“The New Chemistry” -
Sustainable Catalysis with Alcohols

DISSERTATION

zur Erlangung des akademischen Grades eines
Doktors der Naturwissenschaften (Dr. rer. nat.)
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vorgelegt von

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Abbreviations

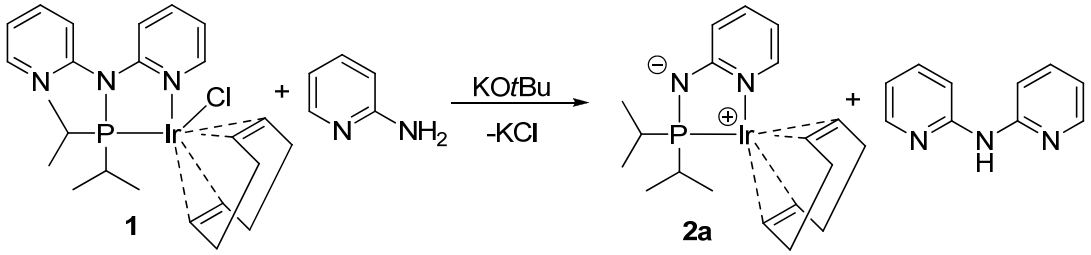
Ar	aryl
Å	Angström
BH/HA	borrowing hydrogen/hydrogen autotransfer
Bn	benzyl
Bu	butyl
br	broad
°C	degree celsius
cod	cis-1,5-cyclooctadiene
d	doublet
δ	chemical shift (ppm)
equiv.	equivalents
g	gram
GC	gas chromatography
h	hours
Hz	Hertz
J	coupling constant (Hz)
K	Kelvin
m	multiplet
min	minute
mL	milliliter
mmol	millimol
MS	mass spectrometry
NMR	nuclear magnetic resonance
q	quartet
rt	room temperature
s	singlet
t	triplet
µL	microliter

Table of Contents

1. Summary

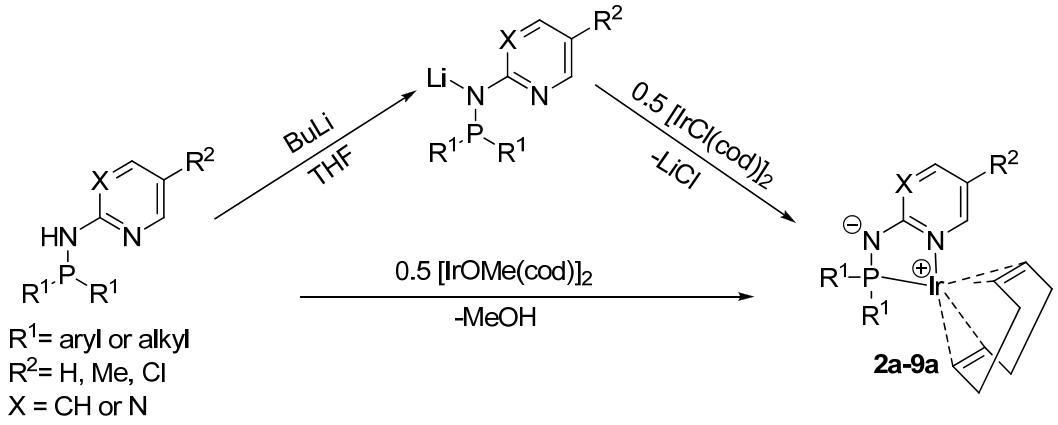
Subject of the thesis are new iridium complexes stabilized by anionic P,N- or P,N,P-ligands. These complexes were used in homogeneous catalysis. Furthermore, mechanistic studies were performed to provide an insight into the catalytic cycles. Synthesis protocols for a multitude of different product classes have been developed.

The iridium complex **1**, stabilized by a neutral P,N-ligand, reacts under basic conditions with 2-aminopyridines. By elimination of dipyridylamine the new catalyst species **2a** was formed, which is more stable than catalyst **1** (Scheme 1).



Scheme 1. Detection of the active catalyst species.

Based on this finding eight new anionic P,N-ligands and the resulting iridium complexes were synthesized (Scheme 2).

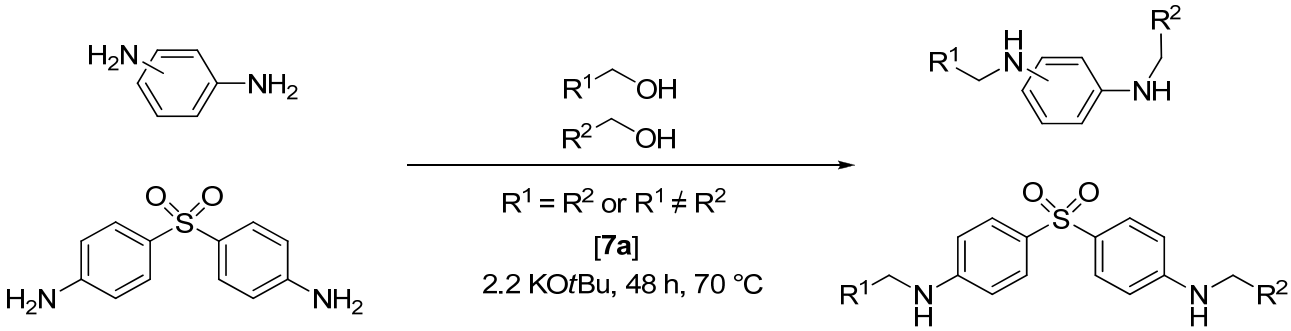


Scheme 2. Synthesis of iridium complexes stabilized by anionic P,N-ligands.

After optimization of the reaction conditions (solvent, base, temperature and catalyst loading) these catalysts were used in BH (borrowing hydrogen)/HA (hydrogen autotransfer) reactions. The selective monoalkylation of anilines with primary alcohols was investigated. In comparative experiments the superiority of the new class of catalysts versus the original

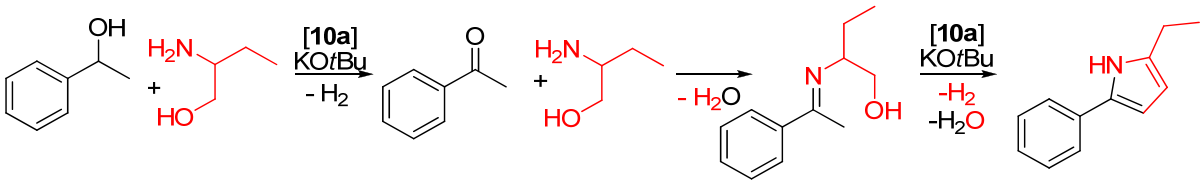
catalyst **1** was clearly shown. Under mild reaction conditions (70 °C) the selectivity profile with respect to the monoalkylation has been preserved.

The catalytic protocol was subsequently extended to the alkylation of aromatic diamines. Therefore various diaminobenzenes were used as substrates. Also Dapsone®, an important drug in treatment of leprosy could be used as starting material. We succeeded in both symmetric and unsymmetric monoalkylations of diamines (Scheme 3). Due to the selectivity profile of the catalyst regarding aromatic amines, also unprotected amino alcohols could be used as alkylating reagents.



Scheme 3. Syntheses of symmetrically and unsymmetrically alkylated diamines.

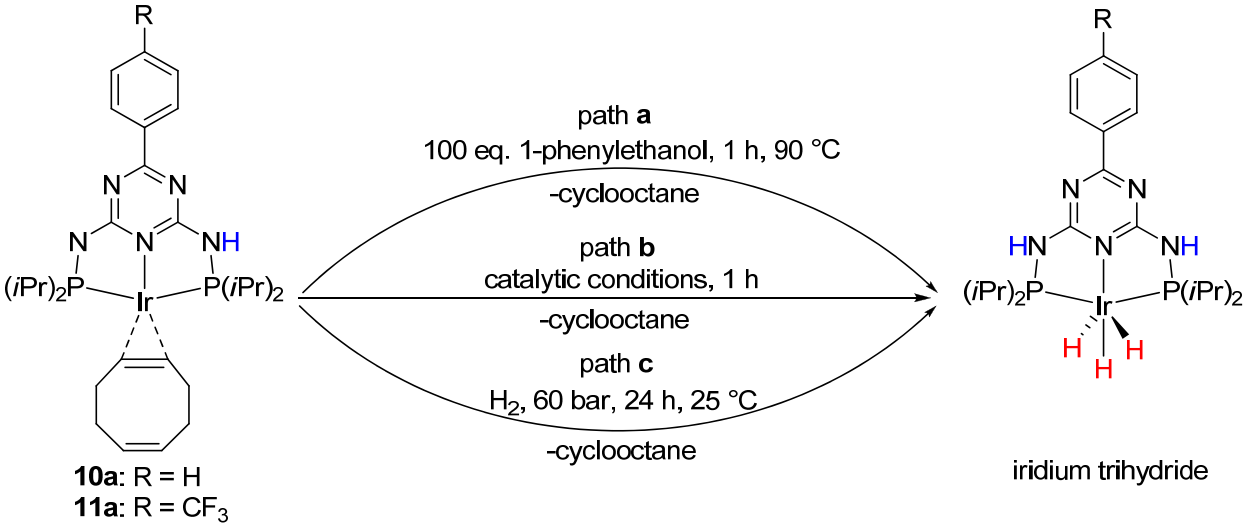
By the use of tridentate P,N,P-ligands, a novel class of more stable catalysts compared to complexes **2a-9a**, could be developed. Due to sealing the synthesis reactor with a semipermeable membrane, the retransfer of the "borrowed" hydrogen could be prevented and H_2 is released. Dehydrogenation and condensation steps are now possible instead of BH/HA. By reacting secondary alcohols with β-amino alcohols, pyrroles were accessible (Scheme 4).



Scheme 4. Pyrrole synthesis.

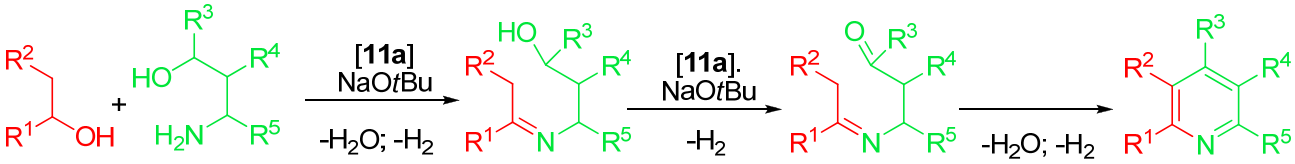
After adapting the synthesis protocol to this new class of products the tolerance of functional groups was tested. Diversely functionalized alcohols were used. Under mild reaction conditions (90 °C) and very low catalyst loadings (down to 0.03 mol% iridium), a large number of novel pyrroles was accessible. Using this protocol 21 differently substituted α,α-pyrroles, 12 bicyclic pyrroles, symmetrically as well as non-symmetrically substituted oligopyrroles and three β-aminopyrroles were synthesized. The catalyst resting state was

identified by NMR experiments and X-ray structure analysis to be an iridium trihydride. This trihydride is formed under catalytic conditions (Scheme 5, path **b**), by treatment of the pre-catalyst with alcohols (Scheme 5, path **a**) or in hydrogen atmosphere (Scheme 5, path **c**).



Scheme 5. Syntheses of the iridium trihydride

In the final part of the work, a catalytic pyridine synthesis was developed (Scheme 6). In this so far unknown heterocycle synthesis up to four different substituents could be introduced within a single reaction step. 2,6-, 2,5-, 2,4- and 2,3-substituted pyridines were synthesized selectively by using variously substituted primary or secondary alcohols and γ-amino alcohols. Furthermore, both the synthesis of bicyclic pyridines as well as the synthesis of pyridines that bear chiral substituents is possible.

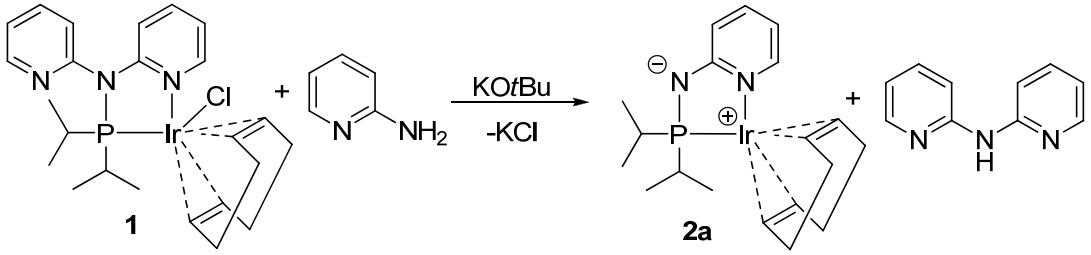


Scheme 6. Pyridine synthesis.

Zusammenfassung

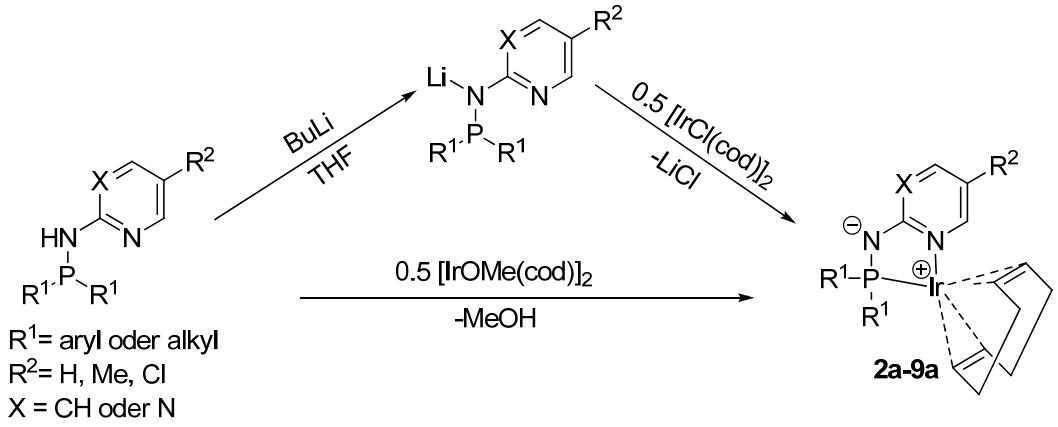
Inhalt der vorliegenden Arbeit sind neue anionische P,N- oder P,N,P-Ligand stabilisierte Iridiumkomplexe, die in der homogenen Katalyse eingesetzt werden. Weiterhin wurden mechanistische Studien durchgeführt, um einen Einblick in die Katalysezyklen zu erhalten. Für eine Vielzahl unterschiedlicher Produktklassen wurden Synthesevorschriften entwickelt.

Der P,N-Neutralligand stabilisierte Iridiumkomplex **1** reagiert unter basischen Bedingungen mit 2-Aminopyridin. Unter Abspaltung von Dipyridylamin bildet sich die neue Katalysatorspezies **2a**, die stabiler als Katalysator **1** ist (Schema 1).



Schema 1. Entdeckung der aktiven Katalysatorspezies **2a**.

Ausgehend von dieser Erkenntnis wurden acht neue anionische P,N-Liganden und die daraus resultierenden Iridiumkomplexe **2a**-**9a** synthetisiert (Schema 2).

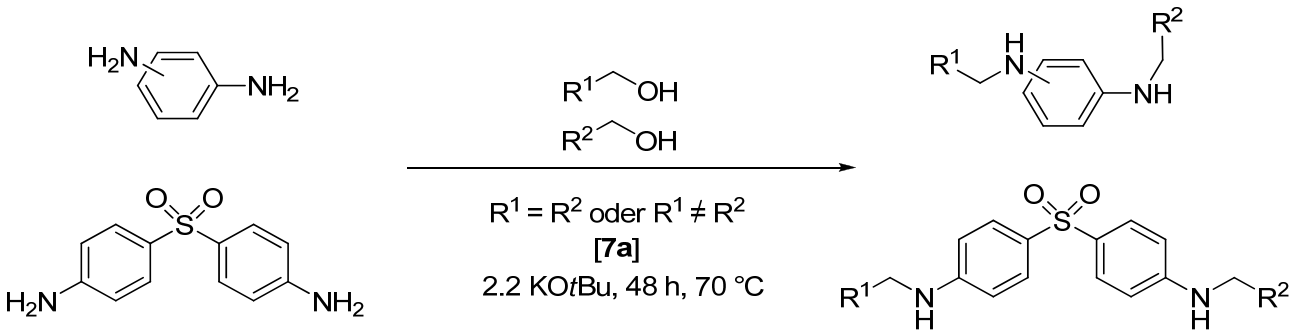


Schema 2. Synthese der anionischen P,N-Ligand stabilisierten Iridiumkomplexe.

Nach Optimierung der Reaktionsbedingungen bezüglich Lösungsmittel, Base und Katalysatorbeladung wurden diese Katalysatoren in BH (borrowing hydrogen)/HA (hydrogen autotransfer) Reaktionen verwendet. Die selektive Monoalkylierung von Anilinen mit primären Alkoholen wurde untersucht. In Vergleichsexperimenten konnte die klare

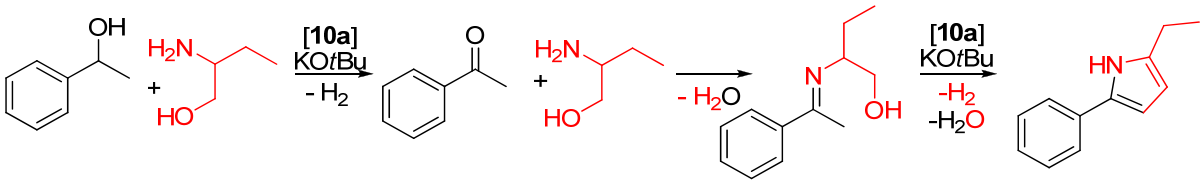
Überlegenheit der neuen Katalysatorklasse (**2a-9a**) gegenüber dem ursprünglichen Katalysator **1** gezeigt werden. Unter milden Reaktionsbedingungen (70 °C) konnte das Selektivitätsprofil bezüglich der Monoalkylierung erhalten werden.

Das Katalyseprotokoll wurde auf die Alkylierung von aromatischen Diaminen ausgeweitet. Hierzu wurden verschiedene Diaminobenzole als Substrate verwendet. Auch Dapson®, was ein wichtiges Medikament bei der Behandlung von Lepra ist, wurde als Edukt verwendet. Es konnte sowohl die symmetrische als auch die unsymmetrische Monoalkylierung der Diamine gezeigt werden (Schema 3). Aufgrund des Selektivitätsprofils des Katalysatorsystems bezüglich aromatischer Amine konnten auch ungeschützte Aminoalkohole als Alkylierungsreagenzien verwendet werden.



Schema 3. Synthese von symmetrisch und unsymmetrisch alkylierten Diaminen.

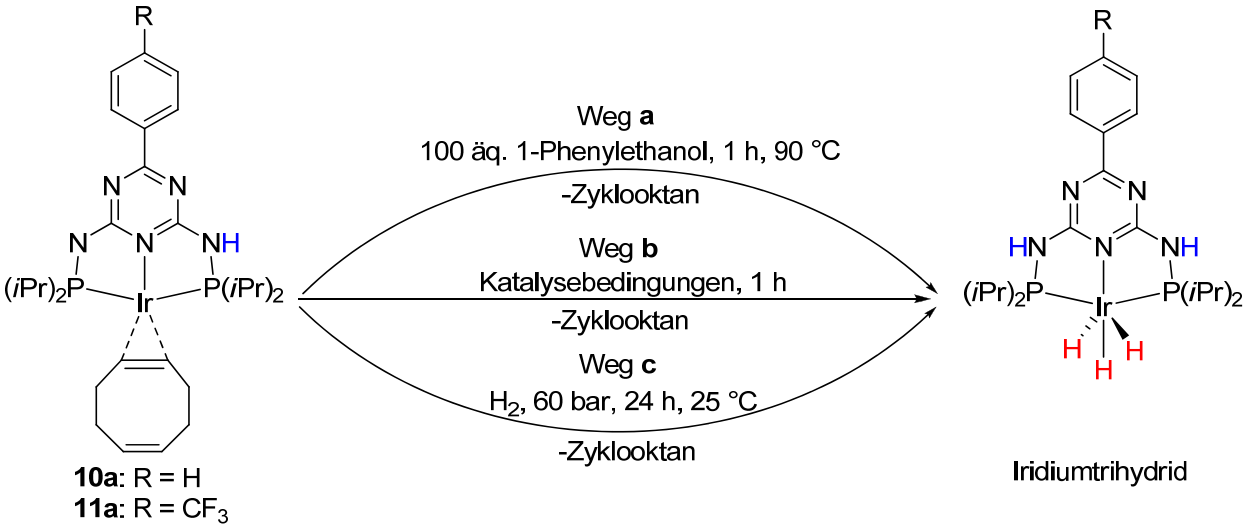
Durch die Verwendung von tridentaten P,N,P-Liganden konnte eine neue Katalysatorklasse, die eine höhere Stabilität als **2a**-**9a** besitzt, entwickelt werden. Unter Verwendung einer semipermeablen Membran wird der "geliehene" Wasserstoff nicht zurückübertragen, sondern als H_2 abgegeben. Anstelle von BH/HA Reaktionen sind nun Dehydrogenierungen und Kondensationsreaktionen möglich. Damit sind Pyrrole ausgehend von sekundären Alkoholen und β-Aminoalkoholen zugänglich (Schema 4).



Schema 4. Pyrrolsynthese.

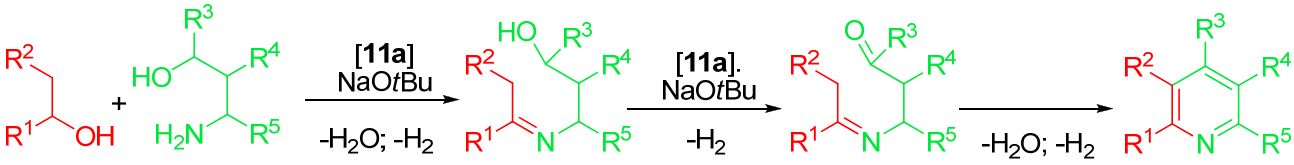
Nach Anpassung des Syntheseprotokolls auf diese neue Produktklasse wurde die Toleranz gegenüber funktionellen Gruppen getestet. Verschiedenst substituierte Alkohole wurden dafür verwendet. Bei milden Reaktionsbedingungen (90 °C) und sehr geringen

Katalysatorbeladungen (0.03 mol% Iridium) war eine Vielzahl neuer Pyrrolderivate zugänglich. Mit Hilfe dieses Syntheseprotokolls konnten 21 unterschiedlich substituierte α,α-Pyrrole, 12 bizyklische Pyrrole, symmetrisch als auch unsymmetrisch substituierte Oligopyrrole und drei β-Aminopyrrole synthetisiert werden. Die in der Katalyse aktive Spezies wurde durch NMR-Experimente und Einkristallröntgenstrukturanalyse als Iridiumtrihydridkomplex identifiziert. Dieser Iridiumtrihydridkomplex bildet sich ausgehend vom Prä-Katalysator (**10a**, **11a**) bei Umsetzung mit Alkoholen (Schema 5, Weg **a**), unter Katalysebedingungen (Schema 5, Weg **b**), oder in einer Wasserstoffatmosphäre (Schema 5, Weg **c**).



Schema 5. Synthese des Iridiumtrihydridkomplexes.

Im finalen Abschnitt der Arbeit wurde eine katalytische Pyridinsynthese entwickelt. In dieser bis dahin unbekannten Heterozyklensynthese konnten bis zu vier verschiedene Reste in einem einzigen Reaktionsschritt eingeführt werden. Darüber hinaus gelang es selektiv 2,6-, 2,5-, 2,4- und 2,3-disubstituierte Pyridine ausgehend von substituierten primären oder sekundären Alkoholen und γ-Aminoalkoholen zu synthetisieren (Schema 6). Ferner war sowohl die Synthese von bizyklischen Pyridinen, als auch die Synthese von Pyridinen die chirale Substituenten tragen, möglich.



Schema 6. Pyridinsynthese.

2. Introduction

The technological level and the economic status of the world is highly dependent on fossil fuels such as oil (1000 barrels per second), natural gas and coal.[1] This includes not only the use as fuel but also secondary products made from petroleum. Due to the increasing demand and the finite nature of fossil resources, a steady increase in price results.[2] In addition to these economic considerations, ecological aspects also play a particularly important role. Thus nature is seriously threatened by both the extraction as well as the consumption of oil, gas and coal. To name just one of the problems, global warming is caused by the release of carbon dioxide from burning fossil fuels.[3] To reverse or at least slow down this trend we are looking for new and especially sustainable resources. Biomass is widely believed to have the greatest chance of success.[4] It is formed in plants by photosynthesis using atmospheric carbon dioxide, water and sunlight.[5] However, the available biomass for chemical and agrochemical industries should not be in competition with food and feed production. Thus, it is limited to by-products of the food industry, wood waste, grasses and agricultural residues. Especially wood waste consists mostly of unused indigestible lignocellulose.[6] By fast pyrolysis this can be transformed to so-called “pyrolysis oil”. Starting from pyrolysis oil, alcohols, diols, and polyols are accessible.[7,8]

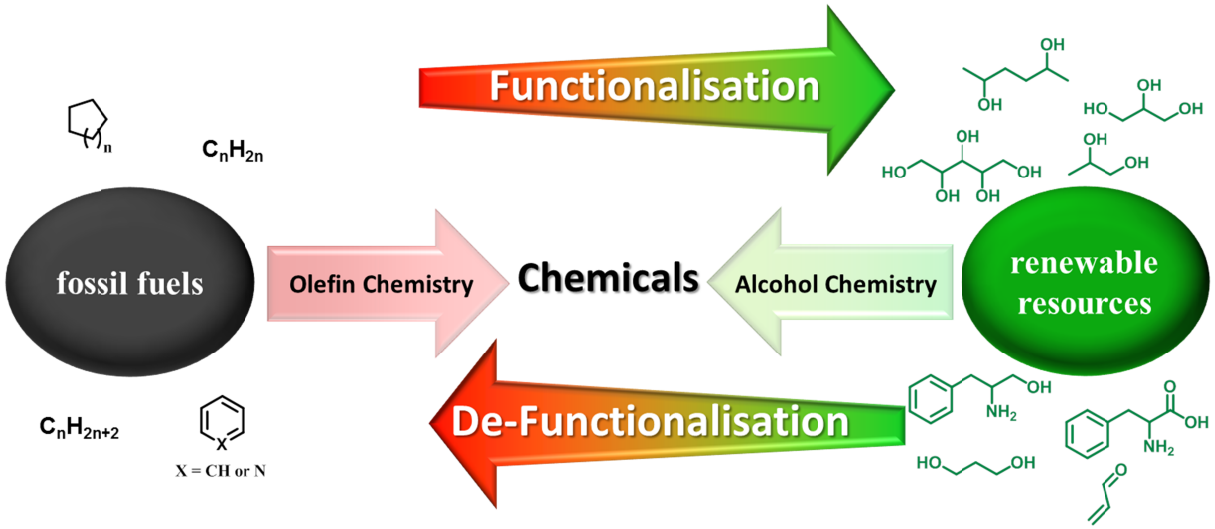


Figure 1. Fossil fuels versus renewable resources.

This highly oxidized feedstock with an oxygen content of up to 60 wt% differs fundamentally from oil-based starting material and is not convertible with the previously developed catalyst

systems.[8] The U.S. Department of Energy (DOE) has set the ambitious goal to achieve 10% of the basic chemical building blocks by 2020 and even 50% by 2050 from renewable resources.[9] To hit this challenging target new catalyst systems that either remove hydroxy groups or ideally implement them directly into useful products are required. A promising concept utilizing alcohols is offered by the so-called "borrowing hydrogen" or "hydrogen autotransfer" (BH/HA) mechanism.[10,11] Using homogeneous transition metal catalysis, unreactive alcohols are transferred to reactive carbonyl compounds. By condensation with an amine and re-transfer of the "borrowed" hydrogen, functionalized amines are received. Water is produced as the only by-product (Figure 2).

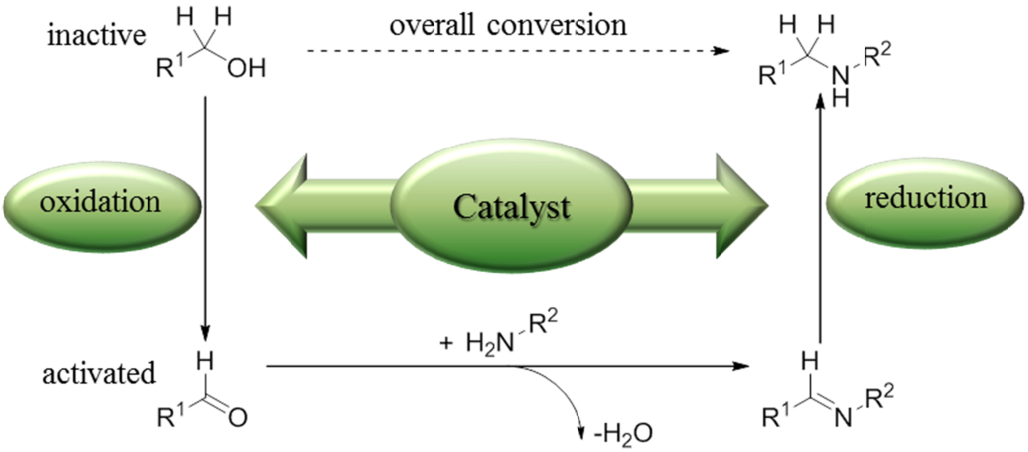


Figure 2. Borrowing Hydrogen/Hydrogen Autotransfer concept (BH/HA).

Through both invention of new catalyst systems and optimization of the reaction conditions, a powerful synthesis concept arised, which enables to work under mild reaction conditions (70 °C) and low catalyst loadings. For this purpose, mono- or bidentate phosphine ligand [12,13], bidentate P,N-ligand[14] or NHC (N-heterocyclic-carbene) ligand[15] stabilized ruthenium or iridium complexes were used. The application of homogeneous catalysis is justified by its high product selectivity regarding primary, secondary or even tertiary amines.

By extending the BH/HA concept the "borrowed" hydrogen could be released in elemental form. In addition to useful hydrogen gas energy-rich products, namely imines or olefins, are obtained.[16]

A new class of iridium complexes, stabilized by P,N-ligands was developed by Kempe and co-workers.[17,18] By using the BH/HA concept these iridium catalysts achieved a good activity in selective monoalkylation reactions of aromatic amines with alcohols. Starting from

these neutral P,N-ligand stabilized iridium complexes a new class of anionic P,N-ligand stabilized iridium complexes is developed within this work.

These are tested in the selective mono-alkylation of deactivated aromatic amines such as anilines or diaminobenzenes with alcohols. Furthermore, a library of tridentate P,N,P-pincer ligands and the corresponding iridium catalysts are synthesized. These are applied in a newly developed dehydrogenative condensation (DC) reaction using primary or secondary alcohols together with amino alcohols to form aromatic N-heterocycles like pyrroles or pyridines. The thereby used alcohols and amino alcohols could be principally derived from renewable recources. In the course of the reaction only non-toxic by-products and useful hydrogen gas are formed.

[1] P. Tertzakian, *A Thousand Barrels a Second*, McGraw-Hill, New York, **2006**.

[2] N. Armaroli, V. Balzani, *Angew. Chem. Int. Ed.* **2007**, *46*, 52-66.

[3] IPCC, **2007**: Climate Change 2007: *The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change* [Solomon, S., D. Qin, M. Manning, Z. Chen, M. Marquis, K.B. Averyt, M. Tignor and H.L. Miller (eds.)]. Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA.

[4] J.A. Kent in *Handbook of Industrial Chemistry and Biotechnology*, 12th ed. (Springer Science+Business Media, New York, **2012**), 1249-1322.

[5] Neil A. Campbell, Jane B. Reece in *Biologie*, 8th ed. (Pearson Studium, München, **2011**), 251-278.

[6] D. L. Klass in *Biomass for Renewable Energy, Fuels and Chemicals* (Academic Press, San Diego, CA, **1998**).

[7] A. J. A. Watson, J. M. J. Williams, *Science* **2010**, *329*, 635-636.

[8] T. P. Vispute, H. Zhang, A. Sanna, R. Xiao, G. W. Huber, *Science* **2010**, *330*, 1222-1227.

[9] A. K. Mohanty, M. Misra, L.T. Drzal, *J. Polym. Enbiron.* **2002**, *10*, 19-26.

[10] R. Grigg, T. R. B. Mitchell, S. Sutthivaiyakit, N. Tongpenyai, *J. Chem. Soc. Chem. Commun.* **1981**, *12*, 611-612.

[11] Y. Watanabe, Y. Tsuji, Y. Ohsugi, *Tetrahedron Lett.* **1981**, *22*, 2667-2670.

[12] D. Hollmann, A. Tillack, D. Michalik, R. Jackstell, M. Beller, *Chem. Asian J.* **2007**, *2*, 403-410.

[13] M. H. S. A. Hamid, J. M. J. Williams, *Chem. Commun.* **2007**, *7*, 725-727.

[14] B. Blank, M. Madalska, R. Kempe, *Adv. Synth. Catal.* **2008**, *350*, 749-758.

[16] A. Prades, R. Corberán, M. Poyatos, E. Peris, *Chem. Eur. J.* **2008**, *14*, 11474-11479.
C. Gunanathan, Y. Ben-David, D. Milstein, *Science* **2007**, *317*, 790-792.

[17] B. Blank, S. Michlik, R. Kempe, *Adv. Synth. Catal.* **2009**, *351*, 2903-2911.

[18] B. Blank, S. Michlik, R. Kempe, *Chem. Eur. J.* **2009**, *8*, 3790-3799.

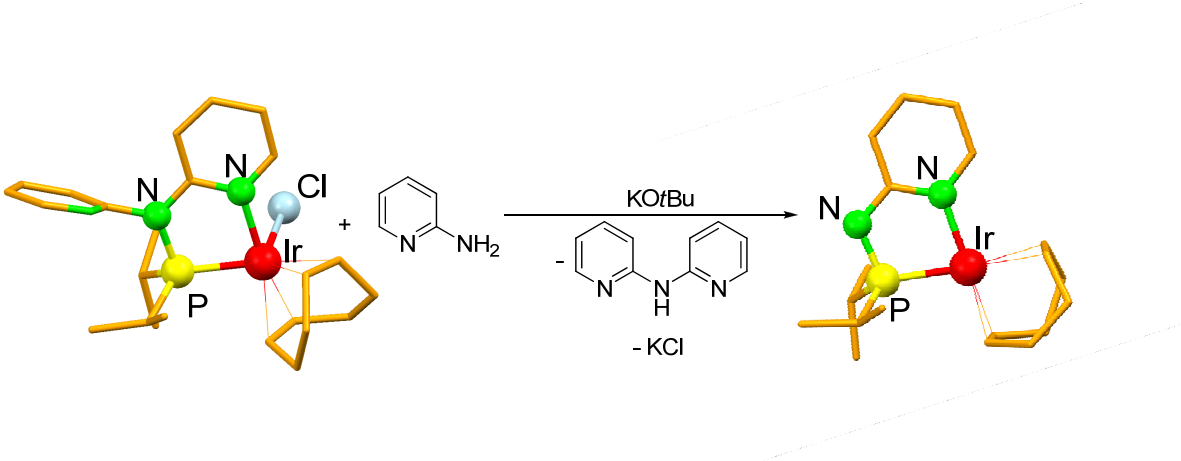
3. Overview of Thesis Results

This thesis contains 4 publications, which are presented in chapter 4-7.

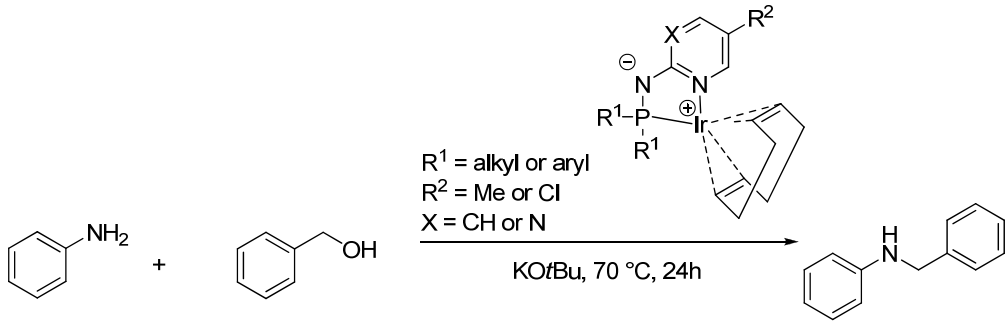
3.1 New iridium catalysts for the efficient alkylation of anilines by alcohols under mild conditions

S. Michlik, R. Kempe, *Chem. Eur. J.* **2010**, *16*, 13193-13198.

Recently, our group reported a novel neutral P,N-ligand stabilized iridium catalyst for the selective mono-N-alkylation of aromatic amines with primary alcohols. It was found that only by the use of 2-aminopyridines as educts low catalyst loadings are possible. When aniline was used as substrate, the catalyst loading had to be increased dramatically. NMR experiments were carried out to get a deeper insight into this issue. Under catalytic conditions the P-N bond of the ligand is cleaved and dipyridylamine is replaced by 2-aminopyridine.



A new catalytically more active and stable species is formed. This reaction cannot take place with anilines. With this finding, eight iridium complexes were synthesized based on eight new anionic P,N-ligands. After optimizing the reaction conditions these iridium complexes were utilized in selective mono-alkylation reactions of aniline with primary alcohols using the BH/HA methodology.

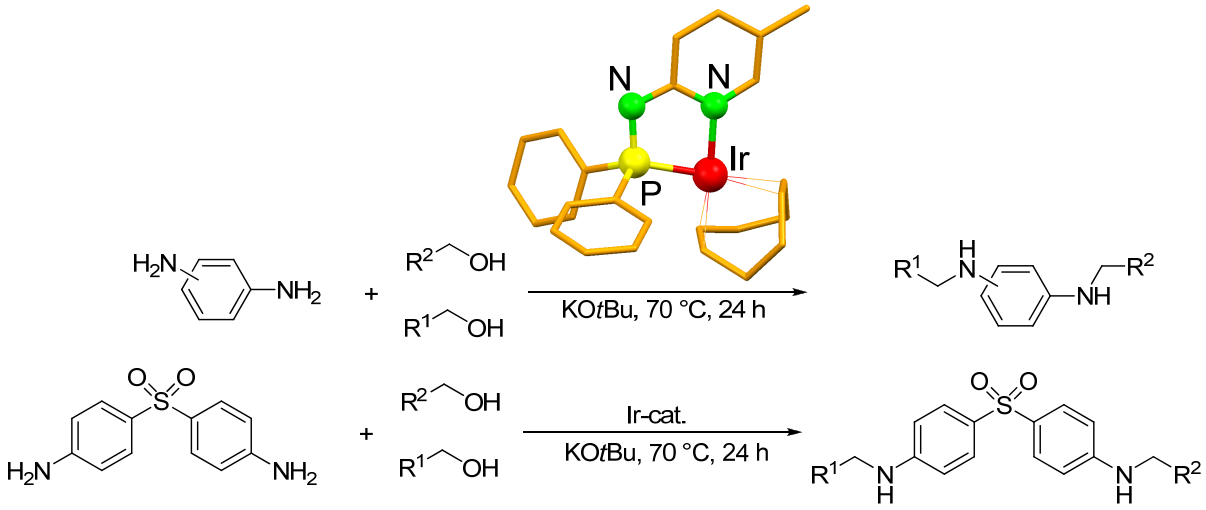


We succeeded in lowering the catalyst loading of the formerly used neutral P,N-ligand stabilized catalyst to about 1/6 by use of the "new" catalyst class.

3.2 The iridium-catalyzed synthesis of symmetrically and unsymmetrically alkylated diamines under mild reaction conditions

S. Michlik, T. Hille, R. Kempe, *Adv. Synth. Catal.* **2012**, *354*, 847-862.

In the previous work, a new class of catalysts for selective monoalkylation reactions of anilines with primary alcohols was developed. Now we were interested in evolving an efficient synthetic procedure for the synthesis of secondary amines starting from aromatic diamines and alcohols. Due to the catalyst stability, we succeeded in developing a synthesis protocol for both symmetrically as well as unsymmetrically alkylated aromatic diamines.

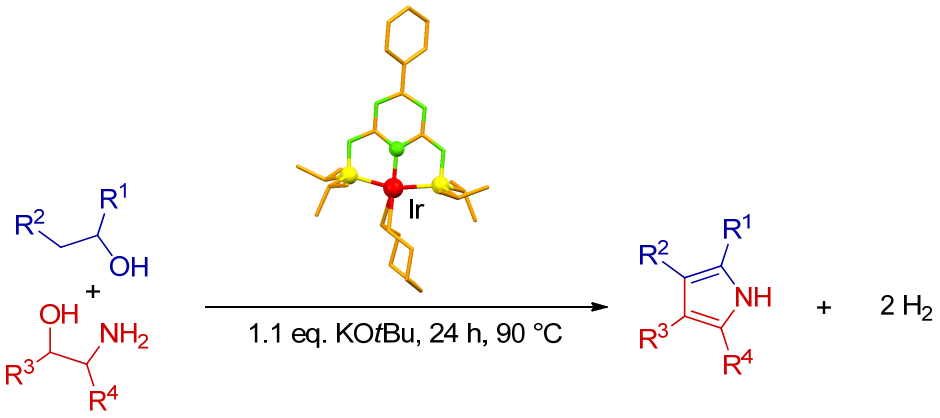


Due to the mild reaction conditions (70 °C) a large variety of functional groups was tolerated. This methodology was further used for the symmetric and non-symmetric alkylation of pharmacologically important 4-aminodiphenylsulfone (Dapsone®). In this way 23 new compounds could be synthesized.

3.3 A sustainable catalytic pyrrole synthesis

S. Michlik, R. Kempe, *Nature Chem.* **2013**, *5*, 140-144.

A more stable iridium catalyst, stabilized by a tridentate P,N,P-ligand had to be developed. By suppressing the retransfer of the "borrowed" hydrogen, we succeeded in developing a new sustainable pyrrole synthesis by dehydrogenative condensation reactions based on β-amino alcohols and secondary alcohols.



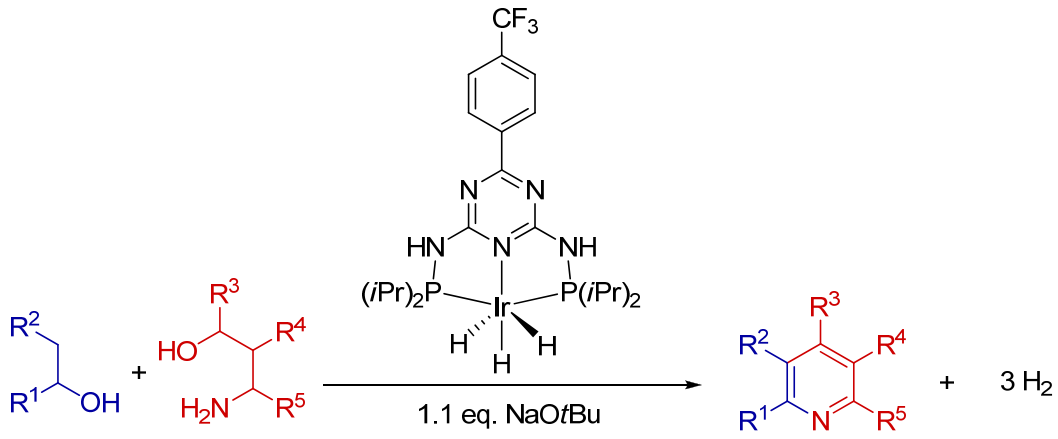
Many of the utilized starting materials can be derived from renewable resources. This fits perfectly into the concept of sustainable chemistry. In addition, only water and two equivalents of useful hydrogen gas are produced. After optimizing the reaction conditions and the synthesis reactor 38 pyrroles could be synthesized among which 30 are previously unknown compounds. Under a mild reaction temperature of 90 °C and very low catalyst loadings a plurality of functional groups, such as chlorides, bromides, organometallic moieties, olefins, amines, alcohols and heteroaromatics were tolerated. Furthermore, the synthetic approach was expanded to fused pyrroles, oligopyrroles and β-aminopyrroles.

3.4 Regioselectively functionalized pyridines from renewable resources

S. Michlik, R. Kempe, *Angew. Chem.* accepted for publication.

Based on primary or secondary alcohols and γ-amino alcohols a new pyridine synthesis catalyzed by a P,N,P-stabilized iridium complex has been developed. In the catalytic cycle two equivalents of water and three equivalents of elemental hydrogen are formed as by-products. The substituents of the pyridine ring can be introduced regioselectively by choice of the alcohols and γ-amino alcohols. Based on this dehydrogenative condensation reaction 2,6-,

2,5-, 2,4- and 2,3-disubstituted pyridines could be synthesized. By using cyclic alcohols even quadruply substituted, non-symmetric pyridines were easily accessible. Starting from natural products such as L-menthol or L-carveol, pyridines that bear chiral substituents are accessible.



The methodology gives rise to diversely and non-symmetrically substituted pyridines. 26 examples were synthesized, among which 21 represent new pyridine derivatives. A large variety of functional groups was tolerated.

3.5 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 the co-authors to the publications are specified. The asterisk denotes the corresponding authors.

Chapter 4

This work was published in Chemistry-A European Journal (*Chem. Eur. J.* **2010**, *16,* 13193-13198) with the title **"New iridium catalysts for the efficient alkylation of anilines by alcohols under mild conditions"**.
Authors: Stefan Michlik and Rhett Kempe*

I synthesized and characterized all ligands and complexes presented in this work, achieved all NMR and GC measurements and wrote the publication. Isabelle Haas performed the X-Ray analyses and solved the crystal structure. Prof. Dr. Rhett Kempe supervised this work, was involved in scientific discussions and the correction of the manuscript.

Chapter 5

This work was published in Advanced Synthesis and Catalysis (*Adv. Synth. Catal*. **2012**, *354*, 847-862) with the title **"The iridium-catalyzed synthesis of symmetrically and unsymmetrically alkylated diamines under mild reaction conditions"**.
Authors: Stefan Michlik, Toni Hille and Rhett Kempe*

All catalytic studies were carried out by me and the publication was also written by me. Toni Hille helped with the development of the catalytic protocol in the course of his B. Sc. thesis. Isabelle Haas performed the X-Ray analyses and solved the crystal structure. Prof. Dr. Rhett Kempe supervised this work, was involved in scientific discussions and the correction of the manuscript.

Chapter 6

This work was published in Nature Chemistry (*Nature Chem.* **2013**, *5*, 140-144) with the title **"A sustainable catalytic pyrrole synthesis"**.
Authors: Stefan Michlik and Rhett Kempe*

I synthesized and characterized all compounds presented in this work. I discovered and established the synthetic protocol, achieved all NMR and GC measurements and wrote the publication along with Prof. Dr. Rhett Kempe. Tobias Bauer performed the X-Ray analyses and solved the crystal structures presented in this work. Prof. Dr. Rhett Kempe supervised this work, was involved in scientific discussions and in the correction of the manuscript.

Chapter 7

This work has been accepted for publication in Angewandte Chemie (*Angew. Chem.*) with the title **“Regioselectively functionalized pyridines from sustainable resources”**.
Authors: Stefan Michlik and Rhett Kempe*

I synthesized and characterized all compounds presented in this work. I discovered and established the synthetic protocol, achieved all NMR- and GC measurements and wrote the publication. Prof. Dr. Rhett Kempe supervised this work, was involved in scientific discussions and the correction of the manuscript.

4. New iridium catalysts for the efficient alkylation of anilines by alcohols under mild conditions

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Keywords: alcohols, alkylation, anilines, iridium, P,N-ligands

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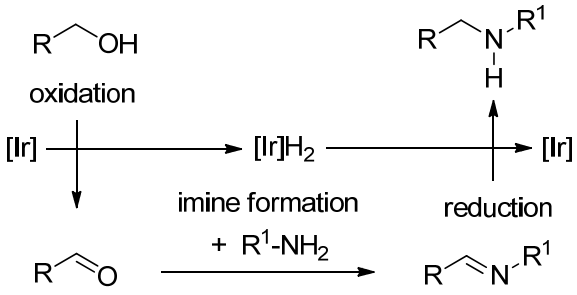
Abstract: The synthesis of eight new iridium complexes containing anionic P,N-ligands is described. These complexes have been investigated as catalysts for amine alkylation reactions, resulting in a highly active catalyst for the selective monoalkylation of anilines with primary alcohols, under mild reaction conditions. Nearly quantitative conversion was observed at 70 °C with a catalyst loading as low as 0.05 mol% iridium.

4.1 Introduction

P,N-ligand stabilized iridium complexes are efficient catalysts for selective C-N[1-3] and C-C[4] coupling reactions involving the borrowing-hydrogen (BH)[5] or hydrogen-autotransfer (HA)[6] catalysis protocols.[7]

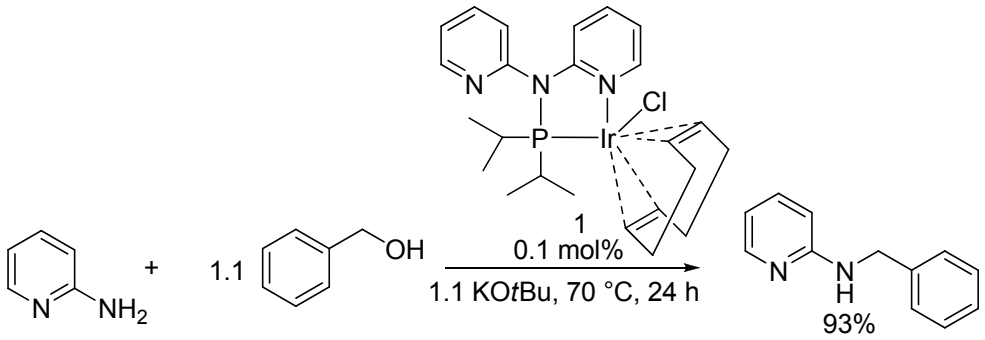


Scheme 1. The metal-complex catalyzed borrowing-hydrogen or hydrogen-autotransfer protocol to selectively alkylate amines ([Ir] = iridium complex).

These protocols proceed for Ir-complex-catalyzed amine alkylations as shown in Scheme 1 and have been developed into efficient synthetic methods by (for instance) the groups of Beller,[8] Grigg,[9] Fujita,[10] Williams[8a,11] and Yus,[12] as well as by us.[1-4] The P,N-ligand-based Ir catalyst system developed by us is especially active in the alkylation of aminopyridines[2,3] and usually requires a stoichiometric amount of base. Both of these observations were not fully understood by us and we became interested in obtaining a more detailed insight into how the catalyst operates within a BH/HA scenario. The observations made led to a new class of catalysts that operates very efficiently under mild conditions.

4.2 Results and Discussion

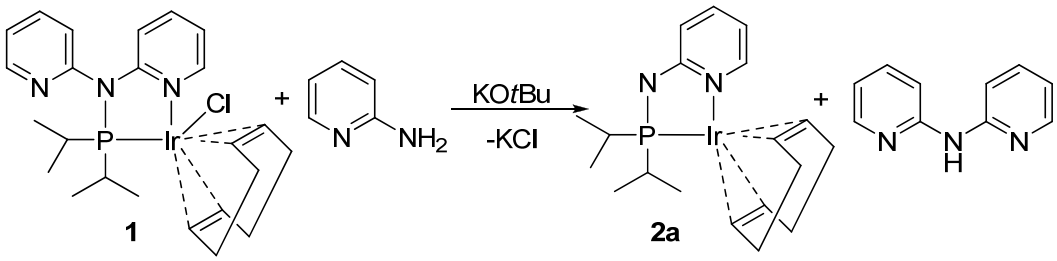
Detection of the catalytically active species in aminopyridine alkylation reactions: In previous work, it has been shown that our catalyst system is highly active in the alkylation of 2-aminopyridines with primary alcohols.[2,3] Therefore, 2-aminopyridine (1.0 equiv.), alcohol (1.1 equiv.) and KO*t*Bu were reacted, at 70 °C, in the presence of the Ir catalyst (0.1 mol%; Scheme 2). Under these conditions, N-(2-pyridyl)benzylamine was isolated in a very good yield of up to 93 %.[2]



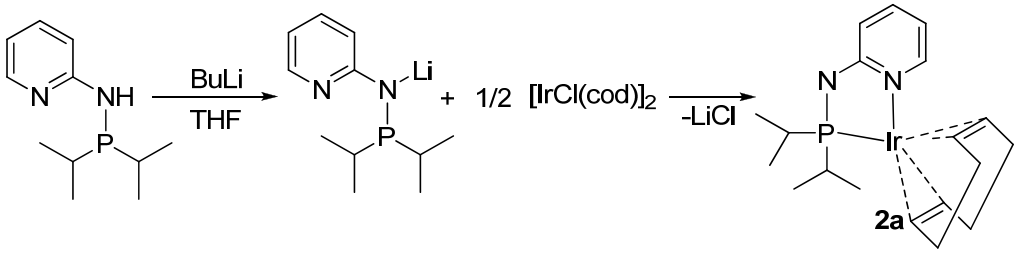
Scheme 2. Alkylation of aminopyridines under mild conditions.

However, these mild reaction conditions could not simply be transferred to the alkylation of anilines. For these compounds it was necessary to increase the catalyst loading up to 0.6 mol% iridium to obtain comparable results. It was concluded that the presence of aminopyridines may change the nature of the catalyst. NMR experiments were carried out to investigate whether the catalyst reacts with the aminopyridine substrate. Stoichiometric amounts of 2-aminopyridine and KO*t*Bu were added to catalyst **1**, under equivalent conditions to the catalysis experiments (Scheme 3). In the ^{31}P NMR spectrum (161 MHz, CD_2Cl_2, 298 K) only one peak, at δ = 94.9 ppm, was detected, which is shifted to higher field in comparison with the chemical shift of complex **1** (δ = 110.4 ppm). This observation indicates

that complex **1** does react with 2-aminopyridine, in the presence of a base, to form a new compound. Independent synthesis of this new compound, complex **2a**, through deprotonation of PyHNP(*i*Pr)$_2$ (Py = pyridine) with *n*BuLi, followed by the addition of [{IrCl(cod)}$_2$] (cod = 1,5-cyclooctadiene), led to **2a** in 80 % isolated yield (Scheme 4).



Scheme 3. The reaction of **1** with 2-aminopyridine, in the presence of KO*t*Bu.



Scheme 4. Synthesis of **2a**.

Crystals suitable for X-ray crystal structure analysis were obtained from a hexane solution. The molecular structure of **2a** is shown in Figure 1. In complex **2a**, both the Ir1-N1 (2.071(5) Å), and the P1-N2 (1.659(5) Å) bond lengths are slightly shorter than those in complex **1**, which contains a neutral P,N-ligand (Ir1-N1 (2.119(3) Å), P1-N2 (1.730(3) Å)), because deprotonation of the amino group means that the electron density is delocalized over the P-N-C-N backbone. Similar observations have been made by Woollins and co-workers for platinum and palladium complexes stabilized by deprotonated 2-(diphenylphosphinoamino)pyridine (dppap).[13] Seidel already succeeded in 1967 in synthesizing a neutral nickel(II) complex by using the deprotonated dppap ligand.[14] It is possible that if complexes like **2a** are formed under the catalytic conditions with alkylated aminopyridines, similar complexes may be formed with anilines. However, no reaction of complex **1** with aniline in the presence of a base was observed. Iridium complexes like **2a**, that is, compounds stabilized by anionic P,N-ligands, might be responsible for the enhanced activity in alkylation reactions of aminopyridines and might be a better class of catalyst than complexes like **1**, namely, ones stabilized by neutral P,N-ligands.

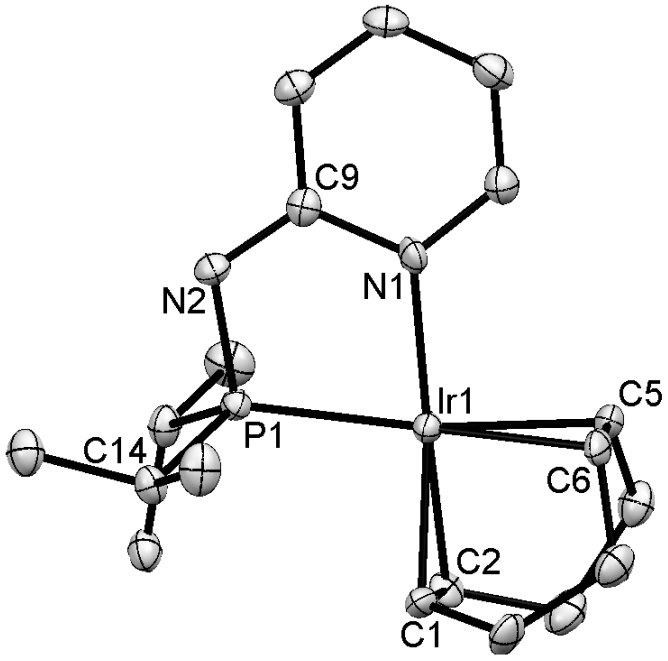
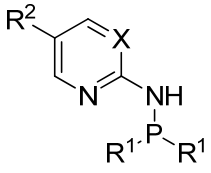


Figure 1. Molecular structure of **2a**. Selected bond length [Å] and angles [°]: Ir1-N1 2.071(5), Ir1-C1 2.109(6), Ir1-C2 2.140(6), Ir1-C5 2.191(6), Ir1-C6 2.216(6), Ir1-P1 2.2806(15), C1-C2 1.402(9), C5-C6 1.381(9), P1-N2 1.659(5), N1-C9 1.405(7), P1-C14 1.835(6), N1-Ir1-C1 157.0(2), N1-Ir1-C2 164.3(2), C1-Ir1-C2 38.5(2), N1-Ir1-C5 95.2(2), N1-Ir1-P1 79.23(14), N2-P1-Ir1 105.53(19), N2-C9-N1 121.7(5).

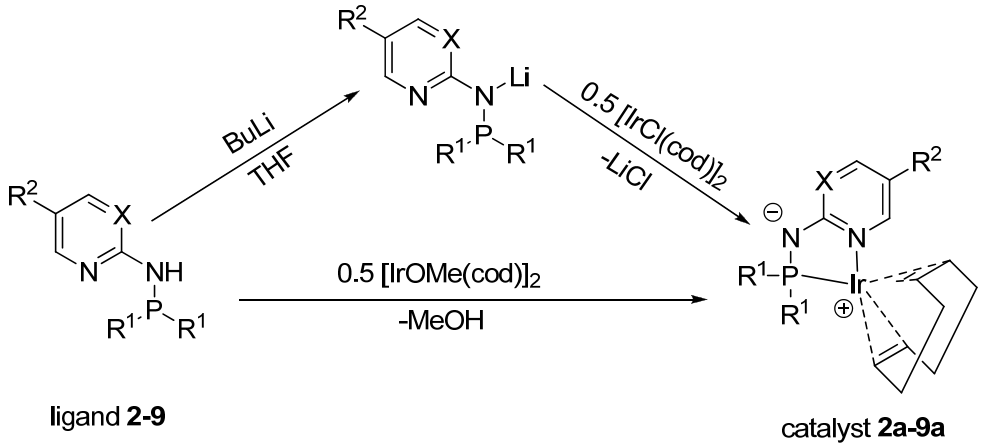
To investigate the potential of this "novel" class of Ir catalysts, a small library of ligands was synthesized from different substituted 2-aminopyridines and 2-aminopyrimidines by reacting them with chlorodiisoproylphosphane or chlorodiphenylphosphane in the presence of a base.



2: X = C; R^1 = *i*Pr; R^2 = H
3: X = C; R^1 = Ph; R^2 = H
4: X = N; R^1 = *i*Pr; R^2 = H
5: X = N; R^1 = Ph; R^2 = H
6: X = C; R^1 = *i*Pr; R^2 = CH_3
7: X = C; R^1 = Ph; R^2 = CH_3
8: X = C; R^1 = *i*Pr; R^2 = Cl
9: X = C; R^1 = Ph; R^2 = Cl

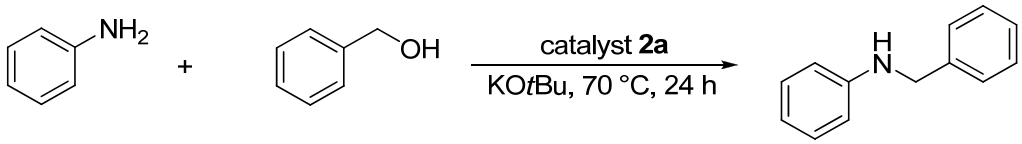
Iridium complexes based upon these ligands were synthesized in two different ways. The first was deprotonation of the corresponding ligand by *n*BuLi, followed by the addition of [{IrCl(cod)}$_2$] (0.5 equiv.). The resulting LiCl was filtered off and the solvent removed under vacuum. The more elegant method was a one-step synthesis of the complexes. For this, the dissolved ligand was added to [{IrOMe(cod)}$_2$] (0.5 equiv.) and the complex was formed by

elimination of methanol in quantitative yield. Iridium complexes **2a**-**9a** were synthesized and characterized (Scheme 5).



Scheme 5. Synthesis of **2a**-**9a**.

Catalyst development: If catalyst systems based upon **2a**-**9a** are responsible for the high efficiency of the alkylation reactions of aminopyridines they should do well in the alkylation of anilines. Since catalyst efficiency depends upon the reaction conditions, these had to be optimized for the new catalyst system. Catalyst **2a** was used for the optimization of the reaction conditions (Scheme 6).



Scheme 6. The model reaction used for finding the optimum reaction conditions.

First of all, the influence of the solvent was determined and various organic solvents were tested. As can be seen from Table 1, diethylene glycol dimethyl ether (diglyme) appears to be the most suitable solvent, because complete conversion and a very good yield (99 %) could only be achieved by using this solvent (Table 1, entry A5). When using THF, toluene or dimethoxyethane (DME), the yields were substantially lower (Table 1, entries A2-A4), indicating an inhibitory influence of the solvent on the reaction. It was also observed that the yield of N-phenylbenzylamine remains the same even with higher catalyst loadings. Interestingly, when DMSO was used as the solvent, no conversion was observed (Table 1, entry A1). Unfortunately, in all recent work the catalyst stock solution was in THF,[1-4] even for the solvent screenings. Since THF seems to deactivate our catalyst, all further stock solutions were made in diglyme. Next, the influence of the base was investigated to determine

whether the results obtained with KO*t*Bu could be improved upon. As can be seen in Table 1, entries B1-B5, only some bases achieved a reasonable yield.

Table 1. Screening of solvent, base and substrate/base ratio

	A		**B**		**C**	
	Solvent	Yield[b,c]	Base	Yield [b]	Substrate/Base	Yield [b,d]
1	DMSO	n.d.	K_3PO_4	23	1 : 1.1	99
2	THF	32	NaOH	10	1 : 1.0	72
3	toluene	34	KOH	9	1 : 0.7	68
4	DME	50	NaO*t*Bu	25	1 : 0.5	45
5	diglyme	99	KO*t*Bu	99	1 : 0.3	36
6					1 : 0.1	31
7					1 : 0	n.d.

[a] Reaction conditions: aniline (1.0 mmol), benzyl alcohol (1.1 mmol), catalyst **2a** (0.4 mol%), base (1.1 mmol), solvent (0.2 mL), 70 °C, 24 h; n.d. = not determined. [b] Yield determined by GC analysis with dodecane as the internal standard. [c] Catalyst stock solutions were made with the corresponding solvent. [d] Mean values after three runs.

However, the problem was that with all bases, except NaO*t*Bu and KO*t*Bu (Table 1, entries B4 and B5), simultaneous to the amine formation, the corresponding imine was also observed. The better results achieved with KO*t*Bu compared with NaO*t*Bu are explained by its excellent solubility in diglyme. The bases used, with the exception of KO*t*Bu, were generally very poorly soluble in diglyme, which could have caused the incomplete conversions.

After these optimizations, we were interested to see if the addition of stoichiometric amounts of base was needed to allow complete conversion or whether catalytic quantities of base are sufficient. Therefore, the influence of the substrate/base ratio was investigated (Table 1, entries C1-C7). The results shown in Table 1, entries C1-C5, suggest that it is necessary to use a substrate/base ratio of 1:1.1, because only in this case (Table 1, entry C1) it was possible to obtain complete conversion and an excellent yield (99 %) within 24 h. However, at a base loading of only 10 mol%, it was possible to achieve a yield of 31 % (Table 1, entry C5), which contradicts the aforementioned stoichiometric requirement for base. For this reason, we investigated whether it is possible to bring the reaction to complete conversion by

the use of 10 mol% of KO*t*Bu. To this end, the reaction time was increased; after 48 h a yield of 45 % and after 4 days a yield of 60 % were obtained. To examine the reaction with catalyst **2a** in detail, a kinetic experiment for the reaction of aniline with benzyl alcohol was performed by utilizing continuous sampling by gas chromatography. As can be seen in Figure 2, it is possible to come to complete conversion and a very good yield (94 %) with catalytic amounts of base. However, a very long reaction time (≈150 h) and a high catalyst loading (2.0 mol% iridium) are needed to get this result. Since these reaction conditions are unfavourable, it is reasonable to use an excess of base to accelerate the reaction and to reduce the catalyst loading.

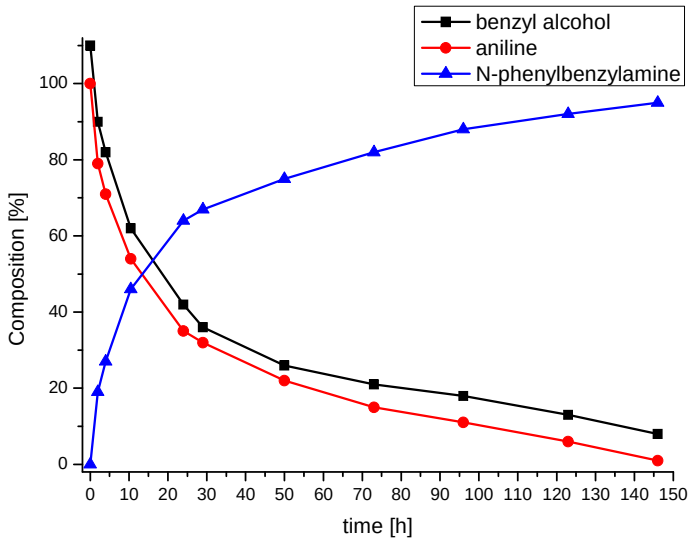
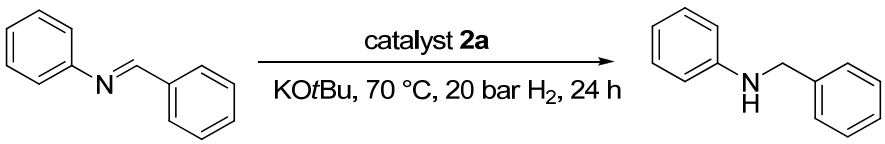


Figure 2. Time conversion plot for the reaction of aniline with benzyl alcohol (▪: benzyl alcohol; •: aniline; ▲: *N*-phenylbenzylamine). Reaction conditions: aniline (4.0 mmol), benzyl alcohol (4.4 mmol), catalyst **2a** (2 mol%), diglyme (1 mL), KO*t*Bu (0.4 mmol) and dodecane (1 mmol) as an internal standard.

To determine whether the base is essential for the imine hydrogenation step or for the activation of the benzyl alcohol, imine hydrogenation experiments were carried out with different base loadings and by using N-benzylidene(phenyl)amine as the starting material to get further insights into this reaction (Scheme 7).



Scheme 7. The hydrogenation of benzylidene(phenyl)amine.

As can be seen from Table 2, the excess of base is not needed for the hydrogenation of the imine, since even 10 mol% of base gives complete conversion and excellent yield (95 %; Table 2, entry 2). At higher base loadings the yield of N-phenylbenzylamine declines (Table 2, entries 3 and 4) and various byproducts are formed.

Table 2. Influence of base ratio on the hydrogenation of benzylidene(phenyl)amine.

	Base [mol%]	Conversion [%]	Yield [b]
1	0	10	9
2	10	100	95
3	50	100	90
4	110	100	70

[a] Reaction conditions: benzylidene(phenyl)amine (1.0 mmol), H_2 (20 bar), catalyst **2a** (0.4 mol%), diglyme (0.2 mL), 70 °C, 24 h. [b] Yield determined by GC analysis with dodecane as the internal standard.

Additionally, the iridium complexes **2a-9a** were tested to determine what effect substitution at the phosphorus and the amino skeleton has on the reaction (Table 3). Evidently, all of the catalysts containing phenyl substituents on the phosphorus (Table 3, entries 2, 4, 6 and 8) gave better results than those containing an isopropyl substituent (Table 3, entries 1, 3, 5 and 7), although isopropyl was always favoured in our earlier work.[1-4]

Table 3. Catalyst screening.[a]

	Catalyst	Yield [%][b]		Catalyst	Yield [%][b]
1	**2 a**	47	5	**6 a**	40
2	**3 a**	61	6	**7 a**	65
3	**4 a**	36	7	**8 a**	49
4	**5 a**	41	8	**9 a**	53

[a] Reaction conditions: aniline (1.0 mmol), benzyl alcohol (1.1 mmol), catalyst (0.05 mol%), KO*t*Bu (1.1 mmol), diglyme (0.2 mL), 70 °C, 24 h. [b] Yield determined by GC analysis with dodecane as the internal standard; mean values after three runs.

Moreover, it is noted that, by using 2-aminopyridines (Table 3, entries 1 and 2, and 5-8) as the amine skeleton, better activities were generally observed than if the corresponding 2-aminopyrimidines (Table 3, entries 3 and 4) were used. The best catalyst for this reaction seems to be catalyst **7a** (Table 3, entry 6), which achieved a 65 % yield at a very low catalyst loading (0.05 mol% iridium). The final screening was performed on the catalyst loading to find the minimum catalyst loading necessary to achieve full conversion and good yields

(Table 4). As shown in Table 4, it was sufficient to use a catalyst loading of 0.1 mol% to obtain a very good yield (92 %) for this reaction (Table 4, entry 4). With catalyst **7a**, the catalyst loading can be reduced to approximately 1/6 of the catalyst loading required when using catalyst **1**. If no catalyst is used a conversion of only 3 % is observed (Table 4, entry 6).

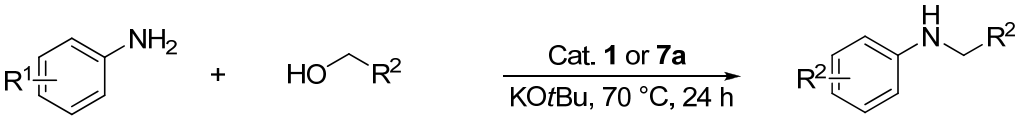
Table 4. Catalyst loading.[a]

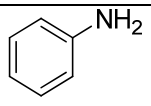
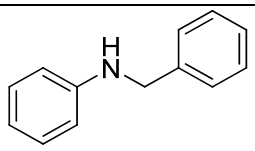
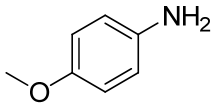
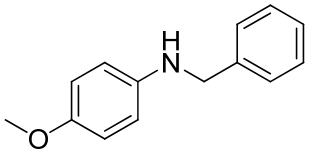
	Ir loading [%]	Yield [%][b]		Ir loading [%]	Yield [%][b]
1	0.4	99	4	0.1	92
2	0.3	99	5	0.05	65
3	0.2	99	6	0.0	3

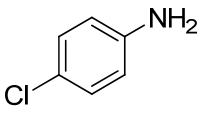
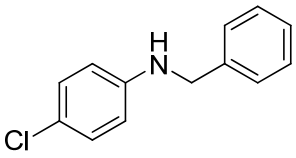
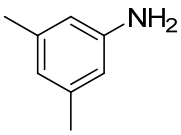
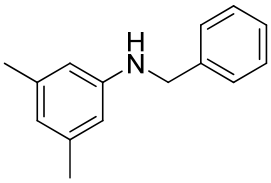
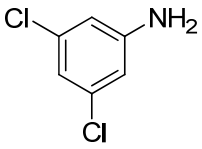
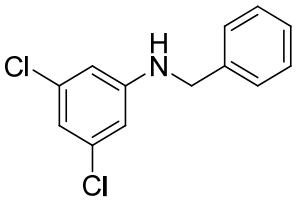
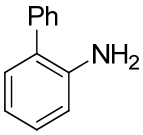
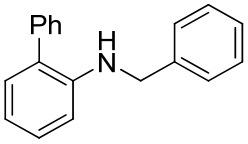
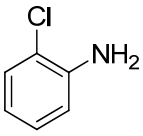
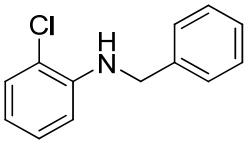
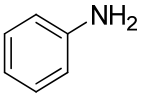
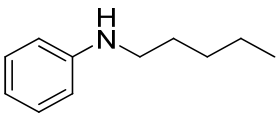
[a] Reaction conditions: aniline (1.0 mmol), benzyl alcohol (1.1 mmol), catalyst **7a**, KO*t*Bu (1.1 mmol), diglyme (0.2 mL), 70 °C, 24 h. [b] Yield determined by GC analysis with dodecane as the internal standard; mean values after three runs.

To confirm the results we achieved for the alkylation of aniline with benzyl alcohol with catalyst **7a,** different aniline derivatives were reacted with primary alcohols (Table 5). To compare results, batches were made both with catalyst **7a** and the original catalyst **1** to show the superiority of the new catalyst system. As can be seen in Table 5, complex **7a** is a significantly better catalyst than **1**. All products were obtained in very good to excellent yields by using complex **7a**. The catalyst loadings are very low and the reaction conditions are very mild in comparison with protocols previously developed for this reaction.[5-12]

Table 5. Catalytic N-alkylation of aniline derivatives with primary alcohols.[a]



	Catalyst loading [mol%]	Amine	Product	Yield [%][b] Catalyst 1	Yield [%][b] Catalyst 7a
1	0.1			38	92
2	0.2			29	92

3	0.05			75	98
4	0.2			33	81
5	0.4			54	98
6	0.2			48	91
7	0.2			73	97
8	0.2			52	98

[a] Reaction conditions: amine (1.0 mmol), benzyl alcohol (1.1 mmol), KO*t*Bu (1.1 mmol), diglyme (0.2 mL), 70 °C, 24 h. [b] Yield determined by GC analysis with dodecane as the internal standard.

4.3 Conclusion

It was shown that our new catalyst system, based upon anionic P,N-ligands, is highly active towards the alkylation of aniline with primary alcohols and far surpasses the original catalyst (based upon a neutral P,N-ligand). Furthermore, the catalysts are characterized by good long-term stability, as confirmed by kinetic experiments over more than five days. In addition, ligands and complexes are easily accessible in very good yields. Further work is directed towards the application of these catalysts to selective C-N and/or C-C coupling reactions using the BH/HA protocol.

4.4 Experimental Section

General considerations

All reactions were carried out in a dry argon or nitrogen atmosphere using standard Schlenk or glove box techniques. Halogenated solvents were dried over P_2O_5 and non-halogenated solvents were dried over sodium benzophenone ketyl. Deuterated solvents were ordered from Cambridge Isotope Laboratories, vented, stored over molecular sieves and distilled. All chemicals were purchased from commercial sources with a purity over 97 % and used without further purification, with the exception of aniline, which was distilled before use in the screening reactions. NMR spectra were performed by using an INOVA 400 MHz spectrometer at 298 K. Chemical shifts are reported in ppm relative to the deuterated solvent. Elemental analysis was carried out on a Vario elementar EL III. GC analyses were carried out on an Agilent 6890N Network GC system equipped with an HP-5 column (30 m×0.32 μm×0.25 μm).

General procedure for the screening reactions

In a pressure tube, the catalyst stock solution (200 µL, 0.02 M) in diethyl glycol dimethyl ether, aniline (1.0 mmol, 91 µL), benzyl alcohol (1.1 mmol, 114 µL), solvent (0.2 mL) and base (1.1 mmol) were combined. The pressure tube was closed with a Teflon cap and stirred at 70 °C for 24 h. The reaction mixture was cooled to room temperature and quenched by the addition of water (2 mL). Then, diethyl ether (10 mL) and dodecane (1.0 mmol, 226 µL, as an internal standard) were added. After agitation, a small fraction of the organic phase was analyzed by GC analysis.

General procedure for ligand synthesis

Arylamine (1.0 equiv.) was dissolved in THF (70-120 mL), triethylamine (1.0 equiv.) was added and the solution was cooled to 0 °C. Then, the corresponding chlorophosphane (1.0 equiv.) was added dropwise, with a syringe. The solution was allowed to warm to room temperature and stirred overnight at 50 °C. The suspension was filtered through a glass filter frit with a pad of Celite (4 cm) and washed with THF. The solvent was concentrated *in vacuo* yielding the corresponding ligands as white solids.

General procedure for complex synthesis

$[\{IrOMe(cod)\}_2]$ (0.5 equiv.) was suspended in THF (5-25 mL) and subsequently a solution of the corresponding ligand (1.0 equiv., **2**-**9**) in THF (5 mL) was added dropwise. A red

solution was obtained and after 30 min the solvent was removed *in vacuo*, affording dark red solids in almost quantitative yields.

Synthesis of (5-Me)PyNHPPh$_2$ (7)

5-Methyl-2-aminopyridine (10.0 mmol, 1.08 g) was suspended in THF (70 mL), triethylamine (10.0 mmol, 1.4 mL) was added and the solution was cooled to 0 °C. Then chlorodiphenylphosphane (10.0 mmol, 1.83 mL) was added dropwise, with a syringe. The solution was allowed to warm to room temperature and stirred for 4 d at room temperature and 12 h at 50 °C. The suspension was filtered over a glass filter frit with a pad of Celite (4 cm) and washed with THF (50 mL). The solvent was removed *in vacuo*, yielding compound **7** as a white solid (9.69 mmol, 97 %). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.92 (s, 1 H), 7.50-7.43 (m, 4 H), 7.41-7.28 (m, 7 H), 6.95 (d, J = 8.6 Hz, 1 H), 5.25 (s, 1 H), 2.19 ppm (s, 3 H); **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 147.7, 139.6, 138.8, 131.2 (d, J = 20.9 Hz), 129.1, 128.5 (d, J = 6.7 Hz), 123.9, 108.4 (d, J = 15.0 Hz), 17.4 ppm; ^{31}P NMR (161 MHz, CD_2Cl_2, 298 K): δ = 27.21 ppm; **Elemental analysis** calcd (%) for $C_{18}H_{17}N_2P$: C 73.96, H 5.86, N 9.58; found: C 73.88, H 5.69, N 9.71.

Synthesis of [{(5-Me)PyNHPPh$_2$}Ir(cod)] (7a)

[{IrOMe(cod)}$_2$] (1.2 mmol, 795 mg) was dissolved in THF (20 mL) and a solution of compound **7** (2.4 mmol, 701 mg) dissolved in THF (5 mL) was subsequently added dropwise. A red solution was obtained and, after 30 min, the solvent was removed *in vacuo* and the residue was recrystallized from hexane/THF (3:1), yielding red crystals (1.03 mmol, 86 %). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.59 (ddd, J = 10.8, 7.3, 1.7 Hz, 4 H), 7.41-7.36 (m, 6 H), 7.23 (s, 1 H), 7.04 (dt, J = 8.9, 2.4 Hz, 1 H), 6.88 (d, J = 8.9 Hz, 1 H), 4.94 (s, 2 H), 3.54 (s, 2 H), 2.25-2.19 (m, 4 H), 2.02 (s, 3 H), 2.04-1.94 (m, 4 H) ppm; **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 143.8 (d, J = 2.7 Hz), 140.7 (d, J = 2.9 Hz), 138.4 (d, J = 0.6 Hz), 137.8 (d, J = 0.5 Hz), 132.5 (d, J = 12.2 Hz), 130.5 (d, J = 2.3 Hz), 128.8 (d, J = 10.3 Hz), 116.6, 116.4 (d, J = 0.5 Hz), 115.9 (d, J = 0.6 Hz), 95.32, 91.7 (d, J = 13.4 Hz), 60.4, 33.5, 29.5, 17.3 ppm; ^{31}P NMR (161 MHz, CD_2Cl_2, 298 K): δ = 72.54 ppm; **Elemental analysis** calcd (%) for $C_{26}H_{28}IrN_2P$: C 52.78, H 4.77, N 4.73; found: C 52.83, H 4.86, N 4.72.

Acknowledgments

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4.5 References

[1] B. Blank, M. Madalska, R. Kempe, *Adv. Synth. Catal*. **2008**, *350*, 749-758.

[2] B. Blank, S. Michlik, R. Kempe, *Chem. Eur. J.* **2009**, *15*, 3790-3799.

[3] B. Blank, S. Michlik, R. Kempe, *Adv. Synth. Catal.* **2009**, *351*, 2903.

[4] B. Blank, R. Kempe, *J. Am. Chem. Soc.* **2010**, *132*, 924-925.

[5] a) T. D. Nixon, M. K. Whittlesey, J. M. J. Williams, *Dalton Trans.* **2009**, 753-762*;* b) G. W. Lamb, J. M. J. Williams, *Chim. Oggi.* **2008**, *26*, 17-19; c) M. H. S. A. Hamid, P. A. Slatford, J. M. J. Williams, *Adv. Synth. Catal.* **2007**, *349*, 1555 - 1575.

[6] a) G. Guillena, D. J. Ramo´n, M. Yus, *Chem. Rev.* **2010,** *110,* 1611-1641; b) G. Guillena, D. J. Ramo`n, M. Yus, *Angew. Chem.* **2007**, *119*, 2410 -2416; *Angew. Chem. Int. Ed.* **2007**, *46*, 2358 -2364.

[7] a) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* **2010**, *110*, 681 - 703; b) D. Gnanamgari, E. L. O. Sauer, N. D. Schley, C. Butler, C. D. Incarvito, R. H. Crabtree, *Organometallics* **2009,** *28,* 321-325; c) D. Gnanamgari, C. H. Leung, N. D. Schley, S. T. Hilton, R. H. Crabtree, *Org. Biomol. Chem.* **2008**, *6*, 4442-4445; d) A. M. Voutchkova, D. Gnanamgari, C. E Jakobsche, C. Butler, S. J. Miller, J. Parr, R. H. J. Crabtree, *Organomet. Chem*. **2008**, 693, 1815-1821; e) D. Gnanamgari, A. Moores, E. Rajaseelan, R. H. Crabtree, *Organometallics* **2007**, 26, 1226-1230.

[8] a) S. Bähn, S. Imm, K. Mevius, L. Neubert, A. Tillack, J. M. J. Williams, M. Beller, *Chem. Eur. J.* **2010**, *16*, 3590-3593; b) S. Imm, S. Bähn, A. Tillack, K. Mevius, L. Neubert, M. Beller, *Chem. Eur. J.* **2010**, *16*, 2705-2709; c) S. Bähn, A. Tillack, S. Imm, K. Mevius, D. Michalik, D. Hollmann, L. Neubert, M. Beller, *ChemSusChem* **2009**, 2, 551-557; d) D. Hollmann, S. Bähn, A. Tillack, R. Parton, R. Altink, M. Beller, *Tetrahedron Lett.* **2008**, *49*, 5742-5745; e) A. Tillack, D. Hollmann, K. Mevius, D. Michalik, S. Bähn, M. Beller, *Eur. J. Org. Che.* **2008**, 4745-4750; f) S. Bähn, D. Hollmann, A. Tillack, M. Beller, *Adv. Synth. Catal*. **2008**, *350*, 2099-2103; g) D. Hollmann, S. Bähn, A. Tillack, M. Beller, *Chem. Commun*. **2008**, 3199-3201; h) D. Hollmann, S. Bähn, A. Tillack, M. Beller, *Angew. Chem*. **2007**, *119*, 8440-8444; i) *Angew. Chem. Int. Ed*. **2007**, 46, 8291-8294; j) D. Hollmann, A. Tillack, D. Michalik, R. Jackstell, M. Beller, *Chem. Asian J*. **2007**, *2*, 403-410; k) A. Tillack, D. Hollmann, D. Michalik, M. Beller, *Tetrahedron Lett*. **2006,** *47*, 8881-8885.

[9] a) S. Whitney, R. Grigg, A. Derrick, A. Keep, Org. Lett. 17, **2007**, 3299-3302; b) C. Löfberg, R. Grigg, M. A. Whittaker, A. Keep, A. Derrick, *J. Org. Chem*. **2006**, *71*, 8023-8027; c) C. Löfberg, R. Grigg, A. Keep, A. Derrick, V. Sridharan, C. Kilner, *Chem. Commun*. **2006**, 5000-5002; d) R. Grigg, T. R. B. Mitchell, S. Sutthivaiyakit, N. Tongpenyai, *J. Chem. Soc. Chem. Commun*. **1981**, 611-612.

[10] a) R. Yamaguchi, Z. Mingwen, S. Kawagoe, C. Asai, K.-i. Fujita, *Synthesis* **2009**, 1220-1223; b) R. Yamaguchi, S. Kawagoe, C. Asai, K.-i. Fujita, *Org. Lett*. **2008**, *10*, 181-184; c) K.-i. Fujita, Y. Enoki, R. Yamaguchi, *Tetrahedron* **2008**, *64*, 1943-1954; d) K.-i Fujita, R. Yamaguchi, *Synlett* **2005**, *4*, 560-571; d) K.-i. Fujita, C. Asai, T. Yamaguchi, F. Hanasaka, R. Yamaguchi, *Org. Lett*. **2005**, *7*, 4017-4019; e) K.-i. Fujita, T. Fujii, R. Yamaguchi, *Org. Lett*. **2004**, *6*, 3525-3528; f) K.-i. Fujita, Z. Li, N. Ozeki, R. Yamaguchi, *Tetrahedron Lett*. **2003**, *44*, 2687-2690; g) K.-i. Fujita, K. Yamamoto, R. Yamaguchi, *Org. Lett*. **2002**, *4*, 2691-2694.

[11] a) O. Saidi, A. J. Blacker, M. M. Farah, S. P. Marsden, J. M. J. Williams, *Angew. Chem*. **2009**, *121*, 7511-7514; b) *Angew. Chem. Int. Ed*. **2009**, *48*, 7375-7378; c) M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson, J. M. J. Williams, *J. Am. Chem. Soc*. **2009**, *131*, 1766-1774; d) G. W. Lamb, A. J. A. Watson, K. E. Jolley, A. C. Maxwell, J. M. J. Williams, *Tetrahedron Lett.* **2009**, *50*, 3374-3377; e) S. J. Pridmore, P. A. Slatford, A. Daniel, M. K. Whittlesey, J. M. J. Williams, *Tetrahedron Lett*. **2007**, *48*, 5115-5120; f) M. H. S. A. Hamid, J. M. J. Williams, *Chem.Commun*. **2007**, 725-727; g) G. Cami-Kobeci, P. A. Slatford, M. K. Whittlesey, J. M. J. Williams, *Bioorg. Med. Chem. Lett*. **2005**, *15*, 535-537; h) G. Cami-Kobeci, J. M. J Williams, *Chem. Commun*. **2004**, 1072-1073.

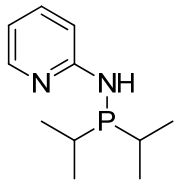
[12] a) R. Martínez, D. J. Ramon, M. Yus, Org. *Biomol. Chem*. **2009**, *7*, 2176-2181; b) R. Martínez, D. J. Ramon, M. Yus, *Tetrahedron* **2006**, *62*, 8982-8987; c) R. Martínez, D. J. Ramon, M. Yus, *Tetrahedron* **2006**, *62*, 8988-9001; d) R. Martínez, G. J. Brand, D. J. Ramon, M. Yus, *Tetrahedron Lett*. **2005**, *46*, 3683-3686.

[13] a) S. M. Aucott, A.M. Z. Slawin, J.D. Woollins, *Phosphorus, Sulfur, and Silicon* **1997**, *124* & *125*, 473-476; b) S. M. Aucott, A.M. Z. Slawin, J. D. Woollins, *J. Chem. Soc, Dalton Trans*. **2000**, 2559-2575.

[14] W. Seidel, *Z.Chem*. **1967,** *12*, 462.

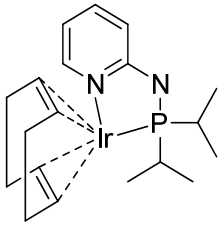
4.6 Supporting Information

Synthesis of PyNHP(*i*Pr)$_2$ (2)



Synthesized via literature methods with slight variations in order to improve the yield.[1] 2-Aminopyridine (20.0 mmol, 1.88 g) was suspended in 100 mL THF and triethylamine (20.0 mmol, 2.8 mL) was added and the solution was cooled to 0 °C. Then chlorodiisopropylphosphin (20.0 mmol, 3.2 mL) was added dropwise with a syringe. The solution was allowed to warm to room temperature and stirred over night at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. The solvent was concentrated *in vacuo* to 10 mL and left to crystallize at -20 °C. The supernatant solution was decanted and the solid washed with 5 mL of cold hexane and subsequently dried *in vacuo* yielding PyNHP(*i*Pr)$_2$ as a white solid (19.2 mmol = 96%). **^{1}H NMR** (400 MHz, C_6D_6, 298 K): δ = 8.18 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.27-7.23 (m, 1H), 7.10 (ddd, *J* = 8.5, 7.2, 1.7 Hz, 1H), 6.37 (ddd, *J* = 7.3, 7.1, 0.9 Hz, 1H), 4.86 (d, *J* = 10.6 Hz, 1H), 1.47-1.36 (m, 2H), 0.96-0.82 (m, 12H) ppm.**^{13}C NMR** (100 MHz, C_6D_6, 298 K): δ = 161.6 (d, *J* = 20.0 Hz), 148.7 (d, *J* = 1.2 Hz), 137.3 (d, *J* = 2.3 Hz), 114.5, 108.6 (d, *J* = 18.6 Hz), 26.5 (d, *J* = 11.6 Hz), 18.7 (d, *J* = 20.4 Hz), 17.1 (d, *J* = 8.0 Hz) ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298 K): δ = 48.83 ppm.

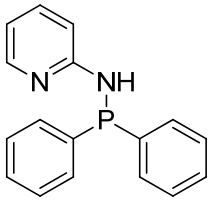
Synthesis of [(PyNP(*i*Pr)$_2$)Ir(cod)] (2a)



PyHNP(*i*Pr)$_2$ **(2)** (2.0 mmol, 420 mg) was suspended in 20 mL THF, cooled to -30 °C and n-BuLi (2.0 mmol, 1.6 M, 1.25 mL) was added dropwise with a syringe. The reaction mixture was stirred at -30 °C for 30 min and was then allowed to warm to room temperature and stirred for 1h. Then the reaction mixture was added to a solution of [IrCl(cod)]$_2$ (1.0 mmol, 671 mg) (with a flexible tube). The reaction mixture was stirred for 30 min at room

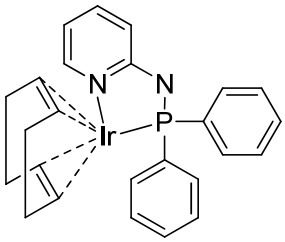
temperature before the solvent was removed *in vacuo*. The residue was suspended in diethyl ether and filtered over a glass filter frit with a pad of celite (1 cm) and washed with 10 mL of cold diethyl ether. Solvent was removed *in vacuo* and the residue was recrystallized from hexane affording dark red crystals (1.6 mmol, 80%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.28 (d, *J* = 6.3 Hz, 1H), 7.05 (dt, *J* = 7.0, 1.7 Hz, 1H), 6.80 (d, *J* = 8.9 Hz, 1H), 5.84 (t, *J* = 6.1 Hz, 1H), 4.64 (s, 2H), 3.85 (s, 2H), 2.27-2.20 (m, 4H), 2.15-2.09 (m, 2H), 2.05-1.99 (m, 2H), 1.85-1.78 (m, 2H) 1.17-1.09 (m, 12H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 161.7, 148.5 (d, *J* = 1.2 Hz), 137.8 (d, *J* = 2.0 Hz), 114.6, 109.1 (d, *J* = 18.9 Hz), 95.4, 26.9 (d, *J* = 11.1 Hz), 19.0 (d, *J* = 20.0 Hz), 17.42 (d, *J* = 8.1 Hz) ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 94.95 ppm. **Elemental analysis** calcd (%) for $C_{27}H_{32}N_2PIr$: C 44.78, H 5.93, N 5.50; found: C 44.77, H 5.68, N 5.53.

Synthesis of $PyNHPPh_2$ (3)



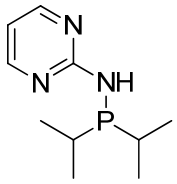
Synthesized via literature methods with slight variations in order to improve the yield.[2] 2-aminopyridine (20.0 mmol, 1.88 g) was suspended in 100 mL THF, triethylamine (20.0 mmol, 2.8 mL) was added and the solution was cooled to 0 °C. Then chlorodiphenylphosphine (20.0 mmol, 3.7 mL) was added dropwise with a syringe. The solution was allowed to warm to room temperature and was stirred over night at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL THF. The solvent was concenrated *in vacuo* to 10 mL and left to crystallize at -20 °C. The supernatant solution was decanted and the solid washed with 5 mL of cold hexane and subsequently dried *in vacuo* yielding $PyNHPPh_2$ as a white solid (16.2 mmol = 81%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ = 8.10 (d, *J* = 4.2 Hz, 1H), 7.47 (dd, *J* = 8.9, 5.7 Hz, 5H), 7.37 (d, *J* = 3.1 Hz, 6H), 7.04 (d, *J* = 8.3 Hz, 1H), 6.71 (t, *J* = 6.0 Hz, 1H), 5.38 (d, *J* = 7.3 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K): δ = 148.2 (d, *J* = 1.1 Hz), 138.02 (d, *J* = 2.3 Hz), 131.5, 131.3, 129.4, 128.7 (d, *J* = 6.7 Hz), 115.2, 109.0 (d, *J* = 15.3 Hz) ppm. **^{31}P NMR** (161 MHz, $CDCl_3$, 298 K): δ = 27.01 ppm.

Synthesis of [PyNPPh$_2$Ir(cod)] (3a)



PyHNPPh$_2$ **(3)** (0.5 mmol, 139 mg) was suspended in 5 mL THF, cooled to -30 °C and n-BuLi (0.5 mmol, 1.6 M, 313 µl) was added dropwise with a syringe. The reaction mixture was stirred at -30 °C for 30 min and was then allowed to warm to room temperature and stirred for 1h. Then the reaction mixture was added to a solution of [IrCl(cod)]$_2$ (0.25 mmol, 166 mg) (with a flexible tube). The reaction mixture was stirred for 30 min at room temperature before the solvent was removed *in vacuo*. The residue was suspended in diethyl ether and filtered over a glass filter frit with a pad of celite (1 cm) and washed with 10 mL of diethyl ether. Solvent was removed *in vacuo* and the residue was recrystallized from THF:hexane = 1:3 affording dark red crystals (0.45 mmol, 90%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.67-7.56 (m, 4H), 7.42-7.30 (m, 6H), 7.17-7.08 (m, 2H), 7.08 (d, *J* = 8.7 Hz, 1H), 5.99 (t, *J* = 6.3 Hz, 1H), 5.02-4.63 (m, 2H), 3.79-3.34 (m, 2H), 2.23 (d, *J* = 8.0 Hz, 4H), 1.95 (d, *J* = 8.6 Hz, 4H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 145.7 (d, *J* = 2.9 Hz), 138.5 (d, *J* = 3.3 Hz), 138.1, 137.5, 132.5 (d, *J* = 11.4 Hz), 130.6 (d, *J* = 2.4 Hz), 128.9 (d, *J* = 10.4 Hz), 116.9 (d, *J* = 23.8 Hz), 107.3, 92.0 (d, *J* = 12.3 Hz), 60.5, 33.5, 29.5 ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 73.46 ppm. **Elemental analysis** calcd (%) for $C_{27}H_{32}N_2PIr$ x 0.5 THF: C 52.84, H 4.93, N 4.56; found: C 53.03, H 4.83, N 4.80.

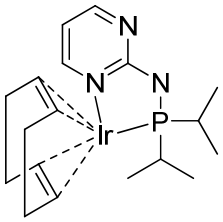
Synthesis of PymNHP(*i*Pr)$_2$ (4)



2-aminopyrimidine (8.0 mmol, 760 mg) was suspended in 90 mL toluene and the solution was cooled to -30 °C. Then n-BuLi (8.0 mmol, 1.6 M, 5.0 mL) was added dropwise with a syringe. The reaction mixture was stirred at -30 °C for 30 min and was then allowed to warm to room temperature and stirred for 2h. The reaction mixture was cooled to -30 °C and chlorodiisopropylphosphine (10.0 mmol, 1.6 mL) was added dropwise with a syringe. The solution was allowed to warm to room temperature and was stirred over night. The suspension

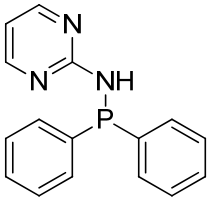
was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of toluene. Solvent was removed *in vacuo* yielding a white solid (6.5 mmol = 81%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ = 8.31 (d, *J* = 4.8 Hz, 2H), 6.59 (t, *J* = 4.8 Hz, 1H), 5.14 (d, *J* = 9.2 Hz, 1H), 1.27-1.18 (m, 2H), 1.10–1.04 (m, 12 H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K): δ = 158.08 (d, *J* = 1.5 Hz), 111.83 (s), 26.14 (d, *J* = 13.4 Hz), 18.58 (d, *J* = 20.5 Hz), 17.30 (d, *J* = 8.7 Hz) ppm. **^{31}P NMR** (161 MHz, $CDCl_3$, 298 K): δ = 49.49 ppm. **Elemental analysis** calcd (%) for $C_{10}H_{18}N_3P$: C 56.86, H 8.59, N 19.89; found: C 56.74, H 8.83, N 19.52.

Synthesis of [(PymNP(*i*Pr)$_2$)Ir(cod)] (4a)



$[IrOMe(cod)]_2$ (0.25 mmol, 166 mg) was dissolved in 5 mL THF and subsequently a solution of PymHNP(*i*Pr)$_2$ **(4)** (0.5 mmol, 106 mg) in THF was added dropwise. A red solution was obtained and after 30 min the solvent was removed *in vacuo*, the residue was recrystallized from toluene:hexane = 1:1 yielding dark red crystals (0.38 mmol, 75%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 8.19 (td, *J* = 4.1, 2.2, 2.1 Hz, 1H), 7.54 (dd, *J* = 6.0, 2.6 Hz, 1H), 5.88 (dd, *J* = 6.0, 4.2 Hz, 1H), 4.53 (d, *J* = 3.3 Hz, 2H), 3.91 (d, *J* = 2.8 Hz, 2H), 2.32-2.20 (m, 4H), 2.18-2.08 (m, 2H), 2.08-1.99 (m, 2H), 1.86-1.76 (m, 2H), 1.20-1.10 (m, 12H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 162.7, 155.4 (d, *J* = 22.5 Hz), 103.8, 89.4 (d, *J* = 11.1 Hz), 58.5, 34.3 (d, *J* = 2.5 Hz), 28.9 (d, *J* = 1.7 Hz), 28.4, 28.0, 17.7 (d, *J* = 3.5 Hz), 17.2 ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 83.49 ppm. **Elemental analysis** calcd (%) for $C_{18}H_{29}IrN_3P$ x 0.25 THF: C 43.17, H 5.91, N 7.95; found: C 43.25, H 6.05, N 7.80.

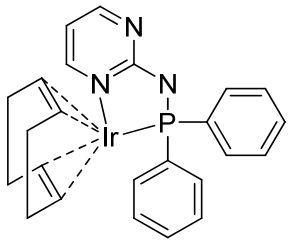
Synthesis of PymNHPPh$_2$ (5)



Synthesized via literature methods with slight variations in order to improve the yield.[3] 2-aminopyrimidine (20.0 mmol, 1.9 g) was suspended in 100 mL THF, triethylamine

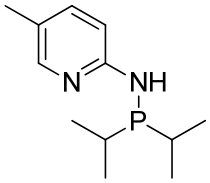
(20.0 mmol, 2.8 mL) was added and the solution was cooled to 0 °C. Then chlorodiphenylphosphine (20.0 mmol, 3.7 mL) was added dropwise with a syringe. The solution was allowed to warm to room temperature and stirred over night at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. The solvent was concenrated *in vacuo* to 10 mL and left to crystallize at -20 °C. The supernatant solution was decanted and the solid washed with 5 mL of cold hexane and subsequently dried *in vacuo* yielding $PymNHPPh_2$ as a white solid (15.2 mmol = 76%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K): δ = 8.25 (d, *J* = 4.3 Hz, 2H), 7.47 (dd, *J* = 5.6, 3.5 Hz, 4H), 7.36 (d, *J* = 1.9 Hz, 6H), 6.64 (td, *J* = 4.8, 0.9 Hz, 1H), 6.12 (d, *J* = 8.3 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K): δ = 148.3 (d, *J* = 1.1 Hz), 138.0 (d, *J* = 2.3 Hz), 131.5, 131.3, 129.4, 128.7 (d, *J* = 6.7 Hz), 115.2, 109.0 (d, *J* = 15.3 Hz) ppm. **^{31}P NMR** (161 MHz, $CDCl_3$, 298 K): δ = 26.90 ppm.

Synthesis of [($PymNPPh_2$)Ir(cod)] (5a)



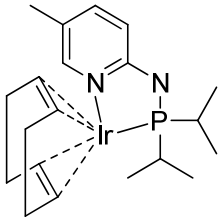
$[IrOMe(cod)]_2$ (0.25 mmol, 166mg) was dissolved in 5 mL THF and subsequently a solution of $PymHNPPh_2$ **(5)** (0.5 mmol, 140 mg) in THF was added dropwise. A red solution was obtained and after 30 min the solvent was removed *in vacuo*, affording a dark red solid in quantitative yield. **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 8.31-8.25 (m, 1H), 7.69-7.59 (m, 5H), 7.47-7.37 (m, 6H), 6.01 (dd, *J* = 5.8, 4.3 Hz, 1H), 4.80 (s, 2H), 3.71–3.64 (m, 2H), 2.24 (d, *J* = 8.2 Hz, 4H), 1.99 (dd, *J* = 15.9, 7.5 Hz, 4H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 162.8 (d, *J* = 3.9 Hz), 155.2 (d, *J* = 4.3 Hz), 132.2 (d, *J* = 11.6 Hz), 130.4 (d, *J* = 2.5 Hz), 128.5 (d, *J* = 10.7 Hz), 104.6, 61.5, 33.2, 29.0 ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 49.49 ppm. **Elemental analysis** calcd (%) for $C_{24}H_{25}N_3PIr$: C 49.81, H 4.35, N 7.26; found: C 49.54, H 4.61, N 7.04.

Synthesis of (5-Me)PyNHP(*i*Pr)$_2$ (6)



5-methyl-2-aminopyridine (10.0 mmol, 1.08 g) was suspended in 70 mL THF, triethylamine (10.0 mmol, 1.6 mL) was added and the solution was cooled to 0 °C. Then chlorodiisopropylphosphine (10.0 mmol, 1.6 mL) was added dropwise with a syringe. The solution was allowed to warm to room temperature and stirred over night at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. The solvent was removed *in vacuo* yielding (5-Me)PyNHP(*i*Pr)$_2$ as a white solid (9.4 mmol = 94%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.86 (s, 1H), 7.28 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.01 (dd, *J* = 8.4, 1.9 Hz, 1H), 4.57 (d, *J* = 10.5 Hz, 1H), 2.18 (s, 3H), 1.81-1.73 (m, 2H), 1.11-1.01 (m, 12H) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2, 298 K): δ = 147.4, 138.6, 123.0, 108.3 (d, *J* = 17.4 Hz), 26.4 (d, *J* = 10.9 Hz), 18.7 (d, *J* = 19.5 Hz), 17.4, 17.0 (d, *J* = 7.8 Hz) ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 49.51 ppm. **Elemental analysis** calcd (%) for $C_{12}H_{21}N_2P$: C 64.26, H 9.44, N 12.49; found: C 64.09, H 9.82, N 12.78.

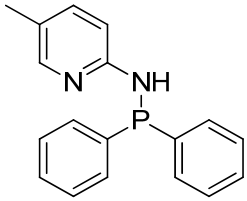
Synthesis of [((5-Me)PyNP(*i*Pr)$_2$)Ir(cod)] (6a)



[IrOMe(cod)]$_2$ (0.25 mmol, 166 mg) was dissolved in 5 mL THF and subsequently a solution of (5-Me)PyHNP(*i*Pr)$_2$ **(6)** (0.5 mmol, 112 mg) dissolved in THF was added dropwise. A red solution was obtained and after 30 min. the solvent was removed *in vacuo*, the residue was recrystallized from hexane yielding dark red crystals (0.34 mmol, 68%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.07 (s, 1H), 6.94 (d, *J* = 8.9 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 4.65 (s, 2H), 3.83 (d, *J* = 1.7 Hz, 2H), 2.29-2.17 (m, 4H), 2.17-2.06 (m, 2H), 2.02 (dd, *J* = 13.5, 7.5 Hz, 2H), 1.96 (s, 3H), 1.81 (dd, *J* = 13.0, 6.4 Hz, 2H), 1.16 - 1.07 (m, 12H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 143.5 (d, *J* = 2.7 Hz), 139.9 (d, *J* = 2.7 Hz), 116.1, 115.9, 56.90, 34.3 (d, *J* = 2.5 Hz), 29.1 (s), 28.70 (s), 28.3 (s), 17.8 (d, *J* = 3.3 Hz), 17.3 (s), 17.1

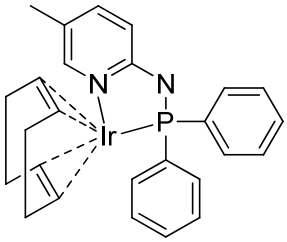
ppm . **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 94.09 ppm. **Elemental analysis** calcd (%) for $C_{20}H_{32}IrN_2P$: C 45.87, H 6.16, N 5.35; found: C 46.13, H 6.52, N 5.51.

Synthesis of (5-Me)PyNHPPh$_2$ (7)



5-methyl-2-aminopyridine (10.0 mmol, 1.08 g) was suspended in 70 mL THF, triethylamine (10.0 mmol, 1.4 mL) was added and the solution was cooled to 0 °C. Then chlorodiphenylphosphine (10.0 mmol, 1.83 mL) was added dropwise with a syringe. The solution was allowed to warm to room temperature and stirred for 4 d at room temperature and 12h at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. The solvent was removed *in vacuo*, yielding (5-Me)PyNHPPh$_2$ as a white solid (9.69 mmol = 97%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.92 (s, 1H), 7.50-7.43 (m, 4H), 7.41 - 7.28 (m, 7H), 6.95 (d, *J* = 8.6 Hz, 1H), 5.25 (s, 1H), 2.19 (s, 3H), ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 147.7, 139.6, 138.8, 131.2 (d, *J* = 20.9 Hz), 129.1, 128.5 (d, *J* = 6.7 Hz), 123.9, 108.4 (d, *J* = 15.0 Hz), 17.4 ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 27.21 ppm. **Elemental analysis** calcd (%) for $C_{18}H_{17}N_2P$: C 73.96, H 5.86, N 9.58; found: C 73.88, H 5.69, N 9.71.

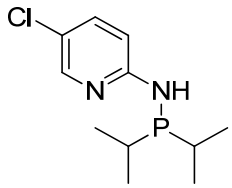
Synthesis of [((5-Me)PyNHPPh$_2$)Ir(cod)] (7a)



[IrOMe(cod)]$_2$ (1.2 mmol, 795 mg) was dissolved in 20 mL THF and subsequently a solution of (5-Me-Py)NHPPh$_2$ **(7)** (2.4 mmol, 701 mg) dissolved in THF was added dropwise. A red solution was obtained and after 30 min. the solvent was removed *in vacuo*, the residue was recrystallized from hexane:THF = 3:1 yielding red crystals (1.03 mmol, 86%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.59 (ddd, *J* = 10.8, 7.3, 1.7 Hz, 4H), 7.41-7.36 (m, 6H), 7.23 (s, 1H), 7.04 (dt, *J* = 8.9, 2.4 Hz, 1H), 6.88 (d, *J* = 8.9 Hz, 1H), 4.94 (s, 2H), 3.54 (s, 2H), 2.25-2.19 (m, 4H), 2.02 (s, 3H), 2.04-1.94 (m, 4H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ =

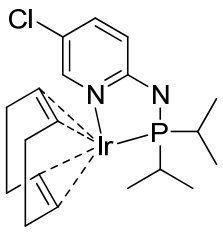
143.8 (d, *J* = 2.7 Hz), 140.7 (d, *J* = 2.9 Hz), 138.4 (d, *J* = 0.6Hz), 137.8 (d, *J* = 0.5 Hz), 132.5 (d, *J* = 12.2 Hz), 130.5 (d, *J* = 2.3 Hz), 128.8 (d, *J* = 10.3 Hz), 116.6, 116.4 (d, *J* = 0.5 Hz), 115.9 (d, *J* = 0.6 Hz), 95.32, 91.7 (d, *J* = 13.4 Hz), 60.4, 33.5, 29.5, 17.3 ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 72.54 ppm. **Elemental analysis** calcd (%) for $C_{26}H_{28}IrN_2P$: C 52.78, H 4.77, N 4.73; found: C 52.83, H 4.86, N 4.72.

Synthesis of (5-Cl)PyNHP(*i*Pr)$_2$ (8)



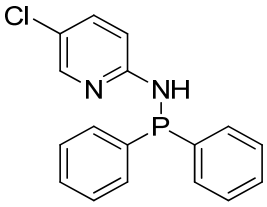
5-chloro-2-aminopyridine (20.0 mmol, 2.57 g) was suspended in 120 mL THF, triethylamine (20.0 mmol, 2.8 mL) was added and the solution was cooled to 0°C. Then chlorodiisopropylphosphine (20.0 mmol, 3.2 mL) was added dropwise with a syringe. The solution was allowed to warm to room temperature and stirred for 2 d at 50 °C. The suspension was filtered on a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. The solvent was concenrated *in vacuo* to 10 mL and left to crystallize at -20 °C. The supernatant solution was decanted and the solid washed with 5 mL of cold hexane and subsequently dried *in vacuo* yielding (5-Cl)PyNHP(*i*Pr)$_2$ as a white solid (18 mmol = 90%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.96 (d, *J* = 2.4 Hz, 1H), 7.40 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.07 (dd, *J* = 8.9, 2.1 Hz, 1H), 4.94 (d, *J* = 8.4 Hz, 1H), 1.85-1.74 (m, 2H), 1.10-1.01 (m, 12H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 160.1 (d, *J* = 20.2 Hz), 146.6, 137.6 (d, *J* = 2.2 Hz), 121.3, 110.1 (d, *J* = 18.6 Hz), 26.9 (d, *J* = 11.6 Hz), 19.0 (d, *J* = 21.1 Hz), 17.4 (d, *J* = 7.7 Hz) ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 51. 65 ppm. **Elemental analysis** calcd (%) for $C_{11}H_{18}N_2PCl$: C 53.99, H 7.41, N 11.45; found: C 53.65, H 7.07, N 11.60.

Synthesis of [((5-Cl)PyNP(*i*Pr)$_2$)Ir(cod)] (8a)



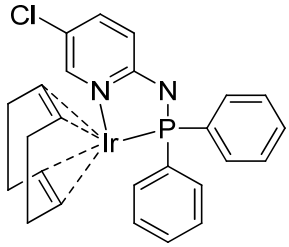
$[IrOMe(cod)]_2$ (0.3 mmol, 199 mg) was dissolved in 10 mL THF and subsequently a solution of (5-Cl-Py)NHP(*i*Pr)$_2$ **(8)** (0.6 mmol, 147 mg) dissolved in THF was added dropwise. A red solution was obtained and after 30 min the solvent was removed *in vacuo*, the residue was recrystallized from hexane:THF = 2:1 yielding red crystals (0.53 mmol = 89%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.23 (d, *J* = 1.6 Hz, 1H), 7.00 (d, *J* = 9.2 Hz, 1H), 6.79 (d, *J* = 9.4 Hz, 1H), 4.60 (d, *J* = 2.7 Hz, 2H), 3.87 (d, *J* = 2.7 Hz, 2H), 2.31-1.98 (m, 8H), 1.87-1.77 (m, 2H), 1.16-1.06 (m, 12H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 143.3 (d, *J* = 2.6 Hz), 137.7, 117.3, (d, *J* = 21.7 Hz), 89.5 (d, *J* = 11.1 Hz), 57.7, 24.3 (d, *J* = 2.5 Hz), 29.0, 28.5 (d, *J* = 38.3 Hz), 17.4 (d, *J* = 52.2 Hz) ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 95.57 ppm. **Elemental analysis** calcd (%) for $C_{26}H_{28}IrN_2P$: C 41.94 , H 5.37 , N 5.15; found: C 42.32, H 5.11, N 5.02.

Synthesis of (5-Cl)PyNHPPh$_2$ (9)



5-chloro-2-aminopyridine (20.0 mmol, 2.57 g) was suspended in 120 mL THF, triethylamine (20.0 mmol, 2.8 mL) was added and the solution was cooled to 0 °C. Then chlorodiphenylphosphine (20.0 mmol, 3.7 mL) was added dropwise with a syringe. The solution was allowed to warm to room temperature and stirred for 2d at 50 °C. The suspension was filtered on a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. Solvent was concenrated *in vacuo* to 10 mL and left to crystallize at -20 °C. The supernatant solution was decanted and the solid washed with 5 mL of cold hexane and subsequently dried *in vacuo* yielding (5-Cl)PyNHPPh$_2$ as a white solid (18 mmol = 90%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.94 (d, *J* = 2.1 Hz, 1H), 7.48-7.42 (m, 4H), 7.40-7.37 (m, 7H), 6.99 (dd, *J* = 8.9, 1.0 Hz, 1H), 5.61 (d, *J* = 7.7 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 146.9 (d, *J* = 0.8 Hz), 139.8 (d, *J* = 11.9 Hz), 138.0 (d, *J* = 1.9 Hz), 132.3 (d, *J* = 10.1 Hz), 131.9, 131.6, 129.9, 129.2 (d, *J* = 6.7 Hz), 110.4 (d, *J* = 14.4 Hz) ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 51.65 ppm. **Elemental analysis** calcd (%) for $C_{17}H_{14}ClN_2P$: C 65.29, H 4.51, N 8.96; found: C 65.03, H 4.12, N 8.73.

Synthesis of [((5-Cl)PyNPPh$_2$)Ir(cod)] (9a)



[IrOMe(cod)]$_2$ (0.3 mmol, 199 mg) was dissolved in 10 mL THF and subsequently a solution of (5-Cl-Py)NHPPh$_2$ **(9)** (2.4 mmol, 147 mg) dissolved in THF was added dropwise. A red solution was obtained and after 30 min the solvent was removed *in vacuo*, the residue was recrystallized from hexane:THF = 3:1 yielding red crystals (0.51 mmol = 85%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.60-7.55 (m, 4H), 7.42-7.38 (m, 7H), 7.10 (dt, *J* = 9.3, 2.4 Hz, 1H) 6.92 (d, *J* = 9.3 Hz, 1H), 4.89 (s, 2H), 3.60 (s, 2H), 2.23-2.21 (m, 4H), 2.01-1.96 (m, 4H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 143.5 (d, *J* = 2.7 Hz), 138.6 (d, *J* = 3.1 Hz), 137.6, 136.7, 132.5 (d, *J* = 11.4 Hz), 130.8 8d, *J* = 2.4 Hz), 128.9 (d, *J* = 10.3 Hz), 117.8 (d, *J* = 23.0 Hz), 113.4, 92.3 (d, *J* = 12.1 Hz), 61.2, 33.5 (d, *J* = 3.1 Hz), 29.5 (d, *J* = 1.7 Hz) ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 73.23 ppm. **Elemental analysis** calcd (%) for $C_{25}H_{25}IrN_2P$: C 41.94, H 5.37, N 5.15; found: C 42.32, H 5.11, N 5.02.

[1] D. B. Garagorria, K. Mereiterb, K. Kirchner, *Collect. Czech. Chem. Commun.* **2007**, *72*, 527-540

[2] S. M. Aucott, A. M. Z. Slawin, J. D. Woollins, *J. Chem. Soc. Dalton Trans.* **2000**, 2559-2575.

[3] U. Florke, H. J. Haupt, T. Kristallogr. **1990**, *191*, 295.

5. The iridium-catalyzed synthesis of symmetrically and unsymmetrically alkylated diamines under mild reaction conditions

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Keywords: alcohols, alkylation, amine alkylation, amines, C-N bond formation, Dapson, diamines, iridium, P,N-ligands, unsymmetrical alkylation

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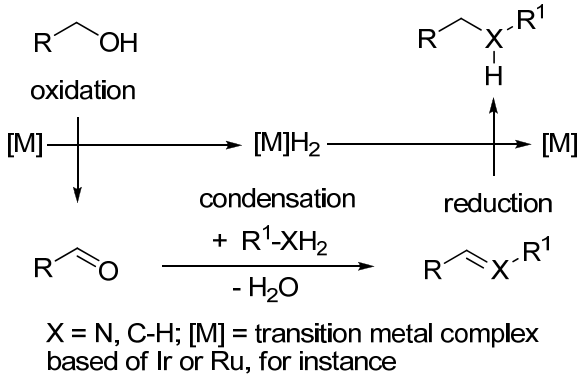
Abstract: An iridium catalyst - stabilized by an anionic P,N-ligand - was used for the symmetric and unsymmetric monoalkylation of *p*-, *m*- and *o*-benzenediamines. Benzyl and aliphatic alcohols were used as alkylating reagents. 28 derivatives were synthesized. 14 of them are new compounds. Furthermore, the alkylation of the pharmacological important diamine Dapson® is described. 14 Dapson® derivatives were synthesized among them 9 new compounds.

5.1 Introduction

The hydrogen autotransfer (= HA)[1] or borrowing hydrogen (= BH)[2] type of reaction has been received a lot of attention during the last few years.[3] It is an efficient protocol for selective C-N and C-C bond formation reactions.[4] The state of the art mechanistic proposal for both types of coupling reactions is shown in Scheme 1. The selective alkylation of amines is an important but challenging reaction. It is important due to the significance of selectively alkylated amines as bulk chemicals, intermediates, pharmaceuticals and agrochemicals. A variety of classic but rather complicated bench top reactions are available, the rather unselective alkylation with harmful alkyl halogens and a variety of catalytic reaction with

certain limitations in scope.[5] The amine alkylation via the BH/HA concept (discovered by Grigg[6] and Watanabe[7]) involves readily available and green alcohols.



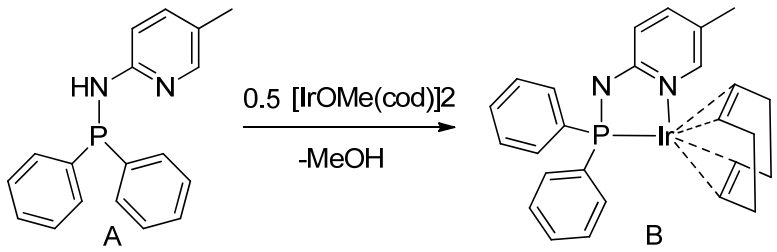
Scheme 1. Selective C-N and C-C coupling reactions via the BH/HA mechanism.

At the beginning, it was a rather unselective reaction requiring harsh conditions and has been developed into a practical synthesis method by (for instance) the groups of Beller,[8] Grigg,[6,9] Fujita,[10] Williams,[8a,11] Yus,[12] and us.[13] Very recently, we discovered a new class of iridium catalysts, stabilized by anionic P,N-ligands.[13d] It was shown that these catalysts are significantly more active in the alkylation of aniline derivatives as the originally (by us) used neutral P,N-ligand complexes[13d] based on dipyridyl amines.[14] Applying mild condition in these amine alkylation reactions is a challenge.[3] Since we can work under mild conditions with the new catalyst class we expected to increase selectivity and functional group tolerance. Here we report on the synthesis of symmetrically or unsymmetrically alkylated benzenediamines and 4,4'-sulfonyldianiline (Dapson®). With the protocol described here appropriate derivatisation is possible. Most of the syntheses were carried out at 70 °C, very mild conditions for amine alkylations using alcohols.[8-13]

5.2 Results and Discussion

Catalyst Synthesis and Structure

The synthesis of the applied Ir catalyst is a very simple two step procedure. In the first step the protonated P,N-ligand **A** is formed quantitative from commercially available 5-methyl-pyridin-2-ylamine and chlorodiphenyl-phosphane with triethylamine as base. In a second step two equivalents of **A** react with one equivalent of $[IrOMe(cod)]_2$ under methanol elimination to yield the catalyst **B** also in nearly quantitative yields (Scheme 2).[13d]



Scheme 2. Catalyst synthesis (nearly quantitative).

Catalyst **B** was identified to be the most active catalyst for aniline alkylations using benzyl and aliphatic alcohols.[13d] Crystals of **B** suitable for X-ray crystal structure analysis (They were not available as we published the catalyst synthesis.) were obtained from a THF solution. The molecular structure of **B** is shown in Figure 1.

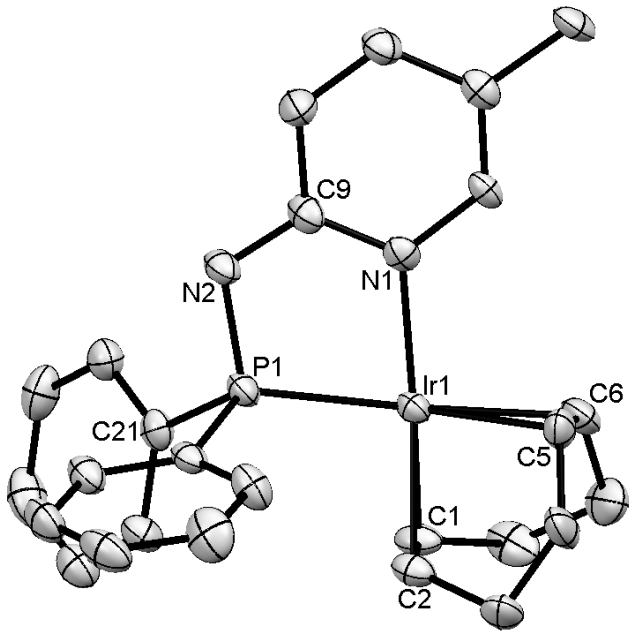


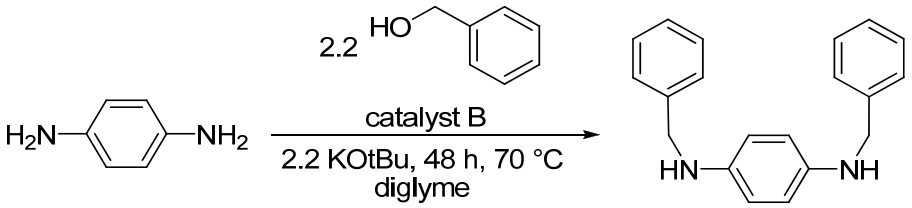
Figure 1. Molecular structure of **B,** selected bond length [Å], and angles [°]:Ir1-N1 2.074(5), Ir1-C1 2.112(6), Ir1-C2 2.135(6), Ir1-C5 2.159(7), Ir1-C6 2.235(8), Ir1-P1 2.2634(18), P1-N2 1.655(6), P1-C21 1.820(6), N1-C9 1.370(9), N2-C9 1.311(8); N1-Ir1-C1 157.7(2), N1-Ir1-C2 163.5(2), N1-Ir1-C5 95.7(2), N1-Ir1-C6 99.3(2), N1-Ir1-P1 78.65(15), N2-P1-C21 106.4(3), N2-C9-N1 123.8(6), N2-P1-Ir1 106.3(2).

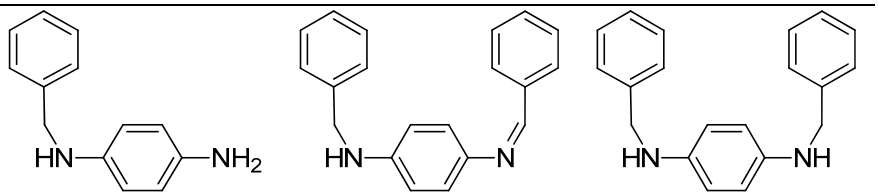
In complex **B**, both the Ir1-N1 [2.074(5) Å], and the P1-N2 [1.659(5) Å] bond lengths are shorter than the length of analogous bonds in related neutral P,N-ligand complexes.[13a-c] This indicates an delocalization of the anionic charge of the ligand over the interior P-N-C-N ligand backbone.

Synthesis of symmetrically alkylated benzenediamines

To find out the ideal catalyst loading for the alkylation of benzenediamines, the model system benzene-1,4-diamine/benzyl alcohol was chosen. It can be seen from Table 1 that a minimum catalyst loading of 1 mol% Ir is sufficient to get an excellent yield of 99% of the favoured dialkylated product.

Table 1. Screening of the catalyst loading.[a]





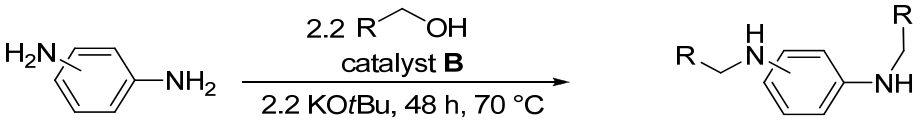
	[mol% Ir]	yield [%][b]	yield [%][b]	yield [%][b]
1	2.0	n.d.	n.d.	>99
2	1.5	n.d.	n.d.	>99
3	1.0	n.d.	n.d.	99
4	0.8	25	12	66
5	0.5	46	12	43
6	0.3	48	13	40
7	0.2	57	11	29
8	0.1	51	12	14

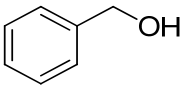
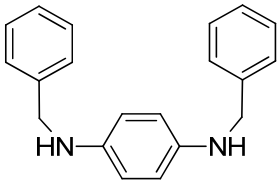
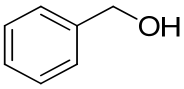
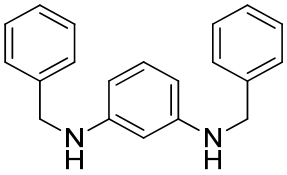
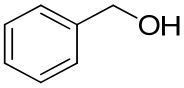
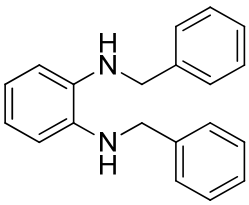
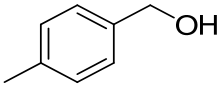
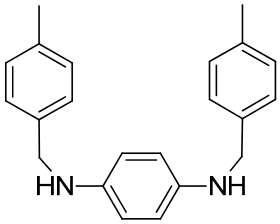
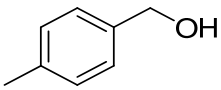
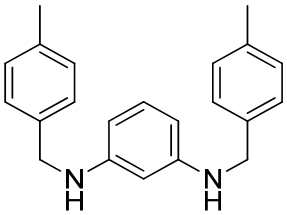
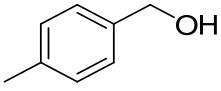
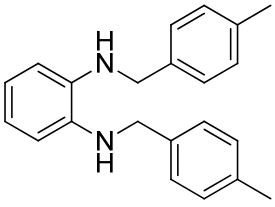
[a] reaction conditions: 1.0 mmol benzene-1,4-diamine, 2.2 mmol benzyl alcohol, 0.4 mL diglyme, 70 °C, 48 h.
[b] yield determined by GC analysis with dodecane as internal standard.

With less than 1 mol% catalyst loading the reaction gets too slow in the given time. The intermediates such as N-benzyl-benzene-1,4-diamine and N-benzyl-N'-benzylidene-benzene-1,4-diamine were detected in certain amounts. Alkylation protocols using the catalyst **B** are listed in Table 2. With benzyl alcohol as an alkylation agent excellent isolated yields could be obtained in combination with p- and m-benzenediamine using the optimized reaction conditions (Table 2, **2a**, **2b**). The catalyst loading had to be increased to 2 mol% Ir for benzyl alcohols bearing electron donating substituents (Table 2, **2d**, **2e**, **2g**, **2h**). Further increase of the catalyst loading (2.5- 4 mol% Ir) was necessary to apply aliphatic alcohols (Table 2, **2j**,

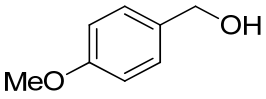
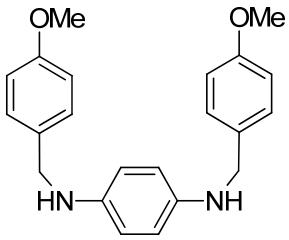
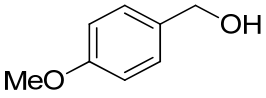
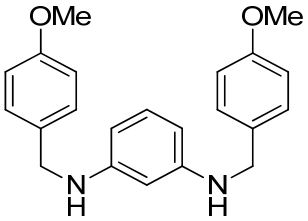
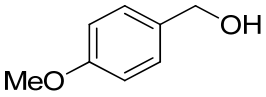
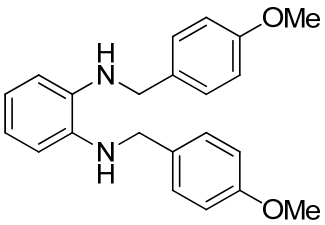
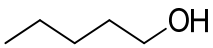
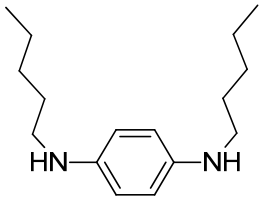
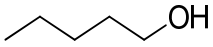
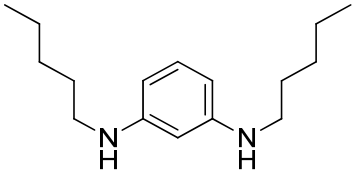
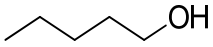
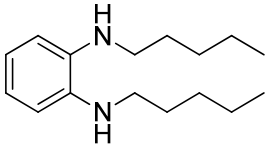
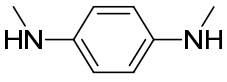
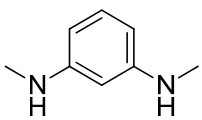
2k, **2m**, **2n**) as well as heteroaromatic alcohols (Table 2, **2p**). In the methylation reaction an excess of methanol had to be added to ensure that enough methanol is available due to the fact that it is refluxing at the given reaction conditions.

Table 2. Synthesis of symmetrically alkylated benzenediamines with primary alcohols.[a]

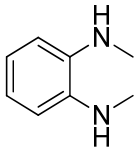
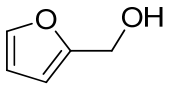
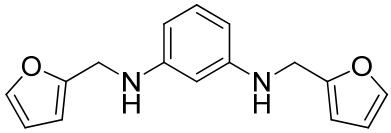


	[mol% Ir]	alcohol	product	yield[%][b]
2a	1.0			99
2b	1.0			94
2c	4.0			45[c]
2d	2.0			99
2e[f]	2.0			96
2f[f]	4.0			35[c]

5. The iridium-catalyzed synthesis of symmetrically and unsymmetrically alkylated diamines under mild reaction conditions

2g	2.0			80
2h	2.0			97
2i[f]	4.0			42[c]
2j	2.5			86
2k[f]	2.5			97
2l[f]	4.0			42[c]
2m	3.0	CH_3OH		88[d]
2n	3.0	CH_3OH		90[d]

5. The iridium-catalyzed synthesis of symmetrically and unsymmetrically alkylated diamines under mild reaction conditions

2o	4.0	CH_3OH		82[c], [d]
2p	4.0			72[e]

[a] reaction conditions: 1.0 mmol benzenediamine, 2.2 mmol primary alcohol, 2.2 mmol KO^{t}Bu, 0.4 mL diglyme, 70 °C, 48 h. [b] isolated yield, [c] 110 °C. [d] 8.8 mmol alcohol. [e] 4.4 mmol alcohol, [f] new compound.

For the alkylation of o-benzenediamine, it was necessary to raise the catalyst loading up to 4.0 mol% Ir as well as the reaction temperature to 110 °C (Table 2, **2c**, **2f**, **2i**, **2l**, **2o**). o-Benzenediamines may act as chelating ligands and compete with the anionic P,N-ligand. Furthermore, steric hindrance which played no role in case of p- and m-benzenediamines is an issue. However, under these conditions it was possible to isolate the accordant products in (at least) low yields.

Synthesis of unsymmetrically alkylated benzenediamines

In reactions in which no complete conversion was achieved the unilateral monoalkylated intermediate was detected as a by-product. Consequently, it was expected to synthesize this intermediate selectively. To explore this option in more detail, a kinetic experiment was performed in which the composition of the reaction mixture was monitored over time by gas chromatography. The reaction of benzene-1,4-diamine with two equivalents benzyl alcohol was studied (Figure 2). This experiment clearly showed that under this reaction conditions it is impossible to isolate the monoalkylated diamine as a main product. At its concentration maximum (after 14 hours) only 40% of N-benzyl-benzene-1,4-diamine is produced. Furthermore, 24% N-benzyl-N`-benzylidene-benzene-1,4-diamine and about 30% dialkylated diamine were formed. By the use of two equivalents of the diamine it was possible to isolate N-benzyl-benzene-1,4-diamine (Table 3, **3a**, 76% yield) and N-benzyl-benzene-1,3-diamine (Table 3, **3b**, 82% yield) as the main products. In the synthesis of N-benzyl-benzene-1,2-diamine (Table 3, **3c**, 91% yield) the fourfold amount of the diamine had to be used. Starting

from these intermediates the second aminofunction could be alkylated with another alcohol to get access to unsymmetrically alkylated diamines.

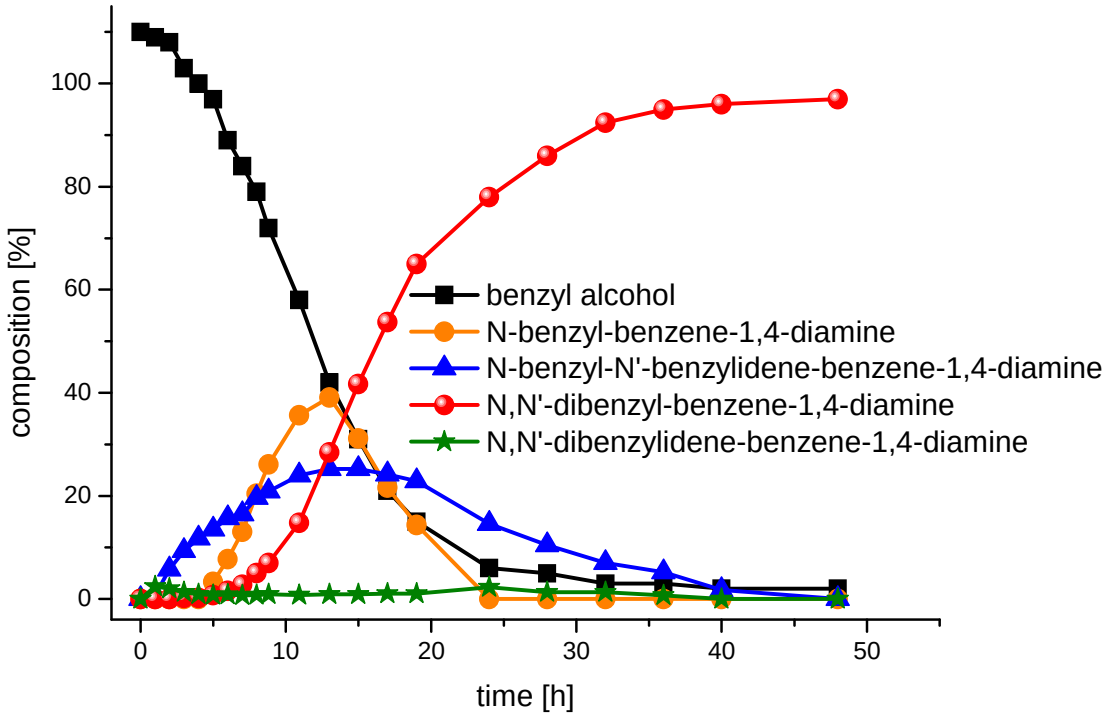
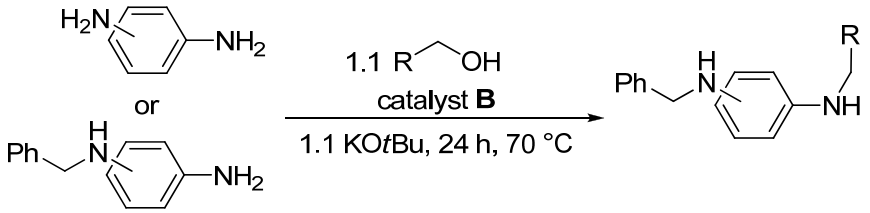
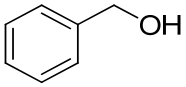
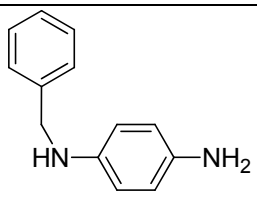


Figure 2. Time conversion plot for the reaction of benzene-1,4-diamine with benzyl alcohol. Reaction conditions: 10.0 mmol benzene-1,4-diamine, 22.0 mmol benzyl alcohol, 1 mol% catalyst **B**, 5.0 mL diglyme, 22.0 mmol KO*t*Bu, 2.5 mmol dodecane as internal standard.

Table 3. Synthesis of unsymmetricially alkylated benzenediamines.[a]



	[mol% Ir]	alcohol	product	yield[%][b]
3a	0.4			76

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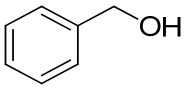
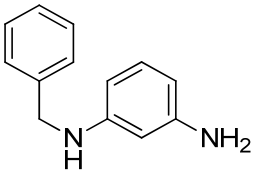
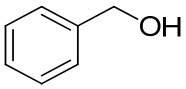
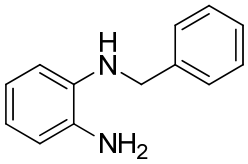
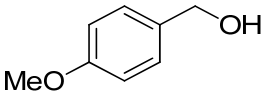
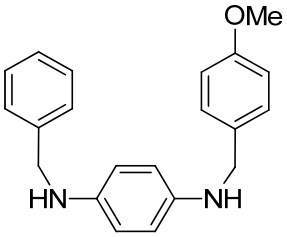
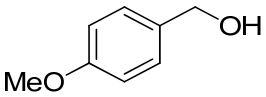
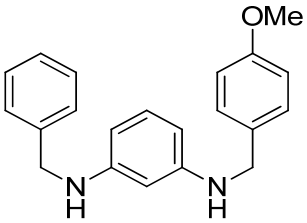
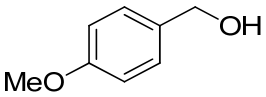
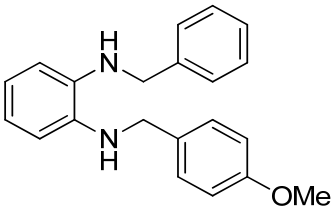
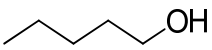
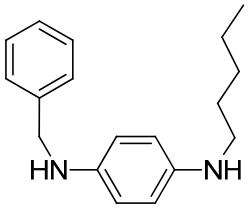
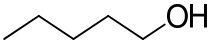
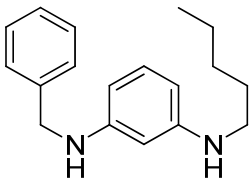
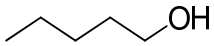
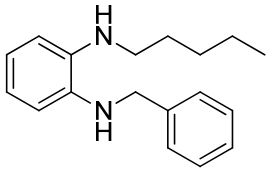
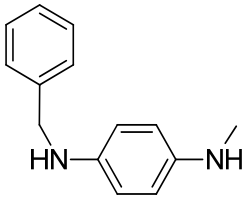
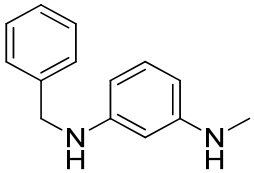
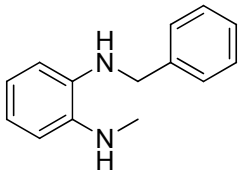
3b	0.2			82
3c	2.0			91
3d[e]	1.0			85
3e[e]	1.0			98
3f[e]	2.0			75[c]
3g[e]	0.4			70
3h[e]	1.0			95

5. The iridium-catalyzed synthesis of symmetrically and unsymmetrically alkylated diamines under mild reaction conditions

3i[e]	2.0			67[c]
3j[e]	1.5	CH_3OH		89[d]
3k[e]	1.5	CH_3OH		80[d]
3l	2.0	CH_3OH		87[c], [d]

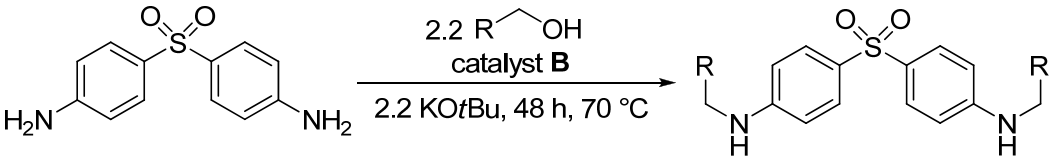
[a] reaction conditions: 1.0 mmol N-benzyl-benzene-diamine, 1.1 mmol primary alcohol, 1.1 mmol KO*t*Bu, 0.4 mL diglyme, 70 °C, 24h. [b] isolated yield, [c] 110 °C. [d] 2.2 mmol methanol. [e] new compound.

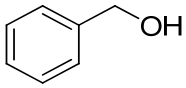
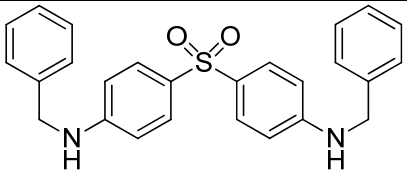
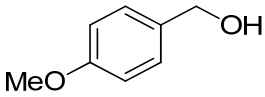
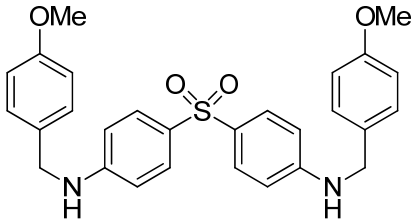
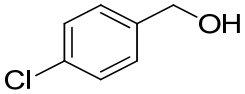
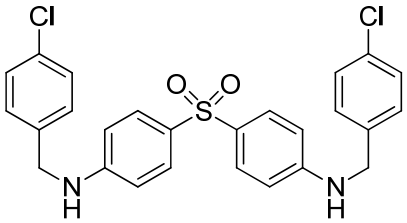
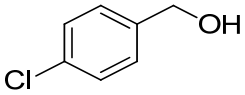
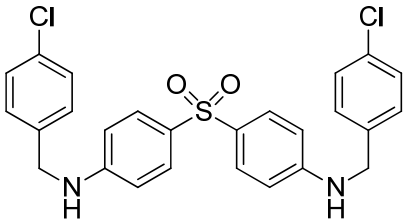
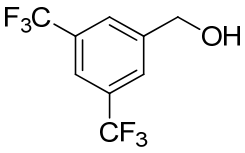
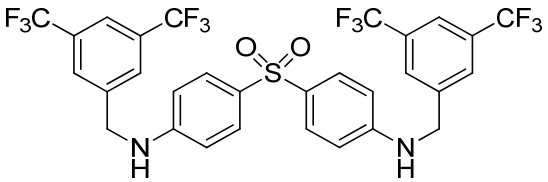
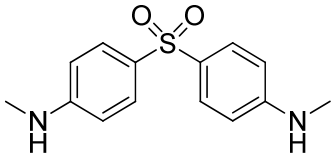
The differently alkylated p- and m-benzenediamines starting from **3a** and **3b** (Table 3) can be made at a moderate reaction temperature of 70 °C, relatively low catalyst loadings of 0.2 mol%-1.5 mol% Ir, and a reaction time of 24 h in good to very good yields. Both benzyl alcohols (Table 3, **3a**, **3b**, **3d**, **3e**) as well as aliphatic alcohols (Table 3, **3g**, **3h**, **3j**, **3k**) are applicable. If methanol is used as the alkylating reagent it is again necessary to use an excess due to the low boiling point of the alcohol (Table 3, **3j-l**). To obtain satisfying yields with the 1,2-benzenediamines both, the catalyst loading and the temperature, had to be increased (Table 3, **3c**, **3f**, **3i**, **3l**).

Synthesis of symmetrically and unsymmetrically alkylated Dapson® derivatives

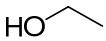
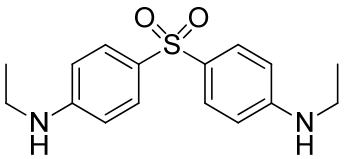
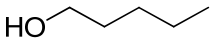
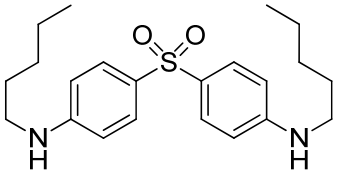
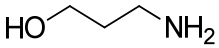
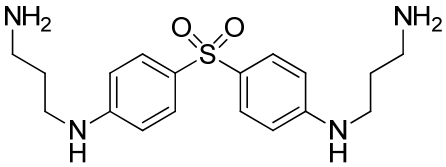
The knowledge that has been collected with the synthesis of symmetrically and unsymmetrically mono-N-alkylated diaminobenzenes should be applicable to the alkylations of 4,4'-sulfonyldianiline, which is known under the trade name Dapson®. Dapson® is an antibiotic effective medicament which finds application in the treatment of leprosy or malaria.[15] However, strong resistance development has appeared.

Table 4. Synthesis of symmetrically alkylated 4,4'-sulfonyldianilines.[a]



	[mol% Ir]	alcohol	product	yield[%][b]
4a	1.0			90
4b[e]	2.0			92
4c[e]	2.5			76
4c[e]	2.5			76
4d[e]	2.5			80
4e	2.5	CH_3OH		97[c]

5. The iridium-catalyzed synthesis of symmetrically and unsymmetrically alkylated diamines under mild reaction conditions

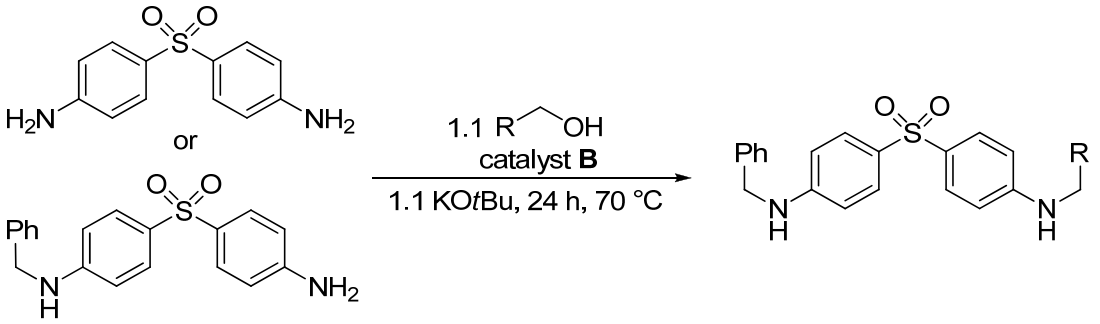
4f	2.5			98[c]
4g	2.5			88
4h[e]	3.0			50[d]

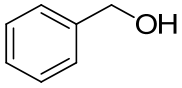
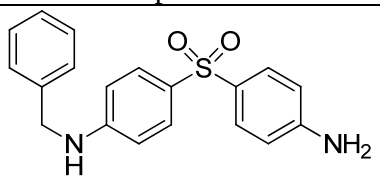
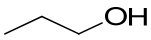
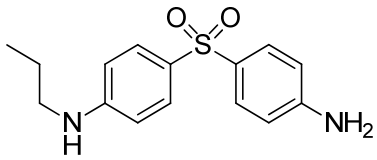
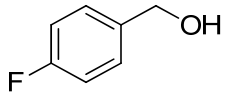
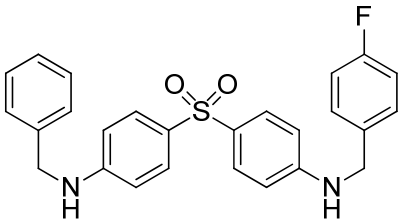
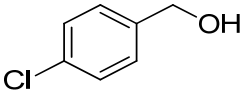
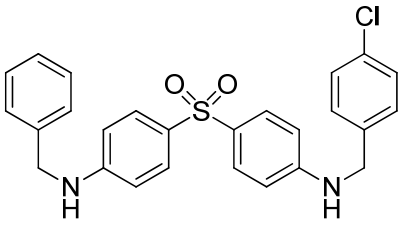
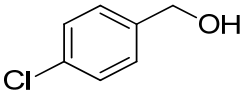
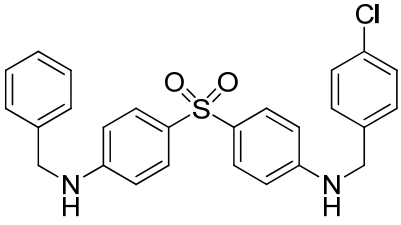
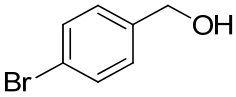
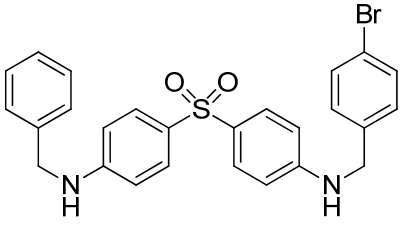
[a] reaction conditions: 1.0 mmol 4,4'-sulfonyldianiline, 2.2 mmol primary alcohol, 2.2 mmol KO*t*Bu, 0.4 mL diglyme, 70 °C, 48h. [b] isolated yield. [c] 4.4 mmol primary alcohol. [d] 2.2 mmol NaO*t*Bu, 110 °C. [e] new compound.

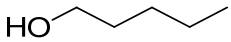
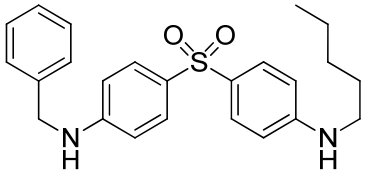
As can be seen in Table 4 the suitable symmetrically alkylated derivatives of 4,4'-sulfonyldianiline were obtained in good up to excellent yields. There is no significant distinction detectable whether benzyl or aliphatic alcohols were used. We also succeeded in using 3-amino-1-propanol to produce N,N'-(sulfonylbis(4,1-phenylene))-bis(propane-1,3-diamine) (Table 4, **4h**) in a one-step reaction without protecting the free aliphatic aminofunction, because alkylation of aliphatic amines is rather slow with our catalysts.[13c] For the synthesis of unsymmetrically alkylated 4,4'-sulfonyldianiline a two-step synthesis must occur analogously to the unsymmetric alkylation of the diaminobenzenes. The first alkylation step can be accomplished with isolated yield of 85% and 86% for benzyl alcohol and propanol, respectively (Table 5). Differently mono-*N*-alkylated 4,4′-sulfonyldianiline derivatives (Table 5, entries **5c**-**5f**) could be obtained in good to very good yields. Both benzyl alcohols as well as aliphatic alcohols can be used under similar reaction conditions. Up to now, these (differently) *N*-alkylated Dapson® derivatives were mostly unknown. Already the first step is difficult to accomplish. Multi-step synthesis protocols including the introduction of a protecting group as well as several oxidation and reduction steps are necessary. For instance, in order to synthesize **5b** (Table 5) 4-amino-4′-nitrodiphenyl sulfide is converted into the corresponding tosylamide by using *p*-toluenesulfonyl chloride in pyridine.

5. The iridium-catalyzed synthesis of symmetrically and unsymmetrically alkylated diamines under mild reaction conditions

Table 5. Synthesis of unsymmetrically alkylated 4,4'-sulfonyldianiline [a]

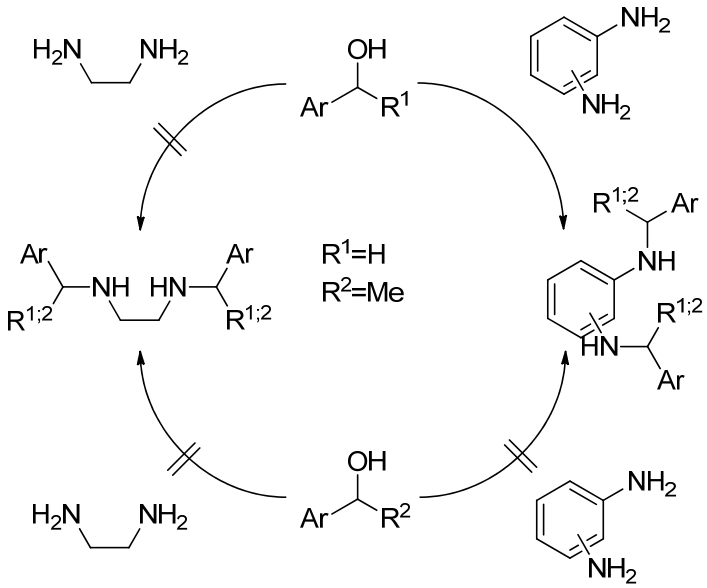


	[mol% Ir]	alcohol	product	yield [%][b]
5a	0.6			85
5b	0.8			86
5c[c]	1.0			73
5d[c]	2.0			88
5d[c]	2.0			88
5e[c]	2.0			67

5f[c]	2.0			91

[a] reaction conditions: 1.0 mmol 4-((4-aminophenyl)sulfonyl)-N-benzylaniline (Table 5, entry 1), 1.1 mmol primary alcohol, 1.1 mmol KO*t*Bu, 0.4 mL diglyme, 70 °C, 24h. [b] isolated yield. [c] new compound.

The amide is then alkylated with *n*-propyl iodide in aqueous KOH and in a further step it gets oxidized by H_2O_2 in acetic acid to (4-*N*-tosyl-*n*-propylamino)-4′-nitrodiphenylsulfone. Subsequently, the nitro group is reduced to the free amino function using hydrogen and Raney nickel. In a final reaction step, the protecting group has to be removed and gives 4-[(4-aminophenyl)sulfonyl]-*N*-propylaniline in an overall yield of 79%.[16] The synthesis protocol developed by us allows us to isolate product **5b** in a yield of 86% in only one step.



Scheme 3. Selectivity of catalyst **B.**

Catalyst **B** seems selective towards aromatic amines and aliphatic amines are alkylated much slower as can be seen from Table 4, last entry. It was not possible to alkylate aliphatic amines in detectable amounts, nor did arylamines react with secondary alcohols, even at higher temperatures of 130 °C and catalyst loadings up to 8 mol% Ir (Scheme 3). Under the given reaction conditions the secondary alcohol was converted nearly quantitatively into the corresponding aldol condensation product.

5.3 Conclusion

It could be shown that the catalyst system based on an anionic P,N-ligand stabilized iridium complex is effectively applicable in mono-*N*-alkylation reactions. The BH/HA concept is the basis of these transformations and primary (benzyl and aliphatic) alcohols as well as aromatic amines (anilines) were used. Symmetrically and unsymmetrically mono-*N*-alkylated diaminobenzenes were synthesized and the methodology could be transferred to pharmacological interesting 4-aminodiphenylsulfone (Dapson®) derivatives. Reactions proceed under mild reaction conditions (mainly 70 °C) which allowed a variety of functional groups to be tolerated, among them also aliphatic amines. 23 new compounds were synthesized.

5.4 Experimental Section

General considerations

All reactions were carried out in a dry argon or nitrogen atmosphere using standard Schlenk techniques or glove-box techniques. Halogenated solvents were dried over P_2O_5, and non-halogenated solvents were dried over sodium benzophenone ketyl. Deuterated solvents were ordered from Cambridge Isotope Laboratories, vented, stored over molecular sieves and distilled. All chemicals were purchased from commercial sources with a purity of over 97% and used without further purification. NMR spectra were obtained using an INOVA 400 or 300 MHz spectrometer at 298 K. Chemical shifts are reported in ppm relative to the deuterated solvent. Elemental analysis was carried out on a Vario elementar EL *III*. GC analyses were carried out on an Agilent 6890N Network GC system equipped with an HP-5 column (30 m×0.32 μm×0.25 μm). GC/MS analyses were carried out on a Thermo Focus GC/Trace DSQ system equipped with a HP-5MS column (30 m×0.32 μm×0.25 μm). X-ray crystal structure analyses were performed with a STOE-IPDS II equipped with an Oxford Cryostream low-temperature unit. CCDC 833733http://www.ccdc.cam.ac.uk/cgi-bin/catreq.cgi contains the supplementary crystallographic data for this paper (compound **B**). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

General procedure for the synthesis of symmetrically alkylated diaminobenzenes

In a pressure tube catalyst **B**, 0.4 mL diglyme, 1.0 mmol diaminobenzene, 2.2 mmol primary alcohol, 2.2 mmol KO*t*Bu were combined. The pressure tube was closed with a Teflon® cap and the mixture stirred at 70 °C (110 °C for the respective alkylated *ortho*-diaminobenzenes) for 48 h. The reaction mixture was cooled to room temperature and quenched by addition of 2 mL of water. The organic phase was extracted three times with 30 mL of Et_2O. The combined organic phases were washed with *ca.* 20 mL of water, and dried over Na_2SO_4. Solvent was evaporated under vacuum and the residue was further purified by column chromatography.

General procedure for the synthesis of non-symmetrically alkylated diaminobenzenes

In a pressure tube the catalyst, 0.4 mL diglyme, 1.0 mmol mono-*N*-alkylated diaminobenzene, 1.1 mmol primary alcohol, and 1.1 mmol KO*t*Bu were combined. The pressure tube was closed with a Teflon® cap and the mixture stirred at 70 °C (110 °C for the respective alkylated mono-*N*-*ortho*-alkylated diaminobenzenes) for 24 h. The reaction mixture was cooled to room temperature and quenched by addition of 2 mL of water. The organic phase was extracted three times with 30 mL of Et_2O. The combined organic phases were washed with *ca.* 20 mL of water and dried over Na_2SO_4. Solvent was evaporated under vacuum and the residue was further purified by column chromatography.

General procedure for the synthesis of symmetrically alkylated dapsone derivatives

In a pressure tube the catalyst, 0.6 mL diglyme, 1.0 mmol Dapson®, 2.2 mmol primary alcohol, and 2.2 mmol KO*t*Bu were combined. The pressure tube was closed with a Teflon® cap and the mixture stirred at 70 °C for 48 h. The reaction mixture was cooled to room temperature and quenched by addition of 2 mL of water. The organic phase was extracted three times with 30 mL of Et_2O. The combined organic phases were washed with *ca*. 20 mL of water and dried over Na_2SO_4. Solvent was evaporated under vacuum and the residue was further purified by column chromatography.

General procedure for the synthesis of non-symmetrically alkylated dapsone derivatives

In a pressure tube the catalyst, 0.6 mL diglyme, 1.0 mmol 4-((4-aminophenyl)sulfonyl)-*N*-benzylaniline **5a**, 1.1 mmol primary alcohol, and 1.1 mmol KO*t*Bu were combined. The pressure tube was closed with a Teflon® cap and the mixture stirred at 70 °C for 24 h. The

reaction mixture was cooled to room temperature and quenched by addition of 2 mL of water. The organic phase was extracted three times with 30 mL of Et_2O. The combined organic phases were washed with *ca.* 20 mL of water and dried over Na_2SO_4. Solvent was evaporated under vacuum and the residue was further purified by column chromatography.

Synthesis of ligand A, (5-Me)PyNHPPh$_2$

2-Amino-5-methyl-pyridine (20.0 mmol, 2.16 g) was suspended in 150 mL of THF, triethylamine (20.0 mmol, 2.8 mL) was added and the solution was cooled to 0 °C. Then chlorodiphenylphosphane (20.0 mmol, 3.66 mL) was added dropwise with a syringe. The solution was allowed to warm to room temperature and stirred overnight at room temperature and for 1 d at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed three times with 30 mL of THF. The solvent was removed under vacuum, affording (5-Me)PyNHPPh$_2$ as a white solid; yield: 19.8 mmol (99%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.92 (s, 1 H), 7.50–7.43 (m, 4 H), 7.41–7.28 (m, 7 H), 6.95 (d, J = 8.6 Hz, 1 H), 5.25 (s, 1 H), 2.19 (s, 3 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 147.7, 139.6, 138.8, 131.2 (d, J = 20.9 Hz), 129.1, 128.5 (d, J = 6.7 Hz), 123.9, 108.4 (d, J = 15.0 Hz), 17.4 ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 27.21 ppm.

Synthesis of catalyst B, [((5-Me)PyNPPh$_2$)Ir(cod)]

[IrOMe(cod)]$_2$ (1.5 mmol, 994 mg) was dissolved in 20 mL of THF and subsequently a solution of (5-Me)-PyNHPPh$_2$ (**A**) (3.0 mmol, 876 mg) dissolved in THF was added dropwise. A red solution was obtained and after 30 min the solvent was removed under vacuum. The residue was recrystallized from hexane:THF = 3:1 affording red crystals; yield: 2.79 mmol (93%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K): δ = 7.59 (ddd, J = 10.8, 7.3, 1.7 Hz, 4 H), 7.41–7.36 (m, 6 H), 7.23 (s, 1 H), 7.04 (dt, J = 8.9, 2.4 Hz, 1 H), 6.88 (d, J = 8.9 Hz, 1 H), 4.94 (s, 2 H), 3.54 (s, 2 H), 2.25–2.19 (m, 4 H), 2.02 (s, 3 H), 2.04–1.94 (m, 4H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K): δ = 143.8 (d, J = 2.7 Hz), 140.7 (d, J = 2.9 Hz), 138.4 (d, J = 0.6 Hz), 137.8 (d, J = 0.5 Hz), 132.5 (d, J = 12.2 Hz), 130.5 (d, J = 2.3 Hz), 128.8 (d, J = 10.3 Hz), 116.6, 116.4 (d, J = 0.5 Hz), 115.9 (d, J = 0.6 Hz), 95.32, 91.7 (d, J = 13.4 Hz), 60.4, 33.5, 29.5, 17 ppm. **^{31}P NMR** (161 MHz, CD_2Cl_2, 298 K): δ = 72.54 ppm.

Synthesis of alkylated diaminobenzenes

***N*,*N′*-Dibenzylbenzene-1,4-diamine (2a):** From **B** (12.0 mg, 0.02 mmol), benzene-1,4-diamine (261 mg, 2.0 mmol), benzyl alcohol (456 µL, 4.4 mmol), 800 µL diglyme, KO-*t*-Bu (497 mg, 4.4 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:Et_2O = 4:1). Yield: 570 mg (1.98 mmol, 99%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.39–7.31 (m, 8 H), 7.28 (ddd, *J* = 7.1, 2.0, 1,8 Hz, 2 H), 6.58 (s, 4 H), 4.27 (s, 4 H), 3.63 (s br, 2 H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 140.7, 140.0, 128.5, 127.6, 127.0, 114.6, 49.5 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 288 (38, M^+), 197 (34), 91 (100), 65 (10).

***N*,*N′*-Dibenzylbenzene-1,3-diamine (2b):** From **B** (12.0 mg, 0.02 mmol), benzene-1,3-diamine (261 mg, 2.0 mmol), benzyl alcohol (456 µL, 4.4 mmol), 800 µL diglyme, KO-*t*-Bu (497 mg, 4.4 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:Et_2O = 4:1). Yield: 542 mg (1.88 mmol, 94%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.38-7.31 (m, 8 H), 7.30-7.25 (m, 2 H), 6.99 (t, *J* = 7.9 Hz, 1 H), 6.07 (dd, *J* = 7.9, 2.0 Hz, 2 H), 5.93 (t, *J* = 2.0 Hz, 1 H), 4.28 (s, 4 H), 3.93 (s br, 2 H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 149.3, 139.6, 130.0, 128.5, 127.5, 127.1, 103.0, 97.2, 48.3 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 288 (92, M^+), 197 (219), 91 (100), 65 (15).

***N*,*N′*-Dibenzylbenzene-1,2-diamine (2c):** From **B** (24.0 mg, 0.04 mmol), benzene-1,2-diamine (108 mg, 1.0 mmol), benzyl alcohol (228 µL, 2.2 mmol), 400 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 110 °C. Purification by column chromatography (pentane:Et_2O = 20:1). Yield: 129 mg (0.45 mmol, 45%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.40–7.32 (m, 8 H), 7.30–7.25 (m, 2 H), 6.75 (ddd, *J* = 29.7, 5.9, 3.6 Hz, 4 H), 4.32 (s, 4 H), 3.64 (s br, 2 H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 139.4, 137.1, 128.6, 127.8, 127.2, 139.4, 112.0, 48.8 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 288 (22, M^+), 197 (25), 118 (24), 91 (24), 65 (16).

