Sustainable Noble Metal Free Catalytic Organic Synthesis

DISSERTATION

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Abbreviations

Ar	aryl
Å	Angström
ADC	acceptor-less dehydrogenative condensation
BH	borrowing hydrogen
bipy	bipyridyl
Bn	benzyl
Bu	butyl
br	broad
°C	degree celsius
d	doublet
δ	chemical shift (ppm)
equiv	equivalents
g	gram
GC	gas chromatography
GC-MS	gas chromatography-mass spectrometry
h	hours
HA	hydrogen auto transfer
Hz	Hertz
J	coupling constant (Hz)
K	Kelvin
m	multiplet
mL	milliliter
MLC	metal ligand cooperation
mmol	millimol
NMR	nuclear magnetic resonance
ppm	parts per million
py	pyridine
q	quartet
rt	room temperature
s	singlet
t	triplet
THF	tetrahydrofurane
XRD	X-ray diffraction
µL	microliter

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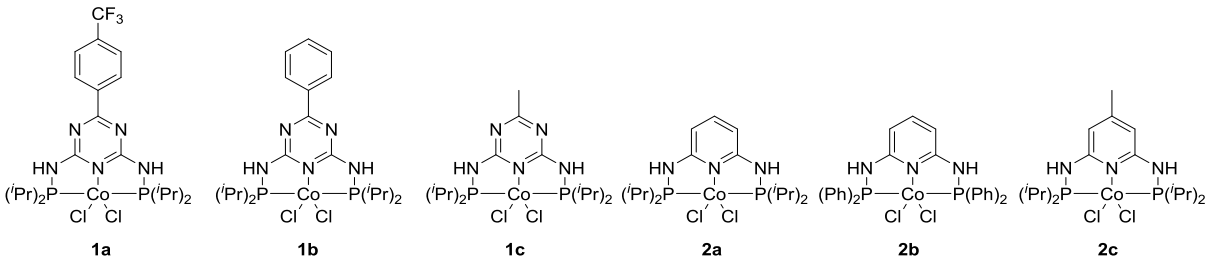
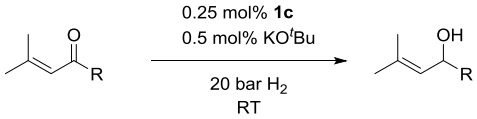
1. Summary

In the present work, the implementation of novel $PN_{3-5}P$ ligand stabilized cobalt complexes in typical noble metal mediated chemistry is described. Hydrogenation reactions, borrowing hydrogen / hydrogen auto transfer (BH/HA) reactions and acceptor-less dehydrogenative condensation reactions (ADC) are preferentially catalyzed by iridium or ruthenium complex catalysts. In order to gain more sustainability, the substitution of these metals by a base metal like cobalt is a very attractive goal.



Scheme 1. Synthesized PN_5P $CoCl_2$ complexes (**1a-c**) and PN_3P $CoCl_2$ complexes (**2a-c**).

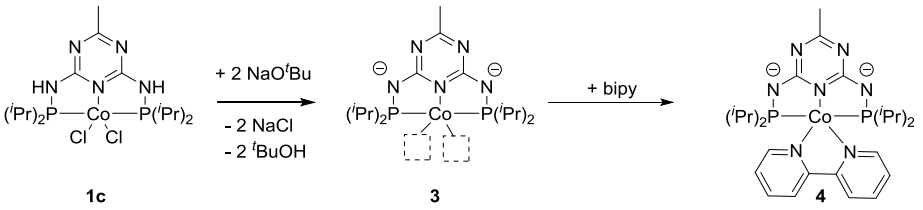
In previous work, it was shown that $PN_{3-5}P$ Ir complexes are highly efficient catalysts for the sustainable synthesis of aromatic N-heterocycles via ADC. Based on this knowledge, six novel $PN_{3-5}P$ cobalt complexes were synthesized and characterized (Scheme 1). The shown complexes **1a-c** and **2a-c** were investigated as pre-catalysts in the hydrogenation of ketones. Interestingly, complex **1c** showed an exceptional activity in the hydrogenation of C=O bonds at 20 bar hydrogen pressure and room temperature.



Scheme 2. Example for the selective hydrogenation of a C=O bond in presence of a C=C bond.

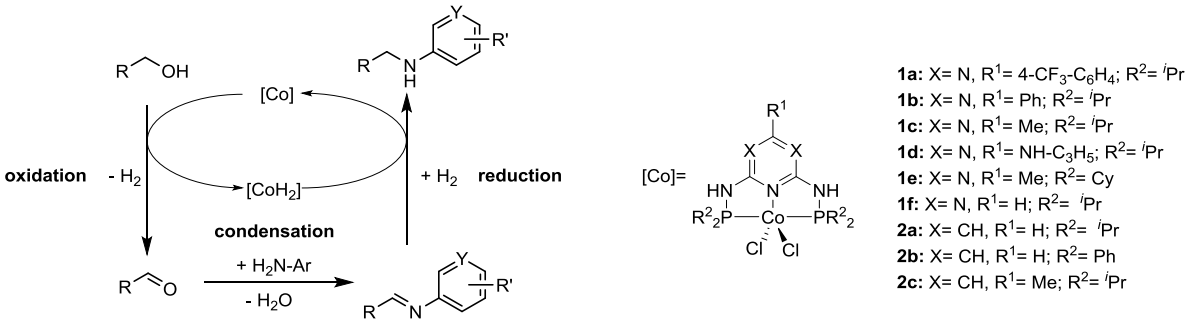
Various aryl-alkyl, aryl-aryl and alkyl-alkyl ketones with several functional groups were reduced (mostly quantitatively) to the corresponding alcohols at catalyst loadings down to 0.25 mol%. Remarkably, a distinct selectivity of this catalyst towards C=O bonds in present of C=C bonds was observed (Scheme 2). Unsaturated alcohols were obtained in quantitative yields with low catalyst loadings about 0.25 mol%.

To get an insight into the supposed active species **3**, complex **1c** was activated with 2 equiv. of NaO^{t}Bu and treated with bipyridine, resulting in **4** (Scheme 3). The oxidation state of the cobalt is not changed in the activation process. The tridentate ligand feature to act as a neutral, mono-anionic or di-anionic ligand seems crucial for the catalyst activation.



Scheme 3. Trapping of the active species **3** with bipyridine results in complex **4**.

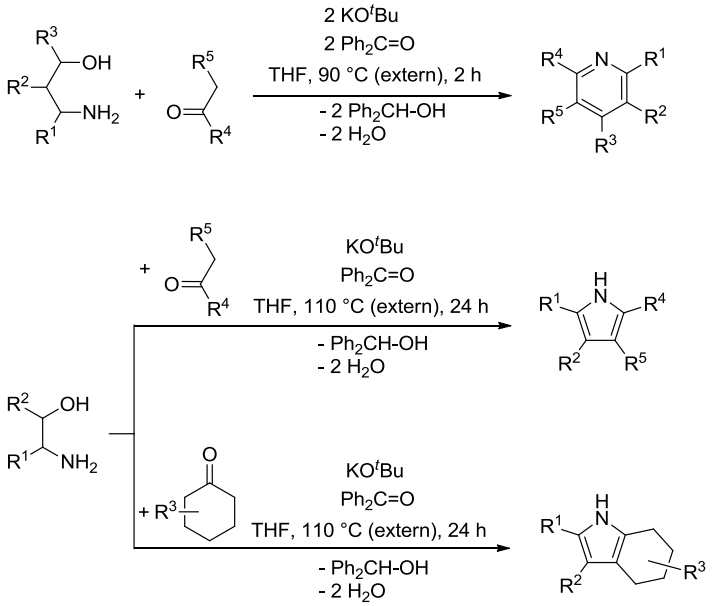
Next, the application of this catalyst family in the field of BH/HA was of interest. The selective mono-alkylation of aromatic amines by alcohols was chosen as a model reaction (Scheme 4). In these reactions, the alcohol was first oxidized by the catalyst to generate the carbonyl compound, which can undergo immediately a condensation reaction with the amine to form the corresponding imine. Subsequent reduction of the imine leads to the saturated, N-alkylated amine.



Scheme 4. BH / HA mechanism and the examined $PN_{3\text{-}5}P$ ligand stabilized Co complexes (**1a-f, 2a-c**).

1d was found as the most active pre-catalyst in the N-alkylation of aniline with benzyl alcohol in a pre-catalyst screening at mild reaction temperatures (80 °C) and catalyst loadings of 2.5 mol%. After optimization of the reaction parameters, aniline and 3-amino pyridine were alkylated with several alcohols. Furthermore, various aniline derivatives were combined with benzyl alcohol to show the broad applicability of the cobalt catalyzed reaction. Remarkably, a broad functional group tolerance was observed. Furthermore, unsymmetrical alkylated diamines were synthesized via a two-step process.

The final part of this thesis is about the transition metal free, base mediated synthesis of N-heterocycles (Scheme 5). This method is based on an observation, which was made in attempting the application of the $PN_{3\text{-}5}P$ ligand stabilized $CoCl_2$ complexes in ADC reactions. Pyrroles, pyridines and indoles are easily available with this synthetic method. KO^{t}Bu mediates the reaction by transferring the hydrogen to a cheap and easy-to-handle hydrogen scavenger like benzophenone. The scavenger is simply removable and recyclable. The reactants are easy-to-handle and commonly available. The presented one-pot synthesis has a broad applicability and is also feasible in larger scale.

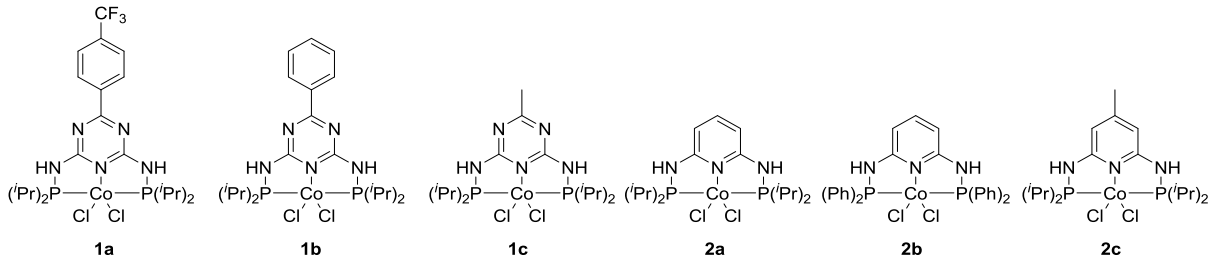


Scheme 5. Base mediated synthesis of pyridines (top), pyrroles (middle) and indoles (bottom)

Zusammenfassung

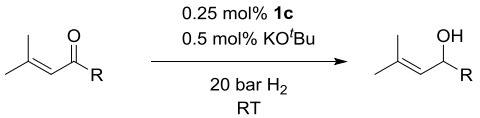
Inhalt der vorliegenden Arbeit ist die Entwicklung neuartiger $PN_{3\text{-}5}P$-Ligand-stabilisierter Kobaltkomplexe und deren Anwendung in der homogenen Katalyse. Diese wurden in katalytischen Reaktionen wie Hydrierung, „Borrowing Hydrogen / Hydrogen Autotransfer“ (BH/HA) und akzeptorloser dehydrierender Kondensation (ADC) eingesetzt. Solche Reaktionen werden typischerweise von Edelmetallen wie z.B. Iridium und Ruthenium katalysiert. Die Substitution dieser Metalle durch ein unedles, billiges Metall wie Kobalt, verleiht den genannten Reaktionen mehr Nachhaltigkeit.

Vorangegangene Arbeiten mit $PN_{3\text{-}5}P$-Ligand-stabilisierten Iridium-Komplexen zeigten, dass diese hervorragende Prä-Katalysatoren für die nachhaltige Synthese einer Vielzahl von N-Heterozyklen via ADC sind. Aufbauend auf diesen Erkenntnissen wurden sechs neuartige $PN_{3\text{-}5}P$-Ligand-stabilisierte $CoCl_2$ Komplexe synthetisiert und charakterisiert (Schema 1).



Schema 1. Synthetisierte PN_5P-Ligand-stabilisierte $CoCl_2$ Komplexe (**1a-c**) und PN_3P-Ligand-stabilisierte $CoCl_2$ Komplexe (**2a-c**).

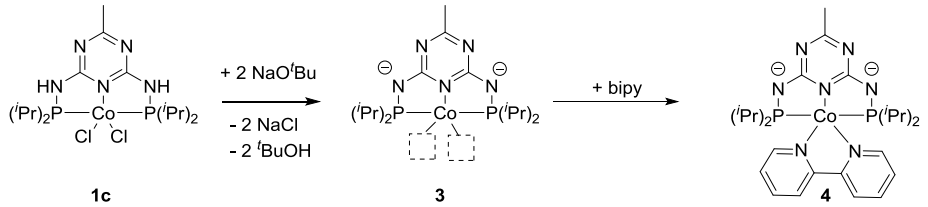
Anschließend wurden **1a-c** und **2a-c** auf ihre Aktivität in der Hydrierung von Ketonen untersucht. Dabei zeigte Komplex **1c** bei Raumtemperatur und unter 20 bar Wasserstoffdruck herausragende Hydriereigenschaften bei niedrigen Katalysatorbeladungen von 0.25 – 0.5 mol%. Es konnte eine Vielzahl von aryl-alkyl-, aryl-aryl- und alkyl-alkyl-Ketonen mit verschiedensten funktionellen Gruppen (meist) quantitativ zu den entsprechenden Alkoholen hydriert werden. Besonders bemerkenswert ist dabei die Selektivität des Katalysators gegenüber C=O Doppelbindungen in Gegenwart einer C=C Doppelbindung (Schema 2). Dabei konnten ungesättigte Alkohole mit Ausbeuten größer 99% dargestellt werden.



Schema 2. Ausgewähltes Beispiel für die selektive Hydrierung der C=O Bindung in Gegenwart einer C=C Bindung.

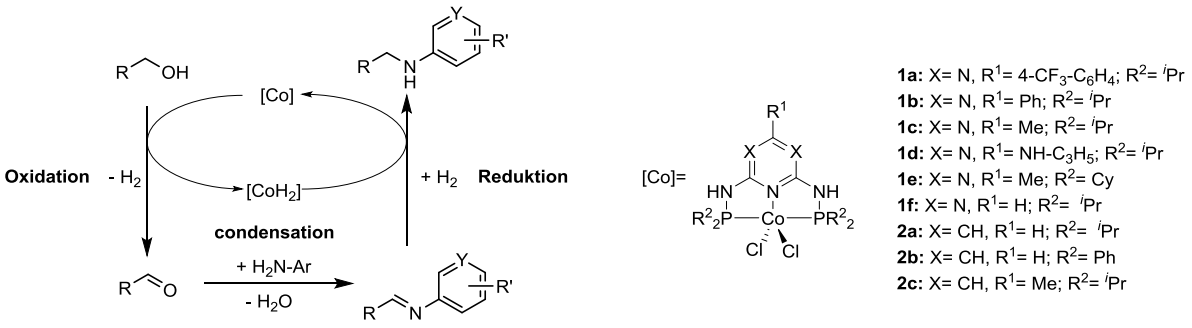
Um eine Vorstellung von der vermuteten aktiven Katalysatorspezies **3** zu erhalten, wurde **1c** in Gegenwart von Bipyridin mit zwei Äquivalenten Base aktiviert. So gelang es, Spezies **4** zu stabilisieren (Schema 3) und mittels Röntgeneinkristallstrukturanalyse zu charakterisieren. Diese Struktur macht

deutlich, dass die Oxidationsstufe des Kobalts auch nach der Aktivierung mit einer Base erhalten bleibt. Dies ist möglich, da die verwendeten tridendaten $PN_{3-5}P$-Liganden sowohl als Neutralliganden, als auch als mono- oder di-anionische Liganden agieren können.



Schema 3. Aktivierung von **1c** mit zwei Äquivalenten NaO^{t}Bu zur aktiven Spezies **3**. Zugabe von einem Äquivalent Bipyridin führt zu Verbindung **4**.

Mit der Affinität der $PN_{3-5}P$-$CoCl_2$ Komplexe zu Wasserstoffübertragungsreaktionen war es von großem Interesse, die Katalysatorklasse in der selektiven Monoalkylierung von aromatischen Aminen nach dem klassischen „Borrowing Hydrogen / Hydrogen Autotransfer“ (BH/HA) Konzept einzusetzen (Schema 4).

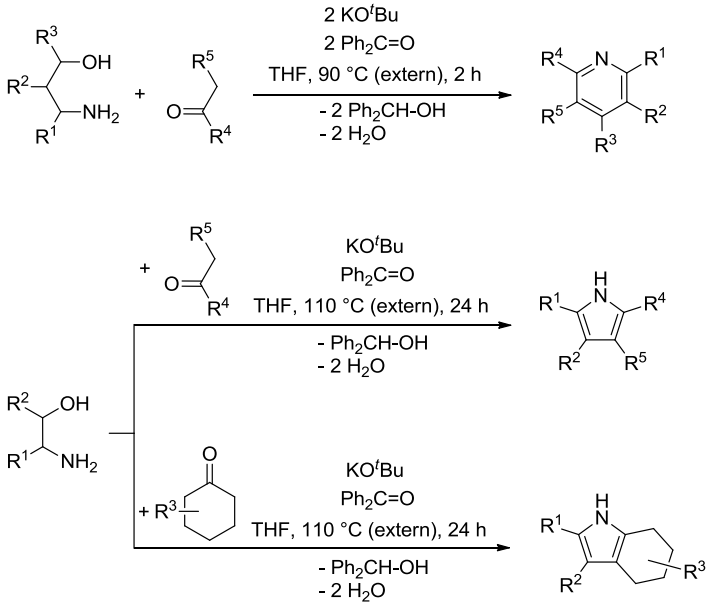


Schema 4. Mechanismus der BH/HA Reaktion und die untersuchten Kobalt Komplexe (**1a-f, 2a-c**).

Dabei wird zunächst der Alkohol vom Katalysator zur entsprechenden Carbonylverbindung oxidiert, welche anschließend mit einem Amin in einer Kondensationsreaktion zum korrespondieren Imin weiter reagieren kann. Durch Rückübertragung des „geliehenen“ Wasserstoffs erhält man das N-alkylierte Amin. In einem Katalysatorscreening bei milden Reaktionstemperaturen (80°C) und niedrigen Katalysatorbeladungen von 2.5 mol% zeigte **1d** die höchste Aktivität in der Alkylierung von Anilin mit Benzylalkohol. Nach Optimierung der Reaktionsparameter wurden Anilin und 3-Aminopyridin mit einer Vielzahl von primären Alkoholen umgesetzt. Des Weiteren wurden verschiedene Anilinderivate mit Benzylalkohol alkyliert. Dabei wurde eine große Toleranz gegenüber verschiedensten funktionellen Gruppen beobachtet. Zuletzt wurden unsymmetrisch alkylierte Diamine über einen zweistufigen Prozess in sehr guten Ausbeuten synthetisiert.

Im letzten Abschnitt dieser Arbeit ist die Übergangsmetall-freie, basenvermittelte Synthese von N-Heterozyklen beschrieben (Schema 5). Diese Synthesemethode wurde aus einer Beobachtung heraus

entwickelt, welche bei Versuchen zur Anwendung der $PN_{3-5}P$-Ligand-stabilisierten $CoCl_2$-Komplexe in ADC Reaktionen gemacht wurde.



Schema 5. Basenvermittelte Synthese von Pyridinen (oben), Pyrrolen (Mitte) und Indolen (unten).

Mit diesem Syntheseprotokoll ist es möglich, Pyridine, Pyrrole und Indole ausgehend von Aminoalkoholen und Carbonylverbindungen unter ausschließlicher Zuhilfenahme von KO^{t}Bu und eines Wasserstoffakzeptors herzustellen. Benzophenon stellte sich als günstiger und einfach handhabbarer Wasserstoffakzeptor heraus, welcher zudem einfach vom Produkt abgetrennt und recycelt werden kann. Die hier vorgestellte Eintopf-Reaktion besticht durch die breite Anwendbarkeit, einfache Handhabung und Zugänglichkeit der Edukte, sowie durch die Möglichkeit, die Reaktion auch im großen Maßstab durchzuführen.

2. Introduction

2.1 Sustainable aspects in environment, ecology and economy

With worlds growing population to over 9 billion people until 2050[1], the demand for an ecologically and economically sustainable use of our resources is becoming predominant. Besides atom economic syntheses, avoidance of waste and toxicity and the use of renewable feed stocks, catalysis is one of the twelve principles of green chemistry (Figure 1).[2] Therefore, the invention of new catalysts and synthetic protocols, which allow atom efficient syntheses from renewable, sustainable feed stocks, has become of growing interest in recent years.

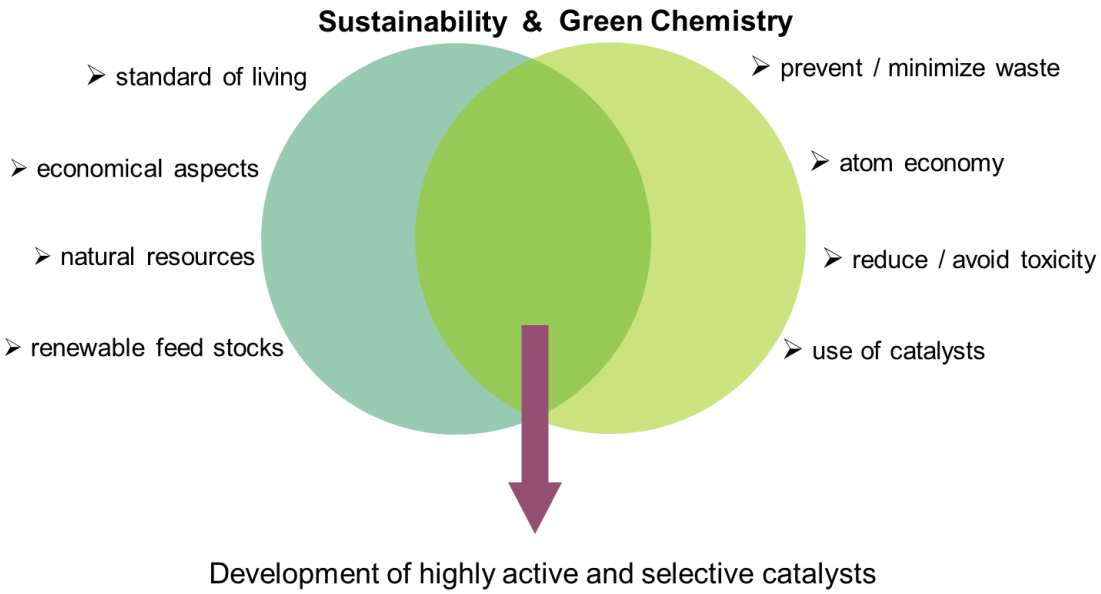


Figure 1. Melting zone of sustainability and green chemistry

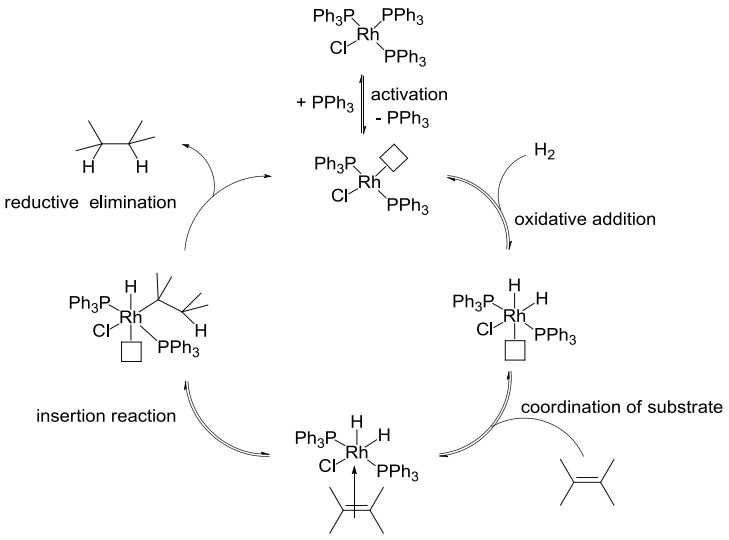
Typically, precious metals such as Ir, Ru, Rh, Pt and Pd show excellent behavior in activity, selectivity and life time in catalytic reactions. However, some of them are also highly important components in electronic devices and therefore meanwhile indispensable for the electronic industry. Furthermore, the resources on these metals are limited to their rare natural occurrence. Thus, with a growing population and an increasing standard of living, the consumption of these metals and therefore the prices are continuously rising.

For instance, the actual price per gram iridium is around 16 US$[3]. In comparison, one gram of cobalt costs around 0.03 US$[3]. In a chemical point of view, the more interesting value is the price per mole of metal, which is around 3075 $/mol for Ir and in comparison 1.8 $/mol for Co. Thus, cobalt is almost 1700 times cheaper than the same amount of iridium. With this background and with the intention to gain more earth abundance, the change in transition metal chemistry towards base metals is more than comprehensible. The development of more sustainable, economically and

environmentally friendly catalysts based on inexpensive, earth abundant base metals such as iron and cobalt is highly desirable.[4]

2.2 Sustainable reactions concepts

Hydrogenation with molecular hydrogen is a prominent example for an atom efficient reaction and is widely used in the chemical industry. Unsaturated compounds are reduced with high selectivity and performances without the generation of any side products or waste by using molecular hydrogen. Commonly, noble transition metal catalysts (Rh, Ir, Ru) play the leading role in the field of homogeneous hydrogenation.[5] A very famous and well understood Rh based hydrogenation catalyst is the Wilkinson complex [$RhCl(PPh_3)_3$] (Scheme 1).[6] The active species [$RhCl(PPh_3)_2$] is generated via ligand (PPh_3) dissociation. Oxidative addition of the dihydrogen molecule results in an unsaturated dihydridorhodium(III) complex. Coordination of the substrate (olefin) leads to a saturated 18 valence electron complex. Insertion of the substrate in the Rh-H bond and consecutive reductive elimination forms the stereo selective hydrogenated product and regenerates the active species [$RhCl(PPh_3)_2$]. A racemic mixture of both enantiomers is obtained by hydrogenation of pro-chiral substrates (e.g. ketones).



Scheme 1. Schematic mechanism of Wilkinson's olefin hydrogenation catalyst.[7]

In case of sophisticated substrates e.g. ketones or imines, two transition states for the hydrogen transfer are proposed. In the classical mechanism the hydrogen is activated by homolytical splitting of the dihydrogen, related to a change in the oxidation state of the metal center. The hydrogen transfer to the substrate takes place via a four-membered transition state (Figure 2, I).

Another concept for the activation of hydrogen is the metal-ligand bifunctional mechanism. This mechanism describes the heterolytical splitting of dihydrogen by generating a metal hydride and a proton, which is captured by a basic site (e.g. amine function) of the ligand.[8] The oxidation state of the metal center is not changed in this mechanism during the hydrogen uptake. The hydrogen

transfer to the substrate is mediated in this case via a six-membered pericyclic transition state (Figure 2, II). Furthermore, this mechanism is also plausible for the activation of hydrogen from organic sources such as alcohols (e.g. in transfer hydrogenation).[9]

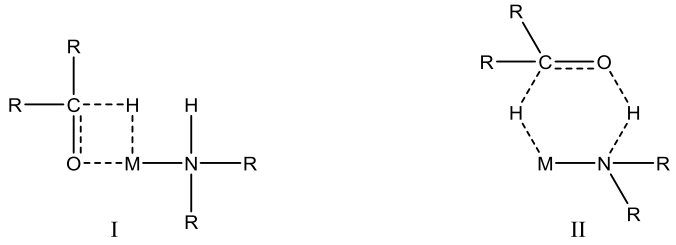
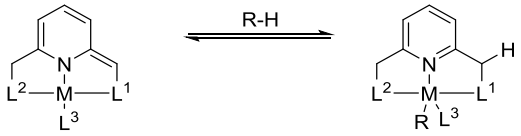


Figure 2. Four-membered transition state (I) in the classical mechanism and six-membered transition state (II) in the metal-ligand bifunctional mechanism for the reduction of C=O bonds. M = transition metal.

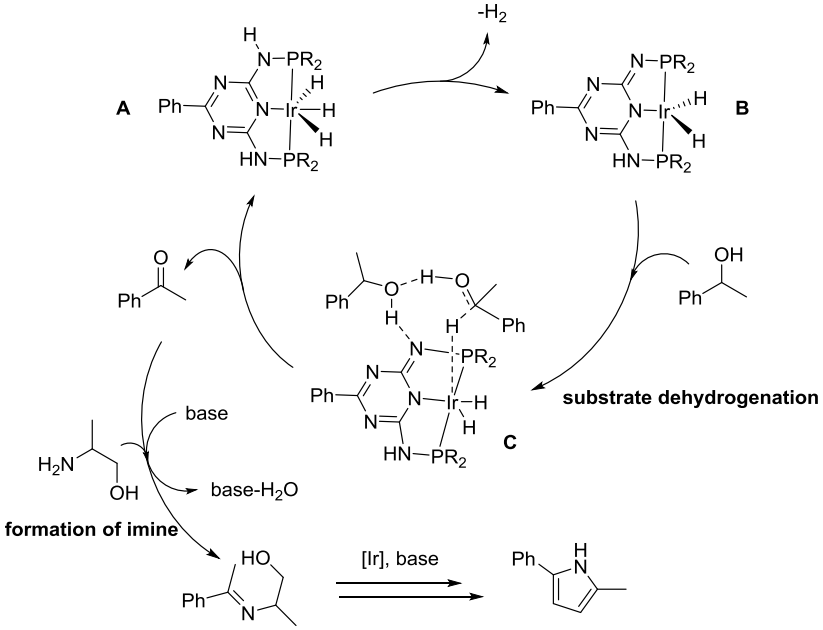
Another type of metal-ligand cooperation (MLC) is also known for pyridine type PNP-pincer complex catalysts.[10] The ligands are involved in the catalytic cycle by dearomatization / aromatization processes (Scheme 2).



Scheme 2. Schematic depiction of MLC in pyridine based LNL pincer type complexes. M = transition metal; L^1,L^2 = PR_2,NR_2; L^3= Cl, COD, PR_2.

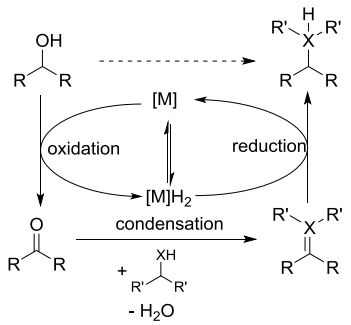
The tridentate $PN_{3\text{-}5}P$ ligands used in this work are also able to act in this manner and enable the iridium catalyzed sustainable synthesis of pyrroles[11], pyridines[12], pyrimidines[13] and other N-heterocycles[14] via acceptor less dehydrogenative condensation (ADC). In a theoretical study of Wang and coworkers the catalytic cycle is discussed in detail (Scheme 3).[15] The catalyst resting state **A** is activated via hydrogen loss. The generated active species **B** can now dehydrogenate the alcoholic substrate via the possible transition state **C** to form the corresponding ketone and regenerate the catalyst to resting state **A**.

The base plays an important role for the further reaction of the formed ketone. It acts as a proton transfer shuttle in the condensation step and mediates the imine formation. The pyrrole is formed by iteration of the cycle followed by an aromatization step. This shows a powerful tool for the sustainable synthesis of several N-heterocycles.



Scheme 3. Elemental steps of the catalytic cycle of Ir catalyzed pyrrole synthesis via ADC . **A** restingstate of the catalyst; **B** active state of the catalyst; **C** possible transition state.[15]

The synthetic concept of ADC has its origin in the concept of "borrowing hydrogen" or "hydrogen autotransfer" (BH/HA).[16] With this method alcohols, which are rather unreactive, are used as alkylating agents for nucleophiles, e.g. primary amines (Scheme 4). With the use of alcohols instead of the typical alkylating agents like alkyl halides, side product and halide wastes could be avoided. Furthermore, alcohols are much easier to handle and show lower toxicities than alkyl halides. The required alcohols could be generated in future exclusively from pyrolysis oil[17] (bio- based oil from biomass, e.g. lignocellulose) in order to minimize the dependence from decreasing oil and natural gas resources.



Scheme 4. Mechanism of BH/HA reaction. M = transition metal; X = N, C

First examples of N-alkylation of amines with alcohols were reported by the groups of Watanabe[16a] and Grigg[16b]. Major contributions to this topic were also made by the groups around Williams[18], Grigg[19], Beller[20], Fujita[21], Yus[22] and the Kempe group[23]. Typically, noble transition metals such as ruthenium and iridium catalyze the alkylation of amines and have been intensively studied.[24]

In consequence to the in chapter 2.1 mentioned issues, the substitution of these precious metals is in progress. However, they are widely unknown in the field of BH/HA. Recently Yan, Feringa and Barta[25] reported on a homogenous Fe catalyst (Knölkers catalyst[26]) for the direct N-alkylation of amines with alcohols. Very similar iron systems were used by the groups of Wills[27] and Zhao[28]. Very recently Darcel and co-workers published an iron catalyzed α-alkylation of ketones.[29] To the best of my knowledge, a homogeneous cobalt catalyst for the N-alkylation of amines by alcohols has not been reported so far.

To find out which kind of cobalt catalyst could be potentially able to transfer hydrogen in a way of BH/HA or ADC, first their potential in hydrogenation with molecular hydrogen should be investigated. However, the number of publications, dealing with cobalt catalyzed homogeneous hydrogenation has grown slowly in recent years. A reason could be the high tendency of 3d metals, especially cobalt, to one electron processes,[30] omitting typical reaction pathways for hydrogenation or related reactions. To overcome this behavior, structurally and electronically well designed ligands are required.[31]

With this knowledge, significant progresses in Co catalyzed C=C bond hydrogenation were made by the group of Budzelaar[31] and the group of Chirik[32]. Homogenous cobalt catalysts for efficient C=O bond reduction are only described by Hanson[33] and co-workers and v. Wangelin[34] and co-workers. Examples of Co catalysts of the state of the art are given in Figure 2. Recently, Milstein and co-workers reported on a homogeneous cobalt catalyzed hydrogenation of esters to alcohols by PNP and NNP ligand stabilized Co complexes.[35]

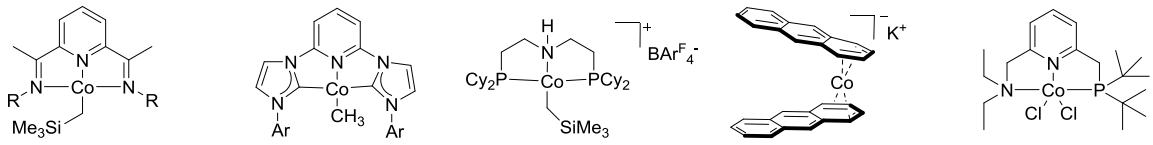


Figure 2. Examples of Co catalysts for homogeneous hydrogenation noted in literature.

These catalysts show a fundamental improvement in cobalt catalyzed hydrogenation. Furthermore, Hanson's PNP ligand stabilized Co complex is the first reported homogeneous Co catalyst being active in acceptor-less dehydrogenation.[36]

Regarding on these promising results, this work follows on the mentioned concepts, aims and ideas.

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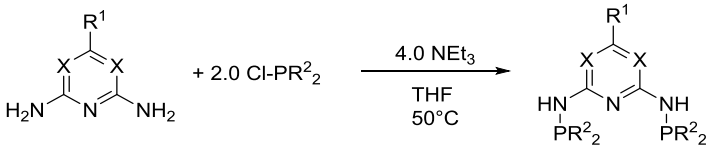
3. Overview of Thesis Results

This thesis contains three publications, which are presented in chapter 4-6.

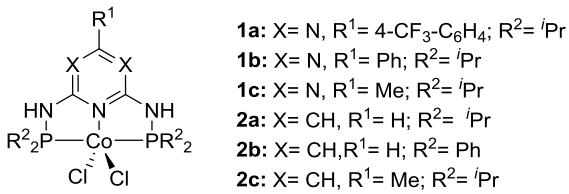
3.1 Synopsis

In previous work of the Kempe group, $PN_{3\text{-}5}P$ ligand stabilized iridium complexes were found as highly active catalysts for the sustainable synthesis of aromatic N-heterocycles. The therein introduced PN_5P ligands are simple in synthesis (Scheme 1) and based on commercially available reactants. Due to the modular design of this ligand class, their steric and electronic properties are highly variable and hence these ligands are potentially appropriate for the stabilization of highly active cobalt cations.

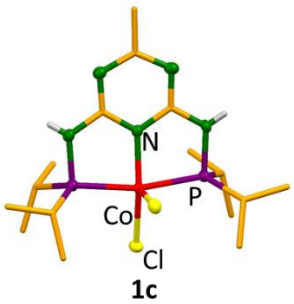


Scheme 1. Schematic depiction of ligand synthesis (X = N or CH).

In the beginning, six novel $PN_{3\text{-}5}P$ ligand stabilized $CoCl_2$ complexes (Figure 1, **1a-c, 2a-c**) were synthesized and characterized. The complexes are easy-to-synthesize, easy-to-handle and stable at ambient conditions as solid materials for a period of a few months. Single crystal structure analyses (XRD) of the crystalline complexes (example of **1c** is shown in Figure 1) showed a pentacoordinated Co(II) cation in a slightly distorted square pyramidal coordination. The neutral PN_5P ligand is coordinated to the cobalt center in the typical tridentate mode. Both N-H hydrogen atoms could be unequivocally located in the difference electron density map. All presented Co complexes showed a paramagnetic behavior and an effective magnetic moment between 2.2 and 2.3 μ_B.



1a: X= N, R^1= 4-CF_3-C_6H_4; R^2= ^{i}Pr
1b: X= N, R^1= Ph; R^2= ^{i}Pr
1c: X= N, R^1= Me; R^2= ^{i}Pr
2a: X= CH, R^1= H; R^2= ^{i}Pr
2b: X= CH,R^1= H; R^2= Ph
2c: X= CH, R^1= Me; R^2= ^{i}Pr



1c

Figure 1. Synthesized PN_5P $CoCl_2$ complexes (**1a-c**) and PN_3P $CoCl_2$ complexes (**2a-c**) and molecular structure of **1c** determined with single crystal X-Ray analysis.

For a first catalytic approach, these complexes were investigated in the homogeneous hydrogenation of C=O bonds. The pre-catalysts were activated *in situ* with two equivalents of base, preferentially NaO^tBu. Remarkably, **1c** showed an unique activity in the hydrogenation of acetophenone (Figure 2). The comparison of **1c** and **2c** reveals the beneficial effect of the triazine ring. Thus, **1c** was used for

further optimization of the reaction conditions (catalyst loading, solvent, hydrogen pressure) and mechanistic investigations.

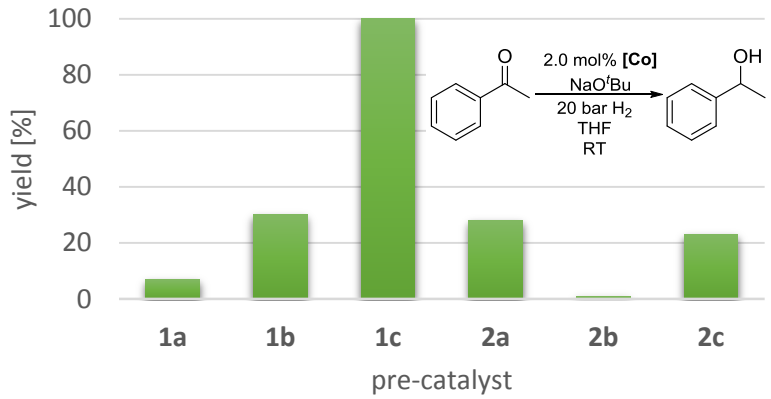


Figure 2. Pre-catalyst screening results of hydrogenation of acetophenone. Reaction conditions: 3.0 mmol acetophenone, 2.0 mol% pre-catalyst, 4.4 mol% NaO^{t}Bu, 2 mL of THF, 20 bar H_2, room temperature, 24 h.

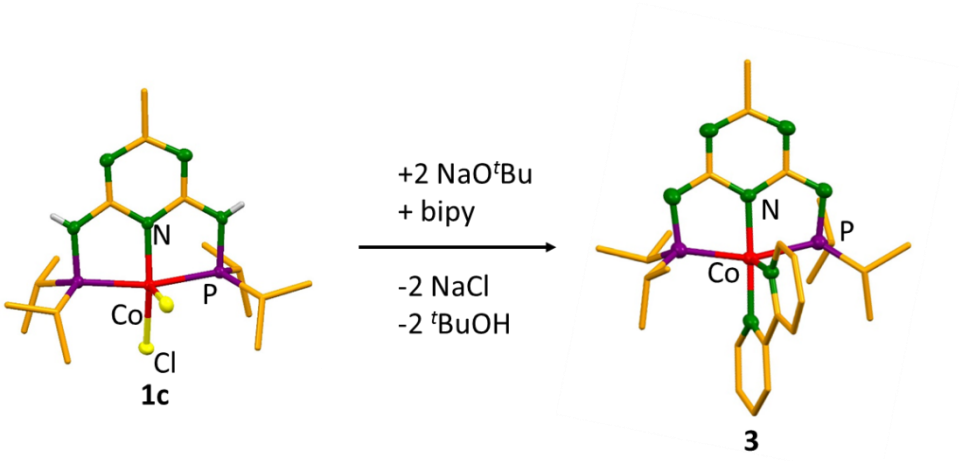


Figure 3. Activation of **1c** with NaO^{t}Bu in presence of bipyridine. The molecular structure of **3** (red orange crystals) was determined with single crystal XRD analysis.

In order to get a more detailed insight into the activation process and the role of the base herein, **1c** was activated with two equivalents of NaO^{t}Bu. The activated species was trapped with bipyridine, resulting in complex **3** (Figure 3). The structure of **3** indicates, that the oxidation state of the cobalt is not affected by the activation procedure. This result is in accordance with the measured effective magnetic moment of 1.9 μ_B for **3**, which is expected for a Co(II) low-spin complex in a pentacoordinated environment. After adaption of the reaction parameters, several carbonyl compounds were hydrogenated. A broad product scope was observed, covering aryl-alkyl, aryl-aryl, alky-alkyl ketones and aldehydes. Several functional groups are well tolerated. In particular, a noteworthy selectivity towards C=O bond hydrogenation in presence of a C=C bond was observed (Figure 4).

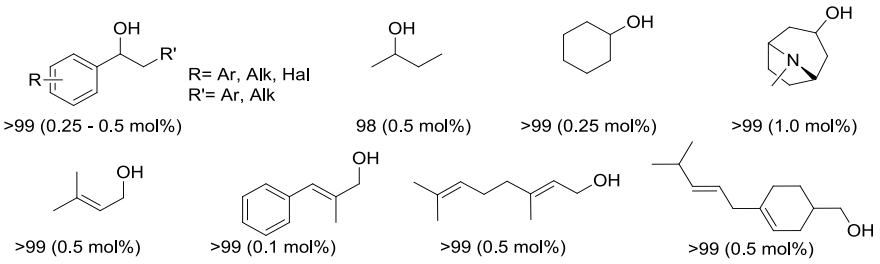
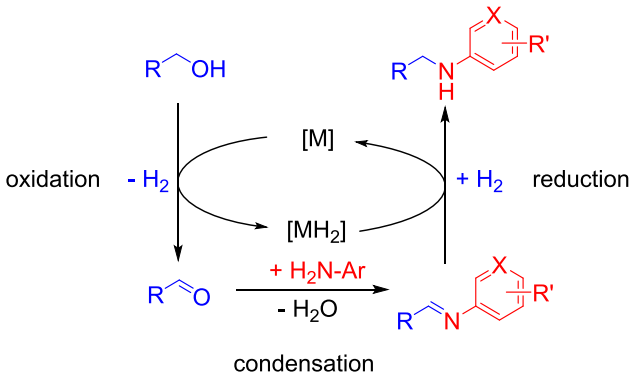


Figure 4. Product scope of cobalt catalyzed hydrogenation. Yield in % and catalyst loading in parentheses.

With these results, it became interesting to expand the catalytic applicability of this catalyst family. The affinity of these catalysts for hydrogen transfer reactions turned the focus on the synthetic concept of the BH/HA reaction. The ability of a catalyst to alcohol dehydrogenation (oxidation reaction), "storage"of the hydrogen and "re-transfer" of the hydrogen to the formed imine (reduction) plays a central role in the mechanism of BH/HA (Scheme 2).



Scheme 2. Mechanism of BH/HA reaction shown exemplarily for the N-alkylation of aniline derivatives with primary alcohols.

For preliminary investigations, the N-alkylation of aniline with benzyl alcohol was chosen as a model reaction. Complex **1c** was used in this experiments as pre-catalyst due to its exceptionally high activity in hydrogenation reactions. 66 % yield of N-benzyl aniline were obtained with a pre-catalyst loading of 5.0 mol% **1c**, without further optimizations at 80 °C reaction temperature. For a broadened catalyst screening, three additional PN_5P $CoCl_2$ complexes were synthesized and characterized (Figures 5 and 6, **1d-f**). Pre-catalyst **1d** was found as the most active in the N-alkylation of aryl amines by primary alcohols. In a test reaction without cobalt and also only with $CoCl_2$ as pre-catalyst, only 3-5 % product were obtained under the above mentioned conditions.

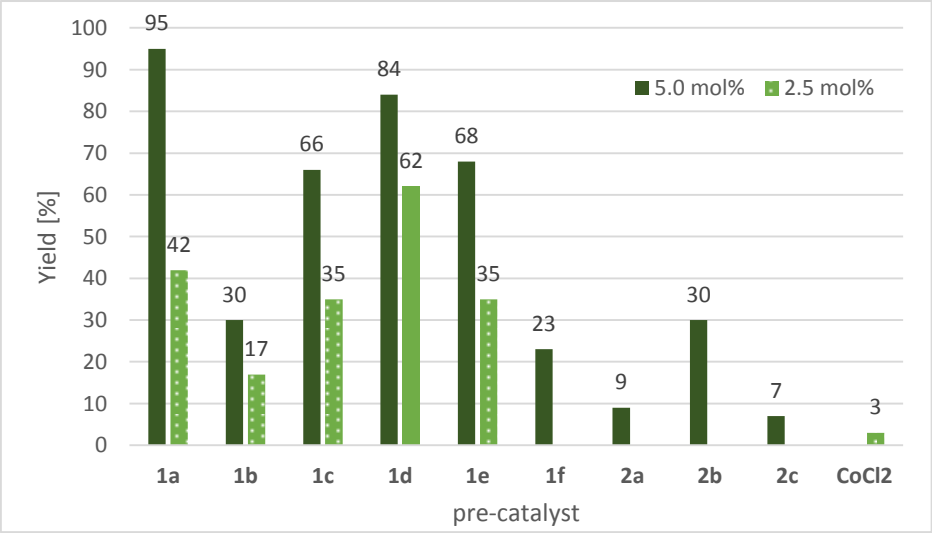
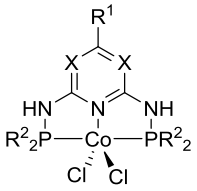


Figure 5. Pre-catalyst screening in alkylation of aniline with benzyl alcohol. Reaction conditions: 1.0 mmol aniline, 1.1 mmol alcohol, 1.0 mmol KO^{t}Bu, 5.0 mol% (dark green) or 2.5 mol% (light green) pre-catalyst, 5 mL toluene, 80 °C, 24 h.



1a: X= N, R^1= 4-CF_3-C_6H_4; R^2= ^{i}Pr
1b: X= N, R^1= Ph; R^2= ^{i}Pr
1c: X= N, R^1= Me; R^2= ^{i}Pr
1d: X= N, R^1= NH-C_3H_5; R^2= ^{i}Pr
1e: X= N, R^1= Me; R^2= Cy
1f: X= N, R^1= H; R^2= ^{i}Pr
2a: X= CH, R^1= H; R^2= ^{i}Pr
2b: X= CH,R^1= H; R^2= Ph
2c: X= CH, R^1= Me; R^2= ^{i}Pr

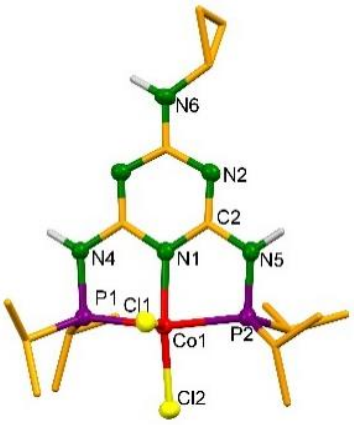


Figure 6. Investigated pre-catalysts in N-alkylation of amines and molecular structure of **1d**.

After optimization of the reaction parameters (reaction temperature, solvent, catalyst loading, base loading, amine to alcohol ratio), the protocol was applied to several substrates. First, aniline was alkylated with several primary alcohols, obtaining good to excellent isolated yields (Figure 7, left). Second, various aniline derivatives were alkylated with benzyl alcohol (Figure 7, middle). On both sides, a broad functional group tolerance was observed. Due to the mild conditions, even bromine and iodine functions were tolerated. Furthermore, the protocol was successfully applied in the N-alkylation of 3-amino pyridines (Figure 7, right). Finally, unsymmetrical alkylated diamines were synthesized via a two-step procedure in good isolated yields (Scheme 3). With this work, the first homogeneous cobalt catalyzed N-alkylation of amines was presented.

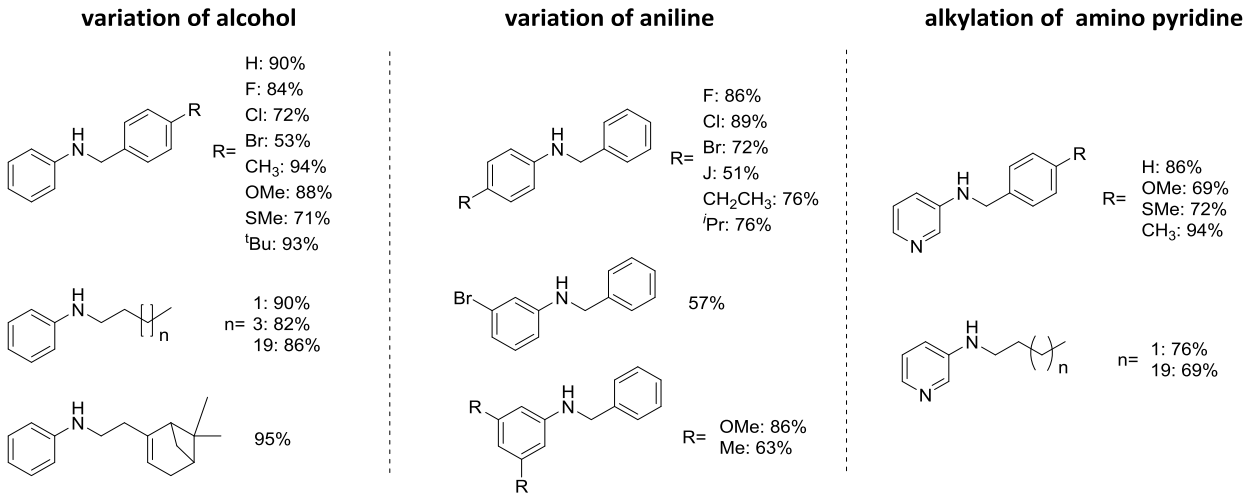
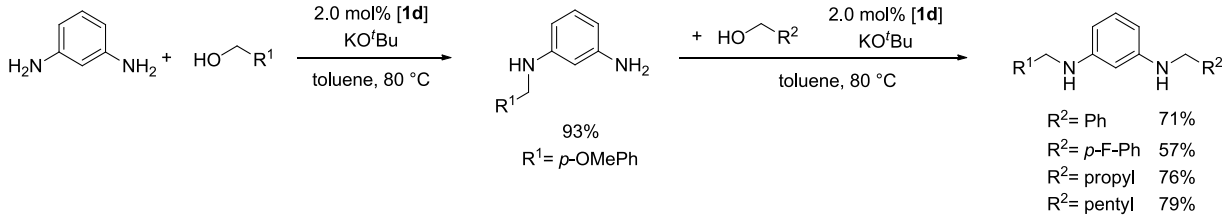
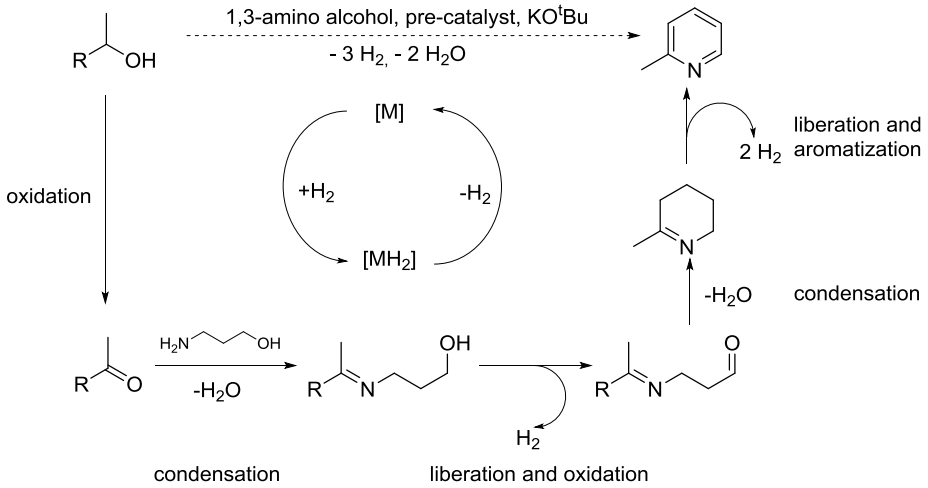


Figure 7. Synthesized products by cobalt catalyzed alkylation of aromatic amines with primary alcohols. Reaction conditions: 1.4 mmol amine, 1.0 mmol alcohol, 1.2 equiv KO^{t}Bu, 2.0 mol% **1d**, toluene, 80 °C, 24 h.



Scheme 3. Synthesis of unsymmetric alkylated diamines via a two step procedure.

Finally, the application of these catalysts in acceptor-less dehydrogenation condensation reactions was the consecutive step to get access to unsaturated compounds such as N-heteroarenes. Therefore, the "re-transfer reaction" of the hydrogen to the unsaturated intermediate must be suppressed, ideally by liberation of the hydrogen (Scheme 4).

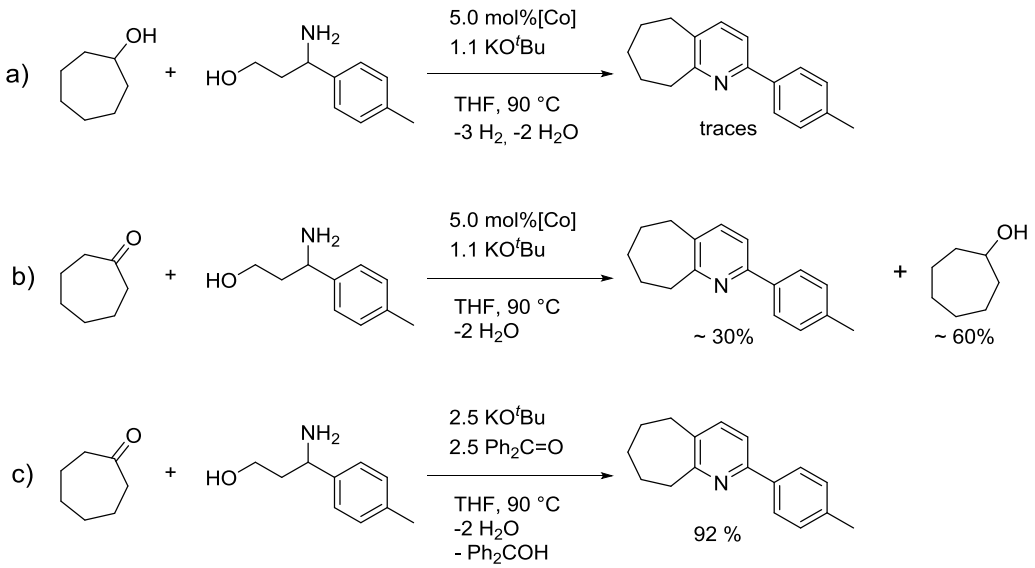


Scheme 4. Schematic mechanism of ADC (acceptor-less dehydrogenative condensation) reaction in the synthesis of pyridines.

As reaction conditions for the first investigations, established parameters for the iridium catalyzed synthesis of pyridines was used. The synthesis of 2-*p*-tolyl-5,6,7,8,9-pentahydro-

cyclohepta[*b*]pyridine was chosen as a model reaction. Cycloheptanol and 3-amino-3-*p*-tolyl-1-propanol was combined with 5.0 mol% of **1c** in presence of 110 mol% base in THF and stirred at 90 °C extern reaction temperature. Unfortunately, only traces of the product were observed after 24 h reaction time (Scheme 5, a). To simplify the reaction, a ketone (cycloheptanone) was used instead of the alcohol (Scheme 5, b). Approximately 30 % of product were observed, while all unreacted ketone was converted into the corresponding alcohol. This suggests, that the ketone acts as an acceptor for the hydrogen and enables the reaction. Several investigations were made to screw up the product yield. Interestingly, while using a hydrogen scavenger high product yields were obtained. During these screening reactions, it was found that the reaction is not driven by the catalyst, it is rather mediated by the base. To confirm this assumption, transition metal free experiments with different hydrogen acceptors were examined (Scheme 5, c). Benzophenone and isobutyrophenone led to the best product yields. Surprisingly, over 90 % yield were obtained with 2.5 equivalents KO^{t}Bu and 2.5 equiv. scavenger with respect to the amino alcohol. This amount of base and scavenger is in correspondence to the theoretical transferred two equivalents of hydrogen in the reaction.

After optimization of the reaction conditions, the applicability of this method was examined. 13 different pyridines were synthesized in good to excellent yields by variation of the ketone and the amino alcohol (Figure 8).



Scheme 5. a) Model reaction for initial experiments, b) simplified reaction by substitution of cycloheptanol to cycloheptanone, c) transition metal free pathway. All reactions were carried out in a seald pressure tube at 90°C extern temperature.

Substitution of the 1,3-amino alcohols by 1,2-amino alcohols led to substituted NH-pyrroles. The reaction parameters were adapted to the needs of the pyrrole synthesis. Base and hydrogen scavenger loadings could be reduced to 1.5 equivalents due to the reduced theoretical hydrogen release in the reaction. The reaction temperature had to be raised to 110 °C extern temperature.

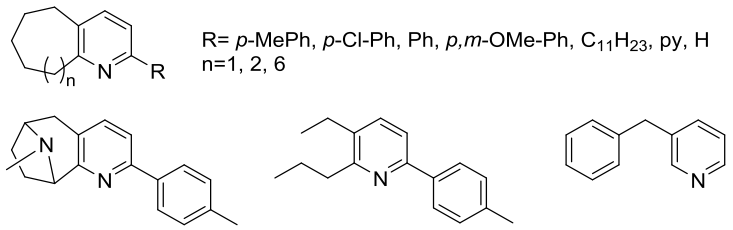


Figure 8. Synthesized pyridines via the transition metal free pathway.

19 different pyrroles and indoles were synthesized with this method, limiting on the side of the amino alcohol by the natural occurrence of their corresponding amino acids. On the ketone side, (bi-) cyclic and symmetric ketones were used to form indoles in case of cycohexanol derivatives and bi-cyclic NH-pyrroles as well as 2,3,5- tri-substituted NH-pyrroles (Figure 9). All compounds could be easily isolated in good yields either by distillation or by column chromatography.

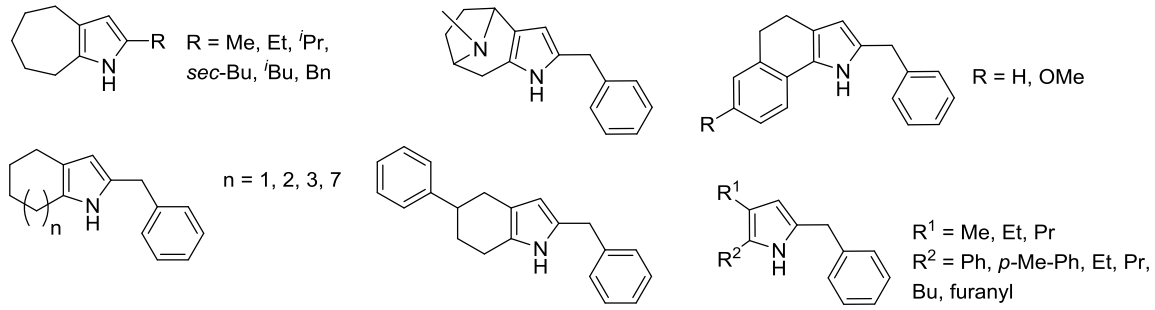


Figure 9. Synthesized NH-pyrroles and indoles.

3.2 Individual contribution to joint publications

The results presented in this thesis were obtained in collaboration with others and are published, submitted or are to be submitted as indicated below. In the following, the contributions of all co-authors to the publications are designated. The asterisk denotes the corresponding authors.

Chapter 4

This work was published in the Journal of the American Chemical Society (*J. Am. Chem. Soc.* **2015**, *137*, 7998-8001) with the title "**A highly active and easily accessible cobalt catalyst for selective hydrogenation of C=O bonds**".

Authors: Sina Rösler, Johannes Obenauf, and Rhett Kempe*

I synthesized and characterized all presented ligands and complexes, run the catalytic experiments and the assigned analytics (GC, GC-MS, NMR) and wrote the publication. Johannes Obenauf performed the X-Ray analyses of the complexes and solved the crystal structures. Prof. Rhett Kempe supervised the work, was involved in scientific discussions and the correction of the manuscript.

Chapter 5

This work was published in Angewandte Chemie International Edition (*Angew. Chem. Int. Ed.* **2015***, 54,* 15046-15050 and *Angew. Chem.* **2015***, 127,* 1526-15264) with the title "**Cobalt catalyzed alkylation of aromatic amines by alcohols**".

Authors: Sina Rösler, Michael Ertl, Torsten Irrgang, and Rhett Kempe*

I synthesized and characterized all ligands, complexes and products presented in this work. I established the synthetic protocols, achieved all NMR and GC measurements and wrote the publication. Michael Ertl worked on preliminary experiments contributing to this topic during his bachelor thesis. Dr. Torsten Irrgang and Prof. Dr. Rhett Kempe were involved in scientific discussions and correction of the manuscript.

Chapter 6

This work is to be submitted with the title "**Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols**".

Authors: Sina Rösler, Torsten Irrgang, and Rhett Kempe*

I synthesized and characterized all compounds presented in this work. I established the synthetic protocols, achieved all NMR and GC measurements and wrote the publication. Dr. Torsten Irrgang and Prof. Dr. Rhett Kempe were involved in scientific discussions and correction of the manuscript.

4. A highly active and easily accessible cobalt catalyst for selective hydrogenation of C=O bonds

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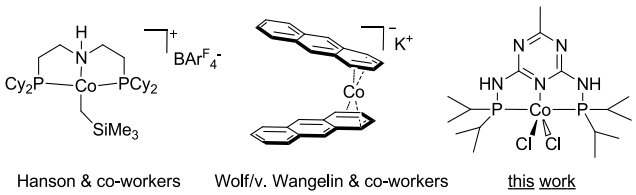
Published in: *J. Am. Chem. Soc.* **2015**, *137*, 7998-8001.

Abstract: The substitution of high-price noble metals such as Ir, Ru, Rh, Pd, and Pt by earth-abundant, inexpensive metals like Co is an attractive goal in (homogeneous) catalysis. Only two examples of Co catalysts, showing efficient C=O bond hydrogenation rates, are described. Here, we report on a novel, easy-to-synthesize Co catalyst family. Catalyst activation takes place via addition of 2 equiv of a metal base to the cobalt dichlorido precatalysts. Aldehydes and ketones of different types (dialkyl, aryl-alkyl, diaryl) are hydrogenated quantitatively under mild conditions partially with catalyst loadings as low as 0.25 mol%. A comparison of the most active Co catalyst with an Ir catalyst stabilized by the same ligand indicates the superiority of Co. Unique selectivity toward C=O bonds in the presence of C=C bonds has been observed. This selectivity is opposite to that of existing Co catalysts and surprising because of the directing influence of a hydroxyl group in C=C bond hydrogenation.

4.1 Introduction

Homogenous hydrogenation with molecular hydrogen is a key step in the industrial synthesis of fine chemicals. Typically, high-price noble metals such as Ir, Ru, Rh, Pd, and Pt play the leading role as catalytically active sites in hydrogenation catalysts.[1] Substitution of these metals by inexpensive, earth-abundant metals like Co would give advantages in terms of costs and sustainability. Furthermore, the unique electronic structural properties of such base metals may allow the observation of unusual activity/selectivity profiles. Despite these and other perspectives, the development of well-defined homogeneous Co hydrogenation catalysts has progressed slowly, especially with regard to the reduction of C=O bonds. However, with the implementation of rational ligand design, a few new Co catalysts for homogeneous hydrogenation have been disclosed in recent years. Hydrogenation of olefins with Co complexes has been described by Budzelaar and coworkers[2] as well as by Chirik and co-workers.[3] A bis-(phosphino)borylcobalt catalyst (for which a boryl–metal cooperativity was observed) has been applied by Peters and co-workers in C=C bond hydrogenation.4

Very recently, Milstein and co-workers reported on the Co-complex-catalyzed hydrogenation of esters.[5]



Scheme 1. Known homogenous cobalt catalysts for C=O bond hydrogenation (left and middle).

To the best of our knowledge, homogeneous Co catalysts for efficient C=O reduction with molecular hydrogen are only described for two examples.[6] Hanson and co-workers reported a bis[2-(dicyclohexylphosphino) ethyl]amine-stabilized cobalt(II)−alkyl catalyst (Scheme 1, left) for C=C, C=N, and C=O reduction.[7] The precatalyst is activated with 1 equiv of $H[BArF_4]\cdot(Et_2O)_2$ (Brookhart's acid,[8] $[BArF_4]^-$ = tetrakis[(3,5-trifluoromethyl)-phenyl]borate) and reduces C=O bonds involving 2.0 mol% catalyst loading within 1–4 bar H_2 pressure at room temperature. Notably, dehydrogenation of alcohols has been observed with this catalyst, too.[9] A heteroatom-free arene-cobalt-ate catalyst for C=C, C=O, and C=N hydrogenation was developed by the group of Wolf and von Wangelin (Scheme 1, middle).[10] Carbonyl compounds are reduced in good to excellent yields with 5.0 mol% of the catalyst, 10 bar H_2 pressure at 60 °C, without previous activation of the catalyst. The above-mentioned Co catalysts, able to mediate C=O bond hydrogenation (Scheme 1), represent impressive progress in hydrogenation chemistry. Unfortunately, they also suffer from disadvantages like labile ligand coordination, expensive activation agents, and restricted capabilities for ligand modifications.

We recently introduced (triazine-based) PN3−5P-Ir complexes (an example of a Co complex is shown in Scheme 1, right) as highly efficient homogeneous catalysts for acceptorless dehydrogenative condensation reactions.[11] Haupt and coworkers introduced such PN_3P ligands,[12] and Kirchner and co-workers demonstrated the broad applicability of the ligand class.[13] Reports on Co complexes stabilized by such ligands are rare.[13e,14,15]

4.2 Results and Discussion

Herein we report on a novel, easy-to-synthesize, and simple-to-activate homogeneous cobalt C=O bond hydrogenation catalyst family (Scheme 1, right). The precatalysts can be synthesized quantitatively up to multigram scale.[16] They are air stable for a period of a few months as a crystalline material. Activation of the precatalysts proceeds via salt elimination by adding 2 equiv of a base and is based on the ability of the used PN3−5P ligand class to act as neutral, monoanionic, or dianionic ligand. The modularly assembled structure of the chosen ligands allows the employment of catalyst libraries for activity screenings. Selective hydrogenation of C=O bonds in the presence of C=C

bonds was observed despite (i) the directing influence of a hydroxyl group in olefin hydrogenation for Co catalysts[3a] and (ii) inverse selectivity patterns as reported for the Hanson catalyst.[7c]

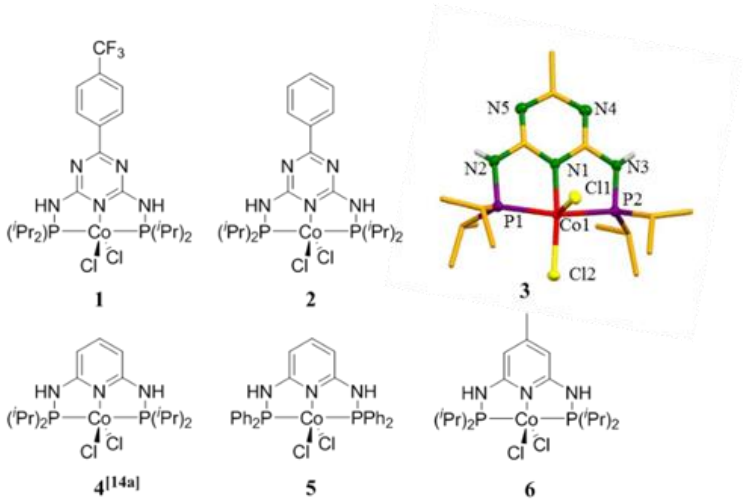
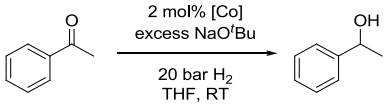


Figure 1. Synthesized $PN_{3-5}P$-stabilized Co(II) chlorido complexes and molecular structure of **3** with 50% probability of thermal ellipsoids. H-atoms (except for the two N−H groups) are omitted for clarity. Selected bond lengths [Å] and angles [°]: Co1−P1 2.220(1); Co1−P2 2.220(1); Co1−Cl1 2.437(1); Co1−Cl2 2.238(1); Co1−N1 1.925(4); P1−Co1−P2 167.04(6); N1−Co1−Cl1 93.0(1); N1−Co1−Cl2 160.3(1); N2−P1−Co1 98.8(2); N3−P2−Co1 99.1(2); C1−N2−P2 119.4(4); C3−N3−P2 118.6(4).

The precatalyst synthesis is performed by addition of an equimolar solution of the ligand to a suspension of anhydrous $CoCl_2$ in THF. The desired precatalysts precipitate as red crystalline solids in quantitative yields. Complexes were characterized by X-ray diffraction (XRD) analysis, elemental analysis, IR spectroscopy, and magnetic measurements. All complexes show paramagnetic behavior and an effective magnetic moment between 2.2 and 2.3 μ_B (studied over a temperature range from 300 to 50 K using a SQUID magnetometer).[17] The molecular structure of **3** is shown in Figure 1. XRD indicates an pentacoordinated Co(II) complex with a slightly distorted square pyramidal coordination. The neutral PN5P ligand is coordinated to the Co center in the typical tridentate mode, with a P1−Co1−P2 angle of 167.04(6)°. Both N−H hydrogen atoms could be located in the difference electron density map. Selected bond distances and angles are given in the caption of Figure 1.

The catalytic activity of complexes **1–6** (Figure 1, Table 1) and the metal precursor $CoCl_2$ was investigated in the hydrogenation of acetophenone (3.0 mmol) using 2.0 mol% precatalyst in THF under 20 bar hydrogen pressure and room temperature. The precatalysts were initially activated with a slight excess (4.4 mol%) of NaO^tBu (^tBu = tert-butyl). Complex **3** was identified as the most active precatalyst. Comparison of **3** and **6** reveals the beneficial effect of the triazine ring. Besides the altered basicity of the coordinating N-atom, an explanation can be the stabilization of the proton shuttle chain via hydrogen-bonding with the N-atoms of the triazine moiety of the PN_5P ligand backbone.[18]

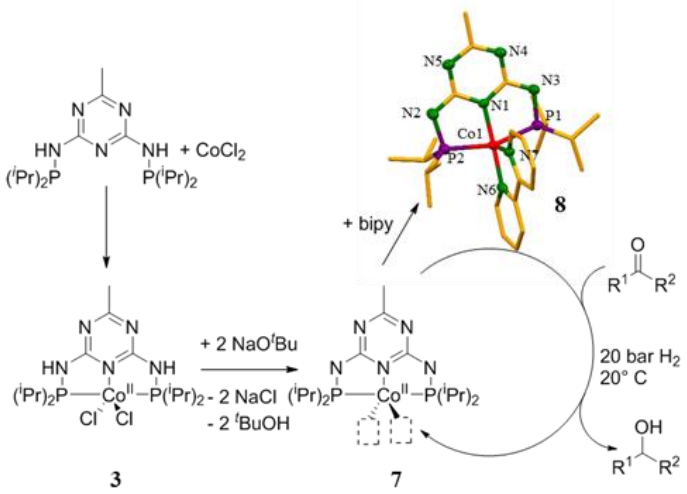
Table 1. Hydrogenation of Acetophenone with Several Cobalt(II) Precatalysts (See Figure 1)[a]



entry	precatalyst	yield[b] [%]
1	1	7
2	2	30
3	3	>99
4	4	28
5	5	0
6	6	23
6	$CoCl_2$	0

[a]Reaction conditions: acetophenone (3.0 mmol), 2.0 mol% Co, NaO^{t}Bu (13 mg, 4.4 mol%), 2 mL of THF, 20 bar H_2, room temperature, 24 h. [b]Determined via GC with dodecane as internal standard.

To understand the role of the base in the activation process, a base-loading screening was carried out (Supporting Information [SI]). A 2 equiv amount of the metal base NaO^{t}Bu is necessary to generate a catalytically active complex. The exact structure of this complex is not fully clear yet. To gain insight, the activated species was trapped with 1 equiv of bipyridine. The resulting red-orange complex (**8**, Figure 2) was analyzed by XRD. Both chlorido ligands as well as both N−H protons were salt-eliminated by the base. The PN_5P ligand acts as a dianionic ligand, coordinating the Co again in the pincerlike tridentate manner with a P1−Co1−P2 angle of 158.18(5)°. The oxidation state of the Co(II) center is not affected by the activation procedure. Complex **8** has an effective magnetic moment of



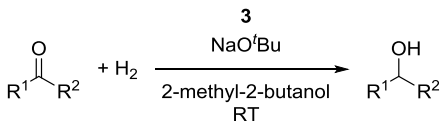
1.9 μ_B, expected for a Co(II) low-spin complex in a pentacoordinated environment.

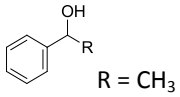
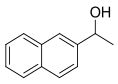
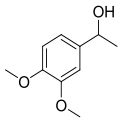
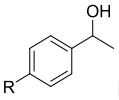
Figure 2. Synthesis and activation of **3** as well as trapping of the activated catalyst with bipyridine (**8**). The molecular structure of **8** is displayed with 50% probability of thermal ellipsoids. H-atoms are omitted for clarity. Relevant bond lengths [Å] and angles [°]: Co1−P1 2.214(1); Co1−P2 2.223(1); Co1−N1 1.915(3); Co1−N6

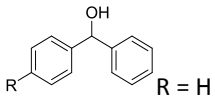
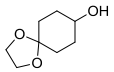
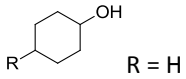
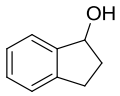
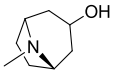
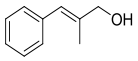
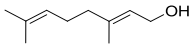
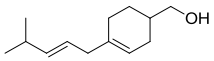
1.930(3); Co1−N7 2.016(3); P1−Co1−P2 158.18(5); N1−Co1−N6 178.0(1); N1−Co1−N7 97.7(1); N2−P2−Co1 102.3(1); N3−P1−Co1 105.1(1); P1−N3−C3 112.0(3); P2−N2−C1 113.3(3).

Next, we became interested in comparing the activity of the catalyst based on **3** with an Ir complex stabilized by the same PN_5P ligand (Figure S2, SI). Under base-free conditions, the iridium catalyst shows no remarkable conversion. With Na-to-Ir ratios of 1 and 2 (Figure S2, green and blue graphs, respectively), a faster conversion is observed. It increases at higher base concentration and is still slower than that with Co (red graphs). Such an activating effect of a metal base is known for other iridium C=O bond hydrogenation catalysts.[19] At very high base loadings (Na/Ir = 10, Figure S2), the Ir catalyst is faster. NaO^tBu addition beyond the 2 equiv needed for its activation is not beneficial for **3**. The comparison indicates that different mechanistic pathways seem relevant and the Co catalyst is superior under base free-conditions or at low base concentrations including identical conditions. Base-free conditions are advantageous since metal bases like NaO^tBu can mediate side reactions of the educts, like aldol-type condensations.

Table 2. Hydrogenation of Aryl-alkyl, Diaryl, and Aliphatic Carbonyl Compounds[a]



Entry	Product	Cat. loading [mol%]	Yield[b] [%]
1	 R = CH_3	0.25	>99
2	R = CH_2CH_3	0.5	>99
3	R = $(CH_2)_4CH_3$	0.5	>99
4	R = H	0.5	>99
5		0.5	>99
6		0.25	>99
7	 R = F	1.0	98 (94[c])
8	R = Cl	1.0	>99
9	R = Br	2.0	64
10		3.0	91
11		3.0	95

12	 R = H	0.25	>99
13	R = Me	0.5	>99 (97[c])
14	R = OMe	0.5	97
15		0.5	98
16		0.5	>99
17	 R = H	0.25	>99
18	R = Ph	0.5	>99 (93[c])
19		0.5	>99
20		1.0	>99 (92[c])
21		0.5	>99
22		1.0	>99 (97[c])
23		0.5	>99
24		0.5	>99 (95[c])

[a]Reaction conditions: 3.0 mmol carbonyl compound, 2.0 mL of 2-methyl-2-butanol, NaO^{t}Bu (2.0 equiv. with respect to the precatalyst), 20°C, 24h, 20 bar H_2, precatalyst **3**, [b]Determined via GC with dodecane as internal standard, [c]isolated yield.

Finally, we optimized the hydrogenation reaction conditions and explored the substrate scope of our Co catalyst. For details, please see the SI. To our delight, a broad product scope was observed. Aryl-alkyl ketones (Table 2, entries 1−11), diaryl ketones (Table 2, entries 12−14), and aliphatic ketones (Table 2, entries 15−20) were reduced to the corresponding alcohols in quantitative yields (except entry 9), tolerating diverse functional groups. In most cases, the catalyst loading amount was 0.25 or 0.5 mol%. In the case of unsaturated carbonyl compounds (Table 2, entries 21−24), a distinct selectivity toward the C=O bond was observed. No directing effect of a (generated) hydroxyl group, as described by Chirik and coworkers,[3a] is noticed. The selectivity we observe is inverse to that of the Hanson catalyst, for which selective hydrogenation of the C=C bond in 2-methyl-5-(prop-1-en-2-yl)cyclohexanone was reported[7c] and for which a bifunctional mechanism has been proposed.[7a,20]

4.3 Conclusion

In conclusion, we report on an easily accessible, inexpensive to activate, and highly active Co catalyst for the homogeneous hydrogenation of C=O bonds. The chosen $PN_{3-5}P$ ligand family allows an easy fine-tuning or optimizing of the catalyst performance, and its flexibility with regard to the

protonation or charge allows an efficient generation of the catalytically active species. The best catalyst operates under mild conditions and addresses a broad substrate scope covering dialkyl, diaryl, and aryl-alkyl ketones. The hydrogenation of C=O bonds in the presence of C=C bonds can proceed highly selectively. Further investigations are focused on better understanding the catalytically active species, the development of enantioselective $PN_{3-5}P$–Co hydrogenation catalysts, and other catalytic applications of the Co catalyst family described here.

Acknowledgments

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[16] The ligand synthesis is similarly easy. For instance, 96% isolated yield starting from commercially available educts for the PN_5P ligand of **3**.

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4.5 Supporting Information

General Considerations:

Nonhalogenated solvents were dried over sodium benzophenone and halogenated solvents were dried over P_2O_5. Deuterated solvents were ordered from Cambridge Isotope Laboratories, vented, stored over molecular sieves and distilled. All chemicals were purchased from commercial sources with purity with over 95% and used without further purification. NMR spectra were received using an INOVA 300 MHz spectrometer. Chemical shifts are reported in ppm relative to the deuterated solvent. GC analyses were carried out on an Agilent Technologies 6890N system equipped with an Optima17 column (30 m x 320 µm x 0.25 µm). GC/MS analyses were carried out on an Agilent 7890A/MSD 5975C system equipped with a HP-5MS column (30 m x 320 µm x 0.25 µm).

X-Ray crystal structure analyses were performed with a Stoe IPDS-II diffractometer and a STOE STADIVARI [λMo-Kα)= 0.71073 Å] equipped with an Oxford Cryostream low temperature unit. Structure solution and refinement were accomplished with SIR97[1] , SHELXL-2013[2] and WinGX[3] .

Magnetic Susceptibility data of the different samples were collected with a Quantum Design MPMS XL-5 SQUID magnetometer under an applied field of 0.1 and 0.2 T over 50–300 K in the sweep and the settle mode. All samples were placed in gelatine capsules held within plastic straws. The data were corrected for the diamagnetic magnetization of the ligands, which were estimated using Pascal's constants, and for the sample holder.

FTIR measurements were carried out under a nitrogen atmosphere on an Agilent Cary 630 FTIR equipped with a Diamond ATR unit.

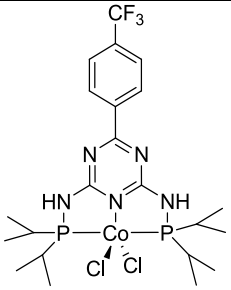
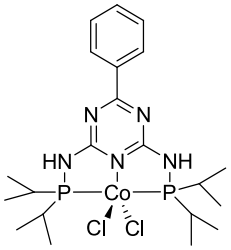
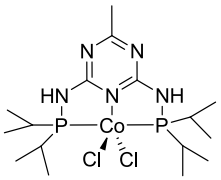
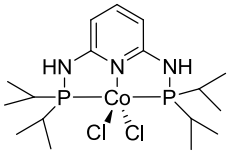
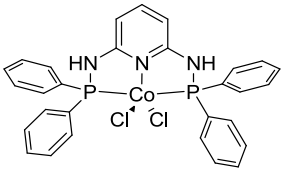
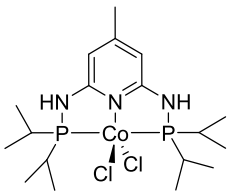
In situ IR measurements were performed with a Mettler Toledo React IR 45m equipped with a silver halide fiber conduit (DiComp, AgX 6.3 mm x 1.5 m fiber).

General procedure for hydrogenation of ketones:

In a nitrogen filled glove box, a 5 mL vial was charged with a magnetic stir bar, acetophenone (3.0 mmol, 350 µL), 250 µL of a solution of precatalyst (0.03 M, 0.0075 mmol, 0.25 mol%) and 250 µL of a solution of NaO*t*Bu (0.06 M, 0.015 mmol, 0.5 mol%) in additional t-amylalcohol (2-methyl-2butanol). The vial was placed in a high pressure autoclave (Parr Instruments) and the reactor was sealed, removed from glove box and purged with hydrogen. After stirring 24 h at room temperature under a pressure of 20bar hydrogen, the reaction was quenched by releasing the hydrogen and addition of 1 mL of water. For quantitative GC analysis dodecane (3.0 mmol, 681 µL) as internal standard was added. The organic layer was extracted with diethyl ether and dried over Na_2SO_4.

Screening Results

Supplementary Table S1 Precatalyst screening

Entry	Precatalyst	Yield [%]
1		7
2		30
3		>99
4		28
5		0
6		23
7	$CoCl_2$	0

Reaction conditions: 3.0 mmol acetophenone, 2.0 mol% precatalyst, 13 mg (0.13 mmol, 4.4 mol%) NaO*t*Bu, 2.0 mL THF, 20 bar H_2, room temperature, 24 h.

Supplementary Table S2 Solvent Screening

Entry	Solvent	Yield [%]
1	THF	83
2	toluene	0
3	*i*PrOH	95
4	MeOH	5
5	*t*BuOH	>99
6	2-methyl-2-butanol	>99

Reaction conditions: 3.0 mmol acetophenone, 0.5 mol% precatalyst **3**, 2.0 mol% NaO*t*Bu, 2.0 mL solvent 20 bar H_2, room temperature, 24 h.

Supplementary Table S3 Catalyst loading screening

Entry	Catalyst loading [mol%]	NaO*t*Bu [mol%]	Yield [%]
1	1.0	2.0	>99
2	0.5	1.0	>99
3	0.25	0.5	>99
4	0.1	0.2	50
5	0.05	0.1	6

Reaction conditions: 3.0 mmol acetophenone, 2.0 mL 2-methyl-2-butanol, 20 bar H_2, room temperature, 24 h , precatalyst **3.**

S**upplementary Table S4** Base loading screening

Entry	NaO*t*Bu [mol%]	Co:Na	Yield [%]
1	0		0
2	2.0	1:1	4
3	4.0	1:2	>99
4	10.0	1:5	96

Reaction conditions: 3.0 mmol acetophenone, 2.0 mol% **3**, 2.0 mL 2-methyl-2-butanol, 20 bar H_2, room temperature, 24h , precatalyst **3.**

Supplementary Table S5 Base screening

Entry	Base	Yield [%]
1	KO*t*Bu	95
2	KH	48
3	KOH	23
4	$KN(SiMe_3)_2$	>99
5	NaO*t*Bu	>99
6	NaOH	36
7	LiO*t*Bu	0
8	LiOH	0
9	none	0

Reaction conditions: 3.0 mmol acetophenone, 0.5 mol% precatalyst **3**, 1.0 mol% base, 2-methyl-2-butanol, 20 bar H_2, room temperature, 24 h.

Supplementary Table S6 H_2 pressure/ catalyst loading screening

Entry	Catalyst loading [mol%]	H_2 pressure [bar]	Yield [%]
1a	1.0	20	>99
1b	1.0	10	>99
1c	1.0	3	>99
2a	0.5	20	>99
2b	0.5	10	>99
2c	0.5	3	94
3a	0.25	20	>99
3b	0.25	10	99
3c	0.25	5	78
3d	0.25	3	55
4a	0.1	20	50
4b	0.1	10	10
4c	0.1	3	0

Reaction conditions: 3.0 mmol acetophenone, 2.0 mL 2-methyl-2-butanol, NaO*t*Bu, room temperature, 24 h , precatalyst **3.**

Supplementary Table S7 Poisoning experiments

Entry	Catalyst loading [mol%]	NaO*t*Bu [mol%]	Poisoning agent	Yield [%]
1	0.25	0.5	-	>99
2	0.25	0.5	Hg	>99
3	0.25	0.5	PMe_3	>99

Reaction conditions: 3.0 mmol acetophenone, 2.0 mL 2-methyl-2-butanol, 20 bar H_2, room temperature, 24 h, precatalyst **3**, poisoning agents (excess related to precatalyst **3**).

Kinetic study of hydrogenation of acetophenone

General procedure:

In a nitrogen filled glove box, a high pressure autoclave (Parr Instruments) was equipped with a 30 mL glass vial with a stirring bar. To a solution of 700 µL (6.00 mmol) acetophenone in 6 mL THF 0.5 mol% pre-catalyst and 1.0 mol% NaO*t*Bu are added. The reactor was sealed and removed from the glove box. The IR probe tip is inserted into the reactor via an adapter under a constant nitrogen flow. The reactor was purged 3x with hydrogen. Monitoring of the reaction was started with setting the hydrogen pressure to 20 bar. Data were collected with the following parameters:

Range: 1900-650 cm^{-1}

Resolution: high (every 4 WN)

Scans per sample: 128

Time intervals: 1 sample every 5 min for 1 h; 1 sample every 10 min for 4 h; 1 sample every 15 min for 12 h. The conversion was determined by integration and normalization of the peak area of the C=O vibrational band (1693 cm^{-1}).

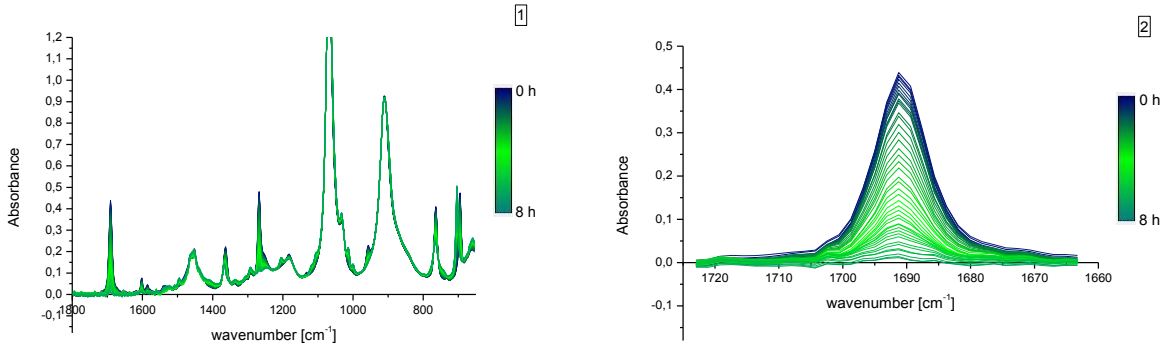
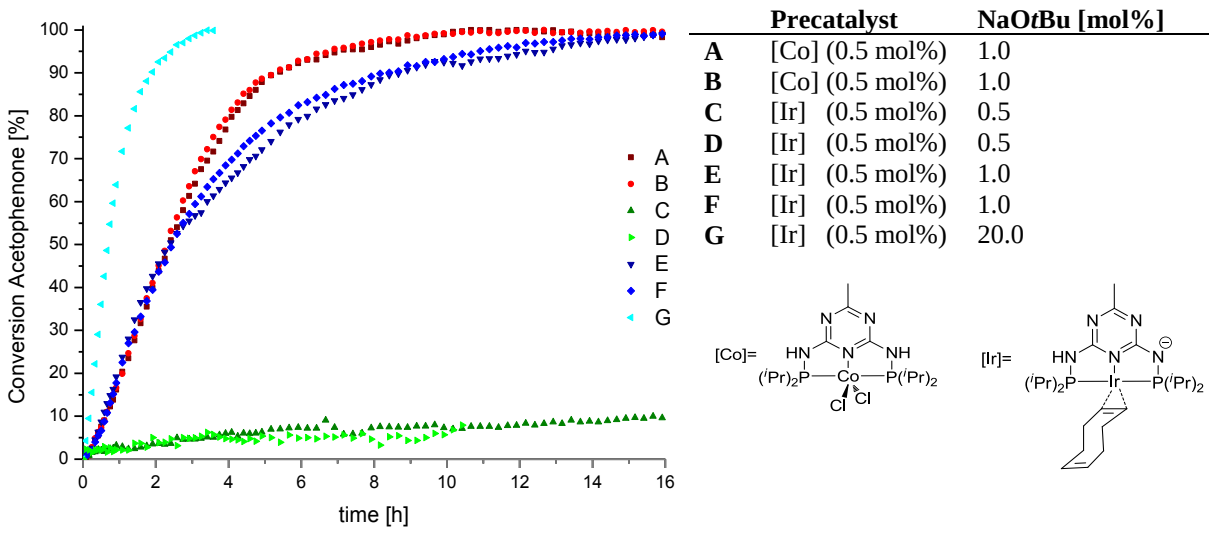


Figure S1. [1]: IR-spectra of hydrogenation of acetophenone with precatalyst **3** in THF. [2]: Decreasing C=O vibrational band.



	Precatalyst	NaO*t*Bu [mol%]
A	[Co] (0.5 mol%)	1.0
B	[Co] (0.5 mol%)	1.0
C	[Ir] (0.5 mol%)	0.5
D	[Ir] (0.5 mol%)	0.5
E	[Ir] (0.5 mol%)	1.0
F	[Ir] (0.5 mol%)	1.0
G	[Ir] (0.5 mol%)	20.0

Figure S2. Conversion vs. time graph for the hydrogenation of acetophenone with precatalyst **3** and a comparable iridium catalyst. Reaction conditions: 6 mmol acetophenone, 0.5 mol% [Co] or [Ir] precatalyst, NaO*t*Bu, 6 mL THF, 20 bar H_2, RT.

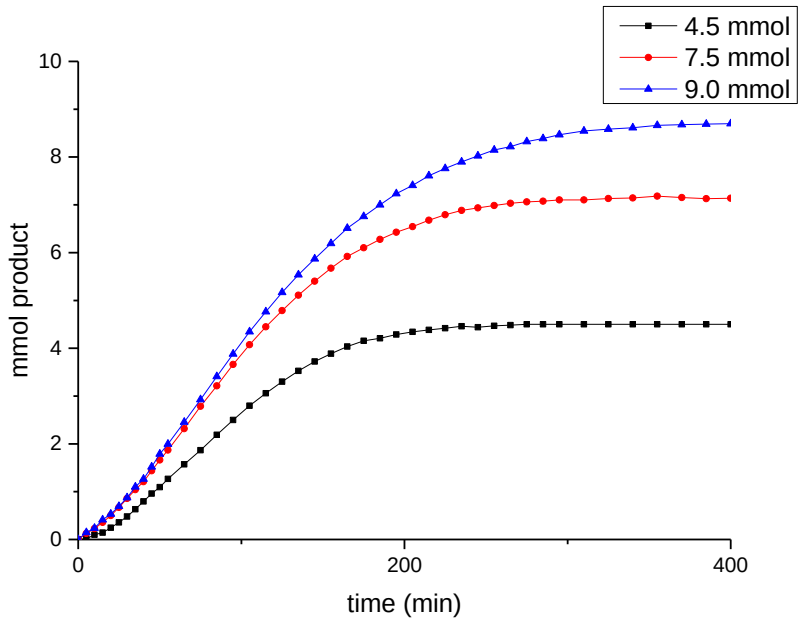


Figure S3. Product formation vs. time graph for the hydrogenation of various amounts of acetophenone with **3** at constant catalyst concentration. Reaction conditions: acetophenone, 0.06 mmol precatalyst **3**, 0.12 mmol NaO*t*Bu, 6 mL THF.

