}C NMR, 100 MHz, $CDCl_3$

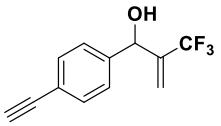




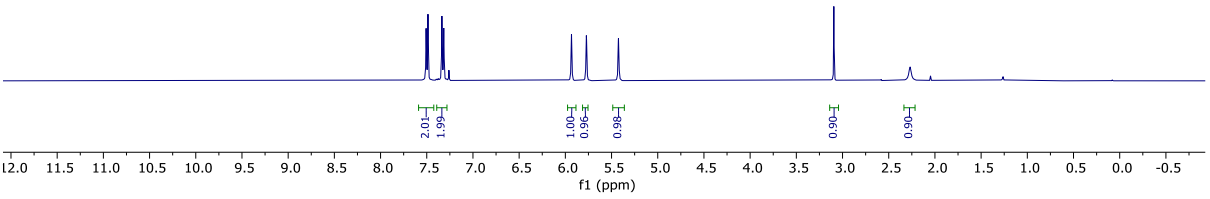
^{19}F NMR, 376 MHz, $CDCl_3$

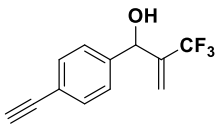


Compound 19

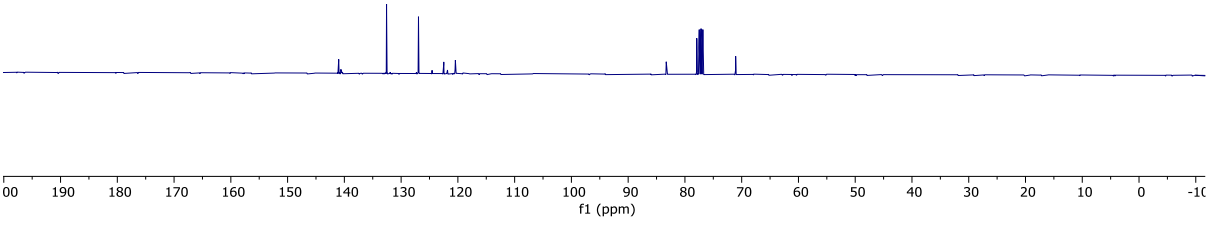


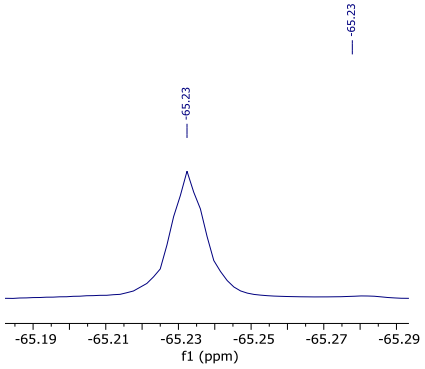
^{1}H NMR, 400 MHz, $CDCl_3$

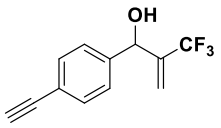




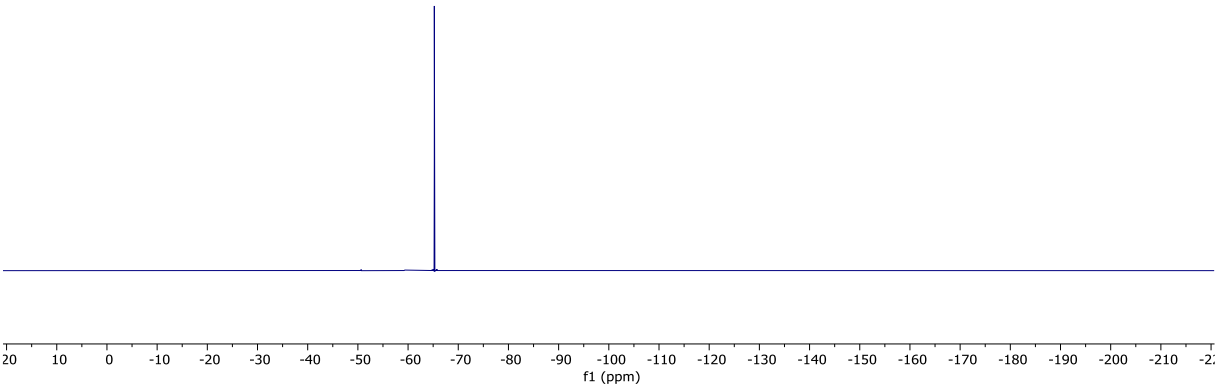
^{13}C NMR, 100 MHz, $CDCl_3$



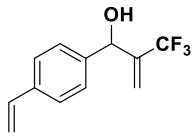




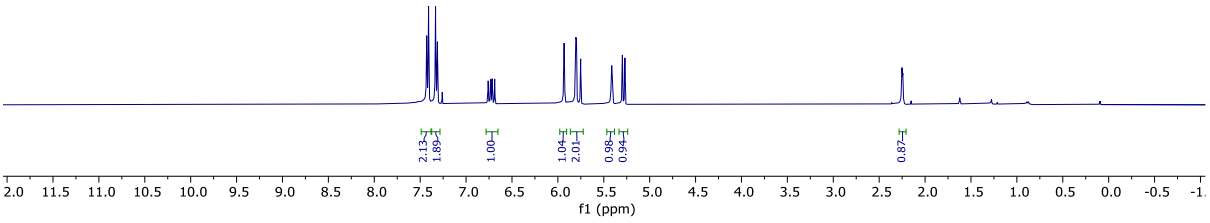
^{19}F NMR, 376 MHz, $CDCl_3$

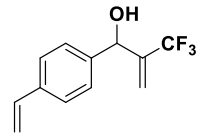


Compound 20

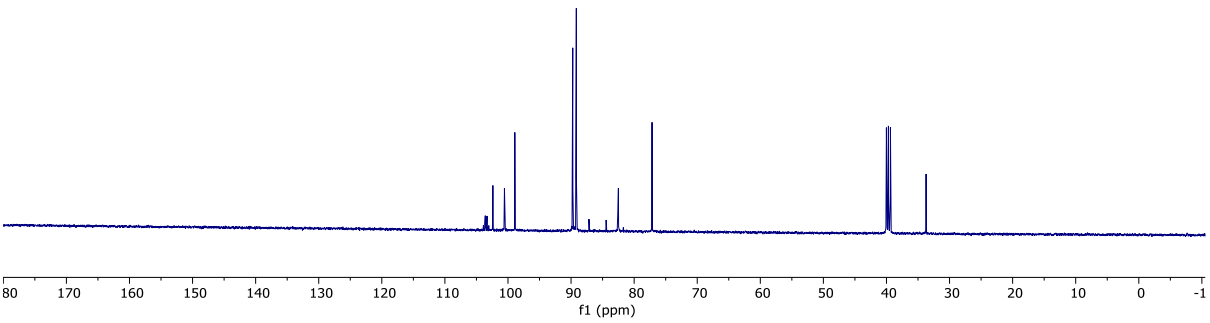


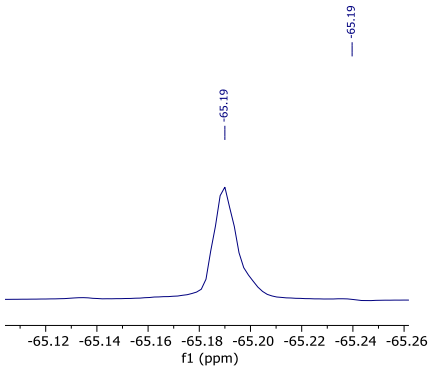
^{1}H NMR, 400 MHz, $CDCl_3$

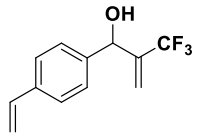




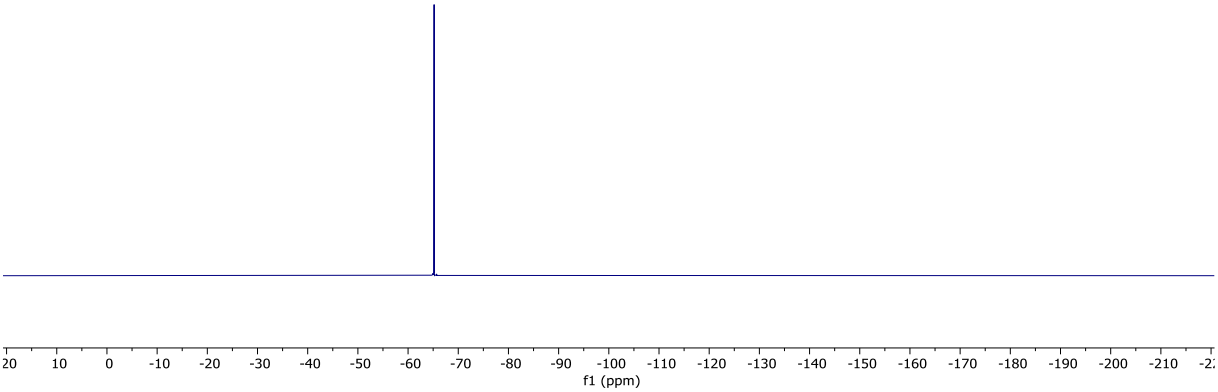
