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Finally, we would like to extend a thanks to our families for their unfailing support throughout our studies.

Abstract

The thesis explores the Kumada-Corriu coupling reaction as a possible handle to further functionalize PAHs. The starting material used was different types of triflate bearing PAHs.

An attempt at preparing phenanthren-9-yl trifluoromethanesulfonate as starting material failed. The compound was attempted synthesised using a D*o*M/DreM approach. The preparation of naphthalen-2-yl trifluoromethanesulfonate (**5b**) and chrysen-3-yl trifluoromethanesulfonate (**6c**) from naphthalen-2-ol (**5a**) and chrysen-3-ol (**6b**) was a success.

The synthesised triflates were reacted with ethylmagnesium bromide (**14**), vinylmagnesium bromide (**15**), isopropylmagnesium chloride lithium chloride complex solution (**16**) and benzylmagnesium bromide (**10a**) using different catalysators. Yields are given in figure 1. The Ni(dppp)Cl_2 catalysator (general procedure A) gave good yields with both Grignard reagent **14** and **16**. Ni(dppe)Cl_2 (general procedure B) and Pd(dppf)Cl_2 (general procedure D) were somewhat suitable catalysators when reacting with Grignard reagent **15**, but in most attempts 2-vinylnaphthalene (**5d**) was lost during workup. A sustainable Fe(acac)$_3$ catalyst (general procedure C) was also used to couple the majority of the Grignard reagents with triflate **5b** and **6c**. The iron catalyst did not seem suitable for the reaction of alkenyl Grignard reagents, nor the self-generated benzylmagnesium bromide (**10a**).

Further investigation could lead to a successful procedure for the coupling of styrylmagnesium bromide, made from (2-bromovinyl)benzene, whose product can be further cyclised to expand the skeletal structure of PAHs.

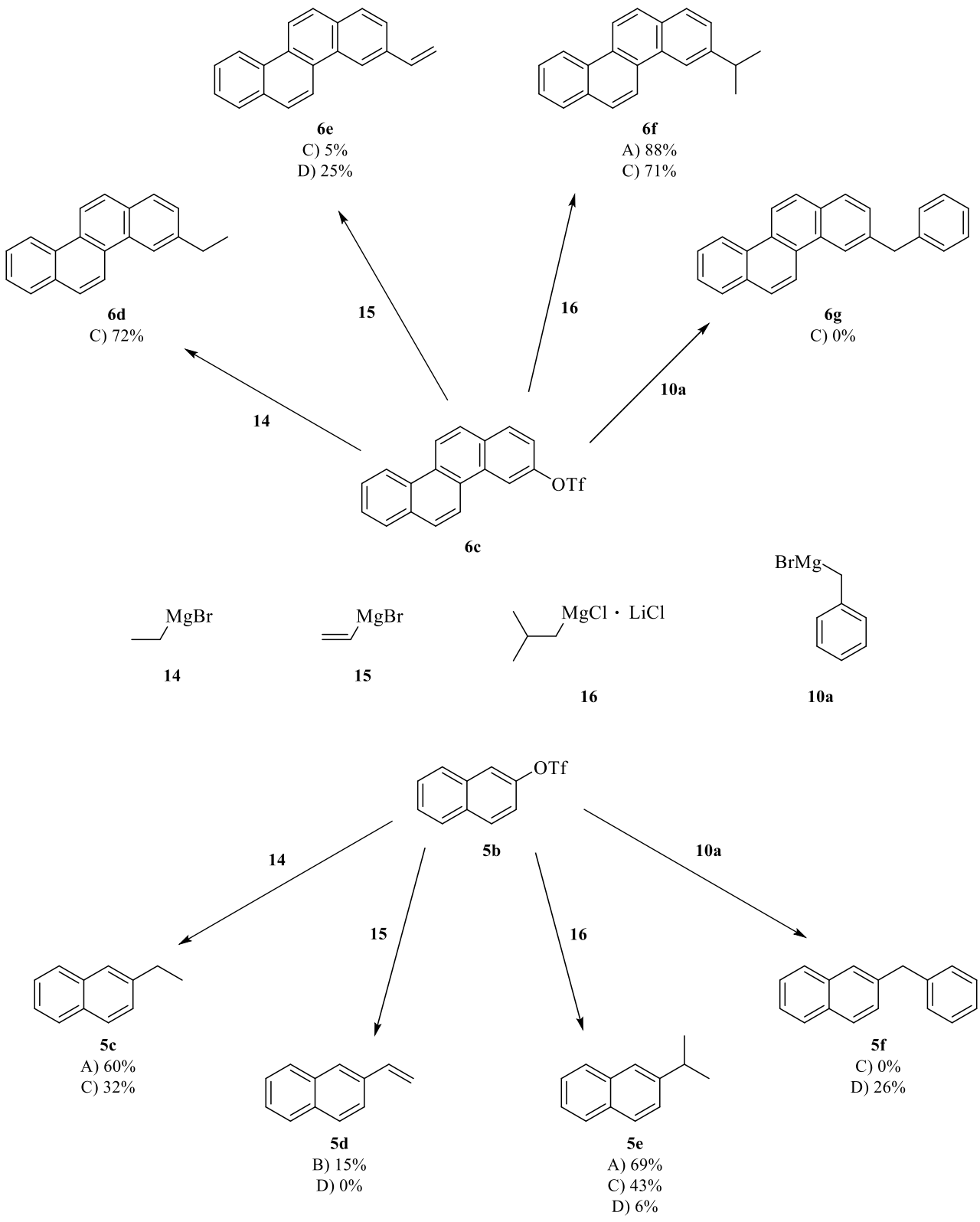

Figure 1: Overview of Kumada-Corriu couplings. A) Ni(dppp)Cl_2 (5 mol%), Et_2O, 0 °C, Reflux 3 hr.B) Ni(dppe)Cl_2 (5 mol%), THF, 0 °C, Reflux 4 hr. C) Fe(acac)$_3$ (5 mol%), THF, 0 °C. D) 1: $ZnBr_2$, LiBr, THF. 2: Pd(dppf)Cl_2 (1 mol%), THF. 3: 50 °C, 24 hr.

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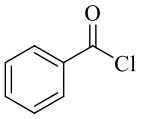
Abbreviations

δ	Chemical shift value
acac	Acetylacetonate
BuLi	Butyllithium
CIPE	Complex-induced proximity effect
d	Doublet
DCM	Dichloromethane
dd	Double doublet
DIA	Diisoproylamine
DME	Dimethoxyethane
DMG	Direct metalation group
DoM	Directed *ortho* metalation
dmpe	1,2-Bis(dimethylphosphino)ethane
dppbz	1,2-Bis(diphenylphosphino)benzene
dppe	1,2-Bis(diphenylphosphino)ethane
dppf	1,1'-Bis(diphenylphosphino)ferrocene
dppp	1,3-Bis(diphenylphosphino)propane
DreM	Directed remote metalation
ds	Double singlet
dt	Double triplet
EA	Ethyl acetate
Eq.	Equivalent(s)
Et	Ethyl
EU	European union
FG	Functional group
Hal	Halogen
Hep	Heptane
hr	Hour
h*ν*	Electromagnetic radiation
Hz	Hertz
i-	*Iso*-
J	Coupling constant, Hz
L	Ligand

LDA	Lithium diisopropylamide
m	Multiplet
M	mol/L
Me	Methyl
MS	Mass spectrometry
NBP	N-butyl-2-pyrrolidone
NHC	N-heterocyclic carbene
NMP	N-Metyl-2-pyrrolidone
NMR	Nuclear magnetic resonance
NORCE	Norwegian Research Centre
o-	*Ortho-*
o.n.	Over night
PAH	Polycyclic Aromatic Hydrocarbon
PCy_2	Dicyclohexylphosphino
Ph	Phenyl
PhD	Philosophiae doctor
Pr	Propyl
q	Quartet
Rf	Retention factor
RT	Room Temperature
s	Singlet
s-	*Sec- (secondary-)*
Salen	N,N′-ethylenebis(salicylimine)
Sat.	Saturated
t	Triplet
Tf	Triflate
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMEDA	N, N, N’, N’-Tetramethylethylenediamine
TMS	Tetramethylsilane
TMSCl	Trimethylsilyl chloride
US EPA	United States Environmental Protection Agency
UV	Ultraviolet

Numbering of molecules



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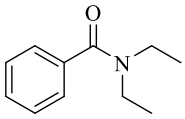

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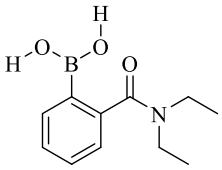

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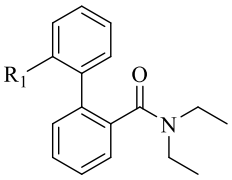
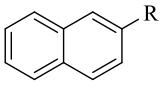
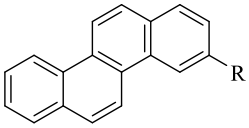


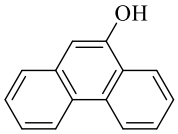
4a: R_1 = Me
4b: R_1 = H



5a: R = OH
5b: R = OTf
5c: R = Etyl
5d: R = Vinyl
5e: R = Isopropyl
5f: R = Benzyl
5g: R = (2-methyl)benzyl



6a: R = OMe
6b: R = OH
6c: R = OTf
6d: R = Etyl
6e: R = Vinyl
6f: R = Isopropyl
6g: R = Benzyl
6h: R = (2-methyl)benzyl



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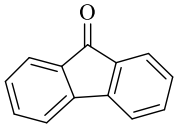

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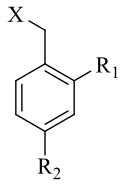
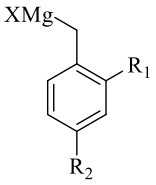
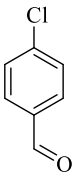


9a: R_1 = H, R_2 = H, X = Br
9b: R_1 = Me, R_2 = H, X = Br
9c: R_1 = H, R_2 = Me, X = Cl



10a: R_1 = H, R_2 = H, X = Br
10b: R_1 = Me, R_2 = H, X = Br
10c: R_1 = H, R_2 = Me, X = Cl



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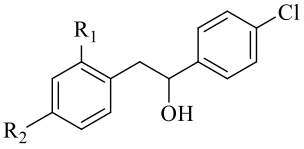
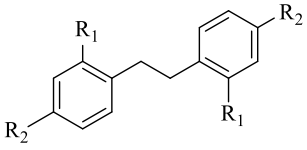
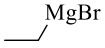


12a: R_1 = H, R_2 = H
12b: R_1 = Me, R_2 = H
12c: R_1 = H, R_2 = Me



13a: R_1 = H, R_2 = H
13b: R_1 = Me, R_2 = H
13c: R_1 = H, R_2 = Me



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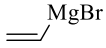

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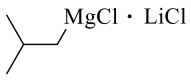

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1. Introduction

The aim of the thesis is to explore the possibility of using Kumada-Corriu coupling to functionalize and expand different systems of PAHs. PAHs are used in different branches of science, including material science, organic synthesis, medical chemistry and astrophysics. PAHs found in marine environments also gets a lot of attention as they are detected in increasing levels and have many effects on marine organisms and human health. The synthesis and functionalization of PAHs is therefore an important area of research. The conventional method of functionalizing PAHs is to install the functionalized groups on the precursor during the synthesis of the PAH. One major reason for this is the inert nature and poor regioselectivity of the C-H bonds in PAHs.[1]

By using the conventional approach, methoxy and hydroxy groups can easily be introduced to PAHs.[2] The introduced group can then easily be converted to a triflate group.[2,3] Triflate is known to be a pseudo halide and can be used in coupling reactions, such as the Kumada-Corriu coupling reaction.[4] By using different coupling partners, this coupling reaction has the potential of becoming a useful handle to work with to further functionalize PAHs. One exciting possibility that has yet to be explored is the potential of increasing the skeleton of the PAH by first coupling with styrylmagnesium bromide, and then photocyclizing the product. This possible pathway is one challenge the thesis aims to explore. The thesis also aims to expand the scope of Kumada-Corriu coupling with triflate bearing PAHs using different catalysators. The $Fe(acac)_3$ catalysator will be thoroughly investigated as it has previously given good results when coupling with triflates.[4] It is also a more environmentally friendly catalysator compared to traditionally used palladium and nickel species.

The synthesis of PAHs has been an area of interest at the University of Stavanger during the last two decades. The project was initiated to provide analytical reference materials for environmental scientists at a local environmental research facility, now known as NORCE. Since 2002, both bachelor students and master students, as well as some PhD students, have been working towards the synthesis of PAHs.[5]

During the first six years the Wittig reaction followed by photocyclization was the main approach to synthesizing PAHs. The general reaction is illustrated in figure 1.1 and was at the time the standard way of making substituted chrysenes.[3] Other types of PAHs can also be synthesized by using the same strategy.

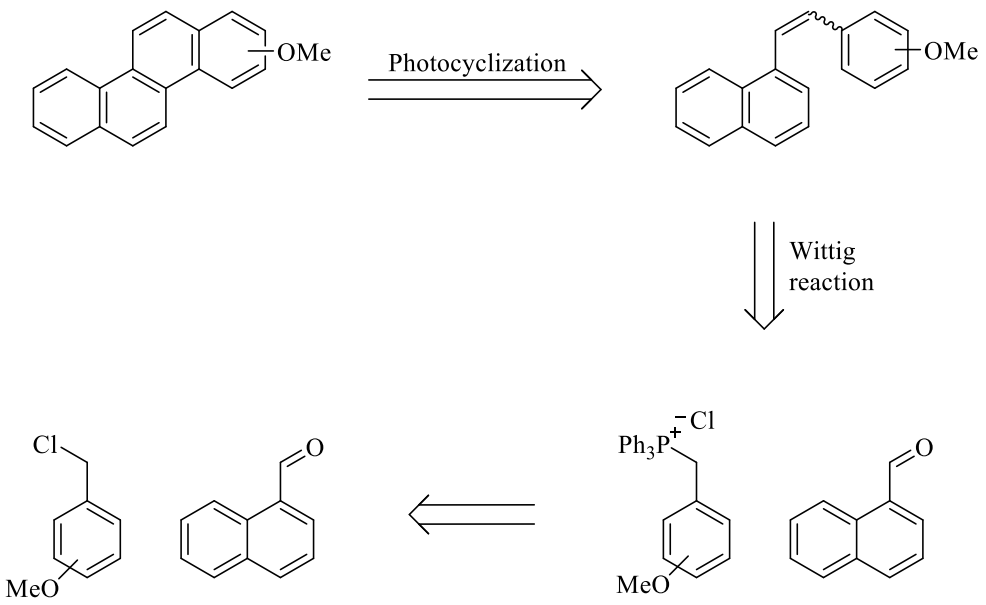


Figure 1.1: Possible retrosynthetic pathway for the construction of methoxychrysene using the Wittig reaction and photocyclization.

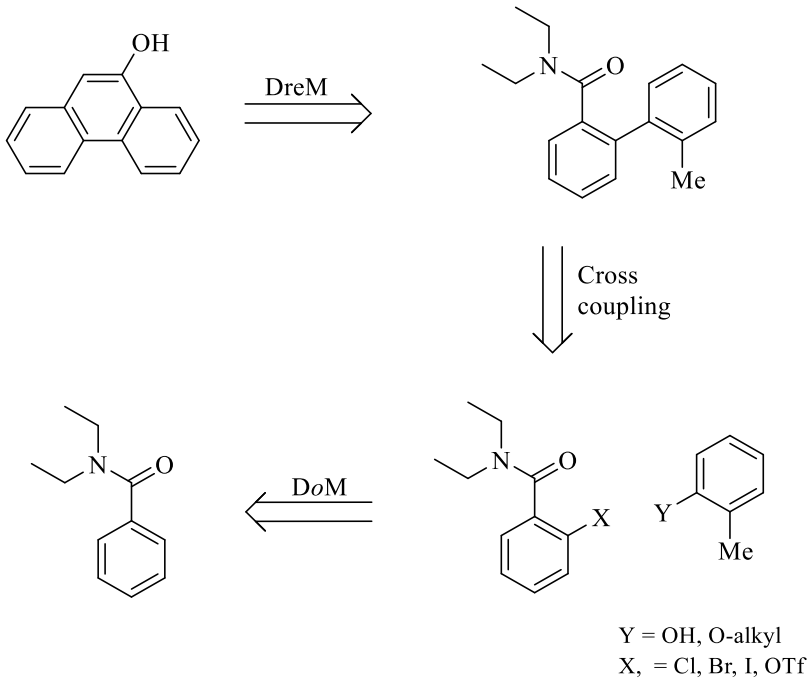


*Figure 1.2: Possible retrosynthetic pathway for the construction of phenanthrol **7** using the DoM/DreM approach.*

More recent experiments have been conducted following a pathway developed by Victor Snieckus which utilizes directed ortho metalation followed by Suzuki-Miyaura coupling and directed remote metalation to synthesise PAHs. All the mentioned reactions are described in subsequent chapters, see 2.2.2, 2.2.3 and 2.2.4. The general approach is illustrated in figure 1.2 and have been performed with both benzene and naphthalene as starting materials to synthesize phenanthrenes and chrysenes.[6,7]

In this thesis triflate bearing naphthalene, phenanthrene and chrysene will be used as starting materials in several Kumada-Corriu couplings. The starting phenanthrene will be synthesized using a D*o*M/DreM approach. The initial starting material is benzoyl chloride (**1**), which will be subjected to an amination creating N,N-diethylbenzamide (**2**).[2] The next step is to react benzamide **2** in a directed *ortho* metalation to create (2-(diethylcarbamoyl)phenyl)boronic acid (**3**).[8,9] The obtained product will then be reacted with 2-bromotoluene to form N,N-diethyl-2'-methyl-[1,1'-biphenyl]-2-carboxamide (**4a**).[9] Lastly a Directed remote metalation will be performed to transform carboxamide **4a** into phenanthren-9-ol (**7**).[9] The mentioned reactions are described in chapter 2.2.1 – 2.2.4 and are illustrated in figure 1.3.

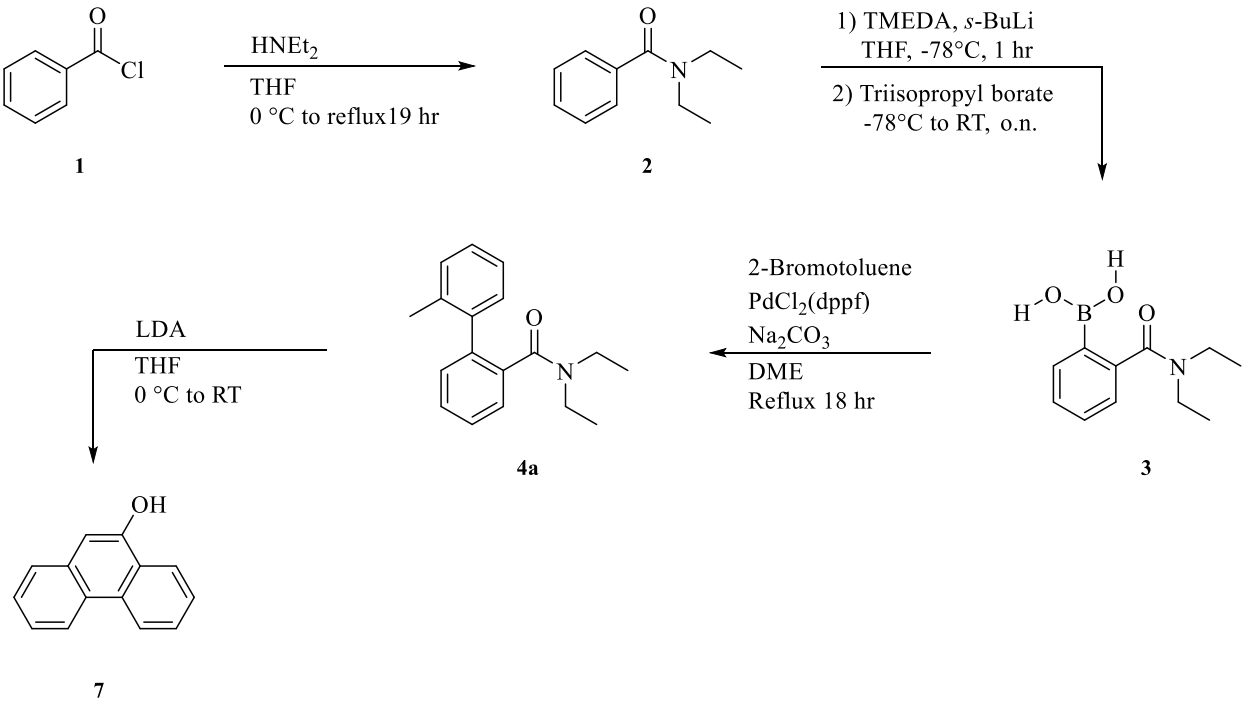


*Figure 1.3: Synthetic pathway that will be used to construct phenanthrol **7**.*

The synthesised phenanthrol will be transformed to a triflate bearing phenanthrene by reaction with triflic anhydride as described in chapter 2.4.[2] Triflate bearing naphthalene will be synthesized using the same procedure from available naphthol **5a**, while chrysenol **6b** can be obtained by demethylation of 3-methoxychrysene (**6a**) using BBr_3 as described in chapter 2.3.[3]

As styrylmagnesium bromide is not available for purchase the reactant will be synthesised from commercially available (2-bromovinyl)benzene. The procedure for creating Grignard reagents is described in chapter 2.5. To be certain that the Grignard reagent has been formed it is possible to react the reagent with an aldehyde to synthesize alcohols.[10] The reaction is known to give almost quantitative yields and is therefore a good indicator for how much Grignard reagent have been synthesised. The reaction of Grignard reagents with aldehydes are described in chapter 2.6.

As there is no standardized method for reacting triflates with styrylmagnesium bromide in a Kumada-Corriu coupling, several approaches will have to be explored to find the best conditions. More information about the Kumada-Corriu coupling reaction is available in chapter 2.7. The photocyclization which will be used to obtain the final products is described in chapter 2.8.

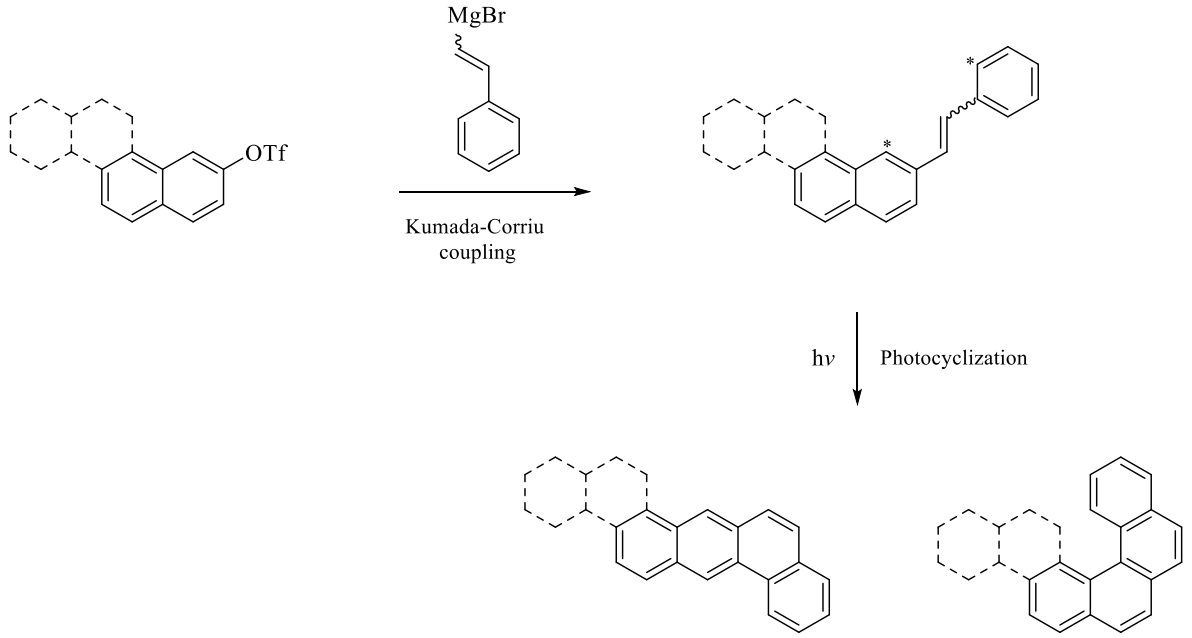


Figure 1.4: Kumada-Corriu coupling can be used together with photocyclization to expand the skeleton of PAHs. The skeleton of the product is dependent on the location of the triflate group. Using different starting triflates will lead to different products than those illustrated.

2. Theory

2.1 Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons, PAHs, are organic species that contain two or more fused aromatic rings. The rings are either five or six membered and built from carbon atoms.[11] The rings can be bonded in angular, linear or cluster arrangements.[12] PAHs include several hundred different compounds which have different chemical properties. Some of these properties are known to cause different health effects, and are considered to be mutagenic, carcinogenic and teratogenic.[13,14] Alkylated PAHs have been shown to be more toxic than the non-alkylated PAHs.[15]

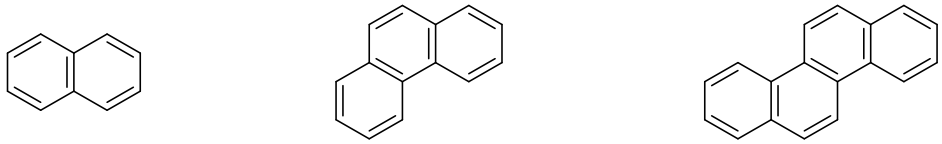


Figure 2.1: Different groups of PAHs.

PAHs occur naturally in crude oil, gasoline and coal, and are as pollutants primarily a result of incomplete combustion of such materials, wood, garbage and tobacco.[11,12,16] PAHs are classified from how they occur. They are divided into four classes called pyrogenic, biological, diagenetic and petrogenic. Pyrogenic PAHs comes from combustion of organic materials like fossil fuel. What specific PAHs that are made in this process are decided by the type of material burned, temperature and access to oxygen. Biological PAHs are produced by certain plants and bacteria. Diagenetic PAHs comes from transformational processes in soil and sediment, over a shorter period of time than the petrogenic. Petrogenic PAHs are found in coal, crude oil, and contaminated water after oil spills. They are also leaked in to the marine environment through natural oil seepage from the seafloor, which are the largest source of oil emission to the oceans.[17,18] The pyrogenic and petrogenic PAHs are most known, and the origin of the species emitted by humans.[12,14] These two groups of PAHs differ in structure. Petrogenic PAHs are either oxygenated to PAH quinones or extensively alkylated, whereas the pyrogenic are not alkylated beyond methyl or ethyl groups.[11,19] This is because PAHs with less alkyl chains tends to be made under higher temperatures.[12] Despite the differences it can in some cases be hard to discriminate between

pyrolytic and petroleum derived products, due to the possible coexistence of contamination and because of the complexity of the distribution of PAHs in the environment.[20]

PAHs are present in most places, and are commonly found in water, air and soil.[21] In the air they are often found in close proximity to certain industrial factories and cities, but they can be spread over long distances by ocean or air currents.[22] The transport of the compounds in air is influenced by the atmospheric partitioning between the particulate and gaseous phases.[12] PAHs can be transferred to soil and water from the air, through rain.[22] They can also be released directly in water through wastewater, industry emissions or spills.[17]

Polycyclic aromatic hydrocarbons are a common pollutant in marine environments and are in increasing levels because of human activity. The pyrogenic and petrogenic PAHs are the two groups that contributes to this in a significant manner.[17] Due to PAHs being big organic molecules, they mostly are hydrophobic and have low aqueous solubility, and will associate to organic particles in the sediments. This causes carcinogenic, toxic and mutagen effects on many living organisms.[14] They are strongly bound to the sediments, but can under specific conditions be released.[12] The bioavailability, and thereby the environmental hazard, of the compounds are largely determined by the characteristics of the PAHs and the composition of the sediments in the area.[17] PAHs have moderate to high toxicity to aquatic life, and it is affected by photo-oxidation and metabolism.[12] The degree of exposure is greatly affected by how the organism obtains food. The PAHs do not necessarily transfer to higher stages in the food chain, even though some organisms on the lower stages are exposed and possibly accumulates PAHs. This is because many organisms have a great ability to break down and excrete PAHs.[17] There has also been done a lot of research on the effect of PAHs on fish and fish embryos.[23] It has been found that generally, in all kinds of fish studied, that PAHs from oil can, among other things, cause problems in the development of the heart, which can cause problems with the circulation system, and malformation of the spine and jaw.[23–25] The malformations will reduce the ability to swim and eat, and can cause death in the larval stage.[23,26,27] In most fish embryo that have been studied it has been the water solvable PAHs that has been bioavailable, but studies on haddock have shown that some fish eggs have hydrophobic shell and can thereby accumulate micro drops of oil that gives strong exposure.[28,29]

PAHs in marine environments gets a lot of attention from the scientific community as they are in increasing levels detected in seawater and sediments, and they have many effects on marine organisms and human health. Even so that there are several PAHs on the priority list of the European Union Water Framework Directive (2000/60/EC), which is there to make a framework for common polices for the EU countries to protect waters from chemical pollution.[30,31] Also the United States Environmental Protection

Agency (US EPA) listed several PAHs as priority pollutants in 1970, including among others naphthalene, phenanthrene and chrysene.[11]

Several PAHs are a potential risk for the health of humans. Many of them are potential carcinogenic and mutagenic, however the effect from indirect, low level exposure are unknown.[16,32] The biggest source of involuntary exposure for humans are in most cases through intake of food.[11] The exposure to PAHs in human can be found by measuring PAH metabolites in urine, to make a basis for comparing and finding health risks.[16] It has also been found that for animals high levels of PAHs has led to difficulty reproducing, higher rates of birth defects and they have been shown to cause harmful effects on skin, body fluids and immune system after both short and long term exposure.[21]

2.2 Preparation of Phenanthrol starting material

As mentioned in the introduction, a DoM/DreM approach will be used to construct the starting material Phenanthrol. The synthetic pathway is illustrated in figure 2.2 and the individual reactions are further described in the subsequent chapters 2.2.1 – 2.2.4.

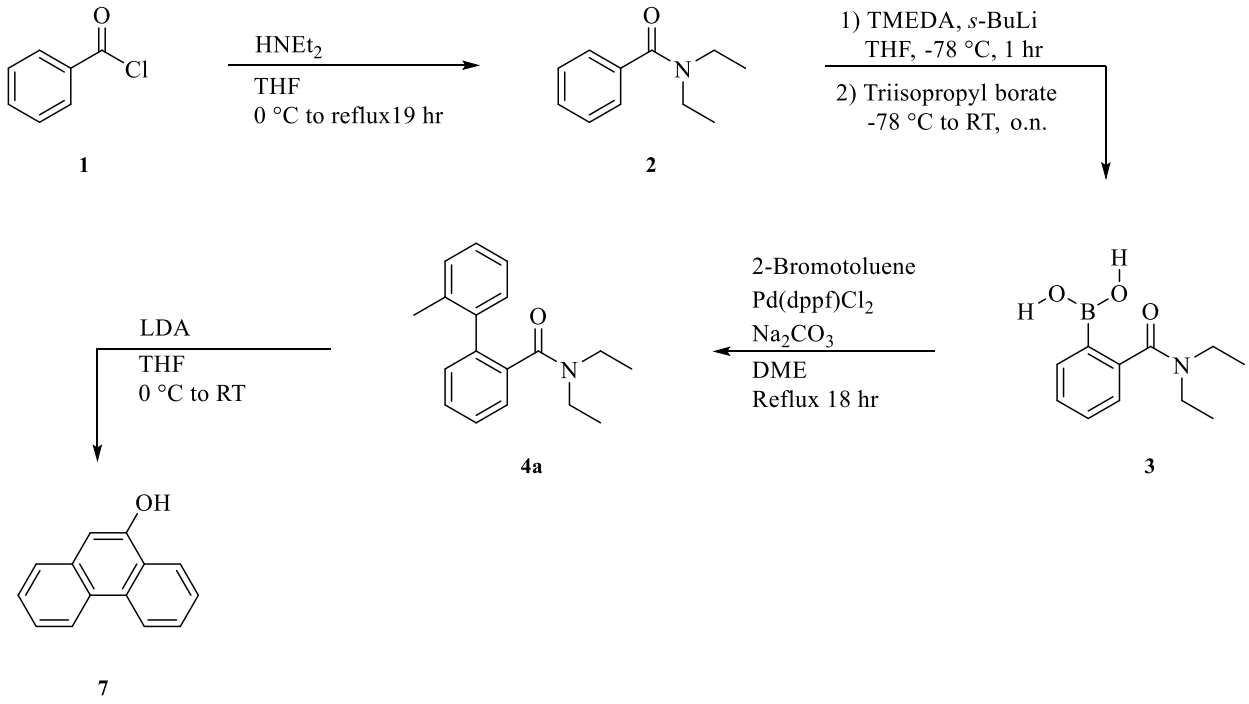


*Figure 2.2: Synthetic pathway of phenanthrol **7** using the DoM/DreM strategy.*

2.2.1 Amination

Amination is the process where an amine group is introduced into an organic molecule. Amination therefore describes a large group of reactions. One such reaction is nucleophilic acyl substitution, where a primary or secondary amine can react with an acid halide to form an amide.[33] The reaction follows a two-step mechanism. First the nucleophile attacks the strongly electrophilic carbonyl group of acid chloride to form a tetrahedral intermediate. The intermediate then expels the chloride ion and loses a proton, thus forming the amide.

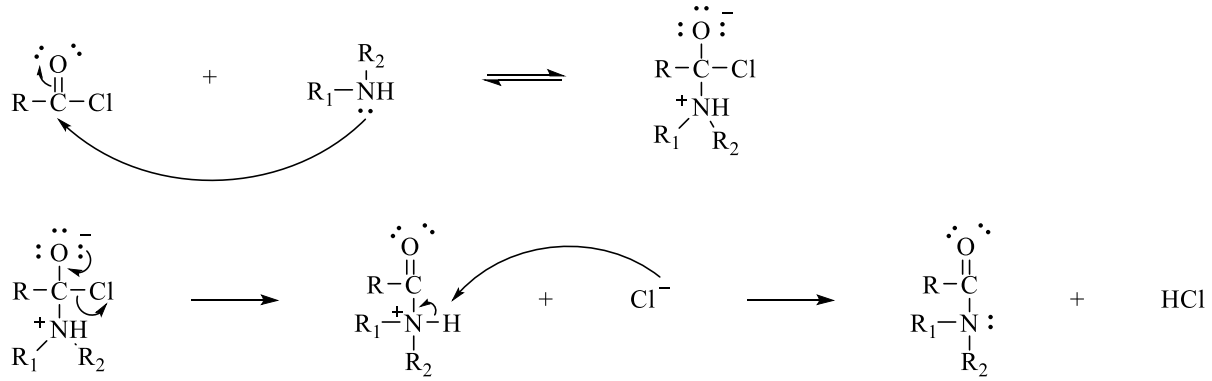


Figure 2.3: Mechanism of the nucleophilic acyl substitution of an amine with acid halide to form an amide.

Amination can be used to synthesize benzamide **2** in good yields by reacting acid chloride **1** with diethylamine in dry THF and refluxing for 18 hours.[2]

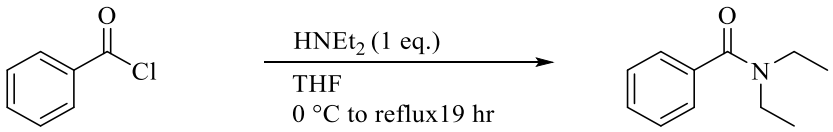


*Figure 2.4: Synthesis of benzamide **2**.*

2.2.2 Directed *ortho* Metalation

Metalation is a chemical process in which a metal atom is introduced into an organic molecule to form an organometallic compound.[34] In directed *ortho* metalation (D*o*M) an electrophile substitutes into *ortho* position due to a directing metalation group (DMG) reacting with alkyllithium.[35] The alkyllithium reagent exists as various aggregates in solution and requires an amine additive, such as TMEDA, which function is to break up the aggregates. The outcome is accelerated reactivity as the basicity is increased.[35]

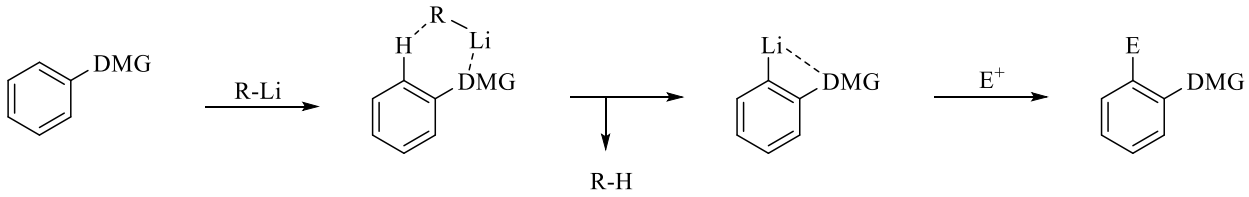


*Figure 2.5: Proposed mechanisms of D*o*M reaction according to CIPE theory.*

The initial mechanism of the reaction can be explained by the complex-induced proximity effect, also called CIPE.[36] According to the CIPE theory, the organolithium is brought into proximity of the DMG group because of Acid-Base Lewis attractions which creates a pre-lithiation complex. The basicity of alkyllithium then promotes deprotonation in *ortho* position, which attracts the lithium cation. By quenching with an electrophile, a polysubstituted aromatic compound is formed where the electrophile takes the place of the lithium cation.

Metalation with organometallic compounds was first discovered by Henry Gilman in 1939 and then independently by Georg Wittig in 1940.[37,38] Metalation has since become significant as it is a unique way to functionalize aromatic and heterocyclic compounds. In recent years the DoM reaction has been increasingly used in the synthesis of highly substituted aromatic systems. The main reason for this is that alternative synthetic pathways tend to be more extensive and less efficient.[39] Another advantage of using the DoM reaction compared to traditional electrophilic substitution, is increased regioselectivity. The DoM reaction will only give *ortho* substituted product while traditional electrophilic substitution gives a mixture of both *ortho* and *para* substituted product.[33]

The DoM reaction can be used to synthesize boronic acid **3** in good yields. By reacting benzamide **2** with *s*-BuLi and TMEDA in THF at -78 °C it is possible to form (2-(diethylcarbamoyl)phenyl)lithium. Upon quenching with triisopropyl borate compound **3** will form.[8,9]

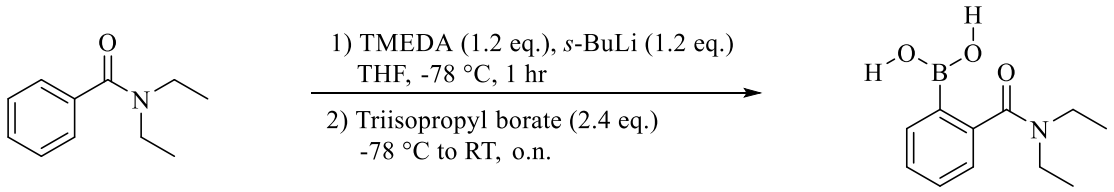


*Figure 2.6: Synthesis of boronic acid **3**.*

2.2.3 Suzuki-Miyaura Cross Coupling

The Suzuki-Miyaura reaction is a catalysed cross coupling between an organic halide and organoborane that can be used to create carbon-carbon bonds.[33,40] The most common catalysts used in the coupling is different palladium species.[41]

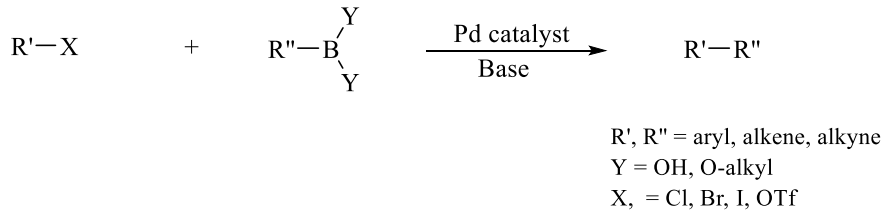


Figure 2.7: The general Suzuki-Miyaura cross coupling reaction.

There exists a widely accepted mechanism for the palladium catalysed Suzuki-Miyaura cross coupling. The proposed mechanism is illustrated in figure 2.8. The mechanism begins with an oxidative addition where the electron-rich Pd^0 is inserted into the organohalide to form an organo-Pd^{II} complex. Some of the base then replaces the halide on the complex, while another part of the base adds to the organoborane to form a borate reagent with a highly nucleophilic R'' group. The next step is a transmetalation where the R'' group of the borate is transferred to the Pd^{II} complex, where it replaces the base. Afterwards a reductive elimination happens where the coupled product is obtained, and the catalyst is regenerated to its initial form.[42]

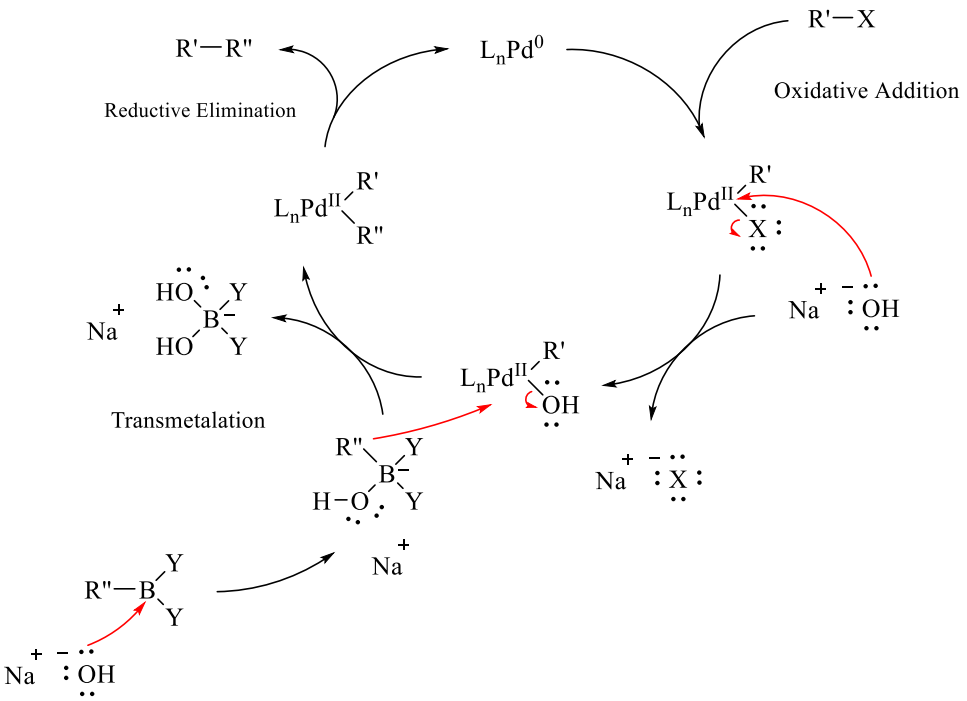


Figure 2.8: Proposed mechanism of the palladium catalysed Suzuki-Miyaura cross coupling reaction.[42]

The catalyst used in the reaction consists of a precursor with ligands. In general, the catalysts have been developed to be electron-rich, which facilitates oxidative addition, and spatially bulky, which facilitates reductive elimination.[41,43] The precursor is most often Pd^0, while the ligands can be several different species. Currently there does not exist an ideal ligand that satisfies all the requirements of the different Suzuki-Miyaura couplings.[43] It is therefore important to consider which ligand is most suitable for a given reaction. Ligands are categorized depending on which atom is coordinated with the metal. There exist three different groups of ligands, namely phosphine ligands, carbon ligands and nitrogen ligands.[41] Today the most commonly used ligands are phosphine-based.[43]

The Suzuki-Miyaura cross coupling reaction was first reported by Akira Suzuki and Norio Miyaura in 1986.[44] The original reaction was between 1-alkynboranes and aryl halides.[44] Boronic acids had already, a decade before, been identified as competent coupling partners by Richard F. Heck. His discovery was however limited by the requirement of stochiometric quantities of palladium.[45] Suzuki and Miyaura overcame this and demonstrated that the reaction could be performed with only catalytic amounts of palladium. Since then, the reaction has been further developed and become an important tool in organic synthesis. Today many different boronate species can be used as coupling partners, though it is still most common to use boronic acids or boronate esters.[46] Suzuki was in 2010, together with Heck and Ei-ichi

Negishi, awarded the Nobel Prize in chemistry for his contribution to palladium-catalysed cross coupling in organic synthesis.[47] The Suzuki-Miyaura reaction is today one of the most utilized cross-coupling reactions in organic chemistry and the most frequently used reaction to form $C(sp^2)$-$C(sp^2)$ bonds in pharmaceutical industry.[44,46]

One of the advantages of the Suzuki-Miyaura reaction is its versatility and broad range of application. Another advantage of the reaction is the mild conditions, which allows for an excellent functional group tolerance. The reaction uses organoboron reagents, which are known to be relatively stable, readily available, and relatively environmentally friendly.[48] The organoboranes are inert to water, which makes it possible to perform the reaction with water as solvent.[49] This can be advantageous in both labs and industrial processes.[33] One limitation of the Suzuki-Miyaura reaction is low reactivity when the halide is chloride. Another known disadvantage is production of side products if a base is not used. The availability of borane can also be a limitation as not all desired R groups can be found on commercially available substrates.[41] Another disadvantage is the possibility of *β*-hydride elimination when working with reactants bearing *β*-hydrides.[50] *β*-hydride elimination is a known side reaction that competes with the transmetalation step in the formation of product. Choosing the right catalysator is important in reducing the possibility of such a side reaction.

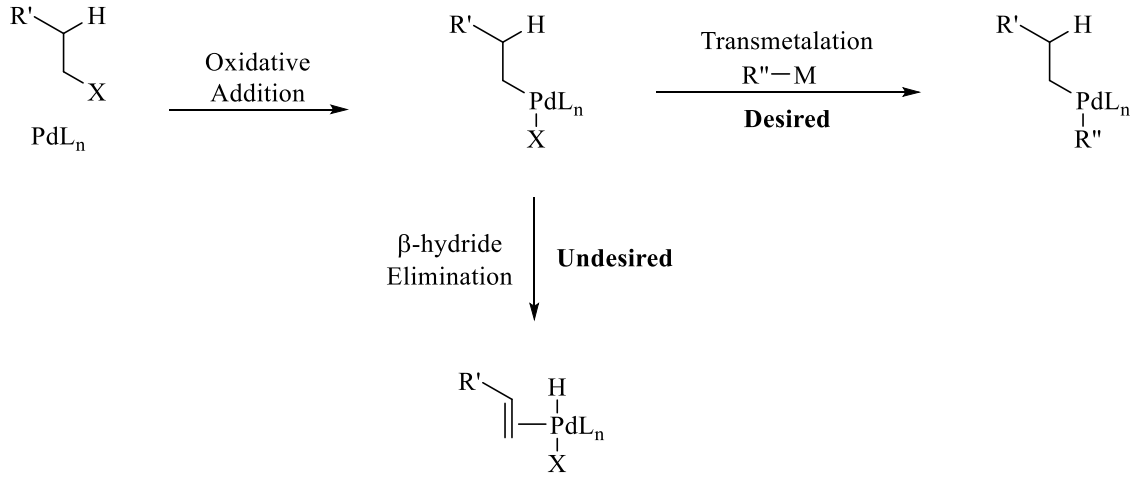


Figure 2.9: Suzuki-Miyaura reagents bearing β-hydrides have the possibility of forming undesired by-products.

The Suzuki-Miyaura cross coupling reaction can be used to synthesize carboxamide **4a** in good yields. The product is obtained by reacting boronic acid **3** with 2-bromotoluene and 2 M Na_2CO_3 catalysed by a palladium species. Both $Pd(dppf)Cl_2$ and $Pd(PPh_3)_4$ have been shown to be suitable catalysators under somewhat different conditions.[6,9]

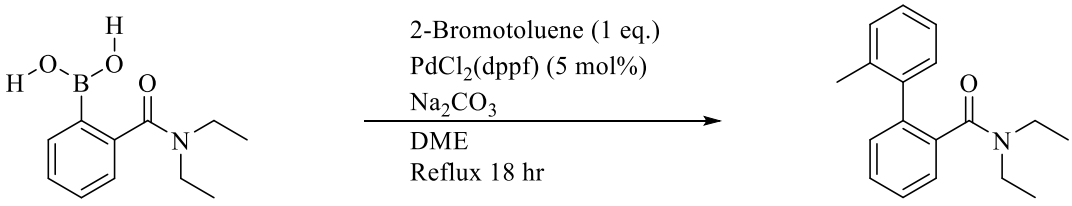


*Figure 2.10: Synthesis of carboxamide **4a**.*

2.2.4 Directed remote Metalation

Directed remote metalation (DreM) may be seen as an extension of the DoM reaction, where the directing property of the DMG group reaches beyond the hydrogen atoms in *ortho* position, to more "remote" hydrogens as illustrated in figure 2.11.

