2022

Rhodium-Catalyzed Decarbonylation of Aroyl Chlorides

Wiktoria M. Koza

LOYOLA UNIVERSITY CHICAGO

RHODIUM-CATALYZED DECARBONYLATION OF AROYL CHLORIDES

A DISSERTATION SUBMITTED TO

THE FACULTY OF THE GRADUATE SCHOOL

IN CANDIDACY FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

PROGRAM IN CHEMISTRY

BY

WIKTORIA M. KOZA

CHICAGO, IL

MAY 2023

ACKNOWLEDGMENTS

I would like to thank Dr. Hee Yeon Cho, who inspired me to pursue chemistry research as an undergraduate. Dr. Cho's laboratory provided me with the resources to grow and develop my skills as a researcher. She taught me how to be patient for good data and how to approach science logically, which helped me develop essential critical thinking skills. Her supervision made the work in this dissertation possible. I would also like to thank Dr. James Devery for his help during this journey and with the writing process. I am also grateful to Dr. Devery for providing me with the opportunity to explore my interests as an educator and trusted me to assist in teaching his undergraduate classes.

I would also like to thank my dissertation committee members. Dr. Linda Brazdil, for her endless support throughout my PhD and for introducing me to the field of chemistry education. As well as Dr. Jacob Ciszek and Dr. Miguel Ballicora for their time, feedback, and support throughout this process.

I would like to thank Loyola University Chicago for their support. Additionally, I would like to thank the National Institute of Health, who provided the financial support for this research.

I would like to thank my lab mates, Dr. Ajit Kale, who taught me all the proper lab techniques and Priya Dhindsa, who was a wonderful undergraduate assistant. I would also like to thank Jordan Delev for his unconditional friendship and his endless words of encouragement. He gave me the push I needed when I struggled to push myself. He recognized qualities in me I

failed to see and challenged me to help me gain the confidence I needed to overcome my fears. His remarkable resilience and strength never ceases to amaze me and continues to inspire me to be a stronger and better person.

I would also like to thank my family. I would like to thank my siblings for their love, patience, and support. Finally, no words will ever be able to express the level of gratitude I have for my parents in their infinite support for my siblings and me. Their courage, dedication, and sacrifices provided us with the opportunities we needed to become successful in life and pursue our dreams. My life today would have not been possible without them.

Though unable to serve on the committee, I would like to add one final acknowledgement for Dr. Hee Yeon Cho. This research originated in her lab under her direction. It was funded, in part, via a grant to the lab, NIH GM122034 and her startup funding. For the first three years of this project, she provided guidance and advice.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

BHC	Benzene hexachloride
Br	Bromine
BINAP	2,2′-Bis(diphenylphosphino)-1,1′-binaphthalene
BrettPhos	2-(Dicyclohexylphosphino)3,6-dimethoxy-2′,4′,6′-triisopropyl-1,1′-biphenyl
Bnep–Bnep	Bis(neopentylglycolato)diboron
$[(CH_3)_2As]_2O$	Cacodyl oxide
Cp*	1,2,3,4,5-pentamethylcyclopentadienyl
C	Carbon
CO	Carbon monoxide
C_{CO}	Carbon of carbonyl
Cl	Chlorine
CN	Cyano
$CuCF_3$	Trifluoromethyl copper
Cy	Cyclohexyl
DG	Directing group
DDT	Dichlorodiphenyltrichloroethane
DPPE	1,2-Bis(diphenylphosphino)ethane
DPPP	1,3-Bis(diphenylphosphino)propane
DIPAMP	1,2-Bis[(2-methoxyphenyl)(phenylphosphino)]ethane
H	Hydrogen
HCl	Hydrochloric acid
I	Iodine

i-Pr	Isopropyl
Me	Methyl
MRSA	Methicillin-resistant *S. aureus*
$Ni(CO)_4$	Nickel tetracarbonyl
N	Nitrogen
P(*i*-Pr)$_{2,}$	Di-isopropyl-phosphine
P(*t*-Bu)$_2$	Di-*tert*-butylphosphine
Pd	Palladium
Pd/C	Palladium on carbon
P	Phosphorous
R	Alkyl group, aryl group, vinyl group
Rt	Room temperature
Rh	Rhodium
$RhCl(PPh_3)_3$	Wilkinson's catalyst
Si	Silicon
S	Sulfur
TPPO	Triphenylphosphine oxide
TBP	*tert*-butyl peroxide
THF	Tetrahydrofuran
TES	Triethylsilyl
O-tol	*ortho*-tolyl
OTf	triflate

t-bu	*tert*-butyl
Xyl	Xylyl
Y	Heteratom
X	Halogen
XantPhos	4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene

CHAPTER 1

INTRODUCTION

In 1760, Louis Claude Cadet prepared what is considered the first organometallic compound synthesized. A reaction with potassium acetate and arsenic trioxide forms an oily liquid, $[(CH_3)_2As]_2O$, also known as cacodyl oxide (Figure 1A). Cacodyl oxide was later isolated in 1837 by Robert Bunsen. [1] Significant organometallic advancements include William Christopher Zeise's preparation of a potassium platinum salt in 1831 with the structure confirmed in the 1950s (Figure 1B) [2, 3, 4] and Edward Frankland's synthesis of an organozinc compound in 1847. [4, 5] Frankland attempted to create an ethyl radical through a reaction with zinc metal and ethyl iodide, but instead made diethylzinc (Figure 1C).

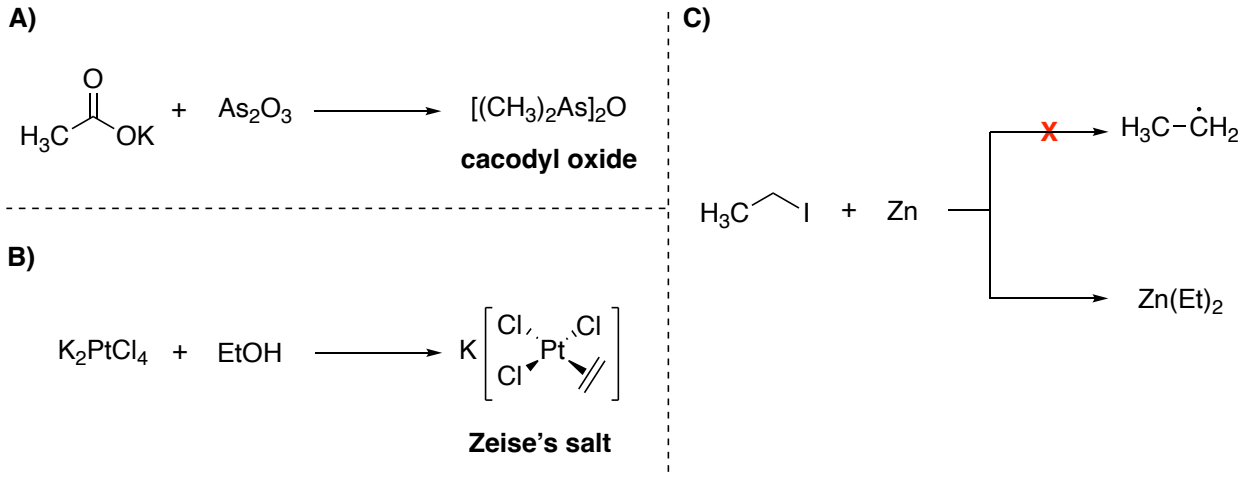


Figure 1. Syntheses of cacodyl oxide (A), Zeise's salt (B) and diethylzinc (C).

The applicability of organometallic reagents was explored in the 1800s. Ludwig Mond synthesized and isolated the first metal–carbonyl complex $Ni(CO)_4$ (Figure 2A).[6] This discovery led to the development of the Mond Process which converts naturally abundant nickel oxides into pure nickel (Figure 2B).[7]

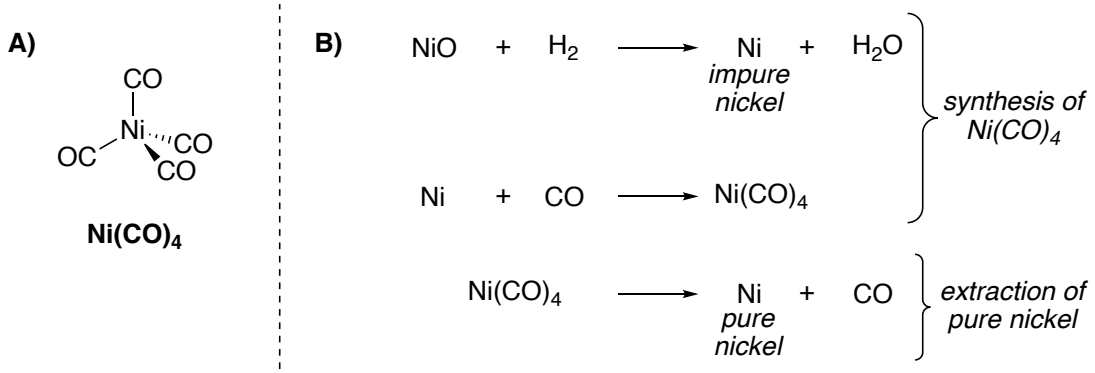


Figure 2. Structure of $Ni(CO)_4$ (A) and the Mond Process (B).

One of the most popular and useful organometallic reagents are Grignard reagents (Figure 3A). These organomagnesium compounds were discovered in the late 1800s and Victor Grignard was awarded the Nobel Prize in Chemistry for this discovery in 1912.[8] The Grignard reaction, discovered in 1900, utilizes Grignard reagents to create new carbon–carbon (C–C) bonds through a nucleophilic reaction with an aldehyde or ketone.[9] Since then, Grignard reagents have been incredibly useful synthetic tools for the creation of new C–C bonds in organic synthesis (Figure 3B).[10]

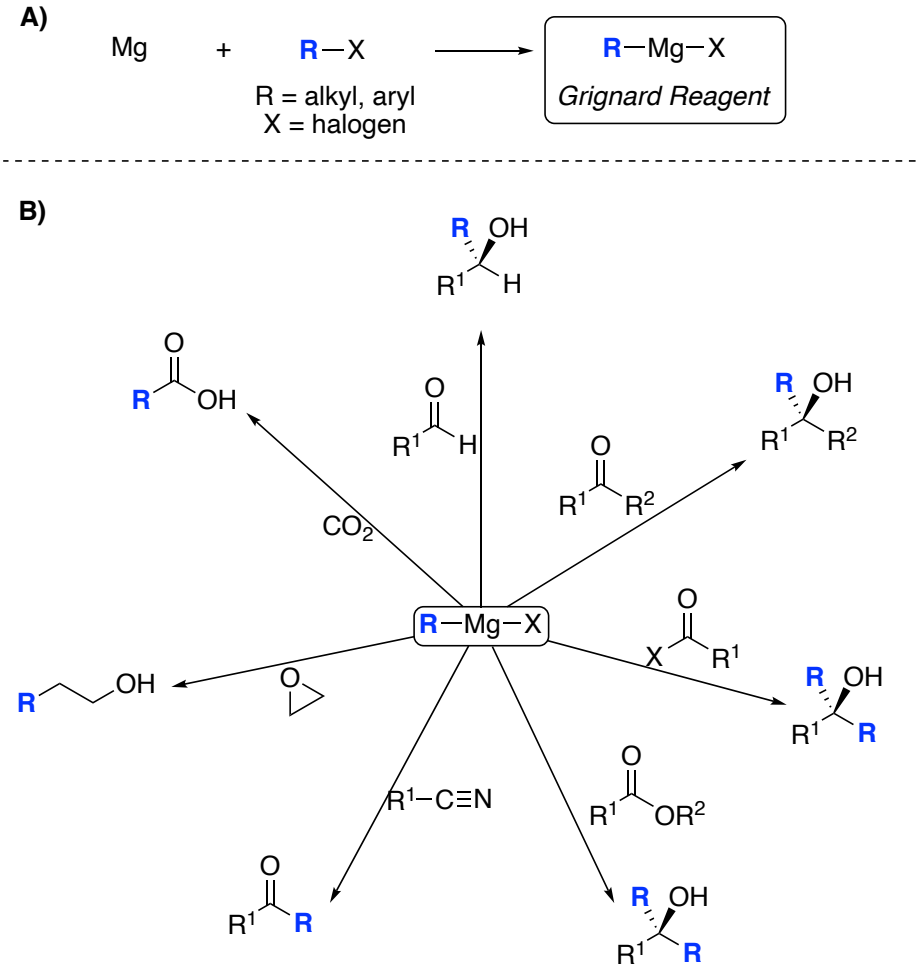


Figure 3. Synthesis of a Grignard reagent (A) and reactions using Grignard reagents (B).

The discovery of Grignard reagents led to the synthesis and isolation of "sandwich" complexes (Figure 4A), including ferrocene. [11, 12] Ernest Otto Fischer and Geoffrey Wilkinson won the Nobel Prize in Chemistry in 1973 for independently determining the "sandwich structure" of ferrocene, a complex with two cyclopentadienyl rings bound to an iron center (Figure 4B). [13, 14] The discovery and characterization of ferrocene is often considered the pioneering work of modern organometallic chemistry. [15]

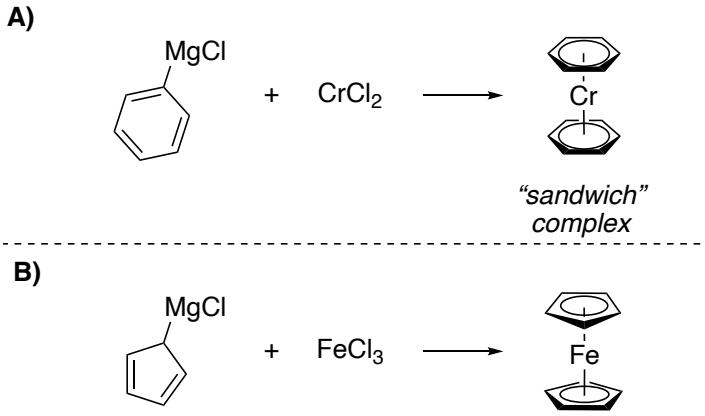


Figure 4. First synthesis of a "sandwich" complex (A) and synthesis of ferrocene (B).

In the 1950s, the impressive utility of organometallic reagents was demonstrated in polymerization reactions. Karl Ziegler and Giulio Natta discovered the organoaluminum and organotitanium system for the catalyzed ethene (Figure 5A) and propene polymerization (Figure 5B). [16, 17] In 1963, Ziegler and Natta were awarded the Nobel Prize in Chemistry for these discoveries. [18, 19]

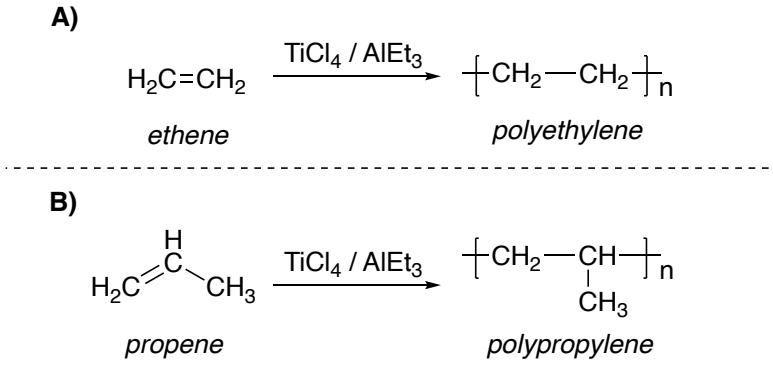


Figure 5. Ziegler–Natta catalyzed polymerization of ethene (A) and propene (B).

For decades, chemists have been working to unlock the full potential of organometallic reagents in organic synthesis. There have been numerous advances in the development and applicability of transition metal organic complexes. Transition metals are elements in the largest block of elements found on the periodic table. These elements can be defined as metals with

partially filled d-subshells, groups 3 through 11.[4] However, groups 3 and 12 are still debated. Group 3 elements, such as scandium, readily form stable cations and therefore do not act as true transition metals. [20, 21, 22]

Advancements in transition metal catalysis include cross-couplings to form new covalent bonds. Cross-coupling reactions are metal-catalyzed nucleophilic substitution reactions that became powerful synthetic tools in recent years. These reactions allow for efficient and selective synthesis of new C–C and carbon–halogen (C–X) bonds. [23, 24] Cross coupling reactions occur between an electrophilic partner and a nucleophilic partner in the presence of a catalyst, often a palladium catalyst. [4, 15] Some of the most notable chemists in the field include Richard Heck, Ei-ichi Negishi, and Akira Suzuki who won the Nobel Prize in Chemistry in 2010. [25, 26, 27]

The Heck reaction, also known as the Mizoroki–Heck reaction, uses a palladium catalyst to activate an alkyl–halogen, aryl–halogen, or vinyl–halogen (R–X) bond of an electrophilic partner, and couple it with an alkene (Figure 6A). [28, 29, 30, 31] The catalytic cycle in the Heck reaction starts with Pd(0) which activates the R–X bond of the electrophilic partner via oxidative addition. The olefin coupling partner then coordinates to the oxidized palladium to form a π-complex which can then undergo migratory insertion to create a new alkylpalladium complex. β-hydride elimination releases the olefin product and Pd(0) is regenerated via reductive elimination (Figure 6B). [32] The Heck reaction has been a useful method for the synthesis of many different pharmaceuticals, including the asymmetric synthesis of morphine (Figure 6C). [33]

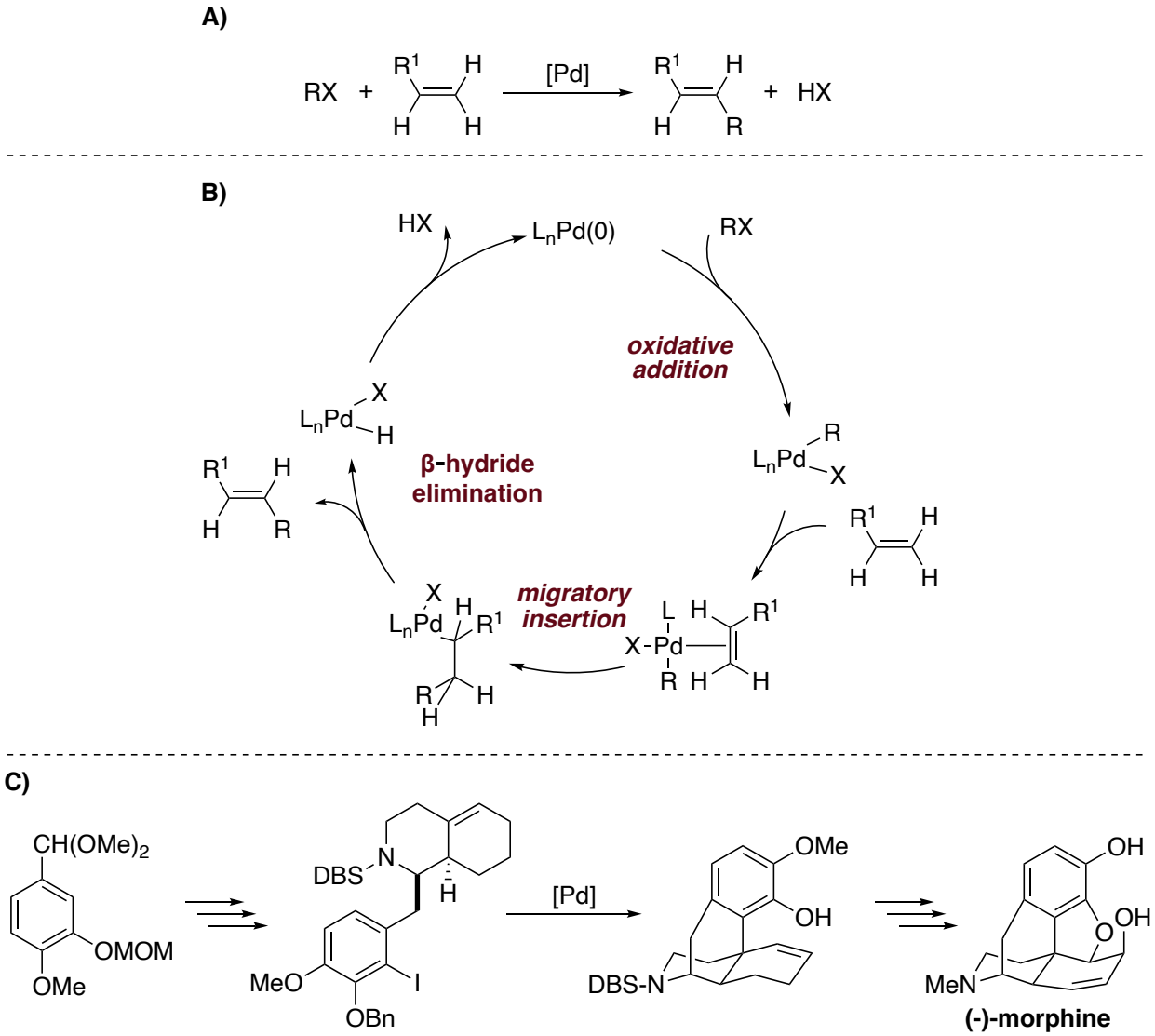


Figure 6. Heck reaction (A) and mechanism (B). Synthesis of (-)-morphine (C).

In contrast to the Heck reaction, Negishi and Suzuki couplings involve an electrophilic partner coupling with an organometallic nucleophile, instead of an alkene. Both Negishi and Suzuki coupling mechanisms require a Pd(0) species, have an oxidative addition step, and an elimination step to yield the desired product. However, the organometallic nucleophile requires an additional transmetallation step, in which the anionic carbon group of the organometallic reagent coordinates to the metal catalyst (Figure 7A). [26, 27] A Negishi coupling uses an

organozinc reagent and has been used for the synthesis of Pumiliotoxin B (Figure 7B). [34, 35, 36] A Suzuki coupling uses an organoboron reagent as the coupling partner and has been used to synthesize capparatriene from naturally abundant citronellal (Figure 7C). [37, 38, 39, 40]

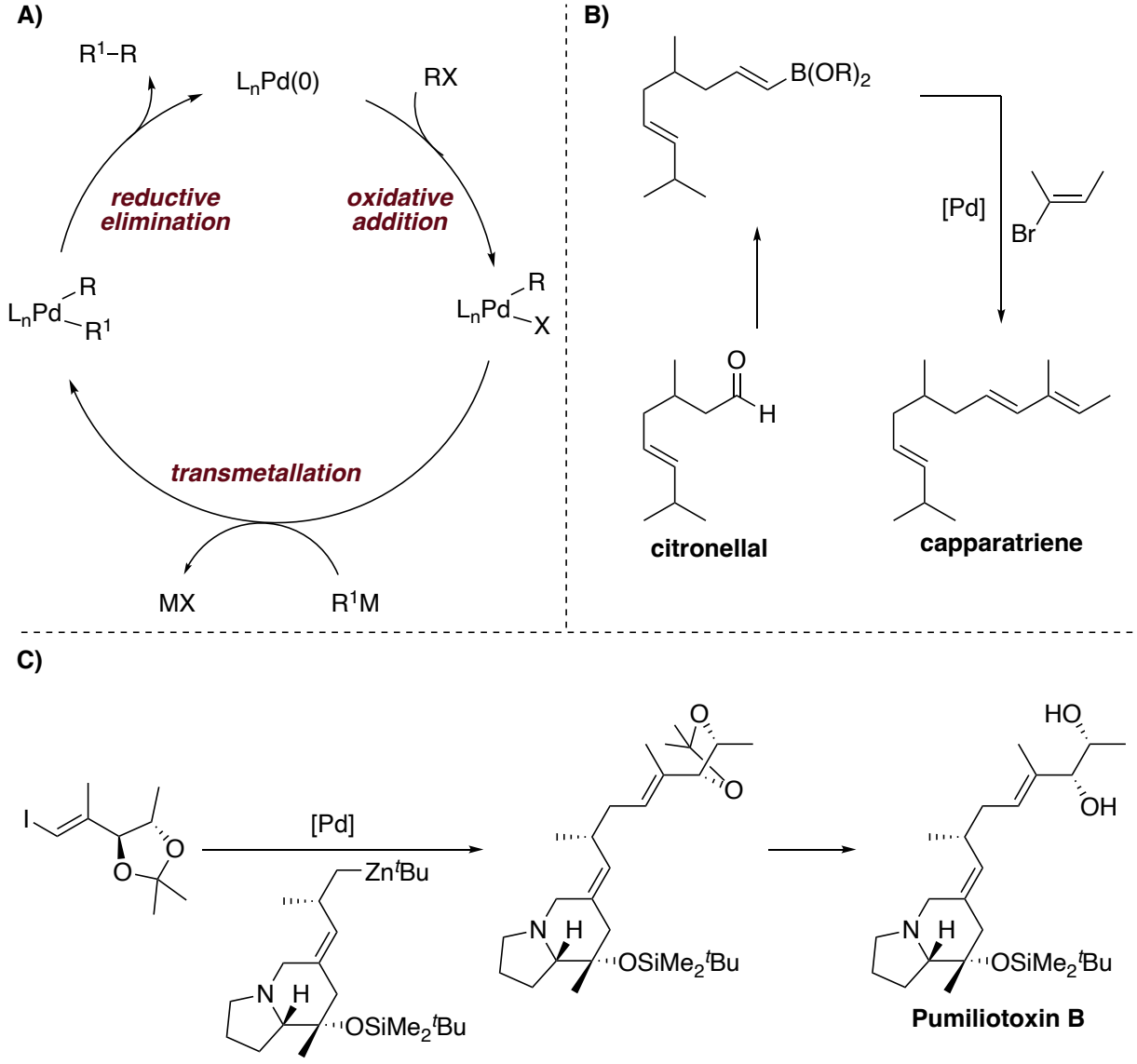


Figure 7. Negishi and Suzuki mechanism (A). Synthesis of capparatriene (B) and Pumiliotoxin B (C).

Other well-known cross-coupling reactions include Kumada coupling, which uses a Grignard reagent as the coupling partner, [41, 42] Stille coupling, which uses an organotin reagent, [43]

and Hiyama coupling, which uses an organosilane reagent (Figure 8A).[44] Sonogashira coupling is another example of a cross-coupling reaction using Pd(0) to catalyze the coupling between a terminal alkyne with an aryl or vinyl halide.[45] Sonogashira coupling uses a copper co-catalyst to transfer an acetylide to palladium in the transmetallation step (Figure 8B). To avoid the use of copper, limit waste, and avoid unwanted byproducts, copper-free Sonogashira methods have been developed (Figure 8C).[46]

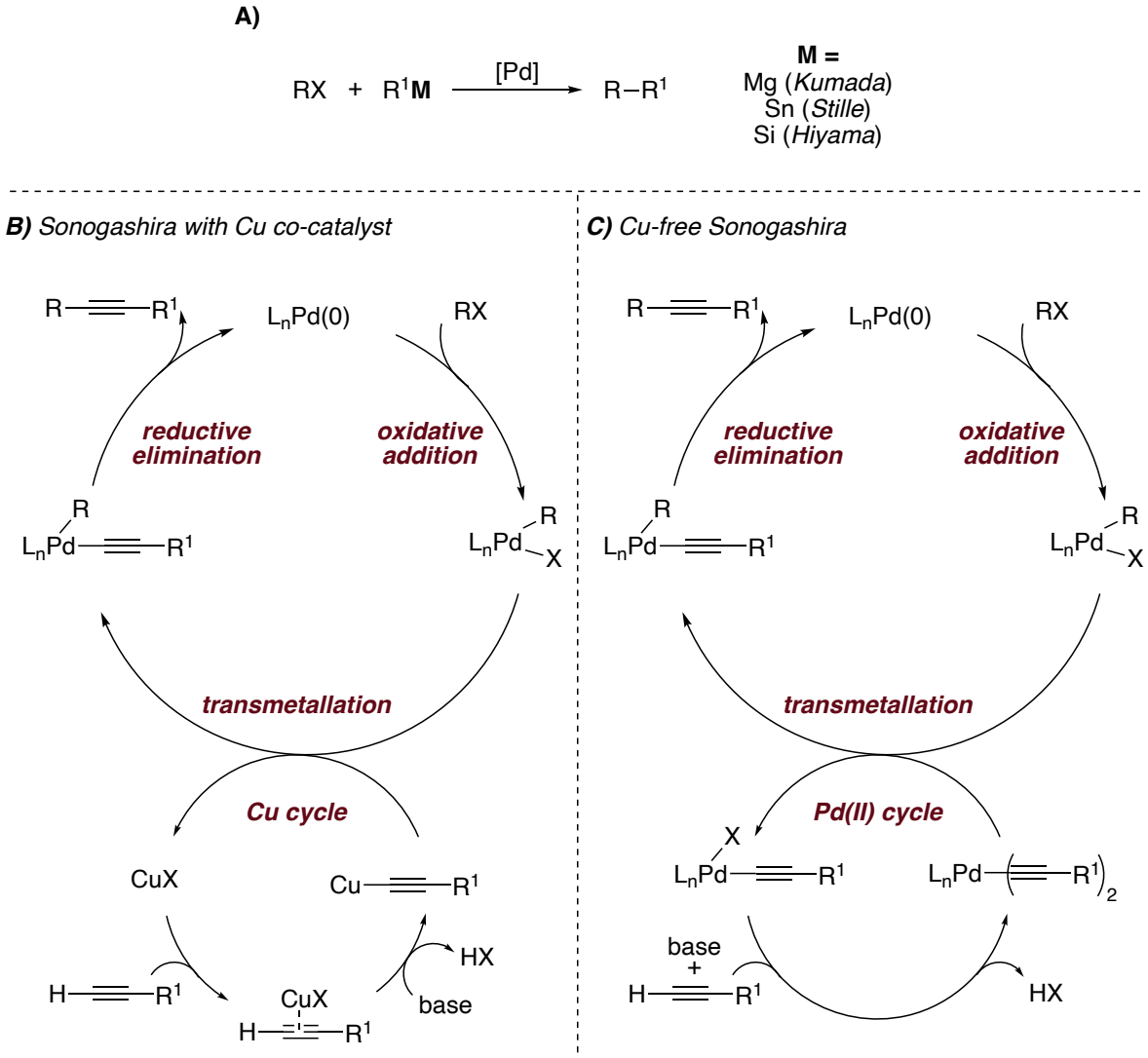


Figure 8. Metal coupling partners used for cross-coupling reactions (A). Sonogashira mechanism (B) and copper-free Sonogashira mechanism (C).

Although palladium is the most common transition metal used for cross-coupling reactions, other metals have proven to be useful. In 1966, Geoffrey Wilkinson set the stage for a rhodium catalyst by using, $RhCl(PPh_3)_3$, known as Wilkinson's catalyst (Figure 9A), for the selective hydrogenation of olefins without reducing any other functional groups attached to the alkene (Figure 9B). [47]

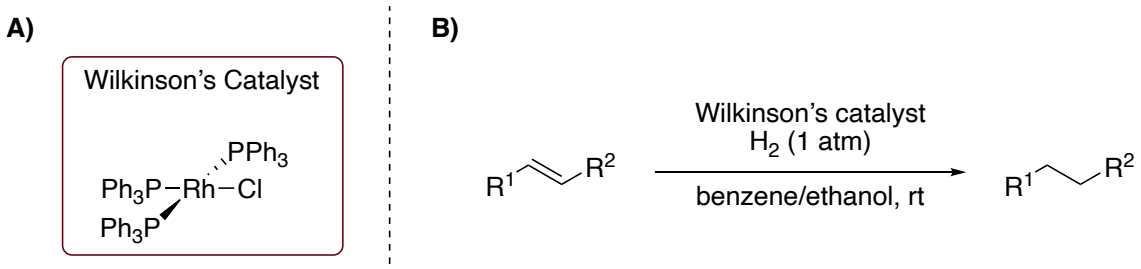


Figure 9. Structure of Wilkinson's catalyst (A) and the selective hydrogenation of olefins using Wilkinson's catalyst (B).

