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Catalysed Functionalisation of Imines

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Abstract

Nitrogen containing compounds are indispensable substructures of valuable pharmaceuticals, as well as interesting building blocks of industrially relevant basic and fine chemicals. With the aim of establishing a one-pot procedure for the synthesis of further functionalised amines, possible follow-up reactions (alkylation and hydrophosphonylation) of the intramolecular hydroamination of aminoalkynes were examined. In order to reach this goal, the reaction conditions were optimised. For this, due to practical reasons, instead of the hydroamination products, aldimines were applied as starting material initially. Moreover, a method to observe the alkylation *via* HPLC was developed, whereas the hydroaminations and the hydrophosphonylations were monitored *via* ^{1}H-NMR spectroscopy and therefore conducted as NMR-scale reactions. It was demonstrated that only one catalyst is sufficient to promote the hydroamination of aminoalkynes and the subsequent hydrophosphonylation of the imine intermediate within a one-pot procedure. In particularly suitable is the zirconium based pre-catalyst [$Zr(NMe_2)_4$], which leads to yields of up to 94% of the corresponding α-amino phosphonate. Additionally, by applying the chiral yttrium-based catalyst [Y((S)-binol-$SiPh_3$)(o-$C_6H_4CH_2NMe_2$)(Me_2NCH_2Ph)], the hydrophosphonylation of aldimines led to yields about 90-96% with enantiomeric excesses of up to 74%.

Zusammenfassung

Stickstoffhaltige Verbindungen sind wesentliche Teilstrukturen wertvoller Arzneimittel und zudem auch interessante Bausteine für Basis- und Feinchemikalien. Um atomökonomische Eintopfverfahren zur Herstellung verschiedenster funktionalisierter Amine zu etablieren, wurden in dieser Arbeit mögliche Folgereaktionen (Alkylierung und Hydrophosphonylierung) für die katalysierte intramolekulare Hydroaminierung von Aminoalkinen untersucht. Zu diesem Zweck wurden zunächst die Reaktionsbedingungen optimiert. Dazu wurden aus praktischen Gründen anstelle der Hydroaminierungsprodukte, Aldimine als Substrate verwendet. Um die Reaktionen zu beobachten, konnte eine Methode zur Verfolgung der Alkylierung mittels HPLC entwickelt werden. Hydroaminierung und Hydrosphophonylierung wurden ^{1}H-NMR spektroskopisch untersucht. Im Zuge der Arbeit konnte erstmalig gezeigt werden, dass es möglich ist mit einem einzigen Katalysator, sowohl die intramolekulare Hydoaminierung von Aminoalkinen, als auch die direkt darauffolgende Hydrophosphonylierung des Imin-Zwischenprodukts zu beschleunigen. Dabei hob sich vor allem der zirkonium-basierte Katalysatorvorläufer [$Zr(NMe_2)_4$] hervor, der zu Ausbeuten von bis zu 94% der gewünschten α-Aminophosponate führte. Des Weiteren konnten auch Hydrophosphonylierungen von aromatischen Aldiminen mit Ausbeuten von 90-96% und einem Enantiomerenüberschuss bis zu 74% realisiert werden, indem ein chiraler yttrium-basierter Katalysator ([$Y((S)\text{-binol-}SiPh_3)(o\text{-}C_6H_4CH_2NMe_2)(Me_2NCH_2Ph)$]) eingesetzt wurde.

Abbreviations

Alox	Aluminium oxide
BINOL	1,1'-Binaphthyl-2,2'-diol
Biphen	5,5',6,6'-Tetramethyl-3,3'-di-*t*-butyl-1,1'biphenyl-2,2'diol
br	Broad signal
CAN	Ceriumammonium hexanitrate
d	Doublet
dd	Doublet of doublet
ddd	Doublet of doublet of doublet
dH_2O	Deionised water
dq	Doublet of quartet
dquin	Doublet of quintet
dsxt	Doublet of sextet
dt	Doublet of triplet
DCM	Dichloromethane
DMF	Dimethylformamide
dpm	Dipivaloylmethane
ee	Enantiomeric excess
eq	Equivalent
Et_2O	Diethylether
EtOAc	Ethylacetate
EtOH	Ethanol
h	Hour(s)
hept	Heptane
HMPA	Hexamethylphosphoramide
HPLC	High Pressure Liquid Chromatography
*i*PrOH	Isopropylalcohol
KPHT	Potassium phthalimide
m	Multiplet
MeOH	Methanol
min	Minute(s)
*n*BuLi	*n*-Butyllithium
NHC	N-heterocyclic carbene
NMR	Nuclear Magnetic Resonance
OTf	Triflate
Ph	Phenyl
ppm	Parts per million
quint	Quintet
rt	Room temperature
s	Singlet
sept	Septet
t	Triplet
td	Triplet of doublet
tfc	Trifluoromethylhydroxymethylene camphorate
tt	Triplet of triplet
THF	Tetrahydrofurane

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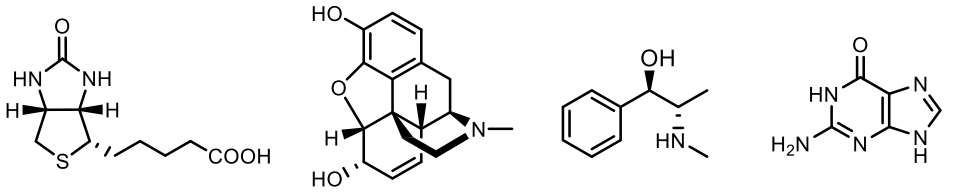
1. Introduction

Nitrogen-containing molecules are substructures of a large number of important biological substances as for instance amino acids, vitamins, alkaloids and nucleic acids (Figure 1). Therefore they are essential in biological systems and processes.[1–3]

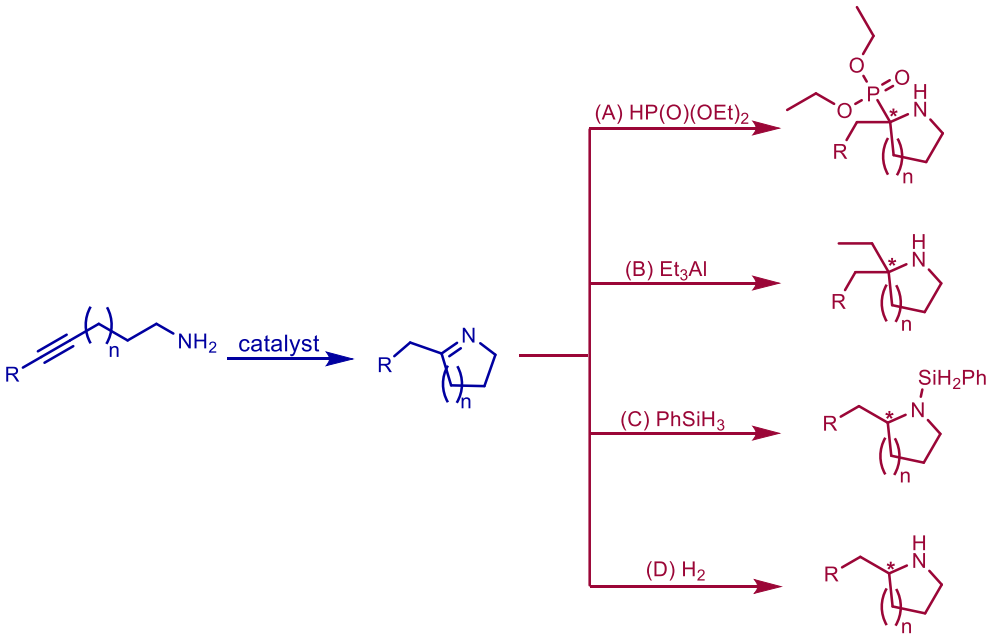


Biotin (vitamin) | Morphine (opiate) | Ephedrine (alkaloid) | Guanine (nucleic acid)

Figure 1: Amines in biological substances[4]

Moreover, nitrogen-containing substances are fundamental pharmaceuticals and important building blocks, as well as industrially relevant basic and fine chemicals. Consequently, the development of their efficient synthesis plays an important role in current catalyst research.[2,5] Among the wide range of synthetic routes for the formation of cyclic and acyclic amines, the hydroamination reaction provides an atom-efficient pathway. A new carbon-nitrogen bond is formed *via* addition of an amine to an unsaturated carbon-carbon bond.[2,3,6]

Comparing the hydroamination of alkenes and alkynes, the hydroamination of alkynes is easier to perform.[6] Moreover, imines, which are products of alkyne hydroamination, are an interesting target for further functionalisation due to their tendency to hydrolysis. One-pot-two-step reaction sequences in which one metal-complex catalyses both reaction steps and thereby introduces additional complexity to the products of the hydroamination of alkynes are attractive in particular.[6] There are different possibilities of functionalisation such as alkylation,[7] hydrosilylation[8] or hydrogenation,[9] which all lead to secondary amines in a convenient way, or hydrophosphonylation which provides α-amino phosphonates (Scheme 1).[10]

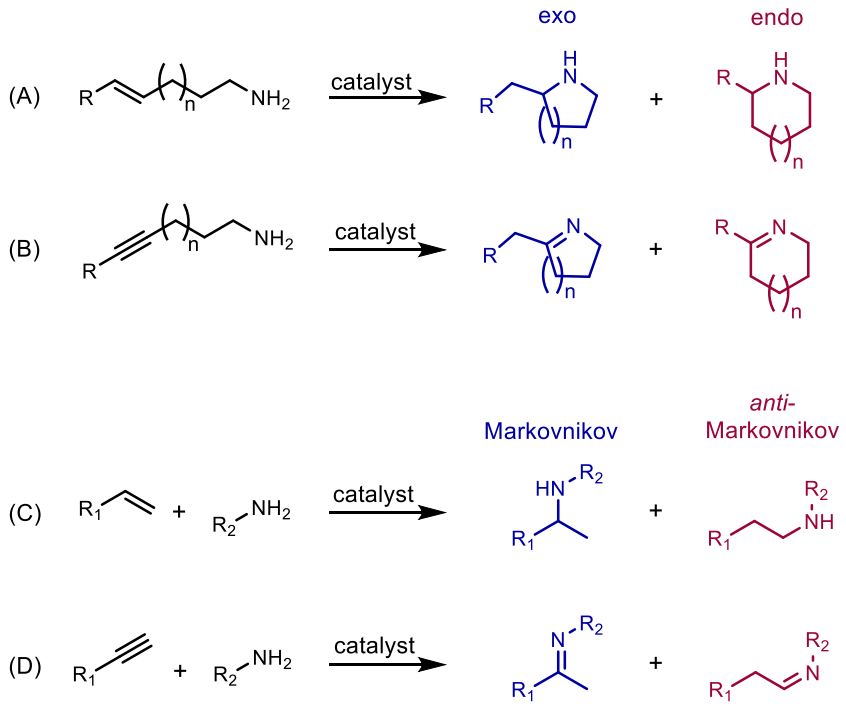


Scheme 1: Different possibilities of combining intramolecular hydroamination of alkynes (blue) with subsequent functionalisation steps (red). (A) Hydrophosphonylation, (B) Alkylation, (C) Hydrosilylation, (D) Hydrogenation.

Since this work is focused on alkylation and hydrophosphonylation, a more detailed introduction on those topics along with hydroamination will be given in the following sections. In the course of that some general information will be provided and the development of suitable catalytic systems, as well as their advances and throwbacks will be outlined.

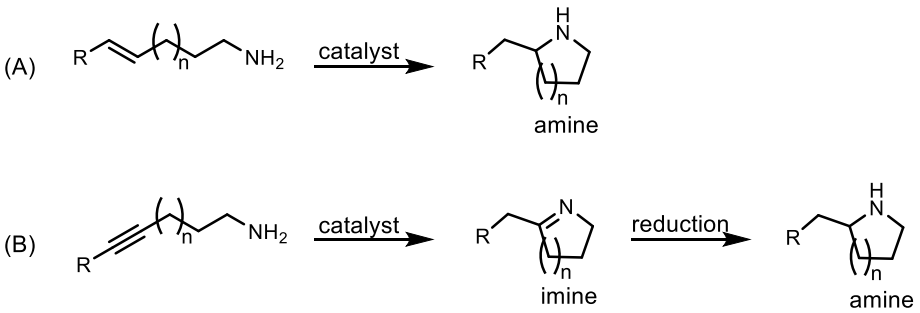
1.1. Hydroamination

The hydroamination of alkenes and alkynes leads to industrial and pharmaceutical valuable nitrogen containing compounds, *via* formation of a new carbon-nitrogen bond in a waste free and highly atom economical way.[6] The reaction can proceed in an intra- or intermolecular fashion and can lead to the exo and endo product, respectively to the Markovnikov and *anti*-Markovnikov product (Scheme 2). However, the formation of the endo and the *anti*-Markovnikov product can only be observed in exceptional cases.[11]



Scheme 2: Overview of catalysed hydroamination: (A) Intramolecular hydroamination of alkenes, (B) Intramolecular hydroamination of alkynes, (C) Intermolecular hydroamination of alkenes, (D) Intermolecular hydroamination of alkynes.[11]

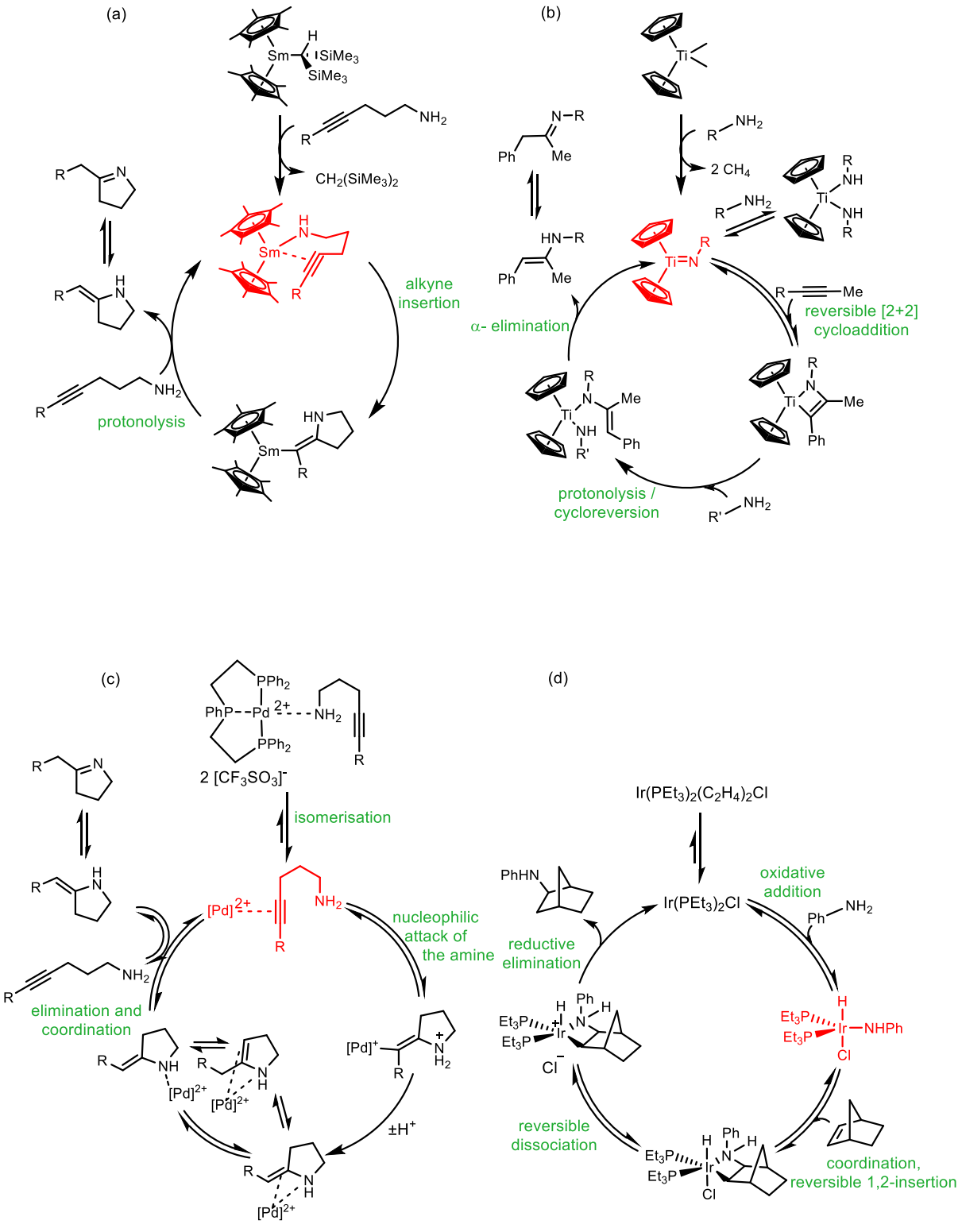
Due to the electrostatic repulsion between the electron lone pair at the nitrogen and the electron rich π-bond of the carbon-carbon multiple bond, a high energy barrier is to overcome in order to add amines to alkenes or alkynes. However, if one raises the reaction temperature to get over that barrier, the equilibrium of the reaction is shifted to the substrates, as hydroaminations have a negative reaction entropy in general.[12] In order to synthesise nitrogen containing compounds in high yields, different catalytic systems and reaction conditions were investigated.[6,13,14] A distinction must be made between the hydroamination of alkenes whereby secondary amines are generated and the hydroamination of alkynes which leads to quite reactive enamines and imines (Scheme 3).[14]



Scheme 3: Different products gained *via* hydroamination of alkenes (A) and alkynes (B).

Due to the higher reactivity and electron density of carbon-carbon triple bonds the hydroamination of alkynes is easier to perform. However, to obtain amines, it is necessary to add a subsequent reduction-step (Scheme 3B). This can be seen as a disadvantage of using alkynes as starting material, but on the other hand this provides an interesting advantage, because it offers the possibility to obtain functionalised nitrogen-containing compounds with a broad diversity within a one-pot-two step synthesis.[6,14]

Based on the great interest in these valuable nitrogen-containing compounds a variety of catalytic systems were investigated to overcome the high activation energy. In general, one can distinguish between two different possibilities of activation: On the one hand alkene or alkyne activation, on the other hand amine activation.[11,15] For example: alkali and alkaline-earth metals[16] or lanthanides[17] as catalytic moiety activate the amine by deprotonation. In the following they form a strongly nucleophilic amido species (e.g. Scheme 4a). Group IV metal catalysts[12,18] activate the amine to form an imido species (e.g. Scheme 4b). On the other hand, late transition metals[13,15] activate the unsaturated moiety *via* complexation (e.g. Scheme 4c) or in the case of them being electron-rich, N-H oxidative addition[20] takes place (e.g. Scheme 4d).



Scheme 4: Different forms of activation depending on the applied system. (a) Lanthanide catalyst,[17] (b) Group IV metal catalyst,[18] (c) Late transition metal catalyst,[15] (d) Electron rich late transition metal catalyst.[20]

In the following section a few examples for investigated catalytic systems are listed:

First of all, organolanthanide complexes were examined especially by Marks and coworkers. Amongst those, especially [$Cp^*_2SmCH(SiMe_3)_2$] (Figure 2a) provided good results for the intramolecular hydroamination of aromatic and aliphatic aminoalkynes *via* a four-centered transition state.[17,21]

Moreover, the working groups of Livinghouse and Lee showed that Group IV metals are suitable catalysts for the intramolecular hydroamination of aminoalkynes. The metal precursors [$Zr(NMe_2)_4$] and [$Ti(NMe_2)_4$] already delivered promising results for the cyclisation, which could be further improved by the variation of ligands.[19,22]

Besides Group IV metals, Livinghouse and Lee examined yttrium-metal precursors, such as [$Y(N(SiMe_3)_2)_3$], and found that they are efficient for intramolecular hydroaminations of primary aminoalkynes.[19] Utilising yttrium as central atom, even promising chiral catalysts (Figure 2b) for the enantioselective intermolecular hydroamination of alkenes were designed by Hultzsch *et al.*.[23]

Various late transition metals were tested as well. $HgCl_2$ was primarily used for intermolecular reactions of terminal alkyl- and arylalkynes with primary and secondary aromatic amines,[24] $Tl(OAc)_3$ for the reaction of phenylacetylene with primary and secondary amines.[25] These reactions were examined by Barluenga and coworkers, but due to the high toxicity of the used systems their application is not recommended. Apart from the mercury- and thallium- systems, many other late-transition metals, as for example copper ([$Cu(CH_3CN)_4$]PF_6) or palladium ([Pd(Triphos)][BF_4]$_2$) (Figure 2c), were explored for the intramolecular reaction of aminoalkynes for instance by Müller and coworkers.[15] In general, it can be said that they tolerate a larger variety of functional groups, since they show a lower affinity to oxygen than early transition metals, lanthanides or actinides.[14]

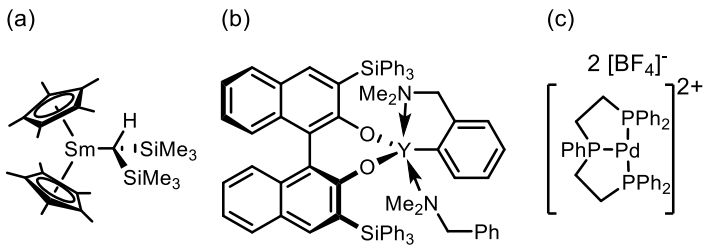


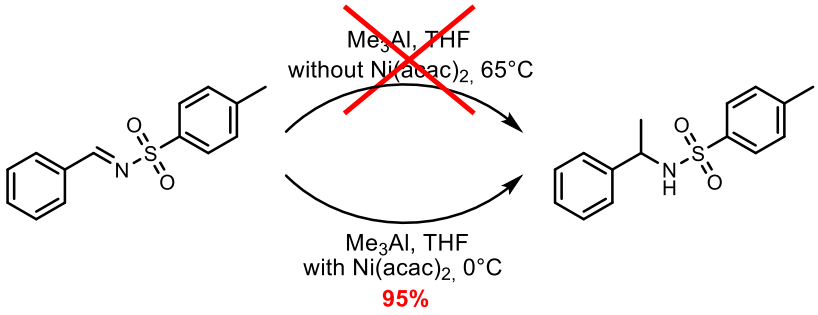
Figure 2: Catalysts used for Hydroaminations: (a) Samarium-based system investigated by Marks *et al.*[17,21], (b) Chiral catalyst for intermolecular hydroamination of alkenes investigated by the research group of Hultzsch[23], (c) Palladium catalyst with bis(diphenylphosphinoethyl)phenylphosphine as ligand used by Müller for the cyclisation of 6-aminohex-1-yne.[15]

1.2. Alkylation of Imines

As already mentioned in the previous sections, amino groups play an important role as substructures in drugs and natural products and as a consequence they are interesting building blocks for pharmaceuticals.[1,26] α-Chiral amines are very valuable substances in particular.[26] Apart from the hydroamination of alkenes, the addition of carbon nucleophiles to imines offers a promising approach for their synthesis.

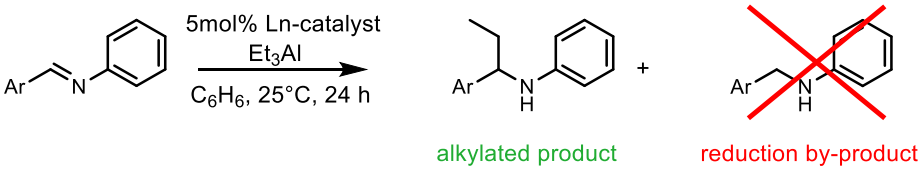
The reagents most commonly used for the addition of alkyl residues to imines are lithium and magnesium organyls. Based on their high reactivity, they lead to racemic product mixtures in general. In contrast, zinc or aluminium organyls hardly react without catalyst with the imine and therefore open the way towards enantioselective functionalisation.[27]
The inertness of dialkylzinc reagents can be explained by their sp-hybridised inert geometry and barely polarised alkyl-metal bond.[28] By using catalytic systems it is possible to add diethyl zinc or higher organyls to imines in an enantioselective fashion. Though, dimethyl zinc reagents still pose problems. This means high catalyst loadings (10 mol%) and a large excess (10-15 equiv.) of dimethyl zinc are necessary.[29]
Due to their tendency to react violently with water, aluminium organyls, especially those with low molecular weight, such as trimethyl aluminium, have been avoided for a relatively long period of time. However, they are commercially available at a cheap price as solutions in hydrocarbons which reduces their pyrophoricity significantly. Apart from the difficulty in their handling, trialkylalanes provide interesting properties: In contrast to other organometallic reagents, such as zinc organyls, the aluminium metal centre shows a high Lewis acidity and reduced Brønsted basicity. This opens the substrate range to more base sensitive substances and in some cases leads to other outcomes of the reaction. Moreover, the alkyl residues in organoaluminium reagents show a reduced nucleophilicity compared to alkyl zinc compounds, but are still strong enough for nucleophilic additions. Generally speaking, their reactivity is in between the one of lithium and zinc organyls. [27,30]

In the following part some different possibilities for the alkylation, which were used as basis of this thesis will be discussed:
The first attempt to alkylate imines by using alkyl alanes was published in 1998 by the research group around Fujisawa. They established a procedure for the addition of trimethylaluminium to aldehydes and ketones by using a nickel catalyst with phosphine ligands. Furthermore, the reaction of N-tosylbenzaldimine catalysed by $Ni(acac)_2$ was investigated and led to 95% of the methylated product, when no background reaction was observed at all (Scheme 5).[31]



Scheme 5: Alkylation of N-tosylbenzaldimine.[31]

Promising results were published for the lanthanide catalysed ethylation of Schiff bases of aromatic aldehydes and anilines by Blum and coworkers (Scheme 6, Table 1).[7]



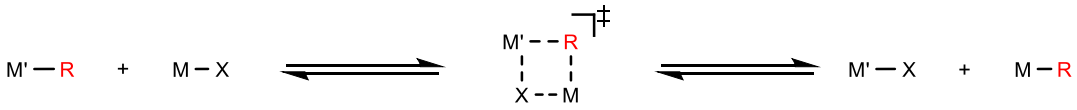
Scheme 6: Ethylation of aromatic imines promoted by lanthanides.[7]

Table 1: Ethylation of aromatic imines promoted by lanthanides.[7]

#	Ar	Catalyst	Yield [%]
1	C_6H_5	$[Eu(dpm)_3]$	73
2	C_6H_5	$[Eu(tfc)_3]$	55
3	C_6H_5	$[Yb(OTf)_3]$	29
4	C_6H_5	$[Pr(tfc)_3]$	11
5	4-OCH_3-C_6H_4	$[Eu(dpm)_3]$	41
6	4-Cl-C_6H_4	$[Eu(dpm)_3]$	82
7	4-CN-C_6H_4	$[Eu(dpm)_3]$	70
8	2-C_5H_4N	$[Eu(dpm)_3]$	99

The best results were gained with $[Eu(dpm)_3]$ as catalyst. For instance, the ethylation of N-Benzylidenamine led to 73% of the desired alkylated product and no reduction by-product at all (Scheme 6). Instead, 25% of starting material was recovered. As no background reaction was observed, there was enough space for enantioselective reactions using catalysts with chiral ligands. Based on these results, Blum *et al.* tested $[(+)\text{-}Eu(tfc)_3]$ and obtained the optically enriched α-Ethyl-4-methyl-N-phenyl-benzenemethanamine with an enantiomeric excess of 82% in 55% yield. Concerning the mechanism of the ethylation, it is

assumed that the reaction proceeds *via* an alkyl lanthanide intermediate which is formed by transmetalation with Et_3Al (Scheme 7).[7]



Scheme 7: General equation for the transmetalation *via* four-centred transition state.[32]

Another possibility is the formation of aluminate complexes. Me_3Al in particular is very prone to build rare-earth tetramethylaluminate complexes with trivalent rare-earth metal complexes (Figure 3).[33,34] This could also be possible for Et_3Al.

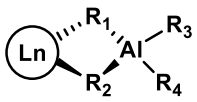
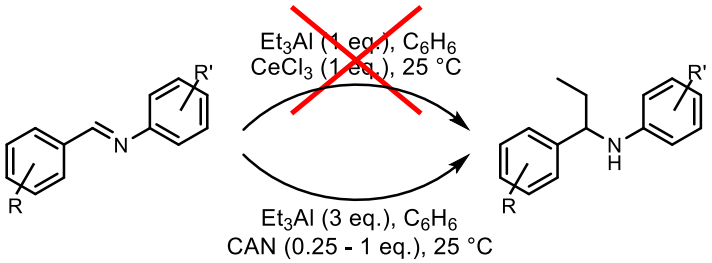


Figure 3: Rare-earth tetraalkylaluminate complex.[33]

The research group of Blum dealt with the ethylation of Schiff bases with triethylaluminium catalysed by cerium as well.[35] $CeCl_3$ was completely inactive. Ethylations were observed at room temperature only by applying Ce(IV) instead of Ce(III). In particular, good conversions (up to 99%) were achieved with cerium ammonium hexanitrate (CAN). However, the necessary quantities of CAN (0.25 to 1.0 equivalents) were very high and the best results were gained by using 3 equivalents of triethyl aluminium (Scheme 8).[35]

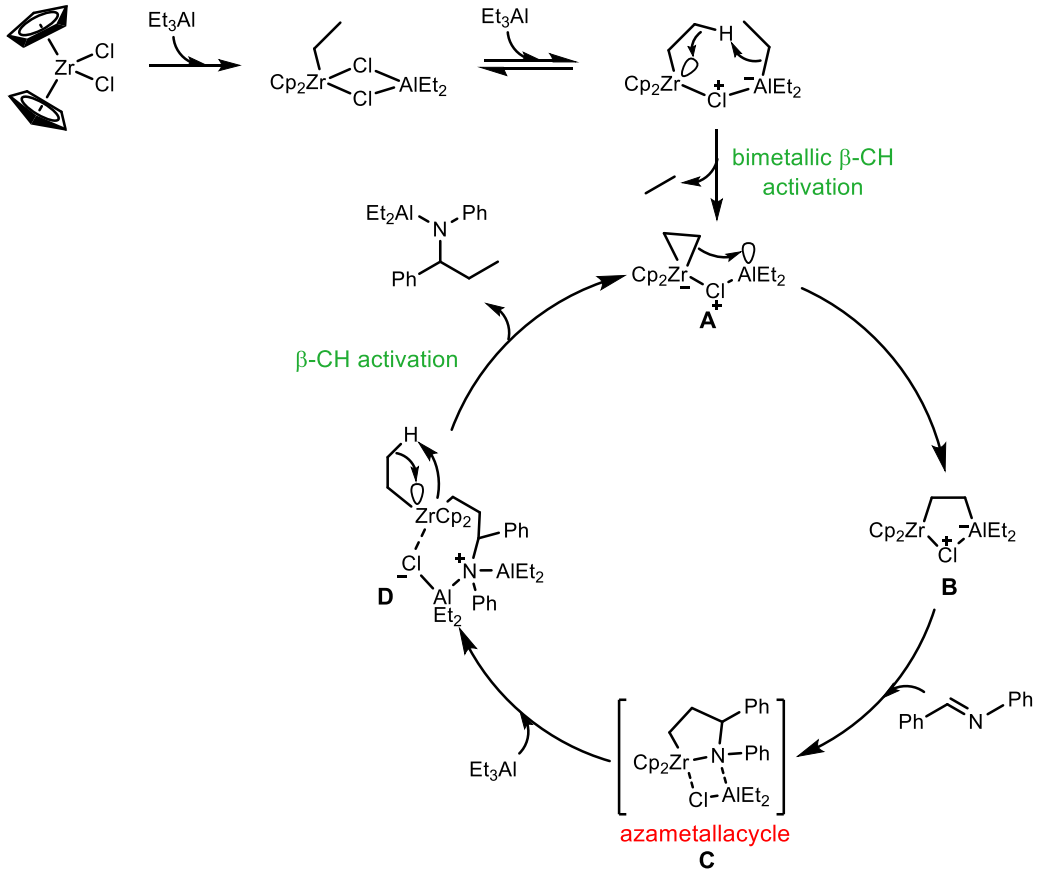


CAN = ceriumammonium hexanitrate

Scheme 8: Ethylation with CAN, investigated by Blum *et al*.[35]

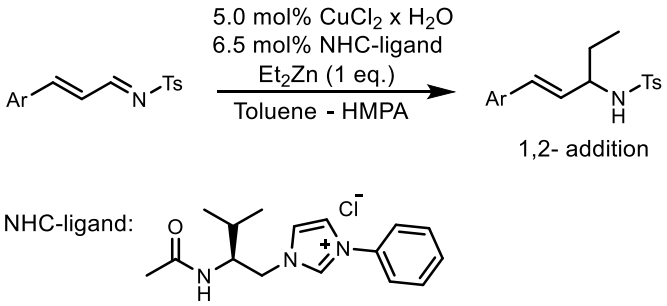
Promising results for the alkylation were also achieved with zirconium(IV)- compounds, which were investigated by the research group of Szymoniak.[36] They performed the ethylation of N-phenylbenzenamine by using 5 mol% of Cp_2ZrCl_2 in DCM at 25 °C and obtained 91% of desired product and no reduction of the imine was observed. However, using *n*-Bu_3Al as alkyldonor decreased the yield (~ 70%) as well as promoted the formation of the reduction by-product. Me_3Al did not lead to the alkylated product at all, which led to the exclusion of the direct acyclic addition mechanism. Instead, a cyclic mechanism was proposed (Scheme 9). In order to promote this catalytic cycle, two equivalents of aluminium reagent are necessary, The first step is the formation of **A** *via* bimetallic β-CH activation, followed by the subsequent generation of **B**,[37] which can react with the imine by formation of the azametallacycle **C**. A

subsequent reaction with Et_3Al leads to complex **D** and a second β-CH activation releases the alkylated product and regenerates complex **A**.[36]



Scheme 9: Proposed mechanism for the alkylation of aromatic aldimines with Et_3Al by using Cp_2ZrCl_2 as catalyst (intermediates not isolated).[36]

To name a current appilication of Et_2Zn as ethyldonor as well, a very interesting approach was developed by Ukaji *et al.* who used chiral NHC ligands and $CuCl_2$ to selective add Et_2Zn to the imine moiety of β-Aryl-α,β-unsaturated N-tosylaldimines (Scheme 10). The NHC ligand controls the chemoselecitivity whereas HMPA increases the yield and acts as efficient co-solvent to improve the enantioselectivity. Based on that they achieved 1,2-selective additions with an *ee* of up to 91%.[38]



Scheme 10: Stereoselective addition of diethyl zinc.[38]

1.3. Hydrophosphonylation of Imines

Hydrophosphonylation of imines provides cyclic and acyclic α-amino phosphonic acids (Figure 4). They are, as well as nitrogen containing compounds, important industrial and pharmaceutical substances.[10]

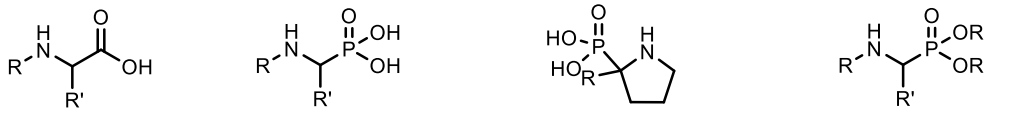


Figure 4: Comparison between different amino acid derivates.[10]

α-Amino phosphonic acids are valuable replacements of α-amino carboxylic acids, which are building blocks of proteins and peptides and therefore play an important role in many physiological processes.[39] Especially interesting in these peptide mimetics is their tetrahedral phosphorus group which is a transition state analogue of peptide hydrolysis. Hence, they can serve as inhibitors for peptidases and proteinases.[10,40] Moreover, they are part of haptens, catalytic antibodies and antibiotics.[39,41] An example for an antibacterial agent is alaphosphin (L-alanyl-L-1-aminoethylphosphonic acid).[39] It selectively inhibits the peptidoglycan biosynthesis in gram-negative as well as in gram-positive bacteria.[42] Only the (S,R)-diastereomer shows inhibitory activity. Therefore, the absolute configuration at the chiral carbon atom α to phosphorus is relevant for the biological activity (Figure 5).[39]

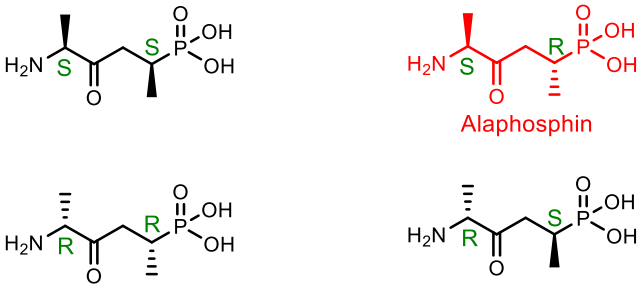
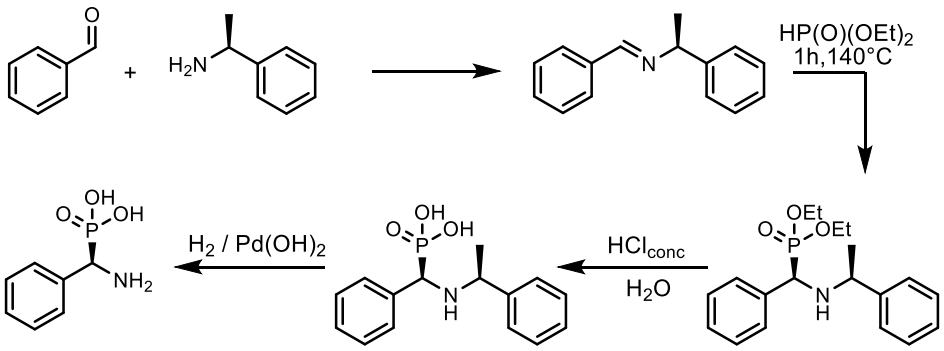


Figure 5: Four diastereomers of Alanyl-1-aminoethylphophonic acid.[39]

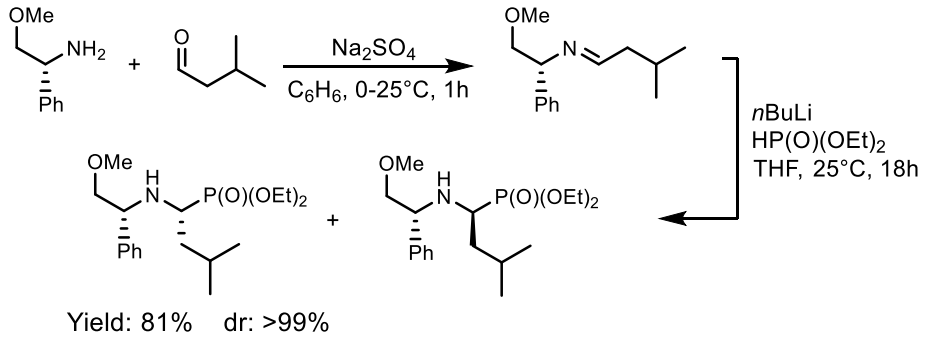
Most approaches for the synthesis of various α-amino phosphonic acids proceed *via* α-amino phosphonate diesters as intermediate. This can be explained by the fact that the resulting α-amino phosphonate diesters are soluble in organic and neutral aqueous media. This enables facile derivatisation of the amine and acid functionalities. Afterwards a conversion into the corresponding acids can be performed under acidic conditions.[39]

Based on the large number of application possibilities of amino phosphonate diesters, various synthetic strategies were investigated and developed. The first approach was published by Gilmore and Mc Bride by using enantiopure α-methylbenzylamine. However they did not disclose the yield and enantiomeric purity of the gained product (Scheme 11).[43]



Scheme 11: First enantioselective approach for the synthesis of amino phosphonic acids developed by Gilmore and Mc Bride: Diastereoselective addition to an imine starting either from (R)-(-)- or (S)-(-)-α-methylbenzylamine.[43]

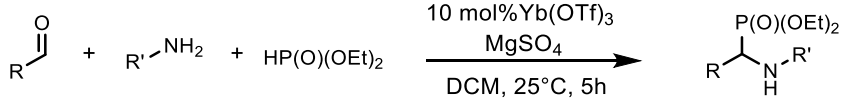
Another interesting approach, with enantiopure starting material was reported by Taylor *et al.* (Scheme 12).[39]



Scheme 12: Diastereoselective reaction tested by Taylor *et al.*[39]

*n*BuLi was used to deprotonate diethylphosphite in order to increase its nucleophilicity, so it could easily add to the imine. The reaction was tested with various aldehydes, whereby the example shown in Scheme 12 led to very good results with 81% of yield and a diasereoselectivity of 99%.