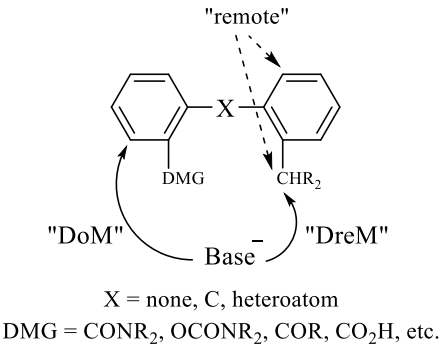


Figure 2.11: The base used in a DreM reaction will react with remote hydrogens.

The regioselective outcome of a directed metalation will depend on several factors. The CIPE theory, the nature and strength of the base, kinetics and the electrophilic and migrating properties of the DMG are of importance. Other factors that can be determining for the regioselective outcome are the acidity of aromatic hydrogen atoms, stability of metalated products and the rigidity of the reactant skeletons. When the reaction is performed on flexible biarylic structures with an electrophilic, non-migrating DMG group,

cyclic compounds will be formed. This is because of an intramolecular nucleophilic substitution of a remote anionic species onto the electrophilic DMG group.[36]

The mechanism of the DreM reaction is dependent on several factors, including most of the factors mentioned above. In 2010 Tilly et al. reported a study on the mechanism of the LDA-mediated *ortho* and remote metalation of N,N-dialkyl-2-biphenyl carboxamides.[51] The study proposes a mechanism for the cyclization of 9*H*-fluoren-9-one (**8**) from N,N-diethyl-[1,1'-biphenyl]-2-carboxamide (**4b**), which is illustrated in figure 2.12. The starting material is believed to equilibrate between the *ortho* and remote lithiated species. When there is no external electrophile available, the DreM product will be synthesized as the cyclization step is irreversible. When an external electrophile is available the D*o*M product will be synthesized as this reaction proceeds faster.

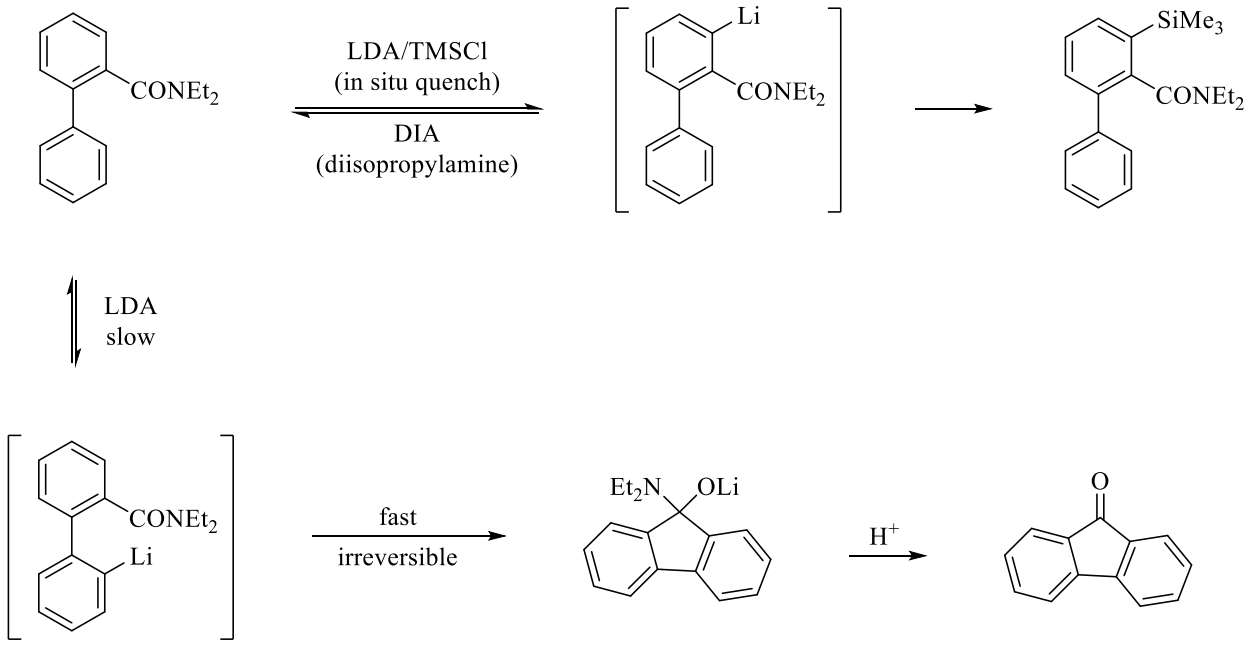


Figure 2.12: Proposed mechanism of LDA-mediated ortho *and remote metalation of* ***4b***.[51]

The DreM reaction can be used to synthesize phenanthrol **7** in good yields. By reacting carboxamide **4a** with LDA in THF at 0 °C (2'-(diethylcarbamoyl)-[1,1'-biphenyl]-2-yl)lithium will be formed. Upon quenching with acid, phenanthrol **7** is synthesised. LDA can be generated in situ by reacting equivalent amounts of *s*-BuLi with diisopropylamine and favours deprotonation of the methyl group.[9]

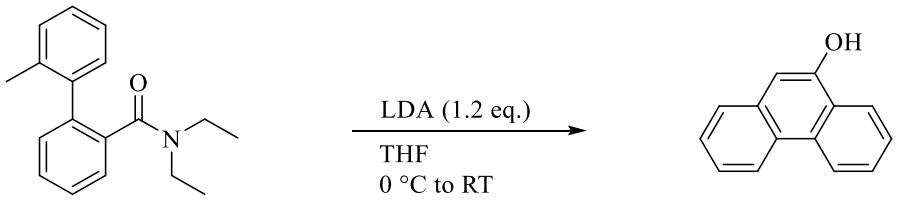


*Figure 2.13: Synthesis of phenanthrol **7**.*

2.3 Demethylation with BBr_3

Demethylation is a deprotection of a methoxy group and can be done with boron tribromide at low temperature, which when quenched with ice gives an alcohol group.

Boron tribromide has a boron centre which is a Lewis acid, this gives it a high reactivity. It can be used in many reactions, but many of them have mechanisms that are not elucidated.[52] Because of its tolerance for many functional groups it is often used as an ether-cleaving reagent, where aryl ethers are divided into phenols and bromoalkanes, and on alkyl ethers the most substituted carbon on the ether bond becomes brominated.[53]

Demethylation was earlier expected to start with the formation of an ether adduct. According to this mechanism both the methyl and the boron centre of the BBr_3 are bound to the ether's oxygen. After this adduct is formed one of the bromides are lost as a free nucleophile. The methyl group of the cationic intermediate is attacked by the bromide and cleaves the C-O bond. The $OBBr_2$ group will in aqueous work-up undergo hydrolysis to form an alcohol.[52]

In 2013 Sousa and Silva proposed an alternative mechanism for the cleavage of ethers, which most likely is the mechanism for cleavage of highly branched aliphatic ethers.[52,53] Insights from their proposal was used by Lord et al. to envision a new possible mechanism through a bimolecular process for demethylation on aryl methyl ethers, where it happens in a three-cycle mechanism to couple four ethers to the boron centre.[52] The three-cycle mechanism is illustrated in figure 2.14.

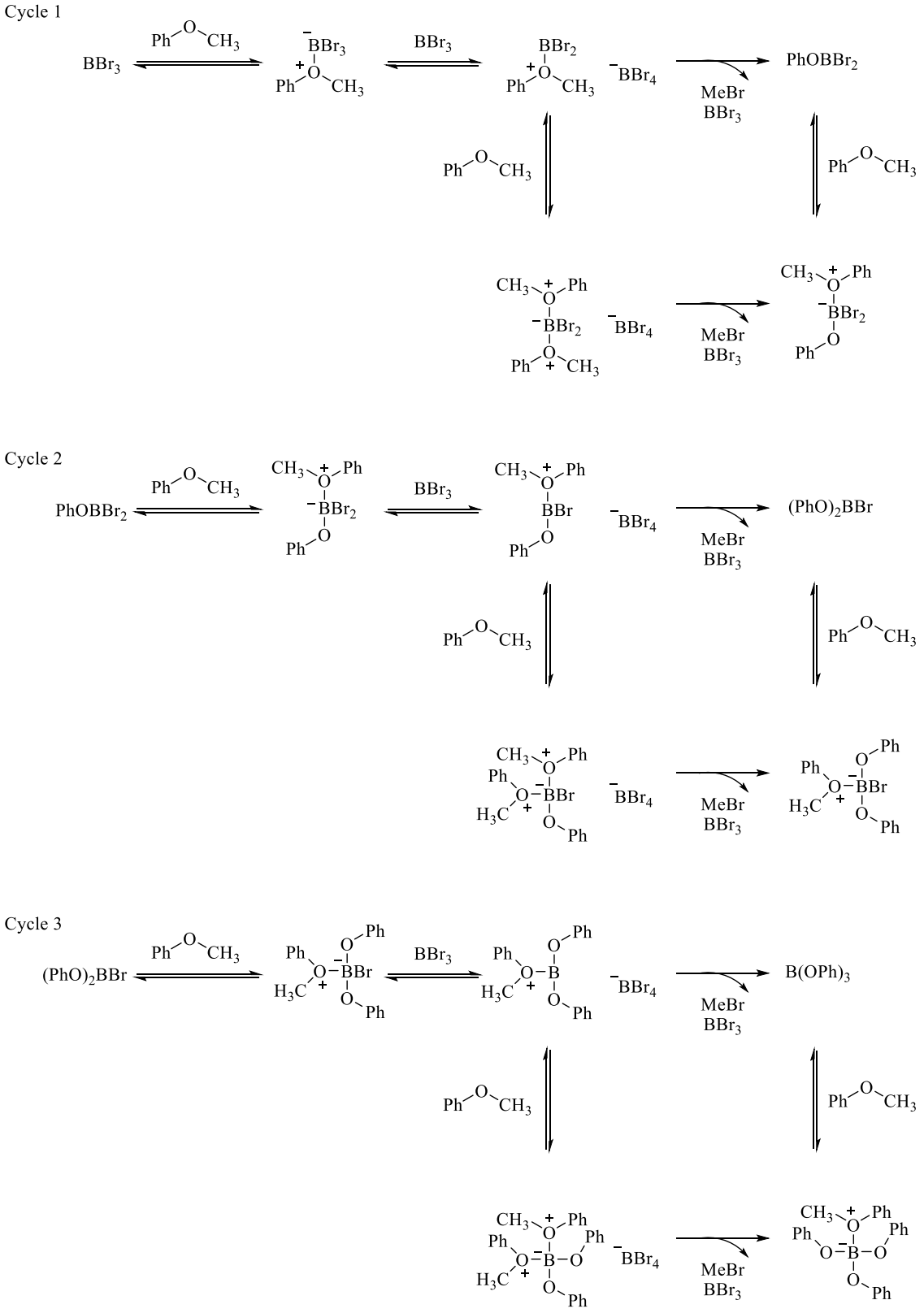


Figure 2.14: Envisioned three-cycle mechanism for the demethylation of methoxybenzene.[52]

A demethylation can be used to synthesise chrysenol **6b** in good yields by reacting 3-methoxychrysene (**6a**) with boron tribromide in DCM at 0 °C followed by quenching with ice.[3]

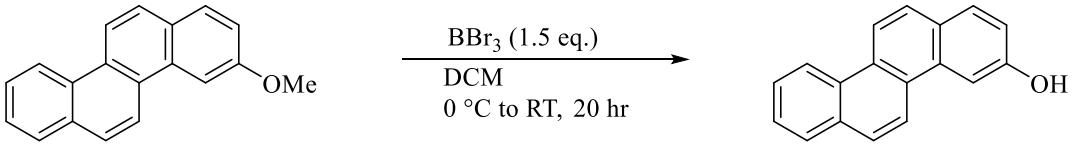


*Figure 2.15: Demethylation for synthesis of chrysenol **6b**.*

2.4 Triflation

Triflation is the process in which a compound reacts to gain a group of trifluoromethanesulfonate, which is a very reactive functional group.[54] The triflate group introduced is an excellent leaving group for nucleophilic substitutions, Suzuki-Miyaura couplings and Heck reactions, among others.[55,56] Earlier tosyl, mesyl and other sulfonyl chlorides were used to convert alcohols into compounds for nucleophilic reactions, but triflate has been shown to have several orders of magnitude, as much as 2×10^4 to 2×10^5 times, increased reactivity.[57,58] Between the different fluorosulfonates there are a much smaller difference in reactivity than between them and other sulfonates. The price and availability are the main things to consider when choosing between them, except for the fact that fluorosulfates can easily decompose into hydrofluoric acid and sulphur trioxide that can be problematic. For the reasons mentioned triflate is the most used perfluoroalkanesulfonate.[58]

In the reaction from an alcohol, it is common to use pyridine to deprotonate the alcohol group before trifluoromethanesulfonic anhydride is added.[54,59] Triflic anhydride is in this reaction used to convert a hydroxyl group to a triflic ester.[60,61] It is one of the most available and inexpensive chemicals that can be used to make a triflate, which makes it a good candidate. The anhydride reacts easily with O-nucleophiles to produce triflates because of its electrophilic character. When this happens the O-S bond in the triflic anhydride is cleaved.[62] This is illustrated in figure 2.16. Pyridine is primarily used because the pyridine-hydrogen cation reacts with the negatively charged rest of the triflic anhydride to make an insoluble salt, and thereby neutralizes the triflic acid that would be formed in the reaction.[59,60] The difficulty of using pyridine in this reaction is that it can react with the newly formed triflate. A solution to this problem is to use derivatives of pyridine like 2,6-dimethyl pyridine, also called 2,6-lutidine, that are less nucleophilic.[60]

Nucleophilicity in alkyl substituted pyridines are affected a lot by steric hinderance, where *ortho* substituted compounds alkylate slower, regardless of base strength. 2,6-lutidine is an approximately 40 times stronger base than pyridine, but a considerably weaker nucleophile.[63]

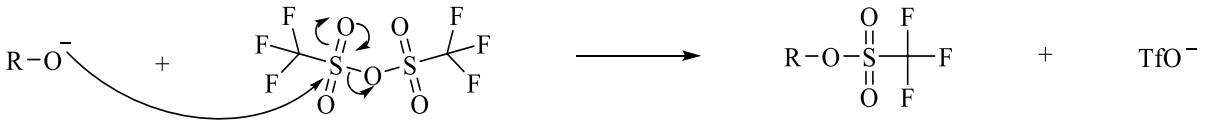


Figure 2.16: Mechanism of the reaction between trifluoromethanesulfonic anhydride and a O-nucleophile to create a triflate.

A common and convenient way to make triflate compounds is with trifluoromethanesulfonate anhydride and pyridine, or 2,6-lutidine, in dichloromethane at 0 °C from the corresponding alcohol.[54,59,60]

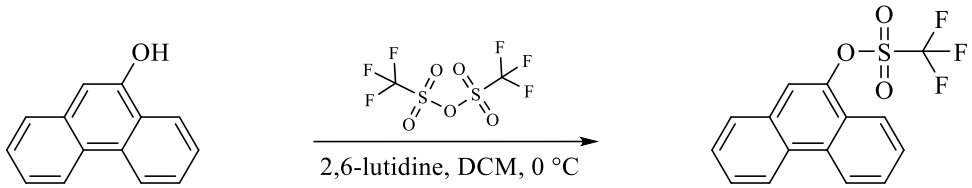


Figure 2.17: Synthesis of phenanthren-9-yl trifluoromethanesulfonate.

2.5 Grignard reagents

Grignard reagent is a term used to describe organomagnesium halides.[64] Such reagents are formed by reacting an organohalide with magnesium metal.[33] The reaction is carried out in anhydrous ether solvents, most commonly diethyl ether and THF, which is needed to stabilize and solvate the Grignard reagent as it forms. Grignard reagents react easily with acidic hydrogens, because of this dry conditions are a must.[65] The exact mechanism of the reaction is not fully understood, but it is generally accepted that radical pathways are contributing.[66] It was Victor Grignard that first discovered the classic preparation of Grignard reagents over 100 years ago. The importance of Grignard's contribution to synthetic chemistry earned him the Nobel prize in Chemistry in 1912.[67]

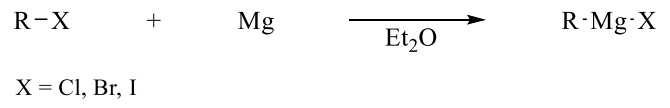


Figure 2.18: The general reaction for synthesising Grignard reagents.

An ethereal solution of a Grignard reagent consists of several different magnesium-containing species that equilibrate.[64] One such equilibrium is illustrated in figure 2.19 and is called the "Schlenk Equilibrium". The halide components in this equilibrium tend to form bridges (Mg-X-Mg) between magnesium atoms, due to Lewis interactions. The degree of bridge formation and magnitude of the equilibrium constant will depend on several factors. These include Lewis basicity and steric properties of the ether solvent, the electronegativity and size of the halogen, and the nature and steric properties of the organic substituent. The overall composition of Grignard reagents in ethereal solvents is therefore very complicated.

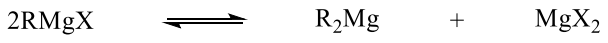


Figure 2.19: The Schlenk equilibrium.

Different halides have different reactivity when it comes to preparing Grignard reagents. Primary, secondary and tertiary alkyl halides are easily transformed while aryl and vinyl halides react somewhat more slowly. Because of this, aryl and vinyl halides are often solvated in THF rather than diethyl ether. THF have a higher boiling point, which leads to better reaction conditions. THF solvates the formed Grignard reagent better, which also increases the efficiency of the reaction. The reactivity is also dependent on the nature of the halogen. Iodine bearing compound are more reactive than bromine bearing ones, which again is more reactive than chlorine bearing compounds. Fluorine bearing compounds are very unreactive and therefore not used to prepare Grignard reagents.[68]

The magnesium used in the Grignard reaction can be of different forms and have different advantages and disadvantages. Magnesium turnings are often used as they are easy to handle. One disadvantage with magnesium turnings is that they can cause abrasiveness to glass lined reaction vessels if stirred over a longer period. Magnesium chips is another alternative and is known to be very pure but less reactive due to decreased surface area. Magnesium powder is known to be more reactive but is also more prone to oxidation. Another disadvantage of using magnesium powder is that it can be pyrophoric. This is a known disadvantage of using the *Rieke*-Mg which is described later in this chapter.[69]

The reaction rate when preparing Grignard reagents is directly proportional to available metal surface.[69] The magnesium used in the reaction, regardless of its form, will most often have a passivating layer of magnesium oxide. By reducing or destroying the passivating layer, it is possible to increase the amount of reactive magnesium available, which again speeds up the reaction rate. Several different methods have been established for activating the magnesium. Mechanical strategies involve crushing of the magnesium, rapid stirring and sonification. Sonification has been shown to initiate the reaction but does not lead to an increase in yield. Sonification prior to the addition of the halide does not show an increase in the initiation, which suggest the ultrasound does not "clean" the surface, but rather removes adsorbed water from the metal surface.[70]

The magnesium of the Grignard reaction can also be added catalytic amounts of iodine to activate the magnesium. The iodine will turn the solution yellow and should be stirred until the colour disappears as this indicates complete activation. The iodine requires refluxing conditions for optimal function. Another activator that can be used is 1,2-dibromoethane. An advantage of using 1,2-dibromoethane is that it does not require refluxing conditions. It has also been shown to be more reliable than activation with iodine. A disadvantage of using 1,2-dibromoethane is its carcinogenic property. In addition to the already mentioned compounds, there exists several other additives that can be used to activate the magnesium and increase the reaction rate.[69]

The traditional method for preparation of Grignard reagents is highly exothermic and performed at the boiling point of the solvent. The reaction therefore has a limited functional group tolerance.[66] A more functionalized method for preparing Grignard reagent is the use of a highly reactive magnesium powder (*Rieke*-Mg) prepared by the reduction of magnesium salts with lithium napthalide.[71] The reactive metal powder is named after Reuben D. Rieke, who first described the recipe for its preparation in 1972.[72] The method allows for preparation at lower temperatures and have higher tolerance for sensitive groups.

In recent years an even better method, with mild reaction conditions, high reactivity and increased functional group tolerance, has been developed by Knochel.[66] The method applies stoichiometric amounts of LiCl to an exchange reagent *i*PrMgCl, resulting in formation of a so-called Turbo-Grignard reagent. The formation of Turbo-Grignard is illustrated in figure 2.20. The method was developed due to electron-rich aromatic compounds resisting the traditional bromine-magnesium exchange. It is suspected that he increased reactivity is a result of the breakup of polymeric aggregates that exist in the classical Grignard reagent.[73] The increased reactivity is also believed to be a result of a negative charge on magnesium in the formed *i*PrMg$Cl_2^-$$LiCl^+$ species. Another advantage of using Turbo-Grignard is inhibition of known side reactions.[73]

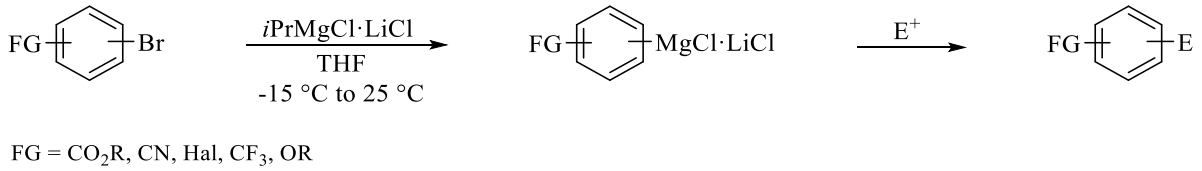


Figure 2.20: The general reaction for synthesising Turbo-Grignard from aryl bromide.

2.6 The Grignard reaction

The Grignard reaction is a common name for a reaction that involves the coupling of an organic compound with a Grignard reagent. A common Grignard reaction is the addition of Grignard reagent (organomagnesium halide) to an aldehyde or a ketone to form an alcohol. The general reaction is illustrated in figure 2.21. If the reactant is formaldehyde, a primary alcohol will be formed. Any other type of aldehyde will result in the formation of a secondary alcohol. If the reactant is a ketone a tertiary alcohol will be formed. Grignard reactions are usually performed in ethereal solutions such as diethyl ether or THF. The final alcohol product is usually obtained by hydrolysis.[74]

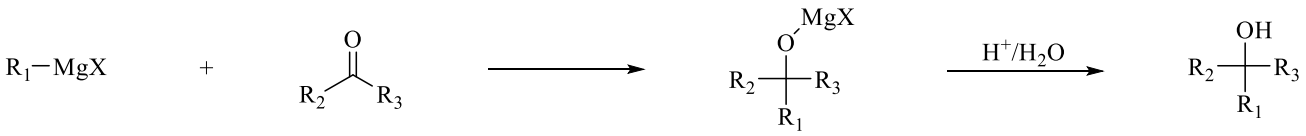


Figure 2.21: The reaction of an aldehyde (ketone) and Grignard reagent to form a secondary (tertiary) alcohol.

The mechanism of the Grignard reaction has been subjected to extensive studies but remains somewhat elusive. At present time, two different competing mechanisms are used to explain the Grignard reaction. The first mechanism is a nucleophilic addition as illustrated in figure 2.22. The second mechanism involves the formation of radical intermediates. The activation of the mechanisms depends on the nature of the substrate, its binding to magnesium and on the dynamics of the solvent. The solvent should be considered a reactant of the reaction as it plays an essential role in the reaction. At thermal equilibrium there exists several different organomagnesium compounds in the Grignard reagent (see chapter 2.5). The different organomagnesium species will have somewhat different reactivity and different reaction

pathways. The Grignard reaction should therefore not be considered as a single process, but rather an assembly of several parallel reactions.[75]

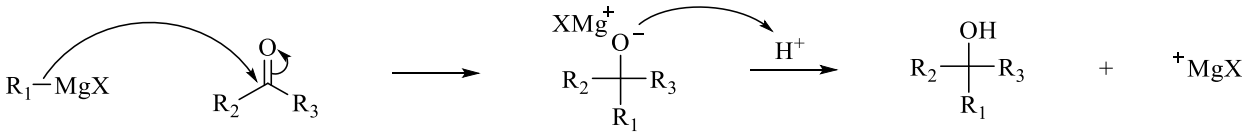


Figure 2.22: Mechanism of the reaction between an aldehyde (ketone) and Grignard reagent to form a secondary (tertiary) alcohol.

The Grignard reaction can be used to synthesize alcohols in almost quantitative yields. By adding an aldehyde dropwise to a solution of Grignard reagent at -40 °C and quenching with acid, it is possible to synthesize the corresponding alcohol in yields of 92-99%.[10] The reaction is illustrated in figure 2.23.

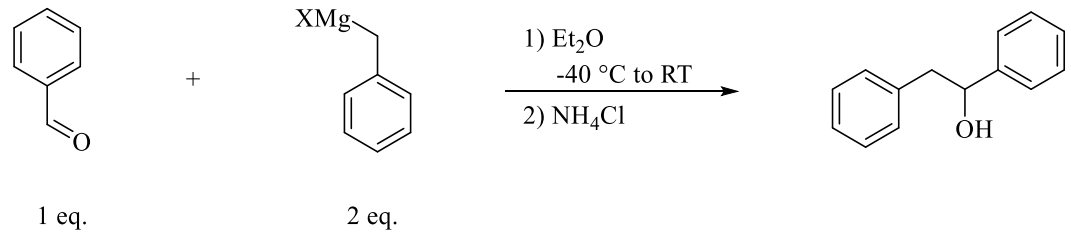


*Figure 2.23: Synthesis of 1,2-diphenylethan-1-ol (**13a**).*

2.7 Kumada-Corriu Coupling

The Kumada-Corriu coupling is a catalysed cross coupling reaction between a Grignard reagent and an organic halide that can be used to create carbon-carbon bonds.[76] The halide of the organic halide, may be a pseudohalide such as triflate.[77,78] The advantage of using Kumada-Corriu coupling, compared to other coupling reactions, is that the Grignard reagents are generally more readily available than alternative organometallic nucleophiles.[79] The reaction is also more straightforward than alternative ones.[77]

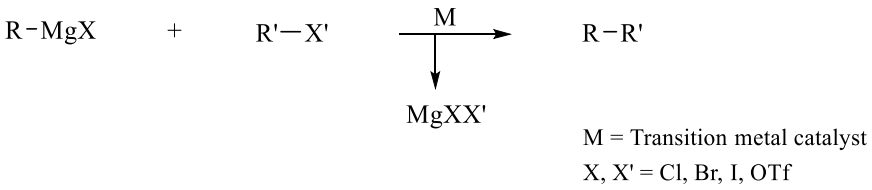


Figure 2.24: The general reaction for Kumada-Corriu Coupling.

2.7.1 Catalysts

Kumada-Corriu coupling was reported independently by the research groups of Robert Corriu and Makoto Kumada in 1972.[80] Initially the catalysts used in the reaction were different types of nickel complexes. However in 1975, not long after the reaction's initial discovery, Shun-Ichi Murahashi reported that also palladium complexes could be used as catalysts.[79] Palladium catalysts tend to have a more controlled reactivity and better chemoselectivity.[81] Still, nickel complexes are often favoured as nickel has lower toxicity, cost and is more abundant than palladium.[82] Another advantage of nickel based complexes is that they are more versatile in terms of substrate scope and group tolerance.[83] Today, other transition metal catalysts are also used in Kumada-Corriu coupling such as copper and iron.

There are many advantages of using iron as catalyst rather than palladium or nickel species. Iron is less toxic, more abundant, and consequently both cheaper and more environmentally friendly. The use of iron as catalyst was proposed by Kochi et al. in 1971 but received little attention in the following decades. According to Wei et al. the key to advancement was the use of NMP as a cosolvent.[84] NMP is short for *N*-methyl-2-pyrrolidone and was discovered to be a good cosolvent by Cahiez in 1998. When Kochi first reported the use of iron, he required three equivalents of halide to one equivalent of Grignard reagent. With the use of NMP Cahiez obtained similar yields without the use of excess halides.[85] A disadvantage is however the toxicity of the additive. In more recent times the scope of iron catalysed couplings has been expanded from that of alkenyl halides and can now be used to couple other electrophiles such as aryl halides but also pseudo halides such as triflate.[86,87] Alternative non-toxic additives such as *N*-butyl-2-pyrrolidone (NBP), has also been found as alternatives to NMP.[88]

2.7.2 Mechanism

There exists a widely accepted mechanism for the palladium catalysed Kumada-Corriu coupling. The proposed mechanism is illustrated in figure 2.25. Palladium's role in the reaction is thought to be analogous to its role in other coupling reactions. The mechanism begins with an oxidative addition where the electron-rich Pd^0 is inserted into the organohalide to form an organo-Pd^{II} complex. This initial step is followed by a transmetalation with the Grignard reagent. In this step, the R' group of the Grignard reagent is transferred to the Pd^{II} complex, where it replaces the halide anion. Afterwards, an isomerization will happen, which brings the organic ligands next to each other. This allows for a reductive elimination where the coupled product is obtained, and the catalyst is regenerated to its initial form.[89]

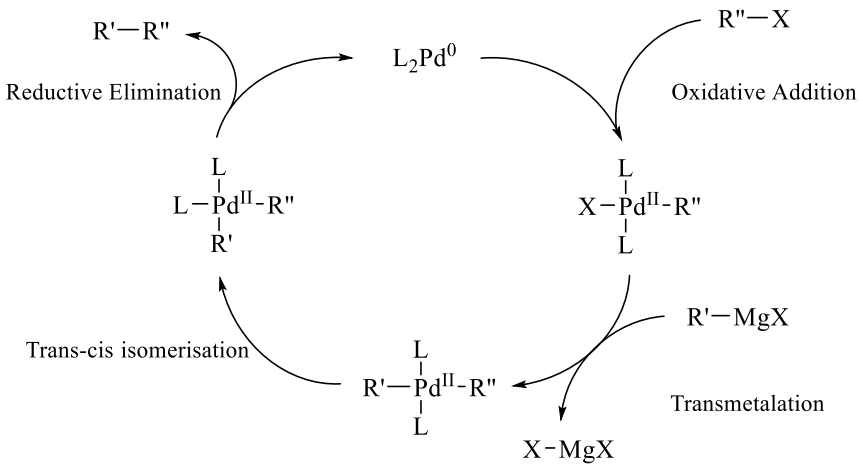


Figure 2.25: Proposed mechanism of the palladium catalysed Kumada-Corriu cross coupling reaction.

The mechanism of the nickel catalysed Kumada-Corriu coupling is not as general and appears to have multiple possible reaction pathways, where the ligand decides the exact mechanism.[83] The mechanism is however in general analogous to that of palladium and consists of the same principal steps.[90] The mechanism of iron catalysed Kumada-Corriu coupling is not as well established as the palladium or nickel catalysed couplings. It is however believed to consists of the same principal steps. The current mechanistic understanding is an initial reduction of Fe^{III} to a reduced species by the Grignard reagent. This leads to FeX_n or $Fe(MgX)_n$ intermediates. The next step is a rate determining oxidative addition with the electrophile. This is followed by a transmetalation with the Grignard reagent. The last step is a reductive elimination which is believed to be fast and restores the iron species to its initial form.[84]

2.7.3 Ligands

According to Kumada, the catalytic activity of the catalyst depends strongly on the nature of the ligand.[80] To illustrate this Kumada performed the coupling of chlorobenzene with *n*-butyl Grignard reagent using different nickel complexes under the same conditions. The greatest yield of 100% was obtained when using dppp as ligand. Another ligand, dmpe, gave a much lower yield of only 47%. Based on this observation, it could be natural to assume that the dppp complex is an overall better catalyst than the dmpe complex. However, this is not the case as both allyl and alkenyl Grignard reagents are virtually unreactive with Ni(dppp)Cl_2. The cross-coupling of allylmagnesium bromide and prop-1-en-1-ylmagnesium bromide with bromobenzene both gave better yields when using Ni(dmpe)Cl_2.[80] The importance of using a suitable catalysator is essential for the yield and outcome of a Kumada-Corriu coupling.

The two main parameters which determines whether a ligand is suitable or not, is its electronic and steric properties. A ligand has three ways in which it can influence the course of the reaction. The ligand may change the electronic properties of the metal centre of the catalyst, change the steric bulk around its metal centre or enforce a preferred bite angle. The bite angle is a geometric parameter which describes the bond angle that separates one ligand (bound to metal) from the other. Change in bite angle can affect both activity and selectivity of a catalytic reaction. The modifications implemented by the ligand will affect the different steps of the catalytic cycle (oxidation, trans-metalation, reductive elimination) in different ways. It is therefore not straight-forward to understand the exact effect and outcome when using a given ligand.[91]

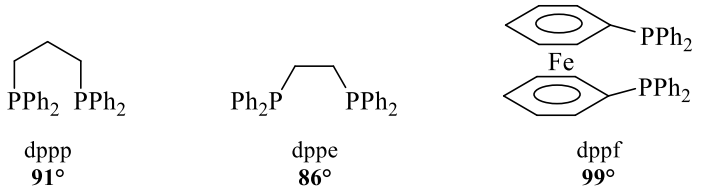


Figure 2.26: Bite angles of common diphosphine ligands.[92]

2.7.4 Reactants

Grignard reagents have a relatively poor functional group compatibility.[79] For a long time this limited the Kumada-Corriu coupling of such reagents to conventional alkyl, aryl and alkenyl Grignard reagents. Knochel and his co-workers later developed conventional methods for preparation and reaction of aryl, heteroaryl and alkenyl Grignard reagents bearing sensitive groups (see 2.5).[79] Since then, several efficient protocols have been reported for aryl-aryl and alkyl-aryl Kumada-Corriu coupling. [79]

In 2015 Xing et al. researched the coupling of various pyrimidin-2-yl phosphates with different Grignard reagents using $Fe(acac)_3$ as catalysator. Xing reported higher yields when using aliphatic Grignard reagents because of their increased activity, compared to aromatic reagents. The electron withdrawing/donating effect of both reactants was also discovered to be of essence. Electron-withdrawing groups on the phenyl ring of the phosphate was reported to increase the yield of the reaction, while electron-donating groups was discovered to decrease the yield. A similar, although opposite effect was true for the Grignard reagents. Better yields were observed when the Grignard reagent had electron-donating groups, while lower yields were observed when the Grignard reagent had electron-withdrawing groups.[93]

2.7.5 Iron catalysed Kumada-Corriu Coupling

In 2002 Fürstner and Leitner reported that iron could be used to couple traditionally less reactive electrophiles bearing chlorine or tosylate. During a screening performed by the pair, it was discovered that both bromine and iodine bearing electrophiles were less reactive under their conditions. Under traditional cross coupling conditions these electrophiles are known to be very reactive substrates. A disadvantage of the Fürstner and Leitner method is therefore its limitation to electron-deficient aryl chlorides, triflates and tosylates. Another disadvantage is its limitation to primary aliphatic Grignard reagents.[4] Later it was discovered that more electron-rich and electron-neutral compounds also could be coupled by using N-heterocyclic carbene ligands (NHC ligands). A disadvantage is the requirement of high temperatures and/or long reaction time.[84]

When Fürstner and Leitner began to explore the use of iron as a coupling catalyst they performed a screening to determine which ligand was ideal. As all the utilized ligands seemed to be suitable, they chose to use the cheap and non-hydroscopic $Fe(acac)_3$ as catalysator. It should be noted that this was true only for primary alkyl Grignard reagents. When reacting with secondary Grignard reagents the use of Fe(salen)Cl gave the best yields. All aryl-, allyl-, and alkenyl Grignard reagents investigated led to poor yields regardless of chosen catalysator.[4] In 2007 the research group of Guérinot reported the successful

coupling of alkyl halides with alkenyl Grignard reagents. The reaction utilized $FeCl_3$ (10 mol%) as catalysator and used TMEDA (1.9 eq.) as additive in THF. The method was attempted using iodobenzene but gave no yields. It was determined that neither aryl halides nor alkyl chloride were reactive under the given conditions.[94] Still today it remains a challenge to utilize iron as catalysator for the coupling of aryl halides with alkenyl Grignard reagents.

For many years it was also a challenge to couple benzyl halides with aryl Grignard reagents when using an iron catalyst. Bedford et al. reported in 2009 that the coupling under such conditions led to low yields and had poor selectivity. According to Bedford, the reaction produced mainly homo-coupled by-products.[95] Under a screening performed by Nakamura in 2013 it was discovered that a strongly donating ligand, such as dppbz could improve the selectivity. Later, it was reported that the dppbz-ligand could be tuned to increase the selectivity even more. The tuned catalysator (mixed PPh_2/PCy_2 ligands) was shown to efficiently catalyse the Kumada coupling of benzylic halides with aryl Grignard reagents. The ligands feature good functional group tolerance while giving high to moderate yields.[96] No coupling of triflate bearing PAHs with styrylmagnesium bromide have previously been reported. It remains a challenge to develop even more active catalyst systems that can be applied to a broader range of coupling partners.

2.8 Photocyclization

A photochemical reaction is when absorption of energy in the form of light is initiating a chemical reaction.[40] This absorption of light will make the molecule go to an exited state, where it has other properties than the original molecule.[97] When a molecule is in its exited state it can either go back to its ground state by emitting the energy as photons or as heat, or it can react chemically. If the excitation energy is higher than the activation energy of the reaction, a reaction with molecules that wouldn't usually react with each other, can happen.[98] Photochemical reactions that are possible to do are in most cases thermally forbidden, and reactions thermally allowed are in most cases photochemically forbidden.[33]

Ultraviolet light is the radiation that is most often used to initiate photochemical reactions.[99,100] The ultraviolet light is electromagnetic radiation in a range of frequencies that are just beyond the visible spectra, therefore giving it more energy.[100] UV light is defined as light with wavelength between 200 and 400 nm, whereas visible light is from 400 nm to 800 nm.[33] Because of the UV light from the sun and

pollutants in the air, mostly form car traffic, photochemical reactions happens naturally especially in big cities to make Los Angeles smog.[101]

Photocyclization is a reaction that can use electromagnetic radiation to make stilbenes into cyclic compounds, among other things. This is the preferred synthesis method for many polycyclic aromatic compounds.[102] Only *cis*- stilbene will react in this reaction, because it will undergo a reversible cyclization to a *trans*-4a,4b-dihydrophenanthrene, and for this to happen the aromatic groups need to be in this position. In practice both *cis*- and *trans*- stilbenes will give the same product, and the stereochemistry be irrelevant, because under irradiation of UV light the stilbene will change back and forth between the isomers rapidly, and the mix of isomers will not influence the yield.[103–105] When it is in the dihydrophenanthrene intermediate it needs to be trapped there to not go back to stilbene. This can be done oxidatively with iodine, oxygen or other hydrogen acceptors.[102,104] The intermediate can also be trapped by an elimination reaction, if one of the aromatic rings has a suitable substituent in *ortho* position.[104] This is illustrated in figure 2.27.

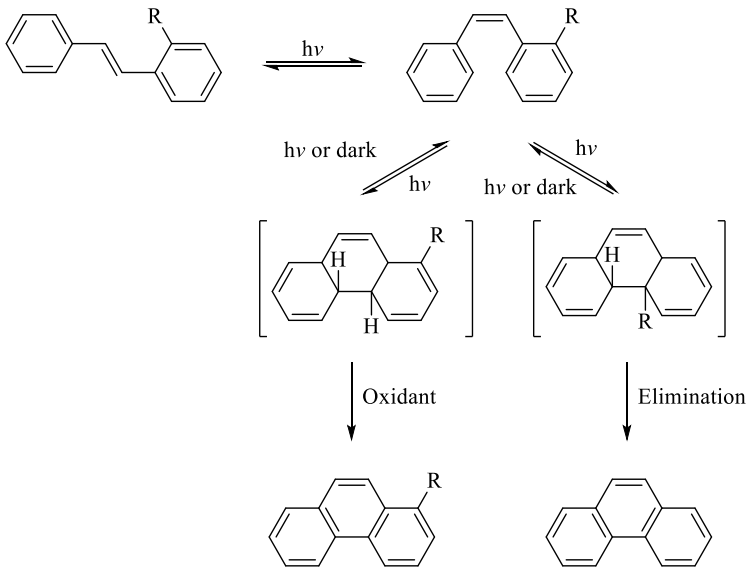


Figure 2.27: Possible photocyclizations of stilbenes.[104]

The possibility to use UV radiation to make phenanthrene from stilbene was, from the sources found, first discovered by Parker and Spoerri in 1950.[106] Oxidative photocyclization of stilbenes in a useful manner was however discovered by Mallory in 1964 when he found that iodine, together with dissolved oxygen, gave much purer products with better yield and less irradiation time needed than dissolved oxygen

alone.[107] Iodine was used in catalytic concentrations, because there were no effect on the reaction rate with increased amounts, but there were an increased risk of side reactions and saturations of the double bond in the stilbene.[104] The proposed mechanism for the iodine is that it is cleaved into radicals by the radiation. These radicals are thought to make a chain reaction where they react with the dihydrophenanthrene intermediate to make hydrogen iodide while oxidizing, and thereby trapping the phenanthrene. The oxygen then oxidizes the hydrogen iodide back to iodine, which can continue to react with other dihydrophenanthrenes.[104] There should under these conditions be an excess of oxygen by bubbling air continuously through the reaction mixture.[108] These conditions has been found to give the best results when using less than 0.01 moles of starting material.[107]

In 1991 a solution to the problem with increased side reactions was proposed, when Katz et al. introduced the use of propylene oxide as a hydrogen iodide scavenger, to remove the source of the problems of side reactions and saturation of the double bond. When the hydrogen iodide is removed, it cannot be reoxidized to iodide and reused. Because of this there are no longer needed just catalytic amounts of iodine, but stoichiometric quantities. Another upside to this is that the reaction can under these conditions be done under inert atmosphere.[109] Oxygen can in addition to hydrogen iodide oxidize other compounds, making the reaction possible in inert atmosphere superior.[109] Katz method has shown to give better yields than the reaction with catalytic iodine, on most occasions.[104,108]

Photocyclization can be used to synthesise polycyclic aromatic hydrocarbons in good yields. By adding the stilbene reactant, iodine and 1,2-epoxybutane in degassed toluene, and irradiating the mixture until the colour of iodine disappears, it is possible to synthesise the corresponding PAH in good yields.[104,109] There has been found no rearrangements in these reactions. When substituted in *ortho-*, *para-*, or α- position oxidative photocyclization gives 1-, 3- or 9- substituted phenanthrene, respectfully. If the stilbene is *meta-*substituted, the product will be a mix of 2- and 4- substituted phenanthrene, that can be difficult to separate.[107] The reaction is illustrated in figure 2.28, as a general procedure that can be done with different amounts of rings and substituents.

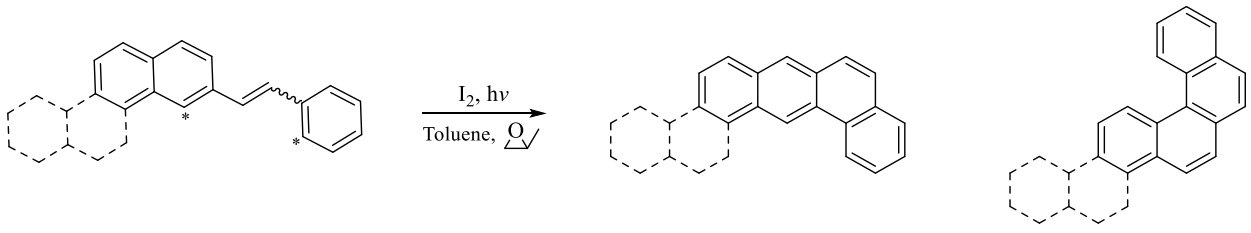


Figure 2.28: Synthesis of PAHs from stilbenes.

3. Results and discussion

3.1 General

Results from the attempted reactions will be presented, compared to literature, and discussed in this chapter. No attempts at photocyclization were done as (2-bromovinyl)benzene did not arrive in time.

3.2 Attempted synthesis of Phenanthren-9-ol

The compound was attempted synthesised using a D*o*M/DreM approach. The initial amination and D*o*M reaction proceeded as planned, yielding 80% of benzamide **2** followed by 75% of boronic acid **3**. The next reaction did not proceed as planned and yielded carboxamide **4b** instead of the expected carboxamide **4a**. It was not possible to continue from here and phenanthrol **7** was not synthesised. Each of the reactions are illustrated in figure 3.1 and are further described in subsequent chapters, see 3.2.1 – 3.2.4.

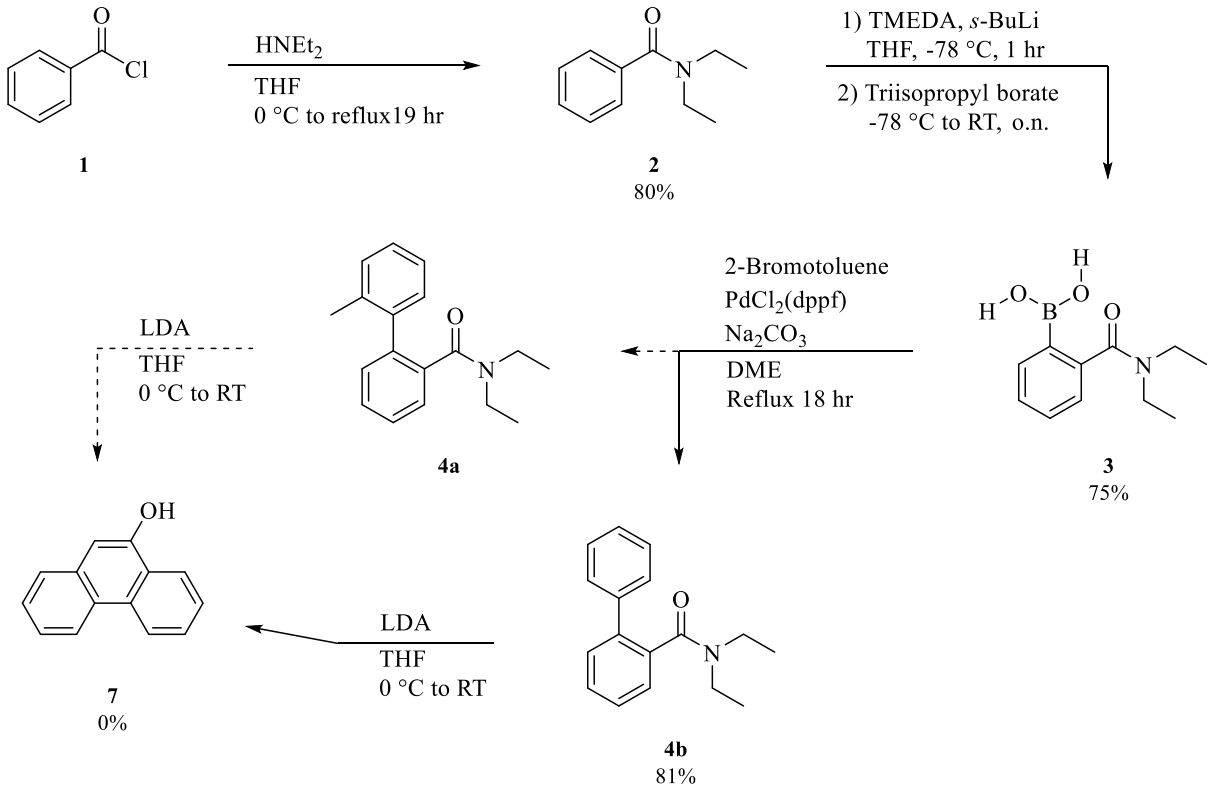
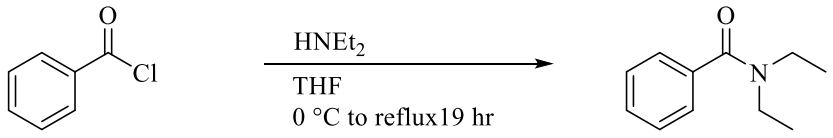


*Figure 3.1: Results from attempt at synthesising phenanthrol **7**.*

3.2.1 Amination

Benzamide **2** was synthesized based on the procedure used by McCabe et al.[110] as illustrated in table 3.1. The reaction was performed in gram scale by reacting 1 equivalent of acid chloride **1** with 1.5 equivalents of diethylamine. See chapter 6.3 for a more detailed description of the reaction procedure.

*Table 3.1: Result from the amination using starting material **1** and the procedure based on McCabe et al.[110]*



1 **2**

Starting material	Mass (g)	Product	Yield (g)	Yield (%)
1	7.826	**2**	8.081	80

The yield of the reaction was good, as seen in table 3.1. Bjelland has previously done the same reaction, under similar conditions, and reported a yield of 93% .[2] TLC analysis of the starting material gave two "spots", which may indicate acid residues present in the reagent. This could be a reason why the obtained yield was lower than Bjelland's. Another source of error is lack of cooling during refluxing. The water supply of the reaction was shut off during the refluxing period and was later turned on again, at an unknown time. This probably has affected the yield of the reaction.