Since then, rhodium has been a useful metal for transition metal catalysis and has been a common catalyst used for carbon–hydrogen (C–H) bond activation. The benefit of C–H bond functionalization over traditional cross-coupling reactions is that there is no need for organohalides or organometallic coupling partners, reducing the amount of toxic byproduct produced. Rhodium's high functional group tolerance and chelating properties make it an excellent metal for C–C bond forming reactions via C–H bond activation. [48] Both Rh(I) and Rh(III) mechanisms have been reported. The Kim group showed the Rh(I)-catalyzed regioselective alkylation of 2-phenylpyridines with olefins via C–H bond activation (Figure 10A). [49, 50] Rh(I) catalyzed C-H bond activation has also been used for the synthesis of pyridines from α,β-unsaturated imines and alkynes (Figure 10B). [51] Rh(III)-catalyzed C–H bond activation reactions include the dehydrogenative coupling of benzoic acid with diphenylacetylene reported by Miura et al. (Figure 10C). [52, 53] Rh(I) and Rh(III) C–H bond activation reactions undergo

different mechanisms. Rh(I) undergoes an oxidative addition pathway and then reduces the rhodium to regenerate Rh(I) (Figure 10D), [54] while the Rh(III) pathway uses Rh(III) as the active catalyst which reduces to Rh(I) upon formation of product and requires an oxidation step to regenerate Rh(III) (Figure 10E). [48, 55]

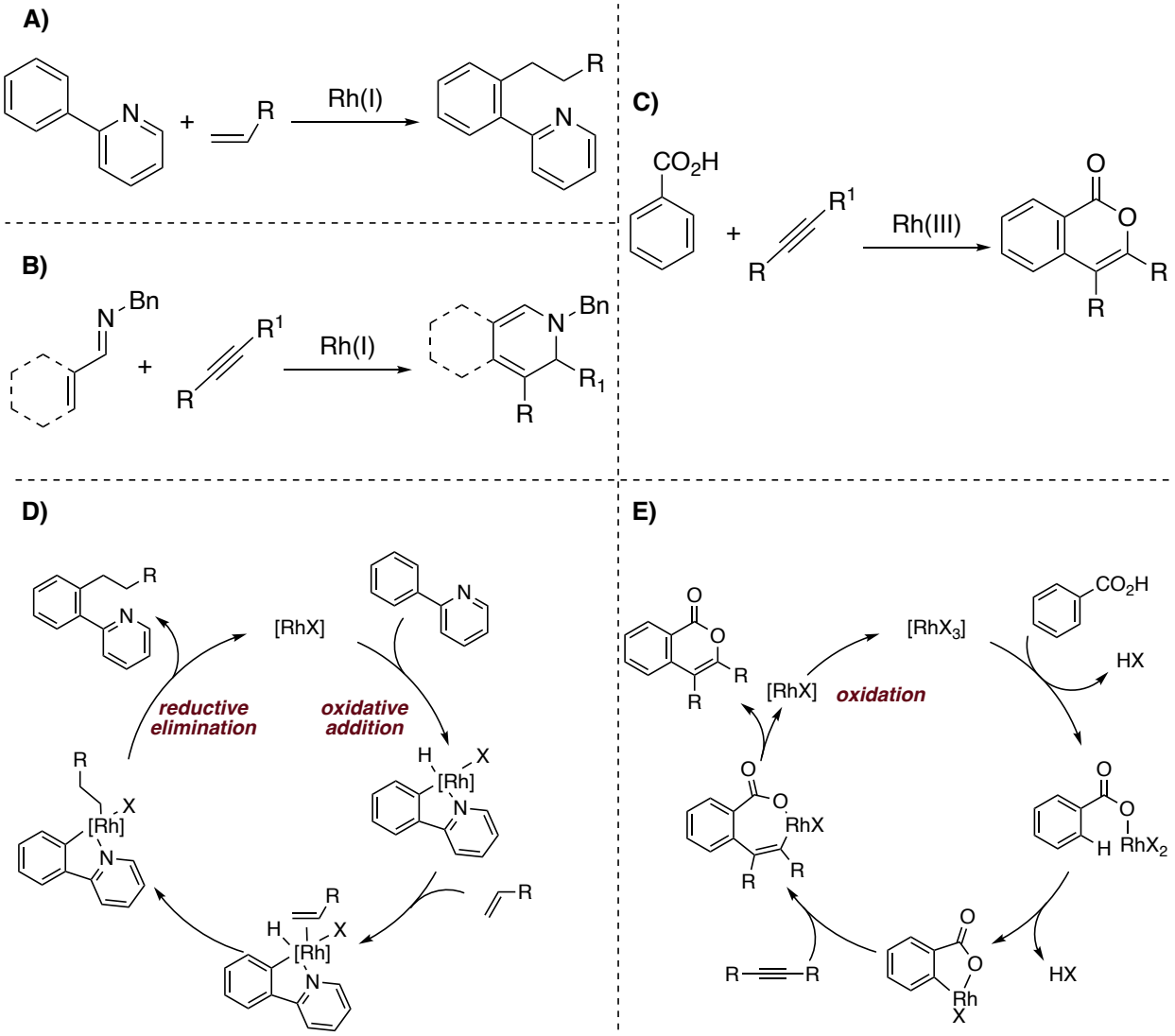


Figure 10. Rh(I)-catalyzed C–H bond activation of 2-phenylpyridines (A) and of α,β-unsaturated imines (B). Rh(III)-catalyzed C–H bond activation of benzoic acid (C). Mechanism of Rh(I)-catalyzed C–H bond activation (D) and Rh(III)-catalyzed C–H bond activation (E).

Transition metal catalysis has many advantages. Many reactions are one pot syntheses, highly efficient, and give good yields with high selectivity. They have also been proved to be very versatile and applicable across a large range of substrates for industrial level syntheses. However, there are also certain disadvantages. Many palladium-catalyzed syntheses involve a transmetallation step before reductive elimination can yield the final desired product. Transmetallation occurs after oxidative addition, and involves an organometallic coupling partner undergoing a ligand exchange with the oxidized metal complex. [4, 15] The transmetallation step does not change the overall oxidation state of the metal center. After this step, the metal complex now bears both coupling partners that will form a new bond to form the desired product. This step requires a toxic or highly basic reagent, which then produces a stoichiometric amount of unwanted, toxic halogenated byproducts. For example, a typical Negishi reaction requires a stoichiometric organozinc coupling partner, a Suzuki reaction requires an organoboron reagent, and a Kumada reaction requires a Grignard reagent. The Heck reaction requires a stoichiometric amount of base for the regeneration of the palladium catalyst. [28, 30, 35, 38, 41]

Intramolecular couplings of carboxylic acids and their derivatives offer a direct method for the formation of new covalent bonds and circumvent the transmetallation step required in many known catalytic syntheses. [56] Transition metal catalyzed decarbonylative processes can limit the amount of toxic byproduct by generating only free carbon monoxide (C–O). The C_{CO}–C bond of a carbonyl is activated via oxidative addition to the metal. CO is removed and the remaining metal complex forms final product with a new C–C bond and reduces the catalyst (Figure 11A). Before decarbonylation can occur, the carbonyl undergoes de-insertion. Since CO is a dative ligand, the de-insertion does not change the oxidation state of the metal. The reverse,

an insertion of CO, is also possible in a process called carbonylation (Figure 11B).[4, 15] Many cross-couplings activate aryl halides and with the right metal-ligand system, a decarbonylative method can also limit the activation of otherwise susceptible bonds.

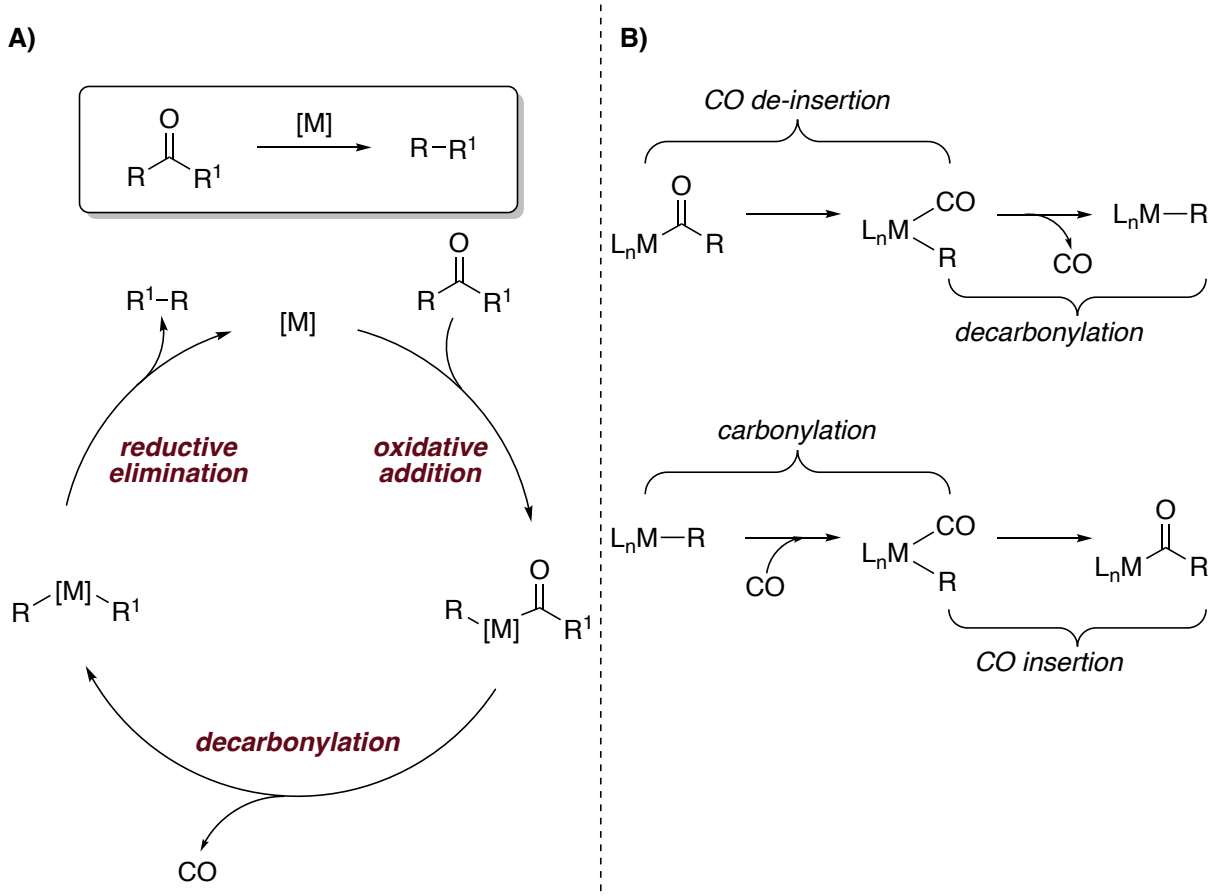


Figure 11. General mechanism of a transition metal-catalyzed decarbonylation (A). CO de-insertion and insertion (B).

Decarbonylation can be used to create new bonds in chemistry, with particular focus on C–C bond forming reactions. Carboxylic acids and their derivatives can undergo both intermolecular couplings and intramolecular couplings via transition metal-catalyzed decarbonylation to form new covalent bonds. Intermolecular decarbonylative couplings have been extensively studied using aldehydes. A rhodium-catalyzed decarbonylative Heck reaction

was reported by Li et al. in 2010[57] with further improvements reported by Yang et al. in 2015 (Figure 12A). [58] In 2010, Li et al. also reported the rhodium-catalyzed decarbonylative Heck cross-coupling of aldehydes and norbornenes (Figure 12B). [59]

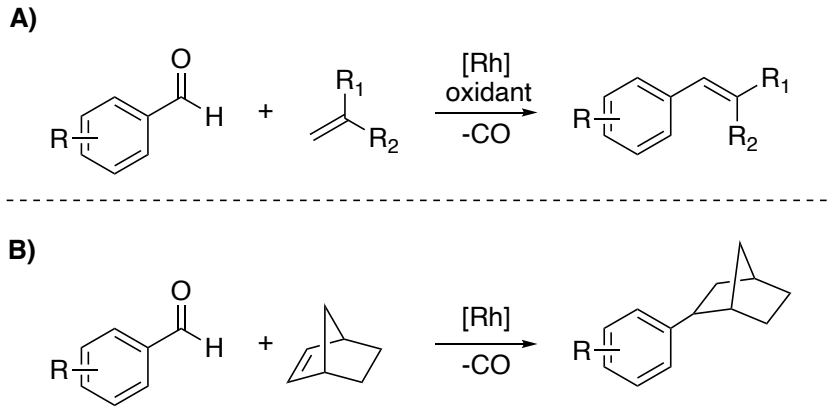


Figure 12. Rhodium-catalyzed decarbonylative Heck cross-coupling of aldehydes and alkenes (A). Rhodium-catalyzed decarbonylative Heck cross-coupling of aldehydes and norbornenes (B).

Li et al. reported the rhodium-catalyzed homo-coupling of aryl aldehydes. His studies illustrate the vast differences in outcomes from ligand choice. When PPh_3 was used as the ligand, the aldehyde underwent a decarbonylative homo-coupling to form biaryls in high yields (Figure 13A). Simply changing the ligand to dppe, the reaction no longer underwent decarbonylation, and afforded a biaryl ketone instead (Figure 13B). [60]

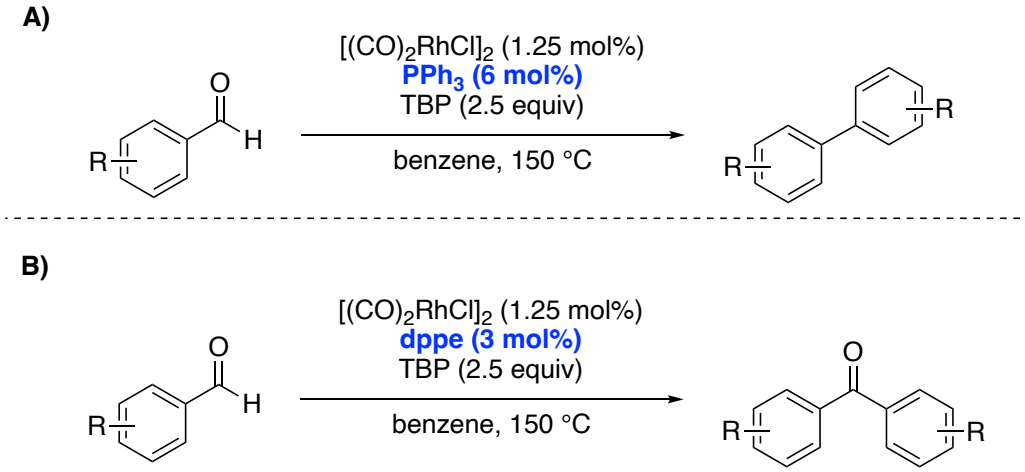


Figure 13. Synthesis of biaryls (A) and biaryl ketones (B) via rhodium-catalyzed homo-coupling of aryl aldehydes.

Li et al. also reported the rhodium-catalyzed decarbonylative cross-coupling of aryl aldehydes with 2-arylpyridines via C–H bond activation (Figure 14A). Addition of an aldehyde to a Rh(I) catalyst generates an oxidized Rh(III) species that can undergo CO de-insertion. The Rh(III) species can undergo decarbonylation and C–H bond activation of 2-arylpyridines. The resulting Rh(III) species can then undergo reductive elimination to form the final product and regenerate Rh(I) (Figure 14B). [61]

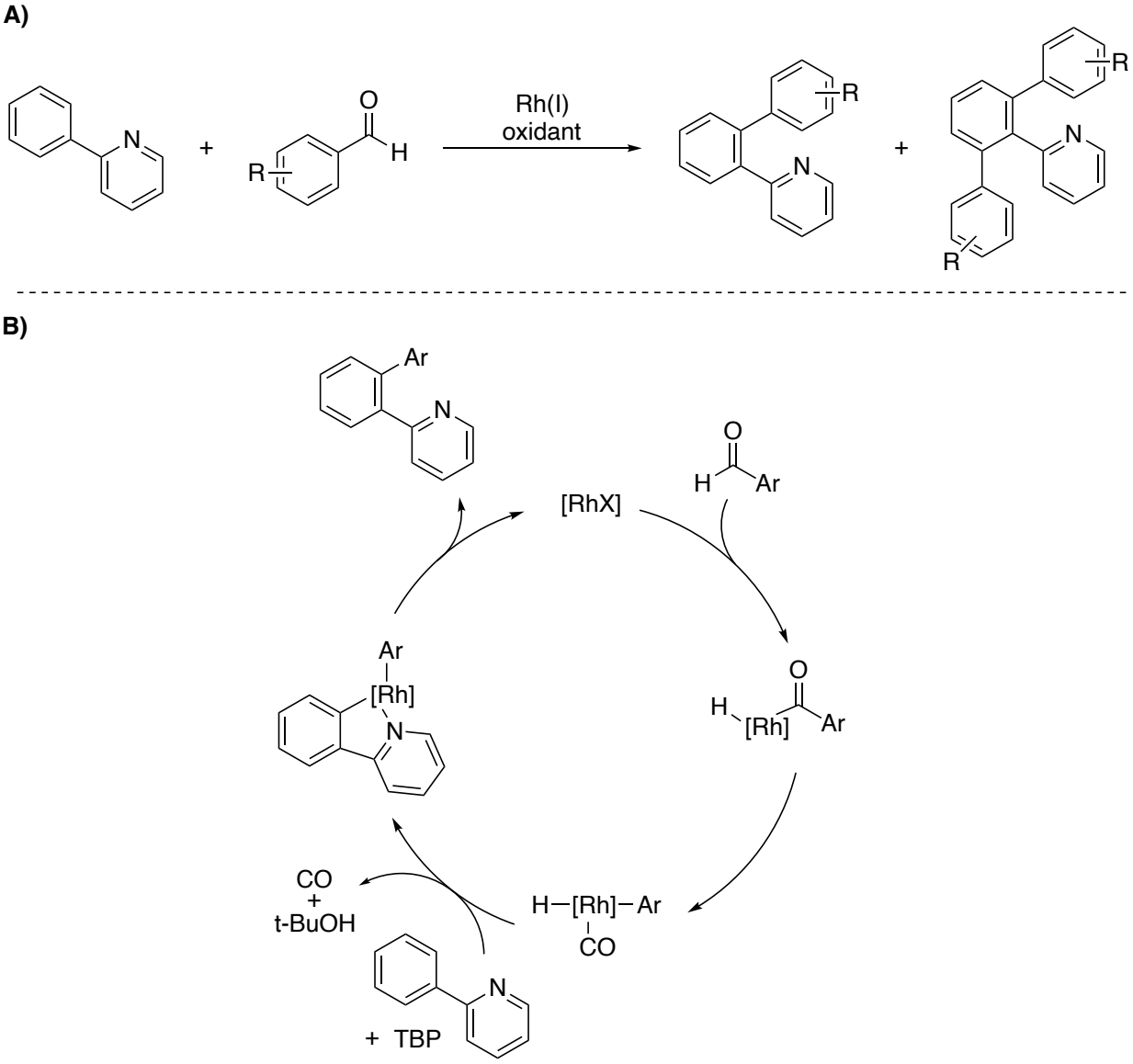


Figure 14. Rhodium-catalyzed decarbonylative cross-coupling of aryl aldehydes with 2-arylpyridines via C–H bond activation (A) and proposed mechanism (B).

Apart from rhodium, other metals have also been reported to catalyze decarbonylative cross-coupling. For example, Li et al. has demonstrated a ruthenium-catalyzed decarbonylative addition of aldehydes to terminal alkynes (Figure 15A). [62] A nickel-catalyzed Suzuki cross-coupling of aldehydes and boronic esters was reported by Rueping et al. in 2019 (Figure 15B). [63]

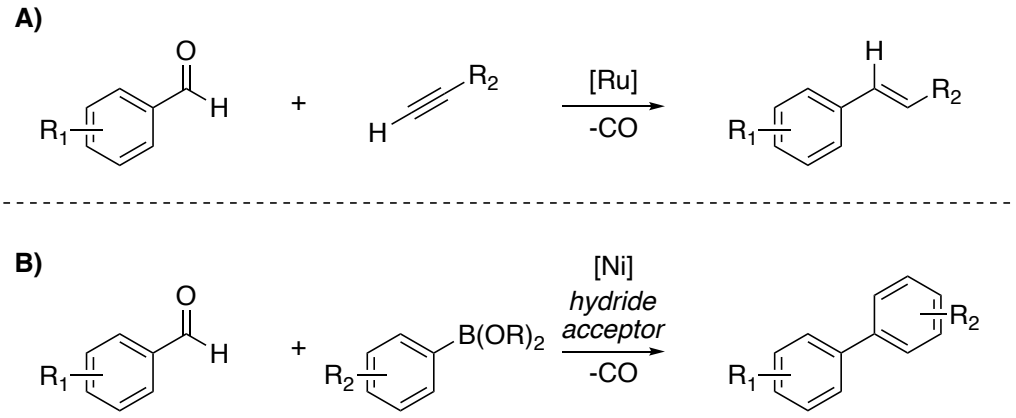


Figure 15. Ruthenium-catalyzed decarbonylative cross-coupling of aldehydes with terminal alkynes (A). Nickel-catalyzed decarbonylative cross-coupling of aldehydes with boronic esters (B).

The pioneering report for intramolecular decarbonylation was the synthesis of apopinene via a palladium-catalyzed intramolecular decarbonylation of myrtenal (Figure 16A). [64] In 1965, Tsuji and Ohno reported a decarbonylation of aldehydes using a palladium catalyst (Figure 16B). [65, 66] They also reported a stoichiometric rhodium decarbonylation of aldehydes using Wilkinson's catalyst. A few years later, they demonstrated decarbonylation of aldehydes using a sub-stoichiometric amount of Wilkinson's catalyst, although it required very high temperatures (Figure 16C). [67, 68] The decarbonylation of aldehydes using palladium and rhodium have been further studied to expand the substrate scope. [69, 70, 71, 72] Carreira et al. reported the synthesis of 1,1-diarylethane compounds via rhodium-catalyzed decarbonylation of aldehydes in high optical purity (Figure 16D). [73] Other examples of the decarbonylation of aldehydes were reported using nickel, [74] iridium, [75, 76] and ruthenium (Figure 16E). [77]

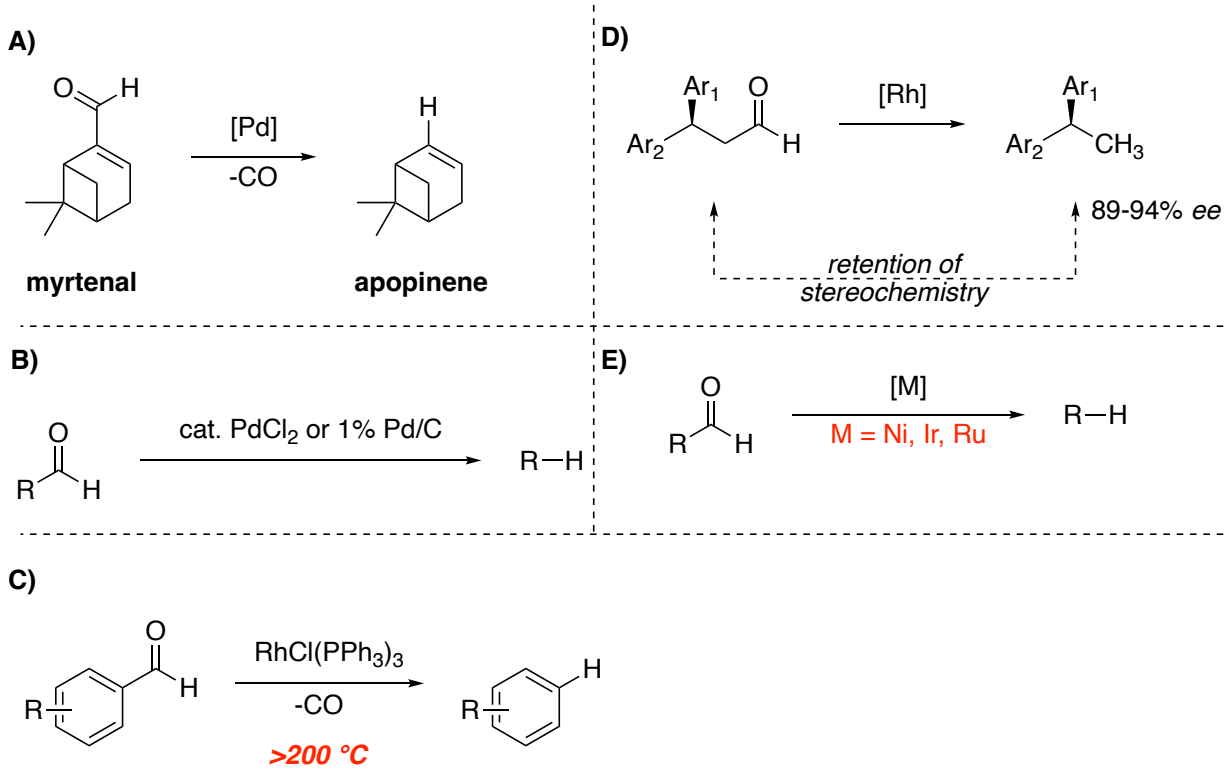


Figure 16. Palladium-catalyzed synthesis of apopinene (A). Decarbonylation of aldehydes using palladium catalysts (B), Wilkinson's catalyst (C). Synthesis of 1,1-diarylethane compounds (D). Decarbonylation of aldehydes using nickel, iridium, and ruthenium catalysts (E).

Besides the decarbonylation of aldehydes, intramolecular decarbonylations have been scarcely reported. Without the need for a coupling partner or stoichiometric oxidants, intramolecular decarbonylations offer an efficient way to form new covalent bonds with minimal organic byproduct. This dissertation describes our work in the development of novel transition metal-catalyzed intramolecular decarbonylations.

CHAPTER 2

DECARBONYLATION OF AROYL CHLORIDES

Compounds containing aryl chlorides represent a wide array of function and importance. Aryl chlorides play an essential role in many industries, including the agricultural and pharmaceutical industries. Therefore, developing diverse and efficient strategies to synthesize aryl chlorides is of utmost importance. Specifically, investigating various transition metal-catalyzed methods of synthesizing aryl chlorides can lead to more economic pathways for the construction of these essential molecules. Within this chapter, an efficient rhodium-catalyzed method for synthesizing aryl chlorides is presented that offers a solution for direct access to these important moieties via decarbonylation.

Aryl chlorides are prevalent moieties in pharmaceuticals[78, 79, 80] and natural products. [81, 82, 83] With over 95% of drugs involving halogenated aromatic or aliphatic carbons[84], the development of novel methods for synthesis of aryl chlorides is always necessary. Aryl chlorides are key structures in drug synthesis. Many drugs on the market contain chlorinated aromatic rings. Aceclofenac, which is a treatment for relieving symptoms of rheumatoid arthritis, contains two aryl chlorides. Temazepam is a treatment for insomnia. Rupatadine is a treatment for allergies, and moclobemide is a treatment for depression and anxiety. Mitotane, which contains two chlorinated aryl groups as well as a dichloromethyl group, is used as a treatment for certain cancers and Cushing syndrome (Figure 17). [85]

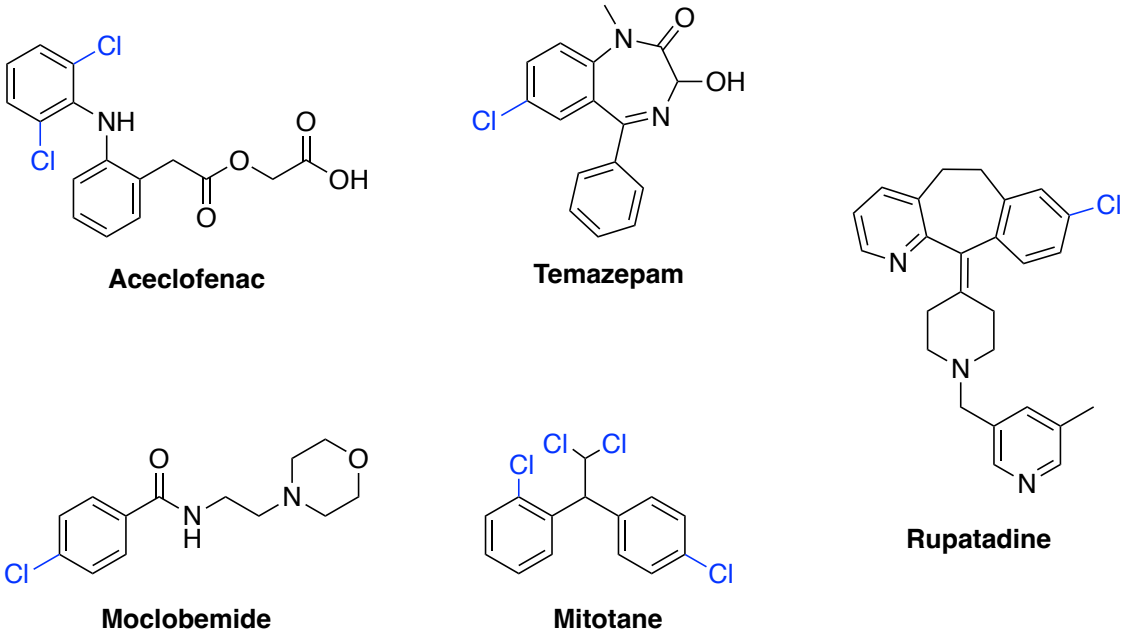


Figure 17. Pharmaceuticals containing aryl chlorides.

Vancomycin, an example of an aryl chloride found in nature, is an antibiotic used to treat many different bacterial infections (Figure 18A). [81, 83] It is often prescribed for life threatening situations, when bacteria are unresponsive to other antibiotics or when the patient is allergic to other antibiotics. The drug is commonly used to treat methicillin-resistant *S. aureus* (MRSA) and highly drug resistant *Staphylococcus epidermidis*. [86] In the case of vancomycin, the chlorinated aryl group is required for the stability and specificity of the binding site. Harris and his group found that upon removal of either one or both chlorines the dechlorinated vancomycin proved ineffective. [87] Neither the monochloro derivative of vancomycin (Figure 18B) nor the didechloro derivative of vancomycin (Figure 18C) showed antibiotic activity. Therefore, the chlorine atoms are necessary for a clinically active conformation of the drug.

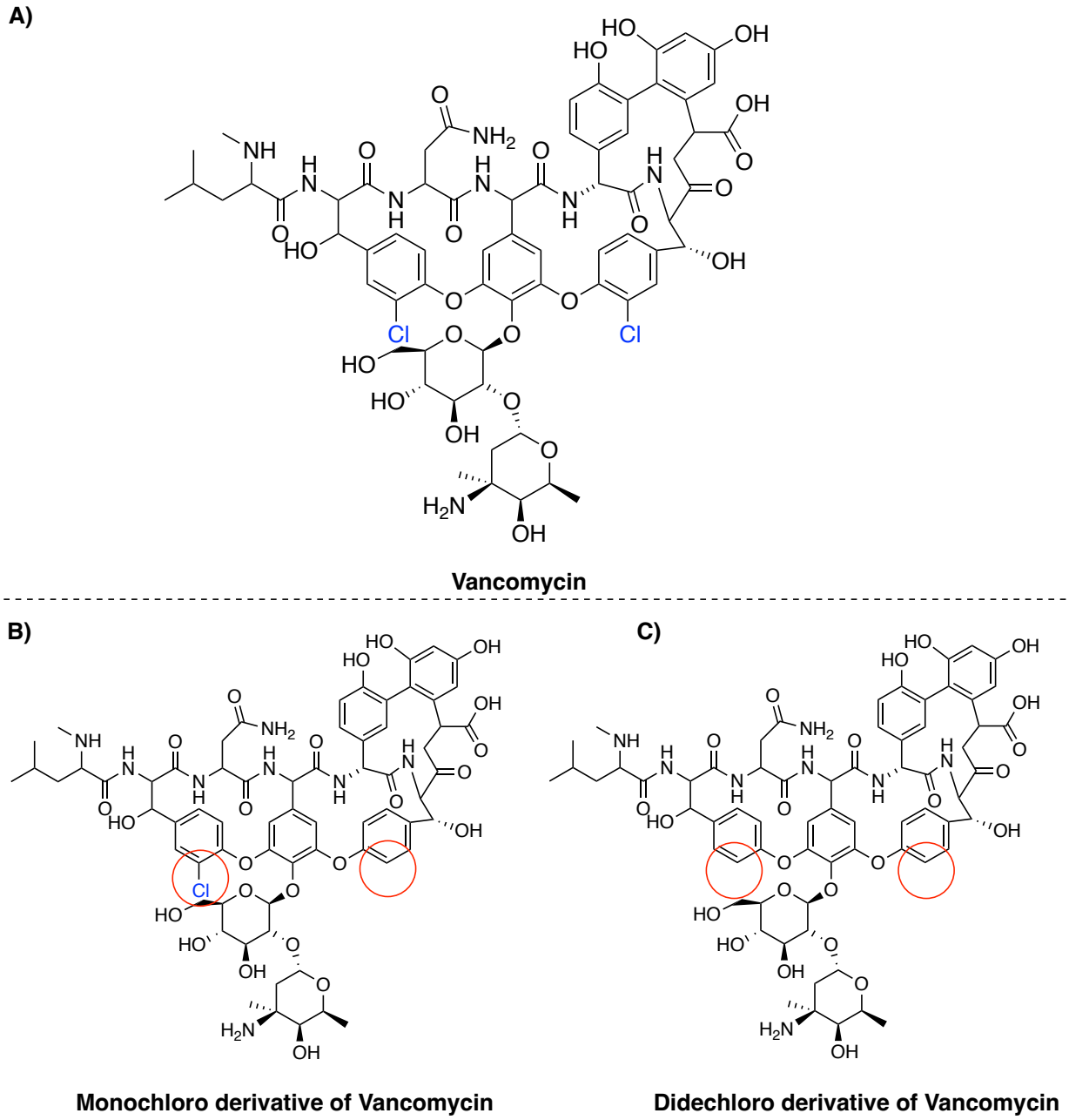


Figure 18. Structure of Vancomycin (A) and structures of de-chlorinated derivates of Vancomycin (B) and (C).