Catalysed one-pot syntheses of α-amino phosphonates starting from amines and aromatic or aliphatic aldehydes showed promising results as well. Huang and coworkers investigated ytterbium triflate as catalyst (Scheme 13).[40]



Scheme 13: One-pot synthesis using ytterbium triflate as catalyst.[40]

When chiral amines were applied they were able to obtain diastereoselectivities of up to 56%. The commercially available (S)-1-methoxy-2-phenylethylamine showed the best results (Figure 6).

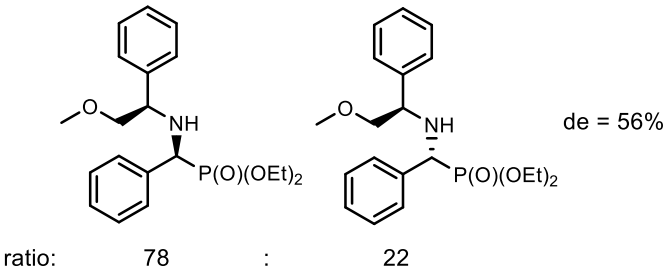
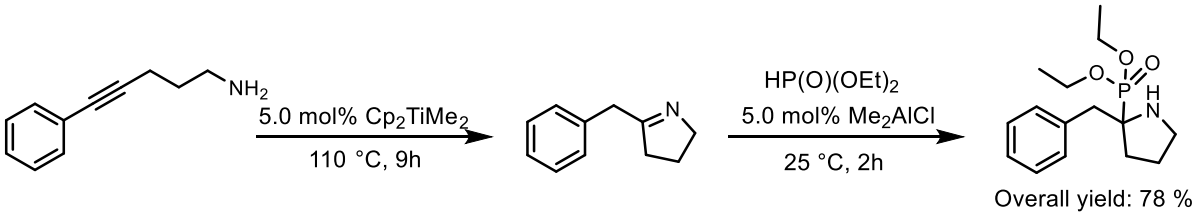


Figure 6: Example of the product distribution of optical active α-amino phosphonates originating from (S)-1-methoxy-2-phenylethylamine.[40]

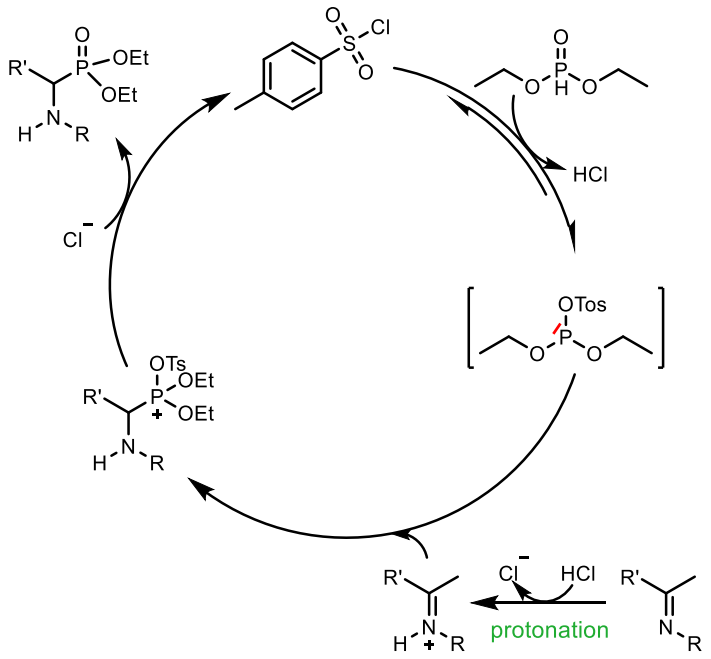
The coupling of these two reaction steps is made possible due to the fact that ytterbium triflate is stable in water. Since water is formed during the formation of the imine, only metal complexes which are stable in water are worth considering as catalyst for this one-pot-two-step synthesis. The catalysts, used for this master thesis, are highly sensitive to water and oxygen and it is not possible to apply them for the one-pot synthesis starting from aldehydes. However, there is the opportunity to apply these catalysts in a one-pot synthesis combining hydroamination and hydrophosphonylation. This idea originates from the work published by Doye and coworkers, who synthesised α-amino phosphonates starting from alkynes in a one-pot synthesis. They used Cp_2TiMe_2 as catalyst for the hydroamination and Me_2AlCl to catalyse the hydrophosphonylation (Scheme 14).[10]



Scheme 14: One-pot synthesis of α-amino phosphonates catalysed by Cp_2TiMe_2 and Me_2AlCl.[10]

They successfully combined inter- and intramolecular catalysis with hydrophosphonylation and gained cyclic and acyclic α-phosphonates without the formation of by-products.

Another convenient method for the hydrophosphonylation of imines was reported by Jafari and Kaboudin, who used 10 mol% tosyl chloride as efficient catalyst. In the course of the catalytic cycle it enables the nucleophilic attack of the phosphorous moiety to the imine by shifting the equilibrium between phosphonate and phosphite towards the latter and protonating the imine (Scheme 15).[44]



Scheme 15: Proposed reaction mechanism for the hydrophosphonylation catalysed by tosyl chloride.[44]

2. Scope of Work

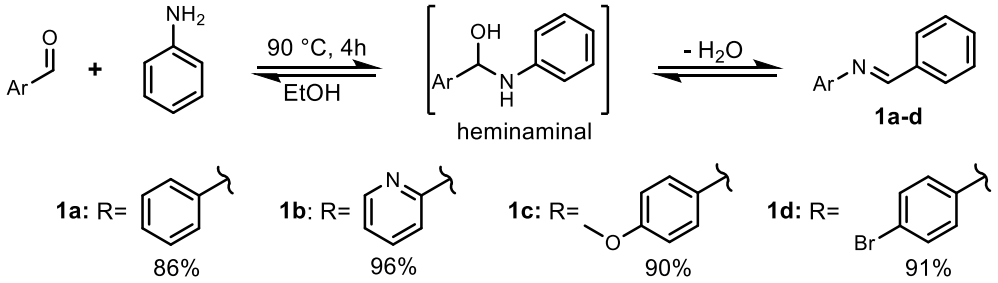
The aim of this master thesis was to develop a one-pot procedure in which one catalyst promotes the intramolecular hydroamination of aminoalkynes, as well as a subsequent functionalisation step of the imine-intermediate. Within this work, the alkylation and the hydrophosphonylation were selected for detailed investigation. In order to reach this goal, the first step was to optimise the reaction conditions, as well as finding a convenient method to monitor the reactions. For this, due to practical reasons, aldimines were used as starting material. In the course of this study, the influence of different, catalytic systems, substrates, temperatures and solvents to the outcome of the reaction was investigated. Moreover, another objective was to increase the enantioselectivity by applying chiral catalytic systems. Then, the established reaction conditions should be adapted to the functionalisation of cyclic imines gained *via* hydroamination to open the way towards convenient one-pot procedures (see Section 1, Scheme 1).

3. Results and Discussion

3.1. Substrate Synthesis

3.1.1. Aldimines

A very convenient way to synthesise aldimines is the condensation of an aldehyde and a primary amine *via* an hemiacetal as intermediate.[45] For the preparation of aromatic aldimines the procedure of Rosa *et al*.[46] was applied. For this purpose, it was sufficient to dissolve aniline with the corresponding aldehyde in EtOH and heat the reaction mixture for 4h to gain between 86-96% of the desired Schiff base (Scheme 16).

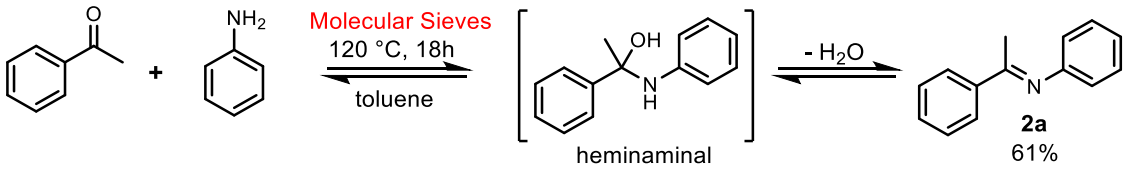


Scheme 16: Synthesis of aldimines.

To make sure that the products were completely pure for the subsequently conducted catalysis, the crude products were purified *via* flash chromatography and dried in *vacuo*, although the NMR-spectra did not show any impurities.

3.1.2. Ketimines

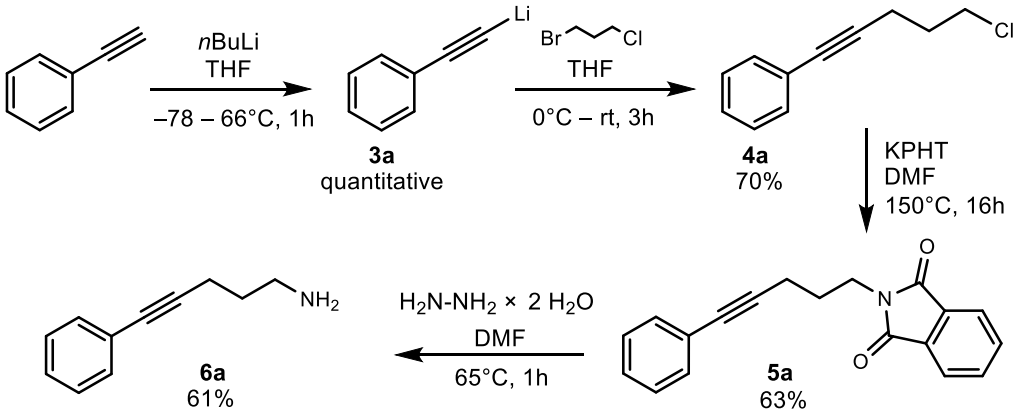
The condensation of acetophenon and aniline to gain the corresponding ketimine was not as convenient as the syntheses of aldimines. Under the same reaction conditions hardly any conversion was observed. Therefore, the procedure from Taguchi and Westheimer was utilised.[47] Molecular sieves and elevated reaction temperature were used to shift the equilibrium to the side of the imine (Scheme 17). Removing unreacted starting material by flash chromatography led to 61% of pure ketimine.



Scheme 17: Synthesis of ketimines.

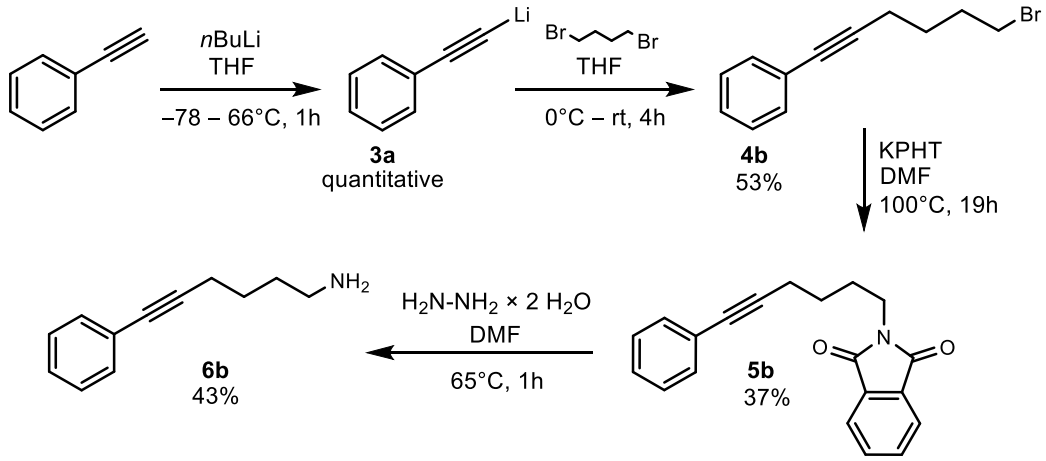
3.1.3. Alkyneamines

To synthesise alkyneamines, the 4-step procedure of Marks and coworkers was utilised.[21] To prepare 5-phenyl-4-pentyn-1-amine (**6a**), the first step was the quantitative lithiation of phenylacetylene followed by a nucleophilic substitution with 1-bromo-3-chloro-propane (S_N2). Then potassium phthalimide was used in a Gabriel synthesis to obtain intermediate **5a**. To liberate the alkyneamine from the phthalimide the intermediate was refluxed with hydrazine (Scheme 18). The overall yield of this multistep synthesis was 27% which is quite good in comparison with the overall yield of 16% of the literature.[21]



Scheme 18: Synthesis of 5-Phenyl-4-pentyn-1-amine.

The synthesis of 6-phenyl-5-hexyn-1-amine (**6b**) resembles the one for 5-phenyl-4-pentyn-1-amine. Just 1,4-dibromobutane was applied instead of 1-bromo-3-chloro-propane to generate the substrate with an additional carbon atom (Scheme 19). The yields of the individual reaction steps were lower in general, but the gained overall yield of 9% was sufficient for the following catalysis. In comparison, the overall yield in the literature was with 4% still lower.[21]

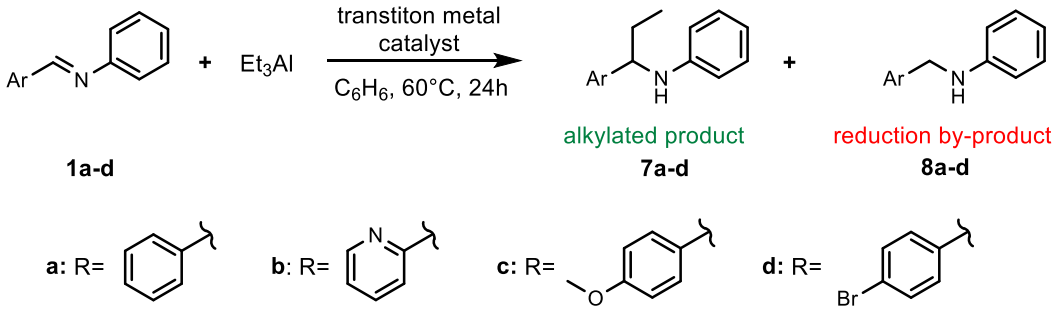


Scheme 19: Synthesis of 6-Phenyl-5-hexyn-1-amine.

For the purpose of applying these substrates for catalytic experiments, they were purified by flash chromatography and distilled from CaH_2.

3.2. Alkylation of Aldimines

In order to alkylate imines, the system of the working group of Blum,[7] who used triethylaluminium to alkylate aromatic aldimines (see Section 1.2, Scheme 6), was applied. Based on their promising results it was attempted to adapt these reaction conditions for the application of transition metal catalysts and precursors. However, the obtained results did not exceed the reactivity of the model system and the major problem was the formation of reduction by-product (Scheme 20).



Scheme 20: Alkylation of aldimines promoted by transition metal catalysts.

It is likely that the by-product is generated by Et_2AlH which reduces the imine double bond. Et_2AlH may originate from Et_3Al. It could either be remaining residues from the preparation or Et_3Al undergoes β-hydride elimination during the reaction.

To improve the outcome of the reaction, various reaction conditions were examined, which are summarised in the following section.

3.2.1. Suitable Catalytic Systems

Catalyst Screening

First of all, various catalysts and precursors were investigated. The table below clearly shows that $[Eu(dpm)_3]$ (Table 2, entry 1) gave the best results. The catalysis yielded 69% of alkylated product, though, in contrast to Blums reports, 14% of by-product were obtained as well. This leads to a ratio of 1 to 0.2 product to by-product. For the newly investigated catalysts $[Y(BDMA)_3]$ delivered the best yield with 44% and a ratio of 1 to 0.5 (Table 2, entry 4). $[La(N(SiHMe_2)_2)_3(THF)_2]$ led to the same amount of alkylated product, but to more by- product (Table 2, entry 5). In contrast to that, the niobium catalyst (Table 2, entry 6 vs. entry 8) did not enhance the reaction at all.

Table 2: Catalyst Screening

#	Catalyst	Yield Product* (**7a**) [%]	Yield By-product* (**8a**) [%]	Ratio (**7a** : **8a**)
1	$[Eu(dpm)_3]$	69	14	1.0 : 0.2
2	$[Y(N(SiMe_3)_2)_3]$	28	30	1.0 : 1.1
3	$[Y(N(SiHMe_2)_2)_3(THF)_2]$	34	52	1.0 : 1.0
4	$[Y(BDMA)_3]$	44	23	1.0 : 0.5
5	$[La(N(SiHMe_2)_2)_3(THF)_2]$	44	52	1.0 : 0.6
6	$[Nb(NMe_2)_5]$	9	25	1.0 : 2.8
7	$[Zr(NMe_2)_4]$	16	35	1.0 : 2.2
8	without catalyst	9	26	1.0 : 2.7

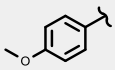
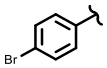
**Determined via HPLC by using a calibration curve*
*Reaction conditions: N-(Phenylmethylene)benzenamine (**1**) as substrate, 5 mol% catalyst, benzene, c = 0.2 M, 60 °C, 24 h.*

Substituent Screening

Secondly, the effect of different substituted starting materials on the outcome of reaction was analysed. The gained results are summarised in Table 3. It is obvious that the substrate with the pyridine residue led to the best yield. The reaction was quantitative and no by-product was observed *via* ^{1}H-NMR, which is outlined by the ratio of 1 to 0 (Table 3, entry 2). However, the uncatalysed background reaction was very fast. A complete conversion was observed within 10 min at –78 °C. Based on that, it would be very challenging to perform this reaction enantioselective. For the phenyl residue the alkylation yield was 44% within 24 h and a product to by-product ratio of 2 to 1 was obtained (Table 3, entry 1).

Moreover, the assumption of Blum[7] that additional functional groups at the phenyl moiety have further impact on the outcome of the reaction was confirmed. Electron-donating groups seem to debase the reaction and lead to an increase of by-product (Table 3, entry 3, methoxy-group), whereas electron-withdrawing groups seem improving (Table 3, entry 4, bromine-residue). However, since the bromine residue is not a classic example for an electron-withdrawing group, other substituents, such as nitrite or cyanide could be tested for further investigation.

Table 3: Residue Screening

#	Imine	Residue	Yield Product* (**7**) [%]	Yield By-product* (**8**) [%]	Ratio (**7** : **8**)
1	**1a**		44	23	1.0 : 0.5
2	**1b**		>99	<5	1.0 : 0.0
3	**1c**		35	37	1.0 : 1.2
4	**1d**		47	21	1.0 : 0.4

**Isolated Yield (after purification by column chromatography)*
Reaction conditions: different aldimines as substrates, 5 mol% [Y(BDMA)$_3$], benzene, c = 0.2 M, 60 °C, 24 h (entry 1,3,4) / 10 min (entry 2).

Dependence on Temperature

By testing at different temperatures, it was found that increasing reaction temperatures lead to increasing yields of product and by-product (Table 4). But between 60 °C and 110 °C the amount of by-product more than doubles, whereas the product only increases by 8%. Thus, the product : by-product ratio deteriorates (Table 4, entry 4 vs. entry 5). As between 0 and 25 °C hardly any product is formed, 60 °C are considered as the most suitable reaction temperature.

Table 4: Temperature Dependence of Reaction Yields

#	Temperature [°C]	Yield Product* (**7a**) [%]	Yield By-product* (**8a**) [%]	Ratio (**7a** : **8a**)
1	0	8	0	1.0 : 0.0
2	25	13	8	1.0 : 0.6
3	45	23	25	1.0 : 1.2
4	60	28	30	1.0 : 1.1
5	110	36	63	1.0 : 1.8

**Determined via HPLC by using a calibration curve*
*Reaction conditions: N-(Phenylmethylene)benzenamine (**1**) as substrate, 5 mol% [Y(N(SiMe$_3$)$_2$)$_3$], benzene, c = 0.2 M, 24 h.*

Solvent Screening

The screening of solvents nearly showed the same results for benzene and toluene (Table 5, entries 1 and 2), whereas the conversion decreased by using DCM (Table 4, entry 3). Hardly any reaction was observed when THF was applied as solvent (Table 4, entry 4), what can be explained by the coordination of THF to triethylaluminium. Due to these results benzene is considered as the best solvent for this catalysis.

Table 5: Solvent Screening

#	Solvent	Yield Product* (**7a**) [%]	Yield By-product* (**8a**) [%]	Ratio (**7a** : **8a**)
1	Benzene	28	30	1.0 : 1.1
2	Toluene	27	30	1.0 : 1.1
3	DCM	20	32	1.0 : 1.6
4	THF	9	3	1.0 : 0.3

**Determined via HPLC by using a calibration line*
*Reaction conditions: N-(Phenylmethylene)benzenamine (**1**) as substrate, 5 mol% [$Y(N(SiMe_3)_2)_3$], c = 0.2 M, 60 °C, 24 h.*

Minimisation of By-Product

Since the above listed screenings did not lead to the desired improvement, some other experiments to reduce the amount of by-product were performed:

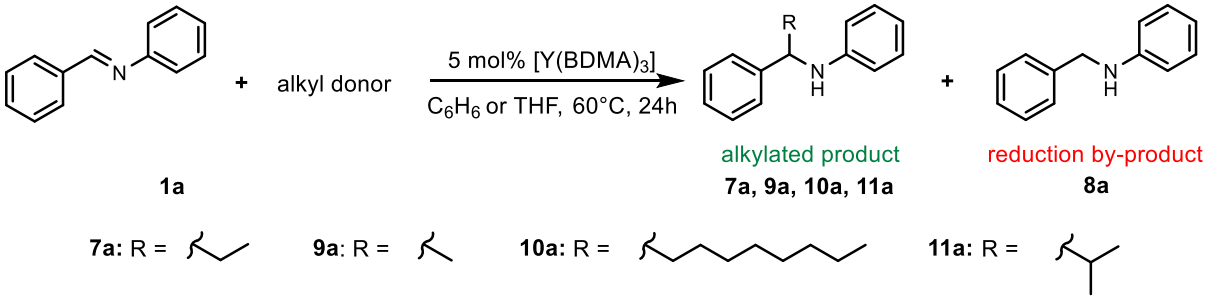
Different concentrations (0.17–1.70 M) were used, the ratio between imine and Et_3Al was varied (1:1–1:3), the order of addition was modified and the reaction was conducted under ethylene atmosphere instead of argon. However, none of these attempts led to an improvement (Table 6). Ethylene atmosphere (Table 6, entry 7 vs. entry 8) and increasing imine concentration (Table 6, entries 1-4) even decreased the yield. By applying more equivalents of Et_3Al the quantities of product and by-product remained the same. This indicates that the mechanism of this catalytic system might not go through a bimetallic β-CH activation proposed for Cp_2ZrCl_2 as catalytic moiety (Section 1.2, Scheme 9). It is more likely that it undergoes transmetalation what is proposed for [$Eu(dpm)_3$] promoted alkylations (Section 1.2, Scheme 7).

Table 6: Reduction of the amount of by-product

#		Yield Product* (**7a**) [%]	Yield By-product* (**8a**) [%]	Ratio (**7a** : **8a**)
1	0.17 M[a][c]	44	23	1.0 : 0.5
2	0.78 M[a][c]	43	22	1.0 : 0.5
3	1.40 M[a][c]	25	31	1.0 : 1.4
4	1.75 M[a][c]	19	44	1.0 : 2.3
5	imine : Et_3Al = 1 : 1[b][c][e]	13	8	1.0 : 0.6
6	imine : Et_3Al = 1 : 3[b][c][e]	12	7	1.0 : 0.6
7	argon atmosphere[b][d][e]	21	5	1.0 : 0.2
8	ethylene atmosphere[b][d][e]	12	8	1.0 : 0.7

**Determined via HPLC by using a calibration line*
*Reaction conditions: N-(Phenylmethylene)benzenamine (**1**) as substrate, 24 h.*
[a] reaction at 60 °C, [b] reaction at 25 °C, [c] 5mol% [$Y(N(SiMe_3)_2)_3$], [d] 5 mol% [$Y(BDMA)_3$], [e] c = 0.2 M

As next step other alkyl donors were tested (Scheme 21). For Oct_3Al, Me_3Al and Et_2Zn[38], hardly any conversion of the starting material was observed (Table 7, entries 1-3). Conversely, Grignard compounds[48] (EtMgCl and *i*PrMgCl·LiCl) increased the yield up to 64% of alkylated product. But the difference of 5-10% between background reaction and catalysed reaction was quite low (Table 7, entries 4 - 7). The last attempt concerning the alkylation was the application of another batch of Et_3Al, which even increased the quantity of by-product (Table 7, entry 8).



Scheme 21: Screening of different alkyl donors

Table 7: Screening of different alkyl donors

	Alkyl donor	Imine	Yield Product* [%]	Yield By-product* (**8a**) [%]	Ratio (**7a, 9a, 10a, 11a** : **8a**)
1	Oct_3Al[c]	**10a**	<5	<5	---
2	Me_3Al[c]	**9a**	11	<5	---
3	Et_2Zn[c]	**7a**	16	<5	---
4	EtMgBr[a][d]	**7a**	53	<5	---
5	EtMgBr[b][d]	**7a**	47	<5	---
6	*i*PrMgCl·LiCl[a][d]	**11a**	64	<5	---
7	*i*PrMgCl·LiCl[b][d]	**11a**	57	<5	---
8	neat Et_3Al[a]	**7a**	7	20	1.0 : 2.9

**Determined via HPLC by using a calibration line*
Reaction conditions: N-(Phenylmethylene)benzenamine as substrate, 24 h.
[a] 5 mol% [Y(BDMA)3], [b] reaction without catalyst, [c] C_6H_6 as solvent, [d] THF as solvent

Finally, it can be said that the formation of by-product is depending on the catalyst and [Eu(dpm)3] performed the best by far. Though, reaction temperature and the applied batch of Et_3Al show an additional impact. Among the newly investigated systems [Y(BDMA)3] as catalyst, Et_3Al as alkyldonor, benzene as solvent and 60 °C as reaction temperature under argon atmosphere are considered as the most suitable reaction conditions.

3.2.2. Evaluation

As already mentioned in Section 1.2., Et_3Al has the tendency to react violently with water. To simplify the handling a solution in toluene was utilised. Due to that fact it was not possible to monitor the reaction by NMR spectroscopy. The relatively large amount of toluene led to intense signals of the toluene in comparison with the signals of substrate or product. Hence, a method to observe the reaction *via* HPLC was developed. A chiral OD-H column with *i*PrOH : Heptane = 2 : 98 (0.5 mL/min, 28 bar, 20 °C) was utilised. To determine the conversion a calibration curve was generated. For this purpose, different ratios of substrate and product were measured (Figure 7).

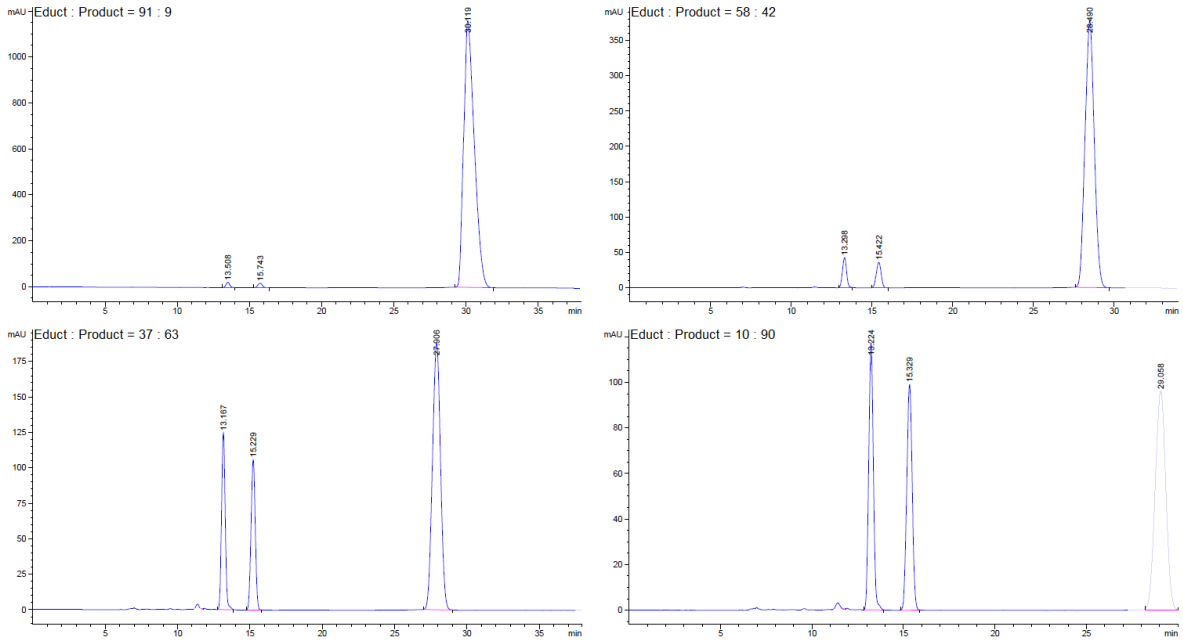


Figure 7: Example of HPLC measurements of substrate-product mixtures to set up a calibration line.

The peaks at 13 and 15 min represent the two enantiomers of the product, whereas the peak at 28 min comes from the substrate. It is clearly evident that the substrate has a much stronger UV-absorption at 280 nm. This can be explained by the imine double bond which leads to a completely conjugated system. In contrast to that, the product, a secondary amine, only has two isolated phenyl residues.

In order to set up a linear calibration curve, the ratios of amount and area were plotted against each other (Figure 8, detailed data see Table 8). Unless otherwise noted, the resulting linear equation was used for the determination of the conversion of all alkylations.

Table 8: Data used to set up the calibration line

Substrate		Product		Ratio	
$Amount_{sub}$ [mol%]	$Area_{sub}$ [%]	$Amount_{pro}$ [mol%]	$Area_{pro}$ [%]	$Area_{sub}$ / $Area_{pro}$ []	$Amount_{sub}$ / $Amount_{pro}$ []
91,29	98,62	8,71	1,38	71,40	10,48
85,77	97,47	14,23	2,53	38,52	6,03
75,02	95,32	24,98	4,68	20,38	3,00
69,95	93,94	30,05	6,06	15,50	2,33
63,36	91,66	36,64	8,34	11,00	1,73
60,85	90,93	39,15	9,07	10,02	1,55
39,31	82,85	60,69	17,15	4,83	0,65
20,21	63,87	79,79	36,13	1,77	0,25

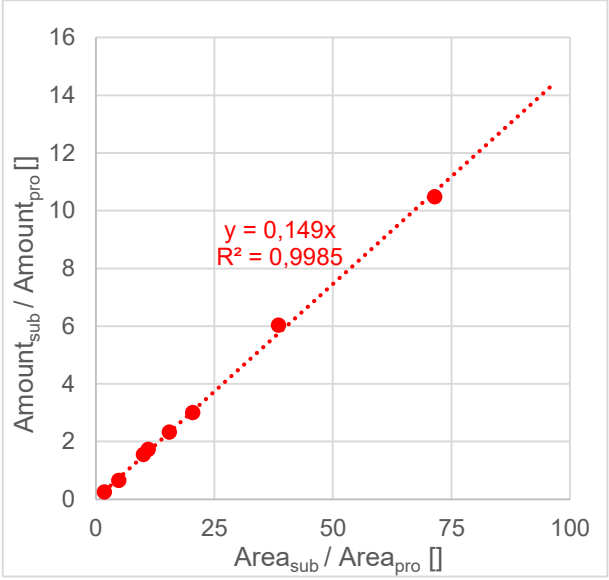


Figure 8: Linear calibration curve.

By applying this calibration curve the conversion into reduction by-product could be determined as well. The by-product has the same aromatic system and therefore the same UV-absorption at 280 nm. Thus, the ratio between by-product to substrate is the same as for product to substrate which was proved by HPLC measurements. The only difference is the retention time with 34 min (Figure 9).

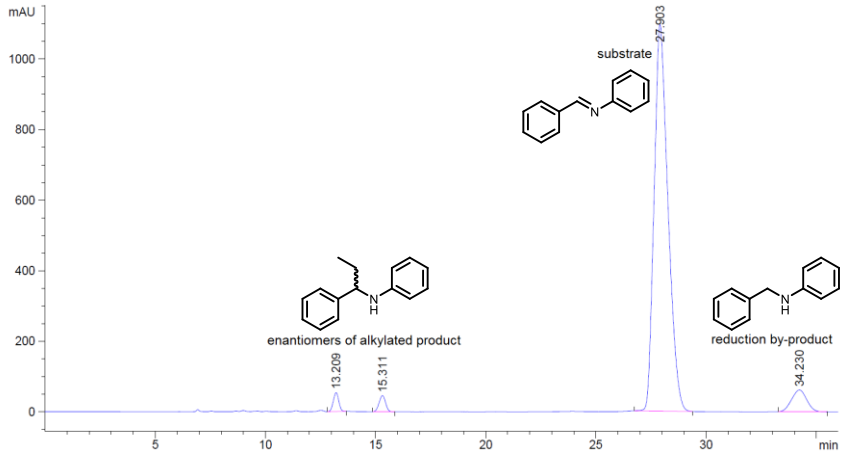


Figure 9: Retention times of substrate, alkylation product and reduction by-product.

Based on that, the following formulas were used to determine the conversion into product and by-product:

$$x = \frac{Area_{substrate}}{Area_{product} + Area_{by\text{-}product}}$$

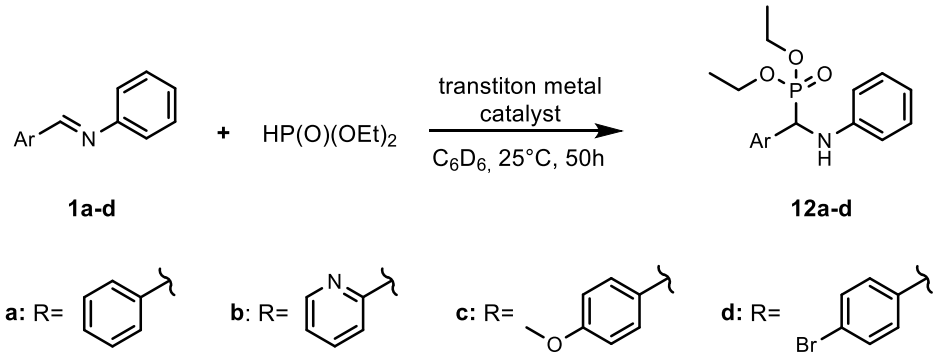
$$Conversion_{overall} = \frac{100}{1 + (0{,}149x)}$$

$$Conversion_{product} = \frac{Area_{product}}{Area_{product} + Area_{by\text{-}product}} \cdot Conversion_{overall}$$

$$Conversion_{by\text{-}product} = \frac{Area_{by\text{-}product}}{Area_{by\text{-}product} + Area_{product}} \cdot Conversion_{overall}$$

3.3. Hydrophosphonylation of Aldimines

The next goal was the hydrophosphonylation of aldimines. For this purpose, diethyl-phosphite was applied as reagent and benzene as solvent (Scheme 22).



Scheme 22: Transition metal catalysed hydrophosphonylation of aldimines.

In general, it can be said that the results were much more promising than for the alkylation and no by-product was formed at all. Detailed reaction conditions and results are listed in the following Section (3.3.1.).

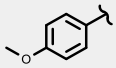
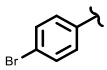
3.3.1. Catalyst and Substrate Screening

The metal precursor [$Y(BDMA)_3$] is quite suitable to catalyse the hydrophoshponylation of aldimines (Table 9, entry 1c). The substrate with the pyridine residue led to the highest conversion again, and in this case no background reaction was observed (Table 9, entry 2), supporting the presumption that there is a possibility to perform this reaction with high enantioselectivity. In contrast to that, the other substrates showed a relatively large percentage of background reaction. Especially for the substrate with the unsubstituted phenyl residue the difference between catalysed and background reaction was really low (Table 9, entries 1c and 1d).

It was tried to reduce the reaction time of 50 h at 25 °C by increasing the reaction temperature to 60 °C. Above all, this led to an increase of background reaction.

As with the alkylation, the methoxy-group led to a slightly decrease of yield, whereas the electron-withdrawing bromine-residue significantly improved the outcome of the reaction (Table 9, entry 3 vs. entry 4).

Table 9: Catalyst and Substrate Screening

		Imine	Residue	Catalyst	Yield product* (**12**) [%]
1	a	**1a**		[Y(N(SiMe$_3$)$_2$)$_3$]	30
	b			[Y(N(SiHMe$_2$)$_2$)$_3$(THF)$_2$]	51
	c			[Y(BDMA)$_3$]	75
	d			---	49
2	a	**1b**		[Y(BDMA)$_3$]	>99
	b			---	<5
3	a	**1c**		[Y(BDMA)$_3$]	71
	b			---	25
4	a	**1d**		[Y(BDMA)$_3$]	92
	b			---	36

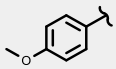
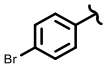
**Determined via ^{1}H-NMR spectroscopy by using hexamethylbenzene as internal standard*
Reaction conditions: 5 mol% catalyst, benzene, c = 0.2 M, 25 °C, 50 h.

3.3.2. Enantioselective Catalysis

In order to perform this hydrophosphonylation in an enantioselective fashion, the chiral catalyst [Y((S)-binol-SiPh$_3$)(o-C$_6$H$_4$CH$_2$NMe$_2$)(Me$_2$NCH$_2$Ph)] (Figure 10) was applied. This binaphtholate complex already showed good results for hydroaminations and can be prepared by arene elimination starting from [Y(BDMA)$_3$].[23,49] First of all, this catalyst obviously increased the conversion. An improvement was observed in particular for the substrate with the phenyl residue (Table 10, entry 1 vs. Table 9, entry 1c) and the one with the additional methoxy-functionality (Table 10, entry 3 vs. Table 9, entry 3a). Thus, for all substrates yields of more than 90% were achieved.