The product was identifiable on both ^{1}H-NMR and ^{13}C-NMR and showed few impurities. The assigned spectral data are given in figure 3.2. Complete spectral data can be found in appendix I and II.

*Figure 3.2: Spectral data from ^{1}H-NMR and ^{13}C-NMR of benzamide **2** assigned to respective atoms in the molecule.*

Based on predictions of ^{1}H-NMR spectra using ChemDraw Professional 17.1[111] a triplet should be observed around 1.2 ppm. Kumar et al. obtained this signal as a doublet.[112] Spectral data of the product in

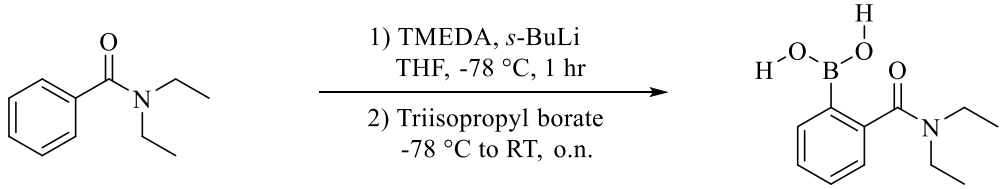
this thesis indicates a singlet at 1.19 ppm due to prevented rotation. The predicted quartet at 3.3 ppm, was also obtained as a singlet due to prevented rotation. The aromatic signals were obtained as a multiplet in the 7.40 – 7.37 ppm area. Due to much overlap, it was not possible to separate the respective aromatic signals from one another on ^{1}H-NMR. Still the area of all peaks was consistent with predictions. The impurity on the ^{1}H-NMR spectra with a shift value of around 1.4 ppm is not associated with the product as it reoccurs in ^{1}H-NMR spectrums of other compounds that use the same solvent. The source of contamination is likely associated with the $CDCl_3$ used.

Based on predicted ^{13}C-NMR spectra two signals should be observed around 13 and 44 ppm. Ren and Yamane obtained each of these signals as two smaller ones.[113] Due to the resolution of the obtained ^{13}C-NMR spectra of this thesis being much lower, it is likely that the signals were lost in noise. The five signals that were identifiable are all in accordance with the shift values obtained by Ren and Yamane.[113]

3.2.2 Directed *Ortho* Metalation

Boronic acid **3** was synthesized following the procedure of Cai et al.[9] as illustrated in table 3.2. The reaction was performed in gram scale by reacting 1 equivalent of benzamide **2** with 1.2 equivalents of *s*-BuLi and TMEDA followed by 2.4 equivalents of triisopropyl borate. See chapter 6.4 for a more detailed description of the reaction procedure.

*Table 3.2: Results from the DoM using starting material **2** and the procedure of Cai et al..*[9]



2 **3**

Starting material	Mass (g)	Product	Yield (g)	Yield (%)
2	1.163	**3**	1.095	75
2	1.199	**3**	1.015	68

The yields of the reaction were acceptable, as seen in table 3.2. The same reaction has previously been done by Cai et al.[9] which reported a yield of 92% and Böhme et al.[8] which reported a yield of 82%. Bjelland has also done the reaction, and discovered that the product is not suitable for purification using

flash column.[2] The reaction was performed twice due to unexpected product formation in the next reaction step (see chapter 3.2.3).

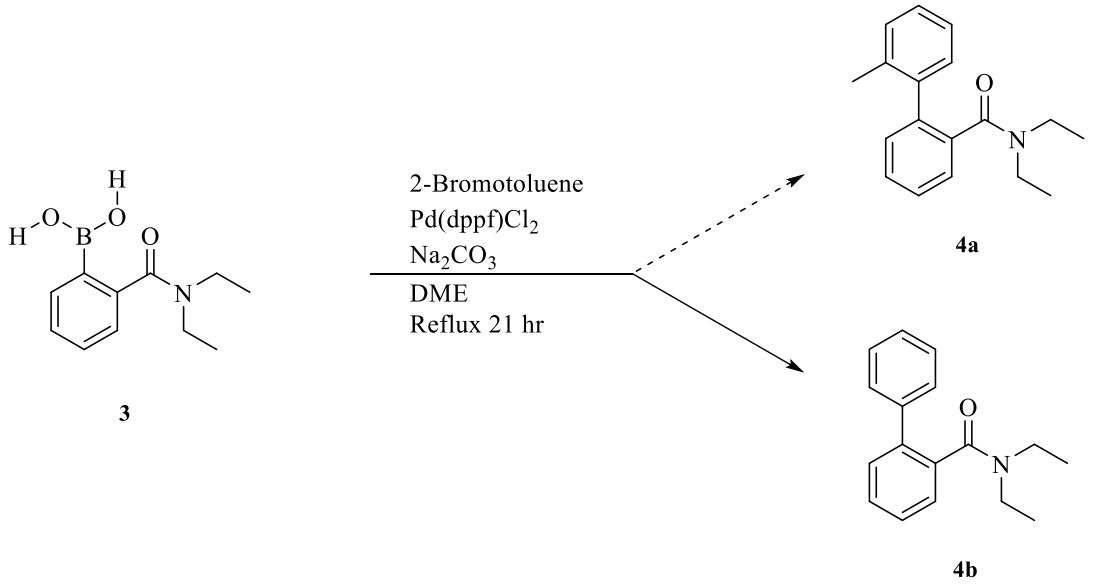
The first attempt at synthesizing boronic acid **3** was done under somewhat uncontrolled temperature. The batteries of the thermometer were running low, and as a result the thermometer showed less and less accurate readings. Since the temperature did not seem to increase, *s*-BuLi may have been added faster than desired. The end temperature according to the thermometer was -150 °C, which is impossible when using dry ice and acetone. During the second attempt at synthesising boronic acid **3** the temperature was more controlled. The thermometer was now working and addition of *s*-BuLi was done over a longer time interval. Surprisingly, better temperature control did not result in a better yield.

The product could somewhat be identified by NMR and was mixed with diisopropyl (2-(diethylcarbamoyl)phenyl)boronate. This became apparent as a signal of 25.3 ppm was observed on the ^{13}C-NMR spectra. Since the product was not purified using flash column chromatography it is likely that other impurities also are present. The lower part of both the ^{1}H-NMR and ^{13}C-NMR spectrums had a big excess of signals. As no previous spectrums of boronic acid **3** or diisopropyl (2-(diethylcarbamoyl)phenyl)boronate were available in literature it was not possible to delegate the observed signals to each of the compounds. Predictions was done using ChemDraw but could neither be used to separate the signals to respective compounds. ^{1}H-NMR and ^{13}C-NMR spectra are available in appendix III and IV.

3.2.3 Suzuki-Miyaura coupling

Carboxamide **4a** was attempted synthesized following the procedure of Cai et al.[9] as illustrated in table 3.3 The reaction was performed in gram scale by reacting 1 equivalent of 2-bromotoluene with 1.5 equivalents of boronic acid **3**. The reaction was catalysed by 5 mol% of Pd(dppf)Cl_2. See chapter 6.5 for a more detailed description of the reaction procedure.

*Table 3.3: Results from the Suzuki-Miyaura reaction using starting material **3** and the procedure of Cai et al..*[9]



3 **4a** **4b**

Starting material	Mass of 2-Bromotoluene (g)	Product	Yield (g)	Yield (%)
3	1.4	**4b**	0.510	81
3	1.4	**4b**	0.367	58

The yields of the reaction were good, as expected, but the product of the reaction was not. The first attempt at the Suzuki-Miyaura reaction seemed to form carboxamide **4b** instead of expected carboxamide **4a**. The product seemed to be lacking the methyl group according to both ^{1}H-NMR and ^{13}C-NMR spectra. Böhme et al.[8] has attempt the same reaction, and had no trouble producing carboxamide **4a** in excellent yield (89%).

The loss of a methyl group during the reaction process seems highly unlikely. A natural explanation would be the use of wrong electrophile. If the reaction had been performed with the use of bromobenzene instead of 2-bromotoluen the outcome would be explainable. Nevertheless, this was not the case as 2-bromotoluene was subjected to a ^{1}H-NMR analysis which confirmed the correct reagent. The spectrum of 2-bromotoluene is available in Appendix XXXIII. Another possible error that was considered was air sensitivity. Palladium catalysators are in general known to be air sensitive. However, the specific catalysator used in this reaction, is reported to be air stable.[114] Nevertheless, it is still a possibility that the catalysator can become sensitive to air during the reaction, as conditions change.

Since there was no clear explanation as to why carboxamide **4b** was formed instead of carboxamide **4a**, the reaction was attempted once again. This time extra care was taken to avoid the presence of oxygen.

Both the solvent used and the Na_2CO_3 solution were properly degassed using liquid nitrogen and reduced pressure. In the end the obtained product was identical to that of the first reaction according to NMR spectra. At this point it was questioned whether the missing methyl group could have been "lost" or hidden under other signals. To be sure that this was not the case, the product was subjected to a DreM reaction (see chapter 2.2.4.). The outcome from this reaction indicated that the product indeed was carboxamide **4b**.

The product was identifiable on both ^{1}H-NMR and ^{13}C-NMR spectra and showed few impurities. There is, however, one unexpected signal of 196.7 ppm on the ^{13}C-NMR spectrum that is not explainable. The assigned spectral data is given in figure 3.3.

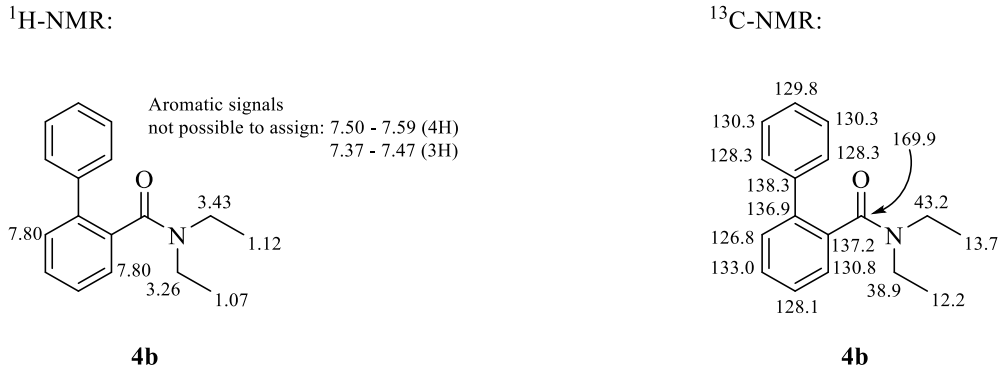


Figure 3.3: Spectral data from ^{1}H-NMR and ^{13}C-NMR assigned to respective atoms in the molecule.

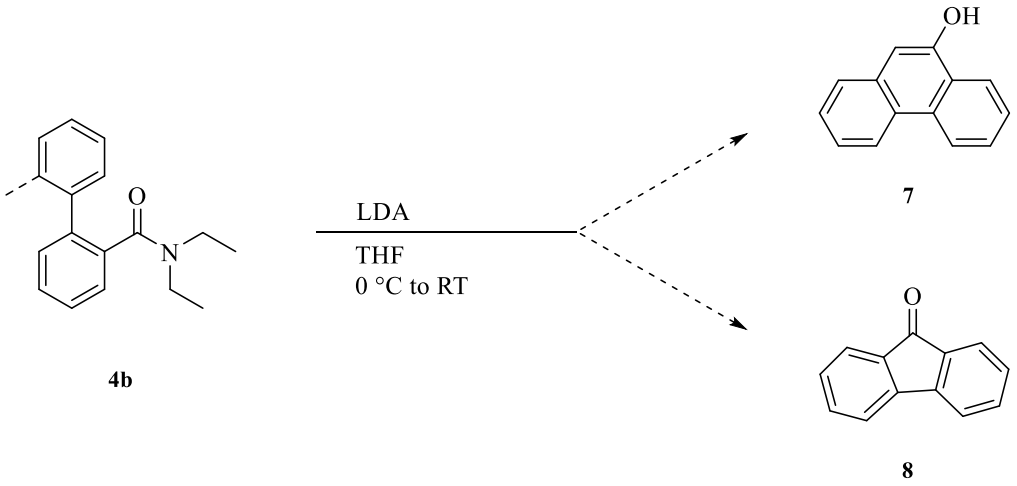
The ratios of the peaks in the ^{1}H-NMR spectra and their respective shift values are all in accordance with the predicted values of carboxamide **4b**. The total amount of hydrogen adds up to 19 as expected for carboxamide **4b**. The total amount of hydrogens should have been added up to 18 had the product been carboxamide **4a**. Zhao and Snieckus[115] have previously obtained ^{1}H-NMR spectra of carboxamide **4b** that seem to match the one in this thesis, although with general lowered ppm values.
The ^{13}C-NMR spectra reported by Zhao and Snieckus[115] also has somewhat different shift values, but seem to otherwise match the spectrum obtained in this thesis. The one signal which does stand out is the mentioned signal of 196.7 ppm on the ^{13}C-NMR spectrum. The shift value indicates the presence of an aldehyde group. However, no aldehyde signal was observed on the^{1}H-NMR spectra. The peak is not derived from acetone as the product was properly dried and no other excessive signals of appropriate magnitude were observed. The aldehyde signal is also observed on the ^{13}C-NMR spectra of the starting material. This may indicate that something crucial happened in the preceding reaction, which could be a

reason as to why the obtained product was formed. Still, further research is necessary to fully explain the outcome.

3.2.4 Directed remote Metalation

Phenanthrol **7** was attempted synthesized following the procedure of Cai et al.[9] as illustrated in table 3.4. The reaction was performed on a scale of approximately 250 milligrams. LDA was generated by reacting 1.2 equivalents of diisopropylamine with 1.2 equivalents of *s*-BuLi. See chapter 6.6 for a more detailed description of the reaction procedure.

*Table 3.4: Result from the DreM reaction using starting material **4b** and the procedure of Cai et al..*[9]



4b **7** **8**

Starting material	Mass (g)	Product	Yield (g)	Yield (%)
4b	0.273	**8**	0.001	0[a]

a: 0.125 g (46%) of starting material was retrieved.

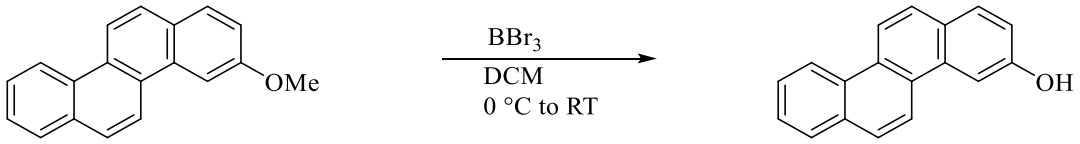
The yield of the reaction was not good. Four different fractions were isolated during flash column chromatography. None of the fractions could be identified as phenanthrol **7** or fluorenone **8**. The biggest fraction of 0.125 g was identified as starting material. The three other fractions seemed to be a mixture of impurities and by-products. Cai et al.[9] has previously shown that the reaction performed on carboxamide **4a** will result in the formation of phenanthrol **7.** Based on the outcome of the DreM reaction it is therefore very likely that the product of the Suzuki-Miyaura coupling was not carboxamide **4a**.

Tilly et al.[51] has previously synthesized fluorenone **8** from carboxamide **4b** in yields of 93%. According to his procedure Tilly allowed the mixture to react at RT for 12 hours and used 1 M HCl for workup. There is a possibility that fluorenone **8** would form under these conditions, but not the ones used in this thesis. It is therefore still reasonable to believe that carboxamide **4b** was synthesised in the Suzuki-Miyaura coupling. Still, further research is necessary to fully explain its outcome. At this point the obtained product cannot be used to construct triflates and is consequently of no use.

3.3 Deprotection with BBr_3

Chrysenol **6b** was synthesized following the procedure of Jørgensen and Joensen[3] as illustrated in table 3.5. The reaction was performed in gram scale by reacting 1 equivalent of ether **6a** with 1.5 equivalents of BBr_3. See chapter 6.7 for a more detailed description of the reaction procedure.

Table 3.5: Result from the demethylation reaction.



6a **6b**

Starting material	Mass (g)	Product	Yield (g)	Yield (%)
6a	1.809	**6b**	1.669	98

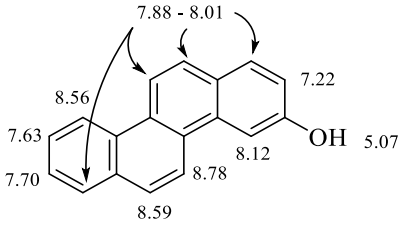
The yield of the reaction was excellent, as seen in table 3.5. Flash column chromatography was not used to purify the product to avoid the possibility of oxidation. Instead, the product was subjected to triflation directly after being concentrated and dried. Jørgensen and Joensen[3] have previously done the same reaction and reported a yield of 58% after mechanical losses. They also did the reaction on similar compounds and obtained yields of 93 – 96%.

Ethyl acetate was used in the extraction, as chrysenol **6b** showed low solubility in DCM. EA has a density that is lower than waters, while DCM has a density that is higher than waters.[116,117] This led to some difficulty when washing the combined organic phases. Most of the organic phase was situated below the

aquatic phase, but some smaller volumes wanted to be above. Extra care was therefore taken to obtain as much of the organic phase as possible.

The product was identifiable on ^{1}H-NMR but not on ^{13}C-NMR. Only half of the expected signals were visible on the ^{13}C-NMR spectrum. This is likely due to a very low concentration of analyte present in the sample, which resulted in a lot of noise. As product **6b** was directly subjected to a triflation, it was not possible to obtain a new ^{13}C-NMR spectrum. The ^{1}H-NMR spectrum obtained was of good quality. Most obtained shift values were in accordance with those reported by Jørgensen and Joensen.[3] One exception was the peak from OH which had a much lower shift value in this thesis than the one reported by Jørgensen and Joensen. This is a result of using different solvent. Jørgensen and Joensen used acetone, while in this thesis $CDCl_3$ was used. Another exception between our spectra and the one obtained by Jørgensen and Joensen is that ours have a high peak around 1.5 ppm that is believed to be an impurity present in the $CDCl_3$ solvent used.

^{1}H-NMR:



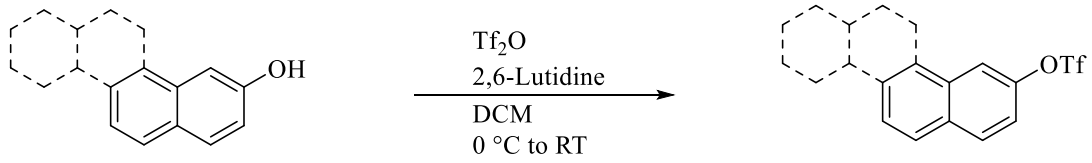
6b

Figure 3.4: Spectral data from ^{3}H-NMR assigned to respective atoms in the molecule.

3.4 Triflation

Triflate **5b** and **6c** were synthesized following the procedure of Cai et al.[9] as illustrated in table 3.6. The reaction was performed in gram scale by reacting 1 equivalent of starting material with 1.2 equivalents of trifluoromethanesulfonic anhydride and 2,6-lutidine. See chapter 6.8 and 6.9 for a more detailed description of the reaction procedures.

Table 3.6: Results from the triflations.



5a / 6b **5b / 6c**

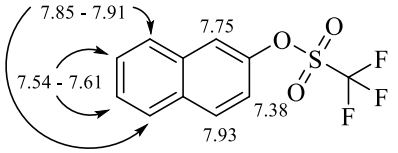
Starting material	Mass (g)	Product	Yield (g)	Yield (%)
5a	1.499	**5b**	2.631	92
5a	1.502	**5b**	2.638	92
6b	1.597	**6c**	1.956	80

The yields of the reaction were very good, as seen in table 3.6. A small part of triflate **6c** was lost during flash column chromatography. This is because some of the product overlapped the starting material. After two rounds of flash column the amount lost seemed negligible compared to the obtained product. There was not performed a third attempt at separating the compounds. Cai et al.[9] have previously used the same procedure to triflate phenanthrenes in yields of 90 – 95%. A similar procedure has also been used by Boehm et al.[118] which produced triflate **5b** in 100% yield.

The melting point of triflate **5b** was observed to be 34.6 – 35.8 °C. This is somewhat higher than the reported 32 – 33 °C by Brimble and Lai[119], but much lower than the reported 58 – 60 °C by Dyke et al.[120] The melting point of triflate **6c** was observed to be 119.7 – 121.0 °C. No previously reported melting point of **6c** could be found in literature. The products were not recrystallized before the melting points were recorded.

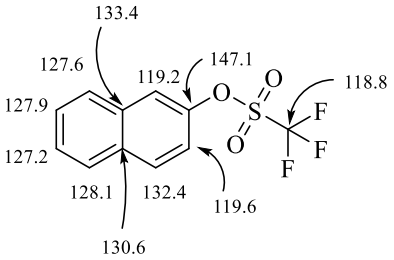
NMR analysis of both triflate **5b** and **6c** showed pure compounds. The spectra of triflate **5b** was in accordance with the spectral data reported by Zhu et al.[121] Only two of the peaks of the quartet at 118.8 ppm were visible through the noise. The coupling constant of 319 Hz was similar to the value of 320 Hz reported by Zhu et al..[121] No previous NMR analysis of triflate **6c** could be found in literature. Predicted values are therefore based solely on ChemDraw's but seem to match well. As with triflate **5b**, only two of the peaks of the quartet were visible through the noise. The assigned spectral data is given in figure 3.5.

^{1}H-NMR:



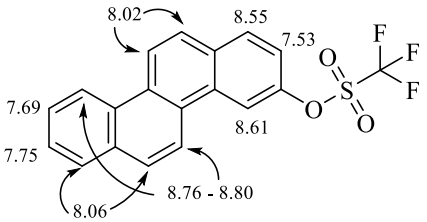
5b

^{13}C-NMR:



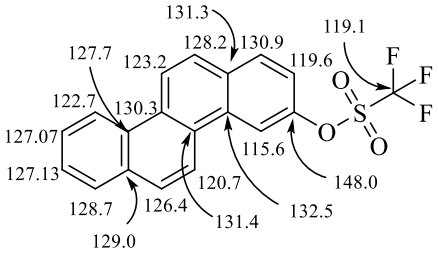
5b

^{1}H-NMR:



6c

^{13}C-NMR:



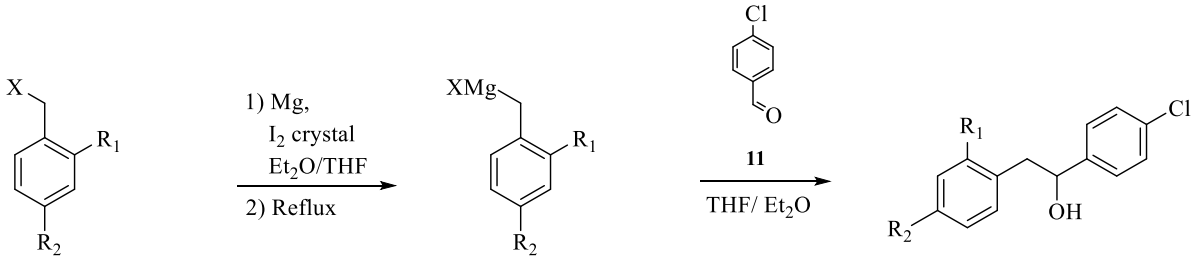
6c

*Figure 3.5: Spectral data from ^{1}H-NMR and ^{13}C-NMR assigned to respective atoms in the molecule. There is a larger degree of uncertainty for the aromatic signals of triflate **6c**.*

3.5 Synthesis of Grignard reagents and reaction with 4-chlorobenzaldehyde

Several attempts at reacting Grignard reagents with 4-chlorobenzaldehyde (**11)** were made. All the attempted reactions were performed using 2 - 4 mmol of starting material which was reacted with 1.0 – 1.4 equivalents of magnesium turnings and 0.53 – 1.0 equivalents of aldehyde. The successful attempt reacted 1 equivalent of benzyl bromide (**9a)** with 1.3 equivalents of Mg and 0.53 equivalents of aldehyde **11**. 24 equivalents of solvent were used to stabilise Grignard reagent **10a**. See chapter 6.10 and 6.11 for a detailed description of all the attempted reactions.

*Table 3.7: Results from the synthesis of Grignard reagents and reaction with **11**.*



9a: R_1 = H, R_2 = H, X = Br
9b: R_1 = Me, R_2 = H, X = Br
9c: R_1 = H, R_2 = Me, X = Cl

10a: R_1 = H, R_2 = H, X = Br
10b: R_1 = Me, R_2 = H, X = Br
10c: R_1 = H, R_2 = Me, X = Cl

12a: R_1 = H, R_2 = H
12b: R_1 = Me, R_2 = H
12c: R_1 = H, R_2 = Me

Starting material	Mg (eq.)	Solvent[a] (eq.)	Aldehyde (eq.)	Conditions Grignard	Conditions Aldehyde	Product	Yield[b] (%)
9a	1.0[c]	10	0.88	I_2, THF, reflux 2 hr. with sonification	THF, -10 °C to RT, 2 hr. stirring	**12a**	0
9a	1.3	24	0.53	Et_2O, 3 hr. stirring at RT	Et_2O, 1 hr. at -40 °C, 3 hr. at RT	**12a**	83
9b	1.1	8.8	0.65	I_2, THF, reflux 2 hr. with sonification	THF, 0 °C to RT, 2 hr. stirring	**12b**	0
9c	1.4[c]	13	1.0	I_2, Et_2O, reflux 30 min. with sonification	Et_2O, 0 °C to RT, 2 hr. stirring	**12c**	0

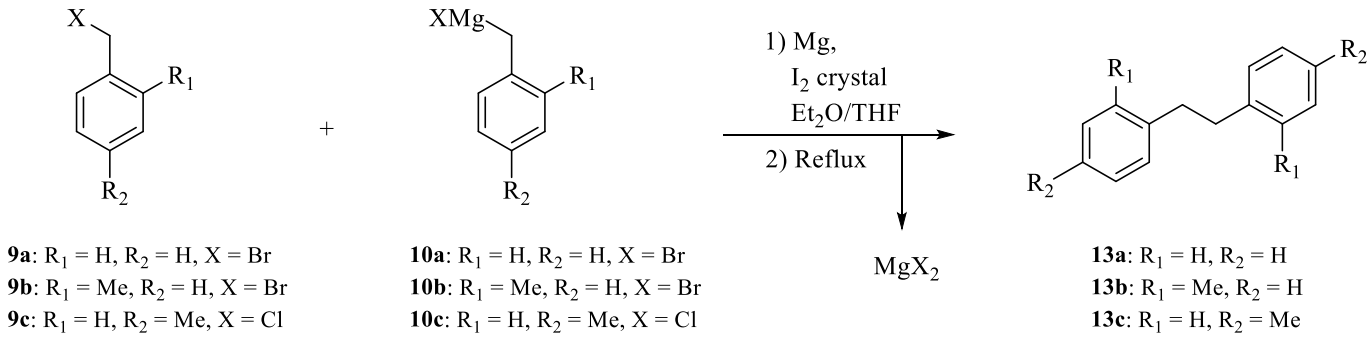
a: Only the solvent used in the synthesis of the Grignard reagent are given in the table. More solvent was added together with the aldehyde, but is not as important for the reaction outcome, and has therefore not been included in the table.

b: Calculation of yield is based on amount of aldehyde.

c: Older magnesium used.

The yields of the reactions were in most attempts not good. This is likely a result of difficulties in the first reaction, where the Grignard reagent was attempted synthesized. It is not possible to directly measure the amount of Grignard reagent made, which is why the reaction with aldehyde was performed. Aldehydes react easily with Grignard reagents in good yields as described in chapter 2.6. Yield of aldehyde obtained is therefore assumed to be directly related to the amount of Grignard reagent made. The successful attempt was based on the procedure previously described by Floresta et al.[10] which obtained yields of 92 – 99% on similar compounds.

The Grignard reaction proved to be more challenging than first expected. Based on the amount of magnesium turnings left and the isolated compounds in the subsequent reactions, it became apparent that only some Grignard was synthesized, and that this reacted with starting material to construct the corresponding bibenzyl, as illustrated in figure 3.6.



9a: R_1 = H, R_2 = H, X = Br
9b: R_1 = Me, R_2 = H, X = Br
9c: R_1 = H, R_2 = Me, X = Cl

10a: R_1 = H, R_2 = H, X = Br
10b: R_1 = Me, R_2 = H, X = Br
10c: R_1 = H, R_2 = Me, X = Cl

13a: R_1 = H, R_2 = H
13b: R_1 = Me, R_2 = H
13c: R_1 = H, R_2 = Me

Figure 3.6: Reaction for the formation of bibenzyl.

The formation of bibenzyl is favoured when the temperatures are high and there is an excess of starting material. It is therefore favourable to add the starting material very slowly, and over a longer time interval as the reaction is exothermal.[122] One reason why the initial attempts failed is probably due to not adding the starting material slowly enough. The attempt that finally succeeded had a very slow addition of starting material, specifically 0.36 ml during the span of 1 hour. All the failed attempts had an addition period smaller than 30 minutes. Another difference between the failed and successful attempts were heating. The successful attempt required no heating but was allowed a longer reaction time. The failed attempts were all heated. It is likely that heating did contribute in synthesizing bibenzyl, but it is probably not the main cause.

Another source of error for the first reactions might be the magnesium used. The first attempts used magnesium that was older and not very shiny in colour. The darker, less shiny colour indicates oxidation. Oxidized magnesium will not react to form Grignard. A new bottle of magnesium turnings was therefore purchased and tried. The first attempts using the new magnesium did not yield any product. This was unexpected because at that time, the magnesium was considered the main source of error. In retrospect the lack of product formation was likely primarily a result of too rapid addition of starting material. Addition at a very slow pace was not tried using the older magnesium. It is therefore a possibility that the older magnesium could have resulted in product formation had it been added more slowly.

Another important aspect is the amount of solvent used in the reaction. Initial attempts were based on larger scale synthesis and was therefore scaled down. The amount of solvent was scaled down according to the same ratio. This probably resulted in there being too little solvent. As mentioned in chapter 2.5 the solvent helps to stabilize the formed Grignard reagent. More solvent will also help to dilute the solution, which decreases the chance of an unfavoured reactions happening. It is therefore essential to have enough solvent. The use of too little solvent probably was a major reason as to why bibenzyl was obtained as the sole product in the first reactions. The successful attempt utilized 2 to 3 times the amount of solvent as the initial, failed attempts.

Another difference between the successful attempt and the failed ones was the addition of an iodine crystal. Iodine was not added in the successful attempt at forming Grignard reagent. It was however added during all the unsuccessful attempts. According to literature the magnesium is fully activated when the yellow colour from iodine disappears. Thus, the starting material should be added when the solution is clear. During all the failed attempts the starting material was added before the colour was clear. An overall conclusion is therefore to be patient when preparing Grignard reagents and to use enough solvent.

NMR analysis of 1-(4-chlorophenyl)-2-phenylethan-1-ol (**12a)** showed signals that were in accordance with the previously reported values of Shannon et al.[123] The assigned spectral data is given in figure 3.7 and spectra are available in appendix XXVII - XXVIII. ^{1}H-NMR and ^{13}C-NMR spectrums of bibenzyl **13a** and 1,2-di-o-tolylethane (**13b)** were also in accordance with literature and can be found in appendix XXIX - XXXII.[124–126] No NMR was taken of 1,2-di-p-tolylethane (**13c)**, however TLC analysis indicated that this was the formed product.

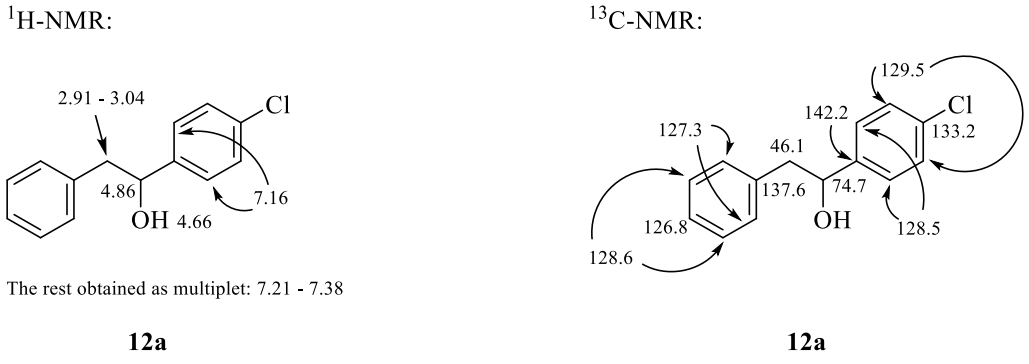


Figure 3.7: Spectral data from ^{1}H-NMR and ^{13}C-NMR assigned to respective atoms in the molecule.

3.7 Kumada-Corriu Coupling

There exists a wide selection of protocols that describes the coupling of different reagents under different conditions. As for the coupling of triflate bearing binaphthalene both the dppp and dppe nickel complexes have been reported to give good yields under different conditions.[127–129] Based on available literature it is reasonable to believe that the dppp ligand works best when coupling with alkyl Grignard reagents, while the dppe ligand is more suitable for alkenyl Grignard reagents.[130] Pd(dppf)Cl_2 has also been reported as a good coupling catalysator when reacting a triflate bearing electrophile with benzylmagnesium bromide.[131] No Kumada-Corriu coupling has been reported between a PAH bearing triflate and styrylmagnesium bromide. A somewhat similar reaction has however been reported between another type of triflate and styrylmagnesium bromide which resulted in a good yield of 81%.[132] The reaction was catalysed by Pd(dppf)Cl_2 and is illustrated in figure 3.8. As there is addition of a zinc salt the reaction might be a Negishi coupling and not a Kumada-Corriu coupling. The reaction type was not specified in the source.

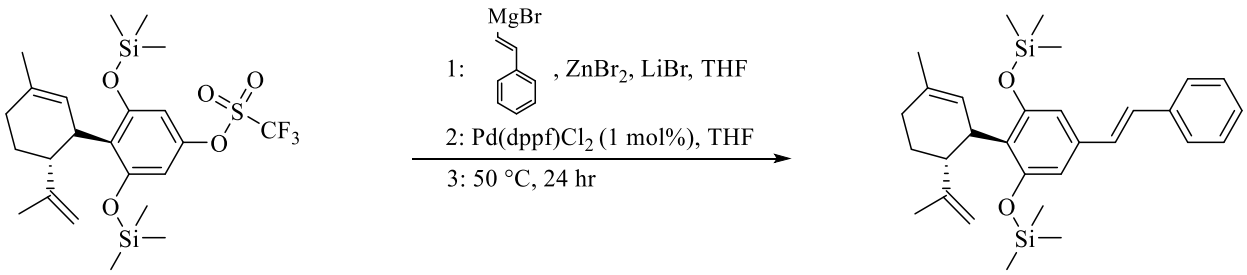


Figure 3.8: The Negishi coupling of (1'R,2'R)-5'-methyl-2'-(prop-1-en-2-yl)-2,6-bis((trimethylsilyl)oxy)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate and styrylmagnesium bromide.

In this thesis four general procedures which utilizes different catalysators, have been established for the coupling of triflate **5b** and **6c** with different Grignard reagents. All the mentioned procedures have been performed using 0.2 – 1.1 mmol of starting triflate. See chapter 6.12 for a detailed description of all the four general procedures. Results from the reactions are illustrated in figure 3.9 and summarised in table 3.8.

General procedure A is based on the procedure reported by Bjelland and utilizes Ni(dppp)Cl_2 as catalysator.[2] The method is assumed to work well for alkyl Grignard reagents and have been used to couple Grignard reagents **14** and **16** to triflate **5b** resulting in the formation of 2-ethylnaphthalene (**5c)** and 2-isopropylnaphthalene (**5e)** respectively. Bot the obtained yields were good. General procedure A has also been used to couple Grignard reagent **16** to triflate **6c** in excellent yield.

General procedure B is loosely based on the procedure reported by Fiorito et al.[130] and utilizes $Ni(dppe)Cl_2$ as catalysator. The method is assumed to be more suitable for alkenyl Grignard reagents and have been used to couple Grignard reagent **15** with triflate **5b** resulting in the formation of 2-vinylnaphthalene (**5d)**. The yield of the first attempt was not good and was mixed with by-product, while the yield from the second attempt was lost during workup.

General procedure C is based on the procedure reported by Fürstner and Leitner[4] and utilizes $Fe(acac)_3$ as catalyst. This procedure has been used to couple triflate **5b** and **6c** with the majority of available Grignard reagents. The best yield was obtained when triflate **6c** was coupled with Grignard reagent **16**. In all attempts the coupling with the chrysene gave better yields than the coupling of the naphthalene when using the same Grignard reagent.

The last procedure referred to as general procedure D utilizes $Pd(dppf)Cl_2$ as catalysator and was originally reported by Abdur-Rashid et al.[132] This procedure has been used to couple triflate **5d** with Grignard reagent **15** and **16**, and triflate **6c** with Grignard reagent **15**. Although TLC indicated good product formation, all attempts at isolating vinylnaphthalene **5d** was unsuccessful. Some alternative versions of general procedure D were also attempted based on other previously reported procedures which utilized the same catalyst. For the coupling of Grignard reagent **10a** with triflate **5b** the procedure previously reported by Hayashi et al.[131] was used. The yield of the reaction was not very good, and the obtained product was mixed with bibenzyl by-product.

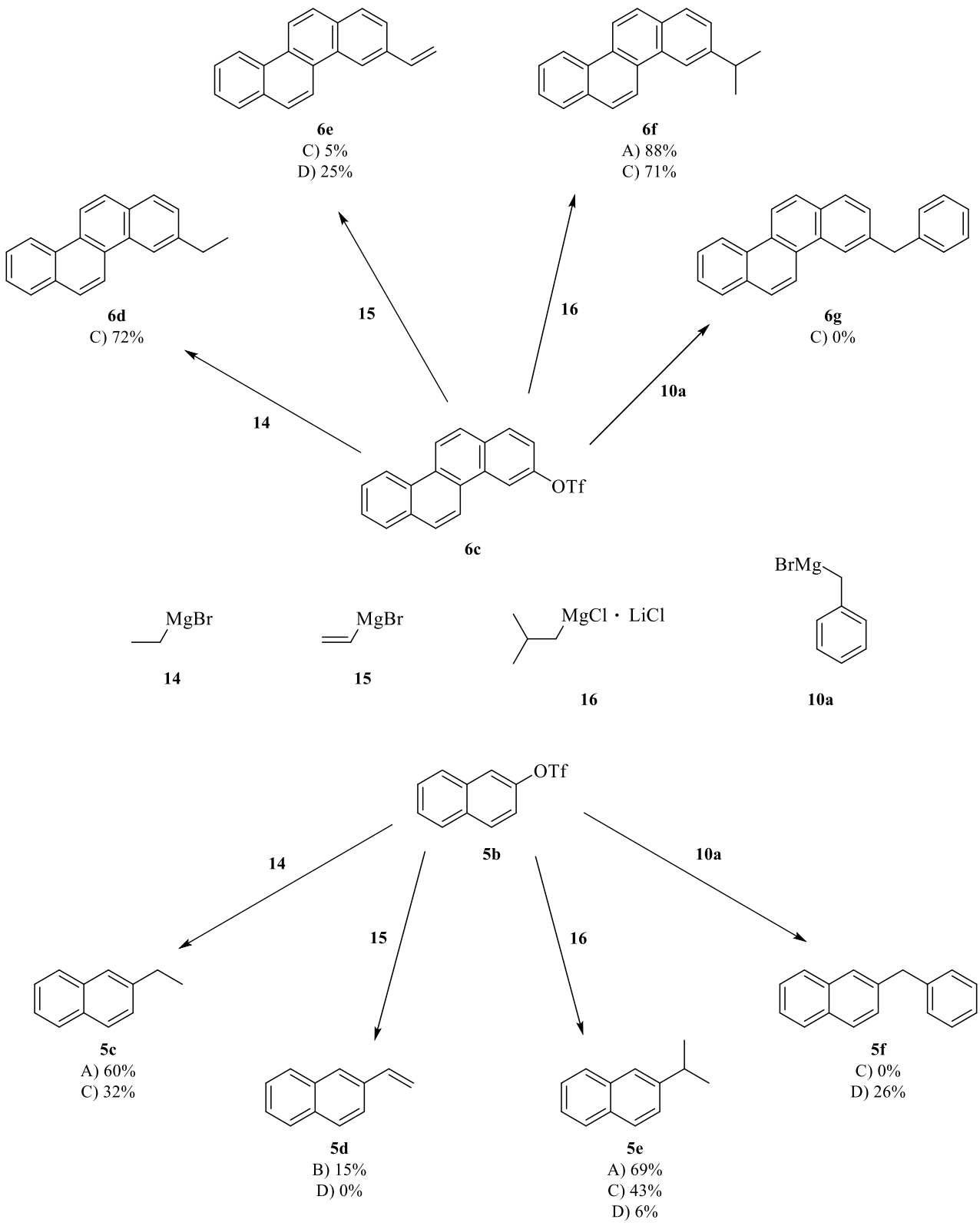


Figure 3.9: Overview of Kumada-Corriu couplings. A) Ni(dppp)Cl_2 (5 mol%), Et_2O, 0 °C, Reflux 3 hr.B) Ni(dppe)Cl_2 (5 mol%), THF, 0 °C, Reflux 4 hr. C) Fe(acac)$_3$ (5 mol%), THF, 0 °C. D) 1: $ZnBr_2$, LiBr, THF. 2: Pd(dppf)Cl_2 (1 mol%), THF. 3: 50 °C, 24 hr.

*Table 3.8: Results from the Kumada-Corriu coupling of Grignard reagents with triflate **5b** and **6c**.*

Starting triflate	Grignard reagent	Eq. of Grignard reagent	Catalyst	Differences from general procedure	Product	Yield (%)
5b	**14**	3.1	$Ni(dppp)Cl_2$	None.	**5c**	60[a]
5b	**14**	3.4	$Fe(acac)_3$	Grignard reagent was not added dropwise. Ice bath was not used under initial addition.	**5c**	32[a]
5b	**15**	1.2	$Ni(dppe)Cl_2$	None.	**5d**	15[a,b]
5b	**15**	3.7	$Ni(dppe)Cl_2$	21 hours of reflux.	**5d**	1[a,b,c]
5b	**15**	1.4	$Pd(dppf)Cl_2$	None.	**5d**	0[a,c,d]
5b	**15**	1.5	$Pd(dppf)Cl_2$	None.	**5d**	0[a,c,d]
5b	**16**	3.0	$Ni(dppp)Cl_2$	None.	**5e**	69
5b	**16**	3.0	$Fe(acac)_3$	None.	**5e**	43
5b	**16**	1.5	$Pd(dppf)Cl_2$	No LiBr added.	**5e**	6
5b	**10a**	3.5[e]	$Pd(dppf)Cl_2$	No LiBr and $ZnBr_2$ was added. Refluxed overnight. Et_2O used instead of THF. Different workup.	**5f**	26[f]
5b	**10a**	3.1[e]	$Fe(acac)_3$	None.	**5f**	0
5b	**10b**	-[g]	$Pd(dppf)Cl_2$	No LiBr and $ZnBr_2$ was added. Refluxed overnight. Different workup.	**5g**	0
5b	**10b**	-[g]	$Pd(dppf)Cl_2$	None.	**5g**	0[d]
6c	**14**	3.1	$Fe(acac)_3$	None.	**6d**	72
6c	**15**	2.7	$Fe(acac)_3$	None.	**6e**	5[b]
6c	**15**	1.6	$Pd(dppf)Cl_2$	None.	**6e**	25[b,d]
6c	**16**	2.9	$Ni(dppp)Cl_2$	None.	**6f**	88
6c	**16**	2.9	$Fe(acac)_3$	None.	**6f**	71
6c	**10a**	1.9[e]	$Fe(acac)_3$	None.	**6g**	0
6c	**10b**	-[g]	$Pd(dppf)Cl_2$	None.	**6h**	0

a: Sublimated when dried *in vacuo*.

b: NMR indicated that the product was mixed with by-product.

c: Product was lost during workup.

d: Possibly a Negishi coupling.

e: Based on 100% yield in synthesis of **10a**.

f: Mixed with bibenzyl by-product.

g: No Grignard reagent was synthesised in the preceding reaction.

3.7.1 Coupling with ethylmagnesium bromide

The coupling of Grignard reagent **14** gave reasonable yields with both triflate **5b** and **6c** as seen in table 3.8. No previous coupling results between these reagents were available in literature.

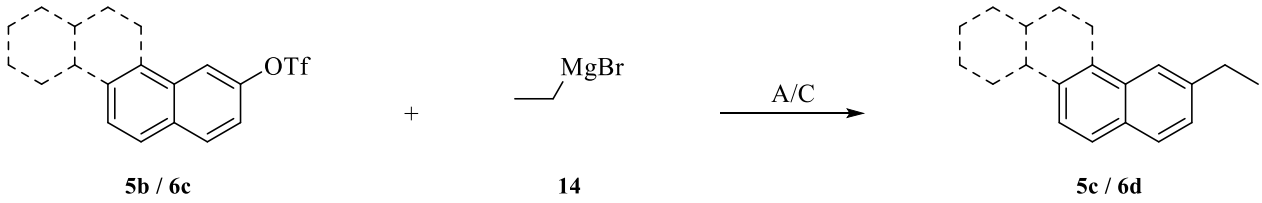


*Figure 3.10: Reaction for synthesis of triflate **5b** and **6c**. A) Ni(dppp)Cl_2 (5 mol%), Et_2O, 0 °C, Reflux 3 hr. C) $Fe(acac)_3$ (5 mol%), THF, 0 °C.*

The reaction of triflate **6c** with Grignard reagent **14** gave the best yield of 72% using general procedure C. The same catalysator yielded ethylnaphthalene **5c** in only 32%. This may be due to somewhat different reaction conditions. When attempting to synthesise ethylnaphthalene **5c** the Grignard reagent was added much faster than it ideally should. On top of that an ice bath was not used before most of the Grignard reagent was added. The mixture was seen boiling when the mixture was put on ice. Heightened temperatures may have contributed to decreased yield. The higher yield of 3-ethylchrysene (**6d)** compared to ethylnaphthalene **5c** may also be a result of ethylchrysene **6c** being more reactive when using general procedure C. When the reaction is compared to the coupling with **16** a greater yield was also achieved when reacting with the chrysene. It can therefore be argued that chrysene seem to have a higher reactivity than naphthalene when catalysed by iron.

The coupling of triflate **5b** using general procedure A obtained a yield of 60%. The true yield of the reaction is believed to be much greater. A TLC analysis was performed during the reaction before and

after quenching. Only product was visible on both plates. This indicates that the majority of reagent had reacted. The low yield is therefore believed to be a result of evaporation of the compound when dried *in vacuo*.

Both Triflate **5c** and **6d** were easily identified on NMR. Both ^{1}H-NMR and ^{13}C-NMR spectra of triflate **5c** was in accordance with reported spectrums of Sloan et al.[133] No previously reported spectra of triflate **6d** was available in literature.