^{13}C NMR, 100 MHz, $CDCl_3$



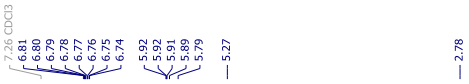


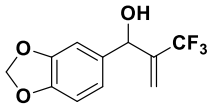


^{19}F NMR, 376 MHz, $CDCl_3$

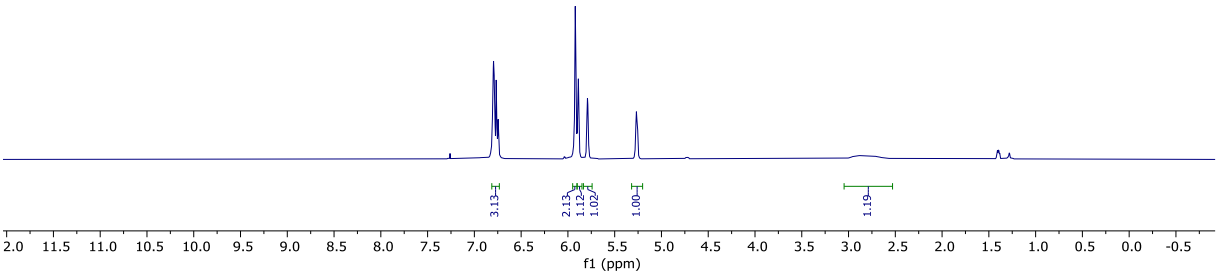


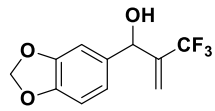
Compound 21



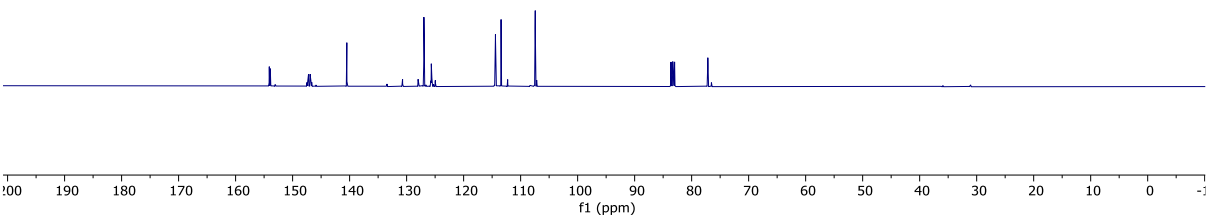


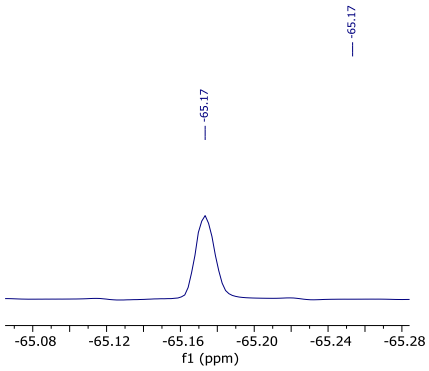
^{1}H NMR, 400 MHz, $CDCl_3$

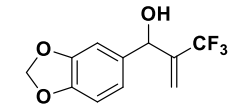




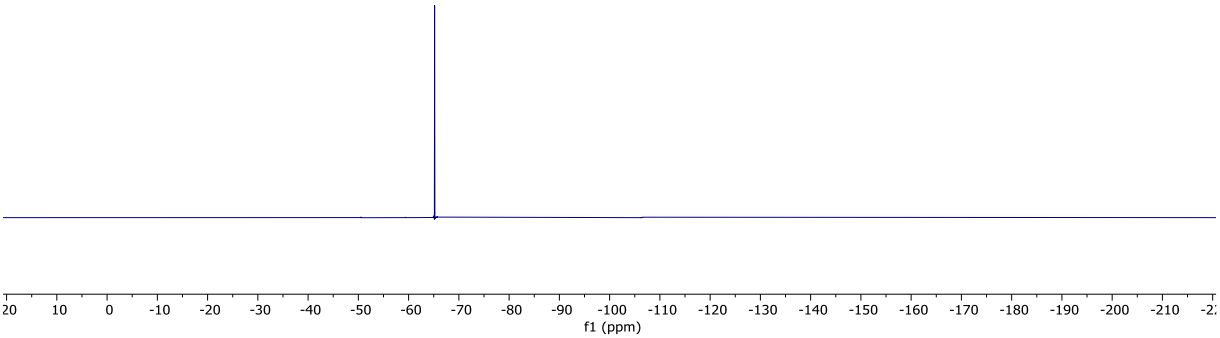
^{13}C NMR, 100 MHz, $CDCl_3$



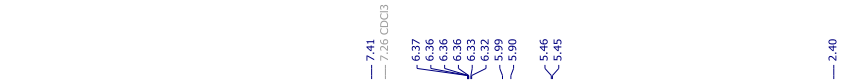


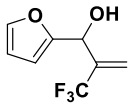


^{19}F NMR, 376 MHz, $CDCl_3$

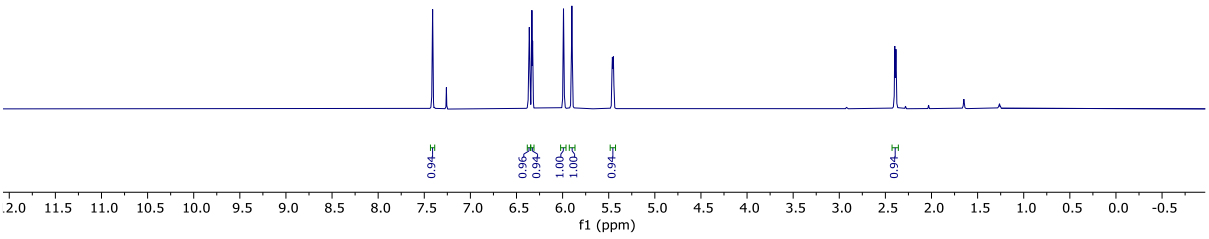


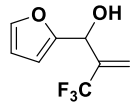
Compound 22



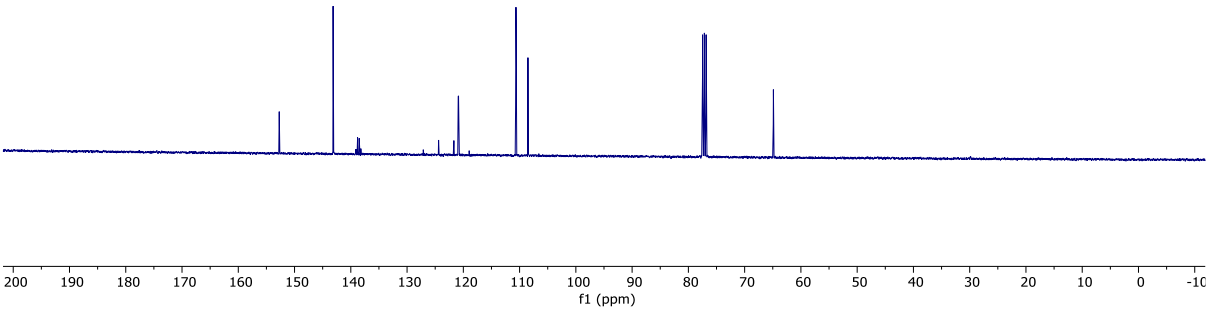


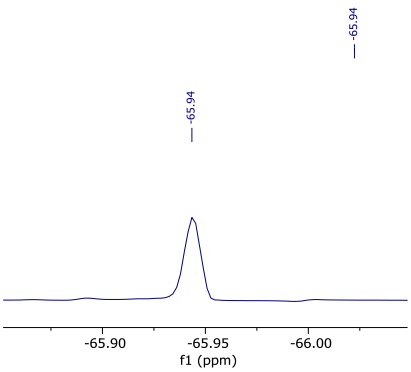
^{1}H NMR, 400 MHz, $CDCl_3$