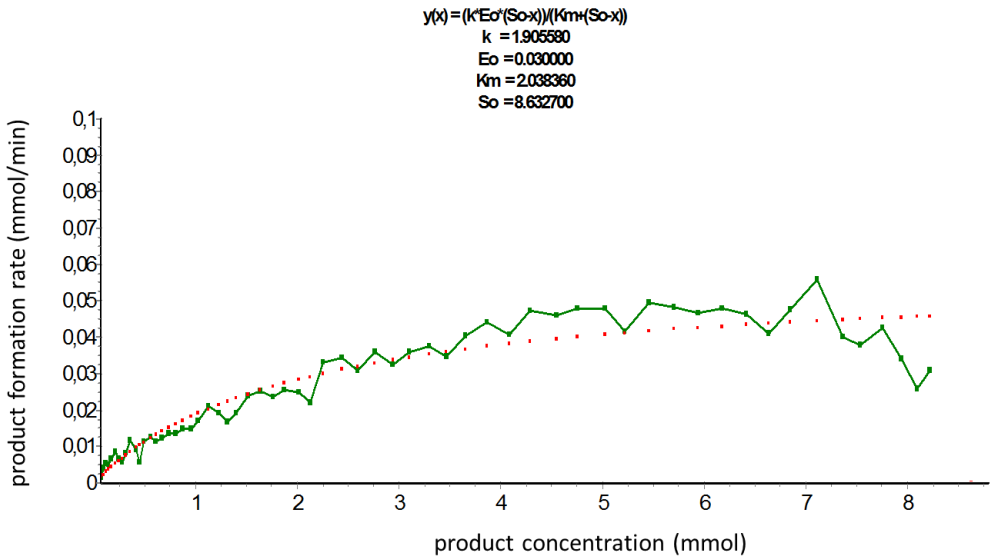
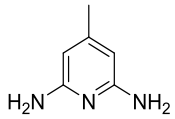


Figure S4. Michaelis-Menten equation for 9 mmol substrate (green: experimental; red: nonlinear calculation; k = rate constant, E_0 = catalyst concentration, S_0 = substrate concentration, K_M = Michaelis constant)

Ligand and complex syntheses:

All ligands were synthesized according to literature procedures[4]

Synthesis of 2,6-Diamino-4-methylpyridine[5]:

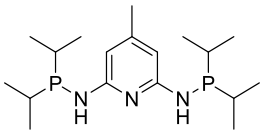


To a solution of sodium amide (9.33 g; 0.24 mol) in N',N-dimethylaniline a solution of 4-methylpyridine (9.31 g, 9.73 mL, 0.1 mol) was added at 130°C over 6 h. Afterwards the reaction was stirred over night at 195°C. The reaction was quenched after cooling to RT by addition of water. The organic layer was extracted with Et_2O, evaporation of the solvent results in a dark brown residue. The product was resublimed as a colorless solid (2.8 g, 0.022 mol, 22%).

^{1}H NMR ($CDCl_3$, 299.86 MHz, 23°C): δ = 5.73 (s, 1 H), 4.16 (br. s., 2 H), 2.11 ppm (s, 2 H)

^{13}C NMR ($CDCl_3$, 75.41 MHz, 23°C): δ = 157.7; 150.6; 98.7; 20.9 ppm.

Synthesis of (4-Me)Py(NHP(iPr)$_2$)$_2$]



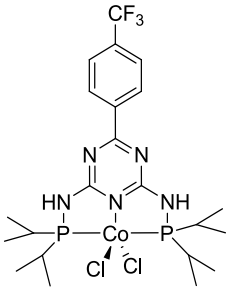
2,6-Diamino-4-methylpyridine (2.46 g, 20.0 mmol) was solved in 150 mL THF and cooled to 0°C. After addition of chlorodiisopropylphosphine (7.0 mL, 44.0 mol), triethylamine (10.6 mL, 80.0 mmol) is added in small portions. The reaction is allowed to warm to RT and stirred over night at 50°C. The suspension is filtered and the solvent is removed. The product is recrystallized from toluene/hexane affording a white solid (5.54 g, 15.6 mmol, 78%).

^{1}H NMR ($CDCl_3$, 299.86 MHz, 23°C): δ = 6.32 (d, *J*=1.8 Hz, 2 H), 2.12 - 2.22 (m, 3 H), 1.75 (quind, *J*=7.0, 1.8 Hz, 4 H), 1.00 - 1.14 (m, 24 H) ppm.

^{13}C NMR ($CDCl_3$, 75.41 MHz, 23°C): δ = 99.1; 98.9; 26.3; 26.1; 18.6; 18.4; 17.0 16.9 ppm.

Elemental analysis calcd (%) for $C_{18}H_{35}N_3P_2$ (M: 355.45): C 60.82 H 9.93 N 11.82; found: C 60.74 H 10.32 N 11.76

Synthesis of [(4-p-CF_3-Ph)Tr(NHP(iPr)$_2$)$_2$$CoCl_2$] **1**:

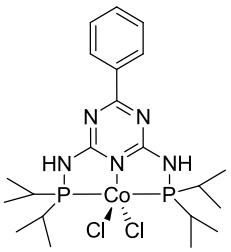


$CoCl_2$ (2.0 mmol, 260 mg) was suspended in 20 mL THF and subsequently a solution of (4-p-CF_3-Ph)Tr(NHP(iPr)$_2$)$_2$ (2.0 mmol, 1.23 g) in THF was added in one portion. Stirring over night at 50°C results in a red-purple suspension. The supernatant solution is filtered off and the residue is dried in vacuo giving a red crystalline powder in quantitative yields (1.07 g, 1.74 mmol, 87%).

Elemental analysis calcd (%) for $C_{22}H_{34}Cl_2CoF_3N_5P_2$ (M: 617.32): C 42.8 H 5.55 N 11.34; found: C 43.07 H 5.42 N 11.15

Magnetic susceptibility: 2.2 μ_B

Synthesis of [(4-Ph)Tr(NHP(iPr)$_2$)$_2$$CoCl_2$] **2**:

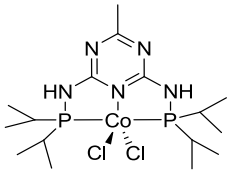


$CoCl_2$ (2.0 mmol, 260 mg) was suspended in 20 mL THF and subsequently a solution of (4-Ph)Tr(NHP(iPr)$_2$)$_2$ (2.0 mmol, 1.1 g) in THF was added in one portion. Stirring over night at 50°C results in a dark red suspension. The supernatant solution is filtered off and the residue is dried in vacuo giving a red crystalline powder in quantitative yields (978 mg, 1.78 mmol, 89%).

Elemental analysis calcd (%) for $C_{21}H_{35}Cl_2CoN_5P_2$ (M: 549.32): C 45.92 H 6.42 N 12.75; found: C 45.95 H 6.46 N 12.62

Magnetic susceptibility: 2.3 μ_B

Synthesis of [(4-Me)Tr(NHP(iPr)$_2$)$_2$CoCl$_2$] **3**:

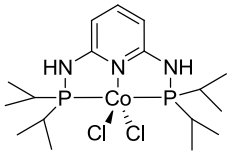


$CoCl_2$ (10.0 mmol, 1.30 g) was suspended in 100 mL THF and subsequently a solution of (4-Me)Tr(NHP(iPr)$_2$)$_2$ (10.0 mmol, 3.57 g) in THF was added in one portion. Stirring over night at 50°C results in a red suspension. The supernatant solution is filtered off and the residue is dried in vacuo giving a red crystalline powder in quantitative yields (4.59 g, 9.42 mmol, 94%).

Elemental analysis calcd (%) for $C_{16}H_{33}Cl_2CoN_5P_2$ (M: 487.25): C 39.44 H 6.83 N 14.37; found: C 39.28 H 6.54 N 14.28 (After storage of the solid material for three months under an aerobic atmossphere, elemental analysis was repeated giving the same values.)

Magnetic susceptibility: 2.3 μ_B

Synthesis of [Py(NHP(iPr)$_2$)$_2$CoCl$_2$] **4**:

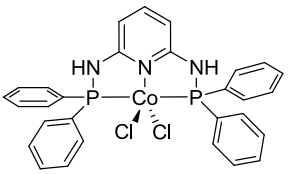


$CoCl_2$ (2.0 mmol, 260 mg) was suspended in 20 mL THF and subsequently a solution of Py(NHP(iPr)$_2$)$_2$ (2.0 mmol, 683 mg) in THF was added in one portion. Stirring over night at 50°C results in a red suspension. The supernatant solution is filtered off and the residue is dried in vacuo giving a red crystalline powder in quantitative yields (877 mg, 1.86 mmol, 93%).

Elemental analysis calcd (%) for $C_{17}H_{33}Cl_2CoN_3P_2$ (M: 471.25): C 43.33 H 7.06 N 8.92; found: C 42.81 H 7.25 N 8.60

Magnetic susceptibility: 2.2 μ_B

Synthesis of [Py(NHP(Ph)$_2$)$_2$CoCl$_2$] **5**:



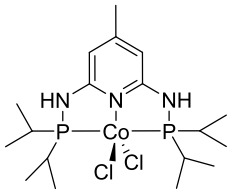
$CoCl_2$ (2.0 mmol, 260 mg) was suspended in 20 mL THF and subsequently a solution of Py(NHP(Ph)$_2$)$_2$ (2.0 mmol, 954 mg) in THF was added in one portion. Stirring over night at 50°C results in a red

suspension. The supernatant solution is filtered off and the residue is dried in vacuo giving a red crystalline powder in quantitative yields (1.14 g, 1.88 mmol, 94%). The red solid was recrystallized from dry acetone for X-ray analysis.

Elemental analysis calcd (%) for $C_{29}H_{25}Cl_2CoN_3P_2$ x C_3H_6O (M: 665.40): C 57.76 H 4.70 N 6.32; found: C 58.24 H 4.75 N 6.35

Magnetic susceptibility: 2.3 μ_B

Synthesis of [4-Me)Py(NHP(iPr)$_2$)$_2$CoCl$_2$] **6**:

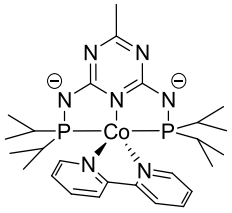


$CoCl_2$ (2.0 mmol, 260 mg) was suspended in 20 mL THF and subsequently a solution of (4-Me)Py(NHP(Ph)$_2$)$_2$ (2.0 mmol, 710 mg) in THF was added in one portion. Stirring over night at 50°C results in a red suspension. The supernatant solution is filtered off and the residue is dried in vacuo giving a red crystalline powder in almost quantitative yields (863 mg, 1.77 mmol, 89%).

Elemental analysis calcd (%) for $C_{18}H_{35}Cl_2CoN_3P_2$ (M: 485.28): C 44.55 H 7.27 N 8.66; found: C 44.46 H 7.69 N 8.63

Magnetic susceptibility: 2.45μ_B

Synthesis of [(4-Me)Tr(NP(iPr)$_2$)$_2$Co(bipy)] **8**:

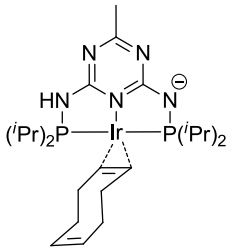


3 (0.5 mmol, 244 mg) was dissolved with bipyridine (0.5 mmol, 78 mg) in 25 mL THF and a solution of KO*t*Bu (1.0 mmol, 112 mg, in THF) was added slowely via a syringe. Red crystals are obtained at -20°C for X-ray analysis. The samples for elemental analysis were prepared in the glovebox. Afterwards the tared tin boat was re-weighted outside directly before the analysis. During this time an increase of the mass to a constant weigt was observed. The CHN analysis was performend on three different days always with double determination (3x2 samples), obtaining exactly the same results.

Elemental analysis calcd. (%) for $C_{26}H_{39}CoN_7P_2$ (M:570.52): C 54.74 H 6.89 N 17.19; found: C 52.87 H 7.15 N 16.50

Magnetic susceptibility: 1.9 μ_B

Synthesis of [(4-Me)Tr(NP(*i*Pr)$_2$)(NHP(*i*Pr)$_2$)Ir(cod)]:



The complex was synthesized and characterized according to literature procedure[5].

Synthesis of 2-methylbenzhydrol:

2-Mehtylbenzophenone (546 mg, 3.0 mmol), 500 µL of a 0.03 M (0.5 mol%) solution of **3** in *t*-amylalcohol, 500 µL (0.1 mol%) of a 0.06 M solution of NaO^{t}Bu in *t*-amylalcohol, 1 mL *t*-amylalcohol, 20 bar H_2, RT, 24h. Reaction is quenched by addition of 1 ml of water. Product is isolated via column chromatography (pentane/Et_2O 10:1) as a colorless solid (534 mg, 2.90 mmol, 97%).

^{1}H NMR ($CDCl_3$, 299.86 MHz, 23°C): δ = 7.44 - 7.50 (m, 1 H), 7.07 - 7.32 (m, 8 H), 5.95 (s, 1 H), 2.20 (s, 3 H), 2.12 (br. s., 1 H) ppm.

^{13}C NMR ($CDCl_3$, 75.41 MHz, 23°C): δ = 142.8, 141.4, 135.3, 130.5, 128.5, 128.4, 127.5, 127.1, 127.0, 126.2, 126.1, 126.1, 73.3, 19.4 ppm.

Synthesis of (4-(4-methylpent-2-en-1-yl)cyclohex-3-en-1-yl)methanol:

(4-(4-Methylpent-2-en-1-yl)cyclohex-3-en-1-yl)carboxaldehyde (384 mg, 2.0 mmol), 500 µL of a 0.03 M (0.5 mol%) solution of **3** in *t*-amylalcohol, 500 µL (0.1 mol%) of a 0.06 M solution of NaO^{t}Bu in *t*-amylalcohol, 1 mL *t*-amylalcohol, 20 bar H_2, RT, 24h. Reaction is quenched by addition of 1 ml of water. Product is isolated via column chromatography (pentane/Et_2O 40:1) as a colorless oil (370 mg, 1.9 mmol, 95%).

^{1}H NMR ($CDCl_3$, 299.86 MHz, 23°C): δ = 5.40 (br. s., 1 H), 5.01 - 5.19 (m, 1 H), 3.47 - 3.63 (m, 1 H), 1.90 - 2.13 (m, 7 H), 1.65 - 1.87 (m, 5 H), 1.61 (s, 4 H), 1.17 - 1.48 (m, 1 H) ppm.

^{13}C NMR ($CDCl_3$, 75.41 MHz, 23°C): δ = 131.4, 124.3, 120.7, 119.4, 67.8, 37.7, 36.4, 28.2, 26.5, 25.7, 24.7, 17.7 ppm.

Synthesis of 1-(4'-fluorophenyl)propan-1-ol:

4' Fluoropropiophenone (417 µL, 3.0 mmol), 1.0 mL of a 0.03 M (1.0 mol%) solution of **3** in *t*-amylalcohol, 1 mL (1.0 mol%) of a 0.06 M solution of NaO^{t}Bu in *t*-amylalcohol, 20 bar H_2, RT, 24h. Reaction is quenched by addition of 1 ml of water. Product is isolated via column chromatography (pentane/Et_2O 5:1) as a colorless oil (438 mg, 2.4 mmol, 94%).

^{1}H NMR ($CDCl_3$, 299.86 MHz, 23°C): δ = 7.44 - 7.62 (m, 2 H), 7.13 - 7.34 (m, 2 H), 4.80 (t, *J*=6.4 Hz, 1 H), 2.51 (d, *J*=8.8 Hz, 1 H), 1.99 (qt, *J*=14.1, 7.0 Hz, 2 H), 1.14 (t, *J*=7.3 Hz, 3 H) ppm.

^{13}C NMR ($CDCl_3$, 75.41 MHz, 23°C): δ = 163.7, 160.4, 140.2, 140.2, 127.6, 127.5, 115.2, 114.9, 75.2, 31.9, 10.0 ppm.

Synthesis of 8-methyl-8-azabicyclo[3.2.1]octan-3-ol:

Tropinone (418 mg, 3.0 mmol), 1.0 mL of a 0.03 M (1.0 mol%) solution of **3** in *t*-amylalcohol, 1 mL (1.0 mol%) of a 0.06 M solution of NaO^{t}Bu in *t*-amylalcohol, 20 bar H_2, RT, 24h. Reaction is quenched by addition of 1 ml of water. Product is isolated via column chromatography (pentane/Et_2O 5:1) as colorless solid (389 mg, 2.76 mmol, 92%).

^{1}H NMR ($CDCl_3$, 299.86 MHz, 23°C): δ = 3.99 (t, *J*=5.0 Hz, 1 H), 3.01 - 3.14 (m, 2 H), 2.24 (s, 3 H), 2.03 - 2.12 (m, 4 H), 1.93 - 2.01 (m, 2 H), 1.64 (d, *J*=14.1 Hz, 2 H) ppm.

^{13}C NMR ($CDCl_3$, 75.41 MHz, 23°C): δ = 64.3, 59.9, 40.4, 39.5, 25.7 ppm.

Synthesis of 4-phenylcyclohexanol:

4-Phenylcyclohexanone (533 mg, 3.00 mmol), 500 µL of a 0.03 M (0.5 mol%) solution of **3** in *t*-amylalcohol, 500 µL (0.1 mol%) of a 0.06 M solution of NaO^{t}Bu in *t*-amylalcohol, 1 mL *t*-amylalcohol, 20 bar H_2, RT, 24 h. Reaction is quenched by addition of 1 ml of water. Product is isolated via column chromatography (pentane/Et_2O 10:1) as colorless solid (489 mg, 2.78 mmol, 93%)

^{1}H NMR ($CDCl_3$, 299.86 MHz, 23°C): δ = 7.18 - 7.40 (m, 5 H), 3.67 - 3.99 (m, 1 H), 2.48 - 2.64 (m, 1 H), 2.07 - 2.20 (m, 1 H), 1.90 - 2.07 (m, 2 H), 1.41 - 1.79 (m, 5 H) ppm.

^{13}C NMR ($CDCl_3$, 75.41 MHz, 23°C): δ = 146.5, 128.3, 126.8, 126.8, 126.1, 125.9, 70.6, 65.6, 43.4, 35.9, 32.4, 27.7 ppm.

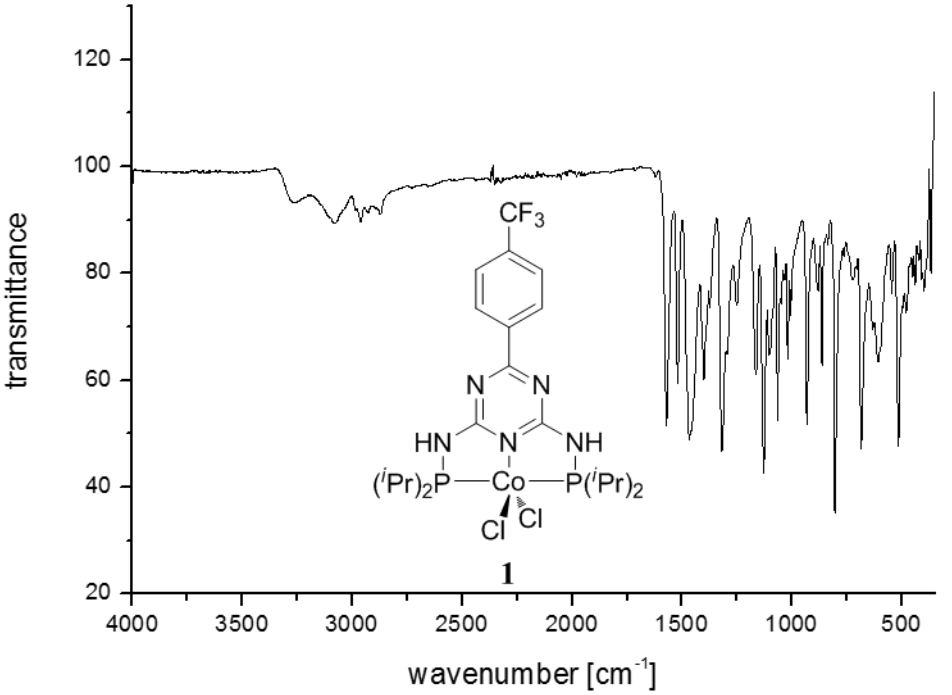
Synthesis of 2-methyl-3-phenyl-prop-2-en-1-ol:

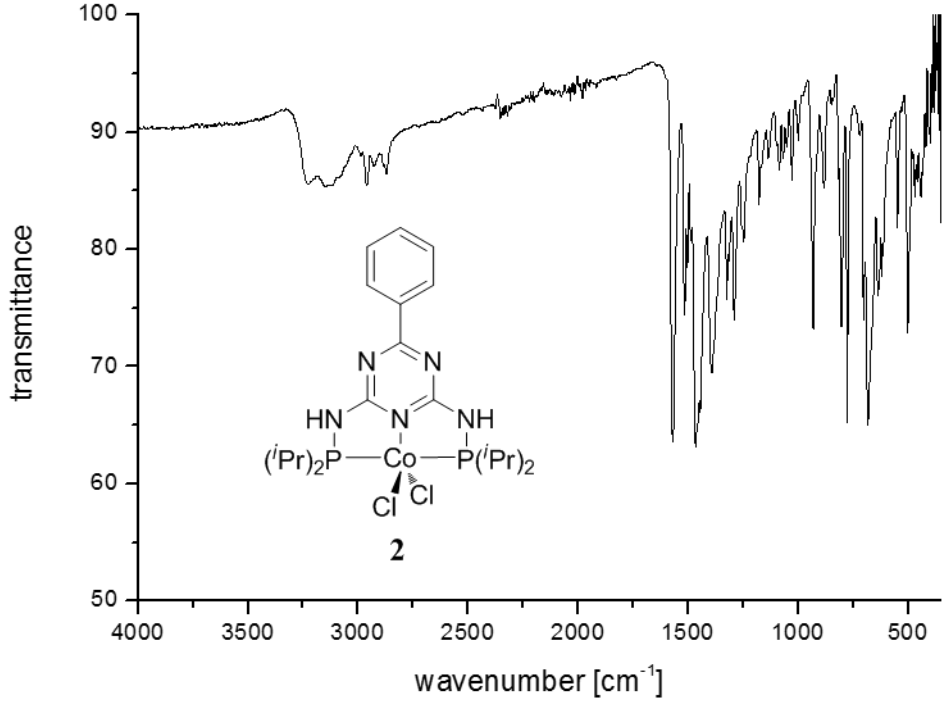
2-Methyl-3-phenylacrylaldehyde (418 µL, 3.0 mmol), 1.0 mL of a 0.03 M (1.0 mol%) solution of **3** in *t*-amylalcohol, 1 mL (1.0 mol%) of a 0.06 M solution of NaO^tBu in *t*-amylalcohol, 20 bar H_2, RT, 24h. Reaction is quenched by addition of 1 ml of water. Product is isolated via column chromatography (pentane/Et_2O 5:1 → 1:1) as colorless oil (431 mg, 2.96 mmol, 97%).

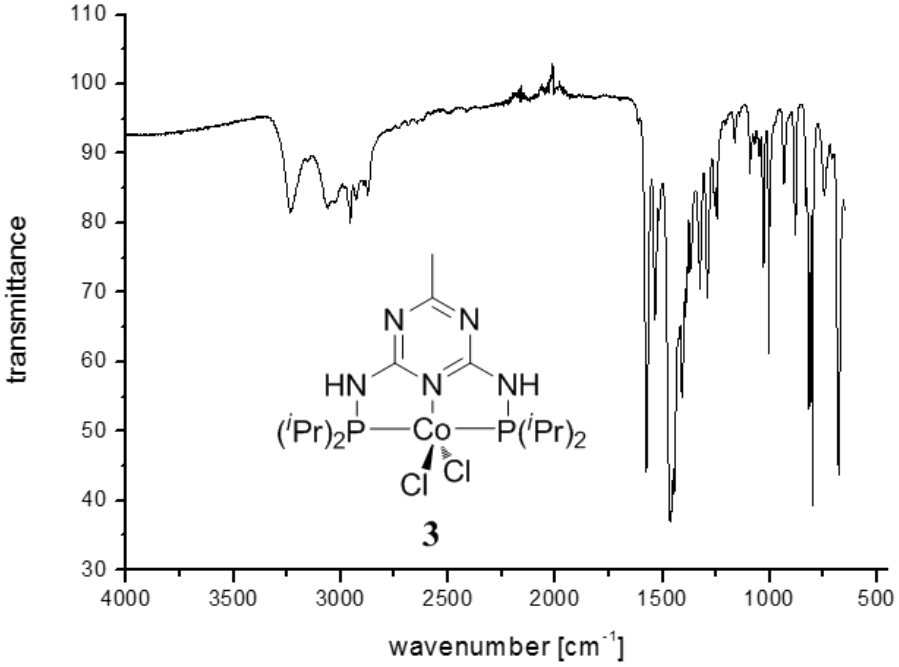
^{1}H NMR ($CDCl_3$, 299.86 MHz, 23°C): δ = 7.13 - 7.45 (m, 5 H), 6.55 (s, 1 H), 4.21 (s, 2 H), 2.15 (br. s., 1 H), 1.92 (s, 3 H) ppm.

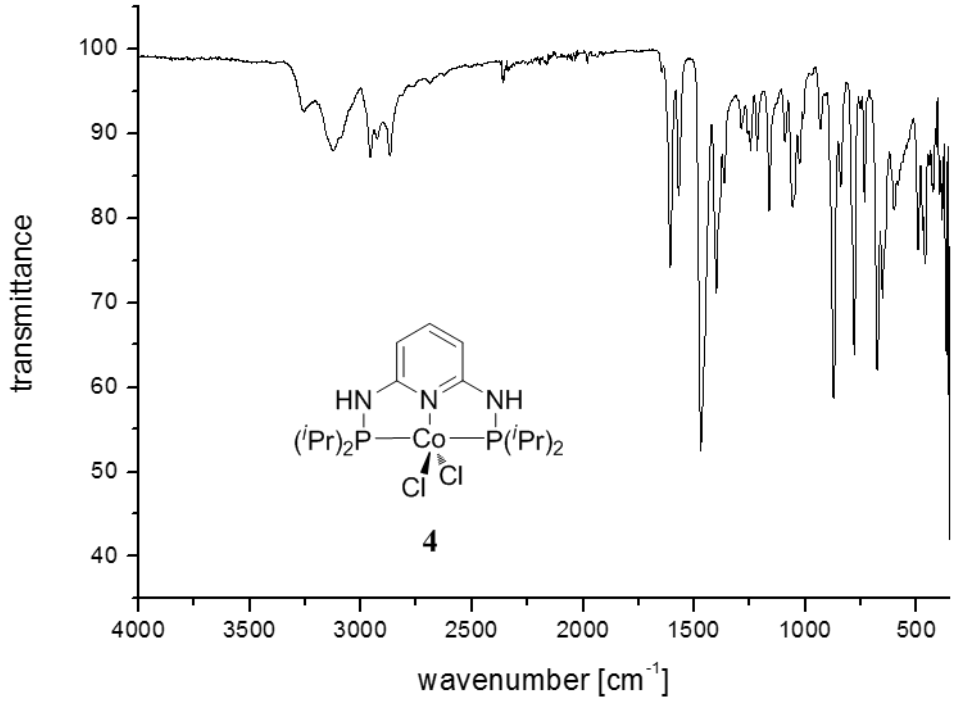
^{13}C NMR ($CDCl_3$, 75.41 MHz, 23°C): δ = 137.6, 137.5, 130.0, 128.8, 128.7, 128.1, 126.4, 125.0, 68.9, 15.2 ppm.

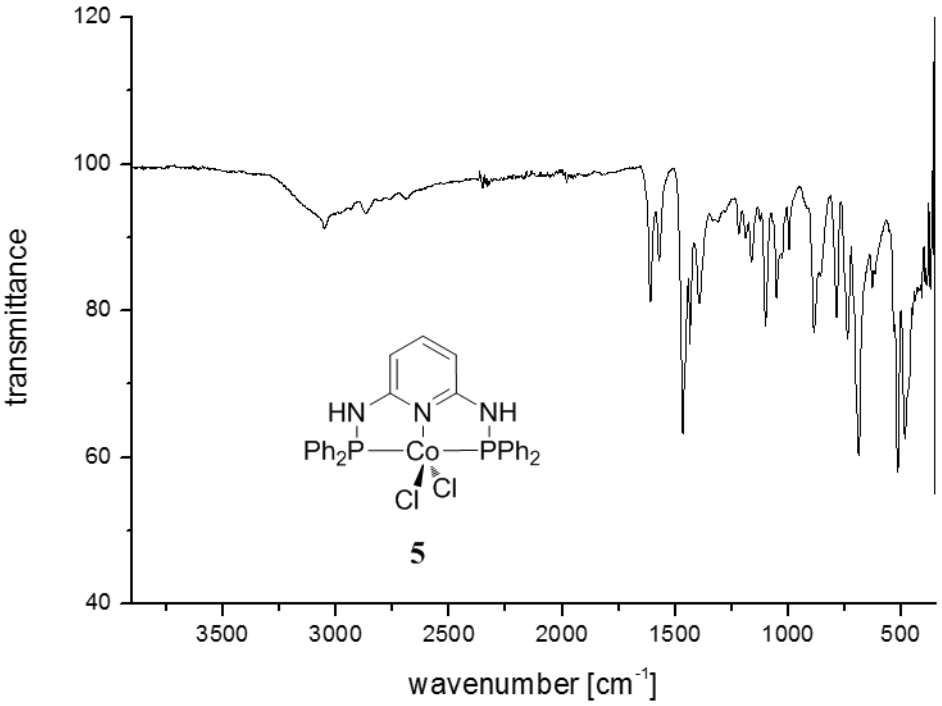
IR spectra of precatalysts 1-6 and 8:

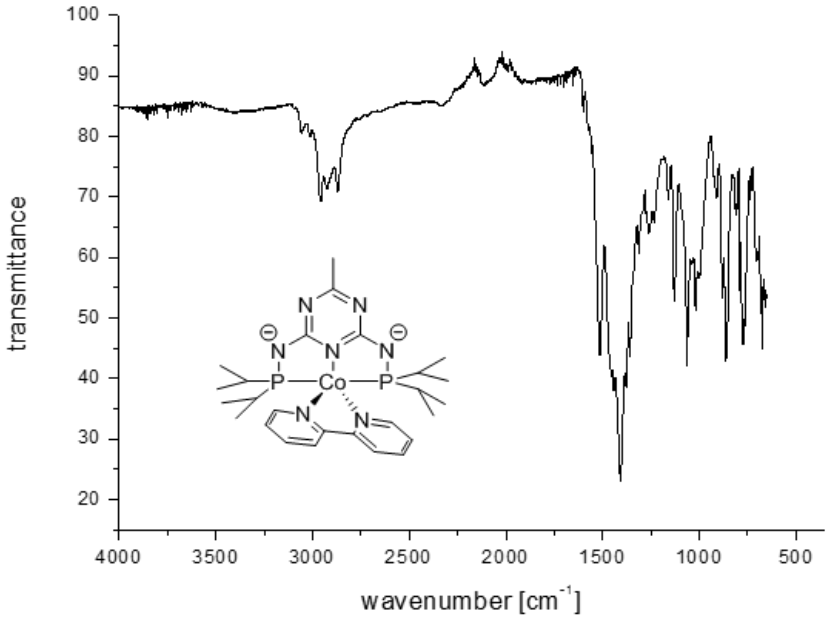





transmittance
wavenumber [cm-1]
3


transmittance
wavenumber [cm-1]
4


transmittance
wavenumber [cm-1]
HN
NH
Ph2P
Co
PPh2
Cl
Cl
5


transmittance
wavenumber [cm-1]

Mechanistic H_2/D_2 experiments

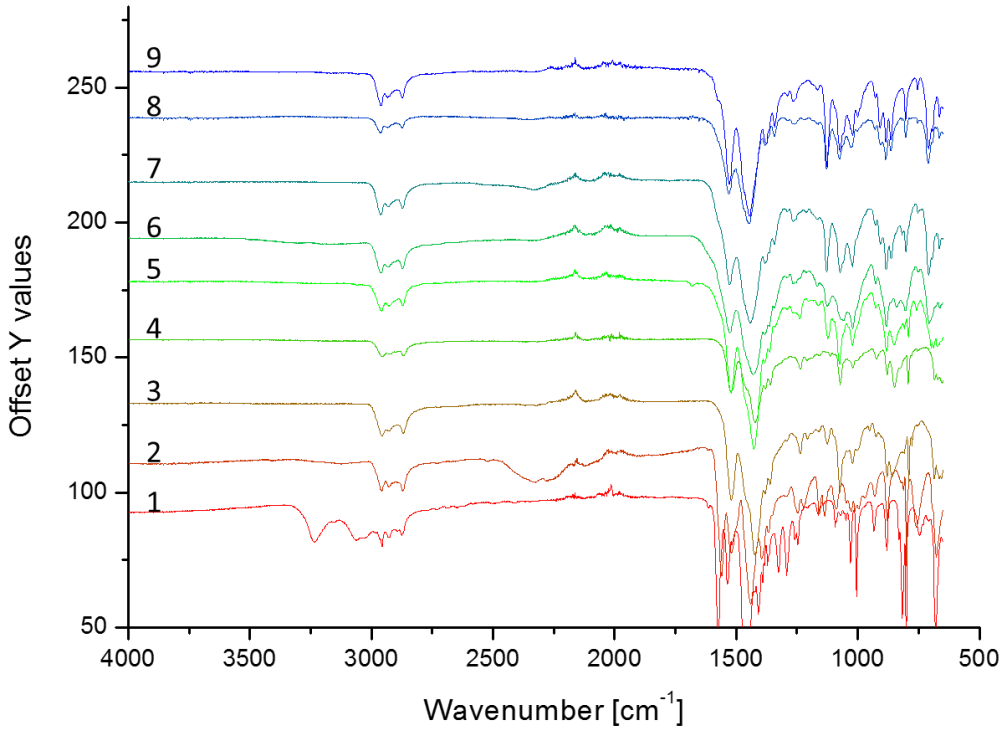


Figure S5. FT-IR spectra of several mechanistic experiments. (1) precatalyst **3**; (2) deuterium labeled pre-catayst **3**; (3) activated precatalyst **3** with 2.0 equivalents NaO^tBu; (4)activated precatalyst **3**, stirred in THF with MeOD-d_4; (5) activated precatalyst **3**, stirred with acetophenone under 10 bar H_2, precipitated with hexane; (6) activated precatalyst **3**, stirred under 10 bar H_2, solvent removed under vacuum; (7) activated precatalyst **3**, stirred under 10 bar D_2, solvent removed under vacuum; (8) activated precatalyst **3**, stirred under 0.6 bar H_2, precipitated under an H_2 atmosphere with hexane; (9) activated precatalyst **3**, stirred under 0.6 bar D_2, precipitated under an D_2 atmosphere with hexane

Procedures:

General: For all experiments, a freshly prepared charge of **3** was used. All FT-IR spectra were recorded from solid materials.

(1) **3** was prepared as described in the given synthesis protocol of $[(4\text{-Me})Tr(NHP(iPr)_2)_2CoCl_2]$.

(2) Exchange of NH with deuterium: 100 mg of **3** was solved in 0.6 mL MeOD-d_4 and stirred for 1 h. Solvent was removed by vacuum.

(3) 98 mg (0.2 mmol) of **3** were activated with 39 mg (0.4 mmol) NaO^tBu in THF. Solvent was removed by vacuum.

(4) 98 mg (0.2 mmol) of **3** were activated with 39 mg (0.4 mmol) NaO^tBu in THF. 300µL MeOD-d_4 was added and stirred for 1 h. Solvent was removed by vacuum.

(5) In an autoclave 98 mg (0.2 mmol) of **3** were activated with 39 mg (0.4 mmol) NaO^{t}Bu in THF and 350 µL (3.0 mmol) acetophenone were added and stirred for 30 minutes under 10 bar H_2. Under a nitrogen stream a solid was precipitated with addition of 20 mL of hexane. Solvent is filtered off and the residue is dried by vacuum.

(6) In an autoclave 98 mg (0.2 mmol) of **3** were activated with 39 mg (0.4 mmol) NaO^{t}Bu in THF and stirred overnight under 10 bar H_2. The solution is transferred into a Schlenk tube, solvent is removed by vaccum.

(7) In an autoclave 98 mg (0.2 mmol) of **3** were activated with 39 mg (0.4 mmol) NaO^{t}Bu in THF and stirred overnight under 10 bar D_2. The solution is transferred into a Schlenk tube, solvent is removed by vaccum.

(8) In a Schlenk tube 98 mg (0.2 mmol) of **3** were activated with 39 mg (0.4 mmol) NaO^{t}Bu in THF and stirred 0.6 bar H_2 for 1 h. A green-brown solid is precipitated by addition of 20 mL of hexane under a hydrogen atmosphere. The Schlenk tube was brought into the glove-box and the suspension was left to settle. A drop of the slurry was placed on the ATR-FTIR and allowed to dry.

(9) In a Schlenk tube 98 mg (0.2 mmol) of **3** were activated with 39 mg (0.4 mmol) NaO^{t}Bu in THF and stirred 0.6 bar D_2 for 1 h. A green-brown solid is precipitated by addition of 20mL of hexane under a deuterium atmosphere. The Schlenk tube was brought into the glove-box and the suspension was left to settle. A drop of the slurry was placed on the ATR-FTIR and allowed to dry.

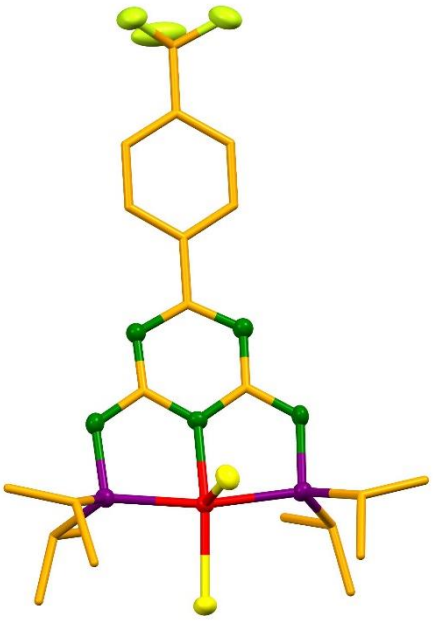


Figure S6 Molecular structure of [(4-p-CF_3-Ph)Tr(NH(iPr)$_2$)$_2$$CoCl_2$] precatalyst **1**. Hydrogen atoms are omitted for clarity.

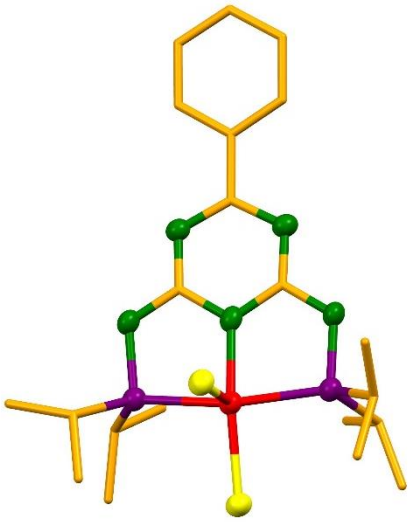


Figure S7 Molecular structure of [(4-Ph)Tr(NH(iPr)$_2$)$_2$CoCl$_2$] precatalyst **2**: Hydrogen atoms are omitted for clarity.

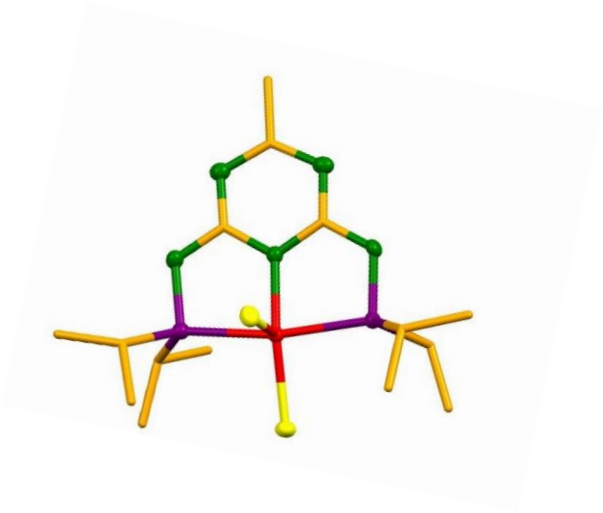


Figure S8 Molecular structure of [(4-Me)Tr(NH(iPr)$_2$)$_2$CoCl$_2$] precatalyst **3**: Hydrogen atoms and solvent molecules are omitted for clarity.

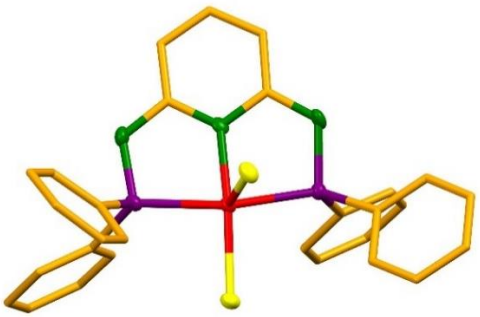


Figure S9 Molecular structure of [Py(NH(Ph)$_2$)$_2$CoCl$_2$] precatalyst **5**: Hydrogen atoms and solvent molecules are omitted for clarity

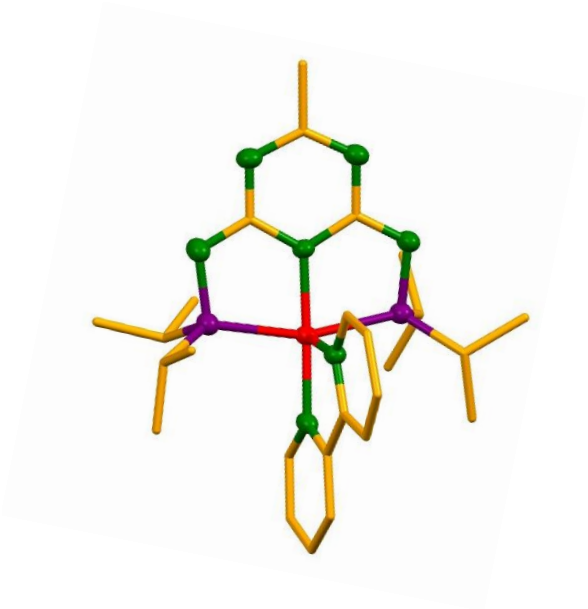


Figure S10 Molecular structure of [(4-Me)Tr(NP(^{i}Pr)$_2$)$_2$Co(bipy)] **8**: Hydrogen atoms and solvent molecules are omitted for clarity

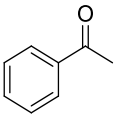
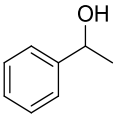
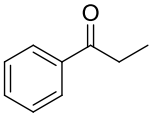
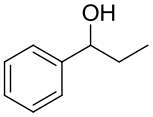
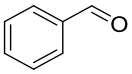
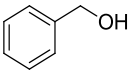
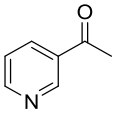
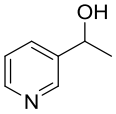
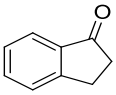
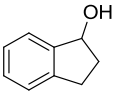
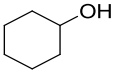
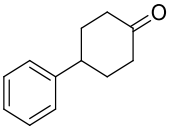
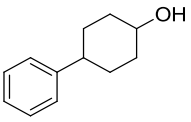
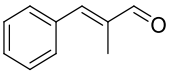
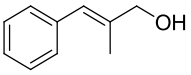
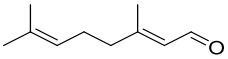
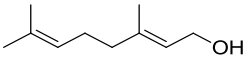
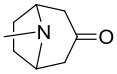
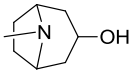
Supplementary Table S7 Crystallographic data

Compound	**1**	**2**	**3**	**5**	**8**
Formula	$C_{22}H_{34}Cl_2CoF_3N_5P_2$	$C_{21}H_{35}Cl_2CoN_5P_2$	$C_{16}H_{33}Cl_2CoN_5P2$, C_4H_8O	$C_{29}H_{25}Cl_2CoN_3P_2$, C_3H_6O	$C_{26}H_{39}CoN_7P_2$
Formula weight	617.31	549.31	559.35	665.37	570.51
Crystal system	orthorhombic	orthorhombic	orthorhombic	orthorhombic	monoclinic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$Pca2_1$	$P2_1/c$
a [Å]	9.6882(3)	10.2011(4)	9.3814(2)	12.2051(5)	16.1656(9)
b [Å]	13.0841(3)	12.1886(4)	13.5379(3)	12.7514(6)	15.8476(6)
c [Å]	21.5222(3)	20.9518(8)	21.3231(6)	19.5704(8)	17.5006(9)
α [°]	90.00	90.00	90.00	90.00	90.00
β [°]	90.00	90.00	90.00	90.00	116.713(4)
γ [°]	90.00	90.00	90.00	90.00	90.00
Cell volume [$Å^3$]	2728.18(11)	2605.09(17)	2078.13(11)	3045.8(2)	4004.9(4)
Z	4	4	4	4	4
Crystal size [mm^3]	0.205x0.197x0.195	0.240x0.168x0.121	0.167x0.121x0.119	0.208x0.104x0.058	0.330x0.311x0.218
Habit	block	block	block	plate	block
Colour	red	red	red	red	red
Density [gcm^{-3}]	1.503	1.401	1.372	1.551	0.946
T [K]	133(2)	133(2)	133(2)	133(2)	133(2)
Theta range	1.82 27.13	1.93 – 25.62	1.78 – 30.04	1.595 – 27.655	1.830 – 26.278
Unique reflections	5800	4910	7192	6862	8036
Observed reflections [I > 2s(I)]	5027	4151	5512	4891	5709
Parameters	332	296	297	380	334
wR_2 (all data)	0.0714	0.1117	0.1211	0.0949	0.1733
R [I > 2s(I)]	0.0360	0.0524	0.0501	0.0565	0.0627

GC-Methods and retentions times of carbonyl compounds and corresponding alcohols

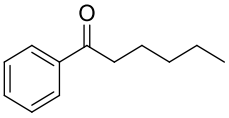
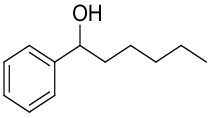
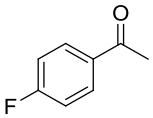
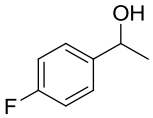
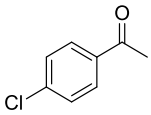
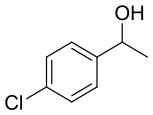
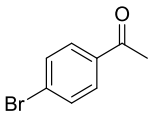
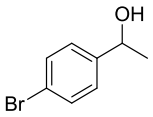
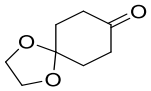
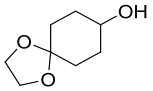
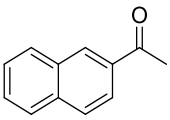
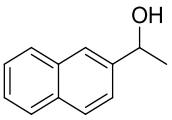
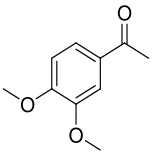
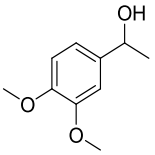
Method 1:

Oven: Initial temp. 60 °C; Initial time 2.00 min; constant flow			
Ramps:	Rate [°C/min]	Final temp [°C]	Final time [min]
1	12.00	200	0.00
2	50.00	300	1.0

Substrate	Retention time [min]	Substrate	Retention time [min]
	7.67		7.35
	8.76		8.34
	6.19		7.14
	8.6o		9.25
	10.84		9.82
	5.27		4.34
	9.84		9.50
	10.84		11.89
	9.08/9.48		8.59/8.95
	9.31		9.07
Dodecan (int. standard)	6.59		

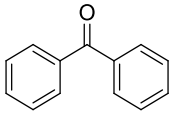
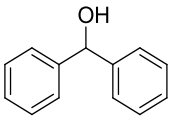
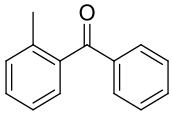
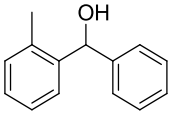
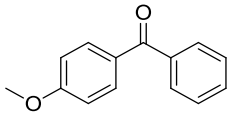
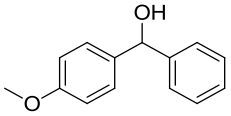
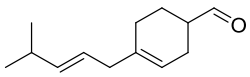
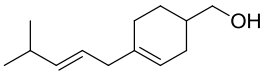
Method 2:

Oven: Initial temp. 90 °C; Initial time 2.00 min; constant flow			
Ramps:	Rate [°C/min]	Final temp [°C]	Final time [min]
1	15.00	300	2.00

Substrate	**Retention time [min]**	**Substrate**	**Retention time [min]**
	8.28		8.06
	5.58		5.49
	6.64		6.74
	7.66		7.74
	7.13		7.26
	10.34		10.18
	9.49		10.02
Dodecan (int. standard)	3.98		

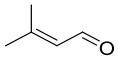
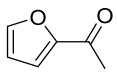
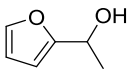
Method 3:

Oven: Initial temp.70 °C; Initial time 2.00 min; constant flow			
Ramps:	Rate [°C/min]	Final temp [°C]	Final time [min]
1	20.00	160	1.00
2	1	170	1.00
3	30	300	2.00

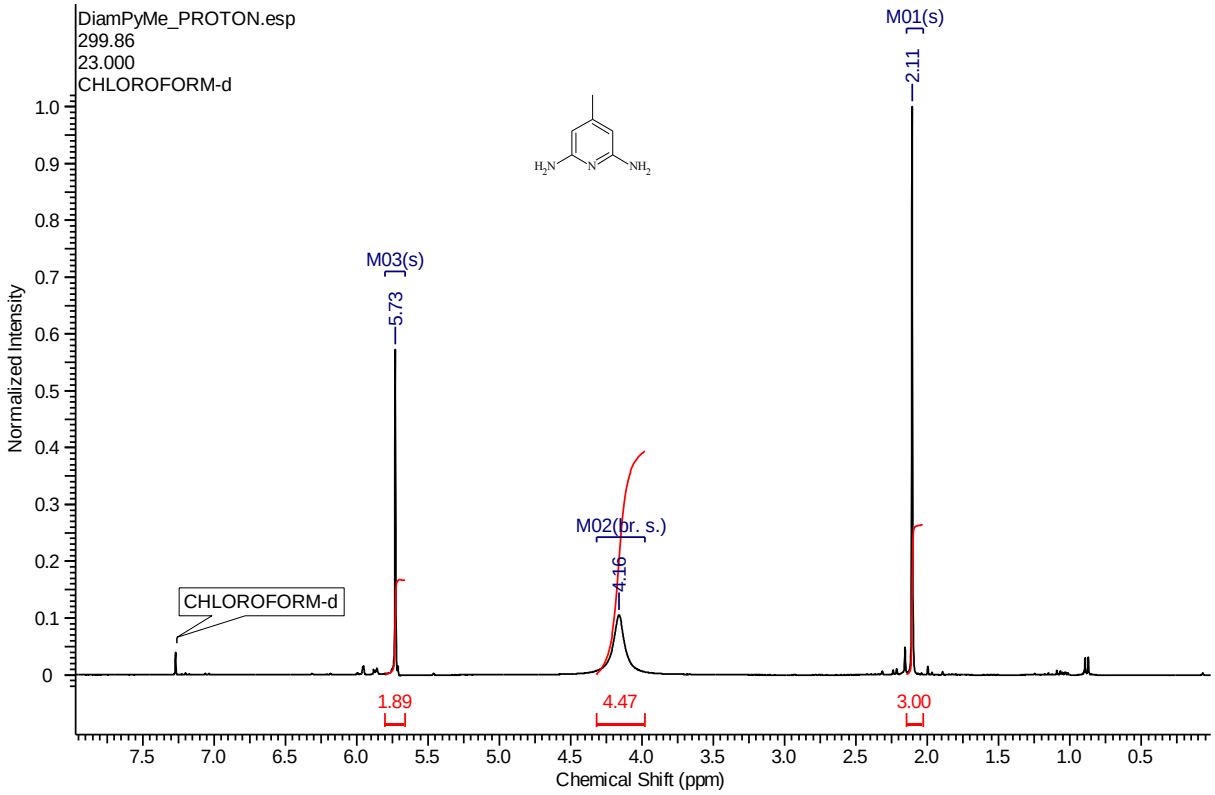
Substrate	Retention time [min]	Substrate	Retention time [min]
	17.76		18.25
	18.84		20.14
	22.19		21.99
	12.70		12.10
Dodecan (int. standard)	5.58		

Method 4:

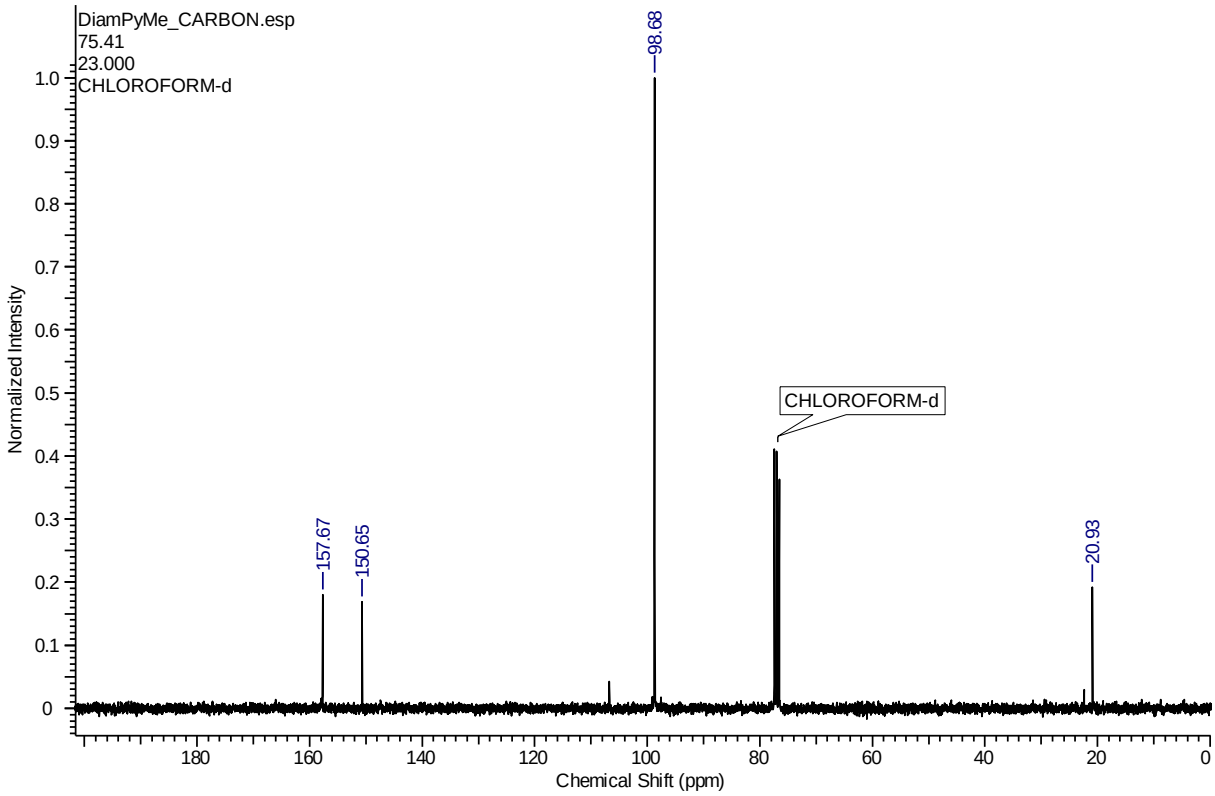
Oven: Initial temp. 35 °C; Initial time 5.00 min; constant flow			
Ramps:	Rate [°C/min]	Final temp [°C]	Final time [min]
1	15.00	100	0.00
2	40	300	2.00

Substrate	Retention time [min]	Substrate	Retention time [min]
	7.47		6.16
	2.38		2.16
	10.296		9.37
Dodecan (int. standard)	11.34		

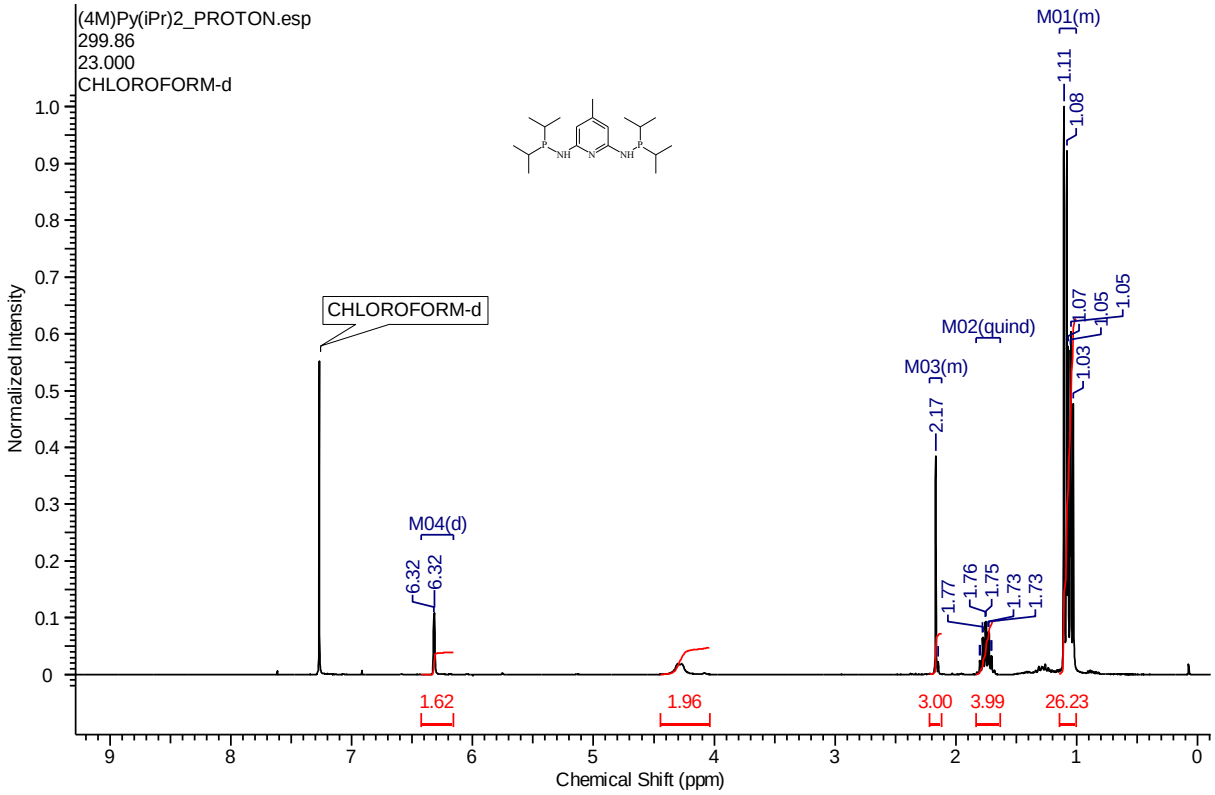
^{1}H NMR Spectra of 2,6-diamino-4-methylpyridine



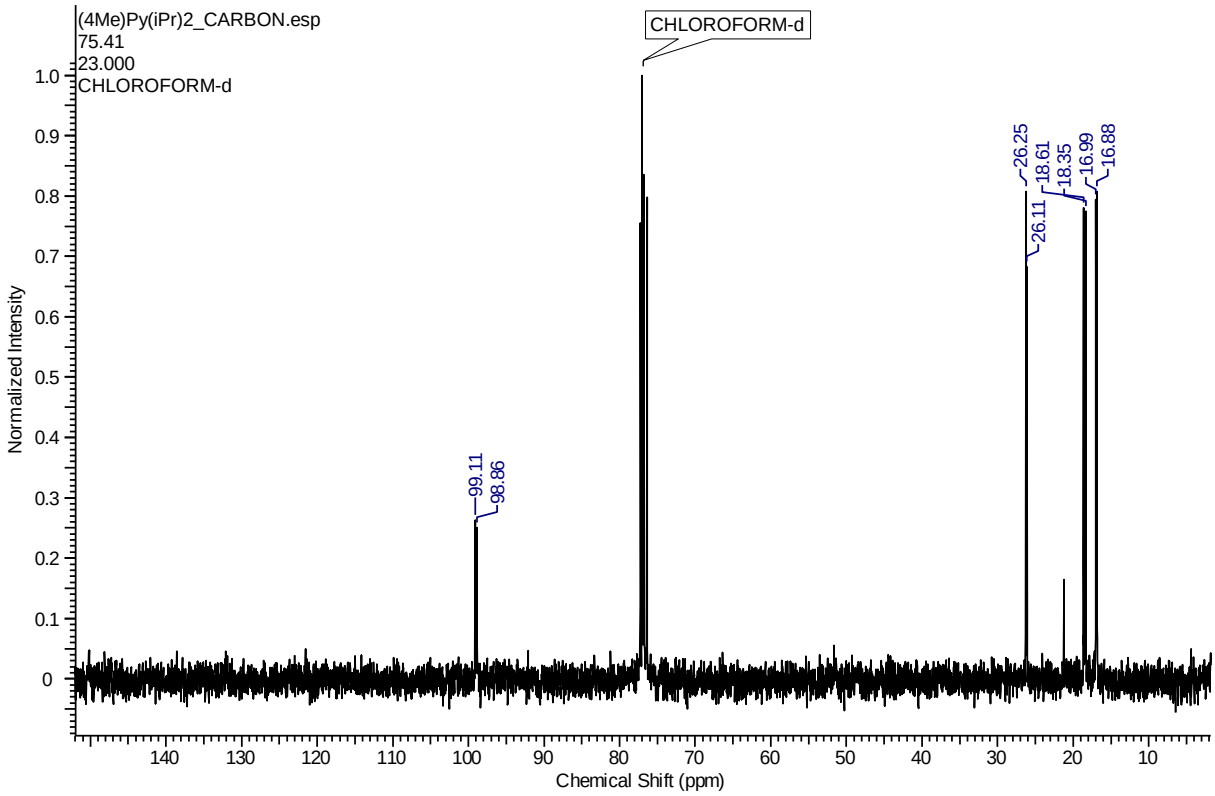
^{13}C NMR Spectra of 2,6-diamino-4-methylpyridine



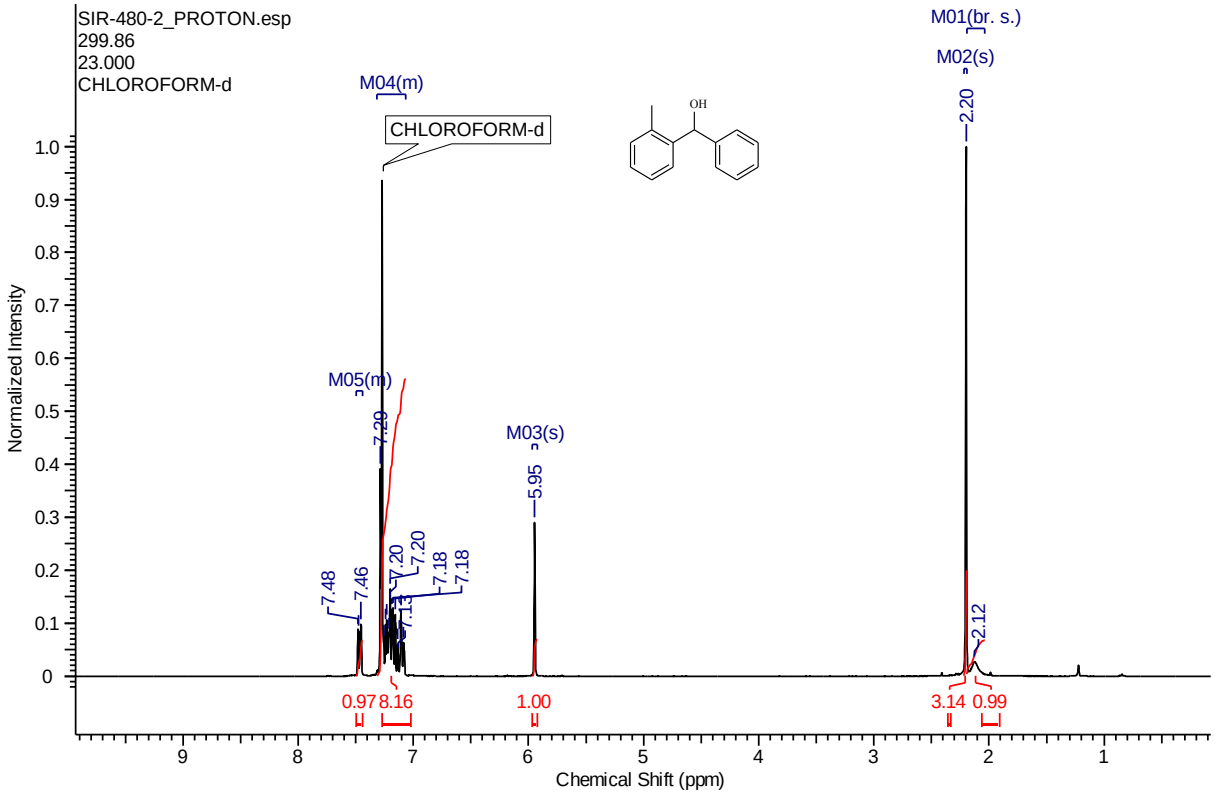
^{1}H NMR Spectra of (4-Me)Py(NHP(iPr)$_2$)$_2$:



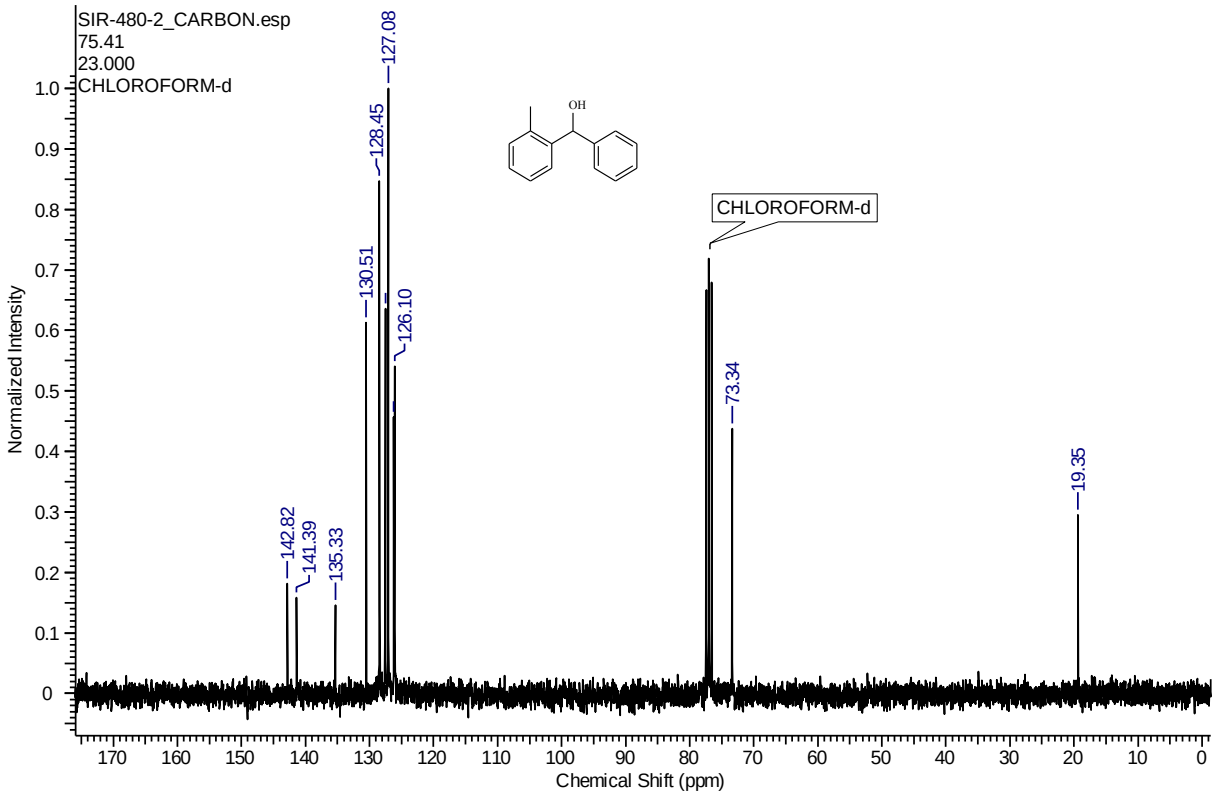
^{13}C NMR Spectra of (4-Me)Py(NHP(iPr)$_2$)$_2$:



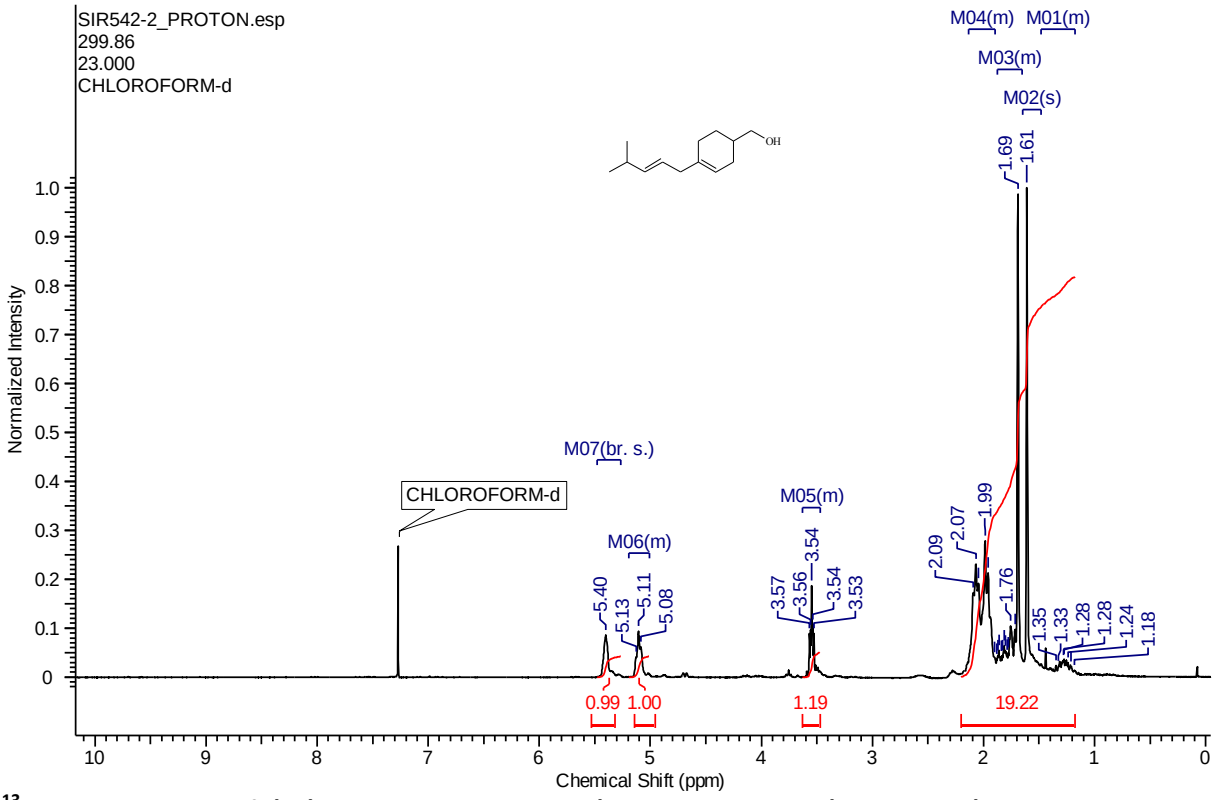
^{1}H NMR Spectra of 2-methylbenzhydrol (299.86 MHz, $CDCl_3$, 23°C)



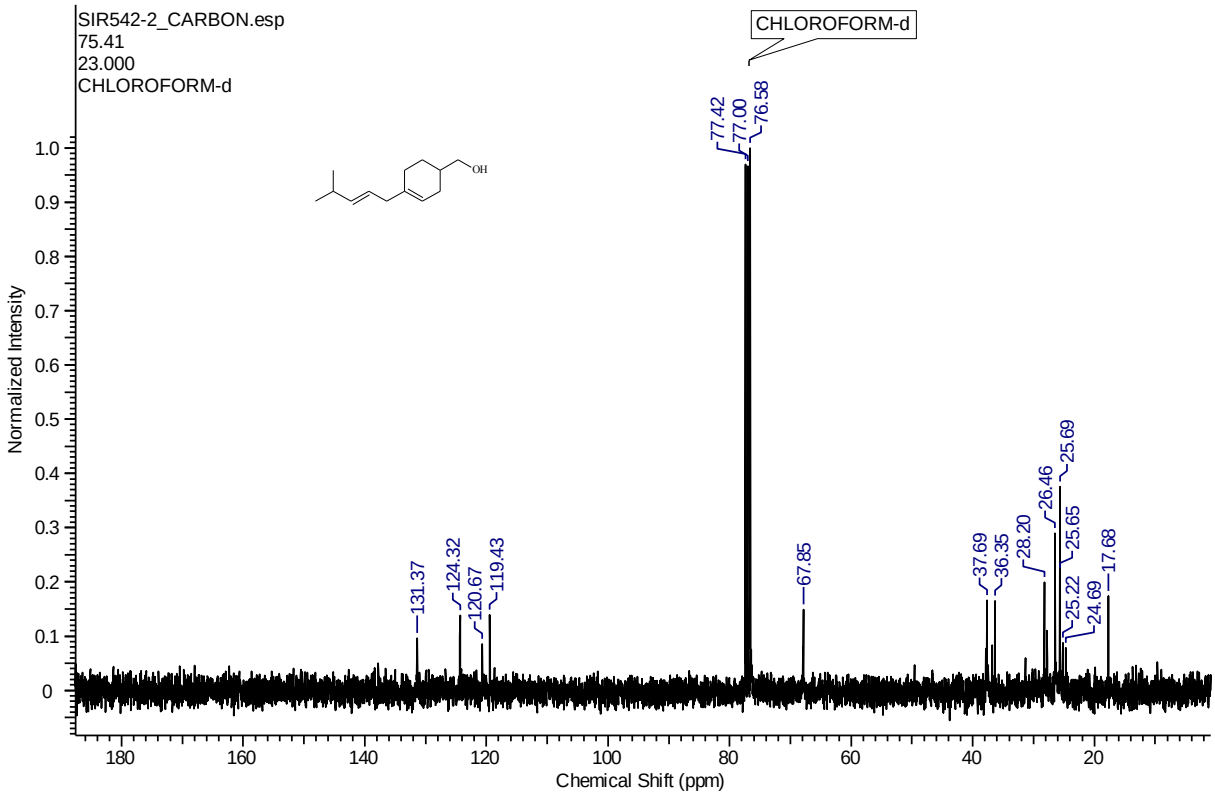
^{13}C NMR Spectra of 2-methylbenzhydrol (75.41 MHz, $CDCl_3$, 23°C)



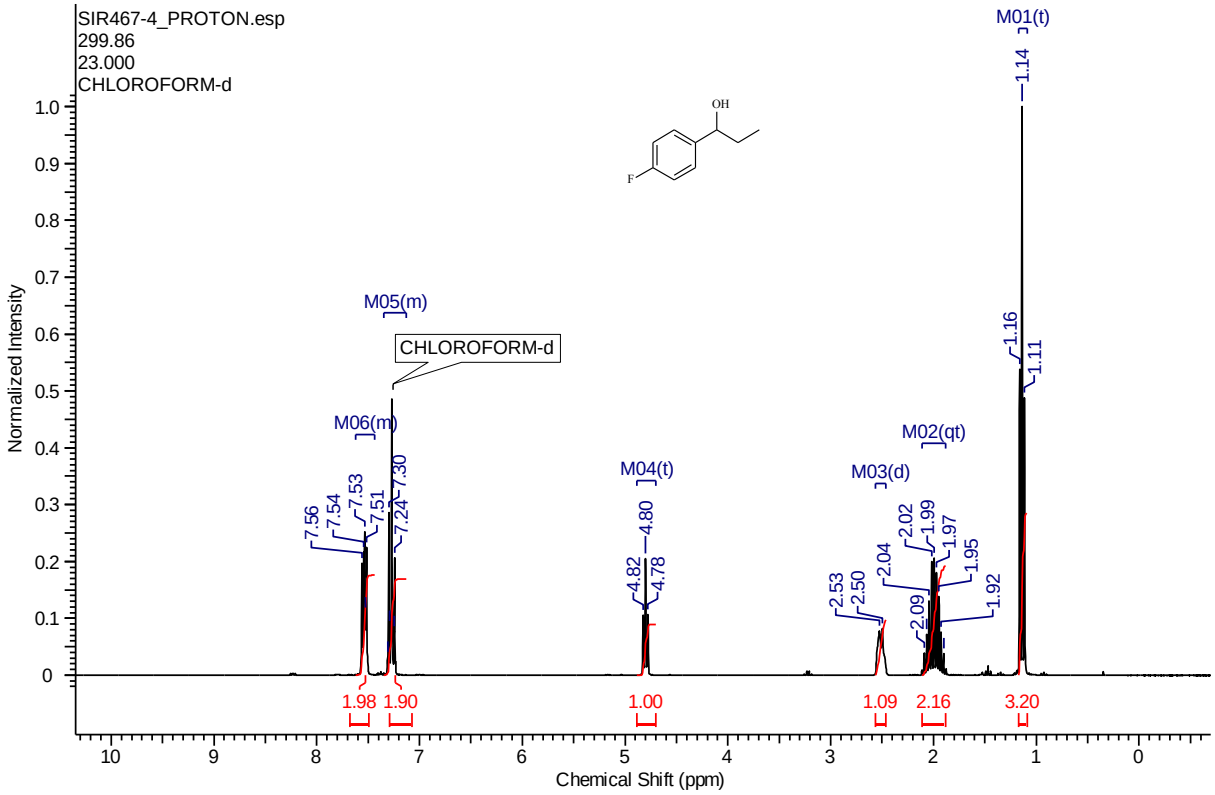
^{1}H NMR Spectra of (4-(4-methylpent-2-en-1-yl)cyclohex-3-en-1-yl)methanol (E/Z mixture) (299.86 MHz, $CDCl_3$, 23°C)



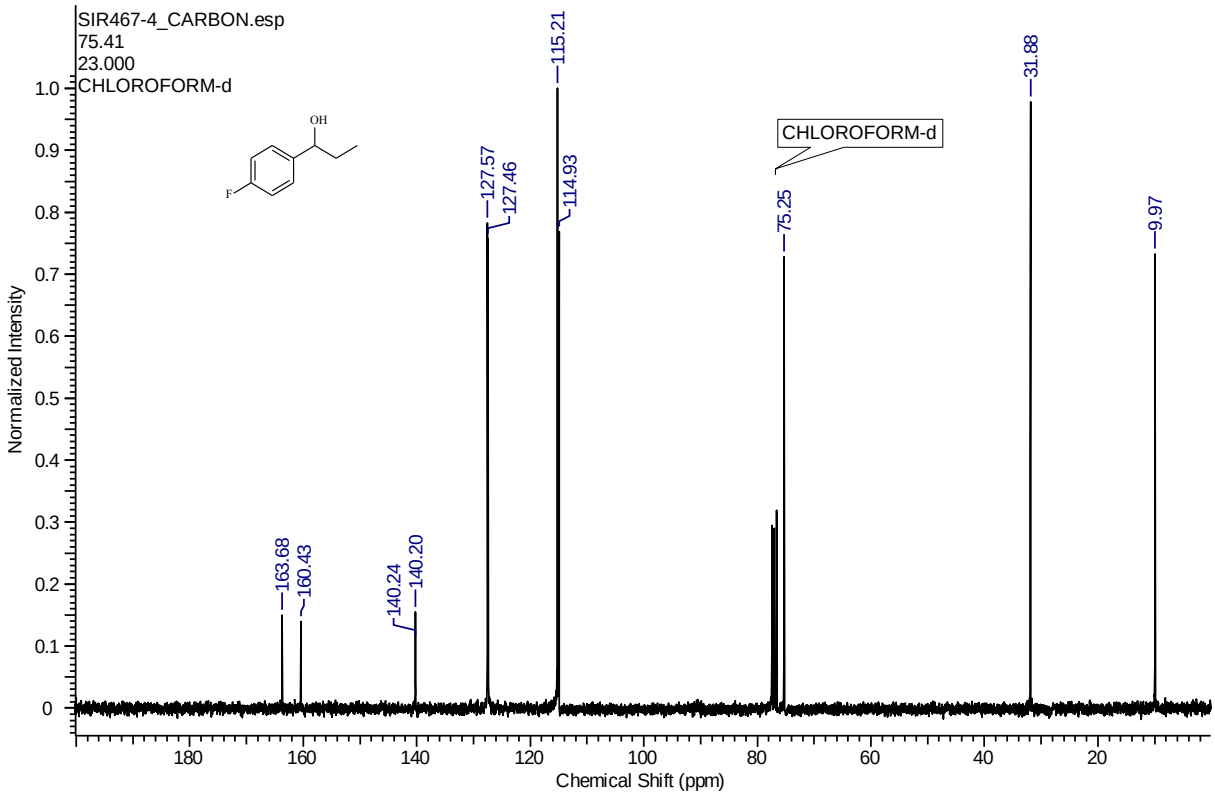
^{13}C NMR Spectra of (4-(4-methylpent-2-en-1-yl)cyclohex-3-en-1-yl)methanol (75.41 MHz, $CDCl_3$, 23°C)



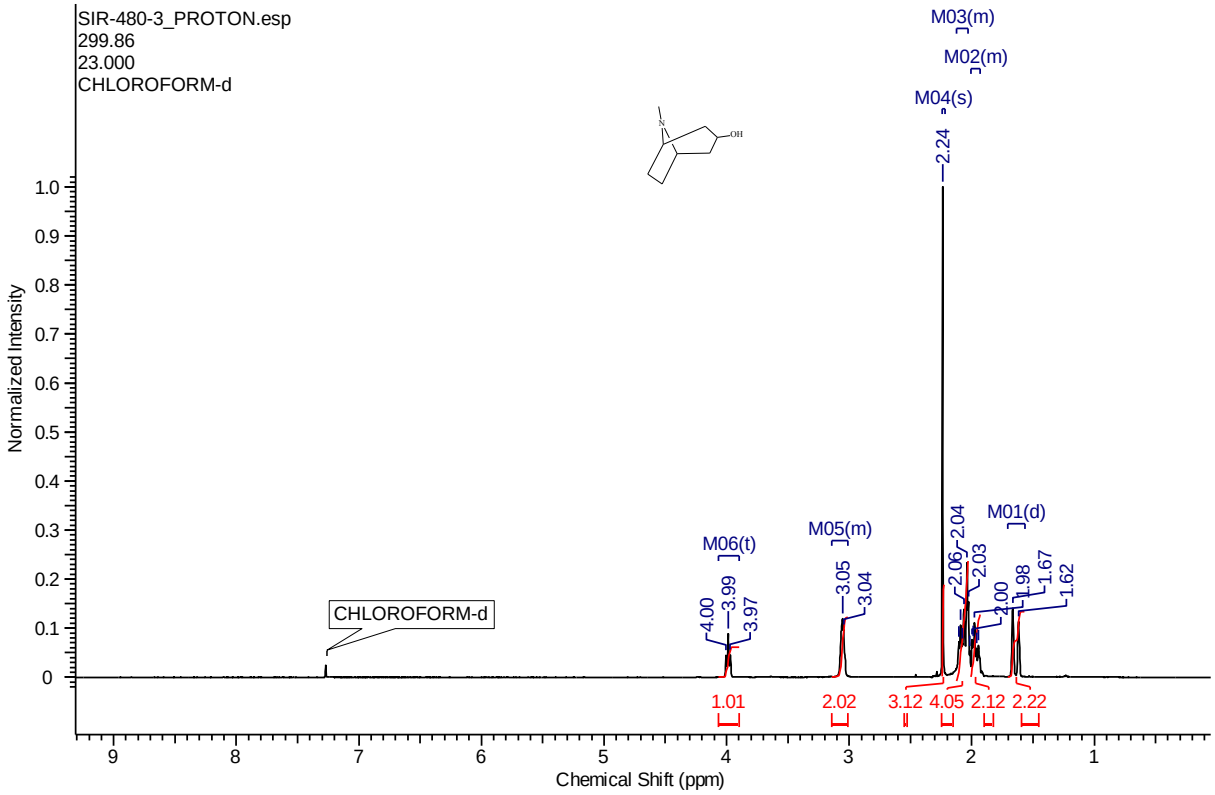
^{1}H NMR Spectra of 1-(4'-fluorophenyl)propan-1-ol (299.86 MHz, $CDCl_3$, 23°C)



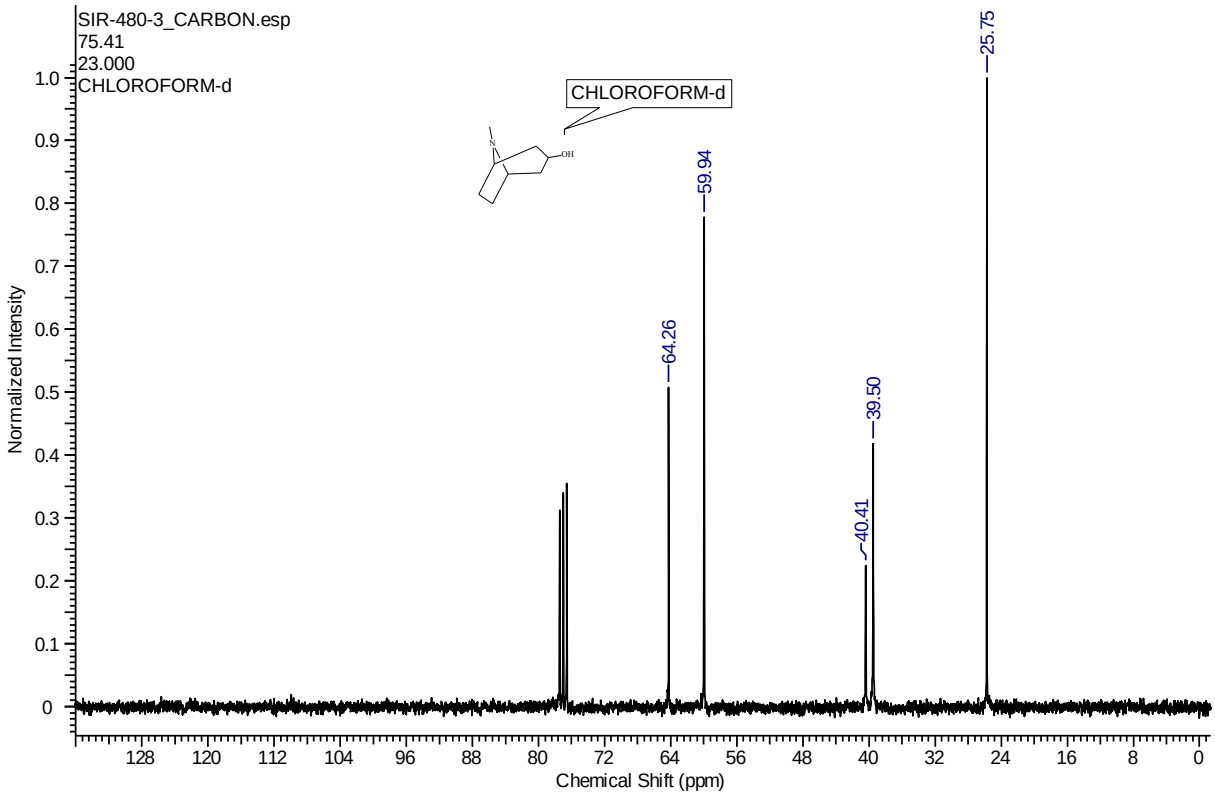
^{13}C NMR Spectra of 1-(4'-fluorophenyl)propan-1-ol (75.41 MHz, $CDCl_3$, 23°C)



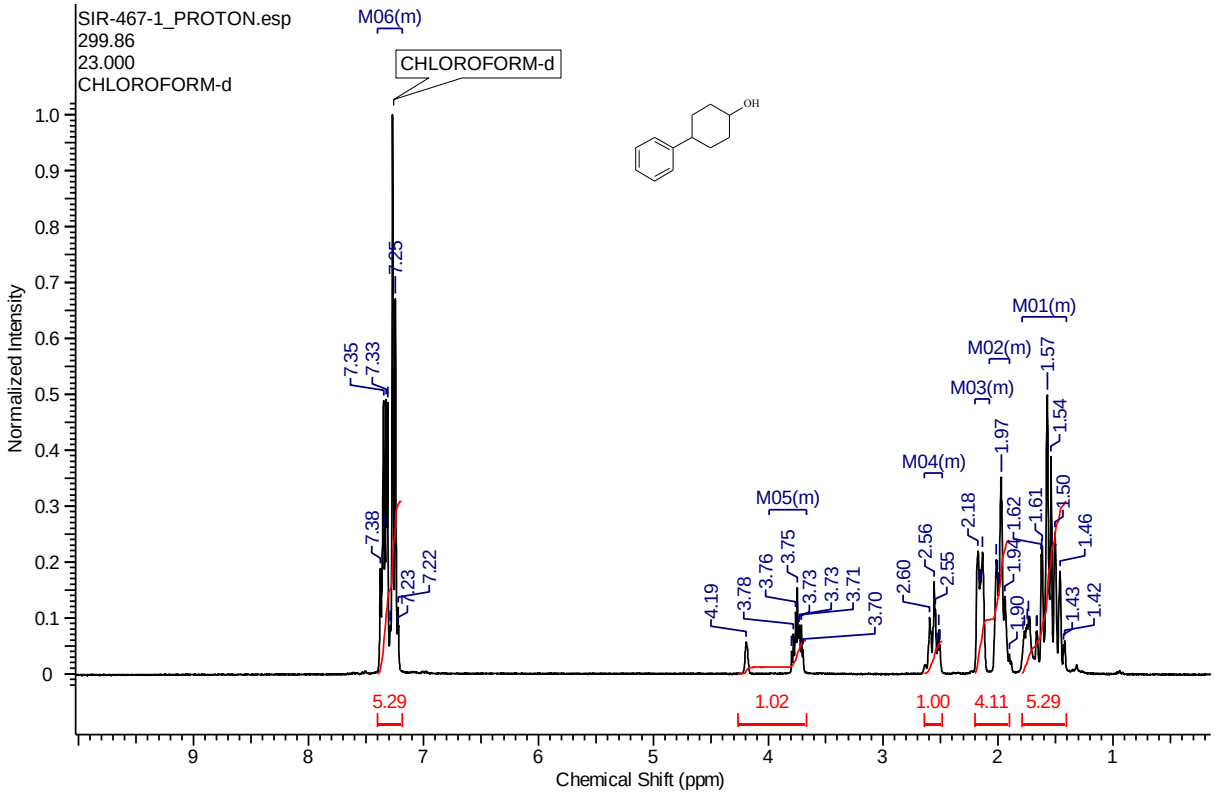
^{1}H NMR Spectra of 8-methyl-8-azabicyclo[3.2.1]octan-3-ol (299.86 MHz, $CDCl_3$, 23°C)



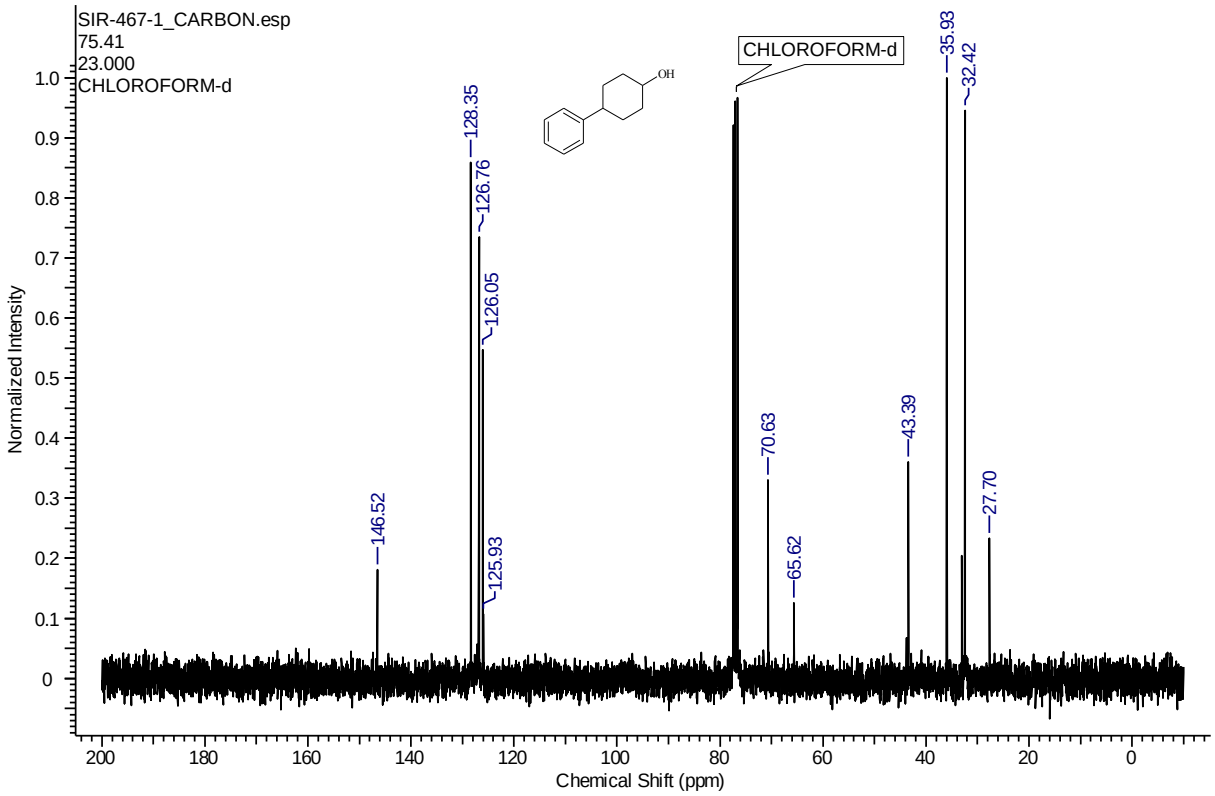
^{13}C NMR Spectra of 8-methyl-8-azabicyclo[3.2.1]octan-3-ol (75.41 MHz, $CDCl_3$, 23°C)



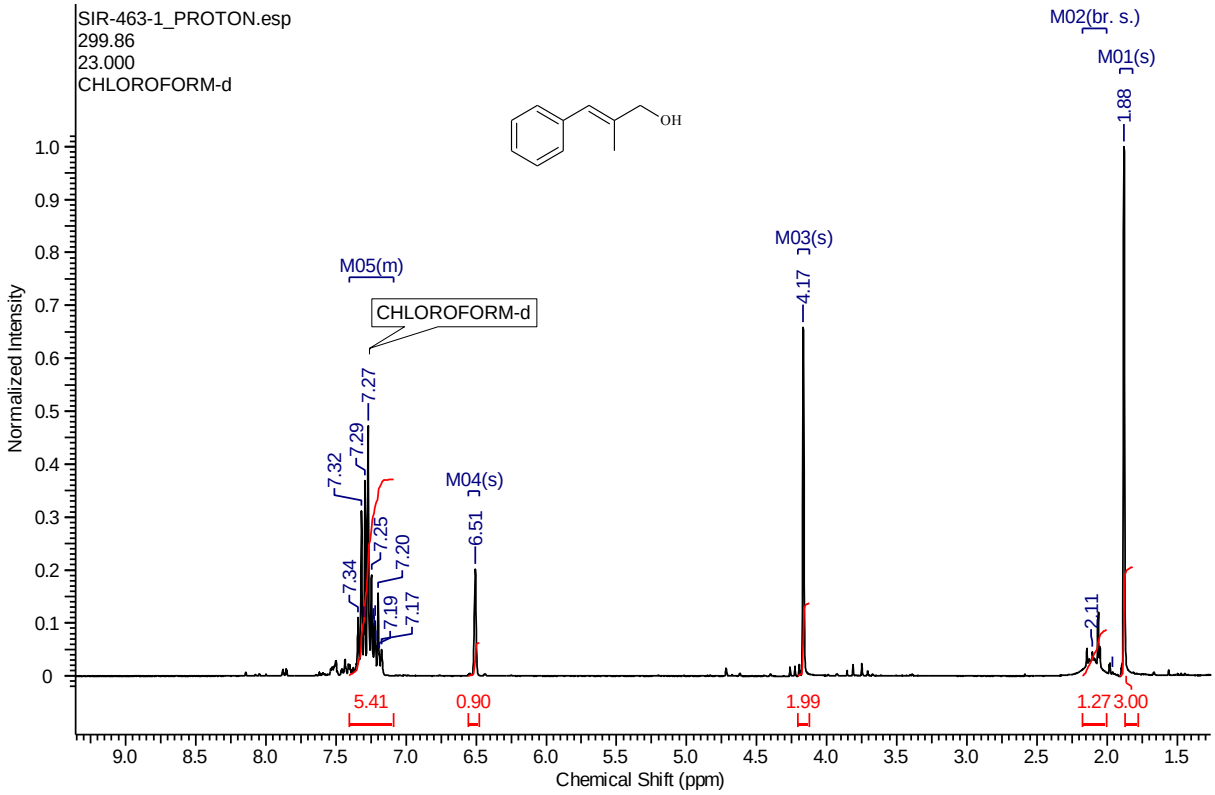
^{1}H NMR Spectra of 4-phenylcyclohexanol (299.86 MHz, $CDCl_3$, 23°C)



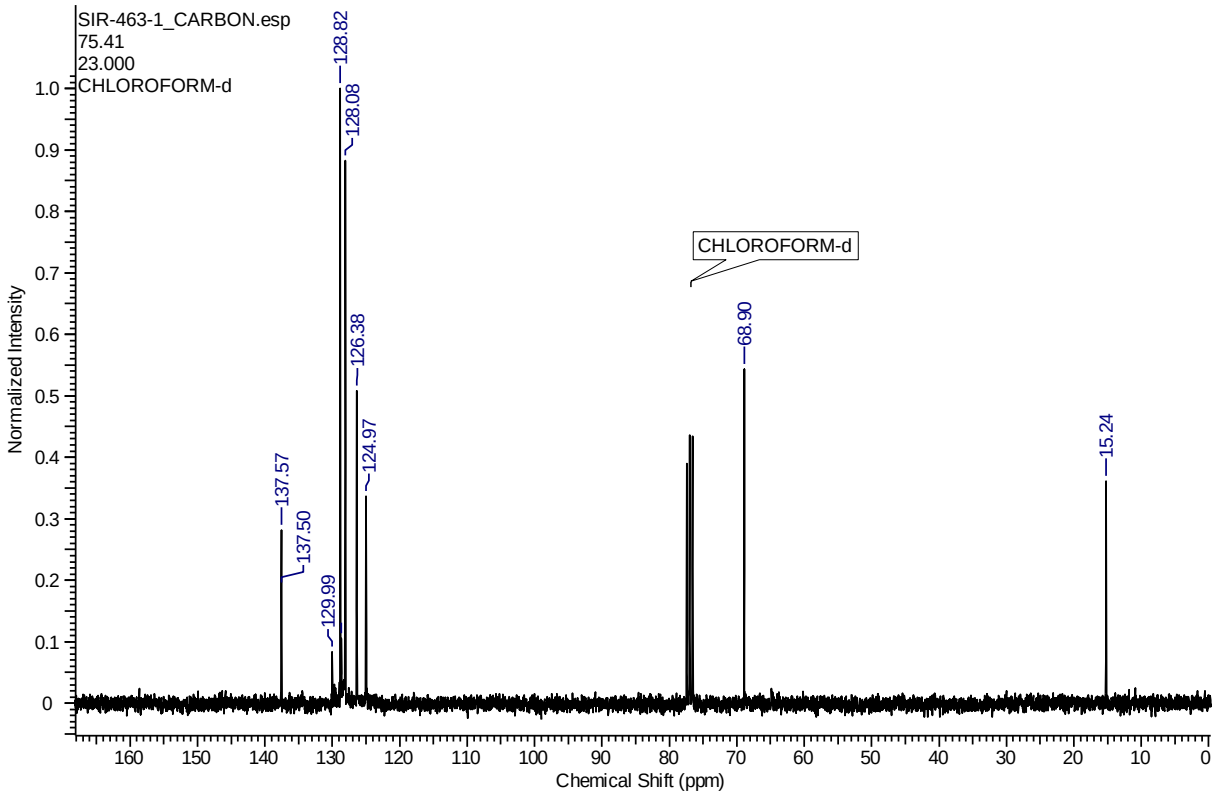
^{13}C NMR Spectra of 4-phenylcyclohexanol (75.41 MHz, $CDCl_3$, 23°C)



^{1}H NMR Spectra of 2-methyl-3-phenyl-prop-2-en-1-ol



^{13}C NMR Spectra of 2-methyl-3-phenyl-prop-2-en-1-ol



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5. Cobalt catalyzed alkylation of aromatic amines by alcohols

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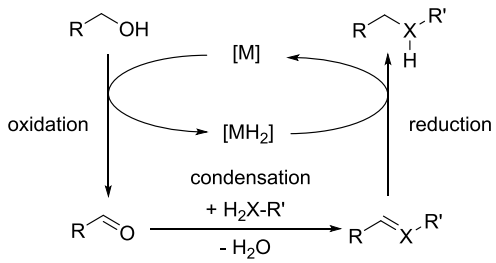
Abstract: The implementation of inexpensive, Earth abundant metals in typical noble-metal-mediated chemistry is a major goal in homogeneous catalysis. A sustainable or green reaction that has received a lot of attention in recent years and is preferentially catalyzed by Ir or Ru complexes is the alkylation of amines by alcohols. It is based on the borrowing hydrogen or hydrogen auto-transfer concept. Herein, we report on the Co-catalyzed alkylation of aromatic amines by alcohols. The reaction proceeds under mild conditions, and selectively generates monoalkylated amines. The observed selectivity allows the synthesis of unsymmetrically substituted diamines. A novel Co complex stabilized by a PN_5P ligand catalyzes the reactions most efficiently.