***N*,*N′*-Bis-(4-methylbenzyl)-benzene-1,4-diamine (2d):** From **B** (12 mg, 0.02 mmol), benzene-1,4-diamine (108 mg, 1.0 mmol), *p*-tolylmethanol (269 mg, 2.2 mmol), KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:Et_2O = 4:1). Yield: 310 mg (0.98 mmol, 98%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.24 (d, *J* = 8.1 Hz, 4 H), 7.13 (d, *J* = 8.1 Hz, 4 H), 6.51 (s, 4 H), 4.19 (s, 4 H), 3.71 (s br, 2 H), 3.71 (s, 6 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 137.2, 129.6, 128.0, 115.0, 95.3, 49.5, 21.3 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 316 (4, M^+), 312 (93), 209 (100), 167 (19), 105 (60), 91 (33).

***N*,*N′*-Bis-(4-methylbenzyl)-benzene-1,3-diamine (2e):** From **B** (12 mg, 0.02 mmol), benzene-1,3-diamine (108 mg, 1.0 mmol), *p*-tolylmethanol (269 mg, 2.2 mmol), KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 4:1). Yield: 306 mg (0.96 mmol, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.29–7.23 (m, 4 H), 7.20–7.13 (m, 4 H), 7.00 (td, *J* = 8.0, 2.4 Hz, 1 H), 6.13 (dt, *J* = 7.7, 2.2 Hz, 2 H), 6.02 (d, *J* = 2.2 Hz, 1 H), 4.71 (s br, 2 H), 4.25 (s, 4 H), 2.35 (s, 6 H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 148.6, 136.9, 135.9, 130.0, 129.2, 127.7, 104.1, 98.4, 48.5, 21.1 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 316 (26, M^+), 211 (18), 194 (5), 105 (100), 79 (23): **Elemental analysis** calcd. (%) for $C_{22}H_{24}N_2$: C 83.50, H 7.64, N 8.85; found: C 83.54, H 7.79, N 8.89.

***N*,*N′*-Bis-(4-methylbenzyl)-benzene-1,2-diamine (2f):** From **B** (12 mg, 0.02 mmol), benzene-1,2-diamine (108 mg, 1.0 mmol), *p*-tolylmethanol (269 mg, 2.2 mmol), KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 110 °C. Purification by column chromatography (pentane:Et_2O = 20:1). Yield: 111 mg (0.35 mmol, 35%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.32–7.25 (m, 4 H), 7.19–7.13 (m, 4 H), 6.75–6.58 (m, 4 H), 4.27 (s, 4 H), 3.67 (s br, 2 H), 2.33 (s, 6 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 137.8, 137.4, 137.2, 129.7, 128.2, 119.6, 112.4, 48.9, 21.4 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 316 (11, M^+), 211 (75), 119 (30), 105 (100), 92 (11), 80 (26), 65 (13); **Elemental analysis** calcd. (%) for $C_{22}H_{24}N_2$: C 83.50, H 7.64, N 8.85; found: C 83.18, H 7.90, N 8.78.

***N*,*N′*-Bis-(4-Methoxybenzyl)-benzene-1,4-diamine (2g):** From **B** (12 mg, 0.02 mmol), benzene-1,4-diamine (108 mg, 1.0 mmol), (4-methoxyphenyl)methanol (273 µL, 2.2 mmol), KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 2:1). Yield: 278 mg (0.80 mmol, 80%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.30 (d, *J* = 8.4 Hz, 4 H), 6.86 (d, *J* = 8.4 Hz, 4 H), 6.64 (s, 2 H), 4.2 (s, 4 H), 3.80 (s, 6 H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 158.9, 129.4, 115.9, 113.9, 94.7, 55.2, 49.8 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 348 (2, M^+), 344 (100), 281 (11), 225 (71), 207 (25), 167 (20), 121 (77), 77 (21).

***N*,*N′*-Bis-(4-methoxybenzyl)-benzene-1,3-diamine (2h):** From **B** (12.0 mg, 0.02 mmol), benzene-1,3-diamine (108 mg, 1.0 mmol), (4-methoxyphenyl)methanol (273 µL, 2.2 mmol), 600 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 4:1). Yield: 338 mg (0.95 mmol, 95%). **^{1}H NMR** (400

MHz, CD_2Cl_2): δ = 7.26 (d, J = 8.4 Hz, 4 H), 6.90 (t, J = 8.1 Hz, 1 H), 6.93–6.88 (m, 4 H), 6.00 (dd, J = 7.7, 2.2 Hz, 2 H), 5.89 (t, J = 2.2 Hz, 1 H), 4.19 (s, 4 H), 3.96 (s br, 2 H), 3.78 (s, 6 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 159.4, 150.0, 132.4, 130.3, 129.2, 114.4, 103.4, 97.7, 55.8, 48.1; **MS** (70 eV, EI): *m*/*z* (%) = 348 (8, M^+), 227 (4), 121 (100), 77 (13).

***N*,*N′*-Bis-(4-methoxybenzyl)-benzene-1,2-diamine (2i):** From **B** (24.0 mg, 0.04 mmol), benzene-1,2-diamine (108 mg, 1.0 mmol), (4-methoxyphenyl)-methanol (273 µL, 2.2 mmol), 600 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 110 °C. Purification by column chromatography (pentane:EtOAc = 10:1). Yield: 146 mg (0.42 mmol, 42%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.35–7.28 (m, 4 H), 6.91–6.85 (m, 4 H), 6.76–6.65 (m, 4 H), 4.25 (s, 4 H), 3.79 (s, 6 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 159.5, 137.8, 132.3, 129.5, 119.7, 114.4, 112.4, 55.8, 48.7 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 348 (2, M^+), 344 (6), 295 (24), 227 (11), 217 (16), 202 (10), 167 (6), 121 (100), 91 (57); **Elemental analysis** calcd. (%) for $C_{22}H_{24}N_2O_2$: C 75.83, H 6.94, N 8.04; found: C 75.78, H 7.02, N 7.98.

***N*,*N′*-Dipentylbenzene-1,4-diamine (2j):** From **B** (15 mg, 0.025 mmol), benzene-1,4-diamine (108 mg, 1.0 mmol), 1-pentanol (239 µL, 2.2 mmol), KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 6:1). Yield: 215 mg (0.86 mmol, 86%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 6.67 (s, 4 H), 3.07 (s, 4 H), 1.63 (s,4 H), 1.39–1.34 (m, 8 H), 1.03–0.81 (m, 6 H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 141.6, 114.9, 45.8, 30.1, 30.0, 23.2, 14.4 ppm. **MS** (70 eV, EI); *m*/*z* (%) = 248 (35, M^+), 204 (6), 191 (100), 189 (10), 147 (6), 105 (10).

***N*,*N′*-Dipentylbenzene-1,3-diamine (2k):** From **B** (15 mg, 0.025 mmol), benzene-1,3-diamine (108 mg, 1.0 mmol), 1-pentanol (239 µL, 2.2 mmol), KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 15:1). Yield: 241 mg (0.97 mmol, 97%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 6.95 (t, J = 8.1 Hz, 1 H), 5.99 (dd, J = 7.9, 2.3 Hz, 2 H) 5.87 (t, J = 2.2 Hz, 1 H), 3.56 (s br, 2 H), 3.10 (t, J = 7.2 Hz, 4 H), 1.70–1.56 (m, 4 H), 1.47–1.37 (m, 8 H), 0.98 (m, 6 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 150.5, 130.3, 103.9, 97.3, 44.6, 30.0, 29.9, 23.2, 14.5 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 248 (40, M^+), 205 (5), 191 (100), 135 (10), 67 (10); Elemental analysis calcd. (%) for $C_{16}H_{28}N_2$: C 77.36, H 11.36, N 11.28; found: C 77.37, H 11.36, N 11.36.

***N*,*N′*-Dipentylbenzene-1,2-diamine (2l):** From **B** (24.0 mg, 0.04 mmol), benzene-1,2-diamine (108 mg, 1.0 mmol), 1-pentanol (478 µL, 4.4 mmol), 400 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 110 °C. Purification by column chromatography (pentane:EtOAc = 10:1). Yield: 104 mg (0.42 mmol, 42%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.66–7.57 (m, 1 H), 7.38–7.26 (m, 1 H), 7.26–7.12 (m, 2 H), 4.14–4.02 (m, 2 H), 2.88–2.77 (m, 2 H), 2.01 (s br, 2 H), 2.07–1.96 (m, 4 H), 1.54–1.21 (m, 8 H), 0.99 (t, *J* = 7.5 Hz, 3 H), 0.90 (t, *J* = 6.9 Hz, 3 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 155.8, 135.8, 109.9, 44.1, 30.1, 29.6, 23.2, 14.2 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 248 (49, M^+), 191 (100), 135 (20), 121 (43), 119 (59), 95 (13), 55 (17); **Elemental analysis** calcd. (%) for $C_{16}H_{28}N_2$: C 77.36, H 11.36, N 11.28; found: C 77.49, H 11.52, N 11.25.

***N*,*N′*-Dimethylbenzene-1,4-diamine (2m):** From **B** (18 mg, 0.03 mmol), benzene-1,4-diamine (108 mg, 1.0 mmol), methanol (356 µL, 8.8 mmol), KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:Et_2O = 1:4). Yield: 120 mg (0.88 mmol, 88%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 6.53 (s, 4 H), 3.34 (s br, 2 H), 2.76 (s, 6 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 142.5, 114.4, 32.1 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 136 (88, M^+), 121 (100), 106 (10), 94 (15), 67 (19).

***N*,*N′*-Dimethylbenzene-1,3-diamine (2n):** From **B** (18.0 mg, 0.03 mmol), benzene-1,3-diamine (108 mg, 1.0 mmol), methanol (356 µL, 8.8 mmol), 400 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 2:3). Yield: 122 mg (0.90 mmol, 90%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 6.94 (t, *J* = 8.1 Hz, 1 H), 5.97 (dd, *J* = 8.1, 2.2 Hz, 2 H), 5.85 (t, *J* = 2.2 Hz, 1 H), 3.65 (s br, 2 H), 2.78 (s, 6 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 151.3, 130.2, 102.7, 96.6, 31.1 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 136 (100, M^+), 106 (41), 94 (9), 77 (8), 67 (16).

***N*,*N′*-Dimethylbenzene-1,2-diamine (2o):** From **B** (24.0 mg, 0.04 mmol), benzene-1,2-diamine (108 mg, 1.0 mmol), methanol (356 µL, 8.8 mmol), 400 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 110 °C. Purification by column chromatography (pentane:EtOAc = 2:3). Yield: 112 mg (0.82 mmol, 82%). **^{1}H NMR** (300 MHz, C_6D_6): δ = 6.96 (dd, *J* = 5.7, 3.4 Hz, 2 H), 6.60 (dd, *J* = 5.6, 3.5 Hz, 2 H), 2.76 (s br, 2 H), 2.42 (s, 6 H) ppm. **^{13}C NMR** (75 MHz, C_6D_6): δ = 139.1, 119.8, 111.1, 31.2 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 136 (100, M^+), 121 (48), 94 (100).

***N*,*N′*-Bis(furan-2-ylmethyl)-benzene-1,3-diamine (2p):** From **B** (24.0 mg, 0.04 mmol), benzene-1,3-diamine (108 mg, 1.0 mmol), furan-2-ylmethanol (190 µL, 4.4 mmol), 400 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:Et_2O 4:1). Yield: 193 mg (0.72 mmol, 72%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.38 (dd, *J* = 1.8, 0.8 Hz, 2 H), 6.96 (t, *J* = 7.9 Hz, 1 H), 6.34 (dd, *J* = 3.2, 1.8 Hz, 2 H), 6.23 (dd, *J* = 3.2, 0.8 Hz, 2 H), 6.07 (dd, *J* = 8.0, 2.2 Hz, 2 H), 5.98 (t, *J* = 2.2 Hz, 1 H), 4.27 (s, 4 H), 4.01 (s br, 2 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 153.8, 149.4, 142.4, 130.4, 110.8, 107.3, 104.0, 98.2, 41.8 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 268 (69, M^+), 239 (4), 225 (6), 187 (10), 159 86), 81 (100); **Elemental analysis** calcd. (%) for $C_{16}H_{16}N_2O_2$: C 71.62, H 6.01, N 10.44.80; found: C 71.28, H 6.18, N 10.57.

***N*-Benzylbenzene-1,4-diamine (3a):** From **B** (71.0 mg, 0.12 mmol), benzene-1,4-diamine (6.48 g, 60.0 mmol), benzyl alcohol (3.12 mL, 30 mmol), 12 mL diglyme, KO-*t*-Bu (3.73 g, 33.0 mmol), 24 h at 70 °C. Purification by column chromatography (pure Et_2O). Yield: 4.5 *g* (22.8 mmol, 76%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.40–7.30 (m, 4 H), 7.29–7.23 (m, 1 H), 6.63–6.45 (m, 4 H), 4.26 (s, 2 H), 3.39 (s br, 3 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 141.7, 140.8, 138.8, 129.0, 128.0, 127.5, 116.9, 114.9, 49.7 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 198 (39, M^+), 119 (3), 107 (100), 91 (15), 80 (13), 65 (10).

***N*-Benzylbenzene-1,3-diamine (3b):** From **B** (35.0 mg, 0.06 mmol), benzene-1,3-diamine (6.48 g, 60.0 mmol), benzyl alcohol (3.12 mL, 30 mmol), 10 mL diglyme, KO-*t*-Bu (3.73 g, 33.0 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:Et_2O = 1:1). Yield: 4.85 g (24.5 mmol, 82%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.45–7.36 (m, 4 H), 7.33–7.30 (m, 1 H), 6.96 (t, *J* = 7.92, Hz, 1 H), 6.08 (dt, *J* = 7.0, 1.1 Hz, 2 H), 5.96 (s, 1 H), 4.32 (s, 2 H), 4.11 (s br, 1 H), 3.62 (s br, 2 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 150.0, 148.4, 140.5, 130.4, 129.0, 127.9, 127.5, 105.2, 104,1. 99.7, 48.5 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 198 (78, M^+), 195 (5), 180 (5), 121 (20), 91 (100), 80 (10), 65 (28).

***N*-Benzylbenzene-1,2-diamine (3c):** From **B** (480 µL, 0.006 mmol, 0.125 M in diglyme), benzene-1,2-diamine (432 mg, 4.0 mmol), benzyl alcohol (108 µL, 1.0 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pure Et_2O). Yield: 180 mg (0.91 mmol, 91%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.46–7.24 (m, 4 H), 7.32–7.25 (m, 1 H), 6.79–6.70 (m, 2 H), 6.69–6.60 (m, 2

H), 4.33 (s, 2 H), 3.77 (s br, 1 H), 3.39 (s br, 2 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.3, 138.2, 135.0, 129.1, 128.2, 127.7, 120.9, 119.2, 116.8, 112.4, 49.0.

***N*-Benzyl-*N′*-(4-methoxybenzyl)-benzene-1,4-diamine (3d):** From **B** (6.0 mg, 0.01 mmol), *N*-benzylbenzene-1,4-diamine **3a** (198 mg, 1.0 mmol), (4-methoxyphenyl)-methanol (137 µL, 1.1 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 10:1). Yield: 317 mg (0.85 mmol, 85%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.30–7.11 (m, 8 H), 6.73 (d, *J* = 8.4 Hz, 1 H), 6.48 (s br, 4 H), 4.13 (s br, 4 H), 4.09 (s br, 2 H), 3.66 (s, 3 H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 159.4, 141.4, 141.2, 140.9, 132.8, 129.3, 129.0, 128.1, 127.5, 115.1, 114.4, 49.8, 49.2 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 318 (10, M^+), 314 (64), 225 (52), 207 (100), 120 (26), 91 (33), 77 (47); **Elemental analysis** calcd. (%) for $C_{21}H_{22}N_2O$: C 79.21, H 6.96, N 8.80; found: C 79.12, H 6.87, N 8.93.

***N*-Benzyl-*N′*-(4-methoxybenzyl)-benzene-1,3-diamine (3e):** From **B** (6.0 mg, 0.01 mmol), *N*-benzylbenzene-1,3-diamine **3b** (198 mg, 1.0 mmol), (4-methoxyphenyl)-methanol (137 µL, 1.1 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 4:1). Yield: 312 mg (0.98 mmol, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.39–7.31 (m, 5 H), 7.26 (d, *J* = 8.1 Hz, 4 H), 7.00 (t, *J* = 8.1 Hz, 1 H), 6.88 (d, *J* = 8.4 Hz, 2 H), 6.10 (dd, *J* = 8.01, 1.5 Hz, 2 H), 5.97 (s, 1 H), 4.30 (s, 2 H), 4.22 (s, 2 H), 3.81 (s, 3 H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 158.8, 131.2, 130.0, 128.9, 128.6, 127.6, 127.1, 113.9, 103.5, 97.7, 95.2, 94.7, 55.3, 48.4, 48.1 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 318 (18, M^+), 121 (100), 91 (34), 77 (10); **Elemental analysis** calcd. (%) for $C_{21}H_{22}N_2O$: C 79.21, H 6.96, N 8.80; found: C 79.56, H 6.96, N 8.93.

***N*-Benzyl-*N′*-(4-methoxybenzyl)-benzene-1,2-diamine (3f):** From **B** (12.0 mg, 0.02 mmol), *N*-benzylbenzene-1,2-diamine **3c** (198 mg, 1.0 mmol), (4-methoxyphenyl)-methanol (137 µL, 1.1 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 110 °C. Purification by column chromatography (pentane:Et_2O = 8:1). Yield: 239 mg (0.75 mmol, 75%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.47–7.25 (m, 7 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 6.80–6.65 (m, 4 H), 4.33 (s, 2 H), 4.26 (s, 2 H), 3.79 (s, 3 H), 3.73 (s br, 1 H), 3.67 (s br, 1 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 159.5, 140.3, 137.8, 132.2, 129.5, 129.1, 128.3, 127.7, 119.7, 114.4, 112.4, 55.8, 49.2, 48.7 ppm. **MS** (70 eV, EI); *m*/*z* (%) = 318 (10, M^+), 227 (14), 197 (65), 180

(5), 121 (100), 91 (79); **Elemental analysis** calcd. (%) for $C_{21}H_{22}N_2O$: C 79.21, H 6.96, N 8.80; found: C 79.16, H 7.12, N 8.71.

N-Benzyl-*N′*-pentylbenzene-1,4-diamine (3g): From **B** (320 µL, 0.004 mmol, 0.125 M in diglyme), *N*-benzylbenzene-1,4-diamine **3a** (198 mg, 1.0 mmol), 1-pentanol (120 µL, 1.1 mmol), 200 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:Et_2O = 4:1). Yield: 188 mg (0.70 mmol, 70%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.40–7.29 (m, 4 H), 7.25 (m, 1 H), 6.52 (d, J = 5.1 Hz, 4 H), 4.25 (s, 2 H), 3.59 (s br, 2 H), 3.01 (t, J = 7.3 Hz, 2 H), 1.59–1.54 (m, 2 H), 1.38–1.34 (m, 4 H), 0.91 (t, J = 7.0, Hz, 3 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 140.7, 128.5, 127.6, 127.0, 114.9, 114.7, 49.6, 49.5, 45.5, 45.4, 29.4, 22.5, 14.0 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 268 (92, M^+), 211 (24), 177 (100), 119 (11), 107 (30), 91 (42), 65 (8); **Elemental analysis** calcd. (%) for $C_{18}H_{24}N_2$: C 80.55, H 9.01, N 10.44; found: C 80.50, H 9.34, N 10.49.

***N*-Benzyl-*N′*-pentylbenzene-1,3-diamine (3h):** From **B** (6.0 mg, 0.01 mmol), *N*-benzylbenzene-1,3-diamine **3b** (198 mg, 1.0 mmol), 1-pentanol (120 µL, 1.1 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:Et_2O = 10:1). Yield: 255 mg (0.95 mmol, 95%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.43–7.33 (m, 4 H), 7.30–7.27 (m, 1 H), 7.01 (td, J = 8.1, 1.5 Hz, 1 H), 7.05–6.98 (m, 2 H), 5.99 (d, J = 1.5 Hz, 1 H), 4.20 (s br, 2 H), 3.08 (td, J = 7.1, 1.5 Hz, 2 H), 1.67–1.57 (m, 2 H), 1.42–1.31 (m, 4 H), 0.93 (m, 3 H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 149.3, 148.7, 139.6, 130.0, 128.6, 127.5, 127.1, 103.6, 103.4, 97.8, 48.4, 44.6, 29.3, 29.0, 22.5, 14.0 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 268 (40, M^+), 211 (100), 197 (5), 133 (16), 91 (100); **Elemental analysis** calcd. (%) for $C_{18}H_{24}N_2$: C 80.55, H 9.01, N 10.44; found: C 80.52, H 9.32, N 10.31.

***N*-Benzyl-*N′*-pentylbenzene-1,2-diamine (3i):** From **B** (12.0 mg, 0.02 mmol), *N*-benzylbenzene-1,2-diamine **3c** (198 mg, 1.0 mmol), 1-pentanol (239 µL, 2.2 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 110 °C. Purification by column chromatography (pentane:EtOAc = 4:1). Yield: 179 mg (0.67 mmol, 67%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.43–7.39 (m, 2 H), 7.38–7.33 (m, 2 H), 7.31–7.25 (m, 1 H), 6.78–6.62 (m, 4 H), 4.32 (br s, 2 H), 3.68 (br s, 1 H), 3.28 (br s, 1 H), 3.09 (t, J = 7.2 Hz, 2 H), 1.71–1.62 (m, 2 H), 1.45–1.34 (m, 4 H), 0.97–0.89 (m, 3 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ

= 140.4, 138.3, 137.5, 129.0, 128.2, 127.7, 119.8, 119.2, 112.2, 111.9, 49.1, 45.0, 30.1, 23.2, 14.4 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 268 (68, M^+), 264 (6), 177 (100), 121 (38), 119 (49), 91 (29); **Elemental analysis** calcd. (%) for $C_{18}H_{24}N_2$: C 80.55, H 9.01, N 10.44; found: C 79.21, H 9.01, N 10.44.

***N*-Benzyl-*N′*-methylbenzene-1,4-diamine (3j):** From **B** (640 µL, 0.008 mmol, 0.125 M in diglyme), *N*-benzylbenzene-1,4-diamine **3a** (198 mg, 1.0 mmol), methanol (89 µL, 2.2 mmol), 200 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:Et_2O = 2:3). Yield: 190 mg (0.89 mmol, 89%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.40–7.35 (m, 4 H), 7.28–7.23 (m, 1 H), 6.58–6.48 (m, 4 H), 4.26 (s, 2 H), 3.52 (s br, 2 H), 2.75 (s, 3 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 142.5, 140.7, 128.7, 127.8, 127.2, 114.8, 114.1, 93.6, 49.6, 31.8 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 212 (35, M^+),121 (100), 94 (8), 91 (20), 67 (5), 65 (10)M; **Elemental analysis** calcd. (%) for $C_{14}H_{16}N_2$: C 79.21, H 7.60, N 13.20; found: C 78.83, H 7.69, N 13.24.

***N*-Benzyl-*N′*-methylbenzene-1,3-diamine (3k):** From **B** (9.0 mg, 0.015 mmol), *N*-benzylbenzene-1,3-diamine **3b** (198 mg, 1.0 mmol), methanol (89 µL, 2.2 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 5:1). Yield: 197 mg (0.93 mmol, 93%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.41–7.31 (m, 4 H), 7.26 (t, *J* = 7.0 Hz, 1 H), 6.93 (t, 8.1 Hz, 1 H), 5.99 (td, *J* = 7.3, 2.0 Hz, 2 H), 5.88 (t, *J* = 2.0 Hz, 1 H), 4.31 (s, 2 H), 3.86 (s br, 2 H), 2.75 (s, 3 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 151.3, 150.0, 140.6, 130.3, 129.0, 128.0, 127.6, 103.1, 97.2, 95.8, 48.7, 31.0 ppm. **MS** (70 eV, EI): *m*/*z* = (%): 212 (100, M^+), 198 (24), 180 (8), 135 (36), 105 (35), 94 (36), 91 (93), 65 (27); **Elemental analysis** calcd. (%) for $C_{14}H_{16}N_2$: C 79.21, H 7.60, N 13.20; found: C 79.20, H 7.59, N 13.07.

***N*-Benzyl-*N′*-methylbenzene-1,2-diamine (3l):** From **B** (24.0 mg, 0.04 mmol), benzene-1,2-diamine (108 mg, 1.0 mmol), methanol (162 µL, 4.0 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 110 °C. Purification by column chromatography (pentane:EtOAc = 20:1). Yield: 186 mg (0.87 mmol, 87%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.47–7.21 (m, 5 H), 6.86–6.61 (m, 4 H), 4.31 (s, 2 H), 3.52 (s br, 2 H), 2.85 (s, 3 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.3, 137.5, 129.1, 128.3, 127.7, 119.9, 119.2, 112.0, 111.0, 49.1, 31.4 ppm.

MS (70 eV, EI): *m*/*z* (%) = 212 (26, M^+), 133 (2), 121 (100), 94 (77), 91 (44), 77 (26), 65 (39).

Dapson® derivatives

4,4′-Sulfonylbis(*N*-benzylaniline) (4a): From **B** (6.0 mg, 0.01 mmol), 4,4′-sulfonyldianiline (248 mg, 1.0 mmol), benzyl alcohol (228 μL, 2.2 mmol), 400 μL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 398 mg (0.93 mmol, 93%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.65–7.56 (m, 4 H), 7.39–7.23 (m, 10 H), 6.64–6.55 (m, 4 H), 6.60 (t, *J* = 5.1 Hz, 2 H), 4.36 (d, *J* = 5.6 Hz, 4 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 152.0, 138.9, 130.8, 129.5, 129.3, 128.0, 127.9, 112.6, 48.0 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 428 (100, M^+), 273 (15), 181 (4), 91 (100), 65 (5).

4,4′-Sulfonylbis[*N*-(4-methoxybenzyl)aniline] (4b): **B** (12.0 mg, 0.02 mmol), 4,4′-sulfonyldianiline (248 mg, 1.0 mmol), (4-methoxyphenyl)-methanol (274 μL, 2.2 mmol), 400 μL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 449 mg (0.92 mmol, 92%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.60 (d, *J* = 8.8 Hz, 4 H), 7.24 (d, *J* = 8.2 Hz, 4 H), 6.87 (d, *J* = 8.2 Hz, 4 H), 6.59 (d, *J* = 8.8 Hz, 4 H), 4.63 (t, *J* = 5.1 Hz, 2 H), 4.28 (d, *J* = 5.3 Hz, 4 H), 3.78 (s, 6 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 159.7, 151.9, 130.7, 130.6, 129.4, 129.4, 129.2, 114.6, 112.5, 55.8, 47.5 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 488 (100, M^+), 366 (8), 333 (8), 303 (12), 211 (9), 167 (11), 121 (100), 181 (28), 77 (41), 65 (10); **Elemental analysis** calcd. (%) for $C_{28}H_{28}N_2O_4S$: C 68.83, H 5.78, N 5.73; found: C 68.45, H 6.06, N 5.34.

4,4′-Sulfonylbis[*N*-(4-chlorobenzyl)aniline] (4c): From **B** (12.0 mg, 0.02 mmol), 4,4′-sulfonyldianiline (248 mg, 1.0 mmol), (4-chlorophenyl)-methanol (316 mg, 2.2 mmol), 400 μL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 306 mg (0.76 mmol, 76%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.60 (d, *J* = 8.8 Hz, 4 H), 7.34–7.24 (m, 8 H), 6.58 (d, *J* = 8.8 Hz, 4 H), 4.72, (t, *J* = 5.7 Hz, 2 H), 4.35 (d, *J* = 5.8 Hz, 4 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 151.4, 137.2, 135.1, 130.7, 129.2, 129.0, 128.8, 112.3, 47.0 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 496 (43, M^+), 462 (35), 307 (6), 125 (100), 91 (25); **Elemental analysis** calcd. (%) for $C_{26}H_{22}Cl_2N_2O_2S$: C 62.78, H 4.46, N 5.63; found: C 62.57, H 4.20, N 5.51.

4,4′-Sulfonylbis{*N*-[3,5-bis(trifluoromethyl)benzyl]aniline} (4d): From **B** (12.0 mg, 0.02 mmol), 4,4′-sulfonyldianiline (248 mg, 1.0 mmol), [3,5-bis(trifluoromethyl)phenyl]-methanol (537 mg, 2.2 mmol), 800 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (Et_2O:pentane = 2:1). Yield: 560 mg (0.80 mmol, 80%). **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 8.01 (s, 4 H), 7.96 (s, 2 H), 7.50 (d, J = 8.8 Hz, 4 H), 7.28 (t, J = 6.2 Hz, 2 H), 6.66 (d, J = 8.8 Hz, 4 H), 4.52 (d, J = 5.9 Hz, 4 H) ppm. **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 131.5, 143.3, 130.2 (q, J = 33.0 Hz), 128.9, 128.6, 127.9, 125.2, 121.5, 111.7, 44.8 ppm. **^{19}F NMR** (282 MHz, DMSO-d_6): δ = −61.75 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 700 (100, M^+), 409 (12), 366 (11), 227 (51); **Elemental analysis** calcd. (%) for $C_{30}H_{20}F_{12}N_2O_2S$: C 51.43, H 2.88, N 4.00; found: C 51.72, H 2.93, N 3.93.

4,4′-Sulfonylbis(*N*-methylaniline) (4e): From **B** (12.0 mg, 0.02 mmol), 4,4′-sulfonyldianiline (248 mg, 1.0 mmol), methanol (180 µL, 4.4 mmol), 600 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 254 mg (0.97 mmol, 97%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.63 (d, J = 8.7 Hz, 4 H) 6.56 (d, J = 8.8 Hz, 4 H), 4.34 (s br, 2 H), 2.82 (s, 6 H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 153.1, 130.3, 129.4, 111.9, 30.4 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 276 (100, M^+), 211 (10), 197 (10), 154 (58), 122 (100), 106 (29), 77 (18), 65 (14).

4,4′-Sulfonylbis(*N*-ethylaniline) (4f): From **B** (12.0 mg, 0.02 mmol), 4,4′-sulfonyldianiline (248 mg, 1.0 mmol), ethanol (250 µL, 4.4 mmol), 600 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 300 mg (0.98 mmol, 98%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.65–7.57 (m, 4 H), 6.59–6.52 (m, 4 H), 4.21 (t, J = 4.1 Hz, 2 H), 3.16, (qd, J = 7.2, 5.4 Hz, 4 H), 1.23 (t, J = 7.2 Hz, 6 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 151.9, 129.9, 129.1 111.8, 38.1, 17.6, 12.5 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 304 (100, M^+), 299 (89), 276 (9), 262 (18), 248 (10), 168 (13), 136 (16), 123 (17), 105 (26), 65 (12).

4,4′-Sulfonylbis(*N*-pentylaniline) (4g): From **B** (12.0 mg, 0.02 mmol), 4,4′-sulfonyldianiline (248 mg, 1.0 mmol), 1-pentanol (240 µL, 2.2 mmol), 400 µL diglyme, KO-*t*-Bu (248 mg, 2.2 mmol), 48 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 344 mg (0.88 mmol, 88%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.67 (dd, J = 8.8, 2.9 Hz, 4 H), 6.58 (dd, J = 8.8, 2.9 Hz, 4 H), 4.78 (s br, 2 H), 3.11 (td, J = 7.2, 2.9 Hz, 4 H), 1.71–

1.51 (m, 4 H), 1.46–1.21 (m, 8 H), 1.00–0.81 (m, 6 H) ppm. **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 151.1, 130.0, 129.1, 112.1, 43.6, 29.1, 28.7, 22.4, 13.9 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 388 (100, M^+), 331 (100), 273 (8), 261 (12), 137 (26), 105 (24), 44 (9); **Elemental analysis** calcd. (%) for $C_{22}H_{32}N_2O_2S$: C 68.00, H 8.30, N 7.21; found: C 67.87, H 8.32, N 7.05.

***N*,*N*′-[Sulfonylbis(4,1-phenylene)]bis(propane-1,3-diamine) (4h):** From **B** (36.0 mg, 0.06 mmol), 4,4′-sulfonyldianiline (496 mg, 2.0 mmol), 3-amino-1-propanol (340 µL, 4.4 mmol), 600 µL diglyme, NaO-*t*-Bu (424 mg, 4.4 mmol), 48 h at 110 °C. Purification by column chromatography (MeOH:Et_3N = 9 :1). Yield: 434 mg (1.2 mmol, 60%). **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 7.49 (d, *J* = 8.8 Hz, 4 H), 6.6 (d, *J* = 7.0 Hz, 4 H), 4.80 (s br, 6 H), 3.38 (q, *J* = 7.0 Hz, 2 H), 2.68 (t, *J* = 6.9 Hz, 2 H), 1.74–1.61 (m, 6 H), 1.09 (t, *J* = 6.9 Hz, 2 H) ppm. **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 175.6, 152.1, 128.5, 111.2, 37.3, 28.3, 25.0 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 362 (100, M^+), 305 (21), 287 (27), 273 (43), 261 (30), 132 (46), 105 (52), 57 (59); **Elemental analysis** calcd. (%) for $C_{18}H_{26}N_4O_2S$: C 59.64, H 7.23, N 15.46; found: C 59.42, H 7.22, N 15.44.

4-[(4-Aminophenyl)sulfonyl]-*N*-benzylaniline (5a): From **B** (3.5 mg, 0.006 mmol), 4,4′-sulfonyldianiline (496 mg, 2.0 mmol), benzyl alcohol (108 µL, 1.0 mmol), 600 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 287 mg (0.85 mmol, 85%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.64–7.57 (m, 4 H), 7.36–7.23 (m, 5 H), 6.67–6.57 (m, 4 H), 4.74 (t, *J* = 4.7 Hz, 1 H), 4.36 (d, *J* = 5.6 Hz, 2 H), 4.18 (s br, 2 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 152.0, 151.3, 138.9, 131.8, 130.5, 129.6, 129.5, 129.2, 128.0, 127.8, 114.5, 112.5, 48.0 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 338 (100, M^+), 261 (6),183 (8), 140 (4), 91 (100), 65 (10).

4-[(4-Aminophenyl)sulfonyl]-*N*-propylaniline (5b): From **B** (4.7 mg, 0.008 mmol), 4,4′-sulfonyldianiline (496 mg, 2.0 mmol), 1-propanol (75 µL, 1.0 mmol), 600 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 255 mg (0.86 mmol, 86%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.61 (dd, *J* = 8.8, 1.8 Hz, 4 H), 6.69–6.52 (m, 4 H), 4.27 (s br, 1 H), 4.15 (s br, 2 H), 3.14–3.05 (m, 2 H), 1.69–1.54 (m, 2 H), 0.97 (td, *J* = 7.4, 1.9 Hz, 3 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 152.4, 151.2, 132.1, 129.7, 129.6, 129.5, 114.5, 112.2, 45.6, 22.9, 11.8 ppm. **MS**

(70 eV, EI): *m*/*z* (%) = 290 (41, M^+), 261 (100), 140 (8), 122 (8), 105 (32), 92 (20), 65 (30), 42 (20).

***N*-Benzyl-4-({4-[(4-fluorobenzyl)amino]phenyl}sulfonyl)- aniline (5c):** From **B** (6.0 mg, 0.01 mmol), 4-[(4-aminophenyl)sulfonyl]-*N*-benzylaniline **5a** (338 mg, 1.0 mmol), (4-fluorophenyl)-methanol (139 µL, 1.1 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 326 mg (0.73 mmol, 73%) **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.61 (d, *J* = 8.8 Hz, 4 H), 7.36–7.22 (m, 7 H), 7.12–6.97 (m, 2 H), 6.59 (dd, *J* = 8.8, 2.3 Hz, 4 H), 4.70 (t, *J* = 4.7 Hz, 1 H), 4.64 (t, *J* = 4.4 Hz, 1 H), 4.39–4.26 (m, 4 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 163.1 (d, *J* = 41.4 Hz), 159.9 (d, *J* = 40.3 Hz), 157.2, 151.9, 151.8, 139.1, 135.2 (d, *J* = 2.8 Hz), 133.4 (*J* = 2.8 Hz), 129.9 (d, *J* = 8.3 Hz), 129.0 (d, *J* = 7.7 Hz),128.4, 127.1, 126.9, 115.2 (d, *J* = 21.5 Hz), 115.3 (d, *J* = 21.5 Hz), 114.8, 111.5, 45.8, 45.1 (d, *J* = 15.5 Hz) ppm. **MS** (70 eV, EI): *m*/*z* (%) = 446 (86, M^+), 291 (12), 273 (8), 109 (100), 91 (96), 65 (8); **Elemental analysis** calcd. (%) for $C_{26}H_{23}FN_2O_2S$: C 69.93, H 5.19, N 6.27; found: C 69.99, H 4.80, N 6.27.

***N*-Benzyl-4-({4-[(4-chlorobenzyl)amino]phenyl}sulfonyl)- aniline (5d):** From **B** (4.7 mg, 0.008 mmol), 4-[(4-aminophenyl)sulfonyl]-*N*-benzylaniline **5a** (338 mg, 1.0 mmol)c, (4-chlorophenyl)-methanol (158 mg, 1.1 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 407 mg (0.88 mmol, 88%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.60 (dd, *J* = 8.8, 1.8 Hz, 4 H), 7.36–7.23 (m, 9 H), 6.58 (ddd, *J* = 8.4, 6.5, 1.8 Hz, 4 H), 4.75 (s br, 2 H), 4.38–4.31 (m, 4 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 152.0, 151.9, 151.7, 138.9, 137.6, 133.5, 131.1 130.6, 129.5, 129.4, 129.3, 129.2, 128.0, 127.8, 112.6, 112.5, 48.0, 47.3 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 462 (61, M^+), 428 (29), 338 (8), 273 (11), 125 (46), 91 (100), 65 (7); **Elemental analysis** calcd. (%) for $C_{26}H_{23}ClN_2O_2S$: C 67.45, H 5.01, N 6.05; found: C 67.27, H 5.00, N 5.97.

***N*-Benzyl-4-({4-[(4-bromobenzyl)amino]phenyl}sulfonyl)- aniline (5e):** From **B** (6.0 mg, 0.01 mmol), 4-((4-aminophenyl)sulfonyl)-*N*-benzylaniline **5a** (338 mg, 1.0 mmol), (4-bromophenyl)-methanol (206 mg, 1.1 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:EtOAc = 1:1). Yield: 344 mg (0.68 mmol, 68%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.64–7.57 (m, 4 H), 7.49–7.44 (m, 2

H), 7.34–7.31 (m, 4 H), 7.30–7.27 (m, 1 H), 7.21 (d, *J* = 8.2 Hz, 2 H), 6.63–6.54 (m, 4 H), 4.74 (s br, 2 H), 4.36 (d, *J* = 5.6, 2 H), 4.32 (d, *J* = 5.9 Hz, 2 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 152.0, 151.7, 138.9, 138.2, 132.3, 131.1, 130.7, 129.6, 129.5, 129.3, 128.0, 127.9, 121.6, 112.7, 112.6, 87.9, 48.0, 47.4 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 508 (18, M^+), 462 (7), 428 (70), 273 (17), 169 (11), 91 (100), 65 (8); **Elemental analysis** calcd. (%) for $C_{26}H_{23}BrN_2O_2S$: C 61.54, H 4.57, N 5.52; found: C 61.85, H 4.99, N 5.41.

N-benzyl-4-{[4-(pentylamino)phenyl]sulfonyl}aniline (5f): From **B** (6.0 mg, 0.01 mmol), 4-[(4-aminophenyl)sulfonyl]-*N*-benzylaniline **5a** (338 mg, 1.0 mmol), 1-pentanol (120 µL, 1.1 mmol), 400 µL diglyme, KO-*t*-Bu (124 mg, 1.1 mmol), 24 h at 70 °C. Purification by column chromatography (pentane:EtOA*c* = 1.5:1). Yield: 371 mg (0.91 mmol, 91%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.60 (dd, *J* = 8.5, 2.1 Hz, 4 H), 7.36–7.30 (m, 4 H), 7.30–7.25 (m, 1 H), 6.57 (dd, *J* = 14.9, 8.5 Hz, 4 H), 4.73 (t, *J* = 5.6 Hz, 1 H), 4.36 (d, 5.6 Hz, 2 H), 4.26 (t, *J* = 5.7 Hz, 1 H), 3.11 (m, 2 H), 1.65–1.54 (m, 2 H), 1.40–1.30 (m, 4 H), 0.95–0.87 (m, 3 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 152.4, 151.9, 139.0, 131.0, 129.9, 129.5, 129.4, 129.3, 128.0, 127.8, 112.6, 112.1, 48.0, 43.9, 29.7, 29.4, 23.0, 14.3 ppm. **MS** (70 eV, EI): *m*/*z* (%) = 408 (100, M^+), 351 (56), 263 (10), 196 (6), 183 (8), 140 (6), 105 (14), 91 (88), 65 (6); **Elemental analysis** calcd. (%) for $C_{24}H_{28}N_2O_2S$: C 70.55, H 6.91, N 6.86; found: C 70.54, H 6.93, N 6.87.

Acknowledgments

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5.5 References

[1] a) G. Guillena, D. J. Ramo´n, M. Yus, *Chem. Rev.* **2010,** *110,* 1611-1641; b) G. Guillena, D. J. Ramo`n, M. Yus, *Angew. Chem. Int. Ed.* **2007**, *46*, 2358-2364.

[2] a) T. D. Nixon, M. K. Whittlesey, J. M. J. Williams, *Dalton Trans.* **2009**, 753-762*;* b) G. W. Lamb, J. M. J. Williams, *Chim. Oggi.* **2008**, *26*, 17-19; c) M. H. S. A. Hamid, P. A. Slatford, J. M. J. Williams, *Adv. Synth. Catal.* **2007**, *349*, 1555-1575.

[3] A. J. A. Watson, J. M. J. Williams, *Science* **2010**, *329*, 635-636**.**

[4] For selected reviews in addition to the ones listed under [1] and [2] or very recent key papers please see: T. Suzuki, *Chem. Rev*. **2011**, *111*, 1825-1845; B. Blank, R. Kempe, *J. Am. Chem. Soc*. **2010**, *132*, 924-925; Y. Iuchi, Y. Obora, and Y. Ishii, *J. Am. Chem. Soc*. **2010**, *132*, 2536-2537; L. J. Allen, R. H. Crabtree, *Green Chemistry* **2010**, *12*, 8, 1362-1364; Y. Iuchi,; M. Hyotanishi, B. E. Miller, K. Maede, Y. Obora, Y. Ishii, *J. Org. Chem.* **2010**, *75*, 1803-1806; R. Grigg, C. Lofberg, S. Whitney, V. Sridharan, A. Keep, A. Derrick, *Tetrahedron* **2009**, *65*, 849-864; R. Grigg, S. Whitney, V. Sridharan, A. Keep, A. Derrick, *Tetrahedron* **2009**, *65*, 7468-7473; T. Jensen, R. Madsen, *J. Org. Chem.* **2009**, *74*, 3990-3992.

a) D. Pingen, C. Müller, D. Vogt, *Angew. Chem. Int. Ed*. **2010**, *49*, 8130-8133; b) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* **2010**, *110*, 681-703; c) D. Gnanamgari, E. L. O. Sauer, N. D. Schley, C. Butler, C. D. Incarvito, R. H. Crabtree, *Organometallics* **2009**, *28*, 321-325; d) D. Gnanamgari, C. H. Leung, N. D. Schley, S. T. Hilton, R. H. Crabtree, *Org. Biomol. Chem.* **2008**, *6*, 4442-4445; e) A. M. Voutchkova, D. Gnanamgari, C. E Jakobsche, C. Butler, S. J. Miller, J. Parr, R. H. Crabtree, *J. Organomet. Chem*. **2008**, *693*, 1815–1821; f) D. Gnanamgari, A. Moores, E. Rajaseelan, R. H. Crabtree, *Organometallics* **2007**, *26*, 1226-1230.

[5] M. B. Smith, J. March, *Advanced Organic Chemistry*, 5th ed.; Wiley: New York, **2001**, 499.

[6] R. Grigg; T. R. B. Mitchell, S. Sutthivaiyakit, N. Tongpenyai, *J. Chem. Soc. Chem. Commun.* **1981**, *12*, 611-612.

[7] a) Y. Watanabe, Y. Tsuji, Y. Ohsugi, T. Ohta, *J. Org. Chem.* **1984**, *49*, 3359-3363. b) Y. Tsuji, H.-T. Huh, Y. Ohsugi, Y. Watanabe. *J. Org. Chem.* **1985**, *50*, 1365-1370.

[8] a) S. Bähn, S. Imm, K. Mevius, L. Neubert, A. Tillack, J. M. J. Williams, M. Beller, *Chem. Eur. J.* **2010**, *16*, 3590–3593; b) S. Imm, S. Bähn, L. Neubert, H. Neumann, M. Beller, *Angew. Chem. Int. Ed*. **2010**, *49*, 8126-8129; c) S. Imm, S. Bähn, A. Tillack, K. Mevius, L. Neubert, M. Beller, *Chem. Eur. J.* **2010**, *16*, 2705-2709; d) F. Shi, M. K. Tse, X. Cui, D. Gördes, D. Michalik, K. Thurow, Y. Deng, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 5912-5915; e) X. Cui, F. Shi, M. K. Tse, D. Gördes, K. Thurow, M. Beller, Y. Denga, *Adv. Synth. Catal*. **2009**, *351*, 2949-2958; f) S. Bähn, A. Tillack, S. Imm, K. Mevius, D. Michalik, D. Hollmann, L. Neubert, M. Beller, *ChemSusChem* **2009**, *2*, 551-557; g) D. Hollmann, S. Bähn, A. Tillack, R. Parton, R. Altink, M.

Beller, *Tetrahedron Lett.* **2008**, *49*, 5742-5745; h) A. Tillack, D. Hollmann, K. Mevius, D. Michalik, S. Bähn, M. Beller, *Eur. J. Org. Chem.* **2008**, 4745-4750; i) S. Bähn, D. Hollmann, A. Tillack, M. Beller, *Adv. Synth. Catal*. **2008**, *350*, 2099-2103; j) D. Hollmann, S. Bähn, A. Tillack, M. Beller, *Chem. Commun*. **2008**, 3199-3201; k) D. Hollmann, S. Bähn, A. Tillack, M. Beller, *Angew. Chem*. **2007**, *119*, 8440-8444; l) *Angew. Chem. Int. Ed*. **2007**, *46*, 8291-8294; m) D. Hollmann, A. Tillack, D. Michalik, R. Jackstell, M. Beller, *Chem. Asian J*. **2007**, *2*, 403-410; n) A. Tillack, D. Hollmann, D. Michalik, M. Beller, *Tetrahedron Lett*. **2006,** *47*, 8881-8885.

[9] a) S. Whitney, R. Grigg, A. Derrick, A. Keep, *Org. Lett.* 9, *17*, **2007**, 3299-3302; b) C. Löfberg, R. Grigg, M. A. Whittaker, A. Keep, A. Derrick, *J. Org. Chem*. **2006**, *71*, 8023-8027; c) C. Löfberg, R. Grigg, A. Keep, A. Derrick, V. Sridharan, C. Kilner, *Chem. Commun*. **2006**, 5000-5002.

[10] a) R. Kawahara, K.-i. Fujita, R. Yamaguchi, *Adv. Synth. Catal.* **2011**, *353*, 1161-1168; b) R. Kawahara, K.-i Fujita, R. Yamaguchi, *J. Am. Chem. Soc*. **2010**, *132*, 15108-15111; c) K.-i. Fujita, A. Komatsubara, R. Yamaguchi, *Tetrahedron* **2009**, *65*, 3624-3628; d) R. Yamaguchi, Z. Mingwen, S. Kawagoe, C. Asai, K.-i. Fujita, *Synthesis* **2009**, 1220-1223; e) K.-i. Fujita, Y. Kida, R. Yamaguchi, *Heterocycles* **2009**, *77*, 1371-1377; f) R. Yamaguchi, S. Kawagoe, C. Asai, K.-i. Fujita, *Org. Lett*. **2008**, *10*, 181-184; g) K.-i. Fujita, Y. Enoki, R. Yamaguchi, *Tetrahedron* **2008**, *64*, 1943–1954; h) K.-i Fujita, R. Yamaguchi, *Synlett* **2005**, *4*, 560-571; i) K.-i. Fujita, C. Asai, T. Yamaguchi, F. Hanasaka, R. Yamaguchi, *Org. Lett*. **2005**, *7*, 4017-4019; j) K.-i. Fujita, T. Fujii, R. Yamaguchi, *Org. Lett*. **2004**, *6*, 3525-3528; k) K.-i. Fujita, Z. Li, N. Ozeki, R. Yamaguchi, *Tetrahedron Lett*. **2003**, *44*, 2687-2690; l) K.-i. Fujita, K. Yamamoto, R. Yamaguchi, *Org. Lett.* **2002**, *4*, 2691-2694.

[11] a) A. J. A. Watson, A. C. Maxwell, J. M. J. Williams, *J. Org. Chem.* **2011**, *76*, 2328-2331; b) O. Saidi, A. J. Blacker, G. W. Lamb, S. P. Marsden, J. E. Taylor, J. M. J. Williams, *Organic Process Research & Development.* **2010**, *14*, 1046-1049; c) O. Saidi, A. J. Blacker, M. M. Farah, S. P. Marsden, J. M. J. Williams, *Chem. Commun.* **2010**, *46*, 1541-1543; d) O. Saidi, A. J. Blacker, M. M. Farah, S. P. Marsden, J. M. J. Williams, *Angew. Chem*. **2009**, *121*, 7511-7514; e) *Angew. Chem. Int. Ed*. **2009**, *48*, 7375-7378; f) M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson, J. M. J. Williams, *J. Am. Chem. Soc*. **2009**, *131*, 1766-1774;

g) G. W. Lamb, A. J. A. Watson, K. E. Jolley, A. C. Maxwell, J. M. J. Williams, *Tetrahedron Lett.* **2009**, *50*, 3374-3377; h) M. Haniti S. A. Hamid, J. M. J. Williams, *Tetrahedron Lett.* **2007**, *48*, 8263-8265; i) M. H. S. A. Hamid, J. M. J. Williams, *Chem. Commun.* **2007**, 725-727; j) G. Cami-Kobeci, P. A. Slatford, M. K. Whittlesey, J. M. J. Williams, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 535-537; k) G. Cami-Kobeci, J. M. J Williams, *Chem. Commun.* **2004**, 1072-1073.

[12] a) A. M.-Asencio, D. J. Ramón, M. Yus, *Tetrahedron* **2011**, *67*, 3140-3149; b) A. M.-Asencio, D. J. Ramón, M. Yus, *Tetrahedron Lett.* **2010**, *51*, 325-327; c) R. Martínez, D. J. Ramon, M. Yus, Org. *Biomol. Chem.* **2009**, *7*, 2176-2181; d) R. Martínez, D. J. Ramon, M. Yus, *Tetrahedron* **2006**, *62*, 8982-8987; e) R. Martínez, D. J. Ramon, M. Yus, *Tetrahedron* **2006**, *62*, 8988-9001; f) R. Martínez, G. J. Brand, D. J. Ramon, M. Yus, *Tetrahedron Lett.* **2005**, *46*, 3683-3686.

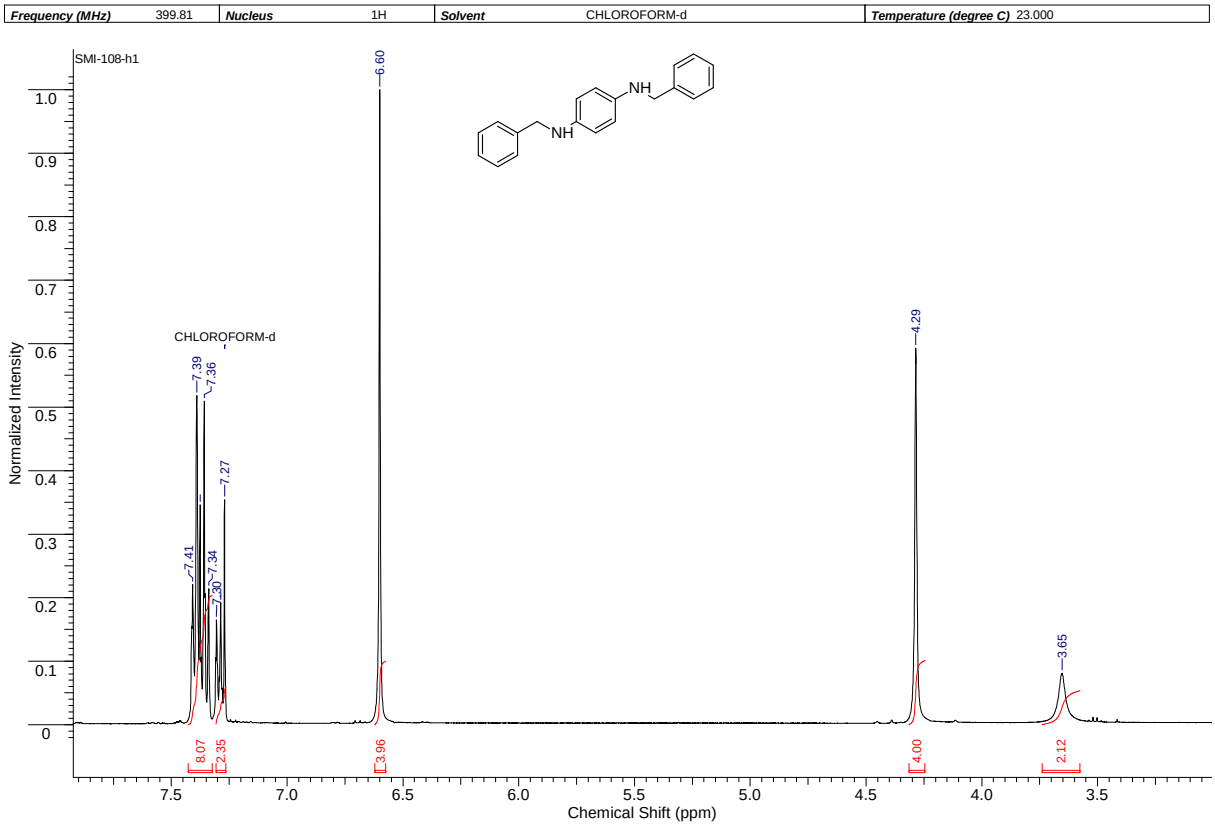
[13] a) B. Blank, M. Madalska, R. Kempe, *Adv. Synth. Catal.* **2008**, *350*, 749-758; b) B. Blank, S. Michlik, R. Kempe, *Chem. Eur. J.* **2009**, *15*, 3790-3799, c) B. Blank, S. Michlik, R. Kempe, *Adv. Synth. Catal.* **2009**, *351*, 2903-2911; d) S. Michlik, R. Kempe, *Chem. Eur. J.* **2010**, *16*, 13193-13198.

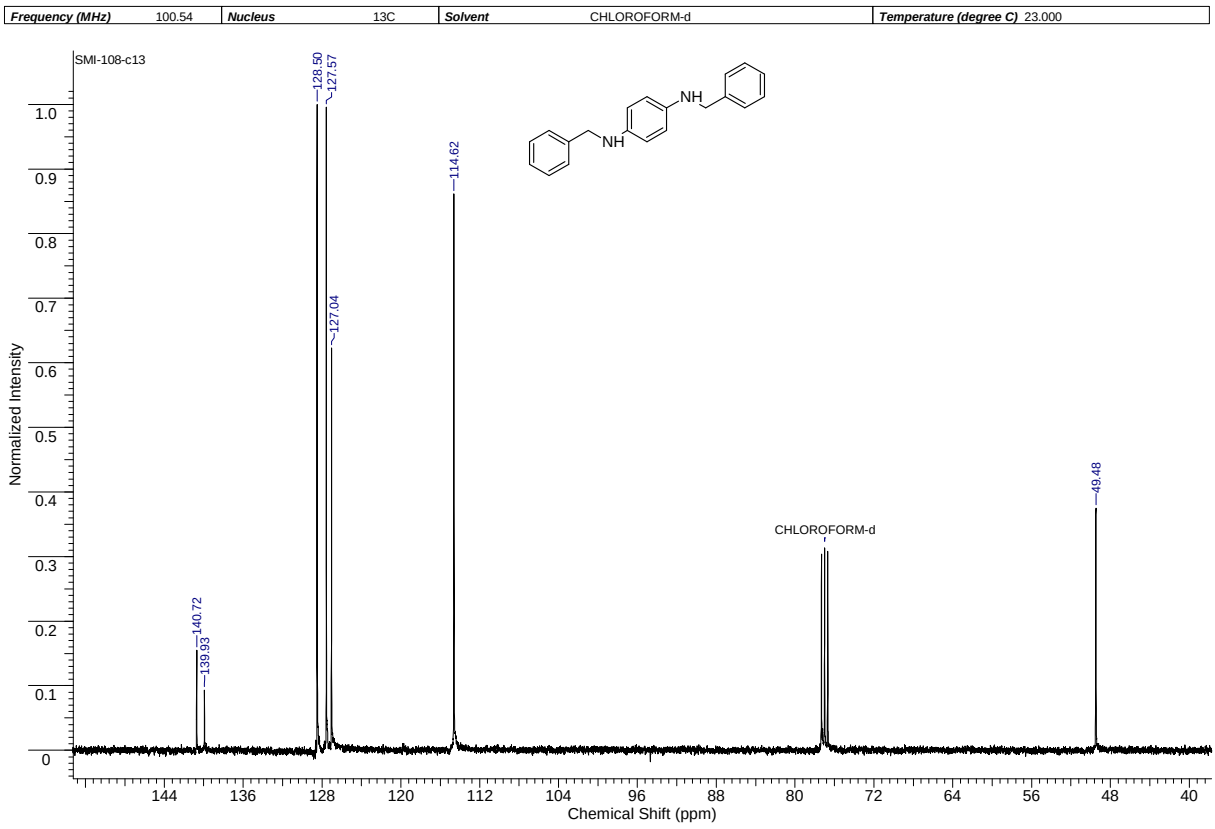
[14] T. Schareina, G. Hillebrand, H. Fuhrmann, R. Kempe, *Eur. J. Inorg. Chem.* **2001**, 2421-2426.

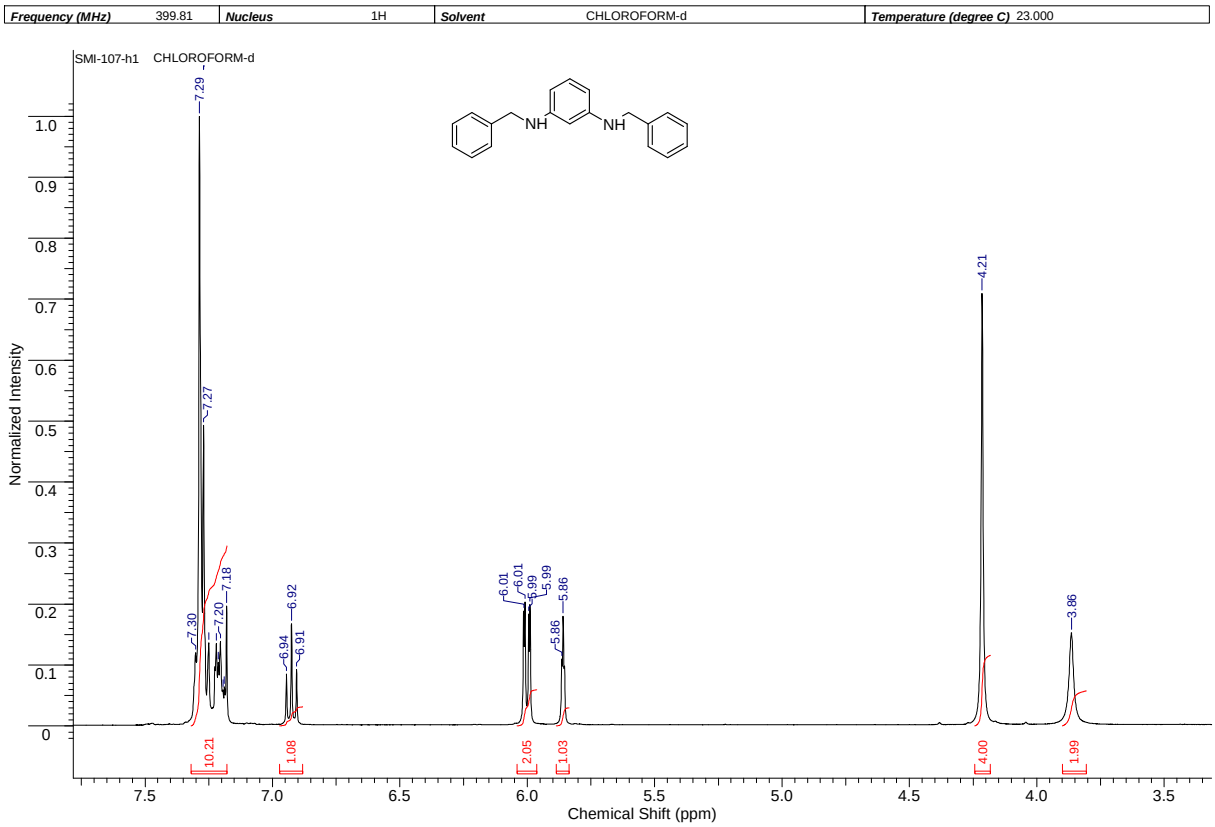
[15] a) G. Edwards, G.A. Biagini, *Br. J. Clin. Pharmacol.* **2006**, *61*, 690-693; b) P. K. Wilairatana, S. Looareesuwan, *Ann. Trop. Med. Parasitol.* **1997**, *91***,** 125–32. c) A. Alloueche, W. Bailey, S. Barton, *Lancet*, **2004**, *363*, 1843-1848. d) P. E. Kremsner. S. Krishna, *Lancet*, **2004**, *364*, 285-294; e) L. Levy, *Antimicrob. agents chemother.* **1978**, 791-793; f) M. D. Coleman, *Gen. Pharmac.* **1995**, *26*, 1461-1467; g) J. Wiesner, R. Ortmann, H. Jomaa, M. Schlitzer, *Angew. Chem. Int. Ed.* **2003**, *42*, 5274-5293.

[16] B. R. Baker, M. V. Querry, A. F. Kadish, *J. Org. Chem.* **1950**, 402-412.

5.6 Supporting Information



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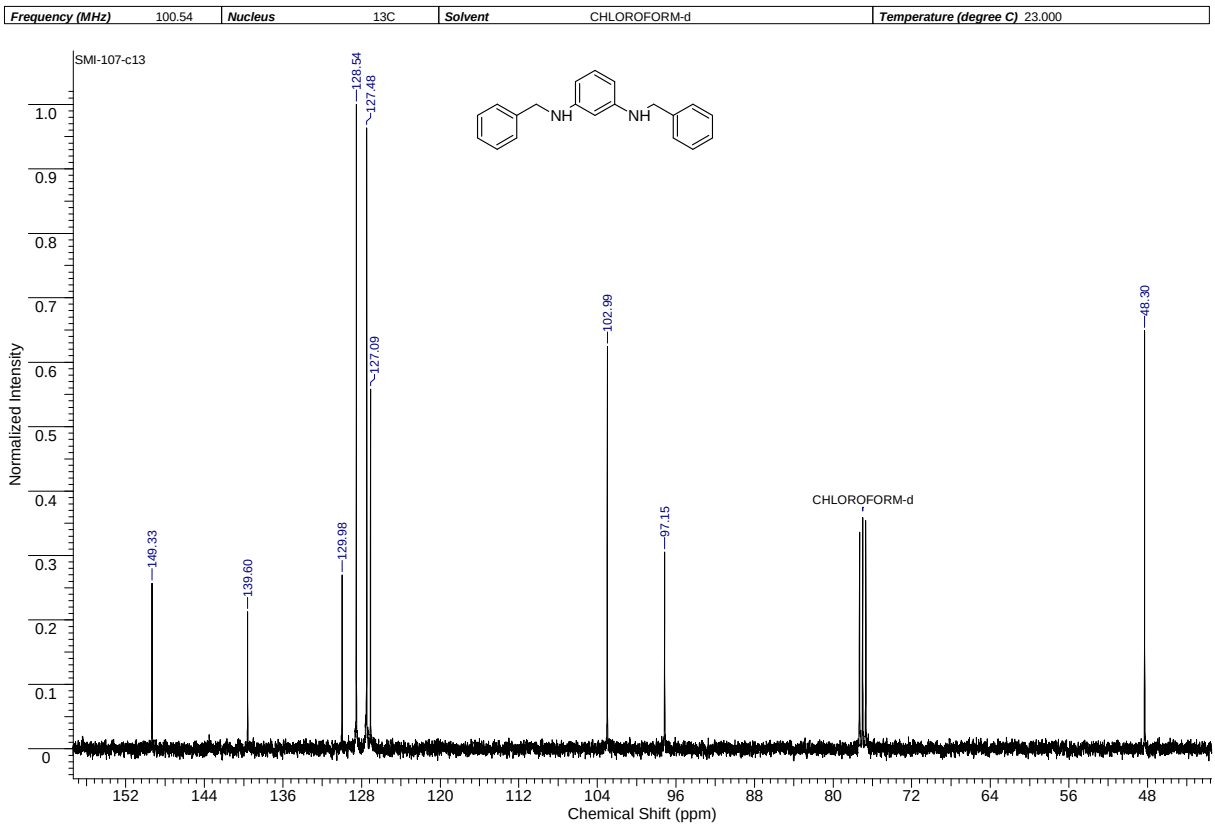
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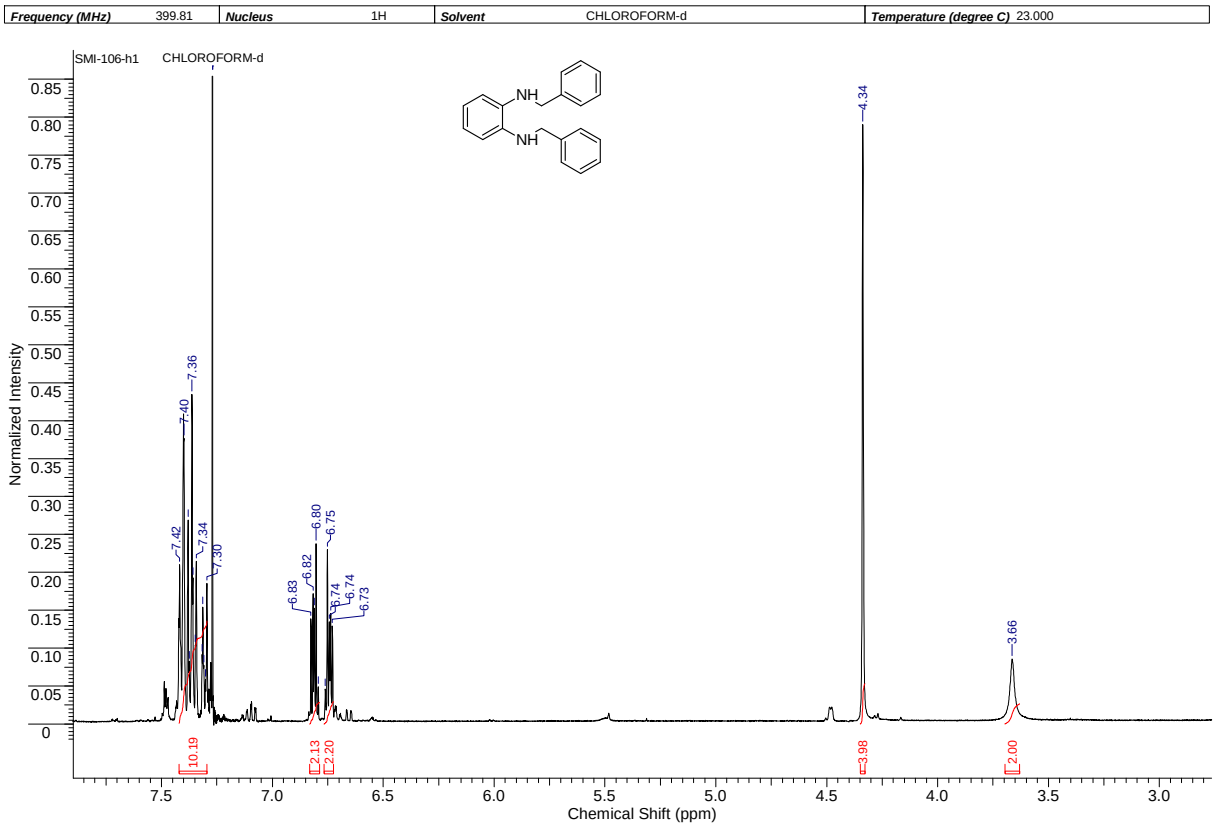
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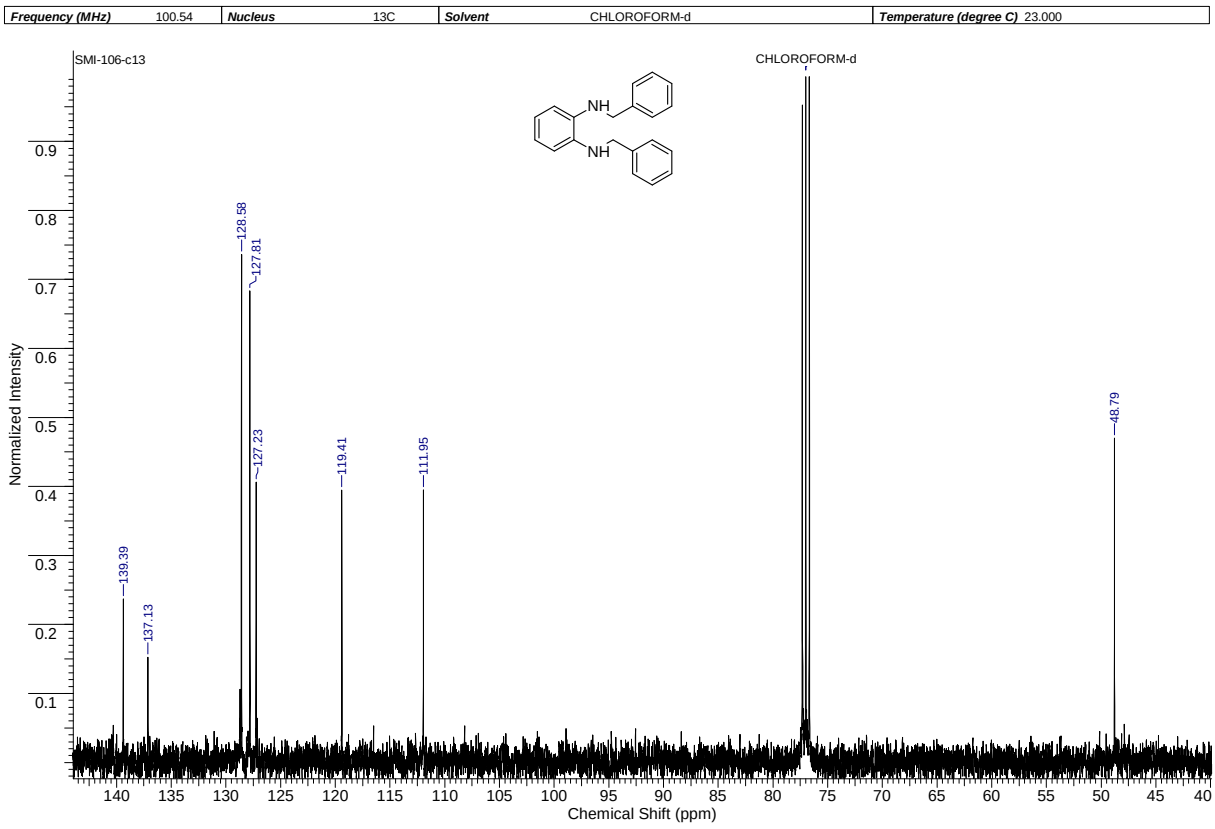
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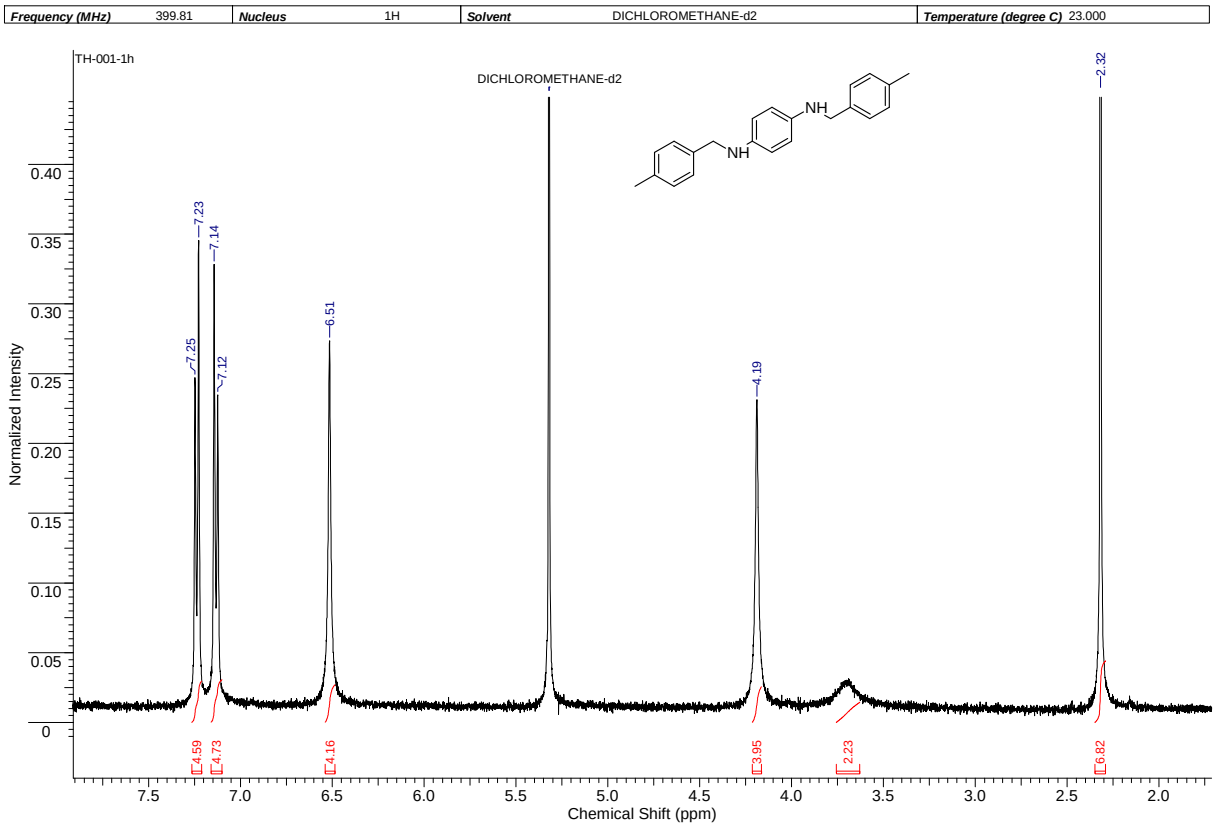
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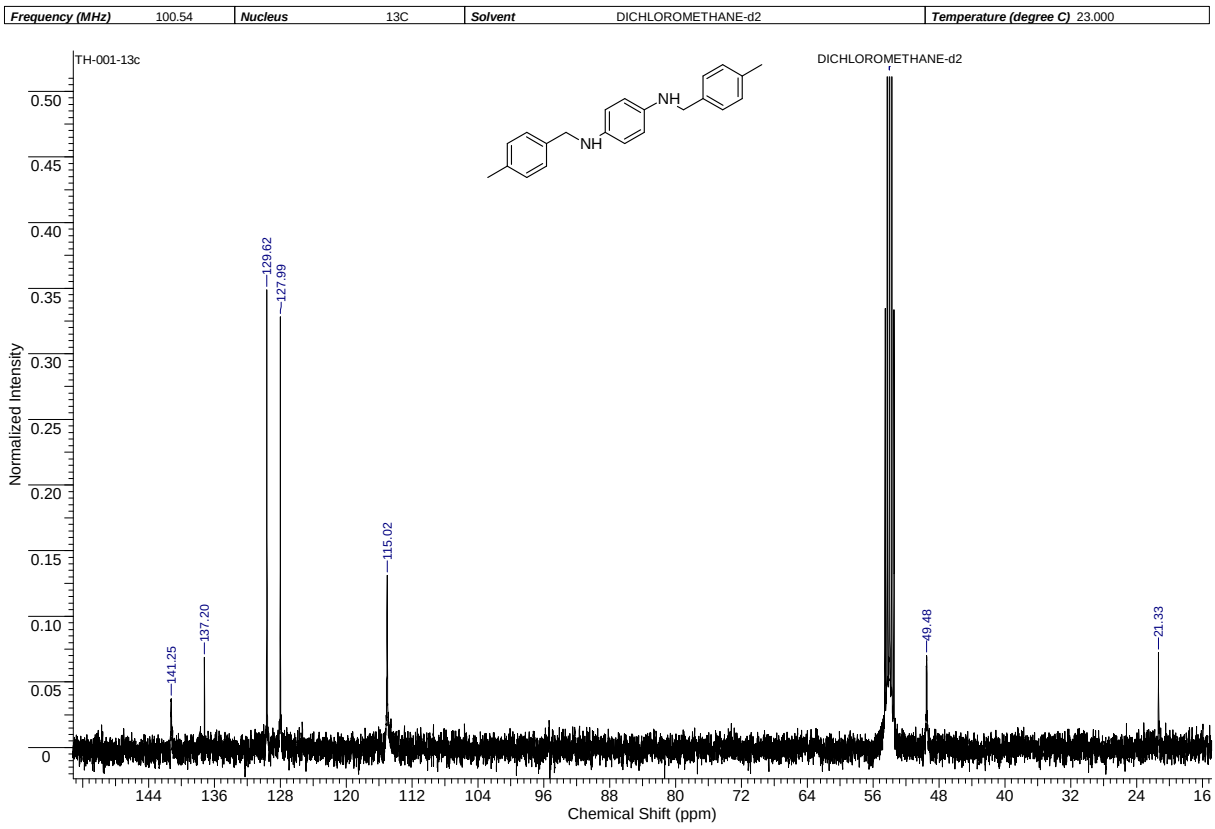
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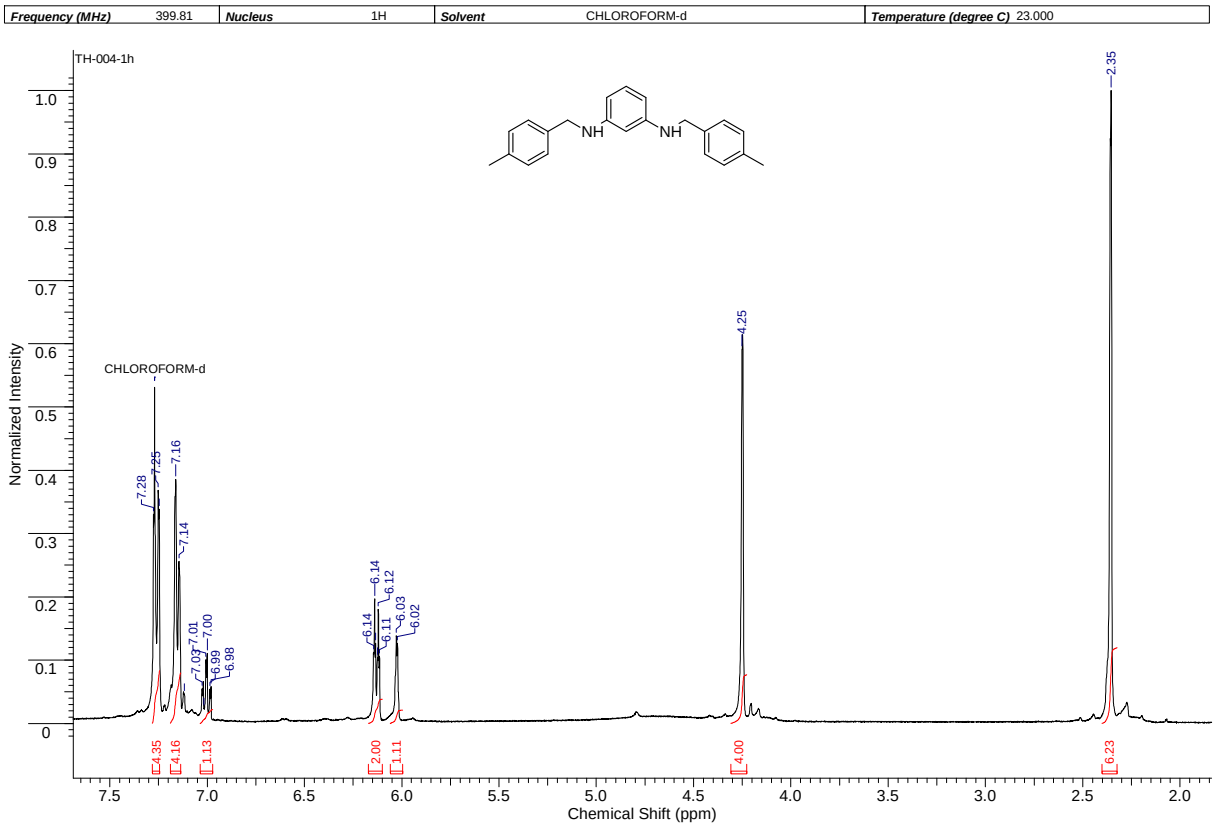
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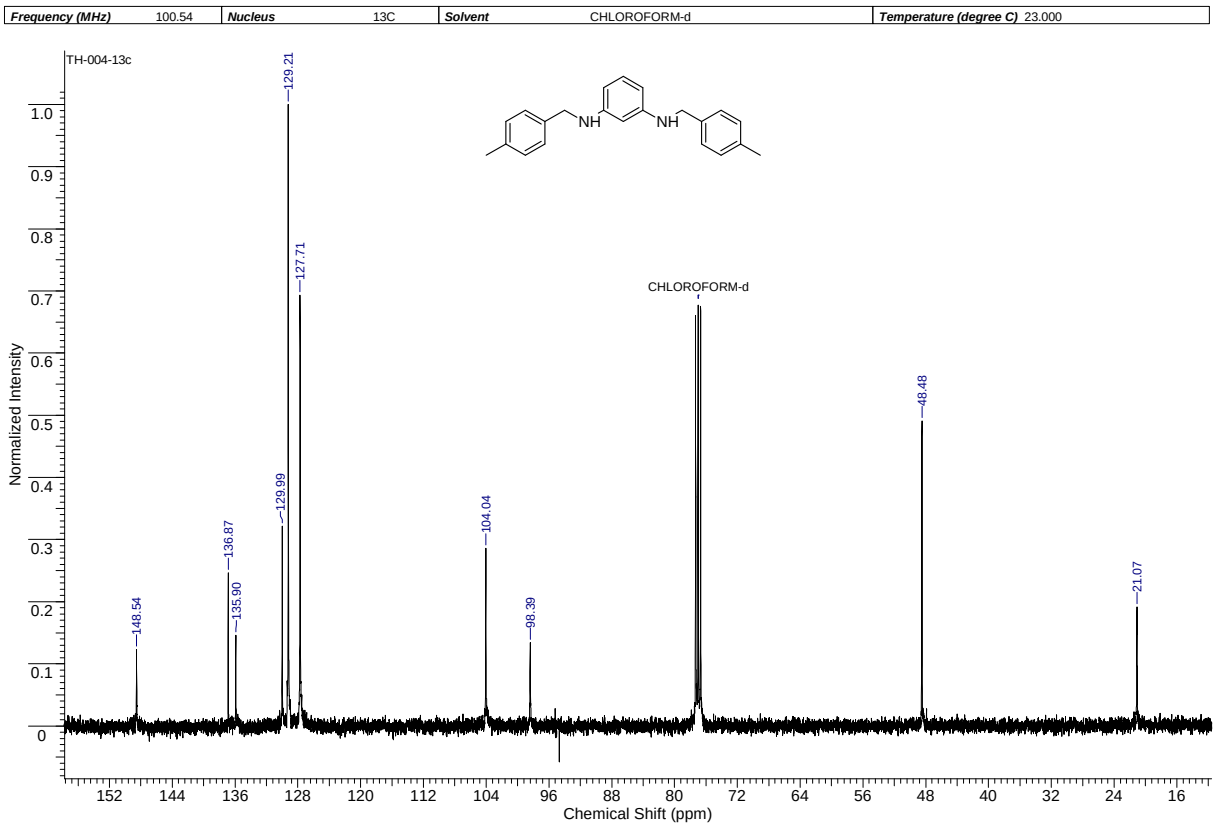
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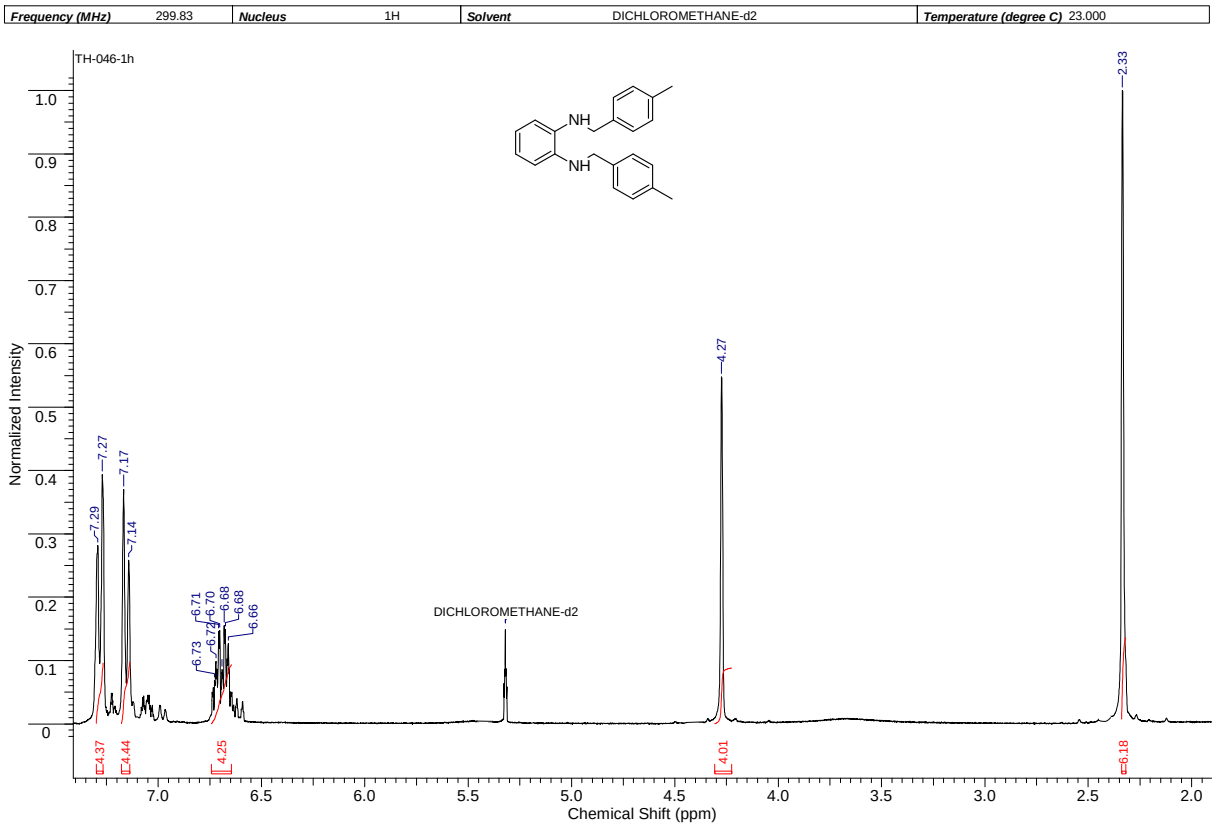
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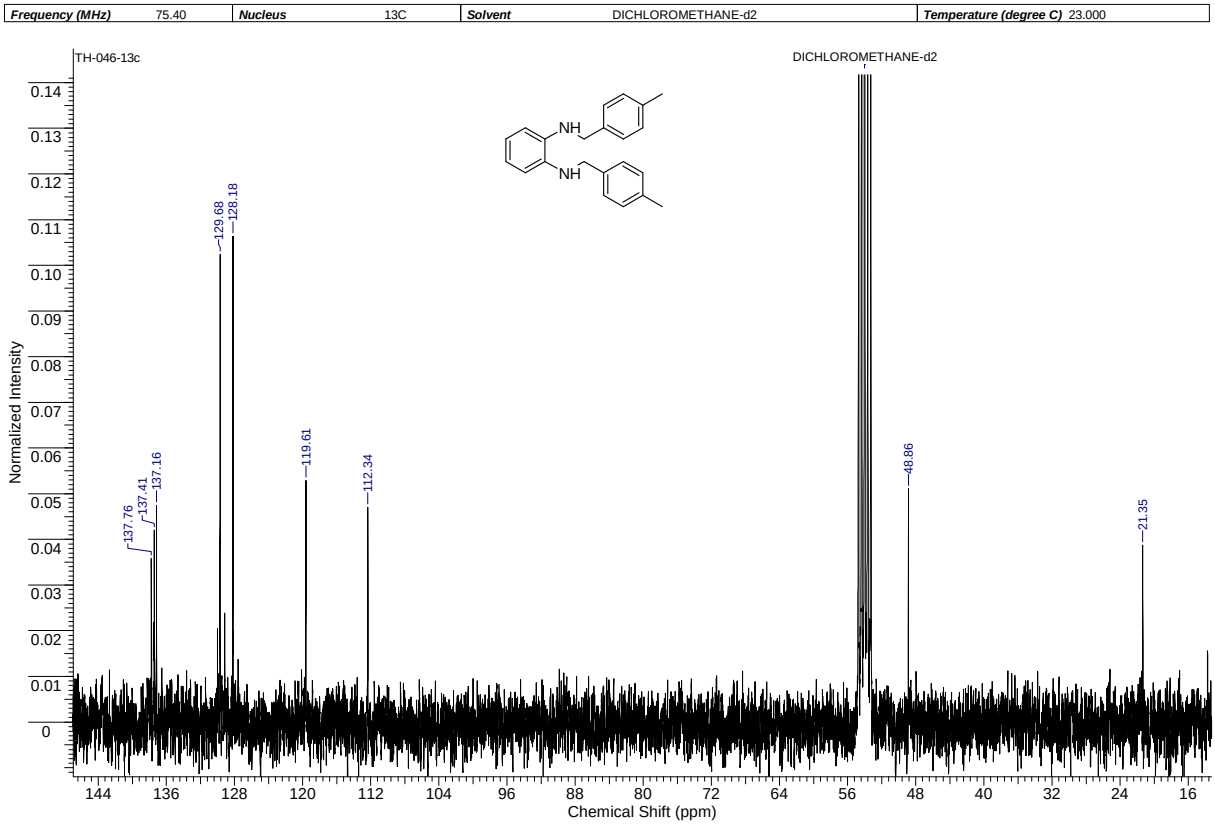
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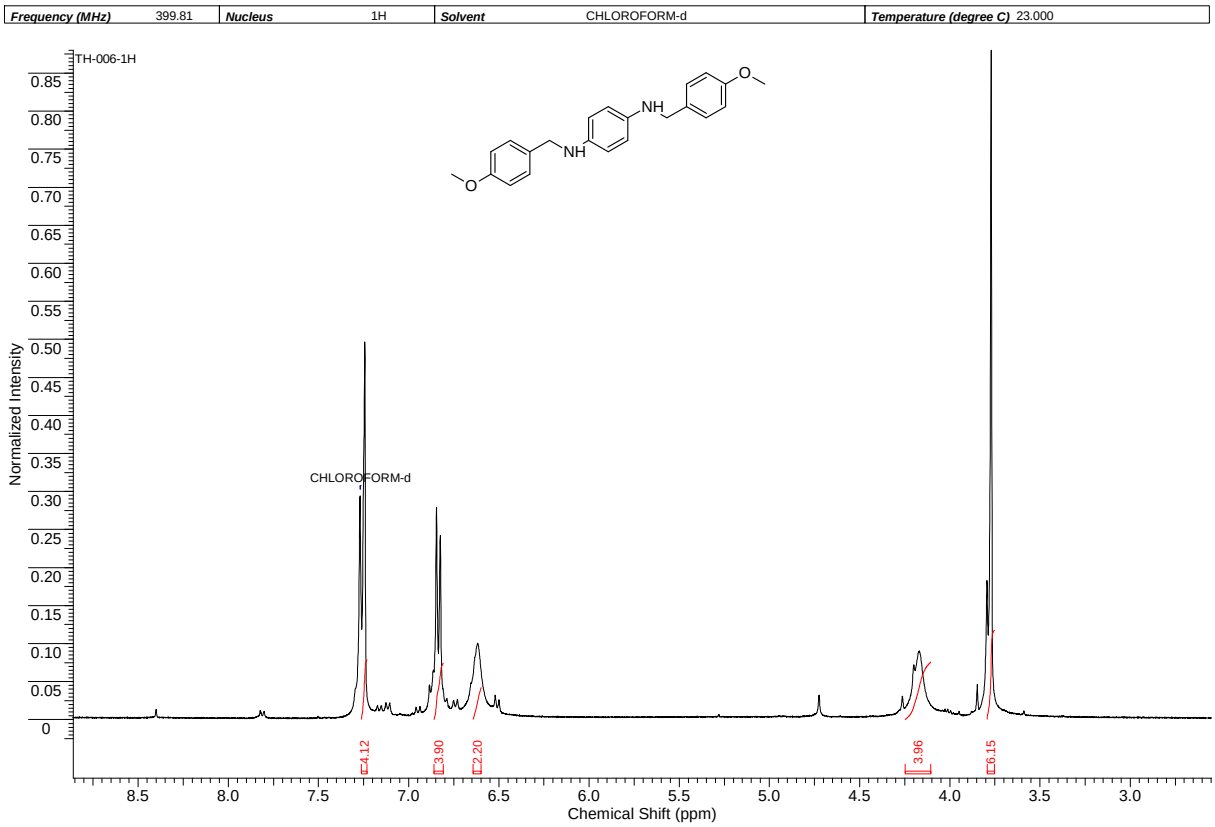
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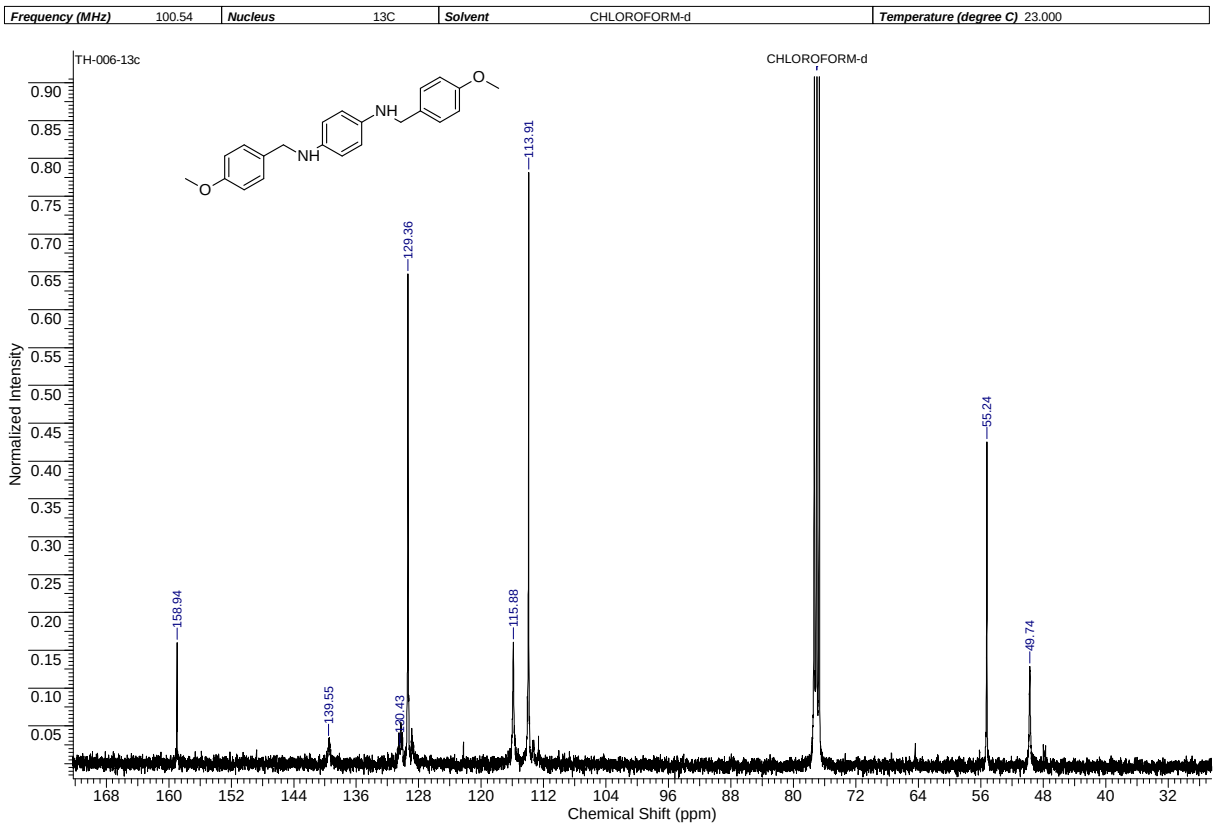
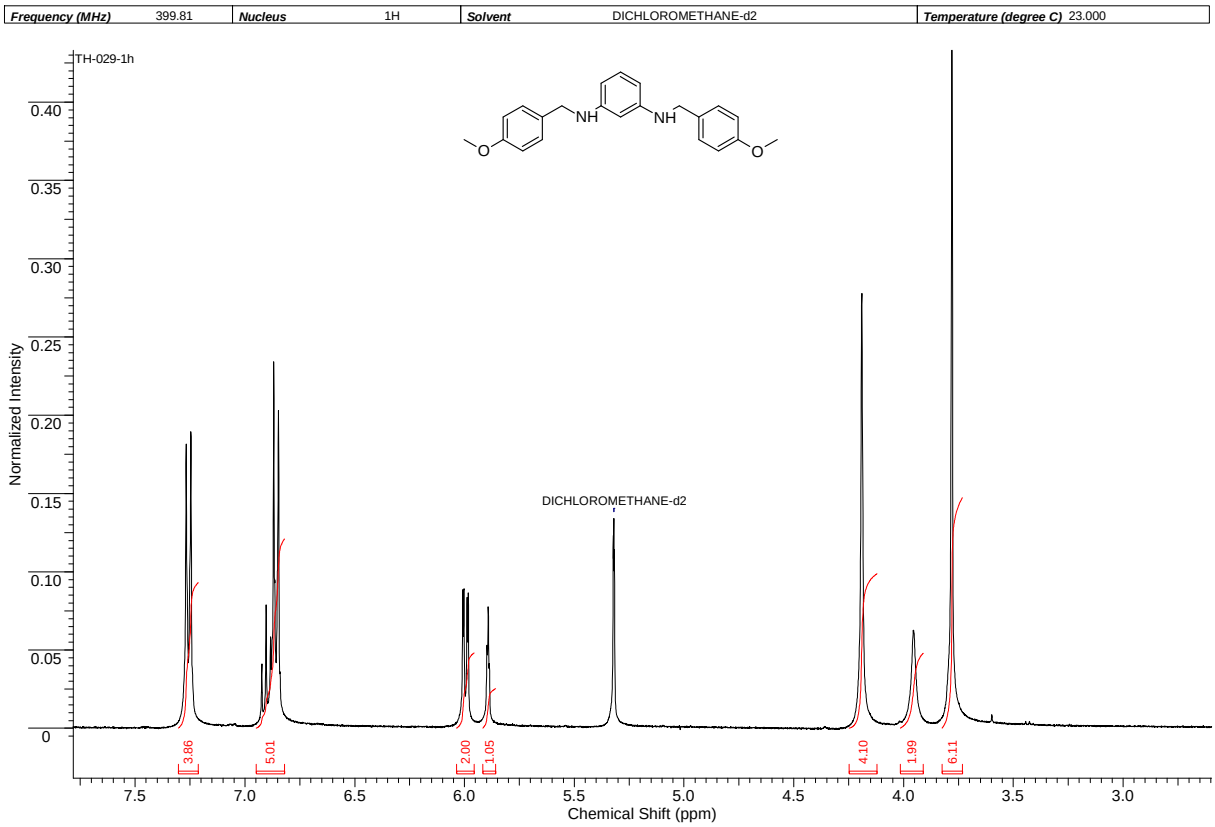
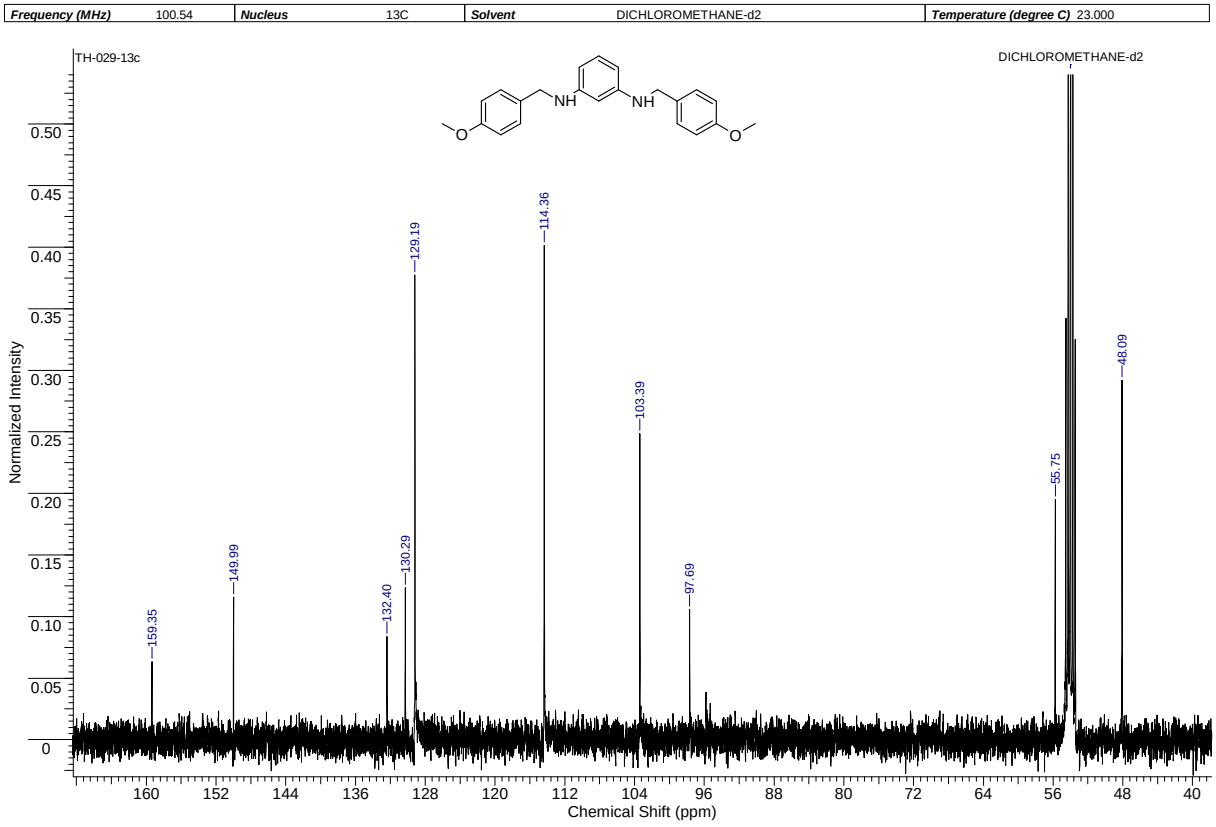
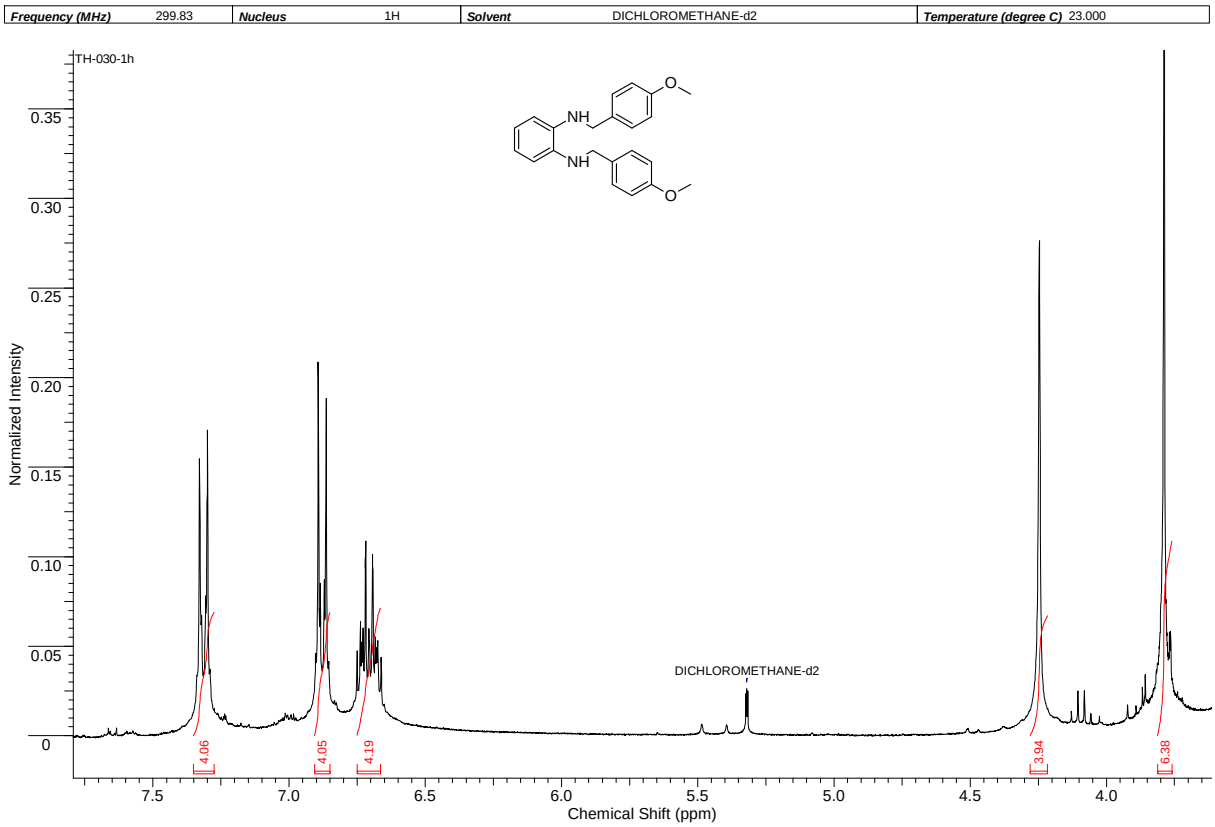
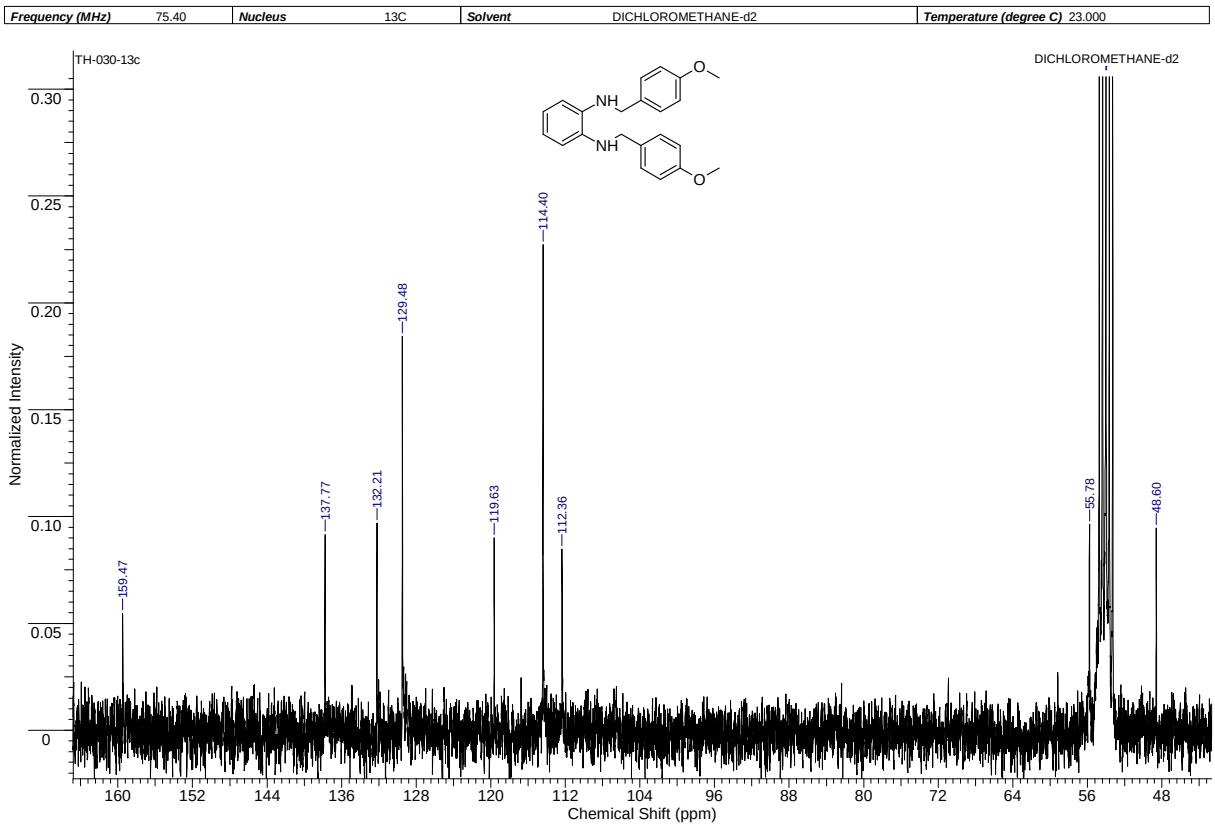
6.15

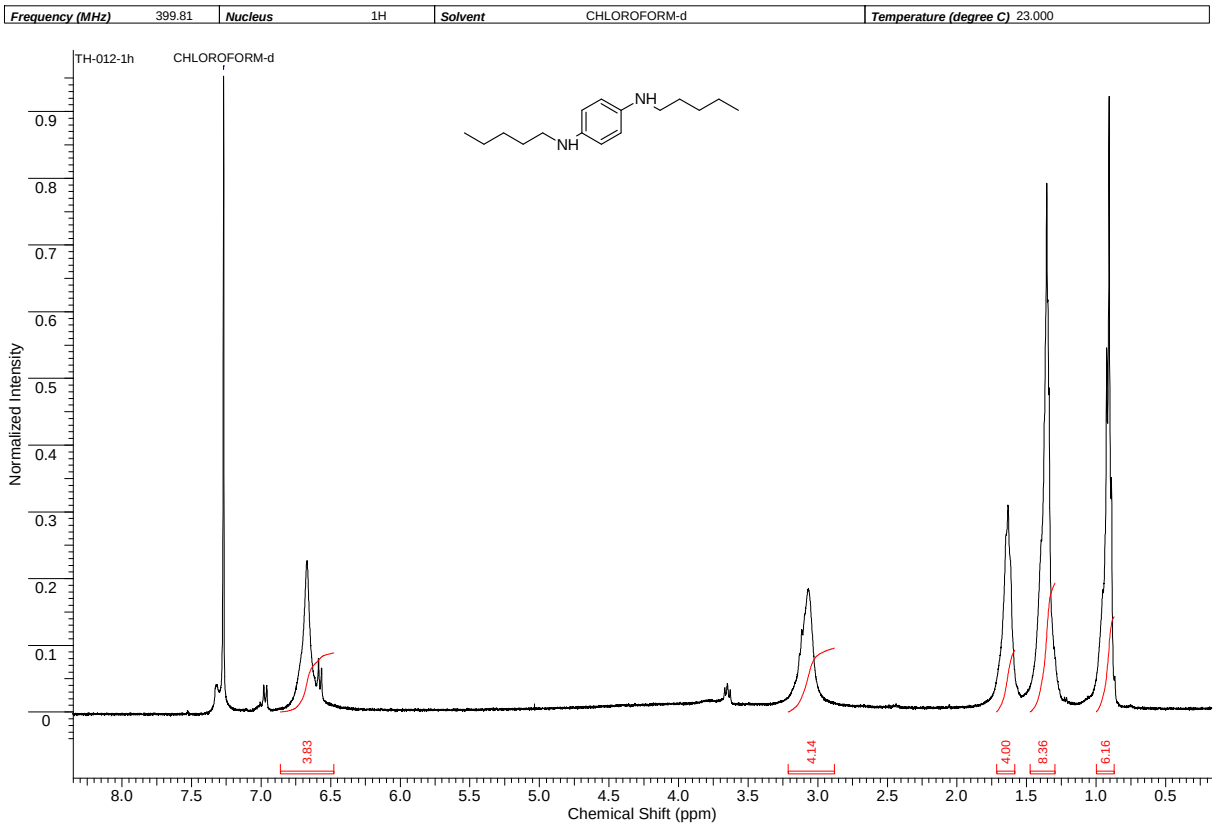

Frequency (MHz) 100.54
Nucleus 13C
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-006-13c
NH
NH
O
O
CHLOROFORM-d
158.94
139.55
130.43
129.36
115.88
113.91
55.24
49.74
Normalized Intensity
Chemical Shift (ppm)

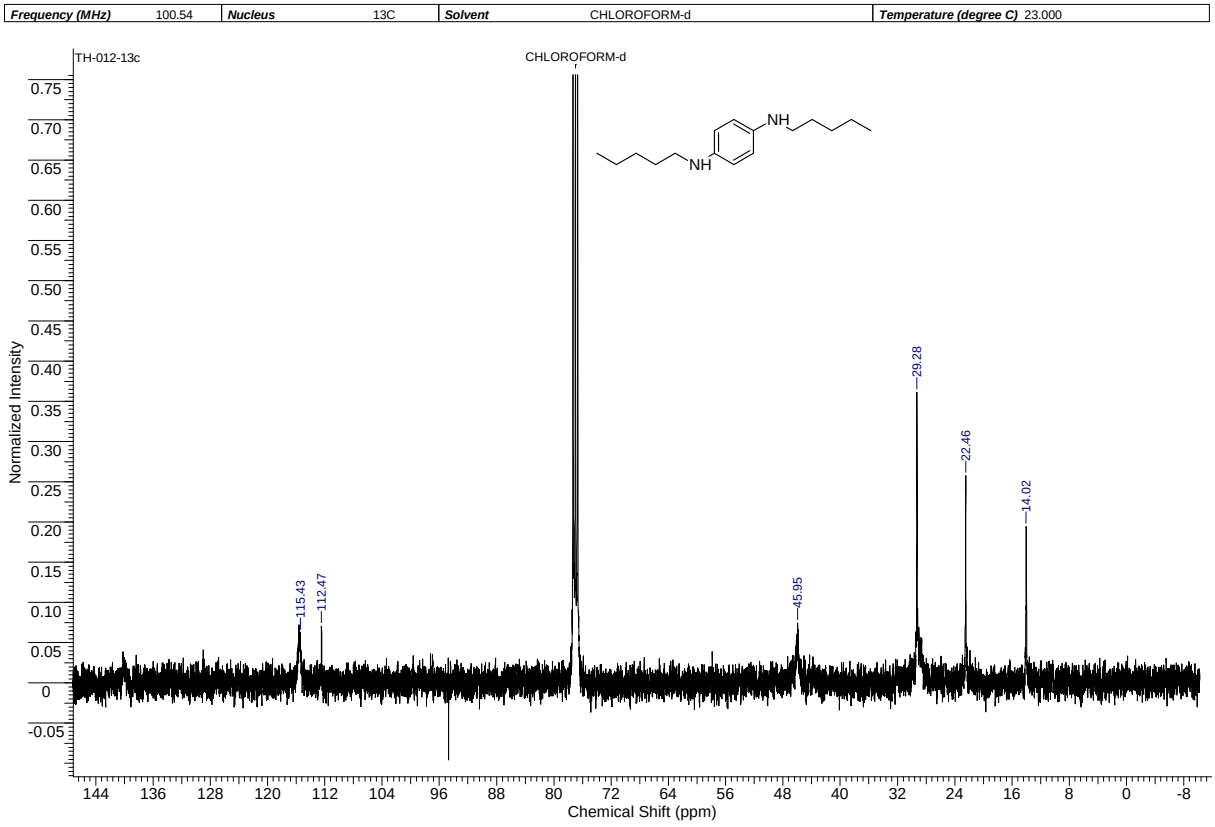

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-029-1h
NH
NH
O
O
DICHLOROMETHANE-d2
Normalized Intensity
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
3.86
5.01
2.00
1.05
4.10
1.99
6.11
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)

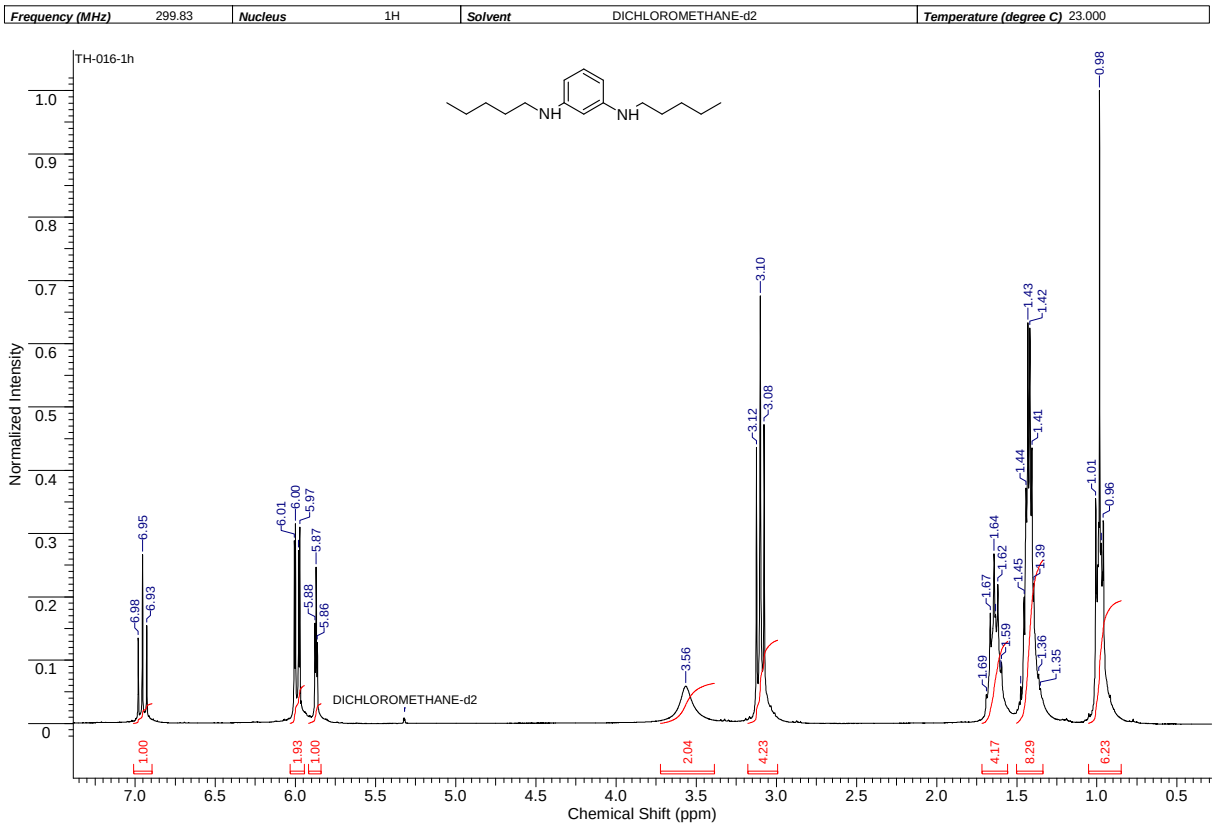

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-029-13c
NH
NH
O
O
DICHLOROMETHANE-d2
Normalized Intensity
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
159.35
149.99
132.40
130.29
129.19
114.36
103.39
97.69
55.75
48.09
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
Chemical Shift (ppm)

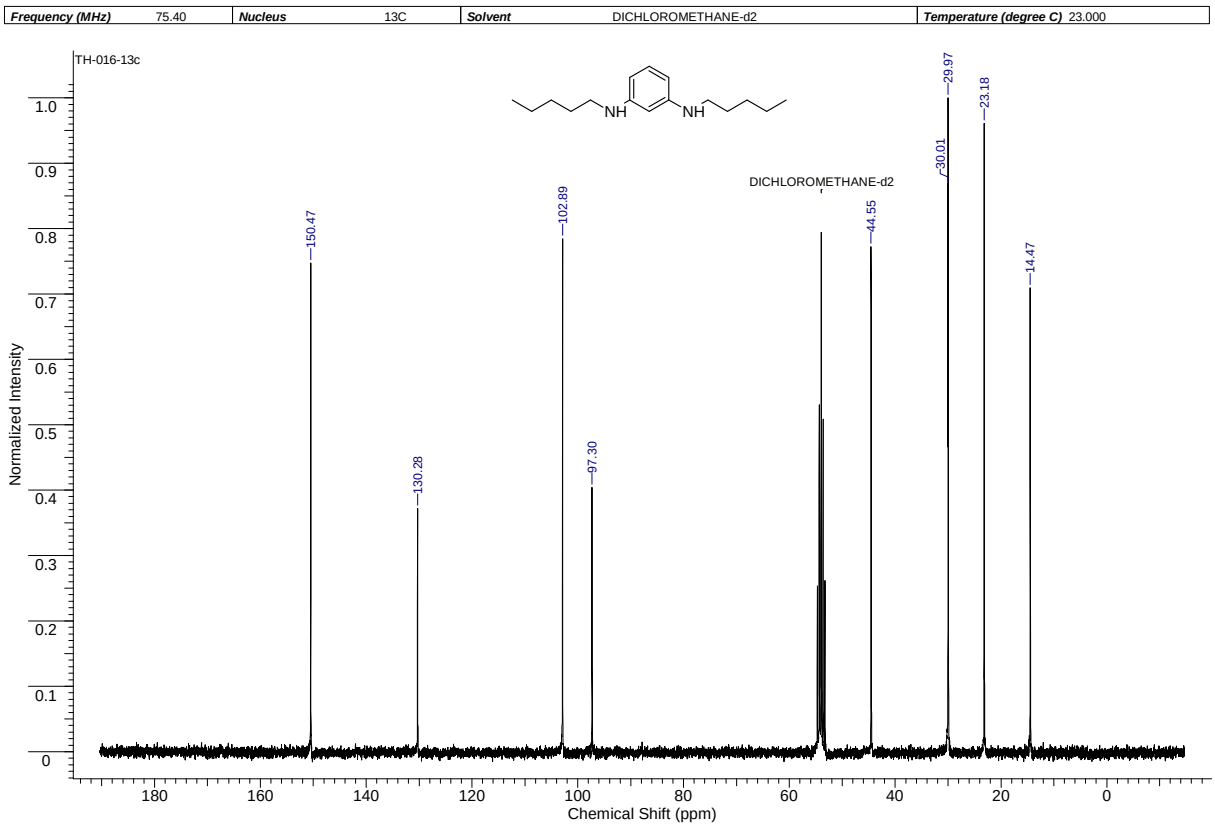

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-030-1h
NH
NH
O
O
DICHLOROMETHANE-d2
4.06
4.05
4.19
3.94
6.38
Normalized Intensity
Chemical Shift (ppm)

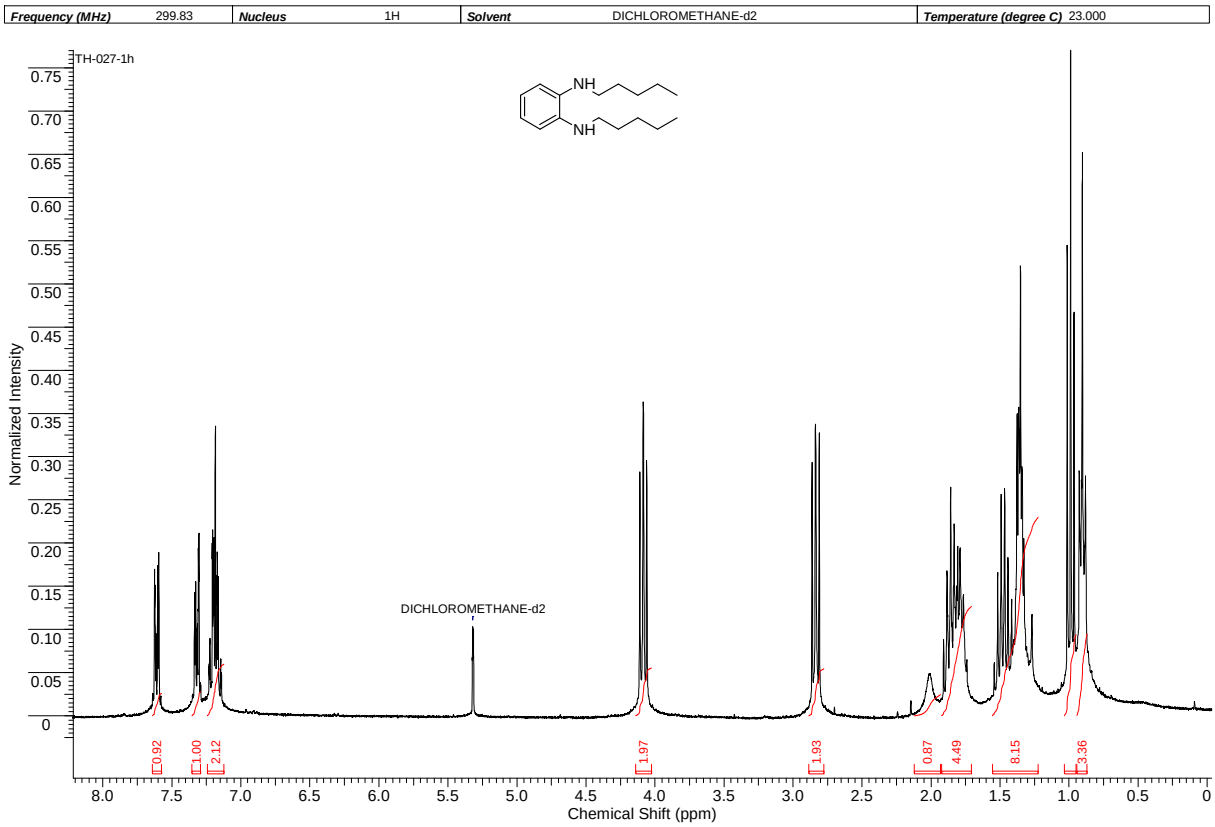

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-030-13c
DICHLOROMETHANE-d2
NH
NH
O
O
159.47
137.77
132.21
129.48
119.63
114.40
112.36
55.78
48.60
Normalized Intensity
Chemical Shift (ppm)

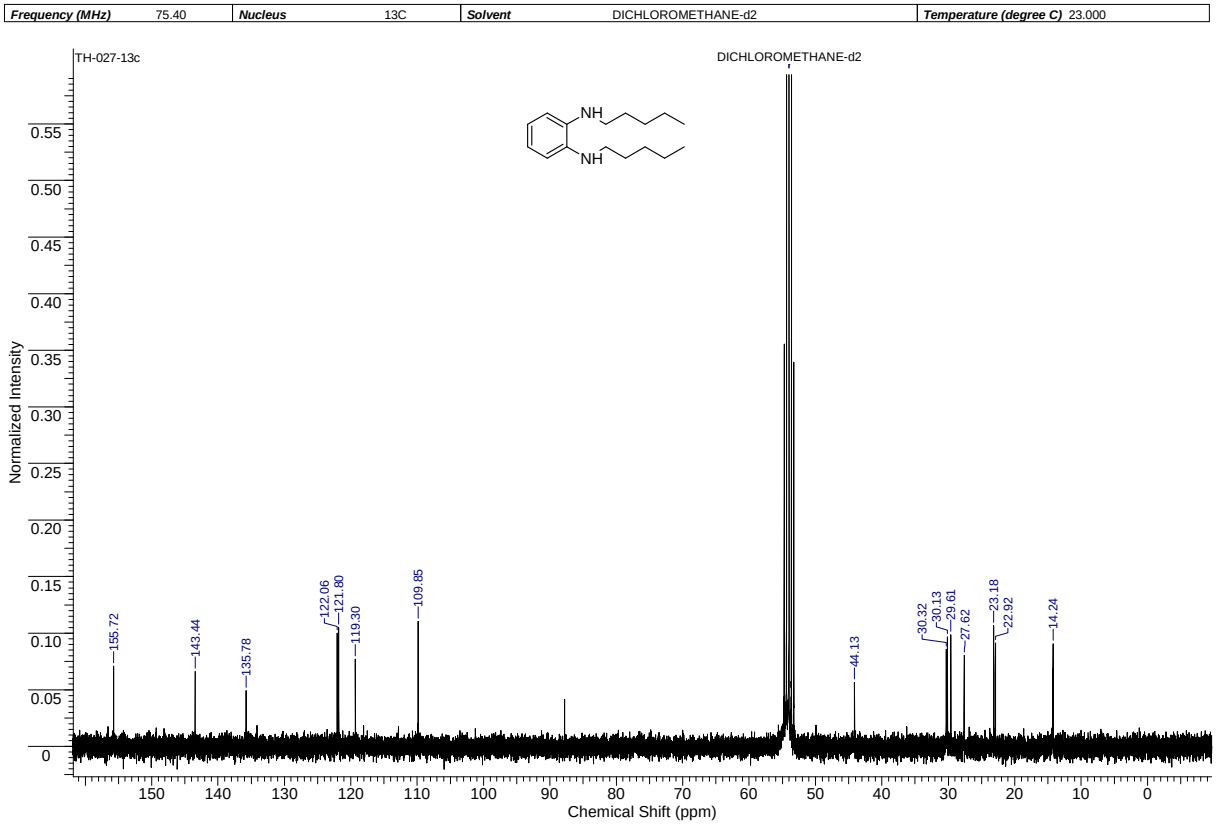

Frequency (MHz) 399.81
Nucleus 1H
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-012-1h
CHLOROFORM-d
NH
NH
Normalized Intensity
Chemical Shift (ppm)
3.83
4.14
4.00
8.36
6.16

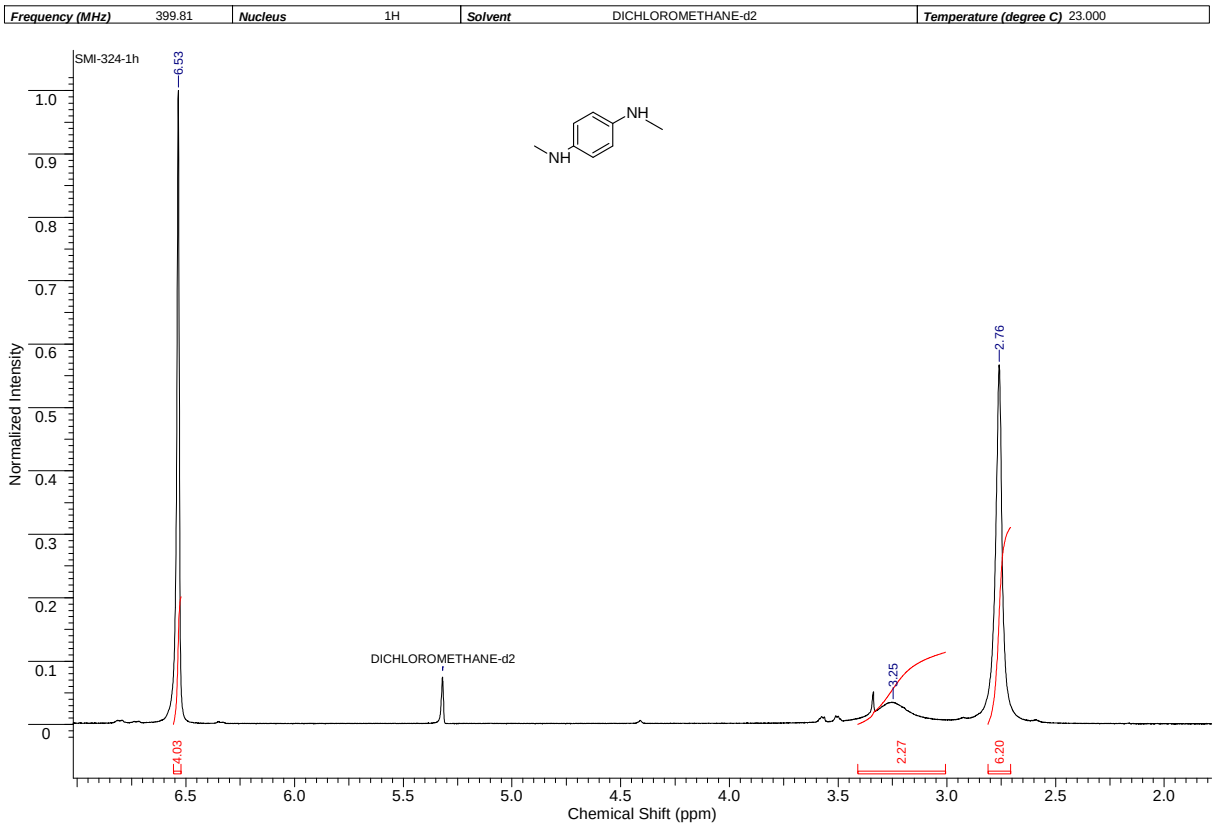

Frequency (MHz) 100.54
Nucleus 13C
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-012-13c
CHLOROFORM-d
NH
NH
Normalized Intensity
Chemical Shift (ppm)
115.43
112.47
45.95
29.28
22.46
14.02

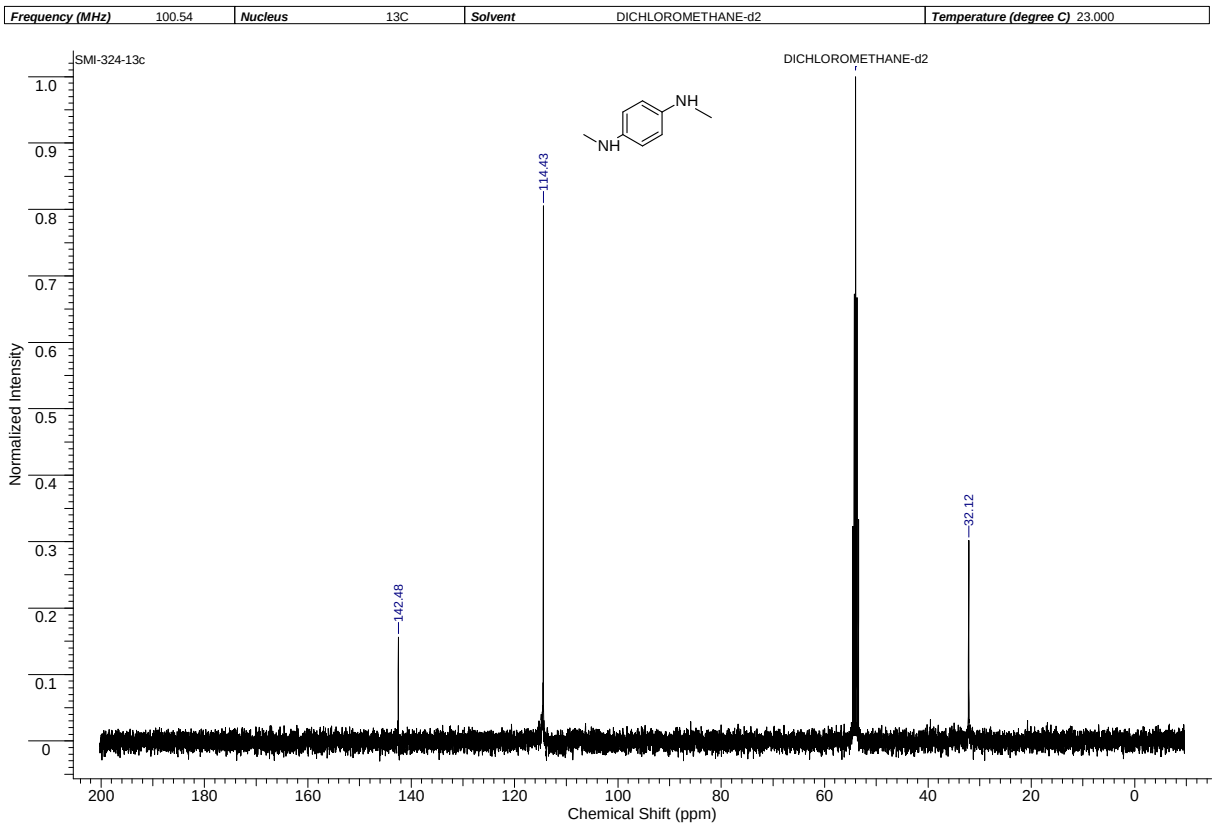

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-016-1h
NH
NH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

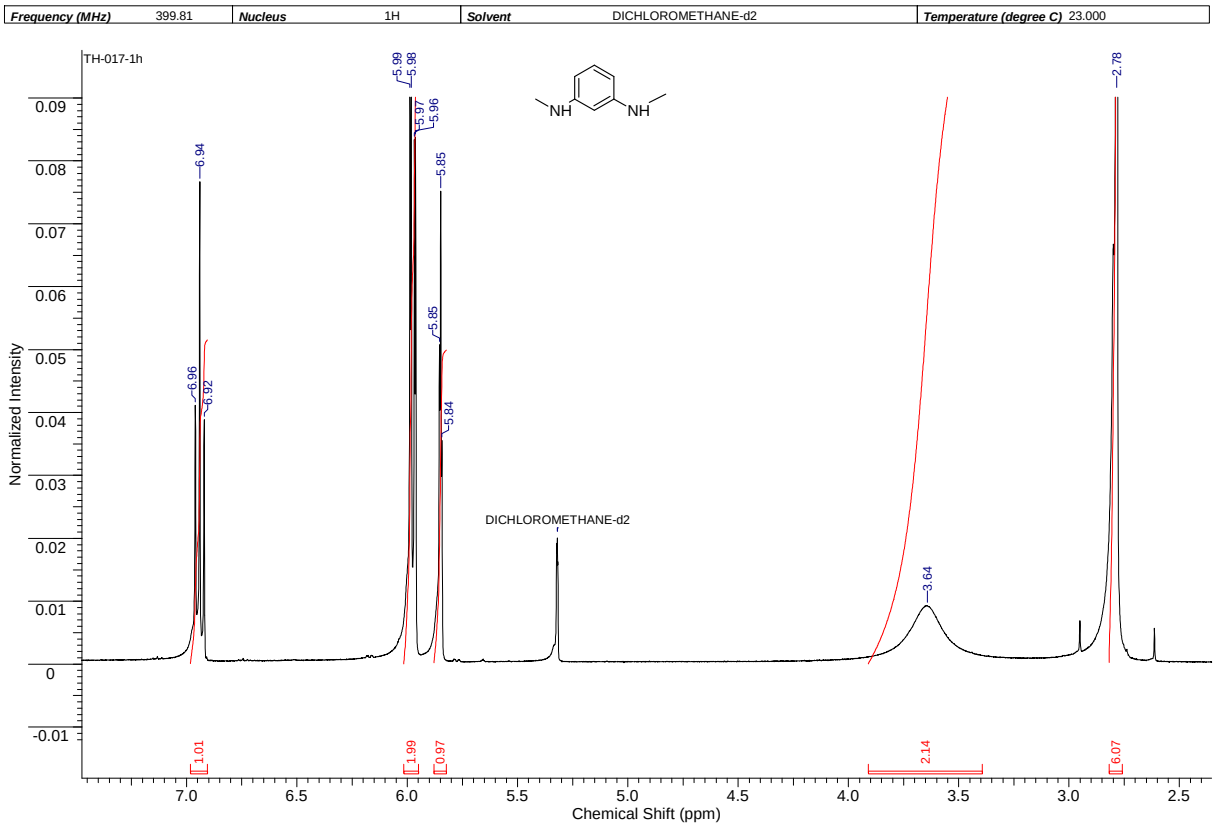

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-016-13c
NH
NH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

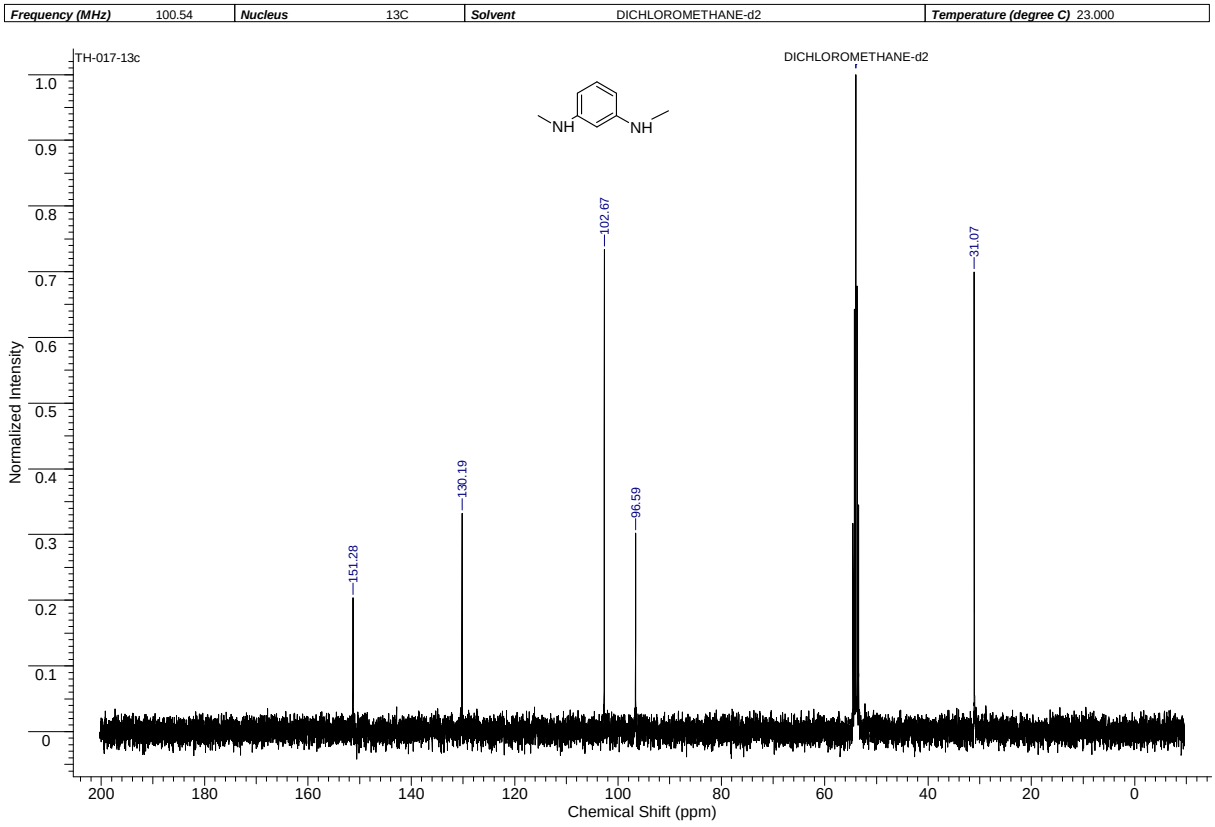

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-027-1h
NH
NH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)
0.92
1.00
2.12
1.97
1.93
0.87
4.49
8.15
3.36

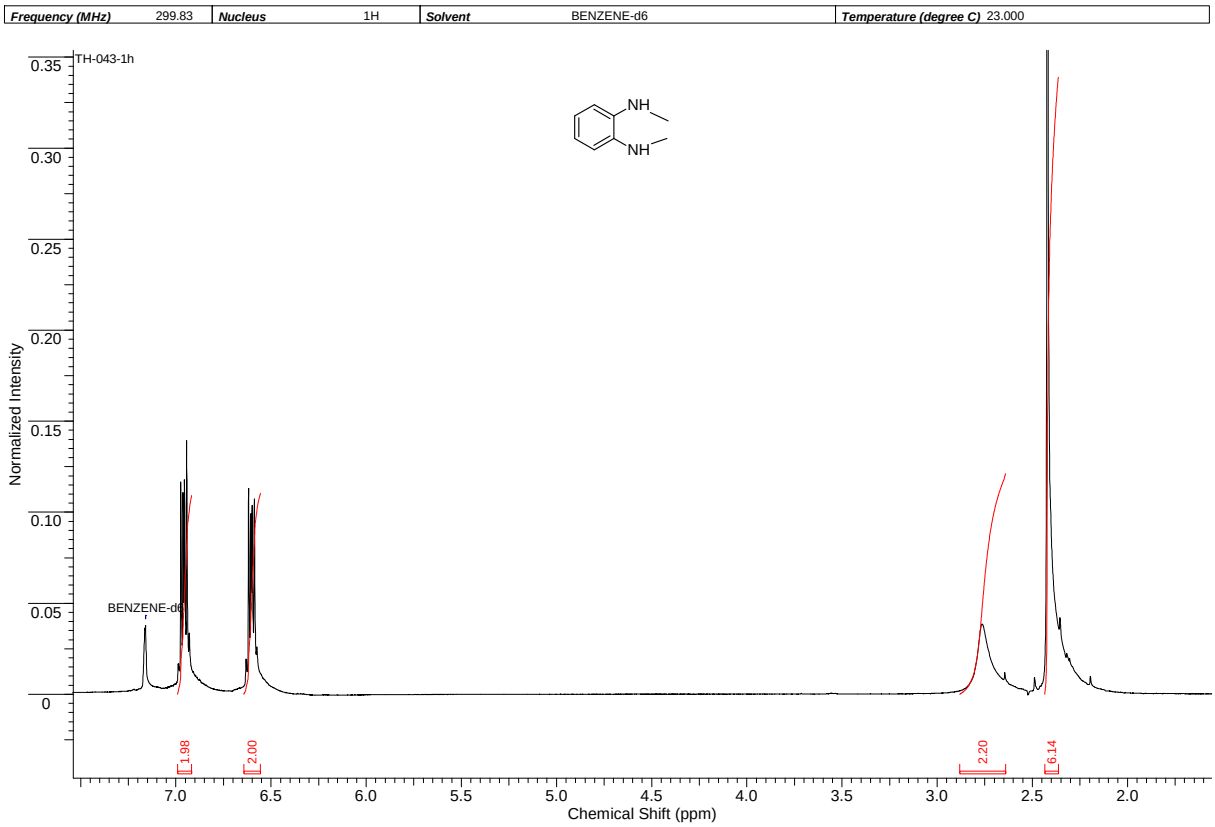

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-027-13c
DICHLOROMETHANE-d2
NH
NH
Normalized Intensity
Chemical Shift (ppm)
155.72
143.44
135.78
122.06
121.80
119.30
109.85
44.13
30.32
30.13
29.61
27.62
23.18
22.92
14.24

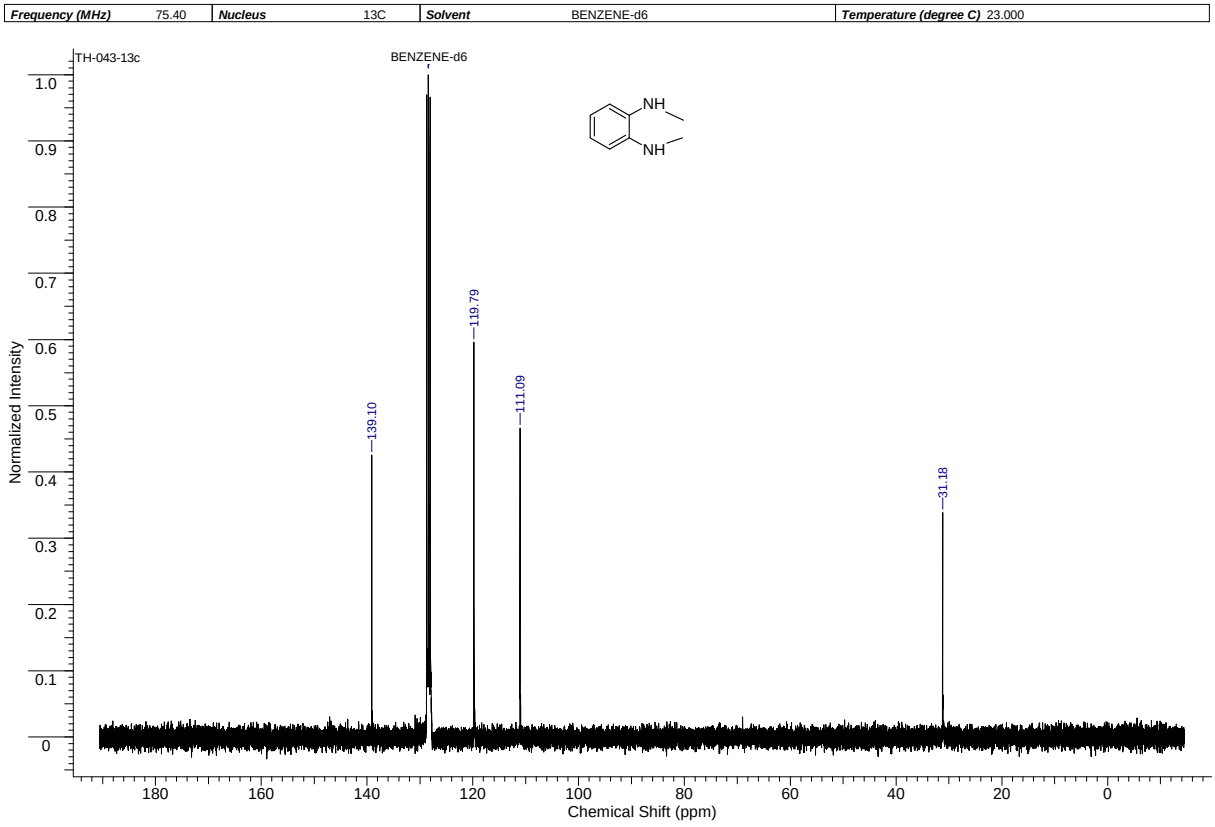

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-324-1h
6.53
2.76
3.25
DICHLOROMETHANE-d2
4.03
2.27
6.20
NH
NH
Normalized Intensity
Chemical Shift (ppm)

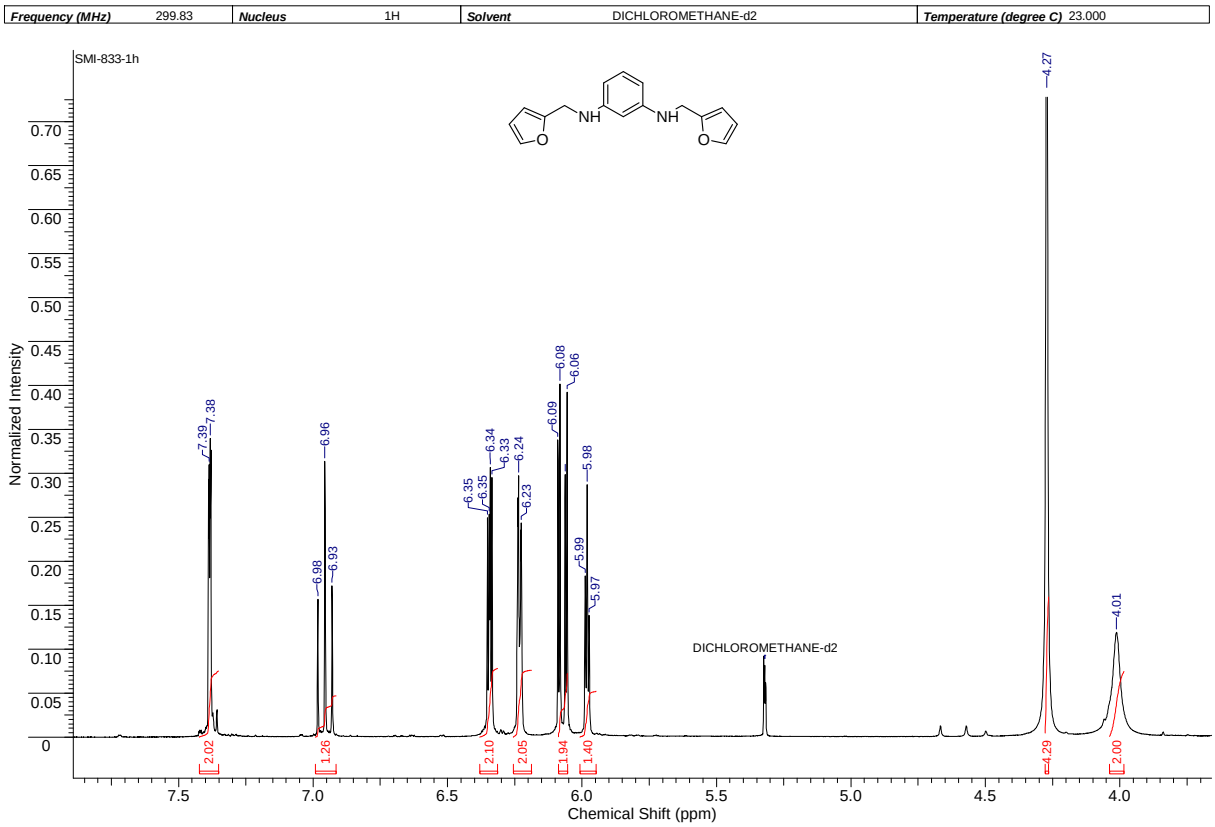

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-324-13c
DICHLOROMETHANE-d2
114.43
142.48
32.12
NH
NH
Normalized Intensity
Chemical Shift (ppm)

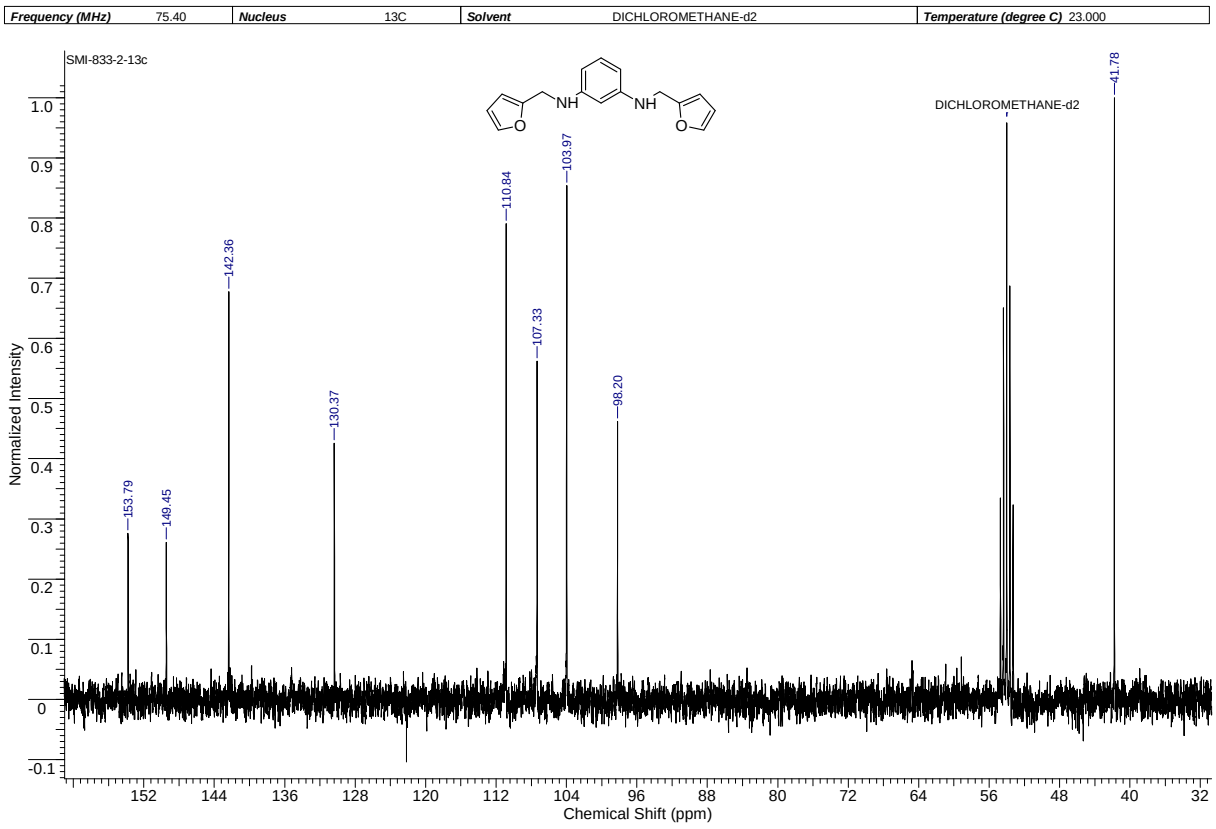

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-017-1h
NH
NH
6.94
6.96
6.92
5.99
5.98
5.97
5.96
5.85
5.85
5.84
DICHLOROMETHANE-d2
3.64
2.78
1.01
1.99
0.97
2.14
6.07
Normalized Intensity
Chemical Shift (ppm)

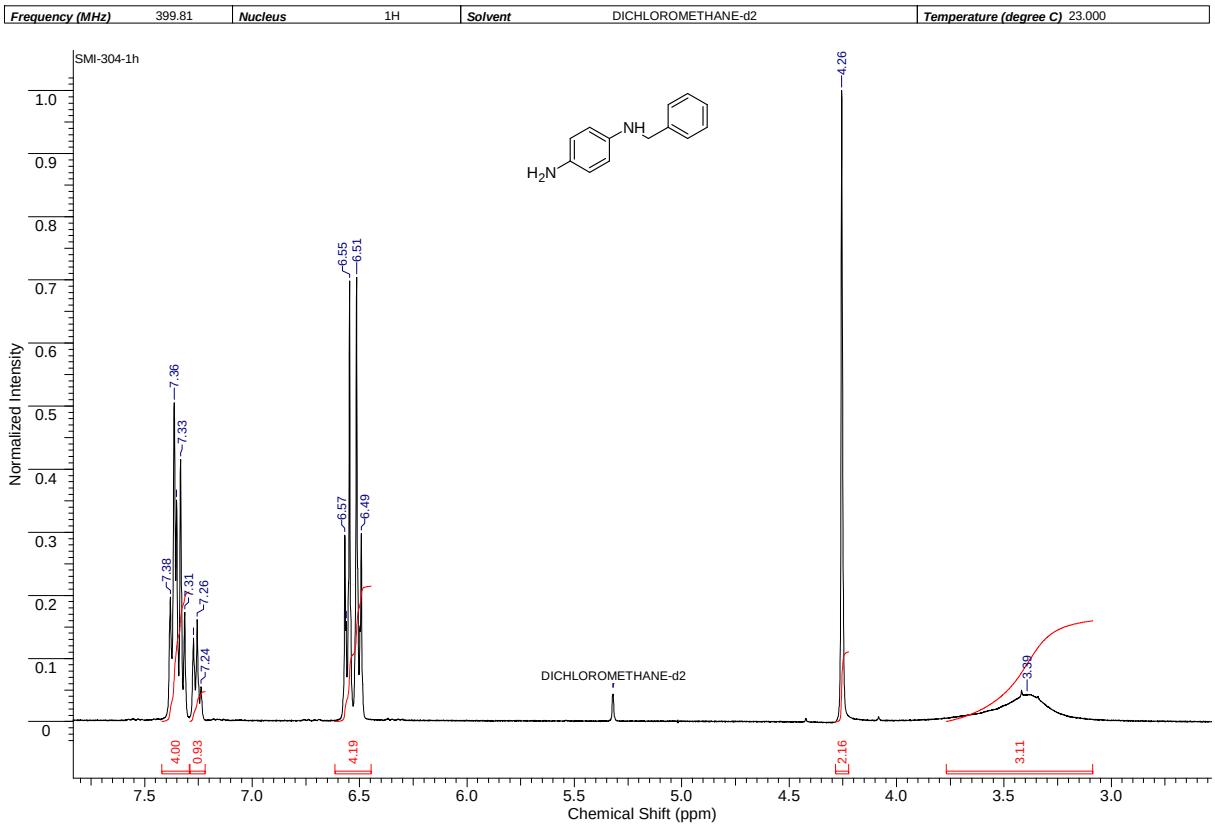

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-017-13c
NH
NH
DICHLOROMETHANE-d2
102.67
31.07
130.19
96.59
151.28
Normalized Intensity
Chemical Shift (ppm)

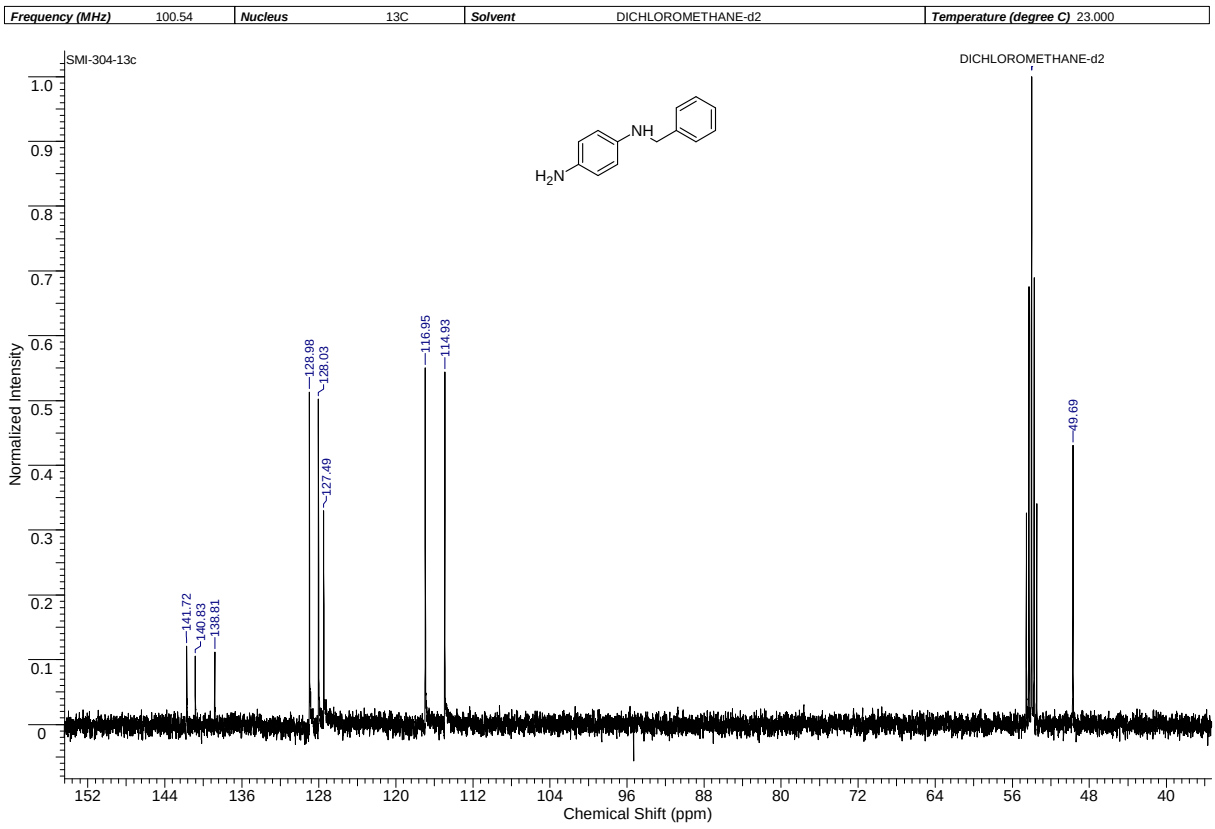

Frequency (MHz) 299.83
Nucleus 1H
Solvent BENZENE-d6
Temperature (degree C) 23.000
TH-043-1h
NH
NH
BENZENE-d6
Normalized Intensity
1.98
2.00
2.20
6.14
Chemical Shift (ppm)