For the starting material with the pyridine residue (Table 10, entry 2) hardly any enantioselectivity was observed, whereas in particular for the one with the phenyl residue (Table 10, entry 1) a quite good enantiomeric excess of 74% was obtained. For the two other substrates (Table 10, entries 3 and 4) moderate to good enantioselectivities were achieved as well. In order to try to explain the high *ee* despite the large amount of background reaction, the reaction was conducted without catalyst, but with Et$_3$N as additive. After 100 h of reaction time, even after heating the mixture to 150 °C no conversion of the starting material was observed. Hence, it is likely that the basicity of Et$_3$N (pK_b~3.3) and the catalyst (pK_b(BDMA)~5.2) supress the background reaction and therefore enable the rather high enantioselectivities. Moreover, this explains that no background reaction was observed for the substrate with the pyridine residue (Table 9, entry 2b), which shows a significant basicity as well. The low *ee* for this substrate may be due to a different binding of the substrate to the catalyst because of the additional electron donor nitrogen atom.

Table 10: Enantioselective Hydrophosphonylation

	Residue	Yield product* (**12**) [%]	*ee*** *[%]*
1		91	74
2		>99	5
3		93	44
4		96	68

**Determined via ^{1}H-NMR spectroscopy by using hexamethyl-benzene as internal standard*
***Determined via HPLC using a chrial OD-H column*
Reaction conditions:
5 mol% [Y((S)-binol-SiPh$_3$)(o-C$_6$H$_4$CH$_2$NMe$_2$) (Me$_2$NCH$_2$Ph)],
c = 0.2 M, benzene, 25 °C, 50 h.

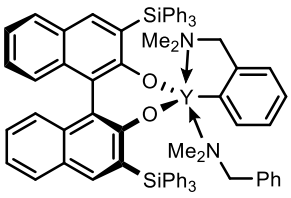
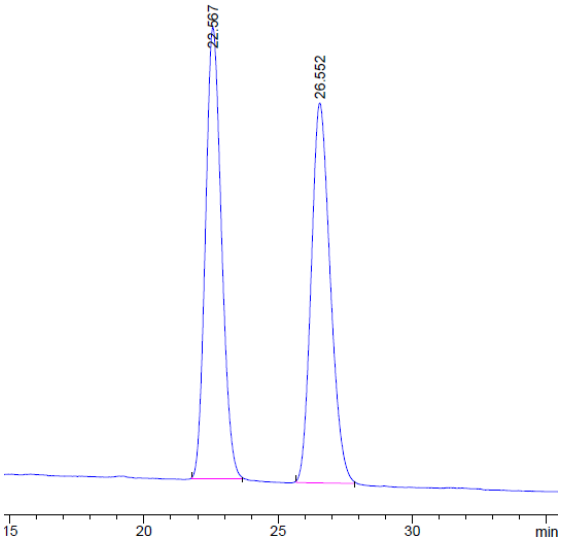
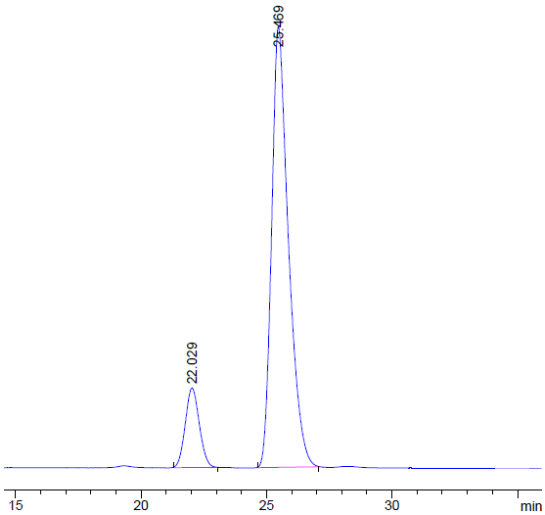


Figure 10: Chiral catalyst.

The enantiomeric excess was determined *via* HPLC using a chiral OD-H column. In the following figure an example of the different distribution of the two enantiomers is shown. In the chromatogram of the racemic mixture on the left side (Figure 11a) the areas of both peaks are nearly the same whereas on the right side (Figure 11b) a significant difference is visible.



(a)



(b)

Figure 11: Separation of the two enantiomers gained after hydrophosphonylation
(a) Reaction with [Y(BDMA)$_3$] as catalyst
(b) Reaction with [Y((S)-binol-SiPh$_3$)(o-C$_6$H$_4$CH$_2$NMe$_2$)(Me$_2$NCH$_2$Ph)] as catalyst.

3.3.3. Evaluation

In contrast to the alkylation, the hydrophosphonylation could be monitored *via* ^{1}H-NMR spectroscopy. The NMR spectrum changes during the reaction (Figure 12). The singlet at 2.1 ppm originates from the internal standard hexamethylbenzene. To determine the conversion, the vanishing aromatic proton of the starting material at 8.1 ppm was considered in relation to the internal standard.

Furthermore, the characteristic peaks of the product are clearly visible. The broad singlet at 5.7 ppm comes from the proton at the nitrogen atom, and the doublet of doublet originates from the tertiary carbon next to the nitrogen and the phosphorus atom.

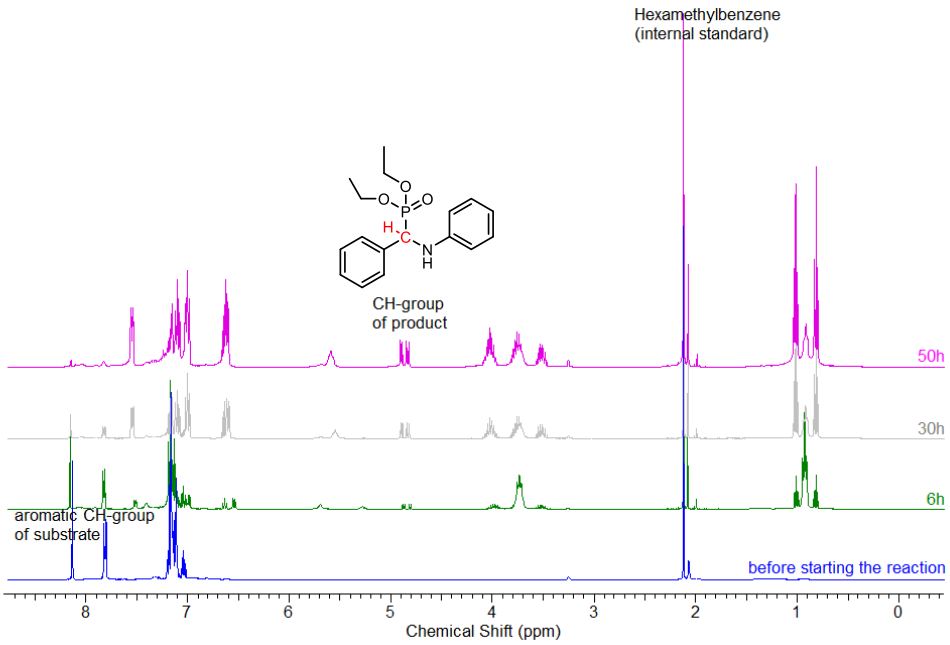
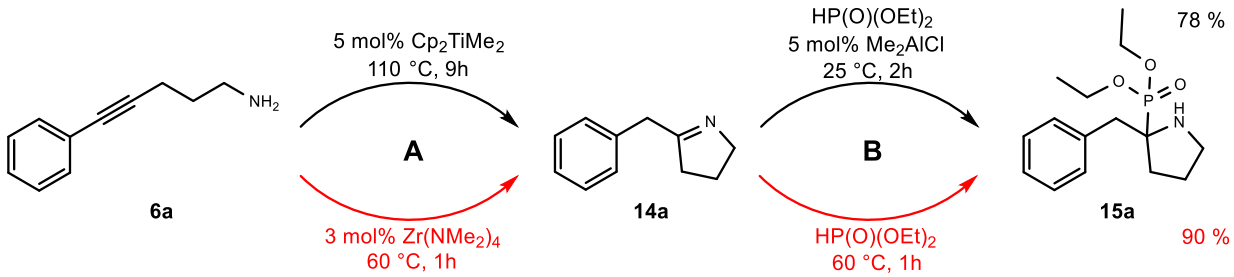


Figure 12: Monitoring of the hydrophosphonylation of aldimines *via* ^{1}H-NMR spectroscopy.

3.4. One-Pot Synthesis of Amino Phosphonates

3.4.1. Suitable Catalytic Systems

After the successful hydrophosphonylation of aldimines, it was planned to apply the established reaction conditions to imines which were obtained *via* hydroamination. In course of this, the idea of the research group of Doye[10] was adapted. Doye used 5 mol% Cp_2TiMe_2 as catalyst for the hydroamination (**A**) and 5mol% Me_2AlCl to catalyse the hydrophosphonylation (**B**), which yielded 78% of the cyclic α-amino phosphonates in a one-pot-two-steps synthesis (Scheme 23, black).



Scheme 23: One-pot-two-step catalysis to generate α-amino phosphonates.

The aim was to perform these two reaction sequences with just one catalyst. Various catalytic systems were tested (Table 11), whereas the zirconium precursor $[Zr(NMe_2)_4]$ was the most suitable one (Table 11, entry 6). A complete conversion was observed within 2 h by using 3 mol% of the catalyst, whereby each reaction step took 1 h. After workup and purification 90% of α-amino phosphonate was obtained (Scheme 23, red). No background reaction took place for the first step. Within the second step 23% of substrate were converted without catalyst (Table 11, entry 1). In contrast to the zirconium catalyst, the other ones based on yttrium or lanthanum were not able to catalyse both reaction steps as quickly and the observed yields were much lower (Table 11, entries 2-5).

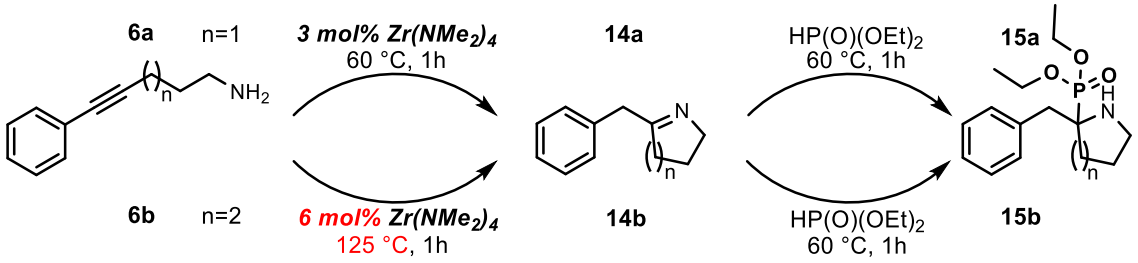
Table 11: Investigation of suitable catalyst for both reaction sequences

	Catalyst	Reaction Conditions				Yield*		
		Loading	Temperature	Time [h]		A	B	Overall
		[mol%]	[mol%]	A	B	[%]	[%]	[%]
1	---	---	60	---	18	---	23[a]	---
2	$[Y(N(SiMe_3)_2)_3]$	3	60	30	18	94	61	57
3	$[Y(N(SiHMe_2)_2)_3(THF)_2]]$	3	60	18	18	>99	62	61
4	$[Y(BDMA)_3]$	3	60	---	17	---	41[a]	---
5	$[La(N(SiHMe_2)_2)_3(THF)_2]]$	3	60	20	20	>99	35	35
6	$[Zr(NMe_2)_4)]$	3	60	1	1	>99	>99	>99

** Determined via ^{1}H-NMR spectroscopy by using hexamethylbenzene as internal standard Reaction conditions: d_6-benzene as solvent.*

[a] To determine the conversion of reaction B, the imine indermediate was formed by using $[Zr(NMe_2)_4)]$ as catalyst. After completion of the first reaction sequence, the catalyst was removed via filtration over silica. Then reaction B was performed without catalyst or by applying $[Y(BDMA)_3]$ as catalyst.

Besides, an attempt was made to apply these conditions to form a six-membered ring. This one-pot-two-step synthesis was carried out successful, though 6 mol% of catalyst and a higher reaction temperature were necessary (Scheme 24).



Scheme 24: Formation of 5- and 6-membered cyclic α-amino phosphonates.

3.4.2. Formation of By-product

After separation of the two enantiomers *via* analytical HPLC with a chiral column, instead of the expected two peaks three peaks were observed using the UV detector at 254 nm (Figure 13). The two outer peaks originate from the two enantiomers, but the third one in the middle could not be explained.

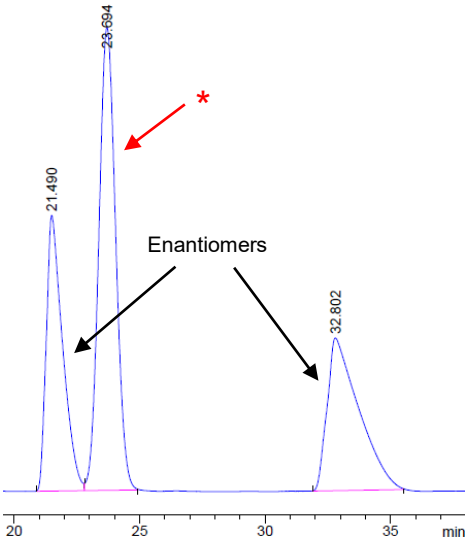


Figure 13: By-product (*) with a strong UV absorption at 254nm and a retention time of 23.7 min

In order to purify the product, the reaction was scaled up to 1 mmol (160 mg) and the peaks were separated by column chromatography. This resulted in 90% of the pure 5-membered cyclic α-amino phosphonate. The peak in the middle led to hardly visible quantities. That is why it was not possible to record a proper NMR-spectrum of the by-product. Despite the low quantities, the UV-peak was quite high, which indicates a strongly conjugated system. Analysis *via* HPLC-MS revealed that this peak has the same molecular mass (m/z 160.1118) as the substrate and the intermediate. However, these two were excluded since they have different retention times than the questionable peak. The proton NMR spectrum of the impure

product showed an additional tiny peak at 5.8 ppm (Figure 14, marked in red; for comparison with the pure product see Section 6.4.2, Sup. 30). Hence, it is assumed that the peak in the HPLC-chromatogram comes from the corresponding enamine (Figure 15).

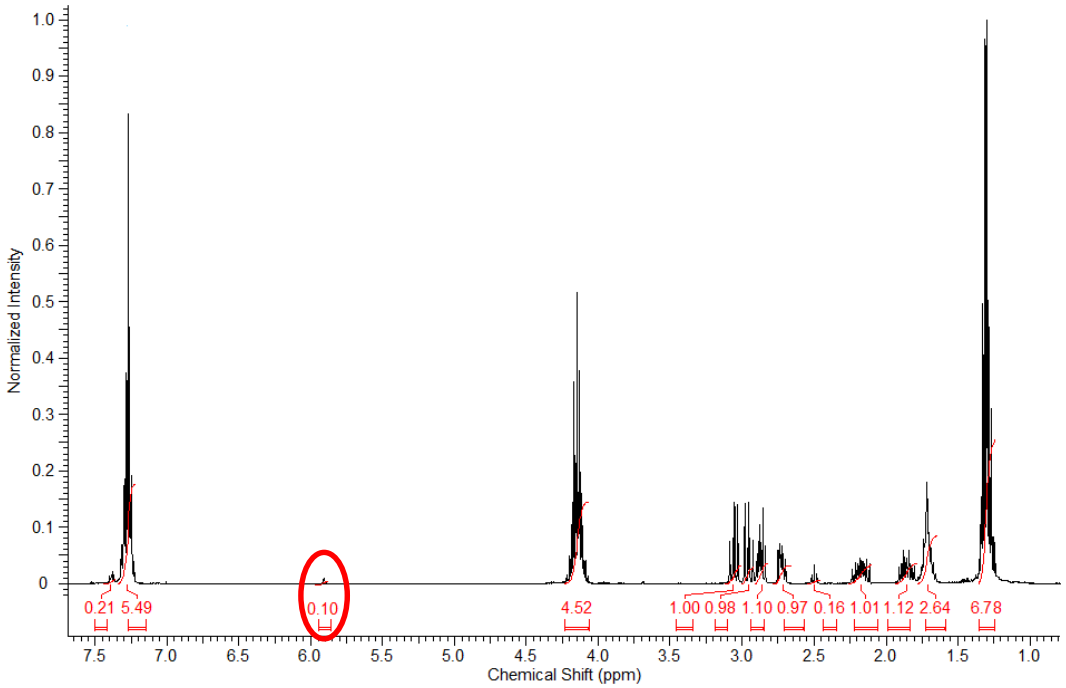


Figure 14: NMR spectrum of impure product with additional peak at 5.8 ppm.

The enamine has a highly conjugated system and the same mass as substrate and intermediate. This presumption is not definitely verifiable because there is no NMR-data of the enamine available. However, the spectrum calculated with ChemBioDraw Ultra 14.0 is suitable.

Interestingly the peak could not be observed after the first reaction step, only after adding diethylphosphite (pK_a=13.5). This leads to the assumption that it possibly shifts the equilibrium a little bit towards the side of the enamine (Figure 15). The new double bond is conjugated with the double bond of the phenyl residue, which leads to further stabilisation. Further investigations showed that the addition of HCl (pK_a=–6.0), H_3PO_4 (pK_a=2.1) or Na_2HPO_4 (pK_a=12.3) to the pure imine do not shift the equilibrium towards the side of the enamine.

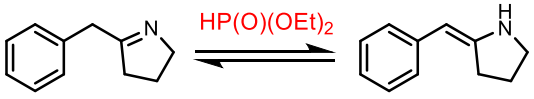


Figure 15: Tautomeric shift between imine and enamine.

For the reaction with aldimines no by-product was observed at all. In this case there is no possibility for the tautomeric shift. Two publications[50,51] reported the observation of the

enamine as main- or by-product as well, dependent on the applied substrate and catalytic system. However, they do not provide any NMR spectroscopic data.

Due to the fact that the yield after purification was quite high and it was possible to purify the product no further analyses on this topic were conducted.

3.4.3. Enantioselective Catalysis

To conduct the catalysis enantioselectively by the chiral catalyst [Y((S)-binol-$SiPh_3$)(o-$C_6H_4CH_2NMe_2$)(Me_2NCH_2Ph)] (Figure 10) was applied again. This catalyst was already used for the intermolecular hydroamination of alkenes[23] and showed good results for the hydrophosphonylation of the aldimines (Section 3.3.2).

Unfortunately, this attempt was not very successful. 10 mol% of catalyst, 125 °C and 4 h of reaction time were necessary to complete the hydroamination of 5-Phenyl-4-pentyn-1-amine. Additional 1 h was required after the addition of diethylphosphite to gain 76% of phosphonylated product, but without any enantioselectivity. Further attempts to increase the enantiomeric excess by decreasing the temperature only led to an extension of reaction time. It is likely that one of the residues has to be sterically more demanding to improve the enantioselectivity. However, there is the restriction, that the CH_2-group (Figure 16, marked in red) is necessary, to enable the hydroamination.

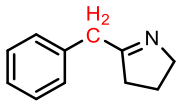
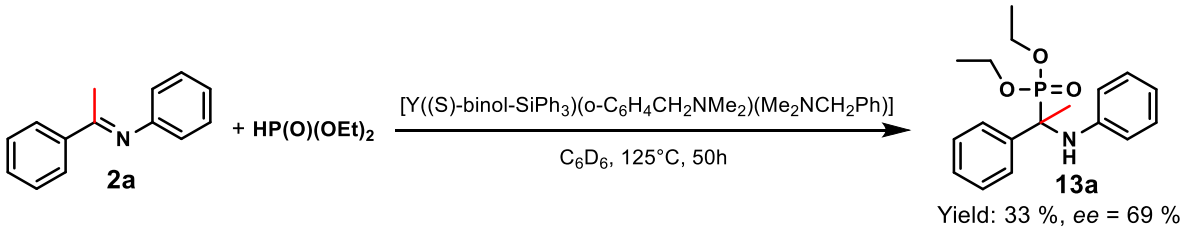


Figure 16: Sterically demanding functional groups to inrease the enantioselectivity.

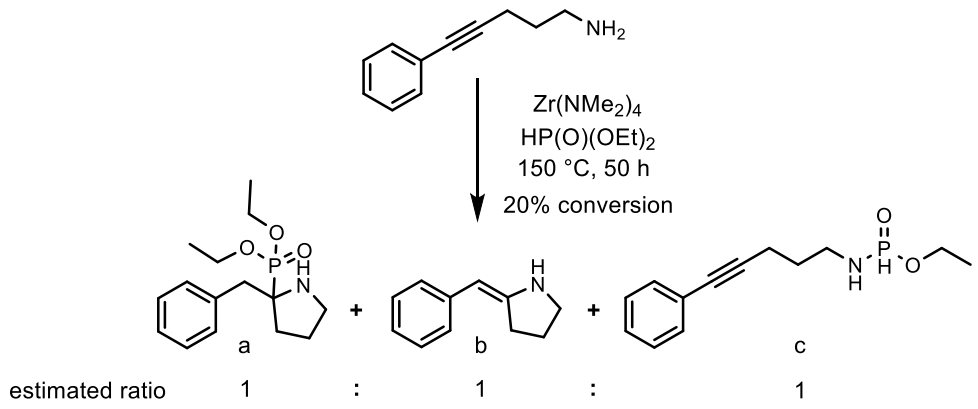
As initial attempt into more demanding substrates, but the last of this master thesis, a ketimine was synthesised and used as starting material for hydrophosphonylation (Scheme 25). But, by applying the established reaction conditions only 8% of desired product was observed. For that reason, the reaction was concentrated from 0.2 M to neat which led to an increase in yield to 33%. It can be said that the ketimine is too sterically demanding and therefore cannot undergo hydrophosphonylation quantitatively. Moreover, applying the chiral catalyst led to 69% *ee*. That means nearly the same compared to the aldimine.



Scheme 25: Hydrophosphonylation of a ketimine.

3.4.4. One-Pot-One-Step Synthesis

Another attempt was to carry out the one-pot-two-step synthesis as a one-pot-one-step synthesis. This means alkyneamine, diethylphosphite and catalyst were directly combined in the beginning and stirred altogether. Unfortunately, this attempt did not lead to the α-amino-phosphonate. Even after 50 h at 150 °C only 20% of substrate were converted. A product mixture was obtained (Scheme 26).

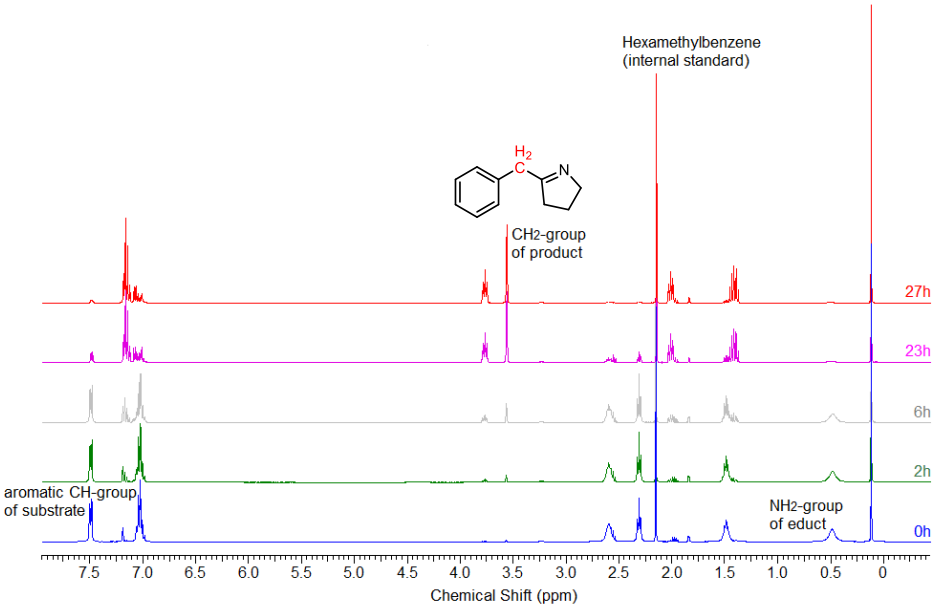


Scheme 26: Product mixture obtained by a one-pot-one-step catalysis

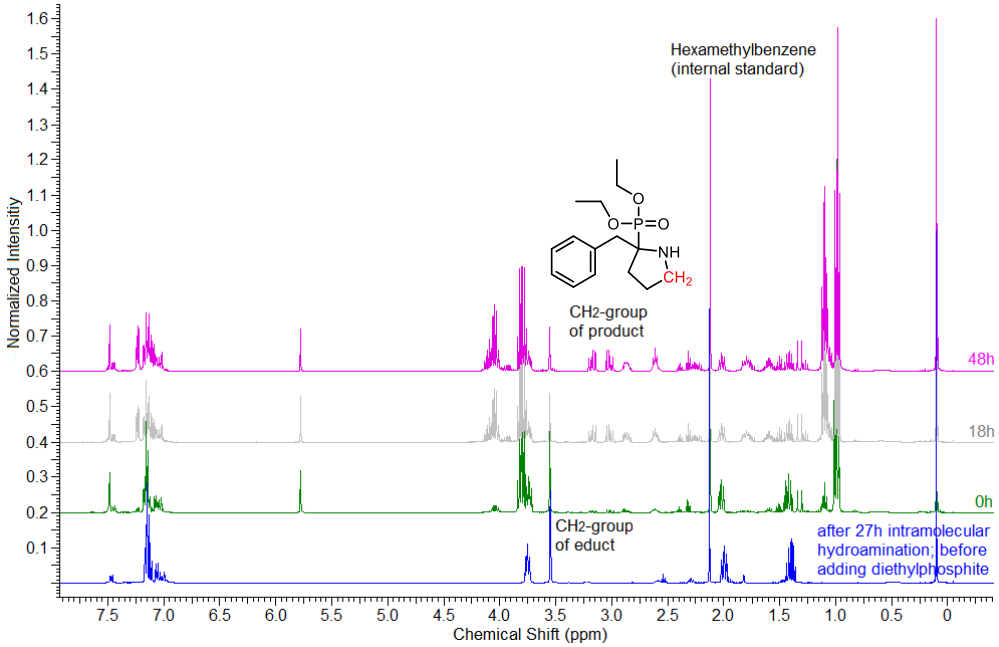
Traces of desired product (Scheme 26 – compound a) were detected in the proton NMR spectrum. By separating the product mixture *via* HPLC, the peak at 23.7 min of the enamine (Scheme 25 – compound b) was found (see also Section 3.4.2). Additionally, it is assumed that tiny amounts of the phosphonylated amine shown in Scheme 25 - compound c are generated as well. This presumption is supported by MS analyses (m/z = 274.0964 $^{+}$Na) and in the ^{13}C-NMR spectrum the carbons of the triple bond, as well as the three secondary carbons between alkyne and amine moiety show doublets due to coupling to ^{31}P. This indicates the binding of the phosphorus to the substrate.

3.4.5. Evaluation

The reactions were monitored *via* proton-NMR spectroscopy. An example for the modification of the NMR spectrum during intramolecular hydroamination (Scheme 27) and subsequent hydrophosphonylation (Scheme 28) is shown below. In both cases hexamethylbenzene was applied as internal standard. To determine the conversion of the hydroamination the disappearing aromatic protons at 7.5 ppm were considered in relation to the internal standard. Especially significant peaks of the imine-intermiediate are two CH_2-groups between 3.5 and 3.8 ppm. To calculate the reaction progress of the hydrophosphonylation the singlet at 3.5 ppm which was formed during the hydroamination, was utilised. It vanishes during the proceeding reaction.



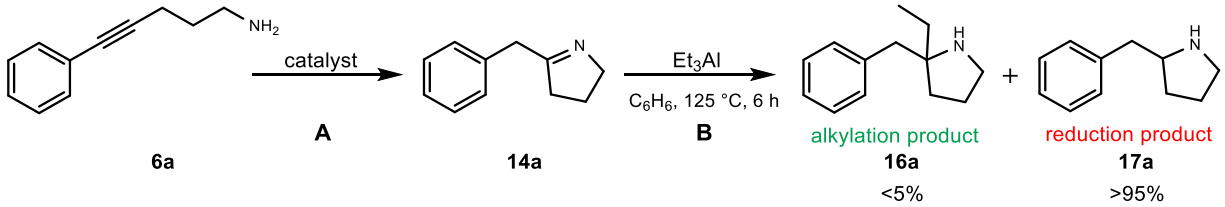
Scheme 27: Monitoring of the intramolecular hydroamination of aminoalkynes *via* ^{1}H-NMR spectroscopy.



Scheme 28: Monitoring of the hydrophosphonylation of imines generated by hydroamination *via* ^{1}H-NMR spectroscopy.

3.5. One-Pot Synthesis of Ethylated Amines

To combine intramolecular hydroamination with alkylation in a one-pot procedure [$Zr(NMe_2)_4$] and [$Y(N(SiHMe_2)_2)_3(THF)_2$] were applied as catalysts (Scheme 29).



Scheme 29: One-pot-two-step synthesis to generate ethylated secondary amines.

However, no conversion was observed at 60 °C. Only after heating the reaction mixture to 125 °C traces (<5%) of desired alkylated product (**16a**) were detected and the reduction product (**17a**) was detected as main product (>95%). Since the detailed investigation of the alkylation of aldimines (Section 3.2) did not lead to very promising results after all, no further investigations concerning this topic were conducted.

4. Conclusion and Outlook

During this work two different possibilities for the functionalisation of imines (alkylation and hydrophosphonylation), as well as their coupling with intramolecular hydroaminations of aminoalkynes were investigated.

The alkylation of aldimines (Scheme 20 and 21) could not be improved by using yttrium, lanthanum, zirconium or niobium catalysts. The most suitable one was [$Eu(dpm)_3$] which was already investigated by the research group of Blum.[7] It was found that the major problem is the formation of reduction by-product, which can be minimised by applying suitable reaction conditions, such as utilised catalyst, solvent and batch of alkyl donor, as well as reaction temperature. Among the newly investigated systems [$Y(BDMA)_3$] showed the best catalytic activity and led up to 44% of desired alkylated product (Table 2). Moreover, Et_3Al as alkyldonor, benzene as solvent and 60 °C as reaction temperature under argon atmosphere are considered as the most suitable reaction conditions.

The hydrophosphonylation of aldimines (Scheme 22) gave promising results. Good yields with even quite good enantioselectivities were achieved. The chiral catalyst [Y((S)-binol$SiPh_3$)(o-$C_6H_4CH_2NMe_2$)(Me_2NCH_2Ph)] (Figure 10) is noteworthy in particular, as it led to the desired α-amino phosphonate in more than 90% of yield and with enantiomeric excesses up to 74% (Table 10). Among the achiral metal precursors, [$Y(BDMA)_3$] performed the best by far (Table 9). Additionally, an influence of different functional groups at the phenyl residue was observed, whereby electron-withdrawing groups improved the outcome of the reaction and electron-donating groups lowered the yield. First attempts to hydrophosphonylate ketimines showed that the steric hindrance is too high to obtain the desired products quantitatively.

Moreover, the combination of hydroamination and hydrophosphonylation was successful (Scheme 23). Former attempts on this topic by the research group of Doye were already successful.[10] However, two catalysts were required, one for each reaction step. Now a one-pot system was established in which one catalyst promotes both reaction in sequence. 3 mol% of catalyst precursor [$Zr(NMe_3)_4$] were sufficient to catalyse the formation of a cyclic five-membered α-amino phosphonate starting from the corresponding aminoalkyne within 2 h. In order to form a six-membered product, higher catalyst loadings and reaction temperatures were necessary (Scheme 24).

Further challenges in this topic will be increasing the enantioselectivity of the hydrophosphonylation of aldimines. In due course, it would be interesting to investigate the influence of other chiral catalysts to the outcome of the reaction. Moreover, to substantiate the assumption of the enhancing effect of electron-withdrawing groups and the debasing effect of electron-donating groups, it is required to examine additional imines as starting material. It would also be attractive to compare the obtained results of the aromatic aldimines with the outcome of the reaction when non-aromatic residues.

Referring to the one-pot synthesis it is necessary to broaden the substrate scope and to find a way to perform it in an enantioselective fashion. Since the achiral zirconium precursor showed promising results a possible prospect is to set up an chiral catalyst based on zirconium. In order to do that [Zr((S)-binolSiPh_3)(NMe_2)$_2$)] could be examined. Sterically more demanding substrates and bulkier ligands on the catalyst might lead to higher enantioselectivities as well.

Besides, to broaden the diversity of the generated amines, additional functionalisation possibilities, such as hydrogenations or hydrosilylations (Scheme 1) should be tested and established.

5. Experimental Section

5.1. General

Unless otherwise noted all reactions were realised under inert conditions, either with a Schlenk line under argon in flame-dried glassware or in an argon filled glovebox. DCM and DMF were distilled from CaH_2, THF, toluene and benzene were distilled from sodium benzophenone ketyl. If not mentioned differently all commercially available starting materials were used without further purification.

All ^{1}H-,^{13}C- and ^{31}P-NMR spectra were recorded on a Bruker Ultrashield^{TM} 400 Plus instrument, whereby the proton NMR spectra were measured at 400.3 MHz, the carbon NMR spectra at 100.6 or 150.9 MHz and the phosphorus NMR spectra at 162.0 MHz. All chemical shifts are noted in ppm. ^{1}H- and ^{31}C- shifts are indicated relative to TMS and were referenced to residual signals of the solvent (^{1}H NMR ($CDCl_3$): 7.27 ppm, ^{1}H NMR (C_6D_6): 7.16 ppm, ^{13}C NMR ($CDCl_3$): 77.0 ppm, ^{13}C NMR (C_6D_6): 128.4 ppm). ^{31}P- shifts were referenced to diethylphosphite. Mass spectra were recorded on two different instruments. ESI-spectra were measured on a Bruker QTOF Maxis-spectrometer, whereas EI-spectra were measured on a Finnigan MAT95S-instrument. Column chromatography was performed by using Biotage® SP4 and Isolera Flash Systems and the applied columns were packed with silica gel 60 Å or aluminium oxide 90 standardised (activity II-III). TLC was performed with commercial Kieselgel 60 F_{254} or ALOX N/UV_{254} and visualised *via* UV lamp. HPLC measurements were conducted on an Agilent Technologies Series 1200 system with 61379B Degasser, 61311A QuatPump, 61329A LLS, 61316A TCC, G1315D DAD.

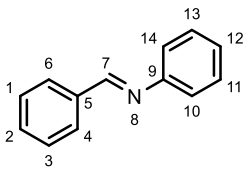
5.2. Synthesis of Substrates, Reagents and Catalysts

5.2.1. Synthesis of N-(Phenylmethylene)benzenamine (**1a**)[46]

This reaction was not performed under inert conditions.

Benzaldehyde (2.12 g, 2.03 mL, 1.04 g/mL, 20.0 mmol) and aniline (1.86 g, 1.83 mL, 1.02 g/mL, 20.0 mmol) were dissolved in EtOH (50 mL). The resulting reaction mixture was stirred for 4 h at 90 °C and then cooled to room temperature overnight. After drying over $MgSO_4$, the product started to crystallise as white needles. To complete the crystallisation, the product was stored in the freezer overnight. The solvent was filtered off and the remaining solid was purified *via* flash chromatography (silica, 5-60% EtOAc in heptane, R_f = 0.65 (heptane:EtOAc (4:1))) to give 3.10 g (17.1 mmol, 86%) of the imine as white crystals. Before further application the product was freeze dried.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 8.48 (s, 1H, H-7), 7.85 – 8.01 (m, 2H, H-4, H-6), 7.46 – 7.59 (m, 3H, H-1, H-2, H-3), 7.36 – 7.46 (m, 2H, H-10, H-14), 7.14 – 7.30 (m, 3H, H-11, H-12, H-13);



^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 160.4 (C-7), 152.7 (C-9), 136.3 (C-5), 131.4 (C-2), 129.1 (C-11, C-13), 128.8 (C-12), 128.7 (C-4, C-6), 125.9 (C-1, C-3), 120.9 (C-10, C-14).

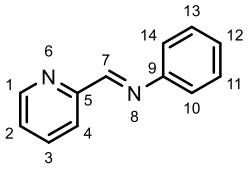
The NMR spectroscopic data is in agreement with the literature.[46]

5.2.2. Synthesis of N-(2-Pyridinylmethylene)benzenamine (**1b**)[46]

This reaction was not performed under inert conditions.

2-Pyridinecarboxybenzalehyde (1.82 g, 1.61 mL, 1.13 g/mL, 17.0 mmol) and aniline (1.58 g, 1.55 mL, 1.02 g/mL, 17.0 mmol) were dissolved in EtOH (35 mL). The resulting reaction mixture was stirred for 4 h at 90 °C and then cooled to room temperature overnight. Drying over $MgSO_4$ and removing the solvent under vacuum led to an orange oil which was purified *via* flash chromatography (silica, 5-80% DCM in heptane, R_f = 0.30 (alox, heptane:DCM (1:1))). After freeze drying, the product was obtained as an orange solid (2.96 g, 16.2 mmol, 96%).

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 8.73 (d, *J* = 4.8 Hz, 1H, H-1), 8.62 (s, 1H, H-7), 8.22 (d, *J* = 8.0 Hz, 1H, H-4), 7.84 (t, *J* = 7.7 Hz, 1H, H-3), 7.35 – 7.49 (m, 3H, H-2, H-10, H-14), 7.22 – 7.34 (m, 3H, H-11, H-12, H-13);



^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 160.7 (C-7), 154.6 (C-9), 151.0 (C-5), 149.7 (C-1), 136.6 (C-4), 129.2 (C-11, C-13), 126.7 (C-3), 125.1 (C-12), 121.9 (C-2), 121.1 (C-10, C-14).

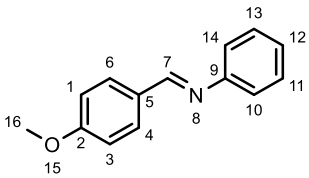
The NMR spectroscopic data is in agreement with the literature.[52]

5.2.3. Synthesis of N-[(4-Methoxyphenyl)methylene]benzenamine (**1c**)[46]

This reaction was not performed under inert conditions.

4-Methoxybenzaldehyde (1.36 g, 1.21 mL, 1.12 g/mL, 10.0 mmol) and aniline (0.93 g, 0.91 mL, 1.02 g/mL, 10.0 mmol) were dissolved in EtOH (25 mL). The resulting reaction mixture was stirred for 4 h at 90 °C and then cooled to room temperature overnight. After drying over $MgSO_4$, the product started to crystallise. To complete the crystallisation, the product was stored in the freezer overnight. The solvent was filtered off and the remaining white solid was purified *via* flash chromatography (silica, 5-60% EtOAc in heptane, R_f = 0.34 (heptane:EtOAc (4:1))) to give 1.90 g (9.0 mmol, 90%) of the imine as white crystals. Before further application the product was freeze dried.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 8.40 (s, 1H, H-7), 7.80 – 7.91 (m, 2H, H-4, H-6), 7.33 – 7.45 (m, 2H, H-10, H-14), 7.14 – 7.26 (m, 3H, H-11, H-12, H-13), 6.94 – 7.05 (m, 2H, H-1, H-3), 3.89 (s, 3H, H-16);



^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ =162.3 (C-2), 159.7 (C-7), 152.4 (C-9), 130.5 (C-4, C-6), 129.3 (C-5), 129.1 (C-11, C-13), 125.5 (C-12), 120.9 (C-10, C-14), 114.2 (C-1, C-3), 88.4 (C-16).

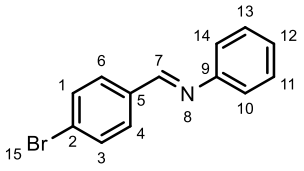
The NMR spectroscopic data is in agreement with the literature.[52]

5.2.4. Synthesis of N-[(4-Bromophenyl)methylene]benzenamine (**1d**)[46]

This reaction was not performed under inert conditions.

