Mn- and Cr-based Complexes for (De-) Hydrogenation Catalysis

DISSERTATION

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Fabian Johann Kallmeier

aus *Auerbach i.d.Opf.*

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Amtierender Dekan: Prof. Dr. Matthias Breuning

Prüfungsausschuss:

Prof. Dr. Rhett Kempe	(Erstgutachter)
Prof. Dr. Rainer Schobert	(Zweitgutachter)
Prof. Dr. Mukundan Thelakkat	(Vorsitz)
Prof. Dr. Birgit Weber	

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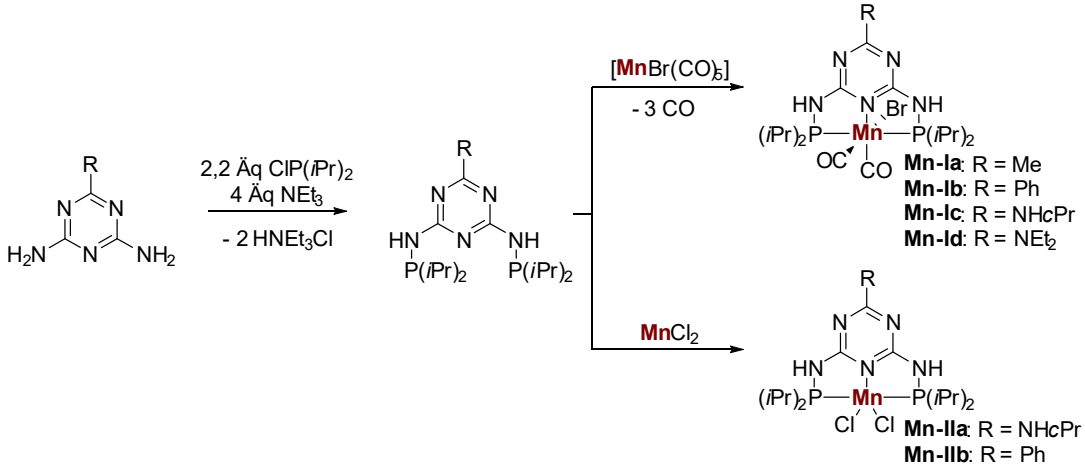
List of Abbreviations

ADC	Acceptorless Dehydrogenative Condensation
Äq	Äquivalent
BAr^F_4	tetrakis[3,5-bis(trifluoromethyl)phenyl]borate
BH / HA	Borrowing Hydrogen / Hydrogen Autotransfer
calcd	calculated
*c*Pr	cyclopropyl
Cy	cyclohexyl
d	doublet
δ	chemical shift [ppm]
diglyme	1-methoxy-2-(2-methoxyethoxy)ethane
dme	1,2-dimethoxyethane
EI	electron ionization
equiv	equivalent
GWP	Global Warming Potential
*i*Pr	isopropyl
J	coupling constant [Hz]
m	multiplet
mp	melting point [°C]
MS	mass spectrometry
Nu	nucleophile
Ph	phenyl
PMP	*para*-methoxyphenyl
q	quartet
R	organic moiety (aliphatic or aromatic moieties) or hydrogen
s	singlet
s_br	broad singlet
t	triplet
*t*Bu	*tert*-butyl
2-MeTHF	2- methyltetrahydrofuran
XRD	X-Ray diffraction

1. Zusammenfassung

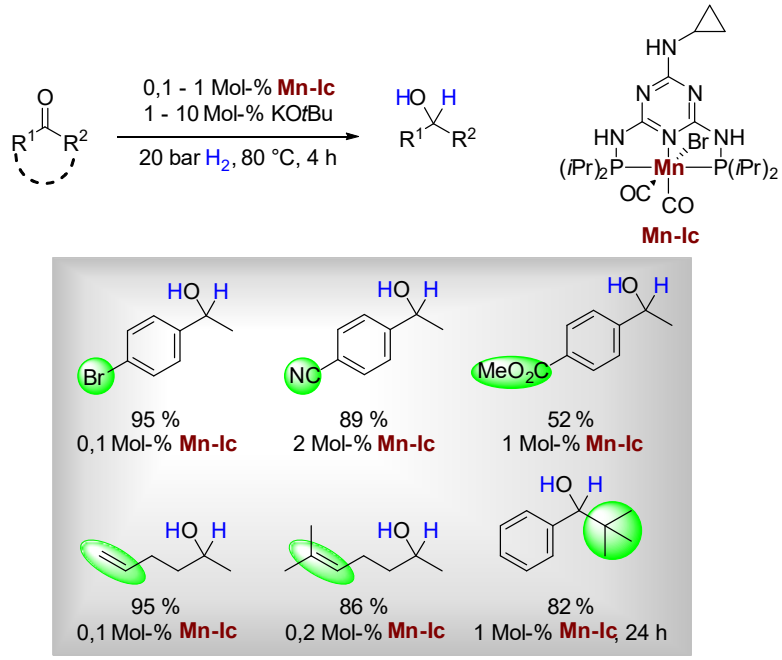
Das Thema der vorliegenden Arbeit ist die Entwicklung und Anwendung von homogenen Katalysatoren, welche auf billigen und reichlich verfügbaren Übergangsmetallen, speziell auf Mangan und Chrom, basieren. Mangan und Chrom wurde aufgrund deren Neigung zu Einelektronenübertragung traditionell keine Aufmerksamkeit in der (De-)Hydrierkatalyse und/oder der „Borrowing Hydrogen“ / Wasserstoff-Autotransfer (BH/HA) Katalyse geschenkt. Um diese Beschränkung zu überwinden wurden im Rahmen der vorliegenden Arbeit bifunktionelle Komplexe synthetisiert, welche – nach Aktivierung mit einer starken Base – eine heterolytische Spaltung von Wasserstoff unter Erhalt der originalen Oxidationsstufe des Metalls erlauben. Diese Komplexe basieren auf Diamino-*s*-triazin-abgeleiteten Liganden, welche von den Gruppen um KEMPE und KIRCHNER in anderen (basismetall-katalysierten) Reaktionen etabliert wurden. Die reibungslose Synthese dieser Liganden, sogar im Multigramm Maßstab, macht diese zu idealen Kandidaten für die Katalysatorentwicklung. Im ersten Teil der vorliegenden Arbeit wurden Mangankomplexe (Mn^{I} und Mn^{II}) durch die Reaktion von P,N,P Liganden mit den entsprechenden Manganpräkursoren [$MnBr(CO)_5$] oder $MnCl_2$ hergestellt (Schema 1.1).



Schema 1.1. Synthese von P,N,P Liganden und deren Mangankomplexe, wie in Kapitel 5 beschrieben. Äq: Äquivalente; *c*Pr: Cyclopropyl.

Diese Komplexe wurden als Präkatalysatoren für die chemoselektive Hydrierung von Carbonylverbindungen angewandt (Kapitel 5). Es wurde festgestellt, dass Mn^{I}-Komplexe unter milden Reaktionsbedingungen katalytisch aktiv waren (typischerweise 0.1 Mol-% Präkatalysatorbeladung, 1 Mol-% KO*t*Bu, 20 bar H_2, 80 °C, 4 h), wohingegen Mn^{II}-Verbindungen als inaktiv befunden wurden. Es wurde weiterhin gezeigt, dass Mangankatalysatoren exzellente Chemoselektivität in der der Hydrierkatalyse aufweisen (Schema 1.2). Ketone und Aldehyde wurden auch in der Anwesenheit von funktionellen Gruppen wie Arylhaliden, Nitrilen, Estern und Alkenen selektiv hydriert. Großer sterischer Anspruch um die Carbonylgruppe des Substrats herum reduzierte die Ausbeute an Produkt, was jedoch durch längere Reaktionszeiten und/oder eine Erhöhung der Katalysatorbeladung überwunden werden konnte. Es wurde insgesamt die Hydrierung von dreißig Beispielen in

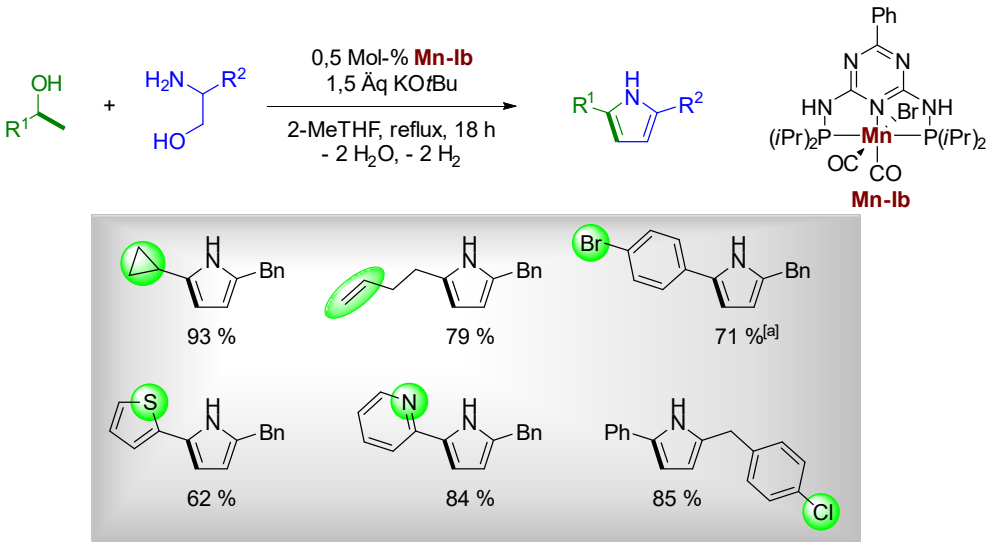
Ausbeuten zwischen 52 % und > 99 % gezeigt, wobei die Ausbeute an Produkt im Mittel mehr als 90 % betrug.



Schema 1.2. Chemoselektivität in der Mn-katalysierten C=O Hydrierkatalyse. Reaktionsbedingungen: Keton (3 mmol), **Mn-Ic** (wie angegeben), KO*t*Bu (10 Äq basierend auf **Mn-Ic**), Toluol (1,5 mL), H_2 (20 bar), 80 °C, 4 h.

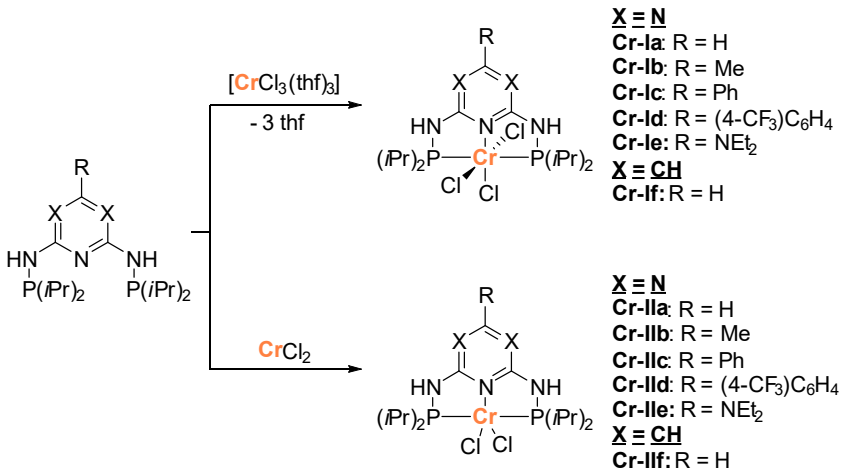
Kapitel 6 der vorliegenden Arbeit beschreibt die Anwendung dieser neu entwickelten Mangankatalysatoren in der Synthese von 1*H*-Pyrrolen ausgehend von sekundären Alkoholen und 1,2-Aminoalkoholen (Schema 1.3). Die Gruppe um KEMPE hat vor Kurzem diese Methode zur Synthese von Pyrrolen basierend auf der Akzeptorlosen Dehydrierenden Kondensation (ADC) von sekundären Alkoholen mit 1,2-Aminoalkoholen veröffentlicht. In diesem Verfahren wird ein Alkohol zu einer Carbonylverbindung dehydriert (d.h. Umkehrreaktion zur Hydrierung), welche im Anschluss eine Kondensation mit dem Aminoalkohol durchläuft; gefolgt von weiteren Dehydrier- und Kondensationsschritten werden die Zielverbindungen, Pyrrole, erhalten. Die Benutzung von Mn-basierten Katalysatoren macht den gesamten Prozess intrinsisch nachhaltiger, indem die Benutzung von teuren und seltenen Iridiumkatalysatoren vermieden wird.

Nachdem für Mn^I Komplexe eine katalytische Aktivität in der Pyrrolsynthese mittels ADC gefunden wurde, wurden die Reaktionsbedingungen optimiert. Die besten Ergebnisse wurden erzielt, wenn 2 Äquivalente des sekundären Alkohols, 1 Äquivalent des 1,2-Aminoalkohols und 1,5 Äquivalente KO*t*Bu unter Benutzung von 0,5 Mol-% des Präkatalysators für 18 Stunden in 2-Methyltetrahydrofuran (2-MeTHF; 0.5 M) unter Rückfluss erhitzt wurden. Die generelle Anwendbarkeit wurde anhand der Synthese und Isolation von 29 Beispielen gezeigt, inklusive Produkte, welche empfindliche funktionelle Gruppen wie Cyclopropane, Alkene, Arylhalide oder Heterozyklen (Thiophen und Pyridin) tragen (Schema 1.3).



Schema 1.3. Highlights der mangankatalysierten Synthese von Pyrrolen. Reaktionsbedingungen: Sekundärer Alkohol (6 mmol, 2 Äq), Aminoalkohol (3 mmol), KO*t*Bu (4,5 mmol, 1,5 Äq), **Mn-Ib** (15 µmol, 0,5 Mol-%), 2-MeTHF (6 mL), reflux, 18 h. [a]: NaO*t*Bu anstelle von KO*t*Bu, 1 Mol-% **Mn-Ib**, 48 h.

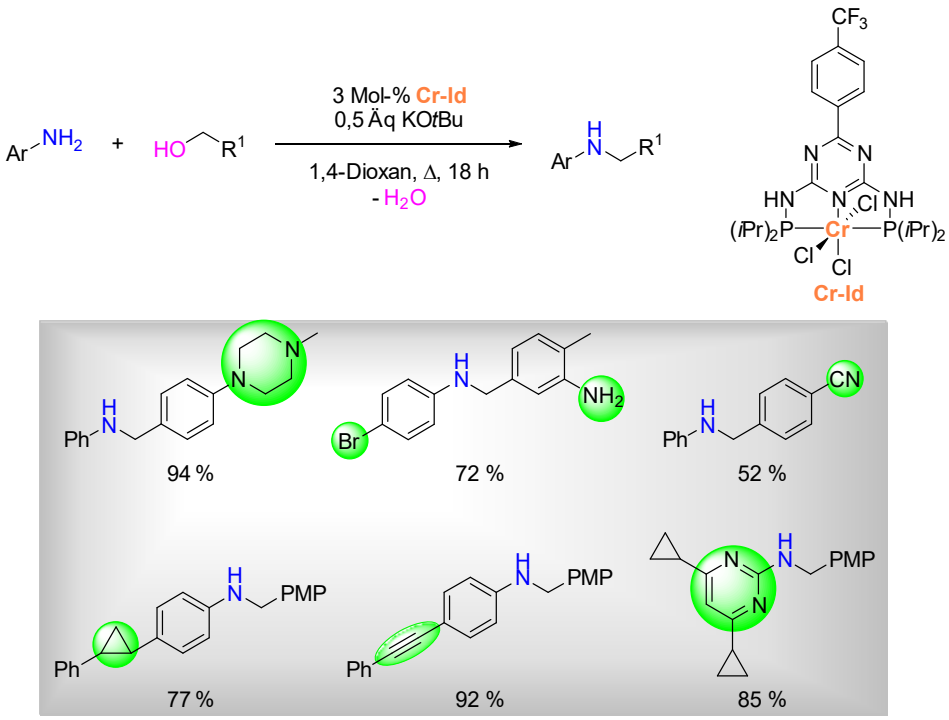
Chrom wurde trotz dessen Verfügbarkeit und günstigen Preises bisher in der Entwicklung von Katalysatoren, welche auf BH/HA Katalyse abzielte, nicht beachtet. In Kapitel 7 der vorliegenden Arbeit wird jedoch am Beispiel der N-Alkylierung von Aminen aufgezeigt, dass Cr tatsächlich derartige bindungsbildende Reaktionen katalysieren kann. Zuerst wurde gemäß Schema 1.4 eine Bibliothek von Cr^{II} und Cr^{III} Komplexen synthetisiert.



Schema 1.4. Bibliothek der als Präkatalysatoren für BH/HA untersuchten Cr^{II} und Cr^{III} Komplexe.

Nach der gründlichen Optimierung der Reaktionsbedingungen unter Benutzung der Reaktion von Anilin mit Benzylalkohol als Modellreaktion (1,2 Äq Benzylalkohol, 1 mmol aromatisches Amin, 0,5 Äq KO*t*Bu, 3 Mol-% Präkatalysator, 1,4-Dioxan (2 M), 150 °C (Ölbad), 18 h), wurden insgesamt 35 N-alkylierte Amine hergestellt und in Ausbeuten von 46 % bis 94 % (im Schnitt betrug die Ausbeute 85 %) isoliert.

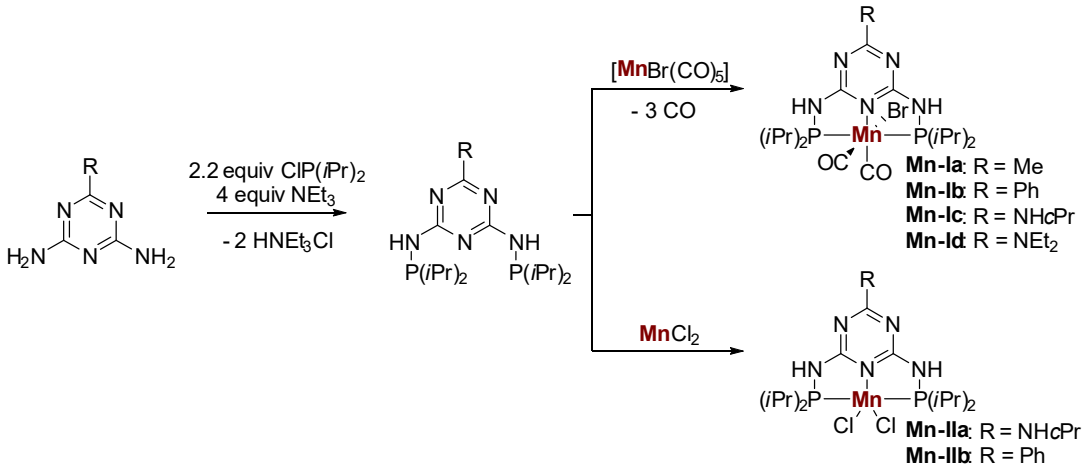
Von dem Katalysatorsystem tolerierte funktionelle Gruppen umfassen primäre und tertiäre Amine, Nitrile, Cyclopropane, C-C Mehrfachbindungen und heteroaromatische Amine (zum Beispiel Pyrimidin, Chinolin, Pyrazol; Schema 1.5).



Schema 1.5. Selektivität in der chromkatalysierten N-Alkylierung von Aminen. Reaktionsbedingungen: Amin (1 mmol), primärer Alkohol (1,2 mmol, 1,2 Äq), **Cr-Id** (30 µmol, 3 Mol-%), KO*t*Bu (0,5 mmol, 0,5 Äq), 1,4-Dioxan (0,5 mL), 150 °C Ölbad, 18 h. PMP: *para*-Methoxyphenyl.

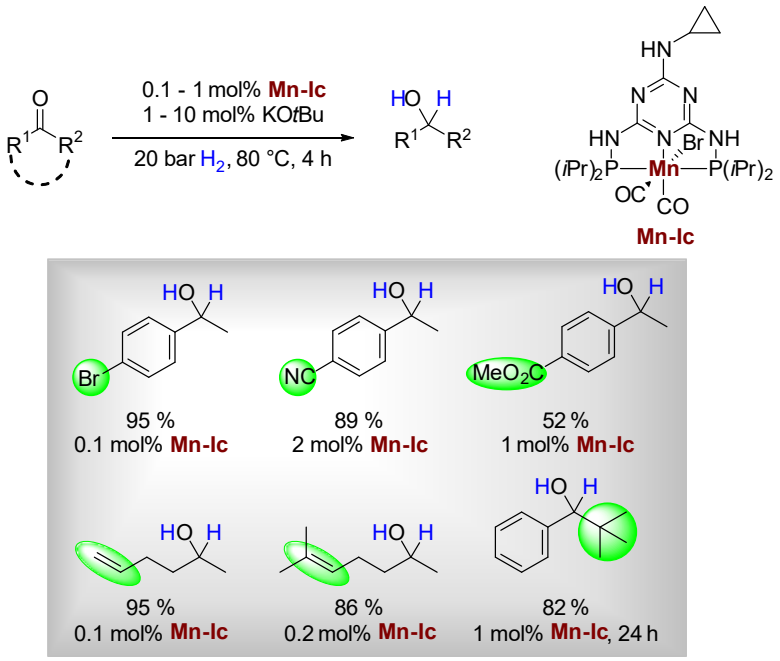
2. Summary

The subject of this thesis is the development and application of homogeneous catalysts that are based on cheap and abundantly available transition metals, specifically manganese and chromium. Manganese and chromium have traditionally received no attention in (De-)Hydrogenation and/or Borrowing Hydrogen / Hydrogen Autotransfer (BH/HA) catalysis, due to their propensity for single-electron-transfer steps. To overcome this limitation, bifunctional complexes have been synthesized in this work, allowing – after activation with a strong base – a heterolytic cleavage of dihydrogen under retention of the original oxidation state of the metal. These complexes are based on diamino-*s*-triazine-derived ligands, which have been established by the groups of KEMPE and KIRCHNER in other (base metal catalyzed) reactions. The seamless synthesis of these ligands, even on multigram scale, makes them ideal candidates for catalyst development. In the first part of this work, manganese (Mn^{I} and Mn^{II}) complexes have been synthesized by the reaction of P,N,P ligands with the corresponding manganese precursors, $[MnBr(CO)_5]$ or $MnCl_2$ (Scheme 2.1).



Scheme 2.1. Synthesis of P,N,P ligands and manganese complexes thereof as described in Chapter 5.

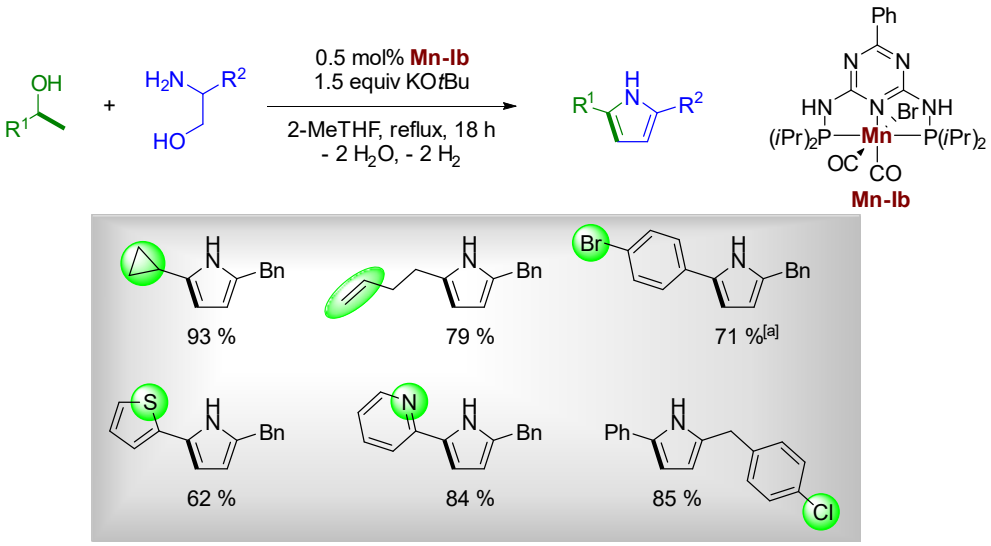
These complexes were applied as precatalysts for the chemo-selective hydrogenation of carbonyl compounds (Chapter 5). It was established that Mn^{I} complexes were catalytically active under mild reaction conditions (typically 0.1 mol% precatalyst loading, 1 mol% KO*t*Bu, 20 bar H_2, 80 °C, 4 h) whereas Mn^{II} compounds were found to be inactive. It was furthermore demonstrated that manganese catalysts exhibit excellent chemo-selectivity in hydrogenation catalysis (Scheme 2.2). Ketones and aldehydes were selectively hydrogenated even in the presence of functional groups like aryl halides, nitriles, esters, and alkenes. Steric bulk around the carbonyl group in the substrate reduced the yield, which was overcome by longer reaction times and/or increased catalyst loading. Overall, the hydrogenation of thirty examples has been reported with yields ranging between 52 % and > 99 % and, on average, the yield of product was well above 90 %.



Scheme 2.2. Chemo-selectivity in Mn-catalyzed C=O hydrogenation catalysis. Reaction conditions: ketone (3 mmol), **Mn-Ic** (as indicated), KO*t*Bu (10 equiv based on **Mn-Ic**), toluene (1.5 mL), H_2 (20 bar), 80 °C, 4 h.

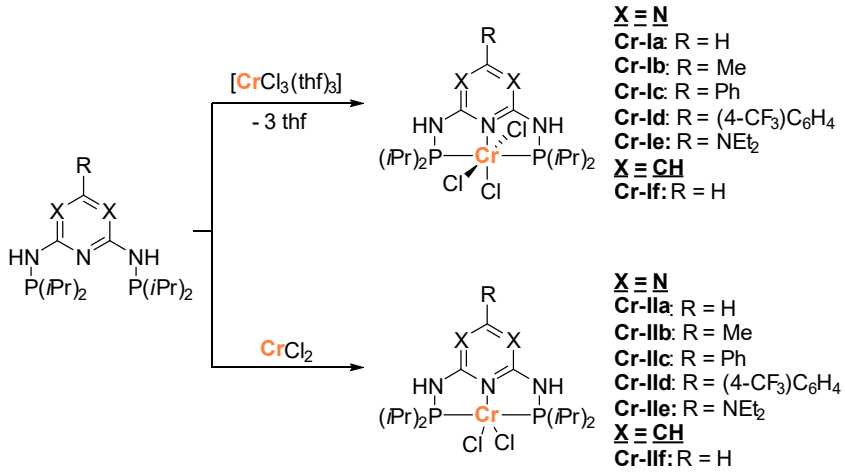
Chapter 6 of this work details the application of these newly developed manganese catalysts in the synthesis of 1*H*-pyrroles from secondary alcohols and 1,2-amino alcohols (Scheme 2.3). The KEMPE group recently reported this method for the synthesis of pyrroles based on the acceptorless dehydrogenative condensation (ADC) of secondary alcohols and 1,2-amino alcohols. In this procedure, an alcohol is dehydrogenated to a carbonyl compound (*i.e.* reverse reaction to hydrogenation) that can then undergo condensation with an amino alcohol, followed by further dehydrogenation and condensation steps to yield the target pyrroles. Using Mn-based catalysts renders the entire process innately more sustainable by avoiding the use of expensive and rare iridium catalysts.

The reaction conditions were optimized after catalytic activity was found for Mn^I complexes in pyrrole synthesis by ADC. The best results were obtained by employing 2 equiv of secondary alcohol, 1 equiv of 1,2-amino alcohol, 1.5 equiv KO*t*Bu when the reaction was refluxed in 2-methyltetrahydrofuran (2-MeTHF; 0.5 M) for 18 hours and 0.5 mol% precatalyst were used. The general applicability was shown by the synthesis and isolation of 29 examples (Scheme 2.3), including products containing sensitive functional groups like cyclopropane, alkene, aryl halides and heterocycles (thiophene and pyridine).



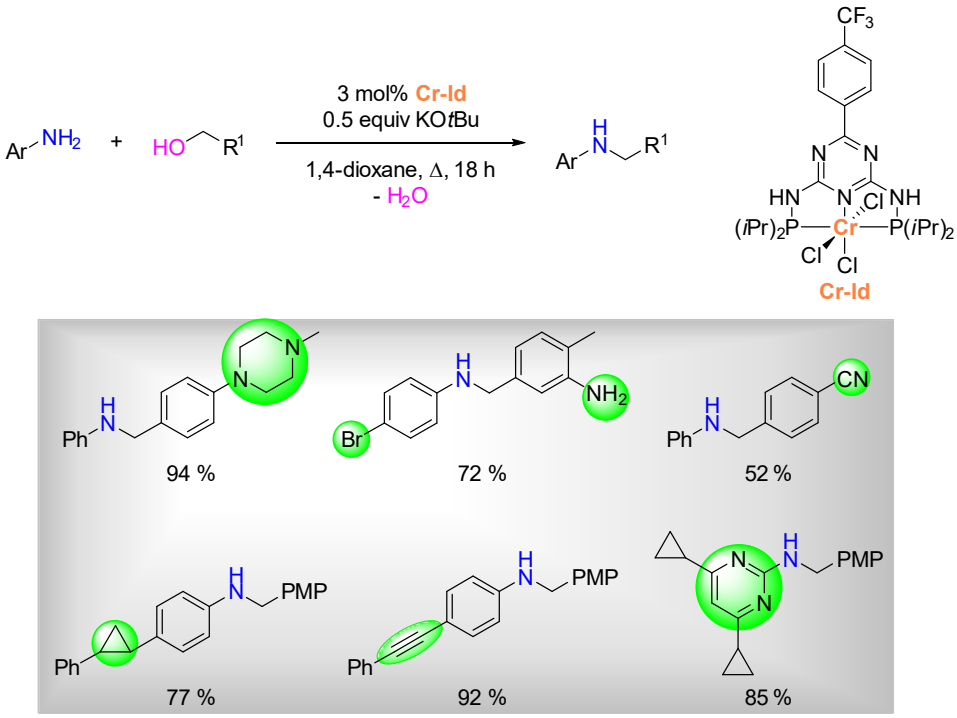
Scheme 2.3. Highlights in manganese-catalyzed pyrrole synthesis. Reaction conditions: Secondary alcohol (6 mmol, 2 equiv), amino alcohol (3 mmol), KO*t*Bu (4.5 mmol, 1.5 equiv), **Mn-Ib** (15 µmol, 0.5 mol%), 2-MeTHF (6 mL), reflux, 18 h. [a]: NaO*t*Bu instead of KO*t*Bu, 1 mol% **Mn-Ib**, 48 h.

Despite its availability and cheap price, chromium has so far been neglected in the development of catalysts aimed at BH/HA catalysis. In Chapter 7 of this work, however, it was demonstrated that Cr can indeed catalyze such bond forming reactions, using the N-alkylation of amines as an exemplary reaction. First, a library of Cr^{II} and Cr^{III} complexes was synthesized according to Scheme 2.4.



Scheme 2.4. Library of the Cr^{II} and Cr^{III} complexes investigated as precatalysts for BH/HA.

After rigorous optimization of the reaction conditions using the reaction of aniline with benzyl alcohol as a model reaction (1.2 equiv benzyl alcohol, 1 mmol aromatic amine, 0.5 equiv KO*t*Bu, 3 mol% precatalyst, 1,4-dioxane (2 M), 150 °C (oil bath) for 18 h), a total of 35 N-alkylated amines was synthesized and isolated in yields from 46 % to 94 % (average yield is 85 %). Functional groups that were tolerated by the catalyst systems include primary and tertiary amines, nitriles, cyclopropanes, C-C multiple bonds and heteroaromatic amines (*e.g.* pyrimidine, quinoline, pyrazole; Scheme 2.5).



Scheme 2.5. Selectivity in the chromium-catalyzed N-alkylation of amines. Reaction conditions: Amine (1 mmol), primary alcohol (1.2 mmol, 1.2 equiv), **Cr-Id** (30 µmol, 3 mol%), KO*t*Bu (0.5 mmol, 0.5 equiv), 1,4-dioxane (0.5 mL), 150 °C oil bath, 18 h. PMP: *para*-methoxyphenyl.

3. Introduction

3.1. Motivation and Sustainability

An increase in human population with an ever-growing demand for an improving lifestyle might lead to a depletion of natural resources and an increase in waste production. The chemical processes needed to sustain human development in an environmentally compatible manner will therefore face the challenge to comply with criteria that have historically played minor roles. These criteria have been proposed by PAUL T. ANASTAS and JOHN C. WARNER as their famous 12 principles of what is now known as Green Chemistry (Figure 3.1).[1] Green Chemistry is a commonly utilized phrase describing the use of renewable raw materials as resources (replacing hazardous/toxic chemicals) to efficiently and selectively synthesize chemical products while avoiding waste generation.[2] The 9th principle, "Catalysis", is of paramount importance because it overlaps with several of the 12 principles. In comparison to stoichiometrically used reagents, the use of catalysts prevents the generation of waste (1st principle); mostly because the atom economy (*i.e.,* the number of total atoms employed in a process *versus* the number of atoms ending up in the final product) is greatly increased (2nd principle). Using less material to produce the same product while reducing waste, which would need to be specially treated, is also of great economical interest. This is reflected in the number of industrial processes (75 to 85 %) that involve the use of catalysts. For newly developed processes that number is closer to 90 % and shows how valuable research in this area is.[3,4] However, the environmental benefits through a more widespread use of catalysts will be insufficient if the feedstocks of the chemical industry won't change, too.

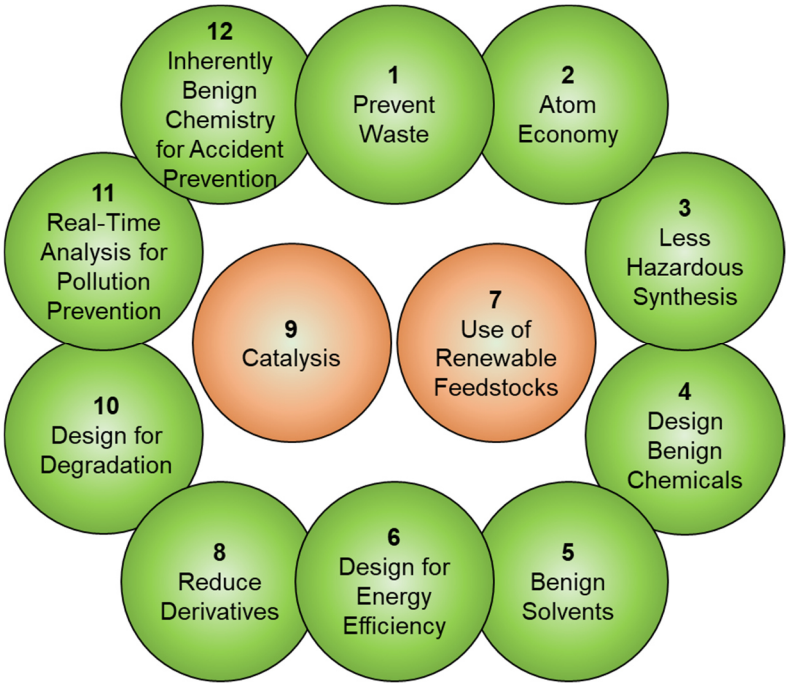
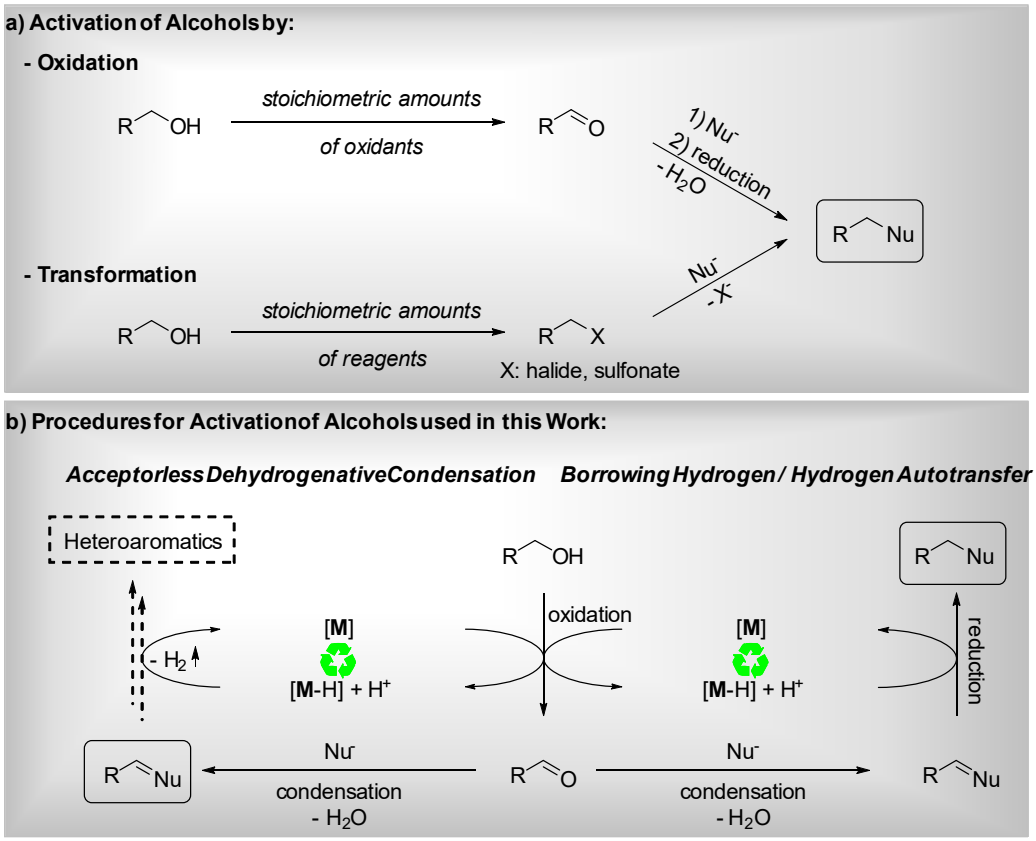


Figure 3.1. The twelve principles of Green Chemistry as proposed by Anastas and Warner.[1] Catalysis and the use of renewable resources are the focus of this work.

Currently, the chemical industry relies heavily on products derived from downstream products of crude oil refining. Crude oil is a finite resource and should therefore be conserved as per the 7th principle of Green Chemistry. Suitable feedstocks should be renewable, abundantly available, and not in competition with food production. One feedstock that is heavily discussed is lignocellulosic biomass, which is produced by woody plants. Lignocellulosic biomass is indigestible and finds little application in industrial processes, despite an estimated world-wide production of 200 billion tons per year.[5] It is a supramolecular assembly of cellulose fibers, hemicellulose, and lignin which can be pyrolyzed to yield low quality bio-oil.[6] Further processing by hydrodeoxygenation and hydrogenation of the acidic, oxygen rich bio-oil yields a mixture of various alcohols.[7] Alcohols are an advantageous class of chemicals for synthesis. Alcohols are relatively stable and due to their low reactivity, also usually less toxic than activated compounds. Hence, they pose less risk to the environment and human health compared to more reactive compounds (conforms with Green Chemistry principles three and twelve). The use of alcohols, however, necessitates a different approach to the synthesis of chemical products, which would have historically been prepared by downstream oxidative chemistry from petroleum-based sources. For alcohols, a re-functionalization-based chemistry is required.[8]



Scheme 3.1. a) "Classic" means of alcohol activation *versus* b) Acceptorless Dehydrogenative Condensation (ADC) and Borrowing Hydrogen / Hydrogen Autotransfer (BH/HA) strategy.[9] Nu: Nucleophile.

Traditionally, the activation of alcohols has been achieved by oxidation using a stoichiometric amount of oxidant (Scheme 3.1a), for example Cr^{VI} salts (*e.g.* Corey-Suggs oxidation[10]) or hypervalent iodine compounds (*e.g.* Dess-Martin oxidation[11]). After transformation of the activated compounds (*i.e.* aldehydes or ketones), a reduction step could be carried out with stoichiometric amounts of reagents like borohydrides or aluminum hydrides, which then leads to more undesirable amounts of potentially problematic waste. Other means of alcohol activation include transformations of the hydroxyl group into "good" leaving groups such as halides or sulfonates. However, this adds additional steps and waste to the overall procedure. One solution to this problem is found in a concept called Borrowing Hydrogen / Hydrogen Autotransfer (BH/HA; Scheme 3.1b).[9] In this scenario, alcohols are dehydrogenated to the corresponding carbonyl compound that can undergo condensation reactions with the nucleophile, liberating water as the only by-product. The resulting unsaturated compound can then be hydrogenated with the hydrogen that had been temporarily "stored" at the catalyst. If the hydrogen is released instead, the unsaturated compound can be obtained together with H_2 (*i.e.* a valuable and easily reusable by-product). This is known as Acceptorless Dehydrogenative Condensation (ADC).

Typically, noble-metal-based catalysts are employed in these kinds of reactions. Besides being scarce, toxic, and expensive[12], noble-metal catalyst precursors are difficult to mine due to their low concentration in earth's upper crust.[13] Furthermore, immense amounts of energy are required during processing and purification. This is reflected in the unfavorable global warming potential (GWP) of the platinum group metals, specifically Rh and Ir (Figure 3.2).[14]

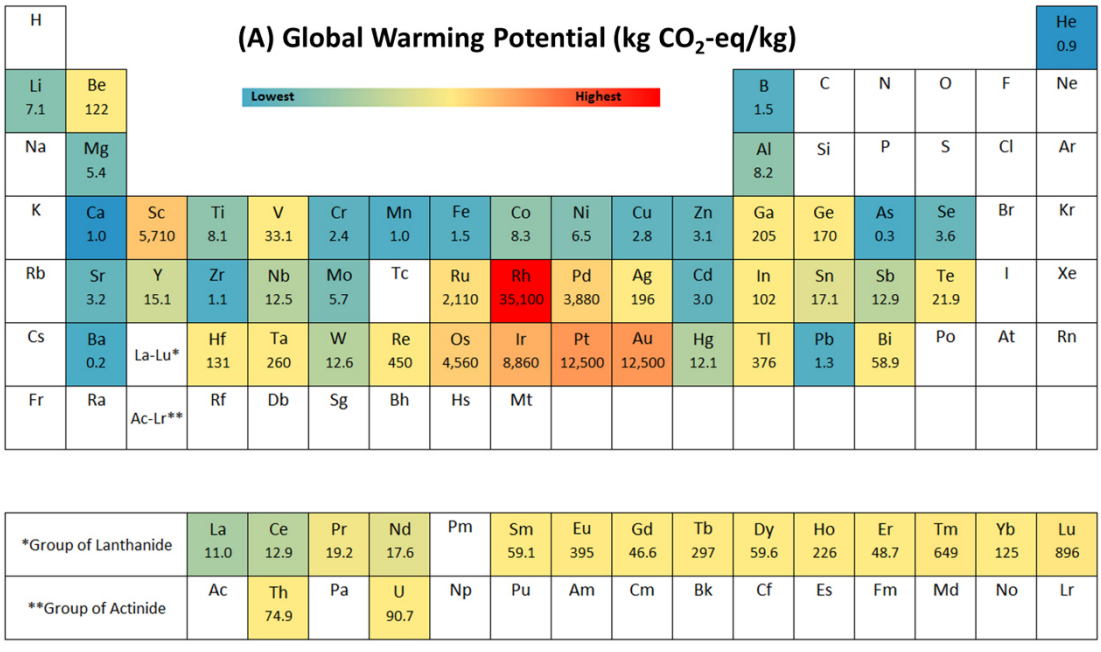


Figure 3.2. Global Warming Potential (GWP) for various elements. "Periodic table of global warming potentials (GWPs)." by P. Nuss and M. Eckelman, used under CC BY 4.0 / trimmed from original.[14]

3.2. Hydrogenation Catalysis

Hydrogenations are one of the most fundamental reactions in academia and industry and have been termed as "*[…] one of the extraordinary success stories of homogeneous catalysis […]*" (R. Morris Bullock in reference 15). The addition of dihydrogen across a $R_2C{=}X$ (X: O, NR, CR_2) double bond is used universally. The thermodynamic and kinetic stability of hydrogen requires the use of catalysts for hydrogenation reactions. Noteworthy early contributions were made by SABATIER, who developed finely distributed Nickel as a heterogeneous catalyst for the hydrogenation of olefins and was awarded the Nobel prize in 1912.[16] The first well-defined, *homogeneous* catalyst for olefin hydrogenation with an activity comparable to heterogeneous catalysts, $[RhCl(PPh_3)_3]$, was developed by WILKINSON over 50 years later.[17] The generally accepted reaction sequence involves oxidative addition of dihydrogen to the rhodium center, followed by olefin coordination. After insertion of the alkene into the [M-H] bond the subsequent reductive elimination liberates the product alkane and regenerates the $[RhCl(PPh_3)_3]$ catalyst (Figure 3.3a).[18] However, this early hydrogenation catalyst preferentially mediates olefin hydrogenation. In Green Chemistry, the production of alcohols by hydrogenation of C=O bonds is a pivotal catalytic reaction. A key development towards this goal was the development of bifunctional ruthenium complexes by NOYORI and co-workers.[19] They developed ruthenium complexes, that could heterolytically activate hydrogen into a nitrogen bonded "protic" H atom and a metal bonded "hydridic" H atom (Figure 3.3b), which allowed the selective hydrogenation of ketones to alcohols. This was also an early step in the development of asymmetric catalytic hydrogenation reactions, for which NOYORI was later awarded the Nobel prize (2001).[20] A relatively new type of metal ligand cooperativity has been found in pincer type complexes (Figure 3.3b). The proton on the linker Y acts in combination with the metal hydride and the formal oxidation state of the metal remains unchanged throughout the catalytic cycle by ligand aromatization-dearomatization.[21]

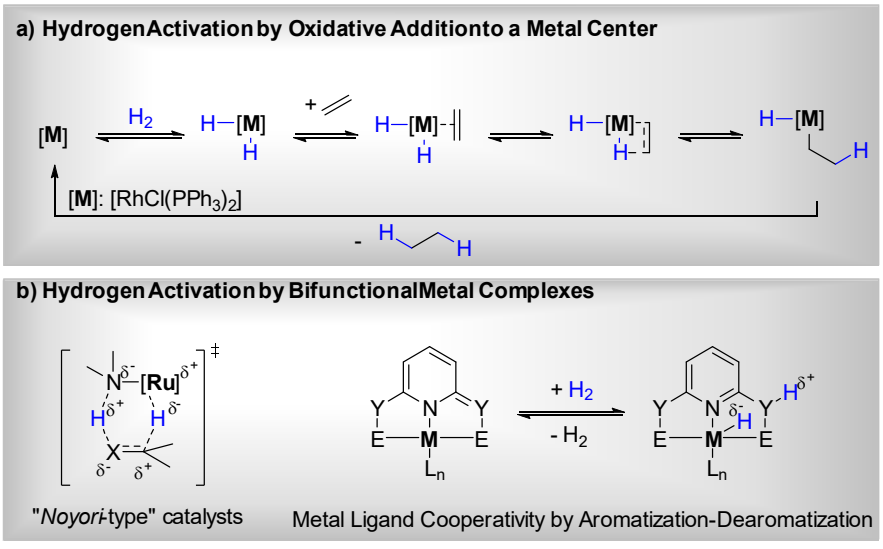
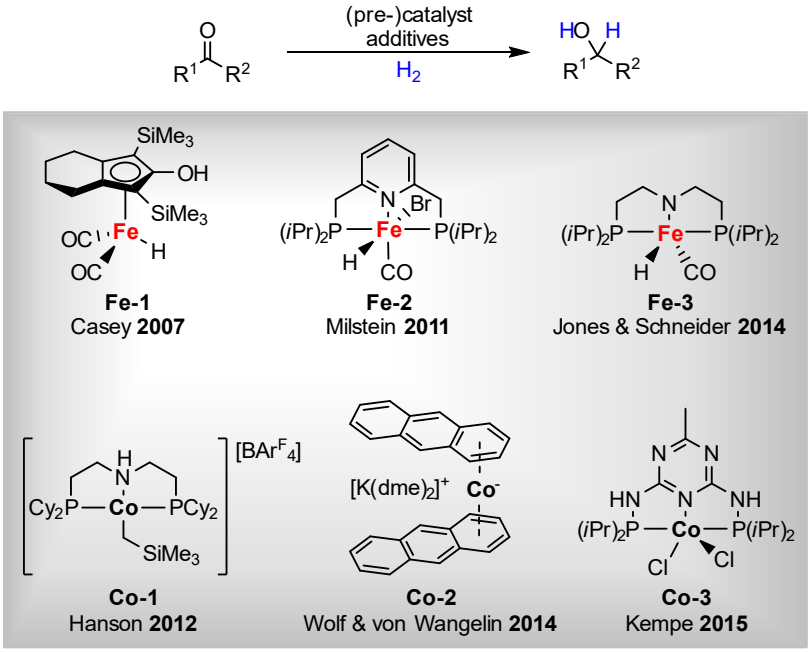


Figure 3.3. Different modes of hydrogen activation. **M**: mostly Ru, Ir; **Y**: CR_2, NR, O, S; **E**: PR_2, NR_2, SR; $\mathbf{L_n}$: CO, Cl, solvent

Considering the disadvantages of noble metal catalysts as discussed in Chapter 3.1, the development of hydrogenation catalysts based on abundantly available 3d-transition-metals became highly feasible (Scheme 3.2); especially for the reduction of C=O bonds in the context of Green Chemistry (*vide supra*). Significant progress has been made in this area using transition metal catalysts. Most notably, complexes based on cobalt and iron were introduced in recent years (Scheme 3.2).

In 2007, CASEY and GUAN reported the first iron complex as catalyst for the hydrogenation of ketones.[22] They successfully employed KNÖLKER's iron complex **Fe-1**[23], due to its resemblance of the active species of SHVO's (Ru) catalyst.[22] The catalyst found significant attention and subsequently, easier-to-use protocols were developed.[24,25] The development of chiral catalysts allowed asymmetric hydrogenation of prochiral compounds.[26,27] The first pincer-ligand based iron complex **Fe-2** was developed by Milstein and showed extraordinary productivity (TON up to 1880).[28] Pincer complex **Fe-3**[29], based on the "MACHO" ligand ($(R_2PCH_2CH_2)_2NH$)[30], showed similar productivity and was further modified for asymmetric catalysis later on.[31,32]

Known for its hydrogenation activity towards alkenes[33], the first report on cobalt complexes for C=O bond hydrogenation was published by HANSON and co-workers in 2012.[34] The precatalyst **Co-1** is based on the MACHO ligand, however, hardly exhibits chemo-selectivity between C=O and C=C double bonds. Some carbonyl hydrogenation selectivity was noted for **Co-2**, but C=C bonds were preferentially hydrogenated by this precatalyst.[35]



Scheme 3.2. State-of-the-art base metal catalysts for hydrogenation of carbonyl compounds. Cy: Cyclohexyl; $[BAr^F_4]$: $B^+(3,5\text{-}(CF_3)_2C_6H_3)_4$; dme: 1,2-Dimethoxyethane

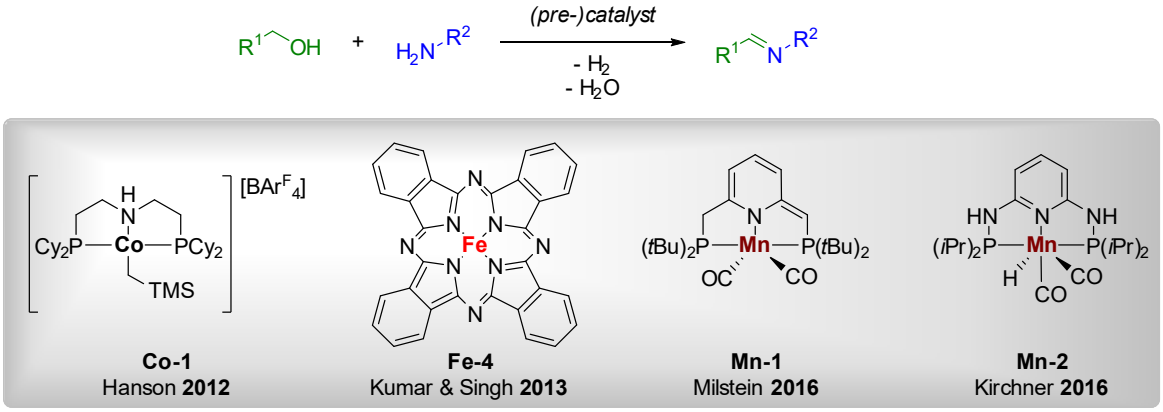
In 2015, the first selective Co precatalyst (**Co-3**) for the hydrogenation of ketones and aldehydes, even in the presence of olefins, was introduced by KEMPE and co-workers.[36] The precatalyst **Co-3** features a diamino-*s*-triazine core and is activated *in-situ* by catalytic amounts of sodium *tert*-butoxide.

Based on this shift of selectivity from C=C bond hydrogenation to preferential C=O hydrogenation by using diamino-*s*-triazine ligands, this ligand class should be a suitable starting point for the development of chemoselective hydrogenation catalysts based on other metals. Specifically, manganese was overlooked in past efforts of finding base metal hydrogenation catalysts, despite the existence of the bifunctional complex $[C_5H_3N\text{-}2,6\text{-}(NHPPh_2)_2Mn(CO)_3]I \cdot H_2O$ since its introduction by HAUPT and co-workers in 1991.[37] In Chapter 5 of this work, manganese complexes based on diamino-*s*-triazine ligands and their application in selective C=O bond hydrogenation will be reported.

3.3. Acceptorless Dehydrogenative Condensation

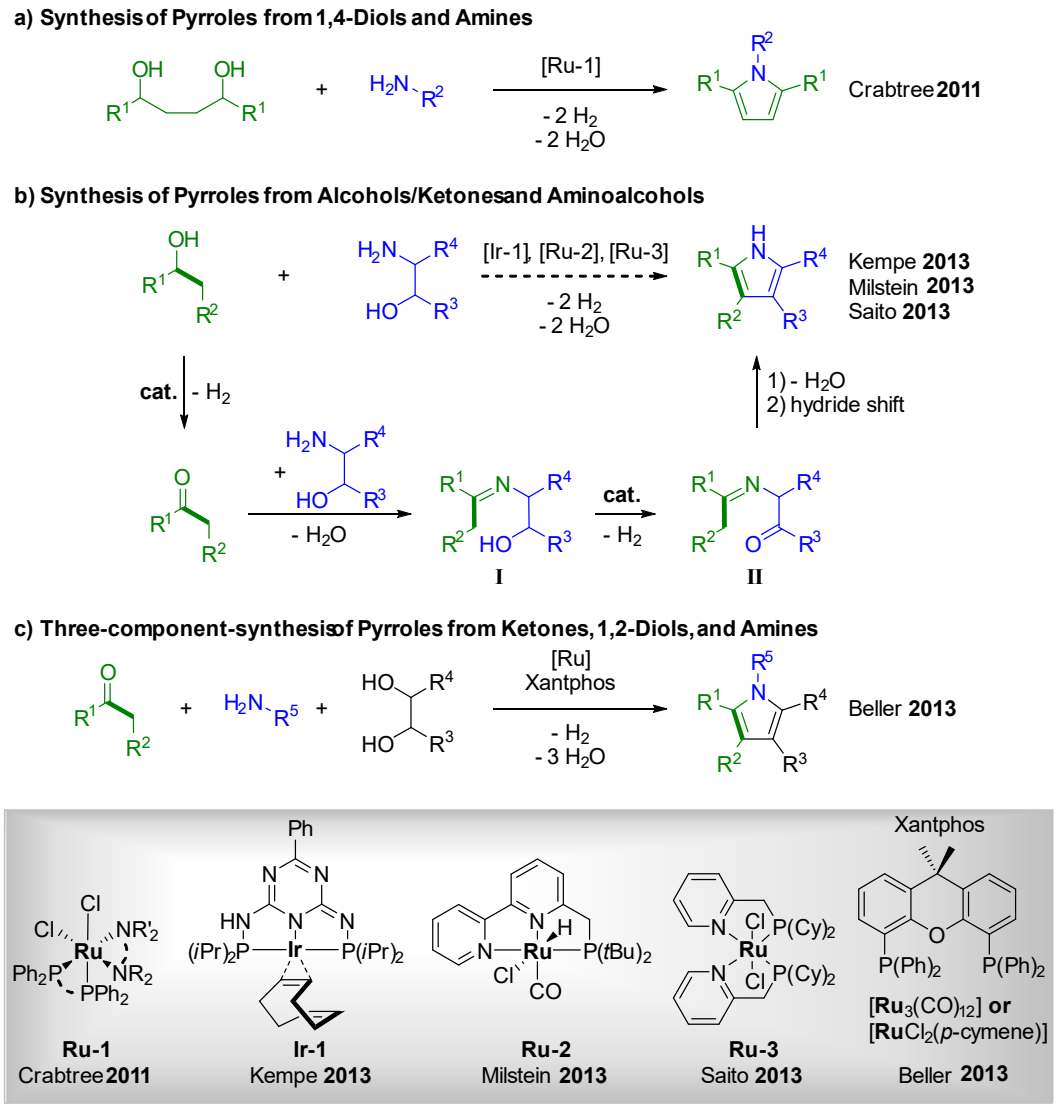
Following the success of base metals in hydrogenation catalysis, the reverse reaction *i.e.* the dehydrogenation of alcohols to form unsaturated products while releasing hydrogen gas was investigated by multiple groups.[38] Since reactive carbonyl compounds are produced from the dehydrogenation of alcohols, a variety of synthetic methods based on further reacting these *in-situ* generated carbonyl compounds have been developed. The most commonly employed reaction type is the condensation of the carbonyl compound with various nucleophiles.[39] If dihydrogen is directly liberated rather than being transferred to a sacrificial substrate, then the reaction sequence is called Acceptorless Dehydrogenative Condensation (ADC). ADC is especially desirable from an atom economic point of view, since hydrogen and water are the only by-products (Scheme 3.1, page 10).

The simplest case of ADC is the dehydrogenation of alcohols to form carbonyl compounds that subsequently undergo condensation with amines in a *Schiff*-type reaction[40] to form imines (Scheme 3.3). This was first reported by the MILSTEIN group in 2010 with a ruthenium catalyst.[41] Reports on ADC reactions catalyzed by base metal complexes are rare. HANSON and co-workers could show that their cobalt precatalyst **Co-1** mediates ADC and forms imines selectively. KUMAR and SINGH and co-workers used iron phthalocyanine **Fe-4** for the synthesis of imines. Manganese complexes were only recently introduced as catalysts for ADC. In 2016, MILSTEIN and co-workers introduced P,N,P pincer complex **Mn-1** as a catalyst for the ADC of alcohols and amines. KIRCHNER and co-workers swiftly followed up this report in the same year using a similar manganese complex (**Mn-2**).



Scheme 3.3. Synthesis of imines by acceptorless dehydrogenative condensation of alcohols and amines.

N-Heteroaromatic compounds are ubiquitously encountered structural motifs in chemistry. However, their synthesis from renewable resources such as alcohols and amino alcohols remains challenging.[42] Pyrroles are one group of privileged compounds due to their prevalence in drugs (Atorvastatin[43]), natural products (porphobilinogen, heme, bilirubin)[44], and material sciences (polypyrroles[45]). In 2011, CRABTREE and co-workers introduced a pyrrole synthesis starting from 1,4-dialcohols and primary amines (similar to the PAAL-KNORR pyrrole synthesis[46,47]) using various ruthenium diphosphine diamine complexes (Scheme 3.4a) as one of the first examples for the selective synthesis of heteroaromatics by acceptorfree dehydrogenative condensation.[48]

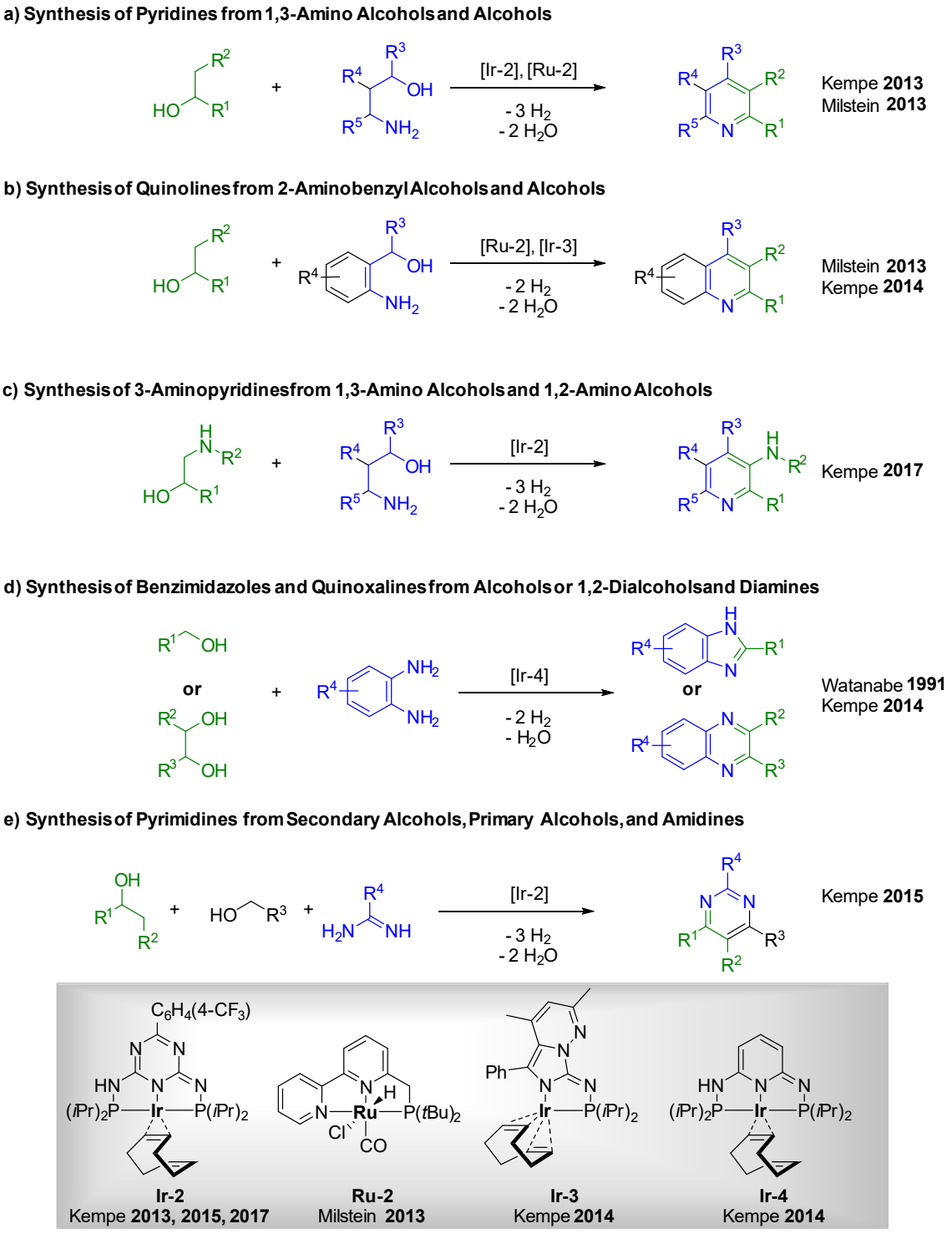


Scheme 3.4. Noble metal catalyzed synthesis of pyrroles from alcohols and amines/amino alcohols

The disadvantage of using 1,4-dialcohols is their poor availability, which then greatly limits the product scope. A breakthrough for increasing the product scope in pyrrole synthesis was achieved by the groups of KEMPE[49] and MILSTEIN[50] (Scheme 3.4b). In 2013, MICHLIK and KEMPE introduced pincer complex **Ir-1** bearing a 2,6-diamino-*s*-triazine based ligand.[49] Using

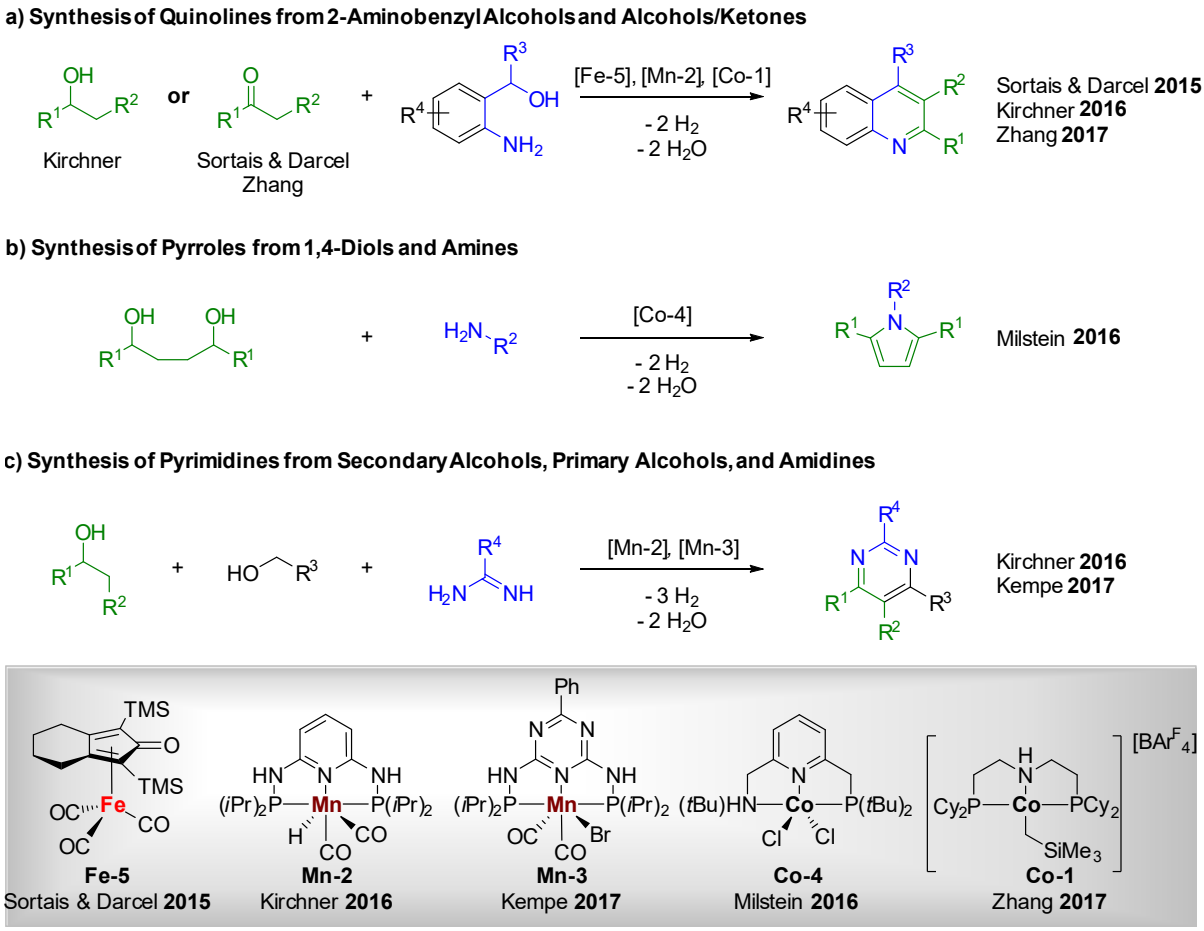
Ir-1 in combination with the strong base potassium *tert*-butoxide, the authors were able to synthesize pyrroles by reacting a secondary alcohol with an 1,2-amino alcohol. A broad range of pyrrole derivatives, most of which had not been reported before, could be synthesized because of the good commercial availability of derivatives of the starting compounds.[49] Mechanistic studies indicate that the alcohol is dehydrogenated and forms imine **I** with the amino alcohol. This intermediate undergoes another dehydrogenation step to intermediate **II**. A subsequent condensation and hydride shift form the pyrrole product.[9,49–51] Shortly after, MILSTEIN and co-workers reported **Ru-2** as a precatalyst for the same reaction.[50] The ruthenium catalyst performed the reaction at a more advantageous alcohol to amino alcohol ratio (Ru: 1:1; Ir: 2:1), albeit at higher catalyst loadings (Ru: 0.5 mol%; Ir: 0.03 to 0.5 mol%). The use of excess secondary alcohol was necessary for **Ir-1** to avoid pyrazine formation through homo-coupling of amino alcohols.[52] Applying a similar concept, SAITO and co-workers showed that **Ru-3** catalyzed the pyrrole synthesis starting from ketones instead of alcohols with only catalytic amounts of KO*t*Bu.[53] A related procedure for pyrrole synthesis was used by BELLER and co-workers, which involved the reaction of *in-situ* generated imine/enamine and 1,2-diols (Scheme 3.4c). This transformation was enabled by using a commercially available combination of a ruthenium source ($[Ru_3(CO)_{12}]$[54] or $[RuCl_2(p\text{-cymene})]$[55]) and Xantphos as the catalyst.

These initial developments demonstrated that noble metal complexes were suitable candidates for developing new reactions based on ADC. Indeed, multiple reactions were developed in the following years (Scheme 3.5), such as the pyridine synthesis by MICHLIK and KEMPE (Scheme 3.5a). They expanded the pyrrole synthesis (Scheme 3.4b) by using a 1,3-amino alcohol instead of a 1,2-amino alcohol to synthesize highly substituted pyridines.[56] The best results were obtained using **Ir-2**, which contained an electron-withdrawing CF_3 group in the ligand backbone. The MILSTEIN group showed that **Ru-2** is also able to mediate the pyridine synthesis (Scheme 3.5a) and extended the synthetic scope to quinolines (Scheme 3.5b) by using 2-aminobenzyl alcohol. This represents the first example of an acceptorless FRIEDLÄNDER-type[57] quinoline synthesis.[58] Subsequent work by KEMPE and co-workers introduced **Ir-3** as a suitable precatalyst for quinoline synthesis.[59] Recent advances in pyridine synthesis allowed the use of N-monosubstituted 1,2-amino alcohols in combination with 1,3-amino alcohols and **Ir-2** to produce 3-aminopyridines in excellent yields (Scheme 3.5c).[60] In 1991, WATANABE and co-workers introduced $[RuCl_2(PPh3)_3]$ as the precatalyst for benzimidazole synthesis (Scheme 3.5d), albeit at a disadvantageous reaction temperature of 215 °C.[61] The pyridine-based iridium precatalyst **Ir-4** enabled the synthesis of benzimidazoles (and related quinoxalines) at much lower temperatures (110 °C and 90 °C, respectively).[62] In 2015, DEIBL and KEMPE developed a multicomponent pyrimidine synthesis starting from a secondary alcohol, a primary alcohol and amidine/guanidine using **Ir-2** (Scheme 3.5e), proving again how heteroaromatics can be obtained in a sustainable fashion.[63]



Scheme 3.5. Reaction development for the hydrogen-acceptor free synthesis of various N-heteroaromatic compounds by noble metal catalysts.

However, the ADC reactions in Scheme 3.5 were developed using expensive noble metal catalysts. Efforts to replace these noble metals by abundantly available base metals have been scarce. SORTAIS and DARCEL and co-workers[64] have demonstrated the iron (**Fe-5**) catalyzed synthesis of quinolines and ZHANG and co-workers[65] reported the cobalt (**Co-1**) catalyzed reaction, respectively (Scheme 3.6a). The base metal catalyzed, CRABTREE-type synthesis of pyrroles (Scheme 3.4a) was achieved by MILSTEIN and co-workers in 2016 using pyridine-based **Co-4** as precatalyst (Scheme 3.6b).[66] **Co-4** was activated *in-situ* by reduction to (P,N,NH)-Co^{I}Cl using NaHBEt$_3$.[66]

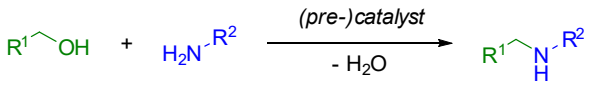


Scheme 3.6. Advancements in base metal catalyzed synthesis of N-heteroaromatics by ADC.

The synthesis of pyrroles has served as a milestone in the development of reactions based on ADC of alcohols and amines/amino alcohols. Chapter 6 of this thesis will describe the first base metal catalyst based on manganese that effectively mediates pyrrole synthesis using alcohols and 1,2-amino alcohols. This demonstrates how ADC reactions can be catalyzed by base metal catalysts under sustainable conditions. While working on this topic, the groups of KIRCHNER[67] and KEMPE[68] reported the manganese-catalyzed synthesis of quinolines (Scheme 3.6a) and pyrimidines (Scheme 3.6c). The activity and selectivity of these base metal catalysts may lead to noble metal catalysts becoming obsolete for future reaction development efforts.

3.4. Borrowing Hydrogen / Hydrogen Autotransfer (BH/HA)

In Borrowing Hydrogen / Hydrogen Autotransfer (BH/HA) catalysis, dehydrogenation and hydrogenation are part of the catalytic cycle; thus, hydrogen is not released but transferred to an unsaturated intermediate compound (Scheme 3.1b, page 10). The procedure therefore allows the synthesis of saturated compounds. Similar to the synthesis of imines by ADC in the previous section, the condensation of the carbonyl intermediate with an amine is the simplest reaction. It leads to valuable alkylated amines as products (Scheme 3.7) since the intermediate imine gets hydrogenated by the catalyst. Compared to more traditional routes (Scheme 3.1a, page 10), this has the added benefit that monoalkylated amines can be obtained selectively.



Scheme 3.7. Alkylation of amines with alcohols using Borrowing Hydrogen / Hydrogen Autotransfer (BH/HA).

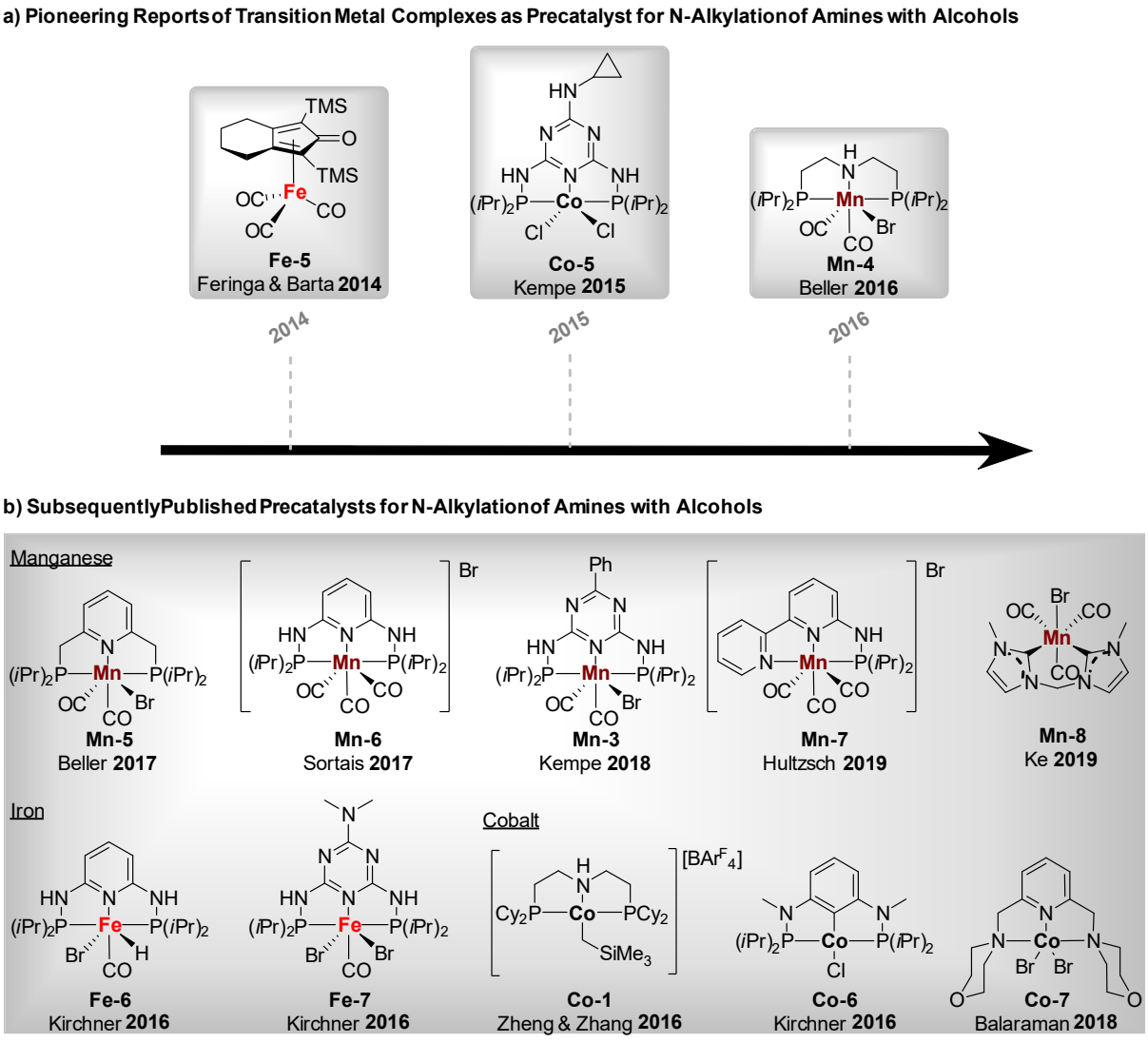
The synthesis of alkylated amines using alcohols as alkylating agents was described as early as 1932 by WINANS and ADKINS, where a heterogeneous nickel catalyst was used.[69] The first homogeneous catalysts were introduced by the groups of GRIGG[70] ([RhH(PPh$_3$)$_4$]) and WATANABE[71] ([RuCl$_2$(PPh$_3$)$_3$]) and since then a plethora of noble metal catalysts have been published.[72–75] In recent years, the aforementioned problems of noble metals (Chapter 3, Section 1) in combination with the idea that 3d-metals can show different or even superior reactivity and selectivity, led to the development of numerous base metal catalysts. Significant developments have been achieved using iron, cobalt, and manganese as catalysts.[76] Pioneering reports on the use of each of those metals are shown in the timeline in Scheme 3.8.

In 2014, FERINGA and BARTA have demonstrated that KNÖLKER'S iron complex **Fe-1** efficiently mediates the N-alkylation of various primary and secondary amines.[77] Primary amines could be doubly alkylated by diols to form the corresponding heterocyclic amines. The catalytically active iron complex **Fe-1** (Scheme 3.2) was formed *in-situ* from the tricarbonyl complex **Fe-5** (Scheme 3.8) by the oxidation of one CO ligand with trimethylamine oxide (Me$_3$NO) and subsequent reaction with an alcohol. Considerable work on the use of KNÖLKER'S iron complex (or derivatives thereof) has been contributed by the groups of ZHAO[78], BARTA[79], SUNDARARAJU[80] and WILLS[81]. KIRCHNER and co-workers used pyridine- and triazine-based iron pincer-complexes **Fe-6**[82] and **Fe-7**[83], respectively (Scheme 3.8). Compared to triazine-based **Fe-7**, pyridine-based pincer complexes required higher temperatures for catalysis to occur efficiently (140 °C vs 80 °C) but did not require base (*cf.* excess KO*t*Bu required for **Fe-7**).

In 2015, the KEMPE group introduced the first cobalt catalyst for the N-alkylation of aromatic amines using **Co-5** (Scheme 3.8).[84] ZHENG and ZHANG and co-workers used HANSON'S cobalt complex **Co-1** to alkylate aromatic and aliphatic amines.[85] The KIRCHNER group demonstrated that a P,C,P-Co^{II} complex **Co-6** (Scheme 3.8) was catalytically active as well, and showed similar selectivity to **Co-5**.[86] BALARAMAN and co-workers demonstrated that phosphine-free **Co-7** was catalytically active, albeit at high temperatures (150 °C).[87]

In 2016, BELLER and co-workers showed that **Mn-4**, which was first introduced for the hydrogenation of C=O and C≡N bonds[88], was a viable catalyst for the N-alkylation of aromatic

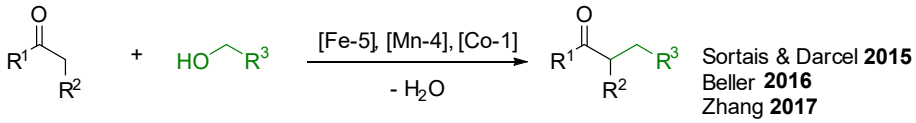
amines.[89] Following this success, catalytic activity of manganese complexes in BH/HA reactions, particularly in N-alkylation of amines, was further explored by multiple groups. The groups of BELLER[90] and SORTAIS[91] used **Mn-5** and **Mn-6**, respectively, for N-methylation of amines using methanol as the alkylating agent. BALARAMAN and co-workers found that combining [$MnBr(CO)_5$] and a simple triamine ligand [$(Me_2N(CH_2)_3)_2NH$] *in-situ* can be used to gain catalytic activity for the N-alkylation of aromatic amines.[92] Catalysts that are able to perform under mild reaction conditions were developed by the groups of HULTZSCH[93] (**Mn-7**, 0.5 mol%, 60 °C) and KE[94] (**Mn-8**, 1.5 mol%, room temperature; Scheme 3.8). Novel selectivity was observed by the KEMPE group with **Mn-3**, where the reaction path was determined by the base[95]. When **Mn-3** was used with NaO*t*Bu, imines were obtained through an ADC process. In contrast, using the same precatalyst in combination with KO*t*Bu yielded amines selectively. This was attributed to kinetic differences in the last hydrogenation step caused by the alkali metal ion.[95,96]



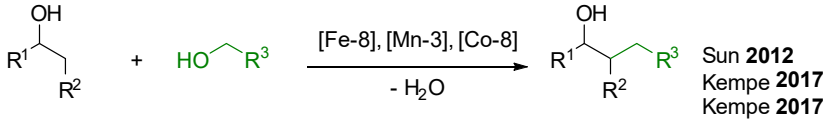
Scheme 3.8. a) First reports of iron, cobalt, and manganese precatalysts for the N-alkylation of amines using alcohols; b) Subsequent work describing base-metal precatalysts for this reaction.

Further applications of the BH/HA methodology using base metal catalysts include the alkylation of various other substrates (Scheme 3.9). SORTAIS and DARCEL were the first to show that KNÖLKER'S iron complex (generated *in-situ* from **Fe-5**) can be used for the α-alkylation of ketones (Scheme 3.9a).[64] BELLER and co-workers also successfully applied their manganese precatalyst **Mn-4** to this reaction.[97] ZHANG and co-workers later showed that HANSON'S cobalt complex **Co-1** also catalyzes the reaction.[65] The β-alkylation of secondary alcohols (Scheme 3.9b) with a base metal catalyst was described for the first time by SUN and co-workers in 2012 using ferrocenecarboxaldehyde.[98] More active catalysts based on **Mn-3**[68] and **Co-8**[99] were developed by the KEMPE group. Precatalyst **Co-8** was previously introduced in the alkylation of esters, alongside **Co-9** for the alkylation of amides (Scheme 3.9c).[100] MILSTEIN and co-workers developed a new synthetic concept incorporating both ADC and BH/HA in the same reaction, which consists of the parallel N-alkylation and N-alkenylation of hydrazine (Scheme 3.9d) using the bipyridine based **Mn-9**.[101]

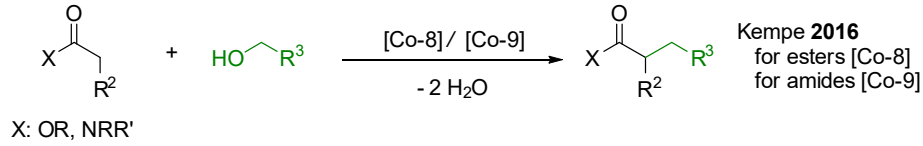
a) Alkylation of Ketones by Primary Alcohols



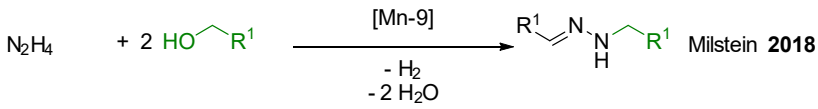
b) Alkylation of Secondary Alcohols by Primary Alcohols

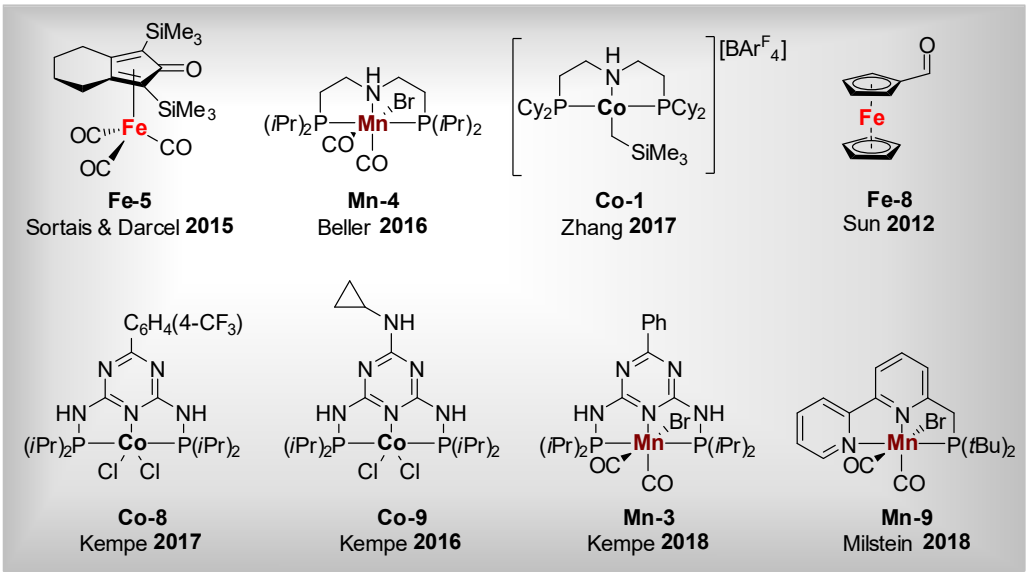


c) Alkylation of Amides/Esters by Primary Alcohols



d) Alkylation of Hydrazone Intermediate





Scheme 3.9. Application of the BH/HA methodology to the alkylation of various substrate classes

The applications discussed in this section show the potential value of discovering new BH/HA-catalysts. In Chapter 7 of this work, chromium-based catalysts for the N-alkylation of amines are introduced. These complexes exhibited unexpected activity and selectivity under catalytic conditions, making Cr-based precatalysts a viable choice for future applications in the BH/HA catalysis field.

3.5. References

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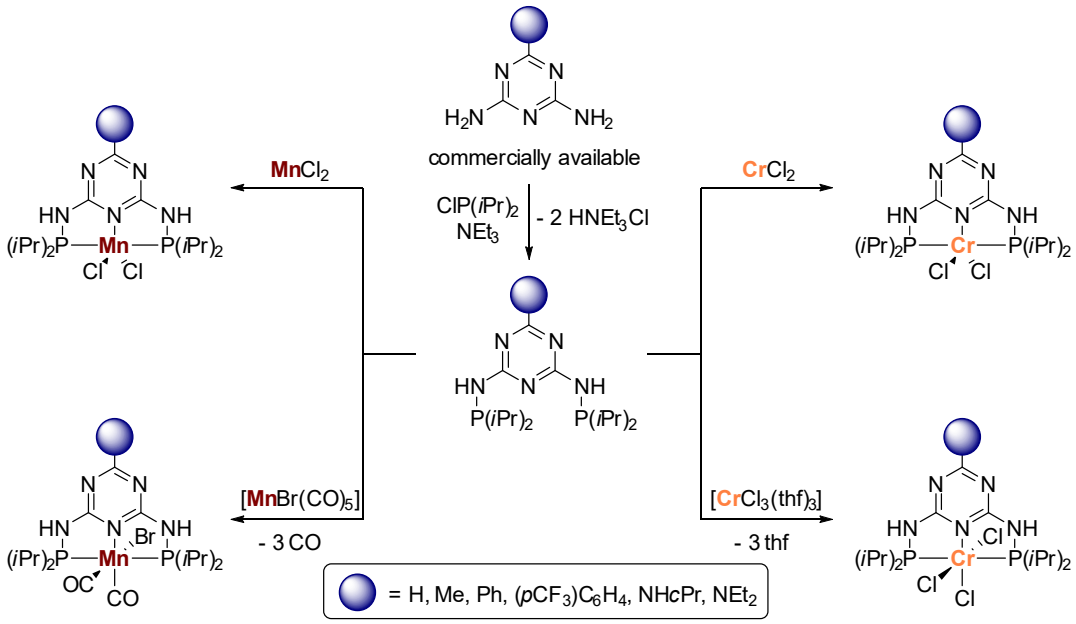
4. Overview of Thesis Results

4.1. Synopsis

This thesis consists of three chapters that introduce manganese and chromium complexes as catalysts for (de-)hydrogenative transformations. The complexes are based on P,N,P ligands that are derived from commercially available diamino-*s*-triazines (Scheme 4.1).

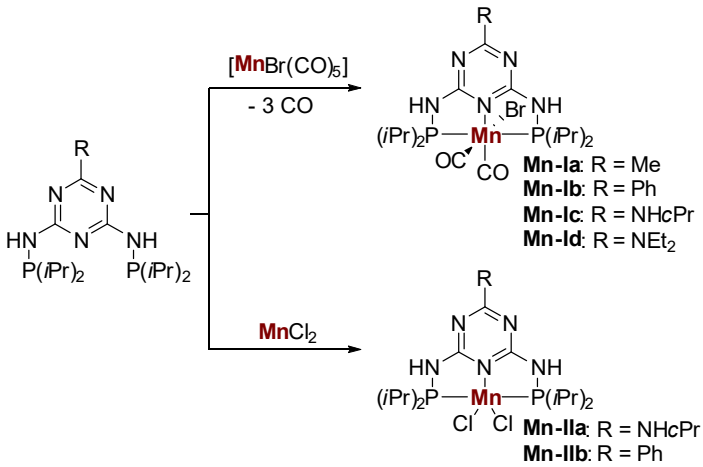
The Mn^{II} and Cr^{II} precatalysts were synthesized from the respective metal chlorides, whereas Mn^{I} complexes have been prepared by elimination of CO from manganese pentacarbonyl bromide [$MnBr(CO)_5$] and Cr^{III} complexes were obtained from the reactions of the ligand with [$CrCl_3(thf)_3$]. The complexes have been analyzed by NMR and IR, the purity was confirmed by elemental analysis and the proposed structures were confirmed by X-Ray analysis for a representative set of the precatalysts. The manganese complexes have then been used as precatalysts for the hydrogenation of C=O bonds and the acceptorless hydrogenative condensation to form pyrroles. The chromium complexes have been applied as precatalysts in Borrowing Hydrogen / Hydrogen Autotransfer reactions, specifically for the N-alkylation of amines with alcohols.



Scheme 4.1. Synthesis of P,N,P ligand-stabilized complexes used in this work.

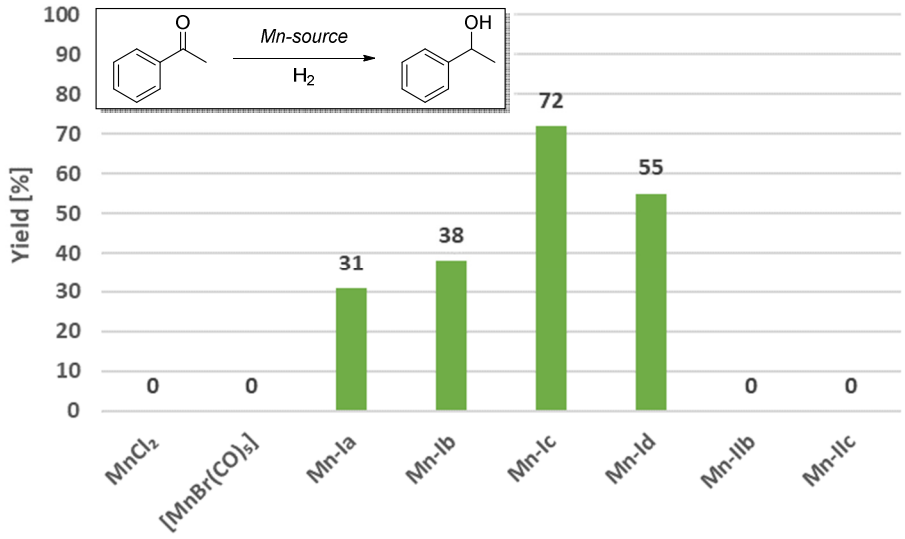
4.1.1. Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State

Despite its abundance, manganese traditionally received no attention in C=O bond hydrogenation catalyst design. The development of catalysts based on Mn would be highly advantageous because it is the third most abundant transition metal in earth's upper crust. To find an active catalyst, a representative library of manganese complexes was prepared. Firstly, manganese complexes based on $MnCl_2$ (**Mn-IIa** and **Mn-IIb**) were synthesized by heating a solution of corresponding P,N,P ligand with $MnCl_2$ in THF at 55 °C for 20 hours. The complexes were isolated by filtration followed by removal of the solvent under reduced pressure and were obtained as analytically pure solids. Next, a series of Mn^I complexes was obtained by refluxing a mixture of corresponding ligand, $[MnBr(CO)_5]$ and toluene overnight and collecting the resulting precipitate by filtration (Scheme 4.2).



Scheme 4.2. Synthesis of the manganese compounds investigated for C=O bond hydrogenation activity.

After successful isolation and analysis of the Mn compounds, their catalytic performance in the hydrogenation of carbonyl bonds was evaluated using the hydrogenation of acetophenone as a model reaction (Scheme 4.3). Manganese salts ($MnCl_2$ and $[MnBr(CO)_5]$) did not catalyze the reaction. Similarly, Mn^{II} complexes were inactive as well, even under more drastic conditions. Mn^I compounds showed significant activity, which increased for electron donating substituents at the triazine core of the Mn complexes (Scheme 4.3).



Scheme 4.3. Activity of manganese compounds in the hydrogenation of acetophenone. Reaction conditions: acetophenone (3 mmol), precatalyst (1 µmol, 0.1 mol%), KO*t*Bu (10 µmol, 1 mol%), toluene (2 mL), H_2 (20 bar), 60 °C, 4 h; for Mn^{II}: acetophenone (1 mmol), precatalyst (50 µmol, 5 mol %), KO*t*Bu (1 mmol), toluene (2 mL), H_2 (60 bar), 60 °C, 16 hours.

Since **Mn-Ic** gave the most active catalyst system, its structure was confirmed by XRD. Crystals of **Mn-Ic**, suitable for X-Ray diffraction analysis could be obtained by slow evaporation of a solution of **Mn-Ic** in benzene / *n*-hexane. The P,N,P ligand is coordinated in the expected meridional manner, while two carbonyl ligands (*cis* to each other) and a bromide ligand complete the slightly distorted octahedral structure of **Mn-Ic**. **Mn-IIb** was likewise crystallized and analyzed by XRD and showed a distorted tetragonal pyramidal structure around the manganese center (Figure 4.1).

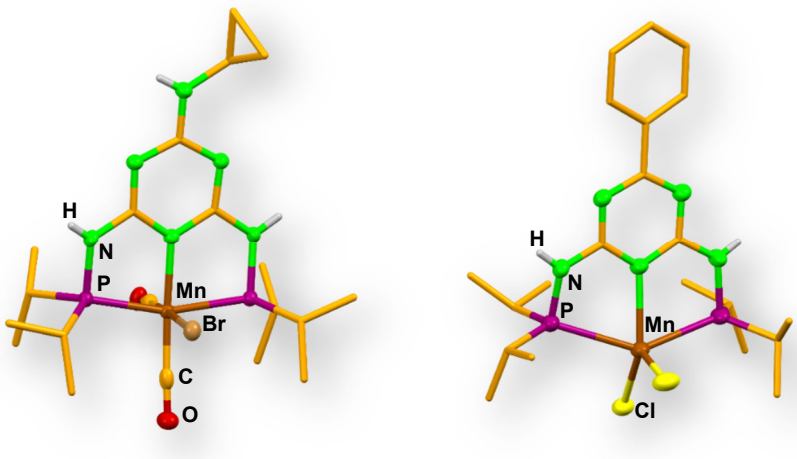
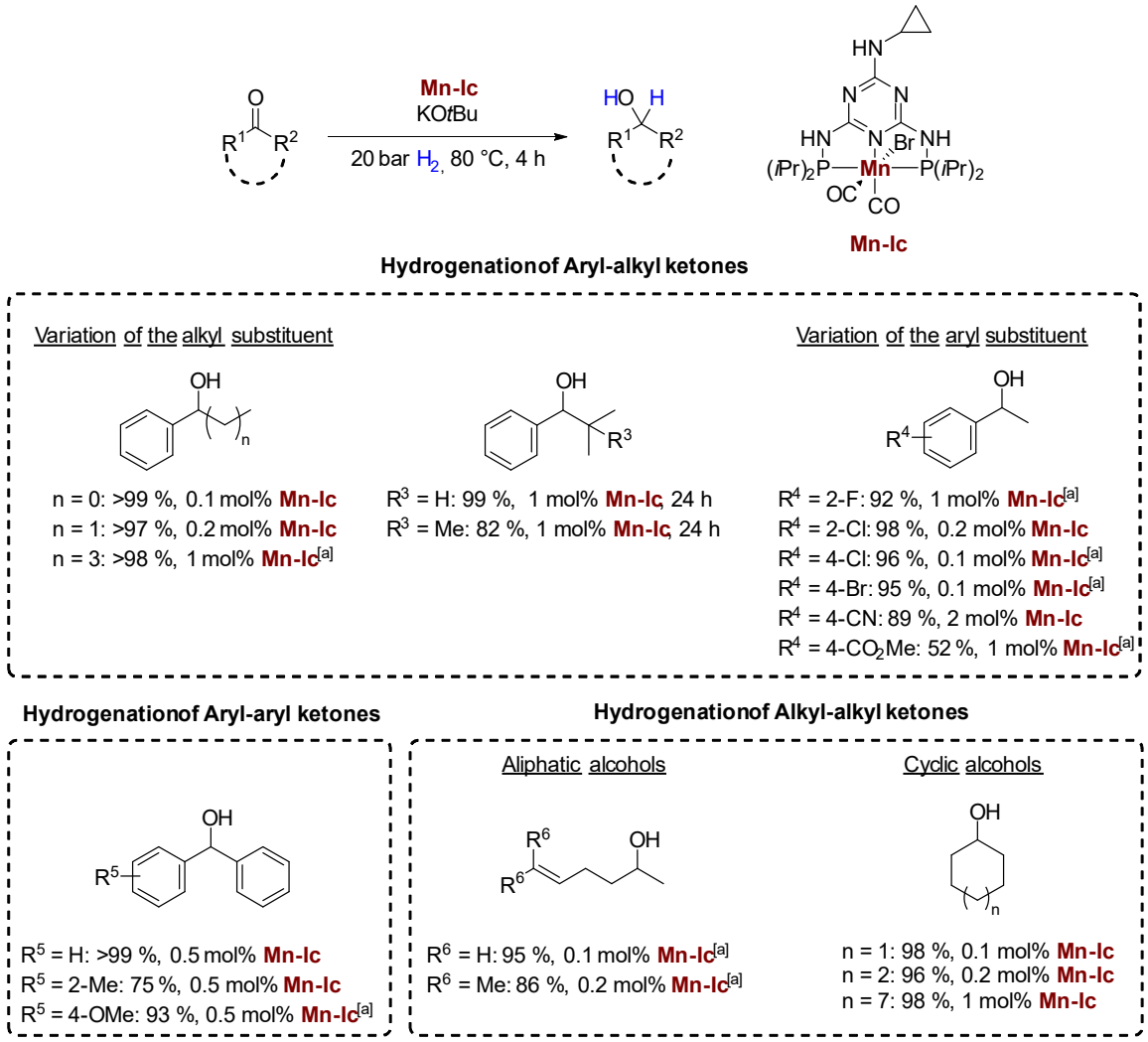


Figure 4.1. Molecular structure of **Mn-Ic** (left) and **Mn-IIb** (right). Solvent molecules and C*H* atoms omitted for clarity; thermal ellipsoids set at 50 % probability.

The reaction conditions were optimized regarding solvent, base, and base loading and finally the temperature and the reaction time were chosen to yield full conversion of acetophenone. The final reaction conditions were as follows: 0.1 mol% of **Mn-Ic**, 1 mol% of KO*t*Bu (10 equivalents with respect to the precatalyst), 3 mmol acetophenone, 1.5 mL of toluene and 20 bar H_2. The optimal reaction temperature was set at 80 °C and the reaction finished within 4 hours. With these conditions at hand, the addressable product scope was investigated by subjecting a variety of ketones to hydrogenation catalysis (Scheme 4.4).



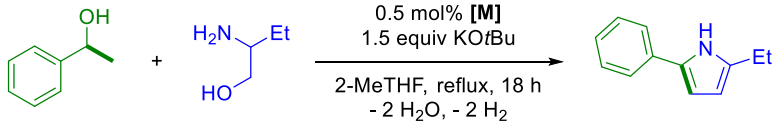
Scheme 4.4 Selected examples of the product scope for manganese-catalyzed C=O bond hydrogenation. Yields determined by GC analysis using *n*-dodecane as standard. [a]: Yield of isolated product.

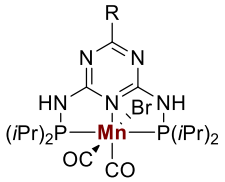
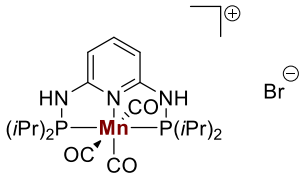
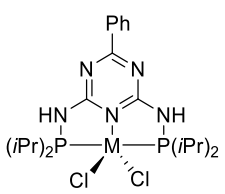
4.1.2. Manganese-Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols

N-Heterocycles are a privileged class of compounds in chemistry due to their multitude of uses in everything from commodity chemicals to pharmaceuticals, materials, and pesticides. Recently, the KEMPE group introduced an iridium-based catalyst for the sustainable synthesis of pyrroles from abundantly available starting materials, namely alcohols and 1,2-amino alcohols (see scheme in Table 4.1). An even more sustainable approach would avoid the use of rare and expensive iridium. Since the manganese complexes developed in this work showed promising results in hydrogenation catalysis, they were investigated as catalysts in the acceptorless dehydrogenative condensation reaction, which involves two dehydrogenation steps (*i.e.* the reverse reaction to the hydrogenation presented in the previous chapter) as key elements of the reaction.

The cheapest manganese complex, **Mn-Ic** (Table 4.1), was used to optimize relevant reaction parameters, like base, solvent, base amount, and reactant ratio. The optimal conditions were with KO*t*Bu (1.5 equiv) as the base and 2-methyltetrahydrofuran (2-MeTHF) as the solvent. The secondary alcohol was used in two-fold excess and the mixture was refluxed for 18 hours. By comparing the rate of consumption of secondary alcohol *versus* the amino alcohol, it could

Table 4.1. Precatalyst screening for the synthesis of pyrroles.

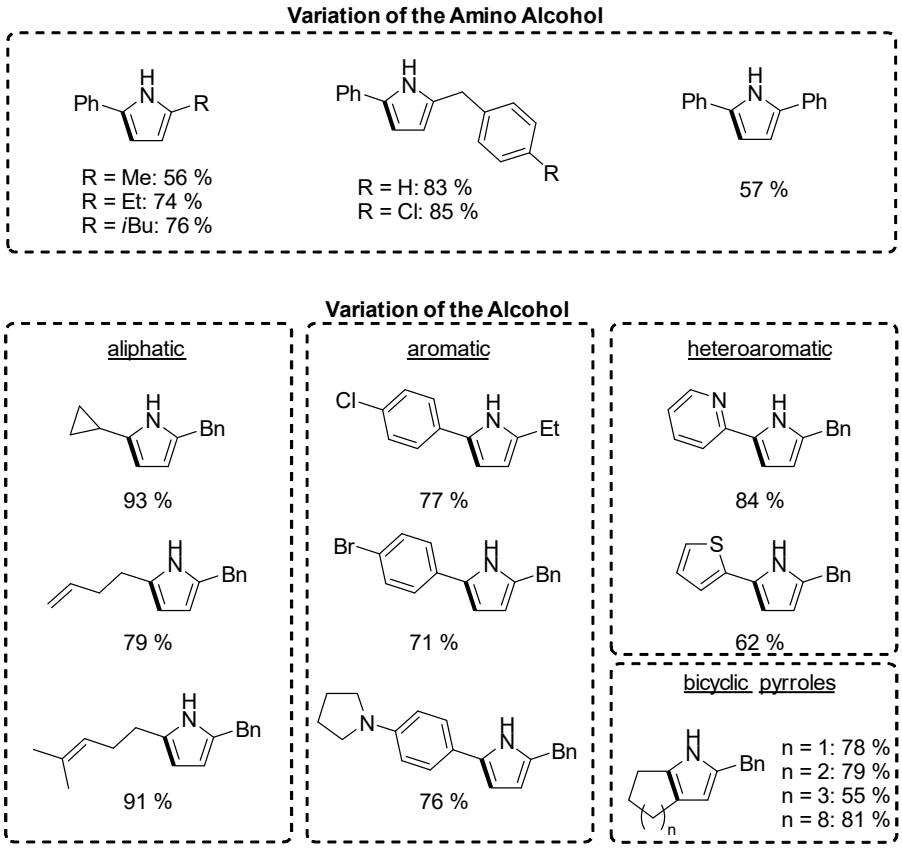


Entry	Precatalyst		Yield [%]
1		R = H	**Mn-Ia** 60
2		R = Me	**Mn-Ib** 58
3		R = Ph	**Mn-Ic** 69
4		R = (4-CF_3)C_6H_4	**Mn-Id** 49
5		R = NH*c*Pr	**Mn-Ie** 37
6		R = NEt_2	**Mn-If** 45
7			32
8		M = Mn	0
9		M = Fe	0
10		M = Co	0

be shown that the use of an excess of secondary alcohol was beneficial to avoid side reactions of the amino alcohol. Lastly, to find the most active catalyst, a library of precatalysts was tested for their activity (Table 4.1).

Notably, **Mn-Ic** performed best and neither electron donating nor electron withdrawing substituents at the triazine ligands improved the product yield. It was noted that **Mn-Ia** performed similarly well and was thus considered an appropriate alternative for more challenging products when evaluating the substrate scope.

Using these optimized reaction conditions, a total of 29 variously substituted 1*H*-pyrroles was synthesized (see Scheme 4.5 for selected examples). The amino alcohol could be varied to obtain pyrroles that incorporated aliphatic, benzylic, and aromatic substituents. Secondary alcohols could be widely varied as well and pyrroles containing functional groups (*e.g.* double bonds, aryl chlorides) and heteroaromatics (pyridine and thiophene) were obtained in adequate yields. For some compounds, slightly better yields could be obtained when unsubstituted-triazine based catalyst **Mn-Ia** was used. Interestingly, a secondary alcohol with an aryl bromide could also be converted to synthetically useful amounts of product. However, sodium *tert*-butoxide had to be used as base to avoid hydro-debromination and the catalyst-loading and reaction time had to be adjusted.

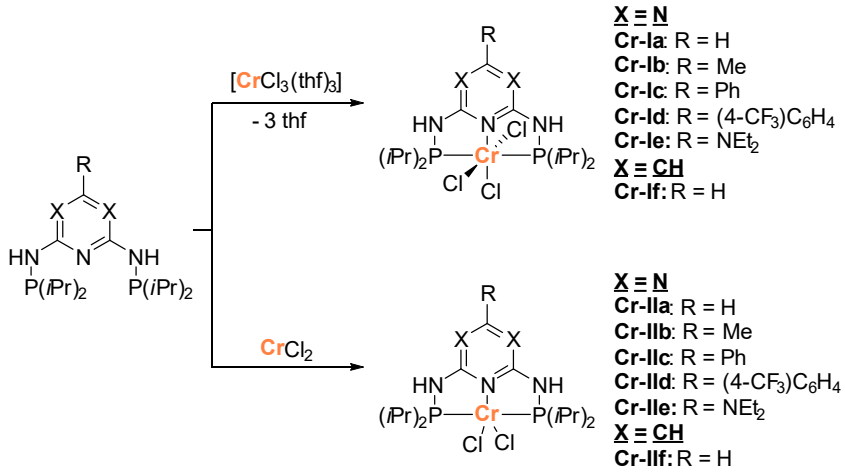


Scheme 4.5. Substrate scope for the manganese-catalyzed synthesis of pyrroles (selected examples). Yields of isolated products are given.

4.1.3. Chromium-Catalyzed Alkylation of Amines by Alcohols

The exploration of 3d-metals in (de-)hydrogenation catalysis is a vivid field that put forth a wide range of catalysts. These compounds show distinct selectivity patterns associated with the specific metal and broadening the scope of potential 3d-metal catalysts would increase the toolbox available to chemists for the selective synthesis of target compounds. One metal that was not yet used as a catalyst for BH/HA is chromium. This work describes the development of Cr^{II} and Cr^{III} coordination compounds that were then applied as catalysts in the N-alkylation of aromatic amines, an example for a reaction that involves both a dehydrogenation and a hydrogenation step.

First, a library of chromium complexes was synthesized using the established P,N,P ligands. Cr^{III} compounds were prepared by heating a mixture of the corresponding ligand with $[CrCl_3(thf)_3]$ and recrystallization. For the synthesis of the analogous Cr^{II} complexes, $CrCl_2$ was reacted with the corresponding ligand and **Cr-IIa-f** were isolated by precipitation and consecutive washing steps.



Scheme 4.6. Library of Cr complexes used in this study.

XRD analysis of **Cr-Id** and **Cr-IId** (Figure 4.2) confirmed the expected molecular structures, namely an octahedral coordination of Cr in **Cr-Id** by the meridionally coordinating P,N,P ligand and three chloride ligands and a distorted tetragonal pyramidal coordination of Cr in **Cr-IId** with two chloride substituents, respectively.

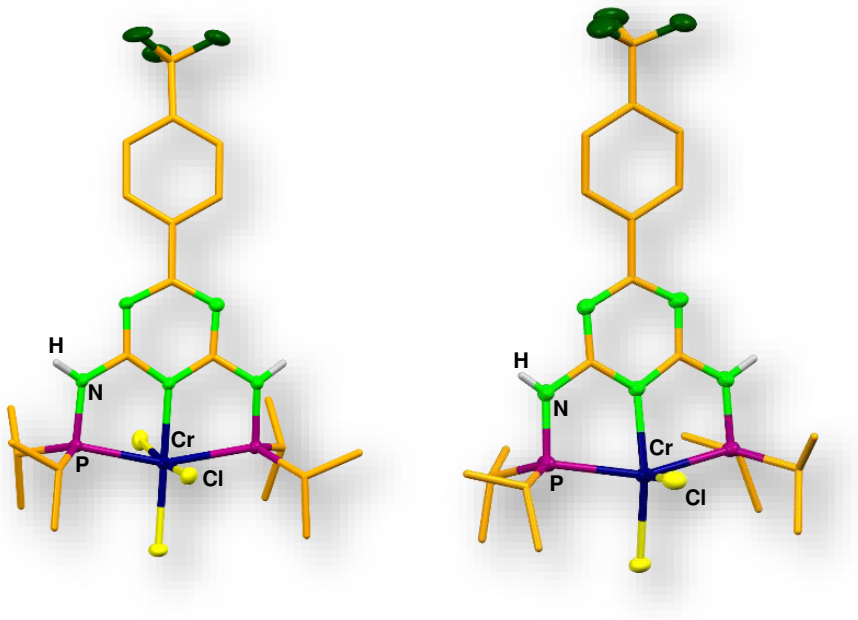
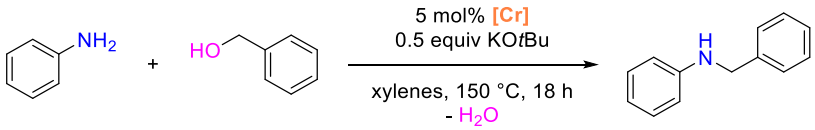


Figure 4.2. Molecular structure of **Cr-Id** (left) and **Cr-IId** (right). Solvent molecules and C*H* atoms omitted for clarity; thermal ellipsoids set at 50 % probability.

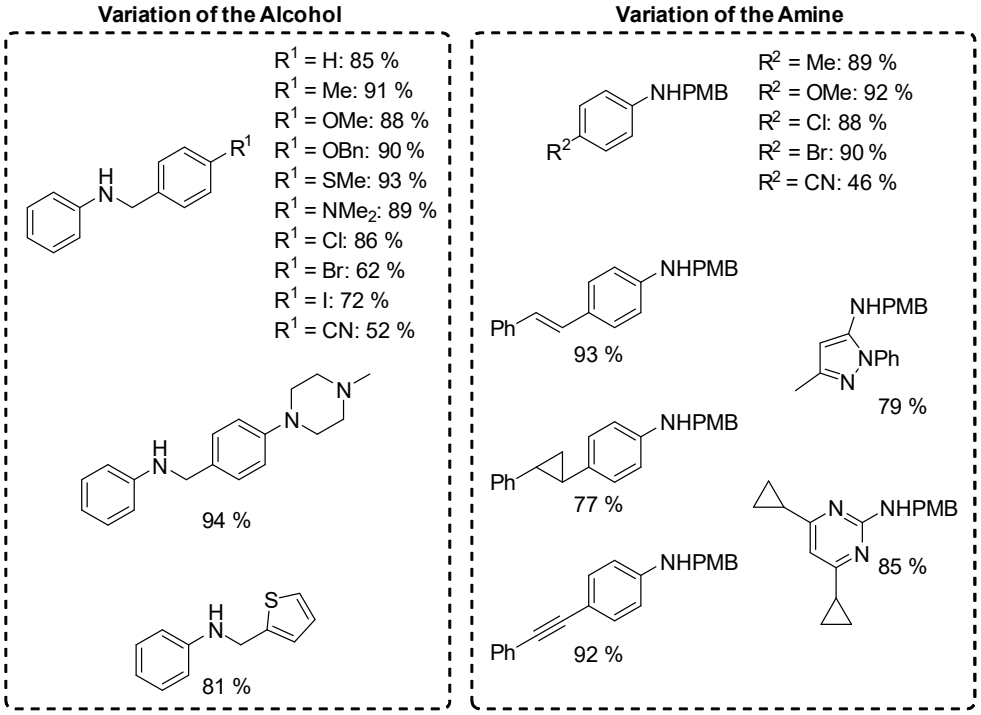
The complexes were then applied as precatalysts in the alkylation of aniline by benzyl alcohol (see scheme in Table 4.2). Initially, the highest conversion was observed when **Cr-IId** was employed as precatalyst. However, contrary to when **Cr-Id** is used, the yield of product could not be increased any further by optimization of reaction parameters.

Table 4.2. Precatalyst screening for the N-alkylation of aniline using a library of Cr complexes. [a]: after optimization of common reaction parameters.



Precatalyst	Yield [%]	Precatalyst	Yield [%]
Cr-Ia	21	**Cr-IIa**	23
Cr-Ib	24	**Cr-IIb**	35
Cr-Ic	29	**Cr-IIc**	22
Cr-Id	52 (97[a])	**Cr-IId**	58
Cr-Ie	18	**Cr-IIe**	31
Cr-If	15	**Cr-IIf**	1

Using the optimized reaction conditions for **Cr-Id** (3 mol% **Cr-Id**, 50 mol% KO*t*Bu, 1.2 equiv alcohol, 1 equiv amine, 0.5 mL 1,4-dioxane, 150 °C oil bath, 18 hours), a total of 35 differently substituted products were obtained in reasonable to excellent yields (see Scheme 4.7 for selected examples). A wide range of functional groups and heterocyclic compounds was found to be compatible.



Scheme 4.7. Substrate scope for N-alkylation of aromatic amines by Cr catalysis (selected examples). PMB: *para*-Methoxybenzyl. Yields of isolated products are given.

4.2. Individual Contributions to Joint Publications

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

Chapter 5

This work was published in 'Angewandte Chemie International Edition' (*Angew. Chem. Int. Ed.* **2016**, *55*, 11806–11809) with the title "Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State".

Authors: Kallmeier, Fabian; Irrgang, Torsten; Dietel, Thomas; Kempe, Rhett*

I conducted the experiments and synthesized and characterized all compounds as presented in the final publication. Thomas Dietel performed the X-Ray analysis and solved the structure of compound **3b** in the manuscript. Torsten Irrgang and Rhett Kempe supervised the work, were involved in scientific discussion, and co-wrote the manuscript with me. Torsten Irrgang and Rhett Kempe co-wrote the translation of the manuscript, which has been published in 'Angewandte Chemie' (*Angew. Chem.* **2016**, *128*, 11984–11988 with the title "Hochaktive und selektive Mangankatalysatoren zur Hydrierung von C=O-Bindungen - die Bedeutung des mehrzähnigen Liganden, der Coliganden und der Oxidationsstufe").

Chapter 6

This work was published in 'Angewandte Chemie International Edition' (*Angew. Chem. Int. Ed.* **2017**, *56*, 7261–7265) with the title "Manganese-Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols".

Authors: Kallmeier, Fabian; Dudziec, Beata; Irrgang, Torsten; Kempe, Rhett*

I conceived the concept, performed the synthesis of starting materials, and conducted the experiments as presented in the final publication. Beata Dudziec conducted the synthesis, purification, and analysis of various products. The help of Martin Schlagbauer in initial reaction development is greatly acknowledged. The help of Thomas Dietel in performing the X-Ray analysis and solving the structure of compound **4c*H** in the manuscript is greatly acknowledged. Torsten Irrgang and Rhett Kempe supervised the work, were involved in scientific discussion, and co-wrote the manuscript with me. Torsten Irrgang and Rhett Kempe co-wrote the translation of the manuscript, which has been published in 'Angewandte Chemie' (*Angew. Chem.* **2017**, *129*, 7367–7371 with the title "Mangan-katalysierte nachhaltige Synthese von Pyrrolen aus Alkoholen und Aminoalkoholen").

Chapter 7

This work was published in 'Angewandte Chemie International Edition' (*Angew. Chem. Int. Ed.* **2020**, *59*, 11789–11793.) with the title "Chromium-Catalyzed Alkylation of Amines by Alcohols".

Authors: Kallmeier, Fabian; Fertig, Robin; Irrgang, Torsten; Kempe, Rhett*

I conceived the concept, performed the synthesis of starting materials, and conducted the experiments as presented in the final publication. Robin Fertig performed the X-Ray analysis and solved the structure of compound **Cr-Id** in the manuscript. The help of Hannah Kurz in performing magnetic measurements on **Cr-Id** and **Cr-IId** in the manuscript is greatly acknowledged. Torsten Irrgang and Rhett Kempe supervised the work, were involved in scientific discussion, and co-wrote the manuscript with me.

5. Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State

Kallmeier, F.; Irrgang, T.; Dietel, T.; Kempe, R.*

Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State.

Angew. Chem. Int. Ed. **2016**, *55* (39), 11806–11809

DOI: 10.1002/anie.201606218

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Hydrogenation Catalysts

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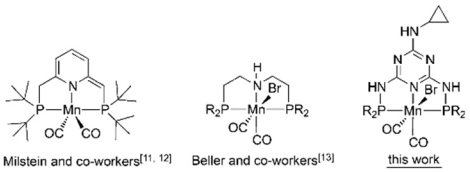
German Edition: DOI: 10.1002/ange.201606218

Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State

*Fabian Kallmeier, Torsten Irrgang, Thomas Dietel, and Rhett Kempe**

Abstract: *The replacement of expensive noble metals by earth-abundant transition metals is a central topic in catalysis. Herein, we introduce a highly active and selective homogeneous manganese-based C=O bond hydrogenation catalyst. Our catalyst has a broad substrate scope, it is able to hydrogenate aryl–alkyl, diaryl, dialkyl, and cycloalkyl ketones as well as aldehydes. A very good functional group tolerance including the quantitative and selective hydrogenation of a ketone in the presence of a non-shielded olefin is observed. In Mn hydrogenation catalysis, the combination of the multidentate ligand, the oxidation state of the metal, and the choice of the right ancillary ligand is crucial for high activity. This observation emphasizes an advantage and the importance of homogeneous catalysts in 3d-metal catalysis. For coordination compounds, fine-tuning of a complex coordination environment is easily accomplished in comparison to enzyme and/or heterogeneous catalysts.*

The hydrogenation of olefins, imines, and ketones or aldehydes is of high academic and industrial interest. Most of the successfully applied catalysts are based on expensive noble metals, such as Ru, Rh, Ir, Pd, and Pt. The low availability of such metals has stimulated a search for alternative catalysts based on transition metals with significantly higher concentration in the earth crust (base metals).[1] The key motivation for this shift of interest results from the need of the conservation of our elemental resources as a central issue of a more sustainable future. In addition, novel mechanistic pathways permitting new activity/selectivity patterns can be expected based on the different redox and magnetic properties of these metals.[2] The application of homogeneous hydrogenation catalysts is especially promising for the reduction of C=O bonds since a bifunctional mechanism involving the ligand can operate for efficient H_2 activation.[3] Recently, we discovered a highly active cobalt C=O bond hydrogenation catalyst stabilized by PN_5P ligands.[4–6] We have had successfully used such ligands to design iridium catalysts[7] and observed for Co, in contrast to Ir, that only very minor alterations of the catalyst structure strongly influenced the hydrogenation activity. Since PN_5P-ligands and the related PN_3P-ligands,[8] introduced by Haupt and co-workers[9] and intensively used by the Kirchner group in recent years,[10] are simple to vary, ligand or catalyst libraries can be used to identify catalytically active species. A base metal which has been overlooked in recent years with regard to catalytic reactions classically associated with noble metals is the third most abundant transition metal of the earth crust, namely manganese. Very recently, Milstein and co-workers introduced homogeneous Mn catalysts for the imine synthesis from alcohols and amines[11] as well as for alkylation chemistry (Scheme 1, left).[12]



Scheme 1. Recently developed manganese complexes able to catalyze reactions classically mediated by noble metals (left and middle) and the pre-catalyst described herein (right).

Herein, we report on the development of a highly active and selective Mn C=O bond hydrogenation catalyst. The pre-catalyst is easy to synthesize in two steps from commercially available starting materials with almost quantitative yield for both steps. In addition, the pre-catalyst is easy to activate by adding a catalytic amount of a metal base, such as KO^{t}Bu (Bu = butyl). The catalyst is active in the hydrogenation of aldehydes as well as aryl–alkyl, dialkyl, diaryl, and cycloalkyl ketones. In addition, functional groups, such as terminal olefins are tolerated. Most importantly, we show that the right choice of the PN_5P ligand, the right oxidation state of the metal, and the right kind and number of ancillary ligands are requirements for catalytic activity. Parallel to our work, Beller and co-workers introduced a Mn catalyst for C=O bond hydrogenation based on a different multidentate ligand (Scheme 1, middle).[13] To the best of our knowledge, this is the only other example of a Mn catalyst able to hydrogenate C=O bonds efficiently.[14] Our catalyst is 10-times more active than the Beller catalyst, operates under milder conditions, and gives quantitative conversion in significantly shorter reaction times.

We first synthesized a representative number of PN_5P-ligand stabilized manganese(II) dichlorido (**2a**,**b**) and manganese(I) bromido dicarbonyl (**3a**–**d**) complexes (Scheme 2).[15] X-ray crystal structure analysis of **2a** was performed to determine the molecular structure (see Sup-

[*] F. Kallmeier, Dr. T. Irrgang, T. Dietel, Prof. Dr. R. Kempe
Anorganische Chemie II—Katalysatordesign
Universität Bayreuth
95540 Bayreuth (Germany)
E-mail: kempe@uni-bayreuth.de

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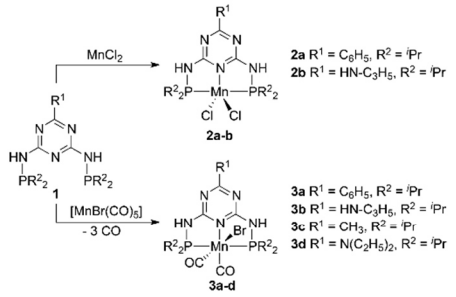
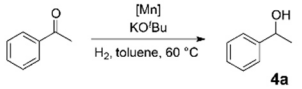


Scheme 2. Synthesis of novel Mn^{II} (**2a,b**) and Mn^{I} (**3a–d**) complexes.

Table 1: Hydrogenation of acetophenone with several Mn pre-catalysts.