Aryl chlorides are also used for the development of agrochemicals. [88] They are frequently seen in synthetic pesticides. [89] About 40% of all pesticides belong to the organochlorine class of chemicals. [90] Dichlorodiphenyltrichloroethane (DDT) was a widely used pesticide developed in

the late 1930s. It was found to be very toxic for insects but showed low toxicity for mammals. The insecticide was later banned when it was found that it does not degrade quickly; the increased concentrations began affecting many different species. Other pesticides which contain aryl chlorides are chloropropylate, 1,4-dichlorobenzene, pentachlorophenol, and benzene hexachloride (BHC) (Figure 1).

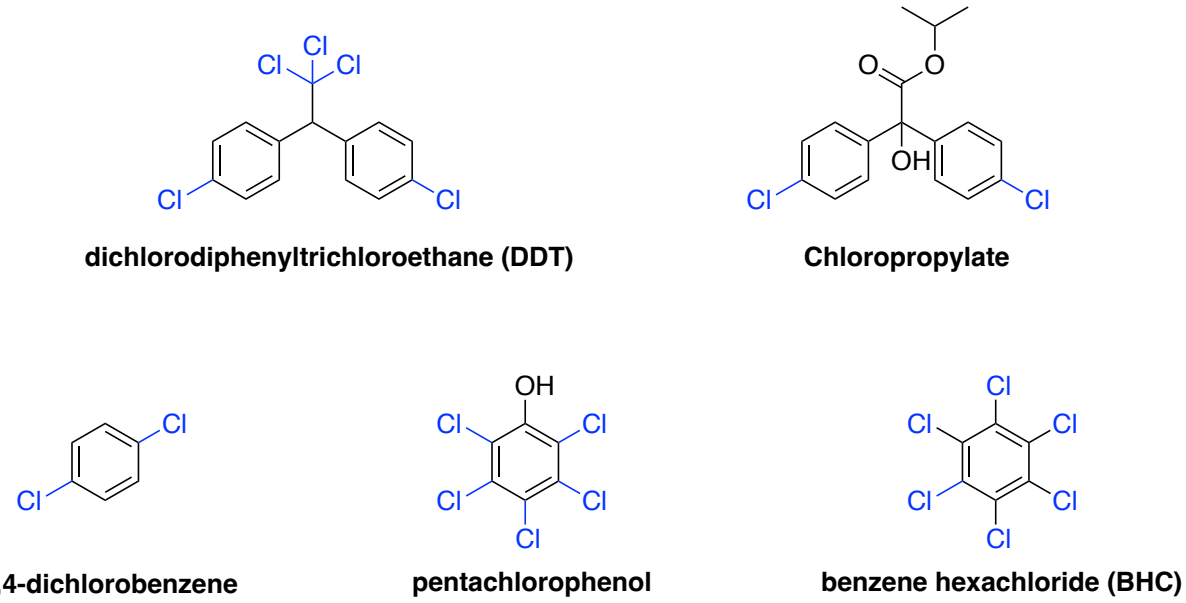


Figure 19. Pesticides containing chlorinated aromatic rings.

In addition to being useful end products, aryl chlorides are key building blocks for complex molecules. The synthesis of Aldara, a topical cream to treat non-melanoma skin cancers, requires a chlorinated nitroquinoline which can then undergo a substitution reaction to form an amine and further modifications make the final drug (Figure 20).[91]

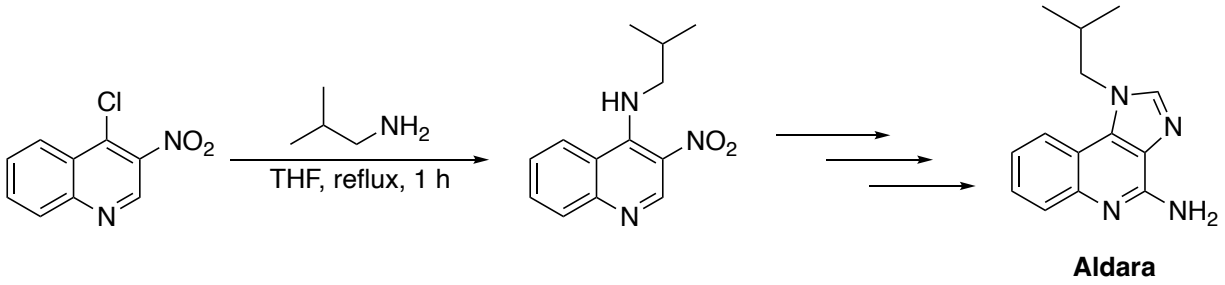


Figure 20. Modification of an aryl chloride for the synthesis of Aldara.

Aryl chlorides are useful starting materials for the synthesis of Grignard reagents (Figure 21A)[9] and anilines (Figure 21B).[10, 92] They are also ideal reagents for transition metal catalyzed cross-coupling reactions (Figure 21C).[23, 93] The versatility of these reagents provides numerous options in organic synthesis. For example, Buchwald et al. reported a palladium-catalyzed trifluoromethylation of aryl chlorides (Figure 21D).[94] Grushin et al. developed a non-catalytic strategy for the same conversion using $CuCF_3$ as the CF_3 source (Figure 21E).[95] The synthesis of biaryls can be achieved via the Ullmann reaction, a copper-mediated homocoupling of aryl halides (Figure 21F),[96] or a palladium-catalyzed Ullmann-type homocoupling (Figure 21G).[97]

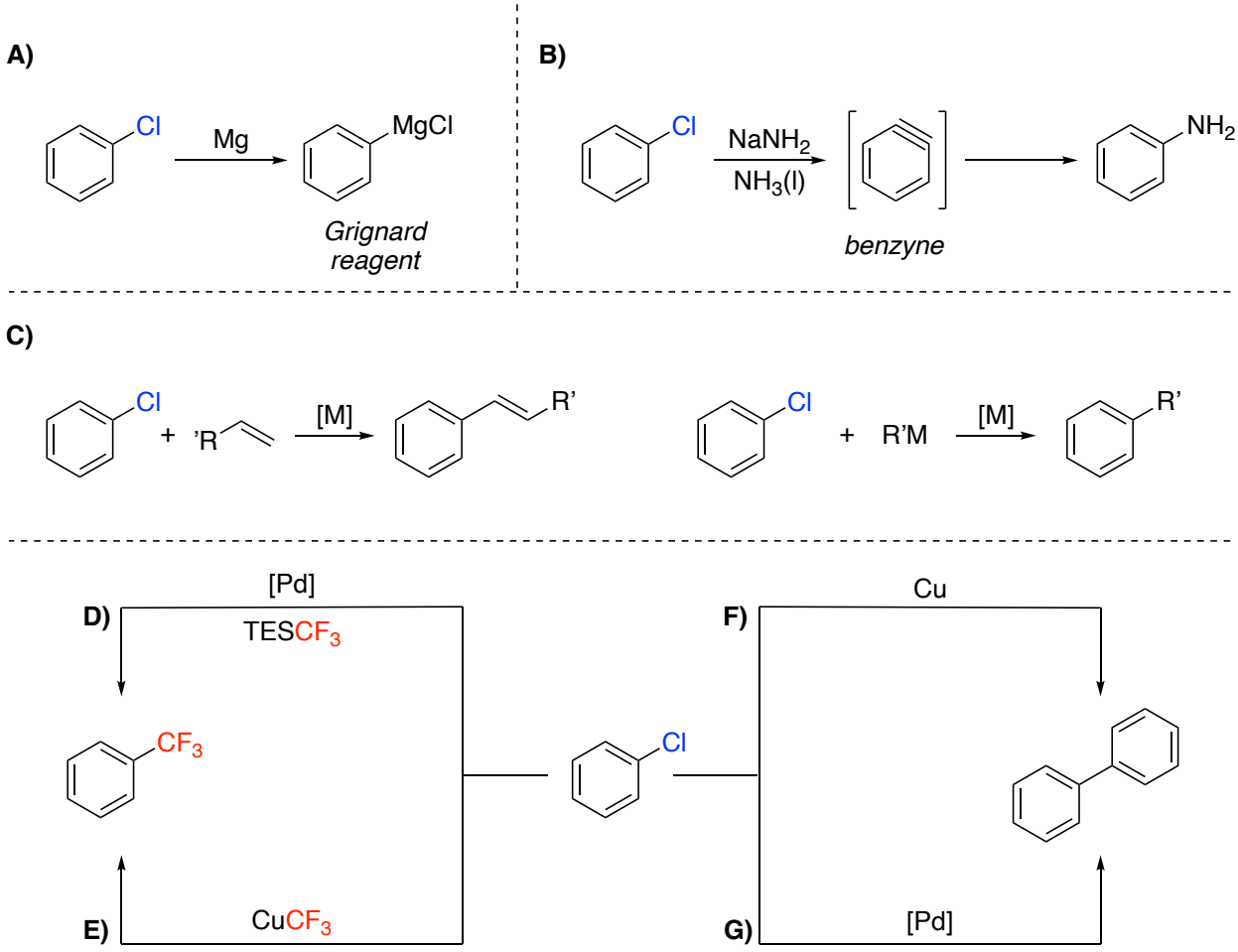


Figure 21. Aryl chlorides as precursors to Grignard reagents (A) and anilines (B). Aryl chlorides as coupling partners in transition-metal catalyzed cross coupling reactions (C). Trifluoromethylation of aryl chlorides via Pd-catalysis (D) and non-catalyzed trifluoromethylation (E). Copper mediated Ullmann synthesis of biaryls (F) and Pd-catalyzed Ullmann type synthesis of biaryls (G).

Two classical methods for the synthesis of aryl chlorides are direct halogenation, such as Friedel–Crafts type halogenation, and chlorination via diazonium salts. [10, 98] Both types of reactions utilize metal salts. Friedel–Crafts type halogenation uses a metal chloride to chlorinate aromatic rings via a substitution reaction (Figure 22A). The Sandmeyer reaction converts anilines to diazonium intermediates which are treated with copper halides to form aryl chlorides (Figure 22B). A modified version of the Sandmeyer reaction, known as the Gattermann reaction,

treats diazonium salts with HCl and copper metal to form the aryl chloride (Figure 22C). [99] Although these protocols for the preparation of aryl chlorides are widely known, they often are subject to low functional group tolerance, stoichiometric byproducts, low regioselectivity, over halogenation or a requirement for shock-sensitive starting materials. [10, 100] These limitations result in difficult purifications, reduced yields, and delicate handling. Therefore, a more efficient strategy for the synthesis of aryl chlorides is desirable.

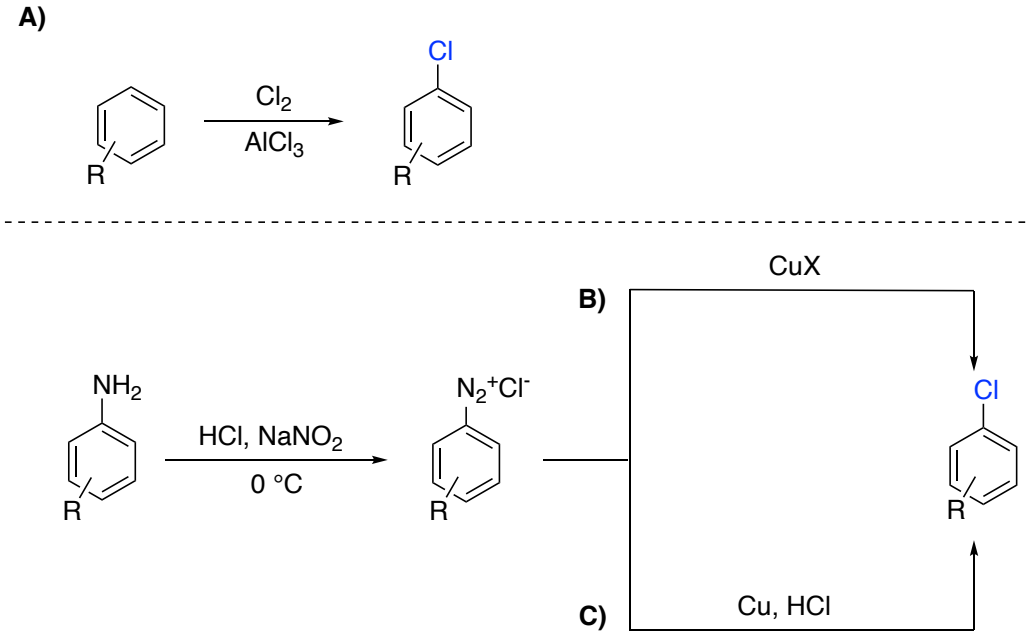


Figure 22. Friedel–Crafts type halogenation (A). The conversion of anilines to aryl chlorides via the Sandmeyer reaction (B) and the Gattermann reaction (C).

Various transition metal-catalyzed aryl–halogen bond formation reactions have been reported. Palladium-catalyzed oxidative C–H halogenation are commonly reported methods, particularly with Pd(II) catalysts. [24, 101] There have been significant advancements in *ortho*-selective C–X elimination from Pd(IV) species. [102, 103, 104] Generally, Pd(II) is oxidized to Pd(IV), and reductive elimination from Pd(IV) forms the new C–X bond. [24] For example, Sanford et al. reported Pd(II) catalyzed oxidative C–H fluorination of 2-aryl pyridines (Figure 23A). [105] In

1970, Fahey reported the Pd(II) catalyzed *ortho*-chlorination of azobenzenes. [106] Pd(II) catalyzed *ortho*-bromination of azobenzenes was later reported (Figure 23B). [107, 108] Raida et al. later reported the Pd(II) catalyzed *ortho*-iodination of azobenzenes (Figure 23C). [109] There have also been examples of C–X bond formation via reductive elimination from a Pd(III) intermediate. [24] The first examples of catalyzed bromination and chlorination via a Pd(III) intermediate were reported with benzo(*h*)quinoline by the Ritter group (Figure 23D). [110, 111]

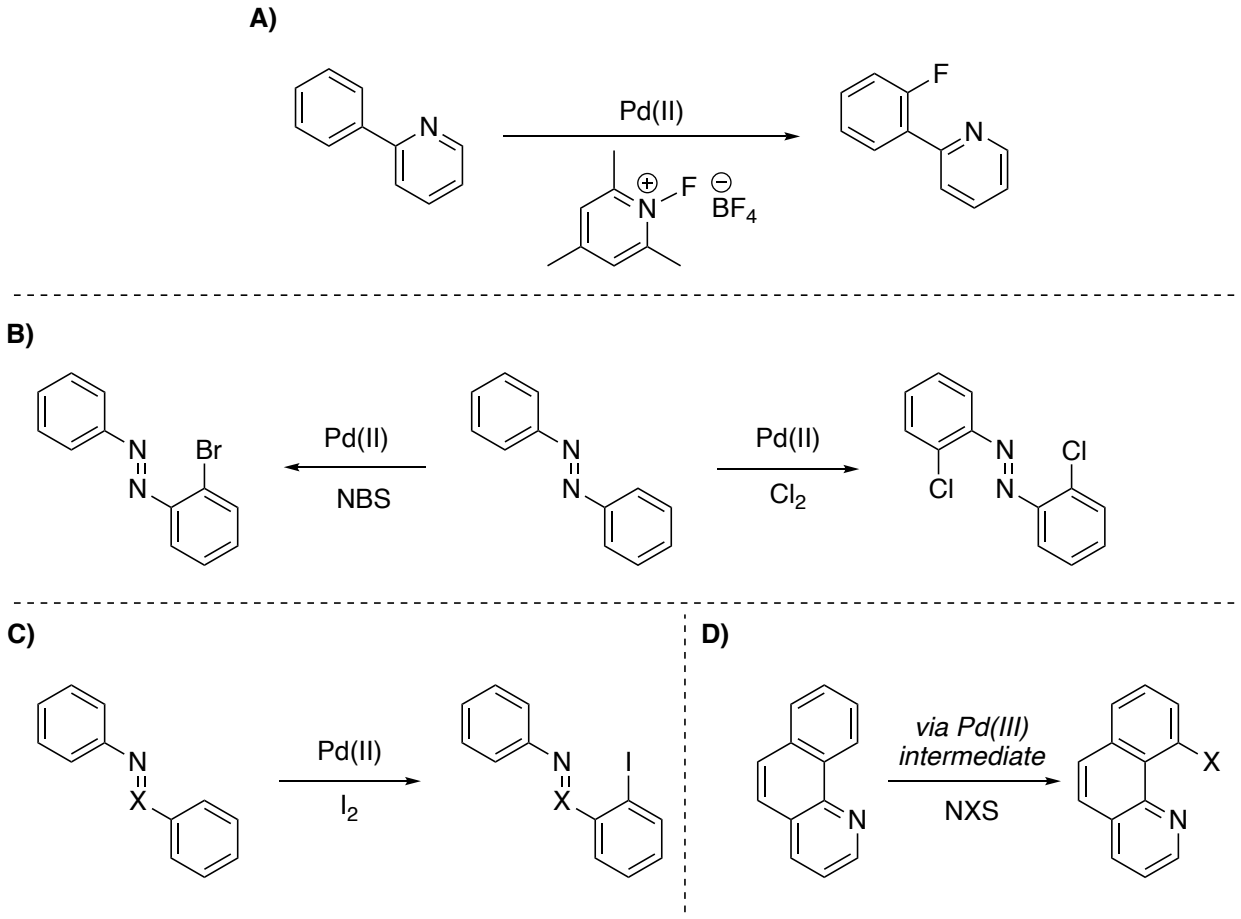


Figure 23. Pd(II)-catalyzed fluorination of 2-aryl pyridines (A). Pd(II)-catalyzed bromination and chlorination (B) and iodination of azobenzenes (C). Halogenation of benzo(*h*)quinolines via Pd(III) intermediate (D).

Oxidative addition of aryl halides to Pd(0) is a fundamental step in many catalytic processes. [30, 32, 39] Typically, the oxidative addition step of aryl halides to Pd(0) is a thermodynamically favorable process. Therefore, compared to the reductive elimination of aryl halides from Pd(IV), reductive elimination from Pd(II) is disfavored. In fact, oxidative addition to Pd(0) is considered an irreversible step. [112, 113] The thermodynamics of oxidative addition to Pd(0) makes the Pd(0) catalyzed synthesis of aryl halides challenging. However, Hartwig's kinetic and thermodynamic stoichiometric studies proved that reductive elimination of aryl halides from a Pd(II) complex is possible (Figure 24A). [114, 115, 116, 117, 118] Electron donating ligands such as halides are known to facilitate oxidative addition, and poor electron donating ligands are known to promote reductive elimination. Hartwig's studies examined the ligand steric effects for promoting reductive elimination. Surprisingly, although an electron donating ligand is not expected to facilitate reductive elimination, the ligand's steric effects can dominate over the electronic effects. [119] This discovery led to Buchwald's groundbreaking development of a Pd(0) catalyzed synthesis of aryl halides via reductive elimination from Pd(II) (Figure 24B). [120]

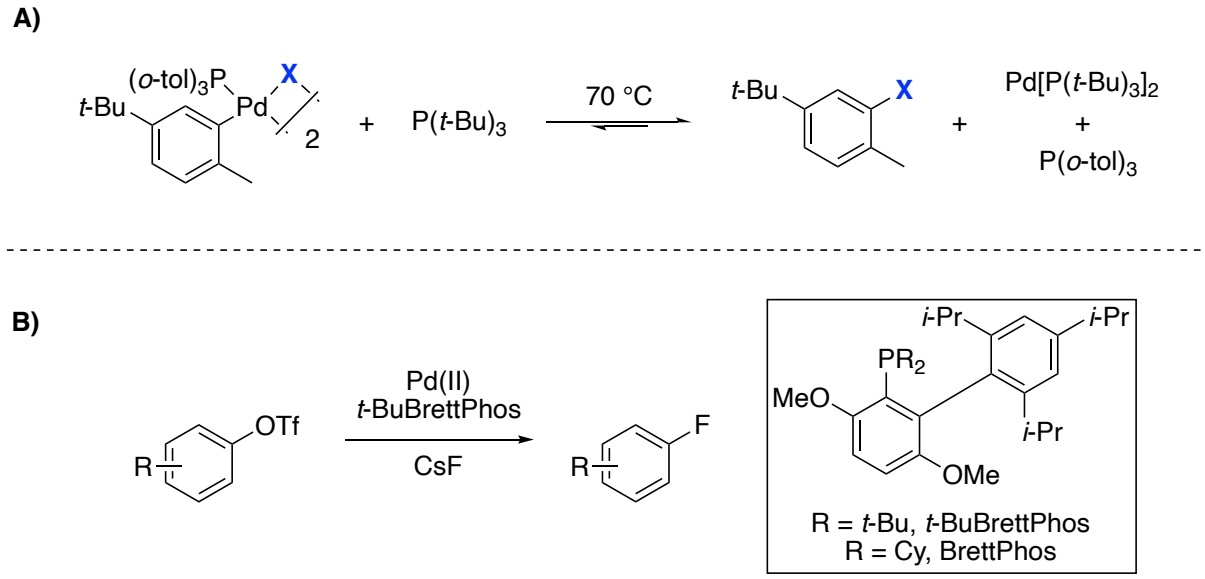


Figure 24. Reductive elimination of aryl halides from Pd(II) (A). Pd(0)-catalyzed conversion of aryl triflates to aryl fluorides (B).

Rhodium catalyzed aryl halide synthesis is commonly reported through Rh(III) catalyzed *ortho*-selective C–H halogenation. [24] For example, Glorius et al. reported the first Rh(III) catalyzed halogenation with halosuccinimides (Figure 25A). The aryl halide is either released from a Rh(III) complex or formed via reductive elimination from an oxidized Rh(V) complex (Figure 25B). [121] Overall, rhodium-catalyzed synthesis of aryl halides have not been extensively studied. However, over-halogenation is a problem in palladium catalyzed halogenations, but not for Rh(III) catalyzed halogenation. [24]

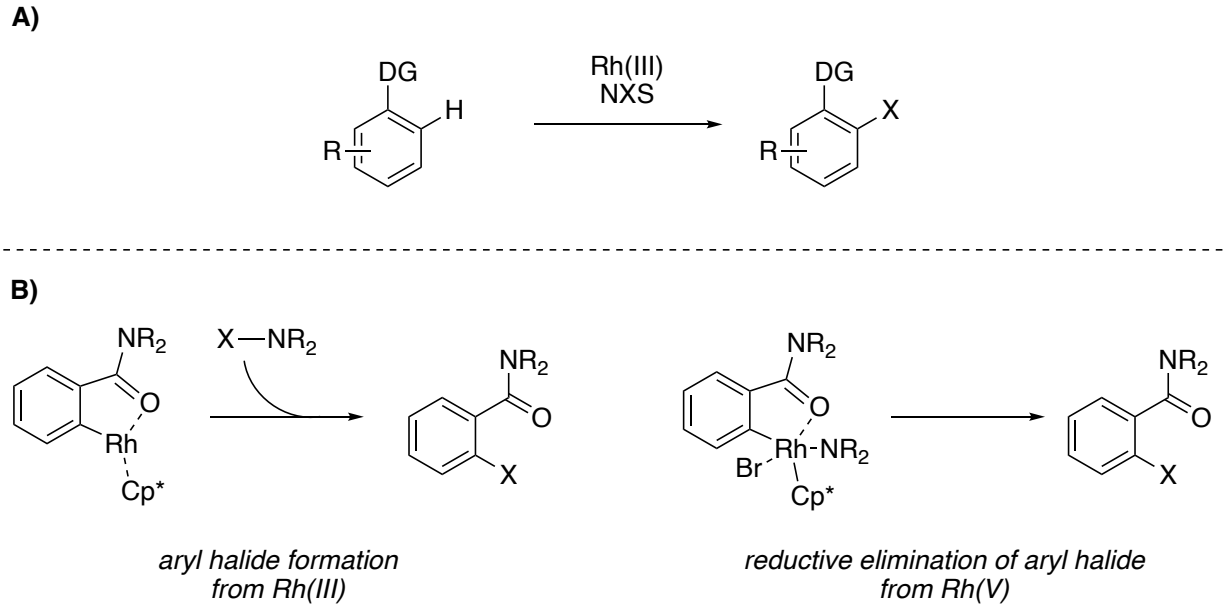


Figure 25. Rh(III)-catalyzed *ortho*-selective halogenation (A) via a Rh(III) complex or reductive elimination from Rh(V) complex (B).

Milstein et al. conducted stoichiometric studies of reductive elimination of Me–X from Rh(III) complexes. Initially, he studied the steric effects on reductive elimination. Upon treatment with CO, a Rh(III) with a bulky bidentate phosphine ligand led to the reductive elimination of Me–I. A less sterically bulky bidentate phosphine ligand formed two different CO adducts with no reductive elimination product observed (Figure 26A). [122] Interestingly, the group suggests that the reductive elimination of Me–I and Me–Br undergoes a non-associative S_N2 mechanism (Figure 26B), while Me–Cl eliminates in a concerted fashion via a three-centered transition state (Figure 26C). Milstein also found the rate of reductive elimination of Me–X to be -X = I > Br > Cl. [123] Similarly, Hartwig's studies on the reductive elimination of aryl halides from Pd(II) showed aryl chlorides to eliminate at the lowest rate. [124]

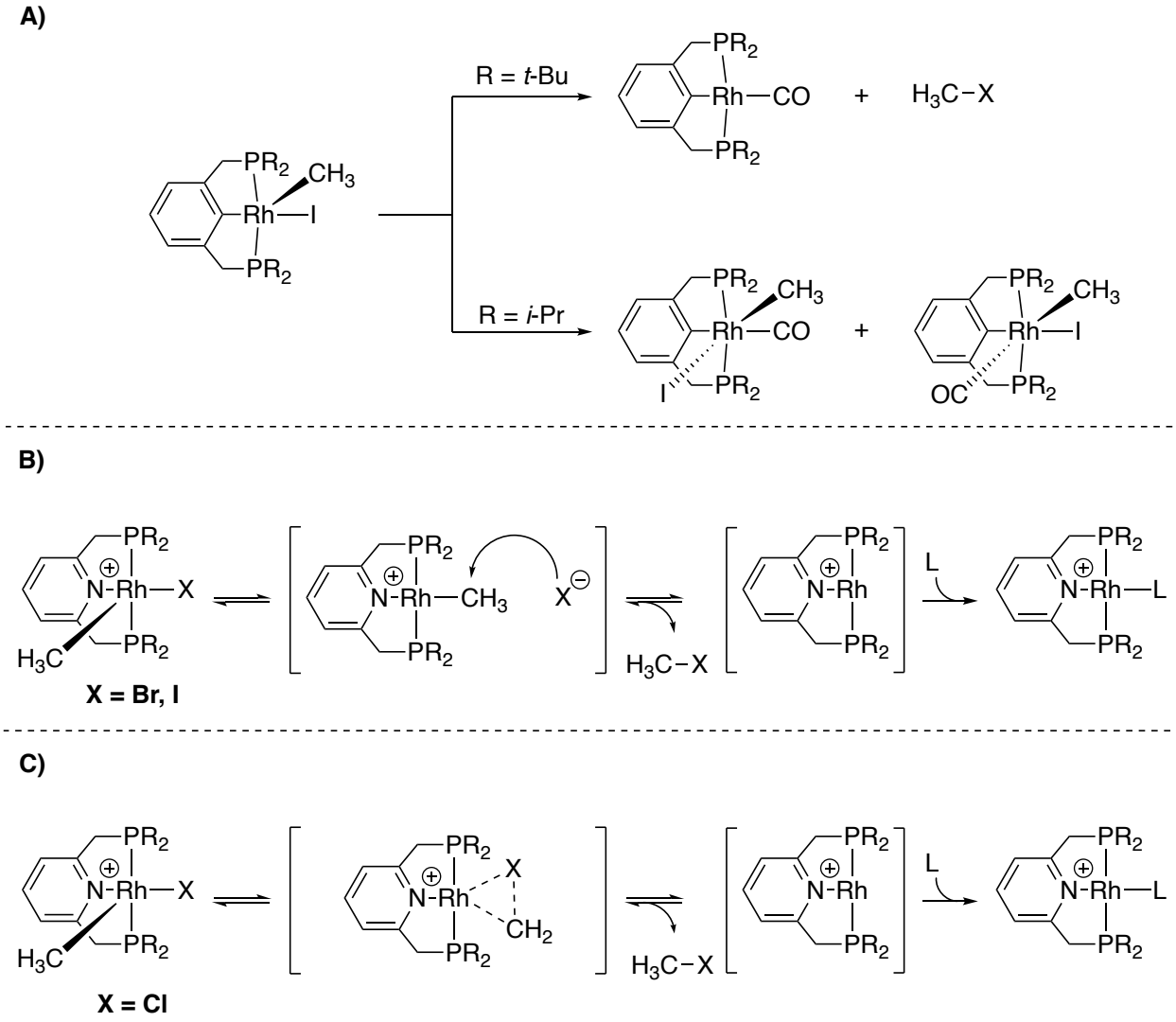


Figure 26. Reductive elimination of Me–X from a rhodium complex with a bulky bidentate phosphine ligand and less bulky bidentate phosphine ligand (A). Reductive elimination of Me–I and Me–Br via a non-associative S_N2 mechanism (B) and reductive elimination of Me–Cl via a concerted mechanism (C).