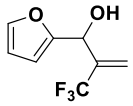




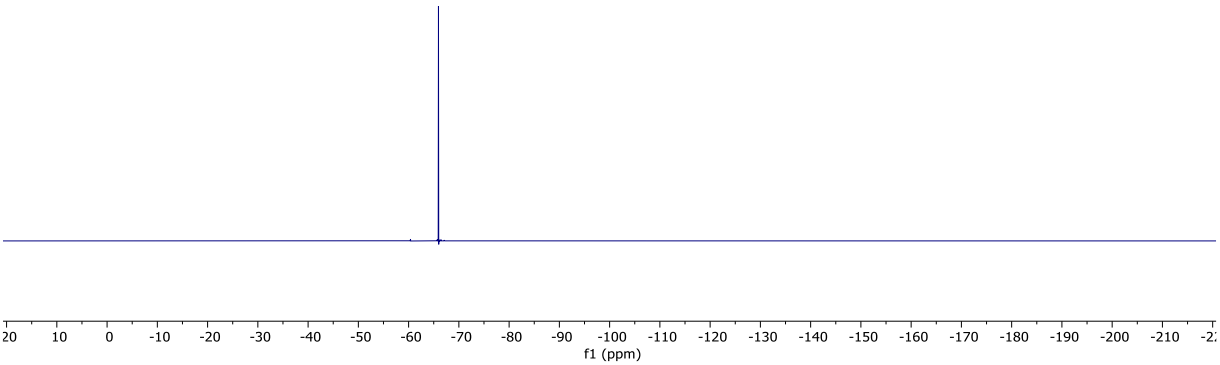
^{13}C NMR, 100 MHz, $CDCl_3$



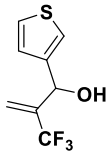




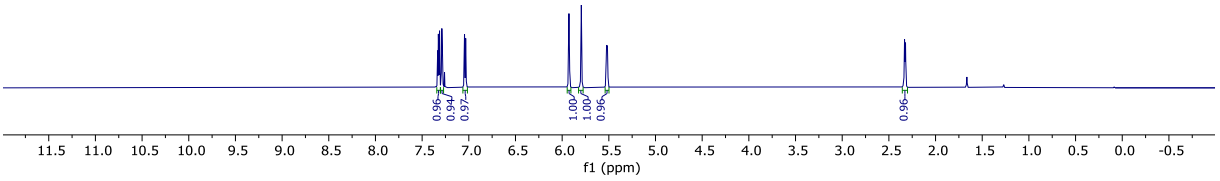
^{19}F NMR, 376 MHz, $CDCl_3$

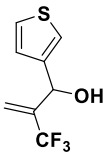


Compound 23

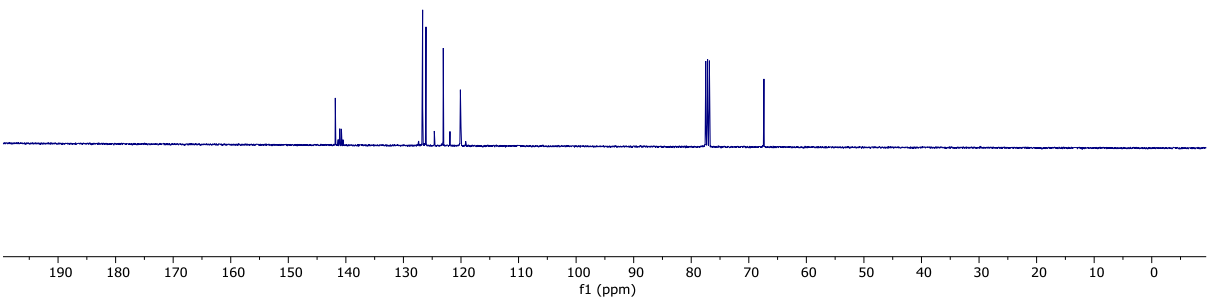


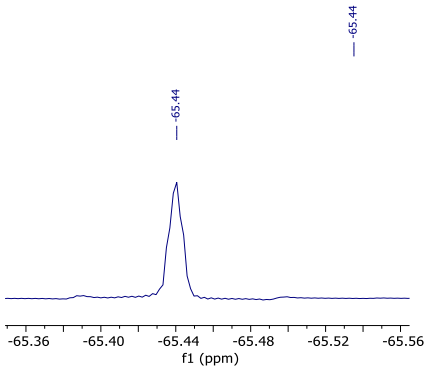
^{1}H NMR, 400 MHz, $CDCl_3$

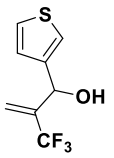




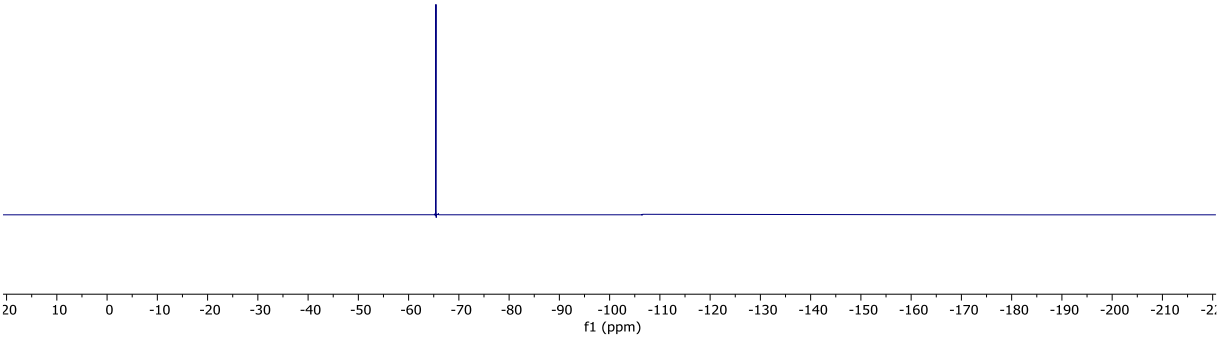
^{13}C NMR, 100 MHz, $CDCl_3$



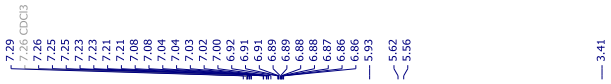


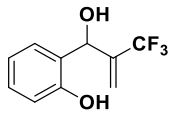


^{19}F NMR, 376 MHz, $CDCl_3$

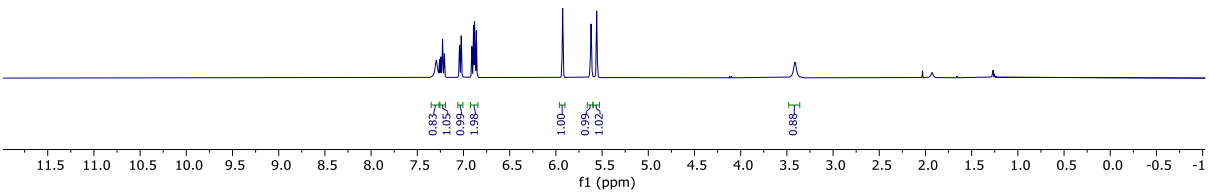


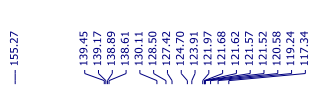
Compound 24

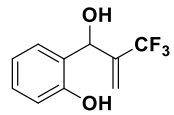




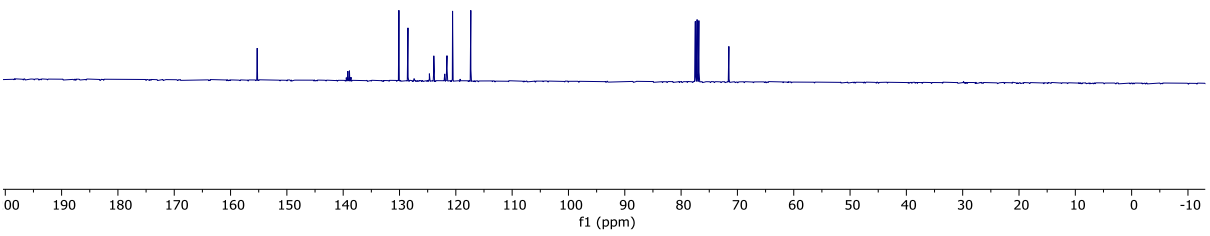