Entry	Pre-catalyst	Yield[c] [%]	Entry	Pre-catalyst	Yield[c] [%]
1	**2a**[a]	0	5	**3c**[b]	31
2	**2b**[a]	0	6	**3d**[b]	55
3	**3a**[b]	38	7	$MnCl_2$	0
4	**3b**[b]	72	8	$[MnBr(CO)_5]$	0

Reaction conditions: [a] 1 mmol acetophenone, 5 mol% pre-catalyst, 100 mol% KO'Bu, 2 mL toluene, 60 bar H_2, 60 °C, 16 h. [b] 3 mmol acetophenone, 0.1 mol% pre-catalyst, 1 mol% KO'Bu, 2 mL toluene, 20 bar H_2, 60 °C, 4 h. [c] Determined by GC with dodecane as internal standard.

porting Information). Next, we investigated the hydrogenation of acetophenone to 1-phenylethanol **4a** (Table 1) as a suitable test reaction to find an active catalyst and optimal hydrogenation reaction conditions. No activity was observed using 5 mol% of **2a,b** in toluene, activated with an excess of KO'Bu, under 60 bar hydrogen pressure and at 60 °C (Table 1, entries 1–2). In contrast, the Mn^{I} bromide complexes **3a–d** were able to hydrogenate the model substrate after activation by a base. After finding an initial hydrogenation activity, with the catalyst based on **3b** being the most active one, we optimized the reaction conditions, such as base amount, pressure, temperature, and catalyst loading (see Supporting Information). The molecular structure of **3b** was confirmed by X-ray crystal structure analysis (XRD) because it gave the most active catalyst (Figure 1). XRD revealed a hexacoordinate Mn^{I} complex with a slightly distorted octahedral coordination. The PN_5P ligand acts as a neutral ligand, coordinating the Mn in a tridentate manner with a P1-Mn1-P2 angle of 162.17(6)°. The CO ligands are coordinated *cis* to each other with a C1-Mn1-C2 angle of 88.55(3)°. To our delight, 0.1 mol% of complex **3b** afforded 1-phenylethanol (**4a**) in quantitative yield (Table 2, entry 1) under relatively mild reaction conditions (80 °C, 20 bar H_2, 4 h). The mildest conditions used by Beller and co-workers to obtain quantitative conversion were 100 °C, 30 bar and 24 h with a catalyst loading of 1 mol%. Our catalyst hydrogenates under milder conditions, in significant shorter time, and with up to 10-times

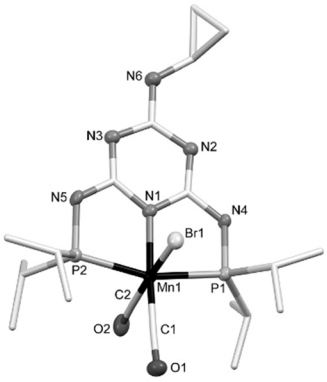
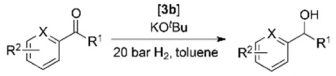


Figure 1. Molecular structure of **3b** is displayed with thermal ellipsoids set at 50% probability.[16] H atoms and one cocrystallized benzene molecule are omitted for clarity. Selected bond lengths [Å] and angles [°]: Mn1–P1 2.265(2), Mn1–P2 2.283(2), Mn1–N1 2.036(4), Mn1–Br1 2.577(1), Mn1–C1 1.800(6), Mn1–C2 1.759(6), P1–N4 1.708(4), P2–N5 1.713(5), C1–O1 1.112(8), C2–O2 1.143(7); P1-Mn1-P2 162.17(6), Mn1-P1-N4 99.67(2), Mn1-P2-N5 100.00(2), P2-Mn1-N1 80.52(1), P1-Mn1-N1 81.78(1), C1-Mn1-Br1 87.35(2), C2-Mn1-Br1 175.89(2), C1-Mn1-N1 174.18(2), C2-Mn1-N1 97.09(2), C1-Mn1-P1 96.75(2), C1-Mn1-P2 100.65(2), C2-Mn1-P1 90.96(2), C2-Mn1-P2 93.31(2), Br1-Mn1-N1 87.01(1).

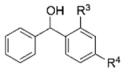
less catalyst loading. The pre-catalyst based on **2b** is completely inactive at these optimized conditions. Since the conditions were optimized for **3b**, we assigned the inactivity of **2b** also to the not optimal reaction conditions. A thorough investigation of the ketone hydrogenation ability of **2b** revealed no activity. Comparing **2b** and **3b**, we see two alterations, the oxidation state [manganese(I) versus (II)] and the presence of the ancillary carbonyl ligands. To see if **2b** becomes active in the +1 oxidation state, reduction of **2b** with one equivalent of potassium graphite was carried out and the corresponding complex was studied in the hydrogenation of the model substrate acetophenone. We could not identify any activity of this carbonyl ligand free "catalyst" and concluded that the combination of the oxidation state and the presence of the ancillary carbonyl ligands is beneficial or even a precondition for ketone hydrogenation activity. The catalytically active species can be formed by the reaction of **3b** with 1 equivalent KO'Bu to form a blue dicarbonyl complex, which reacts with H_2 to form a colorless carbonyl hydride complex.[10a]

Next, we explored the substrate scope applicable to this novel manganese-based hydrogenation catalyst. Starting from the acetophenone motif, we first varied the length (**4a–d**) and the branching (**4e,f**) of the alkyl chain. For increased chain length, the pre-catalyst concentration had to be gradually increased from 0.1 to 1 mol% to reach full conversion. The branched alcohol **4e** could only be obtained quantitatively by increasing the reaction time to 24 h, after which the even bulkier alcohol **4f** could also be obtained in high yields (82%, Table 2, entry 6). A series of 4′-substituted acetophenone derivatives (**4g–l**) were then subjected to hydrogenation,

Table 2: Hydrogenation of aryl–alkyl, diaryl carbonyl compounds and aldehydes.[a]



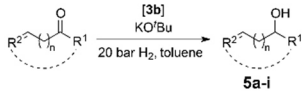
4a-u

Entry	Product		Cat. loading [%]	Yield[d] [%]
1	 R = CH_3	**4a**	0.1	>99
2	R = CH_2CH_3	**4b**	0.2	97
3	R = $(CH_2)_2CH_3$	**4c**	1	>99
4	R = $(CH_2)_3CH_3$	**4d**	1	>99 (98[c])
5	R = $CH(CH_3)_2$	**4e**	1[e]	99
6	R = $C(CH_3)_3$	**4f**	1[e]	82
7	 R = Cl	**4g**	0.1	97 (96[c])
8	R = Br	**4h**	0.1	97 (95[c])
9	R = OCH_3	**4i**	0.2	>99 (91[c])
10	R = CN	**4j**	2	89
11	R = C(O)OMe	**4k**	1	52[c]
12	R = CH_3	**4l**	0.2	>99
13	 R = Cl	**4m**	0.2	98
14	R = F	**4n**	1	>99 (92[c])
15		**4o**	0.5	>99 (92[c])
16	 R^3 = H, R^4 = H	**4p**	0.5	>99
17	R^3 = CH_3, R^4 = H	**4q**	0.5	75
18	R^3 = H, R^4 = CH_3	**4r**	0.5	>99
19	R^3 = H, R^4 = OCH_3	**4s**	0.5	>99 (93[c])
20	 R = H	**4t**	0.1[b]	>99
21	R = NO_2	**4u**	1	>99

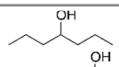
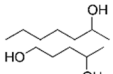
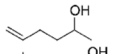
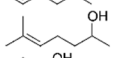
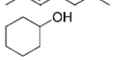
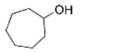
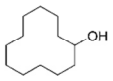
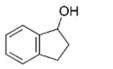
[a] Reaction conditions: 3 mmol substrate, pre-catalyst **3b**, KO^{t}Bu, 1.5 mL toluene, 20 bar H_2, 80 °C, 4 h. [b] 40 °C. [c] Yield of isolated product. [d] Determined by GC with dodecane as internal standard. [e] 24 h.

which were quantitatively hydrogenated under very low catalyst loadings. The 2′-substituted acetophenone derivatives (entries 13–14) could also be obtained quantitatively. Compared to acetophenone, the N-heterocyclic relative 2′-acetylpyridine required higher catalyst loadings to reach full conversion into **4o**, which is probably due to the poisoning of the manganese center by the pyridine moiety. The performance of the catalyst was further evaluated using a series of diaryl ketones (**4p–s**). Generally, higher catalyst loadings (0.5 mol %) were required to reach full conversion, but even the bulkier 2-methylbenzhydrol **4q** was obtained in high yields (75 %, Table 2, entry 17). These substrates could be readily reduced to the alcohols under mild conditions, and correspondingly benzaldehyde was hydrogenated to quantitatively yield benzyl alcohol at only 40 °C. To show the full potential of the catalyst system, the synthesis of **4h** (entry 8) was scaled up to a 45 mmol batch using otherwise unchanged parameters (see Supporting Information for details), still yielding 97 % of essentially pure **4h** after filtration over silica. Since the hydrogenation of various demanding ketones went smoothly, the generally more demanding substrate class of dialkyl ketones was investigated (Table 3). The alcohol **5a**

Table 3: Hydrogenation of dialkyl, and cycloalkyl carbonyl compounds.[a]



5a-i

Entry	Product		Cat. loading [%]	Yield[b] [%]
1		**5a**	0.5	>99
2		**5b**	0.2	95
3		**5c**	1	88
4		**5d**	0.1	>99 (95[c])
5		**5e**	0.2	98 (86[c])
6		**5f**	0.1	98
7		**5g**	0.2	96
8		**5h**	1	58
9		**5i**	1	97

[a] Reaction conditions: 3 mmol substrate, pre-catalyst **3b**, KO^{t}Bu, 1.5 mL toluene, 20 bar H_2, 80 °C, 4 h. [b] Determined by GC with dodecane as internal standard. [c] Yield of isolated product.

was obtained at a rather high pre-catalyst loading of 0.5 mol % most probably because of the position of the C=O bond. Ketones with better accessibility (**5b–e**) of the carbonyl function are reduced very efficiently (**5b**). Ketones bearing a C=C double bond were very selectively converted into the corresponding unsaturated alcohols (**5d,e**). Even a rather exposed unsubstituted double bond remained unharmed during the hydrogenation procedure, resulting in nearly quantitative isolation of **5d**. Lastly, cycloalkyl ketones with various ring sizes were subjected to hydrogenation (**5f–**

h). Cycloalkyl ketones with small ring sizes are herein more readily hydrogenated than ketones with larger ring systems, resulting in only 58% yield of **5h** despite the use of 1 mol% pre-catalyst. The five-membered ring of 1-indanone also required the higher than usual pre-catalyst loading of 1 mol%, but was quantitatively hydrogenated to the corresponding alcohol **5i**.

In summary, we introduced a highly active and easy to synthesize Mn based C=O bond hydrogenation catalyst. The easy modification of the used multidentate ligands makes the catalyst family attractive for fast catalyst identification. Manganese is the third most abundant transition metal in the Earth's crust and we developed a Mn catalyst, which hydrogenates various ketones quantitatively in 4 h with only 0.1 mol% catalyst loading. The substrate scope is broad since aryl–alkyl, diaryl, dialkyl, and cycloalkyl ketones can be hydrogenated smoothly. In addition, we see an impressive functional group tolerance. Hydrogenation of C=O bonds proceeds selectively in the presence of a non-shielded olefin, a nitrile, or a nitro group.

Most importantly, we feel that in Mn hydrogenation catalysis the combination of the multidentate ligand, the oxidation state of the metal, and the choice of the right ancillary ligand is crucial to give high activity. This observation emphasizes an advantage of homogeneous catalysis in the application of base metals as active sites. For coordination compounds, a fine-tuning of a complex coordination environment is easily accomplished in comparison to enzyme catalysis and/or heterogeneous catalysis.

Acknowledgements

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Keywords: alcohols · base metals · hydrogenation · manganese · PNP ligands

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[16] CCDC 1499551 (**2a**) and 1499552 (**3b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via Cambridge Crystallographic Data Centre.

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Supporting Information

Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State

*Fabian Kallmeier, Torsten Irrgang, Thomas Dietel, and Rhett Kempe**

Table of Contents

General

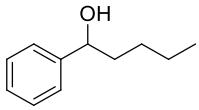
All reactions and manipulations with air sensitive compounds were performed under dry argon (Ar 5.0) or nitrogen (N_2 5.0), using Schlenk and glove box techniques. Non-halogenated solvents were dried over sodium benzophenone and halogenated solvents were dried over P_2O_5. Deuterated solvents were bought from Cambridge Isotope Laboratories, distilled and stored over molecular sieves (3 Å). Chemicals were purchased from commercial sources and used without further purification (purity ≥ 95 %). NMR spectra were received using a Varian INOVA 300 MHz spectrometer. Chemical shifts are reported in ppm relative to the deuterated solvent. GC analyses were carried out on an Agilent Technologies 6890N system equipped with an Optima17 column (30 m, 320 µm, 0.25 µm). GC/MS analyses were carried out on an Agilent 7890A/MSD 5975C system equipped with a HP-5MS column (30 m, 320 µm, 0.25 µm). X-ray crystal structure analyses were performed with a STOE IPDS-II diffractometer and a STOE STADIVARI [λ(Mo-K_α)= 0.71073 Å] equipped with an Oxford Cryostream low temperature unit. Structure solution and refinement were accomplished with SIR97[1], SHELXL-2014[2], WinGX[3] and Mercury 3.5.1[4]. FTIR measurements were carried out under a nitrogen atmosphere on an Agilent Cary 630 FTIR equipped with a Diamond ATR unit. Elemental analyses were performed by using a Vario elementar EL *III*. The hydrogenation experiments were carried out using Parr Instrument stainless steel autoclaves N-MT5 300 mL equipped with heating mantles and temperature controller.

General procedure for ketone hydrogenation:

In a nitrogen filled glovebox, a 10 mL glass vial was charged with a magnetic stirring rod, 500 µL of a stock solution of the pre-catalyst, 1 mL of a stock solution of a base and 3 mmol substrate. The vial was sealed with a perforated screw lid and placed inside a 300 mL Parr Instruments high pressure autoclave, which was then removed from the glovebox and purged 5 times with hydrogen (H_2 5.0). Afterwards, the final pressure was applied and the reaction vessel was heated. The reaction was stopped by releasing the hydrogen and adding 1 mL water to the solution. For quantitative GC analysis, dodecane was added and the mixture diluted with diethyl ether. After vigorous shaking, an aliquot was removed, dried over sodium sulfate and analyzed via gas chromatography.

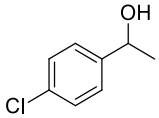
Alcohol syntheses

Synthesis of 1-phenylpentan-1-ol (4d):



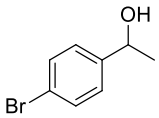
Pre-catalyst **3b** (30 µmol, 1 mol%, 17.7 mg), KO^{t}Bu (300 µmol, 10 mol%, 33.7 mg), 1.5 mL toluene and 1-phenylpentan-1-one (3 mmol, 499 µL) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product was isolated by column chromatography over SiO_2 (ethyl acetate/pentane : 1/9). Yield: 98 % (481 mg) as a colorless oil. ^{1}H NMR ($CDCl_3$, 299.86 MHz, 20 °C): δ = 7.41 - 7.20 (m, 5H), 4.67 (dd, J = 7.3, 6.1 Hz, 1H), 1.85 - 1.64 (m, 3H), 1.48 - 1.15 (m, 4H), 0.89 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 20 °C): δ = 145.1, 128.6, 127.6, 126.0, 74.9, 39.0, 28.1, 22.8, 14.2 ppm.

Synthesis of 1-(4-chlorophenyl)ethanol (4g):



Pre-catalyst **3b** (3 µmol, 0.1 mol%, 500 µL of a 6 mM stock solution), KO^{t}Bu (30 µmol, 1 mol%, 1000 µL of a 30 mM stock solution) and 1-(4-chlorophenyl)ethanone (3 mmol, 389 µL) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product is purified by filtration over a plug of SiO_2. Yield: 96 % (449 mg) as a colorless oil. ^{1}H NMR ($CDCl_3$, 299.86 MHz, 20 °C): δ = 7.54 – 7.43 (m, 2H), 7.30 – 7.21 (m, 2H), 4.87 (q, J = 6.4 Hz, 1H), 1.99 (s, 1H), 1.48 (dd, J = 6.5, 1.5 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 20 °C): δ = 144.9, 131.7, 127.3, 121.3, 69.9, 25.4 ppm.

Synthesis of 1-(4-bromophenyl)ethanol (4h):

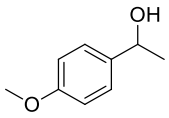


Pre-catalyst **3b** (3 µmol, 0.1 mol%, 500 µL of a 6 mM stock solution), KO^{t}Bu (30 µmol, 1 mol%, 1000 µL of a 30 mM stock solution) and 1-(4-bromophenyl)ethanone (3 mmol, 597 mg) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product is purified by filtration over a plug of SiO_2. Yield: 95 % (574 mg) as an off-white solid. ^{1}H NMR ($CDCl_3$, 299.86 MHz, 20 °C): δ = 7.33 – 7.22 (m, 4H), 4.82 (q, J = 6.4 Hz, 1H), 2.45 (s, 1H), 1.43 (dd,

J = 6.5, 1.0 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 20 °C): δ = 144.3, 133.1, 128.7, 126.9, 69.8, 25.4 ppm.

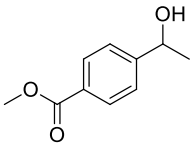
Upscaling: Pre-catalyst **3b** (45 µmol, 0.1 mol%, 26.5 mg), KO^{t}Bu (450 µmol, 1 mol%, 50.5 mg), 1-(4-bromophenyl)ethanone (45 mmol, 8.955 g) and 22.5 mL toluene were added consecutively to a 100 mL beaker. The beaker is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 15 mL water. The product is purified by filtration over a plug of SiO_2. Yield: 97 % (8.780 g) as an off-white solid. The purity was verified by GC-analysis.

Synthesis of 1-(4-methoxyphenyl)ethanol (4i):



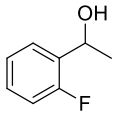
Pre-catalyst **3b** (30 µmol, 1 mol%, 17.7 mg), KO^{t}Bu (300 µmol, 10 mol%, 33.7 mg), 1.5 mL toluene and 1-(4-methoxyphenyl)ethanone (3 mmol, 451 mg) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product was isolated by column chromatography over SiO_2 (ethyl acetate/pentane : 1/3). Yield: 91 % (415 mg) as a colorless oil. ^{1}H NMR ($CDCl_3$, 299.86 MHz, 20 °C): δ = 7.34 – 7.27 (m, 2H), 6.92 – 6.85 (m, 2H), 4.86 (q, *J* = 6.4 Hz, 1H), 3.81 (s, 3H), 1.72 (s, 1H), 1.48 (d, *J* = 6.4 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 20 °C): δ = 159.1, 138.1, 126.8, 114.0, 70.2, 55.5, 25.2 ppm.

Synthesis of methyl-4-(1-hydroxyethyl)benzoate (4k):



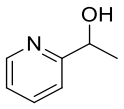
Pre-catalyst **3b** (30 µmol, 1 mol%, 17.7 mg), KO^{t}Bu (300 µmol, 10 mol%, 33.7 mg), 1.5 mL toluene and methyl 4-acetylbenzoate (3 mmol, 535 mg) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product was isolated by column chromatography over SiO_2 (diethyl ether/pentane : 2/1). Yield: 52 % (281 mg) as a colorless oil. ^{1}H NMR ($CDCl_3$, 299.86 MHz, 23 °C): δ = 8.01 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 4.95 (q, *J* = 6.2 Hz, 1H), 3.90 (s, 3H), 2.03 (s, 1H), 1.50 (d, *J* = 6.5 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 23 °C): δ = 166.96, 150.91, 129.84, 125.27, 69.98, 52.10, 25.30 ppm.

Synthesis of 1-(2-fluorophenyl)ethanol (4n):



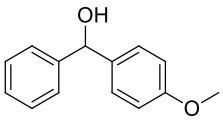
Pre-catalyst **3b** (30 µmol, 1 mol%, 17.7 mg), KO^{t}Bu (300 µmol, 10 mol%, 33.7 mg), 1.5 mL toluene and 1-(2-fluorophenyl)ethanone (3 mmol, 364 µL) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product was isolated by column chromatography over SiO_2 (ethyl acetate/pentane : 1/3). Yield: 92 % (387 mg) as a colorless oil. ^{1}H NMR (C_6D_6, 299.86 MHz, 25 °C): δ = 7.71 – 7.29 (m, 1H), 6.98 – 6.63 (m, 3H), 4.94 (dd, J = 6.3, 2.6 Hz, 1H), 1.29 (d, J = 6.4 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 25 °C): δ = 161.6, 158.3, 128.7, 128.6, 127.1, 127.0, 124.5, 124.4, 115.3, 115.0, 64.1, 24.5 ppm. ^{19}F NMR (C_6D_6, 282 MHz, 25 °C) δ = -120.3 ppm.

Synthesis of 1-(pyridin-2-yl)ethanol (4o):



Pre-catalyst **3b** (15 µmol, 0.5 mol%, 500 µL of a 30 mM stock solution), KO^{t}Bu (150 µmol, 5 mol%, 16.8 mg), 1.0 mL toluene and 1-(pyridin-2-yl)ethanone (3 mmol, 336 µL) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product was isolated by column chromatography over SiO_2 (ethyl acetate/pentane : 3/1). Yield: 92 % (338 mg) as a yellow oil. ^{1}H NMR (C_6D_6, 299.86 MHz, 23 °C): δ = 8.27 (d, J = 3.9 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.77 (d, J = 7.7 Hz, 1H), 6.62 – 6.50 (m, 1H), 4.82 (dd, J = 12.3, 5.9 Hz, 1H), 4.36 (s, 1H), 1.42 (d, J = 6.5 Hz, 3H) ppm. ^{13}C NMR (C_6D_6, 75.41 MHz, 23 °C): δ = 164.1, 148.3, 136.4, 121.9, 119.8, 69.0, 24.7 ppm.

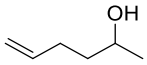
Synthesis of (4-methoxyphenyl)(phenyl)methanol (4s):



Pre-catalyst **3b** (15 µmol, 0.5 mol%, 500 µL of a 30 mM stock solution), KO^{t}Bu (150 µmol, 5 mol%, 16.8 mg), 1.0 mL toluene and (4-methoxyphenyl)(phenyl)methanone (3 mmol, 637 mg) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product was isolated by column chromatography over SiO_2 (ethyl acetate/pentane : 1/5). Yield: 93% (595 mg) as a colorless solid. ^{1}H NMR (C_6D_6, 299.86 MHz, 25 °C): δ = 7.34 (d, J = 7.6 Hz, 2H), 7.19 (d, J = 8.8 Hz, 3H), 7.14 – 7.01 (m, 2H), 6.73 (d, J = 8.6 Hz, 2H), 5.52 (s, 1H), 3.27

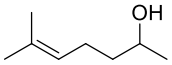
(s, 3H), 1.77 (d, J = 12.6 Hz, 1H) ppm. ^{13}C NMR (C_6D_6, 75.41 MHz, 25 °C): δ = 159.5, 145.2, 137.1, 128.5, 128.3, 127.4, 126.9, 114.1, 75.8, 54.8 ppm.

Synthesis of hex-5-en-2-ol (5d):



Pre-catalyst **3b** (3 µmol, 0.1 mol%, 500 µL of a 6 mM stock solution), KO^{t}Bu (30 µmol, 1 mol%, 1000 µL of a 30 mM stock solution) and hex-5-en-2-one (3 mmol, 348 µL) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product was isolated by column chromatography over SiO_2, which was deactivated prior to use by flushing with triethylamine (diethyl ether/pentane : 1/1). Yield: 95 % (286 mg) as a slightly yellow oil. ^{1}H NMR (C_6D_6, 299.86 MHz, 23 °C): δ = 5.75 (ddt, J = 16.9, 10.1, 6.7 Hz, 1H), 5.07 – 4.88 (m, 2H), 3.61 - 3.42 (m, 1H), 2.19 – 1.88 (m, 2H), 1.49 – 1.04 (m, 3H), 0.97 (d, J = 6.2 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 23 °C): δ = 138.6, 114.3, 66.8, 38.3, 30.1, 23.3 ppm.

Synthesis of 6-methylhept-5-en-2-ol (5e):

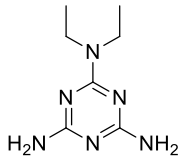


Pre-catalyst **3b** (6 µmol, 0.2 mol%, 500 µL of a 12 mM stock solution), KO^{t}Bu (60 µmol, 2 mol%, 1000 µL of a 60 mM stock solution) and 6-methylhept-5-en-2-one (3 mmol, 441 µL) are added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 4 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. The product was isolated by column chromatography over SiO_2 (diethyl ether/pentane : 3/1). Yield: 86 % (331 mg) as a colorless oil. ^{1}H NMR (C_6D_6, 299.86 MHz, 23 °C): δ = 5.17 (ddd, J = 8.6, 5.8, 1.4 Hz, 1H), 3.58 (dd, J = 12.1, 6.0 Hz, 1H), 2.19 – 1.94 (m, 2H), 1.65 (s, 3H), 1.56 (s, 3H), 1.50 – 1.26 (m, 2H), 1.18 (s, 1H), 1.07 – 0.99 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 23 °C): δ = 131.5, 125.0, 67.4, 39.7, 25.9, 24.9, 23.8, 17.7 ppm.

Ligand syntheses

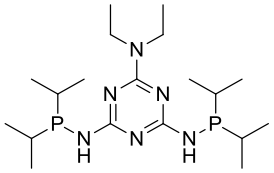
(4-Ph)Triaz(NHP^{i}Pr$_2$)$_2$ (**1a**)[5], (4-NHCpr)Triaz(NHP^{i}Pr$_2$)$_2$ (**1b**, Cpr = Cyclopropyl)[6] and (4-Me)Triaz(NHP^{i}Pr$_2$)$_2$ (**1c**)[5] were prepared according to literature.

Synthesis of N^2,N^2-diethyl-1,3,5-triazine-2,4,6-triamine:



Following the procedure of WÜRTHNER *et al.*[7], a solution of 6-chloro-1,3,5-triazine-2,4-diamine (50 mmol, 7.3 g, 1 eq), diethylamine (55 mmol, 5.8 mL, 1.1 eq) and $NaHCO_3$ (55 mmol, 4.6 g, 1.1 eq) in DMF (200 mL) was heated to reflux for 15 h. After cooling to room temperature, 500 mL of water were added. The aqueous layer was extracted with DCM (5x100 mL), the organic phases were combined, washed with brine, dried over Na_2SO_4 and evaporated. The resulting crude product was recrystallized from warm $CHCl_3$. Yield: 58 % (5.3 g) as colorless crystals. ^{1}H NMR ($CDCl_3$, 299.86 MHz, 23 °C): δ = 4.74 (s, 4H), 3.52 (q, J = 7.1 Hz, 4H), 1.13 (t, J = 7.1 Hz, 6H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 23 °C): δ = 167.5, 165.4, 40.9, 13.4 ppm.

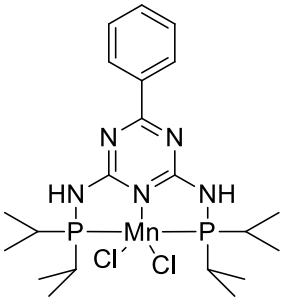
Synthesis of (4-NEt$_2$)Triaz(NHP^{i}Pr$_2$)$_2$ (1d):



To a suspension of N^2,N^2-diethyl-1,3,5-triazine-2,4,6-triamine (16.4 mmol, 3.0 g, 1 eq) in thf (75 mL) at 0 °C, chlorodiisopropylphosphine (36.1 mmol, 6 mL, 2.2 eq) was added. Afterwards, triethylamine (66 mmol, 9.5 mL, 4 eq) was added dropwise and the solution was stirred at 0 °C for an additional 30 min before the solution was heated to 50 °C for 20 h. After filtration, all volatiles were removed *in vacuo* and the resulting crude product was recrystallized from hot toluene to yield 74 % (5 g) of (4-NEt$_2$)Triaz(NHP^{i}Pr$_2$)$_2$ as colorless crystals. ^{1}H NMR ($CDCl_3$, 299.86 MHz, 23 °C): δ = 5.27 (s, 2H), 3.53 (q, J = 7.0 Hz, 4H), 1.70 (s, 4H), 1.16 – 0.84 (m, 32H) ppm. ^{13}C NMR ($CDCl_3$, 75.41 MHz, 23 °C): δ = 41.4, 26.6, 26.4, 19.4, 19.1, 18.2, 13.7 ppm. ^{31}P NMR (C_6D_6, 202 MHz, 23 °C): δ = 49.6 ppm.

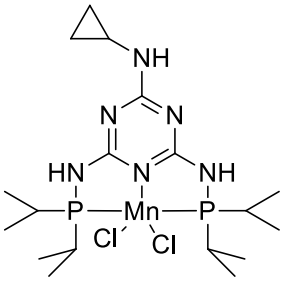
Complex syntheses

Synthesis of (4-Ph)Triaz(NHP^{i}Pr$_2$)$_2$MnCl$_2$ (2a):



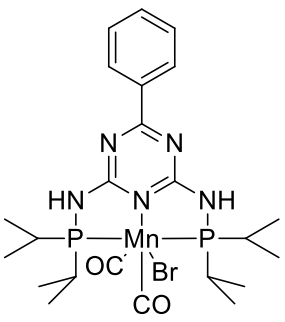
In a Schlenk tube, (4-Ph)Triaz(NHP^{i}Pr$_2$)$_2$ (3 mmol, 1.24 g, 1 eq) and manganese(II) chloride (3 mmol, 378 mg, 1 eq) were dissolved in thf (20 mL) and stirred for 20 h at 55 °C. After filtration, half of the solvent was removed *in vacuo*. After cold filtration, yellow crystals, suitable for X-ray single crystal analysis, were obtained by adding toluene (5 mL) and storing the solution at -20 °C for 3 days. Yield: 1.2 g (75%). Elemental analysis calcd for $C_{21}H_{35}Cl_2MnN_5P_2$ (M: 545.33) [%]: C 46.25, H 6.47, N 12.84; found: C 44.86, H 6.46, N 12.13.

Synthesis of (4-NHCpr)Triaz(NHP^{i}Pr$_2$)$_2$MnCl$_2$ (2b):



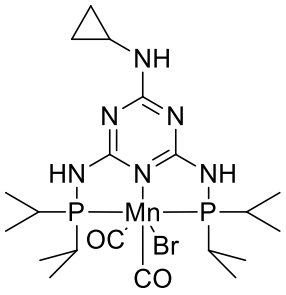
In a Schlenk tube, (4-NHCpr)Triaz(NHP^{i}Pr$_2$)$_2$ (1 mmol, 398 mg, 1 eq) and manganese(II) chloride (1 mmol, 126 mg, 1 eq) were dissolved in thf (20 mL) and stirred for 20 h at 55 °C. After filtration, all volatiles were removed in vacuo to afford (4-NHCpr)Triaz(NHP^{i}Pr$_2$)$_2$MnCl$_2$ (**2b**) as a colorless solid. Yield: 90 % (472 mg). Elemental analysis calcd for $C_{18}H_{36}Cl_2MnN_6P_2$ (M: 524.31) [%]: C 41.23, H 6.92, N 16.03; found: C 41.32, H 7.07, N 15.48.

Synthesis of (4-Ph)Triaz(NHP^{i}Pr$_2$)$_2$Mn(CO)$_2$Br (3a):



In a Schlenk tube, (4-Ph)Triaz(NHP^{i}Pr$_2$)$_2$ (3 mmol, 1.26 g, 1 eq) and manganese pentacarbonyl bromide (3 mmol, 0.82 g, 1 eq) were suspended in toluene (40 mL) and heated to reflux for 16 h. After cooling to room temperature, the supernatant solution was filtered off and the precipitate was dried *in vacuo* at 100 °C to afford (4-Ph)Triaz(NHP^{i}Pr$_2$)$_2$Mn(CO)$_2$Br (**3a**) as a bright yellow powder. Yield: 87 % (1.6 g). Elemental analysis calcd for $C_{23}H_{35}BrMnN_5O_2P_2$ (M: 610.35) [%]: C 45.26, H 5.78, N 11.47; found: C 44.26, H 5.06, N 11.32.

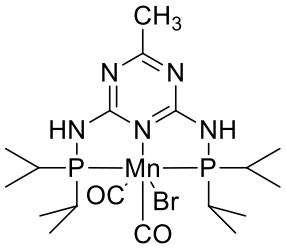
Synthesis of (4-NHCpr)Triaz(NHP^{i}Pr$_2$)$_2$Mn(CO)$_2$Br (3b):



In a Schlenk tube, (4-NHCpr)Triaz(NHP^{i}Pr$_2$)$_2$ (3 mmol, 1.20 g, 1 eq) and manganese pentacarbonyl bromide (3 mmol, 0.82 g, 1 eq) were suspended in toluene (40 mL) and heated to reflux for 16 h. After cooling to room temperature, the supernatant solution was filtered off and the precipitate was dried *in vacuo* at 100 °C to afford (4-NHCpr)Triaz(NHP^{i}Pr$_2$)$_2$Mn(CO)$_2$Br (**3b**) as a bright yellow powder. Yield 91 % (1.6 g). Elemental analysis calcd for $C_{20}H_{36}BrMnN_6O_2P_2$ (M: 589.34) [%]: C 40.76, H 6.16, N 14.26; found: C 41.03, H 6.09, N 13.99.

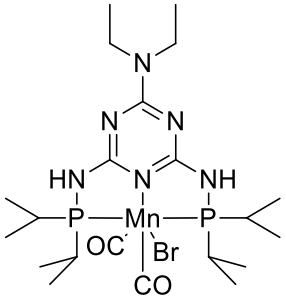
Crystals, suitable for X-ray single crystal analysis, were prepared by layering a saturated solution of the compound in C_6D_6 with *n*-hexane and leave the solution to evaporate in a glovebox.

Synthesis of (4-Me)Triaz(NHP^{i}Pr$_2$)$_2$Mn(CO)$_2$Br (3c):



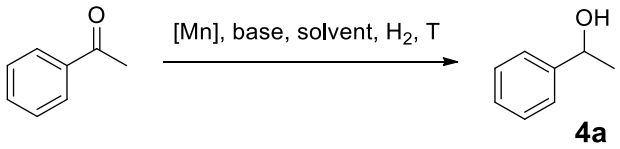
In a Schlenk tube, (4-Me)Triaz(NHP^{i}Pr$_2$)$_2$ (3 mmol, 1.07 g, 1 eq) and manganese pentacarbonyl bromide (3 mmol, 0.82 g, 1 eq) were suspended in toluene (40 mL) and heated to reflux for 16 h. After cooling to room temperature, the supernatant solution was filtered off and the precipitate was dried *in vacuo* at 100 °C to afford (4-Me)Triaz(NHP^{i}Pr$_2$)$_2$Mn(CO)$_2$Br (**3c**) as a bright yellow powder. Yield: 91 % (1.5 g). Elemental analysis calcd for $C_{18}H_{33}BrMnN_5O_2P_2$ (M: 548.28) + 0.5 C_7H_8 (M: 92.14) [%]: C 43.37, H 6.43, N 11.76; found: C 41.69, H 6.14, N 11.23.

Synthesis of (4-NEt$_2$)Triaz(NHP^{i}Pr$_2$)$_2$Mn(CO)$_2$Br (3d):



In a Schlenk tube, (4-NEt$_2$)Triaz(NHP^{i}Pr$_2$)$_2$ (1 mmol, 415 mg, 1 eq) and manganese pentacarbonyl bromide (1 mmol, 275 mg, 1 eq) were suspended in toluene (40 mL) and heated to reflux for 16 h. After cooling to room temperature, the supernatant solution was filtered off and the precipitate was dried *in vacuo* at 100 °C to afford (4-NEt$_2$)Triaz(NHP^{i}Pr$_2$)$_2$Mn(CO)$_2$Br (**3d**) as a bright yellow powder. Yield: 75 % (450 mg). Elemental analysis calcd for $C_{21}H_{40}BrMnN_6O_2P_2$ (M: 605.37) [%]: C 41.66, H 6.66, N 13.88; found: C 41.18, H 6.56, N 13.51.

Screening Reactions



Scheme S1. Model reaction for screening reactions.

Table S1. Solvent Screening[a]

Entry	Solvent	Yield[b] [%]
1	thf	40
2	1,4-dioxane	37
3	**toluene**	**78**
4	xylene	39
5	2-methyl-2-butanol	27
6	1-methoxy-2-(2-methoxyethoxy)ethane (diglyme)	20
7	acetonitrile	3

[a] Reaction conditions: 3 mmol acetophenone, 0.25 mol% pre-catalyst **3c** (7.5 µmol), 5 mol% NaO^{t}Bu (150 µmol), 2 mL solvent, 20 bar H_2, 60 °C, 4 h. [b] Determined via GC with dodecane as internal standard.

Table S2. Base Screening[a]

Entry	Base	Yield[b] [%]
1	LiO^{t}Bu	8
2	NaO^{t}Bu	51
3	**KO^{t}Bu**	**91**
4	LiOH	0
5	NaOH	0
6	KOH	5
7	Cs_2CO_3	0
8	$KN(SiMe_3)_2$	71

[a] Reaction conditions: 3 mmol acetophenone, 0.25 mol% pre-catalyst **3c** (7.5 µmol), 5 mol% base (150 µmol), 2 mL toluene, 20 bar H_2, 60 °C, 4 h. [b] Determined via GC with dodecane as internal standard.

Table S3. Base Amount Screening[a]

Entry	Base Amount (equivalents with respect to the pre-catalyst)	Yield[b] [%]
1	0.5	0
2	1	0
3	1.5	2
4	2	31
5	3	65
6	4	83
7	5	90
8	**10**	**97**
9	20	91

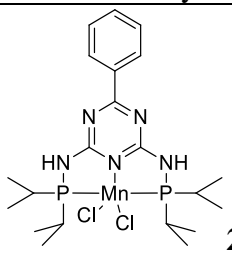
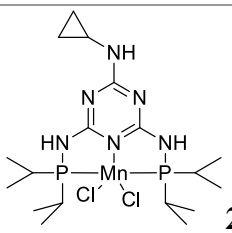
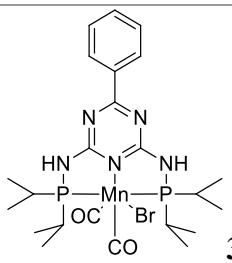
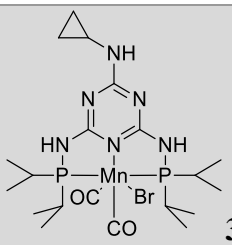
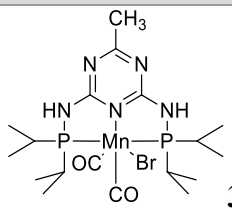
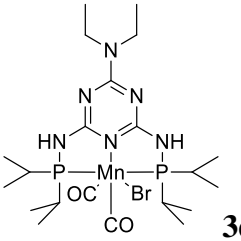
[a] Reaction conditions: 3 mmol acetophenone, 0.25 mol% pre-catalyst **3c** (7.5 µmol), KO^{t}Bu, 2 mL toluene, 20 bar H_2, 60 °C, 4 h. [b] Determined via GC with dodecane as internal standard.

Table S4. Solvent Amount Screening[a]

Entry	Solvent Amount [mL]	Yield[b] [%]
1	0.5	86
2	1	85
3	**1.5**	**90**
4	2	78

[a] Reaction conditions: 3 mmol acetophenone, 0.25 mol% pre-catalyst **3c** (7.5 µmol), 5 mol% KO^{t}Bu, toluene, 20 bar H_2, 60 °C, 4 h. [b] Determined via GC with dodecane as internal standard.

Table S5. Pre-catalyst Screening

Entry	Pre-catalyst	Yield[c] [%]
1	 **2a**[a]	0
2	 **2b**[a]	0
3	 **3a**[b]	38
4	 **3b**[b]	72
5	 **3c**[b]	31
6	 **3d**[b]	55
7	$MnCl_2$ [a]	0
8	$[MnBr(CO)_5]$ [b]	0

Reaction conditions: [a] 1 mmol acetophenone, 5 mol% pre-catalyst, 100 mol% KO^{t}Bu, 2 mL toluene, 60 bar H_2, 60 °C, 16 h. [b] 3 mmol acetophenone, 0.1 mol% pre-catalyst, 1 mol% KO^{t}Bu, 2 mL toluene, 20 bar H_2, 60 °C, 4 h. [c] Determined by GC with dodecane as internal standard.

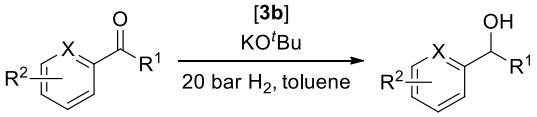
Table S6. Temperature Screening[a]

Entry	Temperature [°C]	Yield[b] [%]
1	40	44
2	60	72
3	**80**	**>99**

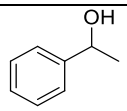
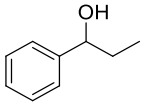
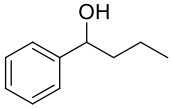
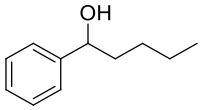
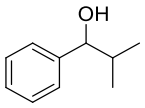
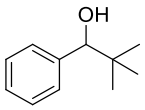
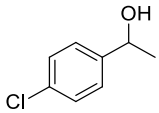
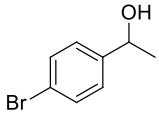
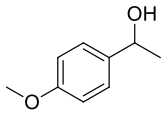
[a] Reaction conditions: 3 mmol acetophenone, 0.1 mol% pre-catalyst **3b** (3 µmol), 1 mol% KO^{t}Bu (30 µmol), 2 mL toluene, 20 bar H_2, 4 h. [b] Determined via GC with dodecane as internal standard.

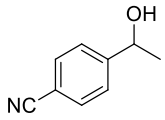
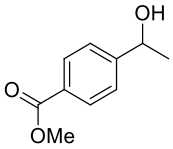
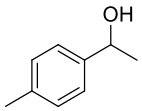
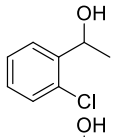
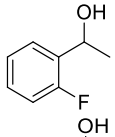
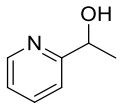
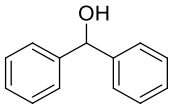
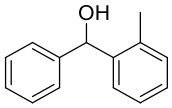
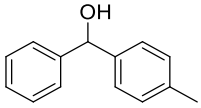
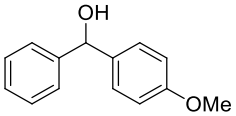
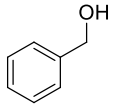
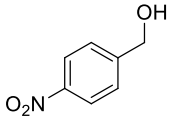
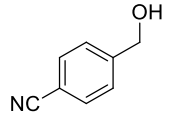
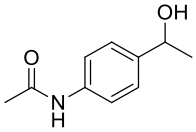
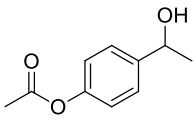
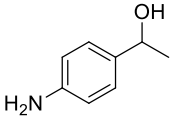
Product Screening

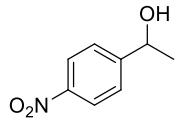
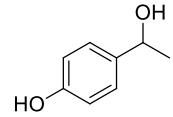
Table S7. Hydrogenation of aryl-alkyl, diaryl carbonyl compounds and aldehydes.[a]



4a-za

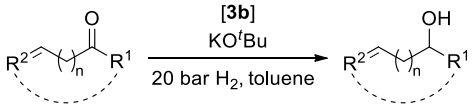
Entry	Product		Pre-cat. loading [mol%]	Yield[d] [%]
1		**4a**	0.1	>99
2		**4b**	0.2 1	97 >99
3		**4c**	0.1 1	64 >99
4		**4d**	1	>99 (98[c])
5		**4e**	1[e]	99
6		**4f**	1[e]	82
7		**4g**	0.1	97 (96[c])
8		**4h**	0.1	97 (95[c])
9		**4i**	0.1 1	70 >99 (91[c])

10		**4j**	2	89
11		**4k**	1	52[c]
12		**4l**	0.2	>99
13		**4m**	0.2	98
14		**4n**	1	>99 (92[c])
15		**4o**	0.1 0.5	79 >99 (92[c])
16		**4p**	0.5	>99
17		**4q**	0.5	75
18		**4r**	0.5	>99
19		**4s**	0.5	>99
20		**4t**	0.1[b]	>99
21		**4u**	1	>99
22		**4v**	1	0 (ester formation was observed)
23		**4w**	1	0 (amide cleavage was observed)
24		**4x**	1	0 (no reaction)
25		**4y**	1	0

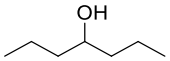
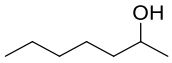
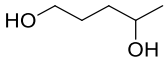
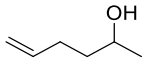
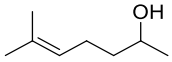
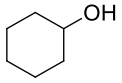
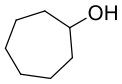
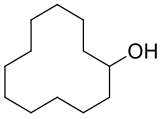
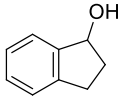
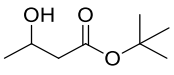
26		**4z**	1	0
27		**4za**	1	0

[a] Reaction conditions: 3 mmol substrate, pre-catalyst **3b**, KO^{t}Bu, 1.5 mL toluene, 20 bar H_2, 80 °C, 4 h. [b] 40 °C. [c] Yield of isolated product. [d] Determined by GC with dodecane as internal standard. [e] 24 h.

Table S8. Hydrogenation of dialkyl, and cycloalkyl carbonyl compounds.[a]

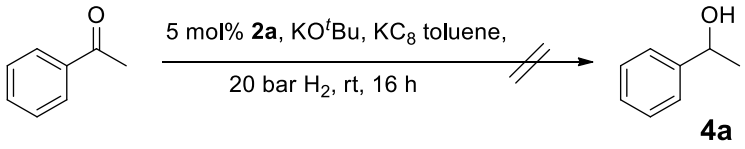


5a-j

entry	product		pre-cat. loading [mol%]	yield[b] [%]
1		**5a**	0.1 0.5	67 >99
2		**5b**	0.2 1	95 >99
3		**5c**	1	88
4		**5d**	0.1	>99 (95[c])
5		**5e**	0.2	98 (86[c])
6		**5f**	0.1	98
7		**5g**	0.2	96
8		**5h**	1	58
9		**5i**	1	97
10		**5j**	1	0

[a] Reaction conditions: 3 mmol substrate, pre-catalyst **3b**, KO^{t}Bu, 1.5 mL toluene, 20 bar H_2, 80 °C, 4 h. [b] Determined by GC with dodecane as internal standard. [c] Yield of isolated product.

Potassium graphite reduction experiment:

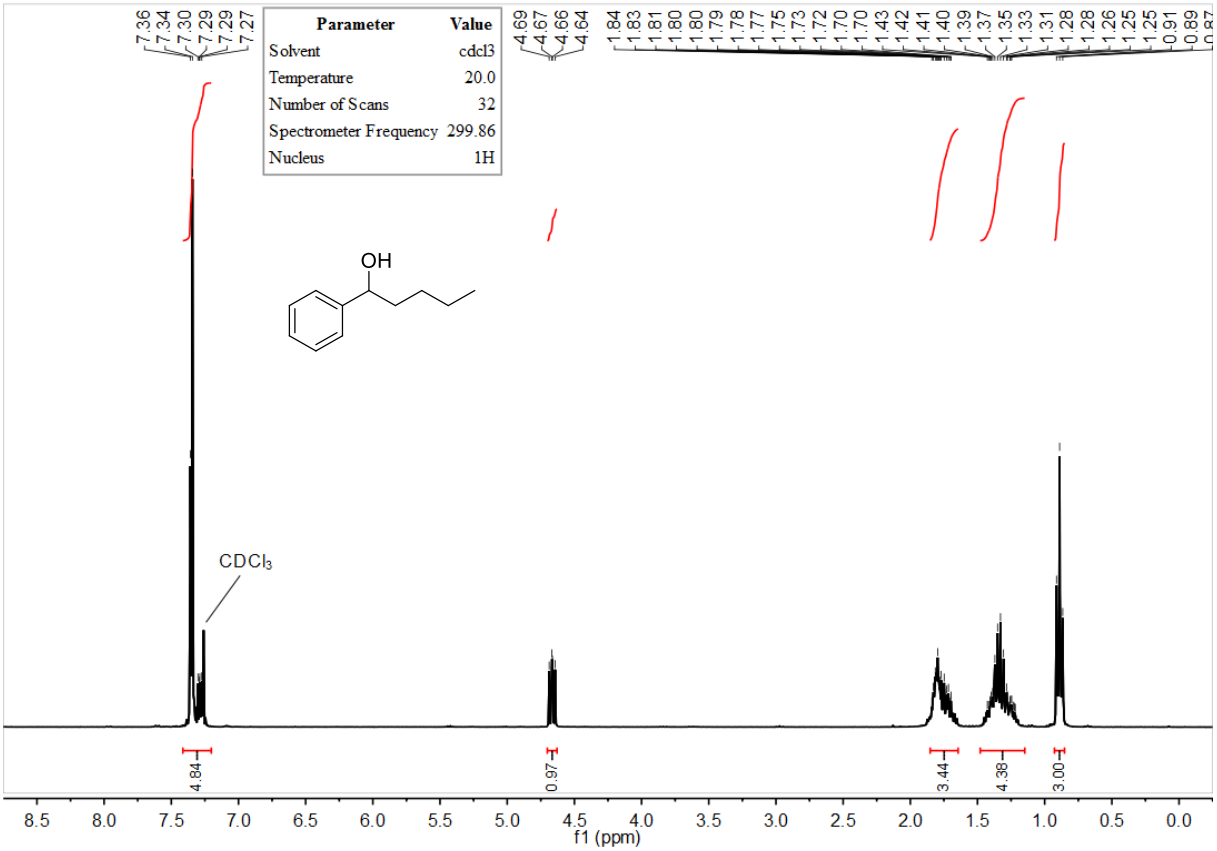


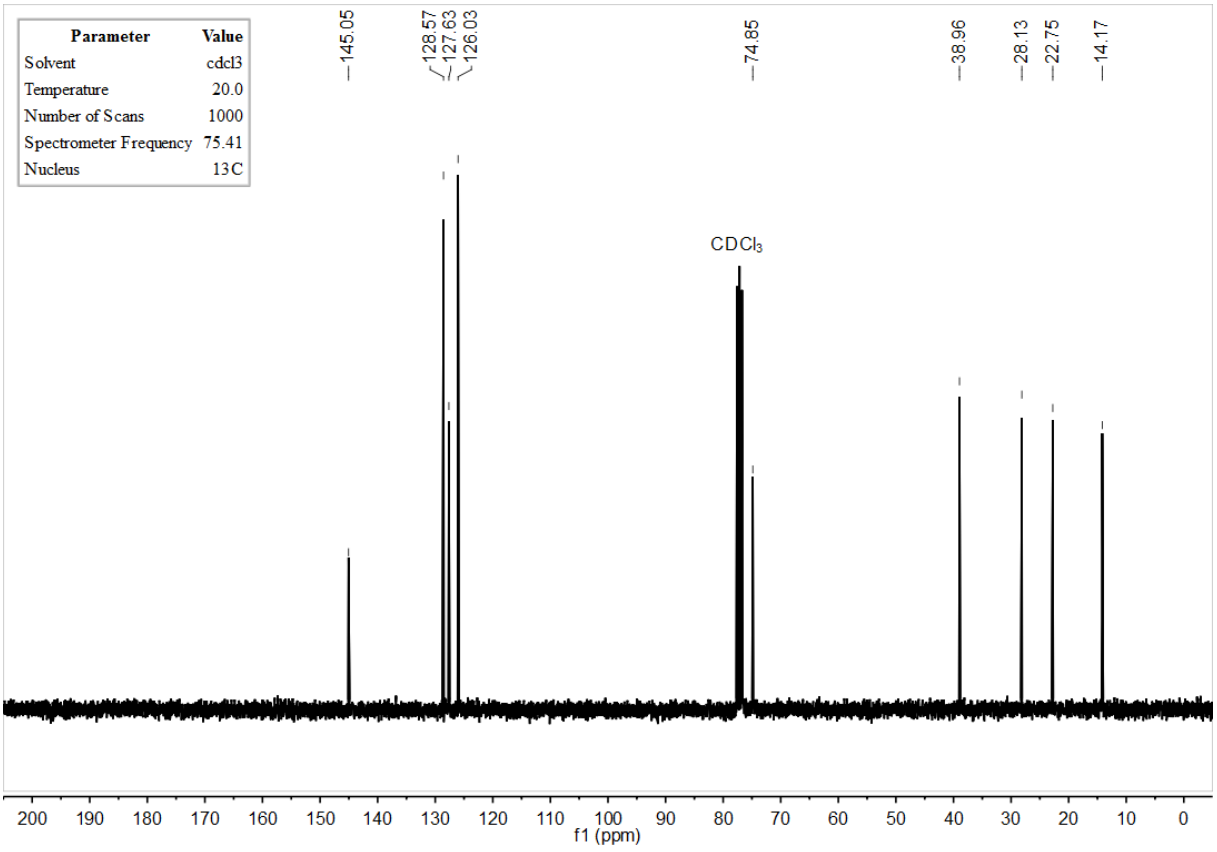
4a

Pre-catalyst **2a** (50 µmol, 5 mol%, 27 mg), KO^{t}Bu (1 mmol, 100 mol%, 112 mg), KC_8 (50 µmol, 7 mg), 1.5 mL toluene and acetophenone (1 mmol, 117 µL) were added consecutively to a glass vial. The glass vial is placed in an autoclave which is purged five times with H_2 gas before it is pressurized with 20 bar H_2. After 16 hours, the reaction is stopped by releasing the hydrogen and the addition of 1 mL water. GC analysis indicated no signs of hydrogenation activity.

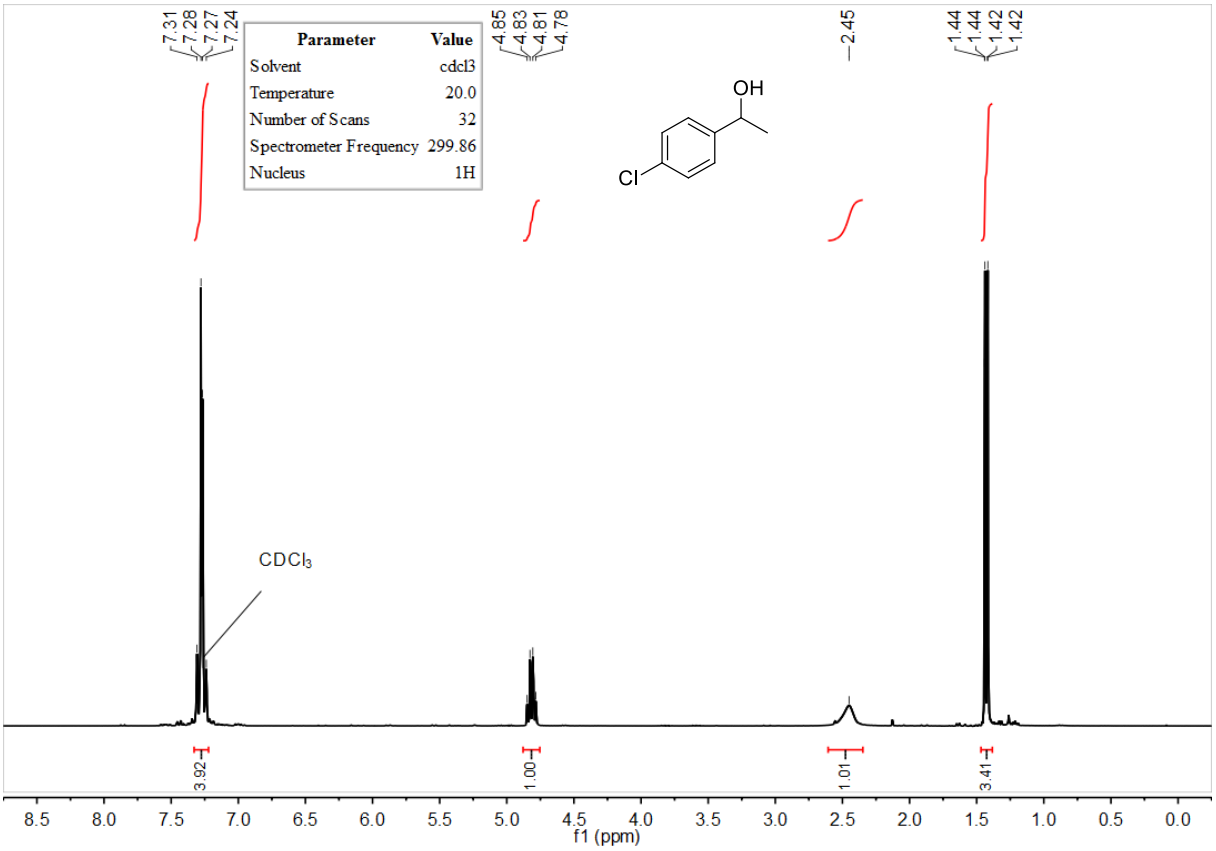
NMR spectra of isolated products

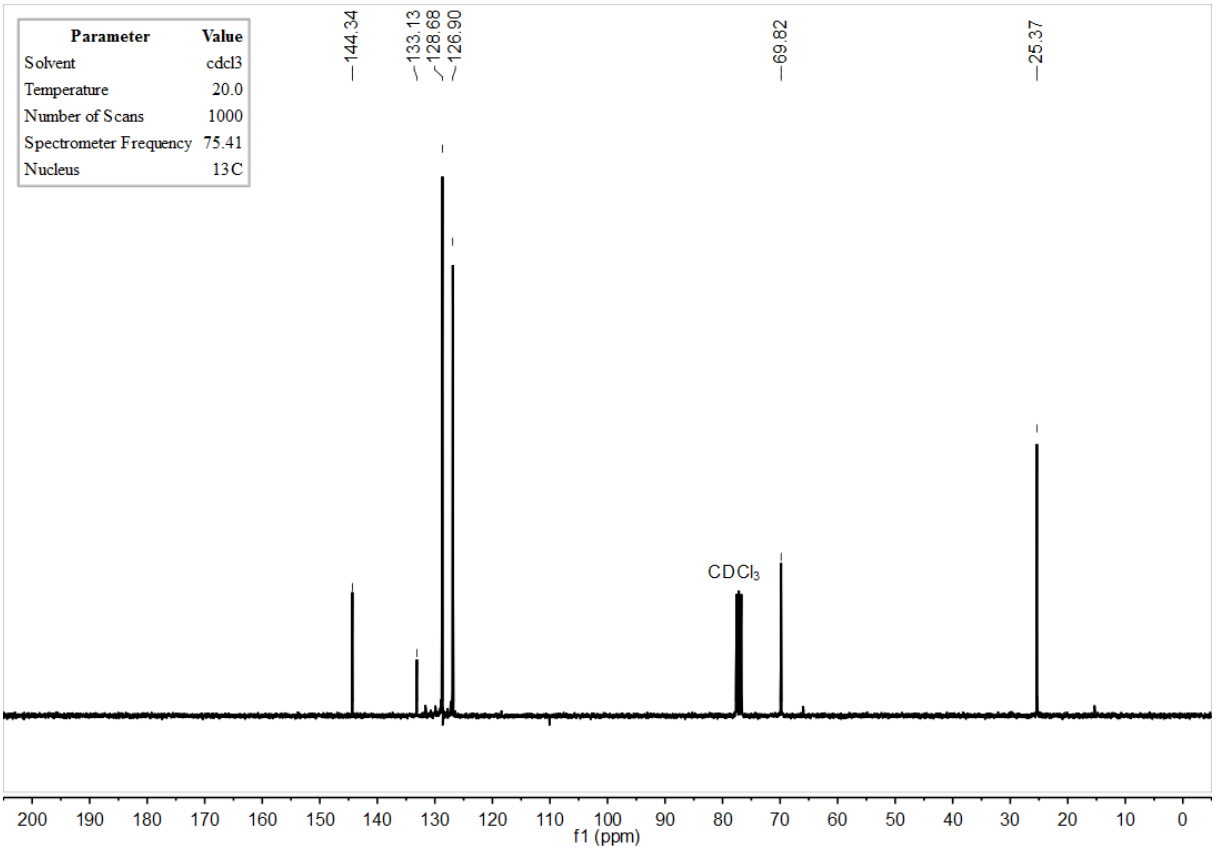
1-phenylpentan-1-ol (4d):



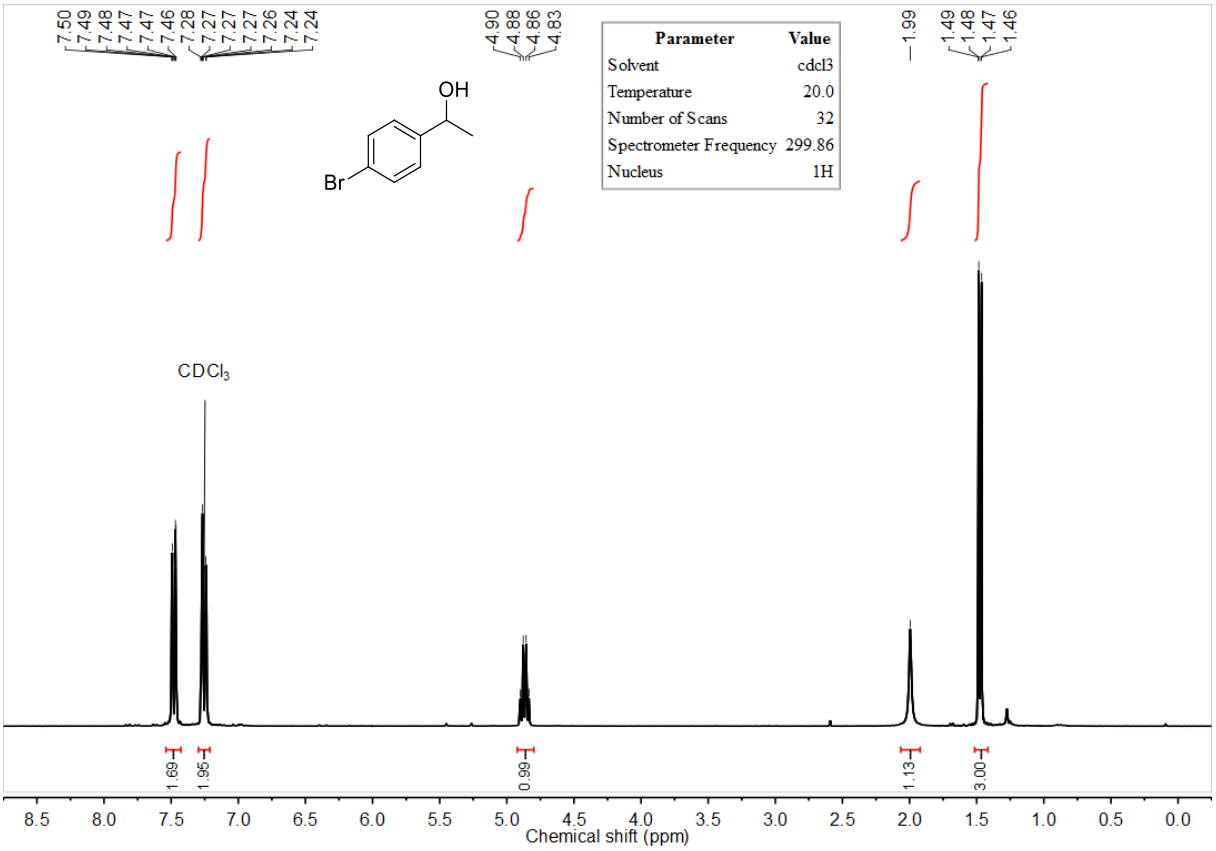


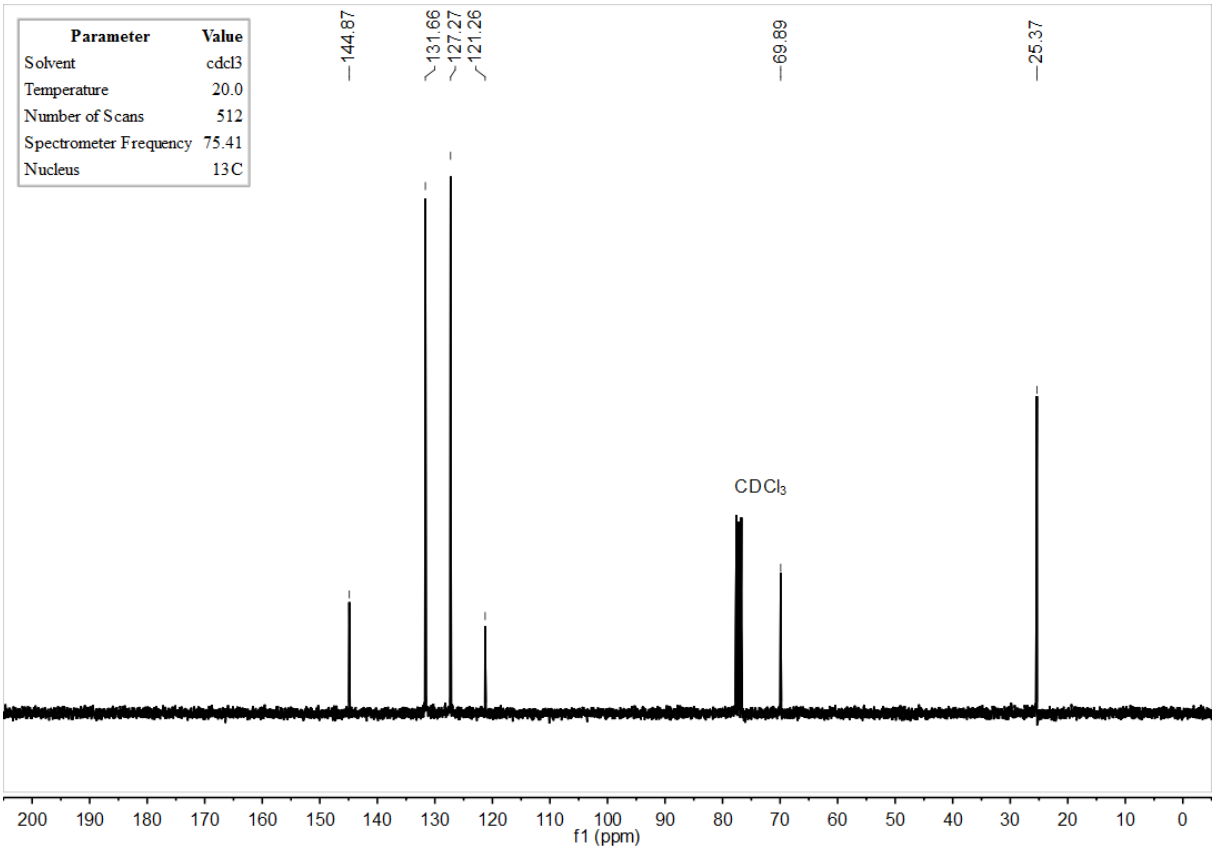
1-(4-chlorophenyl)ethanol (4g)



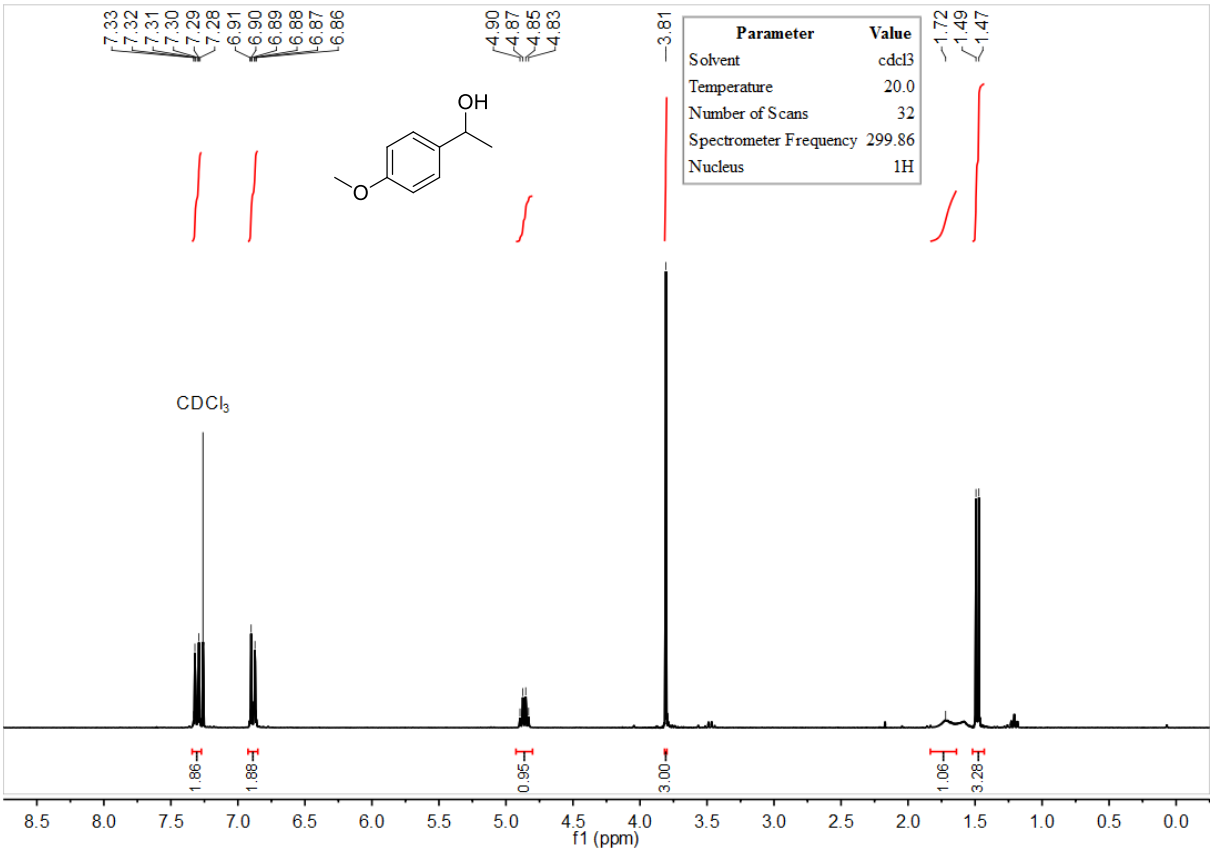


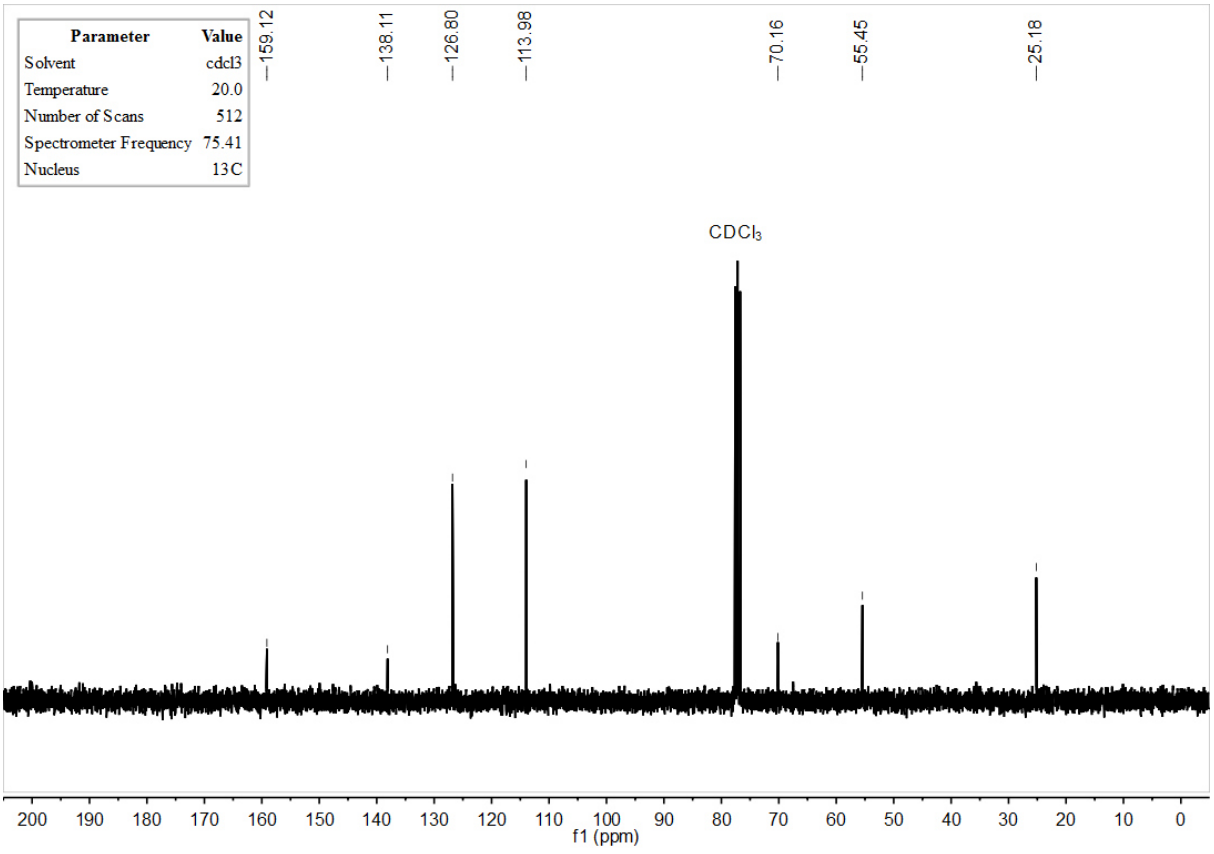
1-(4-bromophenyl)ethanol (4h)



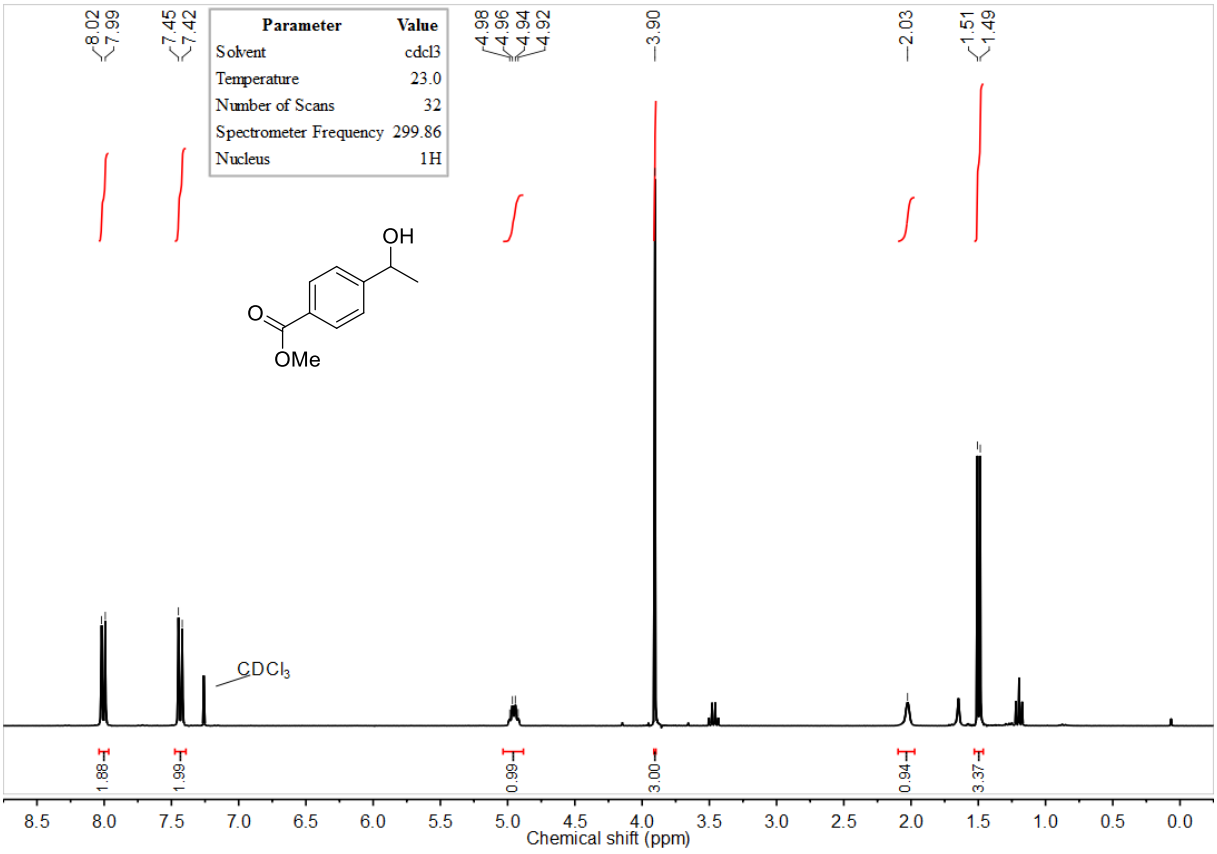


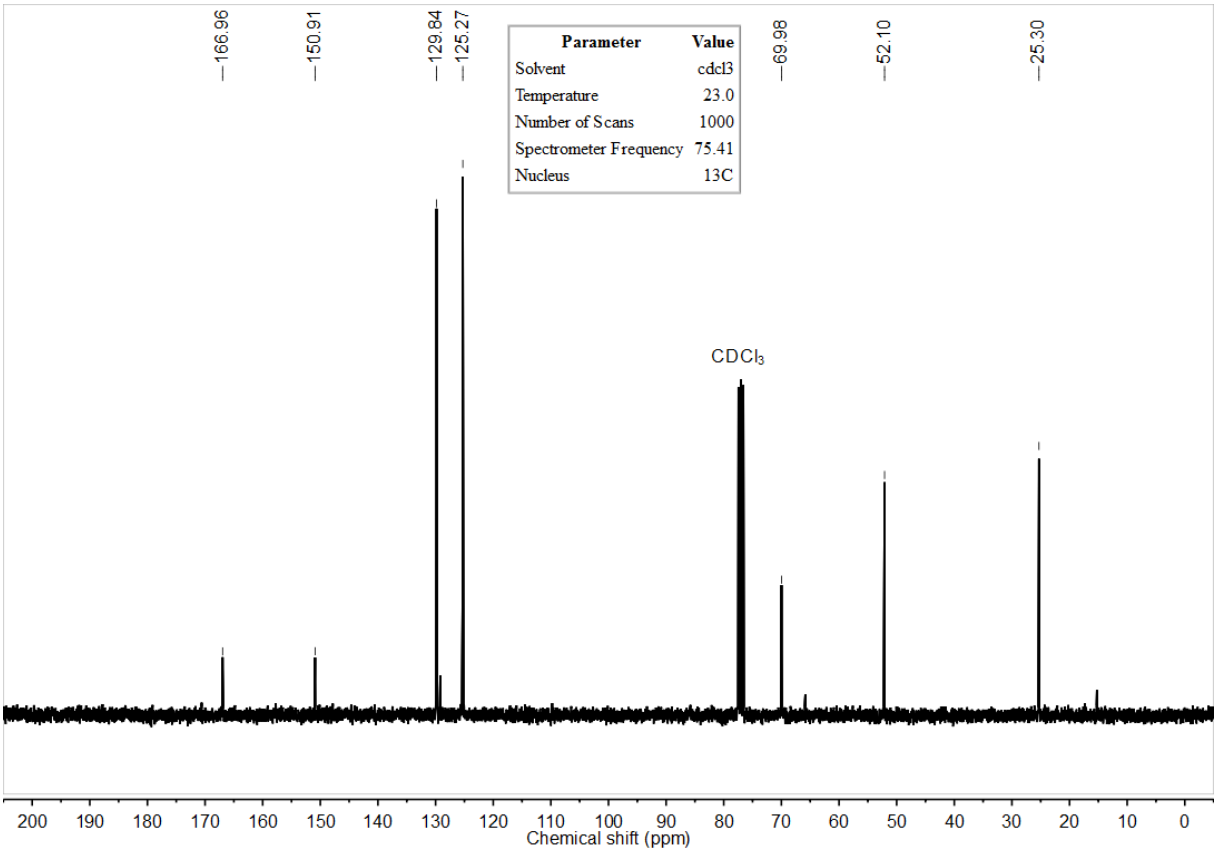
1-(4-methoxyphenyl)ethanol (4i)



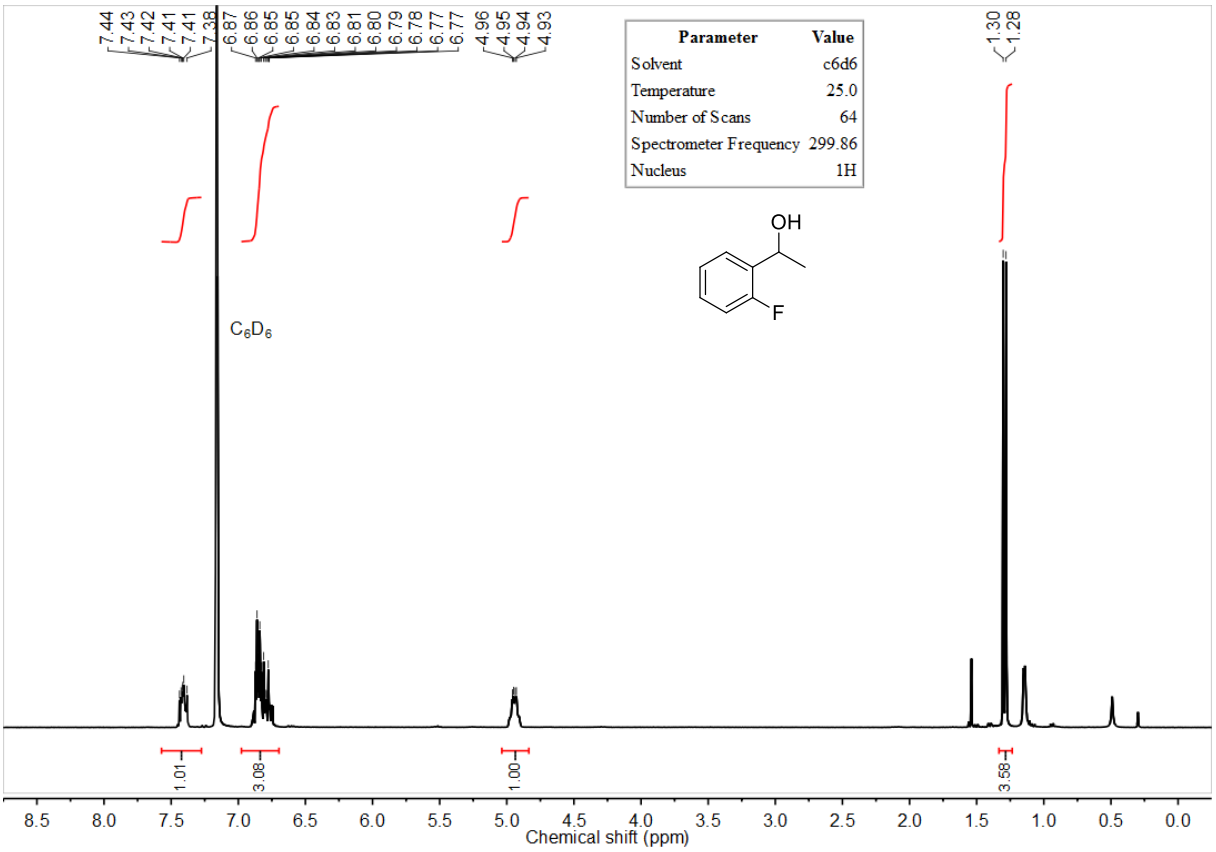


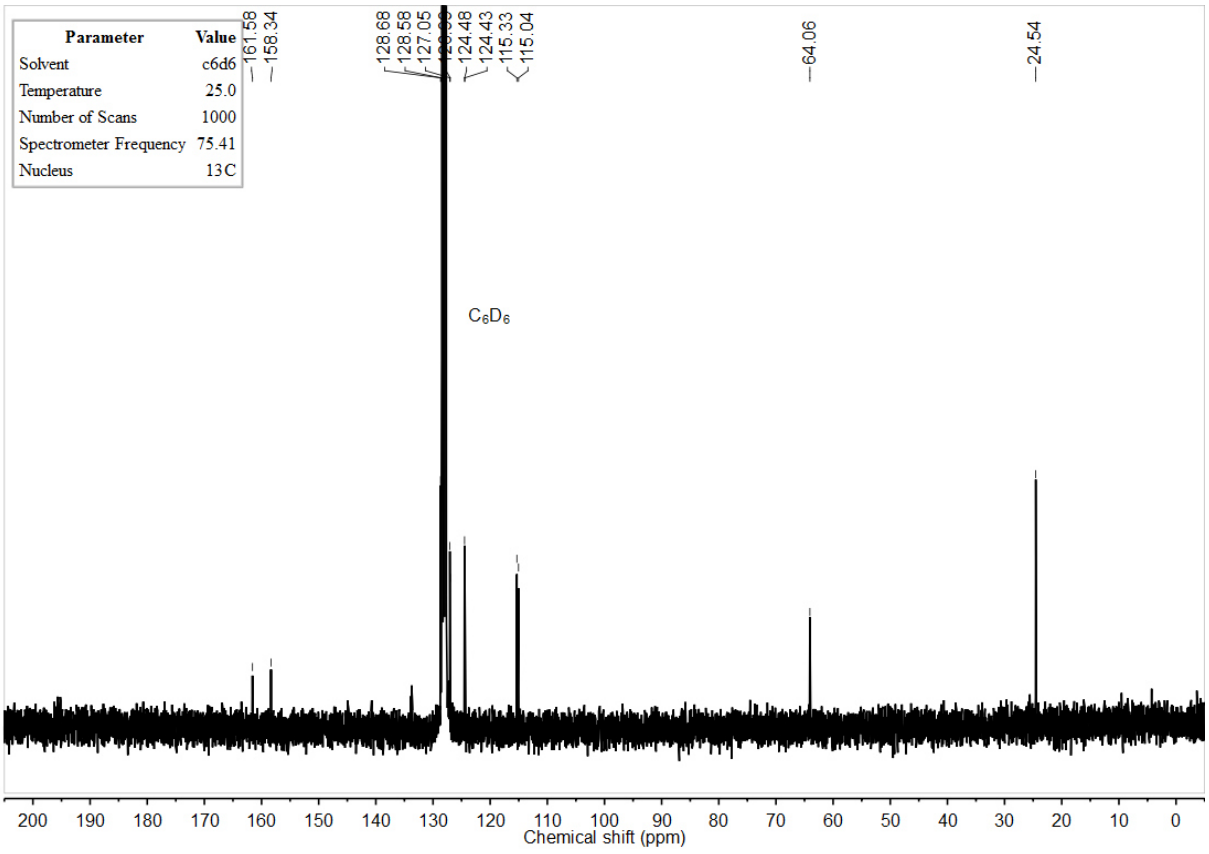
methyl-4-(1-hydroxyethyl)benzoate (4k)

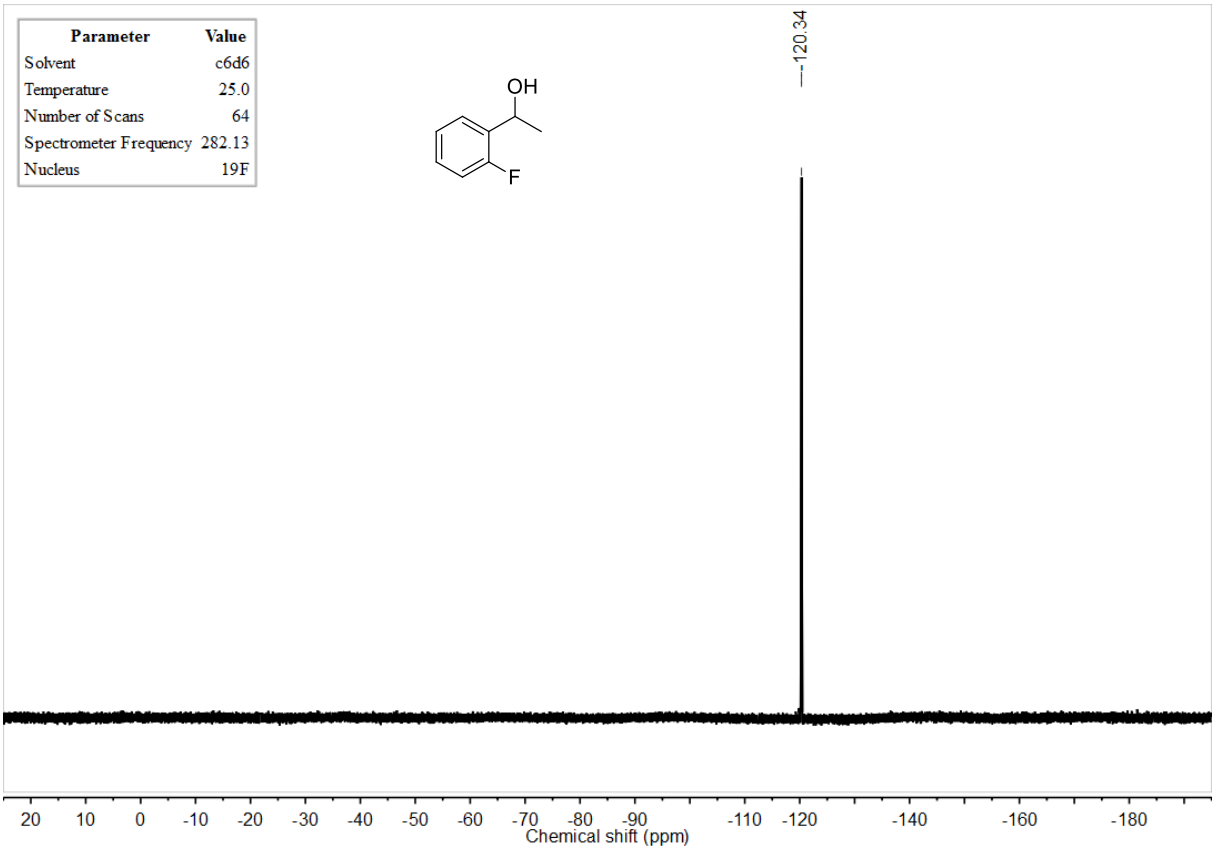




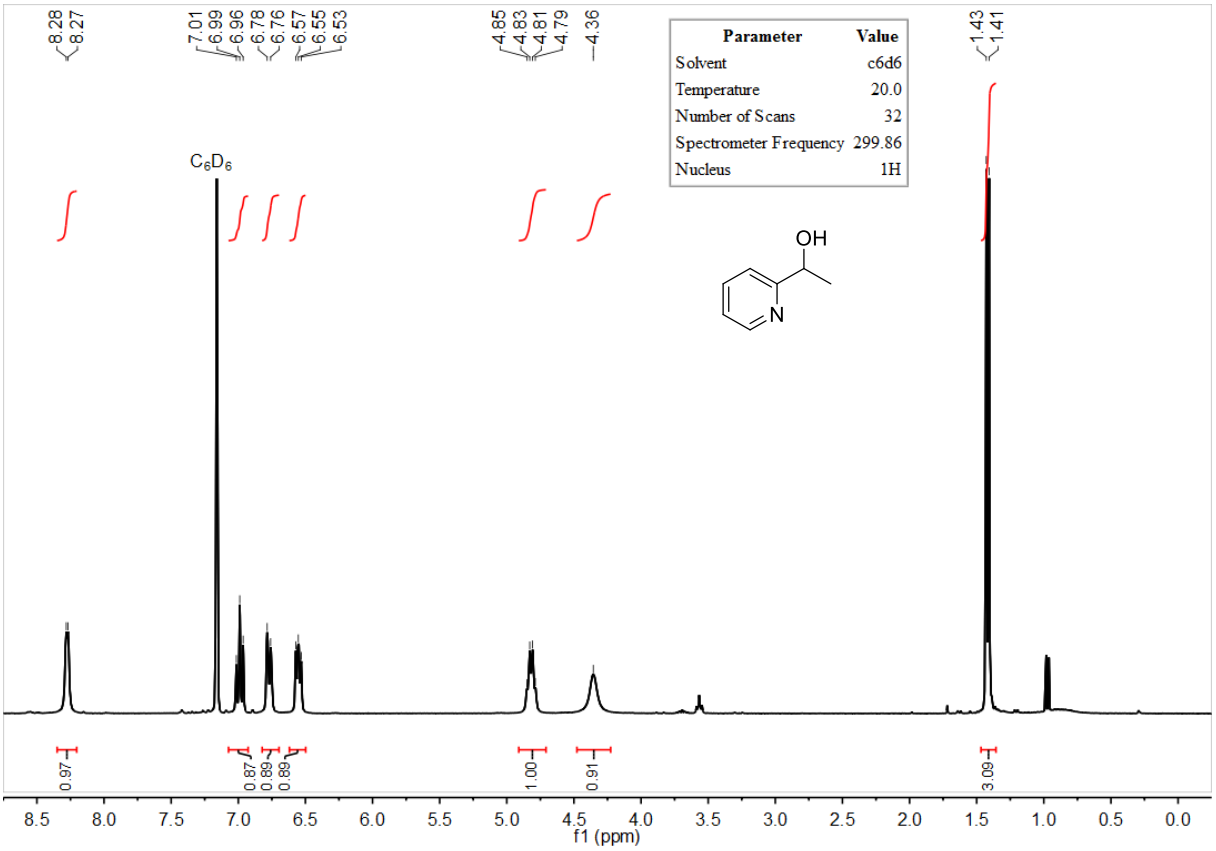
1-(2-fluorophenyl)ethanol (4n)

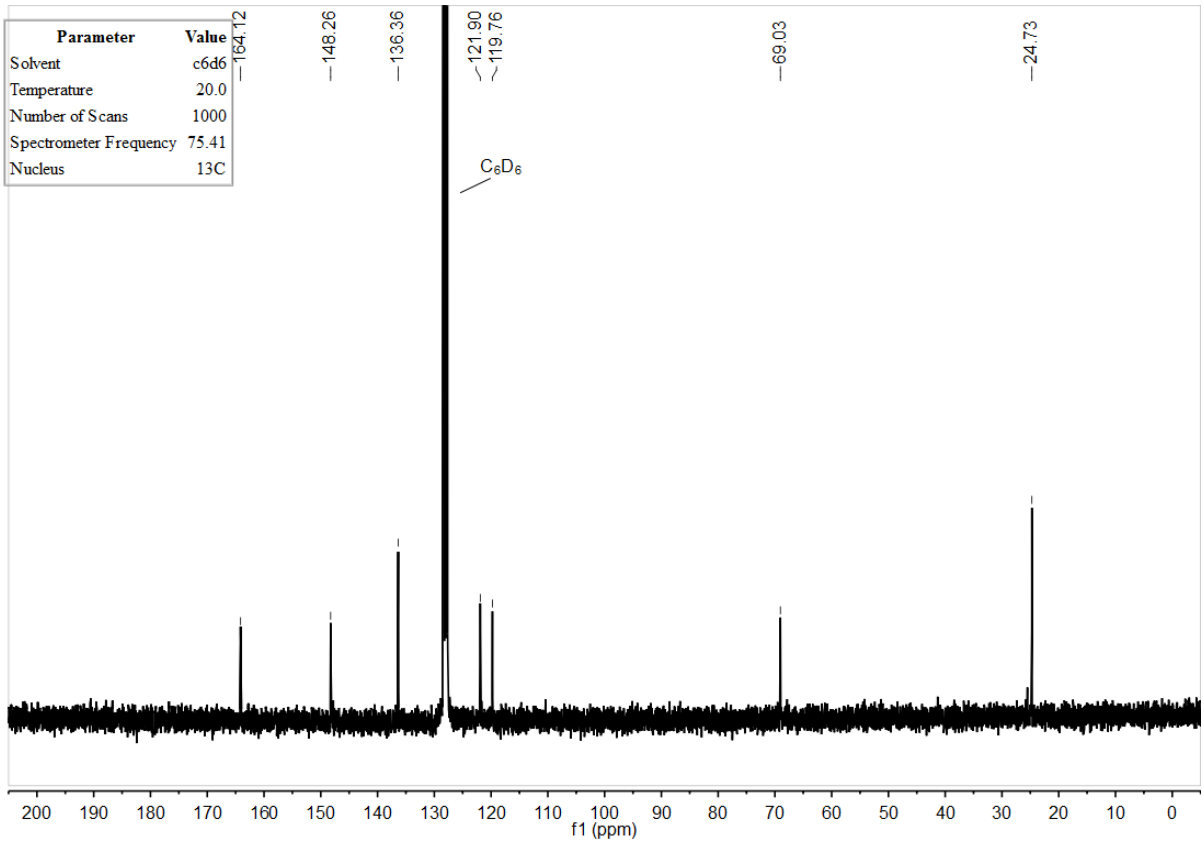




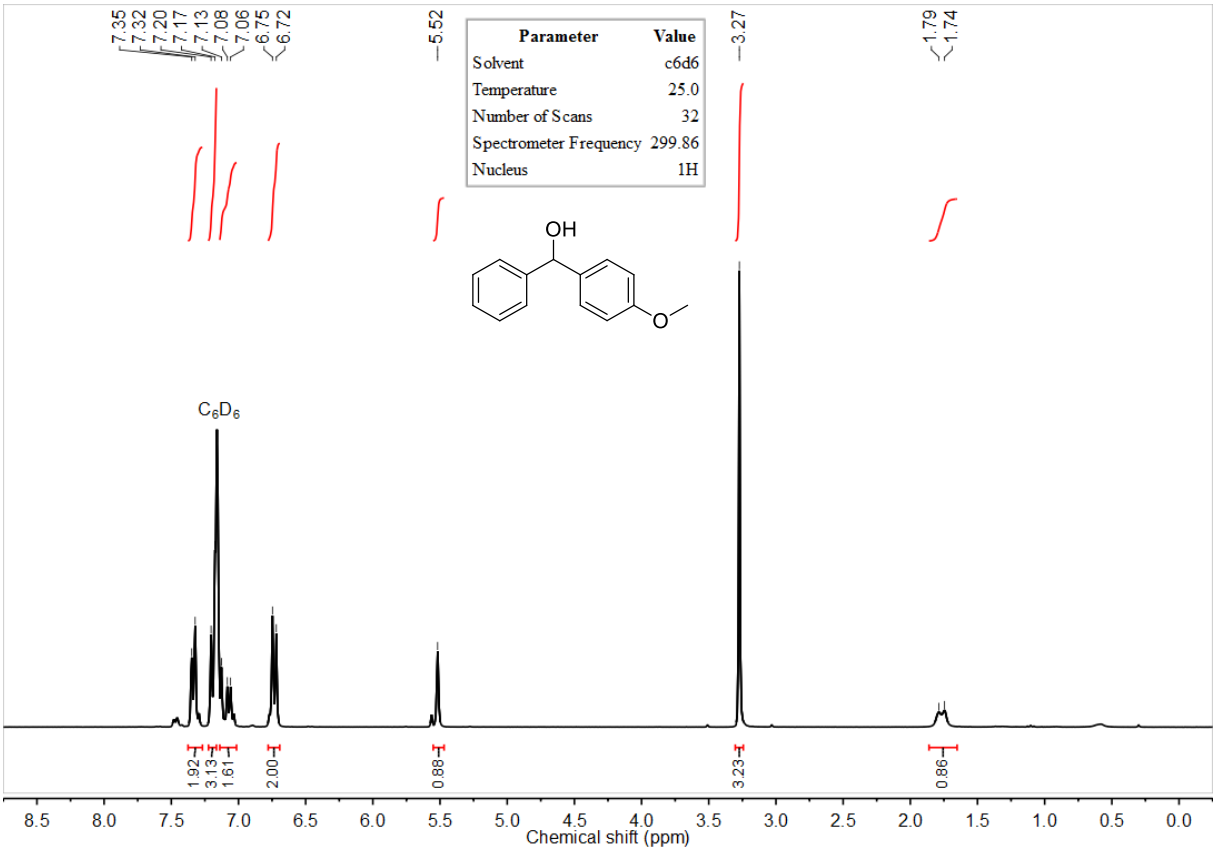

Parameter Value
Solvent c6d6
Temperature 25.0
Number of Scans 64
Spectrometer Frequency 282.13
Nucleus 19F
OH
F
-120.34
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -120 -140 -160 -180
Chemical shift (ppm)

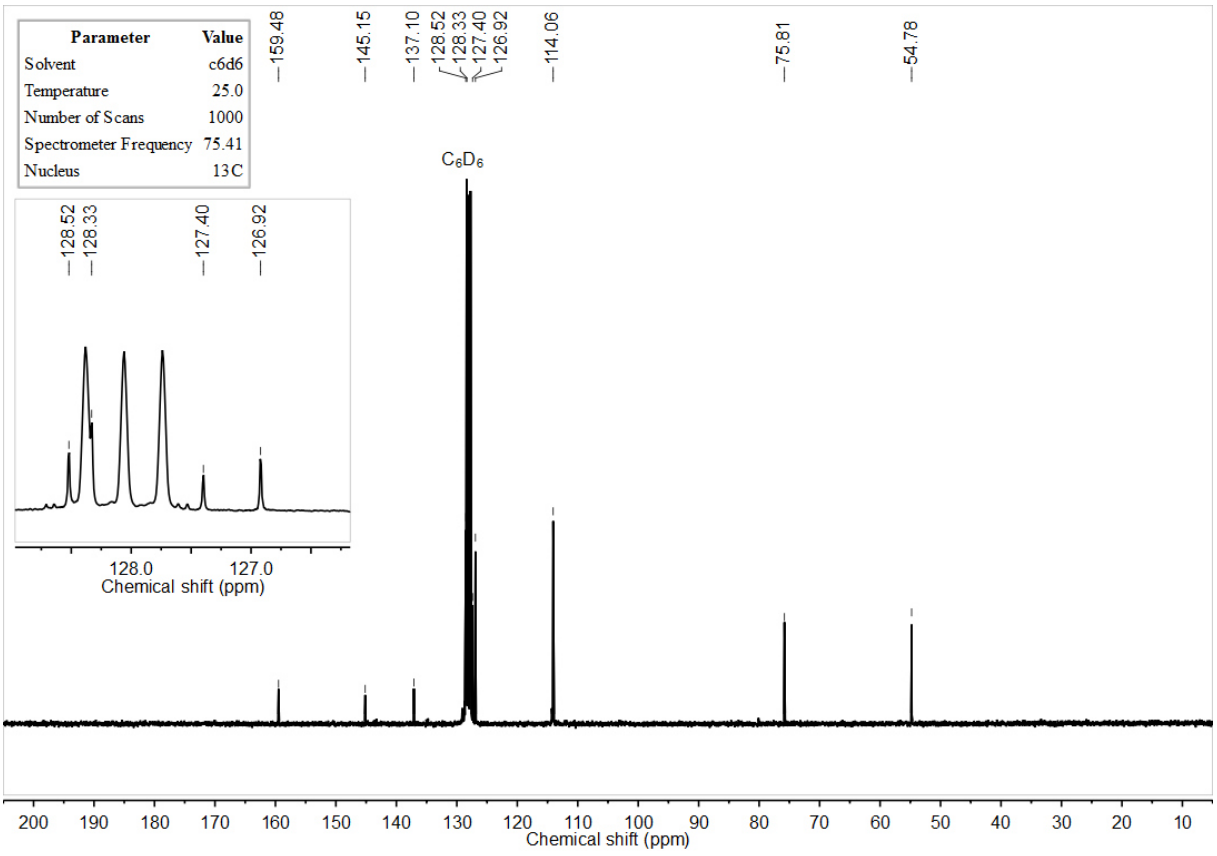
1-(pyridin-2-yl)ethanol (4o)



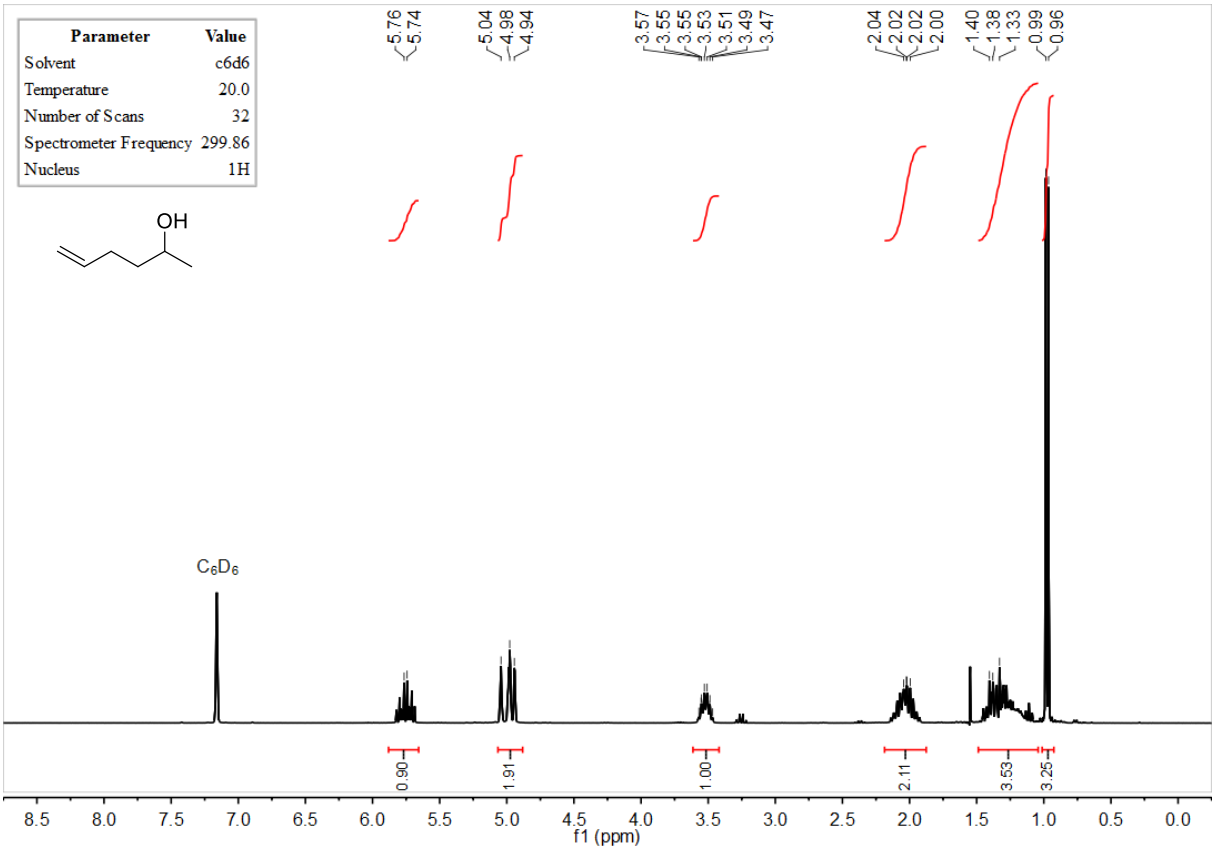


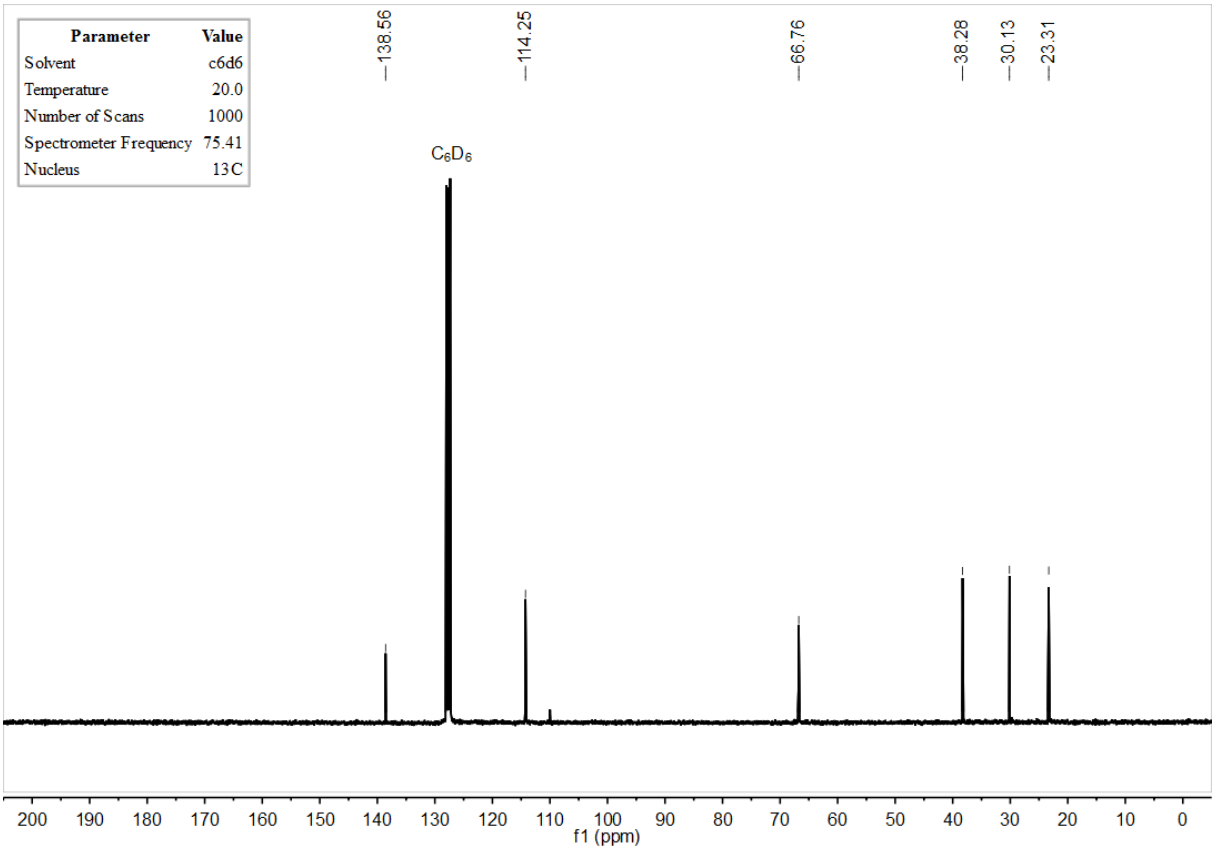
(4-methoxyphenyl)(phenyl)methanol (4s)



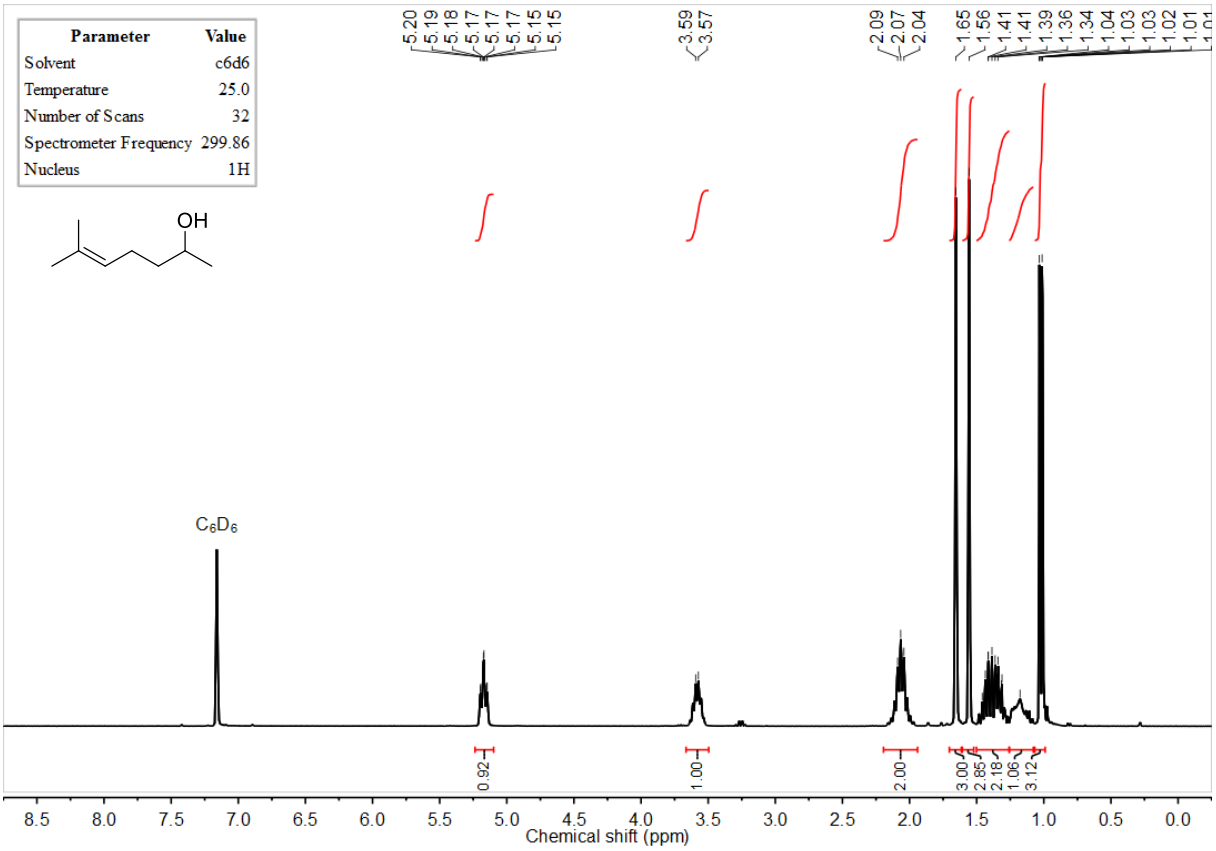


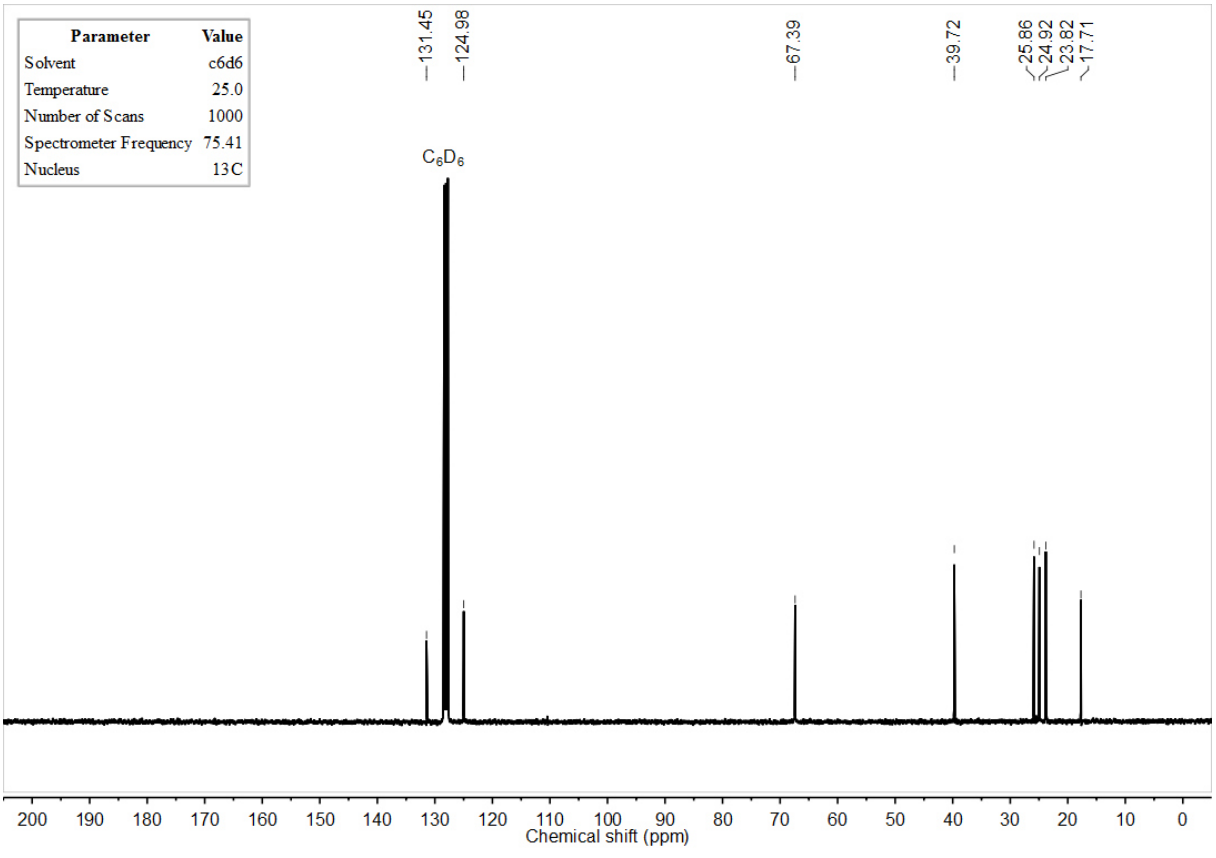
hex-5-en-2-ol (5d)



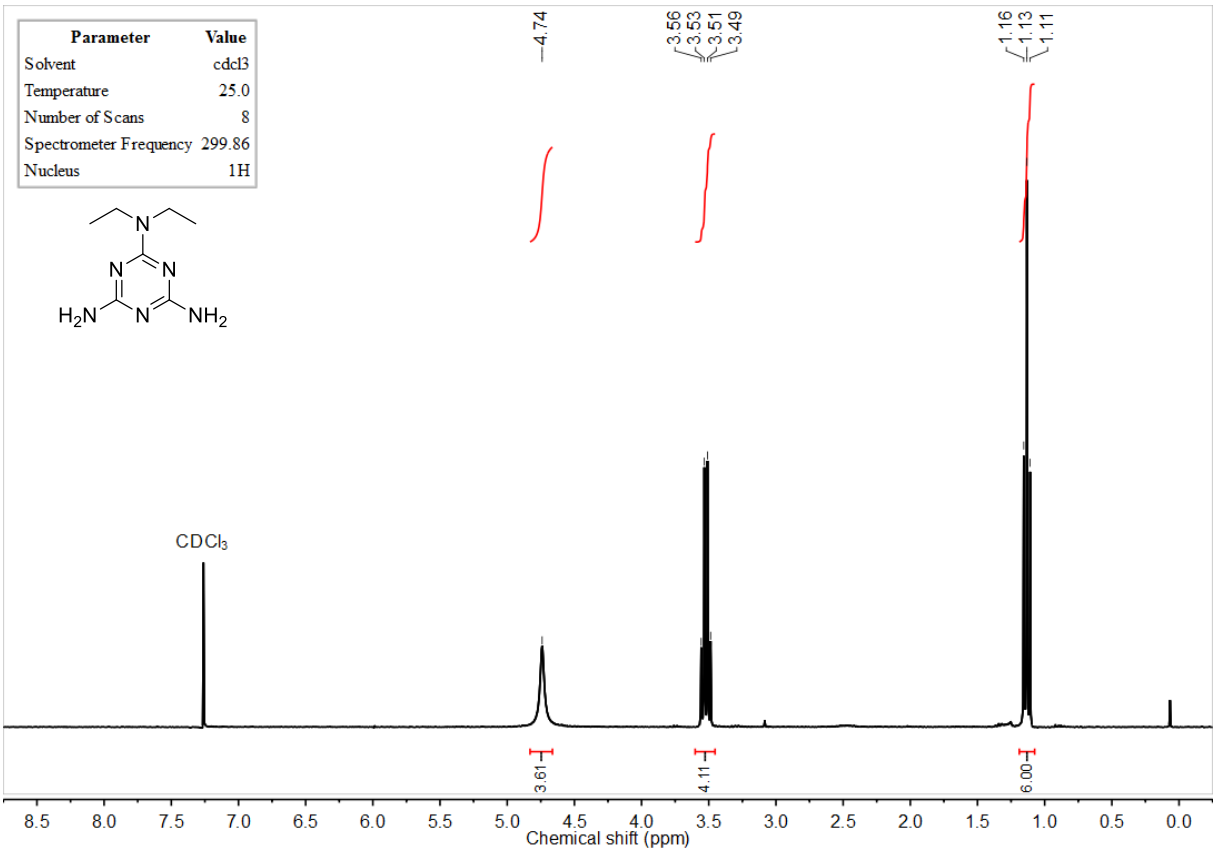


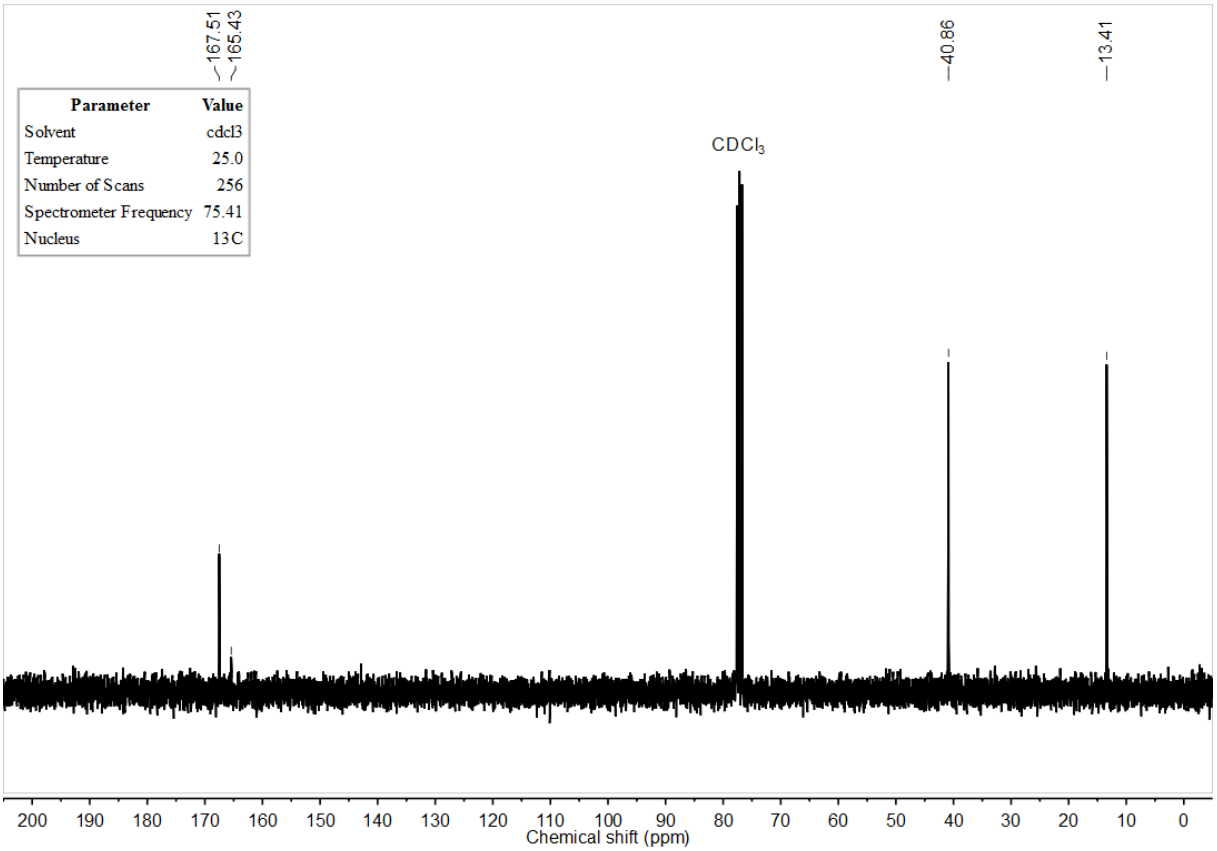
6-methylhept-5-en-2-ol (5e)