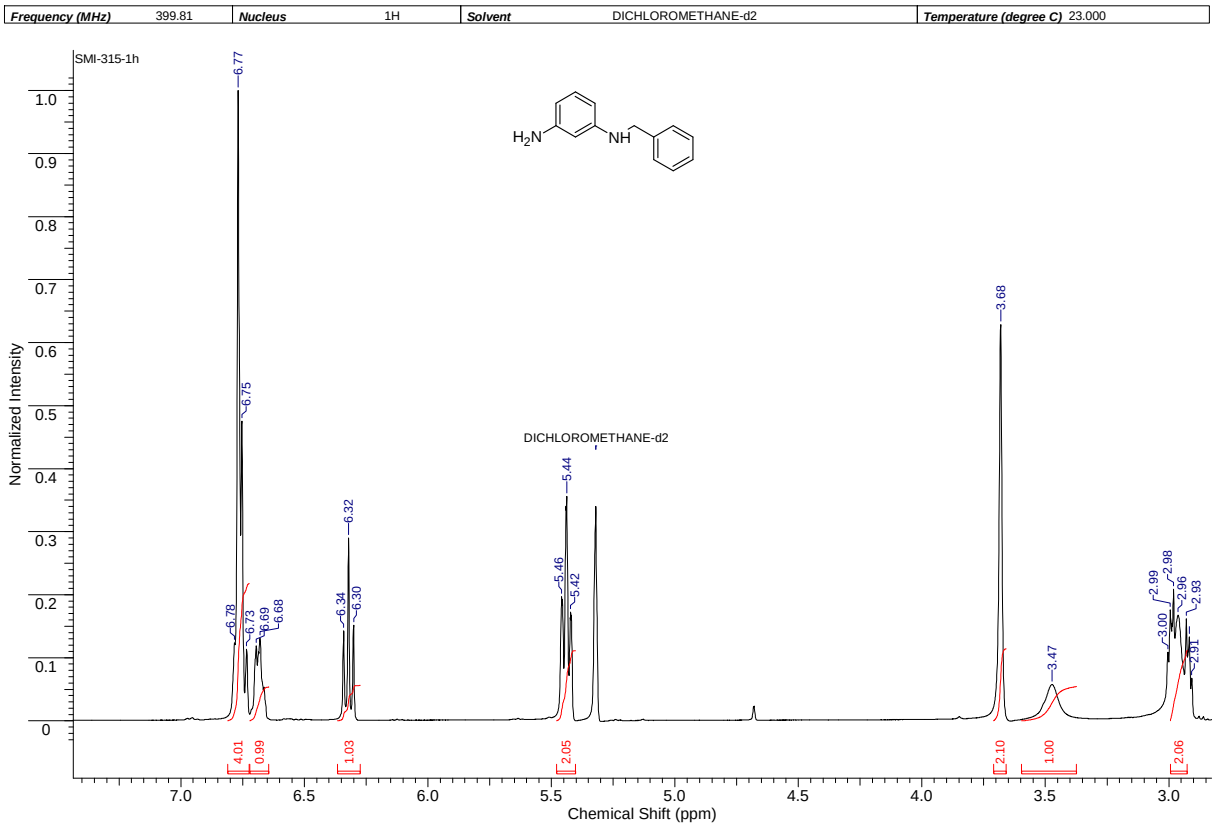

Frequency (MHz) 75.40
Nucleus 13C
Solvent BENZENE-d6
Temperature (degree C) 23.000
TH-043-13c
BENZENE-d6
NH
NH
139.10
119.79
111.09
31.18
Normalized Intensity
Chemical Shift (ppm)

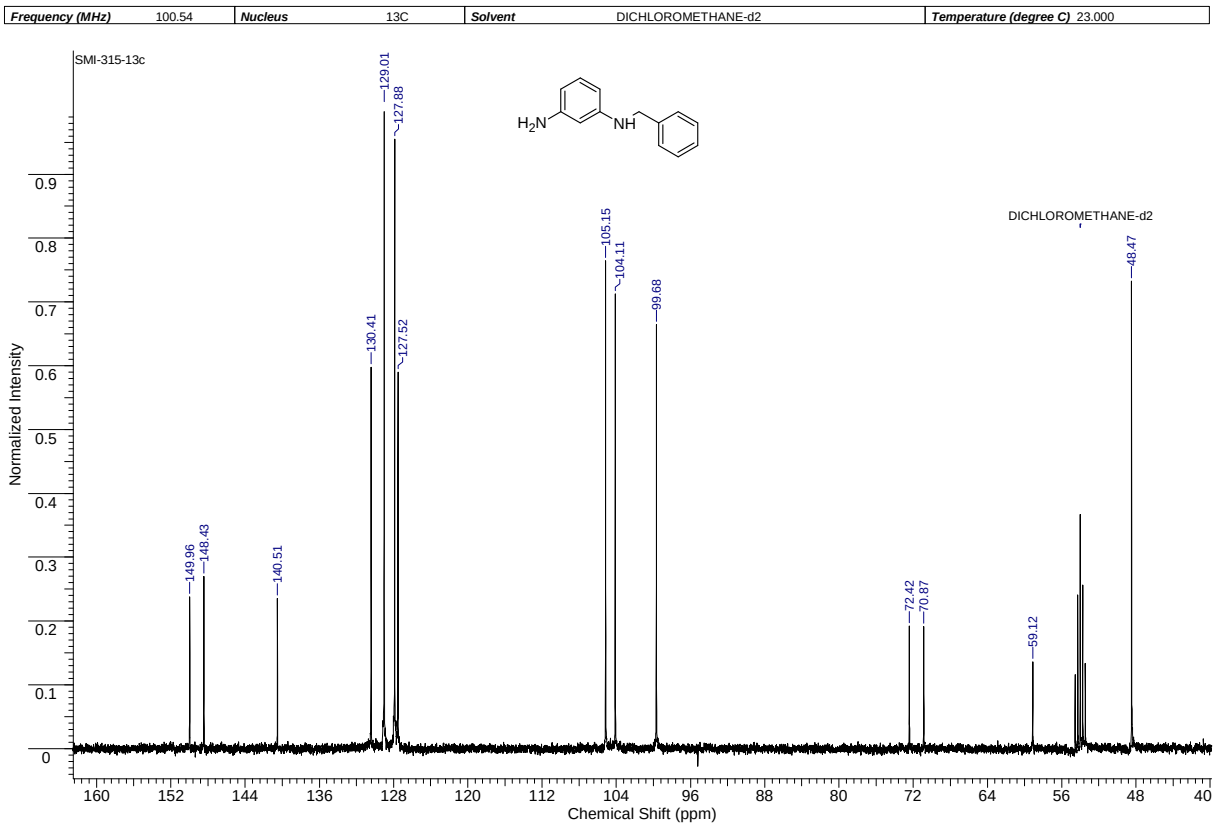

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-833-1h
NH
NH
O
O
4.27
7.39
7.38
6.96
6.98
6.93
6.35
6.35
6.34
6.33
6.24
6.23
6.08
6.06
6.09
5.98
5.99
5.97
DICHLOROMETHANE-d2
4.01
2.02
1.26
2.10
2.05
1.94
1.40
4.29
2.00
Normalized Intensity
Chemical Shift (ppm)

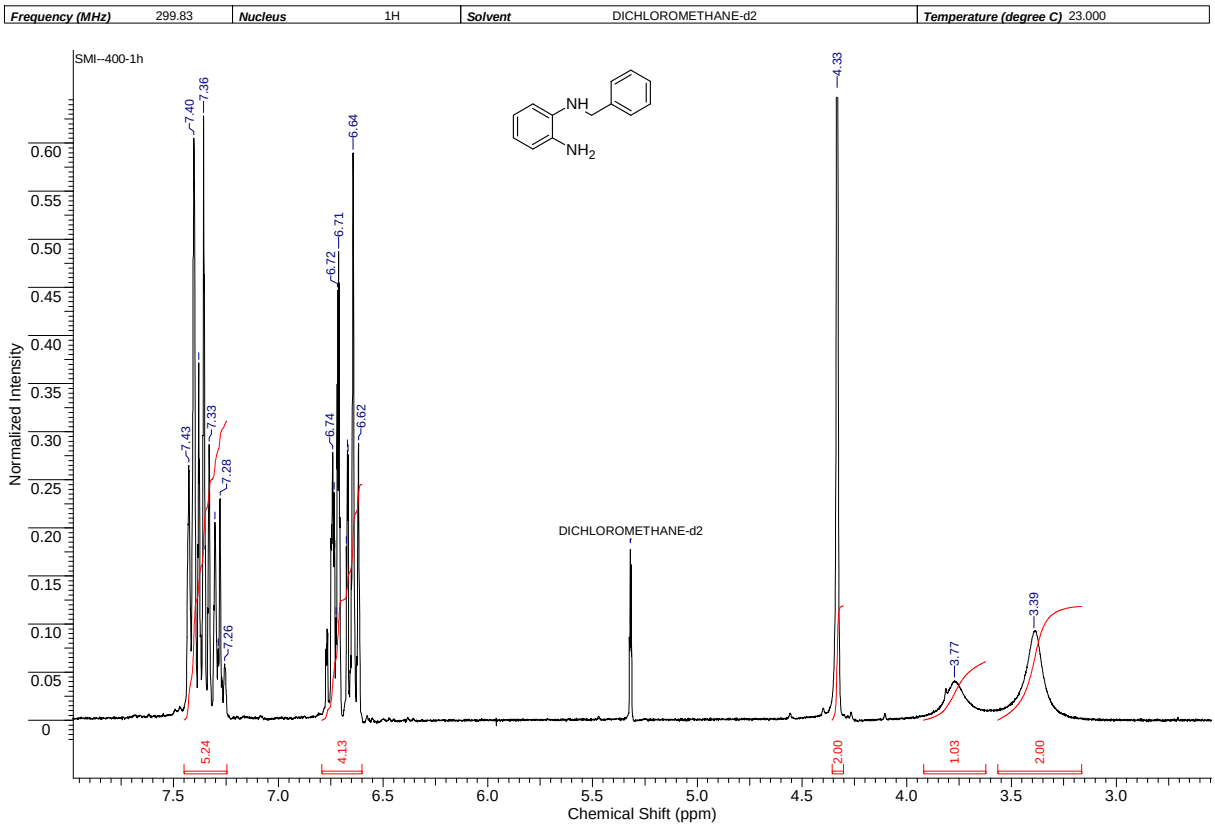

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-833-2-13c
NH
NH
O
O
DICHLOROMETHANE-d2
41.78
110.84
103.97
142.36
107.33
98.20
130.37
153.79
149.45
Normalized Intensity
Chemical Shift (ppm)

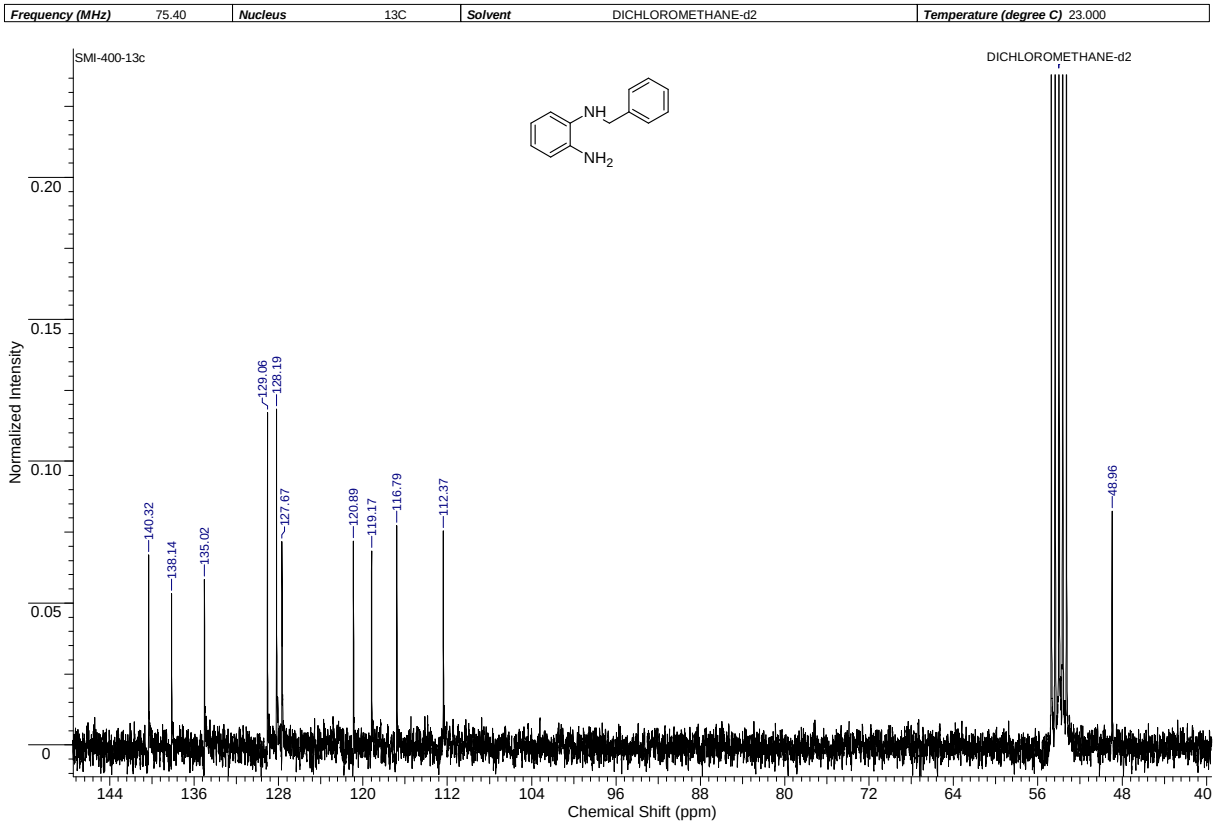

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-304-1h
NH
H2N
4.26
6.55
6.51
7.36
7.33
6.57
6.49
7.38
7.31
7.26
7.24
DICHLOROMETHANE-d2
3.39
4.00
0.93
4.19
2.16
3.11
Normalized Intensity
Chemical Shift (ppm)

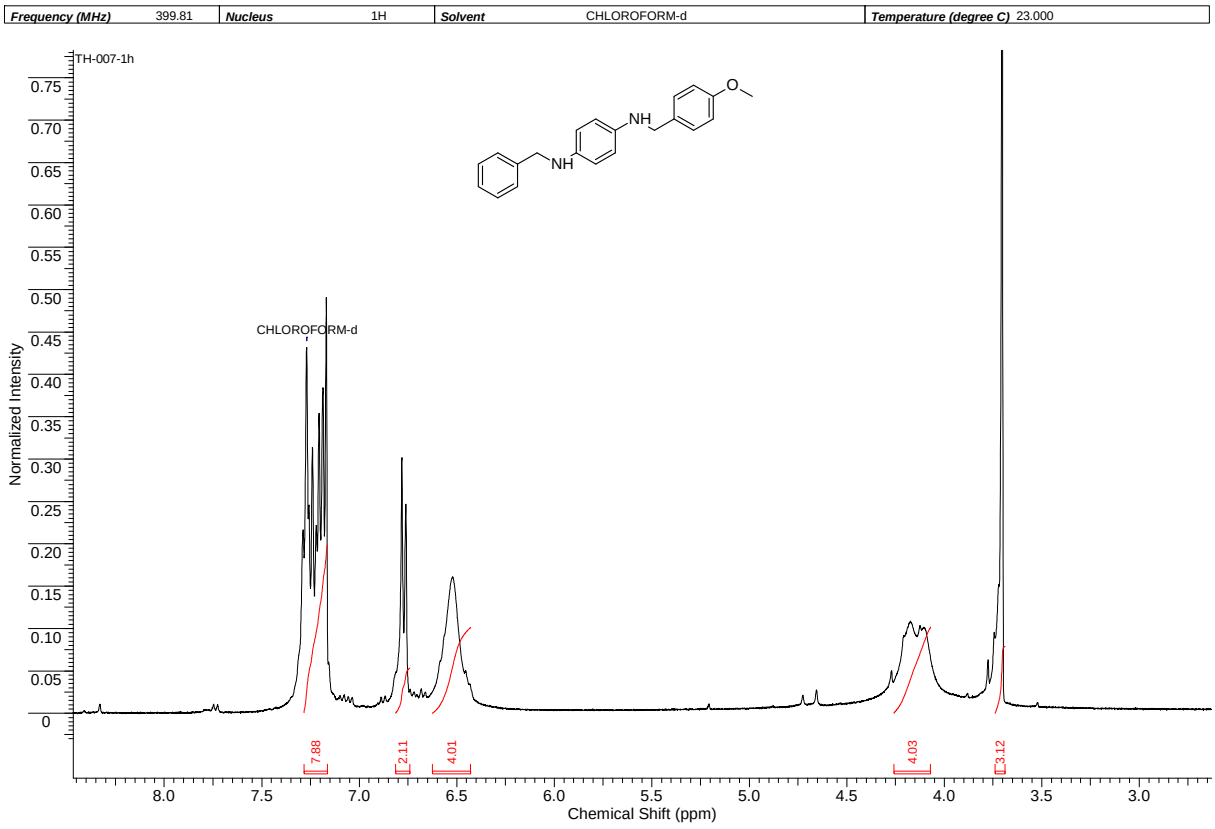

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-304-13c
DICHLOROMETHANE-d2
NH
H2N
128.98
128.03
116.95
114.93
127.49
49.69
141.72
140.83
138.81
Normalized Intensity
Chemical Shift (ppm)

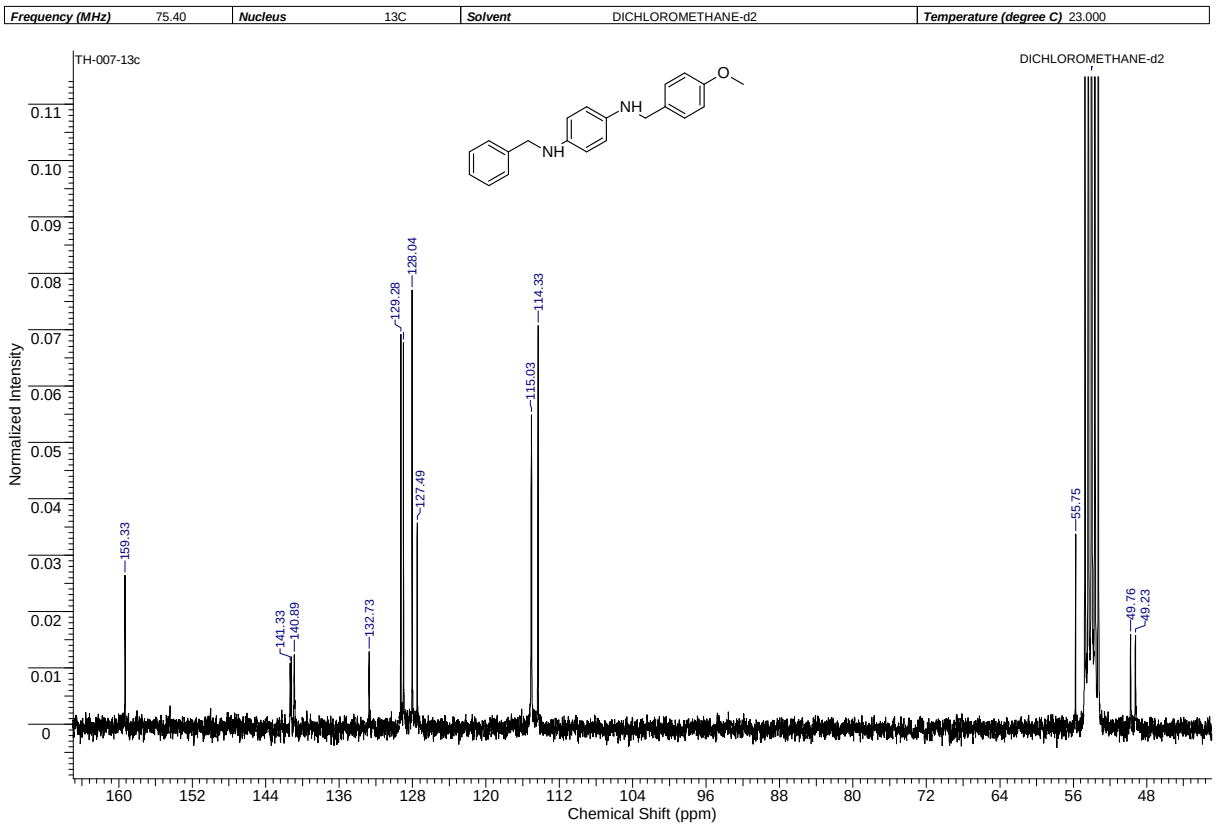

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-315-1h
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
6.77
6.75
6.78
6.73
6.69
6.68
6.34
6.32
6.30
5.46
5.44
5.42
3.68
3.47
2.99
2.98
2.96
2.93
3.00
2.91
4.01
0.99
1.03
2.05
2.10
1.00
2.06

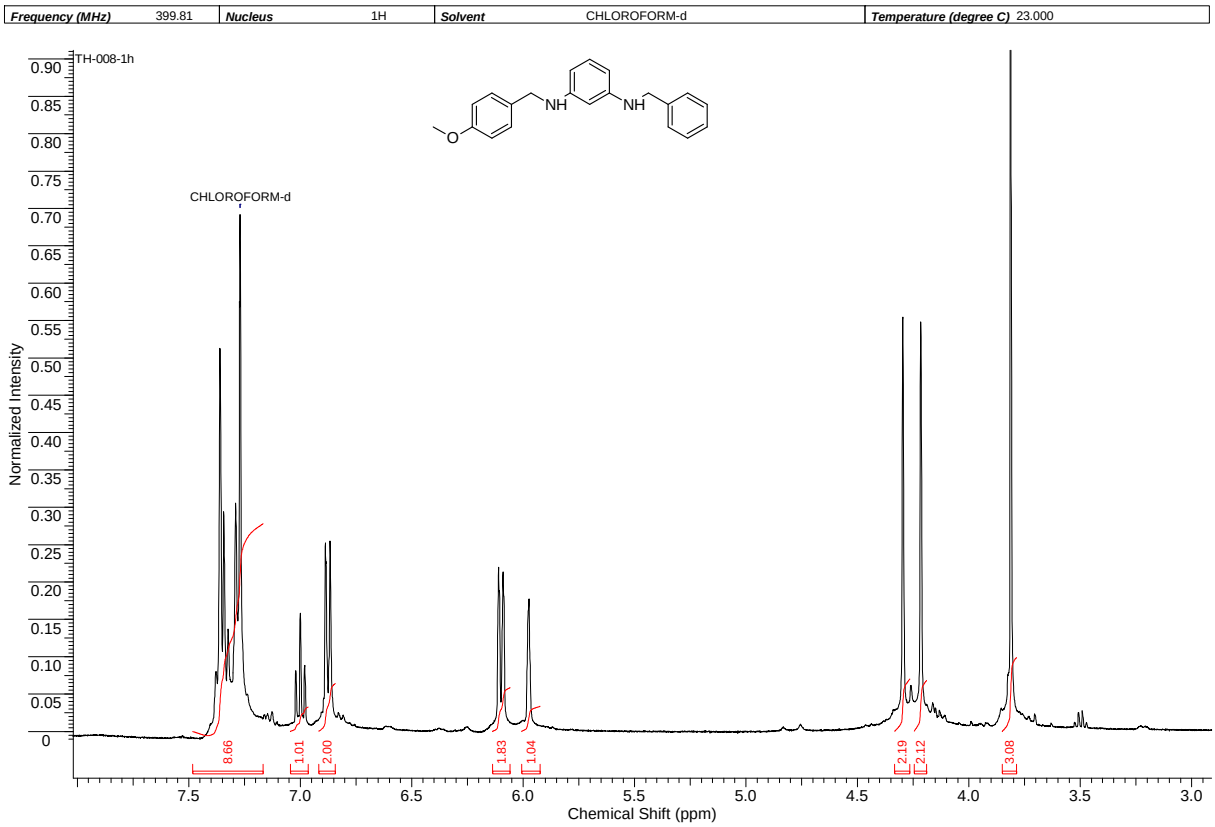

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-315-13c
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
129.01
127.88
130.41
127.52
105.15
104.11
99.68
48.47
149.96
148.43
140.51
72.42
70.87
59.12

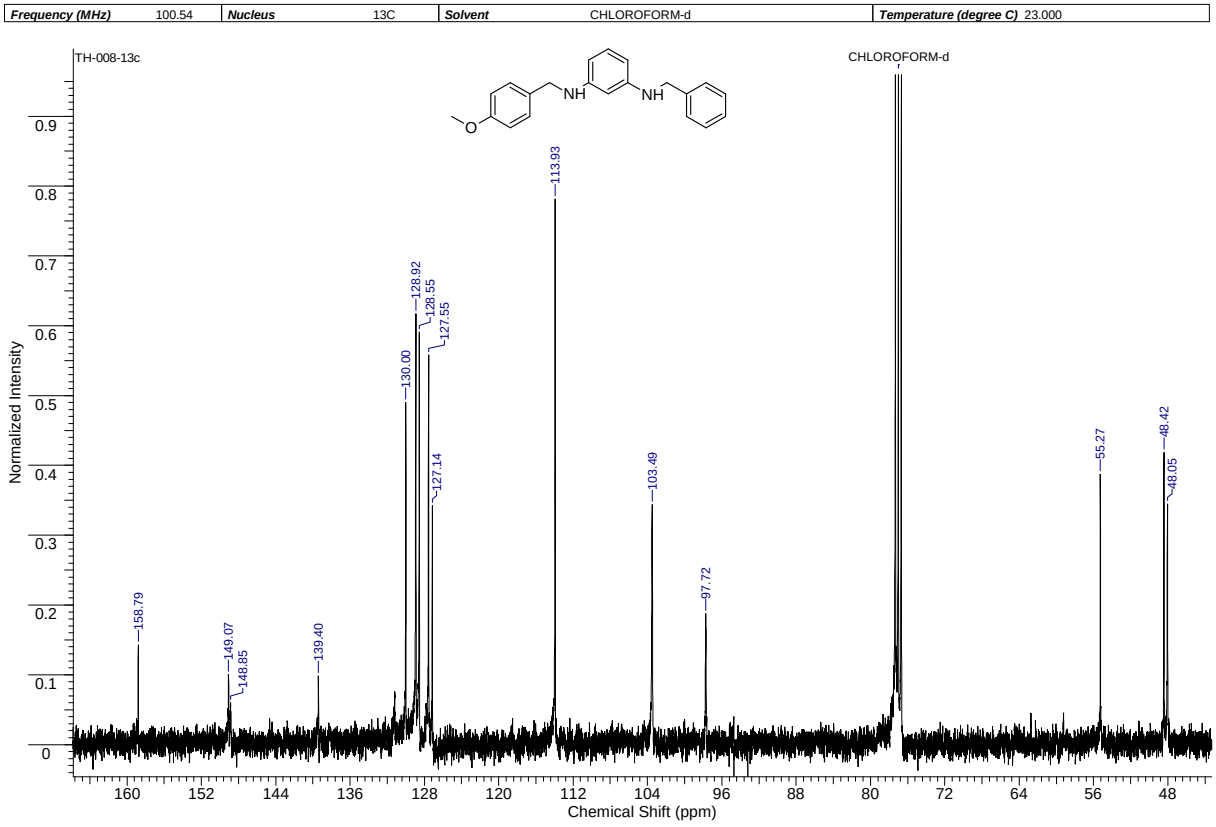

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI--400-1h
NH
NH2
DICHLOROMETHANE-d2
7.40
7.36
6.64
6.72
6.71
7.43
7.33
6.74
6.62
7.28
7.26
4.33
3.77
3.39
5.24
4.13
2.00
1.03
2.00
Normalized Intensity
Chemical Shift (ppm)

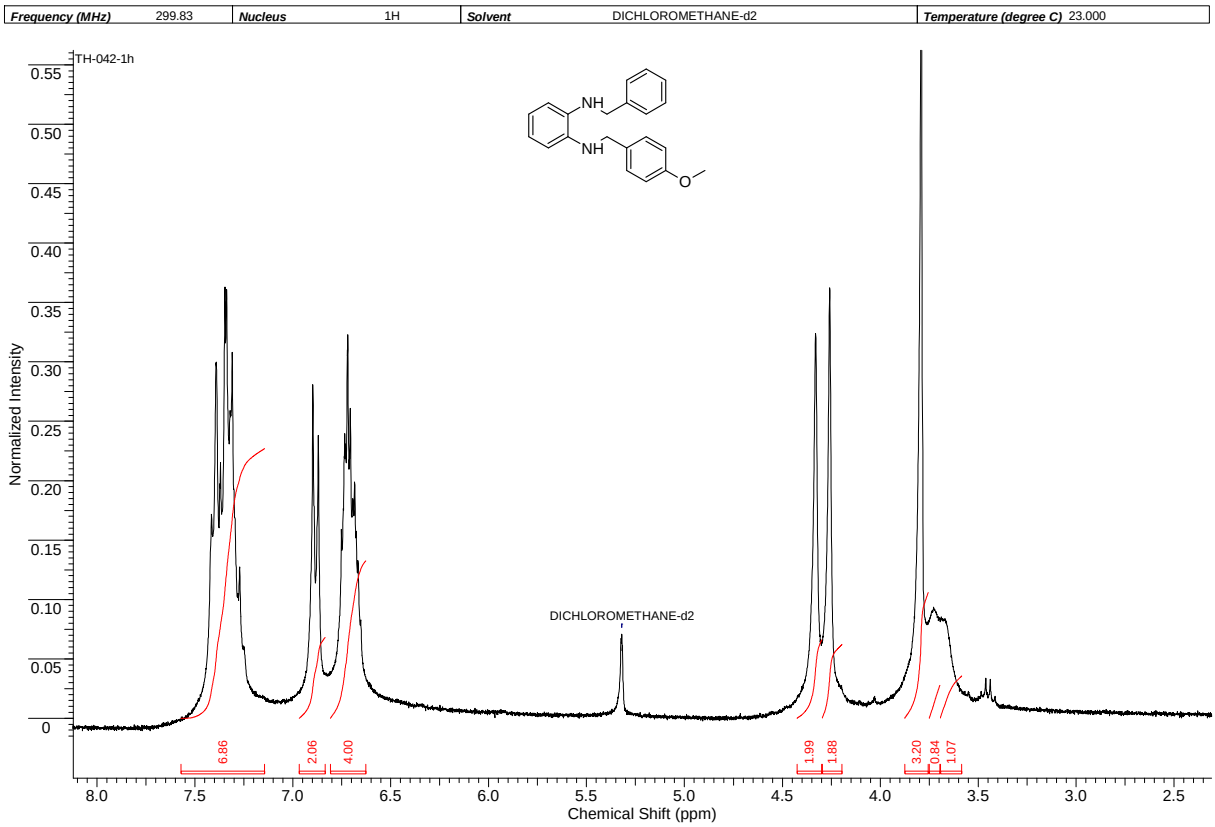

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-400-13c
NH
NH2
DICHLOROMETHANE-d2
129.06
128.19
140.32
138.14
135.02
127.67
120.89
119.17
116.79
112.37
48.96
Normalized Intensity
Chemical Shift (ppm)

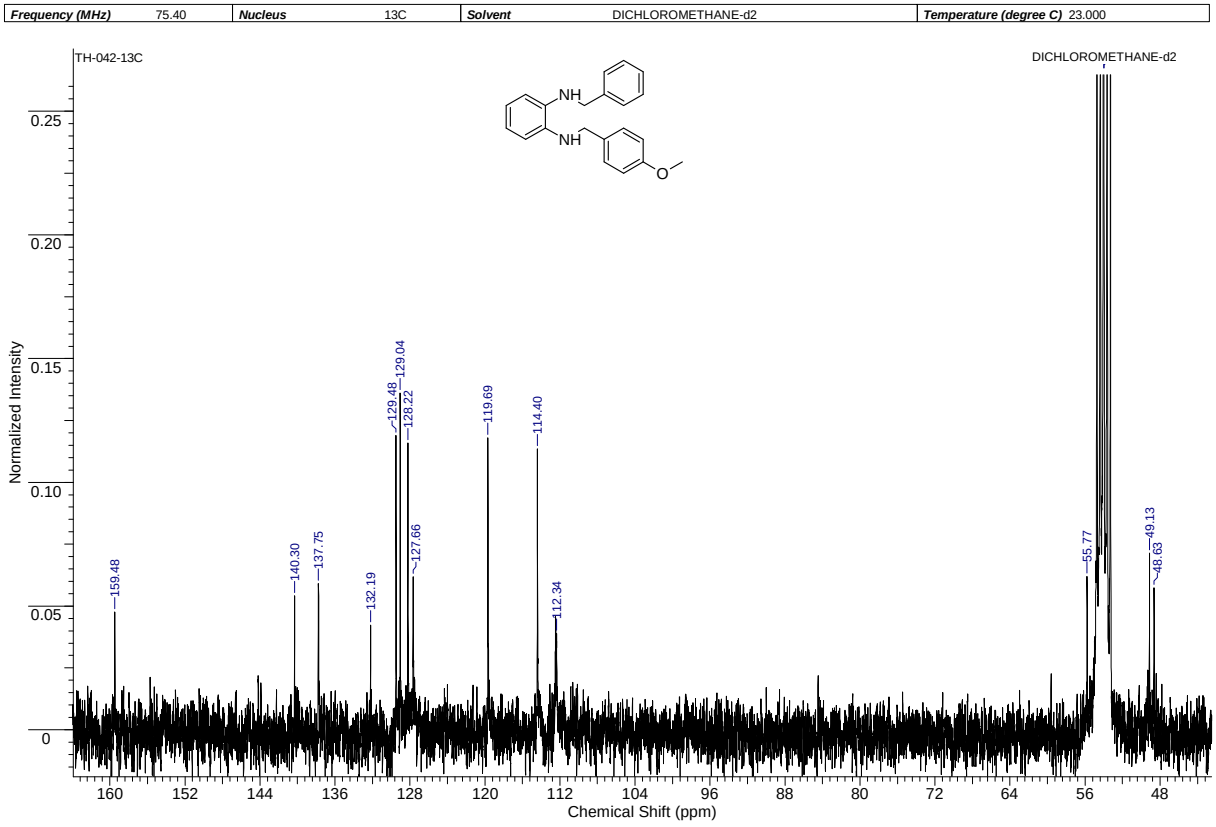

Frequency (MHz) 399.81
Nucleus 1H
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-007-1h
CHLOROFORM-d
7.88
2.11
4.01
4.03
3.12
Normalized Intensity
Chemical Shift (ppm)

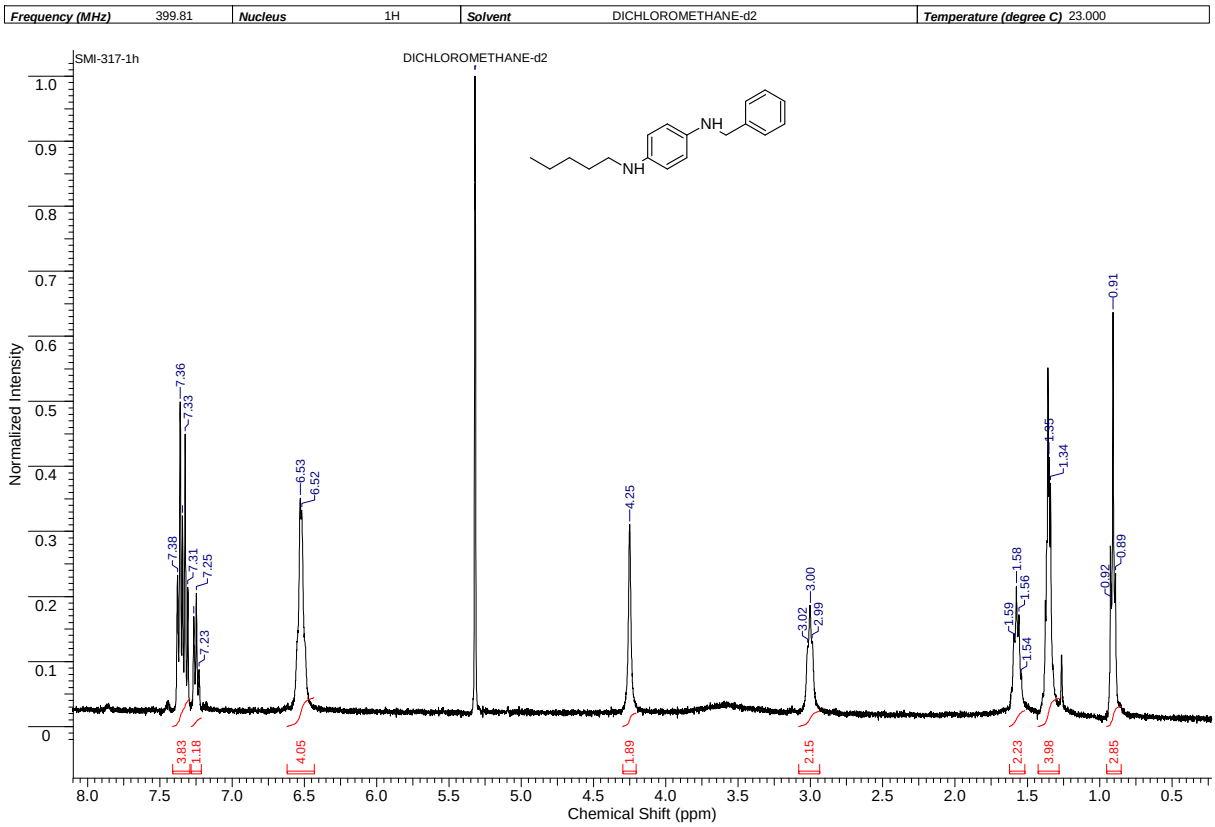

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-007-13c
DICHLOROMETHANE-d2
159.33
141.33
140.89
132.73
129.28
128.04
127.49
115.03
114.33
55.75
49.76
49.23
Normalized Intensity
Chemical Shift (ppm)

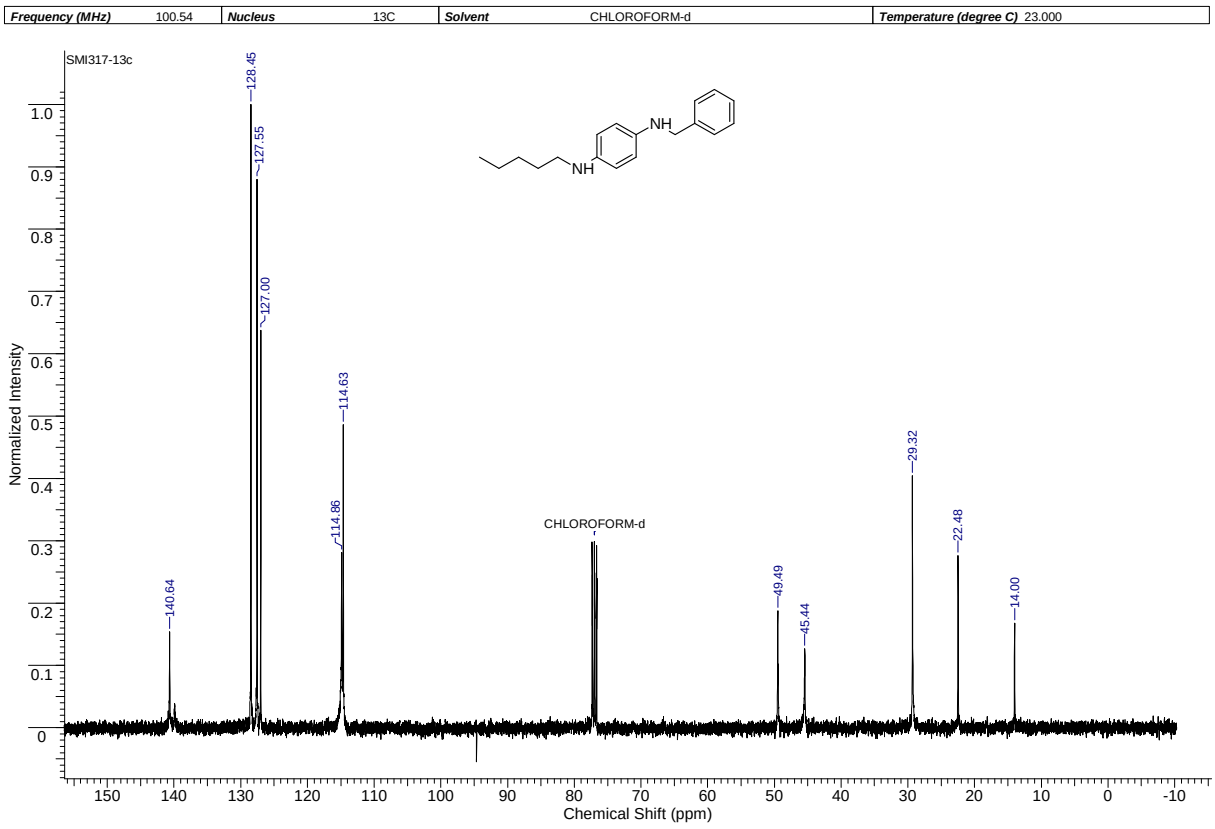

Frequency (MHz) 399.81
Nucleus 1H
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-008-1h
CHLOROFORM-d
NH
NH
O
Normalized Intensity
Chemical Shift (ppm)
8.66
1.01
2.00
1.83
1.04
2.19
2.12
3.08

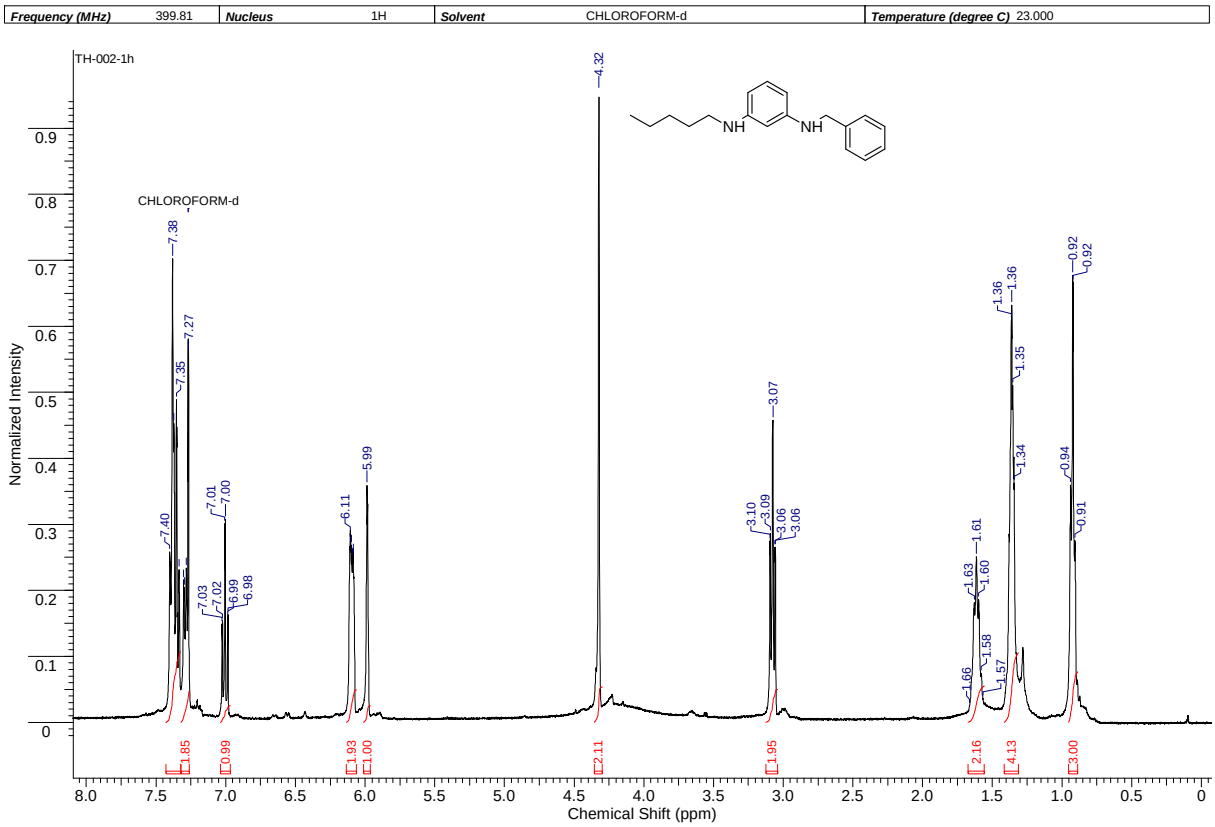

Frequency (MHz) 100.54
Nucleus 13C
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-008-13c
CHLOROFORM-d
NH
NH
O
Normalized Intensity
Chemical Shift (ppm)
158.79
149.07
148.85
139.40
130.00
128.92
128.55
127.55
127.14
113.93
103.49
97.72
55.27
48.42
48.05

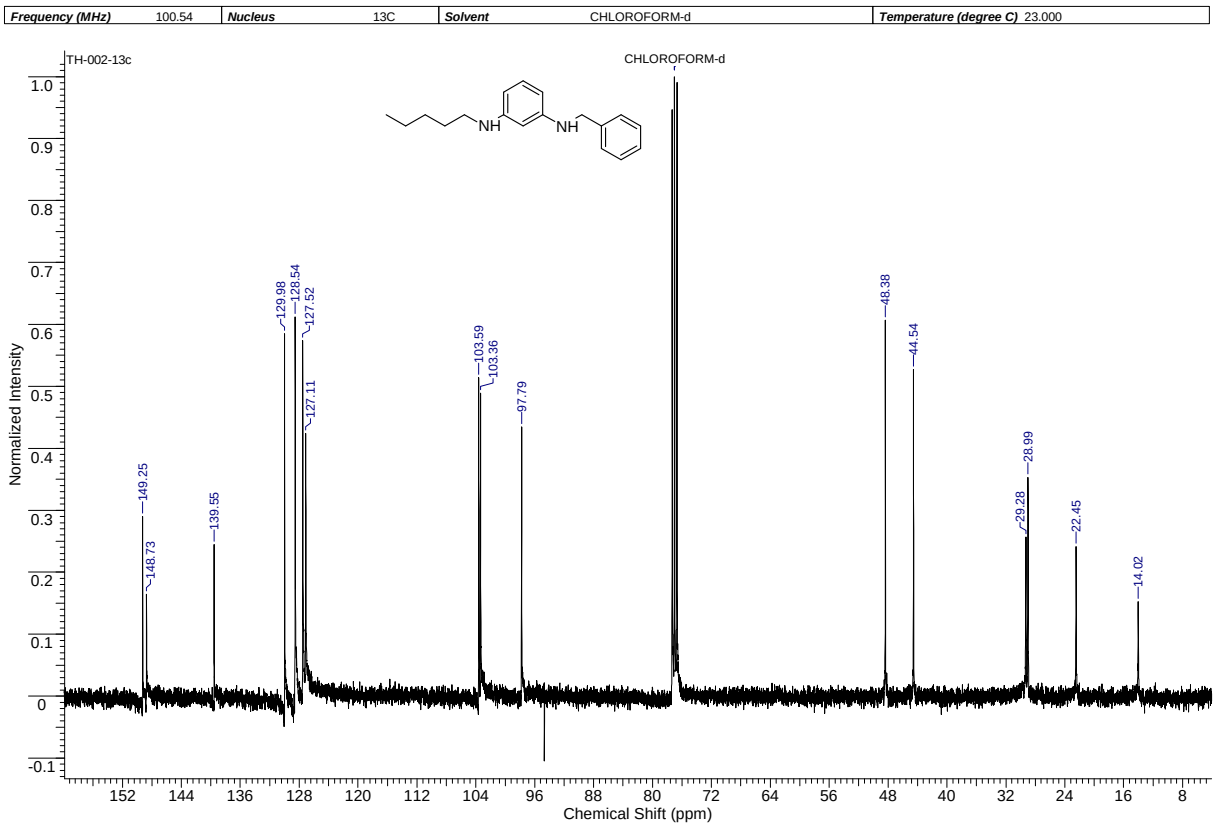

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-042-1h
NH
NH
O
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)
6.86
2.06
4.00
1.99
1.88
3.20
0.84
1.07

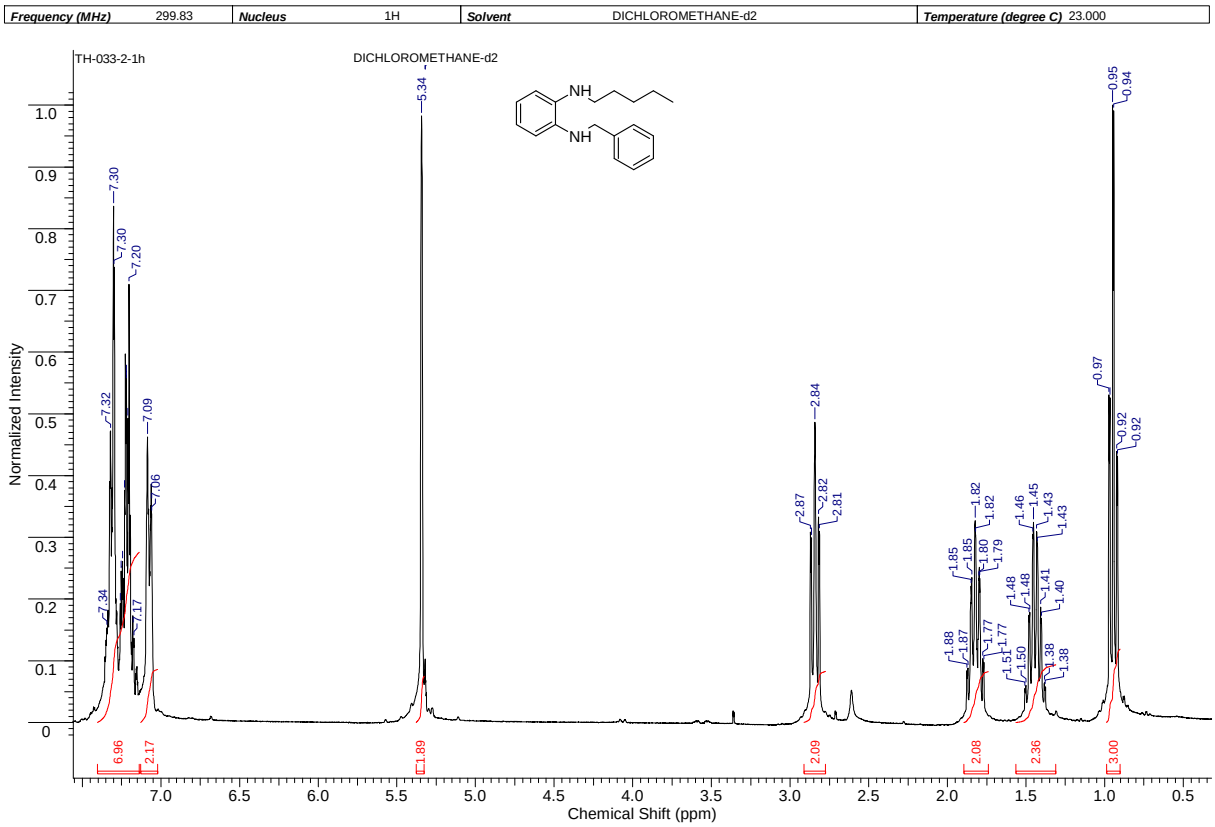

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-042-13C
DICHLOROMETHANE-d2
NH
NH
O
Normalized Intensity
Chemical Shift (ppm)
159.48
140.30
137.75
132.19
129.48
129.04
128.22
127.66
119.69
114.40
112.34
55.77
49.13
48.63

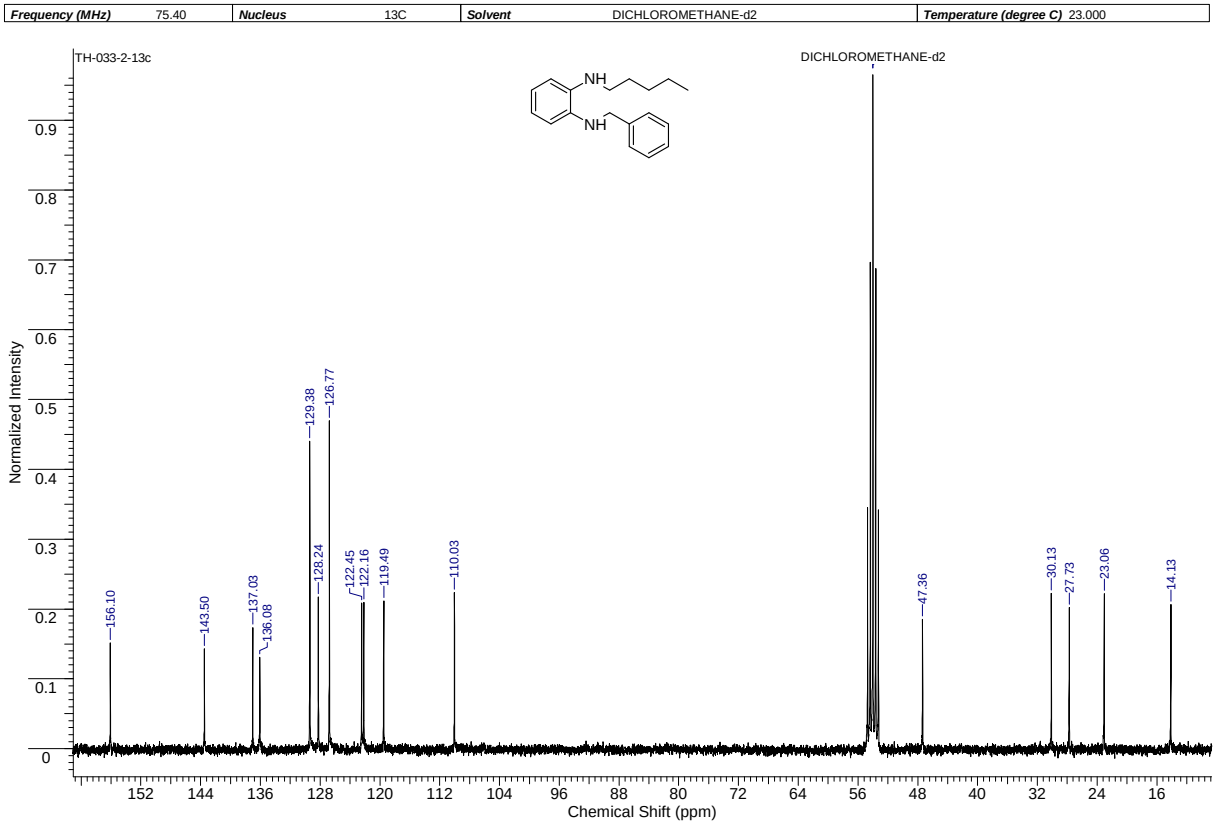

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-317-1h
DICHLOROMETHANE-d2
NH
NH
Normalized Intensity
Chemical Shift (ppm)
7.38
7.36
7.33
7.31
7.25
7.23
6.53
6.52
4.25
3.02
3.00
2.99
1.59
1.58
1.56
1.54
1.35
1.34
0.92
0.91
0.89
3.83
1.18
4.05
1.89
2.15
2.23
3.98
2.85

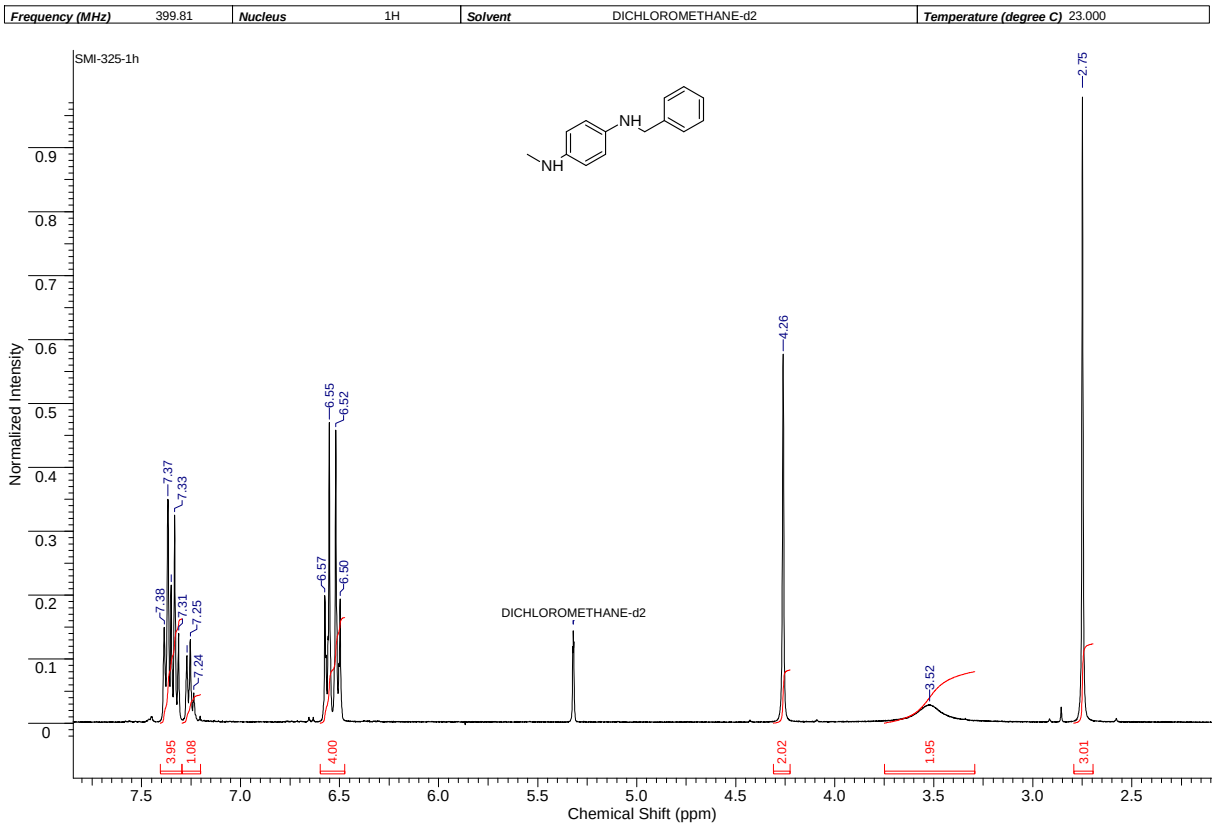

Frequency (MHz) 100.54
Nucleus 13C
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
SMI317-13c
NH
NH
Normalized Intensity
Chemical Shift (ppm)
CHLOROFORM-d
128.45
127.55
127.00
114.63
114.86
140.64
49.49
45.44
29.32
22.48
14.00

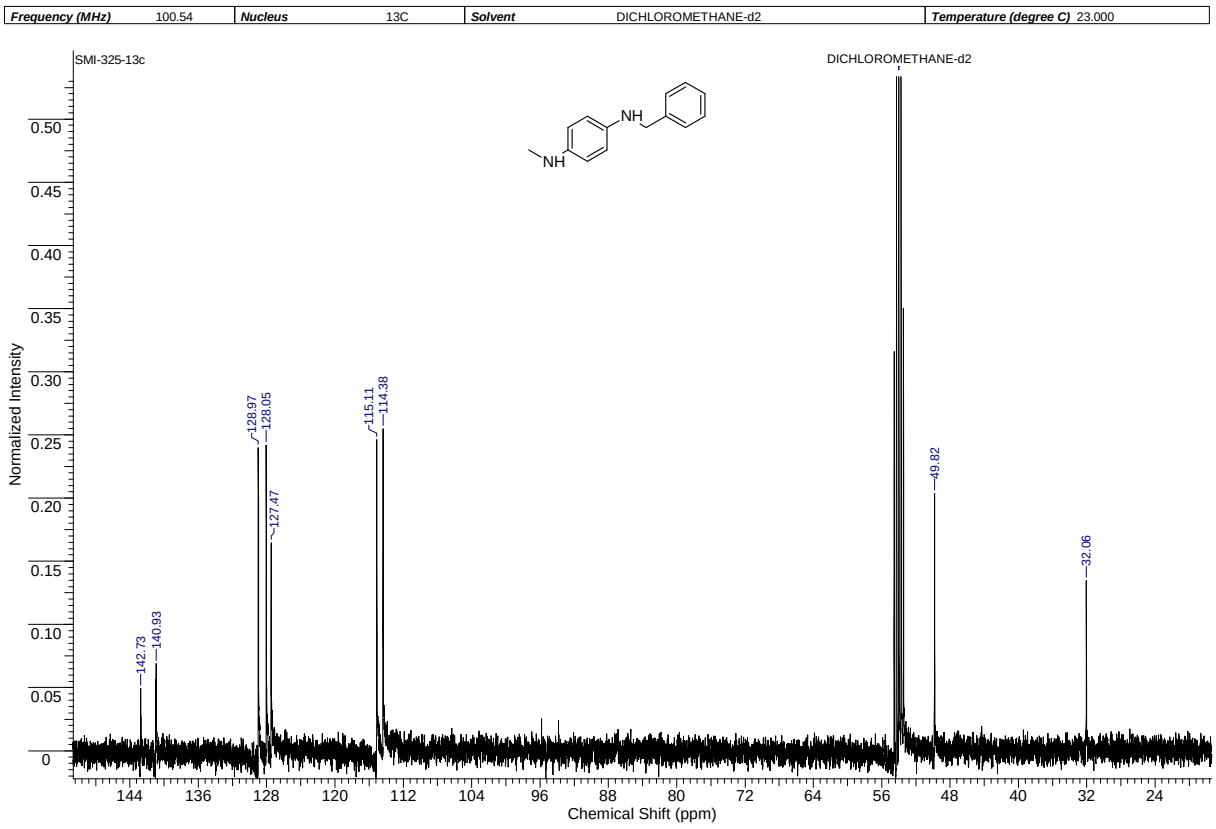

Frequency (MHz) 399.81
Nucleus 1H
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-002-1h
CHLOROFORM-d
NH
NH
Normalized Intensity
Chemical Shift (ppm)

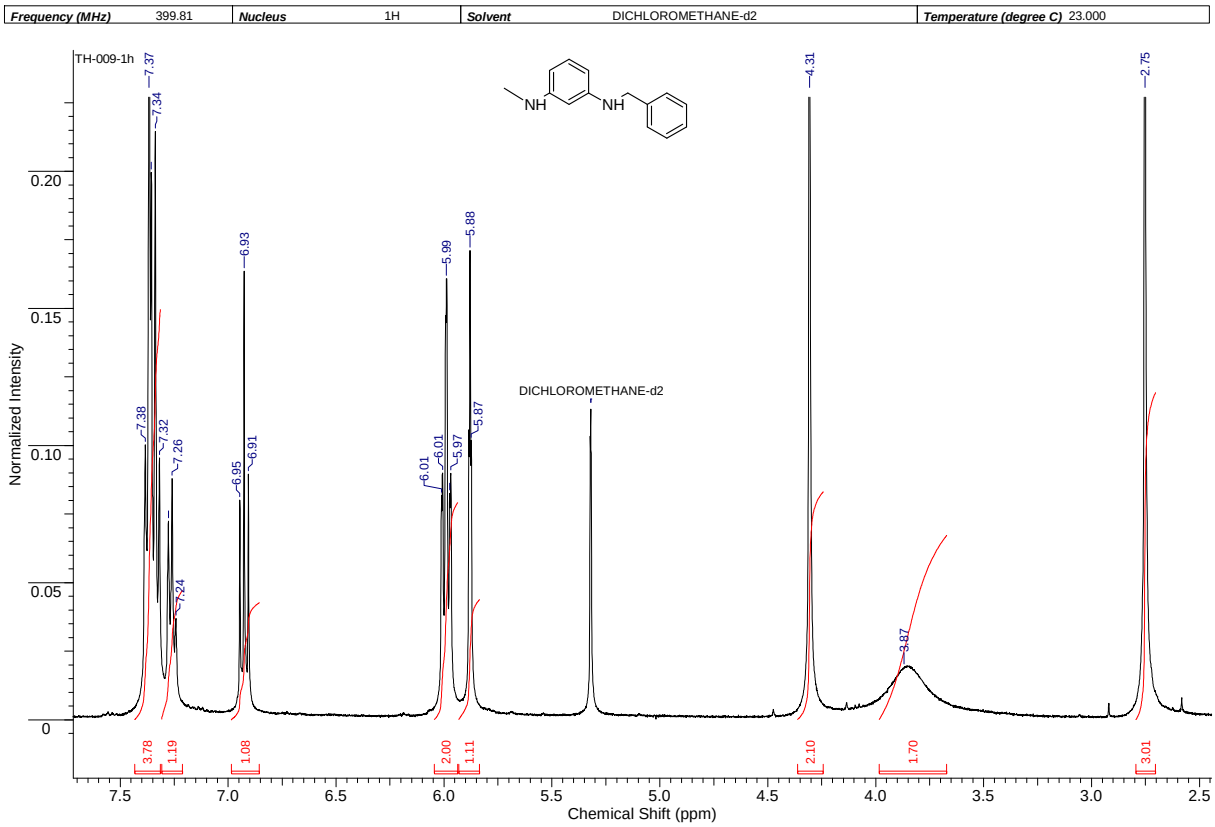

Frequency (MHz) 100.54
Nucleus 13C
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-002-13c
CHLOROFORM-d
NH
NH
Normalized Intensity
Chemical Shift (ppm)

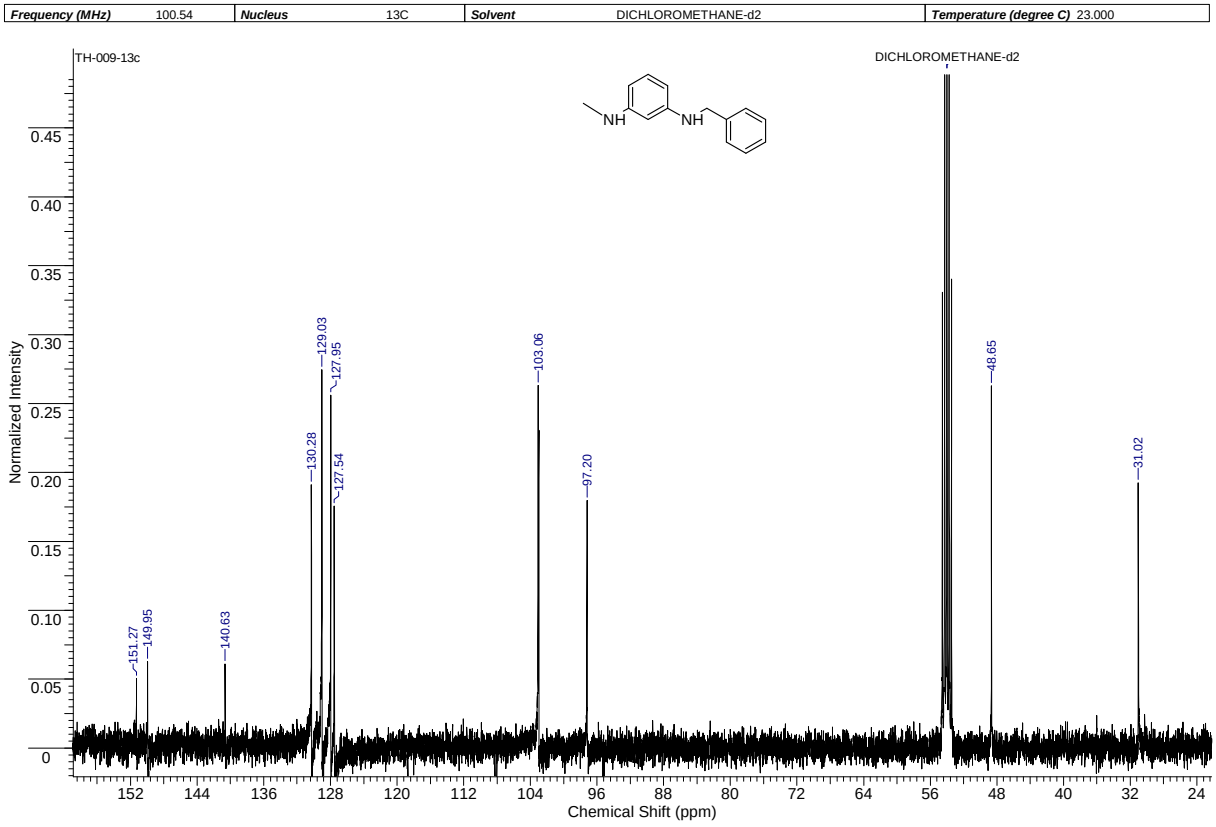

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-033-2-1h
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

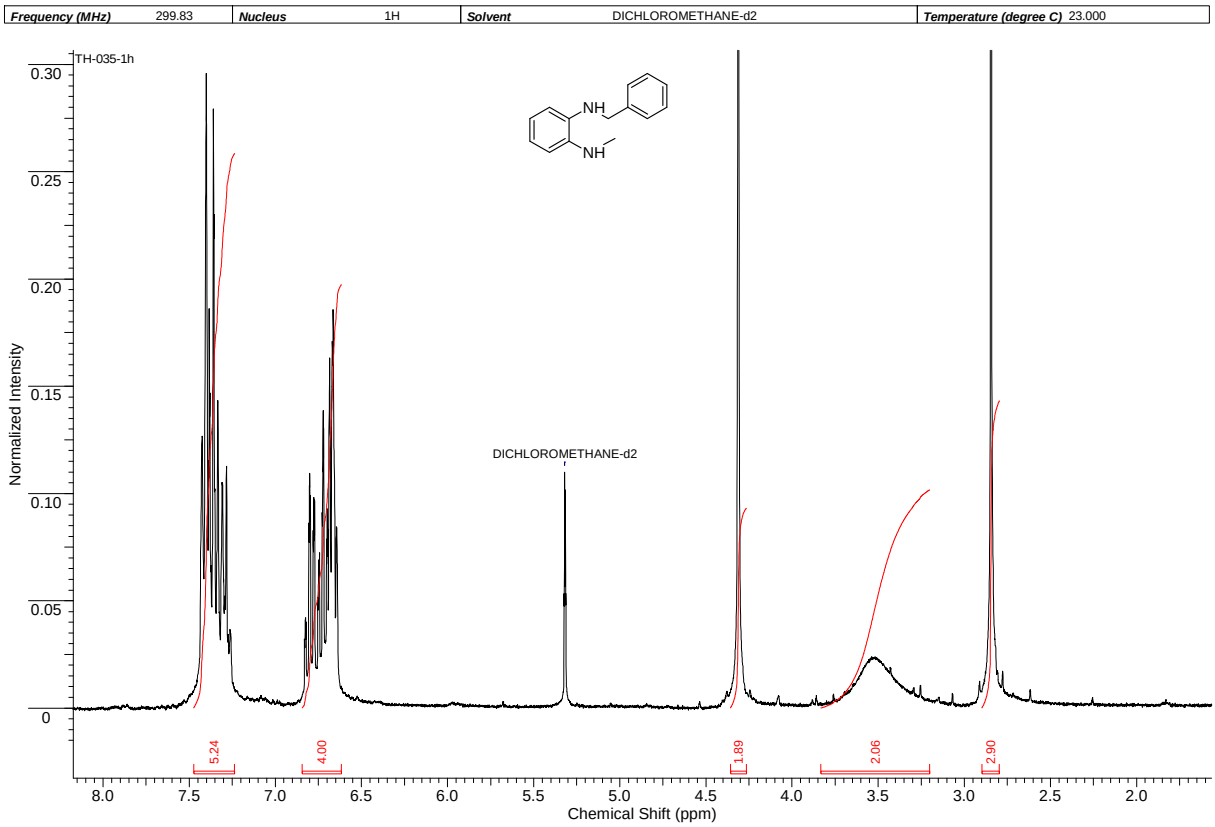

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-033-2-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

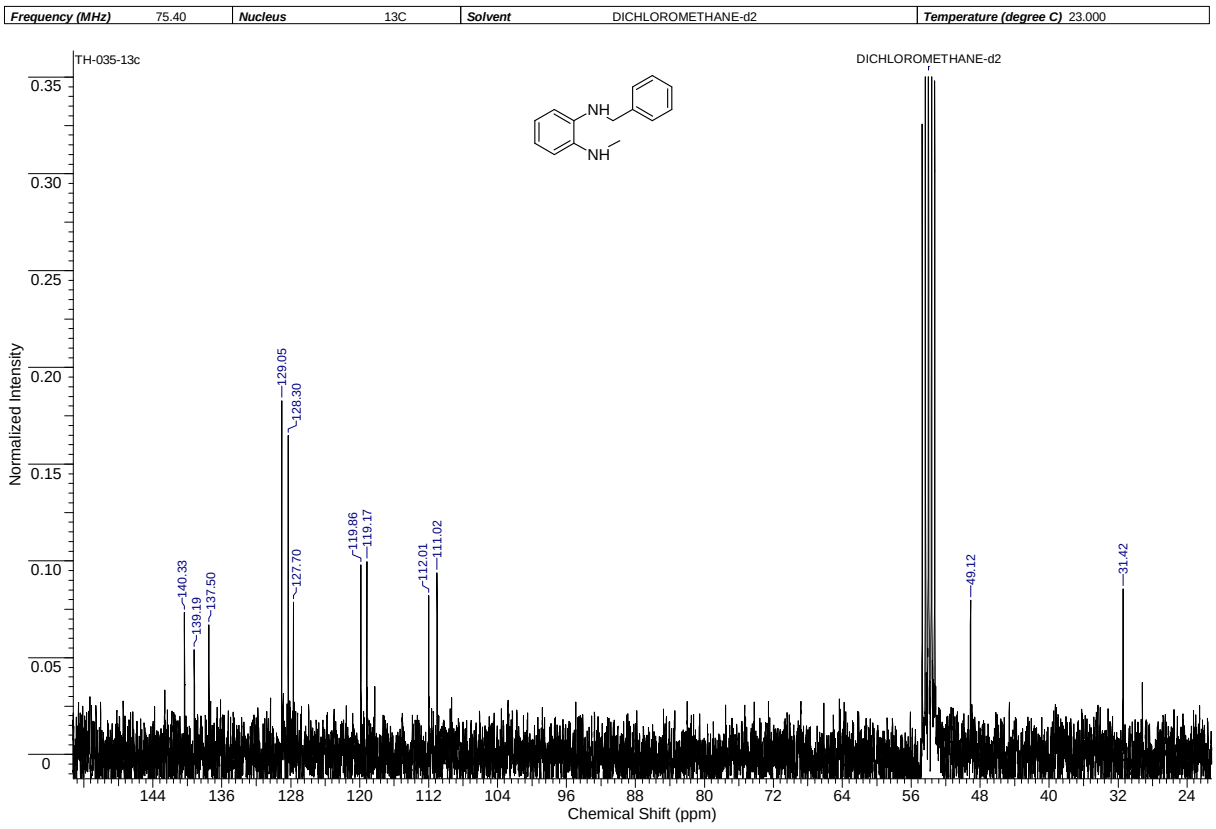

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-325-1h
NH
NH
DICHLOROMETHANE-d2
7.38
7.37
7.33
7.31
7.25
7.24
6.57
6.55
6.52
6.50
4.26
3.52
2.75
3.95
1.08
4.00
2.02
1.95
3.01
Normalized Intensity
Chemical Shift (ppm)

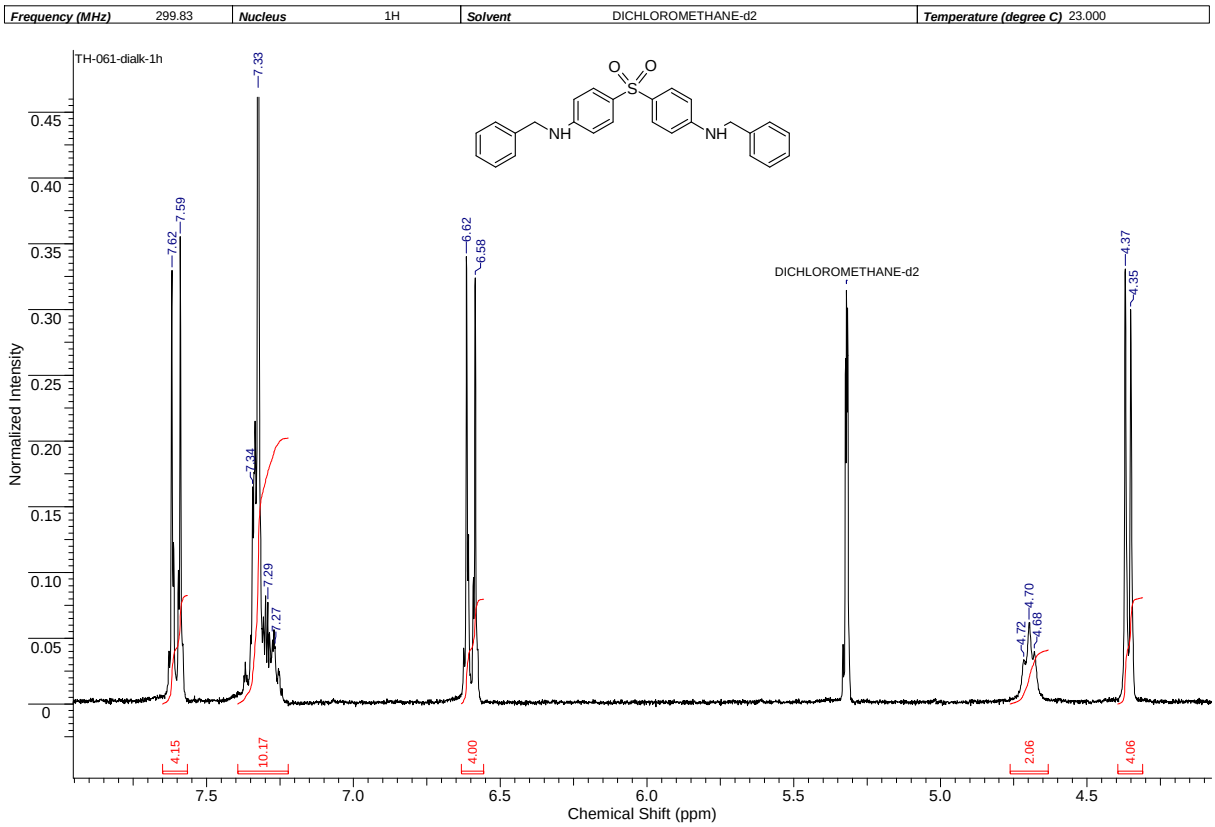

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-325-13c
NH
NH
DICHLOROMETHANE-d2
142.73
140.93
128.97
128.05
127.47
115.11
114.38
49.82
32.06
Normalized Intensity
Chemical Shift (ppm)

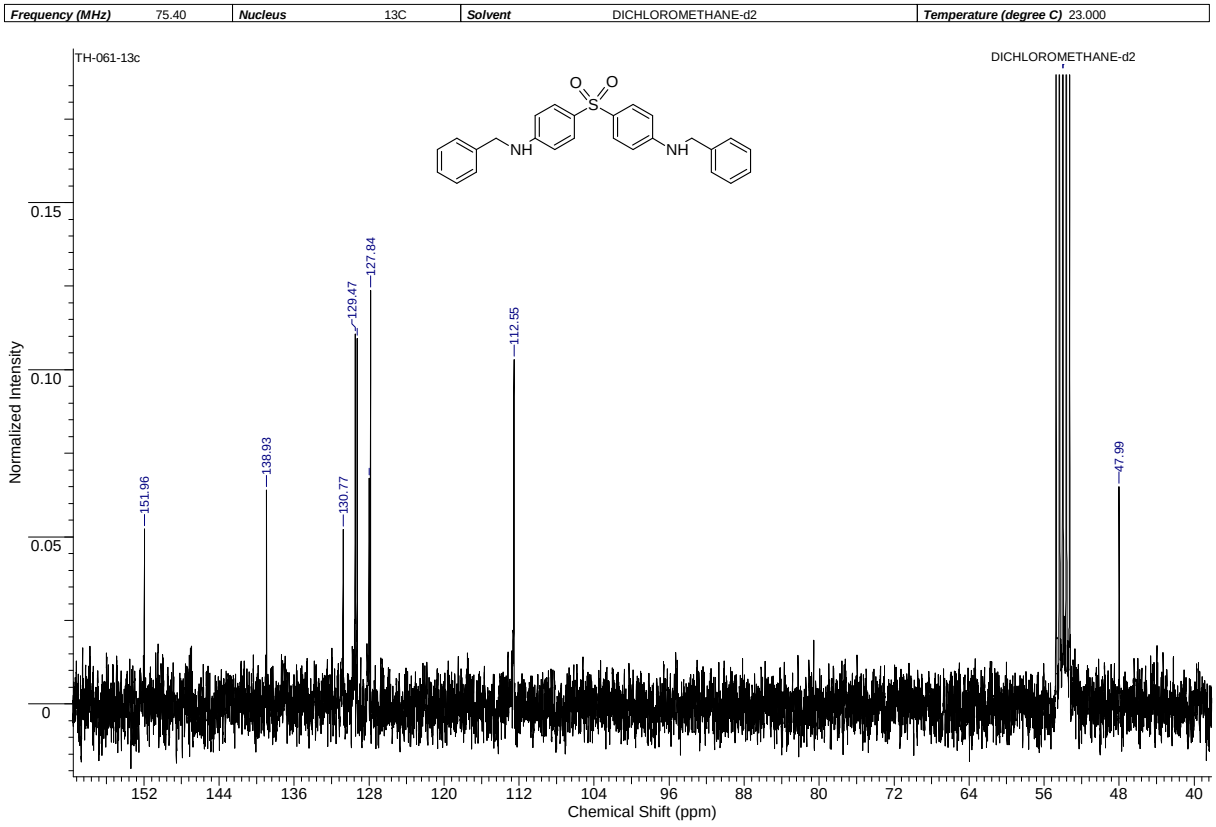

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-009-1h
NH
NH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

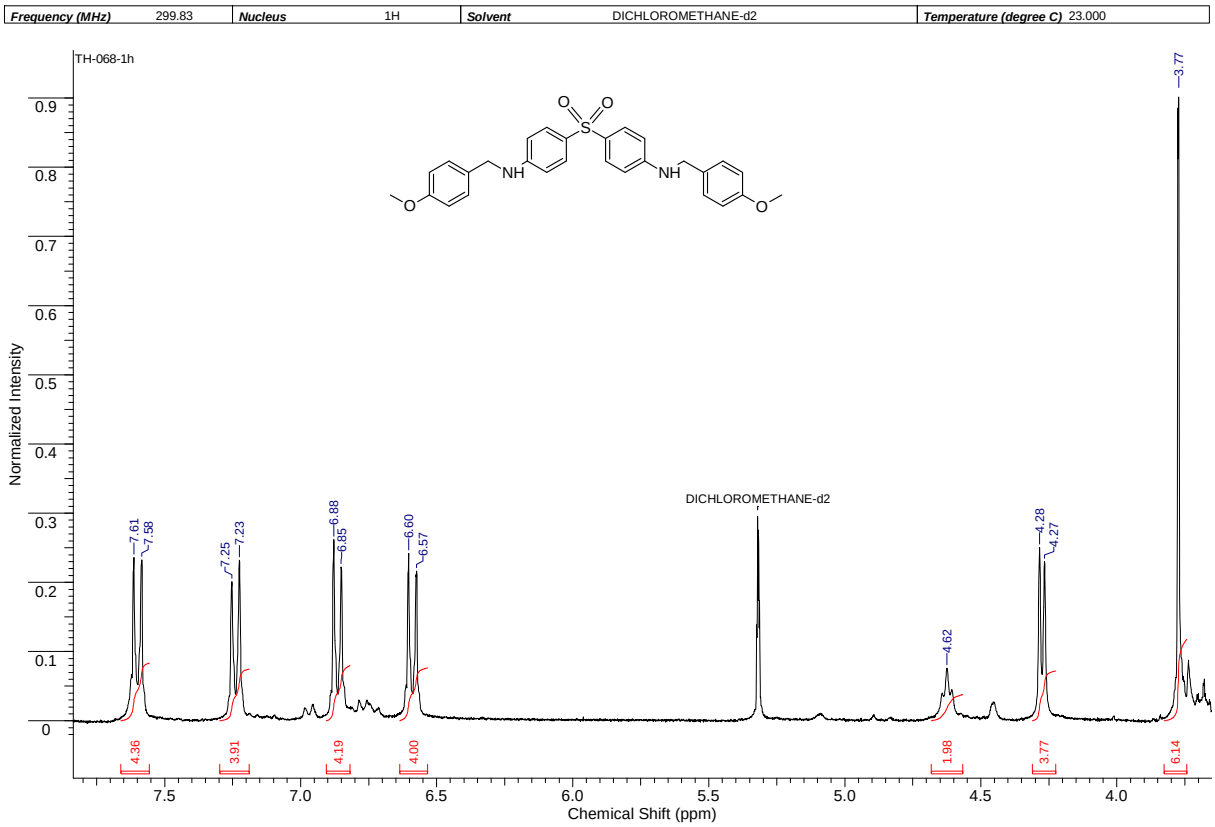

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-009-13c
NH
NH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

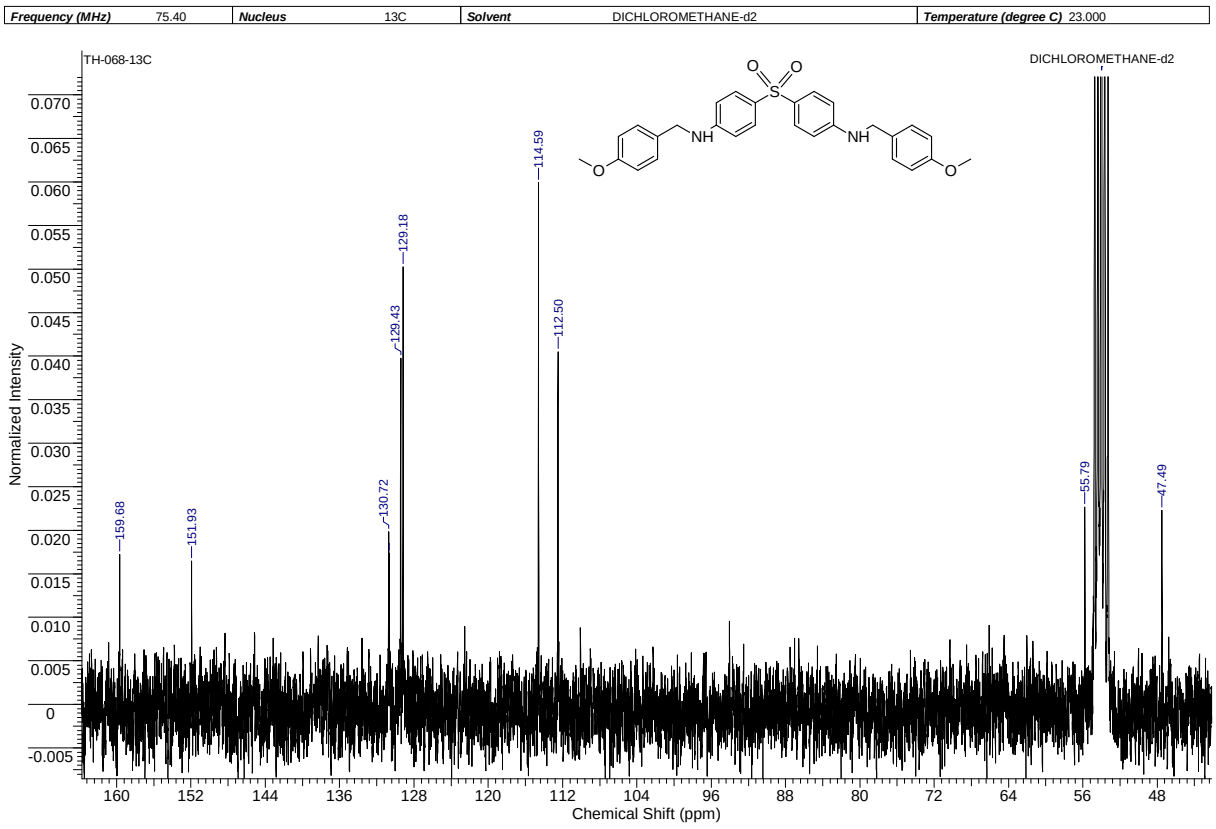

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-035-1h
NH
NH
DICHLOROMETHANE-d2
Normalized Intensity
0.30
0.25
0.20
0.15
0.10
0.05
0
5.24
4.00
1.89
2.06
2.90
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
Chemical Shift (ppm)

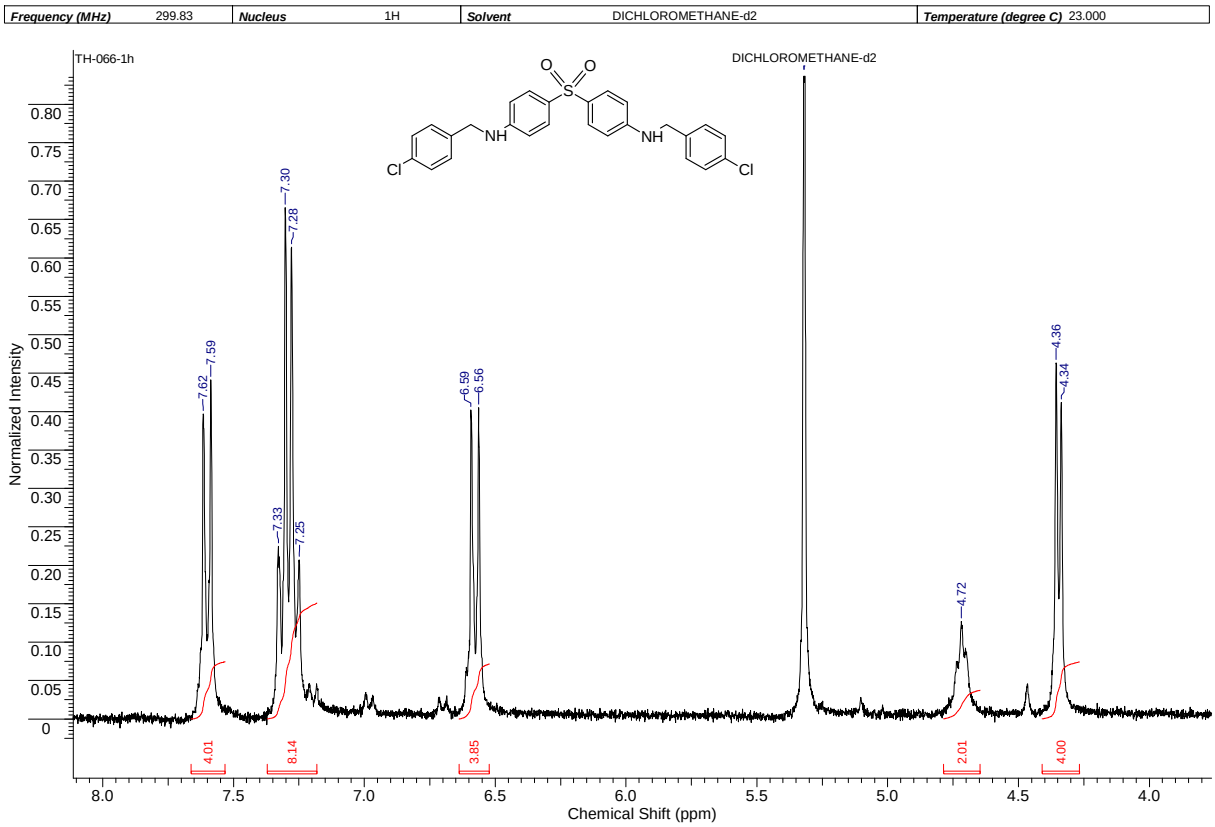

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-035-13c
NH
NH
DICHLOROMETHANE-d2
Normalized Intensity
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
140.33
139.19
137.50
129.05
128.30
127.70
119.86
119.17
112.01
111.02
49.12
31.42
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)

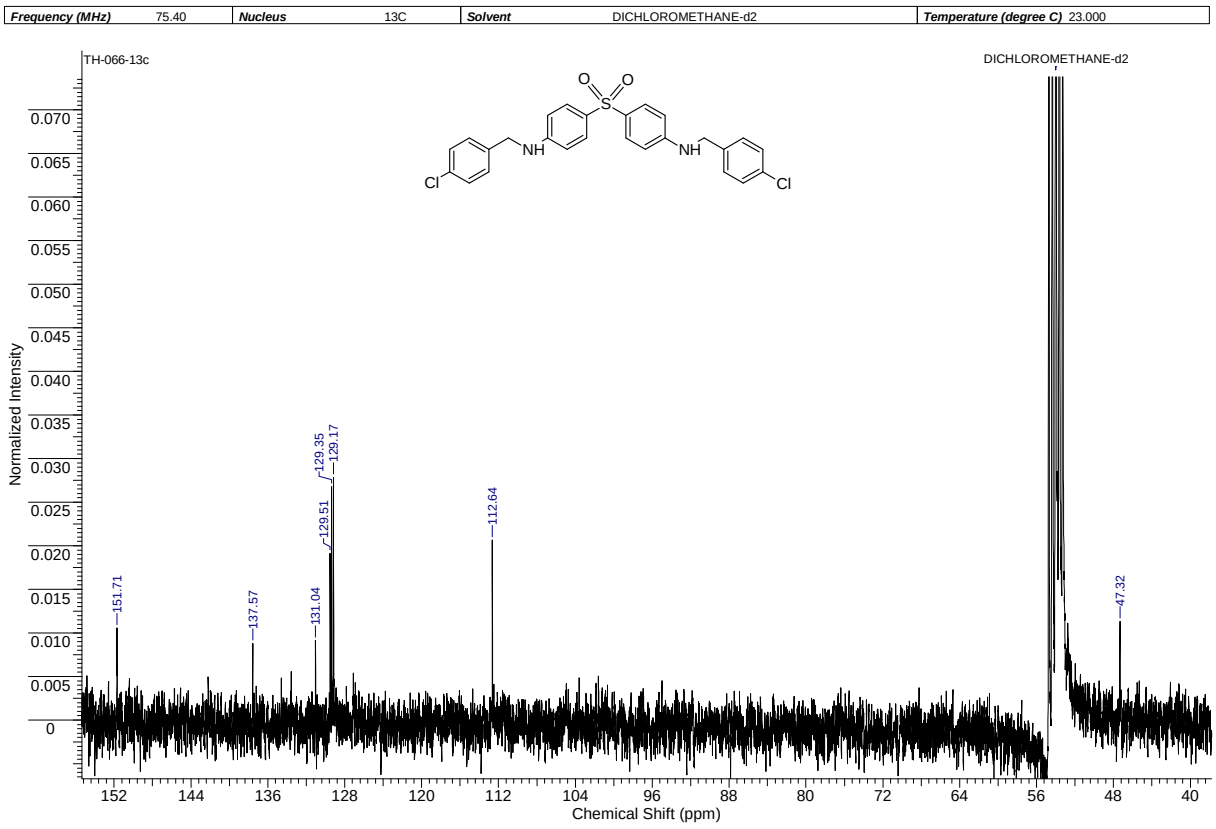

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-061-dialk-1h
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

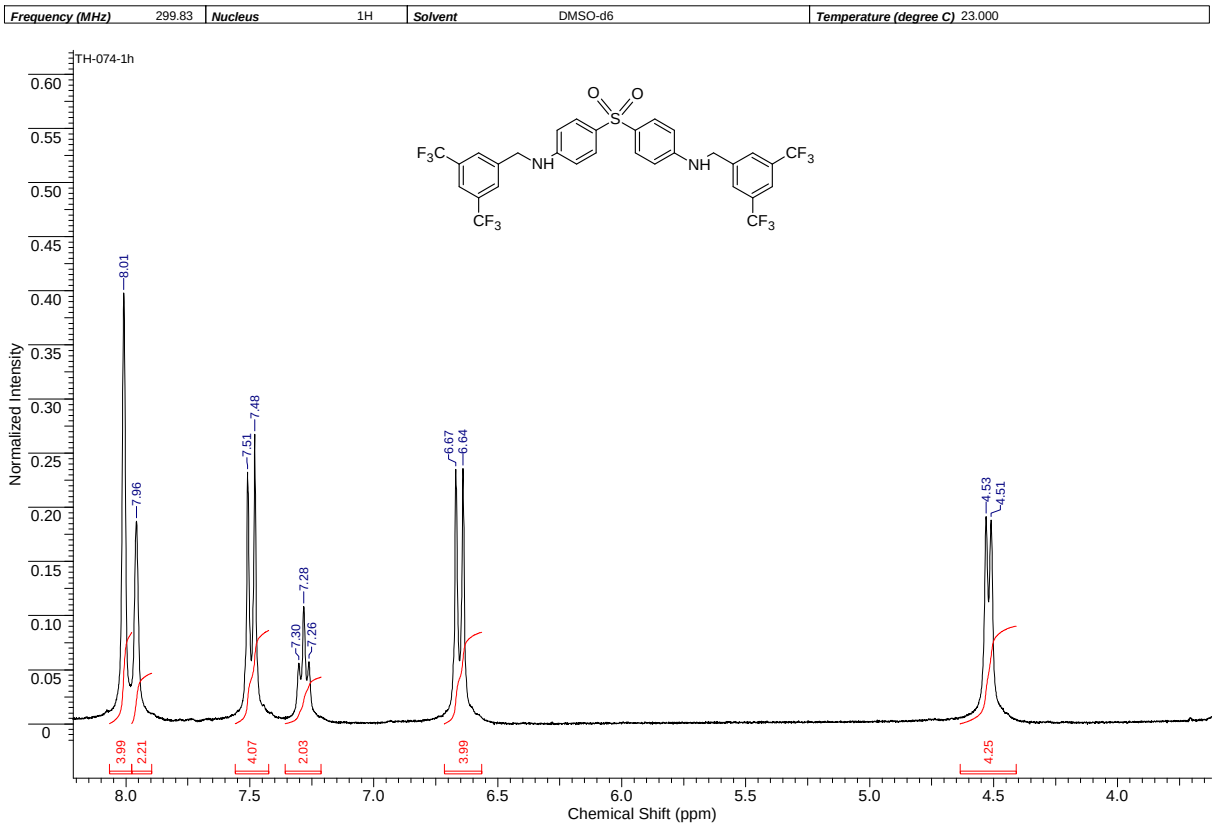

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-061-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

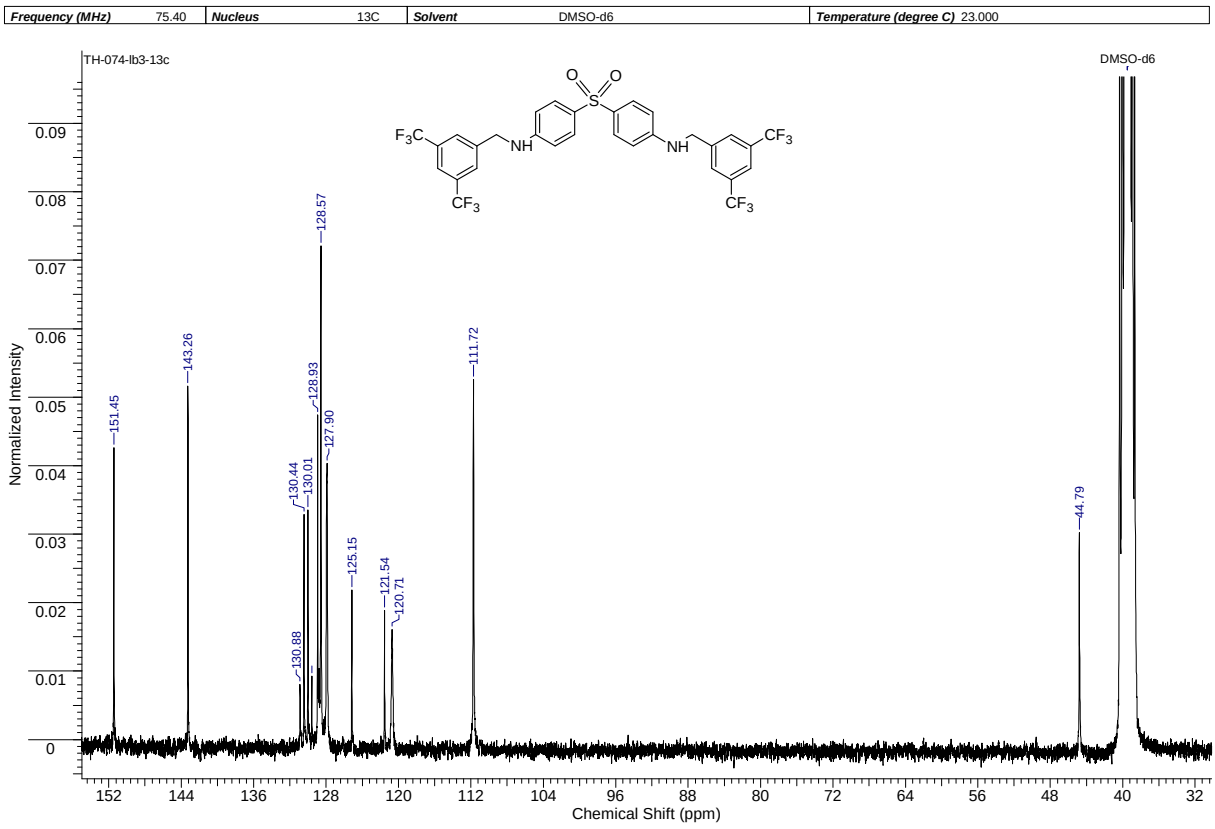

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-068-1h
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
7.61
7.58
7.25
7.23
6.88
6.85
6.60
6.57
4.62
4.28
4.27
3.77
4.36
3.91
4.19
4.00
1.98
3.77
6.14

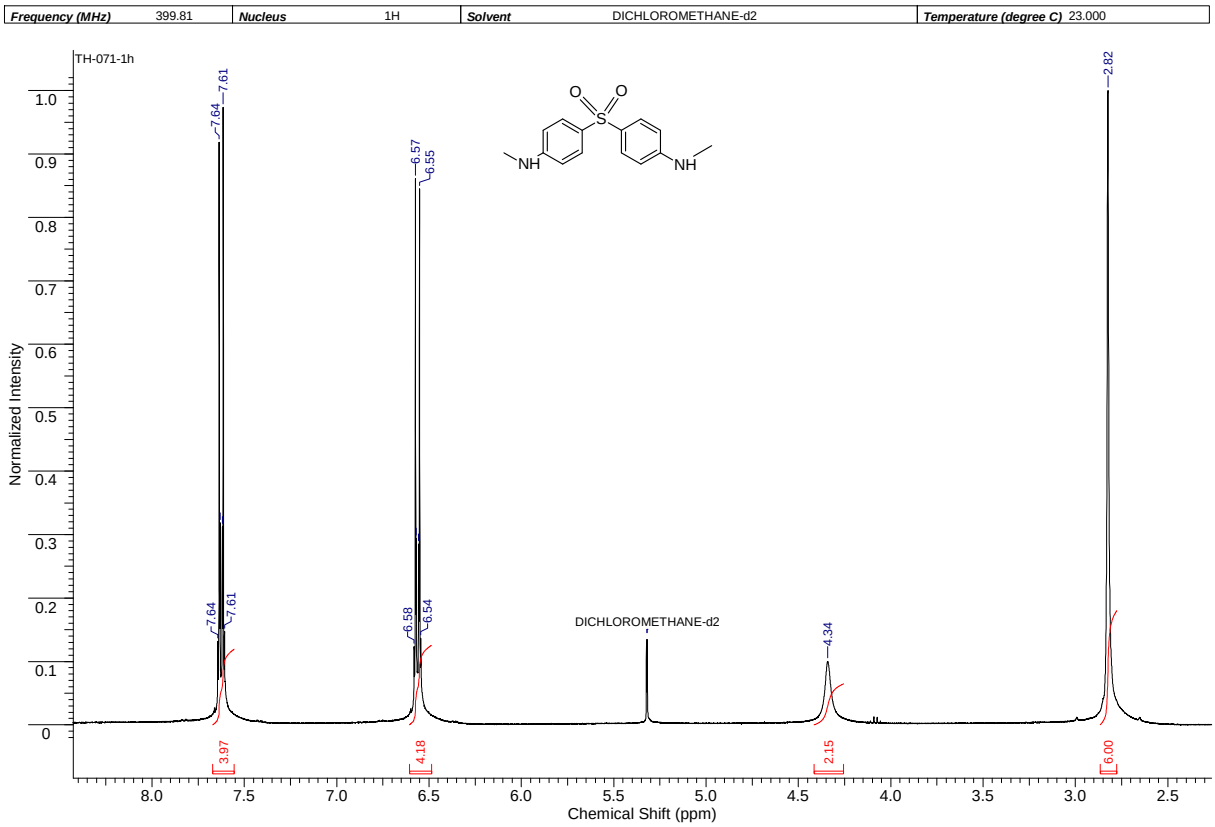

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-068-13C
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)
159.68
151.93
130.72
129.43
129.18
114.59
112.50
55.79
47.49

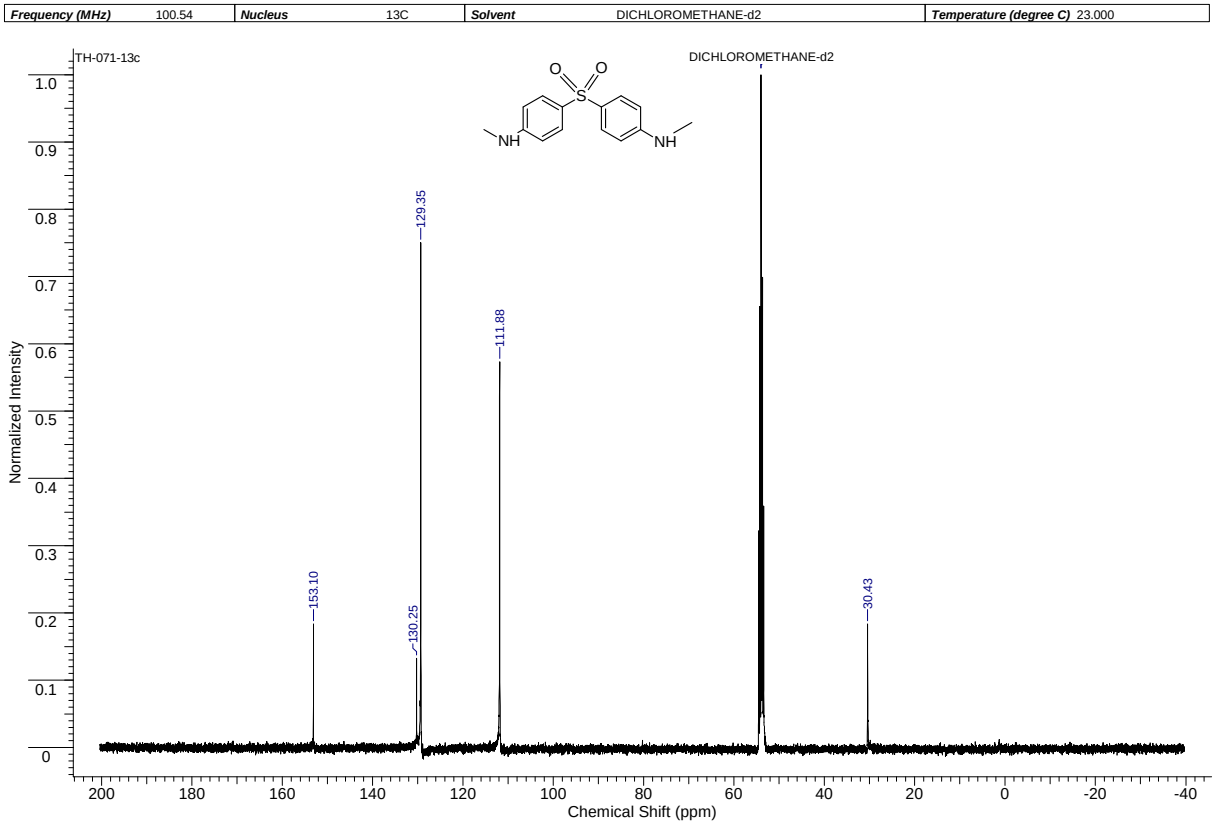

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-066-1h
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)
7.62
7.59
7.33
7.30
7.28
7.25
6.59
6.56
4.72
4.36
4.34
4.01
8.14
3.85
2.01
4.00

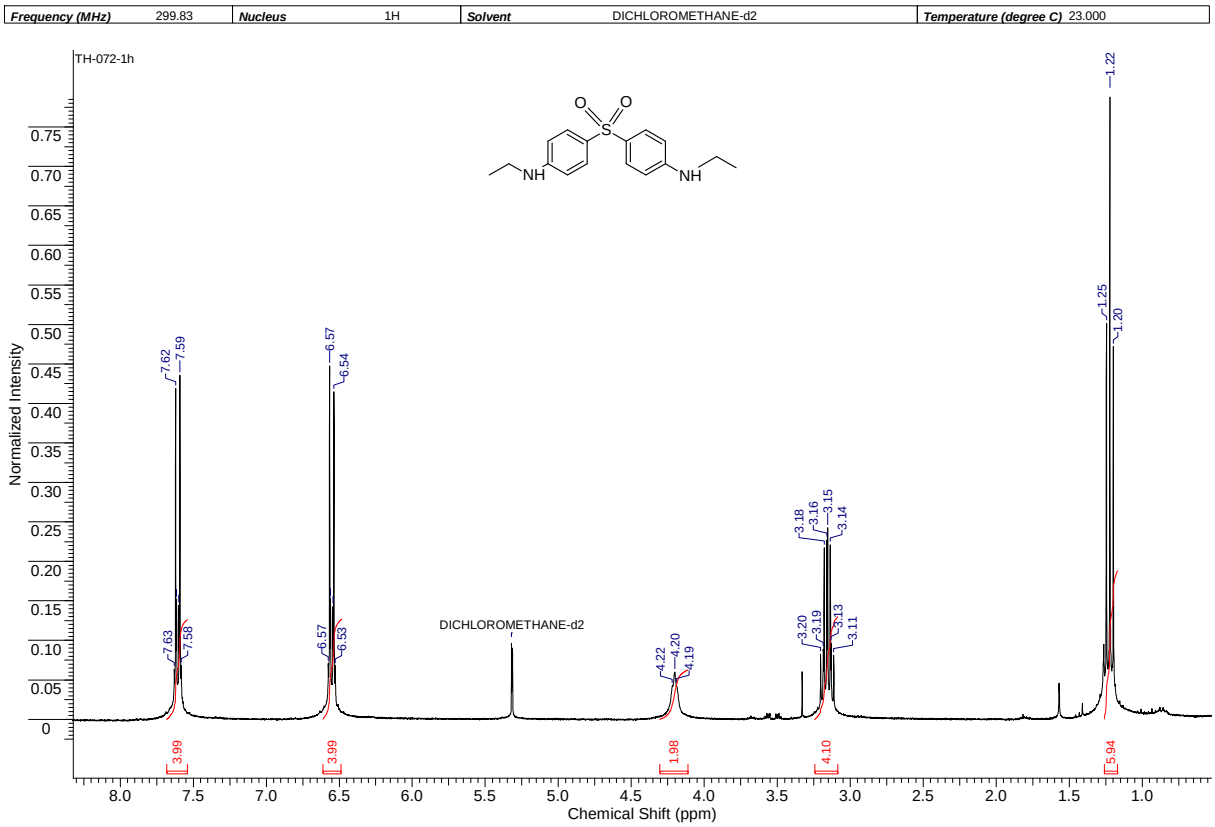

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-066-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)
151.71
137.57
131.04
129.51
129.35
129.17
112.64
47.32

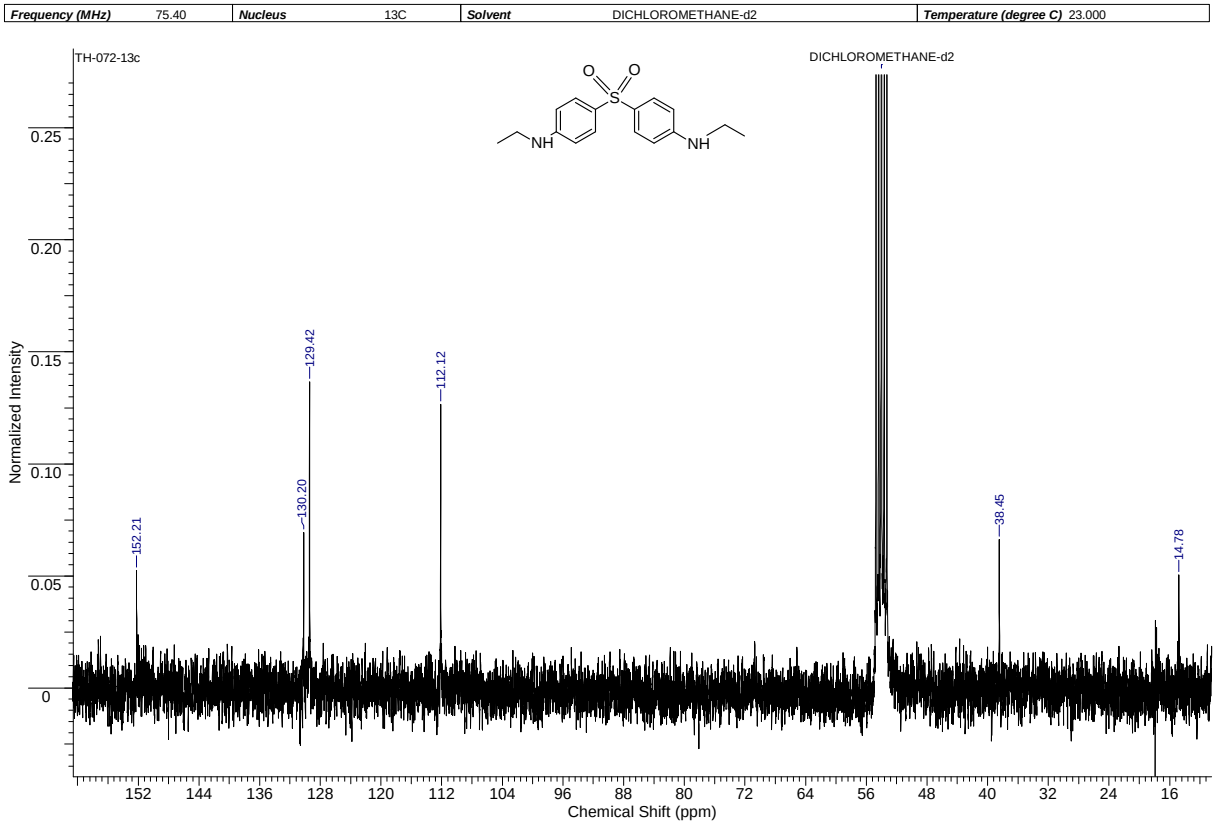

Frequency (MHz) 299.83
Nucleus 1H
Solvent DMSO-d6
Temperature (degree C) 23.000
TH-074-1h
Normalized Intensity
Chemical Shift (ppm)
8.01
7.96
7.51
7.48
7.30
7.28
7.26
6.67
6.64
4.53
4.51
3.99
2.21
4.07
2.03
3.99
4.25

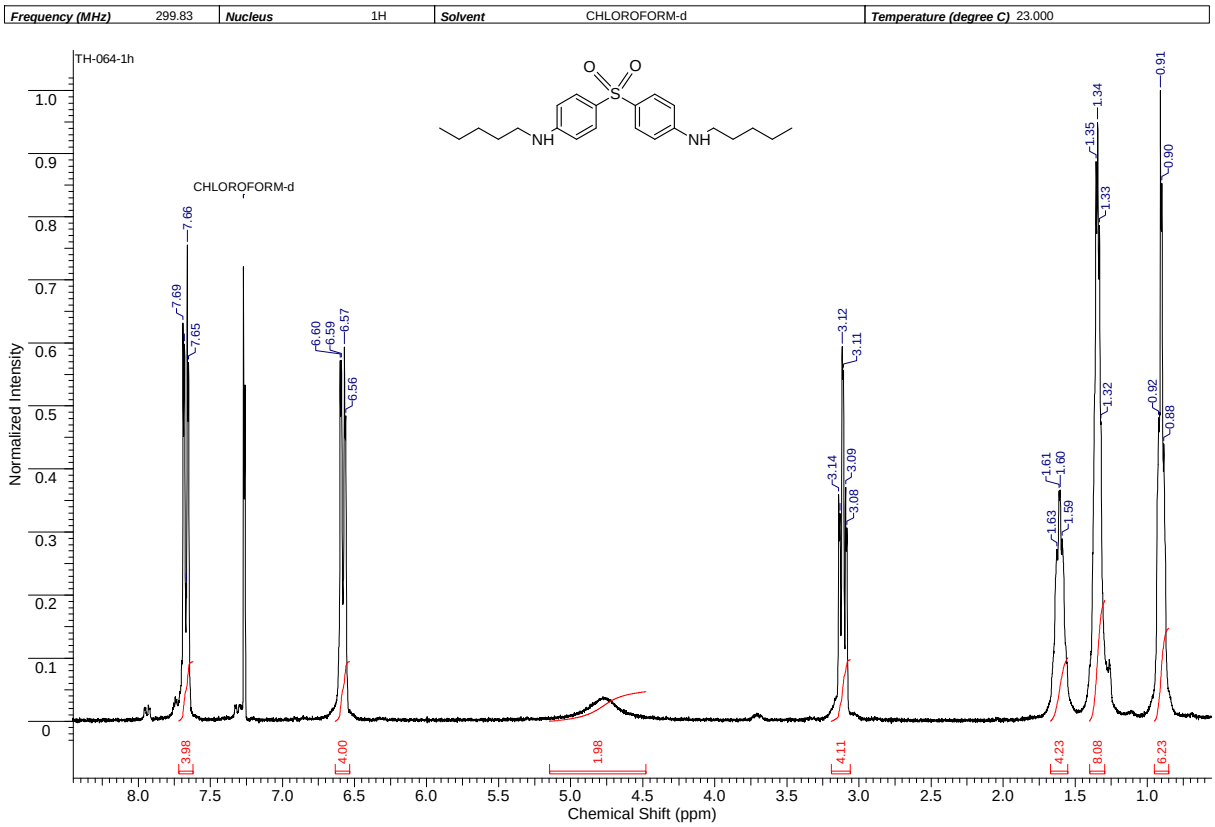

Frequency (MHz) 75.40
Nucleus 13C
Solvent DMSO-d6
Temperature (degree C) 23.000
TH-074-lb3-13c
DMSO-d6
Normalized Intensity
Chemical Shift (ppm)
151.45
143.26
130.88
130.44
130.01
128.93
128.57
127.90
125.15
121.54
120.71
111.72
44.79

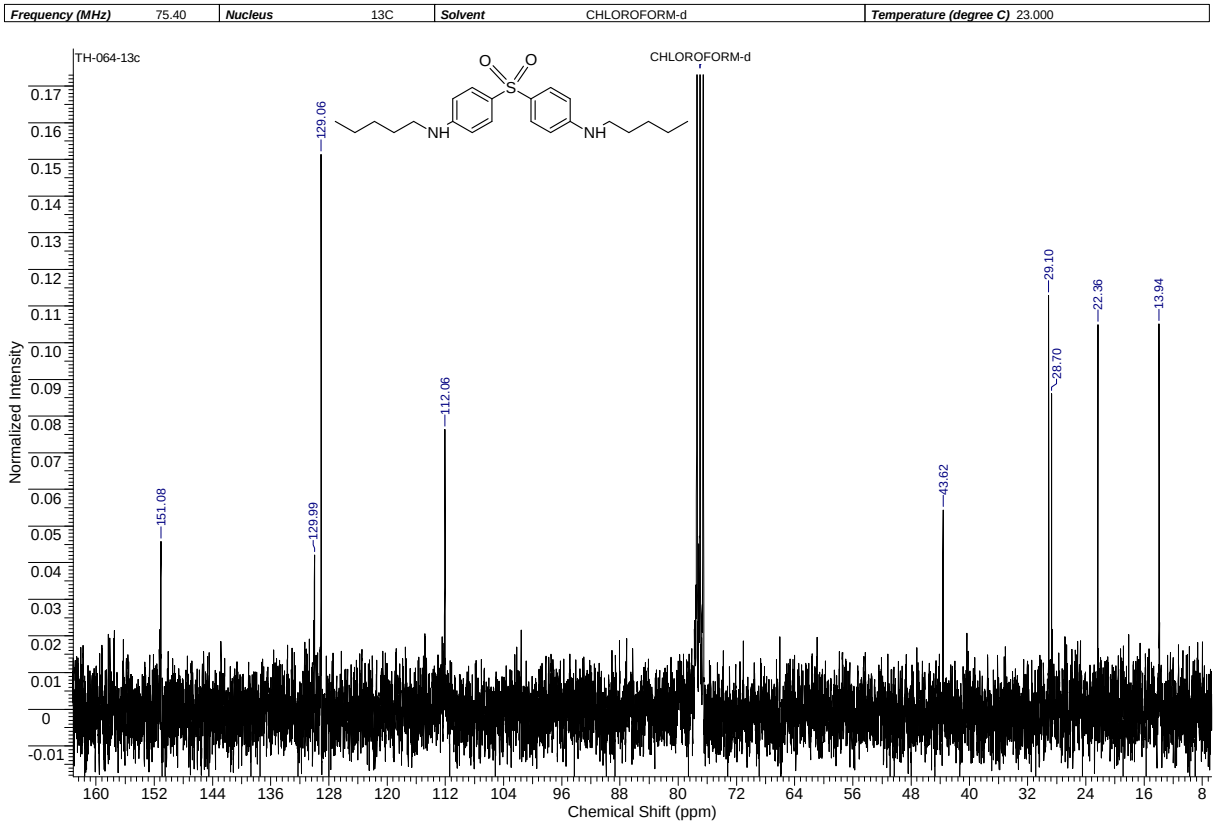

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-071-1h
7.64
7.61
6.57
6.55
2.82
7.64
7.61
6.58
6.54
DICHLOROMETHANE-d2
4.34
3.97
4.18
2.15
6.00
Normalized Intensity
Chemical Shift (ppm)

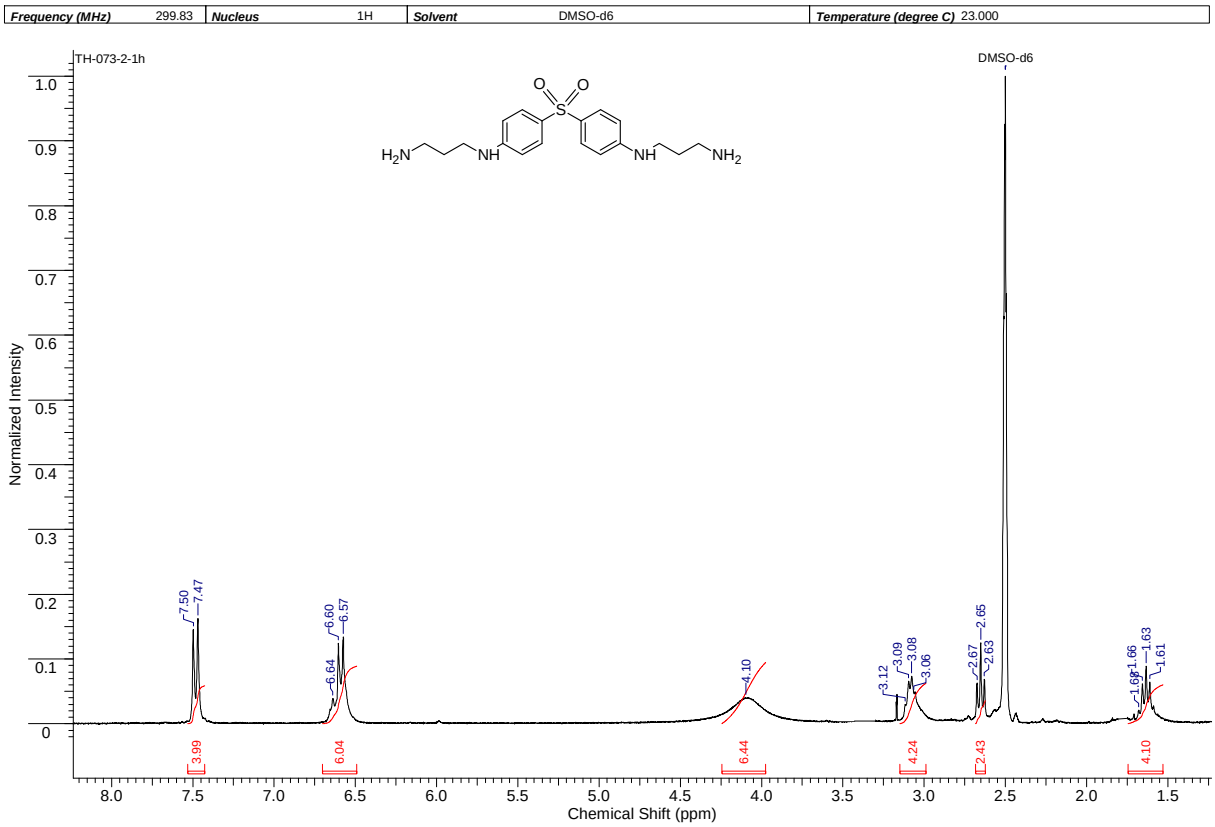

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-071-13c
DICHLOROMETHANE-d2
129.35
111.88
153.10
130.25
30.43
Normalized Intensity
Chemical Shift (ppm)

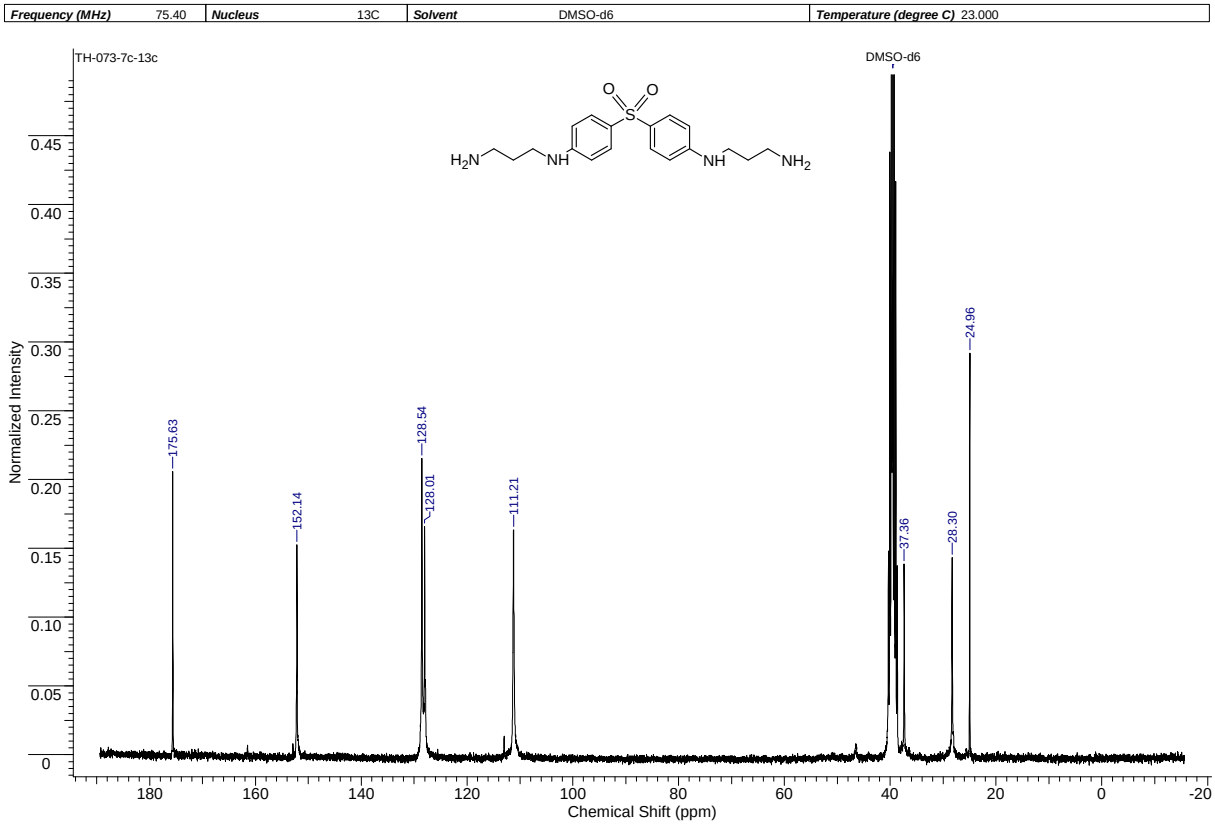

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-072-1h
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

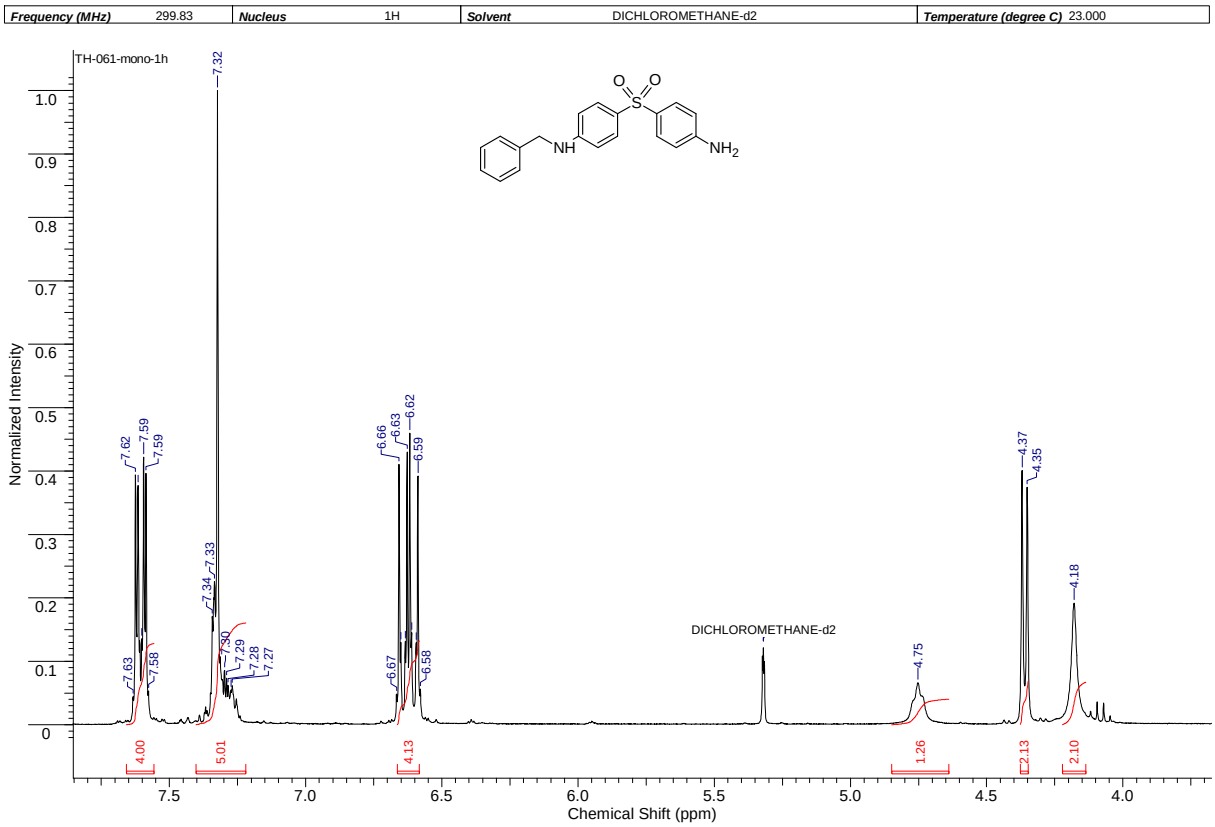

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-072-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

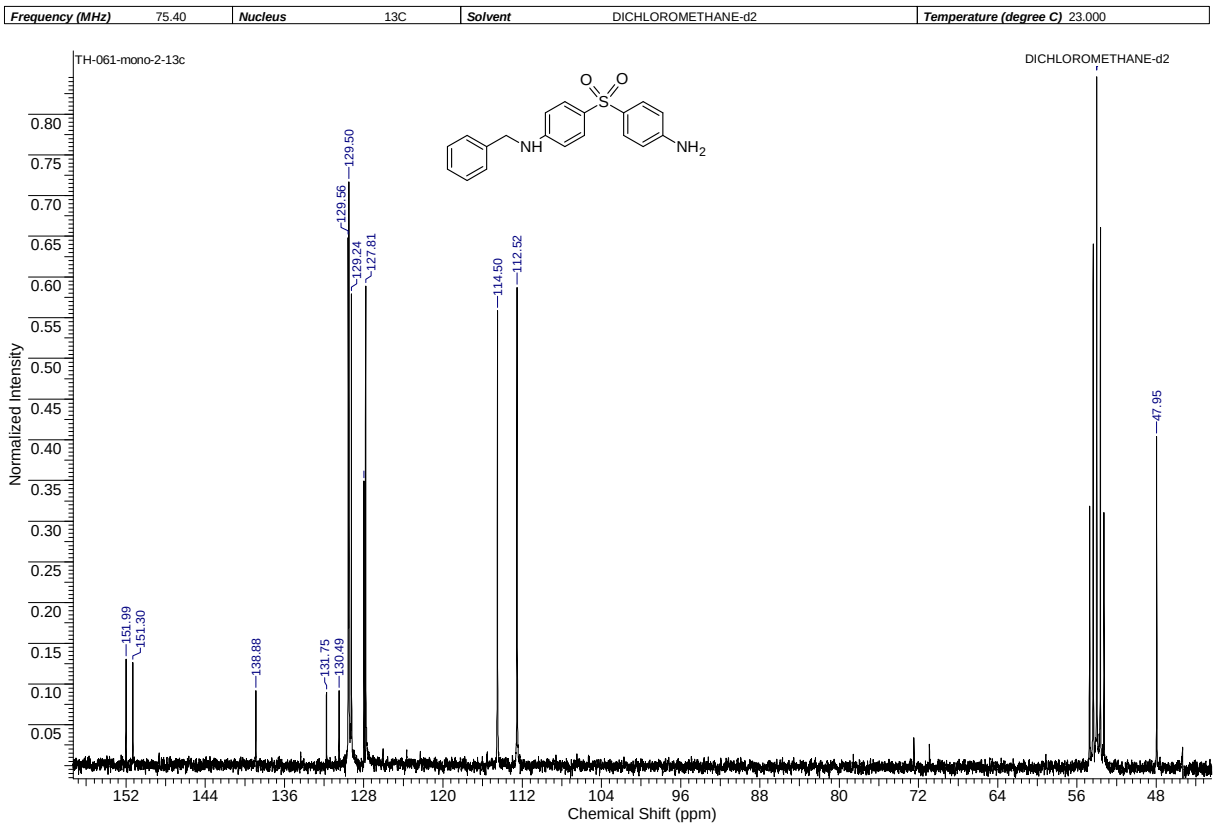

Frequency (MHz) 299.83
Nucleus 1H
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-064-1h
CHLOROFORM-d
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.40
Nucleus 13C
Solvent CHLOROFORM-d
Temperature (degree C) 23.000
TH-064-13c
CHLOROFORM-d
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 299.83
Nucleus 1H
Solvent DMSO-d6
Temperature (degree C) 23.000
TH-073-2-1h
DMSO-d6
Normalized Intensity
Chemical Shift (ppm)
7.50
7.47
6.60
6.57
6.64
4.10
3.12
3.09
3.08
3.06
2.67
2.65
2.63
1.66
1.63
1.61
3.99
6.04
6.44
4.24
2.43
4.10


Frequency (MHz) 75.40
Nucleus 13C
Solvent DMSO-d6
Temperature (degree C) 23.000
TH-073-7c-13c
DMSO-d6
Normalized Intensity
Chemical Shift (ppm)
175.63
152.14
128.54
128.01
111.21
37.36
28.30
24.96


Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-061-mono-1h
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
NH
NH2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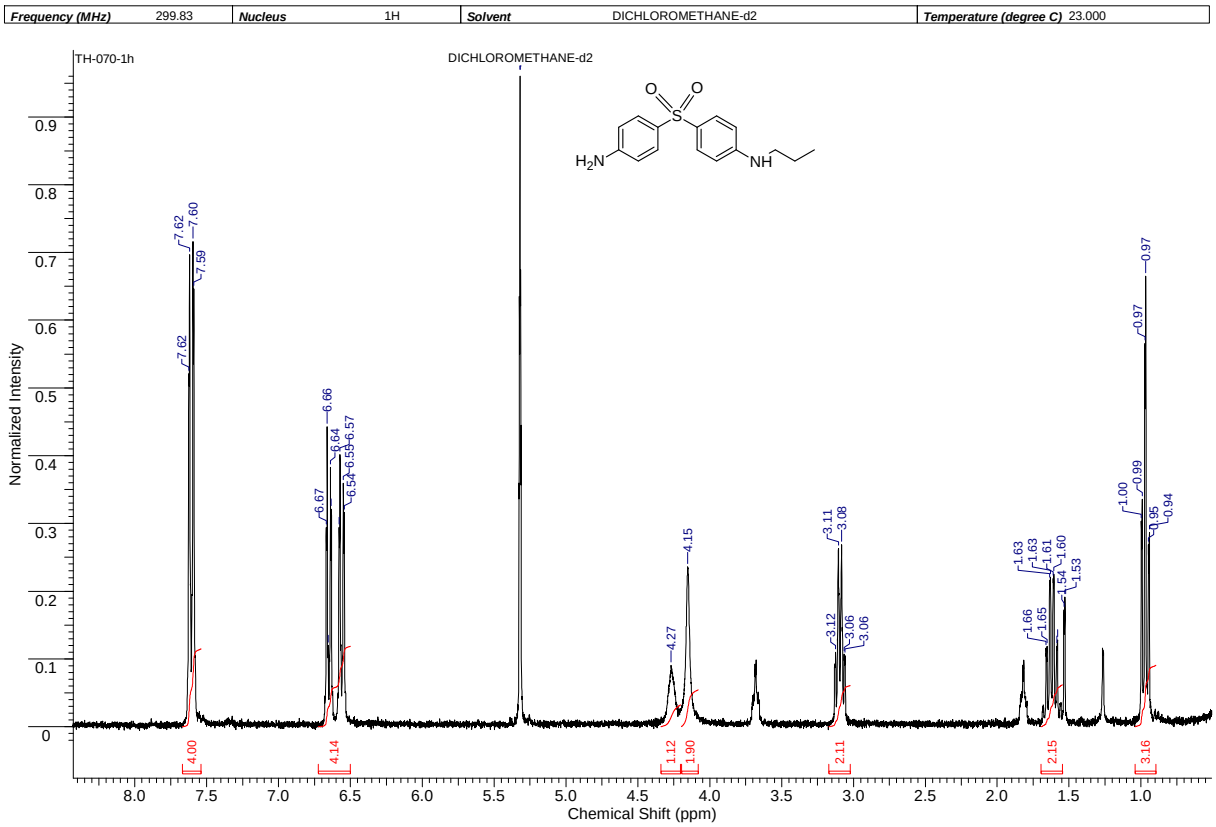
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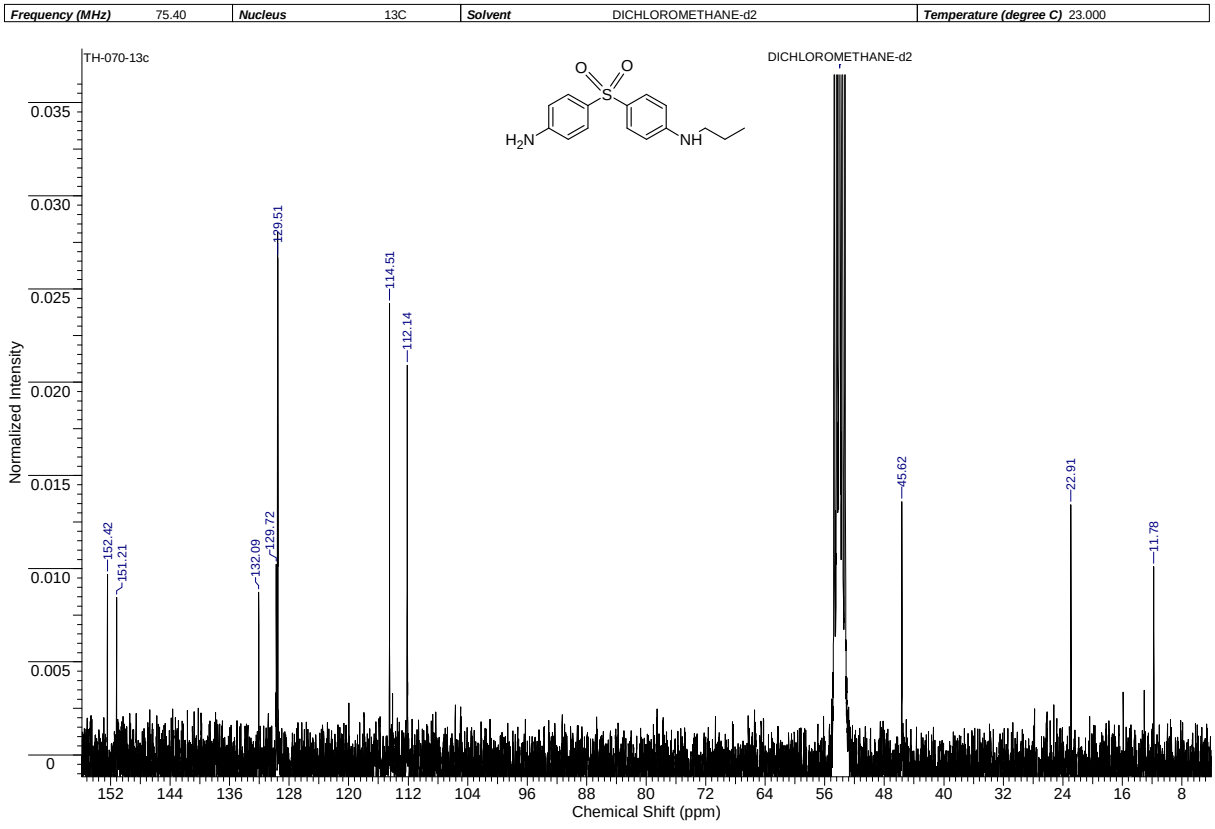
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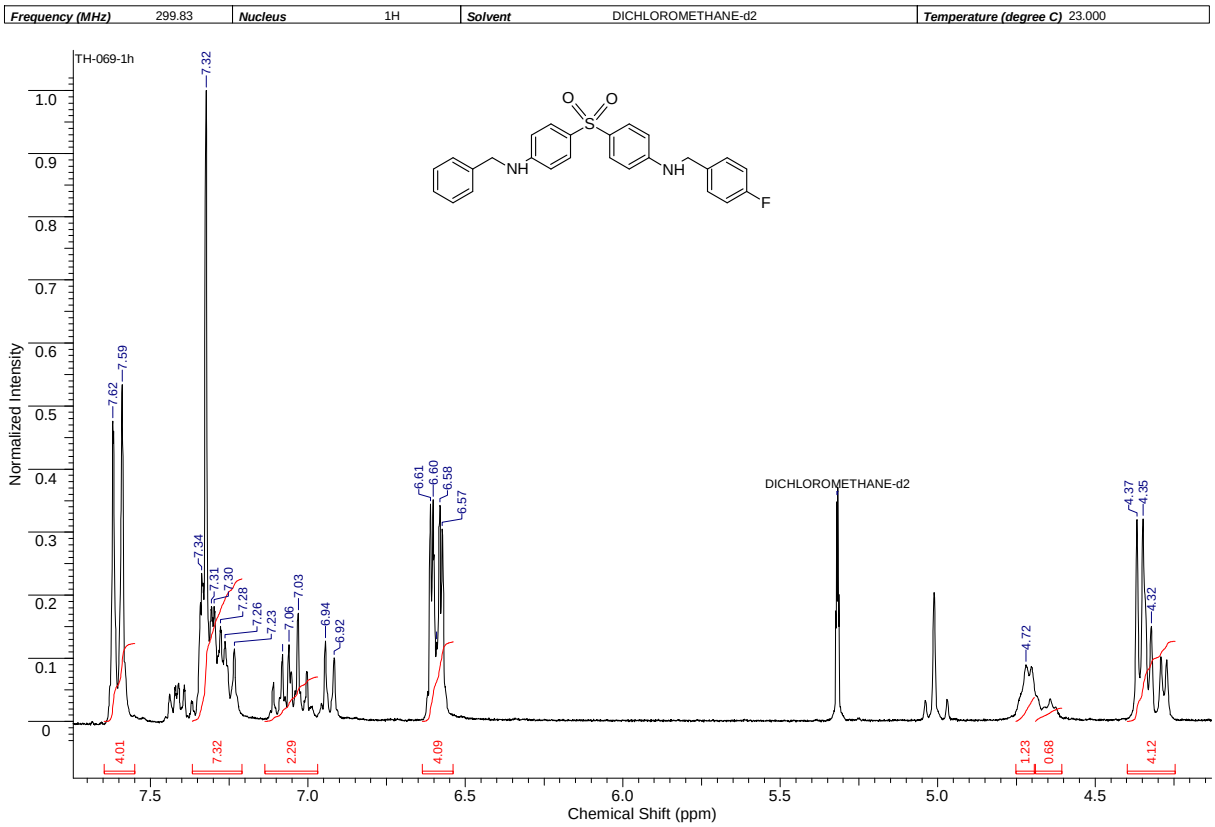
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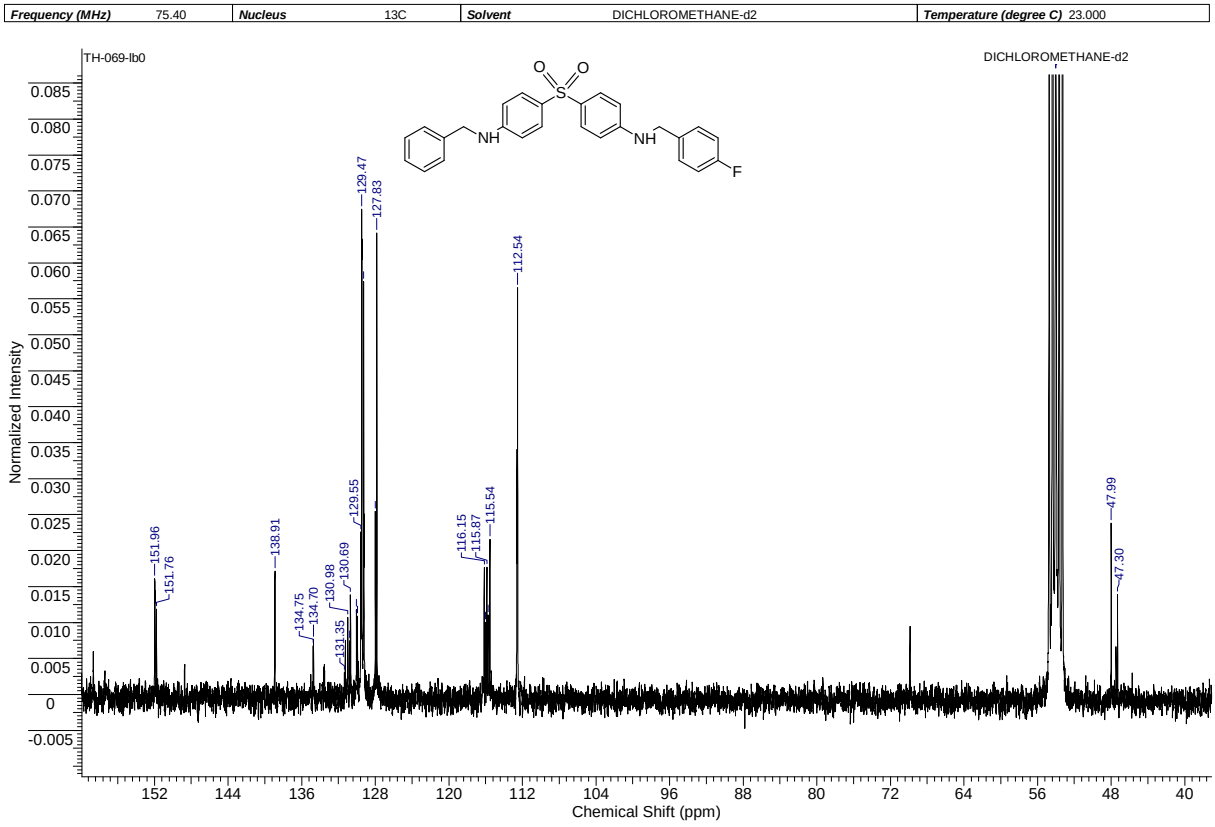
NH
F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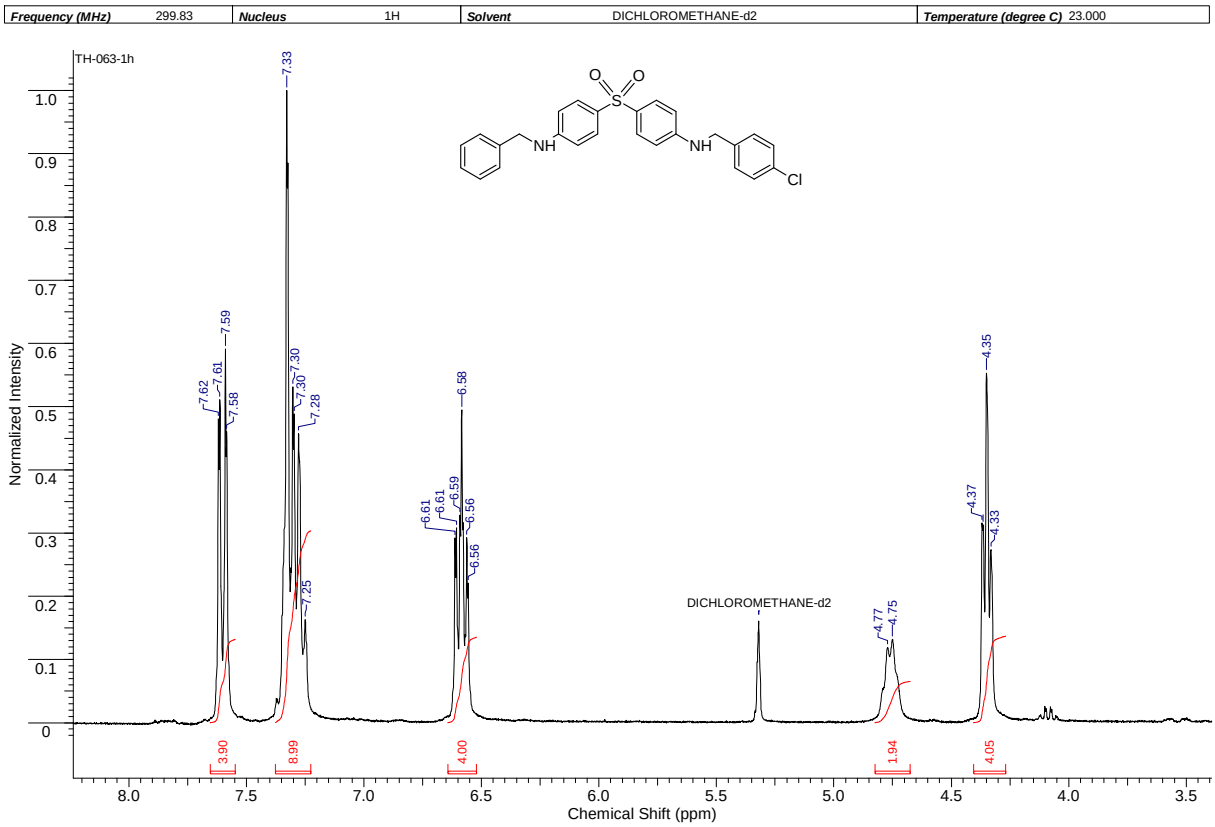
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7.58
7.33
7.30
7.30
7.28
7.25
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4.05
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NH
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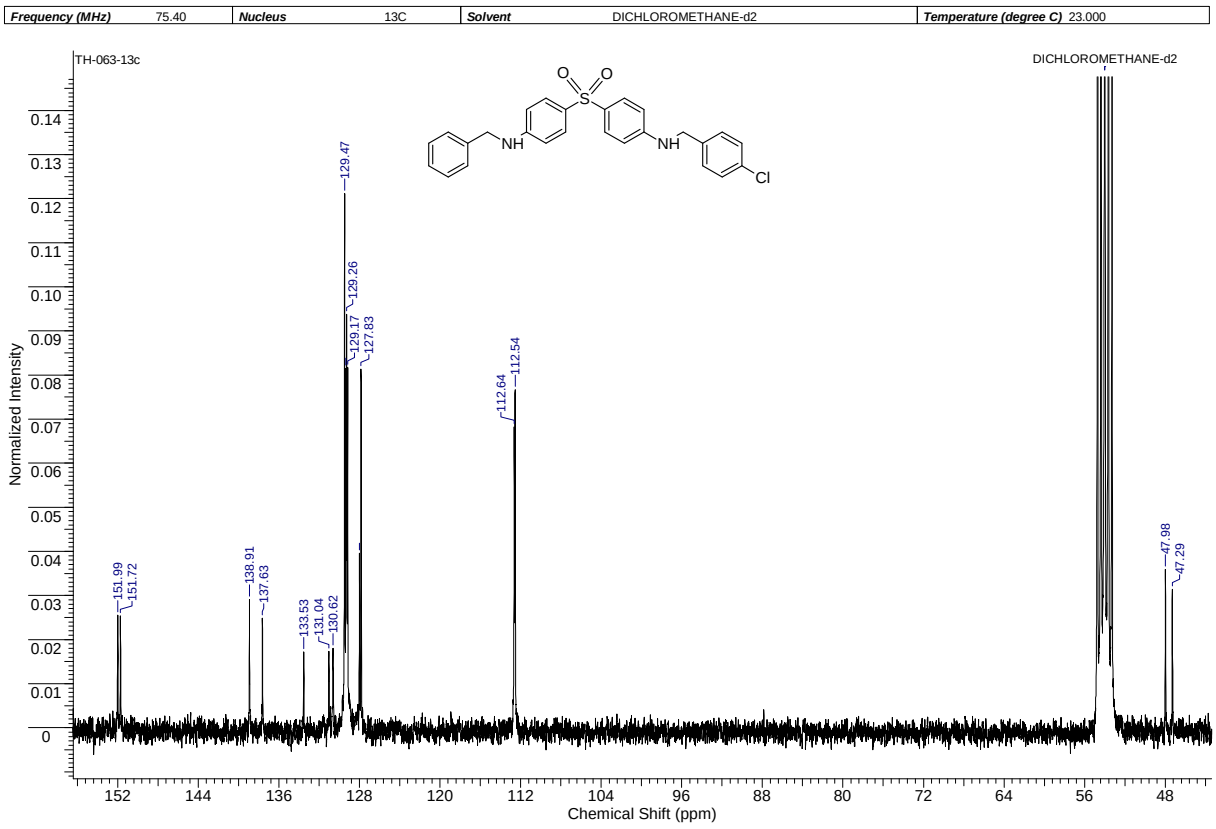
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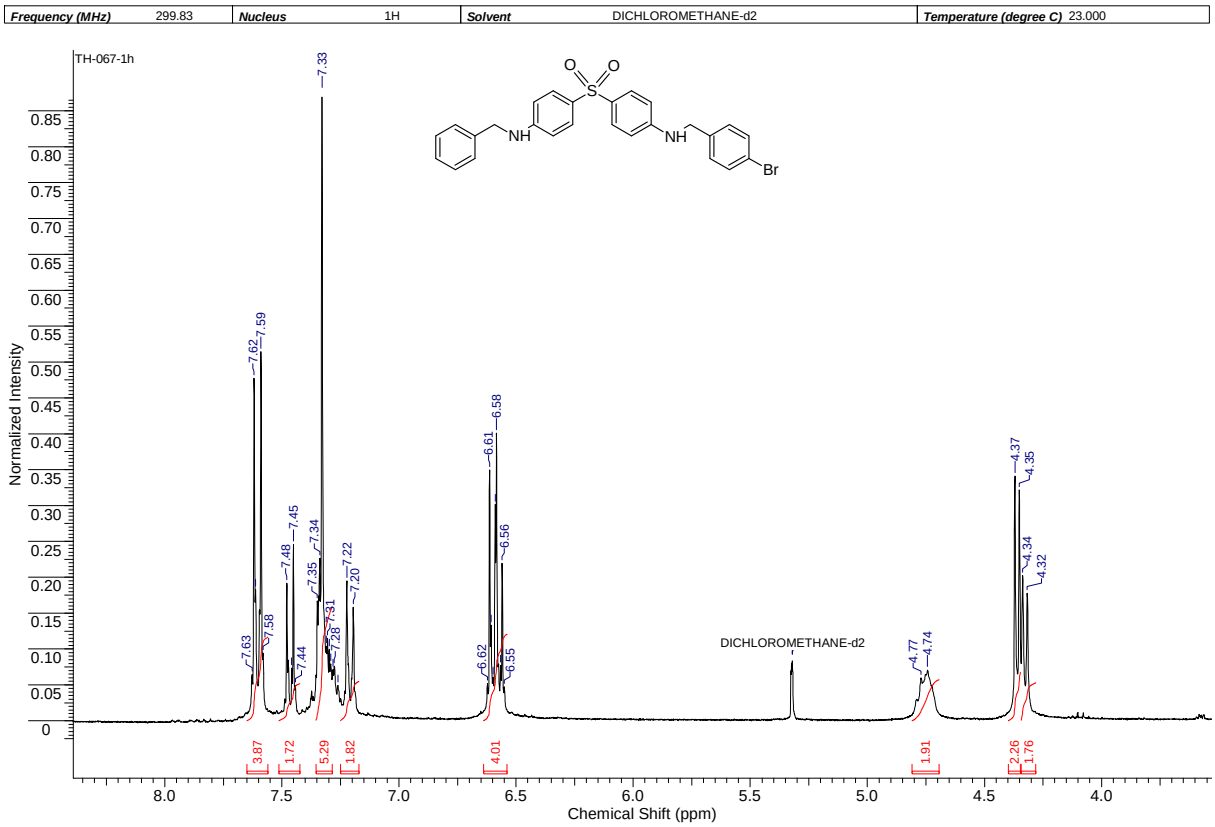
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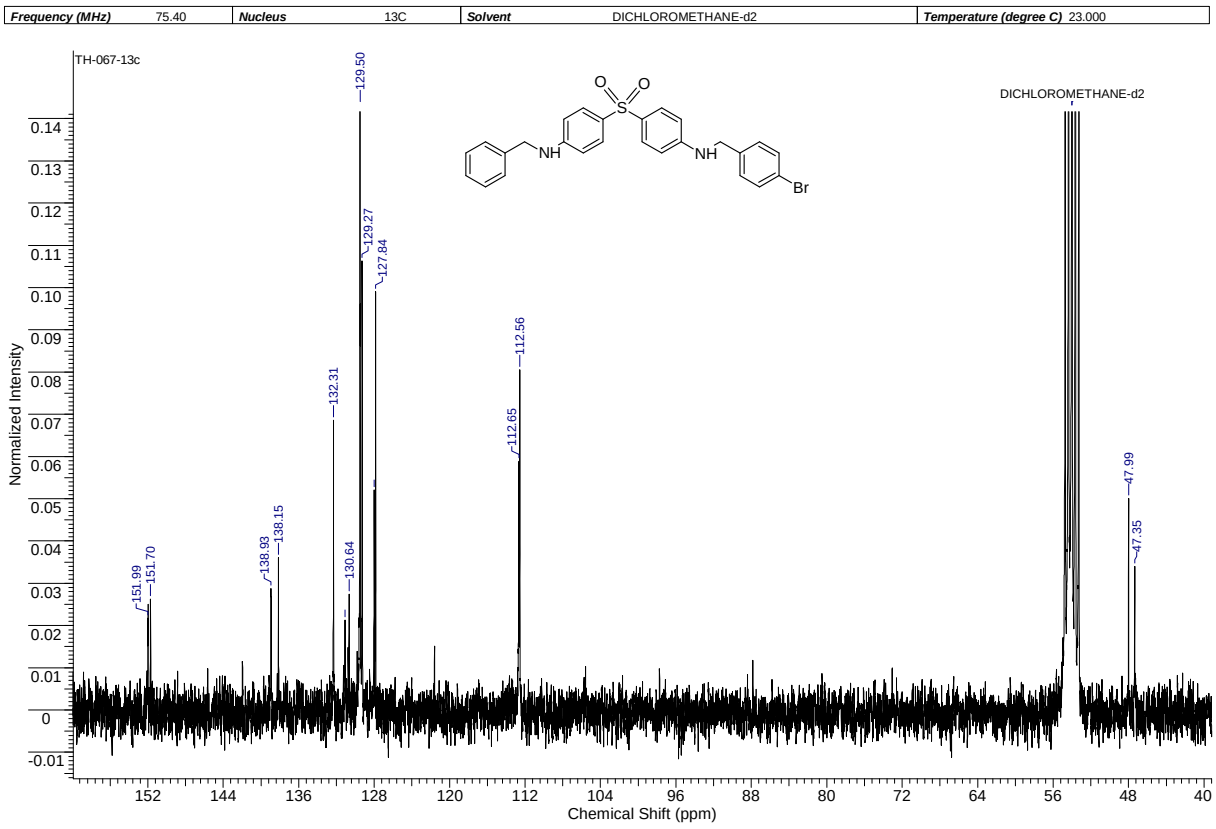
NH
Br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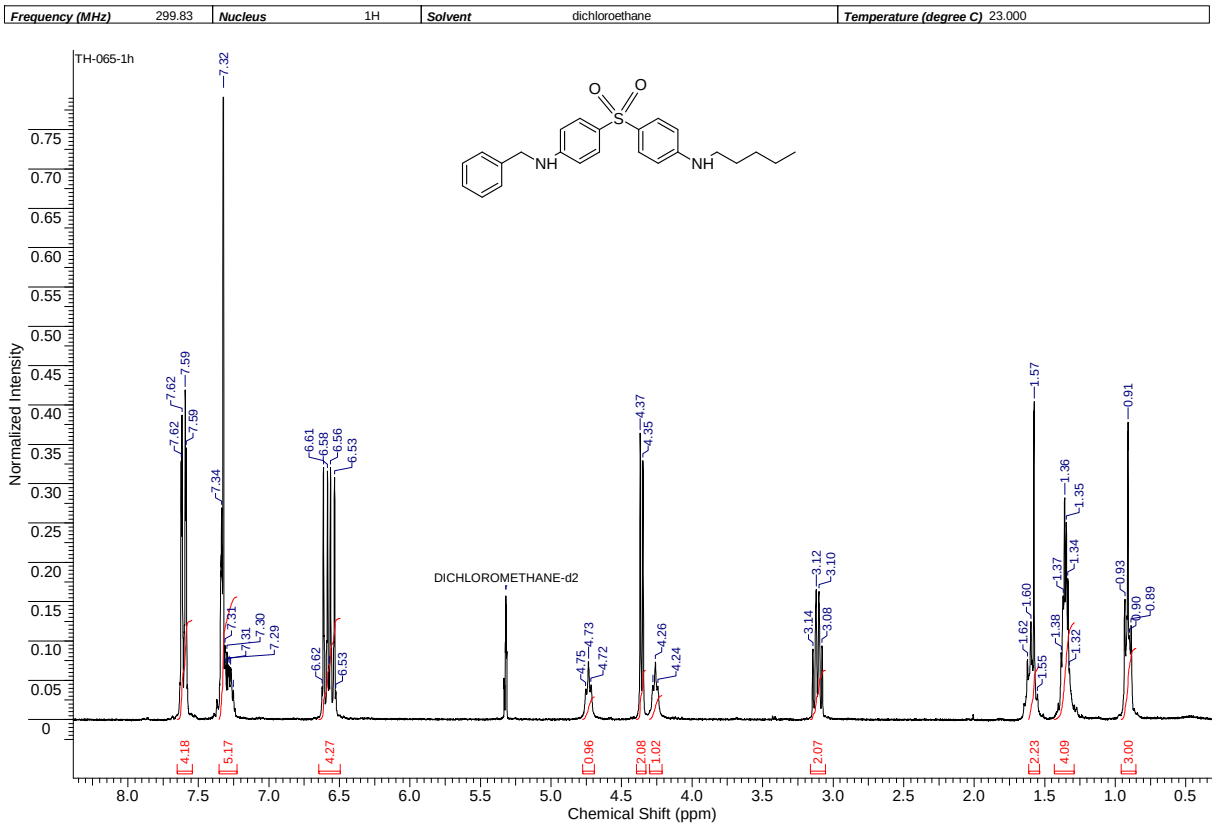
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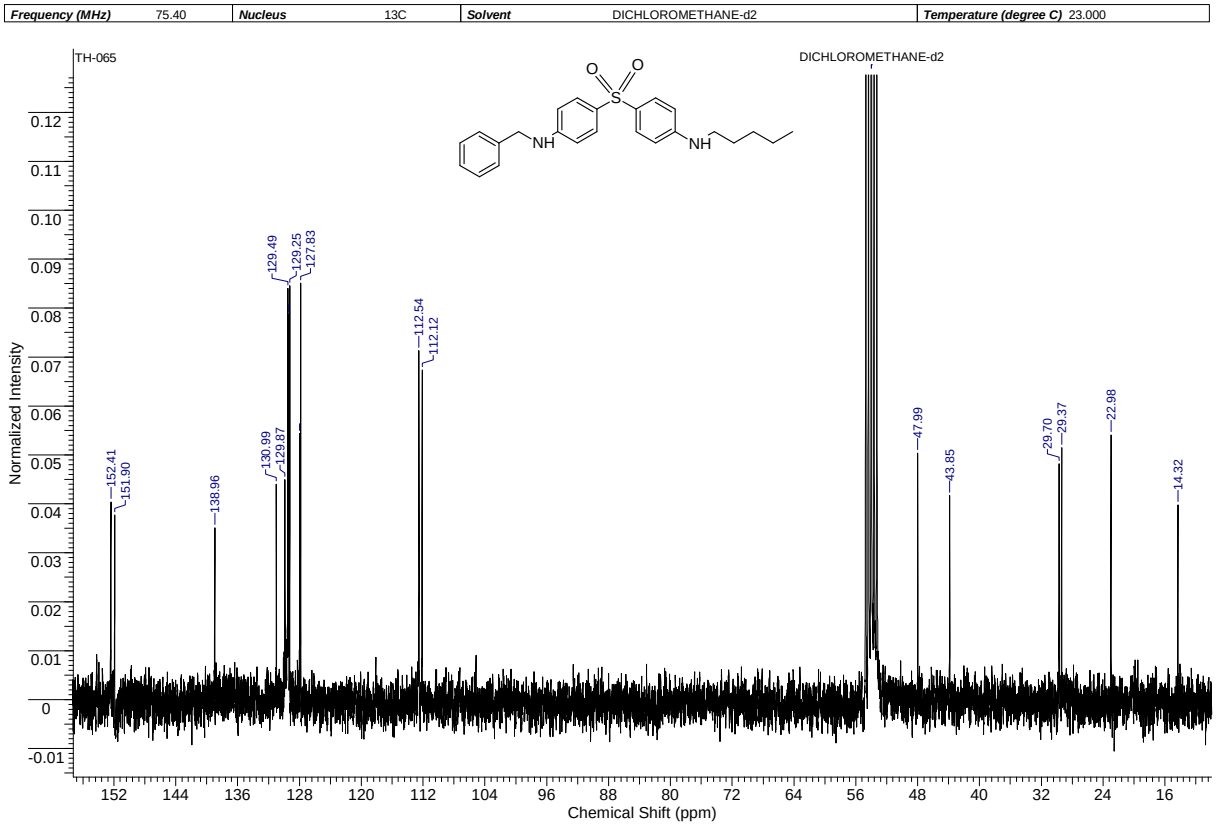
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TH-065
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

6. A sustainable catalytic pyrrole synthesis

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Abstract: The pyrrole heterocycle is a prominent chemical motif and is found widely in natural products, drugs, catalysts, and advanced materials. Here we introduce a sustainable iridium-catalyzed pyrrole synthesis in which secondary alcohols and amino alcohols are deoxygenated and linked selectively via the formation of C-N and C-C bonds. Two equivalents of hydrogen gas are eliminated in the course of the reaction, and alcohols based entirely on renewable resources can be used as starting materials. The catalytic synthesis protocol tolerates a large variety of functional groups, which includes olefins, chlorides, bromides, organometallic moieties, amines and hydroxyl groups. We have developed a catalyst that operates efficiently under mild conditions.