^{1}H NMR, 400 MHz, $CDCl_3$

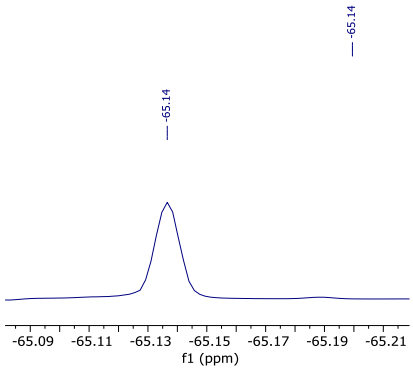


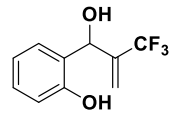




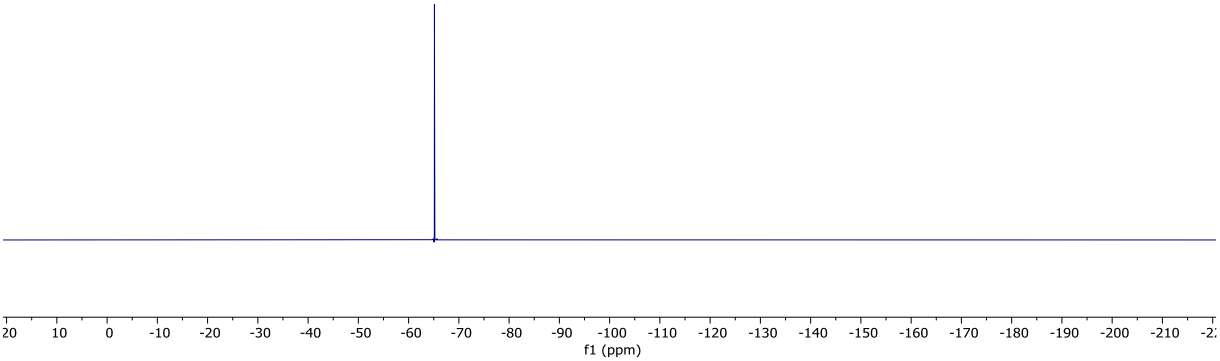
^{13}C NMR, 100 MHz, $CDCl_3$



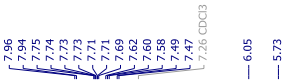


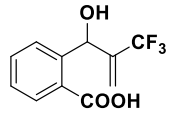


^{19}F NMR, 376 MHz, $CDCl_3$

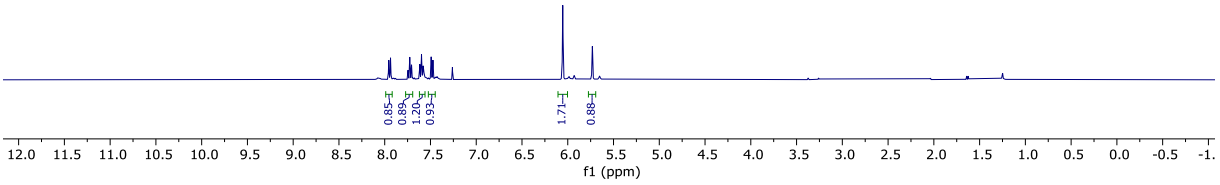


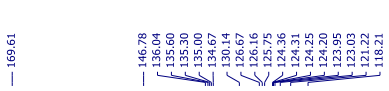
Compound 25

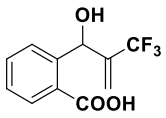




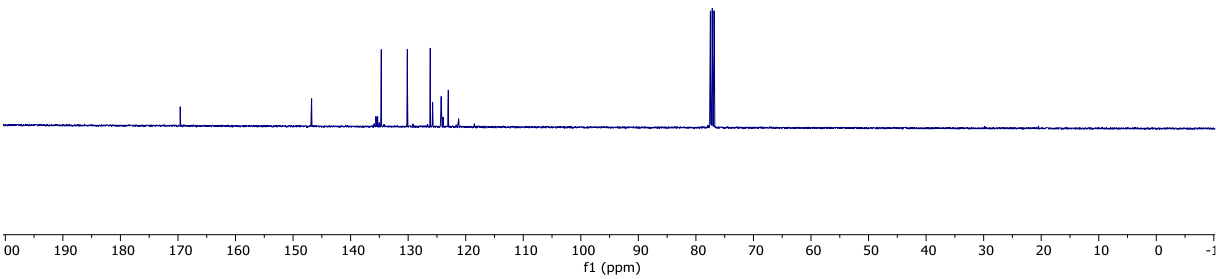
^{1}H NMR, 400 MHz, $CDCl_3$

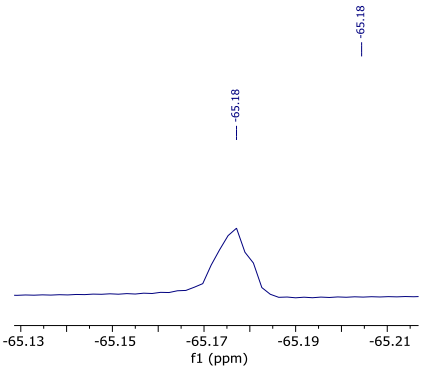


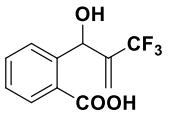




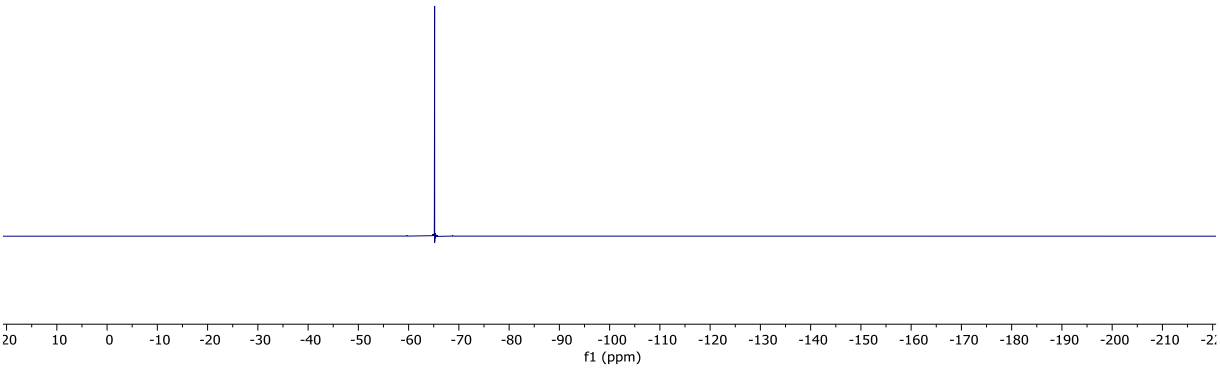
^{13}C NMR, 100 MHz, $CDCl_3$



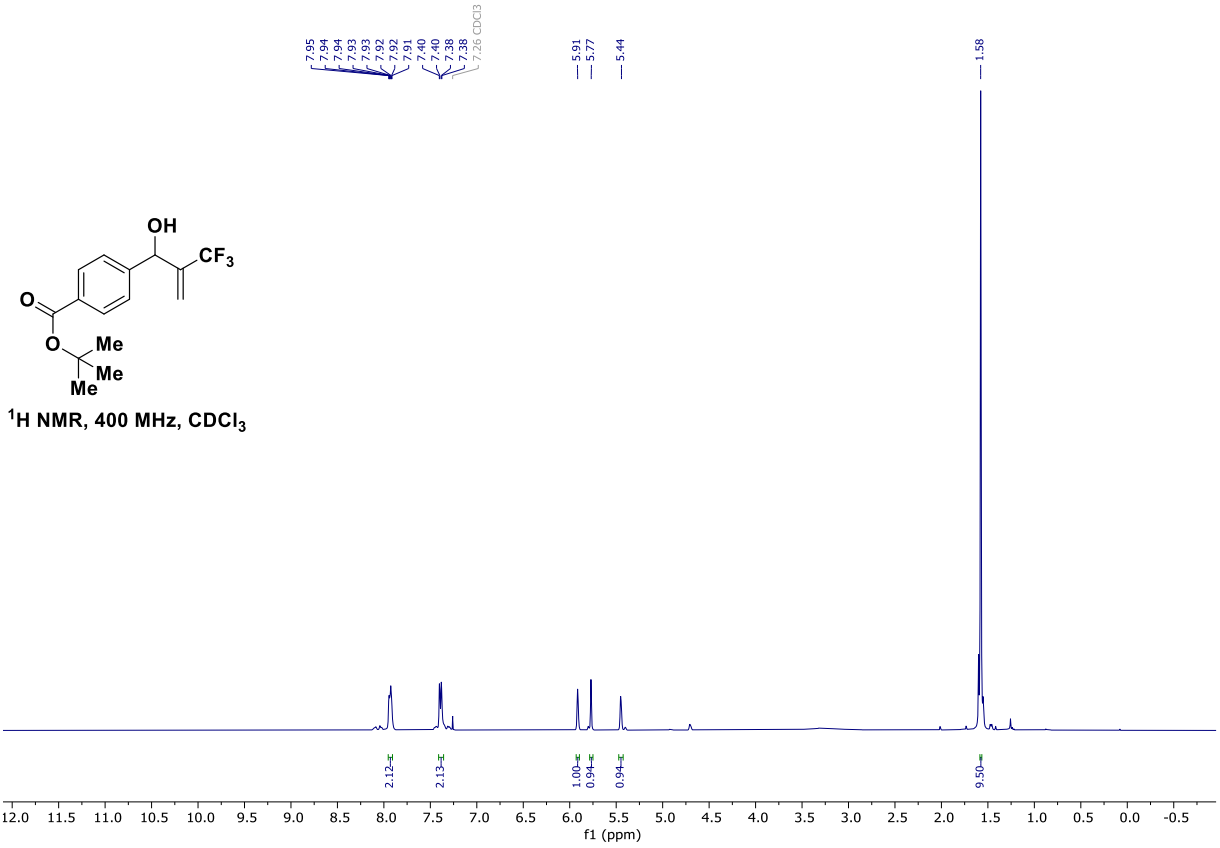




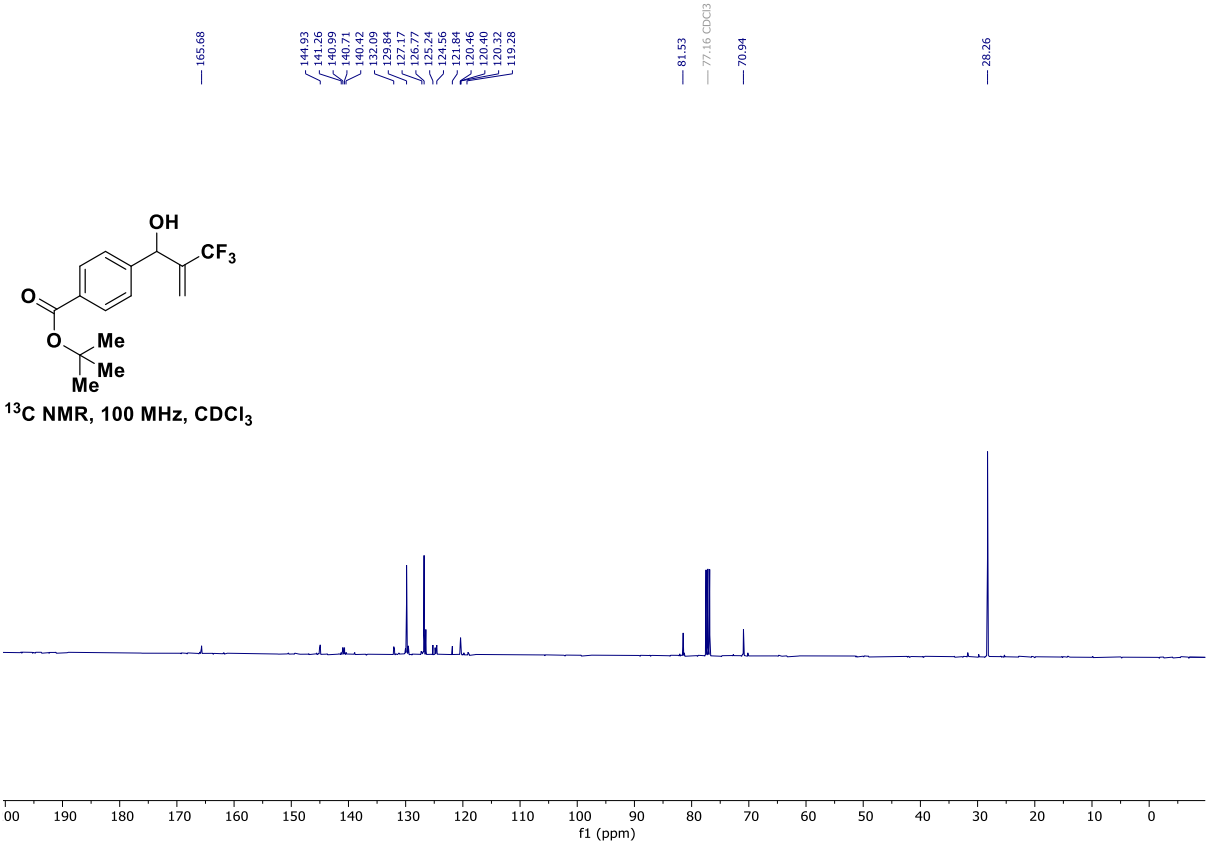
^{19}F NMR, 376 MHz, $CDCl_3$