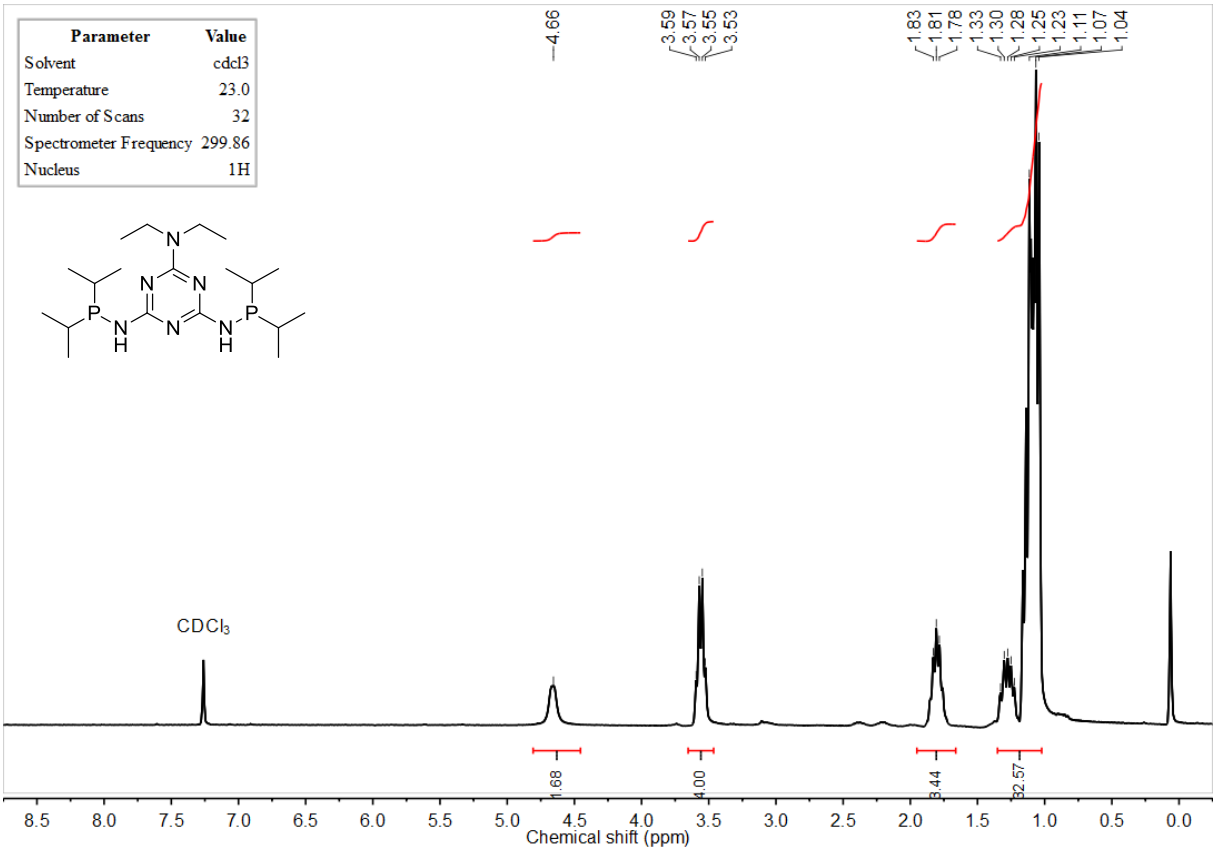




NMR spectra of ligands



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Spectrometer Frequency 299.86
Nucleus 1H
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3.59
3.57
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1.81
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1.33
1.30
1.28
1.25
1.23
1.11
1.07
1.04
CDCl3
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4.00
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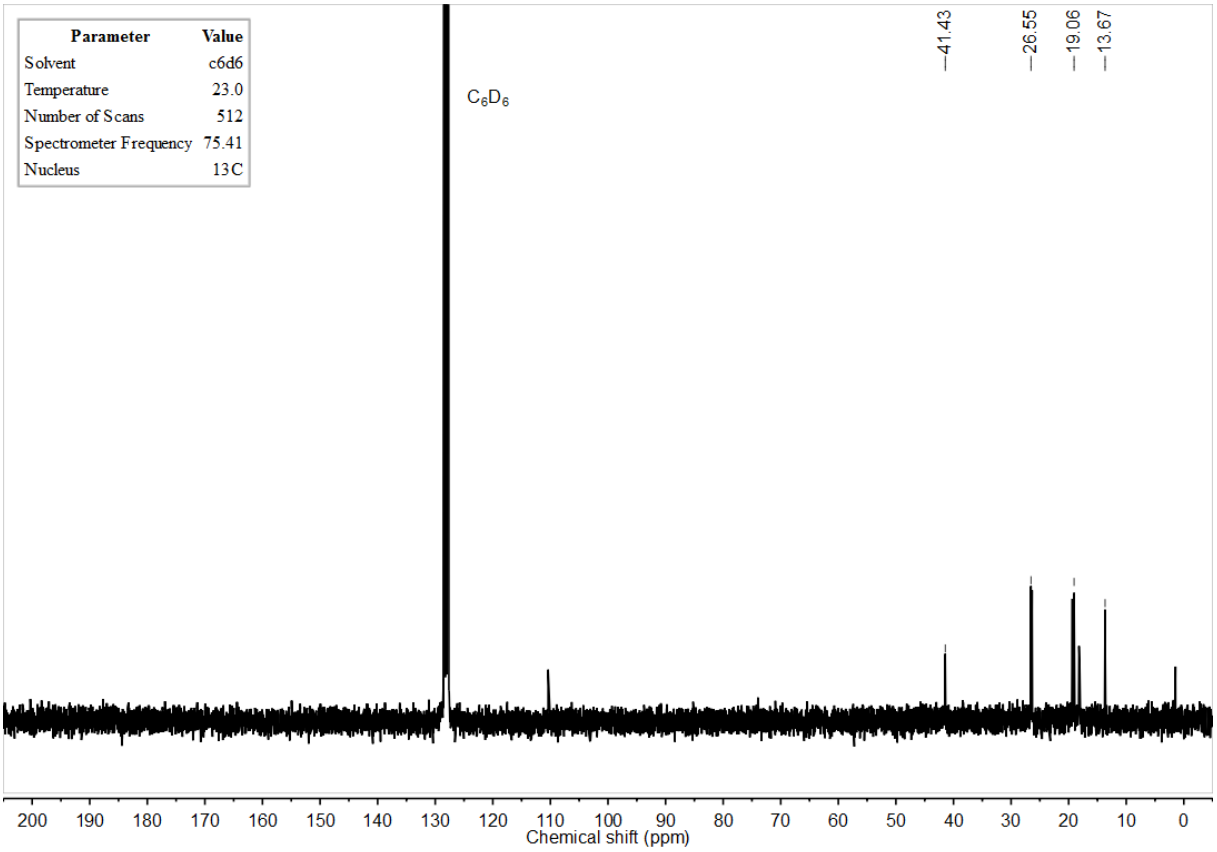
32.57
Chemical shift (ppm)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Spectrometer Frequency 75.41
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C6D6
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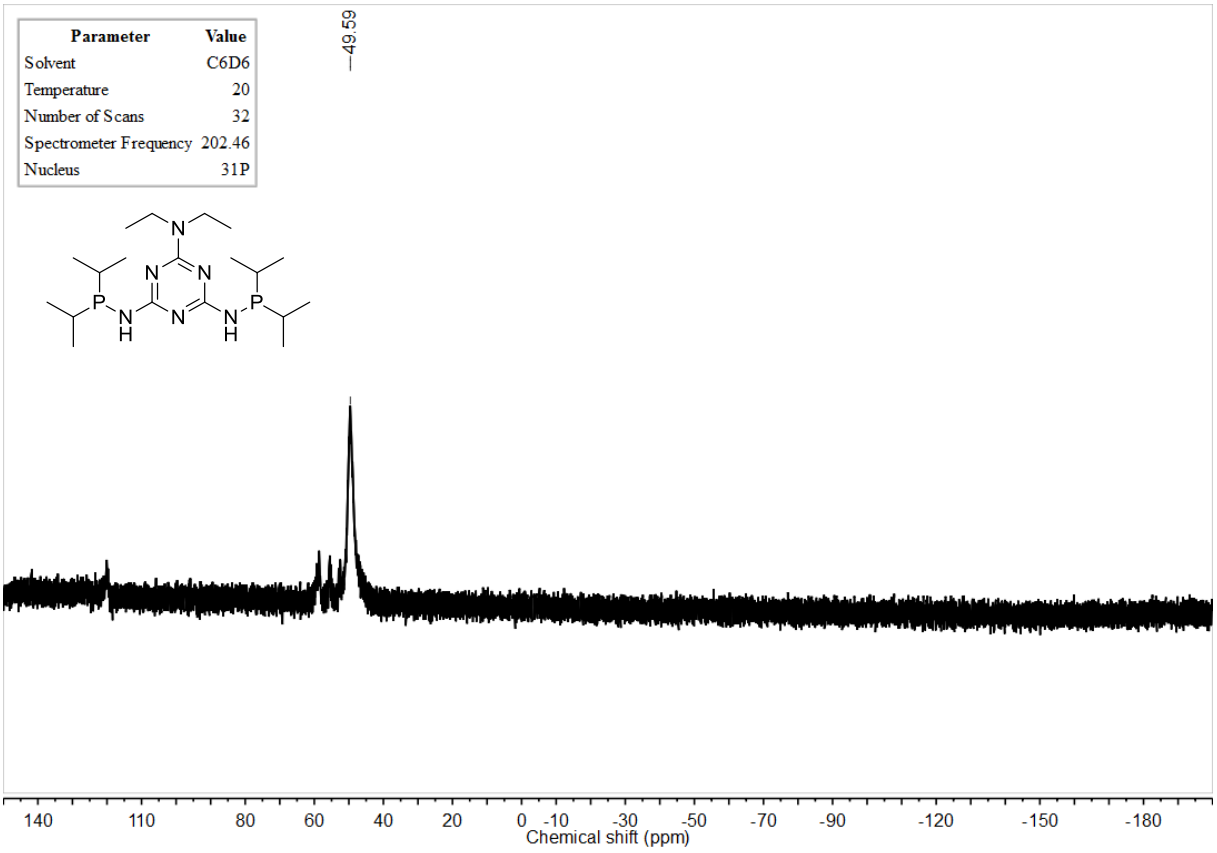
13.67
Chemical shift (ppm)


Parameter Value
Solvent C6D6
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Number of Scans 32
Spectrometer Frequency 202.46
Nucleus 31P
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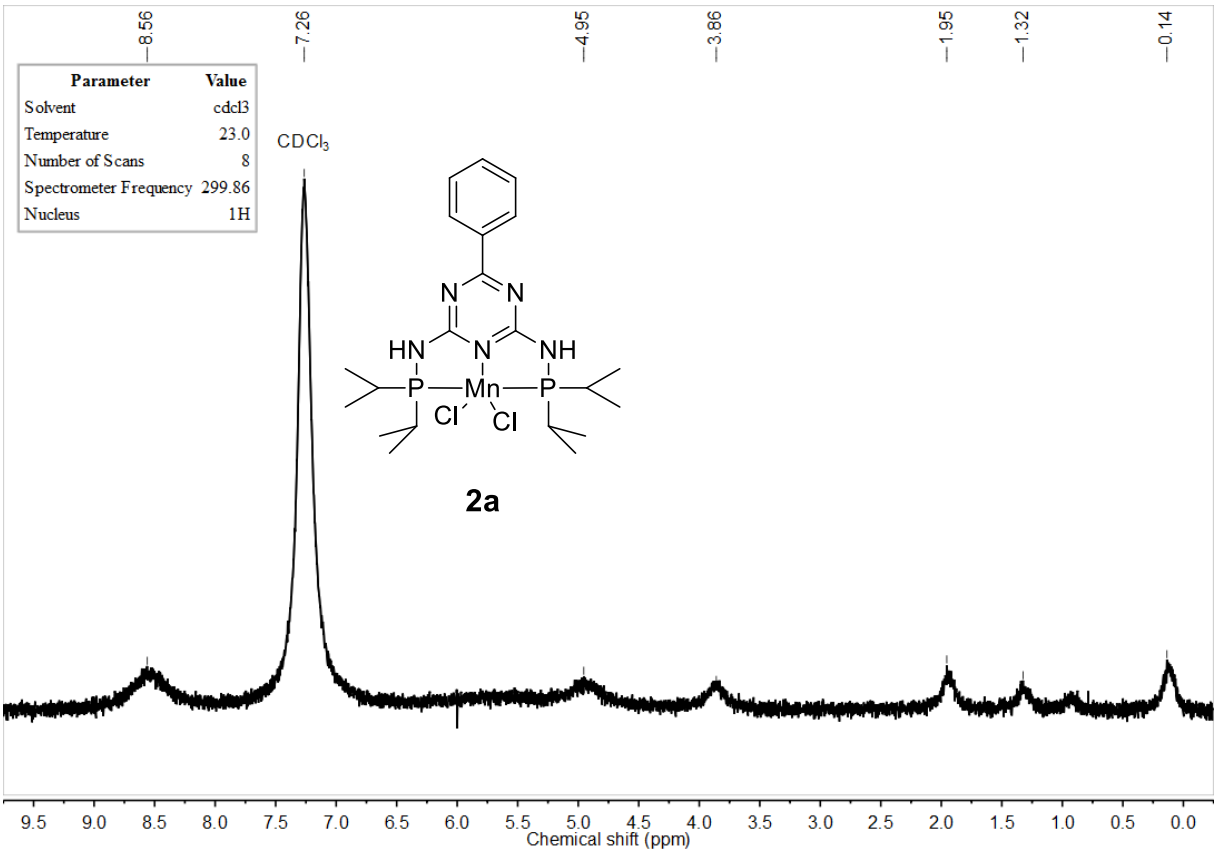
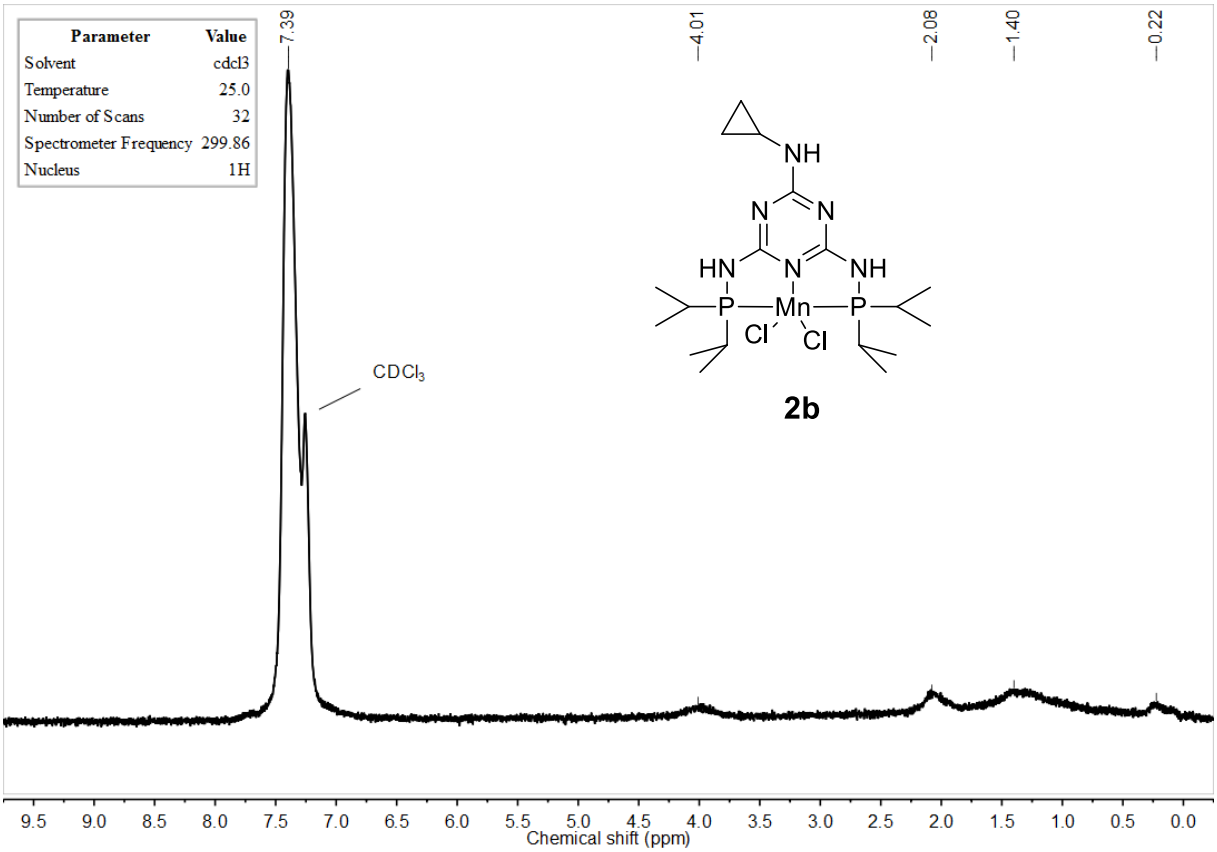
140 110 80 60 40 20 0 -10 -30 -50 -70 -90 -120 -150 -180
Chemical shift (ppm)

^{1}H NMR spectra of complexes

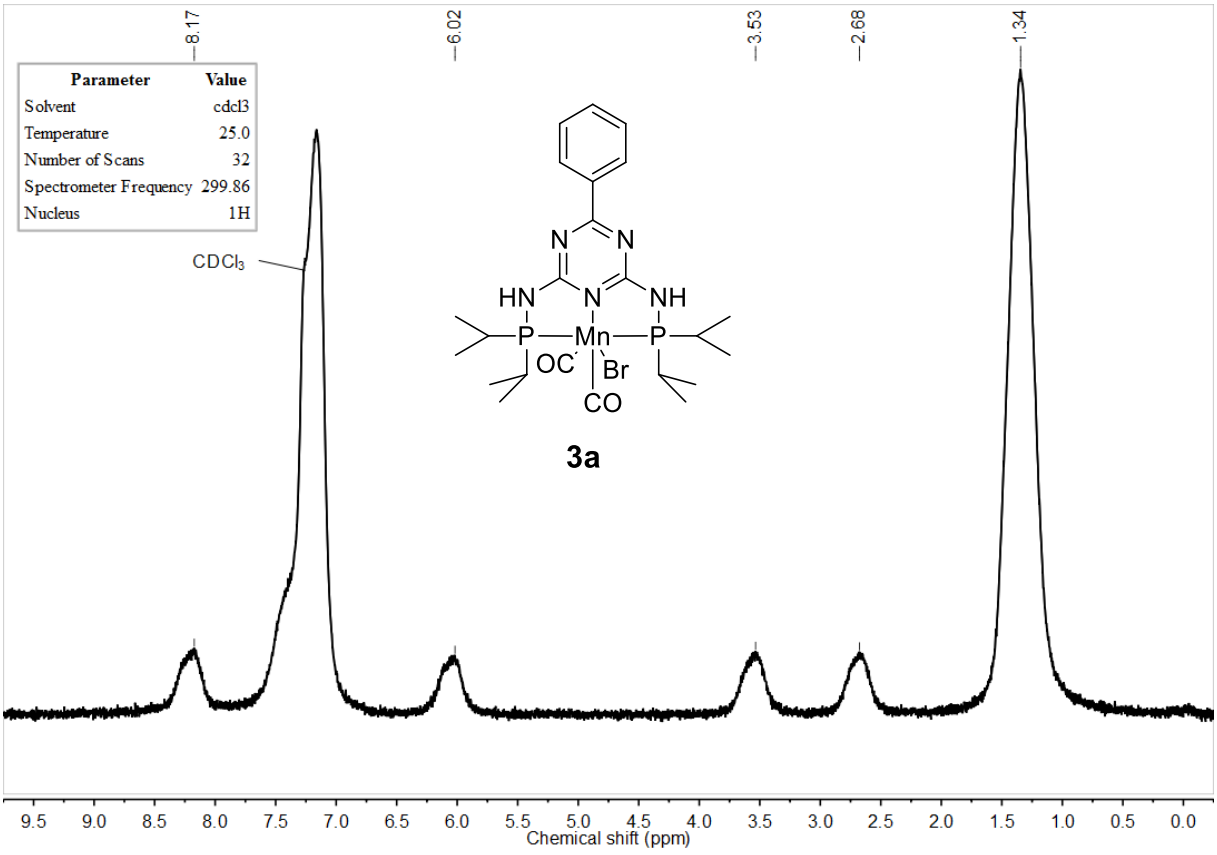
^{1}H NMR spectra of **2a**



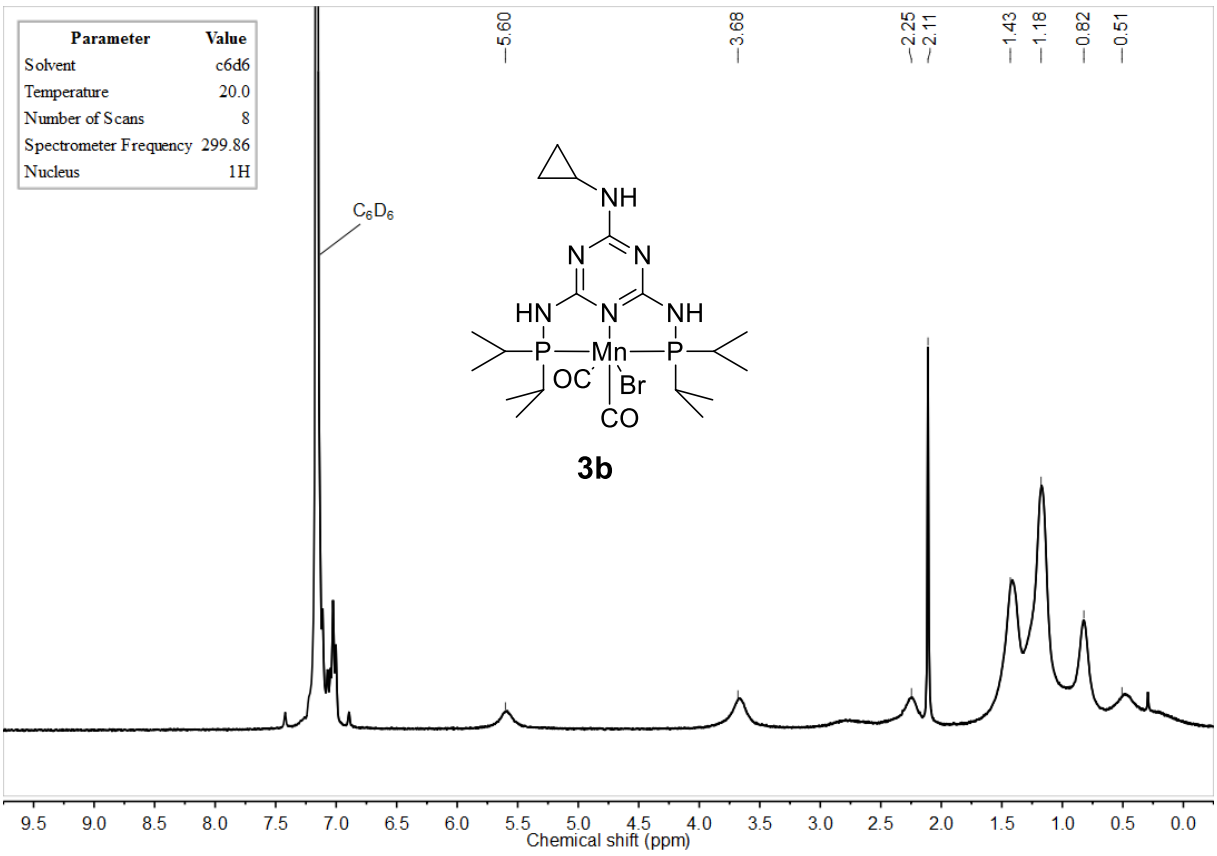
^{1}H NMR spectra of **2b**



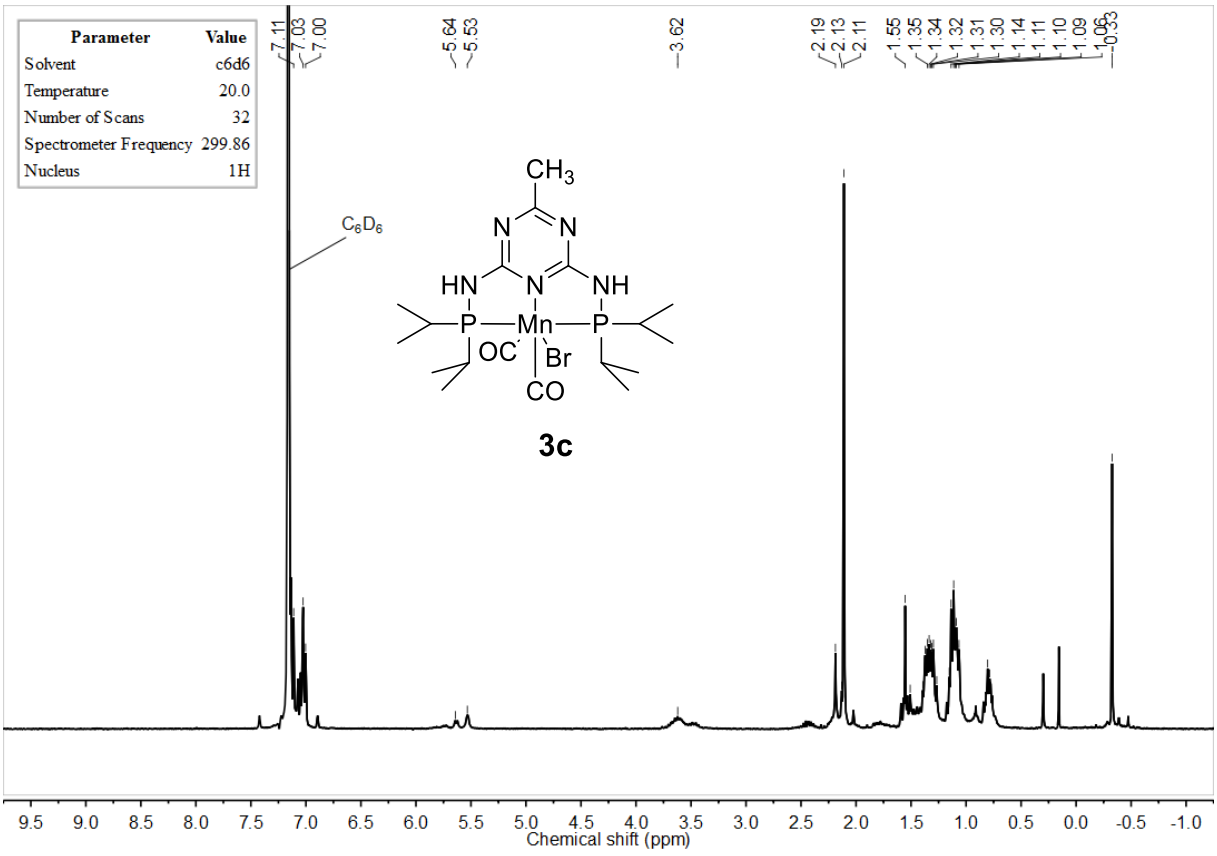
^{1}H NMR spectra of **3a**



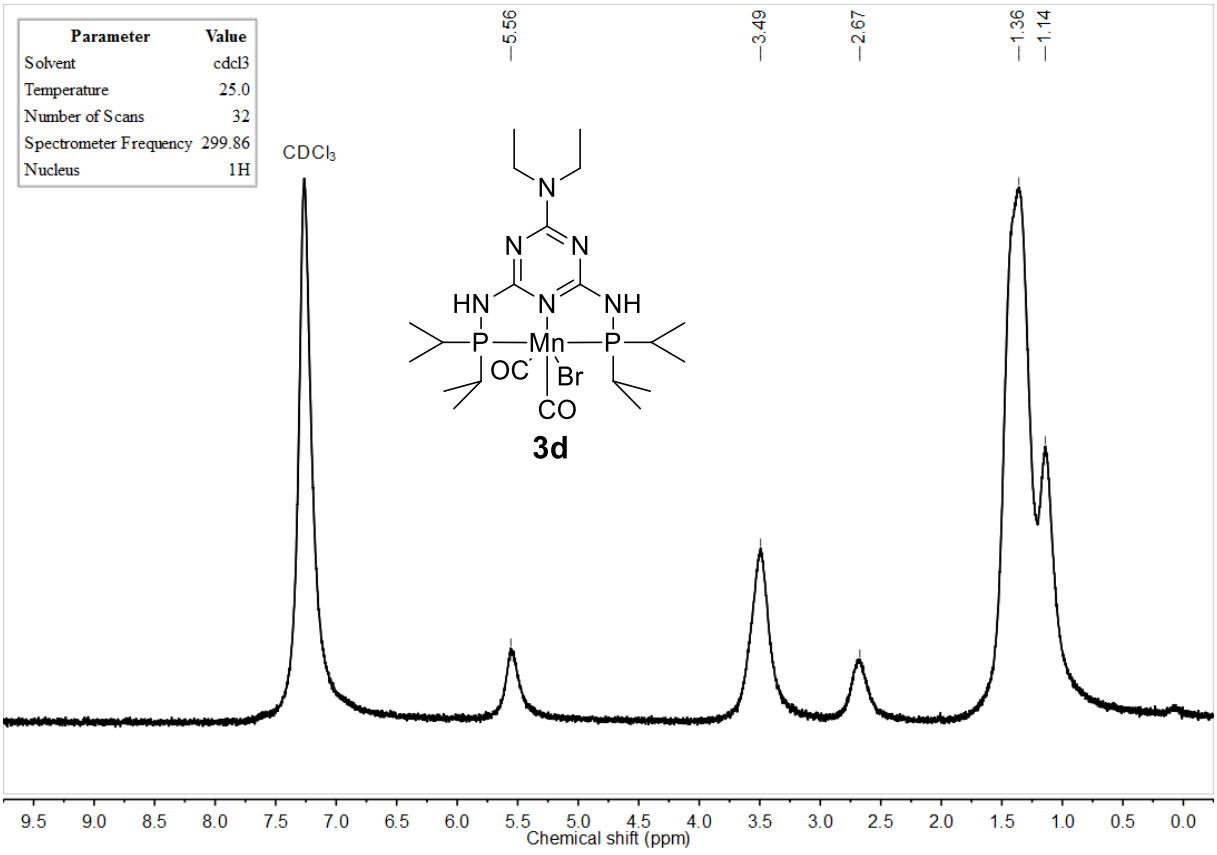
^{1}H NMR spectra of **3b**



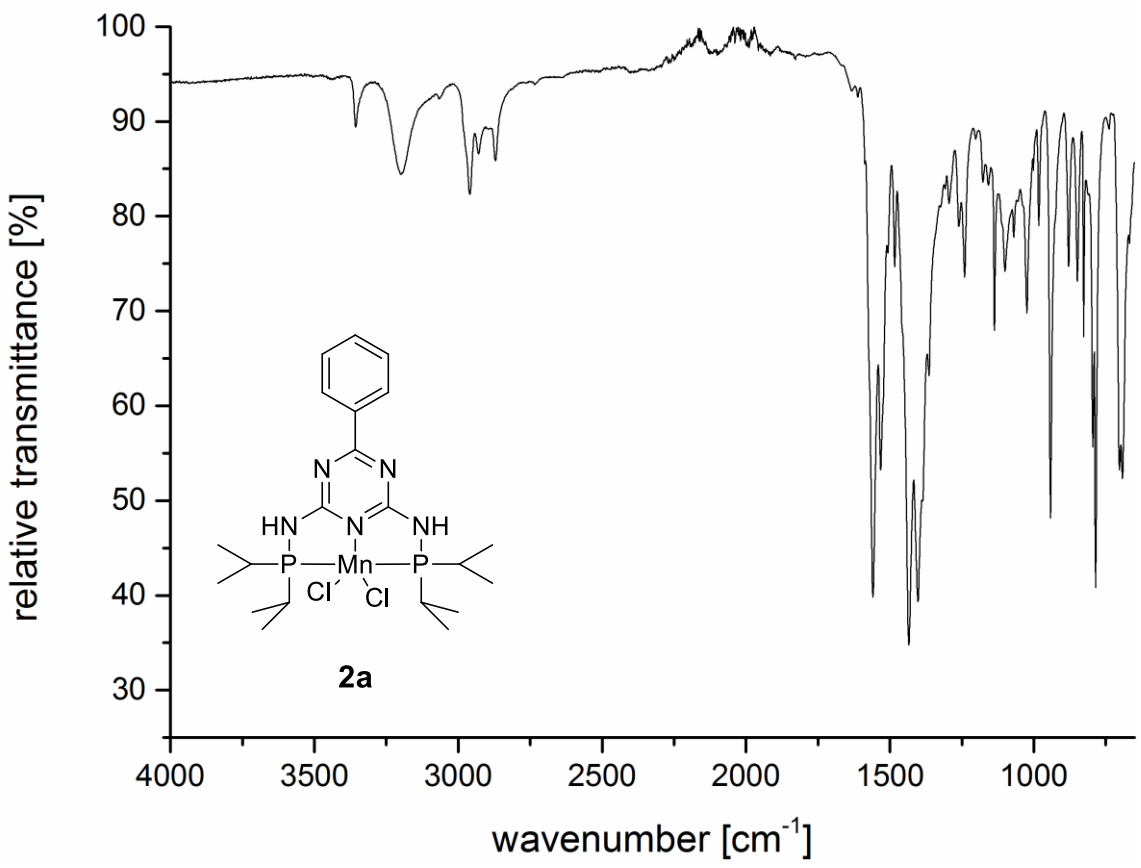
^{1}H NMR spectra of **3c**

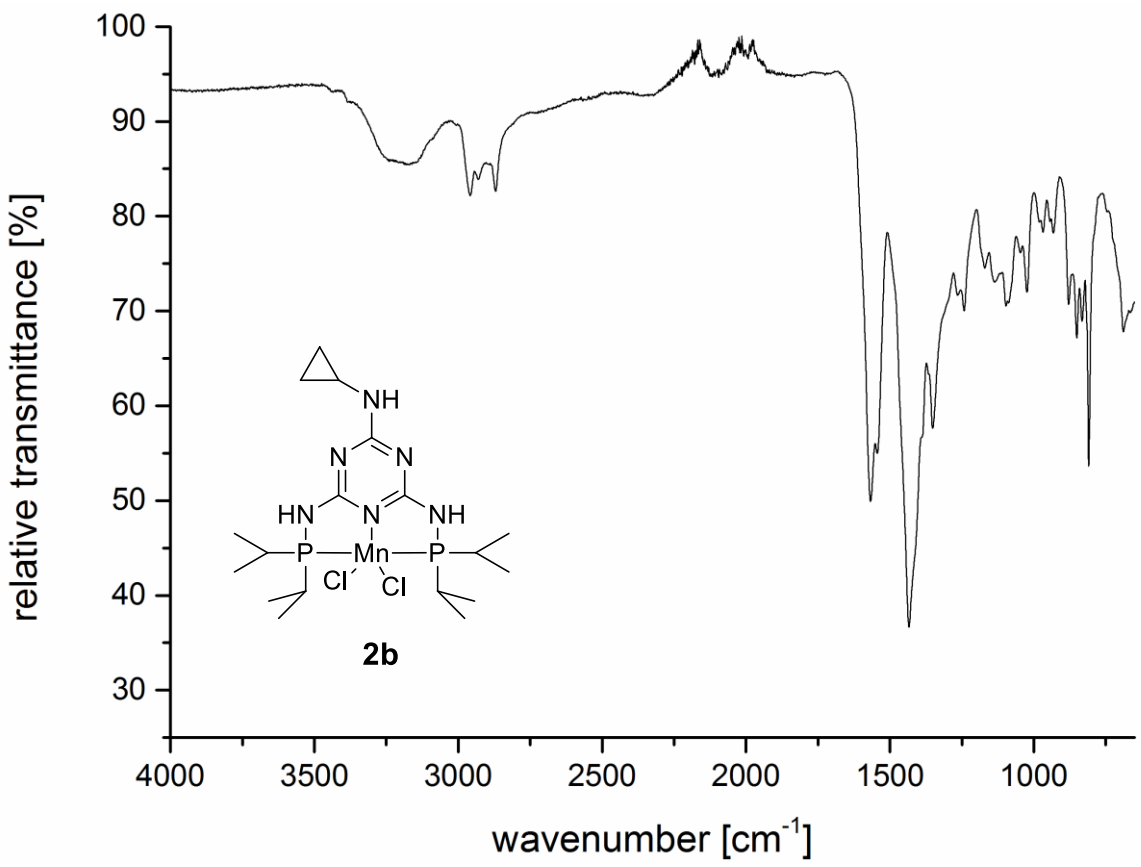


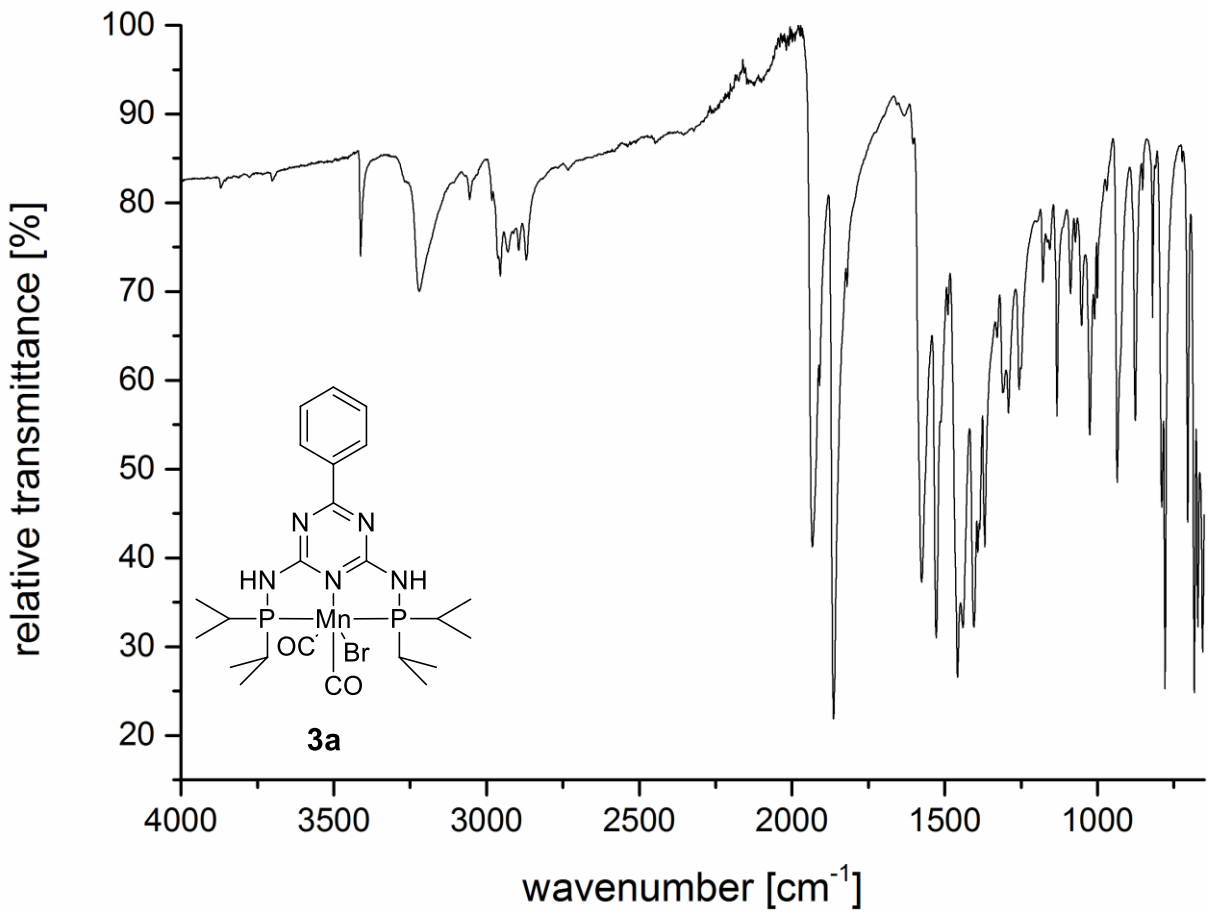
^{1}H NMR spectra of **3d**

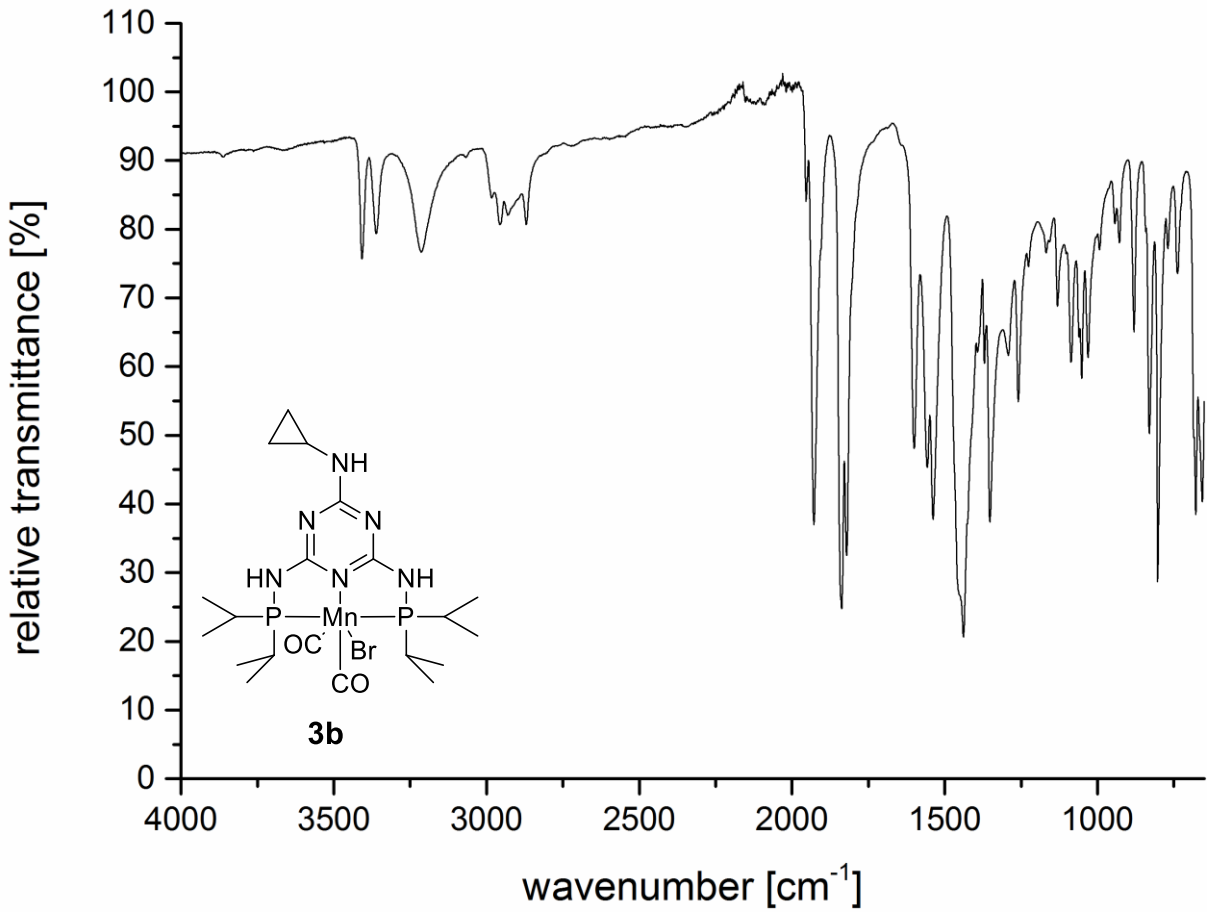


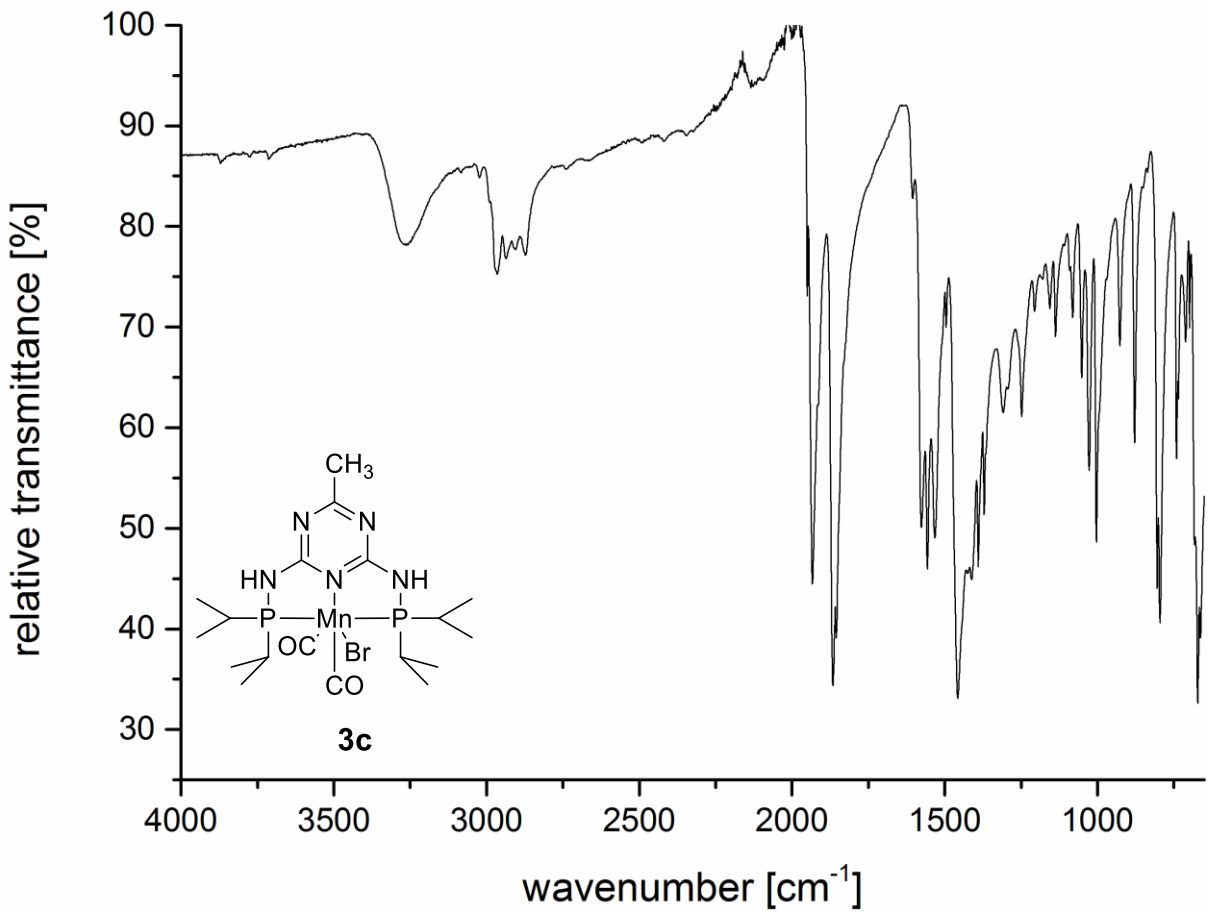
IR Spectra

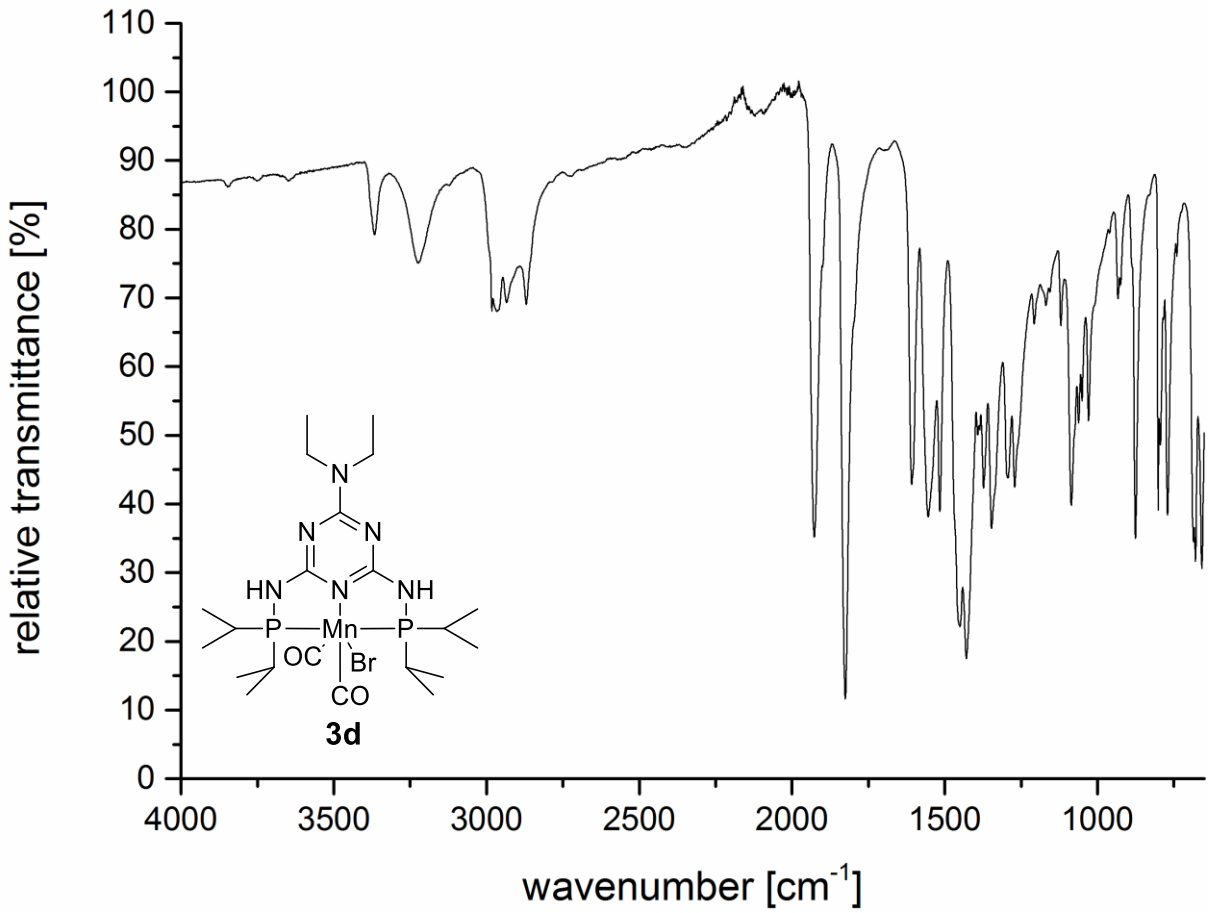

relative transmittance [%]
wavenumber [cm-1]
2a


relative transmittance [%]
wavenumber [cm-1]
2b


relative transmittance [%]
wavenumber [cm-1]
3a

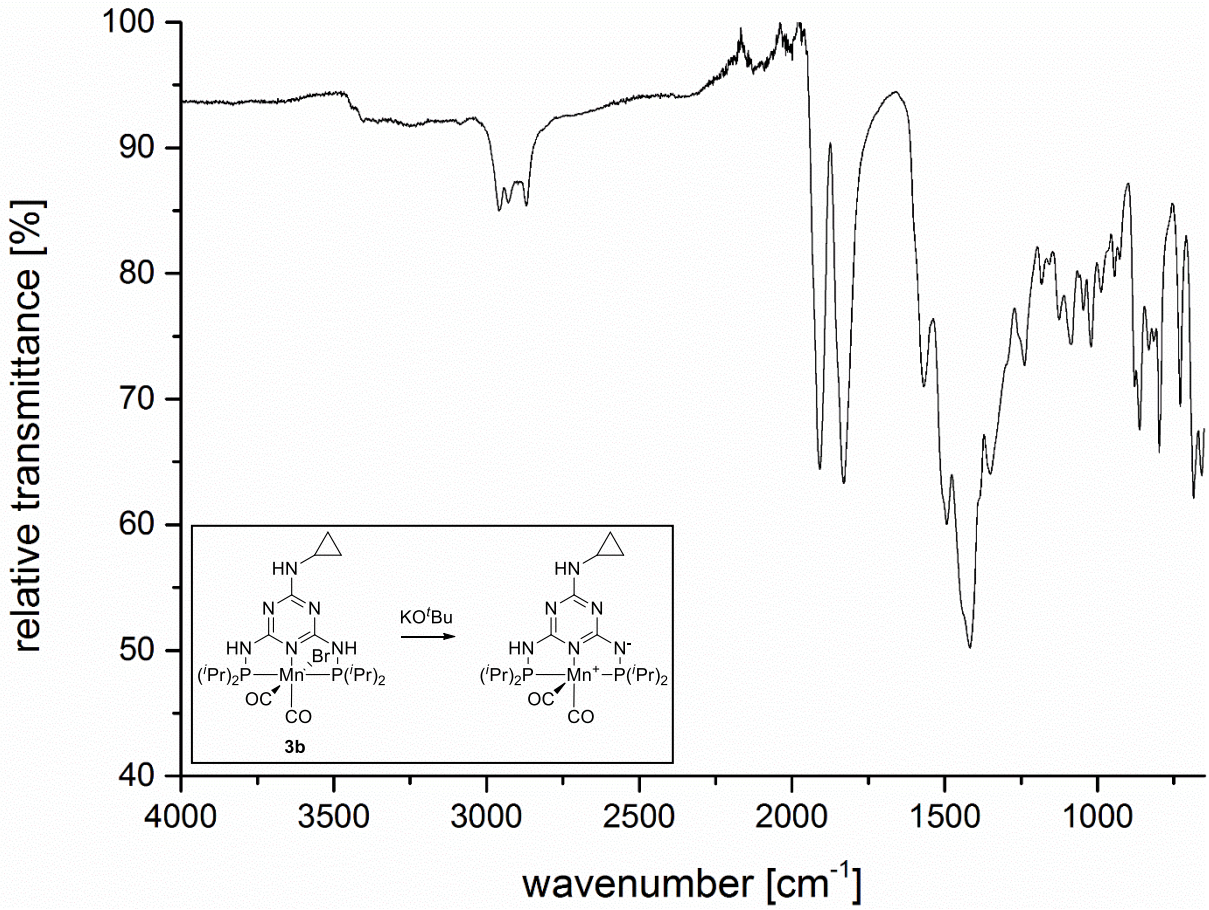

relative transmittance [%]
wavenumber [cm-1]
3b


relative transmittance [%]
wavenumber [cm-1]
CH3
N
N
HN
N
NH
P
Mn
P
OC
Br
CO
3c


relative transmittance [%]
wavenumber [cm-1]
N
N
N
HN
N
NH
P
Mn
P
OC
Br
CO
3d

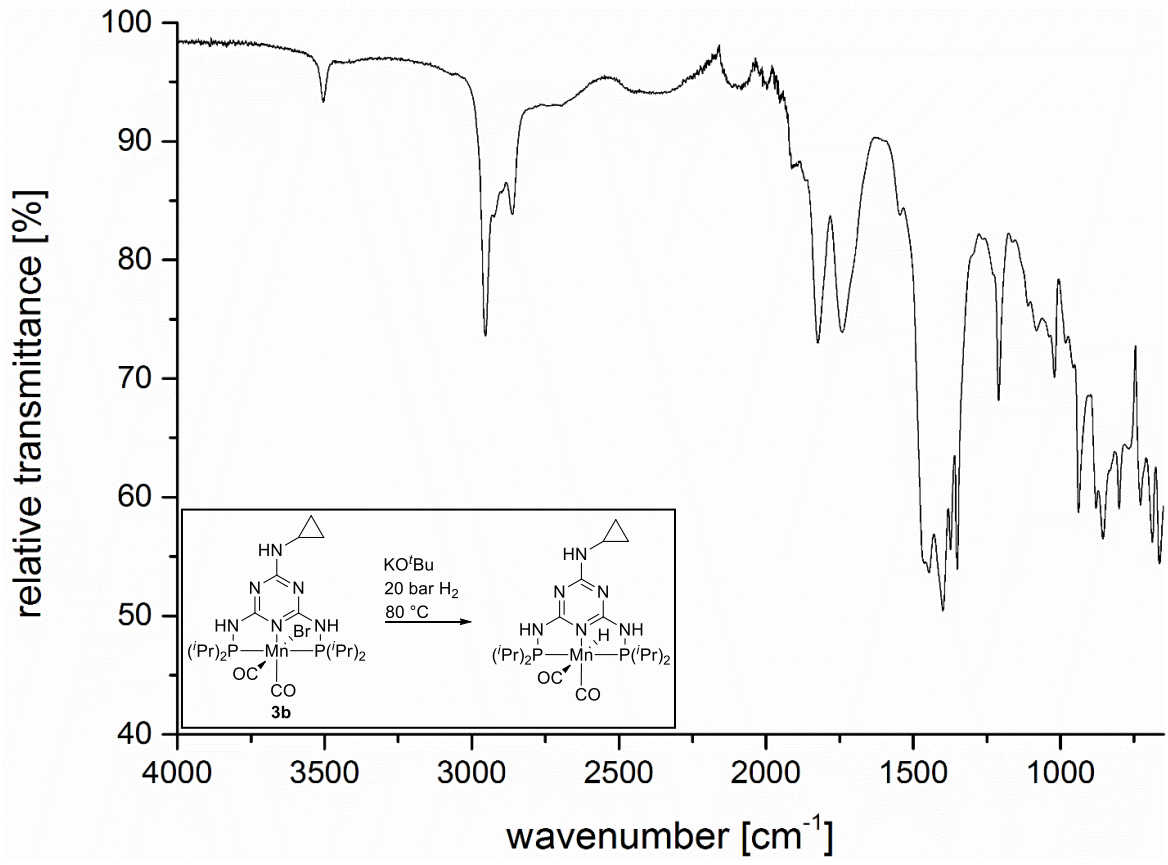
Activation of 3b with KO^{t}Bu:

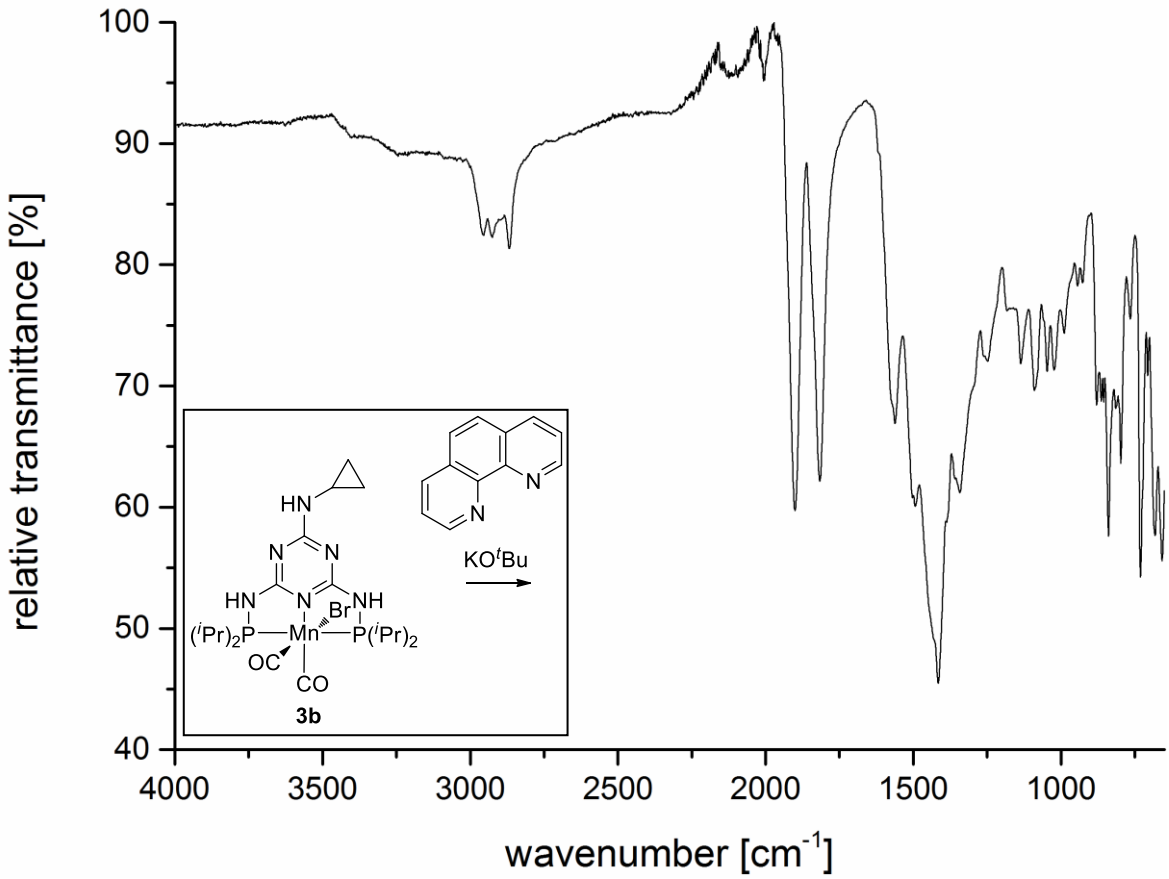
To a solution of **3b** (0.5 mmol, 295 mg, 1 eq) in toluene (10 mL) in a Schlenk tube, potassium *tert*-butoxide (0.5 mmol, 56 mg, 1 eq) was added inside a glovebox. The mixture was then heated to 80 °C for 1 h. After cooling to room temperature, all volatiles were removed under reduced pressure. The resulting solid was then suspended in toluene (5 mL) and the solution was filtered off and dried *in vacuo* to yield a blue powder. ATR-IR: 1908 (ν_{CO}), 1830 (ν_{CO}) cm^{-1}.



Activation of 3b "*in situ*" under hydrogen pressure:

A glass vial was subsequently charged with **3b** (0.1 mmol, 59 mg, 1 eq), KO^{t}Bu (0.1 mmol, 11.2 mg, 1 eq) and toluene (1.5 mL). The glass vial was then placed in an autoclave, which was pressurized to 20 bar hydrogen after purging it 5 times. The autoclave was then heated to 80 °C for 1 h. Afterwards the pressure was reduced to 1 bar and the autoclave was put inside a glovebox. The reaction solution had turned colourless and was directly placed on an IR spectrometer. ATR-IR: 1825 (ν_{CO}), 1740 (ν_{CO}) cm^{-1}.

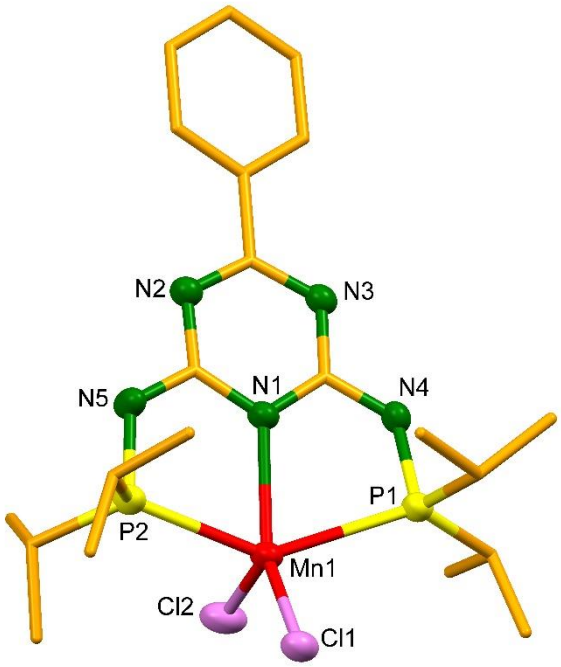



relative transmittance [%]
wavenumber [cm-1]
100
90
80
70
60
50
40
4000
3500
3000
2500
2000
1500
1000
KOtBu
3b

Crystallographic data

Compound	**2a**	**3b**
Formula	$C_{21}H_{35}Cl_2MnN_5P_2$	$C_{20}H_{36}BrMnN_6O_2P_2$
Formula weight	545.33	589.33
Crystal system	triclinic	orthorhombic
Space group	$P\bar{1}$	$P2_12_12_1$
a [Å]	13.644(5)	9.731(5)
b [Å]	15.533(5)	14.214(5)
c [Å]	17.006(5)	21.861(5)
α [°]	101.726(5)	90.000(5)
β [°]	95.589(5)	90.000(5)
γ [°]	100.739(5)	90.000(5)
Cell volume [Å³]	3433(2)	3024(2)
Z	2	4
Crystal size [mm³]	0.533 x 0.296 x 0.164	0.286 x 0.157 x 0.097
Habit	block	block
Color	yellow	orange
Density [gcm^{-3}]	1.264	1.466
T [K]	133(2)	133(2)
Theta range	1.235-28.42	1.709-25.998
Unique reflections	13235	5931
Observed reflections [I>2s(I)]	8989	5023
Parameters	726	363
wR2 (all data)	0.1332	0.0787
R [I>2s(I)]	0.0521	0.0383

Crystallographic data of 2a



checkCIF/PLATON report of 2a

Structure factors have been supplied for datablock(s) shelx

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: shelx

```
Bond precision: C-C = 0.0080 A        Wavelength=0.71069

Cell:      a=13.644(5)          b=15.533(5)     c=17.006(5)
           alpha=101.726(5)     beta=95.589(5)  gamma=100.739(5)
Temperature: 133 K

                      Calculated                Reported
Volume                3433(2)                   3433(2)
Space group           P -1                      P -1
Hall group            -P 1                      -P 1
Moiety formula
                      2(C21 H35 Cl2 Mn N5 P2),
                      3(C4 H8 O)
                                                C42 H70 Cl4 Mn2 N10
                                                P4,3(C4 H8 O)
Sum formula           C54 H94 Cl4 Mn2 N10 O3 P4 C54 H94 Cl4 Mn2 N10
                                                 O3 P4
Mr                    1306.95                   1306.95
```

Dx,g cm-3	1.264	1.264
Z	2	2
Mu (mm-1)	0.662	0.662
F000	1380.0	1380.0
F000'	1383.66	
h,k,lmax	16,19,20	16,19,20
Nref	13494	13235
Tmin,Tmax	0.790,0.897	0.899,0.962
Tmin'	0.703	

Correction method= # Reported T Limits: Tmin=0.899 Tmax=0.962
AbsCorr = NUMERICAL

Data completeness= 0.981 Theta(max)= 25.998

R(reflections)= 0.0521(8989) wR2(reflections)= 0.1442(13235)

S = 0.918 Npar= 726

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

PLAT243_ALERT_4_C High 'Solvent' Ueq as Compared to Neighbors of C46 Check
PLAT243_ALERT_4_C High 'Solvent' Ueq as Compared to Neighbors of C53 Check
PLAT244_ALERT_4_C Low 'Solvent' Ueq as Compared to Neighbors of O1 Check
PLAT244_ALERT_4_C Low 'Solvent' Ueq as Compared to Neighbors of C44 Check
PLAT244_ALERT_4_C Low 'Solvent' Ueq as Compared to Neighbors of O3 Check
PLAT244_ALERT_4_C Low 'Solvent' Ueq as Compared to Neighbors of C52 Check
PLAT341_ALERT_3_C Low Bond Precision on C-C Bonds ..... 0.008 Ang.
PLAT352_ALERT_3_C Short N-H (X0.87,N1.01A) N5 - H5N .. 0.74 Ang.
PLAT360_ALERT_2_C Short C(sp3)-C(sp3) Bond C52 - C53 .. 1.38 Ang.
PLAT411_ALERT_2_C Short Inter H...H Contact H54B .. H54B .. 2.05 Ang.
PLAT906_ALERT_3_C Large K value in the Analysis of Variance ..... 4.411 Check
PLAT911_ALERT_3_C Missing # FCF Refl Between THmin & STh/L= 0.600 253 Report
PLAT976_ALERT_2_C Check Calcd Residual Density 0.71A From O3 -0.49 eA-3

Alert level G

PLAT002_ALERT_2_G Number of Distance or Angle Restraints on AtSite 2 Note
PLAT003_ALERT_2_G Number of Uiso or Uij Restrained non-H Atoms ... 7 Report
PLAT042_ALERT_1_G Calc. and Reported MoietyFormula Strings Differ Please Check
PLAT154_ALERT_1_G The s.u.'s on the Cell Angles are Equal ..(Note) 0.005 Degree
PLAT172_ALERT_4_G The CIF-Embedded .res File Contains DFIX Records 1 Report
PLAT186_ALERT_4_G The CIF-Embedded .res File Contains ISOR Records 2 Report
PLAT432_ALERT_2_G Short Inter X...Y Contact O3 .. C50 .. 2.97 Ang.
PLAT860_ALERT_3_G Number of Least-Squares Restraints ..... 43 Note
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 6 Note
PLAT913_ALERT_3_G Missing # of Very Strong Reflections in FCF .... 1 Note
PLAT961_ALERT_5_G Dataset Contains no Negative Intensities ..... Please Check
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density 1 Note

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0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
13 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
12 **ALERT level G** = General information/check it is not something unexpected

2 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
7 ALERT type 2 Indicator that the structure model may be wrong or deficient
6 ALERT type 3 Indicator that the structure quality may be low
9 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

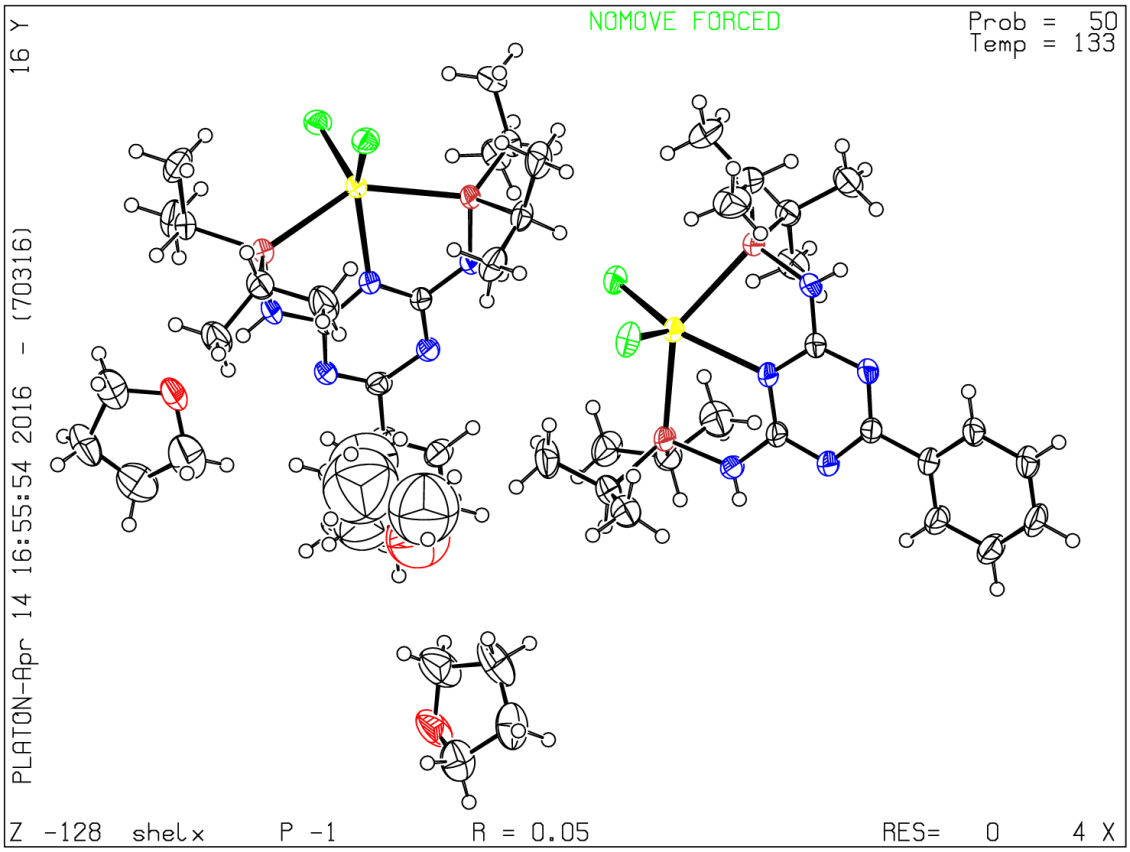
Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

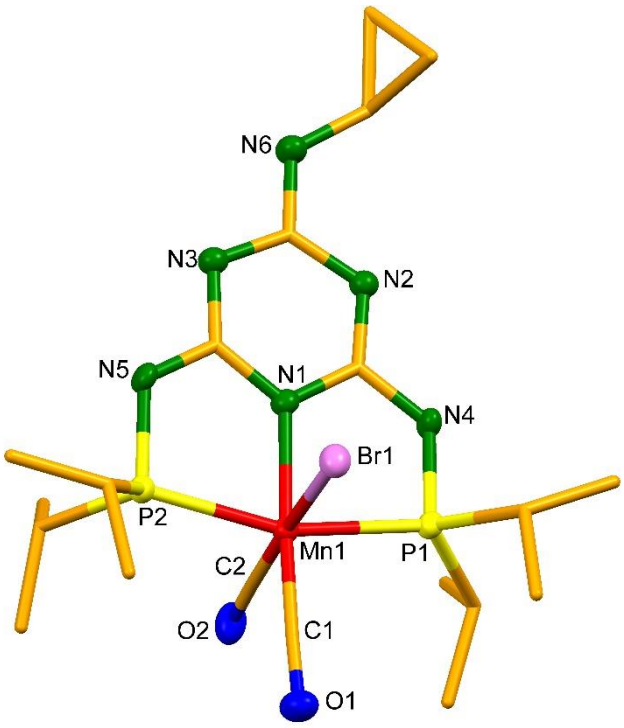
Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 30/03/2016; check.def file version of 30/03/2016



Crystallographic data of 3b



checkCIF/PLATON report of 3b

Structure factors have been supplied for datablock(s) shelx

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: shelx

Bond precision: C-C = 0.0117 A Wavelength=0.71069

Cell:	a=9.731(5)	b=14.214(5)	c=21.861(5)
	alpha=90	beta=90	gamma=90

Temperature: 133 K

	Calculated	Reported
Volume	3024(2)	3024(2)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C20 H36 Br Mn N6 O2 P2, C6 H6	C20 H36 Br Mn N6 O2 P2, C6H6

Sum formula	C26 H42 Br Mn N6 O2 P2	C26 H42 Br Mn N6 O2 P2
Mr	667.44	667.44
Dx,g cm-3	1.466	1.466
Z	4	4
Mu (mm-1)	1.898	1.898
F000	1384.0	1384.0
F000’	1385.36	
h,k,lmax	12,17,26	12,17,26
Nref	5930[3344]	5931
Tmin,Tmax	0.706,0.832	0.902,0.951
Tmin’	0.575	

Correction method= # Reported T Limits: Tmin=0.902 Tmax=0.951

AbsCorr = NUMERICAL

Data completeness= 1.77/1.00 Theta(max)= 25.998

R(reflections)= 0.0383(5023) wR2(reflections)= 0.0827(5931)

S = 0.998 Npar= 363

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

Alert level C

PLAT147_ALERT_1_C s.u. on Symmetry Constrained Cell Angle(s) ..... Please Check

PLAT222_ALERT_3_C Non-Solvent Resd 1 H Uiso(max)/Uiso(min) Range 8.1 Ratio

PLAT245_ALERT_2_C U(iso) H4N Smaller than U(eq) N4 by ... 0.015 AngSq

PLAT245_ALERT_2_C U(iso) H5N Smaller than U(eq) N5 by ... 0.014 AngSq

PLAT245_ALERT_2_C U(iso) H6N Smaller than U(eq) N6 by ... 0.015 AngSq

PLAT250_ALERT_2_C Large U3/U1 Ratio for Average U(i,j) Tensor .... 2.2 Note

PLAT331_ALERT_2_C Small Average Phenyl C-C Dist. C21 -C26 1.36 Ang.

PLAT332_ALERT_2_C Large Phenyl C-C Range C21 -C26 0.17 Ang.

PLAT341_ALERT_3_C Low Bond Precision on C-C Bonds ..... 0.01171 Ang.

PLAT352_ALERT_3_C Short N-H (X0.87,N1.01A) N5 - H5N .. 0.68 Ang.

PLAT352_ALERT_3_C Short N-H (X0.87,N1.01A) N6 - H6N .. 0.75 Ang.

PLAT420_ALERT_2_C D-H Without Acceptor N4 -- H4N ... Please Check

PLAT420_ALERT_2_C D-H Without Acceptor N6 -- H6N ... Please Check

PLAT978_ALERT_2_C Number C-C Bonds with Positive Residual Density 0 Note

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Alert level G

PLAT002_ALERT_2_G Number of Distance or Angle Restraints on AtSite 3 Note

PLAT003_ALERT_2_G Number of Uiso or Uij Restrained non-H Atoms ... 2 Report

PLAT153_ALERT_1_G The s.u.'s on the Cell Axes are Equal ..(Note) 0.005 Ang.

PLAT172_ALERT_4_G The CIF-Embedded .res File Contains DFIX Records 2 Report

PLAT186_ALERT_4_G The CIF-Embedded .res File Contains ISOR Records 1 Report

PLAT232_ALERT_2_G Hirshfeld Test Diff (M-X) Br1 -- Mn1 .. 7.2 s.u.

PLAT232_ALERT_2_G Hirshfeld Test Diff (M-X) Mn1 -- C1 .. 7.7 s.u.

PLAT232_ALERT_2_G Hirshfeld Test Diff (M-X) Mn1 -- C2 .. 6.0 s.u.

PLAT790_ALERT_4_G Centre of Gravity not Within Unit Cell: Resd. # 2 Note

C6 H6

PLAT860_ALERT_3_G Number of Least-Squares Restraints ..... 14 Note

PLAT961_ALERT_5_G Dataset Contains no Negative Intensities ..... Please Check

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0 **ALERT level A** = Most likely a serious problem - resolve or explain

0 **ALERT level B** = A potentially serious problem, consider carefully

14 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight

11 **ALERT level G** = General information/check it is not something unexpected

2 ALERT type 1 CIF construction/syntax error, inconsistent or missing data

14 ALERT type 2 Indicator that the structure model may be wrong or deficient

5 ALERT type 3 Indicator that the structure quality may be low

3 ALERT type 4 Improvement, methodology, query or suggestion

1 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

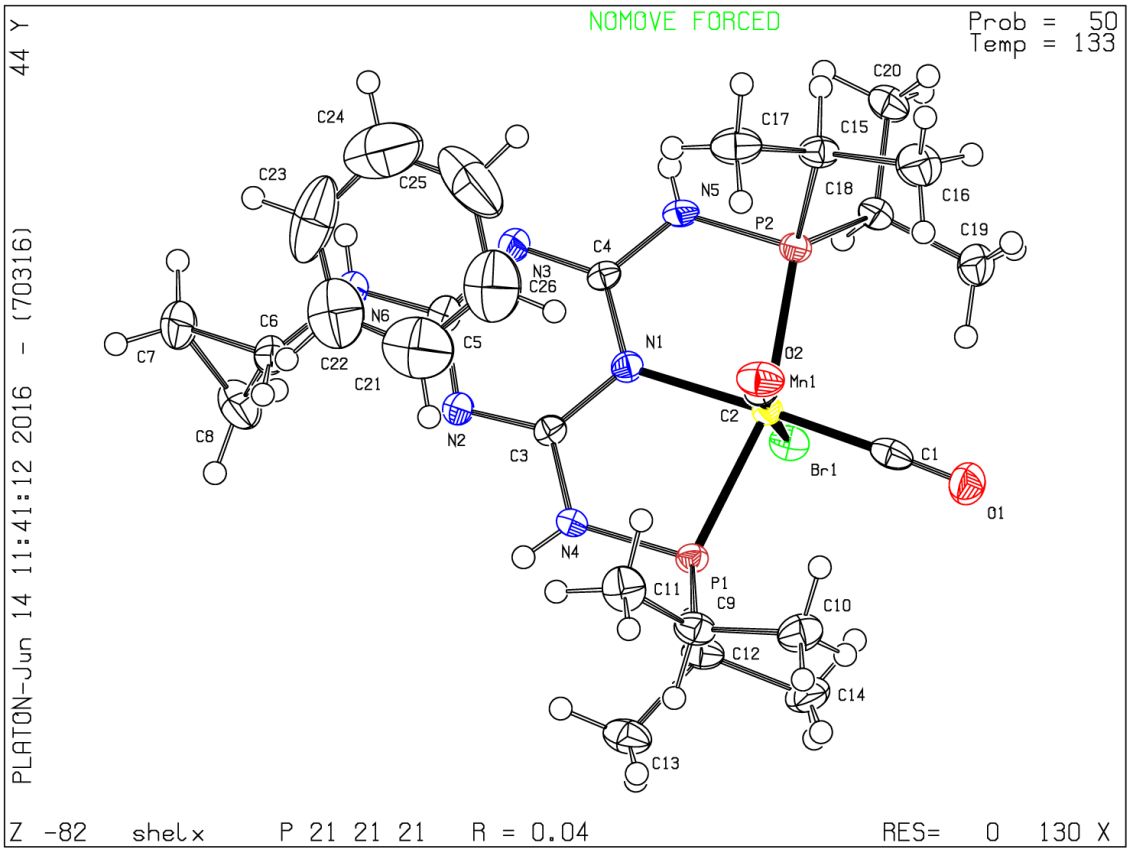
Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 06/05/2016; check.def file version of 05/05/2016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N5
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N3
C26
C6
N6
C5
N1
O2
C7
C22
C21
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O1
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C10
C12
C14
C13
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6. Manganese-Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols

Kallmeier, F.; Dudziec, B.; Irrgang, T.; Kempe, R.*

Manganese-Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols.

Angew. Chem. Int. Ed. **2017**, *56* (25), 7261–7265

DOI: 10.1002/anie.201702543

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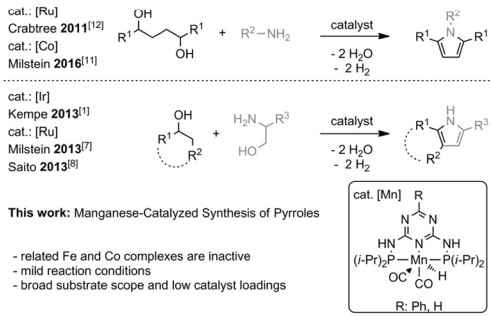
Manganese-Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols

*Fabian Kallmeier, Beata Dudziec, Torsten Irrgang, and Rhett Kempe**

Abstract: *The development of reactions that convert alcohols into important chemical compounds saves our fossil carbon resources as alcohols can be obtained from indigestible biomass such as lignocellulose. The conservation of our rare noble metals is of similar importance, and their replacement by abundantly available transition metals, such as Mn, Fe, or Co (base or nonprecious metals), in key technologies such as catalysis is a promising option. Herein, we report on the first base-metal-catalyzed synthesis of pyrroles from alcohols and amino alcohols. The most efficient catalysts are Mn complexes stabilized by PN_5P ligands whereas related Fe and Co complexes are inactive. The reaction proceeds under mild conditions at catalyst loadings as low as 0.5 mol%, and has a broad scope and attractive functional-group tolerance. These findings may inspire others to use Mn catalysts to replace Ir or Ru complexes in challenging dehydrogenation reactions.*

The development of reactions in which alcohols are converted into important classes of chemical compounds contributes to the conservation of our finite fossil carbon resources and helps to reduce CO_2 emissions.[1] Alcohols can be obtained from indigestible and abundantly available lignocellulose biomass[2] by a combination of hydrogenolysis and hydrogenation.[3] Aromatic N-heterocyclic compounds are of high importance as their motifs are found in many pharmaceuticals, natural products, and functional materials.[4] Unfortunately, their synthesis from biomass-derived starting materials remains challenging.[4] A concept that permits the catalytic synthesis of aromatic N-heterocycles from alcohol starting materials is a combination of catalytic dehydrogenation and condensation steps.[1,5] Condensation steps are used to deoxygenate the alcohols, and dehydrogenation leads to aromaticity. The synthesis of pyrroles from secondary alcohols and amino alcohols is a prominent example of such a conversion of alcohols into N-heterocycles (Scheme 1, bottom). We have shown that a broad range of substrates can be addressed when homogeneous Ir catalysts[1] are used and that reusable Ir catalysts[6] can also mediate this reaction.

[*] F. Kallmeier, Dr. T. Irrgang, Prof. Dr. R. Kempe
Inorganic Chemistry II—Catalyst Design
University of Bayreuth
95440 Bayreuth (Germany)
E-mail: kempe@uni-bayreuth.de
Dr. B. Dudziec
Organometallic Chemistry
Adam Mickiewicz University
61614 Poznań (Poland)
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.201702543.



Scheme 1. Synthesis of pyrroles from diols and amines (top) and from alcohols and amino alcohols (bottom).

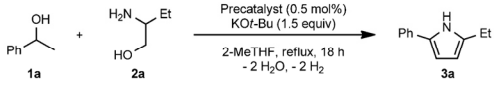
The groups of Milstein[7] and Saito[8] applied homogeneous Ru catalysts, and Beller and co-workers[9] introduced a conceptually similar pyrrole synthesis catalyzed by a Ru complex. Based on these initial findings, a variety of noble-metal-catalyzed reactions for the conversion of alcohols into N-heterocycles have been developed.[10] Aside from the conservation of our fossil carbon resources, the conservation of rare noble metals, which are frequently used in key technologies such as catalysis, is similarly important. It would be highly desirable to combine both sustainability concepts and develop catalysts based on abundantly available transition metals, such as Mn, Fe, and Co (base or nonprecious metals), for the conversion of alcohols into N-heterocycles. Milstein and co-workers showed very recently that a Co complex efficiently catalyzes the synthesis of pyrroles from diols and amines,[11] a reaction originally introduced by the Crabtree group with a Ru catalyst (Scheme 1, top).[12] Kirchner and co-workers[13] and our group[14] described a Mn-complex-catalyzed multicomponent synthesis of pyrimidines from up to three different alcohols and amidines, a reaction originally developed by our group with Ir catalysts.[15] Efficient hydrogenation and dehydrogenation catalysis with Mn has only been reported very recently.[16]

We herein report on the first base-metal-catalyzed reaction of alcohols and amino alcohols into aromatic N-heterocycles. This pyrrole synthesis is catalyzed most efficiently by Mn PN_5P-pincer catalysts developed in our laboratory whereas related Fe and Co complexes do not display any significant activity. The reaction proceeds under mild reaction conditions and at low catalyst loadings, and the desired products were isolated in yields of up to 93%. A

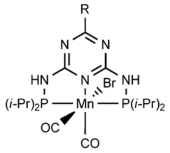
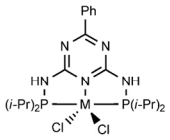
broad scope and very good functional-group tolerance were observed.

We investigated the model reaction between 1-phenylethanol and 2-aminobutan-1-ol to find the optimal reaction conditions (Table 1, top). Suitable and similarly efficient

Table 1: Precatalyst screening.[a]



1a **2a** **3a**

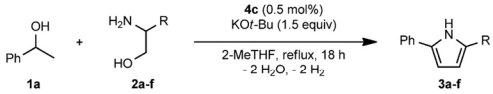
Entry	Precatalyst			Yield of **3a** [%][b]
1		R = H	**4a**	60
2		R = Me	**4b**	58
3		R = Ph	**4c**	69
4		*R* = 4-CF_3(C_6H_4)	**4d**	49
5		R = (C_3H_5)HN	**4e**	37
6		R = NEt_2	**4f**	45
7		M = Co	**5a**	0
8		M = Fe	**5b**	0
9	[$Mn(CO)_5Br$]			0

[a] Reaction conditions: 1-phenylethanol (6 mmol), 2-aminobutan-1-ol (3 mmol), KO*t*-Bu (4.5 mmol), precatalyst (15 µmol, 0.5 mol%), 2-MeTHF (6 mL), reflux, 18 h. [b] Determined by GC analysis using dodecane as an internal standard. 2-MeTHF = 2-methyltetrahydrofuran.

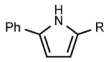
bases are KO*t*Bu, KH, and KN($SiMe_3$)$_2$, 2-MeTHF is the best solvent, 1.5 equiv of the base are optimal, and the alcohol/amino alcohol ratio should be 2:1. These findings were made by using **4c**, the most efficient precatalyst in the multicomponent Mn-catalyzed pyrimidine synthesis.[14] Next, PN_5P-ligand-supported Mn carbonyl complexes were investigated (Table 1, entries 1–6). Precatalyst **4c** gives rise to the most active catalyst. Related complexes of Co complex **5a** have previously been used by our group for hydrogenation/dehydrogenation catalysis,[17] but in this case, **5a** as well as the related Fe complex **5b**, which is also active in the hydrogenation of ketones,[18] showed no activity (entries 7 and 8). In summary, the best results are obtained with 2 equiv of a secondary alcohol with respect to the amino alcohol, 1.5 equiv of KO*t*-Bu, precatalyst **4c** (0.5 mol%), and 2-MeTHF as the solvent. An Ir catalyst[1] stabilized by the same PN_5P ligand as **4c** was investigated to rule out the possibility that Ir contaminations are responsible for the catalytic activity. Interestingly, this Ir catalyst (0.5 mol% precatalyst, 63% of **3a**) did not perform better than our best Mn catalyst (0.5 mol% precatalyst, 69% of **3a**).

We next investigated the substrate scope of the reaction with six different amino alcohols. All reactions afforded phenyl-substituted pyrroles owing to the use of 1-phenylethanol as the secondary alcohol (Table 2, top). These products were isolated in yields of up to 85% (**3e**; Table 2, entry 5). Compound **3e** is also an example of a novel compound. We then varied the secondary alcohol (Table 3). The amino alcohol component was mostly set to 2-amino-3-

Table 2: Substrate scope with respect to the amino alcohol.[a]



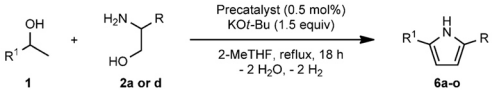
1a **2a-f** **3a-f**

Entry	Product			Yield [%][b]
1		R = Et	**3a**	74
2		R = Me	**3b**	56
3		R = *i*-Bu	**3c**	76
4		R = Bn	**3d**	83
5		R = 4-Cl-Bn	**3e**	85
6		R = Ph	**3f**	57

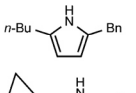
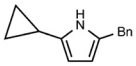
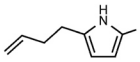
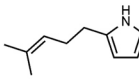
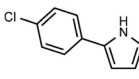
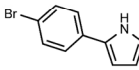
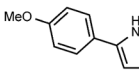
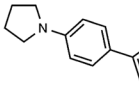
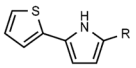
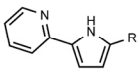
[a] Reaction conditions: 1-phenylethanol (6 mmol), amino alcohol (3 mmol), KO*t*-Bu (4.5 mmol), precatalyst (15 µmol, 0.5 mol%), 2-MeTHF (6 mL), reflux, 18 h. [b] Yield of isolated product.

phenylpropan-1-ol (**2d**). However, we also prepared a representative series of ethyl-substituted pyrroles derived from 2-aminobutan-1-ol to show that the benzyl substituent of the amino alcohol is advantageous in some cases, but by far not a prerequisite (entries 4, 6, 9, 12, and 14). Aliphatic secondary alcohols are readily converted into the corresponding pyrroles and were isolated in yields of up to 93% (**6b**), with **6b** also being a novel compound (entry 2). Aliphatic alcohols containing a terminal (entry 3) or internal (entries 4 and 5) double bond were smoothly converted into the corresponding pyrroles **6c** (79% yield, previously undisclosed compound), **6d**, and **6e** (both isolated in 91% yield). Next, a series of pyrroles derived from 4′-substituted 1-phenylethanol derivatives (entries 6–11) were synthesized. Whereas 1-(4′-chlorophenyl)ethanol gave satisfactory yields (**6f**: 77%, **6g**: 57% yield, entries 6 and 7), dehalogenation was observed for 1-(4′-bromophenyl)ethanol, leading to an inseparable mixture of **3d** and **6h** (in a 1:5 ratio based on GC and NMR analysis). This issue could be solved by using NaO*t*-Bu instead of KO*t*-Bu and 1 mol% of **4c** as well as extending the reaction time to 48 h as the activity of **4c** is lower when used in combination with NaO*t*-Bu. This modification led to the isolation of **6h** in an acceptable 71% yield (entry 8). When 1-(4′-methoxyphenyl)ethanol was used, the corresponding pyrroles **6i** and **6j** were isolated in 76% and 91% yield, respectively (entries 9 and 10). The alcohol 1-(4-(pyrrolidin-1-yl)phenyl)ethanol, which is conveniently prepared from 4′-fluoroacetophenone and pyrrolidine in two high-yielding steps, was readily converted into the novel pyrrole **6k** in 76% yield. Furthermore, we were interested if potentially catalyst-inhibiting heteroaromatic alcohols could be applied. Therefore, 1-(thiophen-2-yl)ethanol was used as a substrate, and the corresponding pyrroles **6l** and **6m** (entries 12 and 13) were isolated in 60% and 62% yield, respectively. Although the

Table 3: Substrate scope with respect to the secondary alcohol.[a]

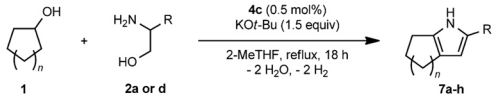


1 2a or d 6a-o

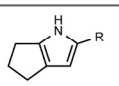
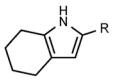
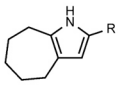
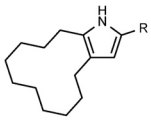
Entry	Product			Yield [%][b]
1			**6a**	74
2			**6b**	93
3			**6c**	79
4		R = Et	**6d**	91
5		R = Bn	**6e**	91[d]
6		R = Et	**6f**	77
7		R = Bn	**6g**	57
8			**6h**	71[c]
9		R = Et	**6i**	76[d]
10		R = Bn	**6j**	91[d]
11			**6k**	76
12		R = Et	**6l**	60
13		R = Bn	**6m**	62
14		R = Et	**6n**	81[d]
15		R = Bn	**6o**	84[d]

[a] Reaction conditions: **1** (6 mmol), **2** (3 mmol), KO*t*-Bu (4.5 mmol), **4c** (15 μmol, 0.5 mol%), 2-MeTHF (6 mL), reflux, 18 h. [b] Yield of isolated product. [c] **4c** (1 mol%), 48 h, NaO*t*-Bu (4.5 mmol). [d] **4a** (0.5 mol%). Upscaling led to 93% of isolated **6d** (5.7 g) and 85% of **6j** (7.8 g).

Table 4: Substrate scope with respect to the secondary alcohol.[a]



1 2a or d 7a-h

Entry	Product			Yield [%][b]
1		R = Et	**7a**	51[c]
2		R = Bn	**7b**	78[c]
3		R = Et	**7c**	61
4		R = Bn	**7d**	79
5		R = Et	**7e**	61
6		R = Bn	**7f**	55
7		R = Et	**7g**	43[c]
8		R = Bn	**7h**	81[c]

[a] Reaction conditions: **1** (6 mmol), **2** (3 mmol), KO*t*-Bu (4.5 mmol), precatalyst **4c** (15 μmol, 0.5 mol%), 2-MeTHF (6 mL), reflux, 18 h. [b] Yield of isolated product. [c] 0.5 mol% **4a** were used.

yields are not impressive, the yields of Ir-catalyzed syntheses reported previously[1,6] could be surpassed. The N-heterocyclic alcohol 1-(pyridine-2-yl)ethanol was used for the synthesis of the substituted 2-(1*H*-pyrrol-2-yl)pyridines **6n** and **6o**, which had not been reported previously. Finally, we investigated the synthesis of 2,3,5-substituted bicyclic compounds containing a pyrrole motif (Table 4).

The dehydrogenation catalyst **4c*H** is generated by salt elimination[13,14,16k,l] and hydrogen addition or alcohol dehydrogenation (Figure 1). The formation of the pyrrole products was not improved when **4c*H** was used as the catalyst (0.5 mol% **4c*H**, 71% of **3a**). The hydrogen liberated during pyrrole formation can be collected (obtained: 40 mL, calculated: 42 mL). 1-Phenylethanol and 2-aminobutan-1-ol are both dehydrogenated by **4c*H** (catalyst resting state) in the presence of base. In addition, base is needed to convert the imine intermediate 2-((1-phenylethylidene)amino)butan-1-ol into **3a**. Complex **4c*H** can also be identified at the end of the catalytic reaction when higher catalyst loadings are used. The use of the secondary alcohol in excess (2 equiv are optimal) increases the dehydrogenation rate of this alcohol by a factor of 1.7 in comparison to the use of one equivalent. The adjustment of the dehydrogenation rates seems to be key to

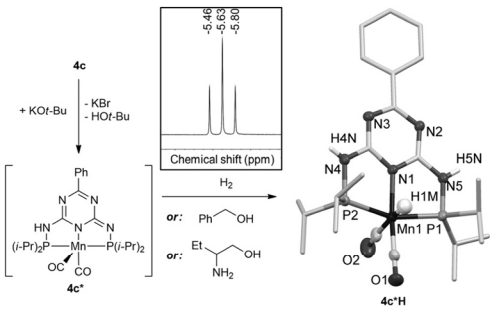


Figure 1. Formation of the catalytically active manganese hydride (**4c*H**) and its molecular structure determined by X-ray analysis.[19] Inset: Hydride region of the ^{1}H NMR spectrum of **4c*H**.

efficient pyrrole formation. When the ketone is used instead of the secondary alcohol, pyrrole formation is lower, and side product formation (self-condensation products such as 2,5-diethylpyrazine) increases.

In summary, we have reported on the Mn-catalyzed synthesis of pyrroles from secondary alcohols and amino alcohols. This is the first example of a base-metal-catalyzed version of this pyrrole synthesis and of any synthesis of aromatic N-heterocycles from alcohol and amino alcohol starting materials. The reaction is catalyzed most efficiently by Mn PN_3P-pincer dicarbonyl hydride catalysts. Co and Fe complexes that are stabilized by the same type of pincer ligand and active in (de)hydrogenation reactions showed no activity in our pyrrole synthesis. The Ir catalyst with the same pincer ligand as the most active Mn catalyst showed lower activity in comparison to the Mn catalyst. The reaction proceeds under mild reaction conditions, and the temperature of 78 °C is lower than that used for the Ir- and Ru-catalyzed versions of this reaction. The reaction has a broad scope, very good functional-group tolerance, and can be easily scaled up to more than 5 g of product. For example, 29 products were isolated in yields of up to 93 %. Seven of these 29 examples are novel pyrroles. The strength of the Co-based diol–amine synthesis of pyrroles (Scheme 1, top) is the variation of the amine, giving rise to symmetric pyrroles with different N substituents, and the fact that it is nearly base-free. Our Mn-catalyzed pyrrole synthesis is strong with regard to the synthesis of differently C-alkylated and C-arylated products, the mild reaction conditions (78 vs. 150 °C), and the low catalyst loading (0.5 vs. 5 mol %).

Acknowledgements

We thank Martin Schlagbauer for his excellent help in the laboratory and Thomas Dietel for X-ray analysis.

Conflict of interest

The authors declare no conflict of interest.

Keywords: alcohols · dehydrogenation · manganese · pyrroles · sustainable synthesis

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[18] Complex **5b** (2 mol%, 20 μmol, 11 mg), KO*t*-Bu (20 mol%, 0.2 mmol, 22 mg), acetophenone (1 mmol, 117 μL), THF (2 mL), 60 bar H_2, 60 °C, 20 h. Conversion (GC): > 99%.

[19] CCDC 1543589 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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Supporting Information

Manganese-Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols

*Fabian Kallmeier, Beata Dudziec, Torsten Irrgang, and Rhett Kempe**

Table of contents

General

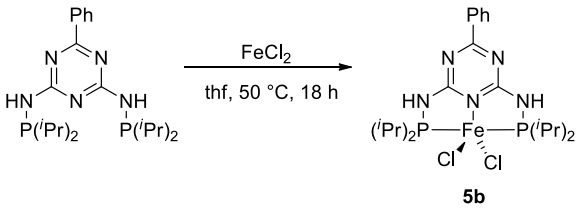
All reactions and manipulations with air sensitive compounds being present were performed under dry argon (Ar 5.0) or nitrogen (N_2 5.0), using Schlenk and glove box techniques. Non-halogenated solvents were dried over sodium benzophenone, 2-methyltetrahydrofuran (2-MeTHF) was dried over calcium hydride, and halogenated solvents were dried over P_2O_5. Deuterated solvents were bought from Cambridge Isotope Laboratories, distilled accordingly, and stored over molecular sieves (3 Å). Other chemicals were purchased from commercial vendors and used without further purification. Alcohols that are not commercially available were obtained by reduction of the corresponding ketones with $LiAlH_4$ or $NaBH_4$ followed by purification via column chromatography or distillation. 1-(4-(pyrrolidin-1-yl)phenyl)ethanol was prepared according to literature.[1] 2-((1-phenylethylidene)amino)butan-1-ol was prepared according to literature.[2] NMR spectra were collected on a Varian INOVA 300 MHz spectrometer, NMR spectra for novel compounds were collected on a Bruker Avance III HD 500. Chemical shifts (δ) are reported in ppm relative to residual solvent signal. Coupling constants (J) are given in Hz (coupling patterns: s: singlet, s_br: broad singlet, d: doublet, t: triplet, q: quartet, m: multiplet). GC analyses were carried out using an Agilent Technologies 6890N system equipped with a Macherey-Nagel (MN) Optima 5 HT column (30 m, 320 µm, 0.25 µm) or an Agilent Technologies 6850 system equipped with a MN Optima 17 column (30 m, 320 µm, 0.25 µm). GC/MS analyses were carried out on an Agilent 7890A/MSD 5975C system equipped with a HP-5MS column (30 m, 320 µm, 0.25 µm). Gas mixtures were analyzed using an Agilent Technologies 6890N equipped with an TCD and an Agilent special plot and molsieve capillary column (30 m, 320 µm, 0.25 µm). FTIR measurements were carried out under a nitrogen atmosphere on an Agilent Cary 630 FTIR equipped with a Diamond ATR unit. Elemental analyses were performed using the Elementar Vario EL *III*. MN silica gel 60 (0.040 – 0.063 mm particle size) was used for flash column chromatography. X-ray crystal structure analysis was performed with a STOE STADIVARI [λ(Mo-K_α) = 0.71073 Å] equipped with an Oxford Cryostream low temperature unit. Structure solution and refinement were accomplished wit SIR97[3], SHELXL-2014[4], WinGX[5] and Mercury 3.5.1[6].

General procedure for the synthesis of pyrroles: In a glovebox, 1.5 eq KO^{t}Bu (4.5 mmol, 505 mg), 0.5 mol% precatalyst (15 µmol, 1000 µL of a 15 mM stock solution in 2-MeTHF), 2 eq of secondary alcohol (6 mmol), 1 eq of amino alcohol (3 mmol) and 2-MeTHF (5 mL) were consecutively added to a Schlenk tube. The tube was sealed, taken outside of the glovebox and a reflux condenser with a bubble counter was attached under argon. The reaction was heated to reflux (oil bath 110 °C) and stirred for 18 h. Afterwards, the reaction was quenched by addition of water (3 mL). The aqueous layer was extracted using *tert*-butyl methyl ether (MTBE), the organic layers were combined, dried using Na_2SO_4 and the solvents removed *in vacuo*. The crude product was purified by column chromatography.

Synthesis of precatalysts

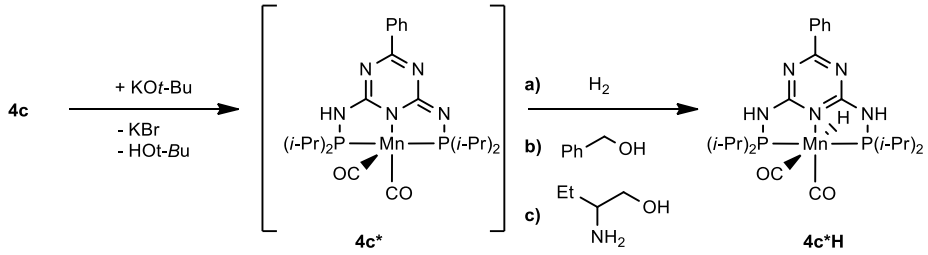
The precatalysts **4a-f**[7,8], **8**[9], **5c**[7], and **5a**[10] were synthesized according to published procedures.

The precatalyst **5b** was prepared following a modified procedure of Kirchner and coworkers.[11]



In a Schlenk tube, to a suspension of $FeCl_2$ (1 eq, 1 mmol, 127 mg) in thf (10 mL) was quickly added a solution of N^2,N^4-bis(diisopropylphosphino)-6-phenyl-1,3,5-triazine-2,4-diamine (1 eq, 1 mmol, 419 mg) in thf (10 mL) under inert gas. The solution was then heated to 50 °C for 18 h upon which the color changed to orange. The solution was filtered and the solvent was removed *in vacuo* to yield **5b** (88 %, 0.88 mmol, 480 mg) as an orange paramagnetic solid. Elemental analysis calcd for $C_{21}H_{35}Cl_2FeN_5P_2$ (M: 546.23) [%]: C 46.18, H 6.46, N 12.82, found: C 45.83, H 6.66, N 12.68.

Synthesis of **4c*H**



a) **H_2:** In a glovebox, a 10 mL glass vial is charged with **4c** (0.33 mmol, 203 mg), KO*t*-Bu (0.33 mmol, 37 mg) and toluene (4 mL). The vial is then transferred to an autoclave (Parr Instrument stainless steel N-MT5 300mL autoclave) which is then sealed, removed from the glovebox, purged three times and finally filled with hydrogen (60 bar). After stirring at room temperature for 16 h the hydrogen is replaced with argon, the autoclave is transferred to a glovebox, and the solution is filtered (Roth, Rotilabo®-Fibre glass syringe filters, Ø 15 mm, 1-2 µm) into a flame dried Schlenk tube. Upon storing the Schlenk tube for 3 days at -24 °C red crystals formed, which were dried over night at high vacuum (1 x 10^{-3} mbar). Yield: 46 % (0.15 mmol, 80 mg) as red crystalline solid. ^{1}H NMR (299.86 MHz, 23.0 °C, C_6D_6): δ = 8.66 (d, J = 6.5 Hz, 2H), 7.32 – 7.21 (m, 3H), 5.79 (d, J = 3.9 Hz, 2H), 2.20 – 2.05 (m, 2H), 1.82 (dt, J = 9.1, 6.9 Hz, 2H), 1.29 (dd, J = 15.3, 7.2 Hz, 6H), 1.23 – 1.09 (m, 12H), 1.03 (dd, J = 14.4, 6.9 Hz, 6H), -5.63 (t, J = 51.0 Hz, 1H) ppm. ^{13}C NMR (125.76 MHz, 20.0 °C, C_6D_6): δ = 170.3, 170.2, 170.1, 168.6, 136.5, 132.2, 128.9, 128.7, 128.6, 33.2, 33.1, 33.0, 31.4, 31.3, 31.2, 18.8, 18.3, 18.2, 18.2 ppm. ^{31}P NMR (202.46 MHz, 20.0 C, C_6D_6): δ = 164.7 ppm.

b) **BnOH:** In a Young NMR tube, **4c** (0.1 mmol, 61 mg), KO*t*-Bu (0.1 mmol, 11 mg), benzyl alcohol (1 mmol, 104 µL, 10 eq.) and C_6D_6 (1 mL) were mixed and heated at

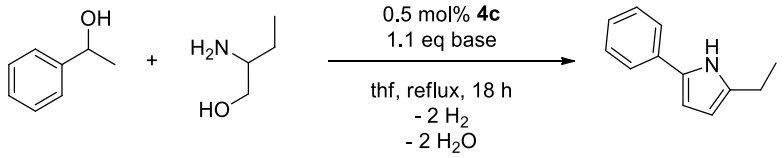
100 °C for 18 h. ^{1}H NMR spectroscopy showed the presence of the characteristic triplet at -5.63 ppm of **4c*H**.

c) **2-Aminobutanol:** In a Young NMR tube, **4c** (0.1 mmol, 61 mg), KO*t*-Bu (0.1 mmol, 11 mg), 2-aminobutan-1-ol (1 mmol, 95 µL, 10 eq.) and C_6D_6 (1 mL) were mixed and heated at 100 °C for 18 h. ^{1}H NMR spectroscopy showed the presence of the characteristic triplet at -5.63 ppm of **4c*H**.

Screening of reaction parameters

Base screening

Table S1: Base screening[a]

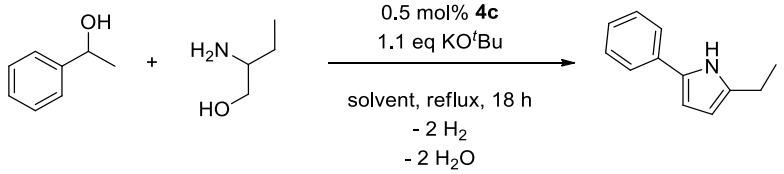


Entry	Base	Yield[b] [%]
1	LiOH	0
2	LiO^{t}Bu	0
3	NaOH	10
4	NaO^{t}Bu	23
5	KH	30
6	KOH	8
7	KO^{t}Bu	29
8	KN(SiMe$_3$)$_2$	30

[a]: Reaction conditions: 0.5 mol% **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1.1 eq base (3.3 mmol), 2 eq 1-phenylethanol (6 mmol, 726 µL), 1 eq 2-amino-1-butanol (3 mmol, 284 µL), 6 mL thf, reflux, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

Solvent screening

Table S2: Solvent screening[a]

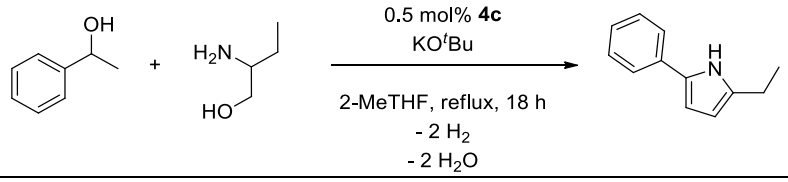


Entry	Solvent	Yield[b] [%]
1	diglyme	25
2	2-methylbutan-2-ol	25
3	thf	29
4	toluene	30
5	benzene	32
6	1,4-dioxane	40
7	2-MeTHF	47

[a]: Reaction conditions: 0.5 mol% **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1.1 eq KO^{t}Bu (3.3 mmol, 370 mg), 2 eq 1-phenylethanol (6 mmol, 726 µL), 1 eq 2-amino-1-butanol (3 mmol, 284 µL), 6 mL solvent, reflux, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

Base amount screening

Table S3: Base amount screening[a]

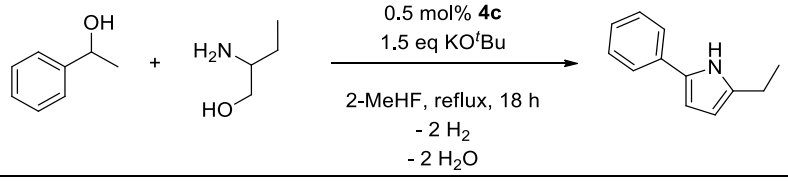


Entry	Base amount [equivalents with respect to the amino alcohol]	Yield[b] [%]
1	0.0	0
2	0.5	37
3	1.0	47
4	1.1	47
5	1.2	55
6	1.3	55
7	1.4	54
8	1.5	69
9	2.0	63

[a]: Reaction conditions: 0.5 mol% **4c** (15 µmol, 1000 µL of a 15 mM stock solution), KO^{t}Bu, 2 eq 1-phenylethanol (6 mmol, 726 µL), 1 eq 2-amino-1-butanol (3 mmol, 284 µL), 6 mL 2-MeTHF, reflux, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

Alcohol to amino alcohol ratio screening

Table S4: Alcohol to amino alcohol ratio screening[a]

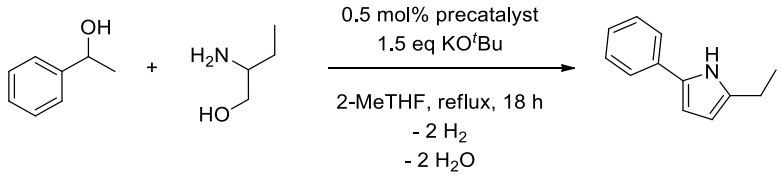


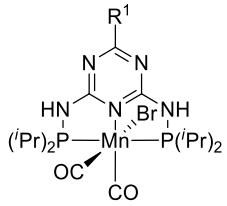
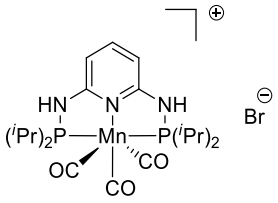
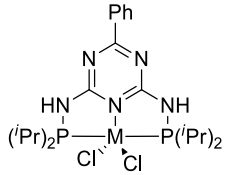
Entry	Ratio (sec. alcohol / amino alcohol)	Yield[b] [%]
1	3.0 / 1.0	63
2	2.0 / 1.0	69
3	1.5 / 1.0	43
4	1.0 / 1.0	40
5	1.0 / 1.5	30

[a]: Reaction conditions: 0.5 mol% **1c** (15 µmol, 1000 µL of a 15 mM stock solution), 1.5 eq KO^{t}Bu (4.5 mmol, 505 mg), 1-phenylethanol, 2-amino-1-butanol, 6 mL 2-MeTHF, reflux, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

Precatalyst screening

Table S5: Precatalyst screening[a]

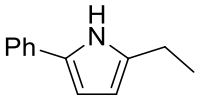


Entry	Precatalyst			Yield[b] [%]
1		$R^1 = H$	**4a**	60
2		$R^1 = CH_3$	**4b**	58
3		$R^1 = C_6H_5$	**4c**	69
4		$R^1 = 4\text{-}CF_3C_6H_4$	**4d**	49
5		$R^1 = NHC_3H_5$	**4e**	37
6		$R^1 = NEt_2$	**4f**	45
7			**8**	32
8		M = Mn	**5c**	0
9		M = Co	**5a**	0
10		M = Fe	**5b**	0
11	$[Mn(CO)_5Br]$			0
12	(pre-)catalyst free (base only)			0

[a]: Reaction conditions: 0.5 mol% precatalyst (15 µmol, 1000 µL of a 15 mM stock solution), 1.5 eq KO^{t}Bu (3.6 mmol, 505 mg), 2 eq 1-phenylethanol (6 mmol, 726 µL), 1 eq 2-amino-1-butanol (3 mmol, 284 µL), 6 mL 2-MeTHF, reflux, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

Characterization data

Synthesis of 2-ethyl-5-phenyl-1*H*-pyrrole (**3a**)



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-phenylethanol (6 mmol, 726 µL), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 Et_2O).

Yield: 74 % (2.22 mmol, 380 mg) as a colorless solid.

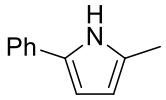
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 8.14 (s_br, 1H), 7.44 (d, J = 8.0 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.17 (t, J = 7.3 Hz, 1H), 6.42 (m, 1H), 5.99 (m, 1H), 2.70 (q, J = 7.6 Hz, 2H), 1.30 (t, J = 7.5, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 135.8, 133.1, 130.7, 128.9, 125.8, 123.5, 106.4, 106.1, 21.2, 13.8 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 13713-06-9.

Synthesis of 2-methyl-5-phenyl-1*H*-pyrrole (**3b**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-phenylethanol (6 mmol, 726 µL), 2-aminopropan-1-ol (3 mmol, 234 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 MTBE).

Yield: 56 % (1.68 mmol, 264 mg) as a colorless solid.

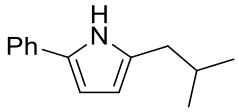
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 8.12 (s_br, 1H), 7.46 (d, J = 7.7 Hz, 2H), 7.37 (t, J = 7.7 Hz, 2H), 7.20 (t, J = 7.2 Hz, 1H), 6.45 (s, 1H), 6.00 (s, 1H), 2.36 (s, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 133.0, 130.9, 129.2, 128.9, 125.8, 123.4, 108.1, 106.3, 13.3 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 3042-21-5.

Synthesis of 2-isobutyl-5-phenyl-1*H*-pyrrole (**3c**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-phenylethanol (6 mmol, 726 µL), 2-amino-4-methylpentan-1-ol (3 mmol, 383 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 MTBE).

Yield: 76 % (2.28 mmol, 454 mg) as an off-white solid.

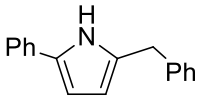
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 8.12 (s_br, 1H), 7.51 – 7.33 (m, 4H), 7.20 (t, 1H), 6.48 (s, 1H), 6.02 (s, 1H), 2.54 (d, J = 7.0 Hz, 2H), 1.94 (m, 1H), 1.01 (d, J = 6.6 Hz, 6H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 133.3, 133.1, 130.5, 128.9, 125.7, 123.4, 108.1, 106.2, 37.5, 29.4, 22.6 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1309456-70-9.

Synthesis of 2-benzyl-5-phenyl-1*H*-pyrrole (**3d**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-phenylethanol (6 mmol, 726 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 Et_2O).

Yield: 83 % (2.48 mmol, 578 mg) as an off white solid.

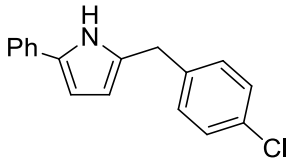
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 8.05 (s, 1H), 7.34 (m, 9H), 6.46 (t, J = 3.1 Hz, 1H), 6.08 (t, J = 3.0 Hz, 1H), 4.05 (s, 2H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 139.4, 132.9, 132.1, 131.6, 128.9, 128.8, 128.8, 126.7, 126.0, 123.6, 108.8, 106.2, 34.5 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 905971-72-4.

Synthesis of 2-(4-chlorobenzyl)-5-phenyl-1*H*-pyrrole (**3e**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-phenylethanol (6 mmol, 726 µL), 2-amino-3-(4-chlorophenyl)propan-1-ol (3 mmol, 557 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 9 : 1 EtOAc).

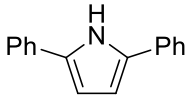
Yield: 85 % (2.56 mmol, 685 mg) as a yellow solid.

^{1}H NMR (500.13 MHz, 20.0 °C, CD_2Cl_2): δ = 8.18 (s_br, 1H), 7.45 – 7.40 (m, 2H), 7.38 – 7.28 (m, 4H), 7.23 – 7.16 (m, 3H), 6.51 – 6.37 (m, 1H), 6.03 – 6.00 (m, 1H), 3.99 (s, 2H) ppm.

^{13}C NMR (125.76 MHz, 20.0 °C, CD_2Cl_2): δ = 138.8, 133.2, 132.6, 132.2, 132.0, 130.6, 129.4, 129.2, 126.4, 123.8, 109.2, 106.7, 34.0 ppm.

Elemental analysis calcd for $C_{17}H_{14}ClN$ (M: 267.75) [%]: C 76.26, H 5.27, N 5.23, found: C 76.12, H 5.18, N 5.29.

Synthesis of 2,5-diphenyl-1*H*-pyrrole (**3f**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-phenylethanol (6 mmol, 726 µL), 2-amino-2-phenylethanol (3 mmol, 412 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 Et_2O).

Yield: 57 % (1.72 mmol, 377 mg) as a colorless solid.

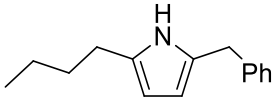
^{1}H NMR (299.86 MHz, 23.0 °C, CD_2Cl_2): δ = 8.72 (s_br, 1H), 7.59 – 7.53 (m, 4H), 7.45 – 7.36 (t, 4H), 7.29 – 7.19 (m, 2H), 6.59 (d, J = 2.6, 2H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, CD_2Cl_2): δ = 133.6, 133.0, 129.5, 126.9, 124.2, 108.4 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 838-40-4.

Synthesis of 2-benzyl-5-butyl-1*H*-pyrrole (**6a**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 2-hexanol (6 mmol, 757 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 Et_2O).

Yield: 74 % (2.23 mmol, 476 mg) as a yellow oil.

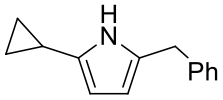
^{1}H NMR (299.86 MHz, 23.0 °C, CD_2Cl_2): δ = 7.62 (s_br, 1H), 7.42 – 7.17 (m, 5H), 5.82 (s, 1H), 5.78 (s, 1H), 3.93 (s, 2H), 2.53 (t, J = 7.6 Hz, 2H), 1.66 – 1.47 (m, 2H), 1.38 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, CD_2Cl_2): δ = 140.9, 132.7, 129.5, 129.1, 129.0, 126.7, 106.8, 1053, 34.7, 32.5, 28.0, 23.0, 14.3 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1422518-33-9.

Synthesis of 2-benzyl-5-cyclopropyl-1*H*-pyrrole (**6b**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-cyclopropylethanol (3 mmol, 587 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 Et_2O).

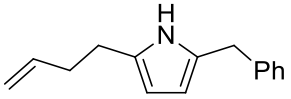
Yield: 93 % (2.79 mmol, 551 mg) as a yellow oil.

^{1}H NMR (500.13 MHz, 20.0 °C, CD_2Cl_2): δ = 7.75 (s_br, 1H), 7.33 (m, 2H), 7.25 (m, 3H), 5.80 (t, J = 2.9 Hz, 1H), 5.71 (t, J = 2.9 Hz, 1H), 3.92 (s, 2H), 1.78 – 1.70 (m, 1H), 0.82 – 0.76 (m, 2H), 0.59 – 0.55 (m, 2H) ppm.

^{13}C NMR (125.76 MHz, 20.0 °C, CD_2Cl_2): δ = 140.7, 134.2, 129.8, 129.1, 129.1, 126.8, 106.7, 104.1, 34.7 ppm.

Elemental analysis calcd for $C_{14}H_{15}N$ (M: 197.28) [%]: C 85.24, H 7.66, N 7.10, found: C 85.04, H 7.66, N 6.62.

Synthesis of 2-benzyl-5-(but-3-en-1-yl)-1*H*-pyrrole (**6c**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), hex-5-en-2-ol (6 mmol, 726 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 98 : 2 Et_2O).

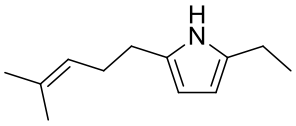
Yield: 79 % (2.36 mmol, 499 mg) as a yellow oil.

^{1}H NMR (500.13 MHz, 20.0 °C, CD_2Cl_2): δ = 7.66 (s_br, 1H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 3H), 5.88 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.82 (t, *J* = 2.6 Hz, 1H), 5.79 (t, *J* = 2.5 Hz, 1H), 5.02 (ddd, *J* = 13.7, 11.0, 0.8 Hz, 2H), 3.92 (s, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.34 (q, *J* = 7.1 Hz, 2H) ppm.

^{13}C NMR (125.76 MHz, 20.0 °C, CD_2Cl_2): δ = 140.8, 138.9, 131.9, 129.8, 129.1, 129.0, 126.8, 115.4, 106.7, 105.5, 34.6, 34.4, 27.7 ppm.

Elemental analysis calcd for $C_{15}H_{17}N$ (M: 211.30) [%]: C 85.26, H 8.11, N 6.63, found: C 85.32, H 8.09, N 6.51.

Synthesis of 2-ethyl-5-(4-methylpent-3-en-1-yl)-1*H*-pyrrole (**6d**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 6-methylhept-5-en-2-ol (6 mmol, 911 µL), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 Et_2O).

Yield: 91% (2.74 mmol, 485 mg) as a yellow oil.

Upscaling: KO^{t}Bu (52.5 mmol, 5.89 g), precatalyst **4c** (175 µmol, 107 mg), 6-methylhept-5-en-2-ol (70 mmol, 10.69 mL), 2-aminobutan-1-ol (35 mmol, 3.31 mL), 2-MeTHF (70 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 Et_2O).

Yield: 93% (32.5 mmol, 5.77 g) as a yellow oil.

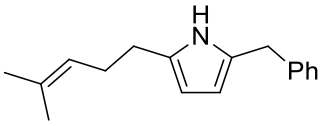
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 7.69 (s_br, 1H), 5.84 (s, 1H), 5.83 (s, 1H), 5.31 – 5.20 (m, 1H), 2.63 (tt, J = 7.6, 3.7 Hz, 4H), 2.34 (q, J = 7.6 Hz, 2H), 1.75 (s, 3H), 1.64 (s, 3H), 1.27 (t, J = 7.6 Hz, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 132.8, 132.5, 131.2, 124.1, 104.7, 103.9, 28.4, 28.0, 25.8, 21.0, 17.8, 13.8 ppm.

The analytical data are consistent with literature.[12]

CAS Registry Number: 1629022-86-1.

Synthesis of 2-benzyl-5-(4-methylpent-3-en-1-yl)-1*H*-pyrrole (**6e**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4a** (15 µmol, 1000 µL of a 15 mM stock solution), 6-methylhept-5-en-2-ol (6 mmol, 911 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 Et_2O).

Yield: 91 % (2.73 mmol, 653 mg) as a yellow oil.

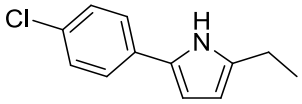
^{1}H NMR (299.86 MHz, 23.0 °C, CD_2Cl_2): δ = 7.64 (s_br, 1H), 7.39 – 7.04 (m, 5H), 5.80 (s, 1H), 5.75 (s, 1H), 5.15 (t, J = 7.0 Hz, 1H), 3.90 (s, 2H), 2.53 (t, J = 7.4 Hz, 2H), 2.24 (q, J = 7.1 Hz, 2H), 1.66 (s, 3H), 1.54 (s, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, CD_2Cl_2): δ = 140.8, 133.0, 132.5, 129.7, 129.1, 129.0, 126.7, 124.4, 106.6, 105.4, 34.7, 28.9, 28.3, 25.9, 17.9 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1422518-35-1.

Synthesis of 2-(4-chlorophenyl)-5-ethyl-1*H*-pyrrole (**6f**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-(4-chlorophenyl)ethanol (6 mmol, 802 µL), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 EtOAc)

Yield: 77 % (2.31 mmol, 475 mg) as an off-white solid.

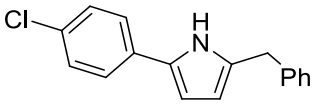
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 8.10 (s_br, 1H), 7.40 – 7.27 (m, 4H), 6.42 (m, 1H), 6.01 (m, 1H), 2.69 (q, J = 7.6 Hz, 2H), 1.31 (t, J = 7.6 Hz, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 136.2, 131.6, 131.2, 129.6, 129.0, 124.6, 106.7, 106.6, 21.1, 13.7 ppm.

The analytical data are consistent with literature.[13]

CAS Registry Number: 1929585-17-0.

Synthesis of 2-benzyl-5-(4-chlorophenyl)-1*H*-pyrrole (**6g**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-(4-chlorophenyl)ethanol (6 mmol, 802 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 30 : 1 MTBE).

Yield: 57 % (1.72 mmol, 461 mg) as an off-white solid.

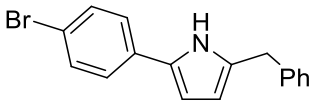
^{1}H NMR (299.86 MHz, 23.0 °C, CD_2Cl_2): δ = 8.15 (s_br, 1H), 7.39 – 7.22 (m, 9H), 6.44 (m, 1H), 6.05 (m, 1H), 4.02 (s, 2H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, CD_2Cl_2): δ = 140.0, 133.4, 132.0, 131.5, 130.7, 129.4, 129.2, 129.1, 127.0, 125.1, 109.3, 107.2, 34.7 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1422518-38-4.

Synthesis of 2-benzyl-5-(4-bromophenyl)-1*H*-pyrrole *(***6h***)*:



NaO^{t}Bu (4.5 mmol, 432 mg), precatalyst **4c** (30 µmol, 18 mg, 1 mol%), 1-(4-bromophenyl)ethanol (6 mmol, 826 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Reaction time: 48 h.