5.1 Introduction

The borrowing hydrogen or hydrogen auto-transfer (BH/HA) concept (Scheme 1) is an elegant method for the green or sustainable formation of C–C and C–N bonds.[1] In this concept, an alcohol is first oxidized by a transition-metal catalyst to the corresponding carbonyl compound. It can then undergo condensation reactions followed by a reduction step using the hydrogen equivalents obtained from the alcohol oxidation.[1,2] The first examples of the N-alkylation of amines by alcohols were reported by the groups of Watanabe[3] and Grigg[4]. In the last 10 years, this type of reaction has received a lot of attention, and elegant synthesis concepts have been developed.[1] Typically, noble transition metals such as ruthenium and iridium catalyze the alkylation of amines efficiently.[1] Our group has contributed to the development of such Ir catalysts.[5]



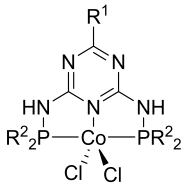
Scheme 1. Mechanism of BH/HA reactions. X= CH, N; [M] = transition metal catalyst

A key challenge in transition-metal-mediated catalysis is the substitution of expensive noble metals by Earth-abundant, inexpensive base metals. Homogenous cobalt catalysts have been reported in

reactions related to the key steps of BH/HA such as hydrogenation (olefins[6], ketones[7], nitriles[8], esters[9] and CO_2[10]) as well as dehydrogenations[11]. However, the use of homogenous cobalt catalysts in amine alkylation reactions by alcohols has not been reported to the best of our knowledge

5.2 Results and Discussion

Herein we describe the efficient alkylation of aromatic amines by alcohols catalyzed by a cobalt complex stabilized by a PN_5P ligand. The catalyst operates under mild conditions and selective monoalkylation is observed. On the basis of this selectivity, the synthesis of unsymmetrically alkylated diamines becomes feasible.



1a: R^1= 4-CF_3-C_6H_4; R^2= ^{i}Pr
1b: R^1= Ph; R^2= ^{i}Pr
1c: R^1= Me; R^2= ^{i}Pr
1d: R^1= NH-C_3H_5; R^2= ^{i}Pr
1e: R^1= Me; R^2= Cy
1f: R^1=H; R^2= ^{i}Pr

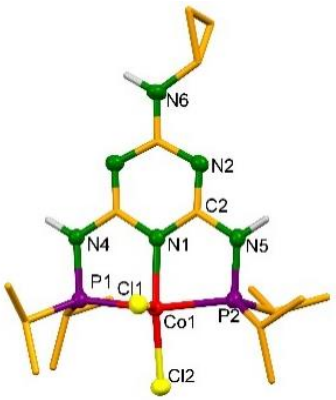
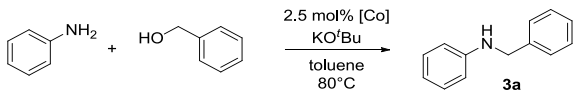


Figure 1. Synthesized Co complexes **1a-f** and molecular structure determined by X-ray crystal structure analysis of **1d** with 50% probability of thermal ellipsoids. Hydrogens (except NH) are omitted for clarity. Selected bond lengths [Å] and angles [°]: P1–Co1 2.202(1); P2–Co1 2.196(1); Co1–Cl1 2.464(1); Co1–Cl2 2.220(1); Co1–N1 1.926(2); C2–N2 1.318(3); P1–Co1–P2 164.36(3); N1–Co1–Cl1 90.34(7); N1–Co1–Cl2 162.43(7); N4–P1–Co1 99.18(8); N5–P2–Co1 99.97(8).

We recently introduced $PN_{3\text{-}5}P$-Ir complexes as highly efficient homogeneous catalysts for the sustainable synthesis of N-heteroarenes such as pyrroles and pyridines.[12] Very recently, we showed that Co complexes stabilized by a PN_5P ligand (triazine backbone) are highly active and selective catalysts for the hydrogenation of C=O bonds.[7a] The Co complexes are easy to synthesize and simple to activate. They can be synthesized quantitatively on a multigram scale and are air-stable as crystalline materials for a few months. The PN_3P ligand system (pyridine backbone) was introduced by Haupt and co-workers[13] and the Kirchner group demonstrated the broad applicability of the ligands class.[14] Reports on Co complexes are rare.[7a,15]

The reaction of aniline with benzyl alcohol was investigated to identify an efficient Co-based catalyst for the alkylation of amines. To our delight, 5.0 mol% complex **1c** (which was the most active pre-catalyst in the hydrogenation of C=O bonds) already afforded N-benzylaniline (**3a**) in 84% yield under relatively mild reaction conditions (80°C). A catalyst screening with 2.5 mo% of the complexes **1a-e** (Figure 1, Table 1) was next carried out. In addition to these already published Co complexes (**1a-c**),[7a] three new $CoCl_2$ complexes stabilized by a PN_5P ligand (**1d-f**) were synthesized, characterized and applied (Figure 1, Table 1; see Table S2 in the Supporting Information).

Table 1. Screening of cobalt complexes in the alkylation of aniline with benzyl alcohol.[a]



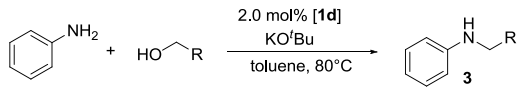
Entry	Pre-catalyst	Yield[b] [%]
1	1a	42
2	1b	17
3	1c	35
4	1d	62
5	1e	35
6	$CoCl_2$	3

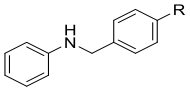
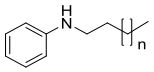
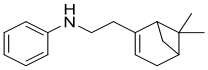
[a] Reaction conditions: 1.0 mmol aniline, 1.1 mmol benzyl alcohol, 1.0 mmol KO^{t}Bu, 5 mL toluene, 80 °C, 20 h. [b] Determined via GC with dodecane as internal standard.

The cobalt precursor, $CoCl_2$, was also investigated, but afforded only 3 % of the alkylated aniline (Table 1, entry 6). Complex **1d** was found to be the most active pre-catalyst in the test reaction. The molecular structure of **1d** was determined by X-ray crystal structure analysis. The N2-C2 and the N3-C1 bonds (1.318 Å) of **1d** are shorter than the corresponding N-C bonds in **1a-c** (averaged 1.331 Å). This indicates a partial double-bond character for these N-C bonds in **1d** and consequently, a more positively charged alkyl amine (N6) and a more negatively charged coordinating N atom (N1). Interestingly, the Co complexes stabilized by a PN_3P ligand (pyridine backbone) resulted in significantly lower rates than their PN_5P (triazine backbone) counterparts (see Table S2). The catalyst based on **1d** was used for the final optimizations of the reaction conditions. The use of precatalyst at a loading of 2.0 mol% led to the formation of 93% N-benzylaniline (Table S7, SI). An amine/ alcohol ratio of 1.4:1 is beneficial.

With these optimized conditions in hand, aniline was alkylated with various alcohol derivatives (Table 2, **3a-l**). Substituted benzyl alcohols (**3a-h**) with several functional groups (halides, alkyl, thioether, methoxy), are applicable as well as aliphatic alcohols (**3i-l**). The resulting N-alkylated anilines were isolated in good to excellent yields except for **3d** where de-bromination lowered the yield.

Table 2. Alkylation of aniline with various primary alcohols.[a]



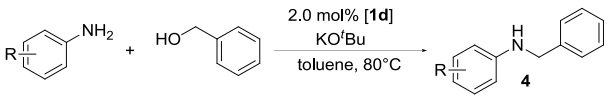
Entry	Alcohol		Product	Yield[b][%]
1	R= C_6H_5	3a		90
2	R= 4-F(C_6H_4)	3b		84
3	R= 4-Cl(C_6H_4)	3c		72
4	R= 4-Br(C_6H_4)	3d		53
5	R= 4-Me(C_6H_4)	3e		94
6	R= 4-OMe(C_6H_4)	3f		88
7	R= 4-SMe(C_6H_4)	3g		71
8	R= 4-*tert*-butyl(C_6H_4)	3h		93
9	1-butanol	3i		90
10	1-hexanol	3j		82
11	$C_{22}H_{45}OH$	3k		86
12	(-)Nopol	3l		96

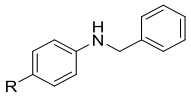
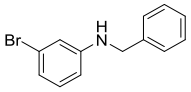
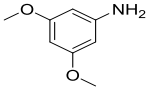
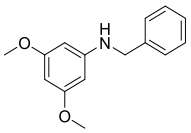
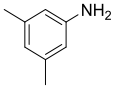
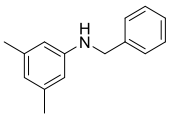
[a] Reaction conditions: 1.4 mmol aniline, 1.0 mmol alcohol, 2.0 mol% pre-catalyst **1d**, 1.2 mmol KO^{t}Bu, 3 mL toluene, 80 °C, 24 h. [b] Yield of isolated product.

Next, substituted anilines were alkylated with benzyl alcohol to show the aniline variability (Table 3). Again, a notable functional group tolerance was observed. Halide (F, Cl, Br and I) substituted N-benzyl anilines (**4a-d, 4g**) as well as 3,5-substituted N-benzyl anilines (**4h,i**) were isolated in good to excellent yields, except for **4d** and **g**, where partially dehalogenation again takes place. In addition, 3-aminopyridine was successfully alkylated with benzyl and aliphatic alcohols (Table 4).

Finally, we were interested in the preferential selective alkylation of diamines with two different alcohols (Table 5). First, a mono-alkylated diamine (**6a**) was synthesized in 91% isolated yield. In a second step, **6a** was alkylated with benzylic and aliphatic alcohols to the corresponding unsymmetrically alkylated diamines (**7b-e**).

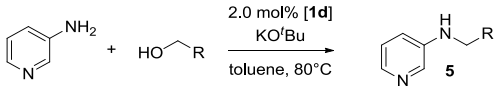
Table 3. Alkylation of various aniline derivatives with benzyl alcohol. [a]

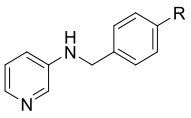
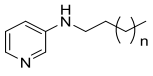


Entry	Amine		Product	Yield[b][%]
1	R= 4-F	4a		86
2	R= 4-Cl	4b		69
3	R= 4-Br	4c		72
4	R= 4-I	4d		51
5	R= 4-Et	4e		76
6	R= 4-^{i}Pr	4f		76
7	R= 3-Br	4g		57
8		4h		86
9		4i		63

[a] Reaction conditions: 1.4 mmol aniline, 1.0 mmol alcohol, 2.0 mol% pre-catalyst **1d**, 1.2 mmol KO^{t}Bu, 3 mL toluene, 80 °C, 24 h. [b] Yield of isolated product.

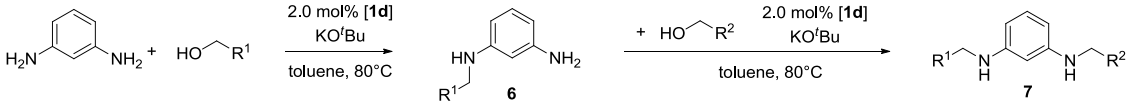
Table 4. Alkylation of 3-aminopyridine with various alcohols.[a]

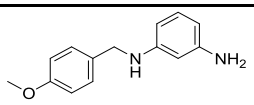
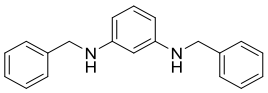
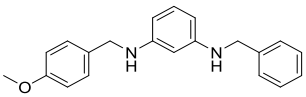
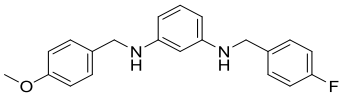
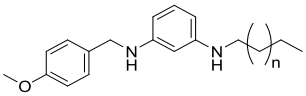


Entry	Alcohol		Product	Yield[b][%]
1	R= C_6H_5	5a		89
2	R= 4-OMe(C_6H_4)	5b		61
3	R= 4-SMe(C_6H_4)	5c		76
4	R= 4-Me(C_6H_4)	5d		94
5	$C_{22}H_{45}OH$	5e		69
6	1-butanol	5f		76

[a] Reaction conditions: 1.4 mmol aminopyridine, 1.0 mmol alcohol, 2.0 mol% pre-catalyst **1d**, 1.2 mmol KO^{t}Bu, 3 mL toluene, 80°C, 24 h. [b] Yield of isolated product.

Table 5. Alkylation of diamines



Entry	Alcohol R^1	Alcohol R^2		Product	Yield[d][%]
1	R^1= 4-OMe(C_6H_4)	-	6a[a]		91
2	R^1= C_6H_5	R^2= C_6H_5	7a[b]		73
3	R^1= 4-OMe(C_6H_4)	R^2= C_6H_5	7b[c]		71
4	R^1= 4-OMe(C_6H_4)	R^2= 4-F-(C_6H_4)	7c[c]		57
5	R^1= 4-OMe(C_6H_4)	R^2= propyl	7d[c]		76
6	R^1= 4-OMe(C_6H_4)	R^2= pentyl	7e[c]		79

[a] 3.0 mmol benzene diamine, 1.0 mmol alcohol, 2.0 mol% pre-catalyst **1d**, 1.2 mmol KO^{t}Bu, 3 mL toluene, 80 °C, 24 h. [b] 1.0 mmol benzene diamine, 2.0 mmol alcohol, 4.0 mol% pre-catalyst **1d**, 2.4 mmol KO^{t}Bu, 3 mL toluene, 80 °C, 24 h. [c] 1.0 mmol **6a**, 1.0 mmol alcohol, 2.0 mol% pre-catalyst **1d**, 1.2 mmol KO^{t}Bu, 3 mL toluene, 80 °C, 24 h. [d] Yield of isolated product.

5.3 Conclusion

In conclusion, we have reported on the first example of an alkylation of amines by alcohols by a cobalt complex. A novel Co catalyst allows the reaction to be carried out under mild conditions (80 °C) with a relatively low catalyst loading (2 mol%). The precatalyst is easily prepared from commercially available reagents in a two-step procedure and in almost quantitative yields. The mild reaction conditions allow the selective mono-alkylation of aromatic amines and the synthesis of unsymmetrically alkylated diamines.

Acknowledgments

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Keywords: alcohols • amine alkylation • base metals • hydrogen-transfer catalysis • cobalt

5.4 References

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5.5 Supporting Information

General considerations

Nonhalogenated solvents were dried over sodium benzophenone and halogenated solvents were dried over P_2O_5. Deuterated solvents were ordered from Cambridge Isotope Laboratories, vented, stored over molecular sieves and distilled. All chemicals were purchased from commercial sources with purity with over 95% and used without further purification. NMR spectra were received using a VARIAN INOVA 300 MHz spectrometer or a Bruker Advance III HD (500 MHz). Chemical shifts are reported in ppm relative to the deuterated solvent. GC analyses were carried out on an Agilent Technologies 6890N system equipped with an Optima17 column (30 m x 320 µm x 0.25 µm). GC/MS analyses were carried out on an Agilent 7890A/MSD 5975C system equipped with a HP-5MS column (30 m x 320 µm x 0.25 µm).

X-Ray crystal structure analysis was performed with a STOE STADIVARI [λ(Mo-Kα)= 0.71073 Å] equipped with an Oxford Cryostream low temperature unit. Structure solution and refinement were accomplished with SIR97[1], SHELXL-2013[2] and WinGX[3].

FTIR measurements were carried out on an Agilent Cary 630 FTIR equipped with a Diamond ATR unit.

General procedure for alkylation of amines:

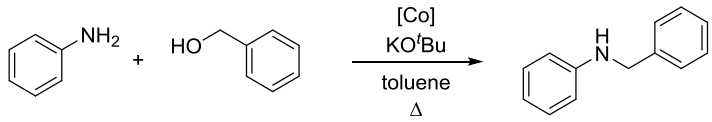


Figure S1. Model reaction for alkylation of aniline

In a nitrogen filled glovebox, a pressure tube was filled with pre-catalyst, KO^{t}Bu (135 mg, 1.2 mmol), aniline (124 µL, 1.4 mmol) and benzyl alcohol (104 µL, 1.0 mmol). 3 mL solvent are added and the tube is closed. The reaction mixture was stirred for 24 h at 80 °C. Reaction was stopped by addition of 1 mL of H_2O. 1.0 Equivalent of dodecane is added as internal standard. For GC analysis, the organic layer is extracted with diethyl ether.

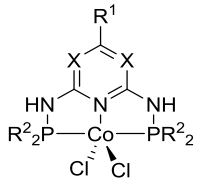
Screening reactions

Table S1. Temperature screening[a]

Entry	Temperature[b] [°C]	Yield[c] [%]
1	25	2
2	40	12
3	60	39
4	**80**	**84**
5	100	59
6	120	48

[a] Reaction conditions: 1.0 mmol aniline, 1.1 mmol benzyl alcohol, 5.0 mol% pre-catalyst **1c**, 1.0 mmol KO^{t}Bu, 5 mL toluene, 20 h. [b] Extern temperature. [c] Determined via GC with dodecane as internal standard.

Table S2. Pre-catalyst screening[a]



1a: X= N, R^1= 4-CF_3-C_6H_4; R^2= ^{i}Pr
1b: X= N, R^1= Ph; R^2= ^{i}Pr
1c: X= N, R^1= Me; R^2= ^{i}Pr
1d: X= N, R^1= NH-C_3H_5; R^2= ^{i}Pr
1e: X= N, R^1= Me; R^2= Cy
1f: X= N, R^1= H; R^2= ^{i}Pr
2a: X= CH, R^1= H; R^2= ^{i}Pr
2b: X= CH,R^1= H; R^2= Ph
2c: X= CH, R^1= Me; R^2= ^{i}Pr

Entry	Pre-catalyst	Pre-catalyst loading[b] [mol%]	Yield[c] [%]
1	**1a**	5.0	95
2	**1a**	2.5	42
3	**1b**	5.0	30
4	**1b**	2.5	17
5	**1c**	5.0	66
6	**1c**	2.5	35
7	**1d**	5.0	84
8	**1d**	**2.5**	**62**
9	**1e**	5.0	68
10	**1e**	2.5	35
11	**1f**	5.0	23
12	**2a**	5.0	9
13	**2b**	5.0	30
14	**2c**	5.0	7
15	**$CoCl_2$**	2.5	3

[a] Reaction conditions: 1.0 mmol aniline, 1.1 mmol benzyl alcohol, 1.0 mmol KO^{t}Bu, 5 mL toluene, 80 °C, 20h. [b] With respect to aniline. [c] Determined via GC with dodecane as internal standard.

Table S3. Solven sceening[a]

Entry	Solvent	Yield[b] [%]
1	**toluene**	**55**
2	*tert*-amyl alcohol	9
3	diglyme	19
4	dioxane	24
5	THF	30
6	acetonitrile	0
7	DMF	0

[a] Reaction conditions: 1.0 mmol aniline, 1.1 mmol benzyl alcohol, 2.5 mol% pre-catalyst **1d**, 1.0 mmol KO^{t}Bu, 5 mL solvent, 80 °C, 18 h. [b] Determined via GC with dodecane as internal standard.

Table S4. Base screening[a]

Entry	Base	Yield[b] [%]
1	**KO^{t}Bu**	**64**
2	$KN(SiMe_3)_2$	61
3	KH	30
4	KOH	0
5	NaO^{t}Bu	16
6	NaOH	0
7	LiO^{t}Bu	0
8	LiOH	0

[a] Reaction conditions: 1.0 mmol aniline, 1.1 mmol benzyl alcohol, 2.5 mol% pre-catalyst **1d**, 1.0 mmol base, 5 mL toluene, 80 °C, 24 h. [b] Determined via GC with dodecane as internal standard.

5. Cobalt catalyzed alkylation of aromatic amines by alcohols

Table S5. KO^{t}Bu loading screening[a]

Entry	KO^{t}Bu loading[b] [mol%]	Yield[c] [%]
1	0	0
2	20	0
3	40	6
4	60	23
5	80	44
6	100	71
7	**120**	**74**
8	140	72

[a] Reaction conditions: 1.0 mmol aniline, 1.1 mmol benzyl alcohol, 2.5 mol% pre-catalyst **1d**, 5 mL solvent, 80 °C, 24 h. [b] With respect to aniline [c] Determined via GC with dodecane as internal standard.

Table S6. Substrate ratio screening[a]

Entry	Aniline [mmol]	Benzyl alcohol [mmol]	Yield[b] [%]
1	1.0	1.0	63
2	1.0	1.2	70
3	1.0	1.4	66
4	1.0	1.6	60
5	1.2	1.0	73
6	**1.4**	**1.0**	**94**

[a] Reaction conditions: 2.5 mol% pre-catalyst **1d**, 1.2 mmol base, 5 mL toluene, 80 °C, 24 h. [b] Determined via GC with dodecane as internal standard.

Table S7. Pre-catalyst **1d** loading sceening[a]

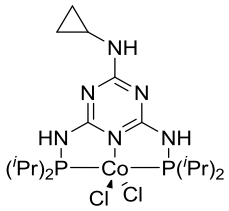
Entry	1d[b] [mol%]	Yield[c] [%]
1	0.5	53
2	1.0	69
3	1.5	82
4	2.0	93
5	2.5	94

[a] Reaction conditions: 1.4 mmol aniline, 1.1 mmol benzyl alcohol, pre-catalyst **1d**, 1.0 mmol KO^{t}Bu, 2 mL toluene, 80 °C, 24 h. [b] With respect to aniline. [c] Determined via GC with dodecane as internal standard.

Synthesis of Ligands and Complexes:

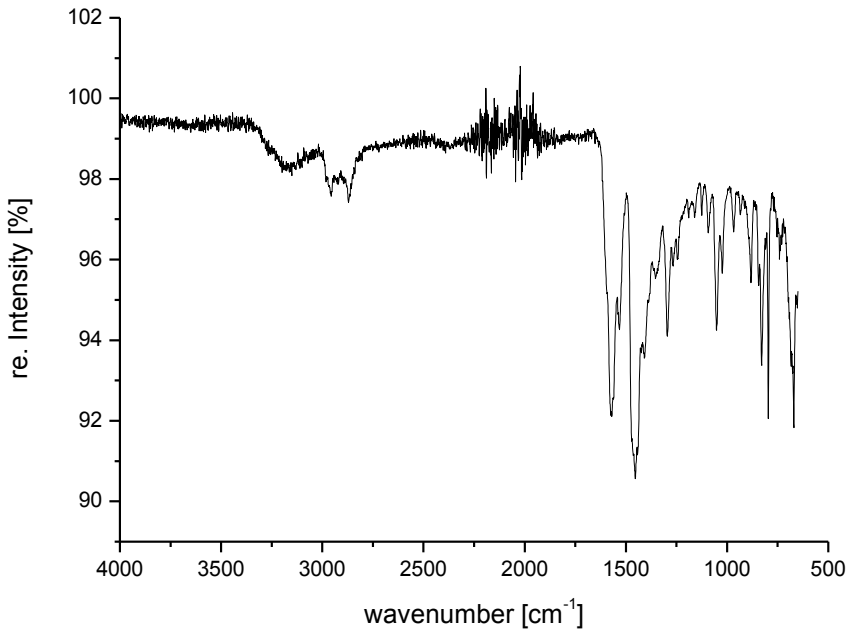
All ligands were synthesized according to literature procedures.[4]

Synthesis of $[(NH\text{-}C_3H_5)Tr(NHP(iPr)_2)_2CoCl_2]$ 1d:

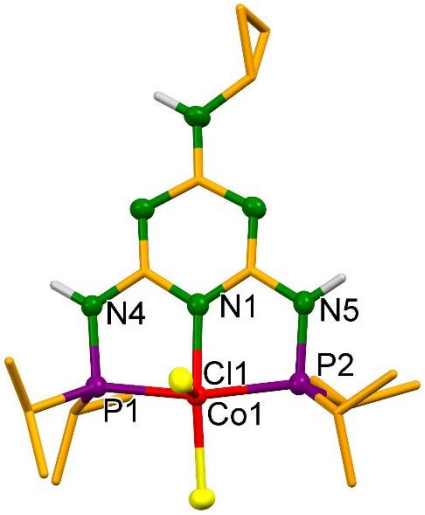


$CoCl_2$ (2.0 mmol, 260 mg) was suspended in 20 mL THF and subsequently a solution of $(NH\text{-}C_3H_5)Tr(NHP(^iPr)_2)_2$ (2.0 mmol, 797 mg) in THF was added in one portion. Stirring over night at 50 °C and cooling to RT results in a purple suspension. The supernatant solution was filtered off and the residue is dried in vacuo giving a red crystalline powder in almost quantitative yield (982 mg, 1.86 mmol, 93 %).
Elemental analysis calcd (%) for $C_{18}H_{34}Cl_2CoN_6P_2$ x $2C_4H_8O$ (M: 528.3): C 46.44 H 7.79 N 12.5; found: C 46.05 H7.72 N 12.57
Magnetic moment : 2.25μ_B

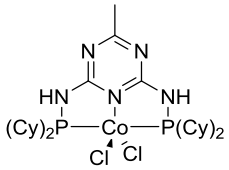
ATR-FT-IR spectra



Crystallographic data of **1d**	
Formula	$C_{18}H_{34}Cl_2CoN_6P_2$, 2 C_4H_8O
Formula weight	528,3
Crystal system	monoclinic
Space group	$P2_1/n$
a [Å]	17.019(5)
b [Å]	11.191(5)
c [Å]	17.932(5)
α [°]	90.000(5)
β [°]	98.896(5)
γ [°]	90.000(5)
Cell volume [$Å^3$]	3374(2)
Z	4
Crystal size [mm^3]	0.328x0.242x0.169
Habit	block
Colour	red
Density [gcm^{-3}]	1.324
T [K]	133(2)
Theta range	1.535 29.455
Unique reflections	6622
Observed reflections [I > 2s(I)]	4567
Parameters	373
wR_2 (all data)	0.0971
R [I > 2s(I)]	0.0391

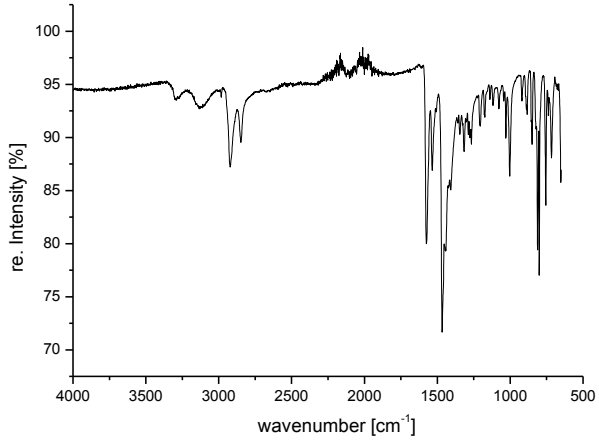


Synthesis of [(4-Me)Tr(NHP(Cy)$_2$)$_2$CoCl$_2$] 1e:

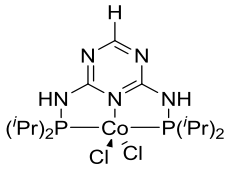


$CoCl_2$ (1.0 mmol, 129 mg) was suspended in 20 mL THF and subsequently a solution of (4-Me)Tr(NHP(Cy)$_2$)$_2$ (1.0 mmol, 517 mg) in THF was added in one portion. Stirring over night at 50 °C and cooling to RT results in a red suspension. The supernatant solution was filtered off and the residue was dried in vacuo giving a red crystalline powder in almost quantitative yield (576 mg, 0.89 mmol, 89 %).
Elemental analysis calcd (%) for $C_{28}H_{49}Cl_2CoN_5P_2$ (M: 647.5): C 51.94 H 7.63 N 10.82; found: C 52.14 H 7.69 N 10.74
Magnetic moment: 2.29 μ_B

ATR-FT-IR spectra

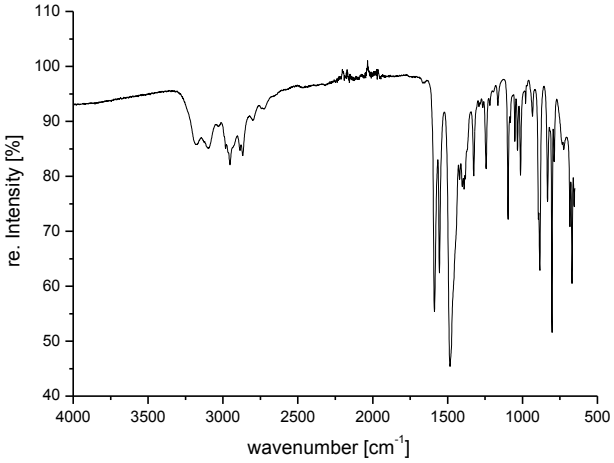


Synthesis of [(H)Tr(NHP(iPr)$_2$)$_2$CoCl$_2$] 1f:



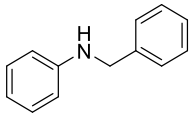
$CoCl_2$ (2.0 mmol, 260 mg) was suspended in 20 mL THF and subsequently a solution of (H)Tr(NHP(^{i}Pr)$_2$)$_2$ (2.0 mmol, 687 mg) in THF was added in one portion. Stirring over night at 50 °C and cooling to RT results in a red suspension. The supernatant solution was filtered off and the residue was dried in vacuo giving a red crystalline powder in almost quantitative yield (878 mg, 1.85 mmol, 93 %).
Elemental analysis calcd (%) for $C_{15}H_{31}Cl_2CoN_5P_2$ (M: 473.2): C 38.07 H 6.60 N 14.80; found: C 38.41 H 6.81 N 14.81

ATR-FT-IR spectra



Products

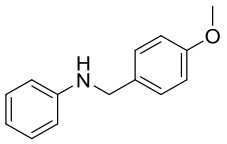
Synthesis of N-benzylaniline (3a):



Chemical Formula: $C_{13}H_{13}N$
Molecular Weight: 183,3

Aniline (1.4 mmol, 124 µL), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (165 mg, 0.90 mmol, 90 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.26 - 7.51 (m, 5 H), 7.11 - 7.25 (m, 2 H), 6.61 - 6.81 (m, 3 H), 4.37 (s, 2 H), 4.17 (br. s., 1 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 148.9, 140.3, 129.7, 129.1, 128.0, 127.7, 117.9, 113.3, 48.6 ppm

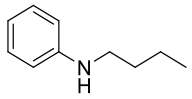
Synthesis of N-((4-methoxy)benzyl)aniline (3f):



Chemical Formula: $C_{14}H_{15}NO$
Molecular Weight: 213,3

Aniline (1.4 mmol, 126 µL), 4-Methoxybenzyl alcohol (1.0 mmol, 127 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 3:1) as a colorless oil (188 mg, 0.882 mmol, 88 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.30 - 7.39 (m, 2 H), 7.15 - 7.25 (m, 2 H), 6.88 - 6.97 (m, 2 H), 6.70 - 6.79 (m, 1 H), 6.62 - 6.70 (m, 2 H), 4.29 (s, 2 H), 4.11 (br. s., 1 H), 3.77 - 3.88 (m, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 159.5, 148.9, 132.2, 129.7, 129.2, 117.8, 114.5, 113.3, 55.7, 48.1 ppm

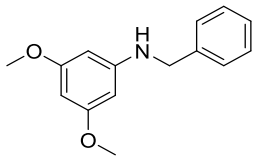
Synthesis of N-(1-butyl)aniline (3i):



Chemical Formula: $C_{10}H_{15}N$
Molecular Weight: 149,2

Aniline (1.4 mmol, 126 µL), 1-Butanol (1.0 mmol, 92 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (135 mg, 0.90 mmol, 90 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.07 - 7.25 (m, 2 H), 6.53 - 6.76 (m, 3 H), 3.67 (br. s., 1 H), 3.12 (t, *J*=7.0 Hz, 2 H), 1.33 - 1.73 (m, 4 H), 0.93 - 1.07 (m, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 149.4, 129.7, 117.3, 113.1, 44.2, 32.2, 20.9, 14.3 ppm

Synthesis of N-benzyl-3,5-dimethoxyaniline (4h):

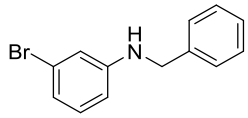


Chemical Formula: $C_{15}H_{17}NO_2$
Molecular Weight: 243,3

3,5-Dimethoxyaniline (1.4 mmol, 214 mg), Benzyl alcohol (1.0 mmol, 104µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The

organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 1:1) as a colorless oil (209 mg, 0.86 mmol, 86 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.33 - 7.42 (m, 4 H), 7.24 - 7.33 (m, 1 H), 5.86 - 5.91 (m, 1 H), 5.83 (d, *J*=2.1 Hz, 2 H), 4.32 (s, 2 H), 4.21 (br. s., 1 H), 3.72 (s, 6 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 162.3, 150.7, 140.2, 129.1, 127.9, 127.7, 92.2, 90.2, 55.6, 48.6 ppm

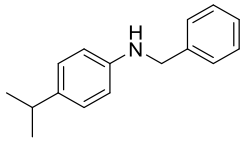
Synthesis of N-benzyl-3-bromoaniline (4g):



Chemical Formula: $C_{13}H_{12}BrN$
Molecular Weight: 262,2

3-Bromoanline (1.4 mmol, 152 µL), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (150 mg, 0.57 mmol, 57 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.35 - 7.41 (m, 4 H), 7.28 - 7.35 (m, 1 H), 6.95 - 7.09 (m, 1 H), 6.83 (ddd, *J*=7.9, 1.8, 0.9 Hz, 1 H), 6.80 (t, *J*=2.1 Hz, 1 H), 6.57 (ddd, *J*=8.2, 2.3, 0.8 Hz, 1 H), 4.32 (d, *J*=4.9 Hz, 2 H), 4.26 (br. s., 1 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 150.1, 139.5, 131.1, 129.2, 128.0, 127.9, 127.9, 123.6, 120.5, 115.8, 113.3, 112.1, 48.4 ppm

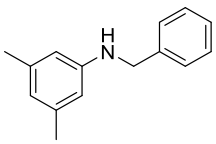
Synthesis of N-benzyl-4-isopropylaniline (4f):



Chemical Formula: $C_{16}H_{19}N$
Molecular Weight: 225,3

4-Isopropylaniline (1.4 mmol, 191 µL), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (170 mg, 0.76 mmol, 76 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.35 - 7.46 (m, 4 H), 7.27 - 7.33 (m, 1 H), 7.03 - 7.10 (m, 2 H), 6.58 - 6.64 (m, 2 H), 4.34 (s, 2 H), 4.07 (br. s., 1 H), 2.83 (dt, *J*=13.7, 6.9 Hz, 1 H), 1.24 (d, *J*=7.0 Hz, 6 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 146.9, 140.6, 138.5, 129.1, 128.0, 127.6, 127.6, 127.5, 113.4, 48.9, 33.8, 24.6 ppm

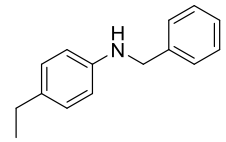
Synthesis of N-benzyl-3,5-dimethylaniline (4i):



Chemical Formula: $C_{15}H_{17}N$
Molecular Weight: 211,3

3,5-Dimethylaniline (1.4 mmol, 174 µL), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (134 mg, 0.63 mmol, 63 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.34 - 7.47 (m, 4 H), 7.24 - 7.34 (m, 1 H), 6.40 (s, 1 H), 6.30 (s, 2 H), 4.33 (s, 2 H), 4.02 (br. s., 1 H), 2.18 - 2.34 (m, 6 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 148.9, 140.6, 139.3, 129.1, 128.0, 127.6, 120.0, 111.3, 48.7, 21.8 ppm

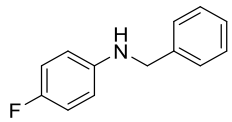
Synthesis of N-benzyl-4-ethylaniline (4e):



Chemical Formula: $C_{15}H_{17}N$
Molecular Weight: 211,3

4-Ethylaniline (1.4 mmol, 174 µL), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (161 mg, 0.76 mmol, 76 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.23 - 7.60 (m, 5 H), 7.04 (d, *J*=8.2 Hz, 2 H), 6.50 - 6.74 (m, 2 H), 4.34 (s, 2 H), 4.03 (br. s., 1 H), 2.57 (q, *J*=7.6 Hz, 2 H), 1.22 (t, *J*=7.6 Hz, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 146.8, 140.6, 133.9, 129.1, 129.0, 128.0, 127.6, 113.5, 48.9, 28.5, 16.5 ppm

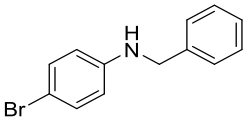
Synthesis of N-benzyl-4-fluoroaniline (4a):



Chemical Formula: $C_{13}H_{12}FN$
Molecular Weight: 201,2

4-Fluoroaniline (1.4 mmol, 135 µL), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (172 mg, 0.86 mmol, 86 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ =7.32 - 7.45 (m, 4 H), 7.27 - 7.32 (m, 1 H), 6.82 - 6.96 (m, 2 H), 6.52 - 6.62 (m, 2 H), 4.31 (s, 2 H), 4.08 (br. s., 1 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 157.2, 155.4, 145.3, 145.3, 140.1, 129.1, 128.0, 127.7, 116.1, 115.9, 114.1, 114.1, 49.2 ppm

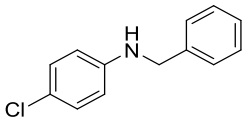
Synthesis of N-benzyl-4-bromoanilne (4c):



Chemical Formula: $C_{13}H_{12}BrN$
Molecular Weight: 262,2

4-Bromoanline (1.4 mmol, 241 mg), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (196 mg, 0.72 mmol, 72 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ =7.18 - 7.45 (m, 7 H), 6.49 - 6.58 (m, 2 H), 4.31 (br. s., 2 H), 4.24 (br. s., 1 H) ppm
^{13}C NMR (CD_2Cl_2, 75MHz): δ = 147.8, 139.7, 132.3, 129.2, 127.9, 127.8, 114.9, 109.2, 48.5 ppm

Synthesis of N-benzyl-4-chloroaniline (4b):

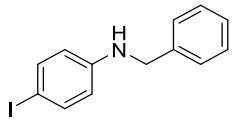


Chemical Formula: $C_{13}H_{12}ClN$
Molecular Weight: 217,7

4-Chloroaniline (1.4 mmol, 179 mg), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (151 mg, 0.69 mmol, 69 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ =7.34 - 7.44 (m, 4 H), 7.26 - 7.34 (m, 1 H), 7.07 - 7.17 (m, 2 H), 6.50 - 6.61 (m, 2 H), 4.32 (d, *J*=4.6 Hz, 2 H), 4.22 (br. s., 1 H) ppm

^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 147.4, 139.8, 129.5, 129.2, 129.2, 127.9, 127.8, 122.2, 114.5, 48.6 ppm

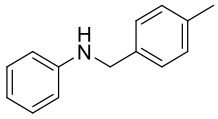
Synthesis of N-benzyl-4-iodoaniline (4d):



Chemical Formula: $C_{13}H_{12}IN$
Molecular Weight: 309,2

4-Iodoaniline (1.4 mmol, 306 mg), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (157 mg, 0.51 mmol, 51 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.39 - 7.43 (m, 2 H), 7.36 (d, *J*=4.3 Hz, 4 H), 7.29 (dq, *J*=8.5, 4.3 Hz, 1 H), 6.41 - 6.46 (m, 2 H), 4.31 (br. s., 2 H), 4.25 (br. s., 1 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 138.2, 129.1, 127.9, 115.6, 48.4 ppm

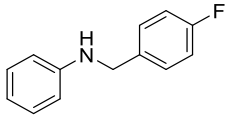
Synthesis of N-(4-methylbenzyl)aniline (3e):



Chemical Formula: $C_{14}H_{15}N$
Molecular Weight: 197,3

Aniline (1.4 mmol, 124 µL), 4-Methylbenzyl alcohol (1.0 mmol, 171 mg), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (185 mg, 0.94 mmol, 94 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.31 (d, *J*=7.9 Hz, 2 H), 7.15 - 7.26 (m, 4 H), 6.73 (t, *J*=7.3 Hz, 1 H), 6.66 (d, *J*=8.2 Hz, 2 H), 4.32 (s, 2 H), 4.13 (br. s., 1 H), 2.39 (s, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 148.9, 137.4, 137.2, 129.8, 129.7, 128.0, 117.8, 113.3, 48.4, 21.4 ppm

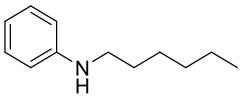
Synthesis of N-(4-fluorobenzyl)aniline (3b):



Chemical Formula: $C_{13}H_{12}FN$
Molecular Weight: 201,2

Aniline (1.4 mmol, 124 µL), 4-Fluorobenzyl alcohol (1.0 mmol, 153 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (168 mg, 0.84 mmol, 84 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.37 (dd, *J*=8.2, 5.5 Hz, 2 H), 7.17 (t, *J*=7.8 Hz, 2 H), 7.00 - 7.11 (m, 2 H), 6.71 (t, *J*=7.3 Hz, 1 H), 6.63 (d, *J*=8.5 Hz, 2 H), 4.32 (s, 2 H), 4.15 (br. s., 1 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 163.5, 161.6, 148.7, 136.1, 129.7, 129.6, 129.5, 118.0, 115.9, 115.7, 113.4, 47.9 ppm

Synthesis of N-(1-hexyl)aniline (3j):

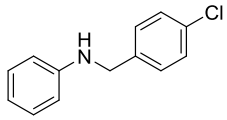


Chemical Formula: $C_{12}H_{19}N$
Molecular Weight: 177,3

Aniline (1.4 mmol, 124 µL), 1-Hexyl alcohol (1.0 mmol, 175 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/

Et_2O 20:1) as a colorless oil (145 mg, 0.82 mmol, 82 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.10 - 7.28 (m, 2 H), 6.56 - 6.73 (m, 3 H), 3.67 (br. s., 1 H), 3.12 (t, *J*=7.0 Hz, 2 H), 1.52 - 1.74 (m, 2 H), 1.25 - 1.52 (m, 6 H), 0.87 - 1.03 (m, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 149.4, 129.7, 117.3, 113.1, 44.5, 32.3, 30.1, 27.5, 23.3, 14.4 ppm

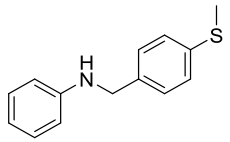
Synthesis of N-(4-chlorobenzyl)anline (3c):



Chemical Formula: $C_{13}H_{12}ClN$
Molecular Weight: 217,7

Aniline (1.4 mmol, 124 µL), 4-Chlorobenzyl alcohol (1.0 mmol, 148 mg), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (156 mg, 0.72 mmol, 72 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.33 (s, 4 H), 7.11 - 7.23 (m, 2 H), 6.70 (t, *J*=7.3 Hz, 1 H), 6.61 (d, *J*=7.6 Hz, 2 H), 4.32 (s, 2 H), 4.18 (br. s., 1 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 148.5, 139.0, 129.7, 129.3, 129.1, 118.1, 113.4, 47.9 ppm

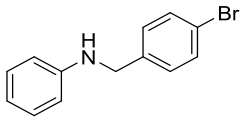
Synthesis of N-(4-methylthiobenzyl)aniline (3g):



Chemical Formula: $C_{14}H_{15}NS$
Molecular Weight: 229,3

Aniline (1.4 mmol, 124 µL), 4-Methylthiobenzyl alcohol (1.0 mmol, 154 mg), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (163 mg, 0.71 mmol, 71 %).
^{1}H NMR (CD_2Cl_2, 500 MHz): δ = 7.28 - 7.38 (m, 2 H), 7.19 - 7.28 (m, 2 H), 7.11 - 7.19 (m, 2 H), 6.69 (td, *J*=7.3, 1.2 Hz, 1 H), 6.57 - 6.65 (m, 2 H), 4.30 (s, 2 H), 4.15 (br. s., 1 H), 2.48 (s, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 126 MHz): δ = 148.7, 137.8, 137.2, 129.7, 128.5, 127.2, 117.9, 113.3, 48.1, 16.2 ppm

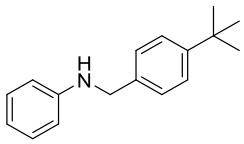
Synthesis of N-(4-bromobenzyl)aniline (3d):



Chemical Formula: $C_{13}H_{12}BrN$
Molecular Weight: 262,2

Aniline (1.4 mmol, 124 µL), 4-Bromobenzyl alcohol (1.0 mmol, 187 mg), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (140 mg, 0.53 mmol, 53 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.48 (d, *J*=8.3 Hz, 2 H), 7.27 (d, *J*=8.3 Hz, 2 H), 7.15 (t, *J*=7.9 Hz, 2 H), 6.56 - 6.75 (m, 3 H), 4.31 (s, 2 H), 4.19 (br. s., 1 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 148.5, 139.5, 132.1, 129.7, 129.6, 121.2, 118.1, 113.4, 48.0 ppm

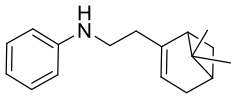
Synthesis of N-(4-*tert*-butyl benzyl)aniline (3h):



Chemical Formula: $C_{17}H_{21}N$
Molecular Weight: 239,4

Aniline (1.4 mmol, 124 µL), 4-*tert*-butyl benzyl alcohol (1.0 mmol, 177 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (222 mg, 0.93 mmol, 93 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = = 7.23 - 7.48 (m, 4 H), 7.11 - 7.23 (m, 2 H), 6.56 - 6.78 (m, 3 H), 4.30 (d, *J*=4.8 Hz, 2 H), 4.12 (br. s., 1 H), 1.33 (s, 9 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 150.7, 149.0, 137.2, 129.7, 127.8, 126.0, 117.8, 113.3, 48.3, 35.0, 31.7 ppm

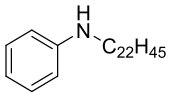
Synthesis of N-(2-(6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl)aniline (3l):



Chemical Formula: $C_{17}H_{23}N$
Molecular Weight: 241,4

Aniline (1.4 mmol, 124 µL), (-)-Nopol (1.0 mmol, 171 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (231 mg, 0.96 mmol, 96 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.08 - 7.21 (m, 2 H), 6.51 - 6.71 (m, 3 H), 5.07 - 5.22 (m, 1 H), 3.41 - 3.80 (m, 3 H), 2.08 - 2.48 (m, 4 H), 1.78 - 2.07 (m, 3 H), 1.37 (d, *J*=9.2 Hz, 1 H), 1.21 - 1.31 (m, 3 H), 0.70 - 0.81 (m, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 149.2, 146.4, 129.6, 119.2, 118.8, 117.5, 113.3, 52.9, 45.9, 41.8, 41.5, 41.4, 41.3, 41.1, 28.1, 26.6, 26.5, 26.3, 25.4, 24.3, 24.2, 22.3, 22.1, 20.3 ppm

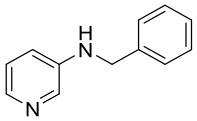
Synthesis of N-(1-docosanoyl)aniline (3k):



Chemical Formula: $C_{28}H_{51}N$
Molecular Weight: 401,7

Aniline (1.4 mmol, 124 µL), $C_{22}H_{45}OH$ (1.0 mmol, 326 mg), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (343 mg, 0.86 mmol, 86 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.15 (dd, *J*=8.6, 7.2 Hz, 2 H), 6.54 - 6.76 (m, 3 H), 3.66 (br. s., 1 H), 3.10 (t, *J*=7.0 Hz, 2 H), 1.52 - 1.70 (m, 2 H), 1.30 (s, 38 H), 0.84 - 1.00 (m, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 149.4, 129.7, 117.4, 113.1, 44.6, 32.6, 30.4, 30.3, 30.2, 30.1, 30.0, 27.8, 23.4, 14.5 ppm

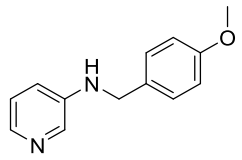
Synthesis of N-(benzyl)pyridine-3-amine (5a):



Chemical Formula: $C_{12}H_{12}N_2$
Molecular Weight: 184,2

3-Aminopyridine (1.4 mmol, 132 mg), Benzyl alcohol (1.0 mmol, 104 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (Et_2O) as a colorless solid (165 mg, 0.89 mmol, 89 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 8.05 (d, *J*=3.1 Hz, 1 H), 7.91 (dd, *J*=4.4, 1.3 Hz, 1 H), 7.25 - 7.44 (m, 5 H), 7.06 (dd, *J*=8.3, 4.4 Hz, 1 H), 6.89 (ddd, *J*=8.2, 2.7, 1.3 Hz, 1 H), 4.22 - 4.59 (m, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 144.7, 139.5, 139.1, 136.6, 129.2, 127.9, 127.9, 124.1, 118.9, 48.2 ppm

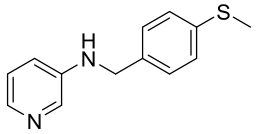
Synthesis of N-(4-methoxybenzyl)pyridine-3-amine (5b):



Chemical Formula: $C_{13}H_{14}N_2O$
Molecular Weight: 214,3

3-Aminopyridine (1.4 mmol, 132 mg), 4-Methoxybenzyl alcohol (1.0 mmol, 124 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (Et_2O) as a colorless solid (131 mg, 0.76 mmol, 61 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.96 - 8.09 (m, 1 H), 7.90 (d, *J*=4.4 Hz, 1 H), 7.20 - 7.36 (m, 2 H), 7.05 (dd, *J*=8.3, 4.8 Hz, 1 H), 6.80 - 6.95 (m, 3 H), 4.27 (s, 2 H), 3.78 (s, 3 H), 2.10 (br. s., 1 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 159.6, 144.8, 139.1, 136.6, 131.3, 129.2, 124.1, 118.9, 114.5, 55.8, 47.7 ppm

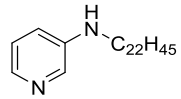
Synthesis of N-(4-methylthiobenzyl)pyridine-3-amine (5c):



Chemical Formula: $C_{13}H_{14}N_2S$
Molecular Weight: 230,3

3-Aminopyridine (1.4 mmol, 132 mg), 4-Methylthiobenzyl alcohol (1.0 mmol, 154 mg), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (Et_2O) as a colorless solid (176 mg, 0.76 mmol, 76 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.97 - 8.08 (m, 1 H), 7.90 (d, *J*=4.4 Hz, 1 H), 7.15 - 7.36 (m, 4 H), 7.05 (dd, *J*=8.2, 4.6 Hz, 1 H), 6.83 - 6.94 (m, 1 H), 4.31 (s, 3 H), 2.47 (s, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 139.3, 138.1, 136.7, 136.2, 128.5, 127.3, 124.1, 118.9, 47.8, 16.2 ppm

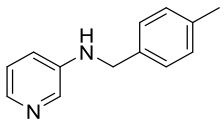
Synthesis of N-(1-docosanoyl)pyridine-3-amine (5d):



Chemical Formula: $C_{27}H_{50}N_2$
Molecular Weight: 402,7

3-Aminopyridine (1.4 mmol, 132 mg), $C_{22}H_{45}OH$ (1.0 mmol, 327 mg), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (Et_2O) as a colorless solid (287 mg, 0.69 mmol, 69 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.98 (d, *J*=2.6 Hz, 1 H), 7.87 (d, *J*=4.8 Hz, 1 H), 7.06 (dd, *J*=8.3, 4.4 Hz, 1 H), 6.86 (dt, *J*=8.3, 1.3 Hz, 1 H), 3.10 (t, *J*=7.0 Hz, 2 H), 1.82 (br. s., 1 H), 1.54 - 1.71 (m, 2 H), 1.27 (s, 38 H), 0.77 - 0.97 (m, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 138.6, 136.4, 124.1, 118.6, 44.1, 32.5, 30.3, 30.2, 30.0, 29.9, 27.6, 23.3, 14.5 ppm

Synthesis of N-(4-methylbenzyl)pyridine-3-amine (5f):

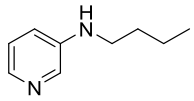


Chemical Formula: $C_{13}H_{14}N_2$
Molecular Weight: 198,3

3-Aminopyridine (1.4 mmol, 132 mg), 4-Methylbenzyl alcohol (1.0 mmol, 171 mg), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless solid (186 mg, 0.94 mmol, 94 %).

^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 8.03 (d, *J*=2.2 Hz, 1 H), 7.90 (dd, *J*=4.4, 1.3 Hz, 1 H), 7.23 - 7.35 (m, 2 H), 7.09 - 7.23 (m, 2 H), 7.00 - 7.09 (m, 1 H), 6.80 - 6.92 (m, 1 H), 4.30 (s, 3 H), 2.34 (s, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 144.7, 139.1, 137.7, 136.7, 136.3, 129.8, 127.9, 124.1, 118.9, 47.9, 21.3 ppm

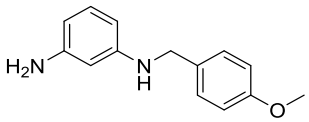
Synthesis of N-(1-butyl)pyridine-3-amine (5e):



Chemical Formula: $C_9H_{14}N_2$
Molecular Weight: 150,2

3-Aminopyridine (1.4 mmol, 132 mg), 1-Butyl alcohol (1.0 mmol, 92 µL), KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 20:1) as a colorless oil (114 mg, 0.76 mmol, 76 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.98 (d, *J*=2.6 Hz, 1 H), 7.81 - 7.93 (m, 1 H), 7.06 (dd, *J*=8.3, 4.4 Hz, 1 H), 6.75 - 6.96 (m, 1 H), 3.79 (br. s., 1 H), 3.03 - 3.21 (m, 2 H), 1.52 - 1.73 (m, 2 H), 1.33 - 1.52 (m, 2 H), 0.96 (t, *J*=7.5 Hz, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 145.2, 138.7, 136.4, 124.1, 118.5, 43.8, 32.0, 20.8, 14.2 ppm

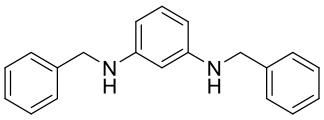
Synthesis of N'-(4-methoxybenzyl)benzene-1,3-diamine (6a):



Chemical Formula: $C_{14}H_{16}N_2O$
Molecular Weight: 228,3

1,3-Diaminobenzen (324 mg, 3.0 mmol), 4-Methoxybenzyl alcohol (127 µL, 1.0 mmol); KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/Et_2O 1:1) as a colorless oil (208 mg, 0.91 mmol, 91 %)
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.29 (d, *J*=8.3 Hz, 2 H), 6.84 - 7.01 (m, 3 H), 5.99 - 6.14 (m, 2 H), 5.91 - 5.98 (m, 1 H), 4.22 (s, 2 H), 3.80 (s, 4 H), 3.64 (br. s., 2 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 159.4, 150.0, 148.4, 132.3, 130.4, 129.2, 114.4, 105.1, 104.2, 99.7, 55.7, 48.0 ppm

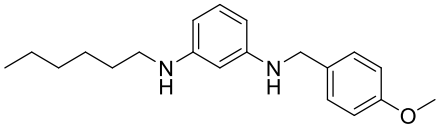
Synthesis of N,N'-(dibenzyl)benzene-1,3-diamine (7a):



Chemical Formula: $C_{20}H_{20}N_2$
Molecular Weight: 288,4

1,3-Diaminobenzole (108 mg, 1.0 mmol), Benzyl alcohol (228 µL, 2.2 mmol); KO^{t}Bu (2.4 mmol, 270 mg), 4.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/Et_2O 5:1) as a light yellow solid (211 mg, 0.73 mmol, 73 %)
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.15 - 7.43 (m, 10 H), 6.93 (t, *J*=7.9 Hz, 1 H), 6.02 (dd, *J*=8.1, 2.0 Hz, 2 H), 5.88 - 5.98 (m, 1 H), 4.28 (d, *J*=3.5 Hz, 4 H), 4.05 (br. s., 2 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 150.0, 140.6, 130.4, 129.0, 127.9, 127.5, 103.4, 97.7, 48.6 ppm

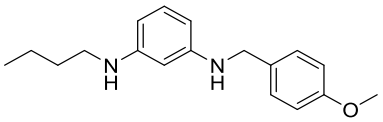
Synthesis of N-(1-hexyl)-N'-(4-methoxybenzyl)benzene-1,3-diamine (7e):



Chemical Formula: $C_{20}H_{28}N_2O$
Molecular Weight: 312,5

N'-(4-Methoxybenzyl)benzene-1,3-diamine (228 mg, 1.0 mmol), 1-Hexyl alcohol (1.0 mmol, 175 µL) KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product wass isolated via column chromatography (pentane/Et_2O 5:1) as a light yellow oil (248 mg, 0.79 mmol, 79 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.30 (d, *J*=8.3 Hz, 2 H), 6.83 - 7.02 (m, 3 H), 5.99 (d, *J*=7.9 Hz, 2 H), 5.88 (s, 1 H), 4.23 (s, 2 H), 3.80 (s, 5 H), 3.05 (t, *J*=7.0 Hz, 2 H), 1.48 - 1.74 (m, 2 H), 1.26 - 1.48 (m, 6 H), 0.85 - 1.04 (m, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 159.4, 150.4, 150.0, 132.5, 130.3, 129.2, 114.4, 103.2, 103.0, 97.5, 55.8, 48.1, 44.5, 32.3, 30.2, 27.4, 23.2, 14.4 ppm

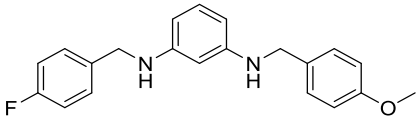
Synthesis of N-(1-butyl)-N'-(4-methoxybenzyl)benzene-1,3-diamine (7d):



Chemical Formula: $C_{18}H_{24}N_2O$
Molecular Weight: 284,4

N'-(4-Methoxybenzyl)benzene-1,3-diamine (228 mg, 1.0 mmol), 1-Butyl alcohol (1.0 mmol, 92 µL) KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/Et_2O 5:1) as a light yellow oil (216 mg, 0.76 mmol, 76 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.30 (d, *J*=8.8 Hz, 2 H), 6.80 - 6.99 (m, 3 H), 5.98 (dt, *J*=8.0, 2.1 Hz, 2 H), 5.85 - 5.92 (m, 1 H), 4.23 (s, 2 H), 3.91 (br. s., 1 H), 3.79 (s, 3 H), 3.55 (br. s., 1 H), 3.05 (t, *J*=7.0 Hz, 2 H), 1.30 - 1.68 (m, 4 H), 0.89 - 1.05 (m, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 159.4, 150.4, 150.0, 132.5, 130.3, 129.2, 114.4, 103.2, 103.0, 97.5, 55.8, 48.2, 44.2, 32.3, 20.9, 14.3 ppm

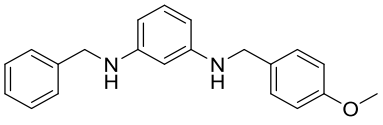
Synthesis of N-(4-fluorobenzyl)-N'-(4-methoxybenzyl)benzene-1,3-diamine (7c):



Chemical Formula: $C_{21}H_{21}FN_2O$
Molecular Weight: 336,4

N'-(4-Methoxybenzyl)benzene-1,3-diamine (228 mg, 1.0 mmol), 4-Fluorobenzyl alcohol (1.0 mmol, 153 µL) KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/Et_2O 5:1) as a light yellow oil (191 mg, 0.57 mmol, 57 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ = 7.20 - 7.46 (m, 4 H), 6.98 - 7.10 (m, 2 H), 6.83 - 6.98 (m, 3 H), 5.97 - 6.09 (m, 2 H), 5.89 (t, *J*=2.2 Hz, 1 H), 4.25 (s, 2 H), 4.20 (s, 2 H), 4.01 (br. s., 2 H), 3.80 (s, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 164.1, 160.9, 159.4, 150.0, 149.8, 136.4, 136.4, 132.4, 130.4, 129.5, 129.4, 129.2, 115.9, 115.6, 114.4, 103.6, 103.4, 97.7, 55.8, 48.1, 47.9 ppm

Synthesis of N-(benzyl)-N'-(4-methoxybenzyl)benzene-1,3-diamine (7b):

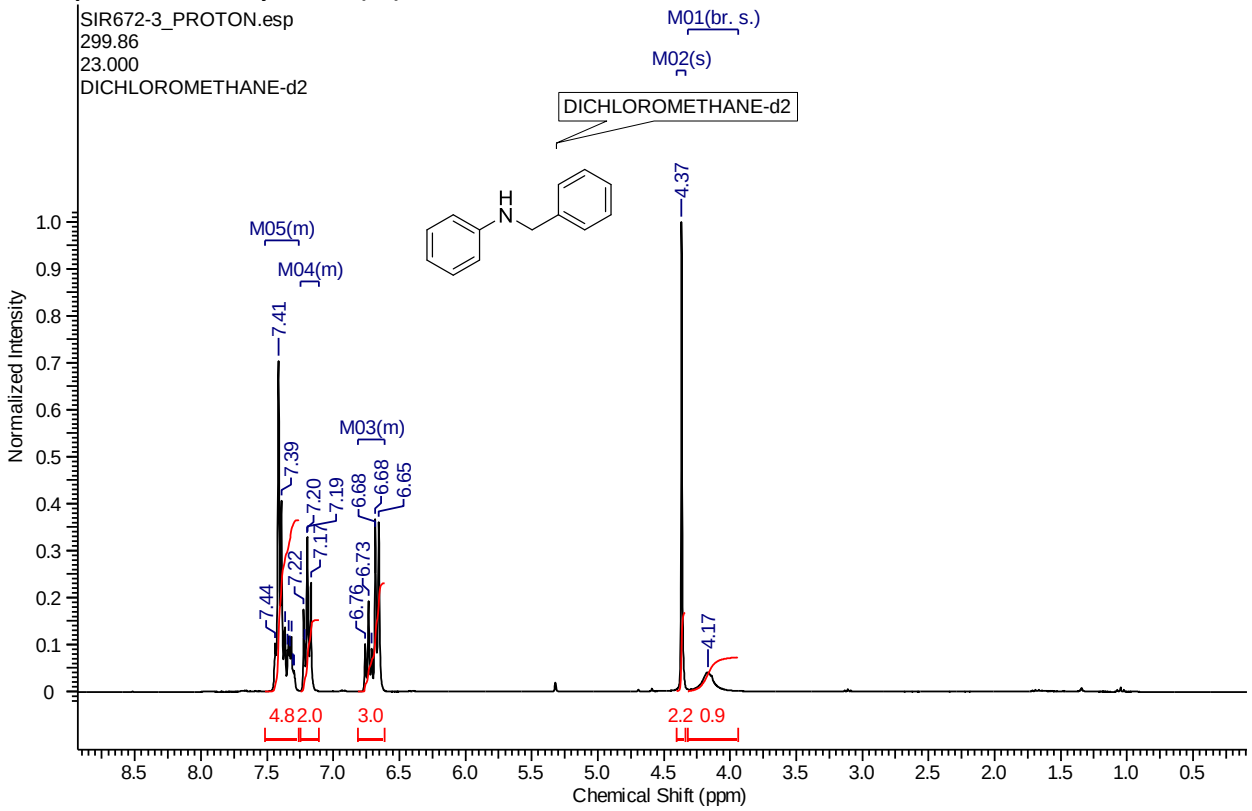


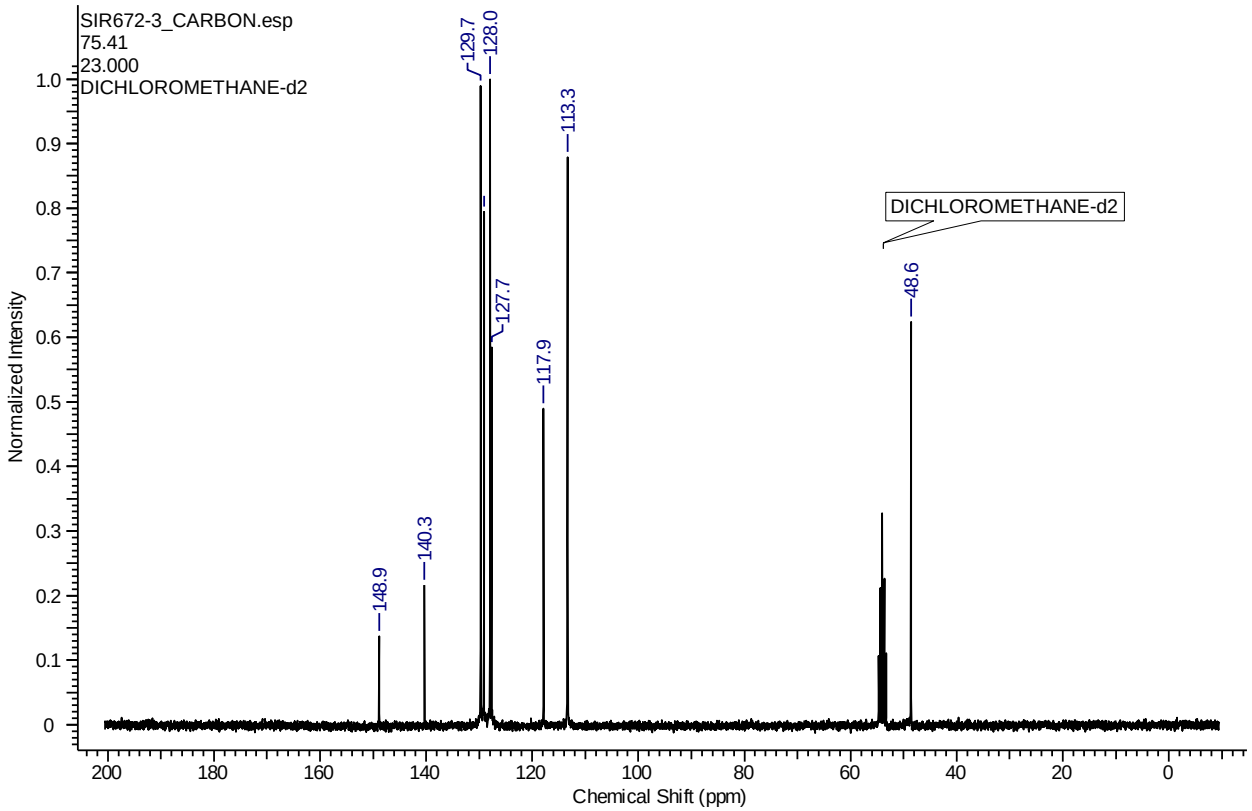
Chemical Formula: $C_{21}H_{22}N_2O$
Molecular Weight: 318,4

N'-(4-Methoxybenzyl)benzene-1,3-diamine (228 mg, 1.0 mmol), Benzyl alcohol (1.0 mmol, 104 µL) KO^{t}Bu (1.2 mmol, 135 mg), 2.0 mol% pre-catalyst **1d**, 3 mL toluene, 80 °C, 24 h. Reaction was quenched by addition of 1 mL of water. The organic layer was diluted with diethyl ether and dried over Na_2SO_4. The product was isolated via column chromatography (pentane/ Et_2O 5:1) as a light yellow oil (227 mg, 0.71 mmol, 71 %).
^{1}H NMR (CD_2Cl_2, 300 MHz): δ =7.18 - 7.47 (m, 7 H), 6.81 - 7.02 (m, 3 H), 6.03 (dd, *J*=7.9, 2.2 Hz, 2 H), 5.92 (t, *J*=1.8 Hz, 1 H), 4.29 (s, 2 H), 4.20 (s, 2 H), 4.01 (br. s., 2 H), 3.80 (s, 3 H) ppm
^{13}C NMR (CD_2Cl_2, 75 MHz): δ = 159.4, 150.0, 150.0, 140.6, 132.4, 130.3, 129.2, 129.0, 129.0, 127.9, 127.5, 114.4, 103.5, 103.4, 97.8, 55.8, 48.6, 48.1 ppm

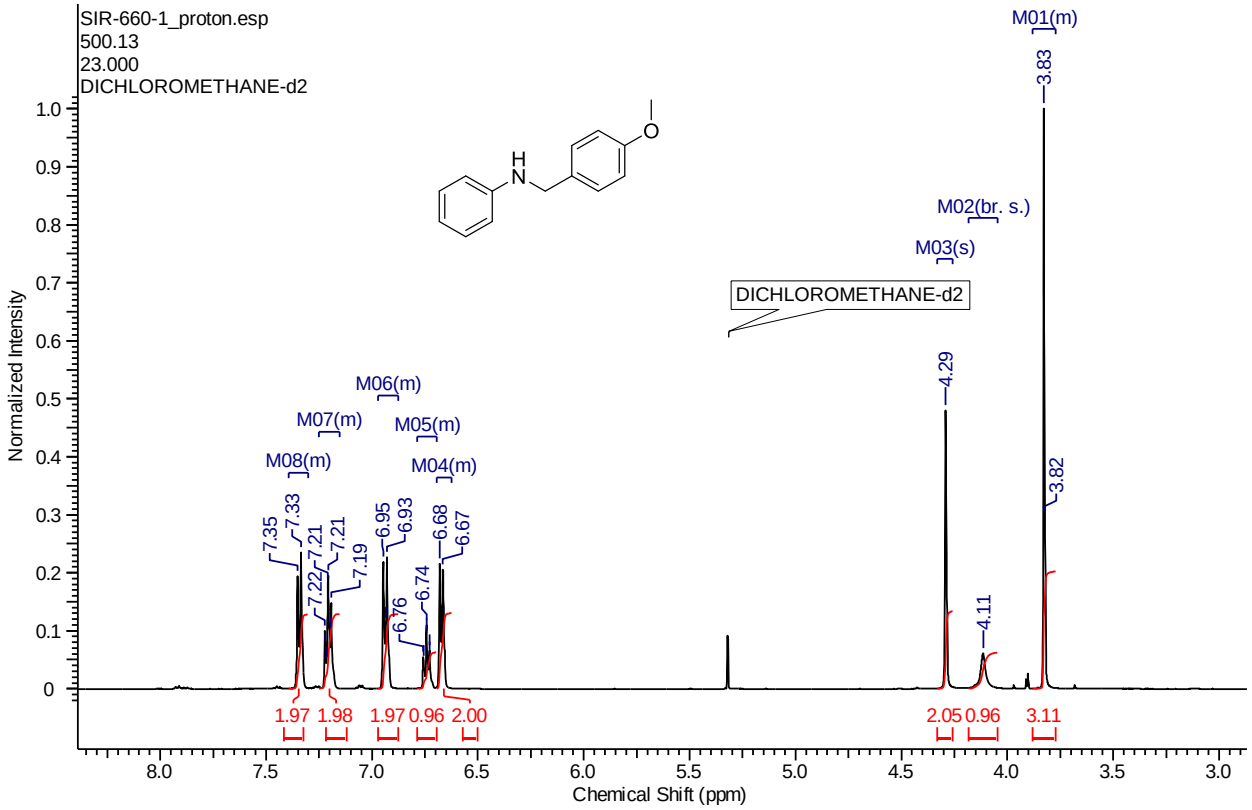
NMR spectra of products

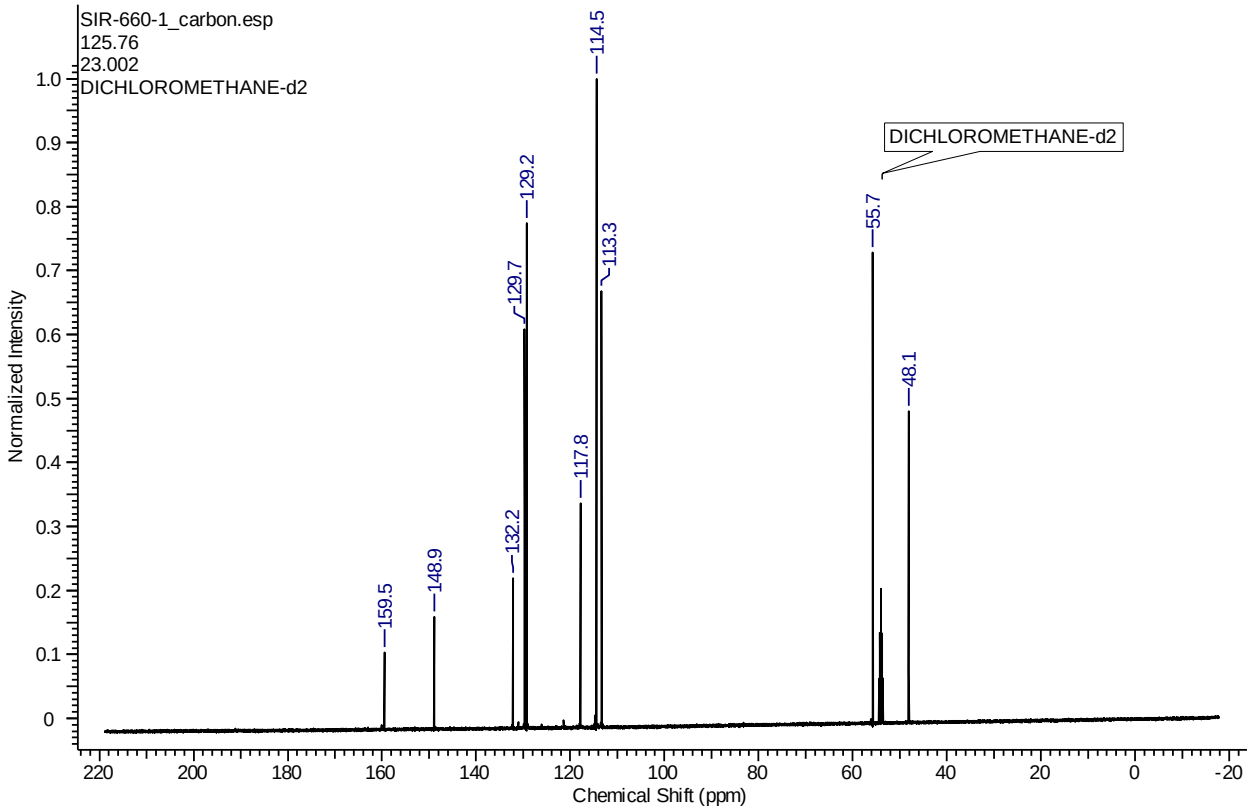
NMR spectra of N-benzylaniline (3a):



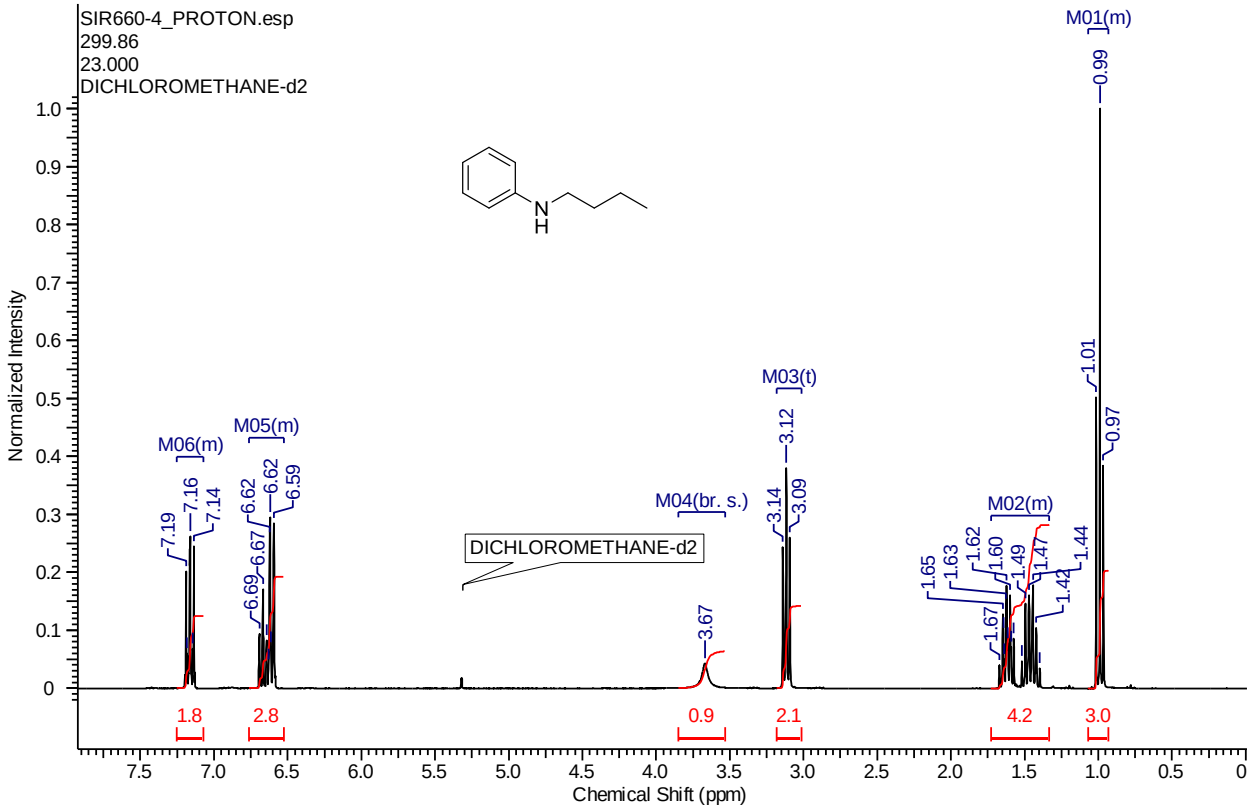


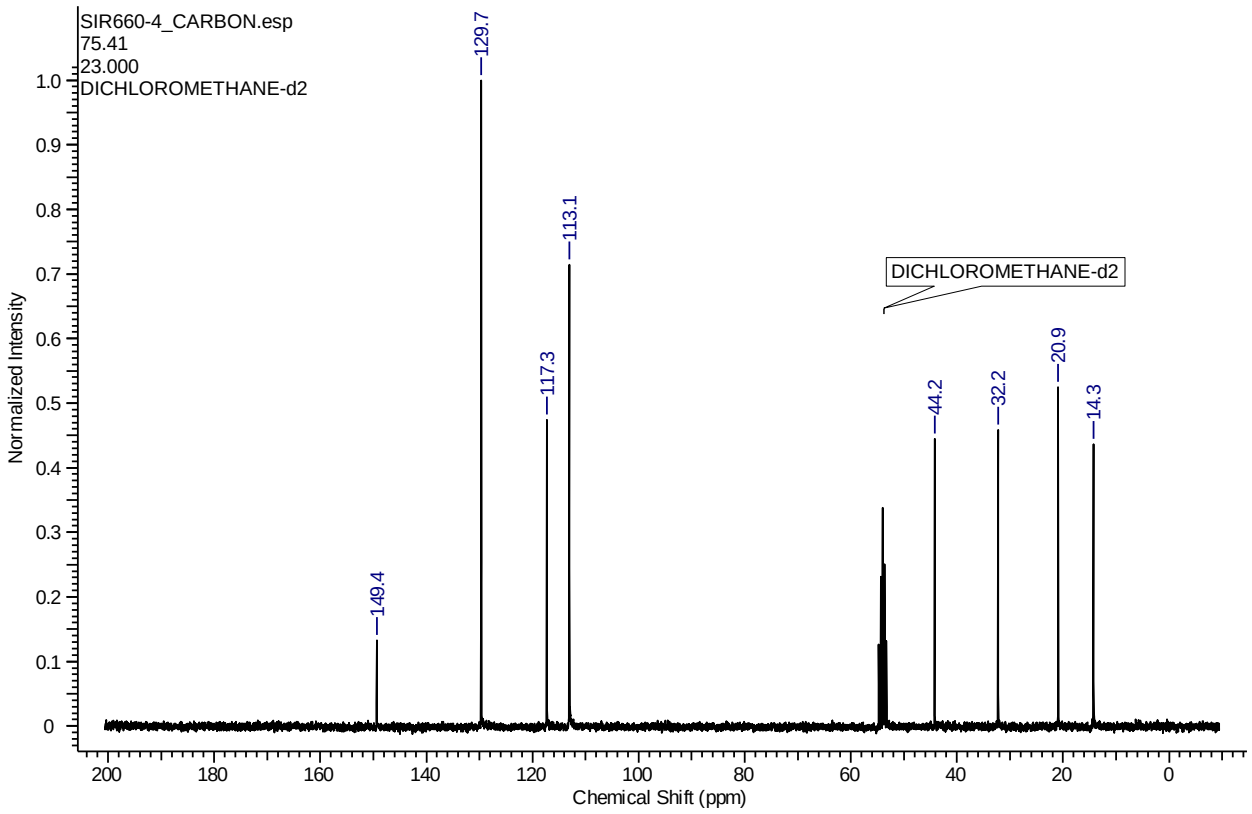
NMR spectra of N-((4-methoxy)benzyl)aniline (3f):