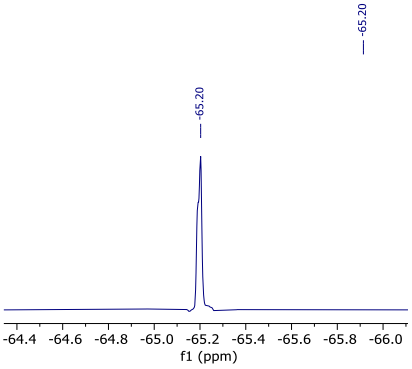
Compound 26

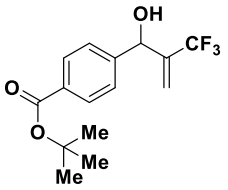


^{1}H NMR, 400 MHz, $CDCl_3$

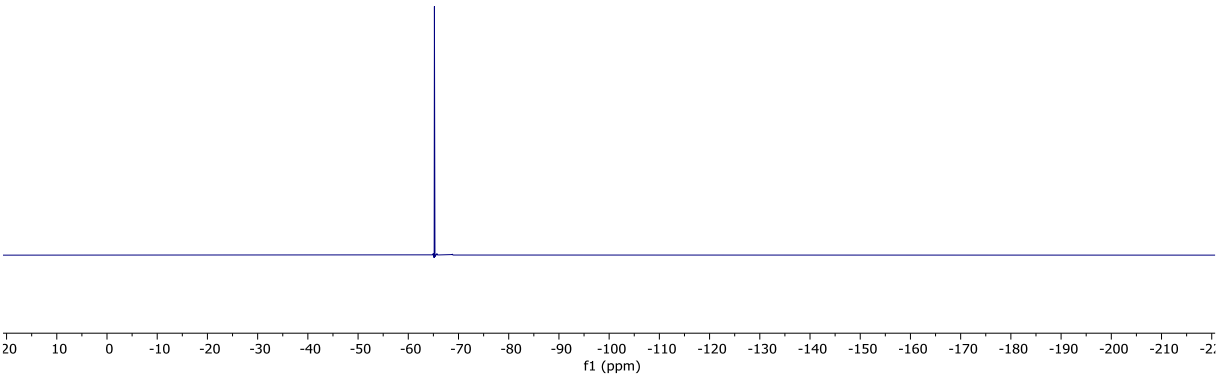


^{13}C NMR, 100 MHz, $CDCl_3$

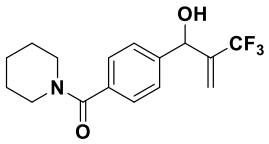




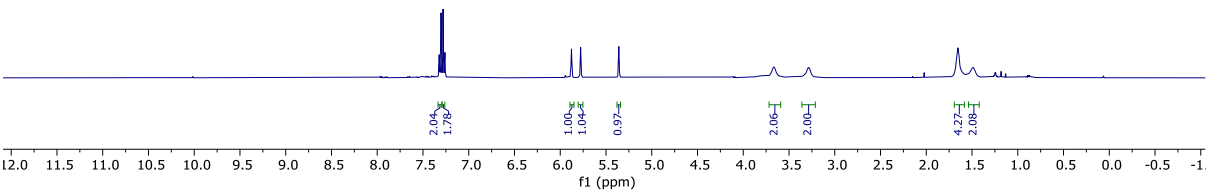
^{19}F NMR, 376 MHz, $CDCl_3$

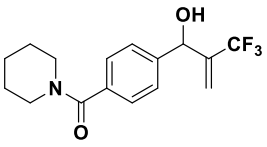


Compound 27

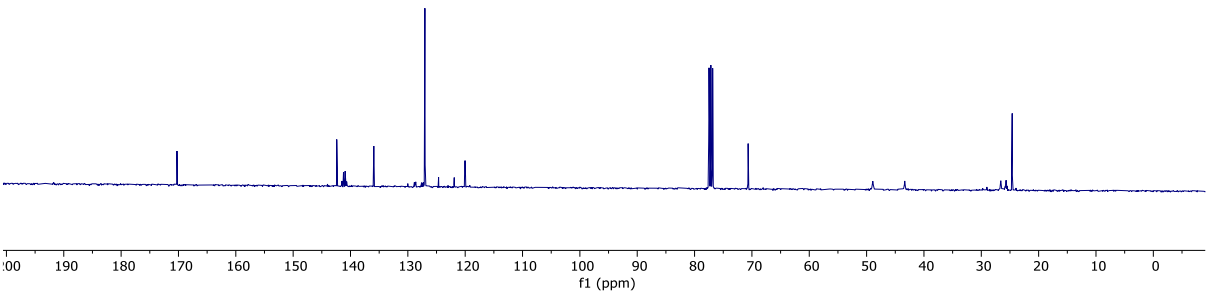


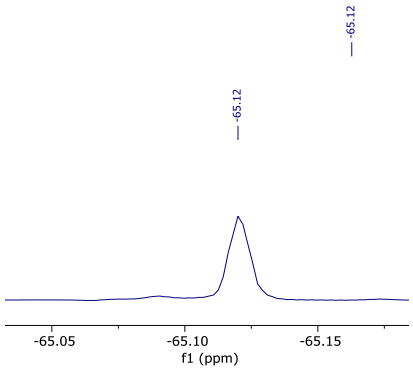
^{1}H NMR, 400 MHz, $CDCl_3$

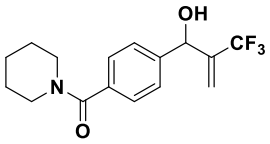




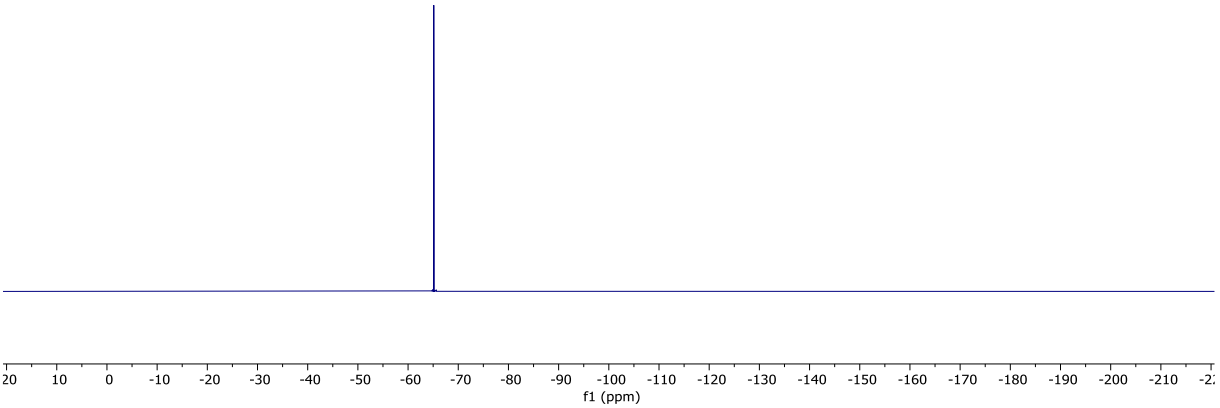
^{13}C NMR, 100 MHz, $CDCl_3$



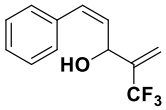




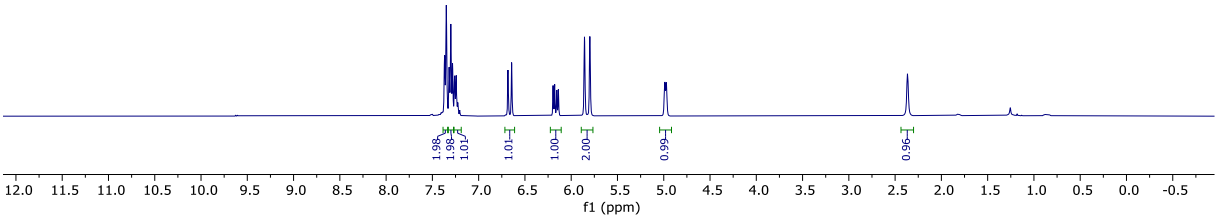
^{19}F NMR, 376 MHz, $CDCl_3$

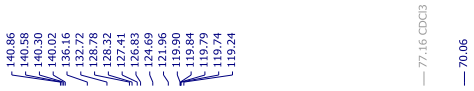


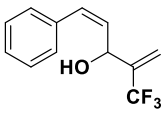
Compound 28