4-Bromobenzaldehyde (1.85 g, 10.0 mmol) and aniline (0.93 g, 0.91 mL, 1.02 g/mL, 10.0 mmol) were dissolved in EtOH (25 mL). The resulting reaction mixture was stirred for 4 h at 90 °C and then cooled to room temperature overnight. After drying over $MgSO_4$, the product started to crystallise as white needles. To complete the crystallisation, the product was stored in the freezer overnight. The solvent was filtered off and the remaining white solid was purified *via* flash chromatography (silica, 5-60% EtOAc in heptane, R_f = 0.41 (heptane:EtOAc (4:1))) to give 2.37 g (9.0 mmol, 91%) of the imine as white crystals. Before further application the product was freeze dried.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 8.42 (s, 1H, H-7), 7.75 – 7.84 (m, 2H, H-4, H-6), 7.59 – 7.67 (m, 2H, H-1, H-3), 7.36 – 7.46 (m, 2H, H-10, H-14), 7.24 – 7.27 (m, 1H, H-12), 7.18 – 7.24 (m, 2H, H-11, H-13);



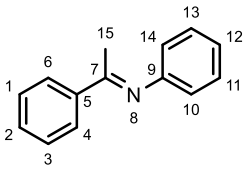
^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ =158.9 (C-7), 151.7 (C-9), 135.2 (C-5), 132.0 (C-1, C-3), 130.1 (C-11, C-13), 129.2 (C-4, C-6), 126.2 (C-12), 125.9 (C-2), 120.8 (C-10, C-14).

The NMR spectroscopic data is in agreement with the literature.[53]

5.2.5. Synthesis of N-(1-Phenylethylidene)benzenamine (**2a**)[47]

In a flame dried schlenk flask, containing molecular sieves 4 Å (8 g), acetophenon (1.20 g 1.17 mL, 1.03 g/mL, 10.0 mmol) and aniline (0.93 g, 0.91 mL, 1.02 g/mL, 10.0 mmol) were dissolved in dry toluene. The resulting reaction mixture was stirred for 16 h at 120 °C and then cooled to room temperature. Then, after removing the solids *via* filtration, the solvent was removed under vacuum. The crude product was purified *via* flash chromatography (silica, 5-35% EtOAc in heptane) to give 1.19 g (6.1 mmol, 61%) of the imine as yellow solid. Before further application the product was freeze dried.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.94 – 8.03 (m, 2H, H-4, H-6), 7.43 – 7.52 (m, 3H, H-1, H-2, H-3), 7.33 – 7.41 (m, 2H, H-11, H-13), 7.07 – 7.15 (m, 1H, H-12), 6.77 – 6.86 (m, 2H, H-10, H-14), 2.25 (s, 3H, H-15);



^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ =165.4 (C-7), 151.7 (C-9), 139.5 (C-5), 130.4 (C-2), 128.9 (C-11, C-13), 128.4 (C-1, C-3), 127.2 (C-4, C-6), 123.2 (C-12), 119.4 (C-10, C-14), 17.3 (C-15).

The NMR spectroscopic data is in agreement with the literature.[54]

5.2.6. Synthesis of 5-Phenyl-4-pentyn-1-amine (**6a**)[21]

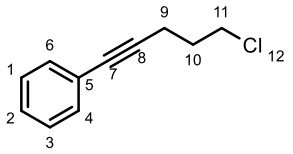
*5.2.6.1. Synthesis of (2-Phenylethynyl)lithium (**3a**)*

In a flame dried two-necked flask, equipped with a dropping funnel, was placed phenylacetylene (3.68 g, 3.95 mL, 0.93 g/mL, 36.0 mmol) dissolved in dry THF (80 mL) and cooled to –78 °C. Then *n*BuLi (2.33 M in hexane, 17.0 mL, 40 mmol) was added dropwise within 30 min and the resulting mixture was stirred for additional 60 min at room temperature to give a yellow- brown solution. In order to analyse the completion of the reaction an aliquot (0.5 mL) was treated with D_2O (1.0 mL). After addition of Et_2O (2 mL) the two layers were separated and the organic layer was dried over $MgSO_4$. Then the solvents were removed under vacuum and a ^{1}H- NMR spectrum was recorded. For the substrate (phenylacetylene) the integrated intensities had been 5.0 for the phenyl protons and 1.0 for the methylidyne proton, after the reaction and deuteration only the phenyl protons were visible. This indicated 100% deuteration and therefore 100% of the phenylethenyllithium.

*5.2.6.2. Synthesis of 5-Chloro-1-phenyl-1-pentyne (**4a**)*

In a flame dried three-necked flask, equipped with a condenser and a dropping funnel, was placed 3-bromo-1-chloropropane (5.51 g, 3.47 mL, 1.59 g/Ml, 35.0 mmol) in dry THF (25 mL) and cooled to 0 °C. Then the (phenylethenyl)lithium (**3a**) prepared before (78 mL, 36 mmol) was added dropwise within 1 h. The resulting reaction mixture was first warmed to room temperature (1 h) and then refluxed at 80 °C for additional 3 h. After cooling to room temperature the reaction was quenched with saturated NH_4Cl-solution (50 mL). The two layers were separated and the water layer was extracted with EtOAc (3 $\times$ 25 mL). All organic layers were combined, washed with saturated NaCl-solution (2 $\times$ 25 mL) and dried over $MgSO_4$. After removing the solvent under vacuum the crude product was purified *via* flash chromatography (silica, 5-60% EtOAc in heptane) which led to 4.38 g (24.4 mmol, 70%) of a yellow oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.39 – 7.46 (m, 2H, H-4, H-6), 7.29 – 7.34 (m, 3H, H-1, H-2, H-3), 3.75 (t, *J* = 6.4 Hz, 2H, H-11), 2.64 (t, *J* = 6.8 Hz, 2H, H-9), 2.01 – 2.15 (m, H, H-10).

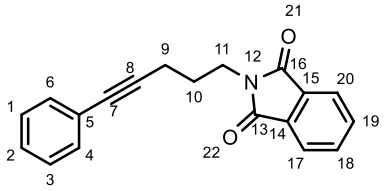


The NMR spectroscopic data is in agreement with the literature.[21]

5.2.6.3. Synthesis of (5-(Phthalimido)-1-pentyn-1-yl)benzene (**5a**)

In a flame dried Schlenk flask equipped with a condenser compound **4a** (4.00 g, 22.4 mmol) and potassium phthalimide (4.56 g, 24.6 mmol) were dissolved in DMF (30 mL) and heated to 150 °C overnight (16 h). The reaction mixture was cooled to room temperature and quenched with a DCM/dH_2O mixture (1:1, 50 mL). The aqueous layer was separated and extracted with DCM (3× 20 mL). In order to remove the unreacted phthalimide all organic layers were combined and washed with 0.2 M KOH (2 × 20 mL) and dH_2O (1 × 20 mL). Then the organic layer was dried over $MgSO_4$ and the solvent was removed under vacuum which led to an orange- white solid. For purification the crude product was washed with Et_2O (3 × 10 mL) and dried under vacuum to give 4.07 g (14.1 mmol, 63%) of a white solid.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.78 – 7.88 (m, 2H, H-18, H-19), 7.63 – 7.75 (m, 2H, H-17, H-20), 7.28 – 7.34 (m, 2H, H-4, H-6), 7.12 – 7.26 (m, 3H, H-1, H-2, H-3), 3.88 (t, *J* = 7.0 Hz, 2H, H-11), 2.51 (t, *J* = 7.0 Hz, 2H, H-9), 2.04 (quin, *J* = 7.0 Hz, 2H, H-10).

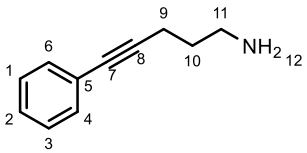


The NMR spectroscopic data is in agreement with the literature.[21]

5.2.6.4. Synthesis of 5-Phenyl-4-pentyn-1-amine (**6a**)

In a flame dried Schlenk flask equipped with a condenser compound **5a** (3.00 g, 10.4 mmol) and hydrazine monohydrate (1.09 g, 1.06 mL, 1.03 g/mL, 21.8 mmol) were suspended in MeOH (30 mL). The reaction mixture was heated to 75 °C which led to a clear yellow solution after 10 min. After 35 min a white precipitate had formed. The suspension was stirred for another 30 min and then cooled to 0 °C. The white solid was filtered off and extracted with MeOH (2 × 10 mL). Removal of the methanol from the organic layer led to a white solid that was extracted with Et_2O (3 × 20 mL). The organic fractions were combined and the ether was removed under vacuum to give 1.00 g (6.3 mmol, 61%) of yellow oil. In order to use it as substrate for catalysis the product was dried over CaH_2 and distilled twice.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.36 – 7.43 (m, 2H, H-4, H-6), 7.24 – 7.30 (m, 3H. H-1, H-2, H-3), 2.88 (t, *J* = 6.9 Hz, 2H, H-11), 2.49 (t, *J* = 6.9 Hz, 2H, H-9), 1.75 (quin, *J* = 6.9 Hz, 2H, H-10), 1.18 (br s, 2H, NH_2-12);



^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 131.5 (C-4, C-6), 128.2

(C-1, C-3), 127.6 (C-2), 123.9 (C-5), 89.6 (C-8), 80.9 (C-7), 41.3 (C-11), 32.5 (C-10), 16.9 (C-9).

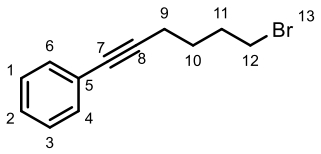
The NMR spectroscopic data is in agreement with the literature.[21]

5.2.7. Synthesis of 6-Phenyl-5-hexyn-1-amine (**6b**)[21]

*5.2.7.1. Synthesis of 6-Bromo-1-phenyl-1-pentyne (**4b**)*

In a flame dried three-necked flask, equipped with a condenser and a dropping funnel, was placed 1,4-Dibromobutane (7.56 g, 4.13 mL, 1.83 g/mL, 35.0 mmol) in dry THF (25 mL) and cooled to 0 °C. Then the (phenylethenyl)lithium (**3a**) prepared above (78 mL, 35 mmol) was added dropwise within 1 h. The resulting reaction mixture was warmed to room temperature (1 h) and then refluxed at 80 °C for additional 4 h. After cooling to room temperature the reaction was quenched with saturated NH_4Cl-solution (50 mL). The two layers were separated and the water layer was extracted with EtOAc (3×25 mL). All organic layers were combined, washed with brine (2×25 mL) and dried over $MgSO_4$. After removing the solvent under vacuum the crude product was purified *via* flash chromatography (silica, 5-60% EtOAc in heptane; $R_f = 0.78$ (30% EtOAc in heptane)) which gave 4.30 g (17.0 mmol, 53%) of a yellow oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.37 – 7.46 (m, 2H, H-1, H-4), 7.20 – 7.36 (m, 3H, H-1, H-2, H-3), 3.49 (t, *J* = 6.7 Hz, 2H, H-12), 2.45 – 2.51 (m, 2H, H-9), 2.00 – 2.08 (m, 2H, H-11), 1.73 – 1.84 (m, 2H, H-10).

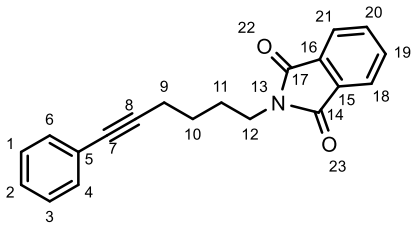


The NMR spectroscopic data is in agreement with the literature.[21]

*5.2.7.2. Synthesis of (6-(Phthalimido)-1-hexyn-1-yl)benzene (**5b**)*

In a flame dried Schlenk flask, equipped with a condenser, compound **4b** (4.00 g, 16.9 mmol) and potassium phthalimide (3.45 g, 18.6 mmol) were dissolved in DMF (30 mL) and heated to 120 °C overnight (19 h). The reaction mixture was cooled to room temperature and quenched with a DCM/dH_2O mixture (1:1, 50 mL). The aqueous layer was separated and extracted with DCM (3×20 mL). In order to remove the unreacted phthalimide all organic layers were combined and washed with 0.2 M KOH (2×20 mL) and dH_2O (1×20 mL). Then the organic layer was dried over $MgSO_4$ and the solvent was removed under vacuum which led to an orange-white solid. For purification the crude product was washed with Et_2O (3×10 mL) and dried under vacuum which gave 1.90 g (6.4 mmol, 37%) of a white solid.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.80 – 7.91 (m, 2H, H-19, H-20), 7.66 – 7.76 (m, 2H, H-18, H-21), 7.35 – 7.44 (m, 2H, H-4, H-6), 7.22 – 7.32 (m, 3H, H-1, H-2, H-3), 3.77 (t, *J* = 7.1 Hz, 2H, H-12), 2.48 (t, *J* = 7.1 Hz, 2H, H-9), 1.84 – 1.95 (m, 2H, H-11), 1.60 – 1.72 (m, 2H, H-10).

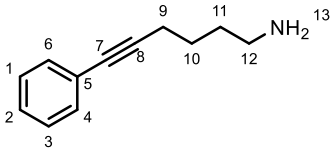


The NMR spectroscopic data is in agreement with the literature.[21]

*5.2.7.3. Synthesis of 6-Phenyl-5-hexyn-1-amine (**6b**)*

In a flame dried Schlenk flask equipped with a condenser compound **5b** (1.90 g, 6.4 mmol) and hydrazine monohydrate (0.65 mL, 13.44 mmol) were suspended in MeOH (30 mL). The reaction mixture was heated to 75 °C which led to a clear yellow solution after 10 min. After 35 min a white precipitate had formed. The suspension was stirred for another 30 min and then cooled to 0 °C. The white solid was filtered off and extracted with MeOH (2 $\times$ 10 mL). Removal of the methanol from the organic residue led to a white solid that was extracted with Et_2O (3 $\times$ 20 mL). The organic fractions were combined and the ether was removed under vacuum to give 0.47 g (2.8 mmol, 43%) of a yellow oil. In order to use it as substrate for catalysis the product was dried over CaH_2 and distilled twice.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.35 – 7.44 (m, 2H, H-4, H-6), 7.22 – 7.33 (m, 3H, H-1, H-2, H-3), 2.76 (t, *J* = 6.8 Hz, 2H, H-12), 2.44 (t, *J* = 6.7 Hz, 2H, H-9), 1.56 – 1.74 (m, 4H, H-10, H-11), 1.22 (br s, 2H, NH_2-13);



^{13}C {^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 131.2 (C-4, C-6), 127.9 (C-1, C-3), 127.2 (C-2), 123.7 (C-5), 89.7 (C-8), 80.5 (C-7), 41.5 (C-12), 32.8 (C-11), 25.8 (C-9), 19.0 (C-10).

The NMR spectroscopic data is in agreement with the literature.[21]

5.2.8. Synthesis of Ethylmagnesium bromide[55]

In a flame dried Schlenk flask, equipped with a dropping funnel, Mg turnings (107 mg, 4.40 mmol) and I_2 (5 mg, 0.02 mmol) were suspended in THF (4 mL). Ethyl bromide (436 mg, 4.00 mmol) dissolved in THF (2 mL), was added *via* dropping funnel within 25 min. The colour of the reaction mixture changed from brown to cloudy white. To complete the reaction, the solution was heated under reflux (65 °C) for 4 h. The ethylmagnesium bromide was separated from the unreacted magnesium *via* teflon cannula and directly used as ethyl donor for catalysis without further investigation or purification.

5.3. Catalysis

5.3.1. Alkylation

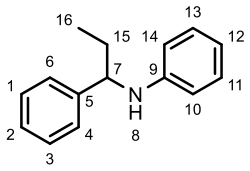
5.3.1.1. General Procedure for the Preparative Alkylation of Imines with Et_3Al[7]

In a flame dried schlenk flask equipped with a stirring bar and a condenser an appropriate imine derivate (2.0 mmol) and [Y(BDMA)$_3$] (49 mg, 0.1 mmol) were dissolved in 8 mL benzene. Then Et_3Al (25 wt% in toluene, 1.02 g, 0.848 g/mL, 1.2 mL, 2.2 mmol) was added and the reaction mixture was stirred for 24 h at 60 °C. In order to quench the reaction, the mixture was cooled to 0 °C and MeOH (14 mL) followed by powdered NaOH (1.0 g) were added. The organic residue was washed with dH_2O (2 × 20 mL) and brine (1 × 20 mL) and dried over $MgSO_4$. Then the solvent was removed under vacuum which led to the crude product. Purification *via* flash chromatography (ALOX, 0-20% DCM in heptane) gave the corresponding alkylation products.

α-Ethyl-N-phenylbenzenemethanamine (**7a**)

The reaction afforded 186 mg (0.9 mmol, 44%) of the alkylated imine as a yellow oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.31 – 7.41 (m, 4H, H-1, H-3, H-4, H-6), 7.22 – 7.30 (m, 1H, H-2), 7.07 – 7.16 (m, 2H, H-11, H-13), 6.66 (tt, *J* = 7.3, 1.9 Hz, 1H, H-12), 6.51 – 6.59 (m, 2H, H-10, H-14), 4.26 (t, *J* = 6.7 Hz, 1H, H-7), 4.09 (br s, 1H, NH-8), 1.78 – 1.96 (m, 2H, H-15), 0.99 (t, *J* = 7.5 Hz, 3H, H-16);



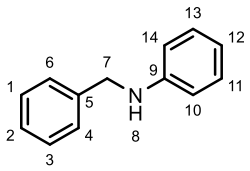
^{13}C {^{1}H} NMR (150.9 MHz, C_6D_6): δ = 148.3 (C-9), 144.7 (C-5), 129.7 (C-11, C-13), 129.1 (C-1, C-3), 128.7 (C-4, C-6), 127.1 (C-2), 118.0 (C-12), 114.1 (C-10, C-14), 80.2 (C-7), 32.1 (C-15), 11.2 (C-16).

The NMR spectroscopic data is in agreement with the literature.[7]

N-Phenylbenzenemethanamine (**8a**)

The reaction afforded 97 mg (0.5 mmol, 23%) of the reduction by-product as a yellow oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.31 – 7.46 (m, 4H, H-1, H-3, H-4, H-6), 7.28 – 7.32 (m, 1H, H-2), 7.11 – 7.24 (m, 2H, H-11, H-13), 6.73 (t, *J* = 7.3, 1H, H-12), 6.58 – 6.69 (m, 2H, H-10, H-14), 4.35 (d, *J* = 5.6 Hz, 2H, H-7), 4.03 (br s, 1H, NH-8).

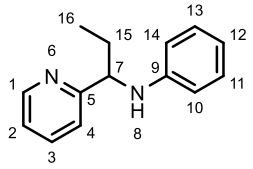


The NMR spectroscopic data is in agreement with the literature.[56]

α-Ethyl-N-phenyl-2-pyridinemethanamine (**7b**)

The reaction afforded 429 mg (2.0 mmol, 99%) of the alkylated imine as an orange oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 8.49 – 8.67 (m, 1H, H-1), 7.61 (td, *J* = 7.7, 1.8 Hz, 1H, H-3), 7.32 (dt, *J* = 7.9, 1.0 Hz, 1H, H-4), 7.06 – 7.18 (m, 3H, H-2, H-11, H-13), 6.65 (tt, *J* = 7.3, 1.1 Hz, 1H, H-12), 6.51 – 6.62 (m, 2H, H-10, H-14), 4.37 – 4.53 (m, 2H, H-7, NH-8), 1.78 – 2.06 (m, 2H, H-15), 0.96 (t, *J* = 7.4 Hz, 3H, H-16);



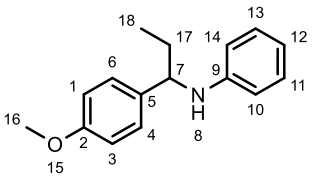
^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 162.8 (C-5), 149.3 (C-1), 147.4 (C-9), 136.5 (C-3), 129.2 (C-11, C-13), 121.9 (C-4), 121.2 (C-2), 117.3 (C-12), 113.4 (C-10, C-14), 80.6 (C-7), 29.9 (C-15), 10.5 (C-16).

The NMR spectroscopic data is in agreement with the literature.[7]

α-Ethyl-4-methoxy-N-phenylbenzenemethanamine (**7c**)

The reaction afforded 168 mg (0.6 mmol, 32%) of the alkylated imine as a slightly yellow oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.21 – 7.26 (m, 2H, H-4, H-6), 7.03 – 7.13 (m, 2H, H-11, H-13), 6.81 – 6.89 (m, 2H, H-1, H-3), 6.63 (tt, *J* = 7.3, 1.1 Hz, 1H, H-12), 6.47 – 6.57 (m, 2H, H-10, H-14), 4.19 (t, *J* = 6.7, 1H, H-7), 4.02 (br s, 1H, NH-8), 3.79 (s, 3H, H-16), 1.73 – 1.88 (m, 2H, H-17), 0.95 (t, *J* = 7.4 Hz, 3H, H-18);



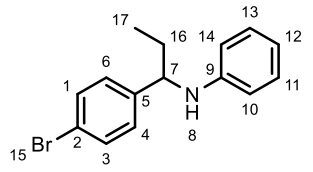
^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 158.5 (C-2), 147.6 (C-9), 135.9 (C-5), 129.0 (C-11, C-13), 127.5 (C-4, C-6), 117.1 (C-12), 113.9 (C-1, C-3), 113.3 (C-10, C-14), 59.1 (C-16), 55.2 (C-7), 31.6 (C-17), 10.8 (C-18).

The NMR spectroscopic data is in agreement with the literature.[7]

4-Bromo-α-ethyl-N-phenylbenzenemethanamine (**7d**)

The reaction afforded 273 mg (0.9 mmol, 47%) of the alkylated imine as a slightly yellow oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.40 – 7.48 (m, 2H, H-1, H-3), 7.18 – 7.26 (m, 2H, H-4, H-6), 7.04 – 7.14 (m, 2H, H-11, H-13), 6.66 (tt, *J* = 7.3, 1.0 Hz, 1H, H-12), 6.45 – 6.52 (m, 2H, H-10, H-14), 4.20 (t, *J* = 6.6 Hz, 1H, H-7), 4.04 (br s, 1H, NH-8), 1.73 – 1.89 (m, 2H, H-16), 0.97 (t, *J* = 7.4, 3H, H-17);



^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 147.2 (C-9), 143.1 (C-5), 131.6 (C-1, C-3), 129.1 (C-11, C-13), 128.2 (C-4, C-6), 120.5

(C-2), 117.5 (C-12), 113.3 (C-10, C-14), 59.3 (C-7), 31.6 (C-16),
10.7 (C-17).

The NMR spectroscopic data is in agreement with the literature.[35]

5.3.1.2. General Procedure for Screening Reactions with Et_3Al

In an argon filled glovebox, a vial, equipped with a magnetic stirring bar, was charged with an imine derivate and solvent (1 mL). The mixture was stirred until everything was dissolved then Et_3Al (25 wt% in toluene) was added and the solution was stirred at the temperatures specified in the table below. The reaction progress was monitored *via* HPLC and led to the results listed in Section 3.2.1.

Note: If other reaction conditions were used, they were stated under the table. More detailed results, such as the ratio between product and by-product are listed in Section 3.2.1.

Preparation of HPLC- samples

To 100 µL of reaction mixture were added 200 µL of solvent (*i*PrOH). In order to remove the catalyst the sample was filtered over silica. For HPLC-analysis the following parameters were used: OD-H column, *i*PrOH:Hept = 2:98 as eluent, 2 µL injection volume, 0.5 mL flow, 26 bar, 20 °C.

Table 12: Screening to optimise the alkylation of aldimines

#	Imine		Catalyst		Solvent	Temperature [°C]	Yield [%]
	Type	Amount [µmol]	Type	Loading [µmol]			
	Substrate						
1	**1a**	200	**C4**	10	Benzene	60	44
2	**1b**						>99
3	**1c**						35
4	**1d**						47
	Solvent						
5	**1a**	200	**C2**	10	Benzene	60	28
6					Toluene		27
7					DCM		20
8					THF		9
	Temperature						
9	**1a**	200	**C2**	10	Benzene	0[a]	8
10						25	13
11						45	23
12						60	28
13						110	36

Table 12 - continued

	Catalyst type					
14	**1a**	200	**C1**	10	Benzene	60	69
15			**C2**				28
16			**C3**				34
17			**C4**				44
18			**C5**				44
19			**C6**				9
20			**C7**				16
21			**C8**				9
	Catalyst amount					
22	**1a**	200	**C2**	0	Benzene	60	9
23				10			28
24				20			41
25				30			65
26				40			78
	Concentration screening					
27	**1a**	100 [b]	**C3**	5	Toluene	60	44
28		700 [c]		35			43
29		700 [d]		35			25
30		700 [e]		35			19
	Imine / Et_3Al- ratio					
31	**1a**	200 [f]	**C1**	10	Benzene	25	13
32		200 [g]					12
	Order of addition					
33	**1a**	750	**C1**	5	Benzene	60	28
34		750[h]				60	29
35		750[i]				60	28
	Argon and ethylene					
36	**1a**	1000[j]	**C3**	5	Benzene	25	21
37		1000[k]					12

Description of catalysts:

***C1**…[Eu(dpm)$_3$],* ***C2**…[Y(N(SiMe$_3$)$_2$)$_3$],* ***C3**…[Y(N(SiHMe$_2$)$_2$)$_3$(THF)$_2$],*
***C4**…[Y(BDMA)$_3$],* ***C5**…[La(N(SiHMe$_2$)$_2$)$_3$(THF)$_2$],* ***C6**…[Nb(NMe$_2$)$_5$],*
***C7**…[Zr(NMe$_2$)$_4$],* ***C8**…[Y((S)-binolSiPh$_3$)(o-C$_6$H$_4$CH$_2$NMe$_2$)(Me$_2$NCH$_2$Ph)]*

[a] *The reaction was performed under Schlenk conditions in a Schlenk flask and cooled with water and ice to 0 °C.*
[b] *Concentration: 0.17 M (0.6 mL solvent)*
[c] *Concentration: 0.78 M (0.9 mL solvent)*
[d] *Concentration: 1.40 M (0.5 mL solvent)*
[e] *Concentration: 1.75 M (0.4 mL solvent)*
[f] *1.0 : 1.1-ratio means 200 µmol of imine and 220 µmol of Et_3Al.*
[g] *1.0 : 3.0-ratio means 200 µmol of imine and 600 µmol of Et_3Al.*
[h] *In a flame dried three-necked flask imine and catalyst were dissolved in benzene (3.8 mL) and heated to 60°C. Then Et_3Al was added dropwise within 5h.*
[i] *In a flame dried three-necked flask Et_3Al and catalyst were dissolved in benzene (3.8 mL) and heated to 60°C. Then the imine was added dropwise within 5h.*
[j] *The reaction was performed in a flame dried Schlenk flask under argon (5 mL of solvent were used).*
[k] *The reaction was performed in a flame dried Schlenk flask under ethylene (5 mL of solvent were used).*

5.3.1.3. General Procedure for the Alkylation of Imines with Neat Et_3Al

In a screw-cap NMR tube in a glovebox, N-(phenylmethylene)benzenamine (18.1 mg, 100 µmol), [Y(BDMA)$_3$] (2.5 mg, 5 µmol) and hexamethylbenzene (3.2 mg, 2 µmol) as internal standard were dissolved in d_6-benzene. Then Et_3Al (11.7 mg, 14 µL, 0.835 g/mL 110 µmol, 1.1 equiv.) was added dropwise and the NMR tube was kept at certain temperatures (0 °C, 25 °C, 100 °C). The reaction was observed *via* ^{1}H-NMR spectroscopy. In all cases <5% of the alkylated product were obtained.

5.3.1.4. General Procedure for the Alkylation of Imines with Ethylmagnesium bromide[57]

In an argon filled glovebox a vial, equipped with a magnetic stirring bar, was charged with an imine derivate (2.0 mmol) and [Y(BDMA)$_3$] (49 mg, 0.1 mmol) in THF (2 mL). This mixture was stirred for 1 h till everything was dissolved, then ethylmagnesium bromide (0.67 M in THF, 3.6 mL, 2.4 mmol) was added and the resulting reaction mixture was stirred for 24h at 25 °C. In order to quench the reaction saturated NH_4Cl solution (4 mL) was added and then filtered through celite. Afterwards the filtrate was extracted with EtOAc (3 × 10 mL) and dried over $MgSO_4$. The solvent was removed under vacuum which led to the crude product. Purification *via* flash chromatography (alox, 0-30% DCM in heptane) gave the corresponding alkylation products.

α-Ethyl-N-phenylbenzenemethanamine (**8a**)

The reaction afforded 224 mg (1.1 mmol, 53%) of the alkylated imine as a yellow oil. NMR spectroscopic data: see section 5.2.1.1.

α-Ethyl-N-phenyl-2-pyridinemethanamine (**8b**)

The reaction afforded 403 mg (1.9 mmol, 95%) of the alkylated imine as an orange oil. NMR spectroscopic data: see section 5.2.1.1.

4-Bromo-α-ethyl-N-phenylbenzenemethanamine (**8d**)

The reaction afforded 331 mg (1.4 mmol, 57%) of the alkylated imine as a slightly yellow oil. NMR spectroscopic data: see section 5.2.1.1.

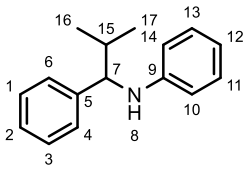
5.3.1.5. General Procedure for the Alkylation of Imines with Isopropylmagnesiumchloride[57]

In an argon filled glovebox a vial, equipped with a magnetic stirring bar, was charged with an imine derivative (2.0 mmol) and [Y(BDMA)$_3$] (49 mg, 0.1 mmol) in THF (2 mL) This mixture was stirred for 1 h, then isopropylmagnesium chloride · lithium chloride (1.30 M in THF, 1.76 g, 1.85 mL, 0.951 g/mL, 2.4 mmol) was added and the resulting reaction mixture was stirred for 24 h at 25 °C. In order to quench the reaction, saturated NH_4Cl solution (4 mL) was added and then filtered through celite. Afterwards the filtrate was extracted with EtOAc (3 × 10 mL) and dried over $MgSO_4$. The solvent was removed under *vacuo* which led to the

crude product. Purification *via* flash chromatography (alox, 0-30% DCM in heptane) gave the corresponding alkylation products.

α-(1-Methylethyl)-N-phenylbenzenemethanamine (**11a**)

The reaction afforded 268 mg (1.3 mmol, 64%) of the alkylated imine as a yellow oil.



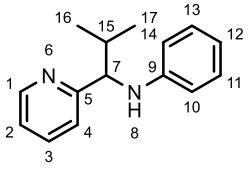
^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.28 – 7.36 (m, 4H, H-1, H-3, H-4, H-6), 7.20 – 7.27 (m, 1H, H-2), 7.04 – 7.14 (m, 2H, H-11, H-13), 6.62 (t, *J* = 7.3, 1H, H-12), 6.48 – 6.55 (m, 2H, H-10, H-14), 4.26 (t, *J* = 6.7 Hz, 1H, H-7), 4.06 – 4.21 (m, 2H, H-7, NH-8), 1.96 – 2.12 (m, 1H, H-15), 1.01 (d, *J* = 6.9 Hz, 3H, H-16 or H-17), 0.94 (d, *J* = 6.9 Hz, 3H, H-16 or H-17);

^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 147.7 (C-9), 142.6 (C-5), 129.3 (C-11, C-13), 128.2 (C-1, C-3), 127.2 (C-4, C-6), 126.8 (C-2), 117.0 (C-12), 113.2 (C-10, C-14), 63.8 (C-7), 34.9 (C-15), 19.7 (C-16 or C-17), 18.6 (C-16 or C-17).

The NMR spectroscopic data is in agreement with the literature.[58]

α-(1-Methylethyl)-N-phenyl-2-pyridinemethanamine (**11b**)

The reaction afforded 400 mg (1.9 mmol, 94%) of the alkylated imine as an orange oil.



^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 8.54 – 8.65 (m, 1H, H-1), 7.57 – 7.62 (m, 1H, H-3), 7.24 – 7.27 (m, 1H, H-4), 7.05 – 7.18 (m, 3H, H-2, H-11, H-13), 6.64 (tt, *J* = 7.3, 1.1 Hz, 1H, H-12), 6.57 – 6.61 (m, 2H, H-10, H-14), 4.51 (d, *J* = 6.7 Hz, 1H, NH-8), 4.29 (t, *J* = 6.5 Hz, 1H, H-7), 2.21 – 2.29 (m, 1H, H-15), 1.01 (d, *J* = 6.9 Hz, 3H, H-16 or H-17), 0.93 (d, *J* = 6.9 Hz, 3H, H-16 or H-17);

^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 162.0 (C-5), 149.2 (C-1), 147.8 (C-9), 136.2 (C-3), 129.1 (C-11, C-13), 122.0 (C-4), 121.8 (C-2), 117.2 (C-12), 113.4 (C-10, C-14), 64.7 (C-7), 33.8 (C-15), 19.7 (C-16 or C-17), 18.4 (C-16 or C-17).

5.3.2. Hydrophosphonylation

5.3.2.1. General Procedure for NMR-scale Hydrophosphonylation with Diethylphosphite[10]

In an argon filled glovebox a, screw cap NMR tube was charged with the appropriate imine (100 µmol), catalyst (5 µmol) and hexamethylbenzene (3.2 mg, 2 µmol) as internal standard. After dissolving the solids in benzene-d_6 (0.5 mL) diethylphosphite (15.0 mg, 14 µL, 1.072 g/mL, 110 µmol) was added. The NMR tube was sealed, removed from the glovebox and placed in the thermostated oil bath. The reaction was observed *via* ^{1}H-NMR

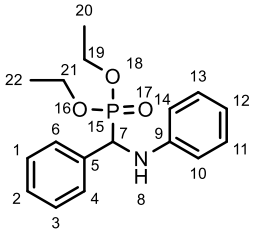
spectroscopy by following the disappearance of the signals of the substrate relative to the internal standard. To quench the reaction dH_2O (2 mL) was added, then 0.2 M KOH was added untill a pH of 9 was reached. The layers were separated and the water layer was extracted with EtOAc (3×5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed in *vacuo*. Purification (pipette column chromatography, silica, 50-90% DCM in heptane) gave the phosphorylated products. The results are listed in Section 3.3.1.

Note: It was possible to scale the reaction up to 1.0 mmol of substrate without reducing the yield.

Diethyl(phenyl(phenylamino)methyl)phosphonate (**12a**)

The reaction afforded the phosphonate as a white solid.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.44 – 7.52 (m, 2H, H-4, H-6), 7.31 – 7.38 (m, 2H, H-1, H-3), 7.27 – 7.31 (m, 1H, H-2), 7.06 – 7.17 (m, 2H, H-11, H-13), 6.67 – 6.73 (m, 1H, H-12), 6.57 – 6.63 (m, 2H, H-9, H-10), 4.68 – 4.86 (m, 2H, H-7, H-8), 4.04 – 4.20 (m, 2H, H-19 or H-21), 3.95 (dt, *J* = 10.1, 7.1 Hz, 1H, H-19 or H-21), 3.61 – 3.76 (m, 1H, H-19 or H-21), 1.29 (td, *J* = 7.1, 0.6 Hz, 3H, H-20), 1.12 (td, *J* = 7.1, 0.6 Hz, 3H, H-22);



^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ =146.3 (d, $^3J_{P\text{-}C}$ = 14.7 Hz, C-9), 135.9 (d, $^2J_{P\text{-}C}$ = 2.9 Hz, C-5), 129.2 (C-11, C-13), 128.6 (d, $^4J_{C\text{-}P}$ = 2.9 Hz, C-1, C-3), 127.9 (d, $^3J_{C\text{-}P}$ = 5.1 Hz, C-4, C-6), 127.8 (C-2), 118.4 (C-12), 113.9 (C-10, C-14), 63.2 (d, $^2J_{C\text{-}P}$ = 2.9, C-19 or C-21), 63.3 (d, $^2J_{C\text{-}P}$ = 2.9, C-19 or C-21), 56.1 (d, $^1J_{P\text{-}C}$ = 150.4 Hz, C-7), 16.4 (d, $^3J_{C\text{-}P}$ = 5.9 Hz, C-20 or C-22), 16.2 (d, $^3J_{C\text{-}P}$ = 5.9 Hz, C-20 or C-22);

^{31}P (162.0 MHz, C_6D_6): δ = 25.5;

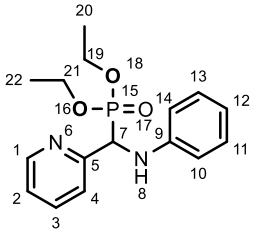
HRMS (ESI): Calc for $C_{17}H_{22}NO_3PNa$ 342.12351, found 342.1262 $[MNa]^+$.

The NMR spectroscopic data is in agreement with the literature.[59]

Diethyl((phenylamino)(pyridine-3-yl)methyl)-phosphonate (**12b**)

The reaction afforded the phosphonate as an orange solid.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 8.61 (d, *J* = 4.8 Hz, 1H, H-1), 7.59 – 7.69 (m, 1H, H-3), 7.51 (d, *J* = 8.0 Hz, 1H, H-4), 7.16 – 7.22 (m, 1H, H-2), 7.09 – 7.16 (m, 2H, H-11, H-13), 6.67 – 6.76 (m, 3H, H-10, H-12, H-14), 5.35 (t, *J* = 7.8 Hz, 1H, NH-8), 4.95 – 5.07 (m, 1H, H-7), 4.10 – 4.23 (m, 2H, H-19 or



H-21), 3.99 – 4.09 (m, 1H, H-19 or H-21), 3.84 – 3.96 (m, 1H, H-19 or H-21), 1.28 (t, *J* = 7.0 Hz, 3H, H-20 or H-22), 1.17 (t, *J* = 7.09 Hz, 3H, H-20 or H-22);

^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 155.9 (d, $^{2}J_{C-P}$ = 1.5 Hz, C-5), 149.2 (d, $^{4}J_{C-P}$ = 2.2 Hz, C-1), 146.5 (d, $^{3}J_{C-P}$ = 11.7 Hz, C-9), 136.6 (C-2), 129.1 (C-11, C-13), 122.8 (d, $^{4}J_{C-P}$ = 3.7 Hz, C-3), 122.7 (d, $^{3}J_{C-P}$ = 8.1 Hz, C-4), 118.5 (C-12), 114.0 (C-10, C-14), 63.5 (d, $^{2}J_{C-P}$ = 6.6, C-19 or C-21), 63.2 (d, $^{2}J_{C-P}$ = 7.3, C-19 or C-21), 58.0 (d, $^{1}J_{C-P}$ = 151.2 Hz, C-7), 16.4 (d, $^{3}J_{C-P}$ = 5.9 Hz, C-20 or C-22), 16.2 (d, $^{3}J_{C-P}$ = 5.9 Hz, C-20 or C-22);

^{31}P (162.0 MHz, C_6D_6): δ = 24.1;

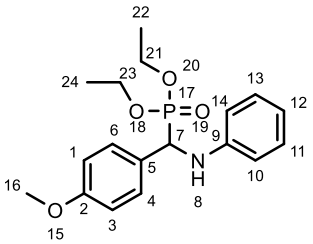
HRMS (ESI): Calc for $C_{16}H_{21}N_2O_3PNa$ 343.1187, found 343.1181 $[MNa]^+$.