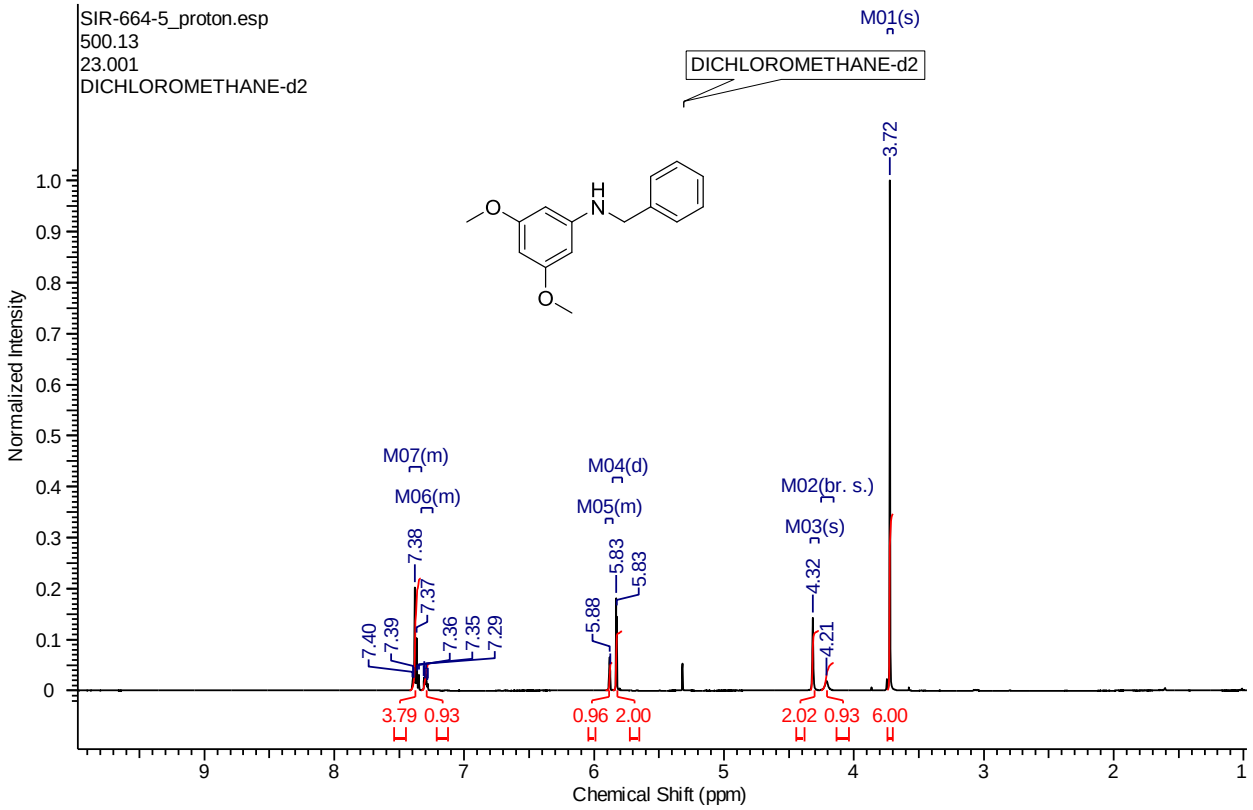


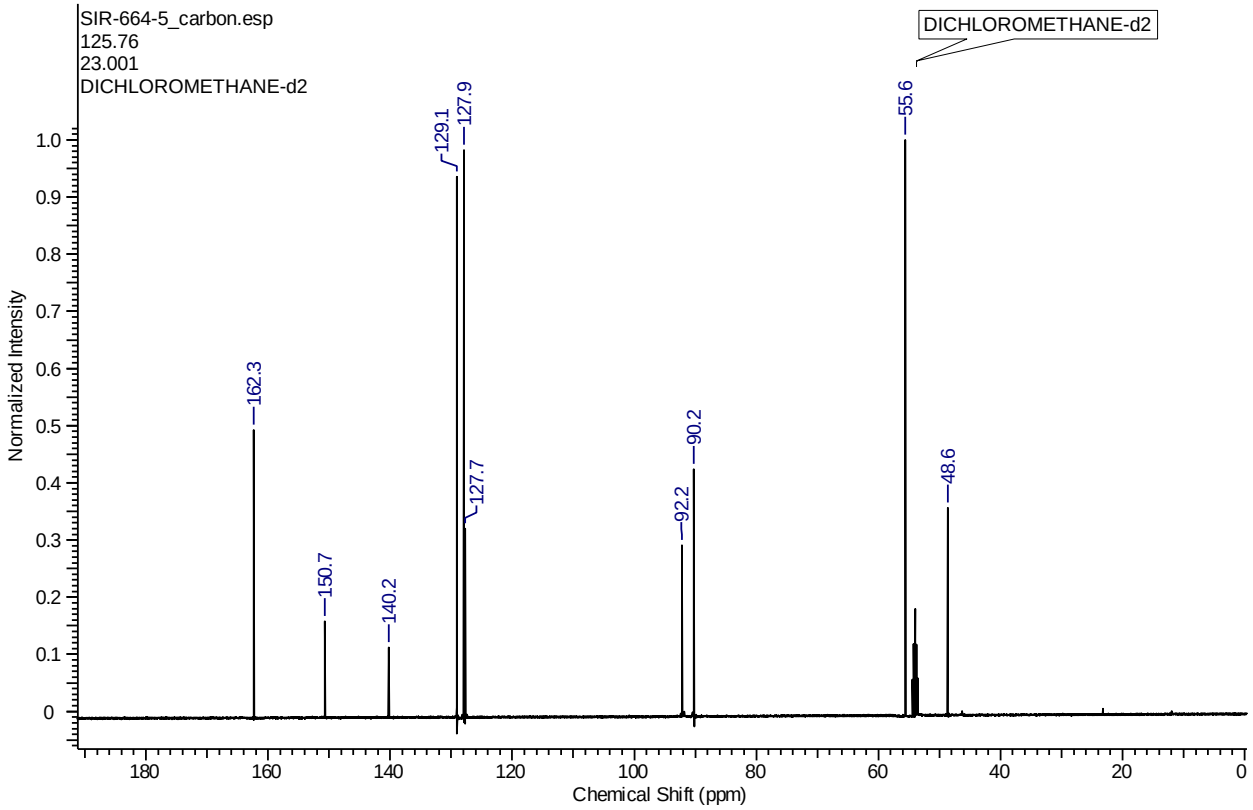
NMR spectra of N-(1-butyl)aniline (3i):



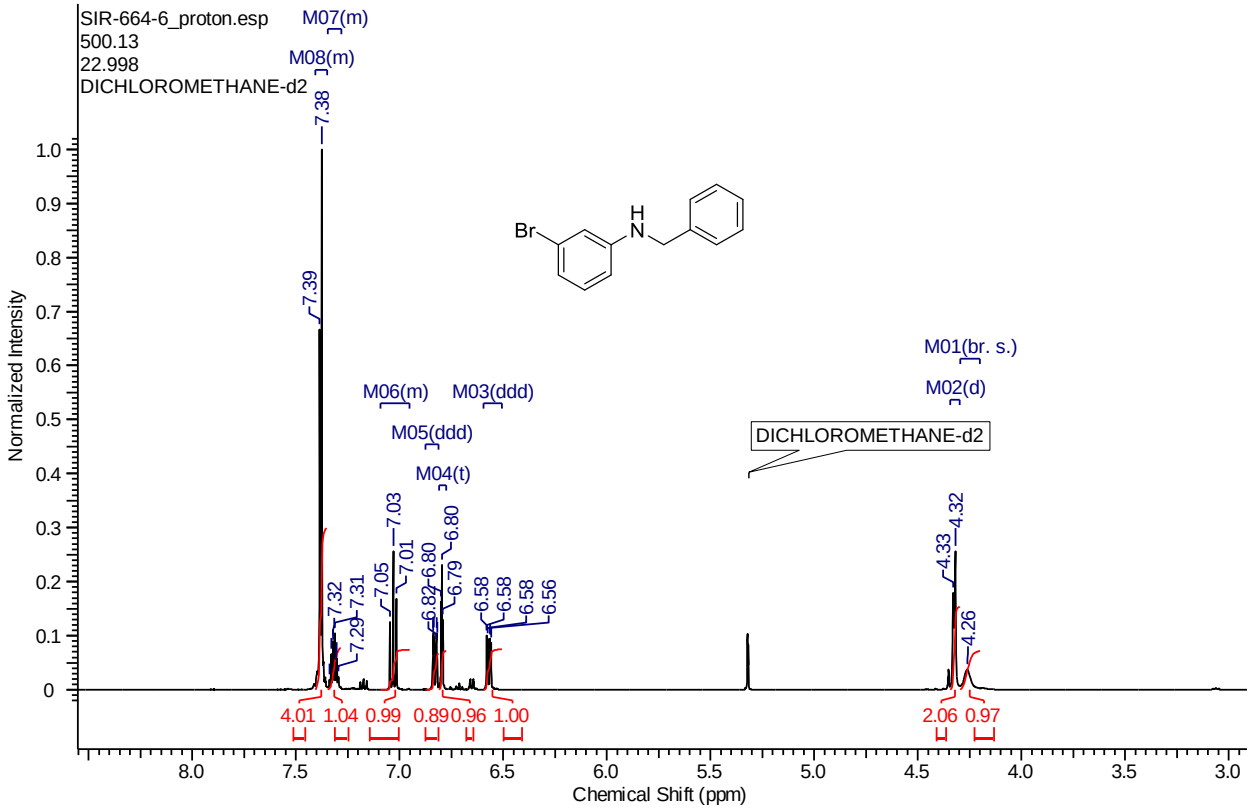


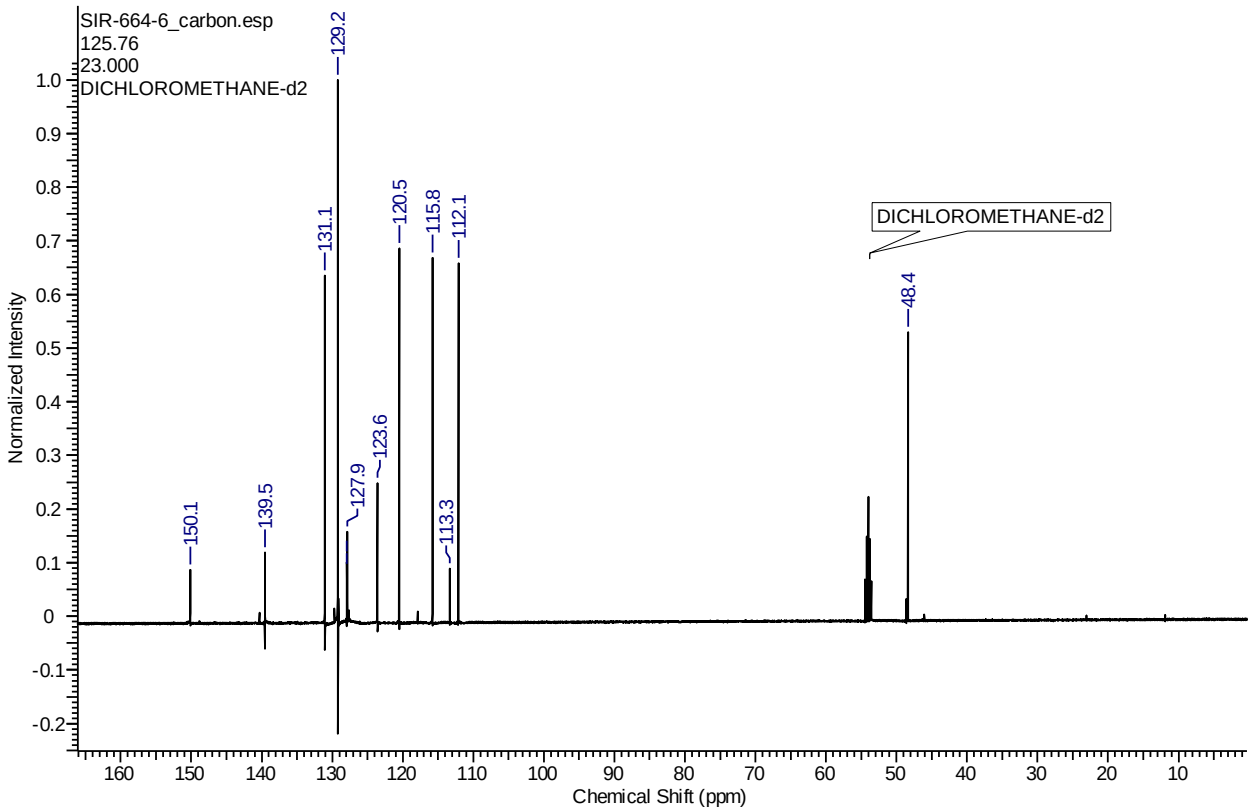
NMR spectra of N-benzyl-3,5-dimethoxyaniline (4h):



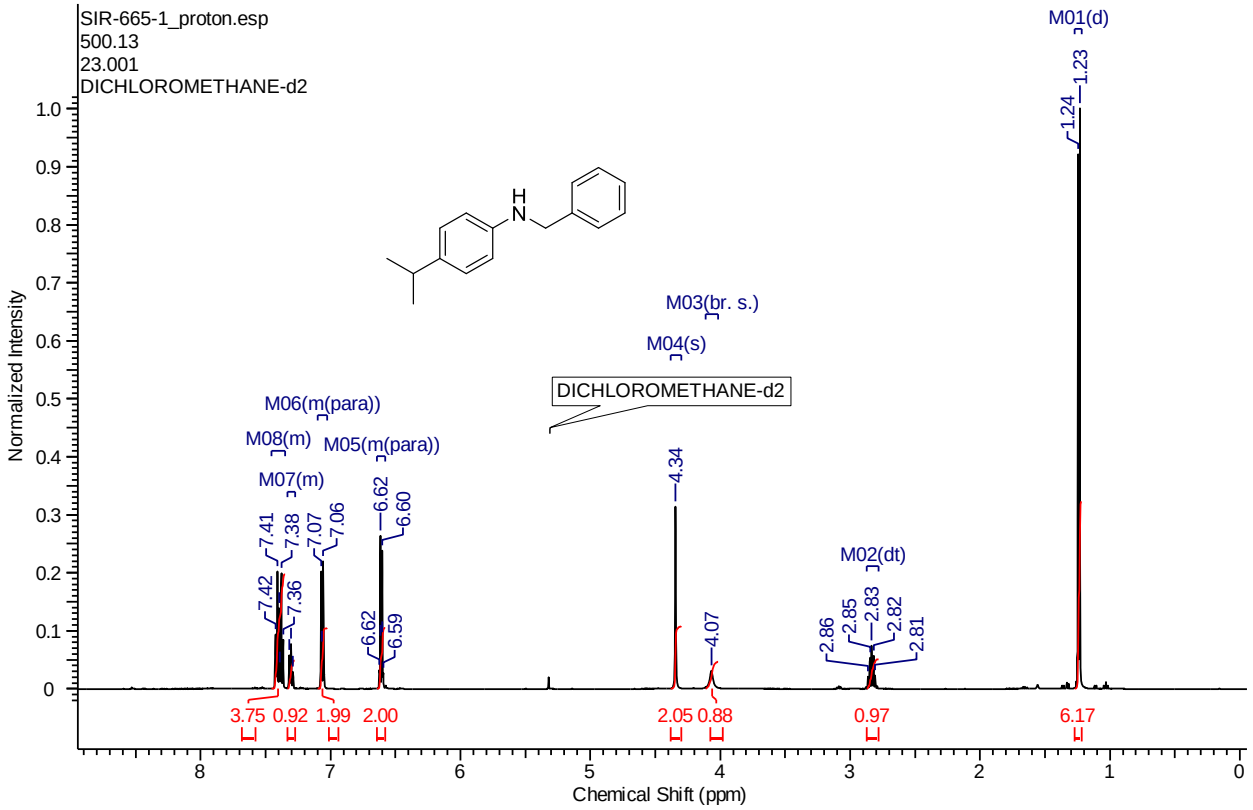


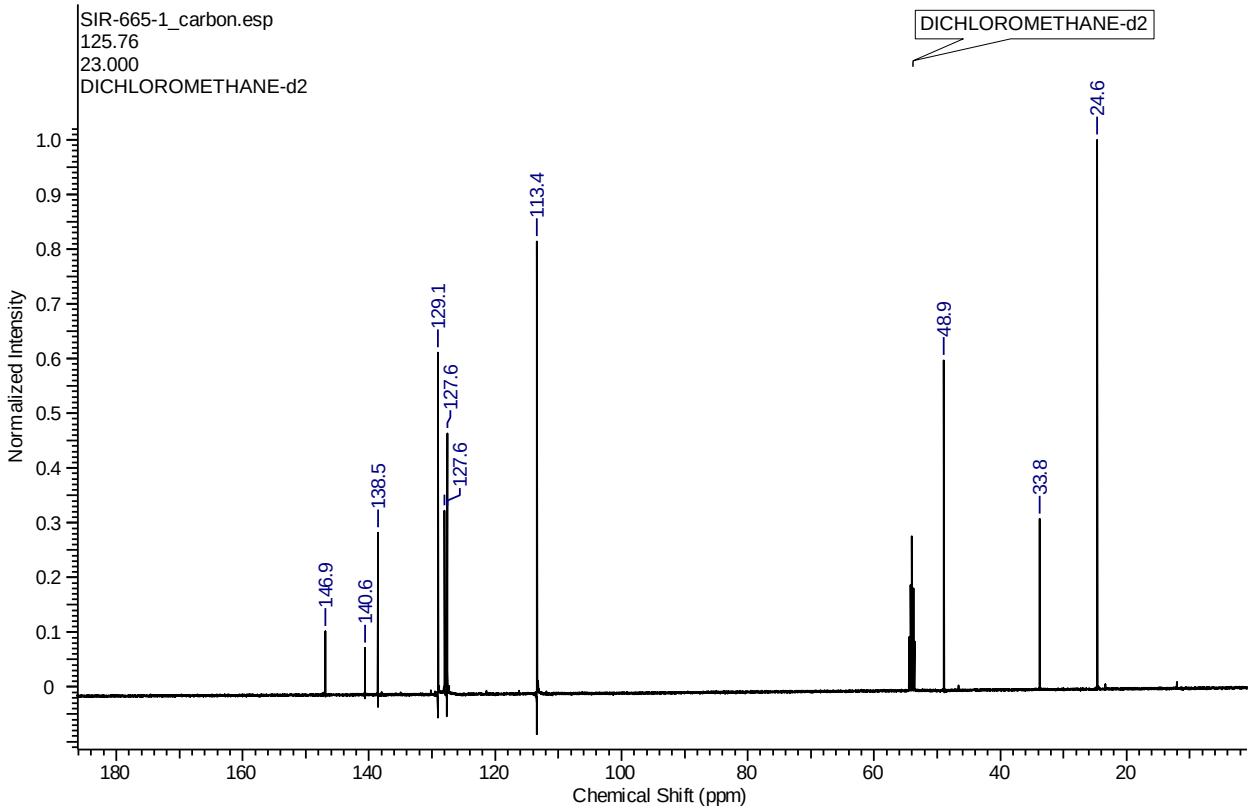
NMR spectra of N-benzyl-3-bromoaniline (4g):



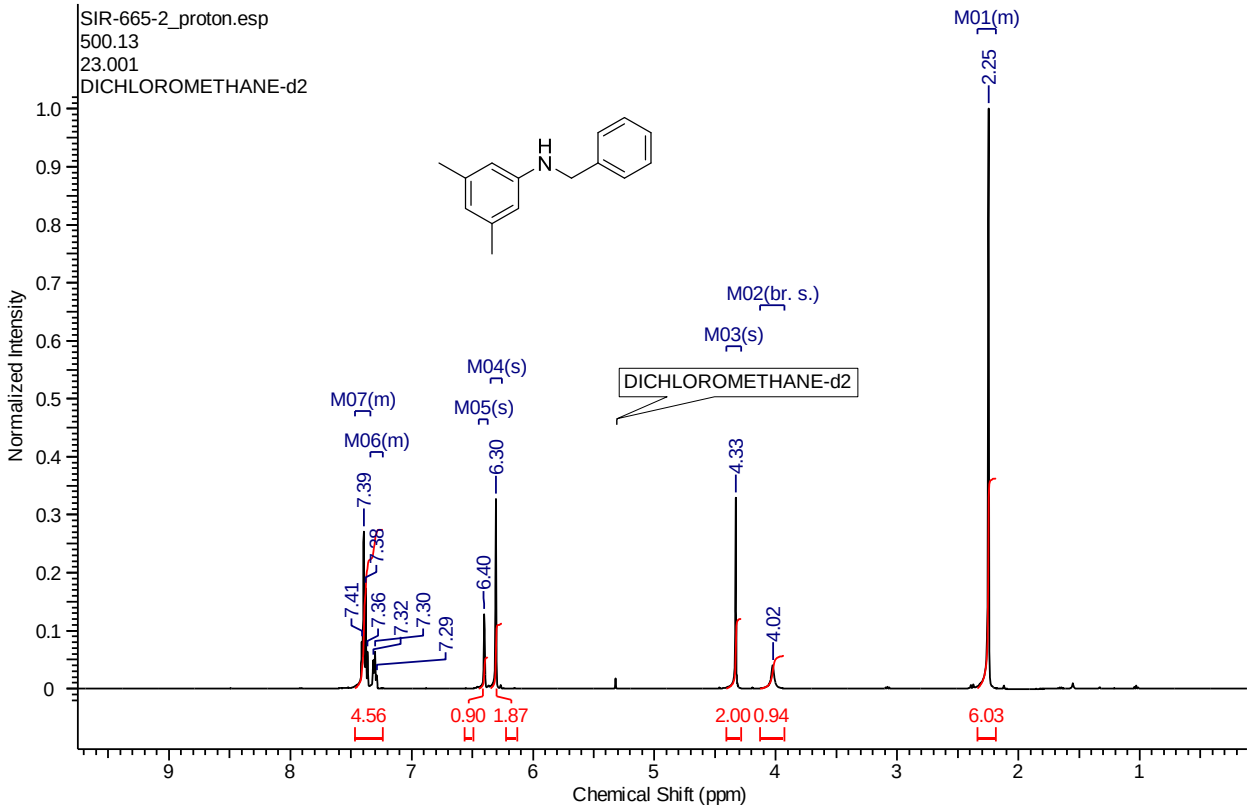


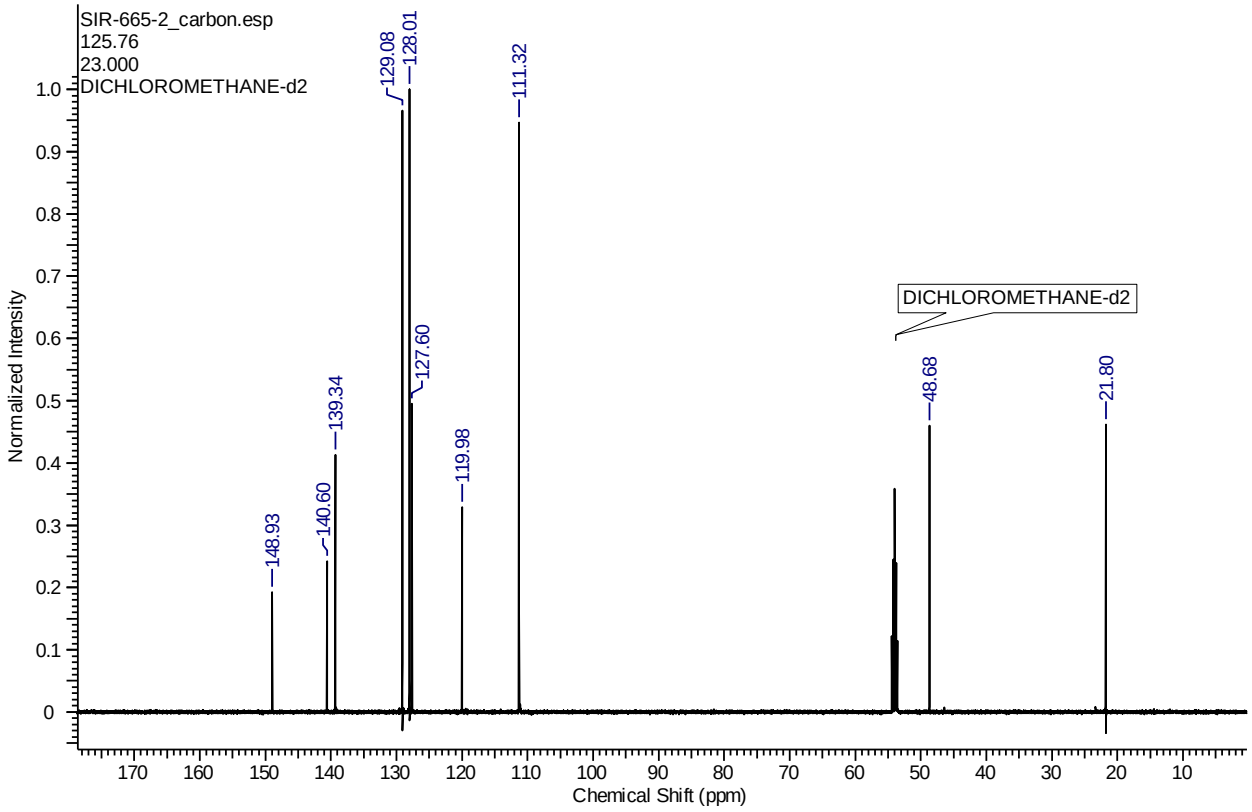
NMR spectra of N-benzyl-4-isopropylaniline (4f):



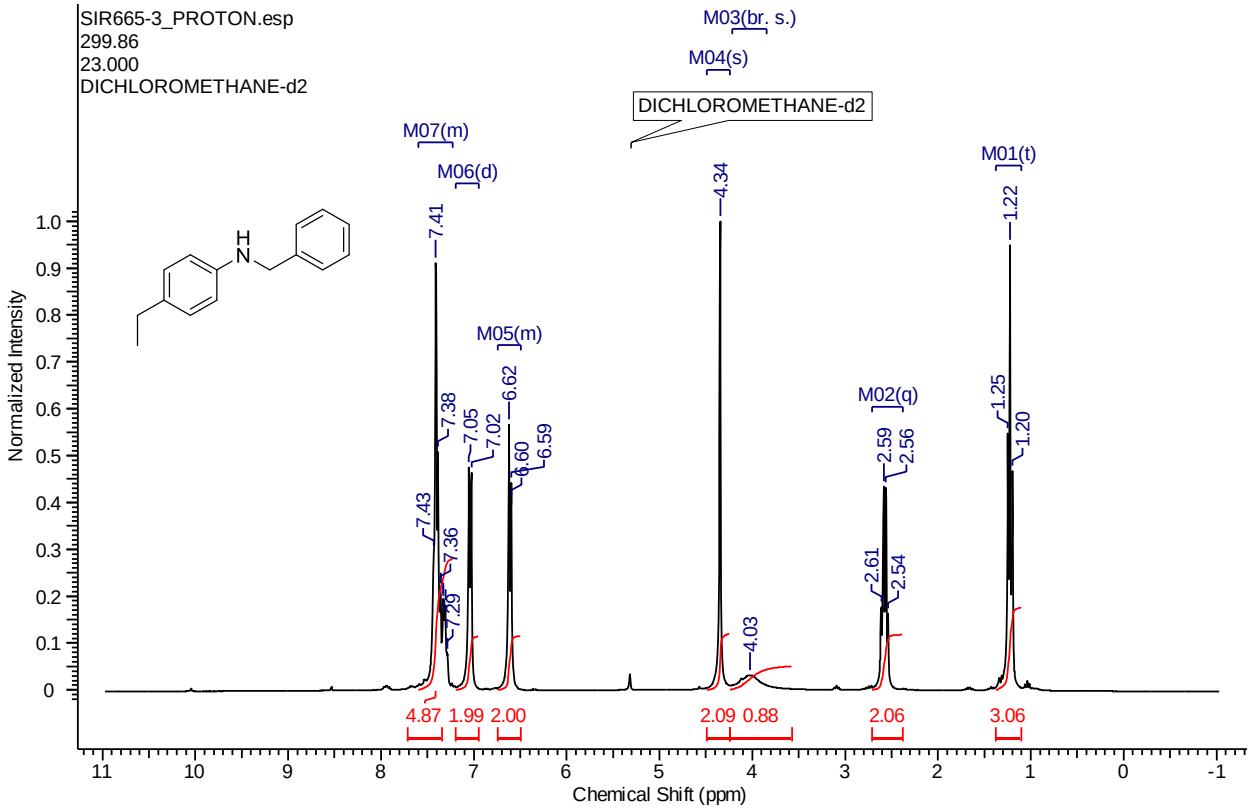


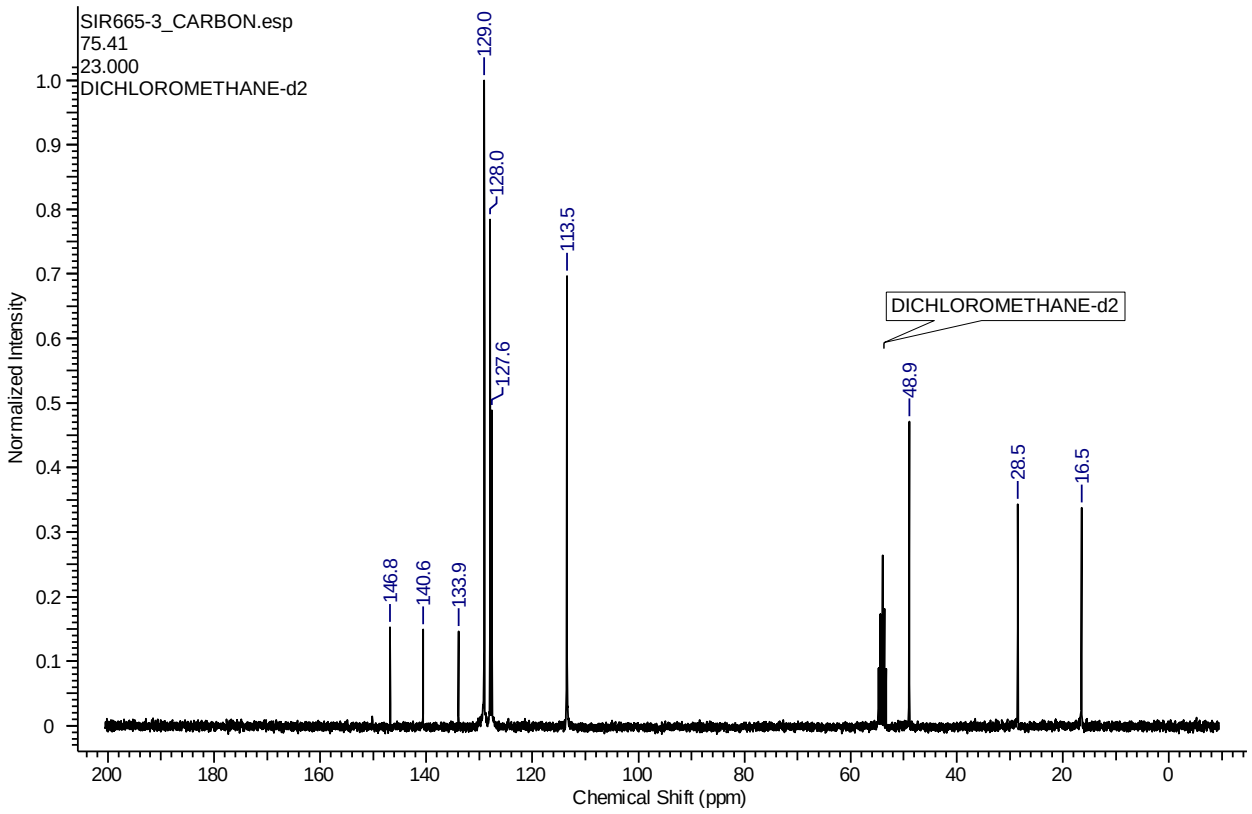
NMR spectra of N-benzyl-3,5-dimethylaniline (4i):



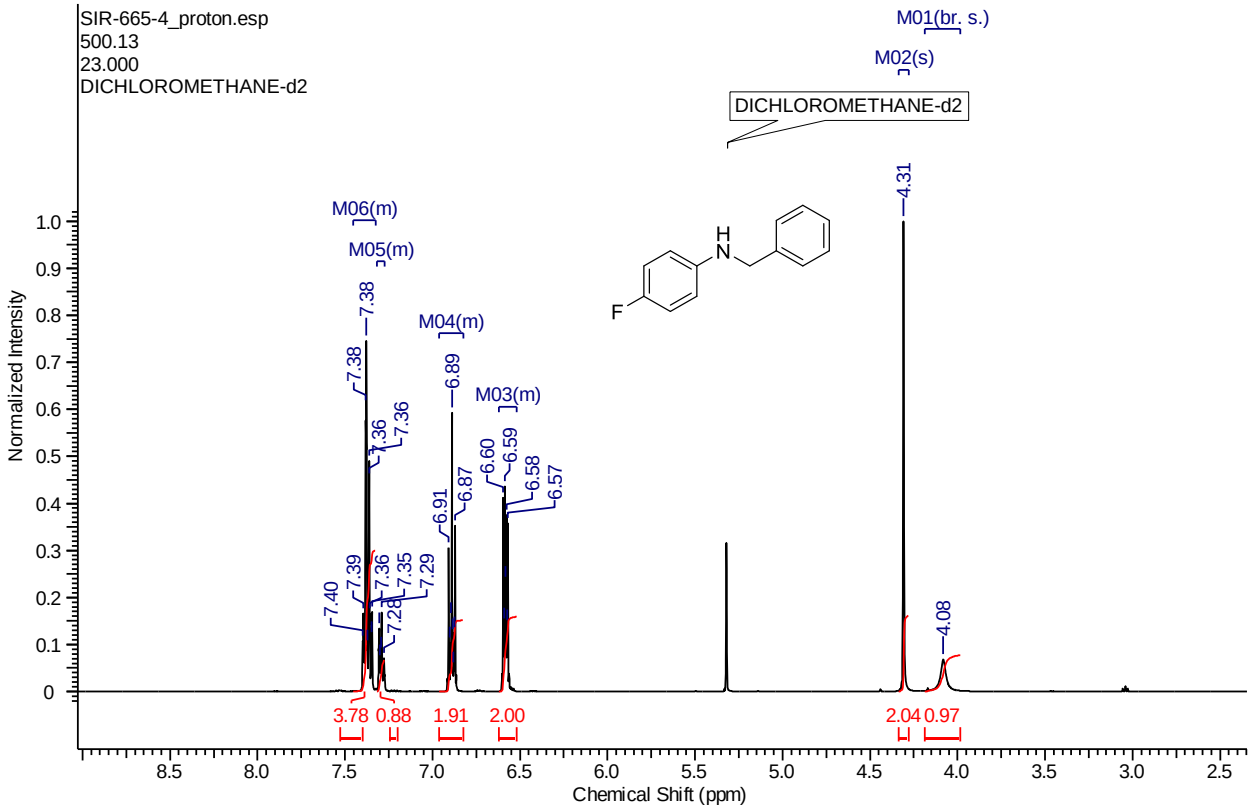


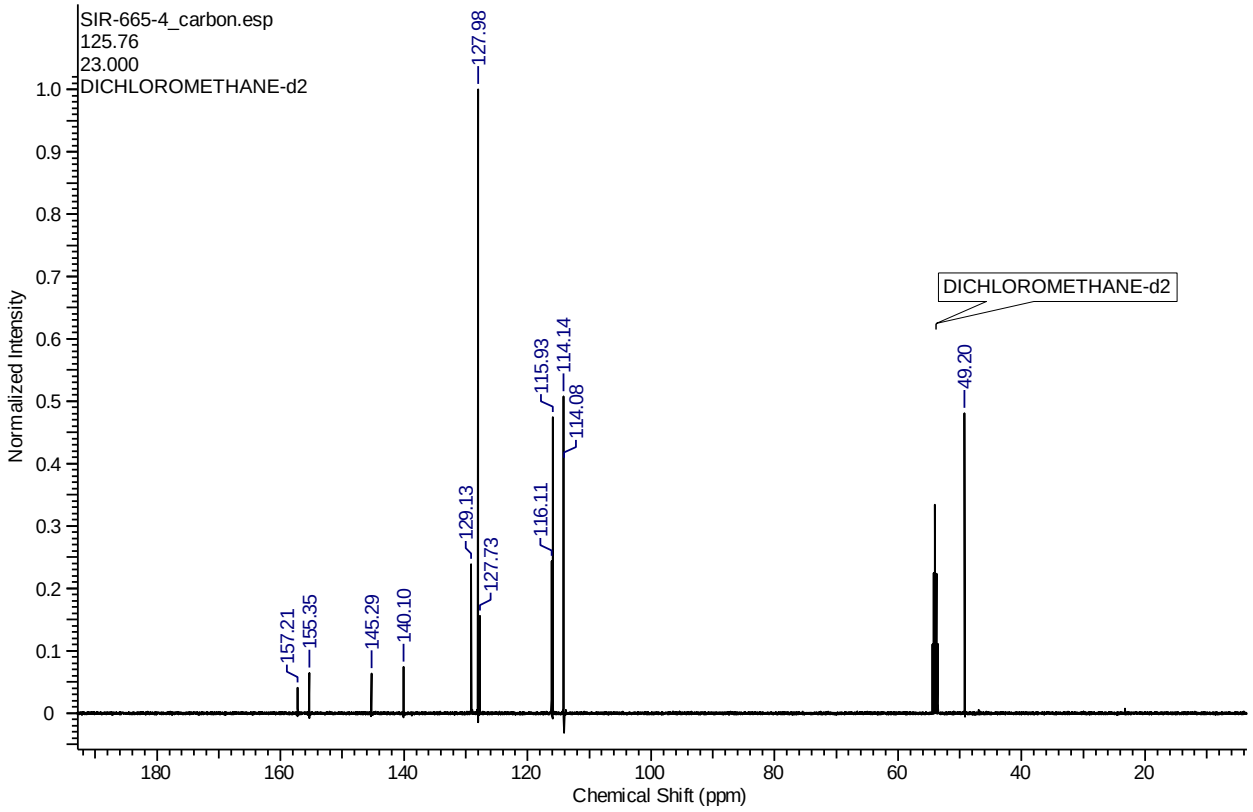
NMR spectra of N-benzyl-4-ethylaniline (4e):



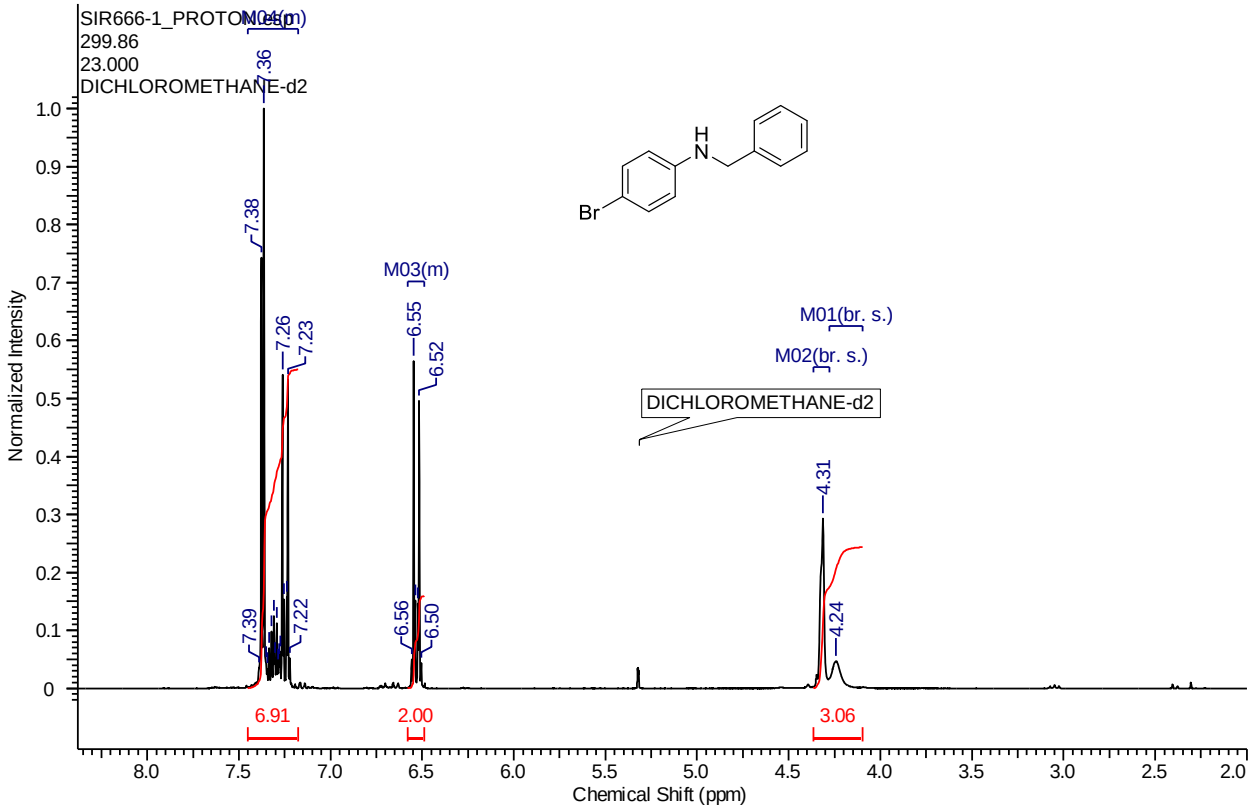


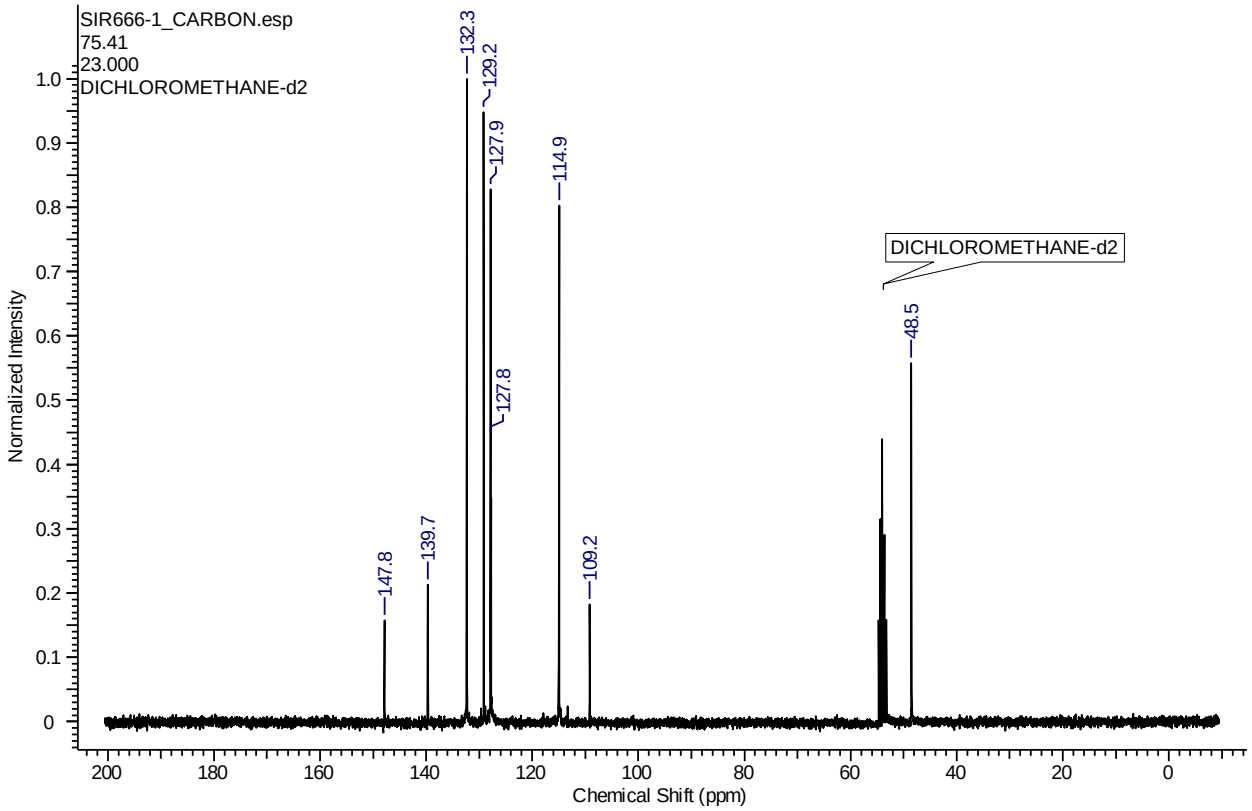
NMR spectra of N-benzyl-4-fluoroaniline (4a):



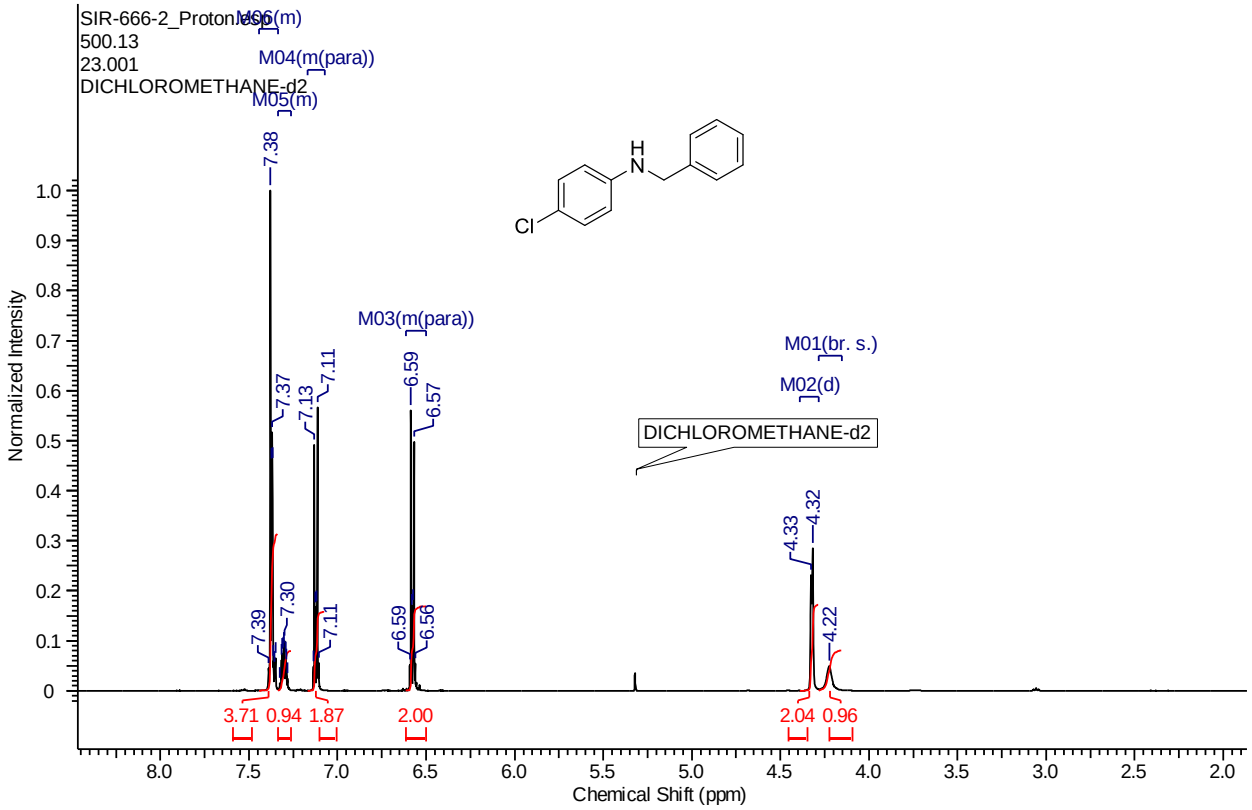


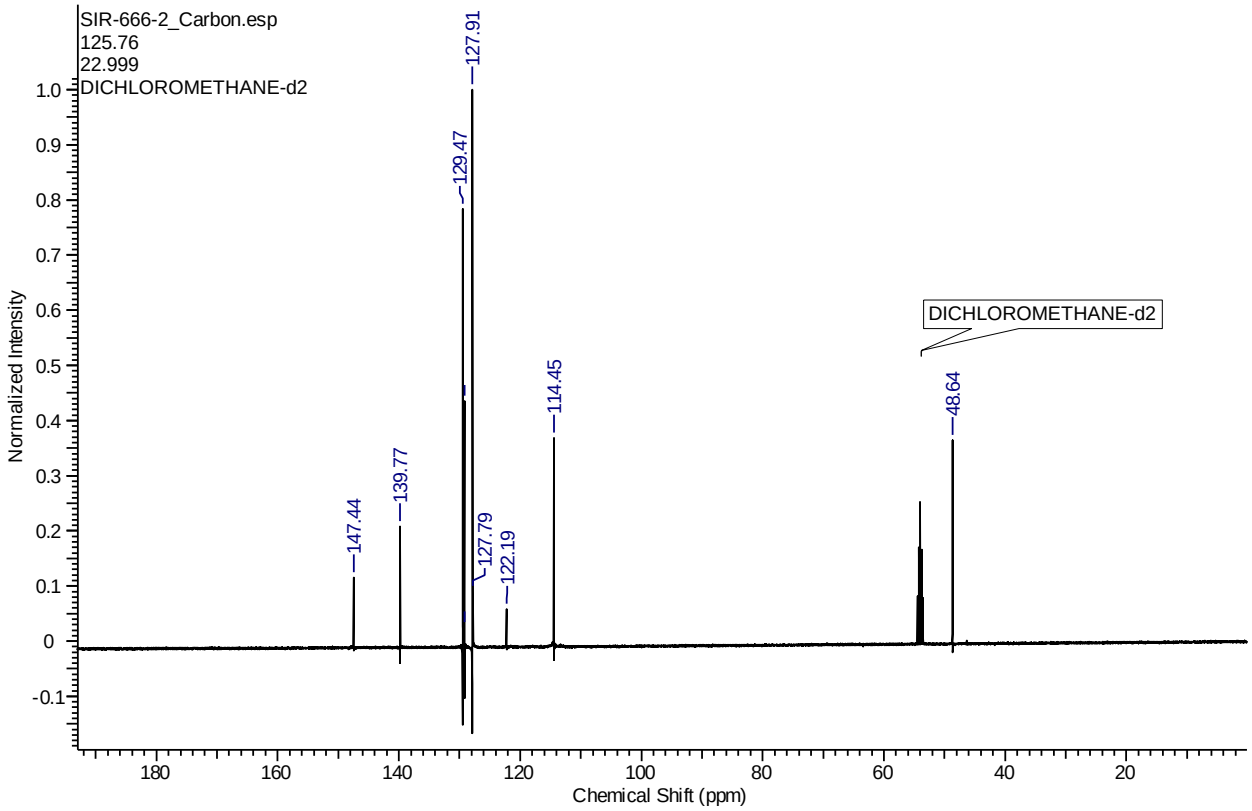
NMR spectra of N-benzyl-4-bromoaniline (4c):



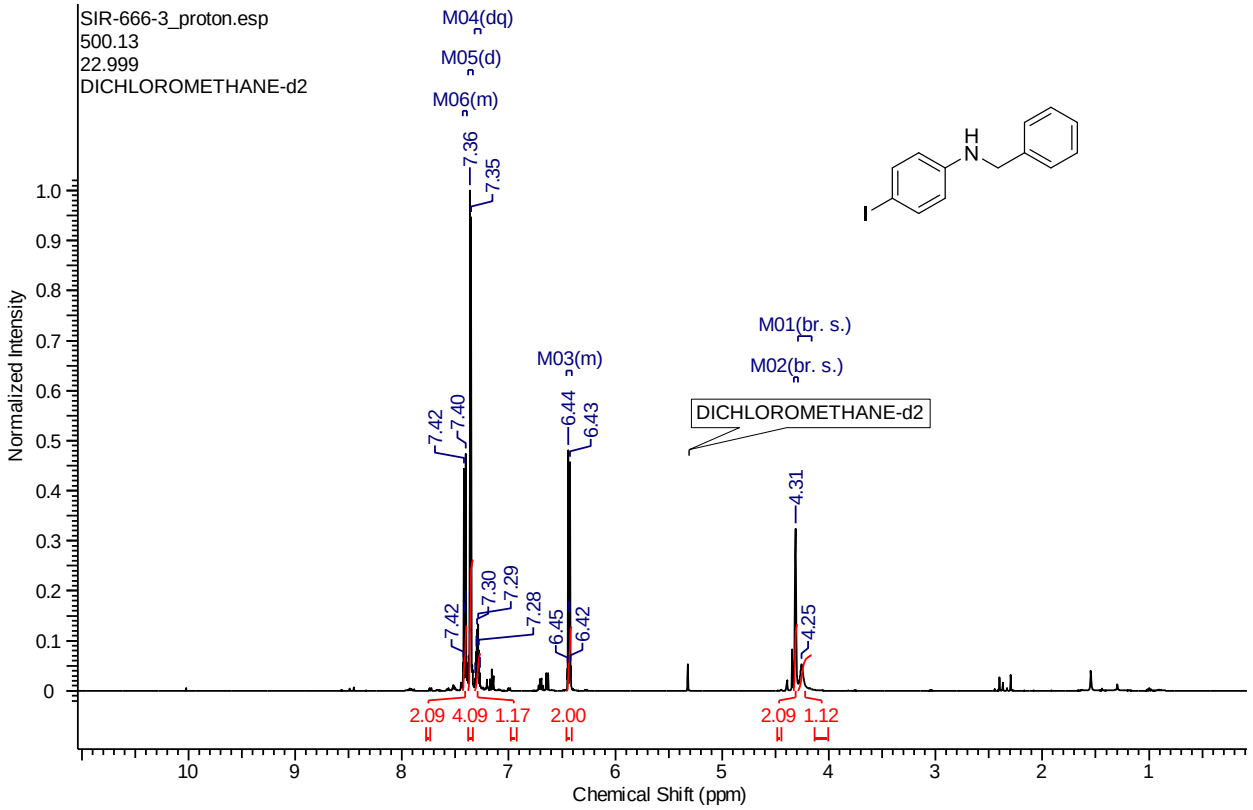


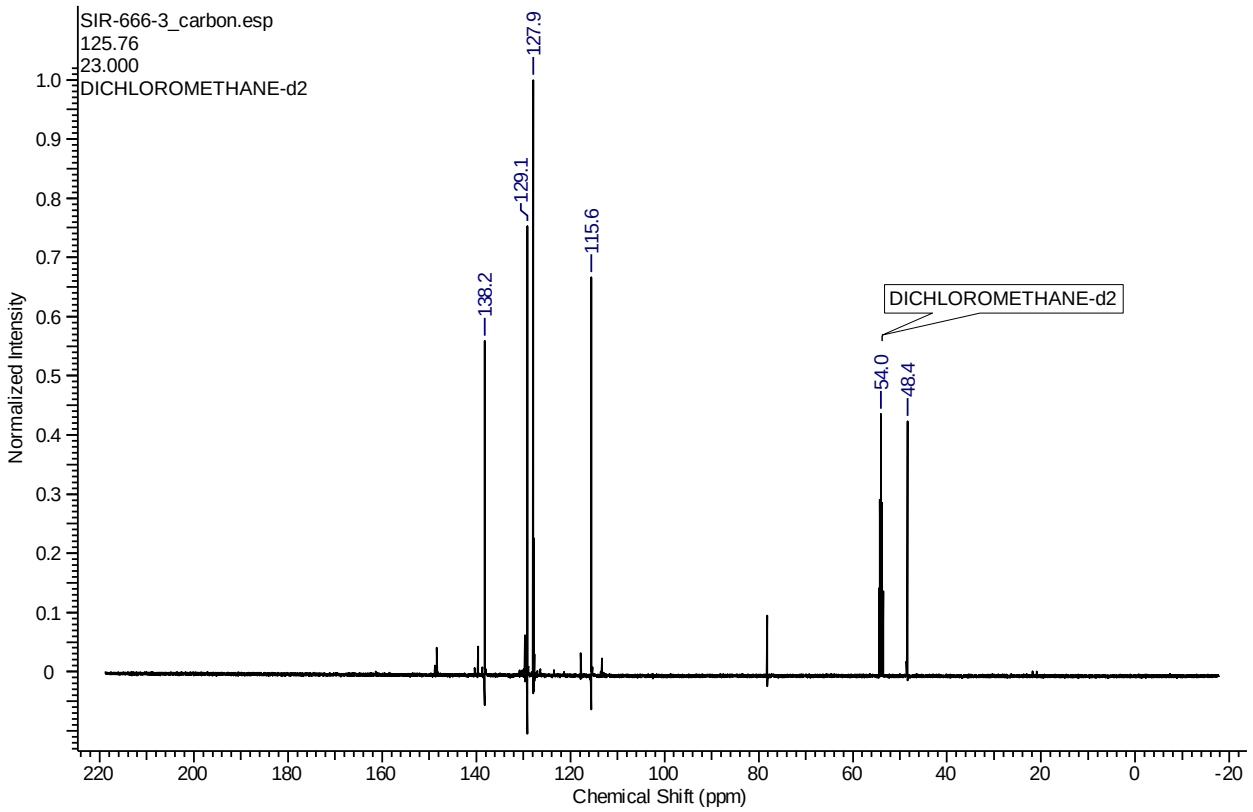
NMR spectra of N-benzyl-4-chloroaniline (4b):



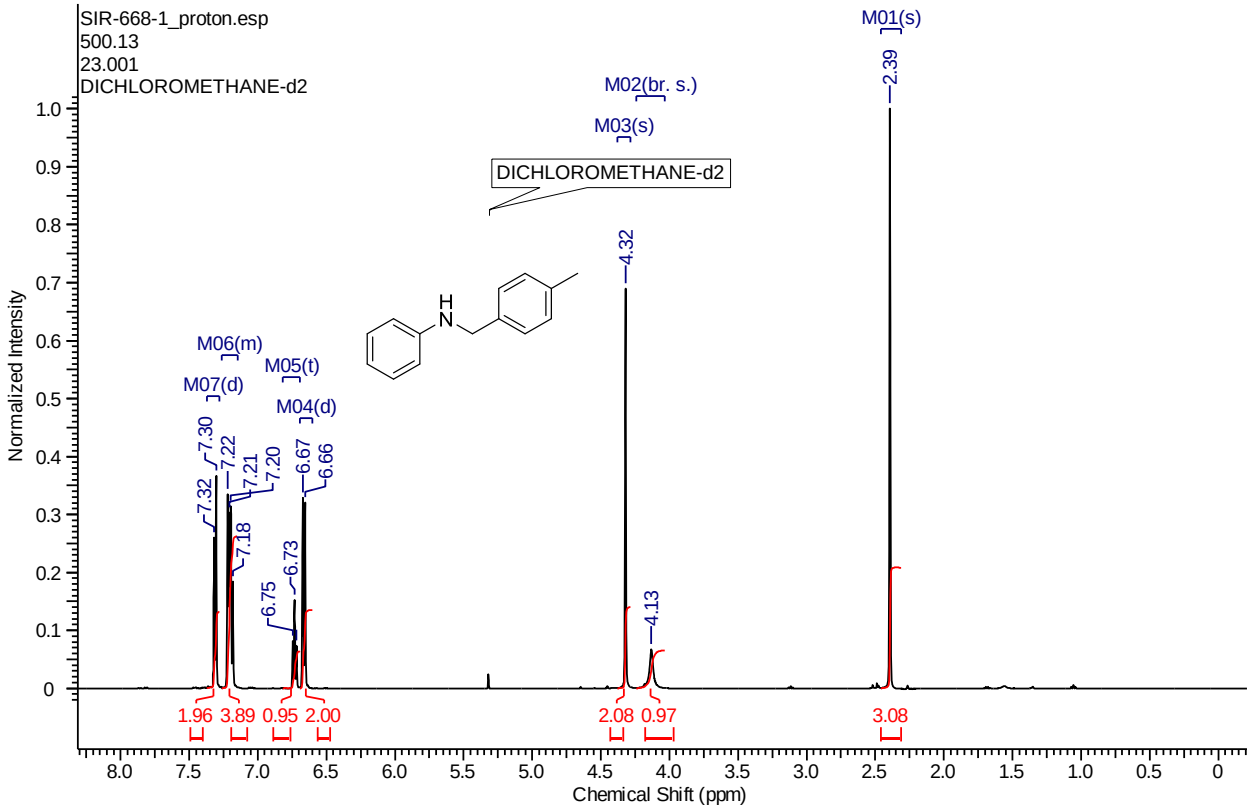


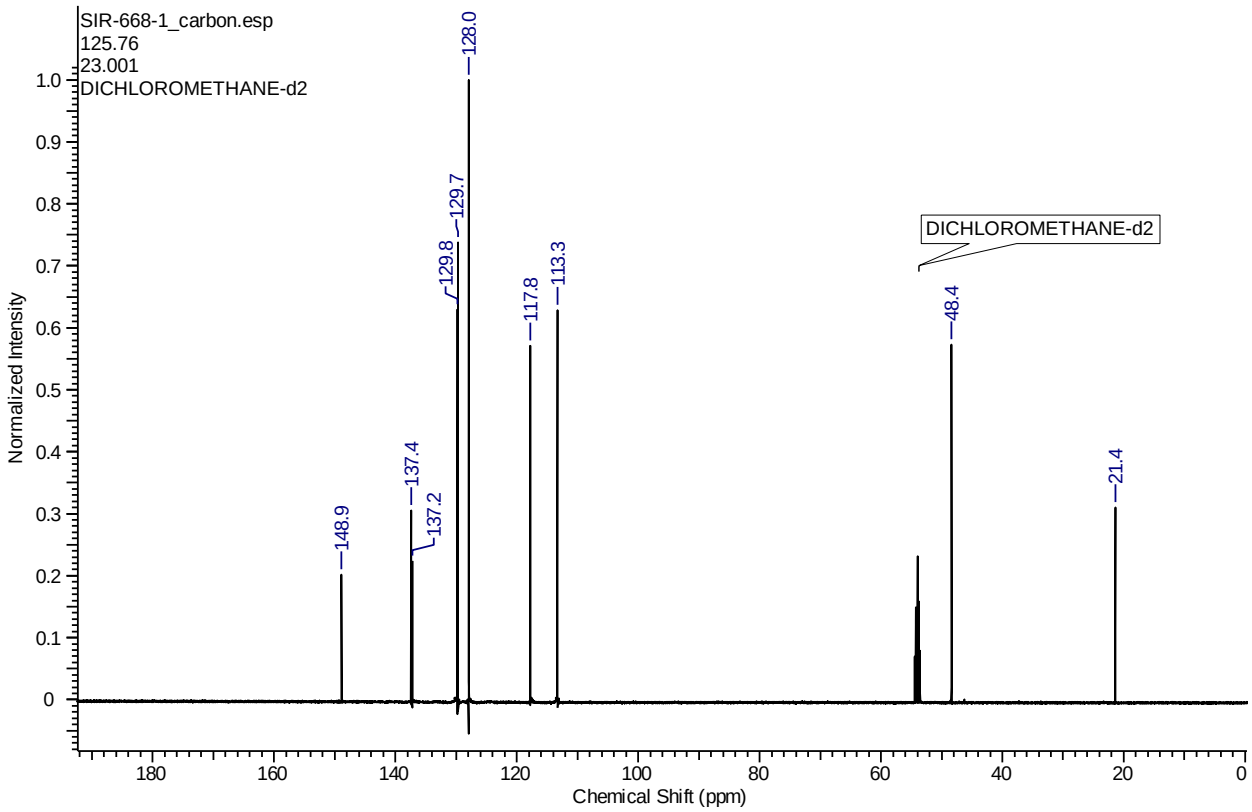
NMR spectra of N-benzyl-4-iodoaniline (4d):



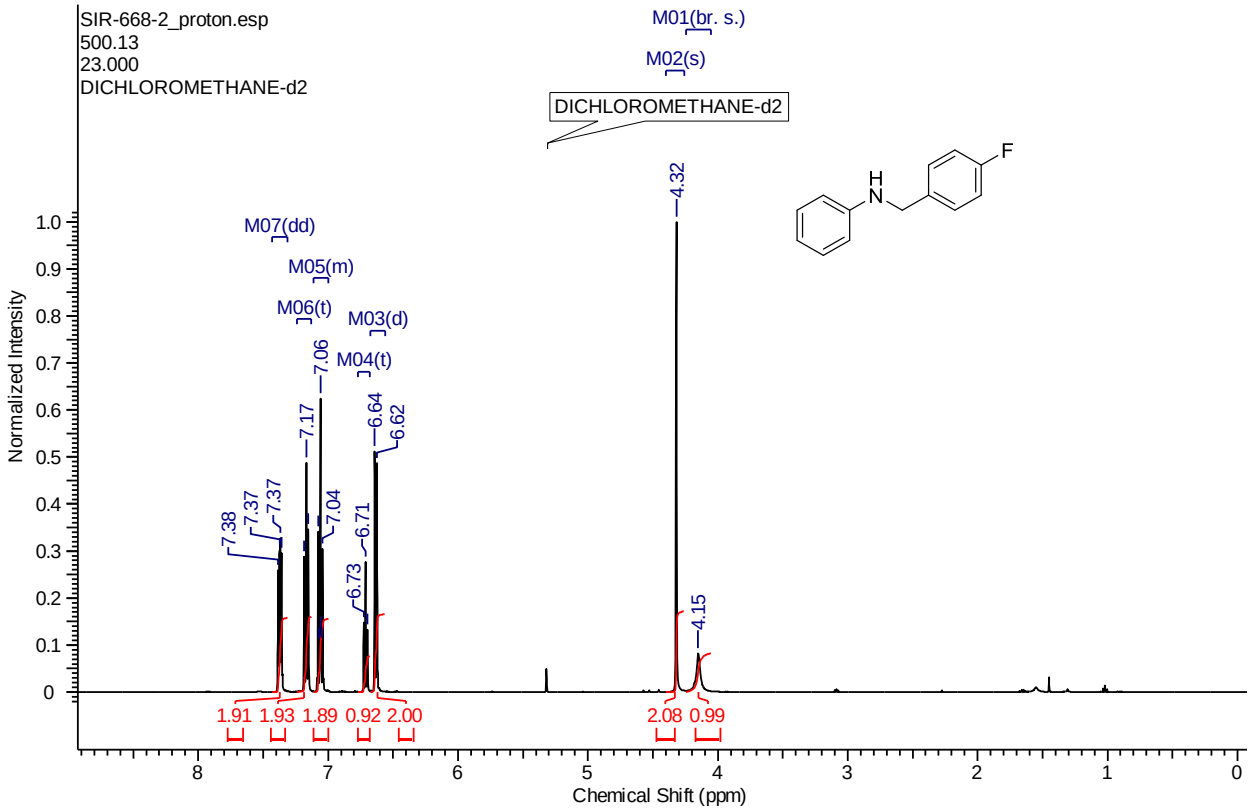


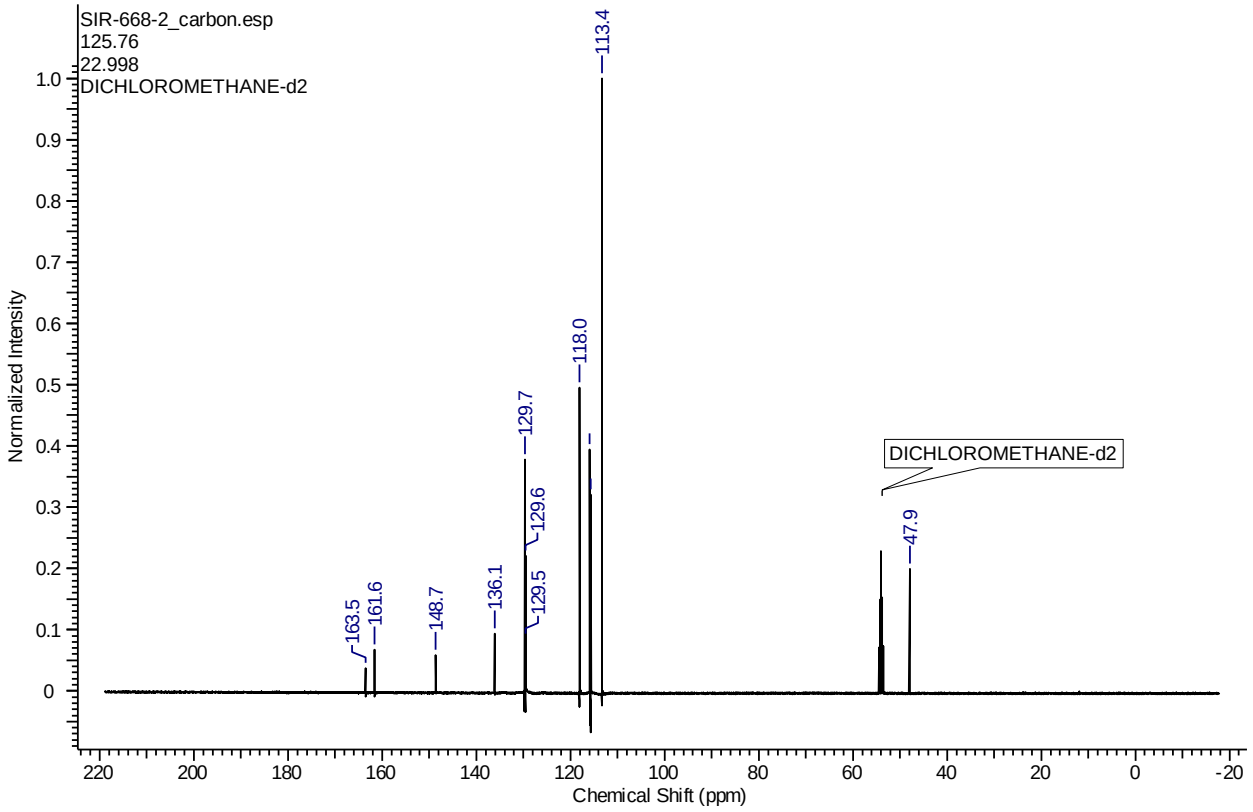
NMR spectra of N-(4-methylbenzyl)aniline (3e):



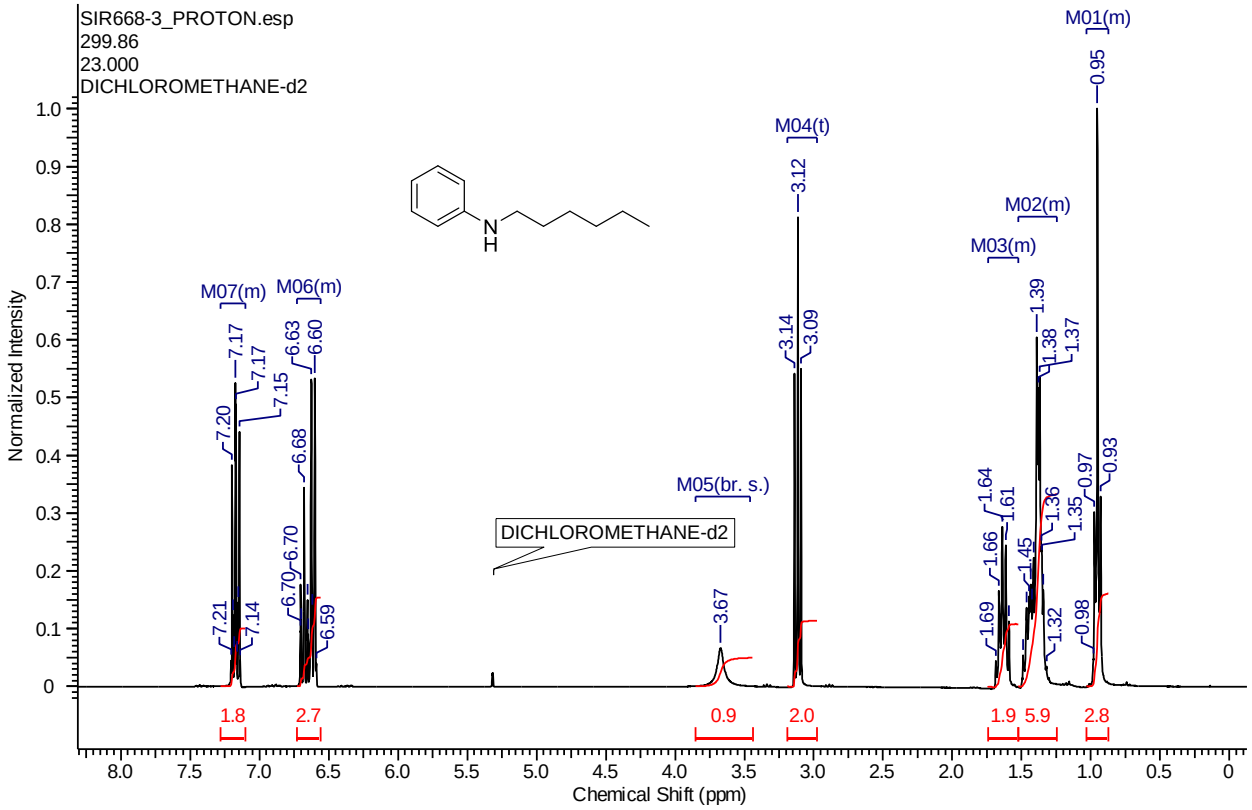


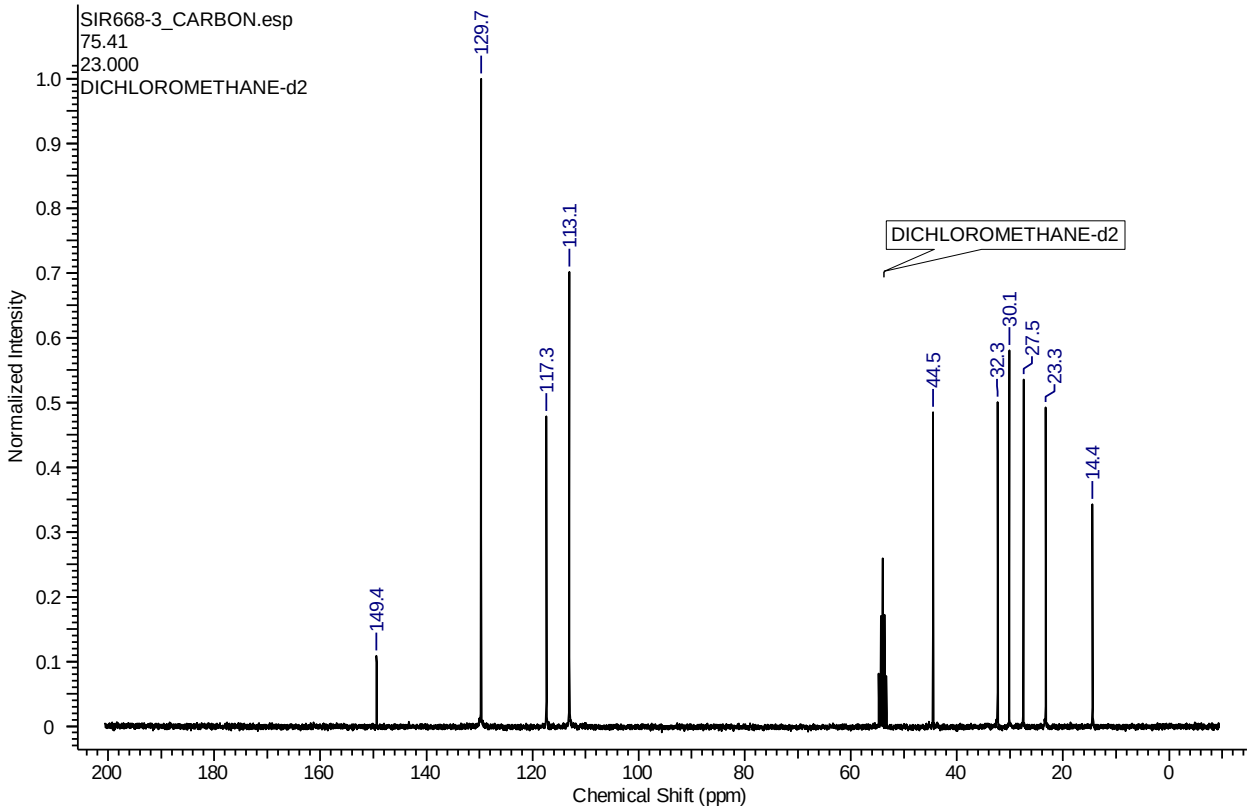
NMR spectra of N-(4-fluorobenzyl)aniline (3b):



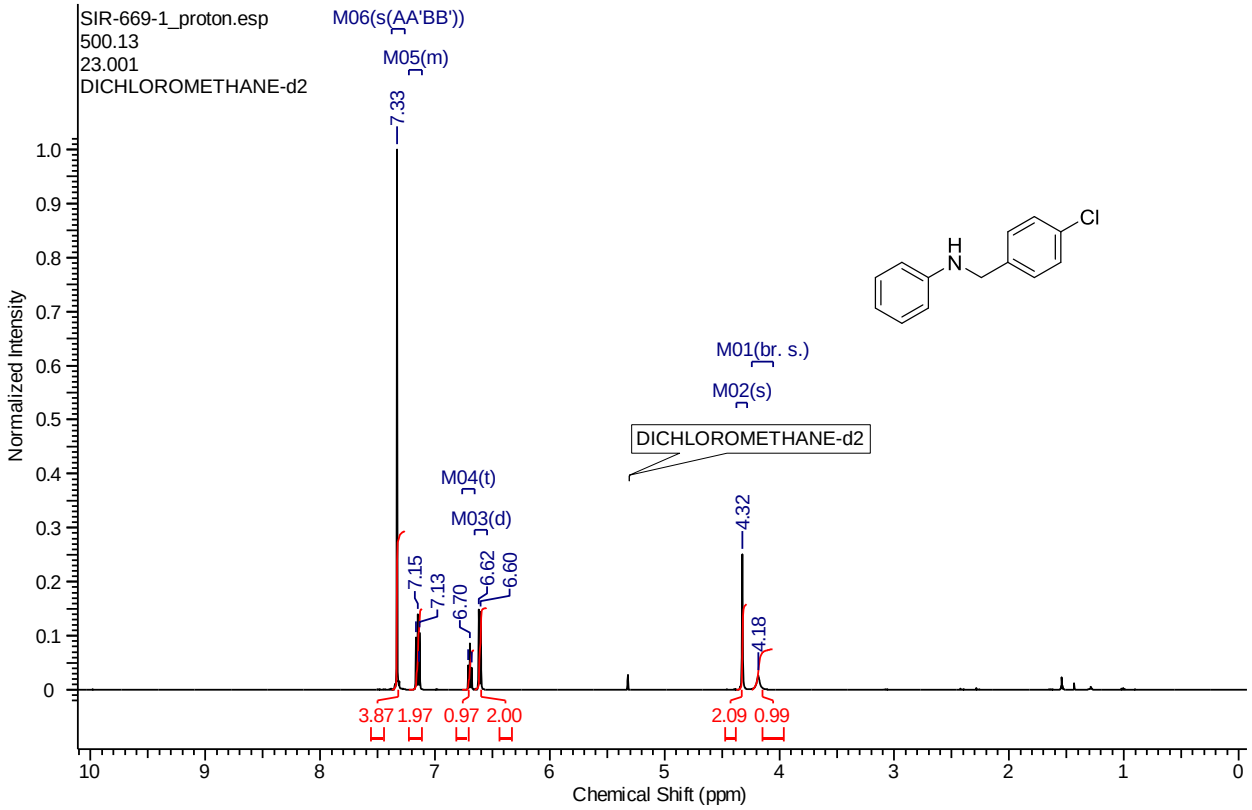


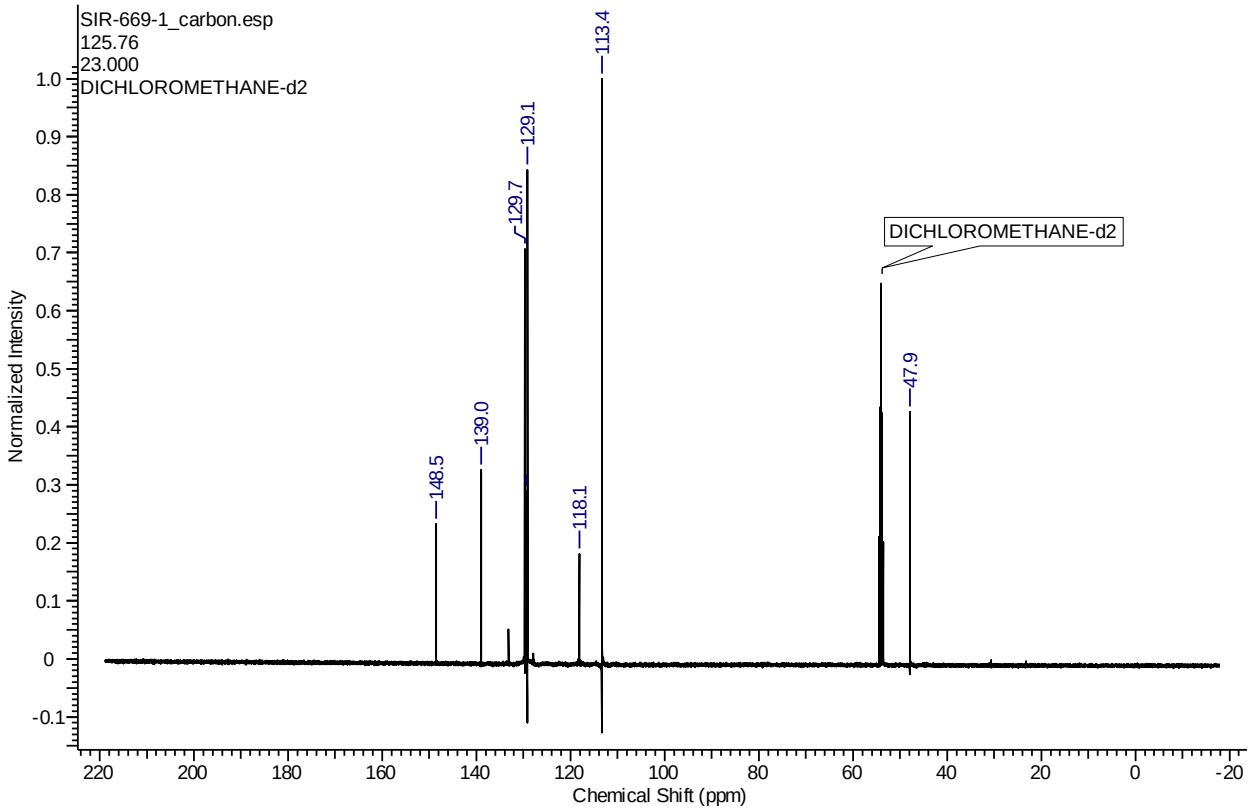
NMR spectra of N-(1-hexyl)aniline (3j):



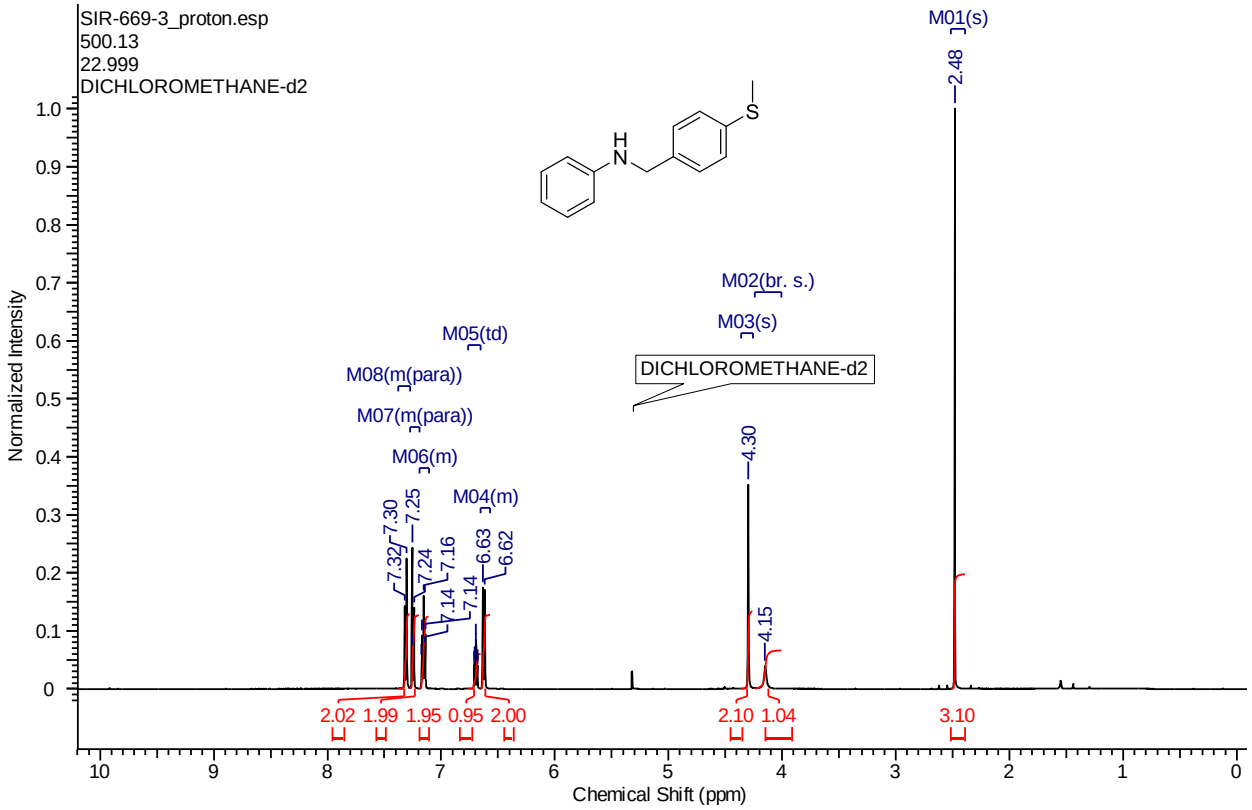


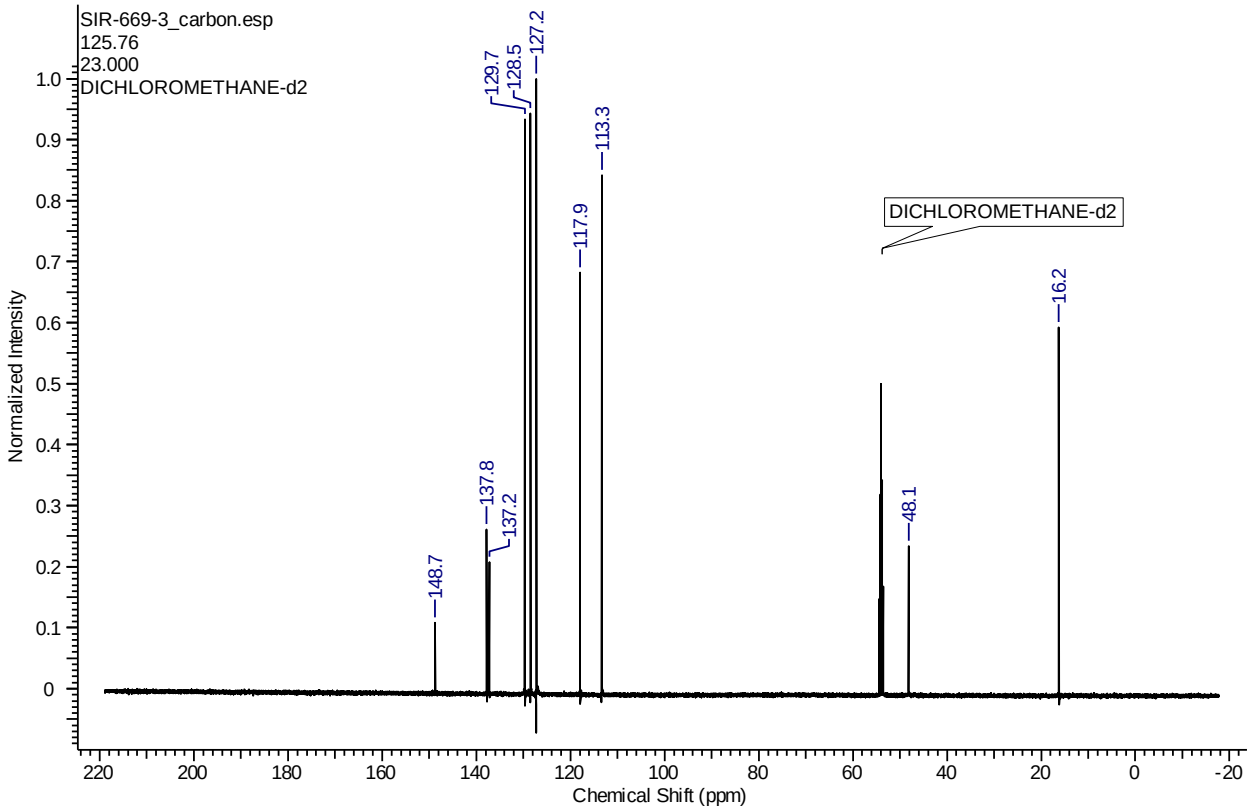
NMR spectra of N-(4-chlorobenzyl)aniline (3c):



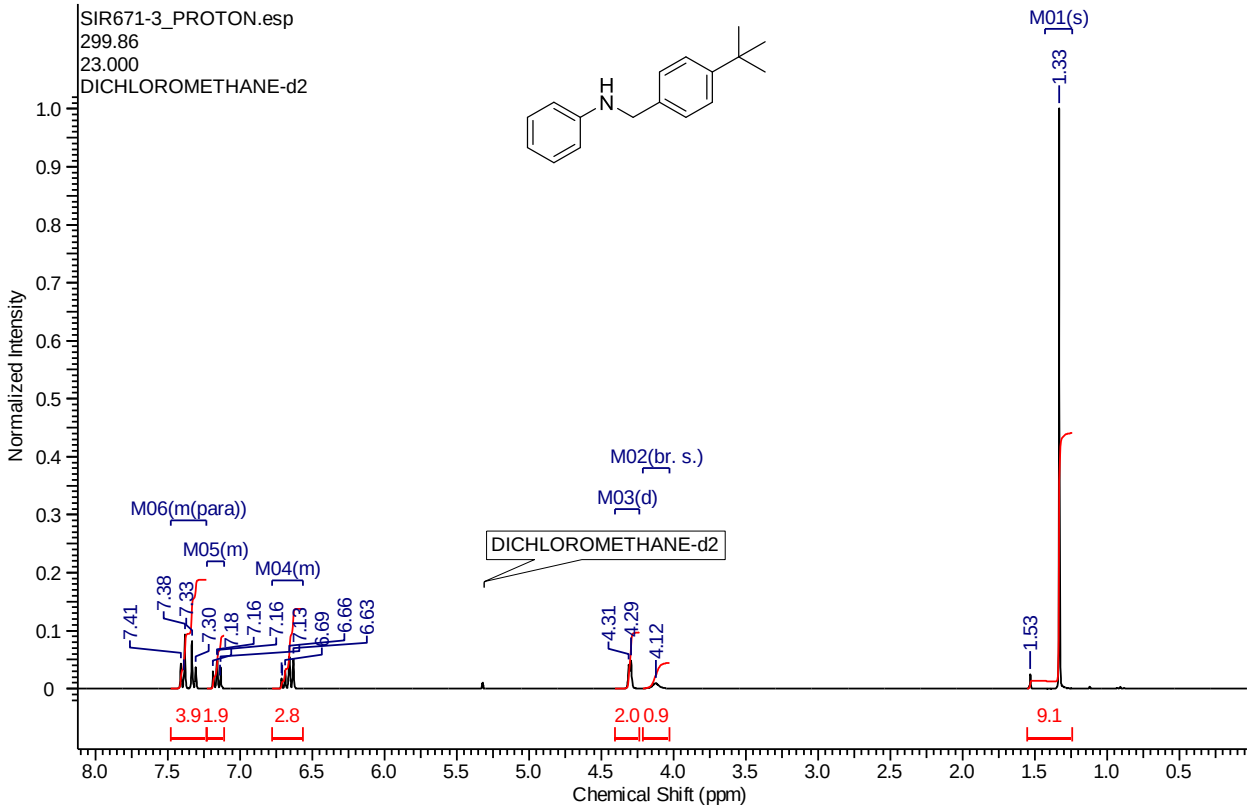


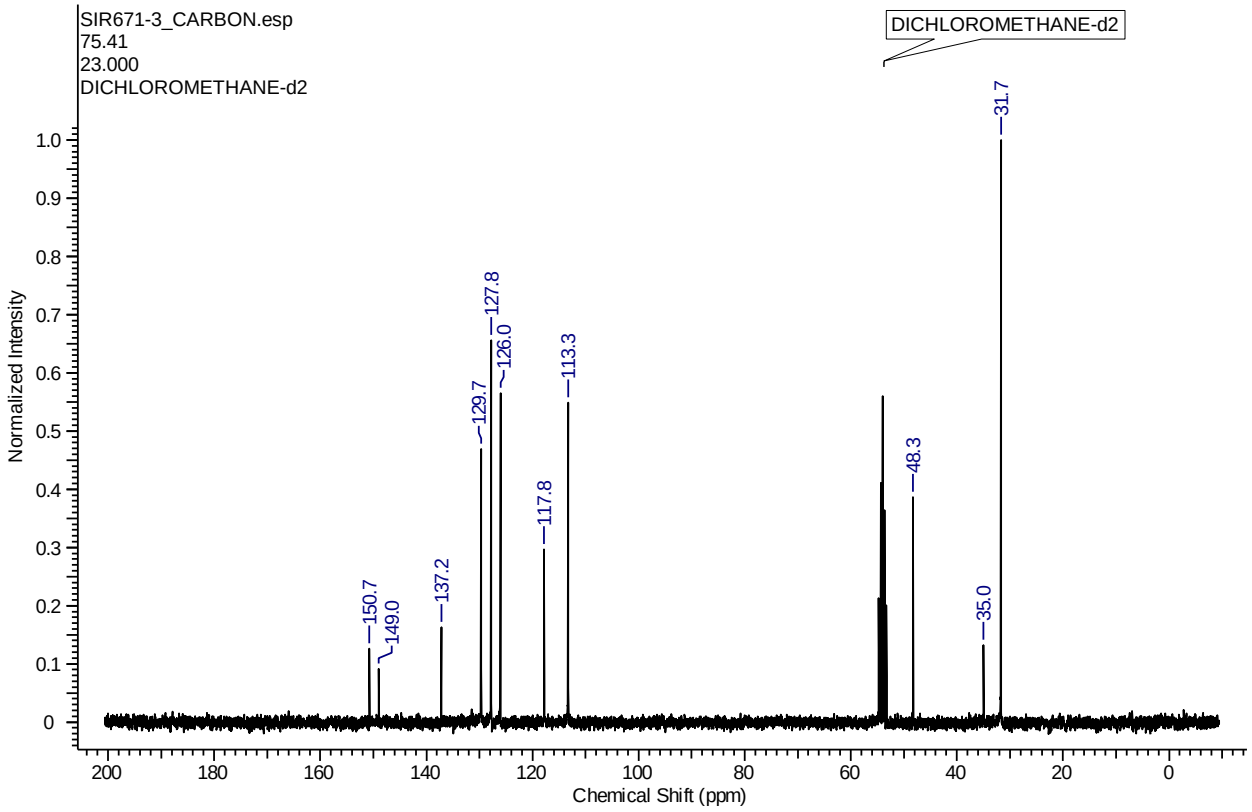
NMR spectra of N-(4-methylthiobenzyl)aniline (3g):