Purification by column chromatography on silica gel (pentane 25 : 1 MTBE).

Yield: 71 % (2.14 mmol, 668 mg) as an off-white solid.

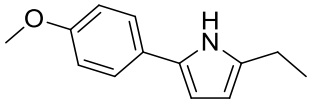
^{1}H NMR (299.86 MHz, 23.0 °C, CD_2Cl_2): δ = 8.15 (s_br, 1H), 7.48 – 7.20 (m, 9H), 6.44 (m, 1H), 6.03 (m, 1H), 4.01 (s, 2H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, 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.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1422518-39-5.

Synthesis of 2-ethyl-5-(4-methoxyphenyl)-1*H*-pyrrole (**6i**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4a** (15 µmol, 1000 µL of a 15 mM stock solution), 1-(4-methoxyphenyl)ethanol (846 µL, 6 mmol), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 EtOAc).

Yield: 76 % (2.28 mmol, 459 mg) as a colorless solid.

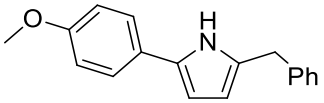
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 8.03 (s_br, 1H), 7.46 – 7.32 (m, 2H), 6.97 – 6.84 (m, 2H), 6.31 (m, 1H), 6.02 – 5.92 (m, 1H), 3.83 (s, 3H), 2.69 (q, J = 7.6 Hz, 2H), 1.30 (t, J = 7.6 Hz, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 158.0, 135.0, 130.8, 126.3, 125.0, 114.4, 106.1, 104.9, 55.5, 21.1, 13.8 ppm.

The analytical data are consistent with literature.[13]

CAS Registry Number: 1929585-16-9.

Synthesis of 2-benzyl-5-(4-methoxyphenyl)-1*H*-pyrrole (**6j**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4a** (15 µmol, 1000 µL of a 15 mM stock solution), 1-(4-methoxyphenyl)ethanol (6 mmol, 846 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 25 : 1 MTBE).

Yield: 91 % (2.73 mmol, 718 mg) as a colorless solid.

Upscaling: KO^{t}Bu (52.5 mmol, 5.89 g), precatalyst **4a** (175 µmol, 94 mg), 1-(4-methoxyphenyl)ethanol (70 mmol, 9.87 mL), 2-amino-3-phenylpropan-1-ol (35 mmol, 5.29 g), 2-MeTHF (70 mL).

Purification by column chromatography on silica gel (pentane 25 : 1 MTBE).

Yield: 85 % (29.7 mmol, 7.83 g) as a colorless solid.

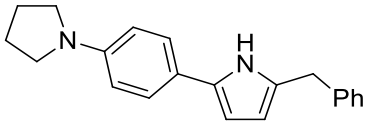
^{1}H NMR (299.86 MHz, 23.0 °C, CD_2Cl_2): δ = 8.09 (s_br, 1H), 7.42 – 7.20 (m, 7H), 6.92 – 6.87 (m, 2H), 6.32 (m, 1H), 6.01 (m, 1H), 4.01 (s, 2H), 3.80 (s, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, CD_2Cl_2): δ = 158.6, 140.4, 132.1, 131.8, 129.1, 129.1, 126.9, 126.4, 125.2, 114.8, 108.8, 105.4, 55.8, 34.7 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1422518-37-3.

Synthesis of 2-benzyl-5-(4-(pyrrolidin-1-yl)phenyl)-1*H*-pyrrole (**6k**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-(4-(pyrrolidin-1-yl)phenyl)ethanol (6 mmol, 1148 mg), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 9 : 1 Et_2O).

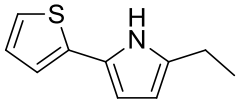
Yield: 76 % (2.29 mmol, 693 mg) as an off-white solid.

^{1}H NMR (500.13 MHz, 20.0 °C, CD_2Cl_2): δ = 8.00 (s_br, 1H), 7.35 – 7.19 (m, 7H), 6.54 (d, J = 8.7 Hz, 2H), 6.20 (t, J = 2.5 Hz, 1H), 5.95 (t, J = 2.9 Hz, 1H), 3.99 (s, 2H), 3.27 (s, 4H), 2.09 – 1.93 (m, 4H) ppm.

^{13}C NMR (125.76 MHz, 20.0 °C, CD_2Cl_2): δ = 147.1, 140.6, 132.8, 131.1, 129.1, 129.1, 126.8, 125.1, 121.0, 112.4, 108.5, 103.8, 48.2, 34.7, 26.0 ppm.

Elemental analysis calcd for $C_{21}H_{22}N_2$ (M: 302.41) [%]: C 83.40, H 7.33, N 9.26, found: C 83.27, H 7.65, N 9.08.

Synthesis of 2-ethyl-5-(thiophen-2-yl)-1*H*-pyrrole (**6l**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-(thiophen-2-yl)ethanol (6 mmol, 769 mg), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 EtOAc).

Yield: 60 % (1.81 mmol, 320 mg) as a yellow oil.

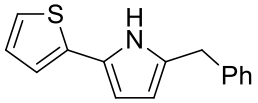
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 7.98 (s_br, 1H), 7.16 – 7.07 (m, 1H), 7.04 – 6.95 (m, 2H), 6.32 (t, J = 3.0 Hz, 1H), 5.98 – 5.93 (m, 1H), 2.67 (q, J = 7.6 Hz, 2H), 1.29 (t, J = 7.6 Hz, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 136.8, 135.4, 127.7, 125.3, 122.1, 120.2, 106.9, 106.2, 21.1, 13.7 ppm.

The analytical data are consistent with literature.[12]

CAS Registry Number: 1629022-85-0.

Synthesis of 2-benzyl-5-(thiophen-2-yl)-1*H*-pyrrole (**6m**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), 1-(thiophen-2-yl)ethanol (6 mmol, 769 mg), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 EtOAc).

Yield: 62 % (1.86 mmol, 445 mg) as a red solid.

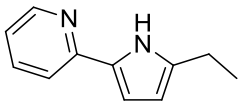
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 7.93 (s_br, 1H), 7.45 – 7.33 (m, 2H), 7.29 (dd, J = 7.0, 3.8 Hz, 3H), 7.15 – 7.11 (m, 1H), 7.03 – 6.94 (m, 2H), 6.37 (t, J = 3.0 Hz, 1H), 6.11 – 6.01 (m, 1H), 4.04 (s, 2H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 139.2, 136.5, 131.8, 128.8, 128.8, 127.7, 126.7, 126.2, 122.4, 120.4, 108.6, 107.0, 34.3 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1422518-42-0.

Synthesis of 2-(5-ethyl-1*H*-pyrrol-2-yl)pyridine (**6n**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4a** (15 µmol, 1000 µL of a 15 mM stock solution), 1-(pyridin-2-yl)ethanol (6 mmol, 739 mg), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 EtOAc).

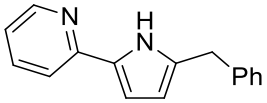
Yield: 81 % (2.43 mmol, 419 mg) as a yellow oil.

^{1}H NMR (500.13 MHz, 20.0 °C, CD_2Cl_2): δ = 9.69 (s_br, 1H), 8.42 (d, J = 4.9 Hz, 1H), 7.61 (td, J = 7.8, 1.8 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.00 (ddd, J = 7.2, 5.0, 0.9 Hz, 1H), 6.65 – 6.59 (m, 1H), 5.99 (t, J = 3.1 Hz, 1H), 2.64 (q, J = 7.6 Hz, 2H), 1.25 (t, J = 7.6 Hz, 3H) ppm.

^{13}C NMR (125.76 MHz, 23.0 °C, CD_2Cl_2): δ = 151.4, 149.3, 137.6, 136.9, 130.5, 120.4, 118.1, 108.0, 107.2, 21.4, 14.0 ppm.

Elemental analysis calcd for $C_{11}H_{12}N_2$ (M: 172.23) [%]: C 76.71, H 7.02, N 16.27, found: C 76.47, H 6.98, N 15.89.

Synthesis of 2-(5-benzyl-1*H*-pyrrol-2-yl)pyridine (**6o**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4a** (15 µmol, 1000 µL of a 15 mM stock solution), 1-(pyridin-2-yl)ethanol (6 mmol, 739 mg), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 EtOAc).

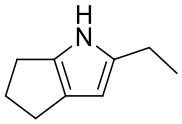
Yield: 84 % (2.52 mmol, 590 mg) as a yellow oil.

^{1}H NMR (500.13 MHz, 20.0 °C, $CDCl_3$): δ = 9.35 (s_br, 1H), 8.41 – 8.34 (m, 1H), 7.62 – 7.55 (m, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.30 (dd, J = 10.2, 4.8 Hz, 2H), 7.26 – 7.20 (m, 3H), 6.97 (ddd, J = 7.3, 5.0, 1.0 Hz, 1H), 6.63 (t, J = 2.9 Hz, 1H), 6.04 (t, J = 2.9 Hz, 1H), 4.01 (s, 2H) ppm.

^{13}C NMR (125.76 MHz, 20.0 °C, $CDCl_3$): δ = 150.7, 148.8, 139.3, 136.5, 133.6, 131.0, 128.8, 128.8, 126.6, 120.2, 117.9, 109.1, 107.7, 34.4 ppm.

Elemental analysis calcd for $C_{16}H_{14}N_2$ (M: 234.30) [%]: C 82.02, H 6.02, N 11.96, found: C 81.98, H 6.10, N 11.71.

Synthesis of 2-ethyl-1,4,5,6-tetrahydrocyclopenta[*b*]pyrrole (**7a**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4a** (15 µmol, 1000 µL of a 15 mM stock solution), cyclopentanol (6 mmol, 544 µL), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 EtOAc). The compound can alternatively be purified by fractional distillation (b.p. 72 °C at 0.7 x 10^{-1} mbar).

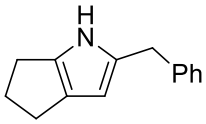
Yield: 51 % (1.53 mmol, 207 mg) as a colorless oil. (Please note that upon being exposed to air, the compound rapidly turns orange within minutes.)

^{1}H NMR (500.13 MHz, 20.0 °C, $CDCl_3$): δ = 7.61 (s_br, 1H), 5.77 (s, 1H), 2.72 (t, J = 7.0 Hz, 2H), 2.70 – 2.62 (m, 4H), 2.50 – 2.40 (m, 2H), 1.29 (t, J = 7.6 Hz, 3H) ppm.

^{13}C NMR (125.76 MHz, 20.0 °C, $CDCl_3$): δ = 137.6, 134.7, 126.5, 100.1, 29.1, 25.7, 25.5, 21.7, 14.1 ppm.

Elemental analysis calcd for $C_9H_{13}N$ (M: 135.21) [%]: C 79.95, H 9.69, N 10.36, found: C 79.27, H 9.68, N 10.02.

Synthesis of 2-benzyl-1,4,5,6-tetrahydrocyclopenta[*b*]pyrrole (**7b**)



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4a** (15 µmol, 1000 µL of a 15 mM stock solution), cyclopentanol (6 mmol, 544 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 Et_2O).

Yield: 78 % (2.34 mmol, 462 mg) as a yellow oil.

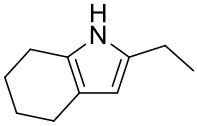
^{1}H NMR (299.86 MHz, 23.0 °C, CD_2Cl_2): δ = 7.52 (s_br, 1H), 7.45 – 7.03 (m, 5H), 5.74 (s, 1H), 3.91 (s, 2H), 2.69 – 2.54 (m, 4H), 2.47 – 2.27 (m, 2H) ppm.

^{13}C NMR (75.41, 23.0 °C, 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.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1422518-51-1.

Synthesis of 2-ethyl-4,5,6,7-tetrahydro-1*H*-indole (**7c**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), cyclohexanol (6 mmol, 633 µL), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 Et_2O).

Yield: 61 % (1.83 mmol, 273 mg) as a yellow oil.

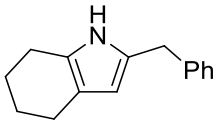
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 7.44 (s_br, 1H), 5.70 (m, 1H), 2.68 – 2.45 (m, 6H), 1.88 – 1.70 (m, 4H), 1.25 (t, J = 7.6 Hz, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 132.6, 125.4, 116.9, 103.5, 24.0, 23.7, 23.0, 22.8, 21.0, 13.9 ppm.

The analytical data are consistent with literature.[12]

CAS Registry Number: 125405-80-3.

Synthesis of 2-benzyl-4,5,6,7-tetrahydro-1*H*-indole (**7d**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), cyclohexanol (6 mmol, 633 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 Et_2O).

Yield: 79 % (2.37 mmol, 501 mg) as a yellow oil.

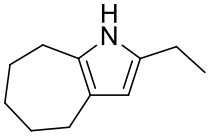
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 7.45 – 7.22 (m, 6H), 5.77 (s, 1H), 3.98 (s, 2H), 2.54 (m, 4H), 2.02 – 1.64 (m, 4H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 139.8, 129.0, 128.9, 128.7, 126.4, 126.3, 117.0, 105.7, 34.5, 24.0, 23.6, 23.0, 22.8 ppm.

The analytical data are consistent with literature.[14]

CAS Registry Number: 233585-17-6.

Synthesis of 2-ethyl-1,4,5,6,7,8-hexahydrocyclohepta[*b*]pyrrole (**7e**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), cycloheptanol (6 mmol, 714 µL), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 Et_2O).

Yield: 61 % (1.83 mmol, 299 mg) as yellow oil.

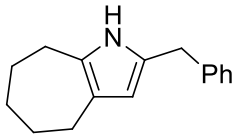
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 7.41 (s_br, 1H), 5.67 (s, 1H), 2.73 – 2.48 (m, 6H), 1.83 – 1.63 (m, 6H), 1.23 (t, J = 7.6 Hz, 3H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 130.0, 128.6, 121.3, 106.4, 32.1, 29.5, 29.3, 28.6, 28.2, 20.8, 13.7 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1422518-47-5.

Synthesis of 2-benzyl-1,4,5,6,7,8-hexahydrocyclohepta[*b*]pyrrole (**7f**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4c** (15 µmol, 1000 µL of a 15 mM stock solution), cycloheptanol (6 mmol, 714 µL), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 25 : 1 Et_2O).

Yield: 55 % (1.64 mmol, 370 mg) as a yellow oil.

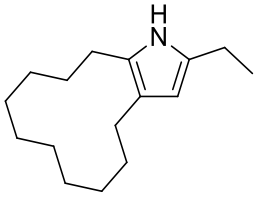
^{1}H NMR (299.86 MHz, 23.0 °C, CD_2Cl_2): δ = 7.40 (s_br, 1H), 7.36 – 7.18 (m, 5H), 5.65 (d, J = 2.9 Hz, 1H), 3.84 (s, 2H), 2.62 – 2.44 (m, 4H), 1.85 – 1.71 (m, 2H), 1.64 (m, 4H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, CD_2Cl_2): δ = 141.0, 129.9, 129.1, 129.0, 126.8, 126.7, 121.8, 108.9, 34.6, 32.6, 30.0, 29.6, 28.9, 28.8 ppm.

The analytical data are consistent with literature.[2]

CAS Registry Number: 1422518-50-0.

Synthesis of 2-benzyl-4,5,6,7,8,9,10,11,12,13-decahydro-1*H*-cyclododeca[*b*]pyrrole (**7g**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4a** (15 µmol, 1000 µL of a 15 mM stock solution), cyclododecanol (6 mmol, 1106 mg), 2-aminobutan-1-ol (3 mmol, 284 µL), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 99 : 1 Et_2O).

Yield: 43 % (1.29 mmol, 301 mg) as a colorless oil.

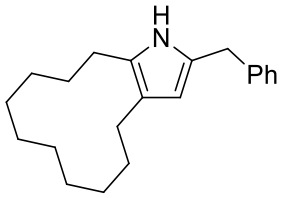
^{1}H NMR (299.86 MHz, 23.0 °C, $CDCl_3$): δ = 7.36 (s_br, 1H), 5.73 – 5.64 (m, 1H), 2.66 – 2.52 (m, 4H), 2.39 (t, J = 6.9 Hz, 2H), 1.71 – 1.56 (m, 4H), 1.53 – 1.15 (m, 18H) ppm.

^{13}C NMR (75.41 MHz, 23.0 °C, $CDCl_3$): δ = 132.5, 126.8, 120.0, 104.1, 29.2, 28.3, 24.9, 24.8, 24.8, 24.6, 22.5, 22.1, 21.1, 13.6 ppm.

The analytical data are consistent with literature.[12]

CAS Registry Number: 1629022-88-3.

Synthesis of 2-ethyl-4,5,6,7,8,9,10,11,12,13-decahydro-1*H*-cyclododeca[*b*]pyrrole (**7h**):



KO^{t}Bu (4.5 mmol, 505 mg), precatalyst **4a** (15 µmol, 1000 µL of a 15 mM stock solution), cyclododecanol (6 mmol, 1106 mg), 2-amino-3-phenylpropan-1-ol (3 mmol, 454 mg), 2-MeTHF (5 mL).

Purification by column chromatography on silica gel (pentane 50 : 1 Et_2O).

Yield: 81 % (2.43 mmol, 718 mg) as an off-white solid.

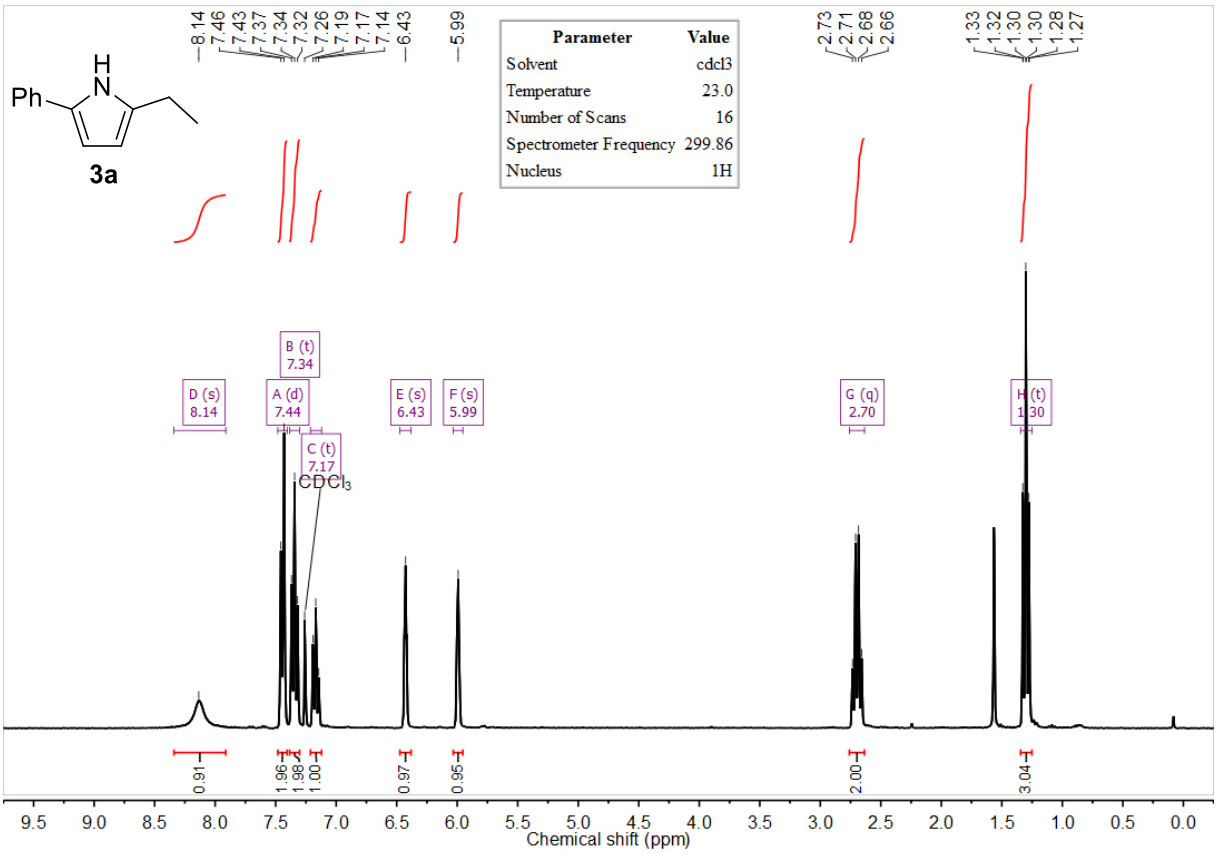
^{1}H NMR (299.86 MHz, 23.0 °C, CD_2Cl_2): δ = 7.30 (m, 6H), 5.71 (s, 1H), 3.90 (s, 2H), 2.53 (t, J = 6.7 Hz, 2H), 2.38 (t, J = 6.8 Hz, 2H), 1.59 (m, 4H), 1.37 (m, 8H), 1.28 (m, 4H) ppm.

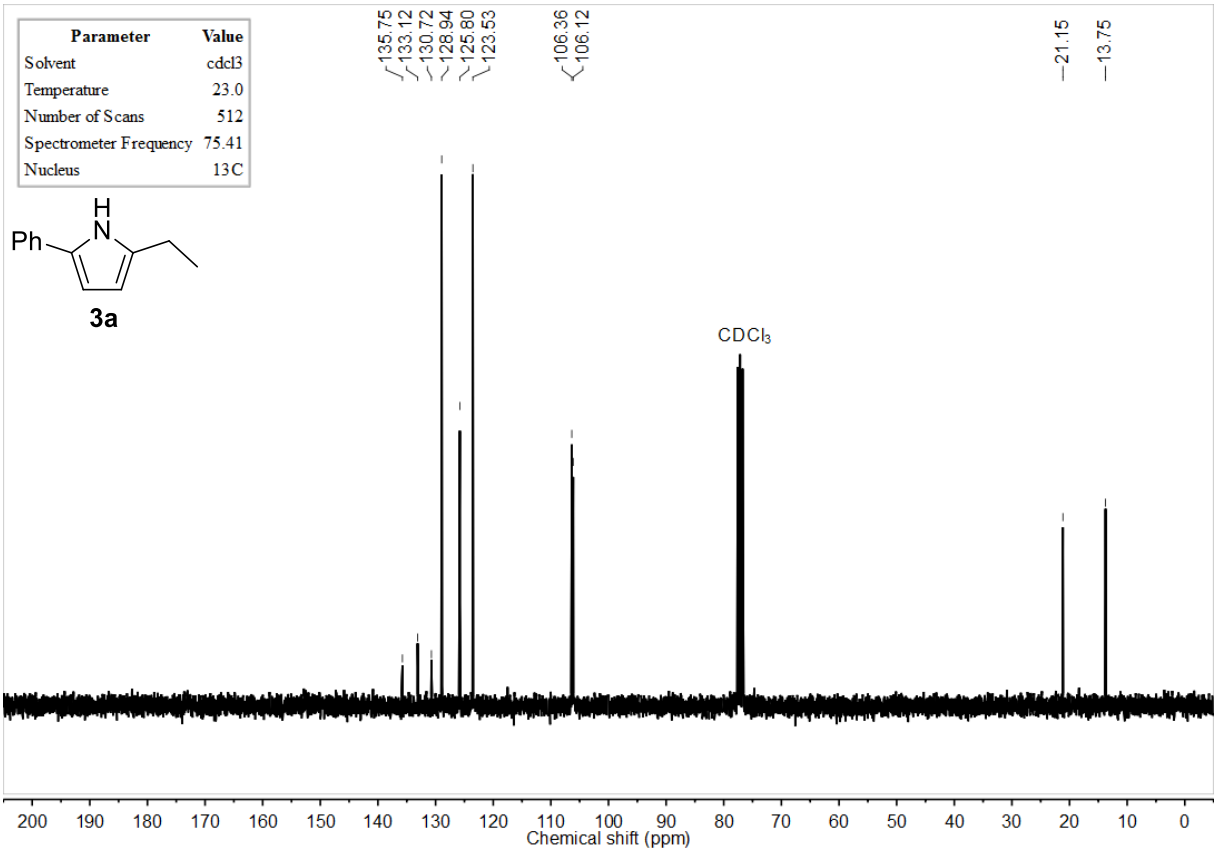
^{13}C NMR (75.41 MHz, 23.0 °C, CD_2Cl_2): δ = 141.0, 129.4, 129.1, 129.0, 128.1, 126.7, 120.5, 107.0, 34.8, 29.6, 28.7, 25.4, 25.3, 25.2, 25.1, 23.0, 23.0, 22.9, 22.5 ppm.

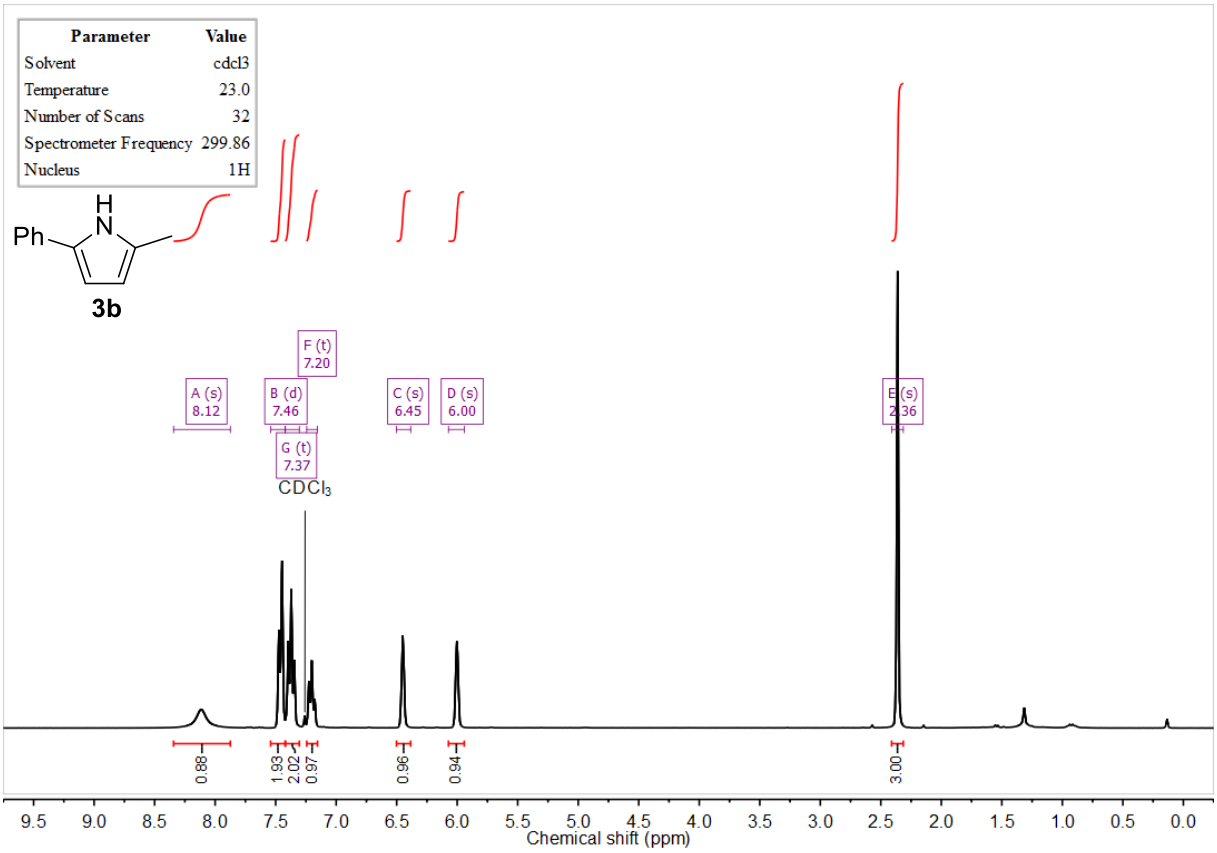
The analytical data are consistent with literature.[2]

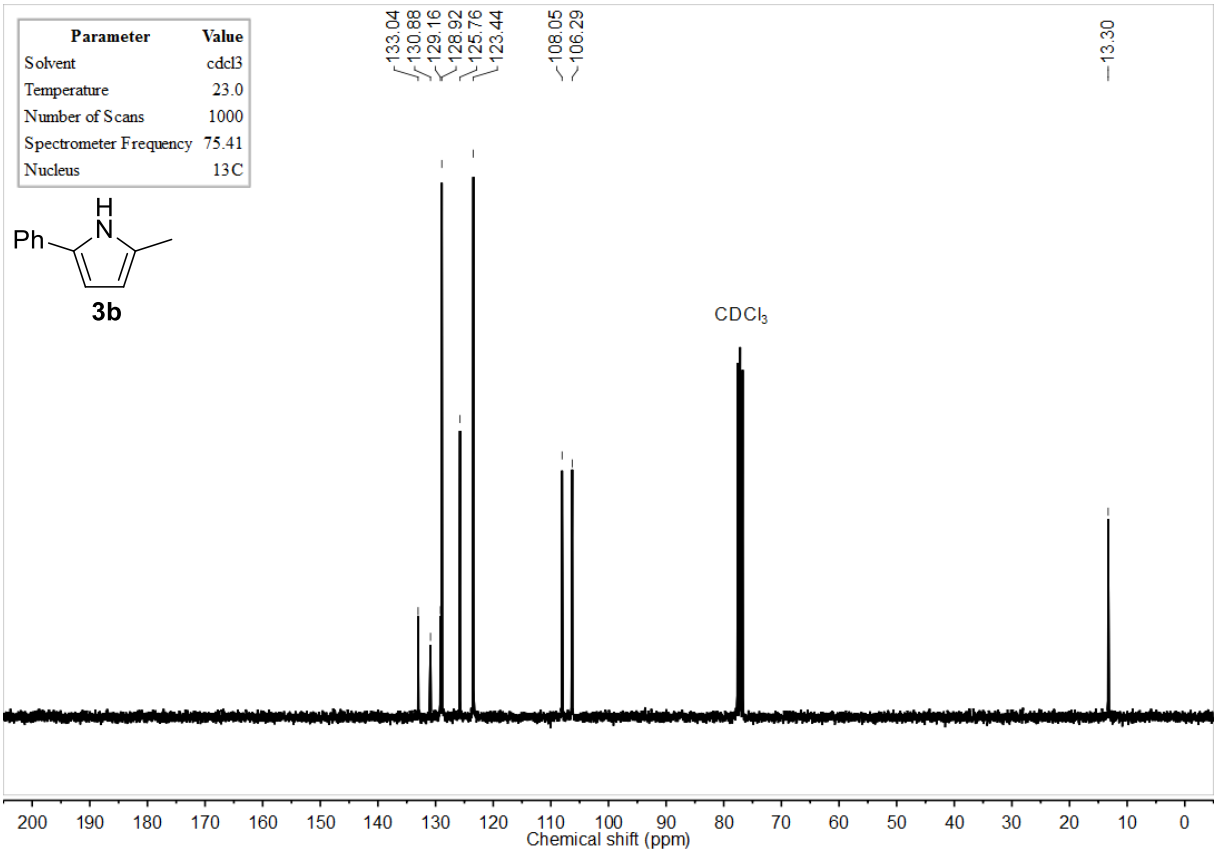
CAS Registry Number: 1422518-53-3.

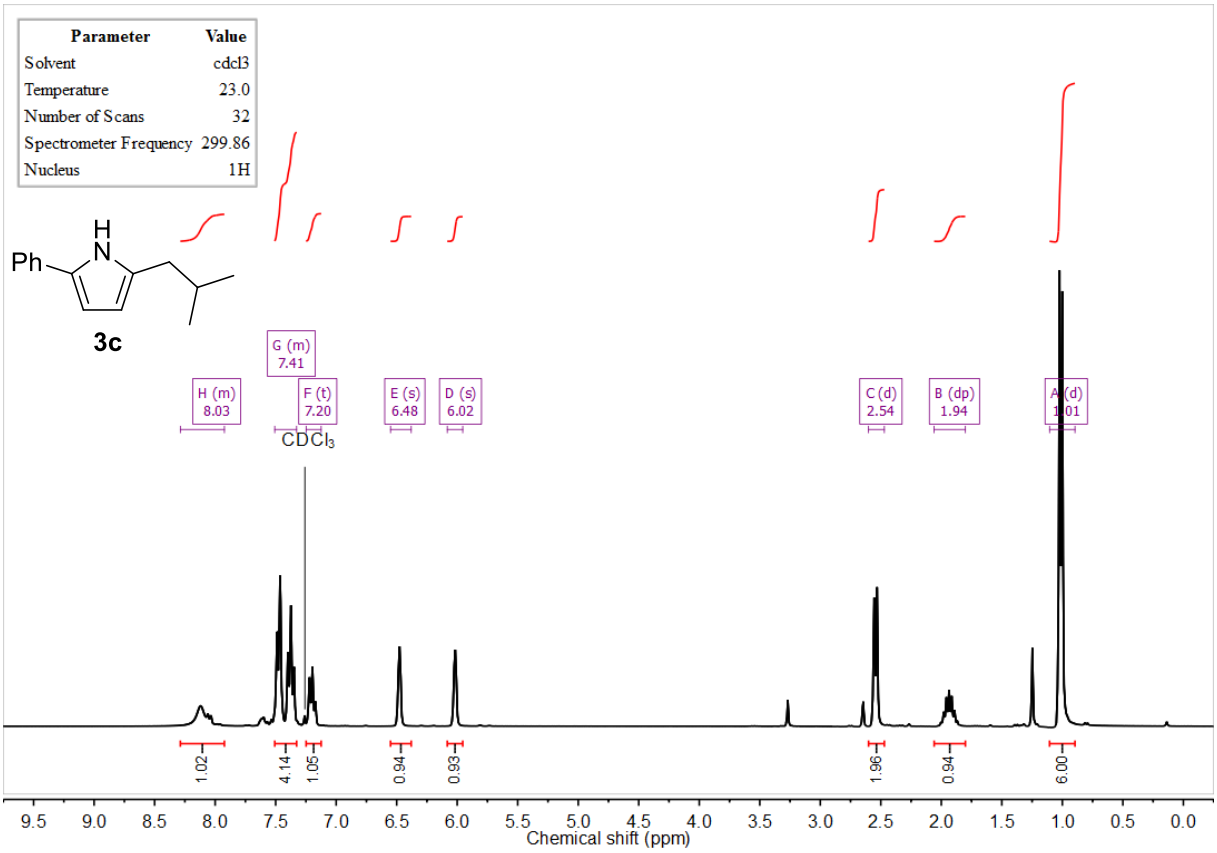
NMR Spectra

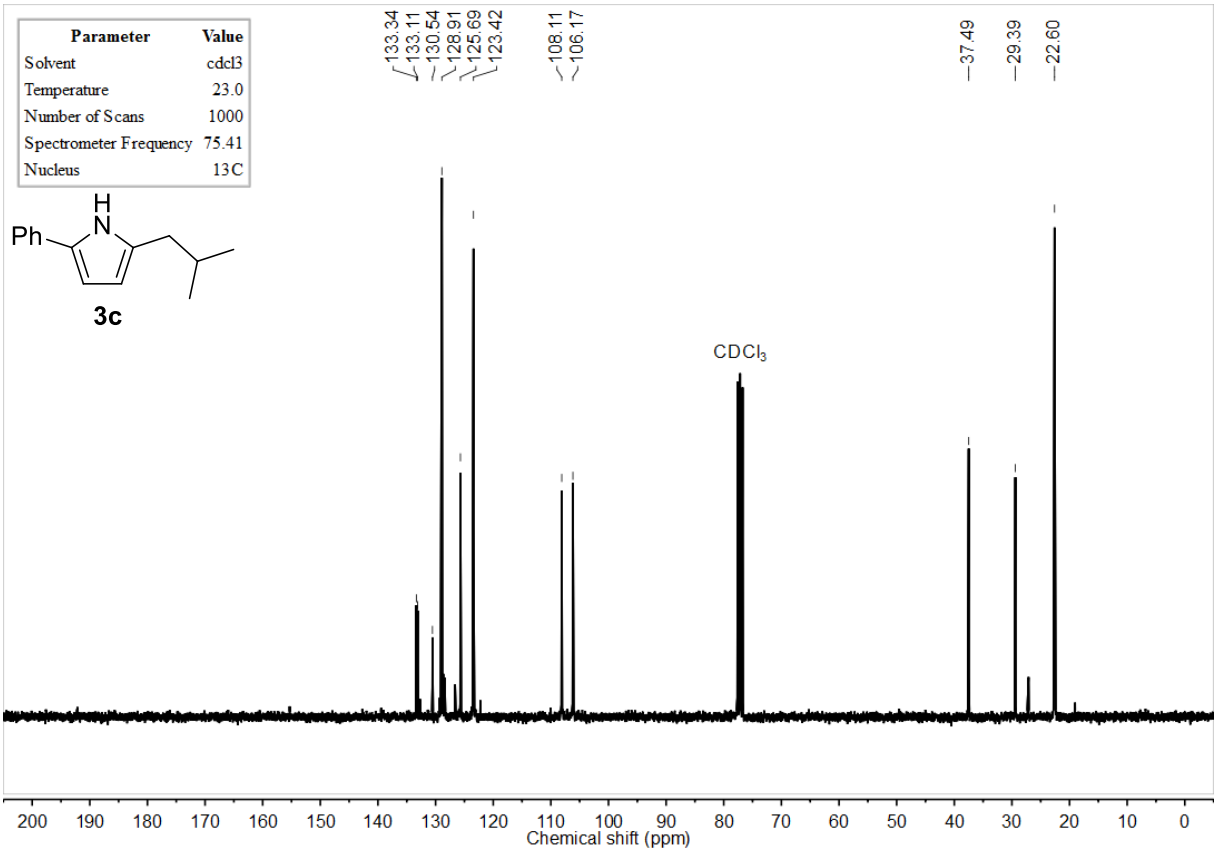

8.14
7.46
7.43
7.37
7.34
7.32
7.26
7.19
7.17
7.14
6.43
5.99
2.73
2.71
2.68
2.66
1.33
1.32
1.30
1.30
1.28
1.27
Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 16
Spectrometer Frequency 299.86
Nucleus 1H
Ph
N
H
3a
B (t) 7.34
D (s) 8.14
A (d) 7.44
E (s) 6.43
F (s) 5.99
G (q) 2.70
H (t) 1.30
C (t) 7.17
CDCl3
0.91
1.96
1.98
1.00
0.97
0.95
2.00
3.04
Chemical shift (ppm)

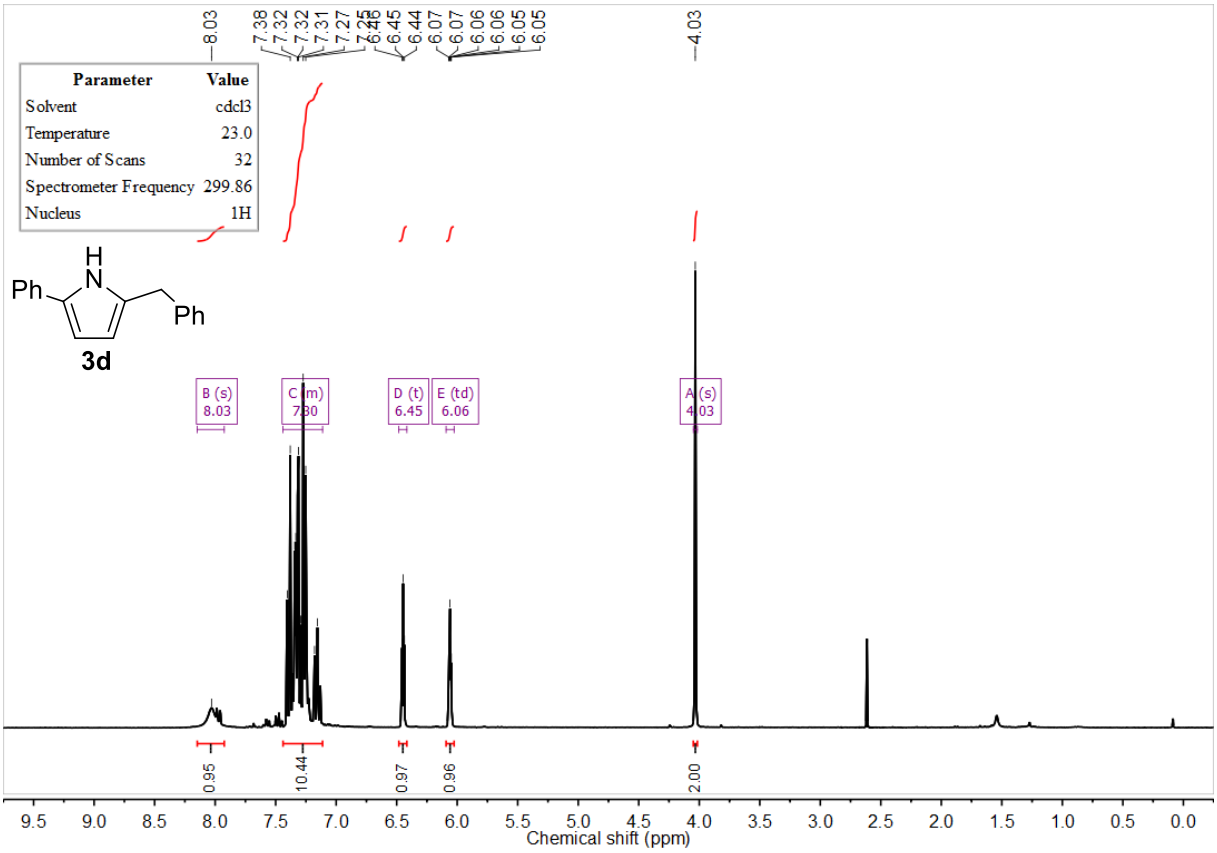

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 512
Spectrometer Frequency 75.41
Nucleus 13C
135.75
133.12
130.72
128.94
125.80
123.53
106.36
106.12
21.15
13.75
Ph
N
H
3a
CDCl3
Chemical shift (ppm)

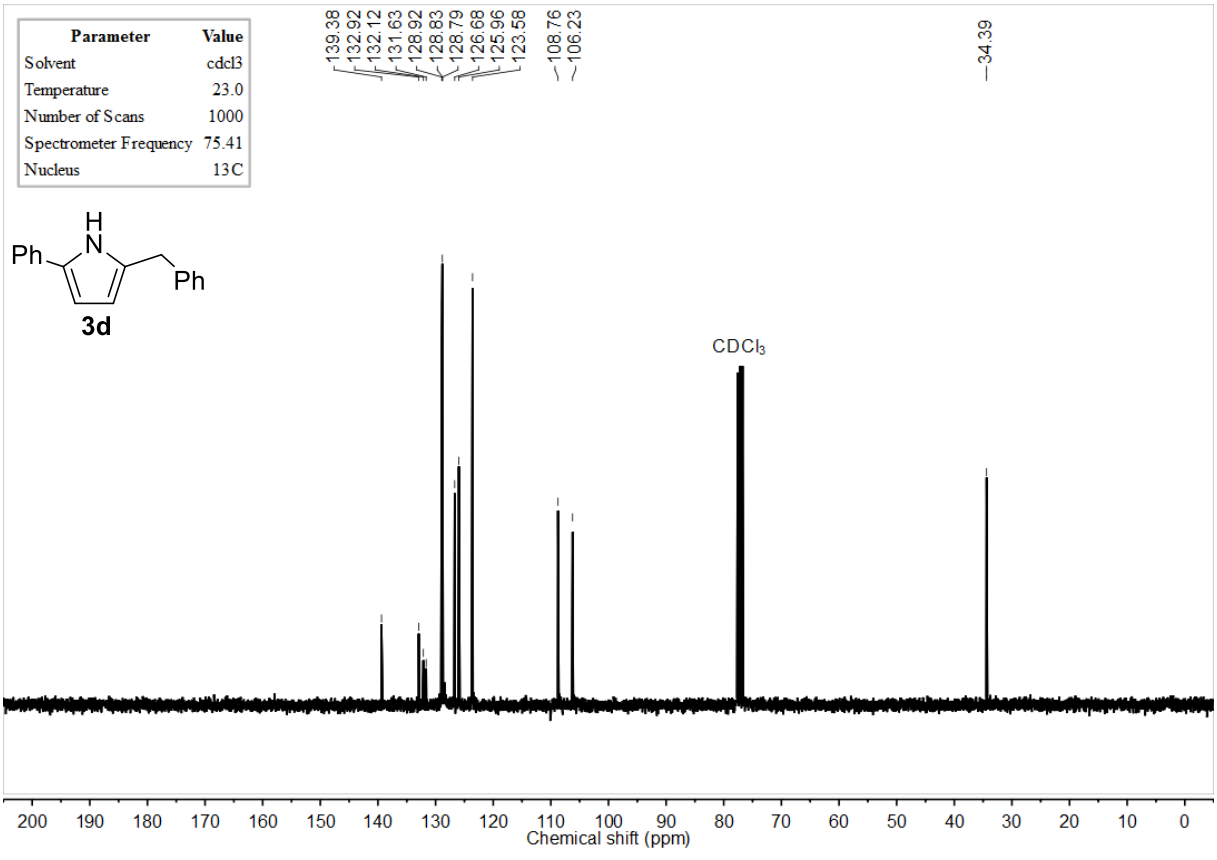

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
Ph
H
N
3b
A (s) 8.12
B (d) 7.46
C (s) 6.45
D (s) 6.00
E (s) 2.36
F (t) 7.20
G (t) 7.37
CDCl3
0.88
1.93
2.02
0.97
0.96
0.94
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical shift (ppm)

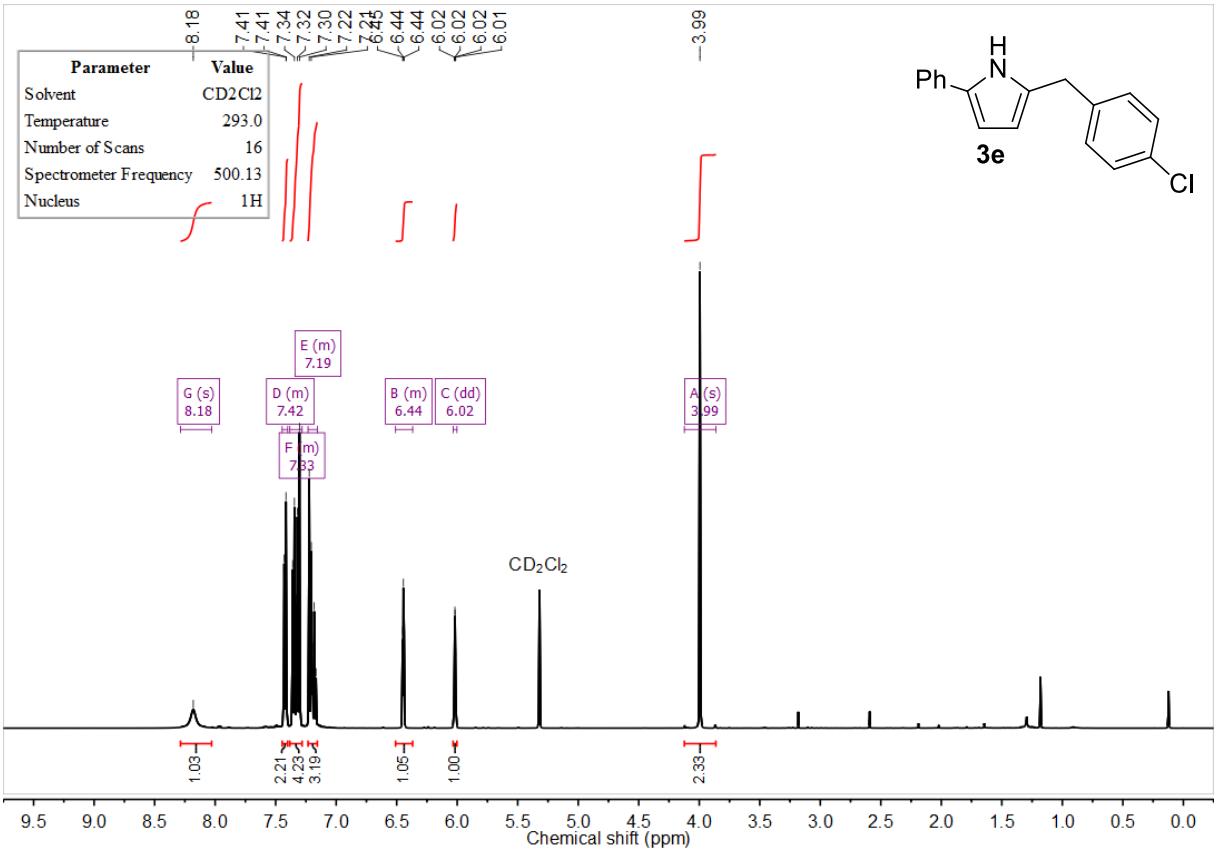

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
Ph
H
N
3b
133.04
130.88
129.16
128.92
125.76
123.44
108.05
106.29
13.30
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

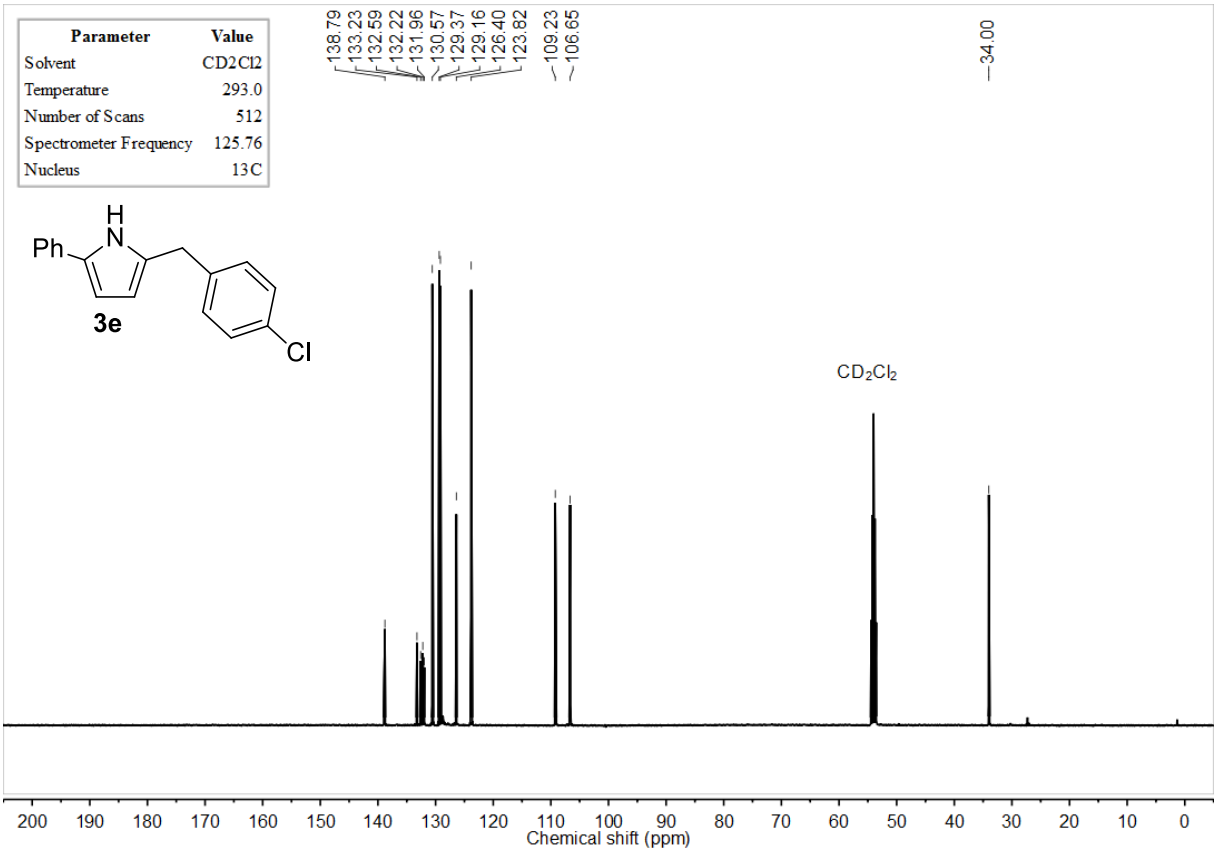

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
Ph
H
N
3c
G (m) 7.41
H (m) 8.03
F (t) 7.20
E (s) 6.48
D (s) 6.02
C (d) 2.54
B (dp) 1.94
A (d) 1.01
CDCl3
1.02
4.14
1.05
0.94
0.93
1.96
0.94
6.00
Chemical shift (ppm)

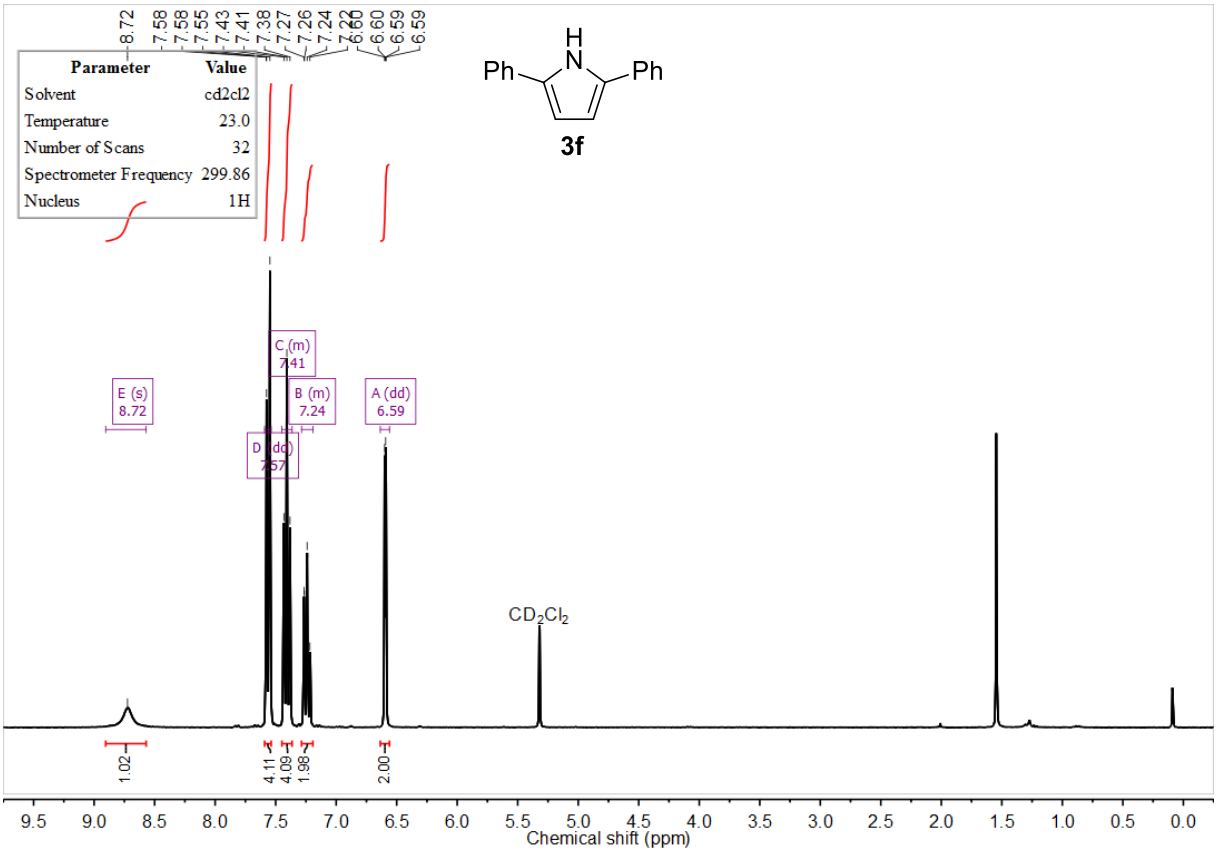

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
Ph
H
N
3c
133.34
133.11
130.54
128.91
125.69
123.42
108.11
106.17
37.49
29.39
22.60
CDCl3
Chemical shift (ppm)

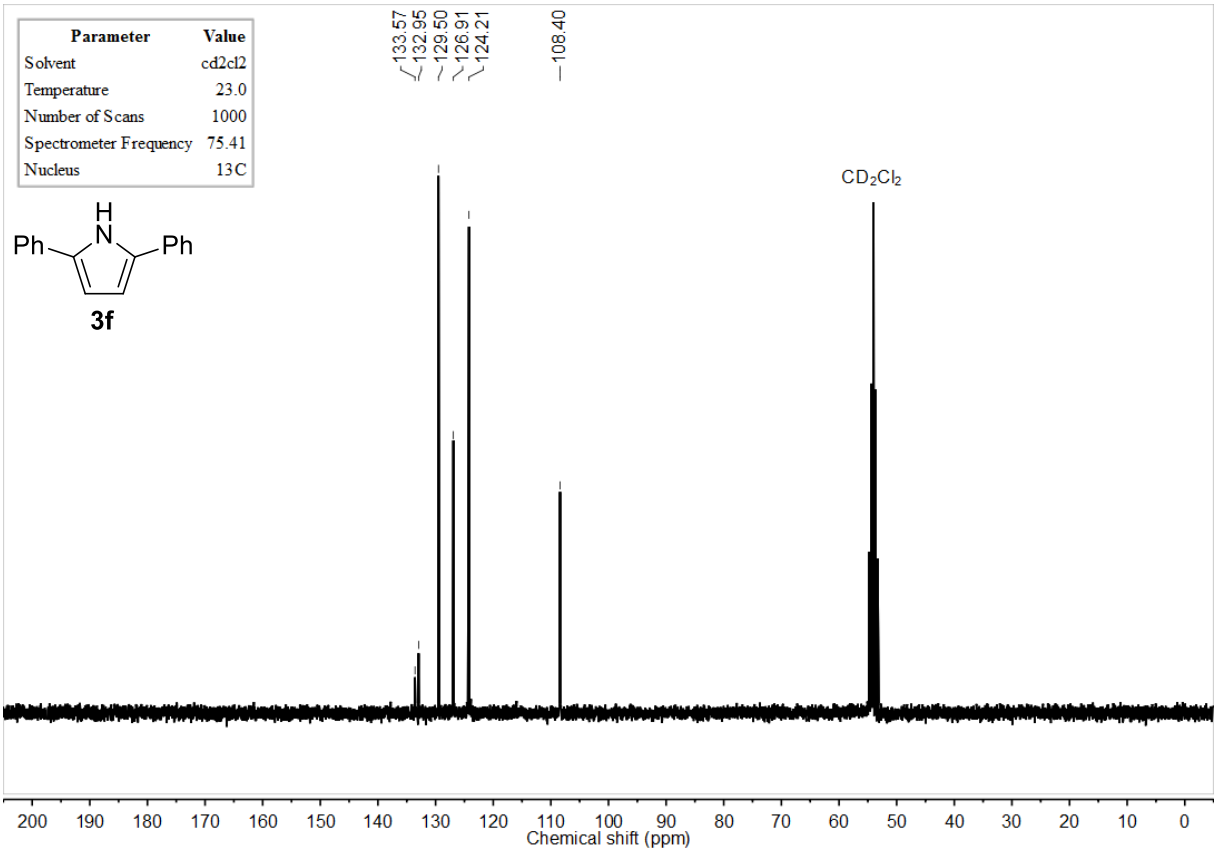

8.03
7.38
7.32
7.32
7.31
7.27
6.45
6.44
6.07
6.06
6.06
6.05
4.03
Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
Ph
N
H
Ph
3d
B (s) 8.03
C (m) 7.30
D (t) 6.45
E (td) 6.06
A (s) 4.03
0.95
10.44
0.97
0.96
2.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical shift (ppm)

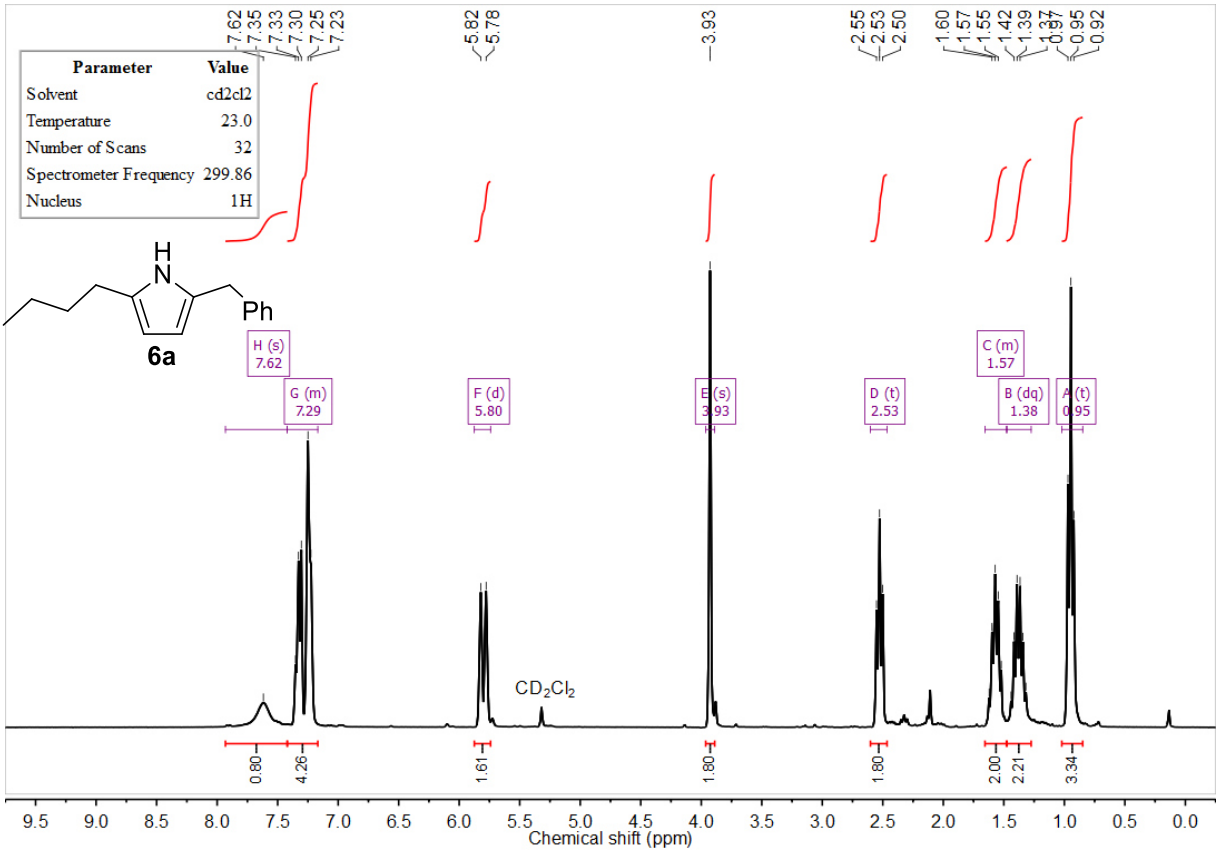

139.38
132.92
132.12
131.63
128.92
128.83
128.79
126.68
125.96
123.58
108.76
106.23
34.39
Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
Ph
N
H
Ph
3d
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

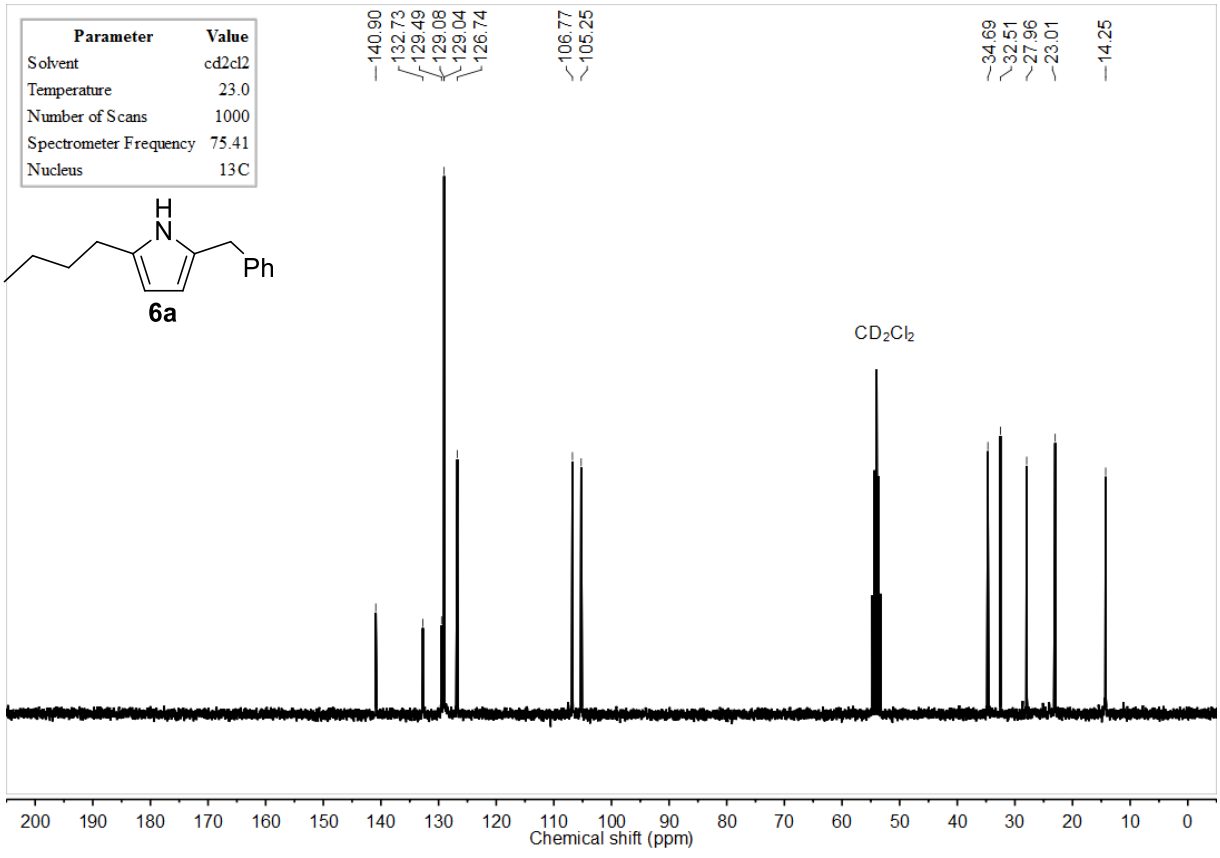

Parameter Value
Solvent CD2Cl2
Temperature 293.0
Number of Scans 16
Spectrometer Frequency 500.13
Nucleus 1H
8.18
7.41
7.41
7.34
7.32
7.30
7.22
6.44
6.44
6.02
6.02
6.01
3.99
Ph
N
H
Cl
3e
E (m) 7.19
G (s) 8.18
D (m) 7.42
F (m) 7.33
B (m) 6.44
C (dd) 6.02
A (s) 3.99
CD2Cl2
1.03
2.21
4.23
3.19
1.05
1.00
2.33
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)

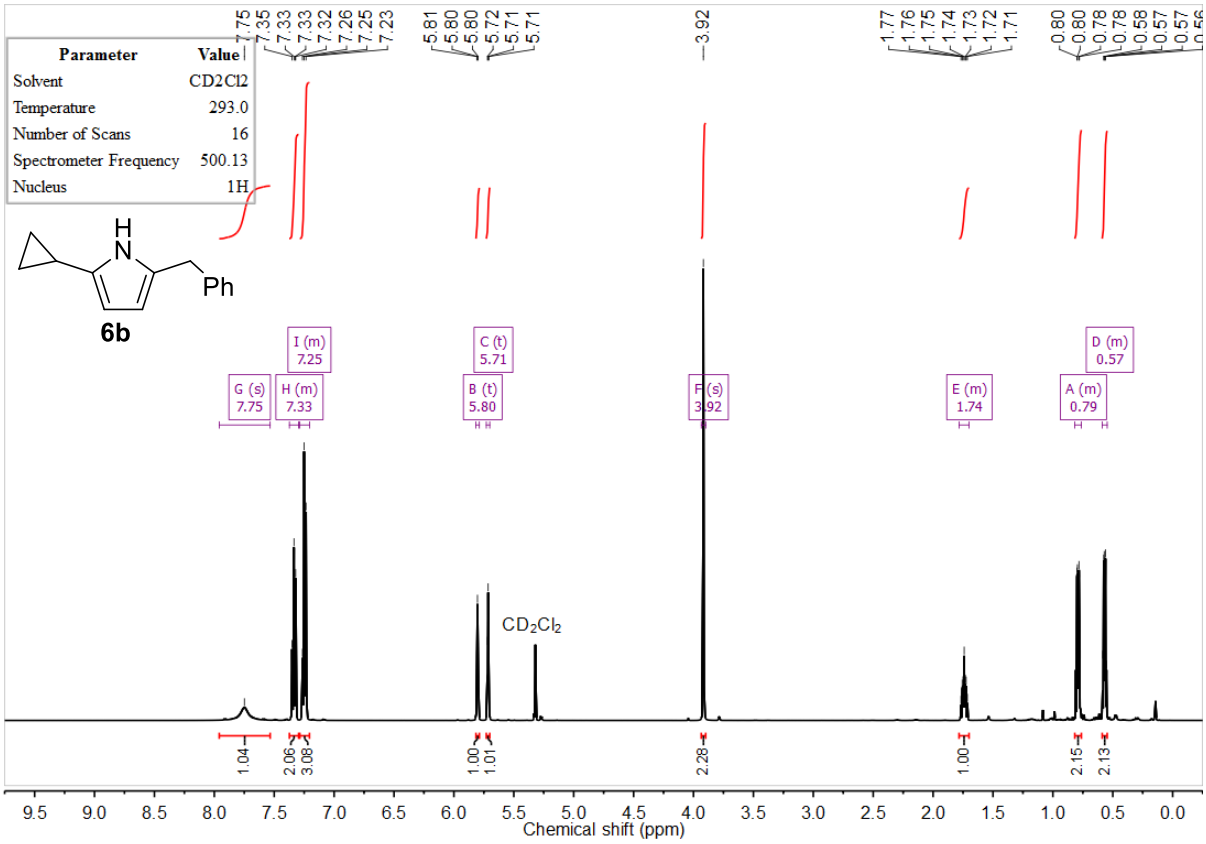

Parameter Value
Solvent CD2Cl2
Temperature 293.0
Number of Scans 512
Spectrometer Frequency 125.76
Nucleus 13C
138.79
133.23
132.59
132.22
131.96
130.57
129.37
129.16
126.40
123.82
109.23
106.65
34.00
Ph
N
H
Cl
3e
CD2Cl2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

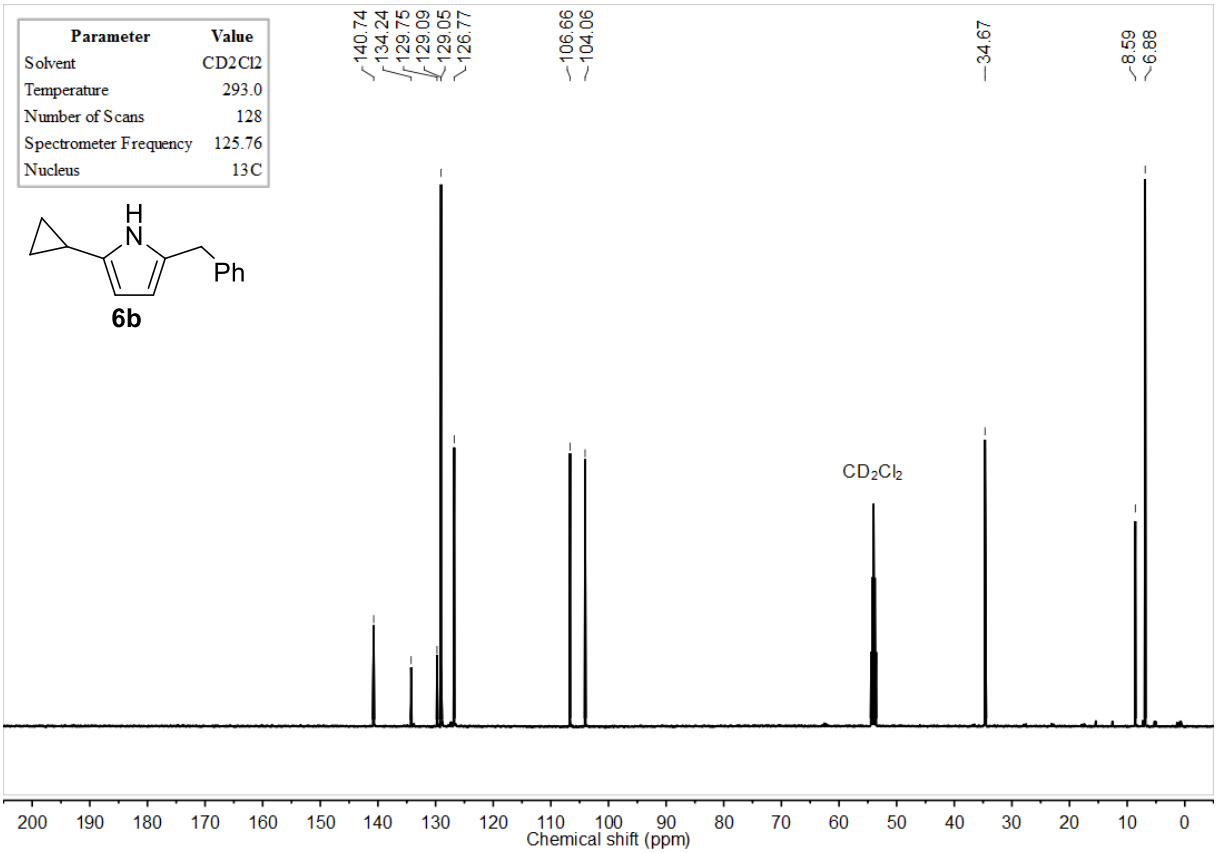

8.72
7.58
7.58
7.55
7.43
7.41
7.38
7.27
7.26
7.24
6.60
6.59
6.59
Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
Ph
N
H
Ph
3f
C (m) 7.41
E (s) 8.72
B (m) 7.24
A (dd) 6.59
D (dd) 7.57
CD2Cl2
1.02
4.11
4.09
1.98
2.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical shift (ppm)

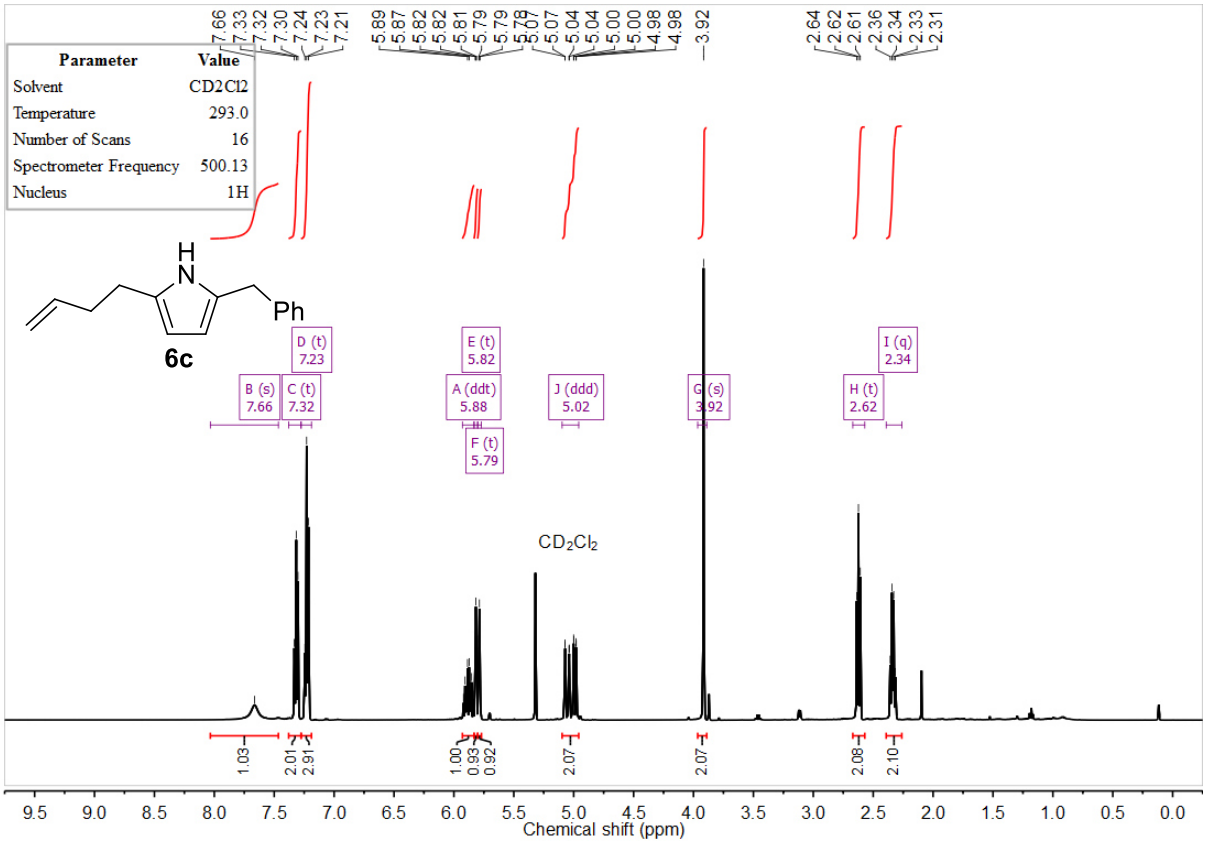

Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
133.57
132.95
129.50
126.91
124.21
108.40
CD2Cl2
Ph
N
H
Ph
3f
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)


Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
7.62
7.35
7.33
7.30
7.25
7.23
5.82
5.78
3.93
2.55
2.53
2.50
1.60
1.57
1.55
1.42
1.39
1.37
0.97
0.95
0.92
H
N
Ph
6a
H (s) 7.62
G (m) 7.29
F (d) 5.80
E (s) 3.93
D (t) 2.53
C (m) 1.57
B (dq) 1.38
A (t) 0.95
CD2Cl2
0.80
4.26
1.61
1.80
1.80
2.00
2.21
3.34
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)


Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
140.90
132.73
129.49
129.08
129.04
126.74
106.77
105.25
34.69
32.51
27.96
23.01
14.25
H
N
Ph
6a
CD2Cl2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)


Parameter Value
Solvent CD2Cl2
Temperature 293.0
Number of Scans 16
Spectrometer Frequency 500.13
Nucleus 1H
H
N
Ph
6b
7.75 7.35 7.33 7.33 7.32 7.26 7.25 7.23
5.81 5.80 5.80 5.72 5.71 5.71
3.92
1.77 1.76 1.75 1.74 1.73 1.72 1.71
0.80 0.80 0.78 0.78 0.58 0.57 0.57
I (m) 7.25
C (t) 5.71
D (m) 0.57
G (s) 7.75
H (m) 7.33
B (t) 5.80
F (s) 3.92
E (m) 1.74
A (m) 0.79
CD2Cl2
1.04 2.06 3.08 1.00 1.01 2.28 1.00 2.15 2.13
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)


Parameter Value
Solvent CD2Cl2
Temperature 293.0
Number of Scans 128
Spectrometer Frequency 125.76
Nucleus 13C
H
N
Ph
6b
140.74 134.24 129.75 129.09 129.05 126.77
106.66 104.06
34.67
8.59 6.88
CD2Cl2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)


Parameter Value
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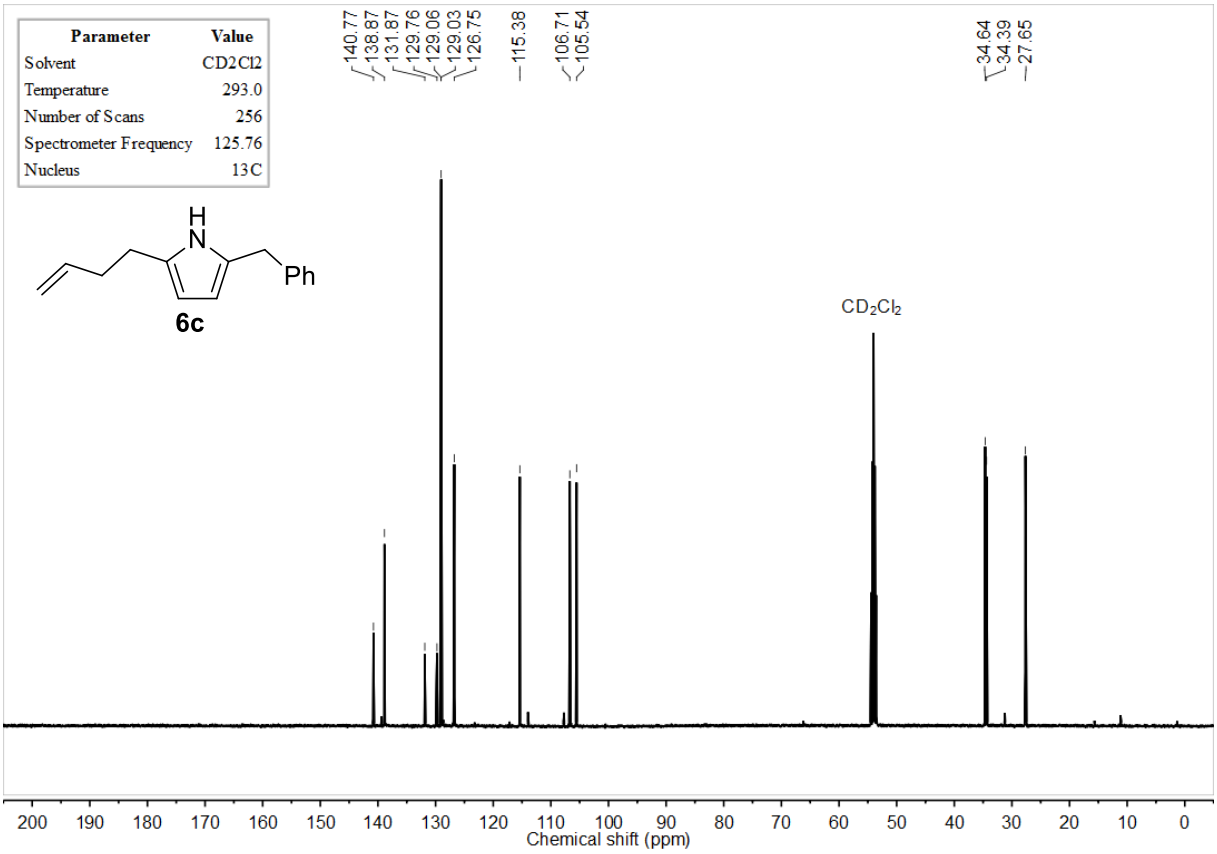
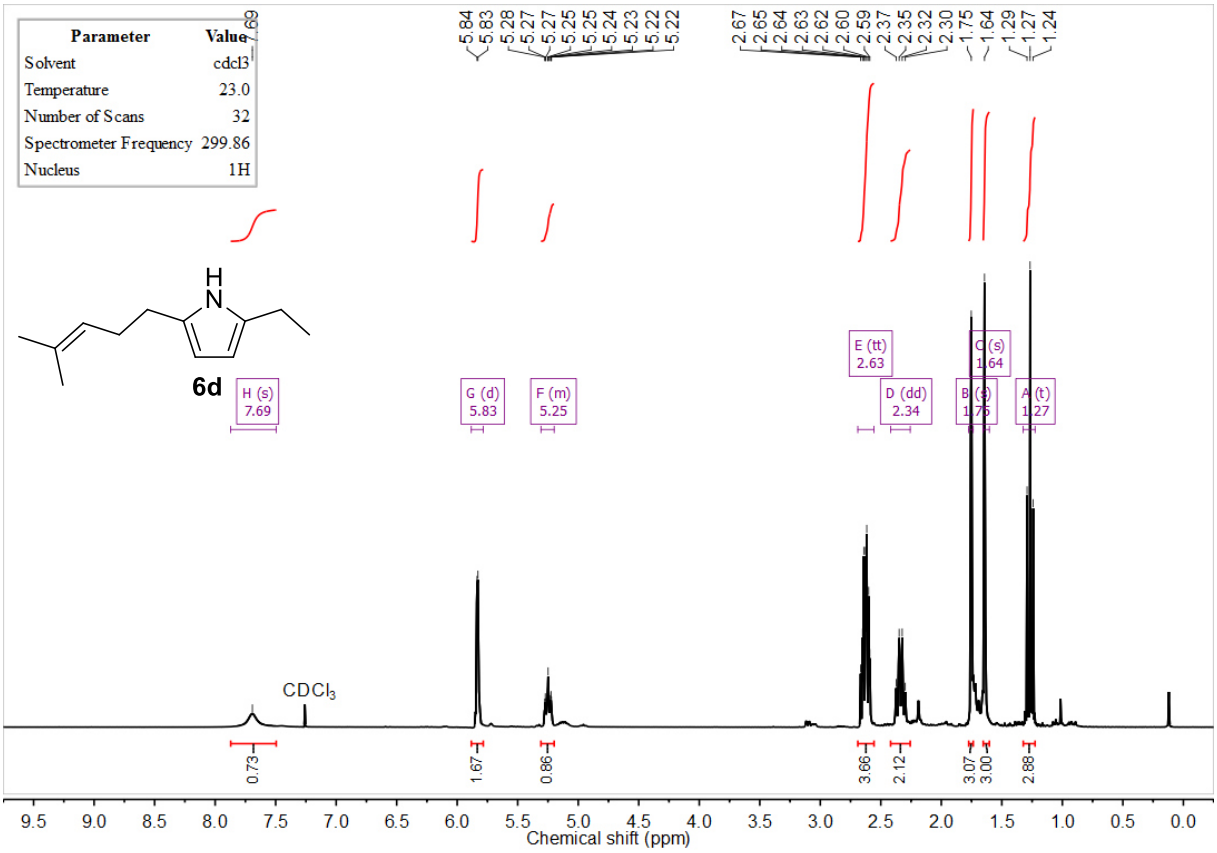
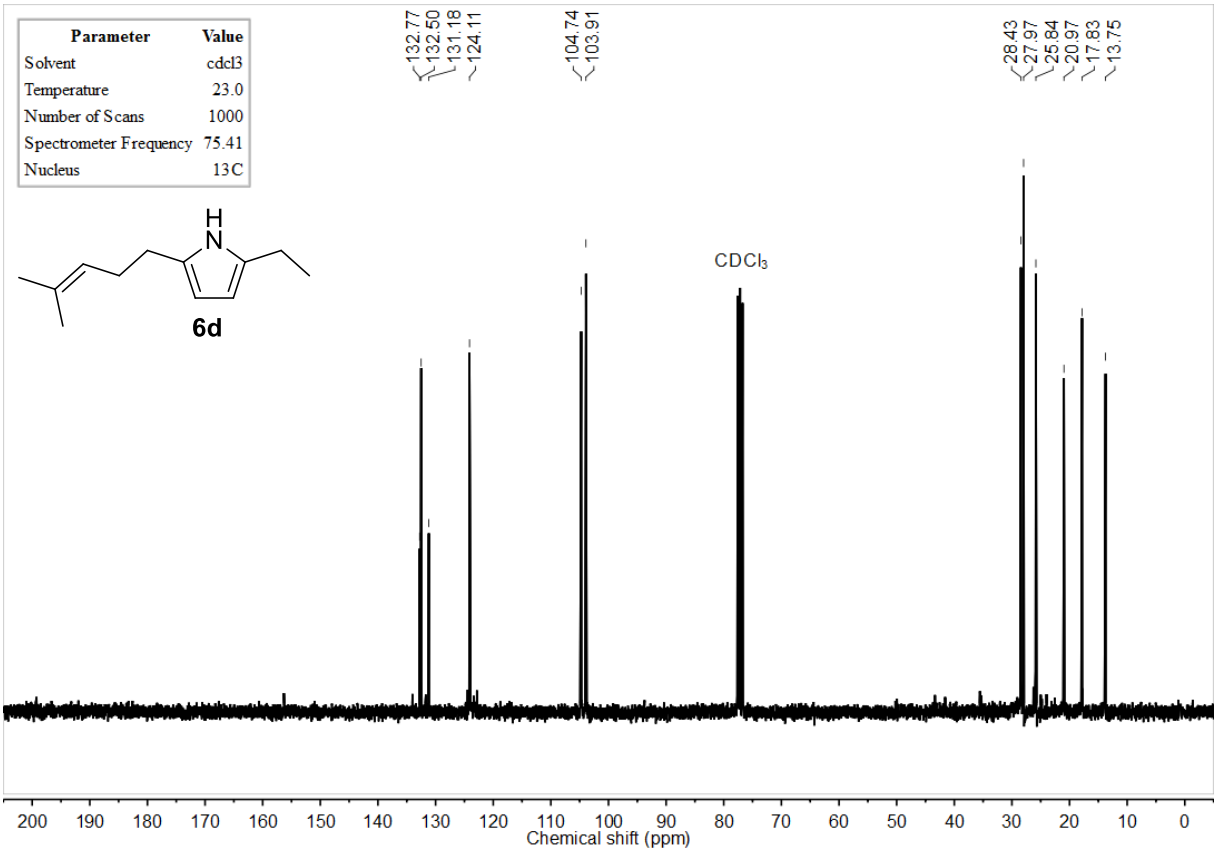
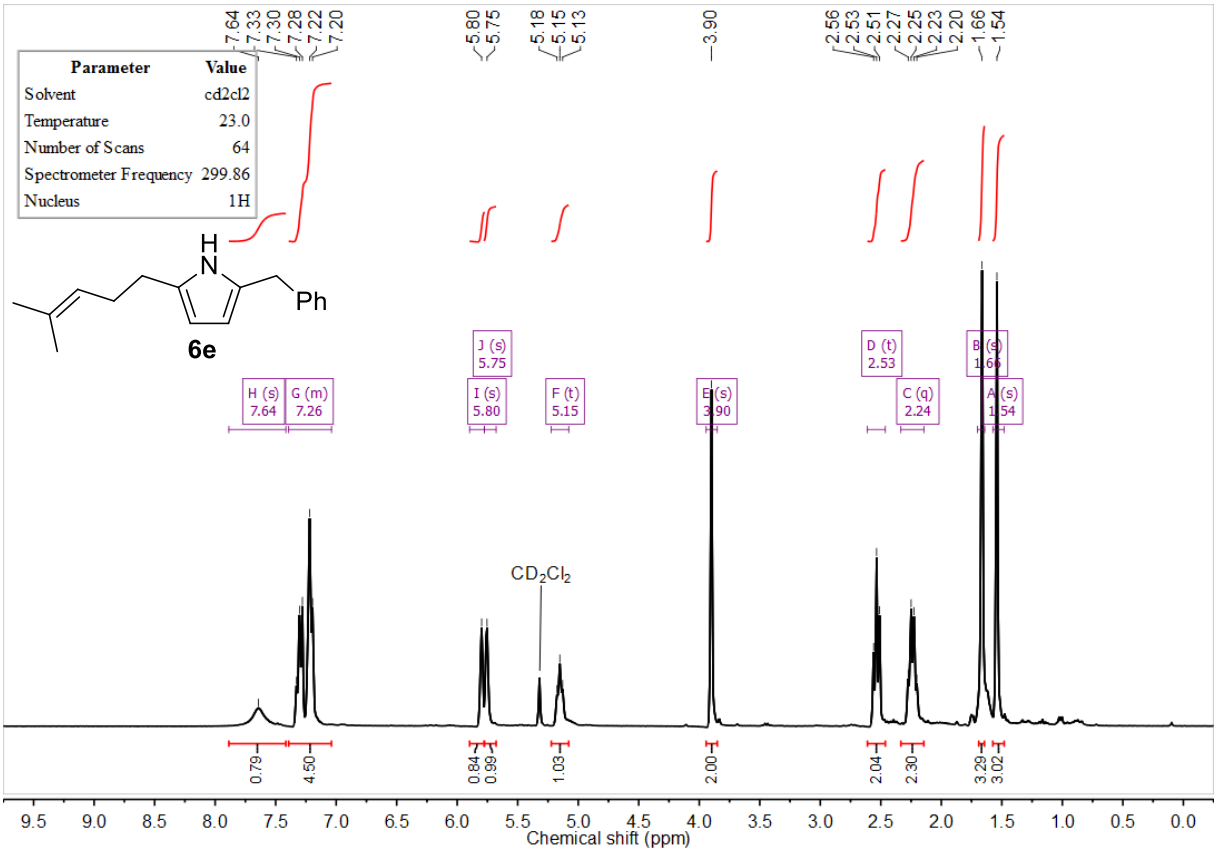
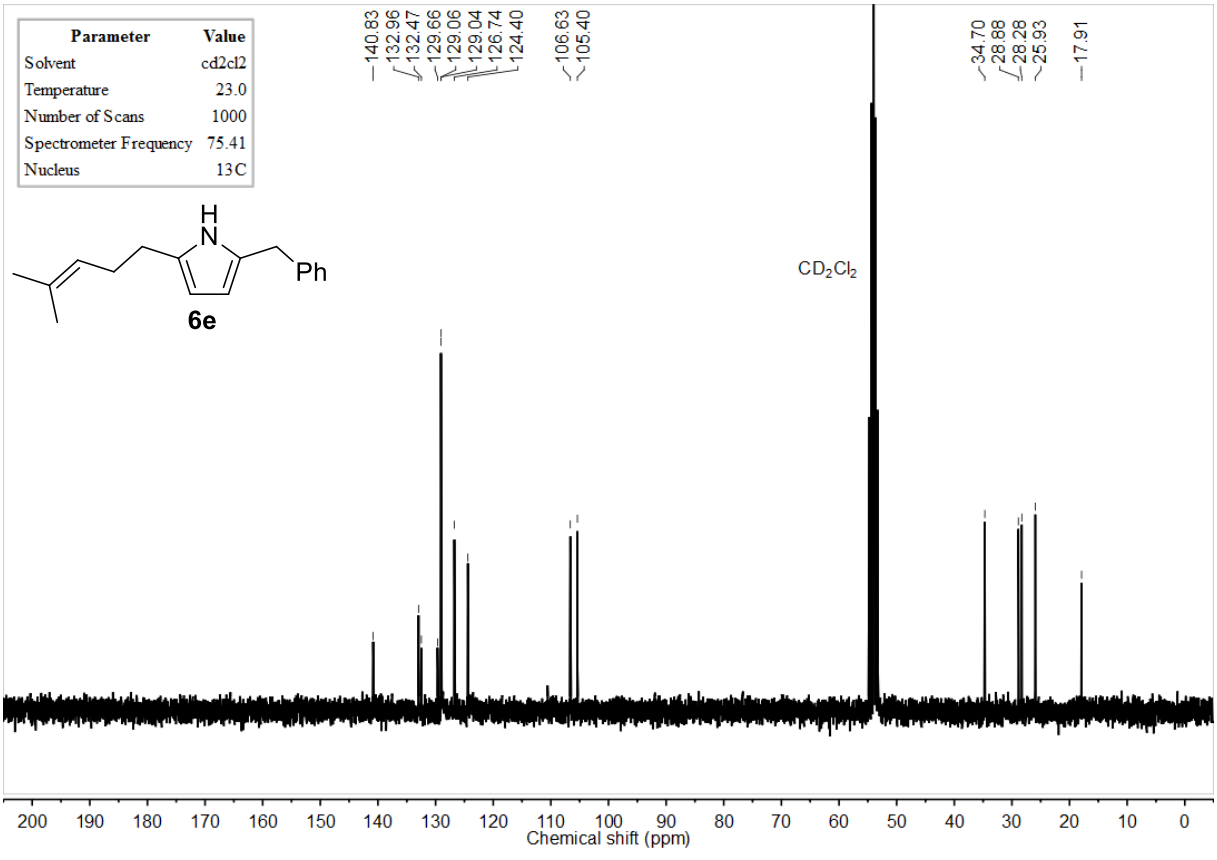
Temperature 293.0
Number of Scans 16
Spectrometer Frequency 500.13
Nucleus 1H
6c
CD2Cl2
Chemical shift (ppm)

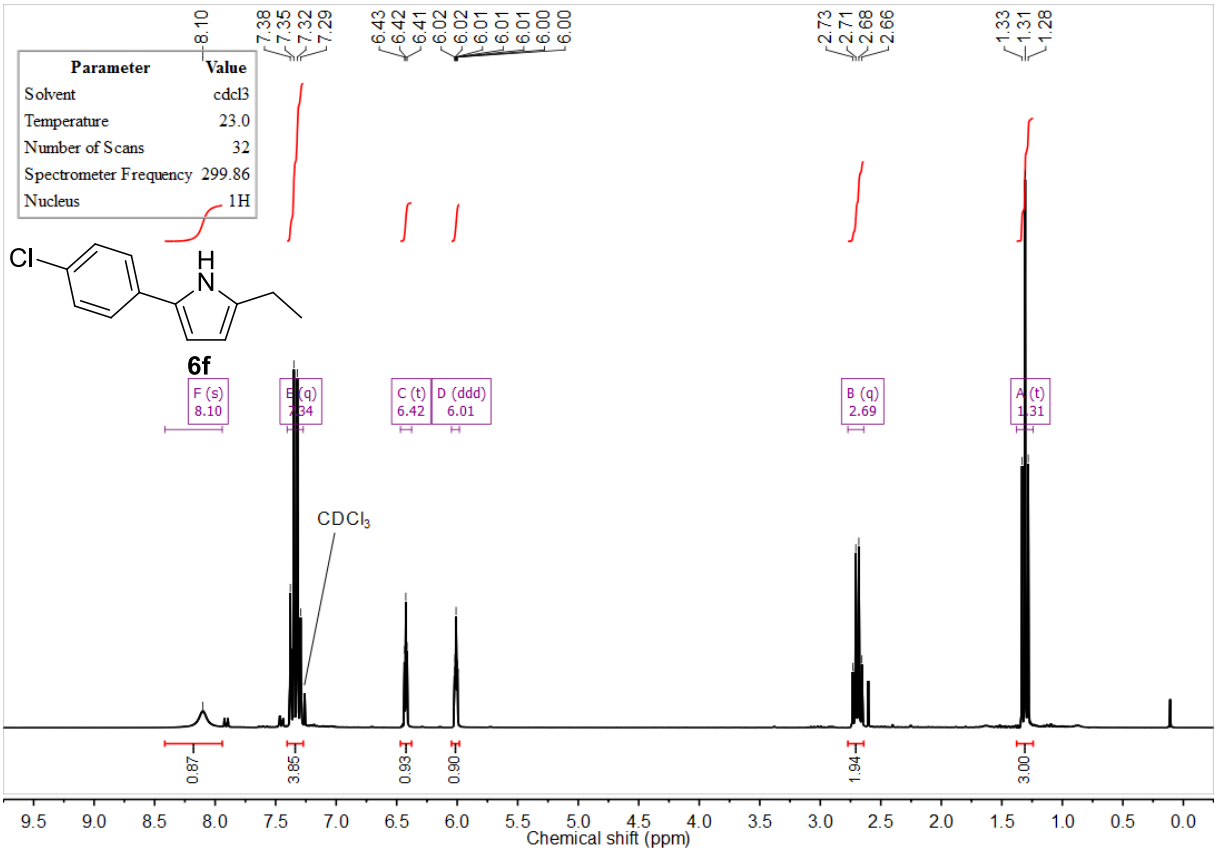

Parameter Value
Solvent CD2Cl2
Temperature 293.0
Number of Scans 256
Spectrometer Frequency 125.76
Nucleus 13C
6c
CD2Cl2
Chemical shift (ppm)

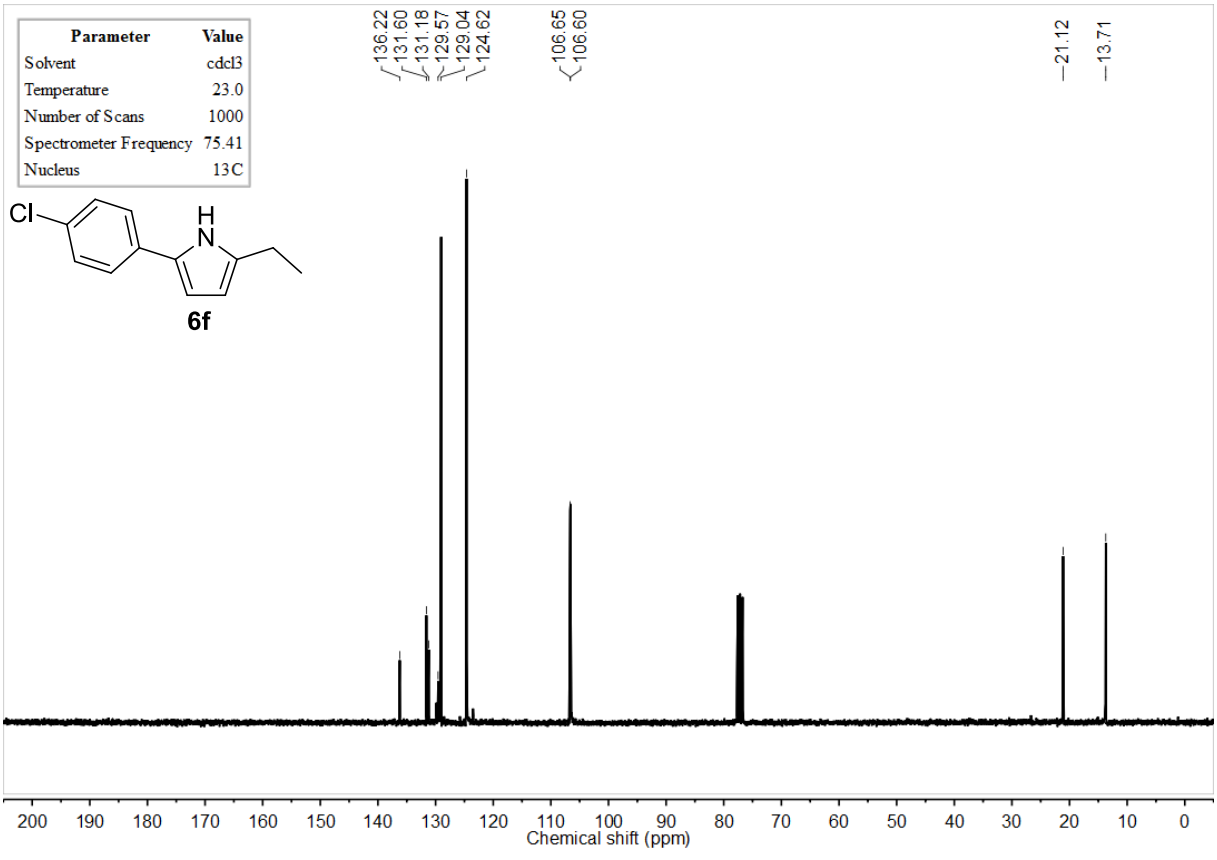

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
6d
H (s) 7.69
G (d) 5.83
F (m) 5.25
E (tt) 2.63
D (dd) 2.34
C (s) 1.64
B (s) 1.75
A (t) 1.27
CDCl3
Chemical shift (ppm)

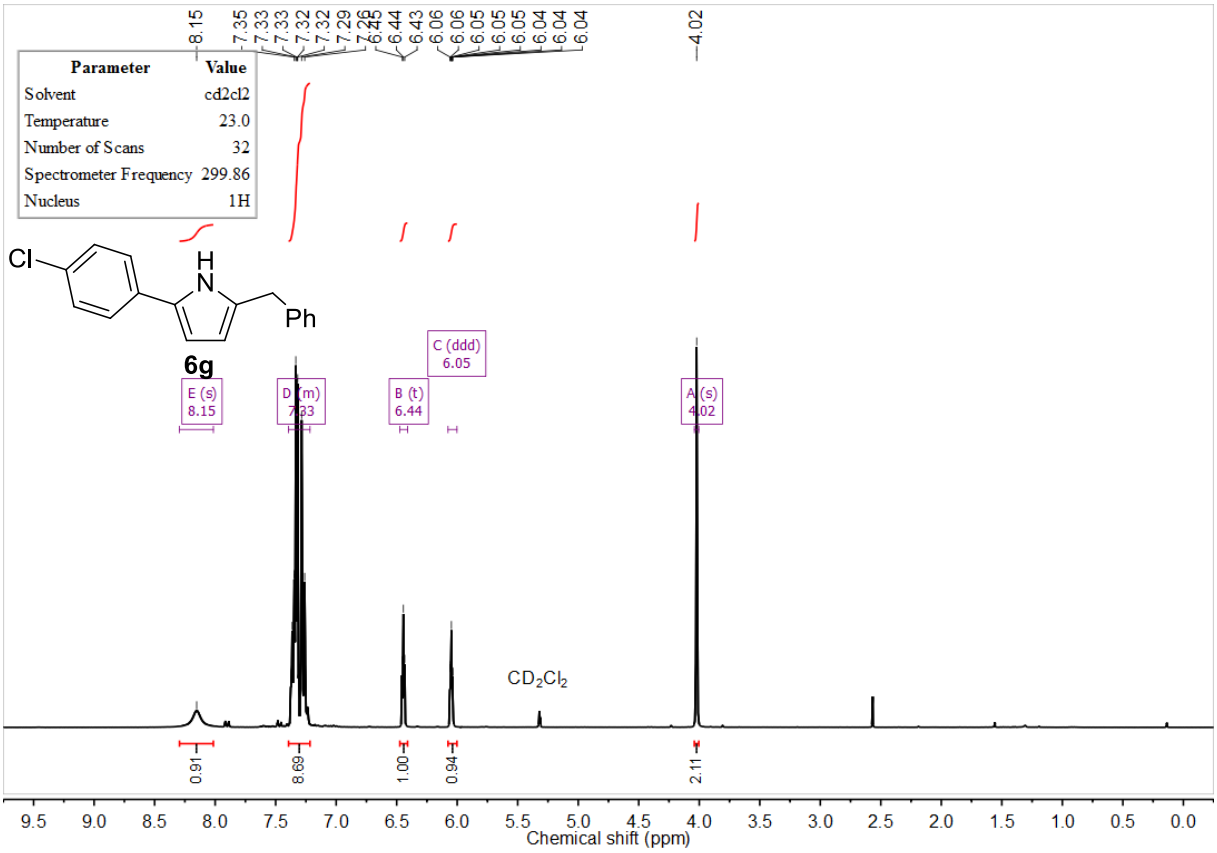

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
6d
CDCl3
Chemical shift (ppm)

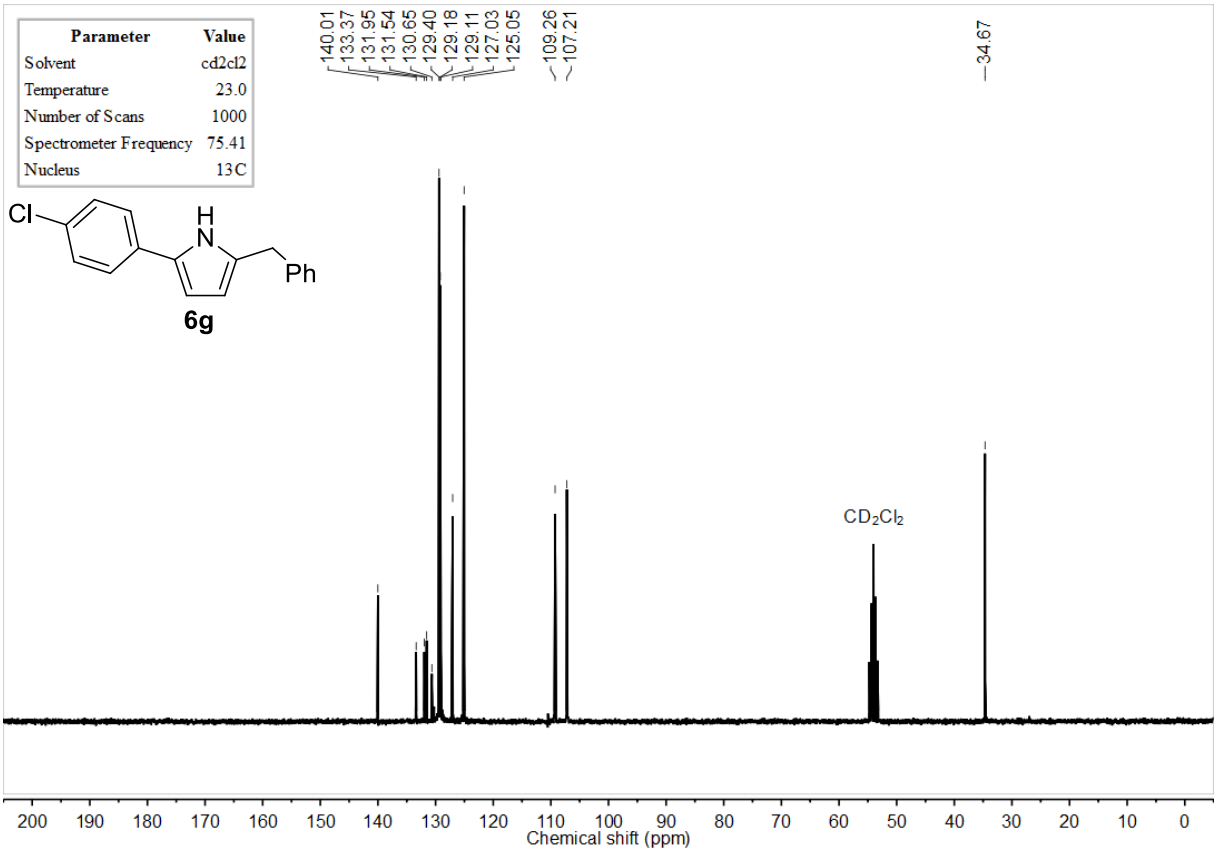

Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 64
Spectrometer Frequency 299.86
Nucleus 1H
H
N
Ph
6e
7.64
7.33
7.30
7.28
7.22
7.20
5.80
5.75
5.18
5.15
5.13
3.90
2.56
2.53
2.51
2.27
2.25
2.23
2.20
1.66
1.54
J (s) 5.75
D (t) 2.53
B (s) 1.66
H (s) 7.64
G (m) 7.26
I (s) 5.80
F (t) 5.15
E (s) 3.90
C (q) 2.24
A (s) 1.54
CD2Cl2
0.79
4.50
0.84
0.99
1.03
2.00
2.04
2.30
3.29
3.02
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)

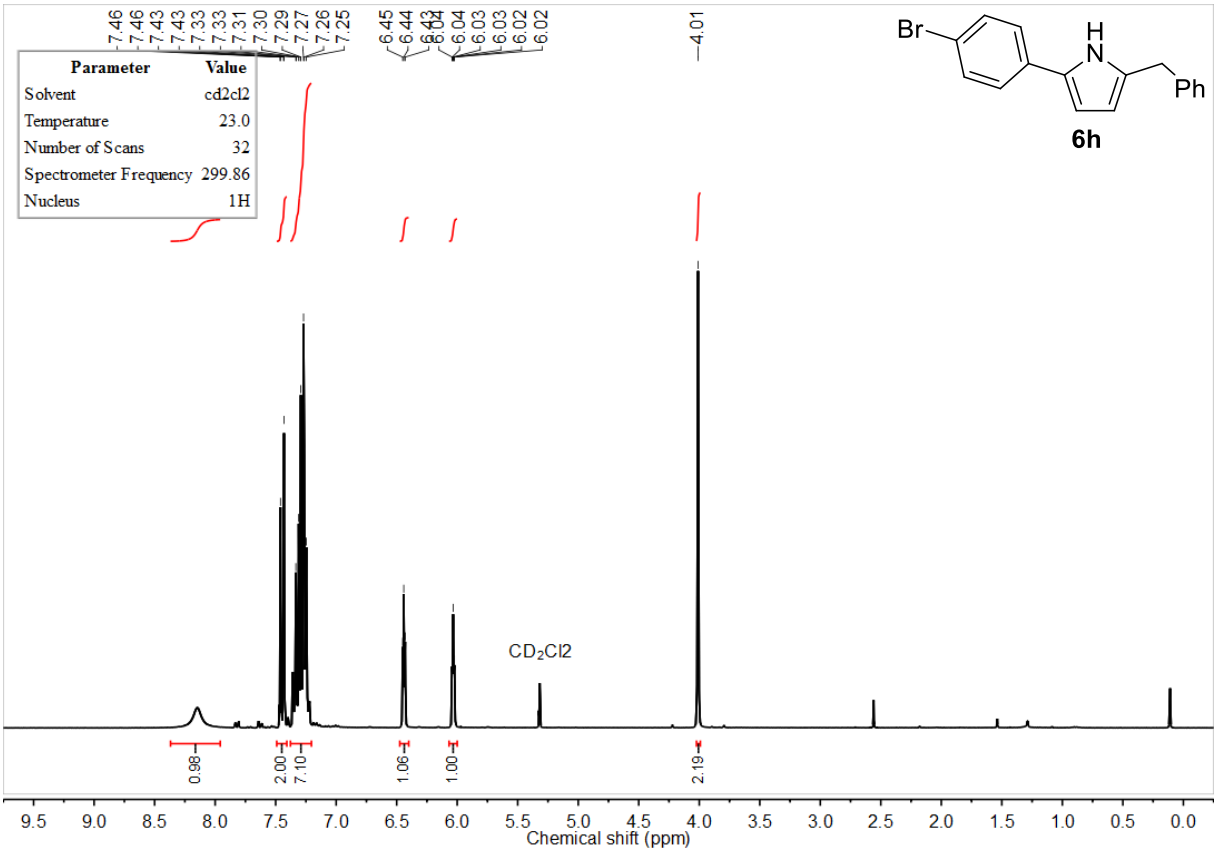

Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
H
N
Ph
6e
140.83
132.96
132.47
129.66
129.06
129.04
126.74
124.40
106.63
105.40
34.70
28.88
28.28
25.93
17.91
CD2Cl2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

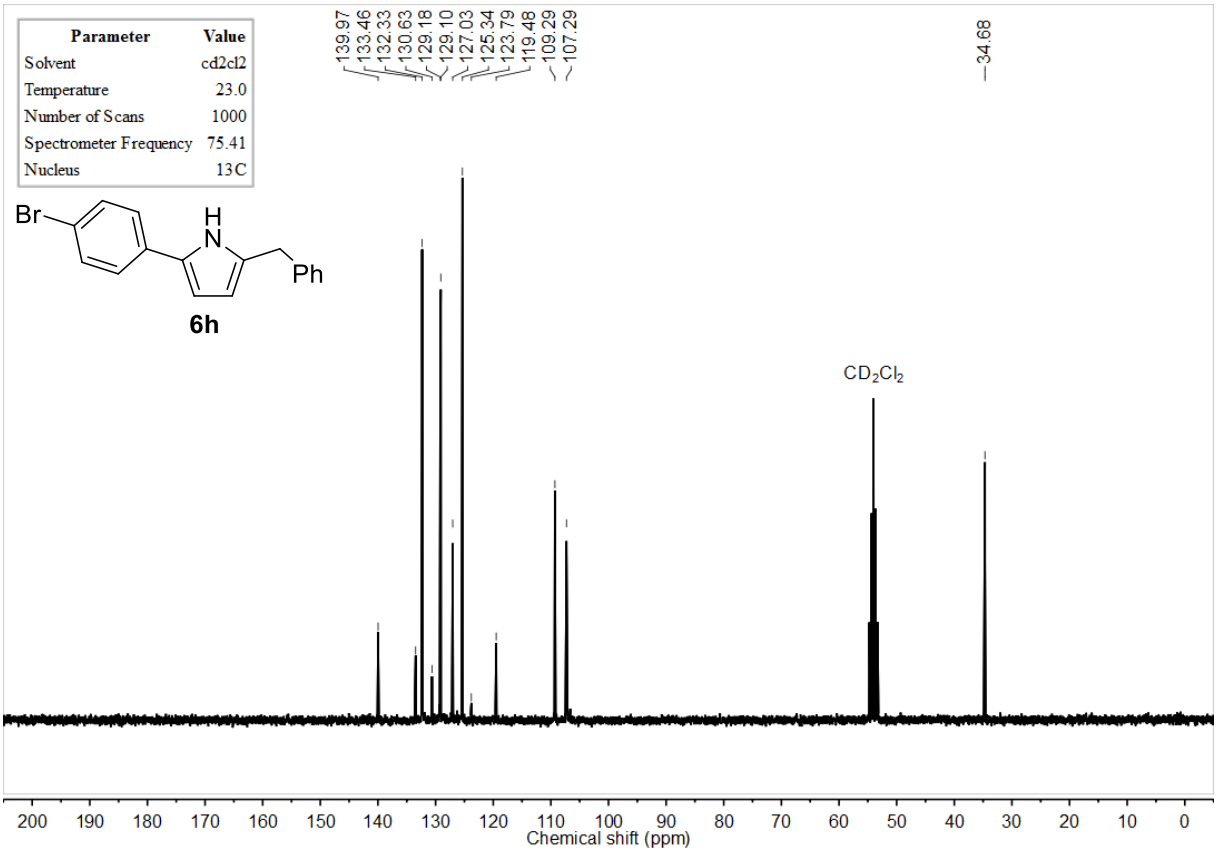

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
8.10
7.38
7.35
7.32
7.29
6.43
6.42
6.41
6.02
6.02
6.01
6.01
6.01
6.00
6.00
2.73
2.71
2.68
2.66
1.33
1.31
1.28
Cl
H
N
6f
F (s) 8.10
C (t) 6.42
D (ddd) 6.01
B (q) 2.69
A (t) 1.31
CDCl3
0.87
3.85
0.93
0.90
1.94
3.00
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)

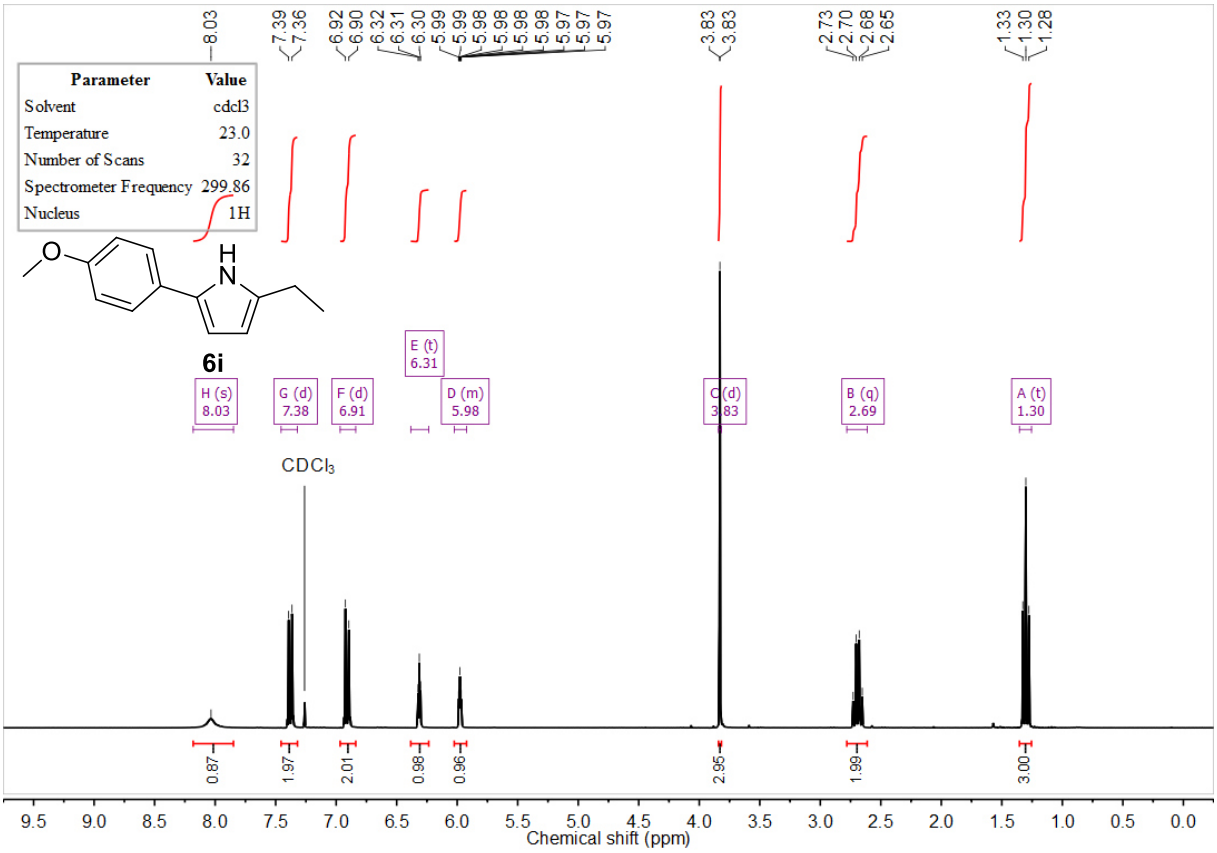

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
136.22
131.60
131.18
129.57
129.04
124.62
106.65
106.60
21.12
13.71
Cl
H
N
6f
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

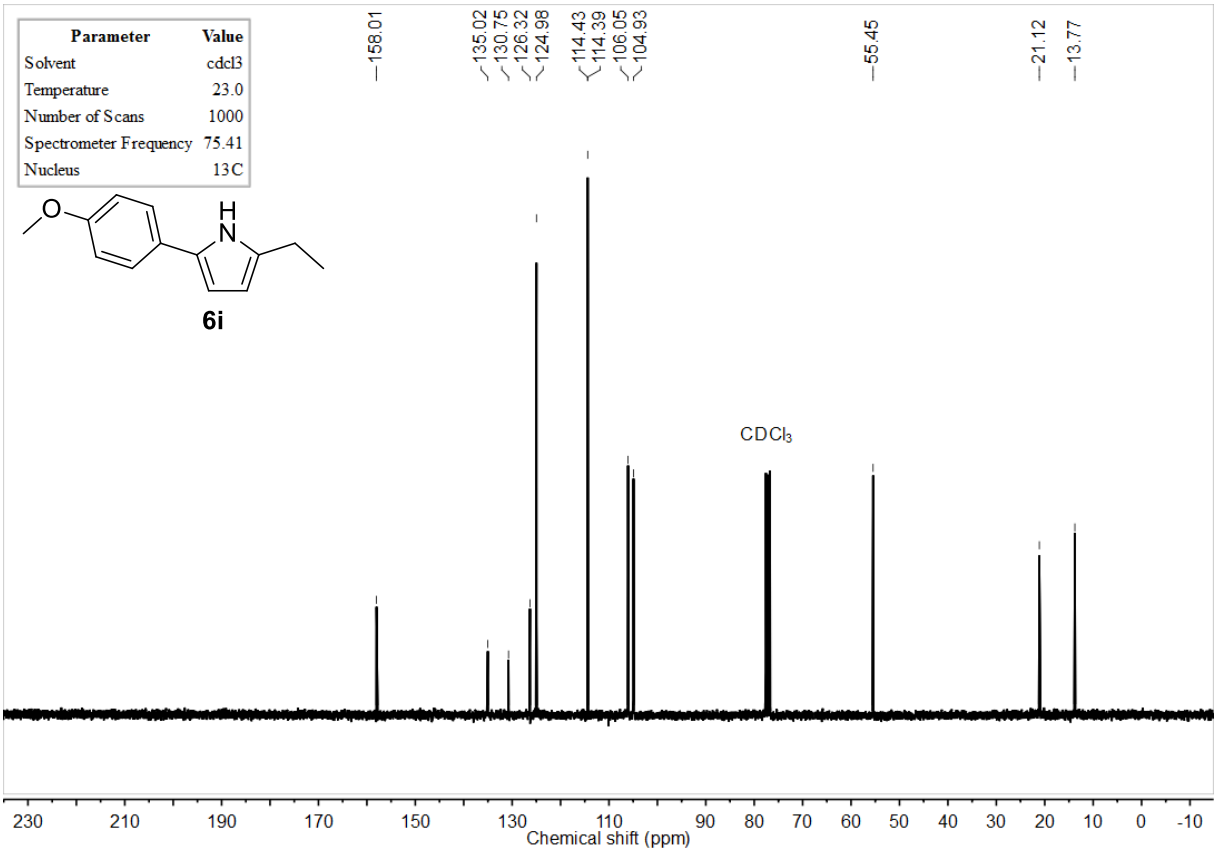

Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
Cl
H
N
Ph
6g
E (s) 8.15
D (m) 7.33
B (t) 6.44
C (ddd) 6.05
A (s) 4.02
CD2Cl2
0.91
8.69
1.00
0.94
2.11
Chemical shift (ppm)