Although significantly less studied, methods for transition metal catalyzed C–X bond formations have been reported. For example, catalyzed halogen exchanges have been reported with copper[125, 126, 127, 128] and nickel (Figure 27A). [129, 130, 131, 132, 133] C–H halogenations have been reported with copper, [134, 135, 136, 137, 138, 139] cobalt, [140] ruthenium, [141, 142, 143, 144] and gold (Figure

27B). [145] The conversion of aryl triflates to aryl halides has also been reported with ruthenium (Figure 27C). [146, 147]

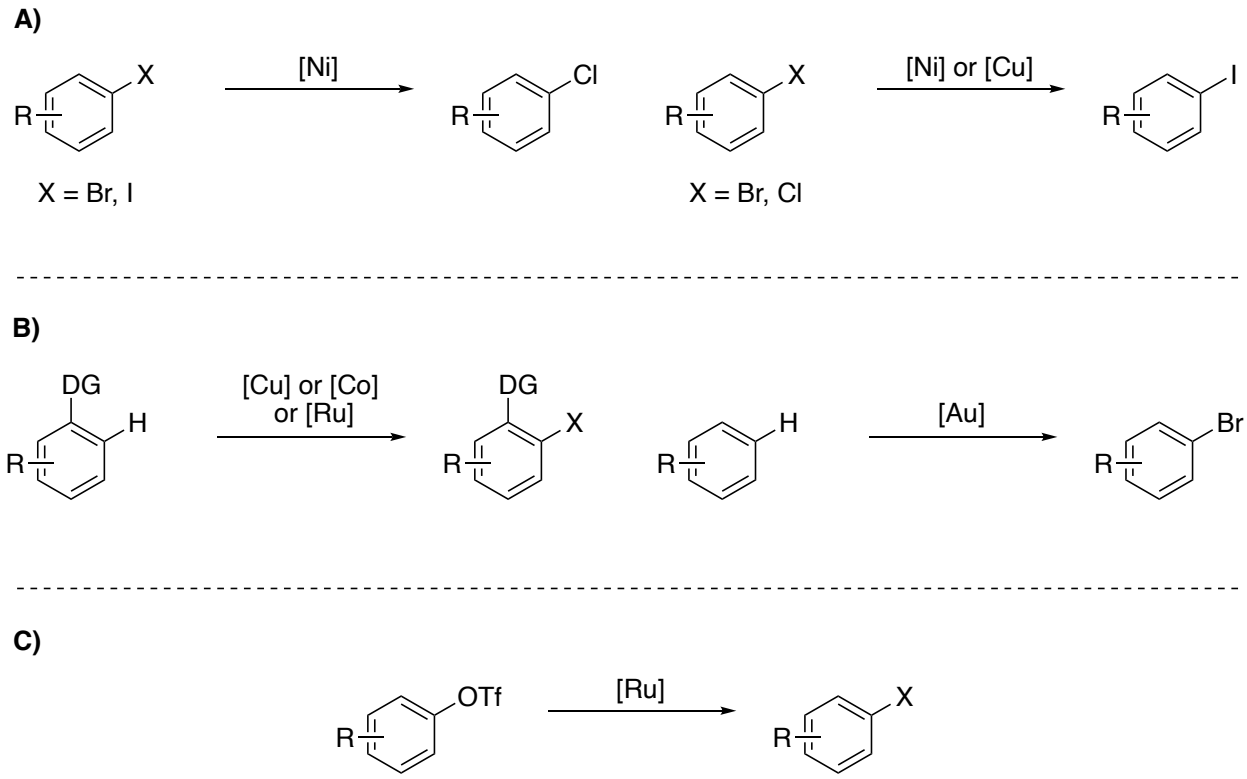


Figure 27. Transition metal-catalyzed halogen exchanges (A). Transition metal-catalyzed C–H halogenations (B). Ruthenium-catalyzed conversion of aryl triflates to aryl halides (C).

The synthesis of C–Y (Y = atom other than carbon hydrogen) via transition metal catalyzed decarbonylation has been significantly developed in recent years. [148] Decarbonylative cross-couplings have been reported for the formation of various aryl–heteroatom bonds (Figure 28A). These reports include synthesis of aryl–N, [149] aryl–CN, [150] aryl–S, [151] and aryl–P bonds. [152] Decarbonylative borylation and silylation have also been reported. [153] There are also examples of intramolecular decarbonylation for aryl–heteroatom bond synthesis (Figure 28B). Intramolecular C–Y bond formation via decarbonylation has been significantly studied for R–S bond synthesis, which has been reported using both palladium and nickel catalysts. [151, 154, 155, 156, 157, 158, 159]

Intramolecular C–CN, [150, 160] C–Si, [161] and C–O[162] bond formation via decarbonylation have also been reported.

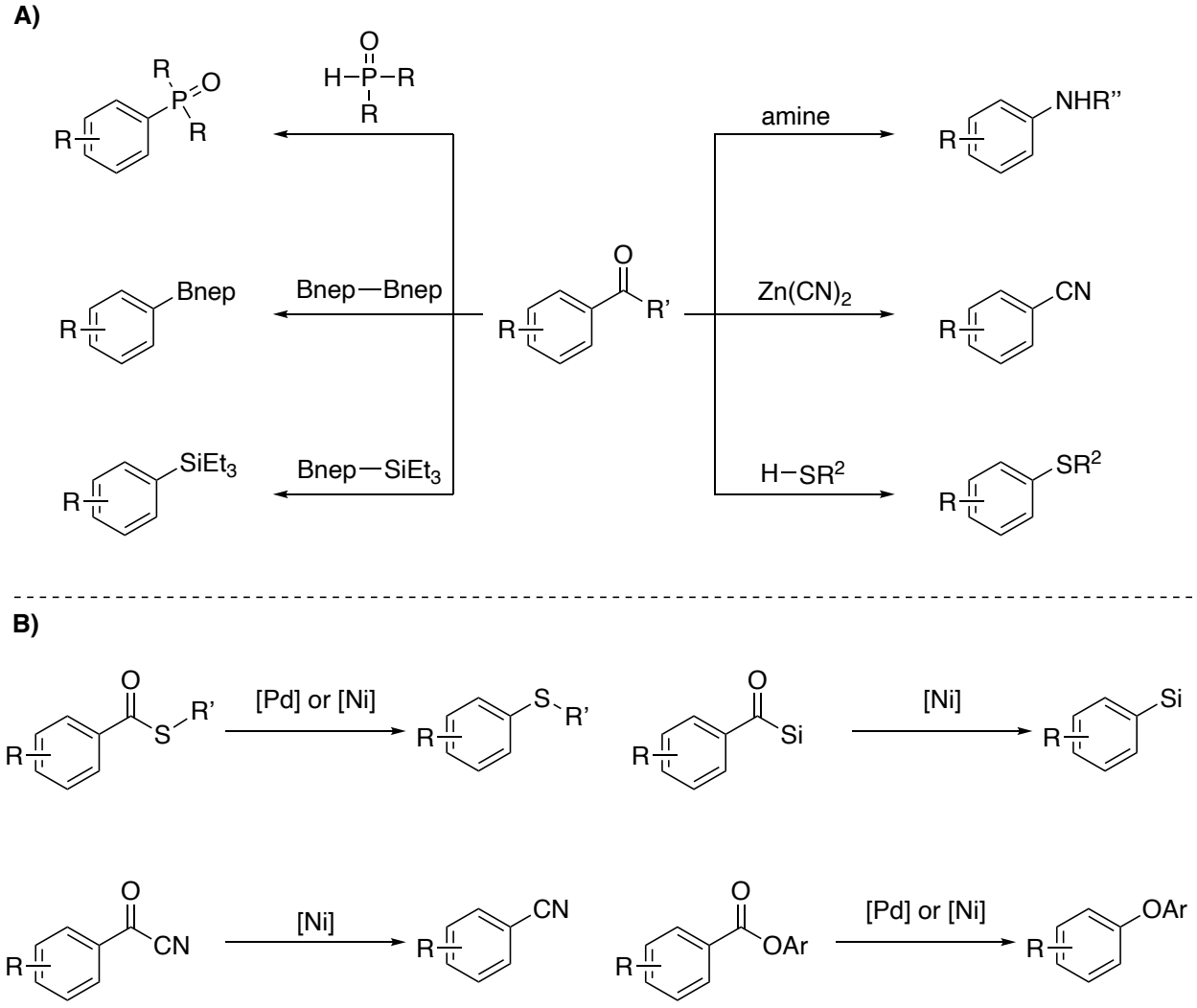


Figure 28. Examples of aryl–heteroatom synthesis via intermolecular decarbonylative cross-couplings (A) and intramolecular decarbonylations (B).

The cross-coupling decarbonylation of aroyl chlorides has been reported with various transition metal catalysts. For example, the decarbonylative reaction of aroyl chlorides with alkynes has been reported with rhodium[163] and iridium[164] catalysts (Figure 29A). Rhodium

catalyzed decarbonylative Heck coupling (Figure 29B) [165] and palladium catalyzed Sonogashira coupling (Figure 29C) [166, 167] have been reported.

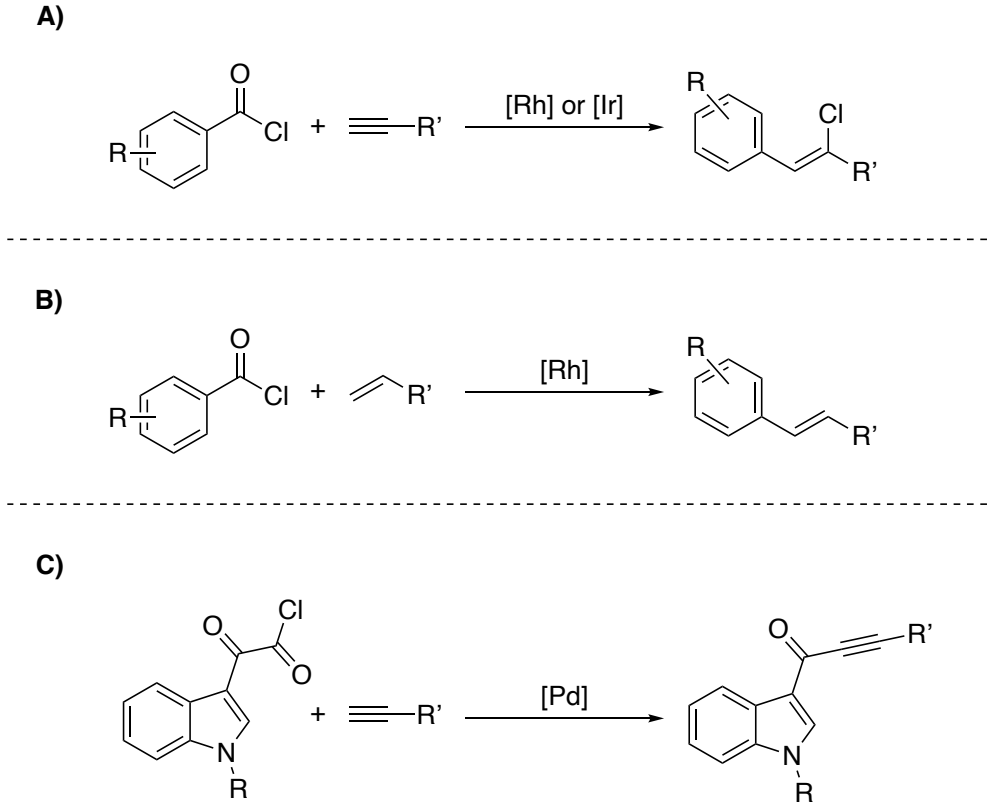


Figure 29. Rh- and Ir-catalyzed decarbonylative addition of aroyl chlorides to terminal alkynes (A). Rh-catalyzed decarbonylative Heck coupling of aroyl chlorides (B). Pd-catalyzed decarbonylative Sonogashira coupling of aroyl chlorides (C).

Although there are many examples of decarbonylative cross coupling of aroyl chlorides, intramolecular decarbonylation of aroyl chlorides for C–Cl bond synthesis has been less extensively studied. In 1982, Verbickey et al. reported the decarbonylation of aroyl chlorides using Pd/C at 360 °C (Figure 30A). [168] More recently, Sanford et al. reported a successful conversion of aroyl chlorides to aryl chlorides with a general procedure using a palladium catalyst at a much lower temperature of 130 °C (Figure 30B). [169]

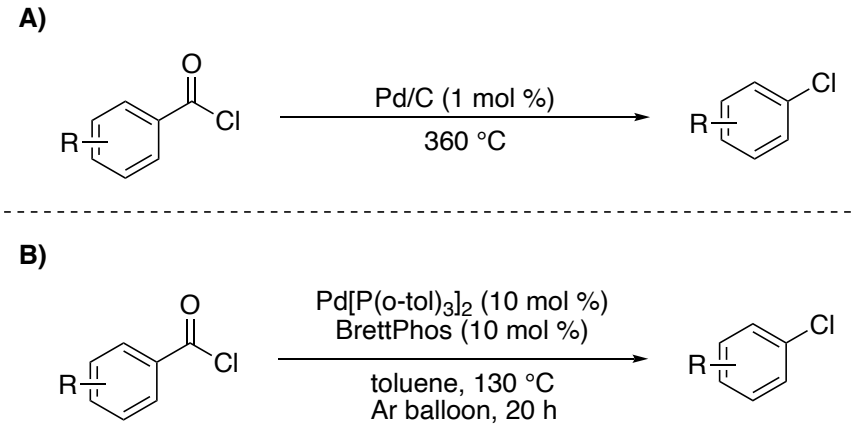


Figure 30. First Pd-catalyzed decarbonylation of aroyl chlorides (A) and conditions of Sanford's improved Pd-catalyzed method (B).

Rhodium catalyzed decarbonylation of aroyl chlorides has also been a subject of interest. However, reports of the corresponding rhodium-catalyzed process are debated in the literature. [122] In 1966, Johanan Blum proposed the decarbonylation of aroyl chlorides using Wilkinson's catalyst. [170] However, the reaction scope is rather limited and requires relatively harsh reaction conditions. The paper reported decarbonylation of aroyl chlorides using a stoichiometric amount of Wilkinson's catalyst as well as a method using a catalytic amount of Wilkinson's catalyst. The stoichiometric decarbonylation of aroyl chlorides was reported to be carried out at temperatures of 30–100 °C. The catalytic decarbonylation was reported to be carried out at temperatures of over 200 °C (Figure 31A). Blum's paper on the decarbonylation of aroyl chlorides was later reevaluated in 1981 by Kampmeier's group. [171, 172] In terms of the stoichiometric reaction, the group found that the aryl chloride Blum originally thought was being formed was actually just the aroyl chloride. It is important to note, that the aroyl chloride is not *unreacted* aroyl chloride, and it did get activated by the rhodium catalyst. They also report the catalytic reaction does indeed give the product; however, it was only tested for one substrate which gave yields

significantly lower than Blum's original report, while still requiring harsh conditions with temperatures of 200 °C or higher (Figure 31B).

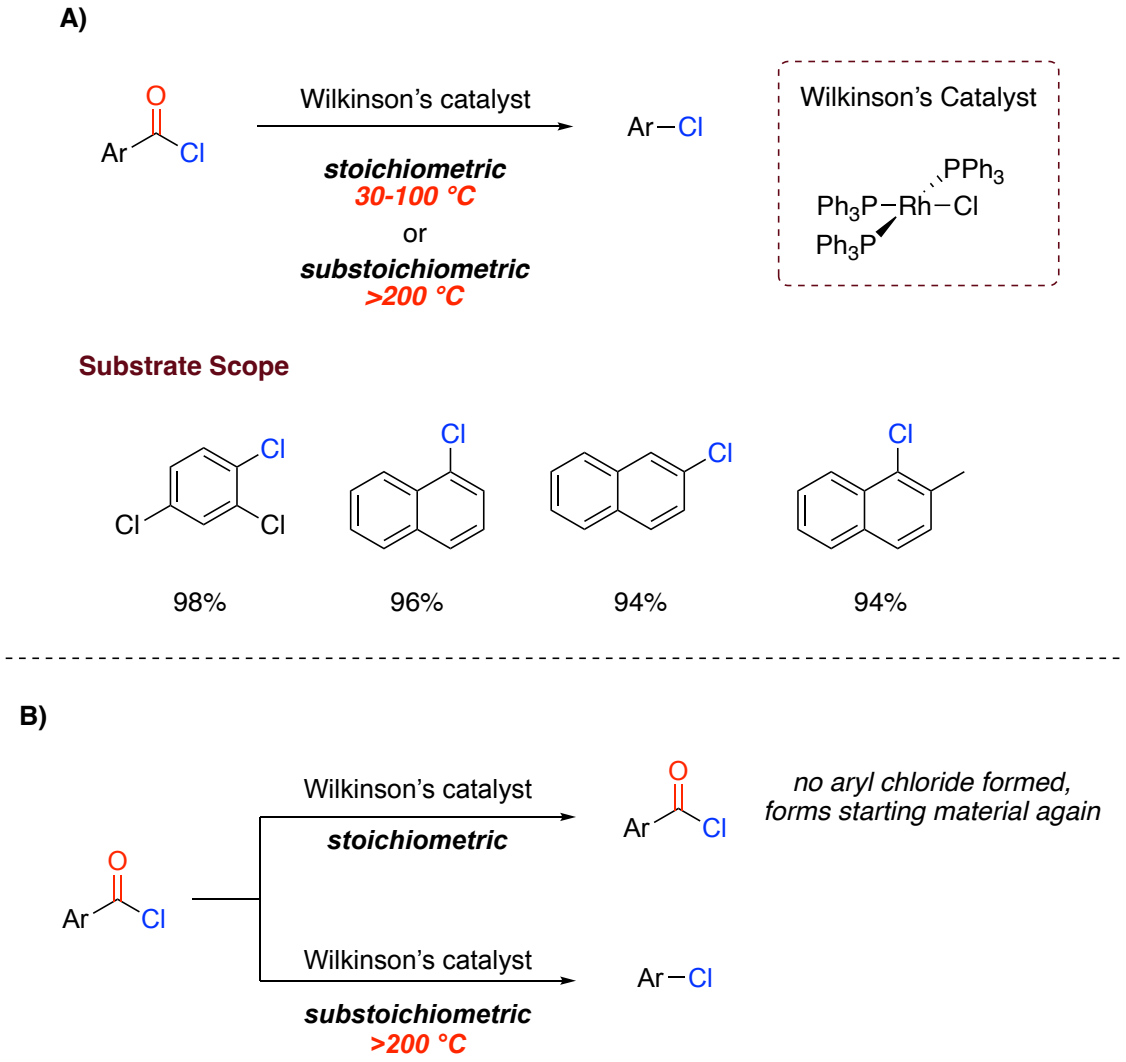


Figure 31. Decarbonylation of aroyl chlorides using Wilkinson's catalyst as reported by Blum (A). Kampmeier's reevaluation of the reaction and their findings (B).

In 1974, Stille et al. proposed a mechanism for stoichiometric and catalyzed decarbonylation of aroyl chlrorides with Wilkinson's catalyst based on Blum's report. [173, 174] The aroyl chloride and Wilkinson's catalyst forms a 5-coordinate complex **1**. Complex **1** undergoes migratory extrusion to form 6-coordinate complex **2**. Stille proposes that reductive elimination

occurs from **2** to form the aryl chloride and a square planar complex **3**, a stable complex, [175] and therefore, at very high temperatures, another equivalent would react with **3** and form **2** and go through the cycle again (Figure 32A). However, after Kampmeier's group's thorough examination of the reaction, they propose a different mechanism to explain their findings. [171, 172] Complex **1** is formed from the aroyl chloride and catalyst. After migratory extrusion, complex **2** releases free CO to form complex **4**. The increased concentration of free CO shifts the equilibrium, and **1** reacts with CO to form complex **3** and the original aroyl chloride. Therefore, in stoichiometric conditions at low temperature, the aryl chloride is not formed. Reductive elimination from **4** can occur at high temperatures (Figure 32B). To the best of our knowledge, this work has not been significantly expanded on and there are no general methods for the rhodium catalyzed decarbonylation of aroyl chlorides.

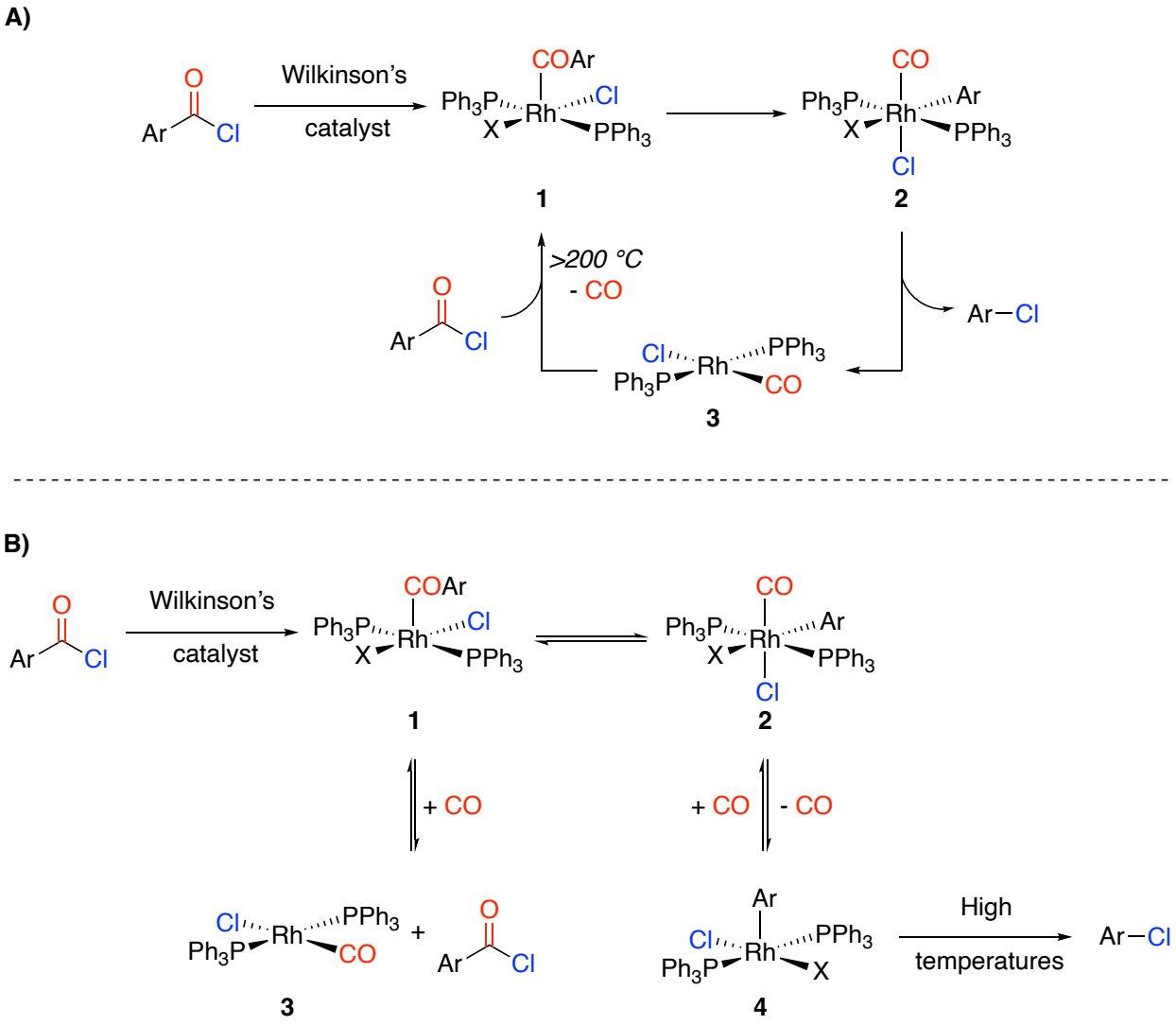


Figure 32. Stille's mechanistic proposal on Blum's conditions for decarbonylation of aroyl chlorides (A). Kampeier's mechanistic proposal after re-evaluation of Blum's report (B).

Our goal was to develop a method for the decarbonylation of aroyl chlorides to synthesize new aryl–Cl bonds using a rhodium catalyst (Figure 33). Aroyl chlorides are easily accessible starting materials which make them an excellent option for the synthesis of regioselective aryl–Cl bonds. Aroyl chlorides are cheap and easily synthesized using simple procedures with quantitative yields.

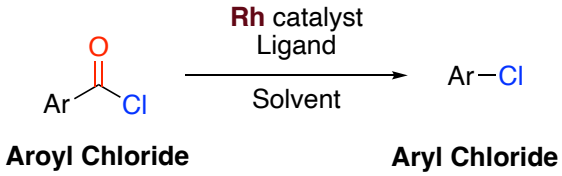
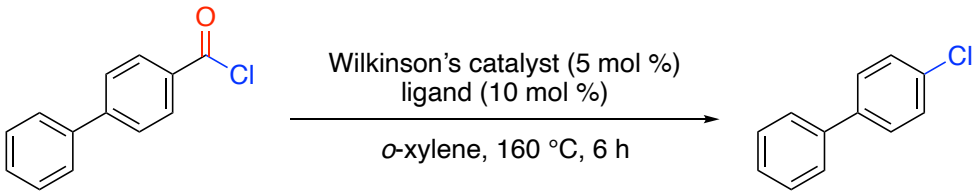


Figure 33. Rhodium-catalyzed decarbonylation of aroyl chlorides.

We began our screening with Wilkinson's catalyst and biphenyl-4-carbonyl chloride as our starting material (Table 1). Different phosphine ligands were screened. Our results were quantified via GC analysis using dodecane as the internal standard. Monodentate ligands gave low yields of decarbonylated product (Entries 1-2). Bidentate ligand DPPP decarbonylated the aroyl chloride in 5% yield (Entry 3). Other bidentate ligands such as DIPAMP and XantPhos slightly increased the product yield (Entries 4-5). *Rac*-BINAP increased the yield to 60% (Entry 6). In accordance to Milstein's studies on the reductive elimination of Me–Cl from Rh(III) complexes, we increased the steric bulk of the ligand. [122] (*S*)-Tol-BINAP and (*S*)-Xyl-BINAP provided an increased yield of 76% and 71% yield respectively (Entries 7-8).

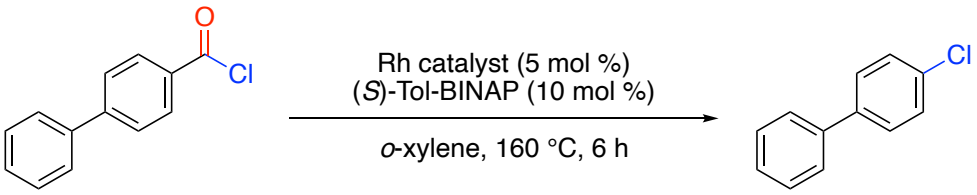


Entry	Ligand	Yield **1b** (%)[a]
1	P(*t*-Bu)$_3$	0
2	BrettPhos	2
3	DPPP	5
4	DIPAMP	6
5	XantPhos	20
6	*rac*-BINAP	60
7	**(*S*)-Tol-BINAP**	**76**
8	(*S*)-Xyl-BINAP	71

[a] GC yields.

Table 1. Ligand screening for rhodium-catalyzed decarbonylation of aroyl chlorides.

(S)-Tol-BINAP was then screened against different rhodium catalysts (Table 2). Rh(I) catalysts showed low yields of decarbonylated product (Entries 1-4). Interestingly, (*S*)-Tol-BINAP with a ($RhBr(PPh_3)_3$), decreased the yield significantly to 48% (Entry 5). Rh(II) catalysts (Entries 6-7) also gave low yields of product. When an Rh(III) catalyst, $RhCl_3$, was used as the catalyst with PPh_3 as the ligand, the product was found in trace yields (Entry 8), but with (*S*)-Tol-BINAP as ligand, the yield increased to 15%.



1a **1b**

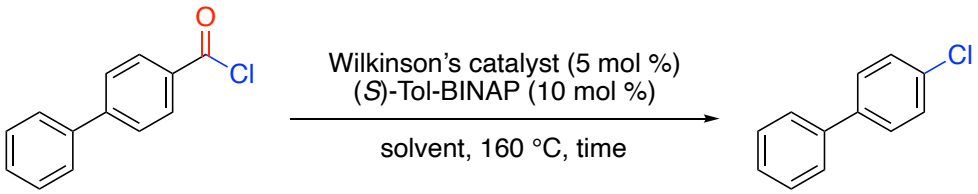
Entry	Catalyst	Yield **1b** (%)[a]
1	$[Rh(nbd)Cl]_2$	15
2	$[Rh(coe)_2Cl]_2$	20
3	$Rh(nbd)_2BF_4$	26
4	$[Rh(cod)Cl]_2$	31
5	$RhBr(PPh_3)_3$	48
6	$[(CF_3COO)_2Rh]_2$	2
7	$Rh_2(OAc)_4$	15
8[b]	$RhCl_3$	<1
9	$RhCl_3$	15

[a] GC yields. [b] PPh_3 as ligand.

Table 2. Catalyst screening of rhodium-catalyzed decarbonylation of aroyl chlorides.

Solvent and time screening were also conducted (Table 3). Toluene provided the product in 60% yield (Entry 1). Interestingly, 1,4-dioxane decarbonylated the starting material in 55% yield (Entry 2). THF decreased the yield significantly (Entry 3). When benzene was used with no ligand present in the system, similar to the conditions Blum originally reported, [170] the yield of product was only 3% (Entry 4). Therefore, *o*-xylene is the optimal solvent. Full conversion of

starting material is achieved at 6 hours (Entry 6), at 3 hours, the yield is 57% with leftover starting material (Entry 5). If the reaction is allowed to run longer than 6 hours, the yield diminishes (Entries 7-9).



1a **1b**

Entry	Solvent	Time (h)	Yield **1b** (%)[a]
1	Toluene	6	60
2	1,4-dioxane	6	55
3	THF	6	16
4[b]	benzene	1	3
5	*o*-xylene	3	57
6	***o*-xylene**	**6**	**76**
7	*o*-xylene	9	55
8	*o*-xylene	12	49
9	*o*-xylene	24	13

[a] GC yields. [b] No ligand

Table 3. Solvent and time screening for rhodium-catalyzed decarbonylation of aroyl chlorides.

The optimal conditions for the decarbonylation of **1a** to **1b** were found to be Wilkinson's catalyst (5 mol %), (*S*)-Tol-BINAP (10 mol %), in *o*-xylene at 160 °C for 6 hours (Figure 34A). These conditions provided full conversion of the starting material. The product was found in 76% GC yield and a protonated byproduct, biphenyl (1c), was found in 20% GC yield (Figure 34B).

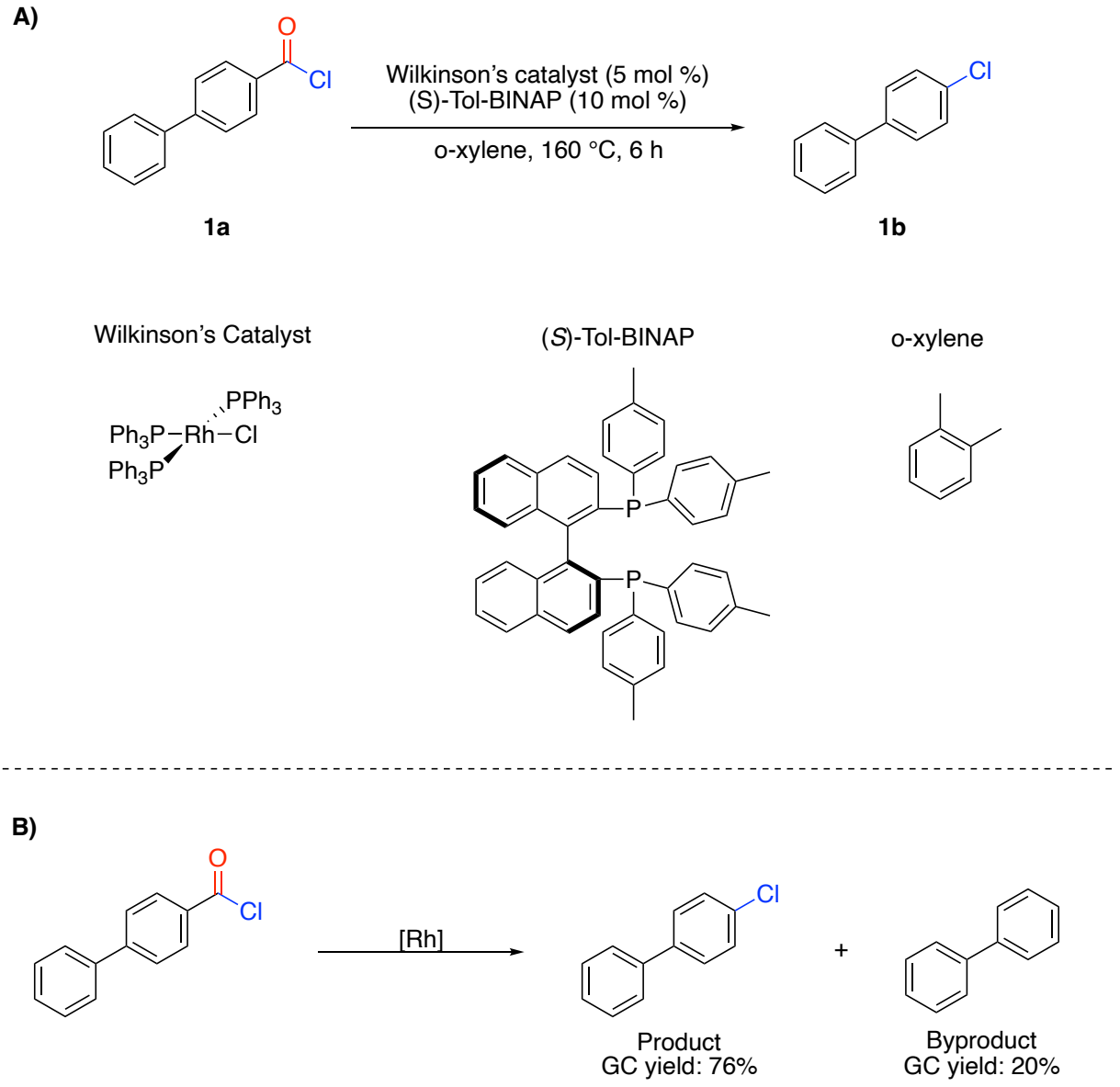


Figure 34. Optimized conditions for the rhodium catalyzed decarbonylation of aroyl chlorides (A). GC yield of product and byproduct after decarbonylation of aroyl chloride (B).