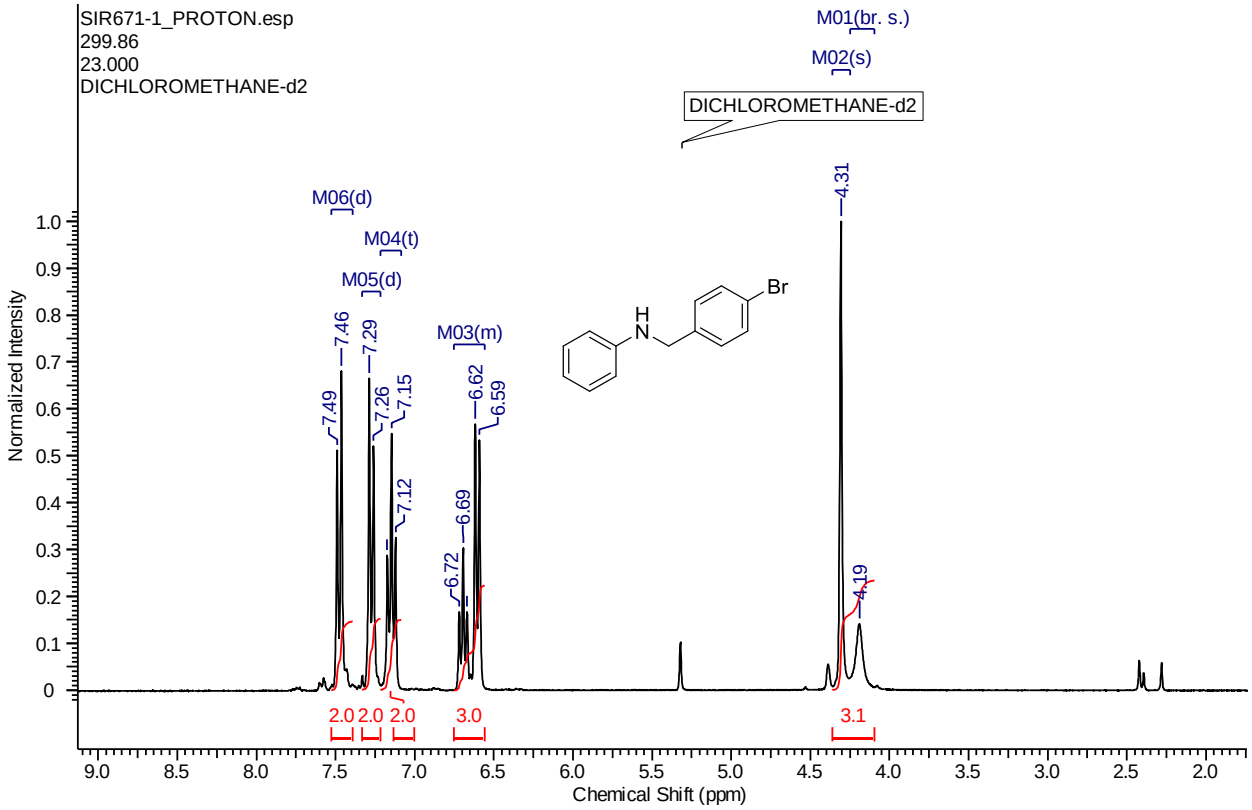


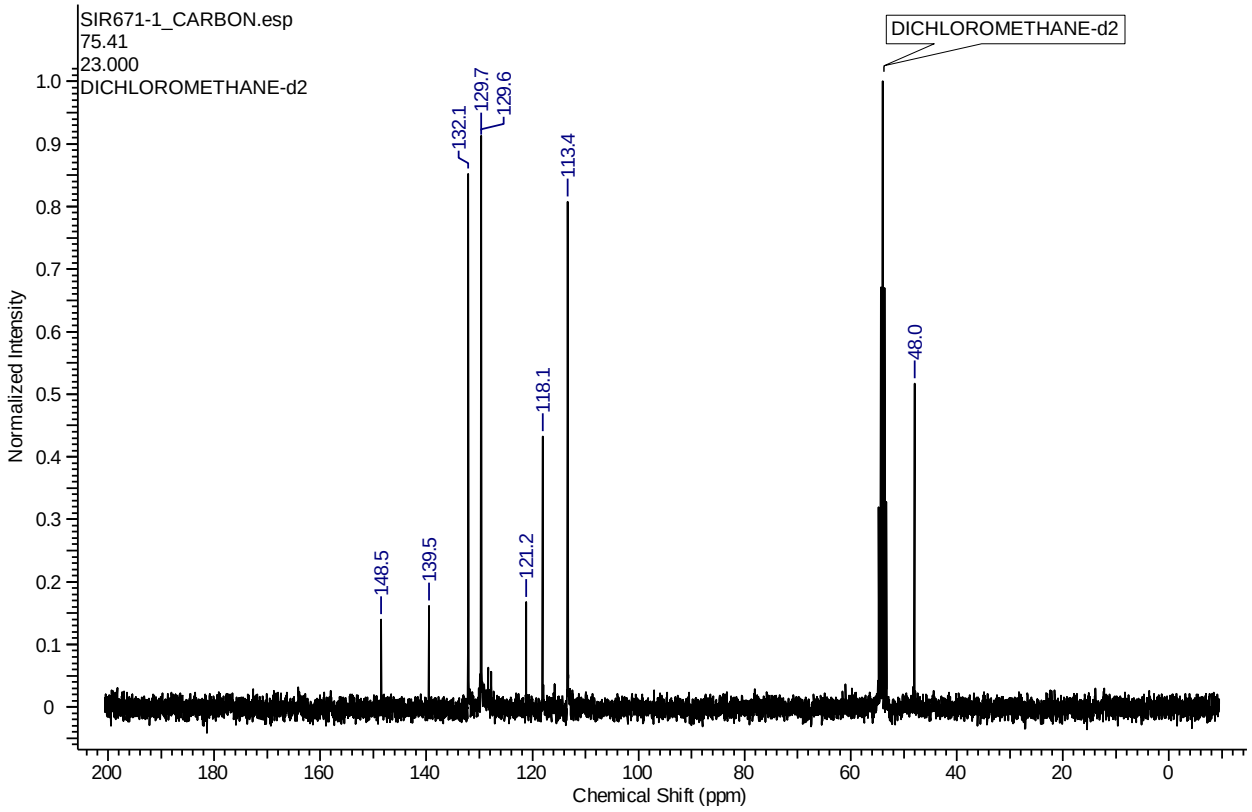
NMR spectra of N-(4-*tert*-butylbenzyl)aniline (3h):



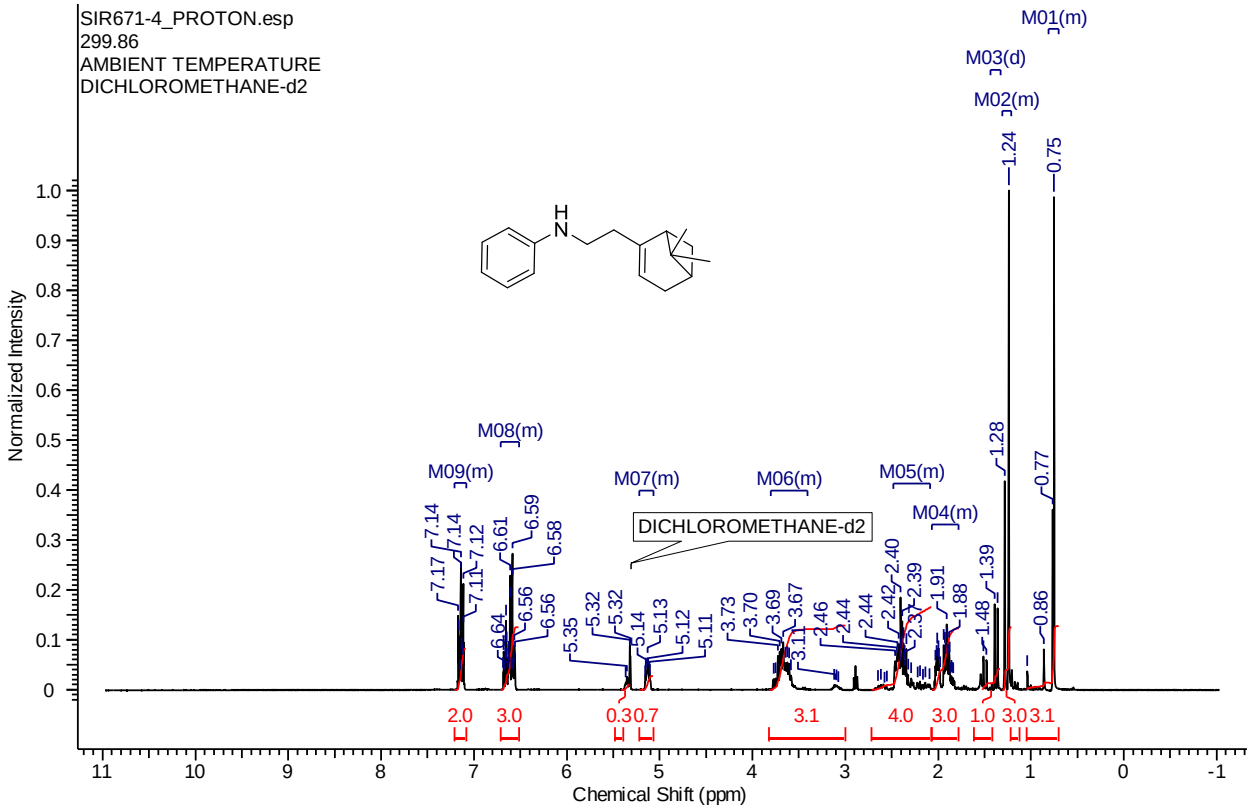


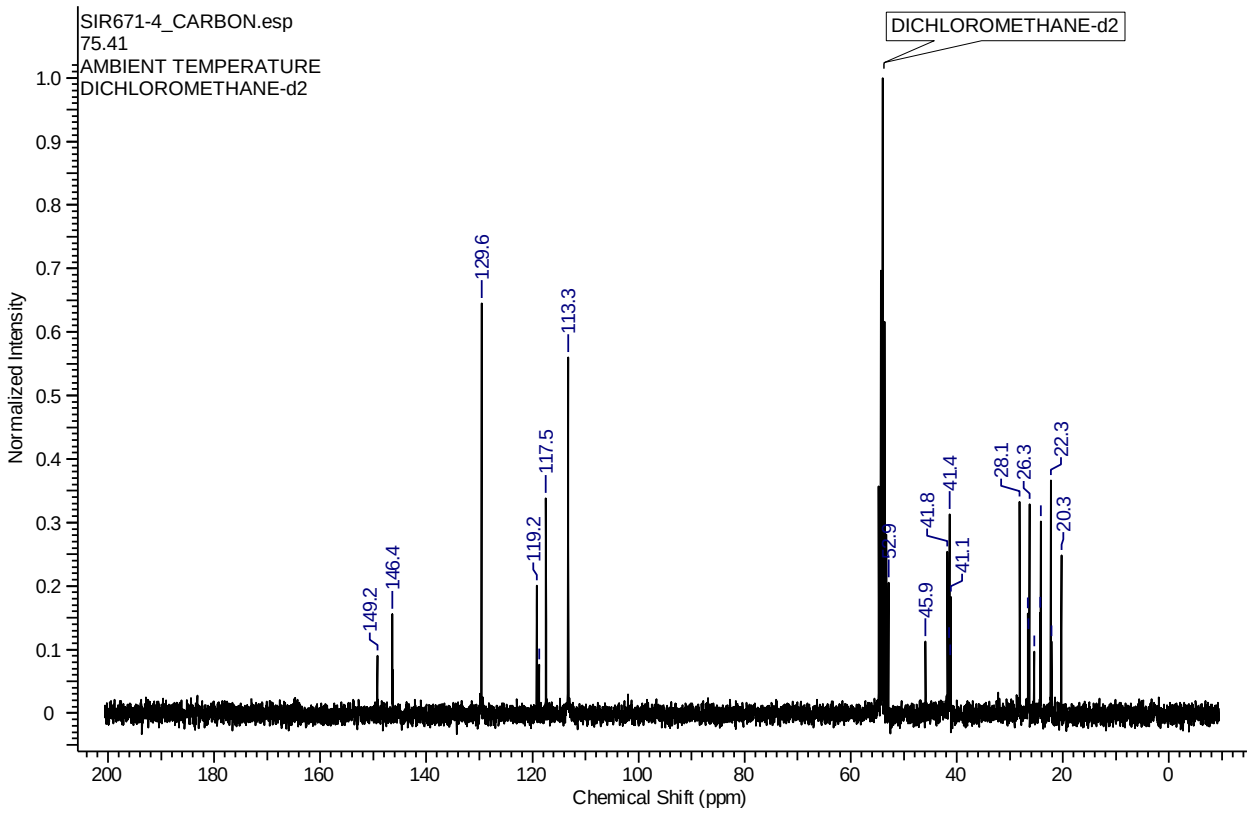
NMR spectra of N-(4-bromobenzyl)aniline (3d):



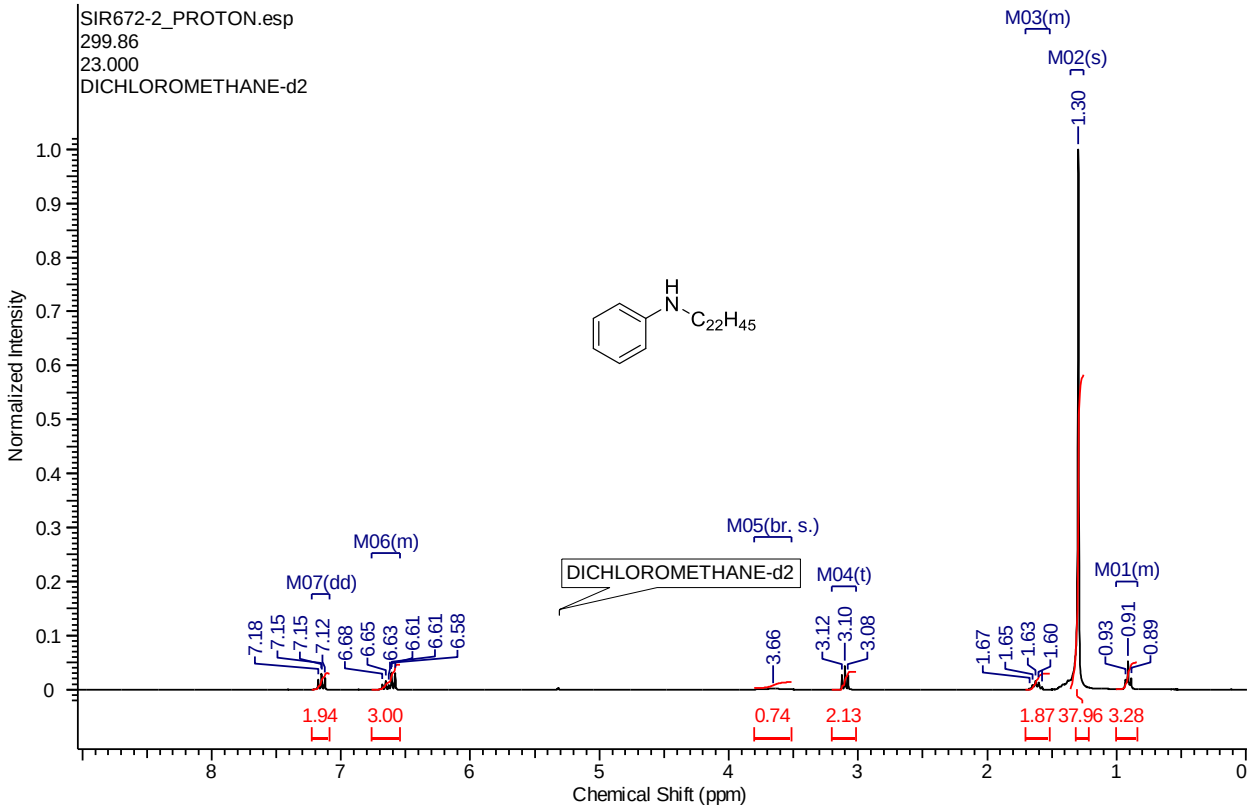


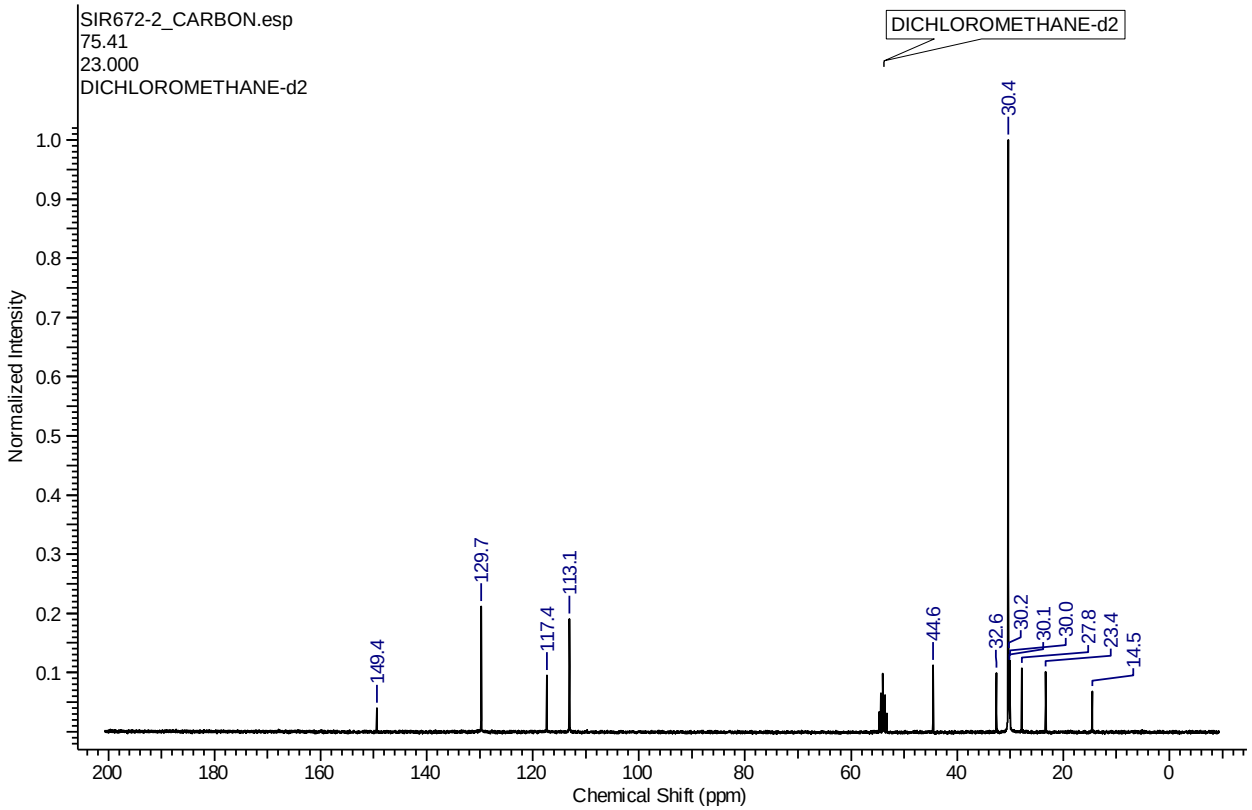
NMR spectra of N-(2-(6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl)aniline (3l):



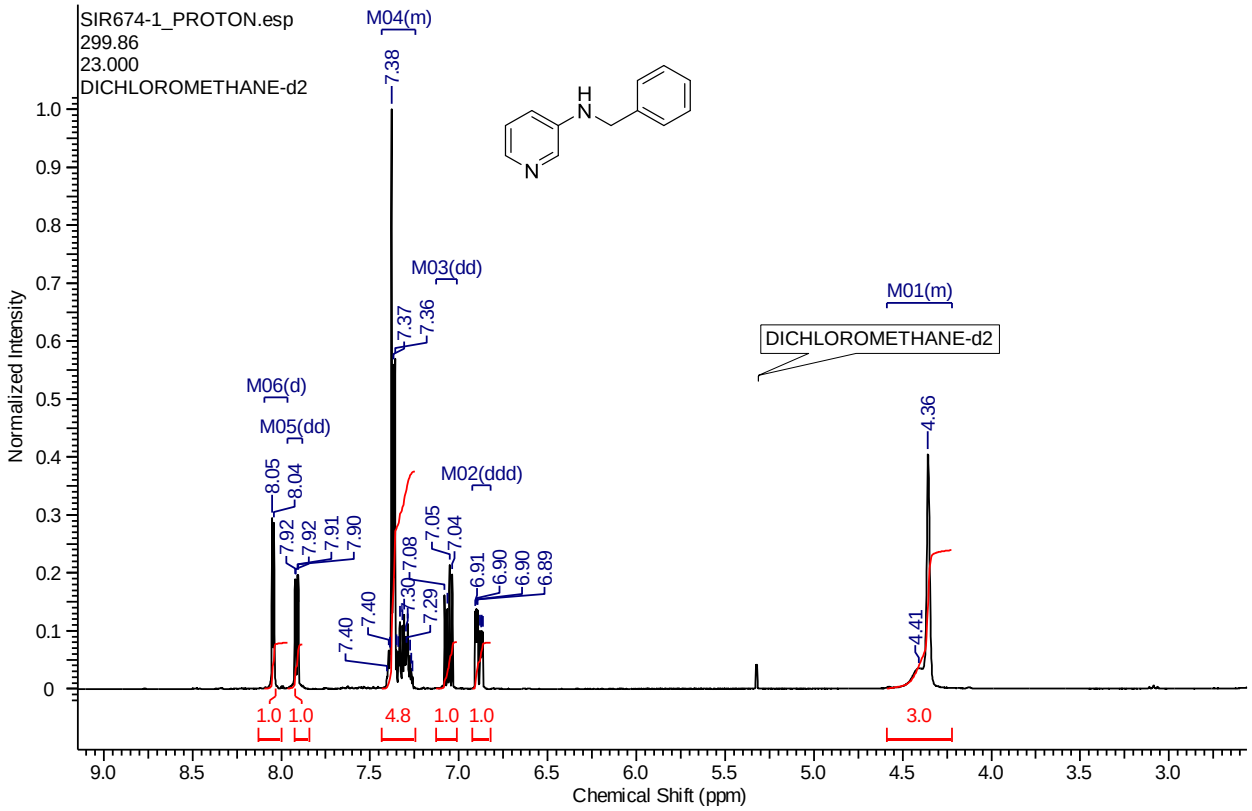


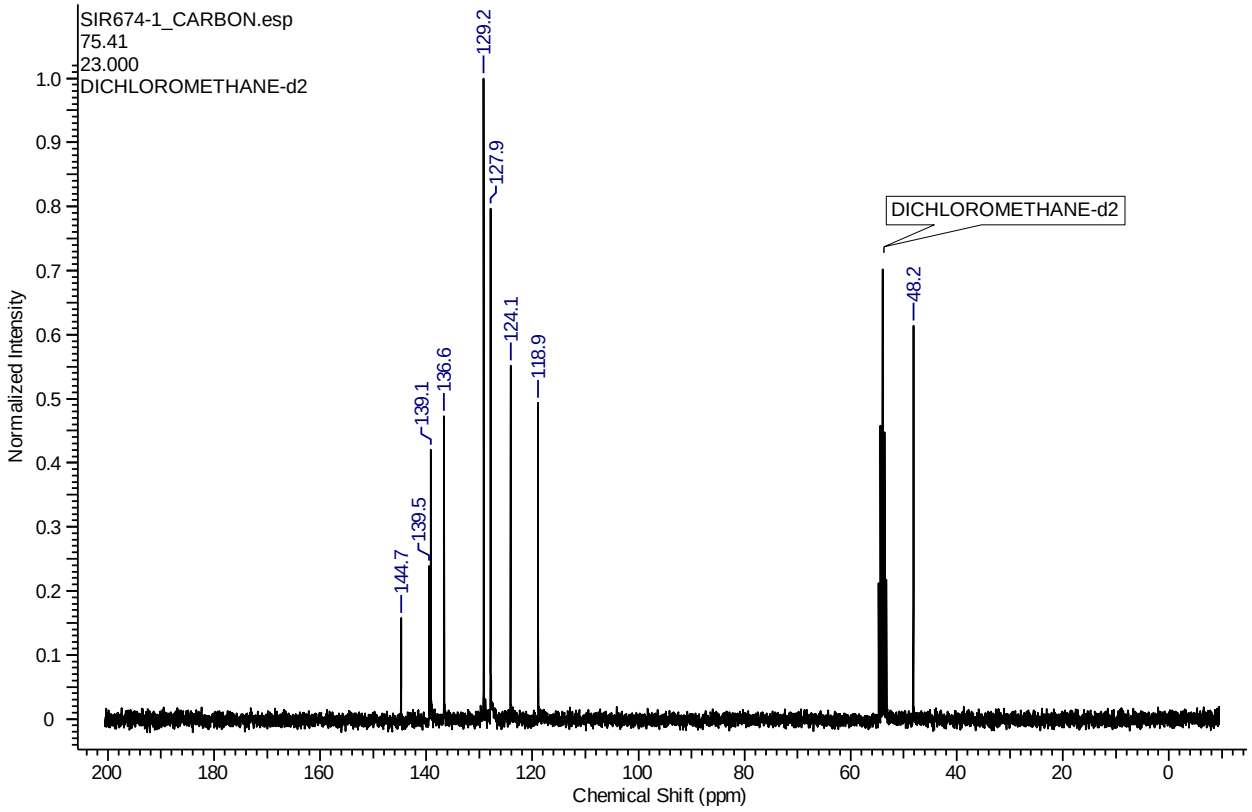
NMR spectra of N-(1-docosanoyl)aniline (3k):



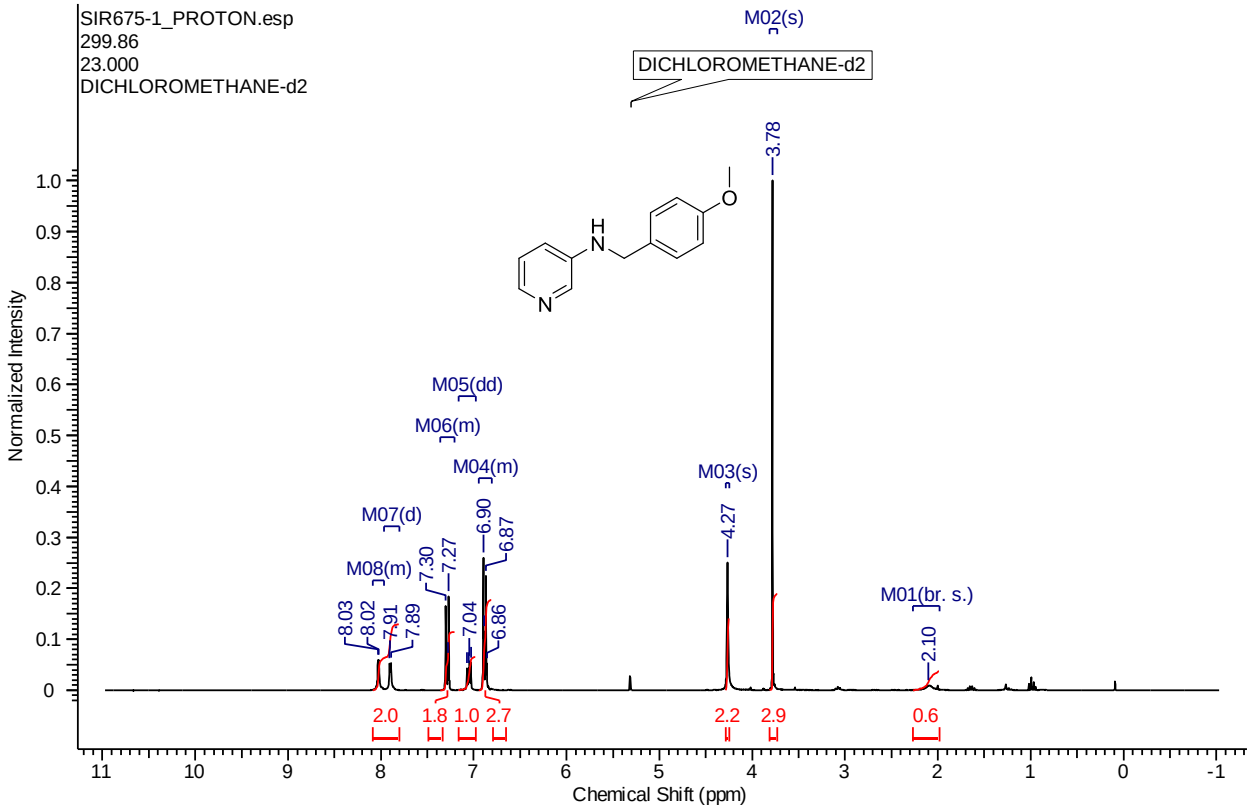


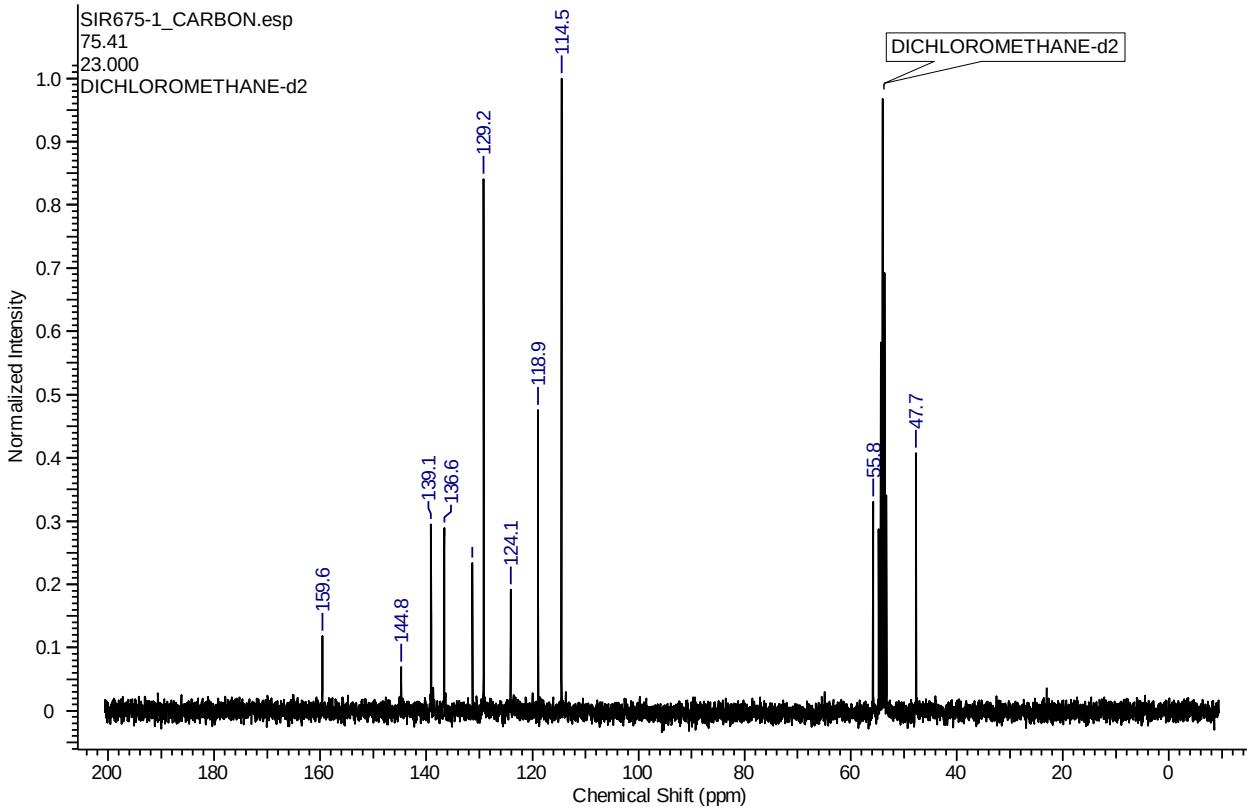
NMR spectra of N-(benzyl)pyridine-3-amine (5a):



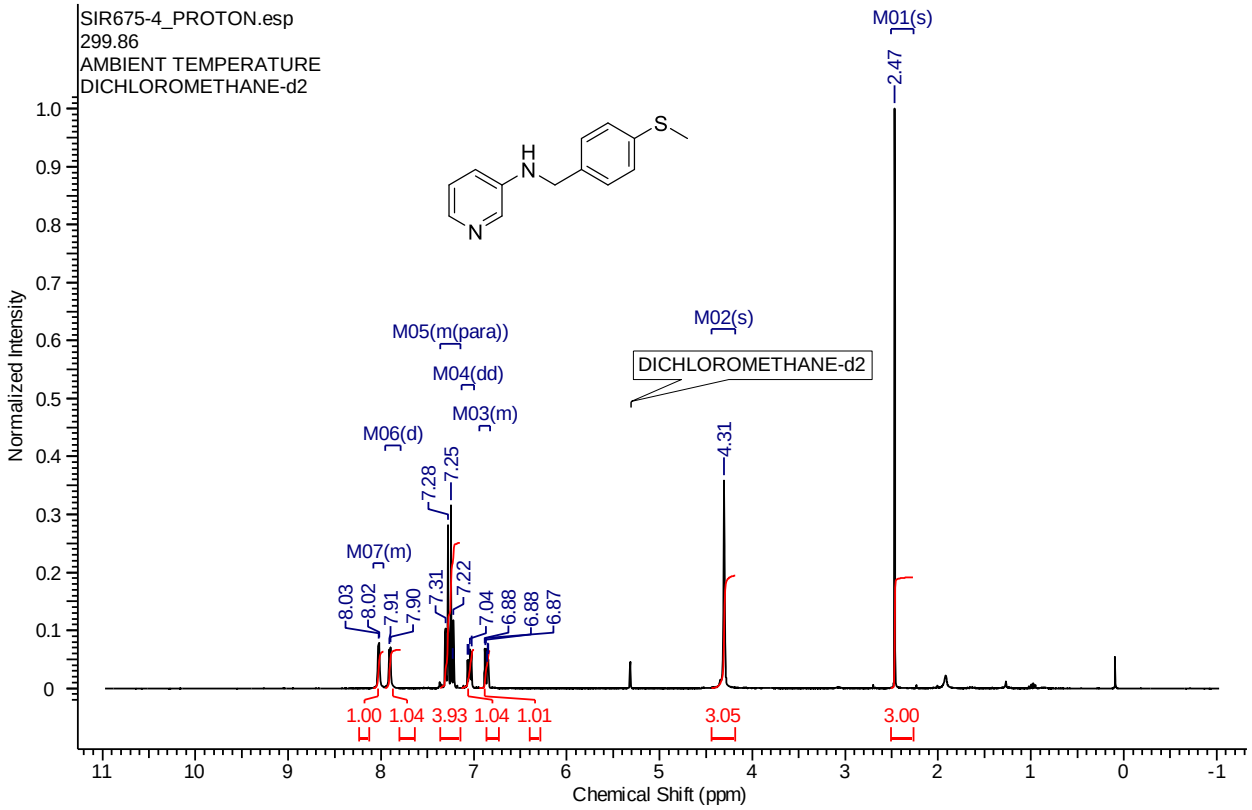


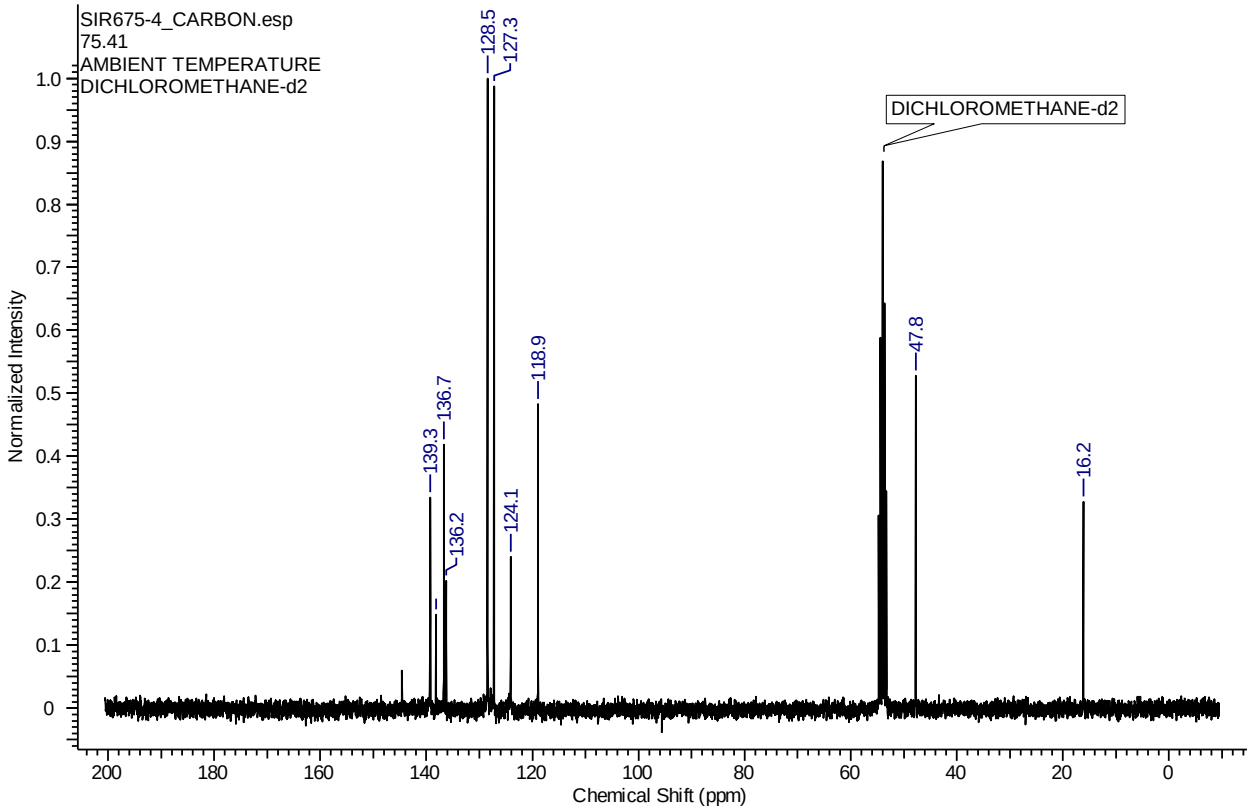
NMR spectra of N-(4-methoxybenzyl)pyridine-3-amine (5b):



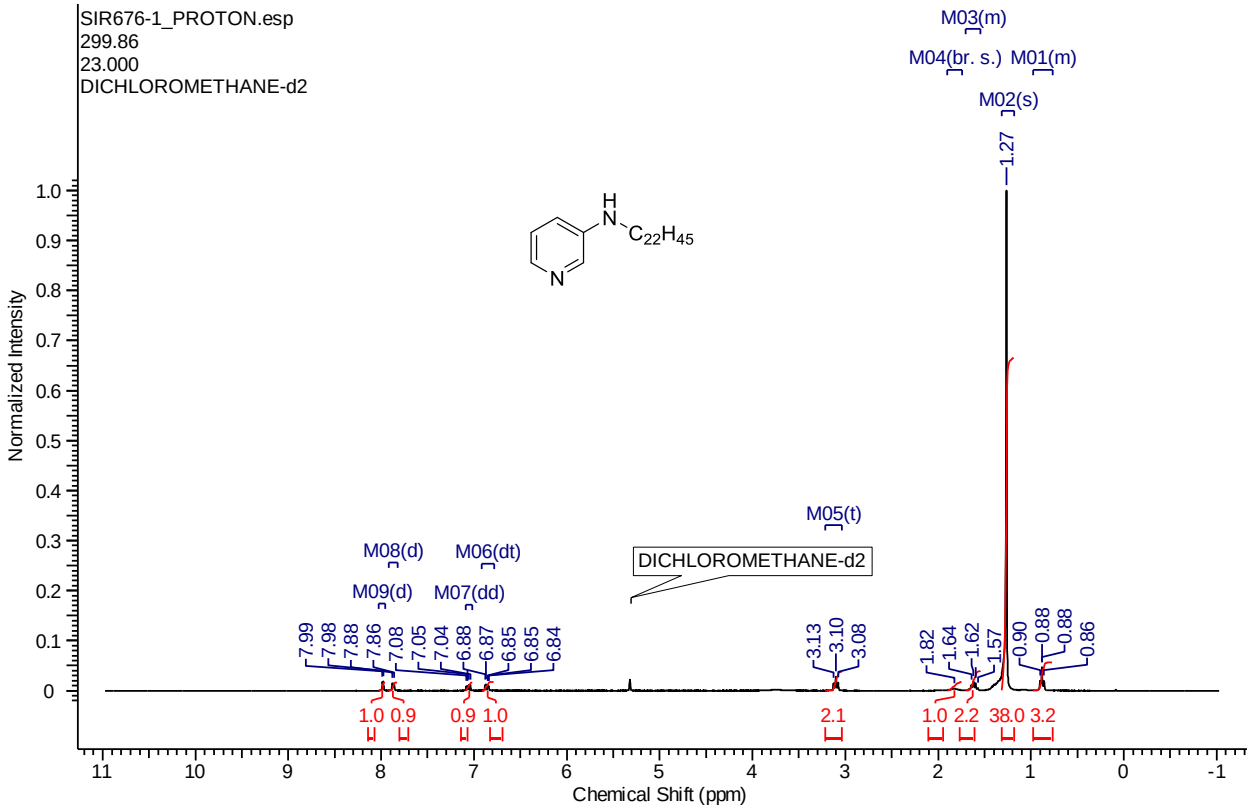


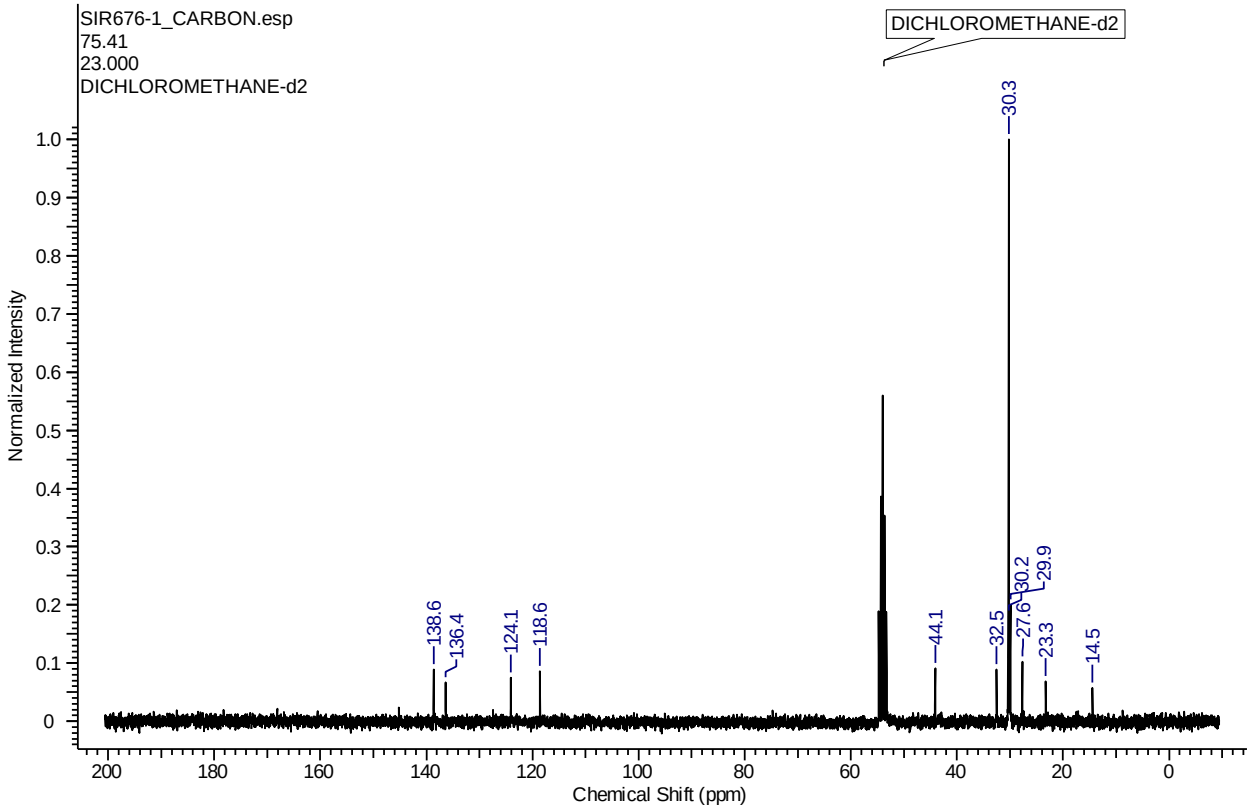
NMR spectra of N-(4-methylthiobenzyl)pyridine-3-amine (5c):



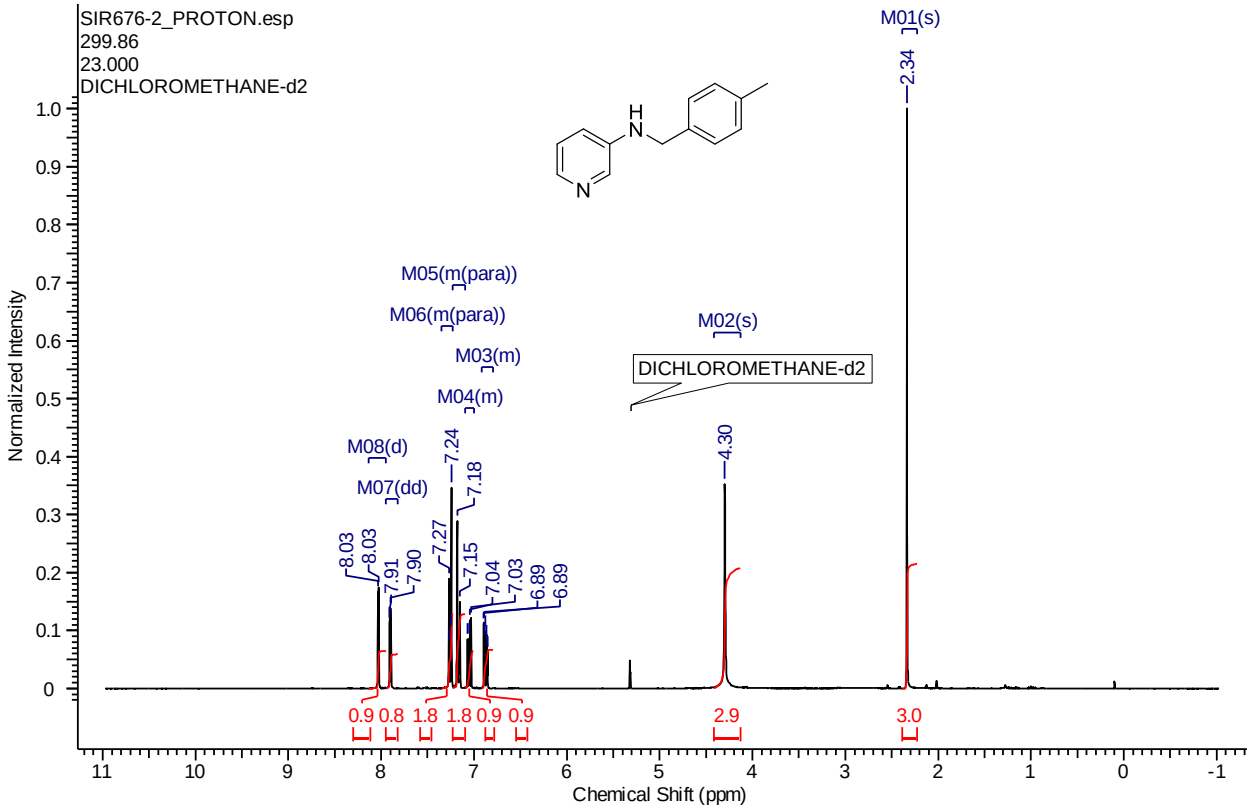


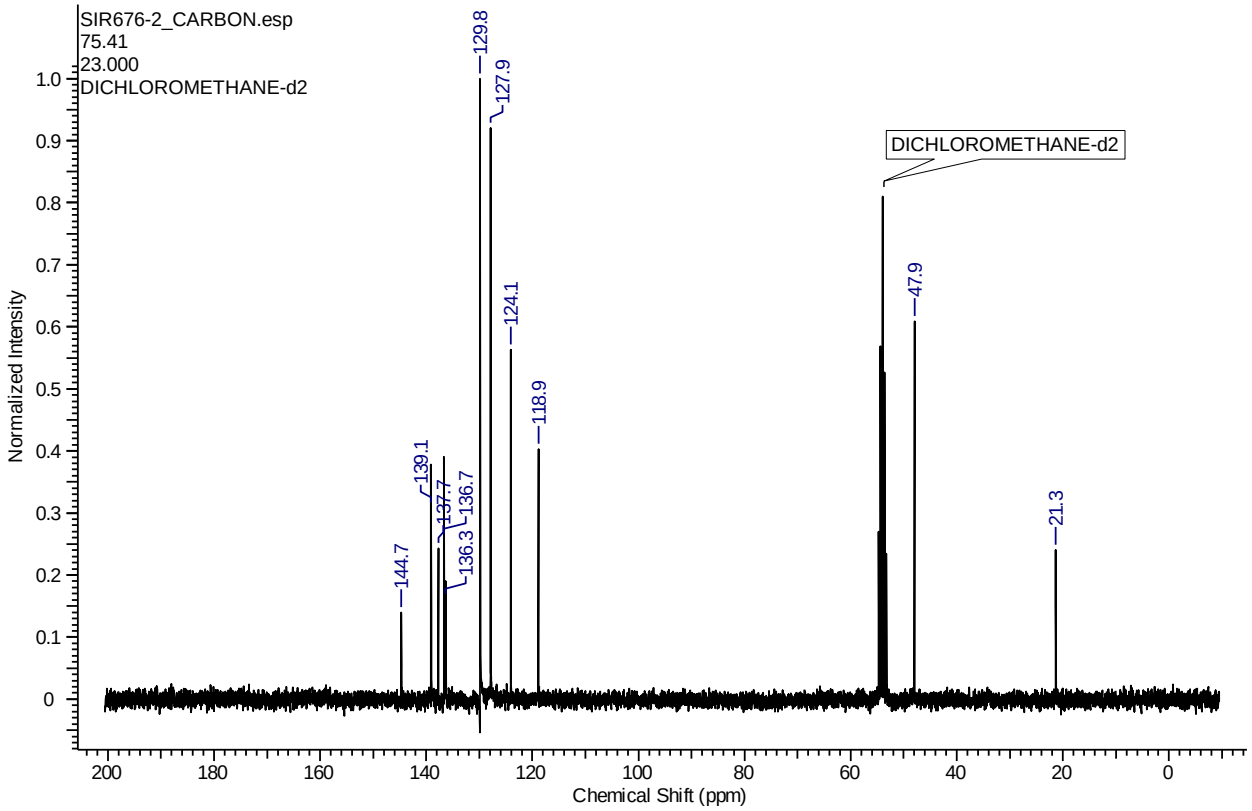
NMR spectra of N-(1-docosanoyl)pyridine-3-amine (5d):



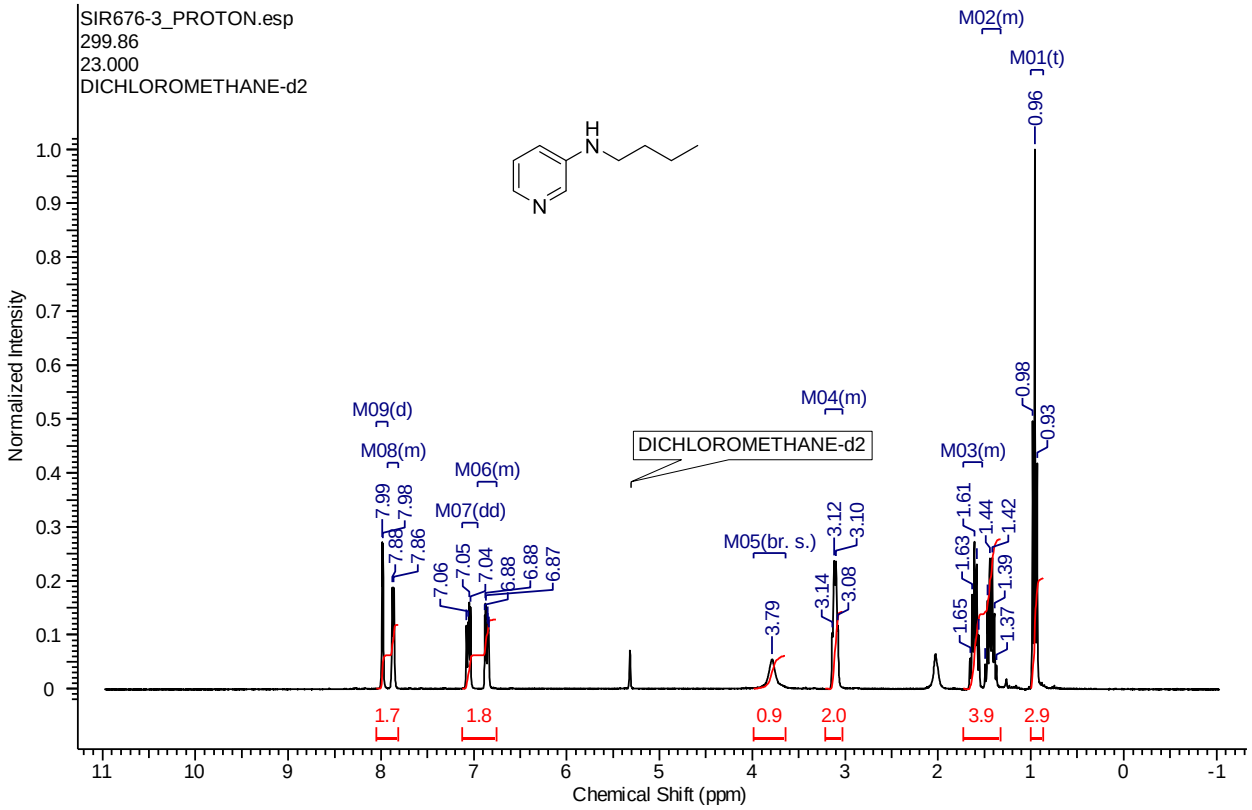


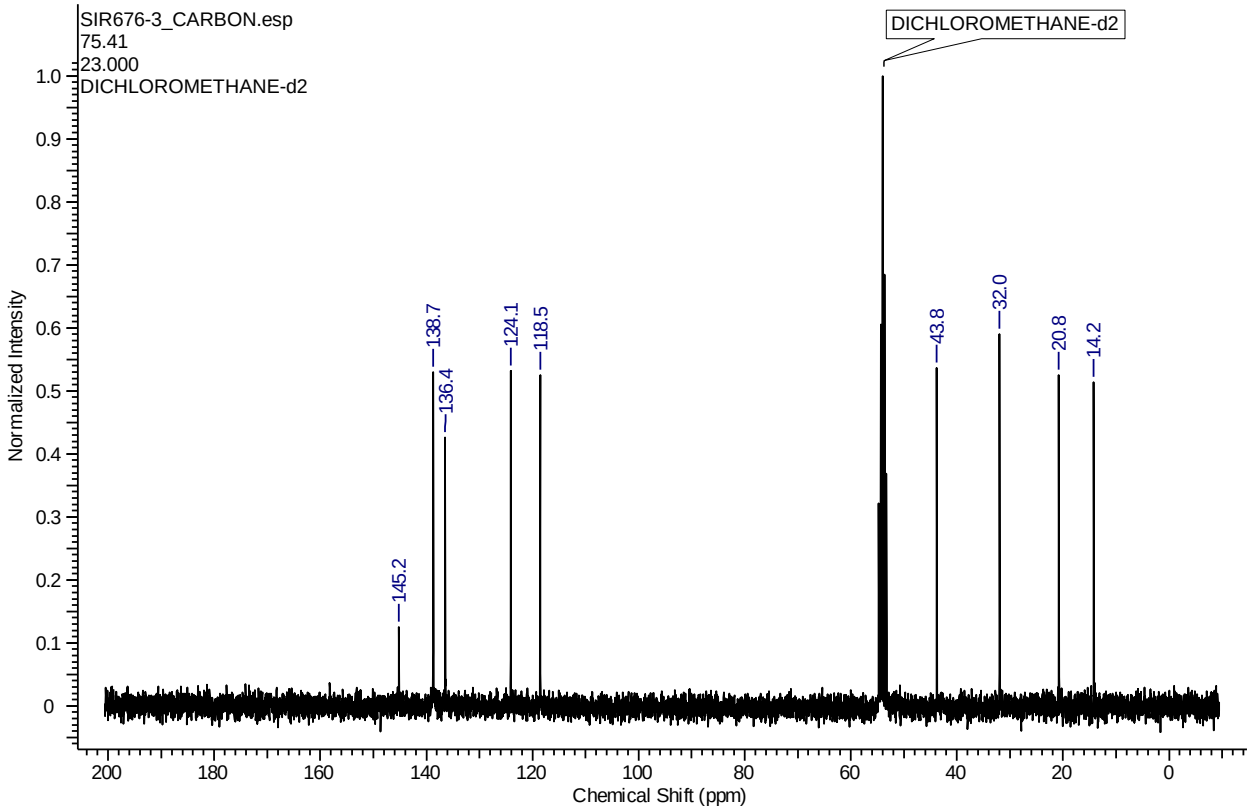
NMR spectra of N-(4-methylbenzyl)pyridine-3-amine (5f):



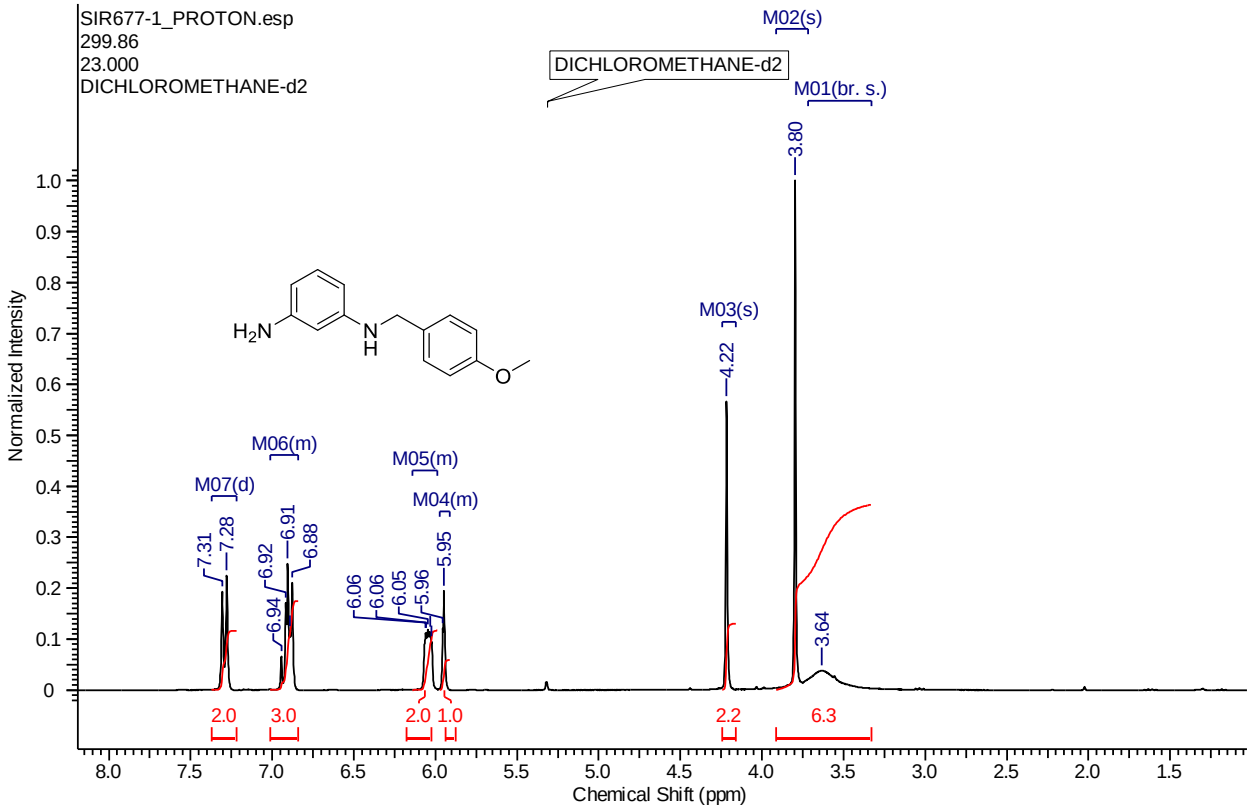


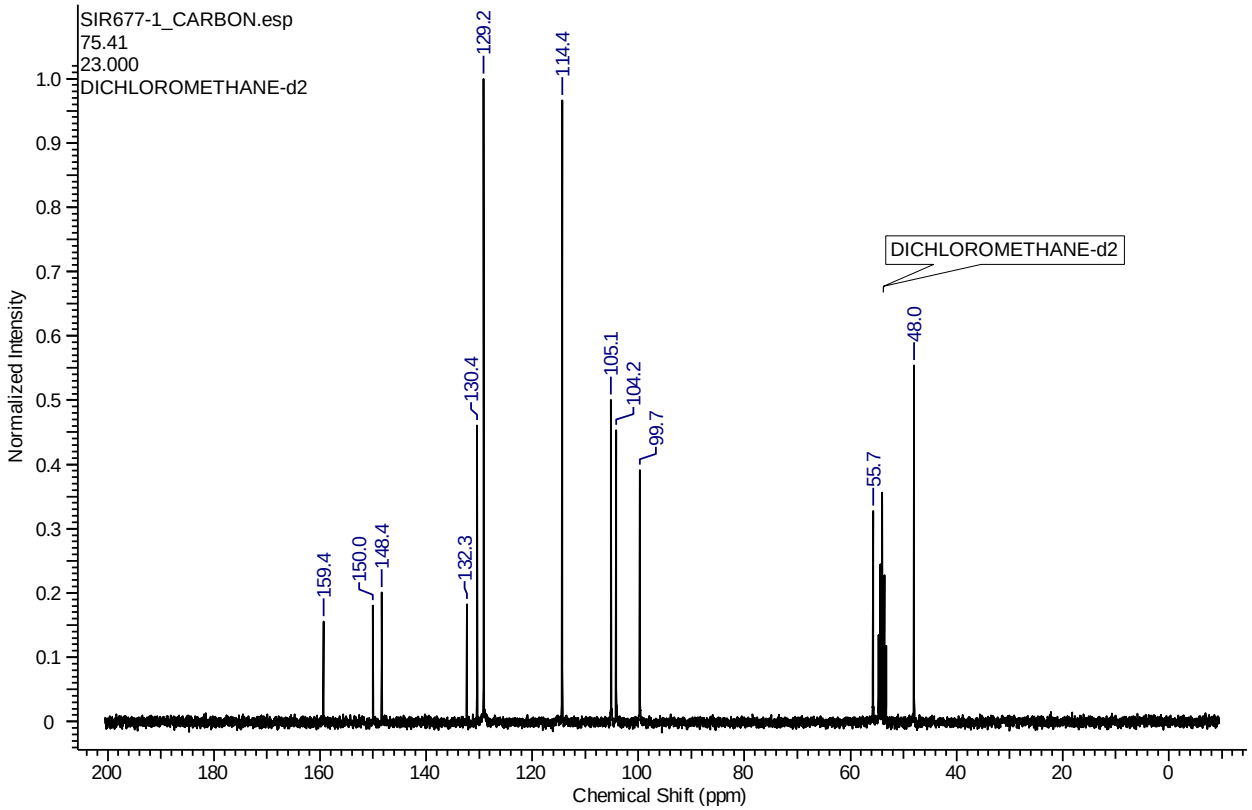
NMR spectra of N-(1-butyl)pyridine-3-amine (5e):



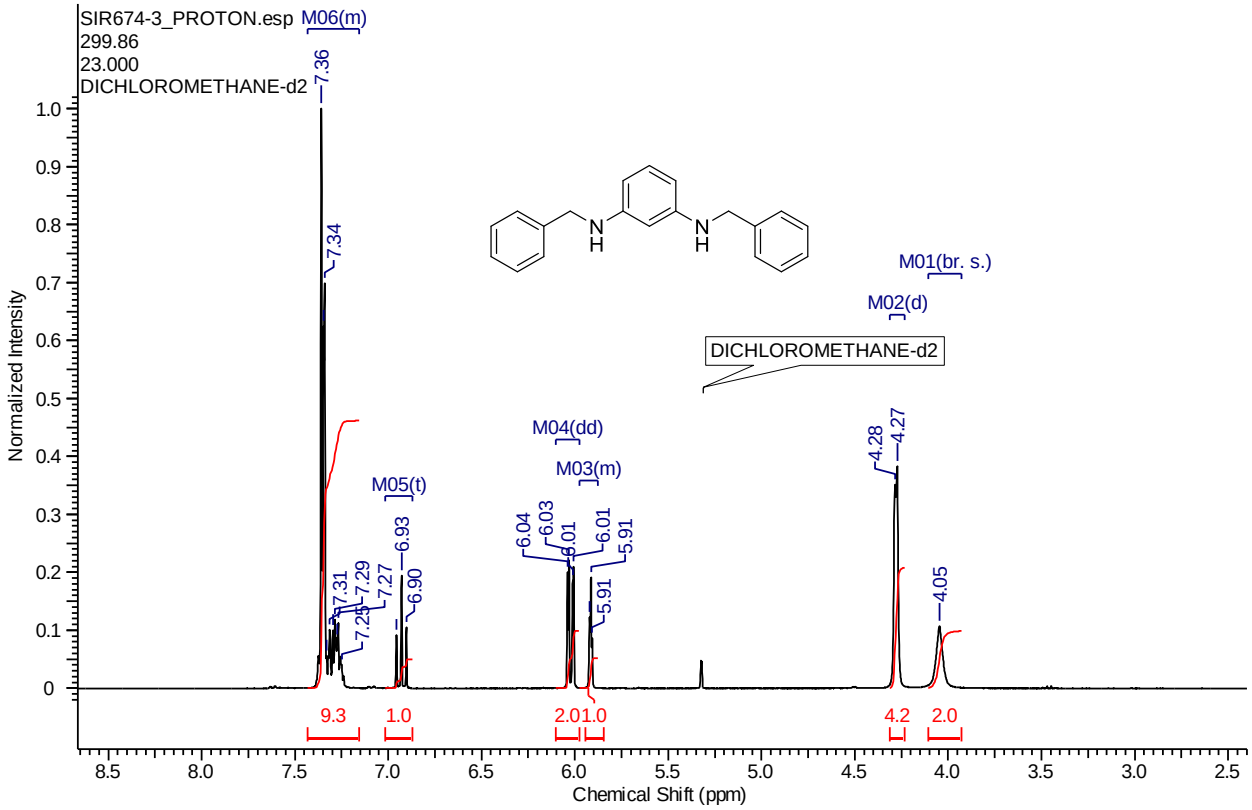


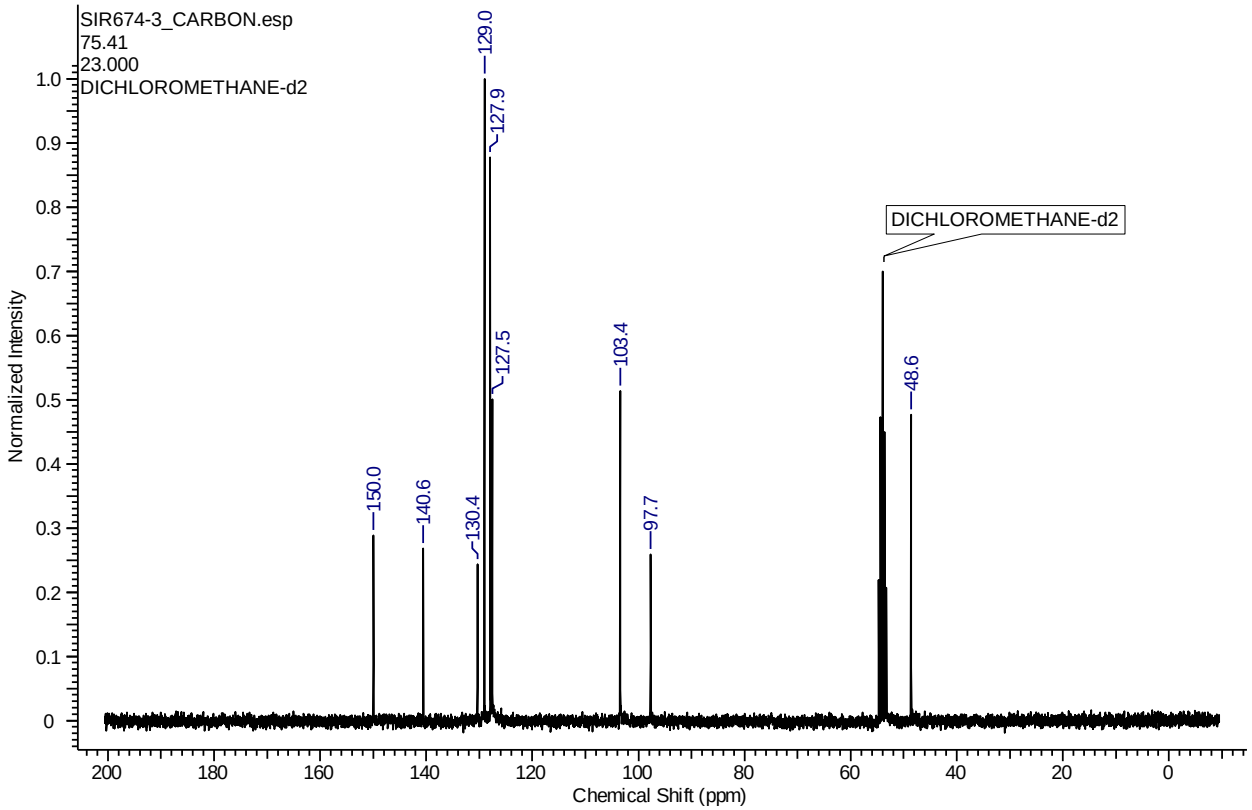
NMR spectra of N'-(4-methoxybenzyl)benzene-1,3-diamine (6a):



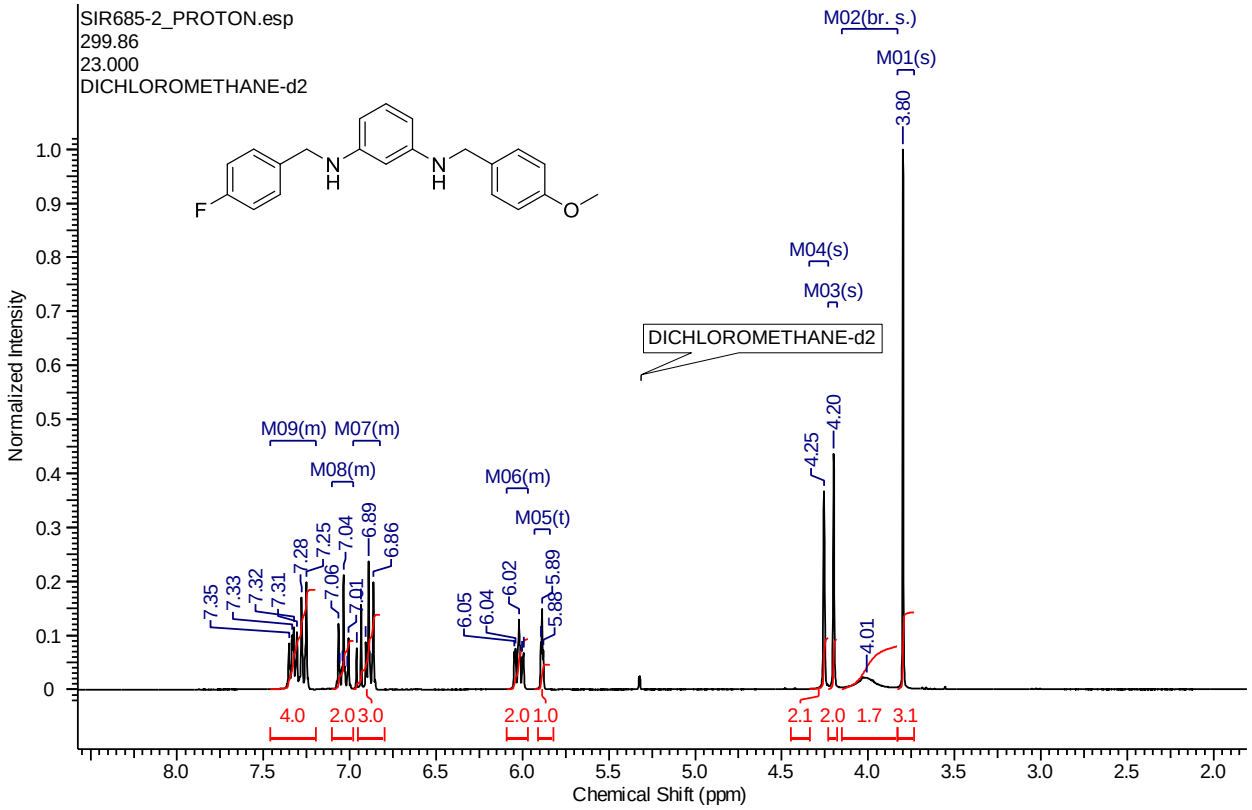


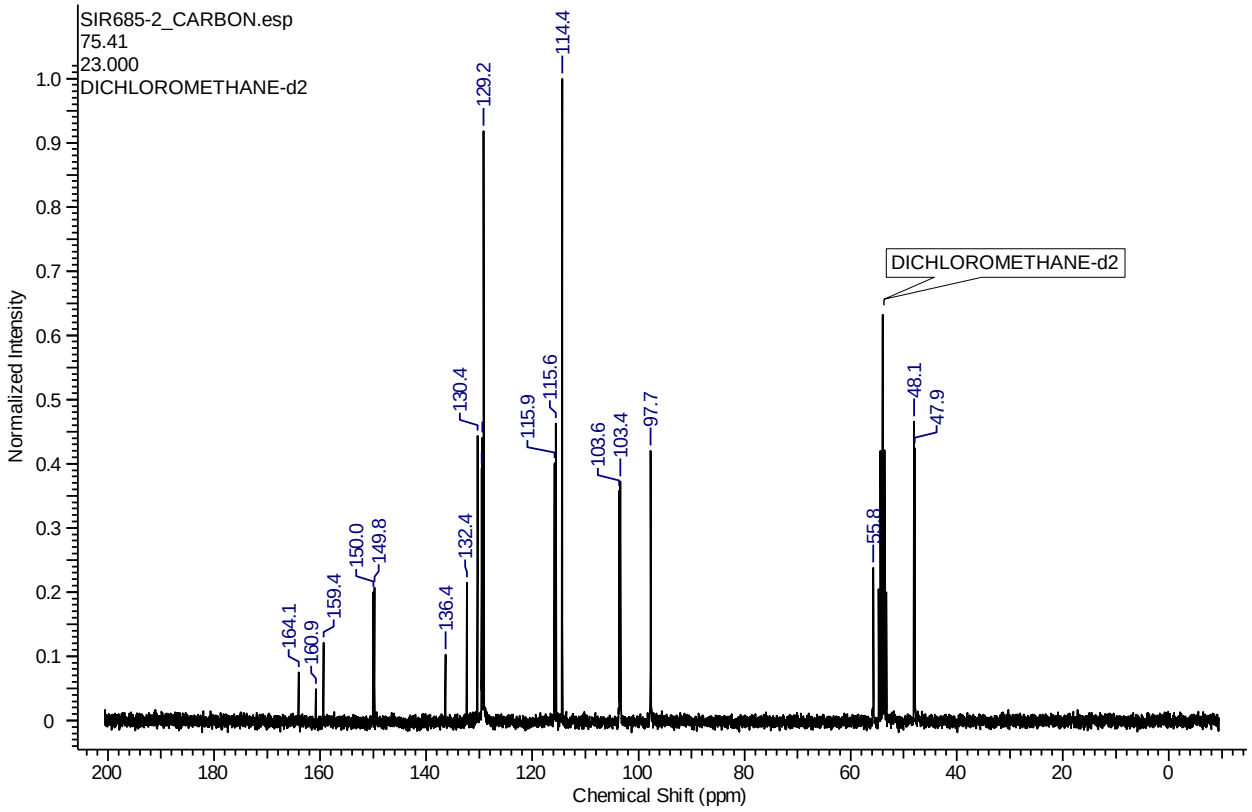
NMR spectra of N,N'-(dibenzyl)benzene-1,3-diamine (7a):



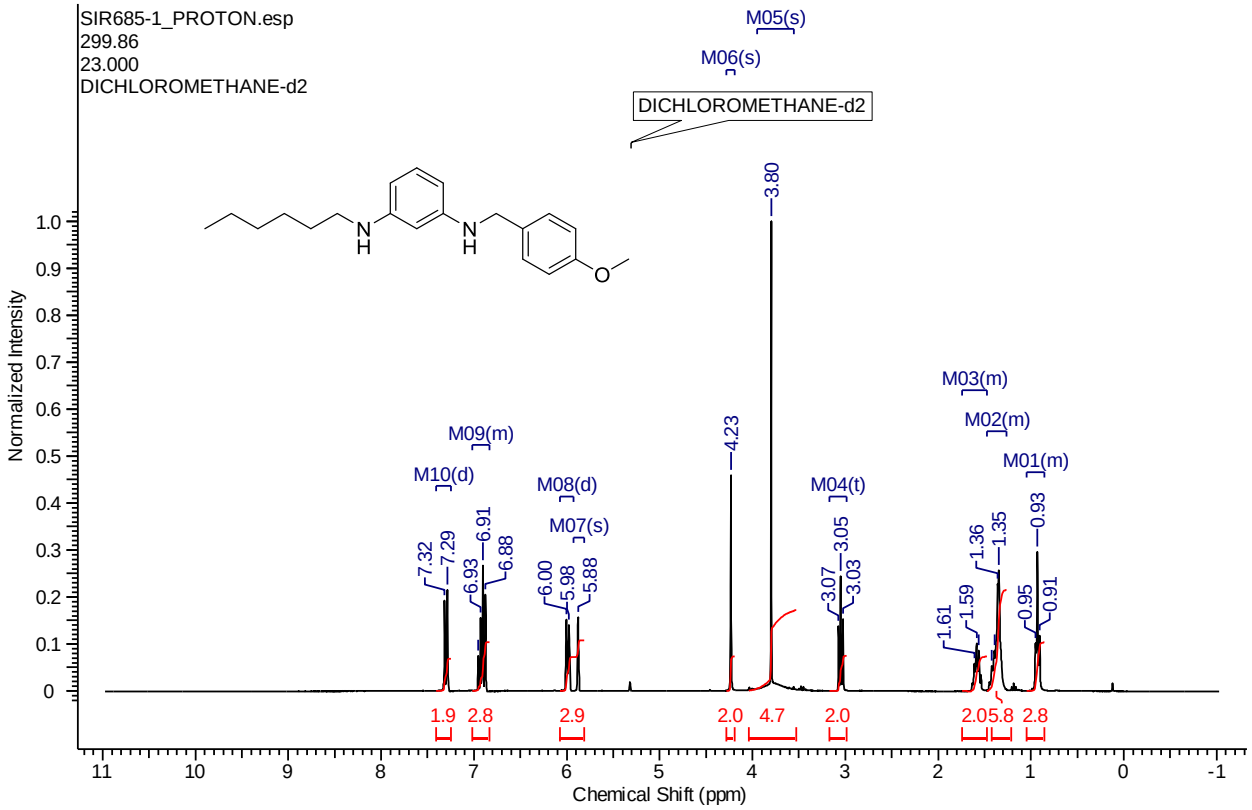


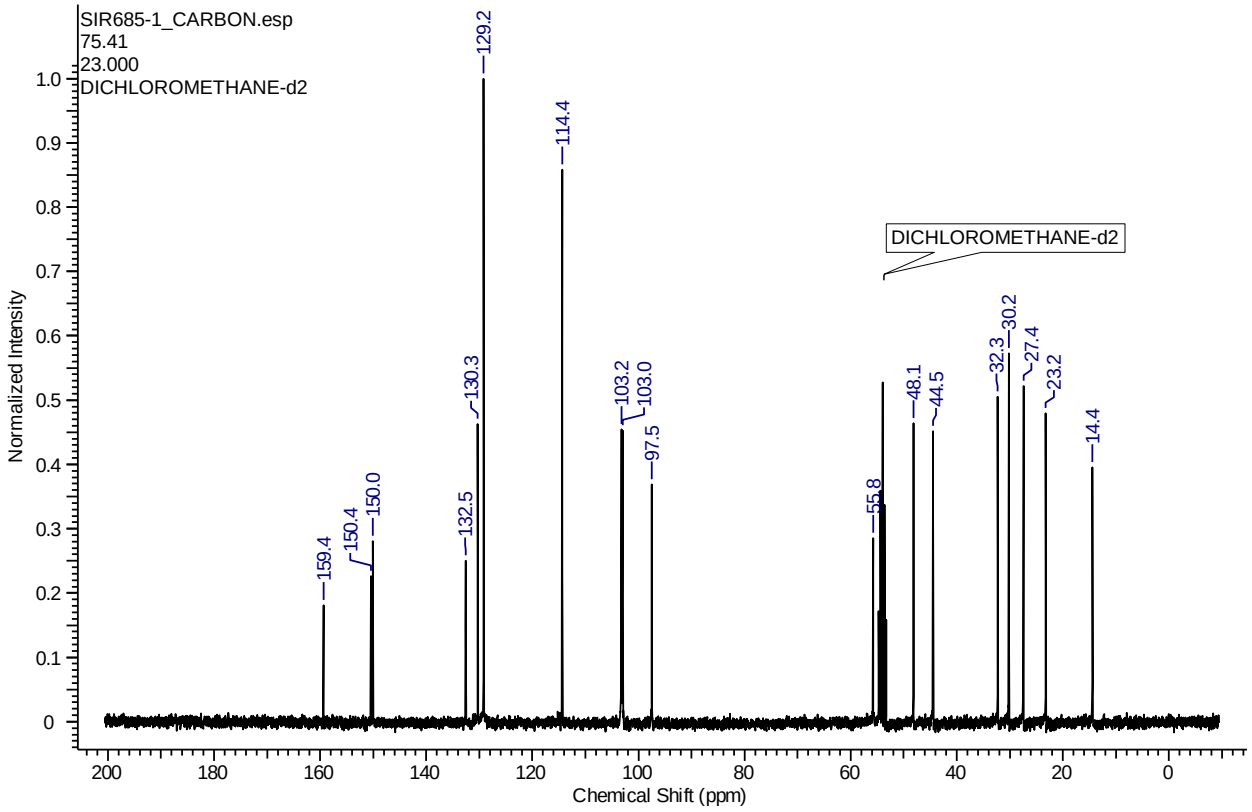
NMR spectra of N-(4-fluorobenzyl)-N'-(4-methoxybenzyl)benzene-1,3-diamine (7c):



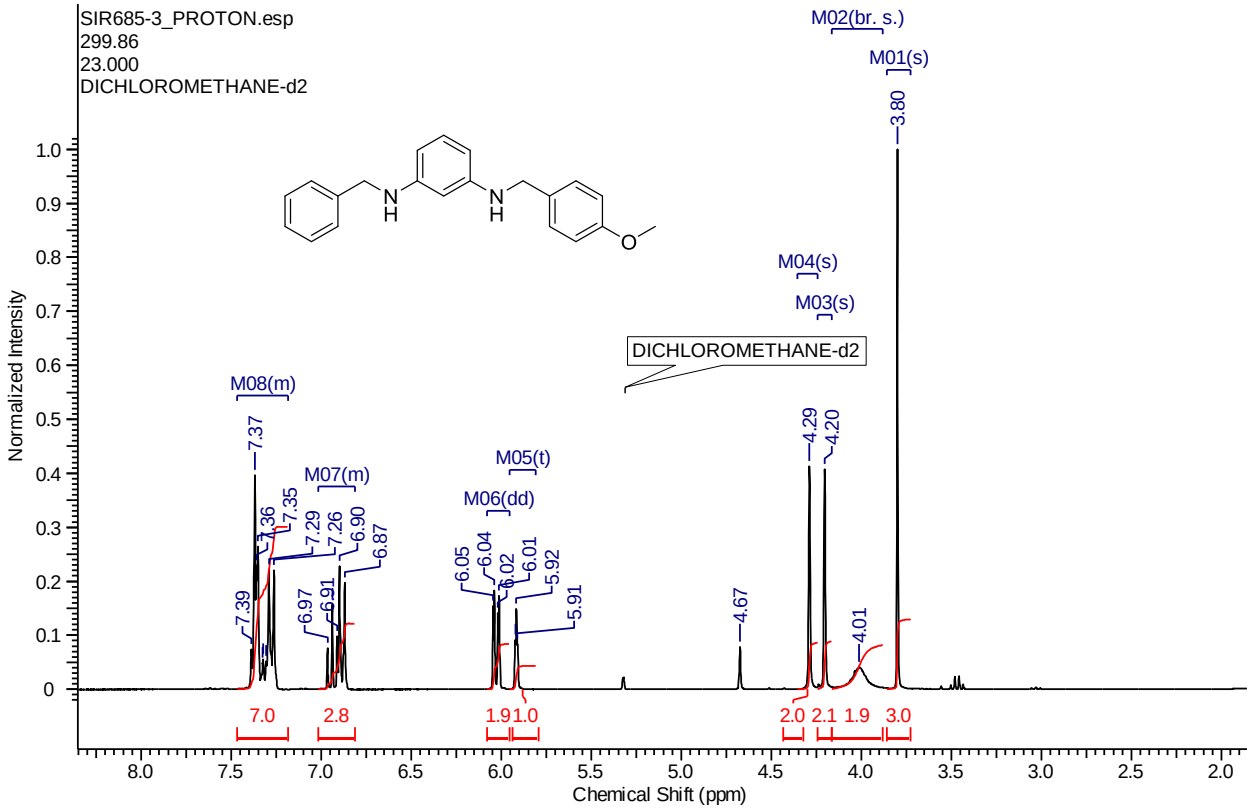


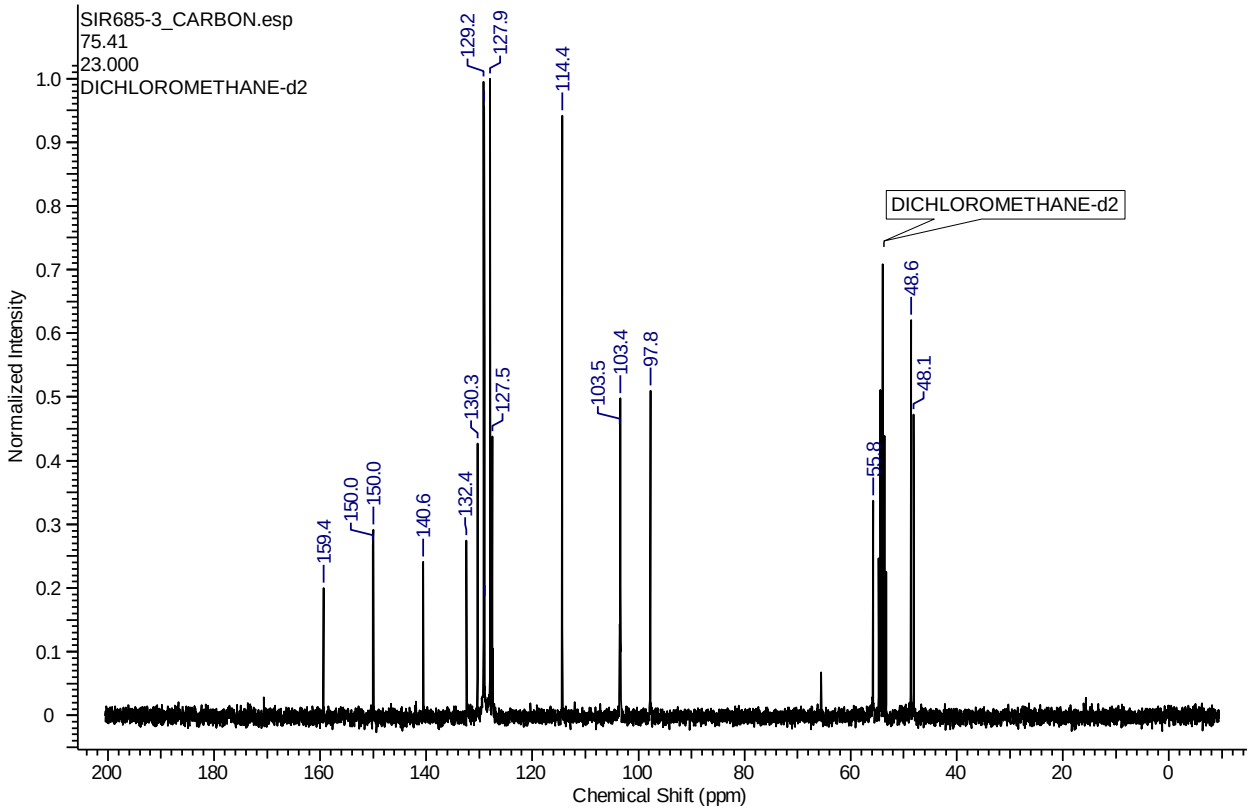
NMR spectra of N-(1-hexyl)-N'-(4-methoxybenzyl)benzene-1,3-diamine (7e):



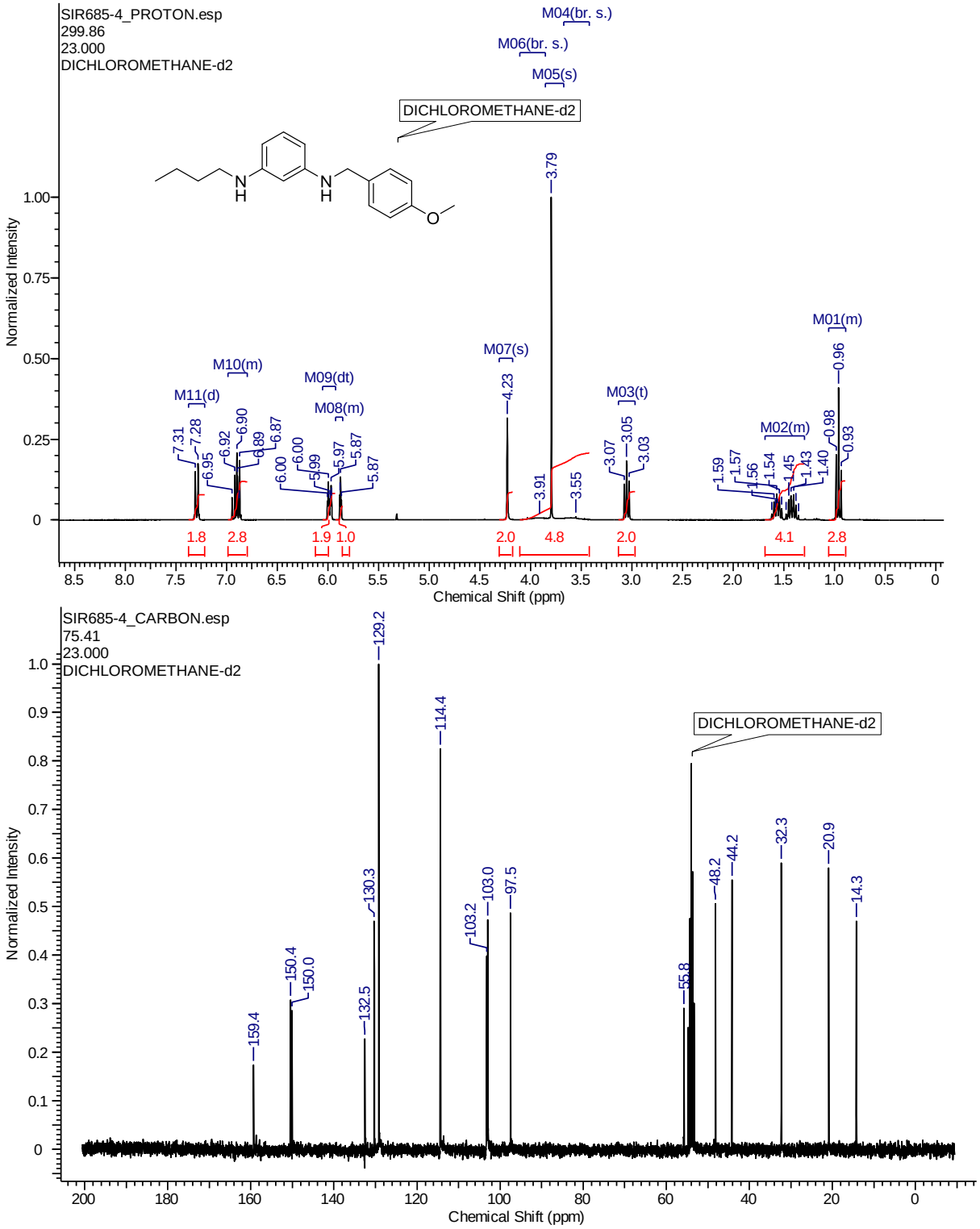


NMR spectra of N-(benzyl)-N'-(4-methoxybenzyl)benzene-1,3-diamine (7b):





NMR spectra of N-(1-butyl)-N'-(4-methoxybenzyl)benzene-1,3-diamine (7d):



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6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

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Abstract: A general and simple method for the synthesis of N-heterocycles such as pyridines, pyrroles and indoles, avoiding toxic reactants and over-stoichiometric waste, is a desirable goal. Here we report on a KO^{t}Bu mediated easy-to handle, broad applicable and simple one pot synthesis of pyridines, pyrroles and N-heterocycles based on such structural motifs starting from stable and easily accessible amino alcohols and ketones. The base mediates the hydrogen transfer to an acceptor molecule, which can be easily removed and recycled.