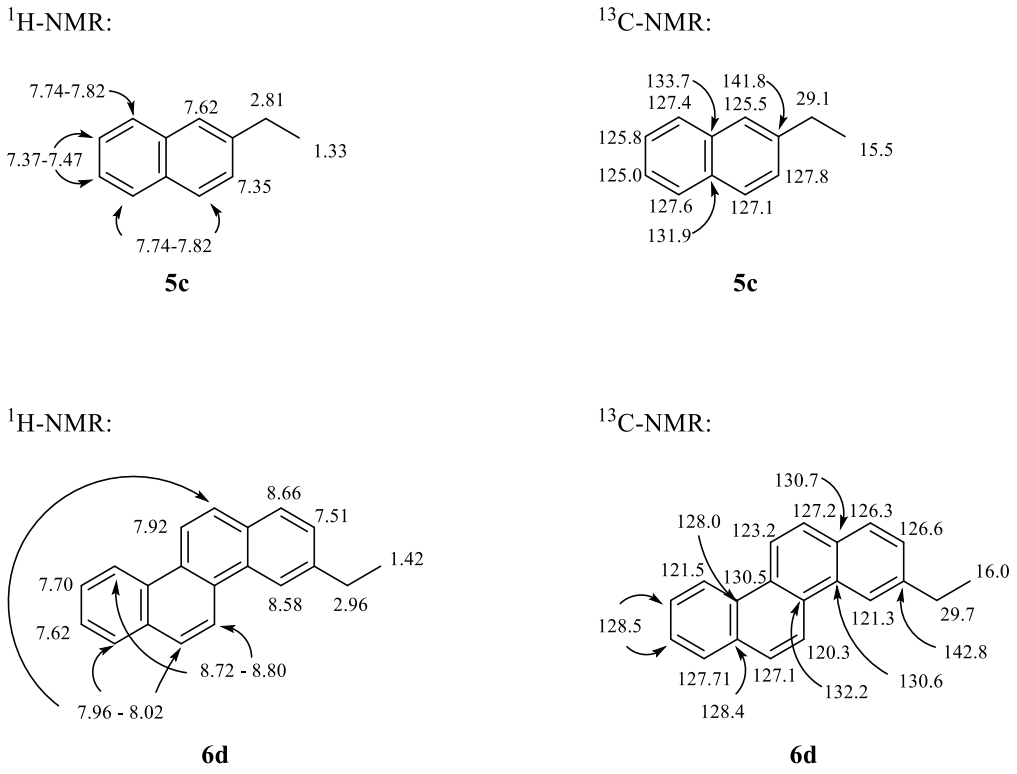
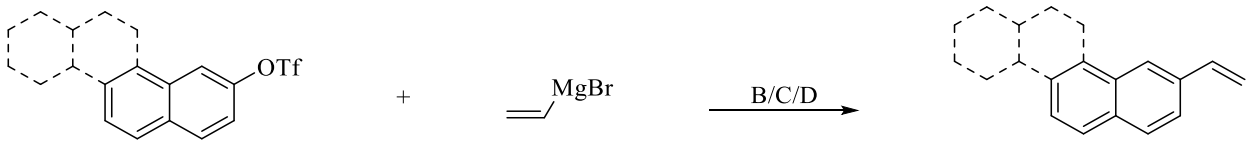


*Figure 3.11: Spectral data from ^{1}H-NMR and ^{13}C-NMR assigned to respective atoms in the molecule. There is a larger degree of uncertainty for the aromatic signals of ethylchrysene **6d**.*

3.7.2 Coupling with vinylmagnesium bromide

The coupling of Grignard reagent **15** gave poor yields with both triflate **5b** and **6c** as seen in table 3.8. No previous coupling results between these reagents were available in literature.



5b/6c **15** **5d/6e**

*Figure 3.12: Reaction for synthesis of triflate **5e** and **6f**. B) Ni(dppe)Cl_2 (5 mol%), THF, 0 °C, Reflux 4 hr. C) Fe(acac)$_3$ (5 mol%), THF, 0 °C. D) 1: $ZnBr_2$, LiBr, THF. 2: Pd(dppf)Cl_2 (1 mol%), THF. 3: 50 °C, 24 hr.*

The reaction of triflate **6c** with Grignard reagent **15** gave the best yield of 25% using general procedure D. The same procedure could not be used to isolate vinylnaphthalene **5d**. When comparing the two TLC plates of vinylnaphthalene **5d** and 3-vinylchrysene (**6e)** there seems to be a much greater product formation of vinylnaphthalene **5d**. During the first synthesis attempt using general procedure D, the product was left in a see-through beaker over the weekend. When the initial attempt at isolating the product failed, it was believed that the product had polymerised. Because of this a second attempt at synthesising vinylnaphthalene **5d** following the same procedure was attempted. This time the purification with flash column was performed directly following the reaction. Nevertheless, no product could be isolated.

*Figure 3.13: TLC plate from the synthesis attempt of vinylnaphthalene **5d** using general procedure D.*

General procedure B was also used to synthesise vinylnaphthalene **5d**. The initial attempt yielded 15%, which makes it the best obtained yield of vinylnaphthalene **5d**. The true yield is however believed to be higher. The product was dried for more than 24 hours *in vacuo*, but still the weight would not stabilise. It was suspected that sublimation could be a problem. Because of this a store-bought sample of vinylnaphthalene **5d** were weighed before it was dried *in vacuo* over the span of 1 hour. Sublimation was confirmed as the weight decreased over 10% during that one hour.

Apart from the original version of general procedure B, an alternative version was attempted. The alternative version had the same problem of isolation as general procedure D, and the product was lost during workup.

There were two major differences between the original procedure B and the alternative one. One of these differences was the amount of Grignard reagent used. The original procedure is based on the optimized reaction conditions of diethyl (1-phenylvinyl) phosphate with Grignard reagent **15** reported by Fiorito et al.[130] According to Fiorito et al. the optimal amount of Grignard reagent **15** is 1.05 equivalent. When increasing the amount of Grignard reagent to 2.50 equivalents under the otherwise same conditions, the yield decreased from 99% to 13%. The alternative procedure reported by Visco et al.[129] uses the same catalysator to react 3.0 equivalents of methylmagnesium bromide to 2'-phenyl-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate. The electrophile used in the procedure of Visco et al. is more similar to vinylnaphthalene **5d**, while the Grignard reagent of Fiorito et al. is identical to Grignard reagent **15**. No major difference in product formation was observed according to the TLC plates.

The second difference between the two procedures was the refluxing period. The procedure of Fiorito et al. only requires 1 hour of refluxing, while that of Visco et al. requires refluxing overnight. When performing the initial attempt at synthesising vinylnaphthalene **5d** the mixture was first refluxed for 1 hour before a TLC analysis was performed. As there still were traces of unreacted starting material, the solution was left to stir for 3 more hours. Afterwards a second TLC analysis was performed but showed no significant difference. Both TLC plates obtained from the original and alternative procedure B showed inferior product formation compared to the TLC plates obtained from following procedure D.

Because of the difficulty in isolating vinylnaphthalene **5d**, it was not attempted to react triflate **5b** with Grignard reagent **15** using general procedure C. The reaction of triflate **6c** with Grignard reagent **15** using general procedure C yielded vinylchrysene **6e** in only 5%. It seems that the iron catalyst used is not suitable for reaction with alkenyl Grignard reagents. This was expected based on reported results from Fürstner and Leitner.[4]

Both vinyl compound **5d** and **6e** were somewhat identifiable on NMR and seemed to be mixed with by-product. Based on the obtained spectra it seems that vinylnaphthalene **5d** is mixed with ethylnaphthalene **5c** and vinylchrysene **6e** is mixed with ethylchrysene **6d**. Both ^{1}H-NMR and ^{13}C-NMR spectra contained the expected signals from the vinyl group as illustrated in figure 3.14. But there were also signals in the lower area of the spectra which match obtained values from ethylnaphthalene **5c** and ethylchrysene **6d**. This was not as visible on the ^{1}H-NMR spectra of vinylnaphthalene **5d** as there was an excess of signal in the lower area, indicating that the product is not properly dried. Further drying could be performed, but there is a great possibility of sublimation which can lead to desired product being lost. There are fewer excess signals in the ^{13}C-NMR spectra of vinylnaphthalene **5d**, where the two biggest peaks of 15.5 and 29.1 ppm are consistent with the ethyl group of ethylnaphthalene **5c**. The ^{1}H-NMR spectra of ethylchrysene **6e** also have an excess of signal in the lower area, which masks the ethyl signals. The ^{13}C-NMR spectra of ethylchrysene **6e** had two peaks of 16.0 and 29.7 ppm which were identical to the obtained values of the ethyl group in ethylchrysene **6d**. Otherwise the spectra of vinylnaphthalene **5d** were in in accordance with reported spectrums of Denmark and Butler.[134] No previously reported spectra of vinylchrysene **6e** was available in literature.

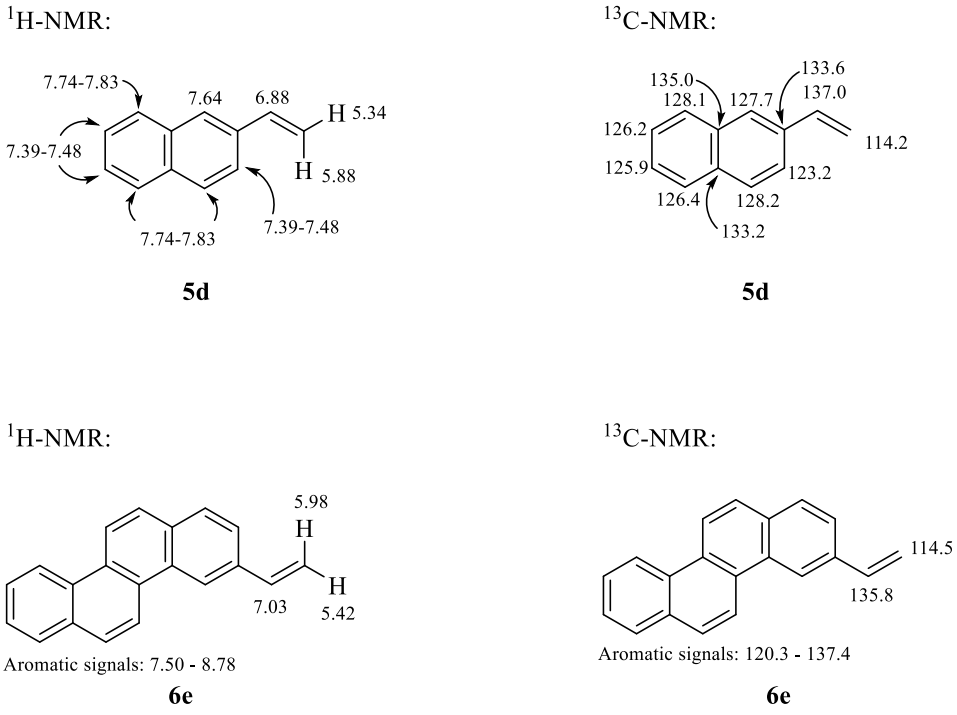
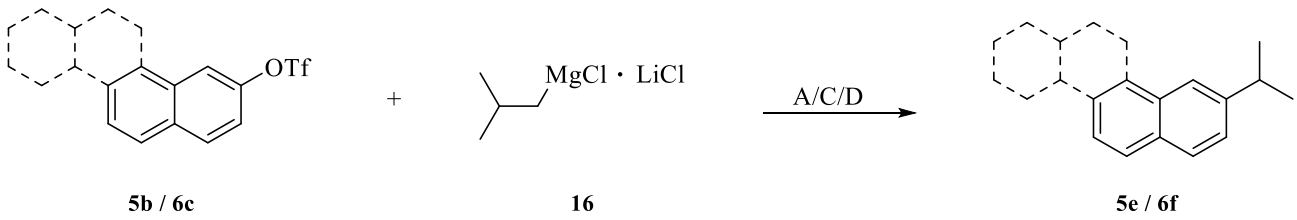


*Figure 3.14: Spectral data from ^{1}H-NMR and ^{13}C-NMR assigned to respective atoms in the molecule. Due to difficulty in separating the aromatic signals of ethylchrysene **6d** from that of product **6e** it was not attempted to assign the aromatic signals of the chrysene to respective atoms in the molecule.*

3.7.3 Coupling with isopropylmagnesium chloride lithium chloride complex

The coupling of Grignard reagent **16** gave reasonable yields with both triflate **5b** and **6c** as seen in table 3.8. No previous coupling results between these reagents were available in literature.



5b / 6c **16** **5e / 6f**

*Figure 3.15: Reaction for synthesis of **5e** and **6f**. A) Ni(dppp)Cl_2 (5 mol%), Et_2O, 0 °C, Reflux 3 hr. C) Fe(acac)$_3$ (5 mol%), THF, 0 °C. D) 1: $ZnBr_2$, LiBr, THF. 2: Pd(dppf)Cl_2 (1 mol%), THF. 3: 50 °C, 24 hr.*

The reaction of triflate **6c** with Grignard reagent **16** gave the best yield of 88% using general procedure A. The second-best yield of 71% was that between the same coupling partners using general procedure C. The Fe(acac)$_3$ catalyst yielded isopropylnaphthalene **5e** in 43%. The reaction conditions were identical, which supports the theory of chrysene being more reactive than naphthalene in coupling reactions using Fe(acac)$_3$ as catalyst. The coupling of triflate **5b** with Grignard reagent **16** was also performed using general procedure A and B. The best yield of 69% was obtained using general procedure A. General procedure D resulted in a yield of only 6%. Since the Grignard reagent used is a Turbo-Grignard, no LiBr was added during this reaction.

Both isopropylnaphthalene **5e** and 3-isopropylchrysene **(6f)** were easily identified on NMR. Both ^{1}H-NMR and ^{13}C-NMR spectra of isopropylnaphthalene **5e** were in accordance with reported spectrums of Madhushaw et al.[135] No previously reported spectra of isopropylchrysene **6f** was available in literature.

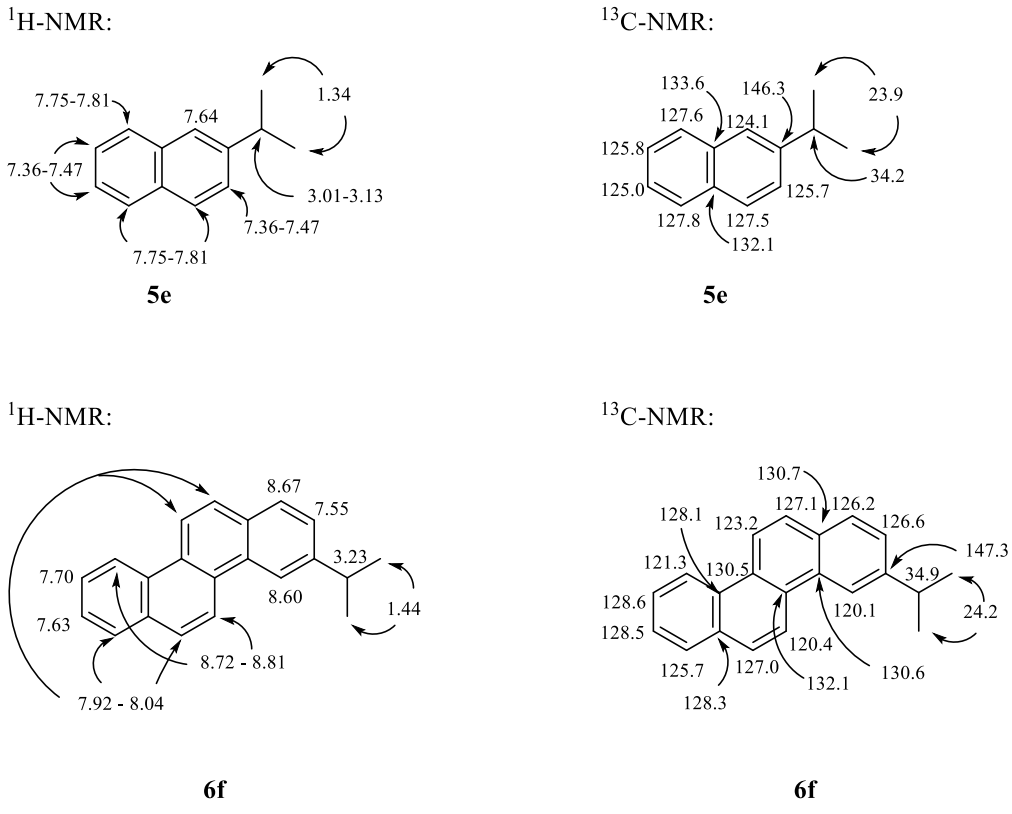


*Figure 3.16: Spectral data from ^{1}H-NMR and ^{13}C-NMR assigned to respective atoms in the molecule. There is a larger degree of uncertainty for the aromatic signals of isopropylchrysene **6f**.*

3.7.4 Coupling with self-generated Grignard reagents

Two couplings were attempted between Grignard reagent **10a** and triflate **5b**. The attempt following a modified version of general procedure D yielded 26% of product. The product had almost the same retention rate as generated bibenzyl. When attempting to separate the two compounds on flash column half the product was overlapping with bibenzyl or starting material. Only the fractions which had visible traces of desired product (according to TLC) was isolated during flash column chromatography. The product which was isolated still seemed to be a mix of 60% benzylnaphthalene **5f** and 40% bibenzyl **13a** (according to NMR analysis). The attempt at synthesising benzylnaphthalene **5f** using general procedure C was unsuccessful. TLC indicated no product formation. The coupling using general procedure C was also attempted with triflate **6c** and yielded no product.

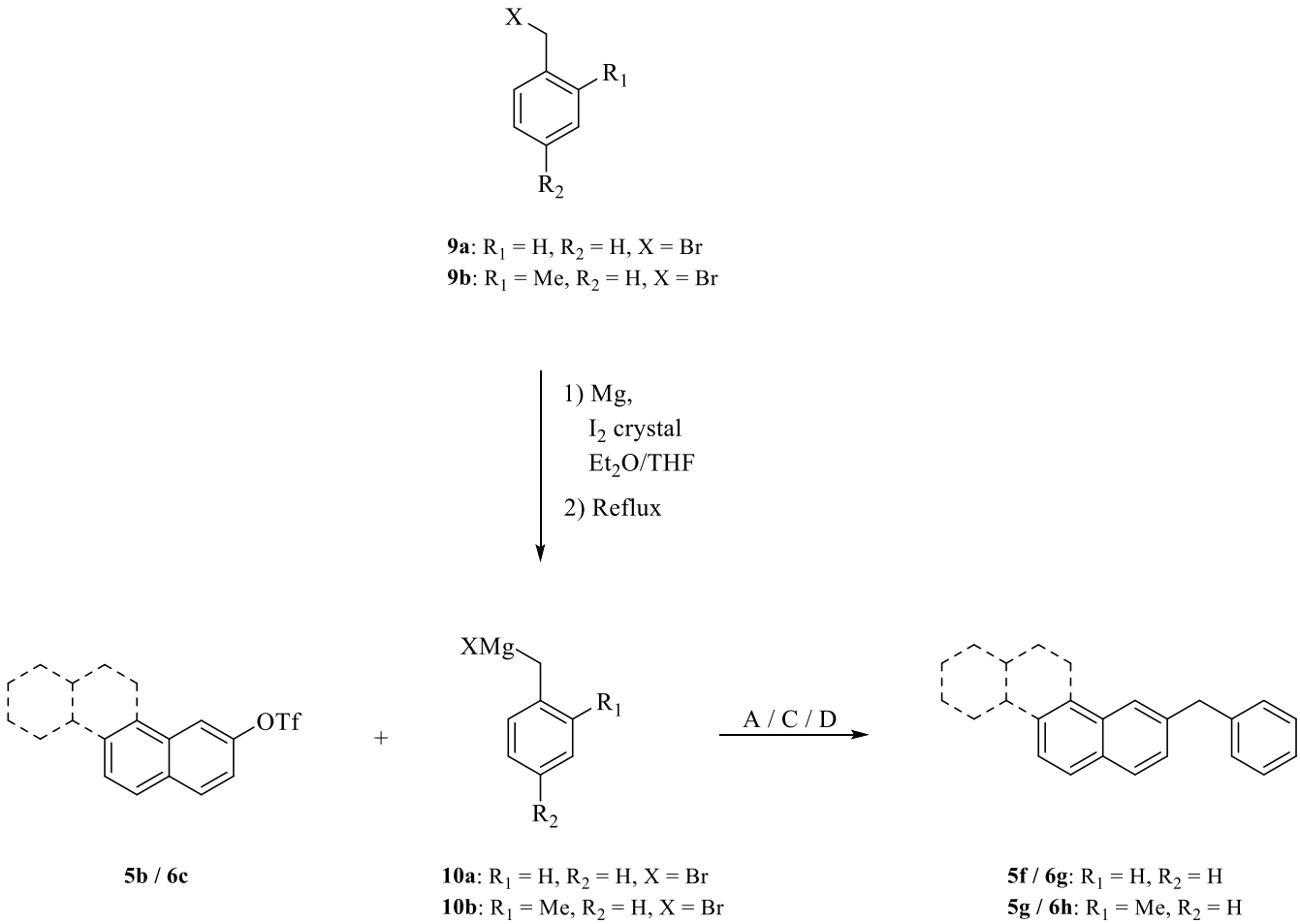


*Figure 3.17: Reaction for the attempted synthesis of **5f**, **5g**, **6g** and **6h**. c) $Fe(acac)_3$ (5 mol%), THF, 0 °C. d) 1: $ZnBr_2$, LiBr, THF. 2: $Pd(dppf)Cl_2$ (1 mol%), THF. 3: 50 °C, 24 hr.*

The Grignard reagent had to be made from available benzyl bromide. For this the procedure of Floresta et al.[10] was used since it already had been used for the successful synthesis of Grignard reagent **10a** in a previous reaction, see chapter 3.5. In all the mentioned attempts the formation of Grignard reagent seemed to be successful, indicated by the disappearance of magnesium turnings.

When attempting to react triflate **5b** with Grignard reagent **10a** a needle was used to transfer the Grignard reagent to the solution containing the triflate. No precipitation was visible in the round flask containing the Grignard reagent. But when the solution was sucked into the needle a black precipitate formed. Based on the similarity to precipitate formed in previously failed attempts at synthesizing Grignard reagents it is reasonable to suspect the formation of bibenzyl. There is no clear explanation as to why the precipitate formed, but it might explain why the following reaction was unsuccessful. The needle used to transfer the Grignard reagent had previously been used to transfer anhydrous THF, but no other reagents or solvents.

Reaction with water is therefore unlikely. A TLC analysis was performed after the attempted Kumada-Corriu reaction. The corresponding bibenzyl was used as a reference together with the triflate to confirm the fear of formed bibenzyl and no product formation. Bibenzyl may also be a by-product from the Kumada-Corriu reaction itself if the two coupling partners is unsuitable for a given catalyst.[95,96]

The successful coupling between Grignard reagent **10a** and triflate **5b** was performed by adding the triflate solution dropwise to the generated Grignard reagent. When attempting to react triflate **6c** with Grignard reagent **10a** the solution containing triflate was also added dropwise to the Grignard reagent. No precipitation was visible during this attempt, but still the major products were bibenzyl and unreacted triflate. It is therefore reason to believe that the use of $Fe(acac)_3$ as catalysator is unsuitable for the coupling of benzylic Grignard reagents.

Attempts at synthesizing 2-(2-methylbenzyl)naphthalene (**5g)** and 3-(2-methylbenzyl)chrysene (**6h)** were performed using general procedure D. Based on the procedure used to make (2-methylbenzyl)magnesium bromide (**10b)**, it is reason to believe that no Grignard reagent was present. Thus, the yield is not representable of the coupling reaction. This is the reason why this reaction is not included in the overview given in figure 3.9. Full descriptions of all the attempted and unsuccessful couplings with self-generated Grignard reagents are available in chapter 6.11.

No previous coupling results using any of the mentioned reagents were available in literature. But several previous spectra of benzylnaphthalene **5f** were available. The spectral data of Inés et al.[136] seem to match the obtained ^{1}H-NMR data in this thesis very well when signals from bibenzyl were removed. A general tendency is however somewhat lowered ppm values in this thesis. The ^{13}C-NMR data of Inés et al. does not match quite as well, even after removing the bibenzyl signals, but still indicates the right compound.

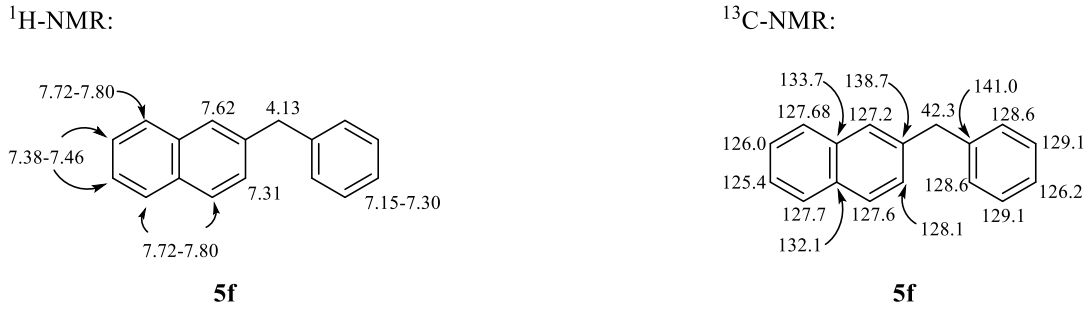


Figure 3.18: Spectral data from ^{1}H-NMR and ^{13}C-NMR assigned to respective atoms in the molecule.

4. Conclusions

The main aim of the thesis was to explore the use of Kumada-Corriu coupling as a possible pathway to functionalise different systems of PAHs. Another aim of the thesis was to explore the possibility of expanding the skeletal structure of starting PAHs by coupling them with styrylmagnesium bromide. The initial strategy to use phenanthren-9-yl trifluoromethanesulfonate as electrophile in the coupling reactions failed. Phenanthren-9-yl trifluoromethanesulfonate was to be synthesised by triflation of phenanthrol **7** which was to be synthesised using a D*o*M/DreM approach. Something seemed to go wrong during the Suzuki-Miyaura coupling which resulted in the formation of carboxamide **4b** and not the expected carboxamide **4a**. At this point, there is no clear understanding of why carboxamide **4b** was formed.

The synthesis of both triflate **5b** and **6c** were successful. The two electrophiles were reacted with four different Grignard reagents catalysed by different catalysators. The Ni(dppp)Cl_2 catalysator gave good yields when coupling Grignard reagent **16** with both triflate **5b** and **6c**. The catalysator also gave reasonable yield when coupling triflate **5b** with Grignard reagent **14**. The coupling of the mentioned reagents using the iron catalyst, Fe(acac)$_3$, all gave inferior yields. Chrysene triflate **6c** showed better reactivity than naphthalene triflate **5b** for all Grignard reagents when using iron as catalyst. Still, it seems that the Ni(dppp)Cl_2 catalyst is an overall better catalyst than Fe(acac)$_3$ when it comes to alkyl Grignard reagents.

The Ni(dppp)Cl_2 catalyst was not used for the coupling of Grignard reagent **15** nor self-generated Grignard reagent **10a**, as it is unsuitable according to literature. As for the coupling of these reagents using the Fe(acac)$_3$ catalyst, only poor yields were obtained. It is therefore highly likely that both the Ni(dppp)Cl_2 and the Fe(acac)$_3$ catalyst will be unsuitable for the coupling of triflate bearing PAH and styrylmagnesium bromide. When attempting to couple vinyl Grignard reagent **15** with triflate **6c** using the Pd(dppf)Cl_2 catalyst a yield of 25% was obtained. Attempts at coupling the same Grignard reagent with triflate **5b,** using the same catalyst, resulted in the product being lost during workup. Nevertheless, TLC analysis indicated good product formation.

The biggest challenge during the work with the thesis was the formation and coupling of self-generated Grignard reagents. All the first attempts at synthesising benzylic Grignard reagents resulted in the formation of undesired bibenzyl. In the end the use of enough solvent and patience seemed to be the key to form Grignard reagent **10a**. Still, when further attempting to react the self-generated Grignard reagent in a Kumada-Corriu coupling, bibenzyl was formed in a side reaction. As bibenzyl and the desired product have similar retention rate, it was difficult to isolate the compounds using flash column chromatography. This led to a poor and highly contaminated yield.

Of the available and used catalysts $Pd(dppf)Cl_2$ worked best for both vinyl Grignard reagent **15** and benzyl Grignard reagent **10a**. These compounds are thought to be more similar to styrylmagnesium bromide than the other Grignard reagents used. It is therefore reason to believe that the $Pd(dppf)Cl_2$ catalyst has the greatest potential of being a suitable catalyst for the coupling of triflate bearing PAH and styrylmagnesium bromide.

5. Future Work

The thesis did fulfil its aim to explore the use of Kumada-Corriu coupling in functionalisation of different systems of PAHs. Nevertheless, much work remains to be explored. In the thesis only four catalysts were used in the coupling reactions. The catalysts were chosen based on results from literature and availability in the lab. During the research process other catalysts also seemed promising, but due to unavailability none of these were attempted used. In the future it would be interesting to broaden the catalyst scope and explore other possibilities than the catalysts mentioned in this thesis.

It would be especially interesting to further explore different versions of the iron catalyst. Iron is a more sustainable catalyst than both nickel and palladium and a better choice for the future. In addition, the use of iron as catalyst in coupling reactions has yet to be explored as much as either nickel or palladium. In this thesis a rather simple iron catalyst without specialized ligands were used. According to literature many other, more specialized iron catalysts have also been established. Alternative additives have also been explored which do not demand the use of toxic NMP as cosolvent.[88] Needless to say, iron has great potential.

A second aim of the thesis was to explore the possibility of expanding the skeletal structure of starting PAHs by coupling them with styrylmagnesium bromide. This was not done as the necessary starting material, (2-bromovinyl)benzene did not arrive in time. Based on the results presented in the thesis, $Pd(dppf)Cl_2$ was deemed a potential catalyst for the coupling. Naturally, the next step would be to use this catalyst in a Kumada-Corriu coupling between styrylmagnesium bromide and triflated PAHs. Before this it could however be advantageous to explore the possibility of transforming (2-bromovinyl)benzene into turbo-Grignard.

When attempting to react self-generated benzyl Grignard reagent in a Kumada-Corriu coupling a major obstacle was the formation of undesired bibenzyl. The formation of bibenzyl resulted in a poorer and more contaminated yield. In the future it would be advantageous to explore pathways which inhibits the side reaction which forms bibenzyl. An alternative is therefore to explore the use of Turbo-Grignard as nucleophile in the Kumada-Corriu coupling. Turbo-Grignard is known to inhibit some known side reactions which usually takes place when forming the Grignard reagent. Another advantage of using Turbo-Grignard is increased reactivity. The use of Turbo-Grignard therefore has the potential of increasing the yield in two ways. Firstly, by inhibiting the formation of bibenzyl and secondly, by increasing the overall reactivity.

6. Experimental

6.1 General

All new compounds were synthesized using standard or similar procedures to previously published literature. All chemicals were used without further purification, but *s*-BuLi and vinylmagnesium bromide were titrated to find the current concentration. DCM was dried and stored on molecular sieves (4Å). The other anhydrous solvents were bought anhydrous. Recrystalising was not performed before recording the melting points of the solids.

Titration of *s*-BuLi was done using a similar procedure to that of Kofron and Baclawski but with the lower temperature as suggested by Burchat et al.[137,138] The titration was performed using diphenylacetic acid in dry THF at -40 °C. The endpoint was indicated by the colour changing from clear to yellow. The titration of vinylmagnesium bromide was done according to the procedure of Krasovskiy and Knochels.[139] The titration was performed using a saturated solution of lithium chloride in dry THF. The endpoint was indicated by a colour change from brown to clear solution.

6.2 Experimental equipment

TLC analysis was done on Merck silikagel 60 F254 plates with UV- radiation of wavelength 254 nm for visualization. Elution liquid was different ratios of heptane and ethyl acetate depending on polarity of analyte.

Flash chromatography was done using silica gel with particle size 40 – 63 µm. Elution liquid was different ratios of heptane and ethyl acetate depending on polarity of analyte. Ratios are specified in each case.

Melting point was measured using Stuart Scientific melting point apparatus SMP3.

NMR spectra was registered on a Bruker Avance III 400 MHz NMR spectrometer with chemical shift given in ppm relative to internal $CDCl_3$ (δ = 77.0 ppm) for ^{13}C-NMR and TMS (δ = 0 ppm) for ^{1}H-NMR. The signals were registered as singlet (s), double singlet (ds), doublet (d), double doublet (dd), triplet (t), double triplet (dt), quartet (q) and multiplet (m).

6.3 Synthesis of N,N-diethylbenzamide (2)

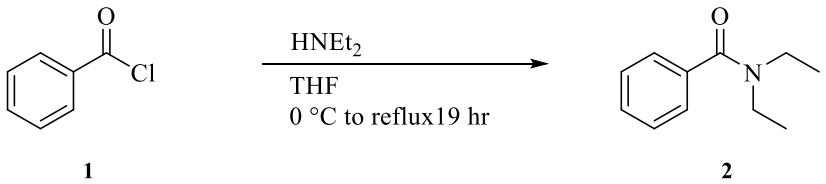


*Figure 6.1: Amination for the synthesis of benzamide **2**.*

Acid chloride **1** (7.826 g, 55.67 mmol) was put under inert atmosphere. Anhydrous THF (150 ml) and Diethylamine (8.5 ml, 82.3 mmol) were added at 0 °C. The mixture was then boiled with reflux for 19 hours. Diethyl ether (200 ml) was added to the product mixture, which was then washed with 1 M HCl (150 ml), sat. aq. $NaHCO_3$ (150 ml) and brine (50 ml). The combined extract was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give **2** as an orange oil (8.081 g, 80%).

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.18 (s, 6 H), 3.41 (s, 4 H), 7.36 – 7.41 (m, 5 H) ppm.

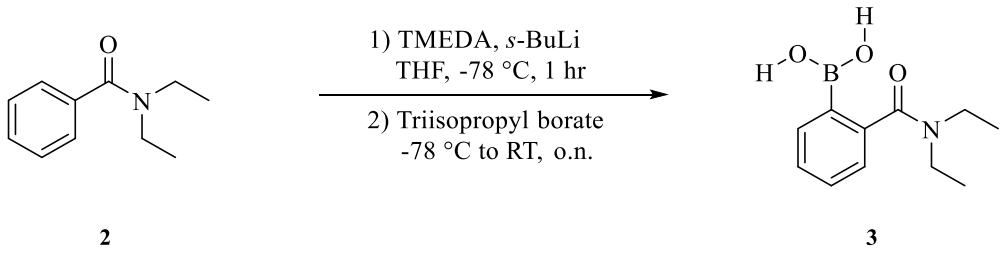
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 126.3, 128.4, 129.2, 137, 171.5 ppm.

The two ethyl-signals of the product were broadened too such a degree that they were not visible on the ^{13}C-NMR spectrum. Broadening was a result of prevented rotation.

Spectra are available in appendix I and II.

NMR data which was visible was in accordance with references.[112,113]

6.4 Synthesis of (2-(diethylcarbamoyl)phenyl)boronic acid (3)



2 **3**

*Figure 6.2: DoM reaction for the synthesis of benzoic acid **3**.*

TMEDA (1.0 ml, 6.7 mmol) was combined with anhydrous THF (20 ml) and put under inert atmosphere. *s*-BuLi (8.5 ml, 6.8 mmol) was then added dropwise at -78 °C. A separate solution of benzamide **2** (1.163 g, 6.561 mmol) in anhydrous THF (20 ml) was added to the mixture, which then was allowed to react for 1 hour at -78 °C. Triisopropyl borate (3.1 ml, 14 mmol) was added to the mixture, and it was allowed to react and reach RT overnight. The reaction was quenched the next day with sat. aq. NH_4Cl (33 ml) and extracted with diethyl ether (3 x 25 ml). The combined organic phases were washed with brine (25 ml). The combined extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give **3** as a yellow oil (1.095 g, 75%).

^{1}H-NMR and ^{13}C-NMR spectra were mixed with impurities and diisopropyl (2-(diethylcarbamoyl)phenyl)boronate.

Spectra are available in appendix III and IV.

6.5 Synthesis of N,N-diethyl-[1,1'-biphenyl]-2-carboxamide (4b)

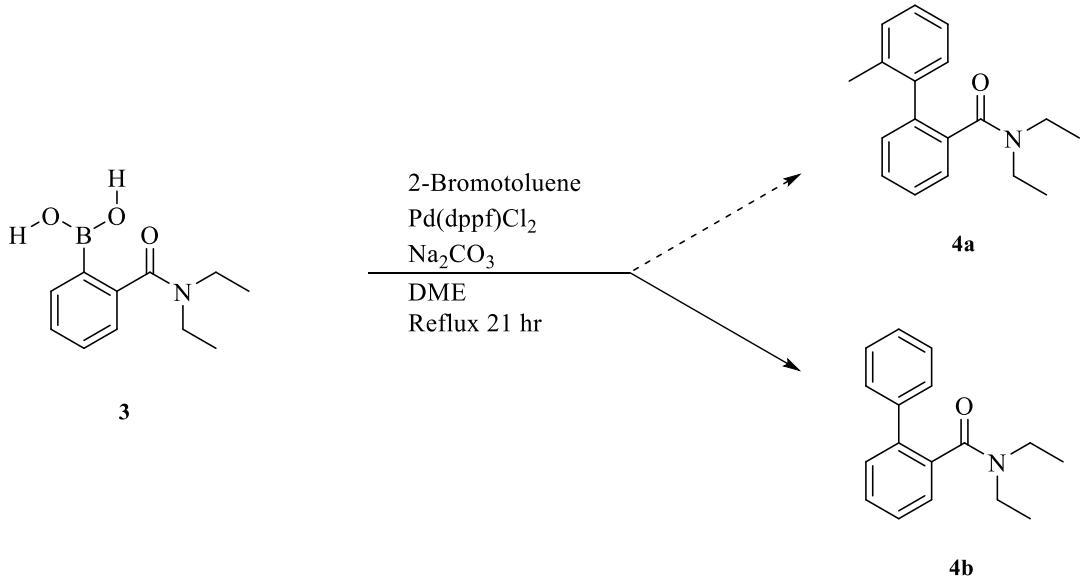


*Figure 6.3: Suzuki-Miyaura coupling reaction for the synthesis of carboxamide **4a** which resulted in the formation of carboxamide **4b**.*

2-bromotoluene (0.30 ml, 2.5 mmol) and Pd(dppf)Cl_2 (0.099 g, 0.12 mmol) were combined and put under inert atmosphere. DME (14 ml) was added and the mixture stirred for 15 minutes. A separate solution of boronic acid **3** (1.095 g, 4.953 mmol) in DME (9 ml) under inert atmosphere, was slowly added to the mixture. Then 2 M Na_2CO_3 (14 ml, 28 mmol) was added, and the mixture was boiled with reflux for 21 hours. The mixture was allowed to cool down to RT the following day, and then extracted with diethyl ether (3 x 20 ml). The combined organic phases were washed with brine (25 ml) and dried over anhydrous Na_2SO_4. The residue was purified by flash column chromatography (*Rf* = 0.2, 1:1 Hep-EA) and dried *in vacuo* to afford **4b** as an orange solid (0.510 g, 76%). Due to the consistency of the product the melting point was hard to determine, based on the attempts it seemed to be around 85 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.07 (t, *J* = 7.1 Hz, 3 H), 1.12 (t, *J* = 7.1 Hz, 3 H), 3.26 (q, *J* = 7.1 Hz, 2 H), 3.43 (q, *J* = 7.1 Hz, 2 H), 7.37 – 7.47 (m, 4 H), 7.50 – 7.59 (m, 3 H), 7.80 (dd, *J* = 8.3, 1.2 Hz, 2 H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 12.2, 13.7, 38.9, 43.2, 126.8, 128.1, 128.3, 129.8, 130.3, 130.8, 133.0, 136.9, 137.2, 138.3, 169.9 ppm.

Spectra are available in appendix V and VI.

NMR data was somewhat in accordance with available reference.[115]

6.6 Attempted synthesis of phenanthrene-9-ol (7) / *9H*-fluoren-9-one (8)

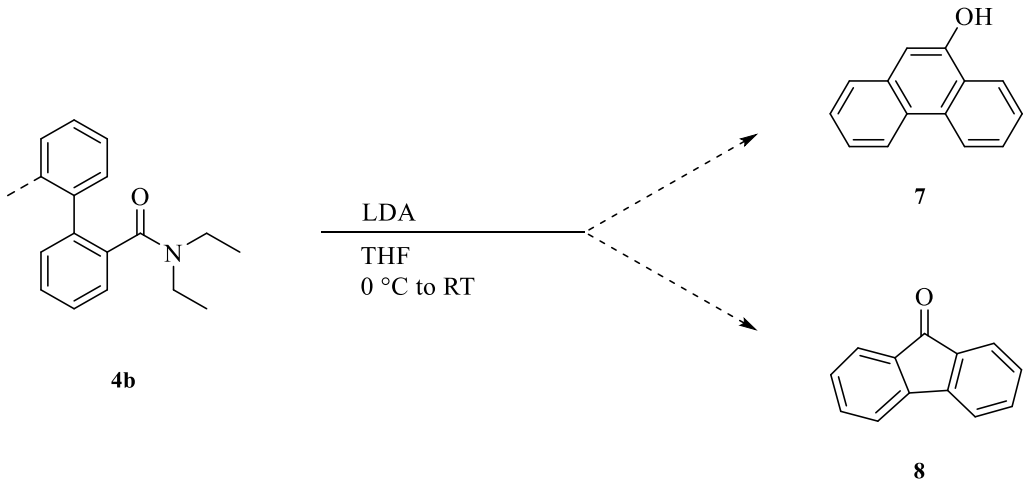
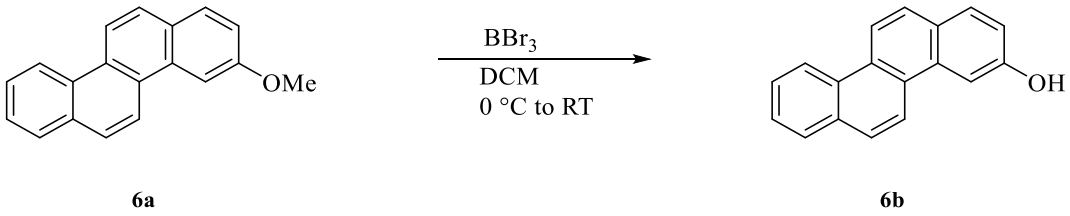


*Figure 6.4: DreM reaction for the synthesis of phenanthrol **7** or fluorenon **8** which resulted in no desired product formation.*

s-BuLi (0.12 mmol, 0.099 g) was added dropwise to a solution of diisopropylamine (0.35 ml, 2.5 mmol) in anhydrous THF (8 ml) under inert atmosphere to create LDA. Afterwards a separate solution of carboxamide **4b** (0.273 g, 1.08 mmol) in anhydrous THF (2 ml) under inert atmosphere, was added to the mixture at 0 °C. The mixture was then allowed to react for 30 minutes at RT. Afterwards it was quenched with sat. aq. NH_4Cl (5 ml) and extracted with diethyl ether (3 x 5 ml). The combined organic phases were washed with brine (5 ml) and dried over anhydrous Na_2SO_4. The residue was purified by flash column chromatography (*Rf* = 0.7, 1:1 Hep-EA) and dried *in vacuo* but only starting material (0.125 g, 46%) was identifiable.

6.7 Synthesis of chrysen-3-ol (6b)



6a **6b**

*Figure 6.5: Deprotection for the synthesis of chrysenol **6b**.*

Ether **6a** (1.809 g, 7.003 mmol) was put under inert atmosphere and added anhydrous DCM (125 ml) and BBr_3 (1.00 ml, 10.4 mmol) at 0 °C. The mixture was first stirred for 20 minutes, and then allowed to reach RT and react overnight. The next day the mixture was quenched by pouring it over ice (400 ml). After 1 hour all the ice had melted, and the mixture was added DCM (300 ml) and 0.1 M NaOH (200 ml). The mixture was then extracted with EA (1 x 200 ml, 1 x 100 ml) and washed with water (300 ml) and brine (300 ml). The combined extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford product **6b** as a white-orange solid compound (1.669 g, 98%). No melting point was recorded as the compound was directly subjected to a triflation.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.07 (s, 1 H), 7.22 (dd, *J* = 8.6, 2.4 Hz, 1 H), 7.63 (dt, *J* = 7.0, 1.3 Hz, 1 H), 7.70 (dt, *J* = 6.9, 1.4 Hz, 1H), 7.88 – 8.01 (m, 4H), 8.12 (ds, *J* = 2.2, 1 H), 8.56 (d, *J* = 7.7 Hz, 1 H), 8.59 (d, *J* = 7.8 Hz, 1H), 8.78 (d, *J* = 8.3 Hz, 1 H) ppm.

Compound was not identifiable on ^{13}C-NMR spectrum as the analyte concentration was too low. There was not enough product to obtain a new spectrum.

Spectra are available in appendix XVII and XVIII.

^{1}H-NMR data was in accordance with available reference.[3]

6.8 Synthesis of naphthalene-2-yl trifluoromethanesulfonate (5b)

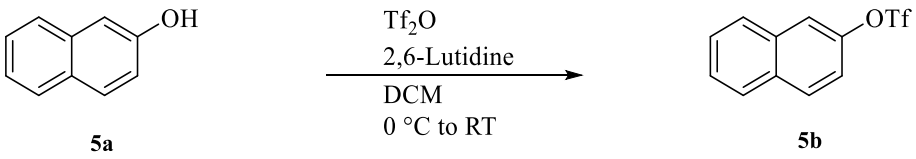


*Figure 6.6: Triflation for the synthesis of triflate **5b**.*

Naphthol **5a** (1.499 g, 10.40 mmol) was put under inert atmosphere. Anhydrous DCM (100 ml) and 2,6-lutidine (1.5 ml, 13.0 mmol) were added, and stirred for 5 minutes at 0 °C. Trifluoromethanesulfonic anhydride (2.1 ml, 12.5 mmol) was added and stirred at RT for 1 hour. The mixture was then quenched with water (50 ml) and extracted with DCM (3 x 50 ml). The combined extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (*Rf* = 0.5, 3:1 Hep-EA) and dried *in vacuo* to afford product **5b** as a yellow-white, solid compound (2.631 g, 92%) with melting point 34.6 – 35.8 °C.

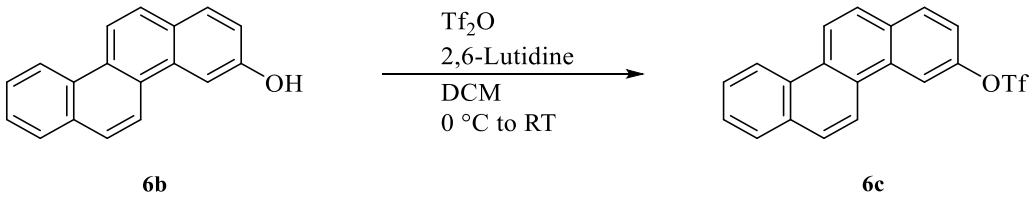
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38 (dd, *J* = 9.2, 2.8 Hz, 1 H), 7.54 – 7.61 (m, 2 H), 7.75 (ds, *J* = 2.8 Hz, 1 H), 7.85 – 7.91 (m, 2 H), 7.93 (d, *J* = 9.2 Hz, 1 H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 118.8 (q, *J* = 319 Hz, CF_3), 119.2, 119.6, 127.2, 127.6, 127.9, 128.1, 130.6, 132.4, 133.4, 147.1 ppm.

See appendix VII and VIII.

NMR data was in accordance with available reference.[121]

6.9 Synthesis of chrysen-3-yl trifluoromethanesulfonate (6c)



6b **6c**

*Figure 6.7: Triflation for the synthesis of triflate **6c**.*

Chrysenol **6b** (1.597 g, 6.537 mmol) was put under inert atmosphere. Anhydrous DCM (100 ml) and 2,6-lutidine (0.98 ml, 8.4 mmol) were added, and stirred for 5 minutes at 0 °C. Trifluoromethanesulfonic anhydride (1.4 ml, 8.4 mmol) was added and stirred at RT for 1 hour. The mixture was then quenched with water (50 ml) and extracted with DCM (3 x 50 ml). The combined extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (*Rf* = 0.2, 9:1 Hep-EA) and dried *in vacuo* to afford product **6c** as a white, solid compound (1.956 g, 80%) with melting point 119.7 – 121.0 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.53 (dd, *J* = 8.8, 2.4 Hz, 1 H), 7.69 (dt, *J* = 7.0, 1.3 Hz, 1 H), 7.75 (dt, *J* = 6.9, 1.5 Hz, 1 H), 8.02 (d, *J* = 8.7, 2 H), 8.06 (dd, *J* = 8.8, 2.5 Hz, 2 H), 8.55 (d, *J* = 9.1 Hz, 1 H), 8.61 (ds, *J* = 5.2 Hz, 1 H), 8.76 – 8.80 (m, 2 H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 115.6, 119.1 (q, *J* = 319 Hz, CF_3), 119.6, 120.7, 122.7, 123.2, 126.4, 127.07, 127.13, 127.7, 128.2, 128.7, 129.0, 130.3, 130.9, 131.3, 131.4, 132.5, 148.0 ppm.

See appendix XIX and XX.