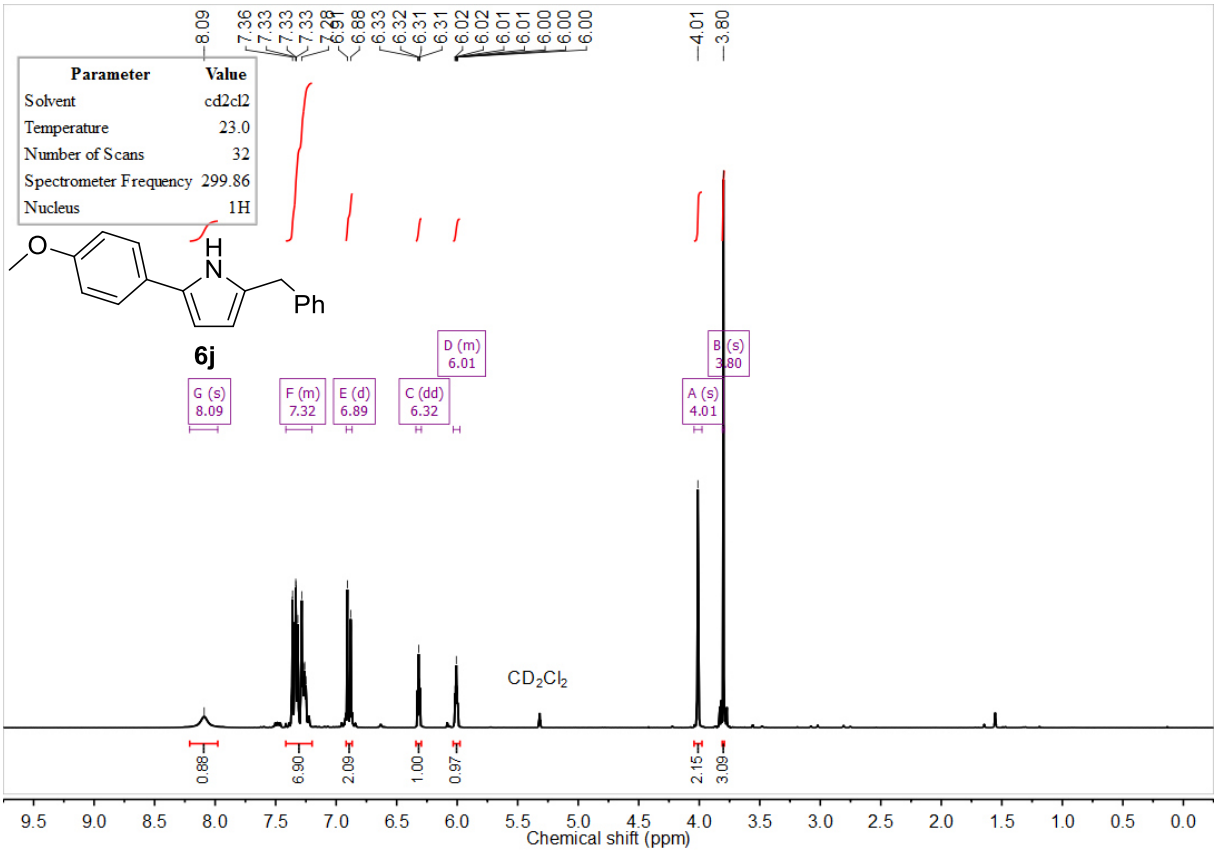

Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
Cl
H
N
Ph
6g
CD2Cl2
Chemical shift (ppm)

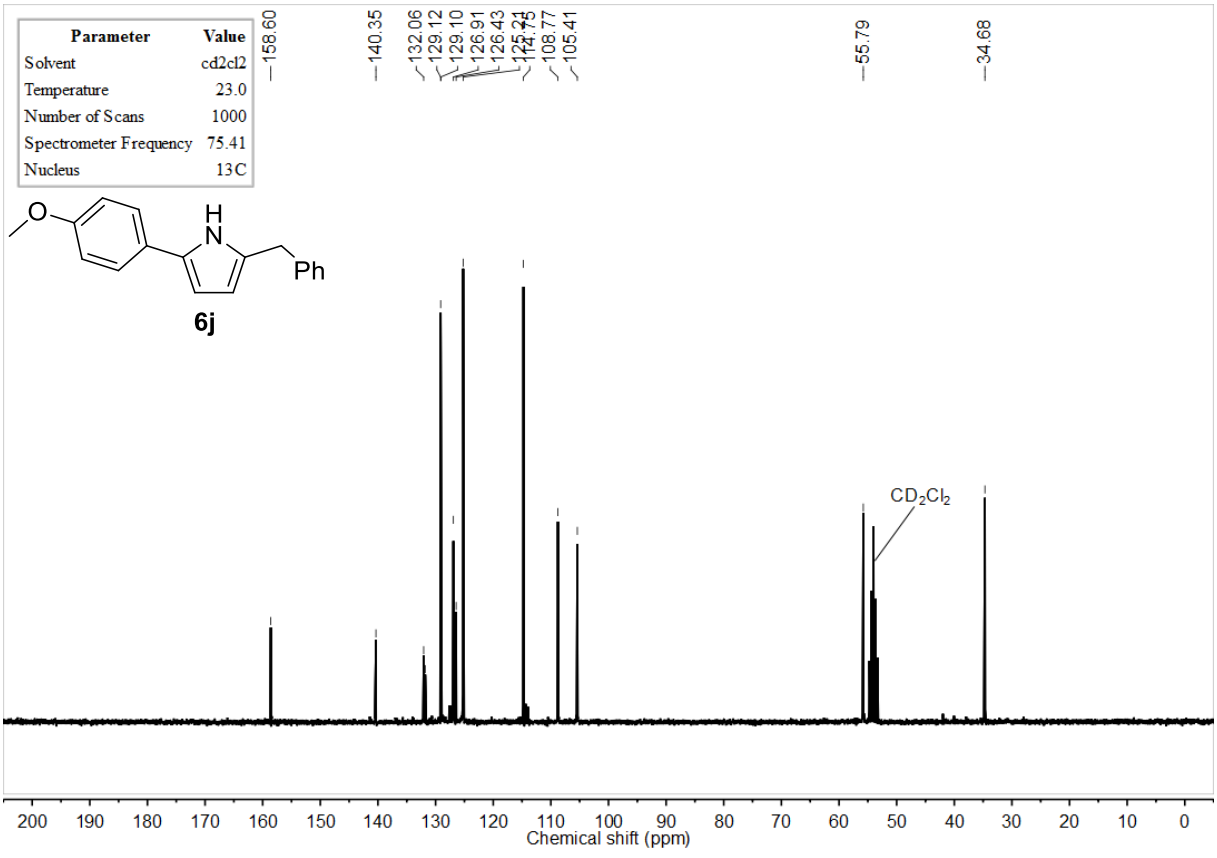

7.46
7.46
7.43
7.43
7.33
7.33
7.31
7.30
7.29
7.27
7.26
7.25
6.45
6.44
6.04
6.04
6.03
6.03
6.02
6.02
4.01
Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
Br
H
N
Ph
6h
CD2Cl2
0.98
2.00
7.10
1.06
1.00
2.19
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical shift (ppm)

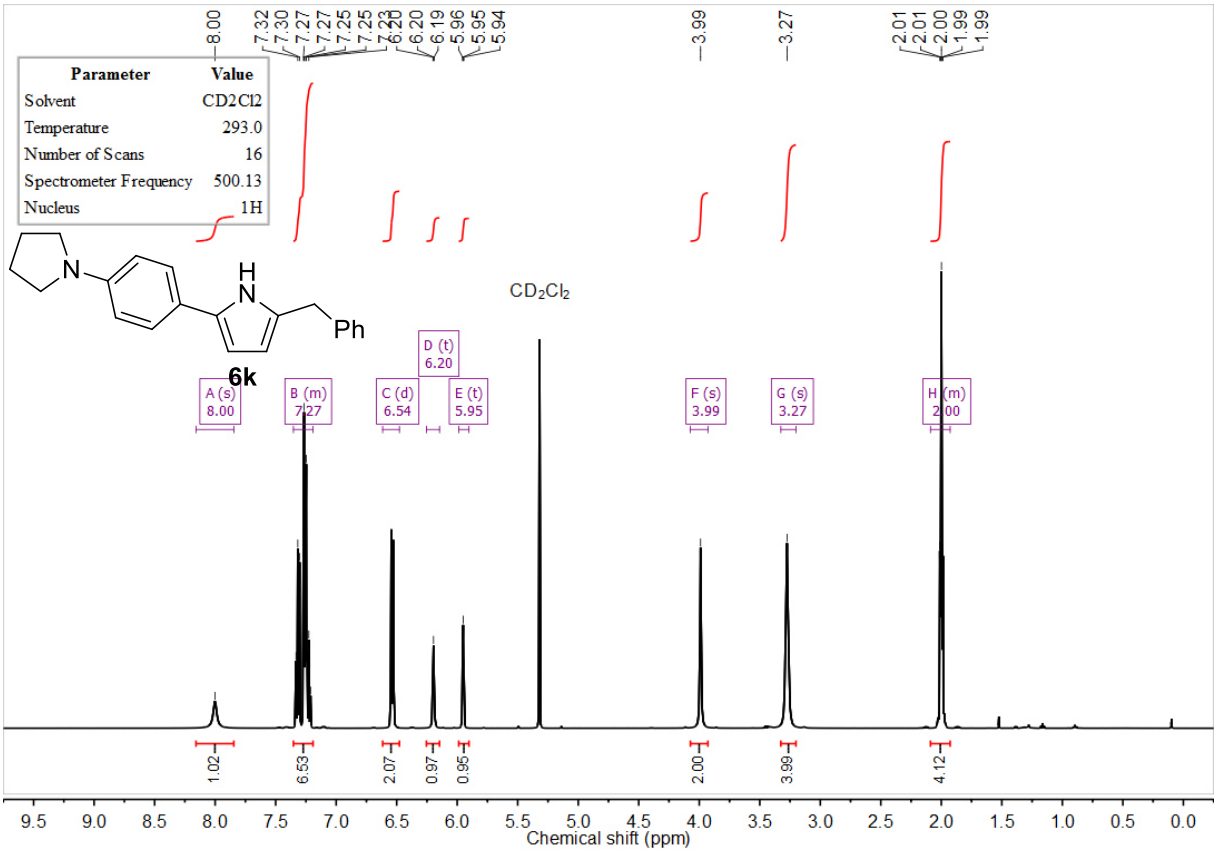

Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
139.97
133.46
132.33
130.63
129.18
129.10
127.03
125.34
123.79
119.48
109.29
107.29
34.68
Br
H
N
Ph
6h
CD2Cl2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

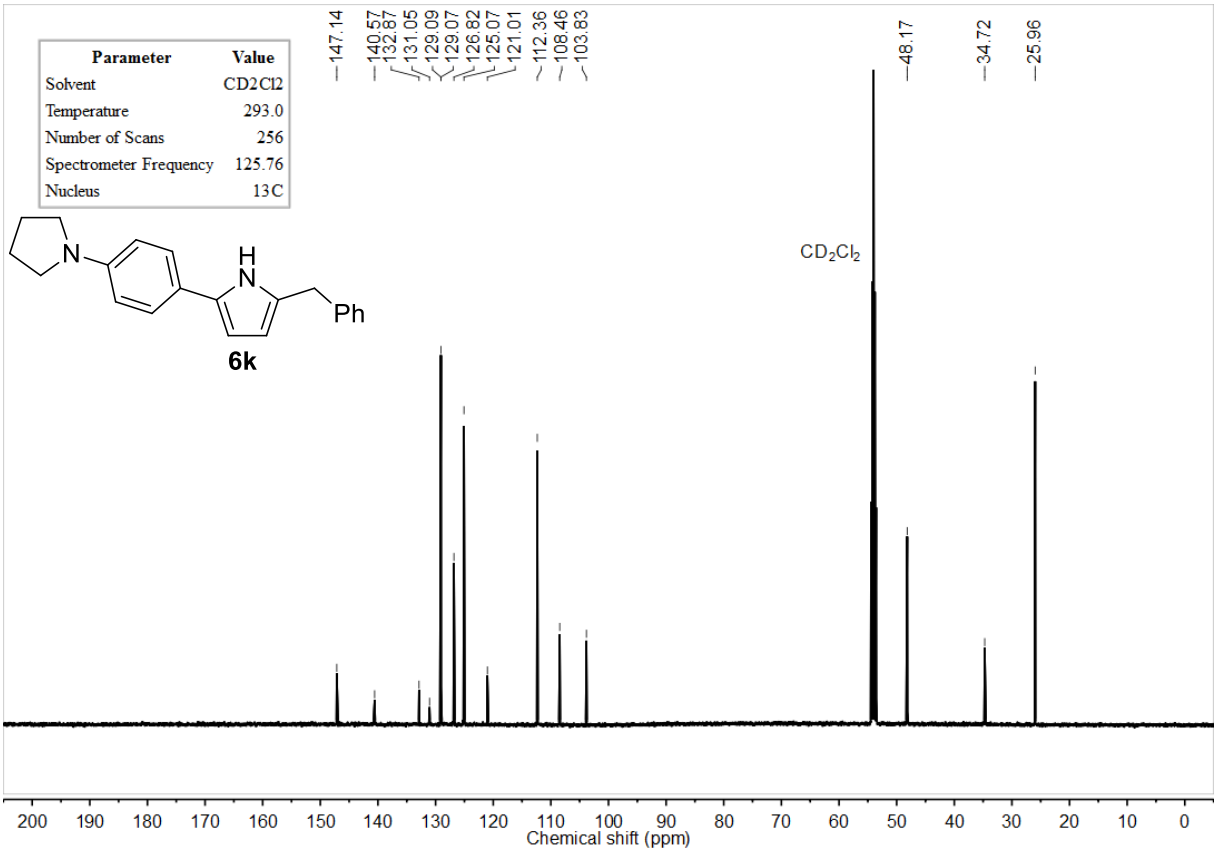

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
6i
H (s) 8.03
G (d) 7.38
F (d) 6.91
E (t) 6.31
D (m) 5.98
C (d) 3.83
B (q) 2.69
A (t) 1.30
CDCl3
Chemical shift (ppm)

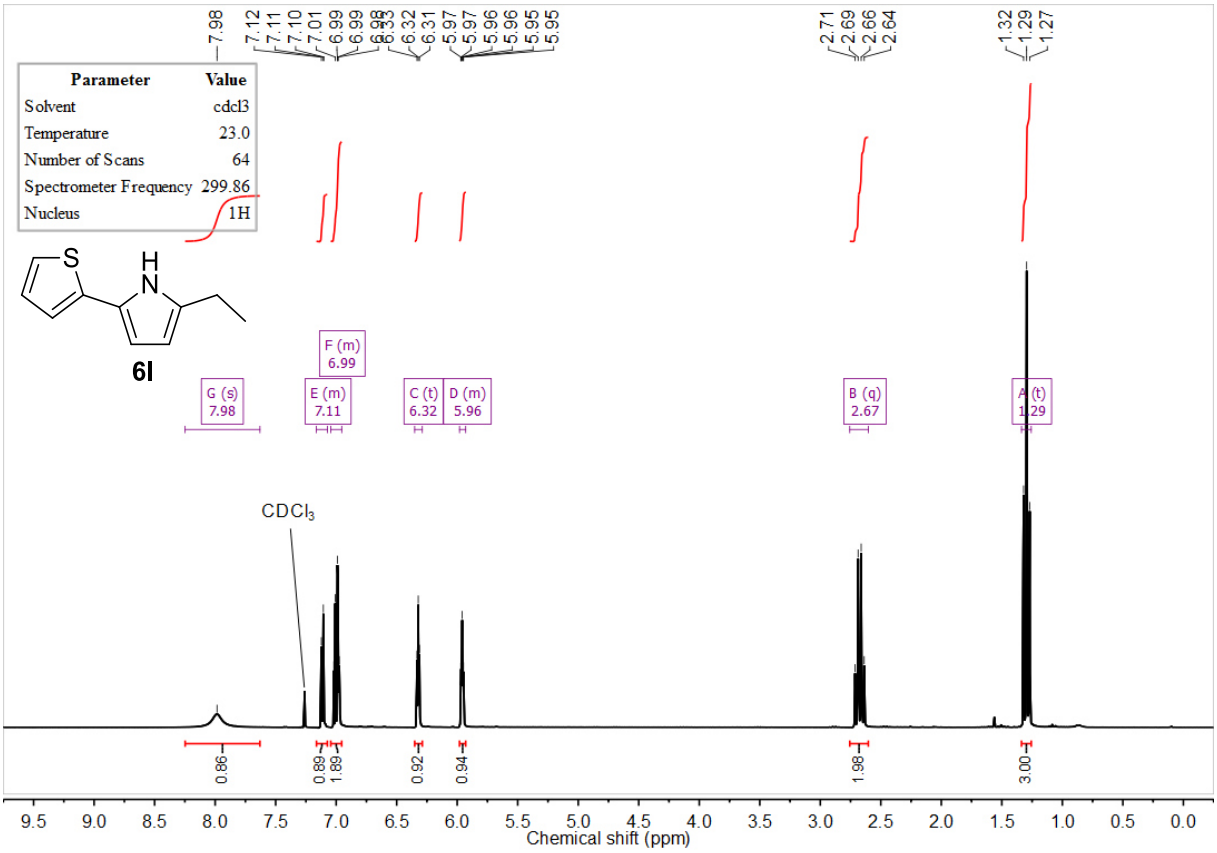

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
6i
158.01
135.02
130.75
126.32
124.98
114.43
114.39
106.05
104.93
55.45
21.12
13.77
CDCl3
Chemical shift (ppm)

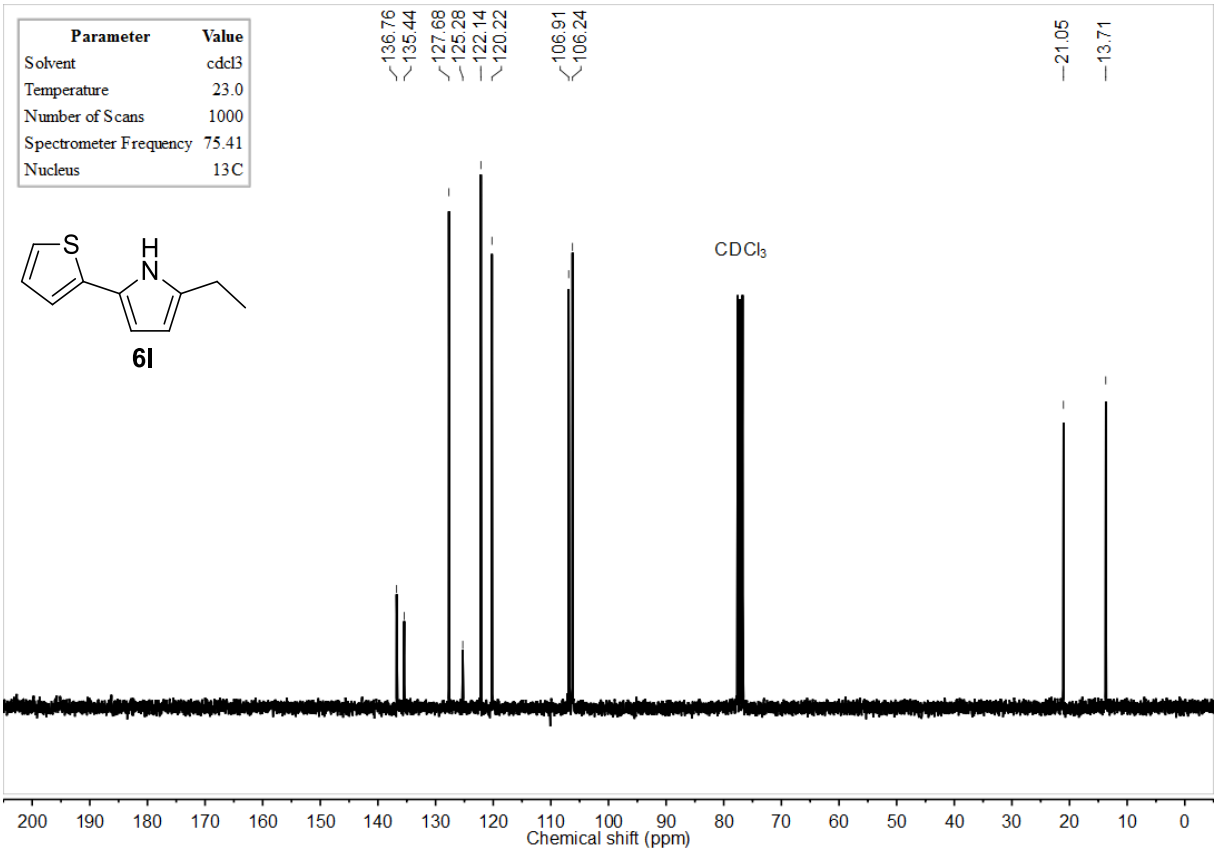

Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
6j
G (s) 8.09
F (m) 7.32
E (d) 6.89
C (dd) 6.32
D (m) 6.01
A (s) 4.01
B (s) 3.80
CD2Cl2
Chemical shift (ppm)

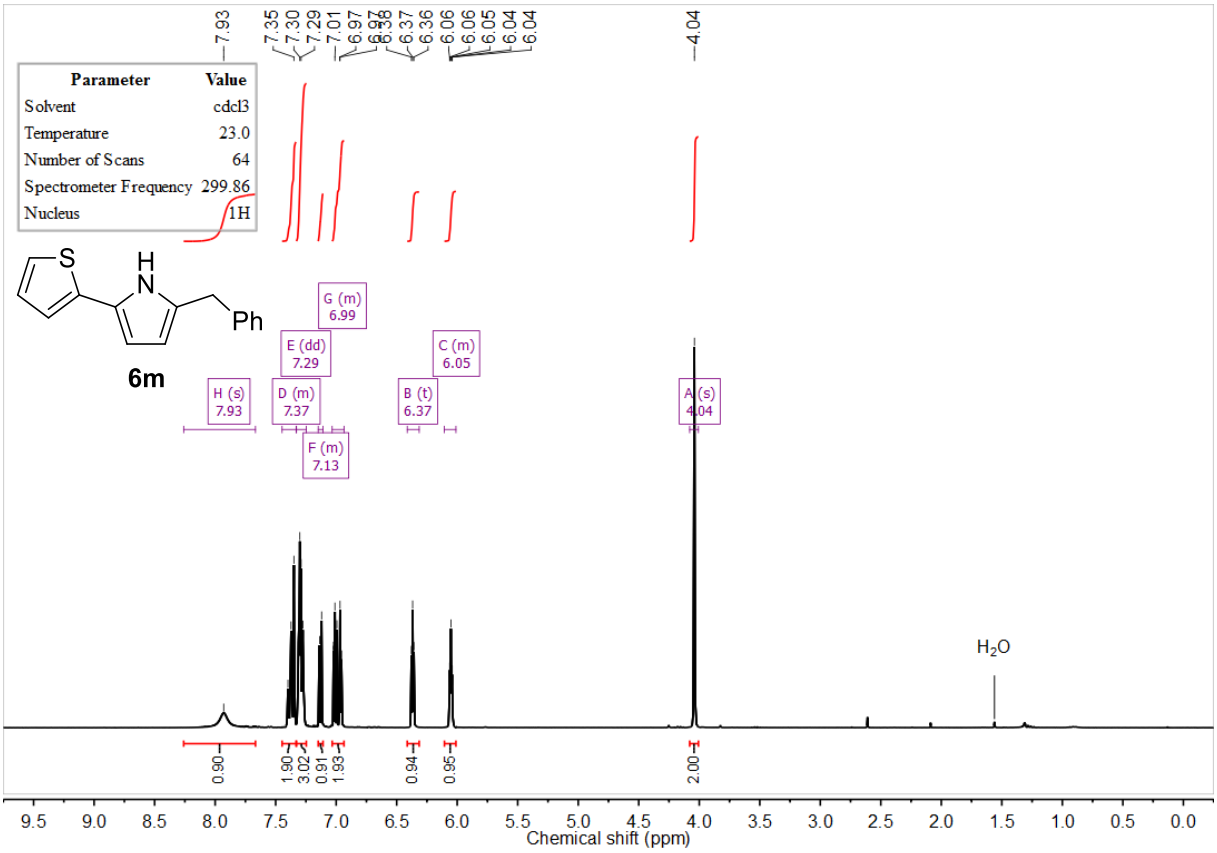

Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
6j
CD2Cl2
Chemical shift (ppm)

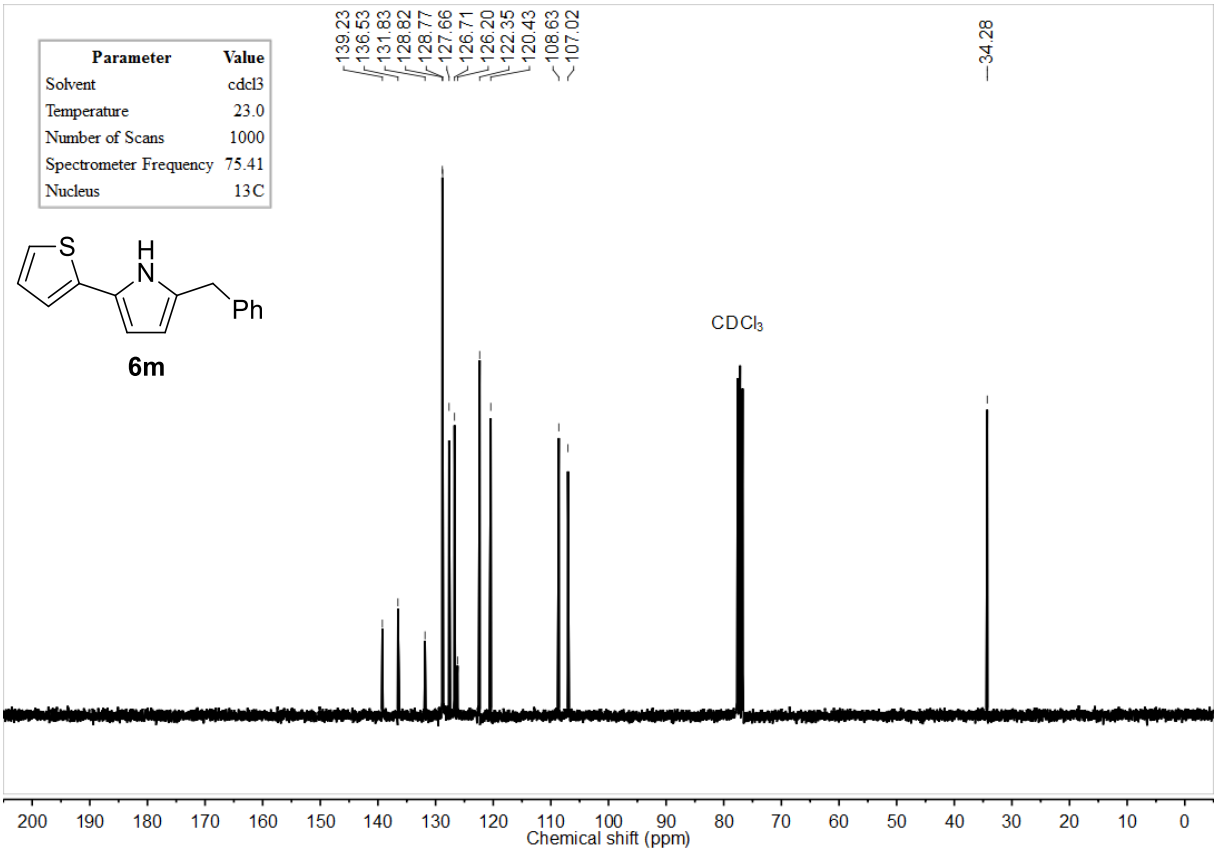

Parameter Value
Solvent CD2Cl2
Temperature 293.0
Number of Scans 16
Spectrometer Frequency 500.13
Nucleus 1H
8.00
7.32
7.30
7.27
7.27
7.25
7.25
6.20
6.19
5.96
5.95
5.94
3.99
3.27
2.01
2.01
2.00
1.99
1.99
N
H
N
Ph
6k
CD2Cl2
A (s) 8.00
B (m) 7.27
C (d) 6.54
D (t) 6.20
E (t) 5.95
F (s) 3.99
G (s) 3.27
H (m) 2.00
1.02
6.53
2.07
0.97
0.95
2.00
3.99
4.12
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)

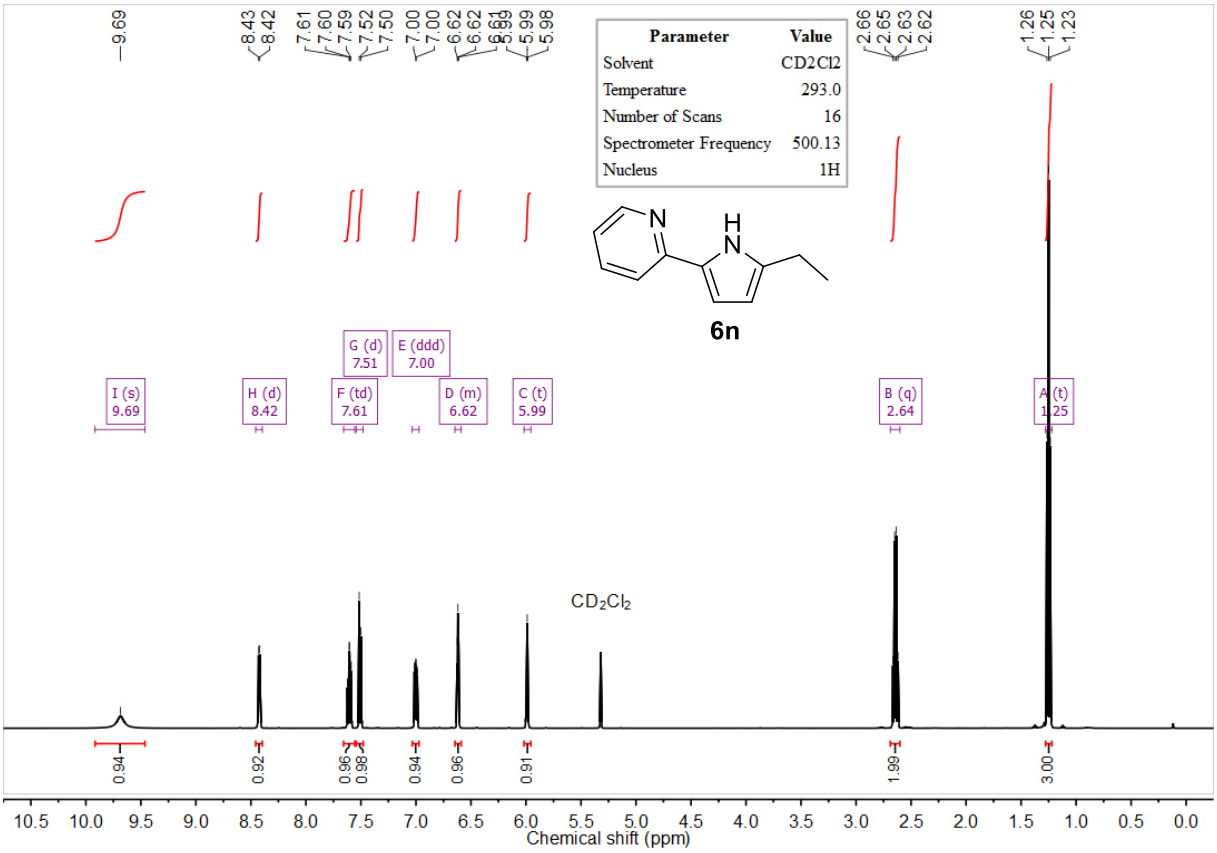

Parameter Value
Solvent CD2Cl2
Temperature 293.0
Number of Scans 256
Spectrometer Frequency 125.76
Nucleus 13C
147.14
140.57
132.87
131.05
129.09
129.07
126.82
125.07
121.01
112.36
108.46
103.83
48.17
34.72
25.96
N
H
N
Ph
6k
CD2Cl2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

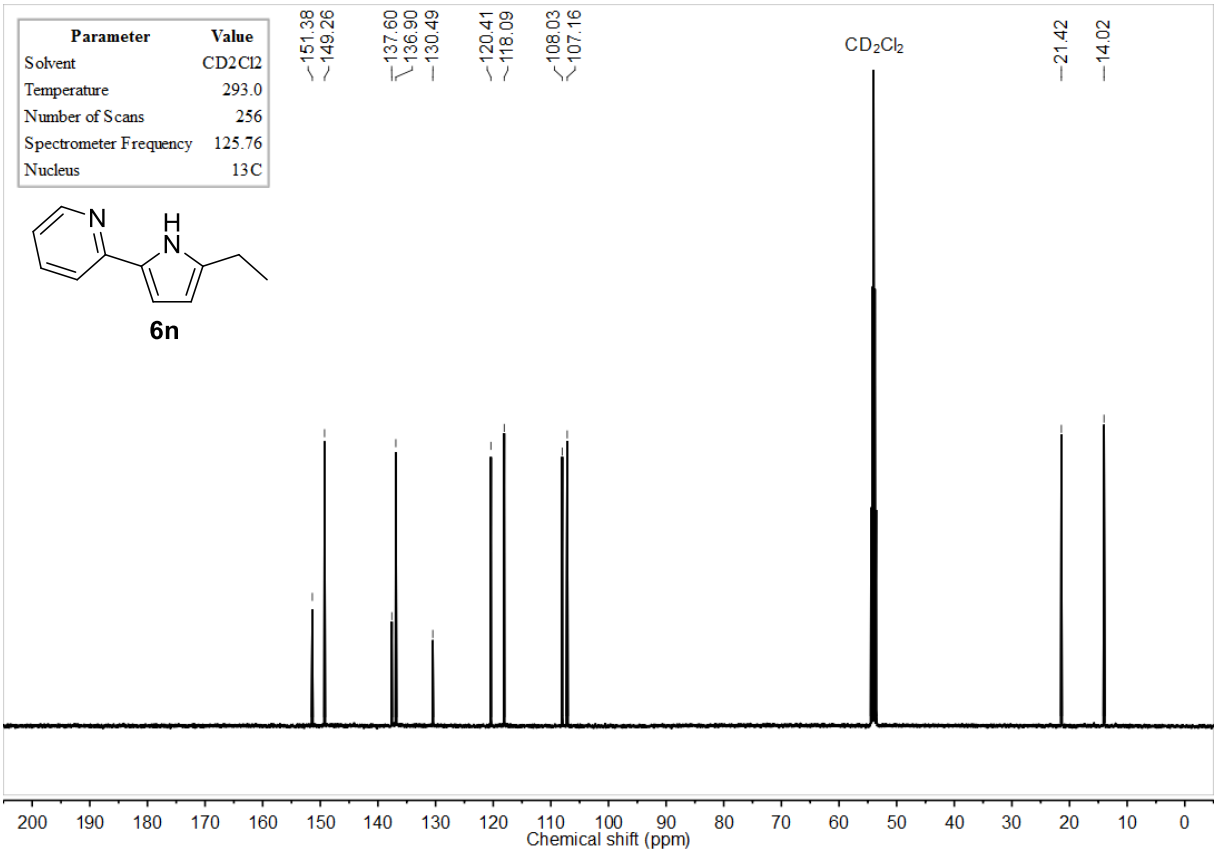

7.98
7.12
7.11
7.10
7.01
6.99
6.98
6.93
6.32
6.31
5.97
5.97
5.96
5.96
5.95
5.95
2.71
2.69
2.66
2.64
1.32
1.29
1.27
Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 64
Spectrometer Frequency 299.86
Nucleus 1H
S
H
N
6l
F (m) 6.99
G (s) 7.98
E (m) 7.11
C (t) 6.32
D (m) 5.96
B (q) 2.67
A (t) 1.29
CDCl3
0.86
0.89
1.89
0.92
0.94
1.98
3.00
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)

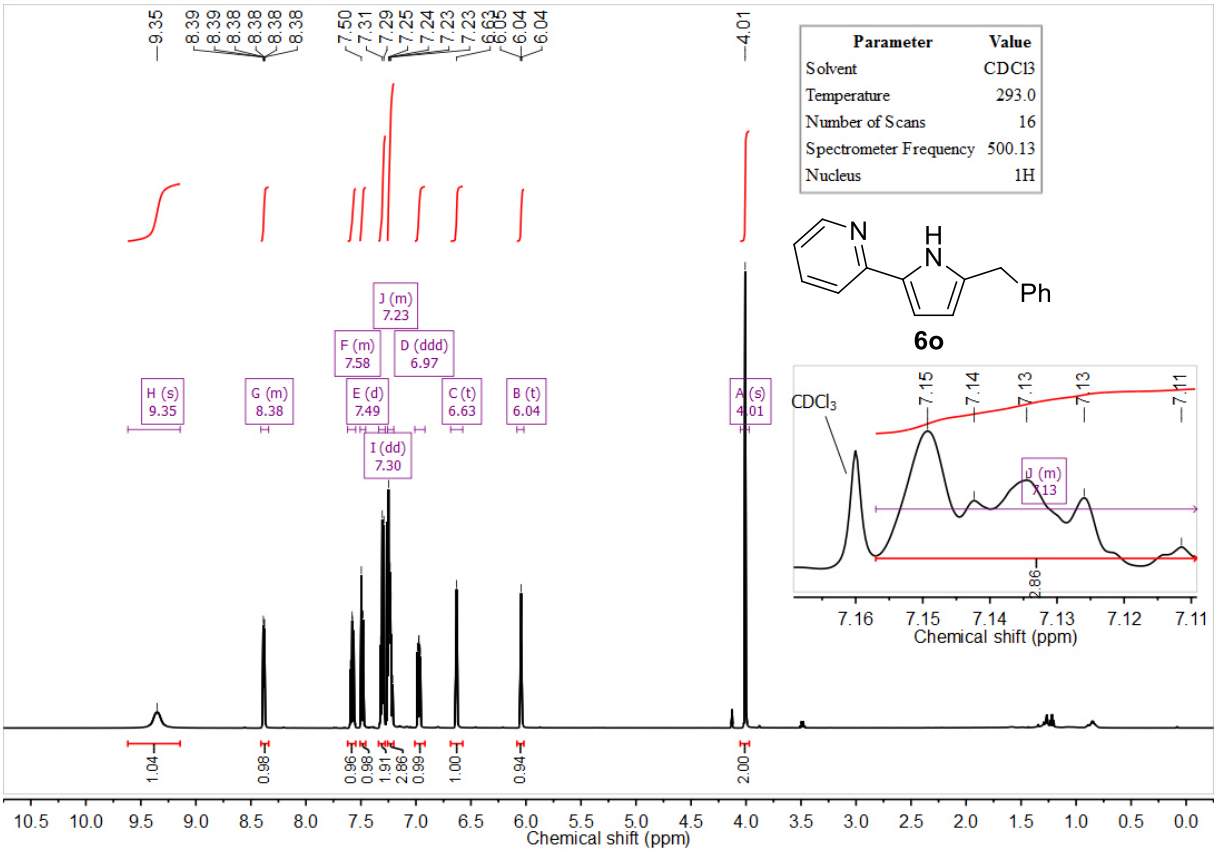

Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
136.76
135.44
127.68
125.28
122.14
120.22
106.91
106.24
21.05
13.71
S
H
N
6l
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

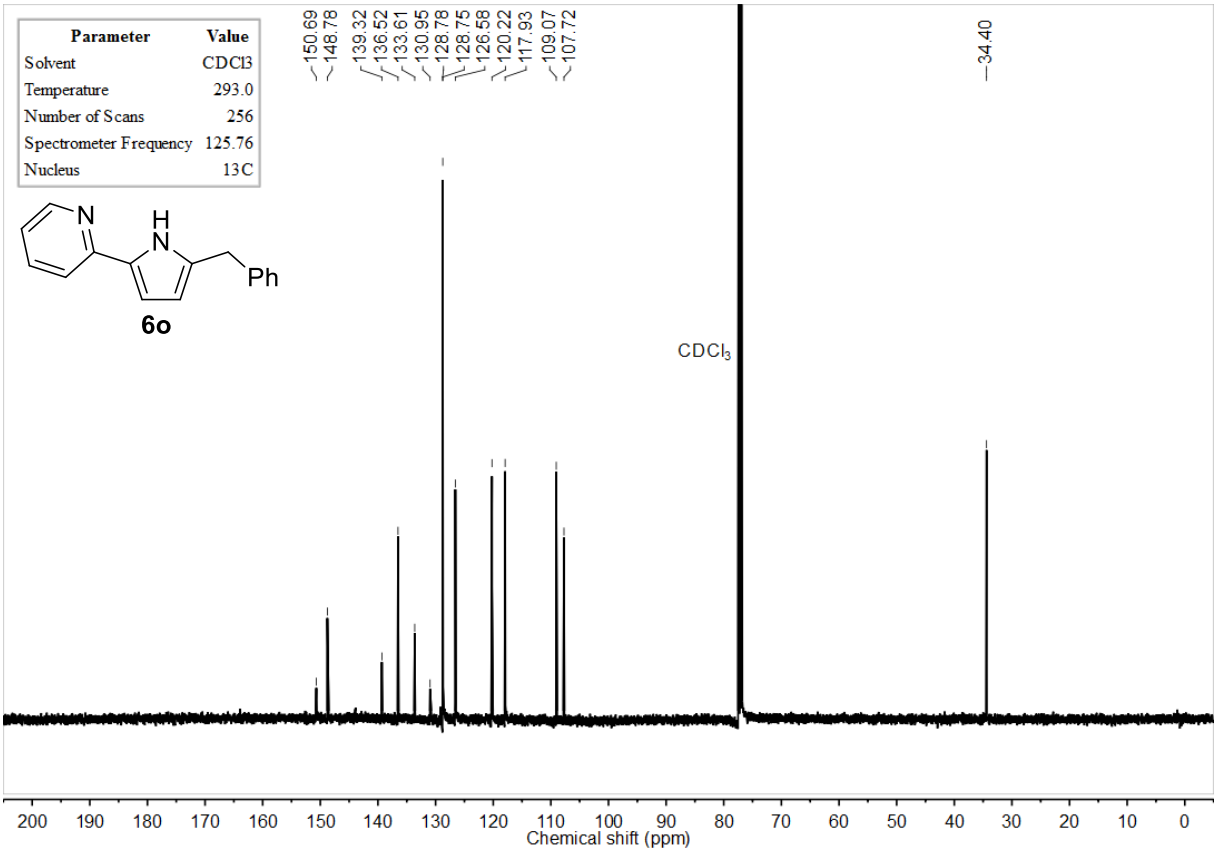

7.93
7.35
7.30
7.29
7.01
6.97
6.38
6.37
6.36
6.06
6.05
6.04
6.04
4.04
Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 64
Spectrometer Frequency 299.86
Nucleus 1H
S
H
N
Ph
6m
G (m) 6.99
E (dd) 7.29
C (m) 6.05
H (s) 7.93
D (m) 7.37
B (t) 6.37
A (s) 4.04
F (m) 7.13
H2O
0.90
1.90
3.02
0.91
1.93
0.94
0.95
2.00
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)

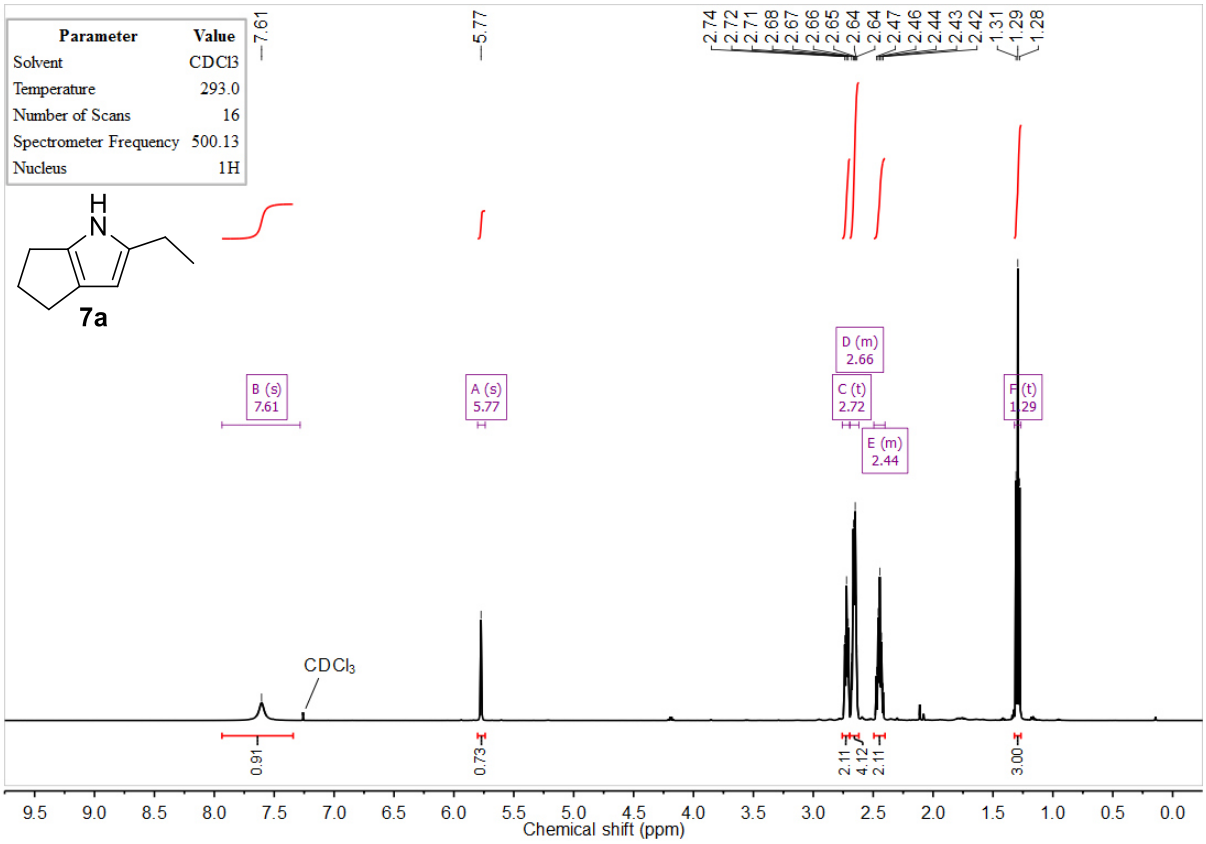

139.23
136.53
131.83
128.82
128.77
127.66
126.71
126.20
122.35
120.43
108.63
107.02
34.28
Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
S
H
N
Ph
6m
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

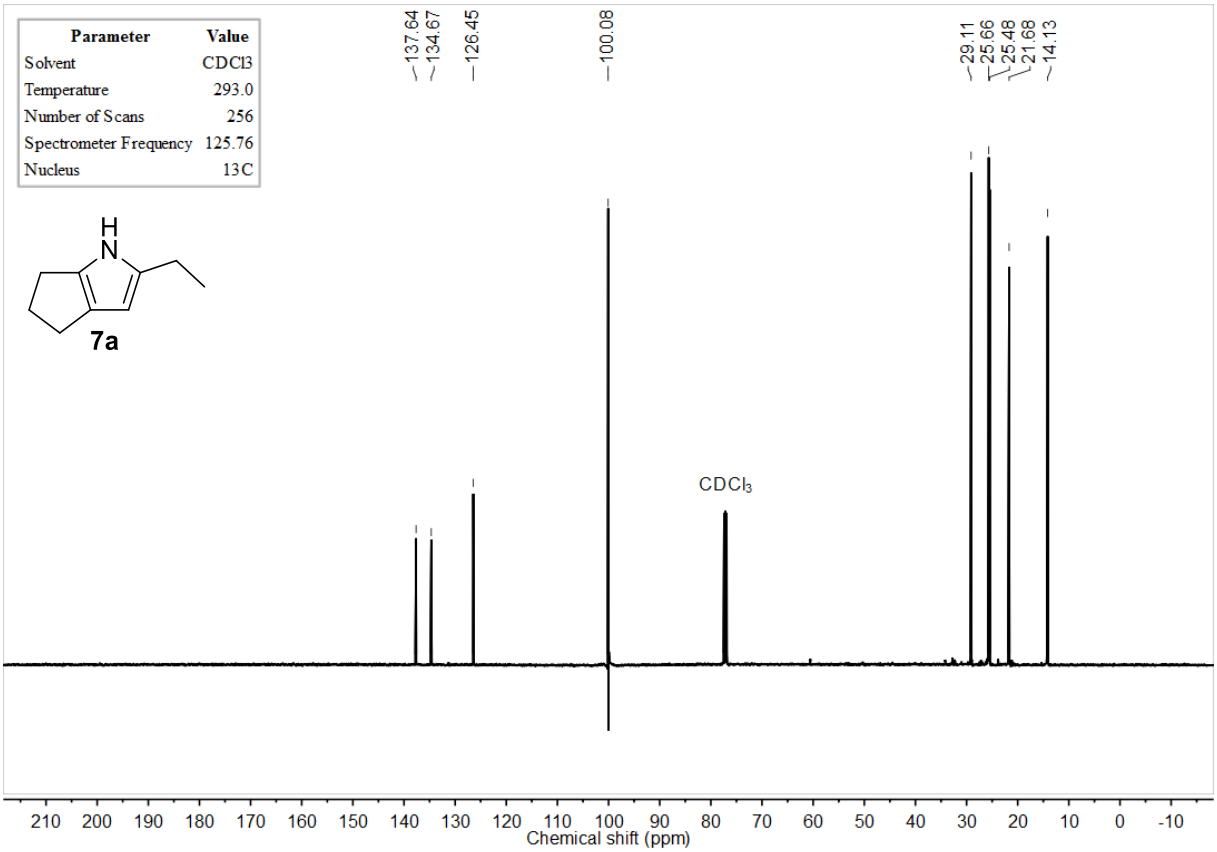

Parameter Value
Solvent CD2Cl2
Temperature 293.0
Number of Scans 16
Spectrometer Frequency 500.13
Nucleus 1H
6n
CD2Cl2
Chemical shift (ppm)

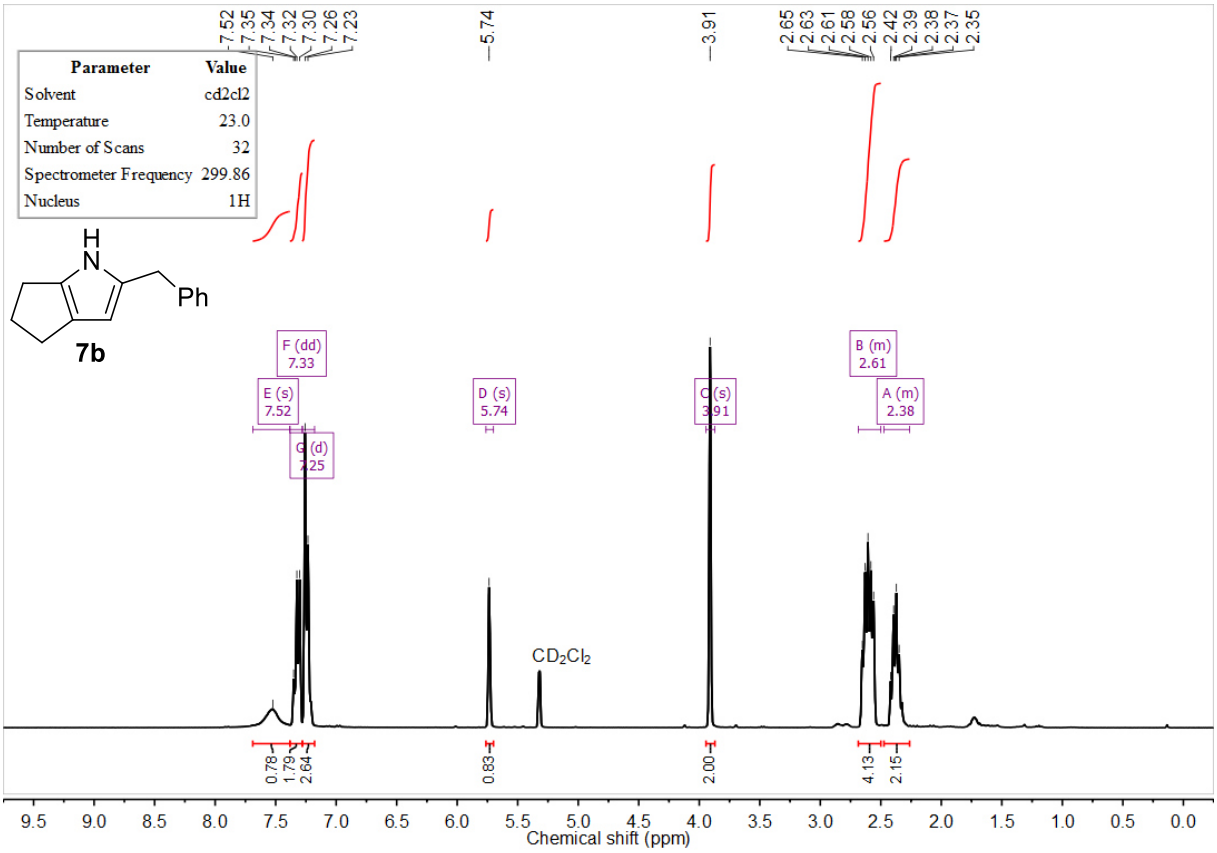

Parameter Value
Solvent CD2Cl2
Temperature 293.0
Number of Scans 256
Spectrometer Frequency 125.76
Nucleus 13C
6n
CD2Cl2
Chemical shift (ppm)

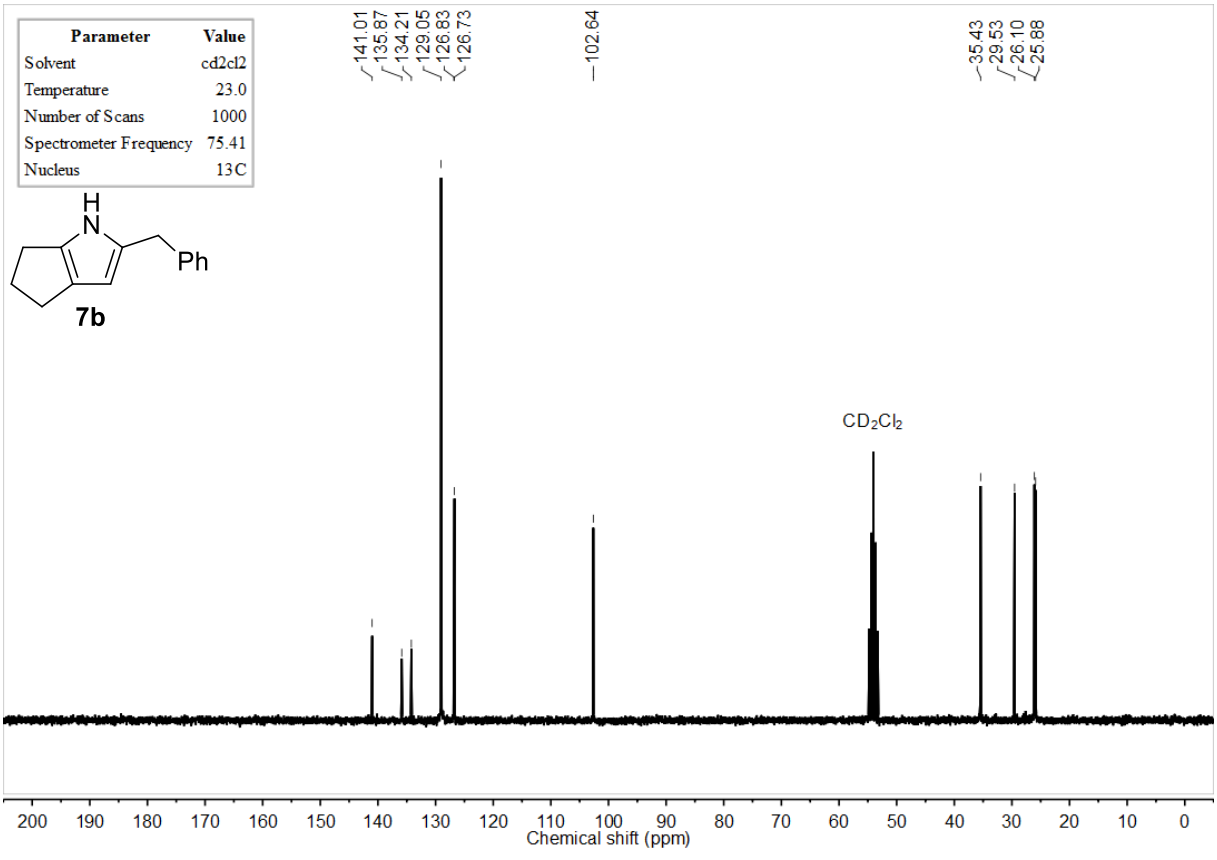

Parameter Value
Solvent CDCl3
Temperature 293.0
Number of Scans 16
Spectrometer Frequency 500.13
Nucleus 1H
6o
H (s) 9.35
G (m) 8.38
E (d) 7.49
I (dd) 7.30
F (m) 7.58
D (ddd) 6.97
J (m) 7.23
C (t) 6.63
B (t) 6.04
A (s) 4.01
CDCl3
Chemical shift (ppm)

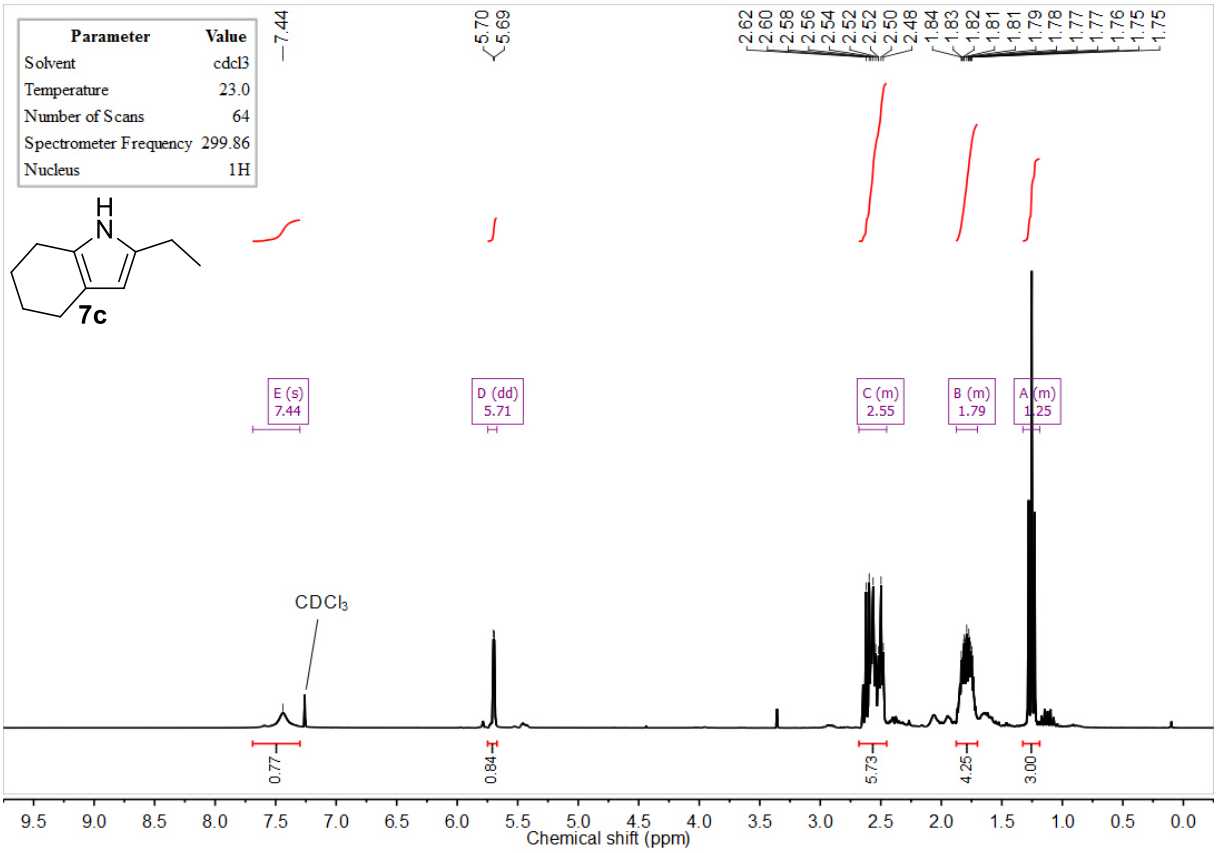

Parameter Value
Solvent CDCl3
Temperature 293.0
Number of Scans 256
Spectrometer Frequency 125.76
Nucleus 13C
6o
CDCl3
Chemical shift (ppm)

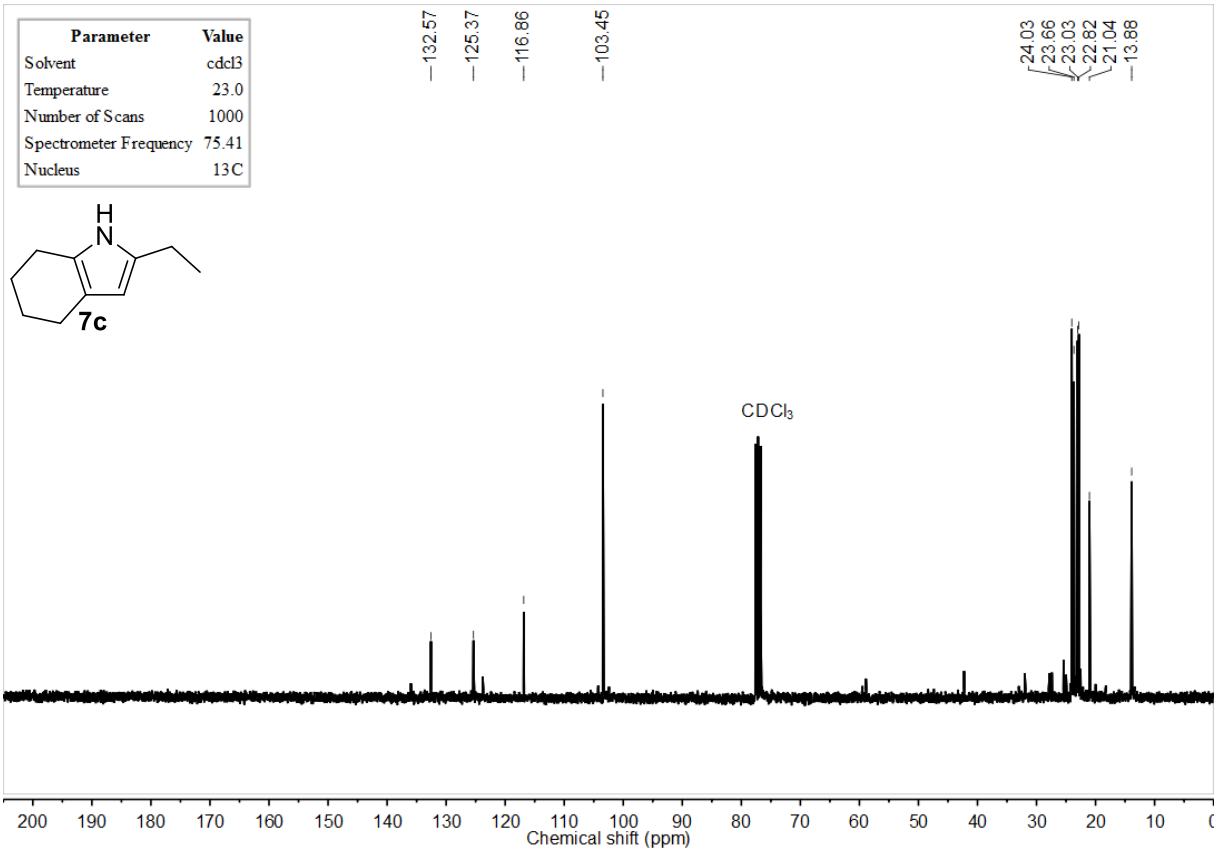

Parameter Value
Solvent CDCl3
Temperature 293.0
Number of Scans 16
Spectrometer Frequency 500.13
Nucleus 1H
7a
7.61
5.77
2.74 2.72 2.71 2.68 2.67 2.66 2.65 2.64 2.64 2.47 2.46 2.44 2.43 2.42 1.31 1.29 1.28
B (s) 7.61
A (s) 5.77
D (m) 2.66
C (t) 2.72
E (m) 2.44
F (t) 1.29
CDCl3
0.91
0.73
2.11
4.12
2.11
3.00
Chemical shift (ppm)

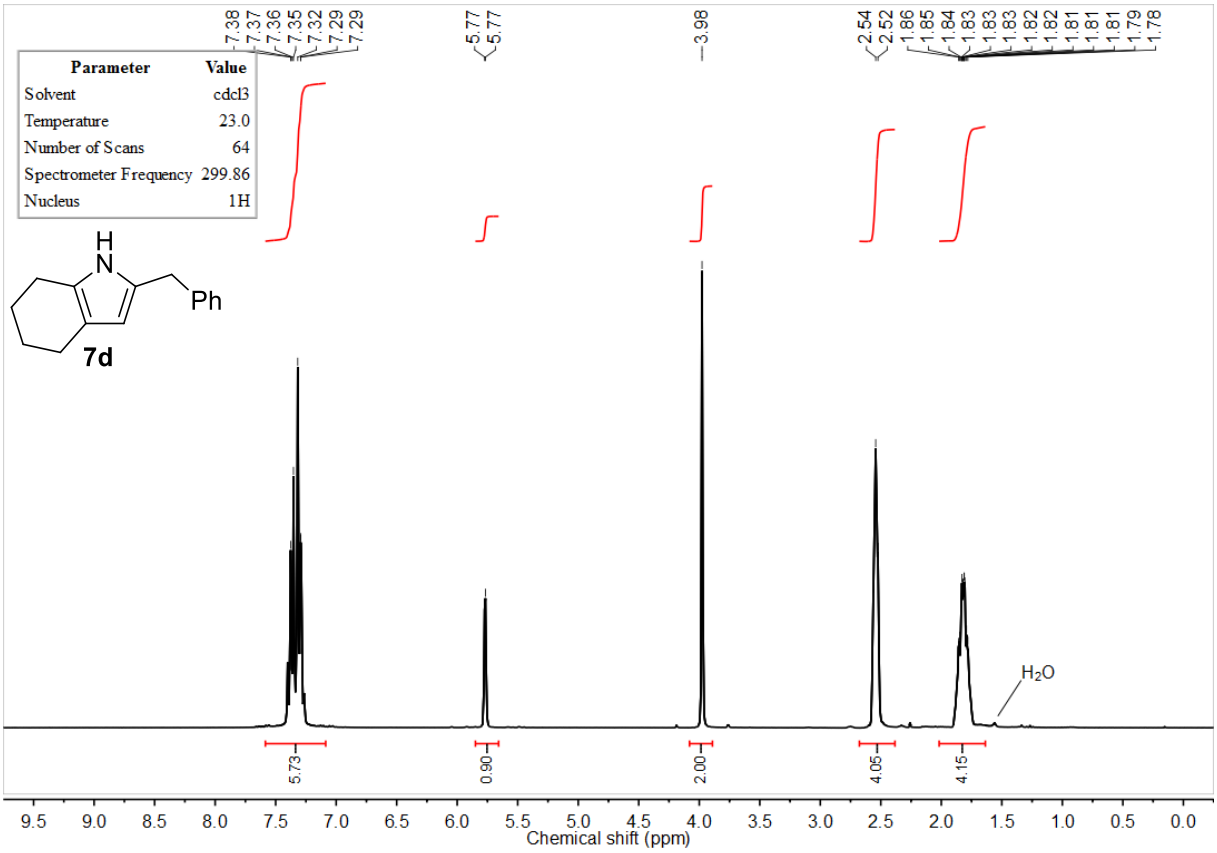

Parameter Value
Solvent CDCl3
Temperature 293.0
Number of Scans 256
Spectrometer Frequency 125.76
Nucleus 13C
7a
137.64
134.67
126.45
100.08
29.11
25.66
25.48
21.68
14.13
CDCl3
Chemical shift (ppm)


Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 32
Spectrometer Frequency 299.86
Nucleus 1H
7.52 7.35 7.34 7.32 7.30 7.26 7.23
5.74
3.91
2.65 2.63 2.61 2.58 2.56 2.42 2.39 2.38 2.37 2.35
H N Ph
7b
F (dd) 7.33
E (s) 7.52
G (d) 7.25
D (s) 5.74
C (s) 3.91
B (m) 2.61
A (m) 2.38
CD2Cl2
0.78 1.79 2.64 0.83 2.00 4.13 2.15
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)


Parameter Value
Solvent cd2cl2
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
H N Ph
7b
141.01 135.87 134.21 129.05 126.83 126.73
102.64
35.43 29.53 26.10 25.88
CD2Cl2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)


Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 64
Spectrometer Frequency 299.86
Nucleus 1H
7c
7.44
5.70
5.69
2.62
2.60
2.58
2.56
2.54
2.52
2.52
2.50
2.48
1.84
1.83
1.82
1.81
1.81
1.79
1.78
1.77
1.77
1.76
1.75
1.75
E (s) 7.44
D (dd) 5.71
C (m) 2.55
B (m) 1.79
A (m) 1.25
CDCl3
0.77
0.84
5.73
4.25
3.00
9.5 9.0 8.5 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 1.5 1.0 0.5 0.0
Chemical shift (ppm)


Parameter Value
Solvent cdcl3
Temperature 23.0
Number of Scans 1000
Spectrometer Frequency 75.41
Nucleus 13C
7c
132.57
125.37
116.86
103.45
24.03
23.66
23.03
22.82
21.04
13.88
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical shift (ppm)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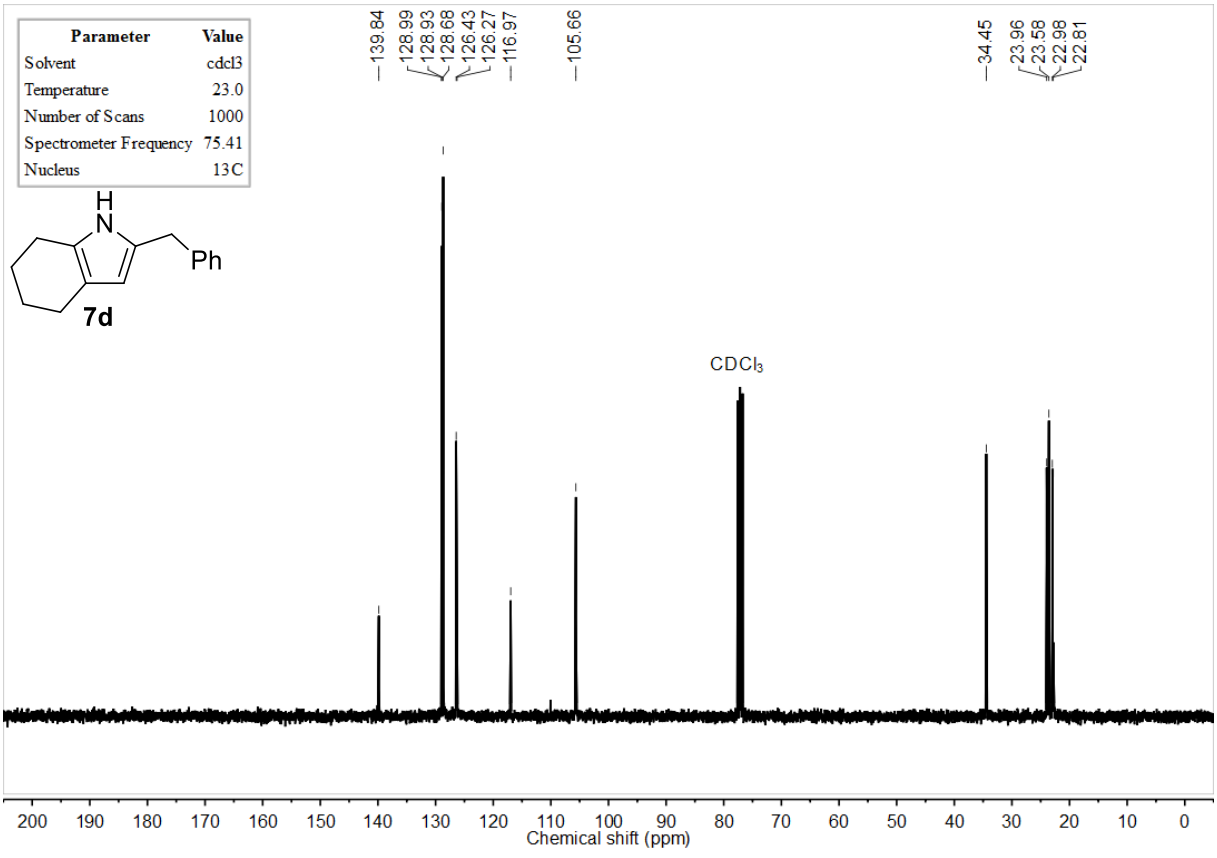
5.77 5.77
3.98
2.54 2.52 1.86 1.85 1.84 1.83 1.83 1.83 1.82 1.81 1.81 1.81 1.79 1.78
H
N
Ph
7d
H2O
5.73
0.90
2.00
4.05
4.15
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical shift (ppm)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105.66
34.45 23.96 23.58 22.98 22.81
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N
Ph
7d
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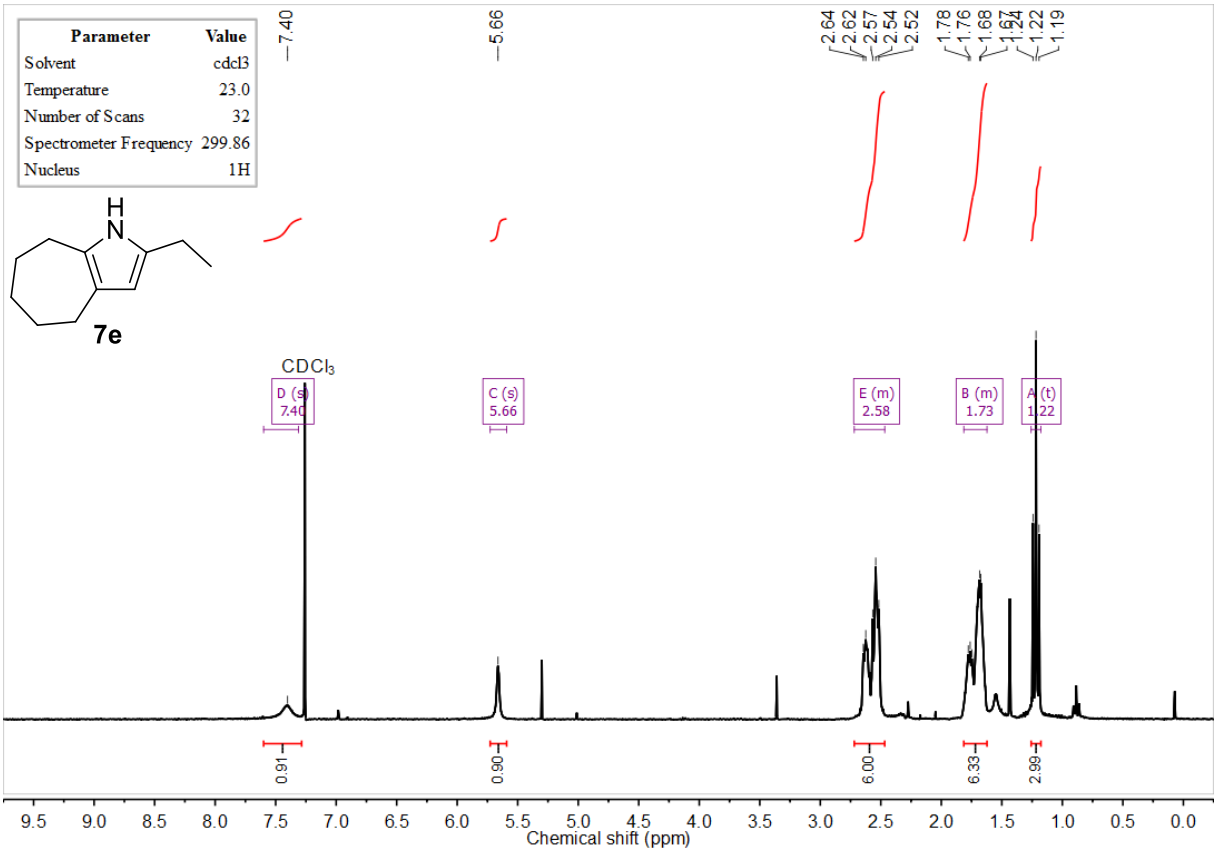
Chemical shift (ppm)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1.22
1.19
CDCl3
D (s) 7.40
C (s) 5.66
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B (m) 1.73
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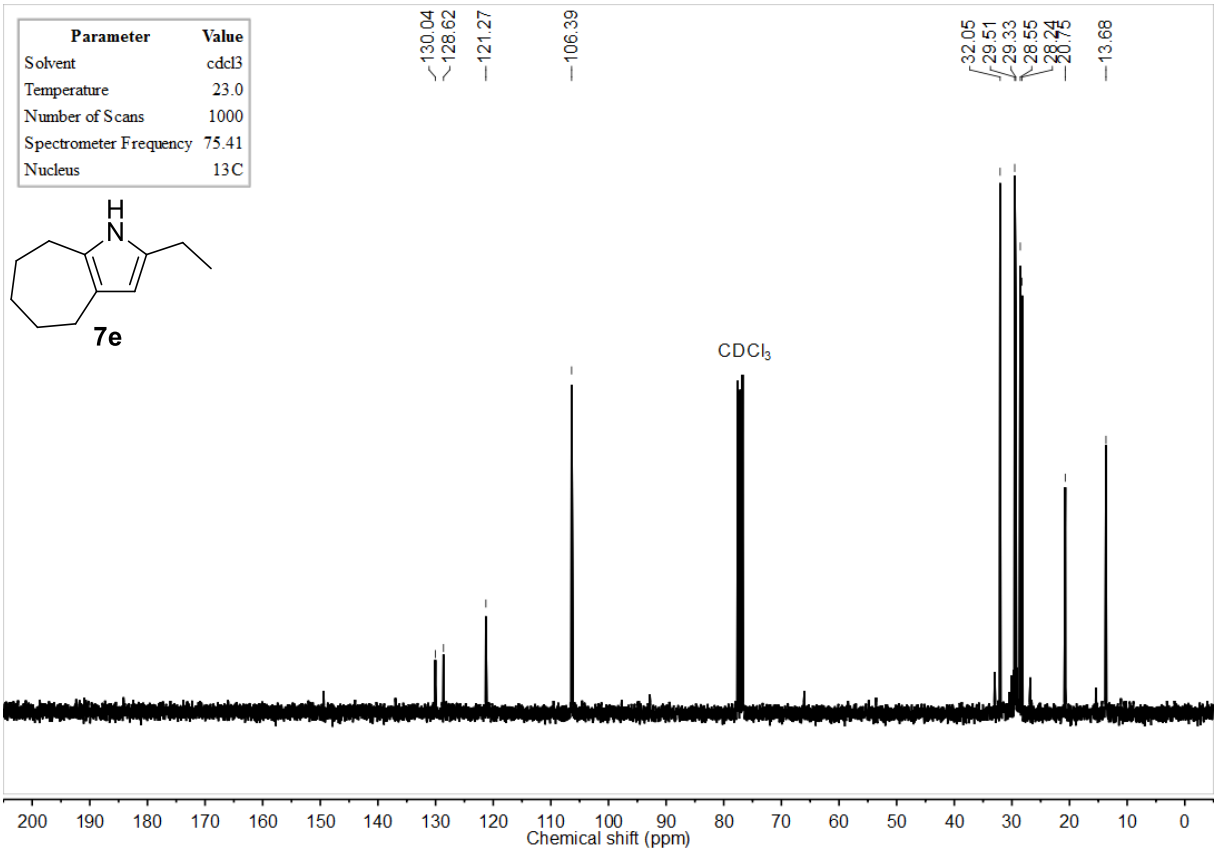
6.00
6.33
2.99
Chemical shift (ppm)


Parameter Value
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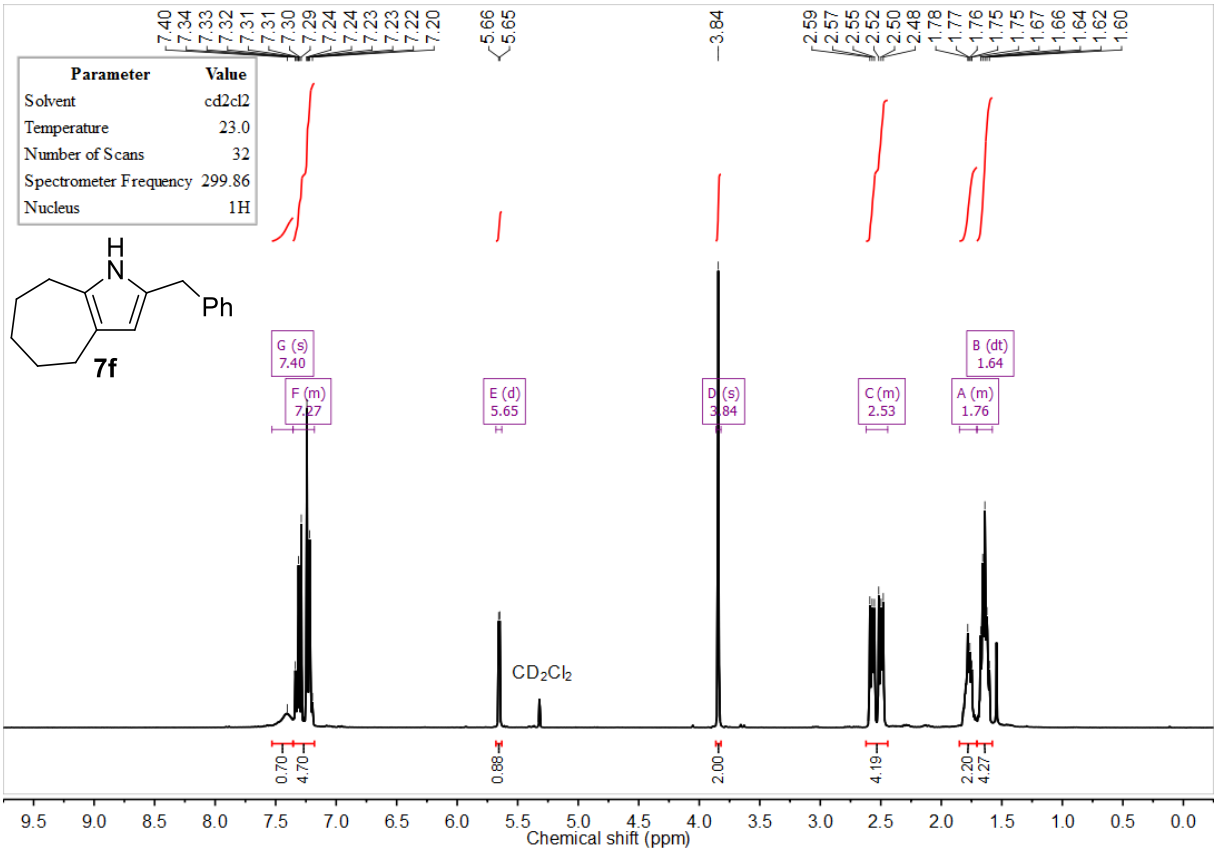
CDCl3
Chemical shift (ppm)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5.66 5.65
3.84
2.59 2.57 2.55 2.52 2.50 2.48
1.78 1.77 1.76 1.75 1.75 1.67 1.66 1.64 1.62 1.60
H
N
Ph
7f
G (s) 7.40
F (m) 7.27
E (d) 5.65
D (s) 3.84
C (m) 2.53
B (dt) 1.64
A (m) 1.76
CD2Cl2
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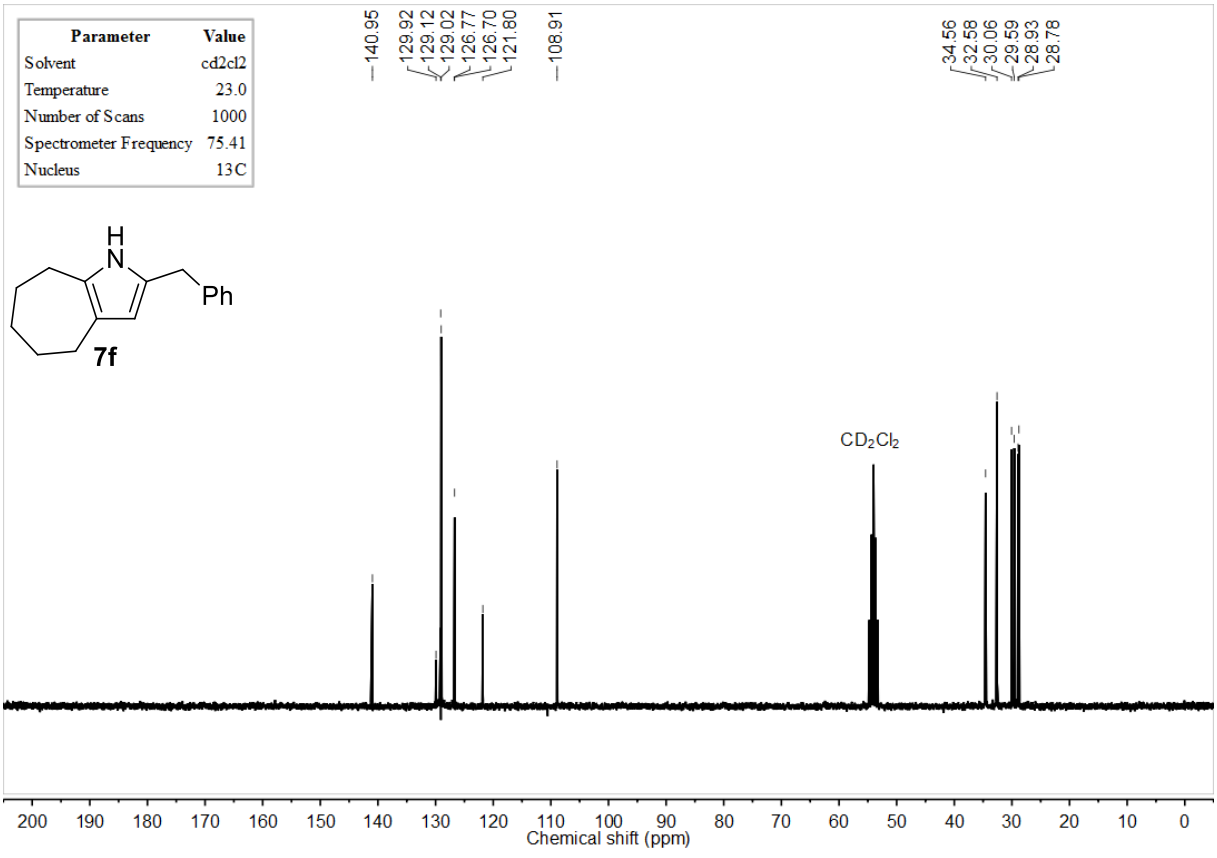
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical shift (ppm)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108.91
34.56 32.58 30.06 29.59 28.93 28.78
H
N
Ph
7f
CD2Cl2
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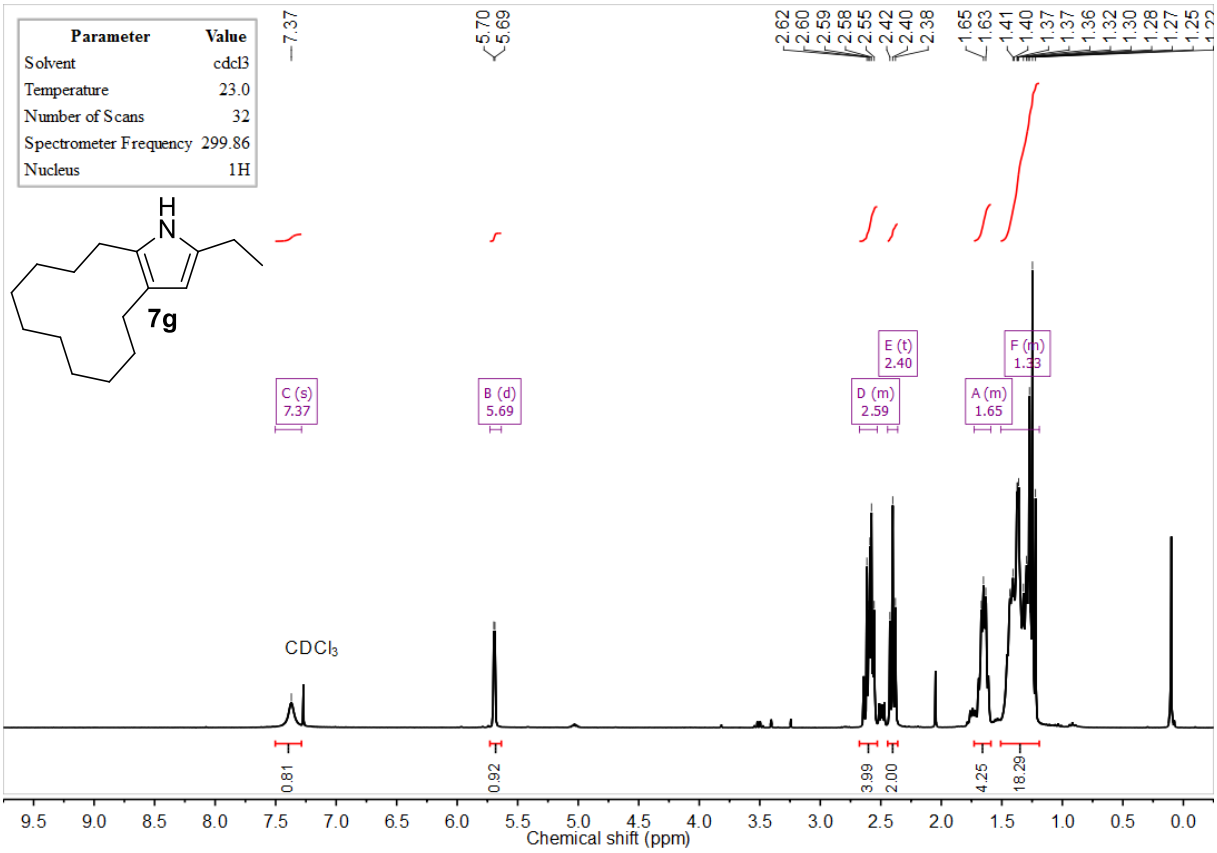
Chemical shift (ppm)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2.40
2.38
1.65
1.63
1.41
1.40
1.37
1.37
1.36
1.32
1.30
1.28
1.27
1.25
C (s) 7.37
B (d) 5.69
D (m) 2.59
E (t) 2.40
A (m) 1.65
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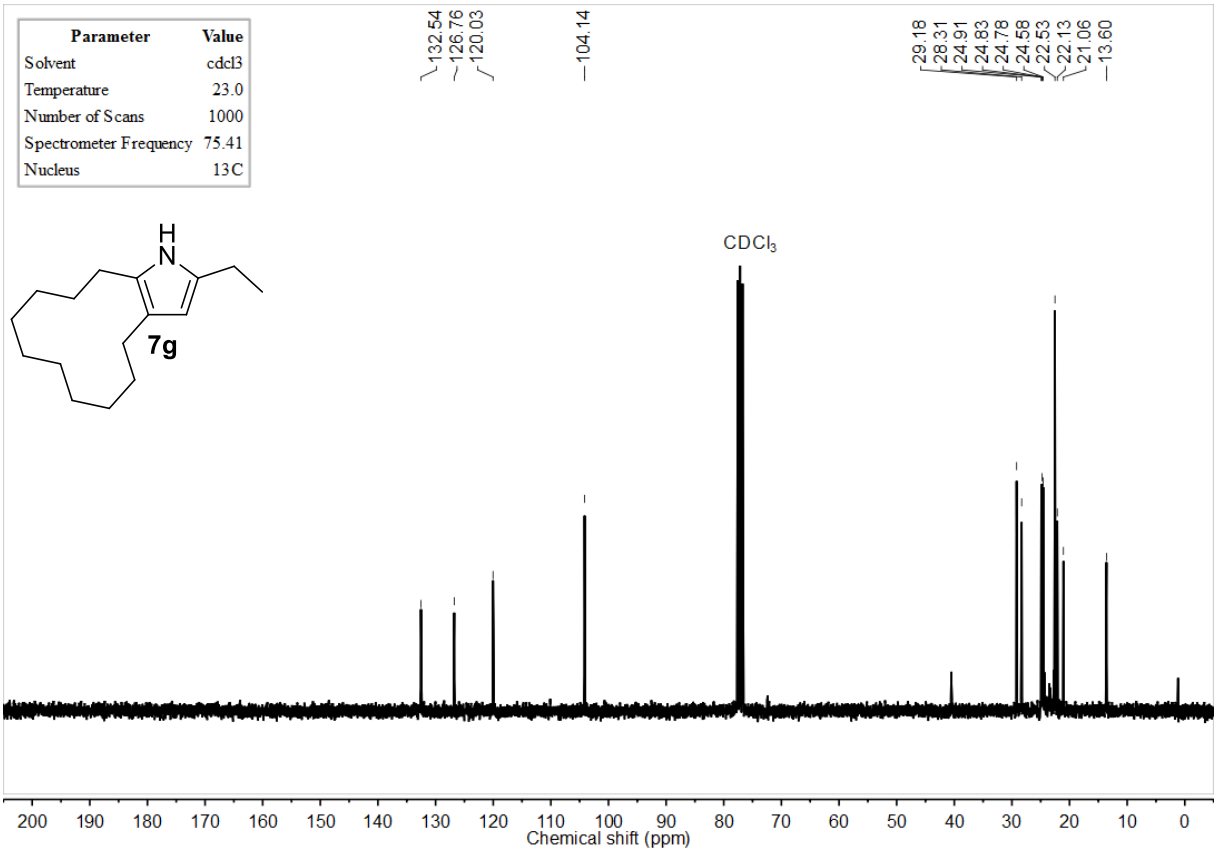
2.00
4.25
18.29
Chemical shift (ppm)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Number of Scans 1000
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21.06
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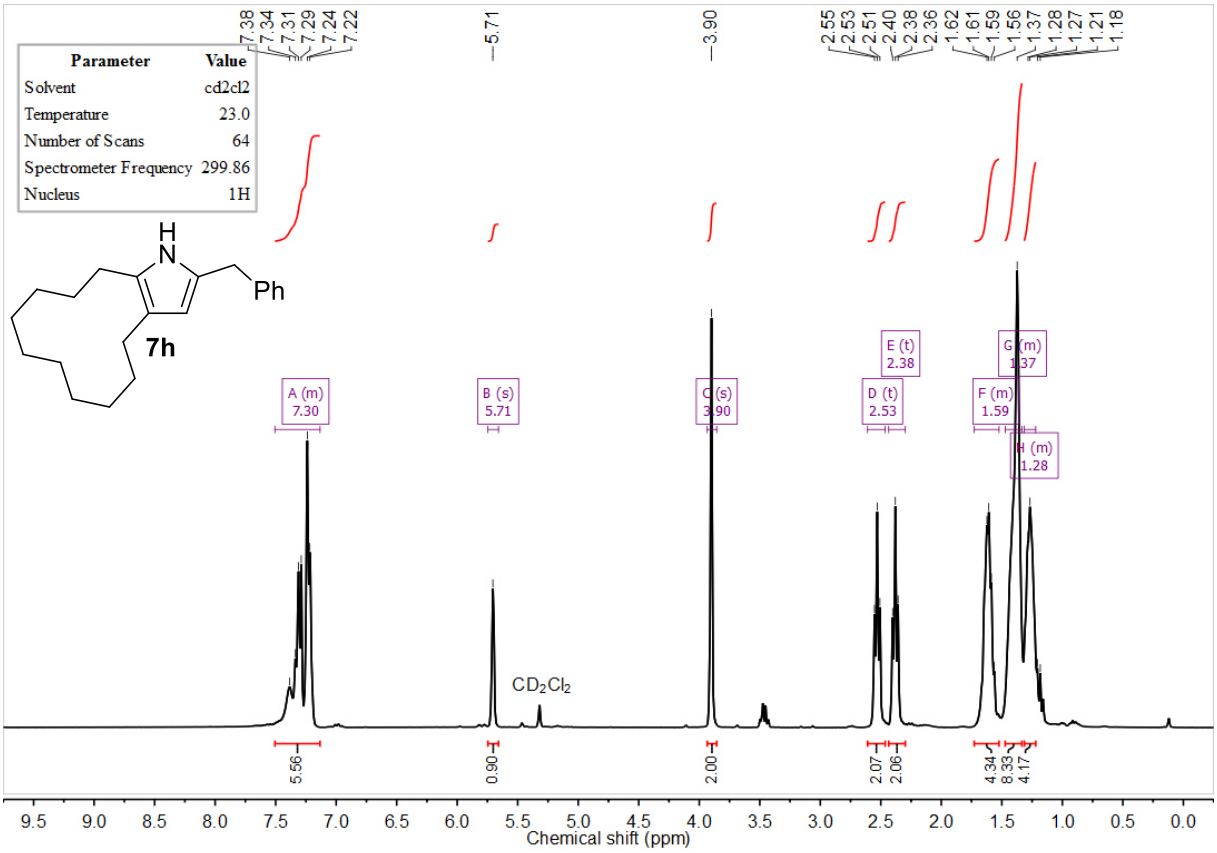
CDCl3
Chemical shift (ppm)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Number of Scans 64
Spectrometer Frequency 299.86
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N
Ph
7h
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5.71
3.90
2.55 2.53 2.51 2.40 2.38 2.36
1.62 1.61 1.59 1.56 1.37 1.28 1.27 1.21 1.18
A (m) 7.30
B (s) 5.71
C (s) 3.90
D (t) 2.53
E (t) 2.38
F (m) 1.59
G (m) 1.37
H (m) 1.28
CD2Cl2
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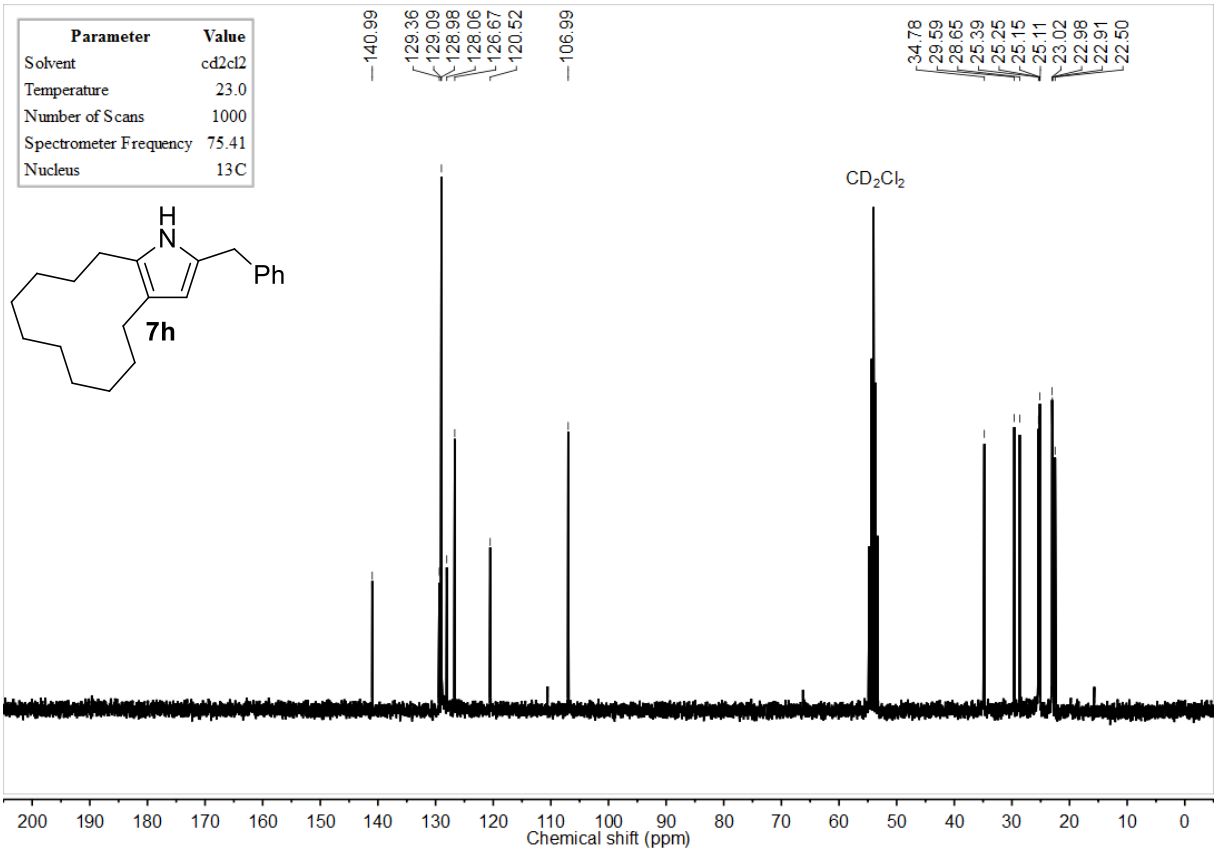
0.90
2.00
2.07
2.06
4.34
8.33
4.17
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical shift (ppm)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Temperature 23.0
Number of Scans 1000
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N
Ph
7h
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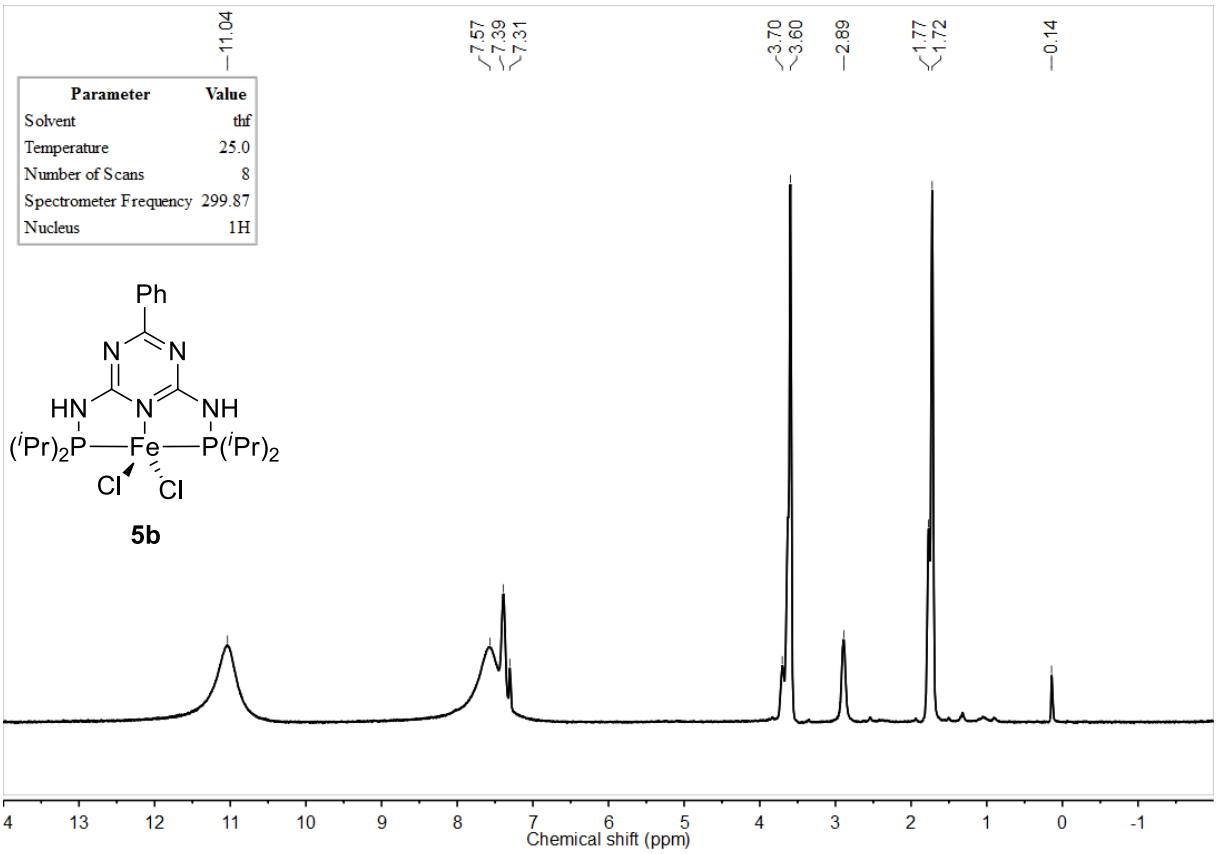
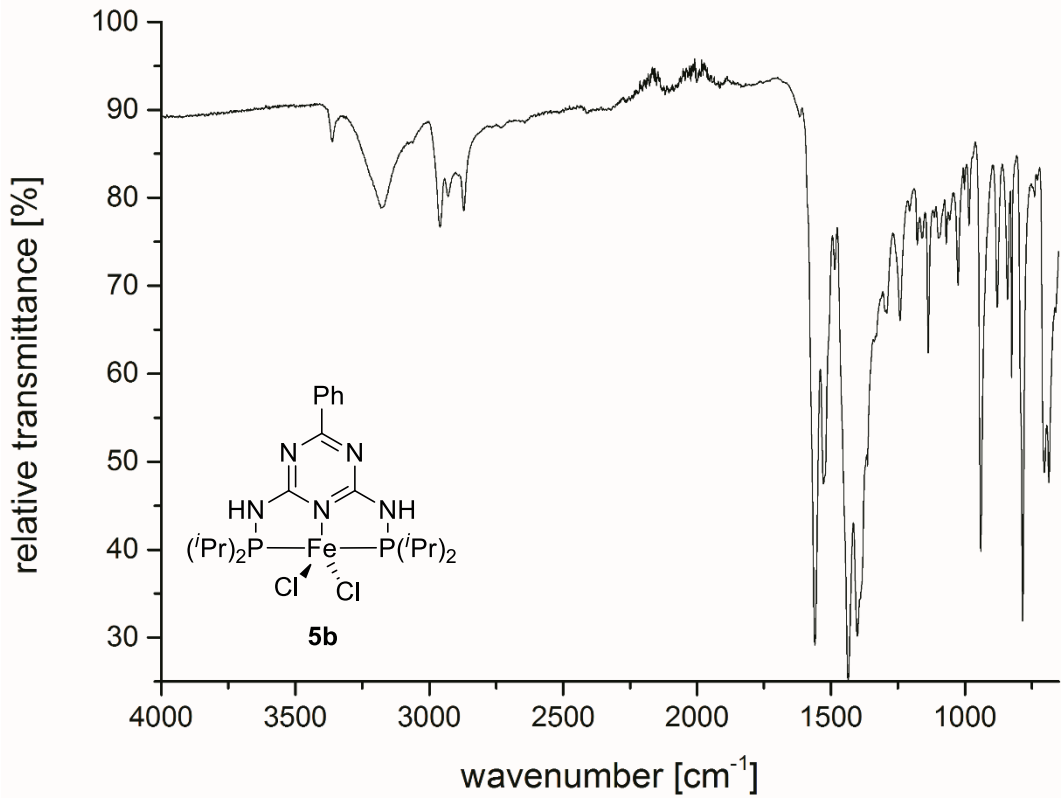
25.25
25.15
25.11
23.02
22.98
22.91
22.50
CD2Cl2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
Chemical shift (ppm)

Characterization of 5b

^{1}H NMR of **5b**

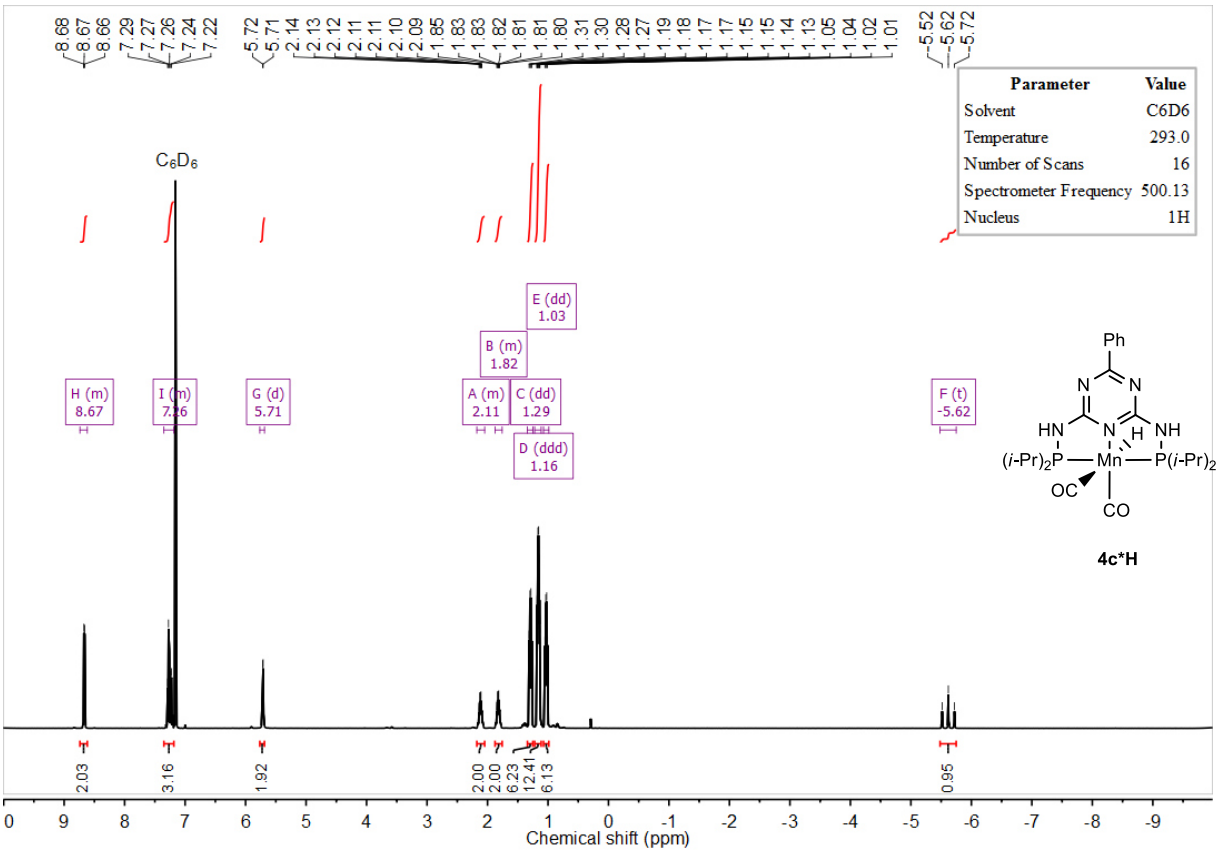


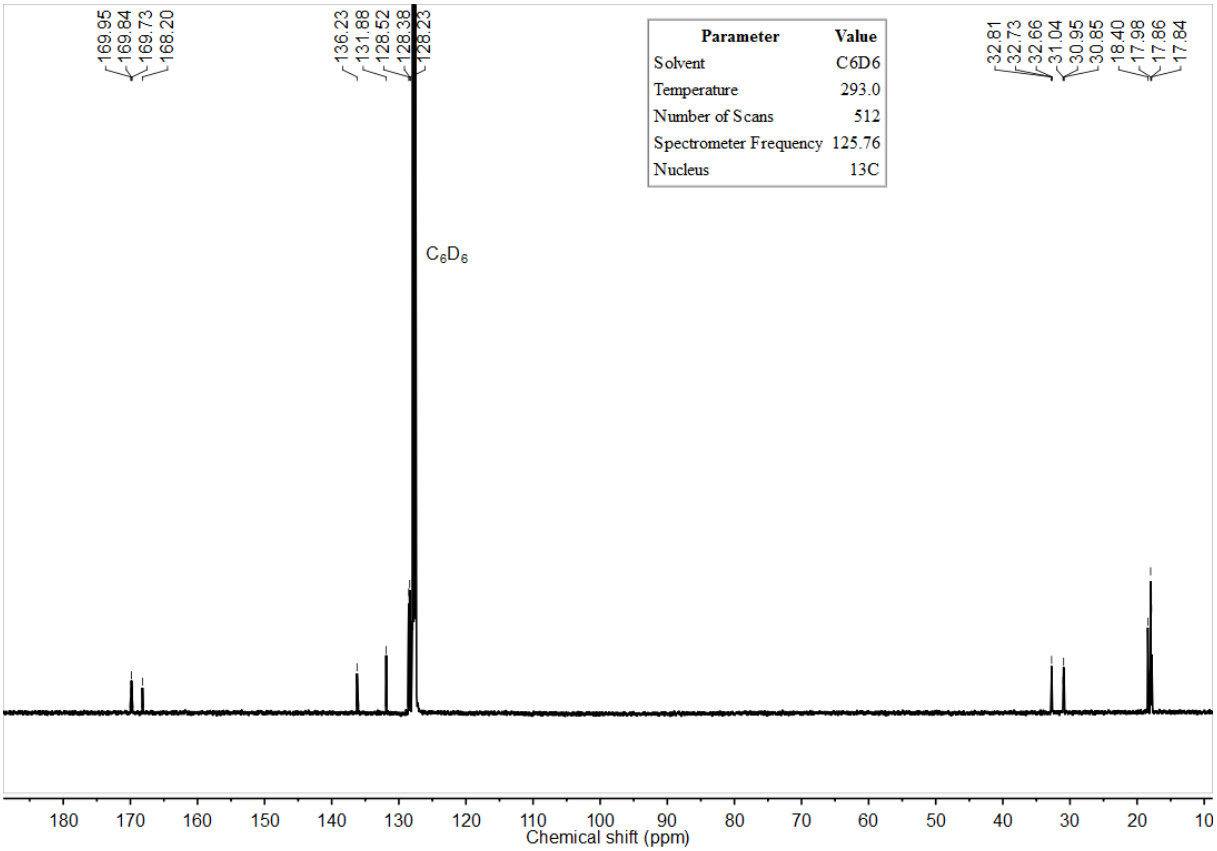
FTIR-spectrum of **5b**

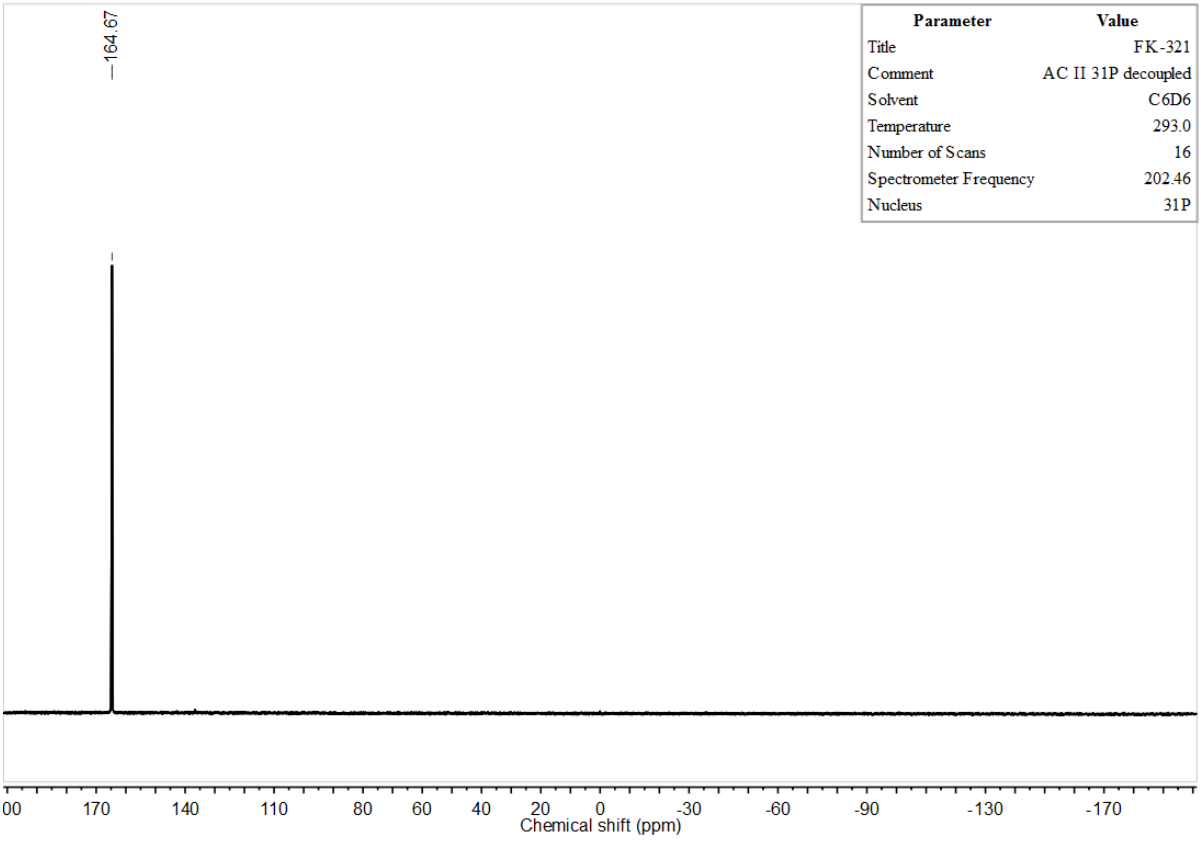


*Characterization of **4c*H***

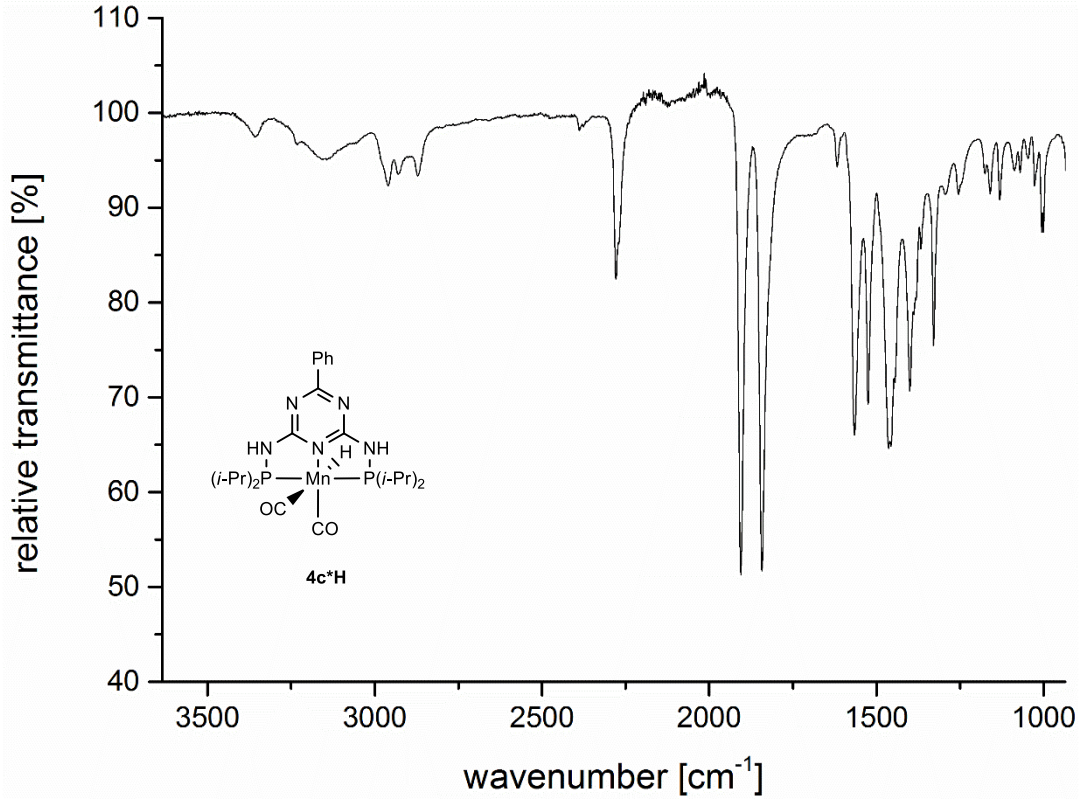
NMR spectra of **4c*H** (from H_2 route)



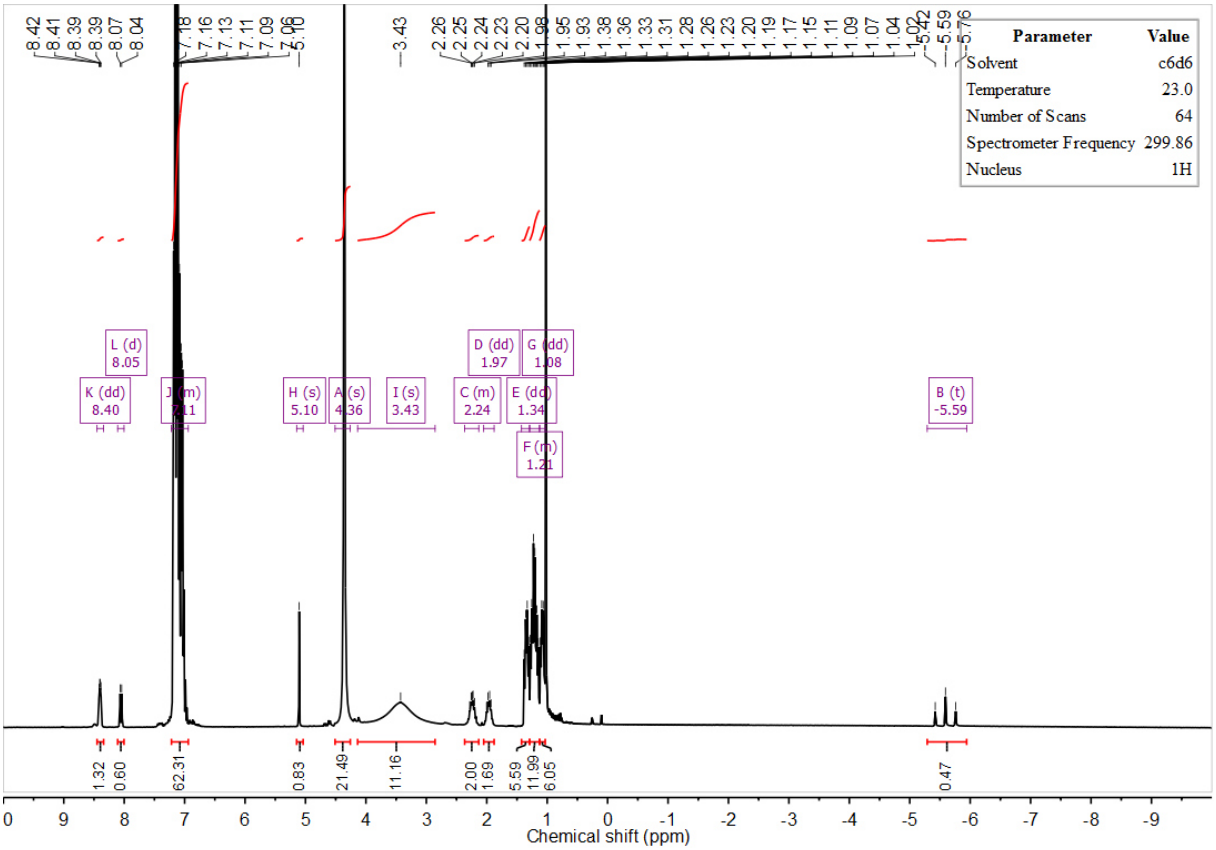




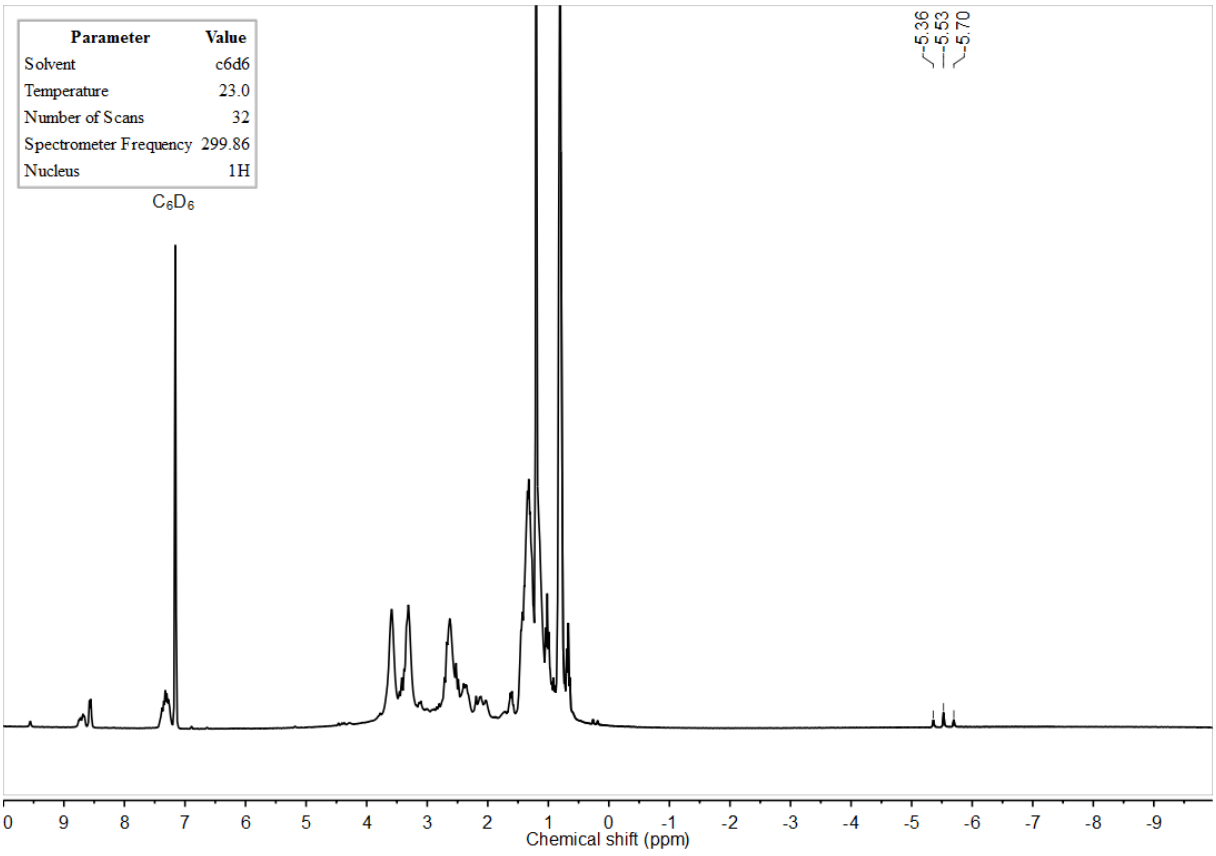
FTIR-spectrum of **4c*H**



1H-NMR spectrum of **4c*H** (from BnOH route, raw mixture)



1H-NMR spectrum of **4c*H** (from 2-aminobutanol route, raw mixture)



Mechanistic Investigations

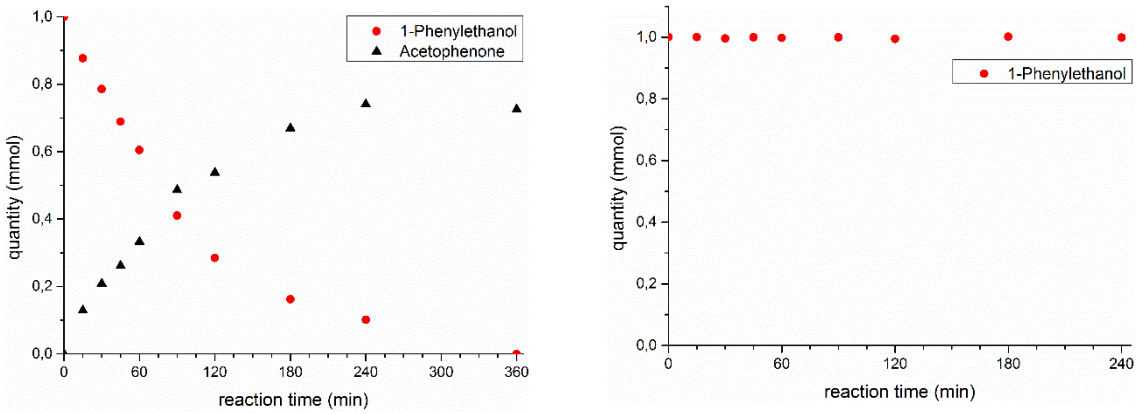


Figure S1: Time conversion plot for the dehydrogenation of 1-phenylethanol in the presence (*left*) and absence (*right*) of base. *Left:* Reaction conditions: 1-phenylethanol (1 mmol, 121 µL), KO*t*-Bu (1 mmol, 112 mg), precatalyst **4c*H** (50 µmol, 27 mg), dodecane (100 µL) as internal standard, 2-MeTHF (2 mL). Oil bath temperature: 110 °C. *Right:* Reaction conditions: 1-phenylethanol (1 mmol, 121 µL), precatalyst **4c*H** (50 µmol, 27 mg), dodecane (100 µL) as internal standard, 2-MeTHF (2 mL). Oil bath temperature: 110 °C. Analysis by GC.