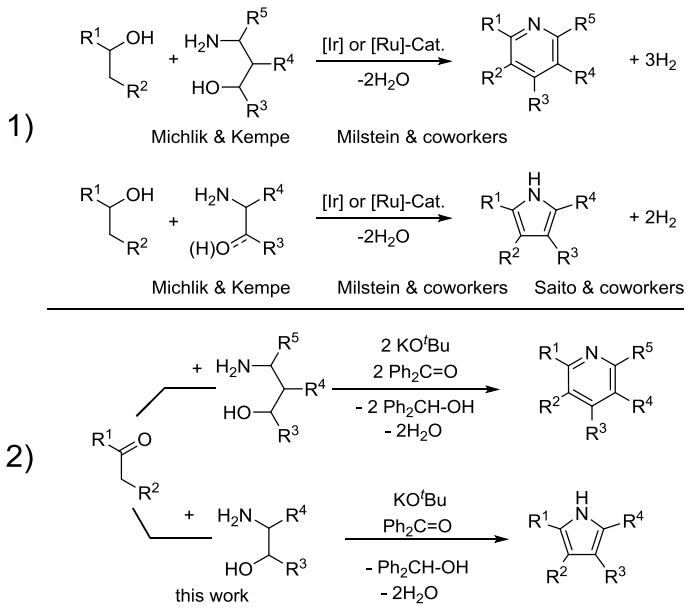
6.1 Introduction

N-Heterocycles such as pyridines and pyrroles are important motifs in several pharmaceuticals and agrochemicals.[1] The catalytic concept of acceptor-less dehydrogenation condensation (ADC) enables the efficient, atom-economical and sustainable synthesis of N-heterocycles. Pioneering work on this topic were made by the groups of Ishii and Crabtree.[2] Inspired from this work, our group reported first on the iridium catalyzed sustainable synthesis of regioselective substituted NH-pyrroles via ADC (Scheme 1).[3] Almost simultaneously the Ru catalyzed synthesis of N-substituted pyrroles and NH-pyrroles starting from ketones, diols and primary amines or ammonia was developed by Beller and coworkers.[4]. The groups of Milstein[5] and Saito[6] (Scheme 1) could show that ruthenium catalysts could be employed in the synthesis of N-heterocycles starting from amino alcohols and alcohols, too.

Based on these concepts[7] our group and several others published a few protocols for the synthesis of pyridines[8], benzimidazoles[9], qinoxalines[10] and quinolines[9b,11]. Very recently, a iridium catalyzed muti component reaction based on the ADC concept was reported by our group.[12]

Due to the high functional group tolerance of the catalysts, a broad substrate scope of various regioselective arylated and alkylated N-heterocycles is accessible.

6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols



Scheme 1. 1) Known transition metal catalyzed synthesis of pyridines and pyrroles via ADC. 2) KO^{t}Bu mediated synthesis of pyrroles, pyridines and such structural motifs, shown in this work.

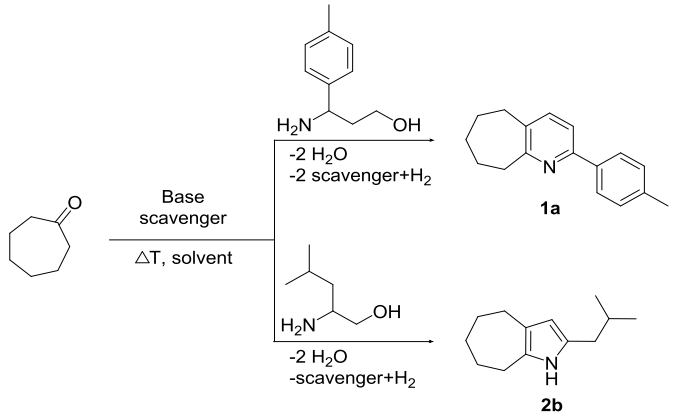
A substantial step in the ADC is the oxidation of the alcohol by the catalyst and the subsequently condensation of the generated carbonyl compound with the amine to build an imine,[13] followed by another ADC step to form the heterocycle. For all known methods catalytic (30 mol%) up to stoichiometric amounts of base, respectively KO^{t}Bu, are needed. In Ir catalyzed systems, the base is known to act as a proton transfer shuttle, and therefore mediates the cyclization.[14]

Due to its broad applicability, easy handling and simple accessibility KO^{t}Bu plays an important role in organic synthesis as well as an affordable base in organometallic chemistry. KO^{t}Bu, assessable in its basicity by the used solvent, mediates or catalyzes a variety of organic reactions[15] such as C-C,[16] C-N,[17] C-E[18] (E= S, Se, O) coupling reactions, exceptional isomerization reactions[19] and oxidation of alcohols[20]. Other alkali metal bases like KOH, K_2CO_3 and NaO^{t}Bu are also known to mediate these reactions.[21] Furthermore, KO^{t}Bu catalyzes the hydrogenation of benzophenone with molecular hydrogen under drastic conditions.[22] In 2008 the groups of Verpoort[23] and Yus[24] published simultaneously a base mediated synthesis of quinolones, starting from 2-aminobenzyl alcohol and several ketones in absence of a transition metal catalyst. In this process, the ketone itself or benzophenone acts as a hydrogen scavenger.

6.2 Results and Discussion

In this context we here report on a KO^{t}Bu mediated synthesis of pyridines, pyrroles and indoles starting from easily accessible and highly stable amino alcohols and carbonyl compounds without any transition metal catalyst. As a model substrate for the synthesis of pyridines, **1a**, starting from cycloheptanone and 3-amino-3-(p-tolyl)-1-propanol, was chosen (Scheme 2, Table 2). For the initial

experiments, benzophenone was used as hydrogen scavenger. To find the ideal conditions in a base screening, KO^{t}Bu was found as the best in selectivity and yield (Table 1) and THF as the ideal solvent at 90 °C extern reaction temperature (for details please see SI). After 2 h reaction time at these conditions, a yield of 97 % of **1a** was obtained. Two equiv. of water and hydrogen are formally released during the reaction. This hydrogen has to be transferred to an acceptor molecule in a Meerwein-Pondorf-Verley-Oppenauer reaction mechanism type.[25] Thus, several ketones (acetone, diisopropylketone, isopropyl-phenyl-ketone and benzophenone) were investigated as hydrogen acceptors. Benzophenone and isopropyl-phenyl-ketone showed the best performances (see SI, Table S1).



Scheme 2. Model reactions for the synthesis of pyridines (**1a**) and pyrroles (**2b**)

Table 1. Screening of base for the synthesis of **1a**[a].

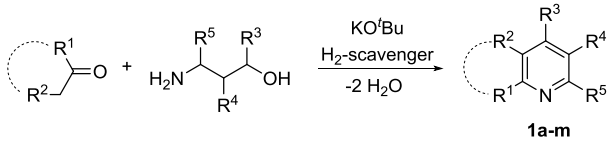
Entry	Base	Yield[b] [%]
1	KOH	29
2	KO^{t}Bu	95
3	KO^{t}Bu (99.99%, sublimed grade)	92
4	KH	63
5	K_2CO_3	traces
6	K[N(SiMe$_3$)$_2$]	70
7	NaOH	9
8	NaO^{t}Bu	63
9	LiO^{t}Bu	10
10	LiOH	-
11	Cs_2CO_3	-

[a] Reaction conditions: cycloheptanone (1.1 mmol), 3-amino-3-p-tolyl-1-propanol (1.0 mmol), benzophenone (2.5 mmol), base (2.5 mmol), 3 mL THF, 90 °C (extern temperature), 2 h. [b] Yield determined via GC with decane as internal standard.

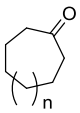
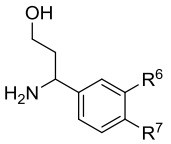
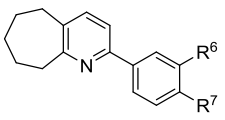
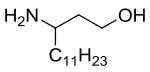
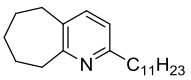
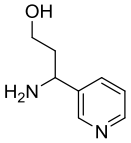
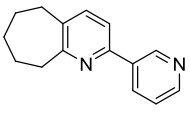
Due to its high accessibility, simple handling and easy removability of the corresponding alcohol, benzophenone was chosen for further experiments. 2.5 equiv. of benzophenone were found to be ideal for the synthesis of pyridines. Starting the reaction with cycloheptanol, the amount of base and scavenger has to be raised to a scavenger (or base) to alcohol ratio of not less than 3:1 (with respect to the amino alcohol). This observation is based on the additional equiv. of hydrogen in the alcohol oxidation step. In this case, **1a** was obtained in 83 % yield. Finally, KO^{t}Bu (reagent grade) is known to have transition metal impurities, which could be responsible for the shown activity. Thus, a run under optimized conditions with KO^{t}Bu (sublimed grade, 99.99 % trace metal basis) was accomplished (Table 1, entry 3). No significant loss in the product yield was observed.

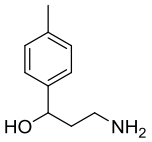
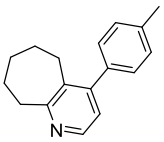
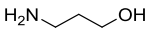
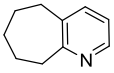
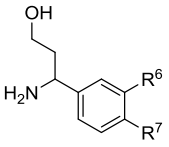
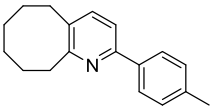
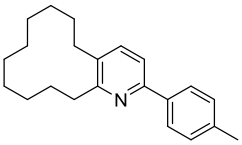
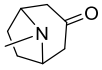
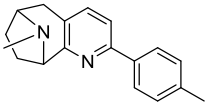
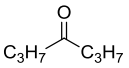
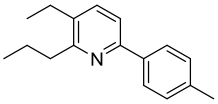
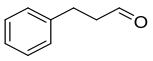
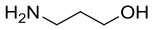
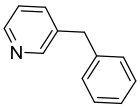
With this protocol pyridines, starting from 1,3-amino alcohols and different ketones were synthesized and isolated by simple acidic basic extraction (Table 2). Bicyclic pyridines were isolated in good to excellent yields (Table 2, **1a-l**), varying the substitution pattern of the 1,3-amino alcohol. Variation of the ring size (C_7-C_{12}) of the cyclic ketone (**1a, 1j-k**) is as well as possible as the use of 1- or 3-substituted 1,3-amino alcohols (**1a-f, 1g**). Remarkably, no products were obtained with C_6 and C_5 ring sizes. Combination of an aliphatic aldehyde and 3-amino-1-propanol results in a 3-substituted pyridine (**1m**). A (symmetric), aliphatic ketone leads to an 2,3,6-substituted pyridine (**1l**) in moderate yield.

Table 2. Synthesized pyridines[a]



1a-m

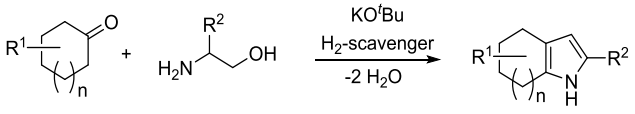
Entry	Nr.	Ketone	Amino alcohol	Product	Yield[b][%]
1	**1a**	 n=1	 R^6=H, R^7=Me		97
2	**1b**	n=1	R^6=H, R^7=Cl		91
3	**1c**	n=1	R^6=H, R^7=H		97
4	**1d**	n=1	R^6=OMe, R^7=OMe		86
5	**1e**	n=1			92[c]
6	**1f**	n=1			79

7	**1g**	n=1			82
8	**1h**	n=1			56 (70[d])
9	**1i**	n=2	 R^6=H, R^7=Me		65[c]
10	**1j**	n=6	R^6=H, R^7=Me		57[e]
11	**1k**		R^6=H, R^7=Me		66
12	**1l**		R^6=H, R^7=Me		57
13	**1m**				35

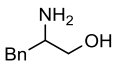
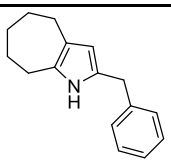
[a] Reaction conditions: 5.5 mmol carbonyl compound, 5.0 mmol amino alcohol, 12.5 mmol benzophenone, 12.5 mmol KO^{t}Bu, 10 mL THF, 90 °C, 2 h. [b] Yield of isolated product. [c] 12.5 mmol Isobutyrophenone. [d] Starting from isolated imine. [e] 12.5 mmol Isobutyrophenone, 110 °C (extern temperature), 24 h.

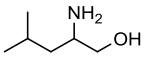
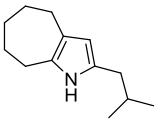
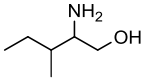
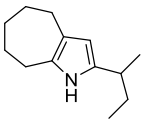
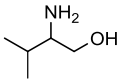
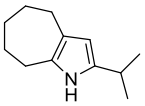
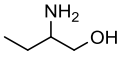
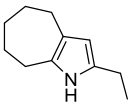
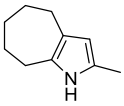
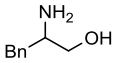
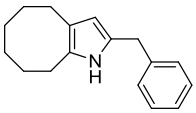
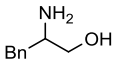
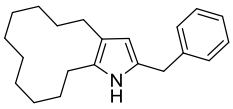
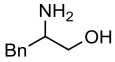
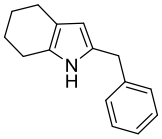
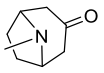
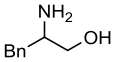
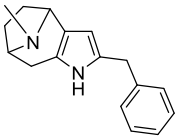
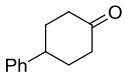
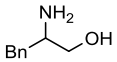
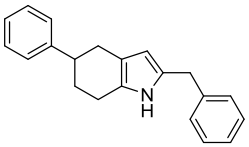
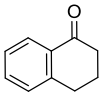
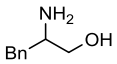
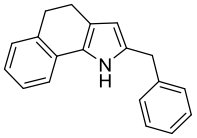
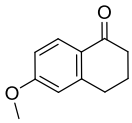
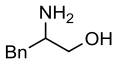
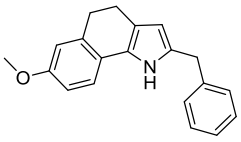
Next, we became interested in the synthesis of substituted pyrroles with this method. Therefore, the protocol was optimized for the preparation of **2b** (Scheme 2, Table 3) as a model compound (see SI). The extern reaction temperature was raised to 110 °C with a reaction time of 24 h. The optimized ratio of base and scavenger to amino alcohol was 1:1. Again, KO^{t}Bu and THF were found as ideal base and solvent. Isobutyrophenone was used as scavenger and was distilled off for product isolation.

Table 3. Synthesized cyclic pyrroles and indoles[a]



2a-m

Entry	Nr.	Ketone	Amino alcohol	Product	Yield[b][%] (GC)[c]
1	**2a**	n=2			59 (79)

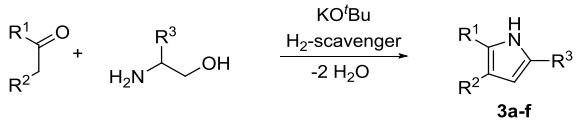
2	**2b**	n=2			66 (80)
3	**2c**	n=2			49 (60)
4	**2d**	n=2			54 (71)
5	**2e**	n=2			78 (89)
6	**2f**	n=2			72 (86)
7	**2g**	n=3			69 (82)
8	**2h**	n=7			45 (67)
9	**2i**	n=1			52 (56)
10	**2j**				65 (72)
11	**2k**				38 (51)
12	**2l**				62 (71)
13	**2m**				52 (65)

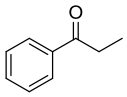
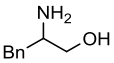
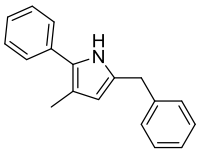
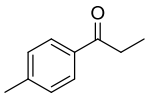
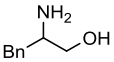
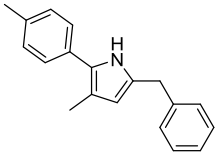
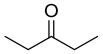
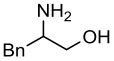
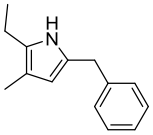
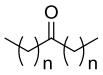
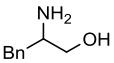
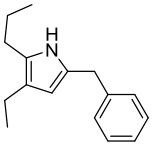
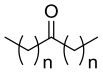
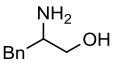
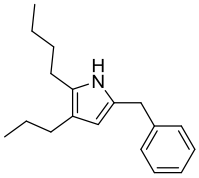
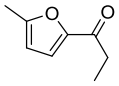
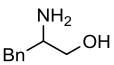
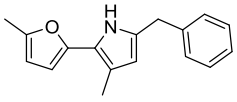
[a] Reaction conditions: 22.0 mmol ketone, 20.0 mmol amino alcohol, 25.0 mmol isobutyrophenone, 25.0 mmol KO^tBu, 20 mL THF, 110 °C (extern temperature), 24 h. [b] Yield of isolated product. [c] Yield determined via GC with decane as internal standard.

To our delight, a broad product scope of 2-substituted bicyclic pyrroles and indoles (Table 3) and 2,3,5-substituted pyrroles (Table 4) were obtained with this method. By variation of the β-amino alcohol, different alkyl and aryl substituents are introduced, limiting to the naturally occurring amino

acids. Various bicyclic pyrroles (**2a-h, 2j**) were synthesized with ring sizes from C_7 to C_{12}. Furthermore, two indoles (**2i, 2k**) and two novel compounds (**2l**, **2m**) were synthesized in good yields. With derivatives of propiophenone, 2,3,5-substituted pyrroles (**3a** and **3b**, Table 4) were received. Halogenated analogues of propiophenone led to a mixture of the desired product and the de-halogenated analogue. Symmetric aliphatic ketones led to aliphatic 2,3,5-substituted pyrroles (Table 4, **3c-e**), whereas with 2-(5-methyl)propionyl-furan a novel heterocyclic substituted pyrrole (**3f**) was synthesized.

Table 4. Synthesized 2,3,5-substituted pyrroles[a]



Entry	Nr.	Ketone	Amino alcohol	Product	Yield[b][%] (GC)[c]
1	**3a**				60 (67)
2	**3b**				41 (57)
3	**3c**				56 (73)
4	**3d**	 n=2			47 (59)
5	**3e**	 n=3			54 (58)
6	**3f**				36 (53)

[a] Reaction conditions: 22.0 mmol ketone, 20.0 mmol amino alcohol, 25.0 mmol isobutyrophenone, 25.0 mmol KO^{t}Bu, 20 mL THF, 110 °C (extern temperature), 24 h. [b] Yield of isolated product. [c] Yield determined via GC with decane as internal standard.

6.3 Conclusion

In conclusion, we here reported on a transition metal free, simple and broad applicable method for the synthesis of various pyridines and pyrroles. Starting from inexpensive starting materials, easily accessible and stable carbonyl compounds and amino alcohols, a broad scope of substituted pyridines, pyrroles and indoles are synthesizable in an one pot reaction. The shown method is reproducible up to gram scales, easy-to-handle and doesn't need any transition metal catalyst.

6.4. References

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6.5 Supporting Information

General considerations:

Nonhalogenated solvents were dried over sodium benzophenone and halogenated solvents were dried over P_2O_5. Deuterated solvents were ordered from Cambridge Isotope Laboratories, vented, stored over molecular sieves and distilled. All chemicals were purchased from commercial sources with purity with over 95 % and used without further purification. NMR spectra were received using an INOVA 300 MHz spectrometer. Chemical shifts are reported in ppm relative to the deuterated solvent. GC analyses were carried out on an Agilent Technologies 6890N system equipped with a HP-5 column (30 m x 320 µm x 0.25 µm). GC/MS analyses were carried out on an Agilent 7890A/MSD 5975C system equipped with a HP-5MS column (30 m x 320 µm x 0.25 µm).

General procedure for Pyridine / Pyrrole / Indole synthesis:

All reactions were carried out under a dry argon / nitrogen atmosphere using schlenk techniques or glove box techniques. Ketone, amino alcohol, base, solvent and scavenger were combined in a pressure tube and closed with a teflon cap. The reaction was stopped by addition of 2 mL of water.

Screening Reactions:

General screening procedure: In a pressure tube ketone, amino alcohol, scavenger, base and solvent were combined and closed with a teflon cap. The reaction was stirred for 1 h at 110 °C. The reaction mixture was cooled to room temperature and decane was added as internal standard. After extraction with Et_2O a GC sample was prepared.

6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

Standard screening reaction for pyridine synthesis:

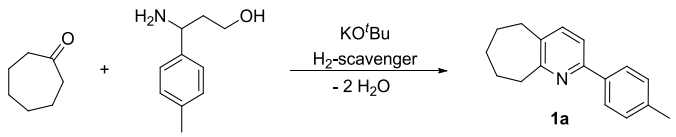
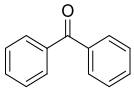
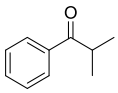


Table S1. Scavenger screening

Scavenger	Yield [%]
——	17
	traces
	32
	93
	91

Reaction conditions: Cycloheptanone (1.1 eq.), 3-amino-3-tolyl-1-propanol, scavenger (3.0 eq.), KO^{t}Bu (3.0 eq.), 5 mL dioxane, 110 °C (extern temperature), 1 h. Yields determined by GC analyses with decane as internal standard.

Table S2. Screening of ratio scavenger to amino alcohol

Scavenger / Amino Alcohol	Yield [%]
1.0 / 1.0	53
1.5 / 1.0	69
2.0 / 1.0	72
2.5 / 1.0	85
3.0 / 1.0	81

Reaction conditions: Cycloheptanone (1.1 eq.), 3-amino-3-tolyl-1-propanol, benzophenone, KO^{t}Bu (3.0 eq.) 5 mL dioxane, 110 °C (extern temperature), 1 h. Yields determined by GC analyses with decane as internal standard.

Table S3. Base screening

Base	Yield [%]
KOH	29
KO^{t}Bu	95
KO^{t}Bu 99.99%	92

KH	63
K_2CO_3	traces
$K[N(SiMe_3)_2]$	70
NaOH	9
NaO^tBu	63
LiO^tBu	10
LiOH	-
Cs_2CO_3	-

Reaction conditions: Cycloheptanone (1.1 eq.), 3-amino-3-tolyl-1-propanol, benzophenone (2.5 eq.), base (2.5 eq.), 3 mL THF, 90 °C (extern temperature), 2 h. Yields determined by GC analyses with decane as internal standard.

Table S4. Amount of KO^tBu

Amino alcohol / KO^tBu	Yield [%]
1.0 / 1.0	62
1.0 / 1.5	67
1.0 / 2.0	91
1.0 / 2.5	93
1.0 / 3.0	92

Reaction conditions: Cycloheptanone (1.1 eq.), 3-amino-3-tolyl-1-propanol, benzophenone (3.0 eq.), KO^tBu, 5 mL dioxane, 110 °C (extern temperature), 1 h. Yields determined by GC analyses with decane as internal standard.

Table S5. Solvent screening

Solvent	Yield [%]
dioxane	81
diglyme	84
THF	92
toluene	78

Reaction conditions: Cycloheptanone (1.1 eq.), 3-amino-3-tolyl-1-propanol, benzophenone (3.0 eq.) KO^tBu (3.0 eq.), 5 mL solvent, 110 °C (extern temperature), 1 h. Yields determined by GC analyses with decane as internal standard.

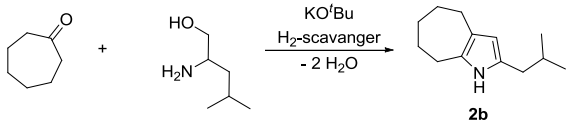
Table S6. Temperature screening

Temperature (extern)	Yield [%]
70 °C	82
90 °C	90
110 °C	89

6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

Reaction conditions: Cycloheptanone (1.1 eq.), 3-amino-3-tolyl-1-propanol, benzophenone (3.0 eq.), KO^{t}Bu (3.0 eq.), 5 mL THF, 1 h. Yields determined by GC analyses with decane as internal standard

Standard screening reaction for pyrrole synthesis:



2b

Table S7. Solvent screening

Solvent	Yield [%]
dioxane	46
diglyme	44
THF	75
toluene	48

Reaction conditions: Cycloheptanone (1.1 eq.), leucinol, isobutyrophenone (1.25 eq), KO^{t}Bu (1.25 eq.), 5 mL solvent, 110 °C (extern temperature), 16 h. Yields determined via GC analyses with decane as internal standard.

Table S8. Reaction time

Reaction time [h]	Yield [%]
4	49
16	75
24	88

Reaction conditions: Cycloheptanone (1.1 eq.), leucinol, isobutyrophenone (1.25 eq.), KO^{t}Bu (1.25 eq.), 5 mL THF, 110 °C (extern temperature). Yields determined by GC analyses with decane as internal standard.

Table S9. Base screening

Base	Yield [%]
KOH	17
NaOH	8
KO^{t}Bu	88
NaO^{t}Bu	30
KH	76

Reaction conditions: Cycloheptanone (1.1 eq.), leucinol, isobutyrophenone (1.25 eq.), base (1.25 eq.), 5 mL THF, 110 °C (extern temperature), 24 h. Yields determined by GC analyses with decane as internal standard.

6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

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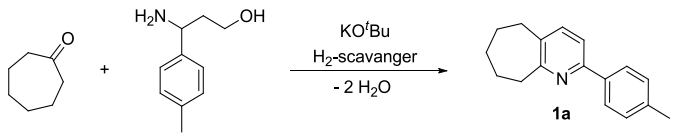
FT-IR measurements



All FT-IR measurements were carried out with a Mettler Toledo React IR 45m with MCT detector equipped with a DiComp (Diamond) AgX 6 mm x 1.5 mm Fibre (silver halide). Reactions were performed in a 100 mL three neck round bottom flask equipped with a magnetic stir bar and a reflux condenser. The FT-IR probe tip was placed inside and a background spectrum was collected. Amino alcohol (825 mg, 5.0 mmol) was dissolved in 5 mL toluene and heated to reflux. After collecting a reference spectrum, isobutyrophenone (1.52 mL, 10 mmol) as scavenger and potassium-*tert*-butoxide (1.20 g, 10 mmol) were added one after another and reference spectra were collected respectively. The reaction was started with addition of cycloheptanone (592 µL, 5.0 mmol). Sample spectra (32 scans, resolution at 4 wavenumbers) were collected from 1900 cm^{-1} to 650 cm^{-1} each 2 minutes, after 40 minutes the sample interval was raised to 10 min.

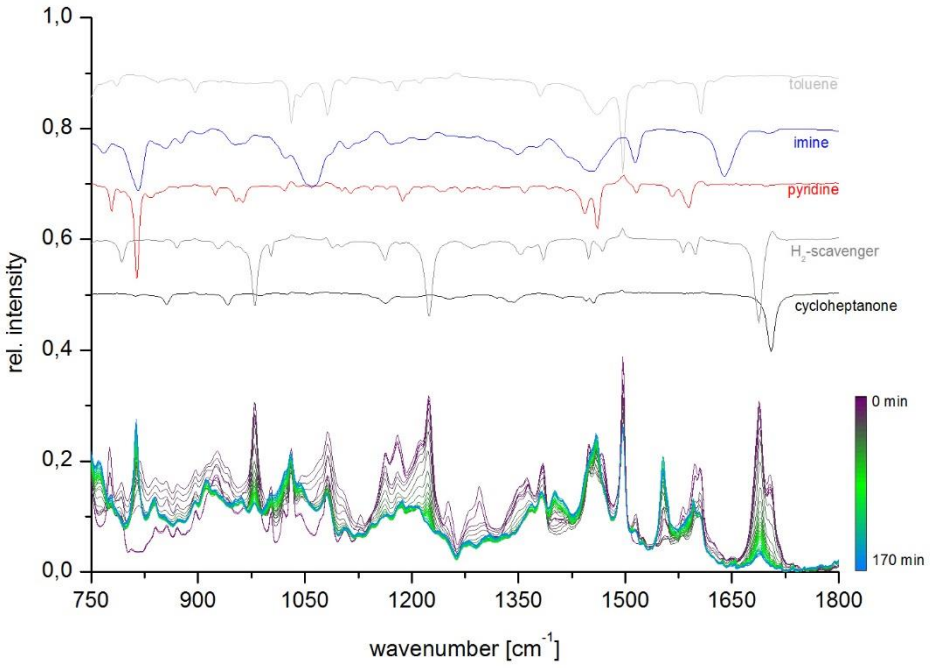


Figure S1. Overview of collected spectra during the reaction.

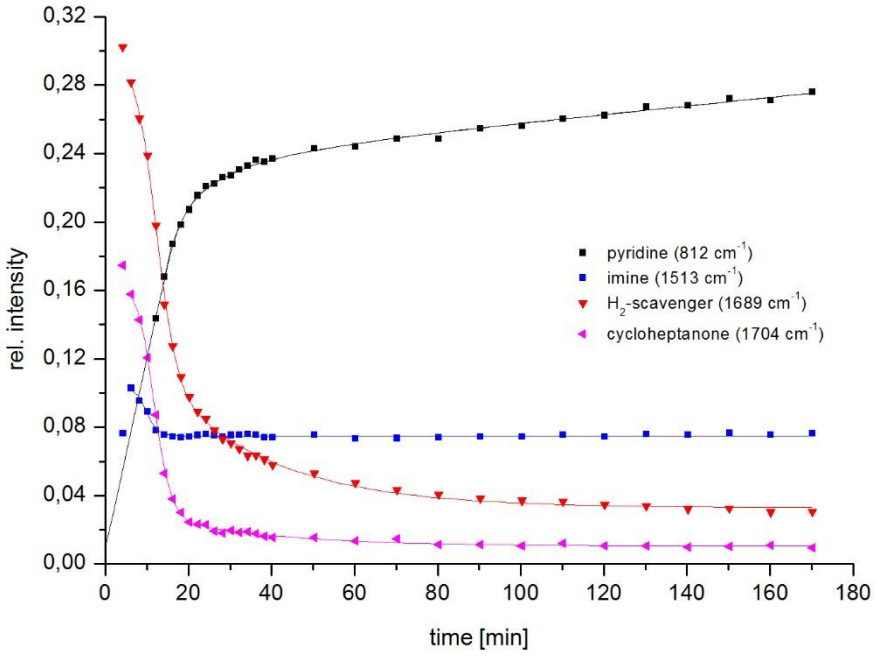
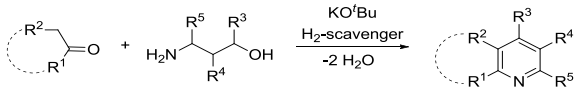
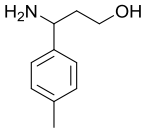
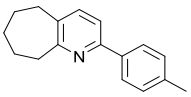
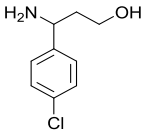
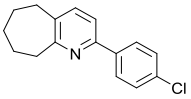
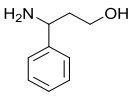
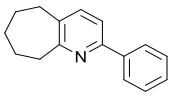
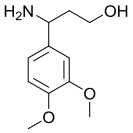
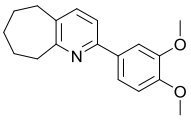
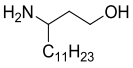
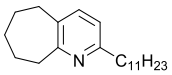
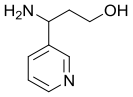
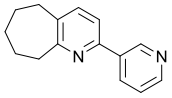
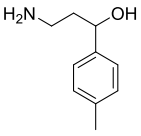
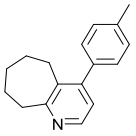
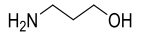
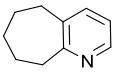
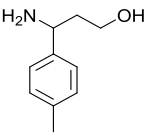
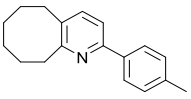
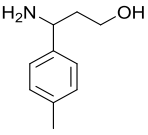
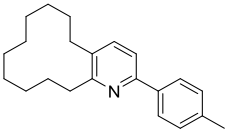
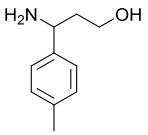
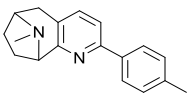
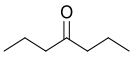
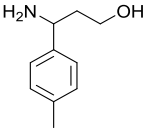
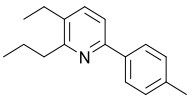


Figure S2. Time vs. rel. intensity plot of representative vibrations.

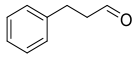
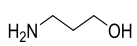
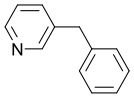
6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

Table S10. Synthesized pyridines[a]

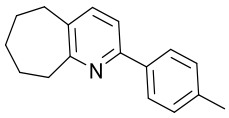


Nr.	Carbonyl Compound	Amino Alcohol	Product	Yield[b] [%]
1a				97
1b				91
1c				97
1d				86
1e				92[c]
1f				79
1g				82
1h				56 (70[e])
1i				65[c]
1j				57[d]
1k				66
1l				57[c]

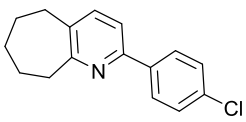
6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

1m				35

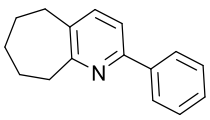
[a] Reaction conditions: 5.5 mmol carbonyl compound, 5.0 mmol amino alcohol, 12.5 mmol benzophenone, 12.5 mmol KO^{t}Bu, 10 mL THF, 90 °C, 1 h. [b] Isolated yield. [c] 12.5 mmol Isobutyrophenone, 90 °C, 2 h. [d] 12.5 mmol Isobutyrophenone, 110 °C (extern temperature), 24 h. [e] Starting from isolated imine.



(1a) 2-*p*-tolyl-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Cycloheptanone (5.5 mmol, 650 µL), 3-amino-3-p-tolyl-1-propanol (5.0 mmol, 826 mg), benzophenone (12.5 mmol, 2.3 g), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 1 h. Purification by acidic/base extraction (3x10 mL 2N HCl, neutralisation, 3x30 mL Et_2O). Yield: 1.162 g = 4.88 mmol = 97 % as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.91 (d, *J* = 8.2 Hz, 2 H); 7.47 - 7.40 (m, 2 H); 7.26 (d, *J* = 8.2 Hz, 2 H); 3.13 - 3.08 (m, 2 H); 2.83 - 2.78 (m, 2 H); 2.40 (s, 3 H); 1.95 - 1.89 (m, 2 H); 1.76 - 1.65 (m, 4 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 163.5; 154.0; 138.8; 137.6; 137.4; 136.9; 129.7; 126.9; 117.6; 40.27; 35.5; 33.2; 28.8; 27.3; 21.5 ppm. **Elemental analysis** for $C_{17}H_{19}N$ calcd: C 86.03 H 8.07 N 5.90; found: C 85.69 H 8.40 N 5.54.

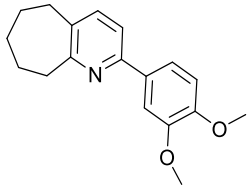


(1b) 2-(4-chlorophenyl)-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Cycloheptanone (5.5 mmol, 650 µL), 3-amino-3-(4-chlorophenyl)-1-propanol (5.0 mmol, 929 mg), benzophenone (12.5 mmol, 2.3 g.), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 1 h. Purification by acid/base extraction (3x10 mL 2N HCl, neutralisation, 3x30 mL Et_2O). Yield: 1.176 g = 4.56 mmol = 91 % as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 8.05 - 7.91 (m, 2 H); 7.49 - 7.38 (m, 4 H); 3.12 - 3.07 (m, 2 H); 2.82 - 2.78 (m, 2 H); 1.95 - 1.85 (m, 2 H); 1.74 - 1.65 (m, 5 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 163.8; 152.6; 138.7; 137.7; 134.6; 129.4; 129.1; 128.1; 117.8; 40.2; 35.4; 33.1; 28.7; 27.2 ppm. **Elemental analysis** for $C_{16}H_{16}ClN$ calcd: C 74.55 H 6.26 N 5.43; found: C 74.63 H 6.12 N 5.43.

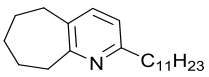


(1c) 2-phenyl-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Cycloheptanone (5.5 mmol, 650 µL), 3-amino-3-phenyl-1-propanol (5.0 mmol, 756 mg), benzophenone (12.5 mmol, 2.3 g), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 1 h. Purification by acid/base extraction: (3x10mL 2N HCl, neutralisation, 3x30 mL Et_2O). Yield 1.088 g = 4.87 mmol = 97 % as light yellow oil. **^{1}H NMR** (300 MHz,

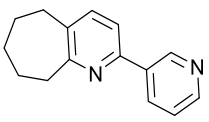
CD_2Cl_2) δ = 8.13 - 7.91 (m, 2 H); 7.53 - 7.35 (m, 5 H); 3.15 - 3.11 (m, 2 H); 2.84 - 2.80 (m, 2 H); 1.96 - 1.89 (m, 2 H); 1.78 - 1.69 (m, 4 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 163.7; 153.9; 140.2; 137.6; 137.3; 129.1; 128.8; 127.1; 118.0; 40.3; 35.5; 33.2; 28.8; 27.3 ppm.



(1d) 2-(3,4-dimethoxyphenyl)-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Cycloheptanone (5.5 mmol, 650 µL), 3-amino-3-(3,4-dimethoxyphenyl)-1-propanol (5.0 mmol, 1.06 mg), benzophenone (12.5 mmol, 2.3 g), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 1 h. Purification by acid/base extraction (3x10 mL 2N HCl, neutralisation, 3x30 mL Et_2O). Yield: 1.22 g = 4.33 mmol = 86 % as yellow solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.67 (d, *J* = 1.8 Hz, 1 H); 7.53 (dd, *J* = 8.3, 2.2 Hz, 1 H); 7.42 (d, *J* = 0.9 Hz, 2 H); 6.94 (d, *J* = 8.3 Hz, 1 H); 3.93 (s, 3 H); 3.88 (s, 3 H); 3.15 - 3.06 (m, 2 H); 2.85 - 2.76 (m, 2 H); 1.95 - 1.85 (m, 2 H); 1.79 - 1.63 (m, 4 H) ppm.**^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 163.4; 153.7; 150.3; 149.9; 137.6; 136.6; 133.1; 119.4; 117.4; 111.8; 110.6; 56.4; 56.4; 40.2; 35.4; 33.1; 28.8; 27.3 ppm. **Elemental analysis** for $C_{18}H_{21}NO_2$ calcd: C 76.29 H 7.47 N 4.94; found: C 76.49 H 7.41 N 4.72.

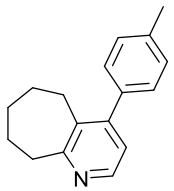


(1e) 2-undecyl-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Cycloheptanone (5.5 mmol, 650 µL), 3-amino-3-undecyl-1-propanol (5.0 mmol, 1.15 g), isopropylphenylketone (12.5 mmol, 1.9 mL), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 1 h. Scavenger is distilled off and the crude prouct is purified by column chromatography pentane/Et_2O 40:1. Yield: 1.40 g = 4.6 mmol = 92 % as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.29 (d, *J* = 7.5 Hz, 1 H); 6.88 (d, *J* = 7.9 Hz, 1 H); 3.05 - 2.97 (m, 2 H); 2.79 - 2.66 (m, 4 H); 1.95 - 1.84 (m, 2 H); 1.75 - 1.63 (m, 6 H); 1.40 - 1.26 (m, 16 H); 0.99 - 0.88 (m, 3 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 163.0; 159.3; 137.1; 135.4; 120.1; 40.1; 38.6; 35.5; 33.3; 32.6; 30.7; 30.4; 30.3; 30.3; 30.3; 30.2: 30.0; 28.9; 27.4; 23.4; 14.6 ppm. **Elemental analysis** for $C_{21}H_{35}N$ calcd: C 83.65 H 11.70 N 4.65; found: C 83.51 H 12.09 N 4.41

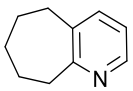


(1f) 2-(pyridin-3-yl)-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Cycloheptanone (5.5 mmol, 650 µL), 3-amino-3-(pyridin-3-yl)-1-propanol (5.0 mmol, 761mg), benzophenone (12.5 mmol, 2.3 g), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 1 h. Purification by acid/base extraction (3x10 mL 2N HCl, neutralisation, 3x30 mL Et_2O). Yield: 890 mg = 3.97 mmol = 79 % as colorless solid. **^{1}H NMR** (300 MHz,

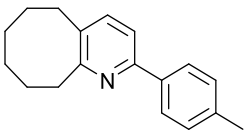
CD_2Cl_2) δ = 9.19 (d, *J* = 2.2 Hz, 1 H); 8.57 (dd, *J* = 4.8, 1.8 Hz, 1 H); 8.38 - 8.26 (m, 1 H); 7.54 - 7.39 (m, 2 H); 7.36 (dd, *J* = 8.1, 4.6 Hz, 1 H); 3.18 - 3.05 (m, 2 H); 2.89 - 2.76 (m, 2 H); 2.01 - 1.83 (m, 2 H); 1.79 - 1.60 (m, 4 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 164.2; 151.5; 149.8; 148.6; 138.1; 137.7; 135.5; 134.3; 123.9; 118.2; 40.2; 35.5; 33.1; 28.7; 27.2 ppm. **Elemental analysis** for $C_{15}H_{15}N_2$ calcd: C 80.32 H 7.19 N 12.49; found: C 80.64 H 7.12 N 12.44



(1g) 3-(p-tolyl)-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Cycloheptanone (5.5 mmol, 650 µL), 3-amino-1-(p-tolyl)-1-propanol (5.0 mmol, 830 mg), benzophenone (12.5 mmol, 2.3 g), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 1 h. Purification by acid/base extraction (3x10 mL 2N HCl, neutralisation, 3x30 mL Et_2O). Yield: 976 mg = 4.11 mmol = 82 % as yellow solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 8.24 (d, *J* = 4.8 Hz, 1 H); 7.26 (m, 2 H); 7.17 (m, 2 H); 6.95 (d, *J* = 5.3 Hz, 1 H); 3.17 - 3.05 (m, 2 H); 2.80 - 2.69 (m, 2 H); 2.41 (s, 3 H); 1.94 - 1.82 (m, 2 H); 1.78 - 1.69 (m, 2 H); 1.62 (ddd, *J* = 10.9, 5.9, 5.6 Hz, 2 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 164.7; 149.2; 145.9; 137.9; 137.7; 129.5; 129.3; 123.1; 40.0; 32.9; 30.1; 28.4; 27.1; 21.4 ppm. **Elemental analysis** for $C_{17}H_{19}N$ calcd: C 86.03 H 8.07 N 5.90; found: C 86.09 H 8.03 N 6.23

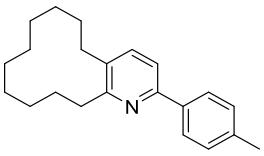


(1h) 5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Cycloheptanone (5.5 mmol, 650 µL), 3-amino-1-propanol (5.0 mmol, 379 µL), benzophenone (12.5 mmol, 2.3 g), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 1 h. Purification by acid/base extraction: (3x10 mL 2N HCl, neutralisation, 3x30 mL Et_2O). Yield 417 mg = 2.84 mmol = 56 % as light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 8.24 (dd, *J* = 4.8, 1.8 Hz, 1 H); 7.36 (dd, *J* = 7.5, 1.8 Hz, 1 H); 6.99 (dd, *J* = 7.5, 4.8 Hz, 1 H); 3.05 - 2.97 (m, 2H); 2.79 - 2.73 (m, 2 H); 1.93 - 1.81 (m, 2 H); 1.72 - 1.57 (m, 4 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 164.0; 146.6; 138.6; 136.6; 121.6; 39.9; 35.8; 33.1; 28.6; 27.1 ppm

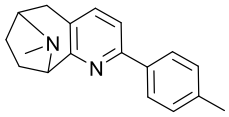


(1i) 2-(p-tolyl)-5,6,7,8,9,10-hexahydro-cycloocta[*b*]pyridine: Cyclooctanone (5.5 mmol, 694 mg), 3-amino-3-p-tolyl-1-propanol (5.0 mmol, 825 mg), isobutyrophenone (12.5 mmol, 1.89 mL), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 2 h. Scavenger is distilled off and the crude product is purified by column chromatography pentane/Et_2O 10:1. Yield: 812 mg = 3.23 mmol = 65 % as light yellow oil.

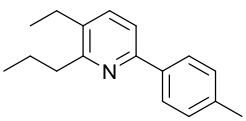
^{1}H NMR (300 MHz, CD_2Cl_2) δ = 8.09 - 7.76 (m, 2 H); 7.57 - 7.38 (m, 2 H); 7.26 (d, *J*=7.9 Hz, 2 H); 3.12 - 2.92 (m, 2 H); 2.85 - 2.65 (m, 2 H); 2.40 (s, 3 H); 1.88 - 1.65 (m, 4 H); 1.41 (ddd, *J*=6.0, 3.0, 2.9 Hz, 4 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 161.3; 154.9; 138.8; 137.6; 137.6; 135.0; 127.9; 127.0; 118.2; 35.4; 32.8; 32.1; 31.3; 26.6; 26.5; 21.5 ppm. **Elemental analysis** for $C_{18}H_{21}N$ calcd: C 86.01 H 8.42 N5.57; found: C 85.85 H 8.43 N 5.52



(1j) 2-*p*-tolyl-5,6,7,8,9,10,11,12,13,14-decahydro-cyclododeca[*b*]pyridine: Cyclododecanone (6.6 mmol, 1.2 g), 3-amino-3-p-tolyl-1-propanol (6.0 mmol, 991 mg), isopropylphenylketone (15.0 mmol, 2.2 mL), KO^{t}Bu (15.0 mmol, 1.7 g); 10 mL THF, 110 °C, 24 h. Scavenger is distilled off. Purification by column chromatography pentane/Et_2O 40:1. Yield: 1.045 g = 3.4 mmol = 57 % as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.96 - 7.89 (m, 2 H); 7.54 - 7.46 (m, 2 H); 7.30 - 7.24 (m, 2 H); 2.89 (t, *J* = 7.5 Hz, 2 H); 2.71 (t, *J* = 7.5 Hz, 2 H); 2.41 (s, 3 H); 2.03 - 1.92 (m, 2 H); 1.80 - 1.70 (m, 2 H); 1.61 - 1.51 (m, 4 H); 1.48 - 1.37 (m, 8 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 160.7; 154.4; 138.9; 138.3; 137.5; 134.8; 129.7; 126.9; 117.7; 32.1; 30.0; 29.1; 28.5; 26.6; 26.2; 25.8; 25.7; 23.6; 23.6; 21.5 ppm. **Elemental analysis** for $C_{22}H_{29}N$ calcd: C 85.94 H 9.51 N 4.56; found: C 85.74 H 9.53 N 4.23

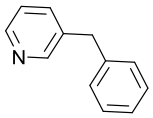


(1k) 2-p-tolyl-5,7,8-trihydro-(N-methyl-azabicyclo[3.2.1]octa)[*b*]pyridine: Tropinone (5.5 mmol, 770 mg), 3-amino-3-p-tolyl-1-propanol (5.0 mmol, 830 mg), benzophenone (12.5 mmol, 2.3 g), KO^{t}Bu (12.5 mmol, 1.4 g); 10 mL THF, 90 °C, 1 h. Purification by column chromatography Et_2O: MeOH 3:1 → 1:1. Yield: 827 mg = 3.8 mmol = 66 % as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.86 (m, 2 H); 7.47 (d, *J* = 7.9 Hz, 1 H); 7.33 (d, *J* = 7.9 Hz, 1 H); 7.26 (m, *J* = 7.9 Hz, 2 H); 3.86 (d, *J* = 5.7 Hz, 1 H); 3.53 (t, *J* = 5.7 Hz, 1 H); 3.31 (dd, *J* = 17.8, 5.1 Hz, 1 H); 2.60 (d, *J* = 17.6 Hz, 1 H); 2.38 (d, *J* = 6.6 Hz, 6 H); 2.32 - 2.22 (m, 2 H); 1.83 - 1.69 (m, 1 H); 1.68 - 1.57(m, 1 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 155.5; 154.6; 139.1; 137.4; 135.2; 134.8; 219.8; 127.0; 118.0; 63.7; 59.1; 37.8; 37.0; 35.1; 29.8, 21.5 ppm.



(1l) 3-ethyl-2-propyl-5-p-tolylpyridine: 4-Heptanone (5.5 mmol, 770 µL), 3-amino-3-p-tolyl-1-propanol (5.0 mmol, 825 mg); isobutyrophenone (12.5 mmol, 2.3 g), KO^{t}Bu (12.5 mmol, 1.4 g), 10 mL THF, 90 °C, 2 h. Scavenger is destilled off and the crude product is purified by column

chromatography pentane/Et_2O 40:1. Yield: 677 mg = 2.83 mmol = 57 % as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.94 (d, *J* = 8.3 Hz, 2 H); 7.50 (s, 2 H); 7.27 (d, *J* = 8.8 Hz, 2 H); 2.91 - 2.77 (m, 2 H); 2.70 (q, *J* = 7.5 Hz, 2 H); 2.41 (s, 3 H); 1.94 - 1.79 (m, 2 H); 1.26 (t, *J* = 7.7 Hz, 3 H); 1.07 (t, *J* = 7.2 Hz, 3 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 160.1; 154.2; 138.9; 137.6; 136.9; 129.8; 127.0; 117.7; 37.4; 25.4; 23.0; 21.5; 15.2; 14.7 ppm.



(1m) 3-benzylpyridine: 3-Phenylpropionaldehyde (5.5 mmol, 723 µL), 3-amino-1-propanol (5.0 mmol, 379 µL); benzophenone (12.5 mmol, 2.3 g), KO^{t}Bu (12.5 mmol, 1.4 g), 10 mL THF, 90 °C, 1 h. Purification by acid/base extraction (3x10 mL 2N HCl, neutralisation, 3x30 mL Et_2O).Yield 301 mg = 1.78 mmol = 35 % as light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 8.52 (s, 1 H); 8.45 (d, *J* = 4.8 Hz, 1 H); 7.61 - 7.44 (m, 1 H); 7.39 - 7.15 (m, 7 H); 3.99 (s, 2 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 150.7; 148.2; 140.7; 137.1; 136.6; 129.4; 129.1; 126.9; 123.8; 39.5 ppm

6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

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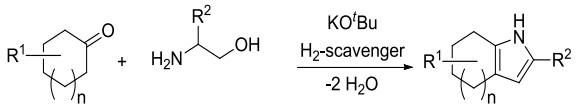
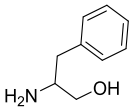
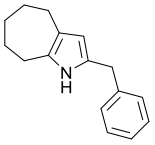
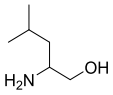
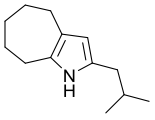
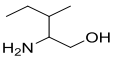
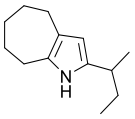
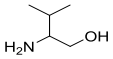
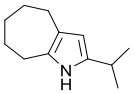
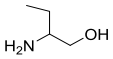
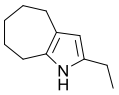
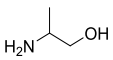
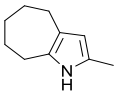
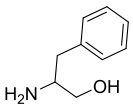
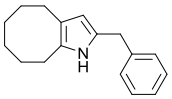
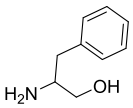
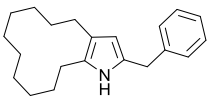
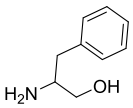
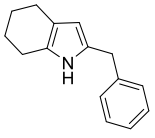
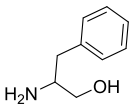
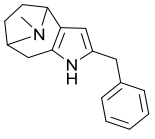
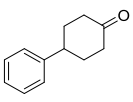
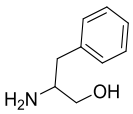
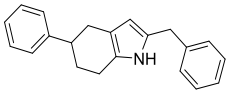
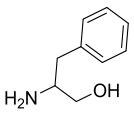
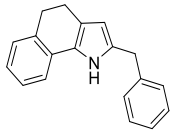
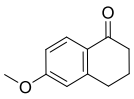
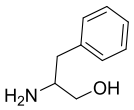
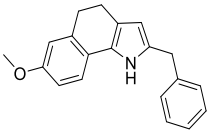
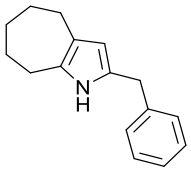
Table S11. Synthesized bicyclic pyrroles[a]



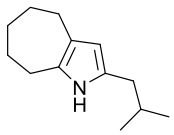
Nr.	Ketone	Amino Alcohol	Product	Yield [%][b] (GC-Yield[c])
2a				59 (79)
2b				66 (80)
2c				49 (60)
2d				54 (71)
2e				44 (72)
2f				36 (81)
2g				69 (82)
2h				45 (67)
2i				52 (56)
2j				65 (72)
2k				38 (51)

2l				62 (71)
2m				52[d] (65)

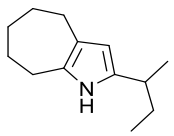
[a] Reaction conditions: 22.0 mmol ketone, 20.0 mmol amino alcohol, 25.0 mmol isobutyrophenone (as scavenger), 25.0 mmol KO^{t}Bu, 20 mL THF, 110 °C, 24 h. [b] Isolated yield. [c] Yield determined via GC with decane as internal standard. [d] 7.20 mmol Ketone, 6.55 mmol amino alcohol, 8.14 mmol isobutyrophenone, 8.14 mmol KO^{t}Bu, 10 mL THF, 110 °C, 24 h.



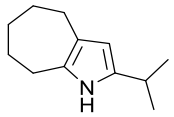
(2a) 2-benzyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cycloheptanone (11.0 mmol, 1.3 mL), phenylalaninol (10.0 mmol, 1.51 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 10 mL THF, 110 °C, 24 h. Scavenger is distilled off and the crude product was purified by column chromatography pentane/Et_2O 40:1. Yield 1.33 g = 5.9 mmol = 59 % as light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) $\delta =$ 7.44 - 7.22 (m, 6 H); 5.72 (d, *J* = 3.1 Hz, 1 H), 3.89 (s, 2 H); 2.59 (dt, *J* = 10.9, 5.5 Hz, 4 H), 1.90 - 1.78 (m, 2 H); 1.76 - 1.62 (m, 4 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) $\delta =$ 141.0; 129.9; 129.2; 126.8; 126.7; 122.8; 109.0; 34.6; 32.6; 30.1; 29.6; 29.00; 28.8 ppm.



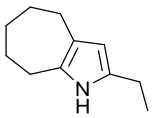
(2b) 2-(2-methyl-propyl)-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cycloheptanone (11.0 mmol, 1.3 mL), leucinol (10.0 mmol, 1,28 mL), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger is distilled off and the crude product was purified by column chromatography pentane/Et_2O 40:1. Yield 1.26 g = 6.58 mmol = 66 % as light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) $\delta =$ 7.41 (br. s., 1 H); 5.59 (d, *J* = 2.6 Hz, 1 H); 2.70 - 2.57 (m, 2 H); 2.55 - 2.47 (m, 2 H); 2.35 (d, *J* = 7.0 Hz, 2 H); 1.87 - 1.74 (m, 3 H); 1.71 - 1.59 (m, 4 H); 0.93 (d, *J* = 6.6 Hz, 6 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) $\delta =$ 128.8; 127.6; 121.6; 108.6; 37.6; 32.6 30.2; 29.9; 29.7; 29.0; 28.9; 22.8 ppm.



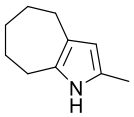
(2c) 2-(1-methyl-propyl)-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cycloheptanone (22.0 mmol, 2.6 mL), isoleucinol (20.0 mmol, 2.34 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger is distilled off and the crude product was purified by column chromatography pentane/Et_2O 40:1. Yield 945 mg = 4.94 mmol= 49 % as light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.45 (br. s., 1 H); 5.59 (d, *J* = 2.6 Hz, 1 H); 2.78 - 2.41 (m, 5 H); 1.86 - 1.73 (m, 2 H); 1.72 - 1.62 (m, 4 H); 1.61 - 1.40 (m, 2 H); 1.19 (d, *J* = 7.0 Hz, 3 H); 0.90 (t, *J* = 7.2 Hz, 3 H) ppm.**^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 133.7; 128.6; 121.3; 106.3; 34.6; 32.6; 30.8; 30.1; 29.7; 29.1; 28.9: 20.5; 12.3 ppm.



(2d) 2-isopropyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cycloheptanone (22.0 mmol, 2.6 mL), valinol (20.0 mmol, 2.06 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger is distilled off and the crude product was purified by column chromatography pentane/Et_2O 40:1. Yield 1.91 g = 10.8 mmol = 54 % as light yellow solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ= 7.48 (br. s., 1 H); 5.60 (d, *J* =3.1 Hz, 1 H); 2.82 (dq, *J* = 7.0, 6.9 Hz, 1 H); 2.68 - 2.57 (m, 2 H); 2.55 - 2.46 (m, 2 H); 1.88 - 1.73 (m, 2 H); 1.67 (ddd, *J* = 10.8, 5.3, 5.1 Hz, 4 H); 1.21 (d, *J* = 7.0 Hz, 6 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 134.9; 128.7; 121.3; 105.6; 32.6; 30.1; 29.7; 29.0; 28.9; 27.4; 23.2 ppm.

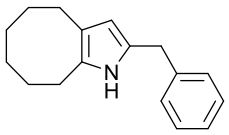


(2e) 2-ethyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cycloheptanone (22.0 mmol, 2.6 mL), 2-amino-1-butanol (20.0 mmol, 1.89 mL), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger is distilled off and the crude product was purified by column chromatography pentane/Et_2O 20:1. Yield 2.53 g = 15.6 mmol= 78% as light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.47 (br. s., 1 H); 5.68 (d, *J* = 3.1 Hz, 1 H); 2.72 - 2.63 (m, 2 H); 2.62 - 2.52 (m, 4 H); 1.91 - 1.80 (m, 2 H); 1.79 - 1.67 (m, 4 H); 1.26 (t, *J* = 7.7 Hz, 3 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 130.1; 128.9; 121.6; 106.9; 32.7; 30.2; 29.9; 29.0; 21.2; 14.4 ppm.

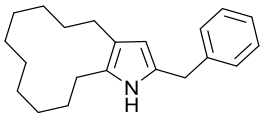


(2f) 2-methyl-1,4,5,6,7,8-hexahydro-cyclohepta[*b*]pyrrole: Cycloheptanone (22.0 mmol, 2.6 mL), 2-amino-1-propanol (20.0 mmol, 1.56 mL), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger is distilled off and the crude product was purified by

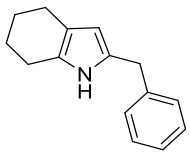
column chromatography pentane/Et_2O 20:1. Yield 2.16 g = 14.2mmol = 72 % as light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.42 (br. s, 1 H); 5.60 (d, *J* = 2.6 Hz, 1 H); 2.72 - 2.56 (m, 2 H); 2.56 - 2.44 (m, 2 H); 2.18 (s, 3 H); 1.87 - 1.77 (m, 2 H); 1.73 - 1.63 (m, 4 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 129.1; 123.3; 121.8; 108.6; 32.7; 30.2; 29.6; 28.9; 13.0 ppm.



(2g) 2-benzyl-1,4,5,6,7,8,9-heptahydro-cycloocta[*b*]pyrrole: Cyclooctanone (22.0 mmol, 2.78 g), phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger is distilled off and the crude product was purified by column chromatography pentane/Et_2O 10:1. Yield: 3.29 g = 13.8 mmol = 69 % as light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ= 7.40 (br. s. 1 H); 7.35 - 7.08 (m, 5 H); 5.68 (s, 1 H); 3.90 (s, 2 H); 2.74 - 2.46 (m, 4 H); 1.81 - 1.53 (m, 4 H); 1.53 - 1.34 (m, 4 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ= 141.1; 129.1; 129.0; 128.1; 127.7; 126.7; 119.5; 108.1; 34.7; 31.3; 30.3; 26.6; 26.3; 26.0; 25.5 ppm.

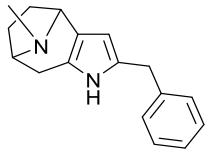


(2h) 2-benzyl-1,4,5,6,7,8,9,10,11,12,13-undecahydro-cyclododeca[*b*]pyrrole: Cyclododecanone (22.0 mmol, 4.12 g), phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. The product was recrystallized from pentane. Yield: 2.67 g = 8.97 mmol = 45 % as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.48 - 7.18 (m, 6 H); 5.69 (d, *J* = 3.1 Hz, 1 H); 3.89 (s, 2 H); 2.52 (t, *J* = 6.8 Hz, 2 H); 2.37 (t, *J* = 6.8 Hz, 2 H); 1.70 - 1.54 (m, 4 H); 1.47 - 1.33 (m, 8 H); 1.33 - 1.20 (m, 5 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 141.0; 129.4; 129.1; 129.0; 128.1; 126.7; 120.5; 107.0; 34.8; 29.6; 28.6; 25.4; 25.2; 25.1; 25.1; 23.0; 23.0; 22.9; 22.5 ppm.

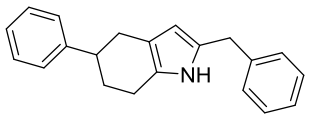


(2i) 2-benzyl-1,4,5,6,7-pentahydroindole: Cyclohexanone (22.0 mmol, 2.28 mL), phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger was distilled off and the crude product was purified by column chromatography pentane/Et_2O 40:1. Yield: 2.20 g = 1.04 mmol= 52 % as orange oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.49 - 7.19 (m, 6 H); 5.72 (d, *J* = 2.6 Hz, 1 H); 3.92 (s, 2 H); 2.52 (q, *J* = 6.0 Hz, 4 H); 1.90 - 1.73 (m, 4 H)

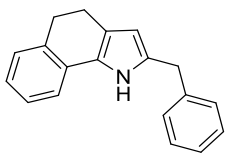
ppm.**^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 141.0; 129.3; 129.1; 129.1; 126.7; 117.2; 106.0; 34.8; 24.6; 24.2; 23.5; 23.2 ppm.



(2j) 2-benzyl -6,7,9-trihydro-(N-methyl-azabicyclo[3.2.1]octa)[*b*]pyrrole: Tropinone (5.5 mmol; 770 mg); phenylalaninol (5.0 mmol; 830 mg); isobutyrophenone (12.5 mmol; 1.84 mL); KO^{t}Bu (12.5 mmol; 1.40 g); 10 mL THF; 110 °C; 24 h. Scavenger is distilled off and the crude product was purified by column chromatography Et_2O/MeOH 3:1 → 1:1. Yield 0.83 g = 3.28 mmol = 65 % as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.99 - 7.71 (m, 2 H); 7.47 (d, *J*=7.9 Hz, 1 H); 7.41 - 7.13 (m, 3 H); 3.86 (d, *J*=5.7 Hz, 1 H); 3.53 (t, *J*=5.7 Hz, 1 H); 3.31 (dd, *J*=17.8, 5.1 Hz, 1 H); 2.60 (d, *J*=17.6 Hz, 1 H); 2.44 - 2.33 (m, 6 H); 2.33 - 2.19 (m, 2 H); 1.84 - 1.54 (m, 2 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 155.5; 154.6; 139.1; 137.4; 134.8; 129.8; 127.0; 118.0; 63.7; 59.1; 37.8; 37.0; 35.1; 29.8; 21.5 ppm.

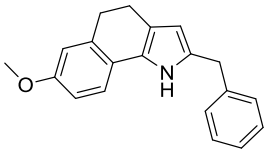


(2k) 2-benzyl-5-phenyl-4,6,7,-trihydro-1*H*-indole: 4-Phenylcyclohexanone (22.0 mmol, 3.82 g), phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger was distilled off and the crude product is purified by column chromatography pentane/Et_2O 40:1. Yield: 2.18 g = 7.85 mmol = 38 % as orange oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.47 (br. s., 1 H); 7.39 - 7.23 (m, 10 H); 5.77 (d, *J* = 2.6 Hz, 1 H); 3.95 (s, 2 H); 3.06 - 2.89 (m, 1 H); 2.86 - 2.59 (m, 4 H); 2.19 - 1.92 (m, 2 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 147.9; 140.9; 129.9; 129.2; 129.1; 128.9; 127.6; 126.8; 126.5; 126.1; 117.4; 105.9; 42.2; 34.9; 31.9; 31.4; 23.5 ppm.



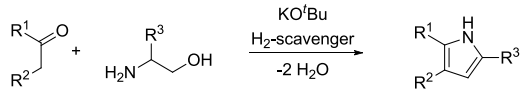
(2l) 2-benzyl-4,5-dihydro-1*H*-benzo[*c*]indole: 1-Tetralone (22.0 mmol, 2.92 mL), phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger was distilled off and the crude product was purified by column chromatography Pentane/Et_2O 20:1→10:1. Yield: 3.25 g = 12.5 mmol = 62 % as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 8.06 (br. s., 1 H); 7.43 - 7.27 (m, 5 H); 7.26 - 7.15 (m, 2 H); 7.07 (d, *J*=7.0 Hz, 2 H); 5.93 (d, *J*=2.2 Hz, 1 H); 4.04 (s, 2 H); 2.95 (t, *J*=7.5 Hz, 2 H); 2.74 (t, *J*=7.6 Hz, 2 H) ppm. **^{13}C NMR** (75.41 MHz,

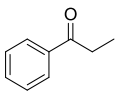
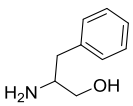
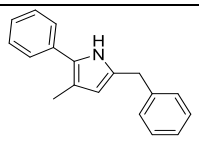
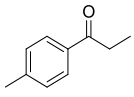
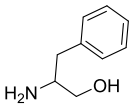
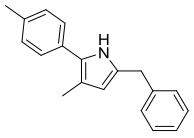
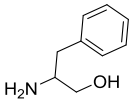
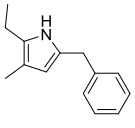
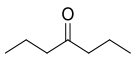
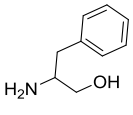
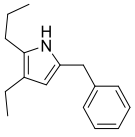
CD_2Cl_2) δ = 140.3; 135.0; 132.5; 123.0; 129.2; 128.8; 127.5; 127.0; 126.9; 125.1; 121.2; 118.3; 107.4; 34.9; 30.6; 22.4 ppm. **Elemental analysis** for $C_{19}H_{17}N$ (M: 259.3) calcd: C 87.99 H 6.61 N 5.40 found: C 88.11 H 6.27 N 5.53

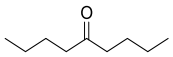
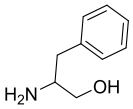
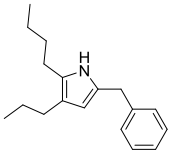
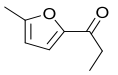
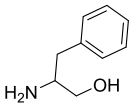
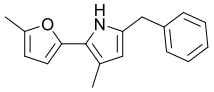


(2m) 2-benzyl-7-methoxy-4,5-dihydro-1*H*-benzo[4,5-*c*]indole: 6-Methoxytetralone (7.2 mmol, 1.27 g), phenylalaninol (6.55 mmol, 990 mg), isobutyrophenone (8.14 mmol, 1.24 mL), KO^{t}Bu (8.14 mmol, 920 mg), 10 mL THF, 110 °C, 24 h. The crude product was purified by column chromatography pentane/Et_2O 10:1→2:1. Yield: 987 mg = 3.4 mmol = 52 % as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.95 (br. s., 1 H); 7.42 - 7.18 (m, 5 H); 6.98 (d, *J* = 8.3 Hz, 1 H); 6.77 (d, *J* = 2.6 Hz, 1 H); 6.74 - 6.63 (m, 1 H); 5.84 (d, *J* = 2.2 Hz, 1 H); 3.98 (s, 2 H); 3.77 (s, 3 H); 2.87 (t, *J* = 7.5 Hz, 2 H); 2.73 - 2.56 (m, 2 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 157.7; 140.5; 137.0; 131.5; 129.1; 127.5; 126.90; 123.4; 119.2; 115.2; 111.6; 107.1; 55.6; 34.9; 31.0; 22.4. **Elemental analysis** for $C_{20}H_{19}NO$ (M: 289.4) calcd: C 83.01 H 6.62 N 4.84 found: C 82.99 H 6.37 N 5.03

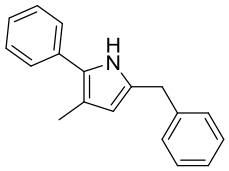
Table S12. Synthesized 2,3,5-substituted pyrroles[a]



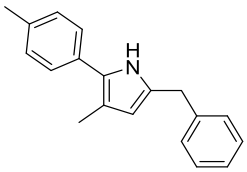
Nr.	Ketone	Amino Alcohol	Product	Yield[b] [%] (GC-Yield[c])
3a				60 (67)
3b				41 (57)
3c				56 (73)
3d				47 (59)

3e				54 (58)
3f				36 (53)

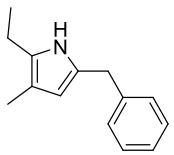
[a] Reaction conditions: 22.0 mmol ketone, 20.0 mmol amino alcohol, 25.0 mmol isobutyrophenone (as scavenger), 25.0 mmol KO^{t}Bu, 20 mL THF, 110 °C, 24 h. [b] Yield of isolated product. [c] Yield determined via GC with decane as internal standard.



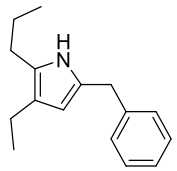
(3a) 5-benzyl-3-methyl-2-phenyl-1*H*-pyrrole: Propiophenone (22.0 mmol, 2.92 mL, phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger was distilled off and the crude product was purified by column chromatography pentane/Et_2O 40:1. Yield: 1.28 g = 11.94 mmol = 60 % as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.97 (br. s., 1 H); 7.55 - 7.32 (m, 11 H) 6.07 (d, *J* = 3.1 Hz, 1 H); 4.09 (s, 2 H); 2.43 (s, 3 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 140.4; 134.5; 131.3; 129.3; 129.2; 129.2; 127.8; 127.0; 126.4; 126.1; 117.0; 111.5; 34.7; 13.1 ppm.



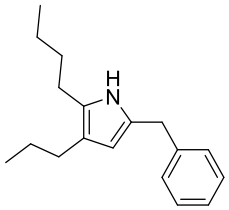
(3b) 5-benzyl-3-methyl-2-tolyl-1*H*-pyrrole: 4-Methylpropiophenone (22.0 mmol, 3.28 mL), phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger was distilled off and the product was crystallized from pentane. Yield: 2.15 g = 8.22 mmol = 41 % as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 7.89 (br. s., 1 H); 7.40 - 7.19 (m, 11 H); 5.90 (d, *J* = 2.6 Hz, 1 H); 3.99 (s, 2 H); 2.39 (s, 3 H); 2.26 (s, 3 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 140.4; 135.8; 131.5; 130.9; 129.9; 129.1; 127.8; 126.9; 126.3; 116.4; 111.1; 34.6; 21.4; 12.9ppm. **Elemental analysis** for $C_{19}H_{19}N$ calcd: C 87.31 H 7.33 N 5.36; found: C 87.15 H 7.01 N 5.53



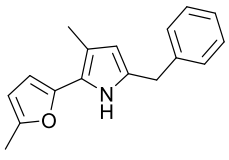
(3c) 5-benzyl-2-ethyl-3-methyl-1*H*-pyrrole: 3-Pentanone (22.0 mmol, 2.34 mL), phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger was distilled off and the crude product was purified by column chromatography pentane/Et_2O 20:1. Yield: 2.25 g = 11.3 mmol = 56 % as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) $\delta =$ 7.56 - 7.23 (m, 6 H); 5.78 (d, *J* = 2.2 Hz, 1 H); 3.96 (s, 2 H); 2.59 (q, *J* = 7.8 Hz, 2 H); 2.09 (s, 3 H); 1.28 - 1.17 (m, 3 H) ppm. . **^{13}C NMR** (75.41 MHz, CD_2Cl_2) $\delta =$ 141.0; 129.4; 129.2; 129.1; 128.3; 126.8; 113.6, 108.9; 34.7; 19.5; 15.0; 11.2 ppm.



(3d) 5-benzyl-3-ethyl-2-propyl-1*H*-pyrrole: 4-Heptanone (22.0 mmol, 3.06 mL), phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger was distilled off and the crude product was purified by column chromatography pentane/Et_2O 20:1. Yield: 2.13 g = 9.36 mmol = 47 % as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) $\delta =$ 7.49 - 7.14 (m, 6 H); 5.77 (d, *J* = 2.6 Hz, 1 H); 3.91 (s, 2 H); 2.54 - 2.34 (m, 4 H); 1.63 - 1.46 (m, 2 H); 1.22 - 1.11 (m, 3 H); 0.95 (t, *J* = 7.2 Hz, 3 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) $\delta =$ 141.1; 129.1; 129.0; 128.5; 127.3; 126.7; 121.6; 106.9; 34.8; 28.3; 24.4; 19.5; 16.5; 14.3 ppm.



(3e) 5-benzyl-2-butyl-3-propyl-1*H*-pyrrole: 5-Nonanone (22.0 mmol, 3.78 mL), phenylalaninol (20.0 mmol, 3.02 g), isobutyrophenone (25.0 mmol, 3.78 mL), KO^{t}Bu (25.0 mmol, 2.8 g), 20 mL THF, 110 °C, 24 h. Scavenger was distilled off and the crude product was purified by column chromatography pentane/Et_2O 40:1. Yield: 2.75 g = 10.8 mmol = 54 % as light yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) $\delta =$ 7.42 (br. s., 1 H); 7.39 - 7.20 (m, 5 H); 5.72 (d, *J* = 2.6 Hz, 1 H); 3.90 (s, 2 H); 2.54 - 2.45 (m, 2 H); 2.38 - 2.30 (m, 2 H); 1.61 - 1.45 (m, 4 H); 1.40 - 1.31 (m, 2 H); 0.95 (q, *J* = 7.0 Hz, 6 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) $\delta =$ 141.0; 129.1; 129.0; 128.4; 127.9; 126.7; 119.8; 107.5; 34.8; 33.4; 28.6; 26.0; 25.4; 23.1; 14.5; 14.3 ppm.



(3f) 5-benzyl-2-(5-methylfuryl)-3-methyl-1*H*-pyrrole: 5-Methyl-propionylfuran (5.5 mmol, 753 µL), phenylalaninol (5.0 mmol, 755 mg), isobutyrophenone (6.25 mmol, 945 µL), KO^{t}Bu (6.25 mmol, 701 mg), 5 mL THF, 110 °C, 24 h. Scavenger was distilled off and the crude product was purified by column chromatography pentane/Et_2O 5:1. Yield: 433 mg = 1.73 mmol = 36 % as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2) δ = 8.08 (br. s., 1 H); 7.36 - 7.29 (m, 2 H); 7.28 - 7.22 (m, 3 H); 6.10 (d, *J*=3.1 Hz, 1 H); 6.05 - 6.00 (m, 1 H); 5.84 (d, *J*=3.1 Hz, 1 H); 3.94 (s, 2 H); 2.31 (s, 3 H); 2.17 (s, 3 H) ppm. **^{13}C NMR** (75.41 MHz, CD_2Cl_2) δ = 149.9; 147.3; 140.4; 130.7; 129.2; 126.9; 120.5; 116.2; 110.7; 107.8; 103.7; 34.6; 13.7; 12.6 ppm. **Elemental analysis** for $C_{17}H_{17}NO$ (M:251.3) calcd.: C 81.24 H 6.82 N 5.57; found: C 81.29 H 6.344 N 5.554

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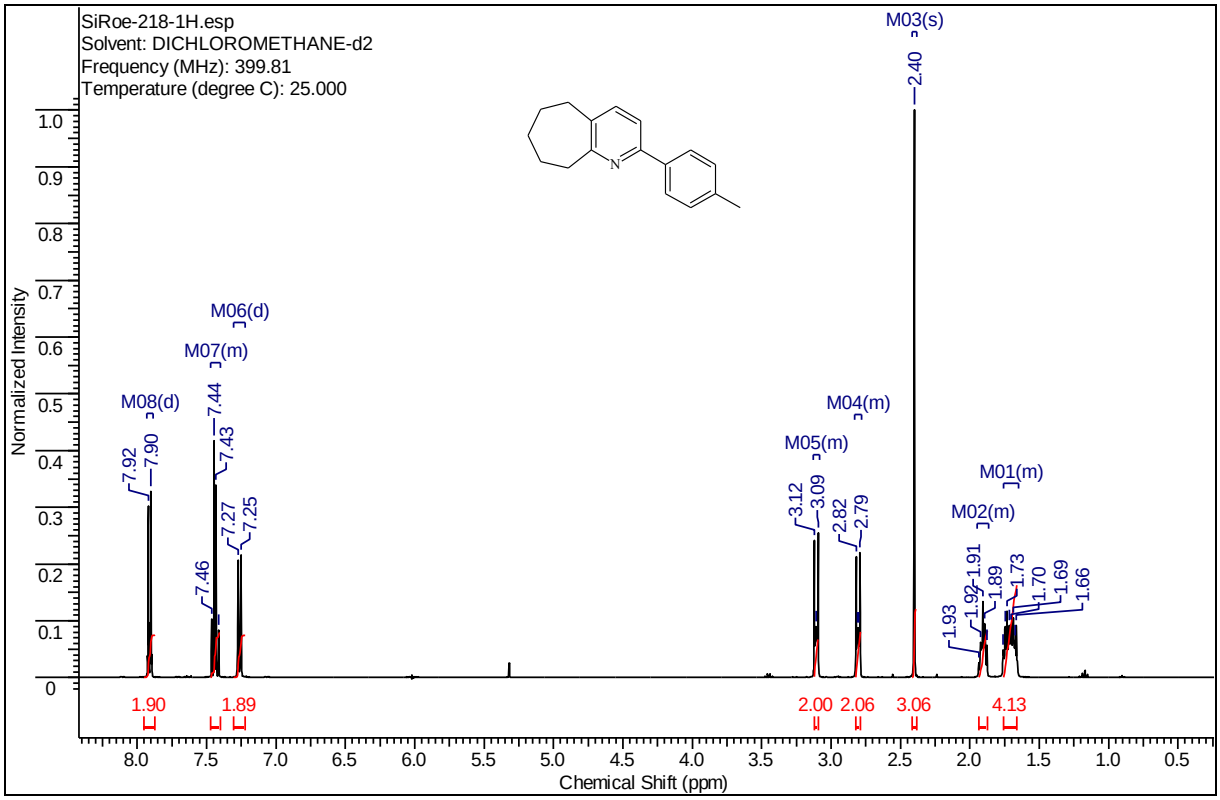
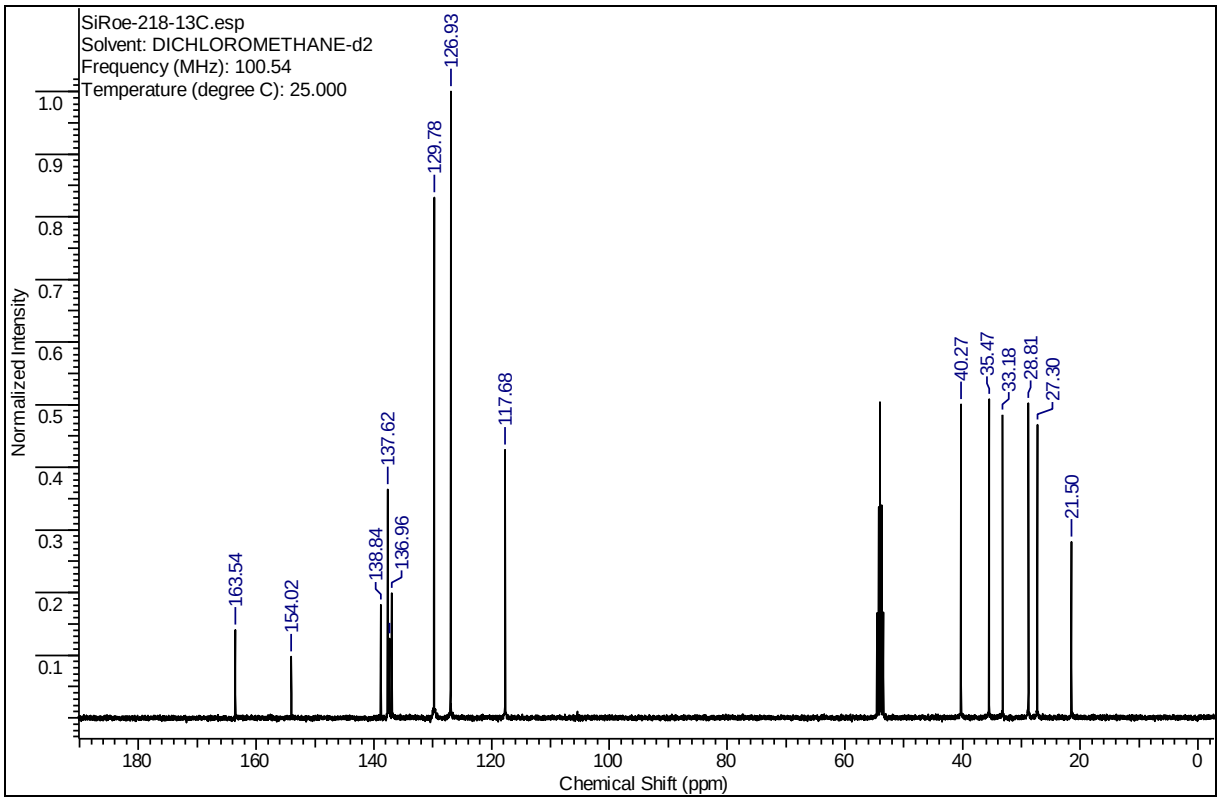
^{1}H and ^{13}C NMR spectra of 2-*p*-tolyl-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine (**1a**)





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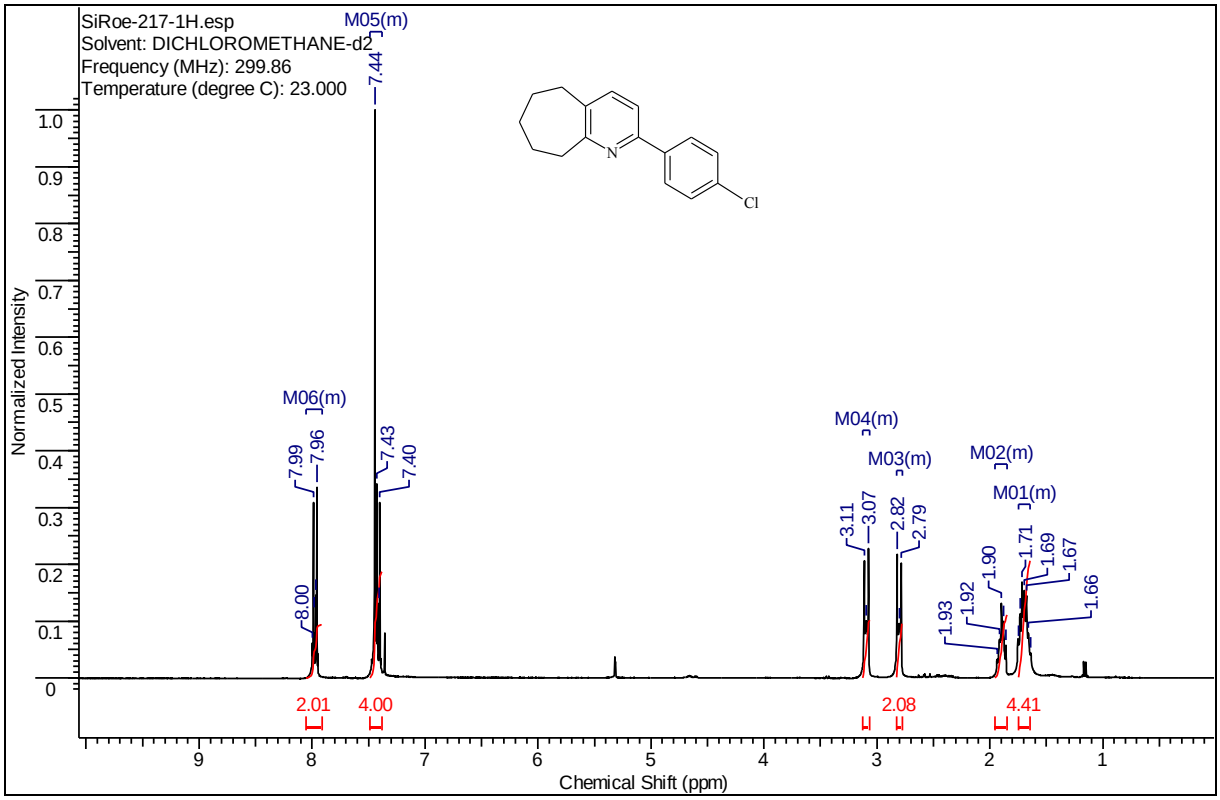
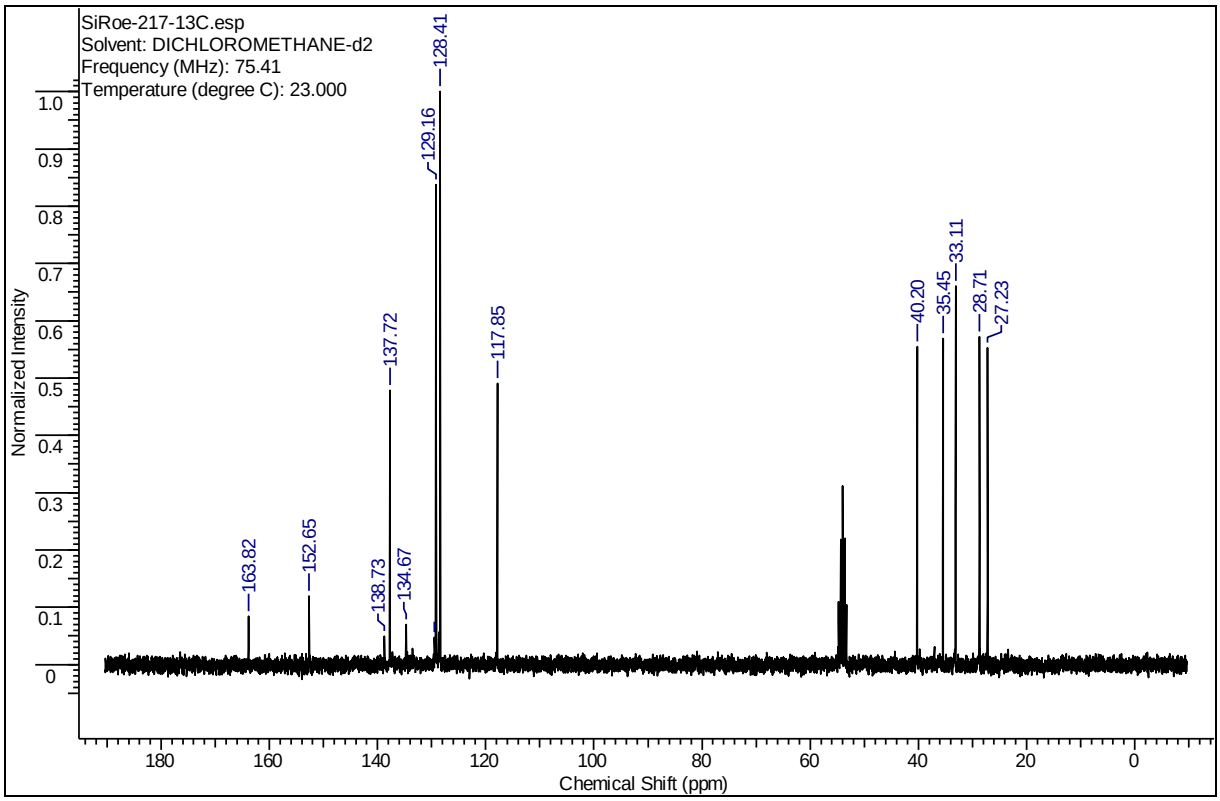
^{1}H and ^{13}C NMR spectra of 2-(4-chlorophenyl)-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine (**1b**)





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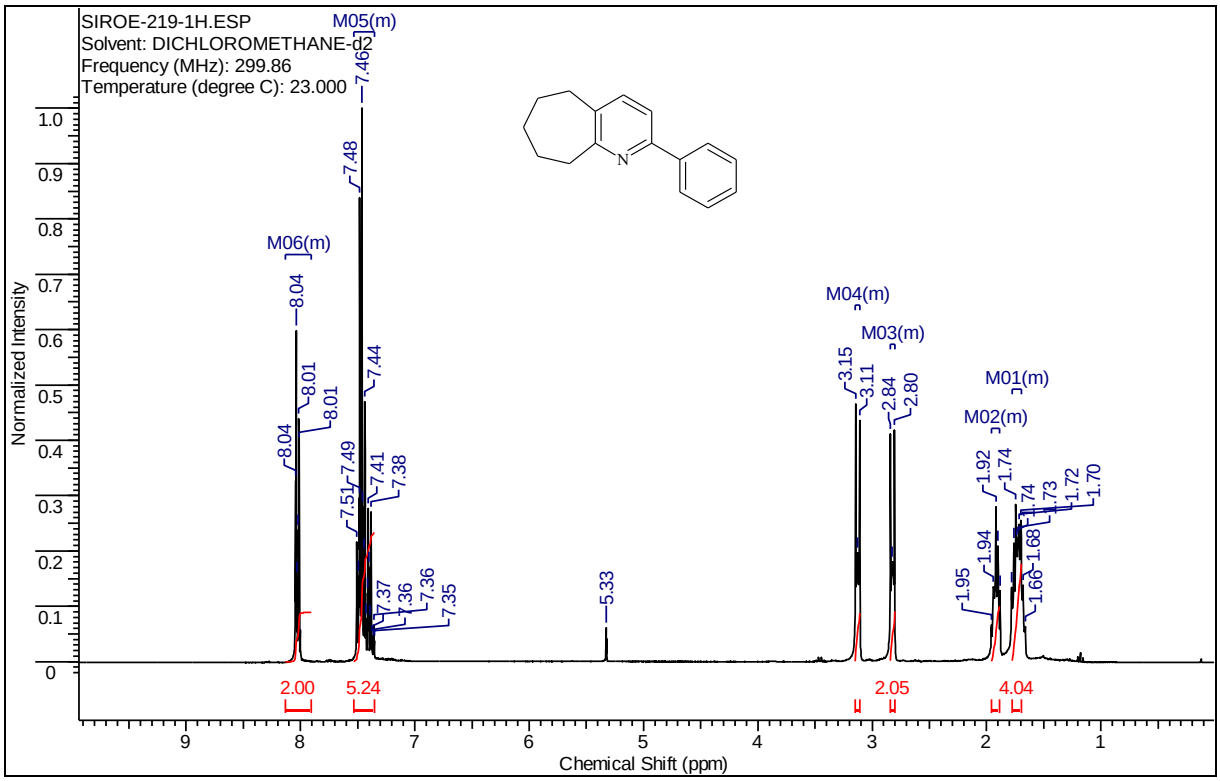
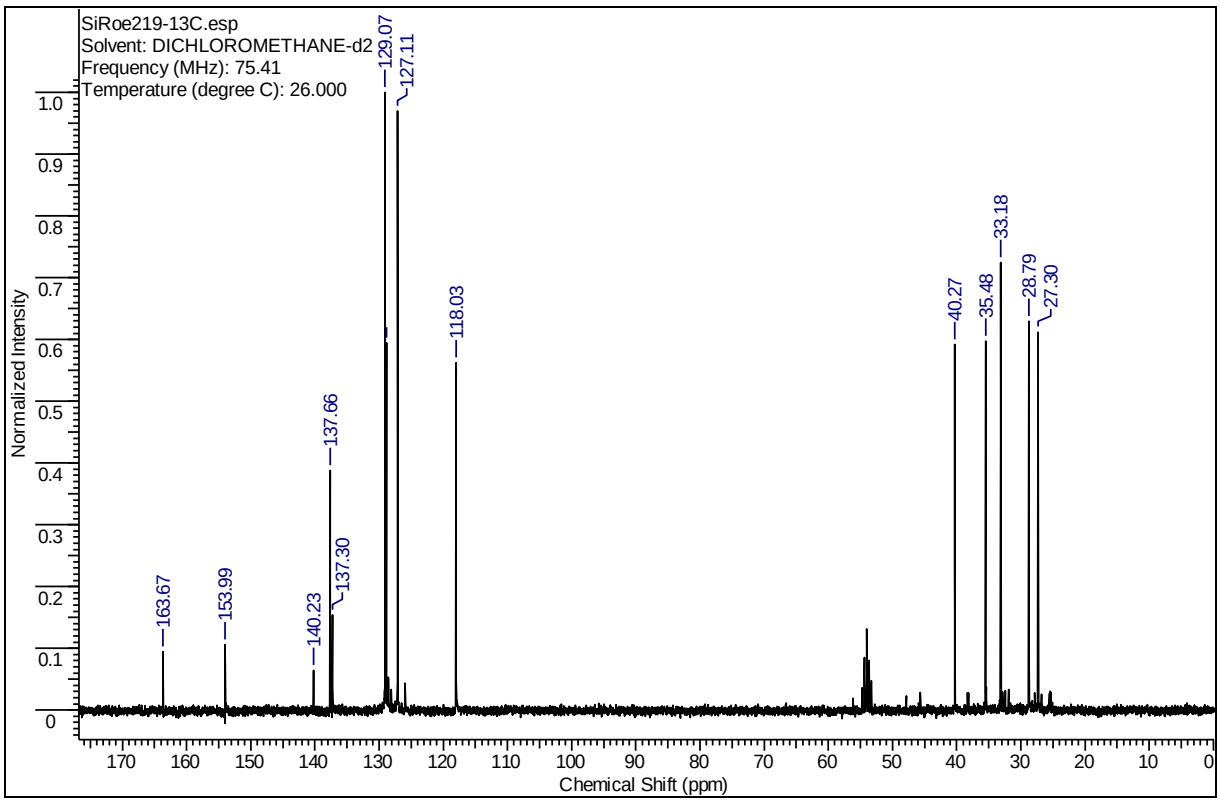
^{1}H and ^{13}C NMR spectra of 2-phenyl-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine (**1c**)