6.1 Introduction

Dwindling reserves of crude oil and the resulting price increase of this and other fossil carbon sources combined with environmental concerns have resulted in a call for the use of alternative, preferably renewable, resources. Aside from fuel, ultimately a wide variety of chemical feedstocks are derived from fossil sources. Renewable lignocellulosic materials are indigestible and therefore not useful as food products and can be processed to give alcohols and polyols.[1] These rather highly oxidized hydrocarbons differ drastically in their chemical nature from the cracking products of crude oil. Thus, there is a high demand for new reactions that utilize such oxidized hydrocarbons and convert them into key chemicals.

Pyrroles are important compounds and present in many natural products, drugs, catalysts and materials. Both the blood respiratory pigment haem and the green photosynthesis pigment chlorophyll are biosynthesized from the pyrrole porphobilinogen.[2] Atorvastatin, the

bioactive component of the best-selling drug by value[2], is a pyrrole derivative. Polypyrroles are conducting polymers used in batteries[3] and solar cells[4]. There are many classic protocols[2] and catalytic transformations[5-7] for the synthesis of pyrroles.

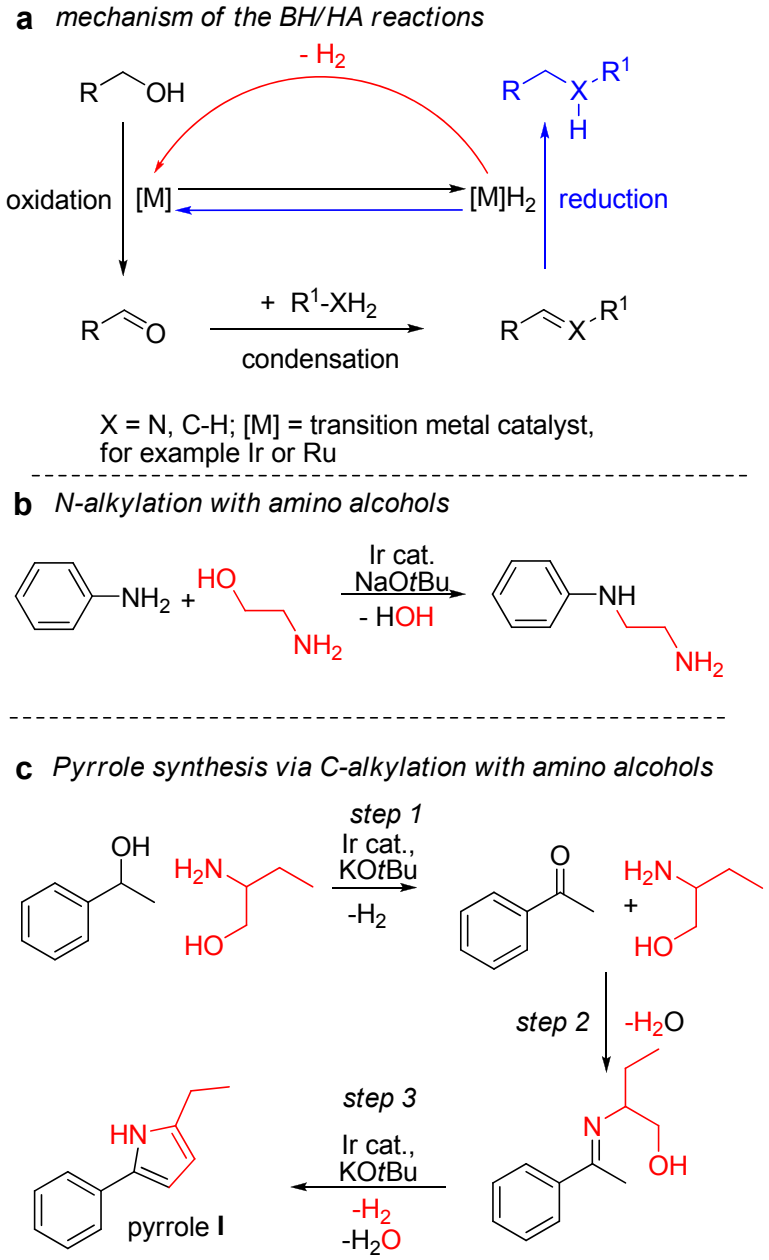


Figure 1. Alkylation reactions using amino alcohols. **a**, The mechanism of the BH/HA reactions (black and blue schemes). The suppression of the reduction step (blue) could give rise to imines or olefins. Catalyst recycling can occur via hydrogen elimination (red). **b**, Selective *N*-alkylation of aromatic amines catalyzed by an iridium complex. **c**, Pyrrole synthesis: step 1, oxidation of the secondary alcohol via the liberation of H_2; step 2, imine formation; step 3, intramolecular C-C coupling via the loss of hydrogen and water followed by isomerization to the pyrrole. (cat. = catalyst, O-*t*-Bu = *t*-butoxide)

The surge of catalytic protocols published recently gives proof of the vibrant activity in this field.[8-21] As a result of both the high demand for new reactions that utilize renewable resources and the importance of pyrroles, a pyrrole synthesis that fully or partially uses renewable resources is a highly desirable goal. Such a reaction would be especially attractive in terms of applicability in organic synthesis (and industrial production) if it extented significantly the scope of existing pyrrole syntheses. The known borrowing hydrogen (BH) methodology[22,23], also called hydrogen autotransfer (HA)[24], converts alcohols into imine or olefin functionalities and reduces them into amines or alkanes (Fig. 1a, black and blue reactions).

Imines or olefins may be accessible if the final reduction or hydrogenation step is suppressed (Fig. 1a, black and red reactions) and the hydrogen atoms (originating from the alcohol substrates) are liberated. The selective linkage of these imine and olefin functionalities can lead to heteroaromatics. Coupling reactions with concomitant liberation of H_2 developed by the Milstein group has attracted considerable attention recently[25-34]. These very useful reactions can also involve condensation steps[29,32,33], but they have not been used to link different alcohols via selective formations of C-C and C-N bonds. The simultaneous use of different alcohols is challenging because homocoupling has to be avoided. In turn, many classes of heteroaromatic compounds might be accessible and unsymmetrically functionalized molecules could be obtained.

6.2 Results and Discussion

Recently, we developed efficient catalysts for the alkylation of amines[35,36] and novel C-C coupling reactions[37] that relied on the BH/HA mechanism. The selectivity pattern of our catalysts tolerated the presence of aliphatic amines.[38] Thus, unprotected aliphatic amino alcohols could be employed to alkylate aromatic amines (Fig. 1b). A catalytic pyrrole synthesis becomes feasible if such catalysts are able to link selectively secondary alcohols and amino alcohols (Fig. 1c). The secondary alcohol is oxidized to a ketone, which undergoes imine formation with the amino alcohol. Subsequently, ring closure can occur via iridium catalyzed amino alcohol dehydrogenation and condensation. Two equivalents of water and hydrogen are eliminated in the course of the reaction (dehydrogenative condensations). To identify a selective catalyst for this process we investigated thoroughly the reaction of 1-phenyl-ethanol with 2-amino-1-butanol. The compound 2-ethyl-5-phenyl-1*H*-pyrrole (pyrrole **I**, Fig. 1c) is formed in this reaction. The best catalyst known to tolerate amino

alcohols (catalyst **I**, Fig. 2a, left[38,39]) afforded only 10% conversion when a catalyst loading of 0.01 mol% was applied. Chemically related catalysts that could provide more stability because of stabilization by three-dentate ligands[40] were thus investigated. The iridium catalyst **II** (Fig. 2a, middle and right) turned out to be the best catalyst and gave 63% conversion under identical conditions. Catalyst **II** as a crystalline material can be handled in air (for instance, for refilling, weighing) asit is not sensitive towards oxygen and moisture for weeks. The optimization of the reaction conditions eventually led to an efficient pyrrole synthesis protocol. (Details in the Supplementary Information and Supplementary Tables S1-S8).

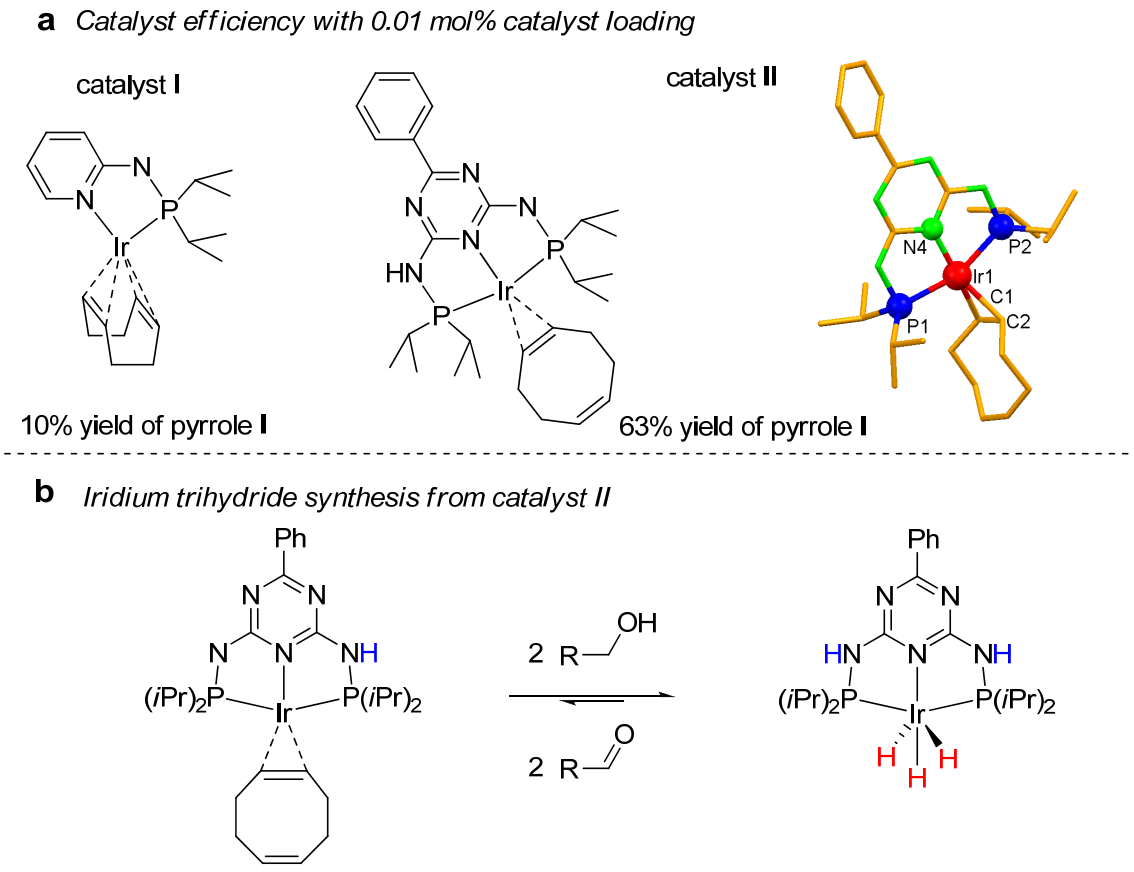
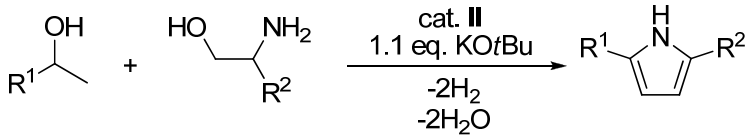


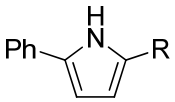
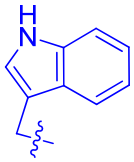
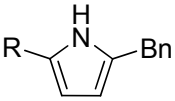
Figure 2. Catalyst design. **a**, Yields of pyrrole **I** using catalysts **I** and **II**. The molecular structure of catalyst **II** was determined by X-ray crystal structure analysis (right). **b**, Synthesis of the catalyst resting state by reacting catalyst **II** with an excess of alcohol. An iridium(III) trihydride species is formed by oxidation of the alcohol. R = alkyl or aryl substituent.

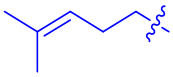
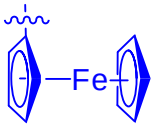
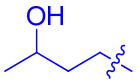
Having found a suitable catalyst and optimum reaction conditions, we addressed the issues of scope and functional group tolerance. Eight pyrroles were synthesized from different amino alcohols (Table 1, **1a-1h**). These examples carry a phenyl substituent that originates from the

secondary alcohol. Additionally, 13 pyrroles were prepared by varying the secondary alcohol (Table 1, **1i-1u**). Here the benzyl substituent that stemms from 2-amino-3-phenylpropan-1-ol was "kept constant". By varying both parameters, 8 x 13 = 104 different α-substituted pyrroles should be accessible, which indicates the versatility of this synthetic protocol. Of the 21 pyrroles we actually prepared, 13 have not been reported previously (Table 1, blue entries). The synthesis protocol is characterized by a very broad functional group tolerance (Table 1). Amines (**1c**), olefins (**1m**), chlorides (**1p**), bromides (**1q**), organometallic moieties (**1r**) and hydroxyl groups (**1u**) remain unaffected. Catalyst loadings as low as 0.03 mol% were sufficient for selected reactions listed in Table 1. All the reactions proceeded under rather mild thermal conditions (90 °C). The methodology is also extendable to 2*H*-pyrroles (Supplementary Table S10).

Table 1. Synthesis of 2,5-disubstituted pyrroles from secondary alcohols and amino alcohols.



	Catalyst **II** Loading: [mol% Ir]	R	Isolated yield [%]
			
1a	0.05	-CH_3	80
1b	0.05	-C_2H_5	93
1c	0.1		65
1d	0.03	-*iso*-propyl	89
1e	0.05	-1-methylpropyl	88
1f	0.1	-*iso*-butyl	69
1g	0.2	-phenyl	86
1h	0.05	-benzyl	79
			

1i	0.03	-CH_3	84
1j	0.03	-C_4H_9	76
1j	0.03	-C_4H_9	76
1k	0.03	-C_6H_{13}	97
1l	0.05	-C_9H_{19}	74
1m	0.1		77
1n	0.1	-*i*-Pr	73
1o	0.05	-(C_6H_4)-4-OMe	84
1p	0.05	-(C_6H_4)-4-Cl	75
1q	0.2	-(C_6H_4)-4-Br	75
1r	0.2		87
1s	0.5	-2-furanyl	42
1t	0.5	-2-thiophenyl	57
1u	0.1		70

Reaction conditions: THF, 90 °C, 24 h.

As the *C*-alkylation step (Fig. 1c) can also take place at a secondary aliphatic carbon atom, this methodology allows for the synthesis of 2,3,5-trisubstituted pyrroles (Fig. 3). Cyclic secondary alcohols afford bicyclic pyrroles. None of the compounds listed in Fig. 3 have been reported previously. These examples give further evidence of the potential of this methodology to complement and augment the conventional organic synthesis of pyrroles. Starting from dioles, dipyrroles can be prepared (Fig. 4a). As intermediates that carry hydroxyl group can be isolated in good yields (Table 1, **1u**), a sequential generation of differently substituted dipyrroles is possible (Fig 4a). Such dipyrrole syntheses generate a remarkable amount of hydrogen (four equivalents). The synthesis of one mole of dipyrrole proceeds with the concomitant generation of about 90 liters of H_2. Furthermore, a combination of selective BH/HA chemistry and dehydrogenative condensations is possible. The alkylation of aryl amines using dioles gives rise to the respective *N*-arylated amino alcohol, which can then be linked selectively with unprotected amino alcohols.

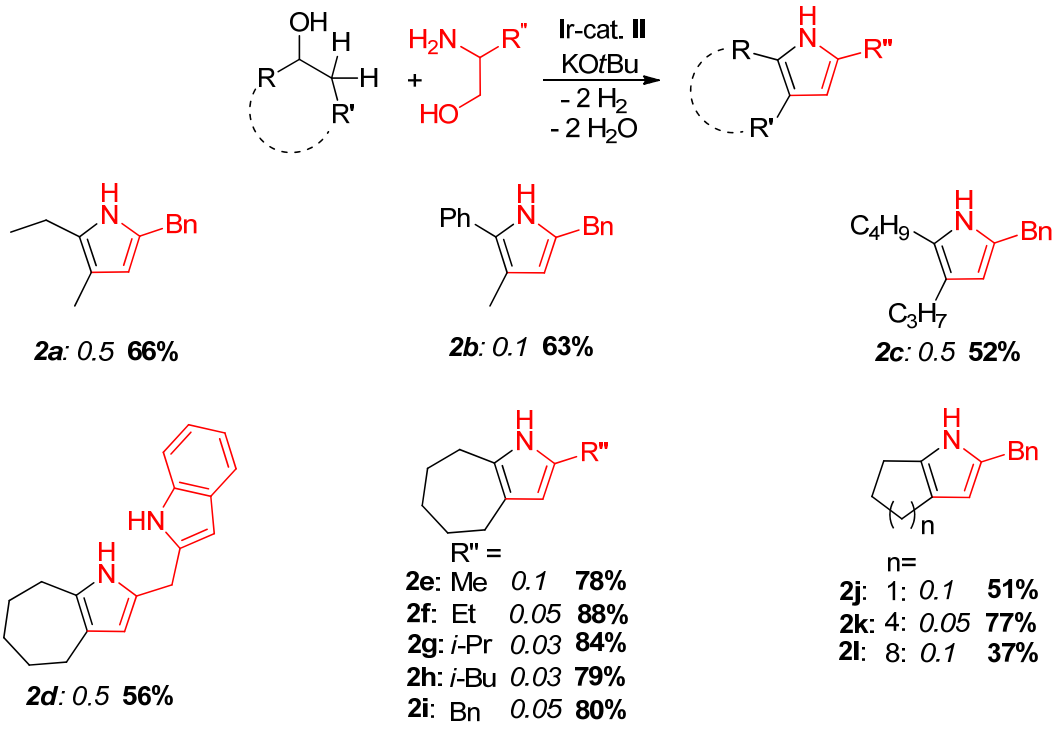


Figure 3. Synthesis of 2,3,5-trisubstituted pyrroles. Fragments that stem from the amino alcohol are shown in red and those contributed by the secondary alcohol are in black. Reaction conditions: THF, 90 °C, 24 h. Italic numbers give the catalyst loadings in mol% (catalyst **II**, Fig. 1d, right) and the bold numbers the isolated yields.

The products, amino pyrroles, were obtained in very good isolated yields (Fig. 4b). The amine functional group tolerance and the selectivity of the C-C and C-N bond formation steps allow access to these compounds. Mechanistically, we propose at this stage a reaction sequence as shown in Fig. 1c. Dehydrogenation of the secondary alcohol is significantly faster than that of the amino alcohol. It affords a ketone, which undergoes a condensation reaction with the amino alcohol to form an imine (Schiff base). Independent synthesis of this imine intermediate and its treatment under catalytic conditions gave pyrrole **I** (Supplementary Figs S8 and S11). Alternatively, intermolecular β-alkylation of 1-phenyl-ethanol using protected amino alcohols (with or without the liberation of H_2) does not proceed significantly under catalytic conditions (Supplementary Figs S12 and S13). Kinetic data indicate that the intramolecular *C*-alkylation is fast in comparison to the oxidation of the secondary alcohol as no imine intermediate was detected (Supplementary Figs S4 and S5). The mechanistic proposal is also in accordance with an observation made by Ishii and co-workers[7]. They reacted 2-aminoethanol and 2-(methylamino)ethanol with three equivalents of propiophenone and observed pyrrole formation in the presence of an iridium catalyst and a base. The catalyst resting state of our pyrrole synthesis is an iridium trihydride complex (Figure 2b).

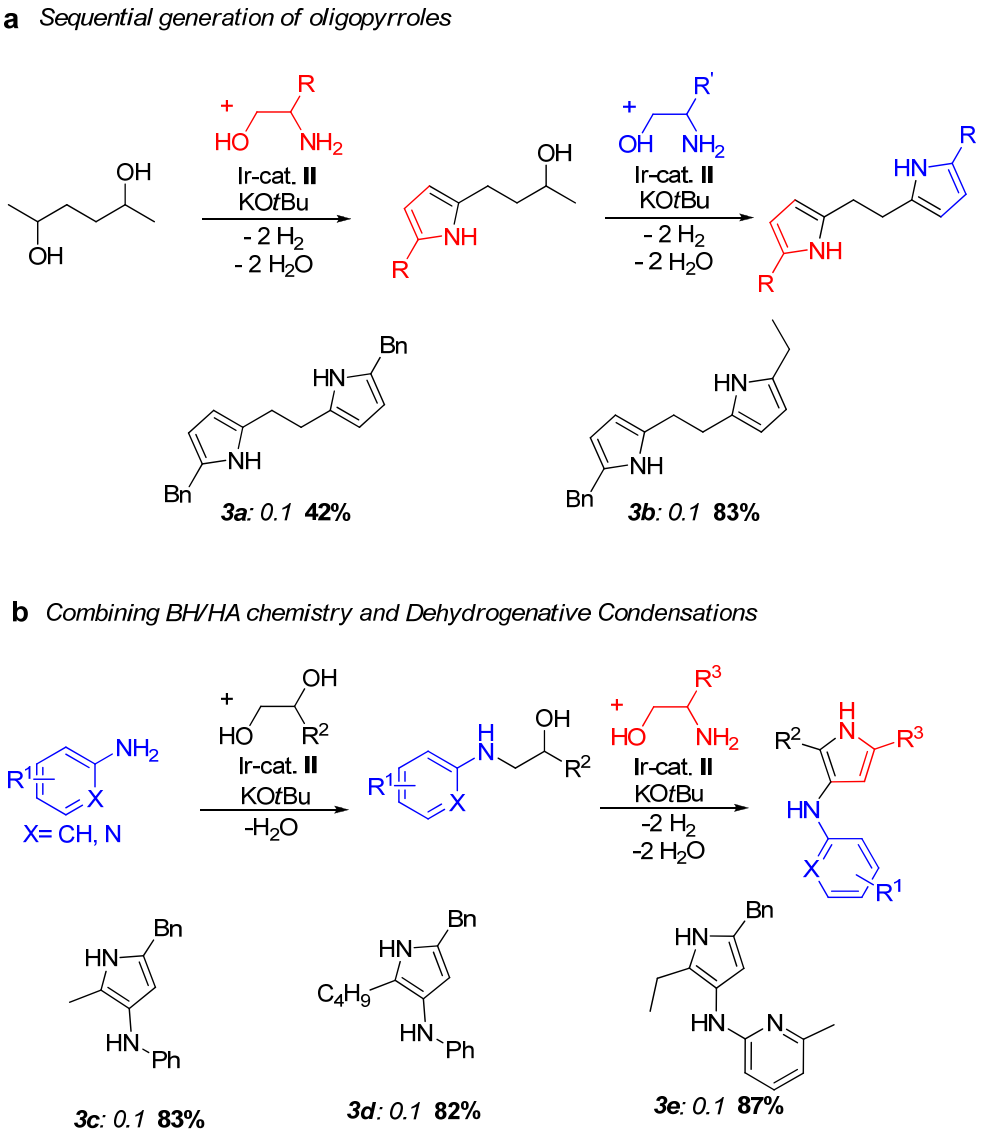


Figure 4. Pyrrole syntheses involving diols. (**a**) Synthesis of symmetric and unsymmetric dipyrroles. (**b**) Synthesis of aminopyrroles. Italic numbers give the catalyst loading in mol% and bold numbers the isolated yields. For the reaction conditions see Table 1.

It can be formed quantitatively (NMR experiment) by reacting catalyst **II** with alcohols or H_2 (Supplementary Fig. S3). Its structure was also determined by X-ray single crystal structure analysis (Supplementary Fig. S15). The role of the iridium catalyst is the oxidation of the two alcohols and the base mediates the C-C coupling/condensation step. In addition, the base accelerates the alcohol oxidation. The base amount was optimized towards an efficient pyrrole formation. In the absence of base essentially nothing happens under catalytic conditions; only iridium trihydride formation is observed. If the catalyst loading is increased, alcohol oxidation accompanied by H_2 liberation takes place (Supplementary Fig. S7). The

somewhat lower yields, for example for **1s** and **1t** (Table 1), result from a rather slow dehydrogenation of the secondary alcohols. Under these circumstances homocoupling of the amino alcohols becomes relevant (the formation of pyrazines[29]; Supplementary Fig. S10). In the case of **1u** (Table 1), oxidation of the second alcohol function and subsequent dipyrrole formation lowers the yield.

6.3 Conclusion

We expect dehydrogenative condensations to become an integral part of what could be termed the "new catalytic chemistry" that taps into the inexhaustible renewable resources for the synthesis of virtually any important organic compound. Such reactions are efficient in the deoxygenation of alcohols, proceed with the evolution of hydrogen and afford diversely substituted products by a series of selective consecutive formations of C-C and C-N bonds. In this paper demonstrate exemplarily how pyrroles may be built up readily by formally connecting an imine and an olefin. More heteroaromatic patterns should now be within reach.

Methods

In a pressure tube (inner diameter 25.4 mm, length 20.3 cm, volume 38 mL) a magnetic stir bar, catalyst **II** (3 to 50 µmol), THF (10 mL), secondary alcohol (20.0 mmol), amino alcohol (10.0 mmol) and KO*t*Bu (11.0 mmol) were combined in a dry nitrogen atmosphere using glove box techniques. The pressure tube was closed with a silicone tube (inner diameter 7 mm, outer diameter 10 mm, length 30 cm) used as a semi-permeable membrane (for details see the Supplementary Information) and stirred at 90 °C for 24 h. The reaction mixture was cooled to room temperature and quenched by the addition of 2 mL of water. The layers were separated and the aqueous layer was extracted with Et_2O (4 x 40 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel.

Acknowledgement

This work was supported by the Deutsche Forschungsgemeinschaft (SFB 840 and KE 756/23-1). S. M. is also grateful for an Elitenetzwerk Bayern grant. We thank Tobias Bauer for solving the structure of catalyst **II** and the Ir trihydride.

6.4 References

[1] Vispute, T. P., Zhang, H., Sanna, A., Xiao, R., Huber, G. W. Renewable Chemical Commodity Feedstocks from Integrated Catalytic Processing of Pyrolysis Oils.

[2] Joule, J. A., Mills, K. in *Heterocyclic Chemistry*, **5th ed.** (Wiley, Chichester, UK, 2010).

[3] Nishide, H., Oyaizu, K. Towards Flexible Batteries. *Science* **319**, 737-738 (2008).

[4] Hagfeldt, A., Boschloo, G., Sun, L., Kloo, L., Pettersson, H. Dye-Sensitized Solar Cells. *Chem. Rev.* **110**, 6595-6663 (2010).

[5] Nakamura, I., Yamamoto, Y. Transition-Metal-Catalyzed Reactions in Heterocyclic Synthesis. *Chem. Rev.* **104**, 2127-2198 (2004).

[6] Patil, N. T., Yamamoto, Y. Metal-mediated synthesis of furans and pyrroles, *Arkivoc* **10**, 121-141 (2007).

[7] Taguchi, K., Sakaguchi, S., Ishii, Y. Synthesis of quinolines from amino alcohol and ketones catalyzed by $[IrCl(cod)]_2$ or $IrCl_3$ under solvent-free conditions. *Tetrahedron Lett.* **46**, 4539-4542 (2005).

[8] Rakshit, S., Patureau, F. W., Glorius, F. Pyrrole Synthesis via Allylic sp^3 C−H Activation of Enamines Followed by Intermolecular Coupling with Unactivated Alkynes. *J. Am. Chem. Soc.* **132**, 9585-9587 (2010).

[9] Maiti, S., Biswas, S. Jana, U. Iron(III)-Catalyzed Four-Component Coupling Reaction of 1,3-Dicarbonyl Compounds, Amines, Aldehydes, and Nitroalkanes: A Simple and Direct Synthesis of Functionalized Pyrroles. *J. Org. Chem.* **75**, 1674-1683 (2010).

[10] Liu, W., Jiang, H., Huang, L. One-Pot Silver-Catalyzed and PIDA-Mediated Sequential Reactions: Synthesis of Polysubstituted Pyrroles Directly from Alkynoates and Amines. *Org. Lett.* **12**, 312-315 (2010).

[11] Donohoe, T. J., Race, N. J., Bower, J. F., Callens, C. K. A. Substituted Pyrroles via Olefin Cross-Metathesis. *Org. Lett.* **12**, 4094-4097 (2010).

[12] Stuart, D. R., Alsabeh, P., Kuhn, M., Fagnou, K. Rhodium(III)-Catalyzed Arene and Alkene C−H Bond Functionalization Leading to Indoles and Pyrroles. *J. Am. Chem. Soc.* **132**, 18326-18339 (2010).

[13] Toshiaki, S., Takuya, S., Reiko I., Norio S., Takeo K. Approach to Trisubstituted 3-Aminopyrrole Derivatives by $Yb(OTf)_3$-Catalyzed [4+1] Annulation of 2-Azadiene with Me_3SiCN. *Eur. J. Org. Chem.* **22**, 4237-4244 (2010).

[14] Lin, M., Hao, L., Ma, R. D., A Novel Indium-Catalyzed Three-Component Reaction: General and Efficient One-Pot Synthesis of Substituted Pyrroles. *Synlett* **15**, 2345-2351 (2010).

[15] Huestis, M. P., Chan, L., Stuart, D. R., Fagnou, K. The Vinyl Moiety as a Handle for Regiocontrol in the Preparation of Unsymmetrical 2,3-Aliphatic-Substituted Indoles and Pyrroles. *Angew. Chem. Int. Ed.* **50**, 1338-1341 **(**2011).

[16] Trost, B. M., Lumb, J.-P., Azzarelli, J. M. An Atom-Economic Synthesis of Nitrogen Heterocycles from Alkynes. *J. Am. Chem. Soc.* **133**, 740-743 (2011).

[17] Ng, E. P. J., Wang, Y.-F., Chiba, S. Manganese(III)-Catalyzed Formal [3+2] Annulation of Vinyl Azides and β-Keto Acids for Synthesis of Pyrroles. *Synlett* **6**, 783-786 (2011).

[18] Cai, Q., Zhou, F., Xu, T., Fu, L., Ding, K. Copper-Catalyzed Tandem Reactions of 1-(2-Iodoary)-2-yn-1-ones with Isocyanides for the Synthesis of 4-Oxo-indeno[1,2-*b*]pyrroles. *Org. Lett.* **13**, 340-343 (2011).

[19] Yamagishi, M., Nishigai, K., Hata, T., Urabe H. Nucleophilic Addition of Sulfonamides to Bromoacetylenes: Facile Preparation of Pyrroles. *Org. Lett.* **13**, 4873-4875 (2011).

[20] Schley, N. D., Dobereiner, G. E., Crabtree, R. H. Oxidative Synthesis of Amides and Pyrroles via Dehydrogenative Alcohol Oxidation by Ruthenium Diphosphine Diamine Complexes. *Organometallics* **30**, 4174-4179 (2011).

[21] Donohoe, T. J., Bower, J. F., Chan, L. K. M. Olefin cross-metathesis for the synthesis of heteroaromatic compounds. *Org. Biomol. Chem*. **10**, 1322-1328 (2012).

[22] Watson, A. J. A., Williams, J. M. J. The Give and Take of Alcohol Activation. *Science* **329**, 635-636 (2010).

[23] Bähn, S., Imm, S., Neubert, L., Zhang, M., Neumann, H., Beller, M. The Catalytic Amination of Alcohols. *ChemCatChem* **3**, 1853-1864 (2011).

[24] Guillena, G., Ramon, D. J., Yus, M. Transition-Metal-Catalyzed Reactions in Heterocyclic Synthesis. *Chem. Rev.* **110**, 1611-1641 (2010).

[25] Gunanathan, C., Ben-David, Y., Milstein, D. Direct Synthesis of Amides from Alcohols and Amines with Liberation of H_2. *Science* **317**, 790-792 (2007).

[26] Gnanaprakasam, B., Milstein, D. Dehydrogenation as a Substrate-Activating Strategy in Homogeneous Transition-Metal Catalysis. *Acc. Chem. Res.* **44**, 588-602 (2011).

[27] Gunanathan, C., Milstein, D. Bond Activation by Metal-Ligand Cooperation: Design of "Green" Catalytic Reactions Based on Aromatization-Dearomatization of Pincer Complexes. *Bifunct. Mol. Cat.* **37**, 55-84 (2011).

[28] Milstein, D. Discovery of Environmentally Benign Catalytic Reactions of Alcohols Catalyzed by Pyridine-Based Pincer Ru Complexes, Based on Metal–Ligand Cooperation. *Top. Catal.* **53**, 915-923 (2010).

[29] Boopathy, G., Balaraman, E., Ben-David, Y., Milstein, D. Synthesis of Peptides and Pyrazines from β-Amino Alcohols through Extrusion of H_2 Catalyzed by Ruthenium Pincer Complexes: Ligand-Controlled Selectivity. *Angew. Chem. Int. Ed.* **50**, 12240-12244 (2011).

[30] Gnanaprakasam, B., Milstein, D. Synthesis of Amides from Esters and Amines with Liberation of H_2 under Neutral Conditions. *J. Am. Chem. Soc.* **133**, 1682-1685 (2011).

[31] Gnanaprakasam, B., Ben-David,Y., Milstein, D. Ruthenium Pincer-Catalyzed Acylation of Alcohols Using Esters with Liberation of Hydrogen under Neutral Conditions. *Adv. Synth. Catal.* **352**, 3169-3173 (2010).

[32] Gnanaprakasam, B., Zhang, J., Milstein, D. Direct Synthesis of Imines from Alcohols and Amines with Liberation of H_2. *Angew Chem. Int. Ed.* **49**, 1468-1471 (2010).

[33] Gunanathan, C., Shimon, L. J., Milstein, D. Direct Conversion of Alcohols to Acetals and H_2 Catalyzed by an Acridine-Based Ruthenium Pincer Complex. *J. Am. Chem. Soc.* **131**, 3146-3147 (2009).

[34] Zhang, J., Leitus, G., Ben-David, Y., Milstein, D. Facile Conversion of Alcohols into Esters and Dihydrogen Catalyzed by New Ruthenium Complexes. *J. Am. Chem. Soc.* **127**, 10840-10841 (2005).

[35] Blank, B., Madalska, M., Kempe, R. An Efficient Method for the Selective Iridium-Catalyzed Monoalkylation of (Hetero)aromatic Amines with Primary Alcohols. *Adv. Synth. Catal*. **350**, 749-758 (2008).

[36] Blank, B., Michlik, S., Kempe, R. Selective Iridium-Catalyzed Alkylation of (Hetero)Aromatic Amines and Diamines with Alcohols under Mild Reaction Conditions. *Chem. Eur. J.* **15**, 3790-3799 (2009).

[37] Blank, B., Kempe, R. Catalytic Alkylation of Methyl-*N*-Heteroaromatics with Alcohols. *J. Am. Chem. Soc.* **132**, 924-925 (2010).

[38] Blank, B., Michlik, S., Kempe, R. Synthesis of Selectively Mono-*N*-Arylated Aliphatic Diamines via Iridium-Catalyzed Amine Alkylation. *Adv. Synth. Catal.* **351**, 2903-2911 (2009).

[39] Michlik S., Hille, T., Kempe, R. The Iridium-Catalyzed Synthesis of Symmetrically and Unsymmetrically Alkylated Diamines under Mild Reaction Conditions. *Adv. Synth. Catal.* **354**, 847-862 (2012).

[40] Schirmer, W., Florke, U., Haupt, H.-J. Darstellung, Eigenschaften und Molekülstrukturen von Komplexen des versteiften dreizähnigen Chelatliganden *N,N′*-Bis(diphenylphosphino)-2,6-diaminopyridin mit M^{II} - und M^{0}-Übergangsmetallen [M^{II} = Ni, Pd, Pt; M^{0} = Cr, Mo, W]. *Z. Anorg. Allg. Chem.* **545**, 83-97 (1987).

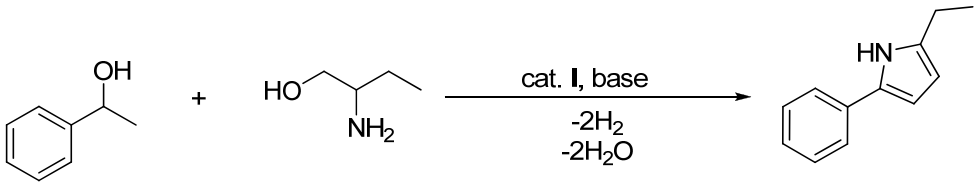
6.5 Supporting Information

General Considerations

All reactions were carried out in a dry argon or nitrogen atmosphere using standard Schlenk techniques or glove box techniques. Halogenated solvents were dried over P_2O_5, and non-halogenated solvents were dried over sodium benzophenone ketyl. 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 97% and used without further purification. NMR spectra were received using an INOVA 400 and 300 MHz spectrometer at 298 K or a BRUKER 300 MHz spectrometer at 300 K. Chemical shifts are reported in ppm relative to the deuterated solvent. Elemental analyses were carried out on a Vario elementar EL *III*. GC analyses were carried out on an Agilent 6890N Network GC system equipped with a HP-5 column (30 m x 0.32 µm x 0.25 µm). GC/MS analyses were carried out on a Thermo Focus GC/Trace DSQ system equipped with a HP-5MS column (30 m x 0.32 µm x 0.25 µm). X-ray crystal structure analyses were performed with a STOE-IPDS II equipped with an Oxford Cryostream low-temperature unit.

Screening Reactions

In a pressure tube catalyst, solvent, secondary alcohol, amino alcohol and base were combined. The pressure tube was closed with a Teflon® cap or a semi-permeable membrane and stirred for 24 h. The reaction mixture was cooled to room temperature and quenched by addition of 2 mL of water. Dodecane as internal standard was added and after shaking, a small fraction of the organic phase was analyzed by GC. The following reaction was investigated.



Supplementary Figure S1. Screening reaction of 1-phenylethanol with 2-amino-1-butanol

Supplementary Table S1. Base screening

Base	Yield [%]
KO*t*Bu	**55**
KOH	32
$KN(SiMe_3)_2$	0
$KOSiMe_3$	0
K_3PO_4	4
KH	47
K_2CO_3	0
KOAc	0
NaO*t*Bu	37
$NaNH_2$	25
NaOAc	0
Na_2CO_3	0
LiH	0
Li^{t}Bu	12
$Mg(O(C_2H_5))_2$	0

Reaction conditions: 1.0 eq. 1-phenylethanol (120 µL), 1.1 eq. 2-amino-1-butanol (104 µL), 1.1 eq. base, 3.0 mL THF, 1 mol% catalyst **I**, 24 h, 110 °C (reaction tubes closed with Teflon® caps). Yields determined by GC analyses with dodecane as internal standard.

Supplementary Table S2. Solvent screening

Solvent	Yield [%]
THF	**55**
DME	54
toluene	41
hexane	49
DMSO	0
diglyme	45
dioxane	48

Reaction conditions: 1.0 eq. 1-phenylethanol (120 µL), 1.1 eq. 2-amino-1-butanol (104 µL), 1.1 eq. KO*t*Bu, 3.0 mL solvent, 1 mol% catalyst **I**, 24 h, 110 °C (reaction tubes closed with Teflon® caps). Yields determined by GC analyses with dodecane as internal standard.

Supplementary Table S3. Amount of KO*t*Bu

Base amount according to secondary alcohol [eq.]	Yield [%]
3.0	8
2.0	19
1.1	**55**
1.0	53
0.5	32
without base	0

Reaction conditions: 1.0 eq. 1-phenylethanol (120 µL), 1.1 eq. 2-amino-1-butanol (104 µL), 3.0 mL solvent, KO^{t}Bu, 1 mol% catalyst **I**, 24 h, 110 °C (reaction tubes closed with Teflon® caps). Yields determined by GC analyses with dodecane as internal standard.

Supplementary Table S4. Alcohol ratio

Amino alcohol /secondary alcohol [eq.]	Yield [%]
3.0 / 1.0	34
2.0 / 1.0	51
1.1 / 1.0	55
1.0 / 1.0	54
1.0 / 1.1	56
1.0 / 2.0	**72**
1.0 / 3.0	77
1.0/ 4.0	77

Reaction conditions: 1.1 mmol KO*t*Bu, 3.0 mL THF, 1 mol% catalyst **I**, 24 h, 110 °C (reaction tubes closed with Teflon® caps). Yields determined by GC analyses with dodecane as internal standard.

Supplementary Table S5. Solvent amount

Solvent amount [mL]	Yield [%]
4.0	77
3.0	**77**
2.0	70
1.0	65
0.5	56
0.25	51

Reaction conditions: 2.0 eq. 1-phenylethanol (240 µL), 1.0 eq. 2-amino-1-butanol (96 µL) 1.1eq. KO*t*Bu, 1 mol% catalyst **I**, 24 h, 110 °C (reaction tubes closed with Teflon® caps). Yields determined by GC analyses with dodecane as internal standard.

Supplementary Table S6. Temperature screening

Temperature [°C] oil bath	Yield [%]
150	76
130	76
110	**76**
90	40
80	23
70	6

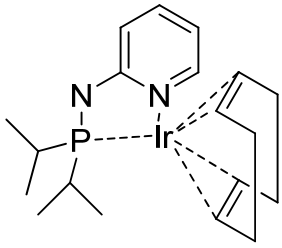
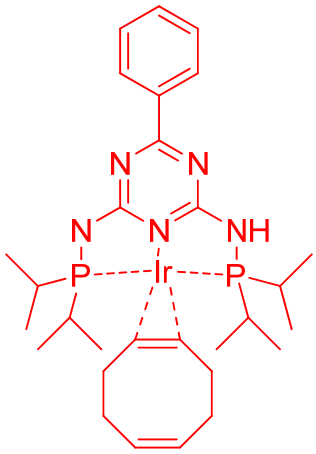
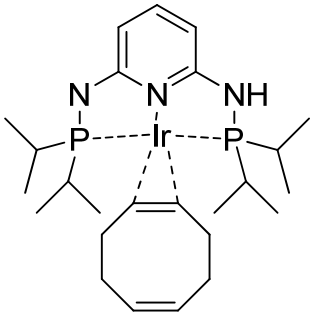
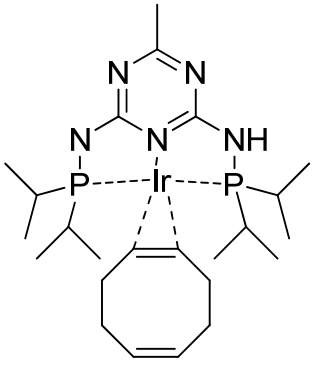
Reaction conditions: 2.0 eq. 1-phenylethanol (240 µL), 1.0 eq. 2-amino-1-butanol (96 µL) 1.1 eq. KO*t*Bu, 1 mol% catalyst **I**, 24 h (reaction tubes closed with Teflon® caps). Yields determined by GC analyses with dodecane as internal standard.

Supplementary Table S7. Catalyst loading

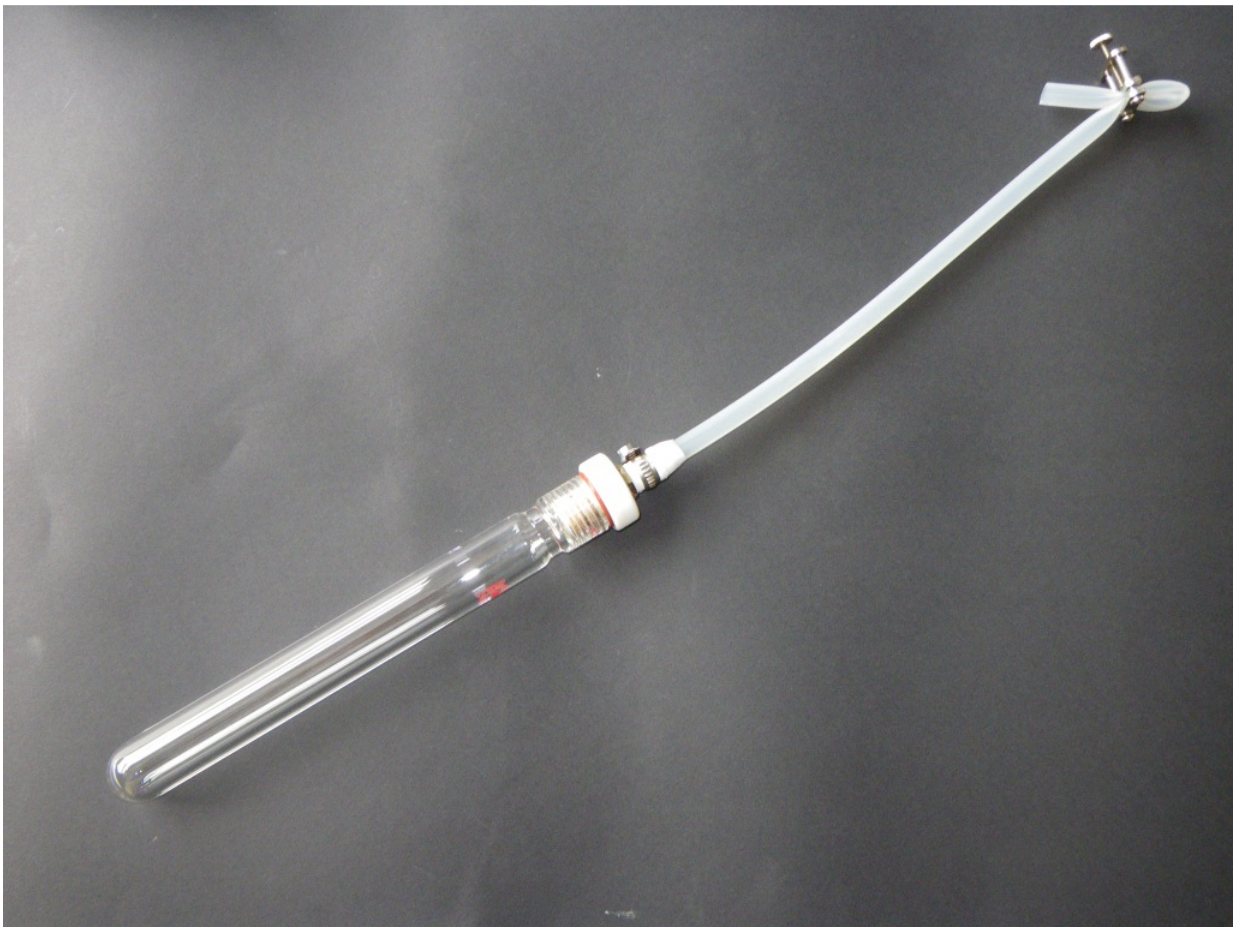
Cat. loading [mol%]	Yield [%]
2.0	65
1.0	75
0.6	**79**
0.4	78
0.2	77
0.1	76
0.05	68
0.01	36
0.005	10

Reaction conditions: 2.0 eq. 1-phenylethanol (240 µL), 1.0 eq. 2-amino-1-butanol (96 µL) 1,1eq. KO*t*Bu, catalyst **I**, 24 h, 110 °C (reaction tubes closed with Teflon® caps). Yields determined by GC analyses with dodecane as internal standard.

Supplementary Table S8. Iridium catalyst screening

	Catalyst	Yield [%]
I		10
II		63
III		33
IV		54
V	$[IrOMe(cod)]_2$	2
VI	$[IrCl(cod)]_2$	3

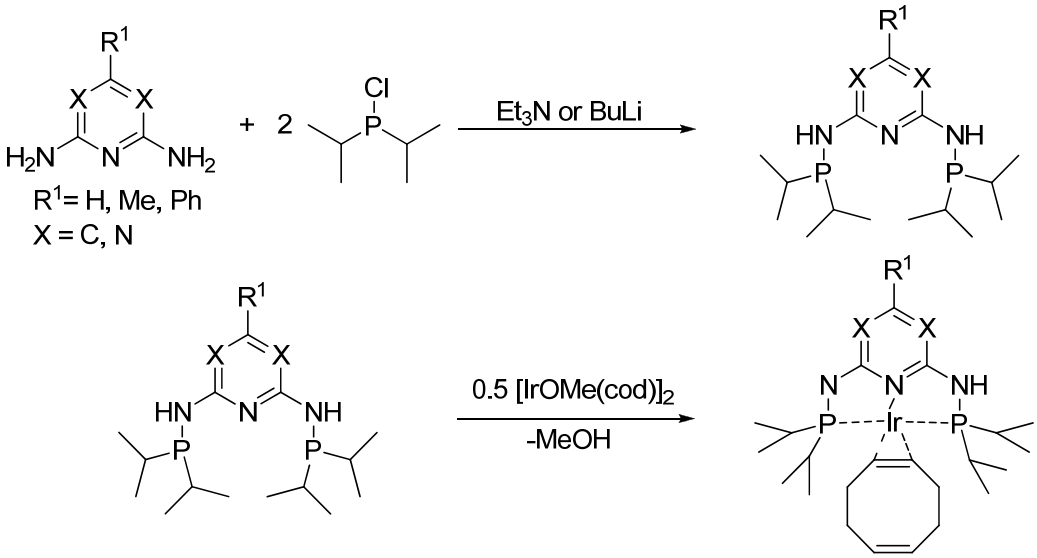
Reaction conditions: 2.0 eq. 1-phenylethanol (2.4 mL), 1.0 eq. 2-amino-1-butanol (0.96 mL) 1.1eq. KO*t*Bu (1.24 g), 0.01 mol% catalyst (1.0 mL, 0.001 M in THF), 10.0 mL THF, 24 h, 90 °C (reaction tubes closed with a semi-permeable membrane, for more details please see Supplementary Figure S2). Yields determined by GC analyses with dodecane as internal standard.



Supplementary Figure S2: Reaction flask with a semi-permeable membrane as used for the pyrrole syntheses. A silicone tube (Rotilabo®) inner diameter 7 mm, outer diameter 10 mm and 30 cm length was used as membrane. A maximum reaction temperature of 90 °C was determined inside the reaction flask due to a pressure increase (1 bar overpressure) caused by the membrane.

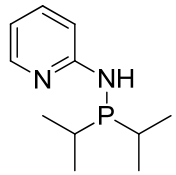
There are a few reasons for using the semi-permeable membrane. 1. low boiling substrates and 2. low boiling solvents which essentially means more solvent flexibility. Low boiling solvents are especially attractive in the work-up procedures since the solvent can be removed easily (also in the presence of products with rather low boiling points). Furthermore, a rather high throughput can be accomplished. One can easily run 60 flasks in a parallel fashion in a rather small fume hood. As a minor drawback the semi-permeable membrane means essentially adding a short rubber tube on top of the reaction flask.

Ligand and Complex Syntheses



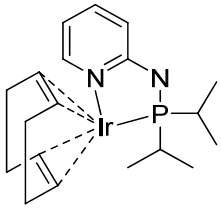
Supplementary Figure S3: Ligand and complex syntheses

Synthesis of PyNHP(*i*Pr)$_2$



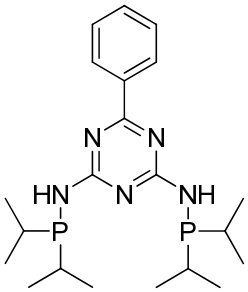
2-Aminopyridine (20.0 mmol, 1.88 g) was dissolved in 100 mL THF and triethylamine (20.0 mmol, 2.8 mL) was added and the solution was cooled to 0 °C. Then chlorodiisopropylphosphine (20.0 mmol, 3.2 mL) was added drop wise with a syringe. The solution was allowed to warm to room temperature and stirred over night at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. The solvent was concentrated *in vacuo* to 10 mL and left to crystallize at -20 °C. The supernatant solution was decanted and the solid washed with 5 mL of cold hexane and subsequently dried *in vacuo* yielding PyNHP(*i*Pr)$_2$ as a colorless solid (19.2 mmol = 96%). **^{1}H NMR** (400 MHz, C_6D_6, 298 K): δ = 8.18 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.27-7.23 (m, 1H), 7.10 (ddd, *J* = 8.5, 7.2, 1.7 Hz, 1H), 6.37 (ddd, *J* = 7.3, 7.1, 0.9 Hz, 1H), 4.86 (d, *J* = 10.6 Hz, 1H), 1.47-1.36 (m, 2H), 0.96-0.82 (m, 12H) ppm.**^{13}C NMR** (100 MHz, C_6D_6, 298 K): δ = 161.6 (d, *J* = 20.0 Hz), 148.7 (d, *J* = 1.2 Hz), 137.3 (d, *J* = 2.3 Hz), 114.5, 108.6 (d, *J* = 18.6 Hz), 26.5 (d, *J* = 11.6 Hz), 18.7 (d, *J* = 20.4 Hz), 17.1 (d, *J* = 8.0 Hz) ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298 K): δ = 48.82 ppm.

Synthesis of [(PyNP(*i*Pr)$_2$)Ir(cod)] (Cat. I)



PyNHP(*i*Pr)$_2$ (2.0 mmol, 420 mg) was dissolved in 20 mL THF, cooled to -30 °C and *n*-BuLi (2.0 mmol, 1.6 M, 1.25 mL) was added drop wise with a syringe. The reaction mixture was stirred at -30 °C for 30 min and was then allowed to warm to room temperature and stirred for 1h. Then the reaction mixture was added to a solution of [IrCl(cod)]$_2$ (1.0 mmol, 671 mg) (with a flexible tube). The reaction mixture was stirred for 30 min at room temperature before the solvent was removed *in vacuo*. The residue was suspended in diethyl ether and filtered over a glass filter frit with a pad of celite (1 cm) and washed with 10 mL of cold diethyl ether. Solvent was removed *in vacuo* and the residue was recrystallized from hexane affording dark red crystals (1.6 mmol, 80%). **^{1}H NMR** (400 MHz, C_6D_6, 298 K): δ = 7.30 (d, *J* = 8.8 Hz, 1H), 7.20 (d, *J* = 6.4 Hz, 1H), 6.86-6.78 (m, 1H), 5.65 (t, *J* = 6.4 Hz, 1H), 4.49-4.41 (m, 2H), 3.78-3.72 (m, 2H), 2.19-2.06 (m, 4H), 1.96-1.78 (m, 4H), 1.61-1.48 (m, 2H), 1.23 (dd, *J* = 13.9, 7.0 Hz, 6H), 1.07 (dd, *J* = 13.9, 7.0 Hz, 6H) ppm. **^{13}C NMR** (100 MHz, C_6D_6, 298 K): δ = 145.5 (d, *J* = 2.9 Hz), 137.6 (d, *J* = 2.5 Hz), 117.7 (d, *J* = 22.5 Hz,) 105.9, 88.3 (d, *J* = 11.3 Hz), 56.14, 34.4, (d, *J* = 2.3 Hz), 29.2 (d, *J* = 1.6 Hz), 28.57 (d, *J* = 38.9 Hz), 17.9 (d, *J* = 3.5 Hz), 17.5 ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298 K): δ = 94.70 ppm. **Elemental analysis** calcd (%) for $C_{27}H_{32}IrN_2P$: C 44.78, H 5.93, N 5.50; found: C 44.77, H 5.68, N 5.53.

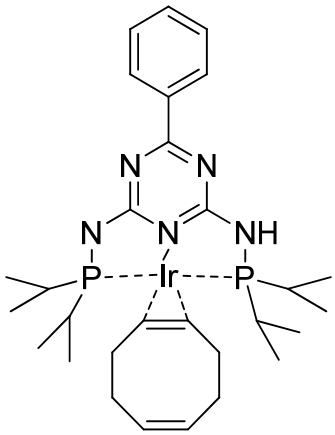
Synthesis of (4-Ph)Tr(NHP(*i*Pr)$_2$)$_2$



Benzoguanamine (30.0 mmol, 5.61 g) was dissolved in 150 mL THF and triethylamine (40.0 mmol, 2.8 mL) was added and the solution was cooled to 0 °C. Then chlorodiisopropylphosphine (60.0 mmol, 9.6 mL) was added drop wise with a syringe. The solution was allowed to warm to room temperature and stirred over night at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with

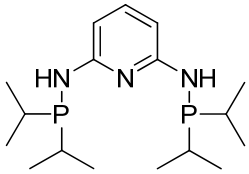
50 mL of THF. The solvent was concentrated *in vacuo*, recrystallized in toluene yielding (4-Ph)Tr(NHP(*i*Pr)$_2$)$_2$ as colorless crystals (12.06 g = 28.8 mmol = 96%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.43-8.29 (m, 2H), 7.54-7.42 (m, 3H), 5.25 (s_br, 2H), 1.99-1.82 (m, 4H), 1.16-1.11 (m, 24H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 171.7, 170.4 (d, *J* = 12.7 Hz), 137.4, 132.0, 128.9, 128.8, 26.8 (d, *J* = 14.4 Hz), 19.2 (d, *J* = 21.0 Hz), 18.0 (d, *J* = 9.3 Hz) ppm. **^{31}P NMR** (161 MHz, C_6D_6 , 298 K): δ = 52.69, 49.47 ppm. **^{31}P NMR** (161 MHz, C_6D_6, 353 K): δ = 54.33 ppm. **Elemental analysis**: for $C_{21}H_{35}N_5P_2$: C 60.13, H 8.41, N 16.70; found: C 60.12, H 8.13, N 16.54.

Synthesis of [(4-Ph)Tr(NP(*i*Pr)$_2$)(NHP(*i*Pr)$_2$)Ir(cod)] (Cat. II)



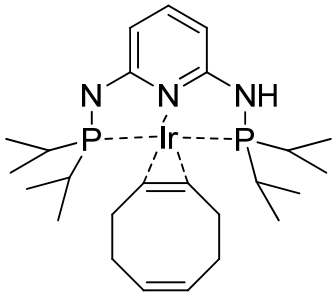
[IrOMe(cod)]$_2$ (2.0 mmol, 1.32g) was dissolved in 40 mL THF and subsequently a solution of (4-Ph)Tr(NHP(*i*Pr)$_2$)$_2$ (4.0 mmol, 1.67 g) dissolved in THF was added drop wise. A red solution was obtained. The solution was stirred over night at 50 °C. The solvent was removed *in vacuo*, yielding a deep red solid in quantitative yield. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.37- 8.32 (m, 2H), 7.48-7.38 (m, 3H), 6.06 (s_br, 1H), 5.68-5.61 (m, 2H), 3.89 (s_br, 2H), 2.42-2.14 (m, 10H), 1.74-1.62 (m, 2H), 1.24-1.12 (m, 24H) ppm.**^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 170.0 (t, *J* = 2.2 Hz), 137.9, 131.6, 130.7, 129.1, 128.7, 55.0, 37.0 (t, *J* = 3.3 Hz), 32.5, 28.5 (s_br), 18.0 (s_br), 16.9 ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298 K): δ = 83.34, 83.11 ppm. **Elemental analysis** (%) for $C_{29}H_{46}IrN_5P_2$ calcd: C 48.45, H 6.45, N 9.74; found: C 48.77, H 6.44, N 9.77.

Synthesis of Py(NHP(*i*Pr)$_2$)$_2$



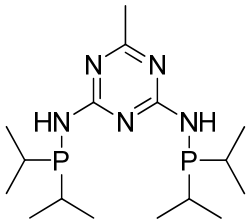
2,6-Diaminopyridine (30.0 mmol, 3.24 g) was dissolved in 150 mL THF and triethylamine (40.0 mmol, 2.8 mL) was added and the solution was cooled to 0 °C. Then chlorodiisopropylphosphine (60.0 mmol, 9.6 mL) was added drop wise with a syringe. The solution was allowed to warm to room temperature and stirred over night at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. The solvent was concentrated *in vacuo,* recrystallized in hexane yielding $Py(NHP(iPr)_2)_2$ as colorless crystals (6.14g = 18.0 mmol = 60%). **^{1}H NMR** (400 MHz, C_6D_6): δ = 7.20 (t, *J* = 7.9 Hz, 1H), 6.72 (dd, *J* = 7.9, 1.8 Hz, 2H), 4.48 (d, *J* = 9.6 Hz, 2H), 1.50-1.40 (m, 4H), 0.99-0.86 (m, 24 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2, 298 K): δ = 159,6 (d, *J* = 20.5 Hz), 140.1, 98.6 (d, *J* = 18.2Hz), 26.9 (d, *J* = 11.6 Hz), 19.0 (d, *J* = 19.9 Hz), 17.4 (d, *J* = 8.3 Hz) ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298 K): δ = 52.40, 49.32 ppm. **^{31}P NMR** (161 MHz, C_6D_6, 353 K): δ = 53.73 ppm.

Synthesis of [Py(NP(*i*Pr)$_2$)(NHP(*i*Pr)$_2$)Ir(cod)] (Cat. III)



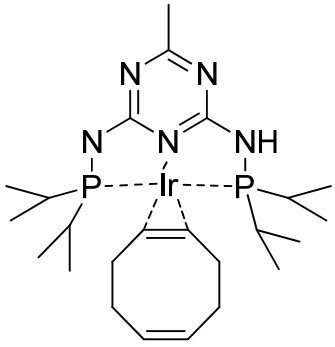
$[IrOMe(cod)]_2$ (1.0 mmol, 662 mg) was dissolved in 20 mL THF and subsequently a solution of $Py(NHP(iPr)_2)_2$ (2.0 mmol, 682 mg) dissolved in THF was added drop wise. A red solution was obtained. The solution was stirred over night at 50 °C. The solvent was removed *in vacuo,* yielding a deep red solid in quantitative yield. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 6.87 (tt, *J* = 7.9, 1.6 Hz, 1H), 5.77 (s_br, 2H), 5.64 (t, *J* = 4.1 Hz, 2 H), 4.84 (s_br, 1H), 3.65-3.76 (m, 2 H), 3.76-3.65 (m, 2H), 2.45-2.24 (m, 4H), 2.22-2.08 (m, 6H), 1.68-1.53 (m, 2 H), 1.26-1.06 (m, 24 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 138.7(t, *J* = 2.2 Hz), 130.8, 51.9, 37.2 (t, *J* = 3.9 Hz), 32.5, 30.0 (t, *J* = 16.5 Hz), 18.2(t, *J* = 2.2 Hz), 16.8 ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298 K): δ = 90.58 ppm. **Elemental analysis** (%) for $C_{25}H_{44}IrN_3P_2$ calcd: C 46.86, H 6.92, N 6.56; found: C 46.98, H 6.89, N 6.42.

Synthesis of (4-Me)Tr(NHP(*i*Pr)$_2$)$_2$



6-Methyl-[1,3,5]triazine-2,4-diamine (30.0 mmol, 3.75 g) was dissolved in 150 mL THF and triethylamine (40.0 mmol, 2.8 mL) was added and the solution was cooled to 0 °C. Then chlorodiisopropylphosphine (60.0 mmol, 9.6 mL) was added drop wise with a syringe. The solution was allowed to warm to room temperature and stirred over night at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. The solvent was concentrated *in vacuo*, recrystallized in toluene yielding (4-Me)Tr(NHP(*i*Pr)$_2$)$_2$ as white crystals (12.06g = 28.8 mmol = 96%). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 5.11 (s_br, 2H), 2.23 (s, 3H), 1.97-1.71 (m, 4H), 1.17-0.97 (m, 24H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 176.3, 169.8 (d, *J* = 13.2 Hz), 46.2, 26.6 (d, *J* = 14.4 Hz), 19.0 (d, *J* = 21.0 Hz), 17.9 (d, *J* = 8.9 Hz) ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298 K): δ = 52.13, 49.00 ppm. **^{31}P NMR** (161 MHz, C_6D_6, 353 K): δ = 53.33 ppm. **Elemental analysis** (%) for $C_{16}H_{33}N_5P_2$ calcd: C 53.77, H 9.31, N 19.59; found: C 53.75, H 9.51, N 19.23.

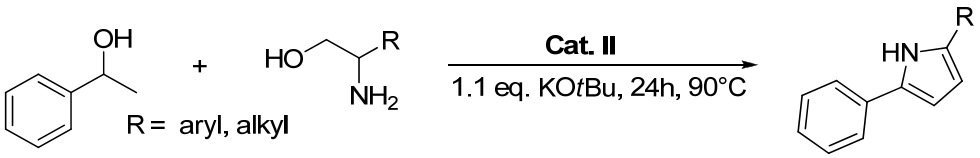
Synthesis of [(4-Me)Tr(NP(*i*Pr)$_2$)(NHP(*i*Pr)$_2$)Ir(cod)] (Cat. IV)

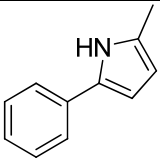
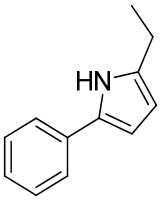
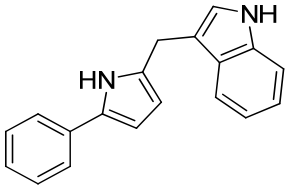
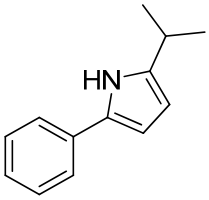
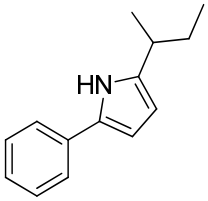
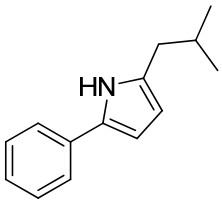


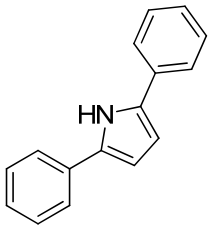
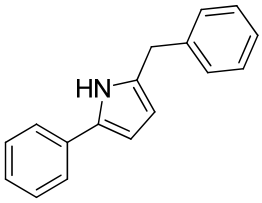
[IrOMe(cod)]$_2$ (0.5 mmol, 332 mg) was dissolved in 40 mL THF and subsequently a solution of (4-Me)Tr(NHP(*i*Pr)$_2$)$_2$ (1.0 mmol, 357 mg) dissolved in THF was added drop wise. A red solution was obtained. The solution was stirred over night at 50 °C. The solvent was removed *in vacuo*, yielding a deep red solid in quantitative yield. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 6.87 (tt, *J* = 7.9, 1.6 Hz, 1H), 5.77 (s_br, 2H), 5.64 (t, *J* = 4.1 Hz, 2 H), 4.84 (s_br, 1H), 3.65-3.76 (m, 2 H), 3.76-3.65 (m, 2H), 2.45-2.24 (m, 4H), 2.22-2.08 (m, 6H), 1.68-1.53 (m, 2 H), 1.26-1.06 (m, 24 H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 138.7, 130.8, 51.9, 37.2 (t, *J* = 3.9 Hz), 32.5, 30.0 (t, *J* = 16.5 Hz), 18.2(t, *J* = 2.2 Hz), 16.8 ppm. **^{31}P NMR** (161 MHz, C_6D_6,

298 K): δ = 84.54, 83.67 ppm. **Elemental analysis** (%) for $C_{24}H_{44}IrN_5P_2$ calcd: C 43.89, H 6.75, N 10.66; found: C 43.86, H 6.52, N 10.32.

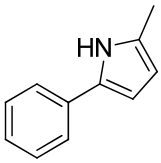
Supplementary Table S9: Reaction of 1-phenylethanol with various amino alcohols



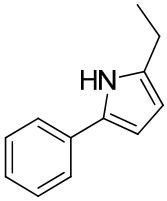
	[mol% **Cat. II**]	Product	Yield [a]
1a	**0.05**		**80%**
1b	**0.05**		**93%**
1c	**0.1**		**65%**
1d	**0.03**		**89%**
1e	**0.05**		**88%**
1f	**0.1**		**69%**

1g	**0.2**		**86%**
1h	**0.05**		**79%**

[a] Isolated yield

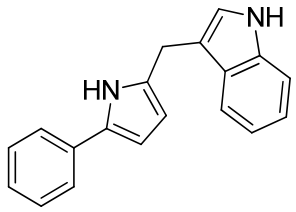


1a: 2-methyl-5-phenyl-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), 1-phenyl-ethanol (2.4 mL, 20.0 mmol), 2-amino-propan-1-ol (797 µL, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 40:1→10:1 pentane:Et_2O; Yield: 1.26 g = 8.0 mmol = 80% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.24 (s_br, 1H), 7.45-7.41 (m, 2H), 7.37-7.30 (m, 2H), 7.19-7.12 (m, 1H), 6.39-6.36 (m, 1H), 5.94-5.90 (m, 1H), 2.32 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 133.5, 131.0, 129.7, 129.4, 126.1, 123.6, 108.4, 106.7, 13.4 ppm. **MS** (70 eV, EI); m/z (%): 157 (65, M^+), 156 (100), 104 (2), 77 (5). **Elemental analysis** (%) for $C_{11}H_{11}N$ calcd C 84.04, H 7.05, N 8.91; found: C 84.20, H 7.34, N 8.88.

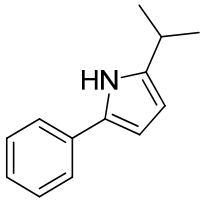


1b: 2-ethyl-5-phenyl-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), 1-phenylethanol (2.4 mL, 20.0 mmol), 2-amino-butan-1-ol (960 µL, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 40:1 pentane: Et_2O; Yield: 1.59 g = 9.3 mmol = 93% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.23 (s_br, 1H), 7.46-7.42 (m, 2H), 7.38-7.31 (m, 2H), 7.19-7.13 (m, 1H), 6.61-6.38 (m, 1H), 5.97-5.93 (m, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 136.3, 133.6, 130.8, 129.4, 126.1, 123.7, 106.7, 21.5, 14.1 ppm.

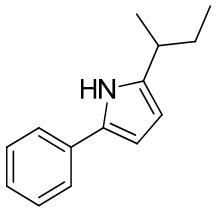
MS (70 eV, EI); m/z (%): 171 (38, M^+), 156 (100), 128 (8), 115 (6), 77 (5). **Elemental analysis** (%) for $C_{12}H_{13}N$ calcd: C 84.17, H 7.65, N 8.18; found: C 84.33, H 7.69, N 8.10.



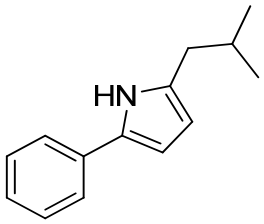
1c: 3-(5-phenyl-1*H*-pyrrol-2-ylmethyl)-1*H*-indole: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), 1-phenylethanol (2.4 mL, 20.0 mmol), 2-amino-3-(1*H*-indol-3-yl)-propan-1-ol (1.90 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 20:1→10:1 pentane:Et_2O;Yield: 1.76 g = 6.5 mmol = 65% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.24 (s_br, 1H), 8.16 (s_br, 1H), 7.57-7.53 (m, 1H), 7.41-7.35 (m, 3H), 7.32-7.26 (m, 2H), 7.21-7.05 (m, 4H), 6.44-6.41 (m, 1H), 6.10-6.07 (m, 1H), 4.16 (s, 2H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 137.1, 133.5, 133.3, 131.2, 129.3, 127.8, 126.1, 123.7, 123.0, 122.7, 120.0, 119.3, 114.1, 111.7, 108.2, 106.6, 24.5 ppm. **MS** (70 eV, EI); m/z (%): 272 (100, M^+), 270 (10), 167 (10), 136 (10), 117 (38), 77 (8). **Elemental analysis** (%) for $C_{19}H_{16}N_2$ calcd: C 83.79, H 5.92, N 10.29; found: C 83.62, H 5.98, N 10.10.



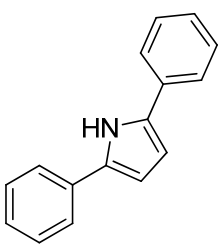
1d: 2-isopropyl-5-phenyl-1*H*-pyrrole: Cat. II (0.3 mL, 0.003 mmol, 0.01 M in THF), 1-phenylethanol (2.4 mL, 20.0 mmol), 2-amino-3-methyl-butan-1-ol (1.03 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 100:1→30:1 pentane:Et_2O; Yield: 1.64 g = 8.9 mmol = 89% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.23 (s_br, 1H), 7.47-7.43 (m, 2H), 7.38-7.31 (m, 2H), 7.20-7.14 (m, 1H), 6.42-6.38 (m, 1H), 5.98- 5.94 (m, 1H), 3.06-2.90 (m, 1H), 1.30 (d, *J* = 6.7 Hz, 6H) ppm.**^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 141.0, 133.6, 130.7, 129.4, 126.1, 123.8, 106.4, 105.5, 27.8, 23.1 ppm. **MS** (70 eV, EI); m/z (%): 185 (28, M^+), 170 (100), 153 (5), 115 (8), 77 (5). **Elemental analysis** (%) for $C_{13}H_{15}N$ calcd: C 84.28, H 8.16, N 7.56; found: C 84.46, H 8.23, N 7.64.



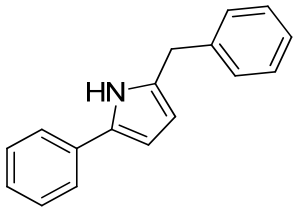
1e: 2-sec-butyl-5-phenyl-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), 1-phenyl-ethanol (2.4 mL, 20.0 mmol), 2-amino-3-methyl-pentan-1-ol (1.17 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1→30:1 pentane:Et_2O; Yield: 1.84 g = 7.9 mmol = 79% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.39-8.00 (s_br, 1H), 7.47-7.43 (m, 2H), 7.38-7.31 (m, 2H), 7.20-7.13 (m, 1H), 6.43-6.39 (m, 1H), 5.98-5.93 (m, 1H), 2.79-2.66 (m, 1H), 1.72- 1.56 (m, 2H), 1.30-1.27 (m, 3H), 0.96-0.89 (m, 3H) ppm.**^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 139.9, 133.6, 130.5, 129.3, 126.1, 123.7, 106.4, 106.2, 35.0, 30.8, 20.5, 12.2 ppm. **MS** (70 eV, EI); m/z (%): 199 (22, M^+), 184 (8), 170 (100), 168 (10), 115 (6), 77 (5). **Elemental analysis** (%) for $C_{14}H_{17}N$ calcd C 84.37, H 8.60, N 7.03; found: C 84.66, H 8.89, N 7.22.



1f: 2-isobutyl-5-phenyl-1*H*-pyrrole: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), 1-phenyl-ethanol (2.4 mL, 20.0 mmol), 2-amino-4-methyl-pentan-1-ol (1.28 mL, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1→20:1 pentane:Et_2O; Yield: 1.39 g = 6.9 mmol = 69% as colorless oil.
^{1}H NMR (300 MHz, CD_2Cl_2): δ = 8.19 (s_br, 1H), 7.47-7.42 (m, 2H), 7.38-7.31 (m, 2H), 7.19-7.13 (m, 1H), 6.43-6.39 (m, 1H), 5.96-5.93 (m, 1H), 2.50 (d, *J* = 7.0 Hz), 1.97-1.82 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 6H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 133.9, 133.6, 130.7, 129.4, 126.0, 123.6, 108.5, 106.6, 37.8, 29.8, 22.7 ppm. **MS** (70 eV, EI); m/z (%): 199 (18, M^+), 156 (100), 115 (5), 77 (5). **Elemental analysis** (%) for $C_{14}H_{17}N$ calcd C 84.37, H 8.60, N 7.03; found: C 84.46, H 8.50, N 7.00.

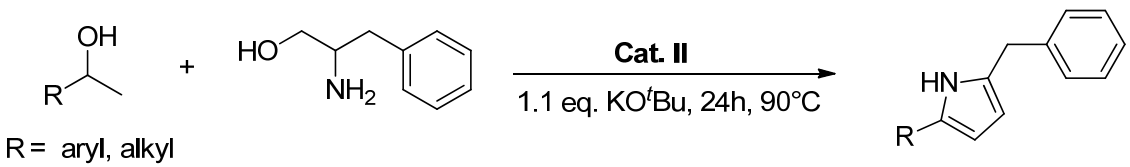


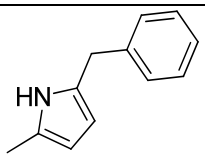
1g: 2,5-diphenyl-1*H*-pyrrole: Cat. II (2.0 mL, 0.02 mmol, 0.01 M in THF), 1-phenylethanol (2.4 mL, 20.0 mmol), 2-amino-2-phenyl-ethanol (1.37 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 10:1→5:1 hexane:Et_2O; Yield: 1.88 g = 8.6 mmol = 86% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.72 (s_br, 1H), 7.58-7.54 (m, 4H), 7.47-7.35 (m, 4H), 7.31-7.18 (m, 2H), 6.59 (d, *J* = 2.6 Hz, 2H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 133.0, 129.5, 127.3, 127.0, 124.2, 108.4 ppm. **MS** (70 eV, EI); m/z (%): 219 (100, M^+), 216 (14), 114 (24), 109 (12), 77 (4). **Elemental analysis** (%) for $C_{16}H_{13}N$ calcd: C 87.64, H 5.98, N 6.39; found: C 87.29, H 5.96, N 6.59.

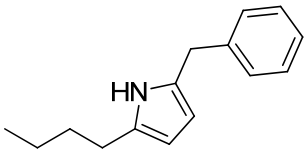
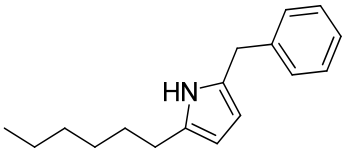
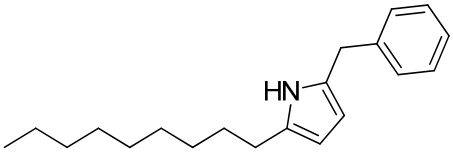
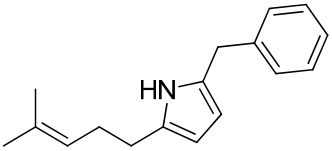
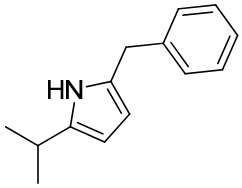
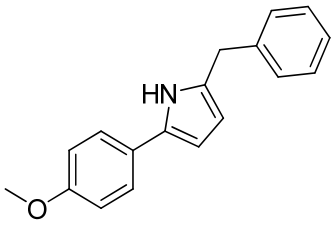
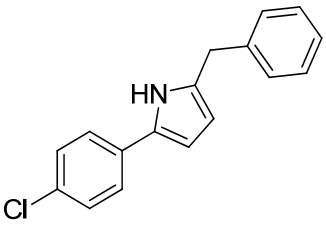
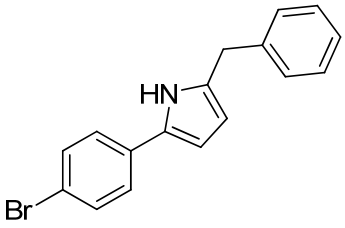


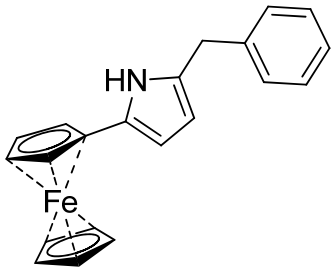
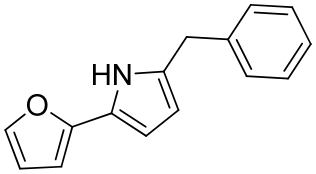
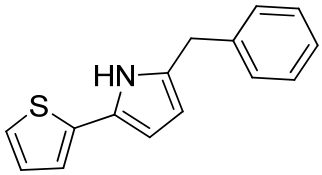
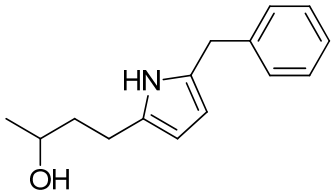
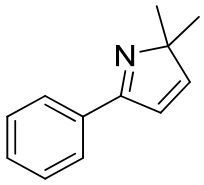
1h: 2-benzyl-5-phenyl-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), 1-phenyl-ethanol (2.4 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 40:1→5:1 pentane:Et_2O; Yield: 1.84 g = 7.9 mmol = 79% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.18 (s_br, 1H), 7.42-7.39 (m, 2H), 7.35-7.30 (m, 4H), 7.29-7.22 (m, 3H), 7.19-7.12 (m, 1H), 6.44-6.41 (m, 1H), 6.03-6.00 (m, 1H), 4.02 (s, 2H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.2, 133.4, 132.9, 129.3, 129.2, 129.1, 127.0, 126.3, 123.8, 109.0, 106.6, 34.7 ppm. **MS** (70 eV, EI); m/z (%): 233 (84, M^+), 156 (100), 128 (15), 115 (8), 77 (6). **Elemental analysis** (%) for $C_{17}H_{15}N$ calcd: C 87.52, H 6.48, N 6.00; found: C 87.62, H 6.21, N 6.02.

Supplementary Table S10. Reaction of 2-amino-3-phenyl-propan-1-ol with various secondary alcohols

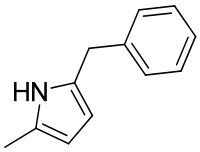


	[mol% **Cat. II**]	Product	Yield [a]
1i	**0.03**		**84%**

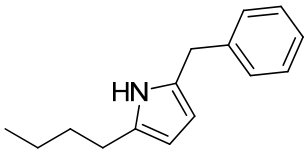
1j	**0.03**		**76%**
1k	**0.03**		**97%**
1l	**0.05**		**74%**
1m	**0.1**		**77%**
1n	**0.1**		**73%**
1o	**0.05**		**84%**
1p	**0.05**		**75%**
1q	**0.2**		**75%**

1r	**0.2**		**78%**
1s	**0.5**		**42%**
1t	**0.5**		**57%**
1u	**0.1**		**70%**
1v	**0.1**		**55%**

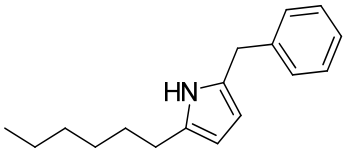
[a] Isolated yield



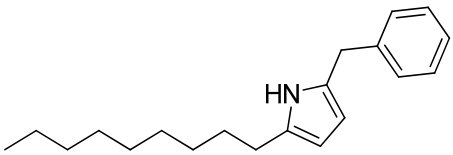
1i: 2-benzyl-5-methyl-1*H*-pyrrole: Cat. II (0.3 mL, 0.003 mmol, 0.01 M in THF), propan-2-ol (3.06 mL, 40.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1→20:1 pentane:Et_2O; Yield: 1.43 g = 8.4 mmol = 85% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.59 (s_br, 1H), 7.34-7.27 (m, 2H), 7.25-7.19 (m, 3H), 5.79 (t, *J* = 2.9 Hz, 1H), 5.74-5.70 (m, 1H), 3.90(s, 2H), 2.18 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.9, 129.8, 129.0, 127.4, 126.8, 106.9, 106.2, 34.7, 13.2 ppm. **MS** (70 eV, EI); m/z (%): 171 (100, M^+), 156 (72), 154 (18), 128 (8), 94 (100), 77 (8). **Elemental analysis** (%) for $C_{12}H_{13}N$ calcd: C 84.17, H 7.65, N 8.18; found: C 84.20, H 7.86, N 8.42.



1j: 2-benzyl-5-butyl-1*H*-pyrrole: Cat. II (0.3 mL, 0.003 mmol, 0.01 M in THF), hexan-2-ol (2.52 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 40:1→30:1 pentane:Et_2O; Yield: 1.62 g = 7.6 mmol = 76% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.61 (s_br, 1H), 7.36-7.28 (m, 2H), 7.27-7.19 (m, 3H), 5.83-5.79 (m, 1H), 5.78-5.75 (m, 1H), 3.92 (s, 2H), 2.55-2.49 (m, 2H), 1.60-1.52 (m, 2H), 1.42-1.32 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.9, 132.7, 129.5, 129.1, 129.0, 126.7, 106.8, 105.2, 34.7, 32.5, 27.9, 23.0, 14.2 ppm. **MS** (70 eV, EI); m/z (%): 213 (60, M^+), 198 (20), 184 (100), 170 (35), 155 (10), 128 (6), 84 (4), 77 (6). **Elemental analysis** (%) for $C_{15}H_{19}N$ calcd: C 84.46, H 8.98, N 6.57; found: C 84.14 H 9.08 N 6.52.

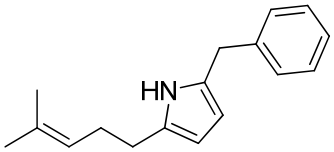


1k: 2-benzyl-5-hexyl-1*H*-pyrrole: Cat. II (0.3 mL, 0.003 mmol, 0.01 M in THF), octan-2-ol (3.1 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 20:1→10:1 pentane:Et_2O; Yield: 2.34 g = 9.7 mmol = 97% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.60 (s_br, 1H), 7.34-7.25 (m, 2H), 7.25-7.17 (m, 3H), 5.83-5.77 (m, 1H), 5.76-5.71 (m, 1H), 3.90 (s, 2H), 2.52-2.47 (m, 2H), 1.59-1.52 (m, 2H), 1.33-1.28 (m, 6H), 0.90-0.87 (m, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.9, 132.8, 129.5, 129.1, 126.7, 107.5, 106.8, 105.2, 34.7, 32.2, 30.3, 29.6, 28.3, 23.2, 14.4 ppm. **MS** (70 eV, EI); m/z (%): 241 (18, M^+), 170 (100), 167 (4), 93 (4), 91 (7), 80 (5). **Elemental analysis** (%) for $C_{17}H_{23}N$ calcd: C 84.59, H 9.60, N 5.80; found: C 84.28, H 9.86, N 5.74.

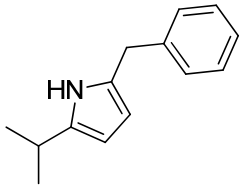


1l: 2-benzyl-5-nonyl-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), undecan-2-ol (4.16 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1→40:1 pentane:Et_2O; Yield: 2.09 g = 7.4 mmol = 74% as colorless oil. **^{1}H NMR** (300

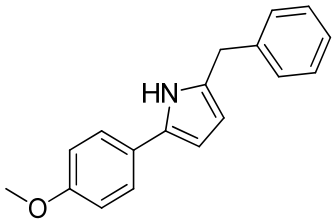
MHz, CD_2Cl_2): δ = 7.60 (s_br, 1H), 7.34-7.26 (m, 2H), 7.25-7.17 (m, 3H), 5.81-5.77 (m, 1H), 5.76-5.73 (m, 1H), 3.91 (s, 2H), 2.52-2.47 (m, 2H), 1.59-1.52(m, 2H), 1.32-1.27 (m, 12H), 0.92-0.87 (m, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.9, 132.8, 129.5, 129.1, 129.0, 126.7, 106.7, 105.2, 34.7, 32.5, 30.4, 30.1, 30.0, 30.0, 29.9, 28.3, 23.3, 14.5 ppm. **MS** (70 eV, EI); m/z (%): 283 (21, M^+), 184 (8), 170 (100), 156 (3), 106 (4), 91 (8), 80 (4). **Elemental analysis** (%) for $C_{20}H_{29}N$ calcd: C 84.75, H 10.31, N 4.94; found: C 84.85, H 10.52, N 6.69.



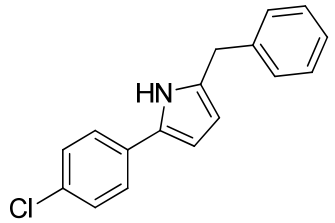
1m: 2-benzyl-5-(4-methyl-pent-3-enyl)-1*H*-pyrrole: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), 6-methyl-hept-5-en-2-ol (3.04 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 70:1→40:1 pentane:Et_2O; Yield: 1.84g = 7.7 mmol = 77% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.64 (s_br, 1H), 7.34-7.27 (m, 2H), 7.25-7.17 (m, 3H), 5.81-5.78 (m, 1H), 5.77-5.73 (m, 1H), 5.20-5.10 (m, 1H), 3.90 (s, 2H), 2.53 (t, *J* = 7.3 Hz, 2H), 2.23 (q, *J* = 7.3 Hz, 2H), 1.66 (d, *J* = 1.2 Hz, 3H), 1.54 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.9, 133.0, 132.5, 129.7, 129.1, 129.0, 126.8, 124.4, 106.7, 105.4, 34.7, 28.9, 28.3, 26.0, 17.9 ppm. **MS** (70 eV, EI); m/z (%): 239 (100, M^+), 224 (44), 184 (6), 170 (20), 148 (48), 133 (8), 94 (8), 91 (32). **Elemental analysis** (%) for $C_{17}H_{21}N$ calcd: C 85.30, H 8.84, N 5.85; found: C 85.65, H 9.13, N 5.69.



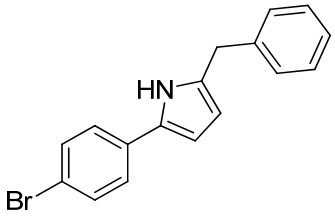
1n: 2-benzyl-5-isopropyl-1*H*-pyrrole: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), 3-methyl-butan-2-ol (2.15 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1→30:1 pentane:Et_2O; Yield: 1.45 g = 7.3 mmol = 73% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.66 (s_br, 1H), 7.36-7.29 (m, 2H), 7.26-7.20 (m, 3H), 5.82-5.75 (m, 2H), 3.93 (s, 2H), 2.91-2.77 (m, 1H), 1.21 (d, *J* = 7.0 Hz, 6H) ppm.**^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.9, 138.8, 129.5, 129.1, 129.0, 126.7, 106.6, 103.3, 34.7, 27.6, 23.1 ppm. **MS** (70 eV, EI); m/z (%): 199 (52, M^+), 184 (100), 106 (16), 91 (26). **Elemental analysis** (%) for $C_{14}H_{17}N$ calcd: C 84.37, H 8.60, N 7.03; found: C 84.16, H 8.29, N 7.05.



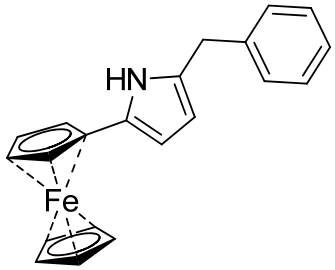
1o: 2-benzyl-5-(4-methoxy-phenyl)-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), 1-(4-methoxy-phenyl)-ethanol (2.82 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 20:1→5:1 pentane:Et_2O; Yield: 2.22 g = 8.4 mmol = 84% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.07 (s_br, 1H), 7.36-7.29 (m, 4H), 7.28-7.19 (m, 3H), 6.90-6.85 (m, 2H), 6.31-6.26, (m, 1H), 6.00-5.95 (m, 1H), 4.00 (s, 2H), 3.79 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 158.6, 140.3, 132.1, 131.8, 129.1, 126.9, 126.4, 125.2, 114.7, 108.8, 105.4, 105.3, 55.8, 34.7 ppm. **MS** (70 eV, EI); m/z (%): 263 (100, M^+), 248 (31), 219 (5), 186 (38), 143 (10), 102 (8), 77 (6). **Elemental analysis** (%) for $C_{18}H_{17}NO$ calcd: C 82.10, H 6.51, N 5.32; found: C 81.92, H 6.57, N 5.01.



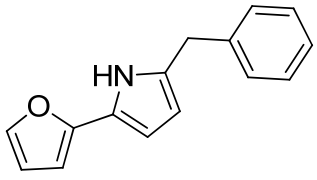
1p: 2-benzyl-5-(4-chloro-phenyl)-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), 1-(4-chloro-phenyl)-ethanol (2.67 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 40:1→5:1 pentane:Et_2O; Yield: 2.02 g = 7.5 mmol = 75% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.14 (s_br, 1H), 7.37-7.20 (m, 9H), 6.44-6.40 (m, 1H), 6.06-5.98 (m, 1H), 4.01 (s, 1H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.0, 133.4, 131.9, 131.5, 130.6, 129.4, 129.2, 129.1, 127.0, 125.0, 109.2, 107.2, 34.7 ppm. **MS** (70 eV, EI); m/z (%): 267 (100, M^+), 230 (5), 192 (22), 190 (82), 154 (18), 127 (12), 101 (8), 77 (8). **Elemental analysis** (%) for $C_{17}H_{14}ClN$ calcd: C 76.26, H 5.27, N 5.23; found: C 76.26, H 5.43, N 5.21.



1q: 2-benzyl-5-(4-bromo-phenyl)-1*H*-pyrrole: Cat. II (2.0 mL, 0.02 mmol, 0.01 M in THF), 1-(4-bromo-phenyl)-ethanol (4.0 g, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 30:1→5:1 pentane:Et_2O; Yield: 2.35 g = 7.5 mmol = 75% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.15 (s_br, 1H), 7.49-7.40 (m, 2H), 7.36-7.21 (m, 7H), 6.47-6.38 (m, 1H), 6.05-5.99 (m, 1H), 4.00 (s, 2H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.0, 133.5, 132.3, 130.6, 129.2, 129.1, 127.0, 125.3, 123.8, 119.5, 109.3, 107.3, 34.7 ppm. **MS** (70 eV, EI); m/z (%): 311 (100), 234 (95), 202 (10), 154 (77), 115 (27), 102 (22), 77 (17). **Elemental analysis** (%) for $C_{17}H_{14}BrN$ calcd: C 65.40, H 4.52, N 4.49; found C 65.54, H 4.60, N 4.52.

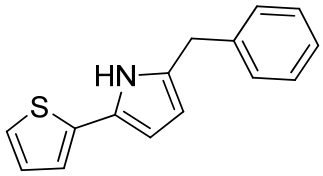


1r: 2-benzyl-5-ferrocenyl-1*H*-pyrrole: Cat. II (2.0 mL, 0.02 mmol, 0.01 M in THF), 1-ferrocenyl-ethanol (4.6 g, 20.0 mmol) 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 40:1→20:1 pentane:Et_2O; Yield: 2.67 g = 7.8 mmol = 78% deep red solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.84 (s_br, 1H), 7.37-7.31 (m, 2H), 7.27-7.21 (m, 3H), 6.10-6.07 (m, 1H), 5.90-5.87 (m, 1H), 4.40- 4.39 (m, 2H), 4.20-4.19 (m, 2H), 4.02 (s, 5H), 3.98 (s_br, 2H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.6, 130.8, 129.5, 129.1, 129.0, 126.9, 108.1, 105.7, 80.0, 69.7, 68.3, 65.5, 34.6 ppm. **MS** (70 eV, EI); m/z (%): 341 (100, M^+), 275 (18), 250 (27), 218 (9), 171 (9), 121 (12), 91 (5), 77 (3). **Elemental analysis** (%) for $C_{21}H_{19}FeN$ calcd: C 73.92, H 5.61, N 4.10; found: C 74.19, H 5.77, N 4.04

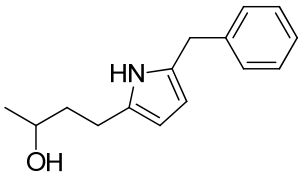


1s: 2-benzyl-5-furan-2-yl-1*H*-pyrrole: Cat. II (5.0 mL, 0.05 mmol, 0.01 M in THF), 1-furan-2-yl-ethanol (2.1 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 20:1→15:1 pentane:Et_2O; Yield: 930 mg = 4.2 mmol = 42% as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.25 (s_br, 1H), 7.37-7.32 (m, 2H), 7.29-7.22 (m, 3H),

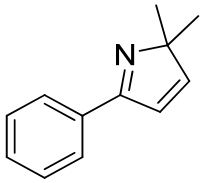
6.43 (dd, *J* = 3.4, 1.9 Hz, 1H), 6.36- 6.33 (m, 1H), 6.30 (dd, *J* = 3.4, 0.7 Hz, 1H), 6.03-5.99 (m , 1H), 4.00 (s, 2H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 149.0, 140.6, 140.1, 132.3, 129.2, 129.1, 127.0, 123.8, 112.0, 108.6, 106.1, 102.1, 34.5 ppm. **MS** (70 eV, EI); m/z (%): 223 (100, M^+), 146 (100), 117 (7), 91 (14), 77 (6). **Elemental analysis** (%) for $C_{15}H_{13}NO$ calcd: C 80.69, H 5.87, N 6.27; found: C 80.60, H 5.94, N 6.55



1t: 2-benzyl-5-thiophen-2-yl-1*H*-pyrrole: Cat. II (5.0 mL, 0.05 mmol, 0.01 M in THF), 1-thiophen-2-yl-ethanol (2.56 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 20:1→15:1 pentane:Et_2O; Yield: 1.36 g = 5.7 mmol = 57% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.06 (s_br, 1H), 7.36-7.29 (m, 2H), 7.28-7.20 (m, 3H), 7.11 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.00-6.94 (m, 2H), 6.31-6.28 (m, 1H), 5.99-5.96 (m, 1H), 3.99 (s, 2H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.0, 137.0, 132.6, 129.2, 129.1, 128.1, 127.0, 126.4, 122.7, 120.7, 108.9, 107.3, 34.6 ppm. **MS** (70 eV, EI); m/z (%): 239 (89, M^+), 204 (6), 162 (100), 102 (6), 91 (7). **Elemental analysis** (%) for $C_{15}H_{13}NS$ calcd: C 75.28, H 5.47, N 5.85; found: C 75.06, H 5.50, N 5.90.

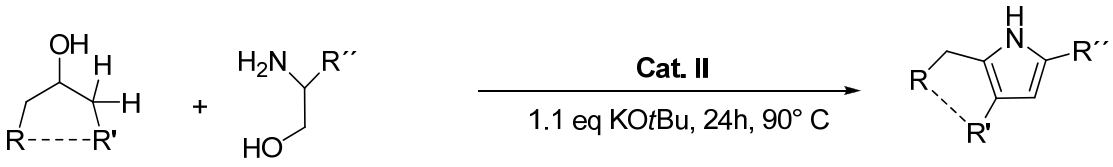


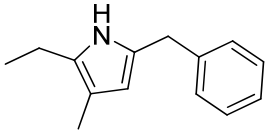
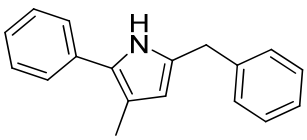
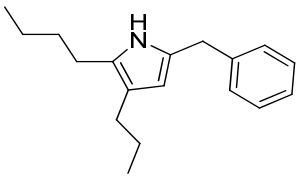
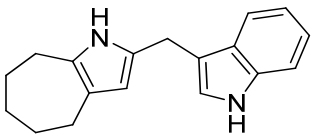
1u: 4-(5-benzyl-1*H*-pyrrol-2-yl)-butan-2-ol: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), hexane-2,5-diol (2.36 g, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 10.0 mmol), 24 h at 90 °C. Purification by column chromatography 2:1→1:1 pentane:Et_2O; Yield: 1.60 g = 7.0 mmol = 70% as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.95 (br_s, 1H), 7.34-7.27 (m, 2H), 7.26-7.17 (m, 3H), 5.81-5.74 (m, 2H), 3.90 (s, 2H), 3.83-3.73 (m, 1H), 2.61 (dt, *J* = 7.7, 2.5 Hz, 1H), 1.71-1.65 (m, 2H), 1.59 (br_s, 1H), 1.18 (d, *J* = 6.4 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.9, 132.0, 129.9, 129.1, 129.0, 126.7, 106.7, 105.4, 68.1, 39.4, 34.7, 24.6, 24.0 ppm. **MS** (70 eV, EI); m/z (%): 229 (56, M^+), 184 (100), 170 (75), 156 (6), 128 (5), 106 (15), 91 (30), 80 (14), 65 (18). **Elemental analysis** (%) for $C_{15}H_{19}NO$ calcd: C 78.56, H 8.35, N 6.11; found: C 78.78, H 8.64, N 5.89.

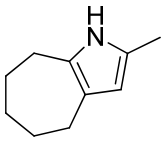
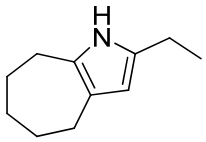
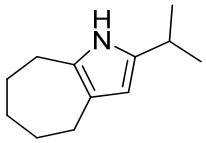
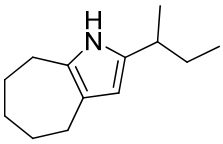
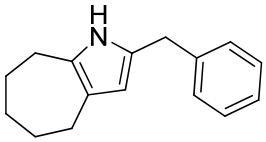
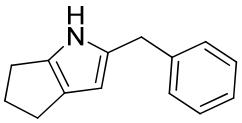
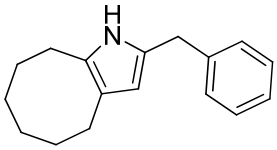
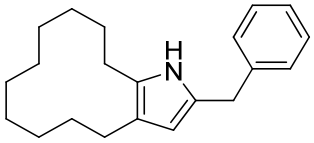


1v: 2,2-dimethyl-5-phenyl-2*H*-pyrrole: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), 1-phenylethanol (2.4 mL, 20.0 mmol), 2-amino-2-methyl-propan-1-ol (1.1 mL, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 40:1→2:1 pentane:Et_2O; Yield: 0.94 g = 5.5 mmol = 55% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.91-7.97 (m, 2H), 7.48-7.43 (m, 3H), 7.41 (d, *J* = 5.0 Hz, 1H), 6.79 (d, *J* = 5.0 Hz, 1H), 1.38 (s, 6H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 169.6, 153.0, 135.0, 130.6, 129.1, 128.1, 123.3, 80.0, 23.7 ppm. **MS** (70 eV, EI); m/z (%): 171 (81, M^+), 170 (100), 156 (37), 129 (12), 104 (18), 77 (12). **Elemental analysis** (%) for $C_{12}H_{13}N$ calcd: C 84.17, H 7.65, N 8.18; found: C 84.03, H 7.88, N 8.61.

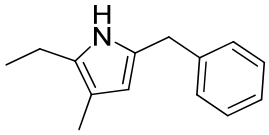
Supplementary Table S11: Reaction of 2-amino-3-phenyl-propan-1-ol with various secondary alcohols and cyclic alcohols



	[mol% **Cat. II**]	Product	Yield [a]
2a	**0.5**		**66%**
2b	**0.1**		**63%**
2c	**0.5**		**52%**
2d	**0.5**		**56%**

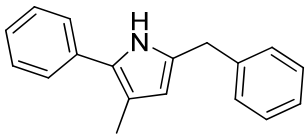
2e	**0.1**		**78%**
2f	**0.05**		**88%**
2g	**0.03**		**84%**
2h	**0.03**		**79%**
2i	**0.05**		**80%**
2j	**0.1**		**51%**
2k	**0.05**		**77%**
2l	**0.1**		**37%**

[a] Isolated yield

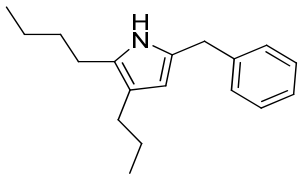


2a: 5-benzyl-3-methyl-2-phenyl-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), 1-phenyl-propan-1-ol (2.74 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1→20:1 hexane:Et_2O; Yield: 1.55 g = 6.2 mmol = 63% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.86 (s_br, 1H), 7.40-7.16 (m, 10H), 5.89 (d, *J* = 2.9 Hz, 1H), 3.97 (s, 2H), 2.23 (s, 3H) ppm.**^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.3, 134.3, 131.3, 129.2, 129.1, 127.7, 127.0, 126.3, 126.0, 116.9, 111.3, 34.6, 12.9 ppm. **MS** (70 eV, EI); m/z

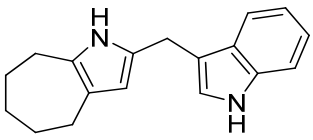
(%): 247 (100, M^+), 232 (47), 170 (83), 128 (6), 115 (11), 77 (6). **Elemental analysis** (%) for $C_{18}H_{17}N$ calcd: C 87.41, H 6.93, N 5.66; found: C 87.31, H 7.01, N 6.03.



2b: 5-benzyl-2-ethyl-3-methyl-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), pentan-3-ol (2.16 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 30:1 hexane:Et_2O; Yield: 1.31 g = 6.6 mmol = 66% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.44 (s_br, 1H), 7.35-7.27 (m, 2H), 7.26-7.17 (m, 3H), 5.67 (d, *J* = 2.6 Hz, 1H), 3.87 (s, 2H), 2.50 (q, *J* = 7.6 Hz, 2H), 1.97 (s, 3H), 1.12 (t, *J* = 7.6 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 129.1, 129.0, 128.3, 126.7, 113.6, 108.8, 34.7, 19.4, 14.9, 11.0 ppm. **MS** (70 eV, EI); m/z (%): 199 (82, M^+), 184 (100), 169 (25), 107 (9), 91 (25), 77 (8). **Elemental analysis** (%) for $C_{14}H_{17}N$ calcd: C 84.37, H 8.60, N 7.03; found: C 84.18, H 8.74, N 7.14

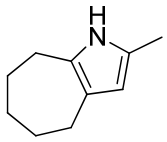


2c: 5-benzyl-2-butyl-3-propyl-1*H*-pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), nonan-5-ol (3.49 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1 pentane:Et_2O; Yield: 1.33 g = 5.2 mmol = 52% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.41 (s_br, 1H), 7.34-7.26 (m, 2H), 7.25-7.14 (m, 3H), 5.69 (d, *J* = 2.9 Hz, 1H), 3.88 (s, 2H), 2.49-2.43 (m, 2H), 2.33- 2.28 (m, 2H), 1.52-1.44 (m, 4H), 1.36-1.29 (m, 2H), 0.95-0.89 (m, 6H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 141.0, 129.1, 129.0, 128.4, 127.9, 126.7, 119.7, 107.4, 34.7, 33.3, 28.6, 25.9, 25.3, 23.1, 14.5, 14.3 ppm. **MS** (70 eV, EI); m/z (%): 255 (31, M^+), 226 (9), 212 (100), 184 (12), 91 (16) ppm. **Elemental analysis** (%) for $C_{18}H_{25}N$ calcd: C 84.65, H 9.87, N 5.48; found: C 84.33, H 10.11, N 5.29.

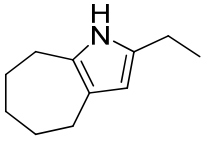


2d: 2-(1*H*-indol-3-ylmethyl)- 1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cat. II (5.0 mL, 0.05 mmol, 0.01 M in THF), cycloheptanol (2.4 mL, 20.0 mmol), 2-amino-3-(1H-indol-3-yl)-propan-1-ol (1.90 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h

at 90 °C. Purification by column chromatography 10:1→2:1 pentane:Et_2O; Yield: 1.49 g = 5.6 mmol = 56 % as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.07 (s_br, 1H), 7.59-7.53 (m, 1H), 7.46 (s_br, 1H), 7.40-7.36 (m, 1H), 7.23-7.16 (m, 1H), 7.12-7.06 (m, 1H), 7.06-7.03 (m, 1H), 5.74 (d, *J* = 2.9 Hz, 1H), 4.01 (s, 2H), 2.56-2.50 (m, 4H), 1.81-1.74 (m, 2H), 1.67-1.60 (m, 4H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 137.0, 129.3, 127.9, 127.0, 122.8, 122.5, 121.7, 119.8, 119.4, 114.8, 111.7, 108.2, 32.6, 30.1, 29.6, 29.0, 28.8, 24.0 ppm. **MS** (70 eV, EI); m/z (%): 264 (100, M^+), 263 (85), 235 (15), 221 (32), 148 (51), 130 (16), 116 (23), 104 (22), 90 (6), 77 (8). **Elemental analysis** (%) for $C_{18}H_{20}N_2$ calcd: C 81.78, H 7.63, N 10.60; found: C 82.12, H 7.95, N 10.49.

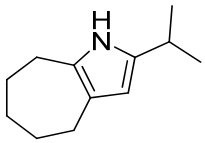


2e: 2-methyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), cycloheptanol (2.4 mL, 20.0 mmol), 2-amino-propan-1-ol (797 µL, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 20:1 hexane:Et_2O; Yield: 1.16 g = 7.8 mmol = 78% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.42 (s_br, 1H), 5.57 (d, *J* = 2.93 Hz, 1H), 2.63-2.58 (m, 2H), 2.51-2.47 (m, 2H), 2.16 (s, 3H), 1.83-1.76 (m, 2H), 1.69-1.62 (m, 4H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 129.1, 123.3, 121.8, 108.5, 32.7, 30.2, 29.6, 28.9, 13.0 ppm. **MS** (70 eV, EI); m/z (%): 149 (88, M^+), 148 (100), 134 (15), 120 (40), 107 (32), 94 (30), 91 (11), 77 (8). **Elemental analysis** (%) for $C_{10}H_{15}N$ calcd: C 80.48, H 10.13, N 9.39; found: C 80.85, H 10.30, N 9.65.

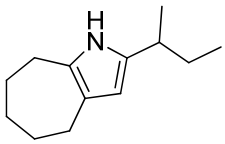


2f: 2-ethyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), cycloheptanol (2.4 mL, 20.0 mmol), 2-amino-butan-1-ol (960 µL, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 40:1→20:1 pentane:Et_2O; Yield: 1.44 g = 8.8 mmol = 88% as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.45 (s_br, 1H), 5.58 (d, *J* = 2.9 Hz, 1H), 2.63-2.59 (m, 2H), 2.55-2.47 (m, 4H), 1.81-1.75 (m, 2H), 1.68-1.61 (m, 4H), 1.18 (t, *J* = 7.6 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 130.1, 128.9, 121.6, 106.9, 32.6, 30.2, 29.6, 29.0, 28.9, 21.2, 14.3 ppm. **MS** (70 eV, EI); m/z (%): 163 (50, M^+), 148 (100), 134 (26), 106 (10), 77 (8).

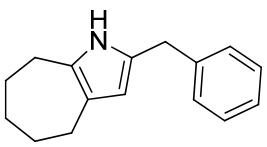
Elemental analysis (%) for $C_{11}H_{17}N$ calcd: C 80.93, H 10.50, N 8.58; found: C 80.60, H 10.87, N 8.83.



2g: 2-isopropyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cat. II (0.3 mL, 0.003 mmol, 0.01 M in THF), cycloheptanol (2.4 mL, 20.0 mmol), 2-amino-3-methyl-butan-1-ol (1.1 mL, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1→40:1 pentane:Et_2O; Yield: 1.49 g = 8.4 mmol = 84% as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.47 (s_br, 1H), 5.63-5.54 (d, *J* = 2.9 Hz, 1H), 2.90-2.72 (m, 1H), 2.64-2.58 (m, 2H), 2.52-2.46 (m, 2H), 1.83-1.74 (m, 2H), 1.70-1.61 (m, 4H), 1.20 (t, *J* = 6.7 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 134.8, 128.7, 121.3, 105.6, 32.6, 30.1, 29.6, 29.0, 28.9, 27.4, 23.2 ppm. **MS** (70 eV, EI); m/z (%): 177 (15, M^+), 162 (100), 106 (5), 77 (6). **Elemental analysis** (%) for $C_{12}H_{19}N$ calcd: C 81.30, H 10.80, N 7.90; found: C 81.40, H 11.14, N 7.84.

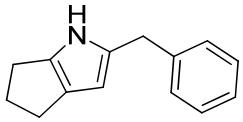


2h: 2-sec-butyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cat. II (0.3 mL, 0.003 mmol, 0.01 M in THF), cycloheptanol (2.4 mL, 20.0 mmol), 2-amino-3-methyl-pentan-1-ol (1.17 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1→40:1 pentane:Et_2O; Yield: 1.52 g = 7.9 mmol = 79 % as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.43 (s_br, 1H), 5.57 (d, *J* = 2.9 Hz, 1H), 2.63-2.58 (m, 2H), 2.58-2.45 (m, 3H), 1.82-1.73 (m, 2H), 1.69-1.61 (m, 4H), 1.59-1.41 (m, 2H), 1.17 (d, *J* = 6.7 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 133.7, 128.6, 121.2, 106.2, 34.6, 32.6, 30.8, 30.1, 29.7, 29.1, 28.9, 20.5, 12.3 ppm. **MS** (70 eV, EI); m/z (%): 191 (10, M^+), 176 (7), 162 (100), 132 (4), 106 (3) 77 (2). **Elemental analysis** (%) for $C_{13}H_{21}N$ calcd: C 81.61, H 11.06, N 7.32; found: C 81.74, H 11.19, N 7.32.

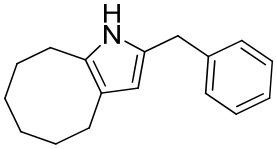


2i: 2-benzyl-1,5,6,7,8,9-hexahydro-cyclohepta[*b*]pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), cycloheptanol (2.4 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column

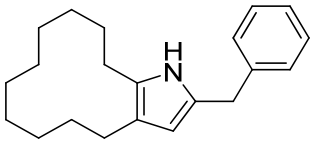
chromatography 30:1→10:1 pentane:Et_2O; Yield: 1.82 g = 8.0 mmol = 80% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.40 (s_br, 1H), 7.34-7.27 (m, 2H), 7.26-7.17 (m, 3H), 5.65 (d, *J* = 2.9 Hz, 1H), 3.84 (s, 2H), 2.59-2.54 (m, 2H), 2.51-2.47 (m, 2H), 1.79-1.74 (m, 2H), 1.67-1.61 (m, 4H) ppm.**^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 141.0, 129.9, 129.1, 129.0, 126.8, 126.7, 121.8, 108.9, 34.6, 32.6, 30.1, 29.6, 28.9, 28.8 ppm. **MS** (70 eV, EI); m/z (%): 225 (100, M^+), 196 (28), 148 (20), 134 (30), 91 (40), 77 (10). **Elemental analysis** (%) for $C_{16}H_{19}N$ calcd: C 85.28, H 8.50, N 6.22; found: C 85.24, H 8.71, N 6.40.



2j: 2-benzyl-1,5,6,7-tetrahydro-cyclopenta[*b*]pyrrole: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), cyclopentanol (1.82 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 30:1→20:1 pentane:Et_2O; Yield: 999 mg = 5.1 mmol = 51% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.53 (s_br, 1H), 7.35-7.26 (m, 2H), 7.26-7.16 (m, 3H), 5.71 (d, *J* = 1.8 Hz, 1H), 3.90-3.88 (m, 4H), 2.39-2.31 (m, 2H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 141.0, 135.9, 134.2, 129.1, 126.8, 126.7, 102.6, 35.4, 29.5, 26.1, 25.9 ppm. **MS** (70 eV, EI); m/z (%): 197 (93, M^+), 196 (100), 182 (10), 169 (25), 152 (5), 120 (81), 106 (22), 91 (34), 85 (15), 77 (13). **Elemental analysis** (%) for $C_{14}H_{15}N$ calcd: C 85.24, H 7.66, N 7.10; found: C 85.55, H 7.79, N 6.97.

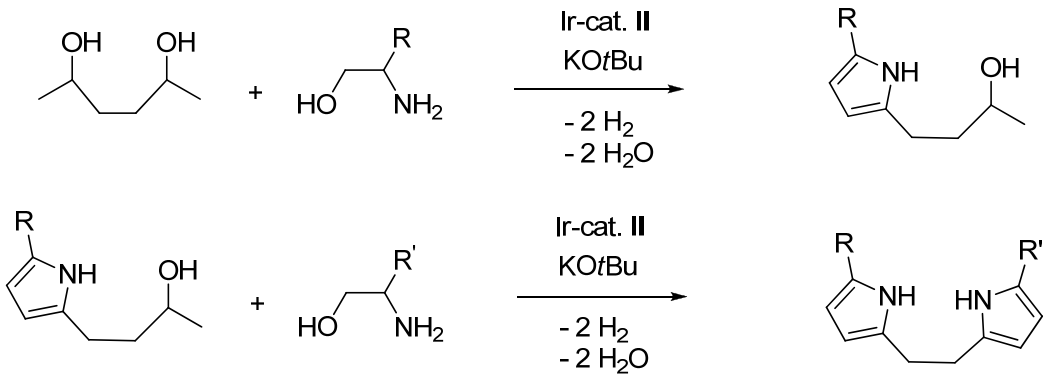


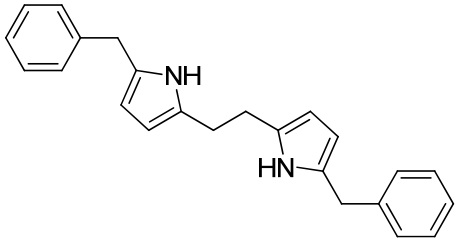
2k: 2-benzyl-5,6,7,8,9,10-hexahydro-1*H*-cycloocta[*b*]pyrrole: Cat. II (0.5 mL, 0.005 mmol, 0.01 M in THF), cyclooctanol (2.64 mL, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 40:1→20:1 pentane:Et_2O; Yield: 1.85 g = 7.7 mmol = 77% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.41 (s_br, 1H), 7.35-7.28 (m, 2H), 7.25- 7.18 (m, 3H), 5.66 (d, *J* = 2.9 Hz, 1H), 3.89-3.88 (m, 2H), 2.63-2.59 (m, 2H), 2.55-2.51 (m, 2H), 1.64-1.59 (m, 4H), 1.46-1.42 (m, 4H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 141.1, 129.1, 129.0, 128.1, 127.7, 126.6, 119.5, 108.0, 34.7, 31.3, 30.3, 26.6, 26.3, 25.9, 25.5 ppm. **MS** (70 eV, EI); m/z (%): 239 (100, M^+), 210 (62), 196 (45), 148 (35), 118 (10), 91 (52). **Elemental analysis** (%) for $C_{16}H_{19}N$ calcd: C 85.30, H 8.84, N 5.85; found: C 85.66, H 8.92, N 5.87.

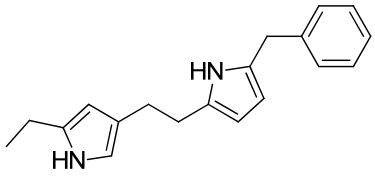


2l: 2-benzyl-5,6,7,8,9,10,11,12,13,14-decahydro-1*H*-cyclododeca[*b*]pyrrole: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), cyclododecanol (3.68 g, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 60:1→40:1 hexane:Et_2O; Yield: 1.1 g = 3.74 mmol = 37% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.37 (s_br, 1H), 7.33-7.26 (m, 2H), 7.25-7.15 (m, 3H), 5.68 (d, *J* = 2.9 Hz, 1H), 3.88 (s, 2H), 2.51 (t, *J* = 6.9 Hz, 2H), 2.36 (t, *J* = 6.9 Hz, 2H), 1.63 (m, 4H), 1.41-1.32 (m, 8H), 1.27-1.20 (m, 4H) ppm. **^{13}C NMR** (75 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, 25.0, 23.0, 22.9, 22.8, 22.5 ppm. **MS** (70 eV, EI); m/z (%): 295 (100, M^+), 266 (7), 252 (14), 238 (12), 210 (30), 204 (35), 196 (40), 184 (38), 171 (40), 91 (40). **Elemental analysis** (%) for $C_{21}H_{29}N$ calcd: C 85.37, H 9.89, N 4.74; found: C 85.11, H 10.11, N 4.91.

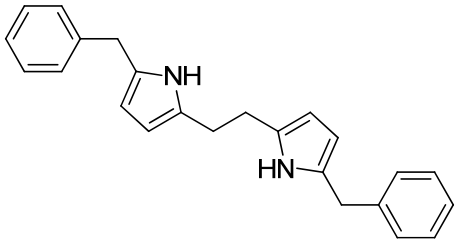
Supplementary Table S12: Reaction of hexane-2,5-diol with various amino alcohols to symmetric and unsymmetric bipyrroles



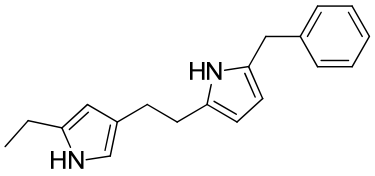
[mol% **Cat. II**]	Product	Yield [a]
3a **0.1**		**42%**

3b	**0.1**		**83%**

[a] Isolated yield

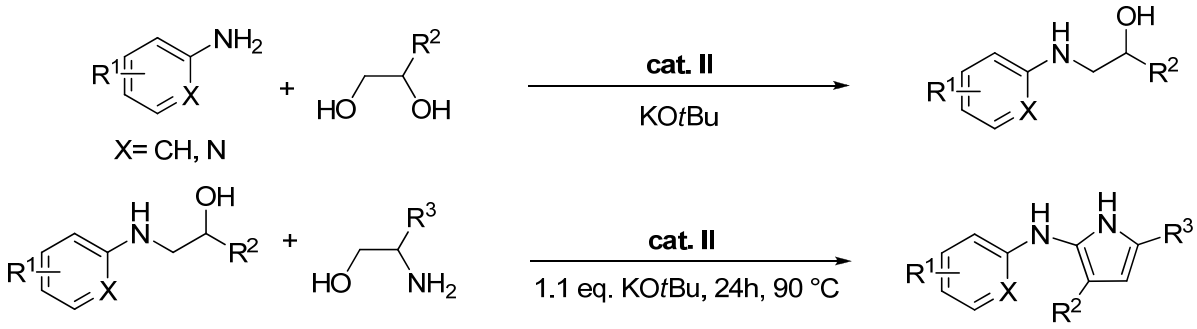


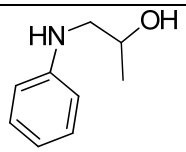
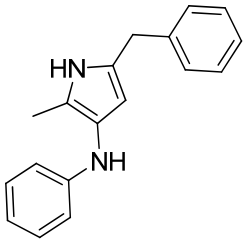
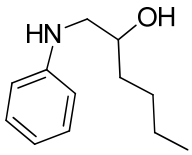
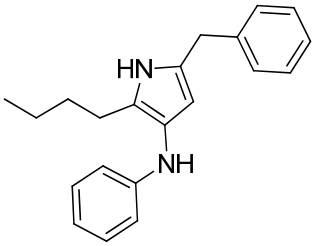
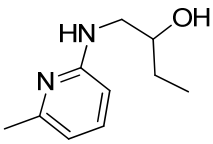
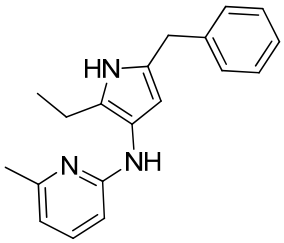
3a: 1,2-bis(5-benzyl-1*H*-pyrrol-2-yl)ethane: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), hexane-2,5-diol (1.18 g, 10.0 mmol), 2-amino-3-phenyl-propan-1-ol (6.04 g, 40.0 mmol), 20 mL THF, KO*t*Bu (2.48 g, 22.0 mmol), 24 h at 90 °C. Purification by column chromatography 8:1→4:1 pentane:Et_2O; Yield: 1.43 g = 4.2 mmol = 42% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.55 (s_br, 2H), 7.34-7.27 (m, 4H), 7.25-7.16 (m, 6H), 5.82-5.75 (m, 4H), 3.86 (s, 4H), 2.77 (s, 4H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.7, 131.7, 130.0, 129.0, 126.8, 106.7, 105.8, 34.6, 28.5 ppm. **MS** (70 eV, EI); m/z (%): 340 (2, M^+), 325 (2), 249 (50), 183 (60), 170 (100), 156 (28), 91 (30). **Elemental analysis** (%) for $C_{24}H_{24}N_2$ calcd: C 84.67, H 7.11, N 8.23; found: C 84.42, H 7.17, N 8.33.



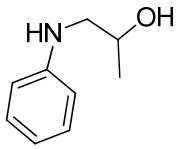
3b: 2-benzyl-5-(2-(5-ethyl-1*H*-pyrrol-2-yl)ethyl)-1*H*-pyrrole: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), 4-(5-benzyl-1*H*-pyrrol-2-yl)-butan-2-ol (4.584 g, 20.0 mmol), 2-amino-1-butanol (960 µL, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 8:1→4:1 pentane:Et_2O; Yield: 2.31 g = 8.3 mmol = 83% as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.58 (s_br, 1H), 7.36-7.28 (m, 2H), 7.27-7.18 (m, 3H), 5.87-5.82 (m, 2H), 5.77-5.73 (m, 2H), 3.89 (s, 2H), 2.81 (s, 4H), 2.53 (q, *J* = 7.6 Hz, 2H), 1.20 (t, *J* = 7.6 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 140.7, 133.4, 131.9, 130.7, 130.1, 129.1, 129.0, 126.8, 106.7, 105.7, 105.6, 104.4, 34.7, 28.7, 28.6, 21.3, 14.2 ppm. **MS** (70 eV, EI); m/z (%): 278 (2, M^+), 186 (1), 170 (100), 108 (75), 93 (12). **Elemental analysis** (%) for $C_{19}H_{22}N_2$ calcd: C 81.97, H 7.97, N 10,06; found: C 81.83, H 8.25, N 10.17.

Supplementary Table S13: Syntheses of *N*-protected amino alcohols and their conversion with 2-amino-3-phenyl-propan-1-ol

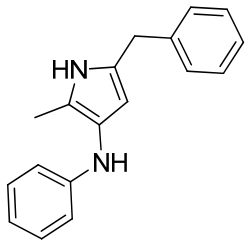


	[mol% **Cat. II**]	Product	Yield [a]
	0.5		**92%**
3c	**0.1**		**83%**
	0.5		**78%**
3d	**0.3**		**82%**
	0.3		**89%**
3e	**0.3**		**87%**

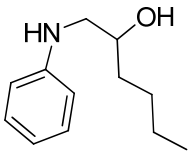
[a] Isolated yield



1-(phenylamino)propan-2-ol: Cat. II (0.4 mmol, 288 mg), aniline (7.28 mL, 80.0 mmol) propane-1,2-diol (23.6 mL, 320.0 mmol), 60 mL THF, KO*t*Bu (9.04 g, 80.0 mmol), 24 h at 110 °C. Purification by HV distillation (3.0x 10^{-2} mbar, 96 °C) 11.11g = 73.5 mmol = 92% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.21-7.11 (m, 2H), 6.74-6.61 (m, 3H), 4.05 (s_br, 1H), 4.02-3.93 (m, 1H), 3.20 (d, *J* = 12.6 Hz, 1H), 2.97 (dd, *J* = 12.6, 8.6 Hz, 1H), 2.21 (s_br, 1H), 1.24 (d, *J* = 6.4 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ =149.1, 129.7, 118.0, 113.6, 66.9, 52.1, 21.3 ppm.

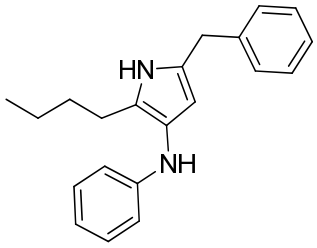


3c: 5-benzyl-2-methyl-N-phenyl-1H-pyrrol-3-amine: Cat. II (1.0 mL, 0.01 mmol, 0.01 M in THF), 1-phenylamino-propan-2-ol (3.02 g, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 2:1→1:1 pentane:Et_2O; Yield: 2.17 g = 8.3 mmol = 83% as deep red oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.51 (s_br, 1H), 7.40-7.30 (m, 2H), 7.30-7.21 (m, 3H), 7.17-7.12 (m, 2H), 6.68-6.64 (m, 3H), 5.82 (d, *J* = 2.9 Hz, 1H), 5.00 (s_br, 1H), 3.91 (s, 2H), 2.07 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 149.2, 141.5, 129.6, 129.12, 129.10, 128.1, 126.9, 122.0, 121.8, 117.6, 113.5, 105.6, 34.9, 10.6 ppm. **MS** (70 eV, EI); m/z (%): 262 (12, M^+), 217 (8), 185 (100), 169 (60), 143 (16), 131 (17), 115 (35), 104 (14), 91 (38), 77 (22). **Elemental analysis** (%) for $C_{18}H_{18}N_2$ calcd: C 82.41, H 6.92, N 10.68; found: C 82.22, H 6.71, N 10.73.

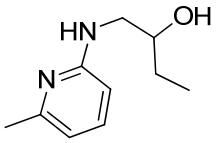


1-(phenylamino)hexan-2-ol: Cat. II (0.4 mmol, 288 mg), aniline (7.28 mL, 80.0 mmol), hexane-1,2-diol (24.8 mL, 200.0 mmol), 40 mL THF, KO*t*Bu (9.94 g, 88.0 mmol), 72 h at 110 °C. Purification by HV distillation (1.3 x 10^{-1} mbar, 133 °C) 11.99g = 62 mmol = 78% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.19-7.11 (m, 2H), 6.72-6.60 (m, 3H), 4.04 (s_br, 1H), 3.80 (s_br, 1H), 3.24 (dd, *J* = 12.6, 2.6 Hz, 1H), 2.97 (dd, *J* = 12.6, 8.6Hz, 1H),

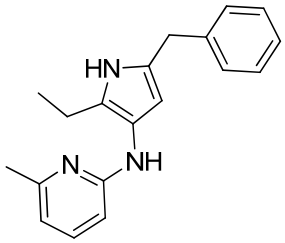
1.95 (d, *J* = 1.9 Hz, 1H), 1.65-1.33 (m, 6H), 0.93 (t, *J* = 6.7 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 149.2, 129.7, 118.0, 113.6, 70.9, 50.8, 35.4, 28.4, 23.3, 14.4 ppm. **MS** (70 eV, EI); m/z (%): 193 (6, M^+), 118 (2), 106 (100), 93 (3), 77 (9).



3d: 5-benzyl-2-butyl-N-phenyl-1H-pyrrol-3-amine: Cat. II (3.0 mL, 0.03 mmol, 0.01 M in THF), 1-phenylamino-hexan-2-ol (3.86 g, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 8:1→4:1 pentane:Et_2O; Yield: 2.49 g = 8.2 mmol = 82% as deep red oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.51 (s_br, 1H), 7.36-7.30 (m, 2H), 7.27-7.20 (m, 3H), 7.15-7.08 (m, 2H), 6.67-6.63 (m, 3H), 5.79 (d, *J* = 2.9 Hz, 1H), 4.96 (s_br, 1H), 3.91 (s, 2H), 2.48-2.42 (m, 2H), 1.51-1.43 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 149.4, 140.5, 129.5, 129.08, 129.07, 128.1, 127.0, 126.8, 121.5, 117.5, 113.5, 105.7, 34.9, 32.4, 25.2, 23.0, 14.2 ppm. **MS** (70 eV, EI); m/z (%): 304 (1, M^+), 261 (66), 244 (13), 169 (100), 115 (15), 91 (15). **Elemental analysis** (%) for $C_{21}H_{24}N_2$ calcd: C 82.85, H 7.95, N 9.20; found: C 82.53, H 8.02, N 9.15.

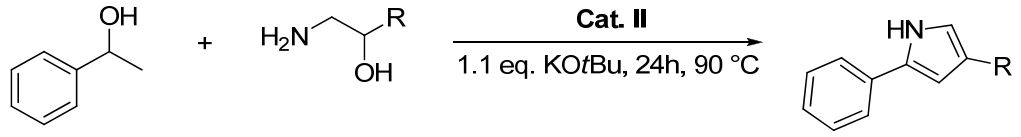


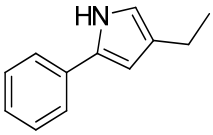
1-(6-methylpyridin-2-ylamino)butan-2-ol: Cat. II (0.3 mmol, 215 mg), 6-methylpyridin-2-amine (10.8 g, 100.0 mmol) butane-1,2-diol (18.4 mL, 250.0 mmol), 60 mL THF, KO*t*Bu (12.4g, 110.0 mmol), 96 h at 110 °C. Purification by HV distillation (2.6x 10^{-2} mbar, 122 °C); Yield: 16.0 g = 89.0 mmol = 89% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.29 (dd, *J* = 8.3,7.2 Hz, 1H), 6.43 (d, *J* = 7.2 Hz, 1H), 6.27 (d, *J* = 8.3 Hz, 1H), 4.98 (s_br, 1H), 3.68-3.57 (m, 1H), 3.45-3.36 (m, 1H), 3.30-3.20 (m, 1H), 2.32 (s, 3H), 1.52-1.45 (m, 2H), 0.94 (t, *J* = 7.6 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ =159.3, 156.5, 138.4, 112.4, 105.6, 74.3, 49.3, 28.7, 24.2, 10.5 ppm.



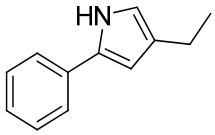
3e: N-(5-benzyl-2-ethyl-1*H*-pyrrol-3-yl)-6-methylpyridin-2-amine: Cat. II (3.0 mL, 0.03 mmol, 0.01 M in THF), 1-(6-methyl-pyridin-2-ylamino)-butan-2-ol (3.60 g, 20.0 mmol), 2-amino-3-phenyl-propan-1-ol (1.51 g, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 2:1→1:2 pentane:Et_2O; Yield: 2.53 g = 8.7 mmol = 87% as deep red oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.14 (s_br, 1H), 7.37-7.21 (m, 6H), 6.46 (d, *J* = 7.0 Hz, 1H), 6.30 (s_br, 1H), 6.27 (d, *J* = 8.5 Hz, 1H), 5.83 (d, *J* = 2.9 Hz, 1H), 3.94 (s, 2H), 2.49 (q, *J* = 7.6 Hz, 2H), 2.34 (s, 3H), 1.11 (t, *J* = 7.6 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 16.1, 157.2, 140.5, 138.3, 129.1, 129.0, 128.6. 128.3, 126.8, 119.3, 112.5, 105.9, 103.3, 34.8, 24.4, 18.8, 14.4 ppm. **MS** (70 eV, EI); m/z (%): 291 (42, M^+), 276 (50), 184 (100), 168 (35), 142 (30), 115 (32), 91 (44). **Elemental analysis** (%) for $C_{19}H_{21}N_3$ calcd C 78.32, H 7.26, N 14.42; found: C 78.08, H 6.97, N 13.61.

Supplementary Table S14: Reaction of 1-phenylethanol with 1-amino-alcohol to 4-substituted pyrroles



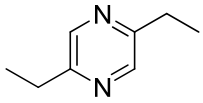
[mol% **Cat. II**]	Product	Yield [a]
0.5		**52%**

[a] Isolated yield

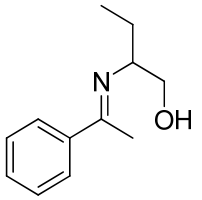


4-ethyl-2-phenyl-1*H*-pyrrole: Cat. II (5.0 mL, 0.05 mmol, 0.01 M in THF), 1-phenylethanol (2.4 mL, 20.0 mmol) 1-aminobutan-2-ol (960 µL, 10.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at 90 °C. Purification by column chromatography 10:1 pentane:Et_2O; Yield: 889 mg = 5.2 mmol = 52% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.28 (s_br, 1H), 7.49-7.42 (m, 2H), 7.39-7.31 (m, 2H), 7.22-7.15 (m, 1H), 6.68-6.61 (m, 1H), 6.43-6.36 (m, 1H), 2.53 (q, *J* = 7.5 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2):

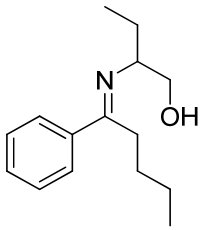
δ = 133.5, 132.1, 129.4, 128.6, 126.4, 124.0, 116.2, 106.5, 20.7, 15.7 ppm. **MS** (70 eV, EI); m/z (%): 171 (46), 156 (100), 128 (20), 115 (10), 78 (19).



2,5-diethylpyrazine: Cat. II (71 mg, 0.1 mmol), 2-aminobutan-1-ol (3.8 mL, 40.0 mmol), 10 mL THF, KO*t*Bu (2.5 g, 22.0 mmol), 24 h at 90 °C. Purification by column chromatography 5:1 pentane:Et_2O; Yield: 0.54 g = 3.9 mmol = 19% as yellow oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.33 (s, 2H), 2.77 (q, *J* = 7.6 Hz, 4H), 1.27 (t, *J* = 7.6 Hz, 6H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 156.2, 143.3, 28.7, 13.9 ppm. **MS** (70 eV, EI); m/z (%): 136, (55, M^+), 135 (100), 121 (96), 108 (8), 94 (4), 80 (5), 67 (6).

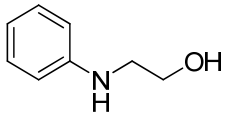


2-(1-phenylethylideneamino)butan-1-ol: acetophenone (35.0 mL, 300.0 mmol) (±)2-aminobutan-1-ol (33.0 mL, 350.0 mmol), molecular sieve 3Å (40 g), 200 mL THF, 48 h reflux. Purification by HV distillation (3.0 x 10^{-3}, 52 °C); Yield: 53.5 g = 279.0 mmol = 93% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.60-7.54 (m, 2H), 7.41-7.21 (m, 3H), 4.09 (dd, *J* = 7.7, 6.9 Hz, 0.31 H), 3.76 (t, *J* = 7.3 Hz, 0.65H), 3.32 (t, *J* = 7.7 Hz, 0.69 H), 3.23-3.16 (m, 0.35 H), 1.85 (s_br, 1H), 1.68-1.31 (m, 5H), 0.97-0.92 (m, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 146.2, 128.5, 127.6, 126.4, 125.9, 71.2, 60.4, 29.9, 27.2, 11.8 ppm. **MS** (70 eV, EI); m/z (%): 190 (1), 176 (100), 160 (75), 145 (8), 132 (7), 114 (50), 105 (63), 91 (33), 77 (32).

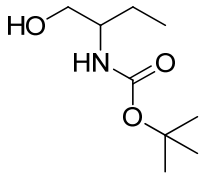


2-(1-phenylpentylideneamino)butan-1-ol: valerophenone (20.0 mL, 120.0 mmol) (±)2-aminobutan-1-ol (19.0 mL, 200.0 mmol), molecular sieve 3Å (20 g), 200 mL THF, 48 h reflux. Purification by HV distillation (3.8 x 10^{-2}, 110 °C); Yield: 21.5 g = 92.2 mmol = 76% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.59-7.45 (m, 2H), 7.41-7.11 (m, 3H), 4.07-4.02 (m, 0.28H), 3.76 (t, *J* = 7.4 Hz, 0.71H), 3.37-3.16 (m, 1H), 3.02-2.83 (m, 1H), 1.95

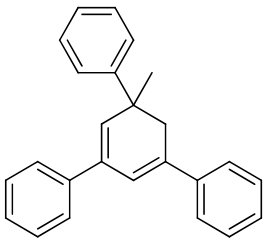
(s_br, 1H), 1.89-1.76 (m, 2H), 1.71-1.56 (m, 1H), 1.56-1.35 (m, 1H), 1.30-1.10 (m, 4H), 0.98-0.88 (m, 3H), 0.88-0.78 (m, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 145.8, 128.2, 127.5, 127.1, 126.5, 71.1, 61.0, 60.1, 42.3, 26.9, 23.5, 14.3, 11.7 ppm. **MS** (70 eV, EI); m/z (%): 233 (1, M^+), 232 (1), 202 (11), 176 (100), 156 (6), 120 (7), 105 (35), 91 (12), 77 (16).



2-(phenylamino)ethanol: cat. II (0.5 mmol, 359 mg), aniline (23.3 mL, 250.0 mmol) ethane-1,2-diol (50.0 mL, 800.0 mmol), 200 mL THF, KO^{t}Bu (31.0 g, 275.0 mmol), 72 h at 110 °C. Purification by HV distillation (2.3 x 10^{-1}, 107 °C); Yield: 10.95 g = 80.0 mmol = 32% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.25-7.13 (m, 2H), 6.77-6.69 (m, 1H), 6.68-6.61 (m, 2H), 4.08 (s_br, 1H), 3.77 (t, *J* = 5.3 Hz, 2H), 3.25 (t, *J* = 5.3 Hz, 2H), 2.44 (s_br, 1H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 149.0, 129.7, 118.1, 113.6, 61.6, 46.6 ppm. **MS** (70 eV, EI); m/z (%): 137 (25, M^+), 106 (100), 77 (20).



tert-butyl-1-hydroxybutan-2-ylcarbamate: To 2-aminobutan-1-ol (18.9 mL, 200 mmol) in 500 mL water and 400 mL THF, Na_2CO_3 (70.0 g, 660 mmol) was added. After cooling to 0 °C, di-tert-butyl-dicarbonate (45.0 g, 206 mmol) dissolved in 100 mL THF was added drop wise. The solution was allowed to warm to room temperature and stirred for further 4h. The solution was extracted 4 times with Et_2O. The combined organic phases were dried over Na_2SO_4, filtered and the solvent was removed by rotary evaporation. Purification by HV distillation (8.8 x 10^{-2} mbar, 99 °C); Yield: 36.5 g = 192 mmol = 96% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 4.73 (s_br, 1H), 3.64-3.55 (m, 1H), 3.55-3.42 (m, 2H), 2.67 (s_br, 1H), 1.62-1.46 (m, 2H), 1.42 (s, 9H), 0.93 (t, *J* = 7.6 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 157.1, 79.6, 65.6, 54.8, 28.7, 25.1, 10.9 ppm.

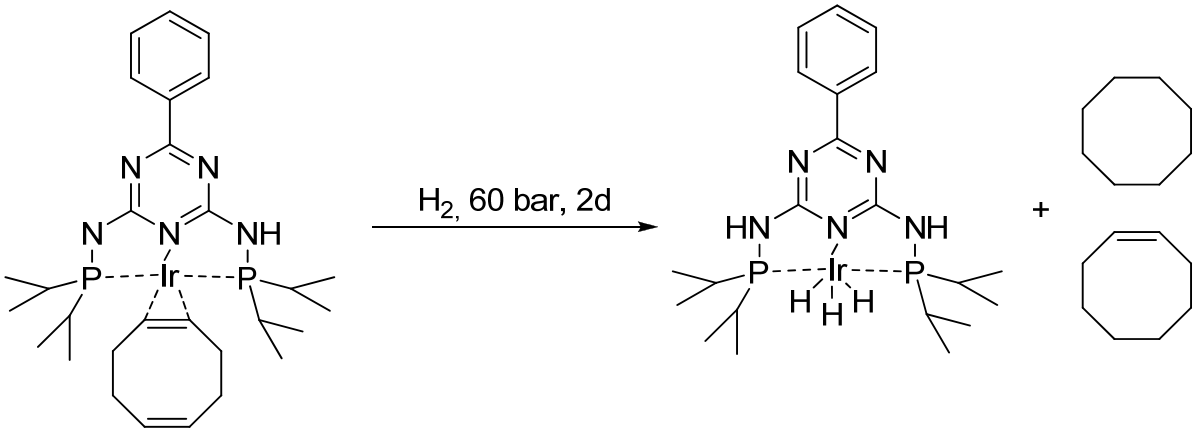


(5-methylcyclohexa-1,3-diene-1,3,5-triyl)tribenzene: Cat. II (36 mg, 0.05 mmol), 1-phenyl-1-ethanol (2.4 mL, 20.0 mmol), 10 mL THF, KO*t*Bu (1.24 g, 11.0 mmol), 24 h at

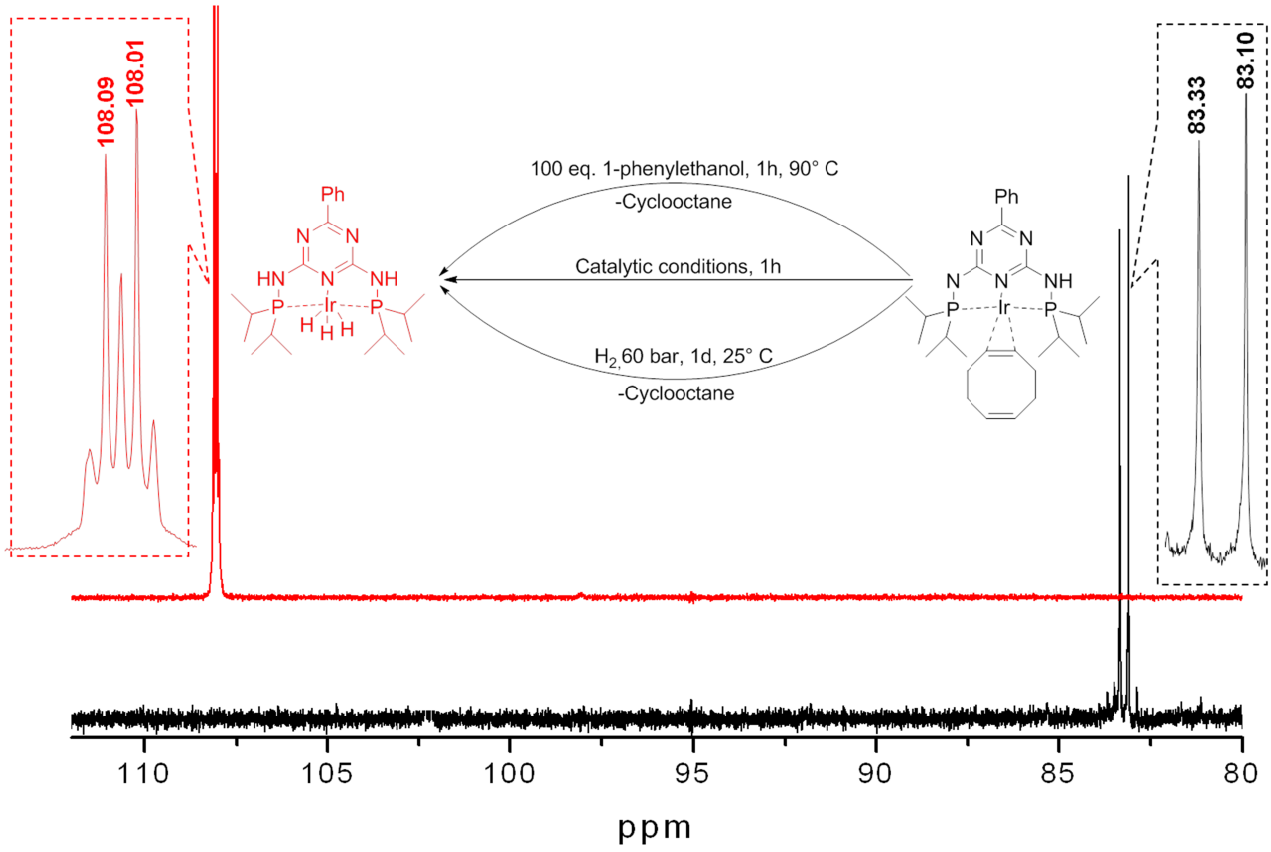
90 °C. Purification by column chromatography 100:1 pentane:Et_2O →3:1 pentane:Et_2O; Yield: = 527 mg = 1.6 mmol = 33% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.62-7.24 (m, 15H), 6.79 (q, *J* = 1.5 Hz, 1H)), 6.27 (d, *J* = 1.5 Hz, 1H), 3.18 (dd, *J* = 16.7, 1.5 Hz, 1H), 2.89 (dd, *J* = 16.7, 1.8 Hz, 1H), 1.64 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 149.3, 141.5, 141.2, 137.6, 136.5, 132.7, 129.1, 129.0, 128.8, 128.0, 127.0, 126.7, 126.6, 126.4, 125.8, 121.9, 41.9, 40.9, 27.5 ppm. **MS** (70 eV, EI); m/z (%): 322 (100, M^+), 307 (80), 291 (14), 265 (8), 231 (24), 215 (31), 202 (12), 165 (8), 115 (9), 105 (29), 91 (17), 77 (10).

Mechanistic Studies

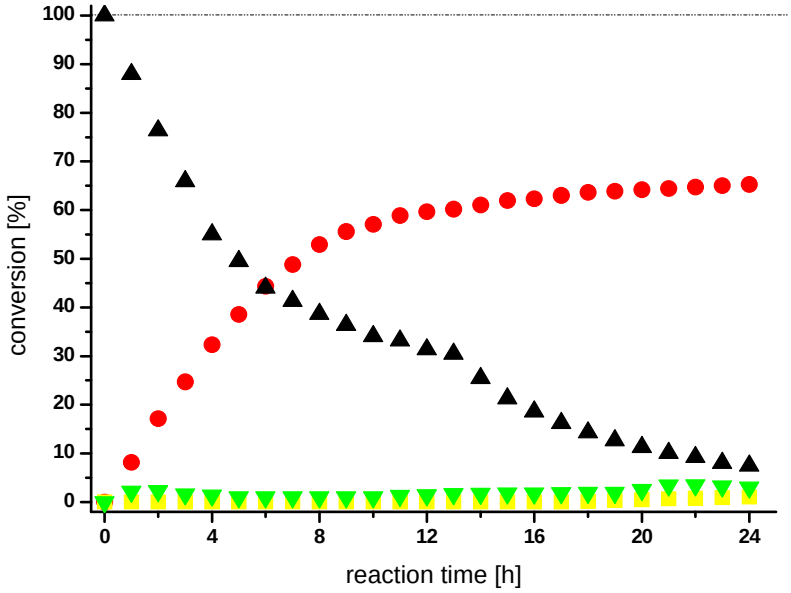
Synthesis of [(4-Ph)Tr(NHP(*i*Pr)$_2$)$_2$IrH$_3$]



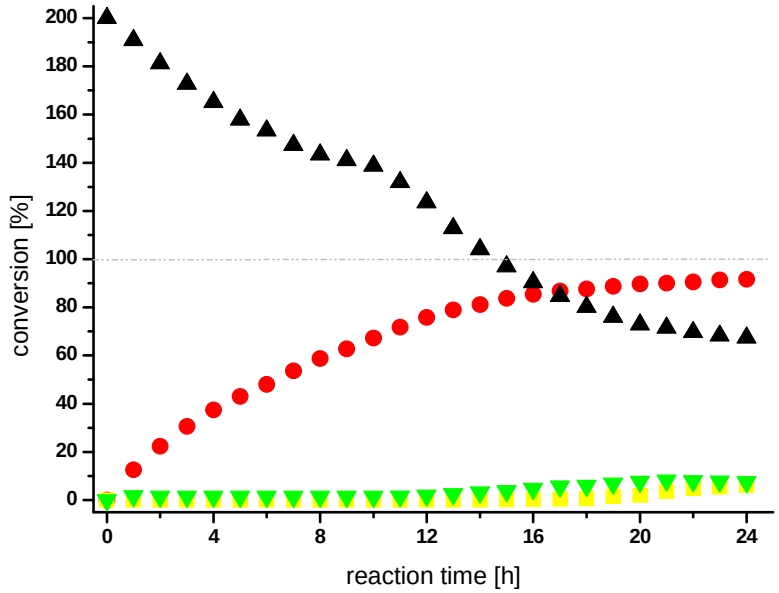
Cat. II (1.0 mmol, 719 mg) was dissolved in 4 mL benzene-d_6 and stirred in a 60 bar H_2 atmosphere at 25 °C for 2 days. An orange solution was obtained. Crystals suitable for X-Ray analysis were obtained from this solution. Due to the high reactivity of this compound NMR-analyses was done directly from the reaction solution. **^{1}H NMR** (400 MHz, C_6D_6): δ = 8.42-8.50 (m, 2H), 7.31-7.27 (m, 3H), 5.90 (s_br, 2H), 1.43-1.37 (m, 4H), 1.08-0.99 (m, 24H), -11.69 (dt, *J* = 18.3, 5.1 Hz, 2H), -18.04 (tt, *J* = 14.6, 5.1 Hz, 1H) ppm. **^{13}C NMR** (100 MHz, C_6D_6): δ = 169.2 (t, *J* = 9.5 Hz), 168.4, 137.1, 132.2, 129.1, 129.0, 69.3, 30.8 (t, *J* = 16.2 Hz), 28.8, 26.2, 23.9, 19.5 (t, *J* = 4.4 Hz), 18.8 ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298 K): δ = 108.05 (dt, *J* = 13.0, 6.7 Hz) ppm. **Elemental analysis** (%) for [$C_{21}H_{35}IrN_5P_2$] x 0.4 C_6D_6 calcd: C 43.35, H 6.65, N 10.80; found: C 43.42, H 6.65, N 10.50.



Supplementary Figure S3: Formation of the catalyst resting state, an iridium trihydride complex. It can be formed quantitatively by reacting catalyst **II** with alcohols, H_2 or under catalytic conditions.

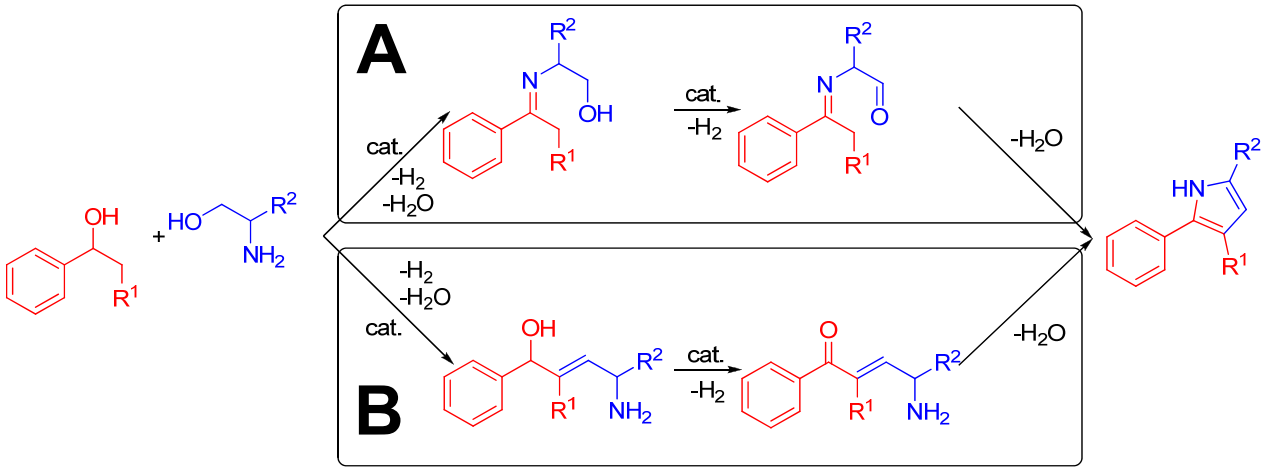


Supplementary Figure S4. Time conversion plot for the reaction of 1-phenylethanol with 2-amino-butan-1-ol. reaction conditions: 1-phenylethanol (2.4 mL, 20.0 mmol), 2-amino-butan-1-ol (1.92 mL, 20.0 mmol), KO*t*Bu (2.48 g, 22.0 mmol), cat. **II** (57 mg, 0.08 mmol), 20 mL dioxane, 1.125 mL dodecane as internal standard, 110 °C ●. 2-ethyl-5-phenyl-1*H*-pyrrole ▲ 1-phenylethanol ▼acetophenone ■ (5-methylcyclohexa-1,3-diene-1,3,5-triyl)tribenzene.



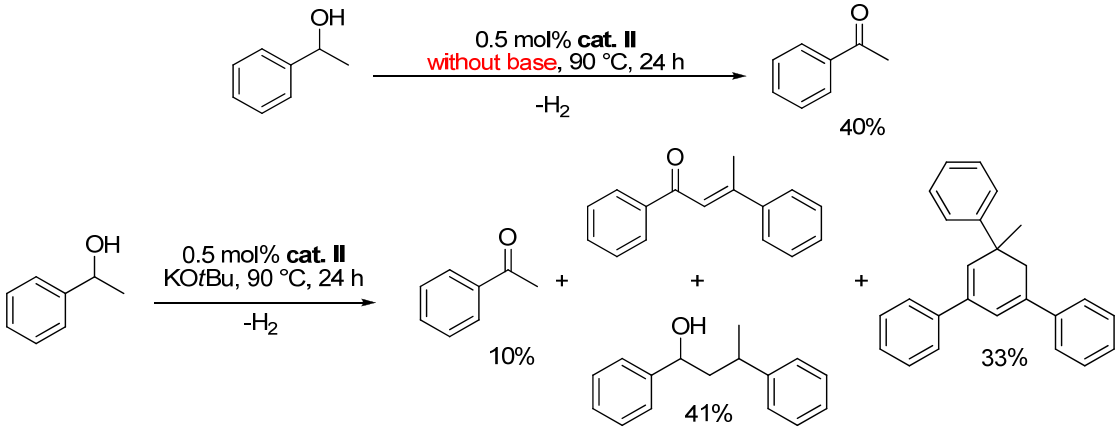
Supplementary Figure S5. Time conversion plot for the reaction of 1-phenylethanol with 2-amino-butan-1-ol. reaction conditions: 1-phenylethanol (4.8 mL, 40.0 mmol), 2-amino-butan-1-ol (1.92 mL, 20.0 mmol), KO*t*Bu (2.48 g, 22.0 mmol), cat. **II** (57 mg, 0.08 mmol), 20 mL dioxane, 1.125 mL dodecane as internal standard, 110 °C. ● 2-ethyl-5-phenyl-1*H*-pyrrole ▲ 1-phenylethanol ▼acetophenone ■ (5-methylcyclohexa-1,3-diene-1,3,5-triyl)tribenzene.

Possible Reaction Pathways



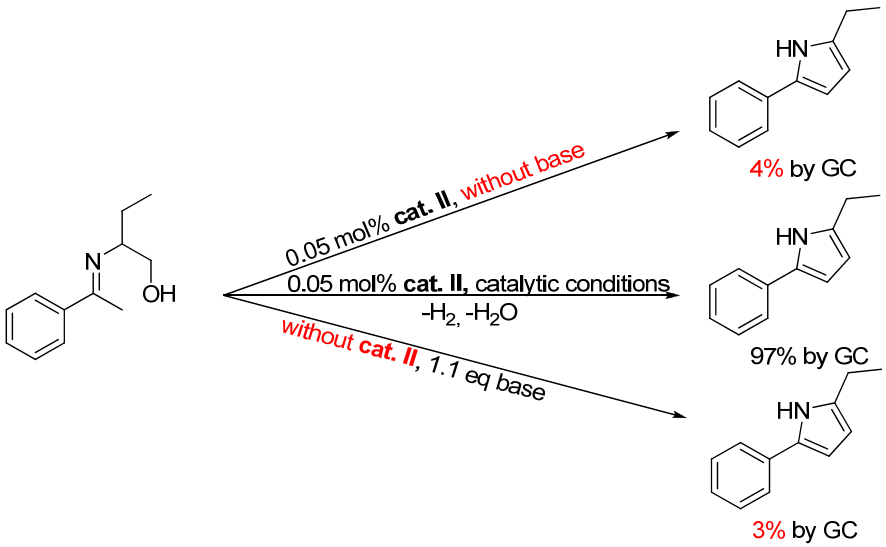
Supplementary Figure S6: Possible reaction pathways for the pyrrole synthesis.

Reactions which confirm Pathway A



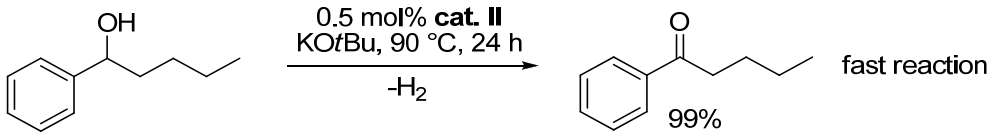
Supplementary Figure S7: Dehydrogenation of 1-phenylethanol.

Without base 1-phenylethanol is converted into acetophenone and H_2 by catalyst **II**, but with base, 1-phenylethanol is converted to acetophenone and several additional aldol condensation products (Supplementary Figure S7). Due to this fact the system 1-phenyl-1-pentanol/valerophenone was used for further mechanistic investigations (Supplementary Figure S9).



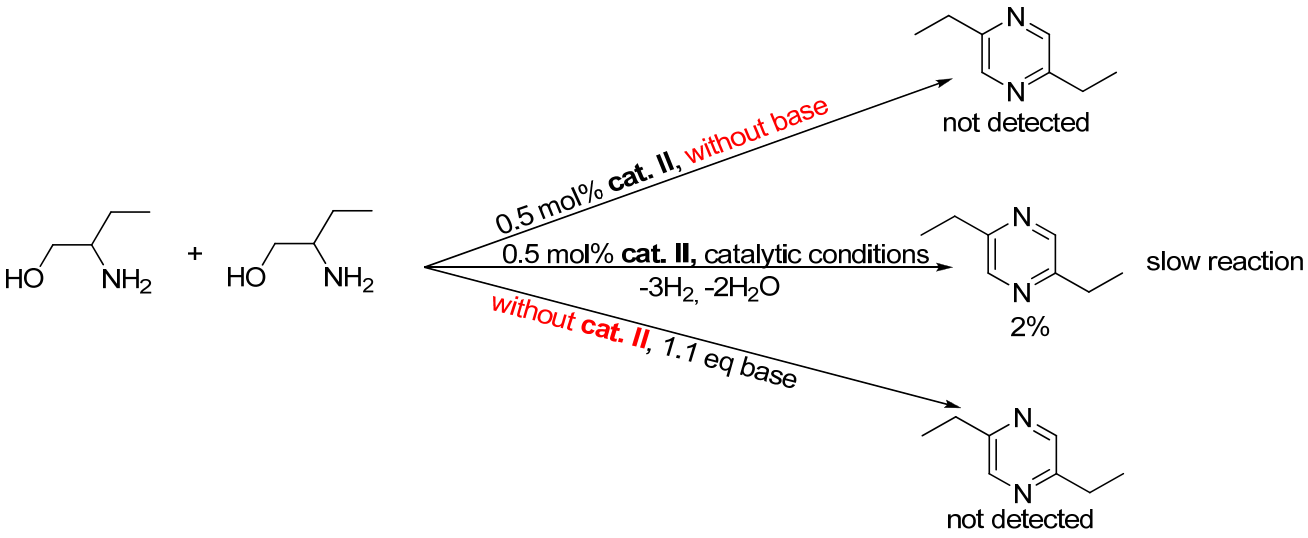
Supplementary Figure S8: Conversion of 2-(1-phenylethylideneamino)butan-1-ol to 2-ethyl-5-phenyl-1*H*-pyrrole.

Under catalytic conditions 2-(1-phenylethylideneamino)butan-1-ol is converted to 2-ethyl-5-phenyl-1*H*-pyrrole in excellent yield (Supplementary Figure S8). If catalyst or base is used exclusively only a very poor conversion of the imine is observed. This fact clearly points out that both catalyst and base in combination are involved in the cyclisation reaction.