The NMR spectroscopic data is in agreement with the literature.[60]

Diethyl((4-methoxyphenyl)(phenylamino)methyl)-phosphonate (**12c**)

The reaction afforded the phosphonate as a white solid.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.32 – 7.47 (m, 2H, H-4, H-6), 7.06 – 7.16 (m, 2H, H-11, H-13), 6.87 (d, *J* = 8.3 Hz, 2H, H-1, H-3), 6.70 (tt, *J* = 7.3, 1.0 Hz, 1H, H-12), 6.60 (d, *J* = 8.6 Hz, 2H, H-10, H-14), 4.63 – 4.79 (m, 2H, H-7, NH-8), 4.04 – 4.20 (m, 2H, H-21 or H-23), 3.87 – 3.99 (m, 1H, H-21 or H-23), 3.79 (s, 3H, H-16); 3.67 – 3.75 (m, 1H, H-21 or H-23), 1.31 (t, *J* = 7.1 Hz, 3H, H-22 or H-24), 1.15 (td, *J* = 7.1 Hz, 3H, H-22 or H-24);



^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 146.5 (C-2), 132.7 (d, $^{3}J_{C-P}$ = 14.7 Hz, C-9), 129.1 (C-11, C-13), 128.9 (d, $^{3}J_{C-P}$ = 5.1 Hz, C-4, C-6), 127.7 (d, $^{2}J_{C-P}$ = 2.9 Hz, C-5), 118.4 (C-12), 114.1 (d, $^{4}J_{C-P}$ = 2.9 Hz, C-1, C-3), 113.9 (C-10, C-14), 63.3 (d, $^{2}J_{C-P}$ = 6.6 Hz, C-21 or C-23), 63.2 (d, $^{2}J_{C-P}$ = 6.6 Hz, C-21 or C-23), 56.4 (d, $^{1}J_{C-P}$ = 150.1 Hz, C-7), 55.2 (C-16), 16.4 (d, $^{3}J_{C-P}$ = 5.9 Hz, C-22 or C-24), 16.3 (d, $^{3}J_{C-P}$ = 5.9 Hz, C-23 or C-24);

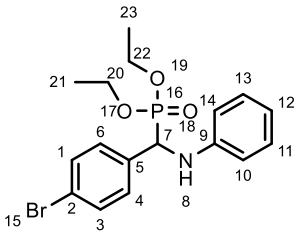
^{31}P (162.0 MHz, C_6D_6): δ = 25.8.

The NMR spectroscopic data is in agreement with the literature.[61]

Diethyl((4-bromophenyl)(phenylamino)methyl)-phosphonate (**12d**)

The reaction afforded the phosphonate as a white solid.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.35 – 7.44 (m, 2H, H-1, H-3), 7.22 – 7.31 (m, 2H. H-4, H-6), 6.97 – 7.10 (m, 2H, H-11, H-13), 6.56 – 6.71 (m, 1H, H-12), 6.42 – 6.53 (m, 2H, H-10, H-14), 4.54 – 4.74 (m, 2H, H-7, H-8), 3.98 – 4.18 (m, 3H, H-20 or H-22), 3.62 – 3.78 (m, 1H, H-20 or H-22), 1.22 (t, *J* = 7.1 Hz, 3H, H-21 or H-23), 1.09 (t, *J* = 7.1 Hz, 3H, H-21 or H-23);



^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 146.1 (d, $^{3}J_{C-P}$ = 14.7 Hz, C-9), 135.2 (d, $^{2}J_{C-P}$ = 2.9 Hz, C-5), 131.7 (d, $^{4}J_{C-P}$ = 2.9 Hz, C-1, C-3), 129.5 (d, $^{3}J_{C-P}$ = 5.1 Hz, C-4, C-6), 129.2 (C-11, C-13), 121.8 (C-2), 118.7 (C-12), 113.9 (C-10, C-14), 63.4 (d, $^{2}J_{C-P}$ = 7.3 Hz, C-20 or C-22), 63.3 (d, $^{2}J_{C-P}$ = 7.3 Hz, C-20 0r C-22), 55.7 (d, $^{1}J_{C-P}$ = 150.1 Hz, C-7), 16.4 (d, $^{3}J_{C-P}$ = 5.9 Hz, C-21 or C-23), 16.2 (d, $^{3}J_{C-P}$ = 5.9 Hz, C-21 or C-23);

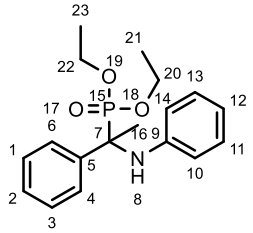
^{31}P (162.0 MHz, C_6D_6): δ = 25.6;

The NMR spectroscopic data is in agreement with the literature.[62]

Diethyl (1-phenyl-1-(phenylamino)ethyl)phosphonate (**13a**)

The reaction afforded the phosphonate as a white solid.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.60 – 7.64 (m, 2H, H-1, H-3), 7.28 – 7.34 (m, 2H, H-4, H-6), 7.02 (t, *J* = 7.89 Hz, 2H, H-11 H-13), 6.69 (t, *J* = 7.34 Hz, 1H, H-2), 6.41 (d, *J* = 7.95 Hz, 2H, H-10, H-14), 4.76 (d, *J* = 11.25 Hz, 1H, H-12), 3.88 – 4.07 (m, 3 H), 3.83 (dd, *J* = 8.38, 7.15 Hz, 1H, NH-8), 2.01 (d, *J* = 16.51 Hz, 3H, H-16), 1.36 (dt, *J* = 16.26, 7.09 Hz, 6H, H-21, H-23);



^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 148.9 (C-9), 142.5 (C-5), 128.6 (C-2), 128.2 (C-11, C-13), 128.1 (d, $^{3}J_{C-P}$ = 5.1 Hz, C-4, C-6), 127.3 (d, $^{4}J_{C-P}$ = 2.9 Hz, C-1, C-3), 118.3 (C-12), 116.7 (C-10, C-14), 63.5 (d, $^{2}J_{C-P}$ = 7.7 Hz, C-20 or C-22), 63.4 (d, $^{2}J_{C-P}$ = 7.7 Hz, C-20 or C-22), 56.9 (d, $^{1}J_{P-C}$ = 150.9 Hz, C-7), 20.1 (d, $^{2}J_{C-P}$ = 2.9 Hz, C-16), 16.4 (d, $^{3}J_{C-P}$ = 5.5 Hz, C-21 or C-23), 16.3 (d, $^{3}J_{C-P}$ = 5.5 Hz, C-21 or C-23);

^{31}P (162.0 MHz, C_6D_6): δ = 35.1.

The NMR spectroscopic data is in agreement with the literature.[62]

5.3.3. Intramolecular Hydroamination[15,19,22,63]

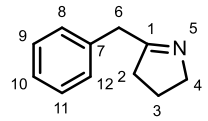
In an argon filled glovebox, a screw cap NMR tube was charged with an aminoalkyne (330 µmol) and hexamethylbenzene (6.4 mg, 4 µmol) as internal standard. After dissolving the

reagents in benzene-d_6 (0.5 mL) the catalyst (3-5 µmol) was added. The NMR tube was sealed, removed from the glovebox and placed in an oil bath with the desired temperature. The progress of the catalysis was monitored *via* ^{1}H NMR spectroscopy. To quench the reaction, EtOAc (2 mL) was added and the solution was filtered through silica (prior to its use the silica was washed with EtOAc/NEt_3=100:1). Remal of the solvent in *vacuo* led to the pure cyclic amine asa yellow oil. The results are listed in section 3.4.1.

3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole (**14a**)

The reaction afforded the cyclic imine as yellow oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.28 – 7.35 (m, 2H, H-9, H-11), 7.19 – 7.27 (m, 3H, H-8, H-10, H-12), 3.84 (t, *J* = 7.3 Hz, 2H, H-4), 3.69 (s, 2H, H-6), 2.40 (t, *J* = 8.2 Hz, 2H, H-2), 1.78 – 1.88 (m, 2H, H-3);



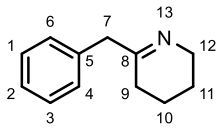
^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 176.7 (C-1), 137.0 (C-7), 129.0 (C-8, C-12), 128.6 (C-9, C-11), 126.6 (C-10), 61.0 (C-4), 40.7 (C-6), 36.5 (C-2), 22.6 (C-3).

The NMR spectroscopic data is in agreement with the literature.[22]

3,4,5,6-Tetrahydro-2-(phenylmethyl)pyridine (**14b**)

The reaction afforded the cyclic imine as a yellow oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.07 – 7.14 (m, 2H, H-1, H-3), 6.96 – 7.07 (m, 3H, H-2, H-4, H-6), 3.39 – 3.51 (m, 2H, H-12), 3.29 (s, 2H, H-7), 1.57 – 1.68 (m, 2H, H-9), 1.41 – 1.57 (m, 4H, H-10, H-11).



^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 169.2 (C-8), 137.6 (C-5), 131.6 (C-4, C-6), 128.2 (C-1, C-3), 127.5 (C-2), 49.2 (C-12), 48.8 (C-7), 27.9 (C-9), 25.0 (C-11), 19.0 (C-10).

The NMR spectroscopic data is in agreement with the literature.[22]

5.3.4. One-Pot Synthesis of Amino Phosphonates[10]

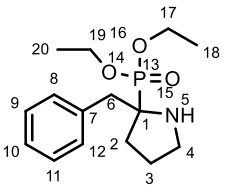
In an argon filled glovebox, a screw cab NMR tube was charged with an aminoalkyne (170 µmol) and hexamethylbenzene (6.4 mg, 4 µmol) as internal standard. After dissolving the reagents in benzene-d_6 (0.5 mL), the catalyst (3-10 µmol) was added. The NMR tube was sealed, removed from the glovebox and placed in an oil bath at the desired temperature. The progress of the reaction was monitored *via* ^{1}H-NMR spectroscopy. After complete consumption of the substrate, the NMR tube was again brought into the glovebox and diethylphosphite (25.7 mg, 24 µL, 1.072 g/mL 190 µmol) was added and the reaction mixture was placed again in an oil bath and monitored *via* ^{1}H-NMR spectroscopy. To quench the

reaction EtOAc (2 mL) was added and the solution was filtered through silica (prior to its use the silica was washed with EtOAc/NEt_3=100:1). Removing of the solvent under vacuum led to the crude product as a yellow oil. After purification *via* pipette column (silica, 5-95% EtOAc and 1% Et_3N in heptane) the amino phosphonates were obtained as slightly yellow solids in yields of up to 98%. The results are listed in section 3.4.1.

Diethyl(2-benzylpyrrolidin-2-yl)phosphonate (**12a**)

The reaction afforded the cyclic α-amino phosphonate as colourless oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.23 – 7.32 (m, 5H, H-8, H-9, H-10, H-11, H-12), 4.08 – 4.21 (m, 4H, H-17, H-19), 3.06 (dd, *J* = 13.5, 10.2 Hz, 1H, H-6), 2.96 (dd, *J* = 13.5,10.2 Hz, 1H, H-6), 2.82 - 2.91 (m, 1H, H-4), 2.70 – 2.76 (m, 1H, H-4), 2.10 – 2.25 (m, 1H, H-2), 1.80 – 1.93 (m, 1H, H-2), 1.64 – 1.75 (m, 3H, H-3, H-5), 1.27 – 1.35 (m, 6H, H-18, H-20);



^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 136.5 (d, $^3J_{C\text{-}P}$ = 11.7 Hz, C-7), 130.9 (C-9, C-11), 128.1 (C-8, C-12), 126.6 (C-10), 63.3 (d, $^1J_{C\text{-}P}$ = 167.6 Hz, C-1), 62.5 (d, $^2J_{C\text{-}P}$ = 7.3 Hz, C-17 or C-19), 62.2 (d, $^2J_{C\text{-}P}$ = 7.3 Hz, C-17 or C-19), 47.2 (d, $^3J_{C\text{-}P}$ = 6.6 Hz, C-4), 41.2 (d, $^2J_{C\text{-}P}$ = 8.1 Hz, C-6), 31.4 (d, $^3J_{C\text{-}P}$ = 2.2 Hz, C-3), 25.8 (d, $^2J_{C\text{-}P}$ = 4.4 Hz, C-3), 16.5 (d, $^3J_{C\text{-}P}$ = 5.1 Hz, C-18, C-20):

^{131}P (162.0 MHz, C_6D_6): δ = 32.0;

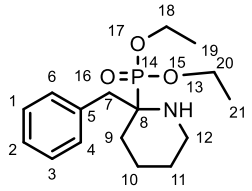
HRMS (ESI): Calc for $C_{15}H_{24}NO_3PNa$ 320.1391, found 320.1382 $[MNa]^+$.

The NMR spectroscopic data is in agreement with the literature.[10]

Diethyl(2-benzylpiperidin-2-yl)phosphonate (**12b**)

The reaction afforded the cyclic α-amino phosphonate as colourless oil.

^{1}H NMR (400.3 MHz, $CDCl_3$): δ = 7.26 – 7.30 (m, 5H, H-1, H-2, H-3, H-4, H-6), 4.13 – 4.20 (m, 2H, H-18 or H-20), 3.86 – 4.03 (m, 2H, H-18 or H-20), 3.10 – 3.23 (m, 1H, H-7), 2.93 – 3.09 (m, 3H, H-7, H-12), 1.93 – 2.11 (m, 2H, H-9), 1.71 – 1.83 (m, 3H, H-11), 1.49 – 1.56 (m, 2H, H-10), 1.25 (t, *J* = 7.1 Hz, 3H, H-19 or H-21), 1.13 (t, *J* = 7.09 Hz, 3H, H-19 or H-21).



^{13}C {^{1}H} NMR (100.7 MHz, $CDCl_3$): δ = 136.4 (d, $^3J_{C\text{-}P}$ = 11.7 Hz, C-5), 131.0 (C-1, C-3), 127.8 (C-4, C-6), 126.3 (C-2), 62.2 (d, $^2J_{C\text{-}P}$ =7.3 Hz, C-18 or C-20), 61.5 (d, $^2J_{C\text{-}P}$ = 7.3 Hz, C-18 or C-20), 57.3 (d, $^1J_{C\text{-}P}$ = 154.3 Hz, C-8), 41.2 (d, $^3J_{C\text{-}P}$ = 9.5 Hz, 2H,

C-12), 39.2 (d, $^{4}J_{C\text{-}P}$ = 4.4 Hz, C-11), 29.6 (C-10), 25.5 (C-9), 19.9 (d, $^{2}J_{C\text{-}P}$ = 8.1 Hz, C-7), 16.5 (d, $^{3}J_{C\text{-}P}$ = 6.0 Hz, C-19 or C-21), 16.2 (d, $^{3}J_{C\text{-}P}$ = 6.0 Hz, C-19 or C-21);

^{31}P (162.0 MHz, C_6D_6): δ = 32.4;

HRMS (ESI): Calc for $C_{16}H_{26}NO_3PNa$ 334.1548, found 334.1534 $[MNa]^+$.

The NMR spectroscopic data is in agreement with the literature.[10]

5.3.5. One-Pot Synthesis of Ethylated Amines

In an argon filled glovebox, a screw cab NMR tube was charged with an aminoalkyne (170 µmol) and hexamethylbenzene (6.4 mg, 4 µmol) as internal standard. After dissolving the reagents in benzene-d_6 (0.5 mL) the catalyst (10 µmol) was added. The NMR tube was sealed, removed from the glovebox and was placed in an oil bath with the desired temperature. The progress of the reaction was monitored *via* ^{1}H-NMR. After complete consumption of the substrate triethylaluminium (190 µmol) was added and the reaction mixture was placed again in an oil bath and monitored *via* ^{1}H-NMR.

2-(1-phenylpropyl)pyrrolidine (**16a**)

The reaction only led to <5% of alkylated product, unreacted starting material, as well as reduction product were observed.

2-(1-phenylpropyl)piperidine (**16b**)

The reaction only led to <5% of alkylated product, unreacted starting material, as well as reduction product were observed.

6. Literature

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7. Appendix

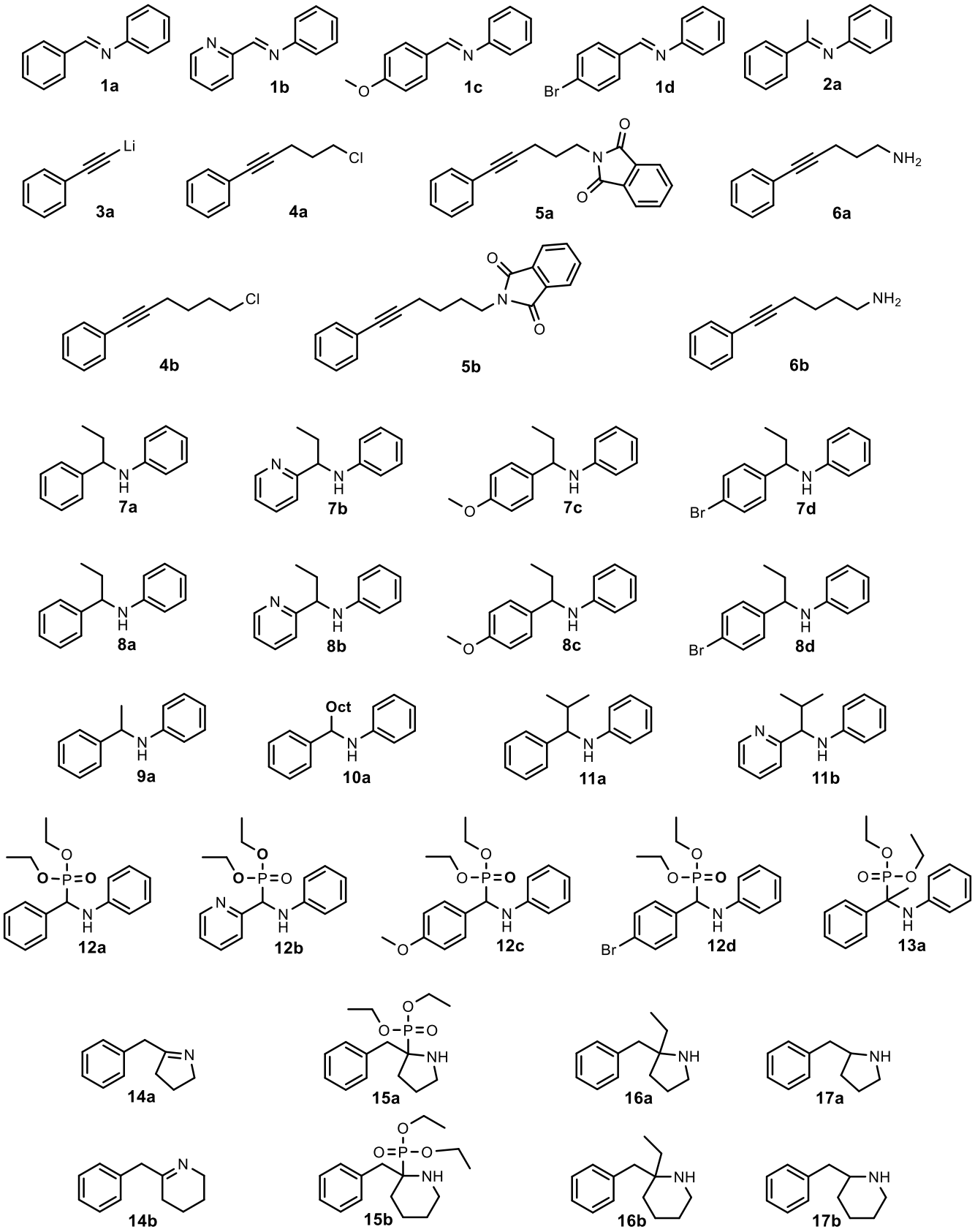
7.1. Figures

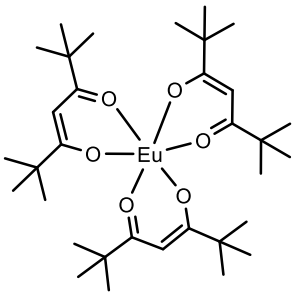
6.2. Schemes

7.3. Tables

7.4. Supplementary Information

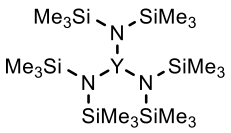
7.4.1. Overview Substrates, Products and Catalysts





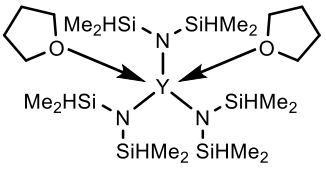
[Eu(dpm)$_3$]

C1



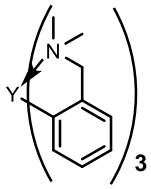
[Y(N(SiMe$_3$)$_2$)$_3$]

C2



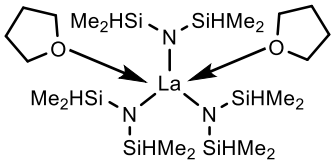
[Y(N(SiHMe$_2$)$_2$)$_3$(THF)$_2$]

C3



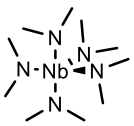
[Y(BDMA)$_3$]

C4



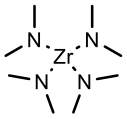
[La(N(SiHMe$_2$)$_2$)$_3$(THF)$_2$]

C5



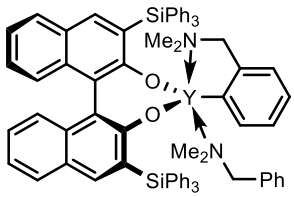
[Nb(NMe$_2$)$_5$]

C6



[Zr(NMe$_2$)$_4$]

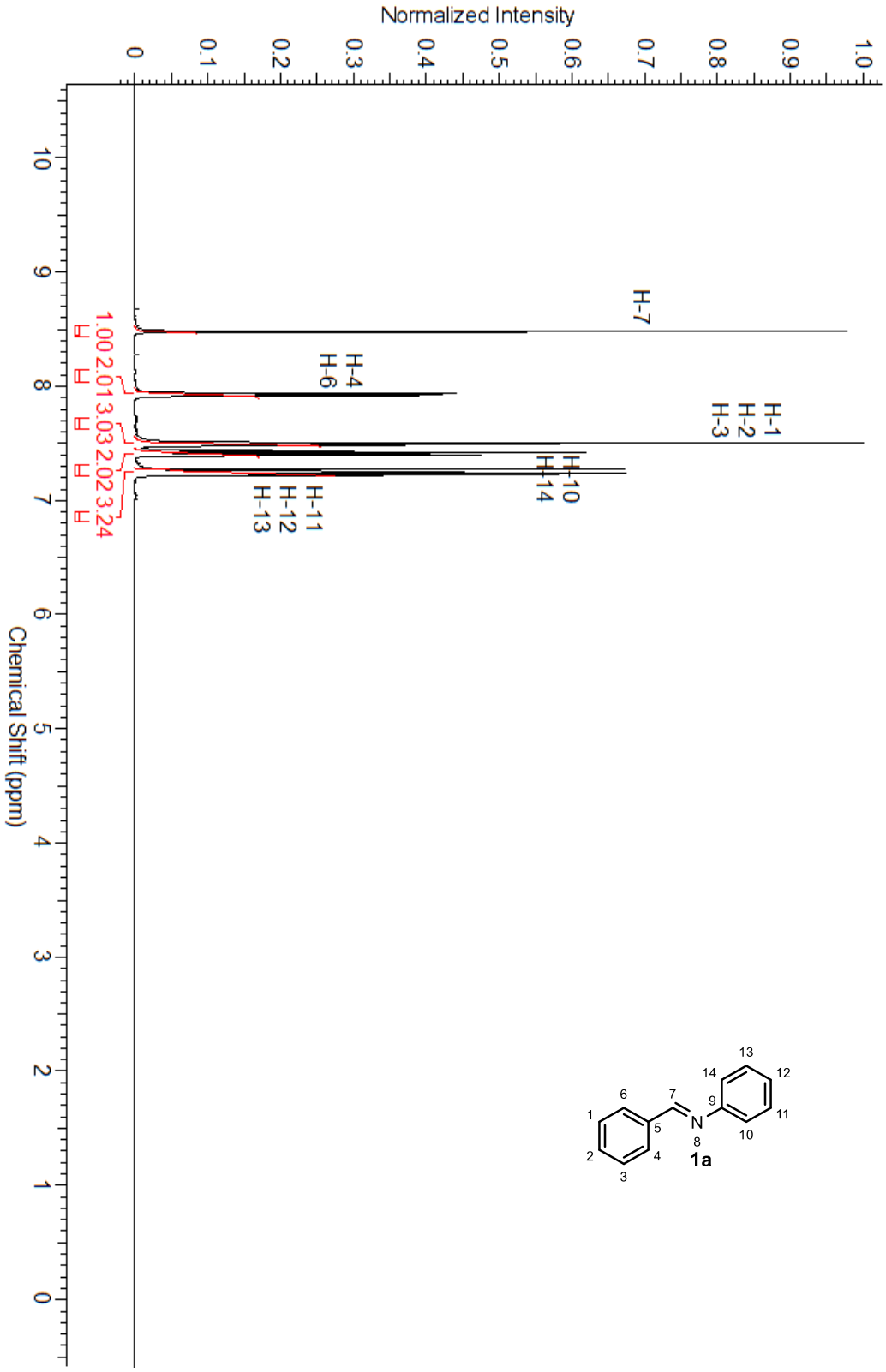
C7



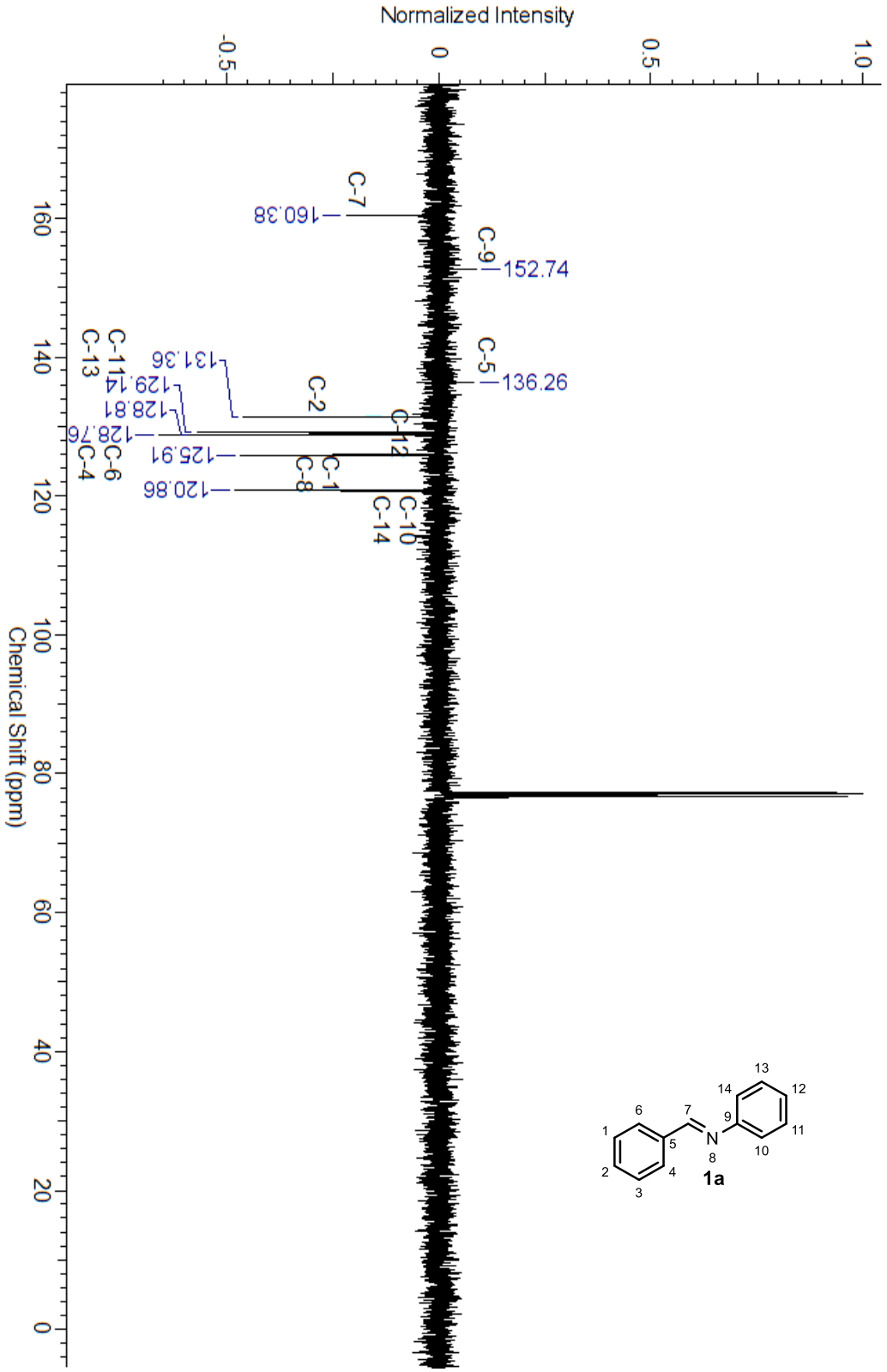
[Y((S)-binol-SiPh$_3$)(o-C$_6$H$_4$CH$_2$NMe$_2$) (Me$_2$NCH$_2$Ph)]

C8

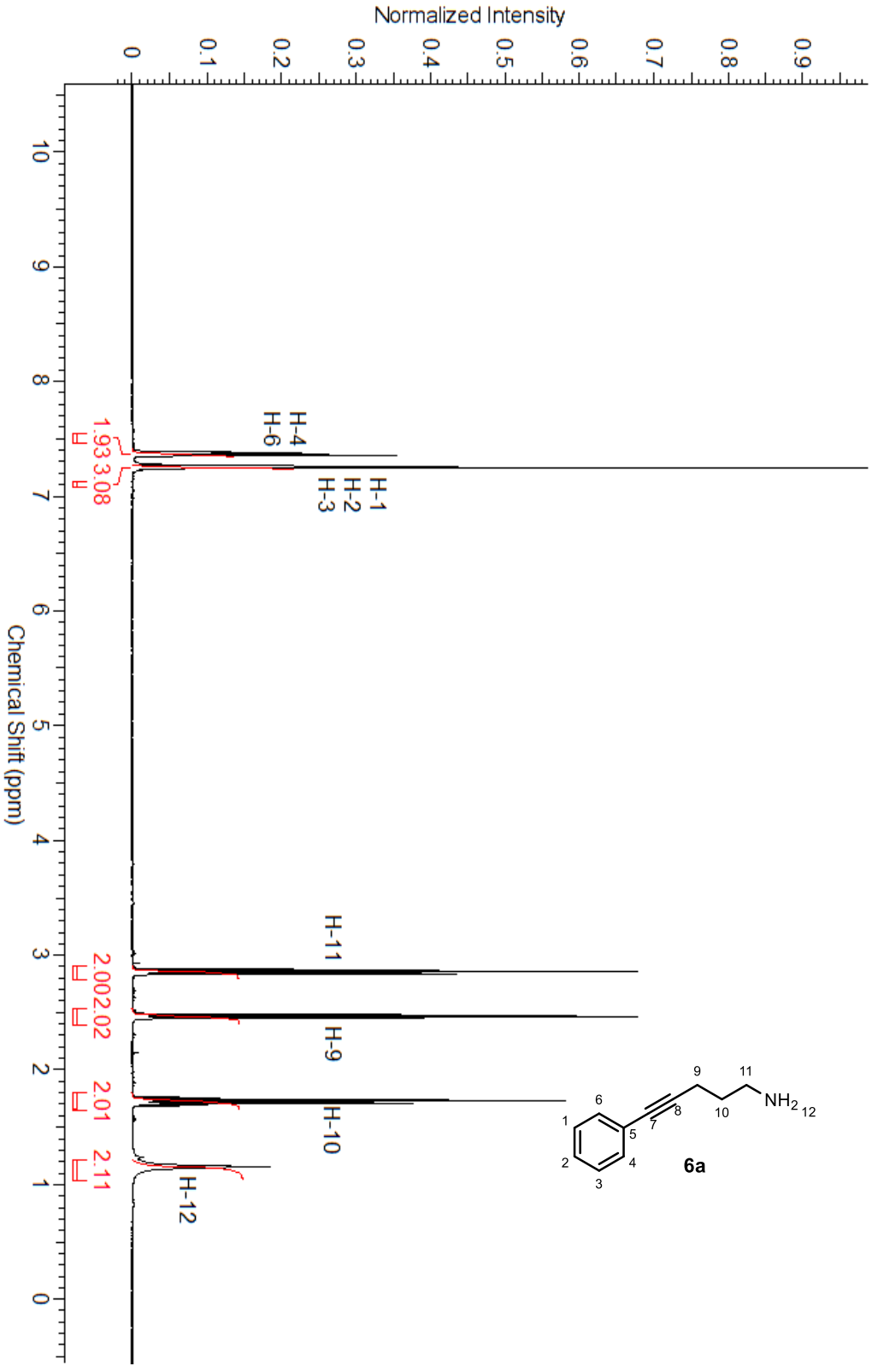
7.4.2. NMR-Spectra



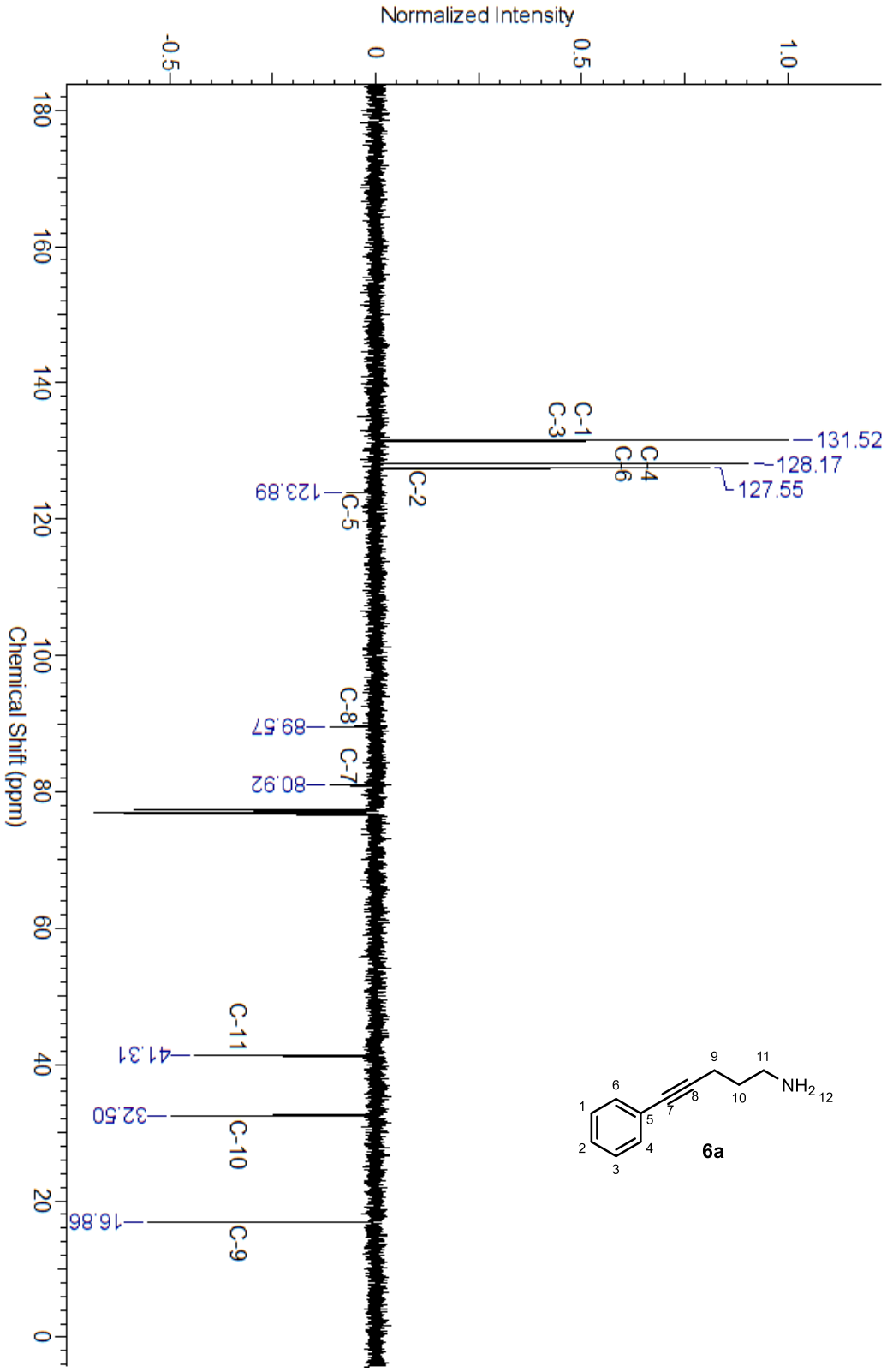
Sup. 1: ^{1}H-NMR spectrum of N-(Phenylmethylene)benzenamine (**1a**); solvent: $CDCl_3$, 400.3 MHz.



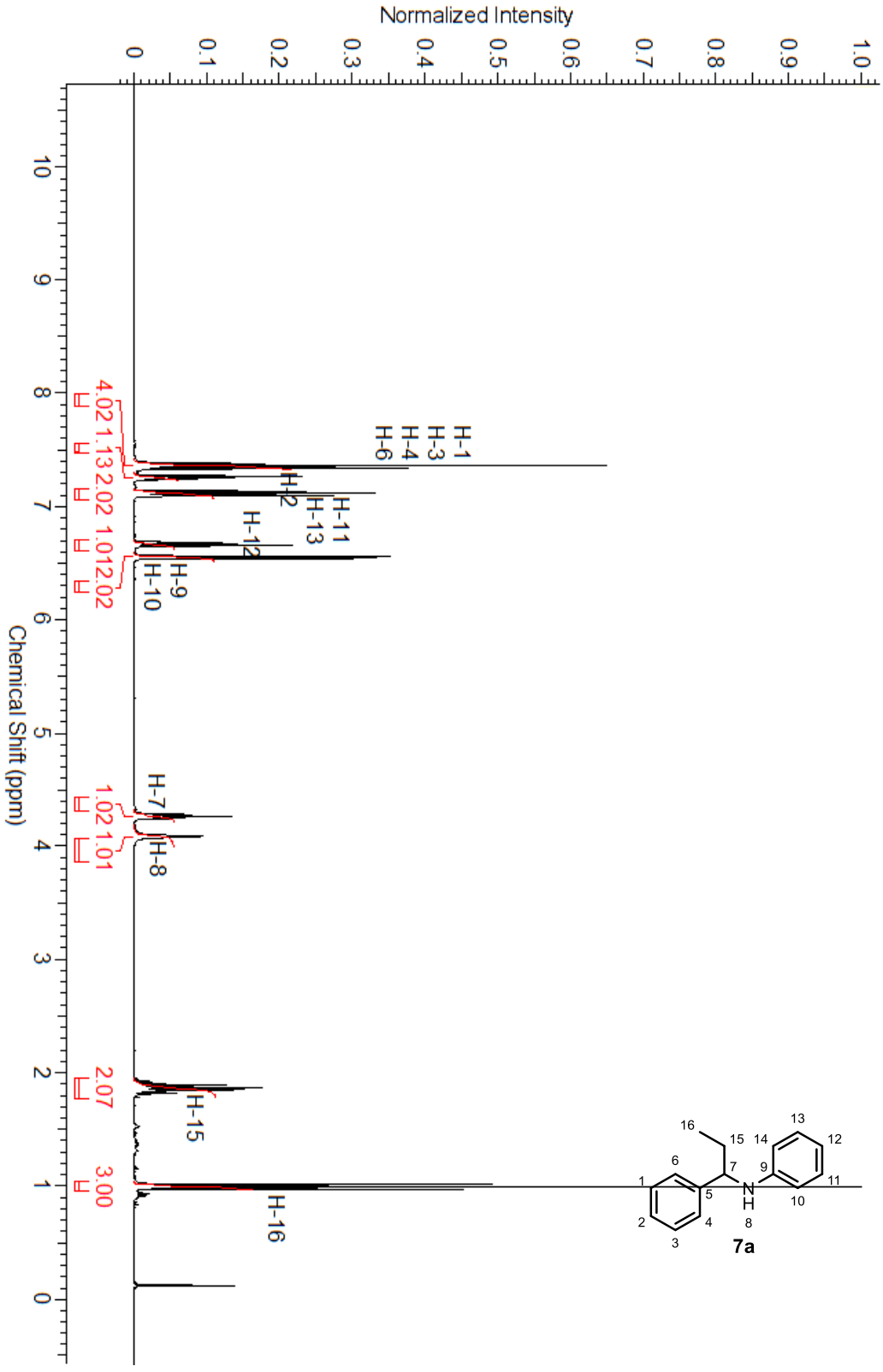
Sup. 2: ^{13}C-NMR (ATP) spectrum of N-(Phenylmethylene)benzenamine (**1a**); solvent: $CDCl_3$, 100.7 MHz.