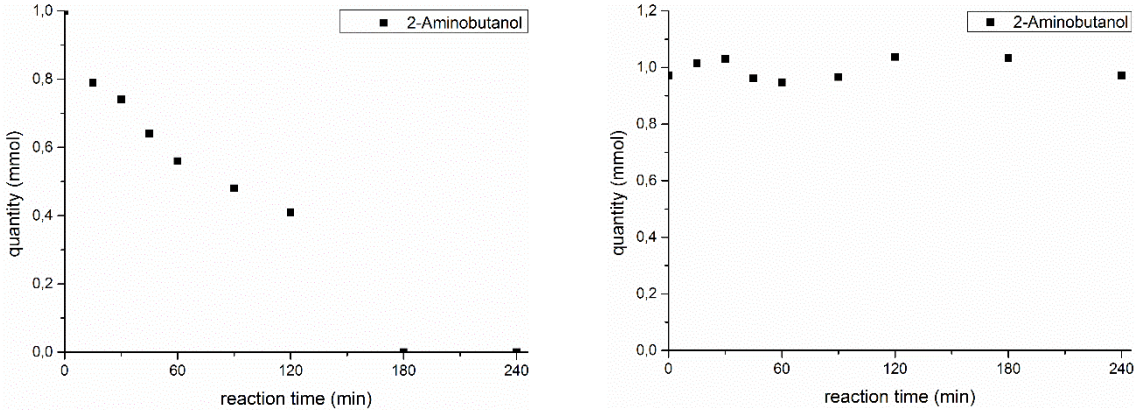


Figure S2: Time conversion plot for the dehydrogenation of 2-aminobutanol in the presence (*left*) and absence (*right*) of base. *Left:* Reaction conditions: 2-aminobutan-1-ol (1 mmol, 95 µL), KO*t*-Bu (1 mmol, 112 mg), precatalyst **4c*H** (50 µmol, 27 mg), dodecane (100 µL) as internal standard, 2-MeTHF (2 mL). Oil bath temperature: 110 °C. *Right:* Reaction conditions: 2-aminobutan-1-ol (1 mmol, 95 µL), precatalyst **4c*H** (50 µmol, 27 mg), dodecane (100 µL) as internal standard, 2-MeTHF (2 mL). Oil bath temperature: 110 °C. Analysis by GC.

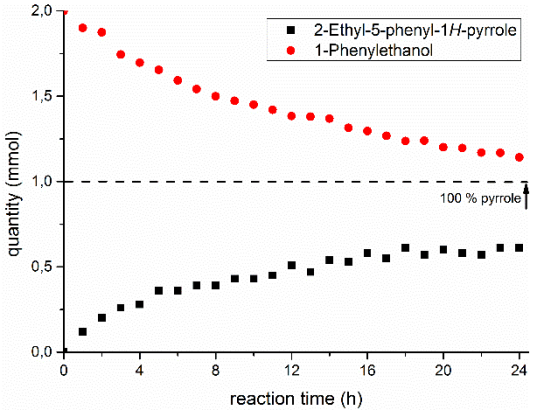


Figure S3: Time conversion plot for the synthesis of **3a**. Reaction conditions: 1-phenylethanol (2 mmol, 242 µL), 2-aminobutan-1-ol (1 mmol, 95 µL), KO*t*-Bu (1.5 mmol, 168 mg), precatalyst **4c** (5 µmol, 3 mg), dodecane (100 µL) as internal standard, 2-MeTHF (2 mL). Oil bath temperature: 110 °C.

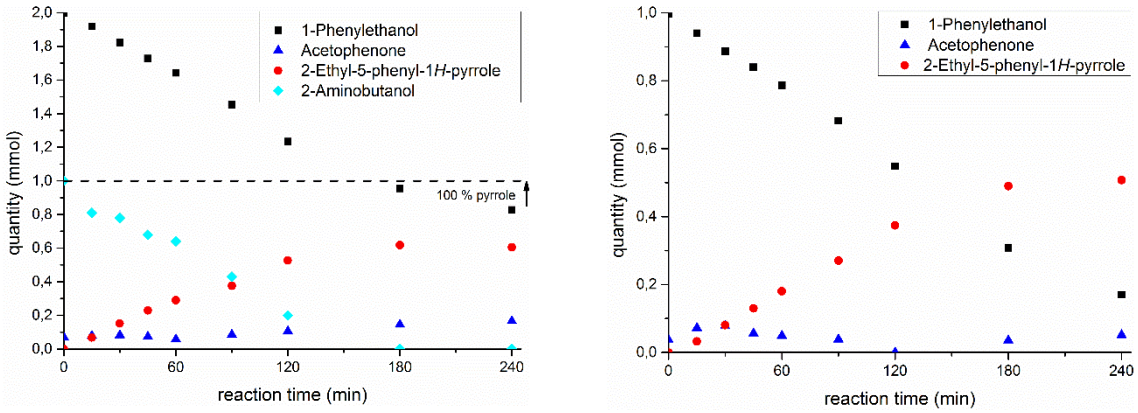


Figure S4: Time conversion plot for the synthesis of **3a** in the presence of two equiv. 1-phenylethanol (*left*) or one equiv. 1-phenylethanol (*right*). *Left:* Reaction conditions: 1-phenylethanol (2 mmol, 242 µL), 2-aminobutan-1-ol (1 mmol, 95 µL), KO*t*-Bu (1.5 mmol, 168 mg), precatalyst **4c*H** (50 µmol, 27 mg), dodecane (100 µL) as internal standard, 2-MeTHF (2 mL). Oil bath temperature: 110 °C. *Right:* Reaction conditions: 1-phenylethanol (1 mmol, 121 µL), 2-aminobutan-1-ol (1 mmol, 95 µL), precatalyst **4c*H** (50 µmol, 27 mg), dodecane (100 µL) as internal standard, 2-MeTHF (2 mL). Oil bath temperature: 110 °C. Analysis by GC.

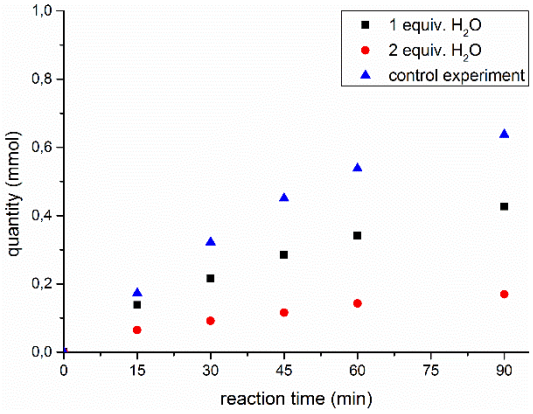
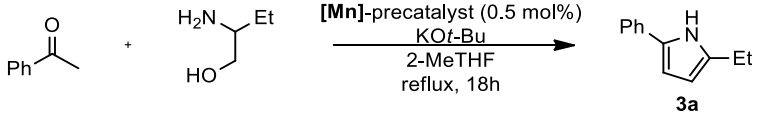


Figure S5: Time conversion plot for the synthesis of **3a** in the presence of 1 equiv. water (black) or 2 equiv. water (red), respectively. Reaction conditions: 1-phenylethanol (2 mmol, 242 µL), 2-aminobutan-1-ol (1 mmol, 95 µL), KO*t*-Bu (1.5 mmol, 168 mg), deionized water (1 equiv.: 1 mmol, 18 mg; 2 equiv.: 2 mmol, 36 mg), precatalyst **4c*H** (50 µmol, 27 mg), dodecane (100 µL) as internal standard, 2-MeTHF (2 mL). Analysis by GC.

Table S6: Investigation of the title reaction using ketone instead of sec. alcohol[a]

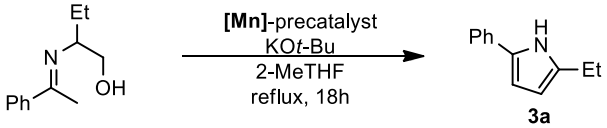


3a

Mn-precatalyst	Amount KO*t*-Bu [equiv.]	Yield[b] [%]
4c	0.5	32
4c	1.5	57
4c*H	0.5	43
4c*H	1.5	56

[a]: Reaction conditions: acetophenone (6 mmol, 700 µL), 2-aminobutan-1-ol (3 mmol, 284 µL), KO*t*-Bu (4.5 mmol, 505 mg), Mn precatalyst (15 µmol), 2-MeTHF (6 mL). [b]: determined by GC using dodecane as internal standard.

Table S7: Cyclization of the proposed imine intermediate[a]



3a

Mn-precatalyst	Amount KO*t*-Bu [equiv.]	Yield[b] [%]
None	1.0	0
4c*H (1 mol%)	1.0	50
4c*H (1 mol%)	0	0

[a]: Reaction conditions: 2-((1-phenylethylidene)amino)butan-1-ol (1 mmol, 191 mg), KO*t*-Bu, Mn precatalyst, 2-MeTHF (2 mL). [b]: determined by GC using dodecane as internal standard.

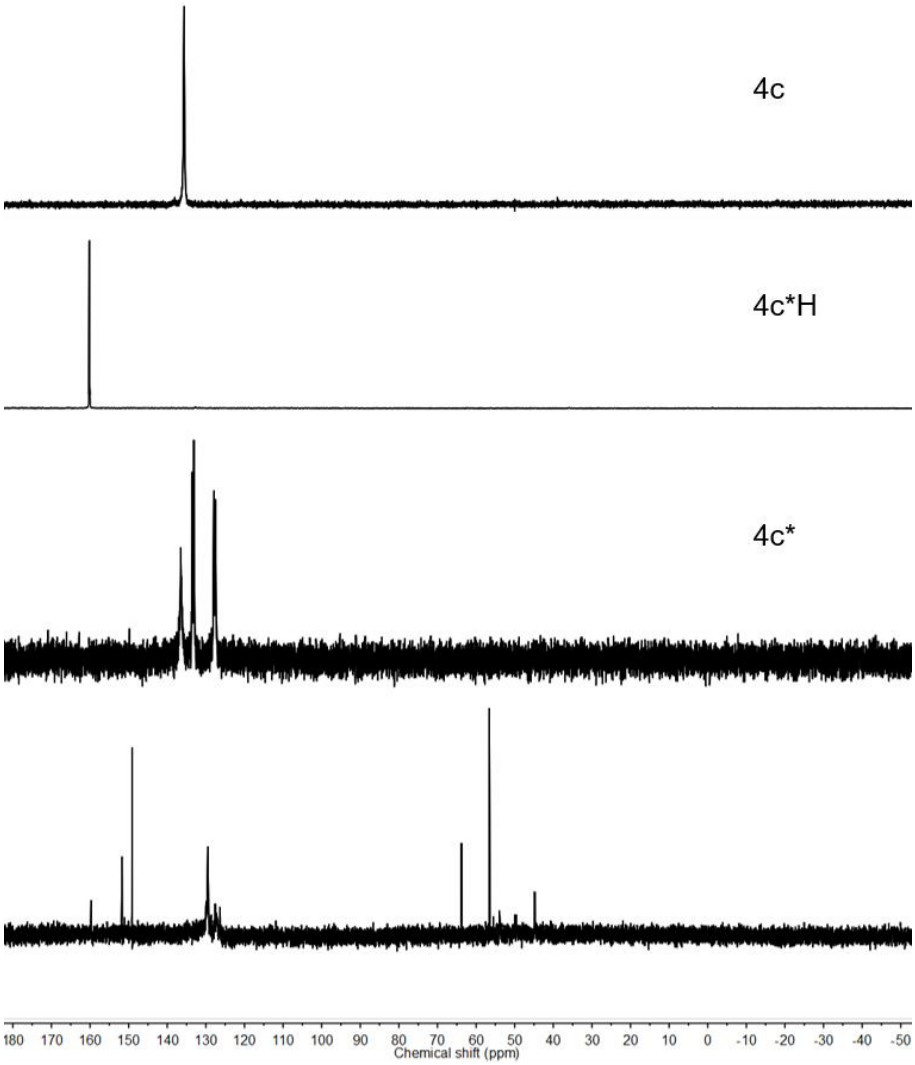
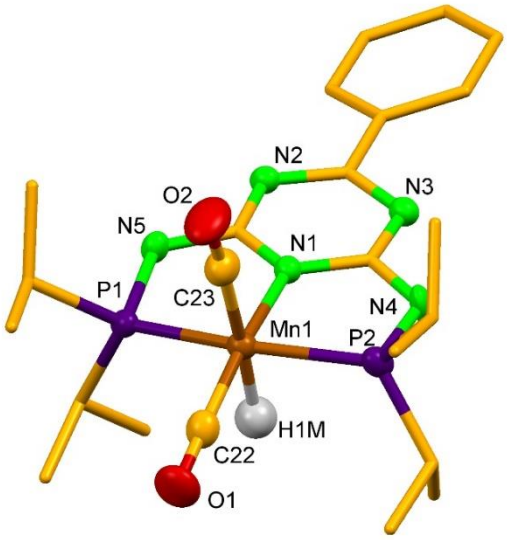


Figure S6: ^{31}P NMR spectra of **4c** (top), **4c*H** (second), **4c*** (third), and after catalysis (bottom). Reaction conditions: 1-phenylethanol (2 mmol, 242 µL), 2-aminobutan-1-ol (1 mmol, 95 µL), KO*t*-Bu (1.5 mmol, 168 mg), **4c** (0.1 mmol, 61 mg), C_6D_6 (2 mL), reflux, 3h; the mixture was filtered inside of a glovebox using a glass syringe filter prior to recording the NMR spectrum.

Crystallographic data

Compound	4c*H
Formula	$C_{46}H_{72}Mn_2N_{10}O_4P_4$, $C_4H_8O_2$
Formula weight	1151.00
Crystal system	monoclinic
Space group	$P2_1/c$
a [Å]	12.025(5)
b [Å]	12.707(5)
c [Å]	37.723(5)
α [°]	90.000(5)
β [°]	91.927(5)
γ [°]	90.000(5)
Cell volume [Å³]	5761(3)
Z	4
Crystal size [mm³]	0.305 x 0.203 x 0.118
Habit	block
Color	red
Density [gcm^{-3}]	1.327
T [K]	133(2)
Theta range	1.691-25.499
Unique reflections	14526
Observed reflections [I>2s(I)]	10572
Parameters	689
wR2 (all data)	0.1367
R [I>2s(I)]	0.0535



Datablock: shelx

Bond precision: C-C = 0.0062 A Wavelength=0.71069

Cell: a=12.025(5) b=12.707(5) c=37.723(5)
alpha=90 beta=91.927(5) gamma=90

Temperature: 133 K

	Calculated	Reported
Volume	5761(3)	5761(3)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	2(C23 H36 Mn N5 O2 P2), C4 H8 O2	C46 H72 Mn2 N10 O4 P4, C4 H8 O2
Sum formula	C50 H80 Mn2 N10 O6 P4	C50 H80 Mn2 N10 O6 P4
Mr	1151.00	1151.00
Dx,g cm-3	1.327	1.327
Z	4	4
Mu (mm-1)	0.604	0.604
F000	2432.0	2432.0
F000'	2437.02	
h,k,lmax	14,15,45	14,15,45
Nref	10731	10572
Tmin,Tmax	0.863,0.931	0.963,0.988
Tmin'	0.832	

Correction method= # Reported T Limits: Tmin=0.963 Tmax=0.988 AbsCorr = NUMERICAL

Data completeness= 0.985 Theta(max)= 25.499

R(reflections)= 0.0535(7156) wR2(reflections)= 0.1367(10572)

S = 1.022 Npar= 689

S = 1.022 Npar= 689

The following ALERTS were generated. Each ALERT has the format **test-name_ALERT_alert-type_alert-level**.
Click on the hyperlinks for more details of the test.

Alert level C

PLAT147_ALERT_1_C s.u. on Symmetry Constrained Cell Angle(s)… Please Check
PLAT220_ALERT_2_C Non-Solvent Resd 1 C Ueq(max)/Ueq(min) Range 3.1 Ratio
PLAT222_ALERT_3_C Non-Solvent Resd 1 H Uiso(max)/Uiso(min) Range 5.3 Ratio
PLAT222_ALERT_3_C Non-Solvent Resd 2 H Uiso(max)/Uiso(min) Range 10.0 Ratio
PLAT230_ALERT_2_C Hirshfeld Test Diff for P4 -- C33… 5.7 s.u.
PLAT244_ALERT_4_C Low 'Solvent' Ueq as Compared to Neighbors of O6 Check
PLAT245_ALERT_2_C U(iso) H9N Smaller than U(eq) N9 by… 0.027 AngSq
PLAT250_ALERT_2_C Large U3/U1 Ratio for Average U(i,j) Tensor… 2.1 Note
PLAT341_ALERT_3_C Low Bond Precision on C-C Bonds… 0.00622 Ang.
PLAT352_ALERT_3_C Short N-H (X0.87,N1.01A) N4 - H4N… 0.75 Ang.
PLAT352_ALERT_3_C Short N-H (X0.87,N1.01A) N5 - H5N… 0.75 Ang.
PLAT352_ALERT_3_C Short N-H (X0.87,N1.01A) N9 - H9N… 0.72 Ang.
PLAT352_ALERT_3_C Short N-H (X0.87,N1.01A) N10 - H1N… 0.73 Ang.
PLAT790_ALERT_4_C Centre of Gravity not Within Unit Cell: Resd. # 1 Note
C23 H36 Mn N5 O2 P2
PLAT906_ALERT_3_C Large K value in the Analysis of Variance… 5.405 Check
PLAT911_ALERT_3_C Missing # FCF Refl Between THmin & STh/L= 0.600 159 Report

Alert level G

PLAT002_ALERT_2_G Number of Distance or Angle Restraints on AtSite 5 Note
PLAT003_ALERT_2_G Number of Uiso or Uij Restrained non-H Atoms ... 4 Report
PLAT042_ALERT_1_G Calc. and Reported MoietyFormula Strings Differ Please Check
PLAT153_ALERT_1_G The s.u.'s on the Cell Axes are Equal ..(Note) 0.005 Ang.
PLAT172_ALERT_4_G The CIF-Embedded .res File Contains DFIX Records 3 Report
PLAT186_ALERT_4_G The CIF-Embedded .res File Contains ISOR Records 1 Report
PLAT230_ALERT_2_G Hirshfeld Test Diff for O2 -- C23 .. 5.3 s.u.
PLAT232_ALERT_2_G Hirshfeld Test Diff (M-X) Mn1 -- C22 .. 5.5 s.u.
PLAT232_ALERT_2_G Hirshfeld Test Diff (M-X) Mn2 -- C45 .. 7.0 s.u.
PLAT232_ALERT_2_G Hirshfeld Test Diff (M-X) Mn2 -- C46 .. 6.5 s.u.
PLAT790_ALERT_4_G Centre of Gravity not Within Unit Cell: Resd. # 2 Note
C23 H36 Mn N5 O2 P2
PLAT790_ALERT_4_G Centre of Gravity not Within Unit Cell: Resd. # 3 Note
C4 H8 O2
PLAT860_ALERT_3_G Number of Least-Squares Restraints ..... 27 Note
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min) 1 Note
PLAT933_ALERT_2_G Number of OMIT Records in Embedded .res File ... 1 Note
PLAT961_ALERT_5_G Dataset Contains no Negative Intensities ..... Please Check
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 1 Note

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
16 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
17 **ALERT level G** = General information/check it is not something unexpected

3 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
12 ALERT type 2 Indicator that the structure model may be wrong or deficient
11 ALERT type 3 Indicator that the structure quality may be low
6 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and

unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

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A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

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Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

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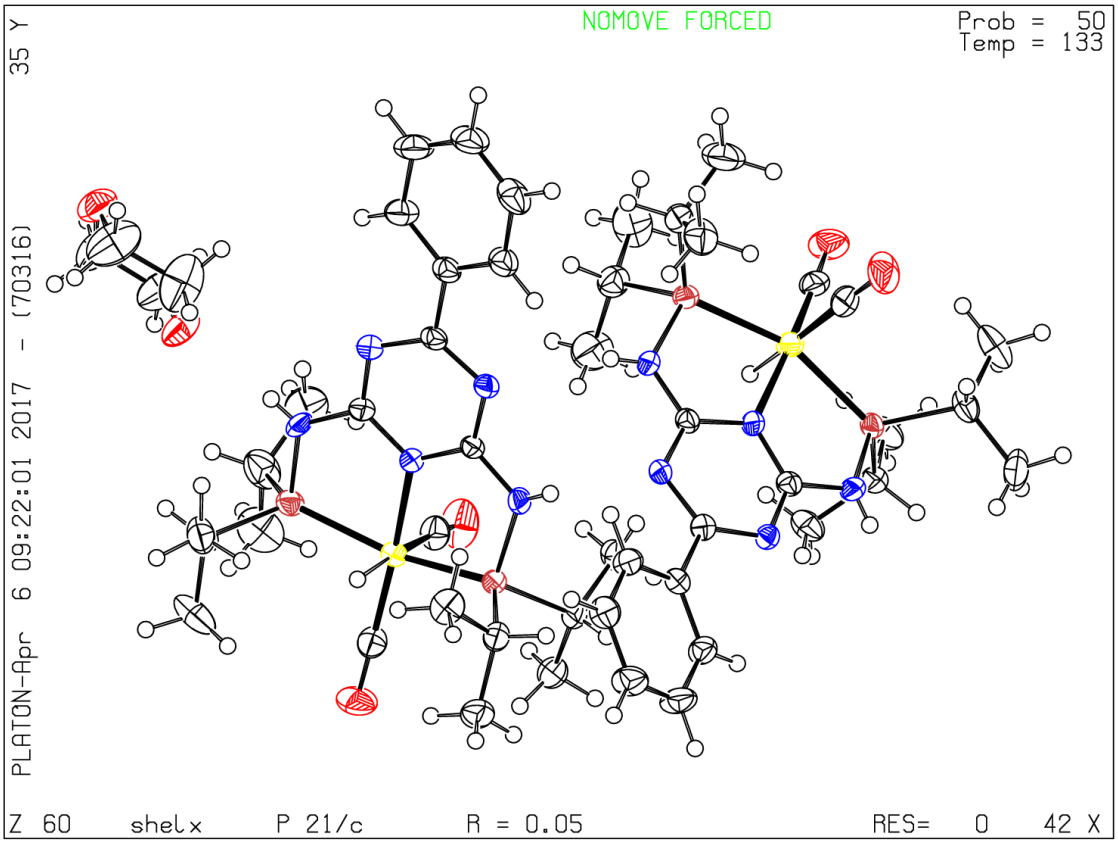

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7. Chromium-Catalyzed Alkylation of Amines by Alcohols

Kallmeier, F.; Fertig, R.; Irrgang, T.; Kempe, R.*

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Chromium-Catalyzed Alkylation of Amines by Alcohols

*Fabian Kallmeier, Robin Fertig, Torsten Irrgang, and Rhett Kempe**

Dedicated to Marlies Schilling

Abstract: *The alkylation of amines by alcohols is a broadly applicable, sustainable, and selective method for the synthesis of alkyl amines, which are important bulk and fine chemicals, pharmaceuticals, and agrochemicals. We show that Cr complexes can catalyze this C–N bond formation reaction. We synthesized and isolated 35 examples of alkylated amines, including 13 previously undisclosed products, and the use of amino alcohols as alkylating agents was demonstrated. The catalyst tolerates numerous functional groups, including hydrogenation-sensitive examples. Compared to many other alcohol-based amine alkylation methods, where a stoichiometric amount of base is required, our Cr-based catalyst system gives yields higher than 90% for various alkyl amines with a catalytic amount of base. Our study indicates that Cr complexes can catalyze borrowing hydrogen or hydrogen autotransfer reactions and could thus be an alternative to Fe, Co, and Mn, or noble metals in (de)hydrogenation catalysis.*

The alkylation of amines by alcohols can proceed via a borrowing hydrogen or hydrogen autotransfer (BH/HA) mechanism (Figure 1, a). The alcohol is dehydrogenated by transferring a proton and a hydride to the catalyst, with the hydride binding to the metal and the proton being accepted by the ligand or support. The so-formed carbonyl compound can undergo a Schiff-base reaction[1] with an amine or ammonia, and the resulting imine is reduced through transfer of the hydride and the proton to it, thereby recycling the catalyst. This amine alkylation is a green or sustainable reaction since alcohols are employed[2] and it permits the selective alkylation of amines.[3] The reaction was discovered by Winans and Adkins[4] in 1932, and the groups of Grigg[5] and Watanabe[6] introduced the first homogeneous catalysts. The development of catalysts based on abundantly available metals to mediate chemical transformations typically associated with rare noble metals is a similarly important green or sustainable approach and may permit the observation of yet unknown selectivity patterns. We recently summarized the

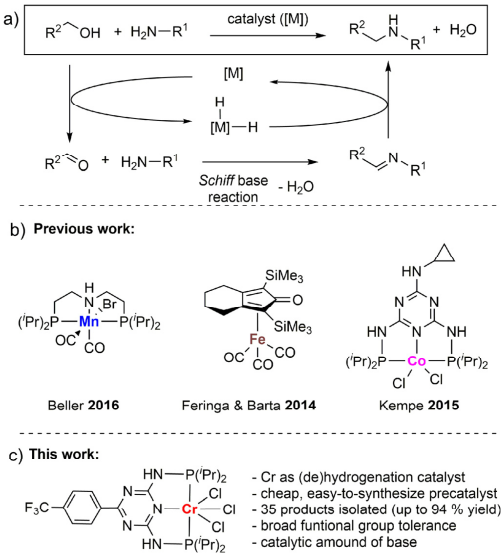

Figure 1. a) Alkylation of amines by alcohols via borrowing hydrogen or hydrogen autotransfer ([M] {transition} metal catalyst). b) Key developments of homogeneous 3d metal catalyst for the alkylation of amines by alcohols. c) Chromium based precatalyst used in this report.

progress made in developing 3d metal catalysts for C–N and C–C bond formation reactions with alcohols using the BH/HA concept[7] and discovered that chromium catalysts have not been reported for these reactions to the best of our knowledge. Homogeneous catalysts of 3d metals for the alkylation of amines by alcohols through BH/HA have been discovered by the groups of Feringa and Barta (Fe),[8] our group (Co),[9] and Beller and co-workers (Mn).[10] Interestingly, these and related complexes have also been used to catalyze a variety of (de)hydrogenation reactions.[11]

Herein, we report that chromium complexes can catalyze the alkylation of amines by alcohols. We synthesized and isolated 35 examples of alkyl amines in yields up to 94%. Thirteen previously undisclosed products were obtained, and selective C–N bond formation by employing amino alcohols as the alkylating agent was demonstrated. Our catalyst tolerates numerous functional groups, among them hydrogenation-sensitive examples. We only use a catalytic amount

[*] F. Kallmeier, R. Fertig, Dr. T. Irrgang, Prof. Dr. R. Kempe
Inorganic Chemistry II—Catalyst Design, University of Bayreuth
95440 Bayreuth (Germany)
E-mail: kempe@uni-bayreuth.de

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of base, and a mechanism following the BH/HA concept is very likely.

Five Cr^{III} precatalysts **Cr-Ia–e** and the corresponding Cr^{II} precatalysts (**Cr-IIa–e**) were synthesized first (Figure 2, for the full synthetic procedure please see the Supporting Information). **Cr-If** and **Cr-IIf** were synthesized according to procedures reported by Kirchner and co-workers.[12] The molecular structure of **Cr-Id** (which turned out to be the precatalyst of the most active catalyst system, see below) was confirmed by X-ray diffraction (XRD) analysis. The magnetic susceptibility μ_{eff} was determined by SQUID measurements to be 3.9, which is fully consistent with a Cr^{III} center.

The reaction of aniline with benzyl alcohol was chosen as a model reaction and the different complexes were tested for their activity at a catalyst loading of 5 mol% (Table 1).

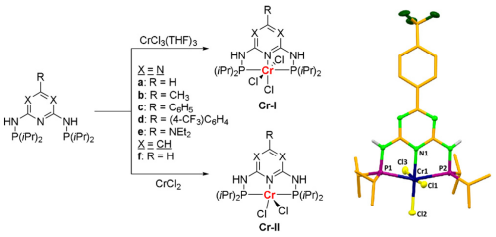
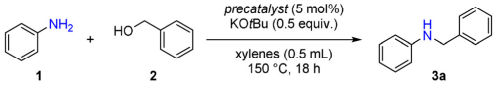


Figure 2. Synthesis of the complexes used in this study and molecular structure of **Cr-Id**. Thermal ellipsoids are shown at 50% probability, solvent molecules and C–H atoms omitted for clarity. Selected bond lengths [Å] and angles [°]: Cr1–N1 2.086(3), Cr1–P1 2.4492(11), Cr1–P2 2.4520(11), Cr1–Cl1 2.3085(11), Cr1–Cl2 2.2877(11), Cr1–Cl3 2.3055(11); P1-Cr1-P2 158.56(4), N1-Cr1-Cl2 179.29(9), Cl3-Cr1-Cl1 173.64(4).

Table 1: Catalyst system screening for the N-alkylation of aniline.[a]



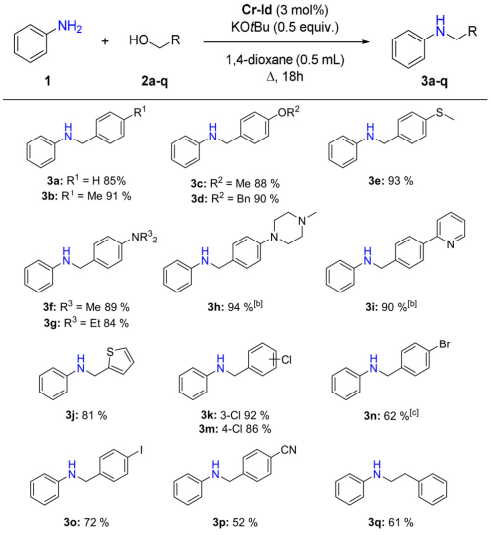
Entry	Precatalyst	Yield[b] [%]
1	**Cr-Ia**	21
2	**Cr-Ib**	24
3	**Cr-Ic**	29
4	**Cr-Id**	52 (97[c])
5	**Cr-Ie**	18
6	**Cr-If**	15
7	**Cr-IIa**	23
8	**Cr-IIb**	35
9	**Cr-IIc**	22
10	**Cr-IId**	58
11	**Cr-IIe**	31
12	**Cr-IIf**	1

[a] Reaction conditions: 5 mol% precatalyst (50 µmol), 0.5 equiv KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL xylenes (mixture of isomers), 1 equiv benzyl alcohol (1 mmol, 104 µL) and 1 equiv aniline (1 mmol, 91 µL), 150 °C oil bath, 18 h. [b] Yield determined by GC-analysis using *n*-dodecane as internal standard. [c] 3 mol% **Cr-Id** (30 µmol), 0.5 equiv KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL 1,4-dioxane, 1.2 equiv benzyl alcohol (1.2 mmol, 125 µL) and 1 equiv aniline (1 mmol, 91 µL), 150 °C oil bath, 18 h, bubble counter with backflow protection.

Electron-donating substituents at the triazine core do not significantly influence the outcome of the reaction (Table 1, entries 1–3 and 7–9), however, the electron-withdrawing substituent in **Cr-Id** and **Cr-IId** leads to a two-fold increase in product yield (Table 1, entries 4 and 10). Notably, switching from a triazine to a pyridine backbone decreases product formation, with the effect being more pronounced in Cr^{II} than Cr^{III} complexes (Table 1, entries 6 and 12). Despite giving the best yield so far (Table 1, entry 10), the result for **Cr-IId** could not be further increased, which is in contrast to the Cr^{III} analogue **Cr-Id** (Table 1, entry 4). When the reaction was run with a slight excess of benzyl alcohol (1.2 equiv) in 1,4-dioxane, the product **3a** was almost quantitatively obtained using only 3 mol% of **Cr-Id** (see the Supporting Information for screening reactions).

Having established optimal reaction conditions, the addressable substrate scope was evaluated using different primary alcohols (Table 2). The screening substrate **3a** was isolated in 85% yield. Substrates containing methyl (**3b**), methoxide (**3c**), and thiomethyl (**3e**) groups were synthesized in slightly better yields of 88–93%. The use of (4-benzyloxy)benzyl alcohol furnished product **3d** in 90% yield without any signs of cleavage of the benzyloxy group. Next, a series of electron rich, *N*,*N*-dialkyl-substituted *para*-aminobenzyl alcohols were tested and the resulting products **3f** and **3g** were isolated in 89 and 84% yield, respectively. The previously undisclosed product **3h**, which contains a piperazine moiety, was isolated almost quantitatively (94%). Heteroaromatic alcohols furnished the pyridine derivative **3i** and thiophene

Table 2: Substrate scope with respect to primary alcohols.[a]



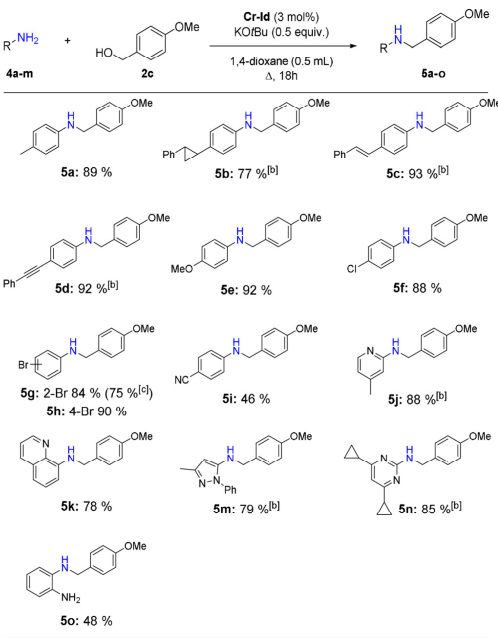
[a] 3 mol% **Cr-Id** (30 µmol), 0.5 equiv KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL 1,4-dioxane, 1.2 equiv alcohol (1.2 mmol) and 1 equiv aniline (1 mmol, 91 µL), 150 °C oil bath, 18 h, bubble counter with backflow protection. Yields refer to isolated product. [b] New compound. [c] 5 mmol scale.

derivative **3j** in 90 and 81 % yield, respectively. Furthermore, halide-substituted benzyl alcohols reacted smoothly to give the products **3k–o** in 62–92 % yield. Notably, the strongly electron-withdrawing nitrile group was tolerated and the corresponding product **3p** was obtained in 52 % yield. Employing 2-phenylethanol instead of a benzylic alcohol resulted in a decrease in yield to 61 % (**3q**).

Next, the substrate scope with respect to the amine was evaluated (Table 3). For this purpose, a series of *para*-substituted anilines was tested. First, 4-methylaniline was reacted under standard conditions and furnished **5a** in 89 % yield. Next, radical-reaction and hydrogenation-sensitive substrates were tested. To our delight, cyclopropanes, double bonds, and triple bonds did not undergo undesired reactions, thus furnishing **5b–d** in very agreeable yields of 77–93 %. A substrate containing an electron-donating methoxide group was converted as efficiently as substrates containing electron-withdrawing groups like halides, leading to the isolation of **5e–h** in similar yields of 84–92 %. The synthesis of **5g** could be easily scaled up to 10 mmol scale, furnishing 2.20 grams (75 %) of product. Product **5i**, which contains the strongly electron-withdrawing nitrile group, was isolated in 46 % yield. Finally, a series of N-heterocyclic amines was subjected to catalytic N-alkylation. Aminopyridine **5j** and aminoquinoline **5k** were synthesized in respectable yields of 88 and 78 %, respectively. The five-membered heteroaromatic aminopyrazole reacted smoothly, affording **5m** in 79 % yield. Finally, 4,6-dicyclopropylpyrimidin-2-amine, which can easily be prepared from alcohols and guanidine by a one-pot procedure,[13] was reacted with *para*-methoxybenzyl alcohol and furnished product **5n** in a satisfying 85 % yield.

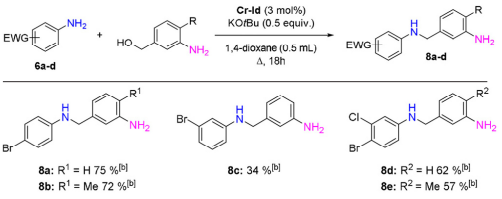
Based on a Hammett study (see the Supporting Information), electron-deficient anilines react faster with alcohols. Therefore, we hypothesized that a selective reaction with an unprotected amino benzyl alcohol should occur readily (Table 4). Indeed, the reaction between 4-bromoaniline with 3-aminobenzyl alcohol furnished **8a** in 75 % yield of isolated material. The yield is significantly affected by using 3-bromoaniline (Table 4; **8c**, 34 %), which is consistent with the findings from our Hammett study, since the position of the electron-withdrawing group in conjugation with the amine is pivotal. With an additional chlorine substituent in the *meta* position, **8d** can be obtained in a similar yield to **8a**. Amino alcohols containing an additional methyl group gave similar results, thus indicating that the selectivity arises from electronic factors rather than steric considerations.

Table 3: Substrate scope with respect to the amine.[a]



[a] 3 mol % **Cr-Id** (30 μmol), 0.5 equiv KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL 1,4-dioxane, 1.2 equiv 4-methoxybenzyl alcohol (1.2 mmol, 149 μL) and 1 equiv amine (1 mmol), 150 °C oil bath, 18 h, bubble counter with backflow protection. Yields refer to isolated product. [b] New compound. [c] 10 mmol scale.

Table 4: Alkylation of anilines using 3-aminobenzyl alcohols.[a]



[a] 3 mol % **Cr-Id** (30 μmol), 0.5 equiv KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL 1,4-dioxane, 1.2 equiv aminobenzyl alcohol (1.2 mmol) and 1 equiv amine (1 mmol), 150 °C oil bath, 18 h, bubble counter with backflow protection. Yields refer to isolated product. [b] new compound. EWG = electron withdrawing group.

Finally, preliminary mechanistic experiments were conducted (Figure 3). A mercury-drop test showed no influence of mercury on the yield of the model reaction (65 % without mercury, 69 % at 225 mol % Hg loading), thus indicating that the active catalyst is likely to be homogeneous in nature. This is further supported by the partial inhibition of the reaction by the phosphine oxide $OPPh_3$ (0.3 mol % $OPPh_3$: 56 % of **3a**). The activation of **Cr-Id** was then examined upon addition of KO*t*Bu to the complex by using IR spectroscopy. The complex exhibits a broad NH resonance at 3214 cm^{-1}, which gradually disappears upon the addition of base. We concluded that a doubly deprotonated species could act as the active catalyst, which is similar to our recent findings with a Mn catalyst.[14] Then, the dehydrogenation and hydrogenation step of the proposed BH/HA cycle were examined. 18 % alcohol was consumed in a closed flask and 27 % was consumed when the same reaction was run using a bubble counter with backflow protection for pressure equalization. Afterwards, the ability

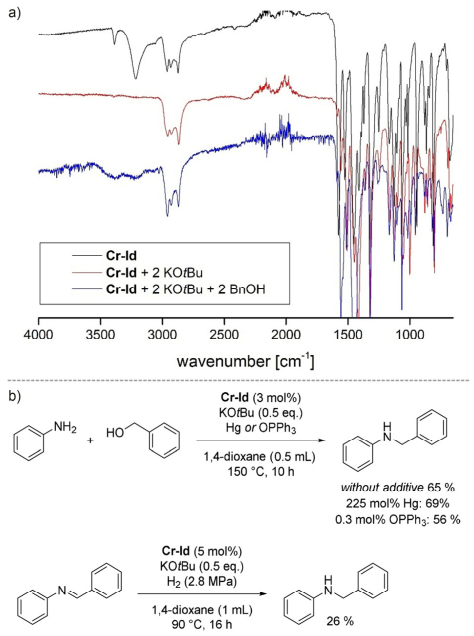


Figure 3. a) IR spectroscopy of **Cr-Id** after activation with 2 equivalents of KO*t*Bu and reaction with benzyl alcohol (normalized). b) Poisoning and hydrogenation experiments.

of the catalyst to hydrogenate the intermediate imine was probed. When employing 5 mol% **Cr-Id** and 50 mol% KO*t*Bu, 26% amine product **3a** was observed. To gain insight into the nature of the rate-determining step, a Hammett study was conducted.[15] It could be observed that electron-donating groups at the anilines like Me and OMe lead to a decreased reaction rate. On the other hand, increased reaction rates are obtained for anilines with electron-withdrawing groups like Cl, Br, and styrene. This leads to the assumption that the rate-determining step is likely hydride transfer to the imine, since electron-withdrawing groups at the aniline can cushion the build-up of negative charge during hydride transfer.

In summary, we have established that Cr complexes can mediate (de)hydrogenation catalysis. The catalytic N-alkylation of amines by alcohols was explored since it is an important and green or sustainable C–N bond-formation reaction. The chromium complexes we use as precatalysts are inexpensive and easy to synthesize. Our catalyst system mediates the alkylation of amines under conditions comparable to other homogeneous 3d metal catalysts with the noteworthy exception that only sub-stoichiometric quantities of base are required. In total, 35 amines (13 of which have not been reported so far) were synthesized and isolated in yields up to 94%. The catalyst system tolerates functional groups such as aryl iodide, CN, and other hydrogenation-sensitive groups like benzyl ether, alkene, and alkyne groups, and unprotected amino benzyl alcohols are efficiently converted. The active catalyst is likely to be homogeneous in nature, as indicated by poisoning experiments. The results of a Hammett study indicate that the rate-determining step is most likely hydride transfer to the imine. Furthermore, a borrowing hydrogen or hydrogen autotransfer mechanism is very likely.

Acknowledgements

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Conflict of interest

The authors declare no conflict of interest.

Keywords: alcohols · alkylation · borrowing-hydrogen reactions · chromium · hydrogen autotransfer

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Supporting Information

Chromium-Catalyzed Alkylation of Amines by Alcohols

*Fabian Kallmeier, Robin Fertig, Torsten Irrgang, and Rhett Kempe**

Table of Contents

General considerations

All water and air sensitive reactions were performed using Schlenk and glovebox techniques (N_2 5.0 or Ar 5.0). Solvents were dried by distillation over sodium or purchased from Acros Organics and stored over molecular sieves (3 Å). Chemicals were purchased from commercial vendors (purity > 96 %) and used without further purification, if not stated otherwise.

Hydrogenation experiments were conducted in vials (10 mL) which were placed in a 300 mL stainless steel Parr Instruments autoclave, that was assembled in a glovebox under inert atmosphere. All tubes were thoroughly flushed with hydrogen gas (H_2 5.0) and subsequently, the autoclave was flushed three times. After the autoclave was pressurised with the desired hydrogen pressure, it was placed in a heating mantle. The reaction was stirred for the indicated time, after which the reaction was stopped by cooling the autoclave in a water bath and releasing the pressure.

NMR Spectra were recorded on a Bruker Avance III HD 500 or a Varian Inova 400. Chemical shifts (δ) are reported in ppm relative to the residual solvent signal. Coupling constants are reported in Hz.

GC Analysis was carried out on an Agilent 6890N system, equipped with an Agilent HP-5 column (30m, 0.32 µm, 0. 25 µm).

GC-MS Analysis was carried out on an Agilent 7890A system, equipped with an Agilent HP-5MS column (30m, 0.32 µm, 0. 25 µm) and an MSD 5975C detector (EI, 70 eV).

Macherey-Nagel silica gel 60 (40 – 63 µm particle size) was used for flash column chromatography.

Elemental analysis was performed on an Elementar Vario El *III* instrument or an Elementar Unicube.

Melting points were determined on a Stuart Scientific SMP3.

X-Ray crystal structure analysis was performed on a STOE STADIVARI [λ(Mo-K_α) = 0.71073 Å] equipped with an Oxford Cryostream low temperature unit. Structure solution and refinement were achieved with ShelXL[1], ShelXT[2] and Olex2[3]. Structures were visualized using Mercury 4.1.3.[4]

Magnetic measurements were carried out using a SQUID MPMS-XL5 magnetometer from Quantum Design. A magnetic field of 5000 Oe was applied and the samples were measured in the range from 300 to 50 K in sweep mode (5 K min^{-1}). The samples were placed in a gelatin capsule held in a plastic straw. The raw data was corrected for the diamagnetism of the sample holder and the organic ligand using tabulated Pascal's constants.

Synthesis/Purification of Chemicals:

$CrCl_3(THF)_3$ was synthesized by Soxhlet extraction of $CrCl_3$ with Zn powder according to literature.[5]

Potassium *tert*-butoxide (KO*t*Bu) was purchased from commercial vendors in > 97 % purity and resublimed under vacuum ($1.0 \cdot 10^{-3}$ mbar) at 130 °C.

4,6-dicyclopropylpyrimidin-2-amine was prepared from guanidine·HCl, cyclopropylmethanol and 1-cyclopropylethanol according to literature[6] and purified by column chromatography.

4-(2-phenylcyclopropyl)aniline was prepared from 1-nitro-4-(2-phenylcyclopropyl)benzene by reduction with Fe/HCl (aq.) in MeOH and purified by column chromatography. 1-nitro-4-(2-phenylcyclopropyl)benzene was prepared from *N'*-(4-nitrobenzylidene)toluenesulfonohydrazide and styrene according to literature.[7] The raw product was filtered through a pad of silica and used in the hydrogenation step without further purification.

4-(phenylethynyl)aniline was prepared from ethynylbenzene and 4-iodoaniline via Pd-catalysed cross coupling according to literature.[8] The product was purified by column chromatography and subsequent recrystallisation from ethyl acetate / pentane.

General procedures

General procedure for the synthesis of Cr(II) complexes (GP1):

In a nitrogen filled glovebox, a Schlenk tube was charged with the corresponding ligand (1.05 mmol, 1.05 equiv) and anhydrous $CrCl_2$ (1.00 mmol, 123 mg, 1.00 equiv). To this was added 20 mL of anhydrous tetrahydrofuran (THF). The Schlenk tube was closed, taken out of the glovebox, placed into a preheated oil bath (40 °C) and stirred for 22 hours. After cooling to room temperature, *n*-hexane (10 mL) was added, the supernatant was filtered off by cannula filtration and the residue was washed with *n*-hexane (10 mL). The solid was dried *in vacuo* yielding the target compound.

General procedure for the synthesis of Cr(III) complexes (GP2):

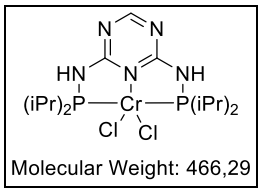
In a nitrogen filled glovebox, a Schlenk tube was charged with a solution of the corresponding ligand (1.00 equiv) in THF (0.2 M) to which $CrCl_3(THF)_3$ (1.00 equiv) and THF (10 mL) were consecutively added. The Schlenk tube was closed, taken out of the glovebox and placed into a preheated oil bath (50 °C) and the solution was stirred for 22 hours. After cooling to room temperature, the solution was concentrated under reduced pressure until precipitation started at which point *n*-hexane (10 mL) was added. Heating the mixture until the solid dissolved and slowly cooling it to 8 °C overnight gave crystals of the product, which were isolated by cannula filtration and washed with *n*-hexane (10 mL). Drying under reduced pressure at 50 °C yielded the target compound.

General procedure for the synthesis of Amines (GP3):

In a nitrogen filled glovebox, a pressure tube (Ace pressure tube, bushing type, Front seal, 38 mL, L 20.3 cm × O.D. 25.4 mm) was charged with KO*t*Bu (0.5 mmol, 56 mg, 0.5 equiv), **Cr-Id** (30 µmol, 22mg, 3 mol%), 1,4-dioxane (250 µL), alcohol (1.2 mmol, 1.2 equiv), aniline (1 mmol, 1 equiv) and 1,4-dioxane (250 µL), in this order. The tube was sealed with a bubble counter with backflow protection, brought out of the glovebox and placed into a preheated oil bath (150 °C). The mixture was stirred for 18 hours, after which the tube was cooled to room temperature in a water bath. The reaction was quenched by the addition of 1.5 mL water. The aqueous phase was extracted three times using methyl *tert*-butyl ether (MTBE), the combined organic phase was dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The crude product was purified by column chromatography.

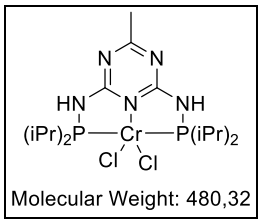
Synthesis of Cr(II) complexes

$^{H}Triaz_{iPr}CrCl_2$ (Cr-IIa)



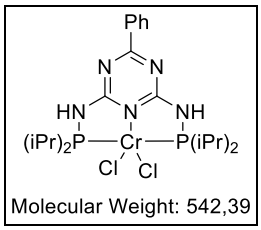
N^2,*N*^{4}-bis(diisopropylphosphanyl)-1,3,5-triazine-2,4-diamine (721 mg, 2.1 mmol) and $CrCl_2$ (246 mg, 2.00 mmol) were reacted according to GP1, yielding the target compound as a dark green solid (825 mg, 1.77 mmol, 88 %). Elemental analysis calcd. for $C_{15}H_{31}Cl_2CrN_5P_2 + C_4H_8O$ (THF): C 42.39, H 7.30, N 13.01; found: C 42.20, H 7.29, N: 13.35. Crystals, suitable for X-Ray analysis were grown by hexane vapor diffusion into a saturated solution of the compound in THF.

$^{Me}Triaz_{iPr}CrCl_2$ (Cr-IIb)



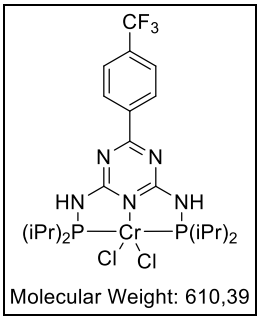
N^2,*N*^{4}-bis(diisopropylphosphanyl)-6-methyl-1,3,5-triazine-2,4-diamine (375 mg, 1.05 mmol) and $CrCl_2$ (123 mg, 1.00 mmol) were reacted according to GP1, yielding the target compound as a dark green solid (322 mg, 0.67 mmol, 67 %). Elemental analysis calcd. for $C_{16}H_{33}Cl_2CrN_5P_2$: C 40.01, H 6.93, N 14,58; found: C 39.62, H 6.73, N 14.24. Crystals, suitable for X-Ray analysis were grown by hexane vapor diffusion into a saturated solution of the compound in THF.

$^{Ph}Triaz_{iPr}CrCl_2$ (Cr-IIc)



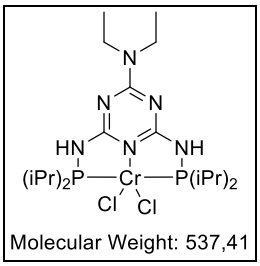
N^2,*N*^{4}-bis(diisopropylphosphanyl)-6-phenyl-1,3,5-triazine-2,4-diamine (440 mg, 1.05 mmol) and $CrCl_2$ (123 mg, 1.00 mmol) were reacted according to GP1, yielding the target compound as a brown solid (447 mg, 0.82 mmol, 82 %). Elemental analysis calcd. for $C_{21}H_{35}Cl_2CrN_5P_2$: C 46.50, H 6.50, N 12.91; found: C 46.15, H 6.49, N 12.66.

$^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz}_{\mathrm{iPr}}\mathrm{CrCl_2}$ (Cr-IId)



N^2,*N*^{4}-bis(diisopropylphosphanyl)-6-(4-(trifluoromethyl)phenyl)-1,3,5-triazine-2,4-diamine (512 mg, 1.05 mmol) and $CrCl_2$ (123 mg, 1.00 mmol) were reacted according to GP1, yielding the target compound as a brown solid (497 mg, 0.81 mmol, 81 %). Reproducing the synthesis on a 5.2 mmol scale gave 2.76 g (87 %) of the product. Elemental analysis calcd. for $C_{22}H_{34}Cl_2CrF_3N_5P_2$: C 43.29, H 5.61, N 11.47; found: C 43.00, H 5.89, N 11.50. Crystals, suitable for X-Ray analysis were grown by hexane vapor diffusion into a saturated solution of the compound in THF. Magnetic susceptibility μ_{eff} = 5.0 μ_B.

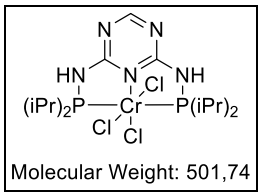
$^{\mathrm{NEt_2}}\mathrm{Triaz}_{\mathrm{iPr}}\mathrm{CrCl_2}$ (Cr-IIe)



N^2,*N*^{4}-bis(diisopropylphosphanyl)-*N*^{6},*N*^{6}-diethyl-1,3,5-triazine-2,4,6-triamine (435 mg, 1.05 mmol) and $CrCl_2$ (123 mg, 1.00 mmol) were reacted according to GP1, yielding the target compound as a blue solid (405 mg, 0.75 mmol, 81 %). Elemental analysis calcd. for $C_{19}H_{40}Cl_2CrN_6P_2$: C 42.46, H 7.50, N 15.64; found: C 42.24, H 7.27, N 15.64. Crystals, suitable for X-Ray analysis were grown by layering the supernatant with 10 mL *n*-hexane.

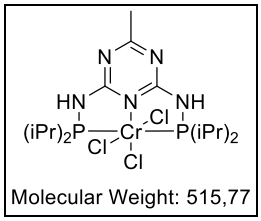
Synthesis of Cr(III) complexes

$^{H}Triaz_{iPr}CrCl_3$ (Cr-Ia)



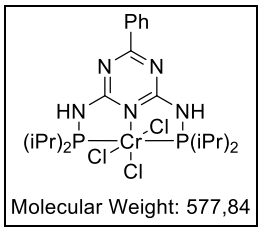
N^2,N^4-bis(diisopropylphosphanyl)-1,3,5-triazine-2,4-diamine (1.03 g, 3 mmol) and $CrCl_3(THF)_3$ (1.12 g, 3 mmol) were reacted according to GP2, yielding the target compound as a dark blue solid (1.40 g, 2.17 mmol, 72 %). Elemental analysis calcd. for $C_{15}H_{31}Cl_3CrN_5P_2$ + 2 C_4H_8O (THF): C 42.77, H 7.33, N 10.84; found: C 42.86, H 7.47, N 11.02. Crystals, suitable for X-Ray analysis were grown by slowly cooling down a hot (80 °C), saturated solution of the compound in THF.

$^{Me}Triaz_{iPr}CrCl_3$(Cr-Ib)



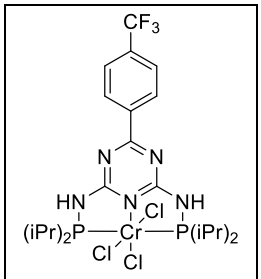
N^2,N^4-bis(diisopropylphosphanyl)-6-methyl-1,3,5-triazine-2,4-diamine (357 mg, 1 mmol) and $CrCl_3(THF)_3$ (375 mg, 1 mmol) were reacted according to GP2, yielding the target compound as a dark blue solid (439 mg, 0.851 mmol, 85 %). Elemental analysis calcd. for $C_{16}H_{33}Cl_3CrN_5P_2$ + C_4H_8O (THF): C 40.86, H 7.03, N 11.91; found: C 40.79, H 6.99, N 11.87. Crystals, suitable for X-Ray analysis were grown by hexane vapor diffusion into a saturated solution of the compound in 1,4-dioxane.

$^{Ph}Triaz_{iPr}CrCl_3$ (Cr-Ic)



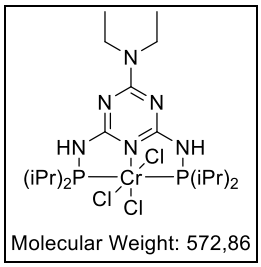
N^2,N^4-bis(diisopropylphosphanyl)-6-phenyl-1,3,5-triazine-2,4-diamine (419 mg, 1.00 mmol) and $CrCl_3(THF)_3$ (375 mg, 1 mmol) were reacted according to GP2, yielding the target compound as a dark blue solid (510 mg, 0.883 mmol, 88 %). Elemental analysis calcd. for $C_{21}H_{35}Cl_3CrN_5P_2$ + C_4H_8O (THF): C 46.20, H 6.67, N 10.78; C 45.79, H 6.54, N 11.19. Crystals, suitable for X-Ray analysis were grown by hexane vapor diffusion into a saturated solution of the compound in THF.

$^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz_{iPr}CrCl_3}$ (Cr-Id)



N^2,N^4-bis(diisopropylphosphanyl)-6-(4-(trifluoromethyl)phenyl)-1,3,5-triazine-2,4-diamine (2.92 g, 6 mmol) and $CrCl_3(THF)_3$ (2.25 mg, 6 mmol) were reacted according to GP2, yielding the target compound as a dark blue solid (2.98 g, 4.61 mmol, 77 %). Elemental analysis calcd. for $C_{22}H_{34}Cl_3CrF_3N_5P_2 + C_4H_8O$ (THF): C 43.50, H 5.90, N 9.75; found: C 43.26, H 5.85, N 9.96. Crystals, suitable for X-Ray analysis were grown by hexane vapor diffusion into a saturated solution of the compound in 1,4-dioxane. Magnetic susceptibility $\mu_{eff} = 3.9\ \mu_B$.

$^{\mathrm{NEt_2}}\mathrm{Triaz_{iPr}CrCl_3}$ (Cr-Ie)



N^2,N^4-bis(diisopropylphosphanyl)-N^6,N^6-diethyl-1,3,5-triazine-2,4,6-triamine (415 mg, 1.00 mmol) and $CrCl_3(THF)_3$ (375 mg, 1.00 mmol) were reacted according to GP2, yielding the target compound as a dark purple solid (464 mg, 0.810 mmol, 81 %). Elemental analysis calcd. for $C_{19}H_{40}Cl_3CrN_6P_2$: C 39.84, H 7.04, N 14.67; found: C 39. 86, H 7.08, N 14.53.

Crystallographic details

Table S1. Molecular structure of the precatalysts used in this study. Thermal ellipsoids at 50 % probability, solvents and (C-)*H* atoms omitted for clarity.

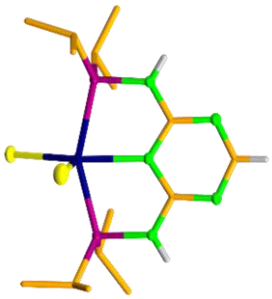
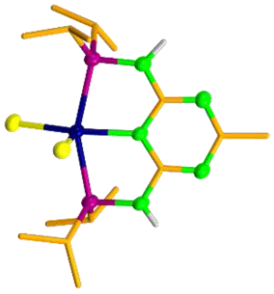
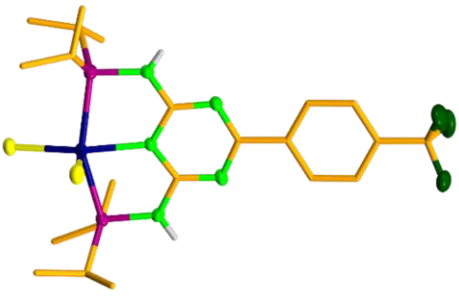
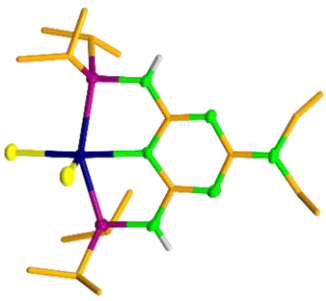
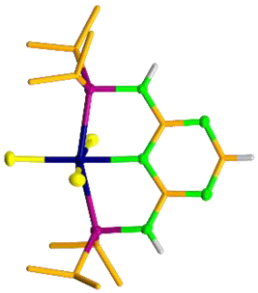
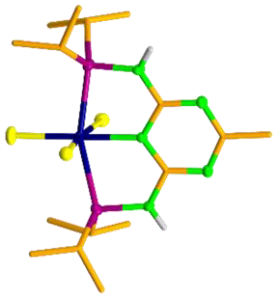
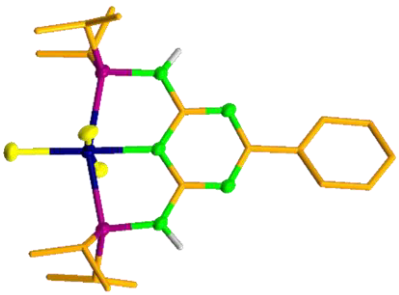
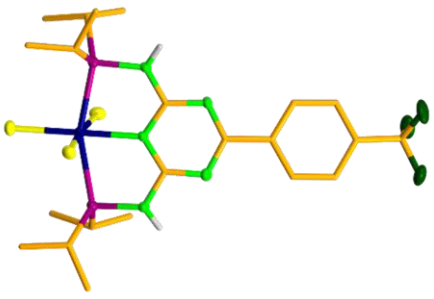
Substituent	H	Me	Ph	^{p}CF$_3$Ph	NEt$_2$
Cr(II)					
Cr(III)					

Table S2. Crystallographic details of Cr(II) complexes used in this study.

Compound	$^{H}Triaz_{iPr}CrCl_2$ (SV501)	$^{Me}Triaz_{iPr}CrCl_2$ (SV490)	$^{pCF_3\text{-}Ph}Triaz_{iPr}CrCl_2$ (SV491)	$^{NEt_2}Triaz_{iPr}CrCl_2$ (SV487)
Formula	C_{15} H_{31} Cl_2 Cr N_5 P_2	0.8 (C_{16} H_{33} Cl_2 Cr N_5 P_2) 0.8 (C_4 H_8 O)	C_{22} H_{34} Cl_2 Cr F_3 N_5 P_2	0.8 (C_{19} H_{40} Cl_2 Cr N_6 P_2) 0.8 (C_4 H_8 O)
Formula weight	466.29	441.93	610.38	487.61
Crystal system	monoclinic	orthorhombic	orthorhombic	orthorhombic
Space group	P 2_1/c (14)	P 2_1 2_1 2_1 (19)	P 2_1 2_1 2_1 (19)	P 2_1 2_1 2_1 (19)
a [Å]	13.050(3)	10.473(2)	10.570(2)	11.070(2)
b [Å]	12.010(2)	12.696(3)	13.130(3)	13.140(3)
c [Å]	14.820(3)	21.129(4)	20.560(4)	21.630(4)
α [°]	90	90	90	90
β [°]	112.80(3)	90	90	90
γ [°]	90	90	90	90
Cell volume [Å³]	2141.3(9)	2809.3(10)	2853.4(10)	3146.3(11)
Z	4	5	4	5
Crystal size [mm³]	0.056*0.047*0.013	0.045*0.042*0.029	0.068*0.047*0.017	0.075*0.065*0.004
Habit	block	plate	plate	block
Colour	green	green	brown	blue
Density [gcm^{-1}]	1.446	1.306	1.421	1.287
T [K]	133	133	133	133
Theta range	2.396 - 28.420	1.871 - 28.537	1.840 - 28.465	1.813 - 28.499
Unique reflections	5120	6062	6325	7408
Observed reflections [I > 2s(I)]	4491	4919	5114	5939
Parameters	234	293	328	327
*wR*2 all data	0.0977	0.1281	0.0643	0.1291
R [I > 2s(I)]	0.0349	0.0482	0.0340	0.0487

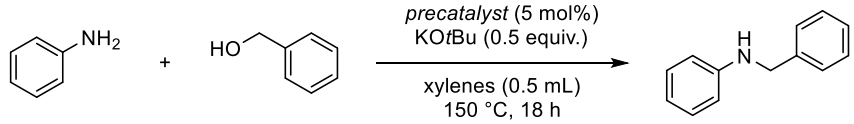
Table S3. Crystallographic details of Cr(III) complexes used in this study.

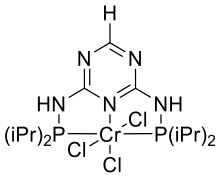
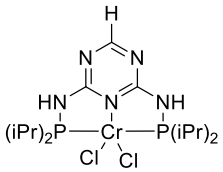
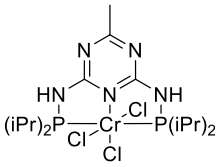
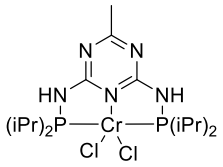
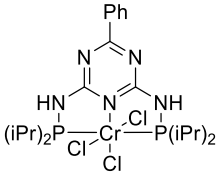
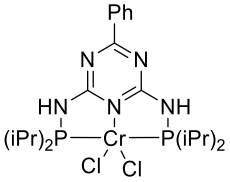
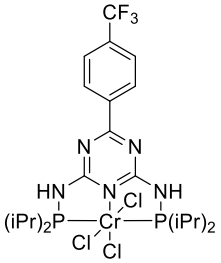
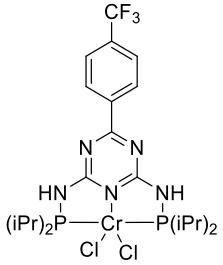
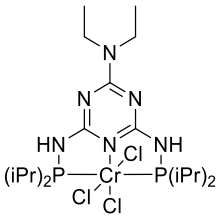
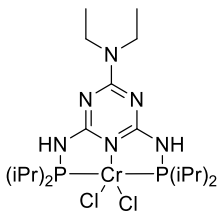
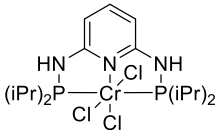
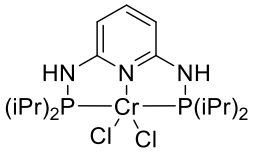
Compound	$^{H}Triaz_{iPr}CrCl_3$ (SV533)	$^{Me}Triaz_{iPr}CrCl_3$ (SV502)	$^{Ph}Triaz_{iPr}CrCl_3$ (SV510)	$^{p-CF_3-Ph}Triaz_{iPr}CrCl_3$ (SV503)
Formula	0.67 (C_{15} H_{31} Cl_3 Cr N_5 P_2) 1.33 (C_4 H_8 O)	0.57 (C_{16} H_{33} Cl_3 Cr N_5 P_2) 1.71 (C_4 H_8 O_2)	0.67 (C_{21} H_{35} Cl_3 Cr N_5 P_2) 2.67 (C_4 H_8 O)	0.57 (C_{22} H_{34} Cl_3 Cr F_3 N_5 P_2) 1.14 (C_4 H_8 O_2)
Formula weight	430.63	445.76	577.49	469.74
Crystal system	monoclinic	monoclinic	triclinic	orthorhombic
Space group	P 2_1/n (14)	P 2_1/n (14)	P $\bar{1}$ (2)	P b c a (61)
a [Å]	11.091(2)	13.650(3)	10.460(2)	22.020(4)
b [Å]	15.286(3)	17.340(4)	11.542(2)	11.440(2)
c [Å]	18.212(4)	16.790(3)	18.584(4)	30.610(6)
α [°]	90	90	84.18(3)	90
β [°]	90.07(3)	103.80(3)	87.60(3)	90
γ [°]	90	90	80.14(3)	90
Cell volume [Å³]	3087.6(11)	3859.3(14)	2198.4(8)	7711(3)
Z	6	7	3	14
Crystal size [mm³]	0.010*0.007*0.003	0.084*0.063*0.057	0.089*0.053*0.025	0.046*0.029*0.027
Habit	block	block	block	needle
Colour	blue	blue	blue	violet
Density [gcm^{-1}]	1.390	1.343	1.309	1.416
T [K]	133	133	133	133
Theta range	2.530 - 28.444	2.855 - 28.449	1.799 - 28.447	1.33 - 28.255
Unique reflections	7350	9148	10279	9117
Observed reflections [I > 2s(I)]	4660	6156	6145	5717
Parameters	333	415	702	444
*wR*2 all data	0.0868	0.0770	0.1549	0.1430
R [I > 2s(I)]	0.0394	0.0349	0.0600	0.0569

Screening of the Reaction Conditions

1) Precatalyst screening

Table S4. Precatalyst screening[a]

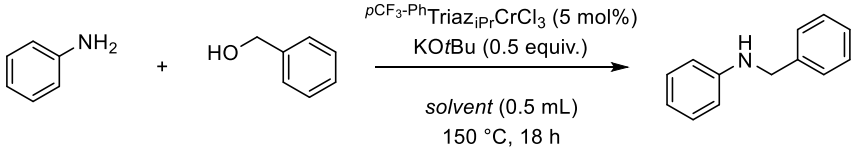


Entry	Catalyst	Yield[b] [%]	Entry	Catalyst	Yield[b] [%]
1	 **Cr-Ia**	21 (15[c])	**8**	 **Cr-IIa**	23
2	 **Cr-Ib**	24 (16[c])	**9**	 **Cr-IIb**	35
3	 **Cr-Ic**	29 (15[c])	**10**	 **Cr-IIc**	22
4	 **Cr-Id**	52 (92[c])	**11**	 **Cr-IId**	58
5	 **Cr-Ie**	18 (87[c])	**12**	 **Cr-IIe**	31
6	 **Cr-If**	15 (17[c])	**13**	 **Cr-IIf**	1
7	No Precatalyst	14	**14**	$CrCl_3(thf)_3$	15

[a]: Reaction conditions: 5 mol% precatalyst (50 µmol), 0.5 equiv KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL xylenes (mixture of isomers), 1 equiv benzyl alcohol (1 mmol, 104 µL) and 1 equiv aniline (1 mmol, 91 µL), 150 °C, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard. [c]: 1,4-dioxane was used as solvent instead of xylenes.

2) Solvent screening

Table S5. Solvent screening[a]

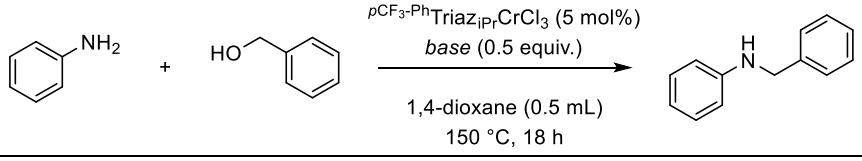


Entry	Solvent	Yield[b] [%]
1	Toluene	71
2	Xylenes (mixture of isomers)	58
3	*p*-Cymene	39
4	Tetrahydrofuran	37
5	1,4-Dioxane	84
6	Bis(2-methoxyethyl) ether	54
7	2-Methylbutan-2-ol	57

[a]: Reaction conditions: 5 mol% $^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz_{iPr}CrCl_3}$ (50 µmol, 32 mg), 0.5 equiv KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL solvent, 1 equiv benzyl alcohol (1 mmol, 104 µL) and 1 equiv aniline (1 mmol, 91 µL), 150 °C, 18 h.
[b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

3) Base screening

Table S6. Base screening[a]

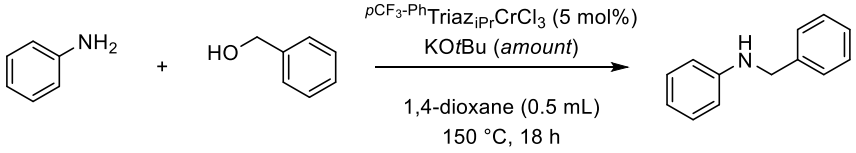


Entry	Base	Yield[b] [%]
1	NaOH	5
2	KOH	0
3	LiO*t*Bu	0
4	NaO*t*Bu	18
5	KO*t*Bu	82
6	K_2CO_3	4
7	1,4-diazabicyclo[2.2.2]octane	9
8	without base	0

[a]: Reaction conditions: 5 mol% $^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz_{iPr}CrCl_3}$ (50 µmol, 32 mg), 0.5 equiv base (0.5 mmol), 0.5 mL 1,4-dioxane, 1 equiv benzyl alcohol (1 mmol, 104 µL) and 1 equiv aniline (1 mmol, 91 µL), 150 °C, 18 h.
[b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

4) Base amount screening

Table S7. Base amount screening[a]

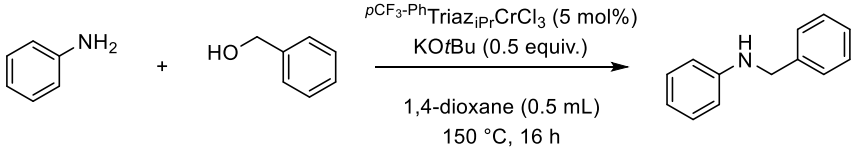


Entry	Base amount	Yield[b] [%]
1	0 equiv	0
2	0.2 equiv	1
3	0.4 equiv	70
4	0.5 equiv	82
5	0.6 equiv	78
6	0.8 equiv	58

[a]: Reaction conditions: 5 mol% $^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz_{iPr}CrCl_3}$ (50 µmol, 32 mg), KO*t*Bu, 0.5 mL 1,4-dioxane, 1 equiv benzyl alcohol (1 mmol, 104 µL) and 1 equiv aniline (1 mmol, 91 µL), 150 °C, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

5) Reactant ratio screening

Table S8. Screening of the reactant ratio[a]

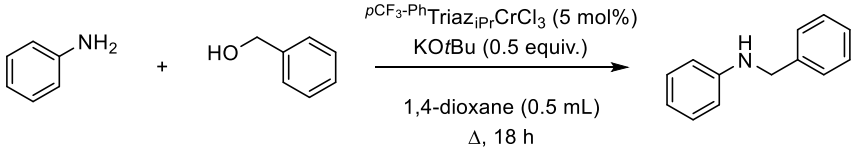


Entry	Molar ratio of reactants (aniline : benzyl alcohol)	Yield[b] [%]
1	1.20 : 1.00	67
2	1.00 : 1.00	66
3	1.00 : 1.20	69
4	1.00 : 1.50	23

[a]: Reaction conditions: 5 mol% $^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz_{iPr}CrCl_3}$ (50 µmol, 32 mg), 0.5 equiv KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL 1,4-dioxane, benzyl alcohol and aniline, 150 °C, 16 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

6) Temperature screening

Table S9. Screening of the oil bath temperature[a]

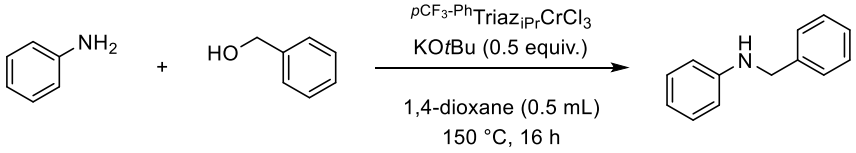


Entry	Temperature [°C]	Yield[b] [%]
1	110	3
2	130	9
3	150	93
4	170	8

[a]: Reaction conditions: 5 mol% $^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz_{iPr}CrCl_3}$ (50 µmol, 32 mg), 0.5 equiv KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL 1,4-dioxane, 1.2 equiv benzyl alcohol (1 mmol, 125 µL) and 1 equiv aniline (1 mmol, 91 µL), Δ, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard.

7) Catalyst loading screening

Table S10. Screening of the catalyst loading[a]

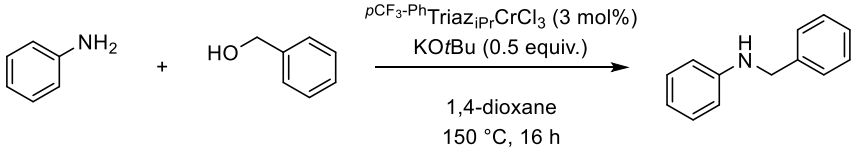


Entry	Precatalyst $^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz_{iPr}CrCl_3}$	Yield[b] [%]
1	1 mol%	49
2	2 mol%	75
3	3 mol%	89
4	4 mol%	65
5	5 mol%	47
6	8 mol%	20[c]

[a]: Reaction conditions: $^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz_{iPr}CrCl_3}$, 0.5 equiv. KO*t*Bu (0.5 mmol, 56 mg), 0.5 mL 1,4-dioxane, 1.2 equiv. benzyl alcohol (1.2 mmol, 125 µL) and 1 equiv. Aniline (1 mmol, 91 µL), 150 °C, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard. [c]: average of three runs.

8) Screening of the solvent amount

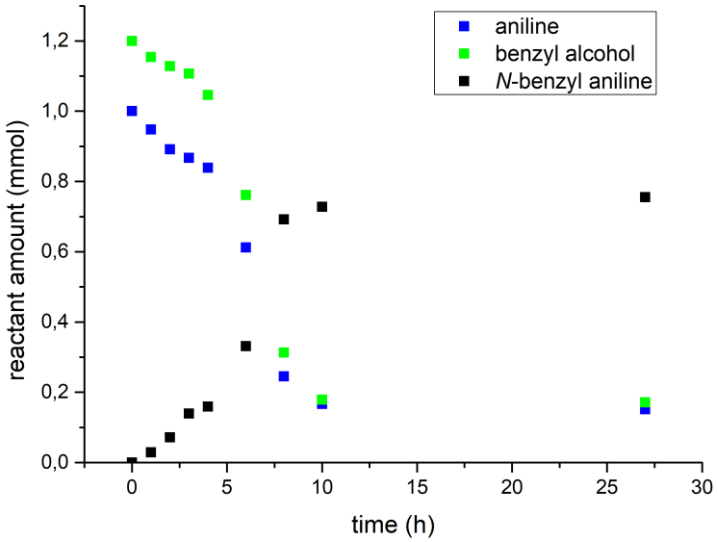
Table S11. Screening of the solvent amount[a]



Entry	Solvent amount [mL]	Yield[b] [%]
1	neat	71
2	0.5	83
3[c]	0.5	97
4	1.0	74
5	2.0	60
6	5.0	46

[a]: Reaction conditions: 3 mol% $^{p\mathrm{CF_3\text{-}Ph}}\mathrm{Triaz_{iPr}CrCl_3}$ (30 µmol, 22 mg), 0.5 equiv. KO*t*Bu (0.5 mmol, 56 mg), 1,4-dioxane, 1.2 equiv. benzyl alcohol (1.2 mmol, 125 µL) and 1 equiv. Aniline (1 mmol, 91 µL), 150 °C, 18 h. [b]: Yield determined by GC-analysis using *n*-dodecane as internal standard. [c]: bubble counter was used for pressure equalization.

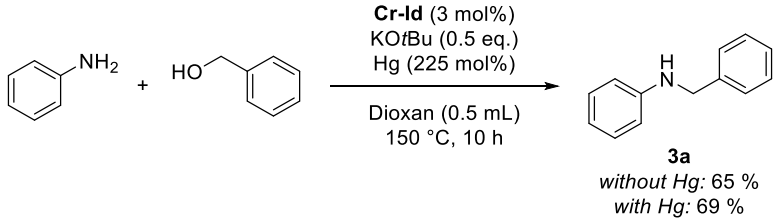
9) Progress of the reaction *versus* time



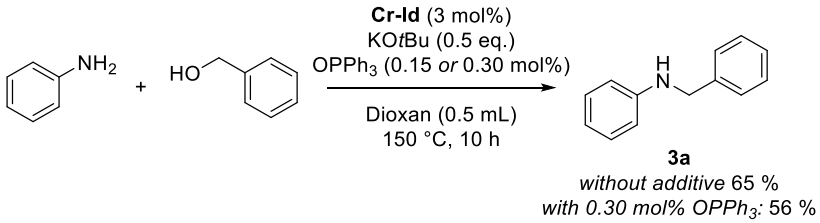
Reaction conditions: **Cr-Id** (30 µmol, 22 mg, 3 mol%), 0.5 equiv. KO*t*Bu (0.5 mmol, 56 mg), 1,4-dioxane (0.5 mL), 1.2 equiv. benzyl alcohol (1.2 mmol, 125 µL) and 1 equiv. Aniline (1 mmol, 91 µL), 150 °C. After the indicated time, the reaction was quenched by the addition of 1.5 mL water and diluted with MtBE (30 mL). Dodecane (100 µL) was added, the mixture thoroughly shaken, and an aliquot was analysed by GC.

Additional Experiments

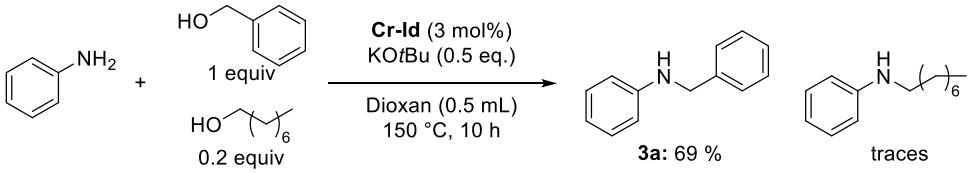
Poisoning Experiments



In a nitrogen filled glovebox, a pressure tube was charged with KO*t*Bu (0.5 mmol, 56 mg, 0.5 equiv), **Cr-Id** (30 µmol, 22mg, 3 mol%), 1,4-dioxane (250 µL), alcohol (1.2 mmol, 1.2 equiv), aniline (1 mmol, 1 equiv) and 1,4-dioxane (250 µL), and mercury (2.25 mmol, 450 mg) in this order. The tube was sealed, brought out of the glovebox and placed into a preheated oil bath (150 °C). The mixture was stirred for 10 hours, after which the tube was cooled to room temperature in a water bath. The reaction was quenched by the addition of 1.5 mL water. The organic phase was diluted with MtBE (30 mL) and *n*-dodecane (100 µL) was as added. After thorough shaking, an aliquot was taken and analysed by GC. Yield of **3a** without mercury under otherwise identical conditions: 65 %. Yield of **3a** with mercury present: 69 %. Yield determined as the average of three entries.

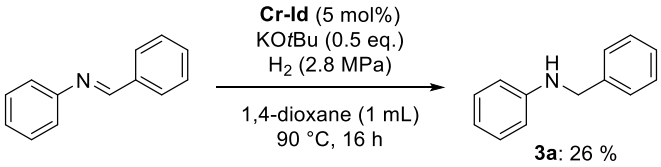


In a nitrogen filled glovebox, a pressure tube was charged with KO*t*Bu (0.5 mmol, 56 mg, 0.5 equiv), **Cr-Id** (30 µmol, 22mg, 3 mol%), 1,4-dioxane (250 µL), alcohol (1.2 mmol, 1.2 equiv), aniline (1 mmol, 1 equiv), triphenylphosphine oxide (3.0 µmol, 200 µL of a 0.015 M stock solution in 1,4-dioxane), and 1,4-dioxane (150 µL or 50 µL, respectively; to bring the overall dioxane amount to 0.5 mL), in this order. The tube was sealed, brought out of the glovebox and placed into a preheated oil bath (150 °C). The mixture was stirred for 10 hours, after which the tube was cooled to room temperature in a water bath. The reaction was quenched by the addition of 1.5 mL water. The organic phase was diluted with MtBE (30 mL) and *n*-dodecane (100 µL) was as added. After thorough shaking, an aliquot was taken and analysed by GC. Yield of **3a** with 0.3 mol% $OPPh_3$: 56 %. Yield determined as the average of three entries.



In a nitrogen filled glovebox, a pressure tube was charged with KO*t*Bu (0.5 mmol, 56 mg, 0.5 equiv), **Cr-Id** (30 µmol, 22mg, 3 mol%), 1,4-dioxane (250 µL), benzyl alcohol (1.0 mmol, 1.0 equiv), octan-1-ol (0.2 mmol, 0.2 equiv), aniline (1 mmol, 1 equiv) and 1,4-dioxane (250 µL), in this order. The tube was sealed, brought out of the glovebox and placed into a preheated oil bath (150 °C). The mixture was stirred for 10 hours, after which the tube was cooled to room temperature in a water bath. The reaction was quenched by the addition of 1.5 mL water. The organic phase was diluted with MtBE (30 mL) and *n*-dodecane (100 µL) was as added. After thorough shaking, an aliquot was taken and analysed by GC. Yield of **3a**: 69 %, conversion of aniline: 74 %.

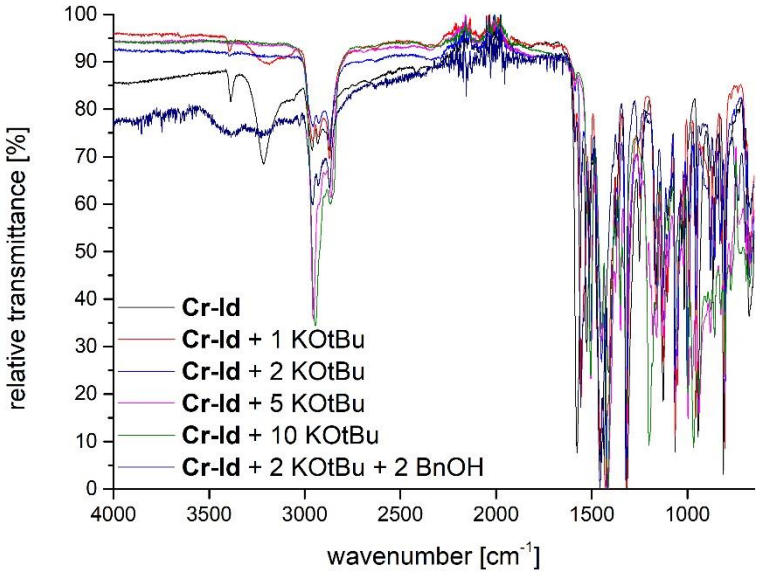
Hydrogenation Experiment

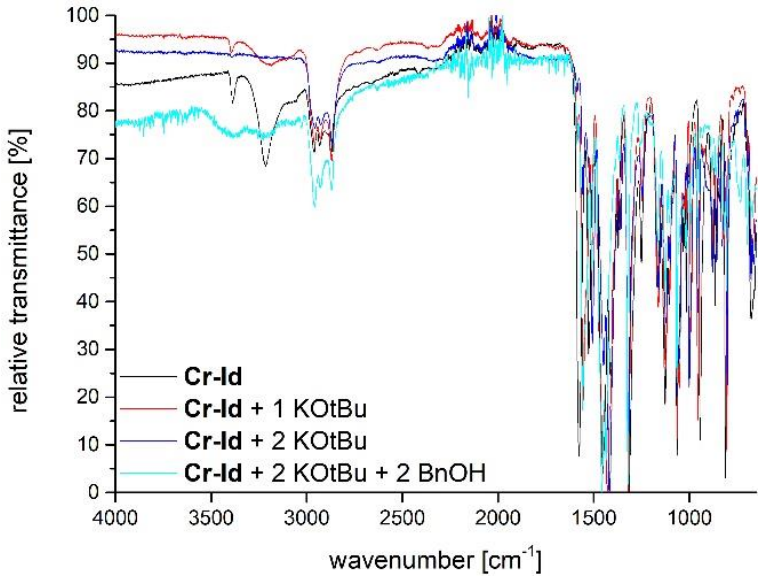


In a glovebox, a 10 mL vial with a magnetic stir bar was charged with **Cr-Id** (50 µmol, 36 mg, 5 mol%), KO*t*Bu (0.5 mmol, 56 mg, 0.5 equiv), the corresponding imine (1 mmol, 181 mg) and 1,4-dioxane (1 mL). The vial was placed in an autoclave, the autoclave was sealed and subsequently flushed (3 times) and pressurised with 2.8 MPa of H_2 at room temperature. Afterwards, the autoclave was heated to 90 °C for 16 hours under stirring (350 rpm). The pressure was released, when the autoclave had reached room temperature, the reaction was quenched by the addition of water (1 mL) and diluted with MtBE (7 mL). To this was added *n*-dodecane (100 µL) and, after vigorous mixing, an aliquot of the organic phase was analysed by GC. Yield of **3a**: 26 %.

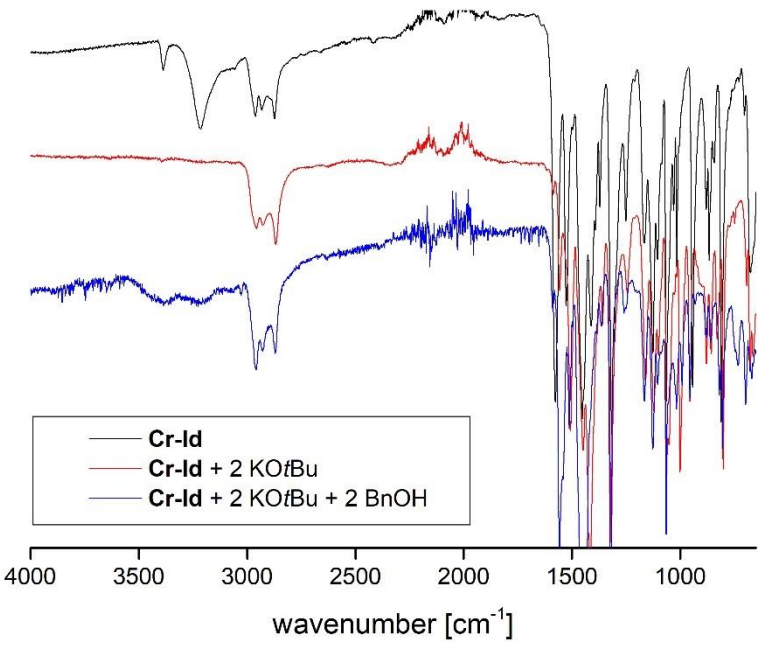
Activation of Cr-Id

In a glovebox, to 100 µL of a 0.02 M stock solution of **Cr-Id** in THF was pipetted the corresponding amount of a 0.2 M stock solution of KO*t*Bu in THF, which was accompanied by an immediate colour change. After 2 minutes of shaking, a few drops of the resulting solution were placed on the ATR unit, and after the THF evaporated the IR spectrum was recorded. For the last experiment, the corresponding amount of a 0.2 M stock solution of benzyl alcohol (BnOH) in THF was added to the mixture.





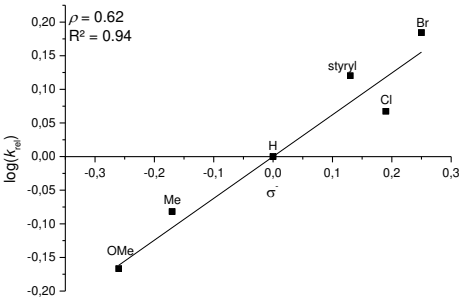
For better visibility, in the following figure is the stacked spectra of key experiments.



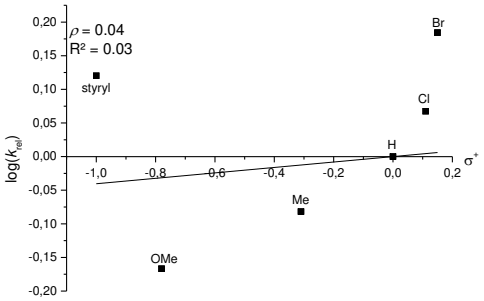
Hammett Study

Cr-Id (30 µmol, 22 mg, 3 mol%), 0.5 equiv. KO*t*Bu (0.5 mmol, 56 mg), 1,4-dioxane (0.25 mL), 1.2 equiv. benzyl alcohol (1.2 mmol, 125 µL), 0.5 equiv. Aniline (0.5 mmol, 45 µL), 0.5 equiv. substituted aniline (0.5 mmol) and 1,4-dioxane (0.25 mL) were reacted according to GP3. After three hours, the reaction was quenched by the addition of 1.5 mL water and diluted with MtBE (30 mL). Dodecane (100 µL) was added, the mixture thoroughly shaken, and an aliquot was analysed by GC.

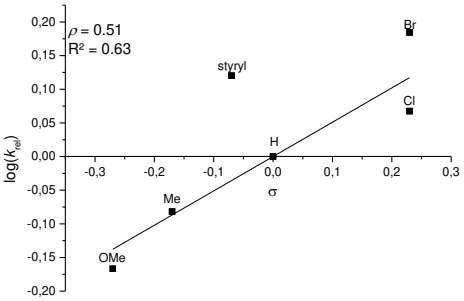
Plot of log(k_{rel}) against σ^-



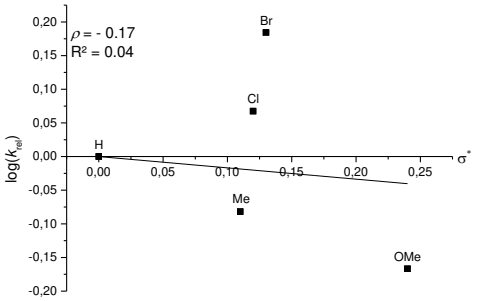
Plot of log(k_{rel}) against σ^+



Plot of log(k_{rel}) against σ

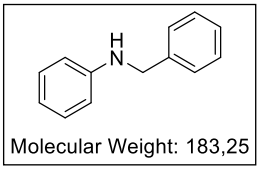


Plot of log(k_{rel}) against σ^*



Synthesis of Amines – Variation of Alcohol

1) *N*-benzylaniline **3a**



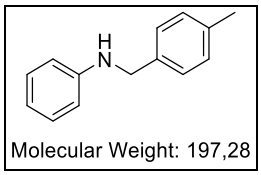
Aniline (91 µL, 1 mmol) and benzyl alcohol (125 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 99:1). Yield: 156 mg (0.851 mmol, 85 %) as a colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 – 7.36 (m, 4H), 7.36 – 7.30 (m, 1H), 7.27 – 7.20 (m, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 2H), 4.37 (s, 2H), 4.06 (s_br, 1H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.3, 139.5, 129.4, 128.7, 127.6, 127.3, 117.7, 112.9, 48.4 ppm.

The spectroscopic data match those reported in literature.[9] (CAS Registry Number: 103-32-2)

2) *N*-(4-methylbenzyl)aniline **3b**



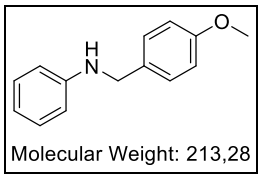
Aniline (91 µL, 1 mmol) and p-tolylmethanol (147 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/ethyl acetate 95:5). Yield: 179 mg (0.907 mmol, 91 %) as a colourless solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.28 (d, *J* = 7.9 Hz, 2H), 7.21 – 7.13 (m, 4H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.63 (d, *J* = 7.7 Hz, 2H), 4.30 (s, 2H), 4.12 (s_br, 1H), 2.36 (s, 3H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 148.9, 137.4, 137.1, 129.7, 129.7, 127.9, 117.8, 113.3, 48.3, 21.4 ppm.

The spectroscopic data match those reported in literature.[10] (CAS Registry Number: 15818-64-1)

3) *N*-(4-methoxybenzyl)aniline **3c**



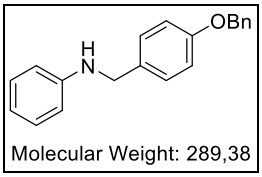
Aniline (91 µL, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 96:4). Yield: 187 mg (0.877 mmol, 88 %) as a colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.3 Hz, 2H), 7.21 (t, *J* = 7.0 Hz, 2H), 6.97 – 6.89 (m, 2H), 6.80 – 6.71 (m, 1H), 6.67 (d, *J* = 8.2 Hz, 2H), 4.28 (s, 2H), 3.97 (s_br, 1H), 3.83 (s, 3H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 158.9, 148.3, 131.5, 129.4, 128.9, 117.6, 114.1, 112.9, 55.4, 47.9 ppm.

The spectroscopic data match those reported in literature.[10] (CAS Registry Number: 3526-43-0)

4) *N*-(4-(benzyloxy)benzyl)aniline **3d**



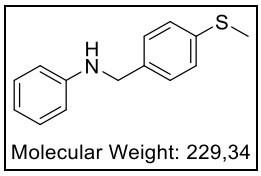
Aniline (91 µL, 1 mmol) and (4-(benzyloxy)phenyl)methanol (257 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, cyclohexane/MTBE 96:4). Yield: 261 mg (0.902 mmol, 90 %) as a colourless solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.46 (d, *J* = 7.5 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.36 (d, *J* = 7.3 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 2H), 7.17 (t, *J* = 7.8 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 8.1 Hz, 2H), 5.08 (s, 2H), 4.27 (s, 2H), 4.10 (s_br, 1H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 158.5, 148.9, 137.8, 132.5, 129.7, 129.3, 129.1, 128.5, 128.1, 117.8, 115.4, 113.3, 70.5, 48.0 ppm.

The spectroscopic data match those reported in literature.[11] (CAS Registry Number: 39860-75-8)

5) *N*-(4-(methylthio)benzyl)aniline **3e**



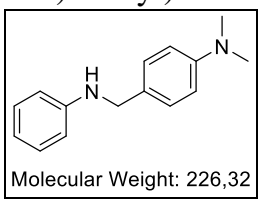
Aniline (91 µL, 1 mmol) and (4-(methylthio)phenyl)methanol (185 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 98:2). Yield: 213 mg (0.929 mmol, 93 %) as a colourless solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.32 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.16 (t, *J* = 7.6 Hz, 2H), 6.75 – 6.66 (m, 1H), 6.63 (d, *J* = 7.7 Hz, 2H), 4.30 (s, 2H), 4.16 (s_br, 1H), 2.49 (s, 3H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 148.7, 137.7, 137.1, 129.7, 128.5, 127.2, 117.9, 113.3, 48.1, 16.2 ppm.

The spectroscopic data match those reported in literature.[12] (CAS Registry Number: 723753-86-4)

6) *N*,*N*-dimethyl-4-((phenylamino)methyl)aniline **3f**



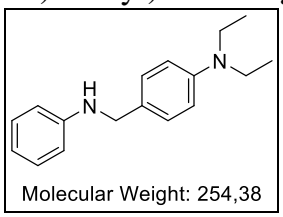
Aniline (91 µL, 1 mmol) and (4-(dimethylamino)phenyl)methanol (181 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 95:5). Yield: 204 mg (0.889 mmol, 89 %) as a colourless solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.25 (d, *J* = 8.6 Hz, 2H), 7.17 (t, *J* = 7.9 Hz, 2H), 6.74 (d, *J* = 8.6 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 2H), 4.22 (d, *J* = 4.8 Hz, 2H), 4.02 (s_br, 1H), 2.95 (s, 6H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 150.6, 149.1, 129.6, 129.1, 127.6, 117.6, 113.3, 113.1, 48.2, 41.0 ppm.

The spectroscopic data match those reported in literature.[13] (CAS Registry Number: 3526-44-1)

7) *N*,*N*-diethyl-4-((phenylamino)methyl)aniline **3g**



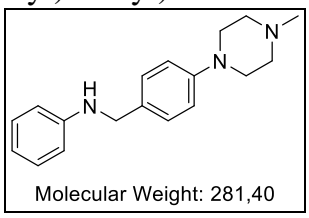
Aniline (91 µL, 1 mmol) and (4-(diethylamino)phenyl)methanol (215 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 95:5). Yield: 213 mg (0.837 mmol, 84 %) as a colourless solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.19 (d, *J* = 8.6 Hz, 2H), 7.14 (t, *J* = 7.9 Hz, 2H), 6.70 – 6.60 (m, 5H), 4.16 (d, *J* = 5.2 Hz, 2H), 3.98 (s_br, 1H), 3.34 (q, *J* = 7.1 Hz, 4H), 1.14 (t, *J* = 7.0 Hz, 6H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 149.1, 147.7, 129.6, 129.4, 126.3, 117.5, 113.2, 112.3, 48.2, 44.9, 12.9 ppm.

The spectroscopic data match those reported in literature.[14] (CAS Registry Number: 940362-30-1)

8) *N*-(4-(4-methylpiperazin-1-yl)benzyl)aniline **3h**



Aniline (91 µL, 1 mmol) and (4-(4-methylpiperazin-1-yl)phenyl)methanol (248 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, methylene chloride/methanol 90:10). Yield: 264 mg (0.938 mmol, 94 %) as a colourless solid (mp = 135 °C).

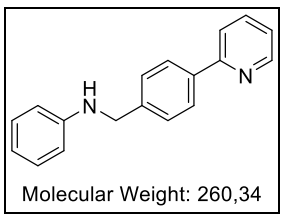
^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.26 (d, *J* = 8.6 Hz, 2H), 7.15 (t, *J* = 7.9 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.67 (t, *J* = 7.3 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 2H), 4.22 (d, *J* = 5.5 Hz, 2H), 4.07 (s_br, 1H), 3.20 – 3.13 (m, 4H), 2.57 – 2.50 (m, 4H), 2.30 (s, 3H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 151.3, 149.0, 130.6, 129.6, 128.9, 117.7, 116.4, 113.3, 55.7, 49.6, 48.1, 46.5 ppm.

MS (EI, 70 eV) *m/z*: 281.1 (M^+), 189.1, 118.1, 93.0.

Elemental analysis calcd. for $C_{18}H_{23}N_3$: C 76.83, H 8.24, N 14.93; found: C 76.53, H 8.11, N 15.01.

9) *N*-(4-(pyridin-2-yl)benzyl)aniline **3i**



Aniline (91 µL, 1 mmol) and (4-(pyridin-2-yl)phenyl)methanol (222 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 95:5). Yield: 234 mg (0.899 mmol, 90 %) as a colourless solid (mp = 122 °C).

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 8.66 (d, *J* = 4.8 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 2H), 7.78 – 7.73 (m, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.27 – 7.20 (m, 1H), 7.16 (t, *J* = 7.9 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 2H), 4.40 (d, *J* = 4.0 Hz, 2H), 4.26 (s_br, 1H).

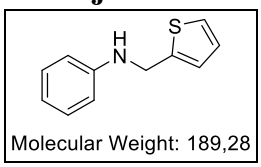
^{13}C NMR (126 MHz, CD_2Cl_2): δ = 157.4, 150.2, 148.8, 141.2, 138.8, 137.2, 129.7, 128.2, 127.5, 122.6, 120.7, 117.9, 113.4, 48.3 ppm.

MS (EI, 70 eV) *m/z*: 260.1 (M^+), 168.1, 77.1.

Elemental analysis calcd. for $C_{18}H_{16}N_2$: C 83.04, H 6.19, N 10.76; found: C 82.23, H 6.27, N 10.80.

(CAS Registry Number: 1532892-14-0, no references, spectroscopic or spectrometric data previously available)

10) *N*-(thiophen-2-ylmethyl)aniline **3j**



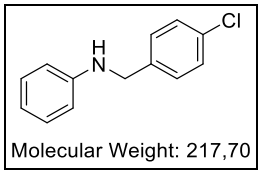
Aniline (91 µL, 1 mmol) and thiophen-2-ylmethanol (114 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 98:2). Yield: 153 mg (0.808 mmol, 81 %) as a yellow solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.24 (d, *J* = 5.1 Hz, 1H), 7.18 (t, *J* = 7.4 Hz, 2H), 7.06 – 7.01 (m, 1H), 6.99 (t, *J* = 4.2 Hz, 1H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 2H), 4.52 (s, 2H), 4.17 (s_br, 1H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 148.3, 144.0, 129.7, 127.4, 125.5, 125.0, 118.4, 113.6, 43.8 ppm.

The spectroscopic data match those reported in literature.[15] (CAS Registry Number: 40625-28-3)

11) *N*-(4-chlorobenzyl)aniline **3k**



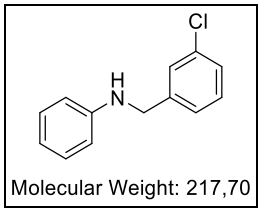
Aniline (91 µL, 1 mmol) and (4-chlorophenyl)methanol (171 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 98:2). Yield: 188 mg (0.864 mmol, 86 %) as a light yellow solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.33 (s, 4H), 7.15 (dd, *J* = 11.6, 4.1 Hz, 2H), 6.69 (td, *J* = 7.3, 0.7 Hz, 1H), 6.61 (d, *J* = 8.2 Hz, 2H), 4.32 (d, *J* = 3.2 Hz, 2H), 4.19 (s_br, 1H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 148.5, 139.0, 133.1, 129.7, 129.3, 129.1, 118.1, 113.3, 47.9 ppm.

The spectroscopic data match those reported in literature.[16] (CAS Registry Number: 4750-61-2)

12) *N*-(3-chlorobenzyl)aniline **3m**



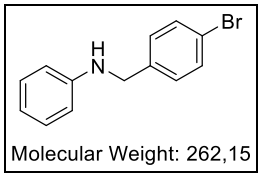
Aniline (91 µL, 1 mmol) and (3-chlorophenyl)methanol (141 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 100:0 → 98:2). Yield: 200 mg (0.922 mmol, 92 %) as a colourless oil.

^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.41 – 7.38 (m, 1H), 7.34 – 7.24 (m, 3H), 7.20 – 7.13 (m, 2H), 6.75 – 6.68 (m, 1H), 6.64 – 6.59 (m, 2H), 4.34 (s, 2H), 4.22 (s_br, 1H) ppm.

^{13}C NMR (101 MHz, CD_2Cl_2): δ = 148.4, 142.7, 134.8, 130.5, 129.7, 127.8, 127.7, 126.0, 118.1, 113.3, 48.1 ppm.

The spectroscopic data match those reported in literature.[17] (CAS Registry Number 10359-19-0)

13) *N*-(4-bromobenzyl)aniline **3n**



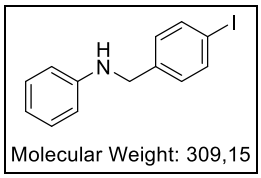
Aniline (456 µL, 5 mmol) and (4-bromophenyl)methanol (1.122 g, 6 mmol) were reacted according to GP3 (5 mmol scale). Purification by column chromatography (silica gel, pentane/ethyl acetate 95:5) gave a yellow oil. The oil was dissolved in pentane (10 mL) and a minimal amount of MTBE was added. The product crystallized over the course of 2 days at -20 °C. Yield: 810 mg (3.09 mmol, 62 %) as colourless crystals.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 8.3 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.09 (t, *J* = 7.6 Hz, 2H), 6.65 (td, *J* = 7.3, 0.8 Hz, 1H), 6.53 (d, *J* = 7.9 Hz, 2H), 4.22 (s, 2H), 3.98 (s_br, 1H) ppm.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 147.9, 138.7, 131.8, 129.4, 129.2, 121.1, 118.0, 113.0, 77.4, 77.2, 76.9, 47.8 ppm.

The spectroscopic data match those reported in literature.[16] (CAS Registry Number 68695-51-2)

14) *N*-(4-iodobenzyl)aniline **3o**



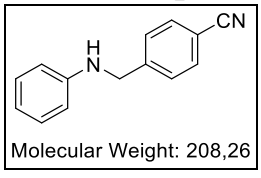
Aniline (91 µL, 1 mmol) and (4-iodophenyl)methanol (281 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 95:5). Yield: 222 mg (0.718 mmol, 72 %) as a colourless solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.68 (d, *J* = 8.2 Hz, 2H), 7.18 – 7.11 (m, 4H), 6.69 (td, *J* = 7.3, 0.8 Hz, 1H), 6.60 (d, *J* = 7.9 Hz, 2H), 4.30 (s, 2H), 4.19 (s_br, 1H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 148.5, 140.2, 138.1, 129.9, 129.7, 118.1, 113.3, 92.6, 48.0 ppm.

The spectroscopic data match those reported in literature.[18] (CAS Registry Number: 349449-94-1)

15) 4-((phenylamino)methyl)benzonitrile **3p**



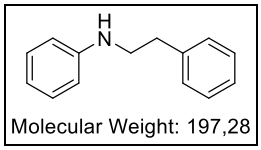
Aniline (91 µL, 1 mmol) and 4-(hydroxymethyl)benzonitrile (160 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 80:20). Yield: 110 mg (0.462 mmol, 46 %) as an off-white solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.63 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.13 (dd, *J* = 8.4, 7.5 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.60 – 6.54 (m, 2H), 4.43 (s, 2H), 4.31 (s_br, 1H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 148.2, 146.2, 132.9, 129.8, 128.2, 119.4, 118.3, 113.3, 111.4, 48.2 ppm.

The spectroscopic data match those reported in literature.[19] (CAS Registry Number: 37812-49-0)

16) *N*-phenethylaniline **3q**



Aniline (91 µL, 1 mmol) and 2-phenylethan-1-ol (144 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 97:3). Yield: 121 mg (0.613 mmol, 61 %) as a colourless oil.

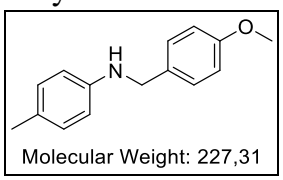
^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.37 – 7.30 (m, 2H), 7.29 – 7.21 (m, 3H), 7.16 (t, *J* = 7.9 Hz, 2H), 6.68 (t, *J* = 7.3 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 2H), 3.75 (s_br, 1H), 3.39 (dd, *J* = 11.2, 6.6 Hz, 2H), 2.92 (t, *J* = 7.1 Hz, 2H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 148.8, 140.1, 129.7, 129.3, 129.0, 126.8, 117.7, 113.3, 45.6, 36.0 ppm.

The spectroscopic data match those reported in literature.[20] (CAS Registry Number: 1739-00-0)

Synthesis of Amines – Variation of Amine

17) *N*-(4-methoxybenzyl)-4-methylaniline **5a**



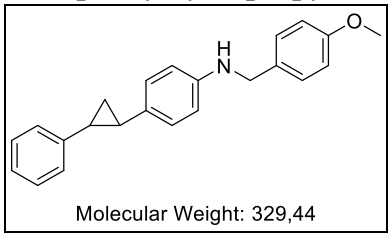
4-Methylaniline (107 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 95:5). Yield: 203 mg (0.893 mmol, 89 %) as a colourless solid.

^{1}H NMR (400 MHz, DMSO-d6): δ = 7.30 – 7.21 (m, 2H), 6.90 – 6.80 (m, 4H), 6.52 – 6.44 (m, 2H), 5.89 (t, *J* = 6.0 Hz, 1H), 4.14 (d, *J* = 6.1 Hz, 2H), 3.71 (s, 3H), 2.12 (s, 3H) ppm.

^{13}C NMR (101 MHz, DMSO-d6): δ = 158.0, 146.4, 132.2, 129.2, 128.4, 124.0, 113.6, 112.5, 55.0, 46.2, 20.1 ppm.

The spectroscopic data match those reported in literature.[21] (CAS Registry Number: 112825-69-1)

18) *N*-(4-methoxybenzyl)-4-(2-phenylcyclopropyl)aniline **5b**



4-(2-phenylcyclopropyl)aniline (209 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, cyclohexane/MTBE 90:10). Yield: 254 mg (0.772 mmol, 77 %) as a colourless solid (mp = 99 °C).

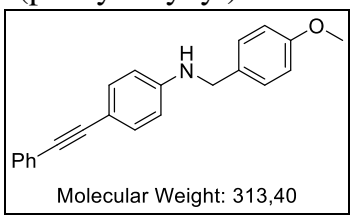
^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.32 – 7.23 (m, 4H), 7.18 – 7.08 (m, 3H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 6.57 (d, *J* = 8.4 Hz, 2H), 4.24 (s, 2H), 4.01 (s, 1H), 3.78 (s, 3H), 2.04 (tdd, *J* = 11.8, 7.2, 4.7 Hz, 2H), 1.33 (t, *J* = 7.3 Hz, 2H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ 159.4, 147.1, 143.7, 132.2, 131.7, 129.2, 128.8, 127.2, 126.0, 126.0, 114.4, 113.5, 55.8, 48.3, 28.1, 27.8, 18.1 ppm.

MS (EI, 70 eV) *m/z*: 329.2 (M^+), 121.1, 91.1.

Elemental analysis calcd. for $C_{23}H_{23}NO$: C 83.85, H 7.04, N 4.25; found: C 83.73, H 6.98, N 4.22.

19) *N*-(4-methoxybenzyl)-4-(phenylethynyl)aniline **5d**



4-(phenylethynyl)aniline (193 mg, 1 mmol)) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/ethyl acetate 90:10). Yield: 288 mg (0.919 mmol, 92 %) as a colourless solid (mp = 139 °C).

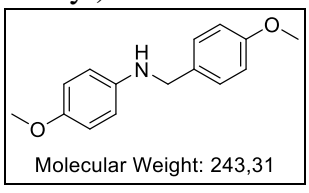
^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.51 – 7.46 (m, 2H), 7.37 – 7.26 (m, 7H), 6.91 – 6.87 (m, 2H), 6.62 – 6.56 (m, 2H), 4.33 (s, 1H), 4.29 (s, 2H), 3.79 (s, 3H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 159.6, 148.9, 133.3, 131.7, 131.5, 129.2, 128.9, 128.1, 124.5, 114.5, 113.0, 111.5, 90.9, 87.6, 55.8, 47.8 ppm.

MS (EI, 70 eV) *m/z*: 313.1 (M^+), 121.1, 77.0.

Elemental analysis calcd. for $C_{22}H_{19}NO$: C 84.31, H 6.11, N 4.47; found: C 84.27, H 5.85, N 4.54.

20)4-methoxy-*N*-(4-methoxybenzyl)aniline **5e**



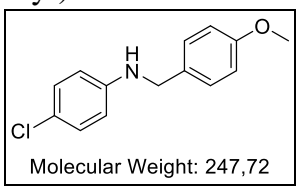
4-Methoxyaniline (123 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 88:12). Yield: 224 mg (0.921 mmol, 92 %) as a colourless solid.

^{1}H NMR (500 MHz, DMSO-d6): δ = 7.27 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 8.9 Hz, 2H), 6.52 (d, *J* = 8.9 Hz, 2H), 5.70 (t, *J* = 6.0 Hz, 1H), 4.12 (d, *J* = 6.0 Hz, 2H), 3.71 (s, 3H), 3.61 (s, 3H) ppm.

^{13}C NMR (126 MHz, DMSO-d6): δ = 158.0, 150.7, 143.0, 132.3, 128.5, 114.5, 113.6, 113.4, 55.3, 55.0, 46.7 ppm.

The spectroscopic data match those reported in literature.[22] (CAS Registry Number 14429-14-2)

21)4-chloro-*N*-(4-methoxybenzyl)aniline **5f**



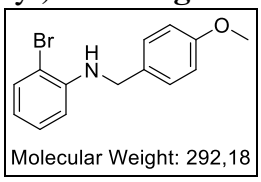
4-Chloroaniline (128 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 90:10). Yield: 218 mg (0.880 mmol, 88 %) as a colourless solid.

^{1}H NMR (500 MHz, DMSO-d6): δ = 7.26 (d, *J* = 8.6 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.56 (d, *J* = 8.9 Hz, 2H), 6.36 (t, *J* = 5.9 Hz, 1H), 4.16 (d, *J* = 5.9 Hz, 2H), 3.72 (s, 3H) ppm.

^{13}C NMR (126 MHz, DMSO-d6): δ = 158.2, 147.6, 131.5, 128.5, 128.4, 118.9, 113.7, 113.6, 55.0, 45.9 ppm.

The spectroscopic data match those reported in literature.[23] (CAS Registry Number: 104329-18-2)

22)2-bromo-*N*-(4-methoxybenzyl)aniline **5g**



2-Bromoaniline (172 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 98:2). Yield: 244 mg (0.835 mmol, 84 %) as a colourless solid.

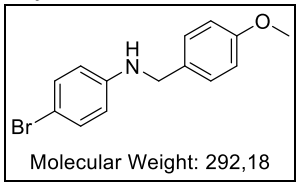
Upscaling (10 mmol scale): 2-Bromoaniline (0.93 mL, 10 mmol) and (4-methoxyphenyl)methanol (1.49 mL, 12 mmol), KO*t*Bu (561 mg, 5 mmol), **Cr-Id** (215 mg, 0.3 mmol) and 1,4-dioxane (500 µL) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 98:2). Yield: 2.20 g (7.53 mmol, 75 %) as a colourless solid.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.43 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.16 – 7.11 (m, 1H), 6.91 – 6.87 (m, 2H), 6.63 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.57 (td, *J* = 7.8, 1.4 Hz, 1H), 4.73 (s, 1H), 4.33 (d, *J* = 5.5 Hz, 2H), 3.79 (s, 3H).

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 159.5, 145.4, 132.8, 131.3, 129.0, 129.0, 118.3, 114.5, 112.2, 110.0, 55.8, 47.8 ppm.

The spectroscopic data match those reported in literature.[24] (CAS Registry Number: 156643-23-1)

23)4-bromo-*N*-(4-methoxybenzyl)aniline **5h**



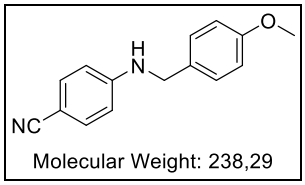
4-Bromoaniline (172 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 90:10). Yield: 264 mg (0.904 mmol, 90 %) as a colourless solid.

^{1}H NMR (500 MHz, DMSO-d6): δ = 7.25 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.52 (d, *J* = 8.8 Hz, 2H), 6.39 (t, *J* = 5.9 Hz, 1H), 4.16 (d, *J* = 5.9 Hz, 2H), 3.72 (s, 3H) ppm.

^{13}C NMR (126 MHz, DMSO-d6): δ = 158.2, 147.9, 131.5, 131.3, 128.4, 114.2, 113.7, 106.2, 55.0, 45.8 ppm.

The spectroscopic data match those reported in literature.[25] (CAS Registry Number: 175357-73-0)

24)4-((4-methoxybenzyl)amino)benzonitrile **5i**



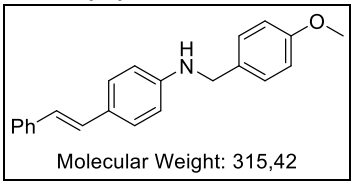
4-Aminobenzonitrile (118 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 80:20). Yield: 110 mg (0.462 mmol, 46 %) as a colourless solid.

^{1}H NMR (500 MHz, DMSO-d6): δ = 7.42 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.6 Hz, 2H), 7.21 (t, *J* = 5.8 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.64 (d, *J* = 8.7 Hz, 2H), 4.25 (d, *J* = 5.9 Hz, 2H), 3.72 (s, 3H) ppm.

^{13}C NMR (126 MHz, DMSO-d6): δ = 158.3, 152.1, 133.3, 130.7, 128.5, 120.6, 113.9, 112.1, 95.8, 55.1, 45.2 ppm.

The spectroscopic data match those reported in literature.[26] (CAS Registry Number: 271242-72-9)

25)(*E*)-*N*-(4-methoxybenzyl)-4-styrylaniline **5c**



4-Aminostilbene (195 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 88:12). Yield: 294 mg (0.932 mmol, 93 %) as an off-white solid (mp = 155 °C).

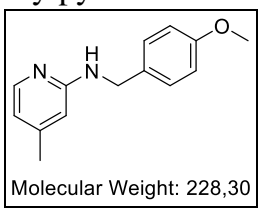
^{1}H NMR (400 MHz, DMSO-d6): δ = 7.54 – 7.43 (m, 2H), 7.35 – 7.24 (m, 6H), 7.20 – 7.14 (m, 1H), 7.10 – 7.02 (m, 1H), 6.89 (dt, *J* = 5.2, 3.7 Hz, 3H), 6.61 – 6.55 (m, 2H), 6.42 (t, *J* = 6.0 Hz, 1H), 4.22 (d, *J* = 6.0 Hz, 2H), 3.72 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d6): δ = 158.1, 148.6, 137.9, 131.8, 129.0, 128.6, 128.4, 127.6, 126.5, 125.7, 124.7, 122.9, 113.7, 112.4, 55.0, 45.8 ppm.

MS (EI, 70 eV) *m/z*: 315.2 (M^+), 194.1, 121.1, 77.0.

Elemental analysis calcd. for $C_{21}H_{22}NO$: C 83.78, H 6.71, N 4.44; found: C 83.88, H 6.63, N 4.44.

26)*N*-(4-methoxybenzyl)-4-methylpyridin-2-amine **5j**



4-methylpyridin-2-amine (108 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, methylene chloride/methanol 100:0 → 90:10). Yield: 200 mg (0.876 mmol, 88 %) as a colourless solid after recrystallisation from methylene chloride/pentane (mp = 121 °C).

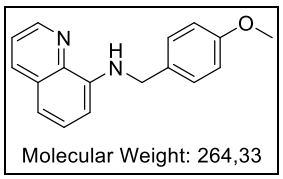
^{1}H NMR (500 MHz, DMSO-d6): δ = 7.81 (d, *J* = 5.1 Hz, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.81 (t, *J* = 5.9 Hz, 1H), 6.35 – 6.26 (m, 2H), 4.37 (d, *J* = 6.0 Hz, 2H), 3.71 (s, 3H), 2.12 (s, 3H) ppm.

^{13}C NMR (126 MHz, DMSO-d6): δ = 159.0, 158.0, 147.3, 146.8, 132.7, 128.4, 113.6, 113.3, 108.0, 55.0, 43.6, 20.6 ppm.

MS (EI, 70 eV) *m/z*: 228.1 (M^+), 213.1, 136.1, 121.1.

Elemental analysis calcd. for $C_{14}H_{16}N_2O$: C 73.66, H 7.06, N 12.27; found: C 73.08, H 6.76, N 12.10.

27)*N*-(4-methoxybenzyl)quinolin-8-amine **5k**



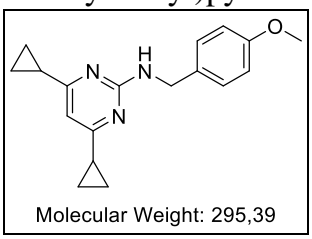
Quinolin-8-amine (144 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 83:7). Yield: 205 mg (0.776 mmol, 78 %) as a light-yellow solid.

^{1}**H NMR** (500 MHz, CD_2Cl_2): δ = 8.70 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.08 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.41 – 7.30 (m, 1H), 7.05 (dd, *J* = 8.1, 0.6 Hz, 1H), 6.91 – 6.86 (m, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 6.61 – 6.51 (m, 1H), 4.48 (d, *J* = 5.8 Hz, 1H), 3.79 (s, 1H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 159.4, 147.5, 145.1, 138.7, 136.4, 131.9, 129.2, 129.1, 128.2, 122.0, 114.43, 114.41, 105.4, 55.8, 47.5 ppm.

The spectroscopic data match those reported in literature.[27] (CAS Registry Number: 1019549-51-9)

28)4,6-dicyclopropyl-*N*-(4-methoxybenzyl)pyrimidin-2-amine **5n**



4,6-Dicyclopropylpyrimidin-2-amine (175 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, methylene chloride/methanol 99:1). Yield: 250 mg (0.846 mmol, 85 %) as a colourless solid (mp = 57 °C).

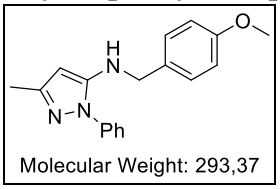
^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.34 – 7.29 (m, 2H), 6.95 – 6.89 (m, 2H), 6.44 (s, 1H), 4.53 (d, *J* = 6.1 Hz, 2H), 3.86 (s, 3H), 1.90 – 1.80 (m, 2H), 1.12 – 1.05 (m, 4H), 1.00 – 0.94 (m, 4H) ppm.

^{13}C NMR (101 MHz, CD_2Cl_2): δ = 171.75, 162.92, 159.22, 133.04, 129.36, 114.17, 106.86, 55.72, 45.19, 16.91, 9.91 ppm.

MS (EI, 70 eV) *m/z*: 295.1 (M^+), 280.1, 136.1, 121.1.