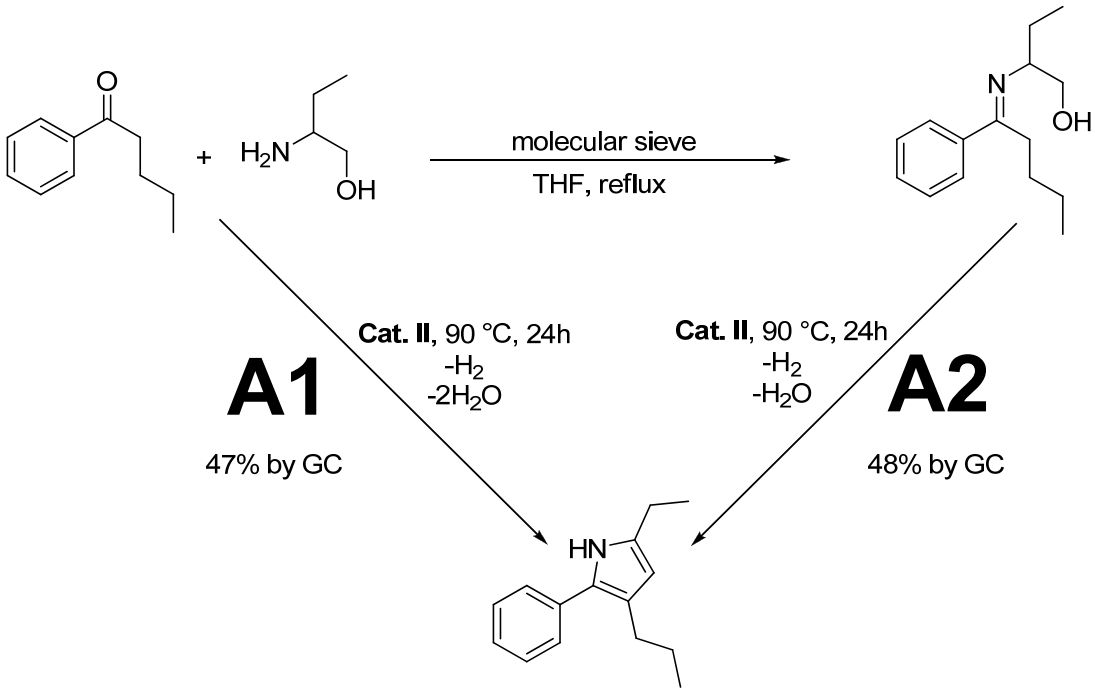
Supplementary Figure S9: Dehydrogenation of 1-phenyl-1-pentanol to valerophenone under catalytic conditions.

Dehydrogenation of 1-phenyl-1-pentanol is fast. Under standard reaction conditions the secondary alcohol is completely converted to the corresponding ketone within 24 h (Supplementary Figure S9).



Supplementary Figure S10: Dehydrogenation and condensation reaction of 2-amino-1-butanol to 2,5-diethylpyrazine**.**

In contrast the dehydrogenation and condensation reaction of the amino alcohol to 2,5-diethylpyrazine is very slow under the given reaction conditions (90 °C), which was already shown in our previous work.[38] (Supplementary Figure S10)

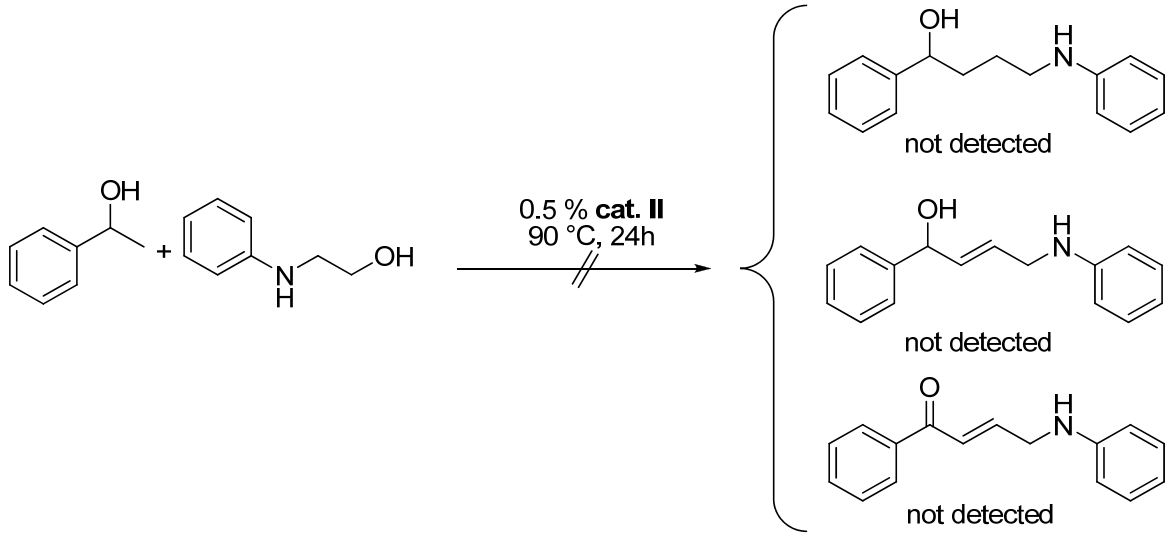


Supplementary Figure S11: Pathway A1: reaction of valerophenone with 2-amino-1-butanol under catalytic conditions (cat II, 0.5 mol%).

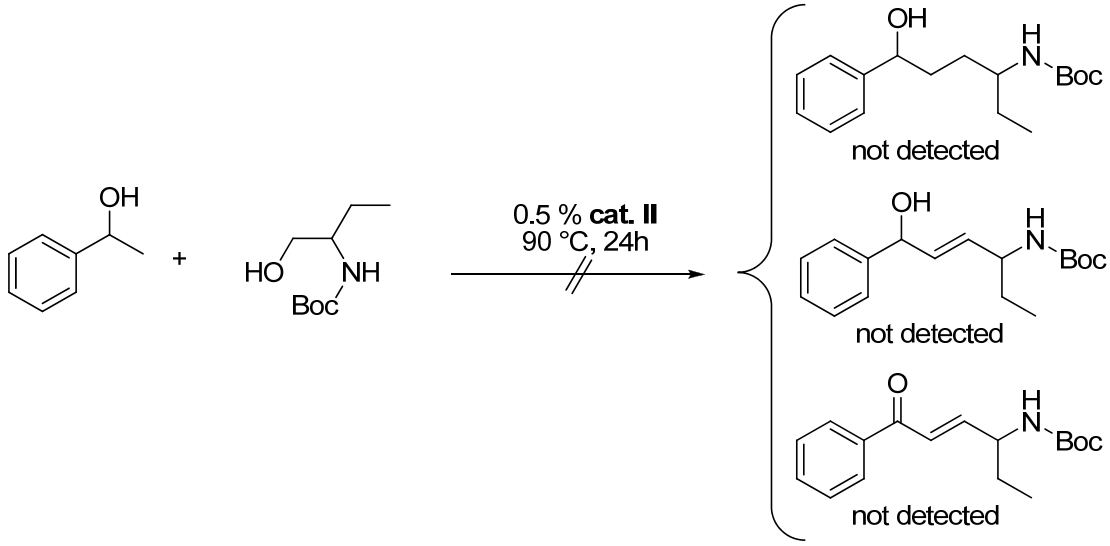
Pathway A2: reaction of 2-(1-phenylpentylideneamino)butan-1-ol under catalytic conditions (cat II, 0.5 mol%).

Regardless whether the reaction was started from ketone and amino alcohol (**A1**, Supplementary Figure S11), or from the preformed Schiff base (**A2**, Supplementary Figure S11), nearly identical yields were obtained. This indicates that the imine formation is very fast.

Reactions which contradict Pathway B



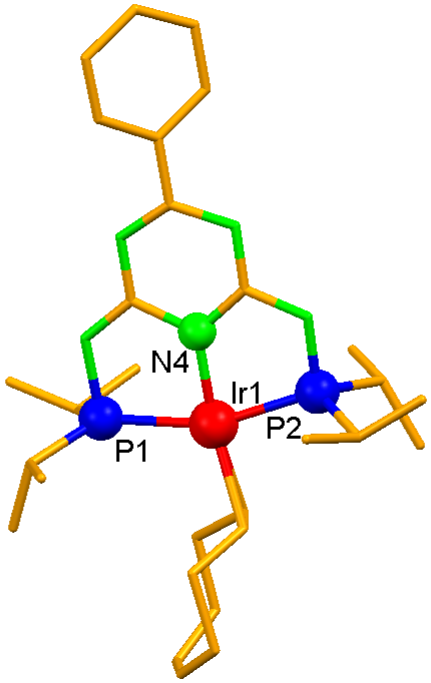
Supplementary Figure S12: Under catalytic conditions no reaction of 1-phenylethanol with 2-(phenylamino)ethanol is observed.



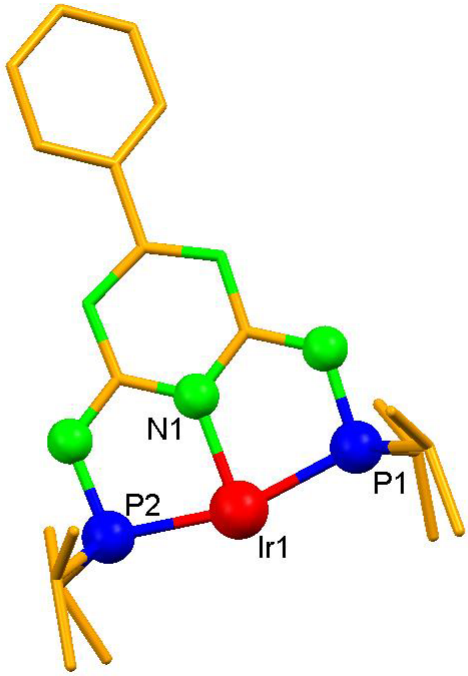
Supplementary Figure S13: Under catalytic conditions no reaction of 1-phenylethanol with *tert*-butyl-1-hydroxybutan-2-ylcarbamate.

No β-alkylation between 1-phenylethanol and the *N*-protected amino alcohol was observed, regardless which protecting group was chosen (Supplementary Figure S12 and Supplementary Figure S13). These experiments show that under the given reaction conditions

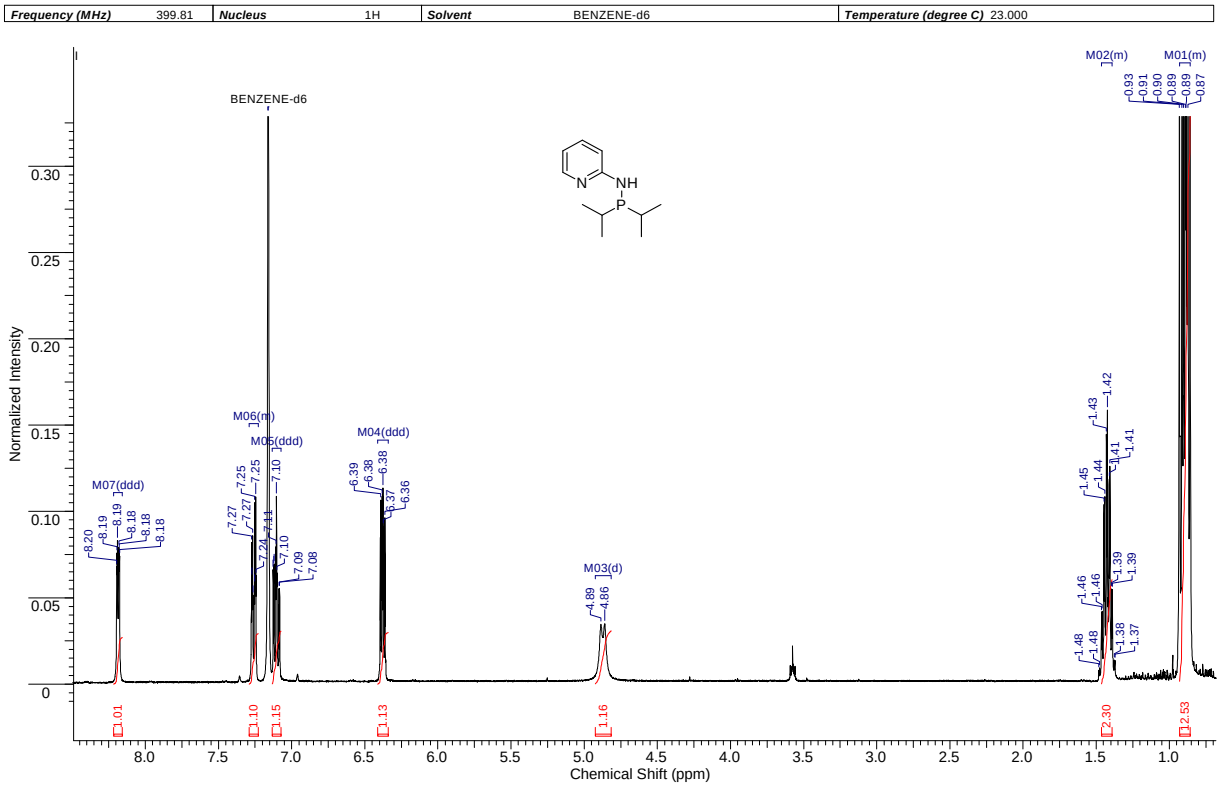
the β-alkylation is very unlikely to be the first reaction step (pathway B, Supplementary Figure S6) in the pyrrole syntheses.



Supplementary Figure S14: Crystal structure of catalyst II.



Supplementary Figure S15. Crystal Structure of [(4-Ph)Tr(NHP(*i*Pr)$_2$)IrH$_3$].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Solvent BENZENE-d6
Temperature (degree C) 23.000
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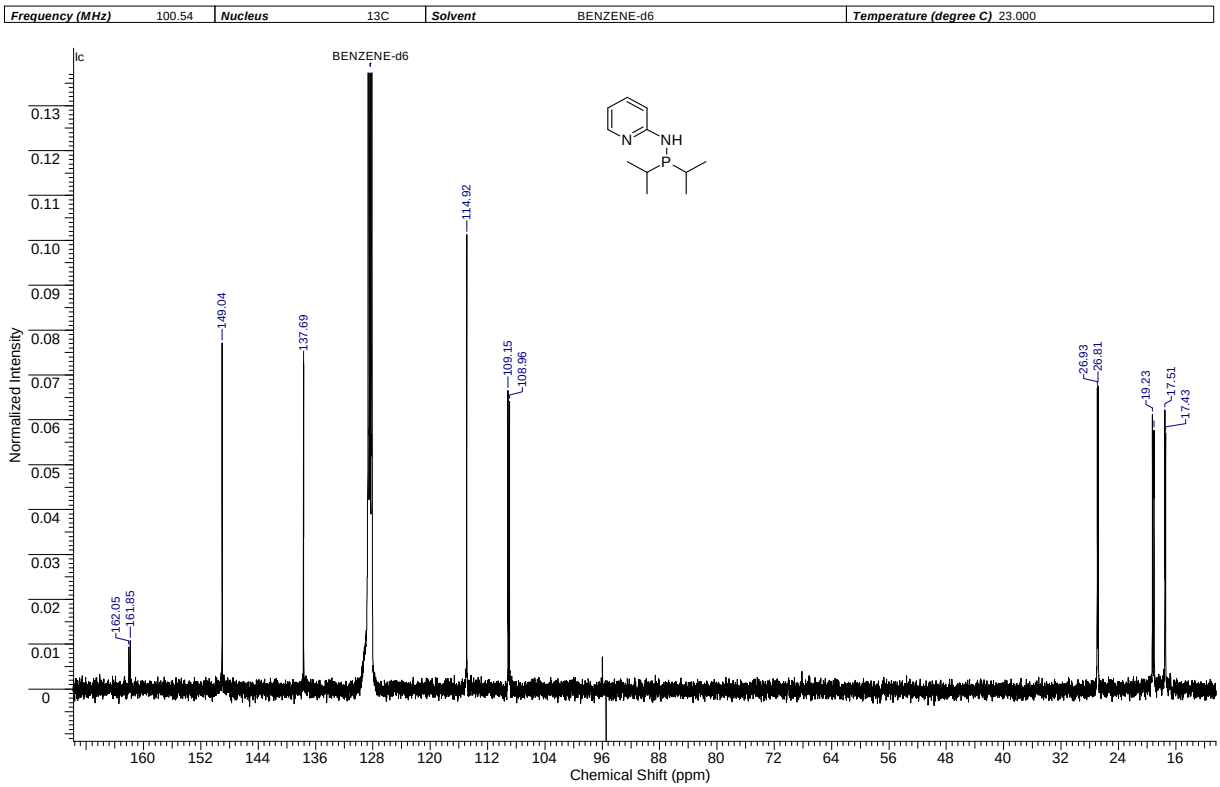
M01(m)
M02(m)
M03(d)
M04(ddd)
M05(ddd)
M06(m)
M07(ddd)
Normalized Intensity
Chemical Shift (ppm)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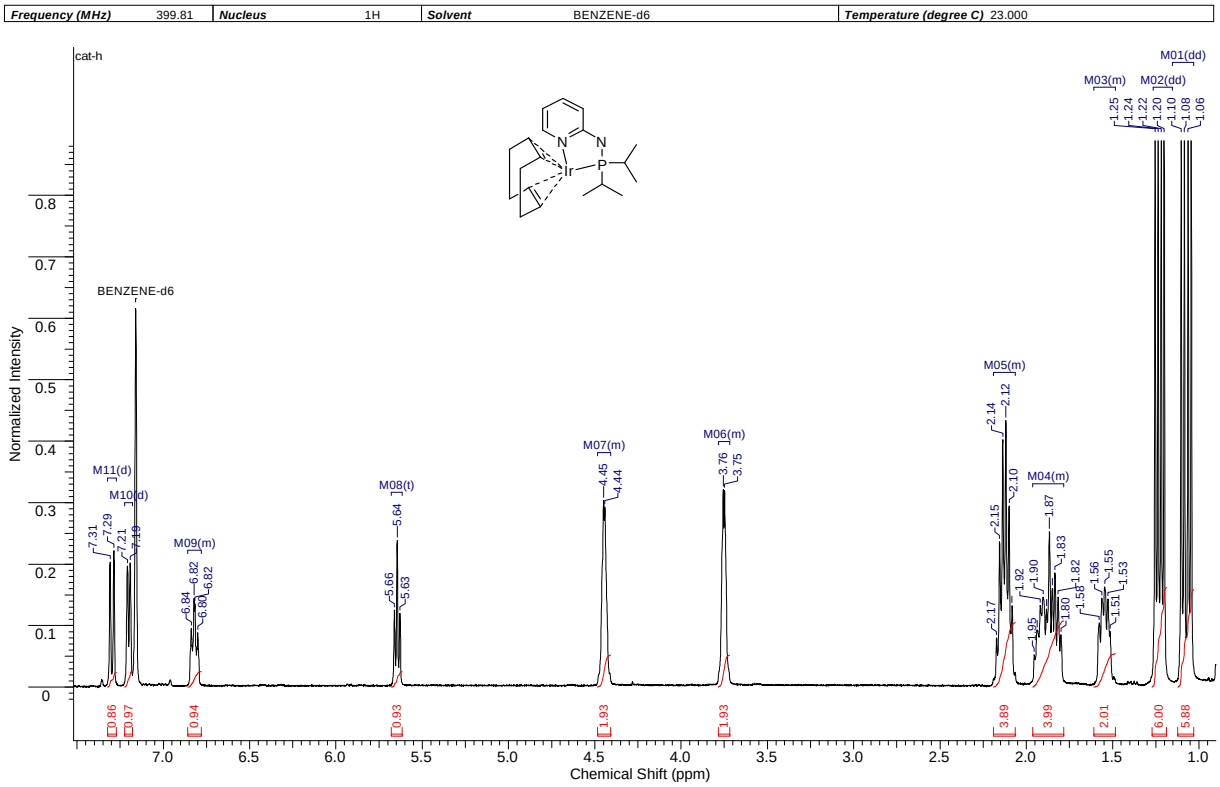
BENZENE-d6
Normalized Intensity
Chemical Shift (ppm)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cat-h
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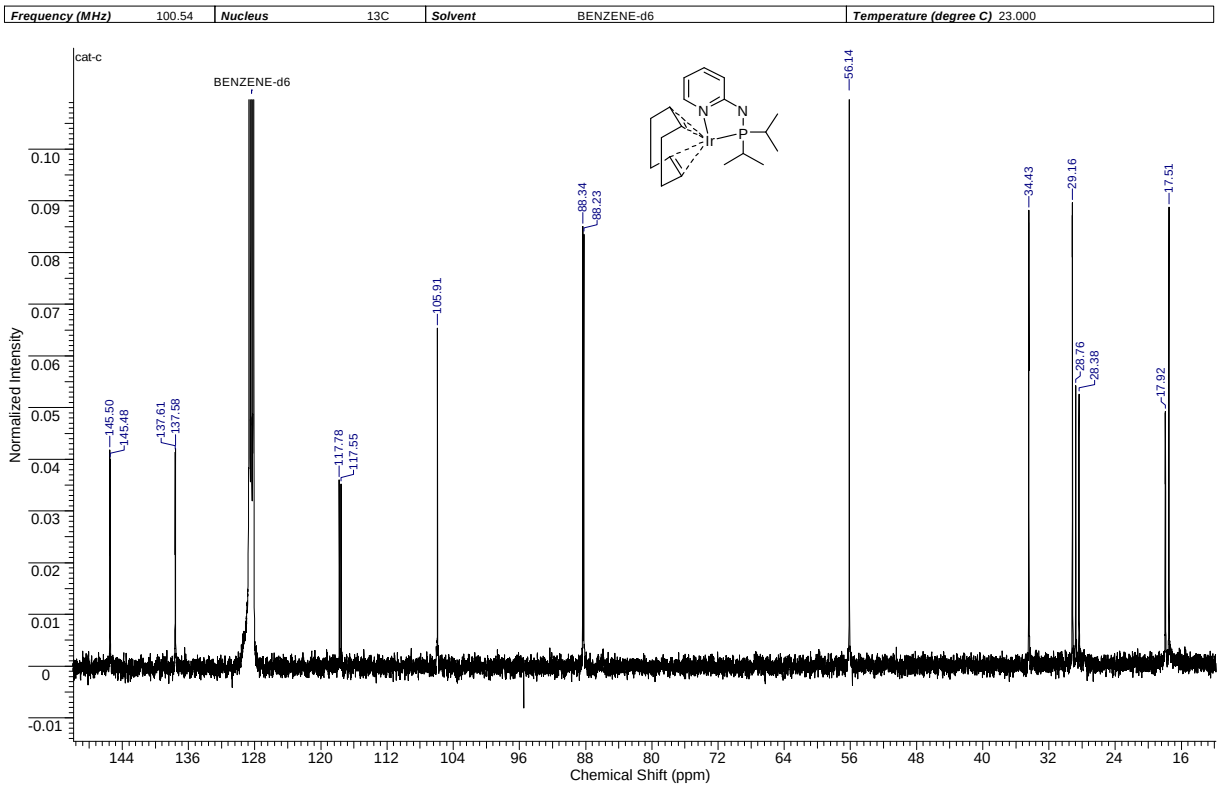
M02(dd)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(t)
M09(m)
M10(d)
M11(d)
Normalized Intensity
Chemical Shift (ppm)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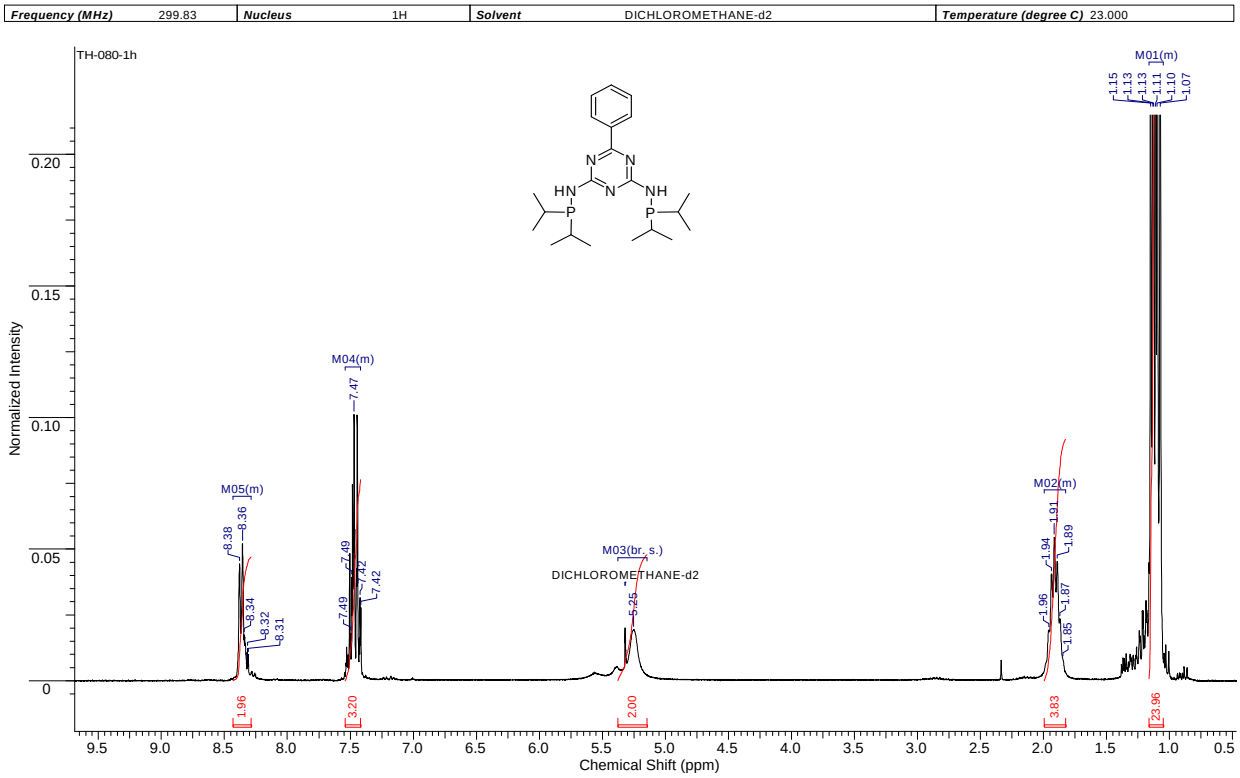
Temperature (degree C) 23.000
cat-c
BENZENE-d6
Normalized Intensity
Chemical Shift (ppm)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Temperature (degree C) 23.000
TH-080-1h
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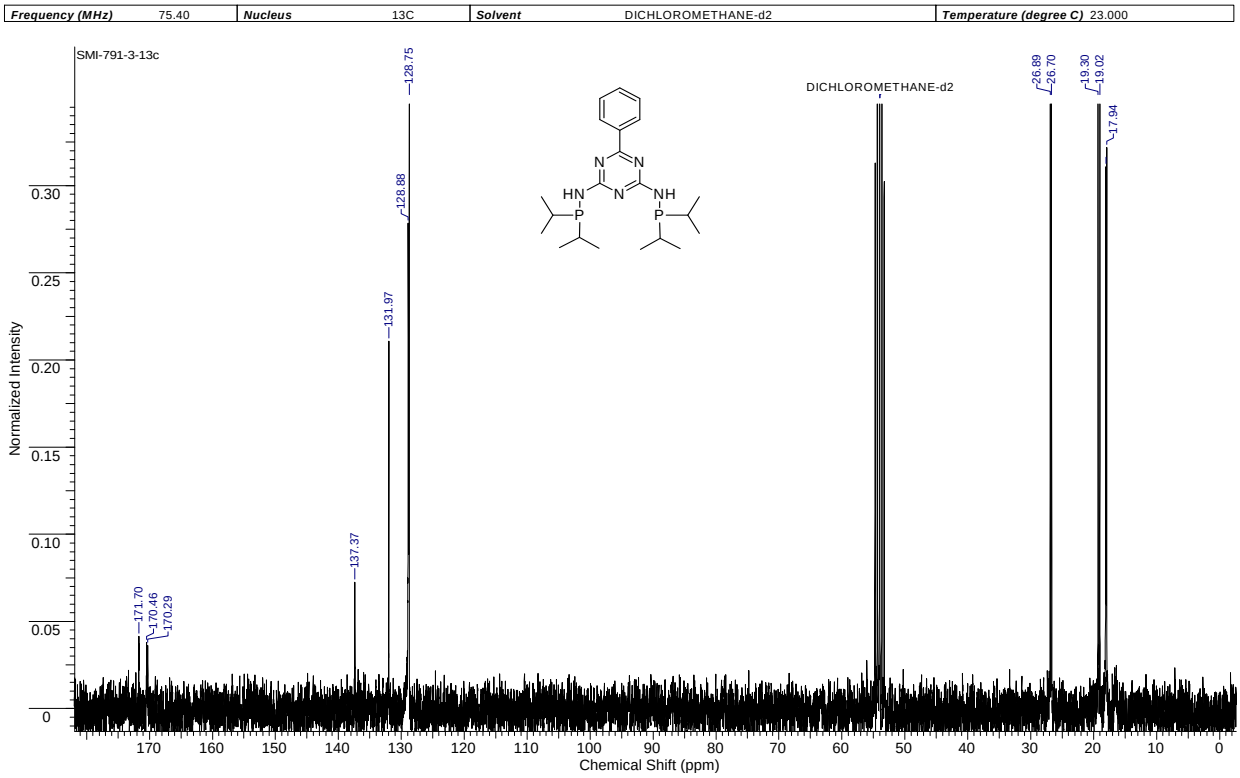
M02(m)
M03(br, s.)
DICHLOROMETHANE-d2
M04(m)
M05(m)
Normalized Intensity
Chemical Shift (ppm)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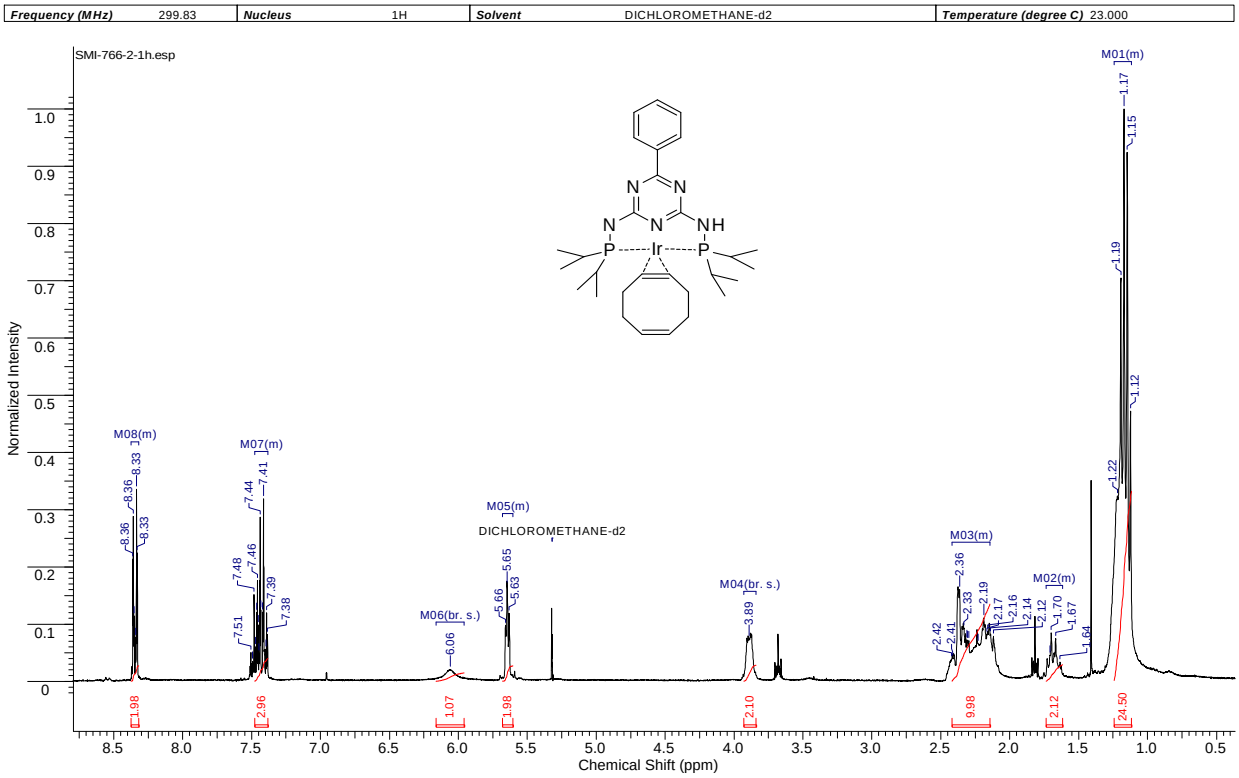
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)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Temperature (degree C) 23.000
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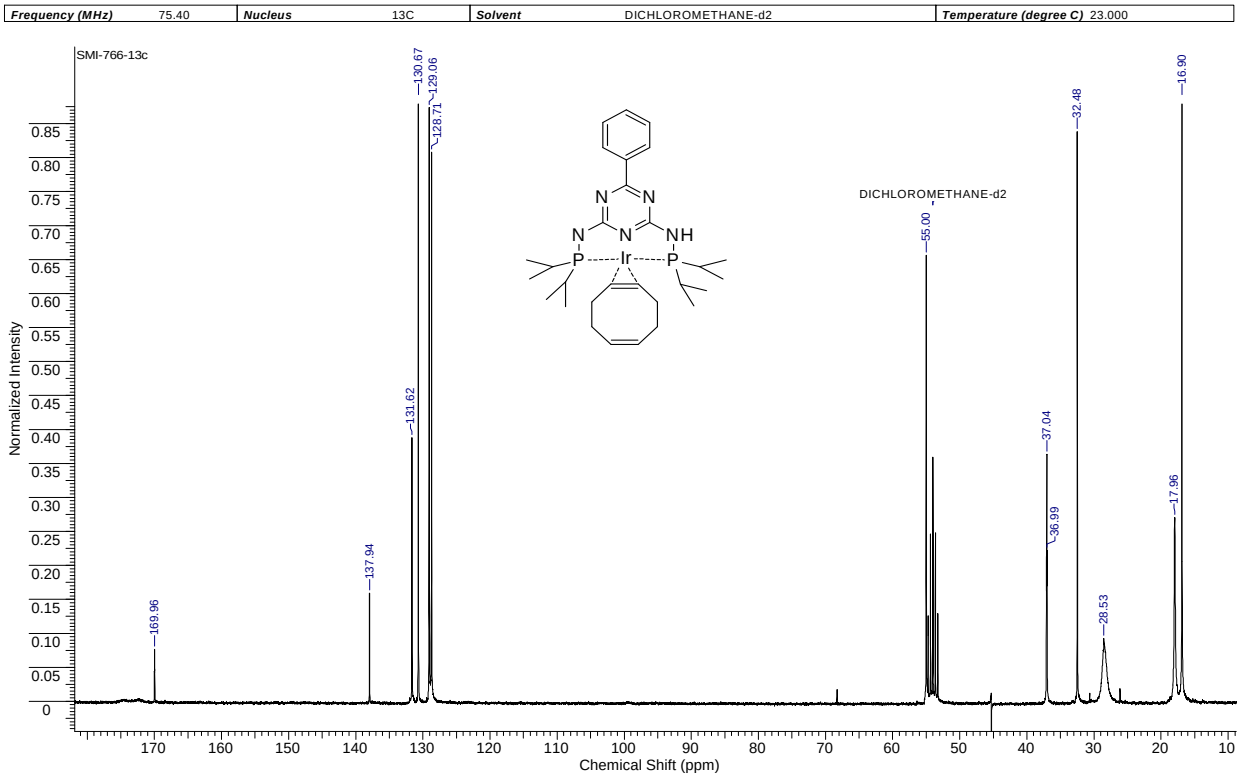
M03(m)
M04(br. s.)
M05(m)
DICHLOROMETHANE-d2
M06(br. s.)
M07(m)
M08(m)
Normalized Intensity
Chemical Shift (ppm)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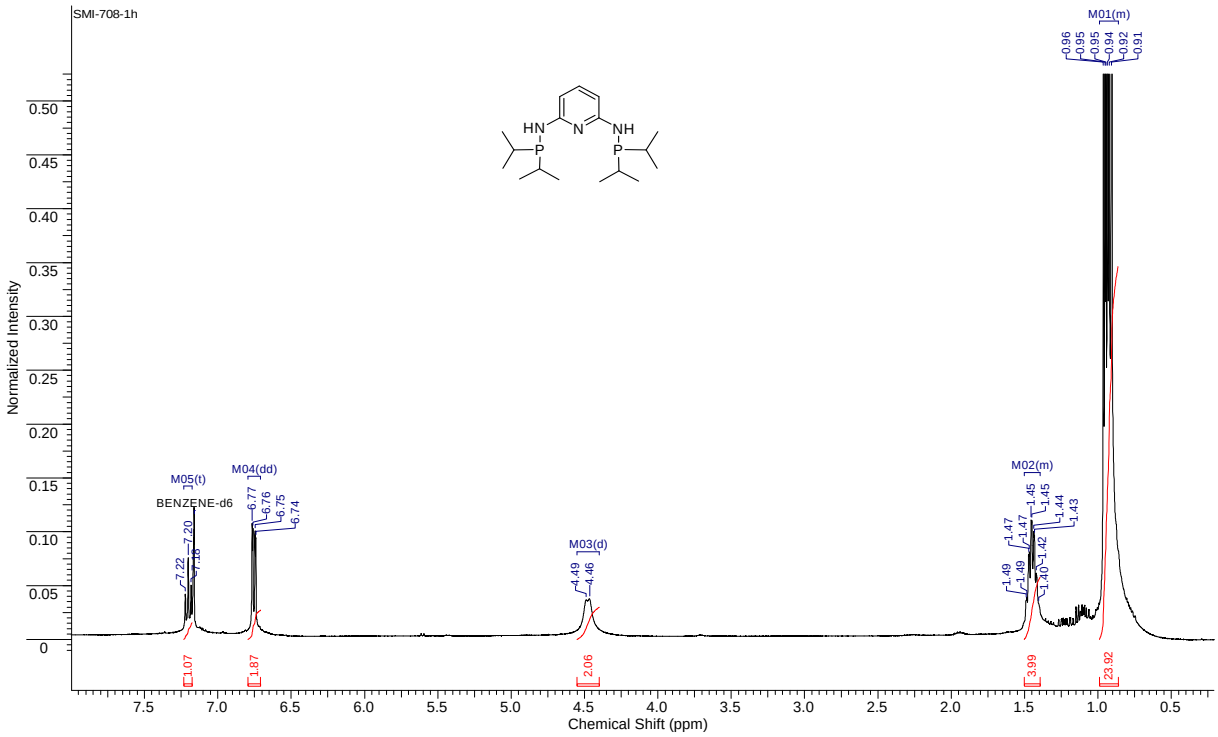
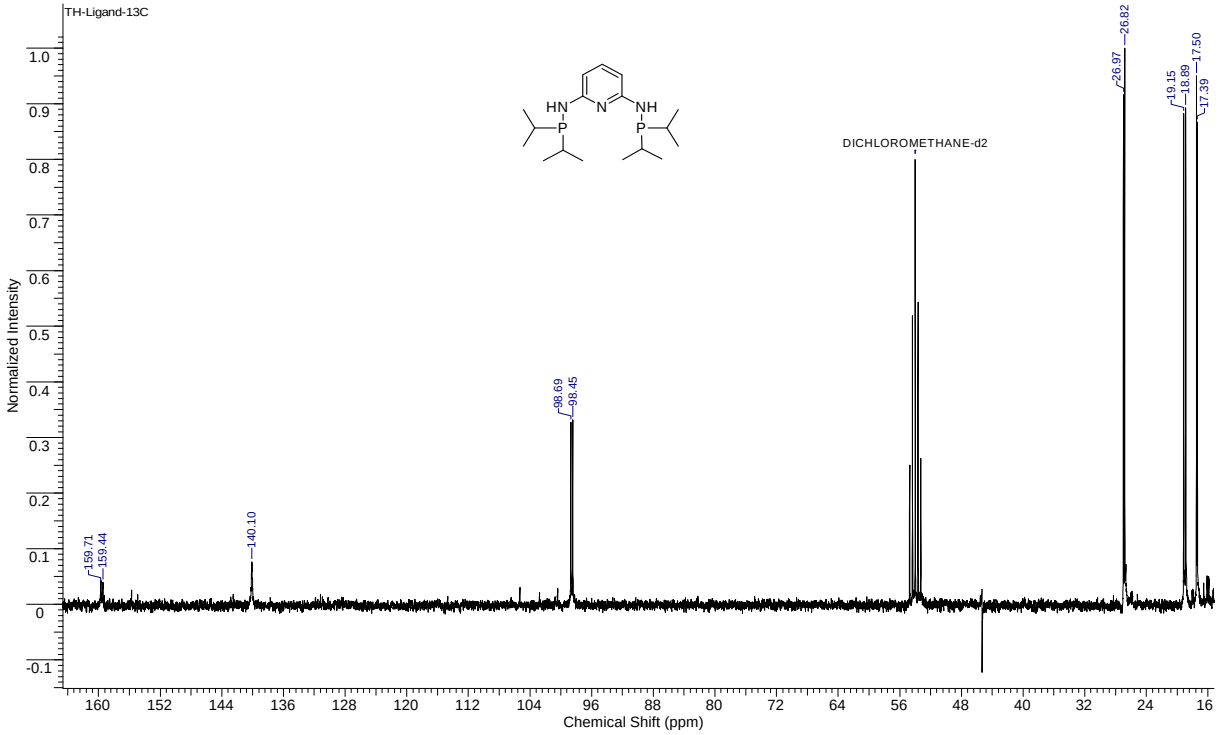
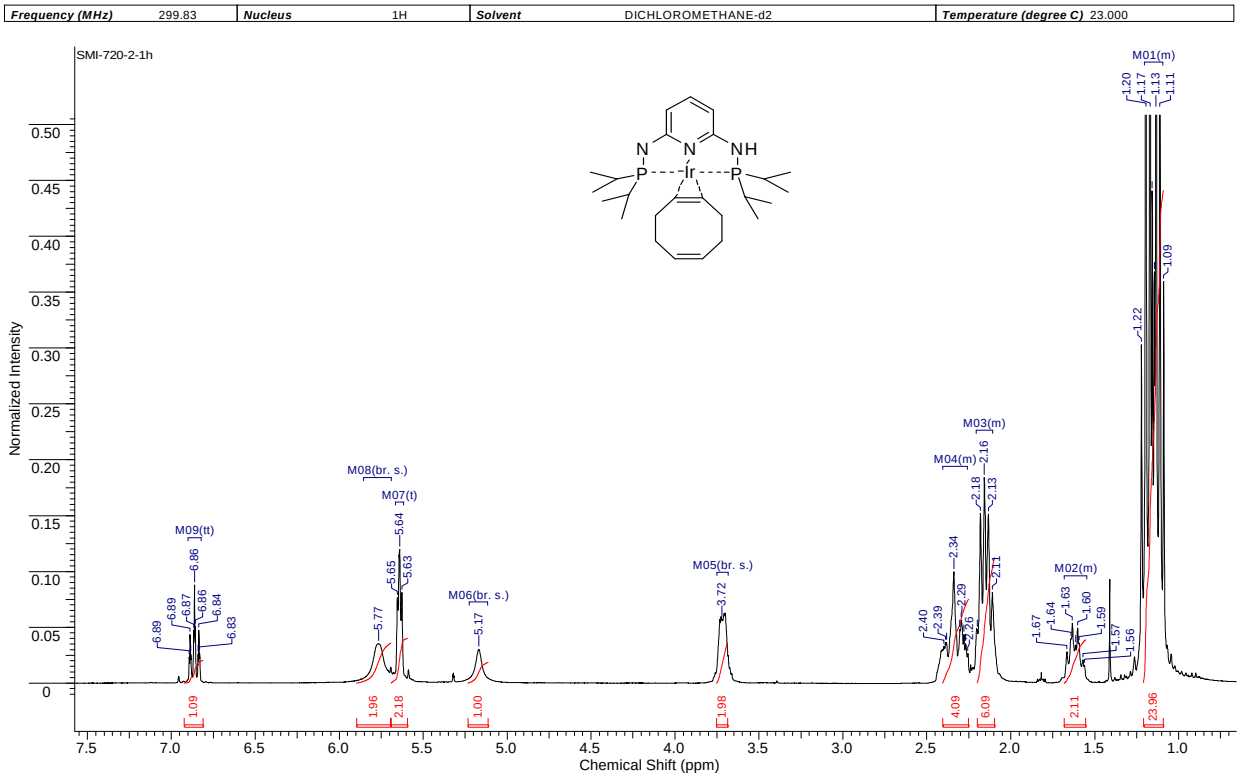
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-766-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

Frequency (MHz)	399.81	Nucleus	1H	Solvent	BENZENE-d6	Temperature (degree C)	23.000



Frequency (MHz)	75.40	Nucleus	13C	Solvent	DICHLOROMETHANE-d2	Temperature (degree C)	23.000

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Chemical Shift (ppm)
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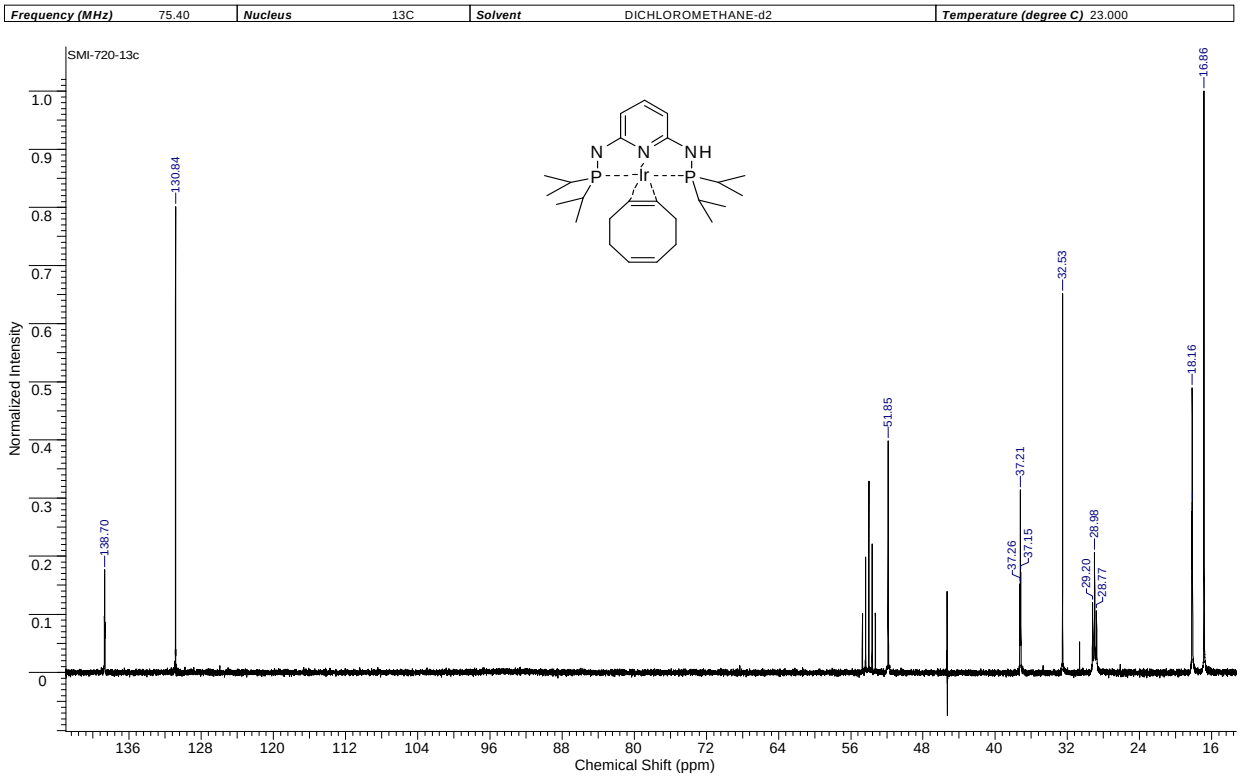
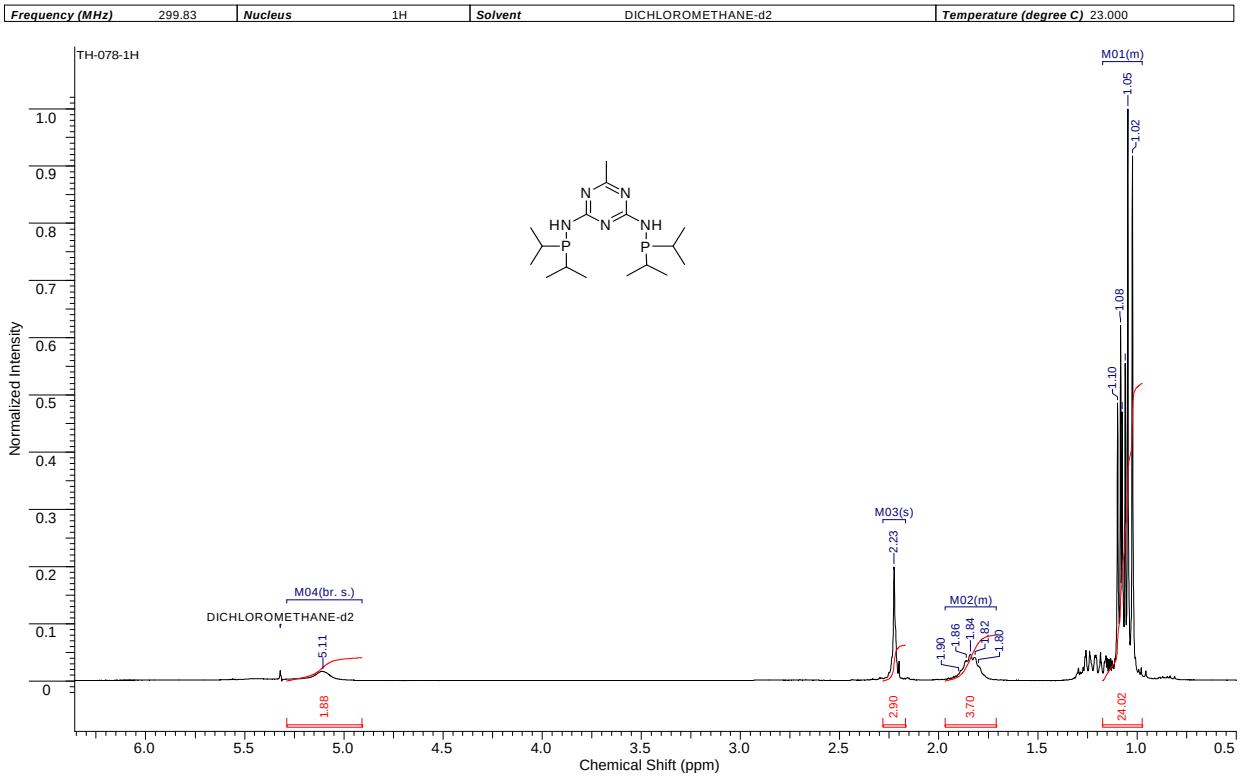
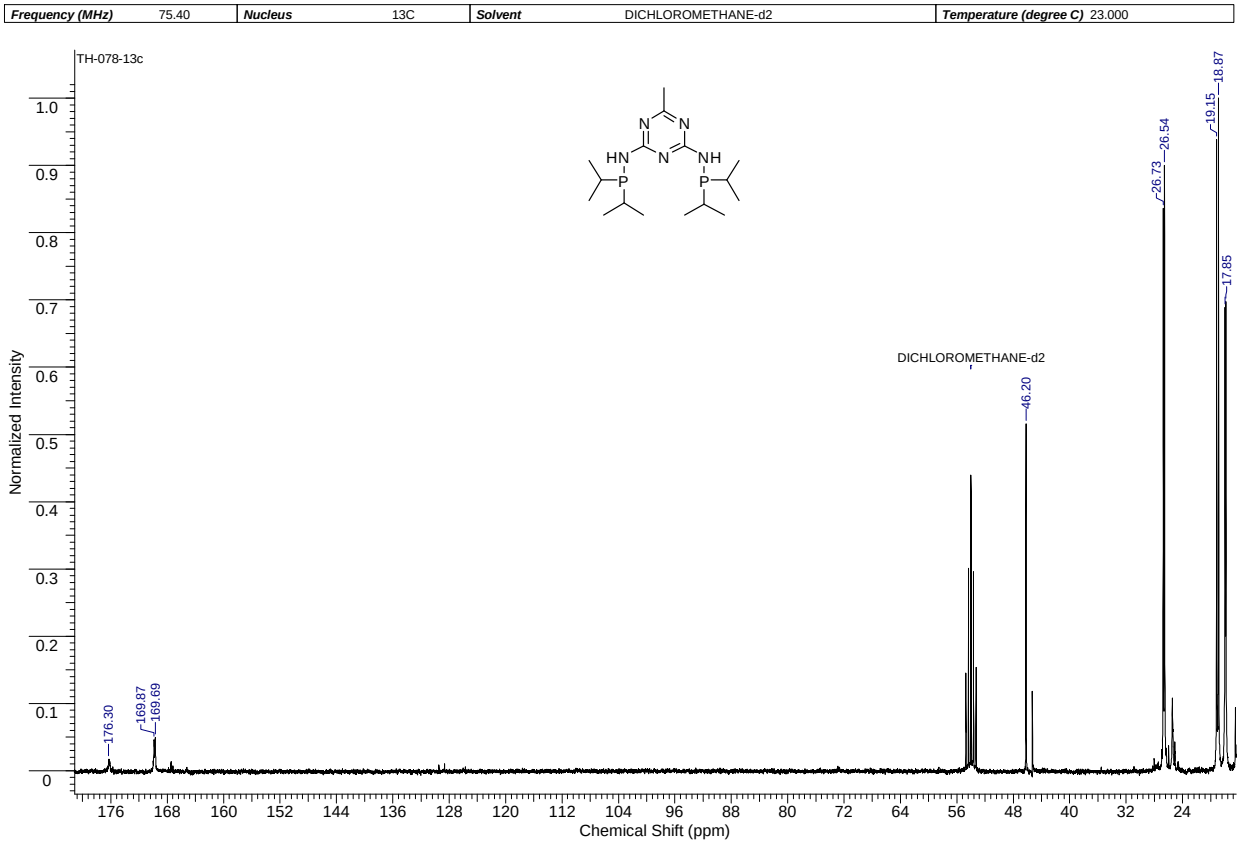
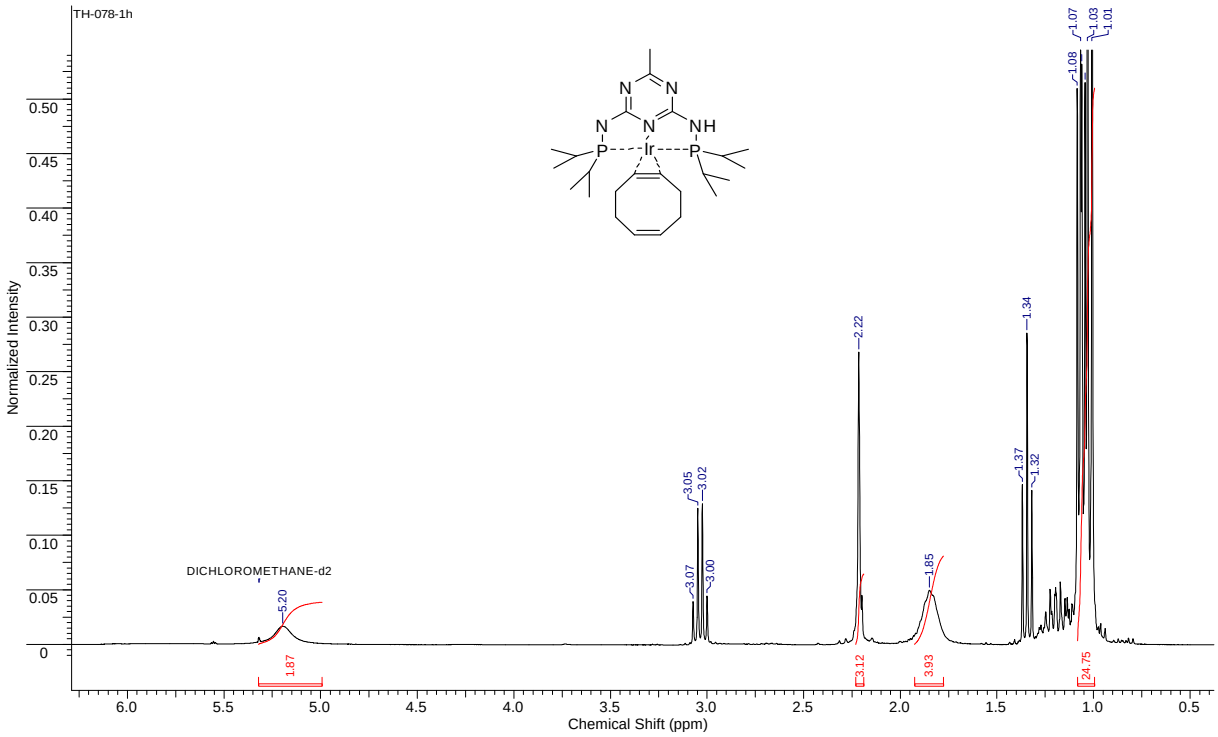
M02(m)
M03(m)
M04(m)
M05(br. s.)
M06(br. s.)
M07(t)
M08(br. s.)
M09(tt)


Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-720-13c
Normalized Intensity
Chemical Shift (ppm)

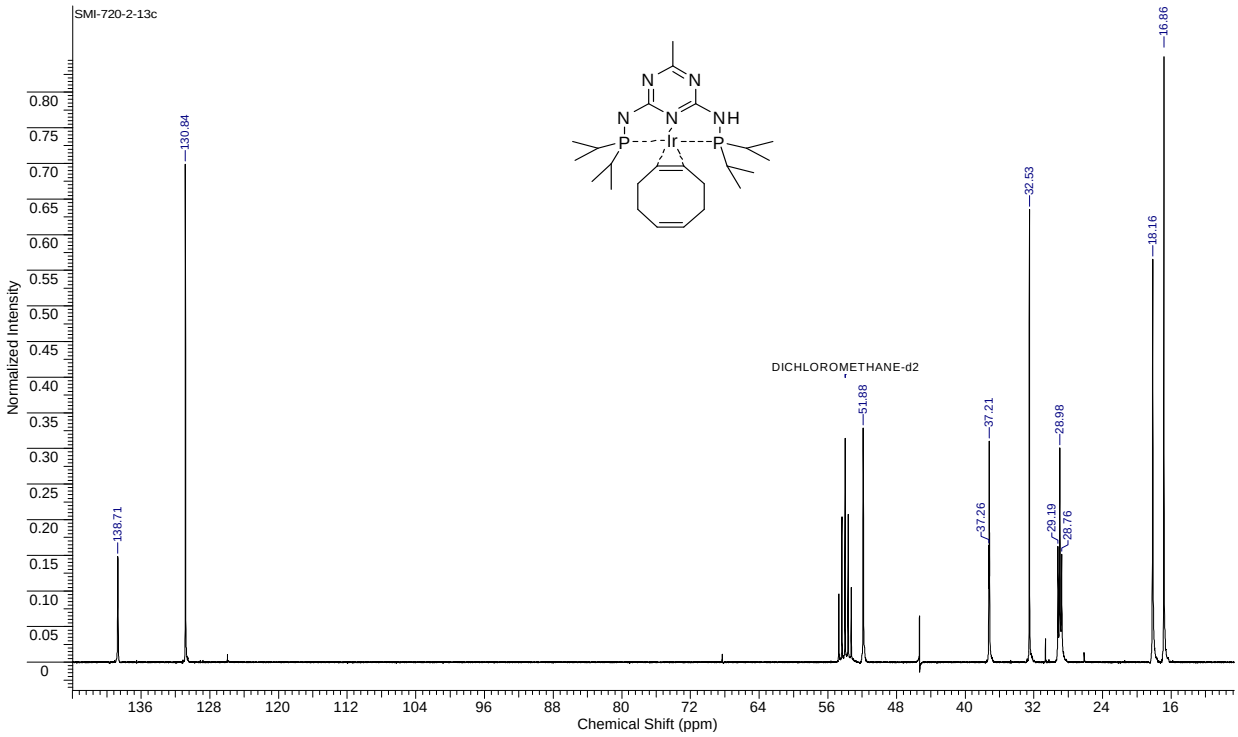

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-078-1H
M01(m)
1.05
1.02
1.08
1.10
M03(s)
2.23
M04(br. s.)
DICHLOROMETHANE-d2
5.11
M02(m)
1.90
1.86
1.84
1.82
1.80
1.88
2.90
3.70
24.02
Normalized Intensity
Chemical Shift (ppm)

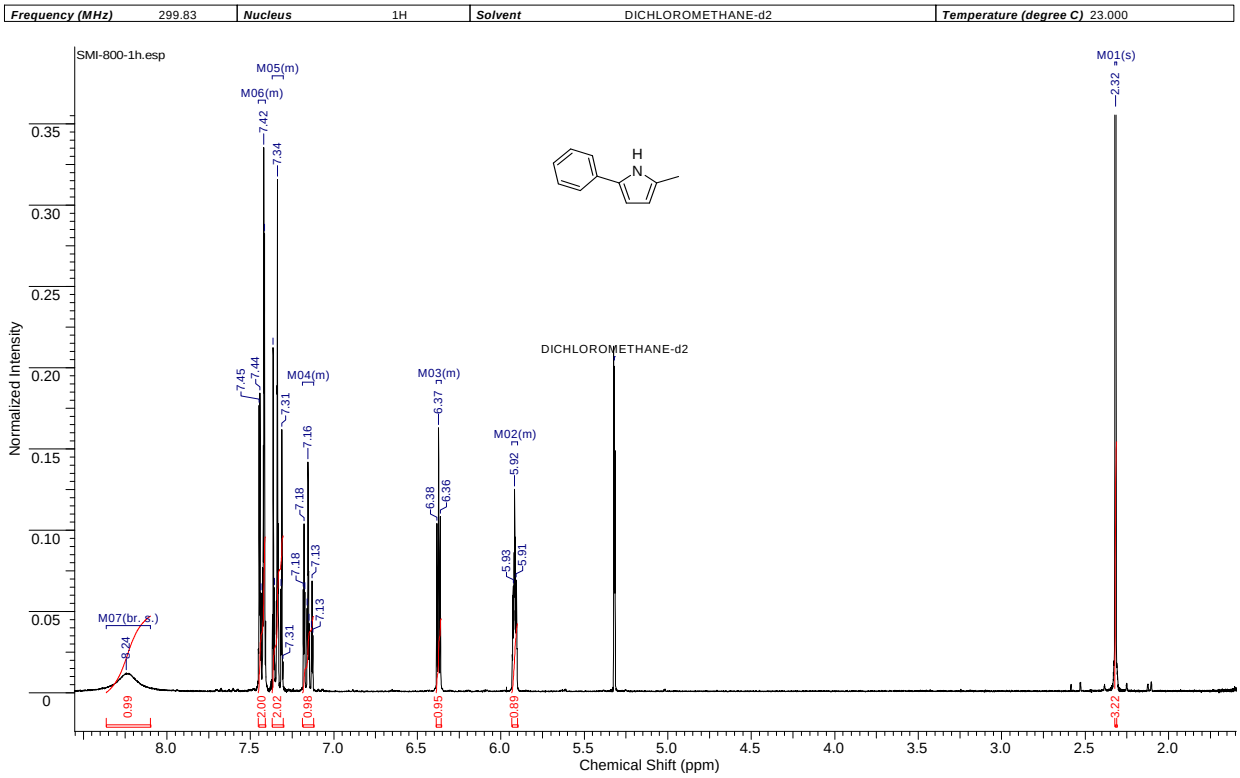

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
TH-078-13c
18.87
19.15
26.54
26.73
17.85
DICHLOROMETHANE-d2
46.20
176.30
169.87
169.69
Normalized Intensity
Chemical Shift (ppm)

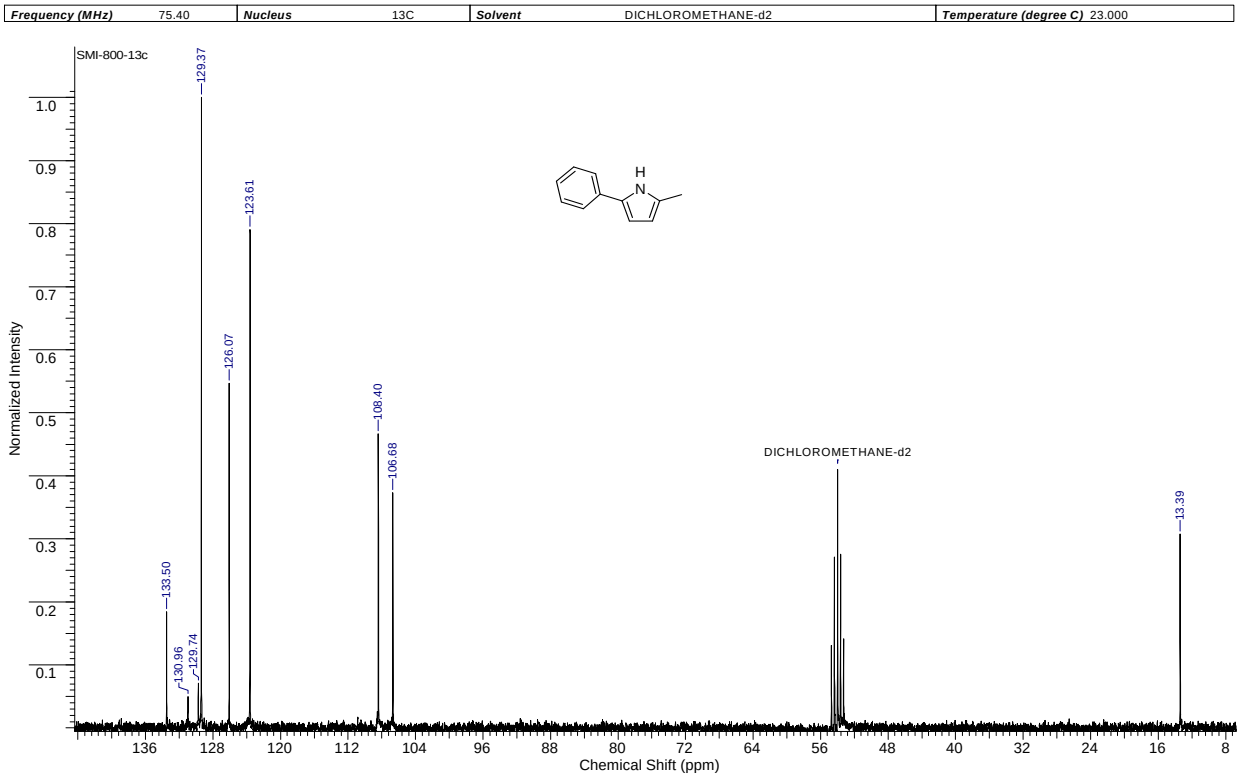
Frequency (MHz)	299.83	Nucleus	1H	Solvent	DICHLOROMETHANE-d2	Temperature (degree C)	23.000

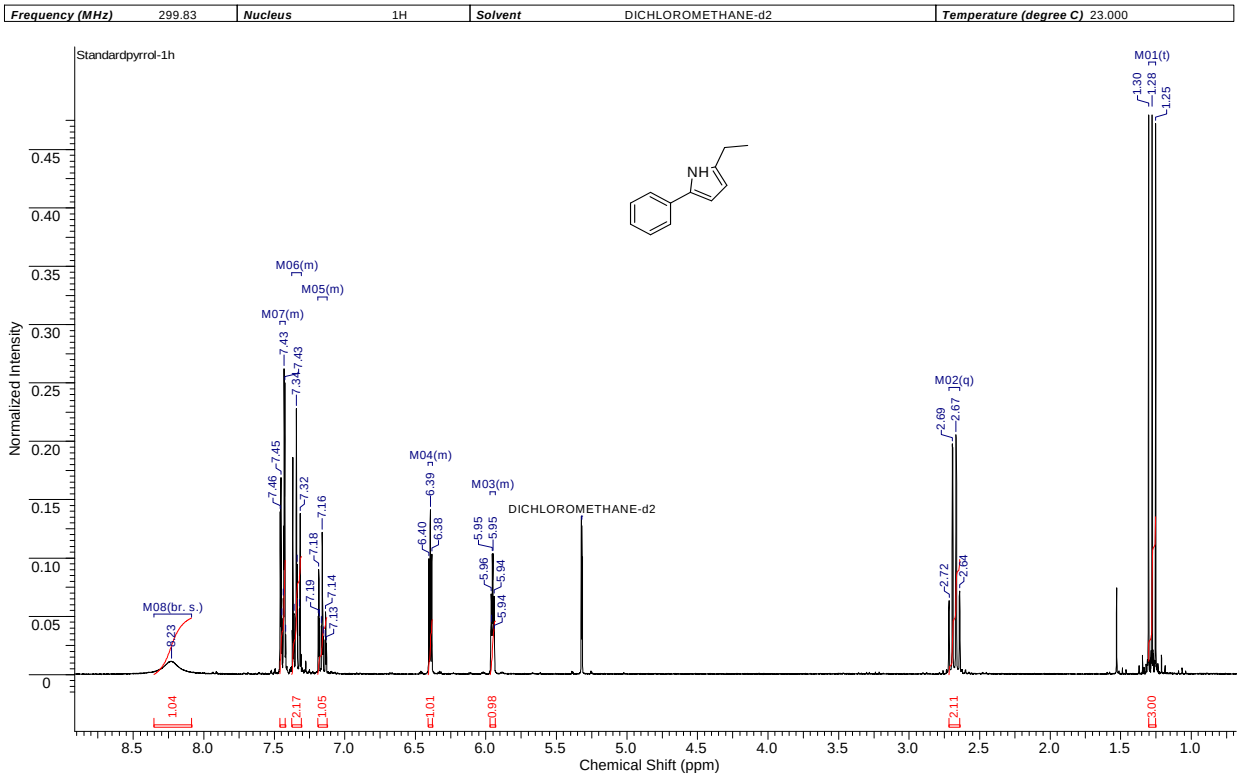


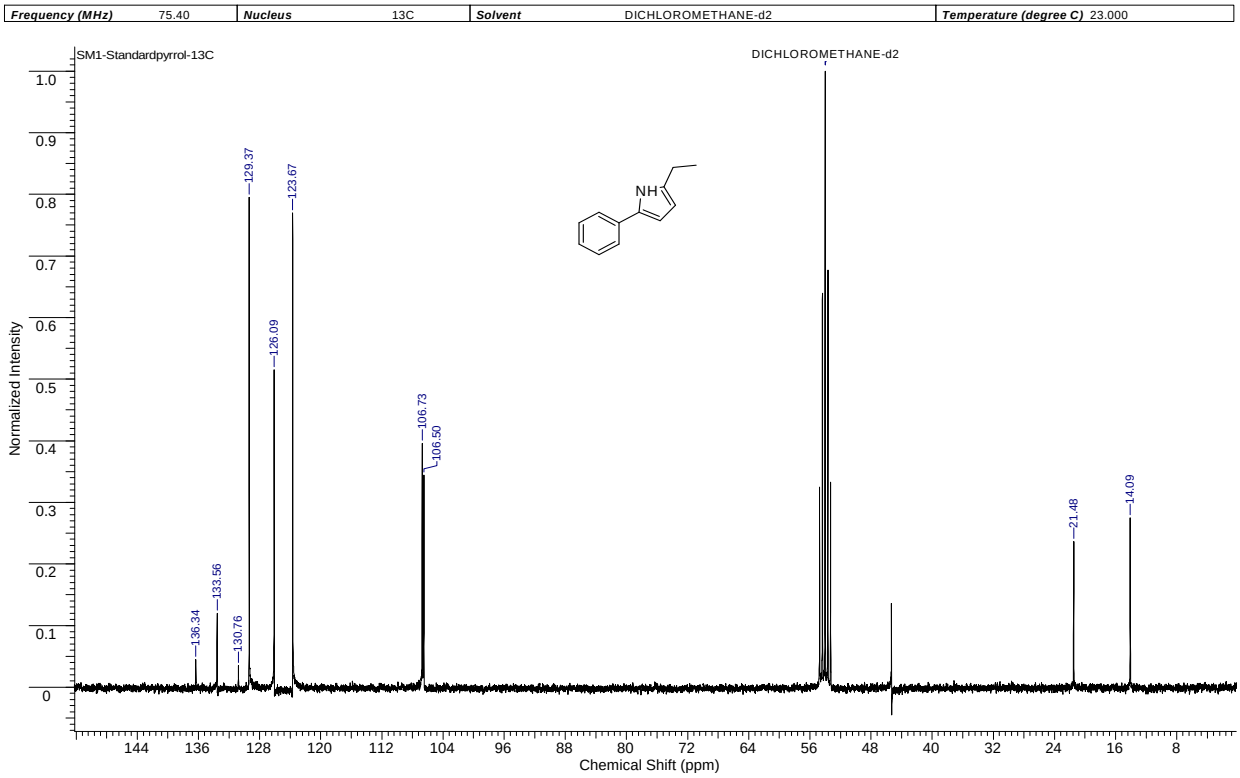
Frequency (MHz)	75.40	Nucleus	13C	Solvent	DICHLOROMETHANE-d2	Temperature (degree C)	23.000

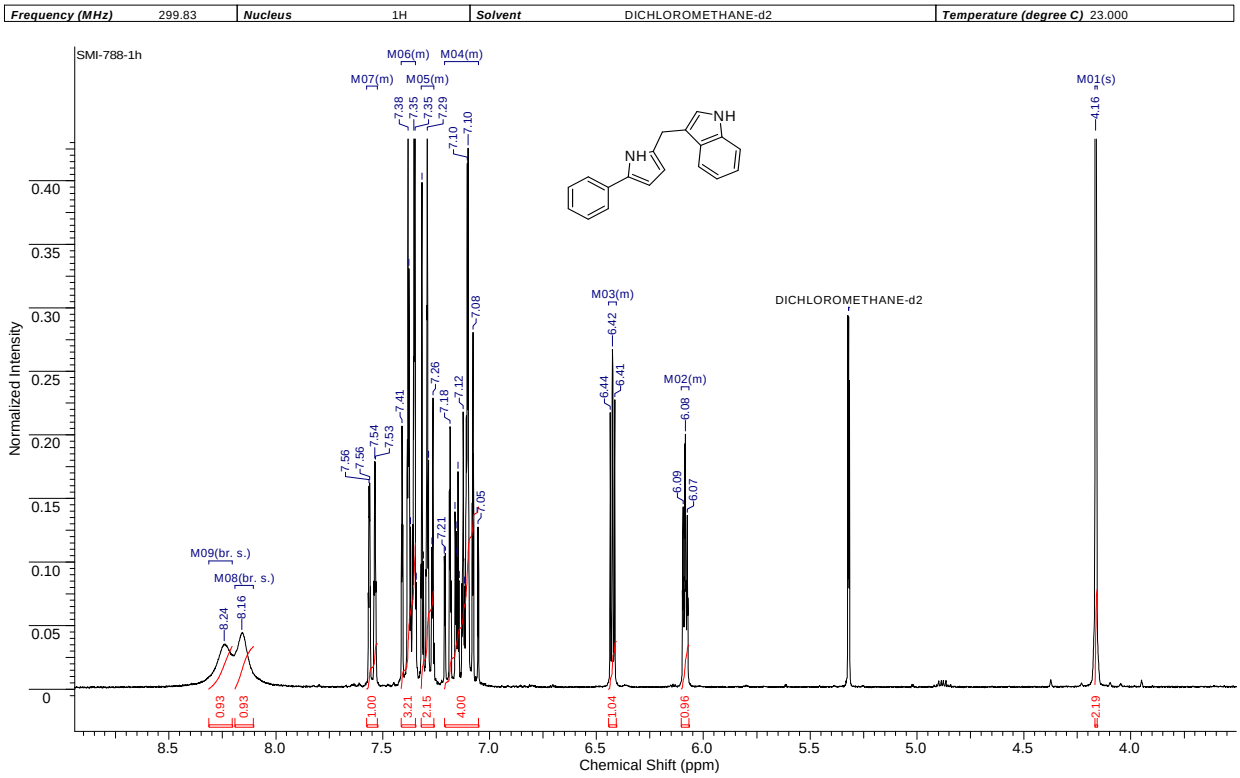


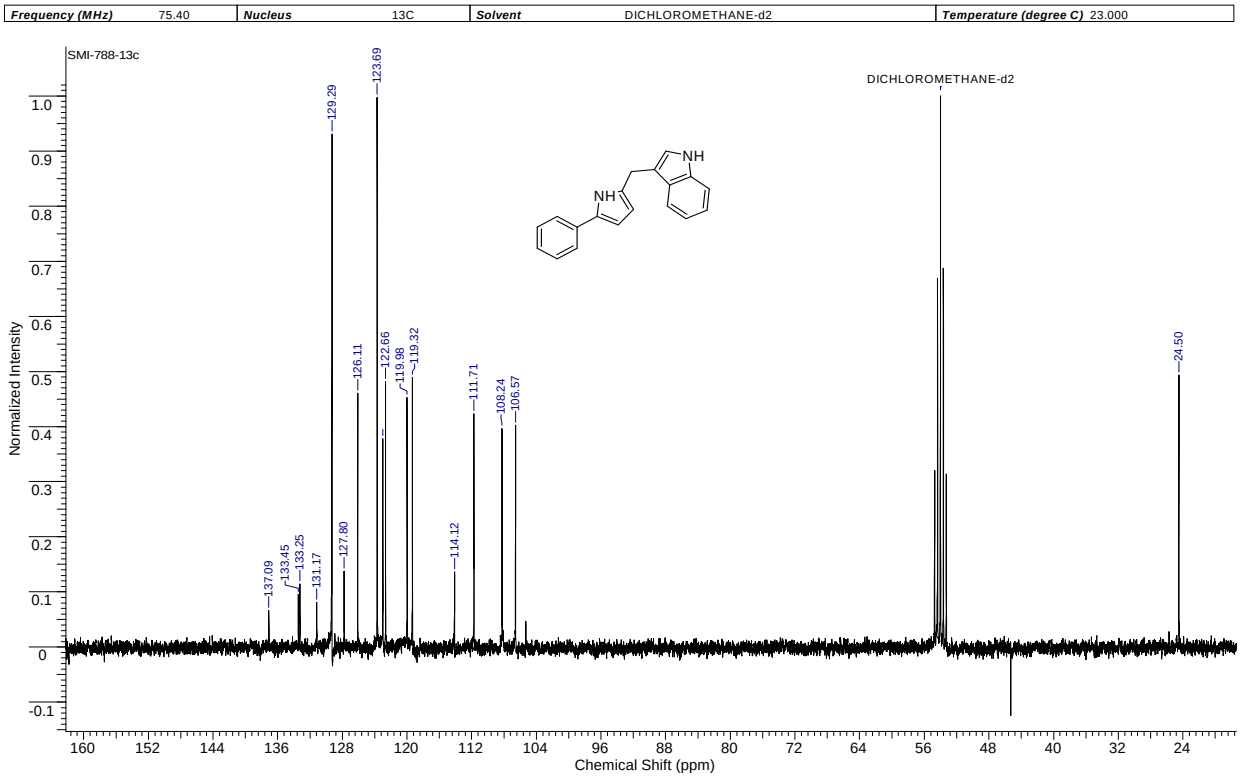

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-800-1h.esp
M05(m)
M06(m)
M01(s)
M04(m)
M03(m)
M02(m)
M07(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

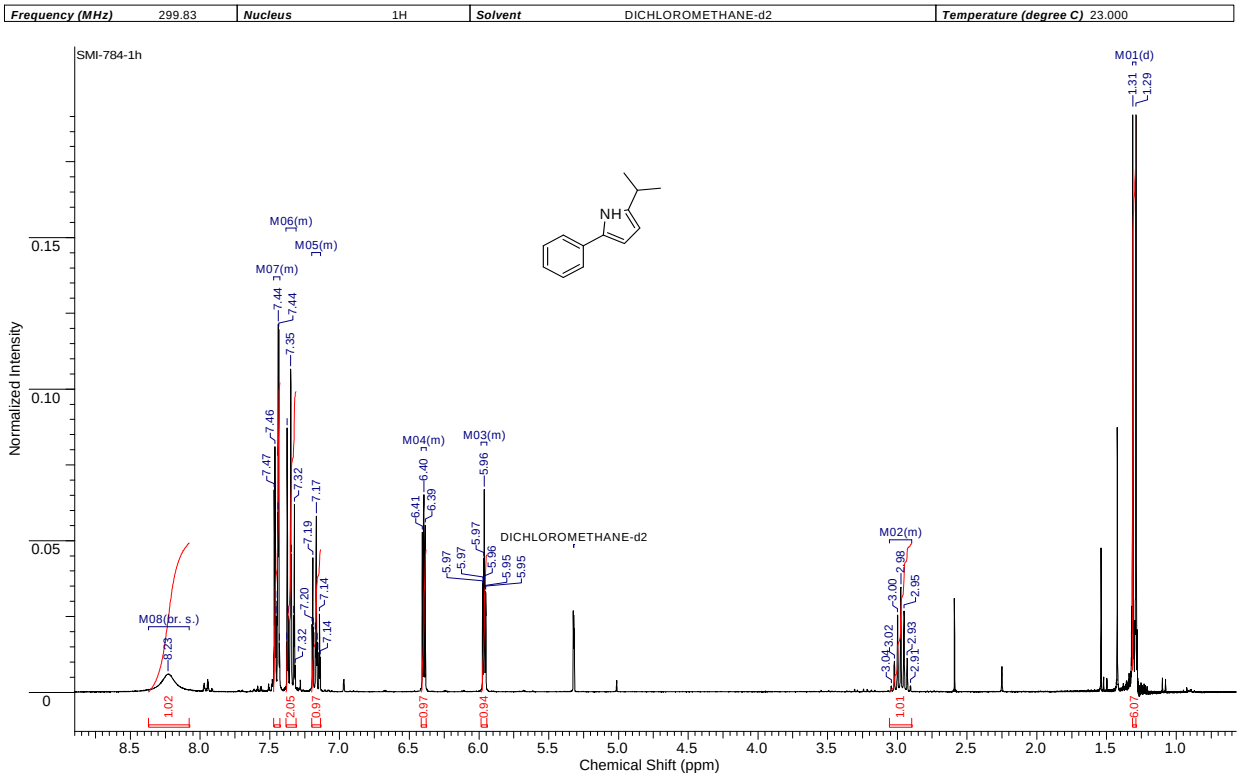

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-800-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

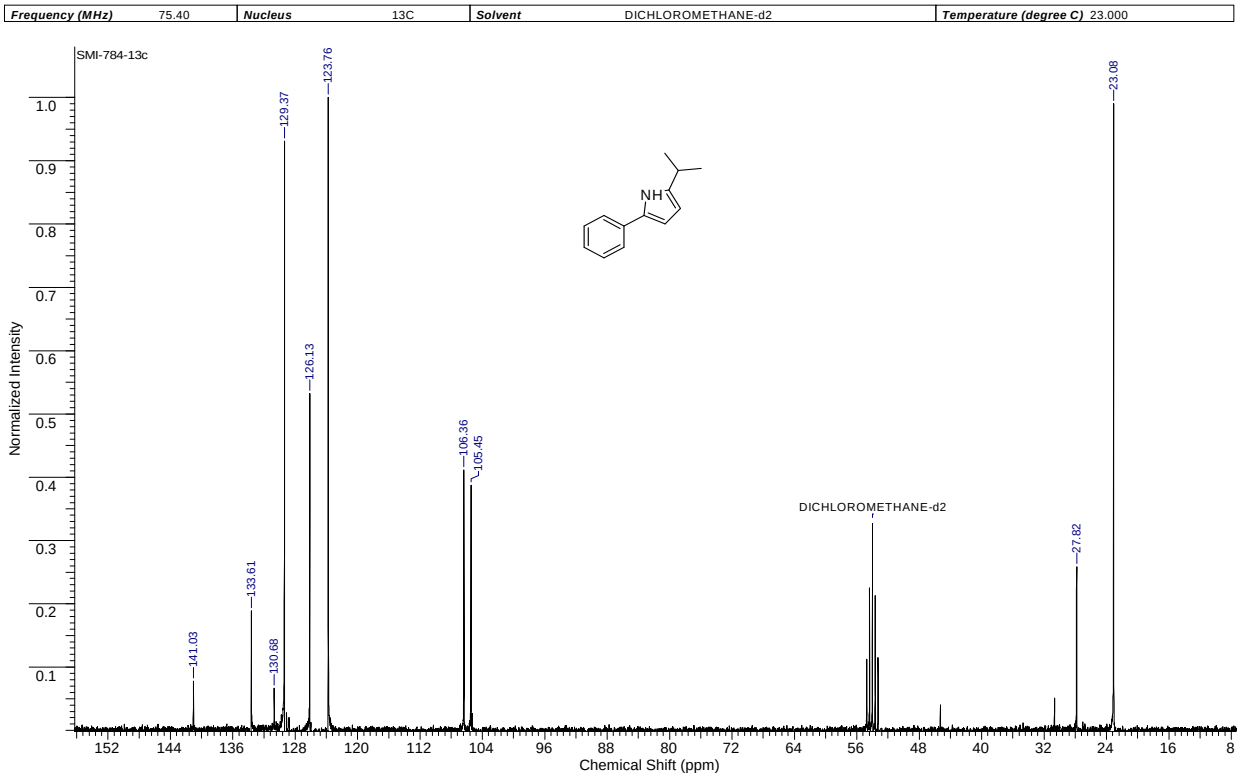

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
Standardpyrrol-1h
Normalized Intensity
Chemical Shift (ppm)
M01(t)
M02(q)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(br. s.)
DICHLOROMETHANE-d2
NH

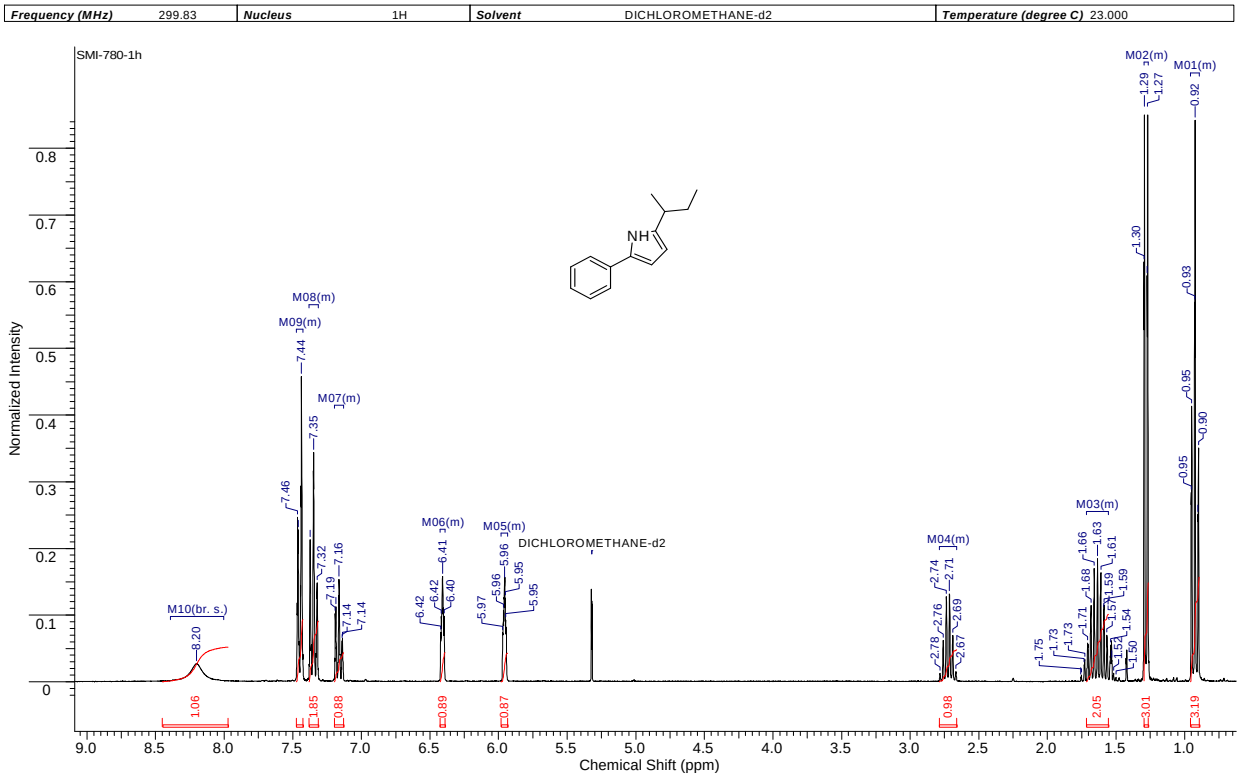

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SM1-Standardpyrrol-13C
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
NH

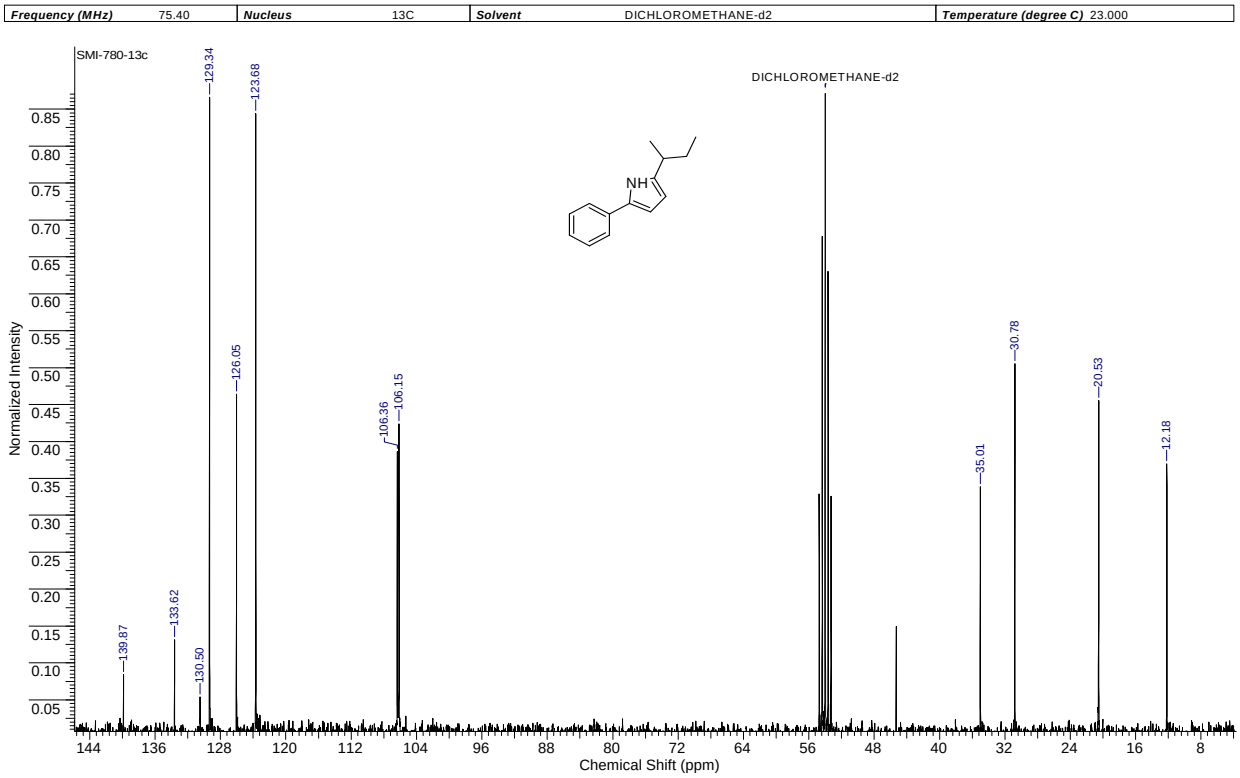

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-788-1h
M06(m) M04(m)
M07(m) M05(m)
M01(s)
M03(m)
M02(m)
M09(br, s.)
M08(br, s.)
DICHLOROMETHANE-d2
NH
NH
Normalized Intensity
Chemical Shift (ppm)

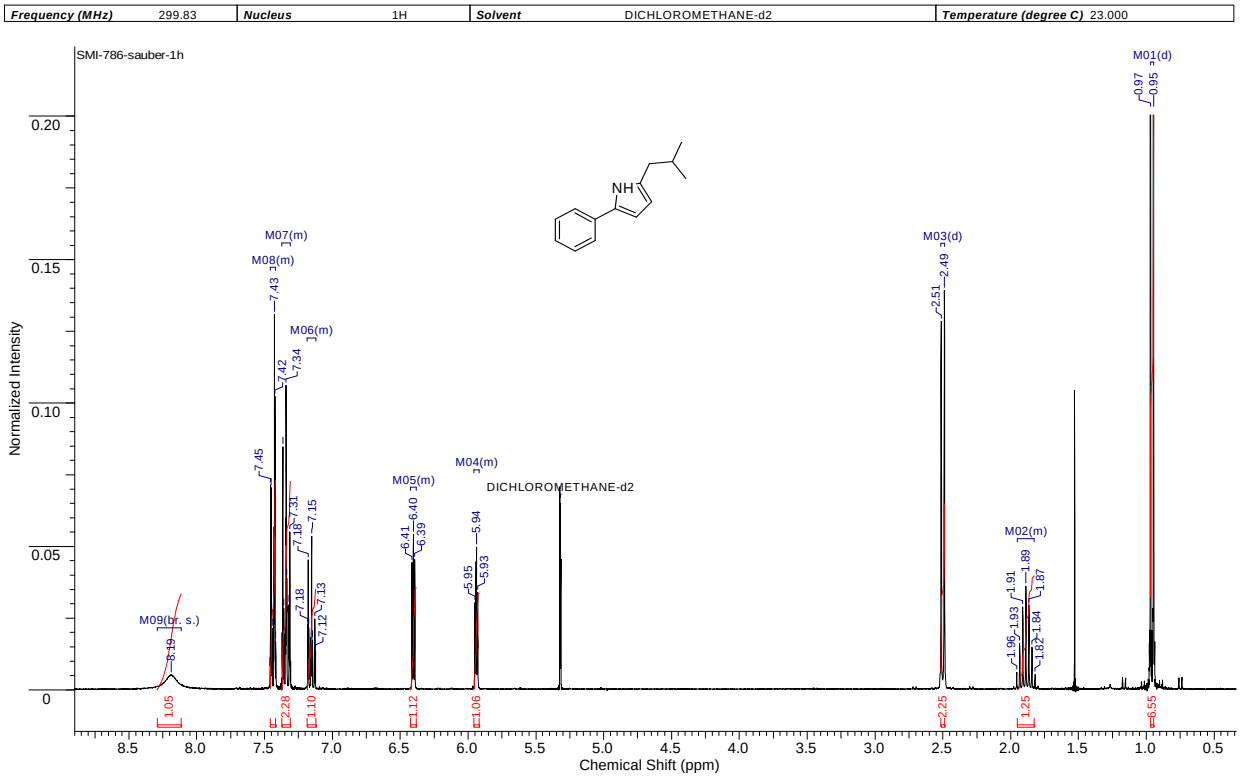

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-788-13c
DICHLOROMETHANE-d2
NH
NH
Normalized Intensity
Chemical Shift (ppm)

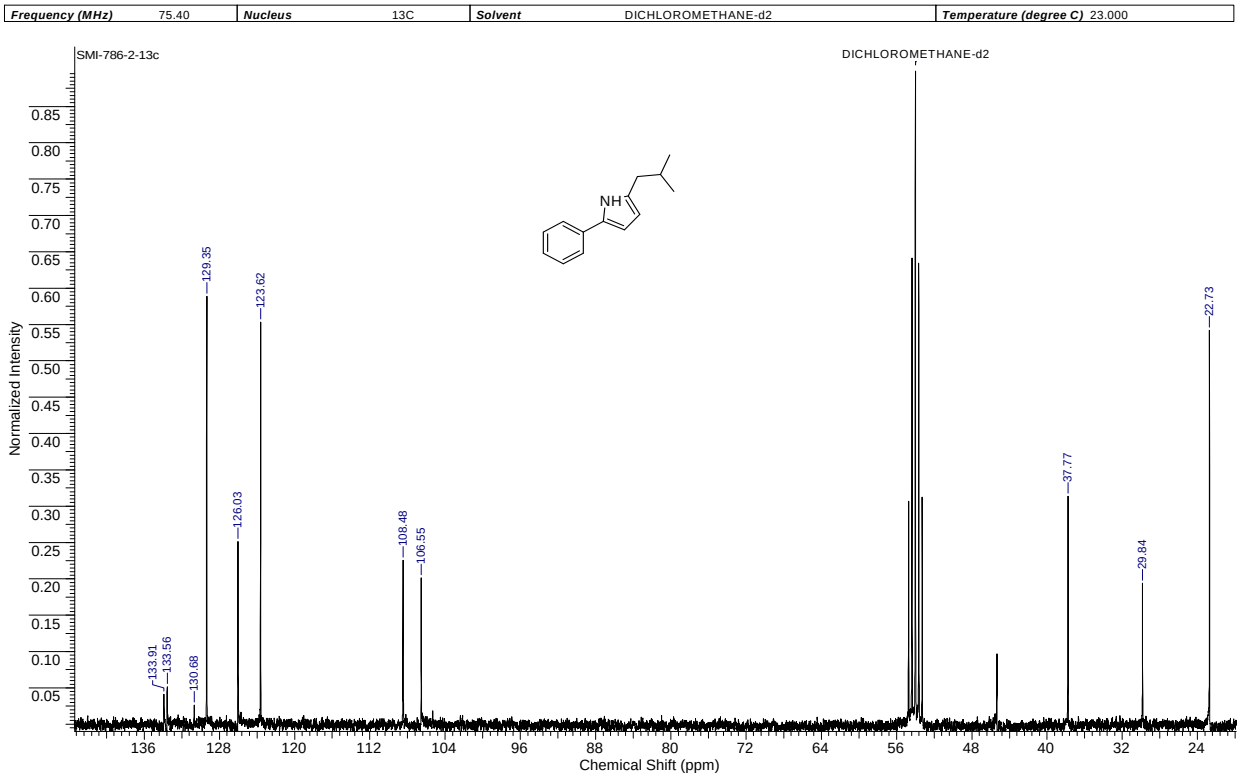

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-784-1h
Normalized Intensity
Chemical Shift (ppm)
M01(d)
M02(m)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(br. s.)
DICHLOROMETHANE-d2
NH

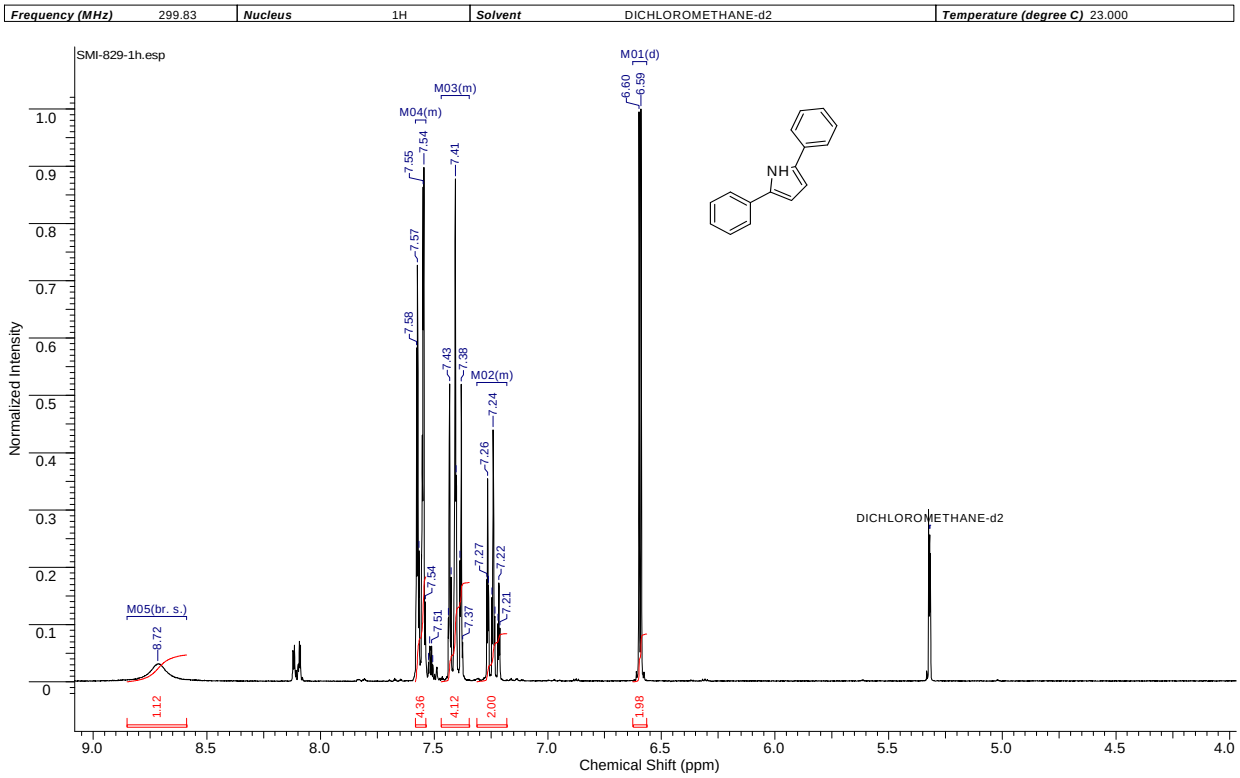

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-784-13c
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
NH

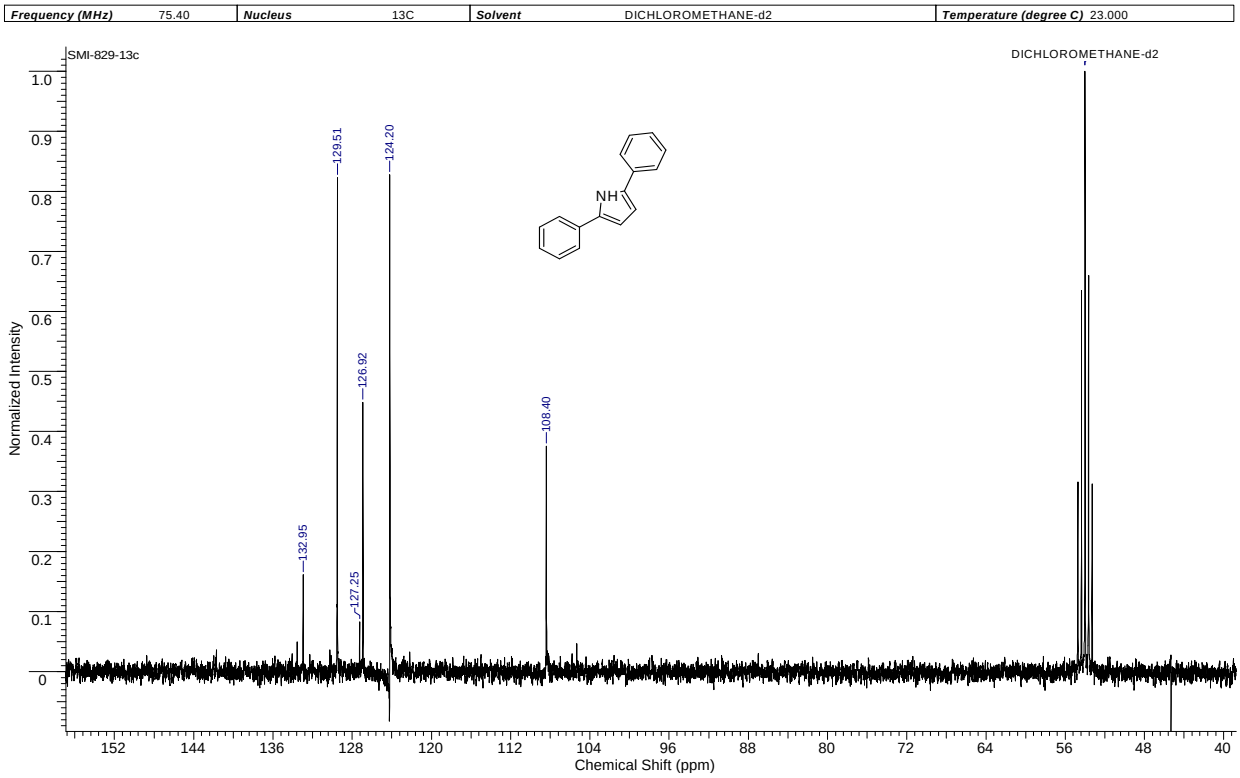

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-780-1h
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
M01(m)
M02(m)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(m)
M09(m)
M10(br. s.)
NH

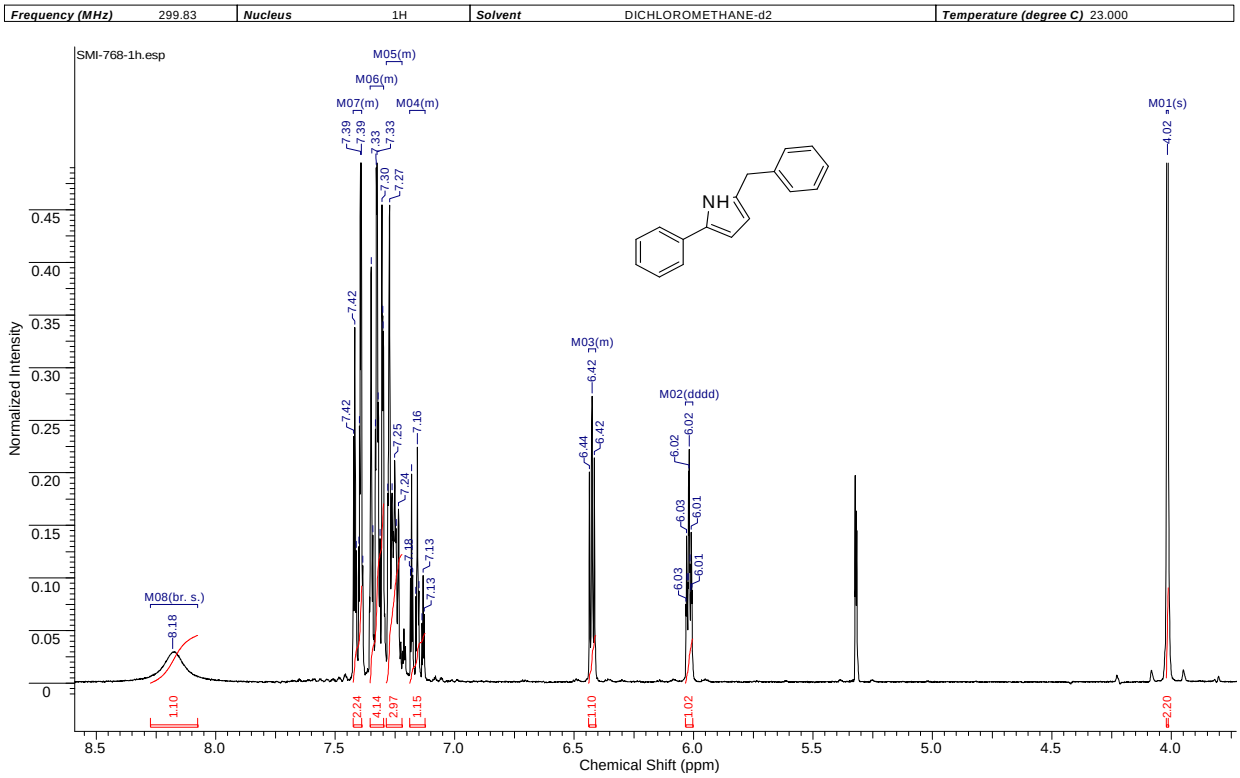

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-780-13c
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
NH

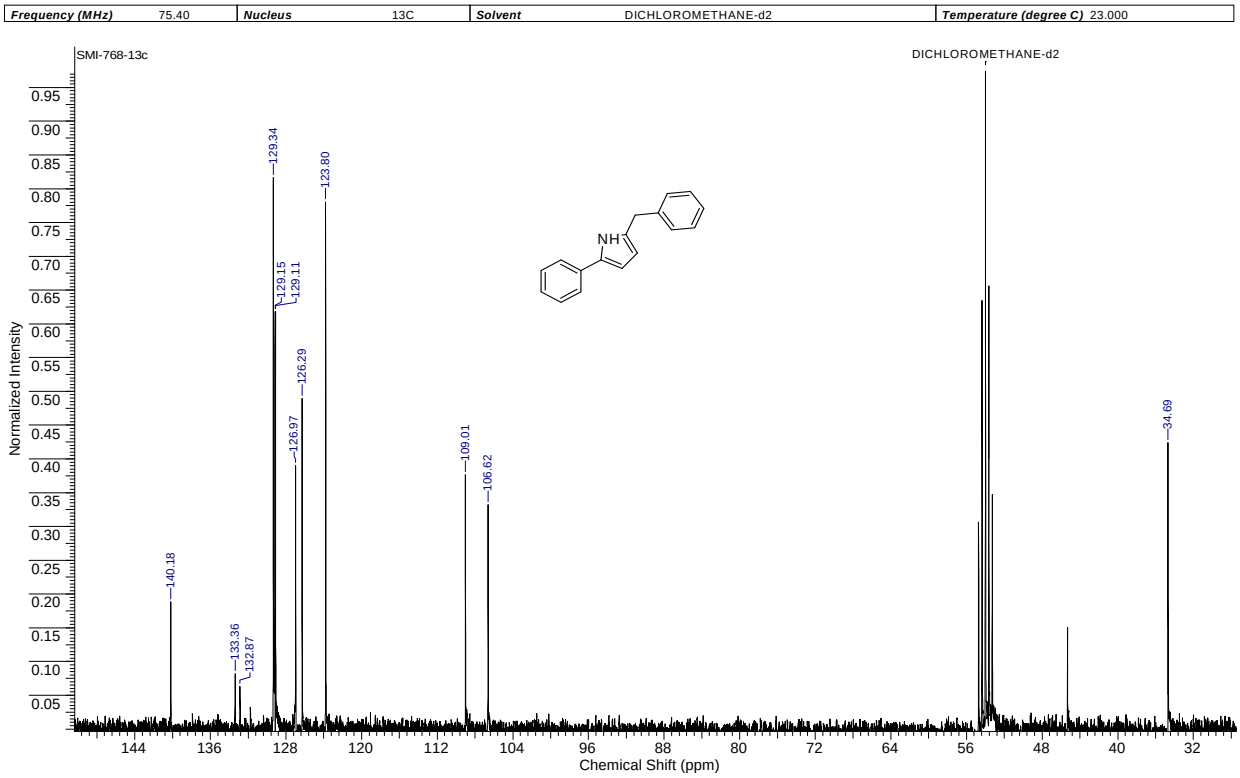

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-786-sauber-1h
Normalized Intensity
Chemical Shift (ppm)
M01(d)
M02(m)
M03(d)
M04(m)
M05(m)
M06(m)
M07(m)
M08(m)
M09(br, s.)
DICHLOROMETHANE-d2
NH

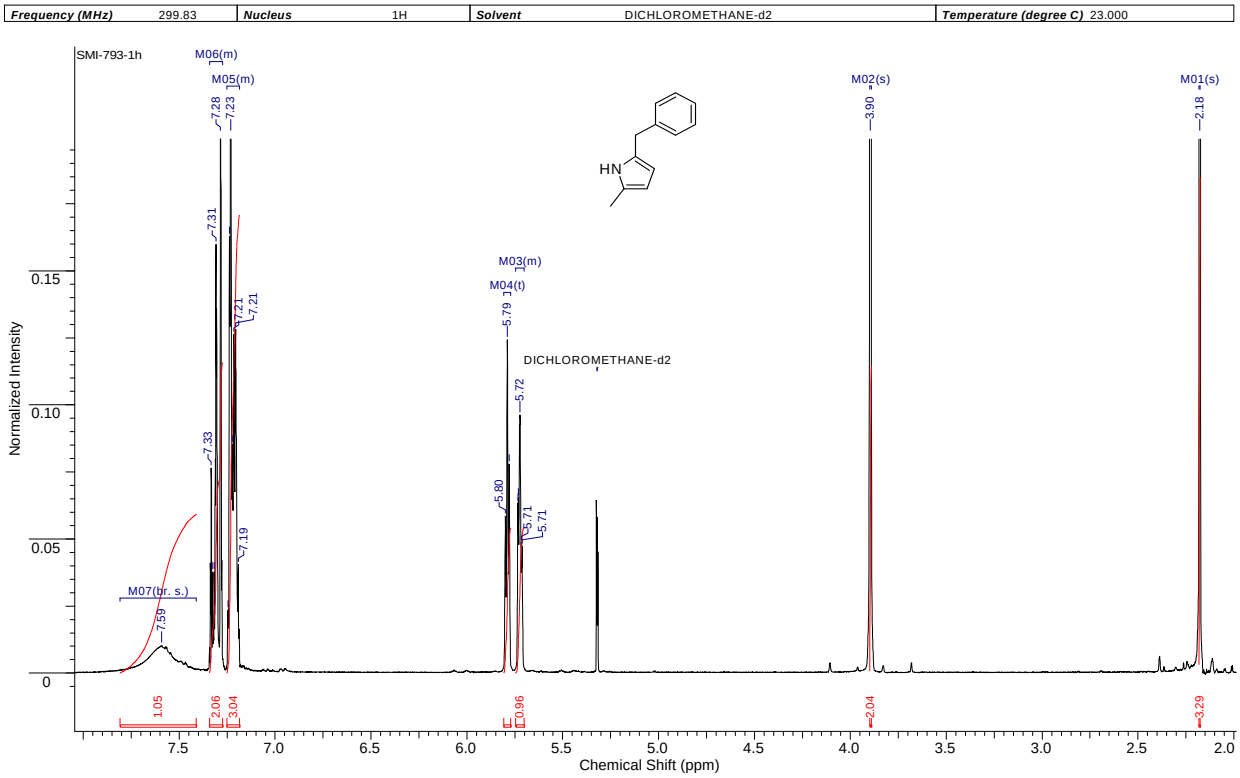

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-786-2-13c
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
NH

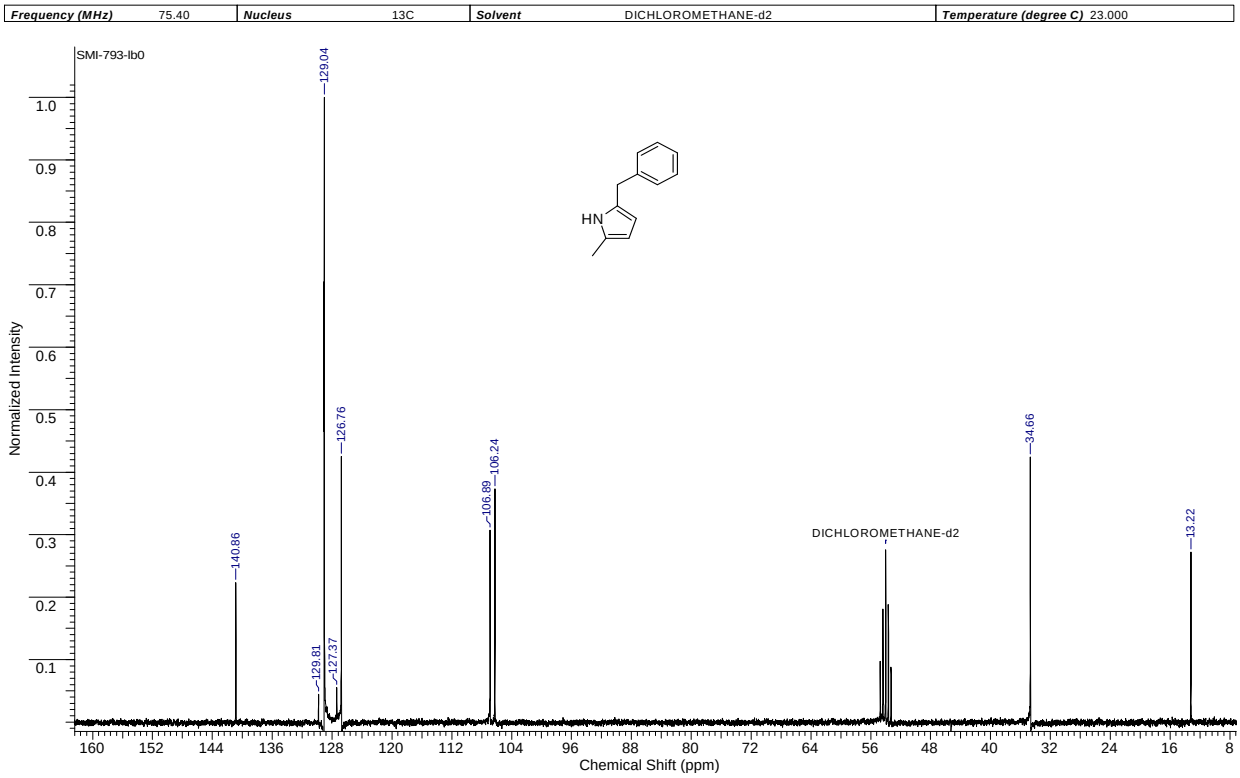

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-829-1h.esp
M01(d)
M02(m)
M03(m)
M04(m)
M05(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

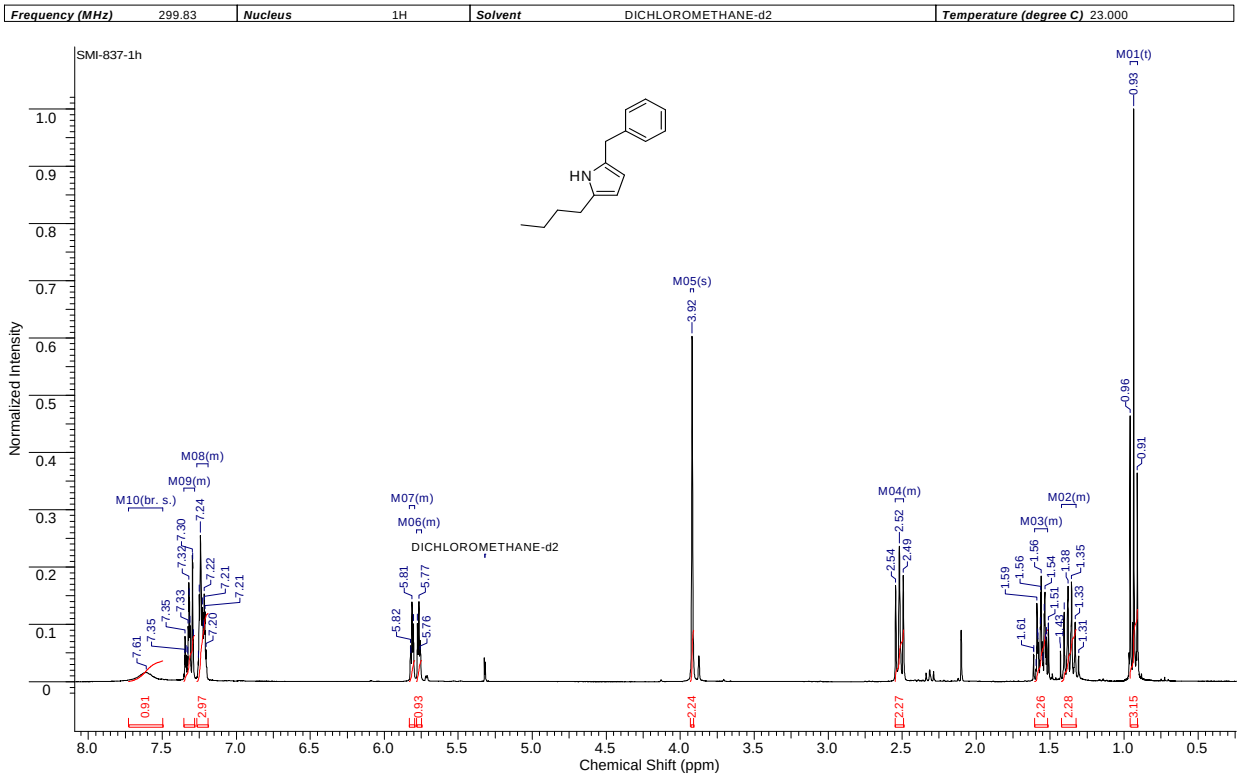

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-829-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

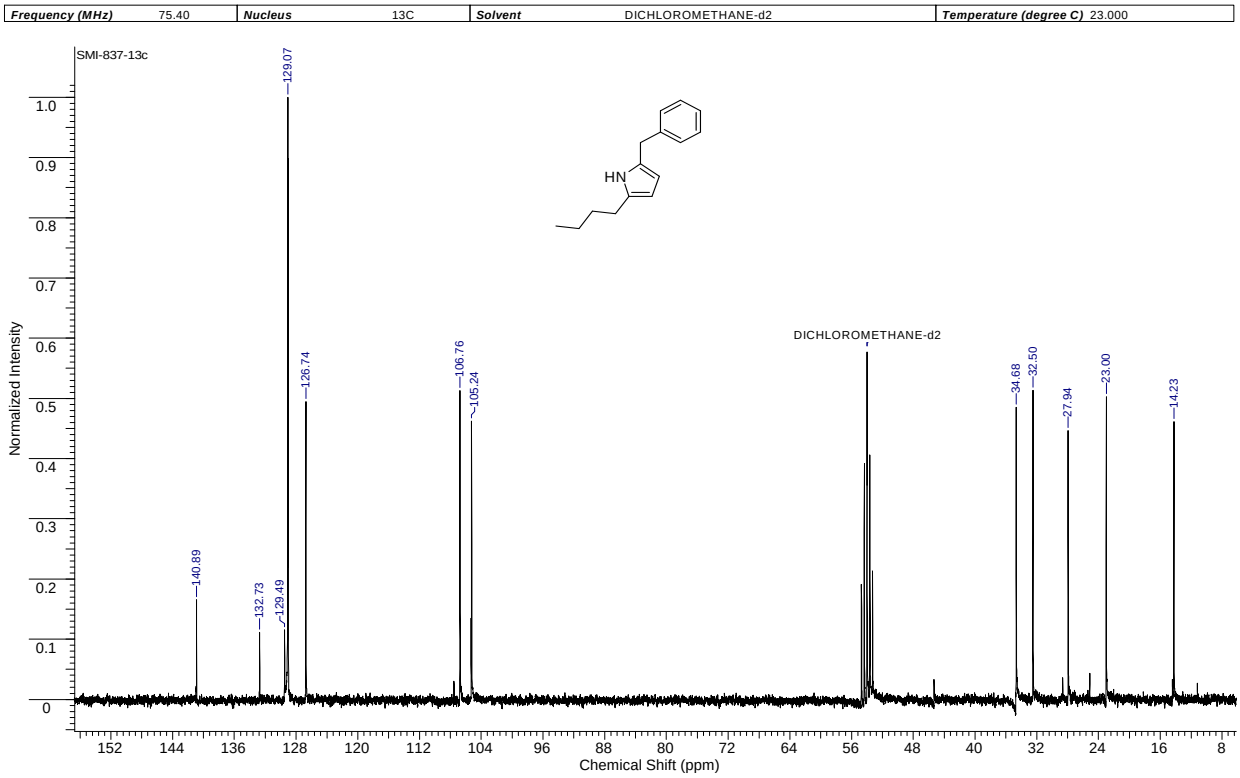

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-768-1h.esp
M05(m)
M06(m)
M07(m)
M04(m)
M01(s)
M03(m)
M02(dddd)
M08(br. s.)
NH
Normalized Intensity
Chemical Shift (ppm)

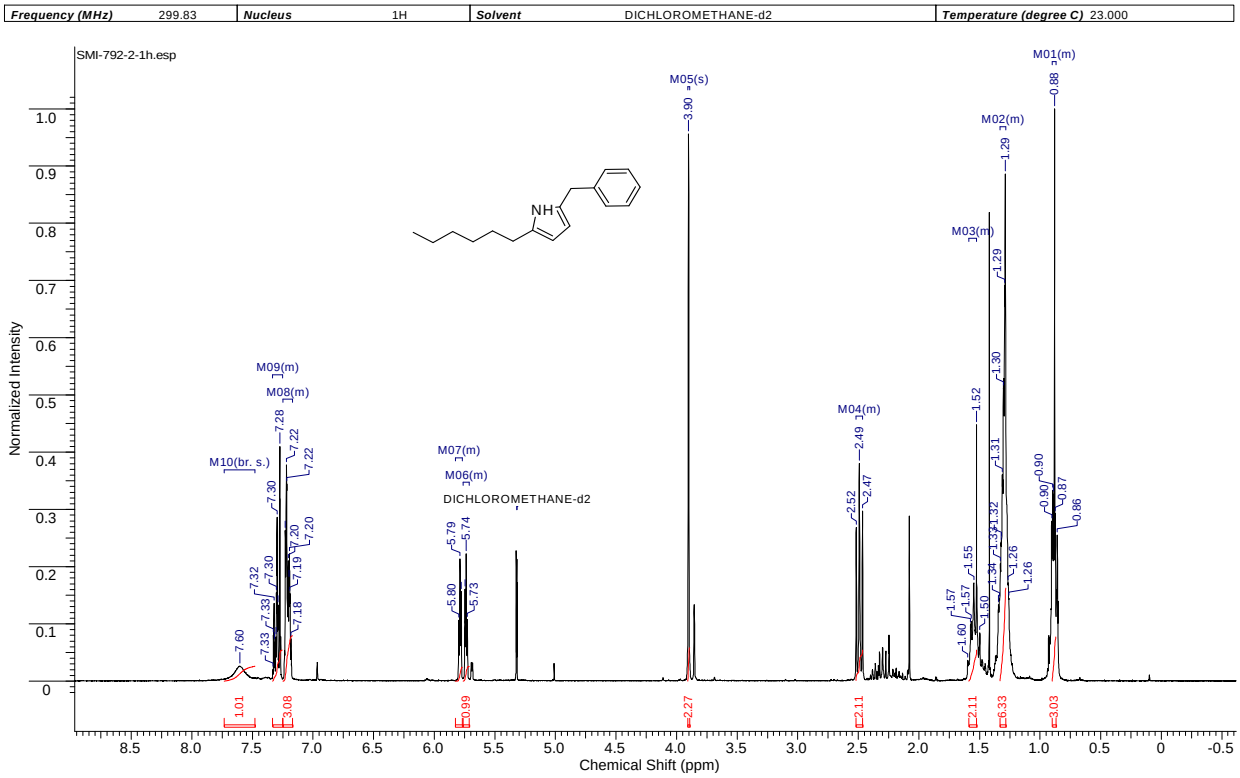

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-768-13c
DICHLOROMETHANE-d2
NH
Normalized Intensity
Chemical Shift (ppm)

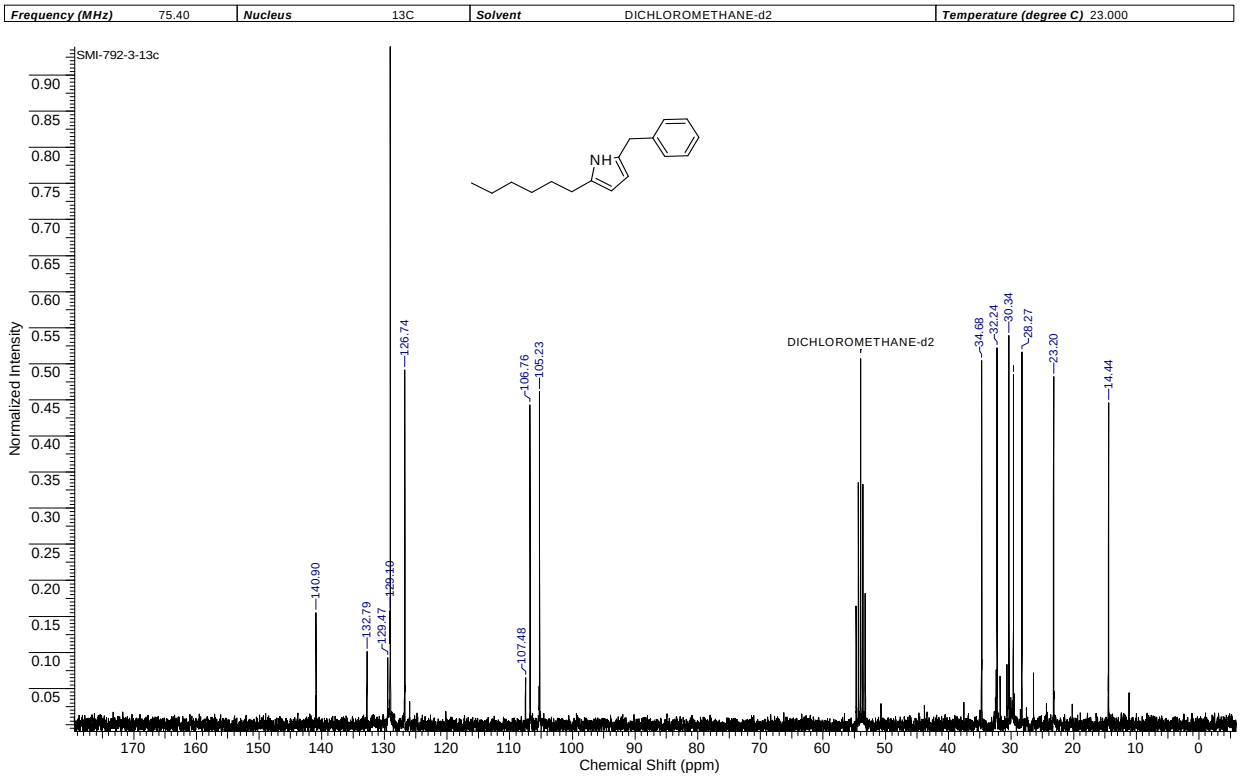

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-793-1h
M06(m)
M05(m)
M02(s)
M01(s)
M03(m)
M04(t)
M07(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

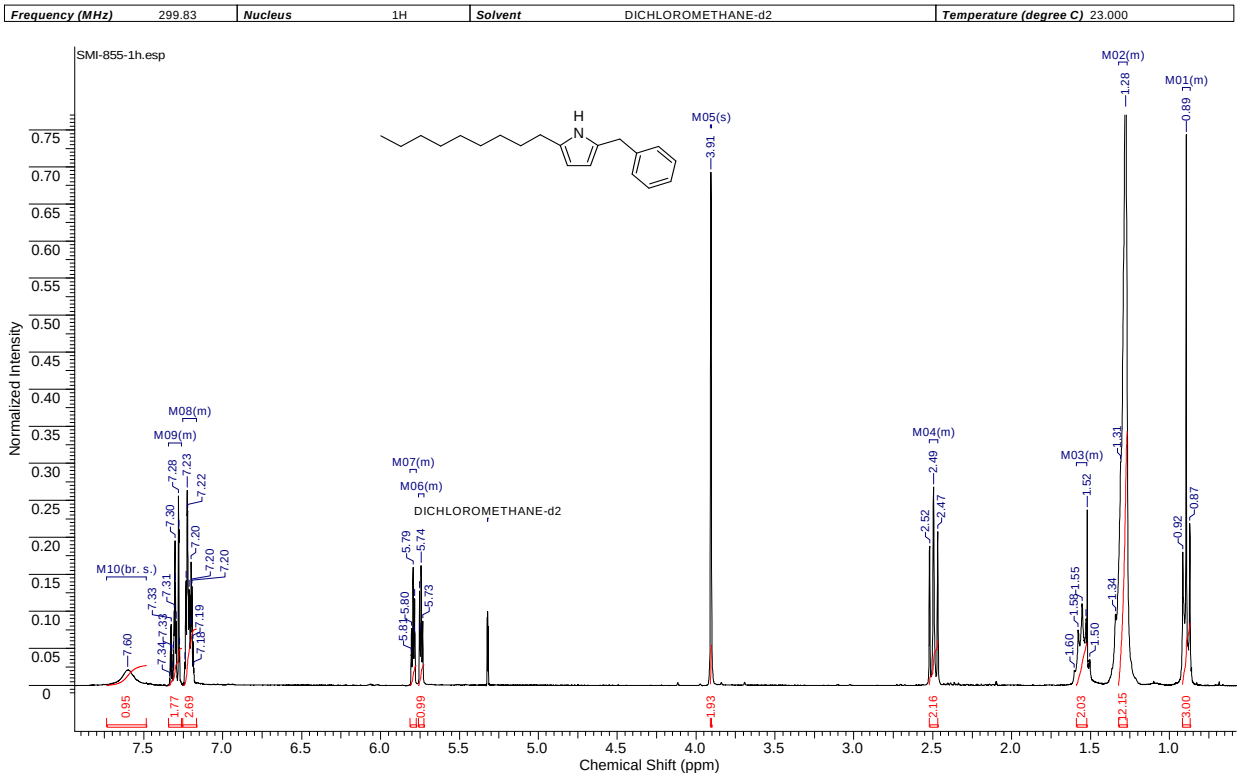

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-793-lb0
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

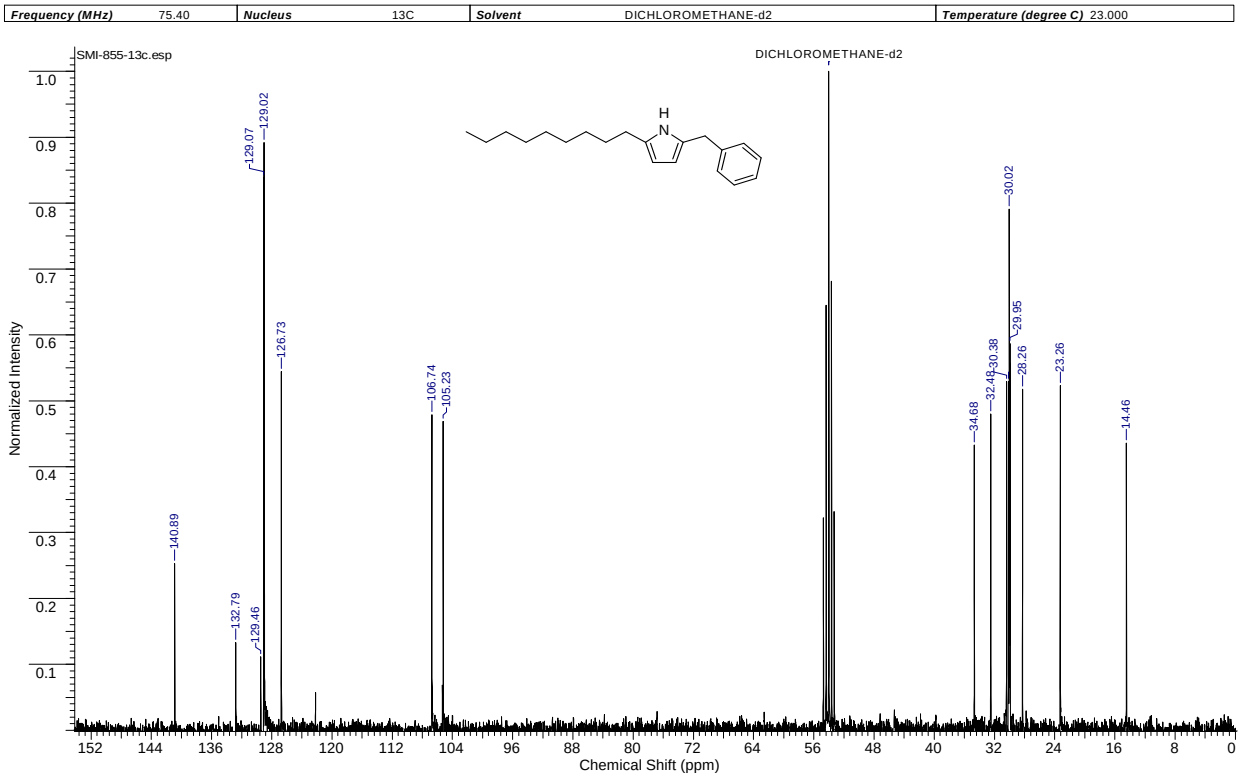

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-837-1h
Normalized Intensity
Chemical Shift (ppm)
M01(t)
M02(m)
M03(m)
M04(m)
M05(s)
M06(m)
M07(m)
M08(m)
M09(m)
M10(br. s.)
DICHLOROMETHANE-d2
HN

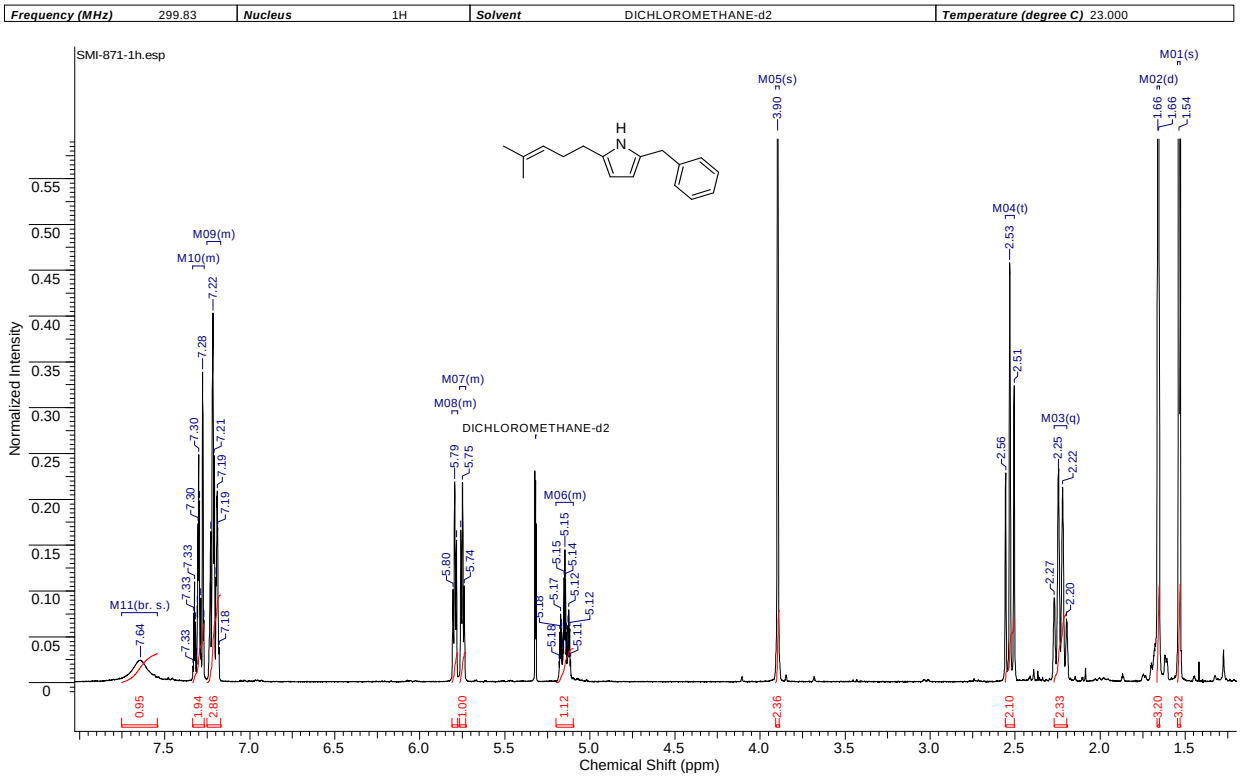

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-837-13c
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
HN

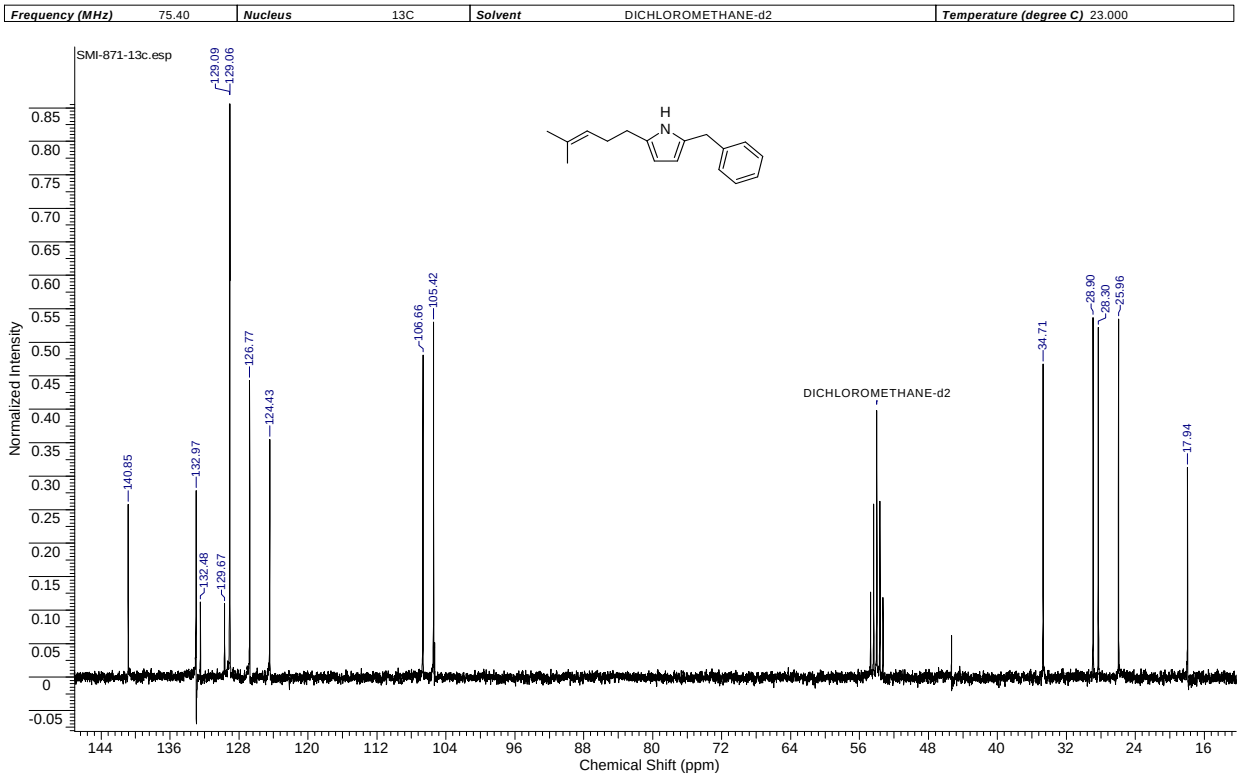

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-792-2-1h.esp
Normalized Intensity
Chemical Shift (ppm)
M01(m)
M02(m)
M03(m)
M04(m)
M05(s)
M06(m)
M07(m)
M08(m)
M09(m)
M10(br. s.)
DICHLOROMETHANE-d2
NH

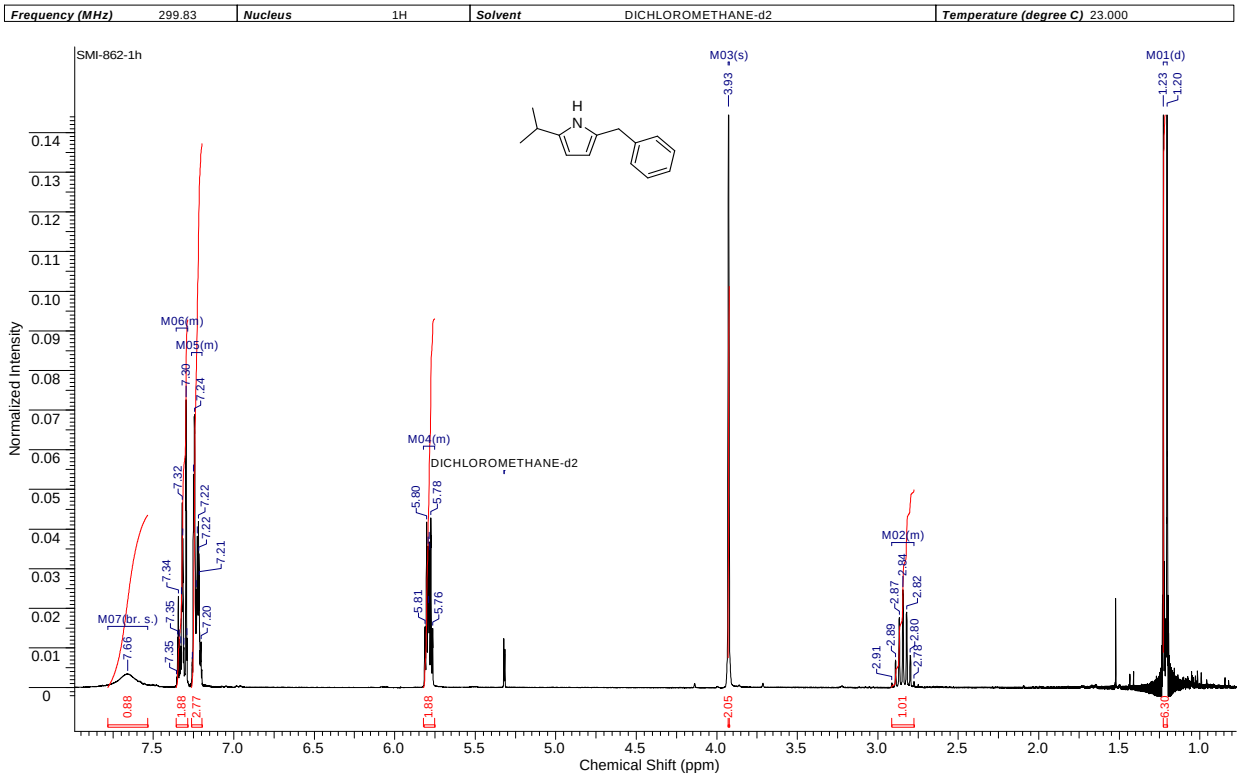

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-792-3-13c
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
NH

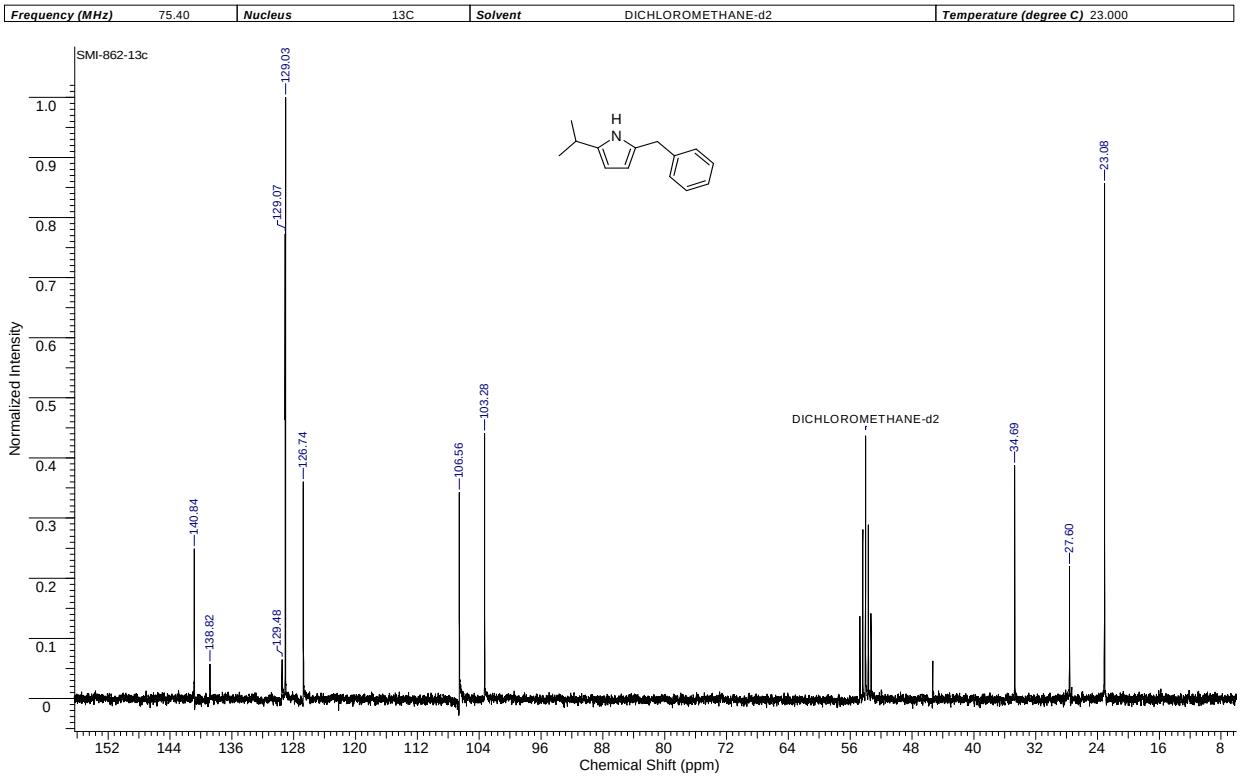

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-855-1h.esp
M01(m)
M02(m)
M03(m)
M04(m)
M05(s)
M06(m)
M07(m)
M08(m)
M09(m)
M10(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

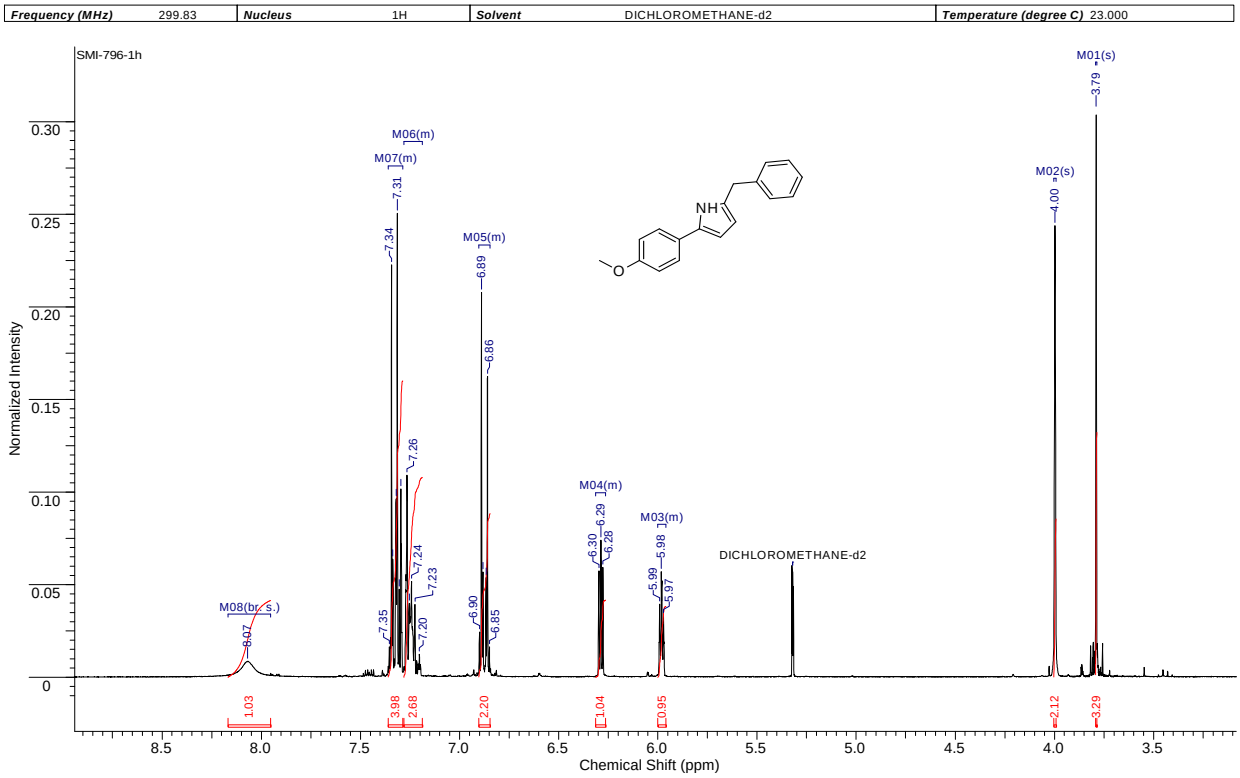

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-855-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

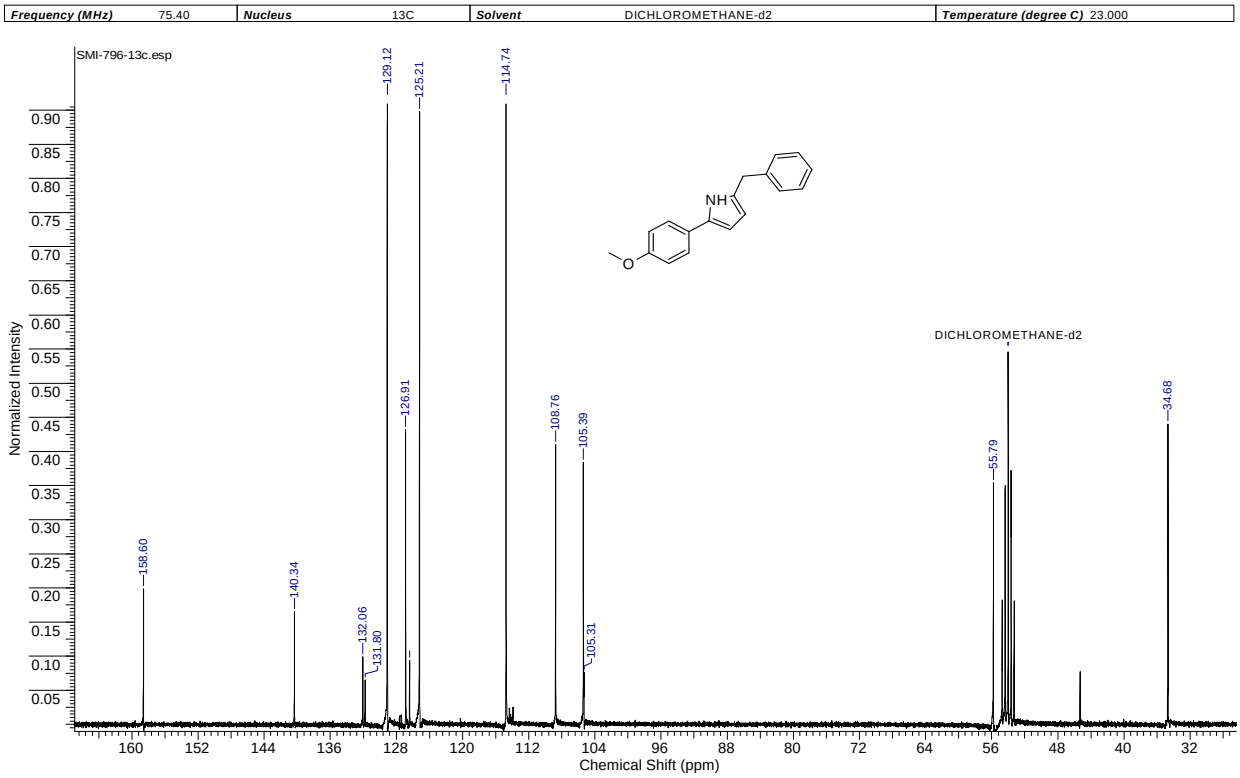

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-871-1h.esp
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(d)
M03(q)
M04(t)
M05(s)
M06(m)
M07(m)
M08(m)
M09(m)
M10(m)
M11(br. s.)
DICHLOROMETHANE-d2

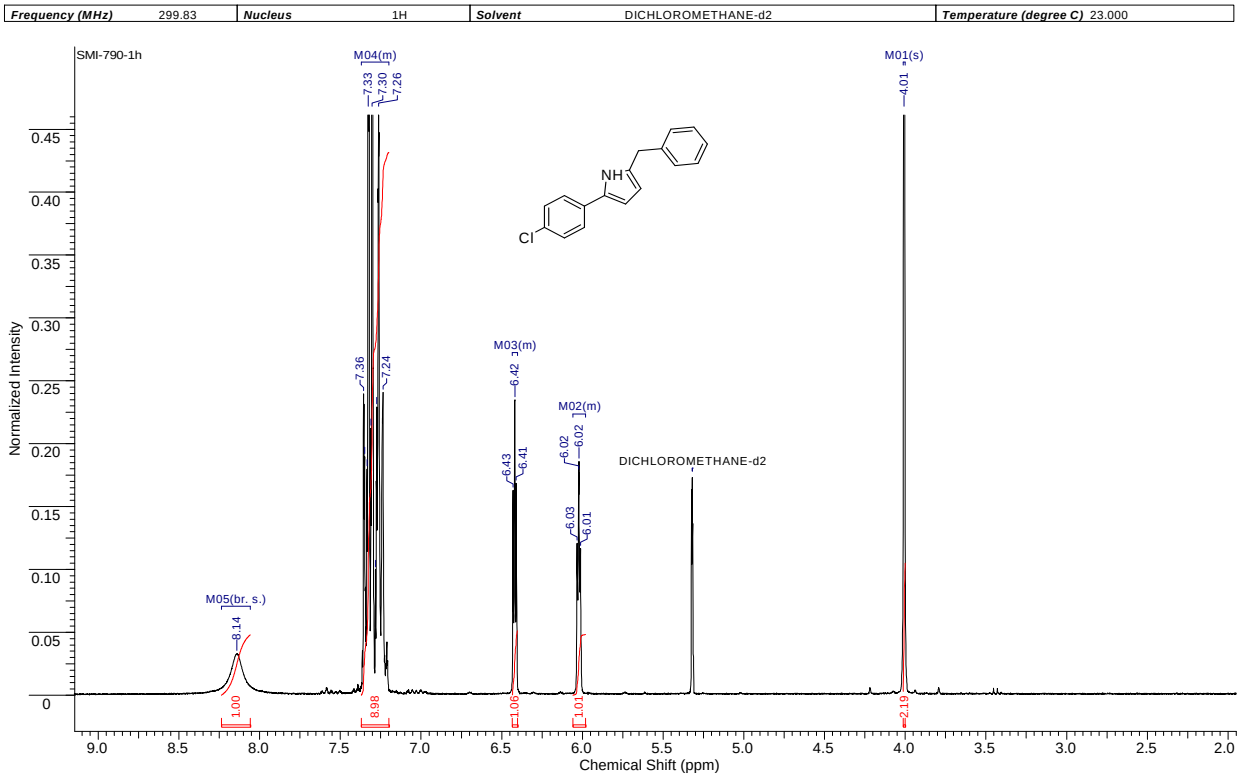

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-871-13c.esp
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2

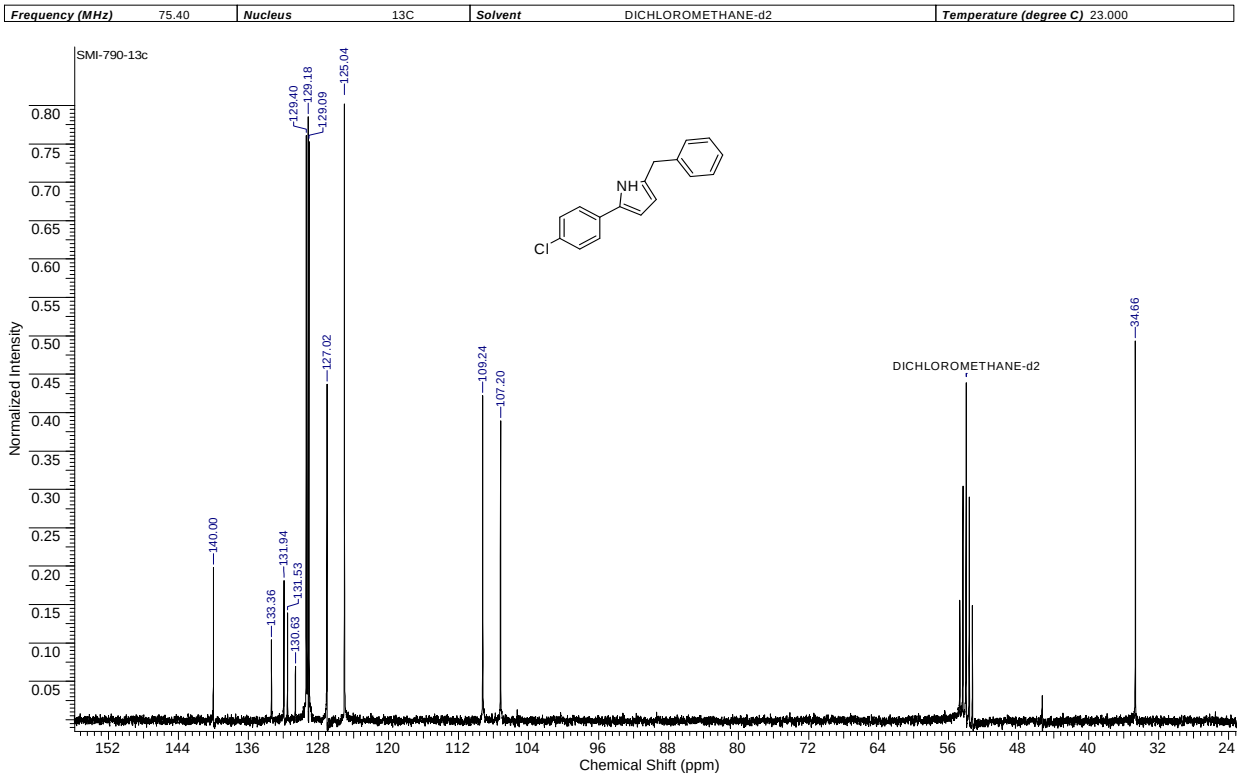

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-862-1h
M03(s)
M01(d)
M06(m)
M05(m)
M04(m)
DICHLOROMETHANE-d2
M02(m)
M07(br. s.)
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-862-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

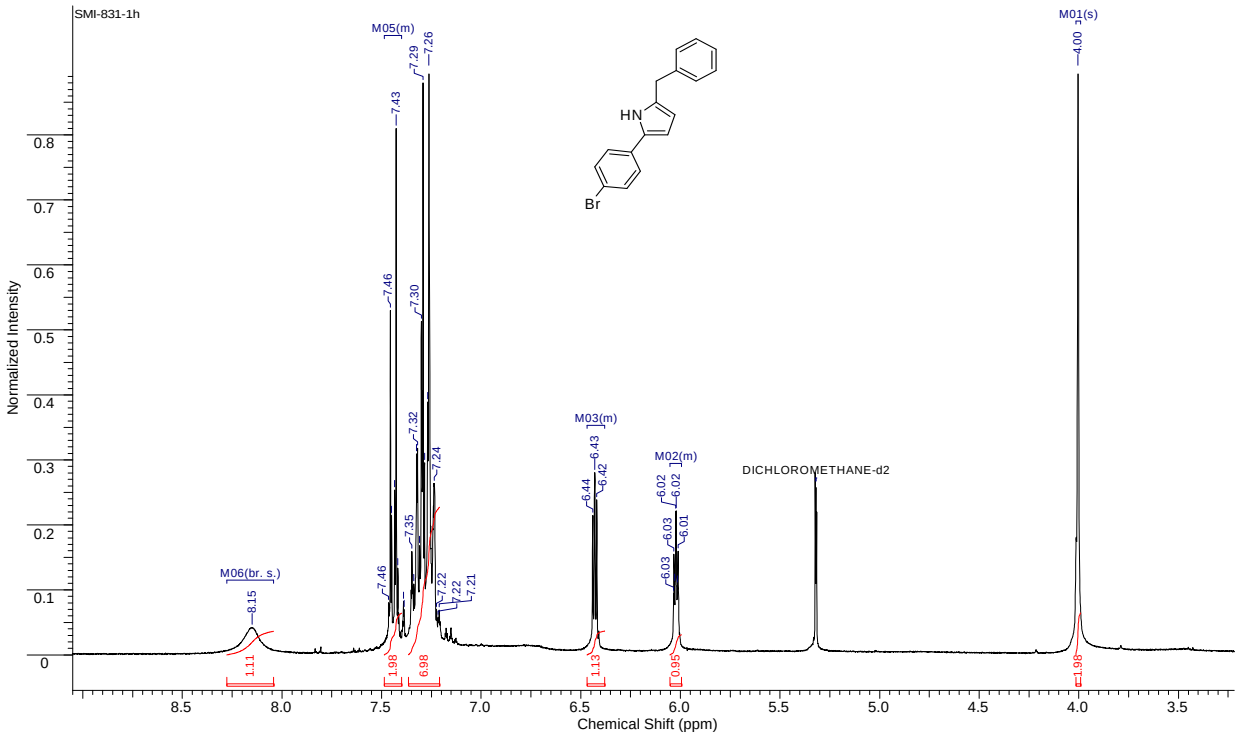

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-796-1h
Normalized Intensity
Chemical Shift (ppm)
M01(s)
M02(s)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(br. s.)
DICHLOROMETHANE-d2
NH
O


Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-796-13c.esp
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
NH
O