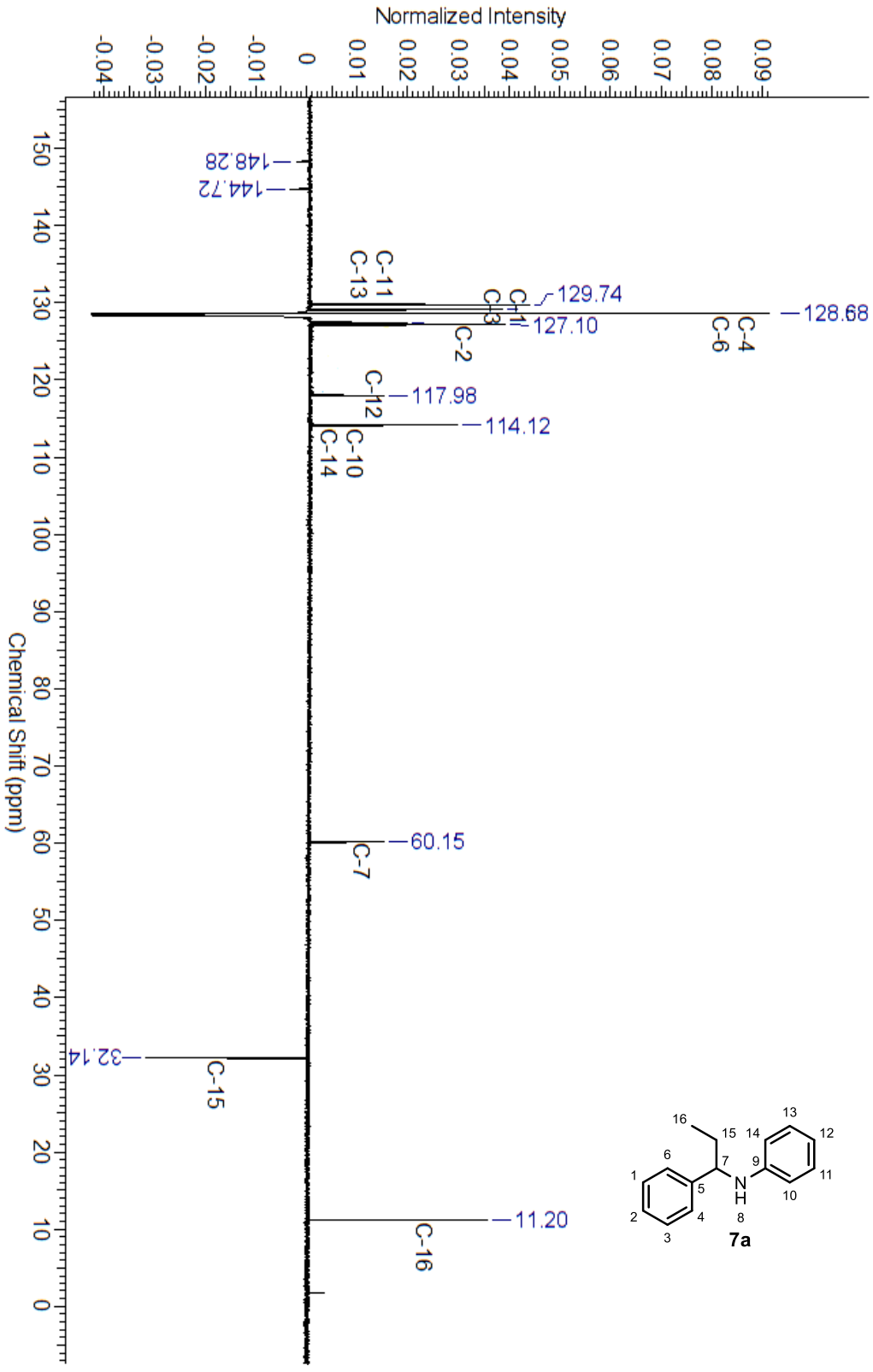
Sup. 3: ^{1}H-NMR spectrum of 5-Phenyl-4-pentyn-1-amine (**6a**);
solvent: $CDCl_3$, 400.3 MHz.



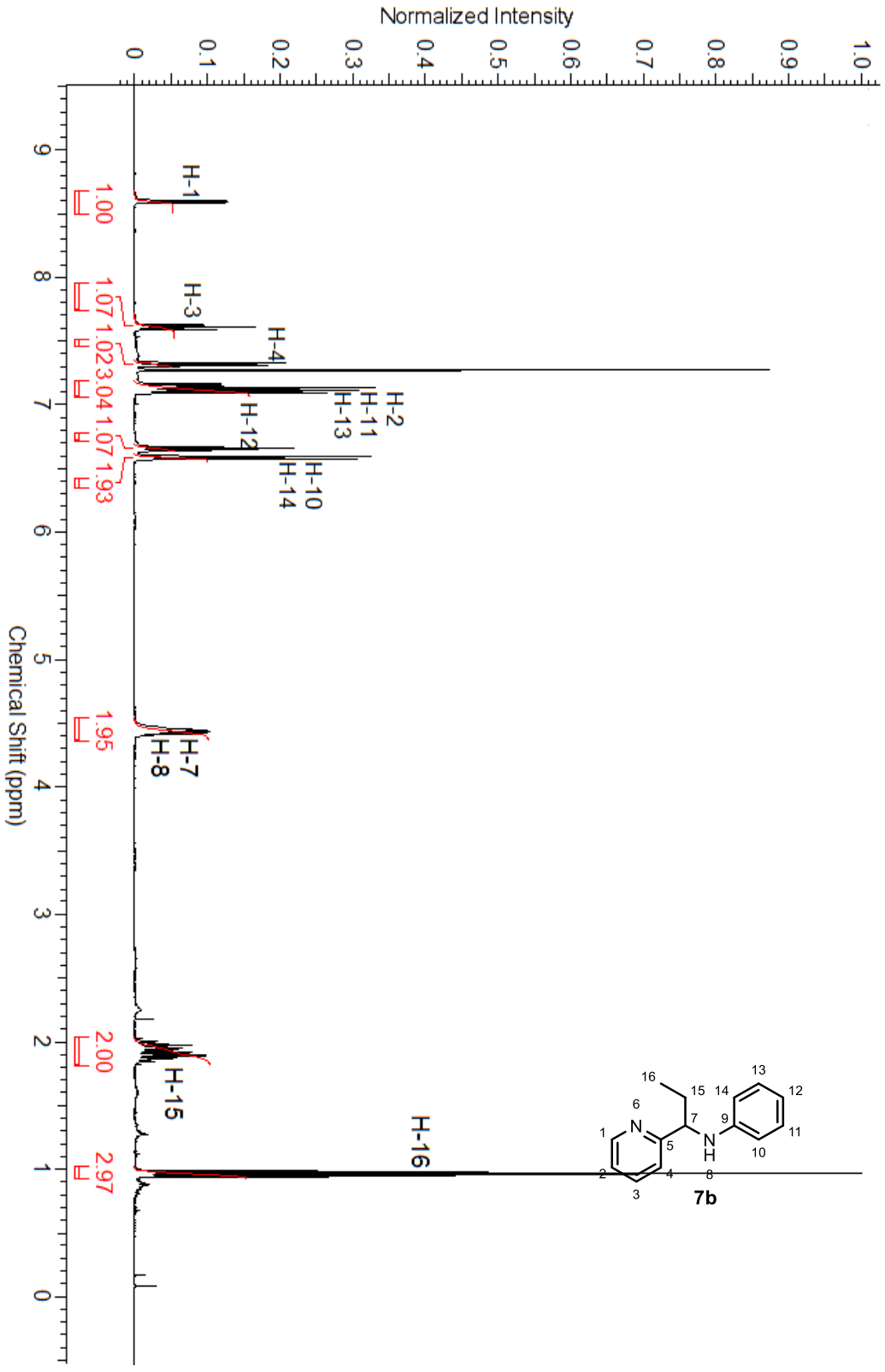
Sup. 4: ^{13}C-NMR (ATP) spectrum of 5-Phenyl-4-pentyn-1-amine (**6a**); solvent: $CDCl_3$, 100.7 MHz.



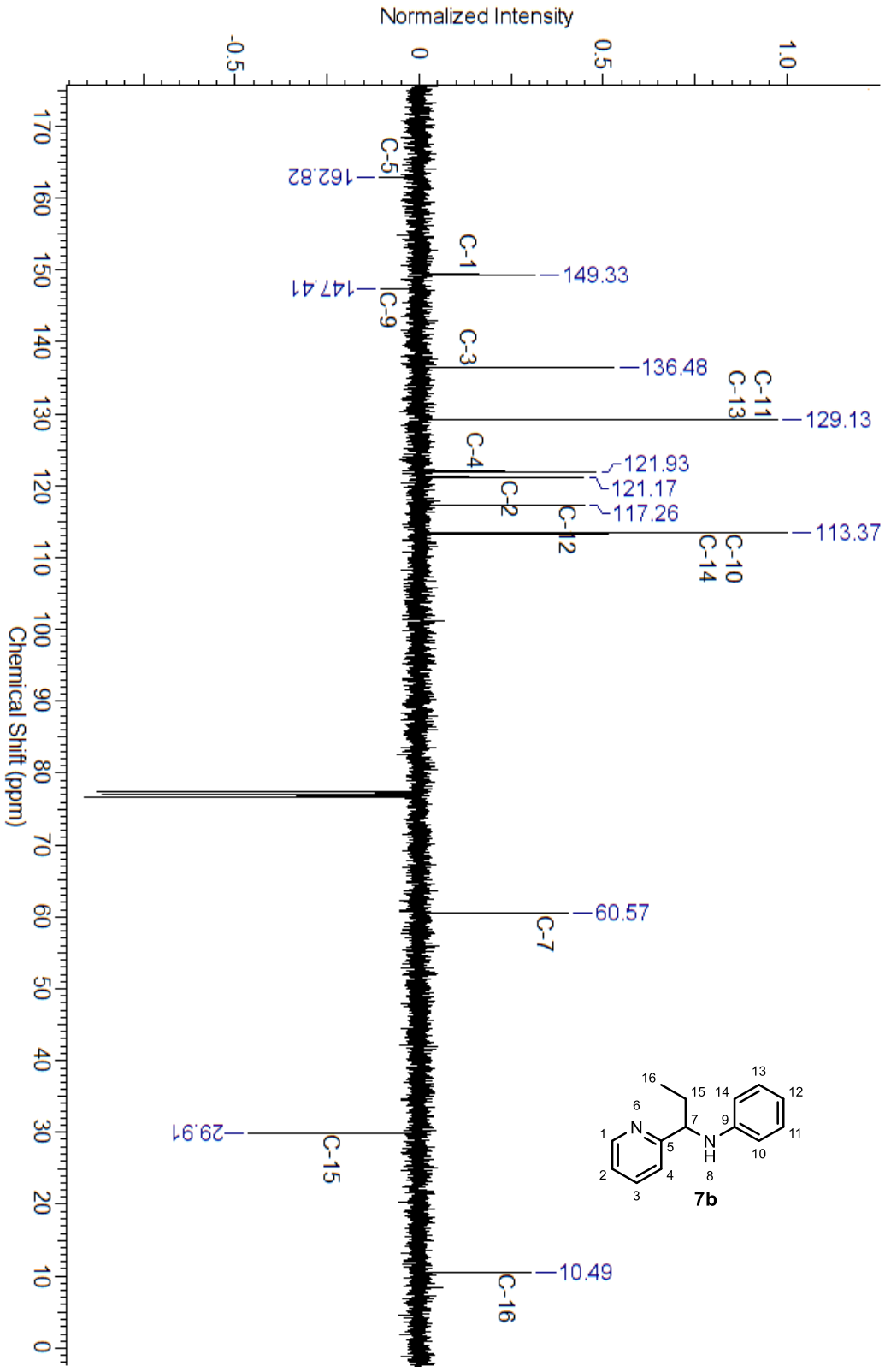
Sup. 5: ^{1}H-NMR spectrum of α-Ethyl-N-phenylbenzenemethanamine (**7a**); solvent: $CDCl_3$, 400.3 MHz.



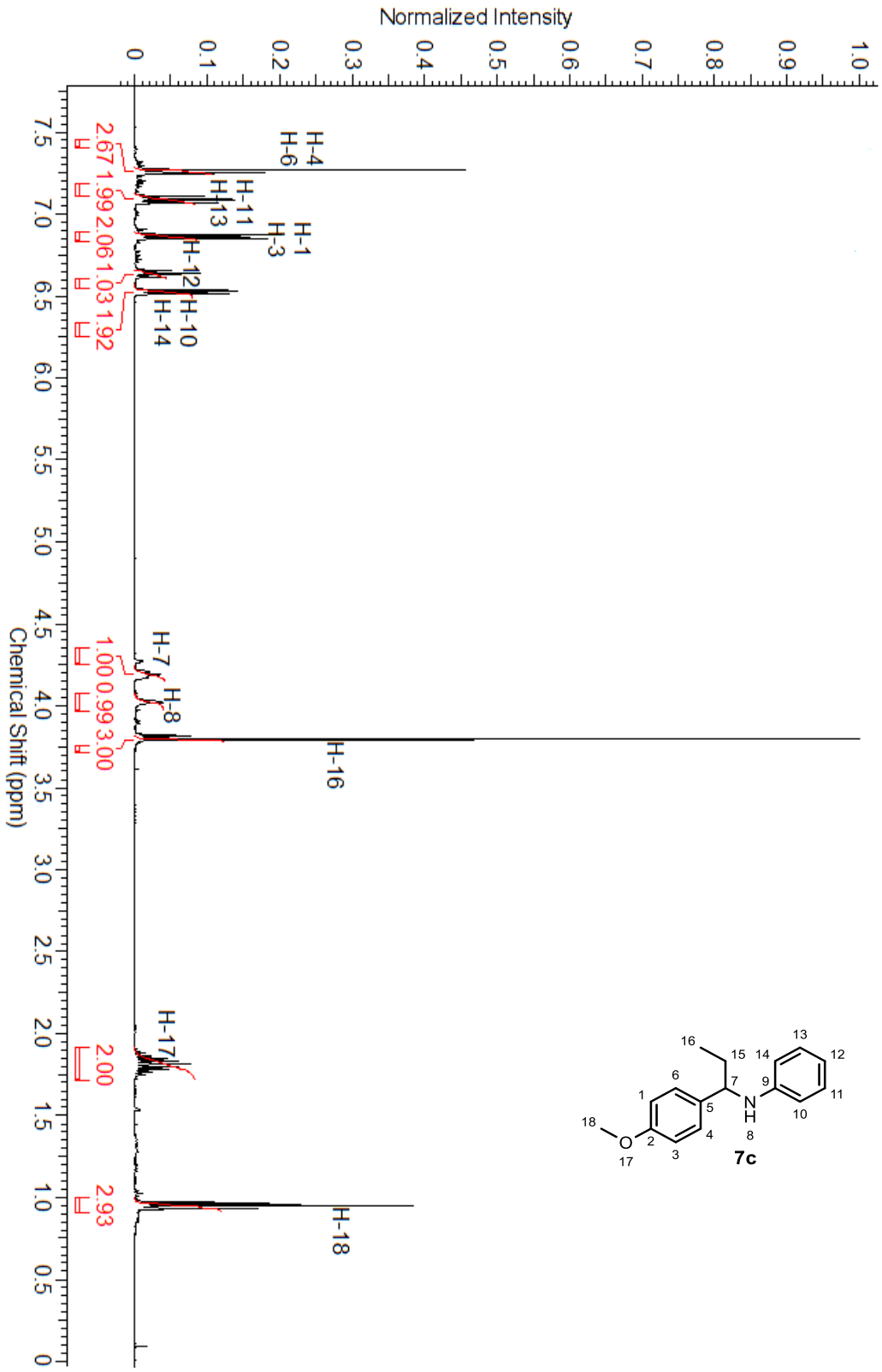
Sup. 6: ^{13}C- NMR (ATP) spectrum of α-Ethyl-N-phenylbenzenemethanamine (**7a**); solvent: C_6D_6, 150.9 MHz.



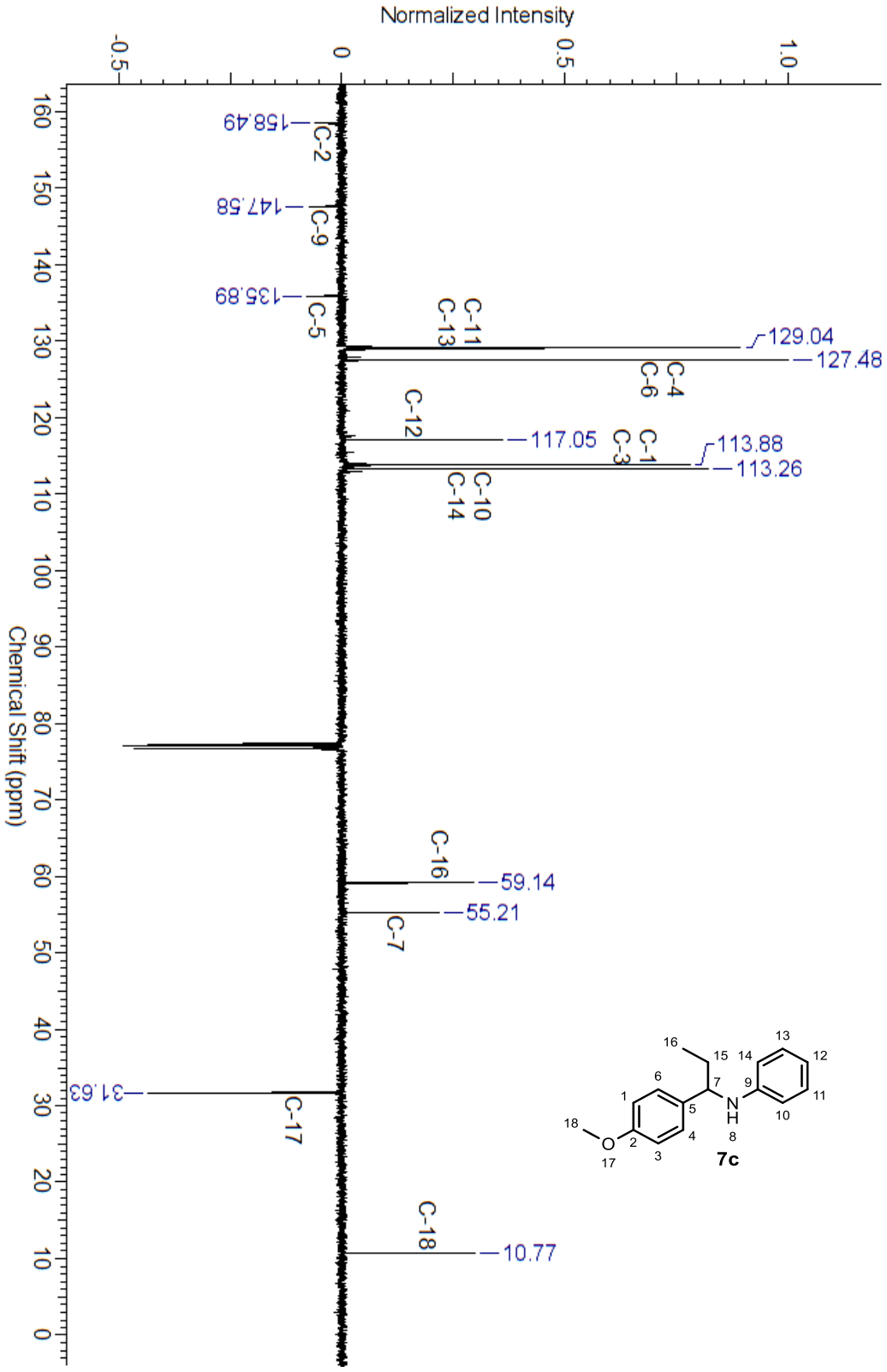
Sup. 7: ^{1}H-NMR spectrum of α-Ethyl-N-pheny-2-pyridinemethanamine (**7b**); solvent: $CDCl_3$, 400.3 MHz.



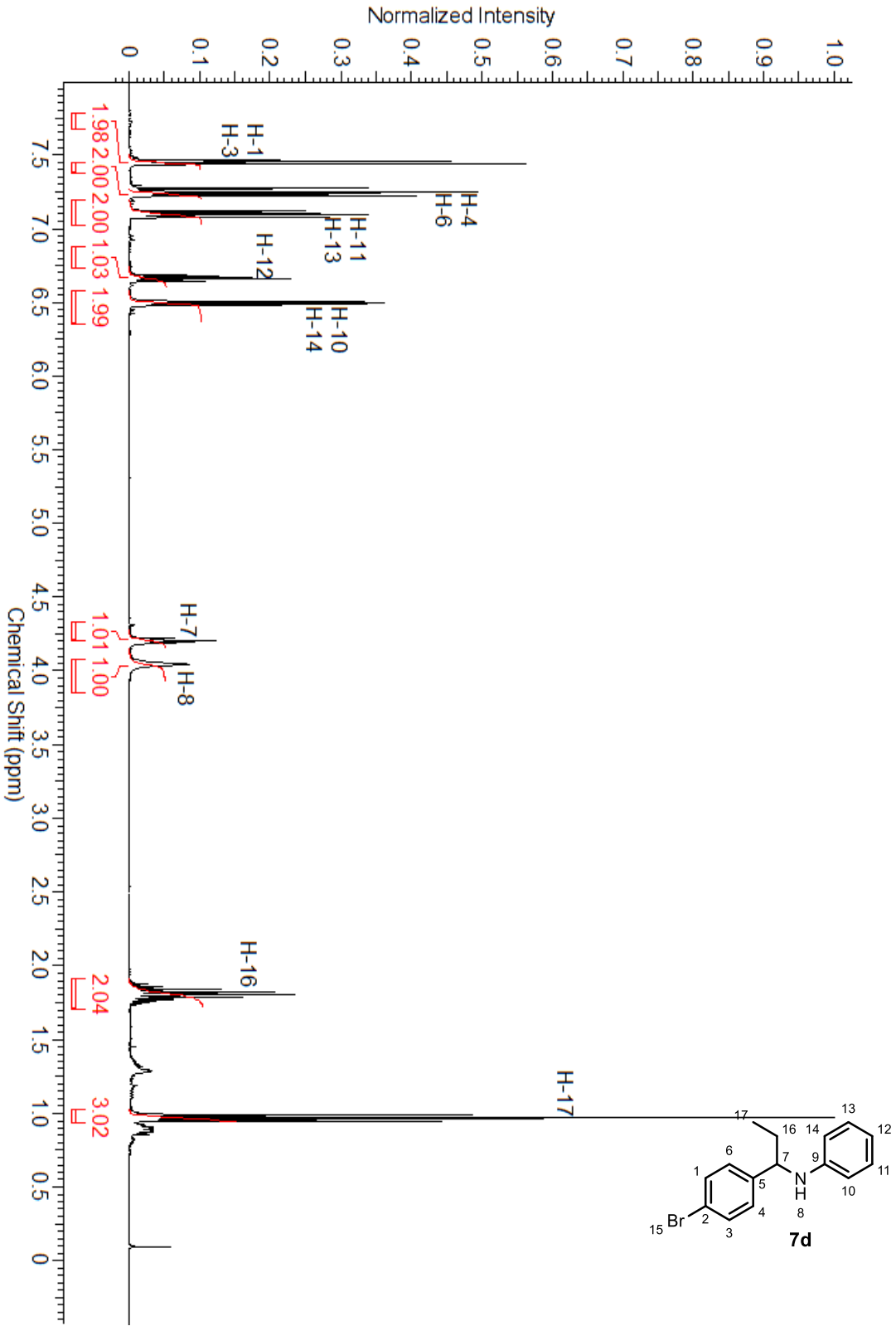
Sup. 8: Sup. 9: ^{13}C- NMR (ATP) spectrum of α-Ethyl-N-pheny-2-pyridinemethanamine (**7b**); solvent: $CDCl_3$, 100.7 MHz.



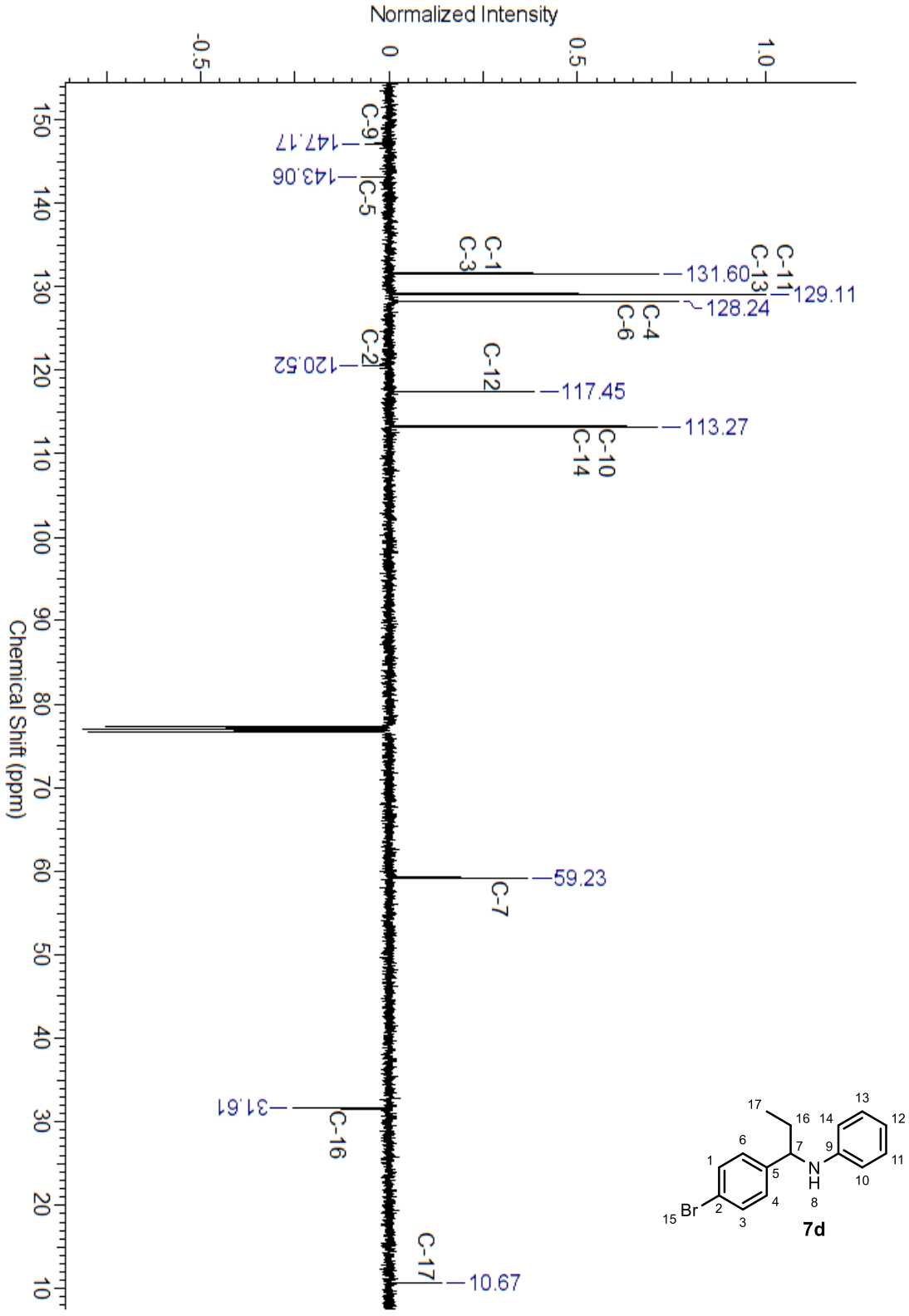
Sup. 10: ^{1}H-NMR spectrum of α-Ethyl-4-methoxy-N-phenylbenzenemethanamine (**7c**); solvent: $CDCl_3$, 400.3 MHz.



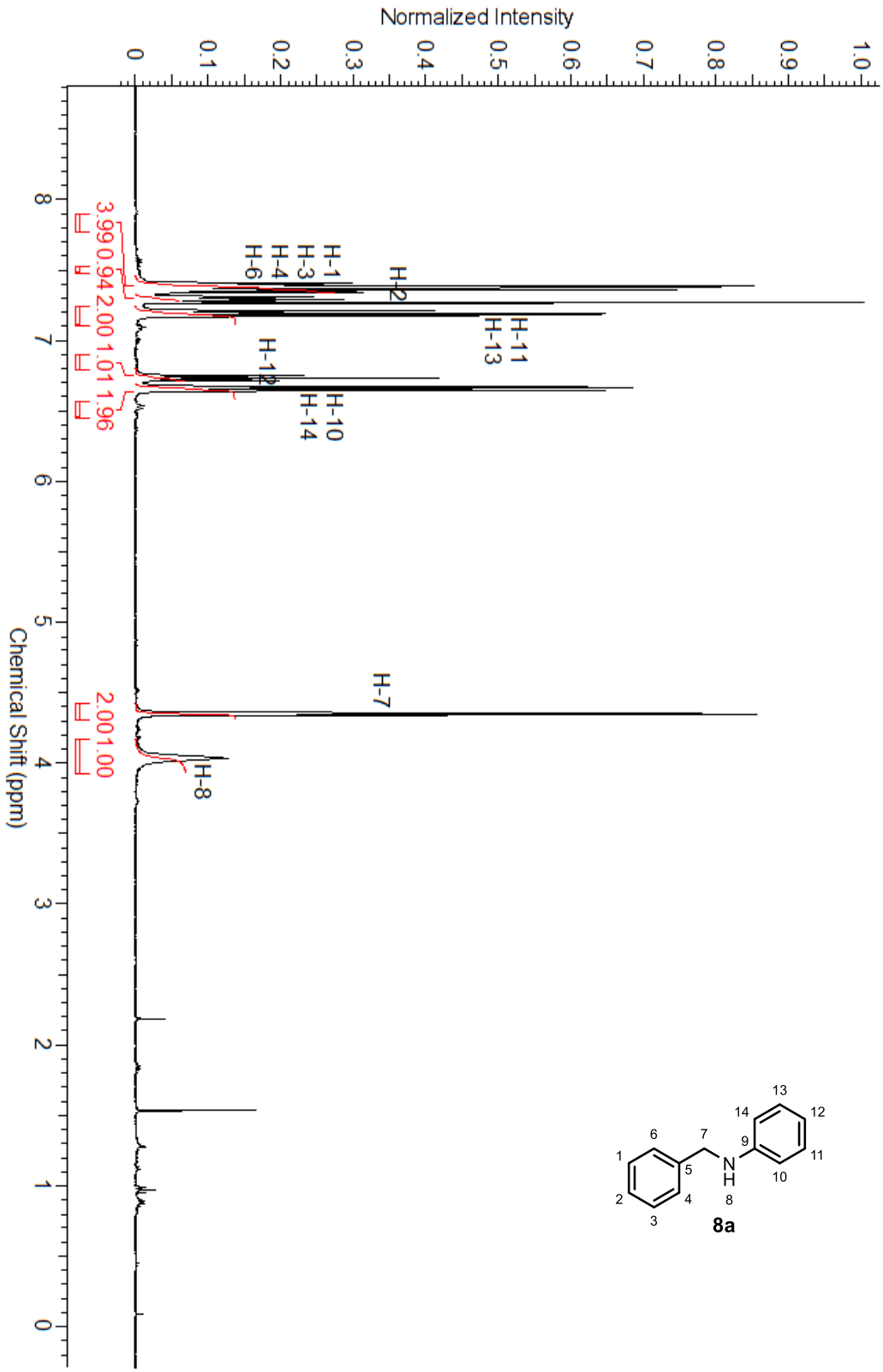
Sup. 11: ^{13}C- NMR (ATP) spectrum of α-Ethyl-4-methoxy-N-phenylbenzenemethanamine (**7c**); solvent: $CDCl_3$, 100.7 MHz.



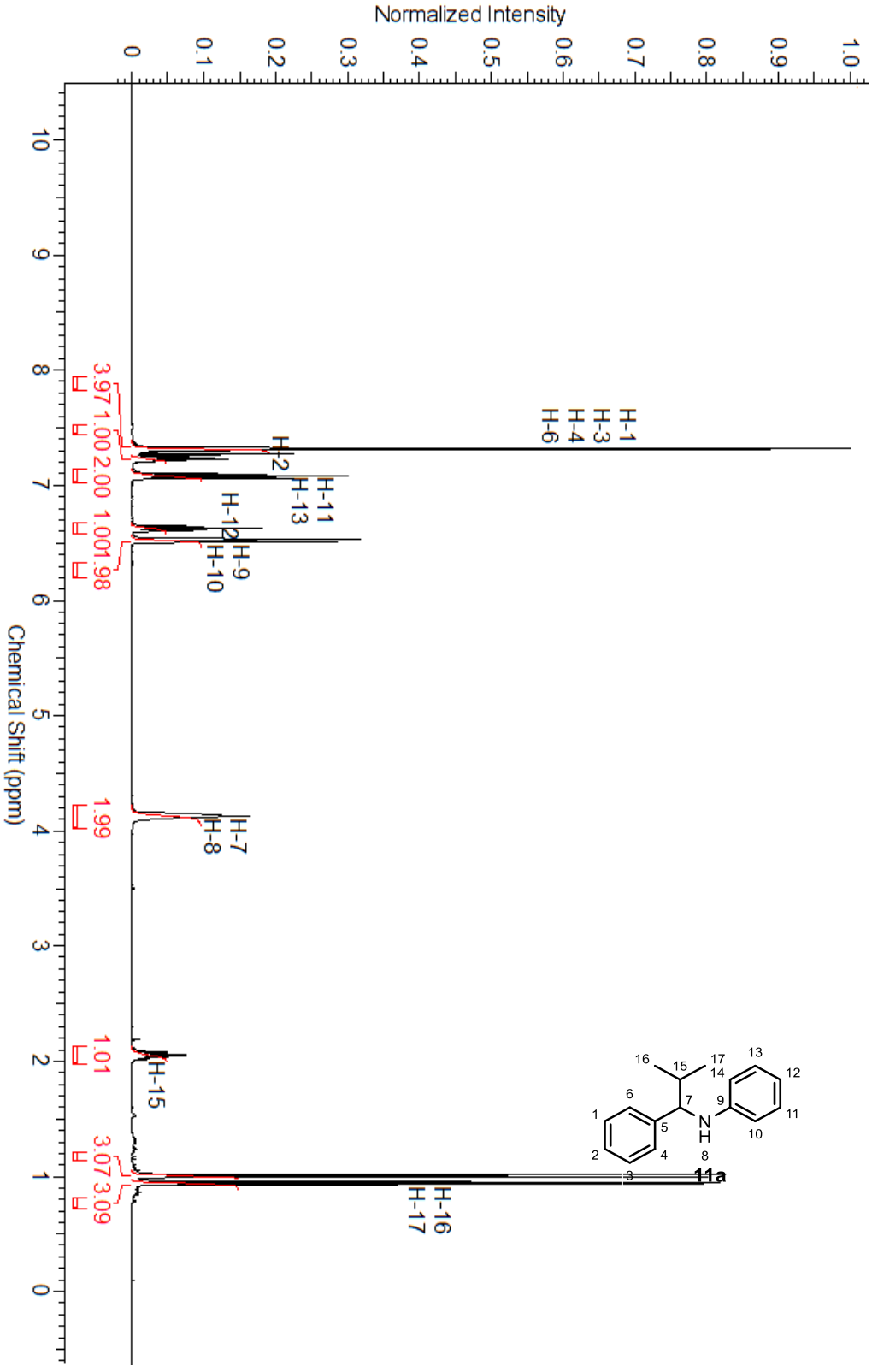
Sup. 12: ^{1}H-NMR spectrum of 4-Bromo-α-ethyl-N-phenylbenzenemethanamine (**7d**); solvent: $CDCl_3$, 400.3 MHz.