Elemental analysis calcd. for $C_{18}H_{21}N_3O$: C 73.19, H 7.17, N 14.23; found: C 72.96, H 7.21, N 14.14.

29)*N*-(4-methoxybenzyl)-3-methyl-1-phenyl-1H-pyrazol-5-amine **5m**



3-Methyl-1-phenyl-1*H*-pyrazol-5-amine (173 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 70:30). Yield: 231 mg (0.787 mmol, 79 %) as a yellow oil.

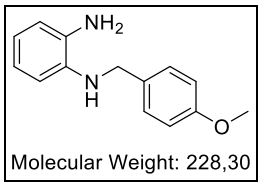
^{1}H NMR (500 MHz, DMSO-d6): δ = 7.60 – 7.53 (m, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.33 – 7.26 (m, 3H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.01 (t, *J* = 5.5 Hz, 1H), 5.25 (s, 1H), 4.10 (d, *J* = 5.6 Hz, 2H), 3.72 (s, 3H), 2.03 (s, 3H) ppm.

^{13}C NMR (126 MHz, DMSO-d6): δ = 158.2, 148.8, 147.9, 139.4, 131.6, 129.1, 128.5, 125.9, 122.9, 113.6, 88.4, 55.0, 48.1, 13.9 ppm.

MS (EI, 70 eV) *m/z*: 293.1 (M^+), 121.1, 77.0.

Elemental analysis calcd. for $C_{18}H_{19}N_3O$: C 73.69, H 6.53, N 14.32; found: C 73.58, H 6.46, N 14.25.

30)*N*-(4-methoxybenzyl)benzene-1,2-diamine **5o**



Benzene-1,2-diamine (108 mg, 1 mmol) and (4-methoxyphenyl)methanol (149 µL, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 40:60). Yield: 110 mg (0.482 mmol, 48 %) as an off-white solid.

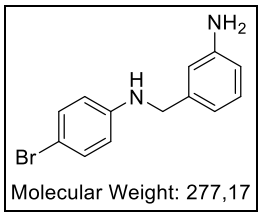
^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.33 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.78 – 6.68 (m, 2H), 6.68 – 6.61 (m, 2H), 4.25 (s, 2H), 3.79 (s, 3H), 3.68 (s, 1H), 3.37 (s, 2H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 159.4, 138.2, 135.0, 132.2, 129.4, 120.8, 119.1, 116.7, 114.4, 112.3, 55.8, 48.4 ppm.

The spectroscopic data match those reported in literature.[28] (CAS Registry Number: 5729-16-8)

Synthesis of Amines – 3-Aminobenzyl Alcohols

31)*N*-(3-aminobenzyl)-4-bromoaniline **8a**



4-Bromoaniline (172 mg, 1 mmol) and (3-aminophenyl)methanol (148 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, methylene chloride/triethylamine 99.9:0.1). Yield: 209 mg (0.754 mmol, 75 %) as a yellow oil.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.22 (d, *J* = 8.7 Hz, 2H), 7.10 (t, *J* = 7.7 Hz, 1H), 6.70 (d, *J* = 7.6 Hz, 1H), 6.65 (s, 1H), 6.57 (dd, *J* = 7.9, 2.2 Hz, 1H), 6.51 (d, *J* = 8.7 Hz, 2H), 4.27 – 4.14 (m, 3H), 3.72 (s, 2H) ppm.

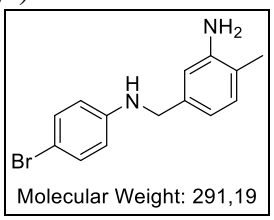
^{13}C NMR (126 MHz, CD_2Cl_2): δ = 147.9, 147.7, 140.9, 132.3, 130.0, 117.6, 114.9, 114.2, 114.1, 109.0, 48.5 ppm.

MS (EI, 70 eV) *m/z*: 276.0/278.0 (M^+), 106.1, 77.0.

Elemental analysis calcd. for $C_{13}H_{13}BrN_2$: C 56.34, H 4.73, N 10.11; found: C 56.42, H 4.75, N 10.18.

(CAS Registry Number: 1557842-58-6, no references, spectroscopic or spectrometric data previously available)

32)*N*-(3-amino-4-methylbenzyl)-4-bromoaniline **8b**



4-Bromoaniline (172 mg, 1 mmol) and (3-amino-4-methylphenyl)methanol (165 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, methylene chloride/triethylamine/methanol 99.83 : 0.10 : 0.07). Yield: 214 mg (0.734 mmol, 73 %) as a colourless solid (mp = 119 °C).

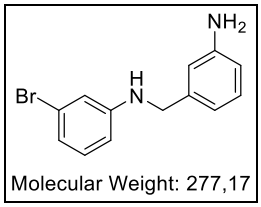
^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.24 – 7.18 (m, 2H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.64 (d, *J* = 6.4 Hz, 2H), 6.53 – 6.46 (m, 2H), 4.17 (s, 3H), 3.65 (s, 2H), 2.12 (s, 3H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 148.0, 145.7, 138.4, 132.3, 131.1, 121.7, 117.7, 114.9, 114.0, 109.0, 48.4, 17.3 ppm.

MS (EI, 70 eV) *m/z*: 290.0/292.0 (M^+), 120.1, 91.1.

Elemental analysis calcd. for $C_{14}H_{15}BrN_2$: C 57.75, H 5.19, N 9.62; found: C 58.09, H 5.15, N 9.77.

33)*N*-(3-aminobenzyl)-3-bromoaniline **8c**



3-Bromoaniline (172 mg, 1 mmol) and (3-aminophenyl)methanol (148 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, methylene chloride/triethylamine 99.9:0.1). Yield: 95 mg (0.343 mmol, 34 %) as a yellow oil.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.10 (t, *J* = 7.7 Hz, 1H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 0.8 Hz, 1H), 6.77 – 6.74 (m, 1H), 6.70 (d, *J* = 7.5 Hz, 1H), 6.66 (s, 1H), 6.58 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.54 (dd, *J* = 8.2, 1.6 Hz, 1H), 4.29 – 4.18 (m, 3H), 3.73 (s, 2H) ppm.

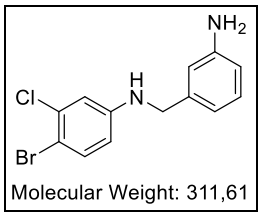
^{13}C NMR (126 MHz, CD_2Cl_2): δ = 150.2, 147.7, 140.7, 131.0, 130.1, 123.6, 120.4, 117.6, 115.6, 114.3, 114.1, 112.1, 48.4 ppm.

MS (EI, 70 eV) *m/z*: 276.0/278.0 (M^+), 106.0, 77.0.

Elemental analysis calcd. for $C_{13}H_{13}BrN_2$: C 56.34, H 4.73, N 10.11; found: C 56.47, H 4.85, N 10.02.

(CAS Registry Number: 1553325-26-0, no references, spectroscopic or spectrometric data previously available)

34)*N*-(3-aminobenzyl)-4-bromo-3-chloroaniline **8d**



4-Bromo-3-chloroaniline (206 mg, 1 mmol) and (3-aminophenyl)methanol (148 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, pentane/MTBE 67:33). Yield: 193 mg (0.619 mmol, 62 %) as a slightly yellow oil.

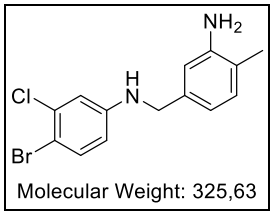
^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.31 (d, *J* = 8.7 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.70 (dd, *J* = 12.7, 5.1 Hz, 2H), 6.64 (s, 1H), 6.58 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.41 (dd, *J* = 8.7, 2.8 Hz, 1H), 4.30 (s, 1H), 4.24 – 4.14 (m, 2H), 3.73 (s, 2H) ppm.

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 149.1, 147.8, 140.3, 135.0, 134.2, 130.1, 117.6, 114.4, 114.2, 114.0, 113.5, 108.4, 48.3 ppm.

MS (EI, 70 eV) *m/z*: 312.0/314.0 (M^+), 231.0, 217.9, 106.0.

Elemental analysis calcd. for $C_{13}H_{12}BrClN_2$: C 50.11, H 3.88, N 8.99; found: C 50.19, H 3.97, N 9.11.

35)*N*-(3-amino-4-methylbenzyl)-4-bromo-3-chloroaniline **8e**



4-Bromo-3-chloroaniline (206 mg, 1 mmol) and (3-amino-4-methylphenyl)methanol (165 mg, 1.2 mmol) were reacted according to GP3. Purification by column chromatography (silica gel, methylene chloride/triethylamine/methanol 99.85 : 0.10 : 0.05). Yield: 185 mg (0.568 mmol, 57 %) as an off-white solid (mp = 109 °C).

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.31 (d, *J* = 8.7 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.71 (d, *J* = 2.7 Hz, 1H), 6.63 (d, *J* = 7.0 Hz, 2H), 6.41 (dd, *J* = 8.7, 2.7 Hz, 1H), 4.32 – 4.22 (m, 1H), 4.16 (d, *J* = 5.5 Hz, 2H), 3.66 (s, 2H), 2.13 (s, 3H) ppm.

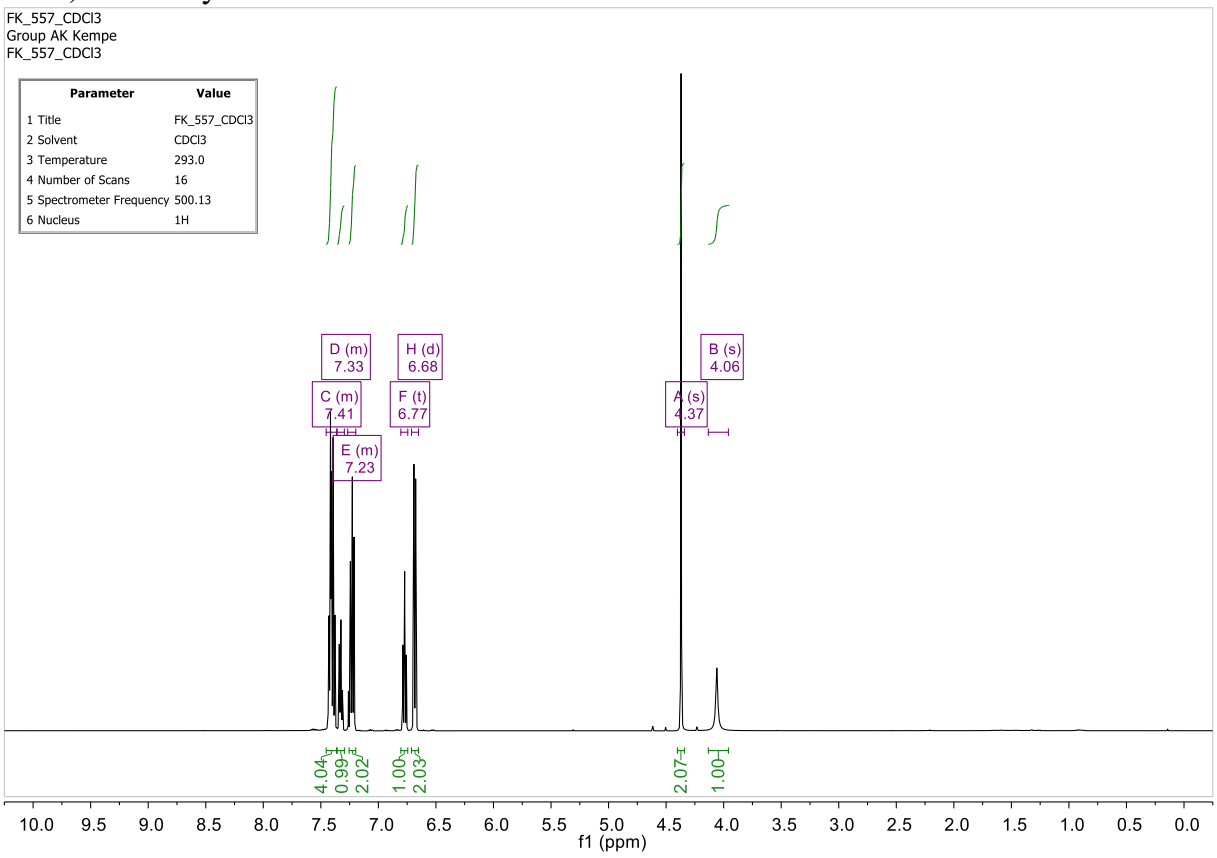
^{13}C NMR (126 MHz, CD_2Cl_2): δ = 148.6, 145.2, 137.3, 134.4, 133.6, 130.6, 121.4, 117.1, 113.7, 113.4, 113.0, 107.8, 47.7, 16.8 ppm.

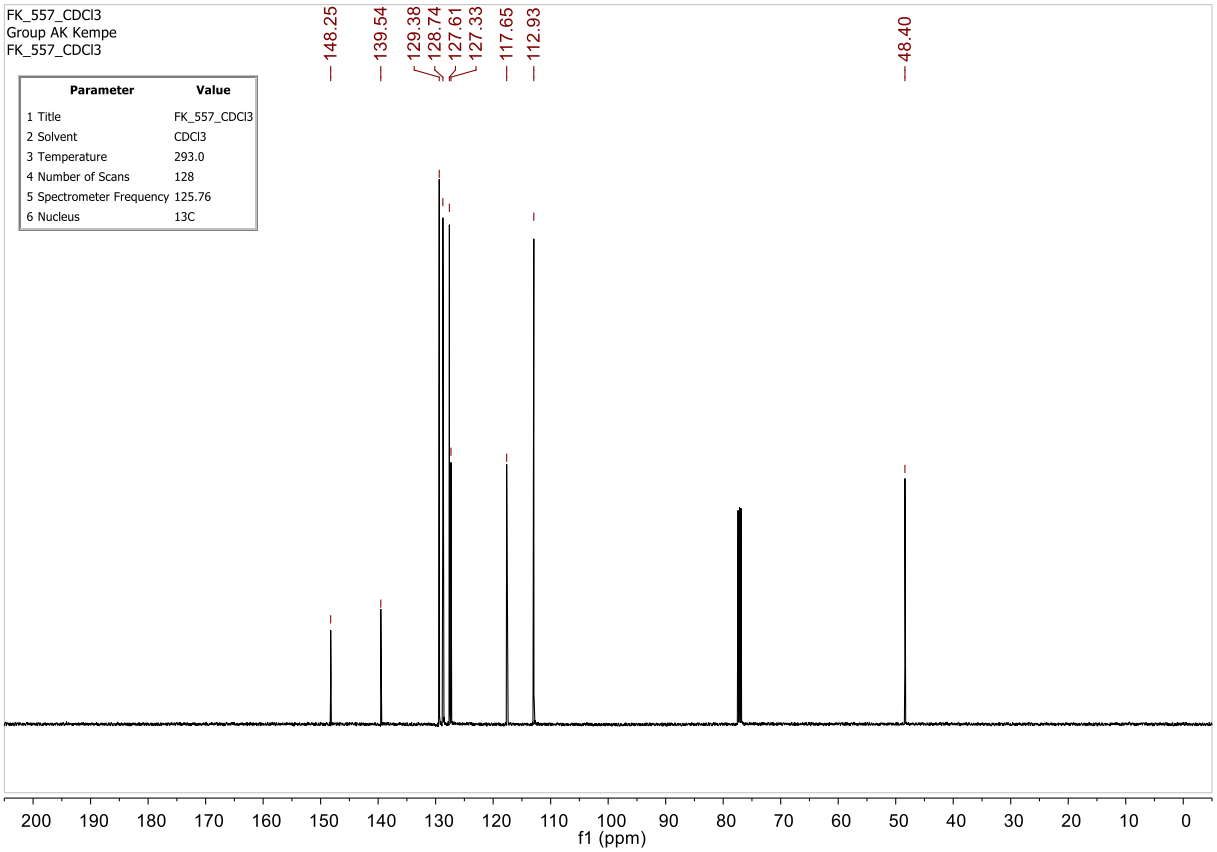
MS (EI, 70 eV) *m/z*: 324.0/326.0 (M^+), 120.1, 77.0.

Elemental analysis calcd. for $C_{14}H_{14}BrClN_2$: C 51.64, H 4.33, N 8.60; found: C 51.87, H 4.29, N 8.54.

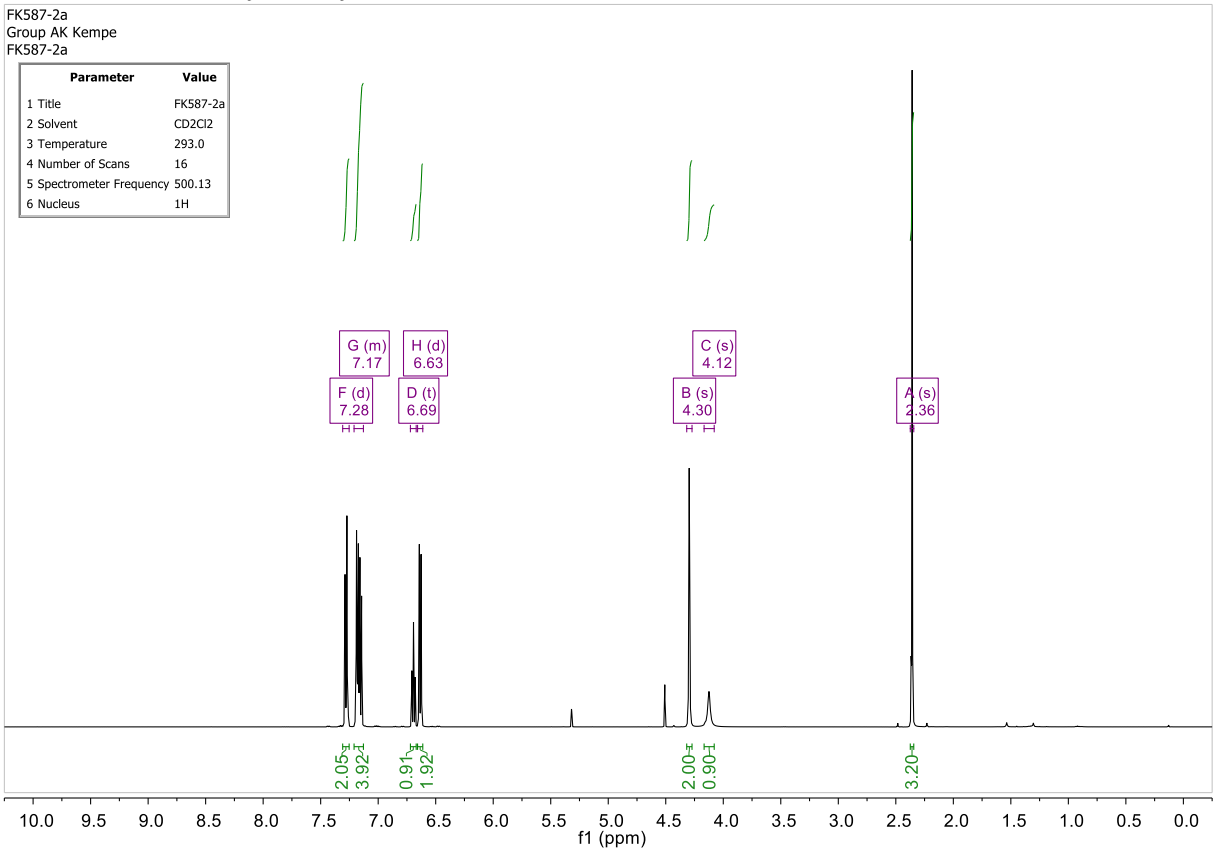
NMR Spectra of Isolated Products

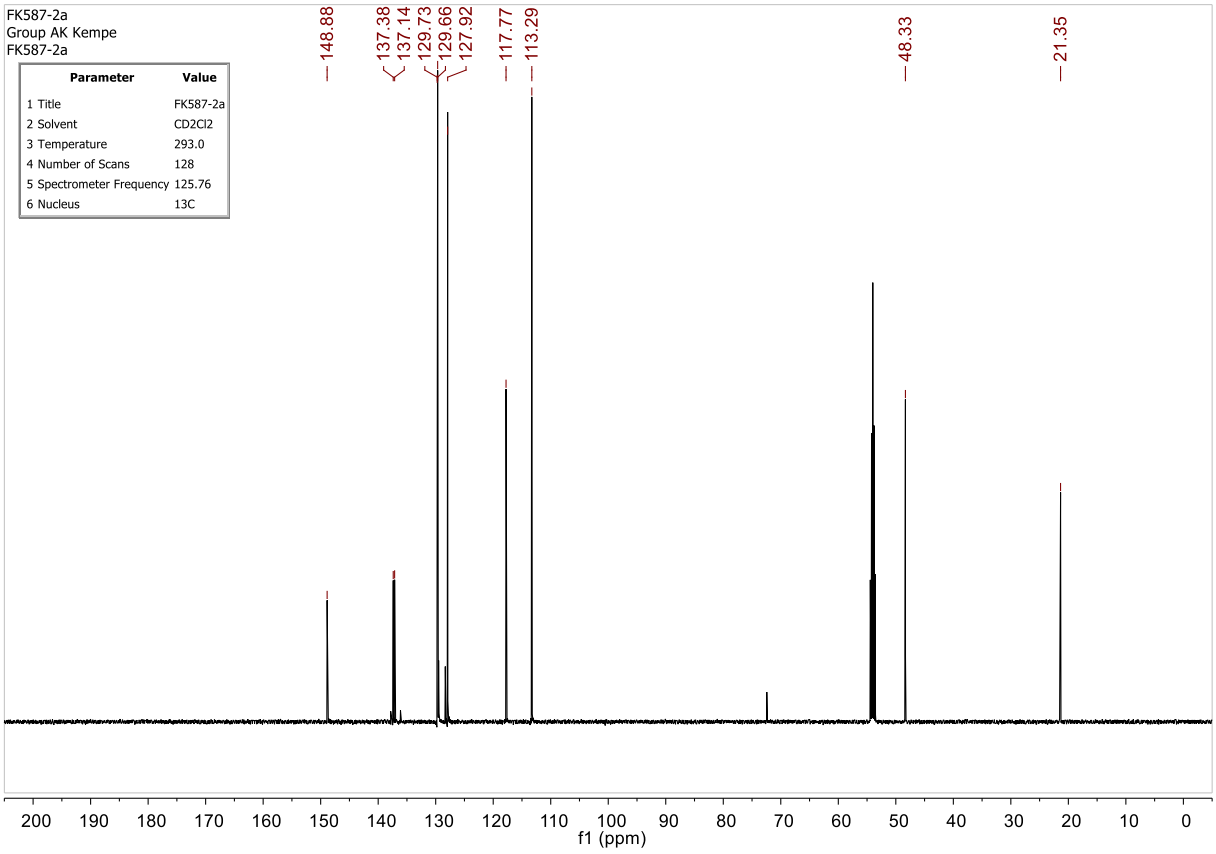
1) N-benzylaniline



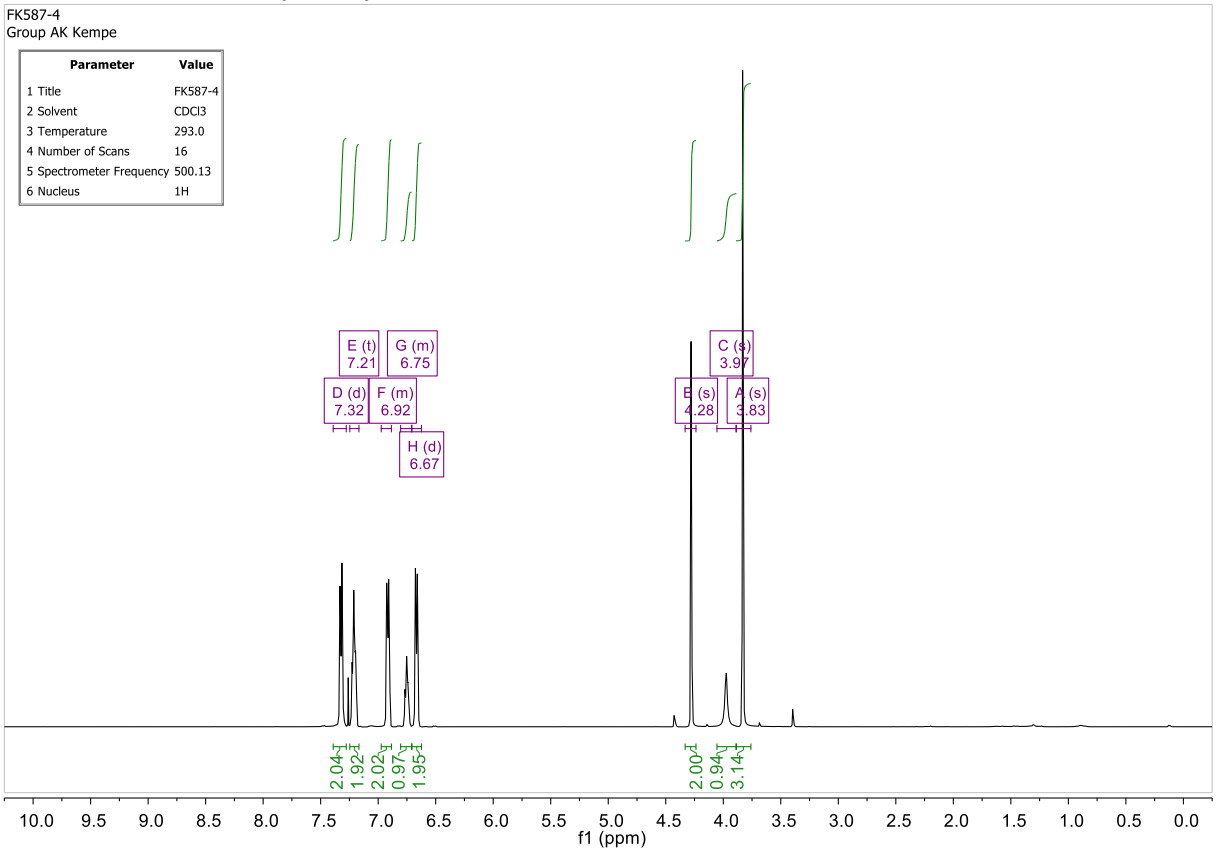


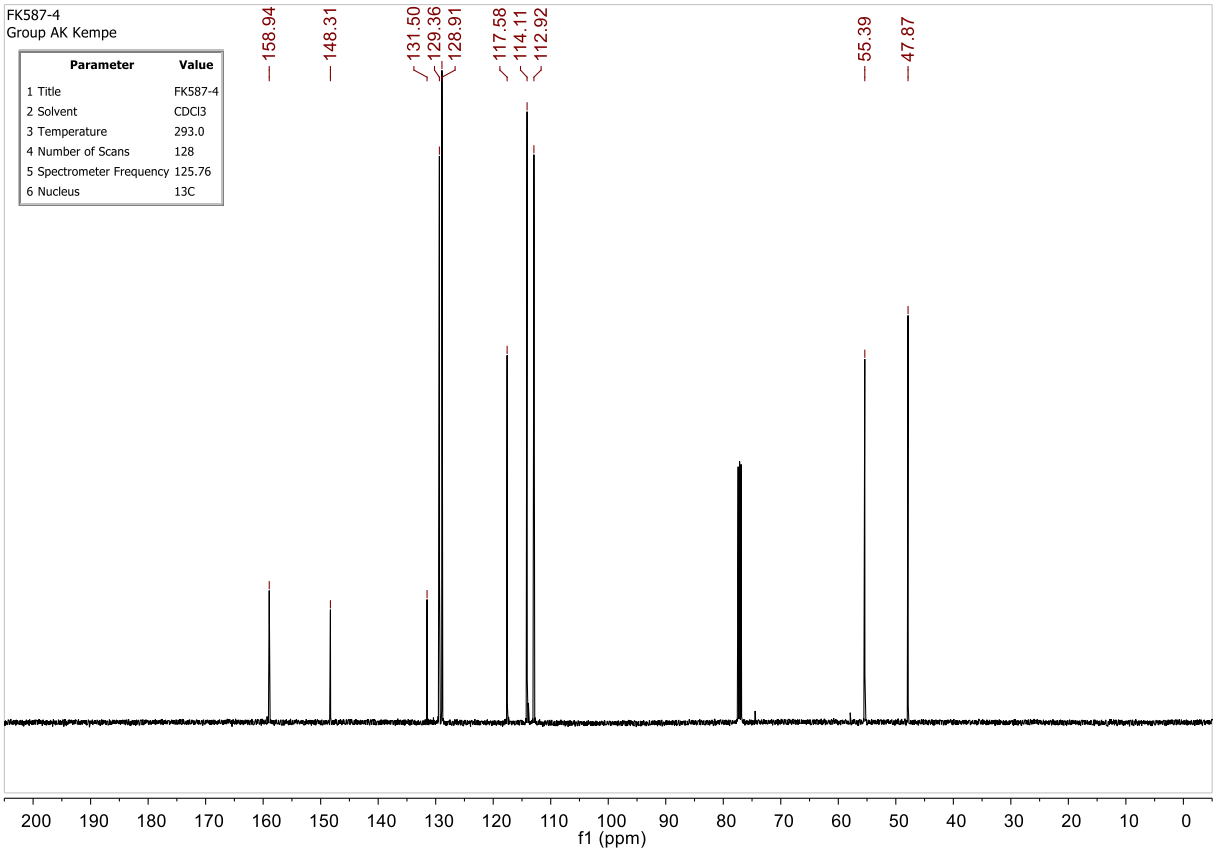
2) N-(4-methylbenzyl)aniline



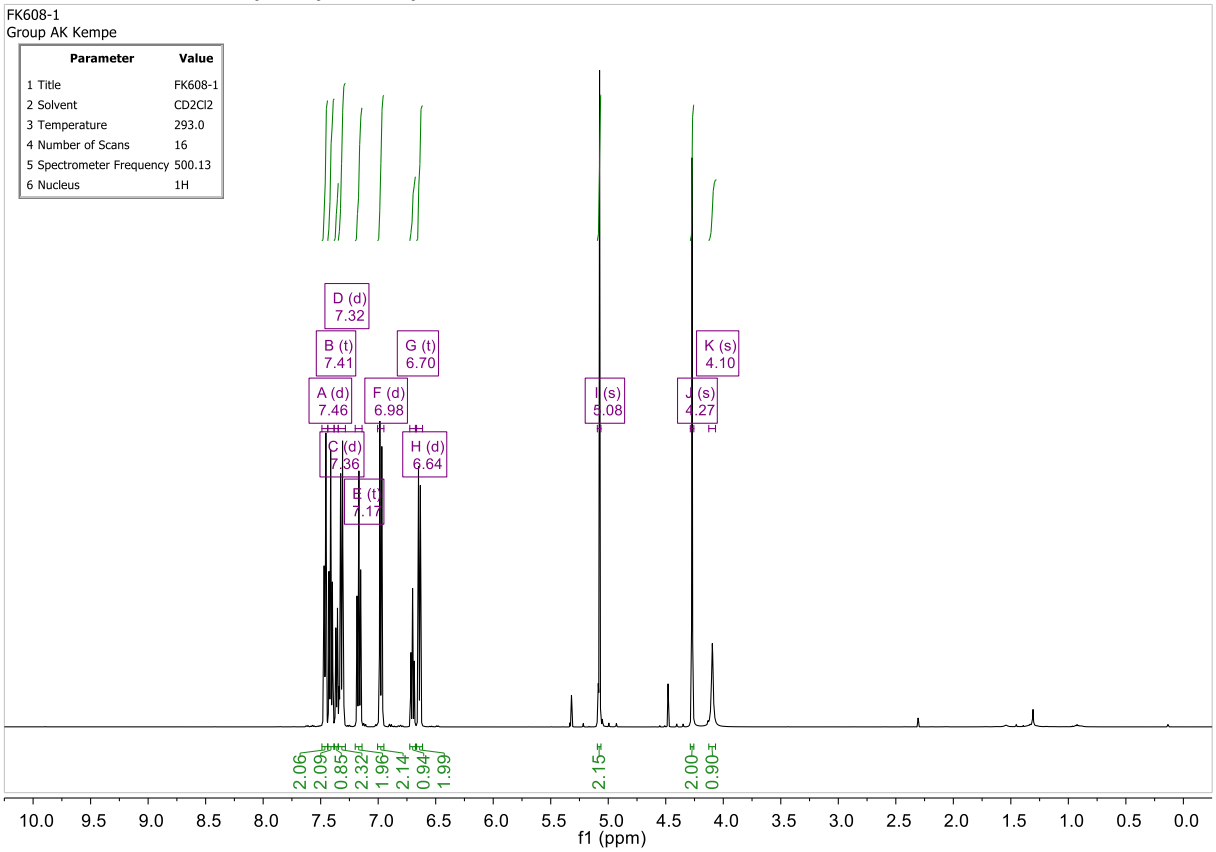


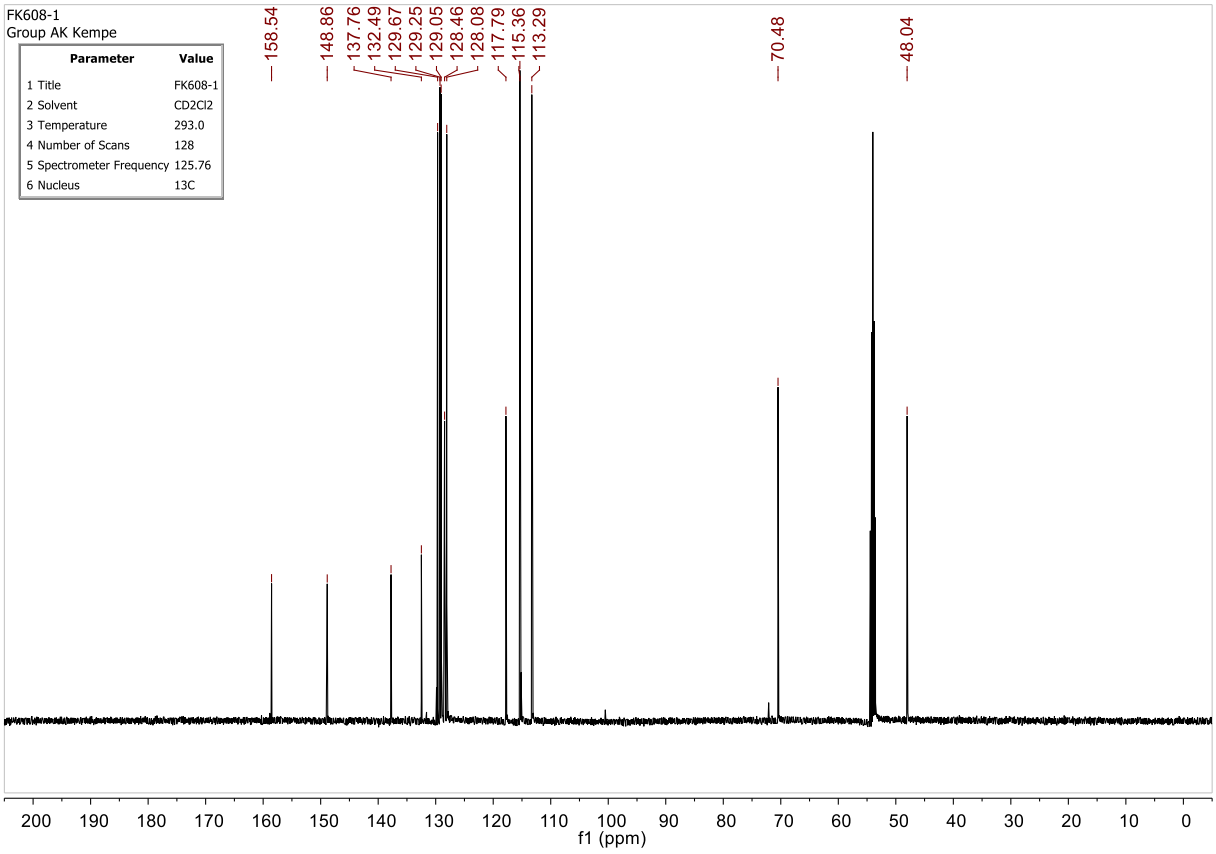
3) N-(4-methoxybenzyl)aniline



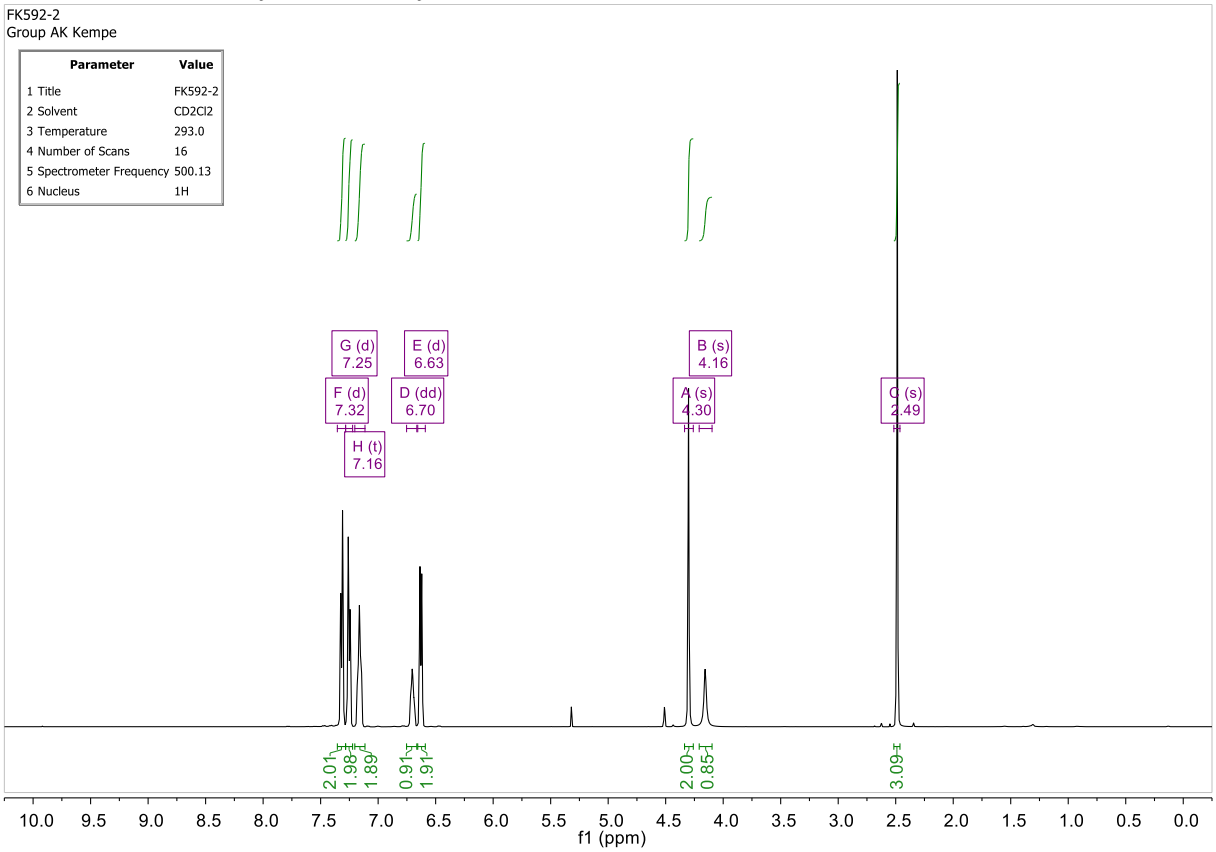


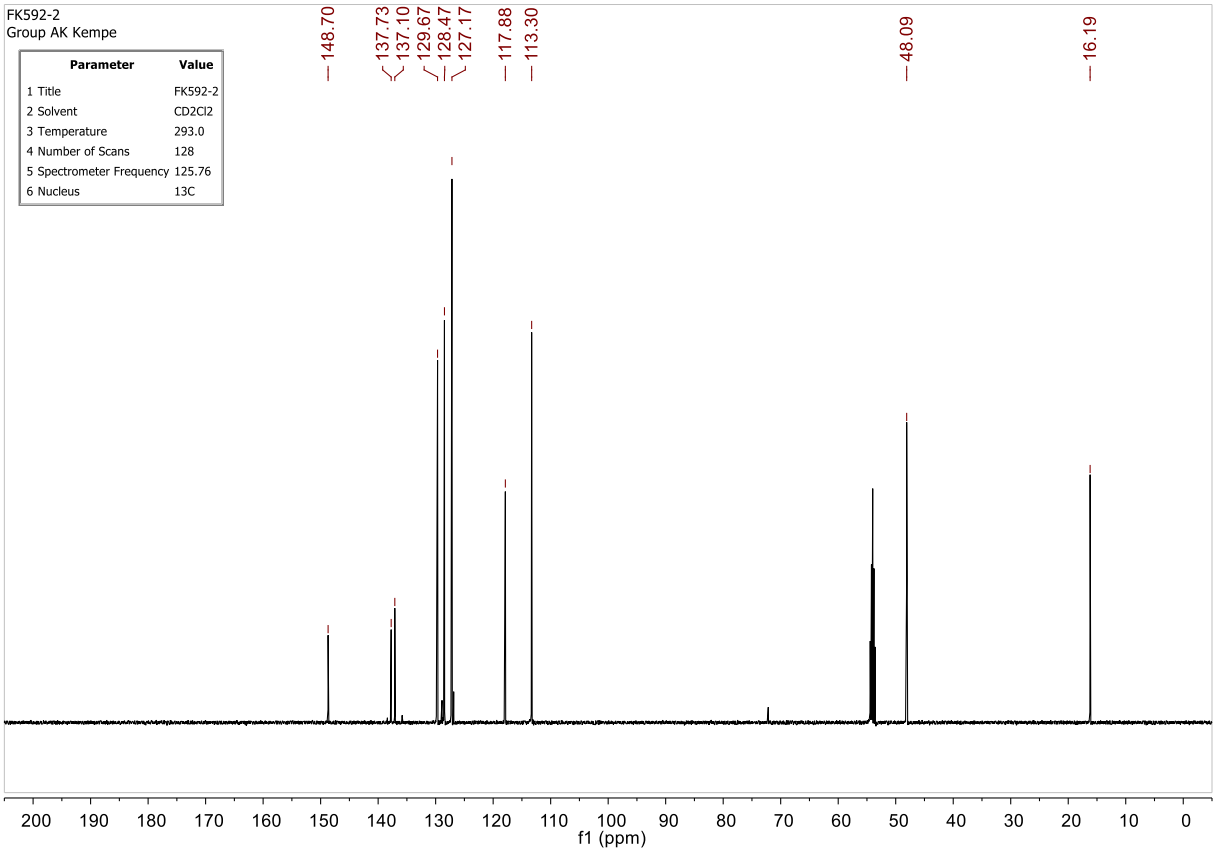
4) N-(4-(benzyloxy)benzyl)aniline



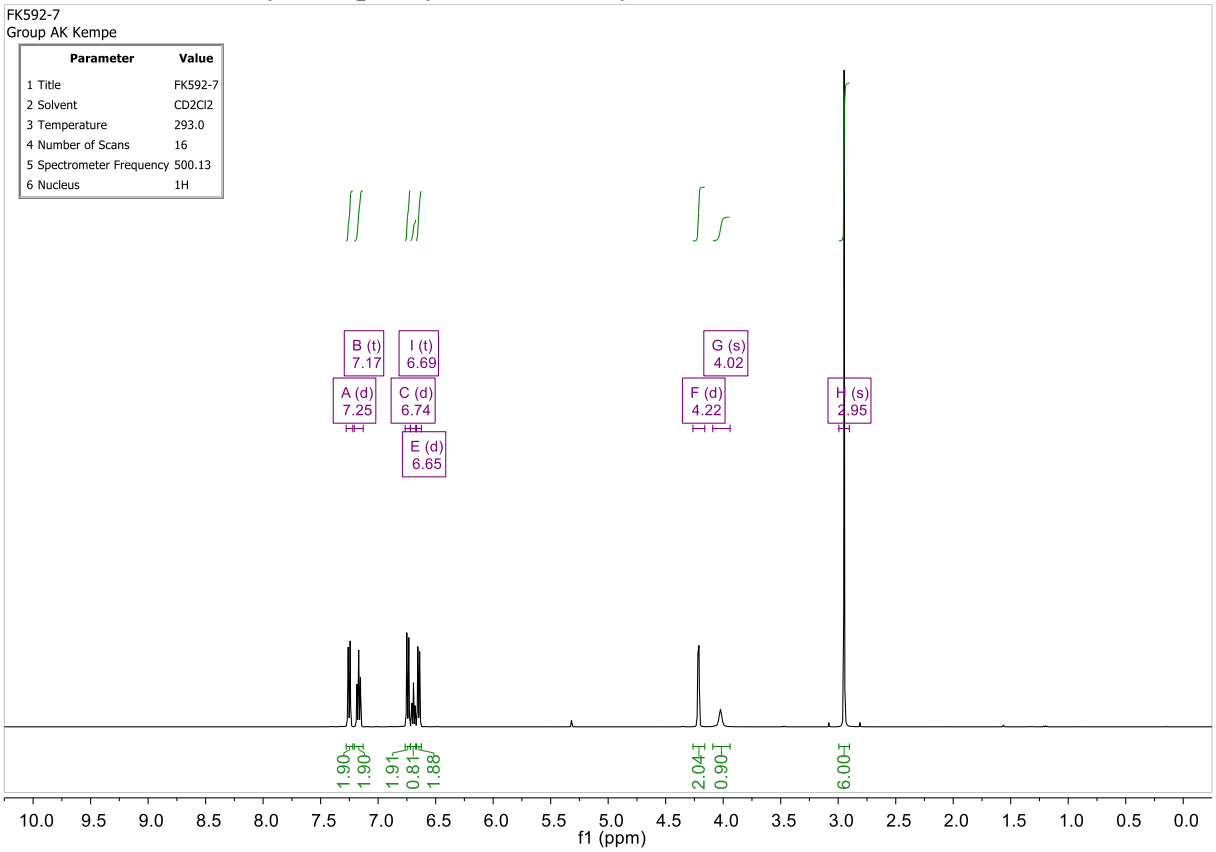


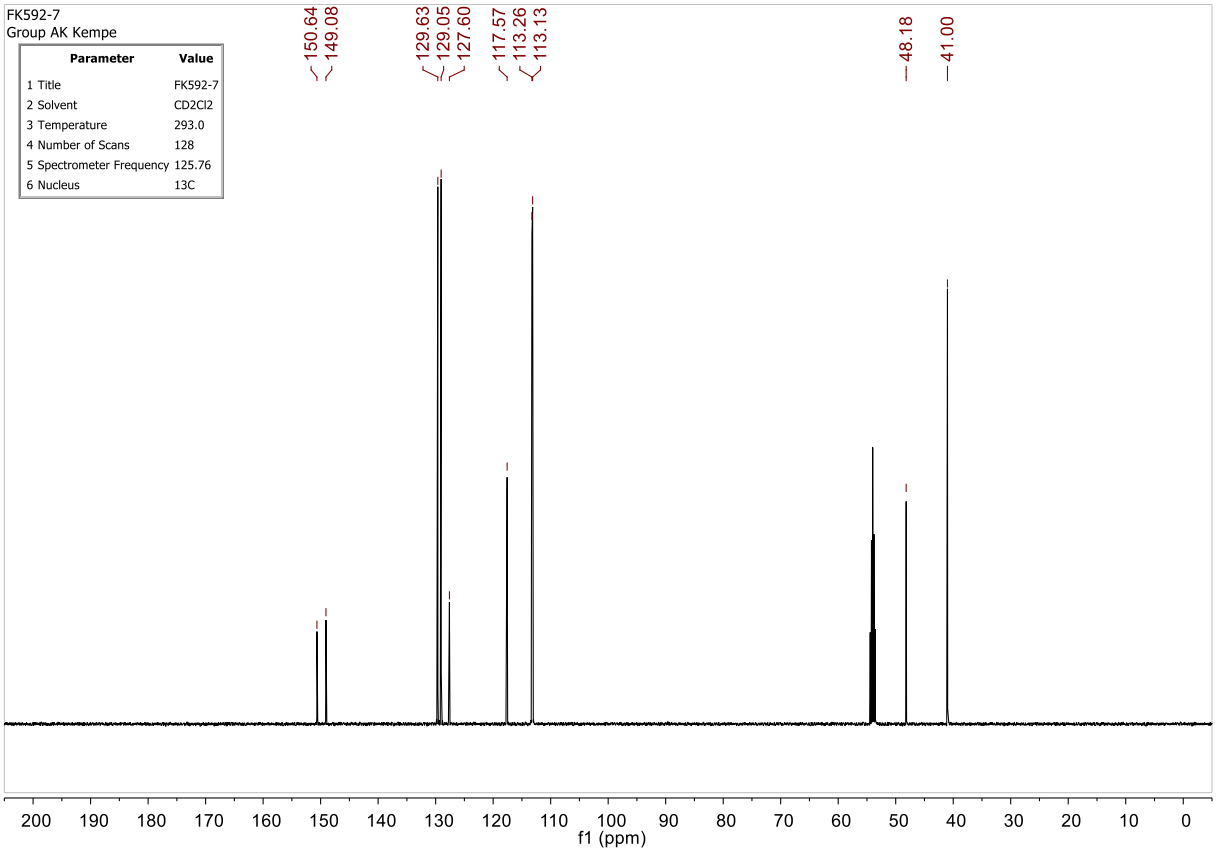
5) N-(4-(methylthio)benzyl)aniline



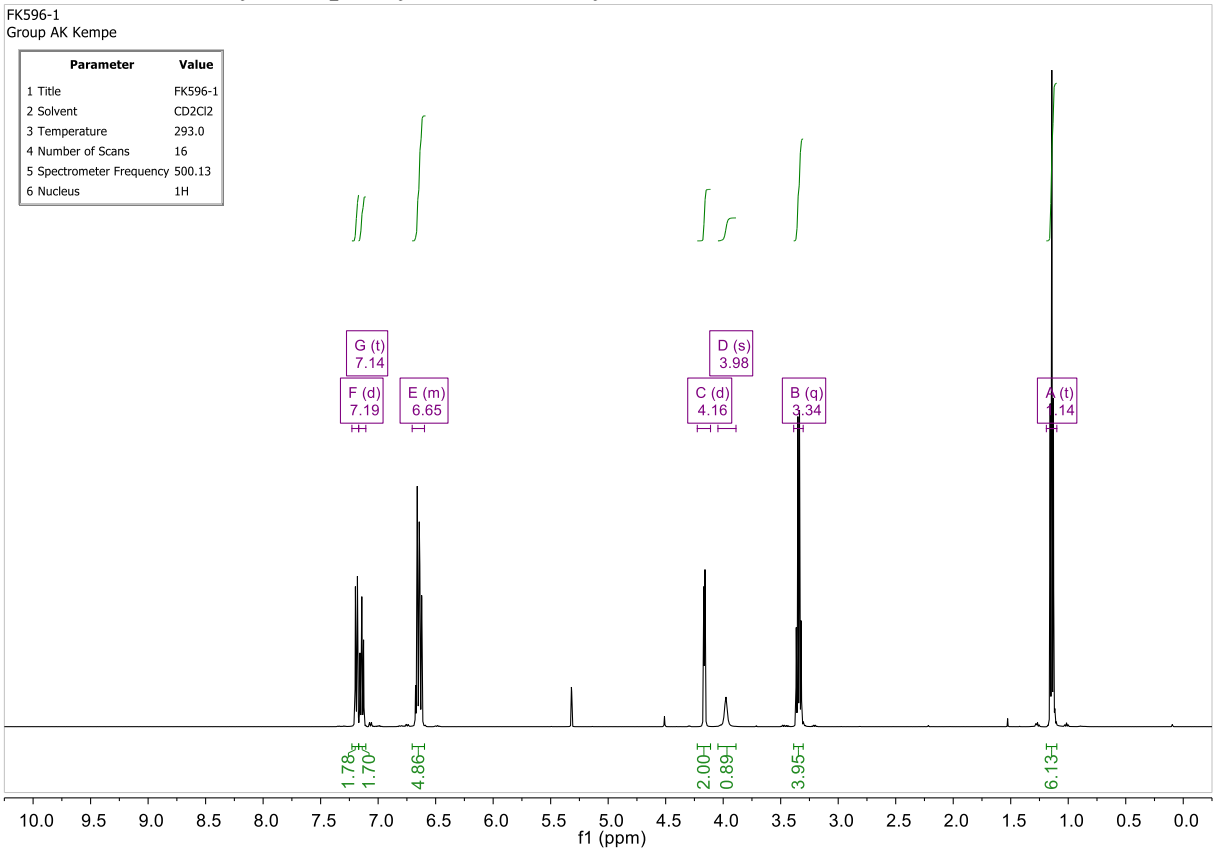


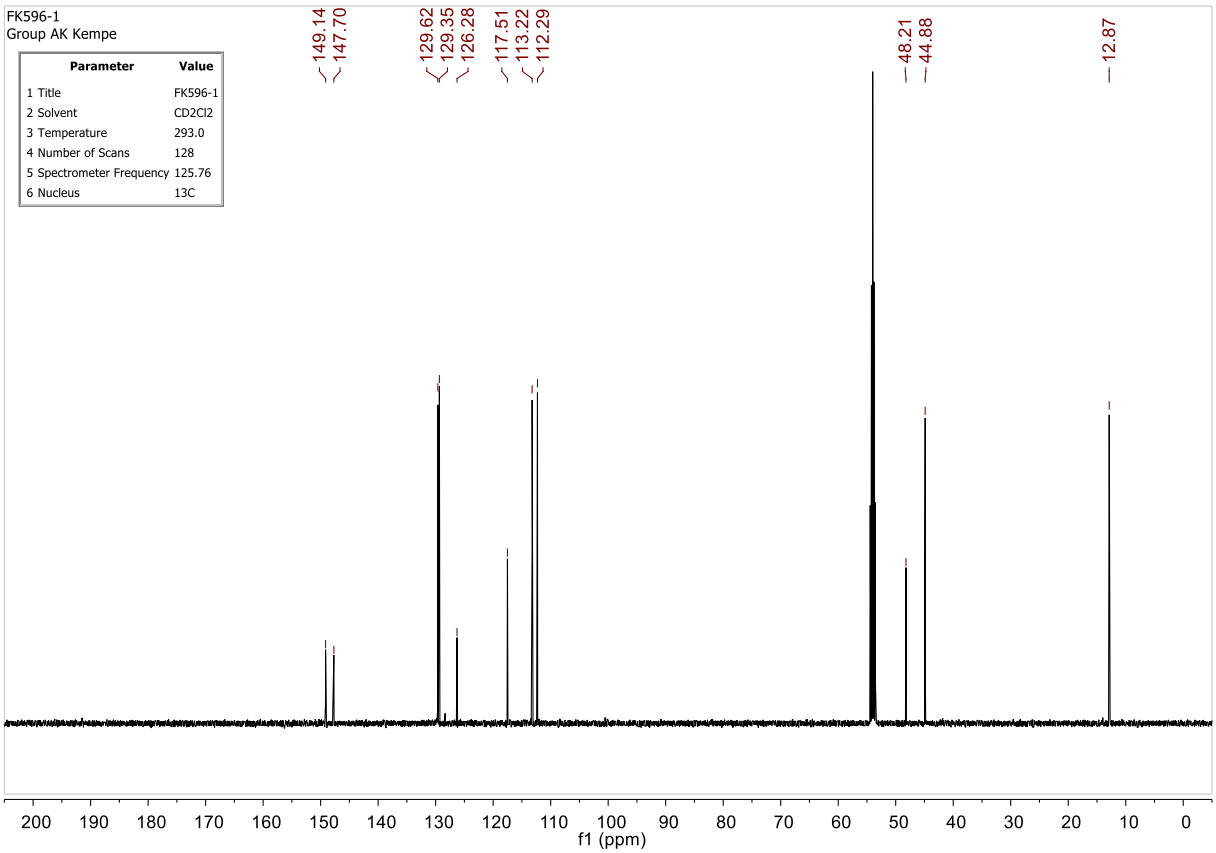
6) N,N-dimethyl-4-((phenylamino)methyl)aniline



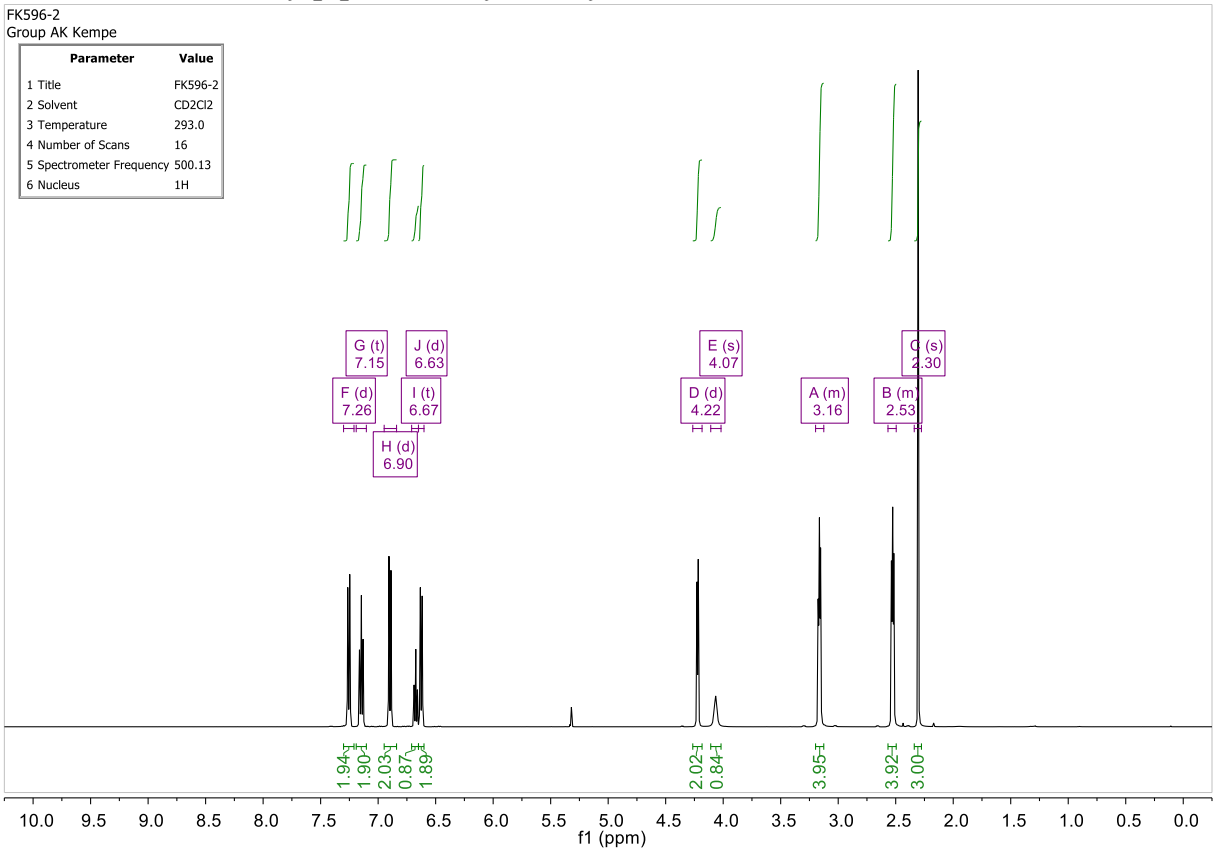


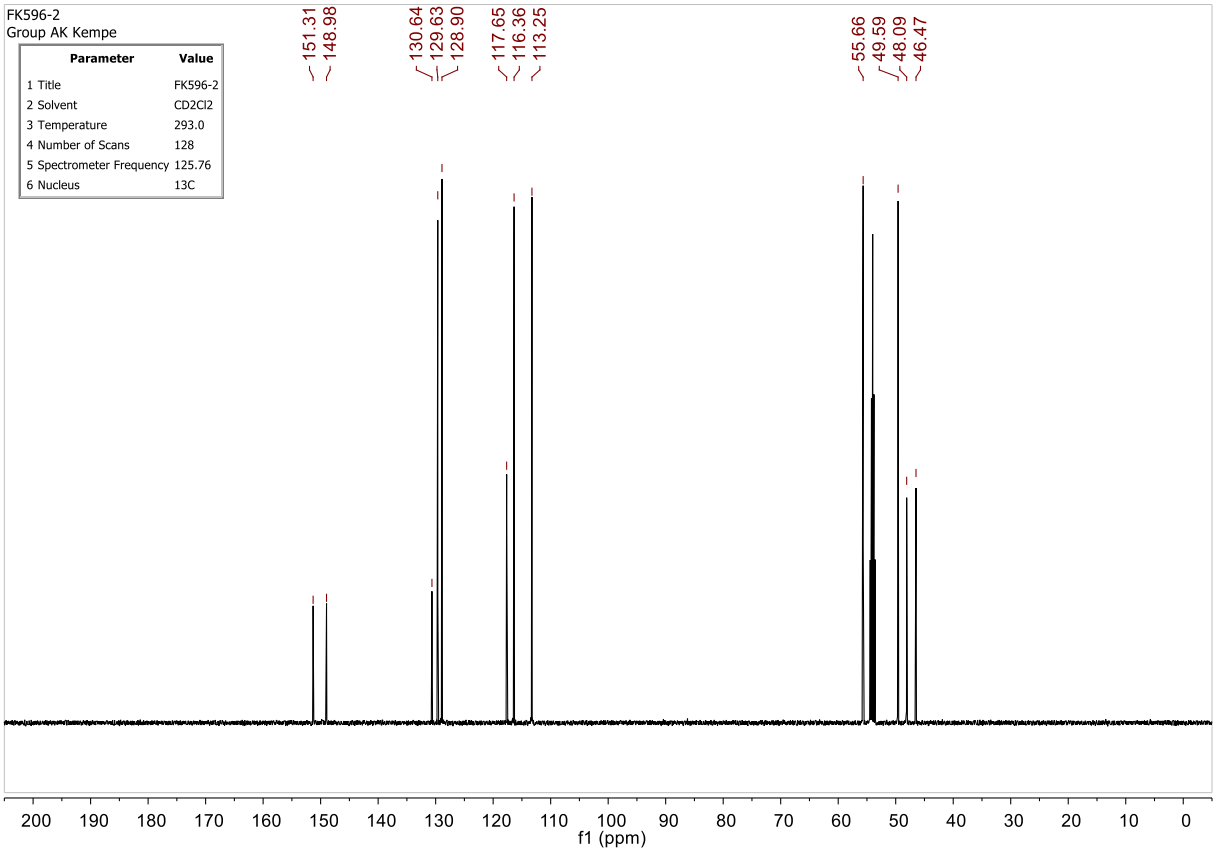
7) N,N-diethyl-4-((phenylamino)methyl)aniline



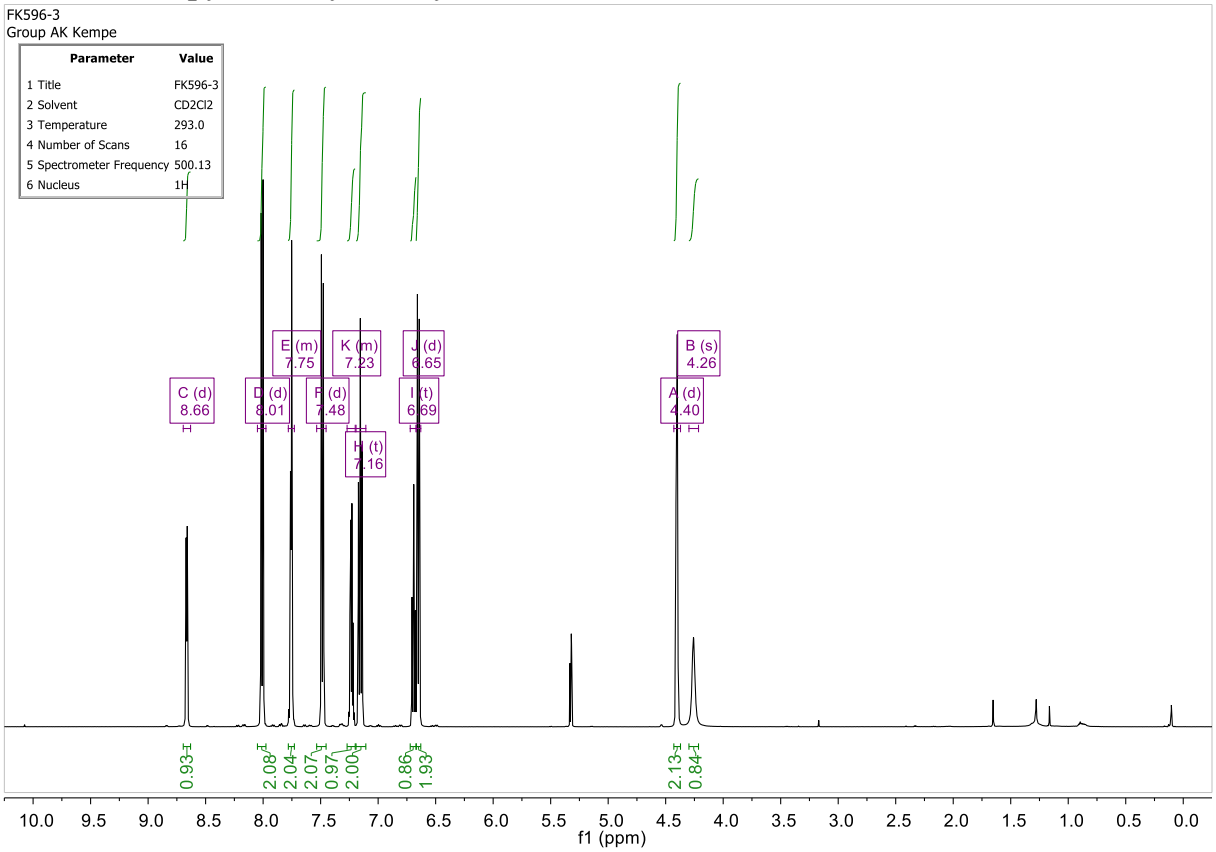


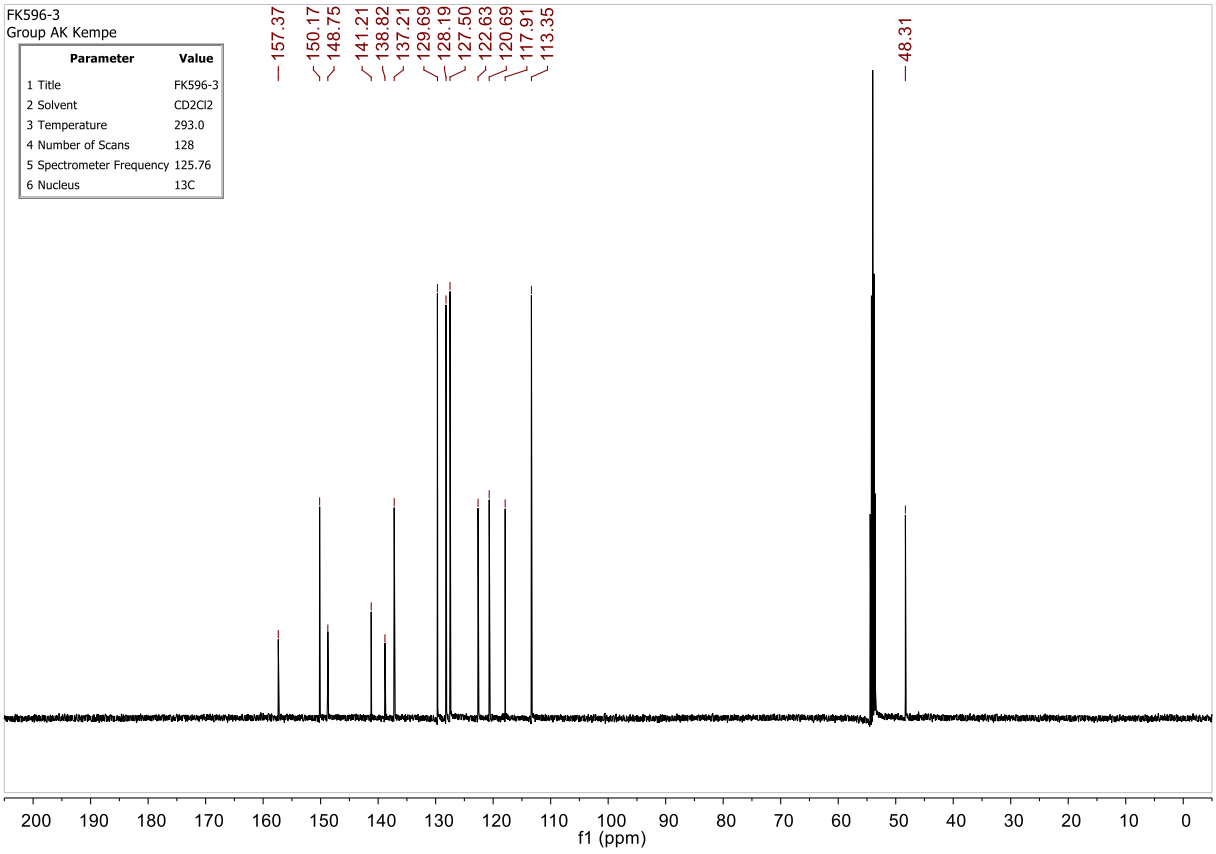
8) N-(4-(4-methylpiperazin-1-yl)benzyl)aniline



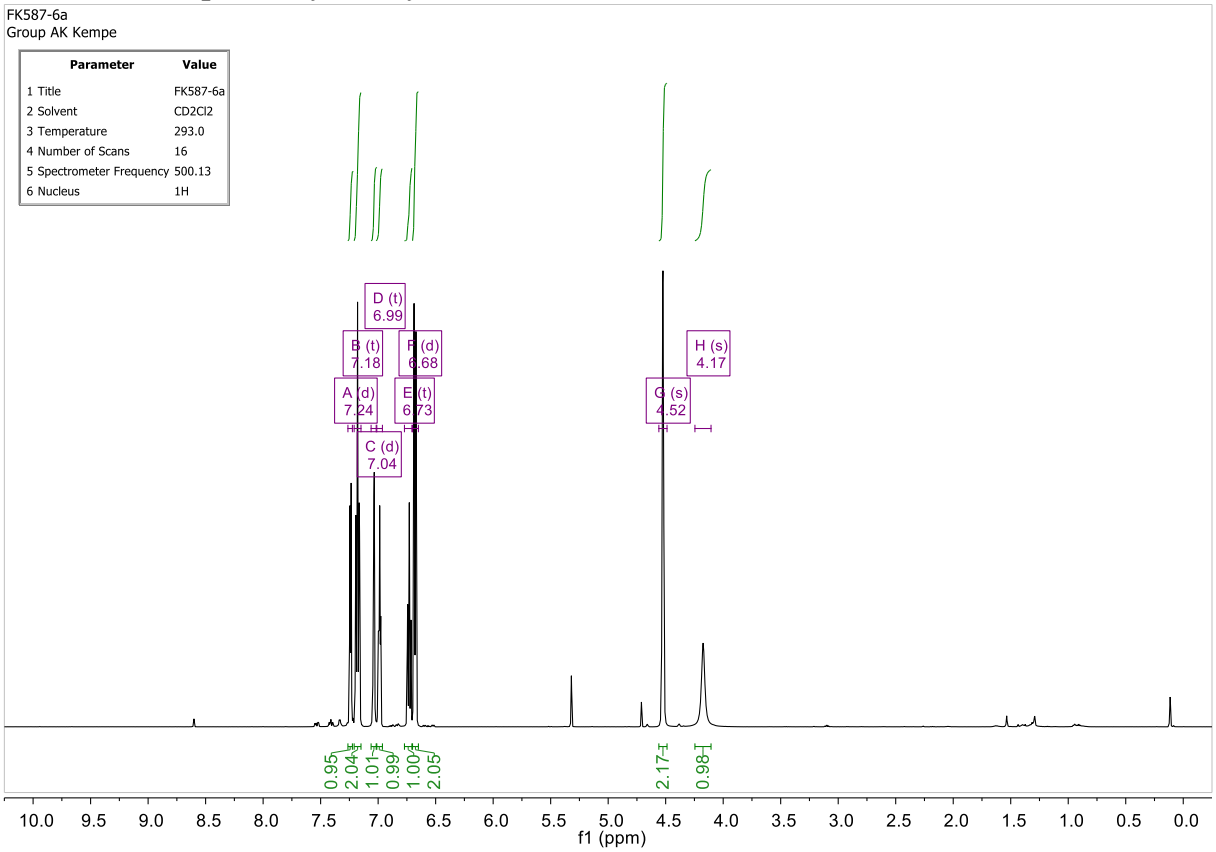


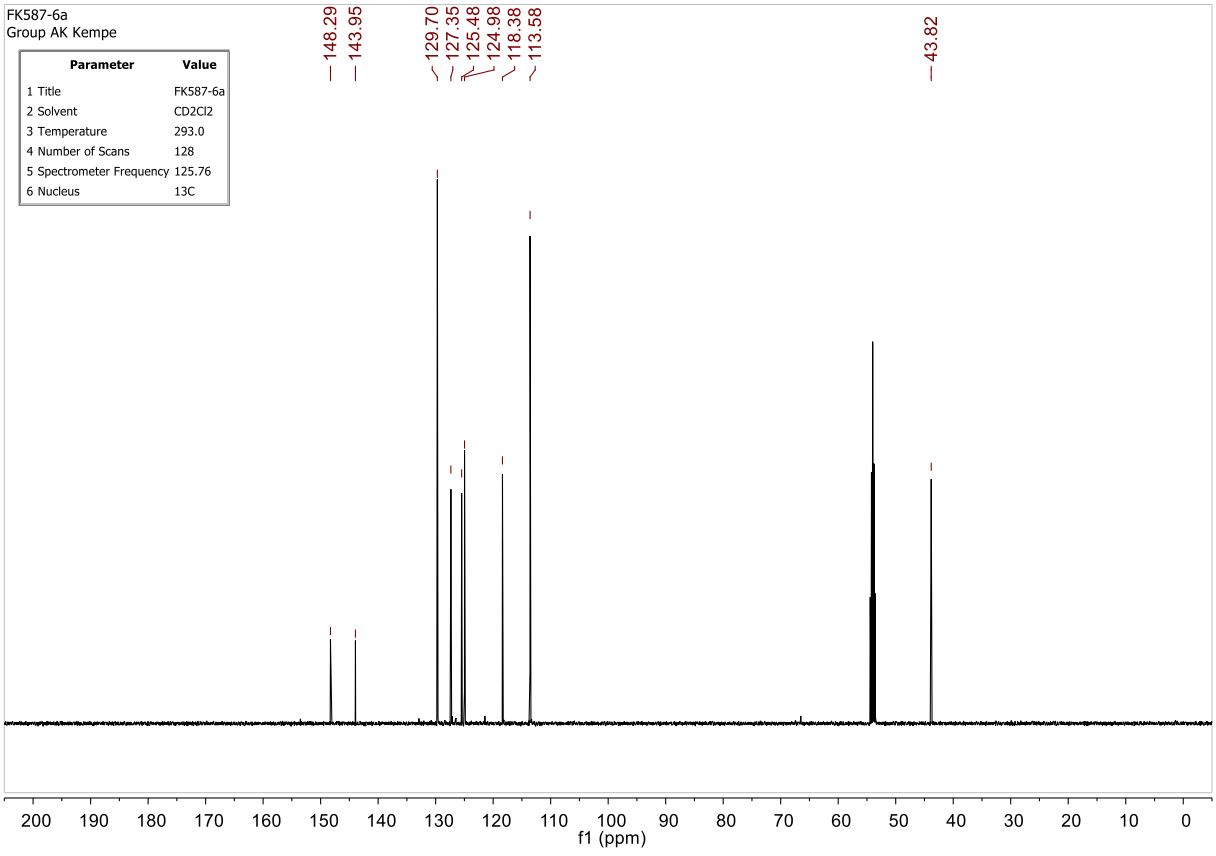
9) N-(4-(pyridin-2-yl)benzyl)aniline



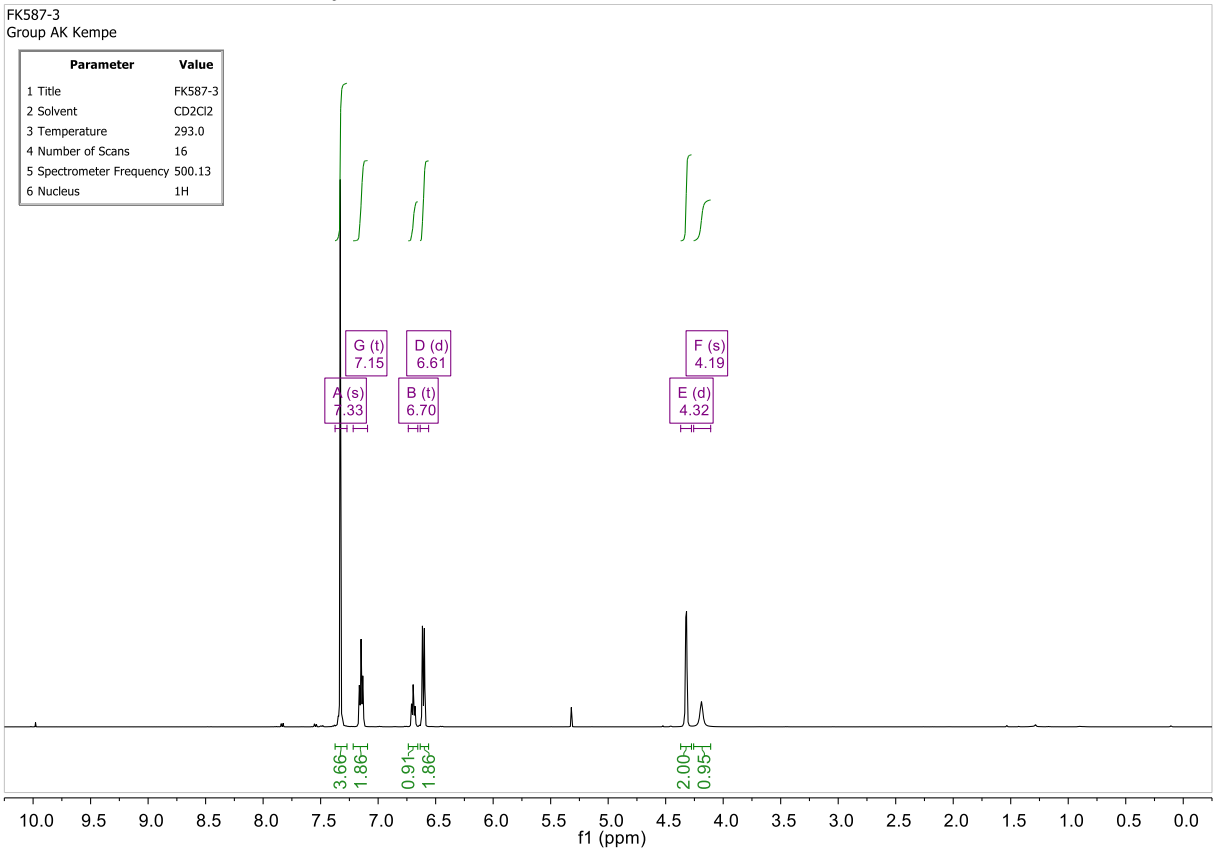


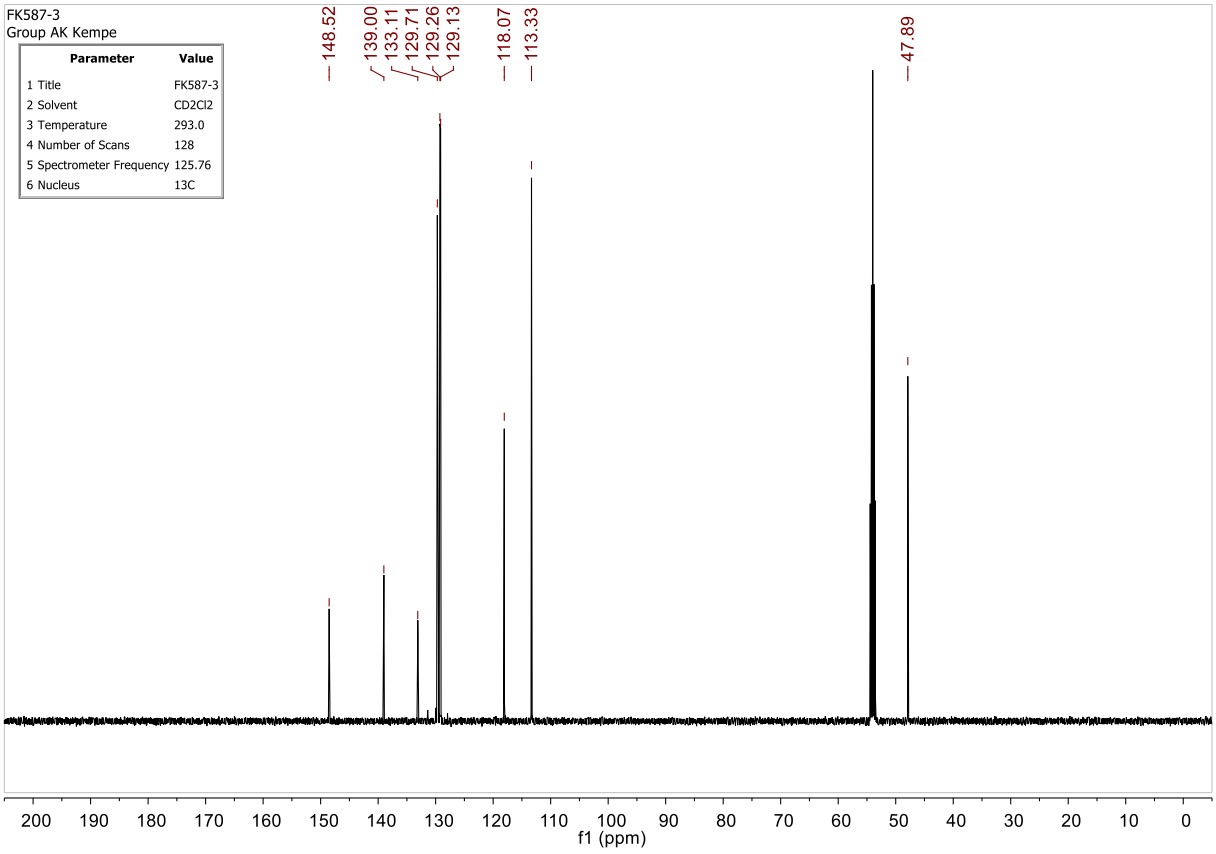
10)N-(thiophen-2-ylmethyl)aniline



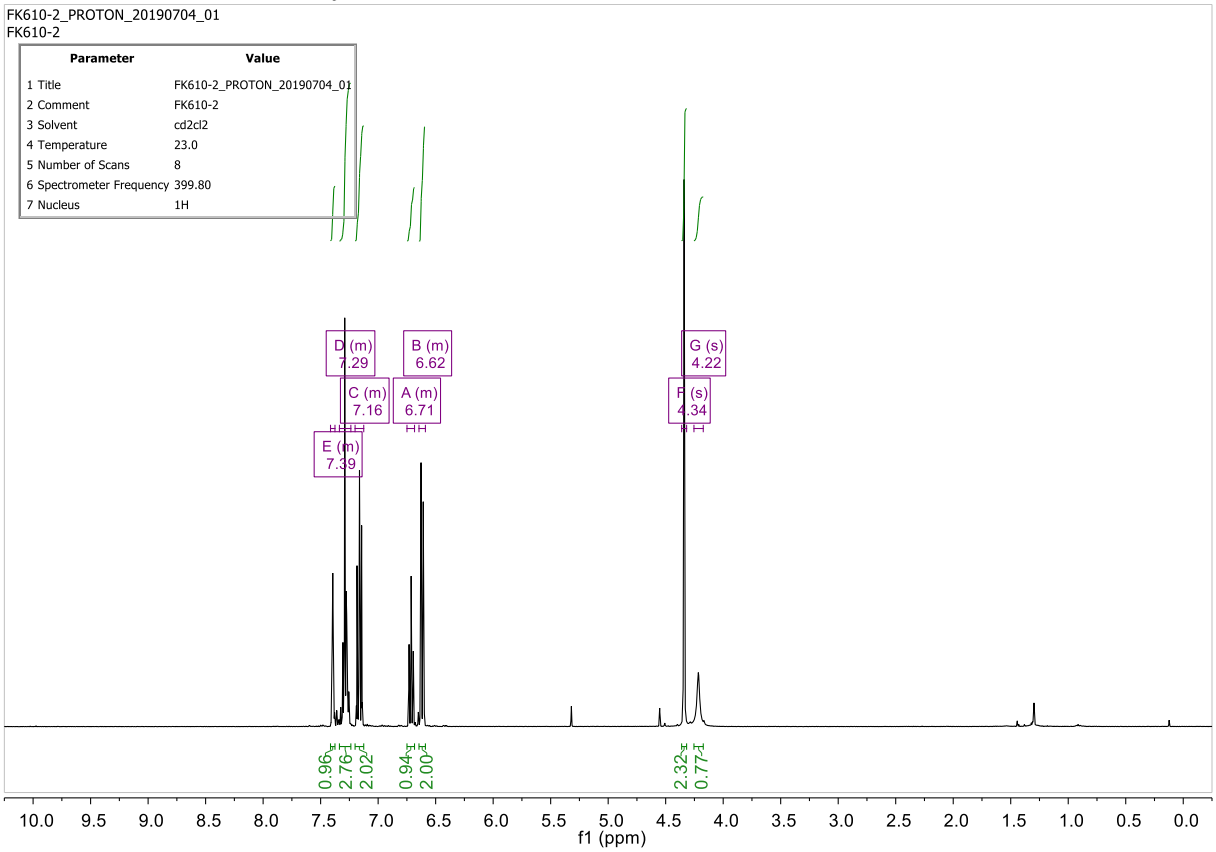


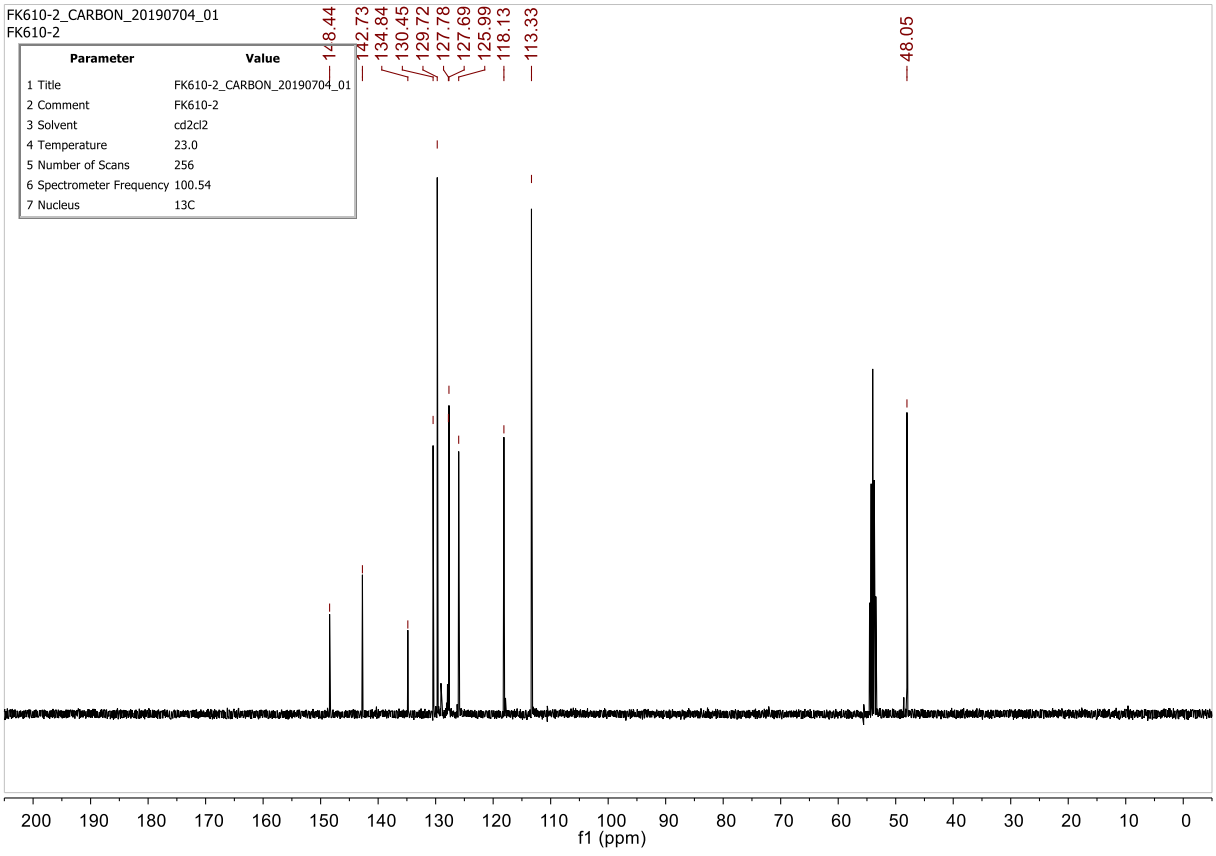
11)N-(4-chlorobenzyl)aniline



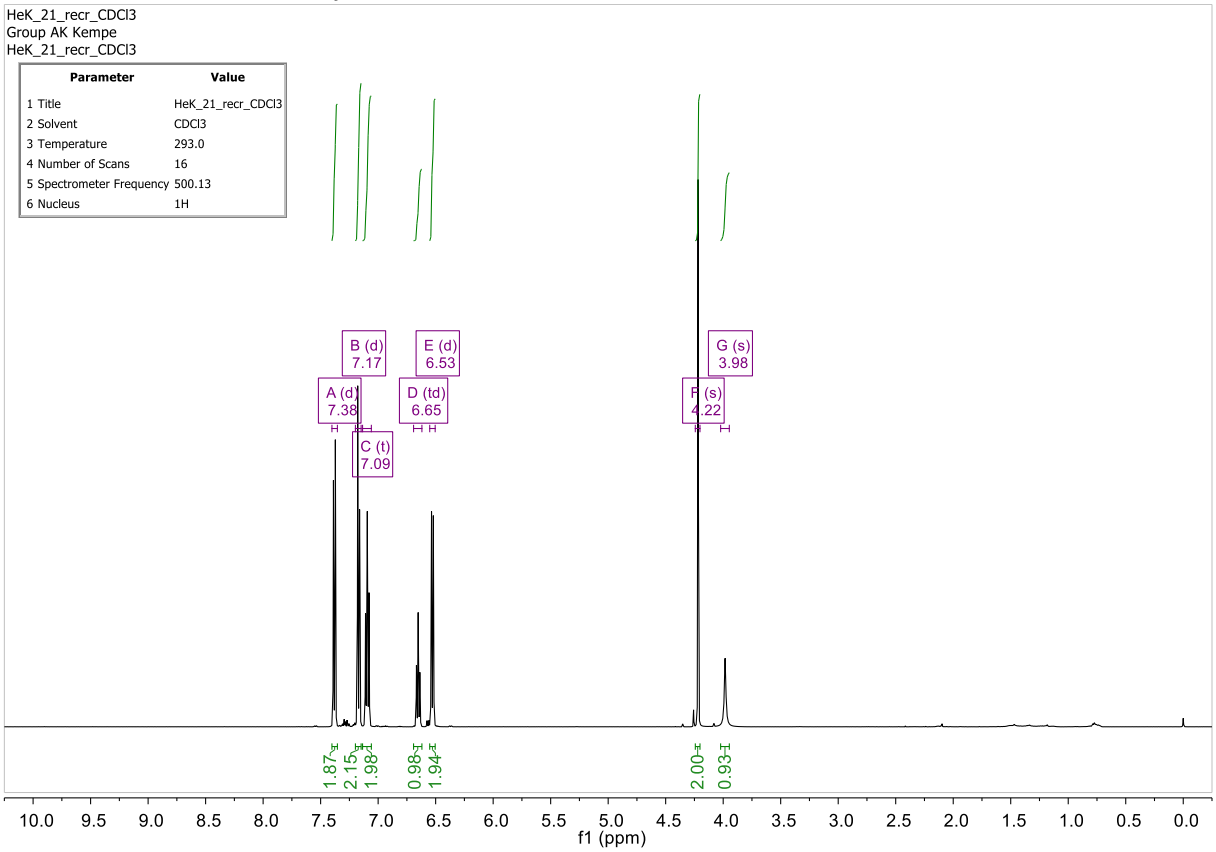


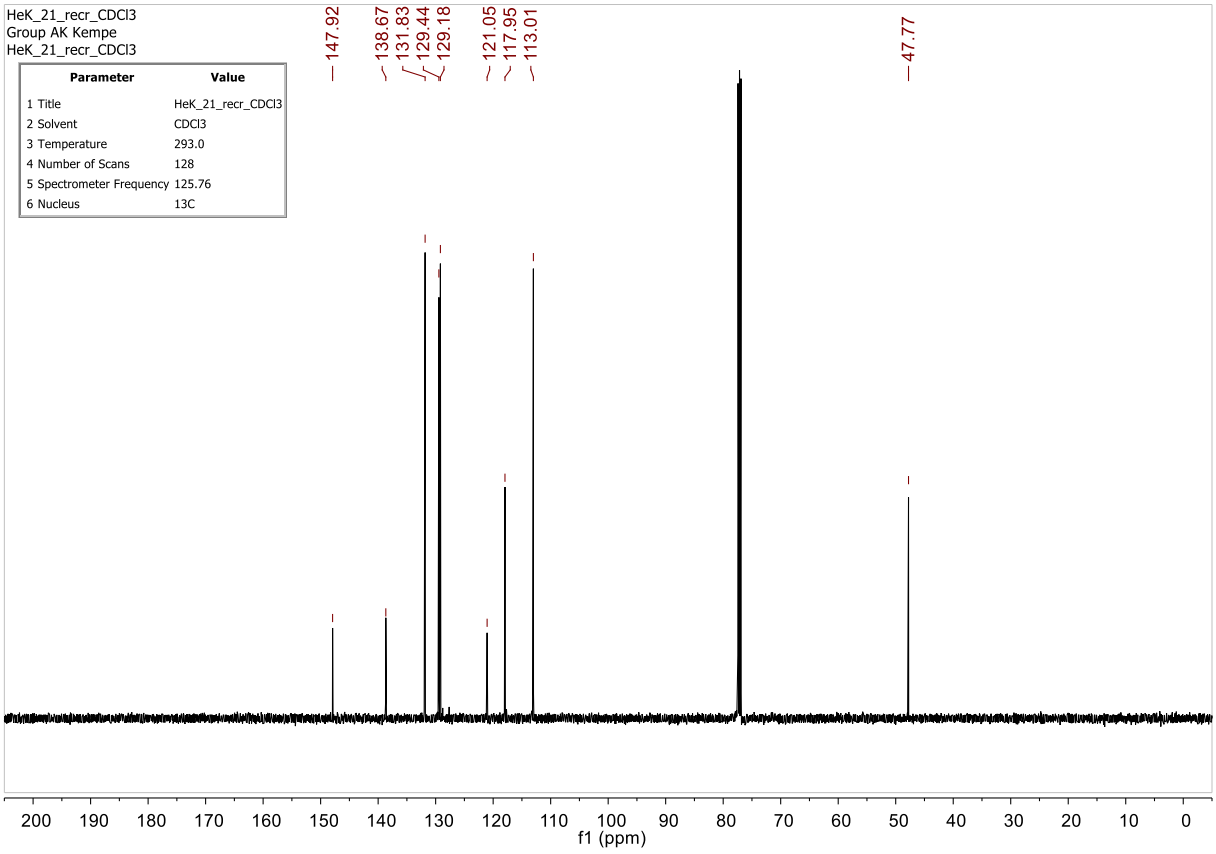
12)N-(3-chlorobenzyl)aniline



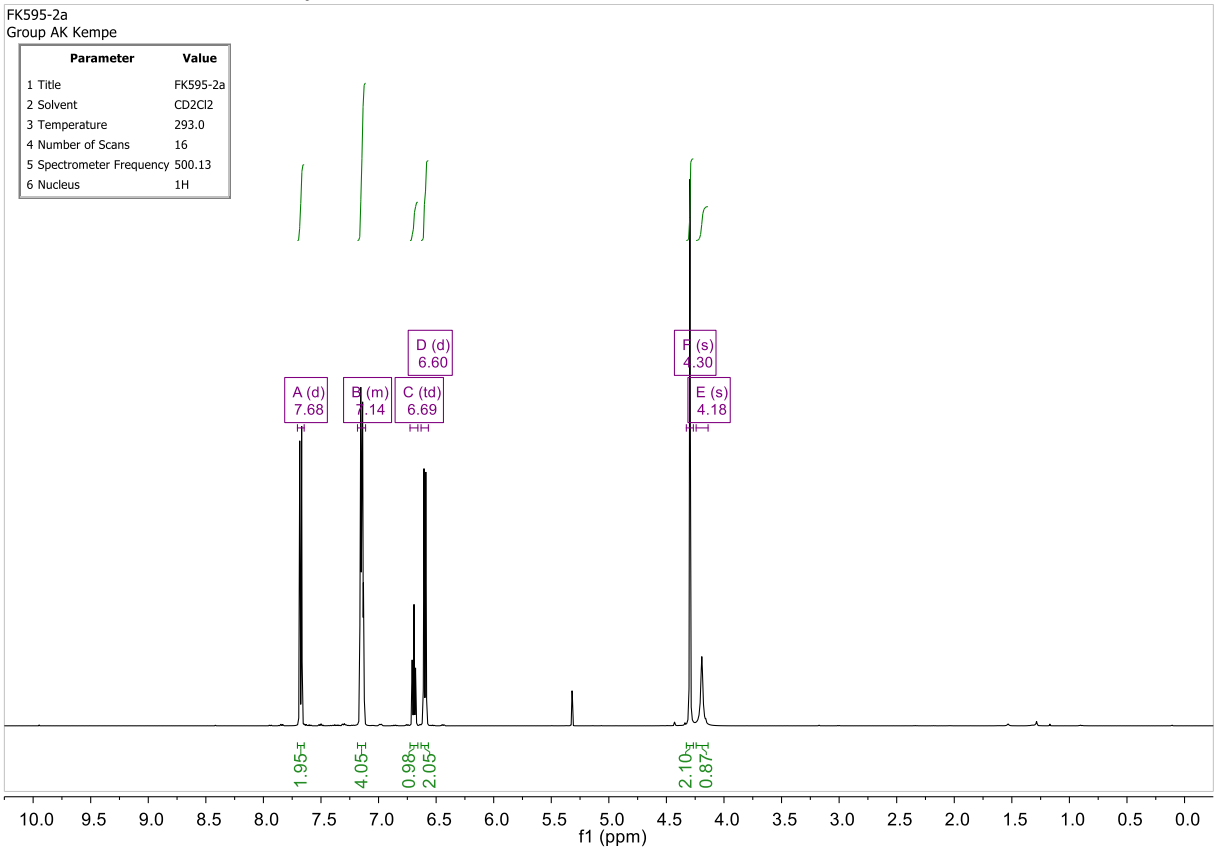


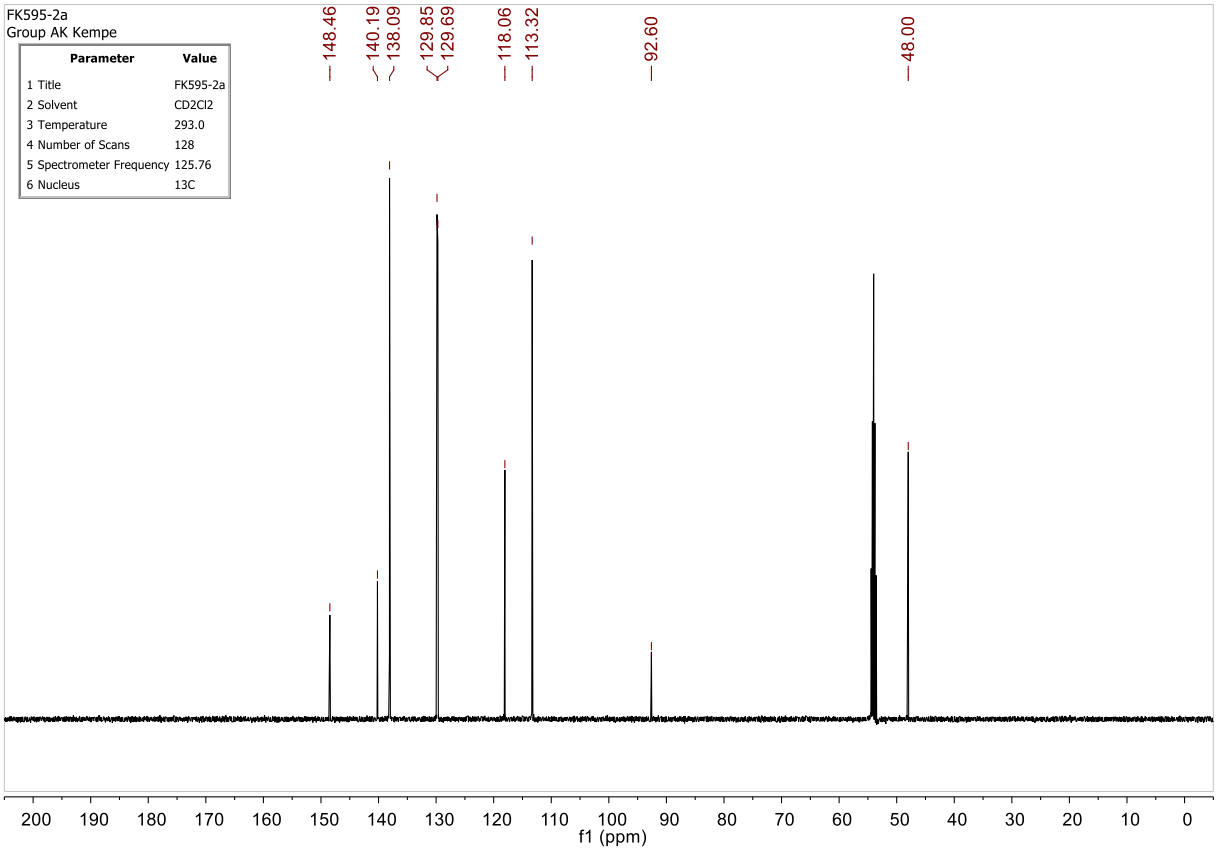
13)N-(4-bromobenzyl)aniline



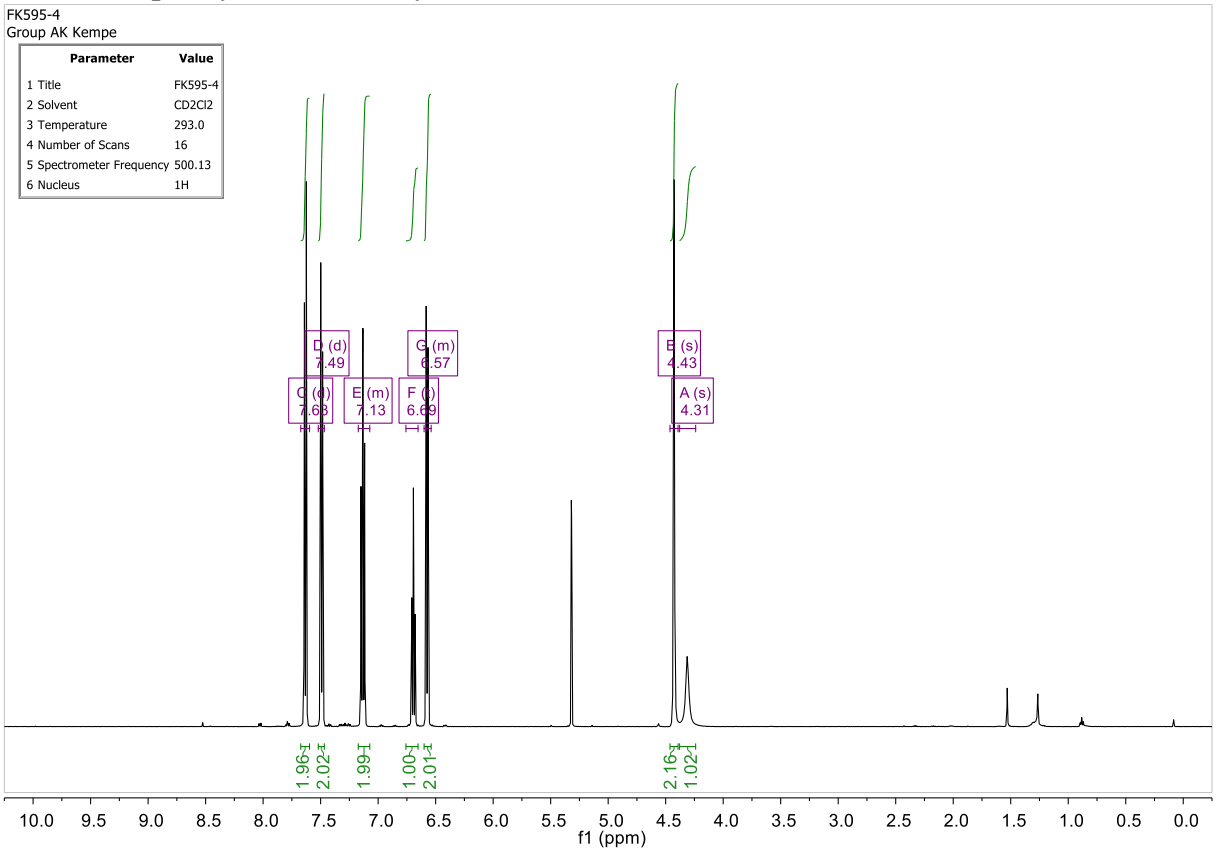


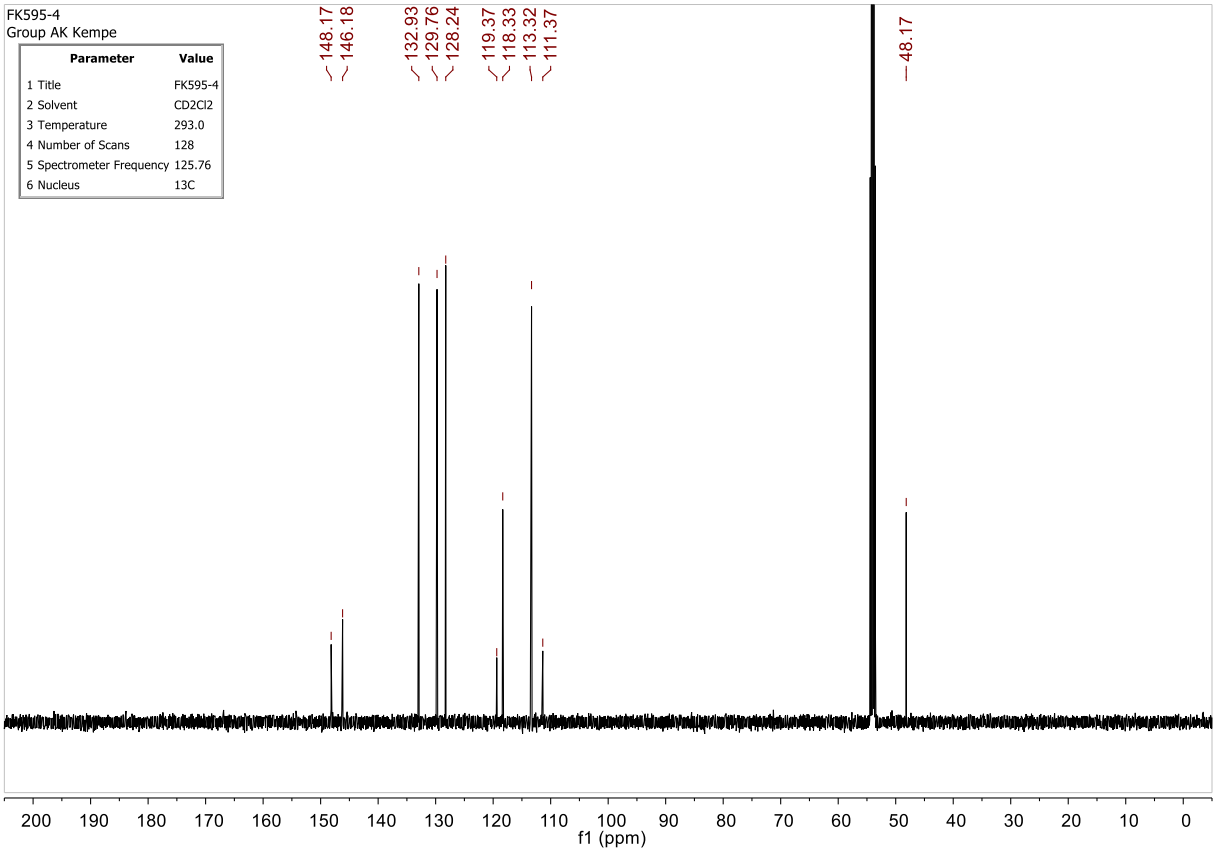
14)N-(4-iodobenzyl)aniline



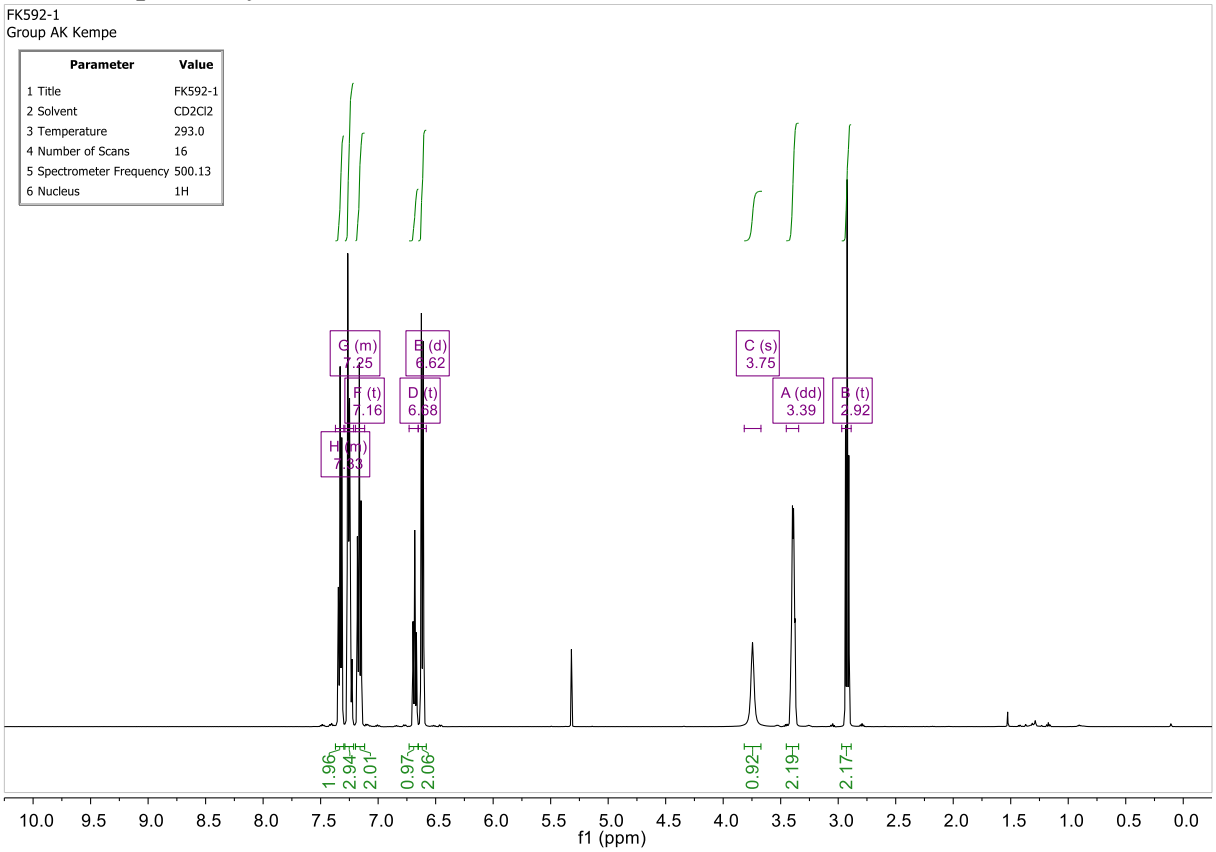


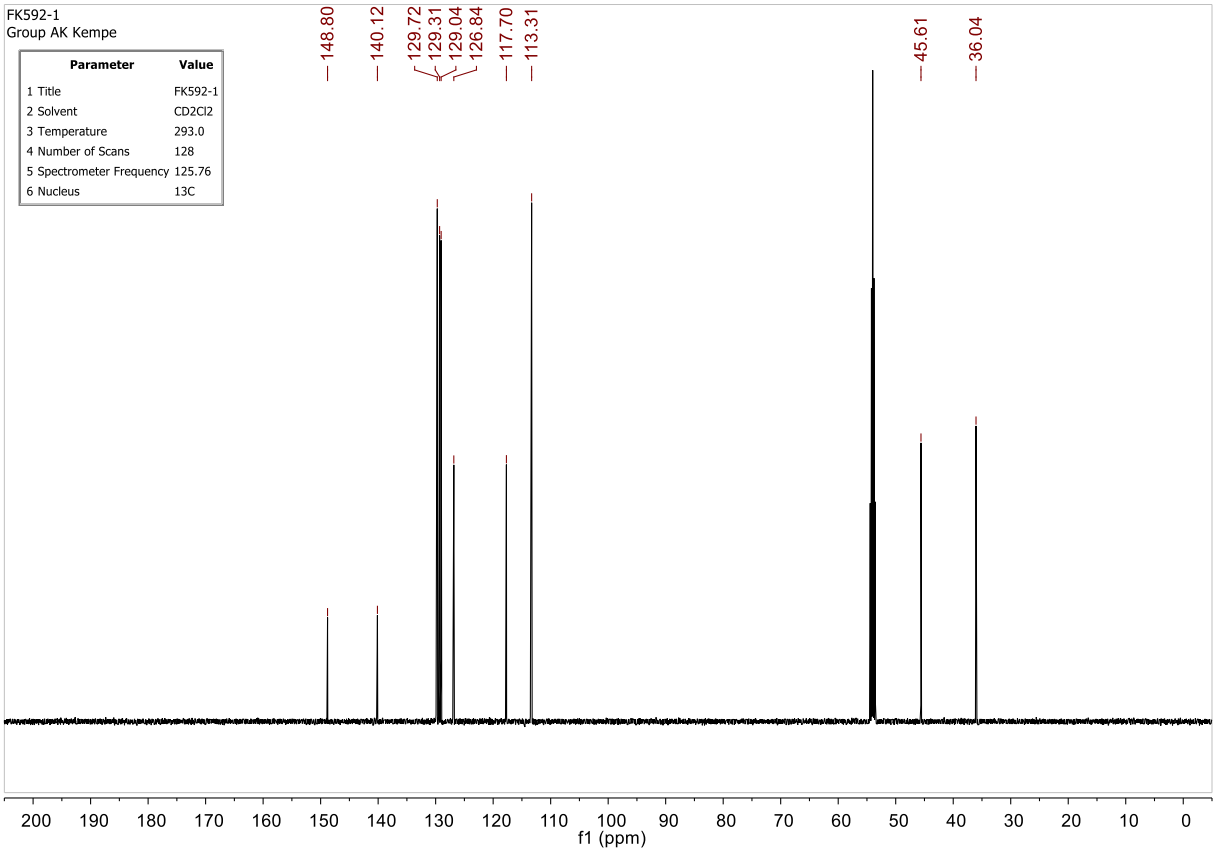
15)4-((phenylamino)methyl)benzonitrile



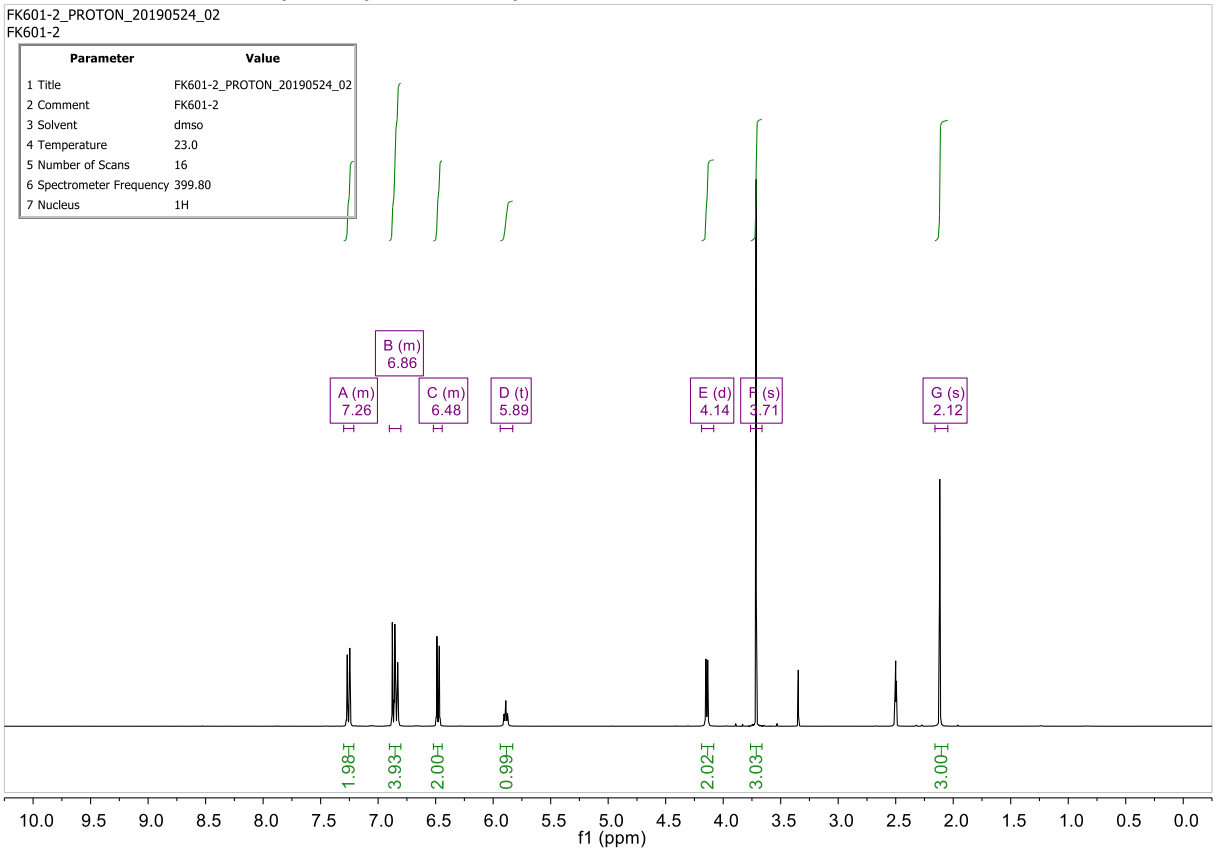


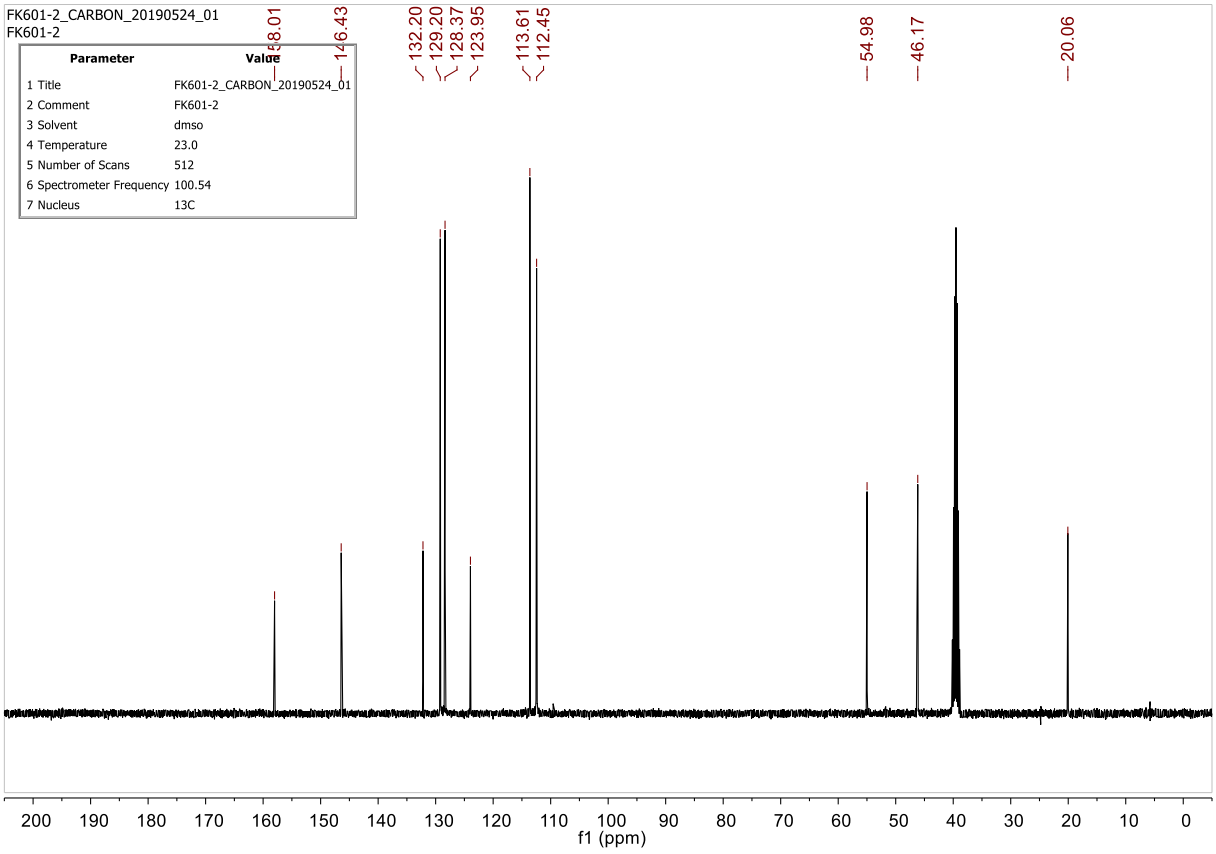
16)N-phenethylaniline



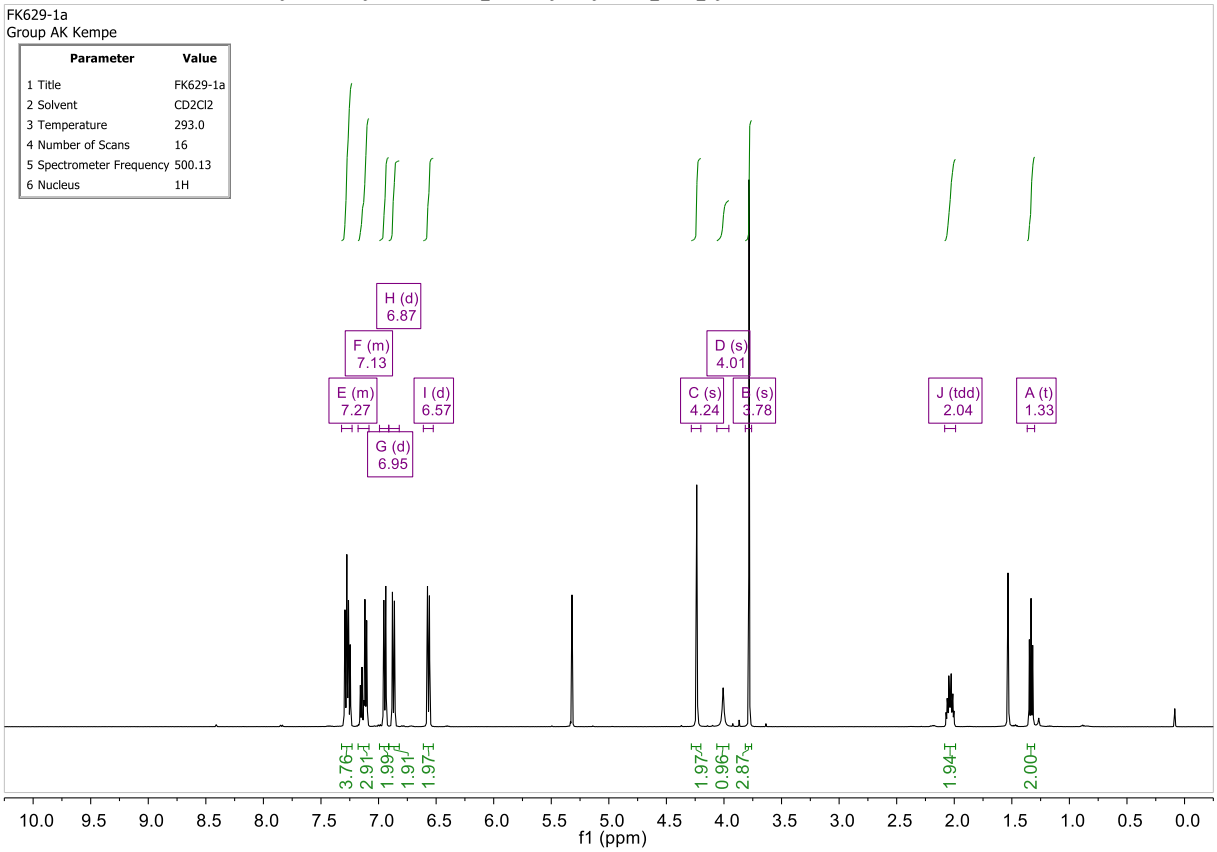


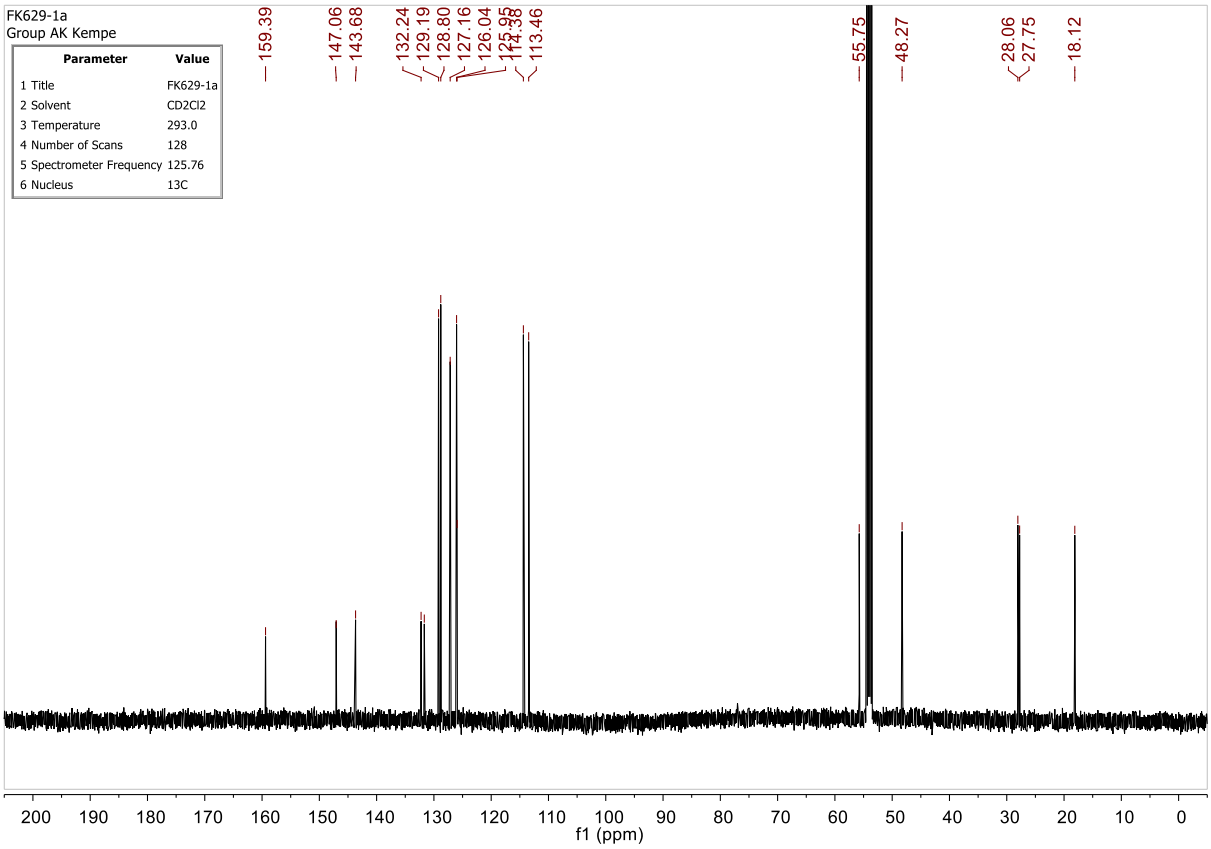
17)N-(4-methoxybenzyl)-4-methylaniline



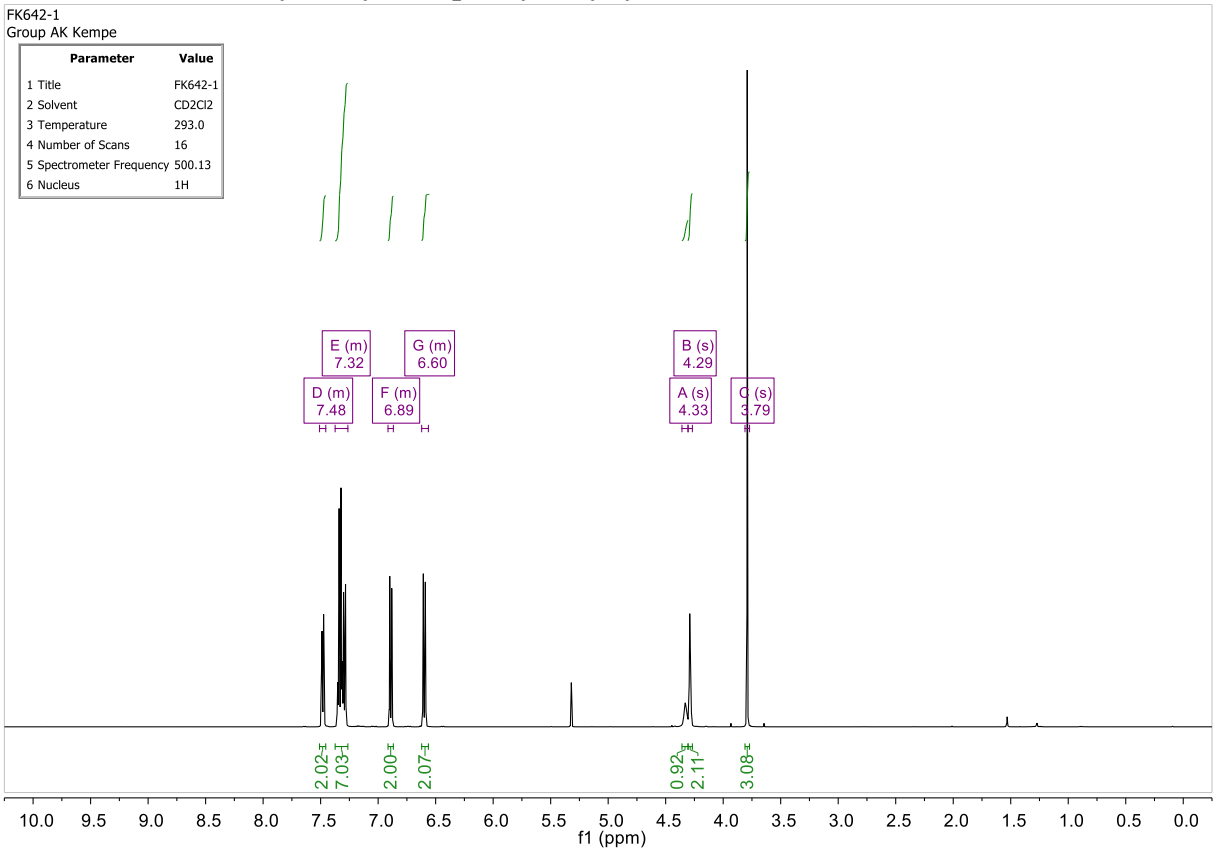


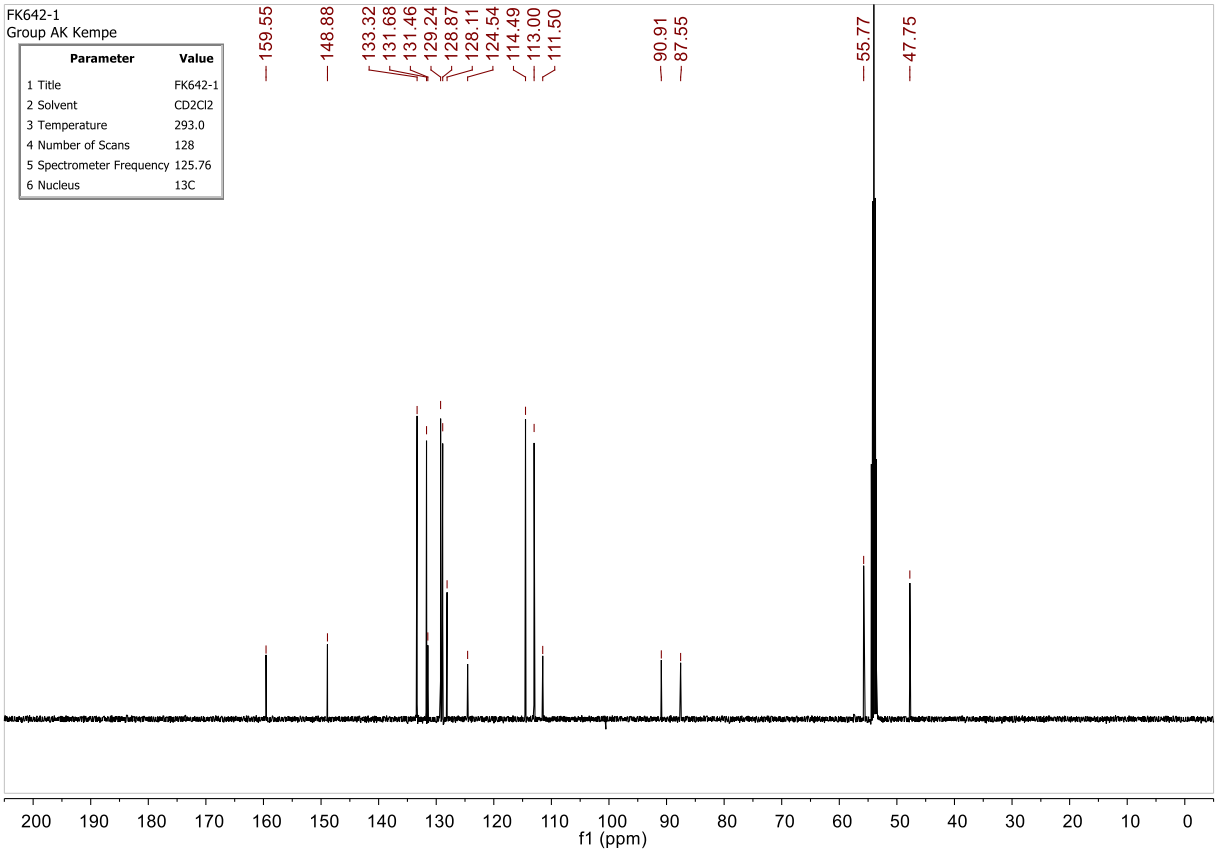
18)*N*-(4-methoxybenzyl)-4-(2-phenylcyclopropyl)aniline