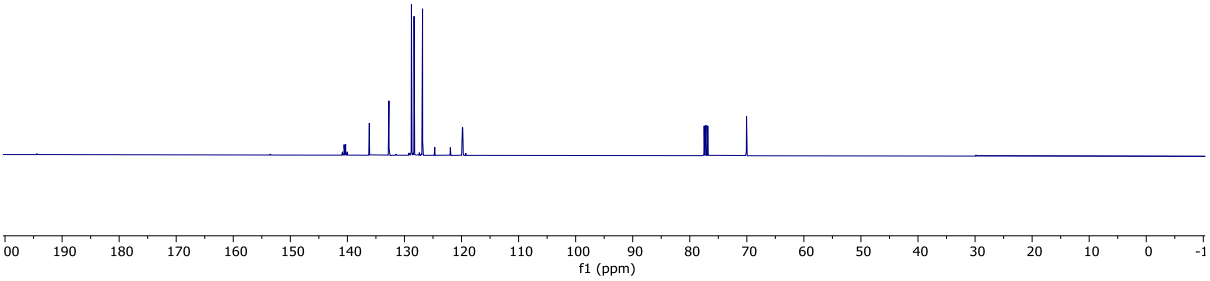
^{1}H NMR, 400 MHz, $CDCl_3$

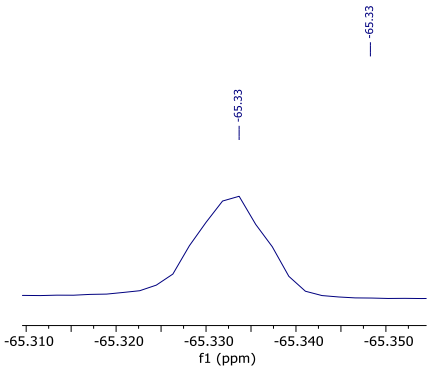


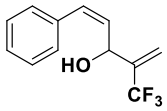




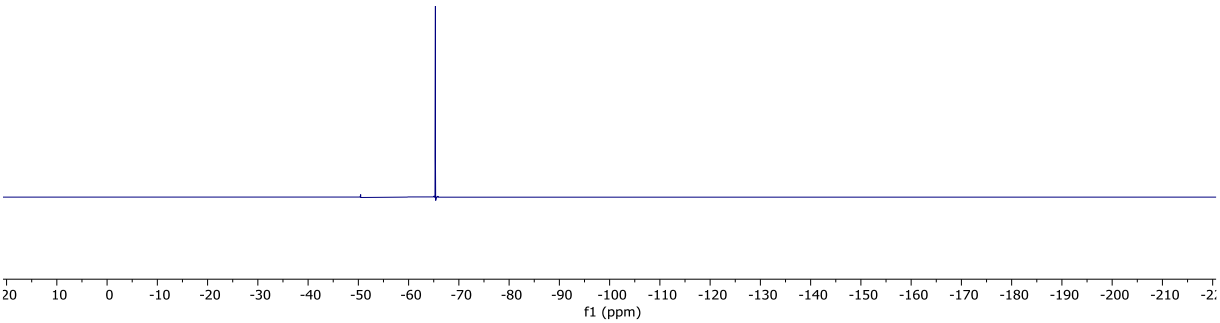
^{13}C NMR, 100 MHz, $CDCl_3$



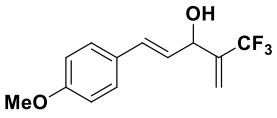




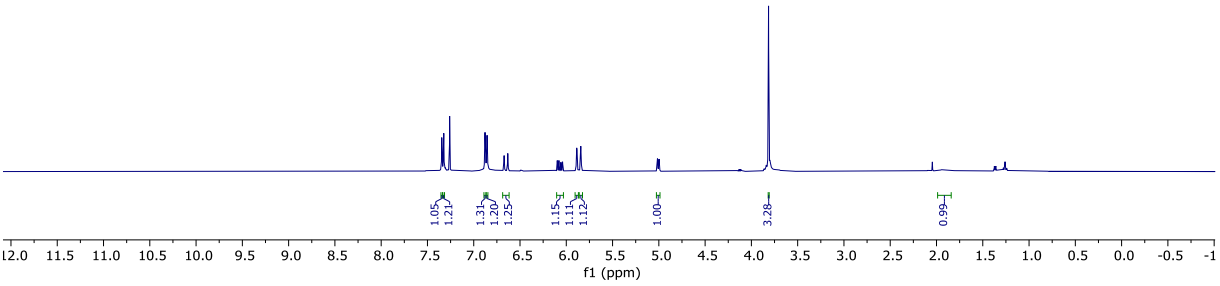
^{19}F NMR, 376 MHz, $CDCl_3$

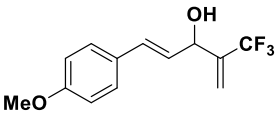


Compound 29

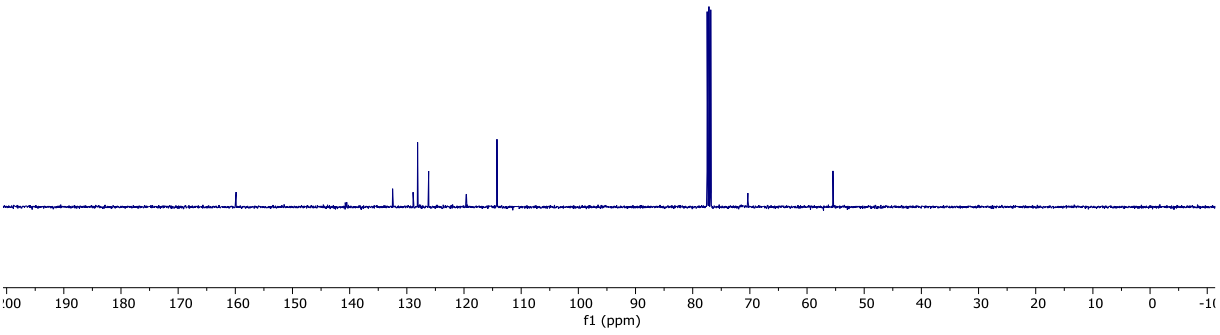


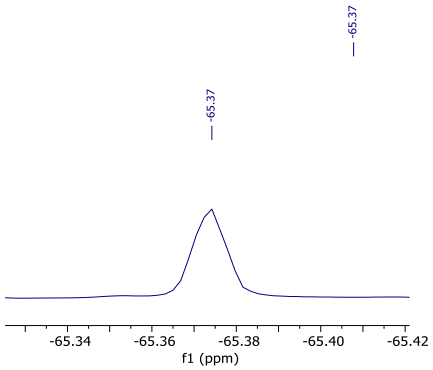
^{1}H NMR, 400 MHz, $CDCl_3$

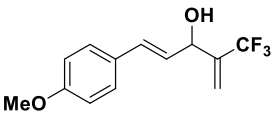




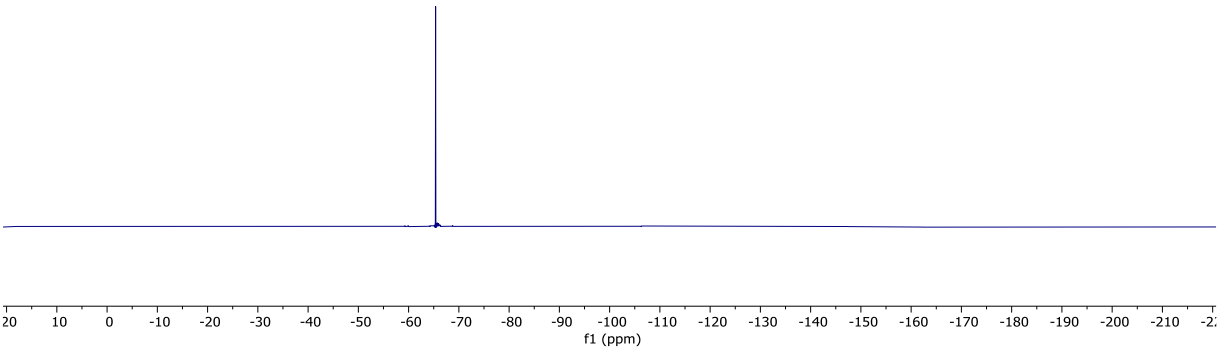
^{13}C NMR, 100 MHz, $CDCl_3$



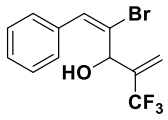




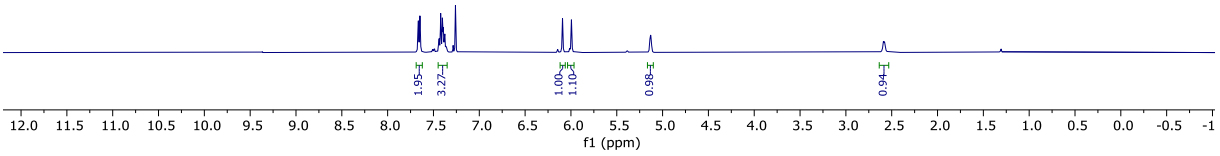
^{19}F NMR, 376 MHz, $CDCl_3$

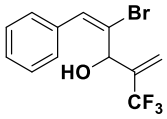


Compound 30