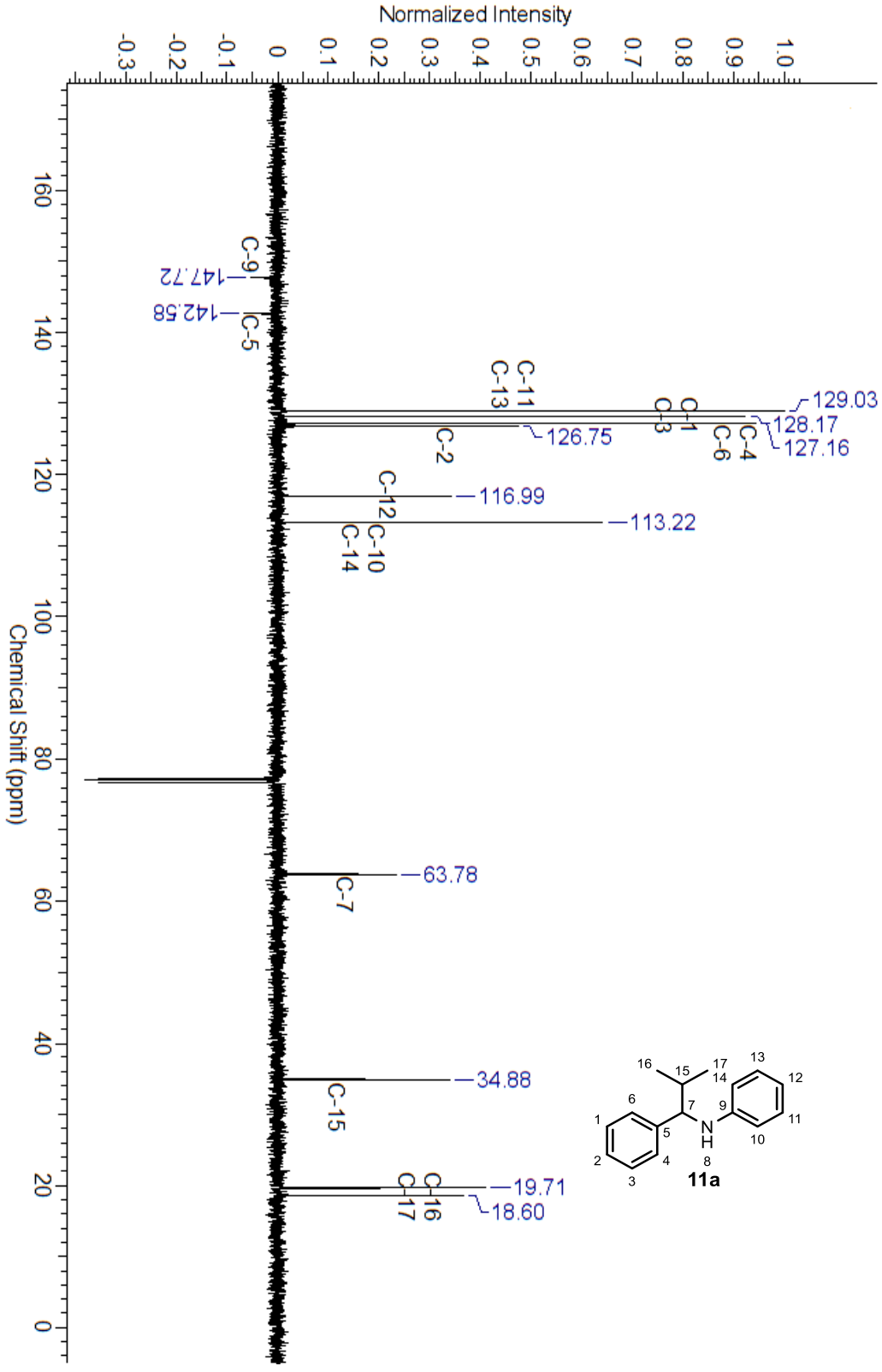
Sup. 13: ^{13}C- NMR (ATP) spectrum of 4-Bromo-α-ethyl-N-phenylbenzenemethanamine (**7d**); solvent: $CDCl_3$, 100.7 MHz.



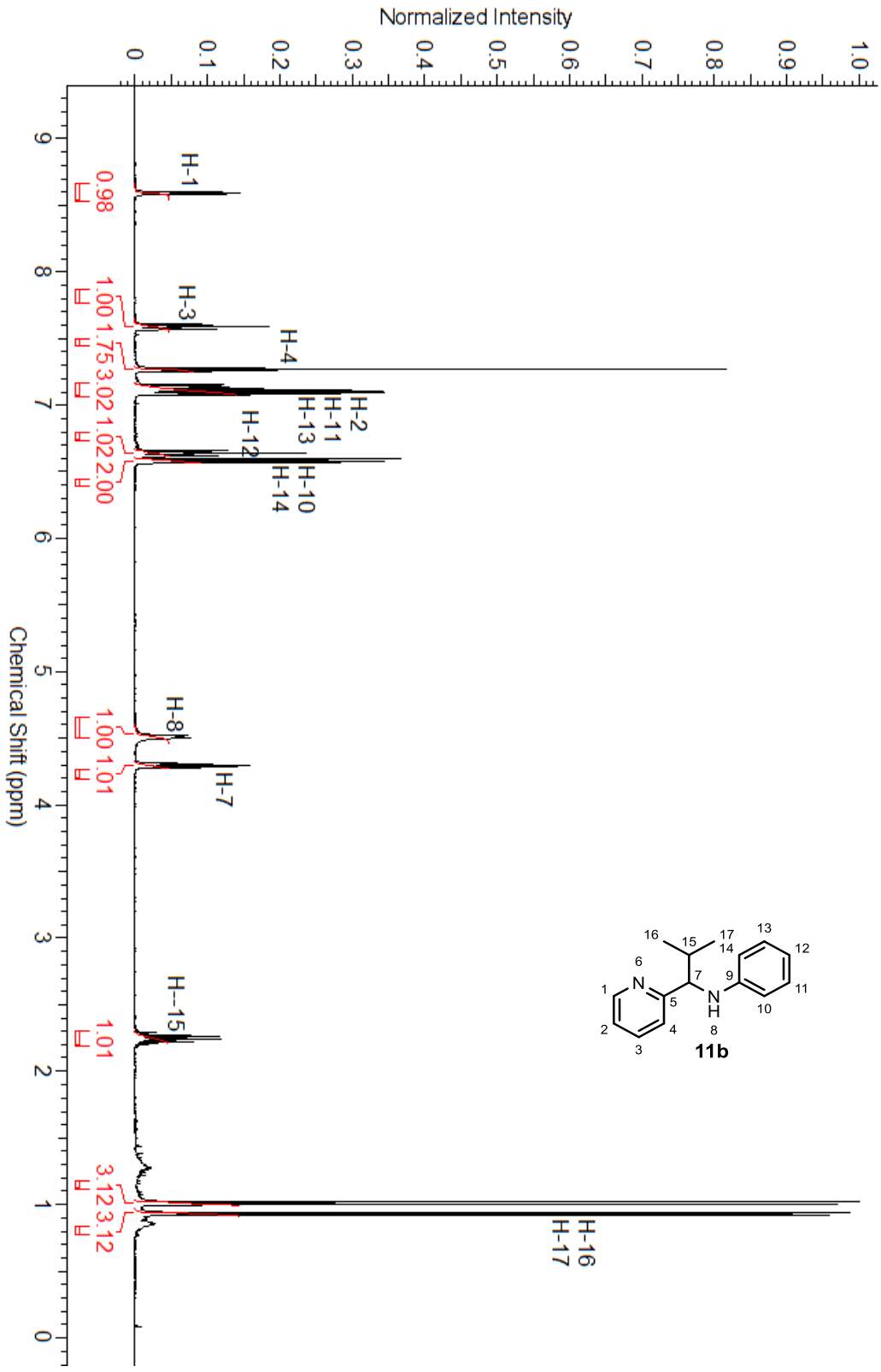
Sup. 14: ^{1}H-NMR spectrum of N-Phenylbenzenemethanamine (**8a**);
solvent: $CDCl_3$, 400.3 MHz.



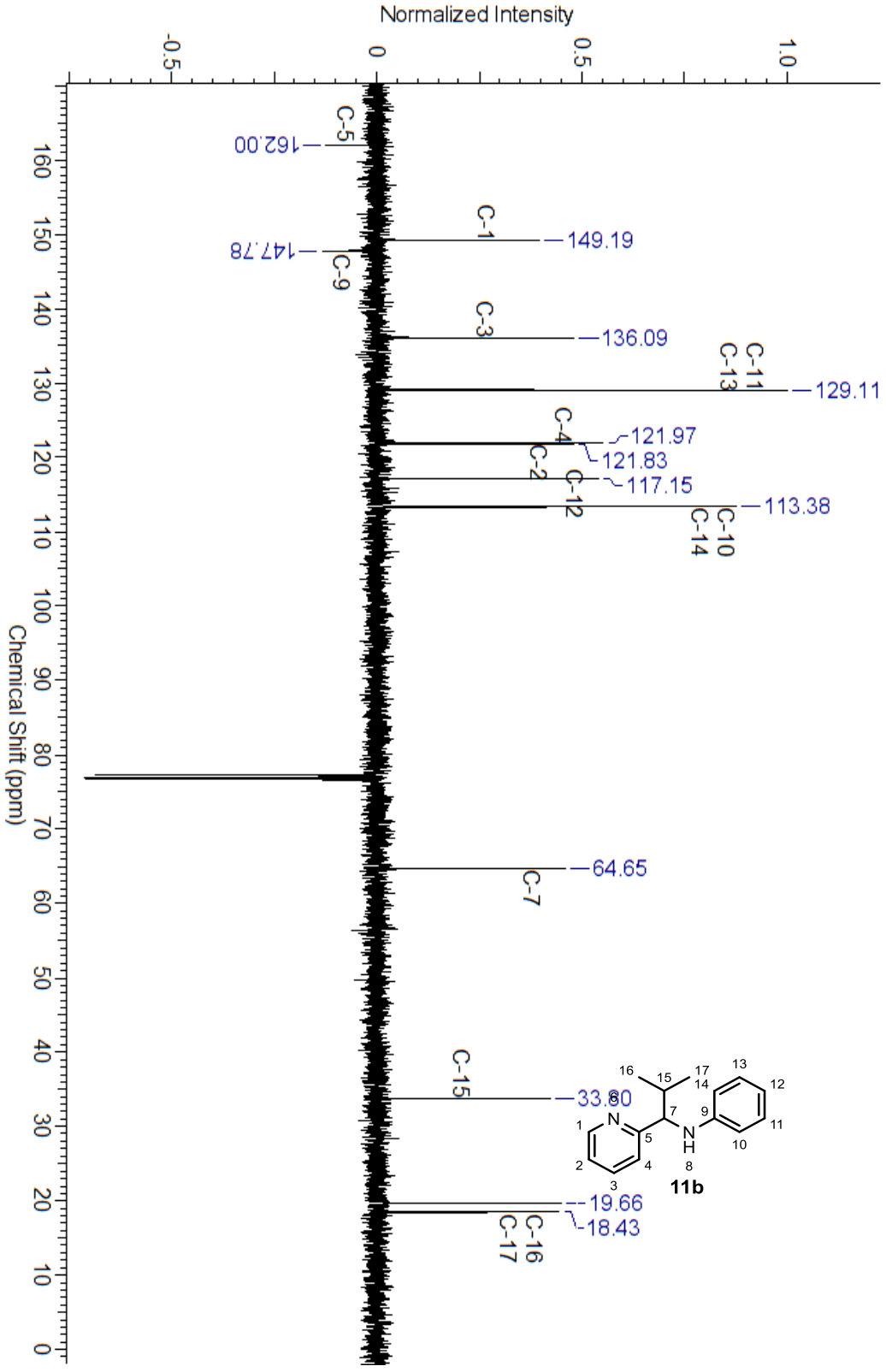
Sup. 15: ^{1}H-NMR spectrum of α-(1-Methylethyl)-N-phenylbenzenemethanamine (**11a**); solvent: $CDCl_3$, 400.3 MHz.



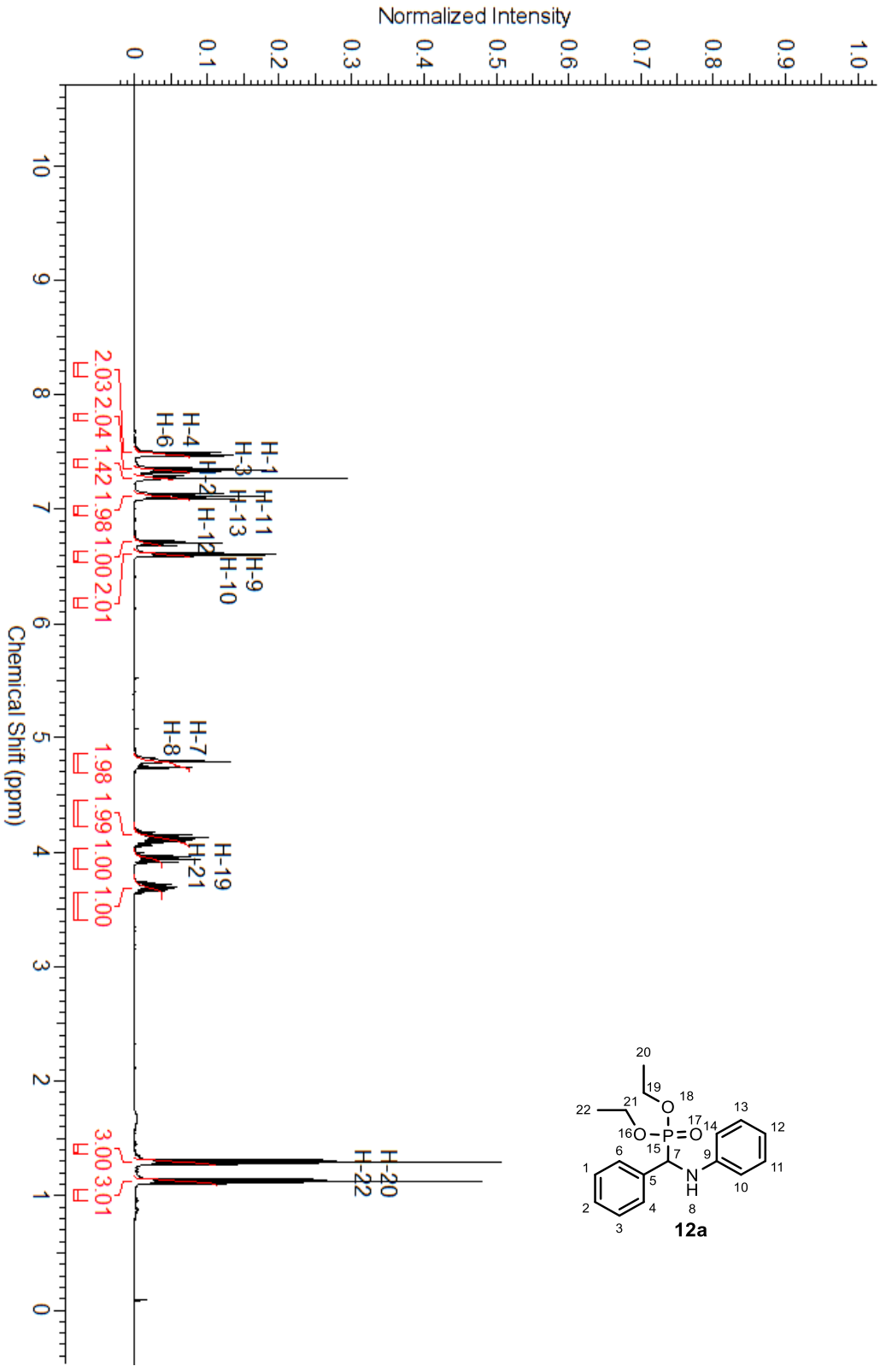
Sup. 16: ^{13}C- NMR (ATP) spectrum of α-(1-Methylethyl)-N-phenylbenzenemethanamine (**11a**); solvent: $CDCl_3$, 100.7 MHz.



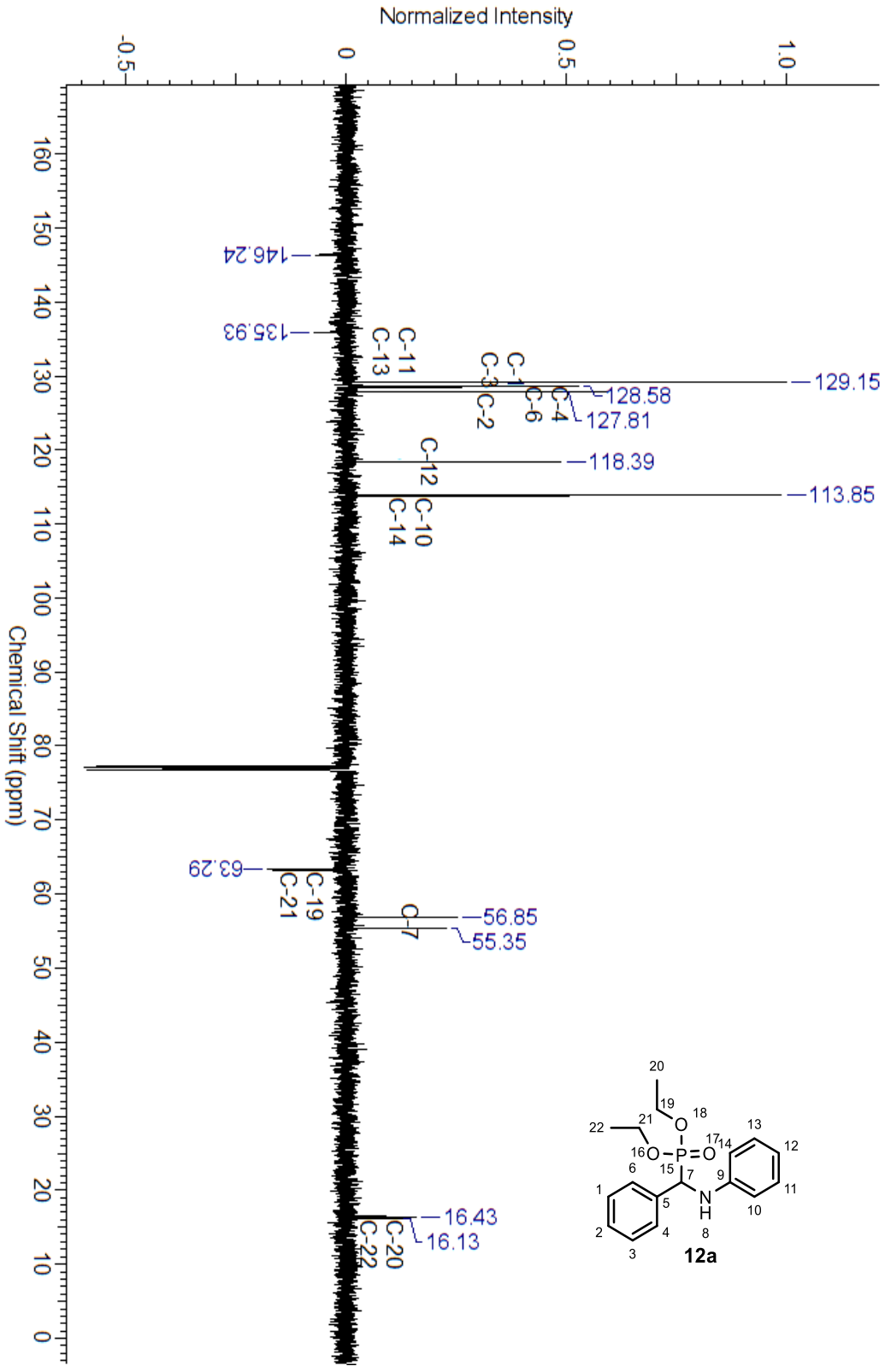
Sup. 17: ^{1}H-NMR spectrum of α-(1-Methylethyl)-N-phenyl-2-pyridinemethanamine (**11b**); solvent: $CDCl_3$, 400.3 MHz.



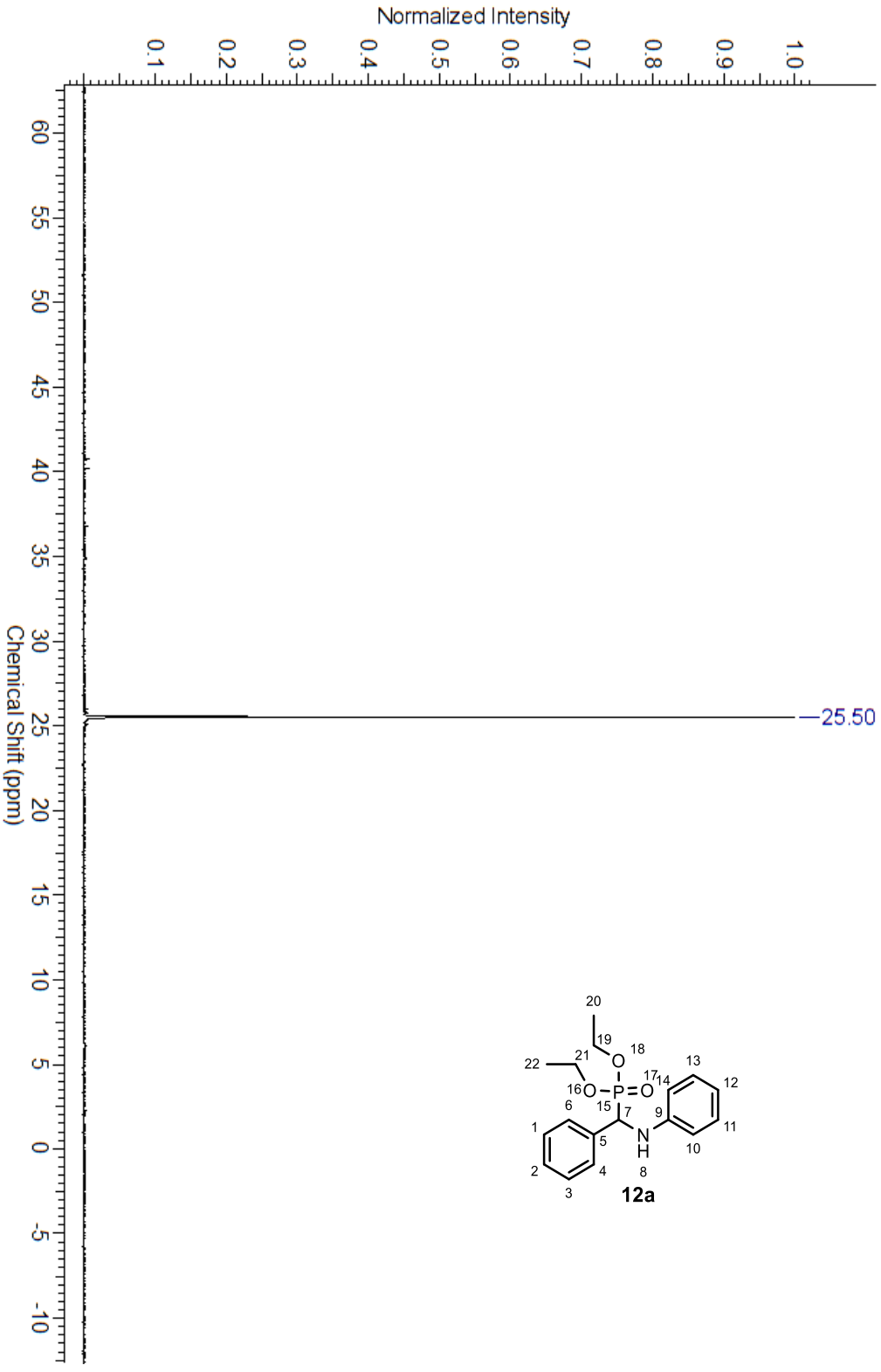
Sup. 18: ^{13}C- NMR (ATP) spectrum of α-(1-Methylethyl)-N-phenyl-2-pyridinemethanamine (**11b**); solvent: $CDCl_3$, 100.7 MHz.



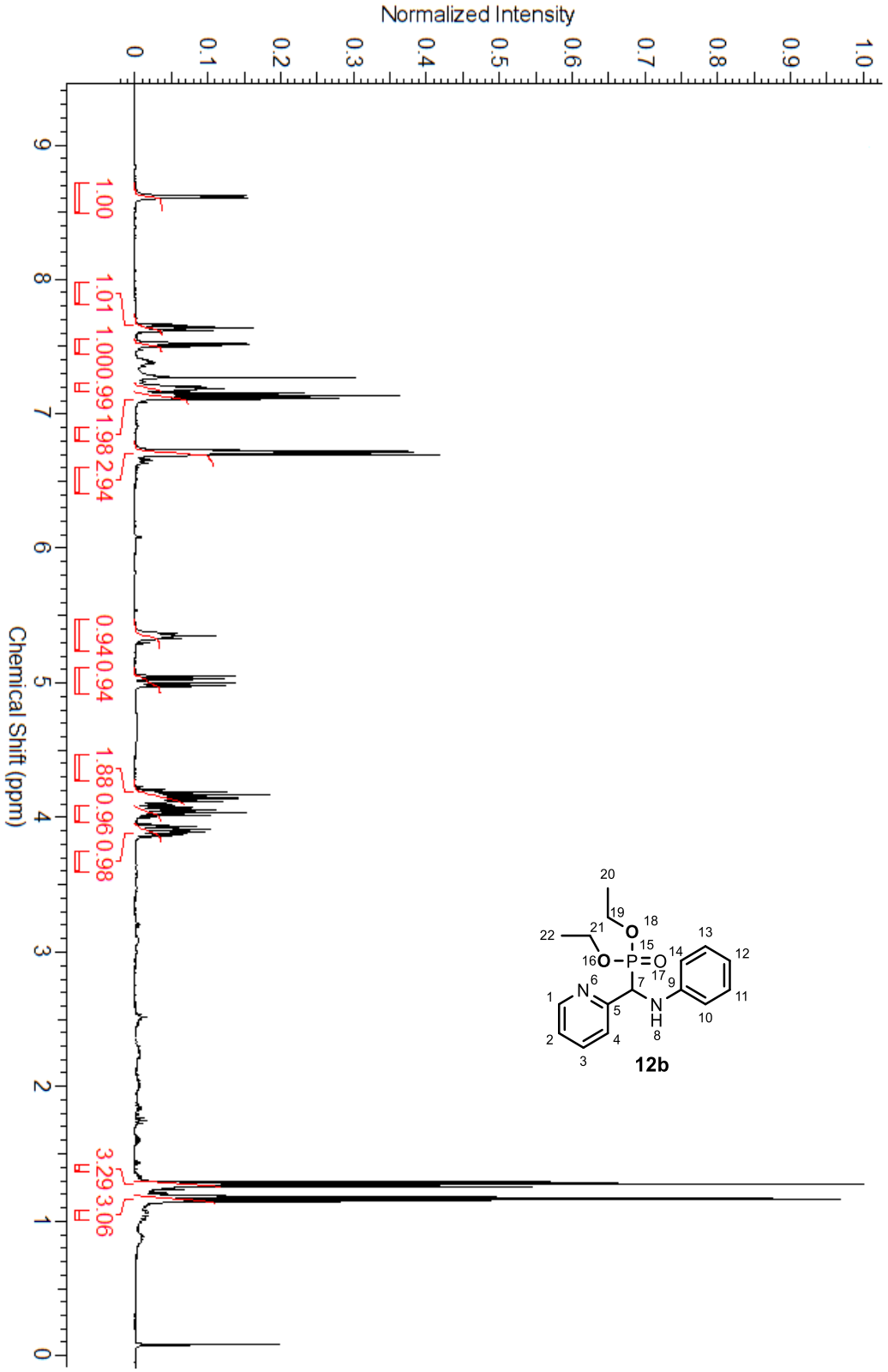
Sup. 19: ^{1}H-NMR spectrum of Diethyl(phenyl(phenylamino)methyl)-phosphonate (**12a**); solvent: $CDCl_3$, 400.3 MHz.



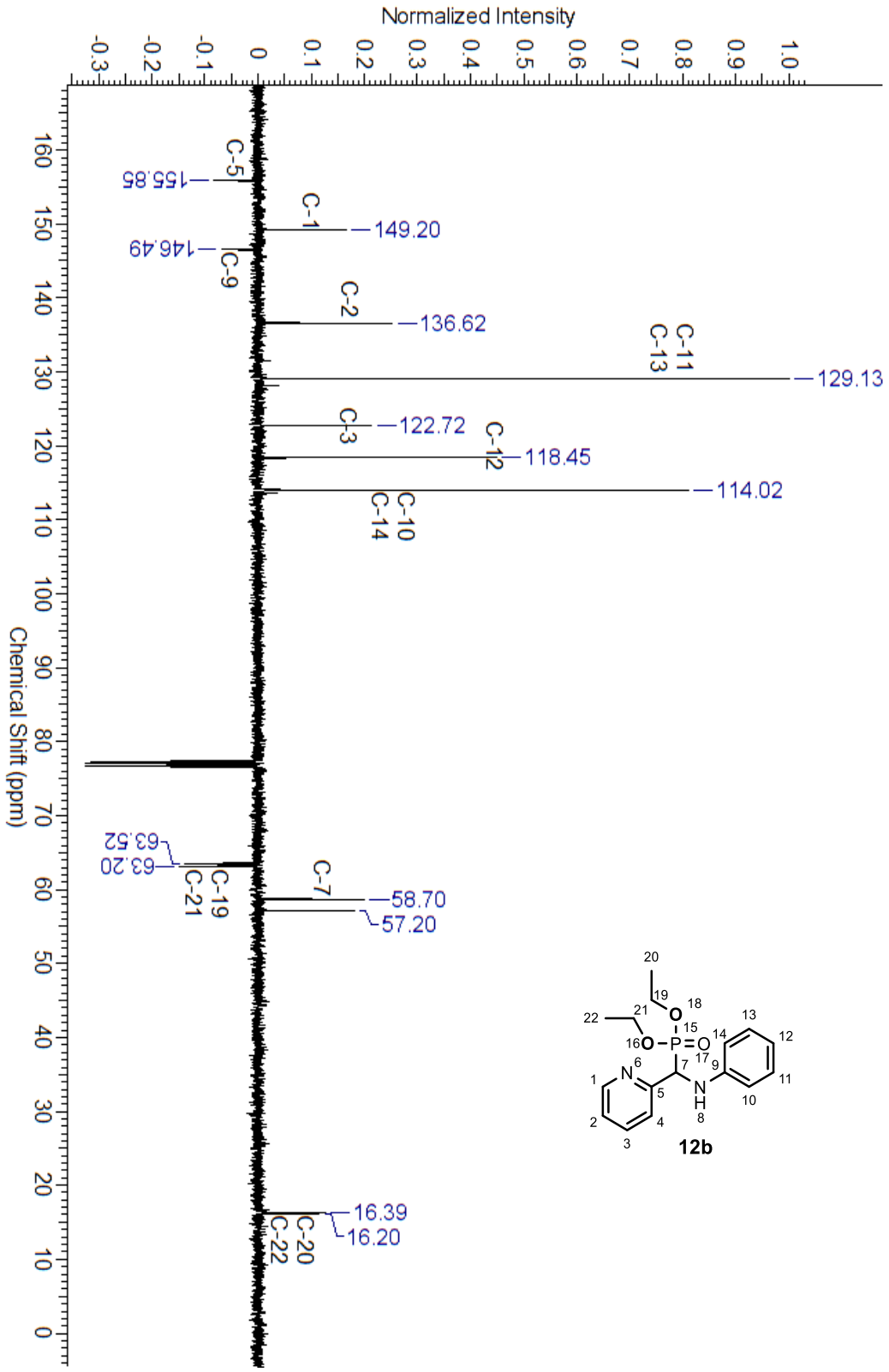
Sup. 20: ^{13}C- NMR (ATP) spectrum of Diethyl(phenyl(phenylamino)methyl)-phosphonate (**12a**); solvent: $CDCl_3$, 100.7 MHz.



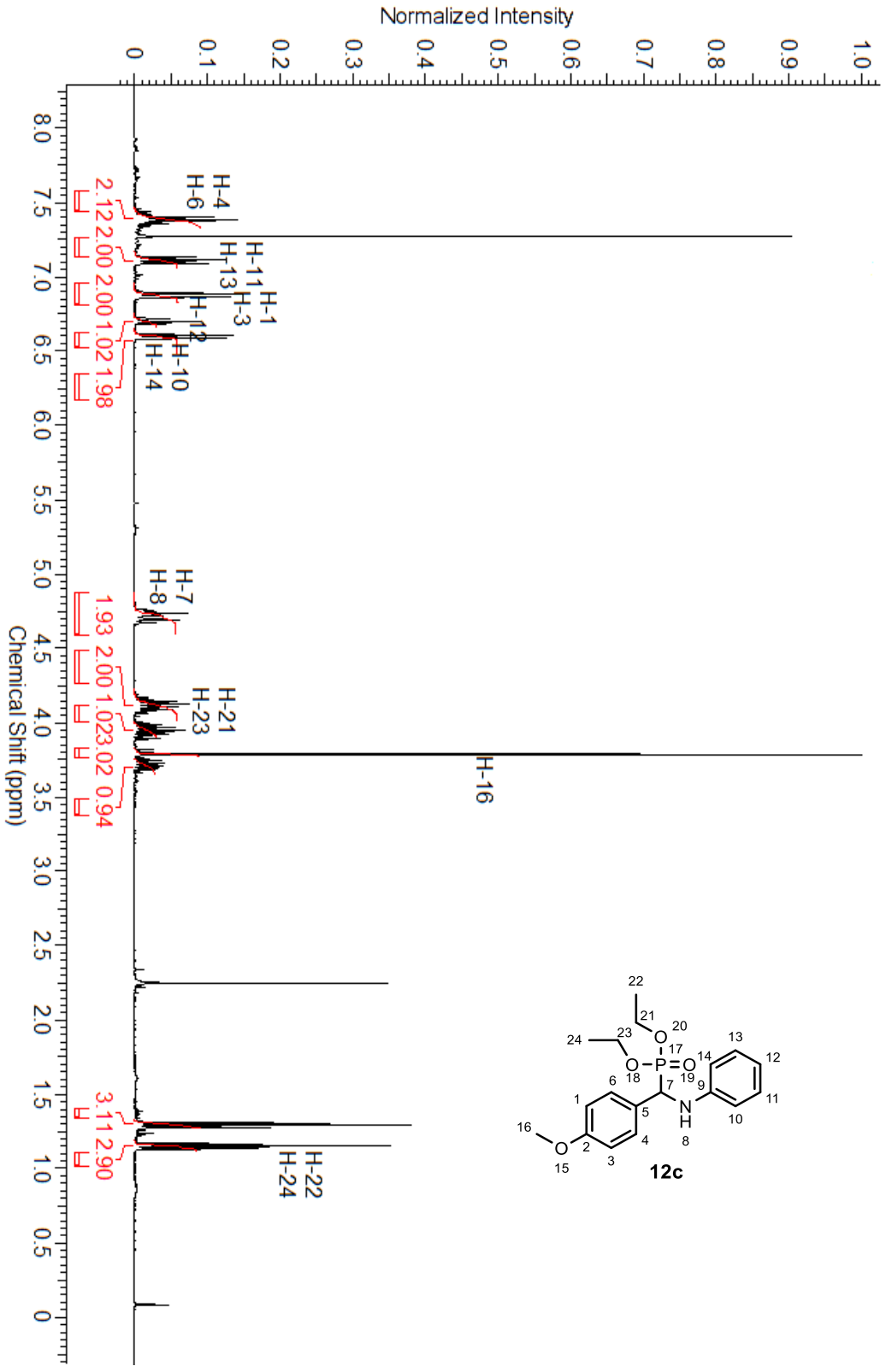
Sup. 21: ^{31}P-NMR spectrum of Diethyl(phenyl(phenylamino)methyl)-phosphonate (**12a**); solvent: C_6D_6, 162.0 MHz.



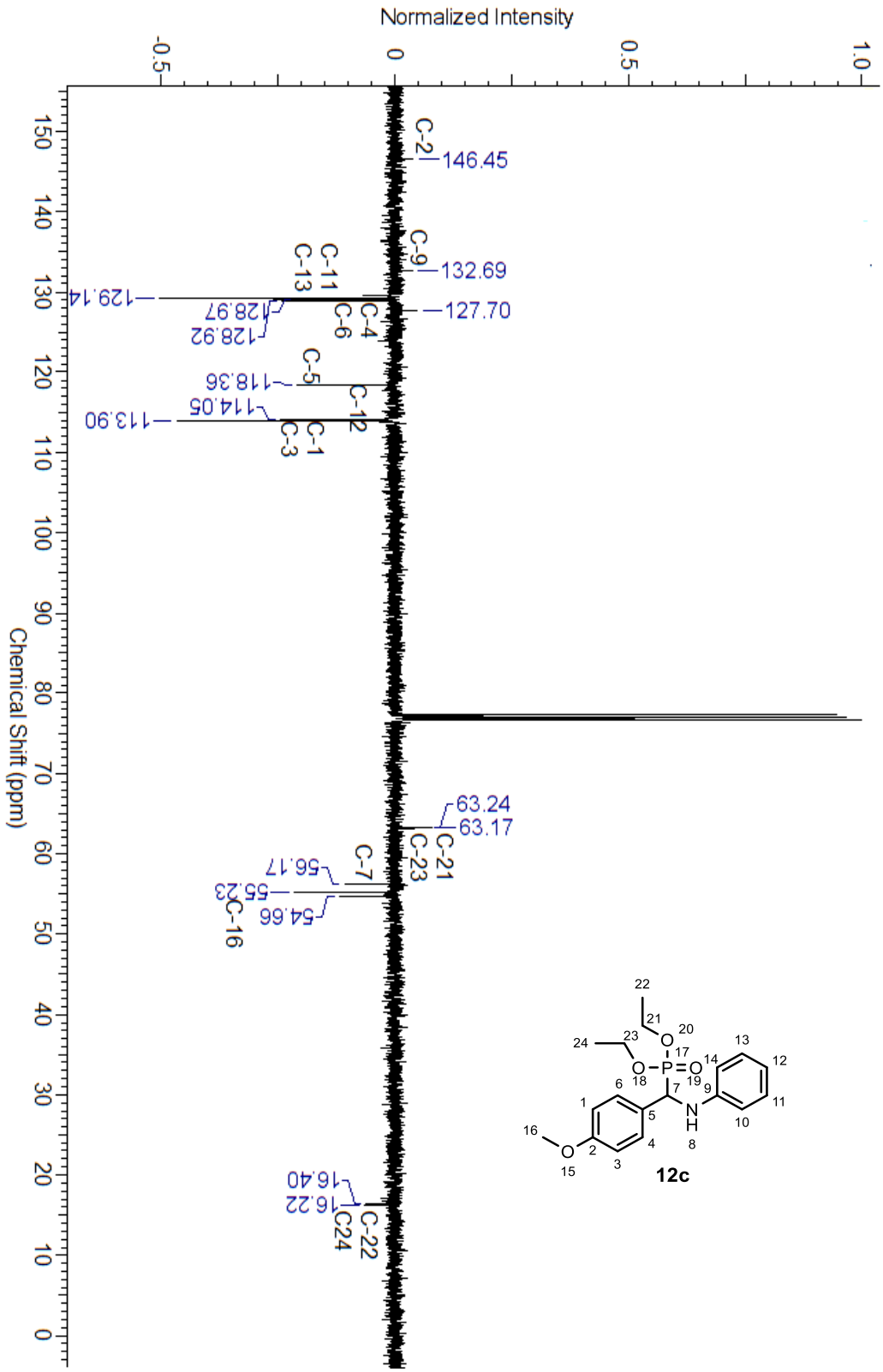
Sup. 22: ^{1}H-NMR spectrum of Diethyl((phenylamino)(pyridine-3-yl)methyl)-phosphonate (**12b**); solvent: $CDCl_3$, 400.3 MHz.