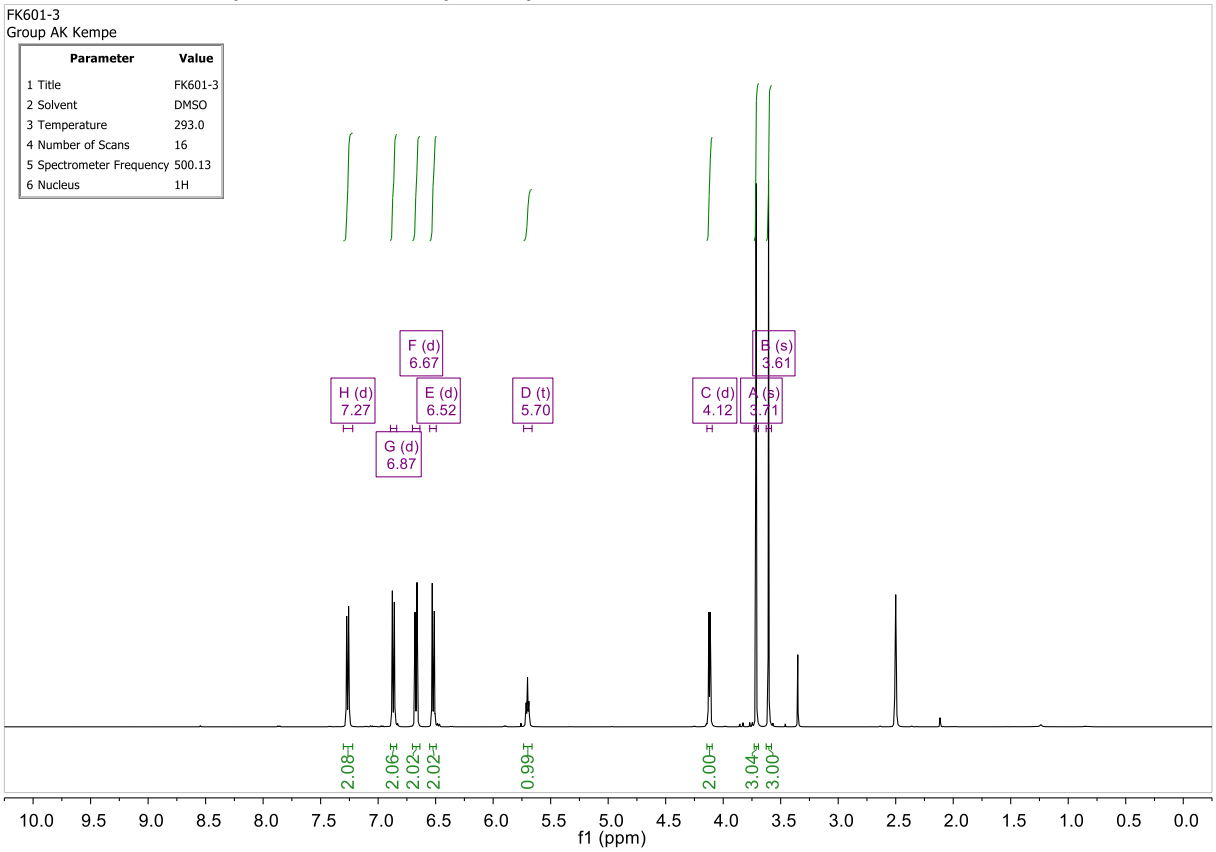


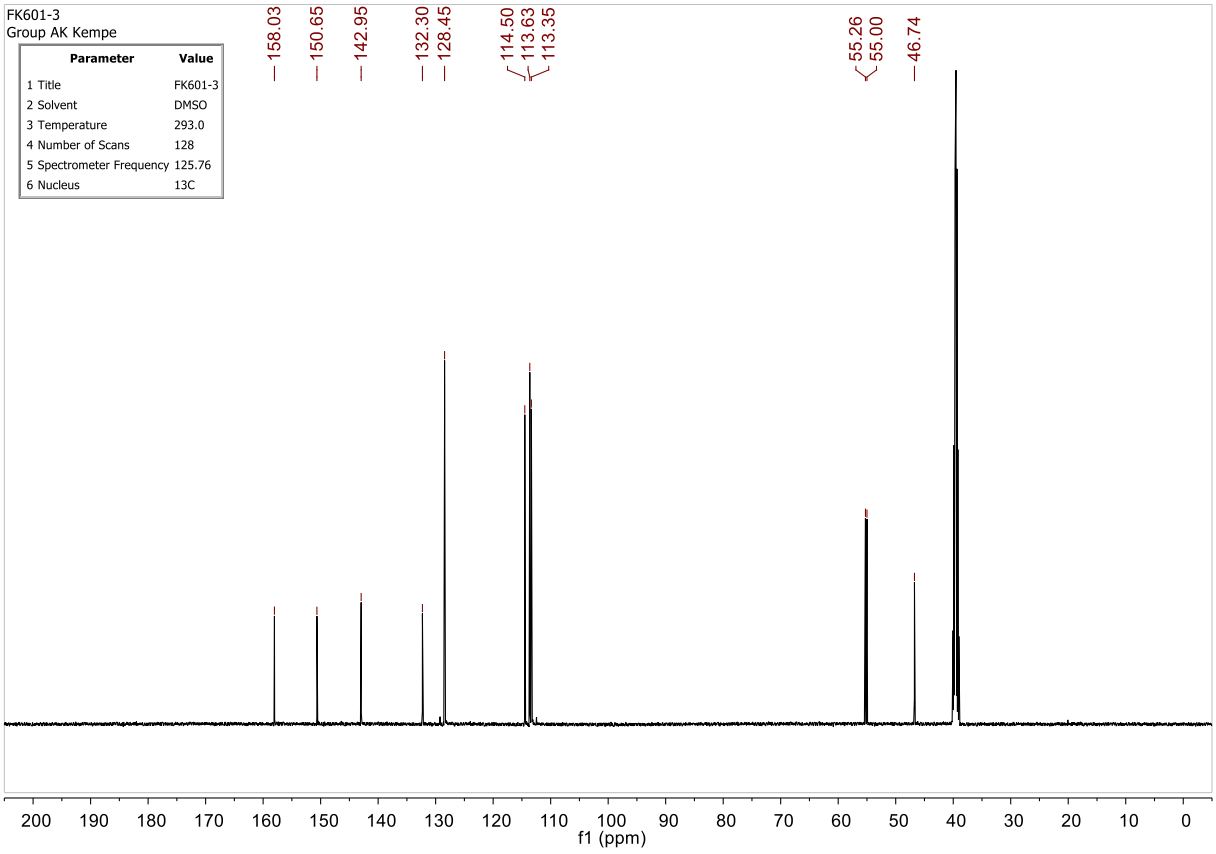
19)*N*-(4-methoxybenzyl)-4-(phenylethynyl)aniline



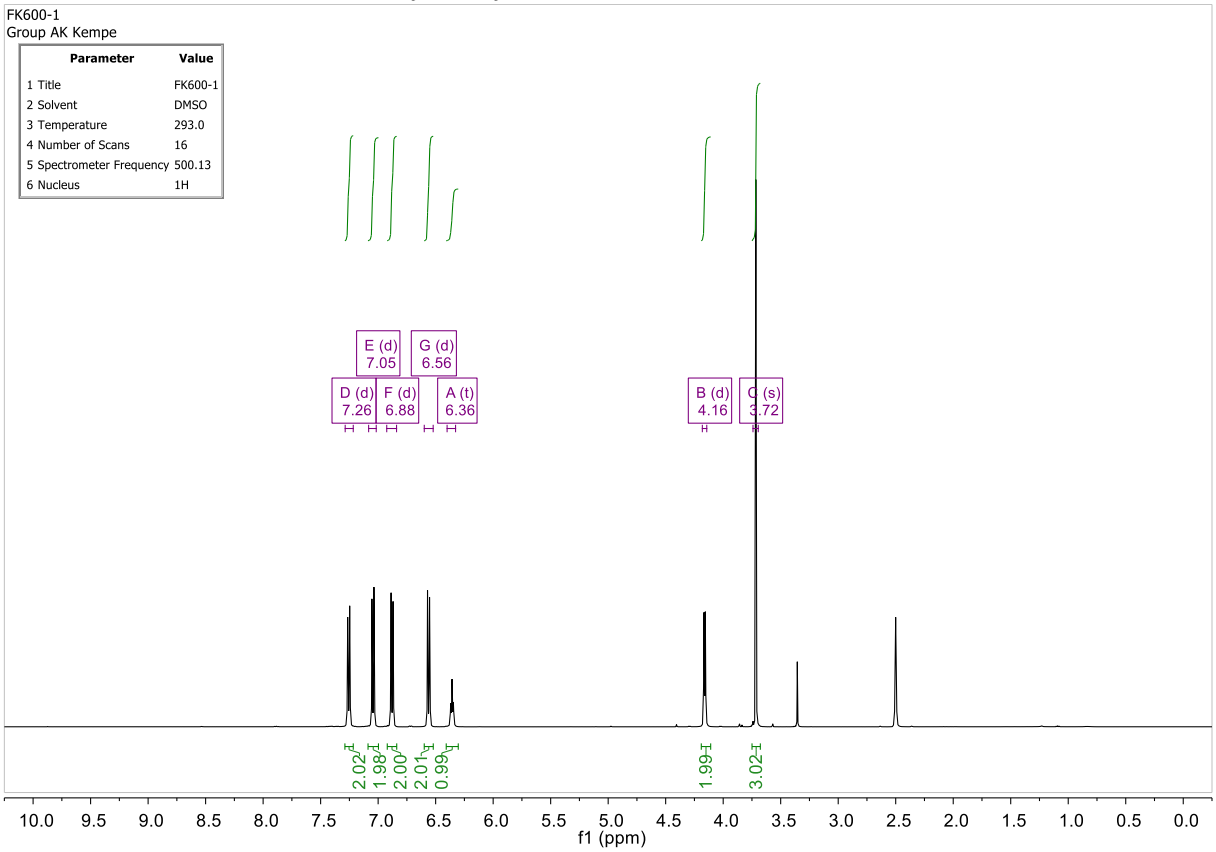


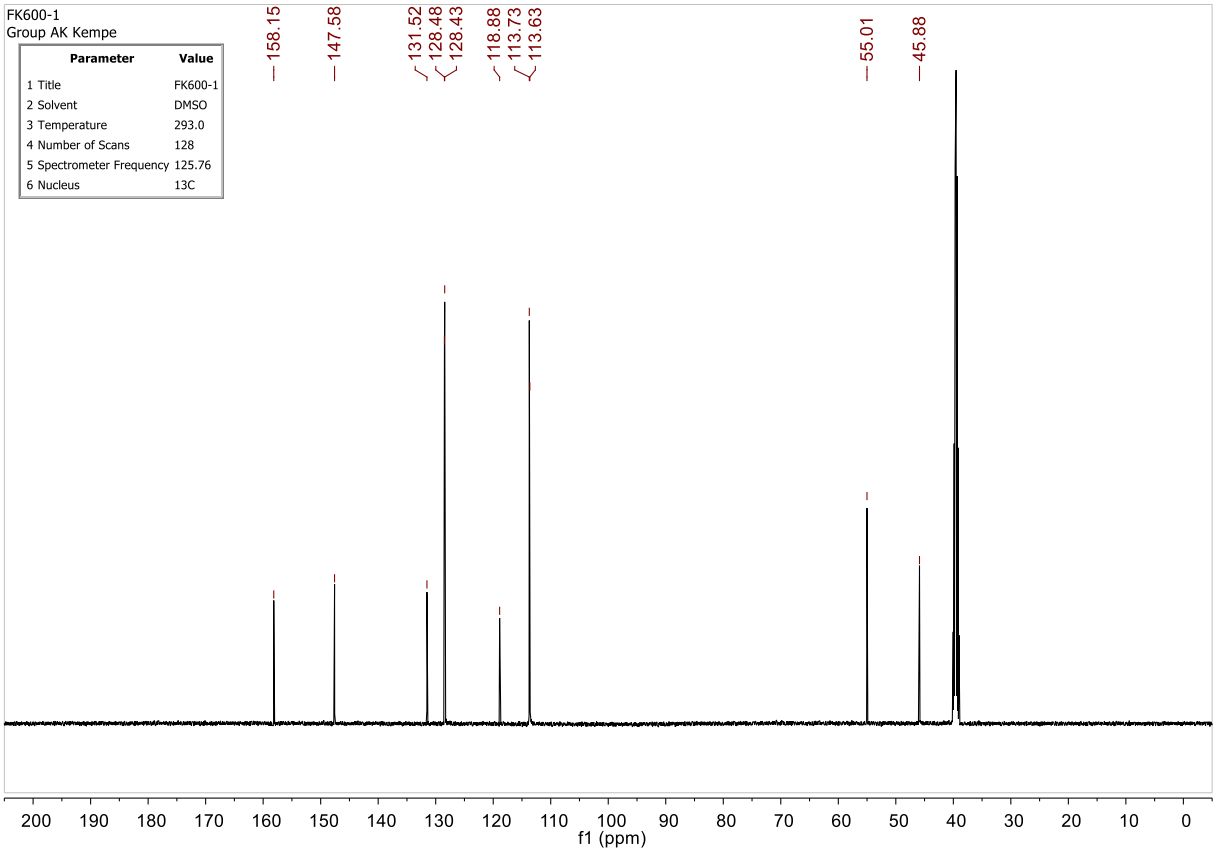
20)4-methoxy-N-(4-methoxybenzyl)aniline



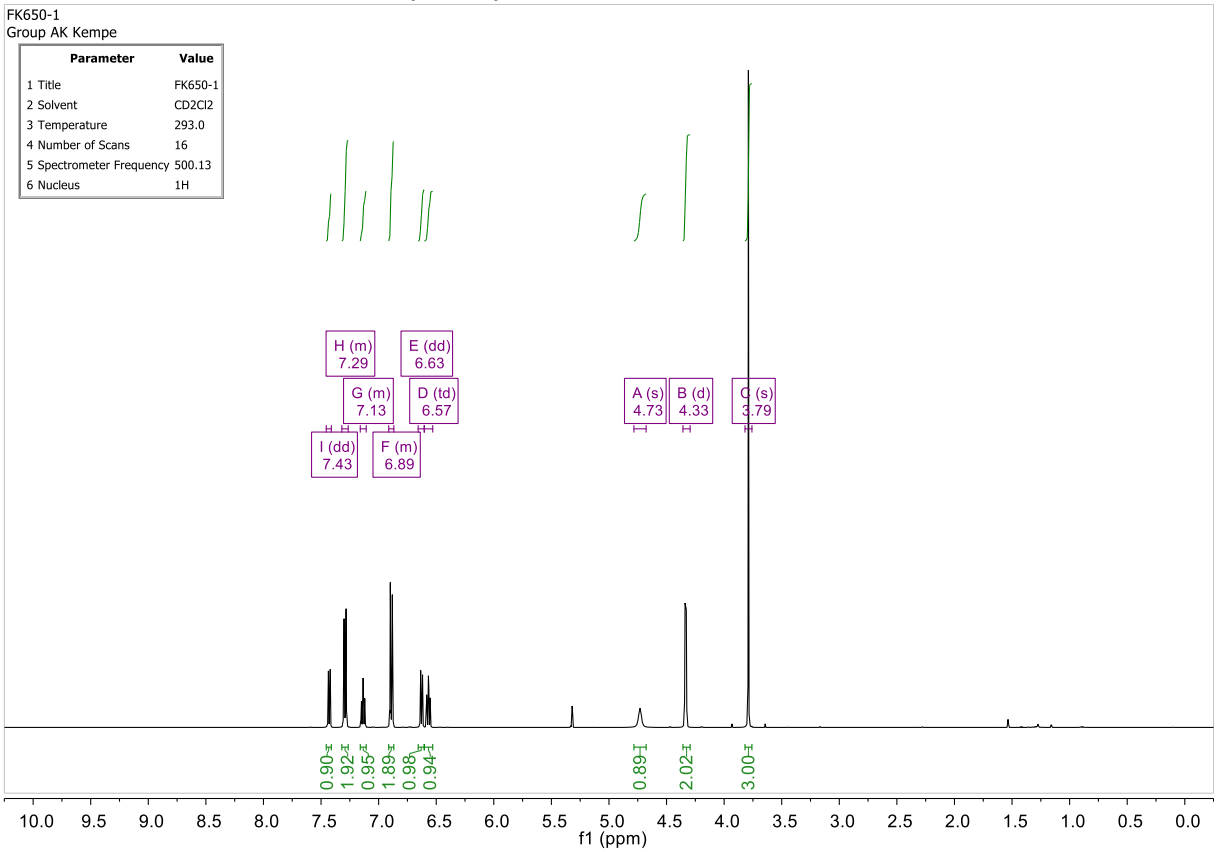


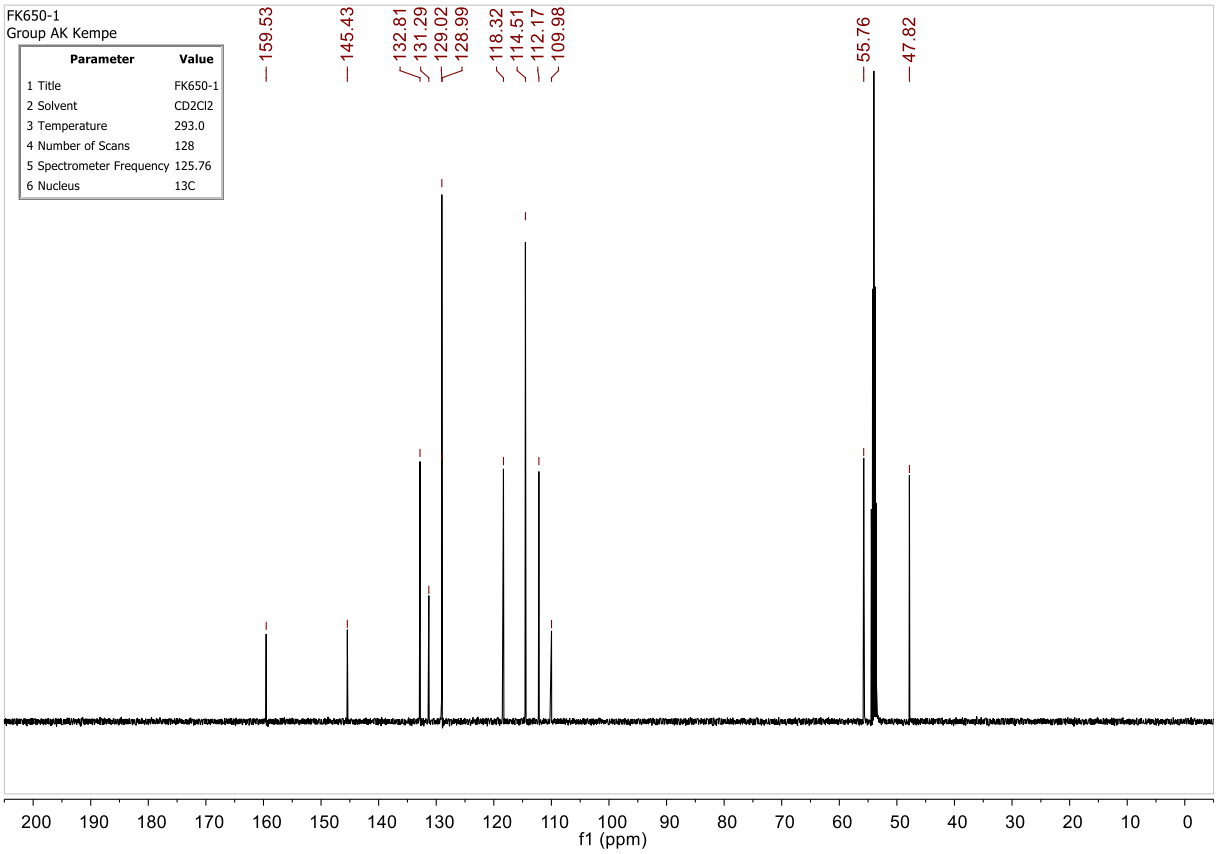
21)4-chloro-N-(4-methoxybenzyl)aniline





22)2-bromo-*N*-(4-methoxybenzyl)aniline





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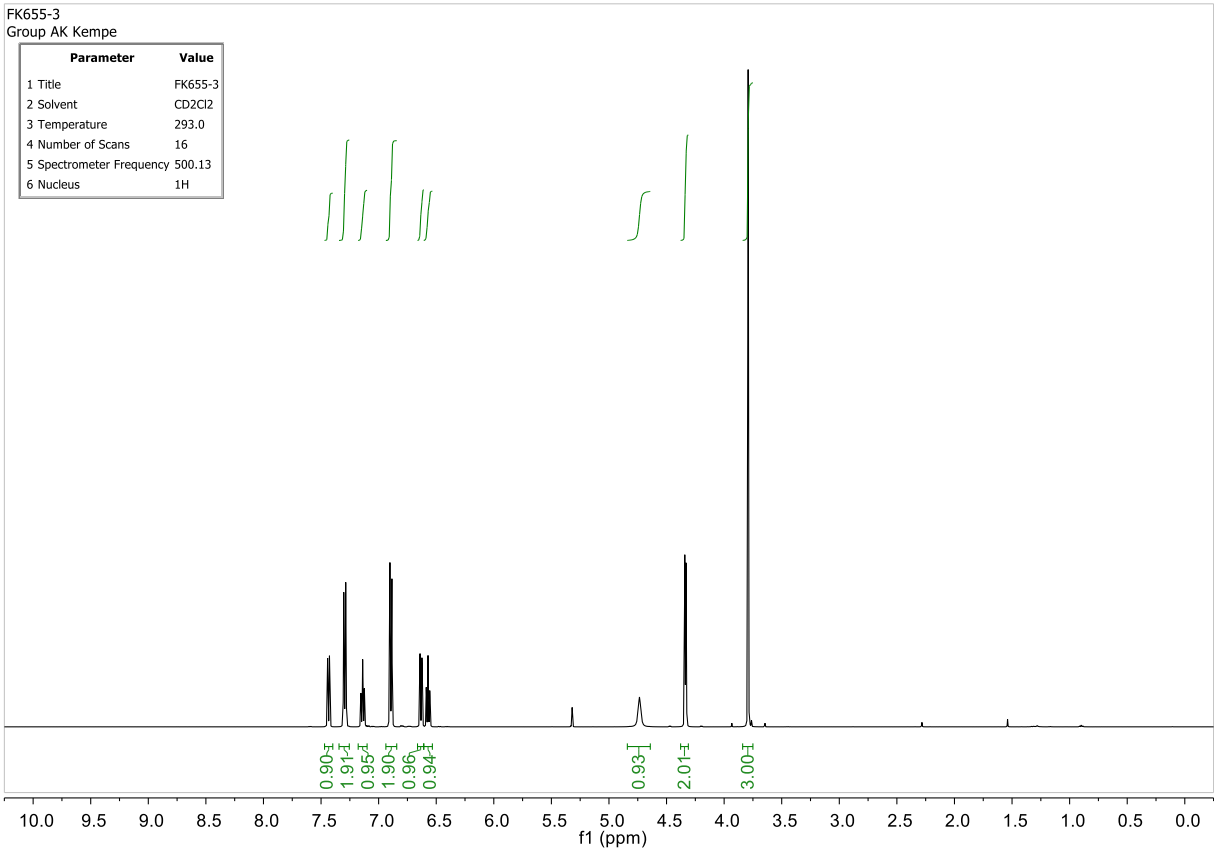
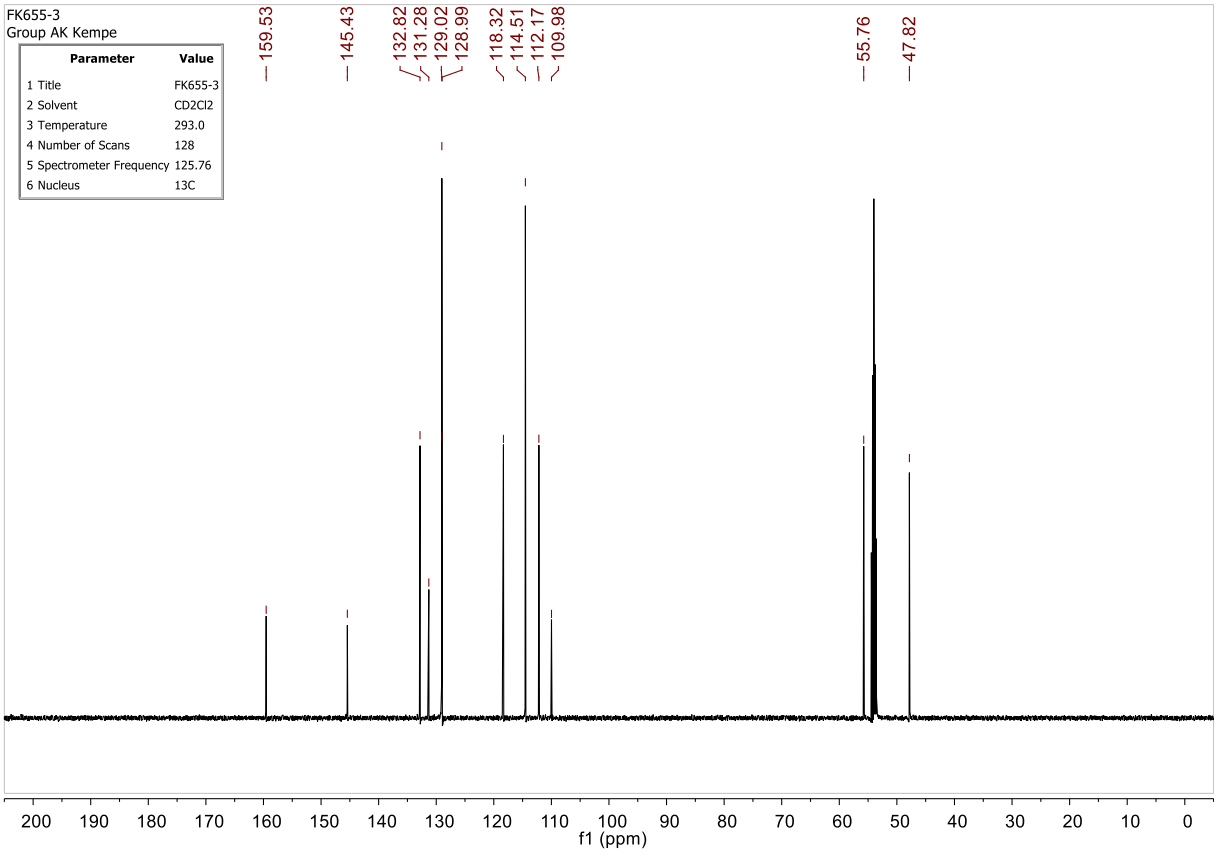
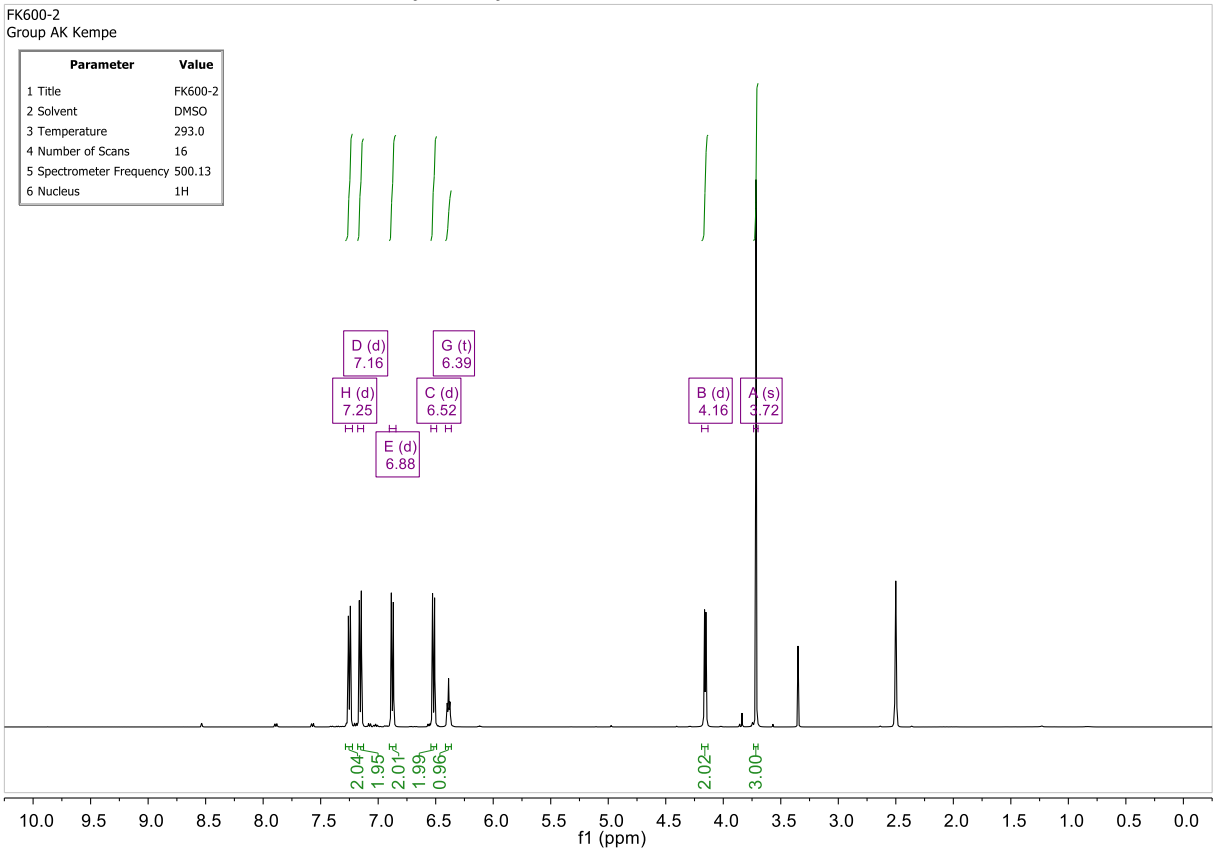
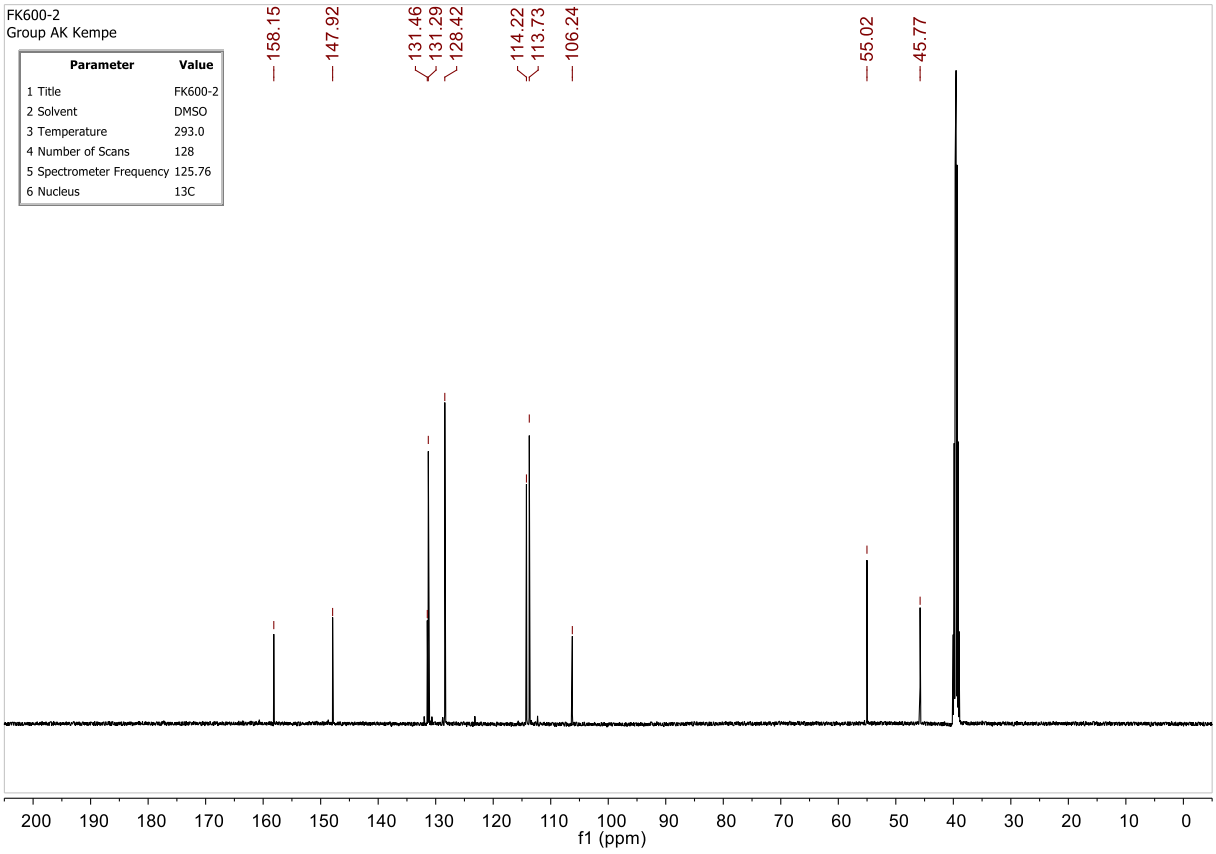


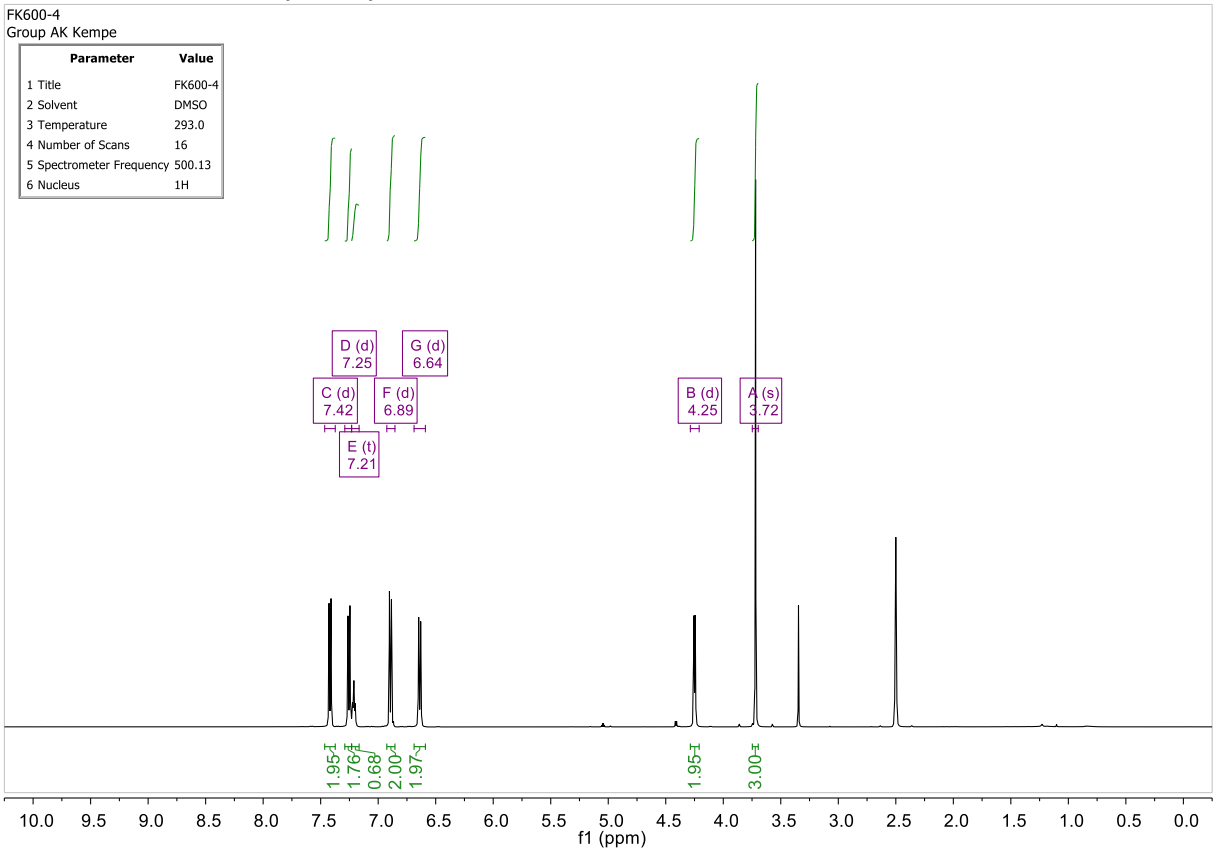


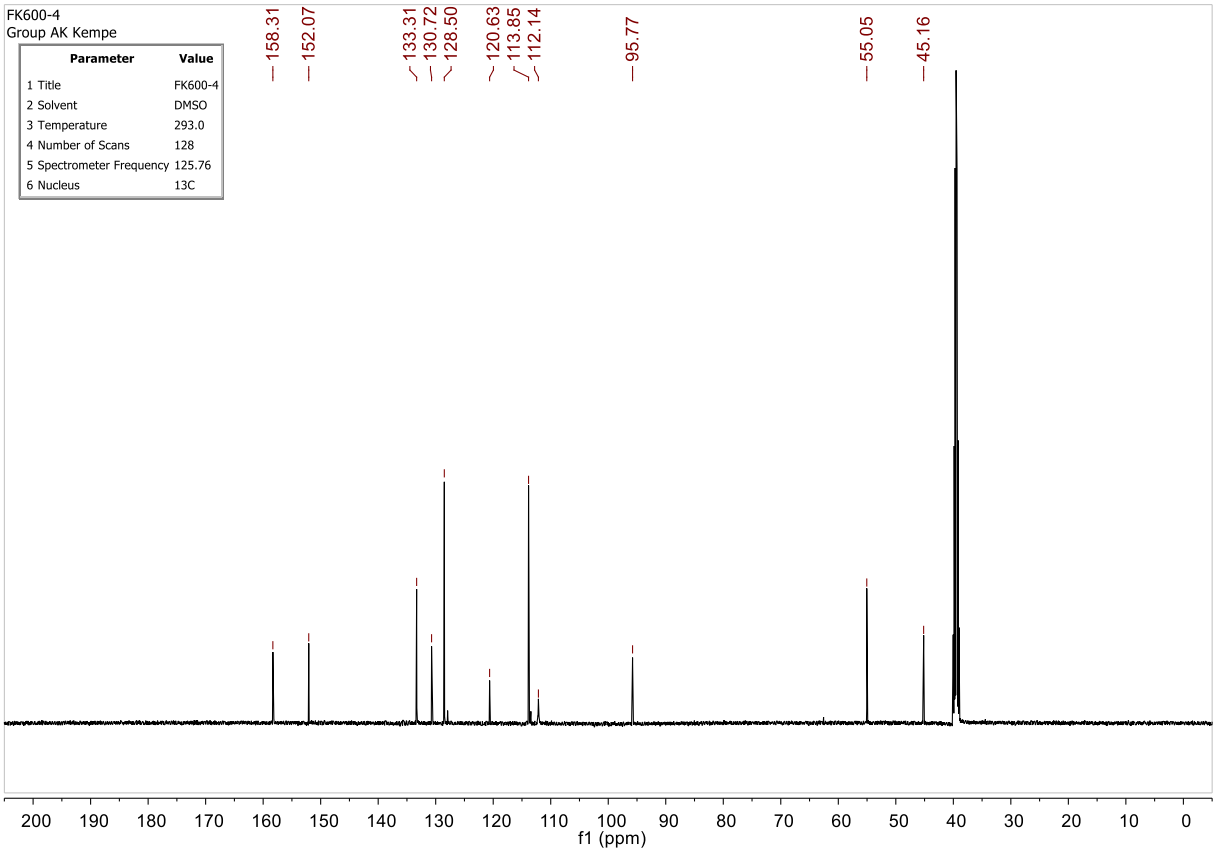
23)4-bromo-N-(4-methoxybenzyl)aniline



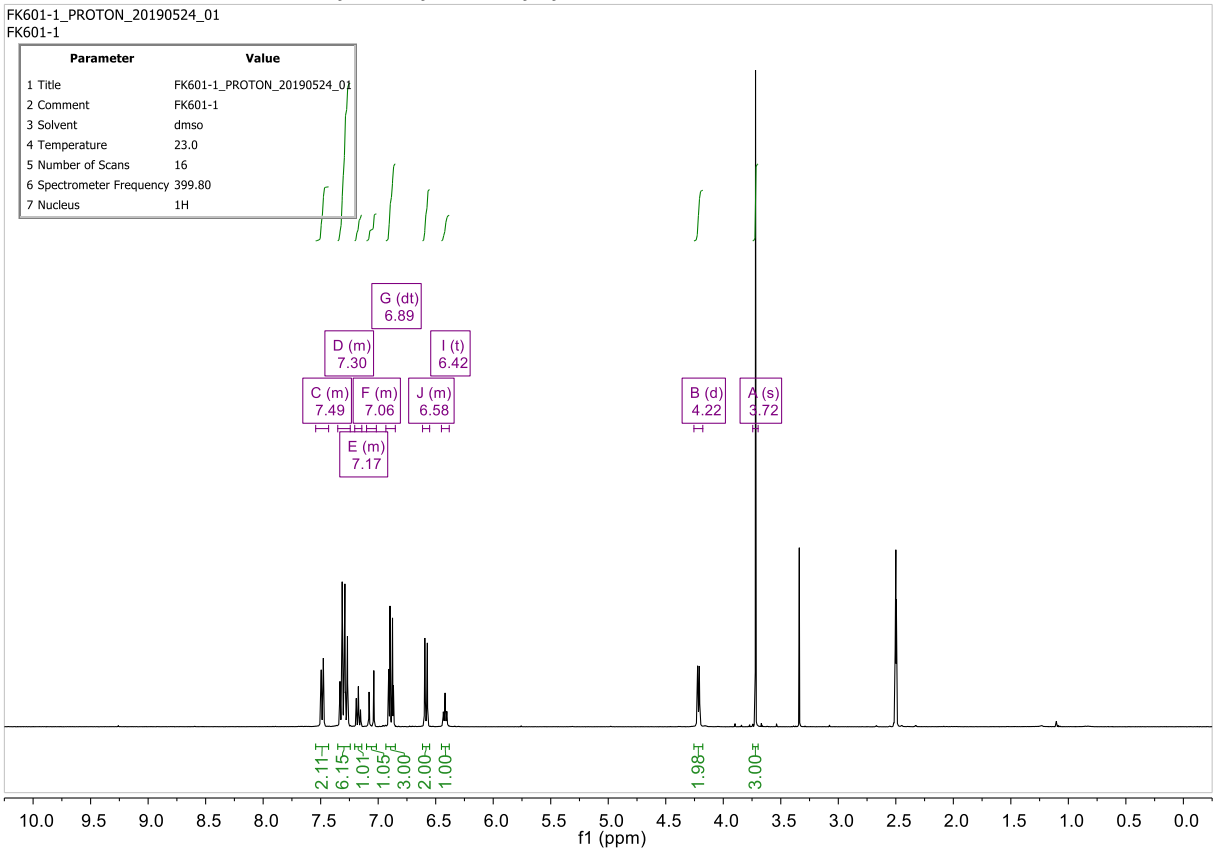


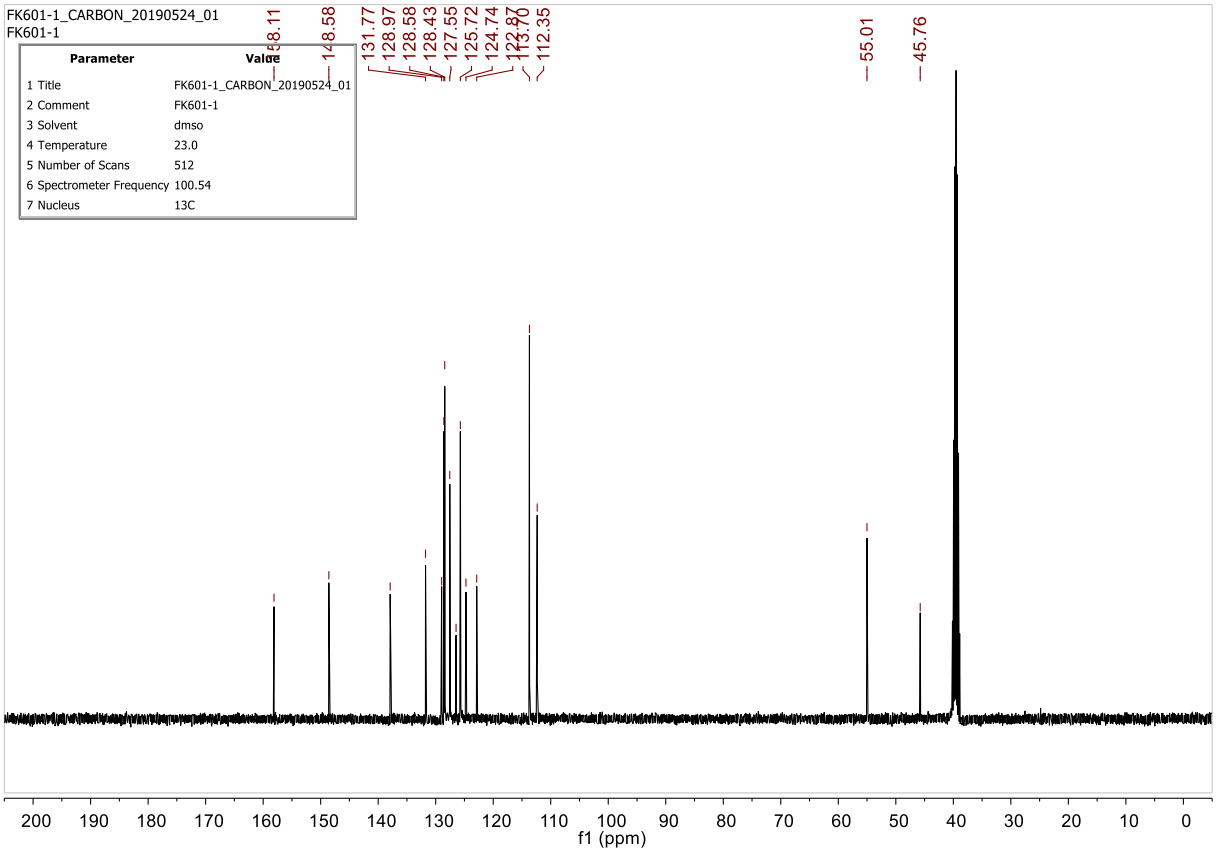
24)4-((4-methoxybenzyl)amino)benzonitrile



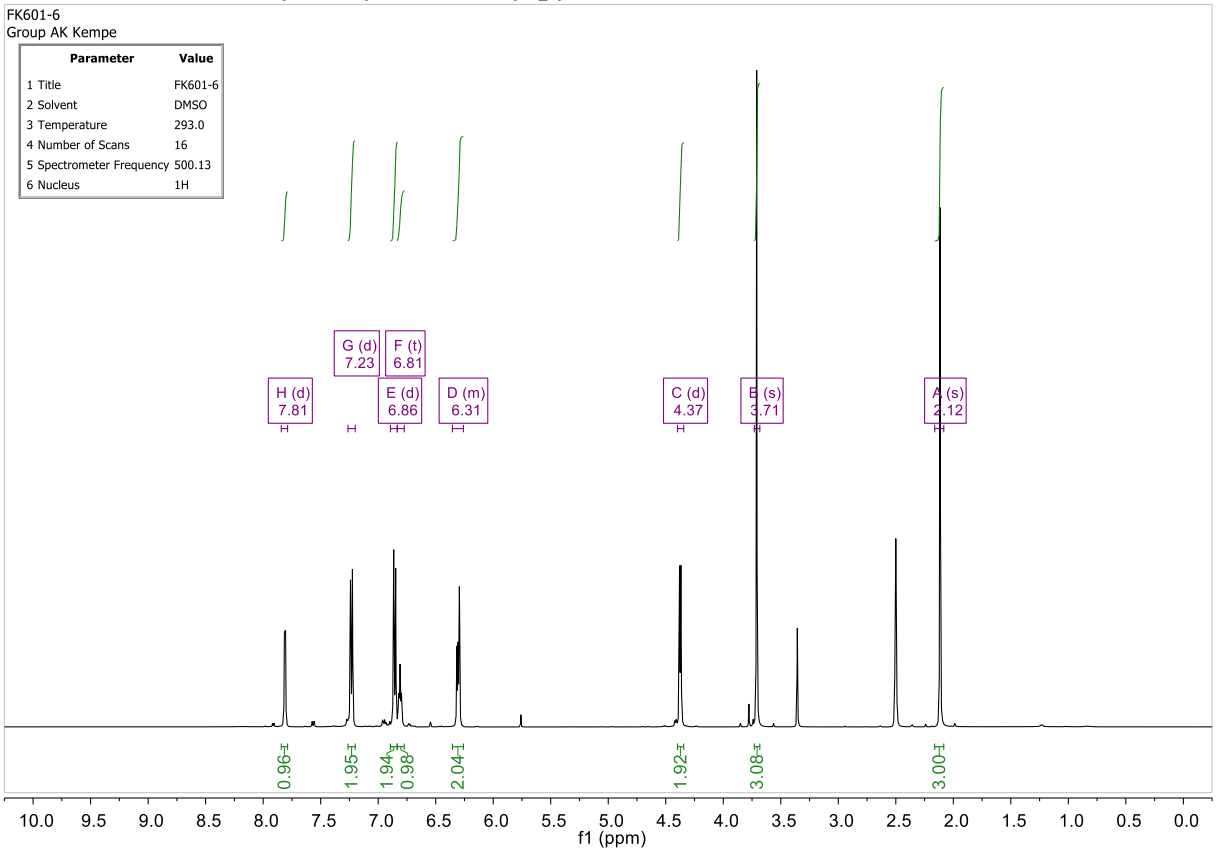


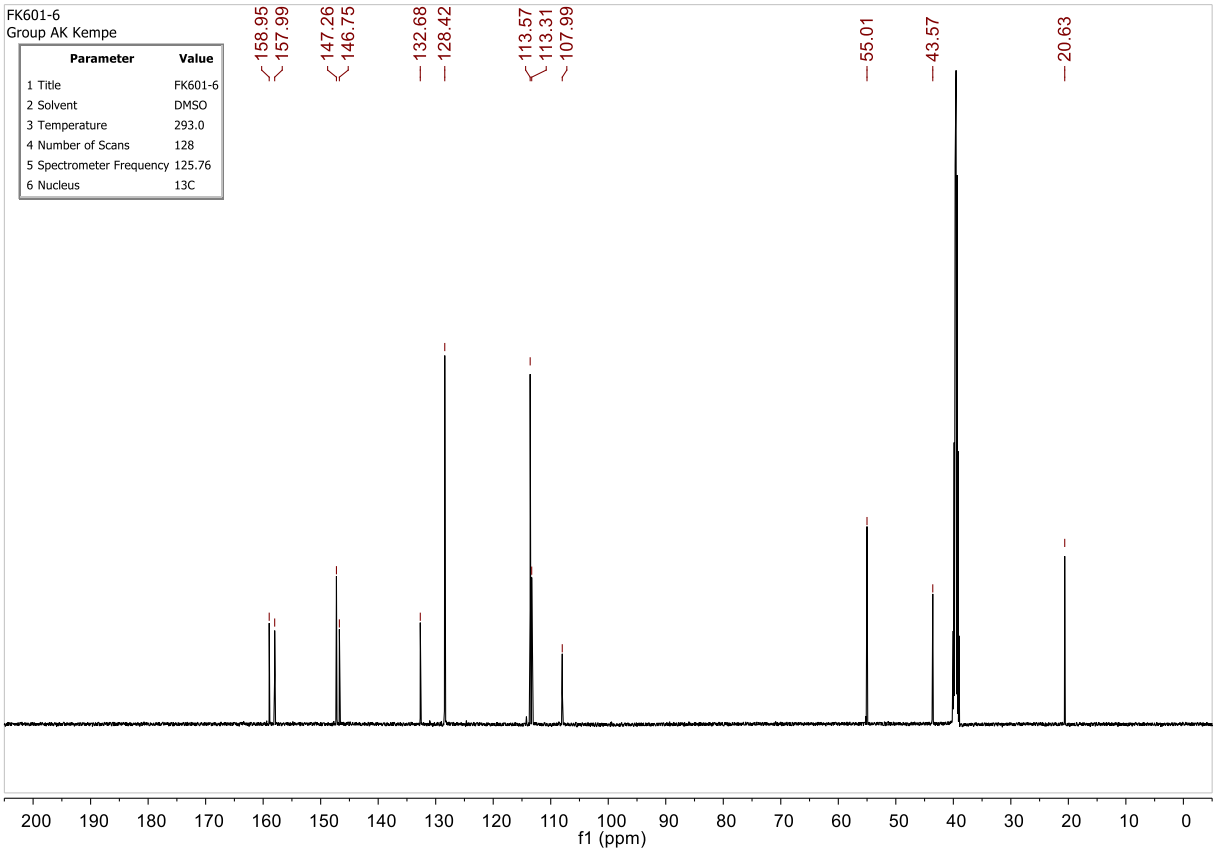
25)(E)-N-(4-methoxybenzyl)-4-styrylaniline



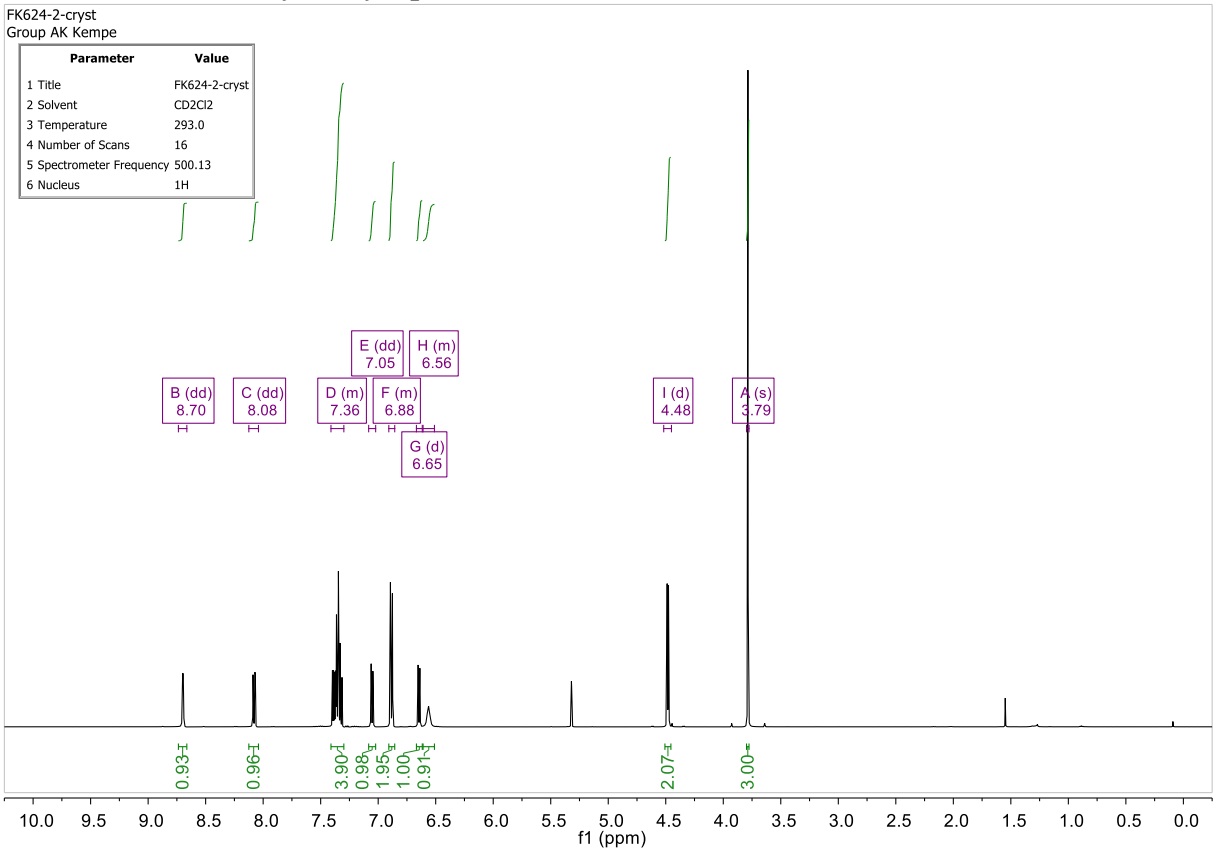


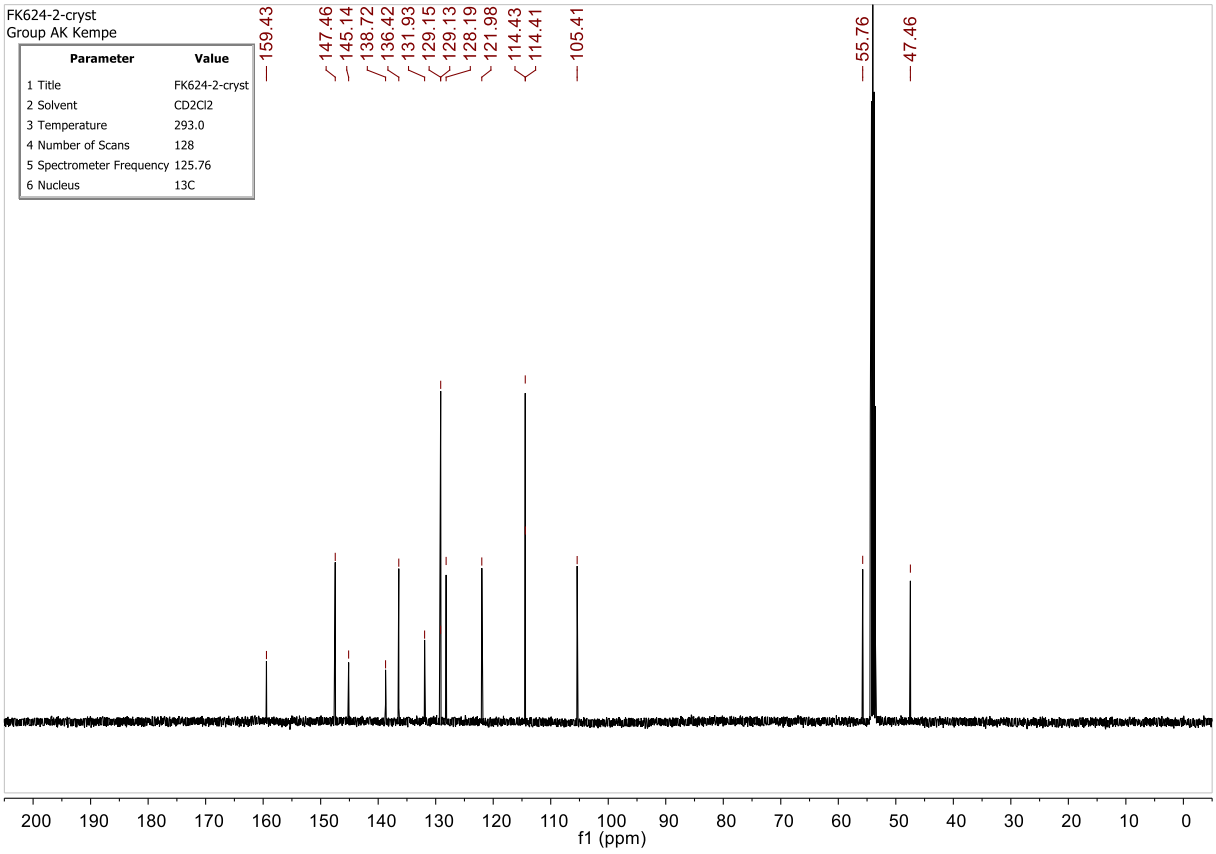
26)N-(4-methoxybenzyl)-4-methylpyridin-2-amine



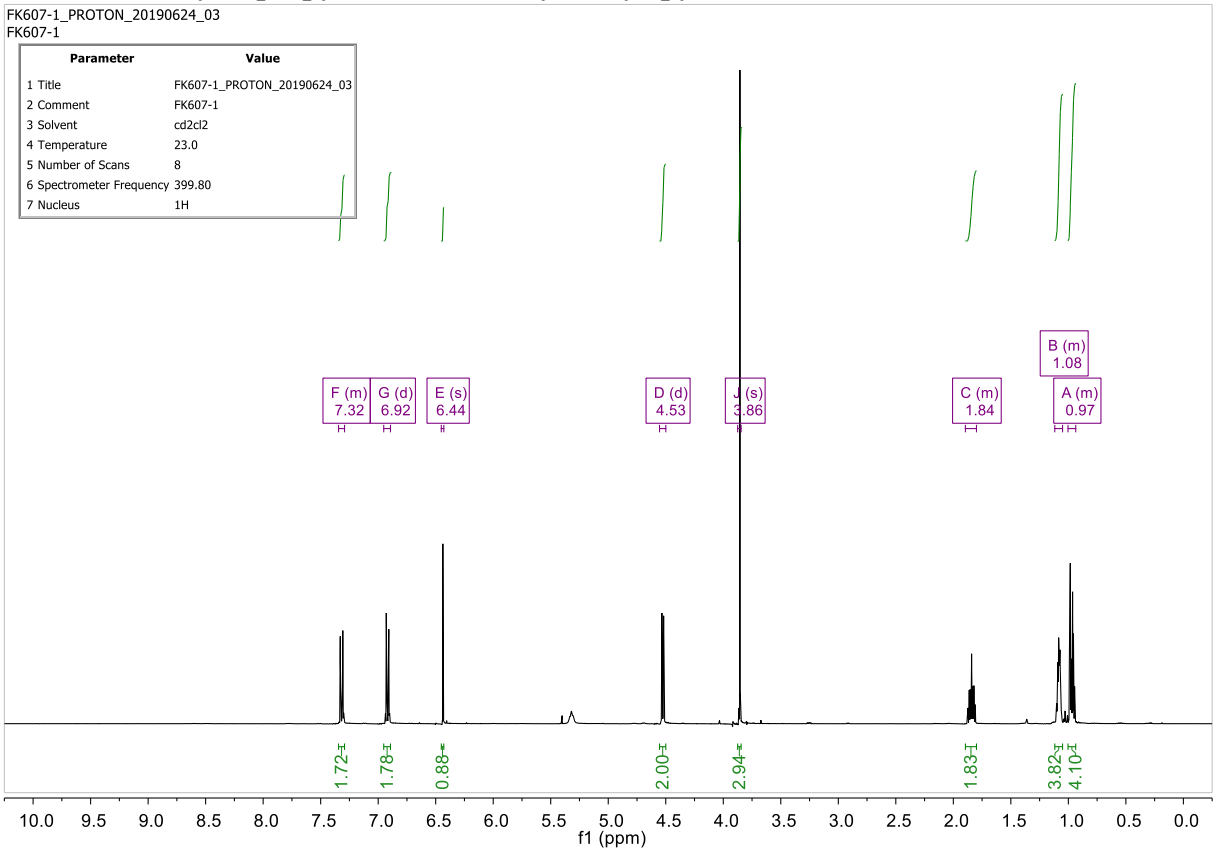


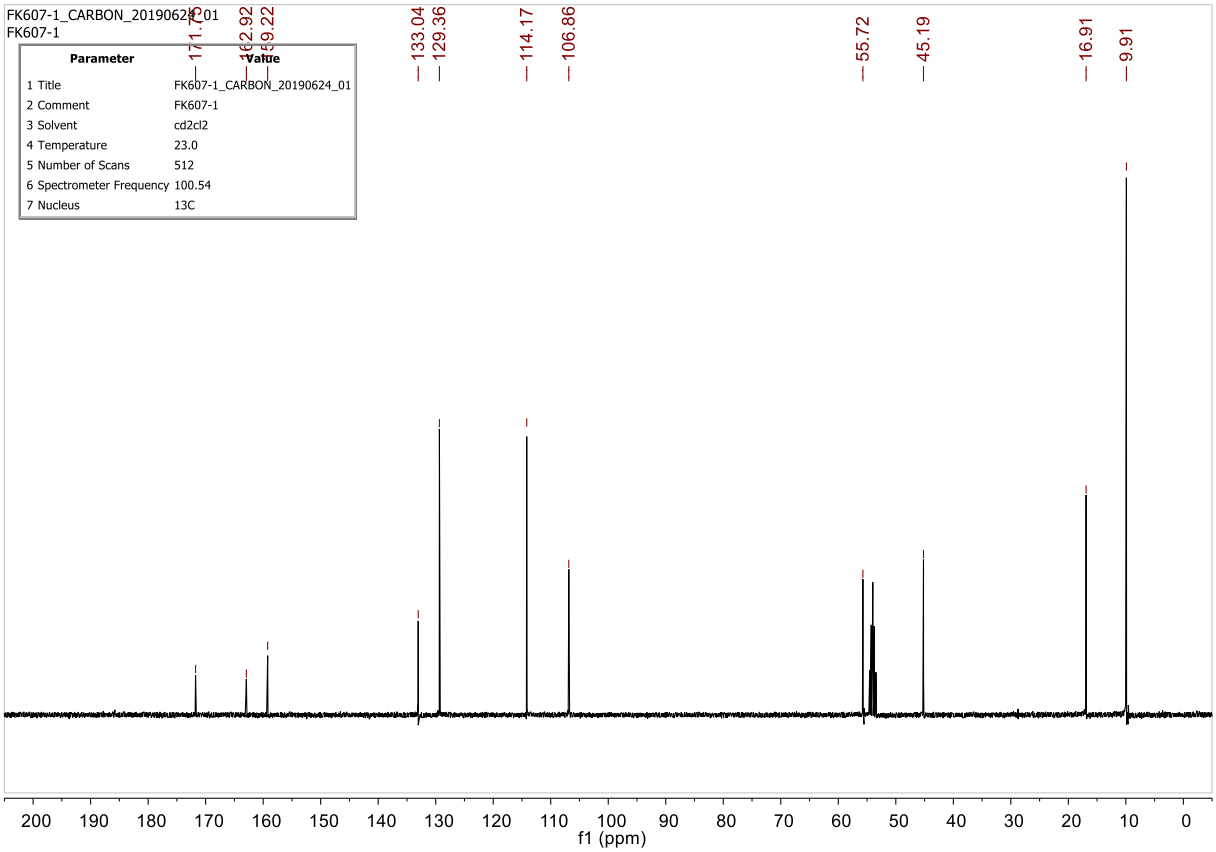
27)N-(4-methoxybenzyl)quinolin-8-amine



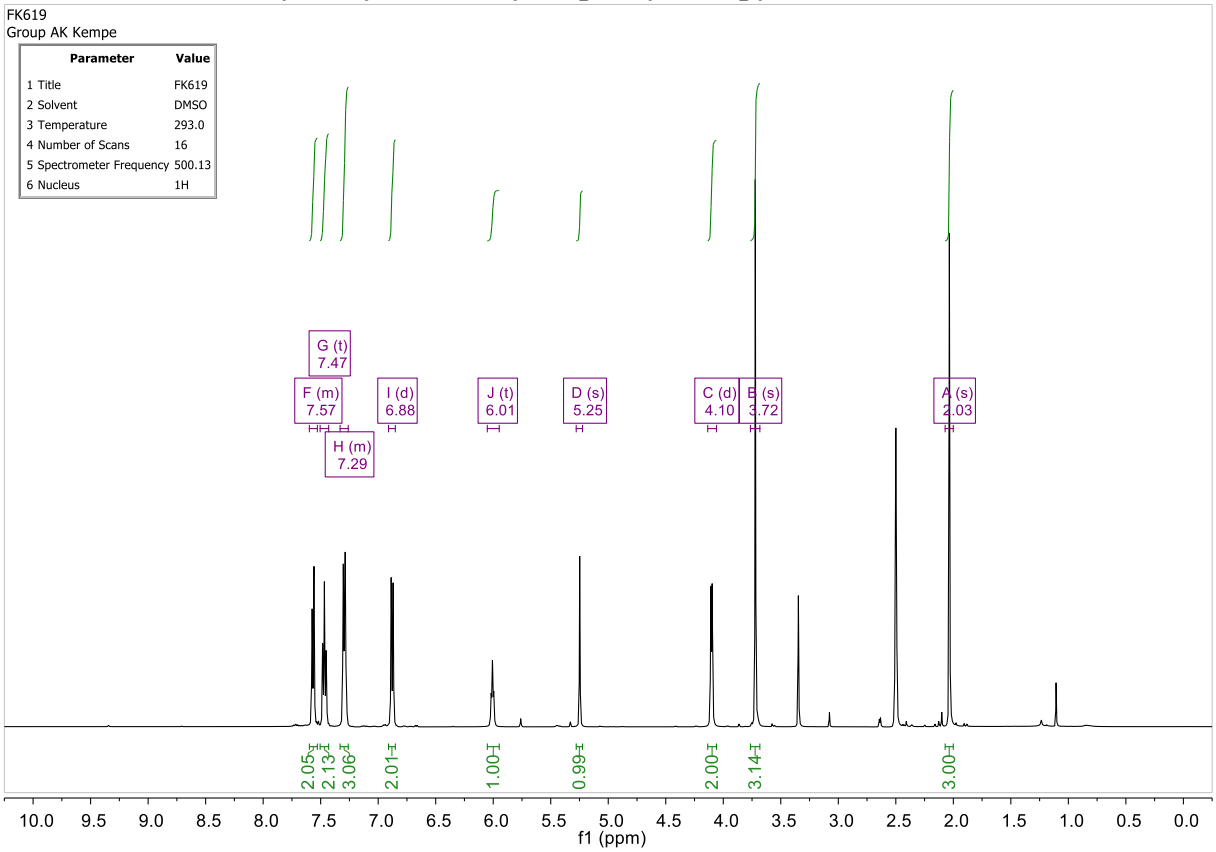


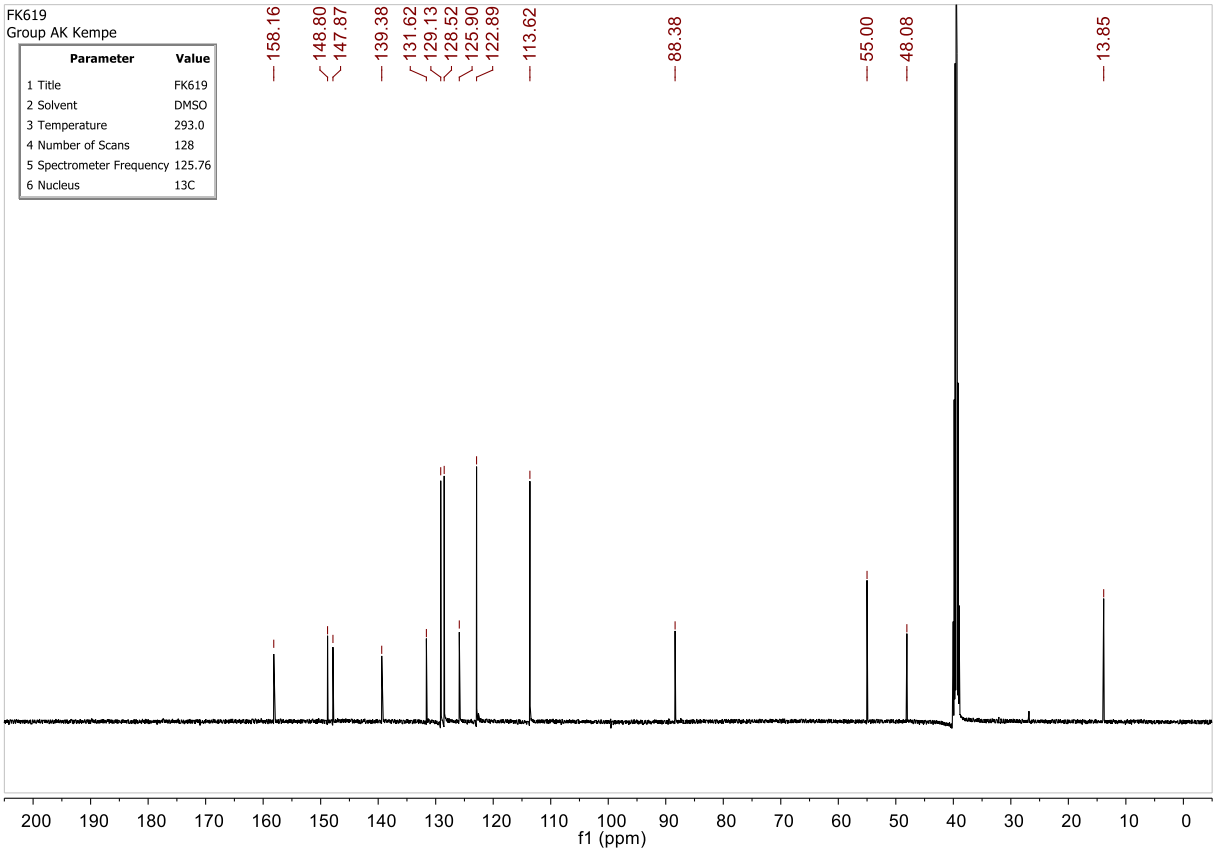
28)4,6-dicyclopropyl-N-(4-methoxybenzyl)pyrimidin-2-amine



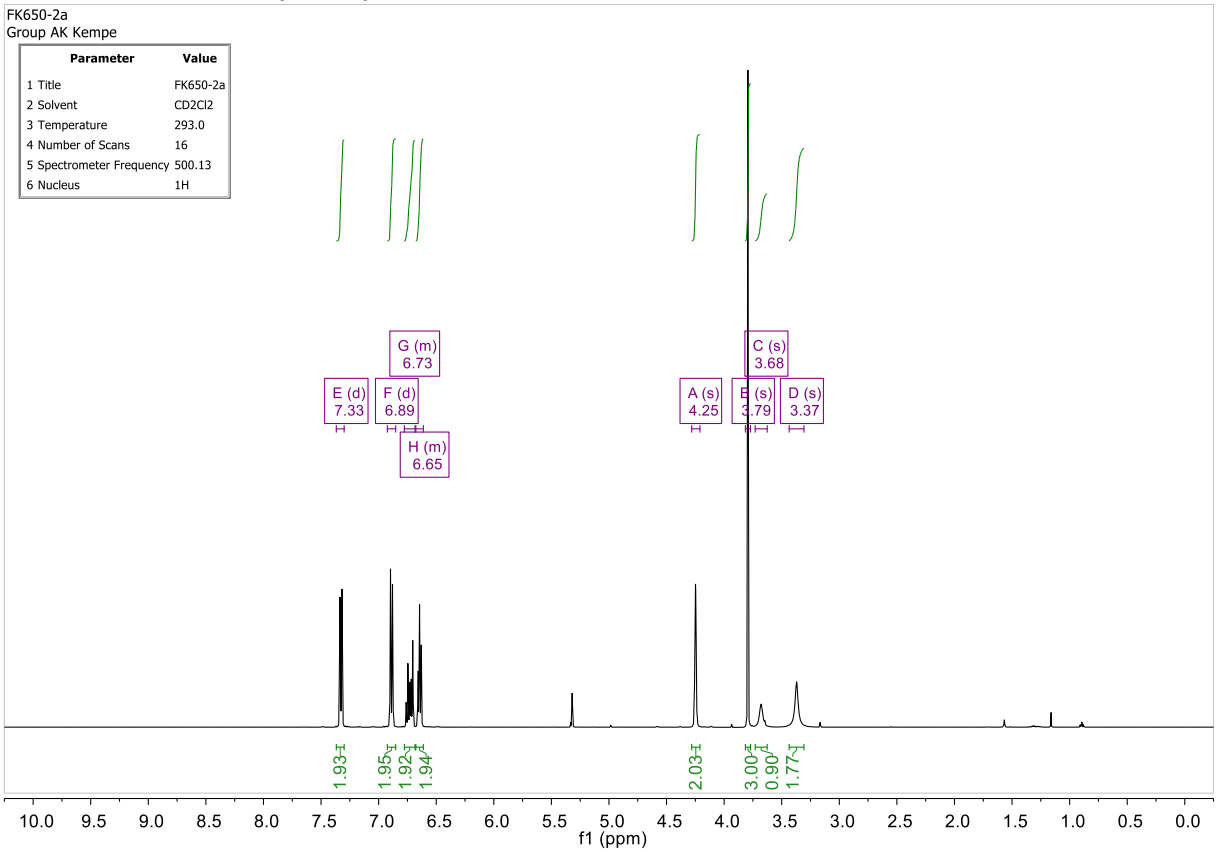


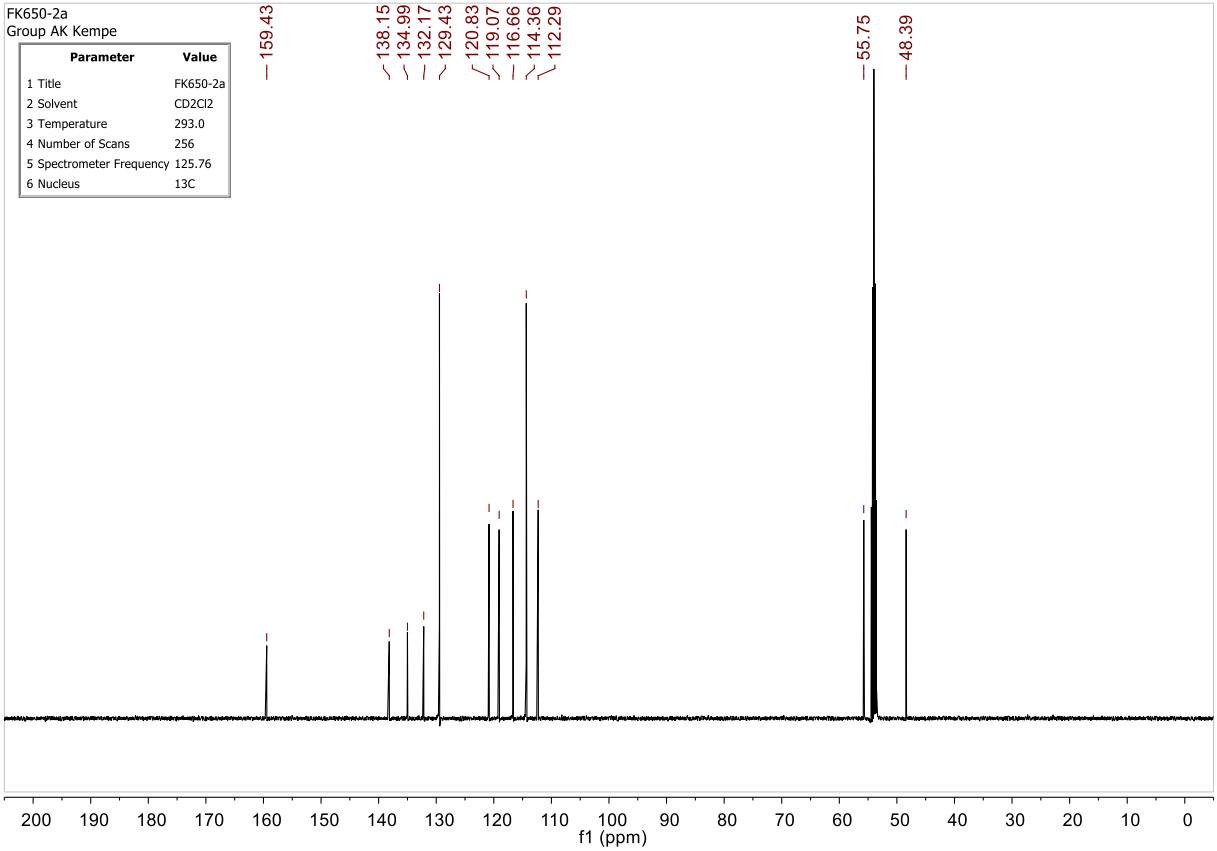
29)N-(4-methoxybenzyl)-3-methyl-1-phenyl-1H-pyrazol-5-amine



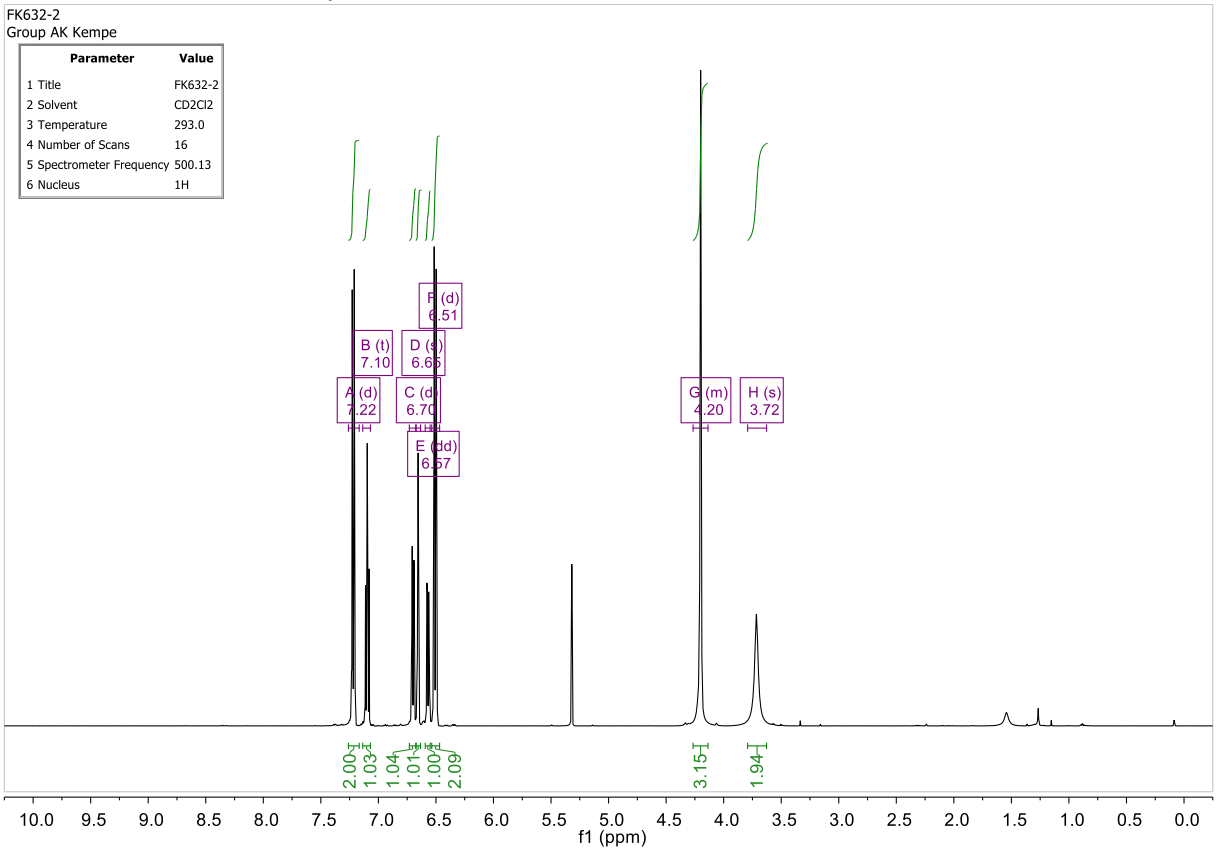


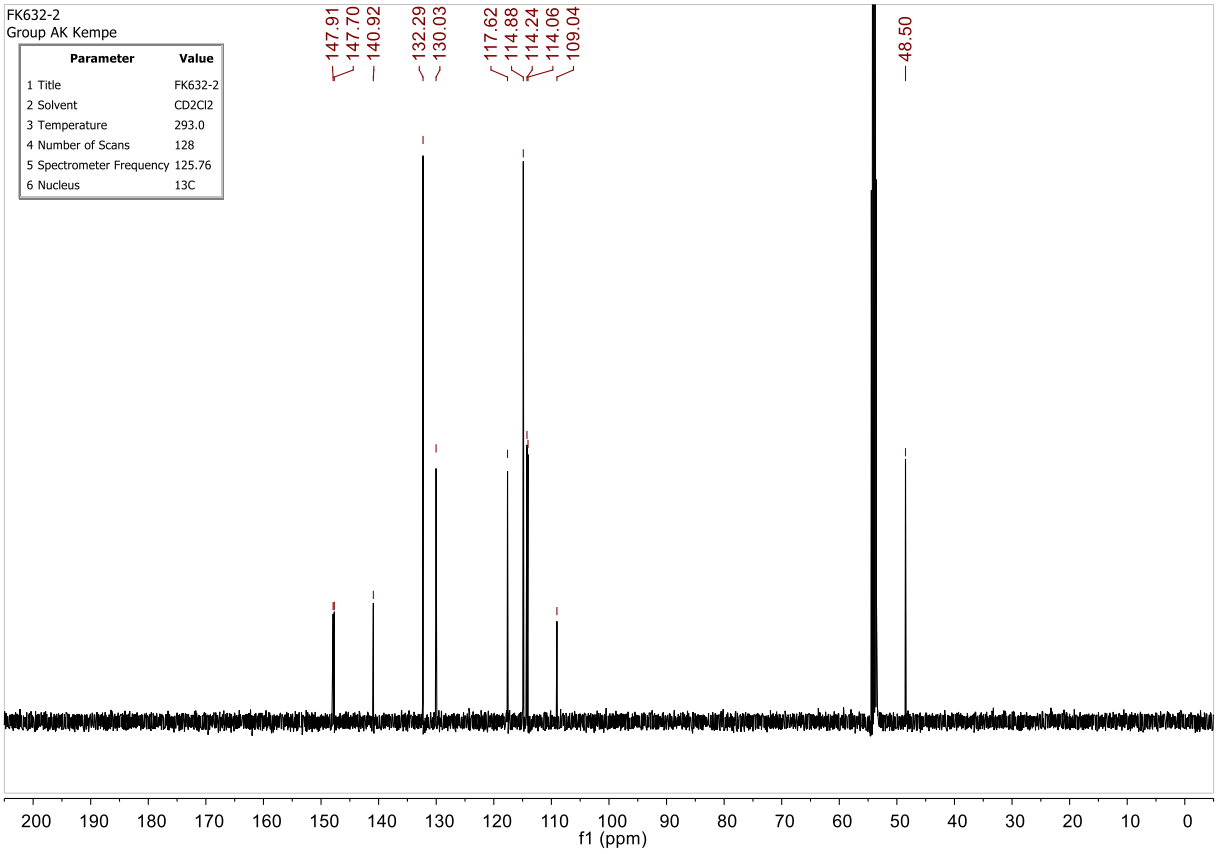
30)*N*-(4-methoxybenzyl)benzene-1,2-diamine



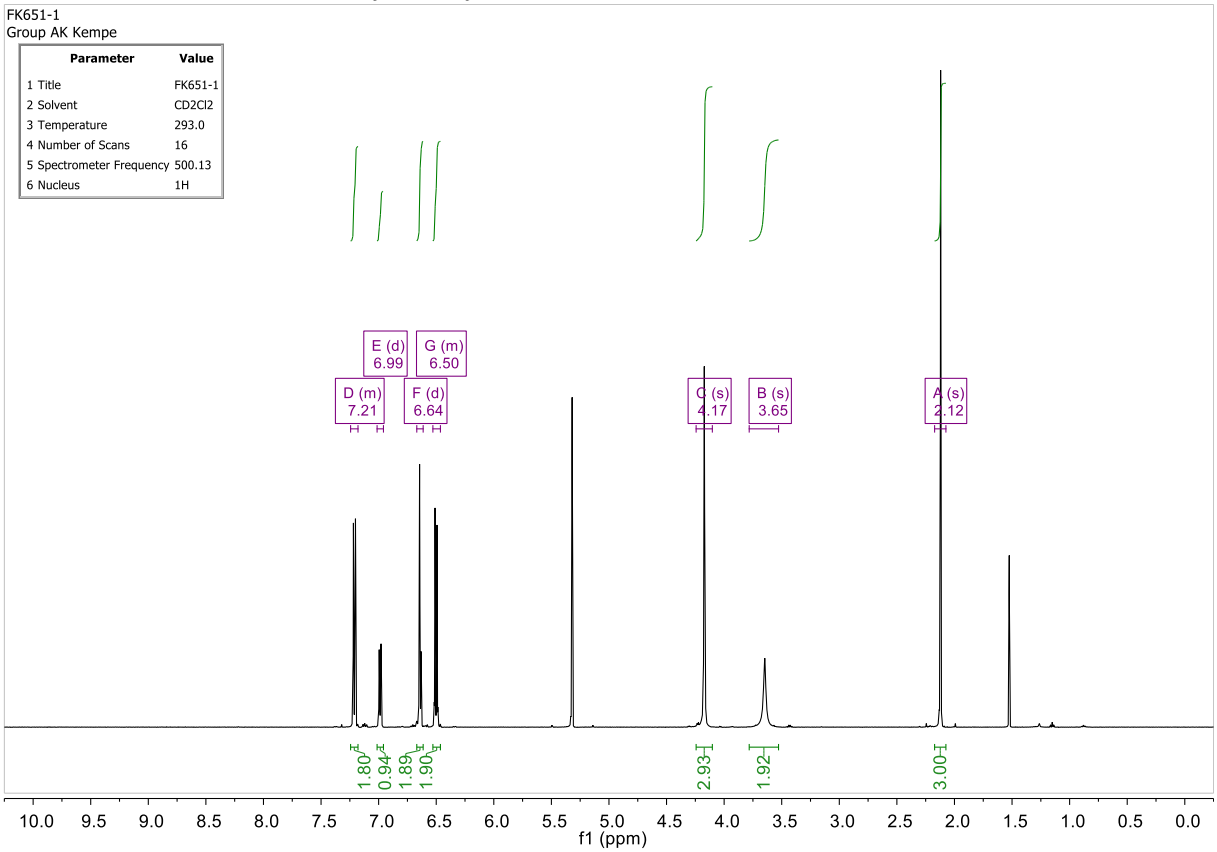


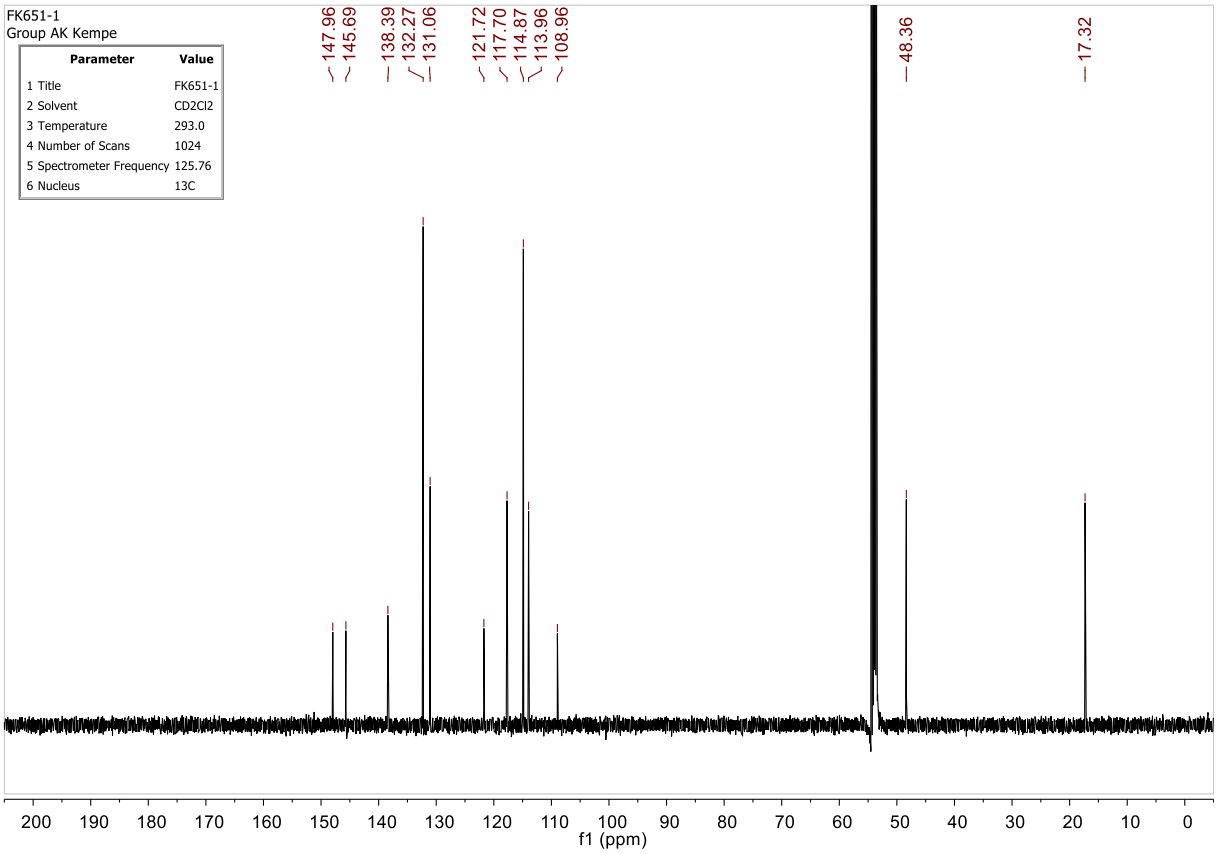
31)*N*-(3-aminobenzyl)-4-bromoaniline



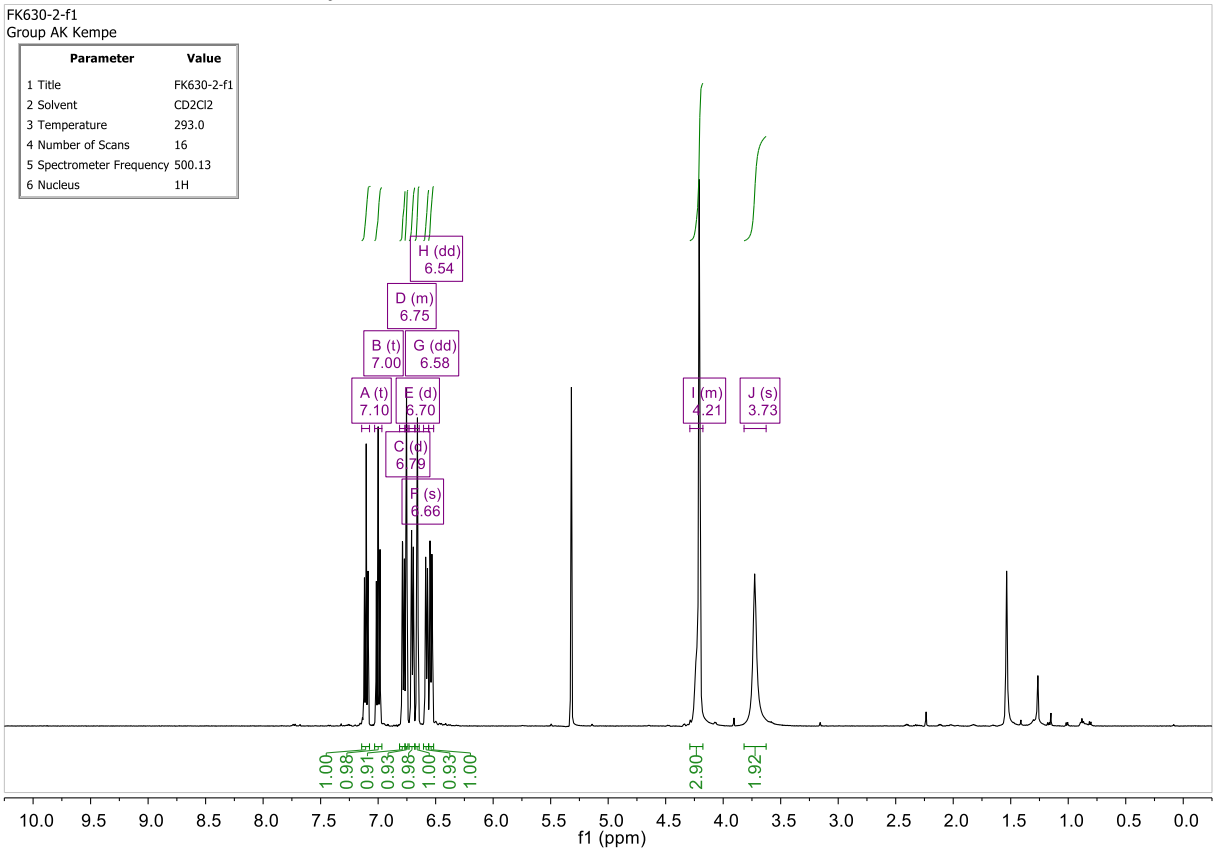


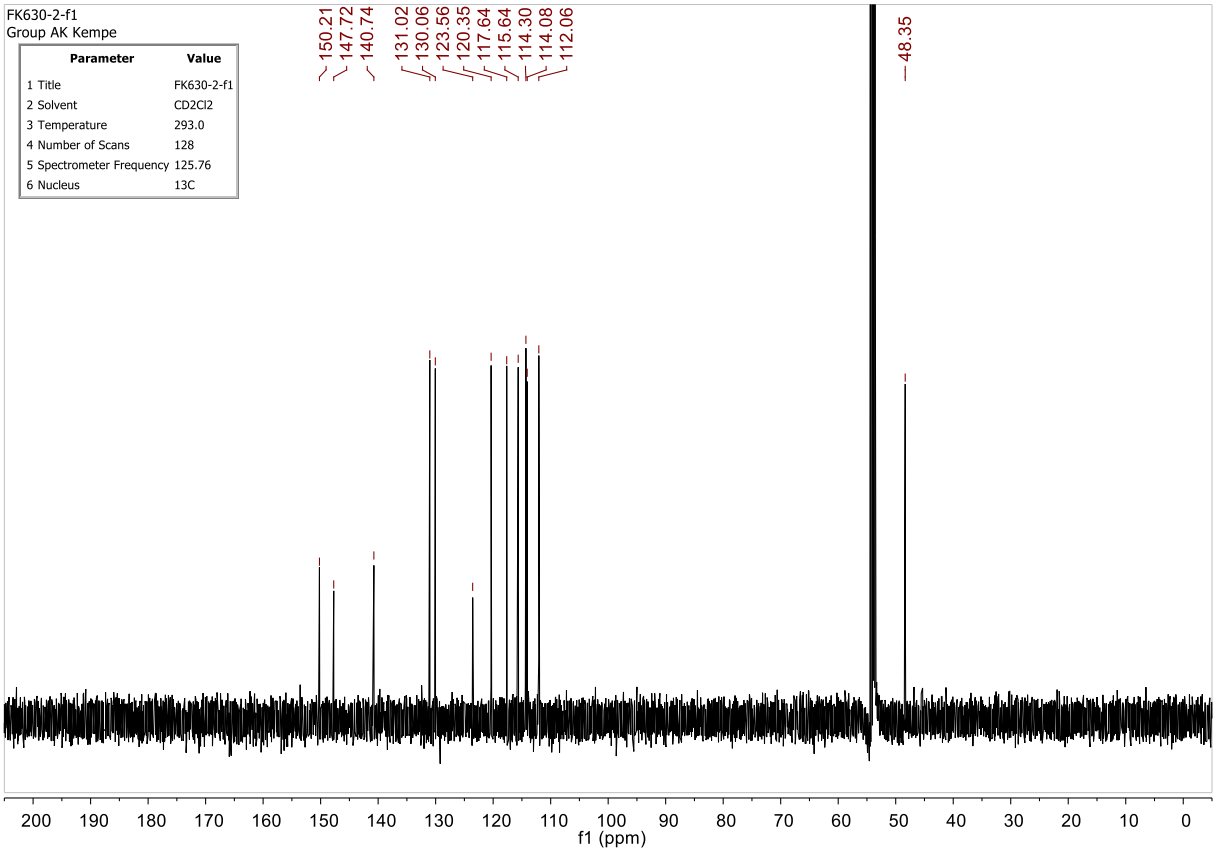
32)*N*-(3-amino-4-methylbenzyl)-4-bromoaniline



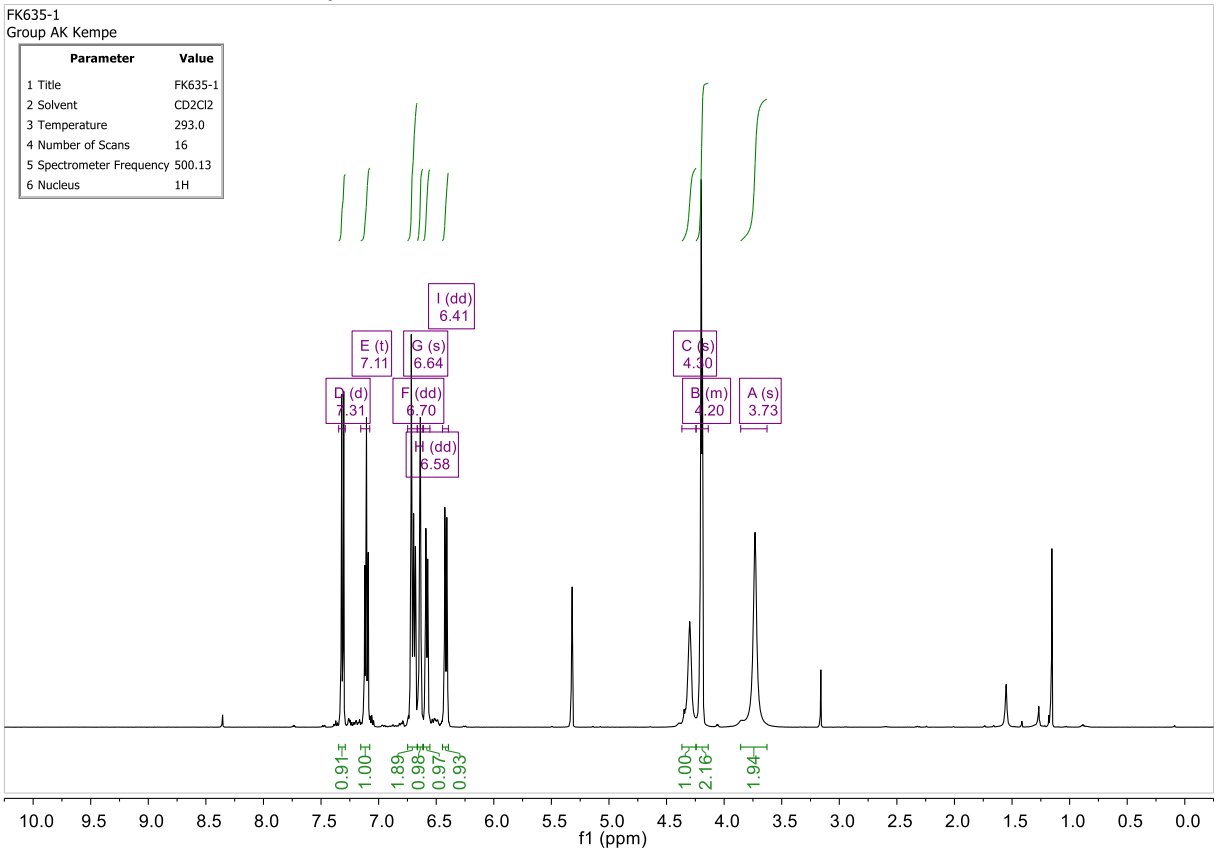


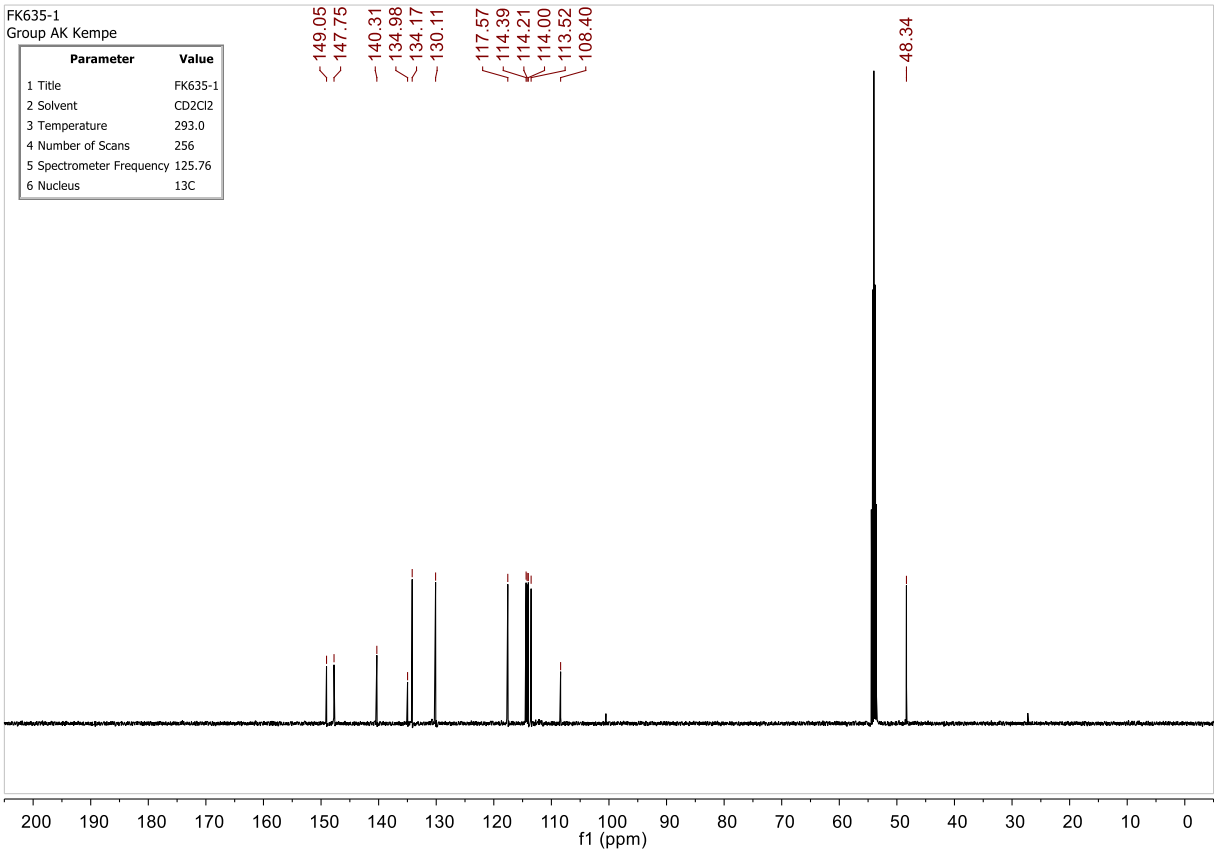
33)*N*-(3-aminobenzyl)-3-bromoaniline



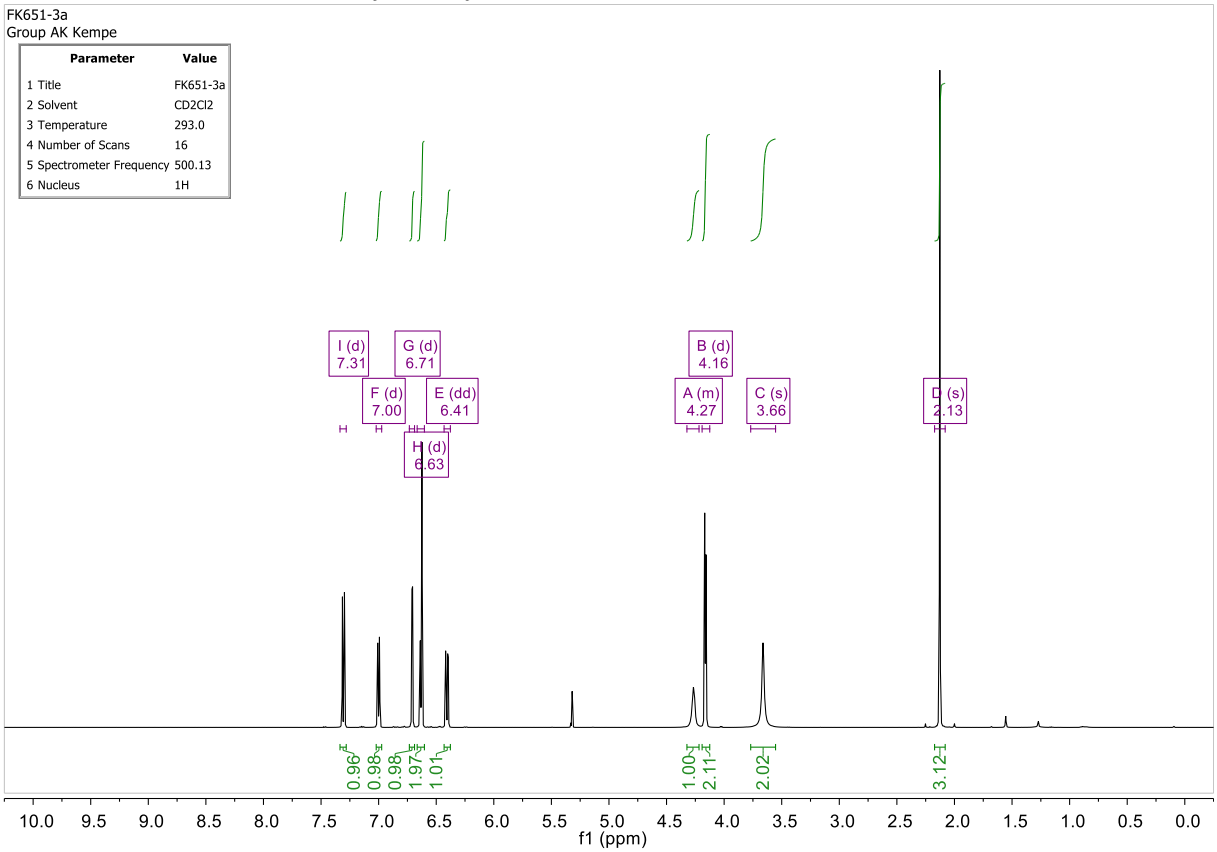


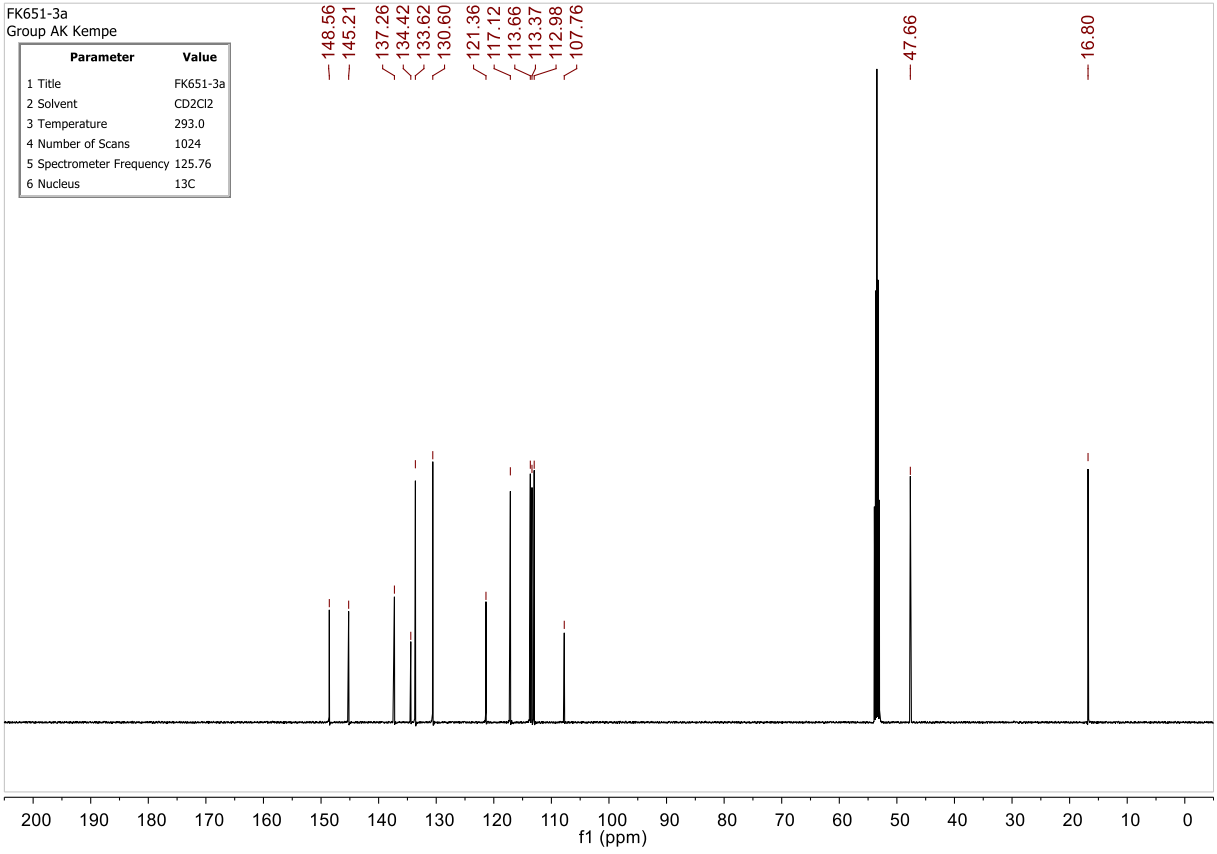
34)*N*-(3-aminobenzyl)-4-bromo-3-chloroaniline





35)*N*-(3-amino-4-methylbenzyl)-4-bromo-3-chloroaniline





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List of Publications

The following publications have been included in this thesis. The asterisk denotes the corresponding author(s).

- Kallmeier, F.; Irrgang, T.; Dietel, T.; Kempe, R.* Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State. *Angew. Chem. Int. Ed.* **2016**, *55* (39), 11806–11809; *Angew. Chem.* **2016**, *128* (39), 11984–11988.

- Kallmeier, F.; Dudziec, B.; Irrgang, T.; Kempe, R.* Manganese-Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols. *Angew. Chem. Int. Ed.* **2017**, *56* (25), 7261–7265; *Angew. Chem.* **2017**, *129* (25), 7367–7371.

- Kallmeier, F.; Fertig, R.; Irrgang, T.; Kempe, R.* Chromium-Catalyzed Alkylation of Amines by Alcohols. *Angew. Chem. Int. Ed.* **2020**, *59* (29), 11789–11793; *Angew. Chem.* **2020,** *132 (29),* 11887-11891.

The following reports have been published parallel to the work on this thesis.

- Kallmeier, F.; Kempe, R.* Manganese Complexes for (De)Hydrogenation Catalysis: A Comparison to Cobalt and Iron Catalysts. *Angew. Chem. Int. Ed.* **2018**, *57* (1), 46–60; *Angew. Chem.* **2018**, *130* (1), 48–63.

- Zhang, G.; Irrgang, T.; Dietel, T.; Kallmeier, F.; Kempe, R.* Manganese-Catalyzed Dehydrogenative Alkylation or α-Olefination of Alkyl-Substituted N-Heteroarenes with Alcohols. *Angew. Chem. Int. Ed.* **2018**, *57* (29), 9131–9135; *Angew. Chem.* **2018**, *130* (29), 9269–9273.

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