6.10 Synthesis of 1-(4-chlorophenyl)-2-phenylethan-1-ol (12a)

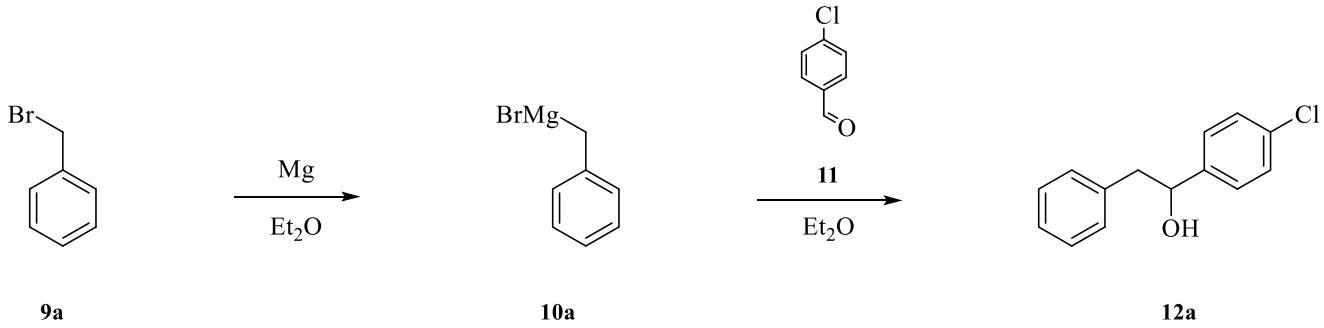


*Figure 6.8: Reaction sequence for the successful synthesis of Grignard reagent **10a** followed by alcohol **12a**.*

Mg-turnings (0.091 g, 3.8 mmol) was put under inert atmosphere and added anhydrous diethyl ether (7.5 ml). Over the next hour, benzyl halide **9a** (0.36 ml, 3.0 mmol) was added dropwise at RT. The mixture was then allowed to react for 3 hours at RT. Afterwards the solution was cooled down to -40 °C. Aldehyde **11** (0.225 g, 1.60 mmol) in anhydrous diethyl ether (7.5 ml) under inert atmosphere was then added dropwise over 1 hour. The mixture was allowed to react for 1 hour at -40 °C before it was allowed to reach RT. Afterwards, the mixture was allowed another 3 hours to react at RT. The resulting mixture was quenched with sat. aq. NH_4Cl (10 ml), extracted with diethyl ether (3 x 10 ml) and washed with water (10 ml) and brine (10 ml). The combined extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (*Rf* = 0.1, 9:1 Hep-EA) and dried *in vacuo* to afford product **12a** as a pale-yellow oil (0.309 g, 83%).

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.91 – 3.04 (m, 2 H), 4.66 (s, OH), 4.86 (s, 1 H), 7.16 (d, *J* = 7.5 Hz, 2 H), 7.21 – 7.38 (m, 7 H)* ppm.

*Integral measured to 8.5 but includes the peak of $CDCl_3$.

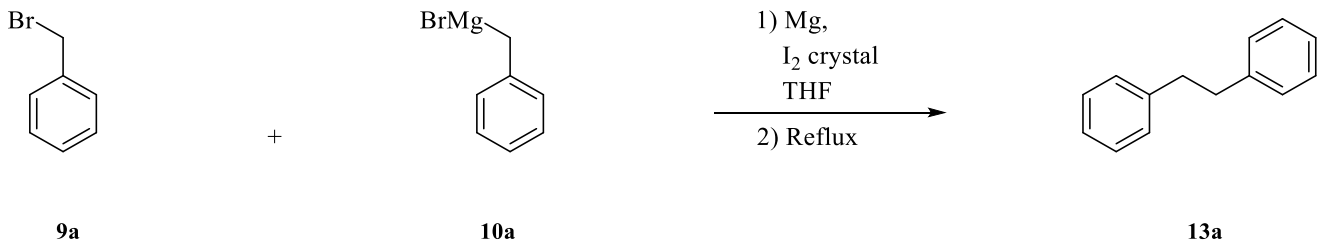
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 46.1, 74.7, 126.8, 127.3, 128.5, 128.6, 129.5, 133.2, 137.6, 142.2 ppm.

See appendix XXVII and XXVIII.

NMR data was in accordance with available reference.[123]

6.11 Synthesis of bibenzyls

6.11.1 Synthesis of 1,2-diphenylethane (13a)



9a **10a** **13a**

*Figure 6.9: Reaction for the formation of bibenzyl which happened during attempted synthesis of Grignard reagent **10a** and led to formation of bibenzyl **13a**.*

*Failed attempt at synthesising alcohol **12a** which resulted in the formation of bibenzyl **13a**:*

Mg-turnings (0.085 g, 3.5 mmol) and one iodine crystal were combined and put under inert atmosphere. Anhydrous THF (3 ml) and benzyl halide **9a** (0.42 ml, 3.5 mmol) were added, and the mixture boiled with reflux for 2 hours with some sonification. Afterwards the solution was cooled down and added to a solution of aldehyde **11** (0.432 g, 3.07 mmol) in anhydrous THF (2.0 ml) at -10 °C under inert atmosphere. The mixture was allowed to reach RT and stirred for 2 hours. The resulting mixture was quenched with sat. aq. NH_4Cl (10 ml), extracted with diethyl ether (3 x 10 ml) and washed with brine (10 ml). The combined extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (*Rf* = 0.6, 9:1 Hep-EA) and dried *in vacuo* to afford bibenzyl **13a** as a white solid (0.046 g) with melting point 52.0 – 53.6 °C.

*Failed attempt at synthesising 2-benzylnaphthalene (**5f**) which resulted in the formation of bibenzyl **13a**:*

Mg-turnings (0.040 g, 1.6 mmol) was put under inert atmosphere and added anhydrous diethyl ether (4.0 ml). Over the next hour, benzyl halide **9a** (0.18 ml, 1.5 mmol) was added dropwise at RT. The mixture was then allowed to react for 3 hours at RT. Afterwards the solution was cooled down and added dropwise over 45 minutes to a solution of triflate **5b** (0.135 g, 0.489 mmol) and $Fe(acac)_3$ (0.017 g, 0.048 mmol) in anhydrous THF (4.3 ml) and NMP (0.4 ml) at 0 °C under inert atmosphere. Then the mixture was allowed to reach RT while it reacted for 45 minutes. The mixture was quenched with 1 M HCl (1.2

ml), extracted with diethyl ether (3 x 10 ml) and washed with water (10 ml) and brine (10 ml). The combined extract was dried over anhydrous Na_2SO_4, and a TLC analysis was performed. The TLC indicated only formation of bibenzyl **13a**, thus the product was discarded.

*Failed attempt at synthesising 3-benzylchrysene **(6g)** which resulted in the formation of bibenzyl **13a**:*

Mg-turnings (0.040 g, 1.2 mmol) was put under inert atmosphere and added anhydrous diethyl ether (4.0 ml). Over the next hour, benzyl halide **9a** (0.12 ml, 1.0 mmol) was added dropwise at RT. The mixture was then allowed to react for 3 hours at RT. Afterwards the solution was cooled down and added dropwise over 30 minutes to a solution of triflate **6c** (0.198 g, 0.526 mmol) and $Fe(acac)_3$ (0.063 g, 0.18 mmol) in anhydrous THF (4.0 ml) and NMP (0.4 ml) at -30 °C under inert atmosphere. Then the mixture was allowed to reach RT while it reacted for 10 minutes. The mixture was quenched with 1 M HCl (0.5 ml), extracted with diethyl ether (3 x 10 ml) and washed with water (10 ml) and brine (10 ml). The combined extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (*Rf* = 0.6, 29:1 Hep-EA) and dried *in vacuo* to afford bibenzyl **13a** as a white solid (0.050 g) with melting point 52.0 – 53.6 °C.

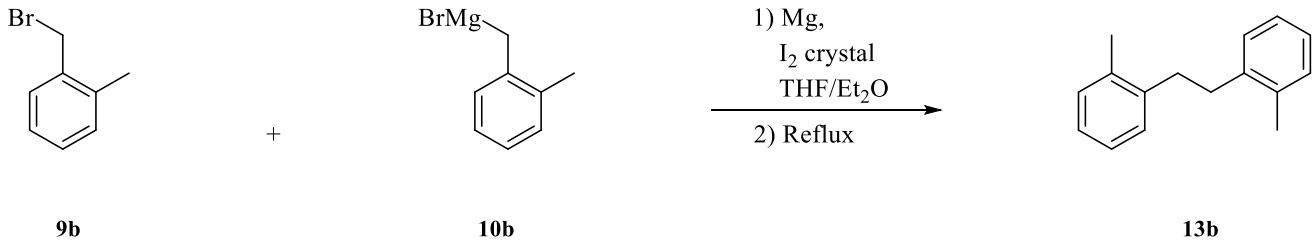
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.92 (s, 4H), 7.16 – 7.22 (m, 6H), 7.25 – 7.30 (m, 4H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 37.94, 125.9, 128.3, 128.4, 141.8 ppm.

See appendix XXIX and XXX.

NMR data was in accordance with available reference.[124]

6.11.2 Synthesis of 1,2-di-*o*-tolylethane (13b)



9b **10b** **13b**

*Figure 6.10: Reaction for the formation of bibenzyl which happened during attempted synthesis of Grignard reagent **10b** and led to formation of bibenzyl **13b**.*

*Failed attempt at synthesising 1-(4-chlorophenyl)-2-(o-tolyl)ethan-1-ol (**12b**) which resulted in the formation of bibenzyl **13b**:*

Mg-turnings (0.073 g, 3.0 mmol) and one iodine crystal were combined and put under inert atmosphere. Anhydrous THF (2.0 ml) and (2-methylbenzyl)magnesium bromide (**9b)** (0.38 ml, 2.8 mmol) were added and the mixture was boiled with reflux for 2 hours. Afterwards the solution was cooled down and added to a solution of aldehyde **11** (0.257 g, 1.83 mmol) in anhydrous THF (2.0 ml) at 0 °C under inert atmosphere. The mixture was allowed to reach RT and then stirred for 2 hours. The resulting mixture was quenched with 1.0 M HCl (25 ml), extracted with diethyl ether (3 x 10 ml) and washed with brine (25 ml). The combined extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (*Rf* = 0.7, 9:1 Hep-EA) and dried *in vacuo* to afford bibenzyl **13b** as a white solid (0.160 g) with melting point 69.9 – 71.1 °C.

*First failed attempt at synthesising (2-methylbenzyl)naphthalene **5g** which resulted in the formation of bibenzyl **13b**:*

Mg-turnings (0.236 g, 9.71 mmol) and one iodine crystal were combined and put under inert atmosphere. Anhydrous diethyl ether (3.0 ml) and benzyl halide **9b** (0.50 ml, 3.7 mmol) were added and the mixture was boiled with reflux for 2 hours with some sonification. Afterwards the mixture was added to a solution of triflate **5b** (0.267 g, 0.967 mmol) and $Pd(dppf)Cl_2$ (0.043 g, 0.053 mmol) in anhydrous diethyl ether (2.0 ml) under inert atmosphere. When all of the solution were combined, the mixture was boiled with reflux overnight. The next day the mixture was quenched with water (2.0 ml) at RT, extracted with diethyl ether (3 x 10 ml) and washed with brine (10 ml). The combined extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (*Rf* = 0.6,

59:1 Hep-EA), and dried *in vacuo* to afford bibenzyl **13b** as a white solid (0.255 g) with melting point 69.9 – 71.1 °C.

*Second failed attempt at synthesising (2-methylbenzyl)naphthalene **5g** which resulted in the formation of bibenzyl **13b**:*

Mg-turnings (0.071 g, 2.9 mmol) and one iodine crystal were combined and put under inert atmosphere. Anhydrous THF (2.0 ml) and benzyl halide **9b** (0.38 ml, 2.8 mmol) were added and the mixture was boiled with reflux for 2 hours. Afterwards some of the solution (1.02 ml) was added to a separate solution which was prepared by combining $ZnBr_2$ (0.382 g, 1.70 mmol), LiBr (0.153 g, 1.76 mmol) and anhydrous THF (2.0 ml) under inert atmosphere. The combined solution was allowed to stir for 30 minutes. A third solution was prepared by combining triflate **5b** (0.301 g, 1.09 mmol), $Pd(dppf)Cl_2$ (0.020 g, 0.024 mmol) and anhydrous THF (2.0 ml) under inert atmosphere. The content of the third solution was added to the second solution after the 30 minutes of stirring were done. The mixture was then allowed to react under stirring at 50 °C over the next 24 hours. The following day the mixture was quenched with water (1.0 ml), added 2 M sulphuric acid (0.5 ml) and stirred for 1 hour. The organic phase was isolated, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (R_f =0.5, 29:1 Hep-EA) and dried *in vacuo* to afford bibenzyl **13b** as a white solid (0.122 g) with melting point 69.9 – 71.1 °C.

*Failed attempt at synthesising (2-methylbenzyl)chrysene **6h** which resulted in the formation of bibenzyl **13b**:*

Mg-turnings (0.071 g, 2.9 mmol) and one iodine crystal were combined and put under inert atmosphere. Anhydrous THF (2.0 ml) and benzyl halide **9b** (0.38 ml, 2.8 mmol) were added and the mixture was boiled with reflux for 2 hours. Afterwards some of the solution (0.84 ml) was added to a separate solution which was prepared by combining $ZnBr_2$ (0.282 g, 1.25 mmol), LiBr (0.104 g, 1.20 mmol) and anhydrous THF (2.0 ml) under inert atmosphere. The combined solution was allowed to stir for 30 minutes. A third solution was prepared by combining triflate **6c** (0.301 g, 1.09 mmol), $Pd(dppf)Cl_2$ (0.010 g, 0.012 mmol) and anhydrous THF (2.0 ml) under inert atmosphere. The content of the third solution was added to the second solution after the 30 minutes of stirring were done. The mixture was then allowed to react under stirring at 50 °C over the next 24 hours. The following day the mixture was quenched with water (1.0 ml), added 2 M sulphuric acid (0.5 ml) and stirred for 1 hour. The organic phase was isolated, dried over

anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (R*f* =0.4, 29:1 Hep-EA) and dried *in vacuo* to afford bibenzyl **13b** as a white solid (0.081 g) with melting point 69.9 – 71.1 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.32 (s, 6H), 2.85 (s, 4H), 7.11 – 7.17 (m, 8H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 19.29, 34.15, 126.06, 126.12, 128.9, 130.2, 135.9, 140.2 ppm.

See appendix XXXI and XXXII.

NMR data was in accordance with available reference.[125,126]

6.11.3 Synthesis of 1,2-di-*p*-tolylethane (13c)

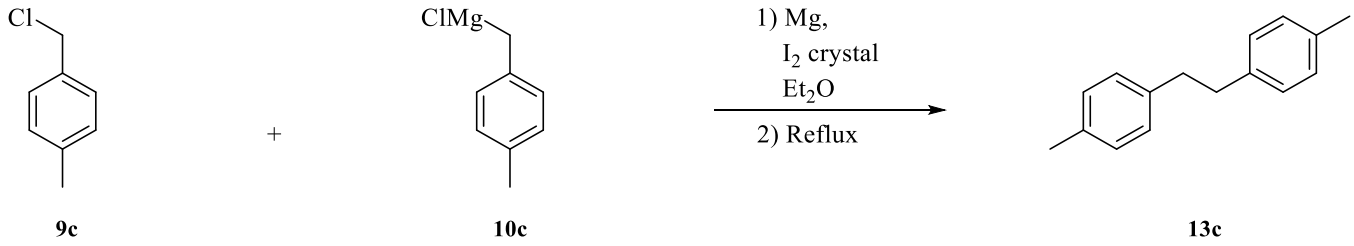


*Figure 6.11: Reaction for the formation of bibenzyl which happened during the attempted synthesis of (4-methylbenzyl)magnesium chloride (**10c**) and led to formation of bibenzyl **13c**.*

*Failed attempt at synthesising 1-(4-chlorophenyl)-2-(p-tolyl)ethan-1-ol (**12c**) which resulted in the formation of bibenzyl **13c**:*

Mg-turnings (0.070 g, 2.9 mmol) and one iodine crystal were combined and put under inert atmosphere. Anhydrous diethyl ether (2.0 ml) was then added to the solution before a few drops of 1-(chloromethyl)-4-methylbenzene (**9c)** (0.299 g, 2.13 mmol) in anhydrous diethyl ether (1.0 ml) were added. The mixture was put on sonification for 15 minutes since there was no sign of reaction. Afterward more diethyl ether (2.0 ml) was added as much of the initial amount had evaporated. Then the rest of the solution containing triflate **9c** was added dropwise over 20 minutes combined with heating between every addition. The mixture was then boiled with reflux for 30 minutes.

Afterwards the solution was cooled down and added to a solution of aldehyde **11** (0.299 g, 2.13 mmol) in anhydrous diethyl ether (2.0 ml) at 0 °C under inert atmosphere. The mixture was allowed to reach RT and then stirred for 2 hours. The resulting mixture was quenched with 1.0 M HCl (25 ml), extracted with diethyl ether (2 x 20 ml, 1 x 10 ml) and washed with brine (25 ml). The combined extract was dried over anhydrous Na_2SO_4. Based on a TLC analysis it was determined that bibenzyl **13c** was the sole product of the reaction. The solution was therefore discarded without further purification.

No NMR analysis was performed.

6.12 Kumada-Corriu coupling of Grignard reagents to triflates

Several methods were used to synthesise Kumada-Corriu coupled product. Four general methods which utilized different catalysators are described below. General procedure D is a Kumada-Corriu coupling with an added Zn salt and can therefore arguably be called a Negishi coupling. All reactions were performed on a scale of 100 – 300 mg.

General procedure A:

Starting triflate (1 eq.) was combined with Ni(dppp)Cl_2 (5 mol%) and put under inert atmosphere. Anhydrous diethyl ether (15 ml per gram starting material) was added to the solution. The Grignard reagent (3 eq.) was slowly added to the mixture at 0 °C. Afterwards the mixture was boiled with reflux for 3 hours. The mixture was quenched with methanol (3 ml per gram starting material) and concentrated *in vacuo*. The residue was purified by flash column chromatography and dried *in vacuo* to afford the product.

General procedure B:

Starting triflate (1 eq.) was combined with Ni(dppe)Cl_2 (5 mol%) and put under inert atmosphere. Anhydrous THF (15 ml per gram starting material) was added to the solution. The Grignard reagent (1.2 eq.) was slowly added to the mixture at 0 °C. Afterwards the mixture was stirred for 1 hour at RT, then boiled with reflux for 4 hours. The mixture was quenched with sat. aq. NH_4Cl (60 ml per gram starting material) and extracted with diethyl ether (3 x 10 ml). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography and dried *in vacuo* to afford the product.

General procedure C:

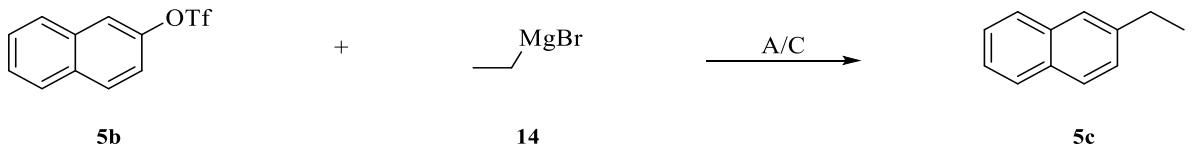
Starting triflate (1.eq) was combined with $Fe(acac)_3$ (5 mol%) and put under inert atmosphere. Anhydrous THF (4 ml) and NMP (0.4 ml) were first added to the solution. Then Grignard (3 eq.) reagent was slowly added dropwise over the span of 30 minutes to 1 hour at 0 °C. Afterwards the mixture was allowed to reach RT while it reacted for 10 – 45 minutes. The mixture was quenched with 1 M HCl (1.2 ml), extracted with diethyl ether (3 x 10 ml) and washed with water (10 ml) and brine (10 ml). The combined

organic phase was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography and dried *in vacuo* to afford the product.

General procedure D:

$ZnBr_2$ (1.5 eq.) and LiBr (1.5 eq.) were combined and put under inert atmosphere. Anhydrous THF (2 ml per mmol) and vinylmagnesium bromide (1.5 eq.) were added and the mixture was allowed to stir for 30 minutes. A separate solution was prepared by combining starting triflate (1 eq.) and $Pd(dppf)Cl_2$ (1 mol%), putting the mixture under inert atmosphere, and adding anhydrous THF (3 ml per mmol). The content of the separate solution was added to the original solution after the 30 minutes were done. The mixture was then allowed to react under stirring at 50 °C over the next 24 hours. The following day the mixture was quenched with water (1.0 ml per mmol), added 2 M sulphuric acid (0.50 ml per mmol) and stirred for 1 hour. The organic phase was isolated, dried over anhydrous Na_2SO_4 and concentrated *in vacuo.* The residue was purified by flash column chromatography to afford the product.

6.12.1 Synthesis of 2-ethyl naphthalene (5c)



5b **14** **5c**

*Figure 6.12: Reaction for the synthesis of ethylnaphthalene **5c**. A) Ni(dppp)Cl_2 (5 mol%), Et_2O, 0 °C, Reflux 3 hr. C) $Fe(acac)_3$ (5 mol%), THF, 0 °C.*

The coupling of triflate **5b** with Grignard reagent **14** following general procedure A yielded ethylnaphthalene **5c** as a clear oil (0.102 g, 60%).

The coupling of triflate **5b** with Grignard reagent **14** following general procedure C but adding **14** much faster and not using an ice bath, yielded ethylnaphthalene **5c** as a clear oil (0.038 g, 32%).

(R*f* =0.7, 29:1 Hep-EA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, *J* = 7.6 Hz, 3 H), 2.81 (q, *J* = 7.2 Hz, 2 H), 7.35 (dd, *J* = 8.4, 1.7 Hz, 1 H), 7.37 – 7.47 (m, 2 H), 7.62 (s, 1 H), 7.74 – 7.82 (m, 3 H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 15.5, 29.1, 125.0, 125.5, 125.8, 127.1, 127.4, 127.6, 127.8, 131.9, 133.7, 141.8 ppm.

See appendix IX and X.

NMR data was in accordance with available reference.[133]

6.12.2 Synthesis of 3-ethyl chrysene (6d)

6c **14** **6d**

*Figure 6.13: Reaction for the synthesis of ethylchrysene **6d**. C) $Fe(acac)_3$ (5 mol%), THF, 0 °C.*

The coupling of triflate **6c** with Grignard reagent **14** following general procedure C yielded ethylchrysene **6d** as a white solid (0.048 g, 72%) with melting point 113.3 – 114.1 °C.

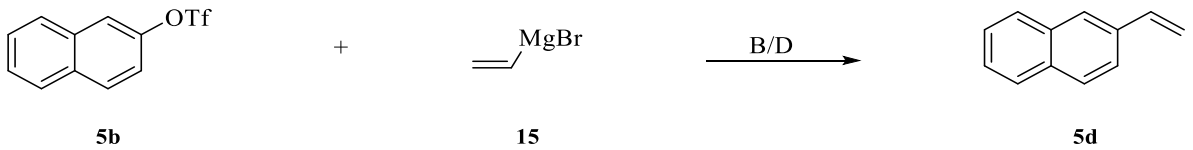
(R*f* =0.4, 29:1 Hep-EA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.42 (t, *J* = 7.6 Hz, 3 H), 2.96 (q, *J* = 7.6 Hz, 2 H), 7.51 (dd, *J* = 8.2, 1.4 Hz, 1 H), 7.62 (dt, *J* = 7.5, 1.1 Hz, 1 H), 7.70 (dt, *J* = 7.0, 1.4 Hz, 1 H), 7.92 (d, *J* = 8.2, 1 H), 7.96 – 8.02 (m, 3 H), 8.58 (s, 1 H), 8.66 (d, *J* = 9.0, 1 H), 8.72 – 8.80 (m, 2 H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 16.0, 29.7, 120.3, 121.3, 121.5, 123.2, 126.3, 126.6, 127.1, 127.2, 127.21, 128.0, 128.4, 128.5, 130.5, 130.6, 130.7, 132.2, 142.8 ppm.

See appendix XXI and XXII.

6.12.3 Synthesis of 2-vinylnaphthalene (5d)



5b **15** **5d**

*Figure 6.14: Reaction for the synthesis of vinylnaphthalene **5d**. B) Ni(dppe)Cl_2 (5 mol%), THF, 0 °C, Reflux 4 hr. D) 1: $ZnBr_2$, LiBr, THF. 2: Pd(dppf)Cl_2 (1 mol%), THF. 3: 50 °C, 24 hr.*

The coupling of triflate **5b** with Grignard reagent **15** following general procedure B yielded vinylnaphthalene **5d** as a clear oil (0.018 g, 15%). Some by-product was also present according to NMR.

The coupling of triflate **5b** with Grignard reagent **15** following general procedure B but with 3.7 equivalents of Grignard reagent **15,** half the amount of solvent and refluxing for 21 hours yielded vinylnaphthalene **5d** as a clear oil (0.001 g, 1%). Some by-product was also present according to NMR.

The coupling of triflate **5b** with Grignard reagent **15** was attempted two times following general procedure D, but the product was lost during workup both times (flash column).

(R*f* =0.6, 29:1 Hep-EA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.34 (dd, *J* = 10.9, 0.5 Hz, 1 H), 5.88 (dd, *J* = 17.6, 0.7 Hz, 1 H), 6.88 (dd, *J* = 17.5, 10.8 Hz, 1 H), 7.39 – 7.48 (m, 3 H), 7.64 (dd, *J* = 8.7, 1.6 Hz, 1 H), 7.74 – 7.83 (m, 3H)* ppm.

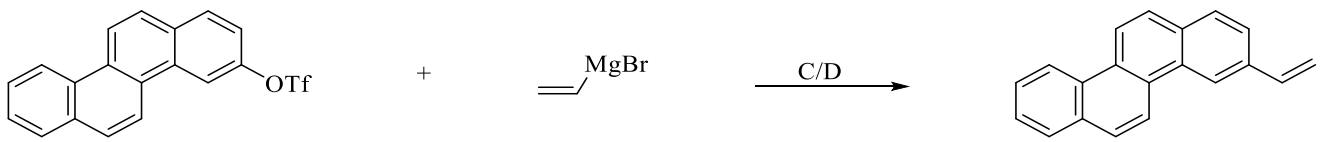
*Because of the apparent presence of ethylnaphthalene **5c**, the spectrum shows a bigger integral than what is reported here.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 114.2, 123.2, 125.9, 126.2, 126.4, 127.7, 128.1, 128.2, 133.2, 133.6, 135.0, 137.0 ppm.

See appendix XI and XII.

NMR data was in accordance with available reference.[134]

6.12.4 Synthesis of 3-vinylchrysene (6e)



6c **15** **6e**

*Figure 6.15: Reaction for the synthesis of vinylchrysene **6e**. C) $Fe(acac)_3$ (5 mol%), THF, 0 °C. D) 1: $ZnBr_2$, LiBr, THF. 2: $Pd(dppf)Cl_2$ (1 mol%), THF. 3: 50 °C, 24 hr.*

The coupling of triflate **6c** with Grignard reagent **15** following general procedure C yielded vinylchrysene **6e** as a white solid (0.008 g, 5%). Some by-product was also present according to NMR.

The coupling of triflate **6c** with Grignard reagent **15** following general procedure D yielded vinylchrysene **6e** as a white solid (0.049 g, 25%). Some by-product was also present according to NMR.

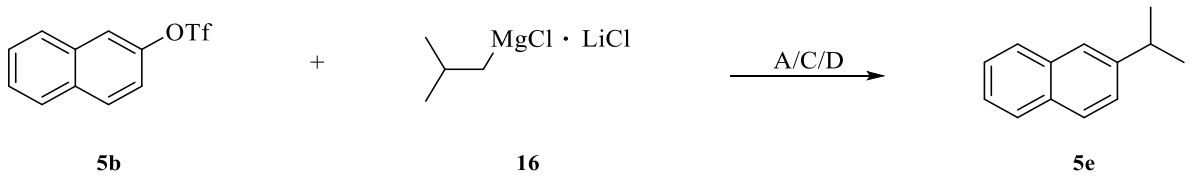
No melting point was recorded as there was not enough of the compound left after NMR analysis.

(R_f =0.7, 9:1 Hep-EA).

The presence of ethylchrysene **6d**, makes it impossible to delegate respective signals of the aromatic area to given atoms in product **6e**.

See appendix XXIII and XXIV.

6.12.5 Synthesis of 2-isopropylnaphthalene (5e)



5b **16** **5e**

*Figure 6.16: Reaction for the synthesis of isopropylnaphthalene **5e**. A) Ni(dppp)Cl_2 (5 mol%), Et_2O, 0 °C, Reflux 3 hr. C) Fe(acac)$_3$ (5 mol%), THF, 0 °C. D) 1: $ZnBr_2$, THF. 2: Pd(dppf)Cl_2 (1 mol%), THF. 3: 50 °C, 24 hr.*

The coupling of triflate **5b** with Grignard reagent **16** following general procedure A yielded isopropylnaphthalene **5e** as a clear oil (0.118 g, 69%).

The coupling of triflate **5b** with Grignard reagent **16** following general procedure C yielded isopropylnaphthalene **5e** as a clear oil (0.032 g, 43%).

The coupling of triflate **5b** with Grignard reagent **16** following general procedure D but without LiBr yielded isopropylnaphthalene **5e** as a clear oil (0.010 g, 6%).

(R*f* =0.6, 29:1 Hep-EA).

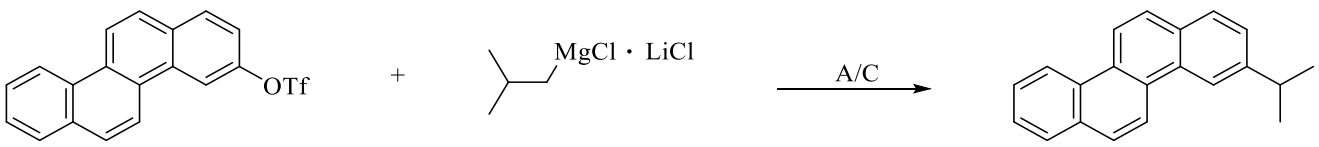
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.34 (d, *J* = 6.9 Hz, 6 H), 3.01 – 3.13 (m, *J* = 7.0 Hz, 1 H), 7.36 – 7.47 (m, 3 H), 7.64 (ds, *J* = 0.7, 1 H), 7.75 – 7.81 (m, 3 H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 23.9, 34.2, 124.1, 125.0, 125.7, 125.8, 127.5, 127.6, 127.8, 132.1, 133.6, 146.3 ppm.

See appendix XIII and XIV.

NMR data was in accordance with available reference.[135]

6.12.6 Synthesis of 3-isopropylchrysene (6f)



6c **16** **6f**

*Figure 6.17: Reaction for the synthesis of isopropylchrysene **6f**. A) Ni(dppp)Cl_2 (5 mol%), Et_2O, 0 °C, Reflux 3 hr. C) Fe(acac)$_3$ (5 mol%), THF, 0 °C.*

The coupling of triflate **6c** with Grignard reagent **16** following general procedure A yielded isopropylchrysene **6f** as a white solid (0.065 g, 88%) with melting point 125.9 – 127.2 °C.

The coupling of triflate **6c** with Grignard reagent **16** following general procedure C yielded isopropylchrysene **6f** as a white solid (0.105 g, 71%) with melting point 125.9 – 127.2 °C.

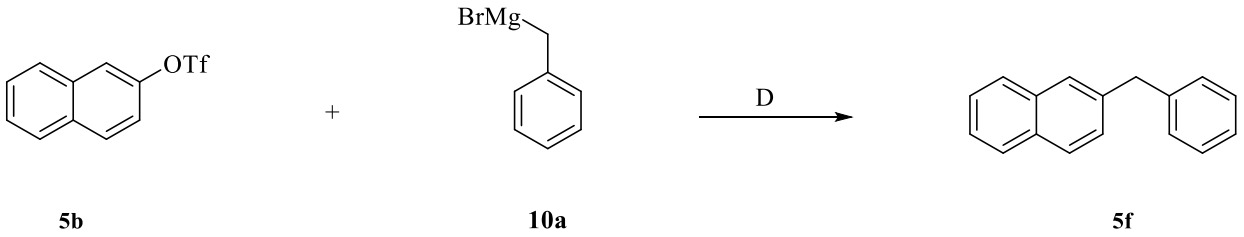
(R*f* =0.4, 29:1 Hep-EA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.44 (d, *J* = 6.9 Hz, 6 H), 3.18 – 3.29 (m, *J* = 6.9 Hz, 1 H), 7.55 (dd, *J* = 8.3, 1.6 Hz, 1 H), 7.63 (dt, *J* = 6.9, 1.2 Hz, 1 H), 7.70 (dt, *J* = 6.9, 1.5 Hz, 1 H), 7.92 – 8.04 (m, 4 H), 8.60 (s, 1 H), 8.67 (d, *J* = 9.0 Hz, 1 H), 8.72 – 8.81 (m, 2 H) ppm.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 24.2, 34.9, 120.1, 120.4, 121.3, 123.2, 125.7, 126.2, 126.6, 127.0, 127.1, 128.1, 128.3, 128.5, 128.6, 130.6, 130.7, 132.1, 147.3 ppm.

See appendix XXV and XXVI.

6.12.7 Synthesis of 2-benzylnaphthalene (5f)



5b **10a** **5f**

*Figure 6.18: Reaction for the synthesis of benzylnaphthalene **5f**. C) $Fe(acac)_3$ (5 mol%), THF, 0 °C. D) 1: $Pd(dppf)Cl_2$ (1 mol%), Et_2O. 2: Reflux, 20 hr.*

The coupling of triflate **5b** with Grignard reagent **10a** following general procedure D but with modified conditions yielded benzylnaphthalene **5f** as a white solid (0.025 g, 26%). No melting point was recorded as it was highly contaminated. Modifications in procedure: No $ZnBr_2$ or LiBr was used. Solvent used was Et_2O. Refluxing was performed for 20 hours. Quenching was performed with water.

(R_f =0.6, 29:1 Hep-EA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.13 (s, 2 H), 7.15 – 7.30 (m, 5H)*, 7.31 (dd, *J* = 6.0, 1.7 Hz, 1 H), 7.38 – 7.46 (m, 2 H), 7.62 (s, 1 H), 7.72 – 7.80 (m, 3H) ppm.
* Spectra shows 11 H. Some of the signals are from the by-product, and some of the signals are from $CDCl_3$ which could not be distinguished from the other signals.

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 42.2, 125.4, 126.0, 126.2, 127.2, 127.6, 127.68, 127.7, 128.1, 128.6, 129.1, 132.1, 133.7, 138.7, 141.0 ppm.

See appendix XV and XVI.

NMR data was in accordance with available reference.[136]

7. References

(1) Kancherla, S. Regioselective Syntheses and Functionalizations of Polycyclic Aromatic Hydrocarbons. *PhD Thesis, University of Stavanger* **2019**.

(2) Bjelland, H. K. Synthesis of Alkylated Phenanthrenes. *Master's thesis, Universitetet i Stavanger.* **2018**.

(3) Jørgensen, K. B.; Joensen, M. Photochemical Synthesis of Chrysenols. *Polycyclic Aromatic Compounds* **2008**, *28* (4–5), 362–372. https://doi.org/10.1080/10406630802374580.

(4) Fürstner, A.; Leitner, A. Iron-Catalyzed Cross-Coupling Reactions of Alkyl-Grignard Reagents with Aryl Chlorides, Tosylates, and Triflates. *Angew. Chem. Int. Ed.* **2002**, *41* (4), 609–612. https://doi.org/10.1002/1521-3773(20020215)41:4%3C609::AID-ANIE609%3E3.0.CO;2-M.

(5) Universitetet i Stavanger. *Synthesis of PAHs (Polycyclic Aromatic Hydrocarbons)*. https://www-uis-no.ezproxy.uis.no/en/synthesis-pahs-polycyclic-aromatic-hydrocarbons (accessed 2022-04-16).

(6) Jørgensen, K. B.; Rantanen, T.; Dörfler, T.; Snieckus, V. Directed Metalation - Suzuki - Miyaura Cross-Coupling Strategies: Regioselective Synthesis Og Hydroxylated 1-Methyl-Phenanthrenes. *J. Org. Chem.* **2015**, *80*, 9410–9424. https://doi.org/10.1021/acs.joc.5b01300.

(7) Kancherla, S.; Lorentzen, M.; Jørgensen, K. B. Directed Ortho-Metalation and Anionic Ortho-Fries Rearrangement of Polycyclic Aromtic O-Carbamates: Regioselective Synthesis of Substituted Chrysenes. *J. Org. Chem.* **2018**, *83* (7), 3590–3598. https://doi.org/10.1021/acs.joc.7b03210.

(8) Böhme, T.; Lorentzen, M.; Jørgensen, K. B. Regiospecific Synthesis of Dimethylphenanthrenes. *Polycyclic Aromatic Compounds* **2017**, *37:2-3*, 106–113. https://doi.org/10.1080/10406638.2016.1179651.

(9) Cai, X.; Brown, S.; Hodson, P.; Snieckus, V. Regiospecific Synthesis of Alkylphenanthrenes Using a Combined Directed Ortho and Remote Metalation - Suzuki-Miyaura Cross Coupling Strategy. *Canadian Journal of Chemistry* **2004**, *82* (2), 195–205. https://doi.org/10.1139/V03-179.

(10) Floresta, G.; Cilibrizzi, A.; Abbate, V.; Spampinato, A.; Zagni, C.; Rescifina, A. *Bioorganic Chemistry*; Elsevier Inc., 2019; Vol. 84.

(11) Huang, M.; Penning, T. M. *Encyclopedia of Food Safety*; Elsevier Inc., 2014; Vol. Volume 2: Hazards and Diseases.

(12) Abdel-Shafy, H. I.; Mansour, M. S. M. A Review on Polycyclic Aromatic Hydrocarbons: Source, Environmental Impact, Effect on Human Health and Remediation. *Egyptian Journal of Petroleum* **2016**, *25* (1), 107–123. https://doi.org/10.1016/j.ejpe.2015.03.011.

(13) *PAH*. Folkehelseinstituttet. https://www.fhi.no/nettpub/luftkvalitet/pah/pah/ (accessed 2022-01-06).

(14) Rocha, A. C.; Palma, C. Source Identification of Polycyclic Aromatic Hydrocarbons in Soil Sediments: Application of Different Methods. *Science of the Total Environment* **2019**, *652*, 1077–1089. https://doi.org/10.1016/j.scitotenv.2018.10.014.

(15) Pampanin, D. M.; Sydnes, M. O. Polycyclic Aromatic Hydrocarbons a Constituent of Petroleum: Presence and Influence in the Aquatic Environment. *In V. Kutcherov, & A. Kolesnikov (Eds.), Hydrocarbon.* **2013**. https://doi.org/10.5772/48176.

(16) Centers for Disease Control and Prevention (CDC). *Polycyclic Aromatic Hydrocarbons (PAHs) Factsheet*. https://www.cdc.gov/biomonitoring/PAHs_FactSheet.html (accessed 2022-04-03).

(17) Ruus, A.; Næs, K.; Grung, M.; Green, N.; Bakke, T.; Oug, E.; Hylland, K. PAH-Forurensing Av Sjøbunn - En Oversikt over Kunnskapsstatus. *Statens forurensningstilsyn (SFT), Norsk institutt for vannforskning (NIVA)* **2009**, *NIVA-rapport 5888-2009*. https://www.miljodirektoratet.no/globalassets/publikasjoner/klif2/publikasjoner/2583/ta2583.pdf.

(18) National Oceanic and Atmospheric Administration. U.S. Department of Commerce. *What is an oil seep?*. https://oceanservice.noaa.gov/facts/oilseep.html (accessed 2022-05-24).

(19) Kong, S.-R.; Yamamoto, M.; Shaari, H.; Hayashi, R.; Seki, O.; Tahir, N. M.; Fadzil, M. F.; Sulaiman, A. The Significance of Pyrogenic Polycyclic Aromatic Hydrocarbons in Borneo Peat Core for the Reconstruction of Fire History. *PLoS ONE* **2021**, *16* (9). https://doi.org/10.1371/journal.pone.0256853.

(20) Cardellicchio, N.; Buccolieri, A.; Giandomenico, S.; Lopez, L.; Pizzulli, F.; Spada, L. Organic Pollutants (PAHs, PCBs) in Sediments from the Mar Piccolo in Taranto (Ionian Sea, Southern Italy). *Marine Pollution Bulletin* **2007**, *55*, 451–458. https://doi.org/10.1016/j.marpolbul.2007.09.007.
(21) Agency for Toxic Substances and Disease Registry. *ToxFAQs for Polycyclic Aromatic Hydrocarbons (PAHs)*. cdc.gov. https://wwwn.cdc.gov/TSP/ToxFAQs/ToxFAQsDetails.aspx?faqid=121&toxid=25 (accessed 2022-04-03).
(22) Miljødirektoratet. *Polysykliske aromatiske hydrokarboner (PAH)*. Miljøstatus. https://miljostatus.miljodirektoratet.no/pah (accessed 2020-04-19).
(23) Risiko for Og Beredskap Mot Akutt Forurensning - Endringer Og Utviklingstrekk. Faggrunnlag for Revisjon Av Forvaltningsplanen for Barentshavet Og Havområdene Utenfor Lofoten. M-1304/2019, 2019.
(24) Barron, M. G.; Carls, M. G.; Heintz, R.; Rice, S. D. Evaluation of Fish Early Life-Stage Toxicity Models of Chronic Embryonic Exposure to Complex Polycyclic Aromatic Hydrocarbon Mixtures. *Toxicological sciences* **2004**, *78* (1), 60–67. https://doi.org/10.1093/toxsci/kfh051.
(25) Incardona, J. P.; Collier, T. K.; Scholz, N. L. Defects in Cardiac Function Precede Morphological Abnormalities in Fish Embryos Exposed to Polycyclic Aromatic Hydrocarbons. *Toxicology and Applied Pharmacology* **2004**, *196* (2), 191–205. https://doi.org/10.1016/j.taap.2003.11.026.
(26) Carls, M. G.; Holland, L.; Larsen, M.; Collier, T. K.; Scholz, N. L.; Incardona, J. P. Fish Embryos Are Damaged by Dissolved PAHs, Not Oil Particles. *Aquatic Toxicology* **2008**, *88* (2), 121–127. https://doi.org/10.1016/j.aquatox.2008.03.014.
(27) Barron, M. G.; Heintz, R.; Rice, S. D. Relative Potency of PAHs and Heterocycles as Aryl Hydrocarbon Receptor Agonists in Fish. *Marine Environmental Research* **2004**, *58* (2–5), 95–100. https://doi.org/10.1016/j.marenvres.2004.03.001.
(28) Sørhus, E.; Incardona, J. P.; Karlsen, Ø.; Linbo, T.; Sørensen, L.; Nordtug, T.; van der Meeren, T.; Thorsen, A.; Thorbjørnsen, M.; Jentoft, S.; Edvardsen, R. B.; Meier, S. Crude Oil Exposures Reveal Roles for Intracellular Calcium Cycling in Haddock Craniofacial and Cardiac Development. *Scientific Reports* **2016**, *6* (31058). https://doi.org/10.1038/srep31058.
(29) Hansen, B. H.; Sørensen, L.; Carvalho, P.; Meier, S.; Booth, A. M.; Altin, D.; Farkas, J.; Nordtug, T. Adhesion of Mechanically and Chemically Dispersed Crude Oil Droplets to Eggs of Atlantic Cod (Gadus Morhua) and Haddock (Melanogrammus Aeglefinus). *Science of the Total Environment* **2018**, *640–641*, 138–143. https://doi.org/10.1016/j.scitotenv.2018.05.207.
(30) Shreadah, M. A.; Abdel Moneim, M. I.; Said, T. O.; Fathallah, E. M. I.; Mahmoud, M. E. PAHs in Seawater of the Semi-Closed Areas along the Alexandria Coast of Egyptian Mediterranean Sea. *Journal of Environmental Protection* **2013**, *4* (11), 1307–1317. https://doi.org/10.4236/jep.2013.411152.
(31) Miljødirektoratet. *EUs viktigste og mest omfattende miljødirektiv*. Vannportalen.no. https://www.vannportalen.no/regelverk-og-foringer/vanndirektivet/ (accessed 2022-04-04).
(32) Tolosa, I.; de Mora, S.; Sheikholeslami, M. R.; Villeneuve, J.-P.; Bartocci, J.; Cattini, C. Aliphatic and Aromatic Hydrocarbons in Coastal Caspian Sea Sediments. *Marine Pollution Bulletin* **2004**, *48*, 44–60. https://doi.org/10.1016/S0025-326X(03)00255-8.
(33) Wade, L. G.; Simek, J. W. *Organic Chemistry*, Ninth Edition.; Pearson Education Limited, 2017.
(34) Encyclopedia Britannica. *Metalation*. Encyclopedia Britannica. https://www.britannica.com/science/metalation (accessed 2022-03-29).
(35) Krawczuk, P. *Directed Metalation: A Survival Guide*. https://www.scripps.edu/baran/images/grpmtgpdf/Krawczuk_March_08.pdf.
(36) Tilly, D.; Magolan, J.; Mortier, J. Directed Remote Aromatic Metalations: Mechanisms and Driving Forces. *Chem. Eur. J* **2012**, No. 18, 3804–3820. https://doi.org/10.1002/chem.201103920.
(37) Wittig, G.; Fuhrmann, G. Über Das Verhalten Der Halogenierte Anisole Gegen Phenyllithium. *Ber. Dtsch. Chem. Ges.* **1940**, *73* (11), 1197–1218. https://doi.org/10.1002/cber.19400731114.

(38) Gilman, H.; Bebb, R. L. Relative Reactivities of Organometallic Compounds. *J. Am. Chem. Soc.* **1939**, *61*, 109–112. https://doi.org/10.1021/ja01870a037.
(39) Knochel, P.; Cole, K. P. Directed Ortho Metalation in 2021: A Tribute to Victor Sniekus (August 1, 1937 - December 18, 2020). *Org. Process Res. Dev.* **2021**, 2188–2191. https://doi.org/10.1021/acs.oprd.1c00271?urlappend=%3Fref%3DPDF&jav=VoR&rel=cite-as.
(40) McMurry, J. *Organic Chemestry*, Ninth edition.; Cengage Learning, 2015.
(41) *Suzuki-Miyaura Coupling*. https://chem.libretexts.org/Bookshelves/Inorganic_Chemistry/Supplemental_Modules_and_Websites_(Inorganic_Chemistry)/Catalysis/Catalyst_Examples/Suzuki-Miyaura_Coupling (accessed 2022-03-09).
(42) Name-reaction.com. *Suzuki cross-coupling*. https://www.name-reaction.com/suzuki-cross-coupling (accessed 2022-03-09).
(43) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. Catalysts for Suzuki-Miyaura Coupling Processes: Scope and Studies of the Effect of Ligand Structure. *J. Am. Chem. Soc.* **2005**, *127* (12), 4685–4696. https://doi.org/10.1021/ja042491j.
(44) Chemler, S. R.; Trauner, D.; Danishefsky, S. J. The B-Alkyl Suzuki-Miyaura Cross-Coupling Reaction: Development, Mechanistic Study, and Applications in Natural Product Synthesis. *Angew. Chem. Int. Ed.* **2001**, *40* (24), 4544–4568. https://doi.org/10.1002/1521-3773(20011217)40:24%3C4544::AID-ANIE4544%3E3.0.CO;2-N.
(45) Johansson Seechurn, C. C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. Palladium-Catalyzed Cross-Coupling: A Historical Contextual Perspective to the 2010 Nobel Prize. *Angew. Chem. Int. Ed.* **2012**, *51*, 5062–5085. https://doi.org/10.1002/anie.201107017.
(46) Blakemore, D. C.; Doyle, P. M.; Fobian, Y. M. *Synthetic Methods in Drug Discovery: Volume 1*; Drug Discovery; The Royal Society of Chemistry, 2016; Vol. 1. https://doi.org/10.1039/9781782622086.
(47) Nobel Prize Outreach AB 2022. *The Nobel Prize in Chemistry 2010*. NobelPrize.org. https://www.nobelprize.org/prizes/chemistry/2010/summary/ (accessed 2022-04-01).
(48) Lennox, A. J. J.; Lloyd-Jones, G. C. Selection of Boron Reagents for Suzuki-Miyaura Coupling. *Chem. Soc. Rev.* **2014**, *43* (412). https://doi.org/10.1039/c3cs60197h.
(49) Maluenda, I.; Navarro, O. Recent Developments in the Suzuki-Miyaura Reaction: 2010-2014. *Molecules* **2015**, *20*, 7528–7557. https://doi.org/10.3390/molecules20057528.
(50) Netherton, M. R.; Dai, C.; Neuschütz, K.; Fu, G. C. Room-Temperature Alkyl-Alkyl Suzuki Cross-Coupling of Alkyl Bromides That Possess Beta Hydrogens. *J. Am. Chem. Soc.* **2001**, *123*, 10099–10100. https://doi.org/10.1021/ja011306o.
(51) Tilly, D.; Fu, J.; Zhao, B.; Alessi, M.; Castanet, A.-S.; Sniekus, V.; Mortier, J. On the Mechanism of the Directed Ortho and Remote Metalation Reactions of N,N-Dialkylbiphenyl 2-Carboxamides. *Org. Lett.* **2010**, *12* (1), 68–71. https://doi.org/10.1021/ol902268h.
(52) Kosak, T. M.; Conrad, H. A.; Korich, A. L.; Lord, R. L. Ether Cleavage Re-Investigated: Elucidating the Mechanism of BBr3-Facilitated Demethylation of Aryl Methyl Ethers. *EurJoc* **2015**, No. 34, 7460–7467. https://doi.org/10.1002/ejoc.201501042.
(53) Sousa, C.; Silva, P. J. BBr3-Assisted Cleavage of Most Ethers Does Not Follow the Commonly Assumed Mechanism. *Eur. J. Org. Chem.* **2013**, No. 23, 5195–5199. https://doi.org/10.1002/ejoc.201300337.
(54) Su, T. M.; Sliwinski, W. F.; Schleyer, P. V. R. Solvolysis of Highly Unreactive Substrates Using the Trifluoromethanesulfonate (Triflate) Leaving Group. *J. Am. Chem. Soc.* **1969**, *91* (19), 5386–5388. https://doi.org/10.1021/ja01047a035.
(55) Chemeurope. *Triflate*. https://www.chemeurope.com/en/encyclopedia/Triflate.html.
(56) Dhakal, B.; Bohé, L.; Crich, D. Trifluoromethanesulfonate Anion as Nucleophile in Organic Chemistry. *J. Org. Chem.* **2017**, *82* (18), 9263–9269. https://doi.org/10.1021/acs.joc.7b01850.