6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

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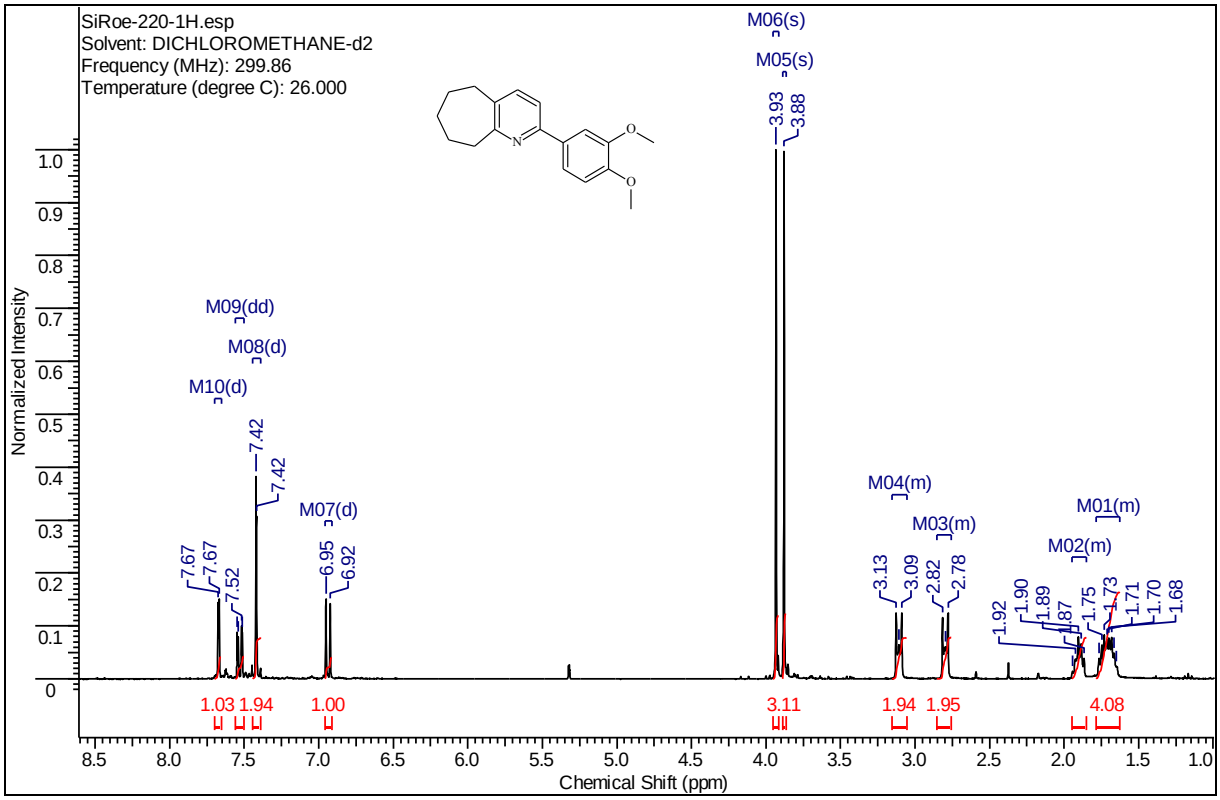
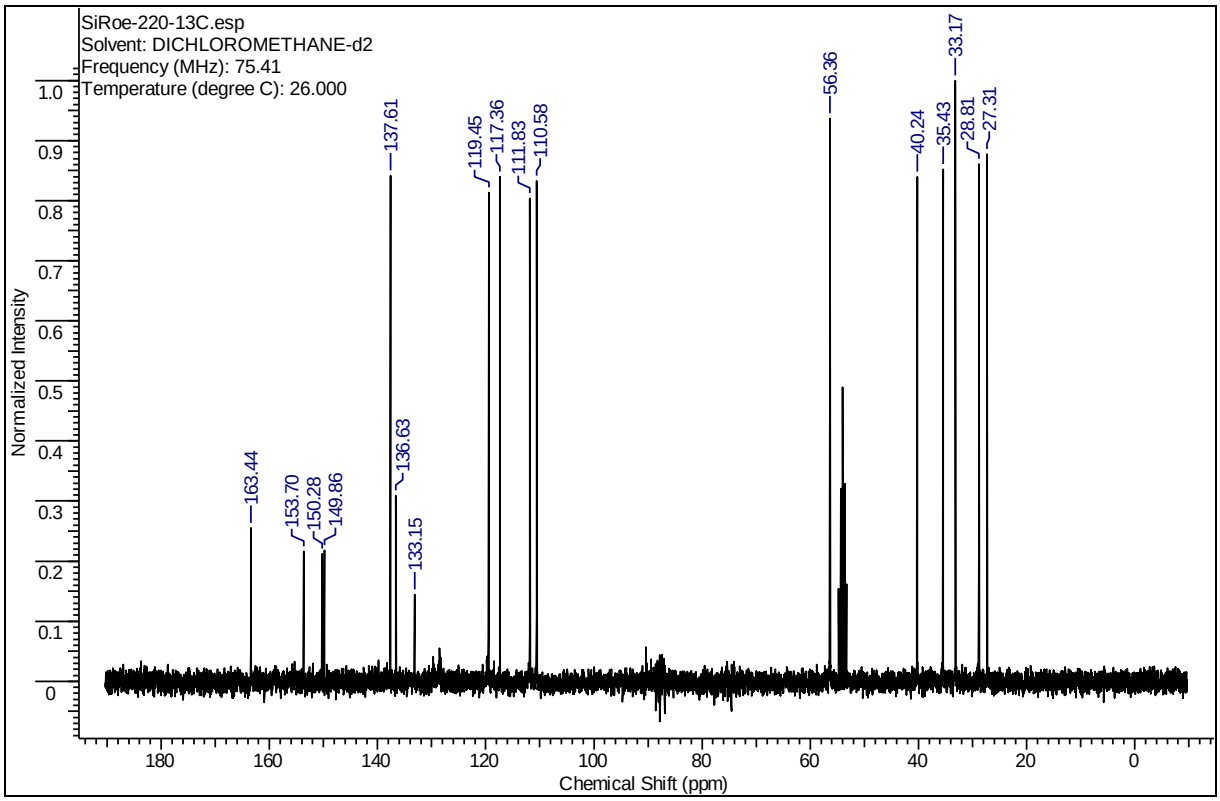
^{1}H and ^{13}C NMR spectra of 2-(3',4'-dimethoxyphenyl)-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine (**1d**)





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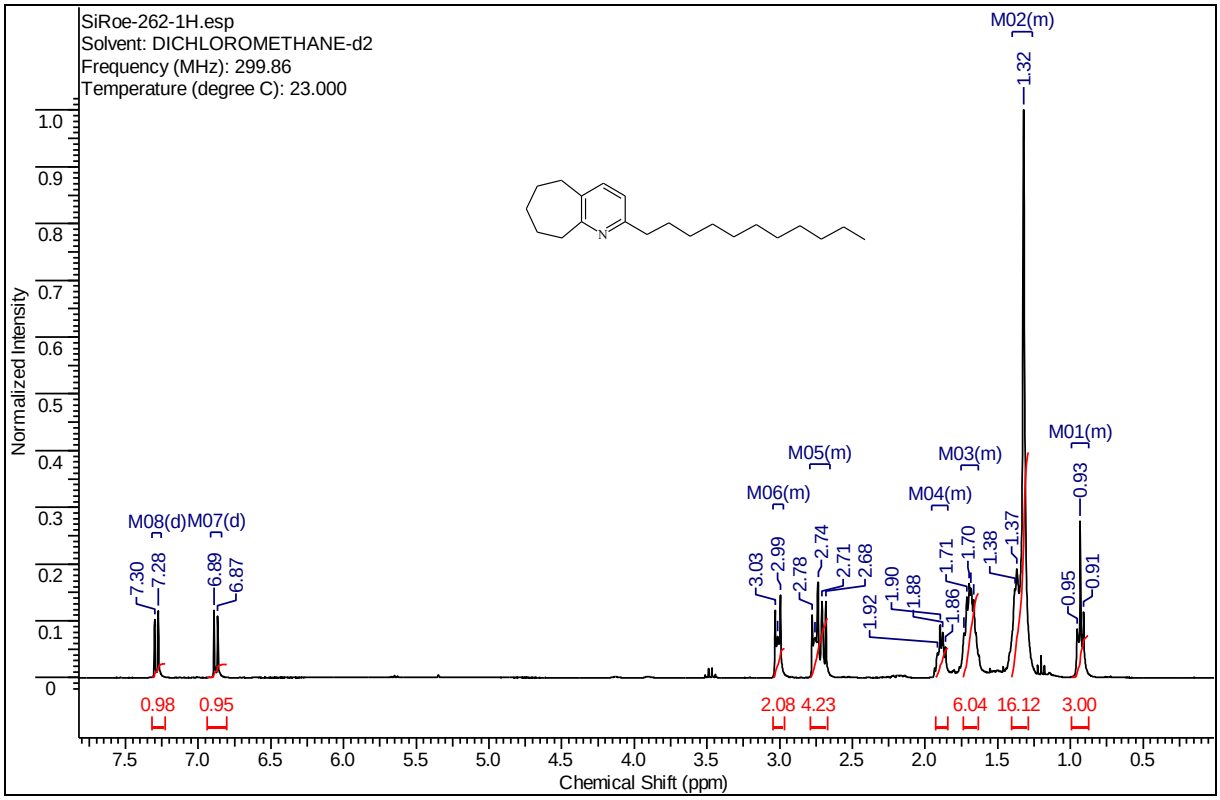
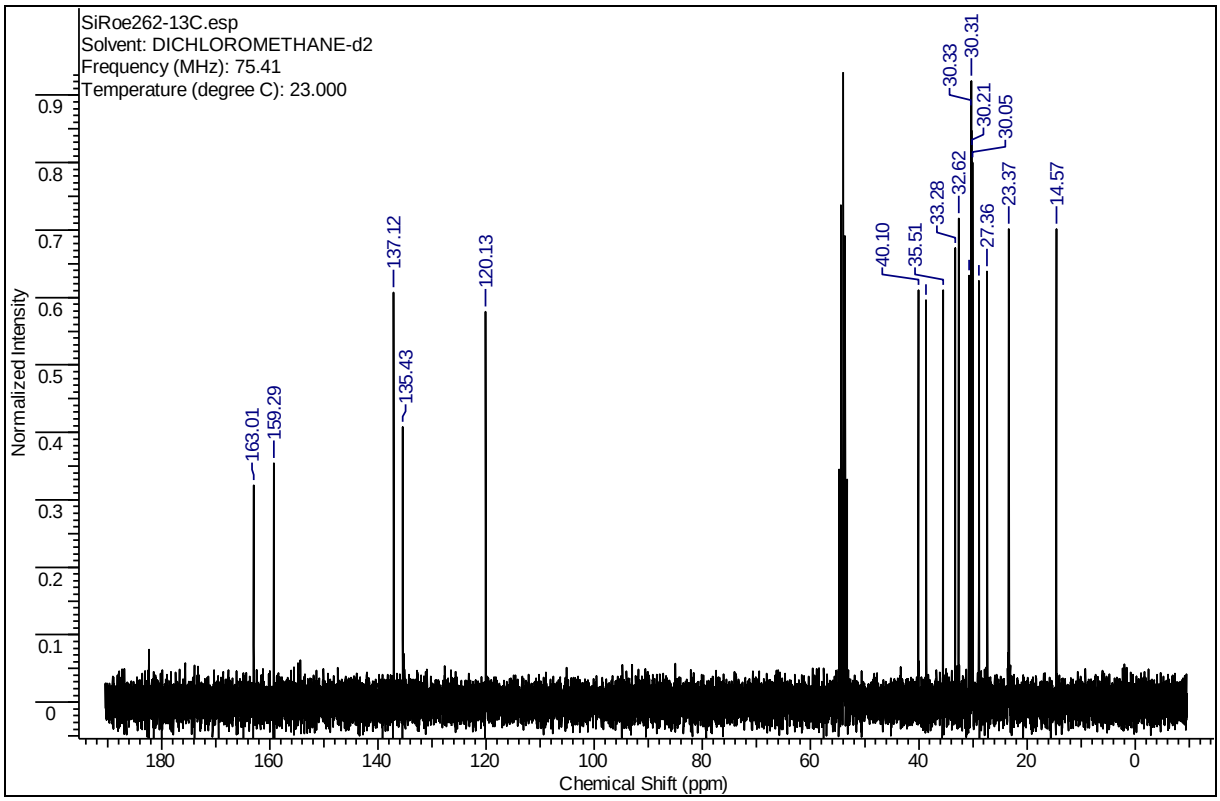
^{1}H and ^{13}C NMR spectra of 2-undecyl-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine (**1e**)





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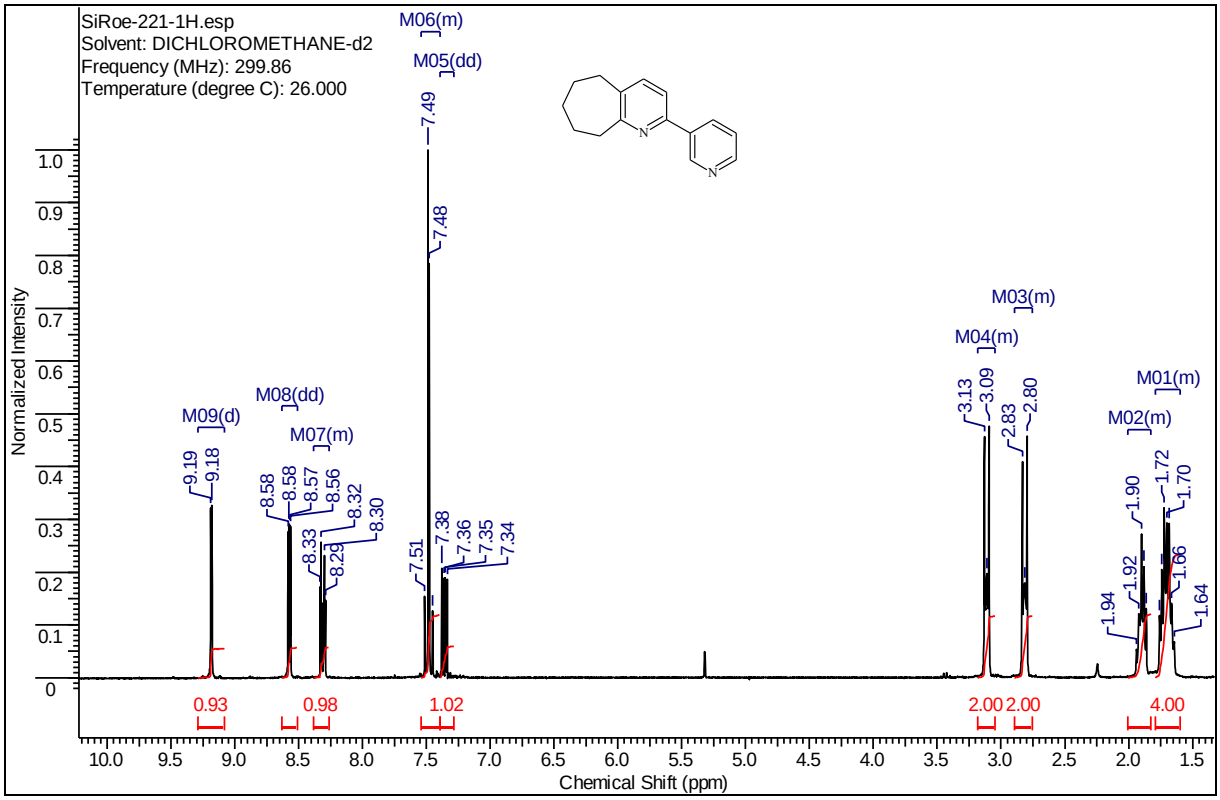
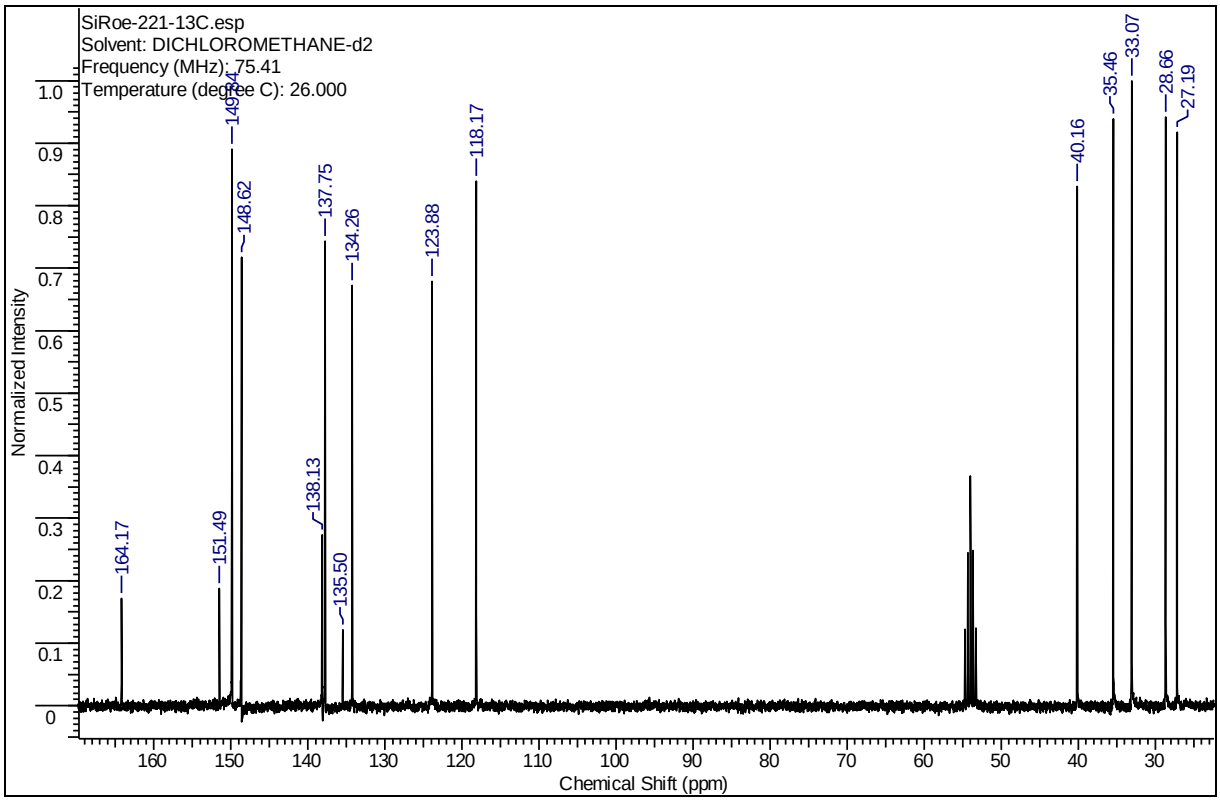
^{1}H and ^{13}C NMR spectra of 2-(pyridin-3-yl)-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine (**1f**)





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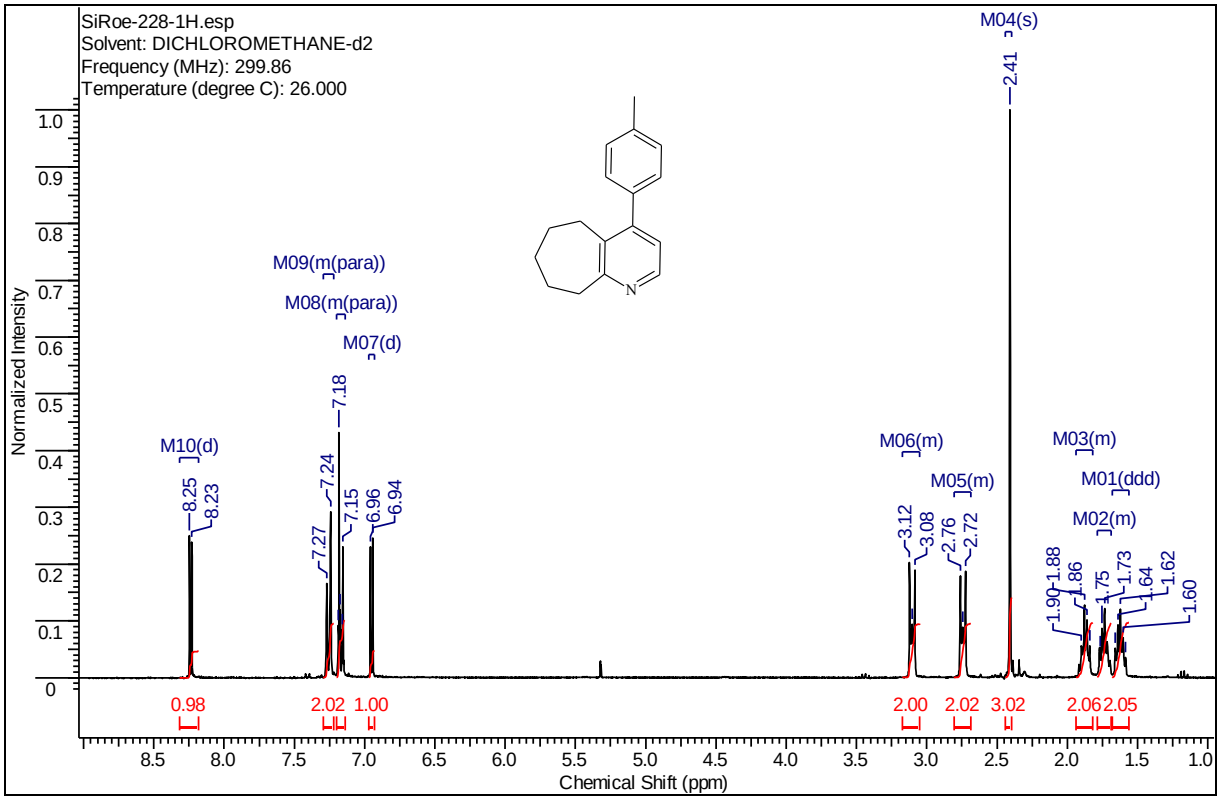
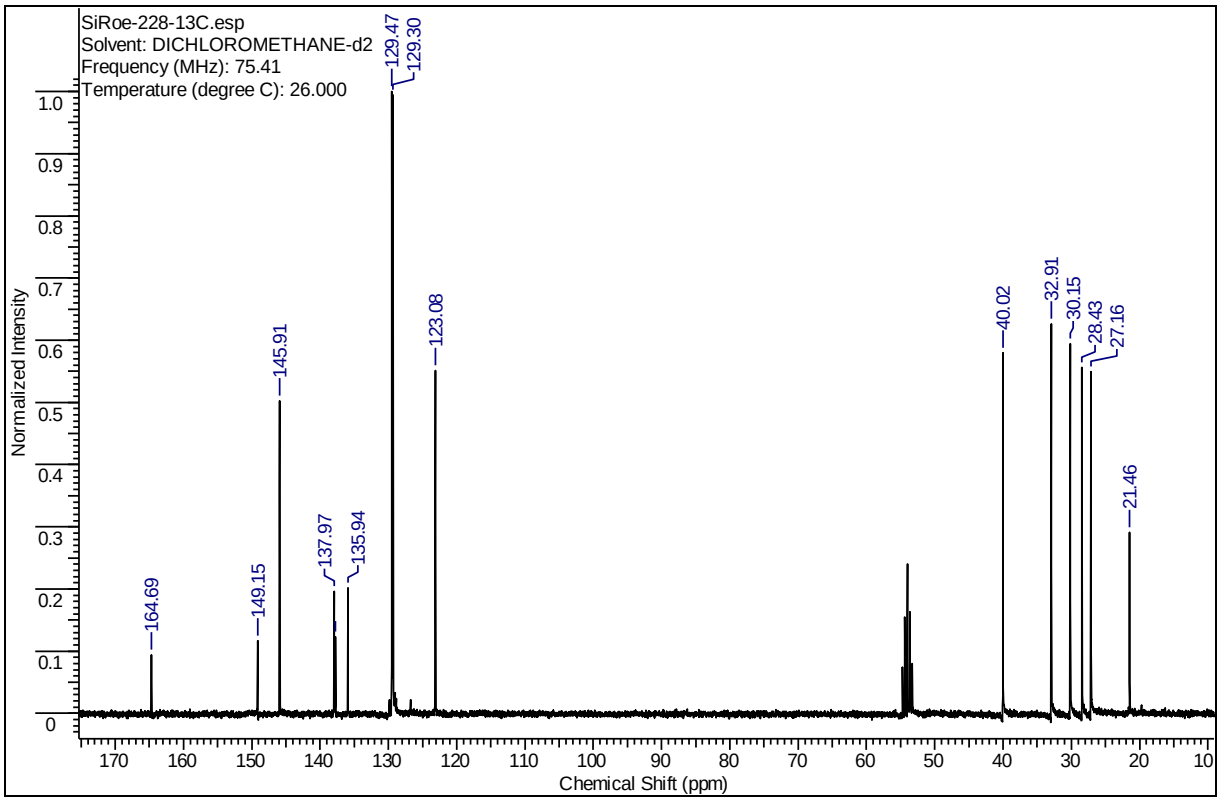
^{1}H and ^{13}C NMR spectra of 3-(p-tolyl)-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine (**1g**)





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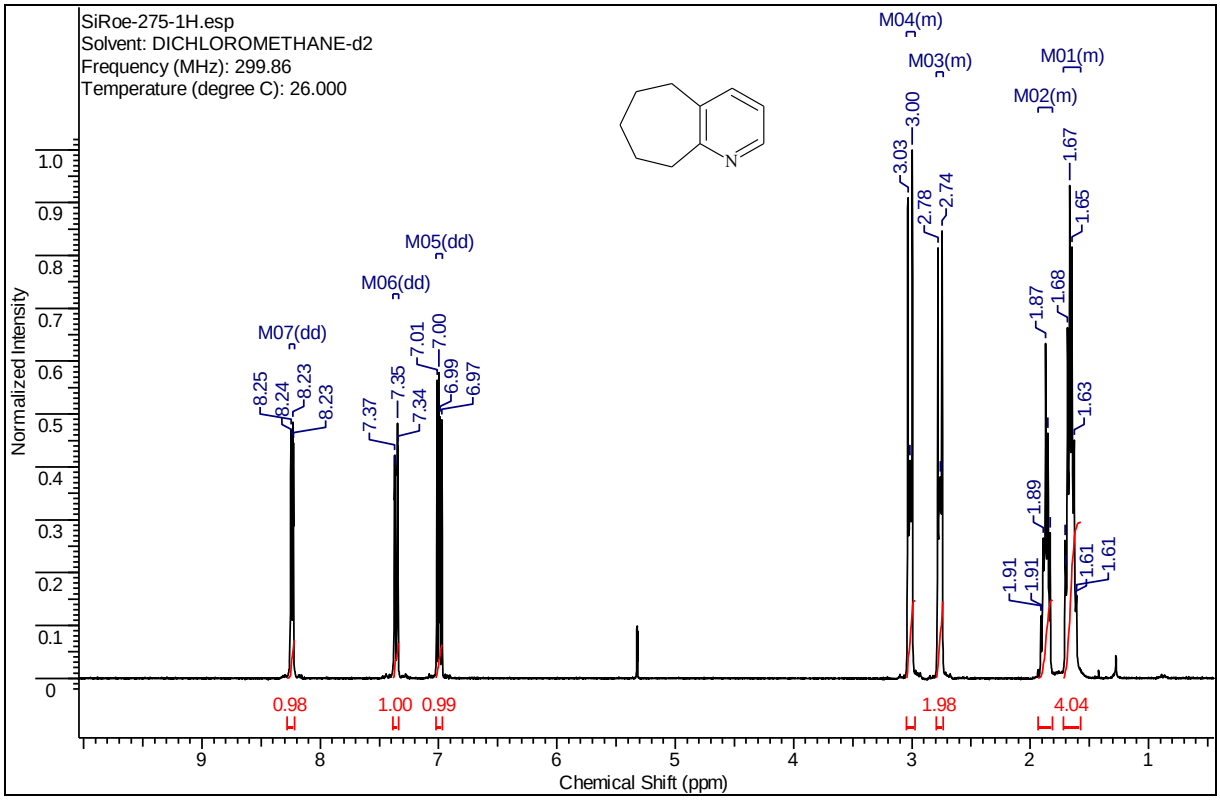
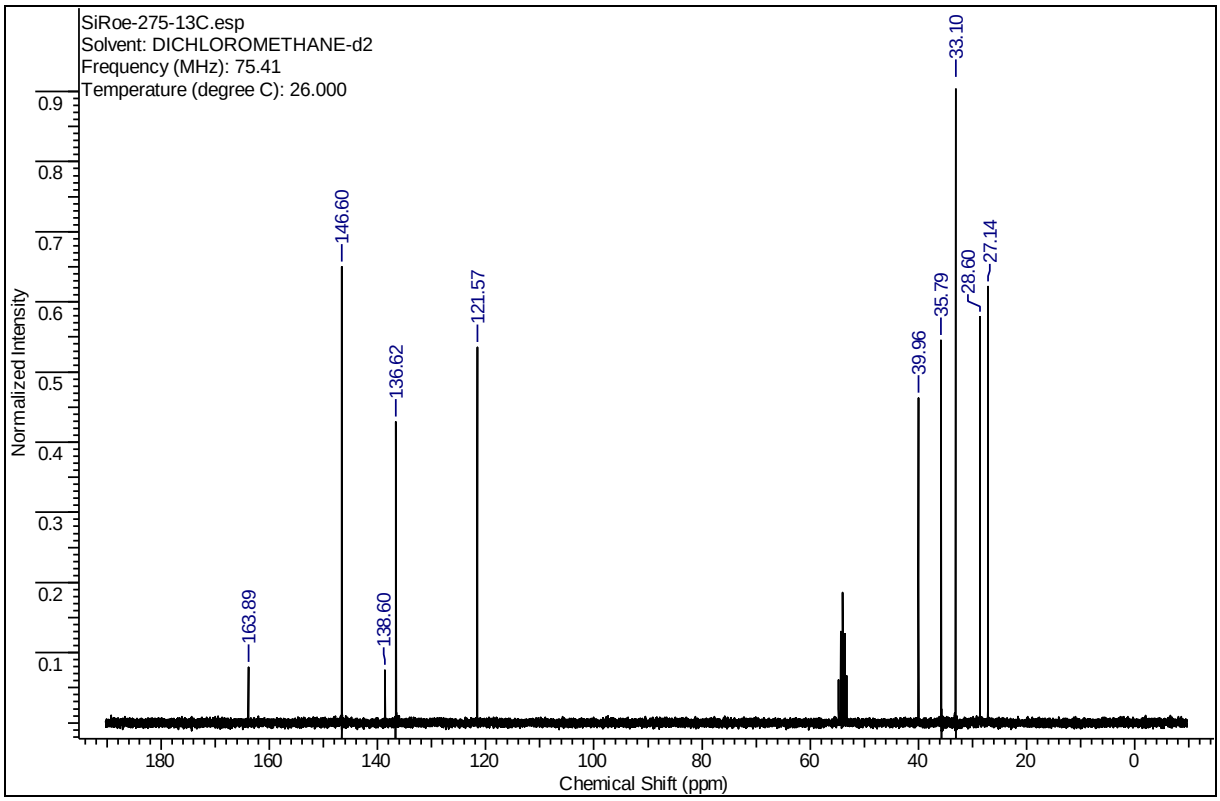
^{1}H and ^{13}C NMR spectra of 5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine (**1h**)





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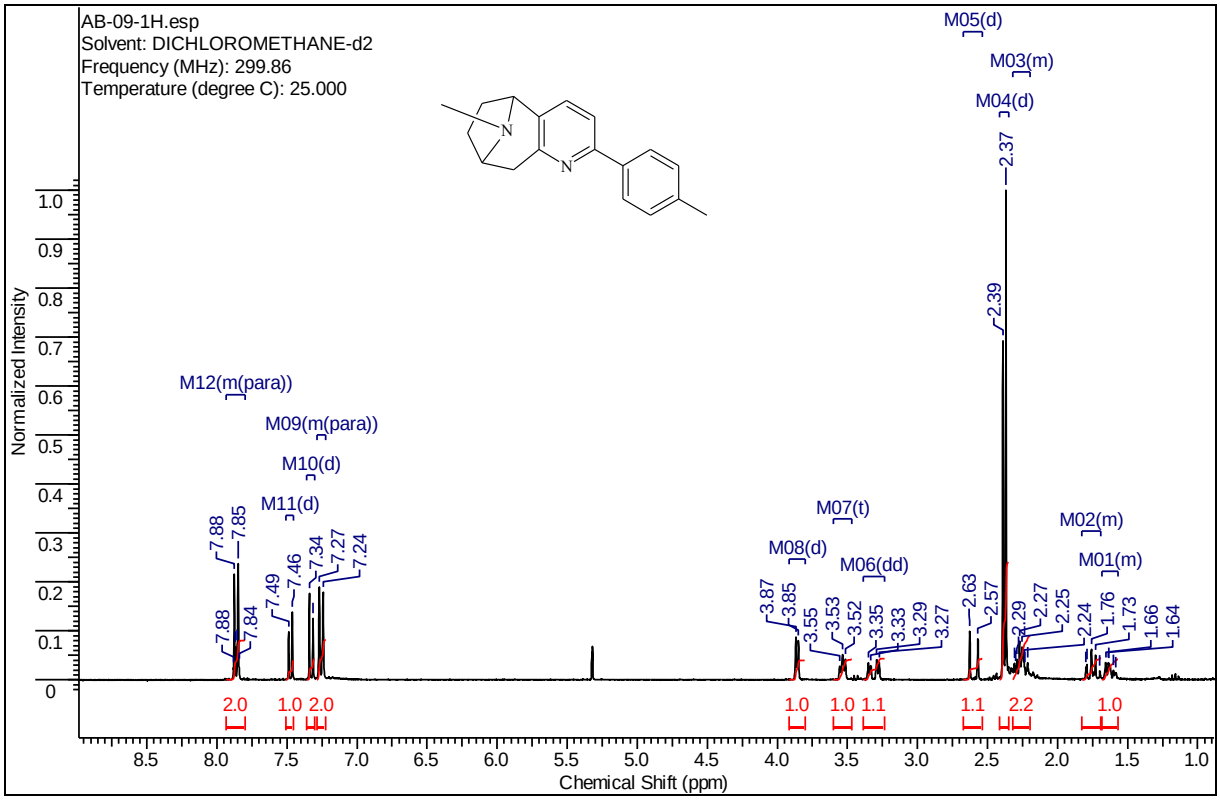
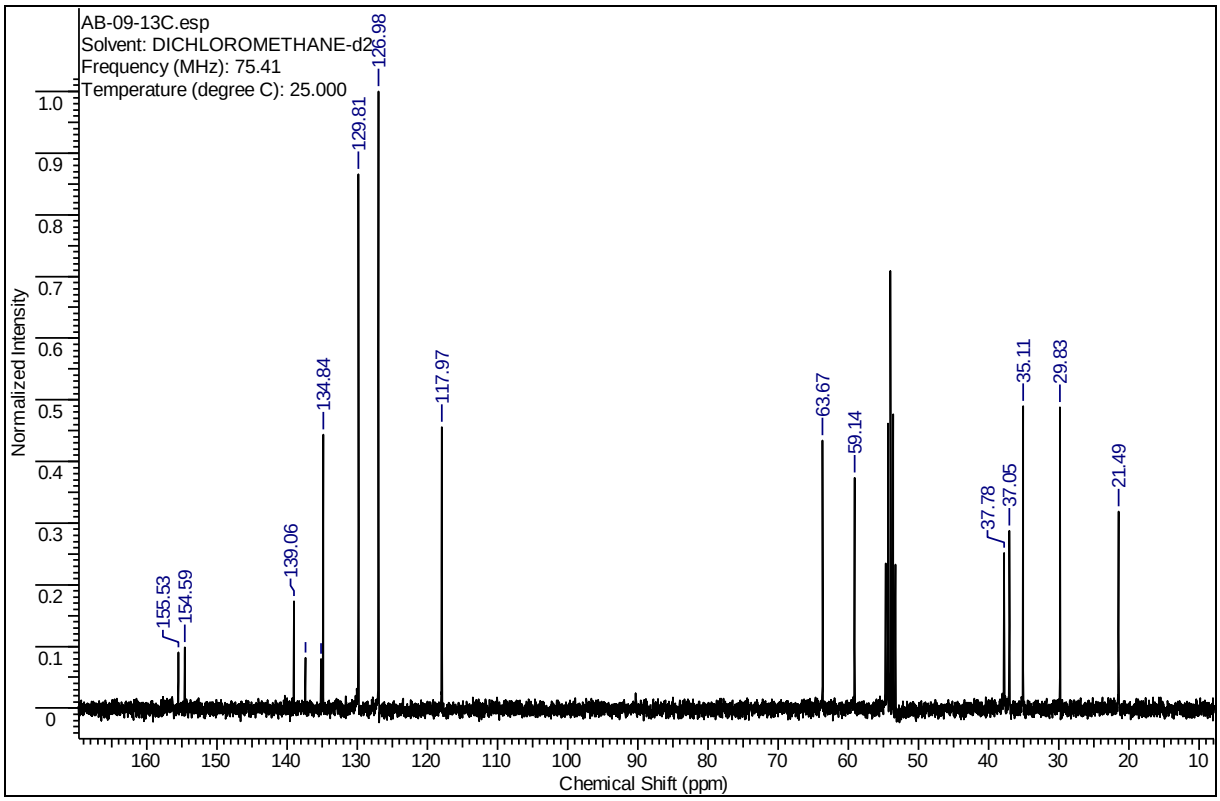
^{1}H and ^{13}C NMR spectra of 2-p-tolyl-5,7,8-trihydro-(N-methyl-azabicyclo[3.2.1]octa)[*b*]pyridine (**1k**)





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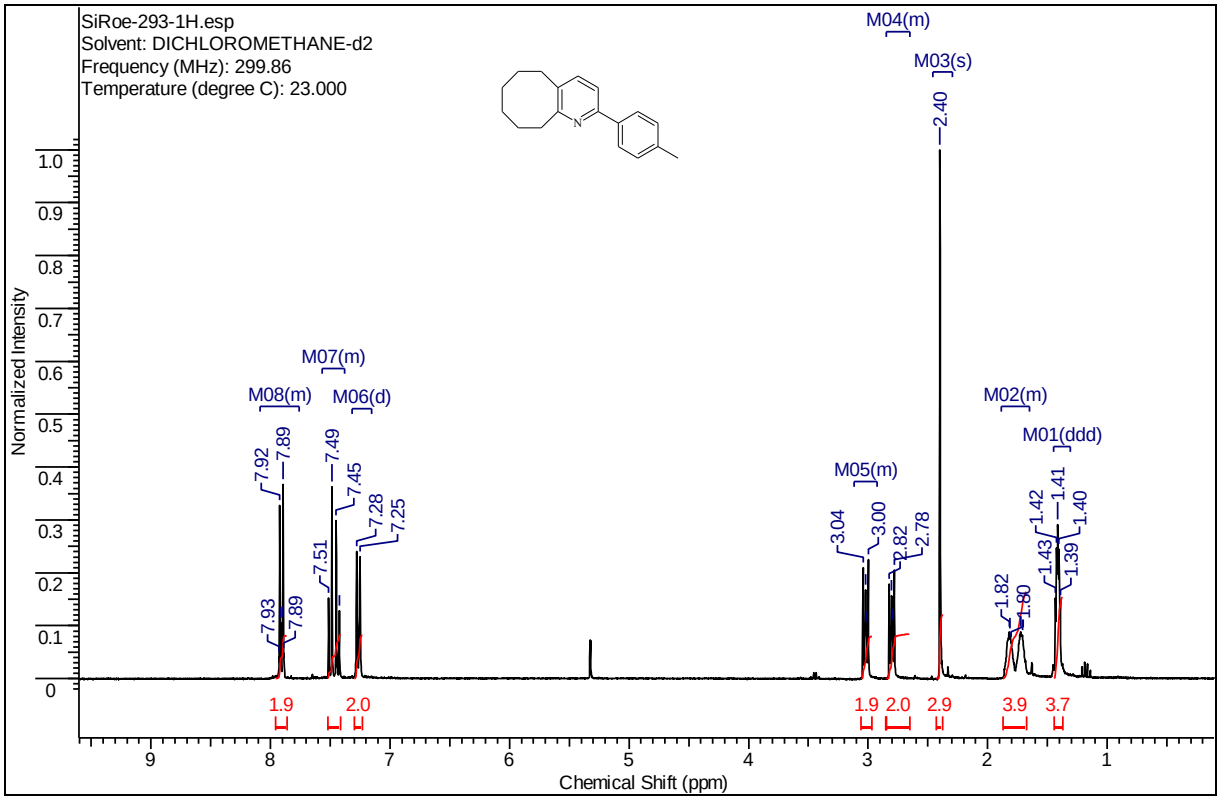
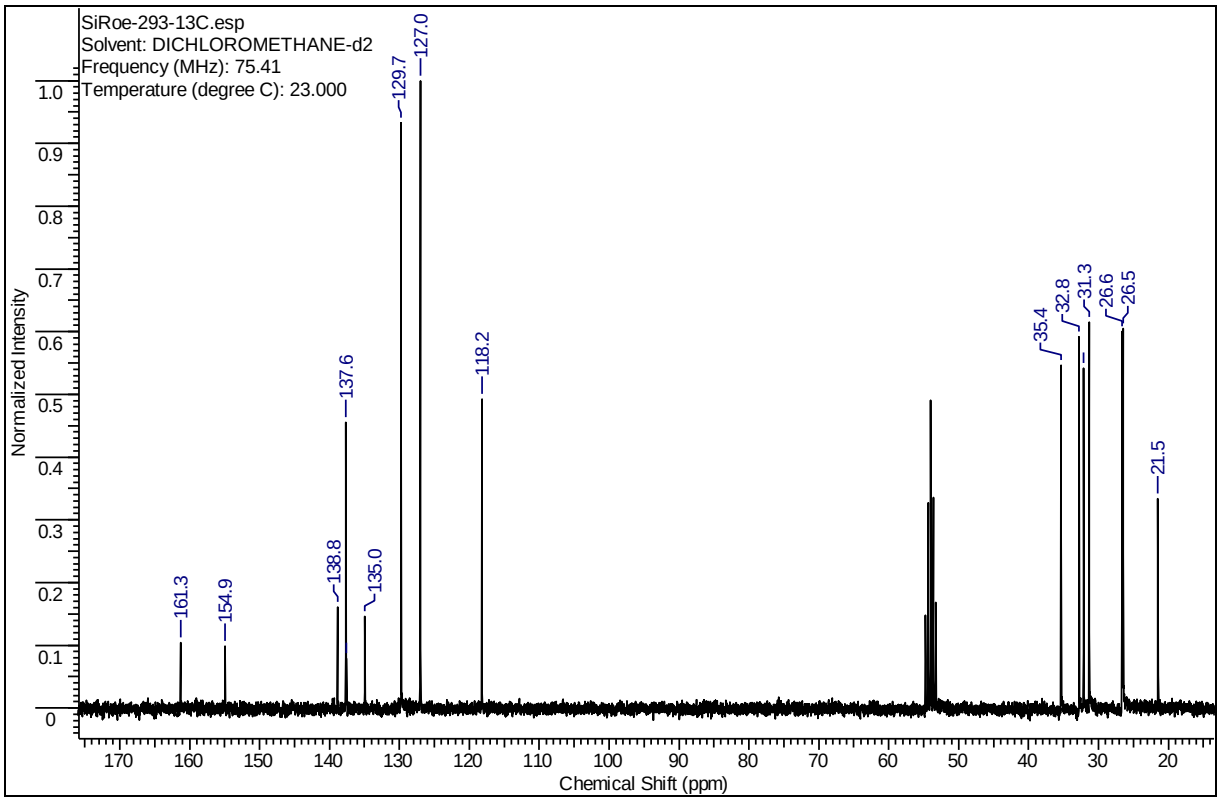
^{1}H and ^{13}C NMR spectra of 2-(p-tolyl)-5,6,7,8,9,10-hexahydro-cycloocta[*b*]pyridine (**1i**)





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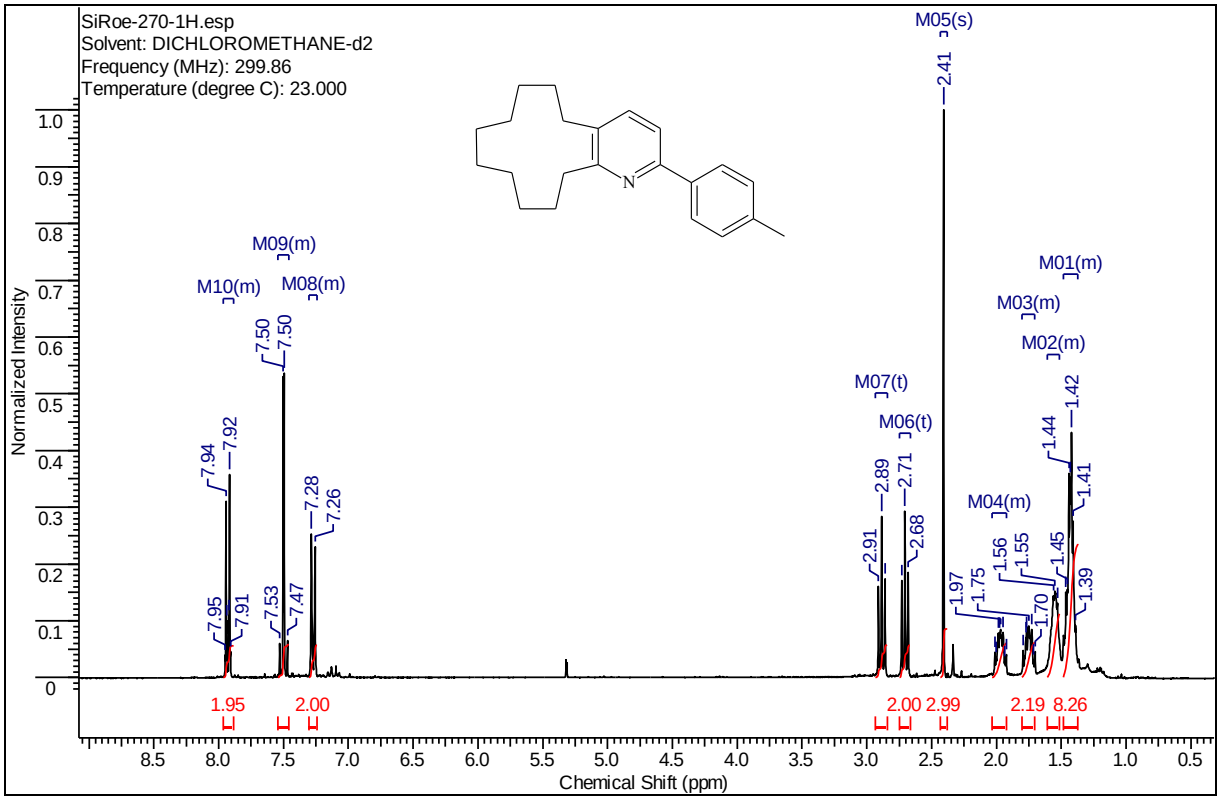
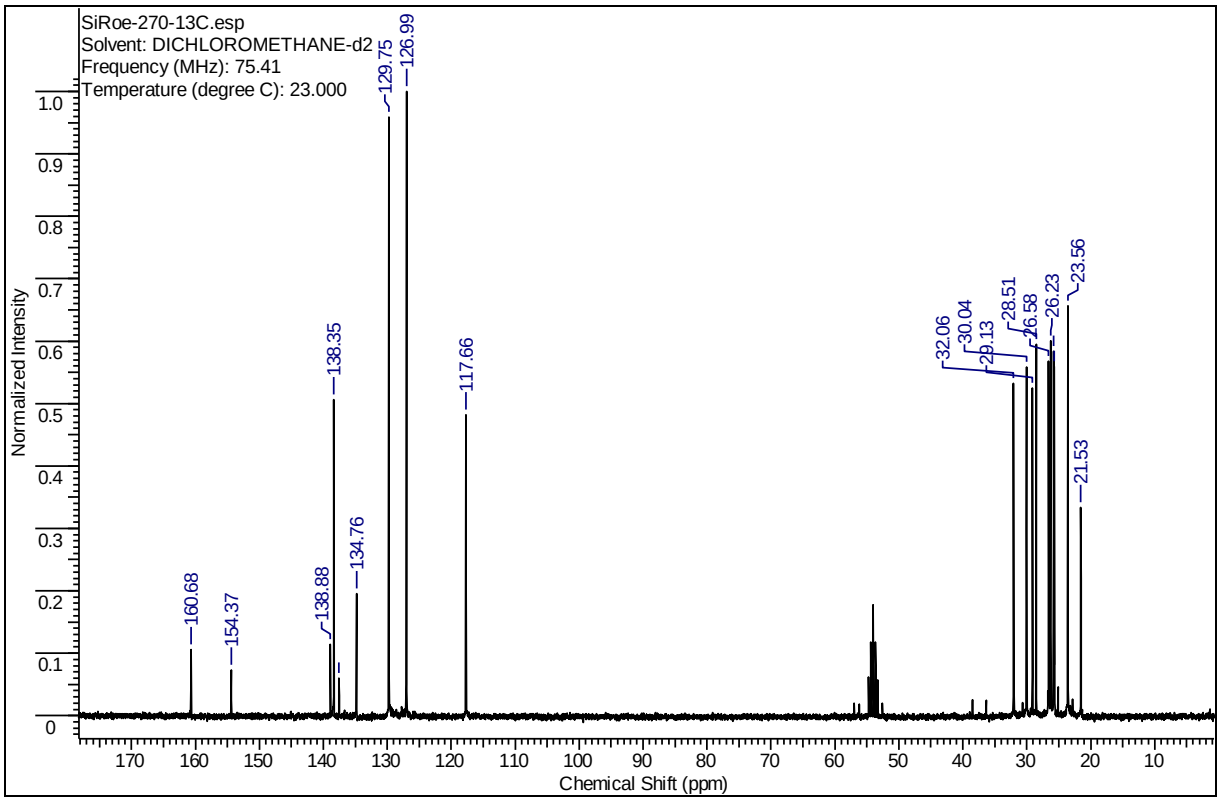
^{1}H and ^{13}C NMR spectra of 2-*p*-tolyl-5,6,7,8,9,10,11,12,13,14-decahydro-cyclododeca[*b*]pyridine (**1j**)





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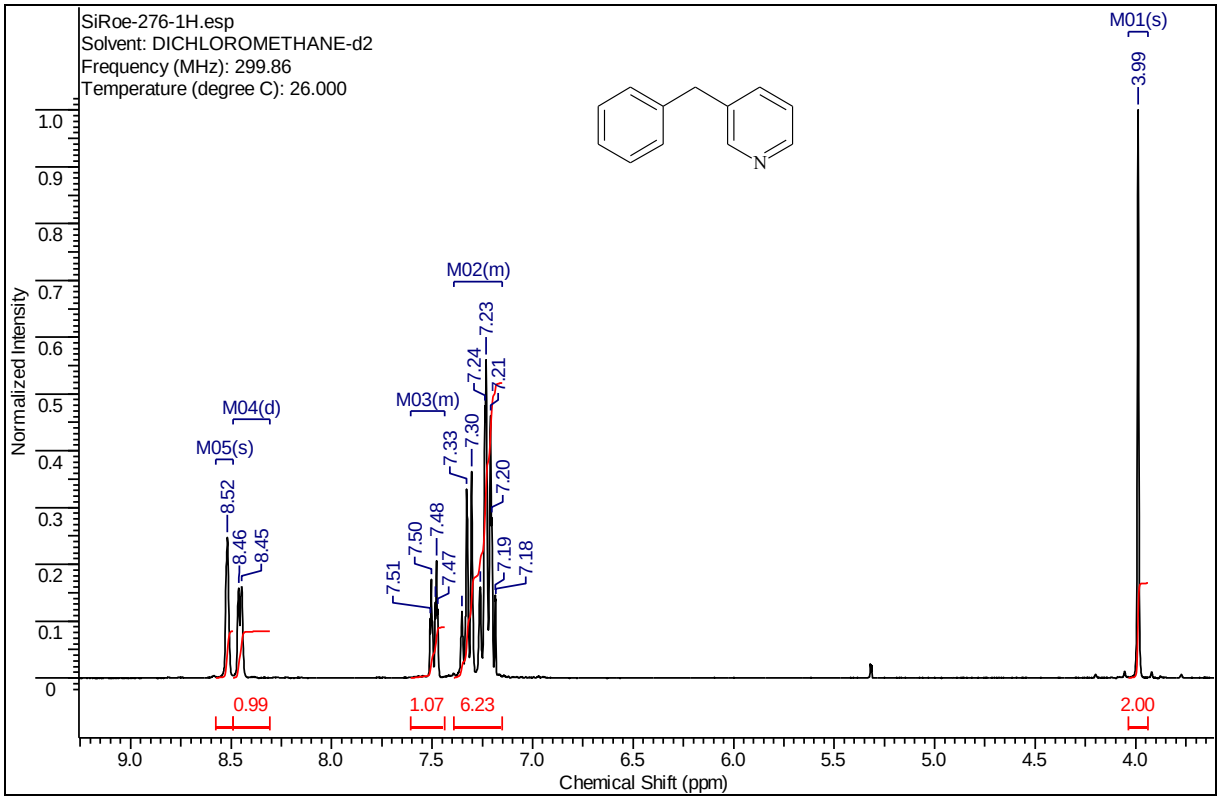
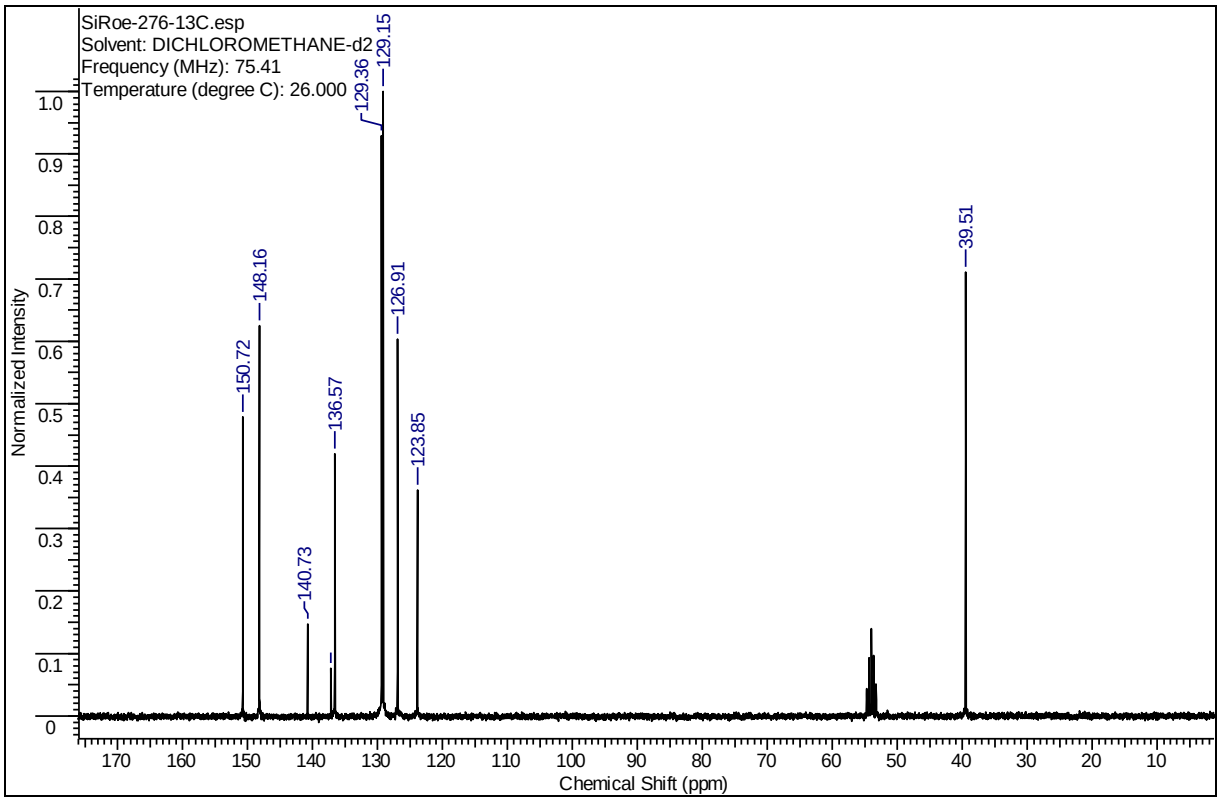
^{1}H and ^{13}C NMR spectra of 3-benzylpyridine (**1m**)





6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

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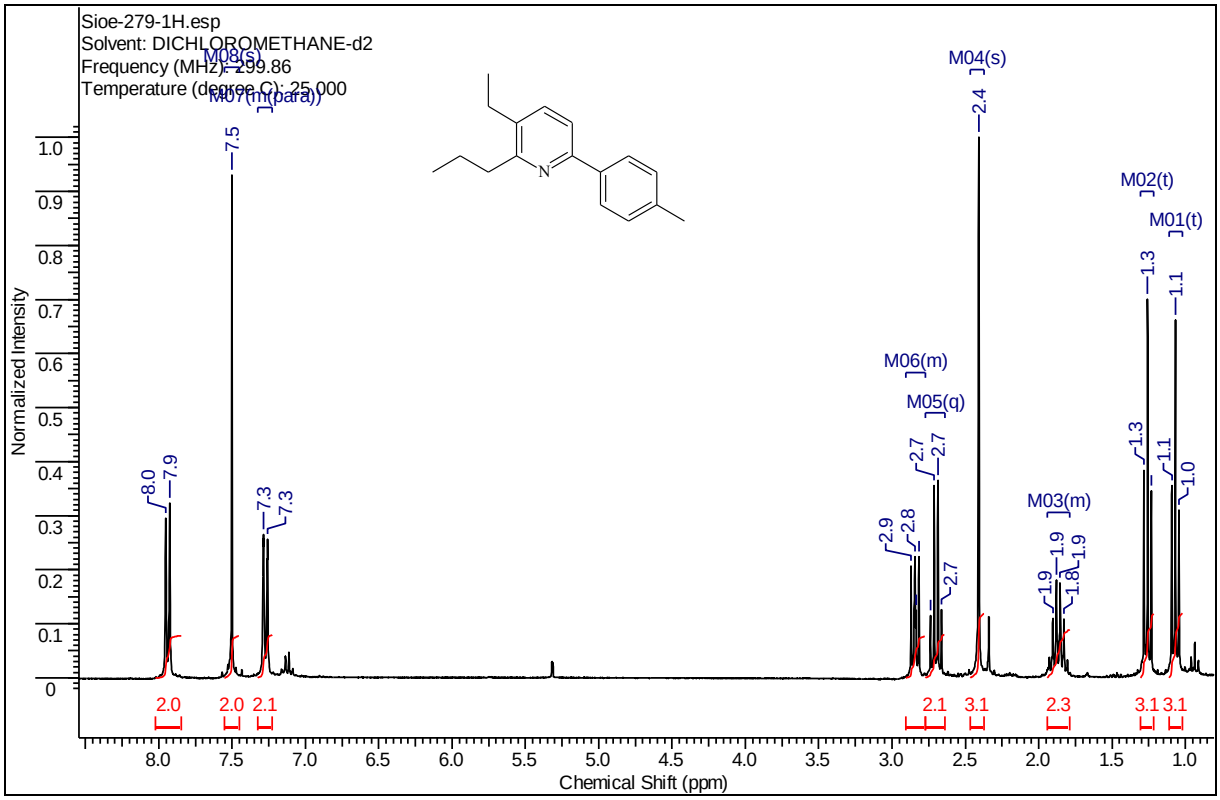
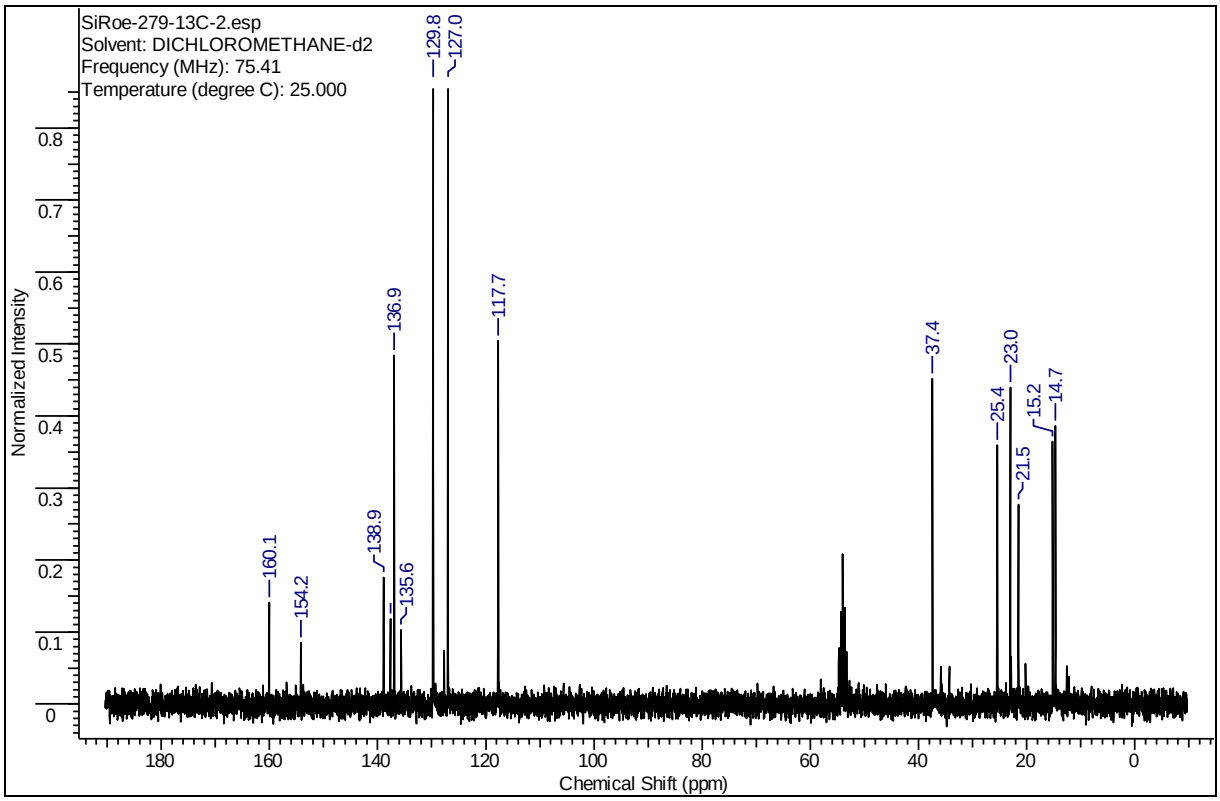
^{1}H and ^{13}C NMR spectra of 3-ethyl-2-propyl-5-p-tolyl-pyridine (**1l**)





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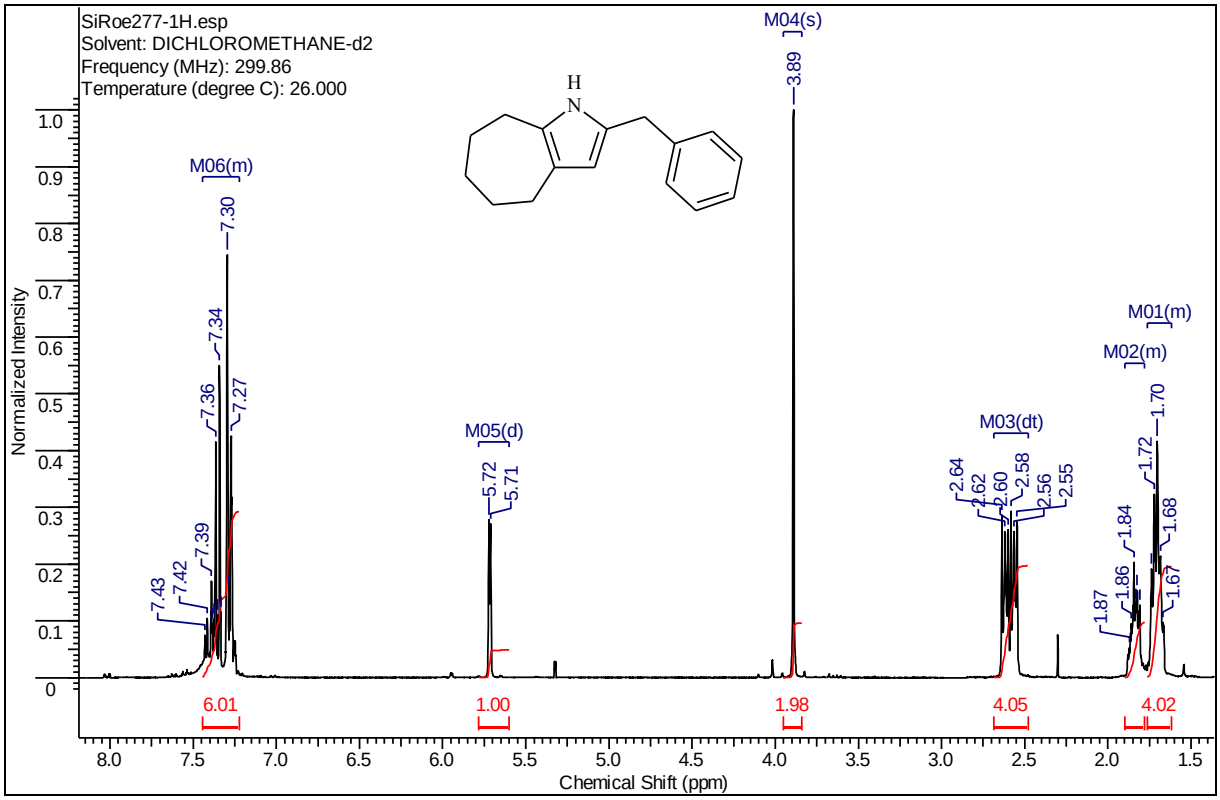
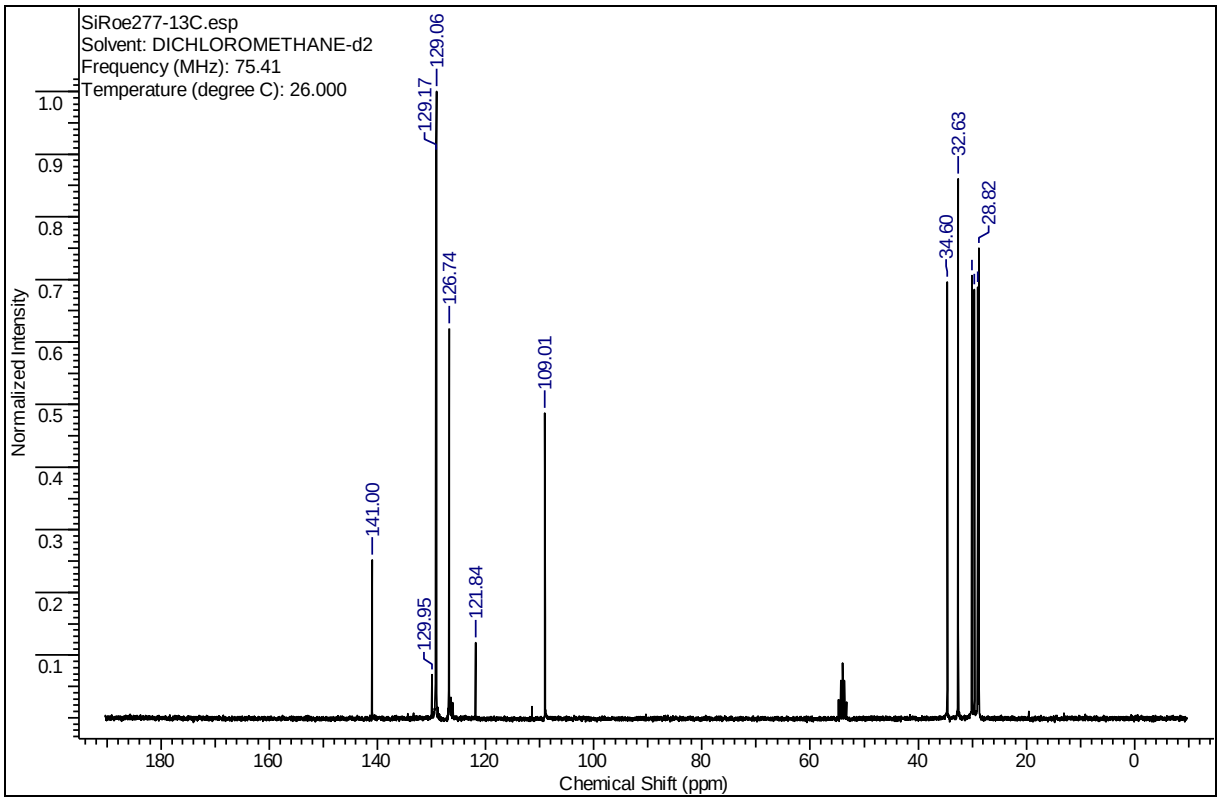
^{1}H and ^{13}C NMR spectra of 2-benzyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole (**2a**)





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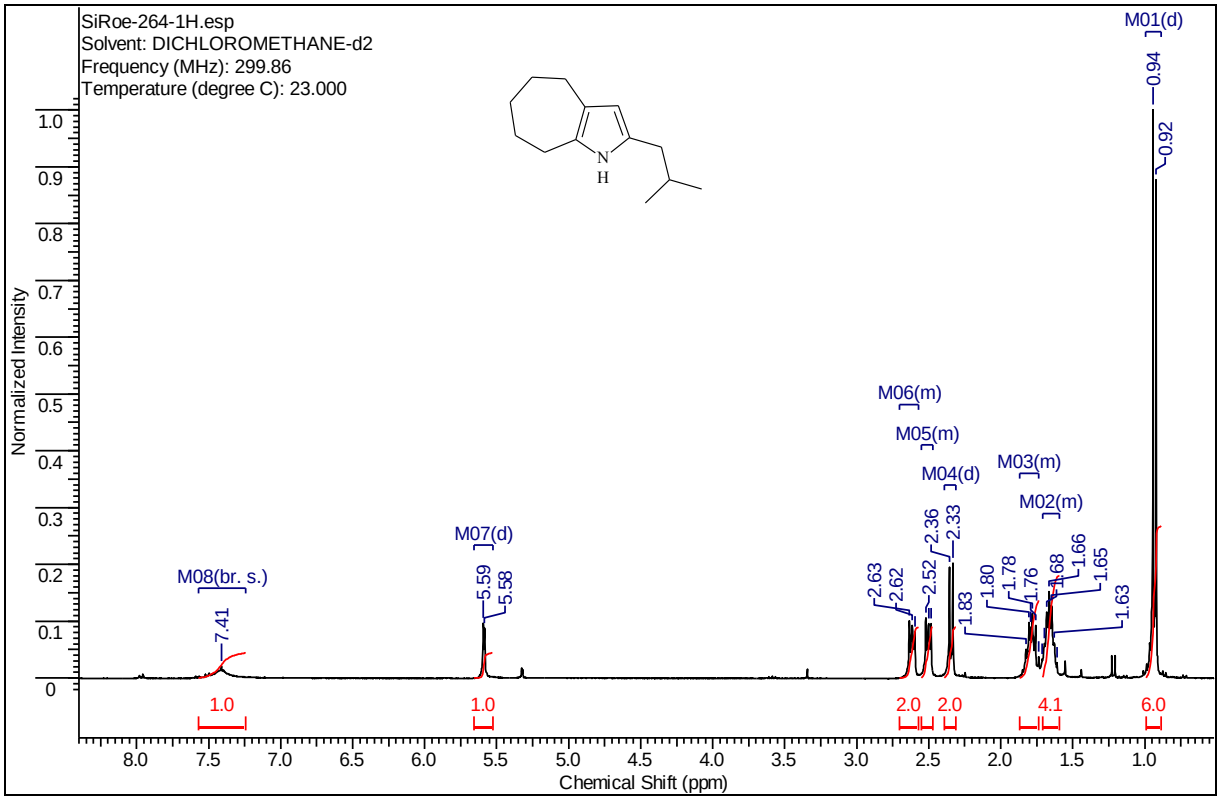
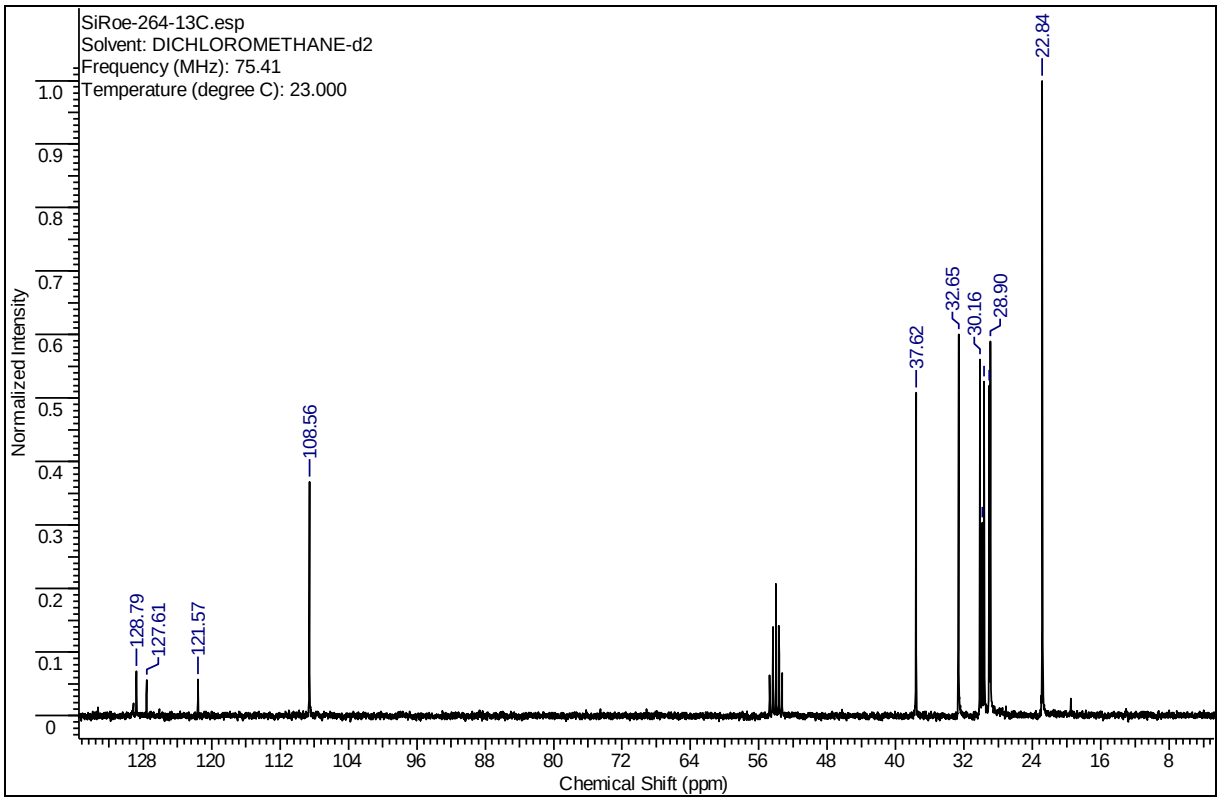
^{1}H and ^{13}C NMR spectra of 2-(2-methyl-propyl)-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole (**2b**)





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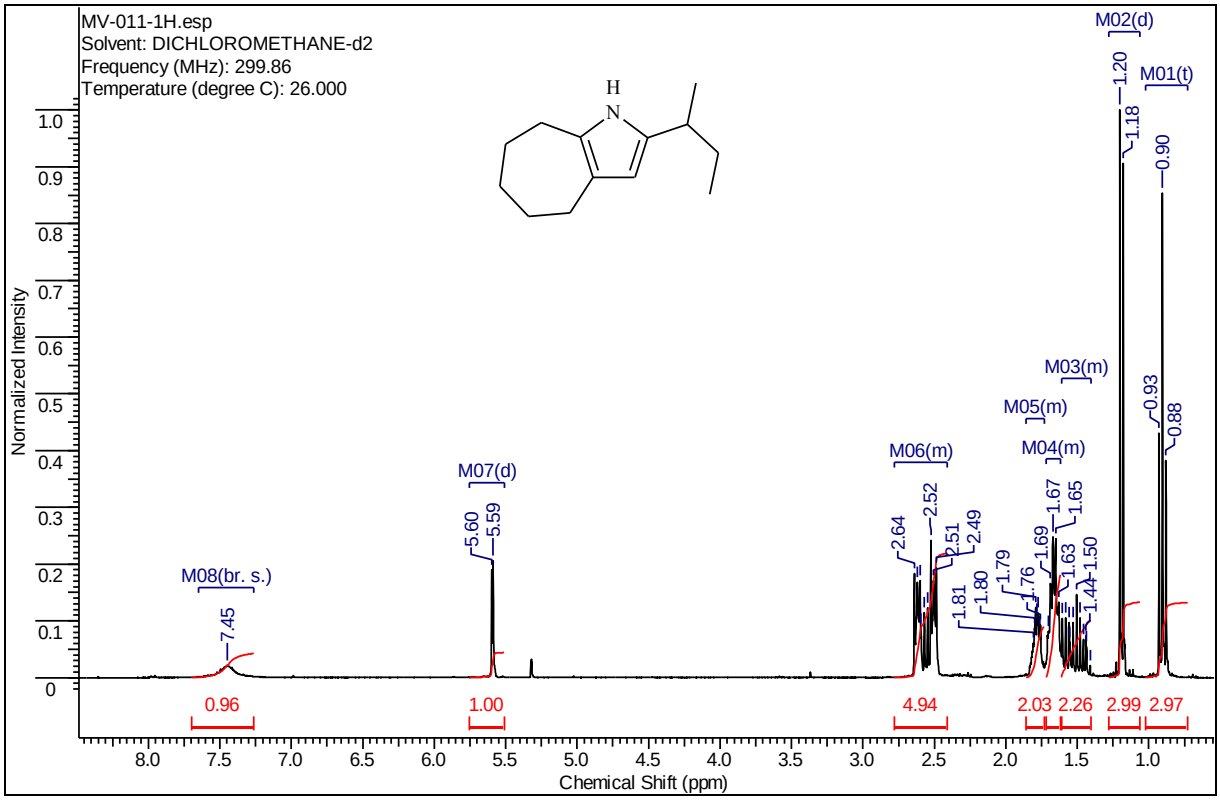
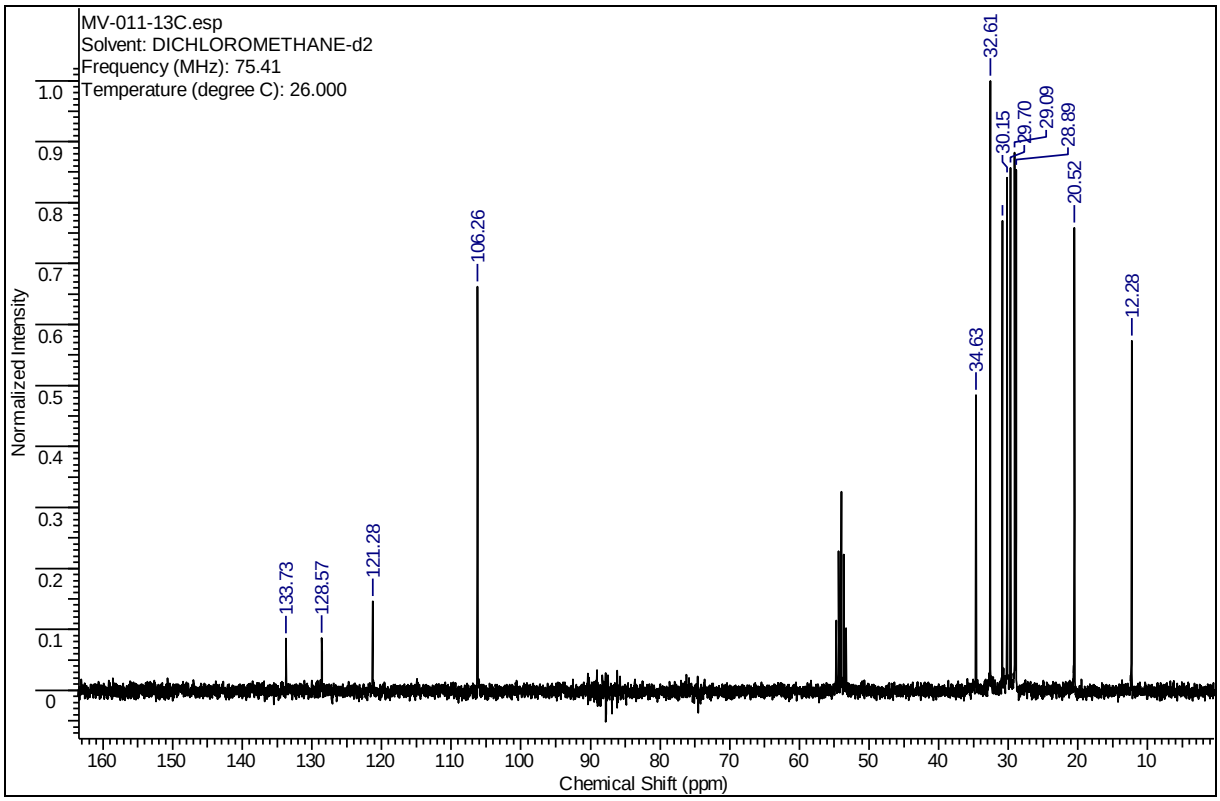
^{1}H and ^{13}C NMR spectra of 2-(1-methyl-propyl)-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole (**2c**)





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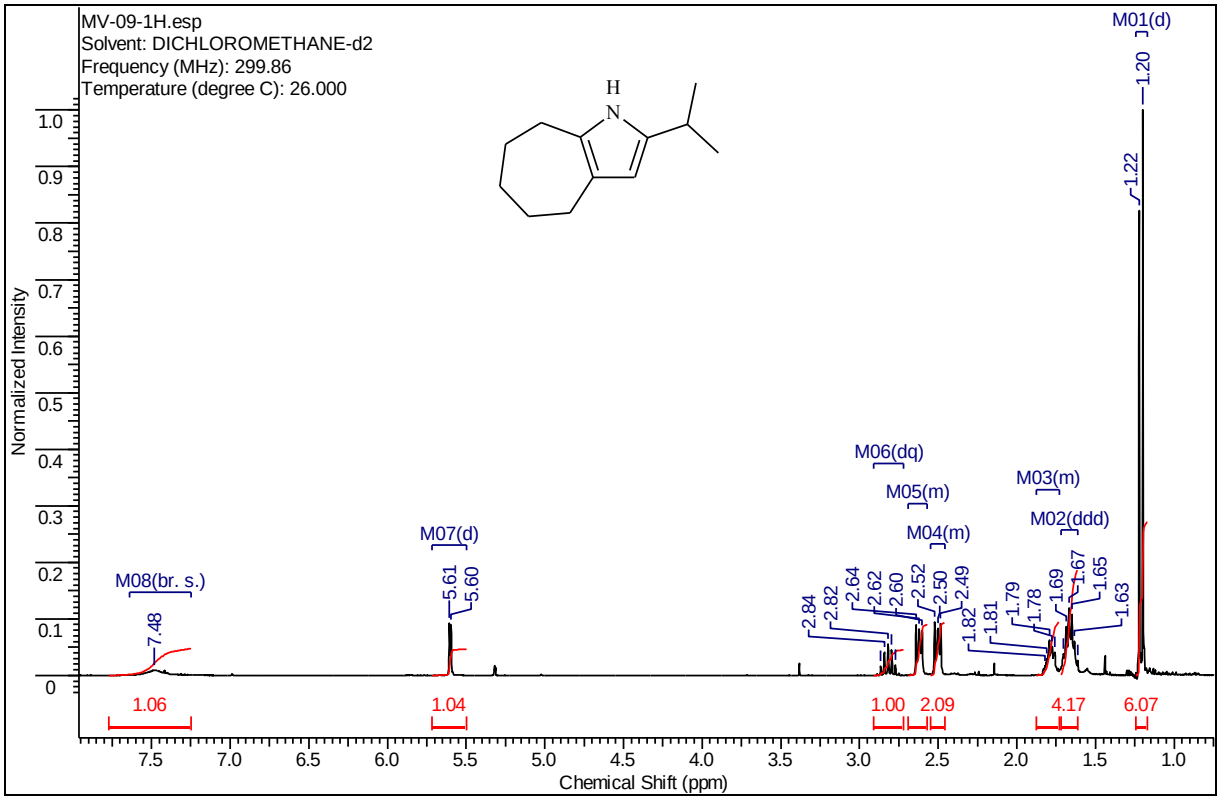
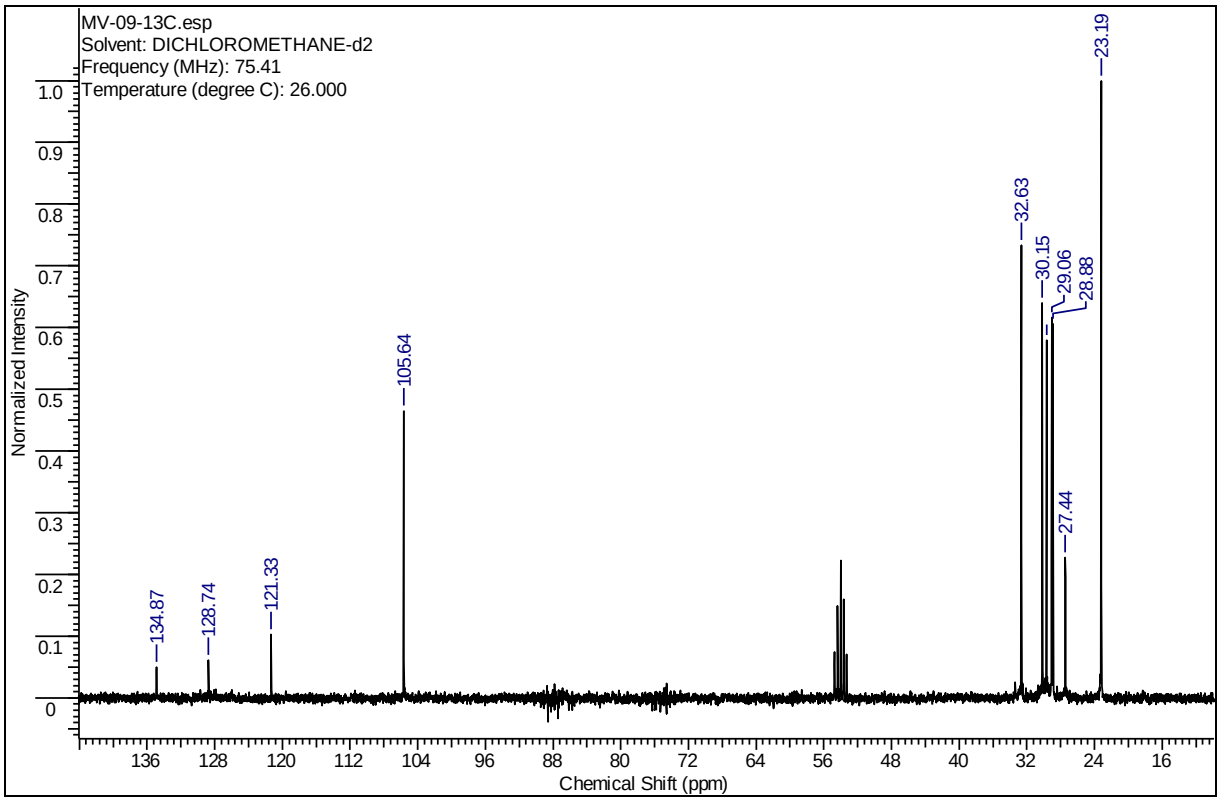
^{1}H and ^{13}C NMR spectra of 2-isopropyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole (**2d**)





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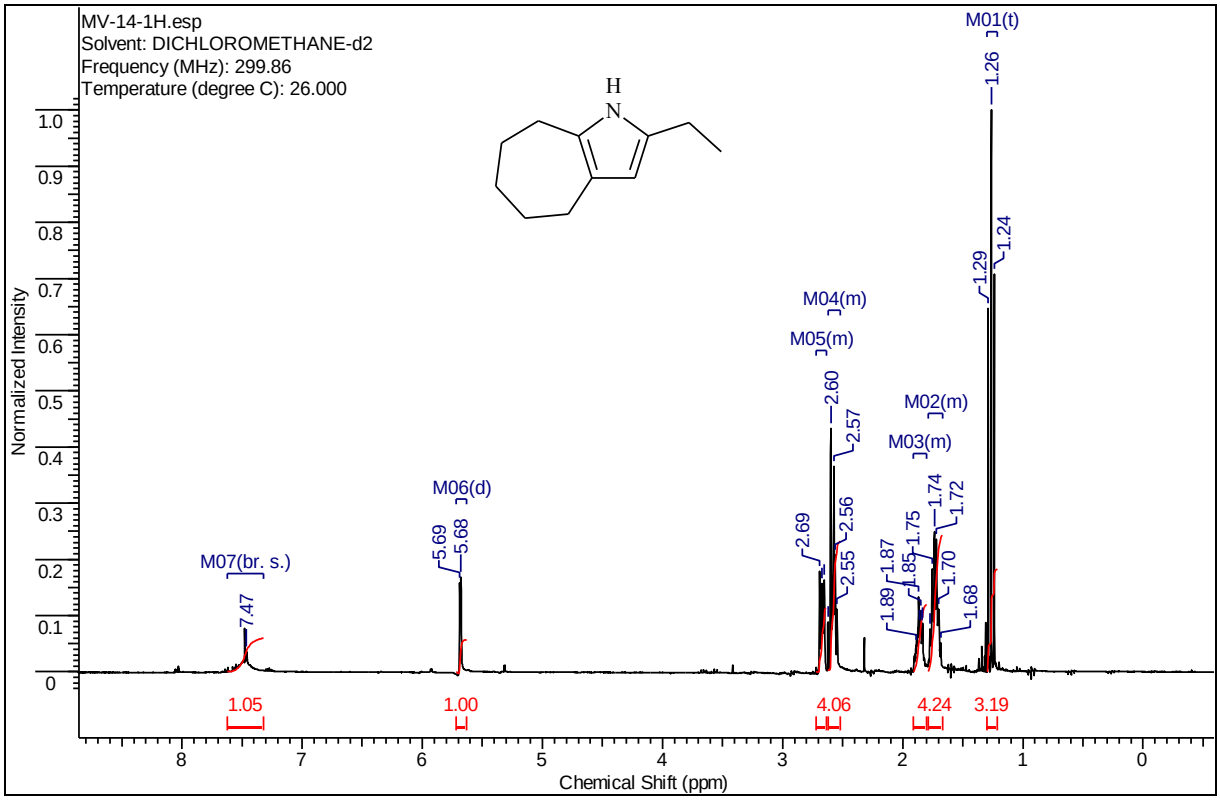
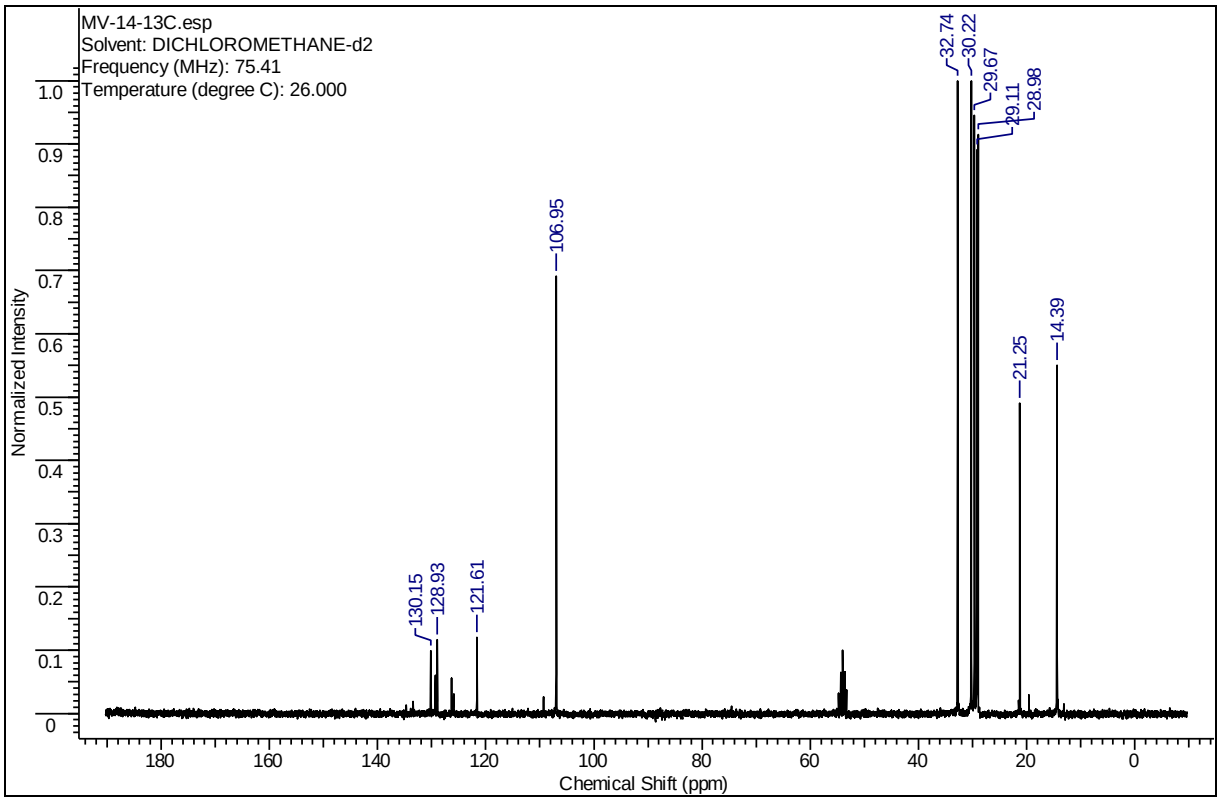
^{1}H and ^{13}C NMR spectra of 2-ethyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole (**2e**)