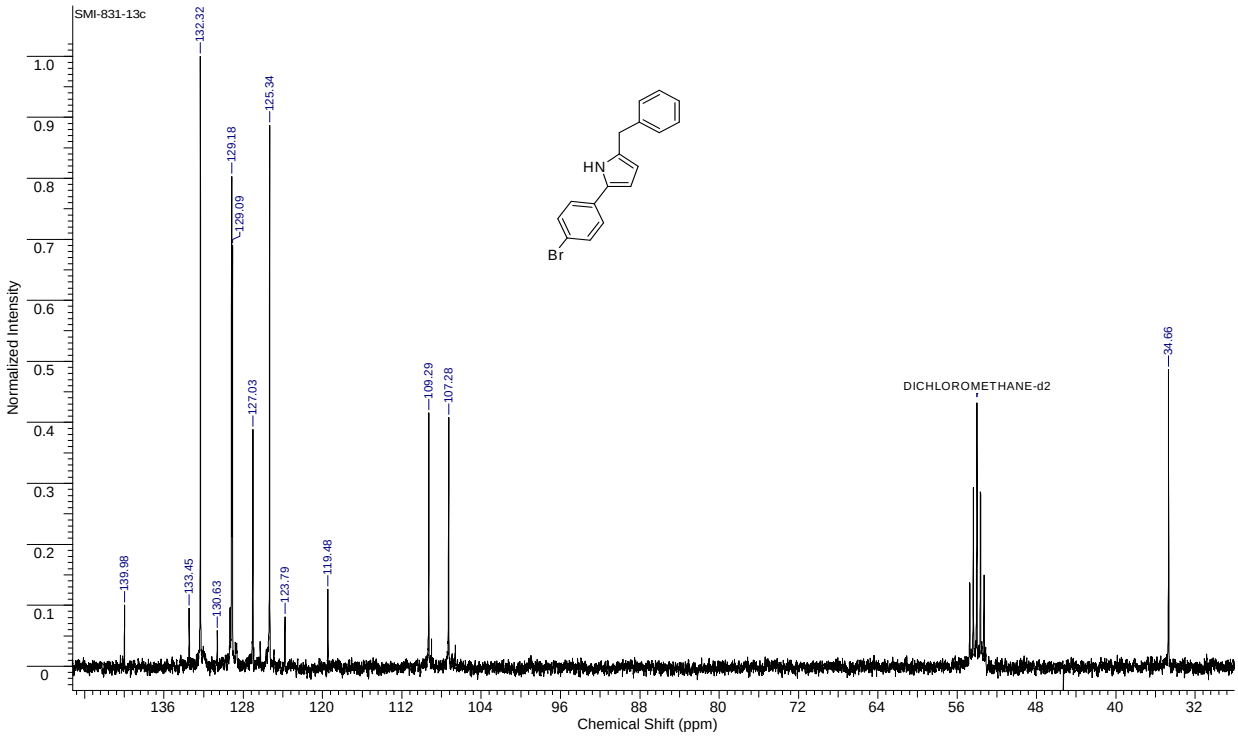

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-790-1h
M04(m)
7.33
7.30
7.26
M01(s)
4.01
NH
Cl
M03(m)
6.42
7.36
7.24
M02(m)
6.02
6.02
6.43
6.41
DICHLOROMETHANE-d2
6.03
6.01
M05(br. s.)
8.14
1.00
8.98
1.06
1.01
2.19
Normalized Intensity
Chemical Shift (ppm)

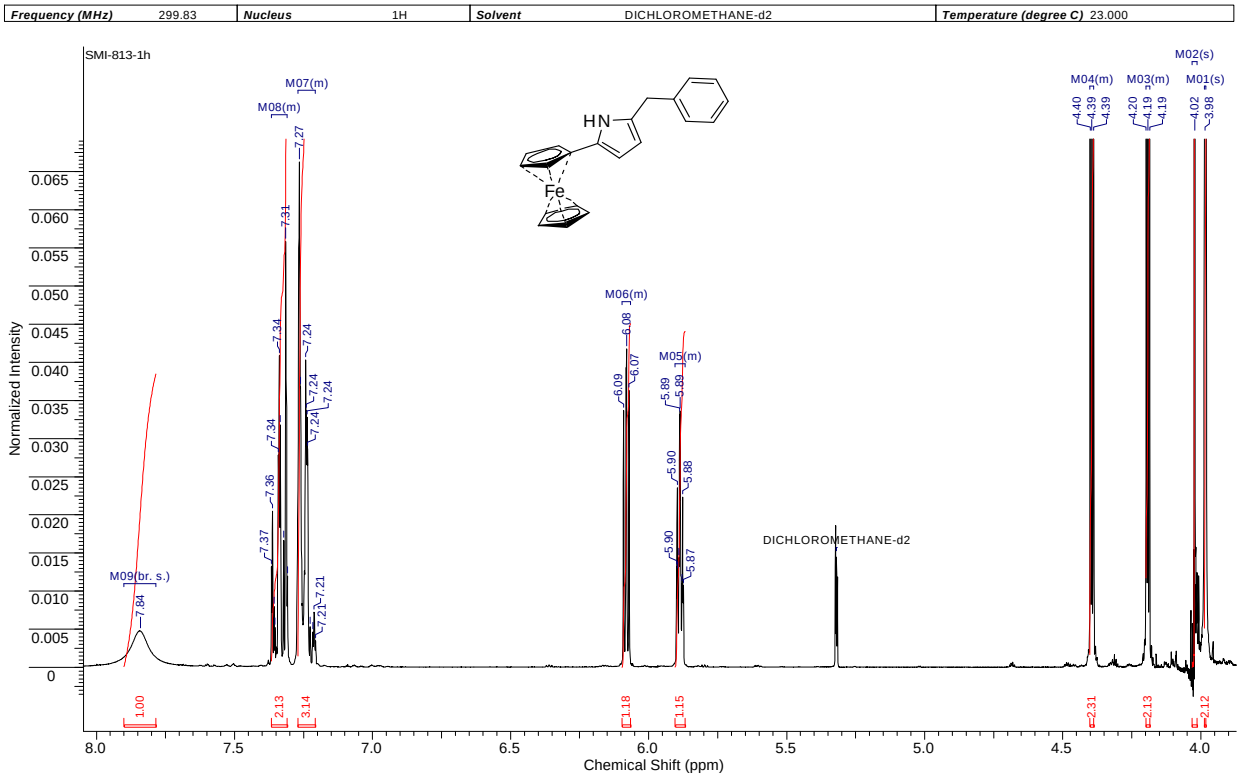

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-790-13c
129.40
129.18
129.09
125.04
NH
Cl
127.02
109.24
107.20
DICHLOROMETHANE-d2
34.66
140.00
131.94
131.53
133.36
130.63
Normalized Intensity
Chemical Shift (ppm)

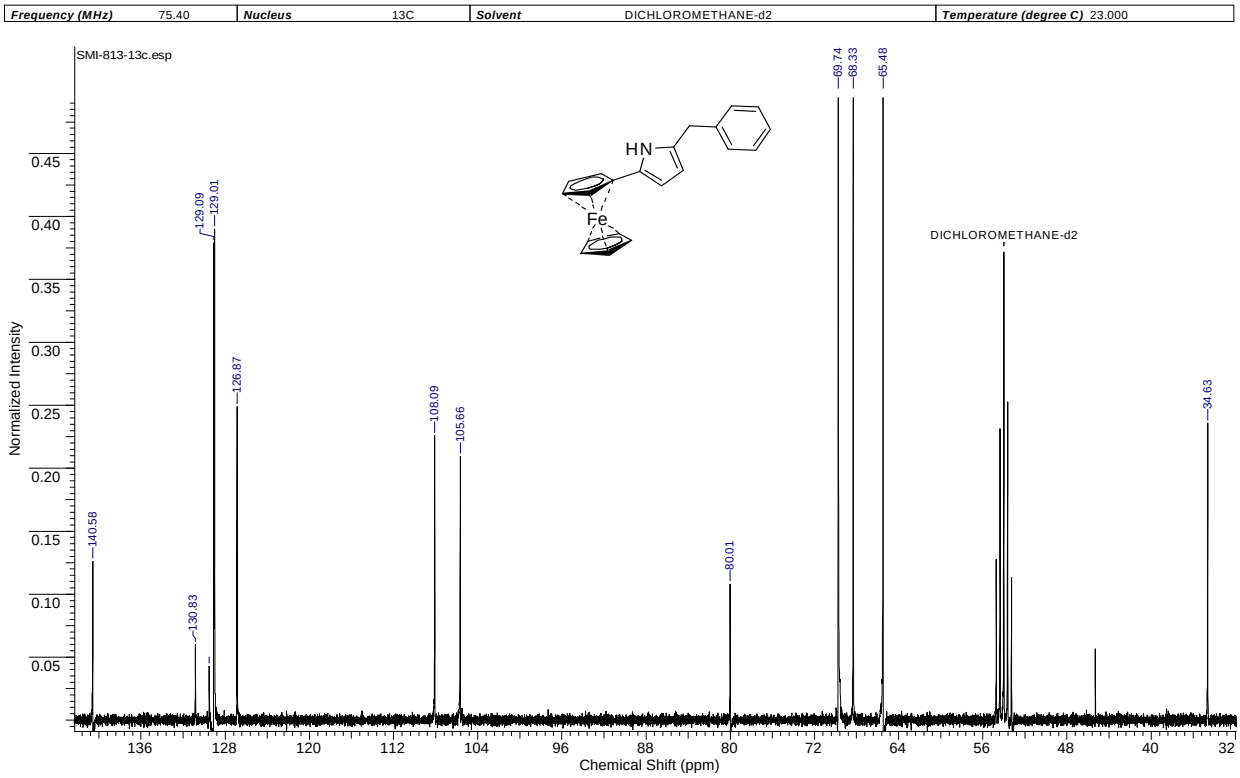
Frequency (MHz)	299.83	Nucleus	1H	Solvent	DICHLOROMETHANE-d2	Temperature (degree C)	23.000

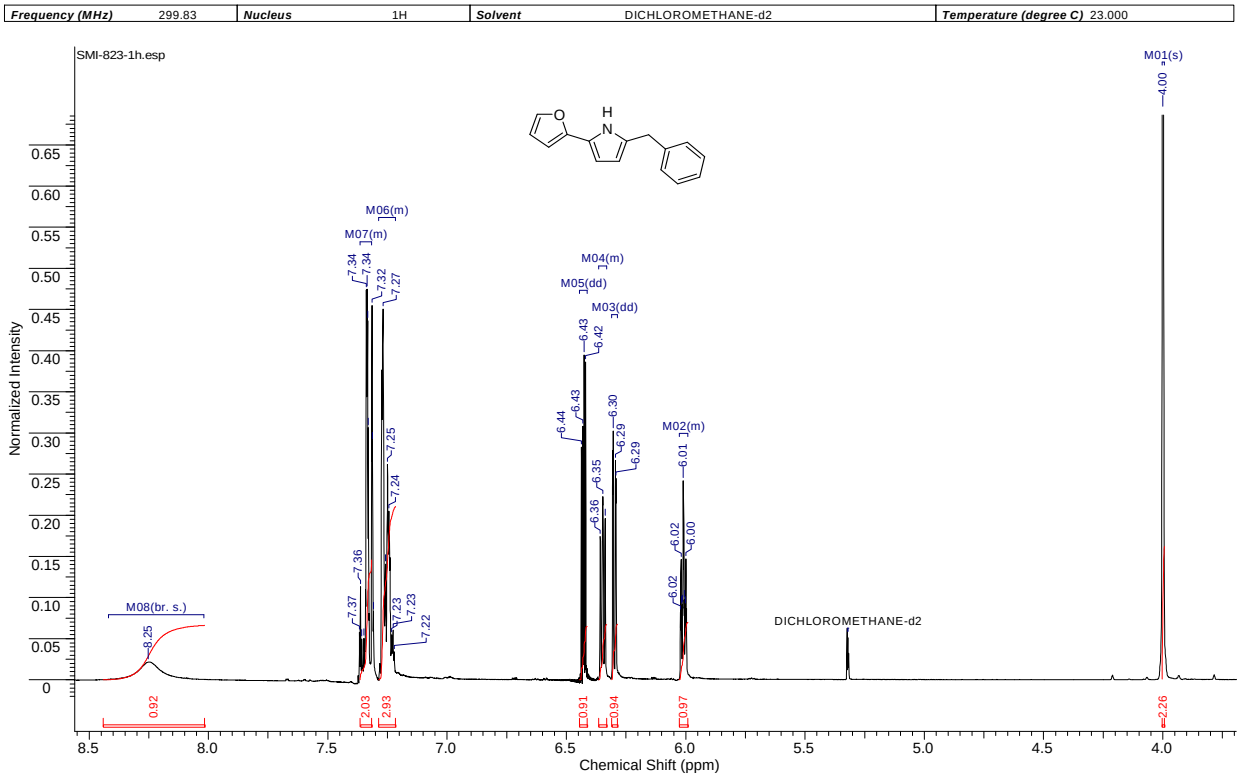


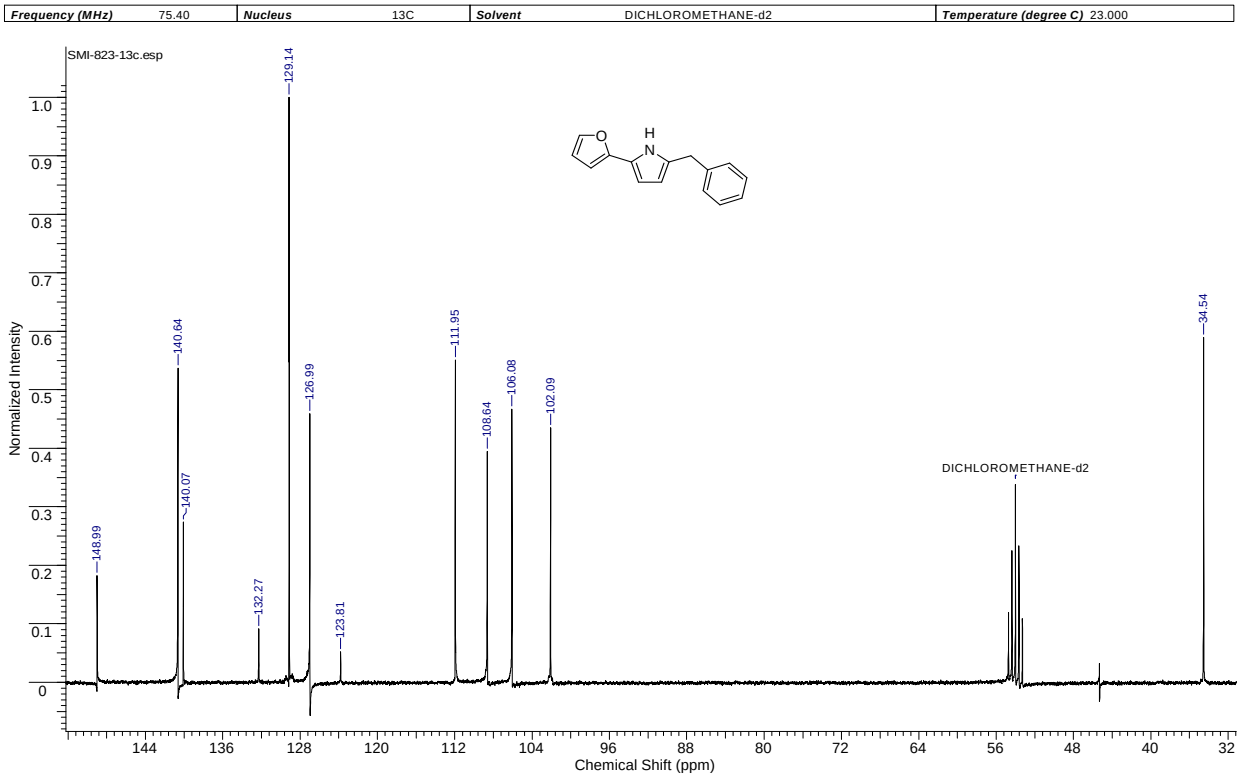
Frequency (MHz)	75.40	Nucleus	13C	Solvent	DICHLOROMETHANE-d2	Temperature (degree C)	23.000

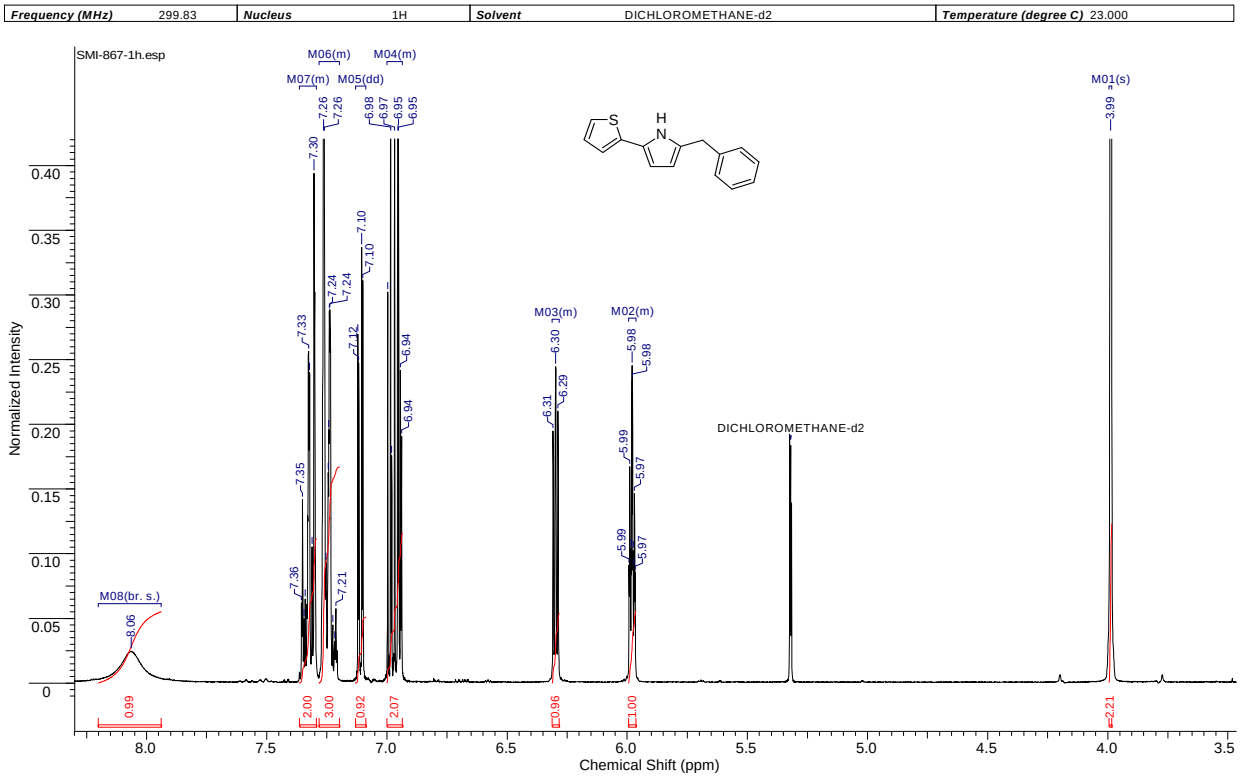


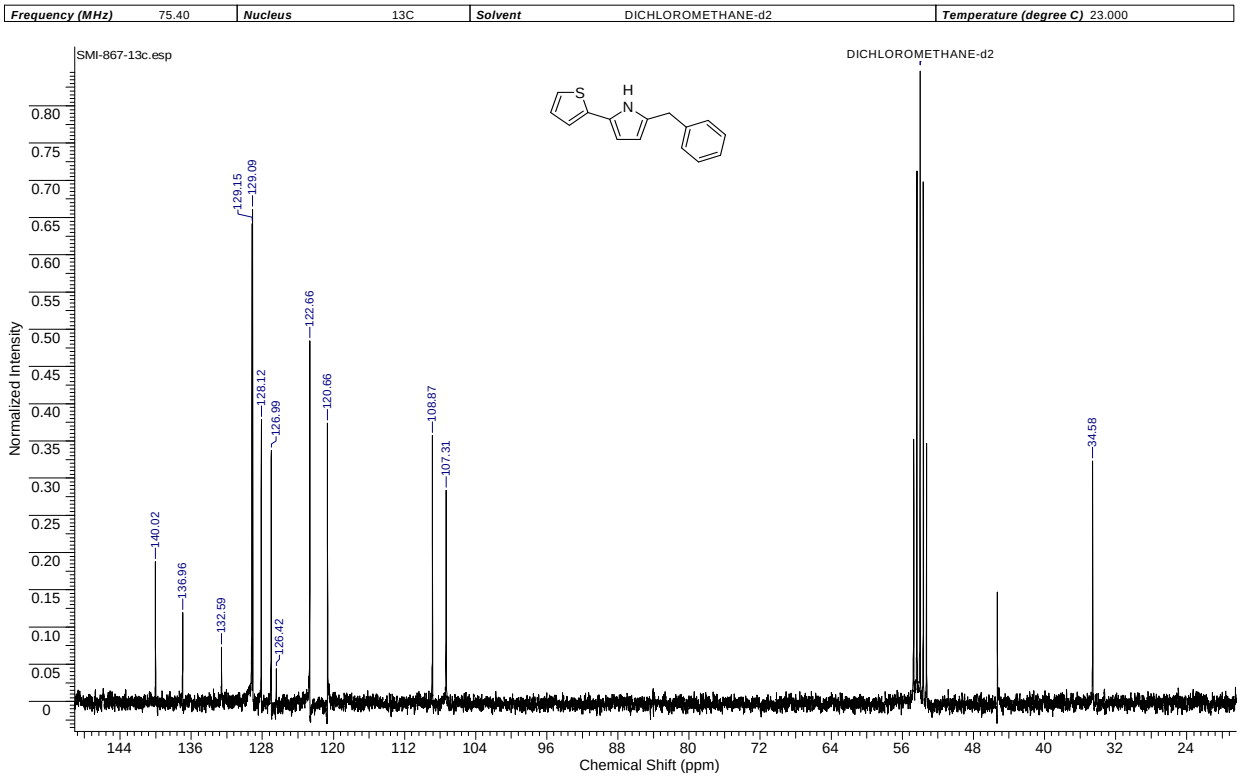

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-813-1h
M01(s)
M02(s)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(m)
M09(br. s.)
DICHLOROMETHANE-d2
HN
Fe
Normalized Intensity
Chemical Shift (ppm)

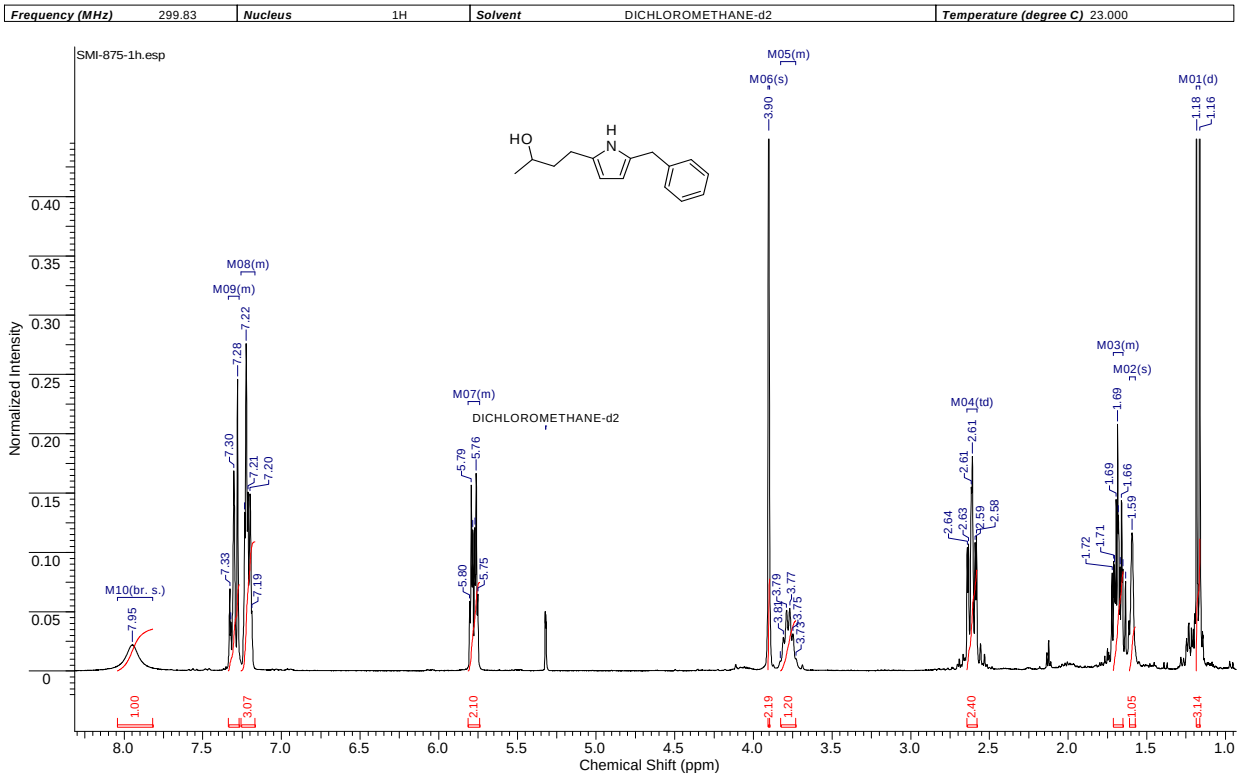

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-813-13c.esp
DICHLOROMETHANE-d2
HN
Fe
Normalized Intensity
Chemical Shift (ppm)

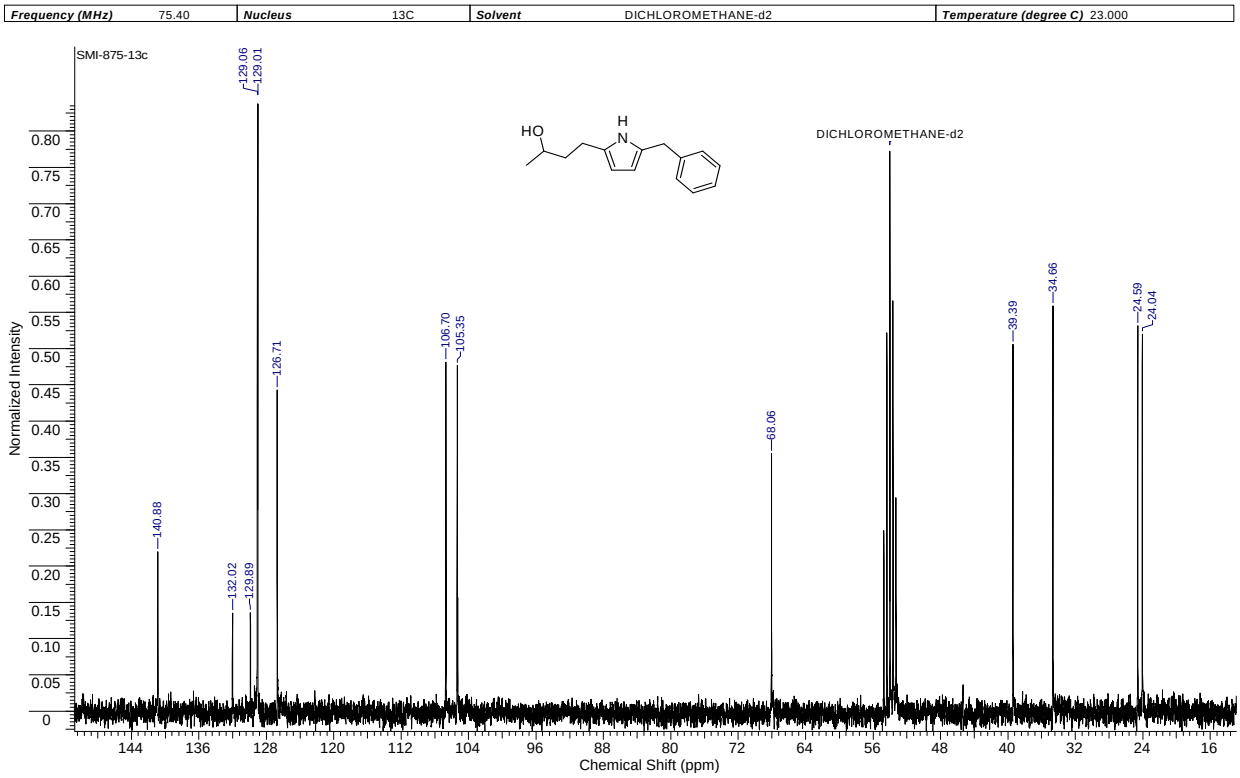

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-823-1h.esp
M01(s)
M02(m)
M03(dd)
M04(m)
M05(dd)
M06(m)
M07(m)
M08(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

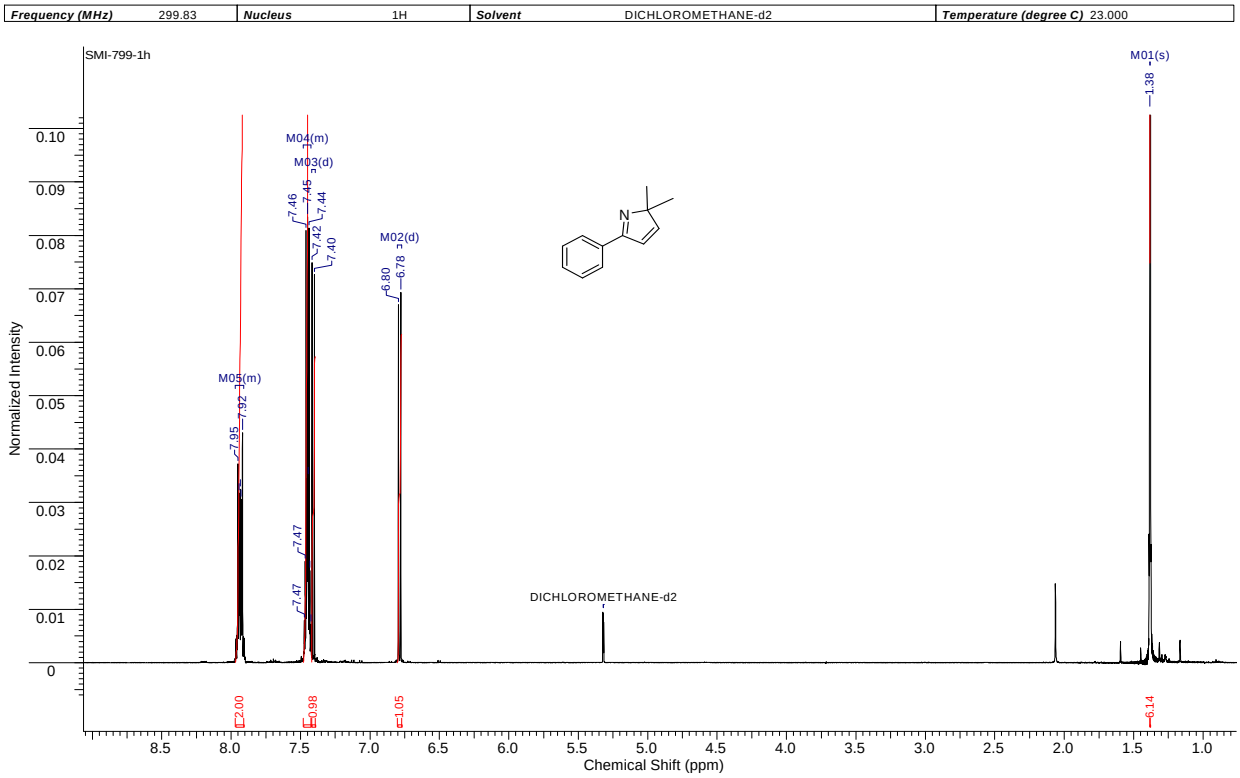

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-823-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

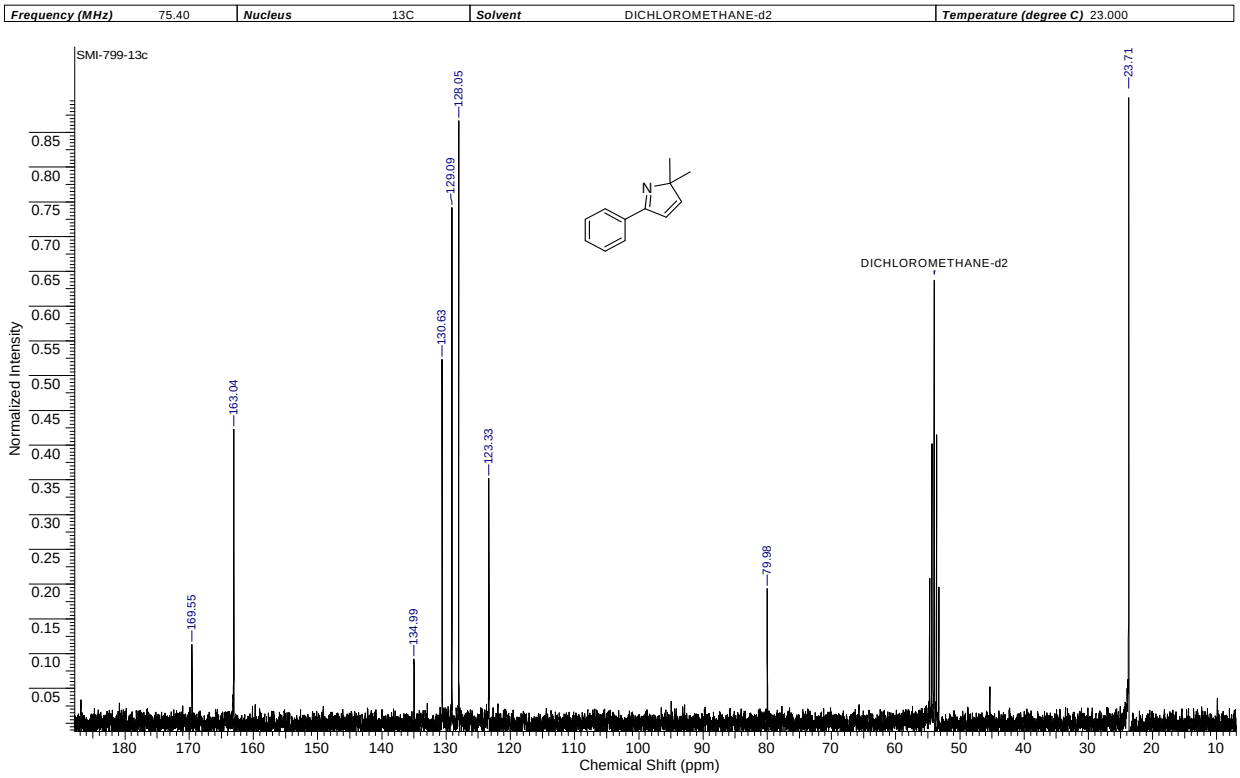

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-867-1h.esp
M06(m)
M04(m)
M07(m)
M05(dd)
M01(s)
M03(m)
M02(m)
M08(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

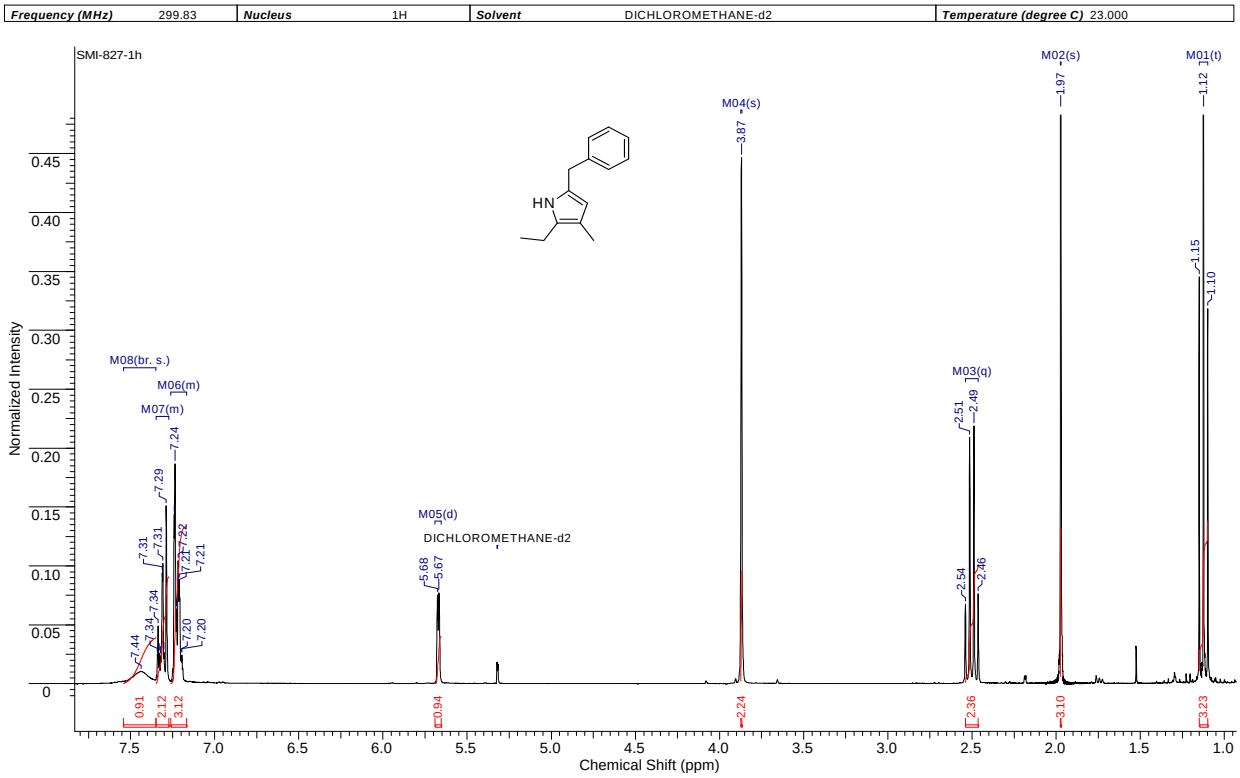

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-867-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

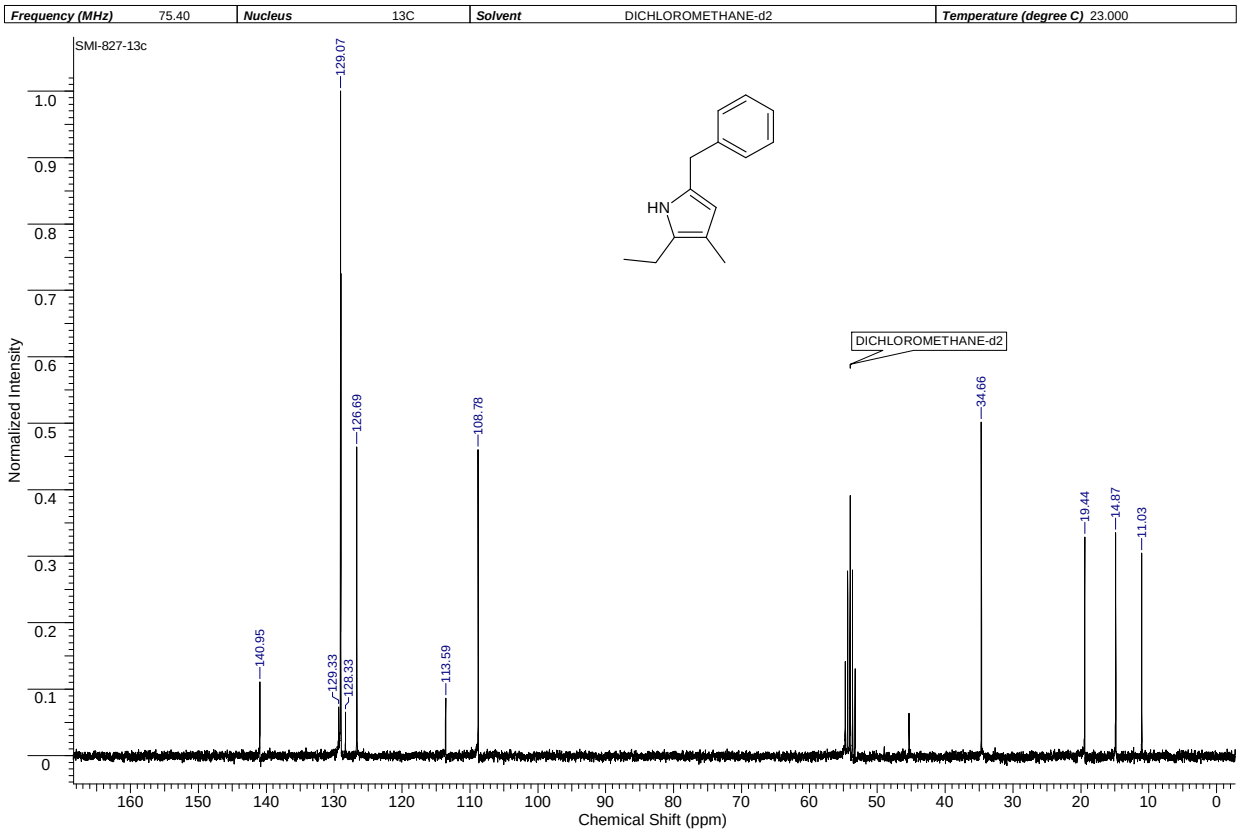

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-875-1h.esp
M05(m)
M06(s)
M01(d)
M08(m)
M09(m)
M07(m)
DICHLOROMETHANE-d2
M04(td)
M03(m)
M02(s)
M10(br. s.)
Normalized Intensity
Chemical Shift (ppm)

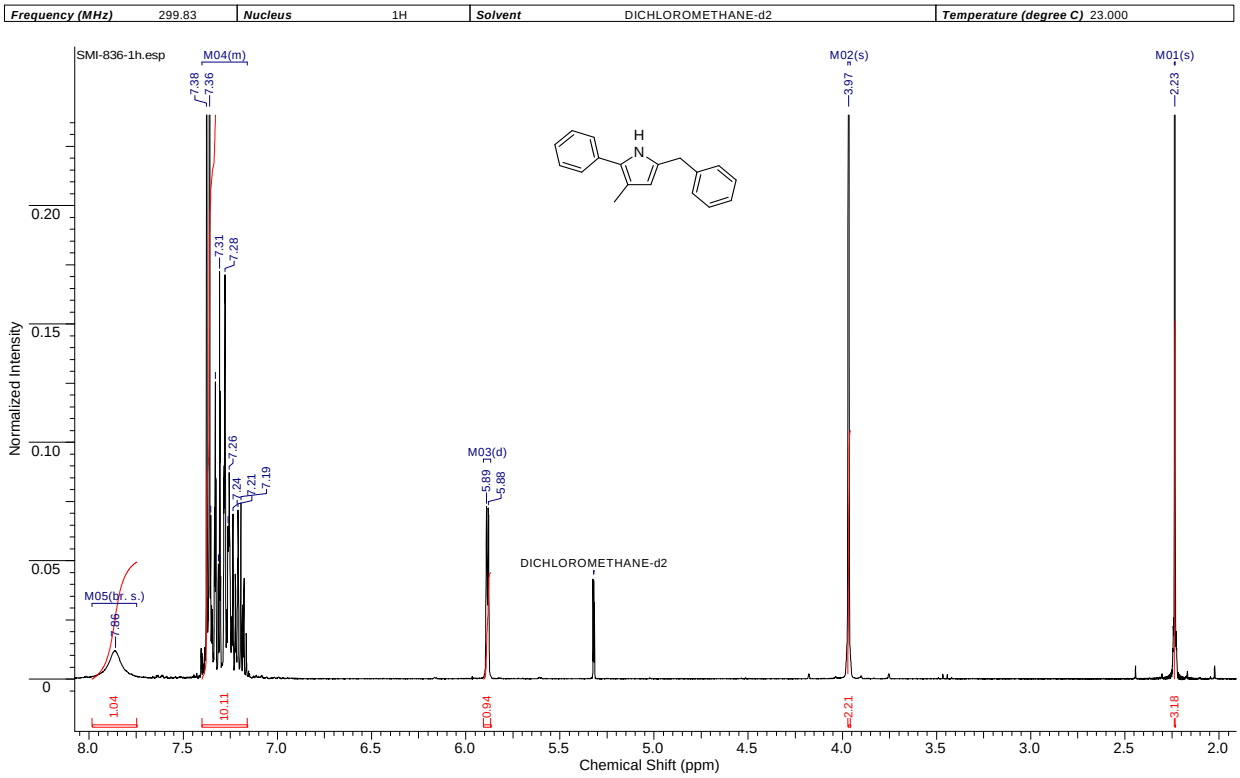

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-875-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

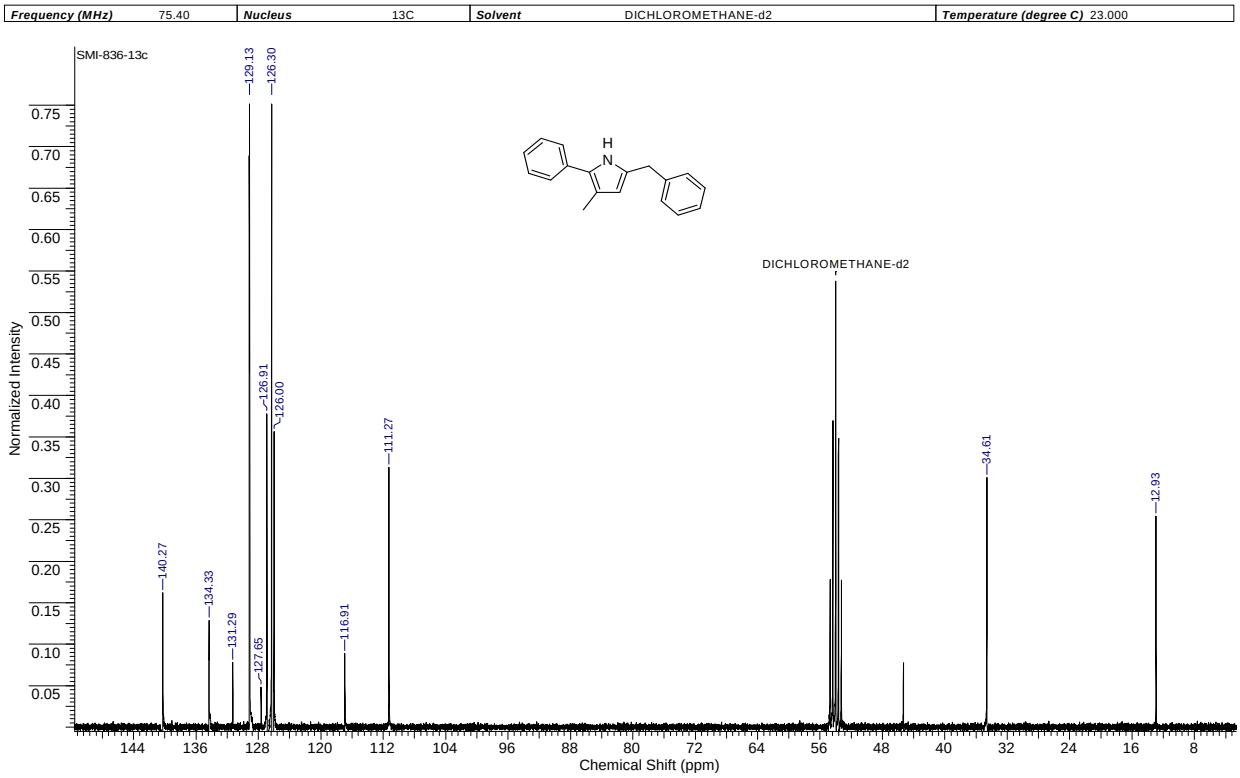

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-799-1h
M01(s)
M02(d)
M03(d)
M04(m)
M05(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

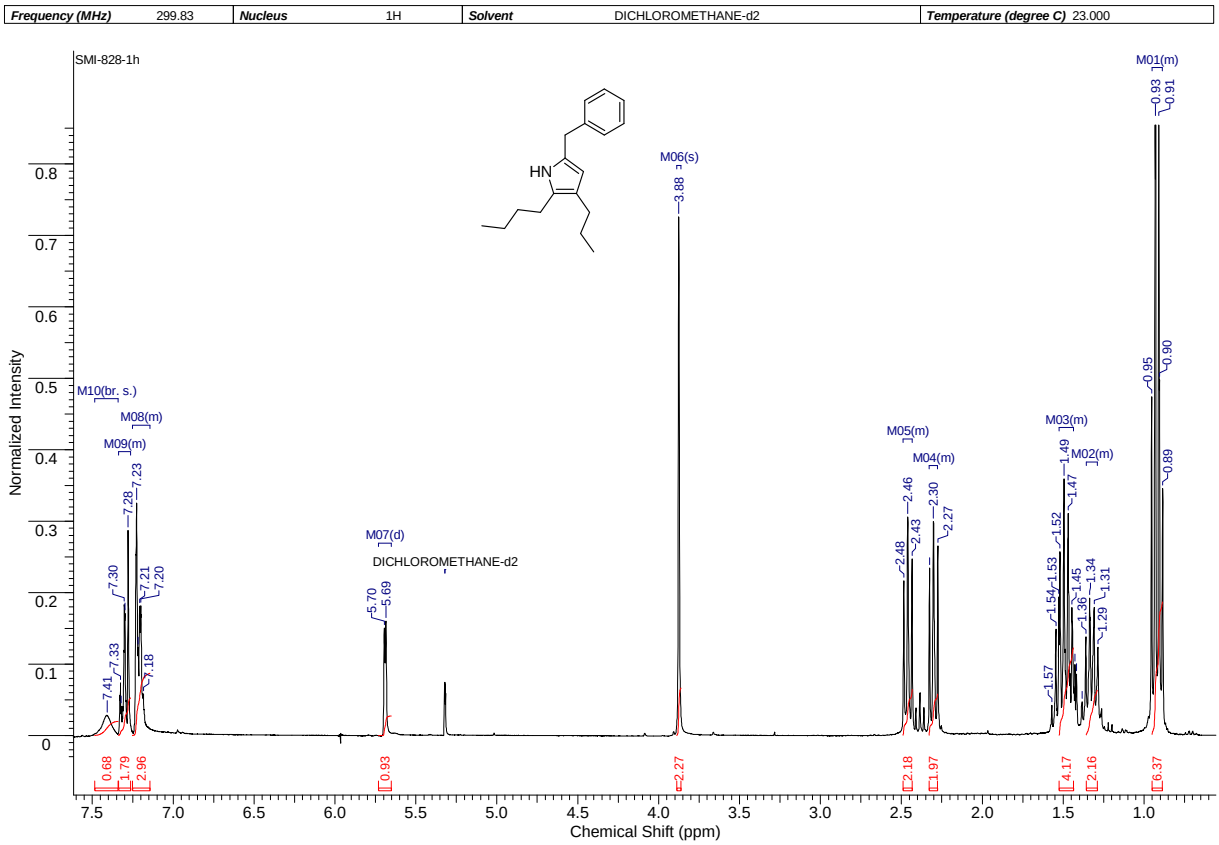

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-799-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

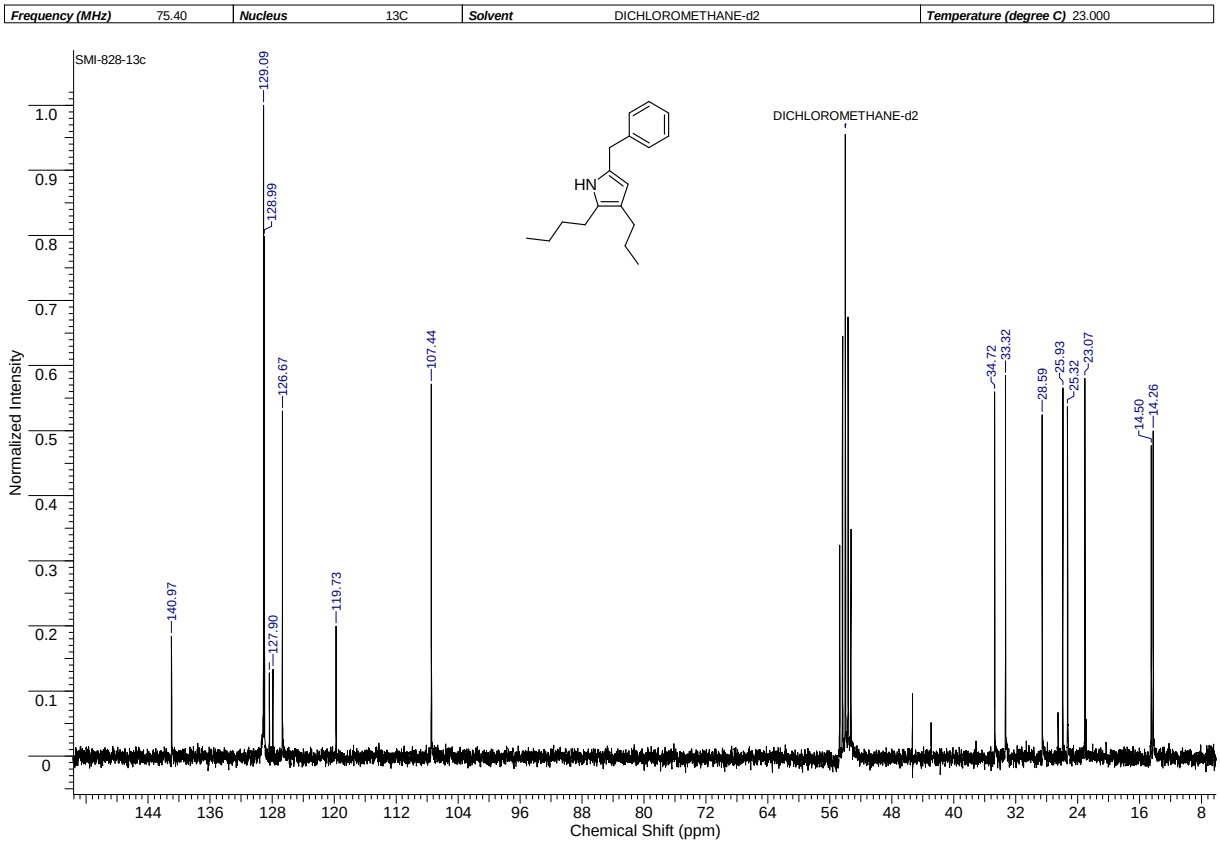

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-827-1h
M08(br. s.)
M06(m)
M07(m)
M05(d)
DICHLOROMETHANE-d2
M04(s)
M03(q)
M02(s)
M01(t)
Normalized Intensity
Chemical Shift (ppm)

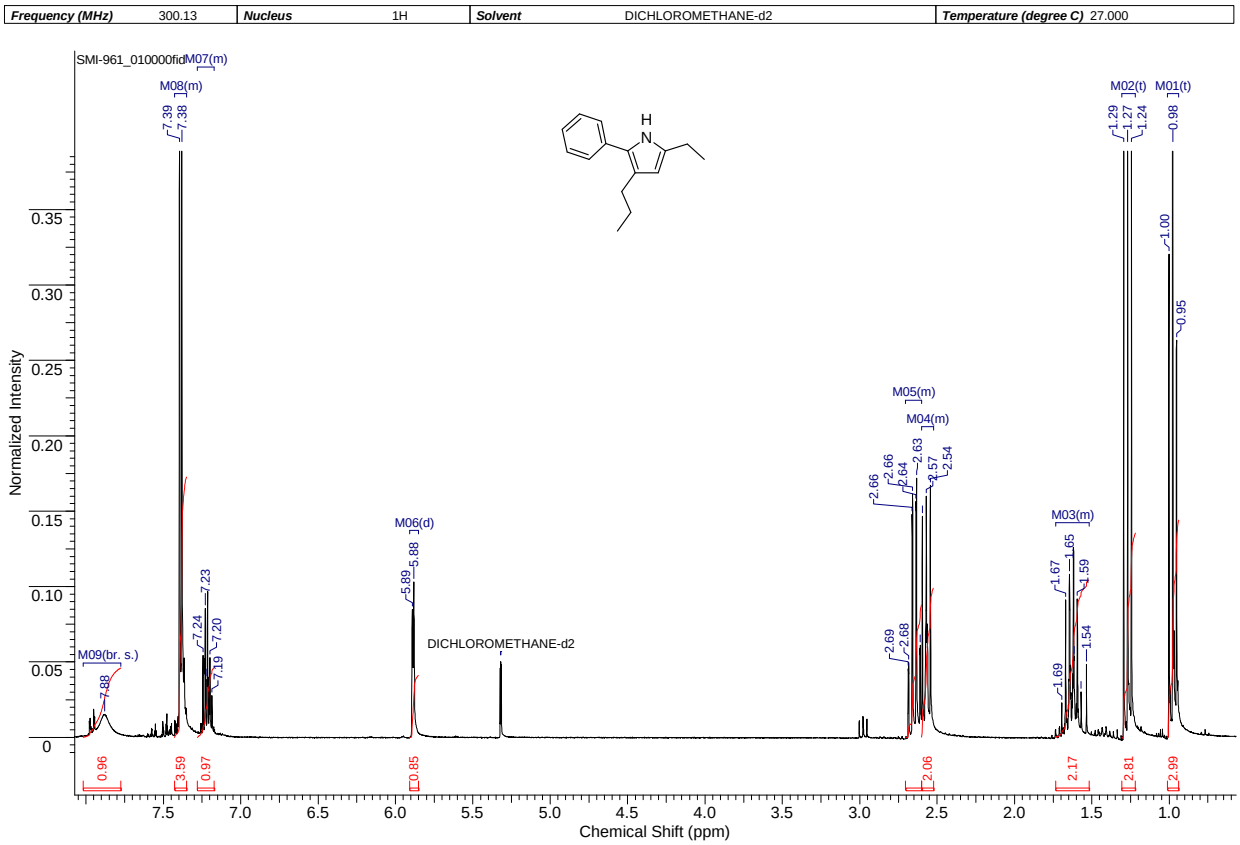

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-827-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

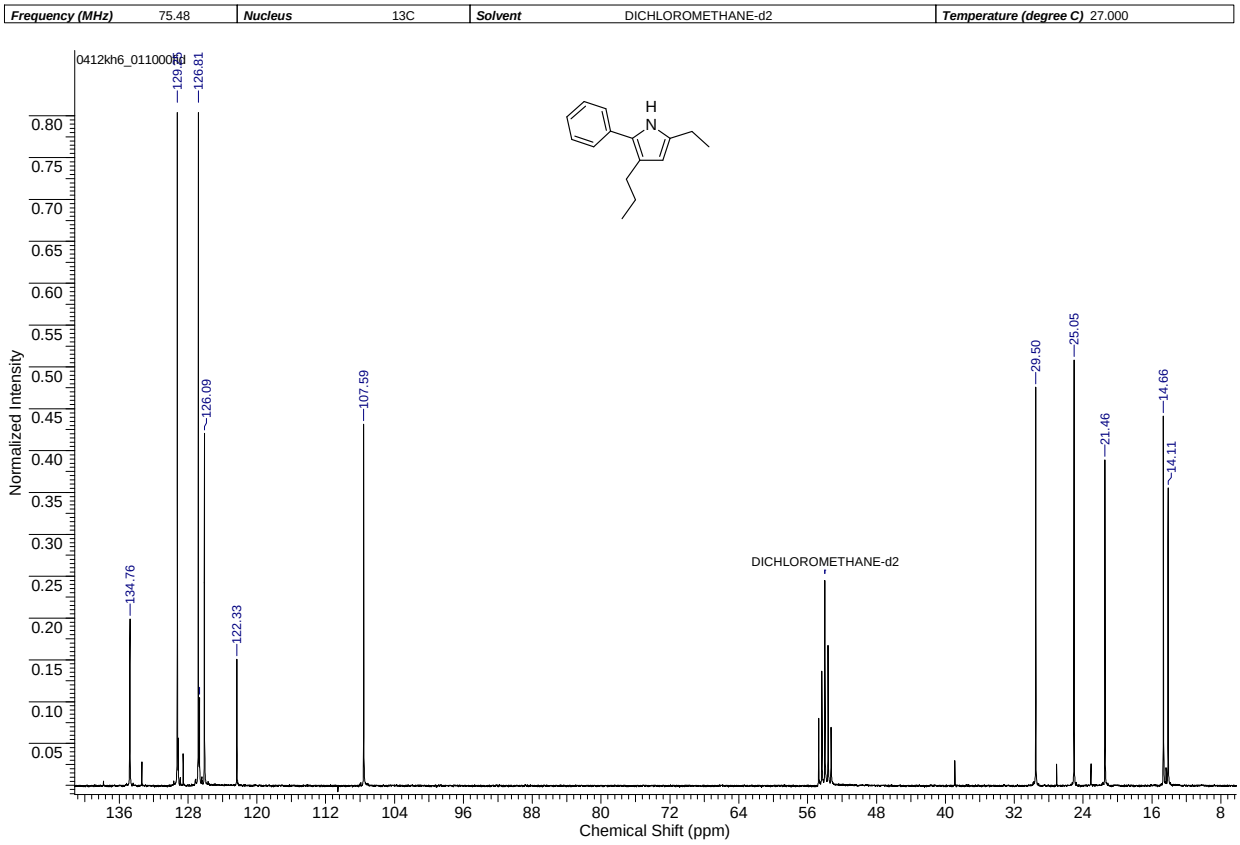

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-836-1h.esp
M04(m)
M02(s)
M01(s)
M03(d)
M05(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

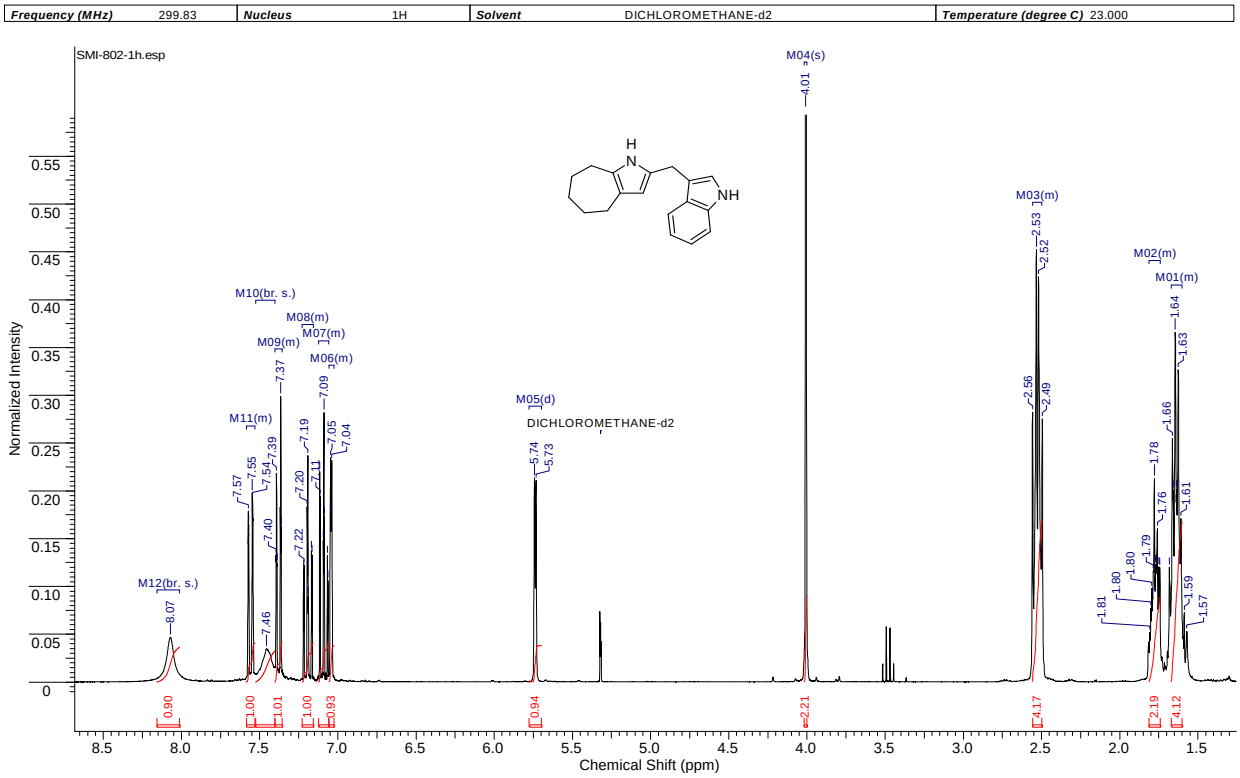

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-836-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

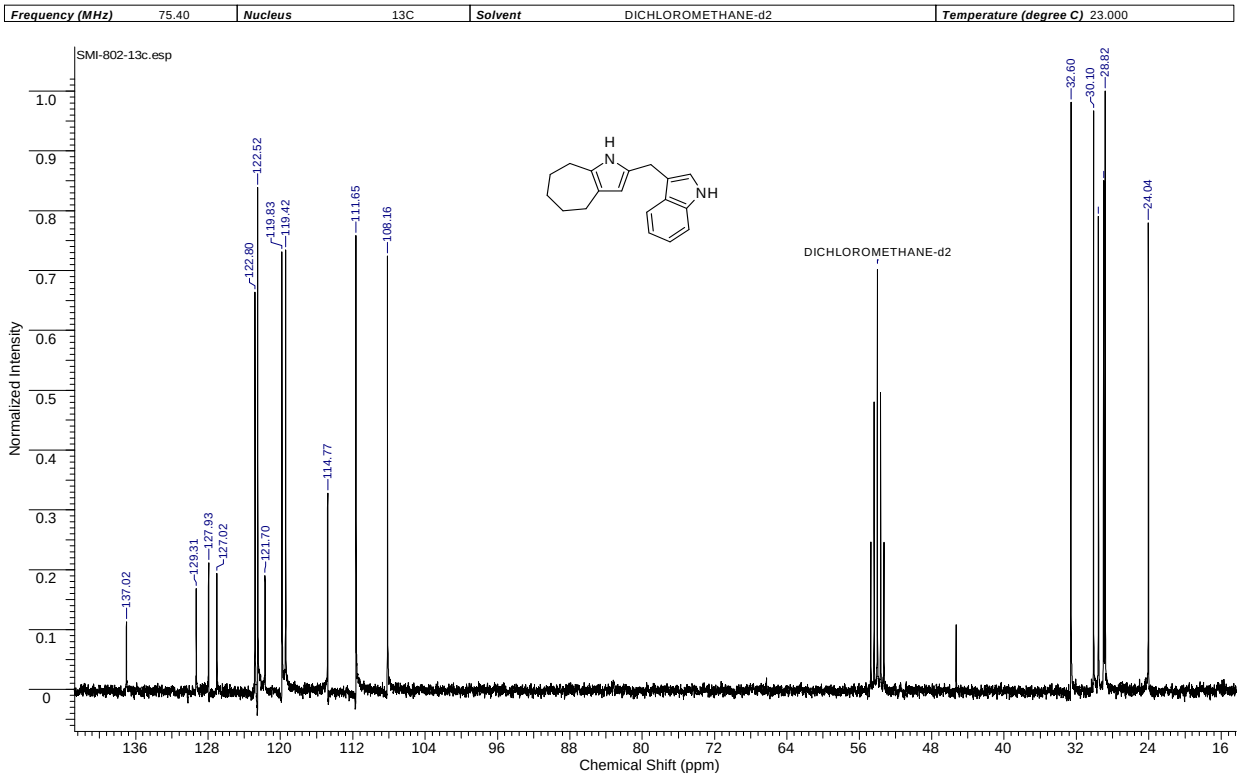

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-828-1h
HN
M01(m)
M02(m)
M03(m)
M04(m)
M05(m)
M06(s)
M07(d)
M08(m)
M09(m)
M10(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

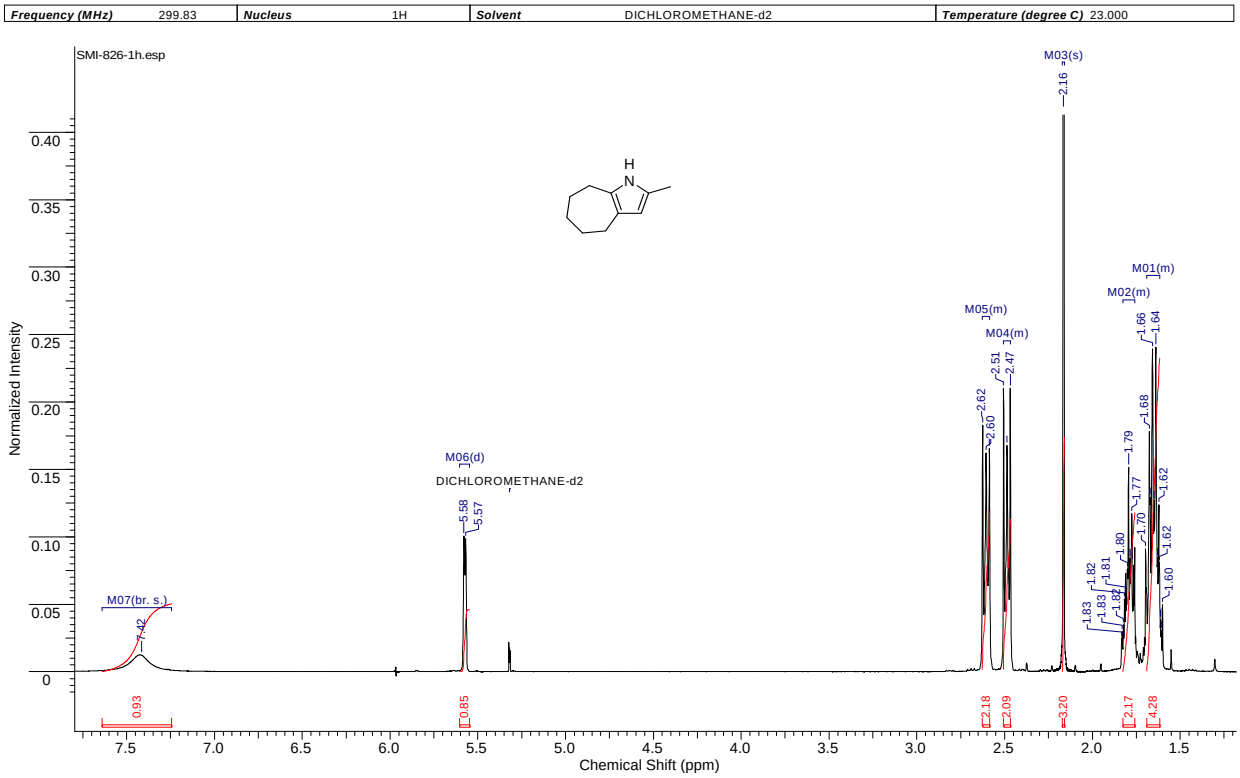

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-828-13c
HN
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

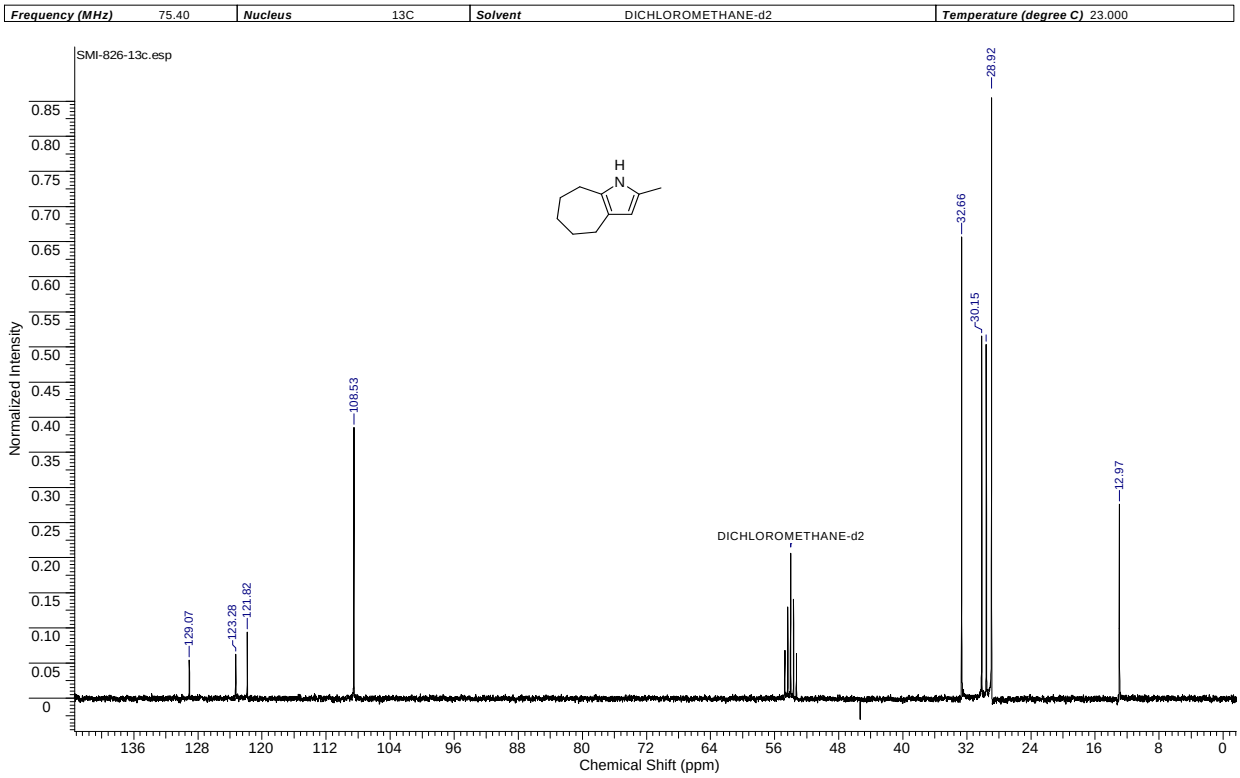

Frequency (MHz) 300.13
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 27.000
SMI-961_010000fid
M07(m)
M08(m)
M02(t)
M01(t)
M05(m)
M04(m)
M06(d)
M03(m)
M09(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

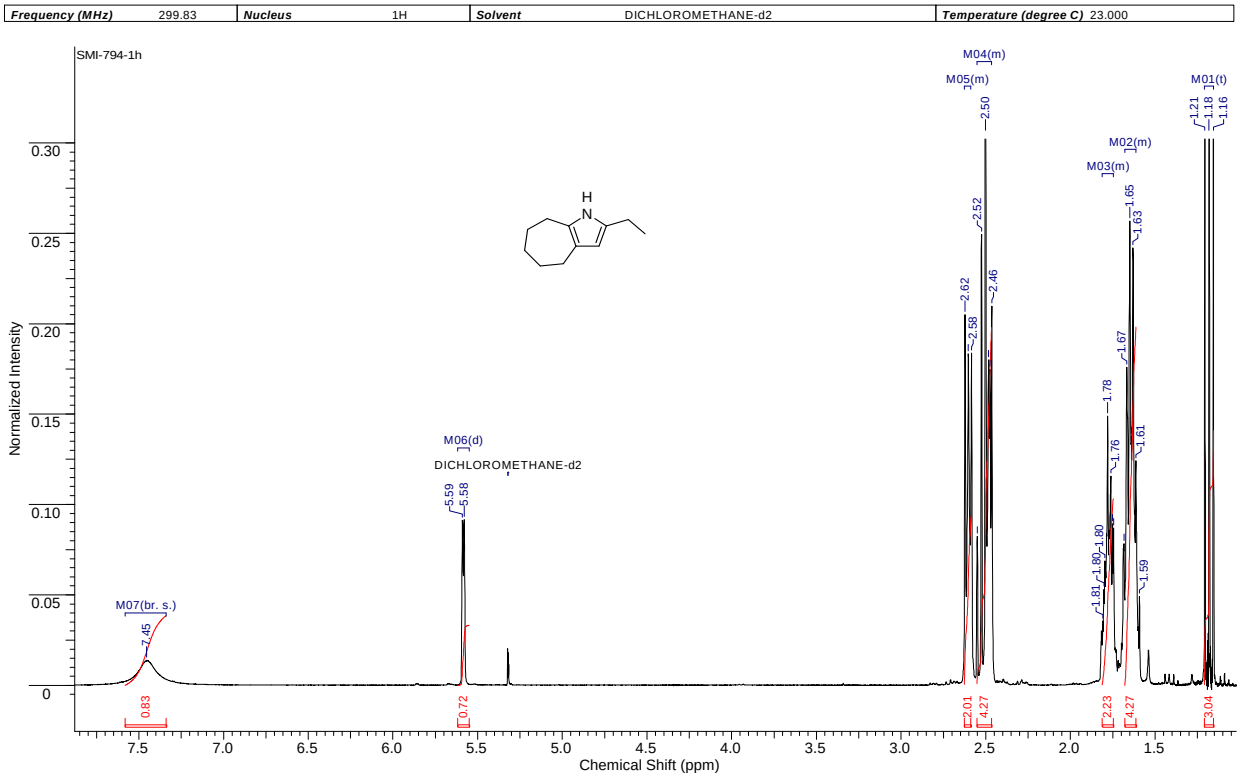

Frequency (MHz) 75.48
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 27.000
0412kh6_011000fid
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

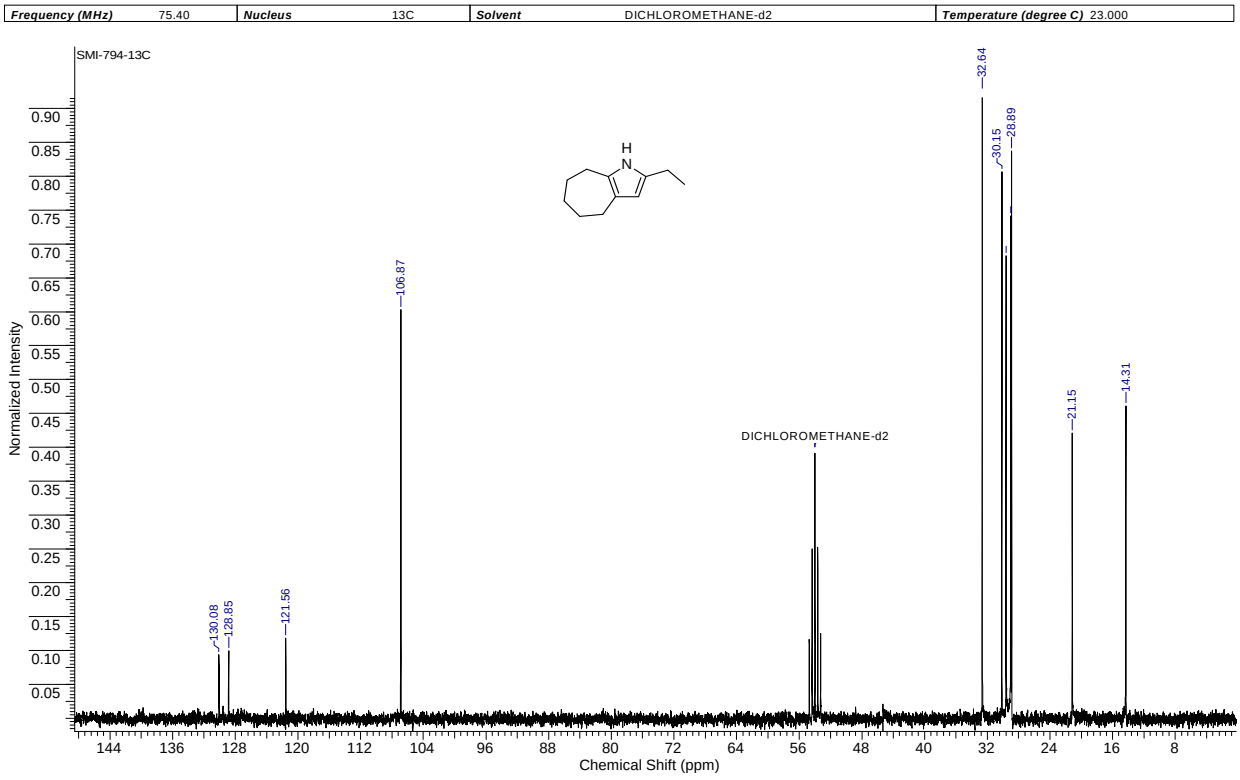

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-802-1h.esp
M04(s)
M03(m)
M02(m)
M01(m)
M10(br. s.)
M08(m)
M09(m)
M07(m)
M06(m)
M11(m)
M05(d)
DICHLOROMETHANE-d2
M12(br. s.)
Normalized Intensity
Chemical Shift (ppm)

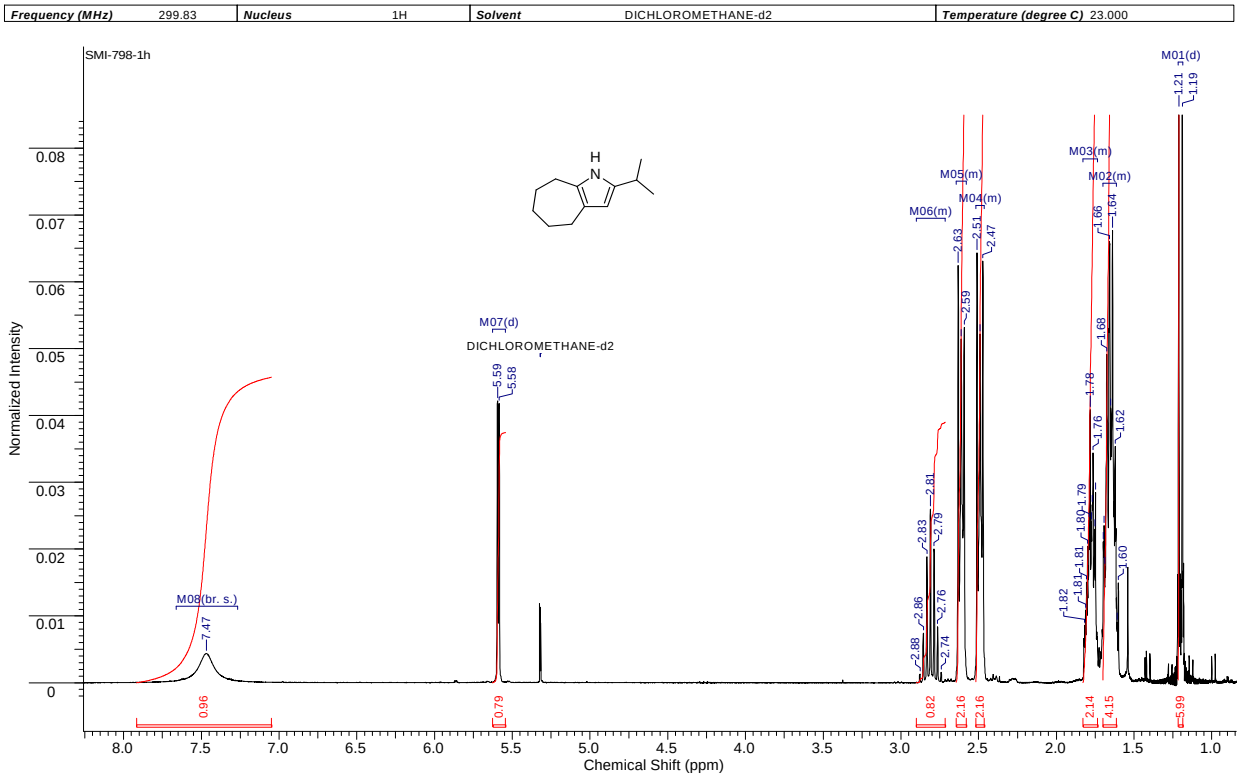

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-802-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

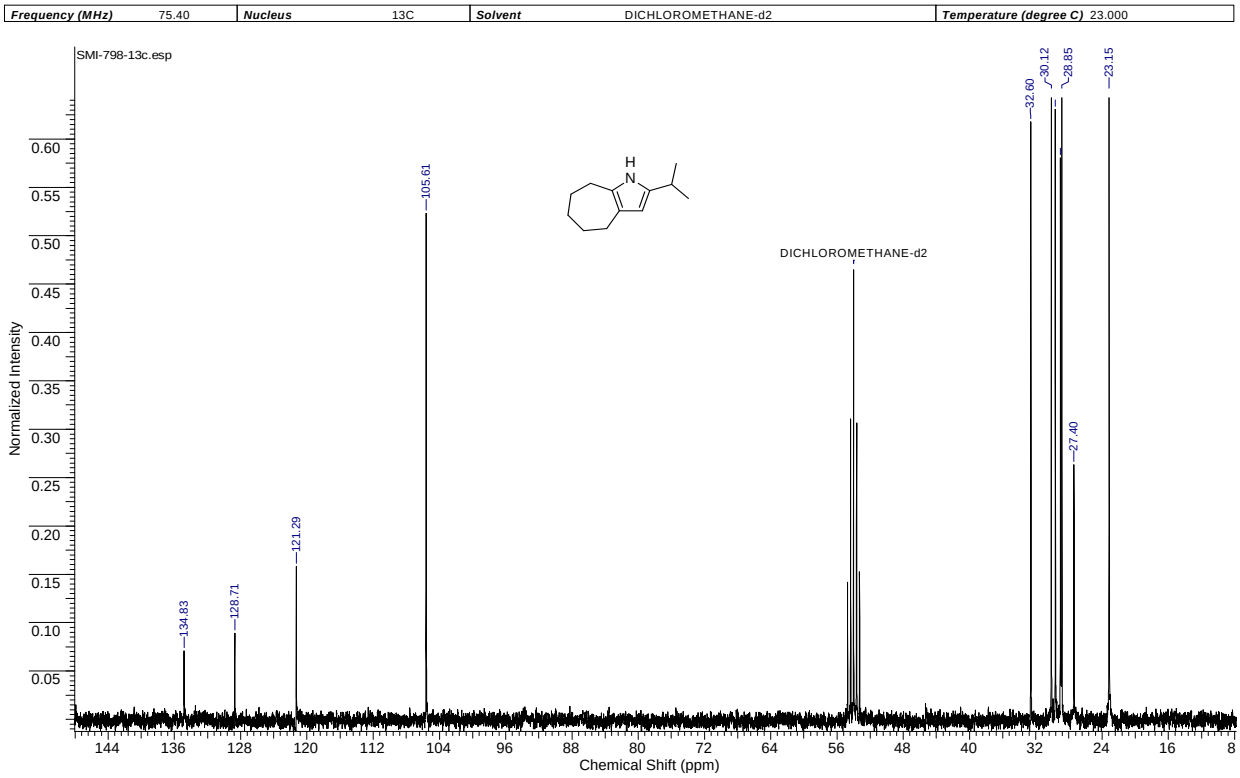

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-826-1h.esp
M03(s)
M01(m)
M02(m)
M05(m)
M04(m)
M06(d)
DICHLOROMETHANE-d2
M07(br. s.)
Normalized Intensity
Chemical Shift (ppm)

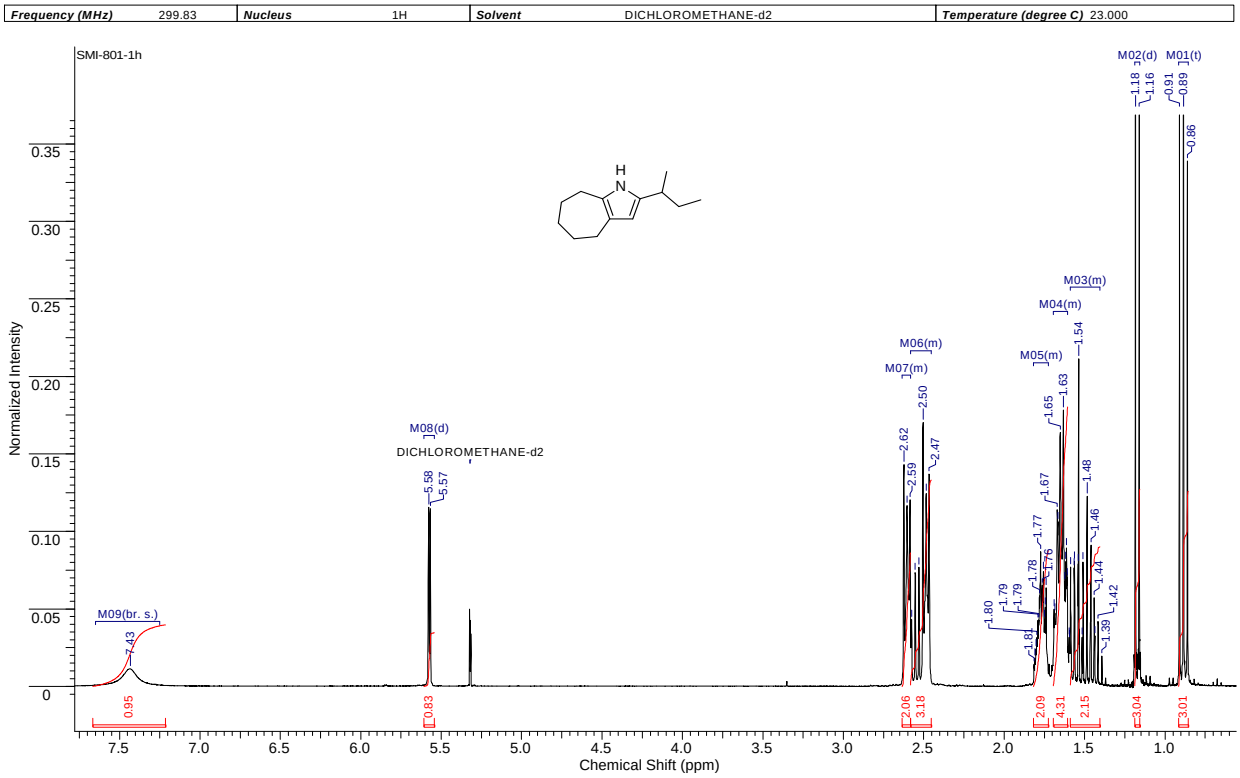

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-826-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

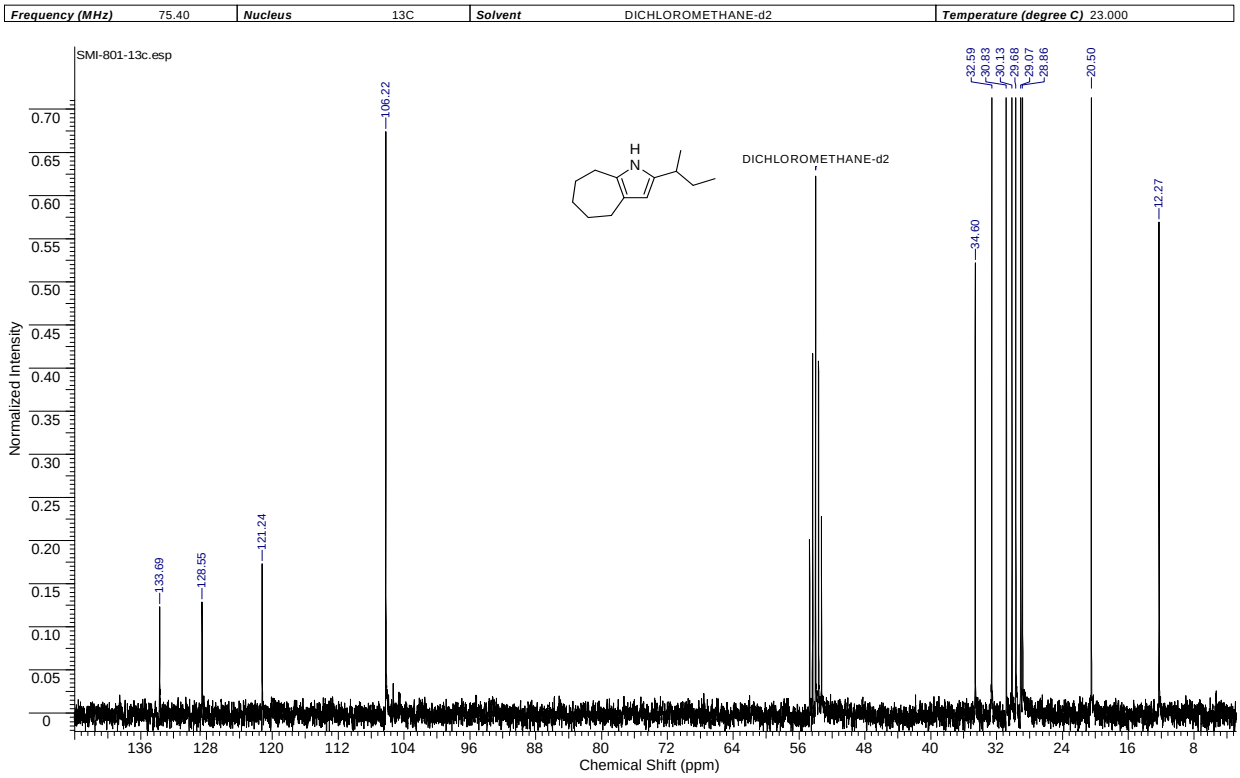

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-794-1h
Normalized Intensity
Chemical Shift (ppm)
M01(t)
M02(m)
M03(m)
M04(m)
M05(m)
M06(d)
DICHLOROMETHANE-d2
M07(br. s.)
7.45
5.59
5.58
2.62
2.58
2.52
2.50
2.46
1.81
1.80
1.78
1.76
1.67
1.65
1.63
1.61
1.59
1.21
1.18
1.16
0.83
0.72
2.01
4.27
2.23
4.27
3.04

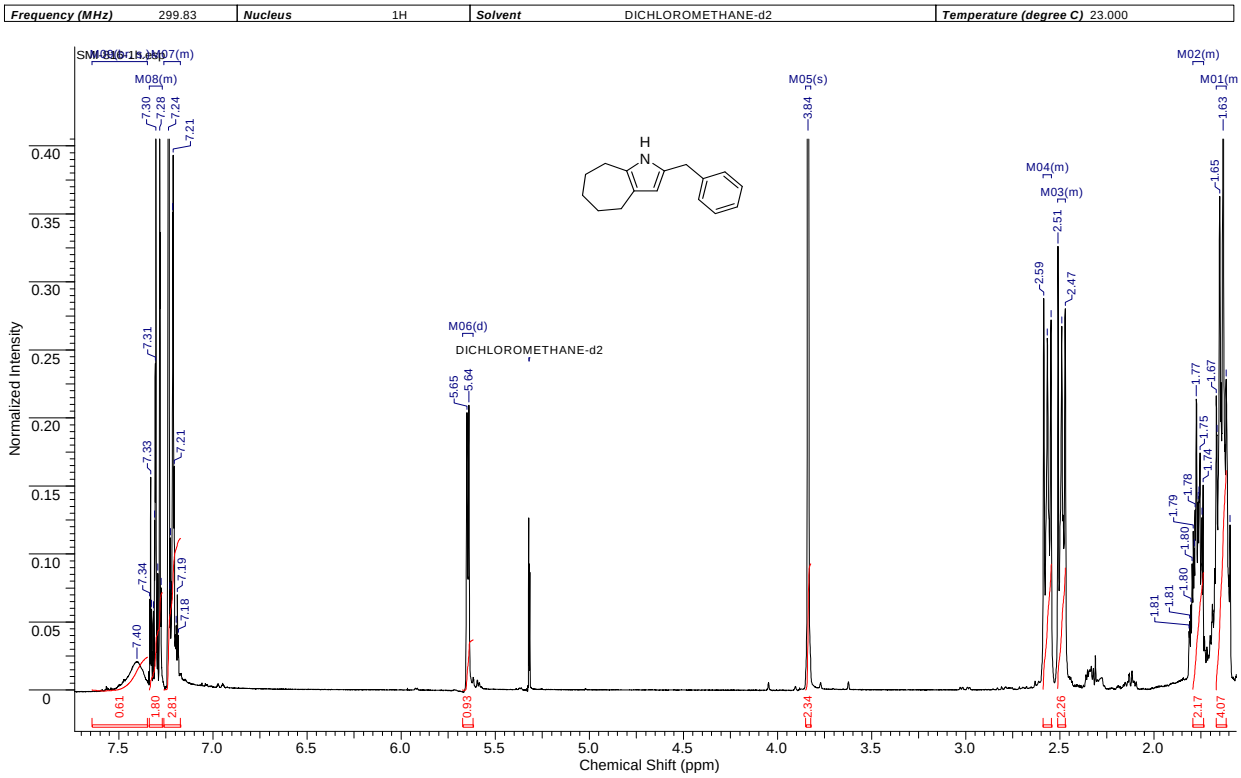

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-794-13C
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
130.08
128.85
121.56
106.87
32.64
30.15
28.89
21.15
14.31

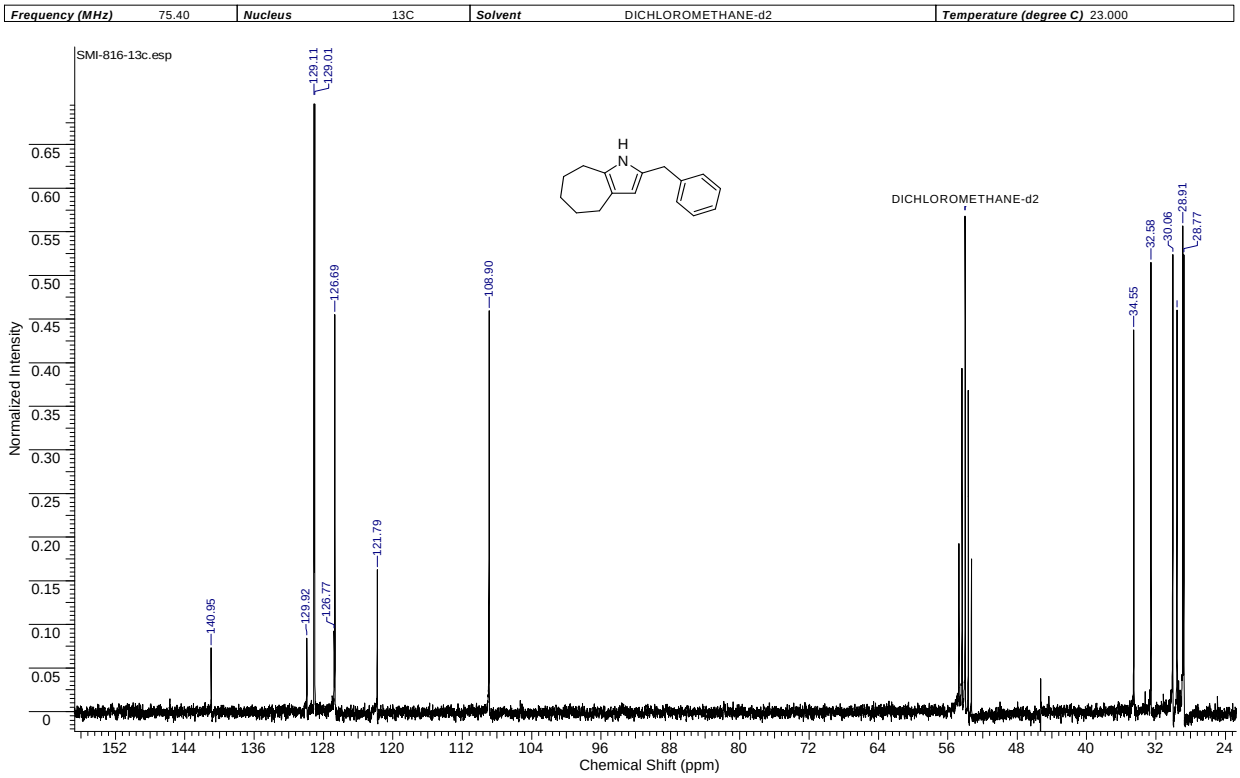

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-798-1h
Normalized Intensity
Chemical Shift (ppm)
M01(d)
M02(m)
M03(m)
M04(m)
M05(m)
M06(m)
M07(d)
DICHLOROMETHANE-d2
M08(br. s.)

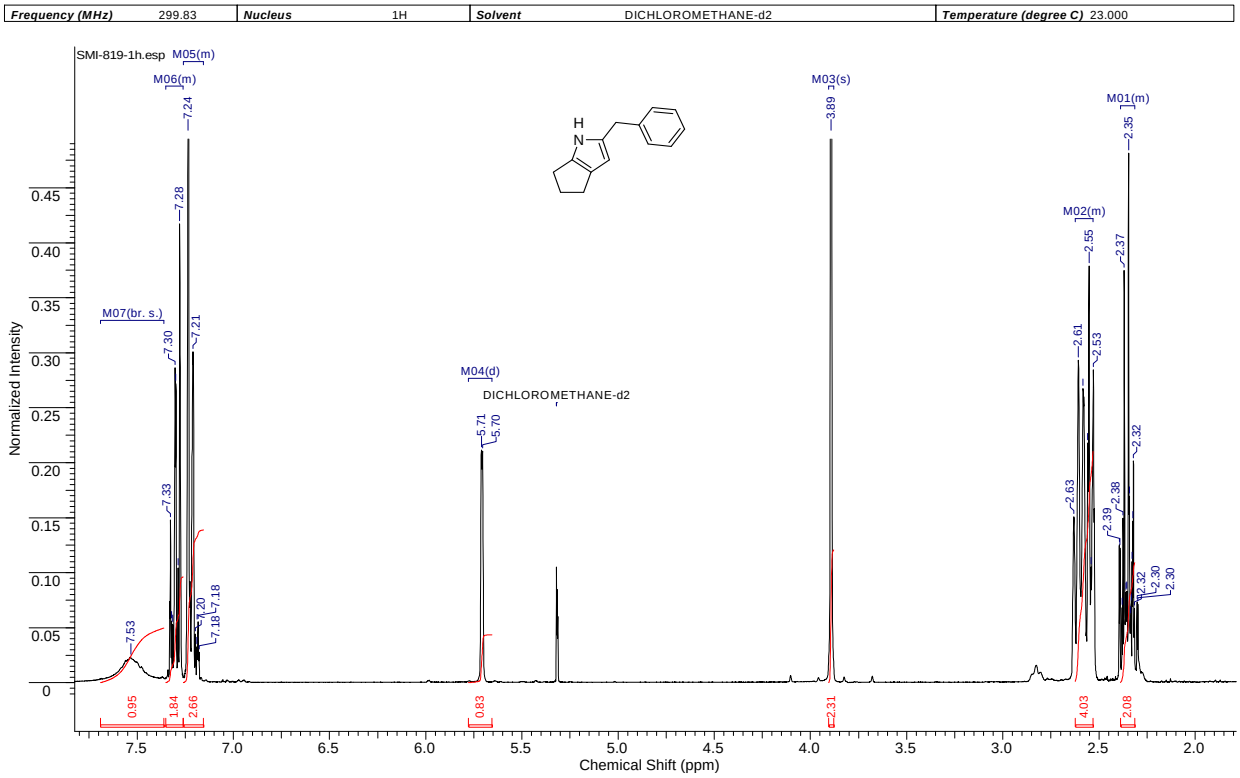

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-798-13c.esp
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2

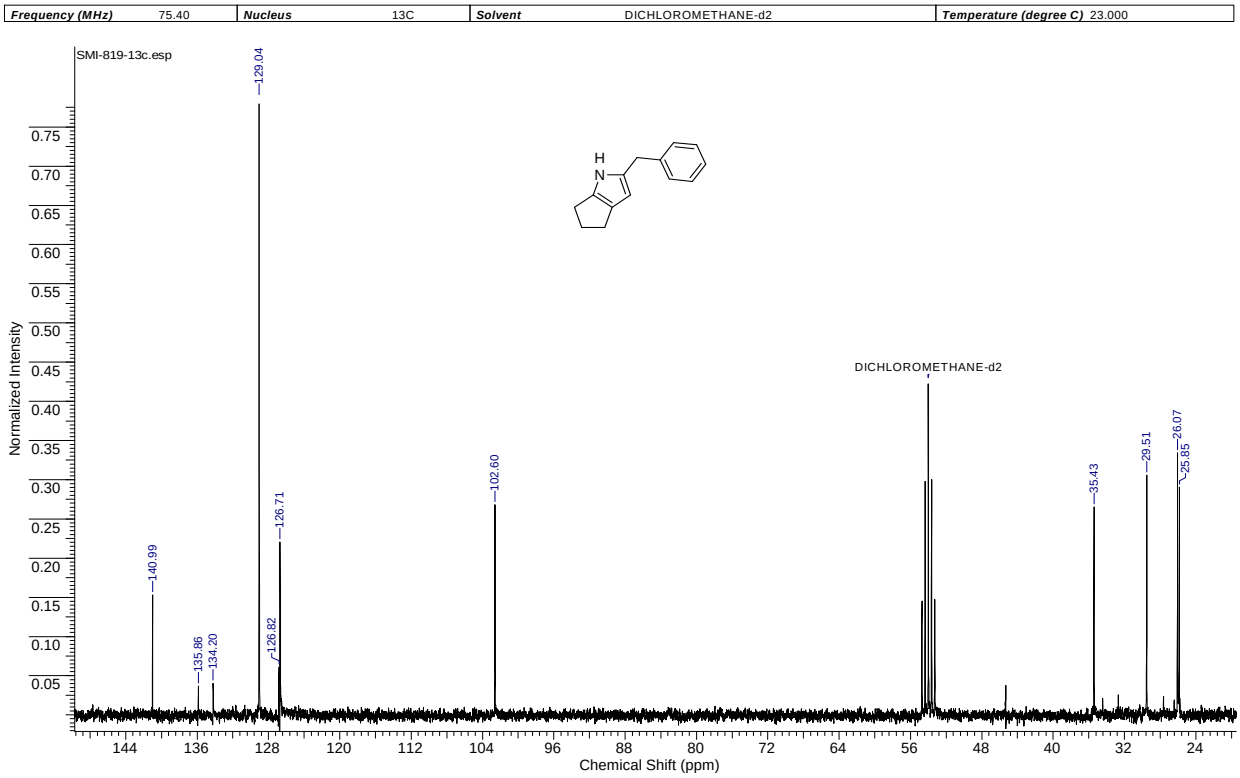

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-801-1h
Normalized Intensity
Chemical Shift (ppm)
M01(t)
M02(d)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(d)
M09(br. s.)
DICHLOROMETHANE-d2

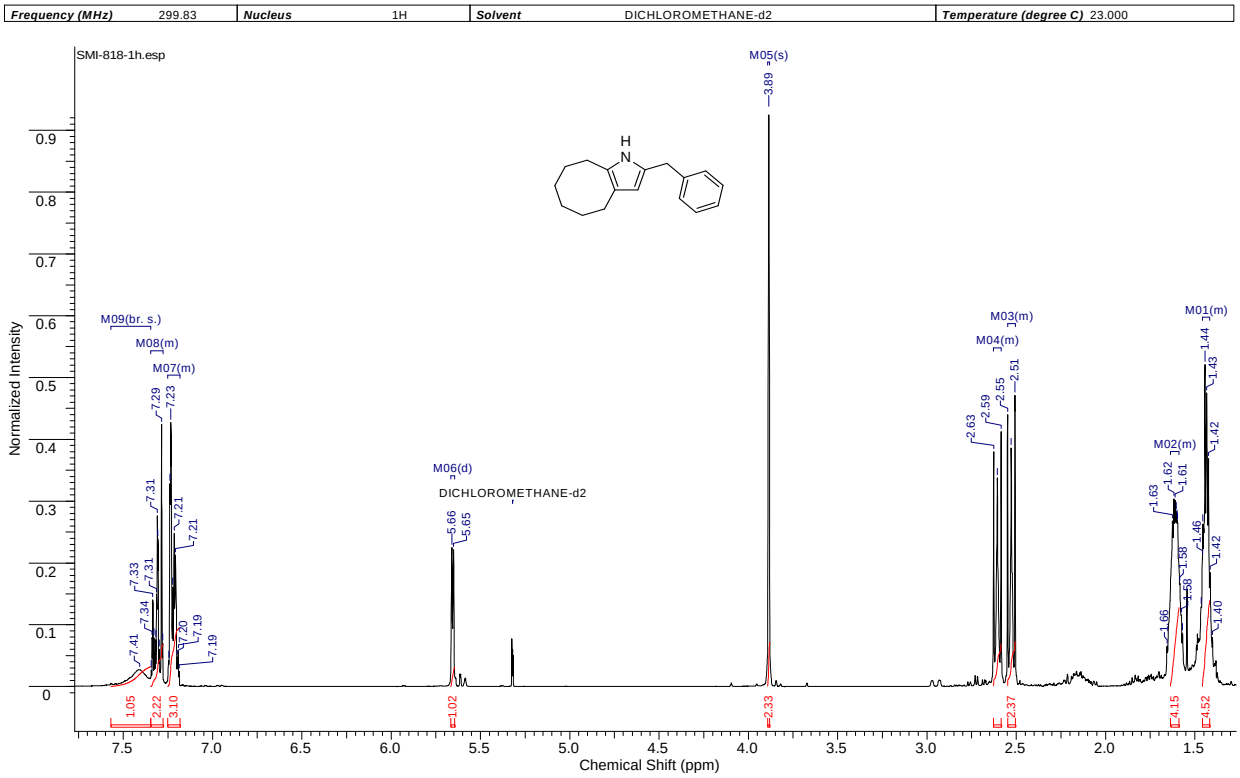

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-801-13c.esp
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2

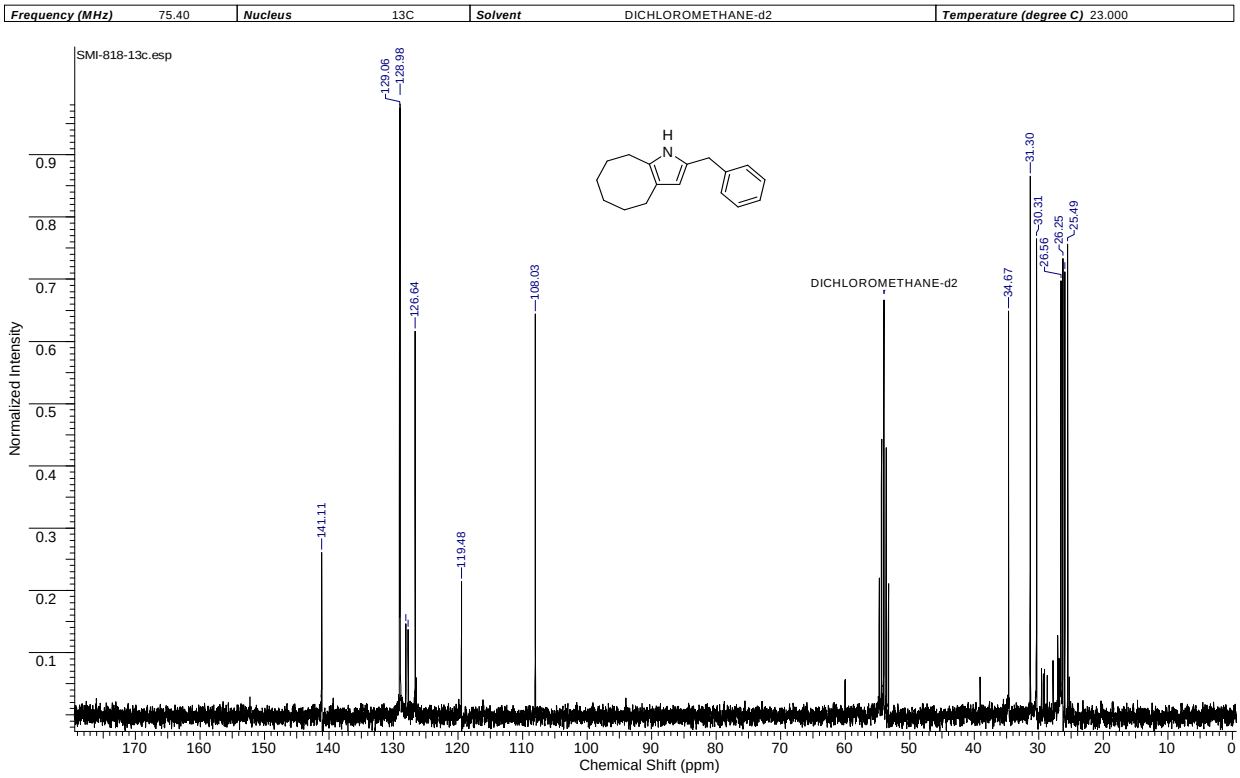

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
M08(m)
M05(s)
M02(m)
M01(m
M04(m)
M03(m)
M06(d)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

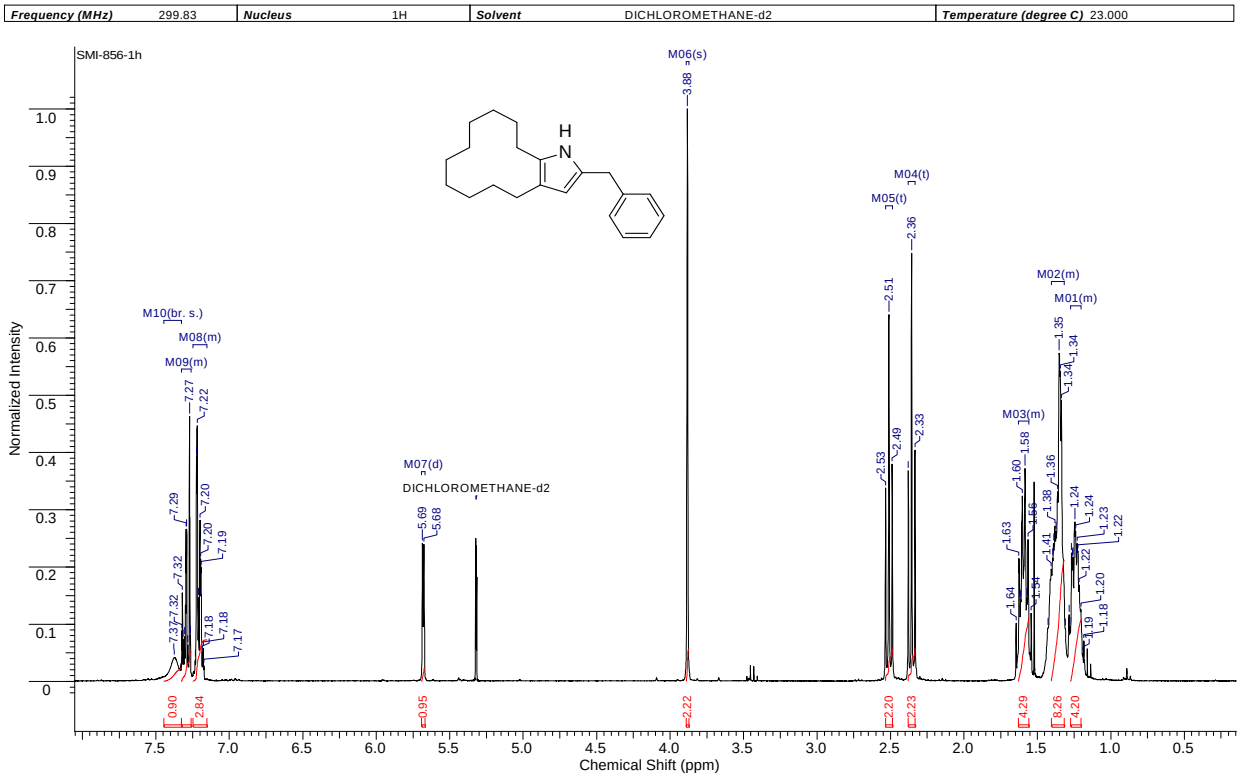

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-816-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

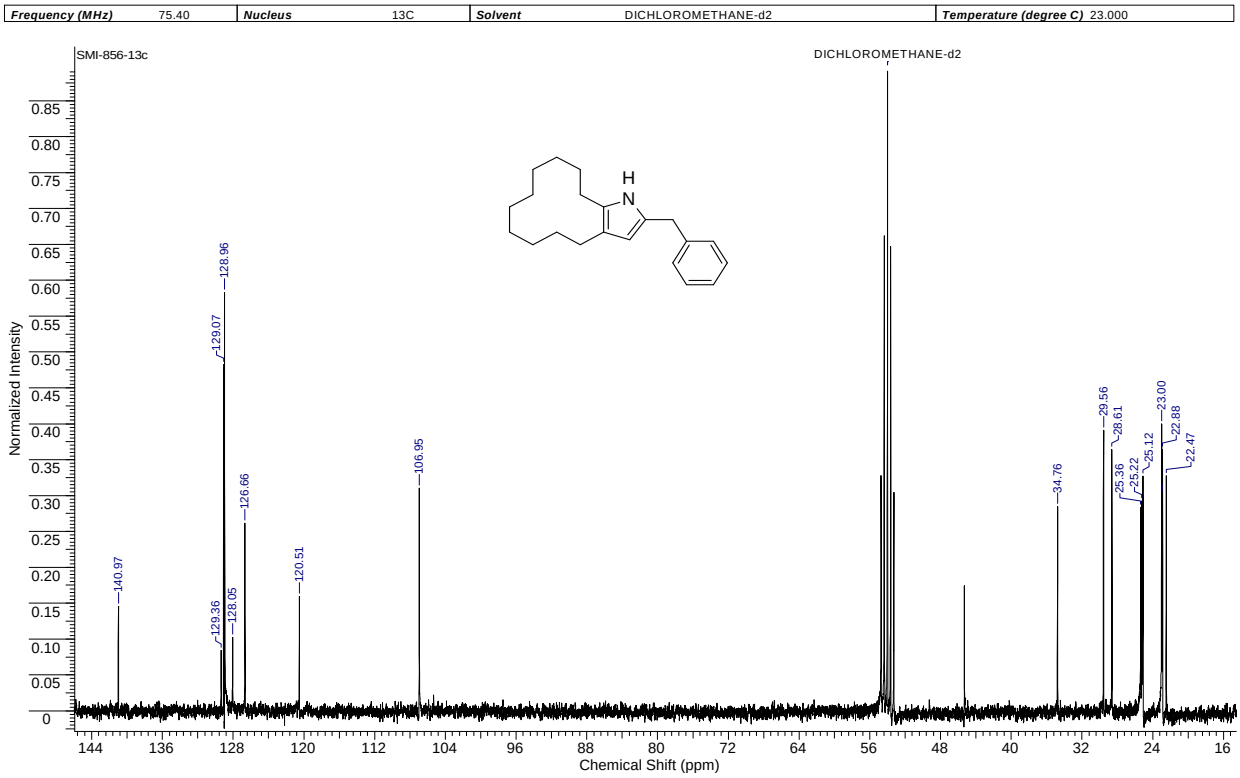

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-819-1h.esp
M05(m)
M06(m)
M03(s)
M01(m)
M02(m)
M07(br. s.)
M04(d)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-819-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

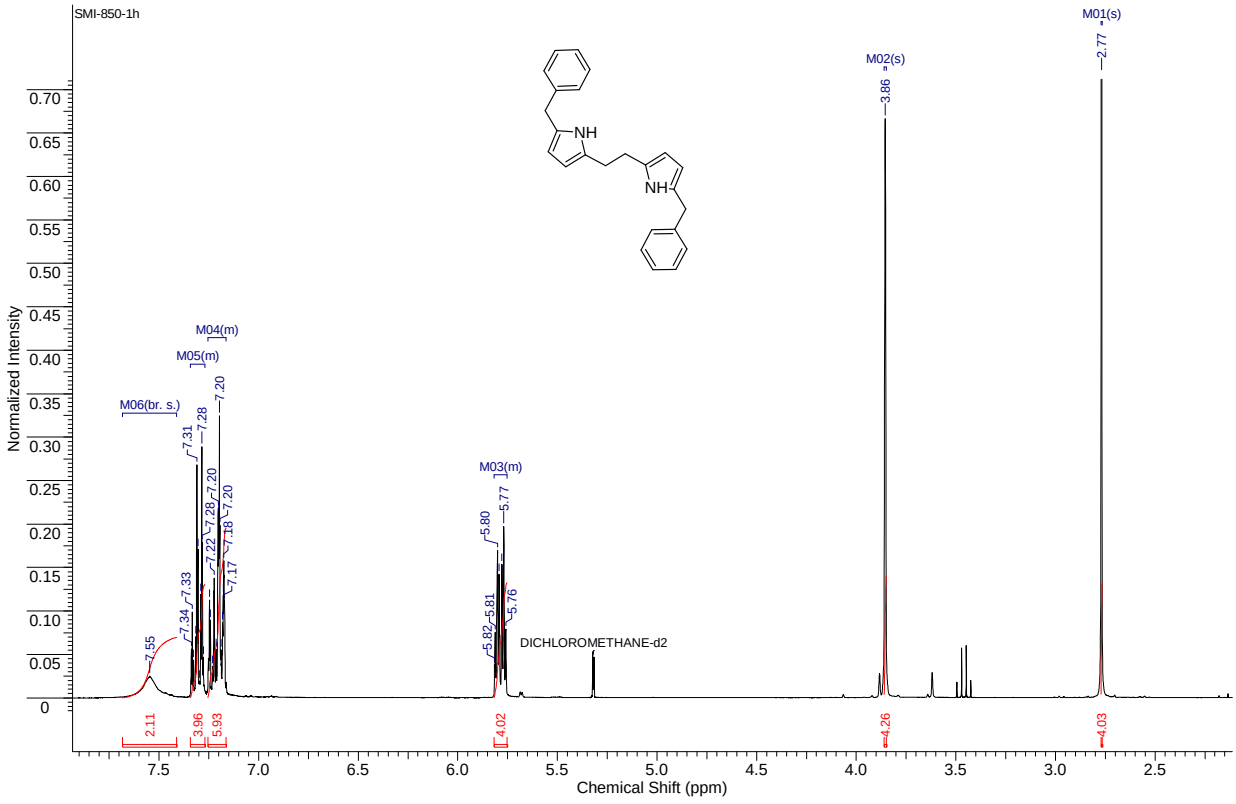

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-818-1h.esp
M09(br. s.)
M08(m)
M07(m)
M06(d)
DICHLOROMETHANE-d2
M05(s)
M04(m)
M03(m)
M02(m)
M01(m)
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-818-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

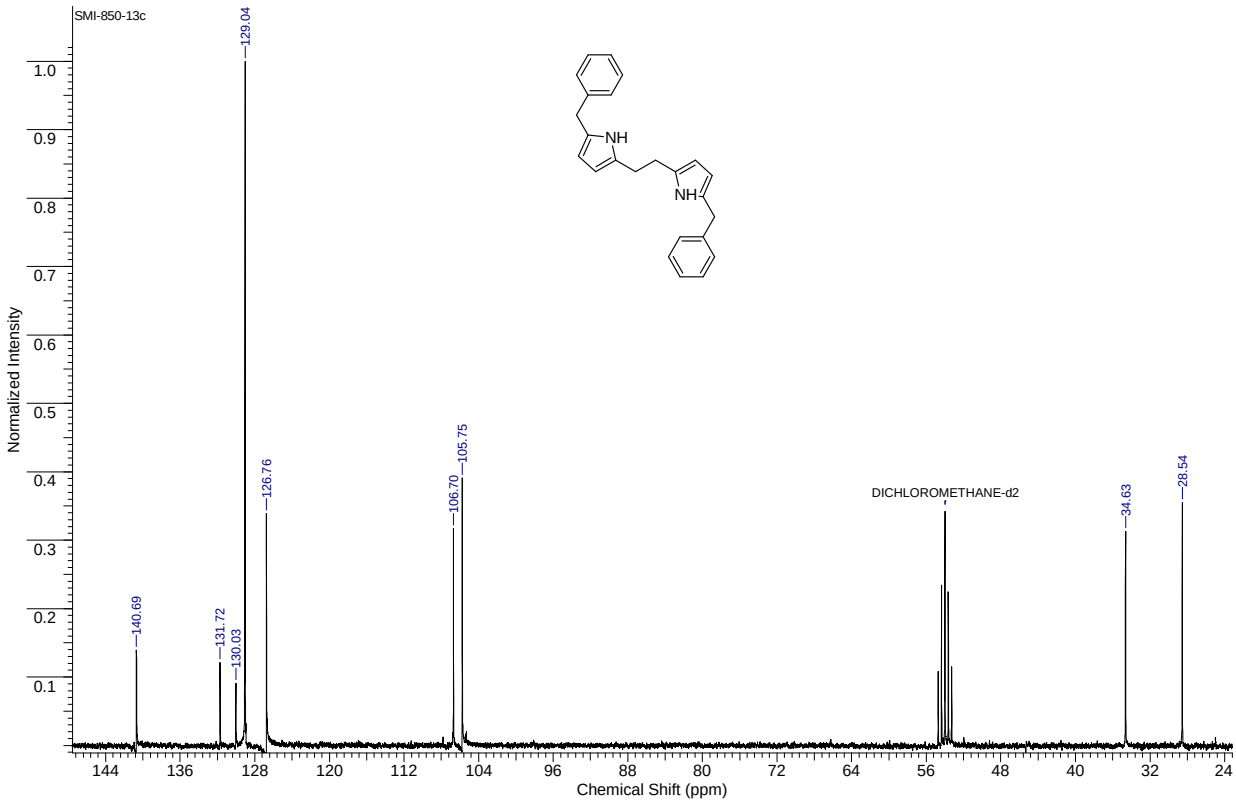

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-856-1h
M06(s)
M04(t)
M05(t)
M02(m)
M01(m)
M10(br, s.)
M08(m)
M09(m)
M03(m)
M07(d)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

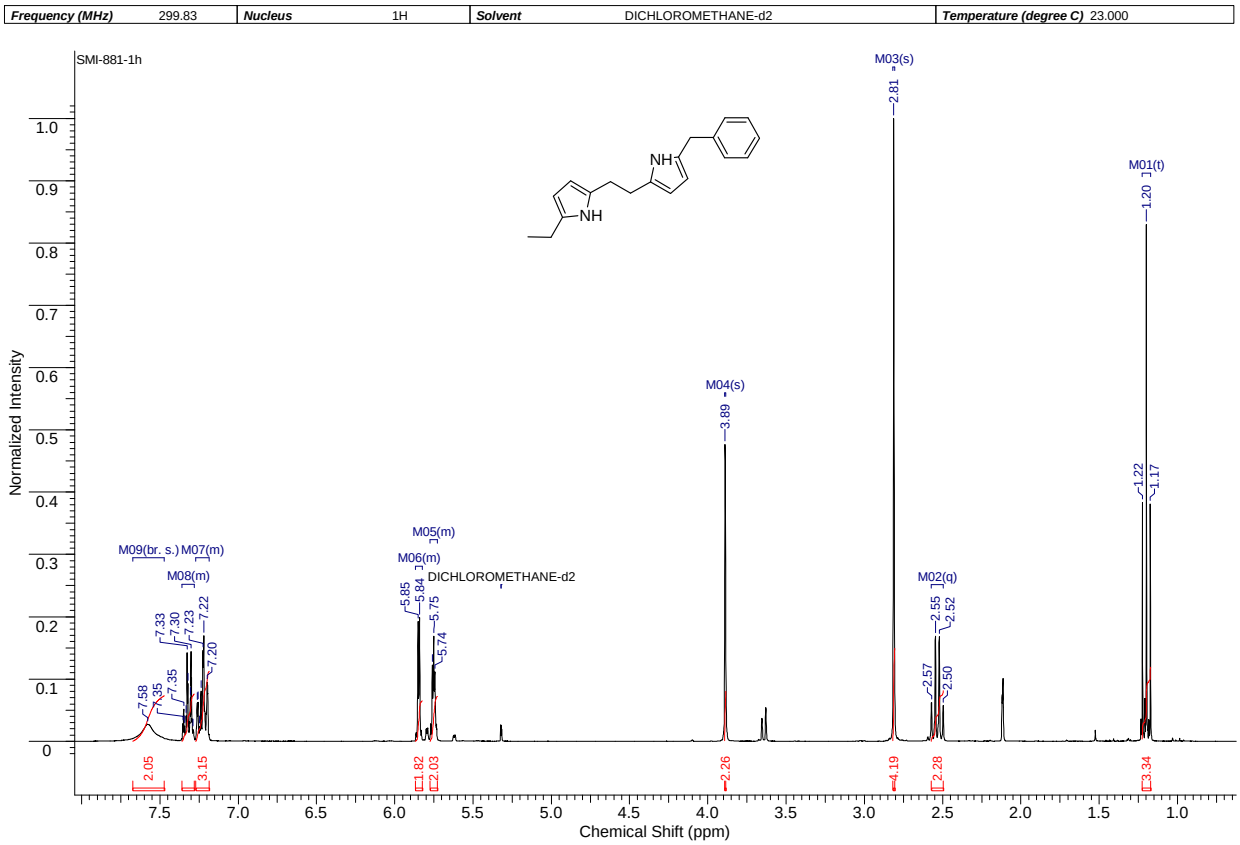

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-856-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

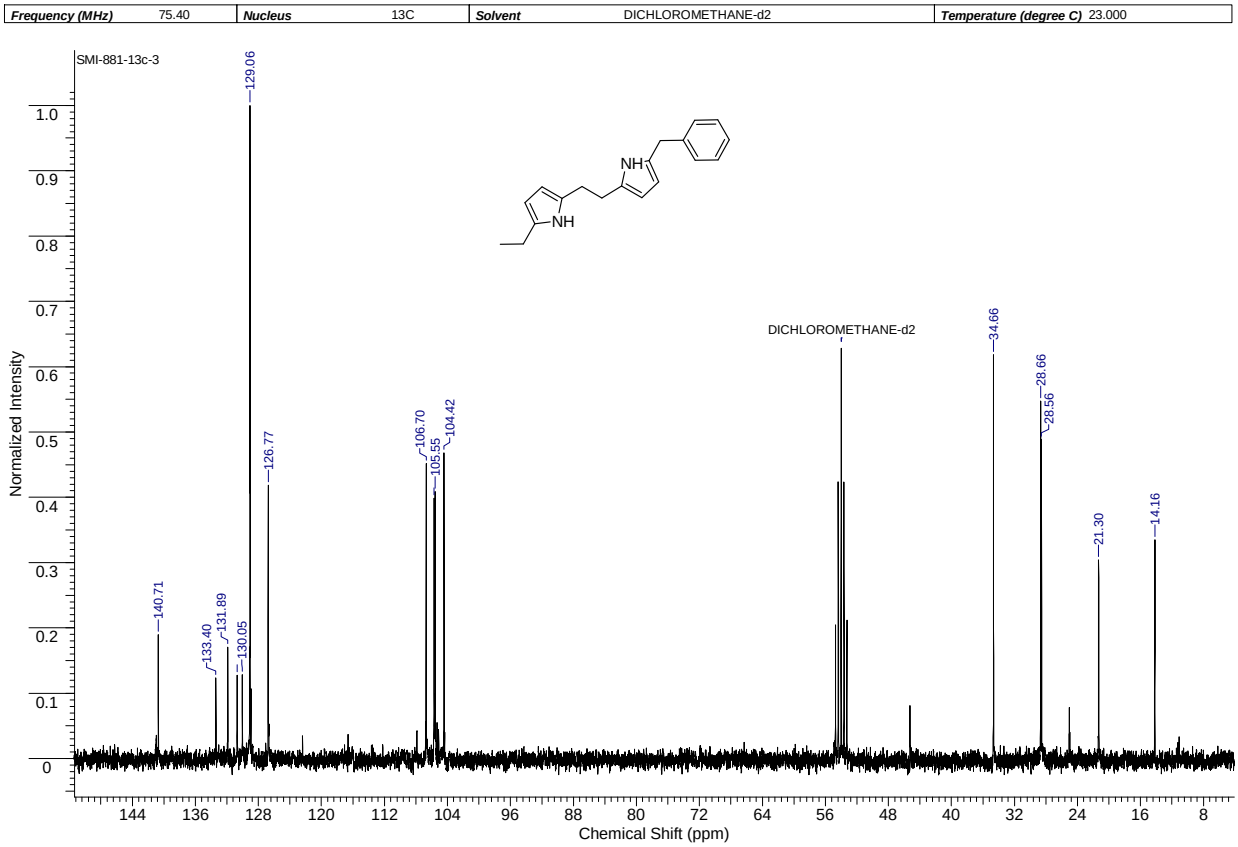
Frequency (MHz)	299.83	Nucleus	1H	Solvent	DICHLOROMETHANE-d2	Temperature (degree C)	23.000

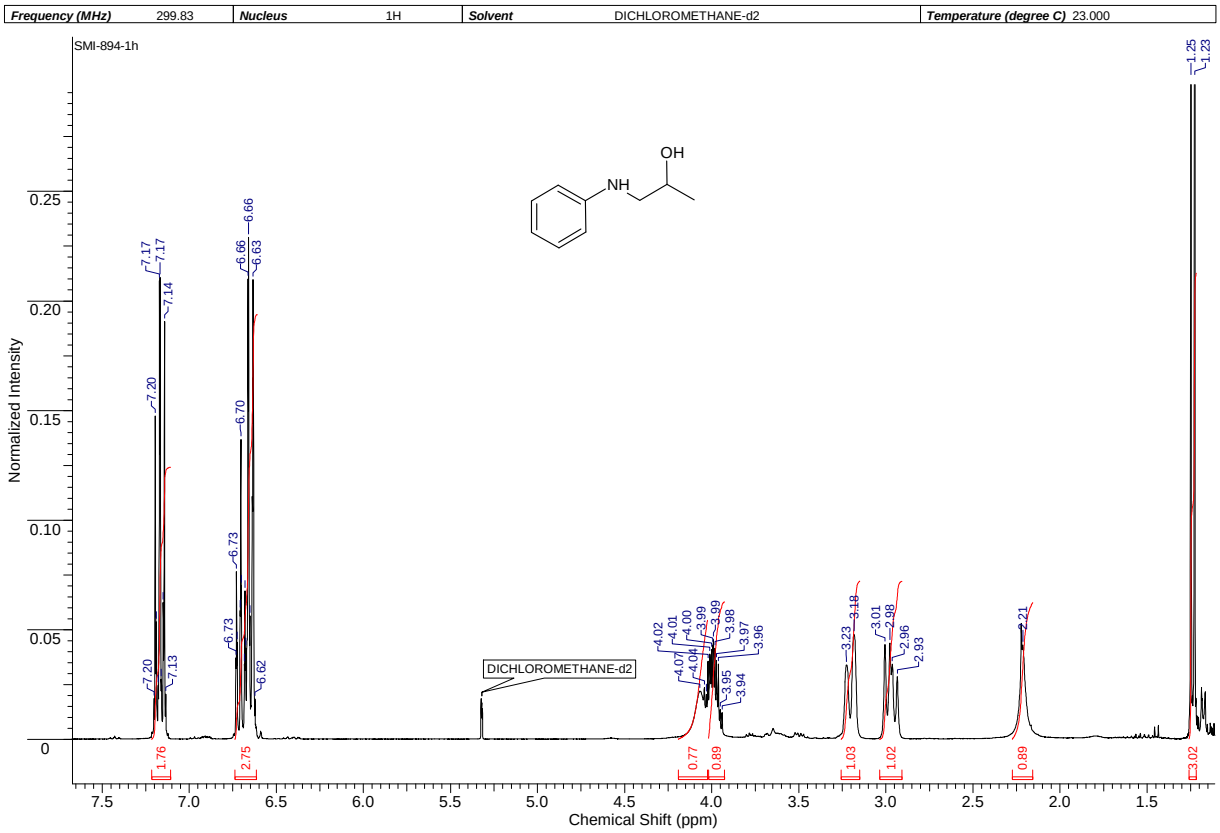


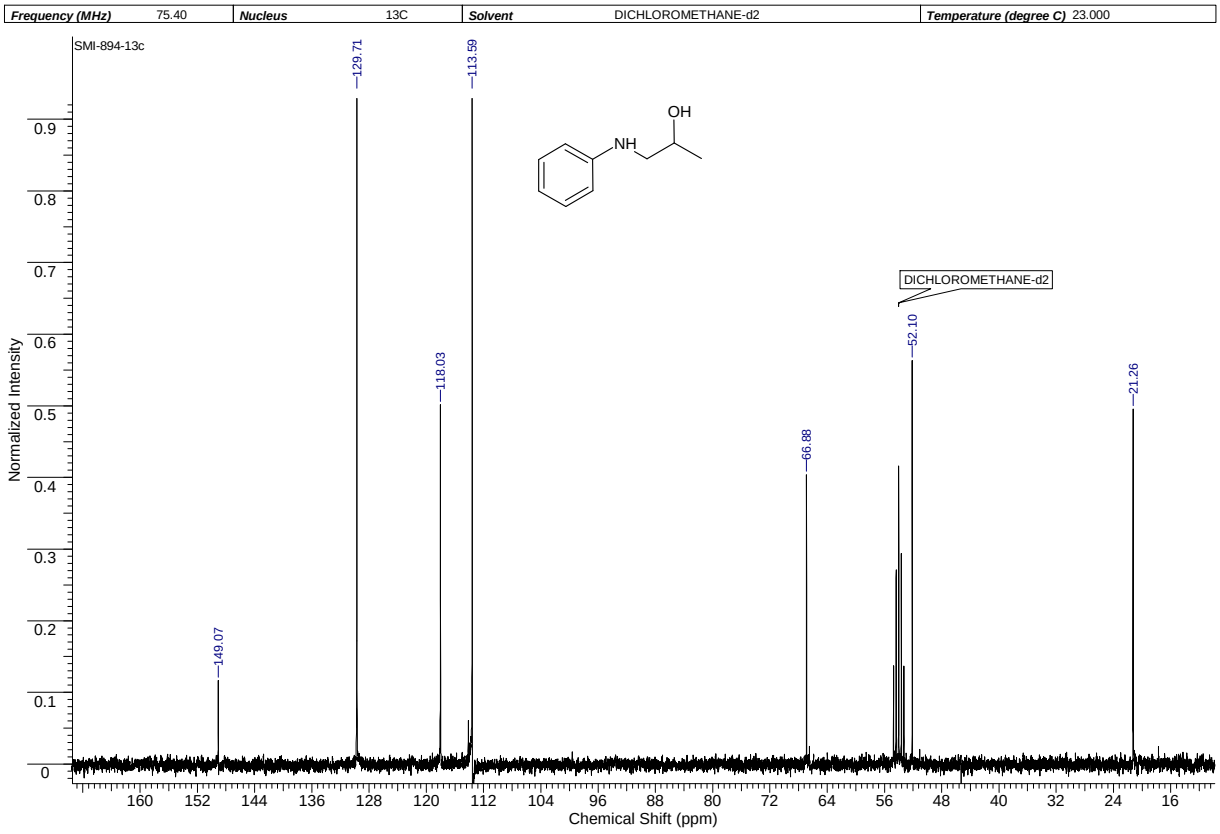
Frequency (MHz)	75.40	Nucleus	13C	Solvent	DICHLOROMETHANE-d2	Temperature (degree C)	23.000

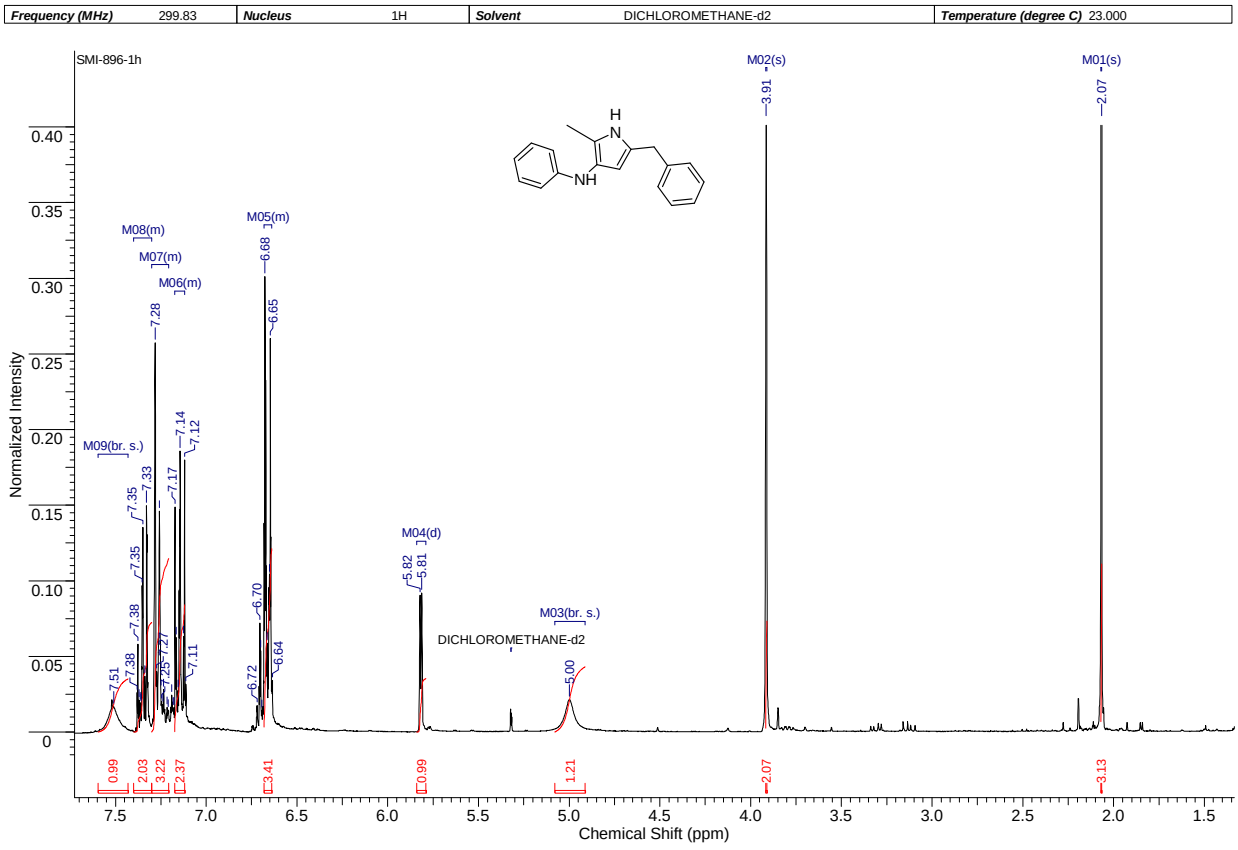


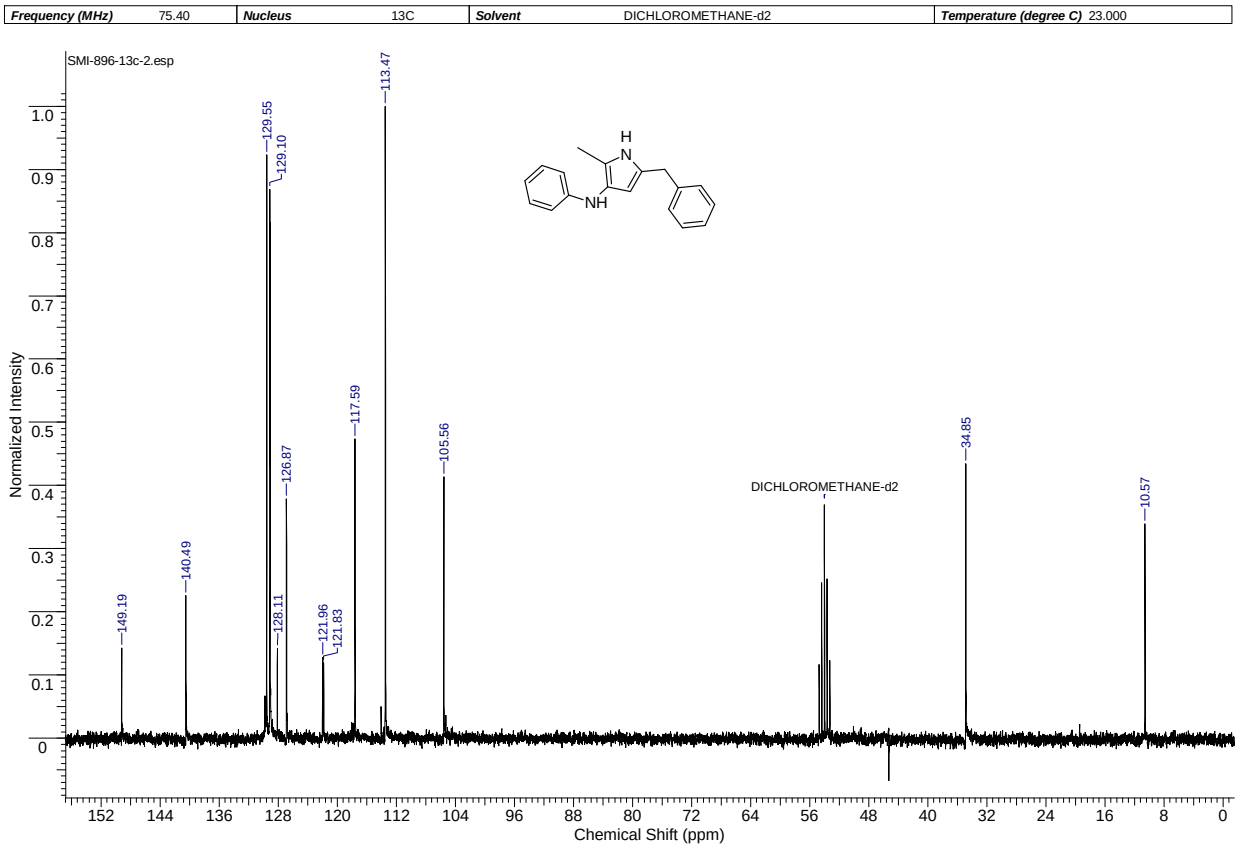

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-881-1h
M03(s)
2.81
M01(t)
1.20
M04(s)
3.89
M05(m)
M06(m)
M09(br. s.)
M07(m)
M08(m)
DICHLOROMETHANE-d2
M02(q)
1.22
1.17
Normalized Intensity
Chemical Shift (ppm)

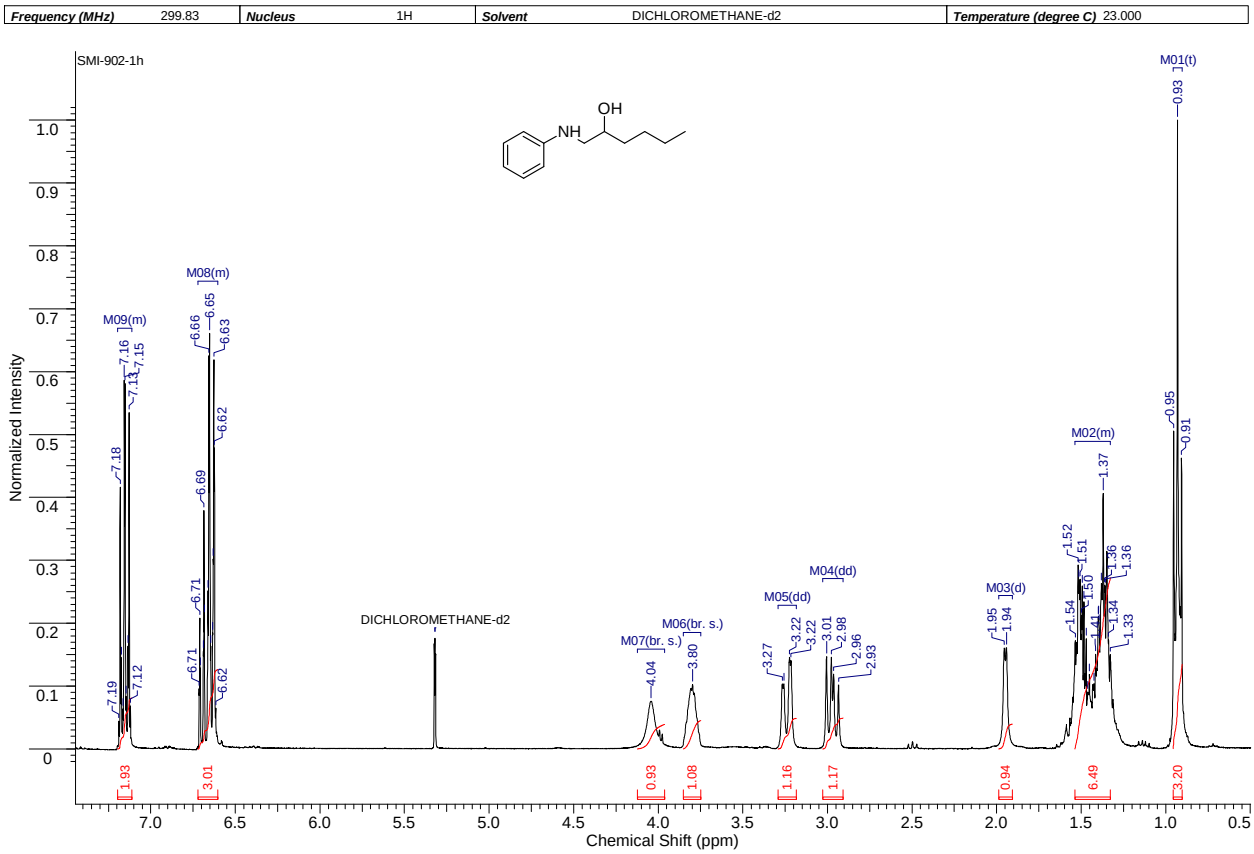

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-881-13c-3
129.06
126.77
106.70
105.55
104.42
140.71
133.40
131.89
130.05
DICHLOROMETHANE-d2
34.66
28.66
28.56
21.30
14.16
Normalized Intensity
Chemical Shift (ppm)

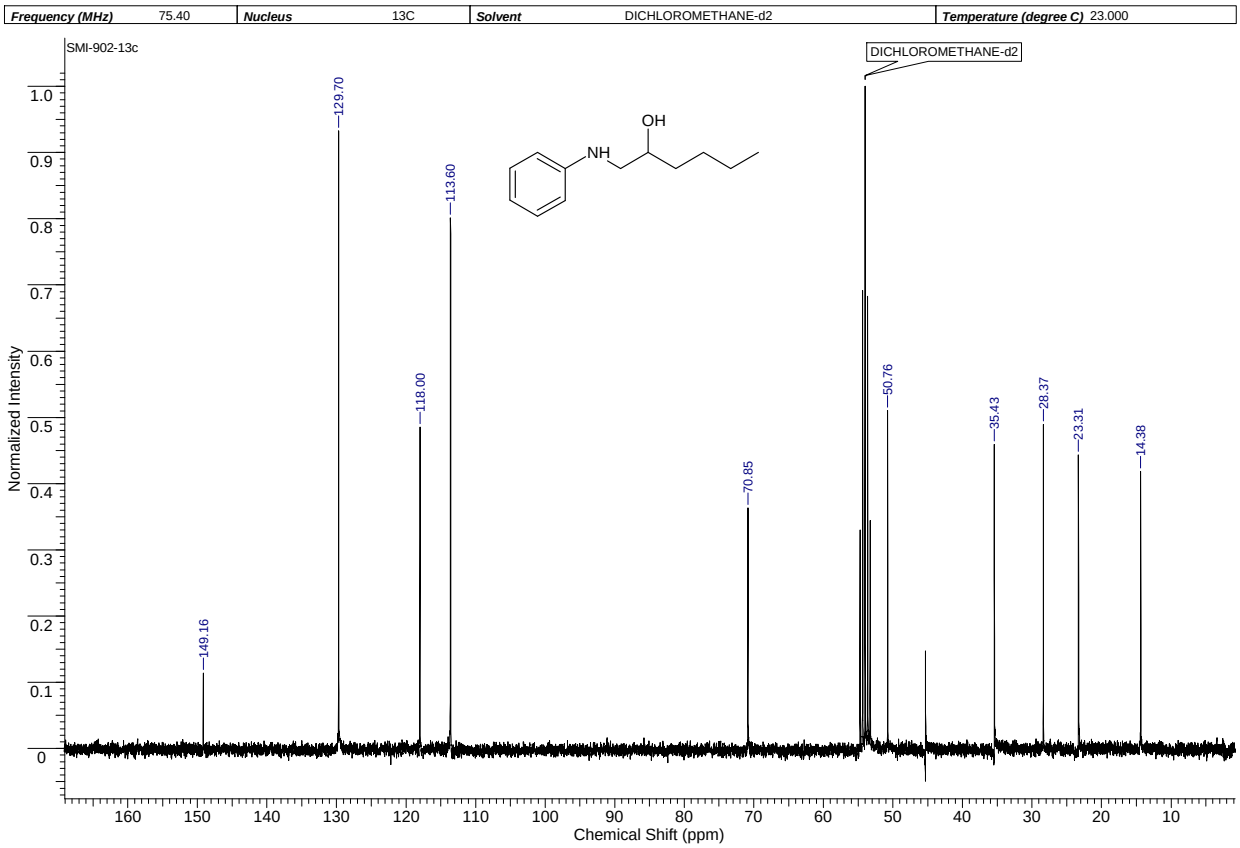

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-894-1h
OH
NH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

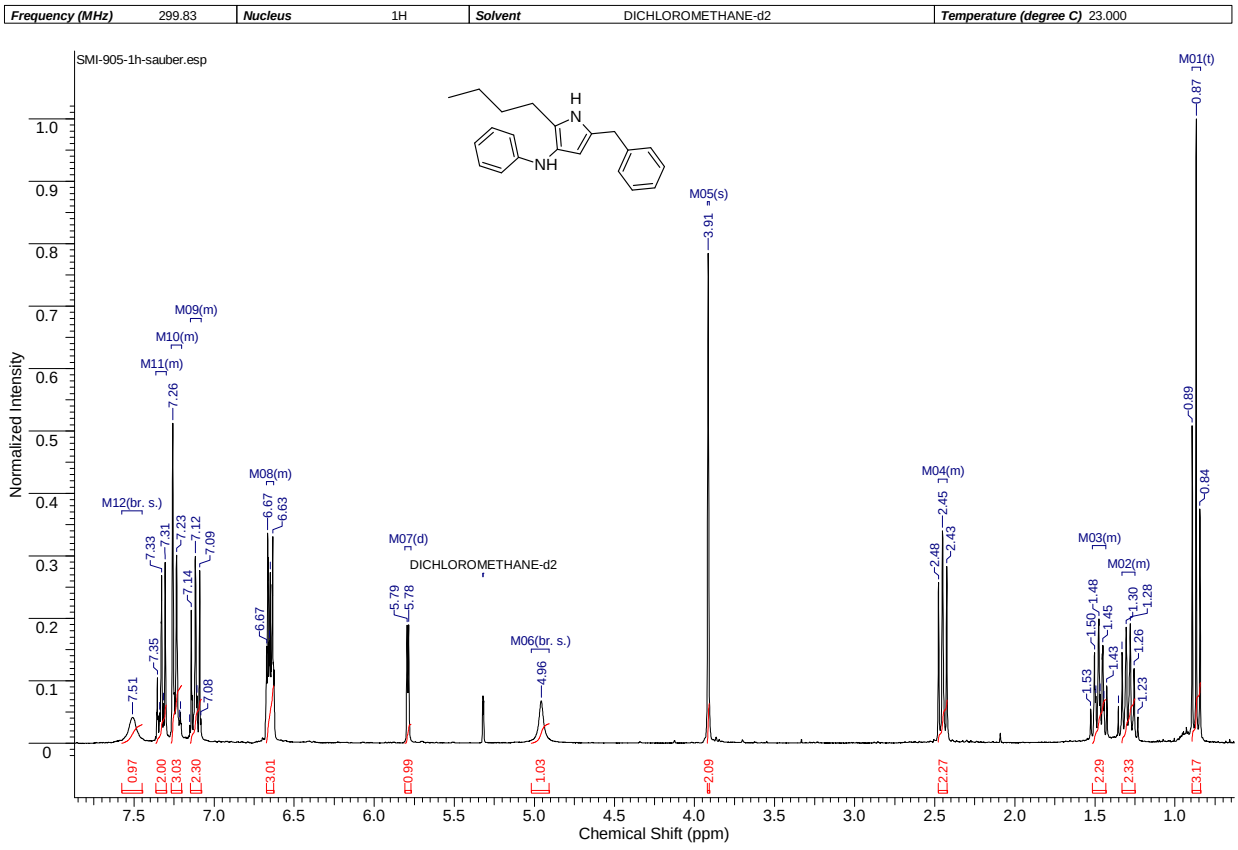

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-894-13c
OH
NH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

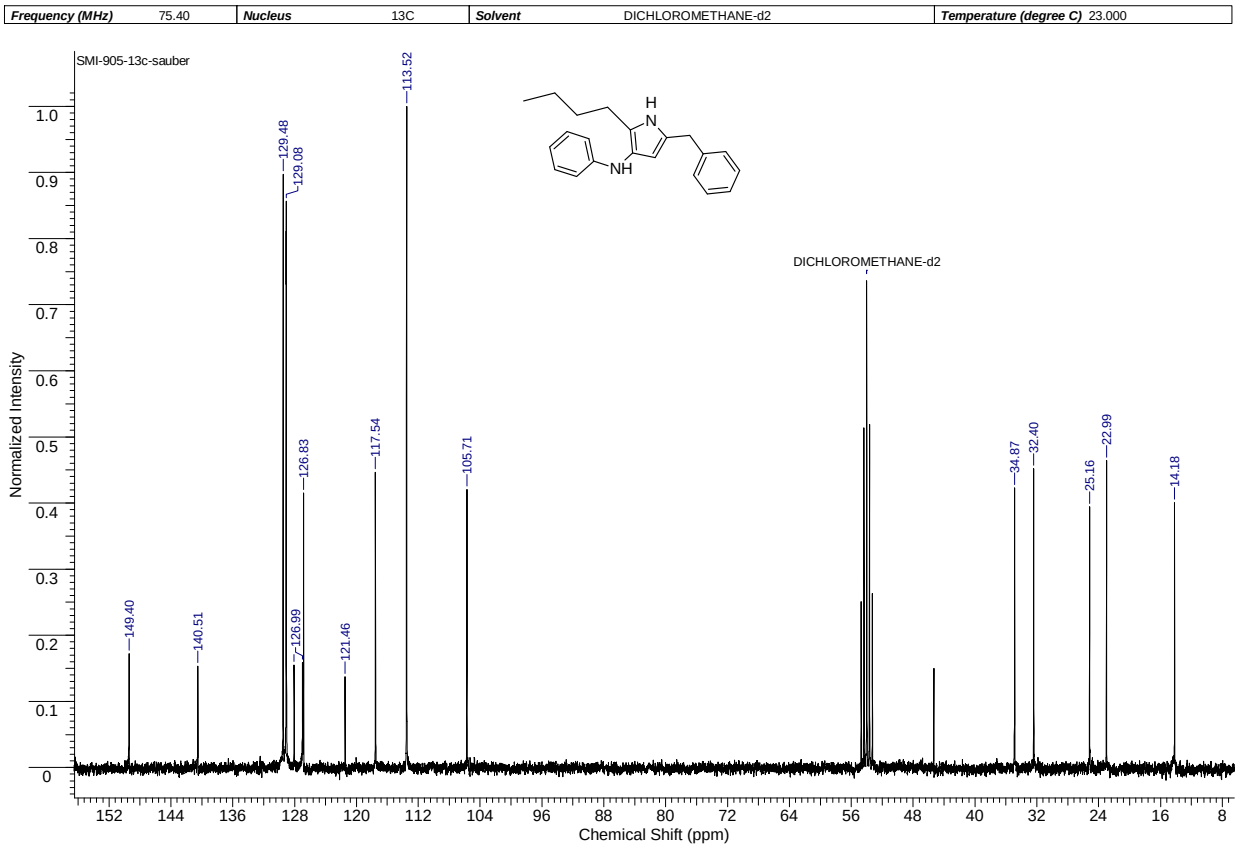

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-896-1h
M02(s)
M01(s)
M08(m)
M07(m)
M06(m)
M05(m)
M09(br. s.)
M04(d)
M03(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

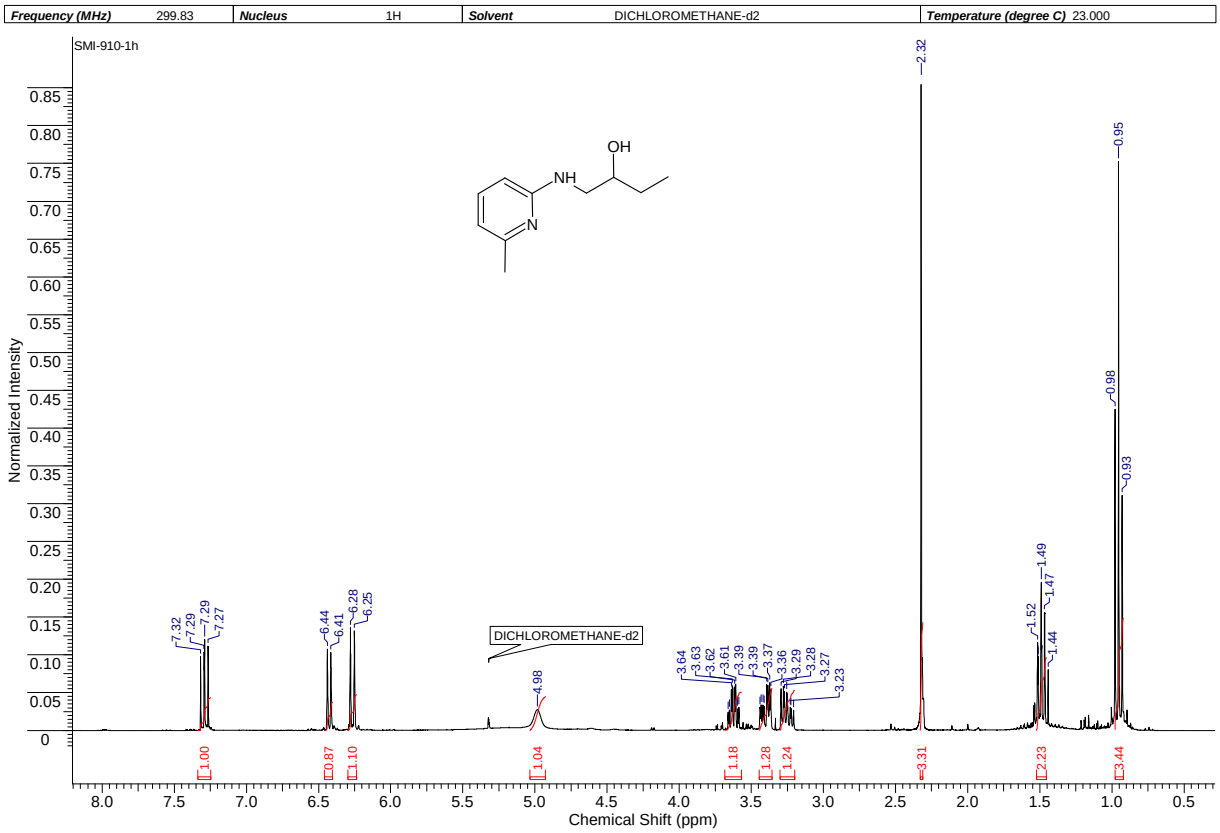

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-896-13c-2.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

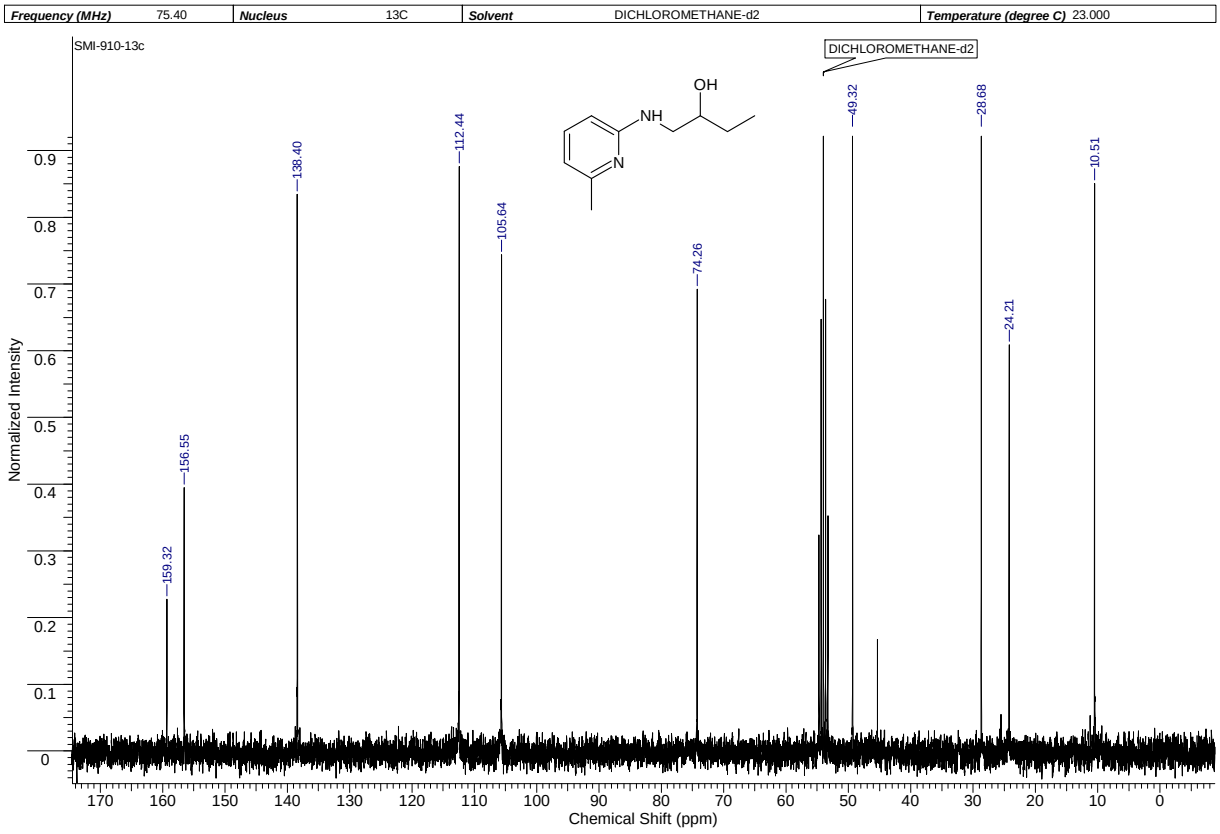

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-902-1h
OH
NH
M01(t)
M02(m)
M03(d)
M04(dd)
M05(dd)
M06(br. s.)
M07(br. s.)
M08(m)
M09(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