(57) Crossland, R. K.; Wells, W. E.; Shiner Jr., V. J. Sulfonate Leaving Groups, Structure and Reactivity. 2,2,2- Trifluoroethanesulfonate. *J. Am. Chem. Soc.* **1971**, *93* (12), 4217–4219. https://doi.org/10.1021/ja00746a021.
(58) Stang, P. J.; Hanack, M.; Subramanian, L. R. Perfluoroalkanesulfonic Esters: Methods of Preparation and Applications in Organic Chemistry. *Synthesis* **1982**, *1982* (2), 85–126. https://doi.org/10.1055/s-1982-29711.
(59) Beard, C. D.; Baum, K.; Grakauskas, V. Synthesis of Some Novel Trifluoromethanesulfonates and Their Reactions with Alcohols. *J. Org. Chem.* **1973**, *38* (21), 3673–3677. https://doi.org/10.1021/jo00961a003.
(60) Binkley, R. W.; Ambrose, M. G. Reaction of 2,6-Dimethyl- and 2,4,6-Trimethylpyridine with Trifluoromethanesulfoic Anhydride. *J. Org. Chem.* **1983**, *48* (10), 1777–1779. https://doi.org/10.1021/jo00158a041.
(61) Merck. *Trifluoromethanesulfonic anhydride solution*. https://www.sigmaaldrich.com/NO/en/product/aldrich/704083 (accessed 2022-02-16).
(62) Ouyang, Y.; Xu, X.-H.; Qing, F.-L. Trifluoromethanesulfonic Anhydride as a Low-Cost and Versatile Trifluoromethylation Reagent. *Angew. Chem. Int. Ed.* **2018**, *57* (23), 6926–6929. https://doi.org/10.1002/anie.201803566.
(63) Sommer, H. Z.; Jackson, L. L. Alkylation of Amines: A New Method for the Synthesis of Quarternary Ammonium Compounds from Primary and Secondary Amines. *Department of the army, Edgewood arsenal, research laboratory* **1969**. https://apps.dtic.mil/sti/pdfs/AD0692840.pdf.
(64) Seyferth, D. The Grignard Reagents. *Organometallics* **2009**, *28* (6), 1598–1605. https://doi.org/10.1021/om900088z.
(65) Ouellette, R. J.; Rawn, J. D. *Organic Chemistry: Structure, Mechanism, and Synthesis*; Elsevier Inc., 2014.
(66) Sämann, C. New Preparations and Reactions of Organometallic Reagents of Mg, Zn and B for the Functionalization of Aromatics and Heteroaromatics, Allylic and Vinylic Compounds as Well as for Adamantyl Derivatives. *PhD Thesis, Ludwig-Maximilians-Universität München* **2013**.
(67) NobelPrize.org; Nobel Prize Outreach AB 2022. *Victor Grignard - Biographical*. https://www.nobelprize.org/prizes/chemistry/1912/grignard/biographical/.
(68) Science Direct. *Grignard Reagent*. https://www-sciencedirect-com.ezproxy.uis.no/topics/chemistry/grignard-reagent (accessed 2022-04-12).
(69) Tilstam, U.; Weinmann, H. Activation of Mg Metal for Safe Formation of Grignard Reagents on Plant Scale. *Organic Process Research & Development* **2002**, *6* (6), 906–910. https://doi.org/10.1021/op025567+.
(70) Ley, S. V.; Low, C. M. R. *Ultrasound in Synthesis*, 1st ed.; Springer, Berlin, Heidelberg, 1989; Vol. 27.
(71) Rieke, R. D. Preparation of Organometallic Compounds from Highly Reactive Metal Powders. *Science* **1989**, *246* (4935), 1260–1264. https://doi.org/10.1126/science.246.4935.1260.
(72) Rieke, R. D.; Hudnall, P. M. Activated Metals. I. Preparation of Highly Reactive Magnesium Metal. *J. Am. Chem. Soc.* **1972**, *94* (20), 7178–7179. https://doi.org/10.1021/ja00775a066.
(73) Merck. *Selective Metalation, Deprotonation, and Additions*. https://www.sigmaaldrich.com/NO/en/technical-documents/technical-article/chemistry-and-synthesis/reaction-design-and-optimization/chemetall (accessed 2022-02-16).
(74) Organic Chemistry Portal. *Grignard Reaction*. https://www.organic-chemistry.org/namedreactions/grignard-reaction.shtm (accessed 2022-04-25).
(75) Peltzer, R. M.; Gauss, J.; Eisenstein, O.; Cascella, M. The Grignard Reaction - Unraveling a Chemical Puzzle. *J. Am. Chem. Soc.* **2020**, *142* (6), 2984–2994. https://doi.org/10.1021/jacs.9b11829?ref=pdf.
(76) Liu, N.; Wang, Z.-X. Kumada Coupling of Aryl, Heteroaryl, and Vinyl Chlorides Catalyzed by Amido Pincer Nickel Complexes. *J. Org. Chem.* **2011**, *76*, 10031–10038. https://doi.org/10.1021/jo201821g.

(77) Martin, R.; Buchwald, S. L. Pd-Catalyzed Kumada-Corriu Cross-Coupling Reactions at Low Temperatures Aloow the Use of Knotchel Type Grignard Reagents. *J. Am. Chem. Soc.* **2007**, *129* (13), 3844–3845. https://doi.org/10.1021/ja070830d.
(78) Busacca, C. A.; Eriksson, M. C.; Fiaschi, R. Cross Coupling of Vinyl Triflates and Alkyl Grignard Reagents Catalyzed by Nickel(0)-Complexes. *Tetrahedon Letters* **1999**, *40* (16), 3101–3104. https://doi.org/10.1016/S0040-4039(99)00439-6.
(79) Adrio, J.; Carretero, J. C. Functionalized Grignard Reagents in Kumada Cross-Coupling Reactions. *Chem. Cat. Chem.* **2011**, *2* (11), 1384–1386. https://doi.org/10.1002/cctc.201000237.
(80) Kumada, M. Nickel and Palladium Complex Catalyzed Cross-Coupling Reactions of Organometallic Reagents with Organic Halides. *Pure & Appl. Chem. 52*, 669–679. https://doi.org/10.1351/pac198052030669.
(81) Chem-Station Int. Ed. *Kumada-Tamao-Corriu Cross Coupling*. https://en.chem-station.com/reactions-2/2014/05/kumada-tamao-corriu-cross-coupling.html (accessed 2022-03-13).
(82) Manar, K. K.; Ren, P. *Advances in Organometallic Chemistry*, 1. Edition.; Elsevier Ltd., 2021; Vol. 76.
(83) Hu, X. Nickel-Catalyzed Cross Coupling of Non-Activated Alkyl Halides: A Mechanistic Perspective. *Chem. Sci.* **2011**, *2*, 1867–1886. https://doi.org/10.1039/c1sc00368b.
(84) Wei, X.-J.; Abdiaj, I.; Sambiagio, C.; Li, C.; Zysman-Colman, E.; Alcázar, J.; Noël, T. Visible-Light-Promoted Iron-Catalyzed C(Sp2)-C(Sp3) Kumada Cross-Coupling in Flow. *Angew. Chem. Int. Ed.* **2019**, *58*, 13030–13034. https://doi.org/10.1002/anie.201906462.
(85) Sears, J. D.; Neate, P. G. N.; Neidig, M. L. Intermediates and Mechanism in Iron-Catalyzed Cross-Coupling. *J. Am. Chem. Soc.* **2018**, *140* (38), 11872–11883. https://doi.org/10.1021/jacs.8b06893.
(86) Blom, C.; Legros, J.; Le Paih, J.; Zani, L. Iron-Catalyzed Reactions in Organic Synthesis. *Chem. Rev.* **2004**, *104*, 6217–6254. https://doi.org/10.1021/cr040664h.
(87) Cahiez, G.; Avedissan, H. Highly Stereo- and Chemoselective Iron-Catalyzed Alkenylation of Organomagnesium Compounds. *Synthesis* **1998**, No. 8, 1199–1205. https://doi.org/10.1055/s-1998-2135.
(88) Bisz, E.; Koston, M.; Szostak, M. N-Butylpyrrolidone (NBP) as a Non-Toxic Substitute for NMP in Iron-Catalyzed C(Sp2)-C(Sp3) Cross-Coupling of Aryl Chlorides. *Green Chem.* **2021**, *23* (19), 7515–7521. https://doi.org/10.1039/D1GC02377B.
(89) Name-reaction.com. *Kumada cross-coupling*. https://www.name-reaction.com/kumada-cross-coupling (accessed 2022-03-03).
(90) Organic Chemistry Portal. *Kumada Coupling*. https://www.organic-chemistry.org/namedreactions/kumada-coupling.shtm (accessed 2022-03-04).
(91) van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. Ligand Bite Angle Effects in Metal-Catalyzed C-C Bond Formation. *Chem. Rev.* **2000**, *100* (8), 2741–2770. https://doi.org/10.1021/cr9902704.
(92) Birkholz, M.-N.; Freixa, Z.; van Leeuwen, P. W. N. M. Bite Angle Effects of Diphosphines in C–C and C–X Bond Forming Cross Coupling Reactions. *Chem. Soc. Rev.* **2009**, *38* (4), 1099–1118. https://doi.org/10.1039/b806211k.
(93) Xing, T.; Zhang, Z.; Da, Y.-X.; Quan, Z.-J.; Wang, X.-C. Iron-Catalyzed Kumada Cross-Coupling Reactions of Pyrimidin-2-Yl Phosphates: An Efficient Approach to C2-Functionalized Pyrimidines. *Asian J. Org. Chem.* **2015**, *4* (6), 538–544. https://doi.org/10.1002/ajoc.201500044.
(94) Guérinot, A.; Reymond, S.; Cossy, J. Iron-Catalyzed Cross-Coupling of Alkyl Halides with Alkenyl Grignard Reagents. *Angew. Chem. Int. Ed.* **2007**, *46* (34), 6521–6524. https://doi.org/10.1002/anie.200702206.
(95) Bedford, R. B.; Huwe, M.; Wilkinson, M. C. Iron-Catalyzed Negishi Coupling of Benzylhalides and Phosphates. *Chem. Commun.* **2009**, *2009* (5), 600–602.
(96) Ma, X.; Wang, H.; Liu, Y.; Zhao, X.; Zhang, J. Mixed Alkyl/Aryl Diphos Ligands for Iron-Catalyzed Negishi and Kumada Cross Coupling Towards the Synthesis of Diarylmethane. *ChemCatChem* **2021**, *13* (24), 5134–5140. https://doi.org/10.1002/cctc.202101237.

(97) Fleming, G. R.; Longworth, J.; Krueger, B. P. *photochemical reaction*. Encyclopedia Britannica. https://www.britannica.com/science/photochemical-reaction (accessed 2022-04-27).
(98) Markali, J.; Uggerud, E. fotokjemi. *Store norske leksikon*; 2021.
(99) Abrajano, T. A.; Yan, B.; O'Malley, V. *Treatise on Geochemistry: Enviromental Geochemistry*, 2nd ed.; Elsevier Ltd., 2014; Vol. 11.
(100) Reusch, W. *Photochemistry*. Michigan State University. https://www2.chemistry.msu.edu/faculty/reusch/virttxtjml/photchem.htm (accessed 2022-05-01).
(101) Boye, N. Chr. *Kjemi Og Miljølære*, 4. utgave.; Gyldendal Norsk Forlag, 2009.
(102) Mallory, F. B.; Mallory, C. W. Photocyclization of Stilbenes and Related Molecules. In *Organic Reactions*; American Cancer Society, 2005; pp 1–456. https://doi.org/10.1002/0471264180.or030.01.
(103) Encyclopedia Britannica. *Photochemical reaction - Photoisomerization*. https://www.britannica.com/science/photochemical-reaction/Photoisomerization (accessed 2022-04-28).
(104) Jørgensen, K. B. Photochemical Oxidative Cyclisation of Stilbenes and Stilbenoids—The Mallory-Reaction. *Molecules* **2010**, *15* (6), 4334–4358. https://doi.org/10.3390/molecules15064334.
(105) Antelo, B.; Castedo, L.; Delamano, J.; Gómez, A.; López, C.; Tojo, G. Photochemical Ring Closure of 1-Tosyl-1,2-Diarylethenes. *J. Org. Chem.* **1996**, *61* (4), 1188–1189. https://doi.org/10.1021/jo951464w.
(106) Parker, C. O.; Spoerri, P. E. Photochemical Conversion of Stilbene to Phenanthrene. *Nature* **1950**, *166* (4223), 603. https://doi.org/10.1038/166603a0.
(107) Wood, C. S.; Mallory, F. B. Photochemistry of Silbenes. IV. The Preparation of Substituted Phenanthrenes. *J. Org. Chem.* **1964**, *29* (11), 3373–3377. https://doi.org/10.1021/jo01034a059.
(108) Neo, A. G.; López, C.; Romero, V.; Antelo, B.; Delamano, J.; Pérez, A.; Fernández, D.; Almeida, J. F.; Castedo, L.; Tojo, G. Preparation of Phenanthrenes by Photocyclization of Stilbenes Containing a Tosyl Group on the Central Double Bond. A Versatile Approach to the Synthesis of Phenanthrenes and Phenanthrenoids. *J. Org. Chem.* **2010**, *75* (20), 6764–6770. https://doi.org/10.1021/jo100742e.
(109) Liu, L.; Yang, B.; Katz, T. J.; Poindexter, M. K. Improved Methodology for Photocyclization Reactions. *J. Org. Chem.* **1991**, *56* (12), 3769–3775. https://doi.org/10.1021/jo00012a005.
(110) McCabe, E. T.; Barthel, W. F.; Gertler, S. I.; Hall, S. A. Insect Repellents. III. N,N-Diethylamides. *J. Org. Chem.* **1954**, *19* (4), 493–498. https://doi.org/10.1021/jo01369a003.
(111) PerkinElmer. *ChemDraw Professional*. https://www.perkinelmer.com/product/chemdraw-professional-chemdrawpro (accessed 2022-04-28).
(112) Kumar, A.; Akula, H. K.; Lakshman, M. K. Simple Synthesis of Amides and Weinreb Amides Using PPh3 or Polymer-Supported PPh3 and Iodine. *Eur. J. Org. Chem.* **2010**, No. 14, 2709–2715. https://doi.org/10.1002/ejoc.200901420.
(113) Ren, W.; Yamane, M. Mo(CO)6-Mediated Carbamoylation of Aryl Halides. *J. Org. Chem.* **2010**, *75* (24), 8410–8415. https://doi.org/10.1021/jo101611g.
(114) Sigma-Aldrich. *Application Guide for Palladium Catalyzed Cross-Coupling Reactions*. https://www.sigmaaldrich.com/deepweb/assets/sigmaaldrich/product/documents/226/818/application-guide-for-palladium-catalyzed-cross-coupling.pdf.
(115) Zhao, Z.; Snieckus, V. Directed Ortho Metalation-Based Methodology. Halo-, Nitroso-, and Boro-Induced Ipso-Desilylation. Link to an in Situ Suzuki Reaction. *Org. Lett.* **2005**, *7* (13), 2523–2526. https://doi.org/10.1021/ol0506563.
(116) National Center for Biotechnology Information. *PubChem Compound Summary for CID 8857, Ethyl acetate*. https://pubchem.ncbi.nlm.nih.gov/compound/Ethyl-acetate (accessed 2022-04-10).
(117) National Center for Biotechnology Information. *PubChem Compound Summary for CID 6344, Dichloromethane*. https://pubchem.ncbi.nlm.nih.gov/compound/Dichloromethane (accessed 2022-04-10).

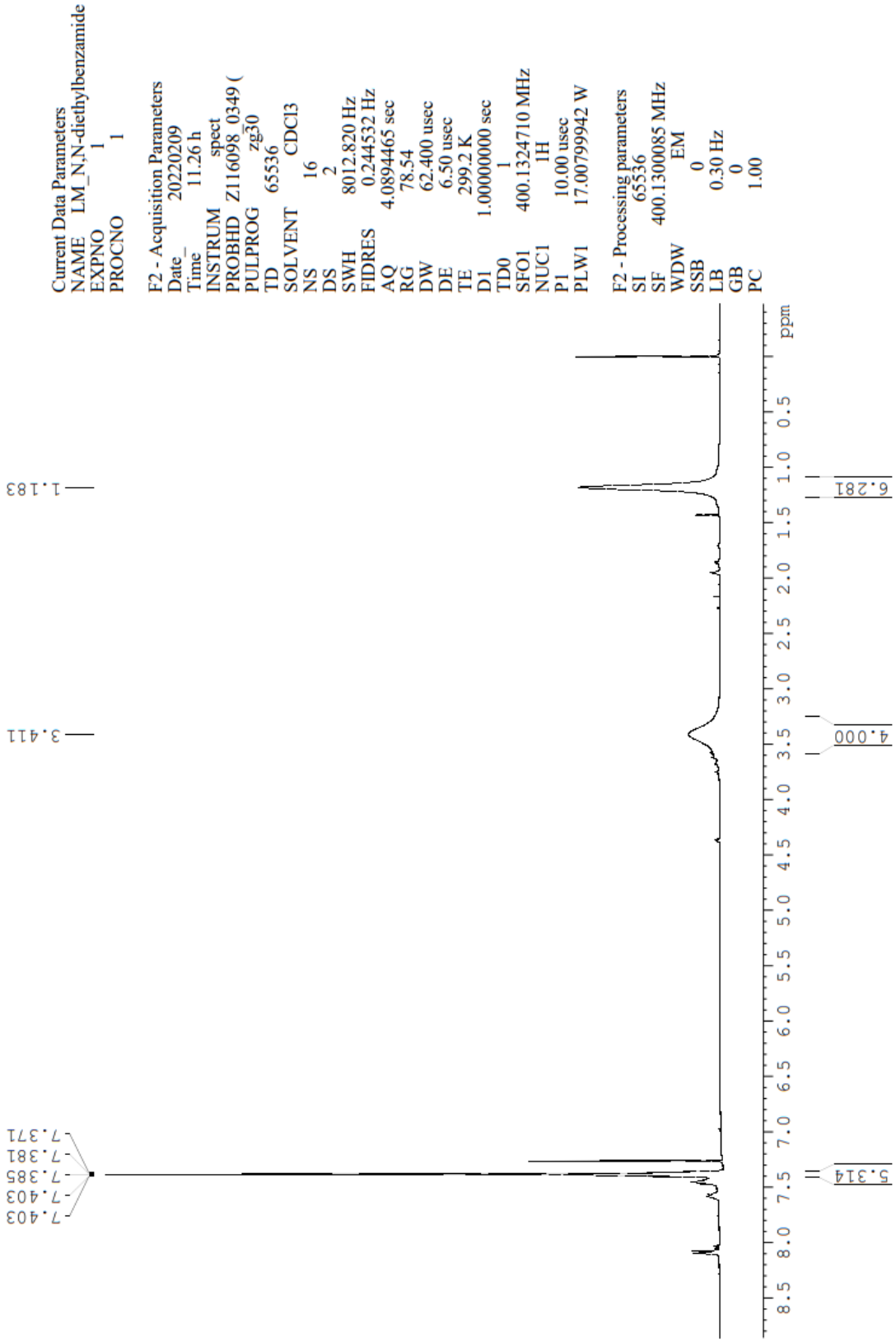
(118) Boehm, P.; Roediger, S.; Bismuto, A.; Morandi, B. Palladium-Catalyzed Chlorocarbonylation Og Aryl (Pseudo) Halides Through In Situ Generation of Carbon Monoxide. *Angew. Chem. Int. Ed. Engl.* **2020**, *59* (41), 17887–17896. https://doi.org/10.1002/anie.202005891.
(119) Brimble, M. A.; Lai, M. Y. H. Suzuki-Miyaura Homocoupling of Naphthyl Triflates Using Bis(Pinacolato)Diboron: Approaches to the Biaryl Skeleton of Crisamicin A. *Org. Biomol. Chem.* **2003**, *1* (12), 2084–2095. https://doi.org/10.1039/B303070A.
(120) Dyke, A. M.; Gill, D. M.; Harvey, J. N.; Hester, A. J.; Lloyd-Jones, G. C.; Muñoz, M. P.; Shepperson, I. R. Decoupling Deprotonation from Metalation: Thia-Fries Rearrangement. *Angew. Chem. Int. Ed.* **2008**, *47* (27), 5067–5070. https://doi.org/10.1002/anie.200800750.
(121) Zhu, S.; Wang, C.; Chen, L.; Liang, R.; Yu, Y.; Jiang, H. Modular Approach for Synthesis of Vicinal Diamines Containing Axial Chiral 1,1'-Binaphthyl from 1,2-Diaminoethane by Pd-Catalyzed N-Arylation Reactions. *Org. Lett.* **2011**, *13* (5), 1146–1149. https://doi.org/10.1021/ol103169z.
(122) UCLA College. Chemistry & Biochemistry. *Meeting 11*. http://www.chem.ucla.edu/~bacher/General/30CL/answers/M11W15.html (accessed 2022-04-20).
(123) Shannon, J.; Bernier, D.; Rawson, D.; Woodward, S. Direct Asymmetric Catalytic 1,2-Addition of RZnX to Aldehydes Promoted by AlMe3 and Reversal of Expected Stereochemistry. *Chem. Commun.* **2007**, *2007* (38), 3945–3947. https://doi.org/10.1039/B710681E.
(124) Xu, X.; Cheng, D.; Pei, W. Iron-Catalyzed Homocoupling of Bromide Compounds. *J. Org. Chem.* **2006**, *71* (17), 6637–6639. https://doi.org/10.1021/jo060673l.
(125) Liu, G.-B.; Zhao, H.-Y.; Dai, L.; Thiemann, T.; Tashiro, H.; Tashiro, M. Raney Ni-Al Alloy-Mediated Reduction of Benzils in Water. *Journal of Chemical Research* **2009**, *9*, 589–581. https://doi.org/10.3184%2F030823409X12506792542783.
(126) Otsubo, T.; Ogura, F.; Yamaguchi, H.; Higuchi, H.; Misumi, S. Pyrolysis of Dibenzyl Selenides to Bibenzyls. *Synthetic Communications* **1980**, *10* (8), 595–601. https://doi.org/10.1080/00397918008063594.
(127) Arthurs, R. A.; Hughes, D. L.; Richards, C. J. Application of a Ferrocene-Based Palladacycle Precatalyst to Enantioselective Aryl-Aryl Kumada Coupling. *Eur. J. Inorg. Chem.* **2022**, *2022* (9). https://doi.org/10.1002/ejic.101077.
(128) Hiramatsu, K.; Honjo, T.; Rauniyar, V.; Toste, F. D. Enantioselective Synthesis of Fluoro–Dihydroquinazolones and −Benzooxazinones by Fluorination-Initiated Asymmetric Cyclization Reactions. *ACS Catal.* **2016**, *6* (1), 151–154. https://doi.org/10.1021/acscatal.5b02182.
(129) Visco, M. D.; Wieting, J. M.; Mattson, A. E. Carbon-Silicon Bond Formation in the Synthesis of Benzylic Silanes. *Org. Lett.* **2016**, *18* (12), 2883–2885. https://doi.org/10.1021/acs.orglett.6b01223.
(130) Fiorito, D.; Folliet, S.; Liu, Y.; Mazet, C. A General Nickel-Catalyzed Kumada Vinylation for the Preparation of 2-Substituted 1,3-Dienes. *ACS Catal.* **2018**, *8* (2), 1392–1398. https://doi.org/10.1021/acscatal.7b04030.
(131) Hayashi, T.; Ueyama, K.; Tokunaga, N.; Yoshida, K. A Chiral Chelating Diene as a New Type of Chiral Ligand for Transition Metal Catalysts: Its Preparation and Use for the Rhodium-Catalyzed Asymmetric 1,4-Addition. *J. Am. Chem. Soc.* **2003**, *125* (38), 11508–11509. https://doi.org/10.1021/ja037367z.
(132) Abdur-Rashid, K.; Jia, W.; Abdur-Rashid, K. Catalytic Cannabinoid Processes and Precursors. WO 2020/232545 A1, November 26, 2020.
(133) Sloan, M. E.; Staubitz, A.; Lee, K.; Manners, I. Scope and Selectivity of Heterogeneous Rh0-Catalyzed Tandem Dehydrocoupling/Hydrogenation Using Me2NH·BH3 as a Stoichiometric H2 Source. *Eur. J. Org. Chem.* **2010**, *2011* (4), 672–675. https://doi.org/10.1002/ejoc.201001332.
(134) Denmark, S. E.; Butler, C. R. Vinylation of Aryl Bromides Using an Inexpensive Vinylpolysiloxane. *Org. Lett.* **2006**, *8* (1), 63–66. https://doi.org/10.1021/ol052517r.
(135) Madhushaw, R. J.; Lo, C.-Y.; Hwang, C.-W.; Su, M.-D.; Shen, H.-C.; Pal, S.; Shaikh, I. R.; Liu, R.-S. Rutheniun-Catalyzed Cycloisomerization of o-(Ethynyl)Phenylalkenes to Diene Derivatives via

Skeletal Rearrangement. *J. Am. Chem. Soc.* **2004**, *126* (47), 15560–15565. https://doi.org/10.1021/ja045516n.
(136) Inés, B.; Moreno, I.; SanMartin, R.; Domínguez, E. A Nonsymmetric Pincer-Catalyzed Suzuki-Miyaura Arylation of Benzyl Halides and Other Nonactivated Unusual Coupling Partners. *J. Org. Chem.* **2008**, *73* (21), 8448–8451. https://doi.org/10.1021/jo8016633.
(137) Kofron, W. G.; Baclawski, L. M. A Convenient Method for Estimation of Alkyllithium Concentrations. *J. Org. Chem.* **1976**, *41* (10), 1879–1880. https://doi.org/10.1021/jo00872a047.
(138) Burchat, A. F.; Chong, J. M.; Nielsen, N. Titration of Alkyllithiums with a Simple Reagent to a Blue Endpoint. *J. Organomet. Chem.* **1997**, *542* (2), 281–283. https://doi.org/10.1016/S0022-328X%2897%2900143-5.
(139) Krasovskiy, A.; Knochel, P. Convenient Titration Method for Organometallic Zinc, Magnesium, and Lanthanide Reagents. *Synthesis* **2006**, *2006* (5), 890–891. https://doi.org/10.1055/s-2006-926345.

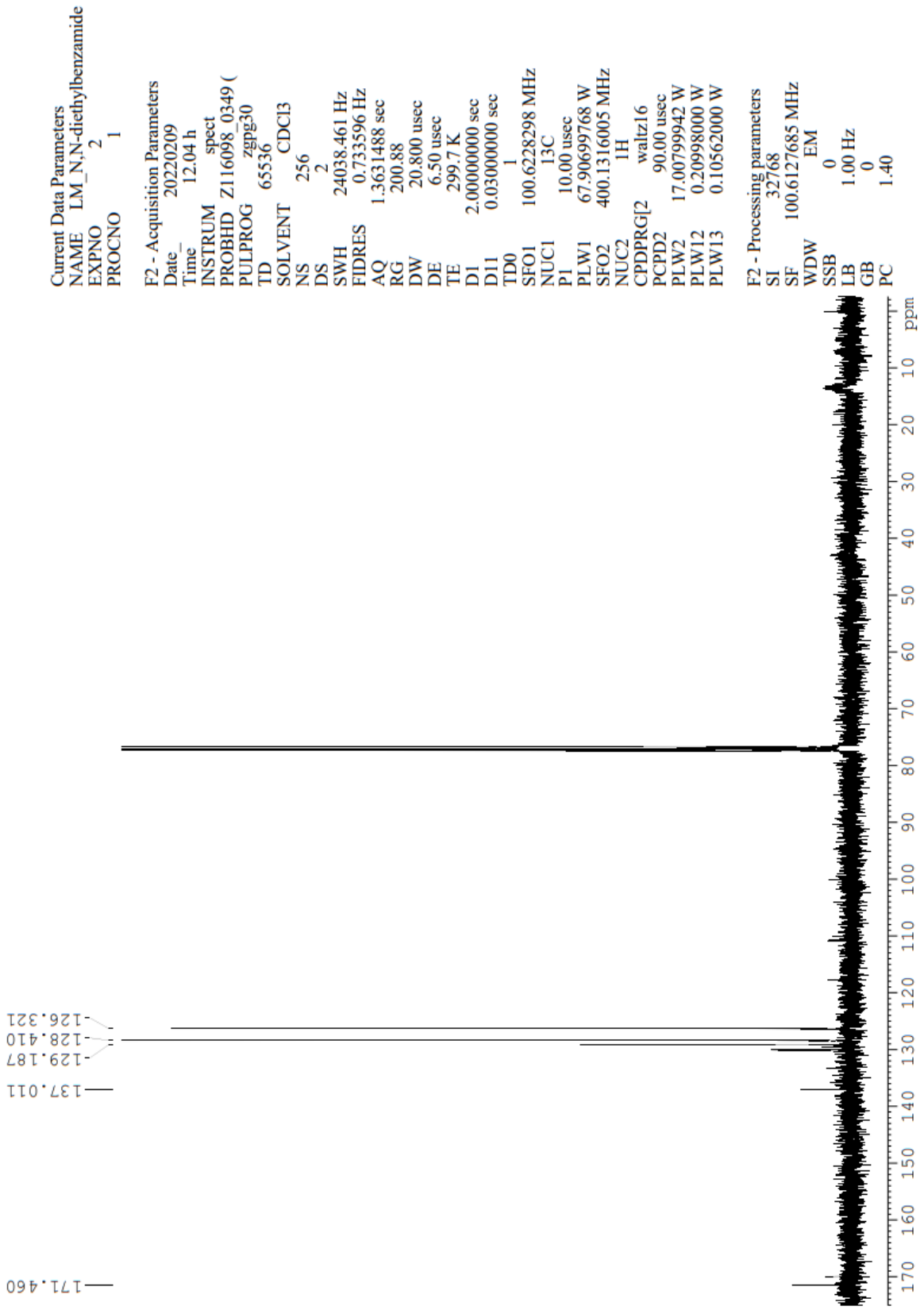
Appendix

Table of contents

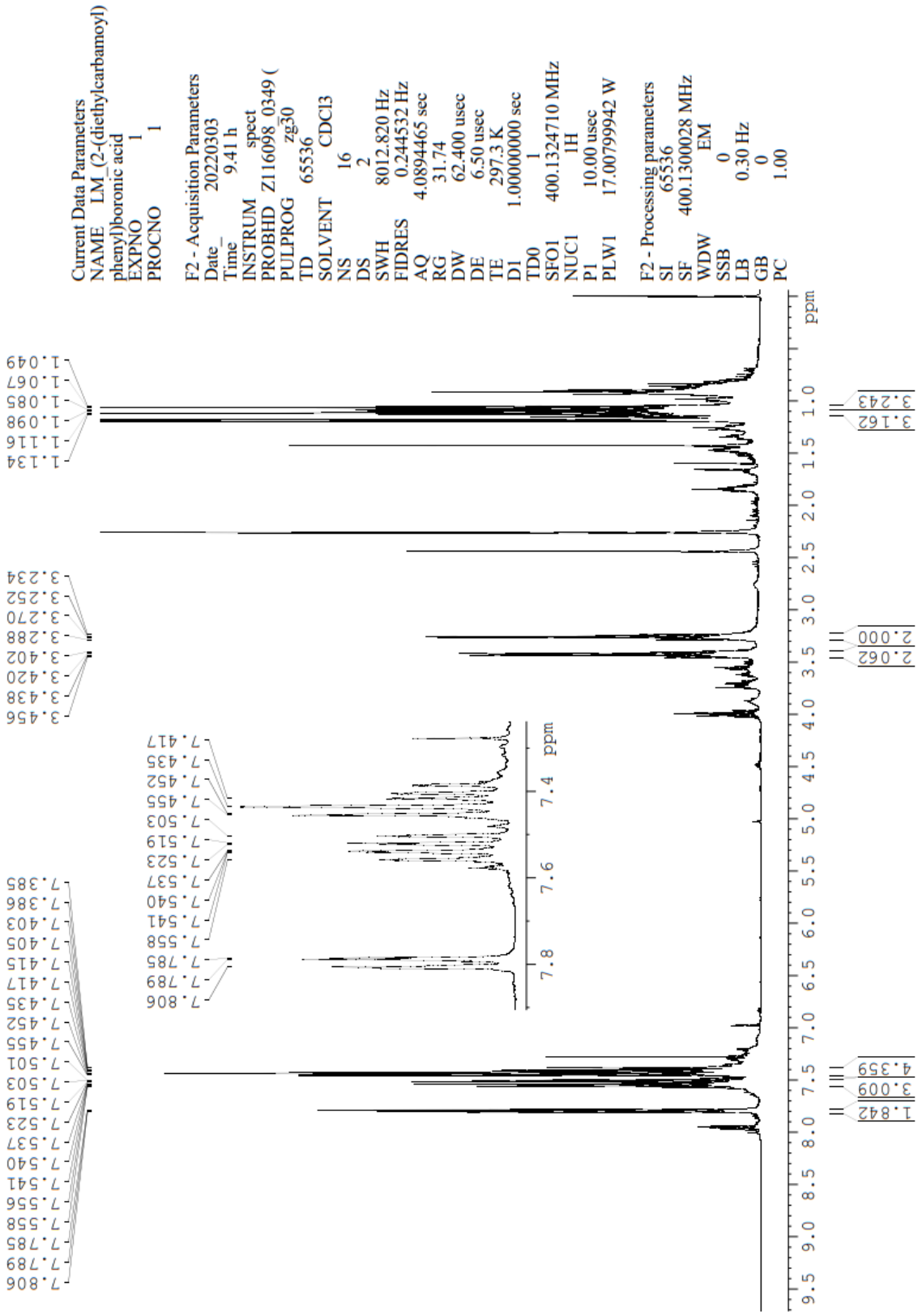
[1]H-NMR N,N-diethylbenzamide (2)



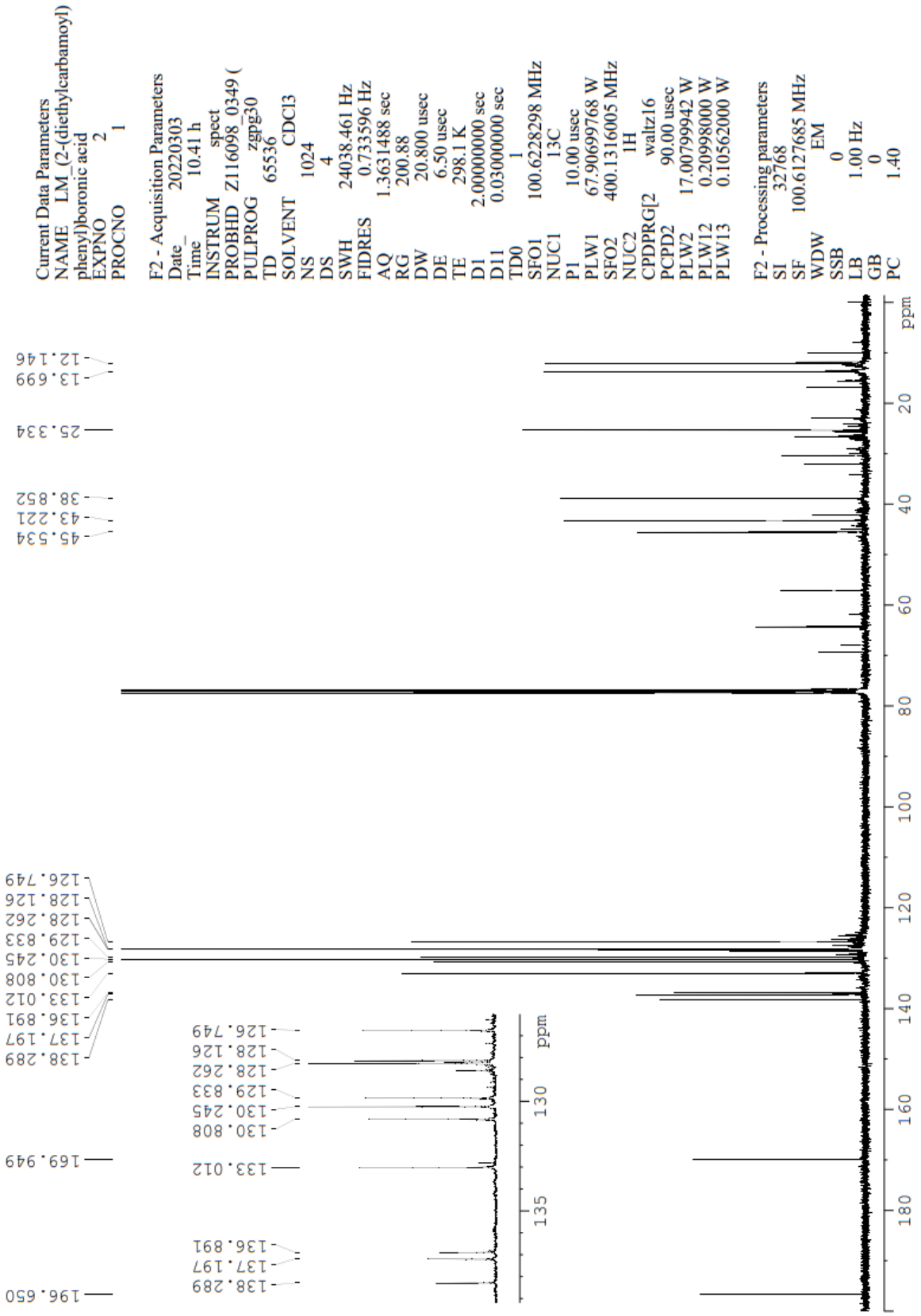
^{13}C-NMR N,N-diethylbenzamide (2)



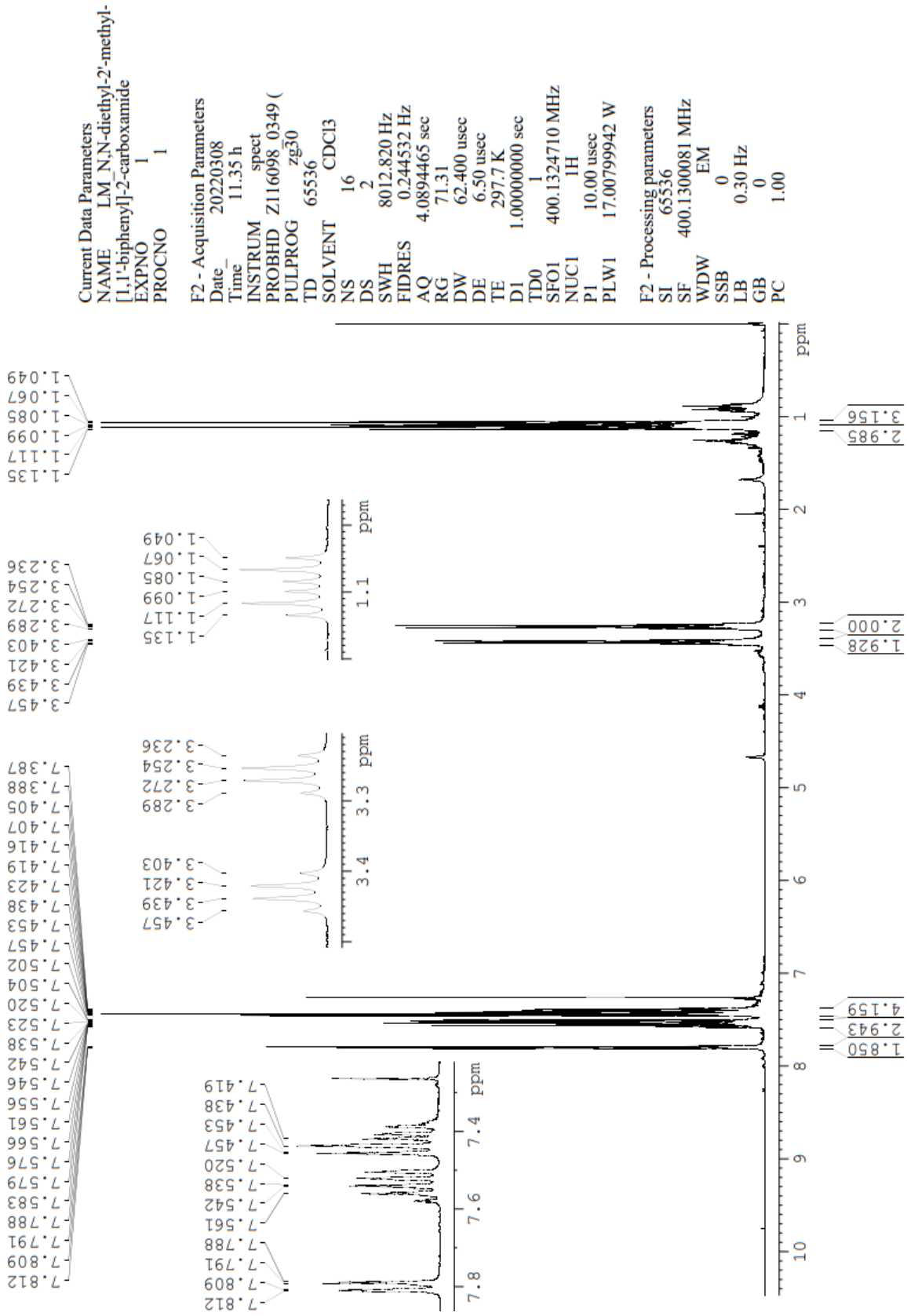
[1]H-NMR (2-(diethylcarbamoyl)phenyl)boronic acid (3)



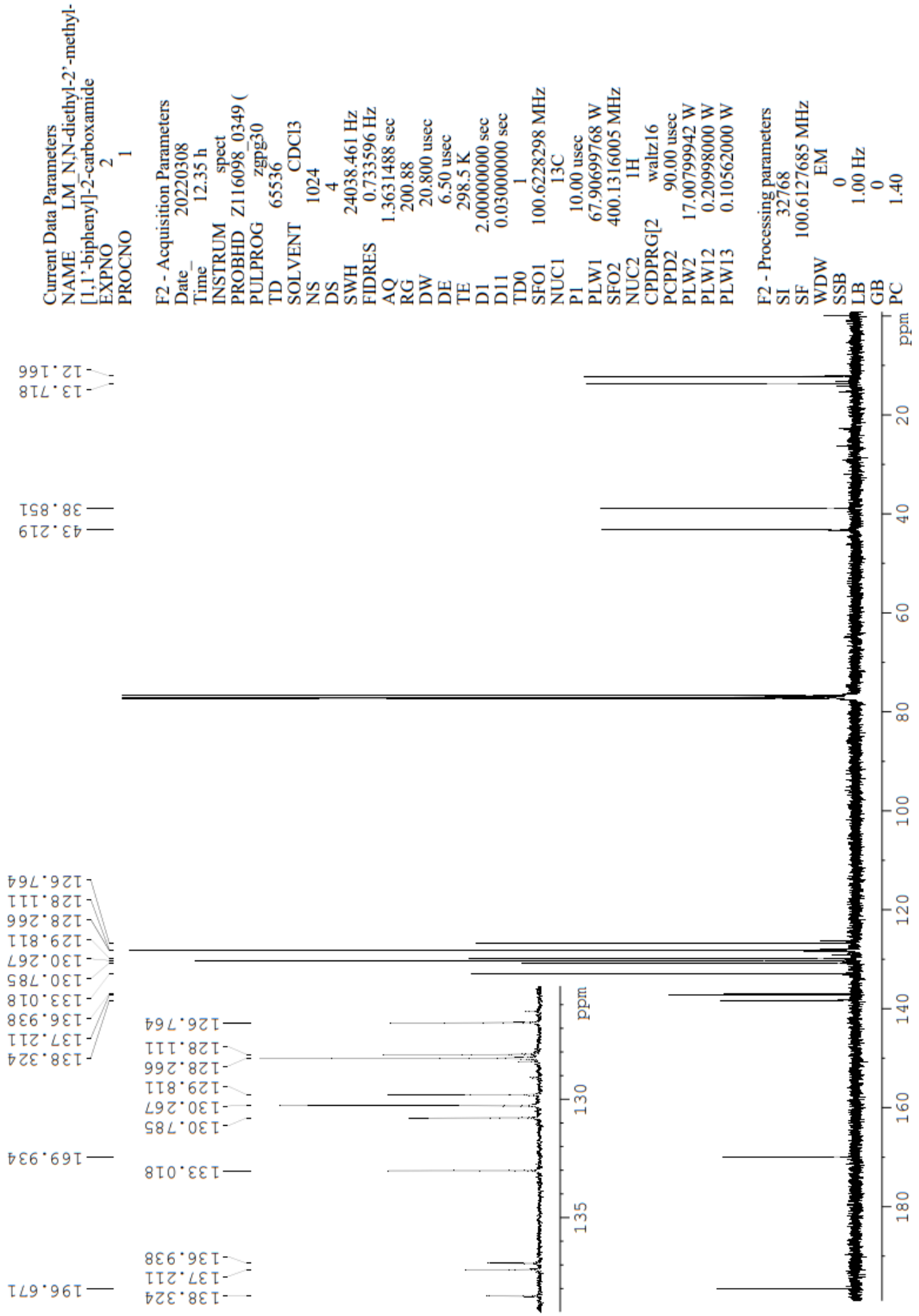
^{13}C-NMR (2-(diethylcarbamoyl)phenyl)boronic acid (3)



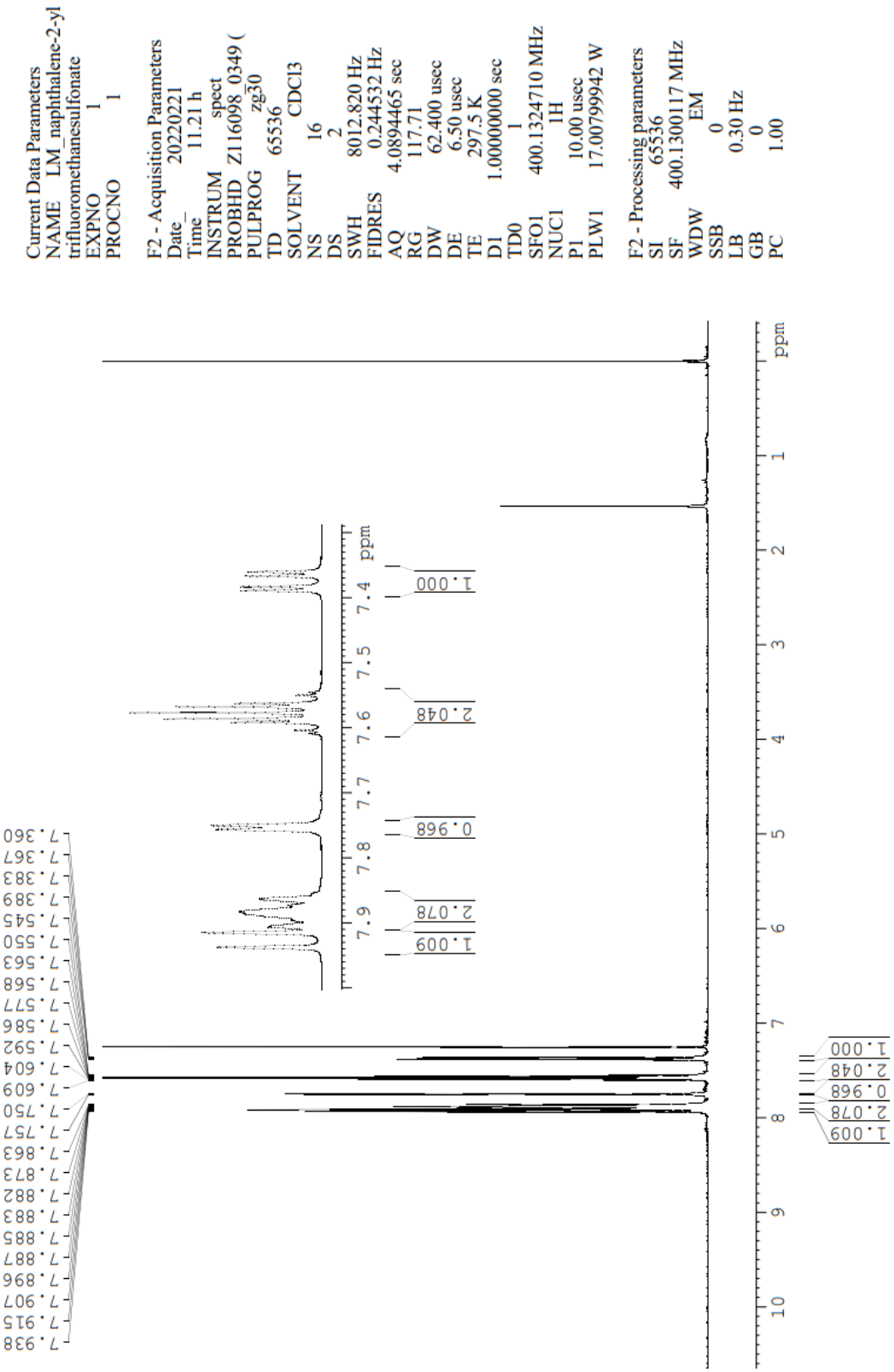
[1]H-NMR N,N-diethyl-2'-methyl-[1,1'-biphenyl]-2-carboxamide (4b)