Through a series of control reactions, we confirmed the rhodium complex is indeed catalyzing the reaction. Without the rhodium catalyst in the solution, we did not achieve any decarbonylated product, confirming there is no decarbonylation occurring exclusively through

heat (Figure 35A). Without the optimal ligand, our yield decreased significantly to 33% (Figure 35B).

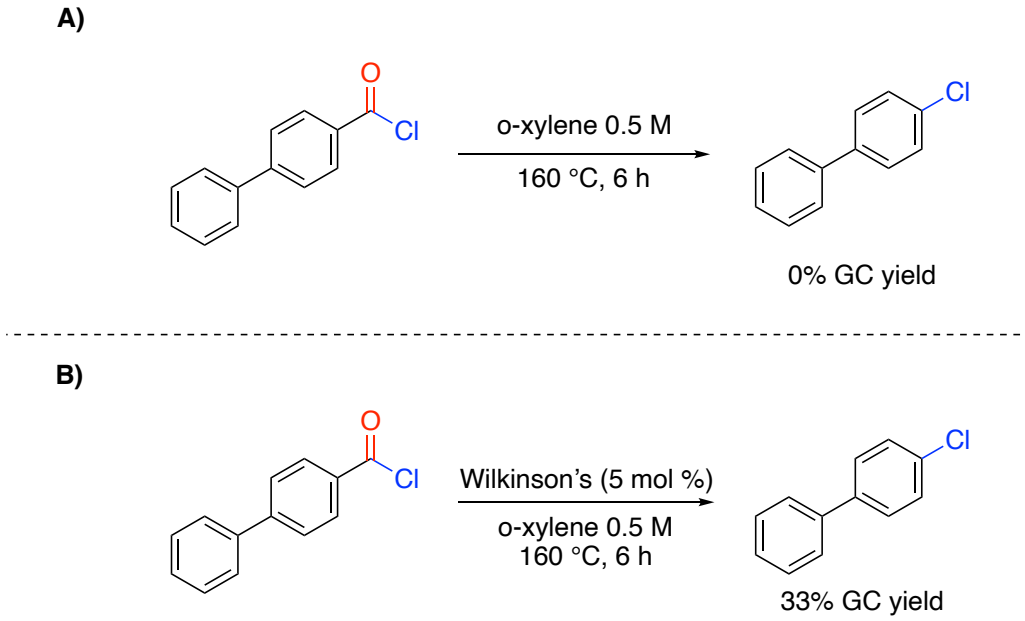


Figure 35. Control reactions without catalyst (A) and without ligand (B).

Most aroyl chlorides are cheap to purchase or are easily synthesized from benzoic acids. Using $(COCl)_2$, we synthesized our starting materials. All starting materials were synthesized in excellent yields and confirmed with GCMS analysis and $^{1}H/^{13}C$ NMR (Figure 36A). Wilkinson's catalyst was prepared using reported procedures with $RhCl_3 \bullet XH_2O$ and PPh_3 and confirmed with $^{1}H/^{13}C$ NMR (Figure 36B). [176]

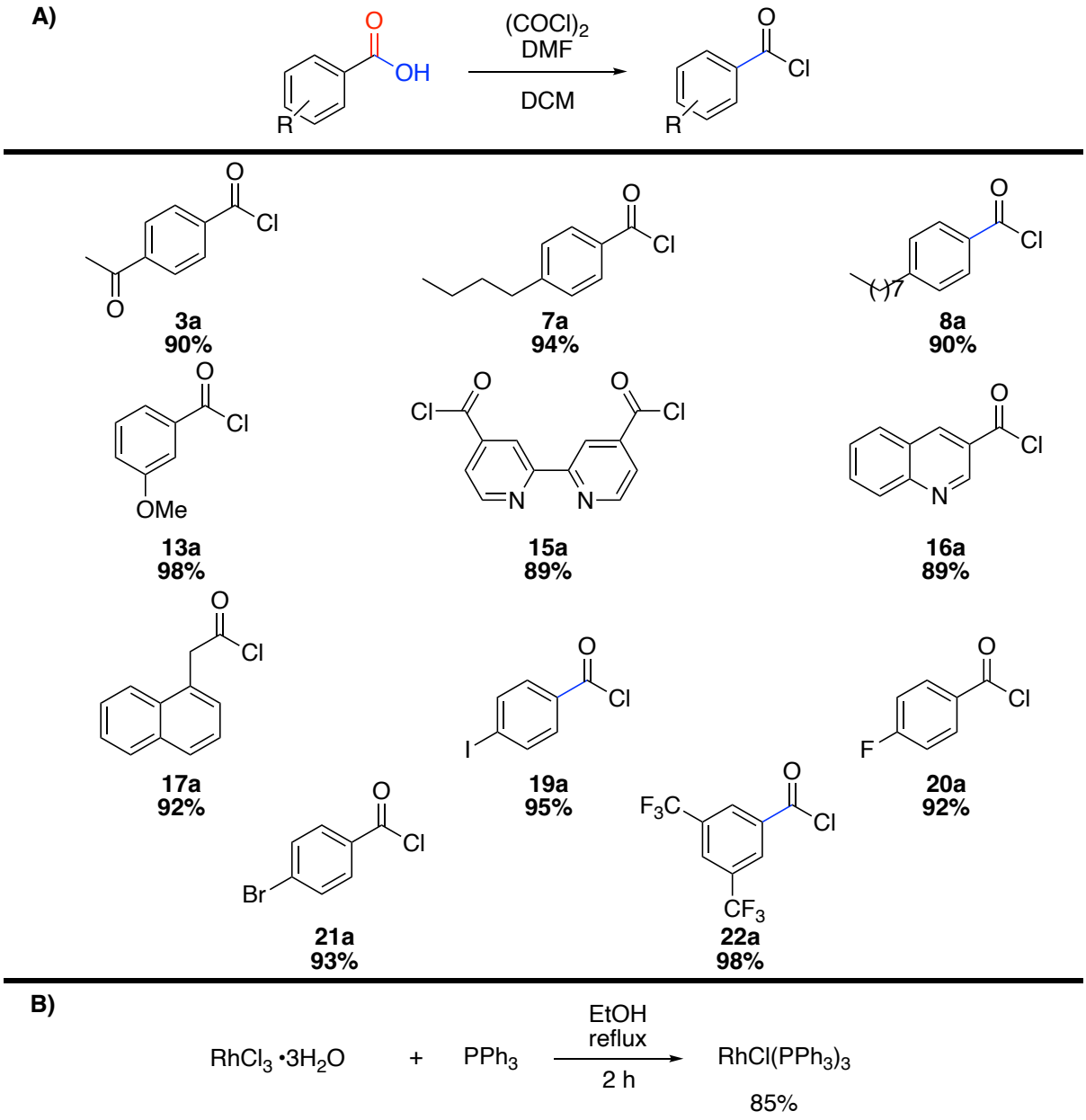
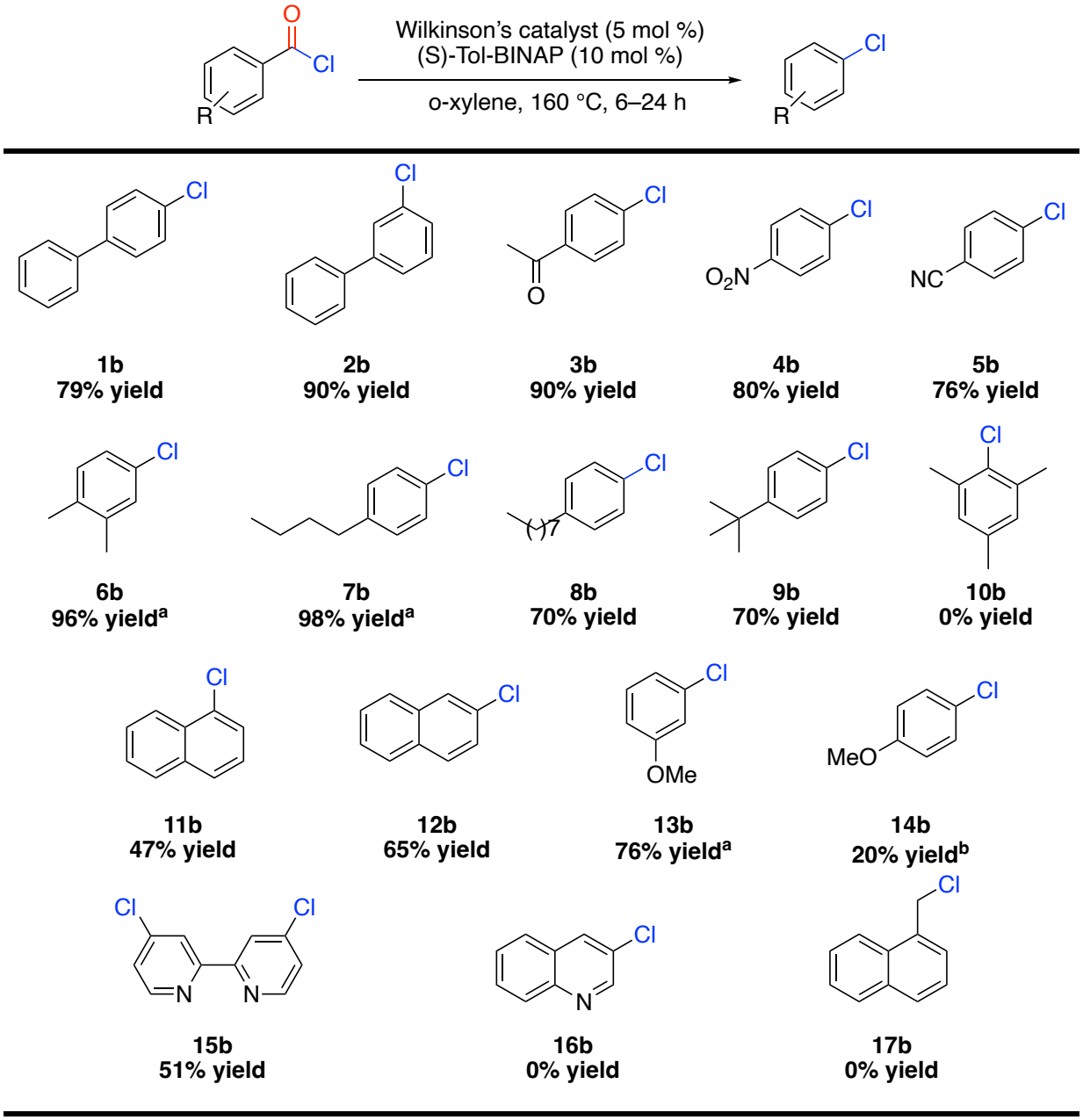


Figure 36. Synthesized aroyl chlorides (A) and synthesis of Wilkinson's catalyst (B).

With the optimized reaction conditions in hand, we investigated the scope of the reaction (Figure 37). We confirmed our previous GC yield calculations and isolated 4-chloro-biphenyl (**1b**) in 79% yield. The product was confirmed and characterized with GCMS analysis and $^{1}H/^{13}C$ NMR. **2b** was isolated in 90% yield. Aryl chlorides with electron withdrawing groups

were also isolated in good yields (**3b-5b**). Alkyl-substituted substrates (**6b-9b**) were produced in good yields, except for **10b** which is likely due to steric hindrance. Naphthalenes **11b** and **12b** were produced in 47% and 65% yield, respectively. Since oxidative addition occurs when with an electron deficient electrophile, it made sense to see strongly electron donating groups, such as the methoxy group on **14b** produced in low yields. **13b**, with the methoxy group on the *meta*-position, gave a 76% NMR yield. **15b**, which requires conversion of two aroyl chlorides, was produced in 51% yield. Unfortunately, there was no yield for 3-chloroquinoline (**16b**) or at the benzyl position in naphthalene (**17b**).

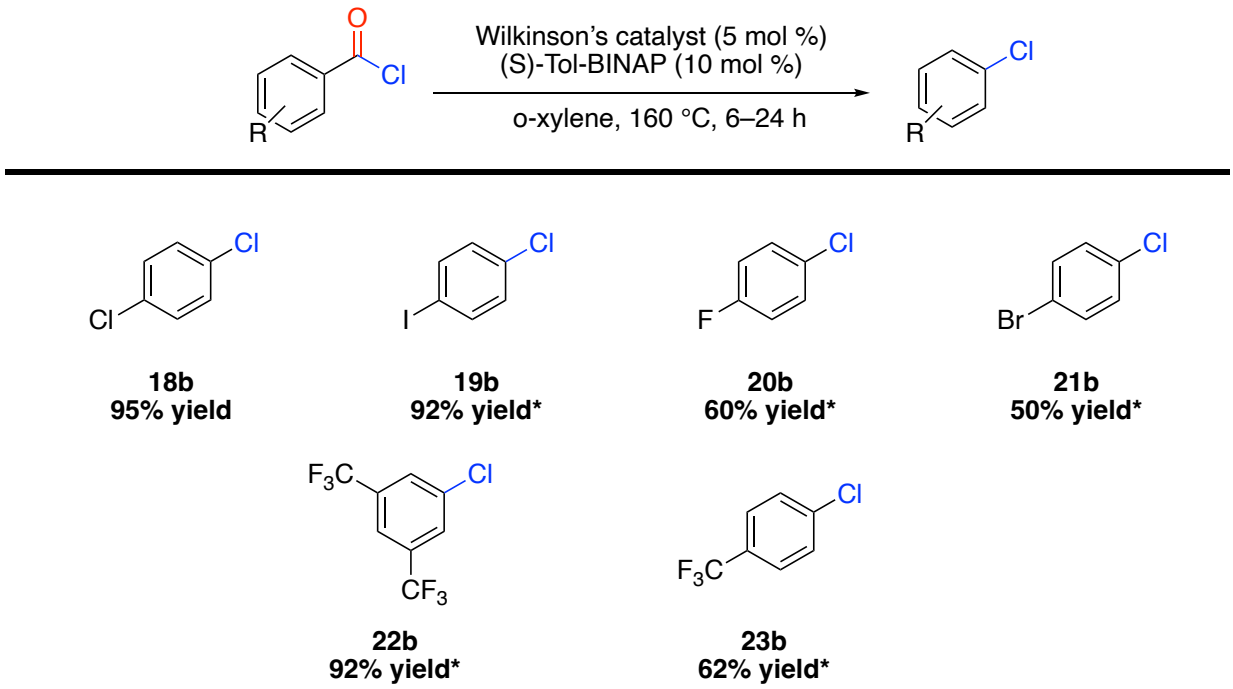


[a] NMR yield. [b] GC yield.

Figure 37. Substrate scope for the rhodium-catalyzed decarbonylation of aroyl chlorides.

We then proceeded to examine the applicability of the conditions to halogenated substrates (Figure 38). Since Pd will often activate aryl halides, using a rhodium catalyst could avoid this by selectively activating the carbonyl position. We were delighted to see that conversion to dichlorobenzene gave a 95% yield (**18b**). Substrates bearing halogens such as

iodine, fluorine, and bromine, gave GC yields of 92%, 60%, and 50% yield (**19b-21b**). Trifluoromethyl-substituted chlorobenzenes are also accessible in modest to excellent yields (**22b-23b**).

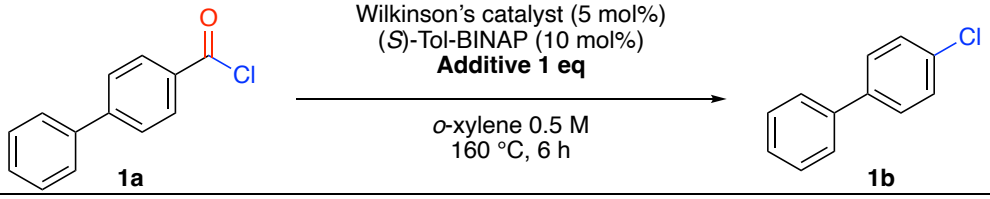


* GC yield

Figure 38. Substrate scope for the rhodium-catalyzed decarbonylation of halogenated aroyl chlorides.

In order to demonstrate the robustness of our conditions, we conducted experiments using Glorius's method of testing new methodologies.[177] Complex pharmaceutical motifs can interfere with a reaction making it an unfavorable procedure, and increased impurities can hinder a reaction significantly. Glorius's method tests a reaction's tolerance to various conditions by introducing equivalents of various additives that can potentially inhibit reactivity in order to demonstrate the applicability of the reaction in those conditions. Using GC analysis, we quantified the yield of desired product and yield of recovered additive to see how much of it was consumed in any side reaction that might be hindering the synthesis of desired aryl chloride

product (Table 4). 5-decyne did not significantly impact the yield of decarbonylated product. Sulfolane increased the decarbonylated product to 92%. Cycloheptanone and (*E*)-stilbene slightly affected the reaction giving a product yield of 52% and 45% respectively.



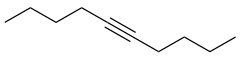
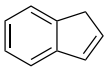
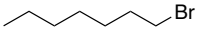
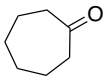
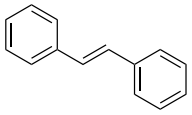
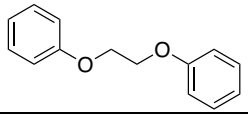
Additive	GC yield 1b (%)	Additive Recovered (% GC yield)	Additive	GC yield 1b (%)	Additive Recovered (% GC yield)
	57	77		38	94
	92	60		6	24
	52	85		45	99
	33	14		30	96

Table 4. Robustness screening.

We evaluated the utility of the reaction by performing it on a gram scale. Using 4-nitro-benzoyl chloride as our starting material. Our reaction was isolated in 89% crude yield containing TPPO as a byproduct (Figure 39A). Removal of TPPO on a larger scale proved to be difficult. We used a method of removing TPPO developed by Weix et al. by adding $ZnCl_2$ in ethanol to form a TPPO zinc salt adduct which is easily filtered out (Figure 39B). [178] Our pure product yield was isolated in 77% which is comparable to the 80% yield we achieved on a much smaller scale (Figure 39C).

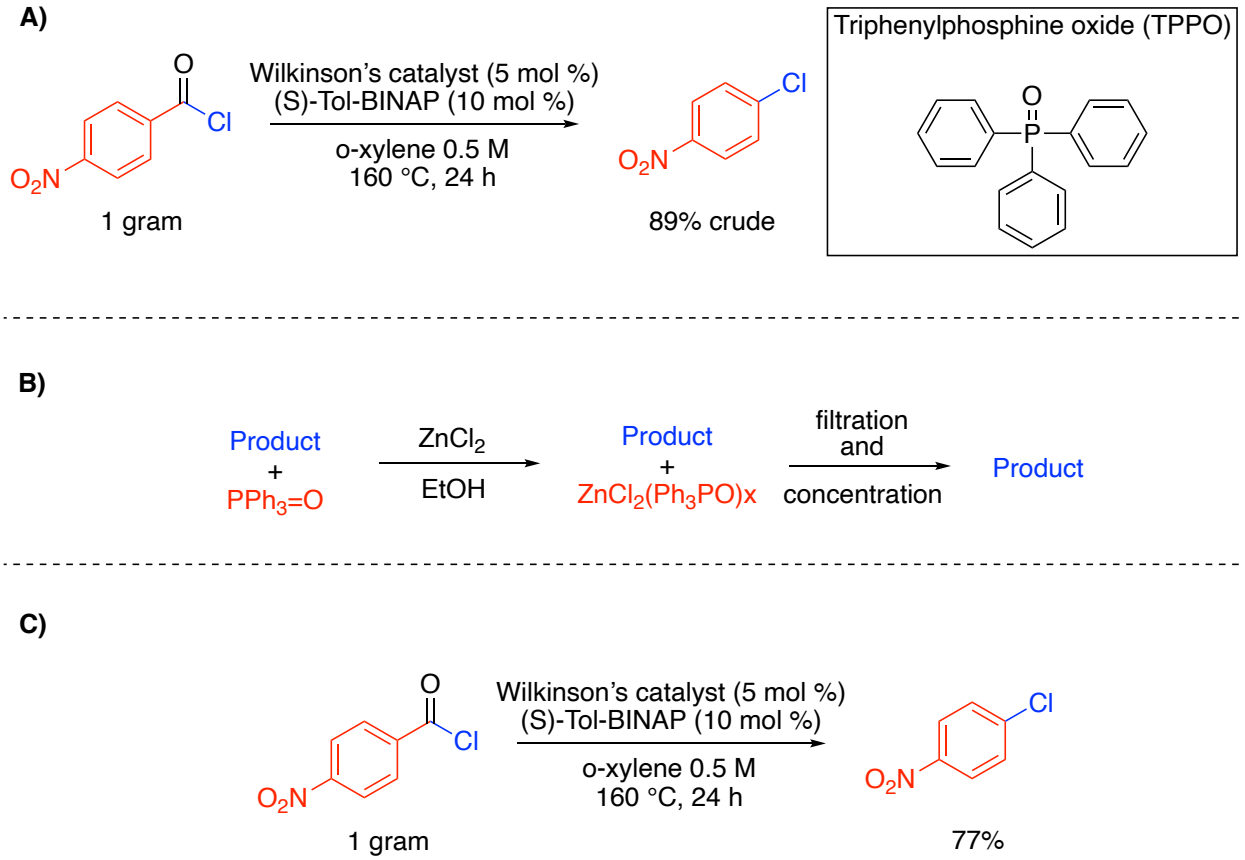


Figure 39. Crude yield of gram-scale decarbonylation of 4-nitrobenzoyl chloride (A). Procedure for removal of TPPO (B). Final yield of gram-scale decarbonylation of 4-nitrobenzoyl chloride (C).

A plausible catalytic cycle is illustrated in Figure 40. Based on previous computational studies on rhodium catalyzed decarbonylations, [175] we propose that the catalytic cycle begins with a coordinatively unsaturated d^8 rhodium complex **I**. This species subsequently undergoes oxidative addition to the starting material, the aroyl chloride, to form an Rh(III) intermediate **II**. **II** can then undergo migratory extrusion to form intermediate **III**. Previous reports suggest that the 6-coordinate complex **III** would reduce to form the desired aryl chloride; however, Milstein's studies suggest reductive elimination of R–X from rhodium is more facile from a 5-coordinate complex. [123] Therefore, we propose that decarbonylation occurs prior to reductive elimination

and forms a 5-coordinate square pyramidal Rh(III) complex **IV**. Reductive elimination of this 5-coordinate Rh(III) complex forms the final aryl chloride product and regenerates Rh(I) complex **I**.

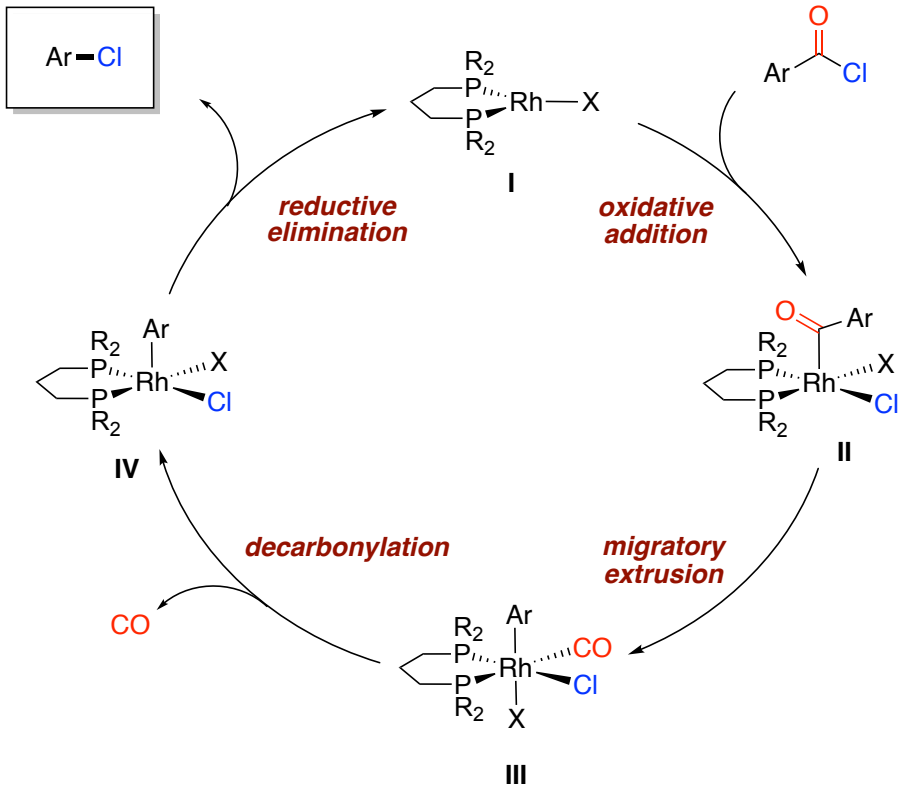


Figure 40. Proposed mechanism for the rhodium-catalyzed decarbonylation of aroyl chlorides.

In conclusion, we describe a Rh-catalyzed decarbonylation of aroyl chlorides. By introducing a bulky ligand, (*S*)-Tol-BINAP, the reductive elimination of aryl chlorides from Rh(III) was achieved. The catalytic system tolerates various functional groups at a lower temperature than previously reported.[11,12] The method allows the use of inexpensive and easily synthesized aroyl chlorides. This work opens the door for further investigations, particularly, into the mechanism which could lead to new discoveries in rhodium catalysis, decarbonylation reactions, as well as reductive eliminations of R–X bonds. Cis/trans effects, as well as bite angle

and cone angle effects of the ligand on the kinetic and thermodynamics in the reaction can also provide useful information for future development. The enantioselectivity of the reaction is also worth exploring, for example, in the synthesis of axially chiral aryl chlorides or for the decarbonylation of aliphatic acid chlorides.

APPENDIX A

SUPPLEMENTARY

GENERAL INFORMATION

^{1}H NMR spectra were recorded using either a Varian INOVA 500 (500 MHz spectrometer) or a Bruker AVANCE 500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ^{1}H NMR ($CDCl_3$: 7.26 ppm). Data is reported in the following format: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), integration. ^{13}C NMR spectra were recorded using either a Varian INOVA 500 (125 MHz spectrometer) or a Bruker AVANCE 500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ^{13}C NMR ($CDCl_3$: 77.16 ppm). GC analyses were performed on a Shimadzu GC-2010 Plus. Melting points were determined with a VWR Basic Melting Point Apparatus.

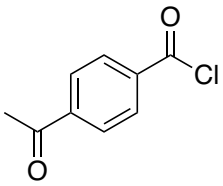
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. All dry solvents (DCM, DMF, Toluene, *o*-xylene) were purchased from Acros and used without further purification. Phosphine ligands were purchased from Strem Chemicals, Inc. and used without further purification. All other reagents were purchased from Acros Organics, Alfa-Aesar, AK Scientific, Fisher, Aldrich etc. and used without further purification.

SYNTHESIS OF ACID CHLORIDES

General Procedure for the Synthesis of Aroyl Chlorides

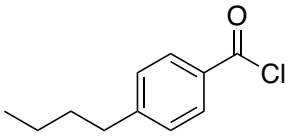
A round bottomed flask with a stir bar was charged with carboxylic acid (1 g, 1.0 equiv), anhydrous DCM (0.5 M), and oxalyl chloride (1.2 equiv) under nitrogen atmosphere at 0 °C. DMF (1 drop) was added to the solution. The reaction mixture was stirred overnight at room temperature. The solvent and unreacted oxalyl chloride were removed under reduced pressure to afford the acid chloride. The crude residue was filtered through a sintered funnel. The pellet was washed with EtOAc. The filtrate was then evaporated *in vacuo*. The resulting aroyl chloride was characterized and used without further purification.

4-acetylbenzoyl chloride (3a)



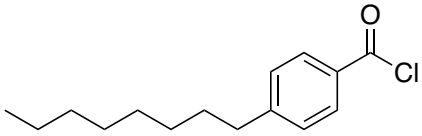
Crude yield: 90%; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.24 (d, *J* = 8.10 Hz, 2H), 8.09 (d, *J* = 8.00 Hz, 2H), 2.69 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.95, 167.88, 141.76, 136.54, 131.53, 128.60, 27.00.

4-butylbenzoyl chloride (7a):



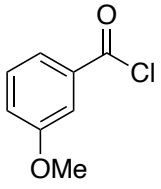
Yield: 94%; Physical appearance light yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): 8.04 (d, *J*= 8.35 Hz, 2H), 7.33 (d, *J*= 8.35 Hz, 2H), 2.72 (t, *J*= 7.7 Hz, 2H), 1.68-162 (m, 2H), 1.42- 1.35 (m, 2H), 0.96 (t, *J*= 7.35 Hz, 3H) δ ; ^{13}C NMR ($CDCl_3$, 125 MHz): δ 168.13, 151.66, 131.64, 130.76, 129.05, 35.79, 33.05, 22.30, 13.87.

4-octylbenzoyl chloride (8a):



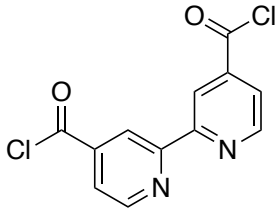
Crude yield: 90%; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.05 (d, *J* = 7.65 Hz, 2H), 7.33 (d, *J* = 7.75 Hz, 2H), 2.71 (t, *J* = 7.7 Hz, 2H), 1.69–1.63 (m, 2H), 1.35–1.29 (m, 10H), 0.91 (t, *J* = 6.95 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 168.12, 151.17, 131.64, 130.75, 129.05, 36.10, 31.85, 30.95, 29.39, 29.24, 29.21, 22.66, 14.10.

3-methoxybenzoyl chloride (13a):



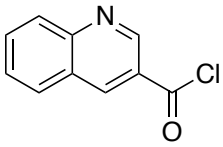
Yield: 98 %; Physical appearance light yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.75 (d, *J*= 7.75 Hz, 1H), 7.61 (s, 1H), 7.44 (t, *J*= 6.25 Hz, 1H), 7.24 (d, *J*= 8.3 Hz, 1H), 3.89 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 126 MHz): δ 168.29, 159.84, 134.46, 129.88, 124.13, 121.95, 115.34, 55.61.

[2,2'-bipyridine]-4,4'-dicarbonyl dichloride (15a):



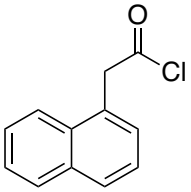
Crude yield: 89%; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.11 (s, 2H), 8.99 (s, 2H), 8.00 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 167.87, 156.38, 150.71, 141.65, 123.90, 121.53.

quinoline-3-carbonyl chloride (16a):



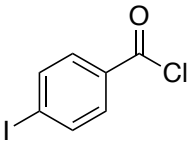
Crude yield: 89%; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.65 (s, 1H), 9.52 (s, 1H), 8.96 (d, J = 8.45 Hz, 1H), 8.35 (d, J = 8.2, 1H), 8.29 (t, J = 7.55 Hz, 1H), 8.06 (t, J = 7.55 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.17, 147.86, 143.93, 140.55, 138.38, 131.89, 130.50, 127.85, 126.98, 123.26.

1-Naphthylacetyl chloride (17a):



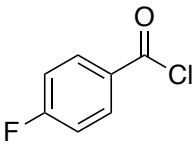
Crude yield: 92%; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.94–7.90 (m, 3H), 7.63–7.55 (m, 2H), 7.52–7.46 (m, 2H), 4.61 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.86, 133.88, 131.16, 129.31, 129.02, 128.87, 127.92, 127.01, 126.20, 125.48, 123.19, 50.88.

4-iodobenzoyl chloride (19a):



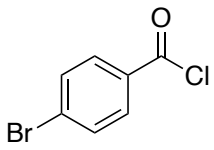
Crude yield: 95%; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.91 (d, J = 8.65 Hz, 2H), 7.83 (d, J = 8.65 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 168.04, 138.43, 132.71, 132.38, 104.27.