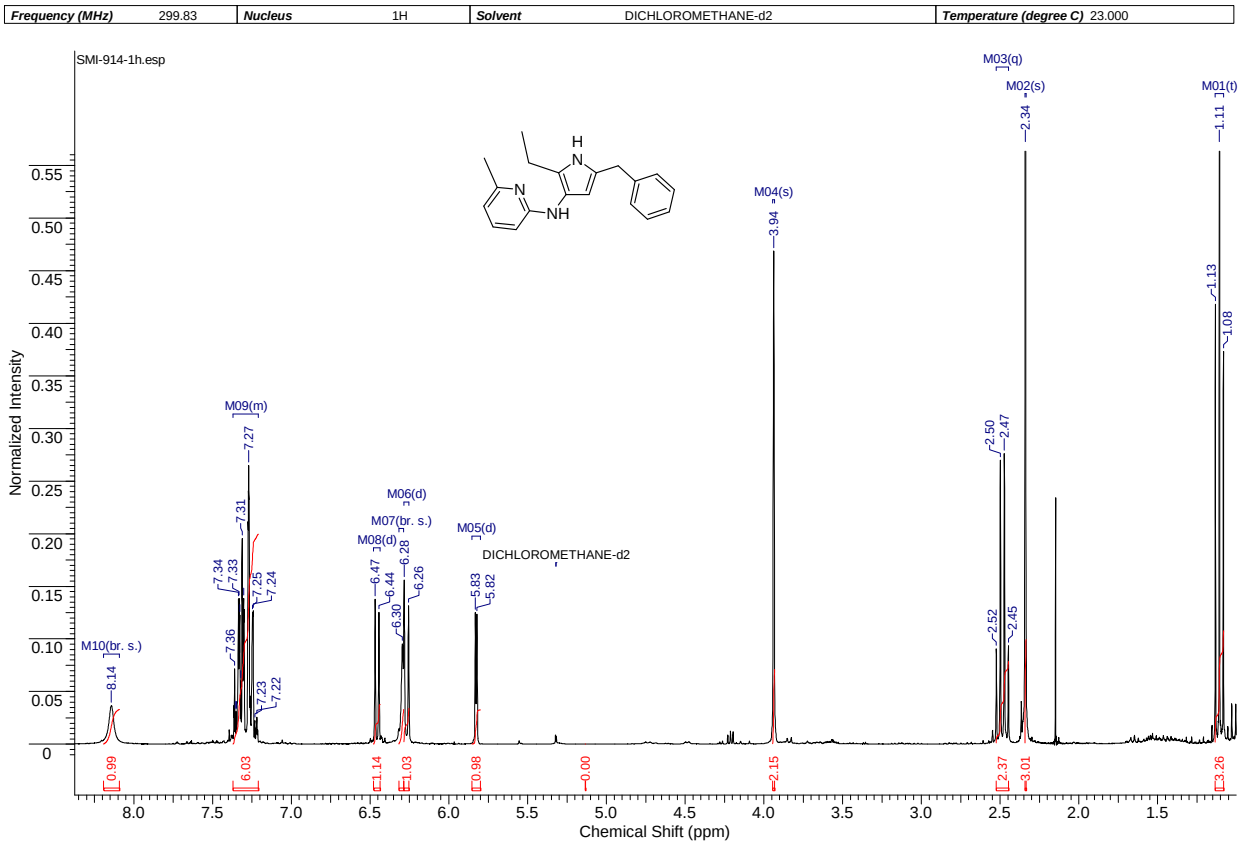

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-902-13c
OH
NH
DICHLOROMETHANE-d2
129.70
118.00
113.60
70.85
50.76
35.43
28.37
23.31
14.38
149.16
Normalized Intensity
Chemical Shift (ppm)

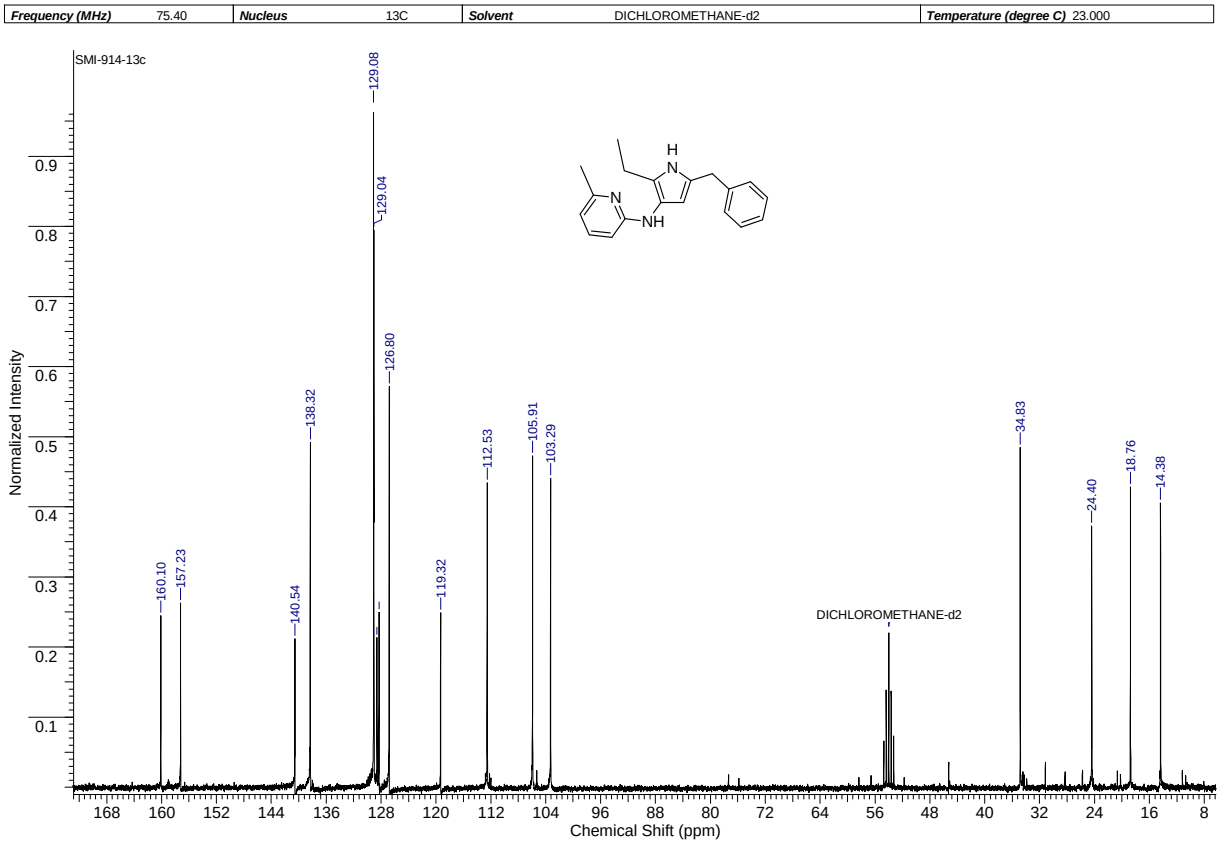

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-905-1h-sauber.esp
Normalized Intensity
Chemical Shift (ppm)
M01(t)
M02(m)
M03(m)
M04(m)
M05(s)
M06(br. s.)
M07(d)
M08(m)
M09(m)
M10(m)
M11(m)
M12(br. s.)
DICHLOROMETHANE-d2

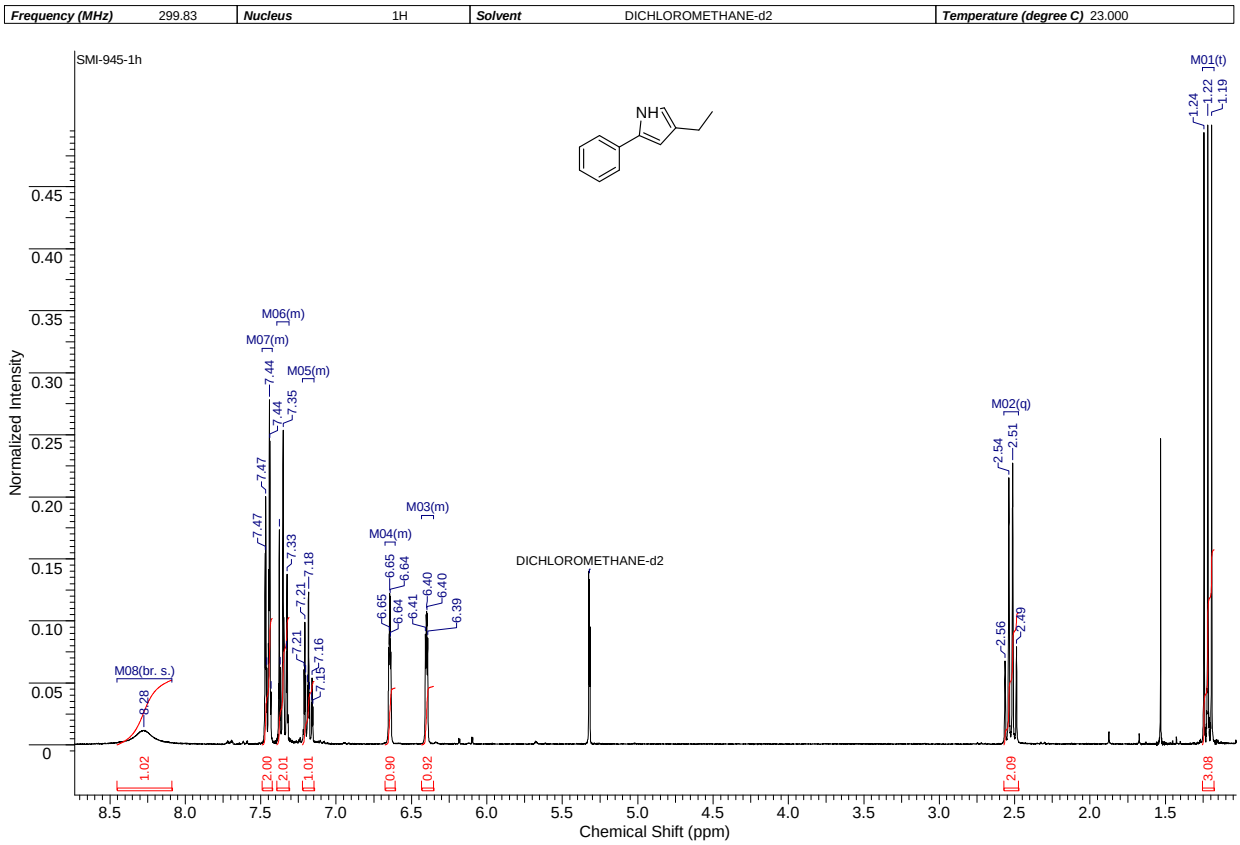

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-905-13c-sauber
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2

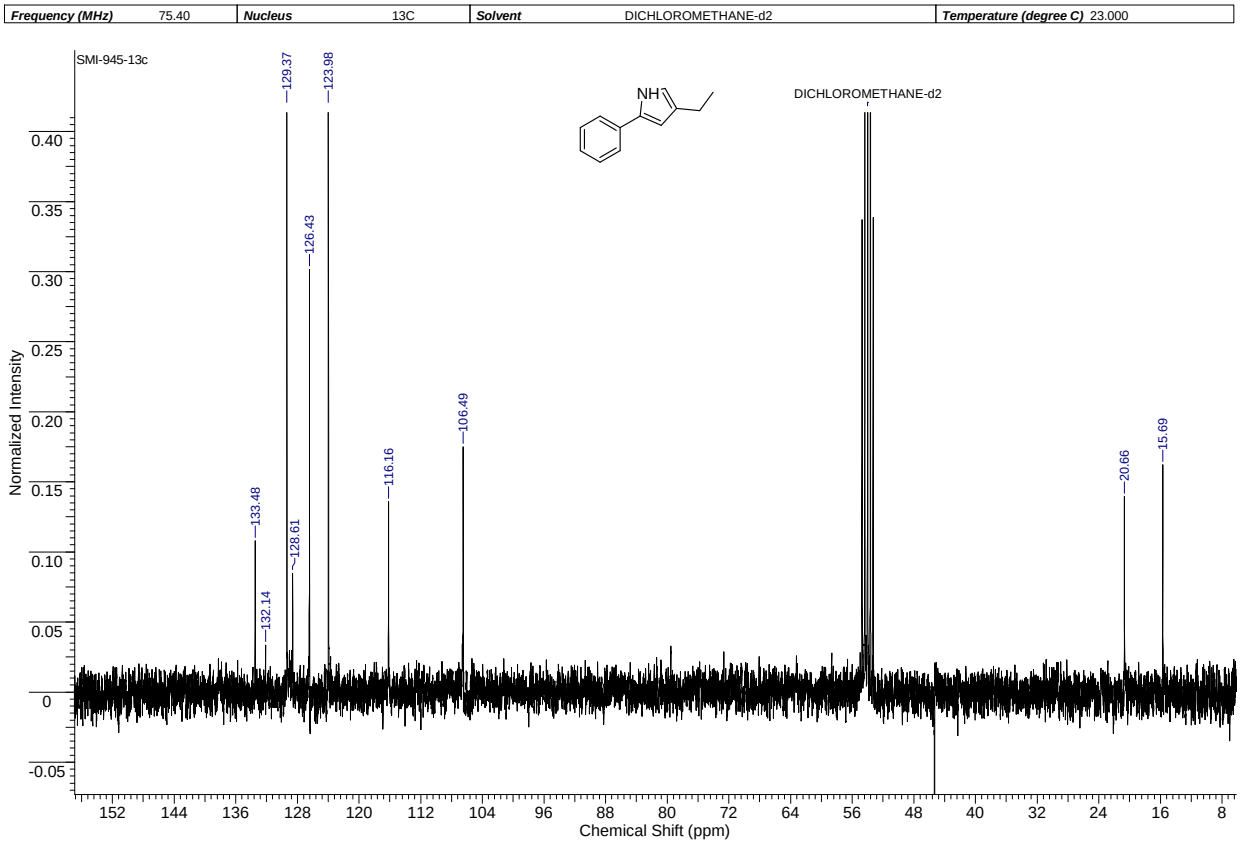

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-910-1h
OH
NH
N
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

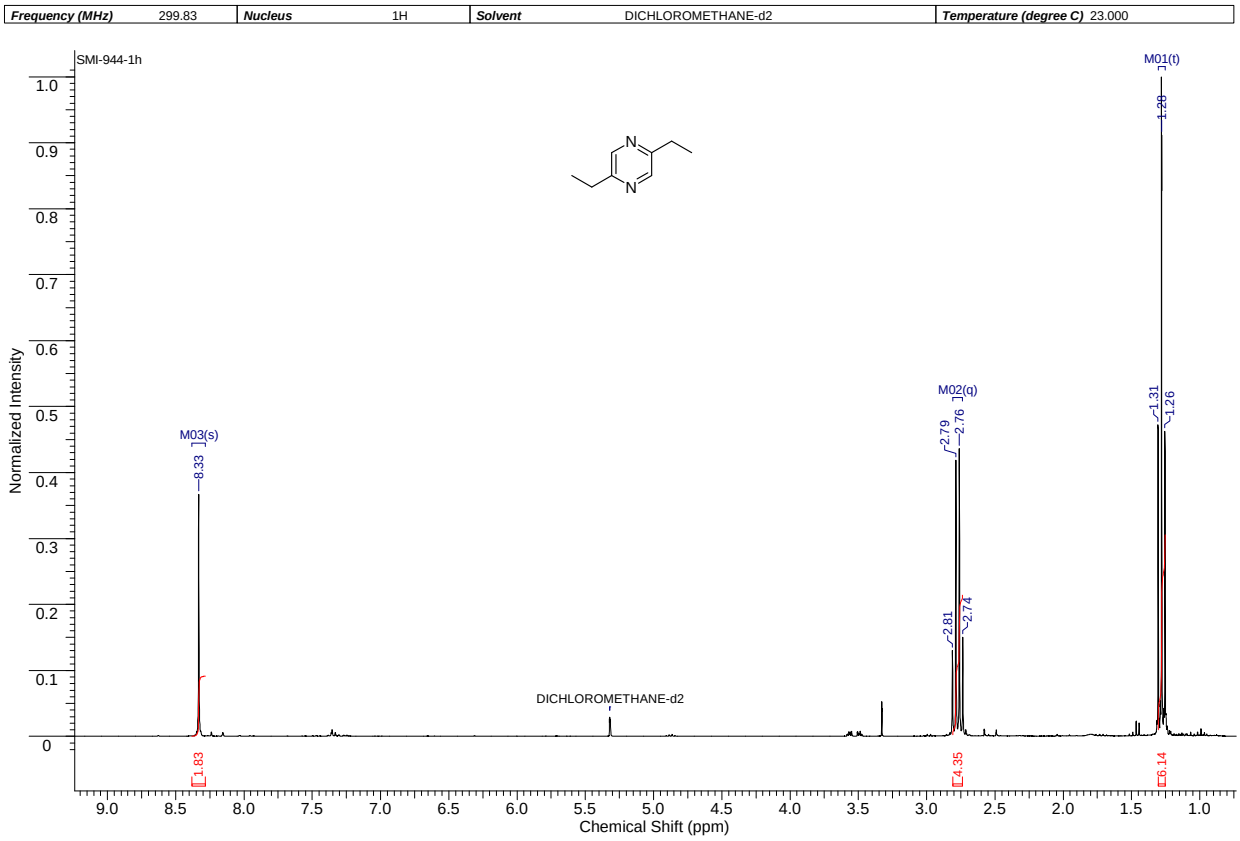

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-910-13c
OH
NH
N
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

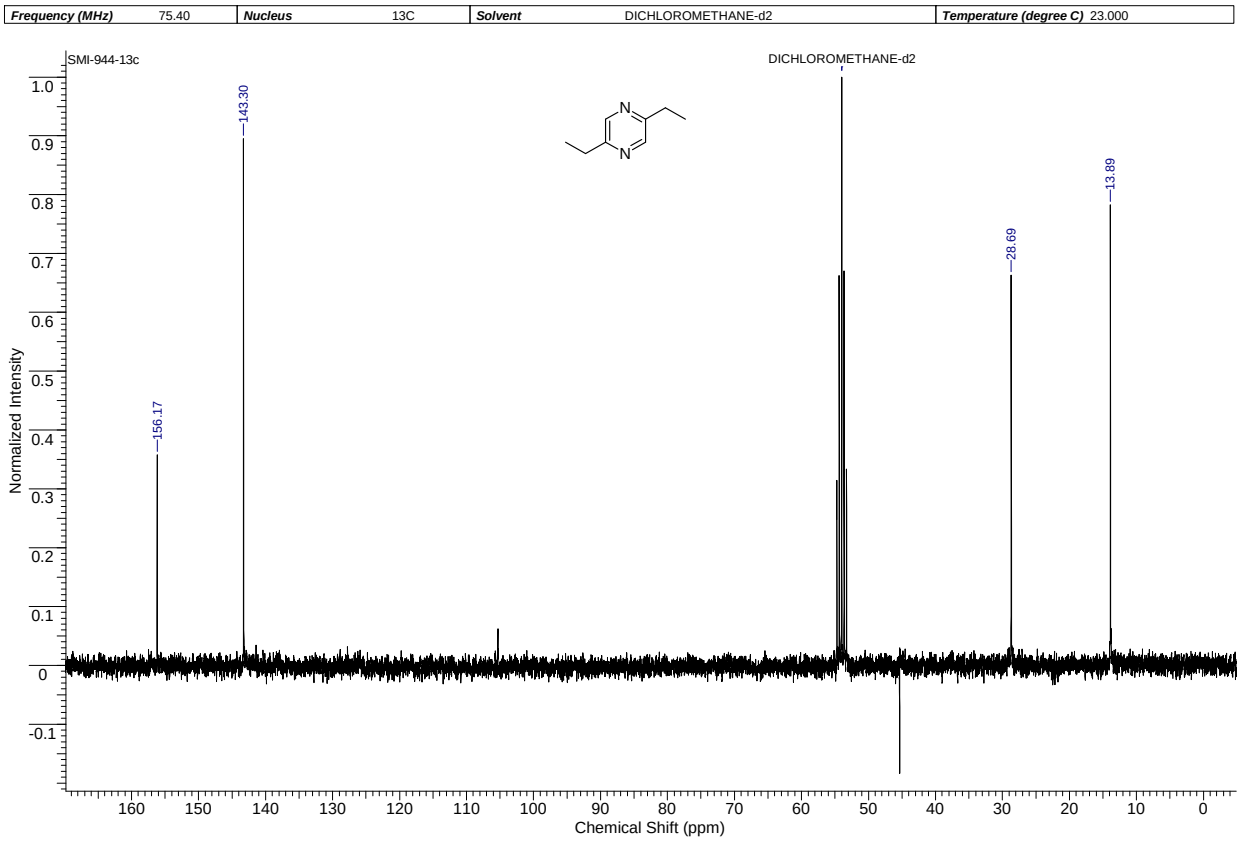

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-914-1h.esp
M10(br. s.)
M09(m)
M06(d)
M07(br. s.)
M08(d)
M05(d)
M04(s)
M03(q)
M02(s)
M01(t)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

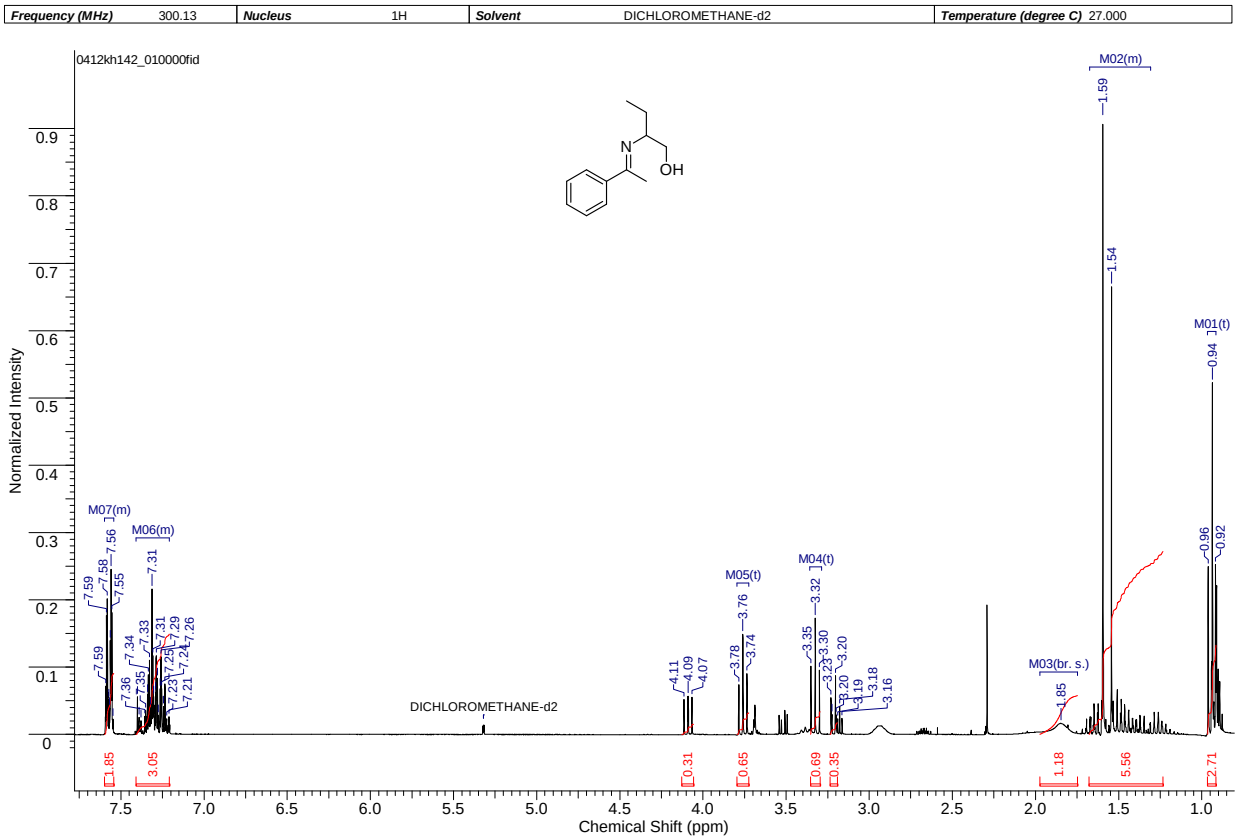

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-914-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

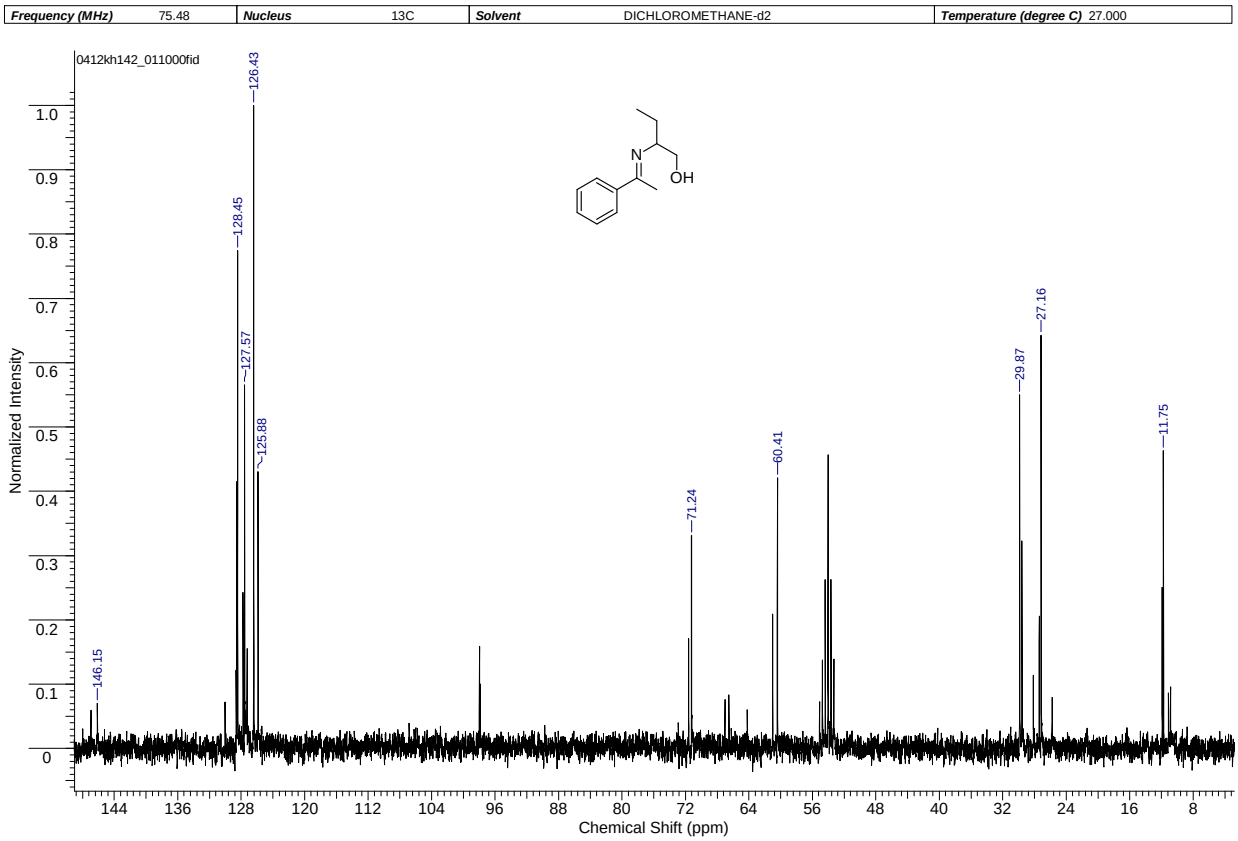

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-945-1h
NH
M01(t)
M02(q)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(br. s.)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

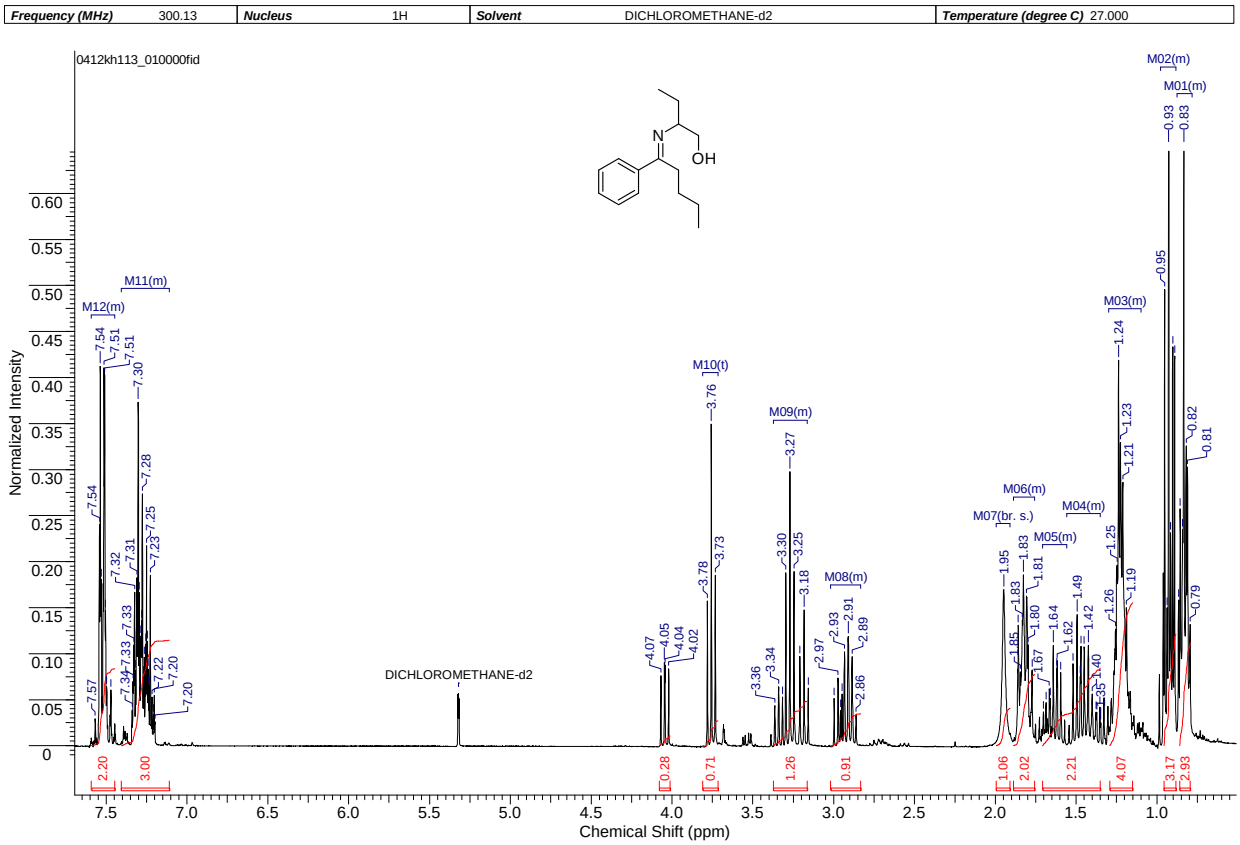

Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-945-13c
NH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

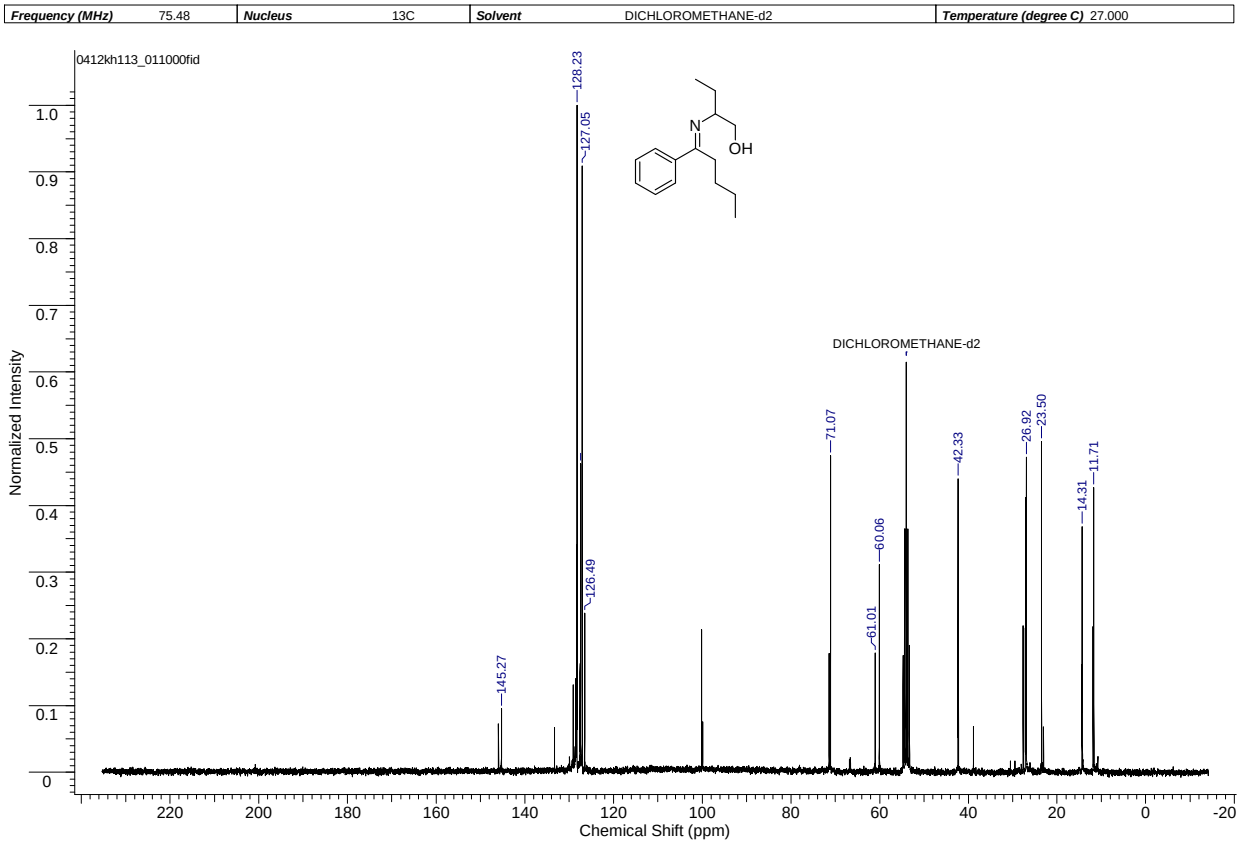

Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-944-1h
M01(t)
M02(q)
M03(s)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-944-13c
DICHLOROMETHANE-d2
143.30
156.17
28.69
13.89
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 300.13
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 27.000
0412kh142_010000fid
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
M01(t)
M02(m)
M03(br. s.)
M04(t)
M05(t)
M06(m)
M07(m)
N
OH


Frequency (MHz) 75.48
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 27.000
0412kh142_011000fid
Normalized Intensity
Chemical Shift (ppm)
N
OH


Frequency (MHz) 300.13
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 27.000
0412kh113_010000fid
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
M01(m)
M02(m)
M03(m)
M04(m)
M05(m)
M06(m)
M07(br. s.)
M08(m)
M09(m)
M10(t)
M11(m)
M12(m)
N
OH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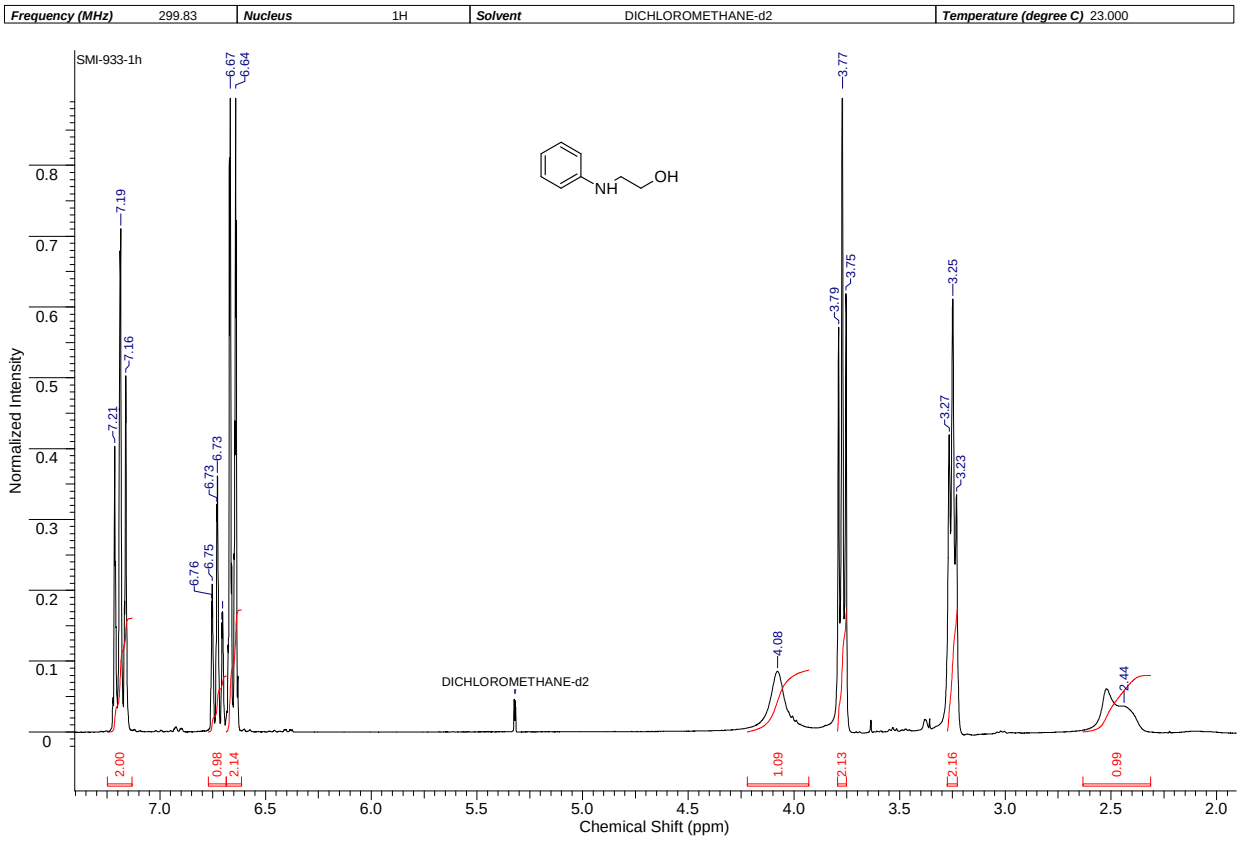
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 27.000
0412kh113_011000fid
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
128.23
127.05
126.49
145.27
71.07
61.01
60.06
42.33
26.92
23.50
14.31
11.71
N
OH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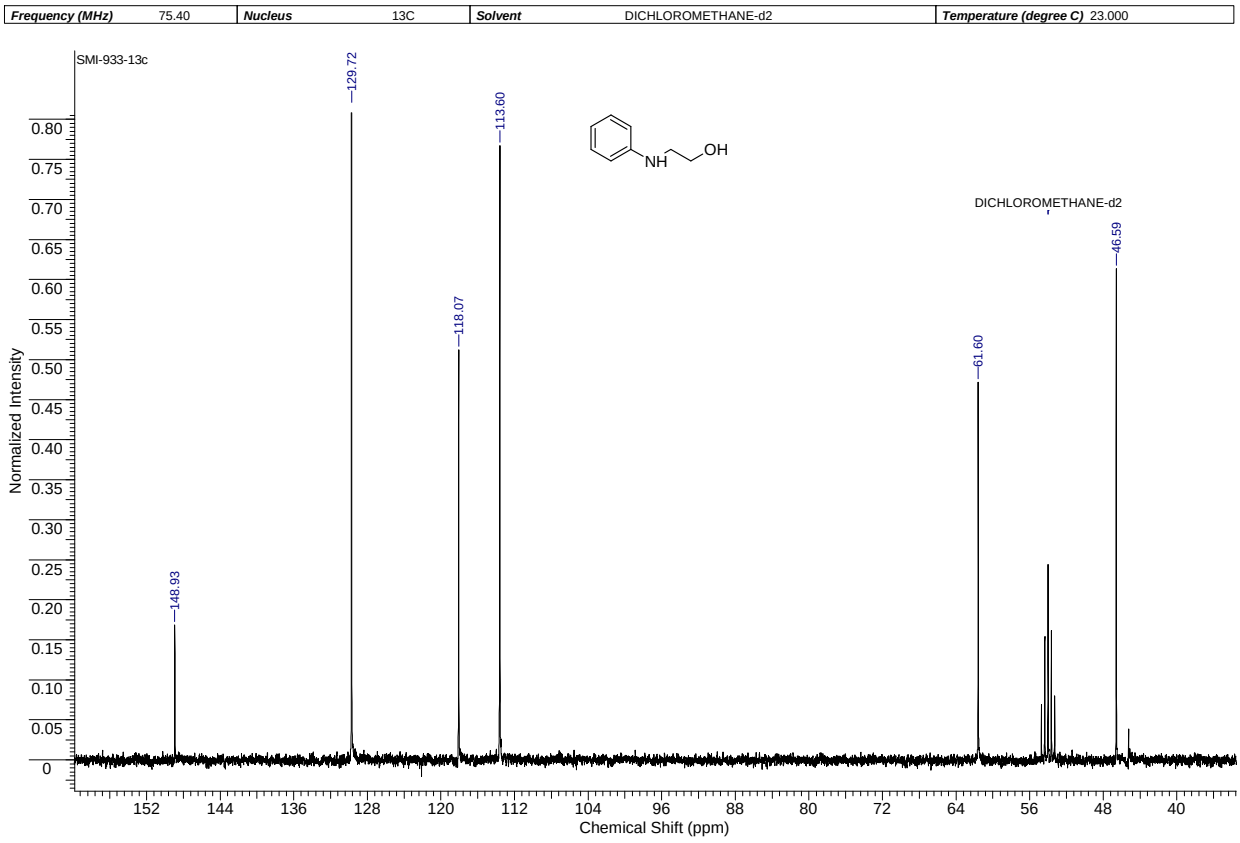
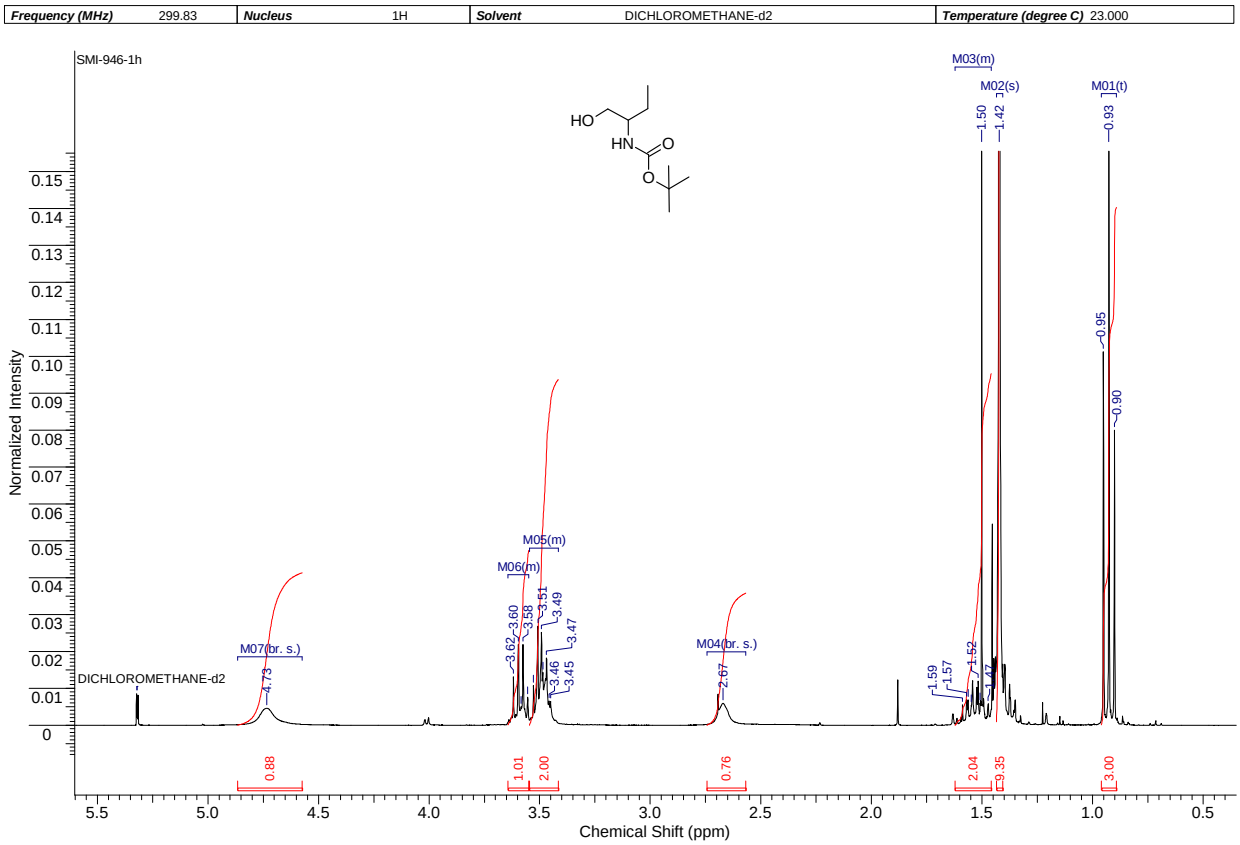
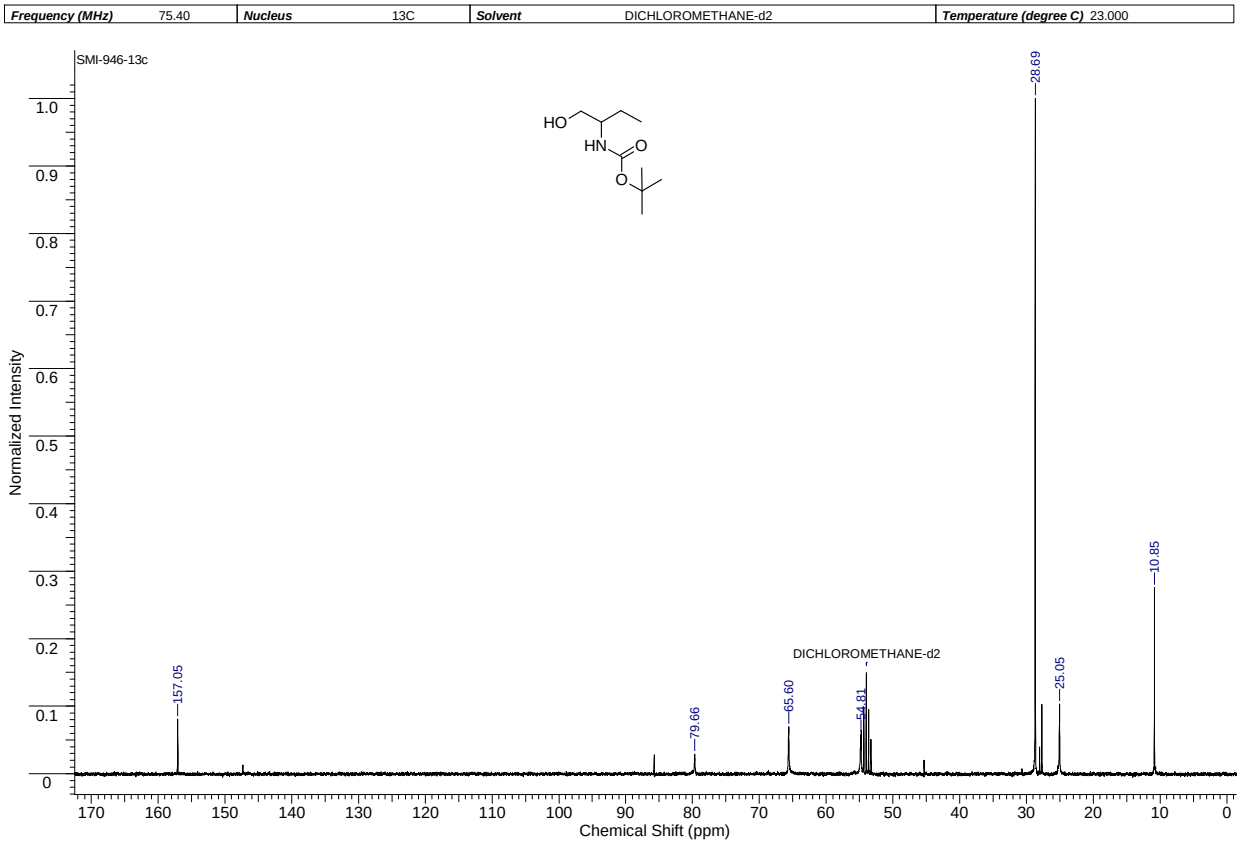
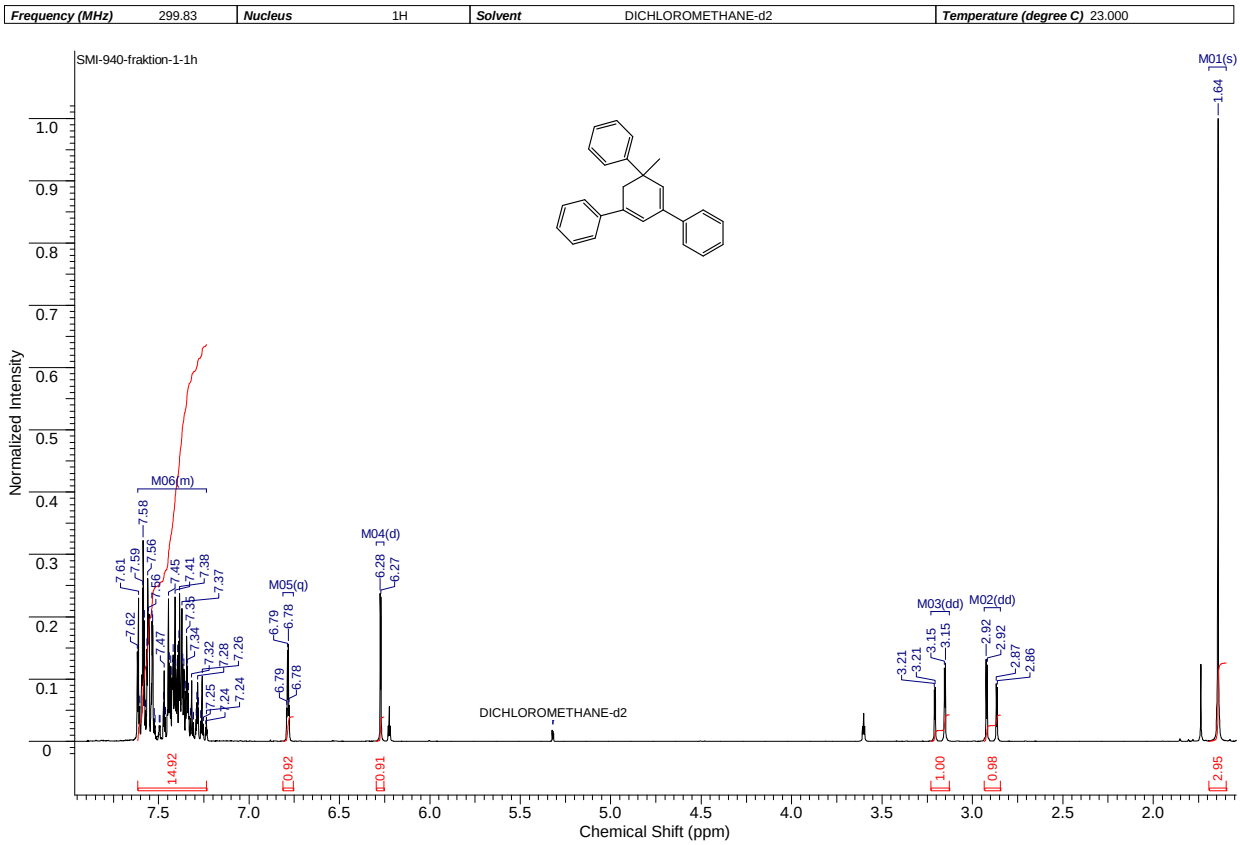
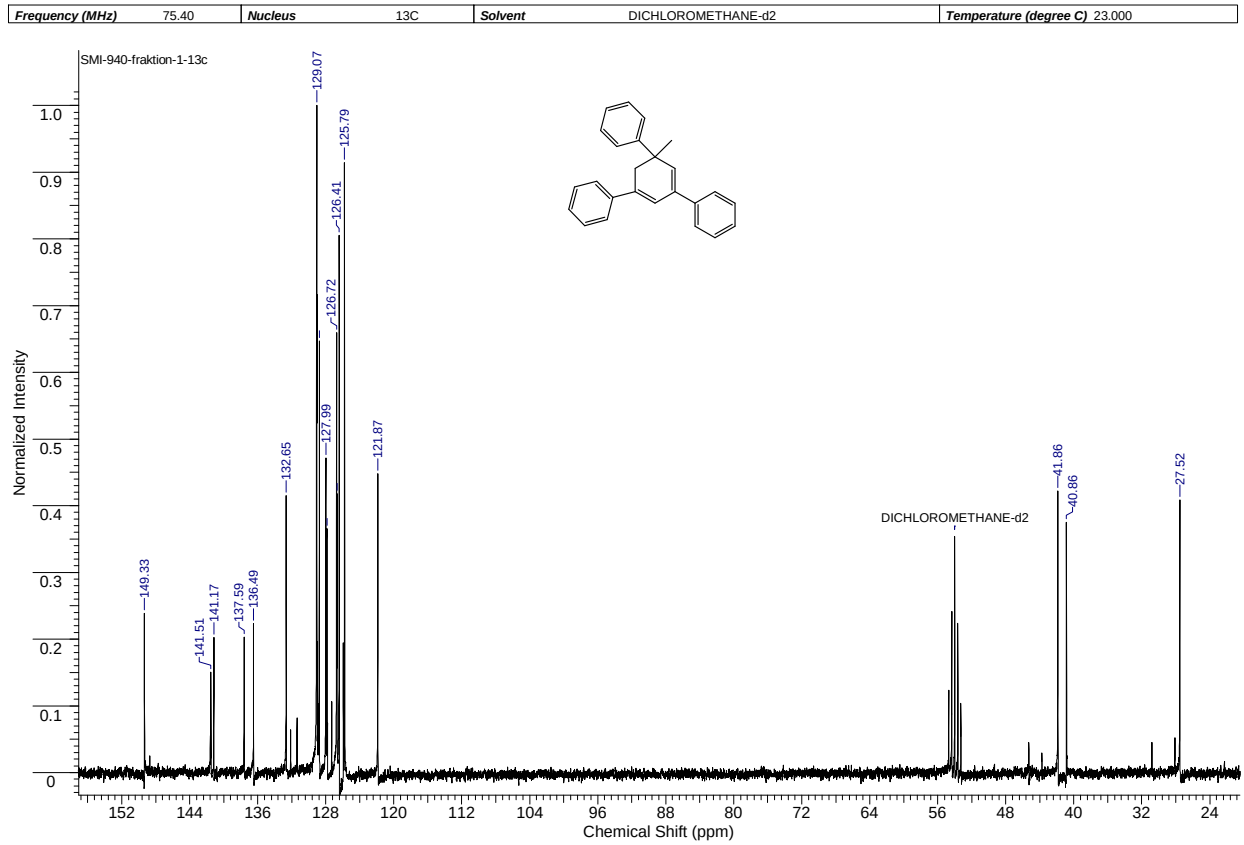
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-933-1h
NH
OH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-933-13c
NH
OH
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-946-1h
HO
HN
O
O
M03(m)
M02(s)
M01(t)
1.50
1.42
0.93
0.95
0.90
M05(m)
M06(m)
3.62
3.60
3.58
3.51
3.49
3.47
3.46
3.45
M07(br. s.)
4.73
M04(br. s.)
2.67
1.59
1.57
1.52
1.47
DICHLOROMETHANE-d2
0.88
1.01
2.00
0.76
2.04
9.35
3.00
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.40
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-946-13c
HO
HN
O
O
28.69
10.85
25.05
157.05
79.66
65.60
54.81
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 299.83
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-940-fraktion-1-1h
M01(s)
M06(m)
M04(d)
M05(q)
M03(dd)
M02(dd)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)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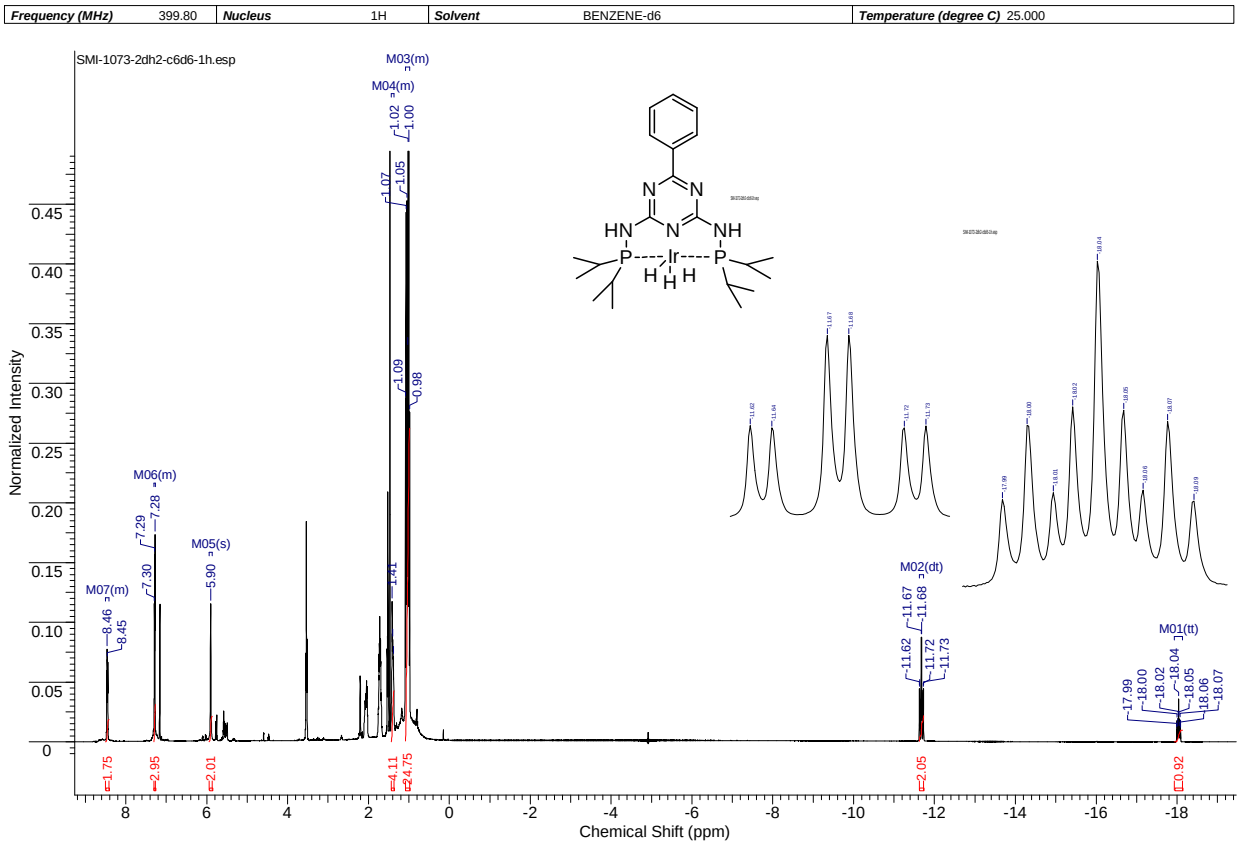
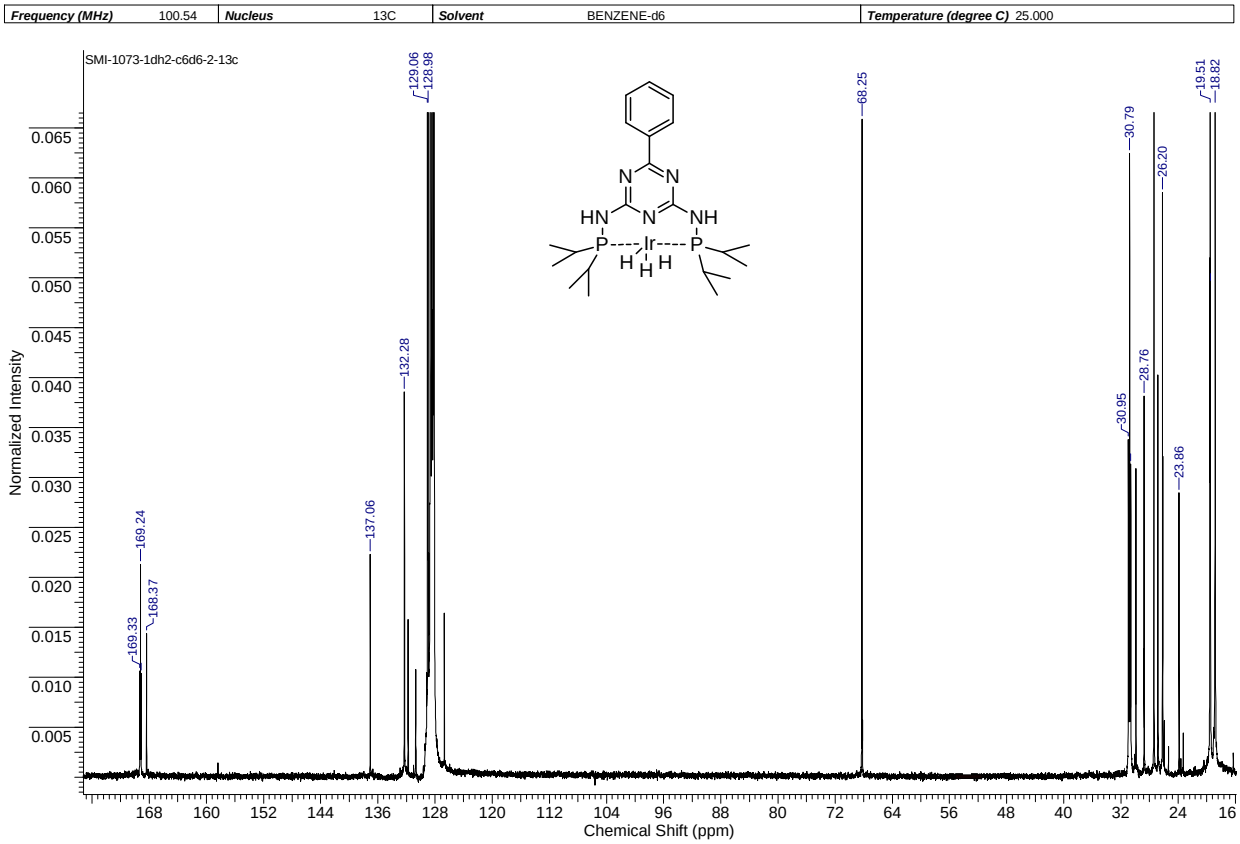
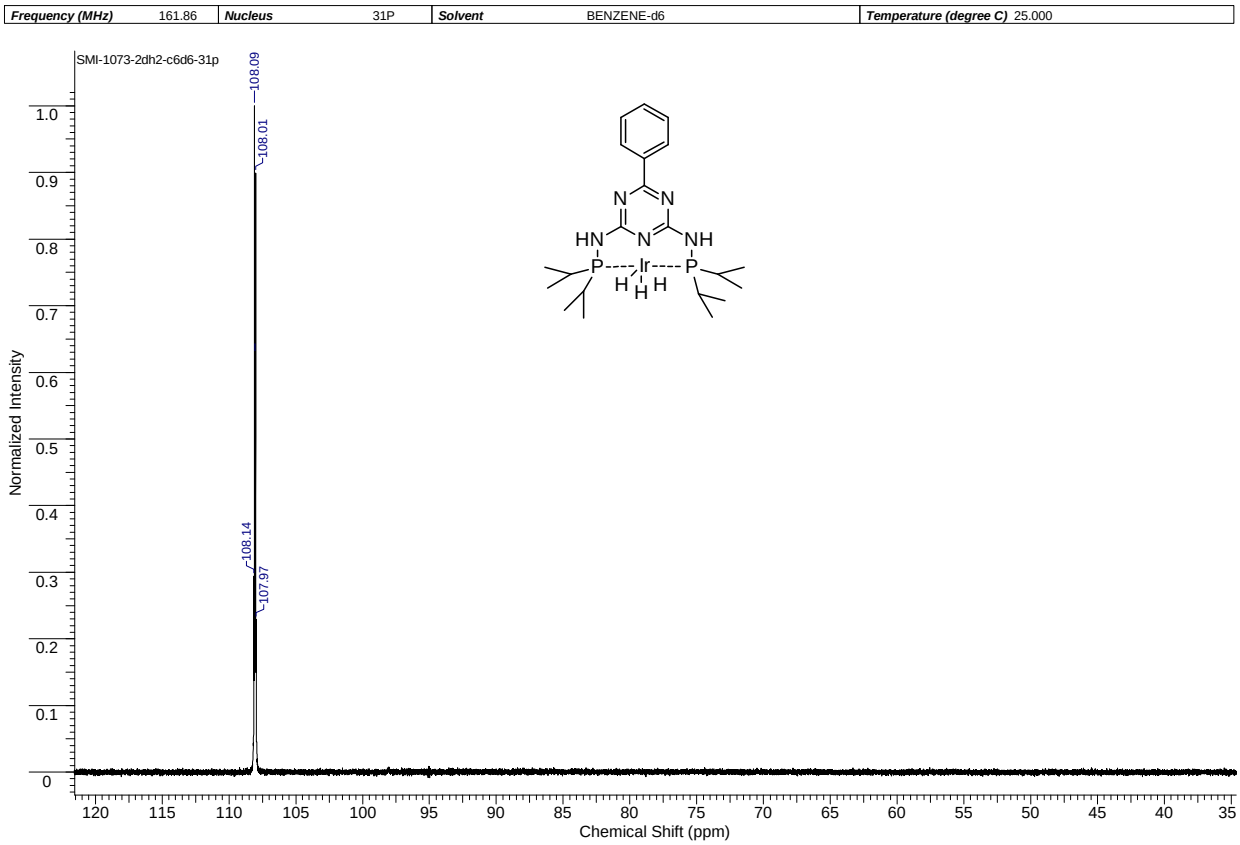
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-940-fraktion-1-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 399.80
Nucleus 1H
Solvent BENZENE-d6
Temperature (degree C) 25.000
SMI-1073-2dh2-c6d6-1h.esp
M03(m)
M04(m)
M06(m)
M05(s)
M07(m)
M02(dt)
M01(tt)
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 100.54
Nucleus 13C
Solvent BENZENE-d6
Temperature (degree C) 25.000
SMI-1073-1dh2-c6d6-2-13c
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 161.86
Nucleus 31P
Solvent BENZENE-d6
Temperature (degree C) 25.000
SMI-1073-2dh2-c6d6-31p
108.09
108.01
108.14
107.97
Normalized Intensity
Chemical Shift (ppm)
N
N
HN
N
NH
P
Ir
P
H
H
H

7. Regioselectively functionalized pyridines from renewable resources

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Keywords: alcohols, dehydrogenative condensation reactions, dehydrogenation, iridium, sustainable resources, pyridine

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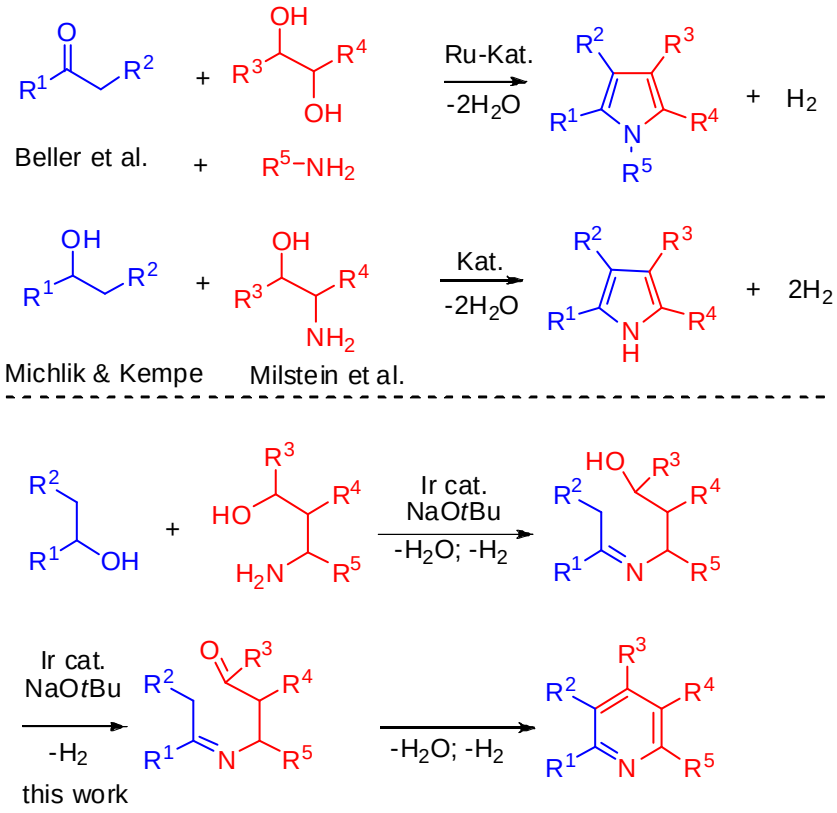
Abstract: The pyridine skeleton is an important structural motif in life sciences. It can be found in a multitude of drugs, herbicides, and fungicides. Herein we present a sustainable iridium catalyzed pyridine synthesis. Primary or secondary alcohols undergo dehydrogenative condensations with γ-amino alcohols followed by a dehydrogenation/aromatization step. Three equivalents of hydrogen gas (and two equivalents of water) are eliminated in the course of the reaction. The required γ-amino alcohols can be made from renewable resources and ammonia. The methodology gives rise to diversely, regioselectively and unsymmetrically substituted pyridines. 26 examples were synthesized among which 21 are new pyridine derivatives. A large variety of functional groups is tolerated.

7.1 Introduction

Pyridines play an important role in life sciences.[1] For instance, many thousands of drugs contain the pyridine motif,[1c,2] as well as many herbicides and fungicides. Furthermore, polymers based on pyridines are used diversely in chemical industry.[3,4] With regard to the importance of the pyridine moiety and the required substitution of petroleum/coal-based chemistry a pyridine synthesis using renewable resources would be an attractive goal. Such a synthesis would be especially attractive and could find significantly faster acceptance if it allows accessing diversely functionalized pyridines that are difficult to prepare applying existing methods. Recently, the Beller group[5], the Milstein group[6a] and our group[6b]

developed sustainable catalytic pyrrole syntheses based on dehydrogenative condensation (= DC) reactions (Scheme 1, upper part). These syntheses are based on observations made by the Ishii group. They reacted 2-aminoethanol or 2-(methylamino)ethanol with an access of propiophenone and observed the formation of two pyrrole derivatives in the presence of a catalyst and a base.[7] Propiophenone is acting as an educt and as H_2 acceptor.

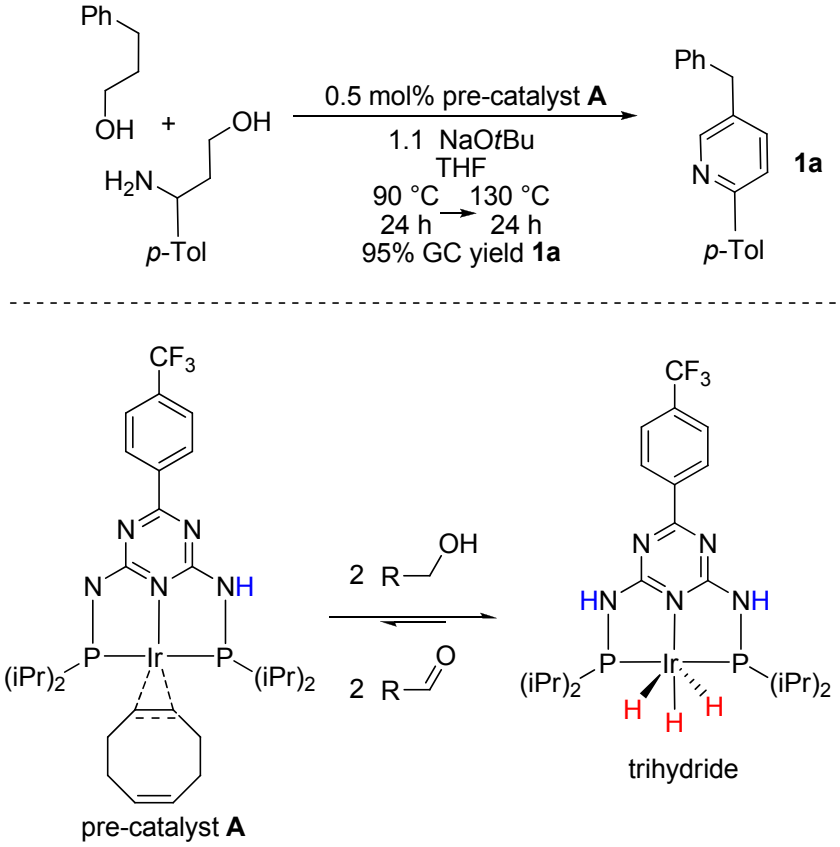


Scheme 1. Known relevant catalytic pyrrole syntheses and the pyridine synthesis presented here.

7.2 Results and Discussion

Considering our pyrrole synthesis (Scheme 1, middle part) and by using γ-amino alcohols (instead of β-amino alcohols) a new [2+4] pyridine synthesis becomes reasonable and is presented here. Primary or secondary alcohols act as a C_2 building block that reacts in the initial step with γ-amino alcohols via an iridium catalyzed dehydrogenative Schiff-base reaction (Scheme 1, middle part).[8] Mechanistic studies reveal a significantly slower amino alcohol oxidation which enables the selective imine formation. Subsequently, the remaining OH-Group becomes dehydrogenated and olefin formation via intramolecular ring closure and water elimination is observed.[9] Finally, aromatization via liberation of H_2 takes place. During the reaction, two equivalents of water and three equivalents of hydrogen gas are eliminated

(Scheme 1). Via the alcohol the substituents in position 2 and 3 of the pyridine ring can be addressed. The positions 4, 5 and 6 are determined by the substitution pattern of the amino alcohol. In this way diversely substituted pyridine derivatives are accessible regioselectively.



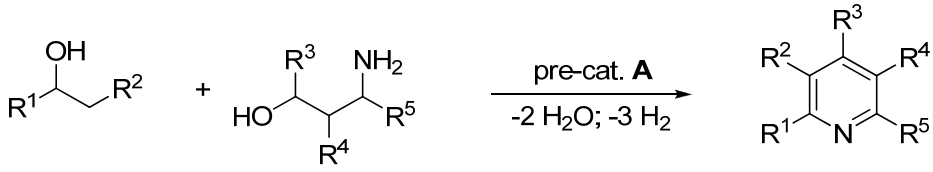
Scheme 2. Optimized reaction conditions (upper part) and formation of the catalyst resting state (iridium trihydride, bottom right).

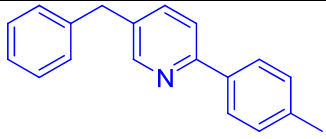
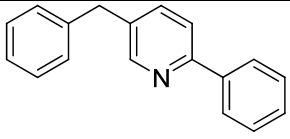
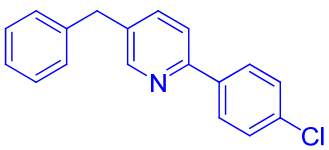
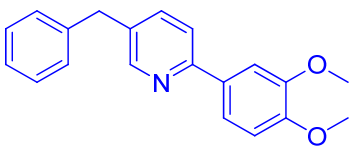
The reaction of 3-phenyl-propanol with 3-amino-3-*p*-tolylpropan-1-ol was investigated (Scheme 2, upper part) to find suitable conditions for the new pyridine synthesis. Starting point regarding the catalyst optimization were Ir complexes stabilized by P,N-ligands that can use aliphatic amino alcohols as alkylating agents without alkylating them at the N atom.[10,6b] Such a selectivity is a prerequisite for the application as catalyst in our pyridine synthesis since amino alcohols are educts. Pre-catalyst **A** gave the highest GC yield in the screening reaction (Scheme 2, upper part). Details of the ligand and complex syntheses are listed in the Supporting Information (SI). After optimizing the reaction conditions (solvent, base, and temperature, for details see SI) 95% yield of **1a** (Scheme 2, upper part) could be observed with 0.5 mol% of pre-catalyst **A**. After a reaction time of 24 h at 90 °C further 24 h at 130 °C are needed to obtain better yields. Beside full conversion of the amino alcohol and the formation of a considerable amount of the desired pyridine; a substantial amount of non-

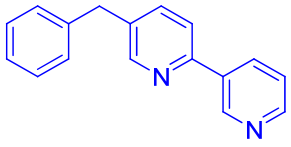
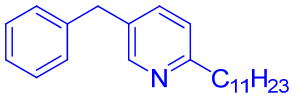
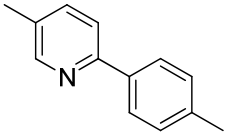
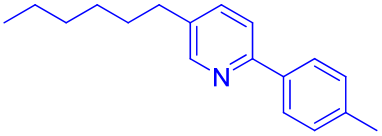
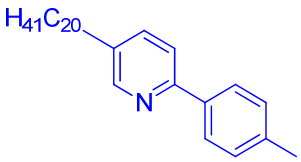
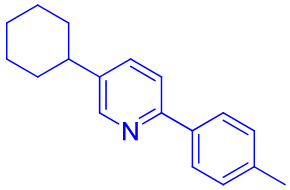
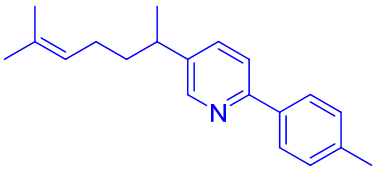
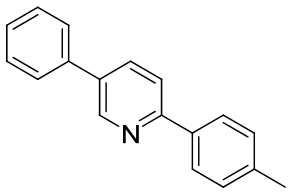
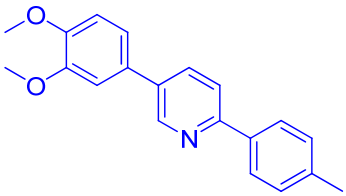
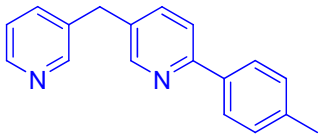
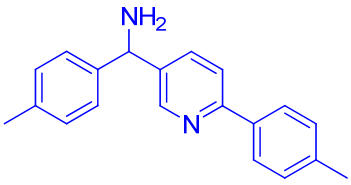
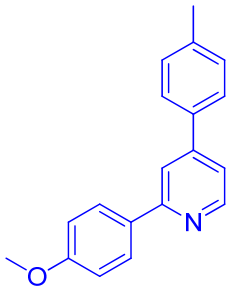
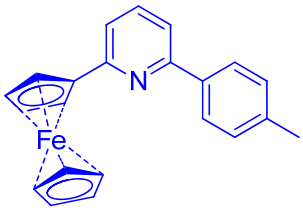
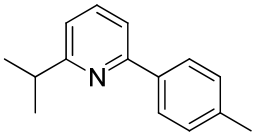
cyclized imino/ketone intermediate (Scheme 1, bottom left) is present after the first 24 hours. The catalyst resting state was found to be an iridium(III)trihydride complex (Scheme 2, bottom right). It can be made by reacting pre-catalyst **A** with (for instance) alcohols at temperatures above 70 °C or with H_2 (Scheme 2, lower part). The trihydride is present during the whole catalytic reaction time as verified by NMR spectroscopy and no noticeable decomposition was observed. For the pyridine syntheses pre-catalyst **A** was used since the trihydride is extremly air sensitive and so more difficult to handle. The trihydride is quantitatively formed from pre-catalyst **A** in less than 30 min under catalytic conditions.

After optimization of the reaction conditions we explored the synthetic scope of the reaction. Via the γ-amino alcohol as well as the primary or the secondary alcohol diverse functional groups can be introduced. Various substituted γ-amino alcohols were reacted with 3-phenyl-propanol and aryl as well as alkyl substituted pyridines (Table 1, **1a-f**) could be obtained in mainly very good isolated yields. Subsequently, we used diverse primary alcohols. These examples (**1g-1o**, Table 1) carry a tolyl substituent in position 2 of the pyridine ring which was brought in by the amino alcohol. Nine different primary alcohols were used among which seven gave rise to new pyridine derivatives, marked blue in Table 1. The lower yield for products **1j**,**k** (Table 1) could be explained by the formation of *p*-tolyl-(6-*p*-tolylpyridin-3-yl)-methanamine (**1o**, Table 1) as a by-product. It is formed by self-condensation of two molecules of amino alcohol since the initial alcohol oxidation step is slow for these examples.

Table 1. Synthesized 2,4-; 2,5- and 2,6-disubstituted pyridines.



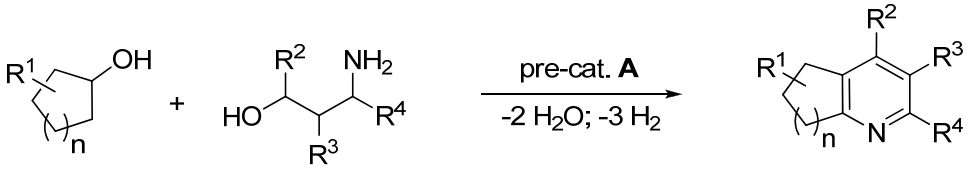
pre-cat.**A** [mol%]		product	yield[a] [%]	pre-cat. **A** [mol%]		product	yield[a] [%]
1a	0.5		90	**1b**	0.5		86
1c	1.5		86	**1d**	0.5		92

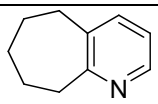
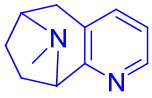
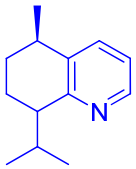
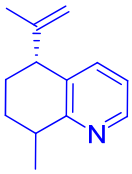
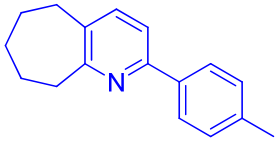
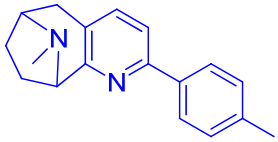
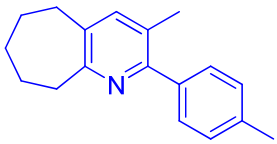
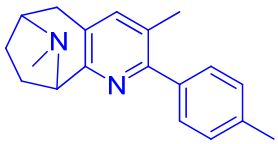
1e	1.5		61	**1f**	0.5		92
1g	1.0		85	**1h**	0.5		94
1i	0.5		70	**1j**	1.0		45
1k	0.5		63	**1l**	0.3		70
1m	0.5		93	**1n**	1.5		94
1o	1.0		35	**1p**	0.5		48
1q	0.05		54 [b]	**1r**	0.5		57 [b]

Reaction conditions: 12.0 mmol alcohol, 3.0 mmol amino alcohol, 3.3 mmol NaO*t*Bu, 10.0 mL THF, pre-catalyst **A**, 24 h/90 °C→24 h/130 °C. [a] isolated yield; [b] 24 h/90 °C. The pyridines marked in blue have not been reported yet.

This side reaction can be “favoured” (35% isolated yield) by adding no other alcohol leading to 5-(aminomethyl)pyridines (**1o**, Table 1). We could show that the new pyridine synthesis works well with primary alcohols. Thus, an efficient access to 2,5-disubstituted pyridines was given. If one uses 1-substituted ethanols 2,6-disubstituted pyridines are in reach. Two examples were synthesized (**1q**,**r** Table 1). However, lower isolated yields were observed since the corresponding cyclic imines or tetrahydropyridines were formed in a side reaction. The unprotected positions 3, 4 and 5 of the pyridine ring allow a rather easy hydrogenation of the via ring closure formed C-C double bond instead of liberation of hydrogen. Furthermore, 2,4-disubstituted pyridines (Table 1, **1p**) are accessible if the appropriately substituted γ-amino alcohols are converted. (For the synthesis of remaining 2,3-disubstituted pyridines see **2a-d**, Table 2, *vide infra*) Due to the tolerance of many functional groups such as chlorides, amines, ethers, olefins, hetero-aromatics and organometallic moieties (Table 1) a wide applicability of the synthesis introduced here is expected.

Table 2. Synthesis of bicyclic pyridines.



pre-cat. **A** [mol%]		product	yield[a] [%]	pre-cat. **A** [mol%]		product	yield[a] [%]
2a	0.5		91	**2b**	0.5		70
2c	0.5		82	**2d**	1.0		76
2e	0.5		96	**2f**	0.5		84
2g	1.0		80	**2h**	1.0		84

Reaction conditions: 12.0 mmol cyclic alcohol, 3.0 mmol amino alcohol, 3.3 mmol NaO*t*Bu, 10.0 mL THF, pre-catalyst **A**, 24 h/90 °C. The pyridines marked in blue have not been reported yet. [a] isolated yield.

The methodology is especially strong regarding the formation of unsymmetrically substituted pyridines. Furthermore, the many first time made pyridines (marked blue examples in Table 1) indicate that our method is extending significantly the scope of existing pyridine syntheses. Finally, we became interested in the formation of bicyclic pyridines starting from cyclic alcohols. The optimization of the reaction conditions was carried out on the model system 3-amino-propan-1-ol/cycloheptanol. By using the optimized conditions, bicyclic pyridines were synthesized among them highly substituted examples (**2g**, **2h**, Table 2). Furthermore, chiral bicyclic pyridines are accessible starting from inexpensive chiral natural products (**2c**,**d**, Table 2). The pyridine synthesis introduced here is sustainable. Not just non-toxic but a very useful by-product namely hydrogen gas is formed. Furthermore, the two educts the alcohols and the γ-amino alcohols can be obtained from renewable resources or waste feedstock. Lignocellulosic materials are available in giant amount,[11] they are indigestible and can be (partially) processed to alcohols or polyoles.[12] The γ-amino alcohols can be made from 1,3-dioles and ammonia using the borrowing hydrogen or hydrogen autotransfer methodology[13,14] or they are accessible from malonic acid, alcohols/aldehydes, and ammonia.[15]

7.3 Conclusion

In summary, a new catalytic pyridine synthesis has been described. It allows accessing diversely regioselectively substituted pyridines and is especially strong in the synthesis of unsymmetric substituted pyridines. A broad spectrum of functional groups is tolerated. In Dehydrogenative Condensation steps three equivalents of H_2 are liberated per formed pyridine. The required starting materials can be obtained from renewable resources with ammonia being the nitrogen atom source. The synthesis method is part of what can be called the “New (Catalytic) Chemistry”, an access to virtually any important organic compound from renewable resources. The broad scope of our pyridine synthesis could result in a faster acceptance of this reaction and by doing so also help the “New Chemistry” to a faster breakthrough.

7.4 References

[1] a) M. D. Hill, *Chem. Eur. J.* **2010**, *16*, 12052-12062; b) G. Jones, *Comprehensive Heterocyclic Chemistry II*, Vol. 5 (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven, A. McKillop), Pergamon, Oxford, **1996**, pp. 167-243; c) G. D. Henry, *Tetrahedron*

2004, *60*, 6043-6060; d) J. A. Joule, K. Mills, *Heterocyclic Chemistry*, 4th ed., Blackwell Science, Cambridge, **2000**, p. 63-120; e) J. P. Michael, *Nat. Prod. Rep*. **2005**, *22*, 627-646; f) *Pharmaceutical Chemistry. Drug Synthesis*, Vol 1, H. J. Roth, A. Kleemann, (Eds.), Prentice Hall Europe, London, **1988**.

[2] MDL Drug Data Registry (MDDR), by MDL Informations Systems, Inc; San Leandro, California, USA.

[3] A. Kirschning, H. Monenschein, R. Wittenberg, *Angew. Chem. Int. Ed*. **2001**, 40, 650-679.

[4] J. M. J. Frechet, M. V. de Meftahi, *Brit. Polym. J.* **1984**, *16*, 193-198.

[5] M. Zhang, H. Neumann, M. Beller, *Angew. Chem. Int. Ed*. **2013**, *52*, 597-601.

[6] S. Michlik, R. Kempe, *Nature Chem.* **2013**, *5*, 140-144.

[7] K. Taguchi, S. Sakaguchi, Y. Ishii, *Tetrahedron Lett.* **2005**, *46*, 4539-4542.

[8] B. Gnanaprakasam, J. Zhang, D. Milstein, *Angew Chem. Int. Ed*. **2010**, *49*, 1468-1471.

[9] B. Blank, R. Kempe, *J. Am. Chem. Soc.* **2010**, *132*, 924-925.

[10] a) B. Blank, S. Michlik, R. Kempe, *Adv. Synth. Catal.* **2009,** *351*, 2903-2911. b) S. Michlik, T. Hille, R. Kempe, *Adv. Synth. Catal.* **2012**, *354*, 847-862.

[11] C. O. Tuck, E. Pérez, I. T. Horváth, R. A. Sheldon, M. Poliakoff, *Science* **2012**, *337*, 695-699.

[12] T. P. Vispute, H. Zhang, A. Sanna, R. Xiao, G. W. Huber, *Science* **2010**, *330*, 1222-1227.

[13] G. Walther, J. Deutsch, A. Martin, F.-E. Baumann, D. Fridag, R. Franke, A. Köckritz, *ChemSusChem*. **2011**, *4*, 1052-1054.

[14] S. Imm, S. Bähn, M. Zhang, L. Neubert, H. Neumann, F. Klasovsky, J. Pfeffer, T. Haas, M. Beller, *Angew. Chem. Int. Ed.* **2011**, *50*, 7599-7603.

[15] C. Y. K. Tan, D. F. Weaver, *Tetrahedron* **2002**, *58*, 7449-7461.

7.5 Supporting Information

General Considerations

All reactions were carried out in a dry argon or nitrogen atmosphere using standard Schlenk techniques or glove box techniques. Halogenated solvents were dried over P_2O_5, and non-halogenated solvents were dried over sodium benzophenone ketyl. 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 400 and 300 MHz spectrometer at 298 K. Chemical shifts are reported in ppm relative to the deuterated solvent. Elemental analyses were carried out on a Vario elementar EL *III*. GC analyses were carried out on an Agilent 6890N Network GC system equipped with a HP-5 column (30 m x 0.32 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 0.32 µm x 0.25 µm).

Screening Reactions

General screening procedure: In a pressure tube catalyst, solvent, alcohol, amino alcohol and base were combined. The pressure tube was closed with a semi-permeable membrane and stirred for 24 h or 48 h. The reaction mixture was cooled to room temperature and quenched by addition of 2 mL of water. Decane as internal standard was added and after shaking, a small fraction of the organic phase was analyzed by GC. The following reaction was investigated.

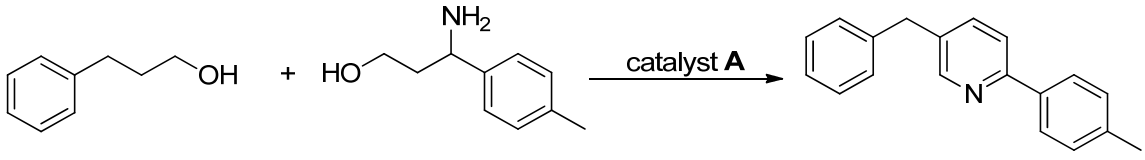


Table 1. Alcohol ratio

amino alcohol /secondary alcohol [eq.]	yield [%]
2.0 / 1.0	23
1.0 / 1.0	10
1.1 / 2.0	27
1.0 / 3.0	34

1.0 / 4.0	**44**

Reaction conditions: 3-phenylpropan-1-ol, 3-amino-3-p-tolylpropan-1-ol, 10.0 mL THF, 1.1 eq KO^{t}Bu, 0.5 mol% catalyst **A**, 24 h, 90 °C (reaction tubes closed with silicone tube). Yields determined by GC analyses with decane as internal standard.

Table 2. Base screening

Base	yield [%]
KO^{t}Bu	44
KOH	48
NaO*t*Bu	**73**

Reaction conditions: 4.0 eq. 3-phenylpropan-1-ol (544 µL), 1.0 eq. 3-amino-3-p-tolylpropan-1-ol (165 mg), 10.0 mL THF, 1.1 eq. base, 0.5 mol% catalyst **A**, 24 h, 90 °C (reaction tubes closed with silicone tube). Yields determined by GC analyses with decane as internal standard.

Table 3. Amount of NaO*t*Bu

base amount according to amino alcohol [eq.]	yield [%]
3.0	52
2.0	56
1.1	**72**
0.5	46
without base	0

Reaction conditions: 4.0 eq. 3-phenylpropan-1-ol (544 µL), 1.0 eq. 3-amino-3-p-tolylpropan-1-ol (165 mg), 10.0 mL THF, NaO^{t}Bu, 0.5 mol% catalyst **A**, 24 h, 90 °C (reaction tubes closed with silicone tube). Yields determined by GC analyses with decane as internal standard.

Table 4. Temperature screening

temperature [°C]	yield [%]
24 h 90 °C	72
24 h 90 °C	77
24 h 90 °C + 24 h 130 °C	**95**

Reaction conditions: 4.0 eq. 3-phenylpropan-1-ol (544 µL), 1.0 eq. 3-amino-3-p-tolylpropan-1-ol (165 mg), 10.0 mL THF, NaO*t*Bu, 0.5 mol% catalyst **A**, (reaction tubes closed with silicone tube). Yields determined by GC analyses with decane as internal standard.

Screening reactions for fused pyridines:

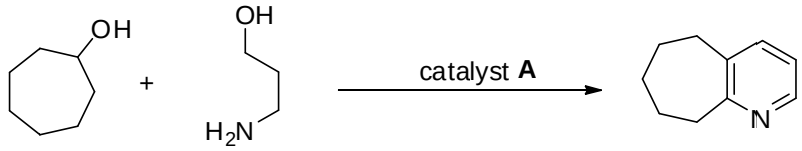


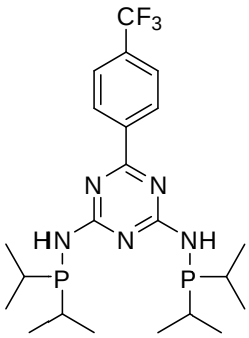
Table 5. Alcohol ratio

amino alcohol /cyclic alcohol [eq.]	yield [%]
1.0 / 4.0	98
1.0 / 2.0	**97**
1.0 / 1.0	56

Reaction conditions: 3-phenylpropan-1-ol, 3-amino-propan-1-ol, 10.0 mL THF, 1.1 eq. NaO*t*Bu, 0.5 mol% catalyst **A**, 24 h, 90 °C (reaction tubes closed with silicone tube). Yields determined by GC analyses with decane as internal standard.

Figure 1. Reaction flask closed with a silicone tube ((Rotilabo®) inner diameter 7 mm, outer diameter 10 mm and 30 cm length) as semi-permeable membrane was used for the pyridine syntheses.

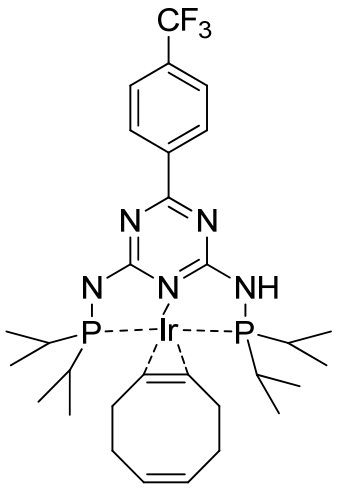
Synthesis of (4-(4-CF_3)-Ph)Tr(NHP(*i*Pr)$_2$)$_2$



6-(4-(Trifluoromethyl)phenyl)-1,3,5-triazine-2,4-diamine (30.0 mmol, 7.65 g) was dissolved in 200 mL THF and triethylamine (80.0 mmol, 11.0 mL) was added and the solution was cooled to 0 °C. Then chlorodiisopropylphosphine (60.0 mmol, 9.6 mL) was added drop wise with a syringe. The solution was allowed to warm to room temperature and stirred over night at 50 °C. The suspension was filtered over a glass filter frit with a pad of celite (4 cm) and washed with 50 mL of THF. The solvent was concentrated *in vacuo*, recrystallized in toluene yielding (4-(4-CF_3)-Ph)Tr(NHP(*i*Pr)$_2$)$_2$ as colorless crystals (13.6 g = 27.9 mmol = 93 %). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.51 (d, *J* = 8.2 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 5.21 (d, *J* =

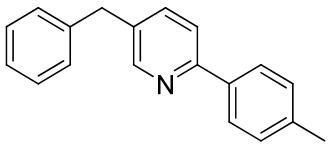
7.0 Hz, 2H), 2.00-1.80 (m, 4H), 1.15-1.08 (m, 24H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 170.5, 141.0, 133.1 (q, *J* = 32.4 Hz), 129.3, 126.2, 125.7 (q, *J* = 3.7 Hz), 123.5, 26.8 (d, *J* =14.0 Hz), 19.1 (d, *J* = 20.6 Hz), 18.0 (d, *J* = 8.8 Hz) ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298K) δ = 57.08 ppm. **Elemental analysis**: for $C_{22}H_{34}F_3N_5P_2$: C 54.20, H 7.03, N 14.37; found: C 54.41, H 7.24, N 14.33.

Synthesis of [(4-(4-CF_3)-Ph)Tr(NP(*i*Pr)$_2$)(NHP(*i*Pr)$_2$)Ir(cod)] (Catalyst A)

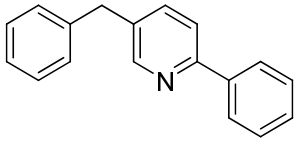


$[IrOMe(cod)]_2$ (2.0 mmol, 1.32g) was dissolved in 40 mL THF and subsequently a solution of (4-(4-CF_3)Ph)Tr(NHP(*i*Pr)$_2$)$_2$ (4.0 mmol, 1.95 g) dissolved in THF was added drop wise. A red solution was obtained. The solution was stirred over night at 50 °C. The solvent was removed *in vacuo*, yielding a deep red solid in quantitative yield. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.49 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 6.35 (s_br, 1H), 5.70-5.60 (m, 2H), 3.98-3.86 (m, 2H), 2.40-2.26 (m, 6H), 2.22-2.05 (m, 4H), 1.75- 1.63 (m, 2H), 1.27-1.07 (m, 24H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 168.7, 141.6, 132.9, 132.6, 130.7, 129.4, 129.1, 125.5 (q, *J* = 3.7 Hz), 123.5, 55.6, 37.1, 32.5, 29.2 (s_br), 29.0 (s_br), 28.1 (s_br), 27.8 (s_br), 18.2 (s_br), 17.8 (s_br), 16.9 (s_br) ppm. **^{31}P NMR** (161 MHz, C_6D_6, 298 K): δ = 85.70, 84.55 ppm. **^{19}F NMR** (376 MHz, C_6D_6, 298 K): δ = -63.45 ppm. **Elemental analysis** (%) for $C_{30}H_{45}F_3IrN_5P_2$ calcd: C 45.79, H 5.76, N 8.90; found: C 45.99, H 5.91, N 8.91.

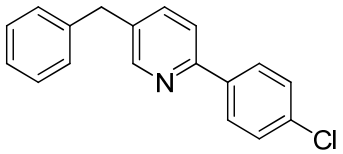
Pyridine products



1a: (5-benzyl-2-p-tolylpyridine): Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), 3-phenylpropan-1-ol (1.63 mL, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg 3.3 mmol), 24h at 90 °C→24h at 130 °C. Purification by column chromatography 20:1 pentane:Et_2O→ 10:1 pentane:Et_2O; Yield: 700 mg = 3.6 mmol = 90% as colorless solid. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.55 (s, 1H), 7.91 (dd, *J* = 8.4, 2.5 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.54 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.40-7.19 (m, 7H), 4.01 (s, 2H), 2.41 (s, 3H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 155.7, 150.4, 140.9, 139.4, 137.5, 137.0, 135.4, 129.9, 129.4, 129.2, 127.0, 126.9, 120.2, 39.2, 21.5 ppm. **MS** (70 eV, EI); m/z (%): 259 (100, M^+), 244 (5), 215 (6), 182 (7), 115 (15), 91 (8). **Elemental analysis** (%) for $C_{17}H_{19}N$ calcd C 87.99, H 6.61, N 5.40; found: C 88.15, H 6.36, N 5.45.

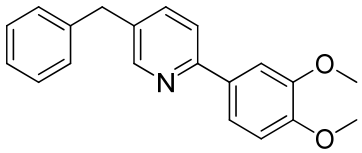


1b: 5-benzyl-2-phenylpyridine: Catalyst A (0.9 mL, 0.009 mmol, 0.01 M in THF), 3-phenylpropan-1-ol (1.63 mL, 12.0 mmol), 3-amino-3-phenylpropan-1-ol (453 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→24h at 130 °C. Purification by column chromatography 10:1 pentane:Et_2O; Yield: 632 mg = 2.58 mmol = 86% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.56-8.60 (m, 1H), 8.04-8.00 (m, 2H), 7.71-7.67 (m, 1H), 7.69 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.51-7.40 (m, 3H), 7.37-7.30 (m, 2H), 7.28-7.21 (m, 3H), 4.03 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 155.6, 150.5, 140.8, 139.8, 137.5, 135.8, 129.4, 129.2, 129.1, 127.2, 126.9, 120.5, 39.2 ppm. **MS** (70 eV, EI); m/z (%): 245 (100, M^+), 215 (6), 202 (7), 168 (10), 141 (12), 115 (20), 115 (20), 91 (6), 77 (4).

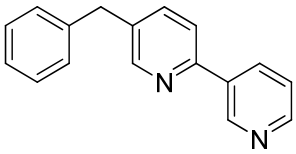


1c: 5-benzyl-2-(4-chlorophenyl)pyridine: Catalyst A (4.5 mL, 0.045 mmol, 0.01 M in THF), 3-phenylpropan-1-ol (1.63 mL, 12.0 mmol), 3-amino-3-(4-chlorophenyl)propan-1-ol (555 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→24h at 130 °C. Purification by column chromatography 10:1 pentane:Et_2O Yield: 635 mg = 2.58 mmol = 86% as yellow oil. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.56 (dd, *J* = 2.3, 0.8 Hz, 1H), 7.97 (d, *J* = 9.0 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.56 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.44 (d, *J* = 9.0 Hz, 2H), 7.35-7.31 (m, 2H), 7.28-7.21 (m, 3H), 4.01 (s, 2H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 154.4, 150.6, 140.7, 138.3, 137.7, 136.1, 135.2, 129.4, 129.3, 129.2, 128.5, 127.0, 120.4, 39.2 ppm. **MS** (70 eV, EI); m/z (%): 279 (100, M^+), 244 (12), 215 (13), 202 (13), 139 (20),

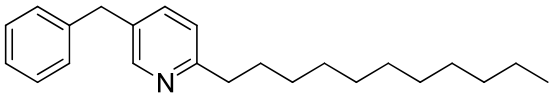
121 (15), 115 (16), 91 (15). **Elemental analysis** (%) for $C_{17}H_{19}N$ calcd C 77.28, H 5.04, N 5.01; found: C 77.03, H 4.70, N 5.04.



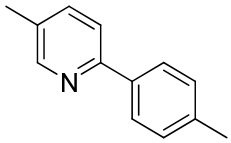
1d: 5-benzyl-2-(3,4-dimethoxyphenyl)pyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), 3-phenylpropan-1-ol (1.63 mL, 12.0 mmol), 3-amino-3-(3,4-dimethoxyphenyl)propan-1-ol (633 mg, 3.0 mmol), 10 mL THF, NaO^tBu (317 mg, 3.3 mmol), 24h at 90 °C→24h at 130 °C. Purification by column chromatography 2:1 pentane:Et_2O→ 1:2 pentane:Et_2O; Yield: 842 mg = 2.76 mmol = 92% as colorless solid. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.52 (d, *J* = 2.3 Hz, 1H), 7.66 (d, *J* = 2.0 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.53-7.50 (m, 3H),7.34-7.29 (m, 2H), 7.27-7.19 (m, 3H), 6.94 (d, *J* = 8.6 Hz, 1H), 4.00 (s, 2H), 3.92 (s, 3H), 3.88 (s, 3H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 155.3, 150.6, 150.2, 150.0, 141.0, 137.5, 135.1, 132.6, 129.4, 129.2, 126.9, 119.9, 119.5, 111.8, 110.5, 56.4, 39.2, 31.2 ppm. **MS** (70 eV, EI); m/z (%): 305 (100, M^+), 290 (26), 274 (24), 262 (20), 259 (23), 218 (24), 91 (20). **Elemental analysis** (%) for $C_{17}H_{19}N$ calcd C 78.66, H 6.27, N 4.59; found: C 78.57, H 6.37, N 4.59.



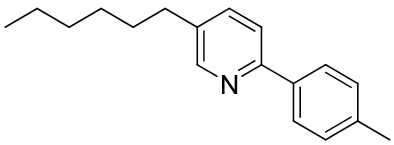
1e: 5-benzyl-2,3'-bipyridine: Catalyst A (4.5 mL, 0.045 mmol, 0.01 M in THF), 3-phenylpropan-1-ol (1.63 mL, 12.0 mmol), 3-amino-3-(pyridin-3-yl)propan-1-ol (456 mg, 3.0 mmol), 10 mL THF, NaO^tBu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography pure Et_2O. Yield: 450 mg = 1.83 mmol = 61% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 9.20-9.16 (m, 1H), 8.62-8.58 (m, 2H), 8.32-8.28 (m, 1H), 7.72-7.69 (m, 1H), 7.40-7.36 (m, 1H), 7.35-7.29 (m, 2H), 7.27-7.20 (m, 3H), 4.03 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 153.2, 150.7, 150.2, 148.6, 140.6, 137.7, 136.6, 135.1, 134.4, 129.4, 129.2, 127.0, 124.0, 120.7, 39.2 ppm. **MS** (70 eV, EI); m/z (%): 246 (100), 218 (10), 169 (7), 141 (10), 115 (15), 91 (10), 65 (5). **Elemental analysis** (%) for $C_{17}H_{14}N_2$ calcd C 82.90, H 5.73, N 11.37; found: C 83.18, H 5.34, N 11.50.



1f: 5-benzyl-2-undecylpyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), 3-phenylpropan-1-ol (1.63 mL, 12.0 mmol), 3-aminotetradecan-1-ol (687 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography 15:1 pentane:Et_2O →10:1 pentane:Et_2O Yield: 892 mg = 2.76 mmol = 92% as yellow oil. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.38 (d, *J* = 2.3 Hz, 1H), 7.38 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.32-7.27 (m, 2H), 7.24-7.18 (m, 3H), 7.06 (d, *J* = 7.8 Hz, 1H), 3.93 (s, 2H), 2.74-2.70 (m, 2H), 1.70-1.66 (m, 2H), 1.34-1.27 (m, 16H), 0.91-0.87 (m, 3H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 161.0, 149.9, 141.2, 136.9, 134.1, 129.3, 129.1, 126.8, 122.8, 39.2, 38.5, 32.5, 30.5, 30.3, 30.22, 30.18, 30.1, 30.0, 29.9, 23.3, 14.5 ppm. **MS** (70 eV, EI); m/z (%): 323 (3, M^+), 308 (1), 294 (2), 280 (2), 266 (2), 252 (2), 238 (3), 224 (3), 219 (10), 196 (18), 183 (100), 106 (10), 91 (8). **Elemental analysis** (%) for $C_{17}H_{19}N$ calcd C 85.39, H 10.28, N 4.33; found: C 85.01, H 10.62, N 4.50.

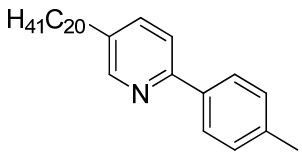


1g: 5-methyl-2-p-tolylpyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), 1-propanol (897 µL, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography 10:1 pentane:Et_2O. Yield: 467 mg = 2.55 mmol = 85% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.50-8.47 (m, 1H), 7.93-7.88 (m, 2H), 7.66-7.61 (m, 1H), 7.58-7.52 (m, 1H), 7.31-7.25 (m, 2H), 2.41 (s, 3H), 2.36 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 154.9, 150.5, 139.1, 137.7, 132.0, 129.9, 126.0, 119.9, 21.5, 18.4 ppm. **MS** (70 eV, EI); m/z (%): 183 (100, M^+), 167 (20), 153 (4), 128 (4), 115 (10), 91 (8), 65 (6).

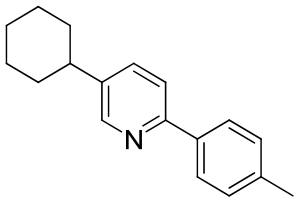


1h: 5-hexyl-2-p-tolylpyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), 1-octanol (1.88 mL, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography 10:1 pentane:Et_2O. Yield: 714 mg = 2.82 mmol = 94% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.48 (d, *J* = 1.8 Hz, 1H), 7.94-7.86 (m, 2H), 7.69-7.62 (m, 1H), 7.60-7.52 (m, 1H), 7.31-7.23 (m, 2H), 2.68-2.59 (m, 2H), 2.40 (s, 3H), 1.71-1.58 (m,

2H), 1.45-1.26 (m, 6H), 0.97-0.83 (m, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 155.1, 150.2, 139.1, 137.2, 137.0, 136.9, 129.9, 126.9, 120.0, 33.2, 32.2, 31.7, 29.4, 23.2, 21.5, 14.4 ppm. **MS** (70 eV, EI); m/z (%): 253 (50, M^+), 196 (10), 182 (100), 167 (8), 155 (12), 129 (6), 115 (6). **Elemental analysis** (%) for $C_{18}H_{23}N$ calcd C 85.32, H 9.15, N 5.53; found: C 85.28, H 9.17, N 5.60.

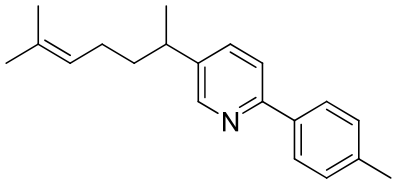


1i: 5-icosyl-2-p-tolylpyridine: Catalyst A (4.5 mL, 0.045 mmol, 0.01 M in THF), docosan-1-ol (1.96 g, 6.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography pure toluene. Yield: 943 mg = 2.1 mmol = 70% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.47 (d, *J* = 1.5 Hz, 1H), 7.92-7.85 (m, 2H), 7.68-7.61 (m, 1H), 7.58-7.51 (m, 1H), 7.30-7.22 (m, 2H), 2.68-2.58 (m, 2H), 2.39 (s, 3H), 1.74-1.54 (m, 2H), 1.27-1.26 (m, 34H), 0.90-0.86 (m, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 155.1, 150.2, 139.1, 137.2, 137.0, 136.9, 129.9, 126.9, 120.0, 41.2, 33.2, 32.5, 31.8, 31.5, 30.7, 30.3, 30.2, 30.0, 29.9, 29.8, 27.4, 23.3, 21.5, 14.5 ppm. **MS** (70 eV, EI); m/z (%): 449 (20, M^+), 434 (2), 420 (7), 406 (10), 392 (10), 378 (14), 364 (14), 350 (16), 336 (16), 322 (14), 308 (13), 294 (12), 280 (10), 266 (10), 252 (12), 238 (10), 224 (7), 210 (10), 196 (95), 183 (100), 167 (6), 155 (14), 57 (14). **Elemental analysis** (%) for $C_{32}H_{51}N$ calcd C 85.46, H 11.43, N 3.11; found: C 85.44, H 11.12, N 3.03.

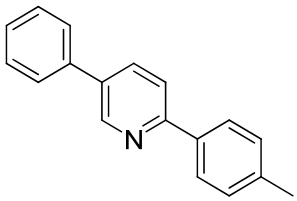


1j: 5-cyclohexyl-2-p-tolylpyridine: Catalyst A (3.0 mL, 0.03 mmol, 0.01 M in THF), 2-cyclohexylethanol (1.67 mL, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography 15:1 pentane:Et_2O. Yield: 339 mg = 1.35 mmol = 45% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.51 (d, *J* = 2.0 Hz, 1H), 7.93-7.86 (m, 2H), 7.69-7.62(m, 1H), 7.61-7.54 (m, 1H), 7.31-7.23 (m, 2H), 2.65-2.50 (m, 1H), 2.40 (s, 3H), 1.97-1.83 (m, 4H), 1.82-1.74 (m, 1H), 1.55-1.39 (m, 4H), 1.39-1.26 (m, 1H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 155.3, 129.2, 131.8, 129.1, 137.2, 135.3, 129.9, 126.9, 120.1, 42.3, 34.7, 27.3, 26.6, 21.5 ppm. **MS** (70 eV, EI); m/z (%): 251 (100), 208 (75), 195 (20), 182 (30), 115

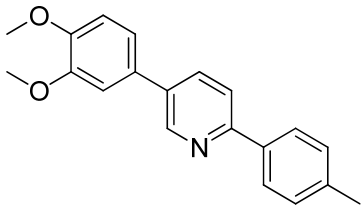
(6), 91 (6). **Elemental analysis** (%) for $C_{18}H_{21}N$ calcd C 86.01, H 8.42, N 5.57; found: C 86.09, H 8.15, N 5.67.



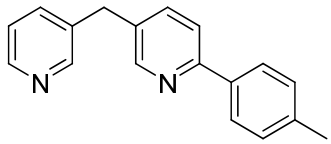
1k: 5-(6-methylhept-5-en-2-yl)-2-p-tolylpyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), 2,7-dimethyloct-6-en-1-ol (2.19 mL, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography 10:1 pentane:Et_2O. Yield: 527 mg = 1.89 mmol = 63% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.49 (d, *J* = 2.1 Hz), 7.95-7.88 (m, 2H), 7.71-7.65 (m, 1H), 7.60-7.54 (m, 1H), 7.32-7.25 (m, 2H), 5.16-5.08 (m, 1H), 2.85-2.72 (m, 1H), 2.41 (s, 3H), 2.00-1.89 (m, 2H), 1.72-1.64 (m, 5H), 1.54 (s, 3H), 1.30 (d, *J* = 7.0 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 155.4, 149.6, 141.5, 139.2, 137.2, 135.4, 132.3, 129.9, 127.0, 124.7, 120.1, 38.6, 37.2, 26.6, 26.0, 22.5, 21.5, 18.0 ppm. **MS** (70 eV, EI); m/z (%): 279 (18, M^+), 264 (10), 236 (8), 222 (14), 210 (100), 196 (100), 183 (12), 169 (6), 128 (7). **Elemental analysis** (%) for $C_{20}H_{25}N$ calcd C 85.97, H 9.02, N 5.01; found: C 86.30, H 9.20, N 5.34.



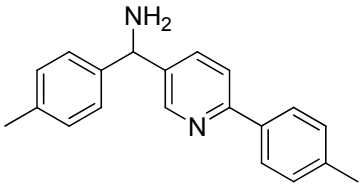
1l: 5-phenyl-2-p-tolylpyridine: Catalyst A (0.9 mL, 0.009 mmol, 0.01 M in THF), 2-phenylethanol (1.46 mL, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography 20:1 pentane:Et_2O. Yield: 478 mg = 1.95 mmol = 65% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.92 (dd, *J* = 2.5, 0.7 Hz, 1H), 8.02-7.93 (m, 3H), 7.82 (dd, *J* = 8.4, 0.7 Hz, 1H), 7.70-7.64 (m, 2H), 7.55-7.46 (m, 2H), 7.46-7.38 (m, 1H), 7.35-7.29 (m, 2H), 2.42. (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 156.4, 148.5, 139.7, 138.3, 136.7, 135.4, 135.0, 130.0, 129.6, 128.5, 127.4, 127.1, 120.3, 21.6 ppm. **MS** (70 eV, EI); m/z (%): 245 (100, M^+), 202 (6), 123 (6), 102 (5).



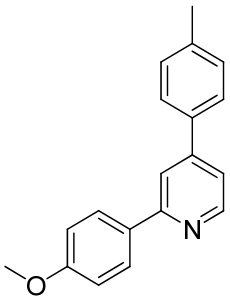
1m: 5-(3,4-dimethoxyphenyl)-2-p-tolylpyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), 2-(3,4-dimethoxyphenyl)ethanol (1.64 g, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography 1:1 Et_2O:pentane → pure Et_2O. Yield: 851 mg = 2.79 mmol = 93% as colorless solid **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.90-8.86 (m, 1H), 7.99-7.95 (m, 2H), 7.92 (dd, *J* = 8.4, 2.5 Hz, 1H), 7.79 (dd, *J* = 8.4, 0.7 Hz, 1H), 7.33-7.28 (m, 2H), 7.24-7.19 (m, 1H), 7.16 (d, *J* = 2.1 Hz, 1H), 6.99 (d, *J* = 8.2 Hz, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 2.41 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 155.9, 150.2, 150.0, 148.2, 139.6, 136.7, 135.0, 134.9, 131.0, 130.0, 127.0, 120.2, 119.8, 112.5, 110.8, 56.5, 56.4, 21.5 ppm. **MS** (70 eV, EI); m/z (%): 305 (100, M^+), 290 (16), 262 (40), 218 (12), 204 (5), 153 (12), 115 (5), 91 (5). **Elemental analysis** (%) for $C_{20}H_{19}NO_2$ calcd C 78.66, H 6.27, N 4.59; found: C 78.98, H 6.54, N 4.62.



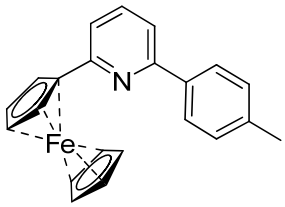
1n: 5-(pyridin-3-ylmethyl)-2-p-tolylpyridine: Catalyst A (4.5 mL, 0.045 mmol, 0.01 M in THF), 3-(pyridin-3-yl)propan-1-ol (1.55 mL, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography pure Et_2O→ 1:1 Et_2O:acetone. Yield: 733 mg = 2.82 mmol = 94% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.53 (dd, *J* = 5.0, 1.8 Hz, 2H), 8.46 (dd, *J* = 5.0, 1.8 Hz, 1H), 7.92-7.87 (m, 2H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.56-7.49 (m, 2H), 7.31-7.19 (m, 3H), 4.01 (s, 2H), 2.39 (s, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 156.0, 150.7, 150.3, 148.5, 139.5, 137.5, 136.8, 136.6, 136.2, 134.2, 129.9, 127.0, 124.0, 120.3, 36.4, 21.5 ppm. **MS** (70 eV, EI); m/z (%): 260 (100, M^+), 232 (5), 217 (4), 182 (7), 167 (5), 142 (5), 115 (8), 65 (5). **Elemental analysis** (%) for $C_{18}H_{16}N_2$ calcd C 83.04, H 6.19, N 10.76; found: C 83.13, H 6.12, N 10.72.



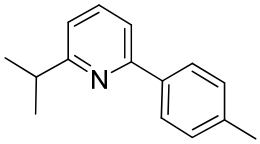
1o: p-tolyl(6-p-tolylpyridin-3-yl)methanamine: Catalyst A (3.0 mL, 0.03 mmol, 0.01 M in THF), 3-amino-3-p-tolylpropan-1-ol (990 mg, 6.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography pure EtOAc. Yield: 300 mg = 1.05 mmol = 35% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.66 (d, *J* = 2.3 Hz, 1H), 7.91-7.86 (m, 2H), 7.76-7.71 (1H), 7.66 (dd, *J* = 7.3, 0.9 Hz, 1H), 7.33-7.24 (m, 4H), 7.17-7.12 (m, 2H), 5.25 (s, 1H), 2.39 (s, 3H), 2.32 (s, 3H), 1.77 (s_br, 2H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 156.3, 149.0, 142.8, 140.1, 139.4, 137.5, 136.9, 135.6, 129.9, 129.8, 127.2, 127.1, 120.1, 57.7, 21.5, 21.3 ppm. **MS** (70 eV, EI); m/z (%): 288 (20, M^+), 271 (40), 207 (8), 197 (48), 170 (100), 141 (8), 120 (38), 91 (24), 77 (10), 65 (11). **Elemental analysis** (%) for $C_{18}H_{16}N_2$ calcd C 83.30, H 6.99, N 9.71; found: C 83.19, H 7.36, N 9.43.



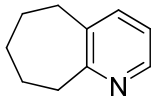
1p: 2-(4-methoxyphenyl)-4-p-tolylpyridine: Catalyst A (3.0 mL, 0.03 mmol, 0.01 M in THF), 1-(4-methoxyphenyl)ethanol (1.69 mL, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C→ 24h at 130 °C. Purification by column chromatography pure Et_2O. Yield: 396 mg = 1.44 mmol = 48% as colorless solid. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.64 (dd, *J* = 5.1, 0.8 Hz, 1H), 8.08-8.01 (m, 2H), 7.92-7.89 (m, 1H), 7.66-7.60 (m, 2H), 7.40 (dd, *J* = 5.1, 1.8 Hz, 1H), 7.36-7.30 (m, 2H), 7.05-6.98 (m, 2H), 3.87 (s, 3H), 2.42 (s, 3H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 161.2, 157.9, 150.5, 149.4, 139.8, 136.2, 132.6, 130.3, 128.7, 127.4, 119.9, 117.9, 114.6, 55.9, 21.5 ppm. **MS** (70 eV, EI); m/z (%): 275 (100, M^+), 260(22), 232 (15), 217 (10), 189 (4), 138 (6), 115 (8). **Elemental analysis** (%) for $C_{19}H_{17}NO$ calcd C 82.88, H 6.22, N 5.09; found: C 82.90, H 6.35, N 5.10.



1q: 2-ferrocenyl-6-p-tolylpyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), 1-ferrocenyl-ethanol (2.76 g, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10.0 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24 h at 90 °C. Purification by column chromatography 60:1 pentane:Et_2O Yield: 571 mg = 1.62 mmol = 54% as orange solid. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 8.02 (d, *J* = 8.2 Hz, 2H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.54 (dd, *J* = 7.81, 0.8 Hz, 1H), 7.35 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.31, (d, *J* = 7.8 Hz, 2H), 5.03-5.02 (m, 2H), 4.42-4.41 (m, 2H), 4.06 (s, 6H), 2.43 (s, 3H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 159.3, 156.7, 139.4, 137.4, 137.1, 129.8, 127.2, 118.7, 117.2, 84.9, 70.3, 70.1, 68.0, 21.6 ppm. **MS** (70 eV, EI); m/z (%): 353 (100), 288 (26), 231 (6), 207 (8), 191 (6), 177 (8), 121 (8), 56 (6). **Elemental analysis** (%) for $C_{17}H_{19}N$ calcd C 74.80, H 5.42, N 3.97; found: C 74.61, H 5.33, N 3.96.

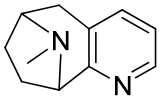


1r: 2-isopropyl-6-p-tolylpyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), 3-methylbutan-2-ol (1.08 mL, 12.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24 h at 90 °C. Purification by column chromatography 10:1 pentane:Et_2O Yield: 361 mg = 1.71 mmol = 57% as colorless oil. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.97-7.92 (m, 2H), 7.68-7.63 (m, 1H), 7.53 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.30-7.25 (m, 2H), 7.10 (d, *J* = 7.8 Hz, 1H), 3.16-3.04 (m, 1H), 2.40 (s, 3H), 1.34 (d, *J* = 7.0 Hz, 6H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 167.5, 156.6, 139.3, 137.6, 137.5, 129.8, 127.2, 119.3, 117.7, 37.0, 22.9, 21.5 ppm. **MS** (70 eV, EI); m/z (%): 211 (30), 196 (100), 183 (40), 168 (15), 154 (8), 128 (8), 115 (10), 91 (9), 77 (8).

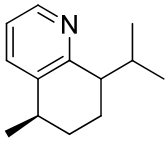


2a: 5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Catalyst A (0.9 mL, 0.009 mmol, 0.01 M in THF), cycloheptanol (725 µL, 6.0 mmol), 3-amino-1-propanol (229 µL, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C. Purification by column chromatography 10:1 pentane:Et_2O. Yield: 401 mg = 2.73 mmol = 91% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.23 (dd, *J* = 4.7, 1.5 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.99 (dd, *J* = 7.6,

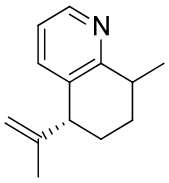
4.7 Hz, 1H) 3.03-2.99 (m, 2H), 2.78-2.74 (m, 2H), 1.90-1.83 (m, 2H), 1.69-1.63 (m, 4H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 163.9, 146.6, 138.6, 136.6, 121.6, 40.0, 35.8, 33.1, 28.6, 27.1 ppm. **MS** (70 eV, EI); m/z (%): 147 (80, M^+), 132 (40), 118 (100), 104 (8), 91 (8), 77 (7), 65 (10).



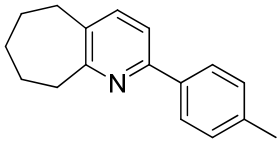
2b: 5,7,8-Trihydro-(N-methyl-azabicyclo[3.2.1]octa)[*b*]pyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01M in THF), tropin (845 mg, 6.0 mmol), 3-amino-1-propanol (229 µL, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24 h at 90 °C. Purification by column chromatography 3:1 Et_2O:MeOH; Yield: 365 mg = 2.1 mmol = 70% as orange oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.32 (dd, *J* = 4.7, 1.8 Hz, 1H), 7.26 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.05-6.98 (m, 1H), 3.80 (d, *J* = 5.6 Hz, 1H), 3.52-3.44 (m, 1H), 3.24 (dd, *J* = 17.9, 5.6 Hz, 1H), 2.52 (d, *J* = 17.9 Hz, 1H), 2.32 (s, 3H), 2.27-2.17 (m, 2H), 1.76-1.68 (m, 1H), 1.61-1.53 (m, 1H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 155.0, 148.0, 136.9, 133.9, 121.5, 63.8, 59.1, 37.6, 37.1, 35.0, 29.7 ppm. **MS** (70 eV, EI); m/z (%): 174 (15, M^+), 145 (100), 118 (8), 104 (4), 82 (6). **Elemental analysis** (%) for $C_{11}H_{14}N_2$ calcd C 75.82, H 8.10, N 16.08; found: C 75.85, H 8.25, N 16.25.



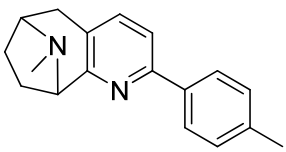
2c: (5R)-8-isopropyl-5-methyl-5,6,7,8-tetrahydroquinoline: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), L-menthol (1.87 g, 12.0 mmol), 3-amino-1-propanol (228 µL, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C. Purification by column chromatography 20:1 pentane:Et_2O. Yield: 465 mg = 2.46 mmol = 82% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.39-8.32 (m, 1H), 7.55-7.35 (m, 1H), 7.08-6.96 (m, 1H), 3.01-2.67 (m, 3H), 2.05-1.86 (m, 1H), 1.86-1.65 (m, 2H), 1.65-1.35 (m, 1H), 1.29-1.22 (m, 3H), 1.07-0.99 (m, 3H), 0.71-0.55 (m, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 160.2, 160.0, 147.1, 146.9, 138.6, 136.5, 134.6, 121.1, 121.0, 47.2, 46.8, 33.4, 33.1, 31.8, 30.8, 30.3, 29.0, 23.3, 21.9, 21.7, 21.2, 21.1, 18.6, 17.3, 17.1 ppm. **MS** (70 eV, EI); m/z (%): 189 (24, M^+), 174 (22), 147 (95), 146 (100), 144 (16), 132 (60), 130 (55), 117 (20), 91 (6), 77 (10). **Elemental analysis** (%) for $C_{13}H_{19}N$ calcd C 82.48, H 10.12, N 7.40; found: C 82.51, H 9.98, N 7.63. **Optical rotation** $[\alpha]_D^{25}$ = -5.4° (± 0.1) (c = 1; CH_2Cl_2).



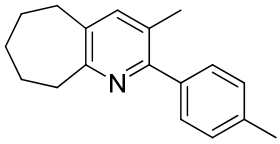
2d: (5R)-8-methyl-5-(prop-1-en-2-yl)-5,6,7,8-tetrahydroquinoline: Catalyst A (3.0 mL, 0.03 mmol, 0.01 M in THF), (5S)-2-methyl-5-(prop-1-en-2-yl)cyclohexanol (1.85 g, 12.0 mmol), 3-amino-1-propanol (228 µL, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C. Purification by column chromatography 3:1 pentane:Et_2O. Yield: 426 mg = 2.28 mmol = 76% as colorless oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 8.37 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H), 7.29 (ddd, *J* = 7.8, 1.8, 0.9 Hz, 1H), 7.02 (ddd, *J* = 7.8, 4.6, 0.7 Hz, 1H), 4.95-4.92 (m, 1H), 4.69-4.66 (m, 1H), 3.61-3.52 (m, 1H), 3.02-2.87 (m, 1H), 2.17-2.04 (m, 1H), 1.99-1.87 (m, 1H), 1.8-1.71 (m, 1H), 1.61 (dd, *J* = 1.5, 0.9 Hz, 3H), 1.60-1.45 (m, 1H), 1.35 (d, *J* = 1.4 Hz, 3H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 162.0, 148.7, 147.6, 136.9, 133.5, 121.3, 114.4, 48.3, 36.7, 30.6, 26.9, 21.2, 19.6 ppm. **MS** (70 eV, EI); m/z (%): 187 (20), 172 (30), 158 (25), 144 (100), 130 (42), 117 (15), 91 (5), 77 (10). **Elemental analysis** (%) for $C_{13}H_{17}N$ calcd C 83.37, H 9.15, N 7.48; found: C 83.45, H 9.44, N 7.67. **Optical rotation** $[\alpha]_D^{25}$ = +51.6° (± 0.1) (c = 1; CH_2Cl_2).



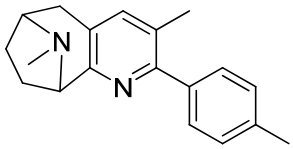
2e: 2-p-tolyl-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Catalyst A (1.5 mL, 0.015 mmol, 0.01 M in THF), cycloheptanol (723 µL, 6.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C. Purification by column chromatography 40:1 pentane:Et_2O. Yield: 683 mg = 2.88 mmol = 96% as colorless solid. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.91 (d, *J* = 8.2 Hz, 2H), 7.47-7.40 (m, 2H), 7.26 (d, *J* = 8.20 Hz, 2H), 3.13-3.08 (m, 2H), 2.83-2.78 (m, 2H), 2.40 (s, 3H), 1.95-1.87 (m, 2H), 1.76-1.65 (m, 4H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 163.5, 154.0, 138.8, 137.6, 137.4, 137.0, 129.8, 126.9, 117.7, 40.3, 35.5, 33.2, 28.8, 27.3, 21.5 ppm. **MS** (70 eV, EI); m/z (%): 237 (100, M^+), 222 (16), 208 (40), 183 (6), 91 (6). **Elemental analysis** (%) for $C_{17}H_{19}N$ calcd C 86.03, H 8.07, N 5.90; found: C 85.91, H 8.31, N 5.95.



2f: 2-p-Tolyl-5,7,8-trihydro-(N-methyl-azabicyclo[3.2.1]octa)[*b*]pyridine: Catalyst A (2.4 mL, 0.024 mmol, 0.01 M in THF), tropin (845 mg, 6.0 mmol), 3-amino-3-p-tolylpropan-1-ol (495 mg, 3.0 mmol), 10.0 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24 h at 90 °C. Purification by column chromatography 10:1 Et_2O:MeOH→ 3:1 Et_2O:MeOH; Yield: 665 mg = 2.52 mmol = 84% as yellow oil. **^{1}H NMR** (400 MHz, CD_2Cl_2): δ = 7.86 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 2H), 3.85 (d, *J* = 5.9 Hz, 1H), 3.53 (t, *J* = 6.1 Hz, 1H), 3.31 (dd, *J* = 17.6, 5.1 Hz, 1H), 2.59 (d, *J* = 17.6 Hz, 1H), 2.39 (s, 3H), 2.36 (s, 3H), 2.32-2.20 (m,2H), 2.12 (s, 2H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 155.5, 154.6, 139.1, 137.4, 135.3, 134.8, 129.8, 127.0, 118.0, 63.7, 59.2, 37.9, 37.1, 35.1, 29.8, 21.5 ppm. **MS** (70 eV, EI); m/z (%): 264 (15, M^+), 235 (100), 222 (3), 219 (5), 208 (5), 117 (15). **Elemental analysis** (%) for $C_{17}H_{19}N$ calcd C 81.78, H 7.63, N 10.60; found: C 81.51, H 7.92, N 10.46.



2g: 3-methyl-2-p-tolyl-5,6,7,8,9-pentahydro-cyclohepta[*b*]pyridine: Catalyst A (3.0 mL, 0.03 mmol, 0.01 M in THF), cycloheptanol (725 µL, 6.0 mmol), 3-amino-2-methyl-3-p-tolylpropan-1-ol (534 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24h at 90 °C. Purification by column chromatography 10:1 pentane: Et_2O. Yield: 655 mg = 2.61 mmol = 87% as colorless solid. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.47-7.38 (m, 2H), 7.30-7.22 (m, 3H), 3.07-3.03 (m, 2H), 2.82-2.77 (m, 2H), 2.43 (s, 3H), 2.30 (s, 3H), 1.94-1.88 (m, 2H), 1.75-1.68 (m, 4H) ppm. **^{13}C NMR** (75 MHz, CD_2Cl_2): δ = 160.7, 155.1, 139.6, 138.8, 137.7, 136.8, 129.5, 129.1, 128.1, 39.7, 35.3, 33.2, 28.9, 27.5, 21.5, 19.8 ppm. **MS** (70 eV, EI); m/z (%): 251 (45, M^+), 234 (4), 222 (5), 194 (3), 115 (3), 91 (4), 77 (3). **Elemental analysis** (%) for $C_{18}H_{21}N$ calcd C 86.01, H 8.42, N 5.57; found: C 86.22, H 8.12, N 5.68.

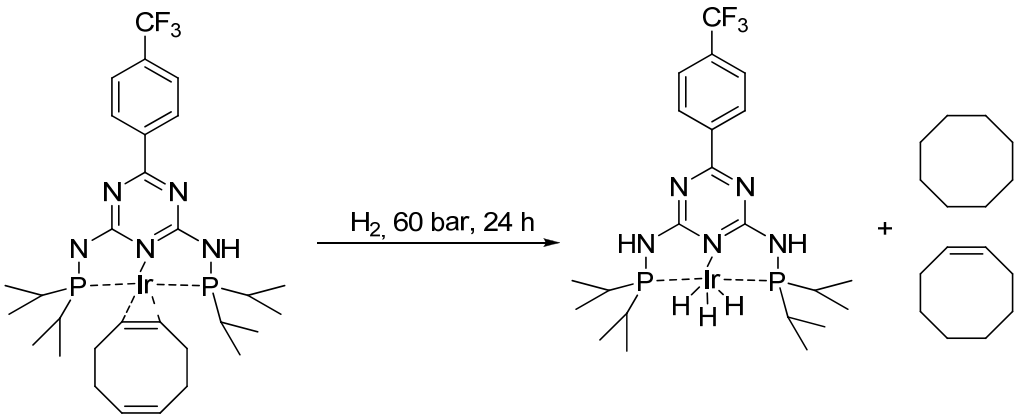


2h:2-p-tolyl-2-methyl-5,7,8-trihydro-N-methyl-azabicyclo[3.2.1]octa[*b*]pyridine:
Catalyst A (3.0 mL, 0.03 mmol, 0.01M in THF), tropin (845 mg, 6.0 mmol), 3-amino-2-methyl-3-p-tolylpropan-1-ol (537 mg, 3.0 mmol), 10 mL THF, NaO^{t}Bu (317 mg, 3.3 mmol), 24 h at 90 °C. Purification by column chromatography 3:1 Et_2O:MeOH; Yield: 700 mg = 2.52 mmol = 84% as orange oil. **^{1}H NMR** (300 MHz, CD_2Cl_2): δ = 7.41-7.35 (m, 2H), 7.27-7.21 (m, 2H), 7.16 (s, 1H), 3.83 (d, *J* = 5.9 Hz, 1H), 3.55-3.48 (m, 1H), 3.25 (dd, *J* = 17.6, 5.0

Hz, 1H), 2.52 (d, *J* = 17.6 Hz, 1H), 2.40 (s, 3H), 2.37 (s, 3H), 2.43-2.31 (m, 1H), 2.28 (s, 3H), 2.26-2.20 (m, 1H), 1.80-1.73 (m, 1H), 1.66-1.56 (m, 1H) ppm. **^{13}C NMR** (100 MHz, CD_2Cl_2): δ = 156.8, 151.6, 138.7, 137.8, 136.5, 135.0, 129.4, 129.1, 128.4, 63.5, 59.1, 37.1, 37.0, 35.1, 29.8, 21.5, 20.0 ppm. **MS** (70 eV, EI); m/z (%): 278 (10, M^+), 249 (100), 222 (5), 117 (13), 91 (4). **Elemental analysis** (%) for $C_{19}H_{22}N_2$ calcd C 81.97, H 7.97, N 10.06; found: C 82.11, H 8.33, N 10.23.

Mechanistic Studies

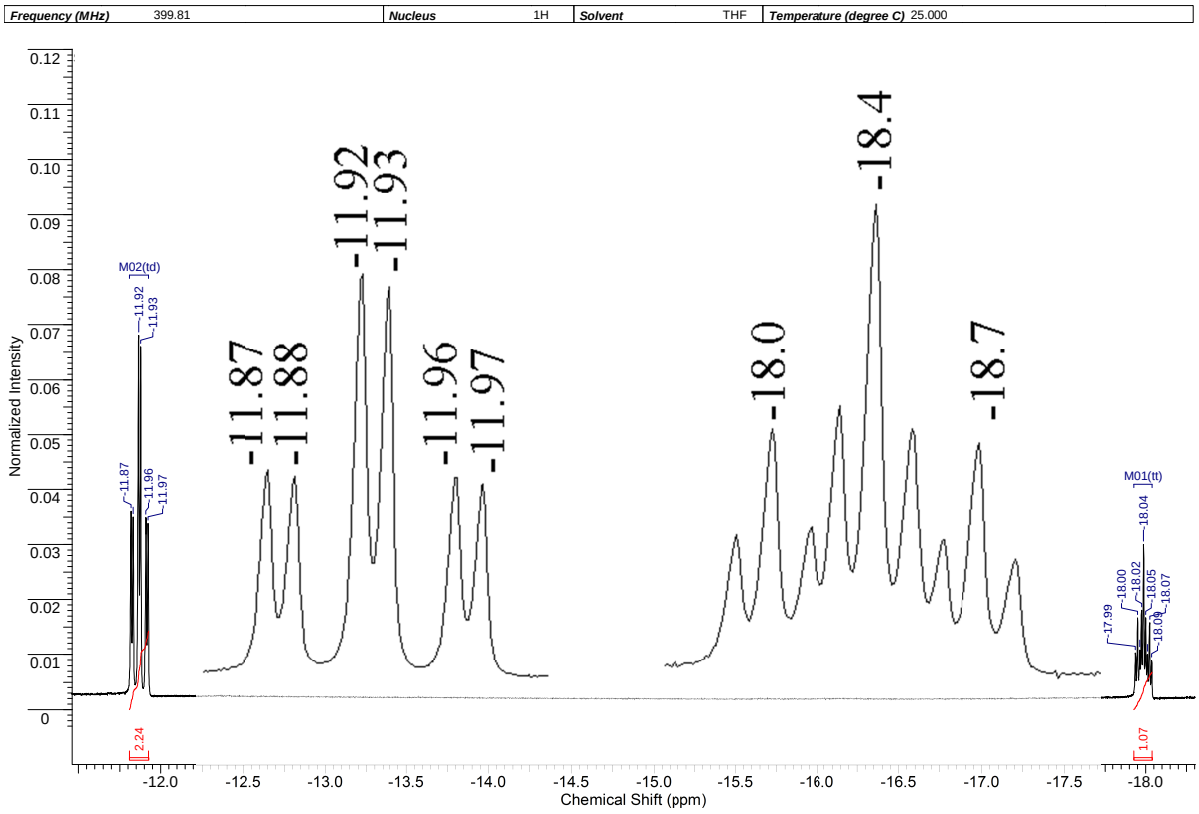
Synthesis of [(4-(4-CF_3)-Ph)Tr(NHP(*i*Pr)$_2$)$_2$IrH_3]

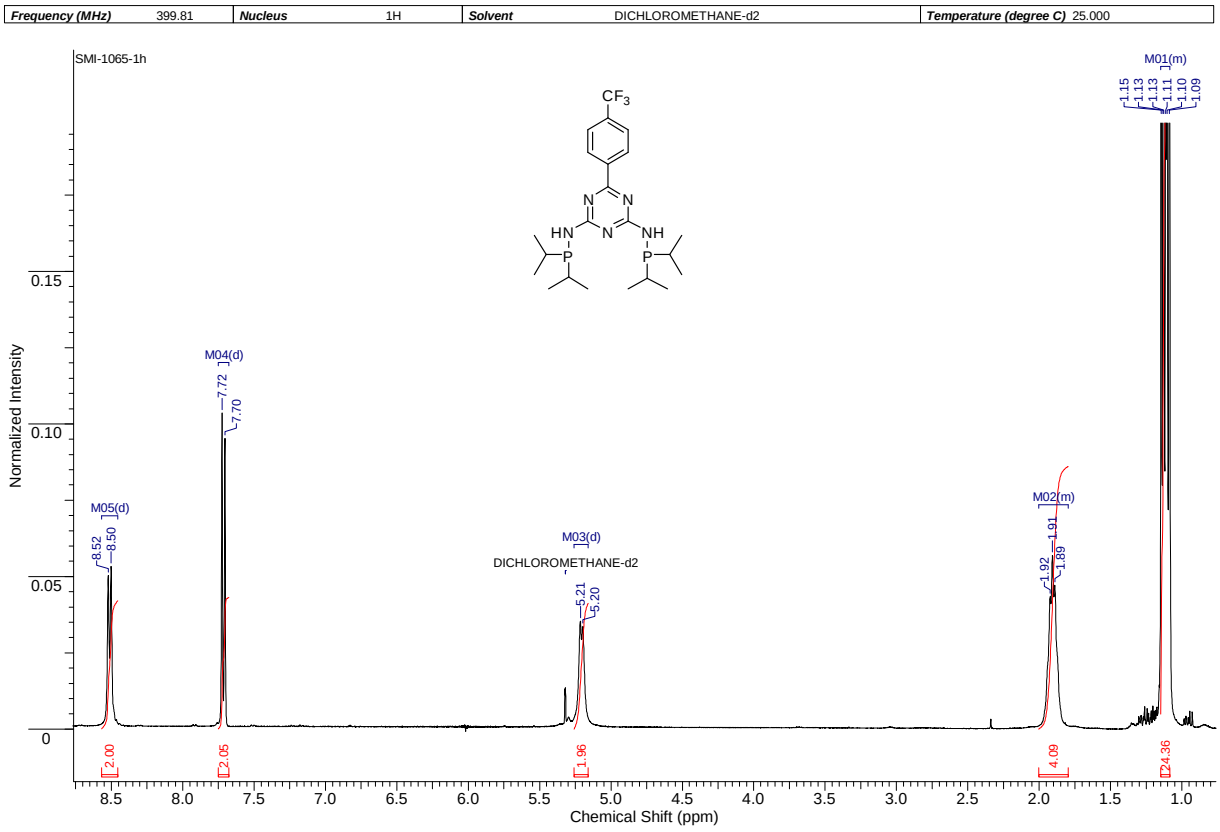


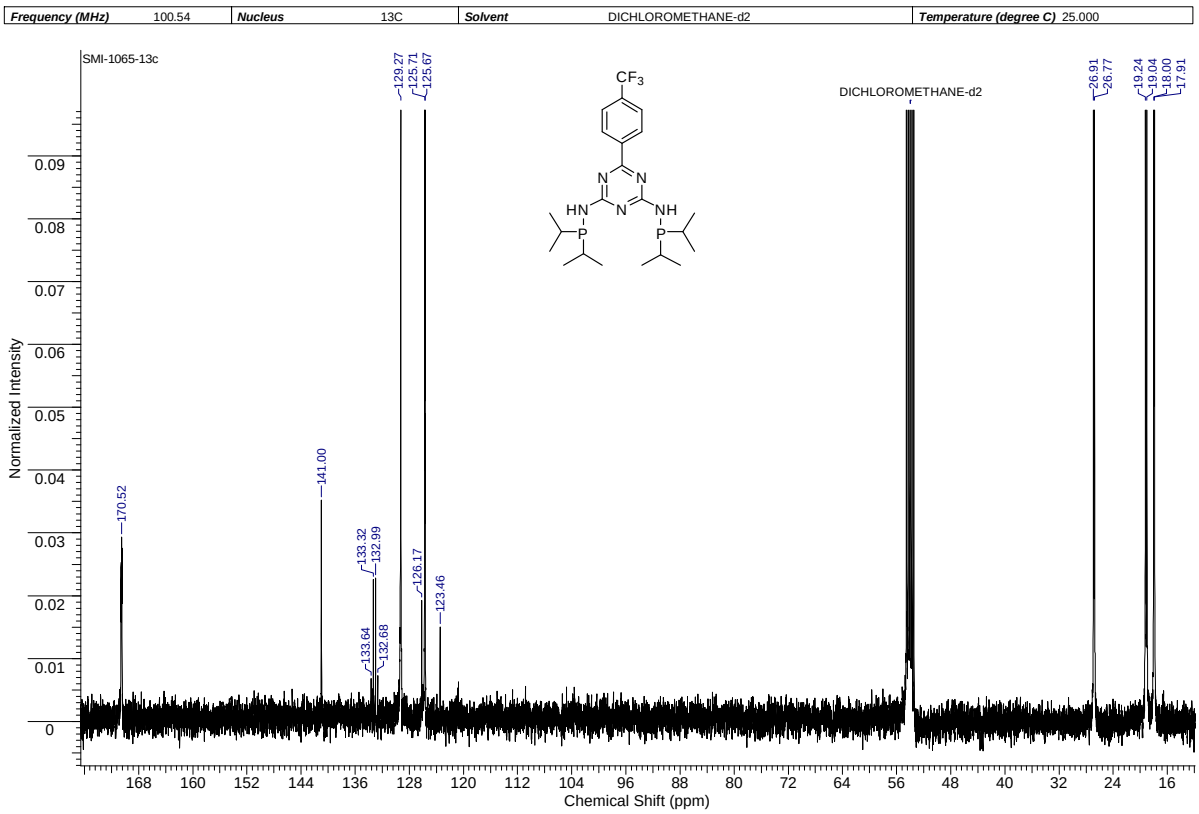
31P NMR (161 MHz, THF-d_8):
δ= 83.09, 82.40 ppm.

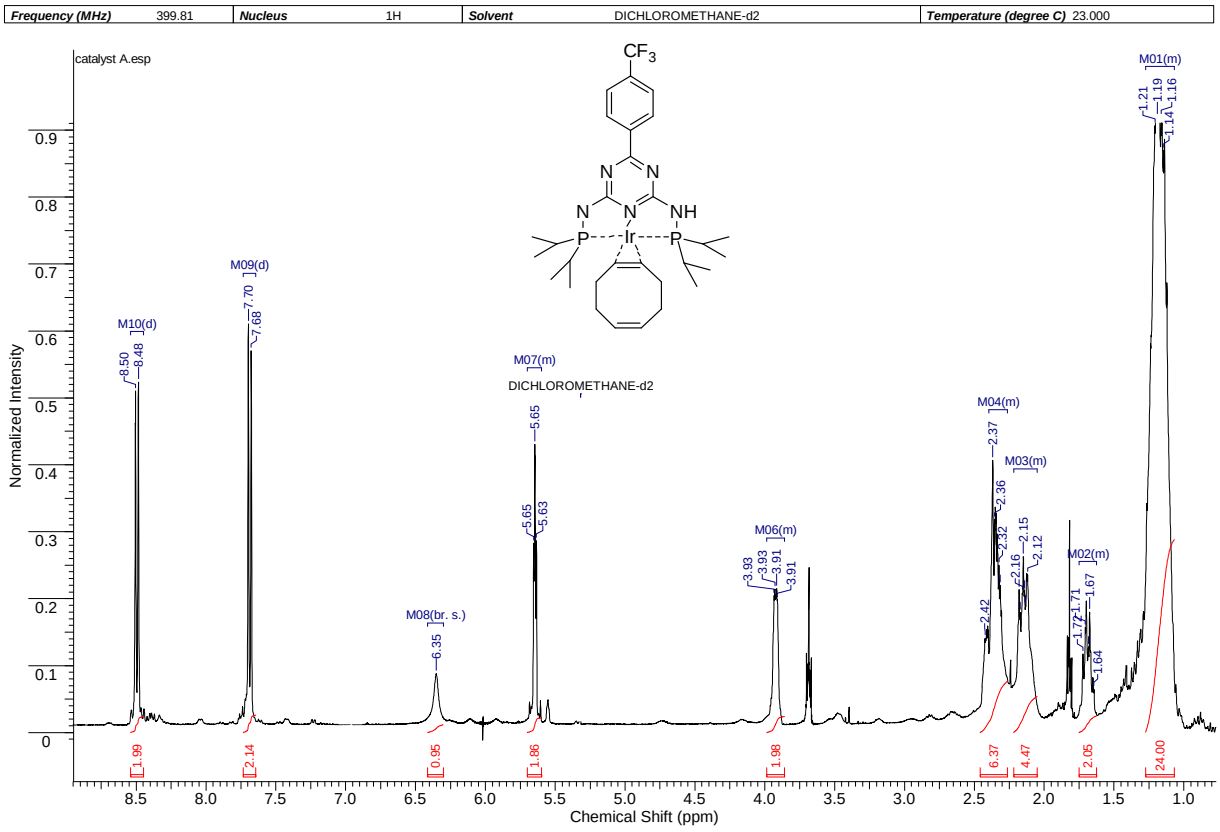
31P NMR (161 MHz, THF-d_8):
δ= 108.25 (d, *J* = 12.5 Hz) ppm.

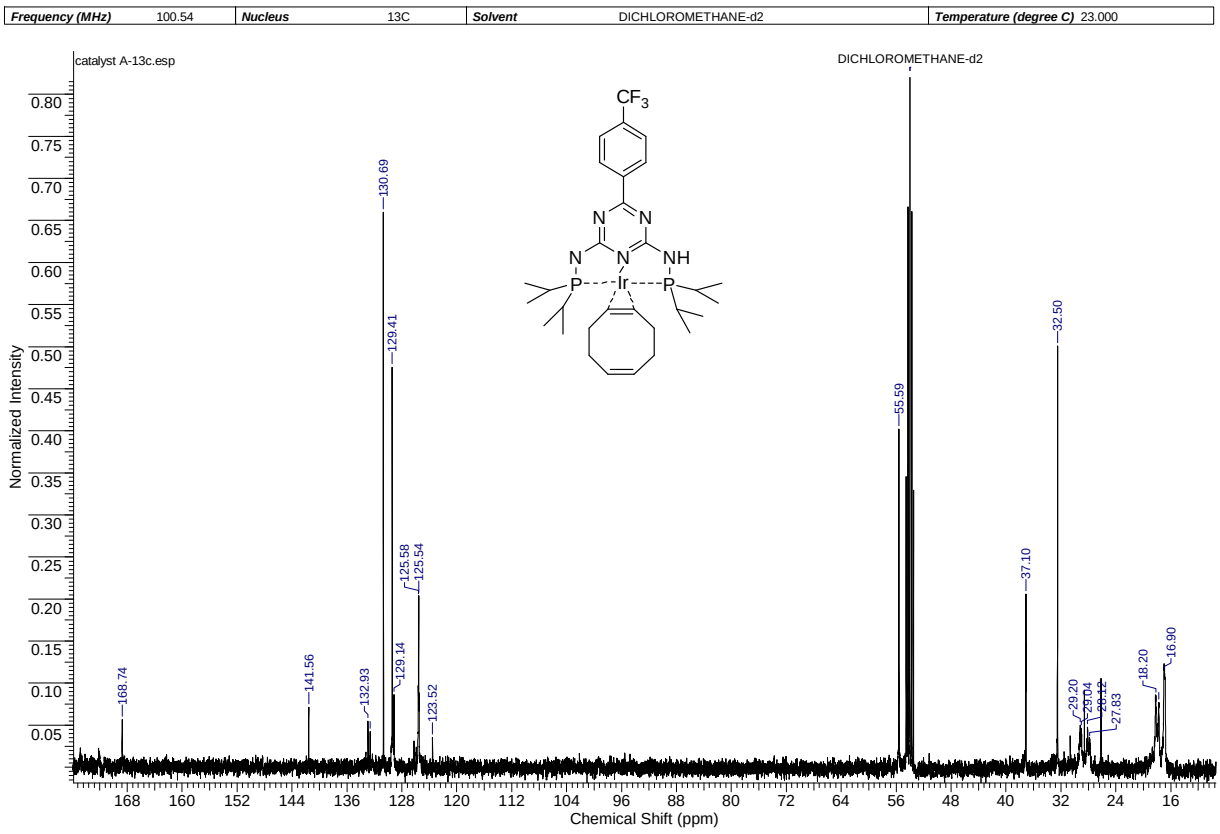
Catalyst A (0.1 mmol, 78 mg) was dissolved in 1 mL THF-d_8 and stirred in a 60 bar H_2 atmosphere at 25 °C for 24 h. An orange solution was obtained. Due to the high reactivity of this compound NMR-analyses was done directly from the reaction solution.