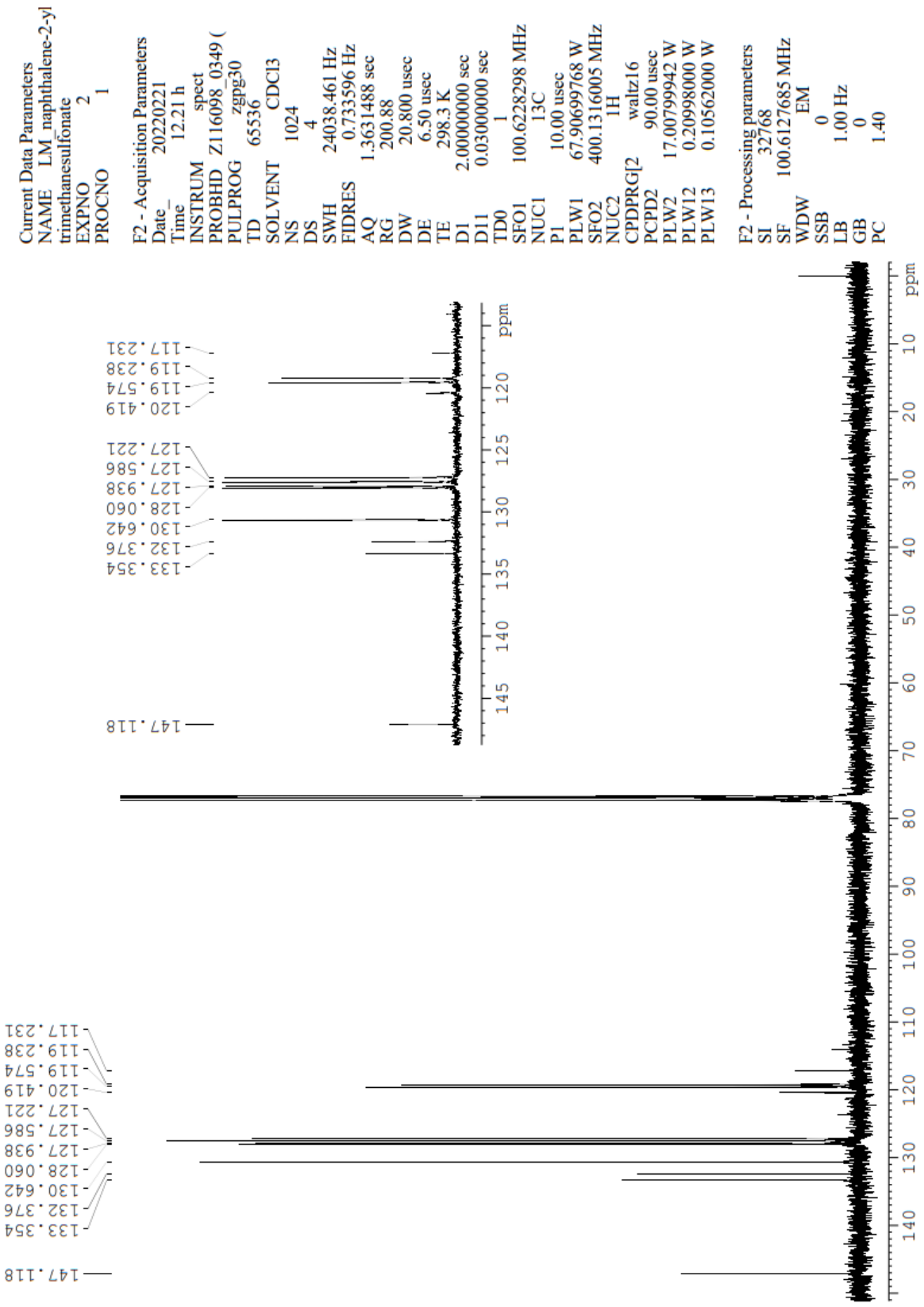
^{13}C-NMR N,N-diethyl-2'-methyl-[1,1'-biphenyl]-2-carboxamide (4b)



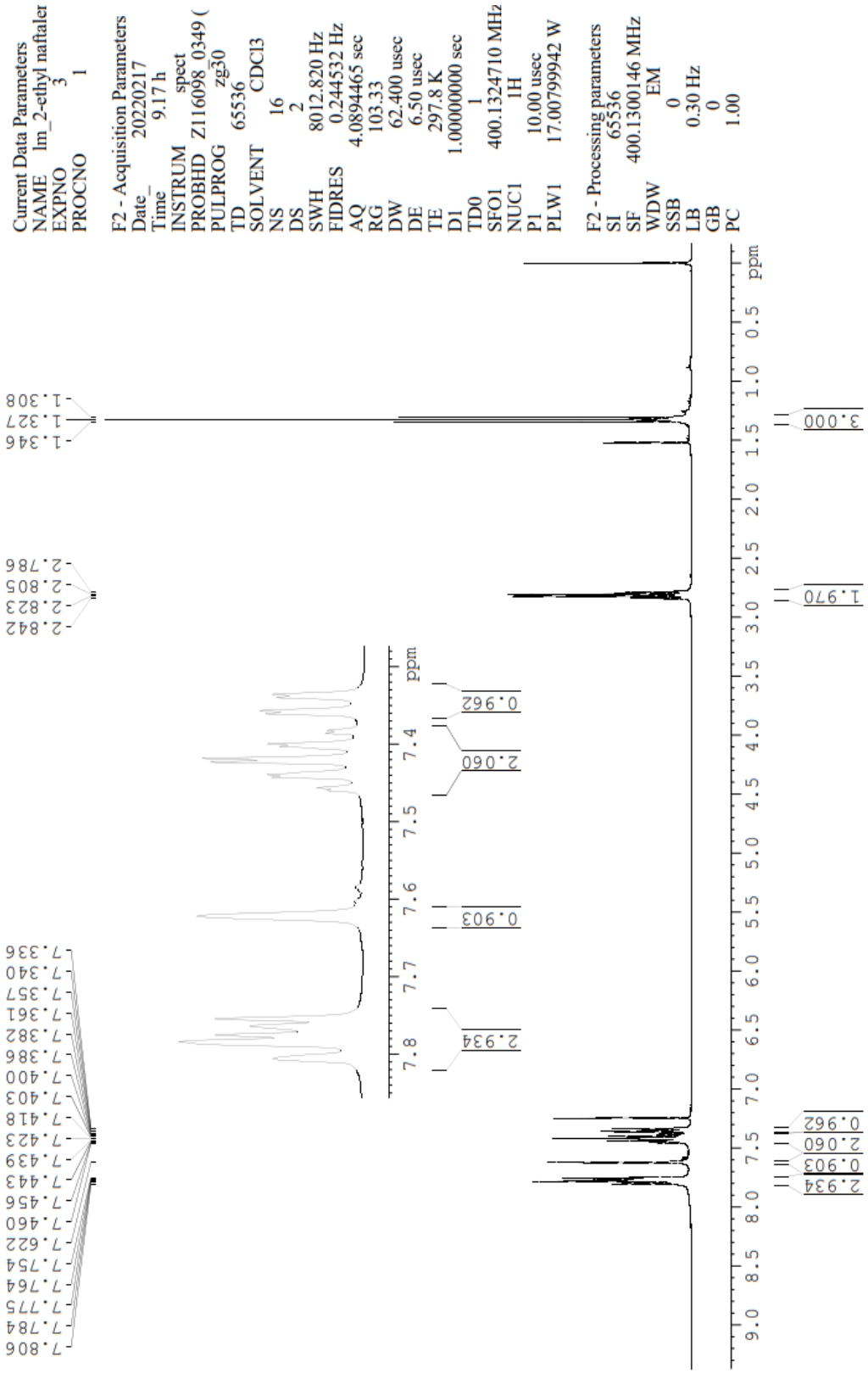
[1]H-NMR Naphthalene-2-yl trifluoromethanesulfonate (5b)



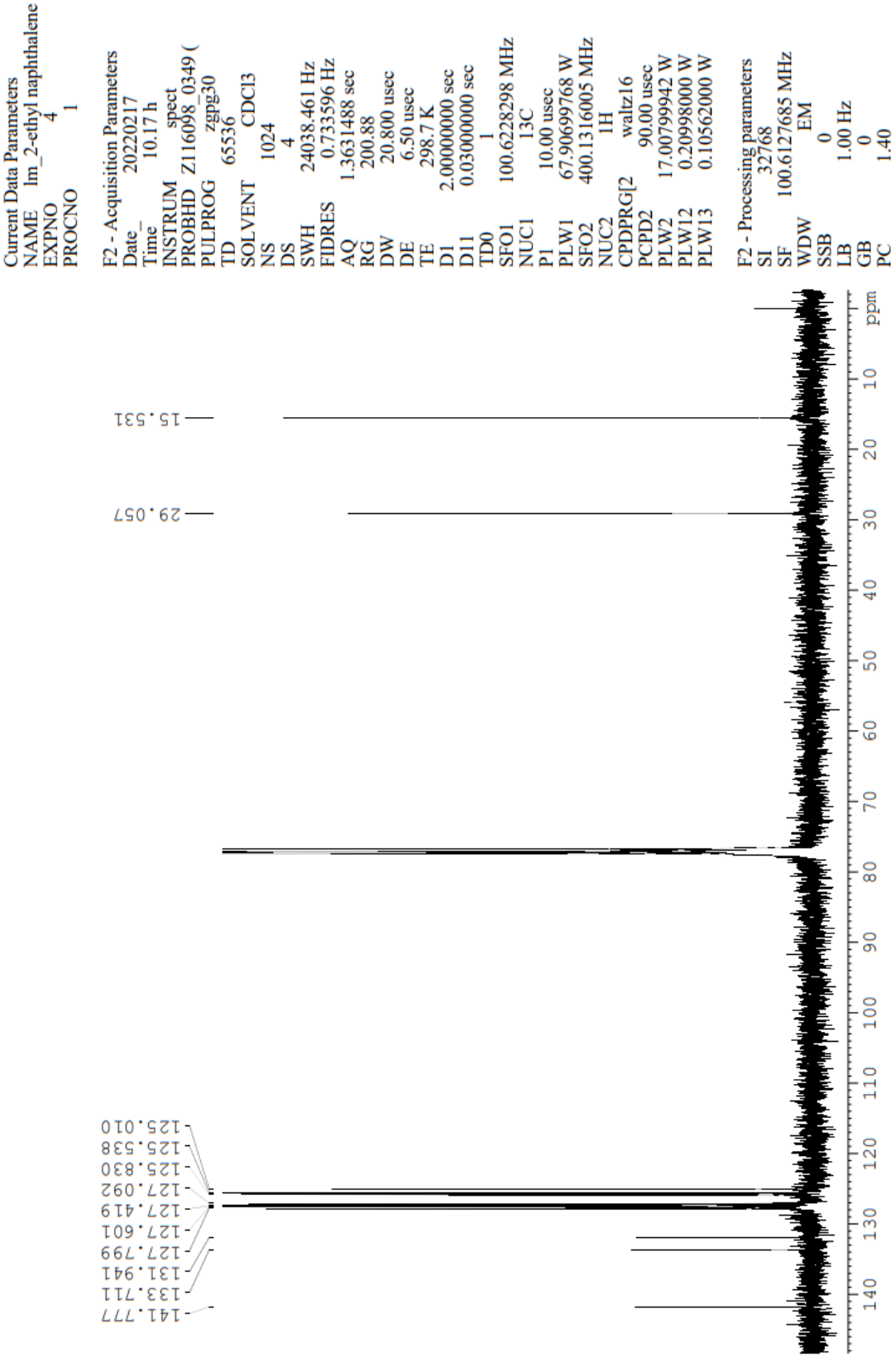
^{13}C-NMR Naphthalene-2-yl trifluoromethanesulfonate (5b)



[1]H-NMR 2-ethylnaphthalene (5c)

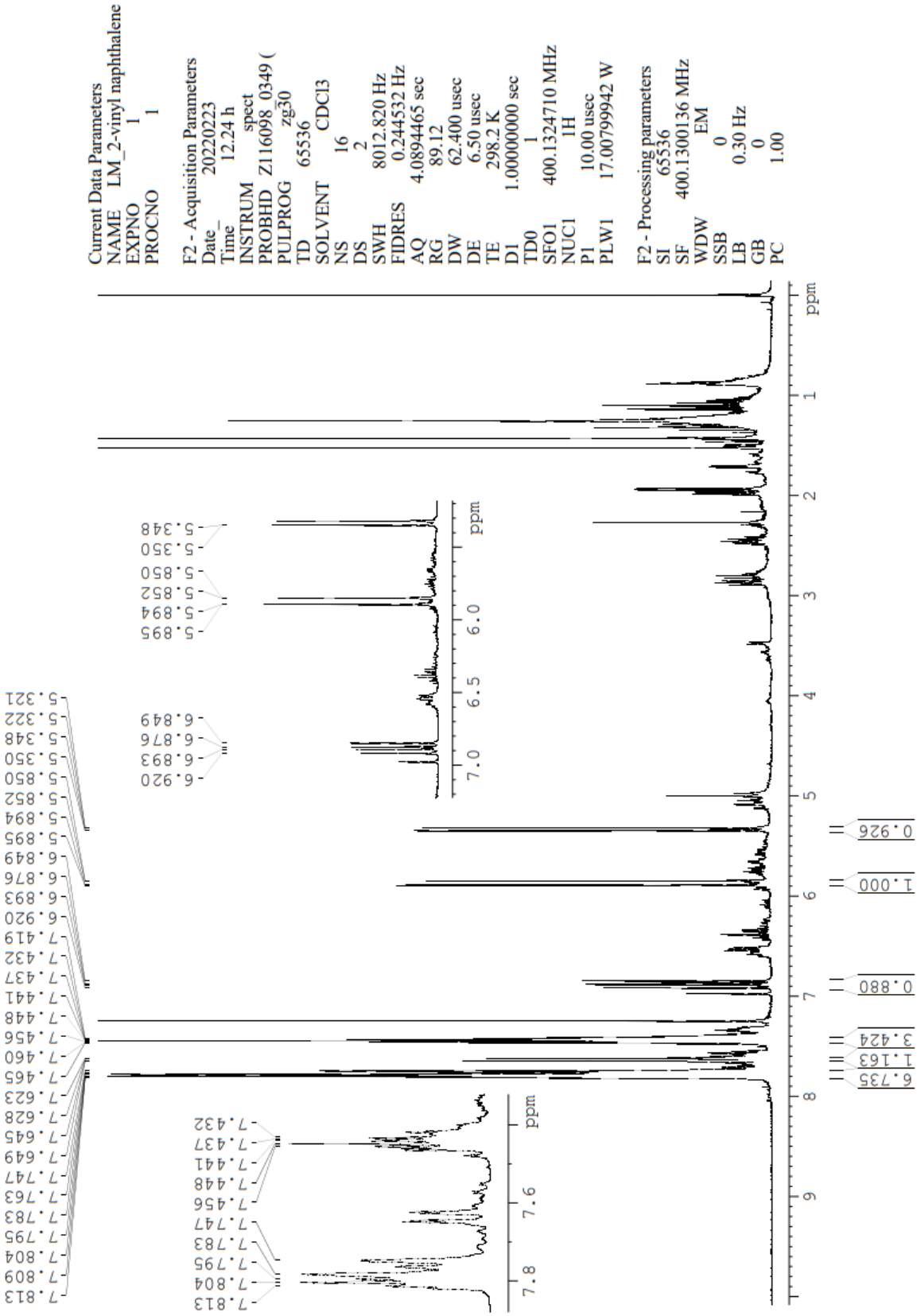


^{13}C-NMR 2-ethylnaphthalene (5c)

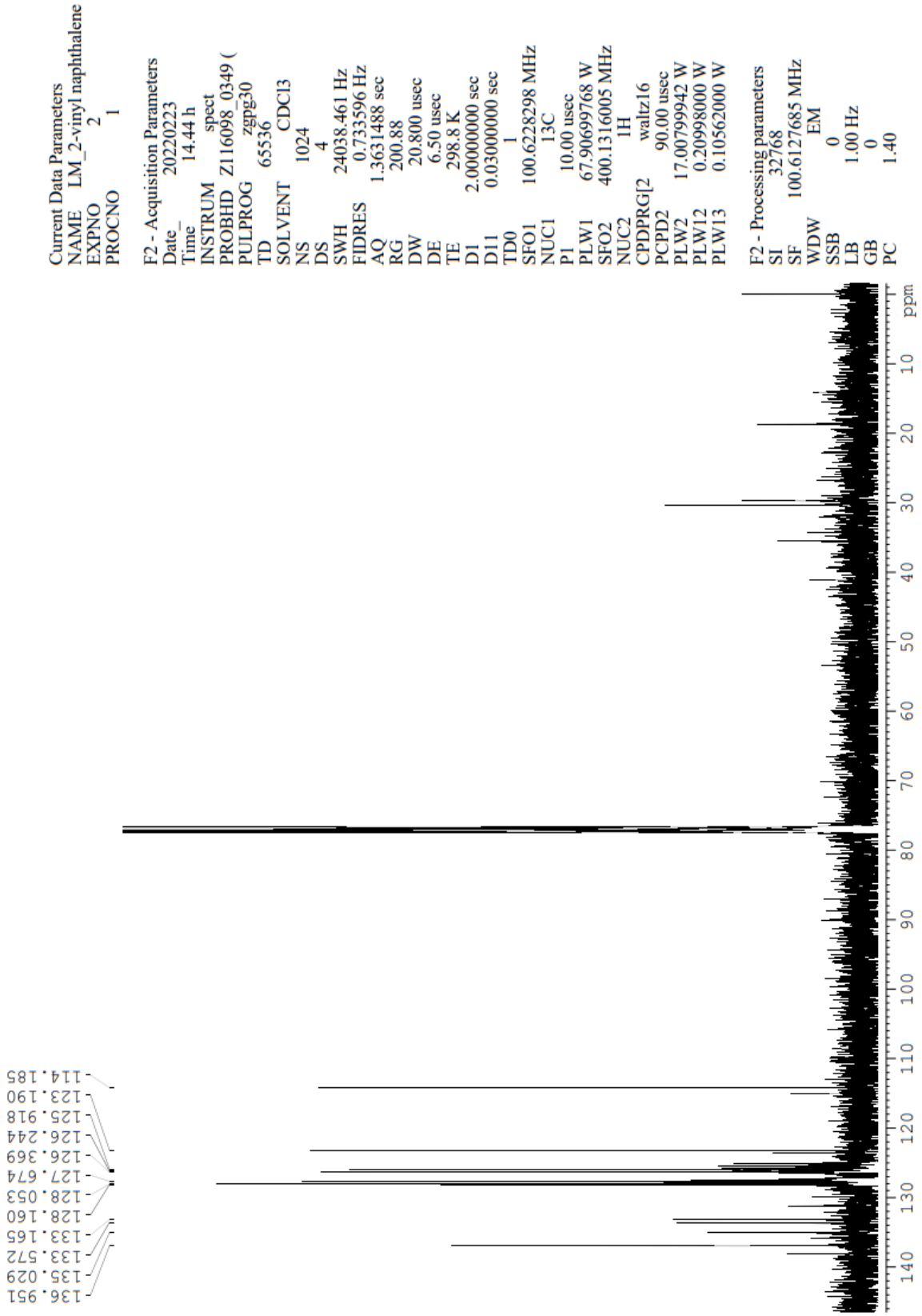


X

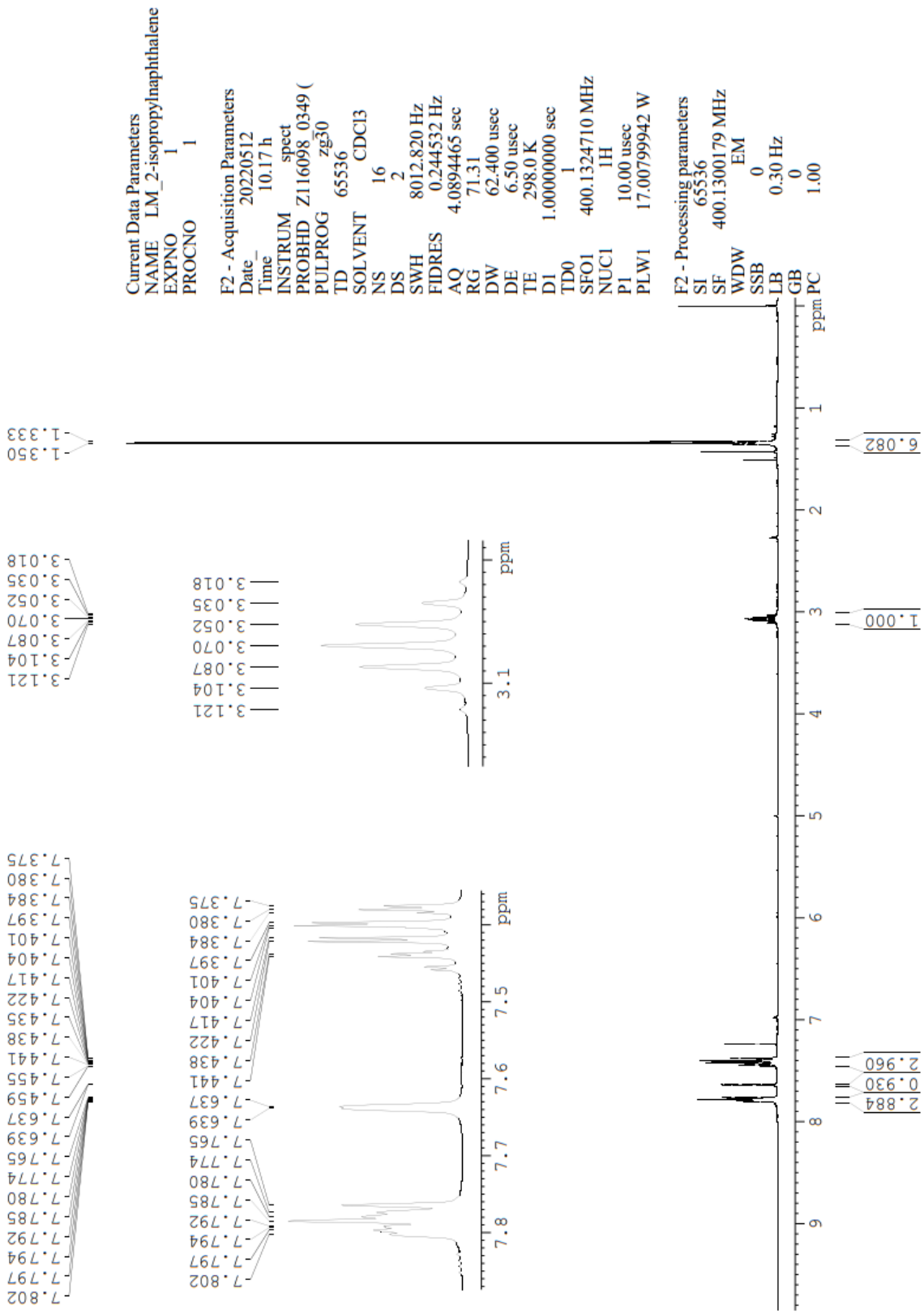
[1]H-NMR 2-vinylnaphthalene (5d)



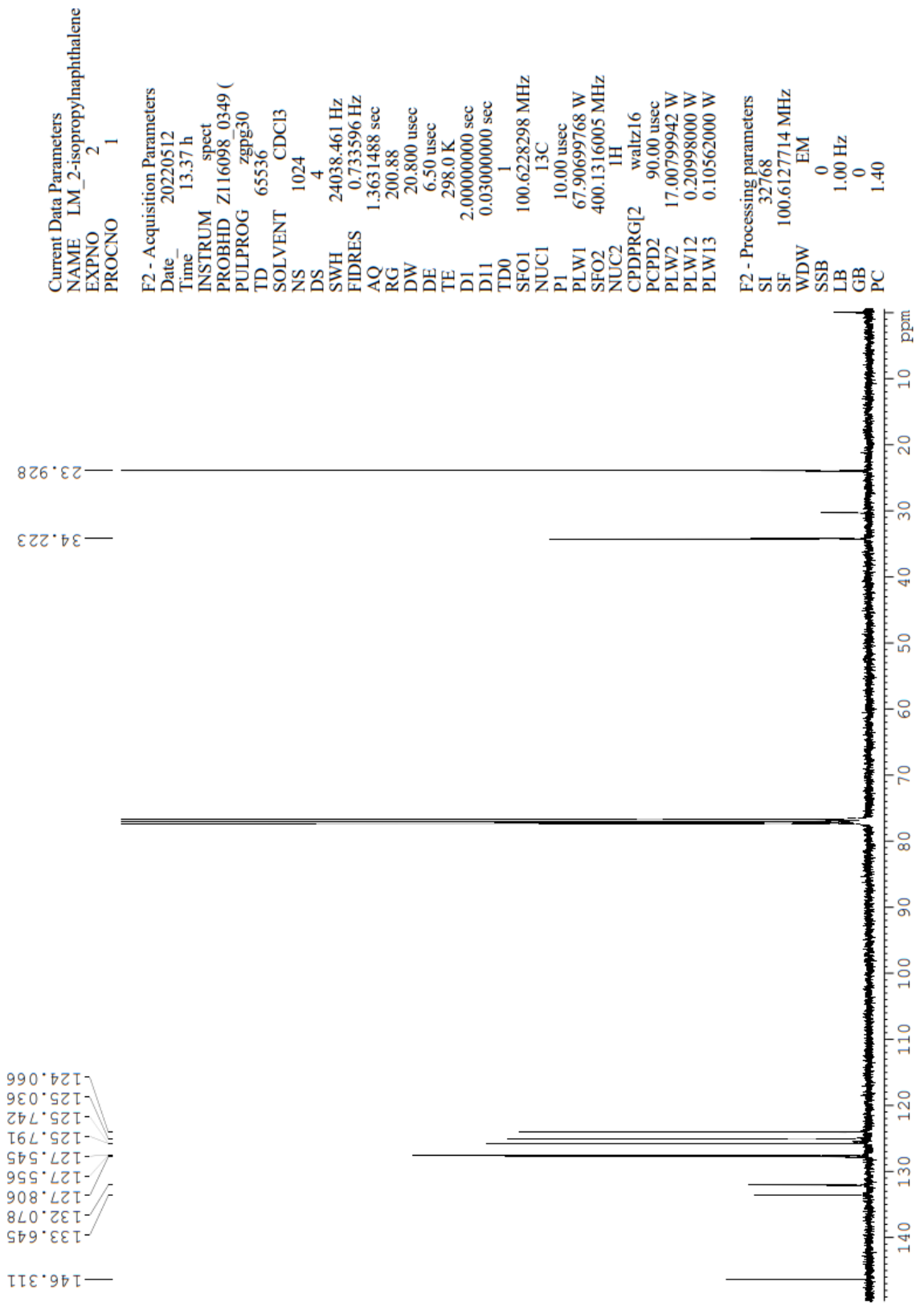
^{13}C-NMR 2-vinylnaphthalene (5d)



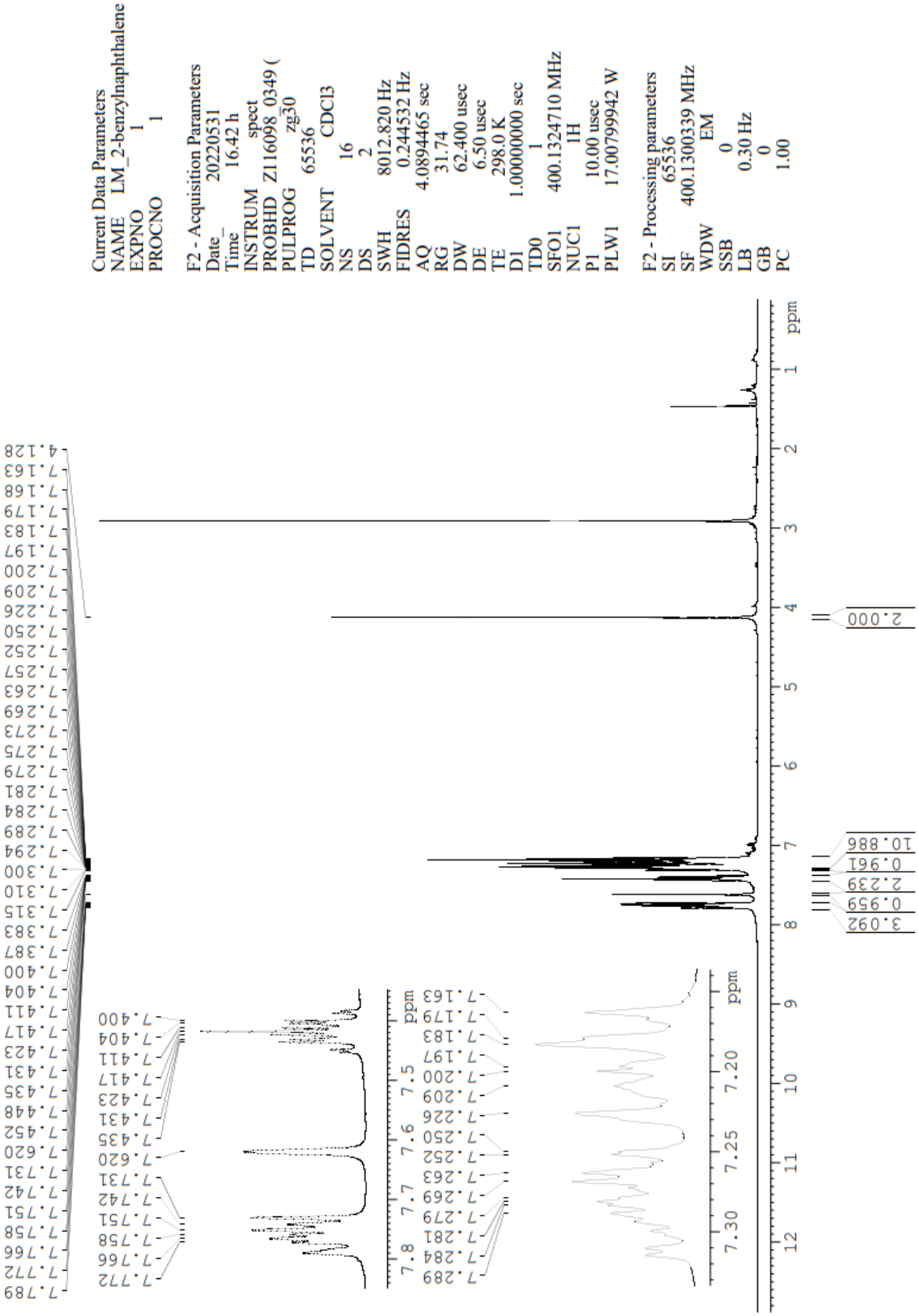
[1]H-NMR 2-isopropylnaphthalene (5e)



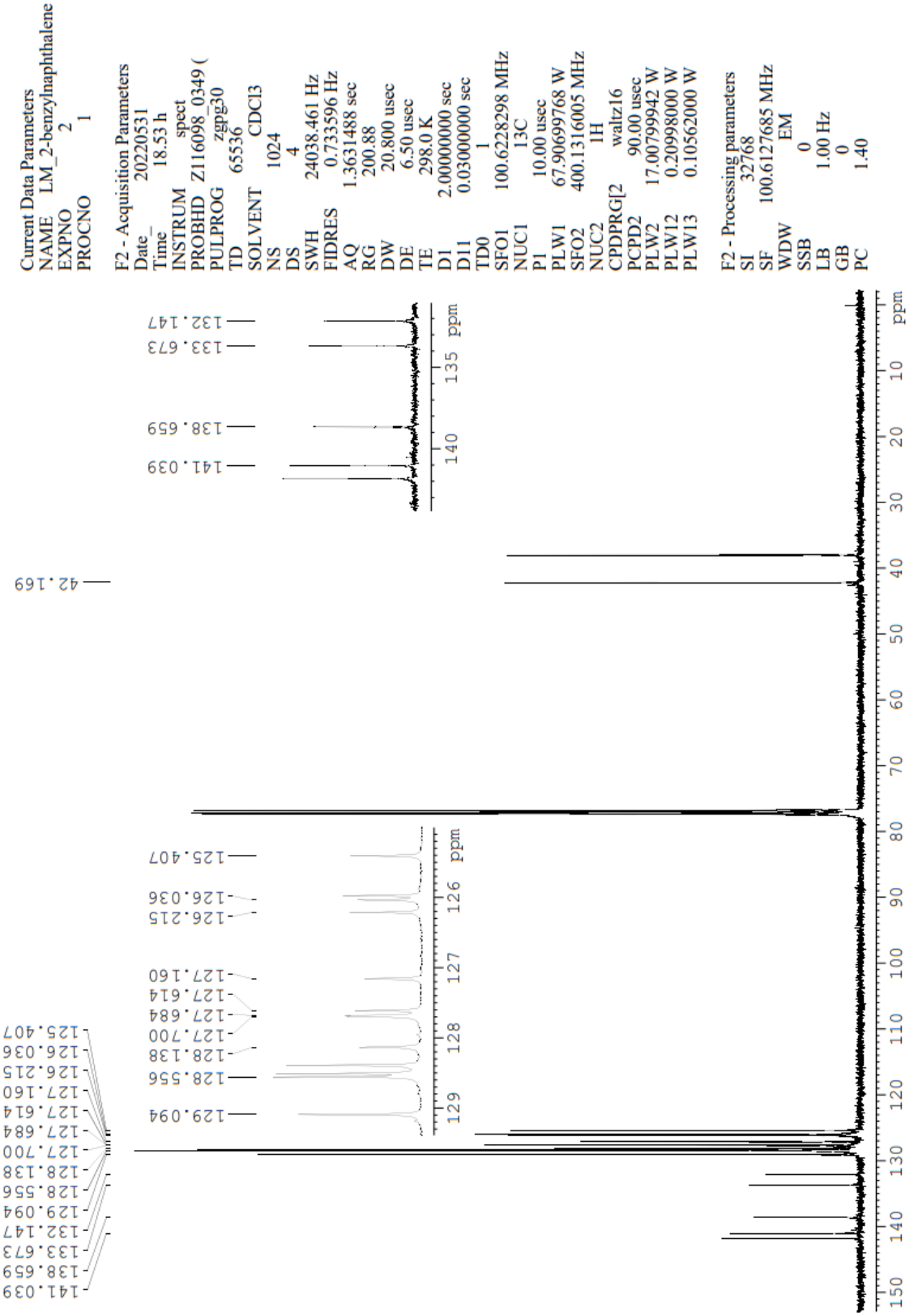
^{13}C-NMR 2-isopropylnaphthalene (5e)



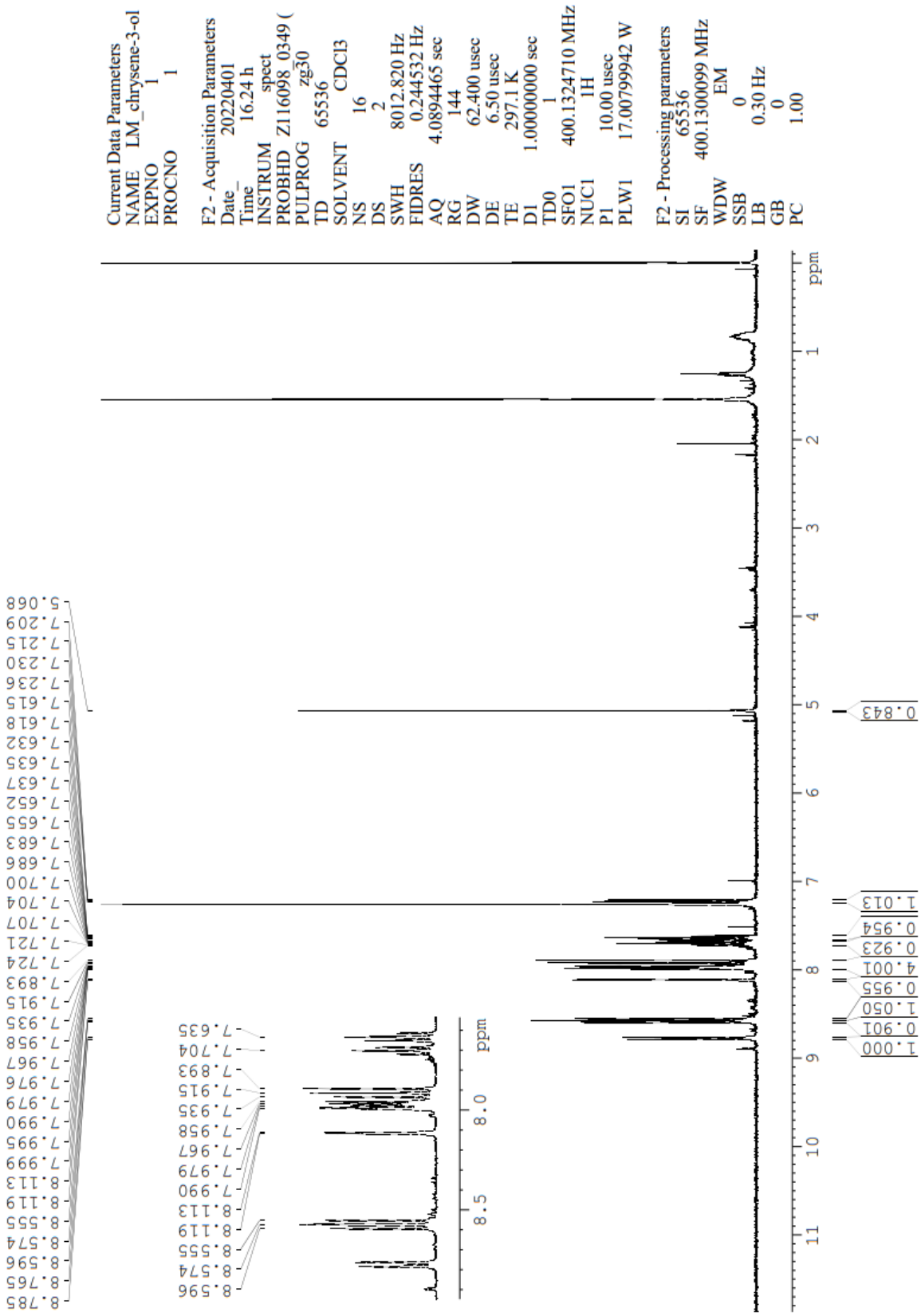
[1]H-NMR 2-benzylnaphthalene (5f)



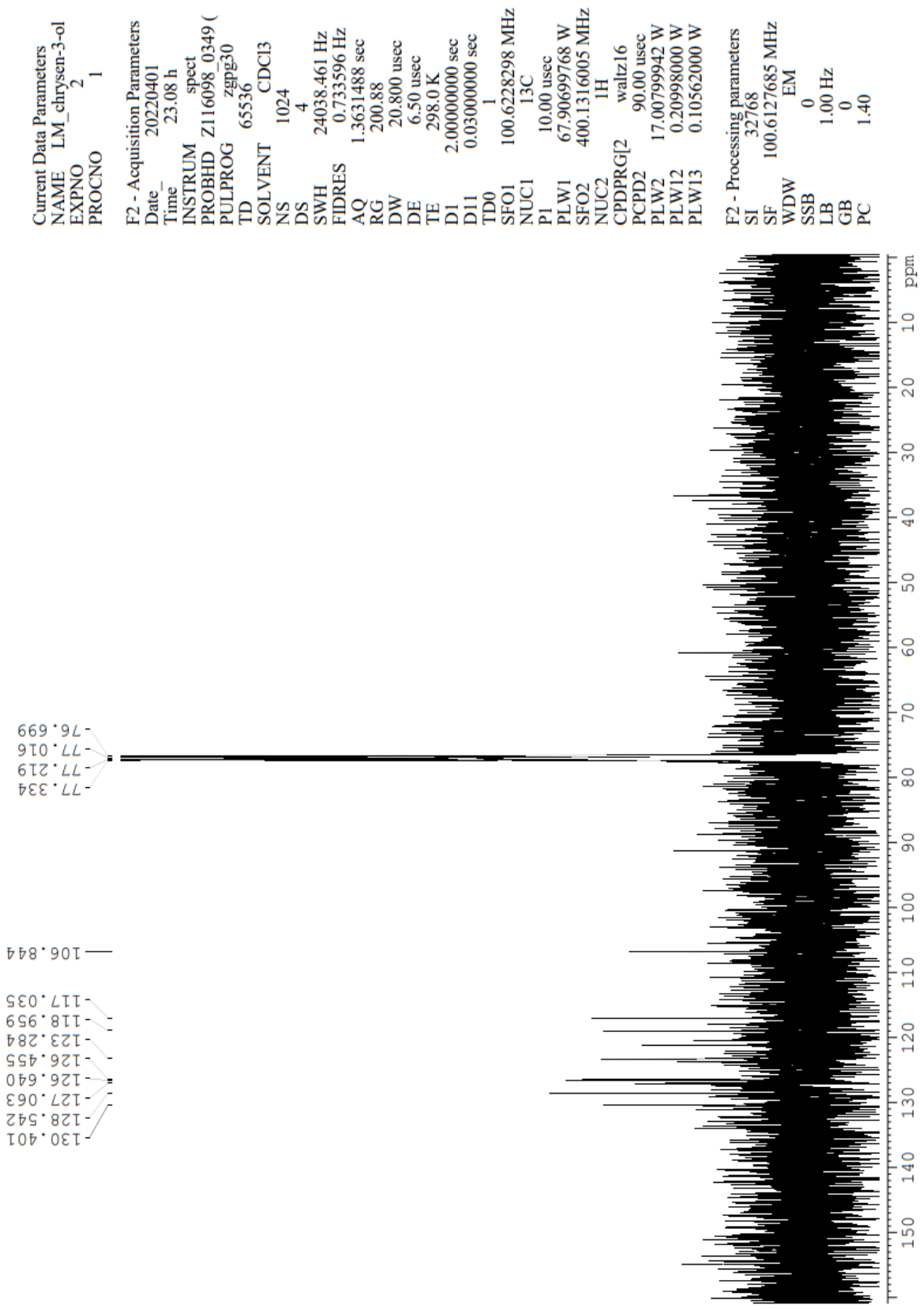
^{13}C-NMR 2-benzylnaphthalene (5f)



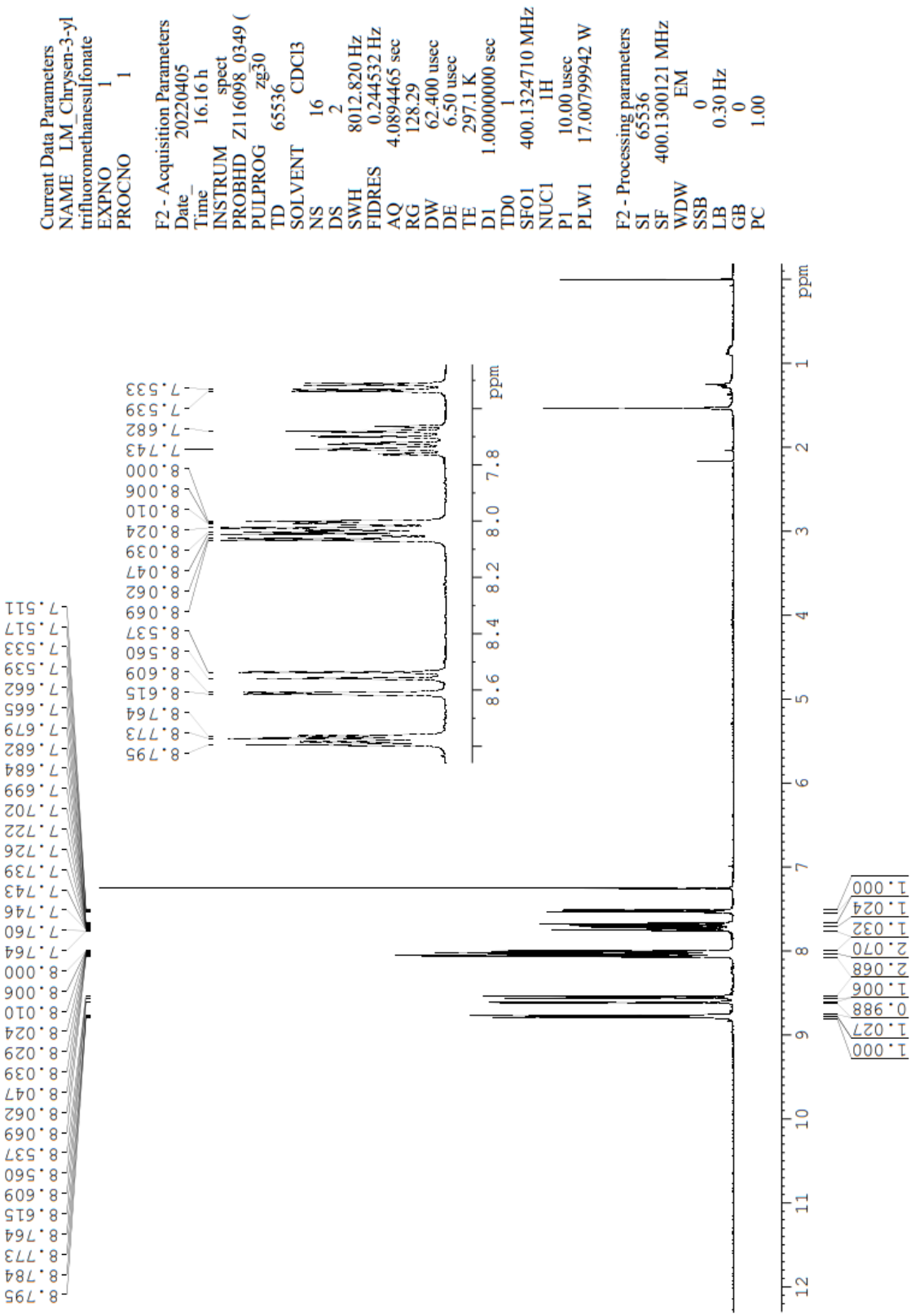
[1]H-NMR Chrysen-3-ol (6b)