4-fluorobenzoyl chloride (20a):



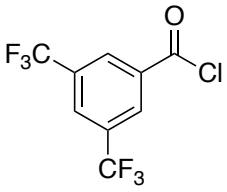
Crude yield: 92%; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.19–8.16 (m, 2H), 7.23–7.20 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 168.16, 167.00, 166.10, 134.26, 116.41.

4-bromobenzoyl chloride (21a):



Crude yield: 93%; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.99 (d, J = 8.7 Hz, 2H), 7.68 (d, J = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 167.55, 132.61, 132.39, 132.07, 131.18.

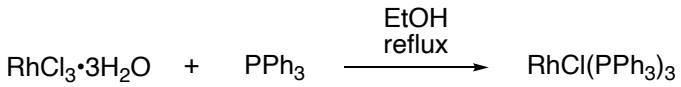
3,5-bis(trifluoromethyl)benzoyl chloride (22a):



Crude yield: 98 %; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.59 (s, 2H), 8.22 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.31, 135.28, 133.18, 130.93, 128.43, 125.69, 123.51, 121.34, 119.17.

SYNTHESIS OF ARYL CHLORIDES

General Procedure for the Synthesis of Wilkinson's Catalyst[176]



An oven dried 250 mL round-bottom flask with a magnetic stir-bar was charged with ethanol (100 mL) and triphenylphosphine (3 g, 11.5 mmol), was placed in an oil bath under nitrogen atmosphere, and the solution was heated to just below its boiling point (78 °C). Hydrated rhodium(III) chloride (0.5 g, 2 mmol) was added to the solution before the solution reached reflux. The resulting solution was heated to reflux and allowed to react for 2 hours. While hot, the resulting burgundy-red crystals were collected by filtration through sintered funnel and washed with diethyl ether (3 x 20.0 mL). The crystals were then dried *in vacuo* to provide the desired catalyst.

Optimization Studies for Rh-Catalyzed Decarbonylation

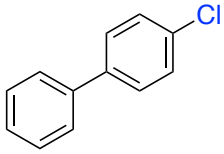
In an argon-filled glove box, acid chloride **1a** (1 equiv, 0.2 mmol) was weighed into an oven dried 3 mL pressure vial equipped with a magnetic stir-bar. Rh catalyst, ligand, and solvent (0.5 M) were added. The pressure vial was sealed with a cap and removed from the glovebox. The reaction mixture was allowed to stir at designated temperature. The reaction mixture was cooled to room

temperature and the crude mixture was filtered through a silica plug and analyzed by GC using undecane or dodecane as a standard. Results are summarized in Tables 1 and 2.

General Procedure for Rh-Catalyzed Decarbonylation of Aroyl Chlorides

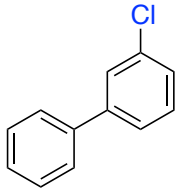
In an argon-filled glove box, an oven-dried 15 mL pressure vessel, equipped with a magnetic stir-bar, was charged with Wilkinson's catalyst (0.02 mmol, 5 mol%) and (*S*)-Tol-BINAP (0.04 mmol, 10 mol%). The aroyl chloride (0.4 mmol, 1.0 equiv.) and *o*-xylene (0.8 mL, 0.5 M) were added via syringe. The pressure vessel was sealed with a polypropylene cap and removed from the glove box. The reaction mixture was then allowed to stir at 160 °C for 3-24 h. Upon cooling to room temperature, the reaction mixture was diluted with EtOAc and the resulting solution was filtered through a silica plug and concentrated under reduced pressure. The products were purified via column chromatography on silica gel (pentane) or (hexane/EtOAc). The solvent was evaporated *in vacuo* to afford the aryl chloride.

4-chlorobiphenyl (1b):



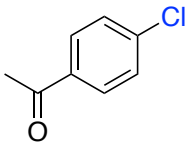
Yield: 79%; Purification by column chromatography on silica gel (pentane) afforded a white solid; mp 76–77 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.58–7.52 (m, 4H), 7.48–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 140.24, 139.92, 133.62, 129.14, 129.11, 128.62, 127.81, 127.22.

3-chlorobiphenyl (2b):



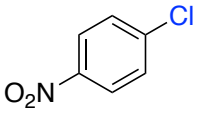
Yield: 90%; Purification by column chromatography on silica gel (pentane) afforded a clear colorless liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.61–7.58 (m, 3H), 7.50–7.45 (m, 3H), 7.41–7.35 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 143.33, 140.06, 134.90, 130.21, 129.13, 128.09, 127.54, 127.49, 127.35, 125.53.

4-chloroacetophenone (3b):



Yield: 90%; Purification by column chromatography on silica gel (17:3 hexanes: EtOAc) afforded a clear colorless liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, J = 8.6 Hz, 2H) 7.43 (d, J = 8.6 Hz, 2H), 2.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ. 196.79, 139.53, 135.41, 129.71, 128.86, 26.53.

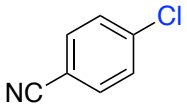
1-chloro-4-nitrobenzene (4b):



Yield: 80%; Purification by column chromatography on silica gel (19:1 hexanes: EtOAc) afforded a yellow solid; mp 79–80 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.22–8.20 (m, 2H), 7.55–7.53 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 146.80, 141.60, 129.80, 125.15.

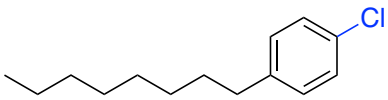
Method for 1 gram scale: In a glove box under an argon atmosphere, an oven-dried 48 mL pressure vessel, equipped with a magnetic stir-bar, was charged with Wilkinson's catalyst (0.27 mmol, 5 mol%) and (*S*)-Tol-BINAP (0.54 mmol, 10 mol%). Aroyl chloride **1d** (1 g, 5.4 mmol, 1.0 equiv.) and *o*-xylene (11 mL, 0.5 M) were added via syringe. The pressure vessel was sealed with a polypropylene cap and removed from the glove box. The reaction mixture was heated to 160 °C and allowed to stir for 24 h. Upon cooling to room temperature, the reaction mixture was diluted with EtOAc and the resulting solution was filtered through a silica plug and concentrated under reduced pressure. To remove triphenylphosphine oxide (TPPO) from the reaction mixture, the resulting products were dissolved in EtOH. $ZnCl_2$ was added in 15 mol% and the mixture was allowed to stir at room temperature for 12-16 hours. The $ZnCl_2$:TPPO salt was removed by filtration through a sintered funnel. [178] The filtrate was then evaporated *in vacuo.* The product was purified via column chromatography on silica gel in 19:1 (Hex/EtOAc). The solvent was evaporated *in vacuo* to afford the aryl chloride in 77% yield.

4-chlorobenzonitrile (5b):



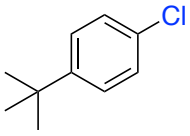
Yield: 76%; Purification by column chromatography on silica gel (19:1 hexanes: EtOAc) afforded a white solid; mp 90–91 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.63–7.59 (m, 2H), 7.50–7.47 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 139.79, 133.60, 129.92, 118.15, 111.06.

1-chloro-4-octylbenzene (8b):



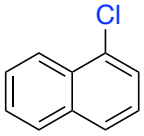
Yield: 70%; Purification by column chromatography on silica gel (pentane) afforded a clear colorless liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.05 (d, J = 8.5, 2H), 7.32 (d, J = 8.5, 2H), 2.71 (t, J = 7.7 Hz, 2H), 1.69–1.63 (m, 2H), 1.34–1.29 (m, 10H), 0.91 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 141.34, 131.21, 129.73, 128.28, 35.31, 31.88, 31.41, 29.44, 29.25, 29.21, 22.67, 14.11.

1-(*tert*-butyl)-4-chlorobenzene (9b):



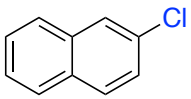
Yield: 70%; Purification by column chromatography on silica gel (pentane) afforded a clear colorless liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.32 (d, J = 8.7 Hz, 2H) 7.27 (d, J = 8.7 Hz, 2H), 1.32 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 149.60, 131.14, 128.08, 126.76, 34.48, 31.30.

1-chloronaphthalene (11b):



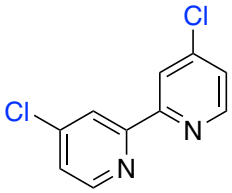
Yield: 47%; Purification by column chromatography on silica gel (hexanes) afforded a brown liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.30 (d, J = 8.45 Hz, 1H), 7.88 (d, J = 8.15 Hz, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.64–7.55 (m, 3H), 7.39 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 134.82, 132.19, 131.07, 128.45, 127.39, 127.27, 126.91, 126.39, 125.94, 124.66.

2-chloronaphthalene (12b):



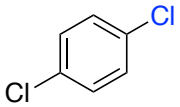
Yield: 65%; Purification by column chromatography on silica gel (hexanes) afforded a white solid; mp 58–59 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.85–7.76 (m, 4H), 7.54–7.42 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 134.26, 131.89, 131.80, 129.71, 128.02, 127.29, 127.13, 127.00, 126.82, 126.34.

4,4'-dichloro-2,2'-bipyridine (15b):



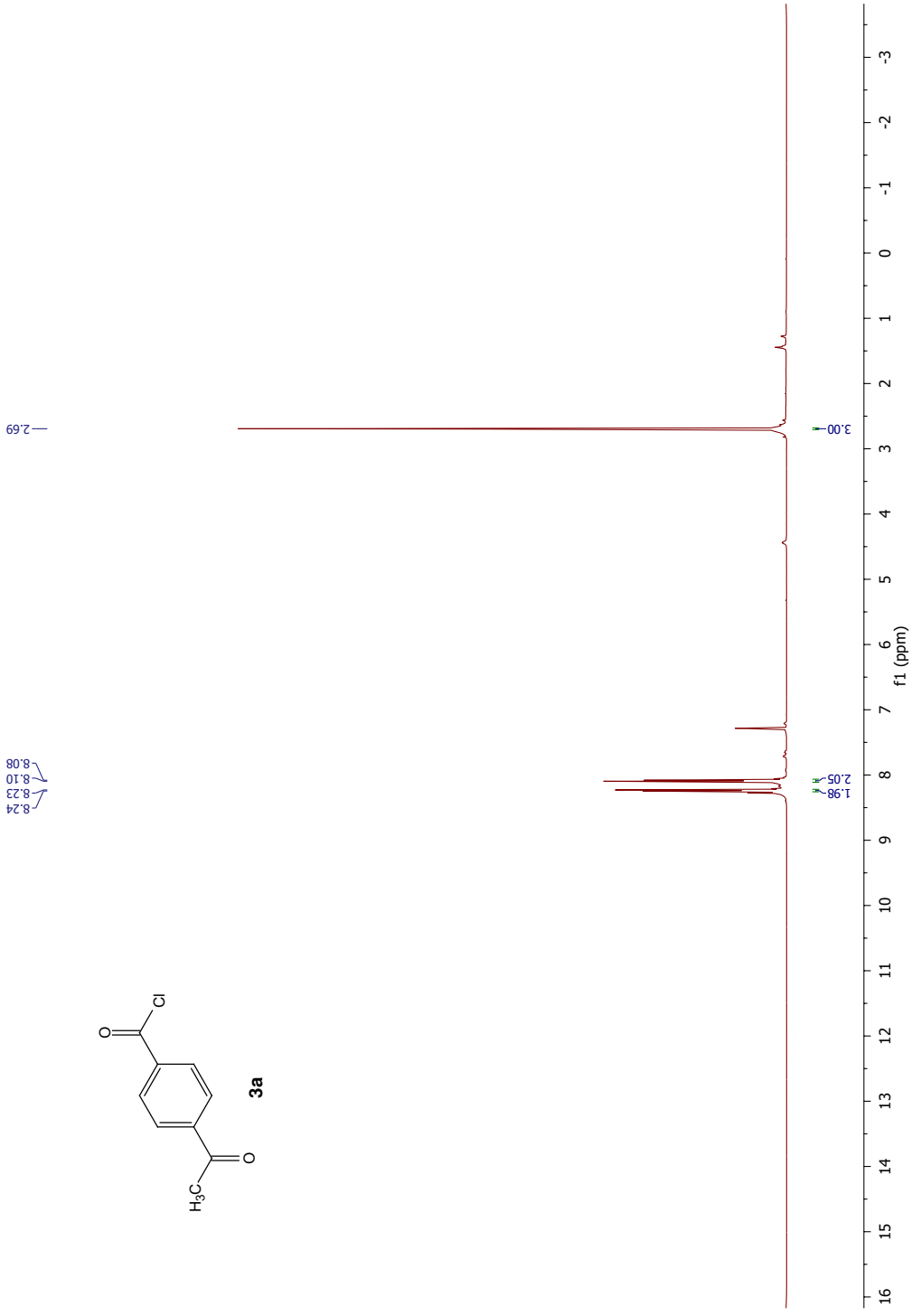
Yield: 51%; Purification by column chromatography on silica gel (17:3 hexanes: EtOAc) afforded a white solid; mp 129–130 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.59 (d, J = 5.05, 2H) 8.48 (s, 2H), 7.37 (d, J = 5.15, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 156.25, 150.01, 145.48, 124.49, 121. 85.

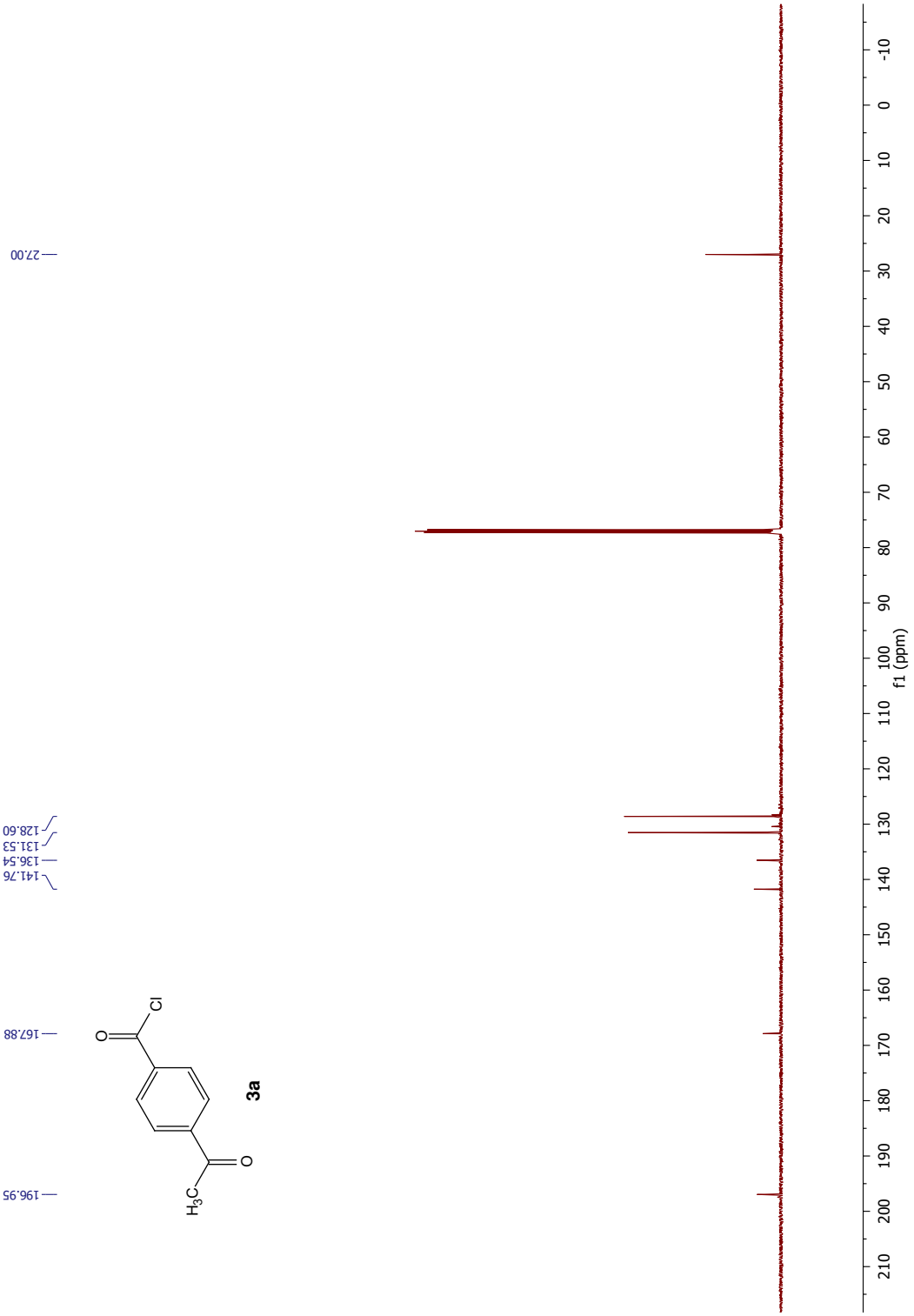
1,4-dichlorobenzene (18b):

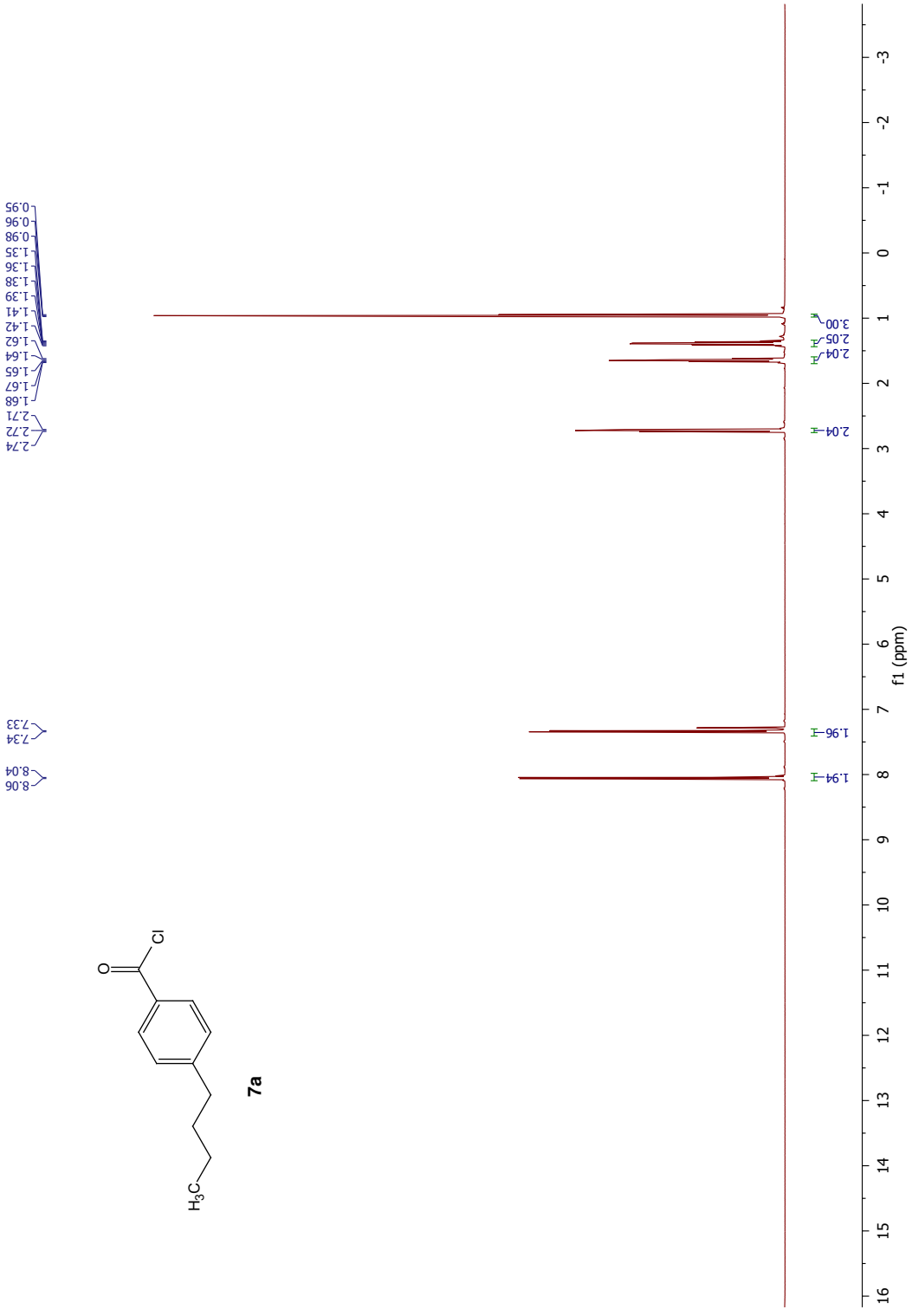


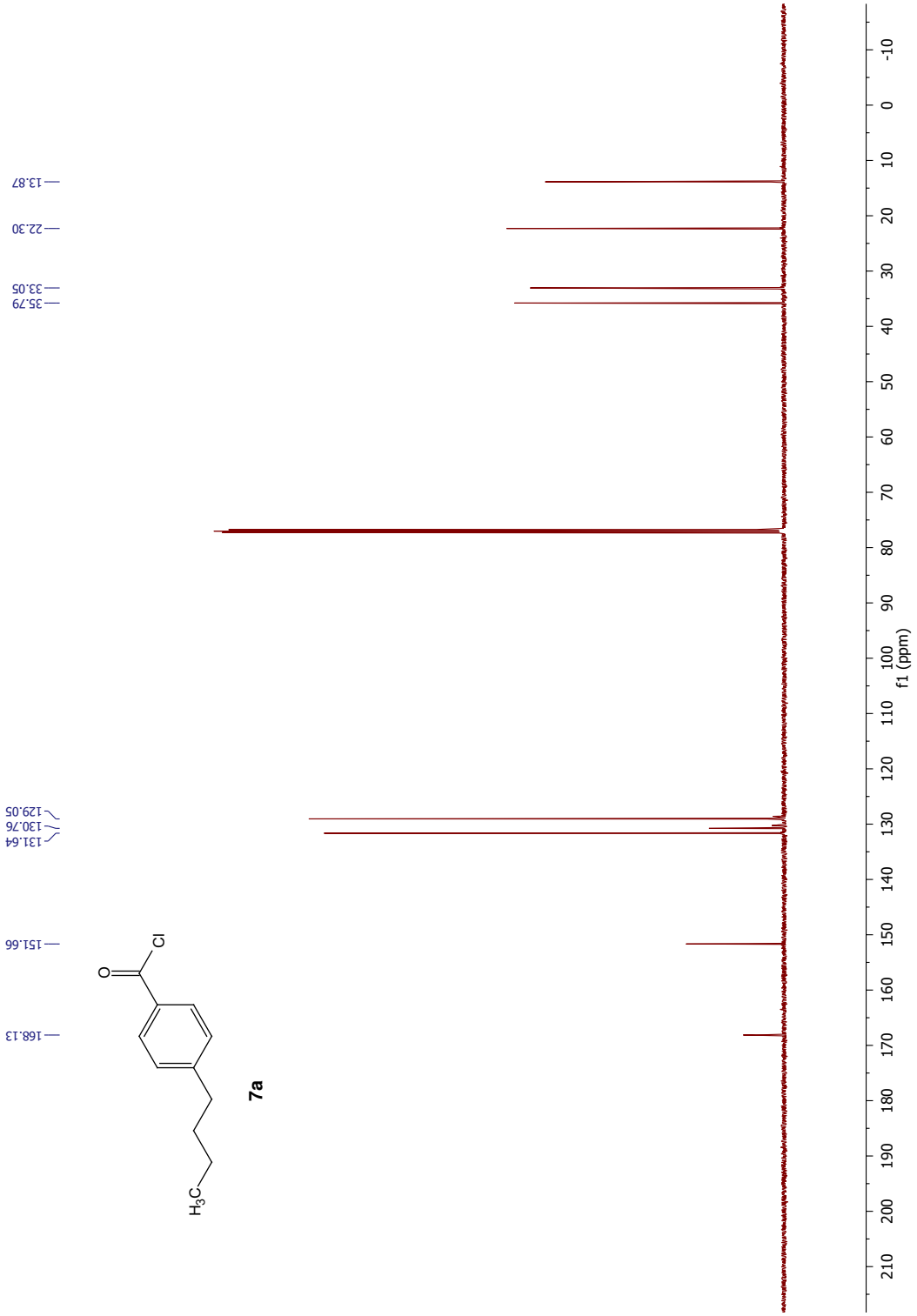
Yield: 95%; Purification by column chromatography on silica gel (hexanes) afforded a white solid; mp 49–51 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.28 (s, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 132.76, 130.0

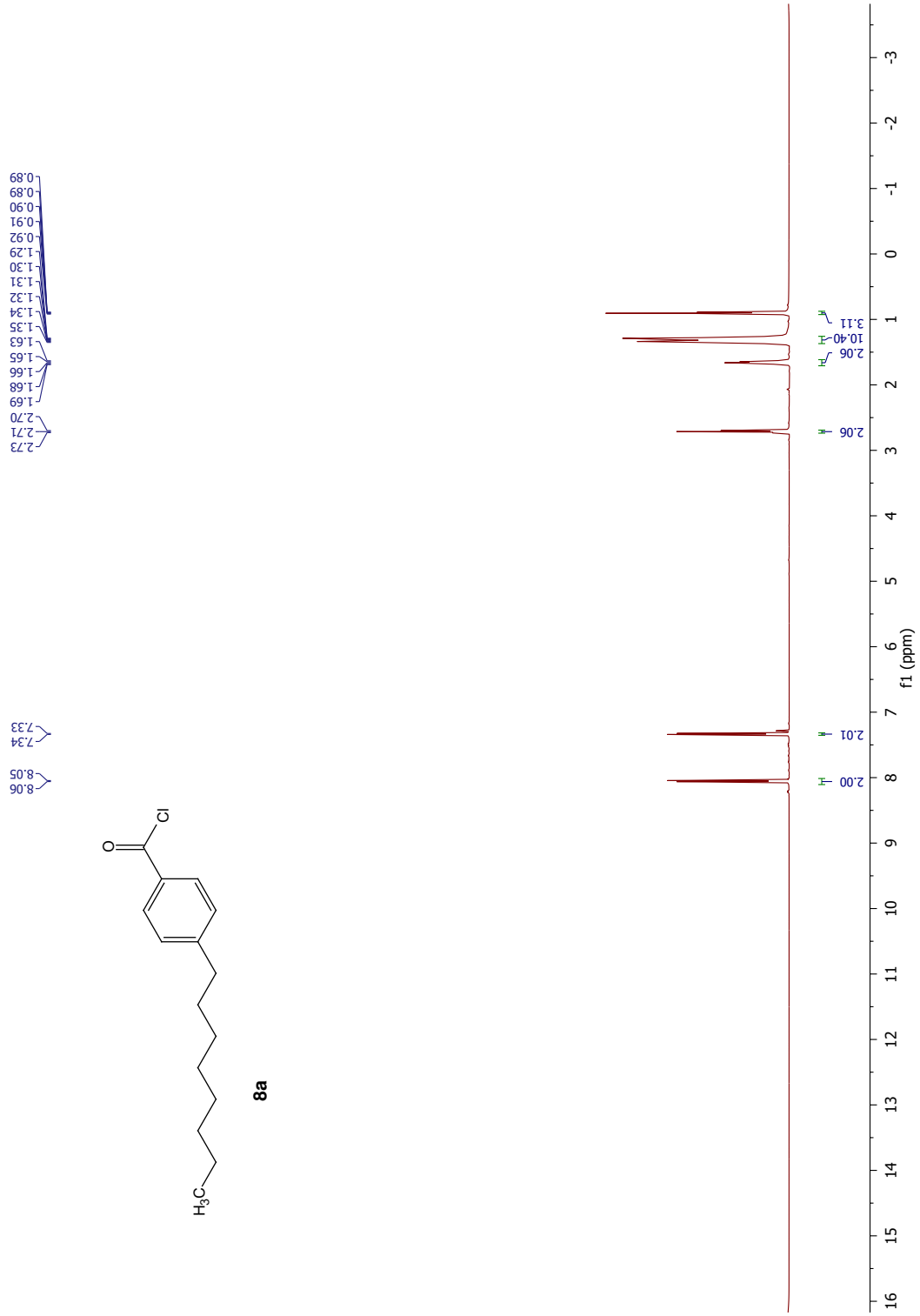
^{1}H AND ^{13}C NMR SPECTRA

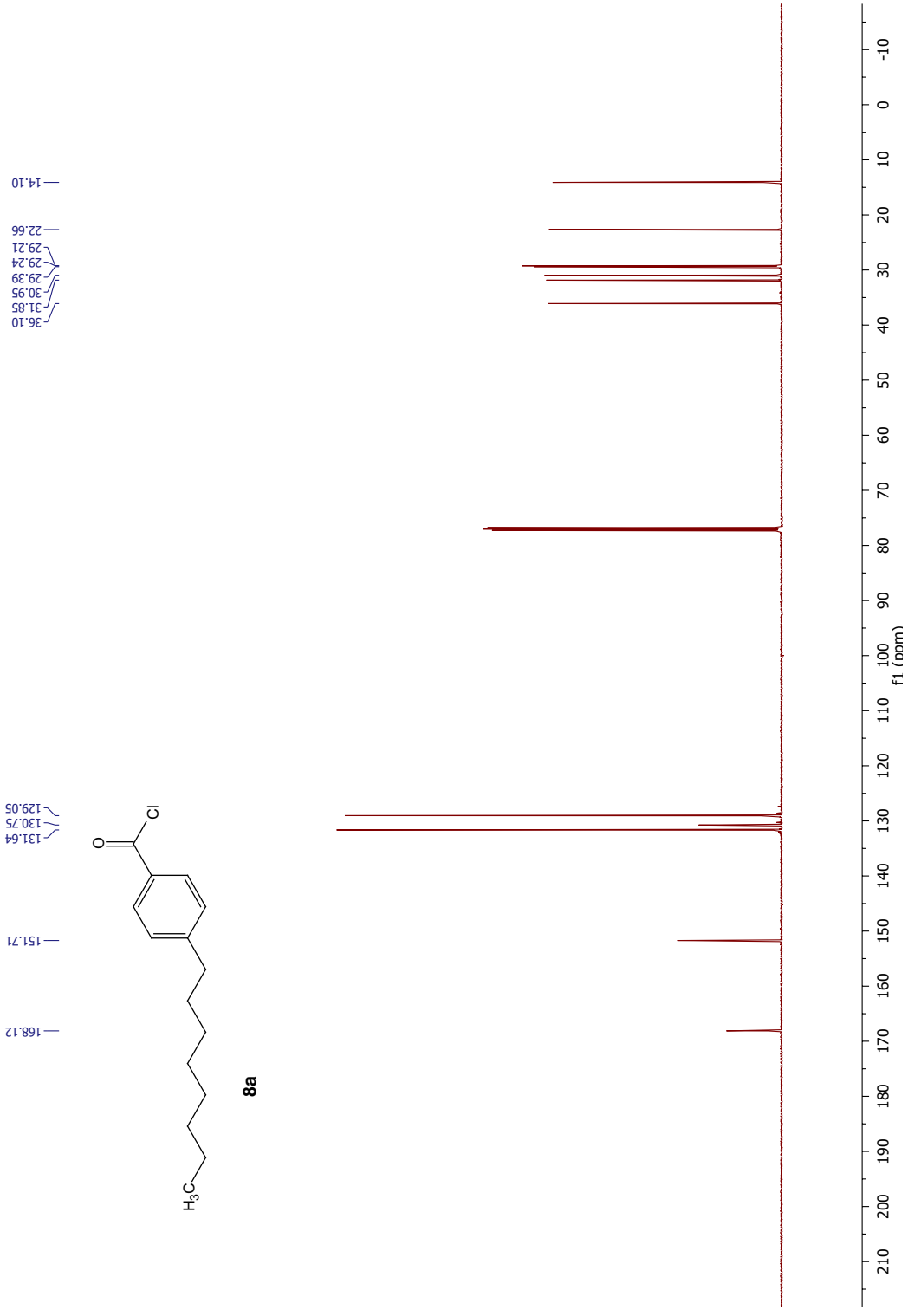


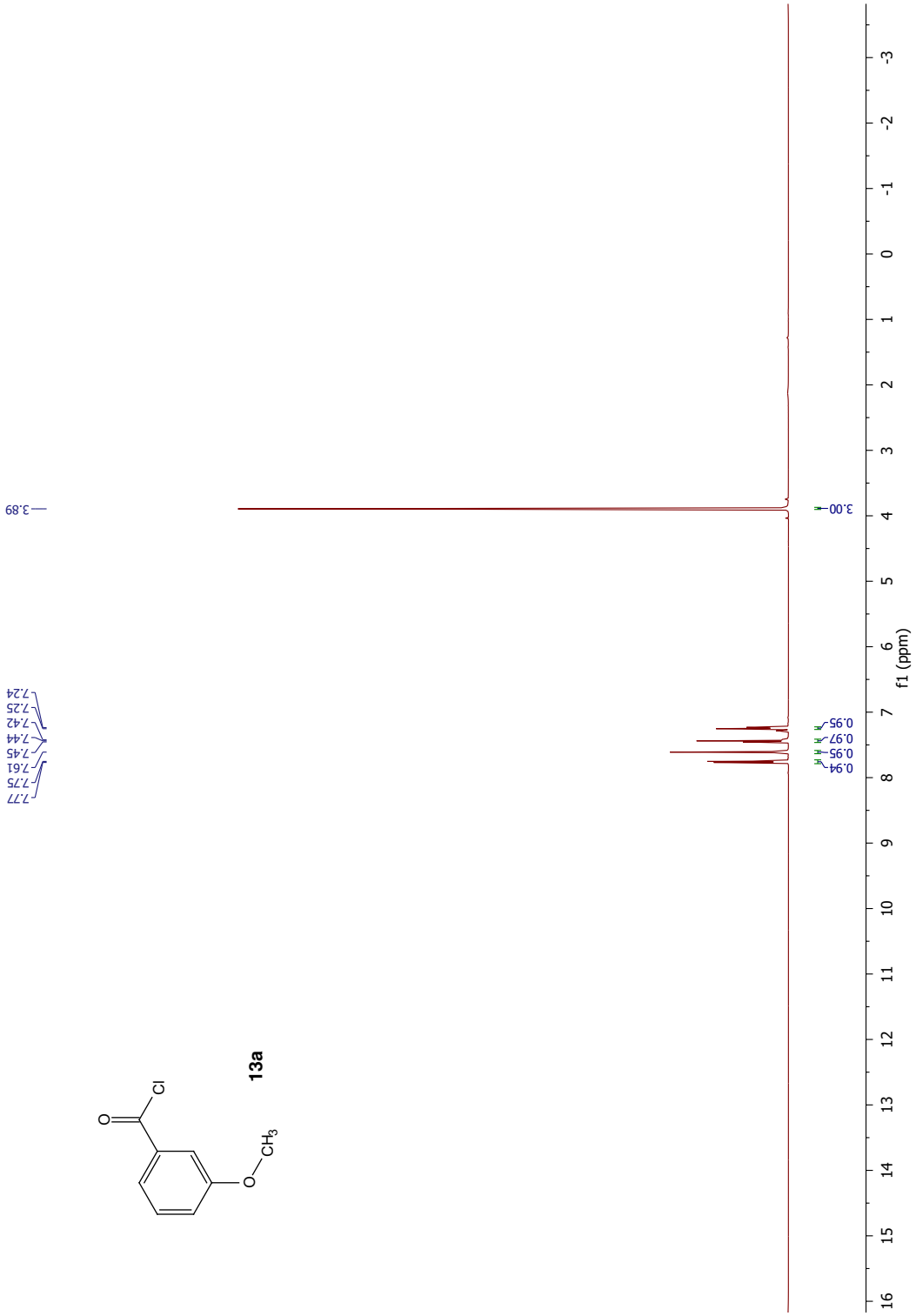

27.00
128.60
131.53
136.54
141.76
167.88
196.95
Cl
O
O
H_3C
3a
f1 (ppm)