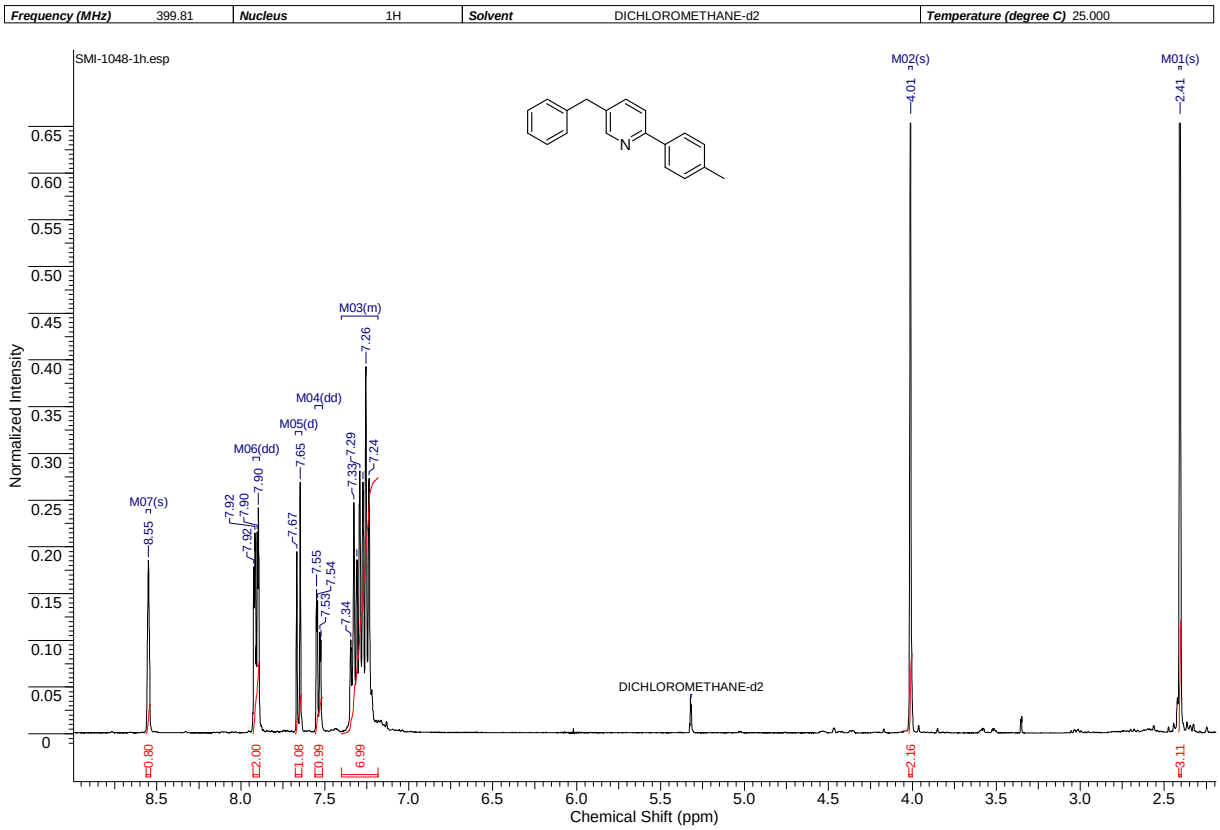

Frequency (MHz) 399.81
Nucleus 1H
Solvent THF
Temperature (degree C) 25.000
Normalized Intensity
Chemical Shift (ppm)
-11.87
-11.88
-11.92
-11.93
-11.96
-11.97
-18.0
-18.4
-18.7
M02(td)
M01(tt)
2.24
1.07

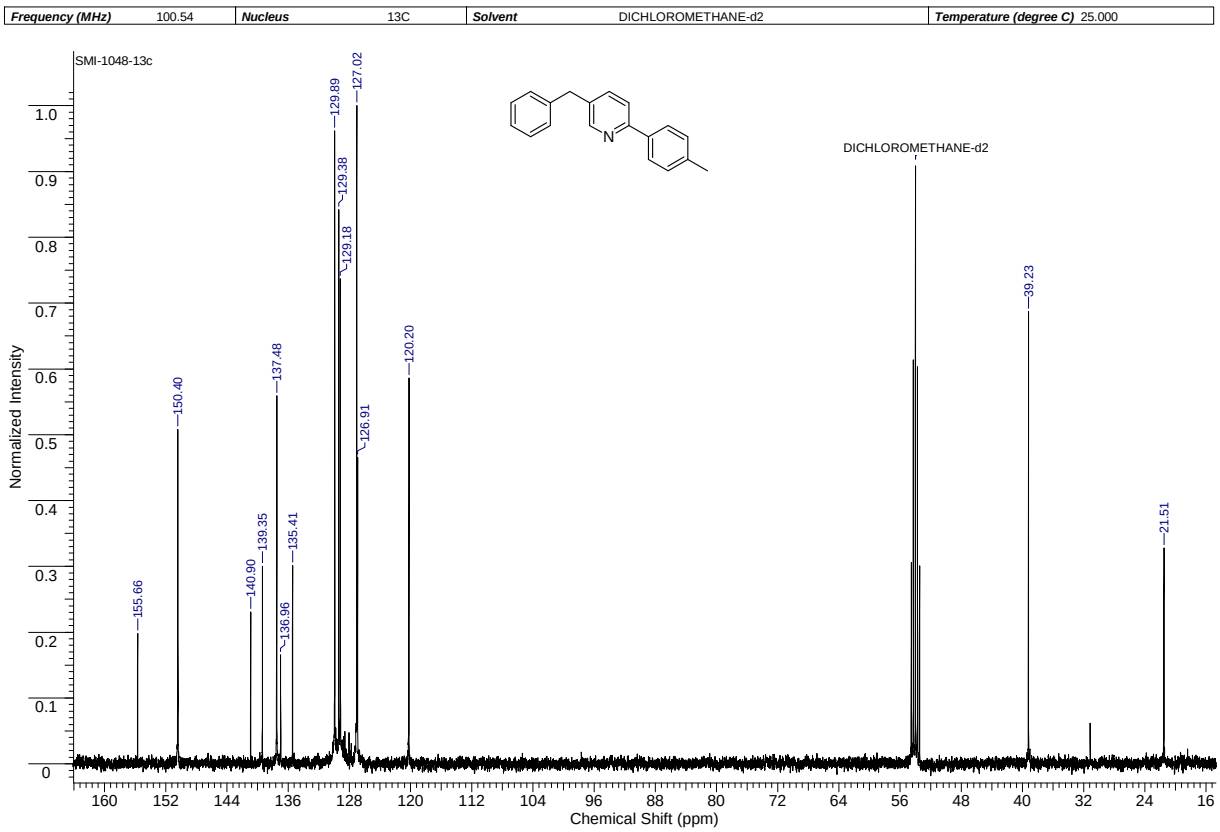

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1065-1h
CF3
HN
NH
P
M01(m)
1.15
1.13
1.13
1.11
1.10
1.09
M04(d)
7.72
7.70
M05(d)
8.52
8.50
M03(d)
DICHLOROMETHANE-d2
5.21
5.20
M02(m)
1.92
1.91
1.89
2.00
2.05
1.96
4.09
24.36
Normalized Intensity
Chemical Shift (ppm)

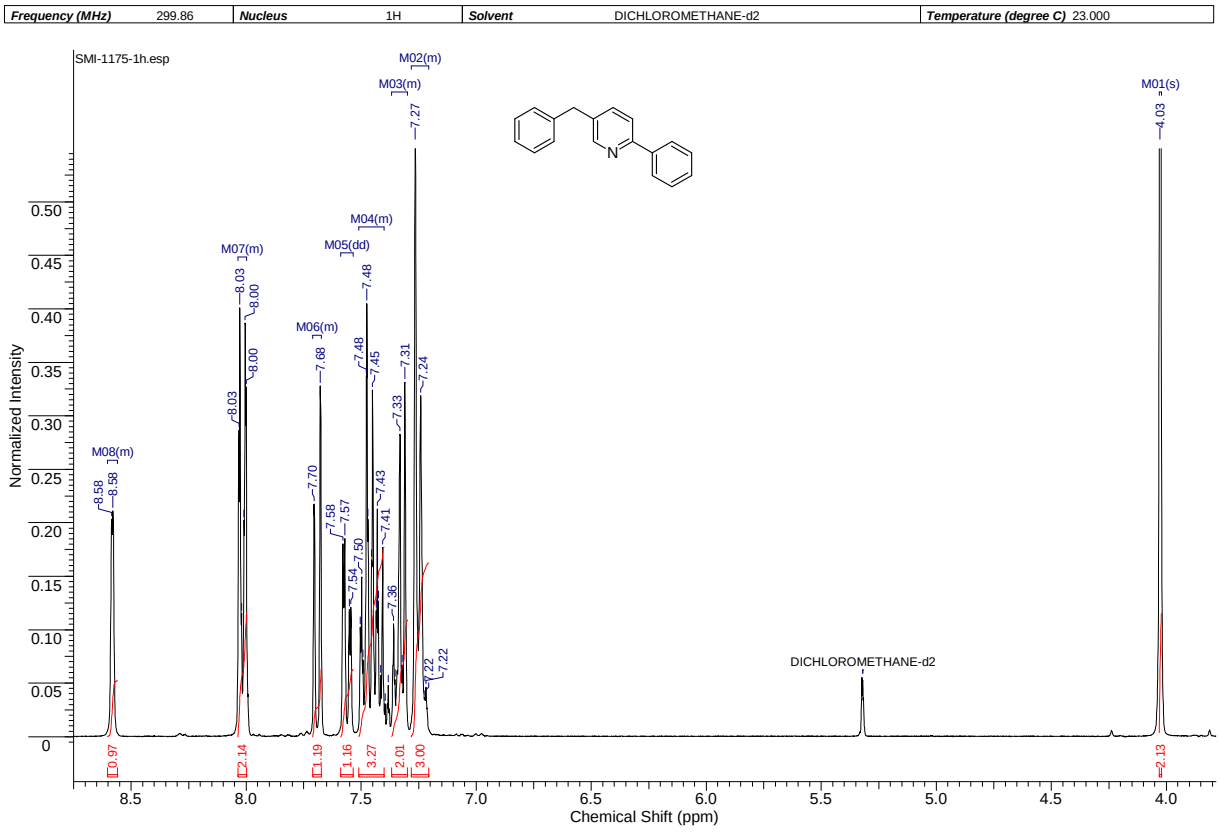

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1065-13c
CF3
HN
NH
P
129.27
125.71
125.67
DICHLOROMETHANE-d2
26.91
26.77
19.24
19.04
18.00
17.91
170.52
141.00
133.32
132.99
133.64
132.68
126.17
123.46
Normalized Intensity
Chemical Shift (ppm)

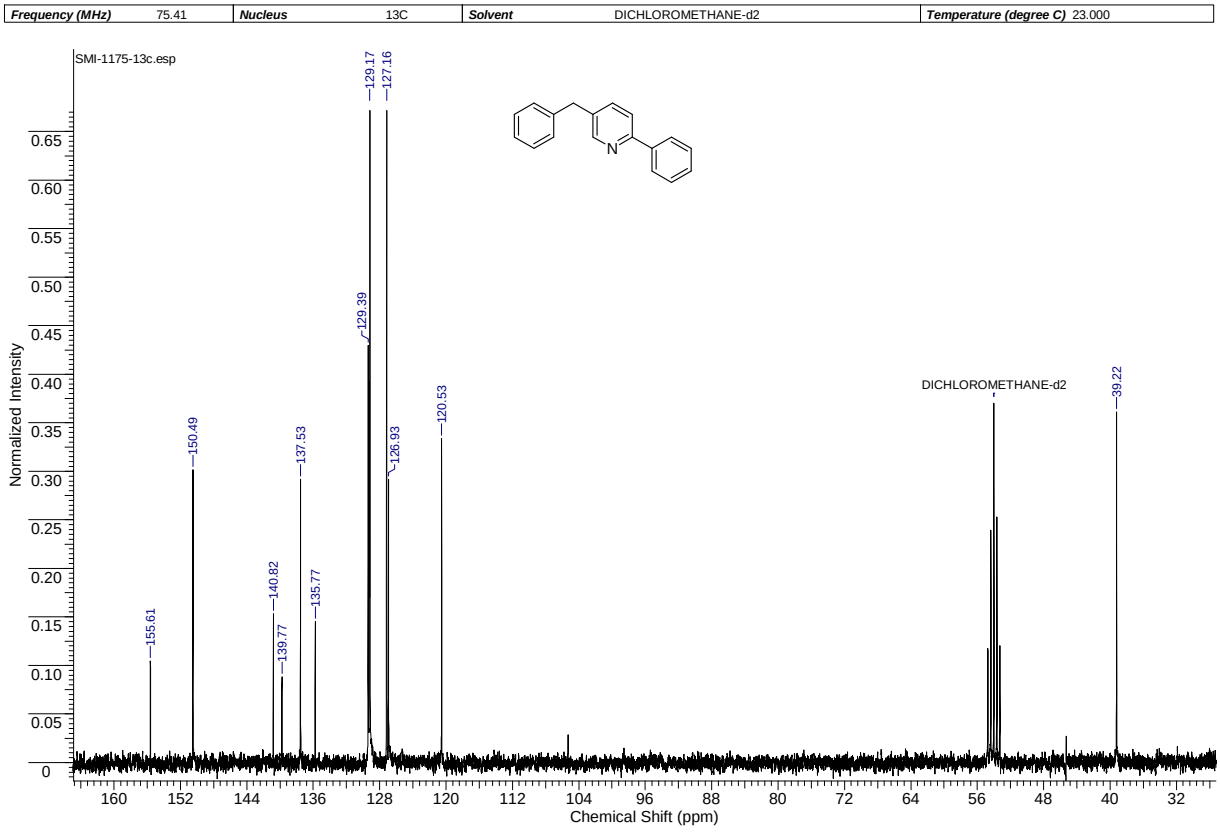

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
catalyst A.esp
CF3
N
N
N
N
NH
P
Ir
P
M01(m)
M02(m)
M03(m)
M04(m)
M06(m)
M07(m)
DICHLOROMETHANE-d2
M08(br. s.)
M09(d)
M10(d)
Normalized Intensity
Chemical Shift (ppm)

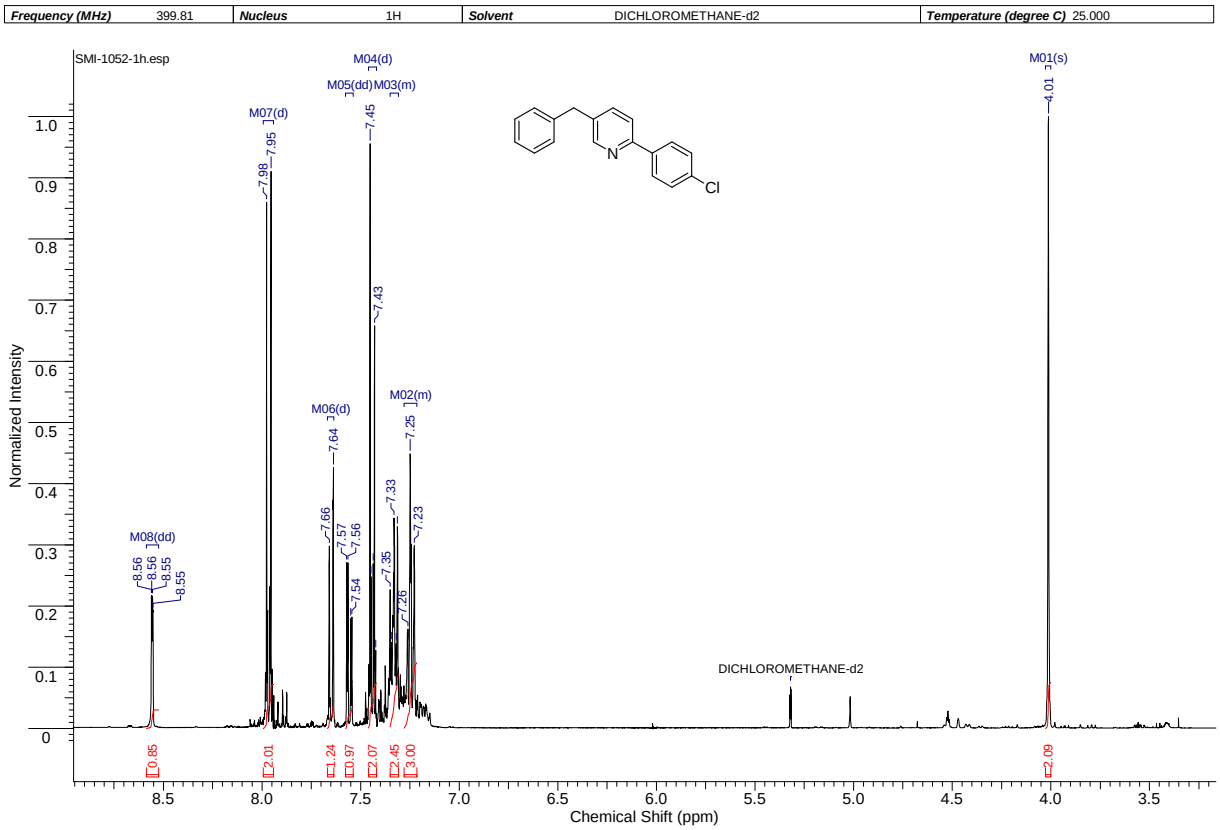

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
catalyst A-13c.esp
DICHLOROMETHANE-d2
CF3
N
N
N
N
NH
P
Ir
P
Normalized Intensity
Chemical Shift (ppm)

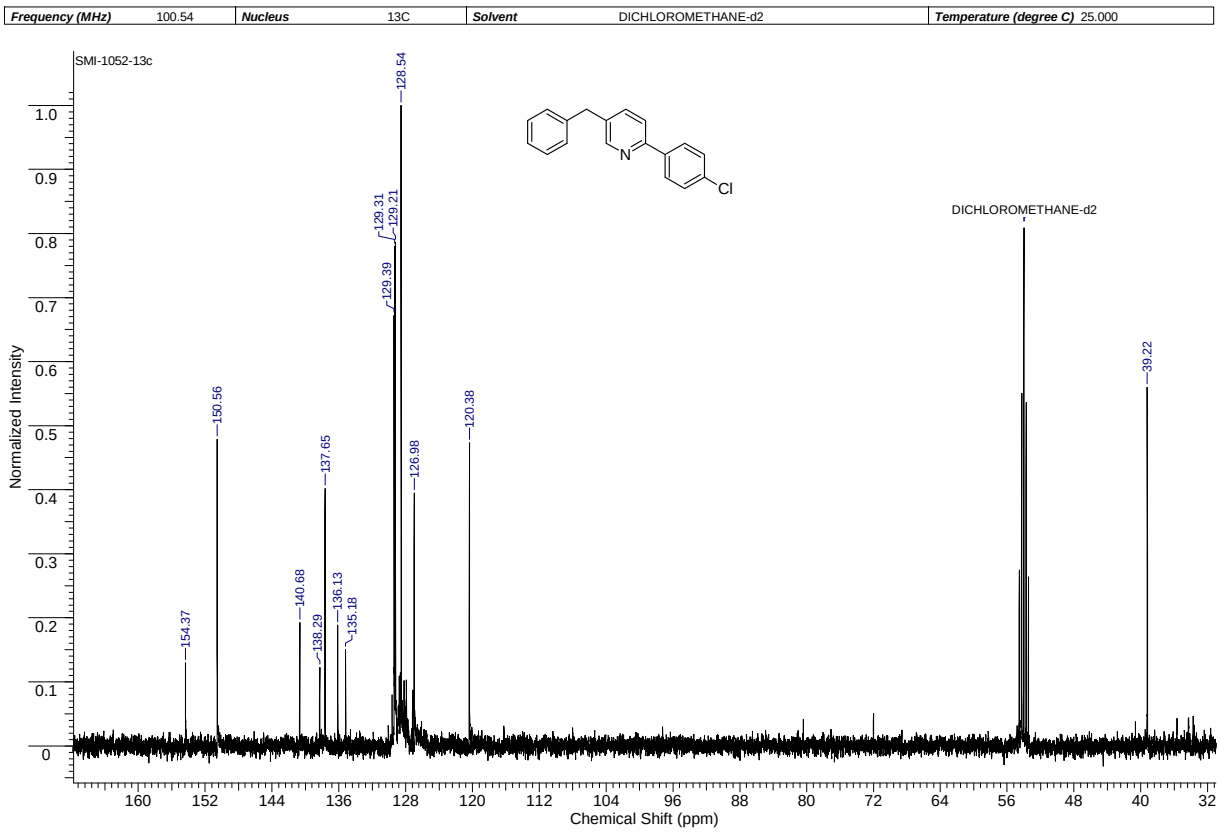

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1048-1h.esp
M01(s)
M02(s)
M03(m)
M04(dd)
M05(d)
M06(dd)
M07(s)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

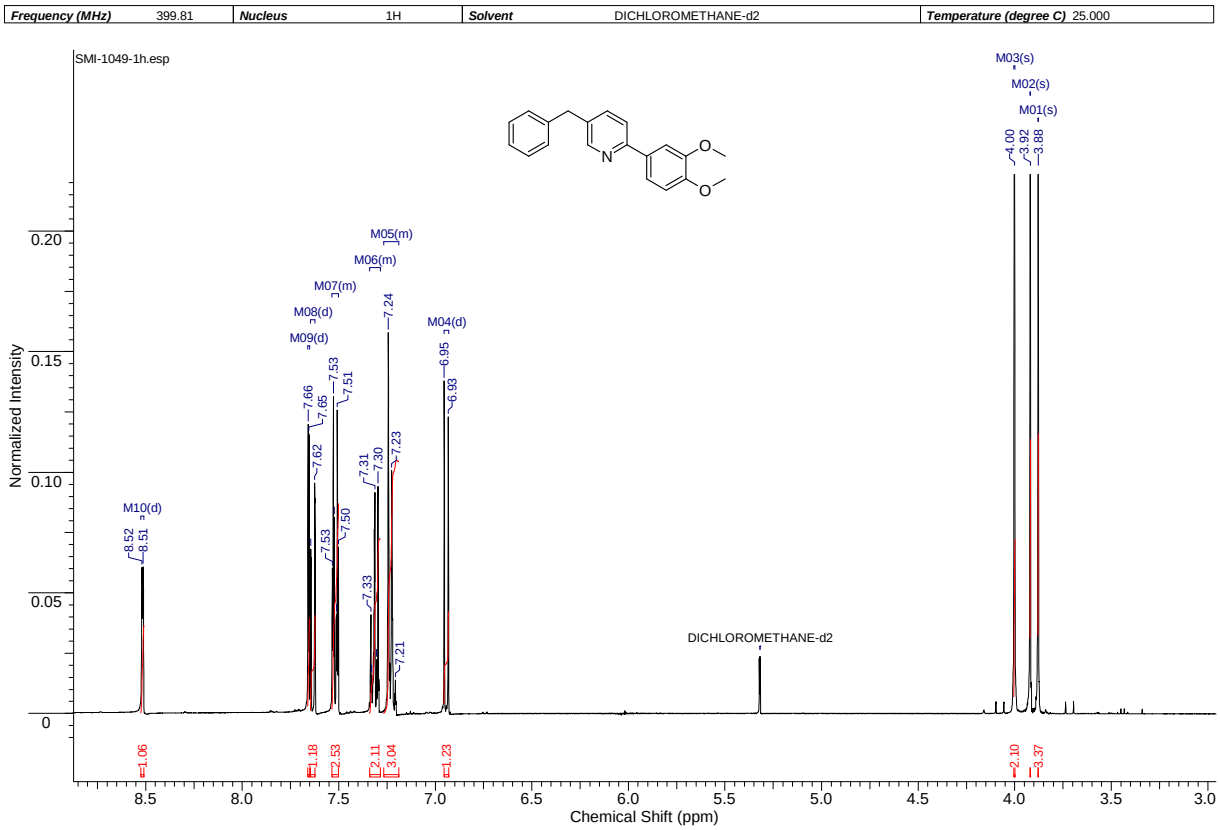

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1048-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

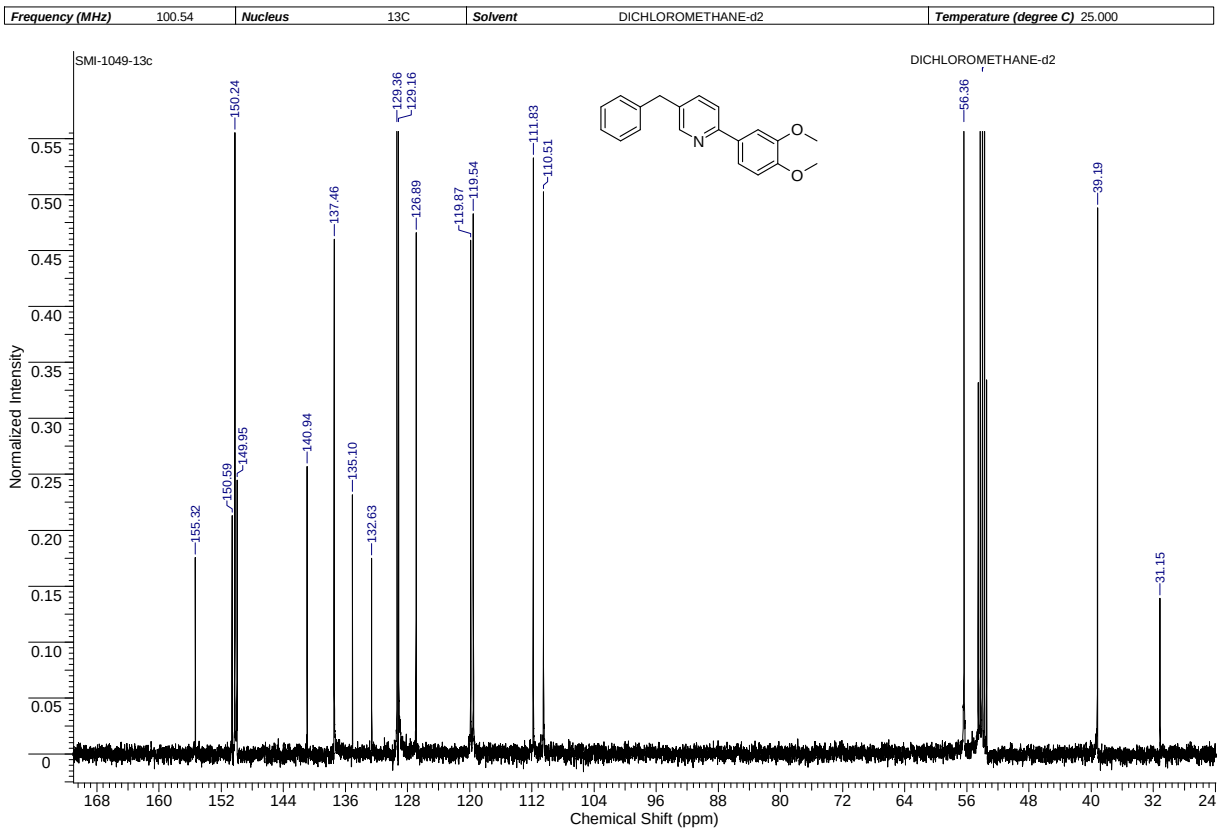

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1175-1h.esp
M01(s)
M02(m)
M03(m)
M04(m)
M05(dd)
M06(m)
M07(m)
M08(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

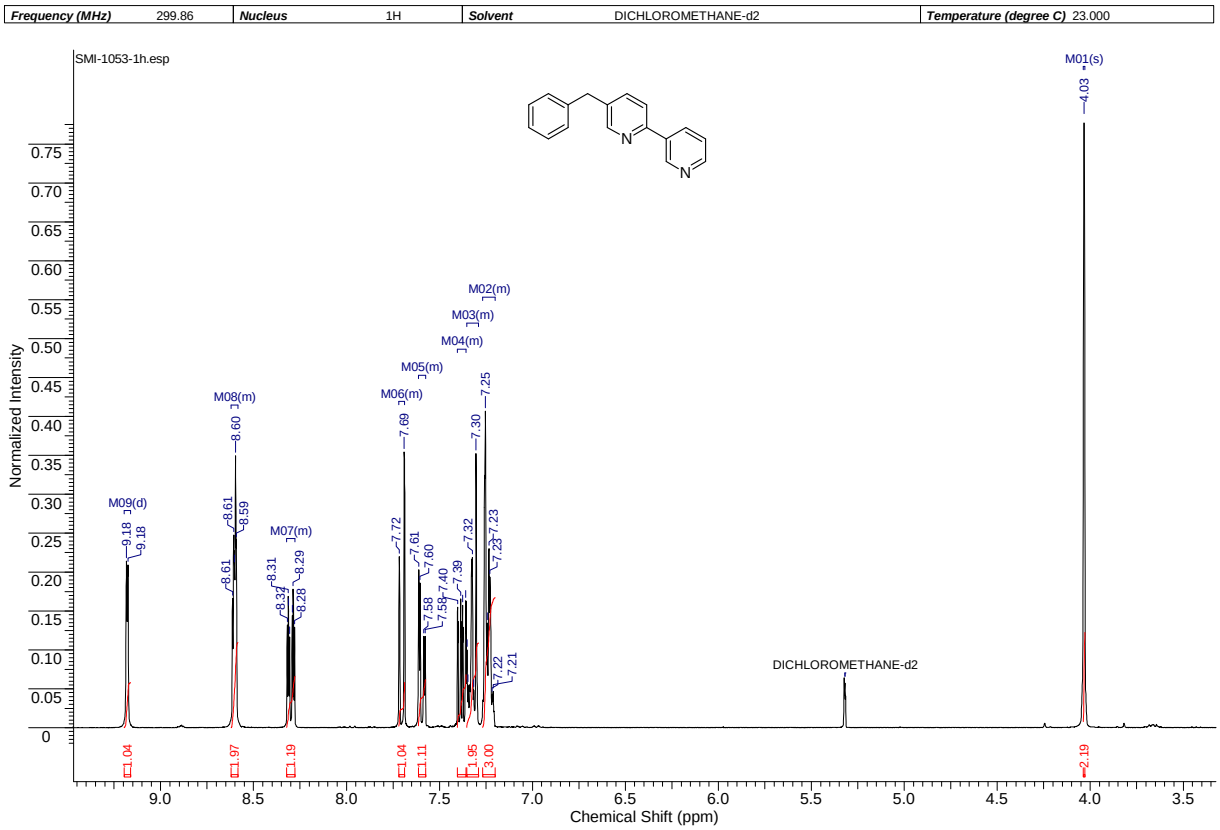

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1175-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

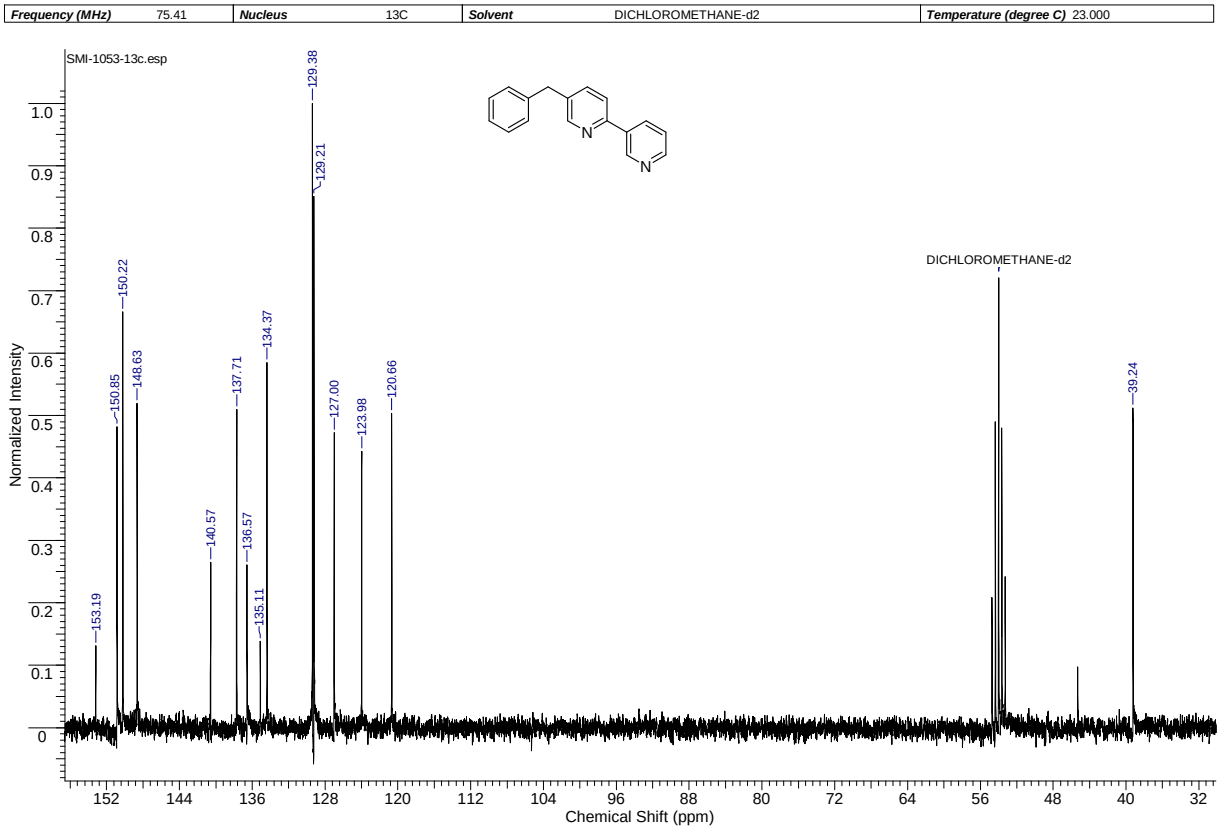

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1052-1h.esp
M04(d)
M05(dd)
M03(m)
M07(d)
M01(s)
M06(d)
M02(m)
M08(dd)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

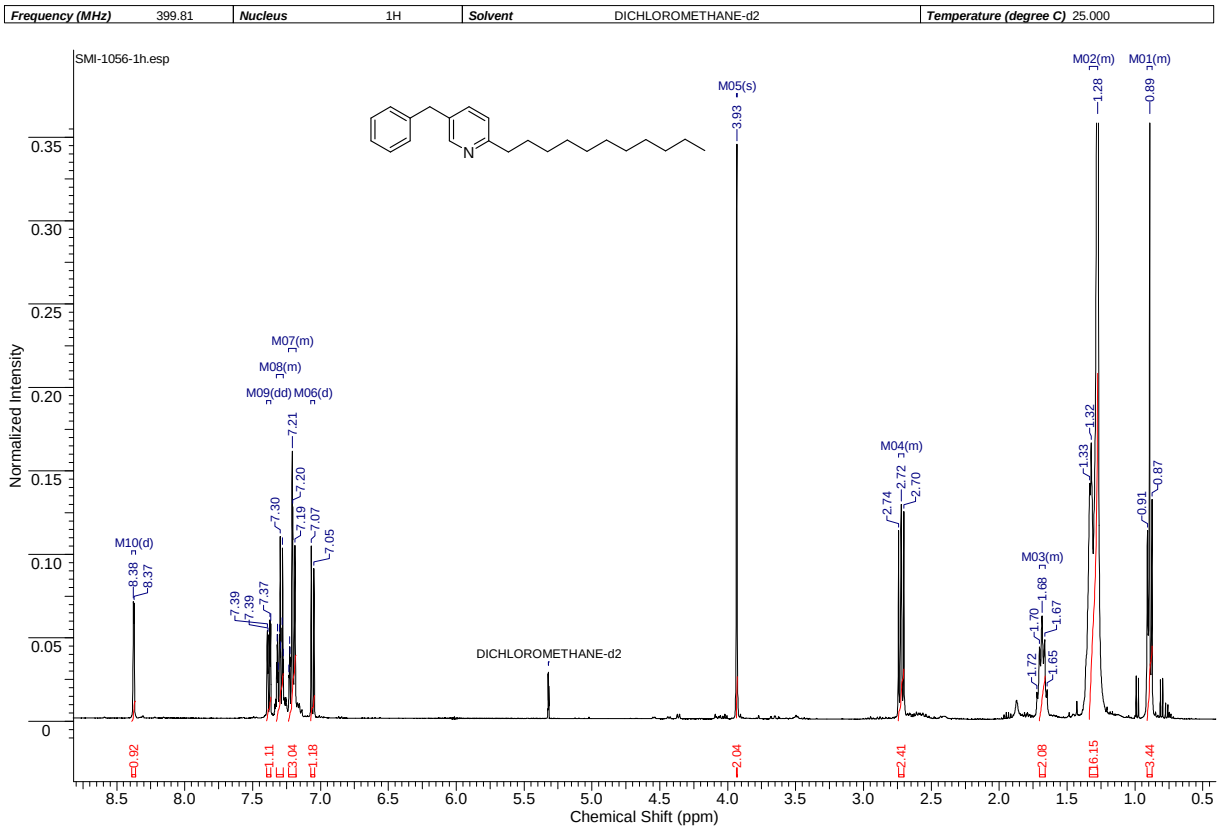

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1052-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

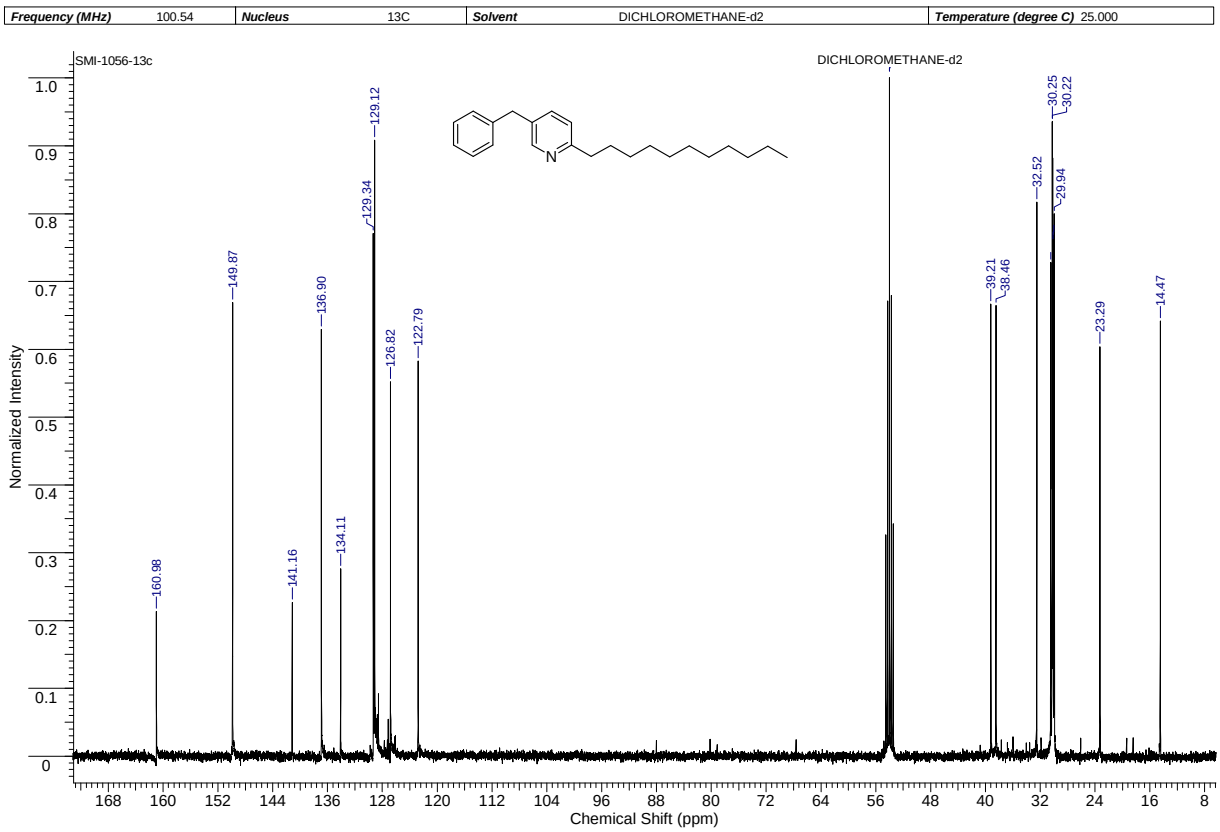

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1049-1h.esp
M03(s)
M02(s)
M01(s)
4.00
3.92
3.88
M05(m)
M06(m)
M07(m)
M08(d)
M09(d)
M04(d)
7.24
6.95
6.93
7.66
7.65
7.62
7.53
7.51
7.31
7.30
7.23
M10(d)
8.52
8.51
7.53
7.50
7.33
7.21
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

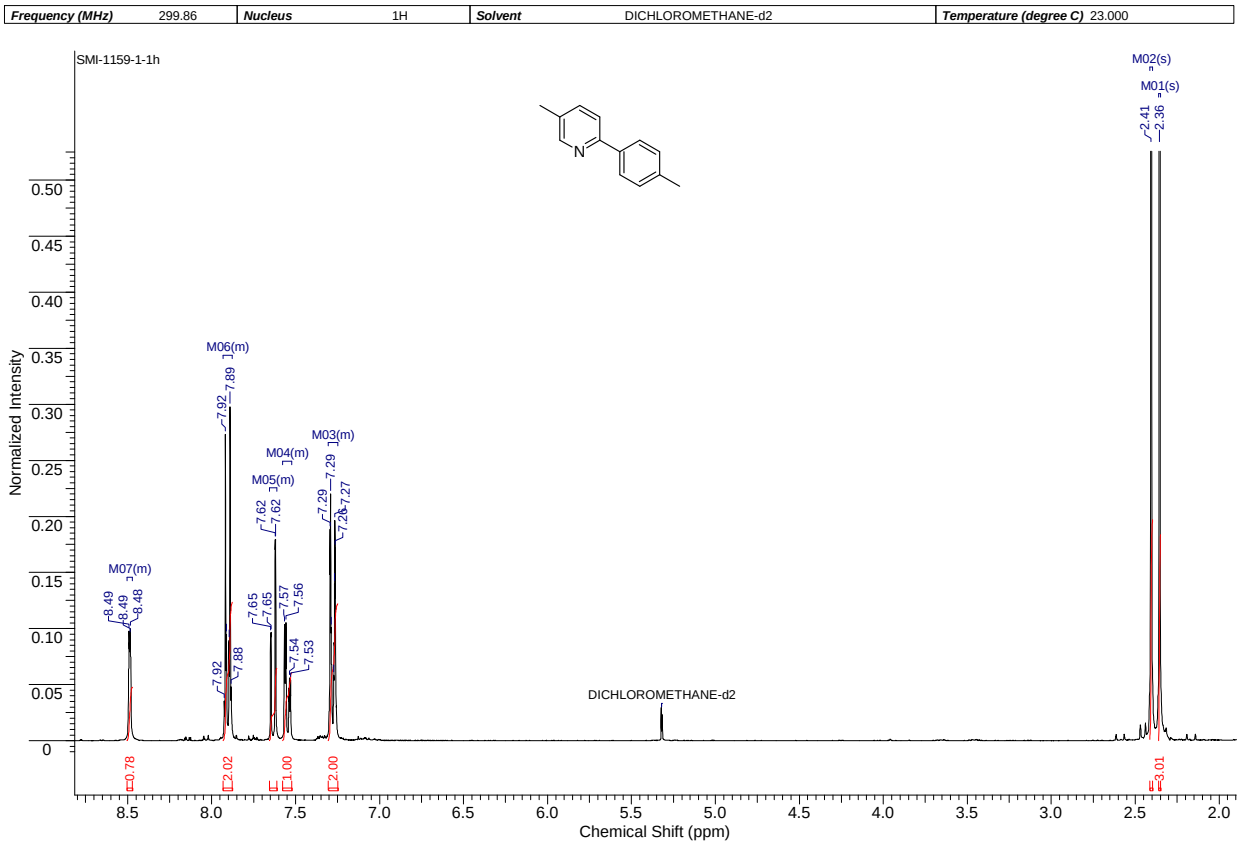

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1049-13c
DICHLOROMETHANE-d2
150.24
129.36
129.16
111.83
110.51
137.46
126.89
119.87
119.54
56.36
39.19
155.32
150.59
149.95
140.94
135.10
132.63
31.15
Normalized Intensity
Chemical Shift (ppm)

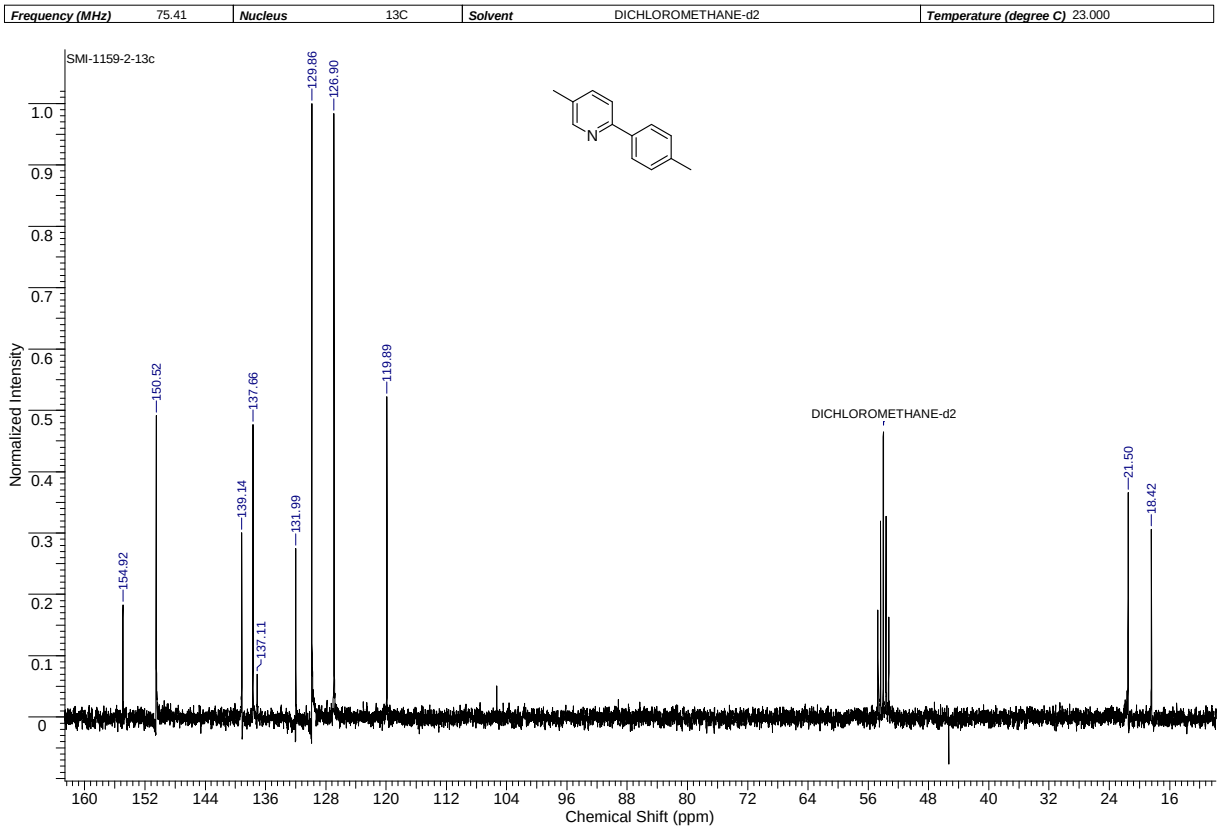

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1053-1h.esp
M01(s)
M02(m)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(m)
M09(d)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

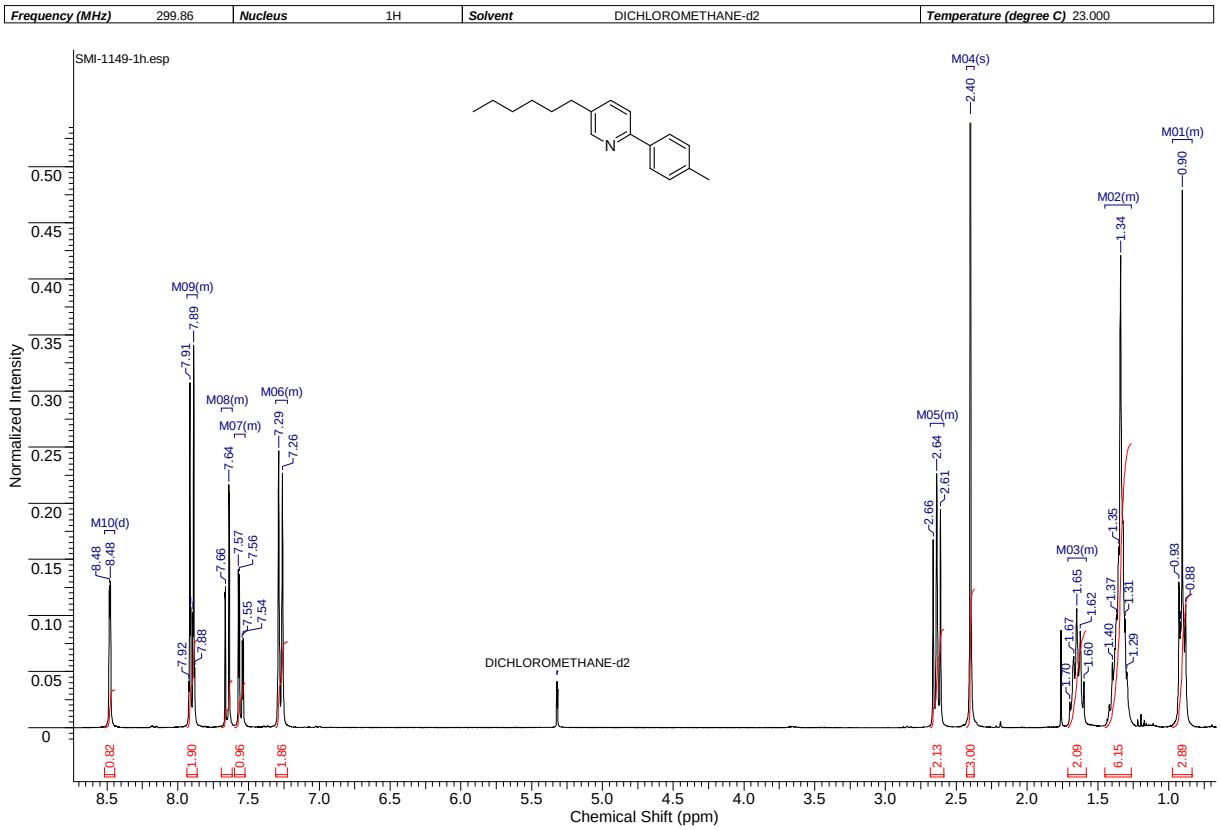

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1053-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

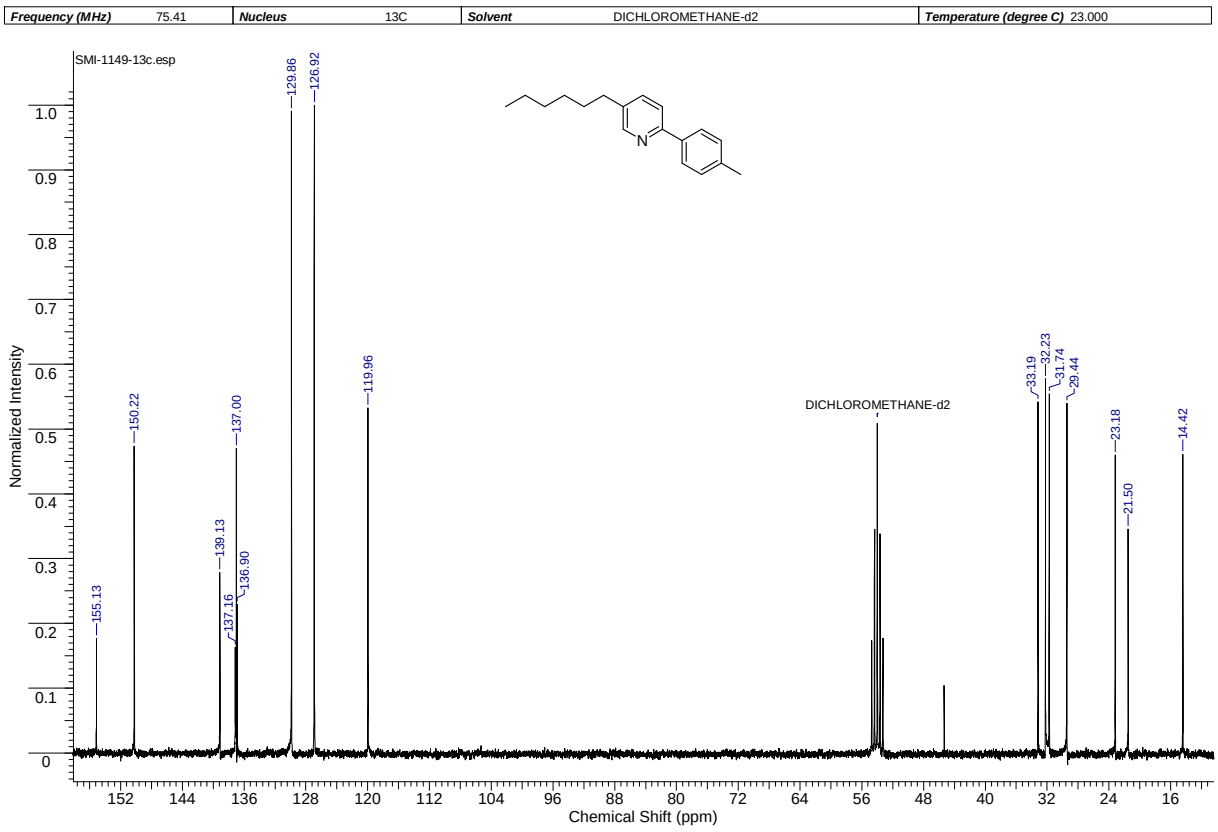

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1056-1h.esp
M05(s)
M02(m)
M01(m)
M07(m)
M08(m)
M09(dd)
M06(d)
M10(d)
M04(m)
M03(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

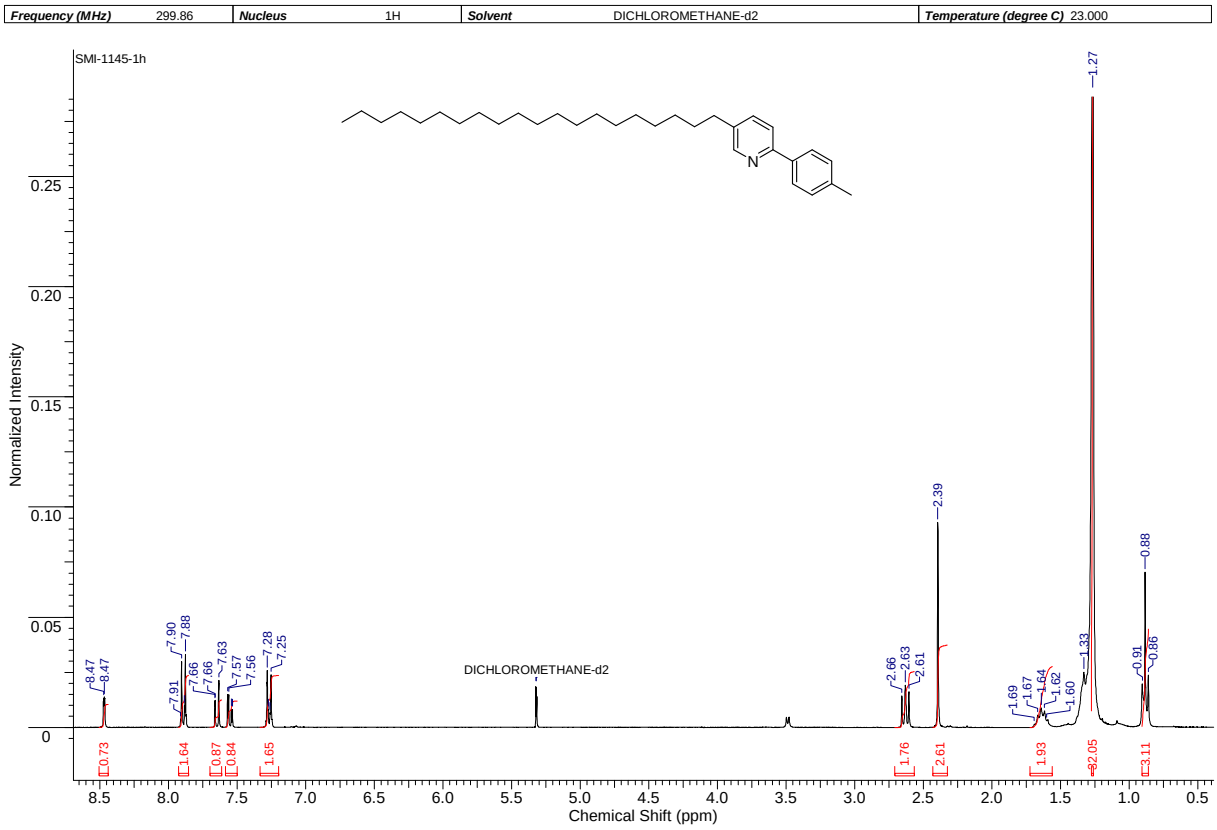

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1056-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

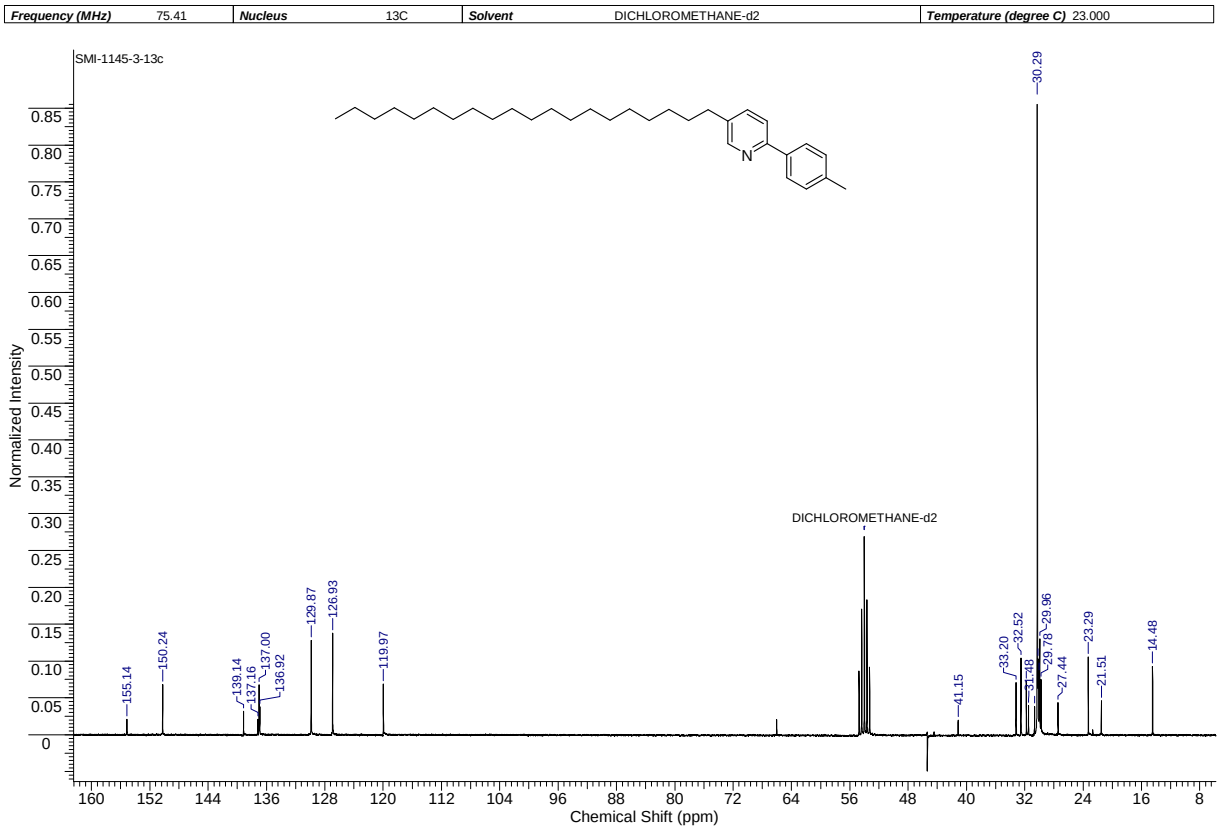

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1159-1-1h
M02(s)
M01(s)
2.41
2.36
M06(m)
7.92
7.89
M03(m)
M04(m)
M05(m)
7.62
7.62
7.29
7.29
7.27
7.26
M07(m)
8.49
8.49
8.48
7.65
7.65
7.57
7.56
7.92
7.88
7.54
7.53
DICHLOROMETHANE-d2
0.78
2.02
1.00
2.00
3.01
Normalized Intensity
Chemical Shift (ppm)

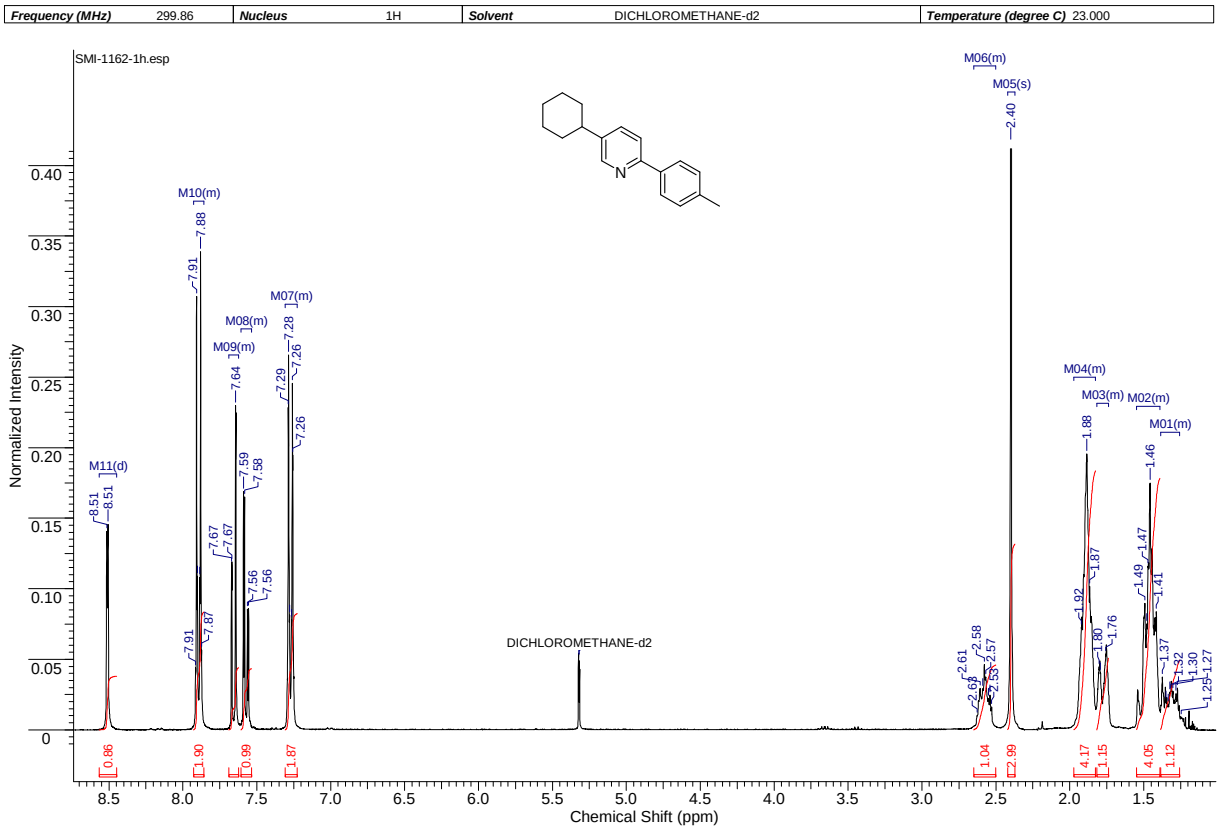

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1159-2-13c
129.86
126.90
150.52
137.66
119.89
139.14
131.99
154.92
137.11
DICHLOROMETHANE-d2
21.50
18.42
Normalized Intensity
Chemical Shift (ppm)

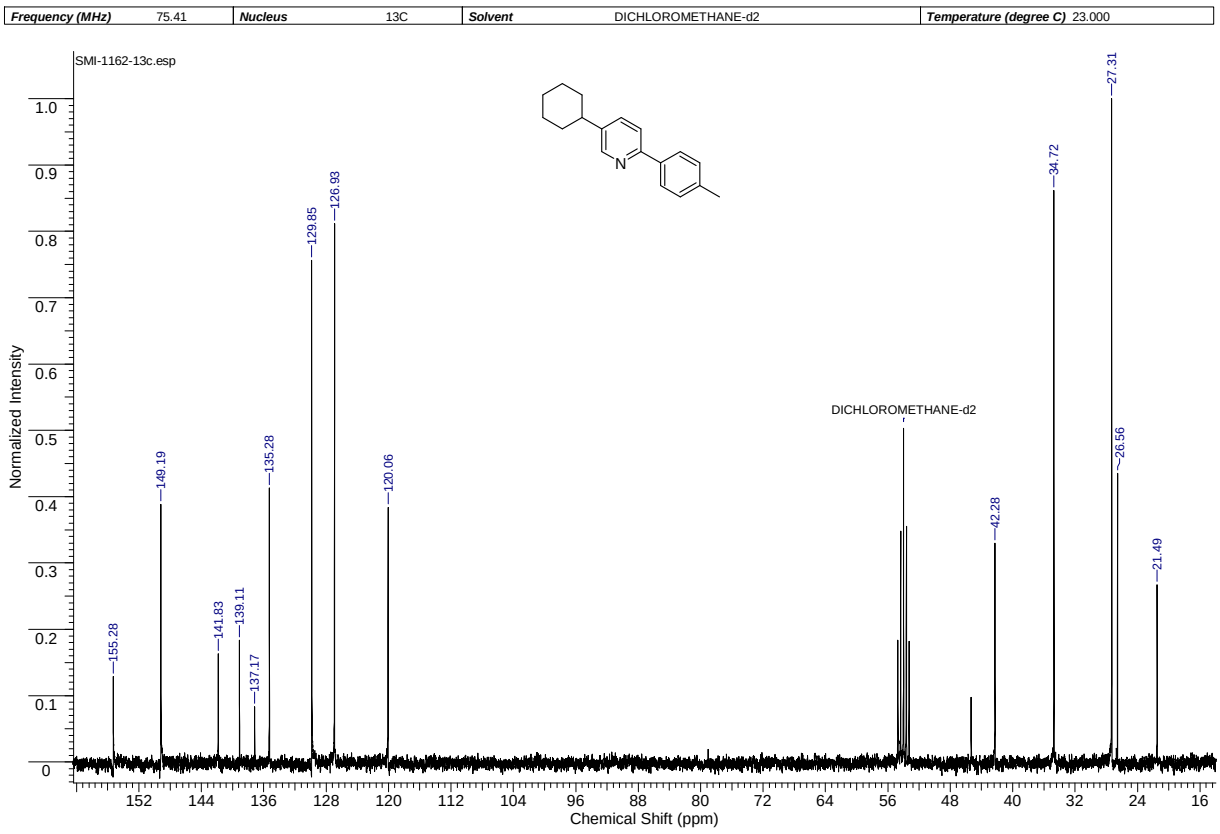

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1149-1h.esp
M04(s)
M01(m)
M02(m)
M09(m)
M08(m)
M06(m)
M07(m)
M05(m)
M10(d)
M03(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

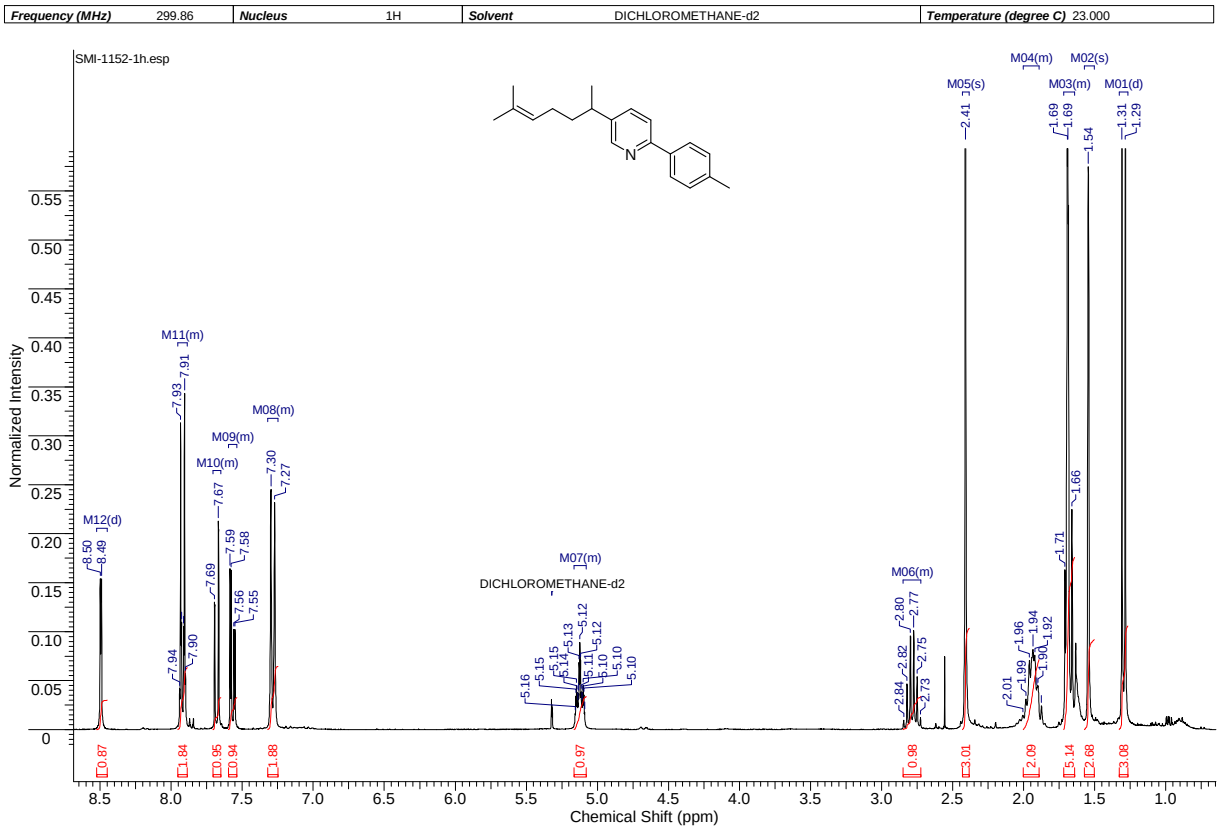

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1149-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

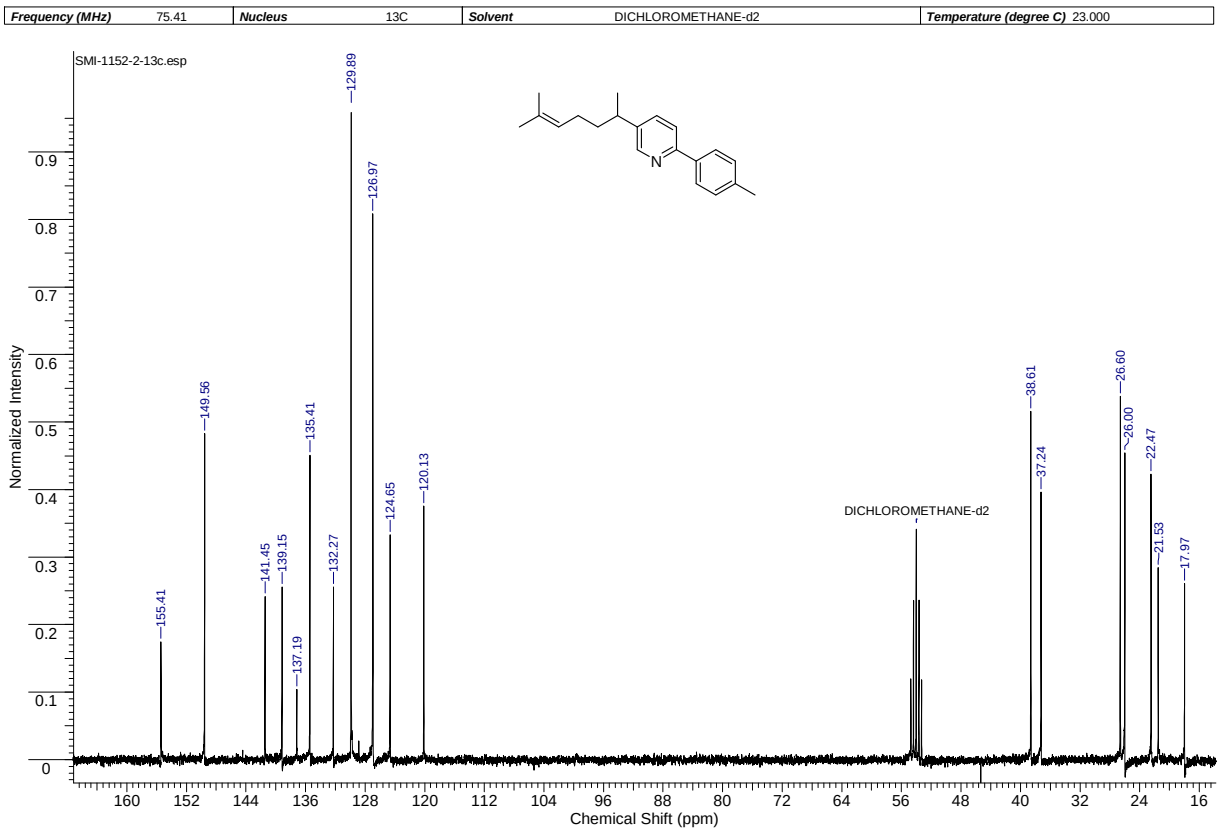

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1145-1h
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
8.47
8.47
7.91
7.90
7.88
7.66
7.66
7.63
7.57
7.56
7.28
7.25
2.66
2.63
2.61
2.39
1.69
1.67
1.64
1.62
1.60
1.33
1.27
0.91
0.88
0.86
0.73
1.64
0.87
0.84
1.65
1.76
2.61
1.93
82.05
3.11

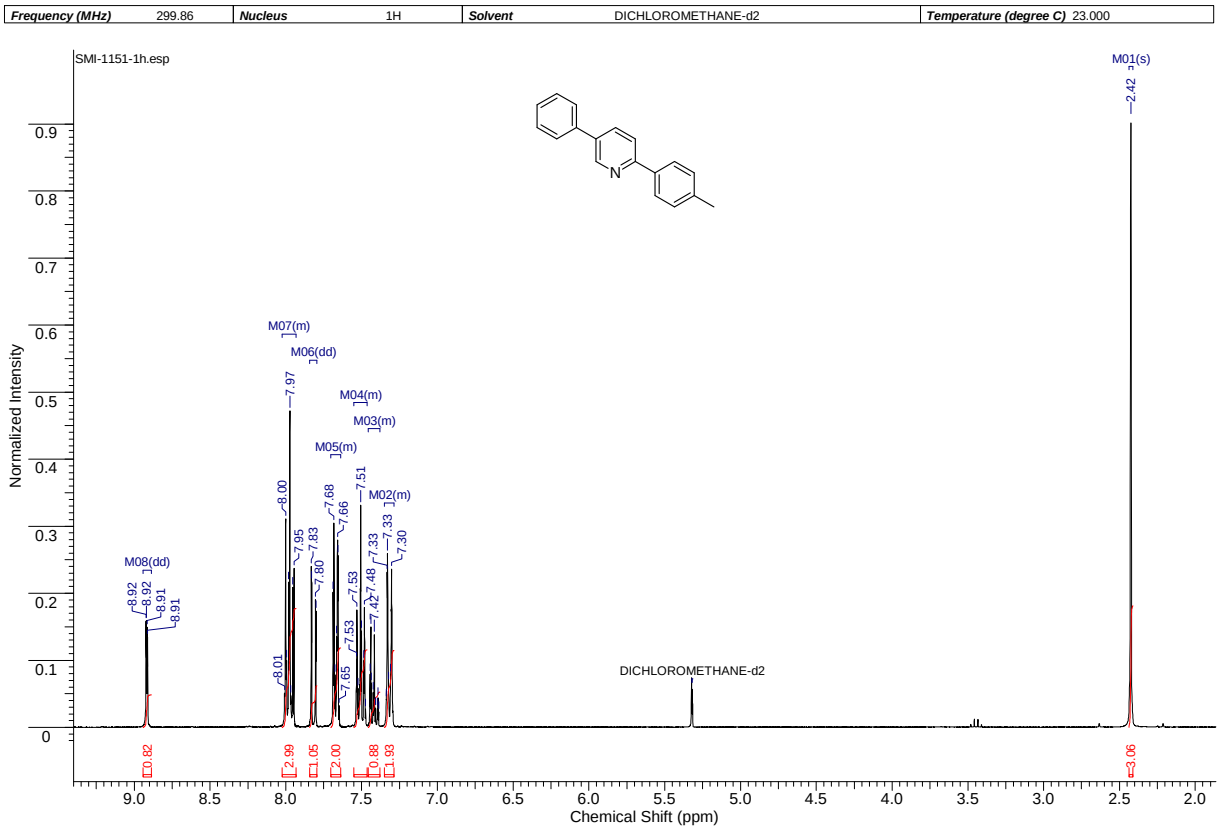

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1145-3-13c
Normalized Intensity
Chemical Shift (ppm)
DICHLOROMETHANE-d2
155.14
150.24
139.14
137.16
137.00
136.92
129.87
126.93
119.97
41.15
33.20
32.52
31.48
30.29
29.96
29.76
27.44
23.29
21.51
14.48

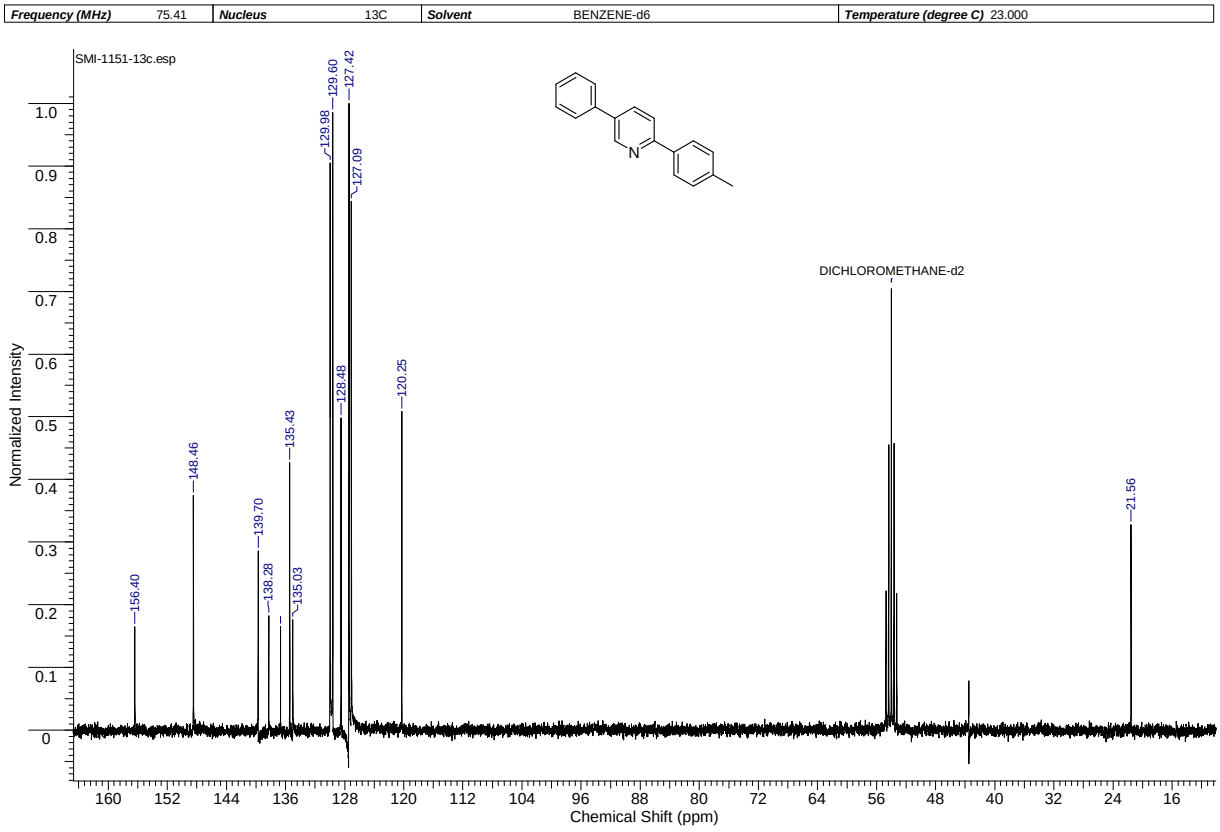

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1162-1h.esp
M06(m)
M05(s)
M10(m)
M07(m)
M08(m)
M09(m)
M04(m)
M03(m)
M02(m)
M01(m)
M11(d)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

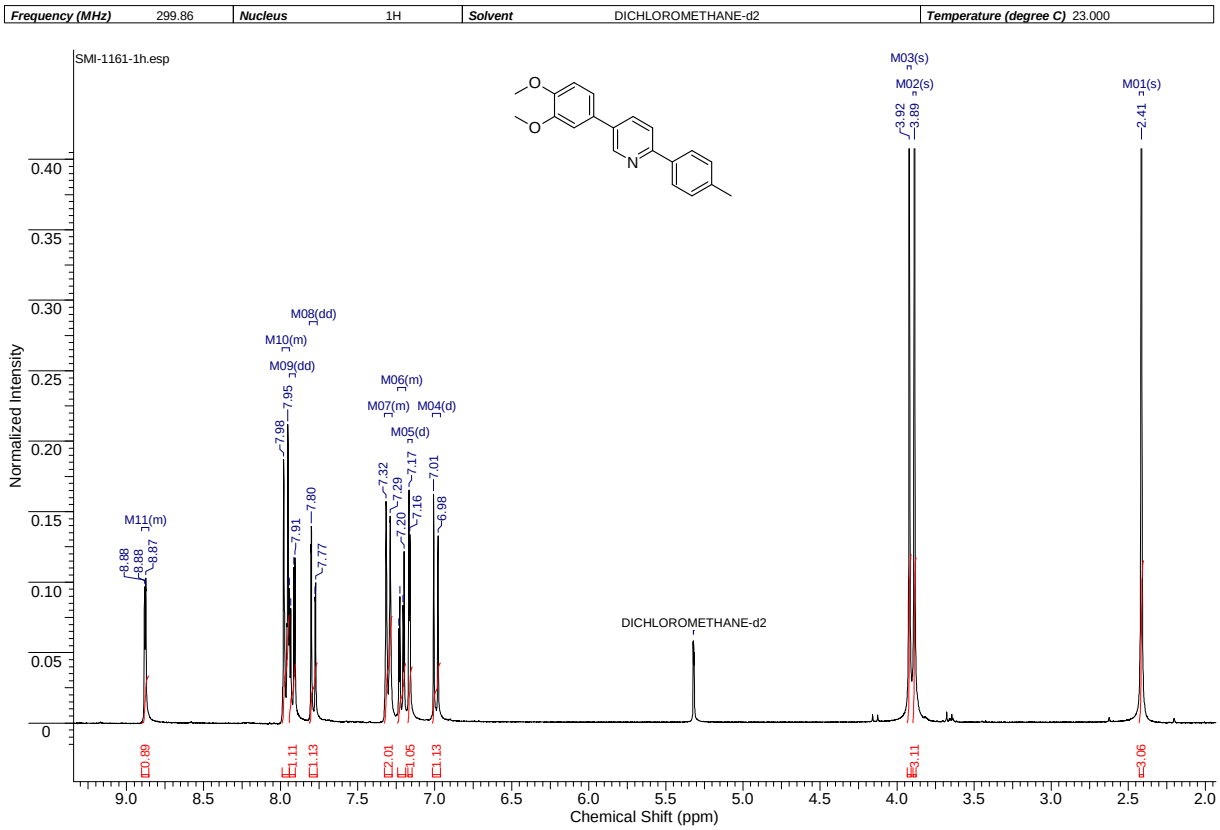

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1162-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

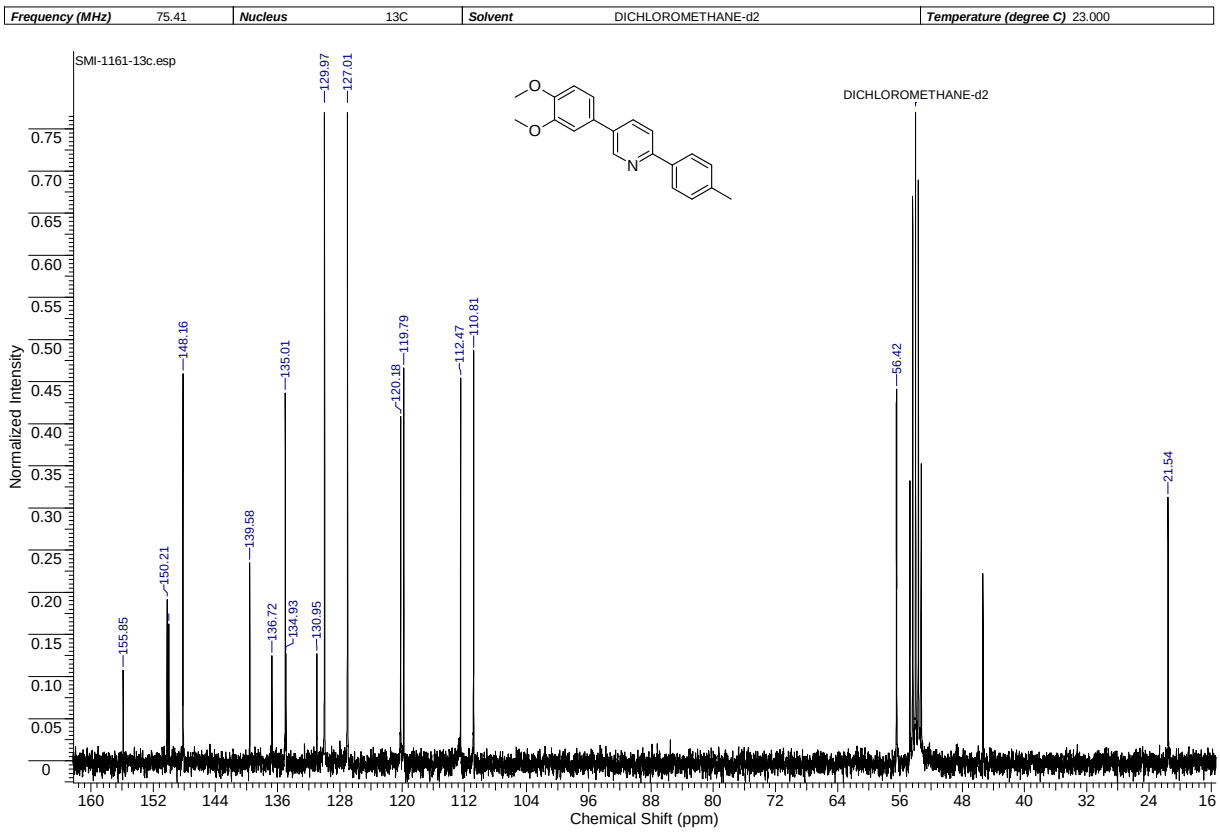

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1152-1h.esp
M12(d)
M11(m)
M10(m)
M09(m)
M08(m)
M07(m)
DICHLOROMETHANE-d2
M06(m)
M05(s)
M04(m)
M03(m)
M02(s)
M01(d)
Normalized Intensity
Chemical Shift (ppm)

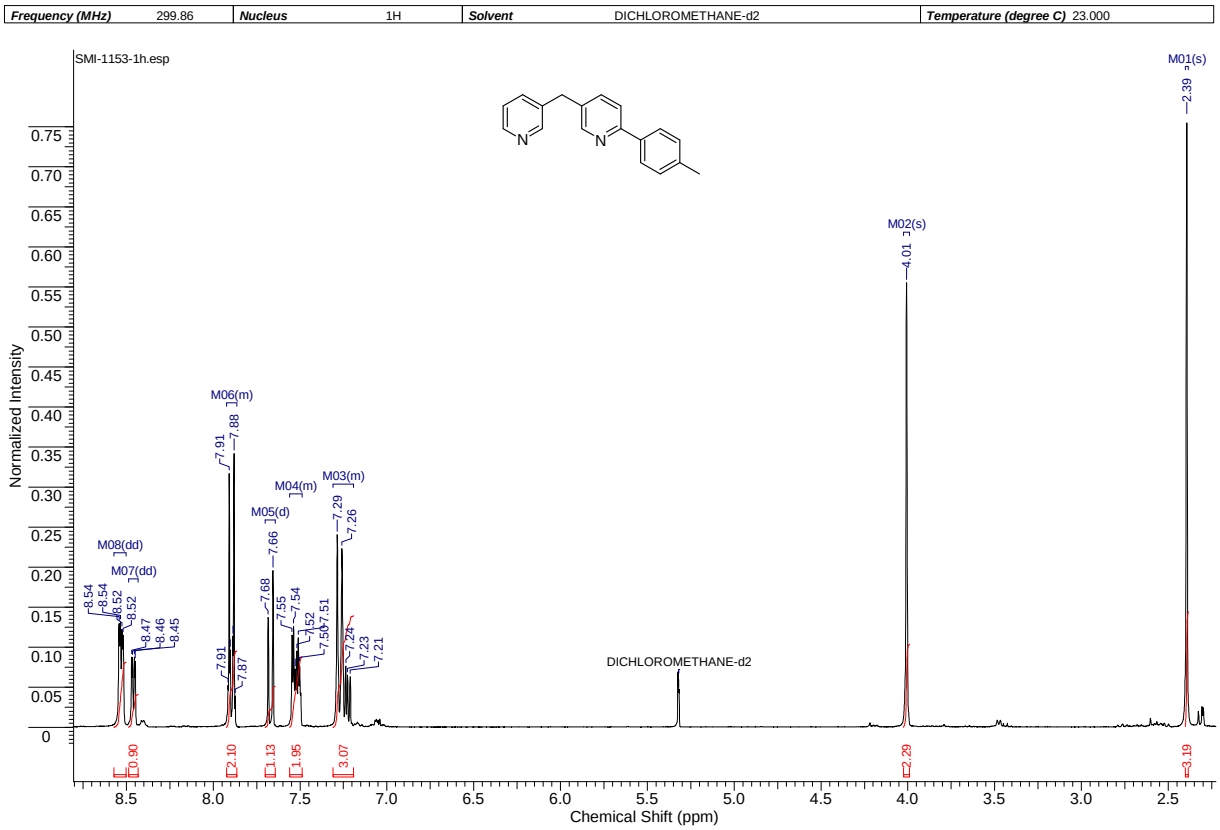

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1152-2-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

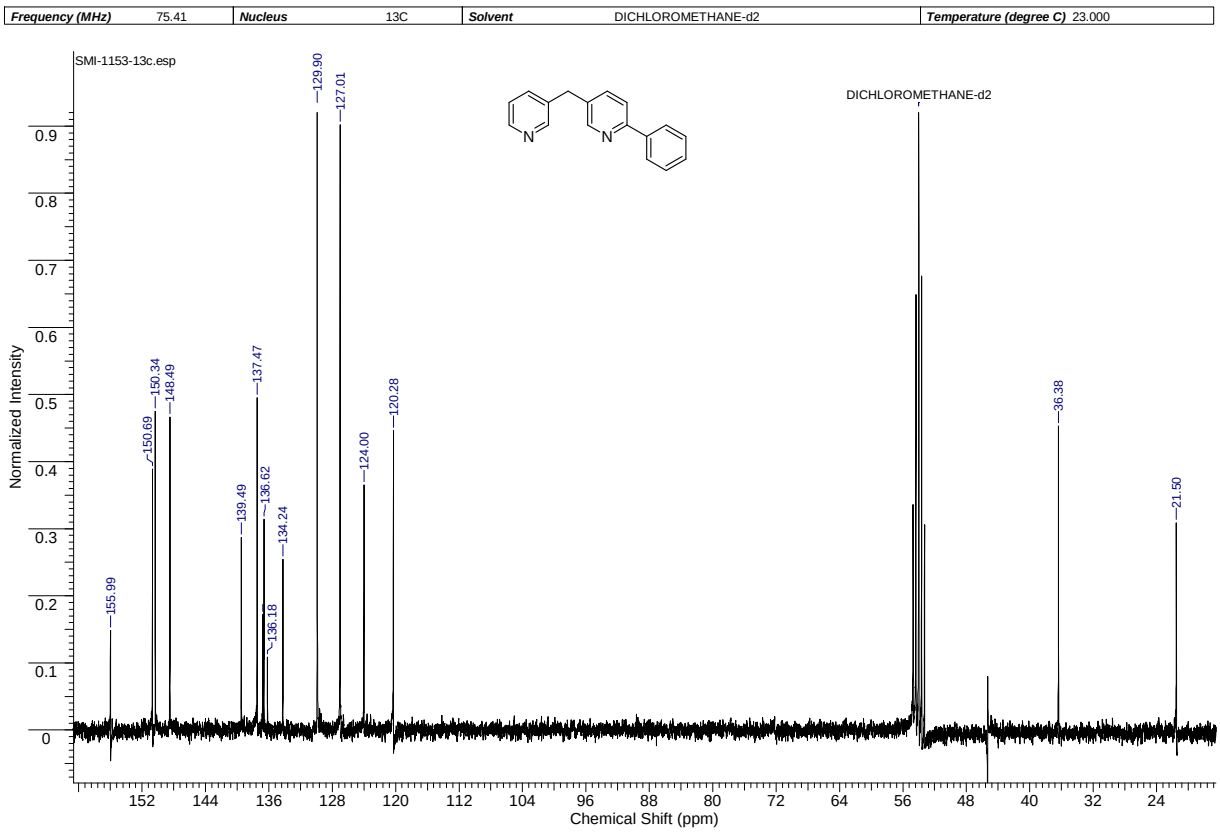

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1151-1h.esp
M01(s)
M02(m)
M03(m)
M04(m)
M05(m)
M06(dd)
M07(m)
M08(dd)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

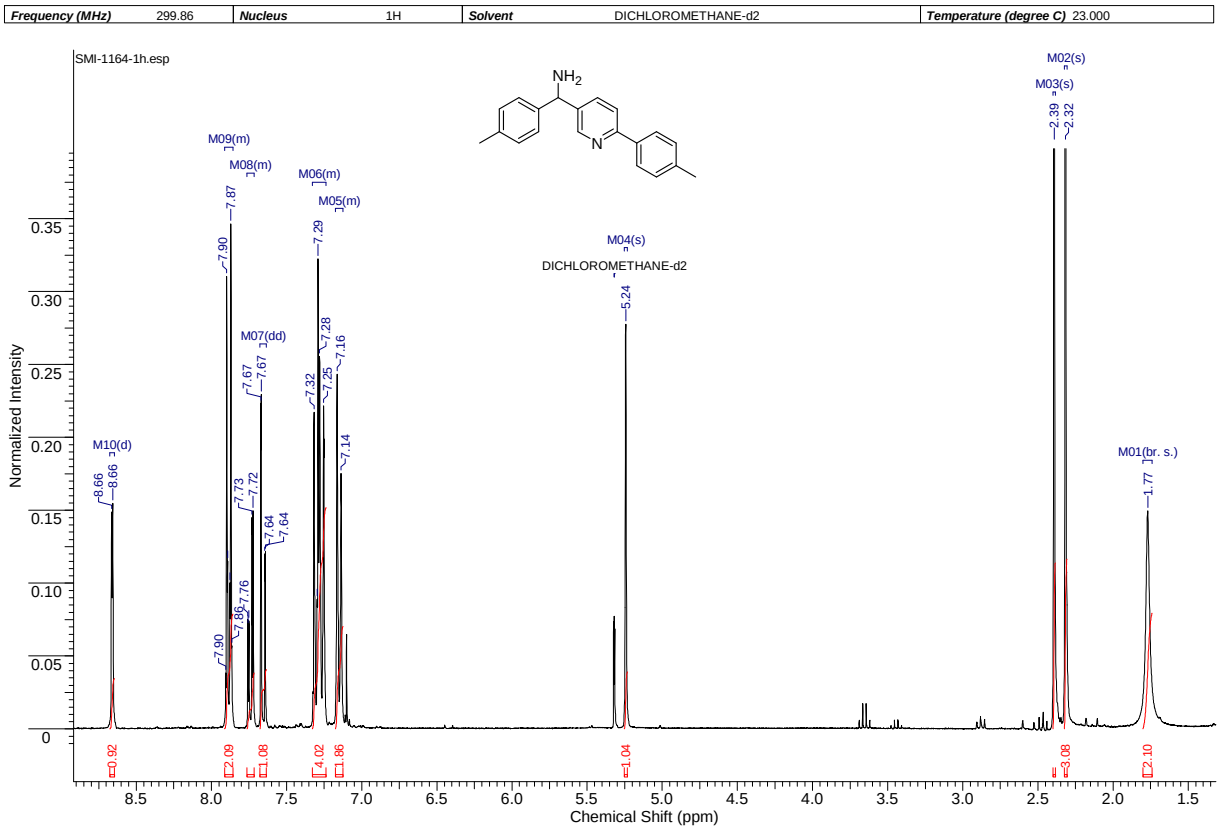

Frequency (MHz) 75.41
Nucleus 13C
Solvent BENZENE-d6
Temperature (degree C) 23.000
SMI-1151-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

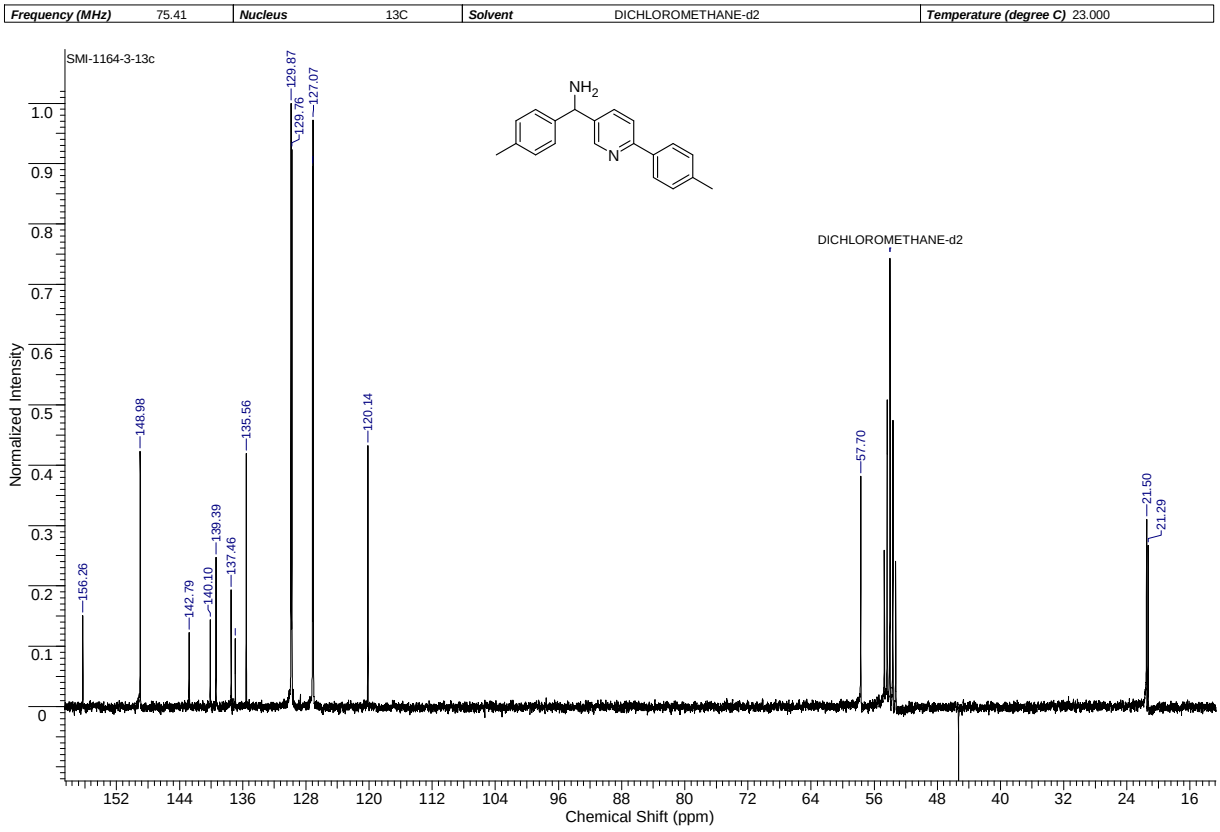

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1161-1h.esp
M03(s)
M02(s)
M01(s)
M08(dd)
M10(m)
M09(dd)
M06(m)
M07(m)
M04(d)
M05(d)
M11(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

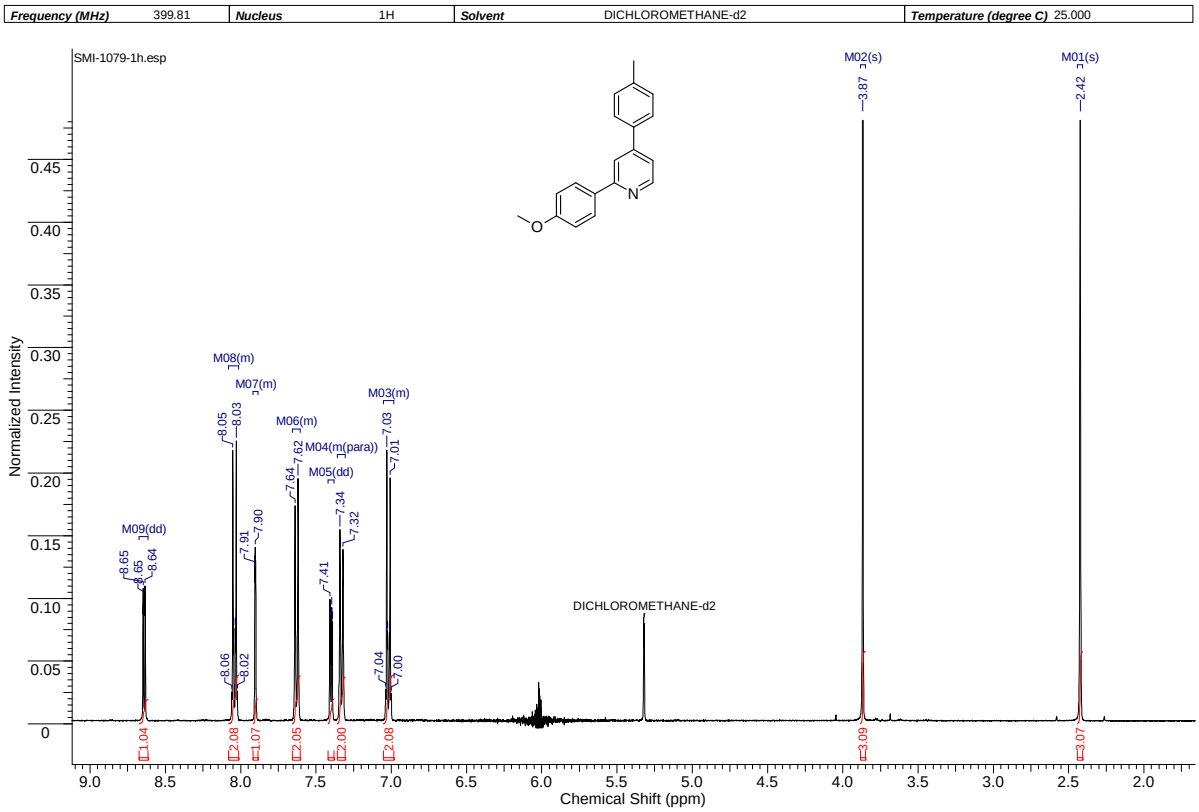

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1161-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

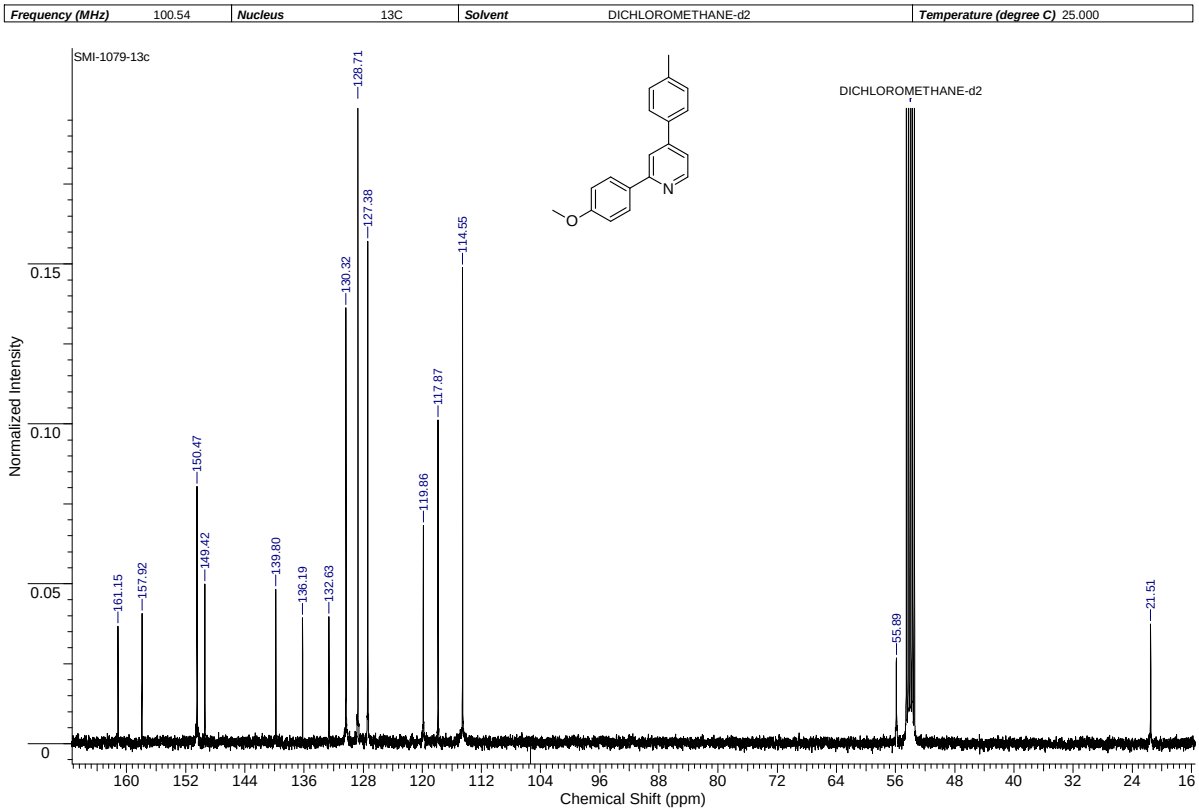

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1153-1h.esp
M01(s)
M02(s)
M03(m)
M04(m)
M05(d)
M06(m)
M07(dd)
M08(dd)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

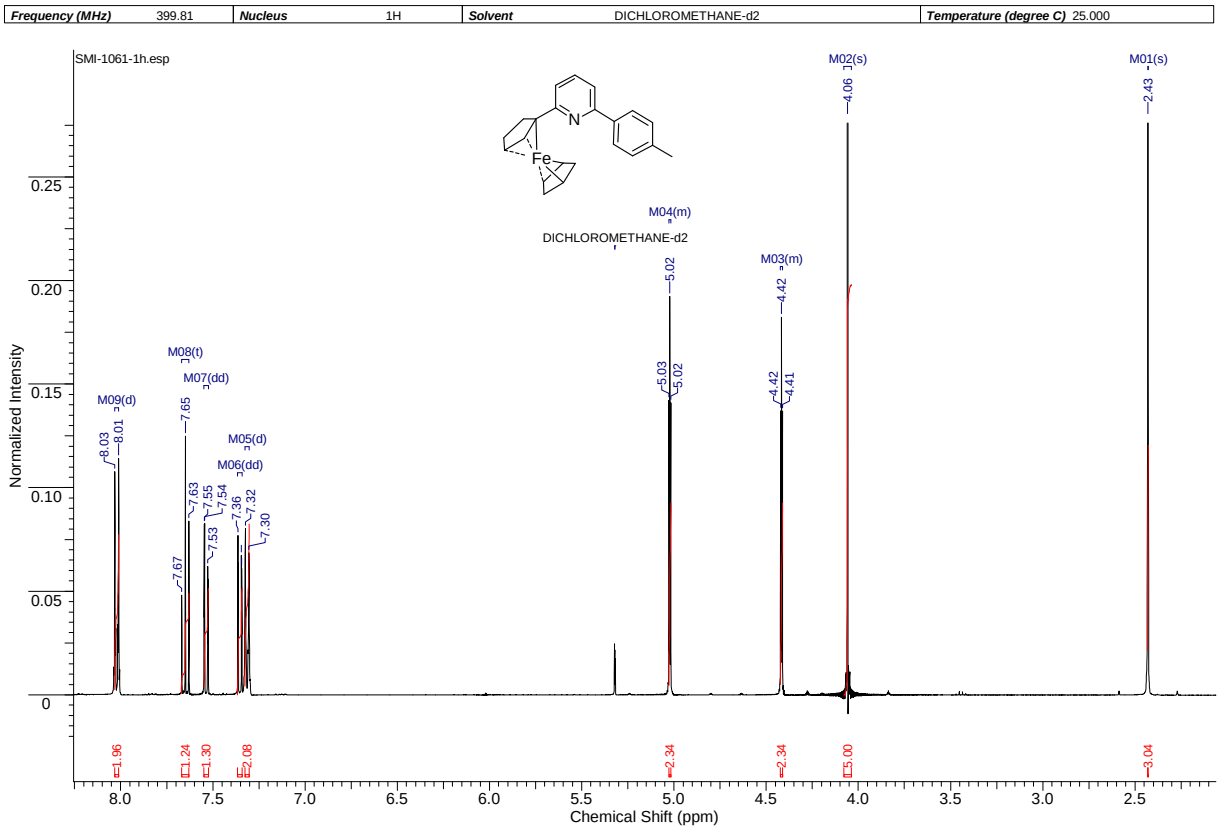

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1153-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

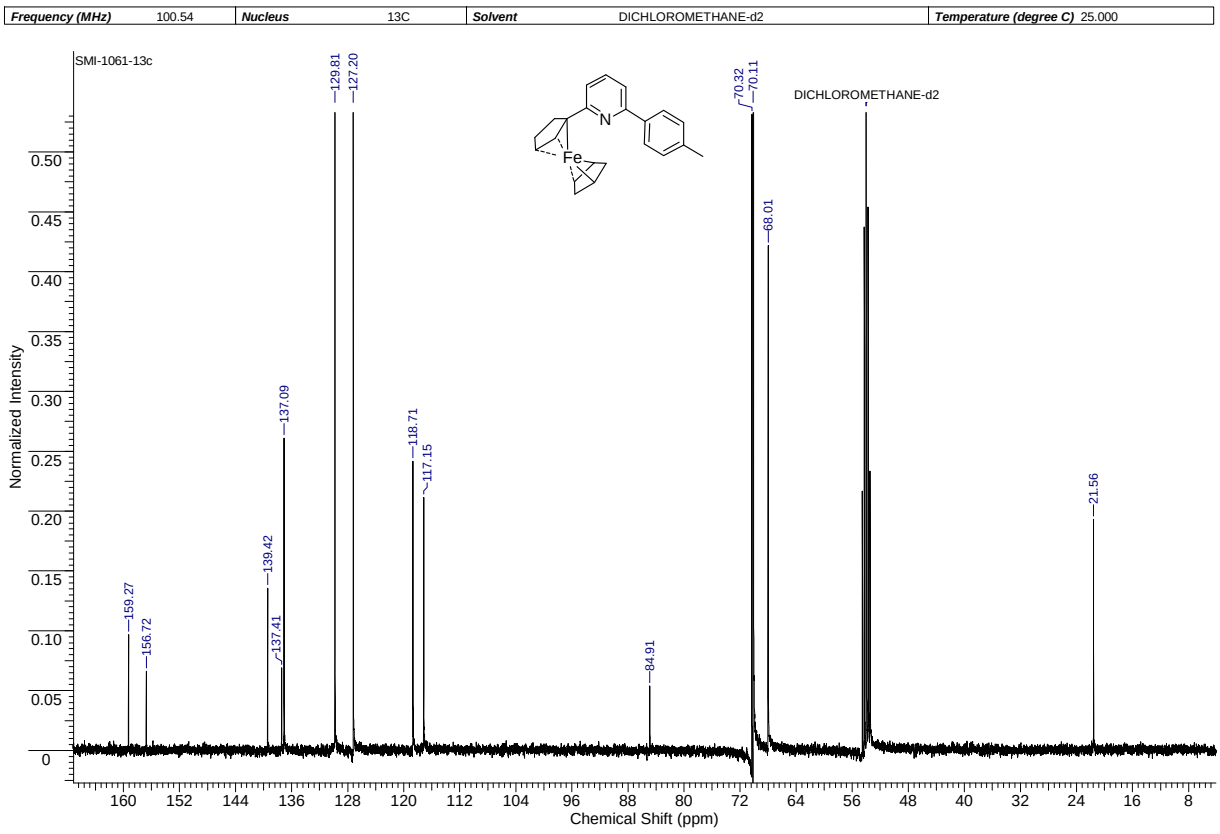

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1164-1h.esp
NH2
N
M09(m)
M08(m)
M06(m)
M05(m)
M02(s)
M03(s)
M04(s)
DICHLOROMETHANE-d2
M07(dd)
M10(d)
M01(br. s.)
Normalized Intensity
Chemical Shift (ppm)

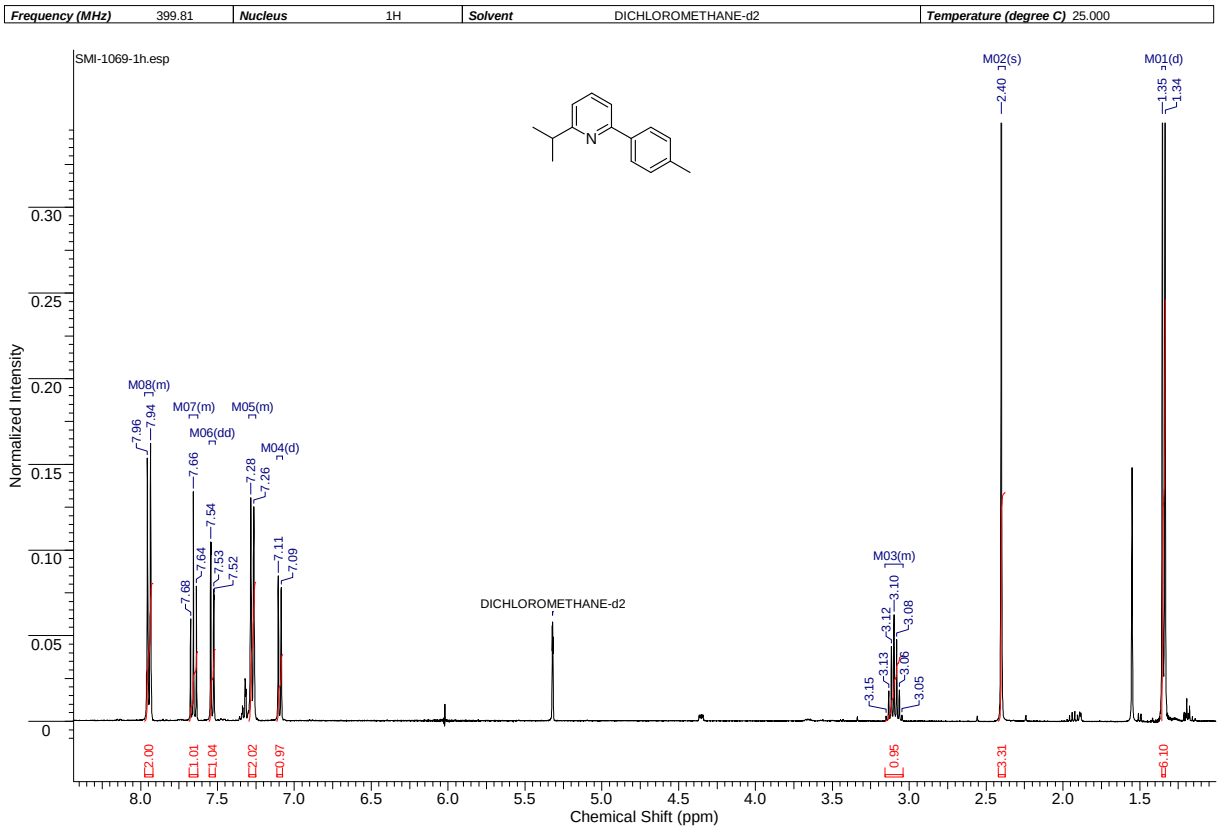

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1164-3-13c
NH2
N
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

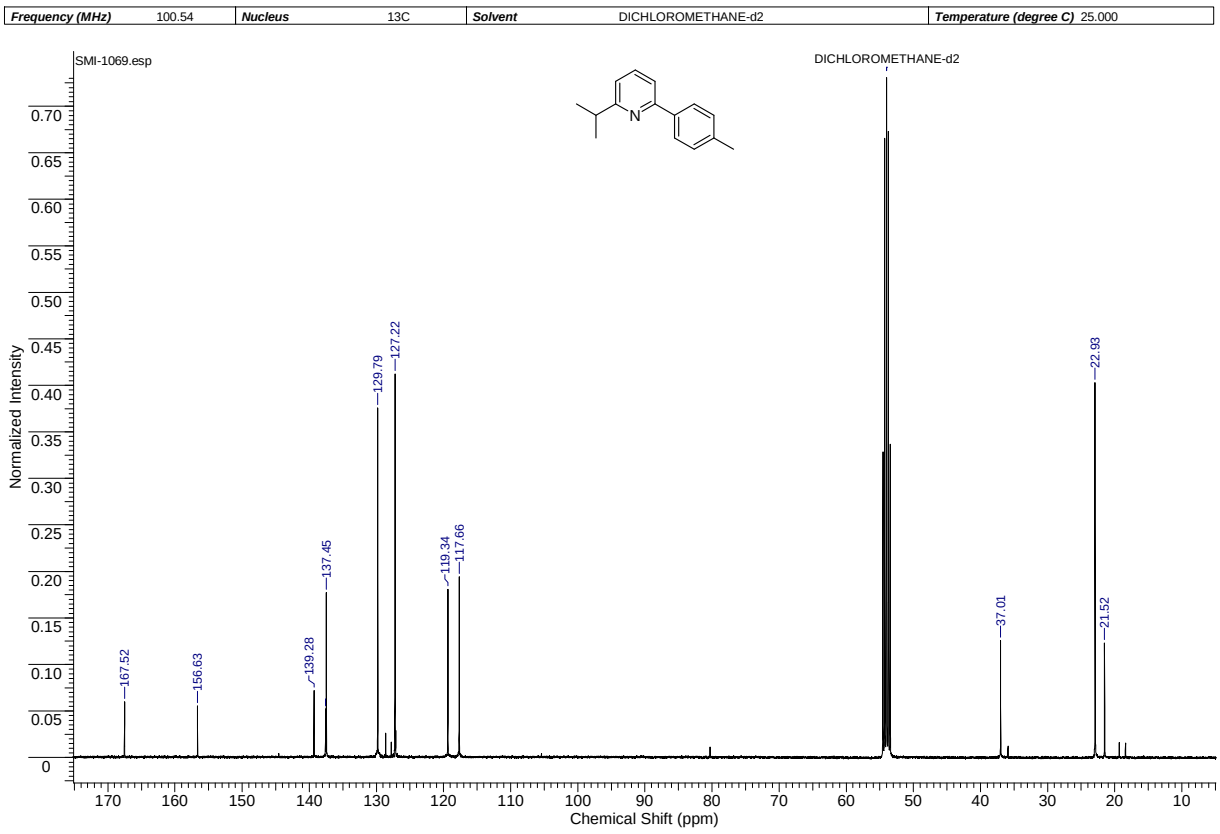

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1079-1h.esp
M01(s)
M02(s)
M03(m)
M04(m(para))
M05(dd)
M06(m)
M07(m)
M08(m)
M09(dd)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

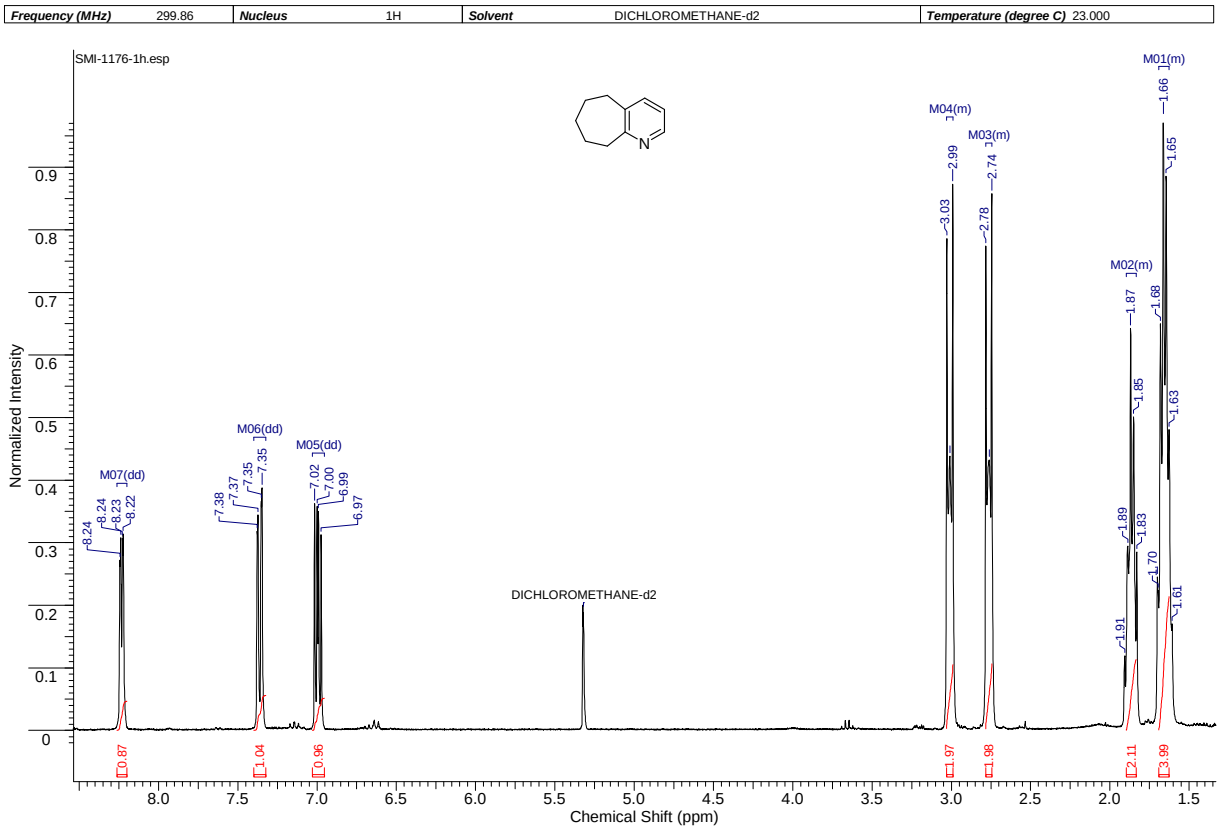

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1079-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

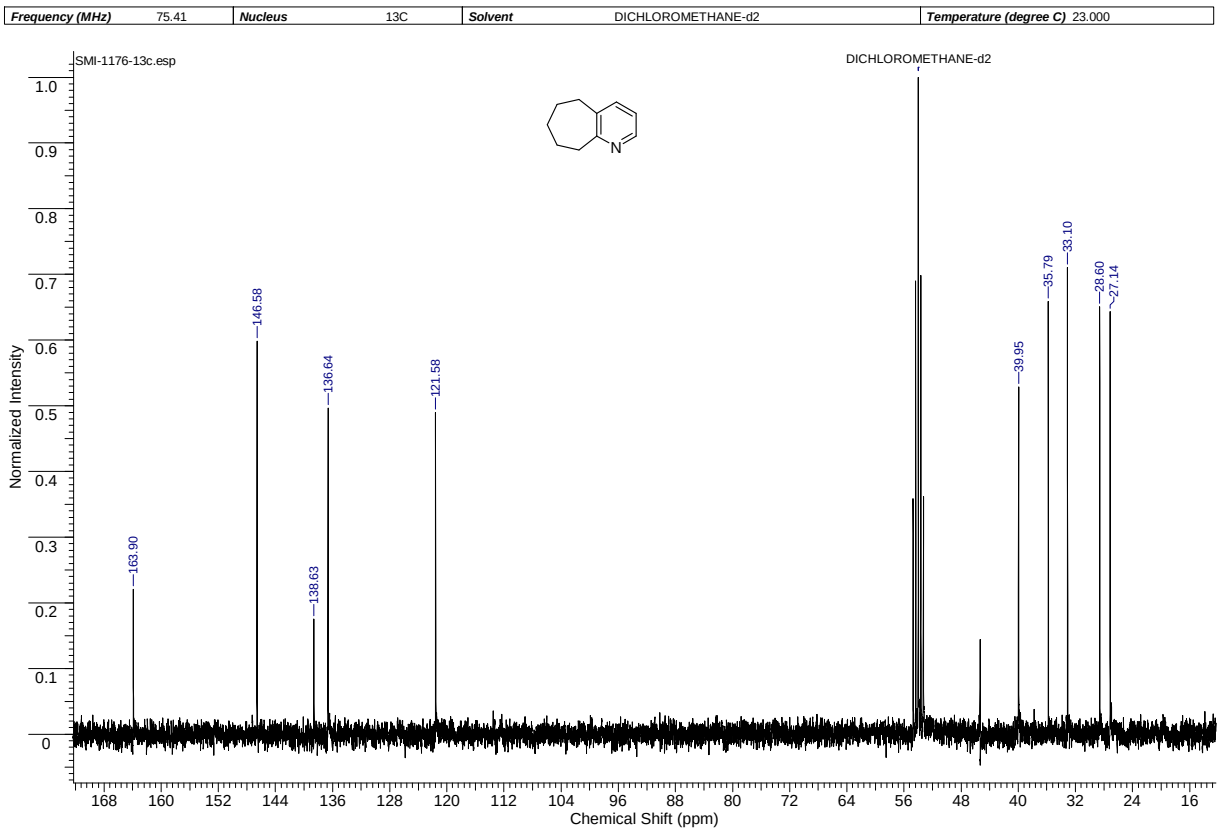

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1061-1h.esp
M02(s)
M01(s)
M04(m)
DICHLOROMETHANE-d2
M03(m)
M08(t)
M07(dd)
M09(d)
M05(d)
M06(dd)
Normalized Intensity
Chemical Shift (ppm)

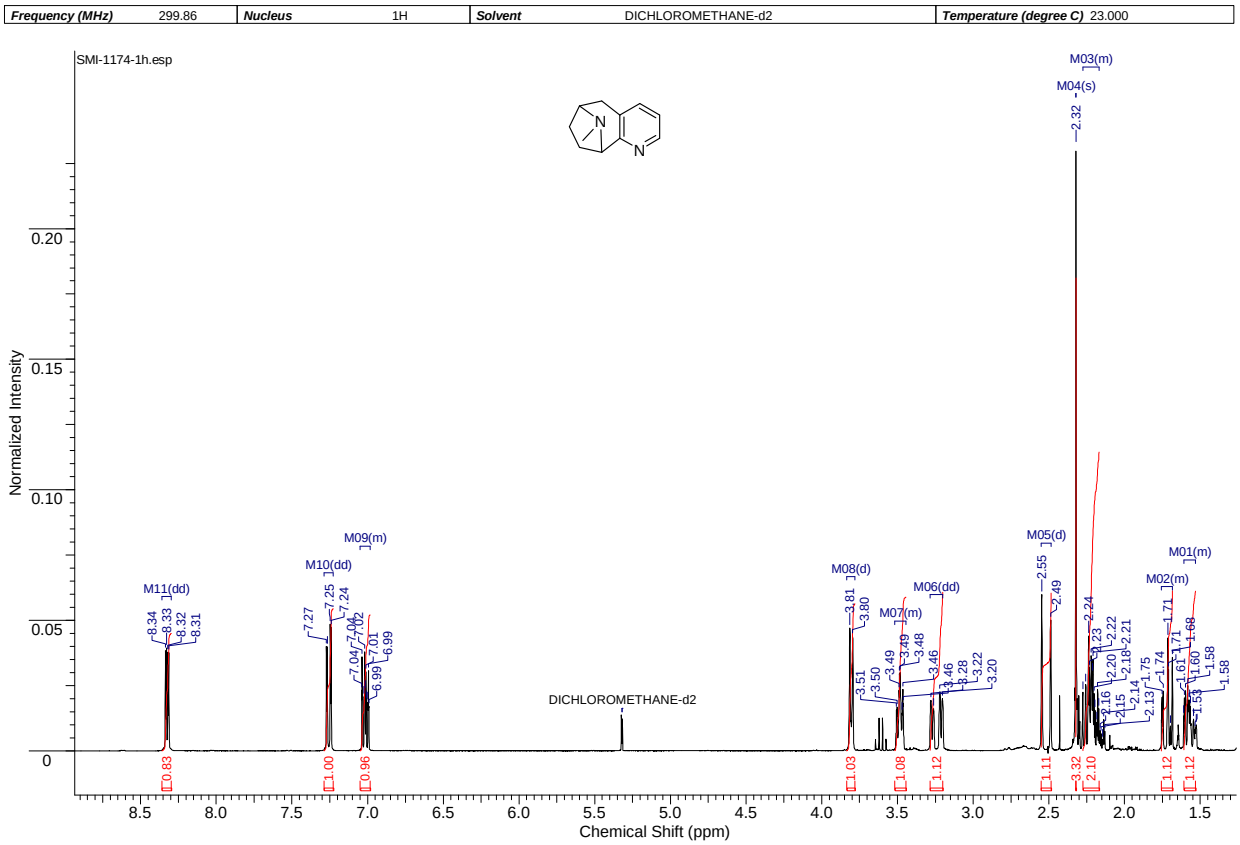

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1061-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

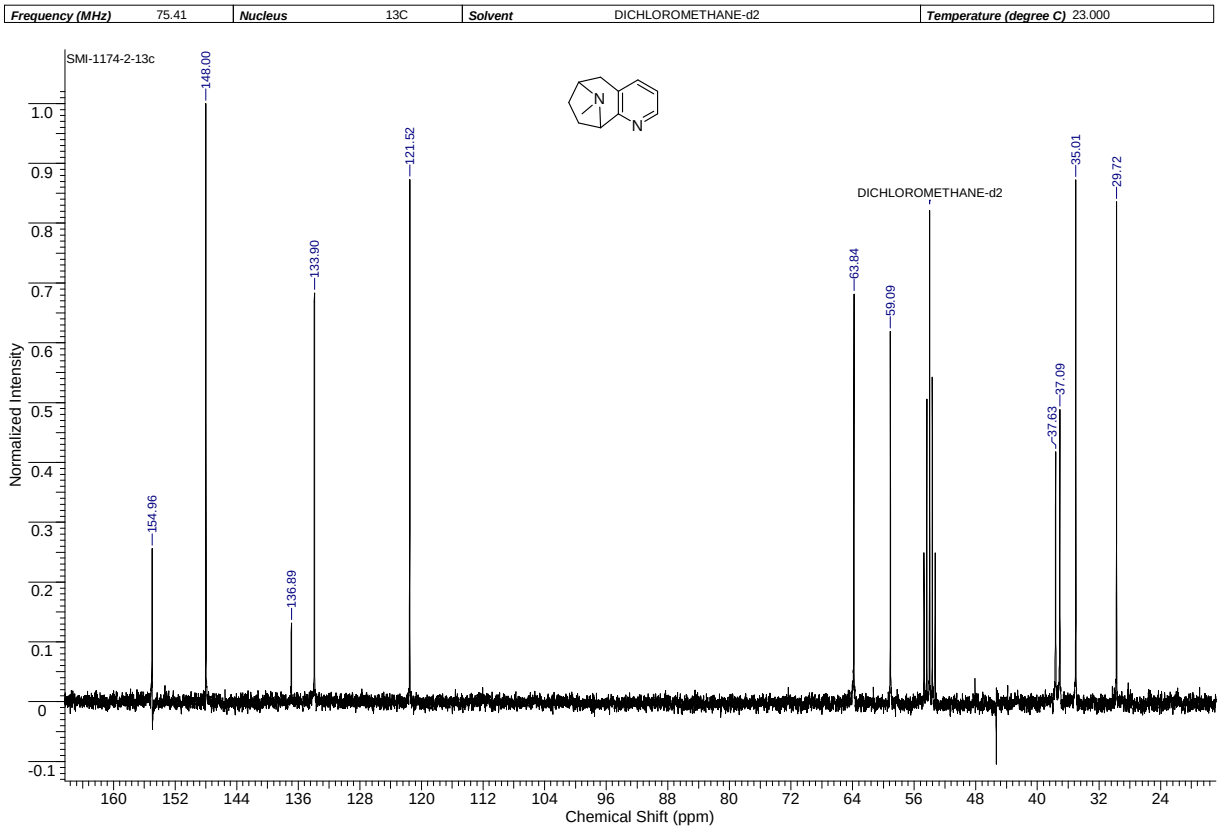

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1069-1h.esp
M08(m)
M07(m)
M06(dd)
M05(m)
M04(d)
M03(m)
M02(s)
M01(d)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

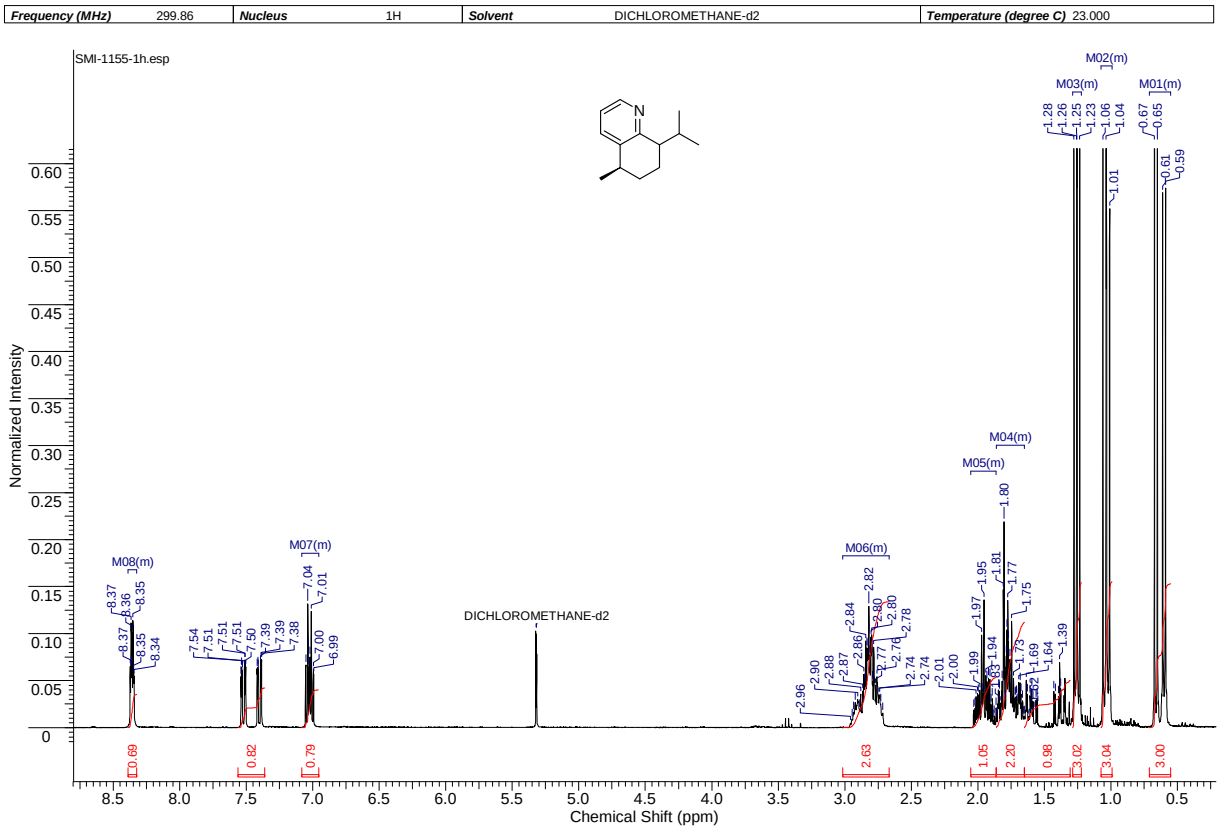

Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1069.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

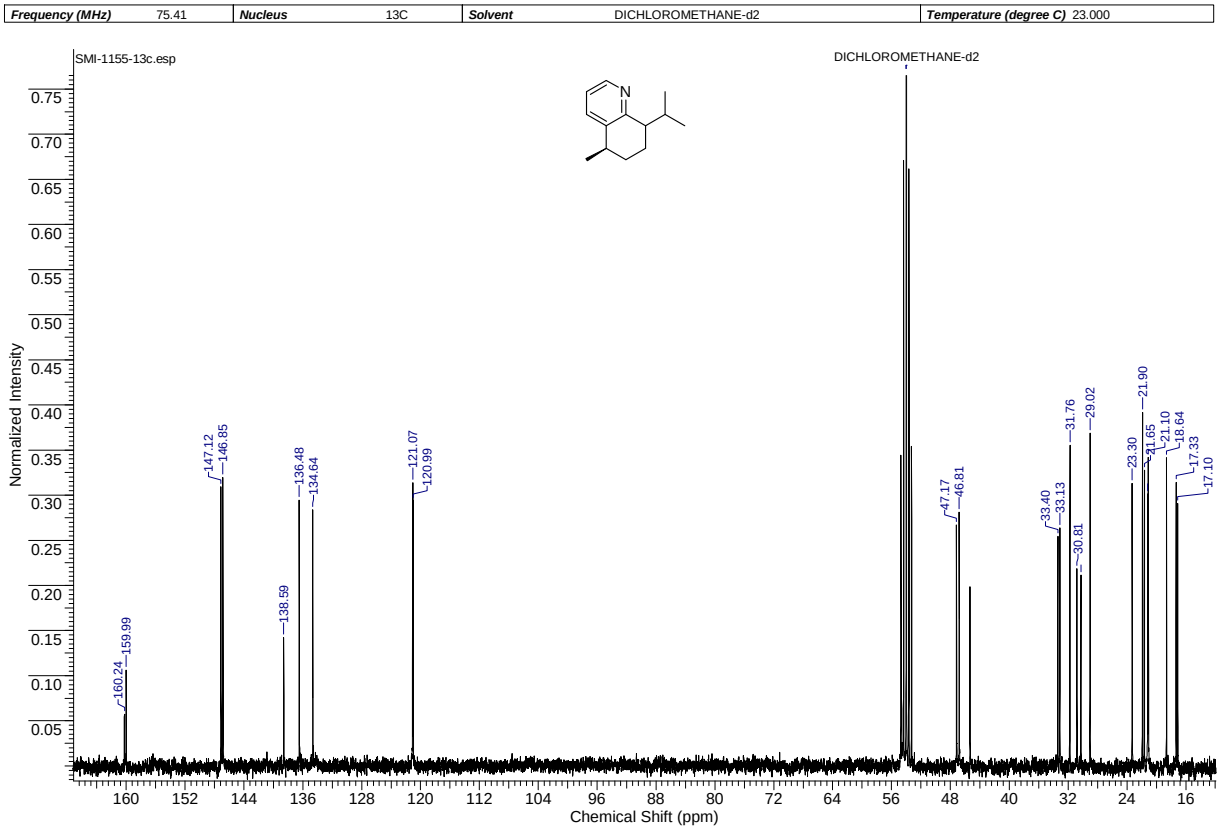

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1176-1h.esp
M01(m)
M02(m)
M03(m)
M04(m)
M05(dd)
M06(dd)
M07(dd)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

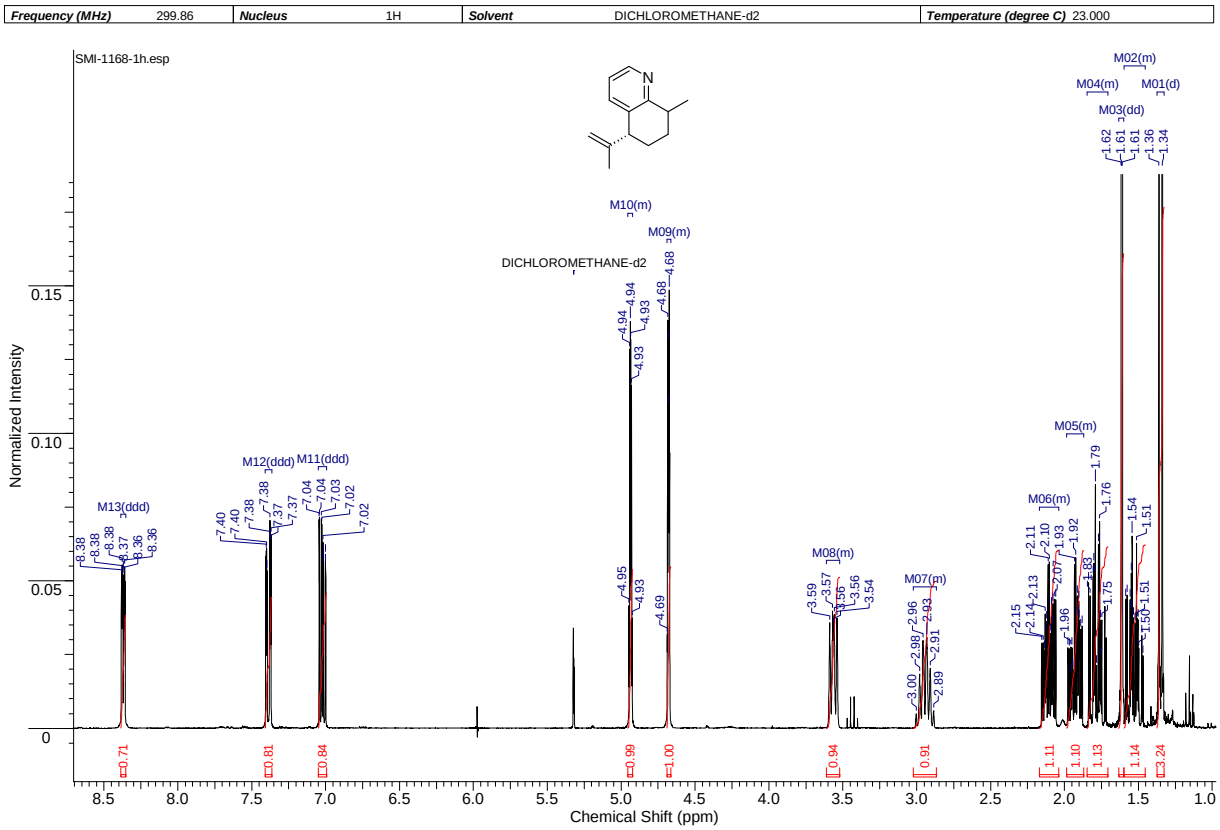

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1176-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

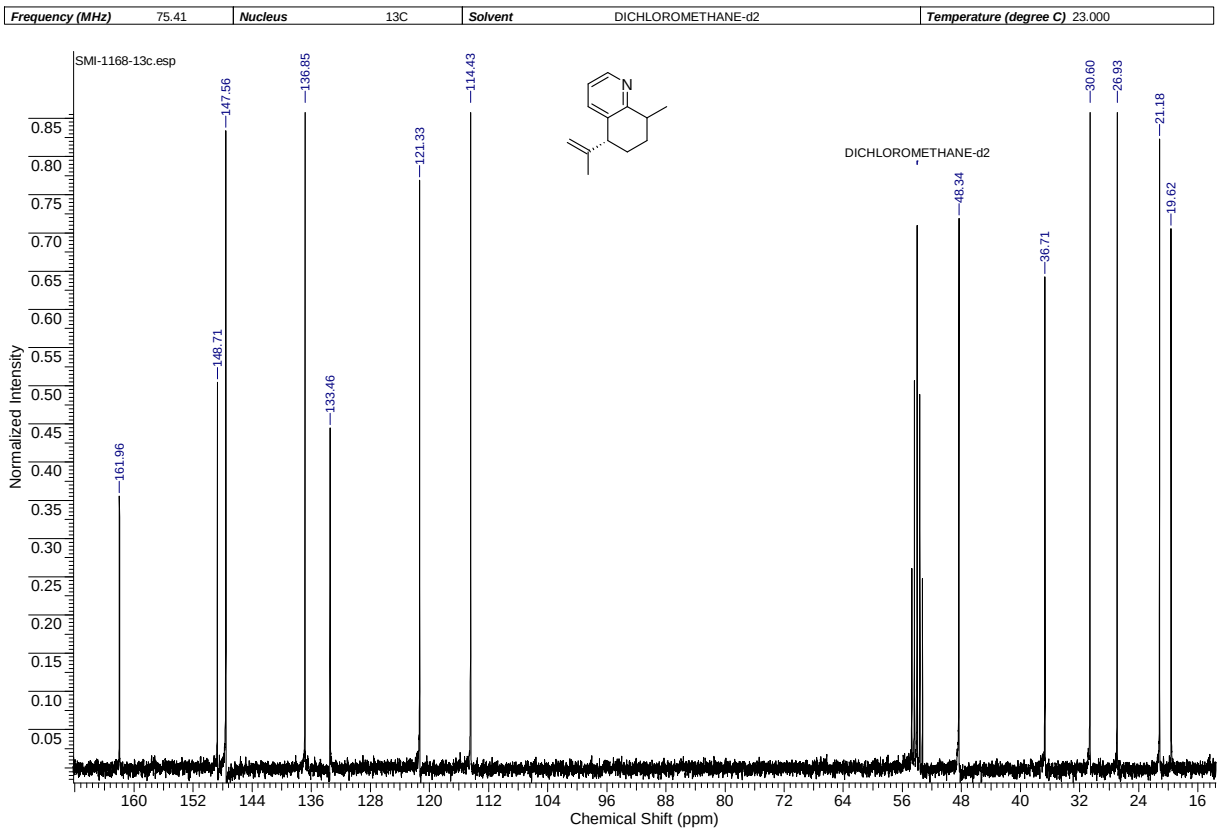

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1174-1h.esp
M03(m)
M04(s)
M09(m)
M10(dd)
M11(dd)
M08(d)
M06(dd)
M07(m)
M05(d)
M01(m)
M02(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

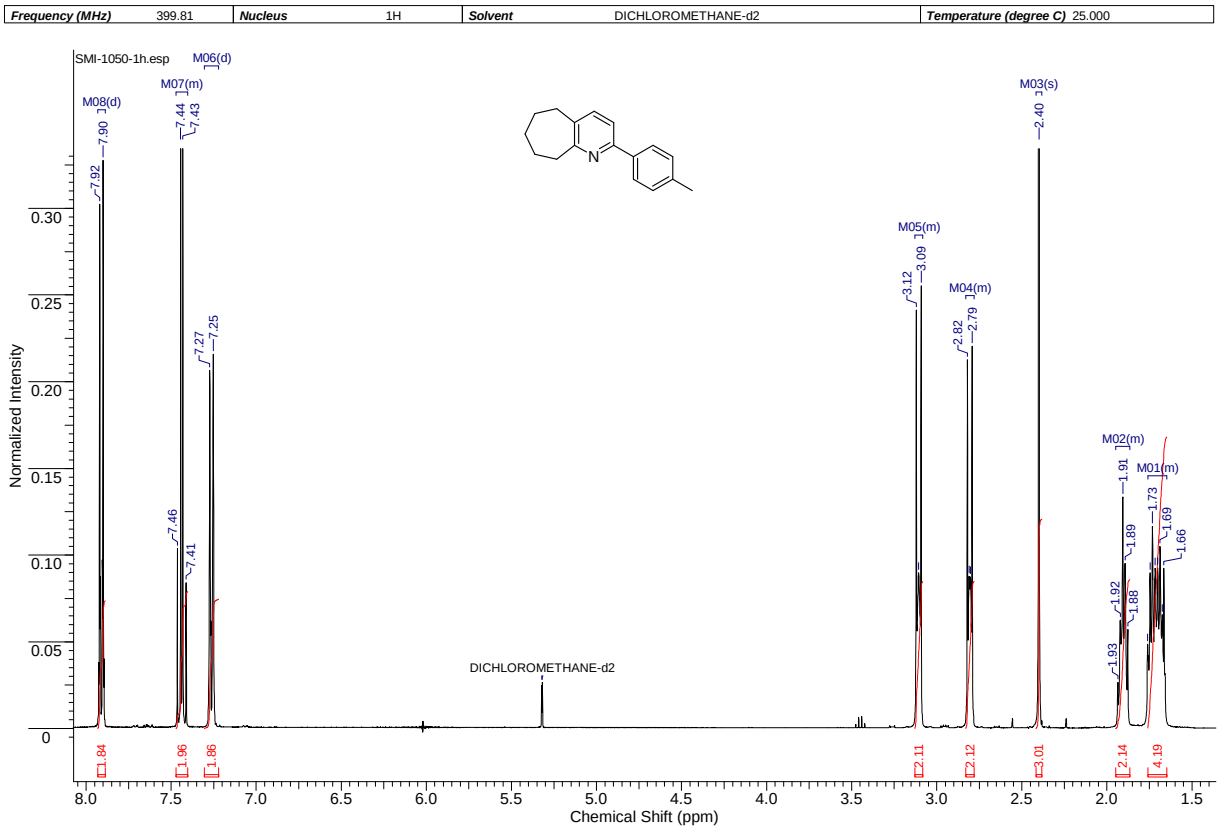

Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1174-2-13c
148.00
121.52
133.90
154.96
136.89
63.84
59.09
DICHLOROMETHANE-d2
35.01
29.72
37.09
37.63
Normalized Intensity
Chemical Shift (ppm)

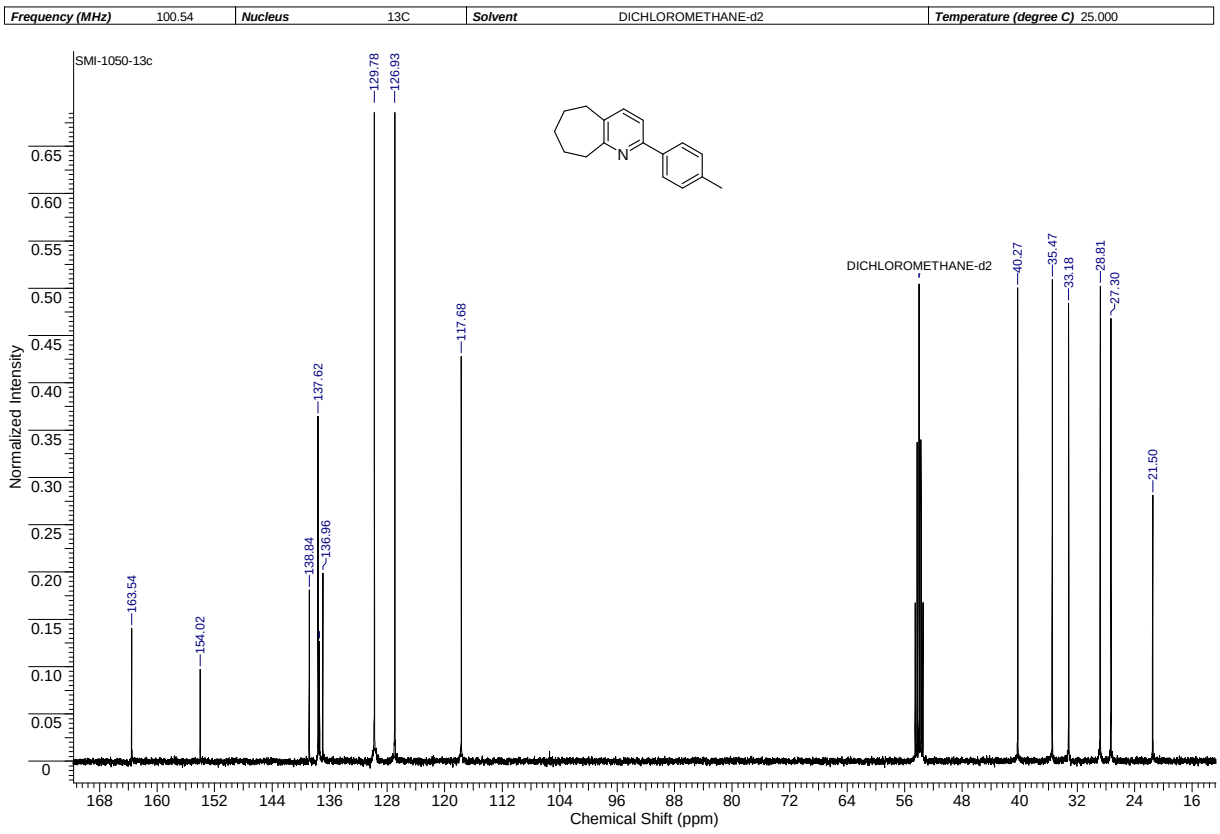

Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1155-1h.esp
DICHLOROMETHANE-d2
M01(m)
M02(m)
M03(m)
M04(m)
M05(m)
M06(m)
M07(m)
M08(m)
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1155-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1168-1h.esp
DICHLOROMETHANE-d2
M01(d)
M02(m)
M03(dd)
M04(m)
M05(m)
M06(m)
M07(m)
M08(m)
M09(m)
M10(m)
M11(ddd)
M12(ddd)
M13(ddd)
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1168-13c.esp
DICHLOROMETHANE-d2
161.96
148.71
147.56
133.46
136.85
121.33
114.43
48.34
36.71
30.60
26.93
21.18
19.62
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1050-1h.esp
M08(d)
M07(m)
M06(d)
M05(m)
M04(m)
M03(s)
M02(m)
M01(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)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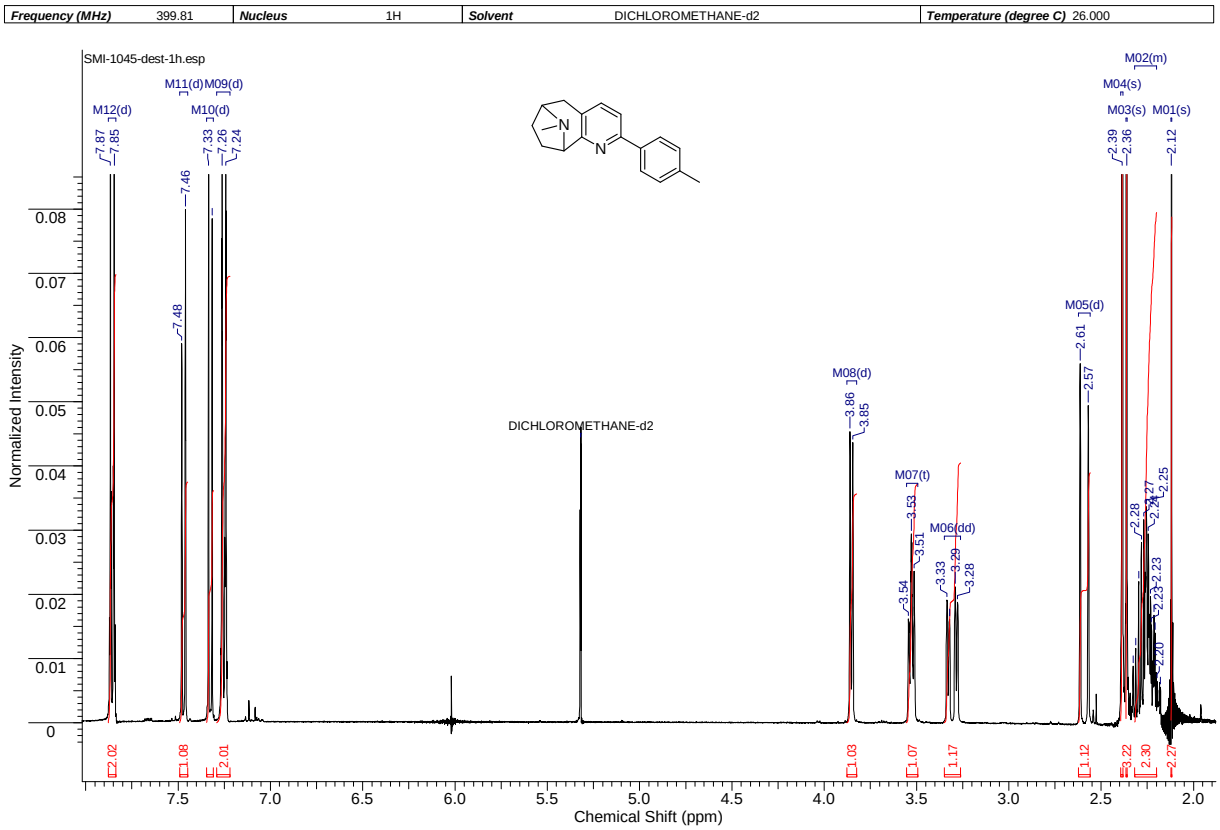
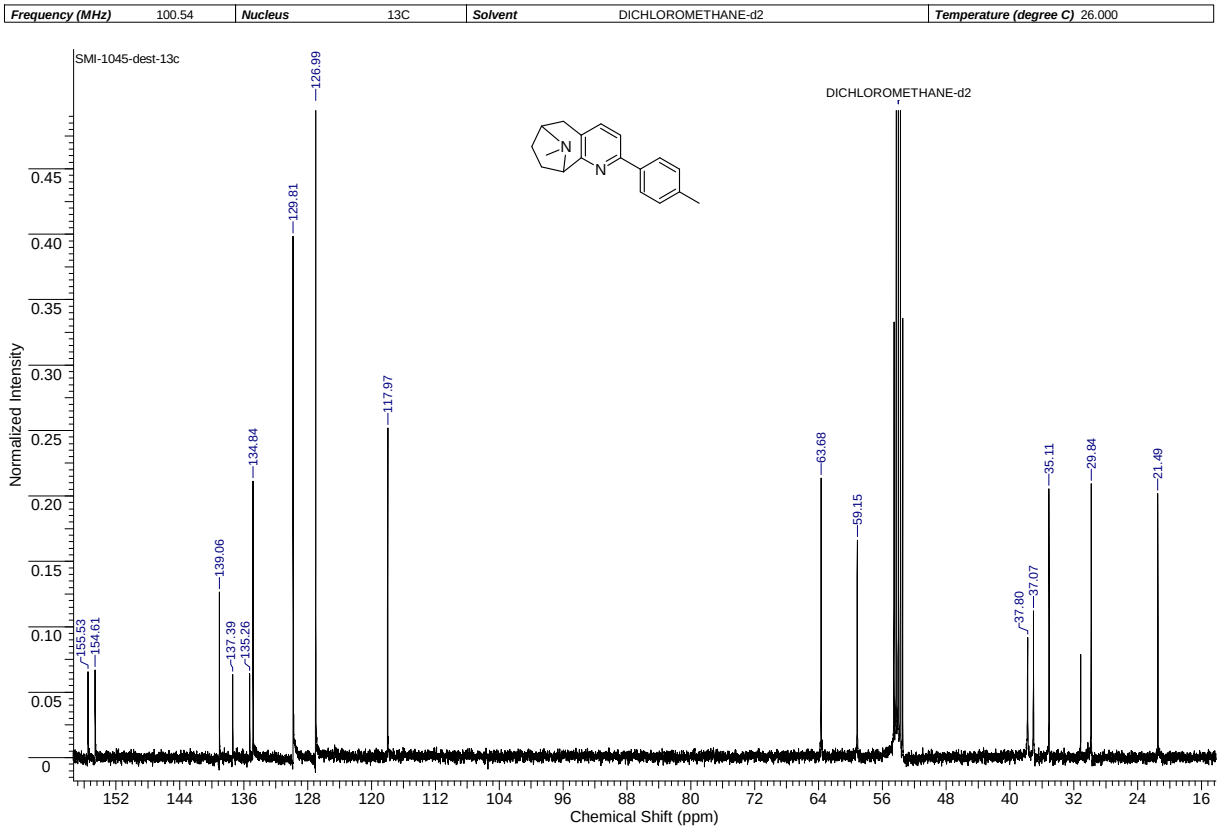
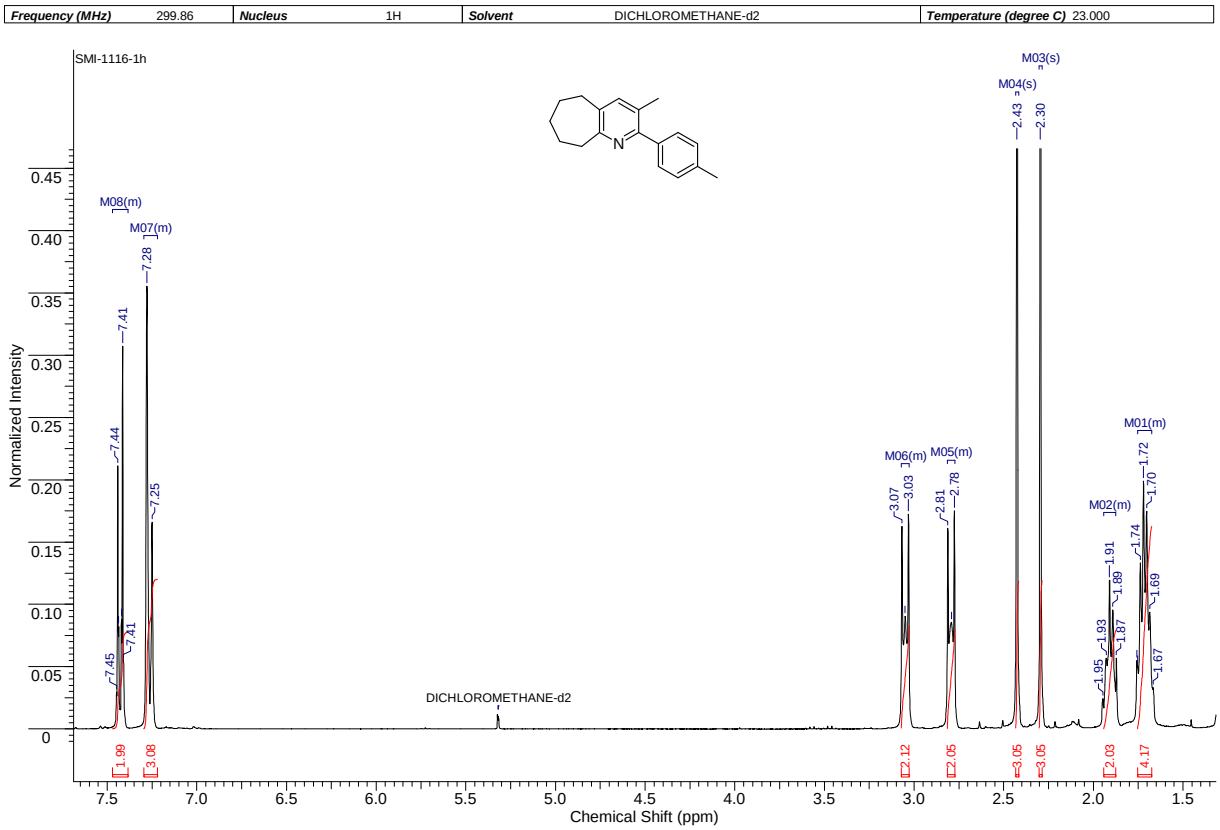
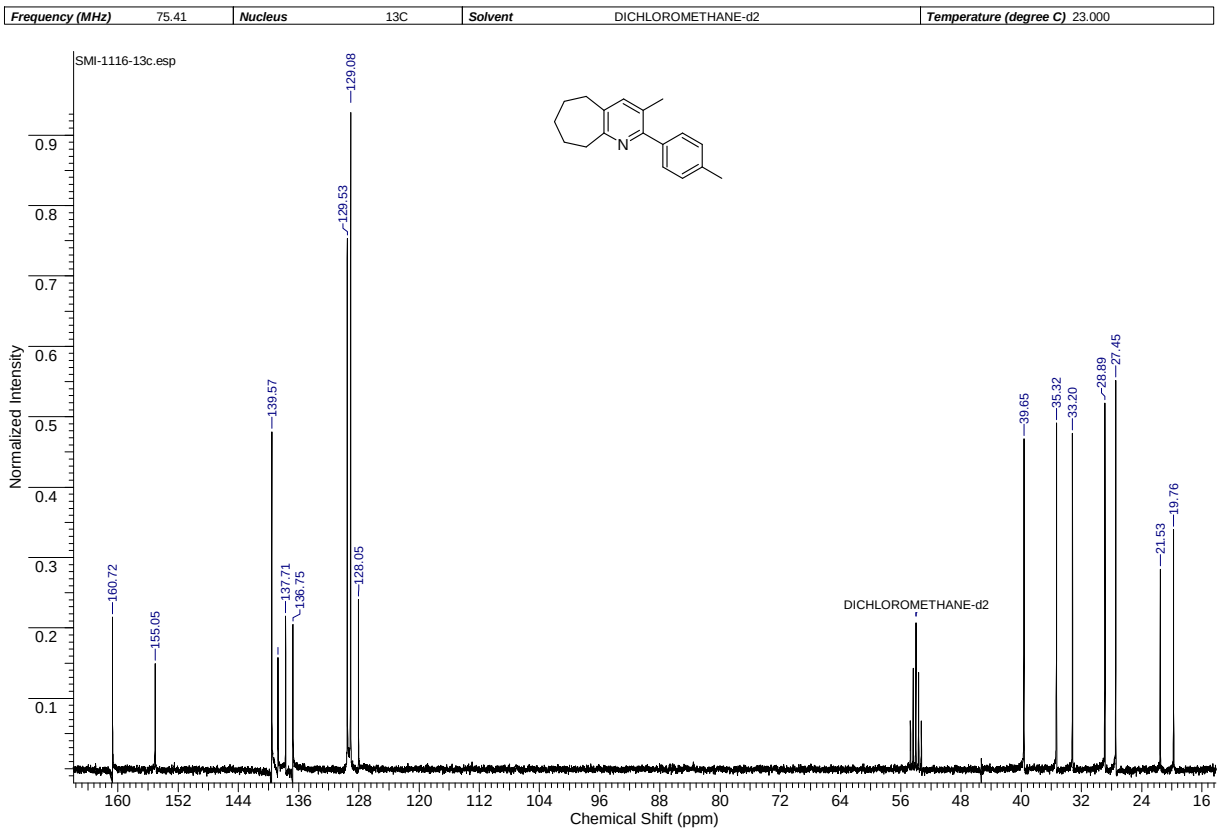
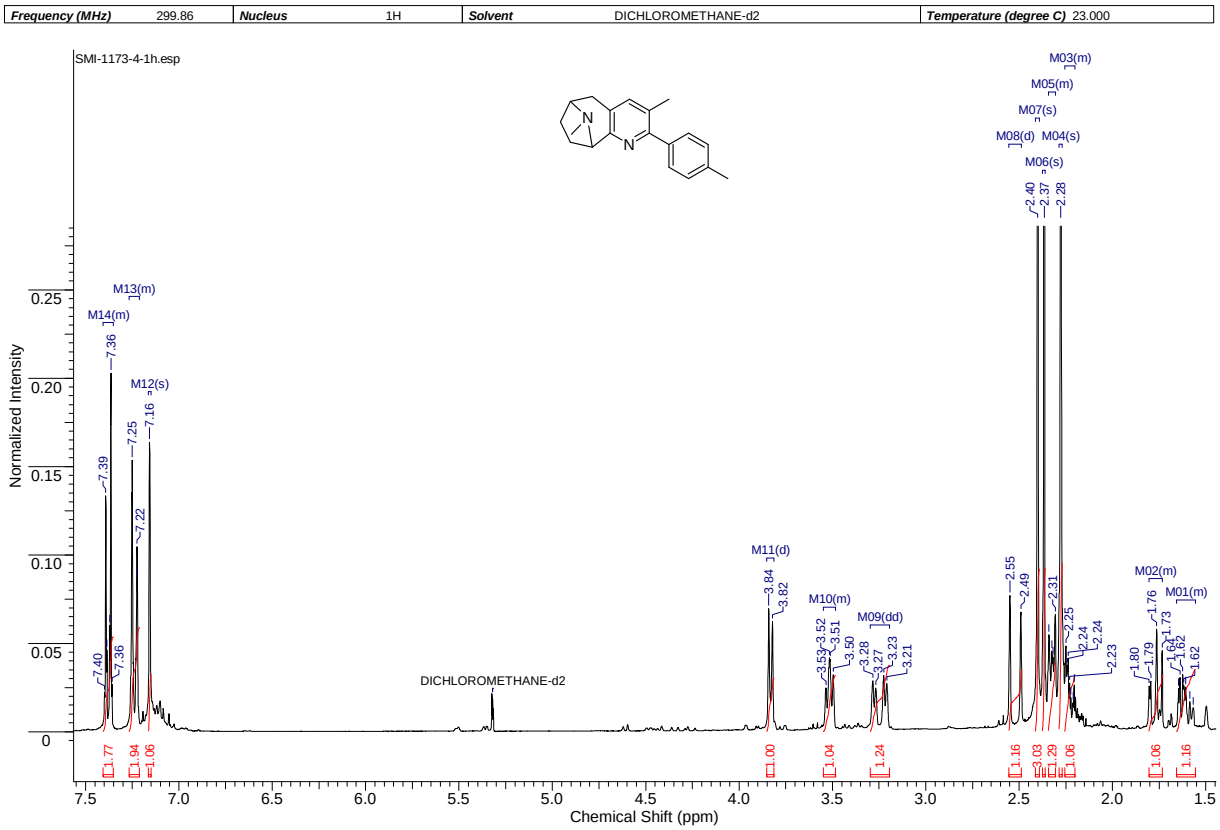
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 25.000
SMI-1050-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

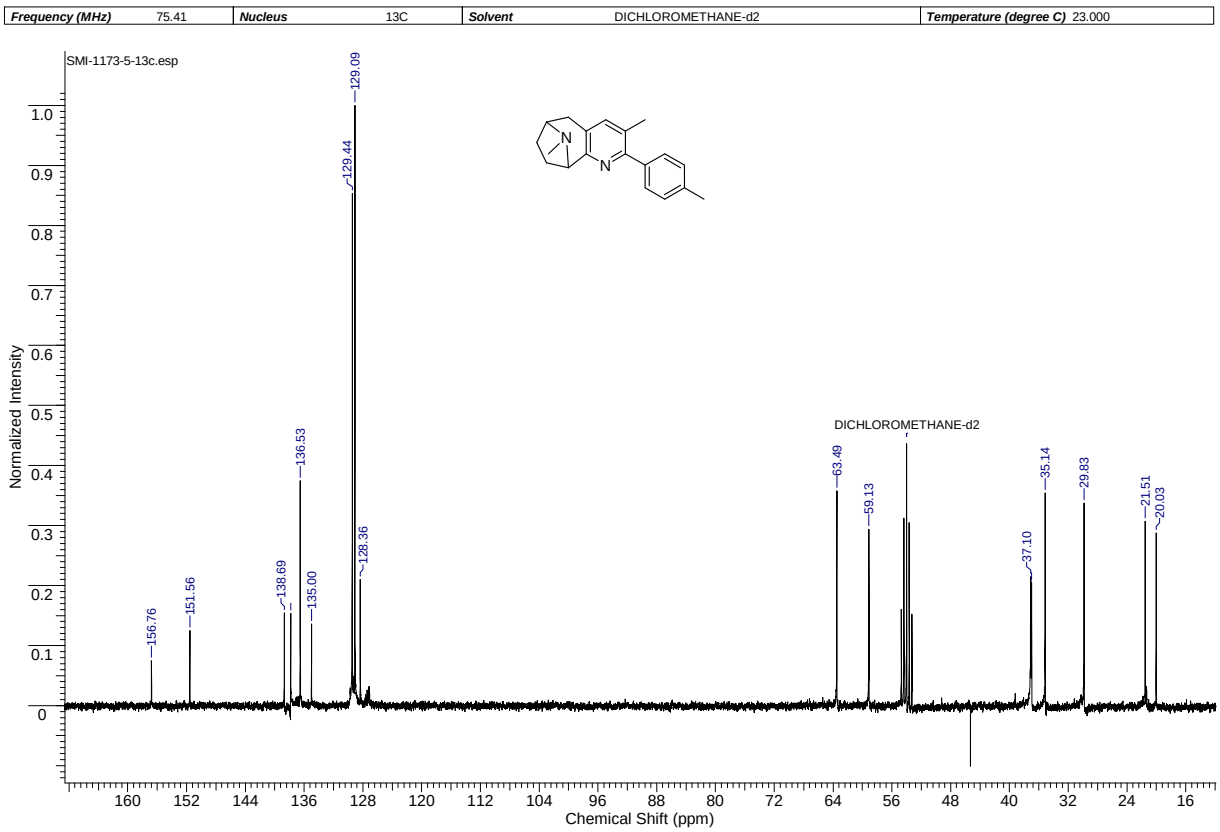

Frequency (MHz) 399.81
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 26.000
SMI-1045-dest-1h.esp
M12(d)
M11(d)
M09(d)
M10(d)
M02(m)
M04(s)
M03(s)
M01(s)
M05(d)
M08(d)
M07(t)
M06(dd)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 100.54
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 26.000
SMI-1045-dest-13c
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1116-1h
M08(m)
M07(m)
M03(s)
M04(s)
M06(m)
M05(m)
M01(m)
M02(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1116-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 299.86
Nucleus 1H
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1173-4-1h.esp
M03(m)
M05(m)
M07(s)
M08(d) M04(s)
M06(s)
M13(m)
M14(m)
M12(s)
M11(d)
M10(m)
M09(dd)
M02(m)
M01(m)
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)


Frequency (MHz) 75.41
Nucleus 13C
Solvent DICHLOROMETHANE-d2
Temperature (degree C) 23.000
SMI-1173-5-13c.esp
DICHLOROMETHANE-d2
Normalized Intensity
Chemical Shift (ppm)

8. List of Publications

The following publications were published prior to working on this thesis:

1) B. Blank, S. Michlik and R. Kempe, *Chem. Eur. J.* **2009**, *15*, 3790-3799.
"Selective iridium-catalyzed alkylation of (hetero)aromatic amines and diamines with alcohols under mild reaction conditions"

2) B. Blank, S. Michlik and R. Kempe, *Adv. Synth. Catal.* **2009**, *351*, 2903-2911.
"Synthesis of selectively mono-N-arylated aliphatic diamines *via* iridium-catalyzed amine alkylation"

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

3) S. Michlik and R. Kempe, *Chem. Eur. J.* **2010**, *16*, 13193-13198.
"New iridium catalysts for the efficient alkylation of anilines by alcohols under mild conditions"

4) S. Michlik, T. Hille and R. Kempe, *Adv. Synth. Catal.* **2012**, *354*, 847-862.
"The iridium-catalyzed synthesis of symmetrically and unsymmetrically alkylated diamines under mild reaction conditions"

5) S. Michlik, R. Kempe, *Nature Chem.* **2013**, *5*, 140-144.
"A sustainable catalytic pyrrole synthesis"

6) S. Michlik, R. Kempe, T. Irrgang, Deutsche Patentanmeldung (Nr. 102012018403.4)
"Verfahren zur katalytischen Synthese von N-Heterozyklen"

7) S. Michlik, R. Kempe, *Angew. Chem.* accepted for publication.
"Regioselectively functionalized pyridines from sustainable resources"

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Special thanks are due to my father, who has always believed in me, but cannot be with us to experience the completion of this work. Equally I want to thank my mother, who always supported me especially in hard times.

A very special thanks goes to my wife Christiane, who was there for me all the time.

Danksagung

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10. Declaration / Erklärung

I hereby declare that I have written this work by myself and that no other sources than those mentioned in this work have been used.

I further declare that I have not tried, with or without success, to submit this thesis elsewhere. I have not finally failed any similar doctoral thesis at any other university.

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

Ferner erkläre ich, dass ich anderweitig mit oder ohne Erfolg nicht versucht habe, diese Dissertation einzureichen. Ich habe keine gleichartige Doktorprüfung an einer anderen Hochschule endgültig nicht bestanden.

Bayreuth, den _____ _____

(Stefan Michlik)