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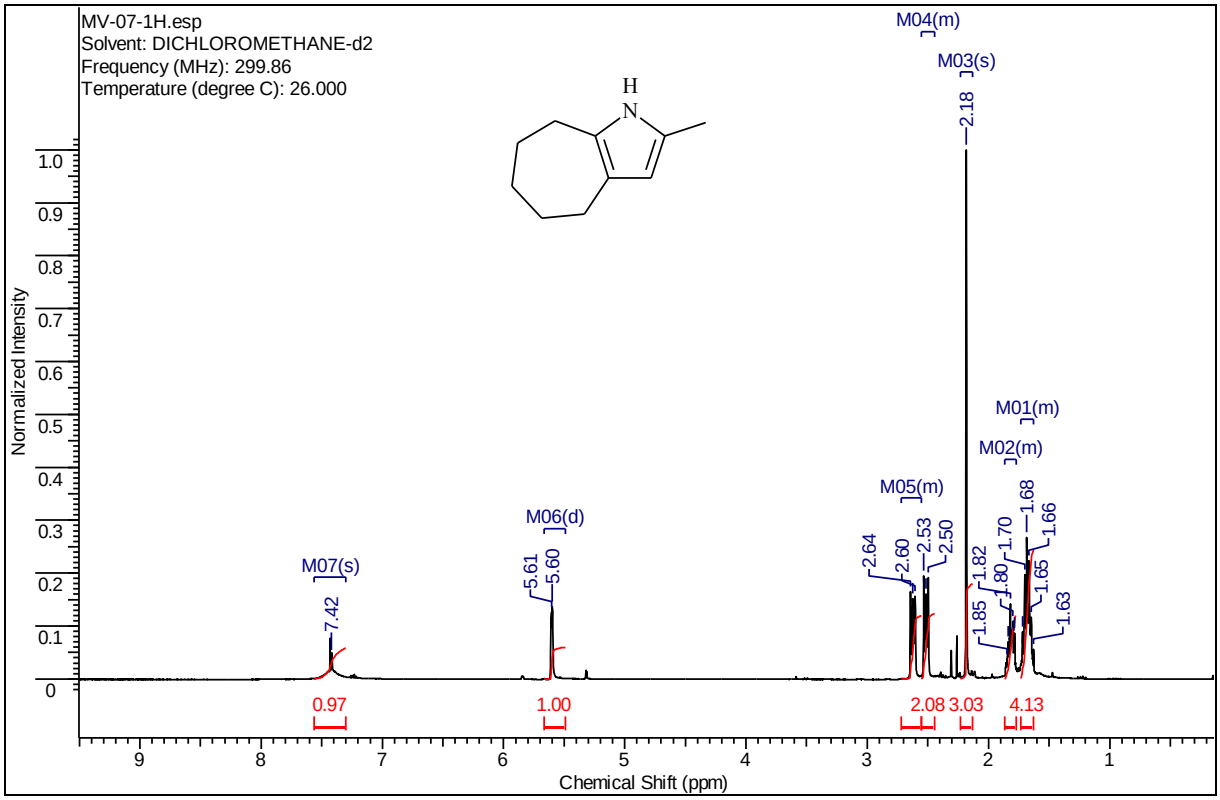
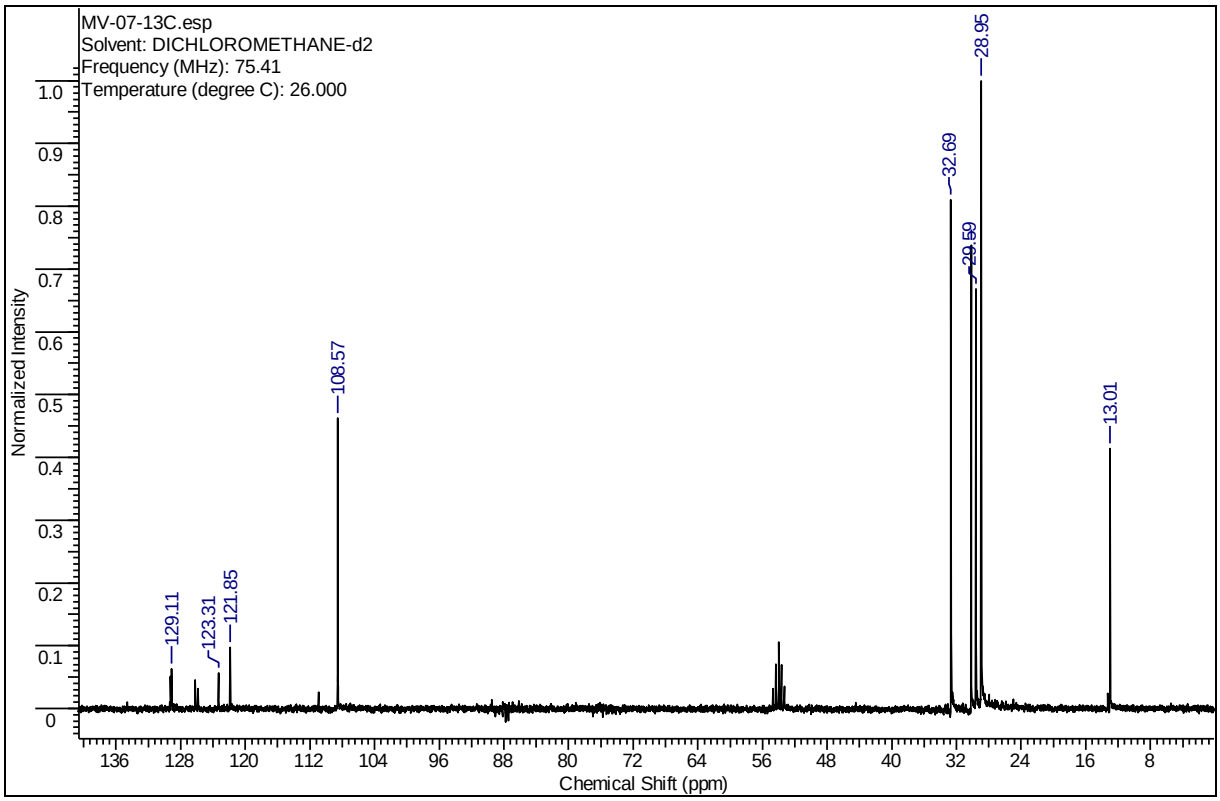
^{1}H and ^{13}C NMR spectra of 2-methyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole (**2f**)





6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

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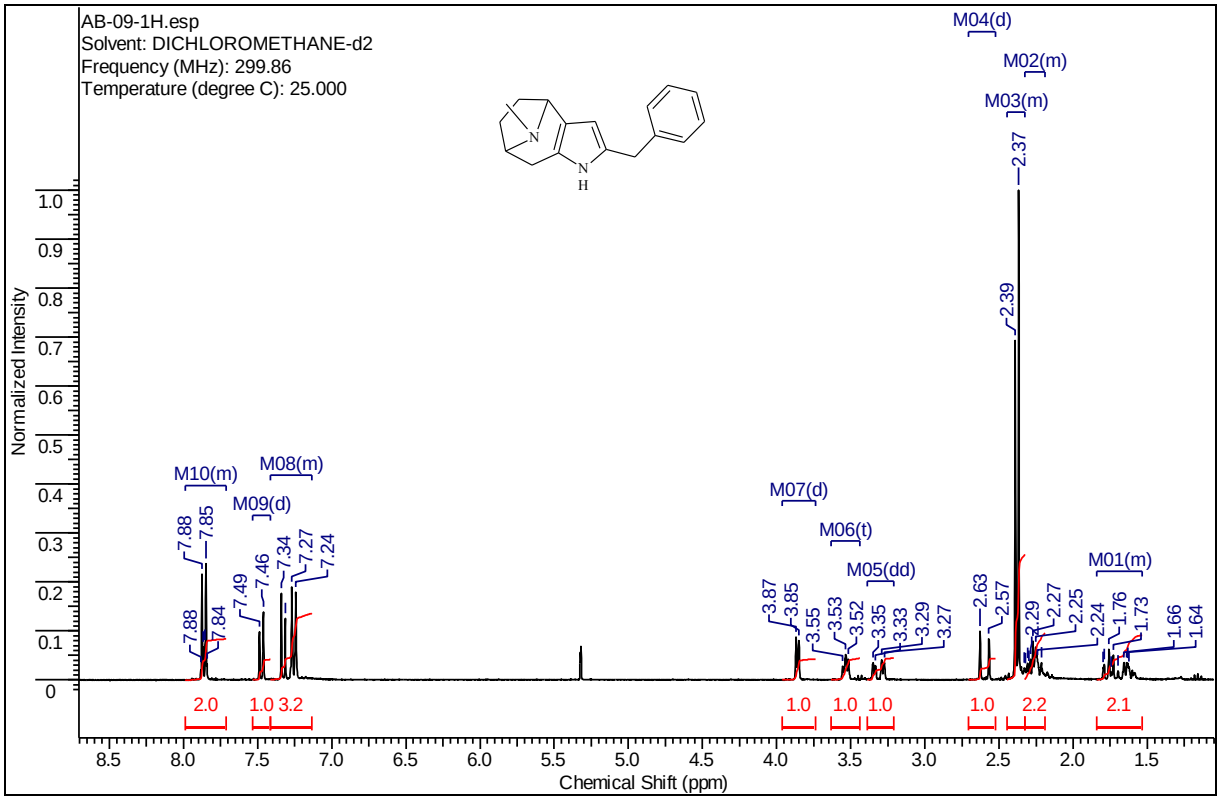
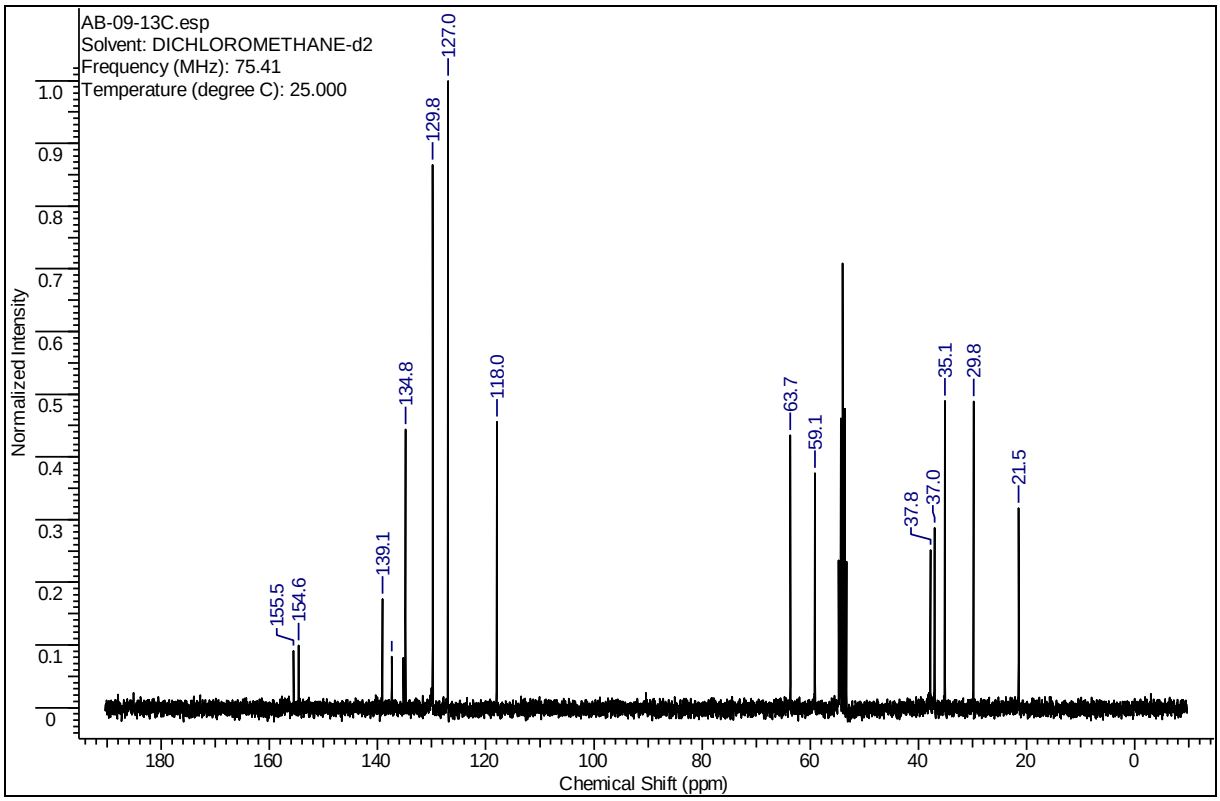
^{1}H and ^{13}C NMR spectra of 2-benzyl-6,7,9-trihydro-(N-methyl-azabicyclo[3.2.1]octa)[*b*]pyrrole (**2j**)





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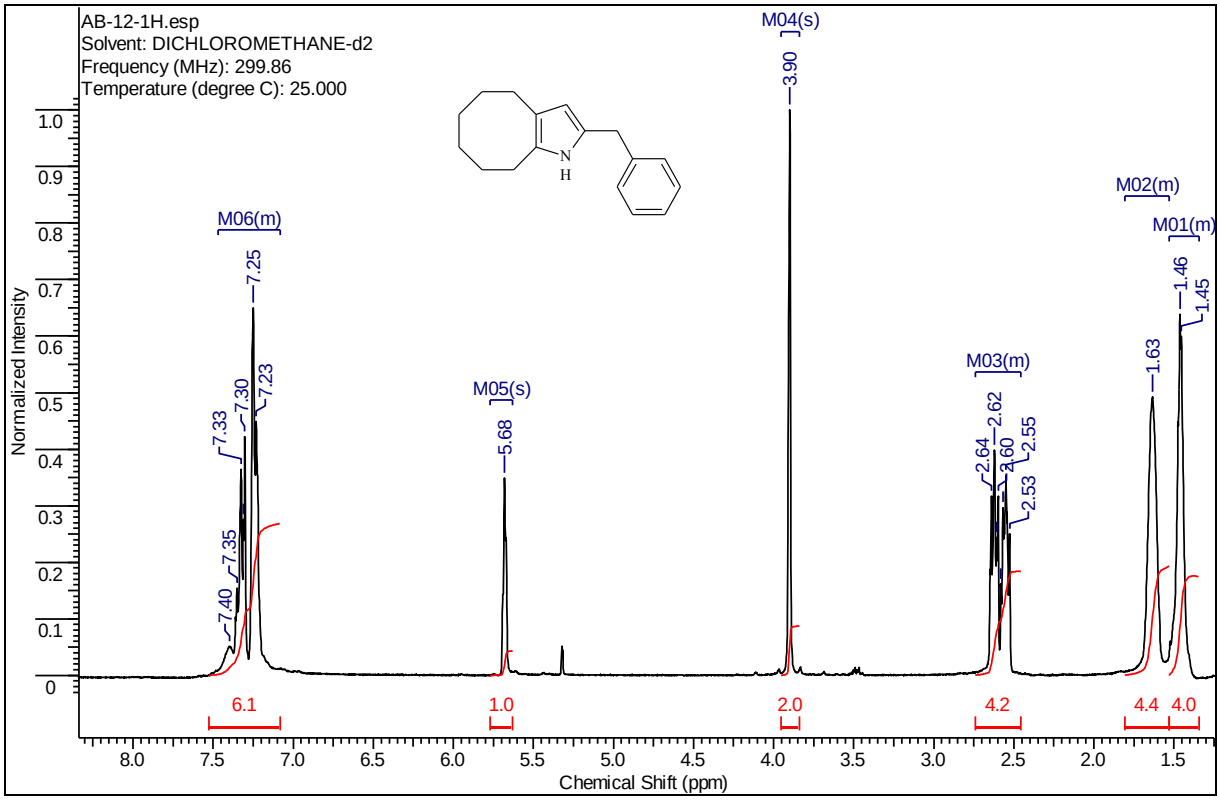
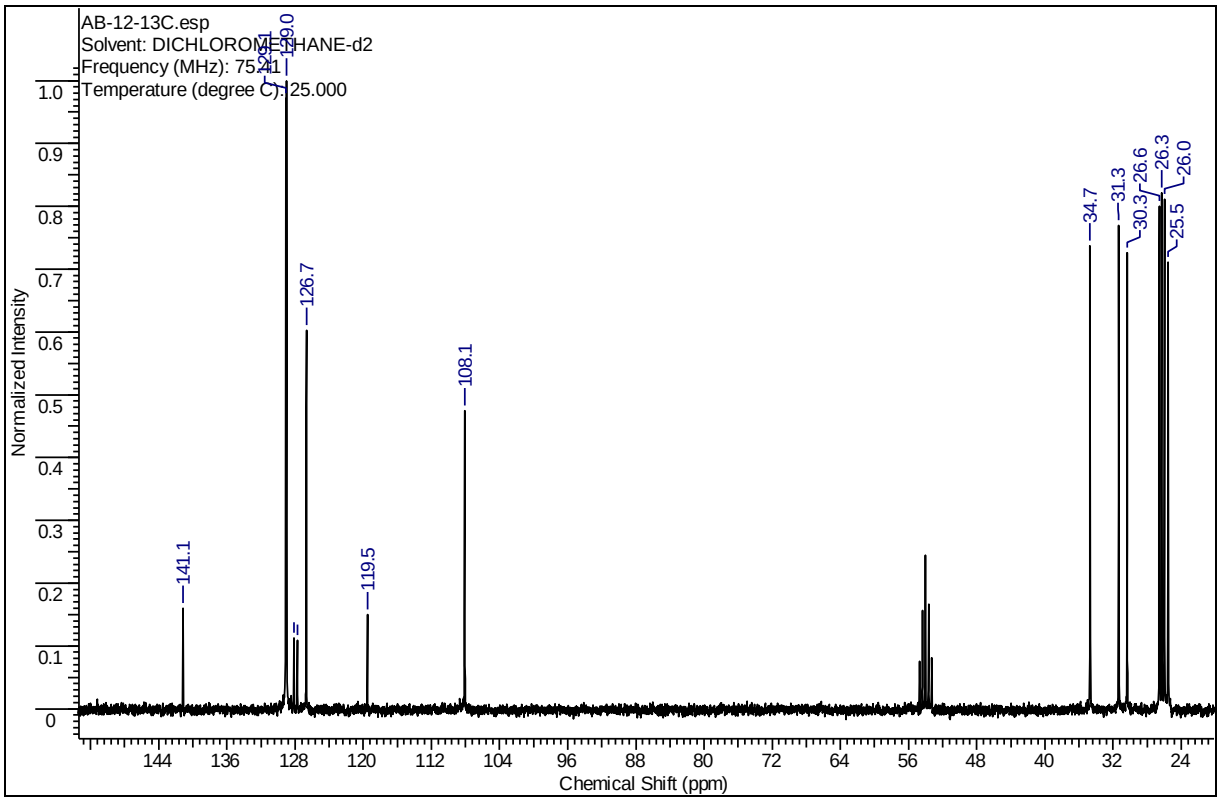
^{1}H and ^{13}C NMR spectra of 2-benzyl-1,4,5,6,7,8,9-heptahydro-cycloocta[*b*]pyrrole (**2g**)





6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

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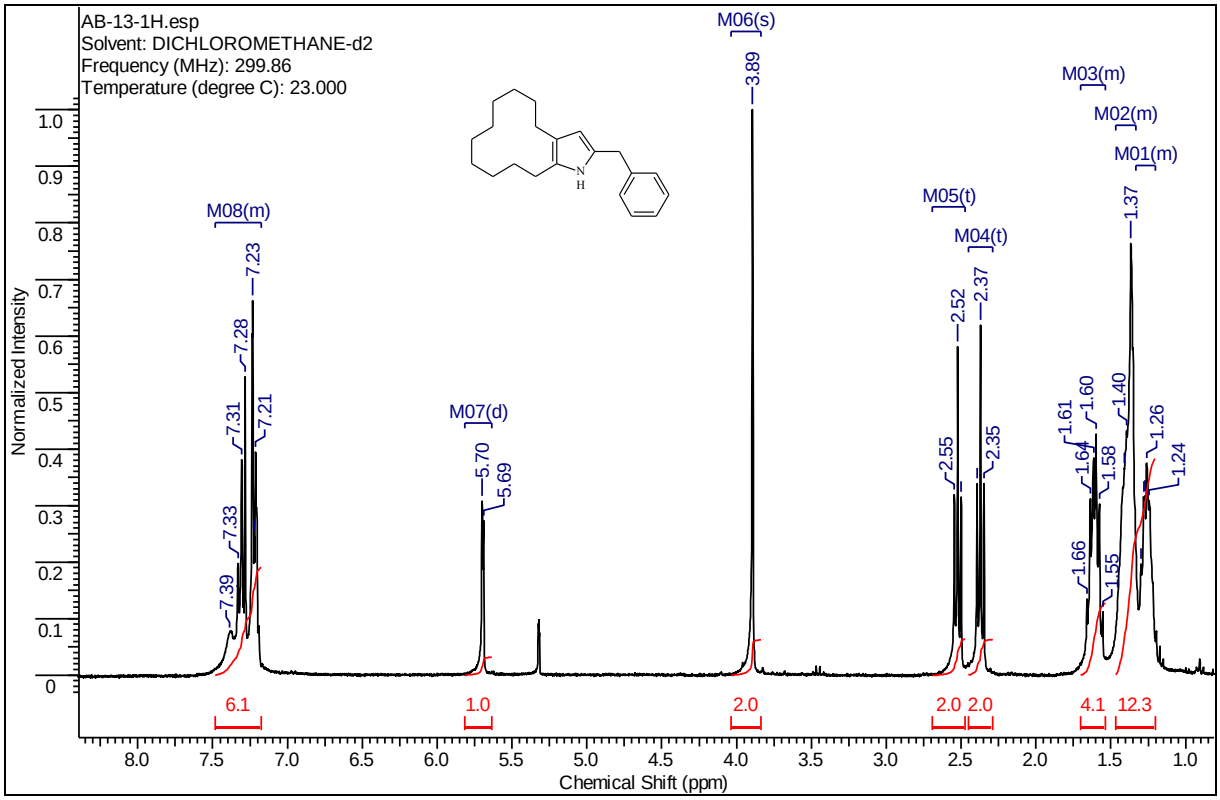
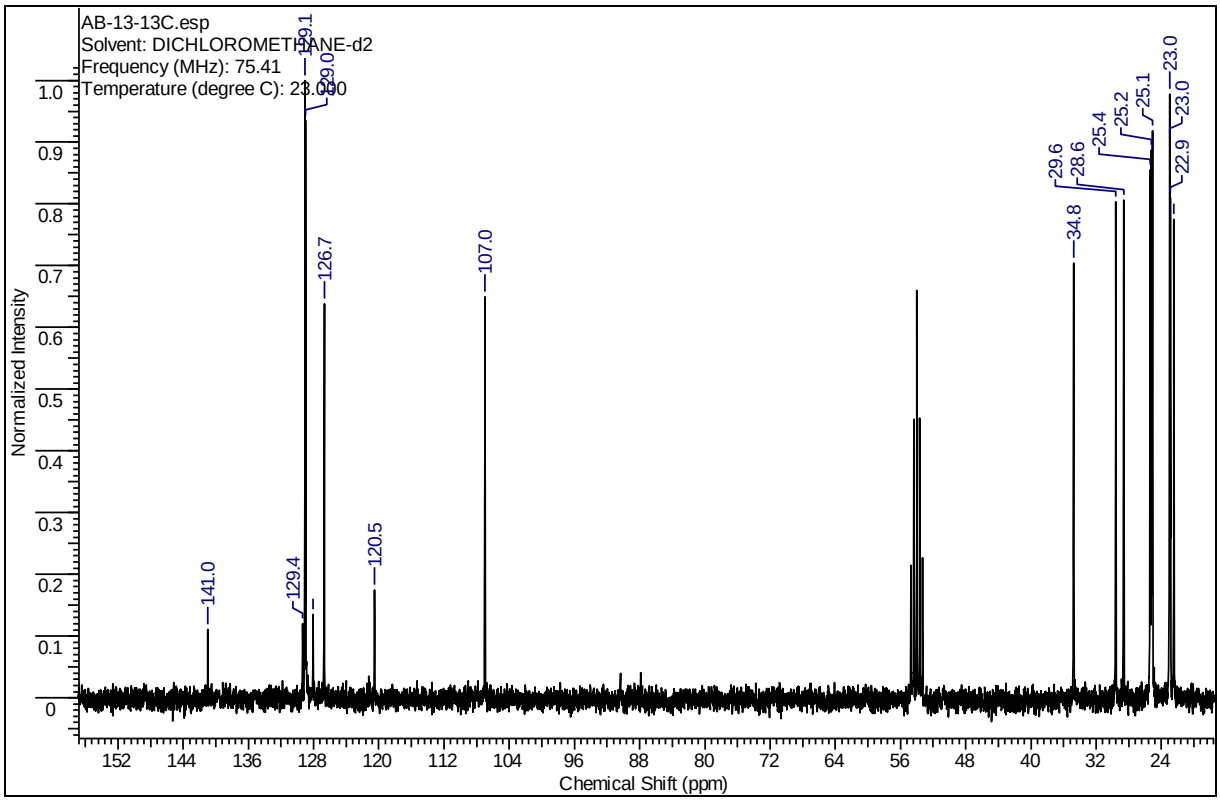
^{1}H and ^{13}C NMR spectra of 2-benzyl-1,4,5,6,7,8,9,10,11,12,13-undecahydro-cyclododeca[*b*]pyrrole (**2h**)





6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

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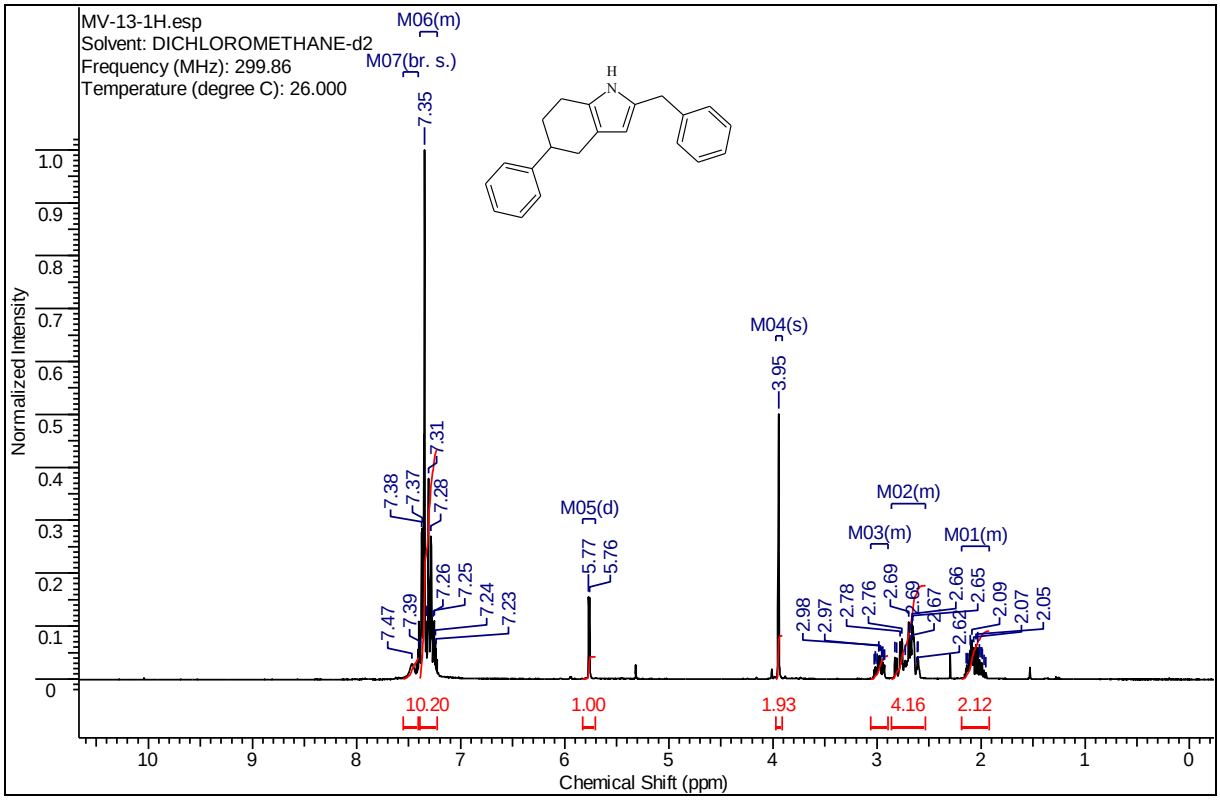
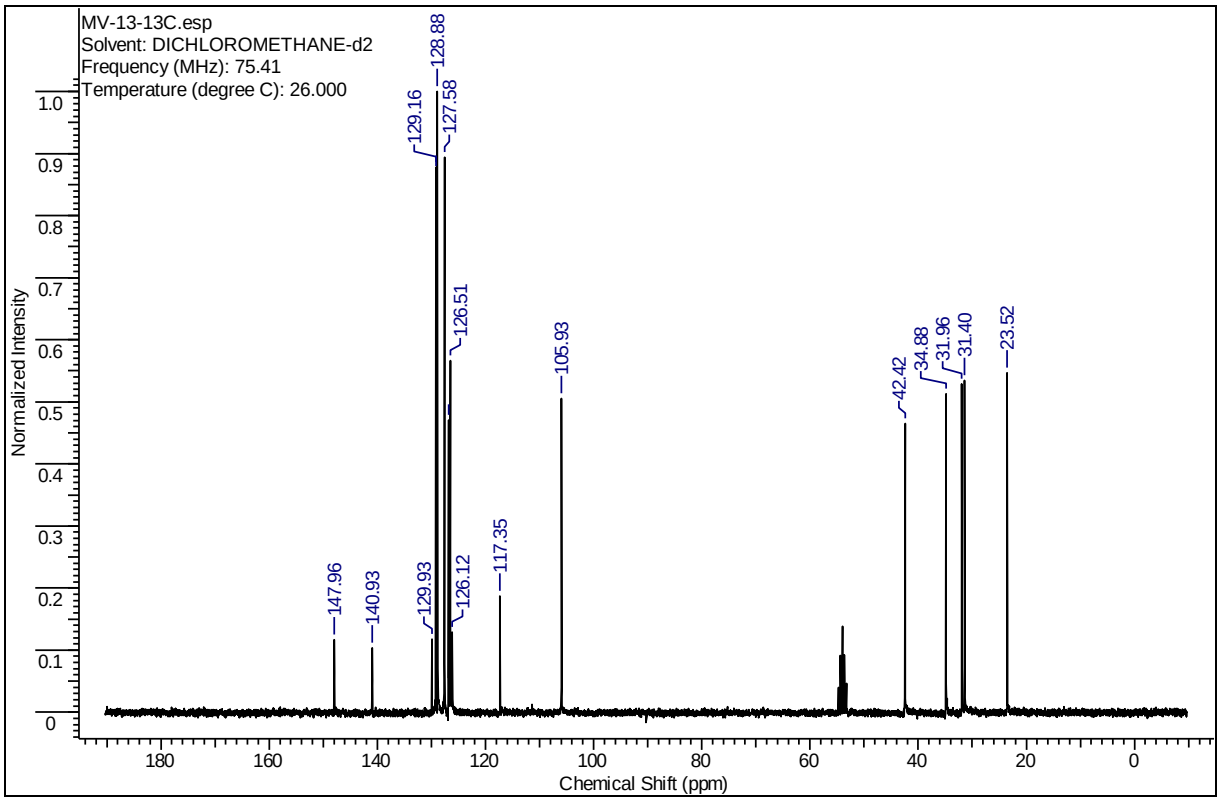
^{1}H and ^{13}C NMR spectra of 2-benzyl-5-phenyl-4,5,6,7,-tetrahydro-1*H*-indole (**2k**)





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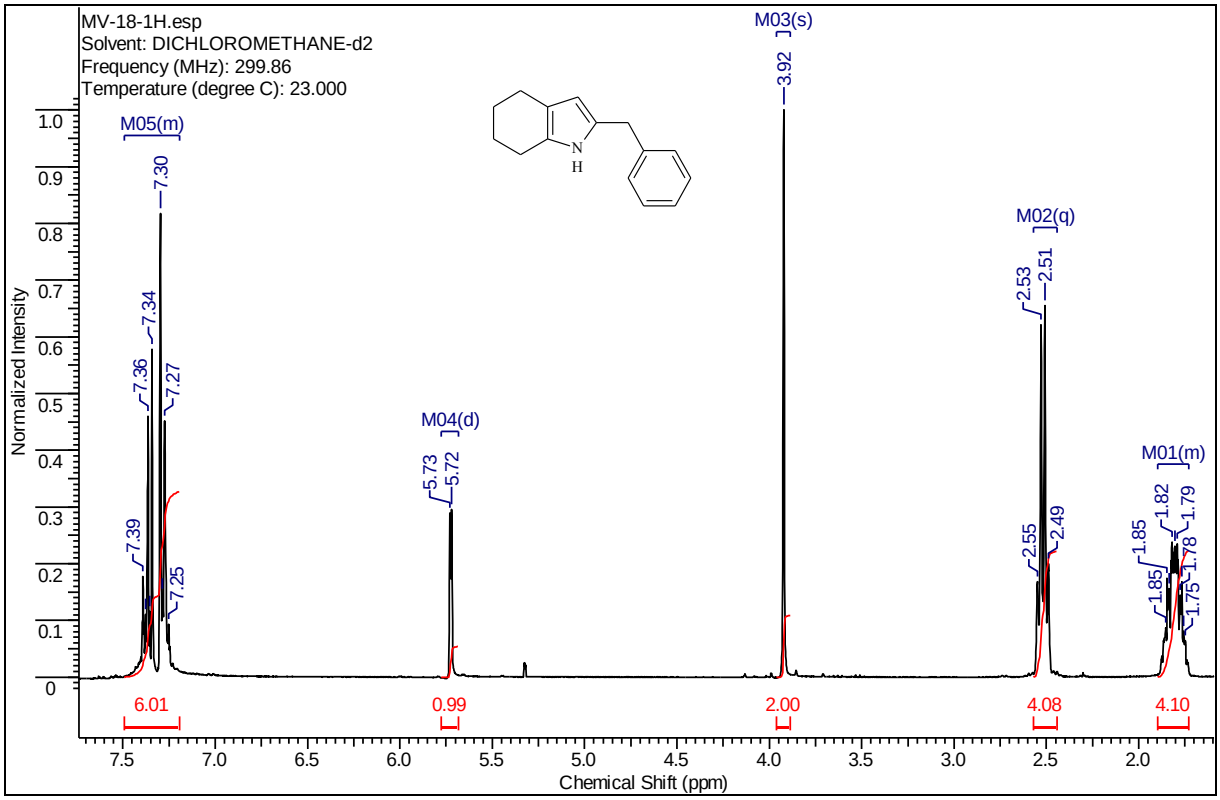
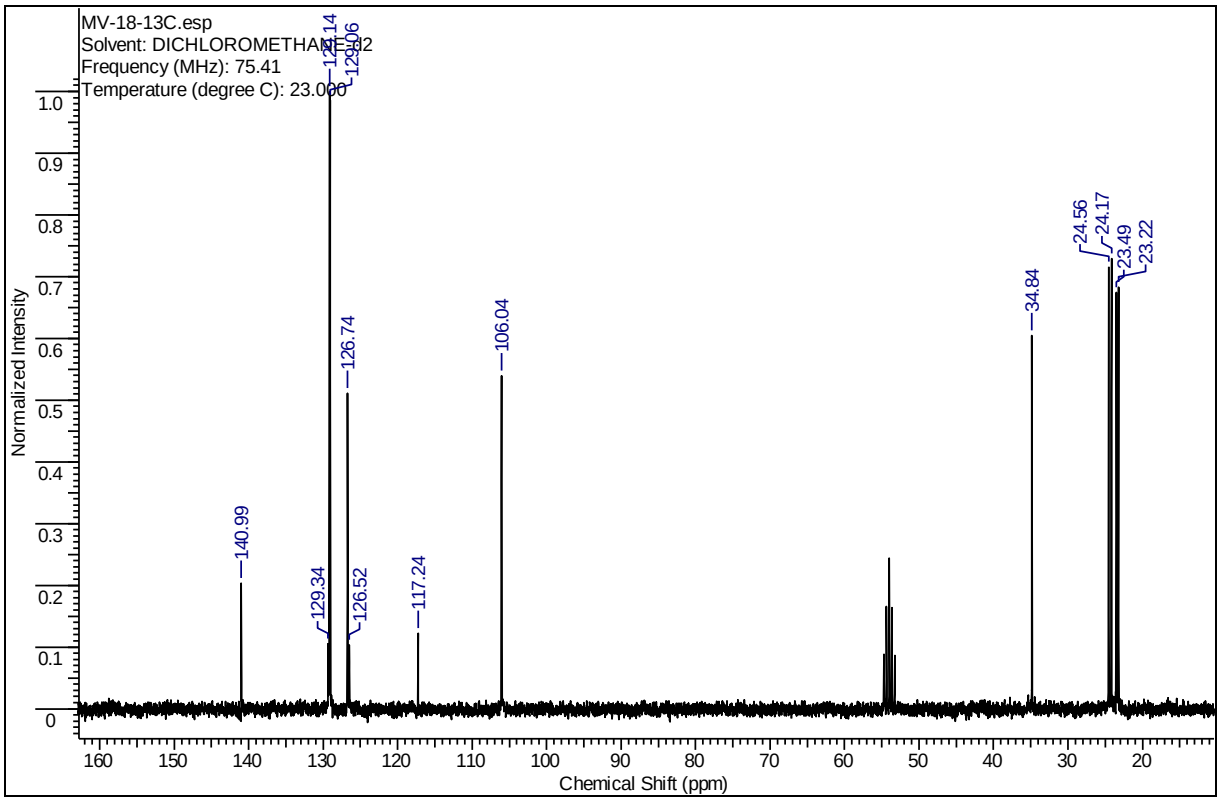
^{1}H and ^{13}C NMR spectra of 2-benzyl-1,4,5,6,7-pentahydro-cyclohexa[*b*]pyrrole (**2i**)





6. Base mediated, transition metal free regioselective synthesis of pyridines, pyrroles and indoles from ketones and amino alcohols

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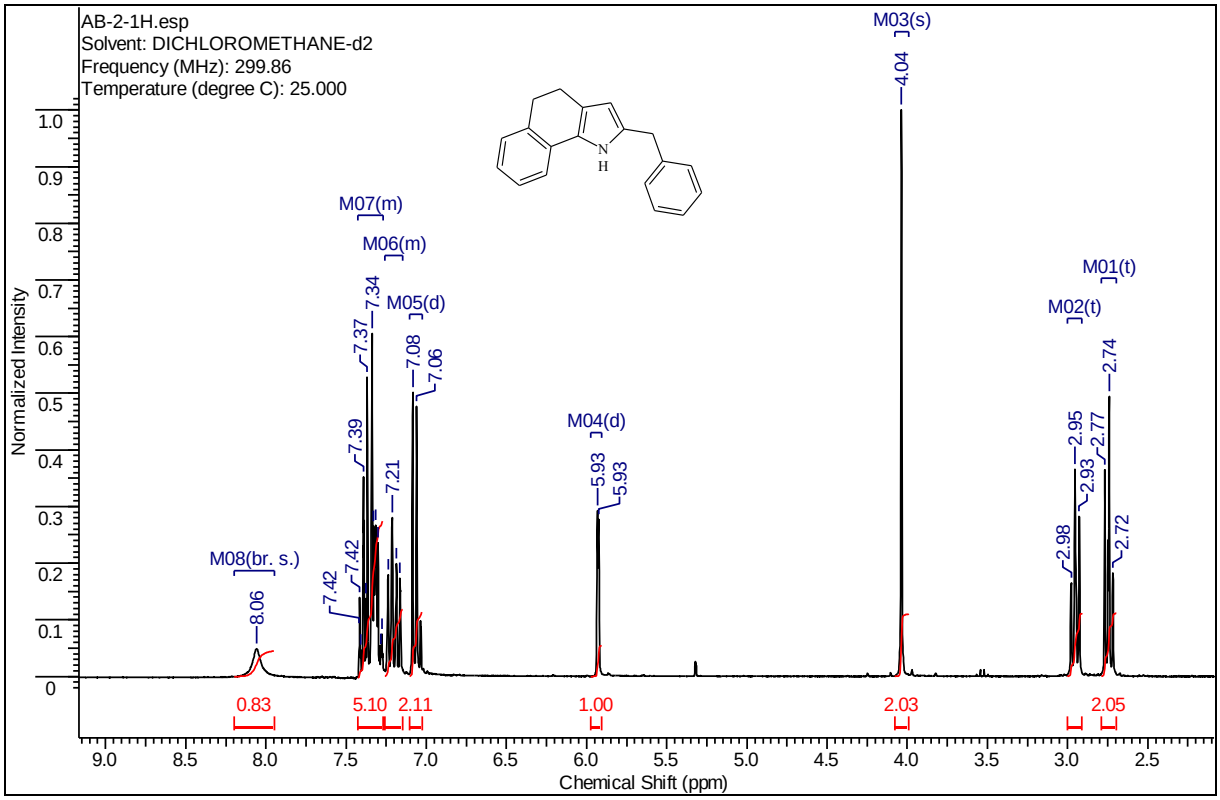
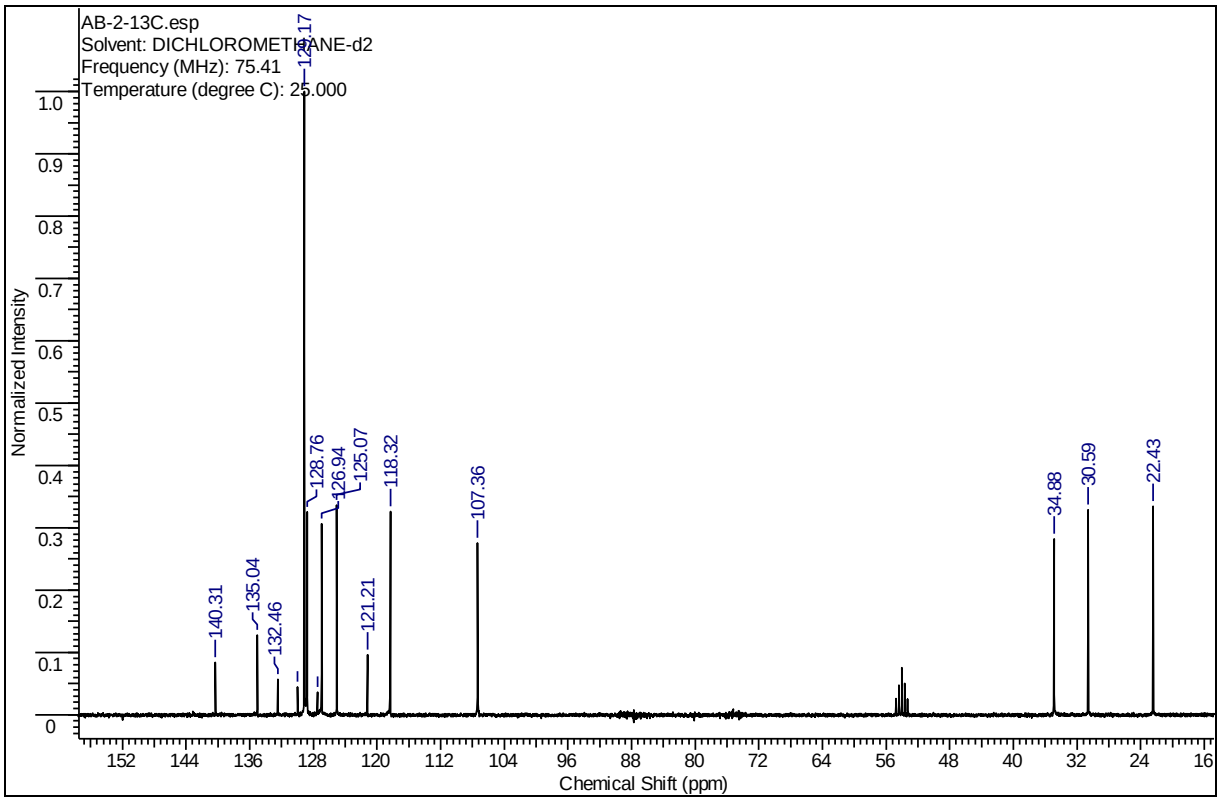
^{1}H and ^{13}C NMR spectra of 2-benzyl-4,5-dihydro-1*H*-benzo[*c*]indole (**2l**)





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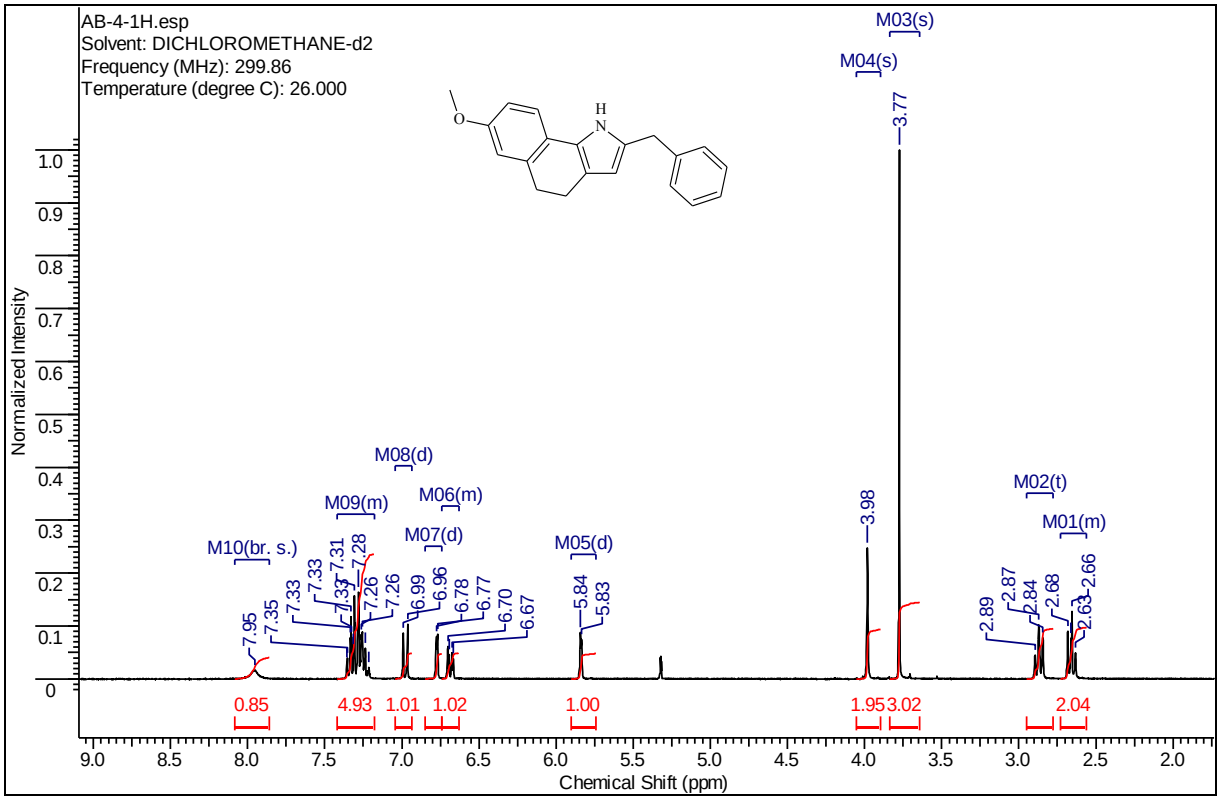
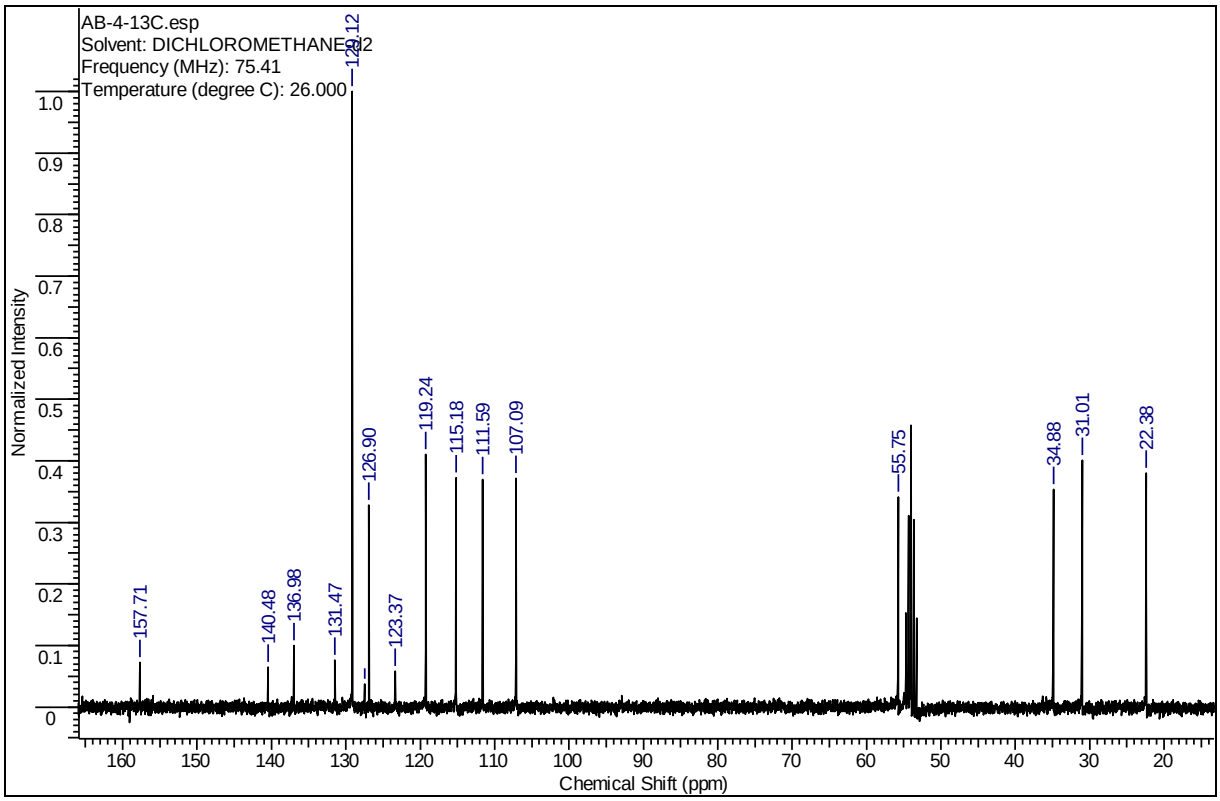
^{1}H and ^{13}C NMR spectra of 2-benzyl-7-methoxy-4,5-dihydro-1*H*-benzo[4,5-*c*]indole (**2m**)





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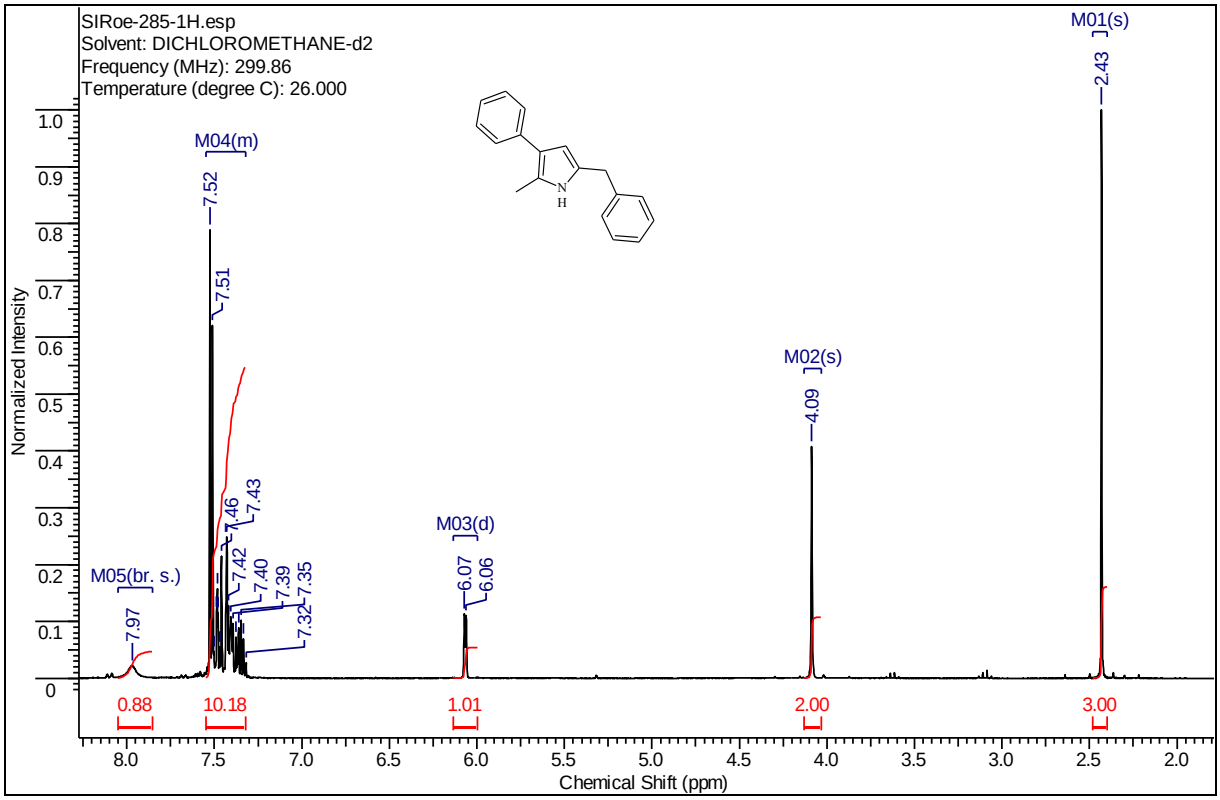
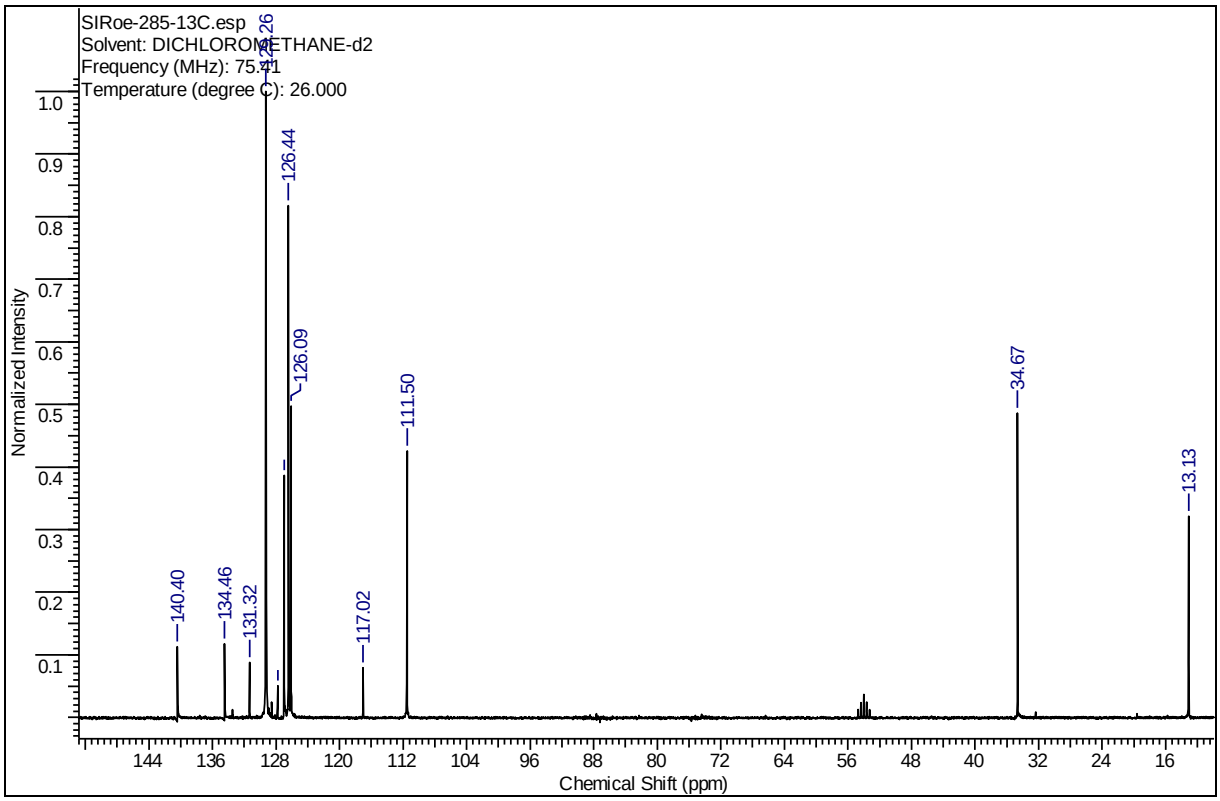
^{1}H and ^{13}C NMR spectra of 5-benzyl-3-methyl-2-phenyl-1*H*-pyrrole (**3a**)





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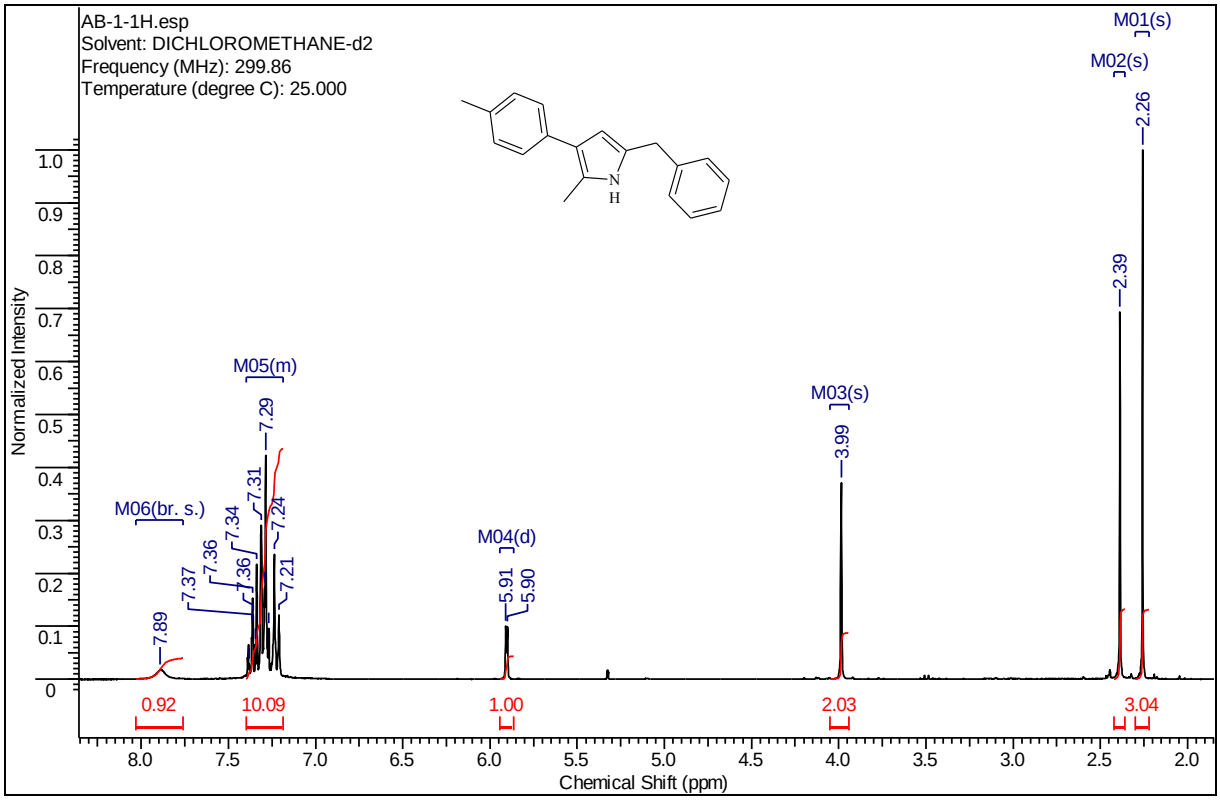
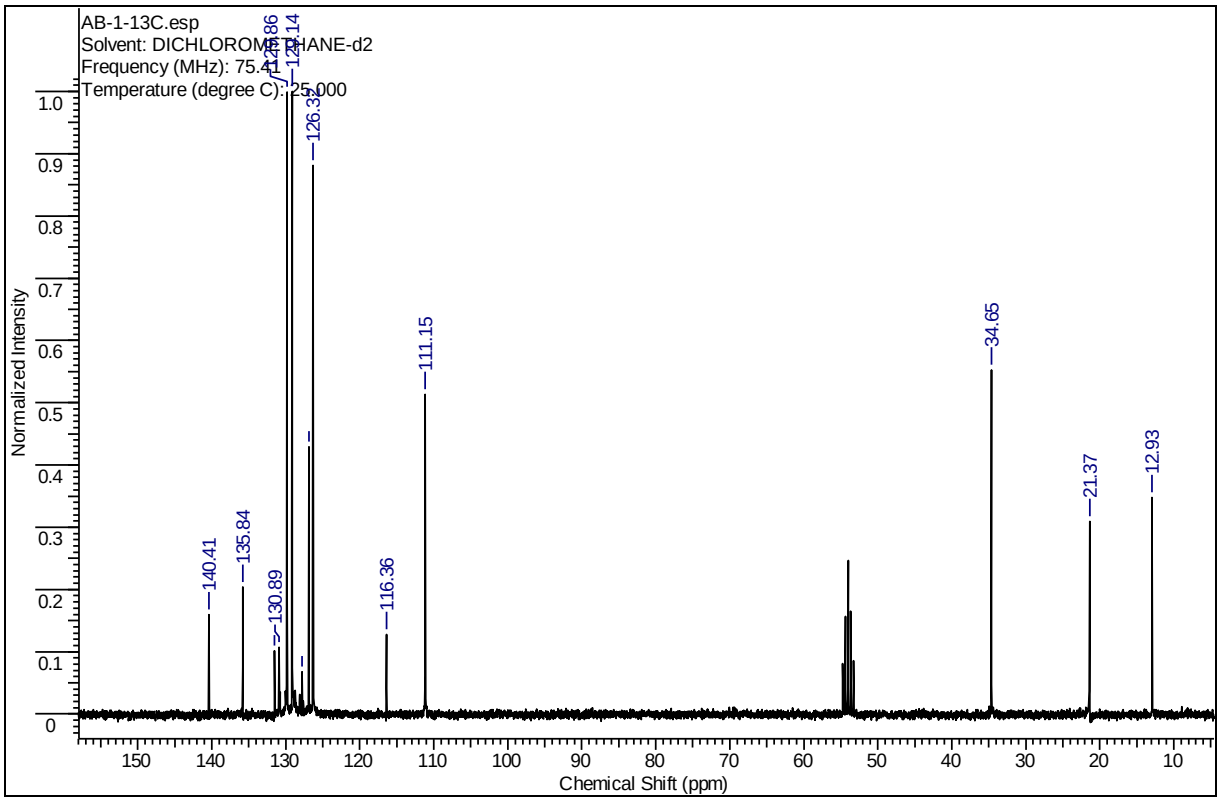
^{1}H and ^{13}C NMR spectra of 5-benzyl-3-methyl-2-tolyl-1*H*-pyrrole (**3b**)





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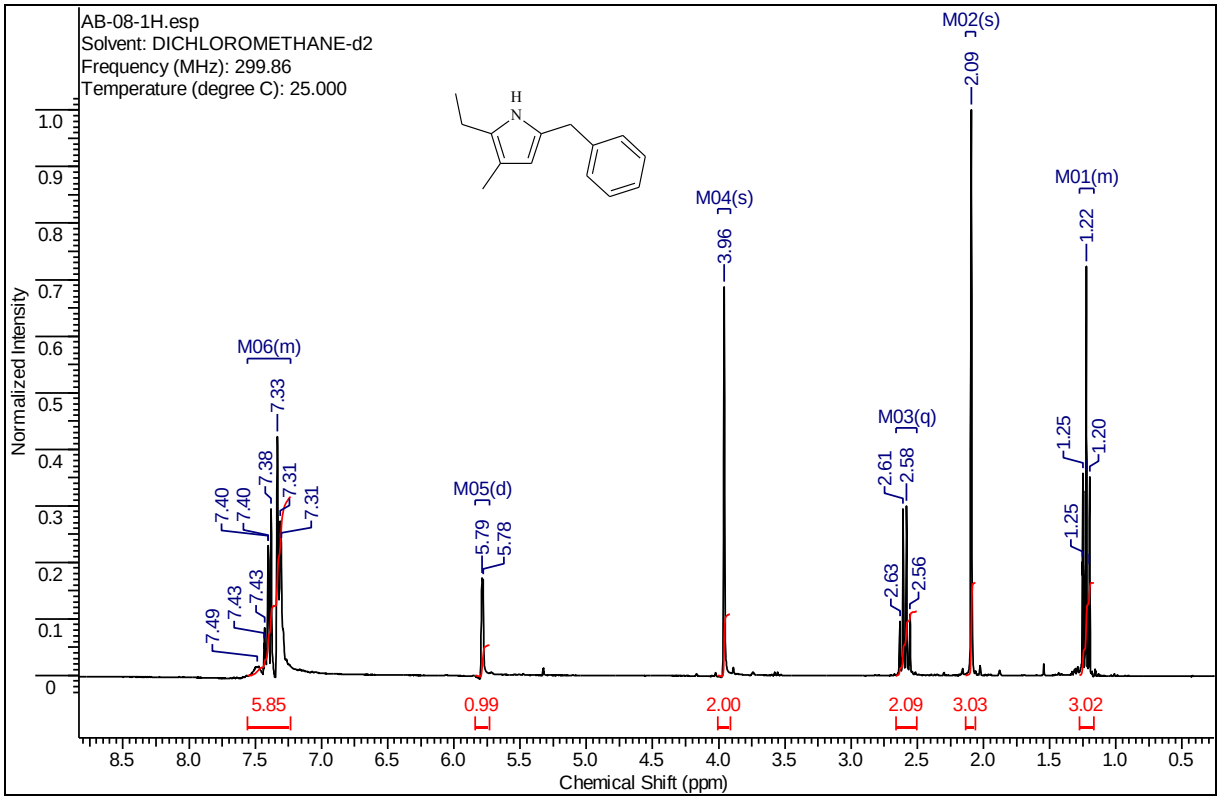
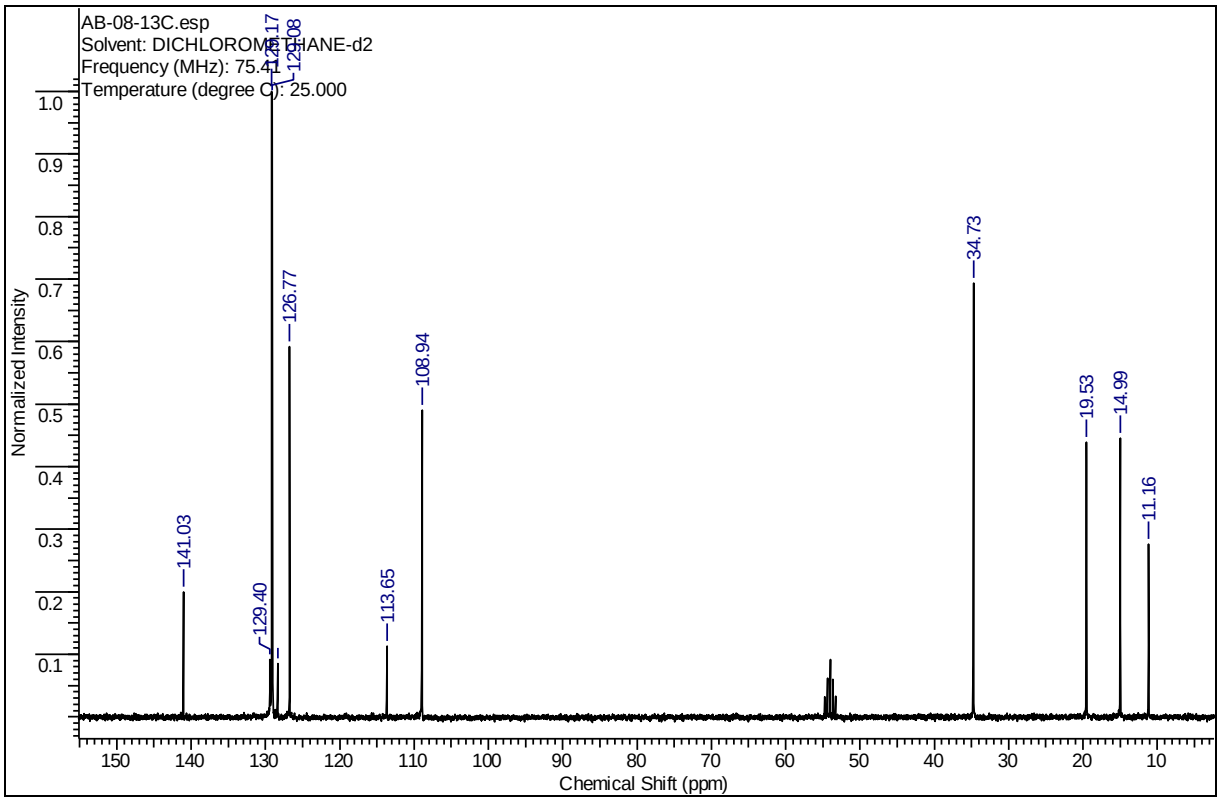
^{1}H and ^{13}C NMR spectra of 5-benzyl-2-ethyl-3-methyl-1*H*-pyrrole (**3c**)





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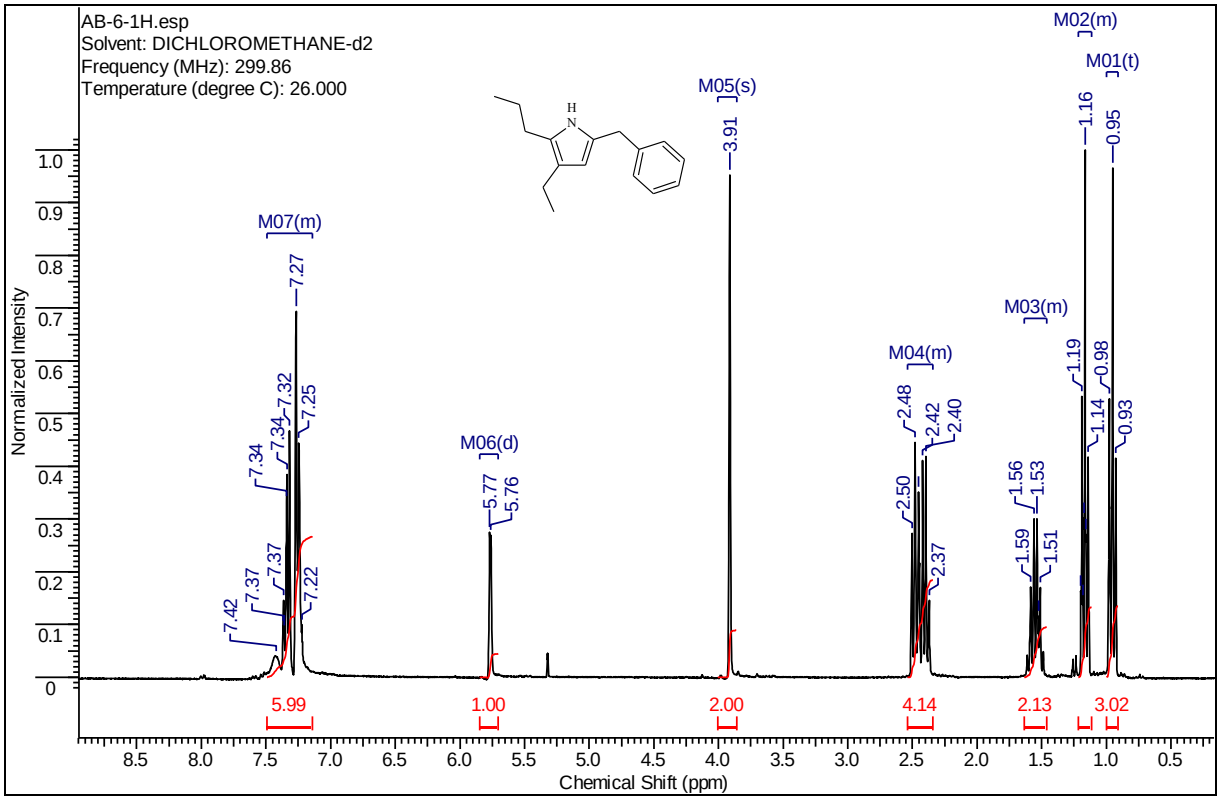
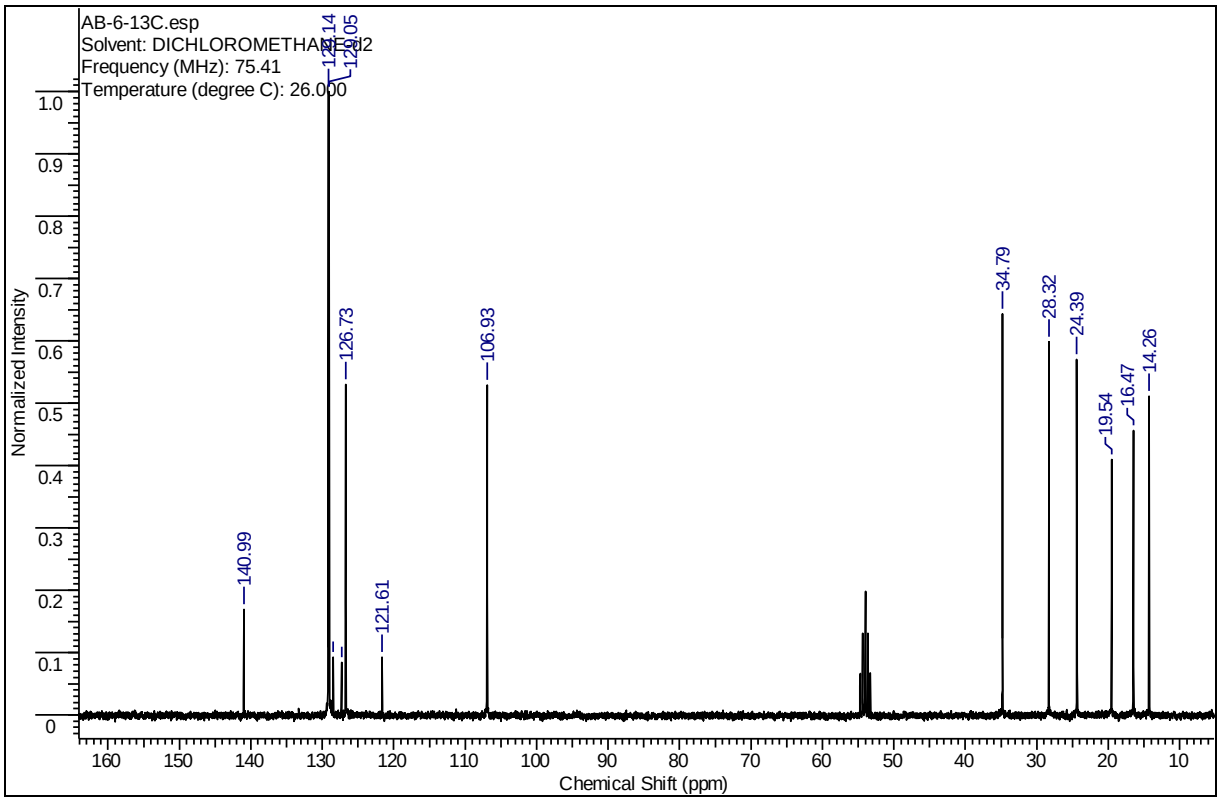
^{1}H and ^{13}C NMR spectra of 5-benzyl-3-ethyl-2-propyl-1*H*-pyrrole (**3d**)





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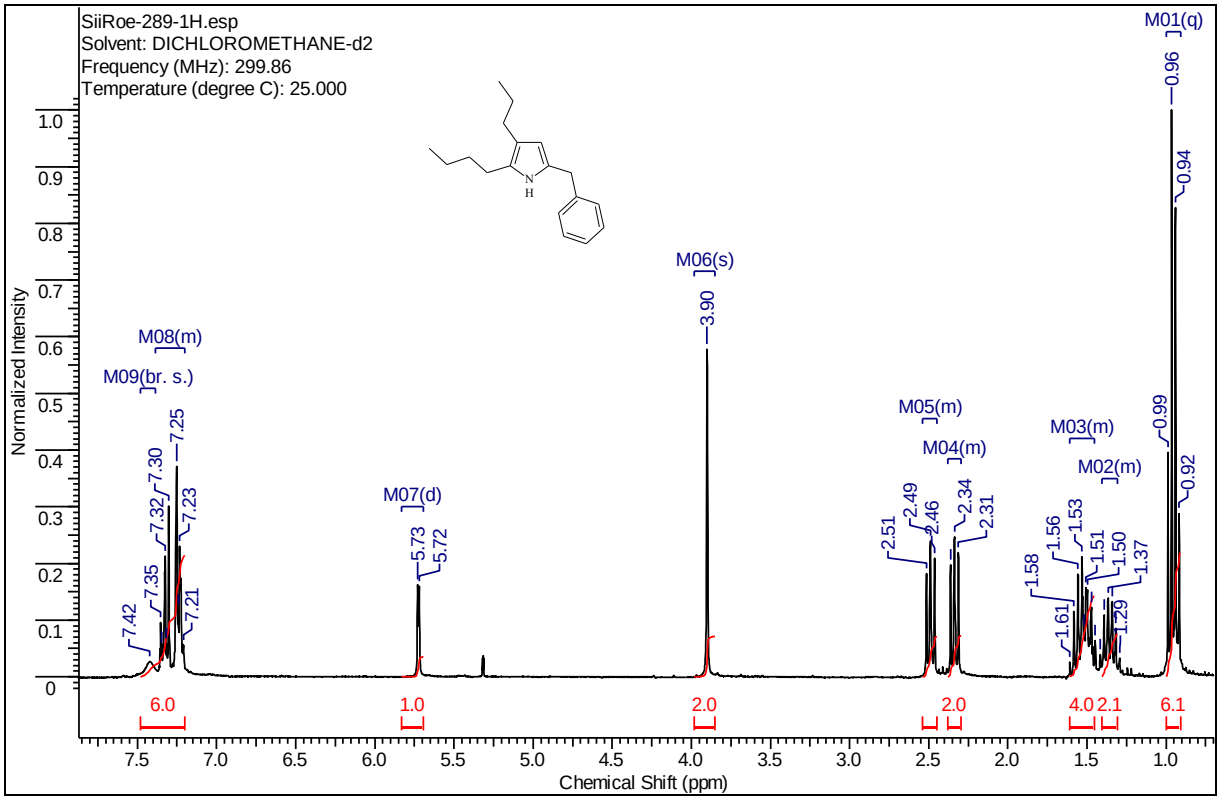
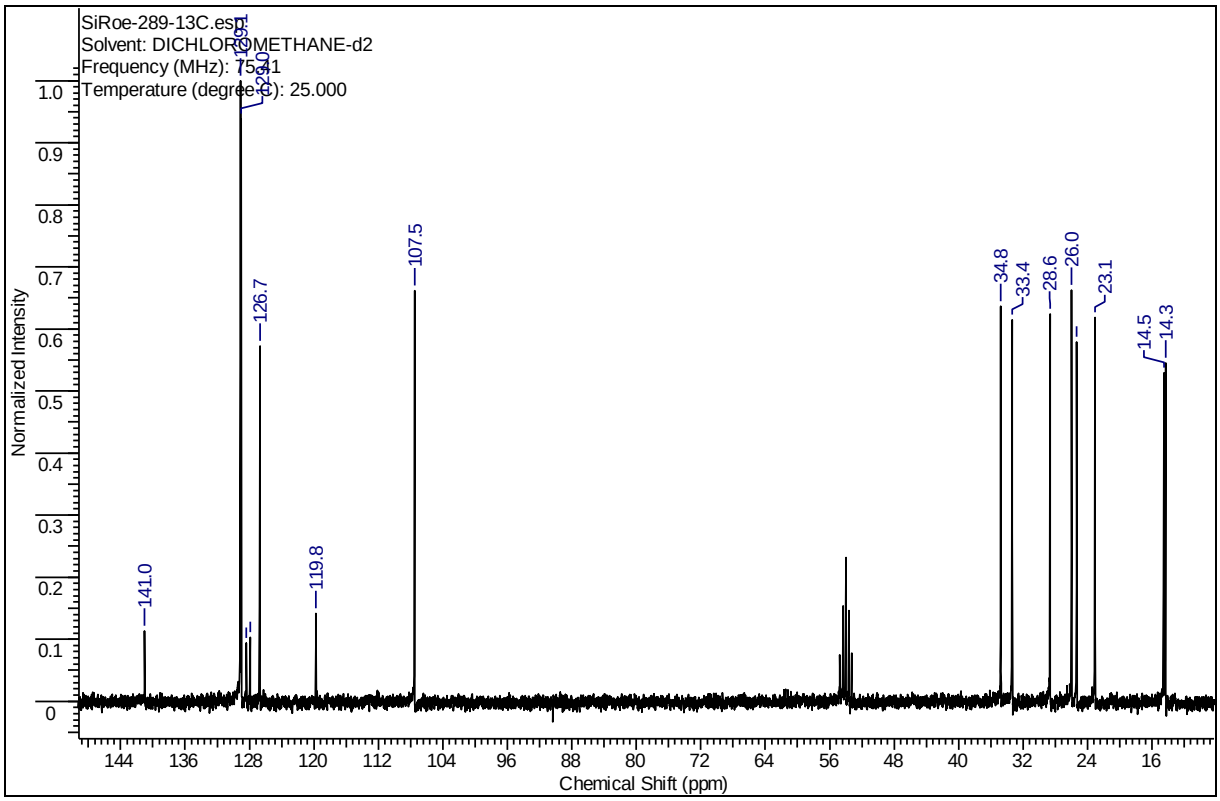
^{1}H and ^{13}C NMR spectra of 5-benzyl-2-butyl-3-propyl-1*H*-pyrrole (**3e**)





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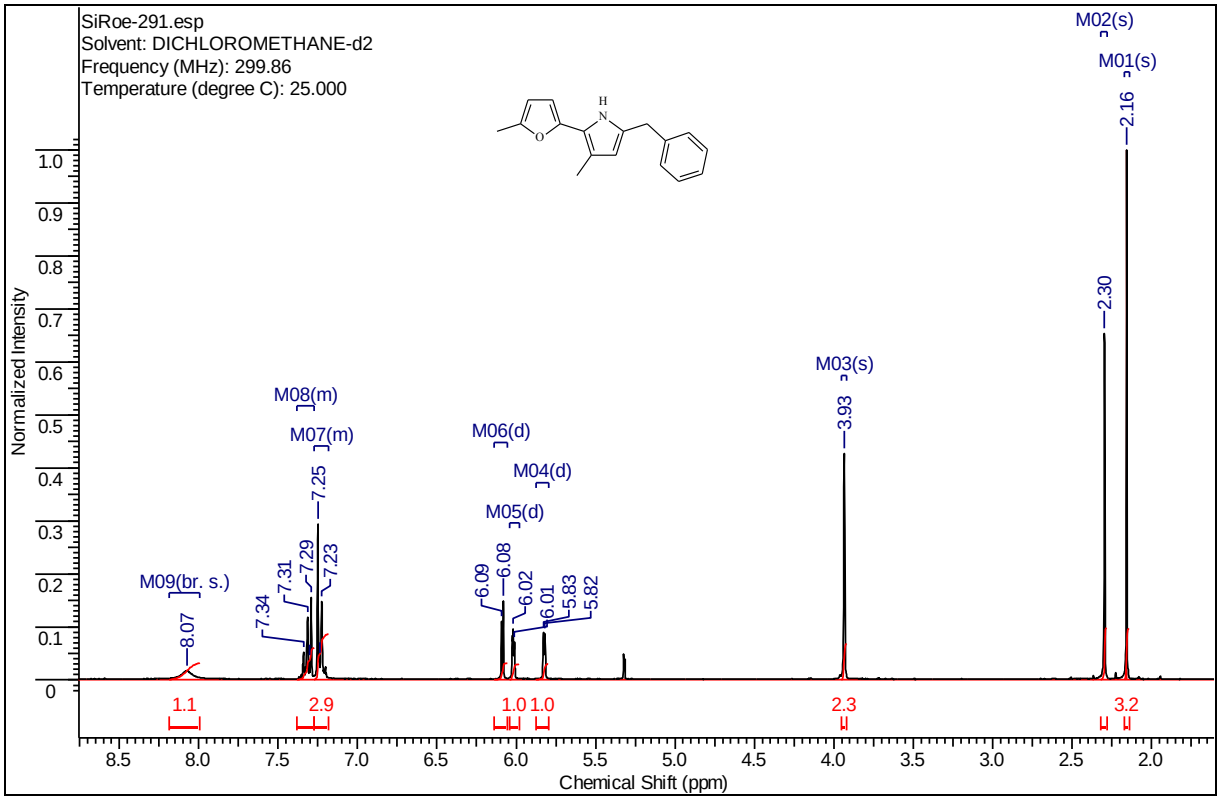
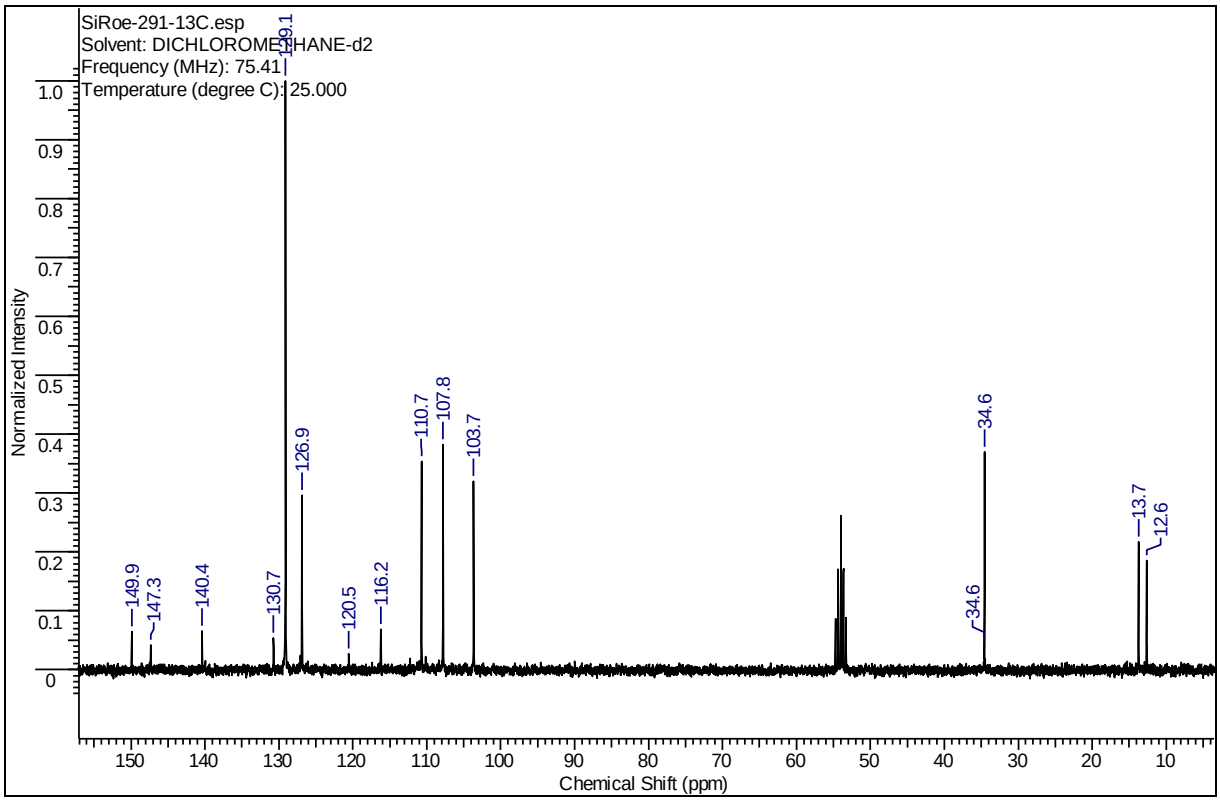
^{1}H and ^{13}C NMR spectra of 5-benzyl-2-(5-methylfuryl)-3-methyl-1*H*-pyrrole (**3f**)





7. List of Publications

The following publication was published prior to working on this thesis:

(1) P. Ott, J. Gensel, S. Roesler, K. Trenkenschuh, D. Andreeva, A. Laschewsky, A. Fery, „*Cross-Linkable Polyelectrolyte Multilayer Films of Tailored Charge Density*“, *Chem. Mater.* **2010**, *22*, 3323-3331.

The following publications have been published or were submitted during the work on this thesis:

(2) S. Roesler, J. Obenauf, R. Kempe, „*A highly active and easily accessible cobalt catalyst for selective hydrogenation of C=O bonds*“*, J. Am. Chem. Soc.* **2015**, *137*, 7998-8001.

(3) S. Roesler, M.Ertl, T. Irrgang, R. Kempe, „*Cobalt catalyzed alkylation of aromatic amines by alcohols*“, *Angew. Chem. Int. Ed.* **2015***, 54,* 15046-15050 and *Angew. Chem.* **2015***, 127,* 15260-15264

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Prof. Dr. Rhett Kempe

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9. Declaration / Erklärung

(§ 5 Nr. 4 PromO)

Hiermit erkläre ich, dass keine Tatsachen vorliegen, die mich nach den gesetzlichen Bestimmungen über die Führung akademischer Grade zur Führung eines Doktorgrades unwürdig erscheinen lassen.

(§ 8 S. 2 Nr. 5 PromO)

Hiermit erkläre ich mich damit einverstanden, dass die elektronische Fassung meiner Dissertation unter Wahrung meiner Urheberrechte und des Datenschutzes einer gesonderten Überprüfung hinsichtlich der eigenständigen Anfertigung der Dissertation unterzogen werden kann.

(§ 8 S. 2 Nr. 7 PromO)

Hiermit erkläre ich eidesstattlich, dass ich die Dissertation selbständig verfasst und keine anderen als die von mir angegebenen Quellen und Hilfsmittel benutzt habe.

(§ 8 S. 2 Nr. 8 PromO)

Ich habe die Dissertation nicht bereits zur Erlangung eines akademischen Grades anderweitig eingereicht und habe auch nicht bereits diese oder eine gleichartige Doktorprüfung endgültig nicht bestanden.

(§ 8 S. 2 Nr. 9 PromO)

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Sina Rösler