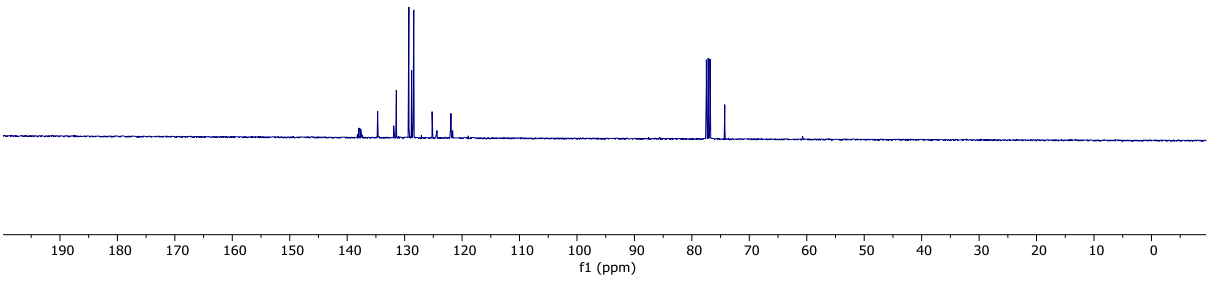


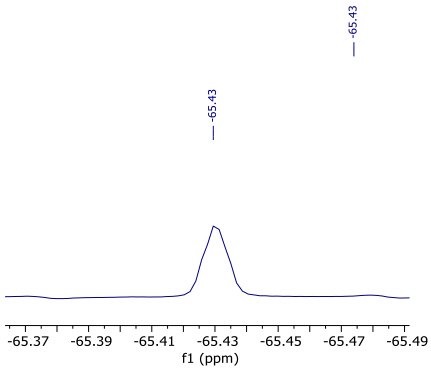
^{1}H NMR, 400 MHz, $CDCl_3$

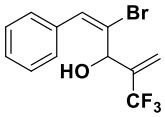




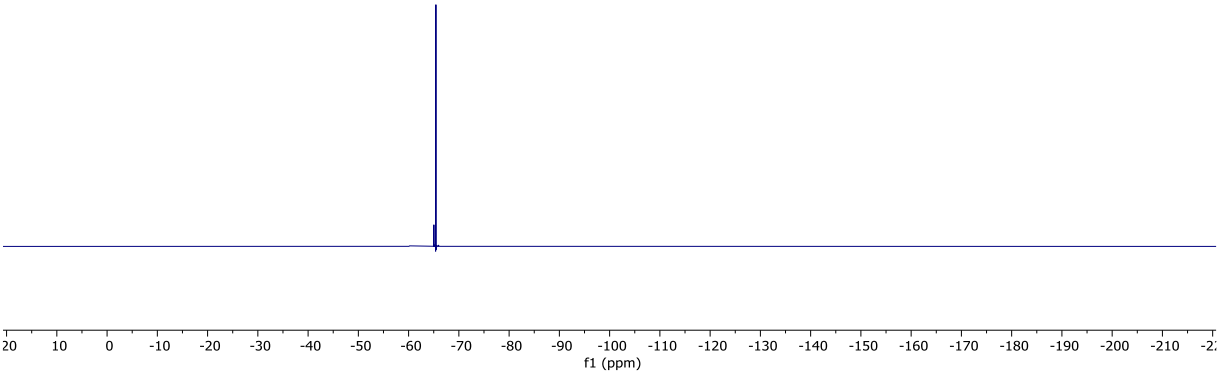
^{13}C NMR, 100 MHz, $CDCl_3$



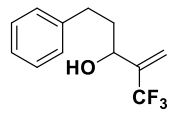




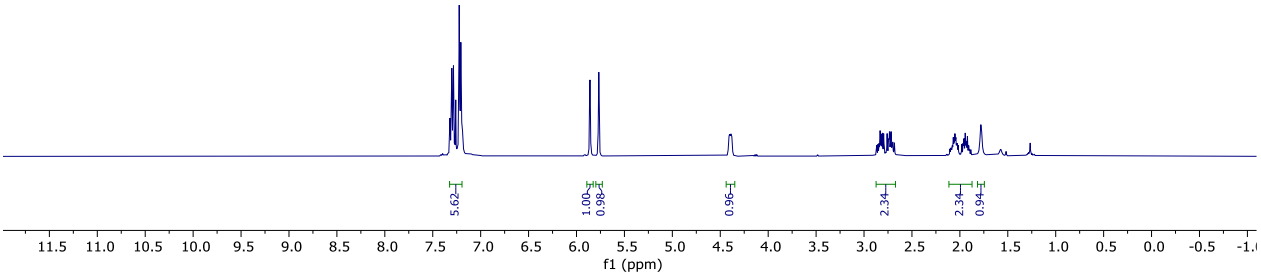
^{19}F NMR, 376 MHz, $CDCl_3$

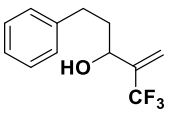


Compound 31

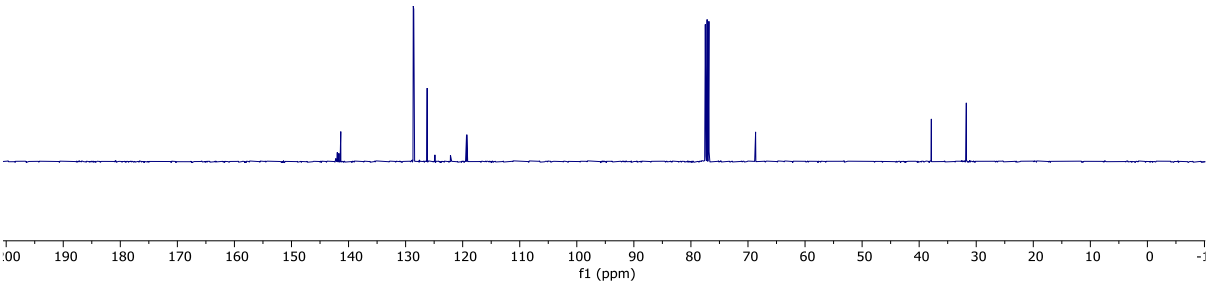


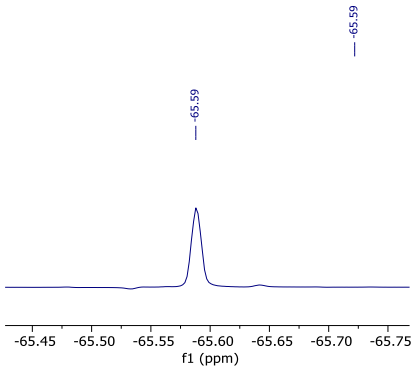
^{1}H NMR, 400 MHz, $CDCl_3$

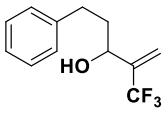




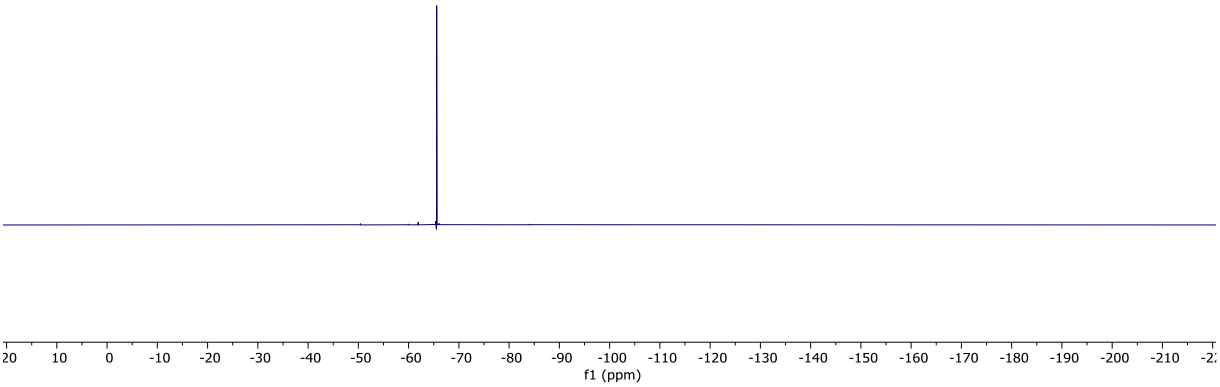
^{13}C NMR, 100 MHz, $CDCl_3$



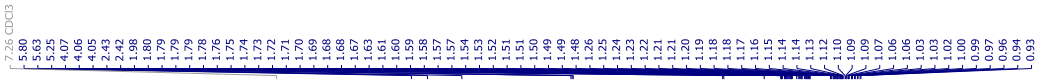


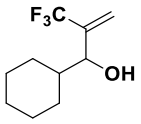


^{19}F NMR, 376 MHz, $CDCl_3$

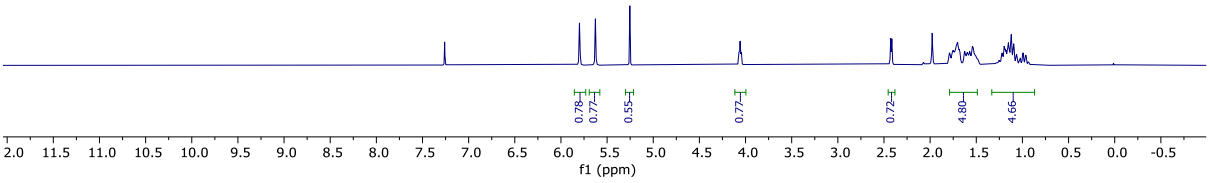


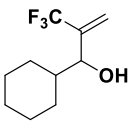