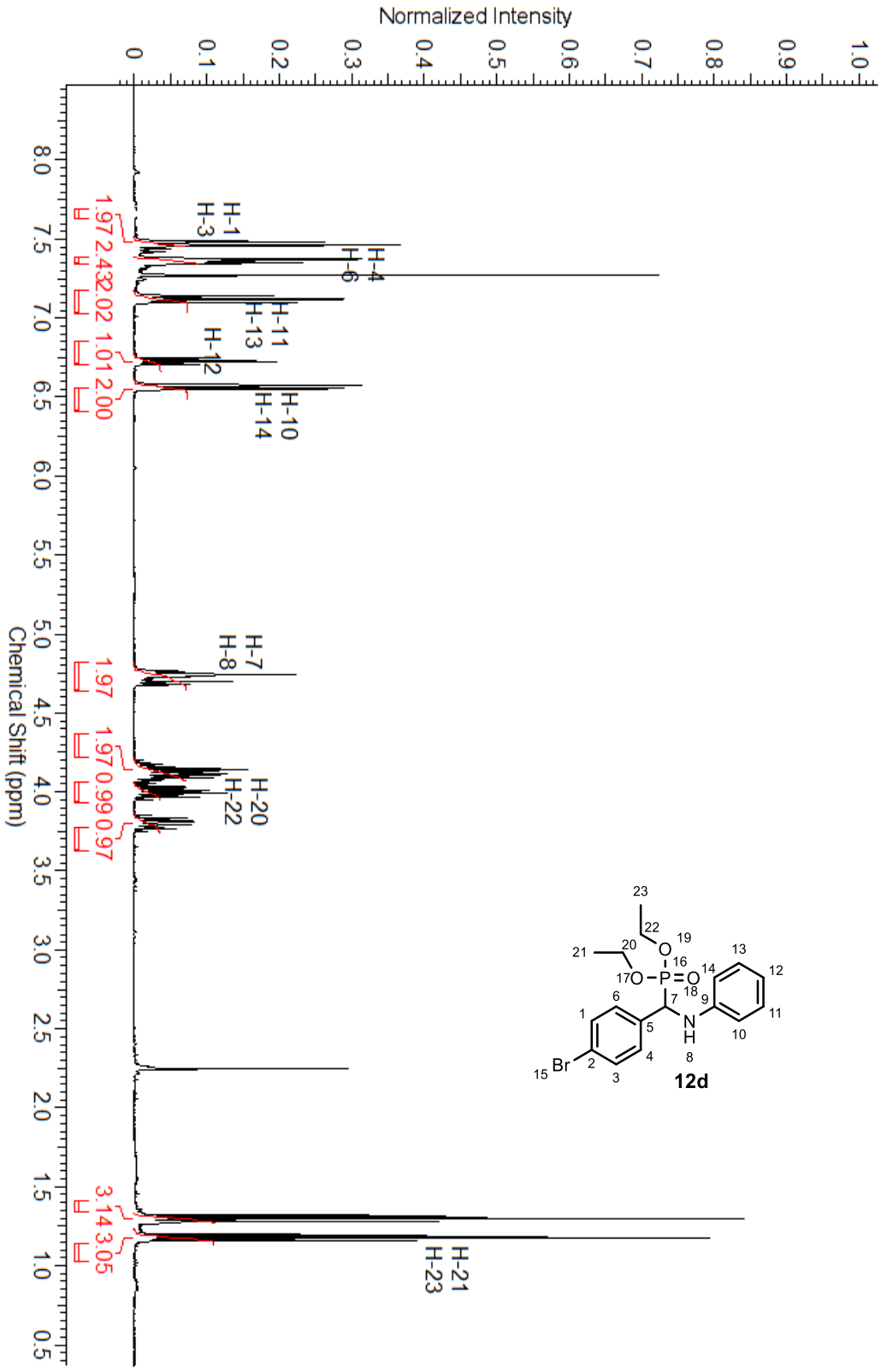
Sup. 23: ^{13}C- NMR (ATP) spectrum of Diethyl((phenylamino)-(pyridine-3-yl)methyl)-phosphonate (**12b**); solvent: $CDCl_3$, 100.7 MHz.



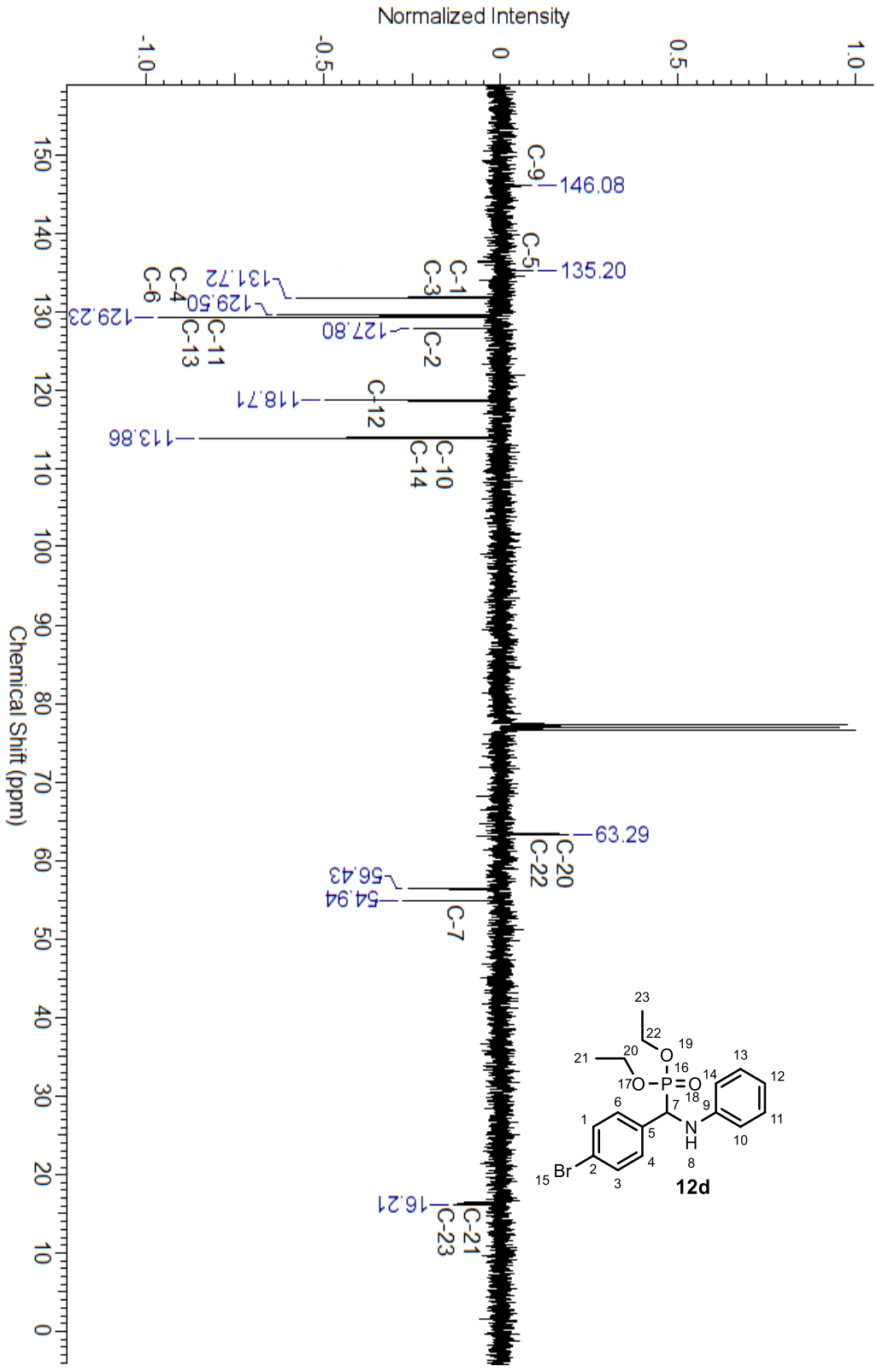
Sup. 24: ^{1}H-NMR spectrum of Diethyl(4-methoxyphenyl(phenylamino)methyl)-phosphonate (**12c**); solvent: $CDCl_3$, 400.3 MHz.



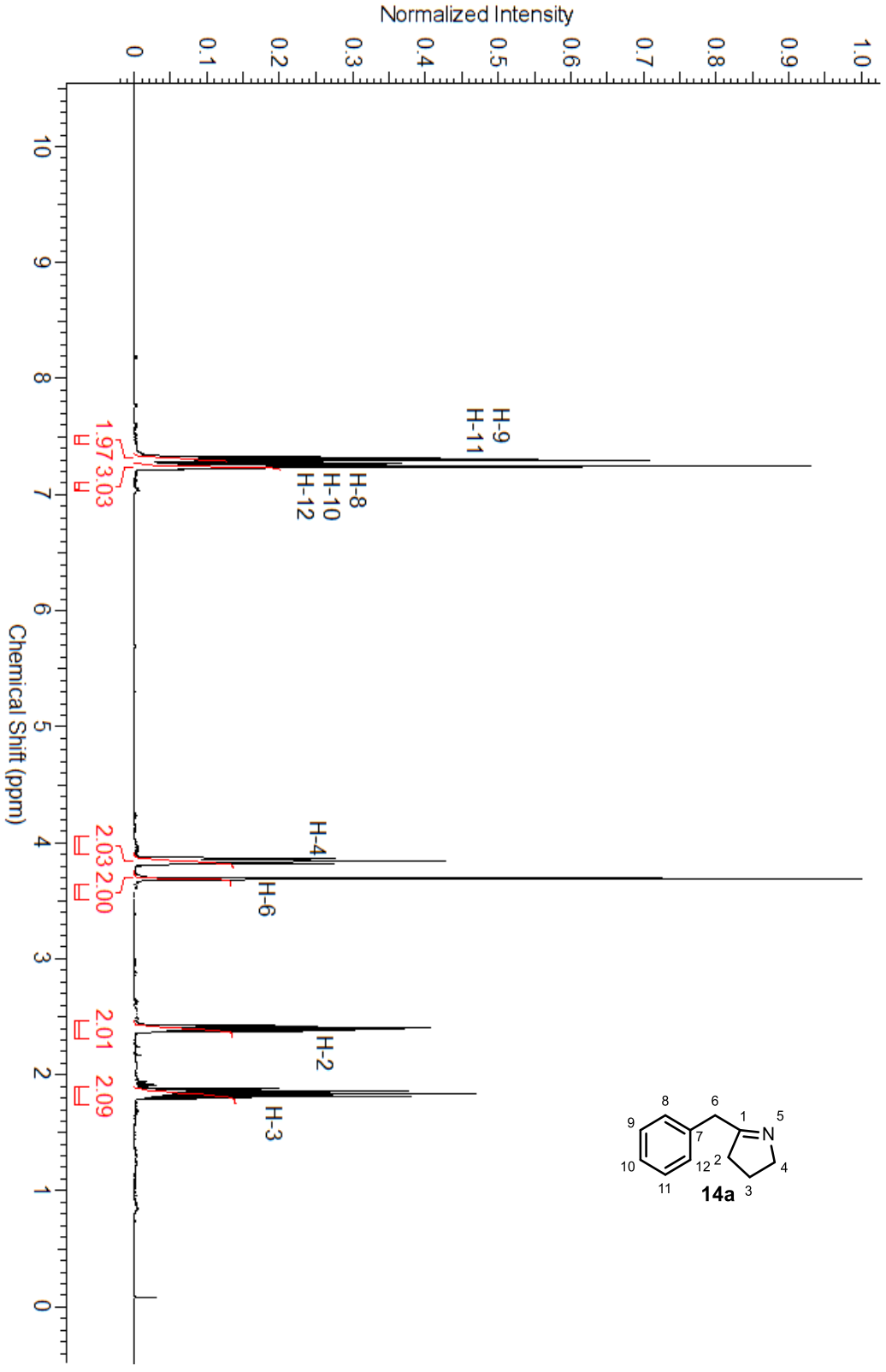
Sup. 25: ^{13}C- NMR (ATP) spectrum of Diethyl(4-methoxyphenyl(phenylamino)methyl)-phosphonate (**12c**); solvent: $CDCl_3$, 100.7 MHz.



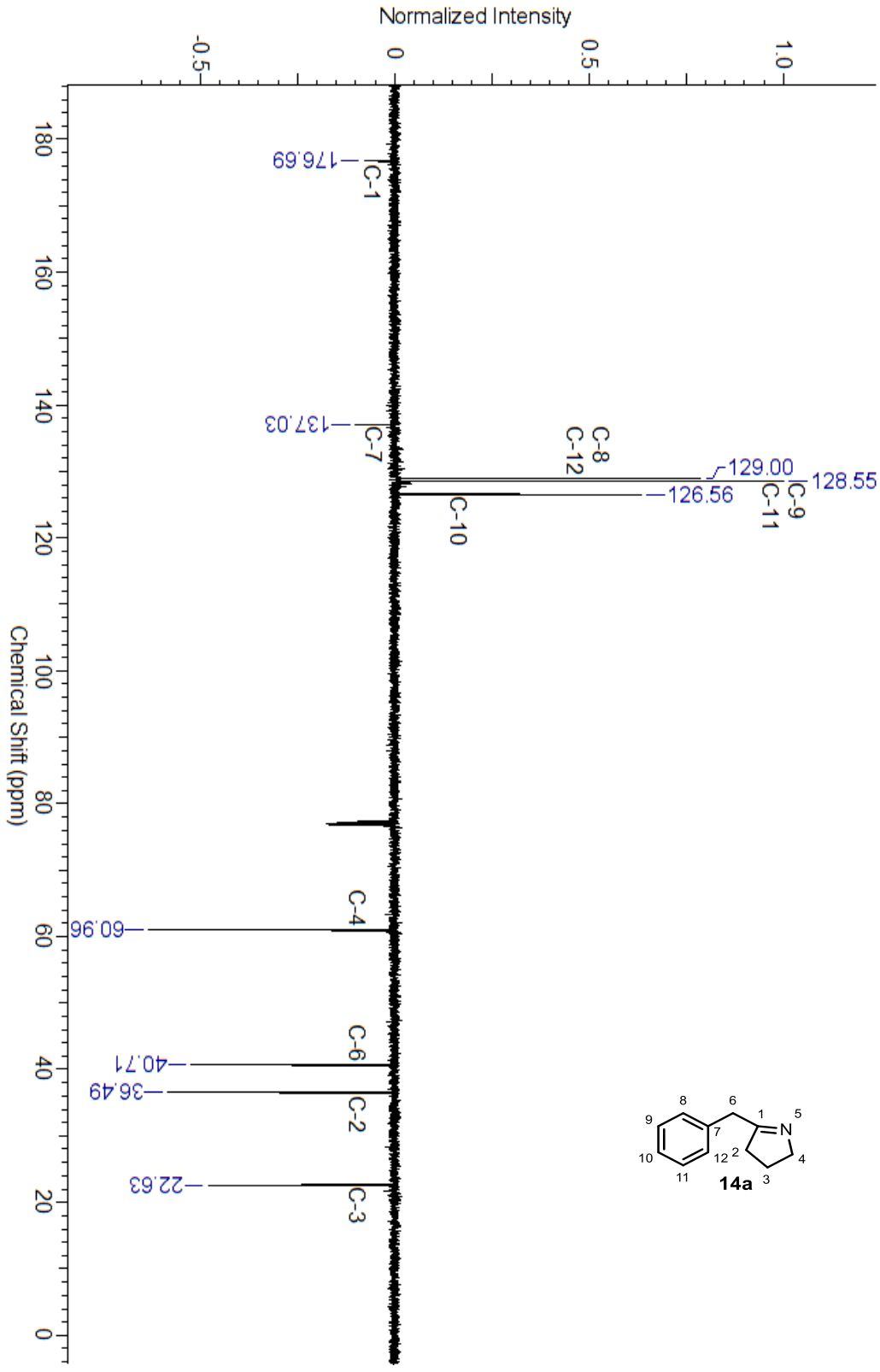
Sup. 26: ^{1}H-NMR spectrum of Diethyl(4-bromophenyl(phenylamino)methyl)-phosphonate (**12d**); solvent: $CDCl_3$, 400.3 MHz.



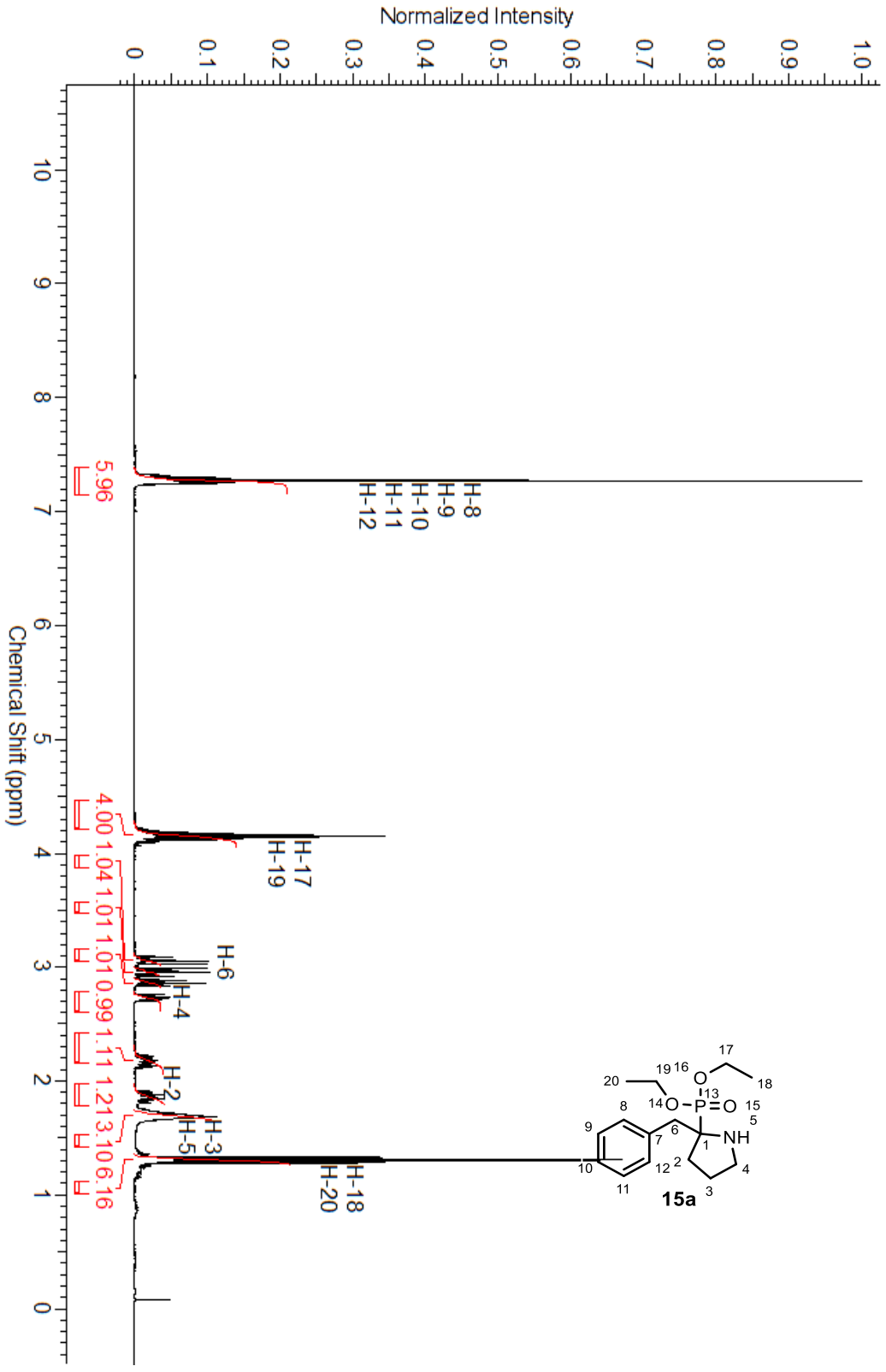
Sup. 27: ^{13}C- NMR (ATP) spectrum of Diethyl(4-bromophenyl(phenylamino)methyl)-phosphonate (**12d**); solvent: $CDCl_3$, 100.7 MHz.



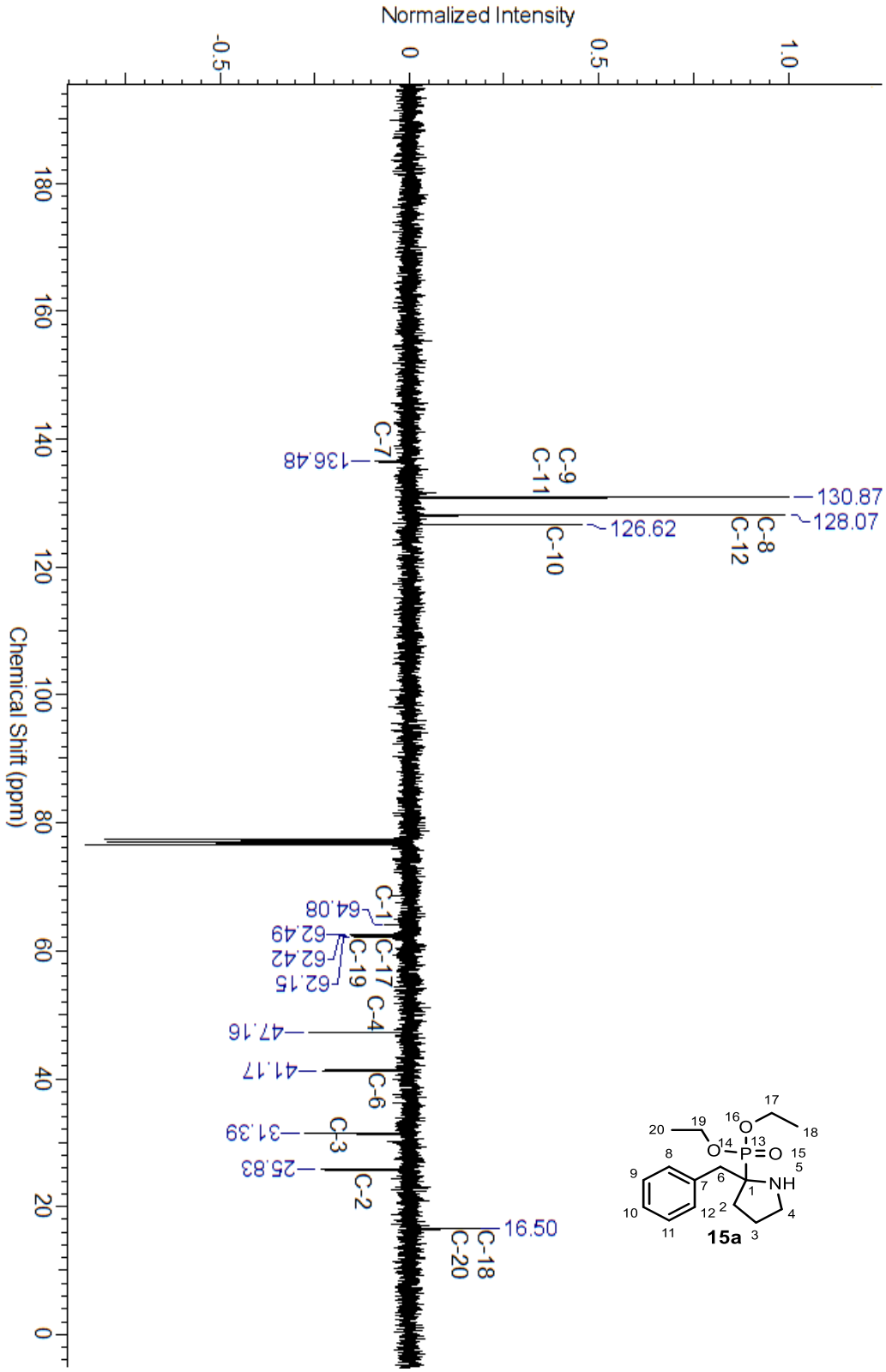
Sup. 28: ^{1}H-NMR spectrum of 3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole (**14a**); solvent: $CDCl_3$, 400.3 MHz.



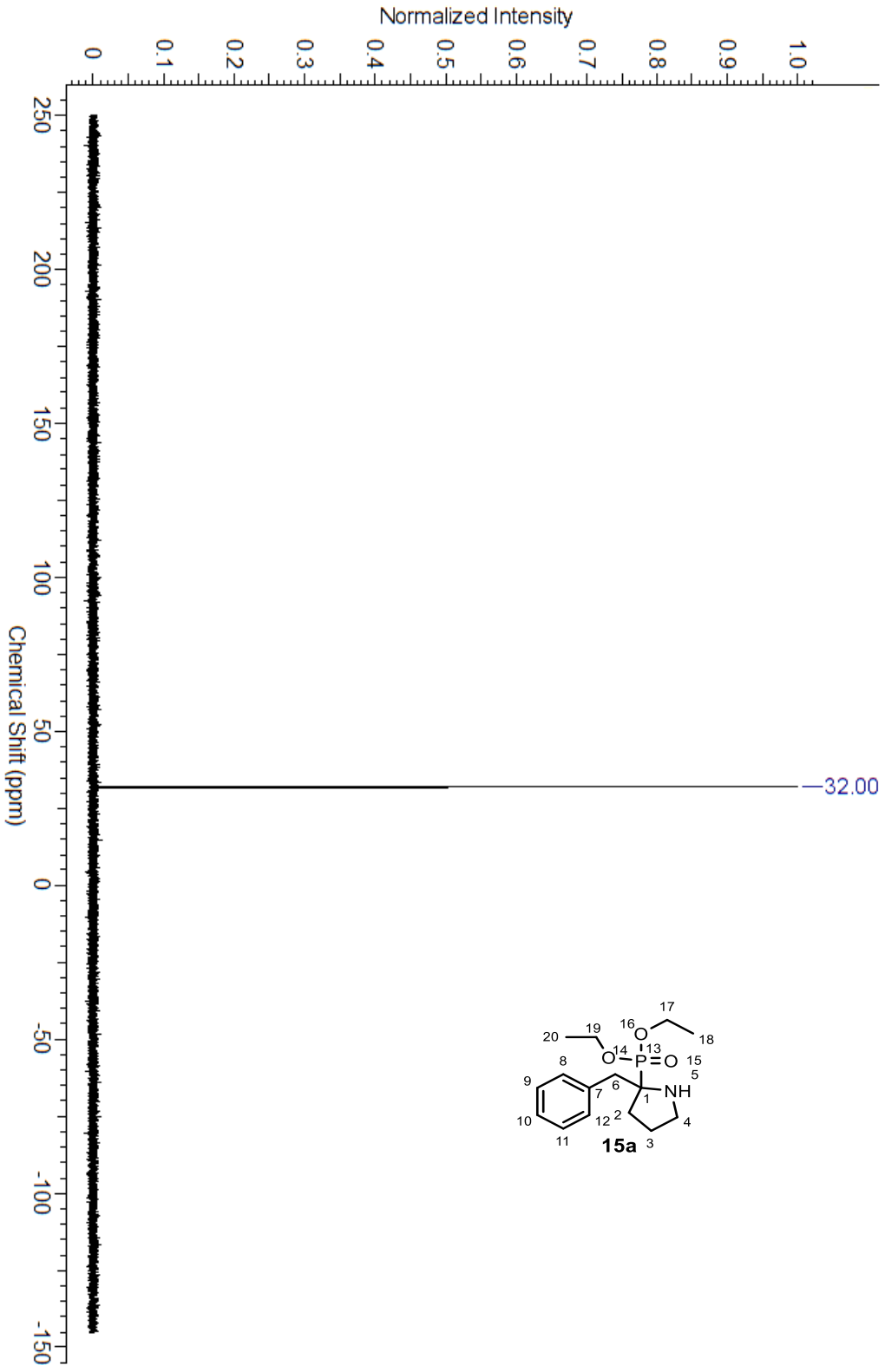
Sup. 29: ^{13}C- NMR (ATP) spectrum of 3,4-Dihydro-5-(phenylmethyl)-2H-pyrrole (**14a**); solvent: $CDCl_3$, 100.7 MHz.



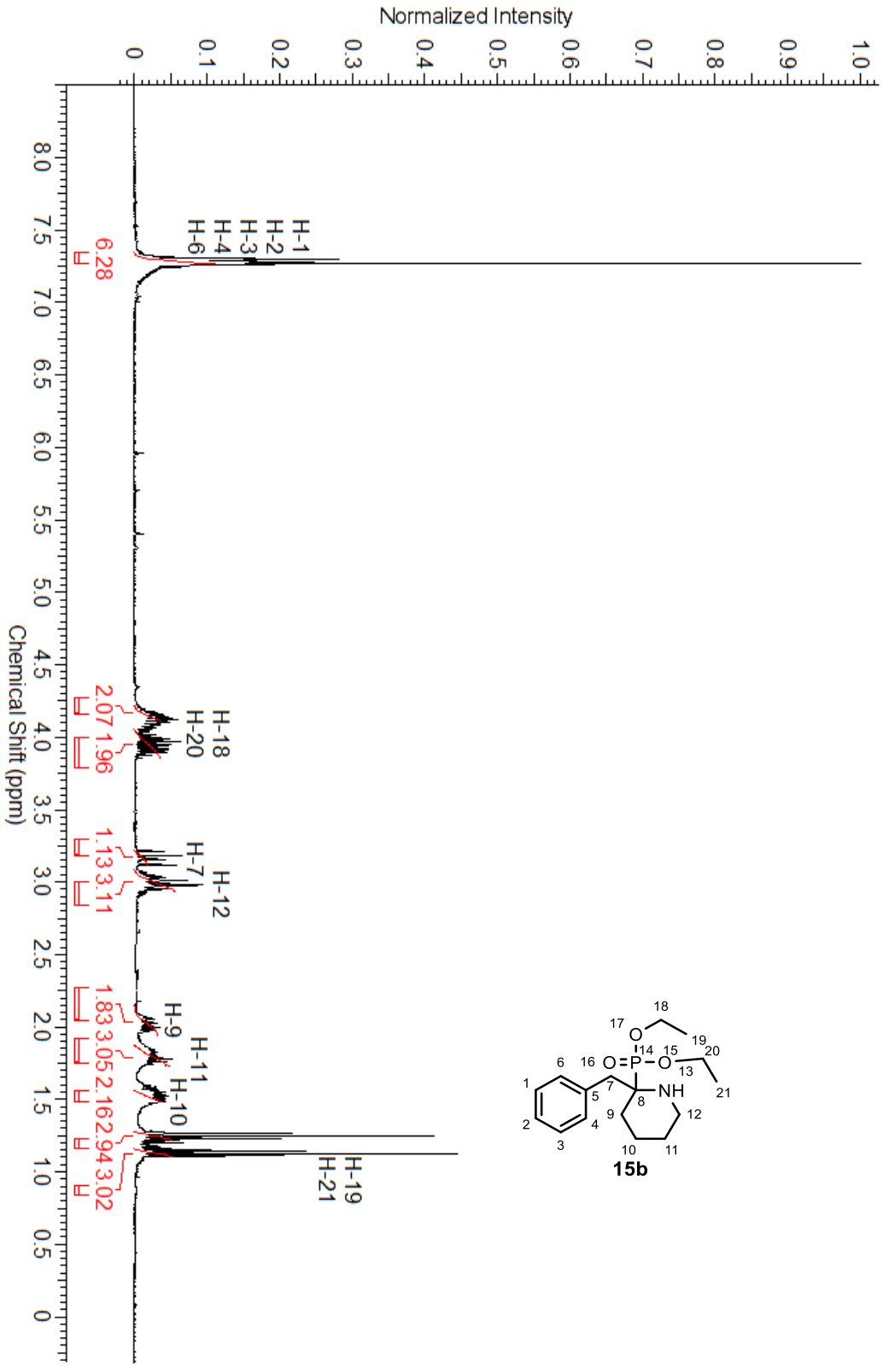
Sup. 30: ^{1}H-NMR spectrum of Diethyl(2-benzylpyrrolidin-2-yl)phosphonate (**15a**); solvent: $CDCl_3$, 400.3 MHz.



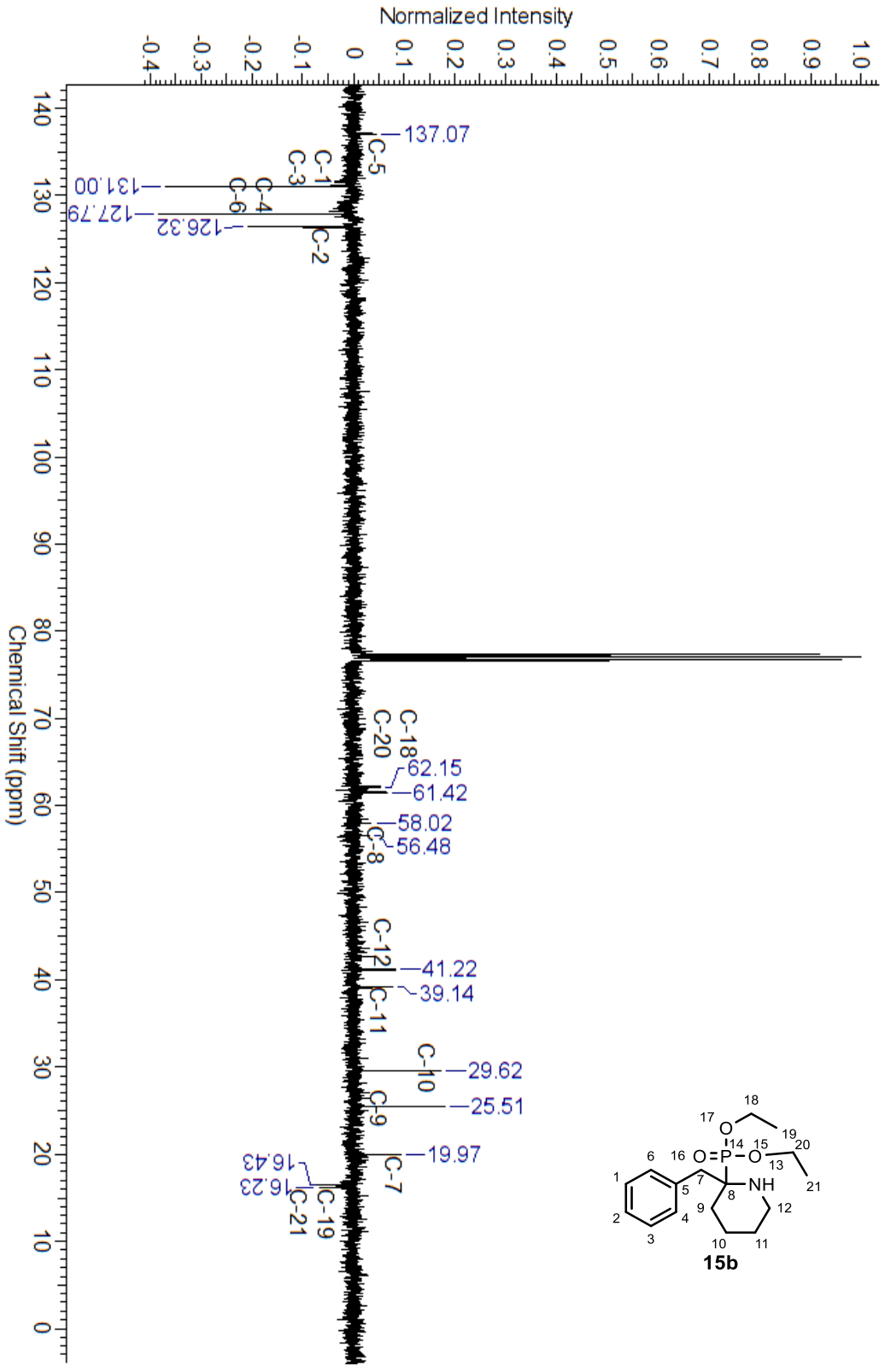
Sup. 31: ^{13}C- NMR (ATP) spectrum of Diethyl(2-benzylpyrrolidin-2-yl)phosphonate (**15a**); solvent: $CDCl_3$, 100.7 MHz.



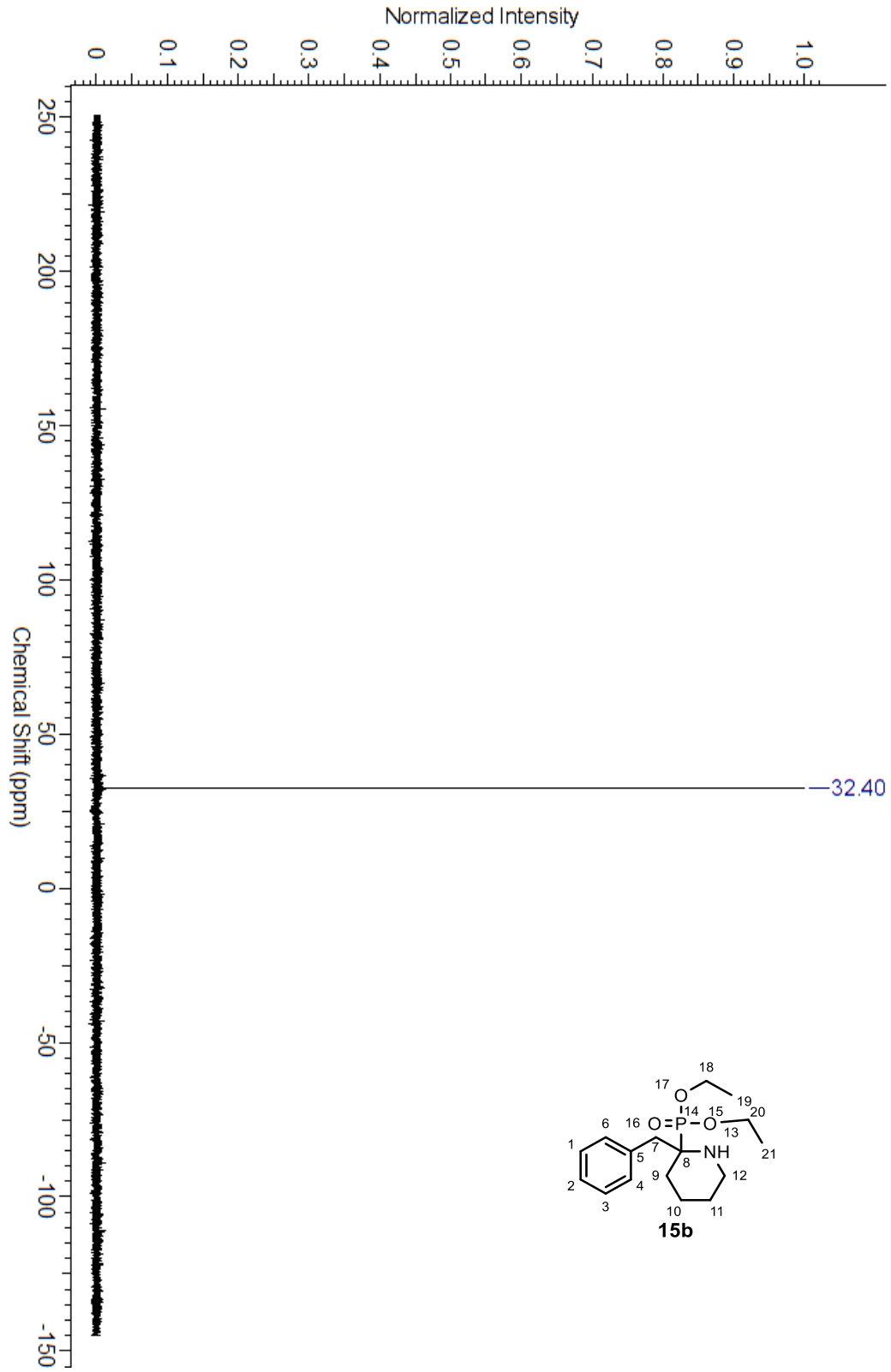
Sup. 32: ^{31}P-NMR spectrum of Diethyl(2-benzylpyrrolidin-2-yl)phosphonate (**15a**); solvent: C_6D_6, 162.0 MHz.



Sup. 33: ^{1}H-NMR spectrum of Diethyl(2-benzylpiperidin-2-yl)phosphonate (**15b**); solvent: $CDCl_3$, 400.3 MHz.



Sup. 34: ^{13}C- NMR (ATP) spectrum of Diethyl(2-benzylpiperidin-2-yl)phosphonate (**15b**); solvent: $CDCl_3$, 100.7 MHz.



15b

Sup. 35: ^{31}P-NMR spectrum of Diethyl(2-benzylpiperidin-2-yl)phosphonate (**15b**); solvent: C_6D_6, 162.0 MHz.