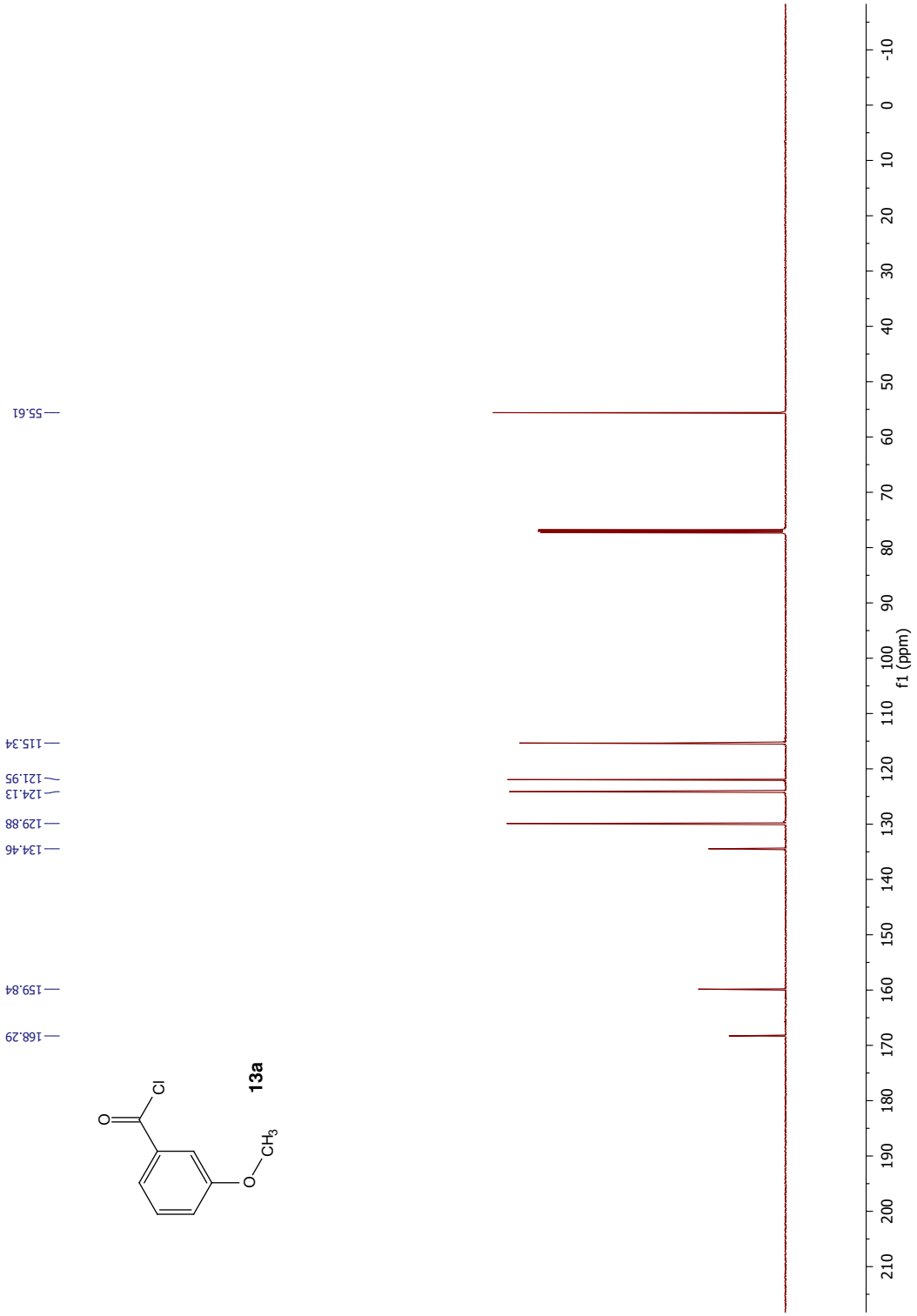

f1 (ppm)
3.00
2.05
2.04
2.04
1.96
1.94
8.06
8.04
7.34
7.33
2.74
2.72
2.71
1.68
1.67
1.65
1.64
1.62
1.42
1.41
1.39
1.38
1.36
1.35
0.98
0.96
0.95
Cl
O
H3C
7a

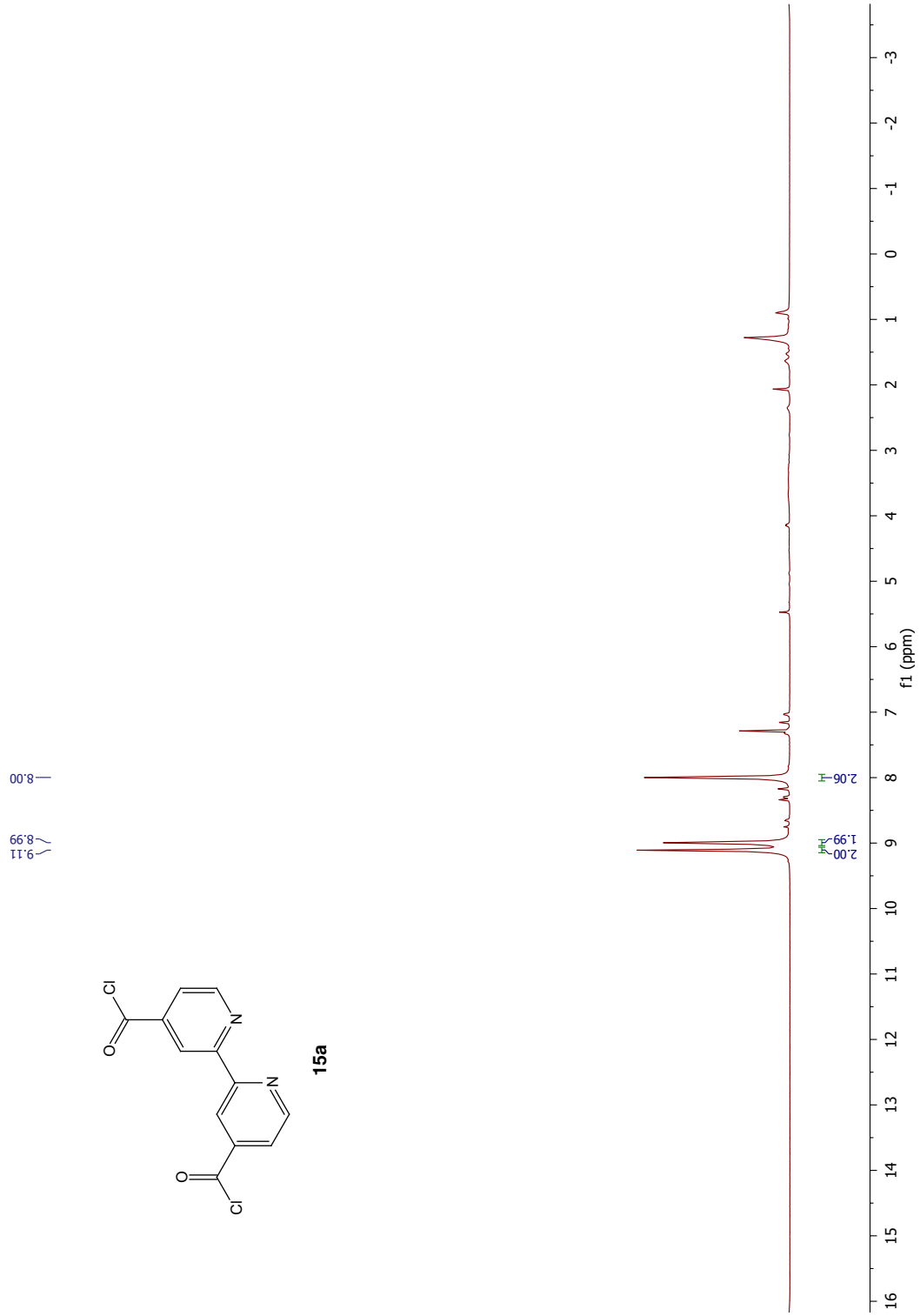

13.87
22.30
33.05
35.79
129.05
130.76
131.64
151.66
168.13
Cl
O
H3C
7a
f1 (ppm)

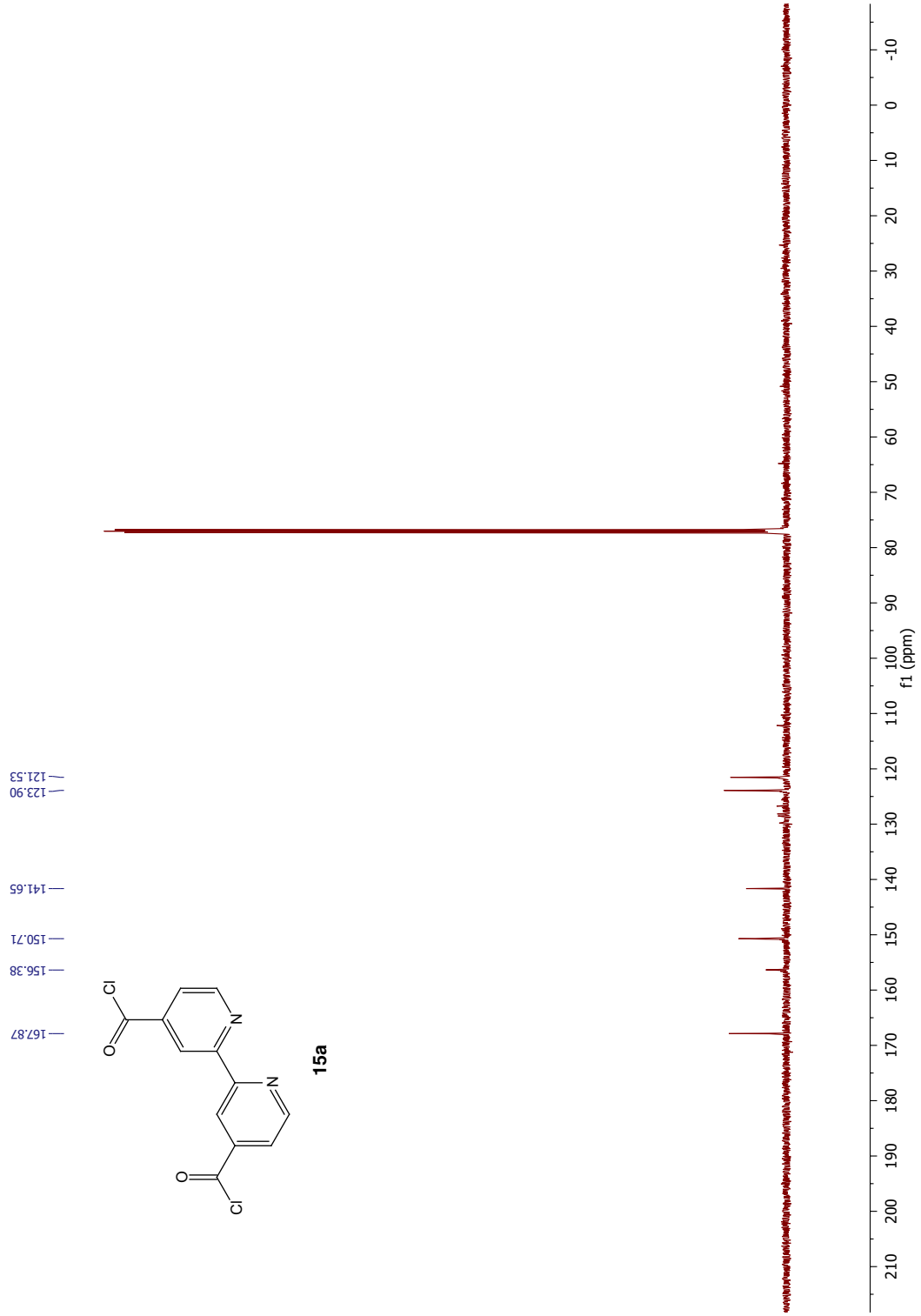

8.06
8.05
7.34
7.33
2.73
2.71
2.70
1.69
1.68
1.66
1.65
1.63
1.35
1.34
1.32
1.31
1.30
1.29
0.92
0.91
0.90
0.89
0.89
O
Cl
H3C
8a
2.00
2.01
2.06
10.40
3.11
f1 (ppm)

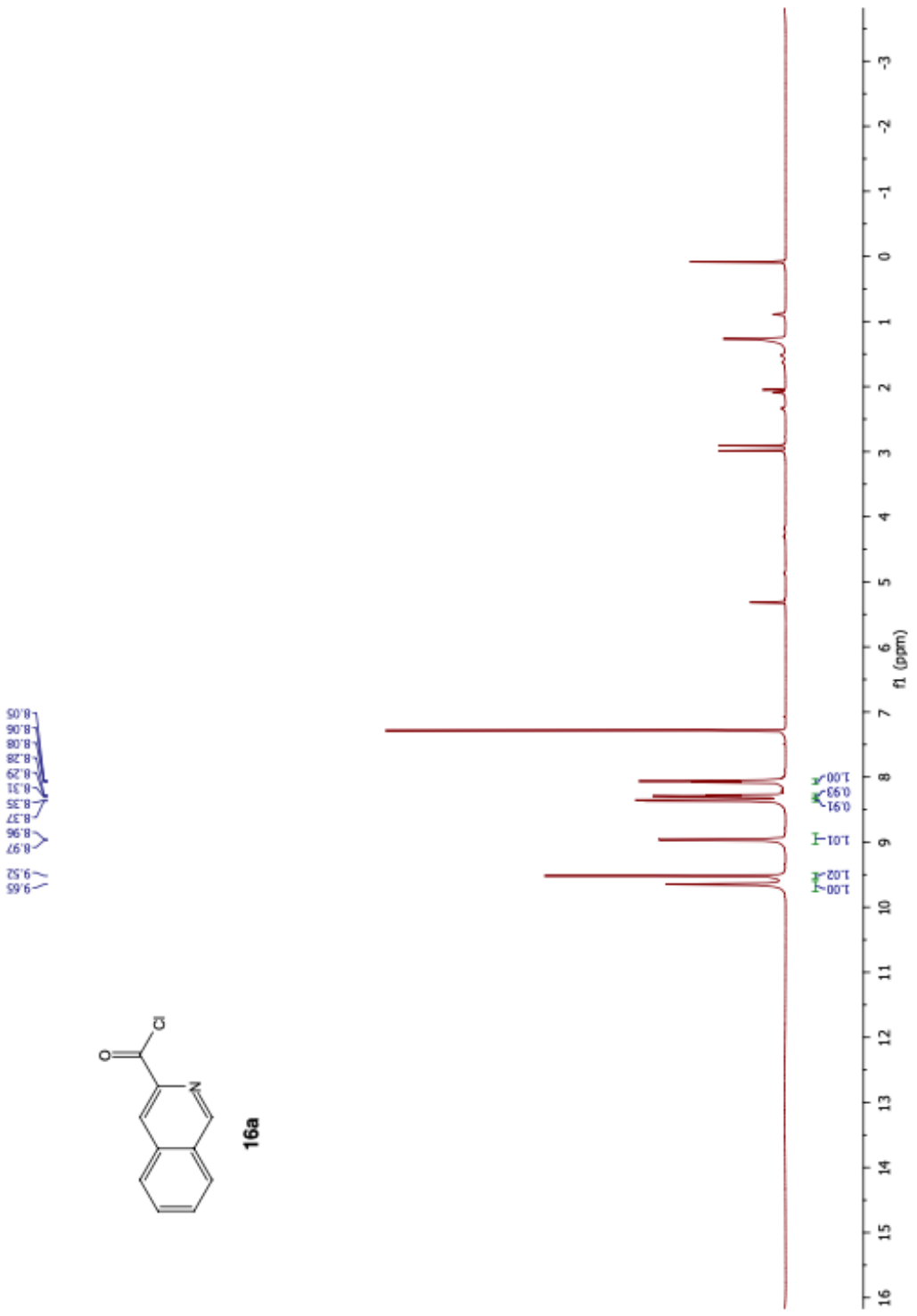

14.10
22.66
29.21
29.24
29.39
30.95
31.85
36.10
129.05
130.75
131.64
151.71
168.12
O
Cl
H3C
8a
f1 (ppm)

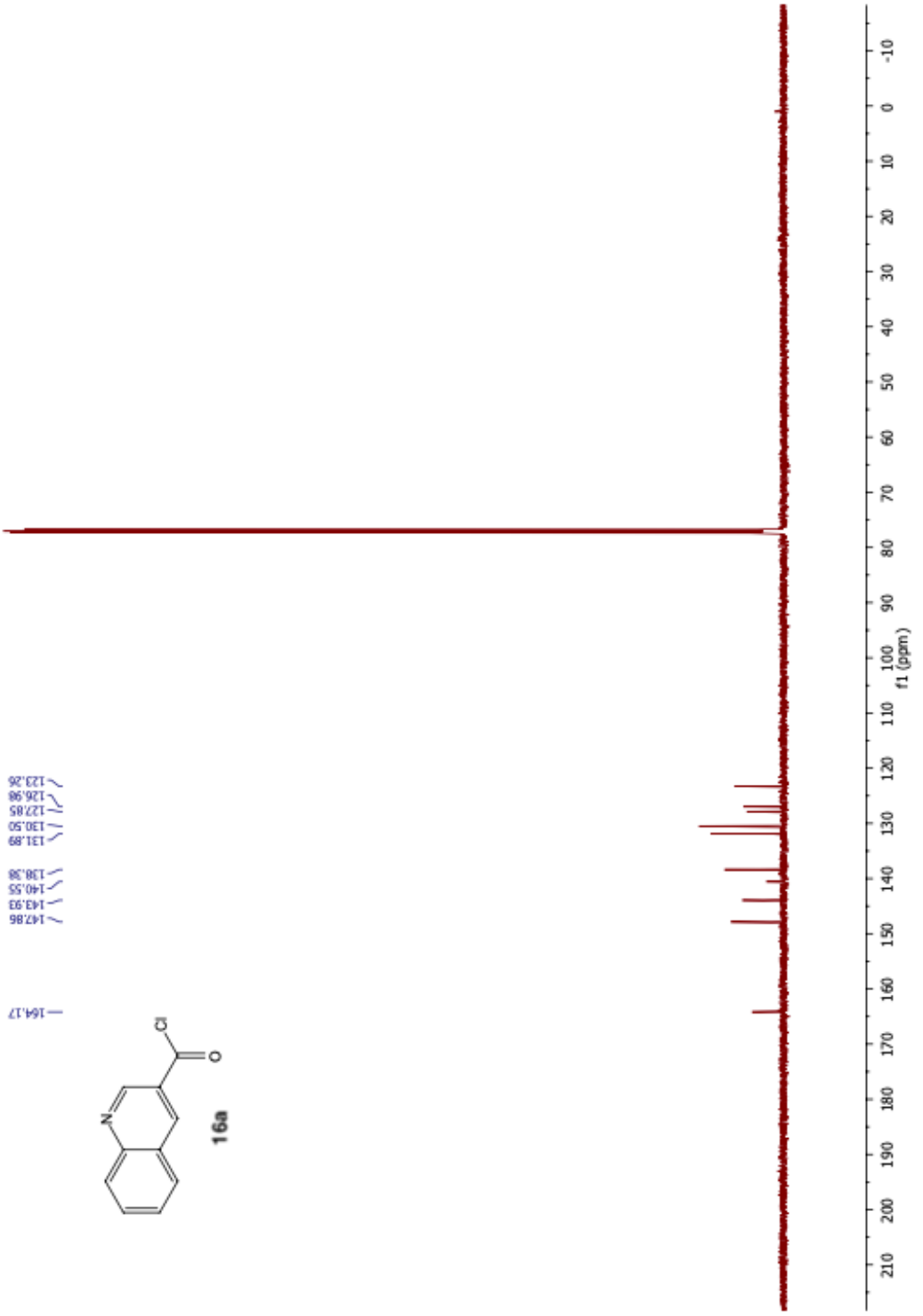

13a
Cl
O
O
CH3
7.77
7.75
7.61
7.45
7.44
7.42
7.25
7.24
3.89
0.94
0.95
0.97
0.95
3.00
f1 (ppm)

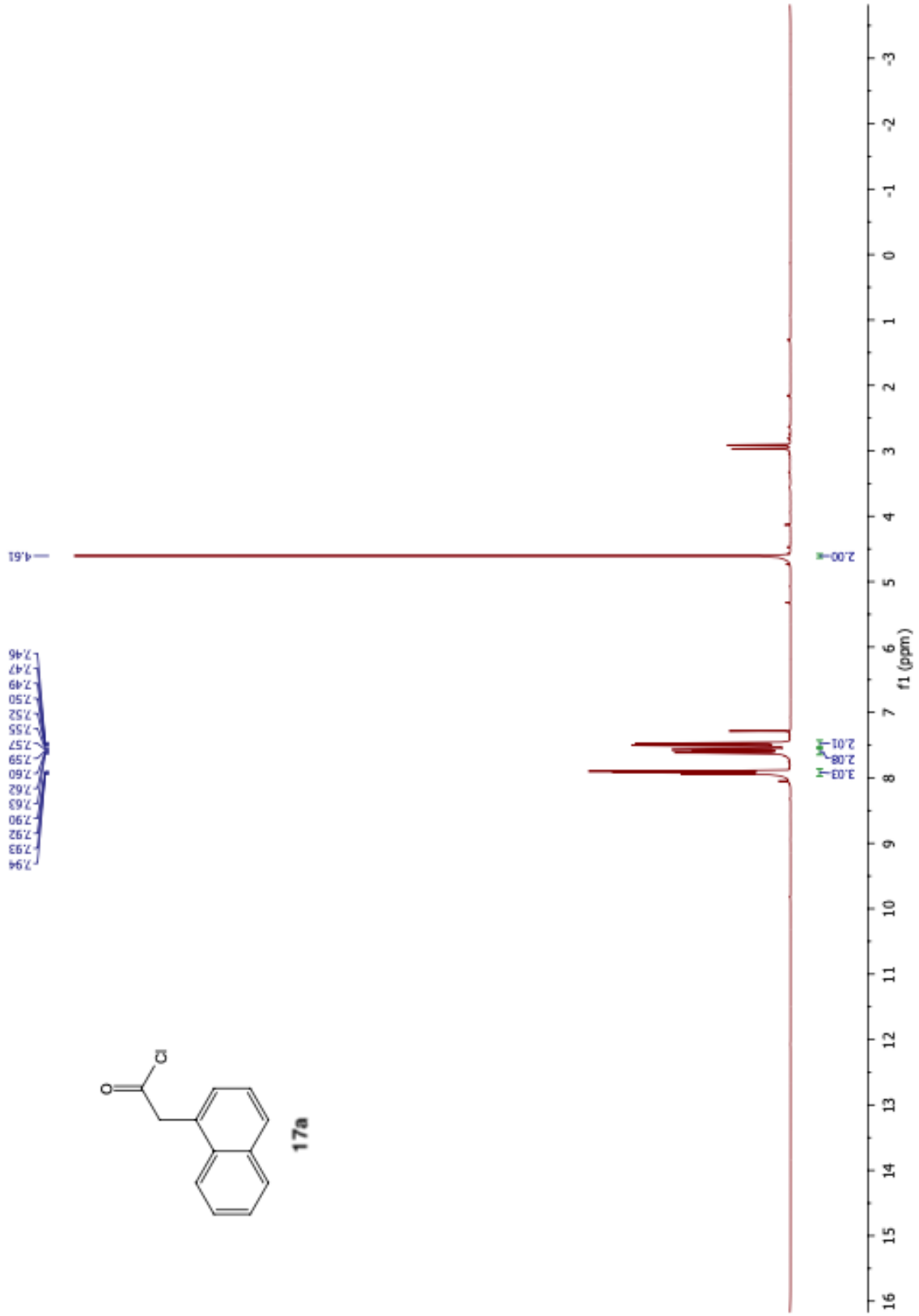

55.61
115.34
121.95
124.13
129.88
134.46
159.84
168.29
Cl
O
O
CH3
13a
f1 (ppm)

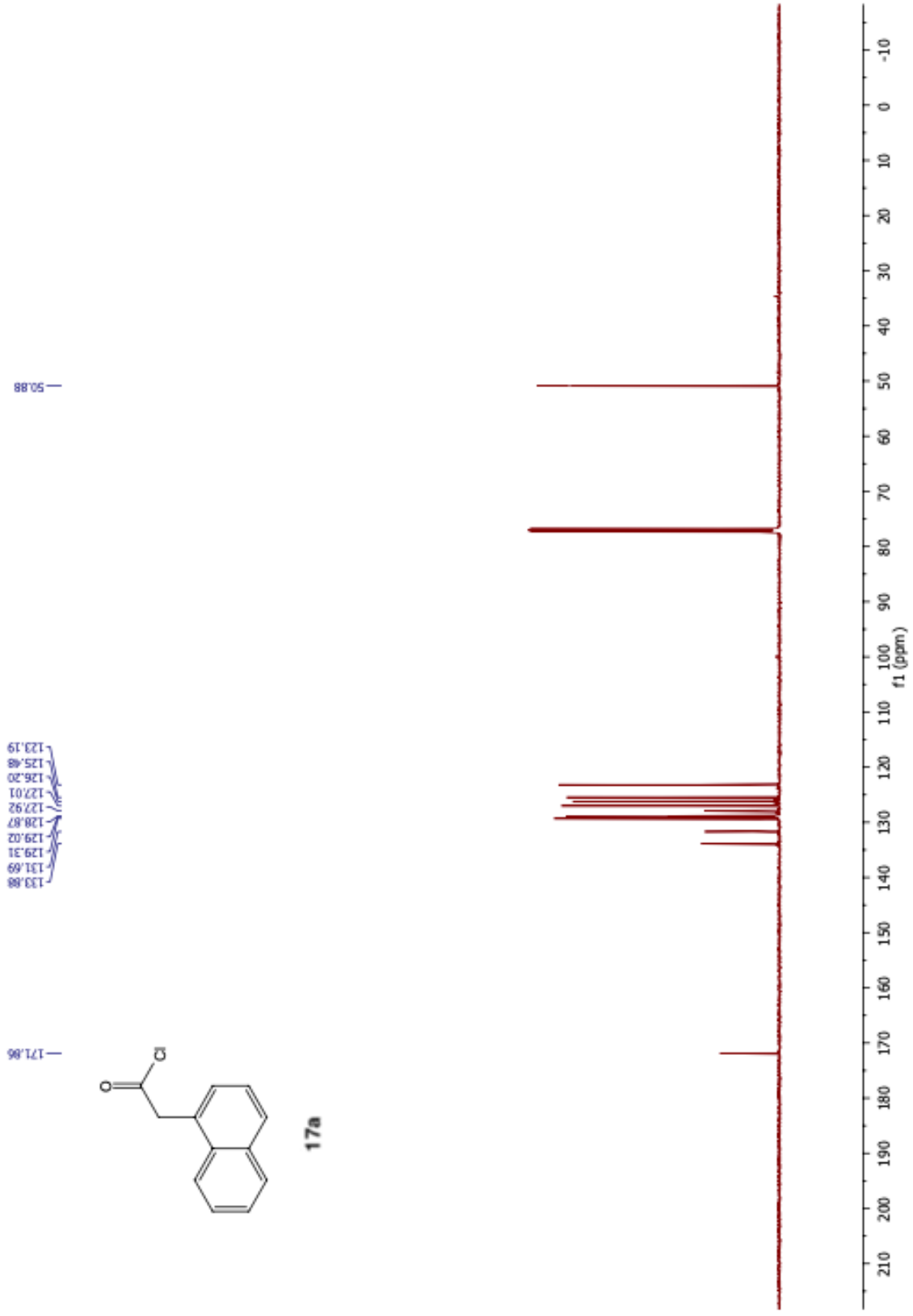

8.00
8.99
9.11
2.06
1.99
2.00
f1 (ppm)
15a

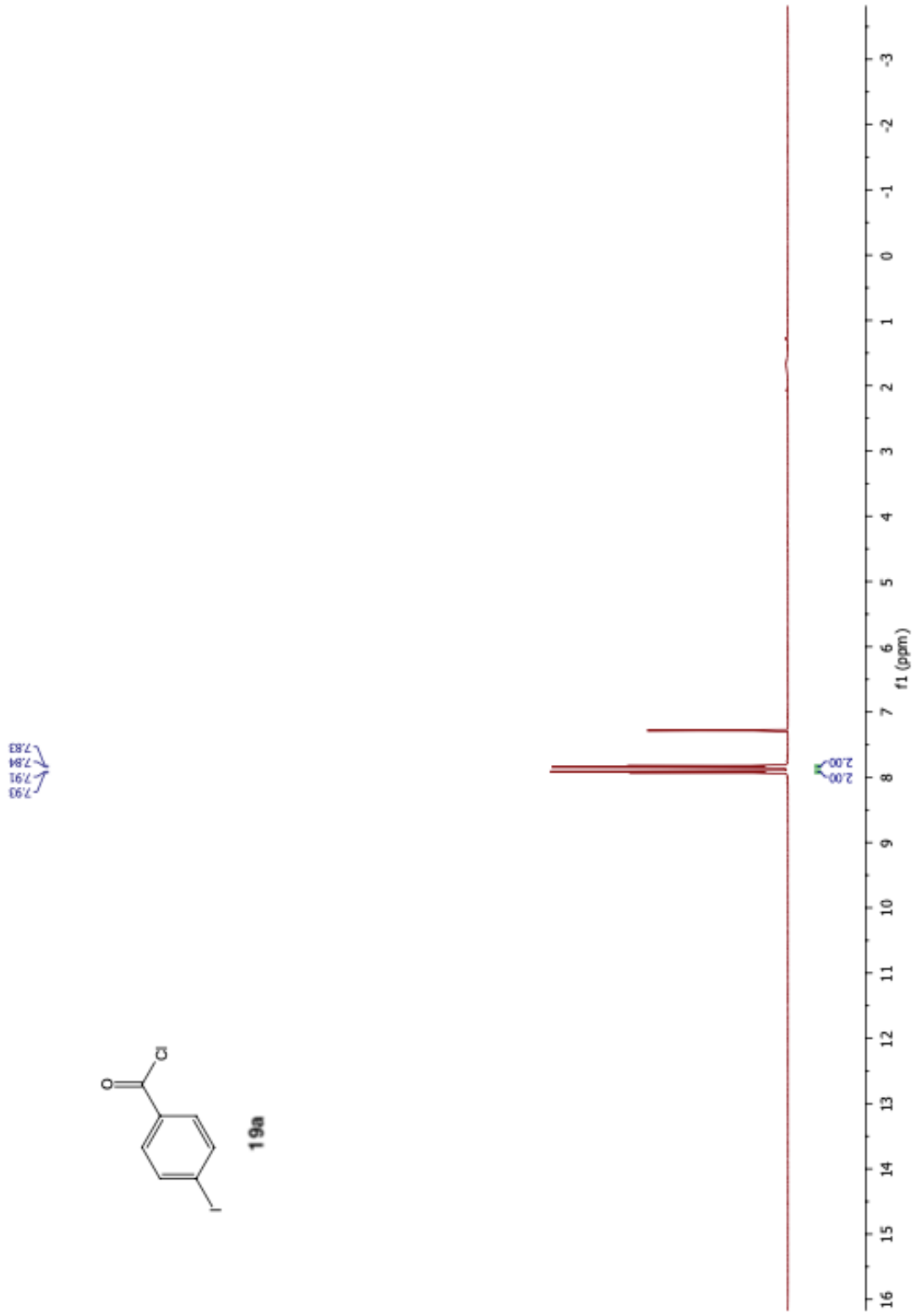

167.87
156.38
150.71
141.65
123.90
121.53
15a
f1 (ppm)