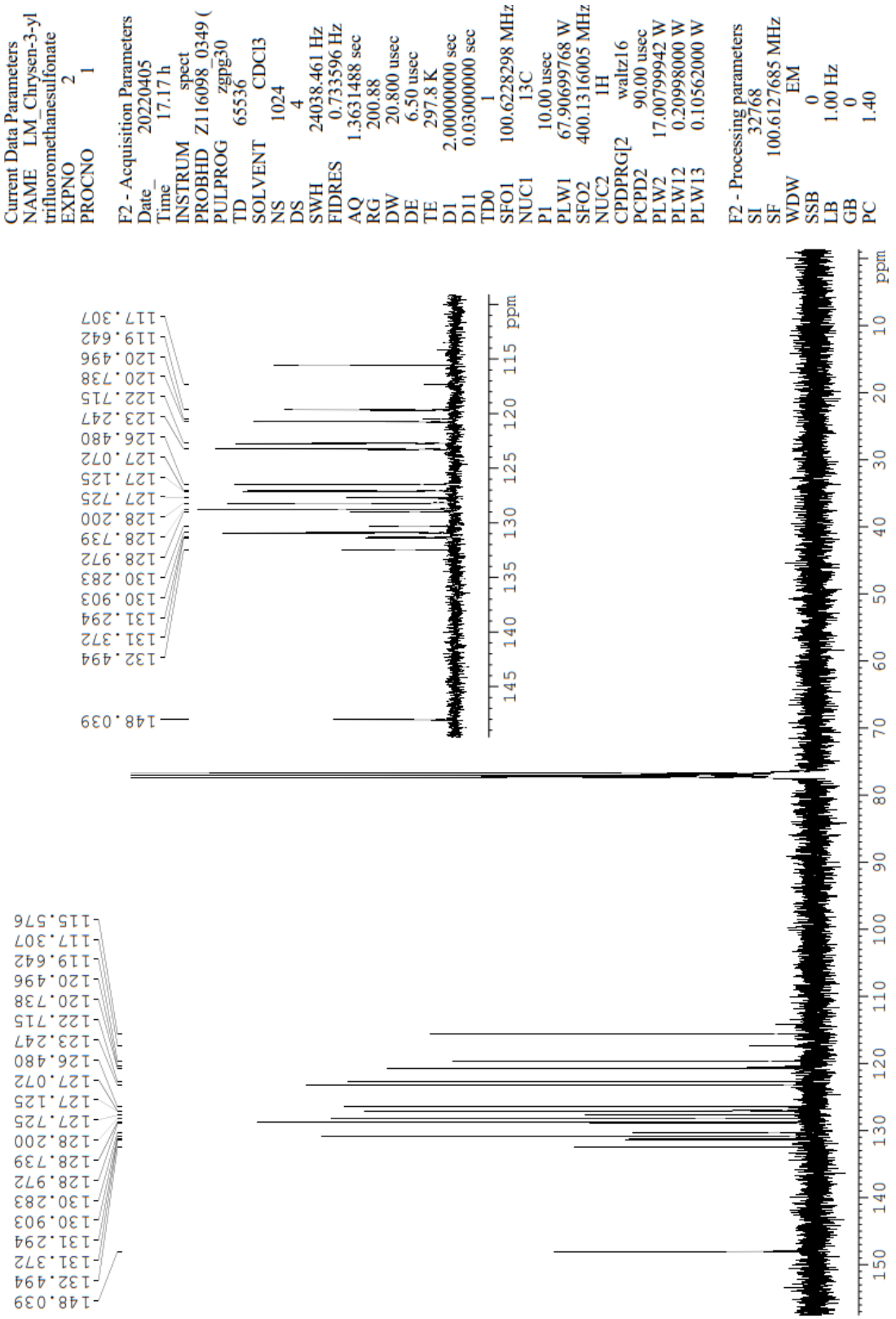
^{13}C-NMR Chrysen-3-ol (6b)



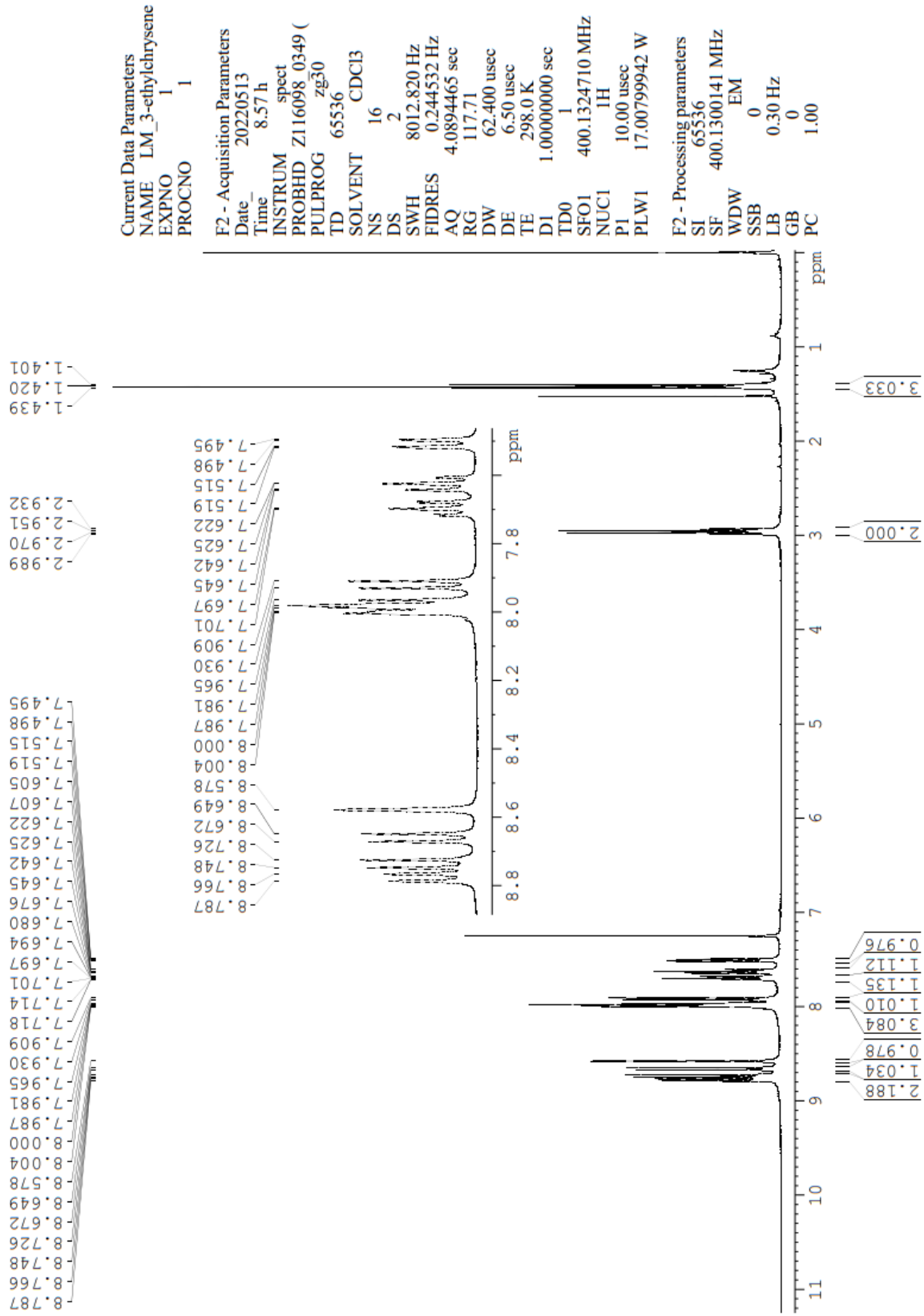
[1]H-NMR Chrysen-3-yl trifluoromethanesulfonate (6c)



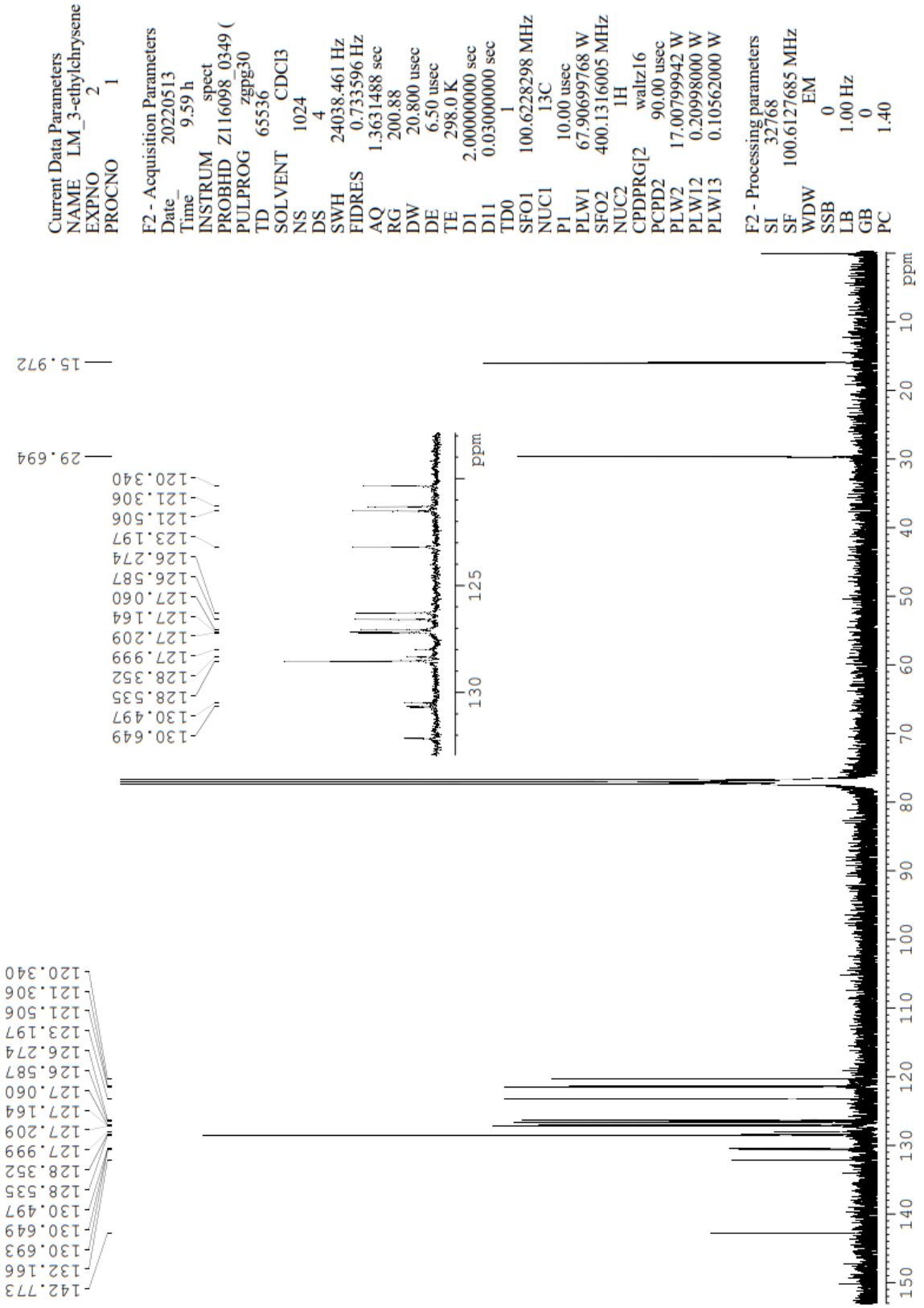
^{13}C-NMR Chrysen-3-yl trifluoromethanesulfonate (6c)



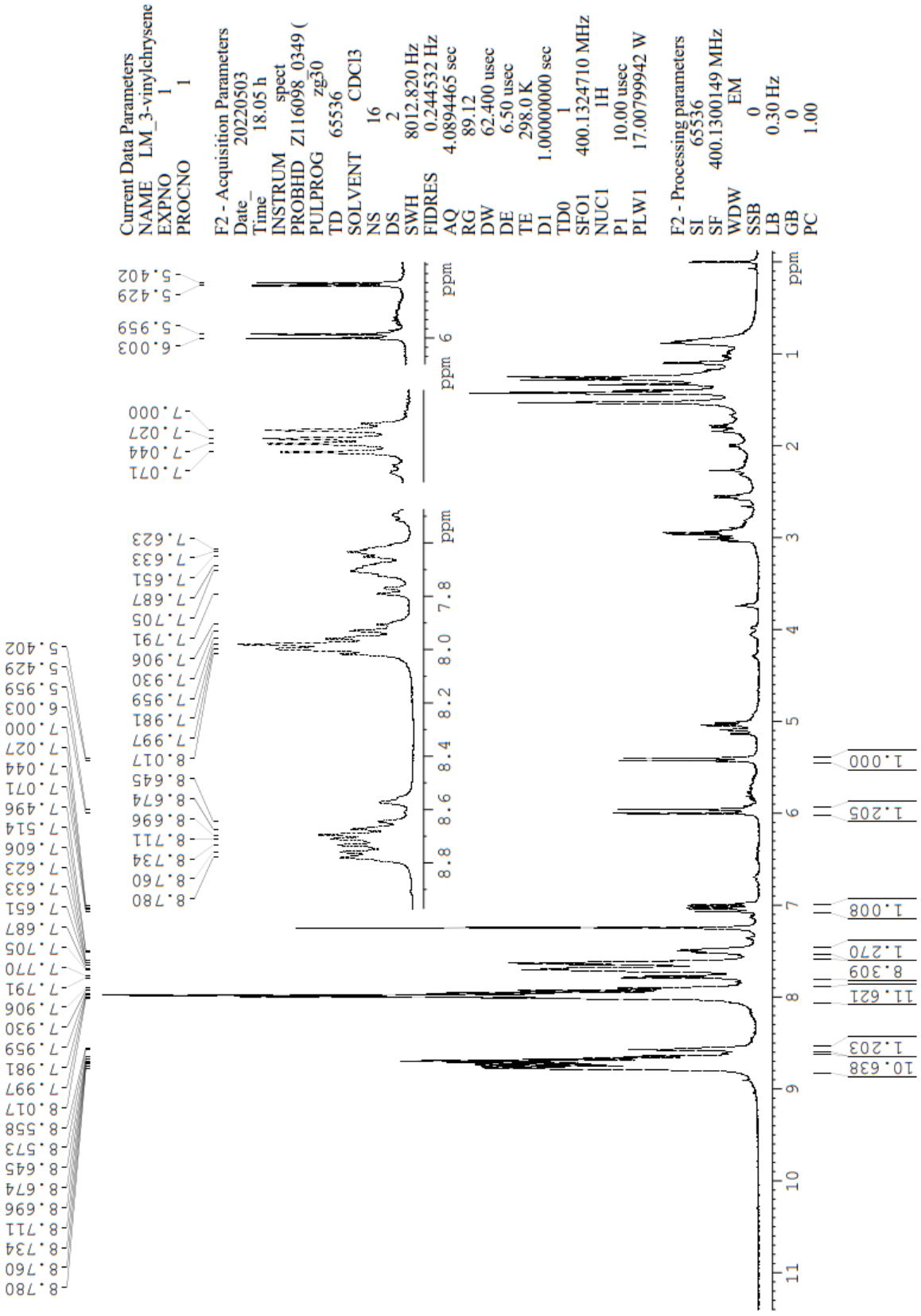
[1]H-NMR 3-ethylchrysene (6d)



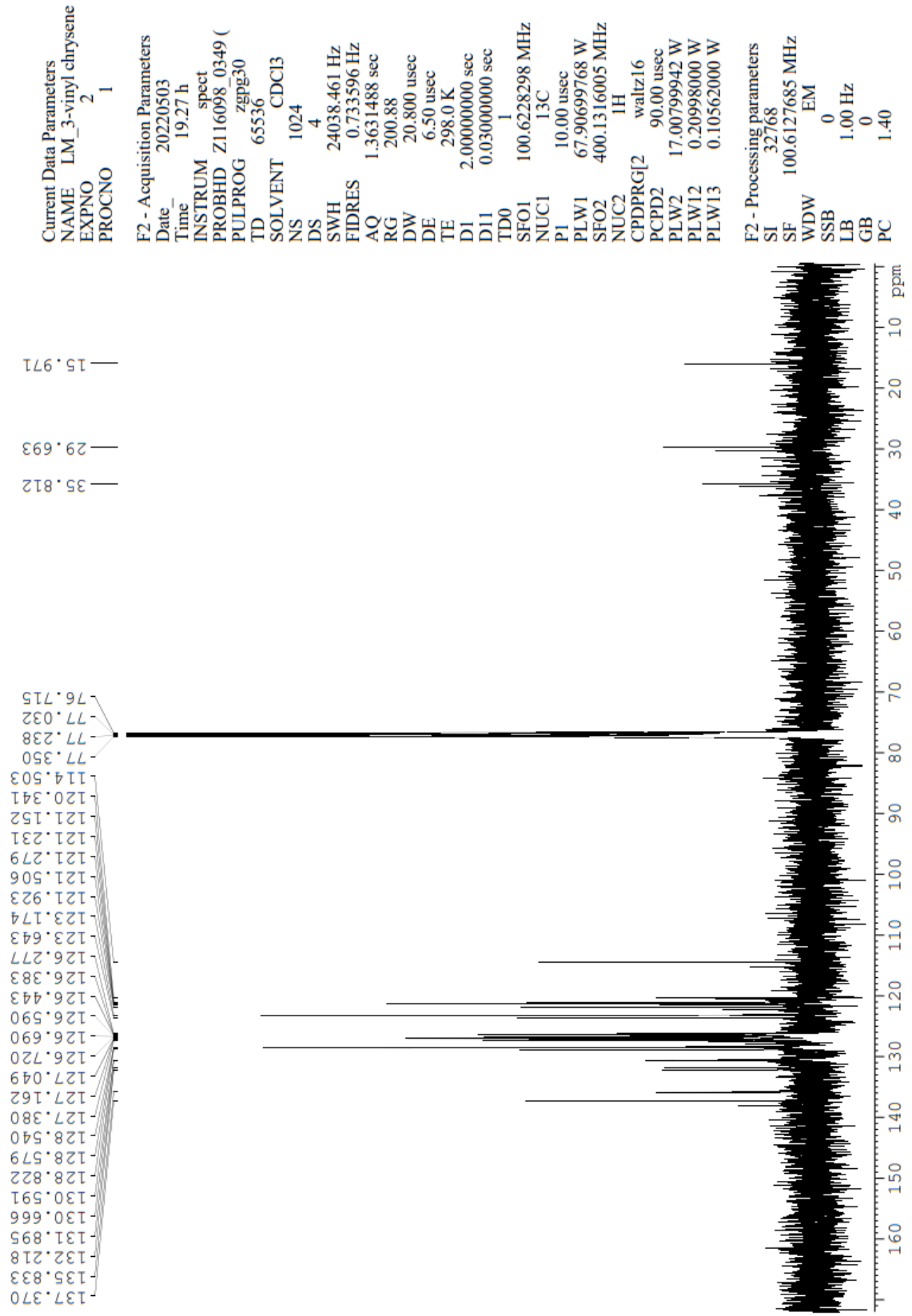
^{13}C-NMR 3-ethylchrysene (6d)



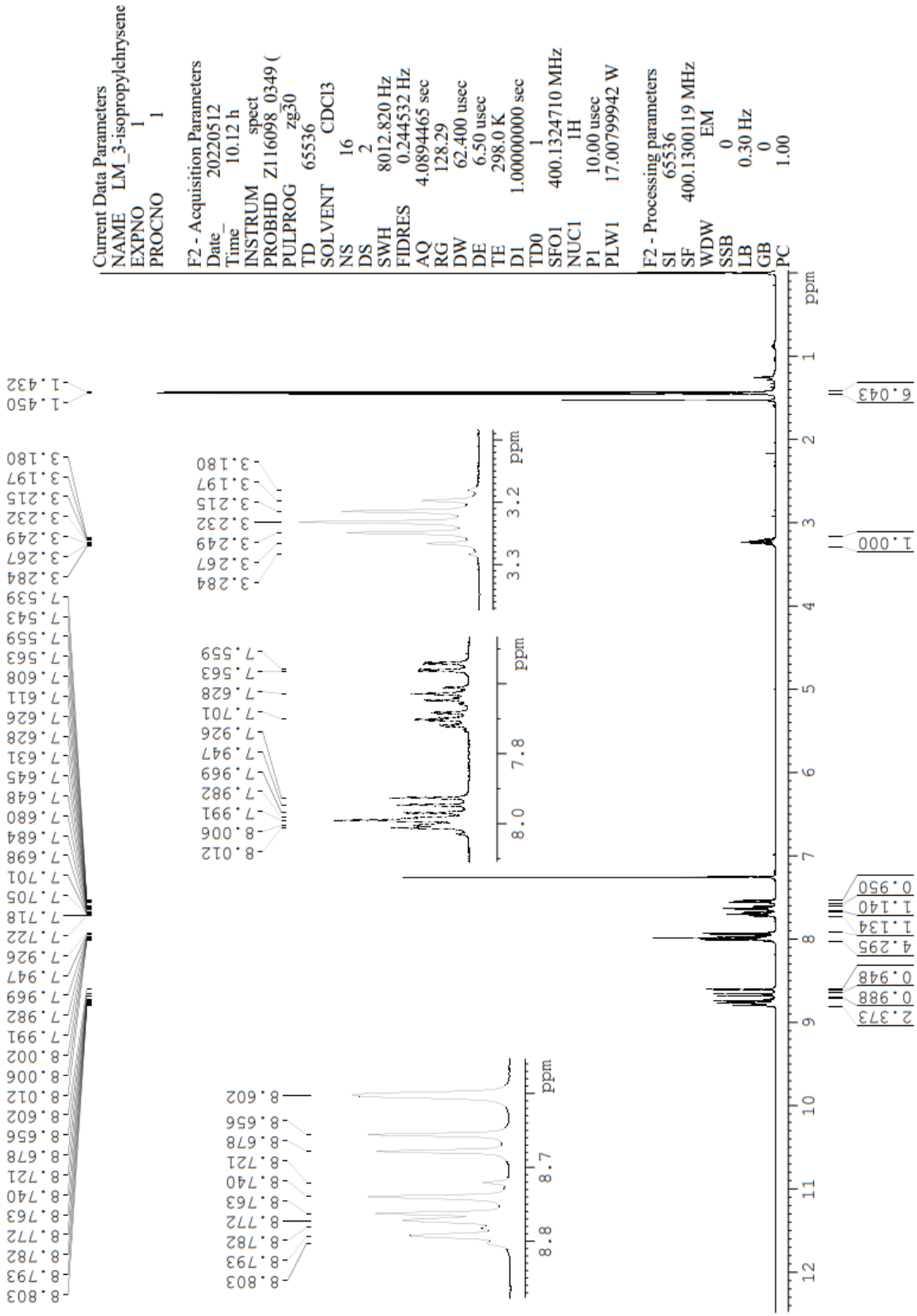
[1]H-NMR 3-vinylchrysene (6e)



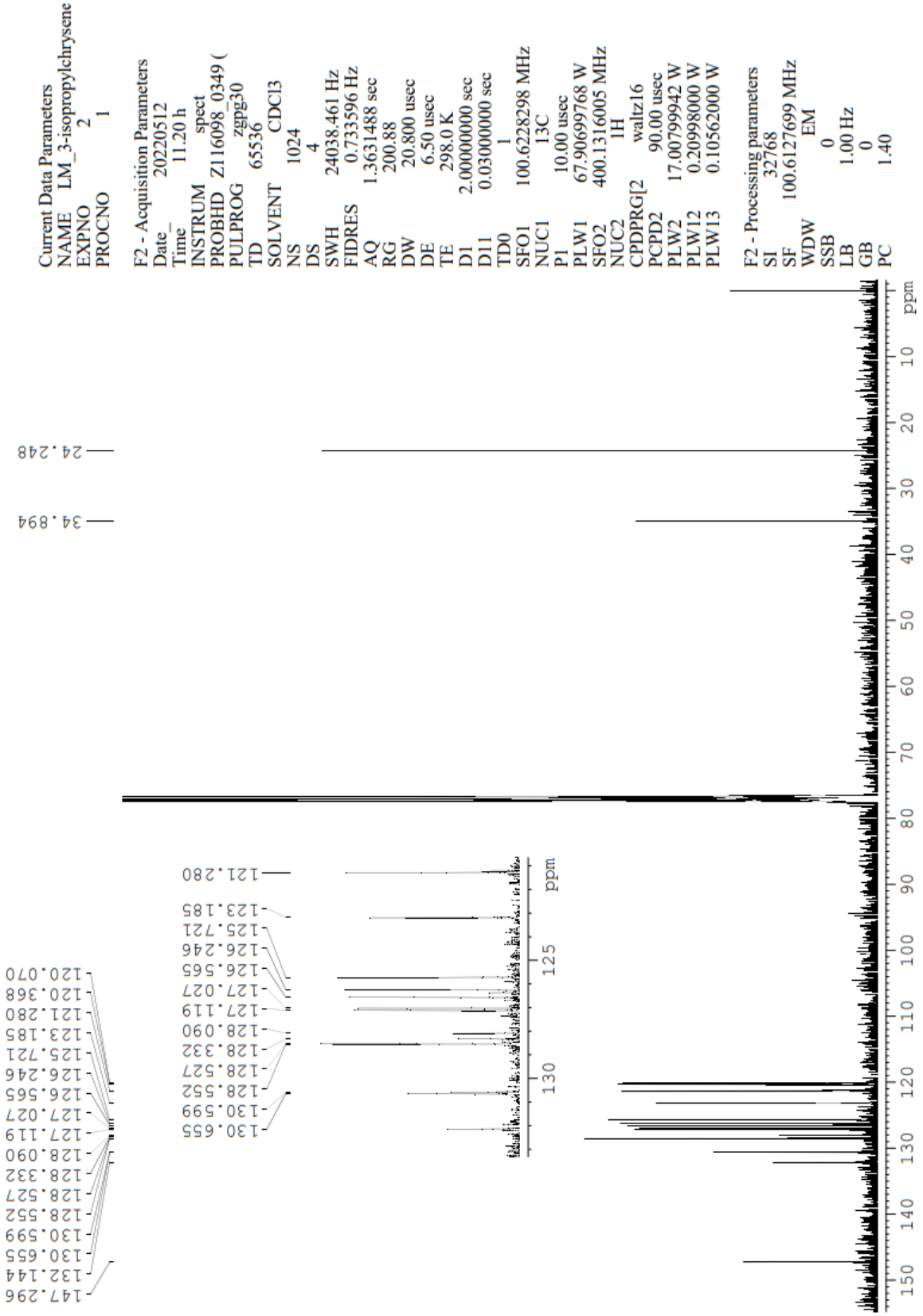
^{13}C-NMR 3-vinylchrysene (6e)



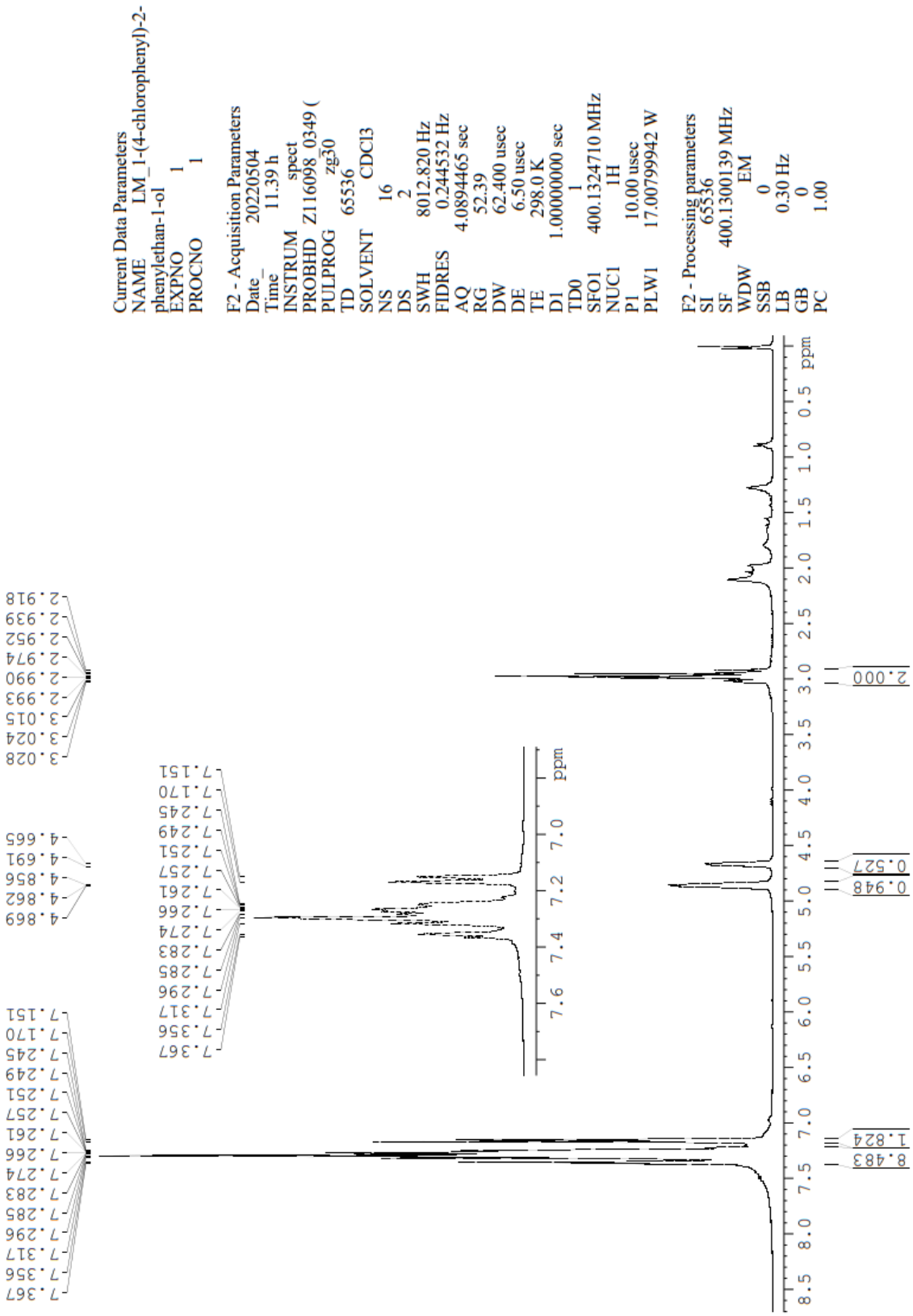
[1]H-NMR 3-isopropylchrysene (6f)



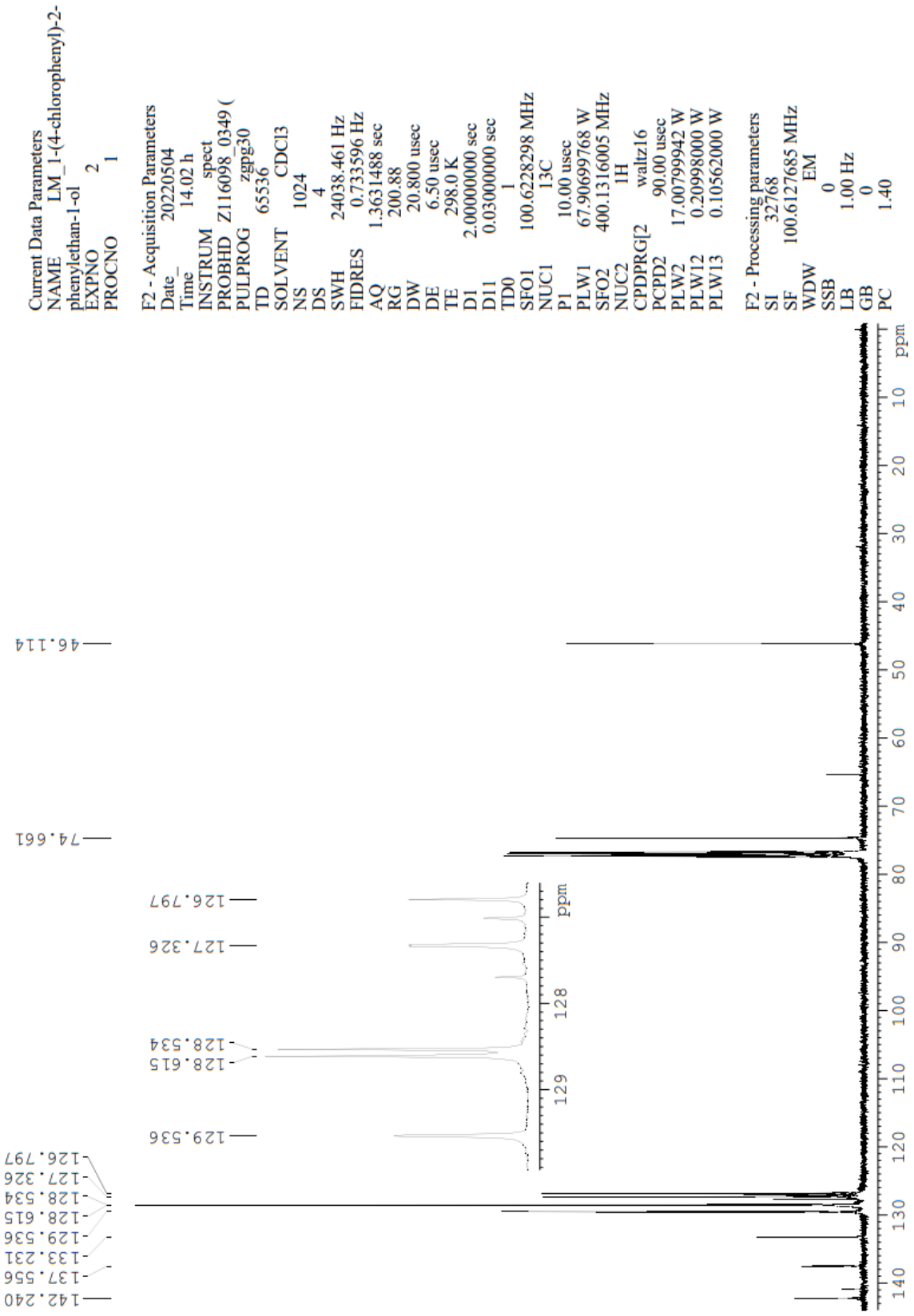
^{13}C-NMR 3-isopropylchrysene (6f)



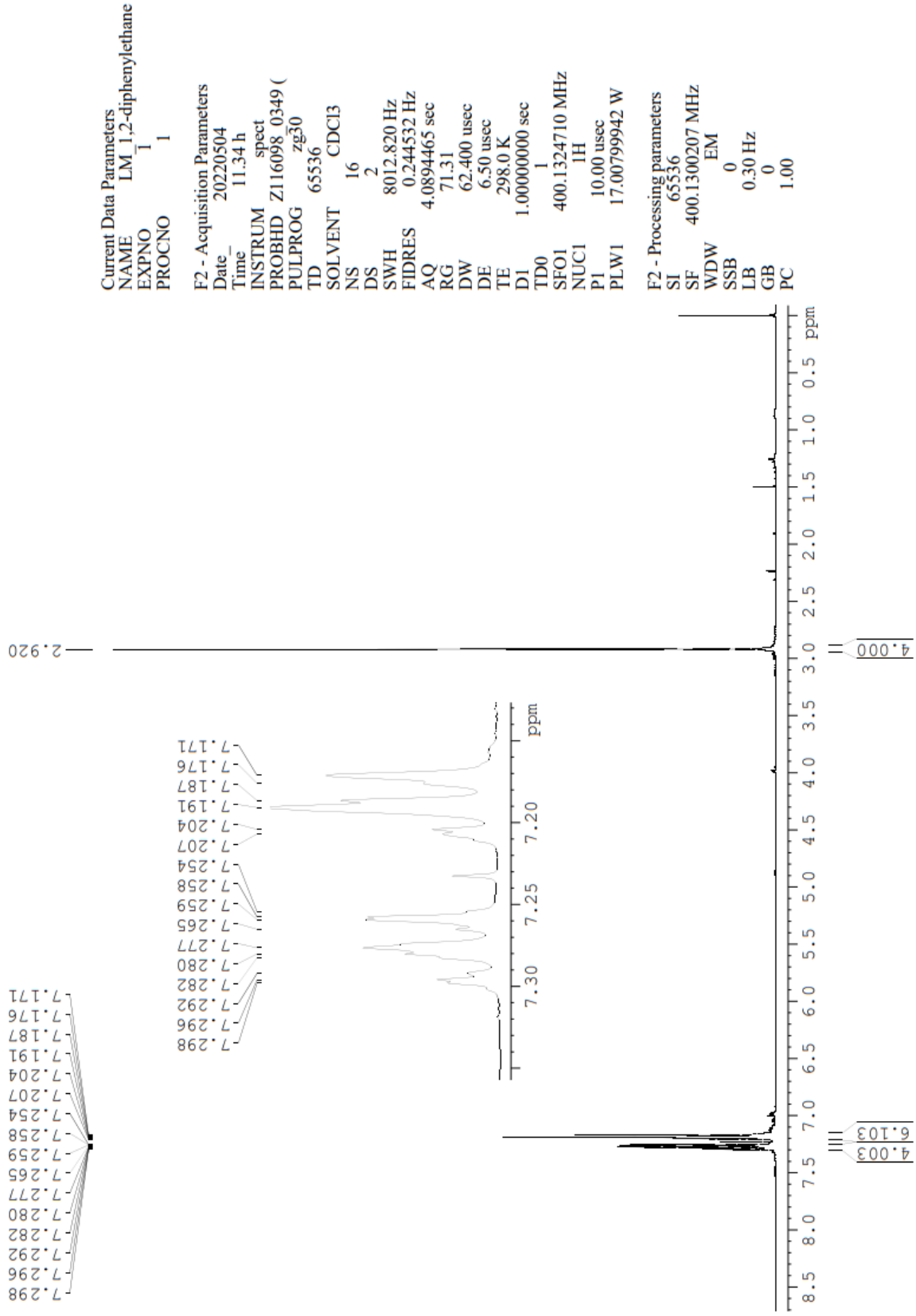
[1]H-NMR 1-(4-chlorophenyl)-2-phenylethan-1-ol (12a)



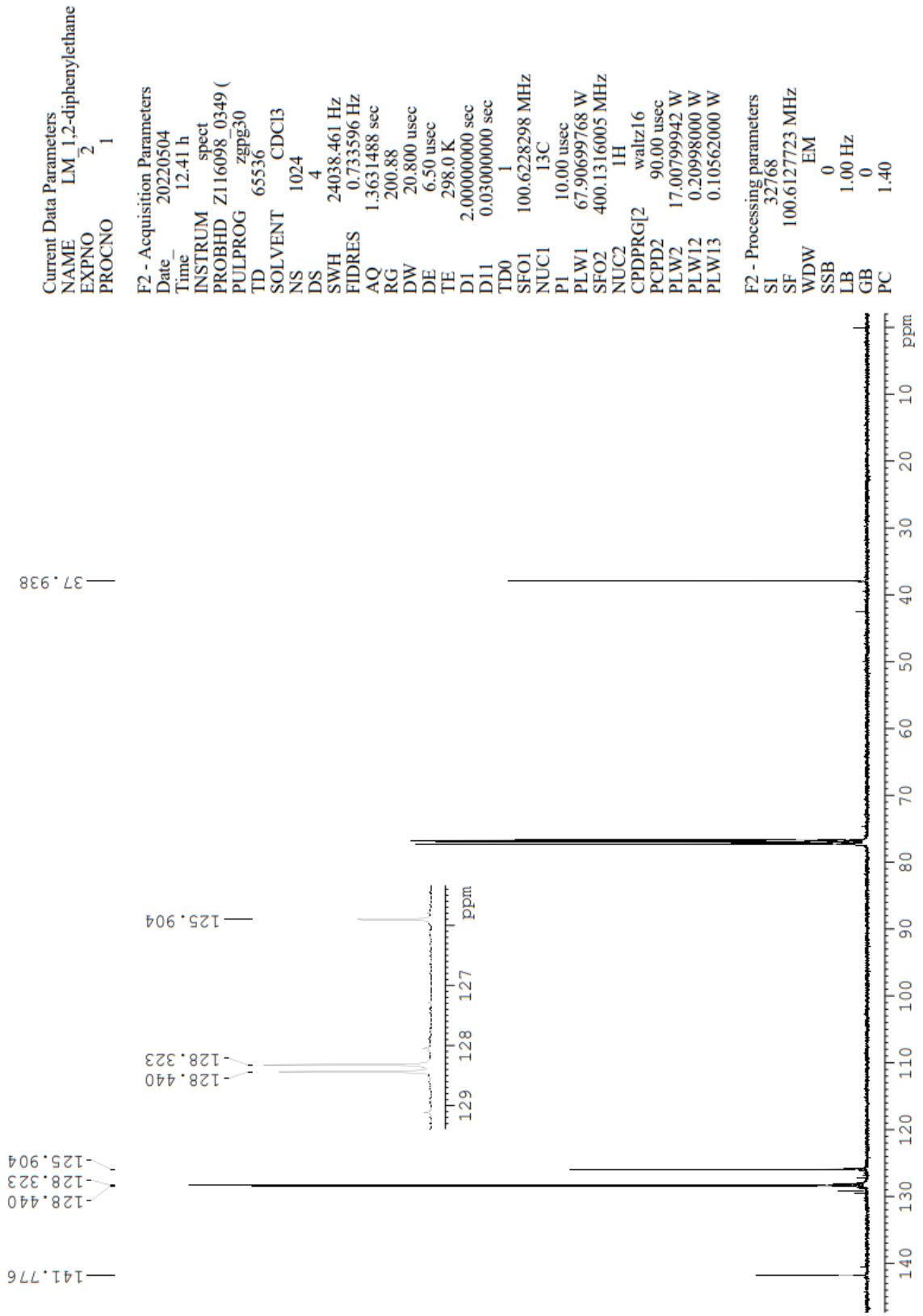
^{13}C-NMR 1-(4-chlorophenyl)-2-phenylethan-1-ol (12a)



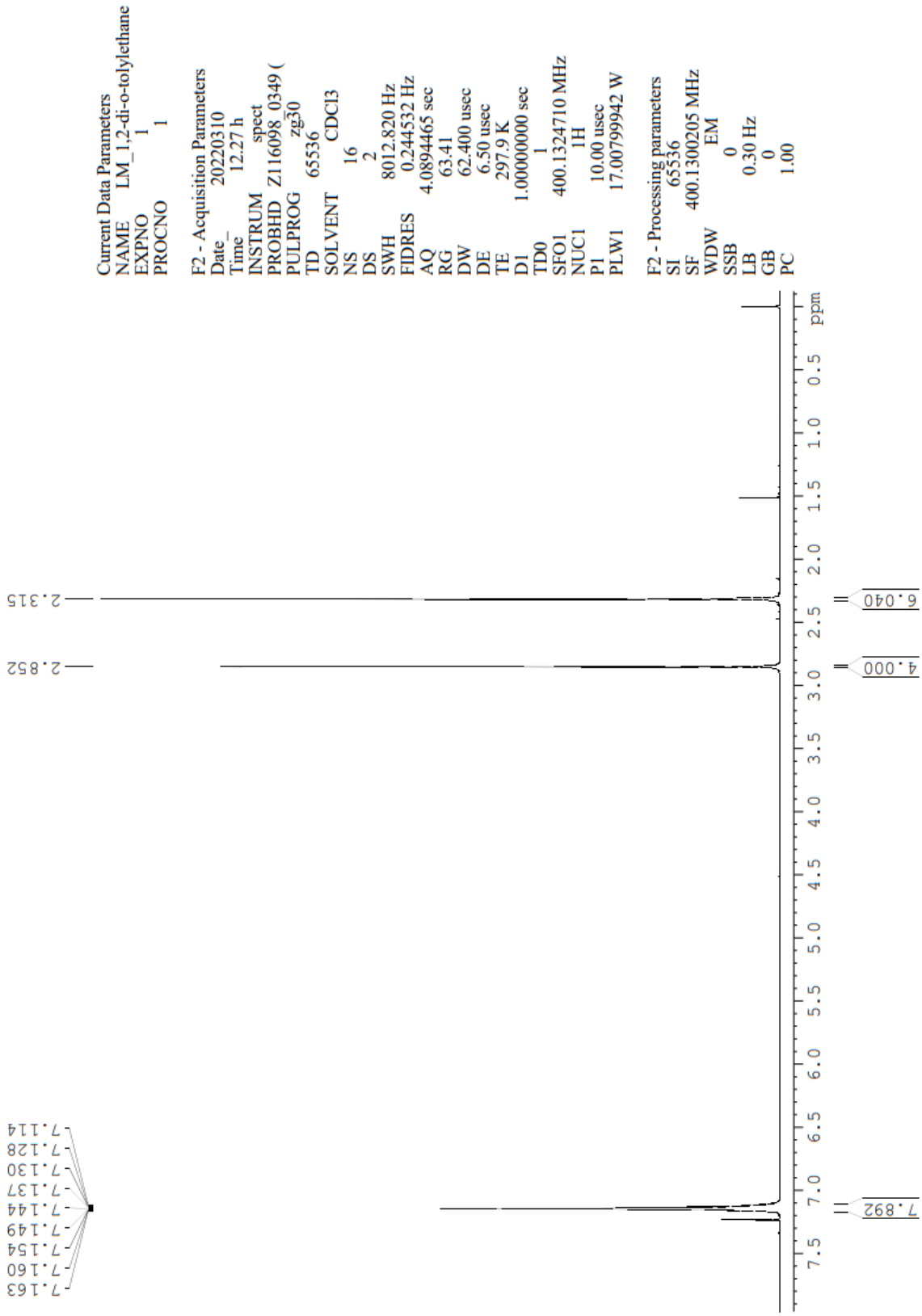
[1]H-NMR 1,2-diphenylethane (13a)



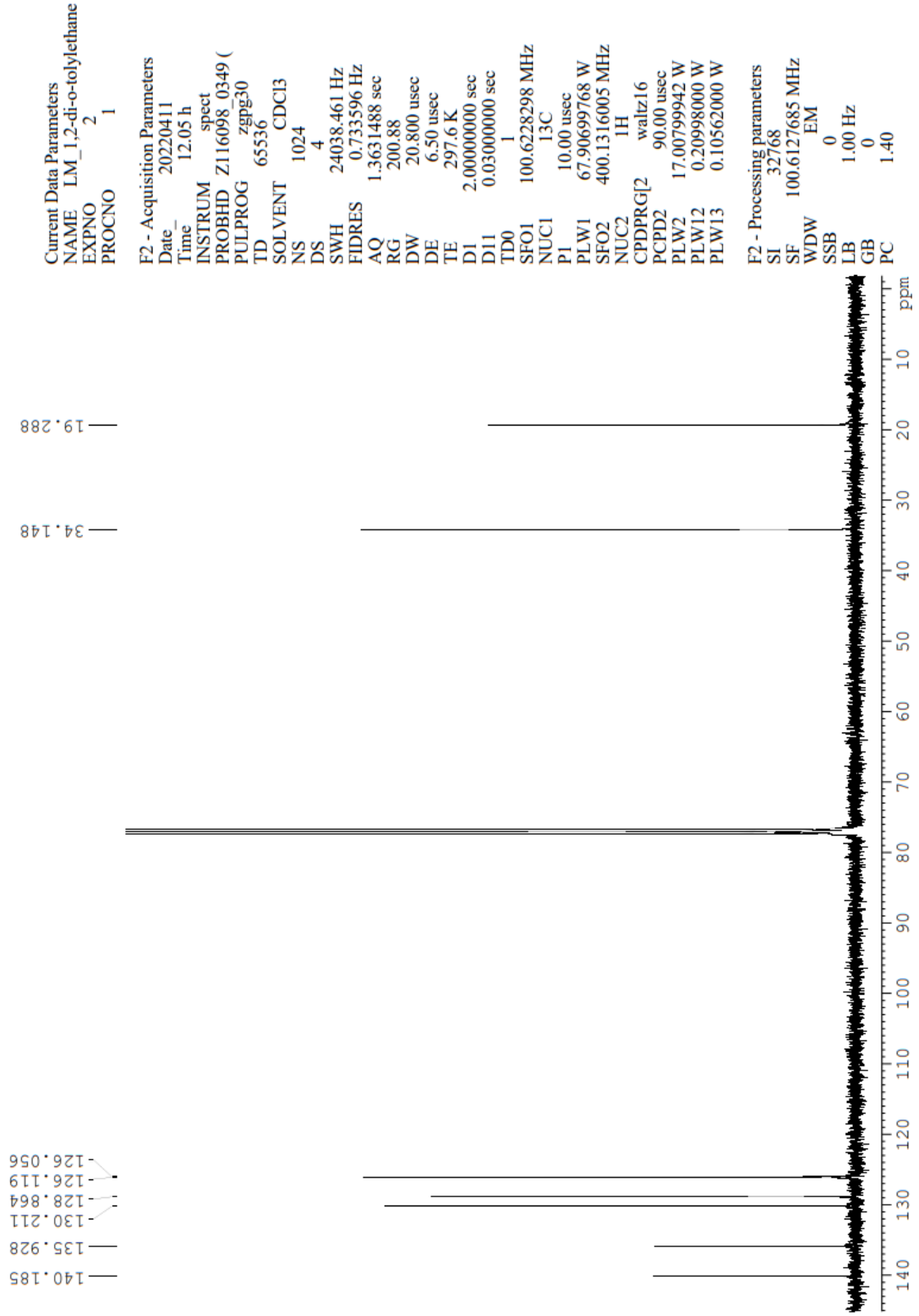
^{13}C-NMR 1,2-diphenylethane (13a)



[1]H-NMR 1,2-di-*o*-tolylethane (13b)



^{13}C-NMR 1,2-di-*o*-tolylethane (13b)



[1]H-NMR 2-bromotoluene