Compound 32



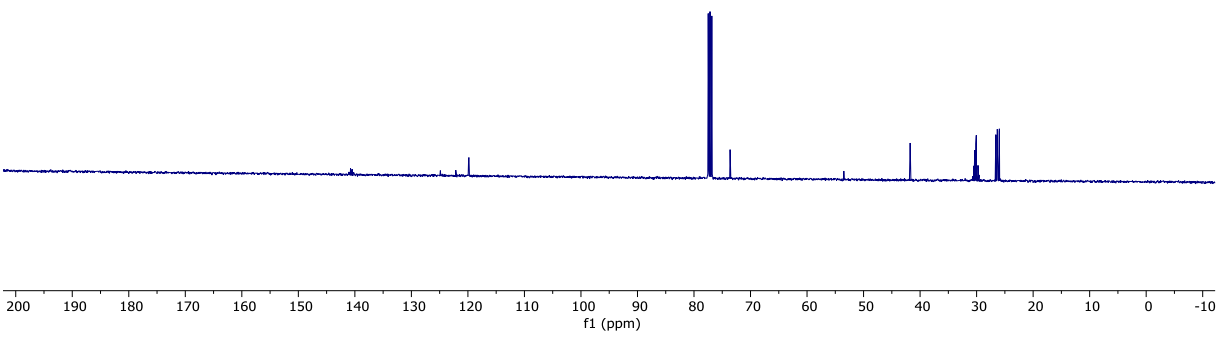


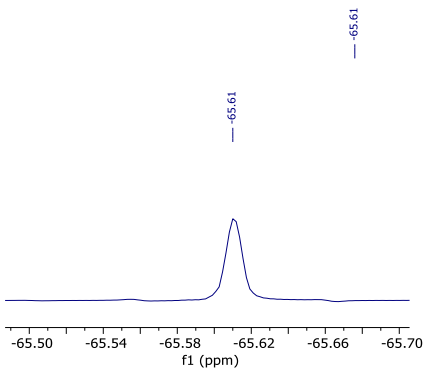
^{1}H NMR, 400 MHz, $CDCl_3$

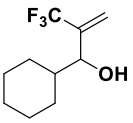




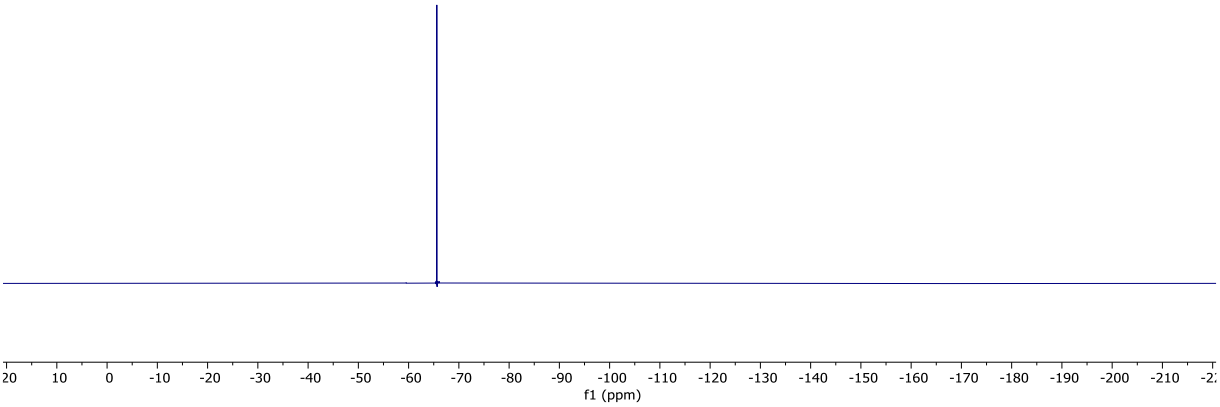
^{13}C NMR, 100 MHz, $CDCl_3$



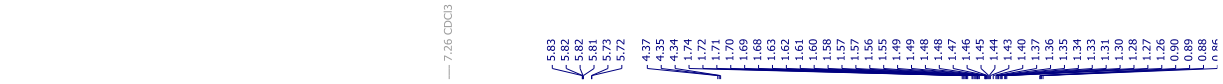


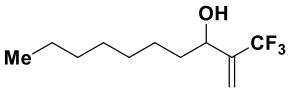


^{19}F NMR, 376 MHz, $CDCl_3$

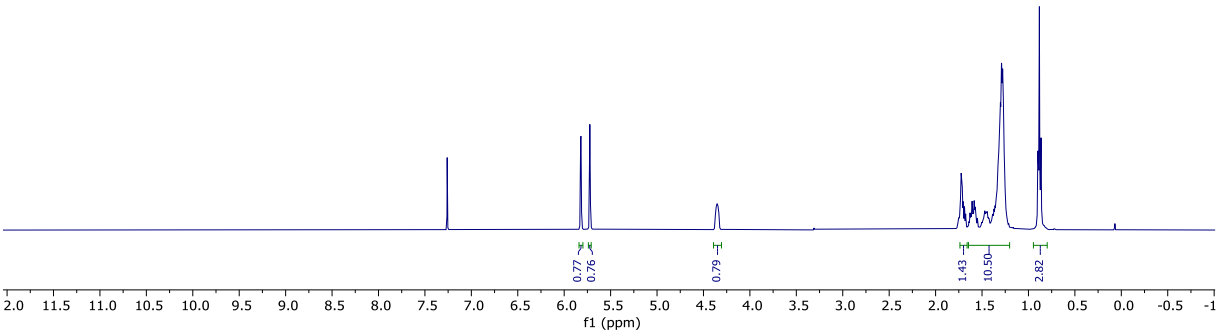


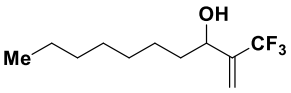
Compound 33



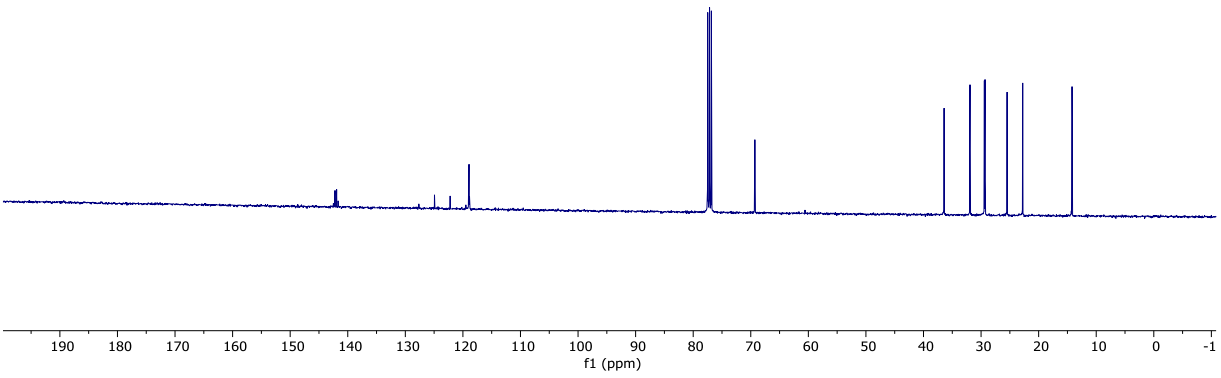


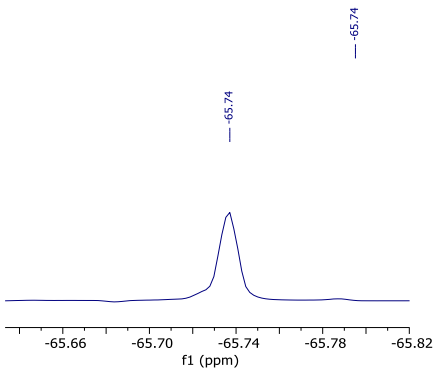
^{1}H NMR, 400 MHz, $CDCl_3$

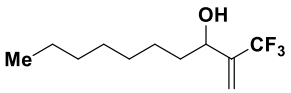




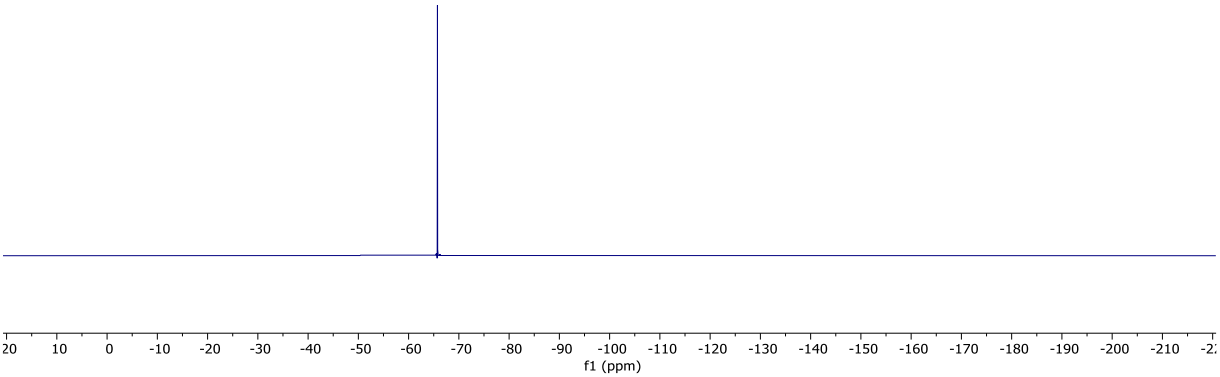
^{13}C NMR, 100 MHz, $CDCl_3$







^{19}F NMR, 376 MHz, $CDCl_3$



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6. LIST OF SCHEMES