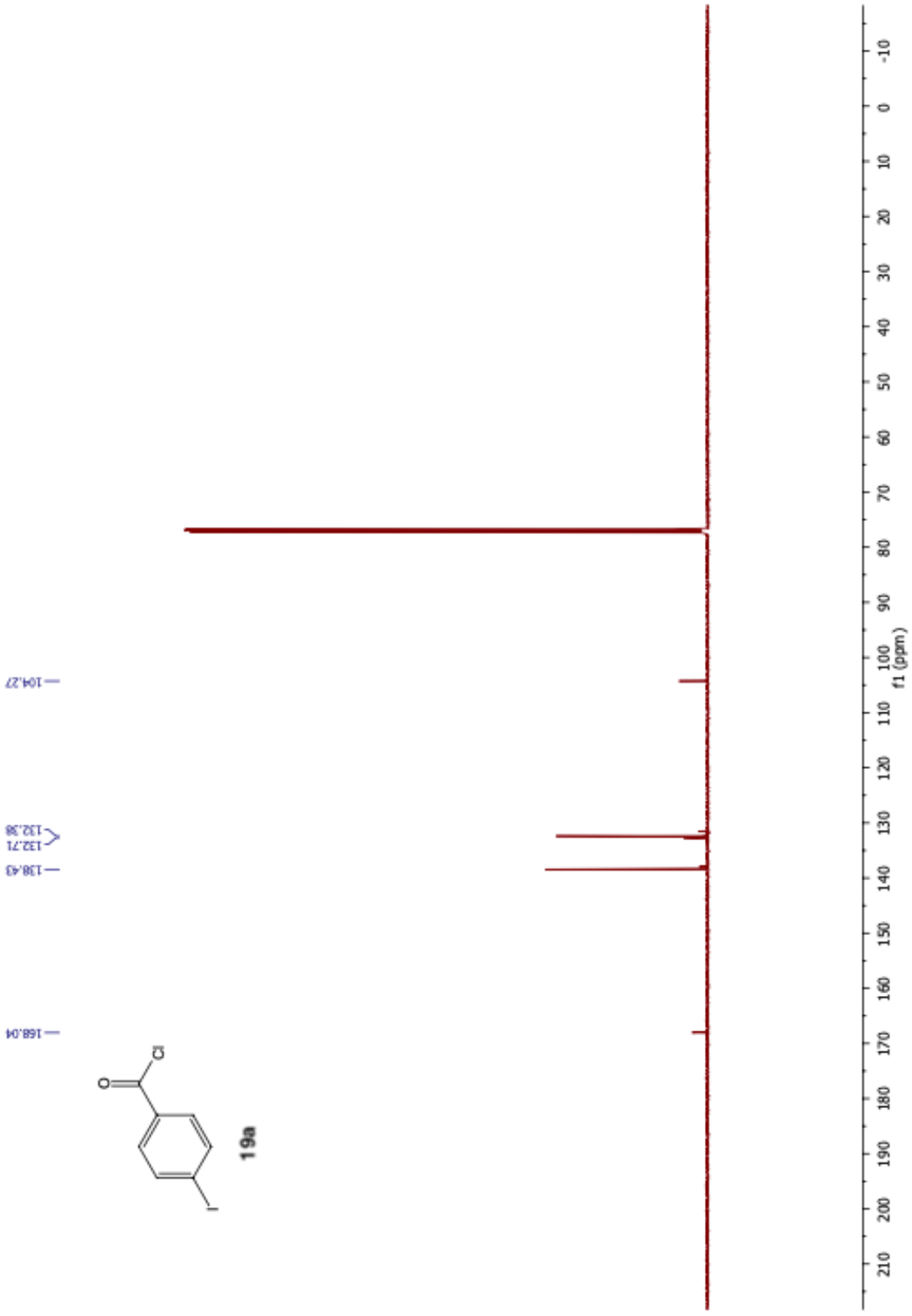

9.65
9.52
8.97
8.96
8.37
8.35
8.31
8.29
8.28
8.08
8.06
8.05
1.00
1.02
1.01
0.99
0.91
1.00
f1 (ppm)
16a

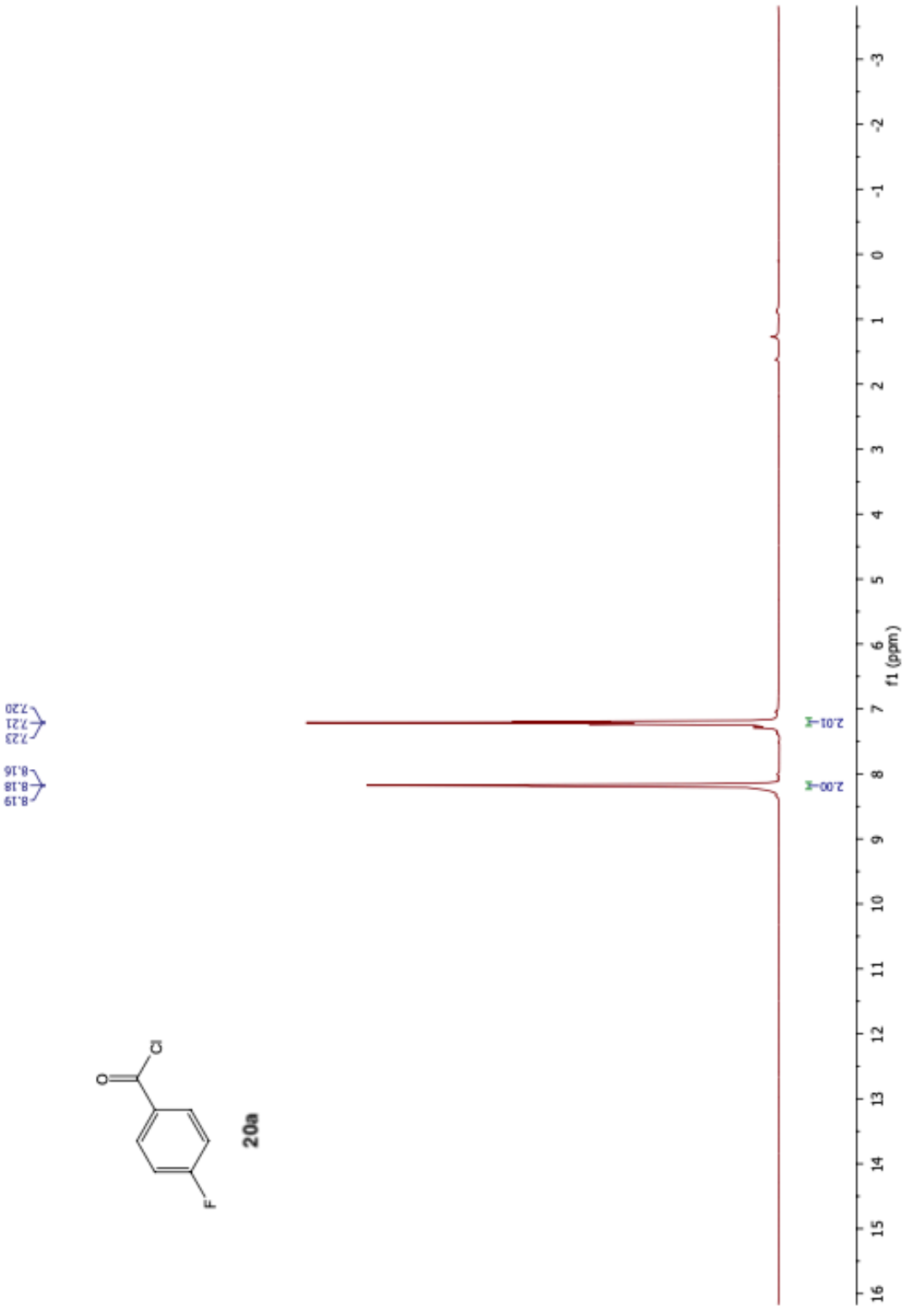

164.17
147.86
143.93
140.55
138.38
131.89
130.50
127.85
126.98
123.26
Cl
O
N
16a
f1 (ppm)

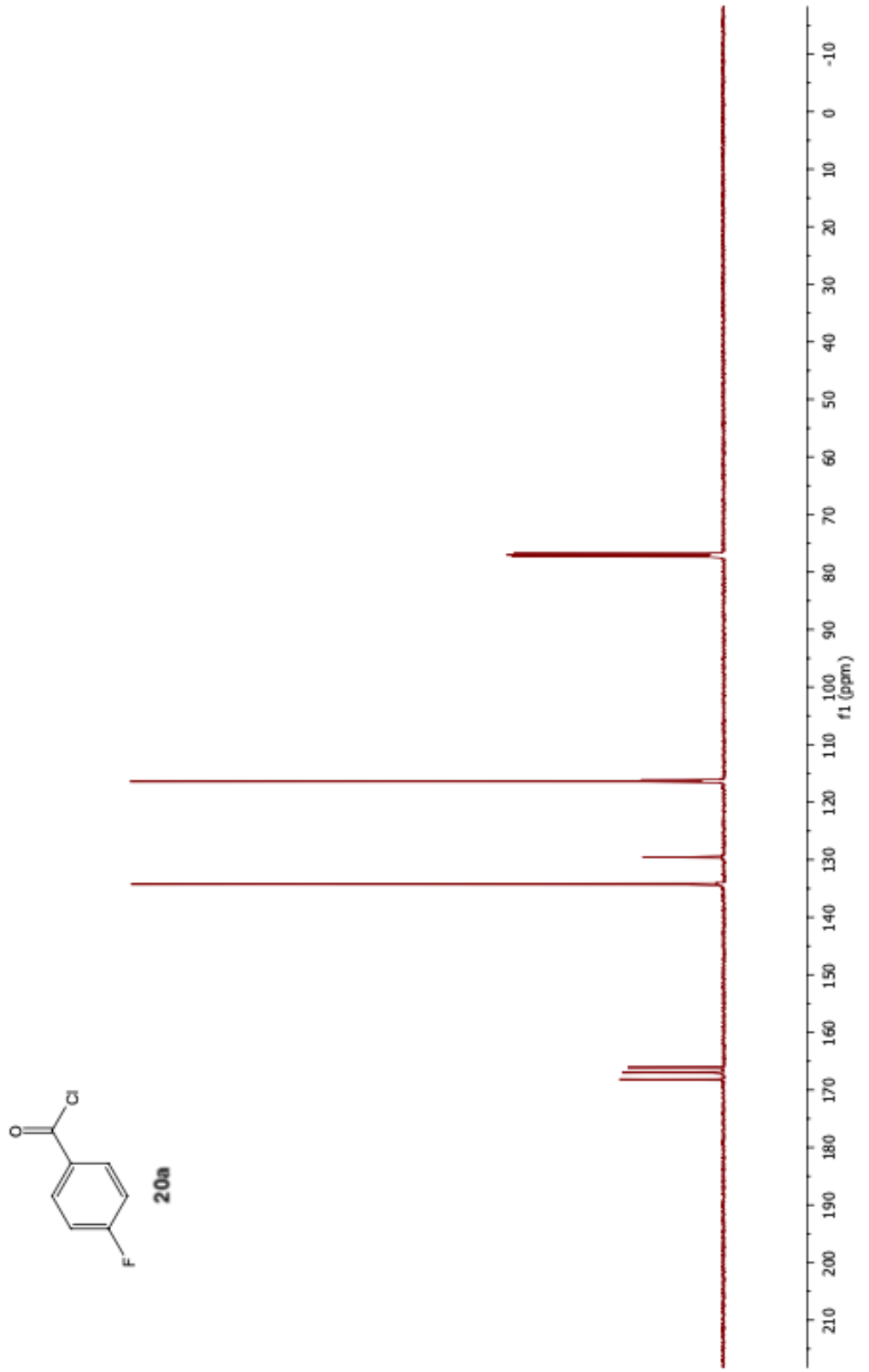

4,61
7,46
7,47
7,49
7,50
7,52
7,55
7,57
7,59
7,60
7,62
7,63
7,90
7,92
7,93
7,94
2,00
3,03
2,08
2,01
f1 (ppm)
O
Cl
17a

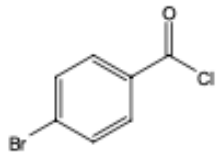

171.86
133.88
131.69
129.31
129.02
128.87
127.92
127.01
126.20
125.48
123.19
50.88
f1 (ppm)
17a


7.93
7.91
7.84
7.83
2.00
2.00
f1 (ppm)
19a


168.04
138.43
132.71
132.38
104.27
O
Cl
I
19a
f1 (ppm)

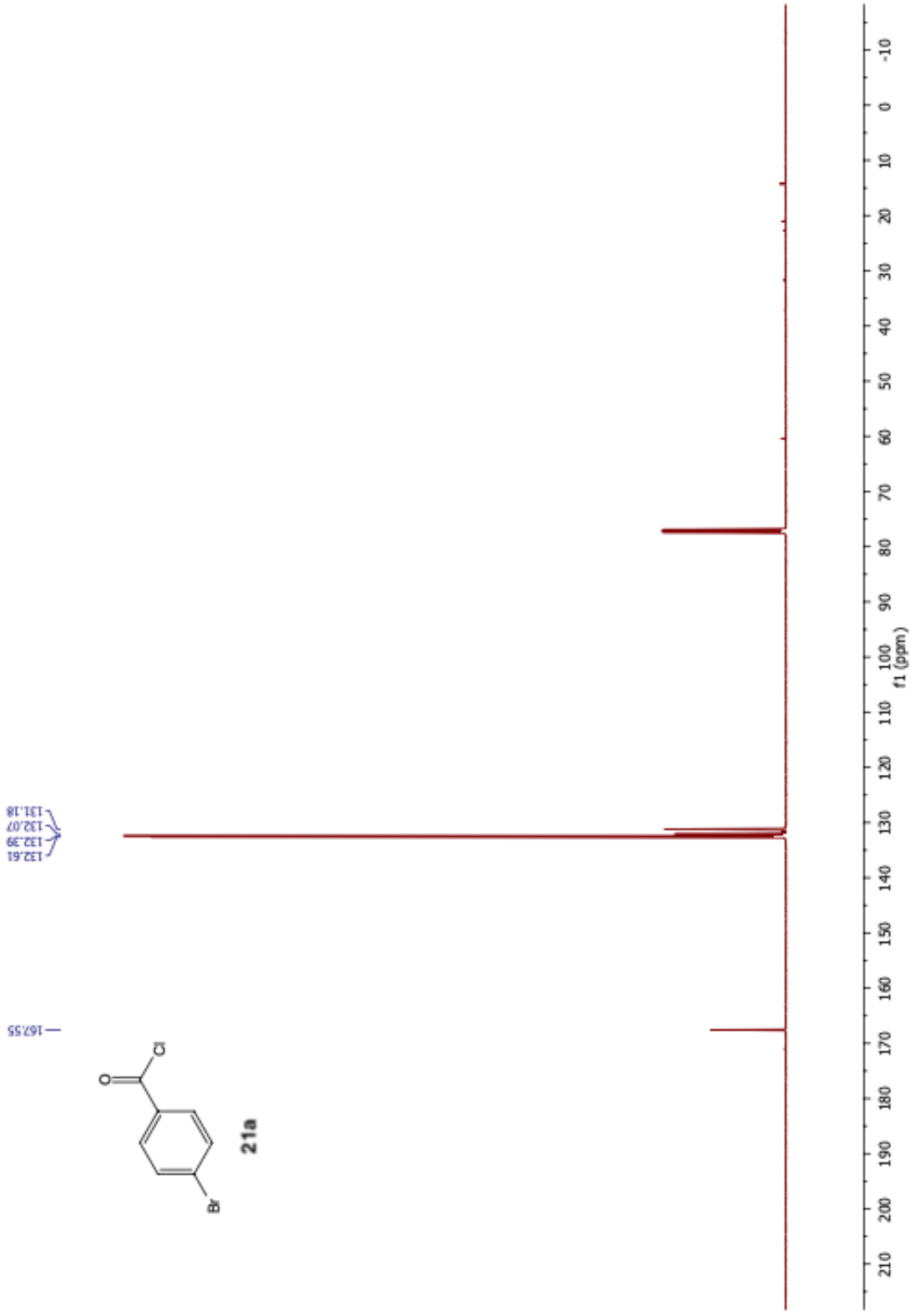

8.19
8.18
8.16
7.23
7.21
7.20
2.01
2.00
f1 (ppm)
20a

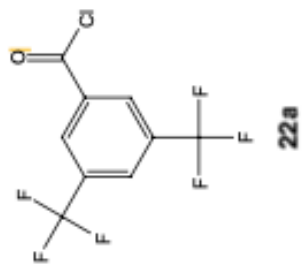

O
Cl
F
20a
f1 (ppm)


O
Cl
Br

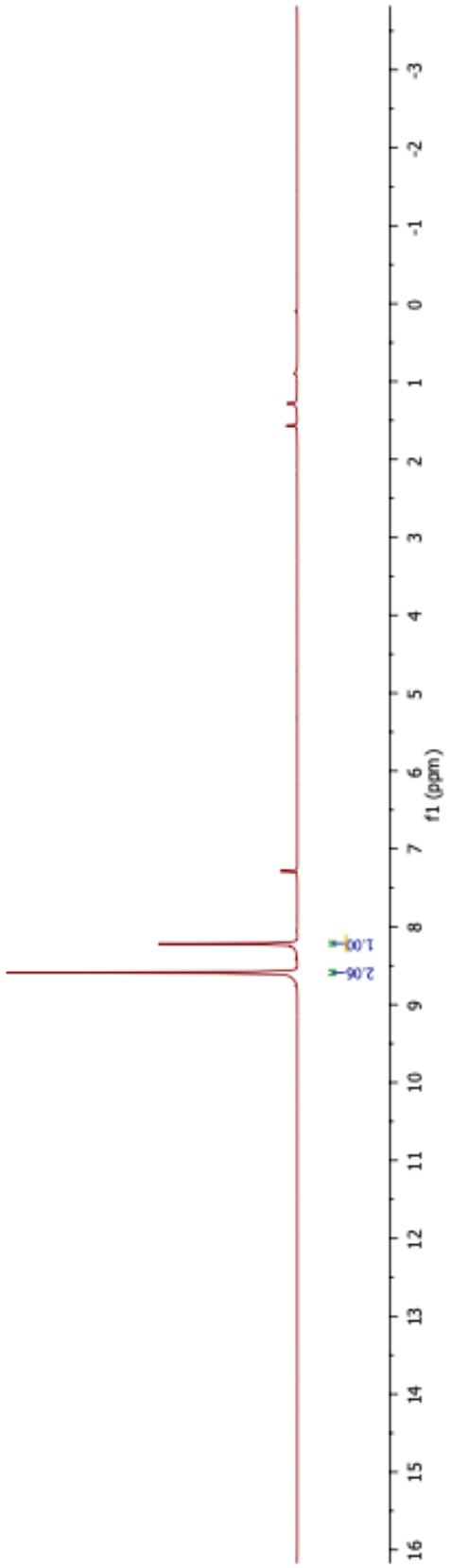
21a

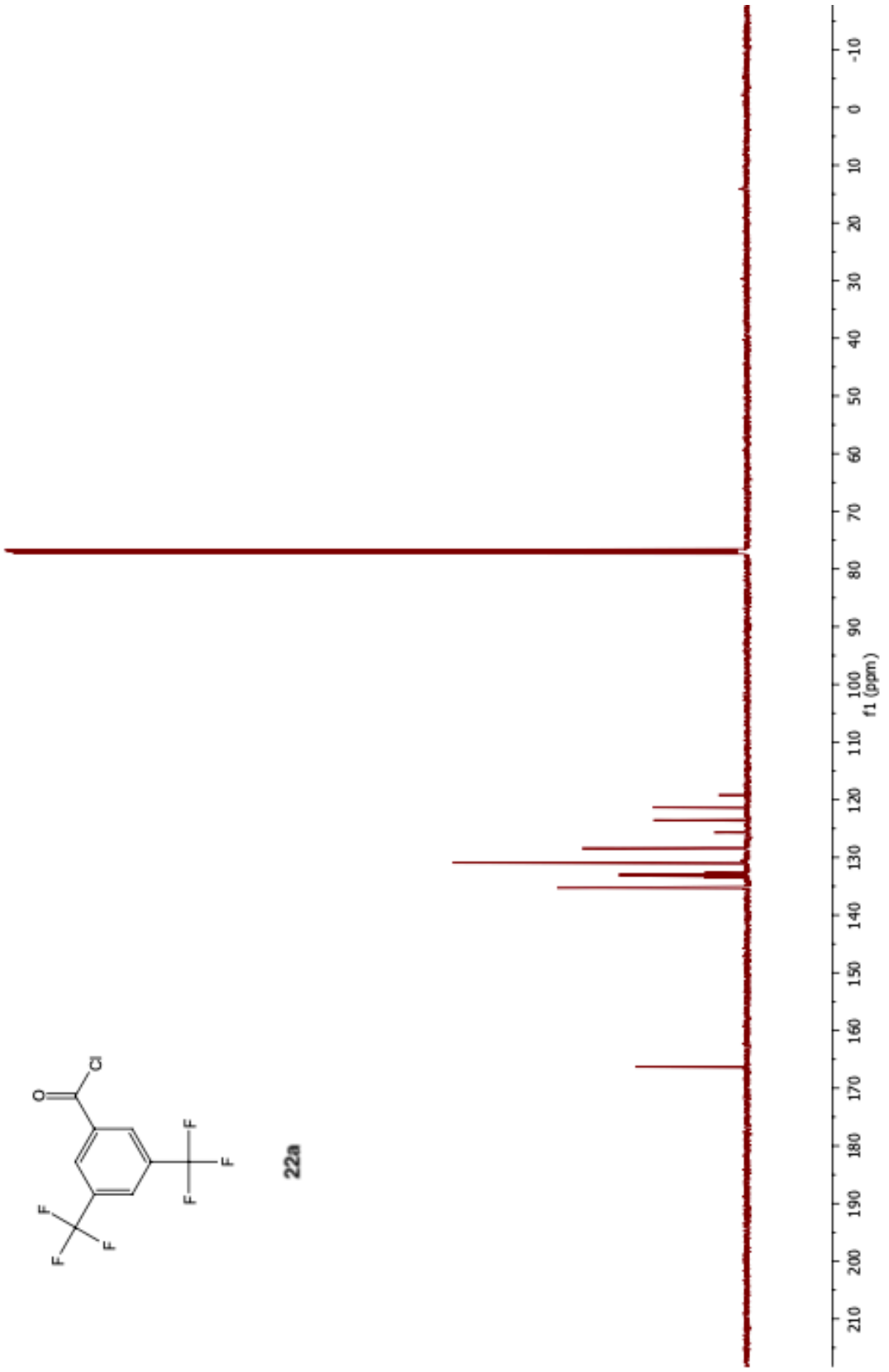
8.01
7.99
7.70
7.68
2.00
2.00
0.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f1 (ppm)


167.55
132.61
132.39
132.07
131.18
O
Cl
Br
21a
f1 (ppm)

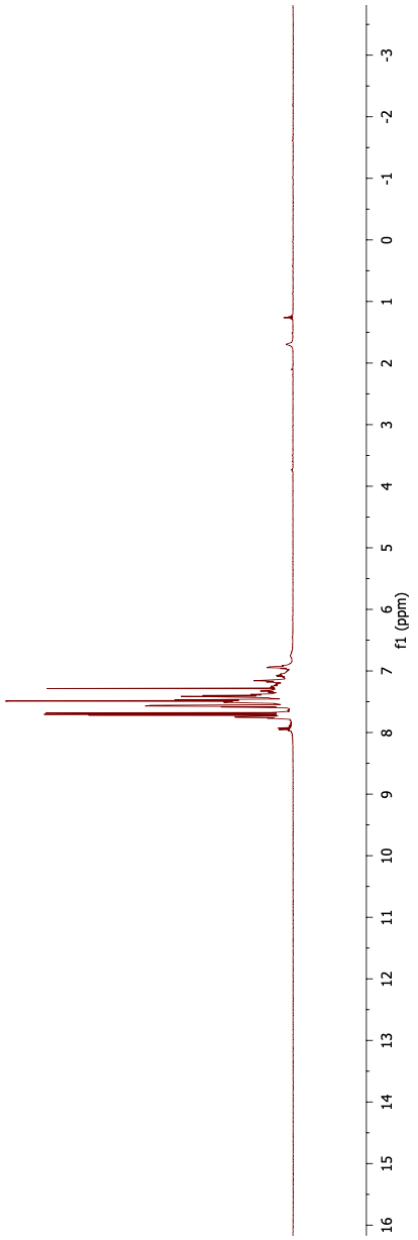


22a

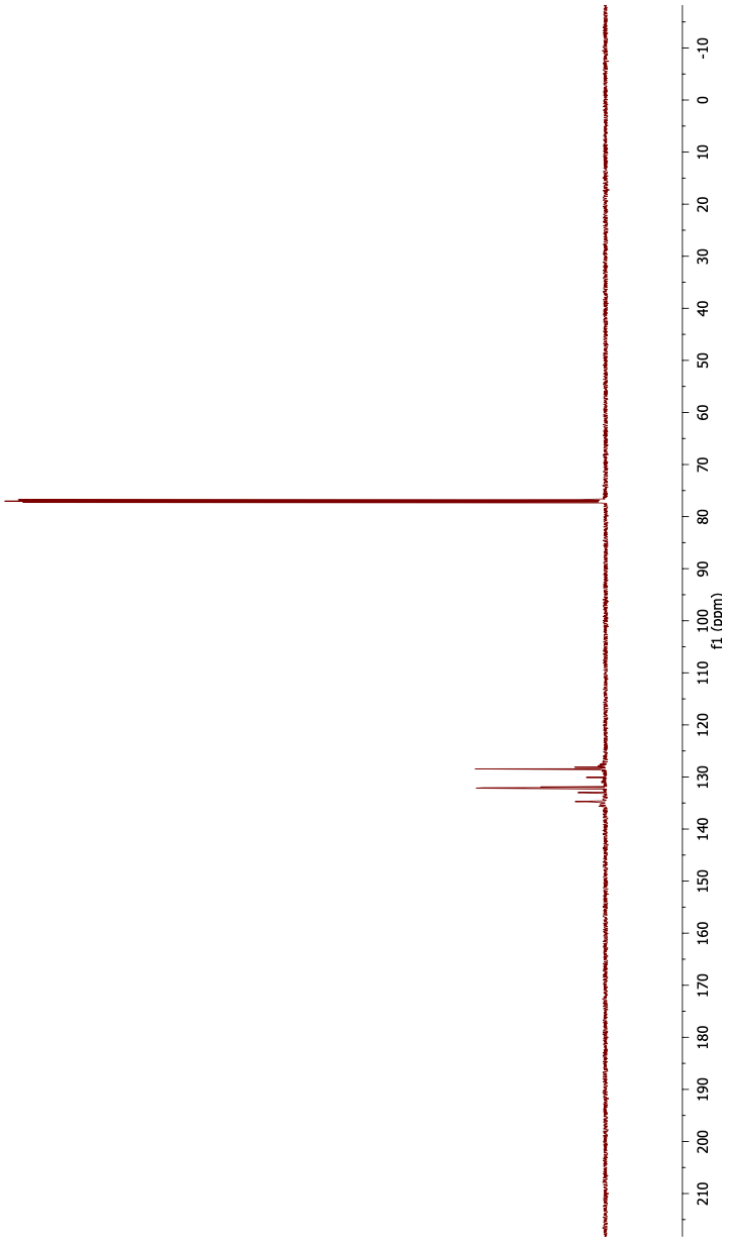



O
Cl
F
F
F
F
F
F
22a
f1 (ppm)
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210

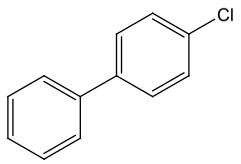
Wilkinson's Catalyst



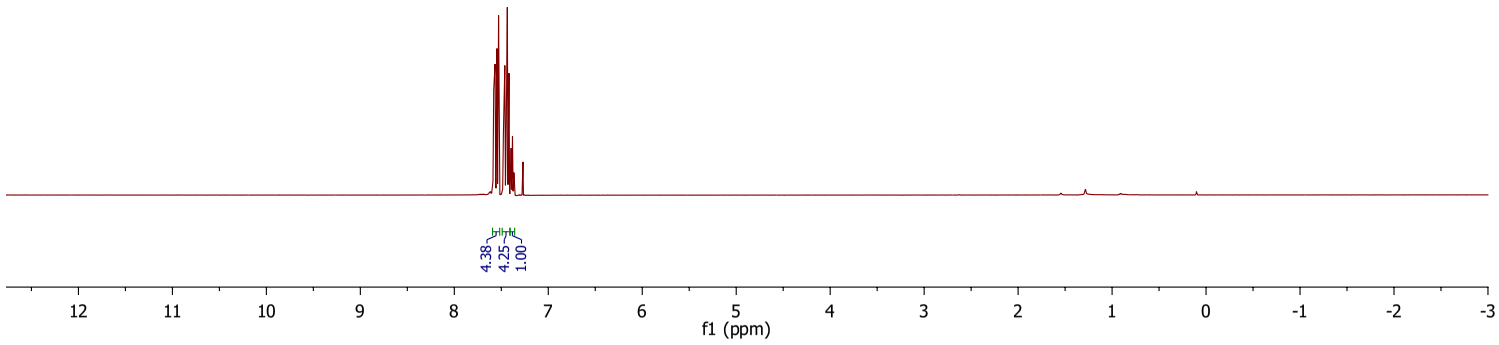
Wilkinson's Catalyst

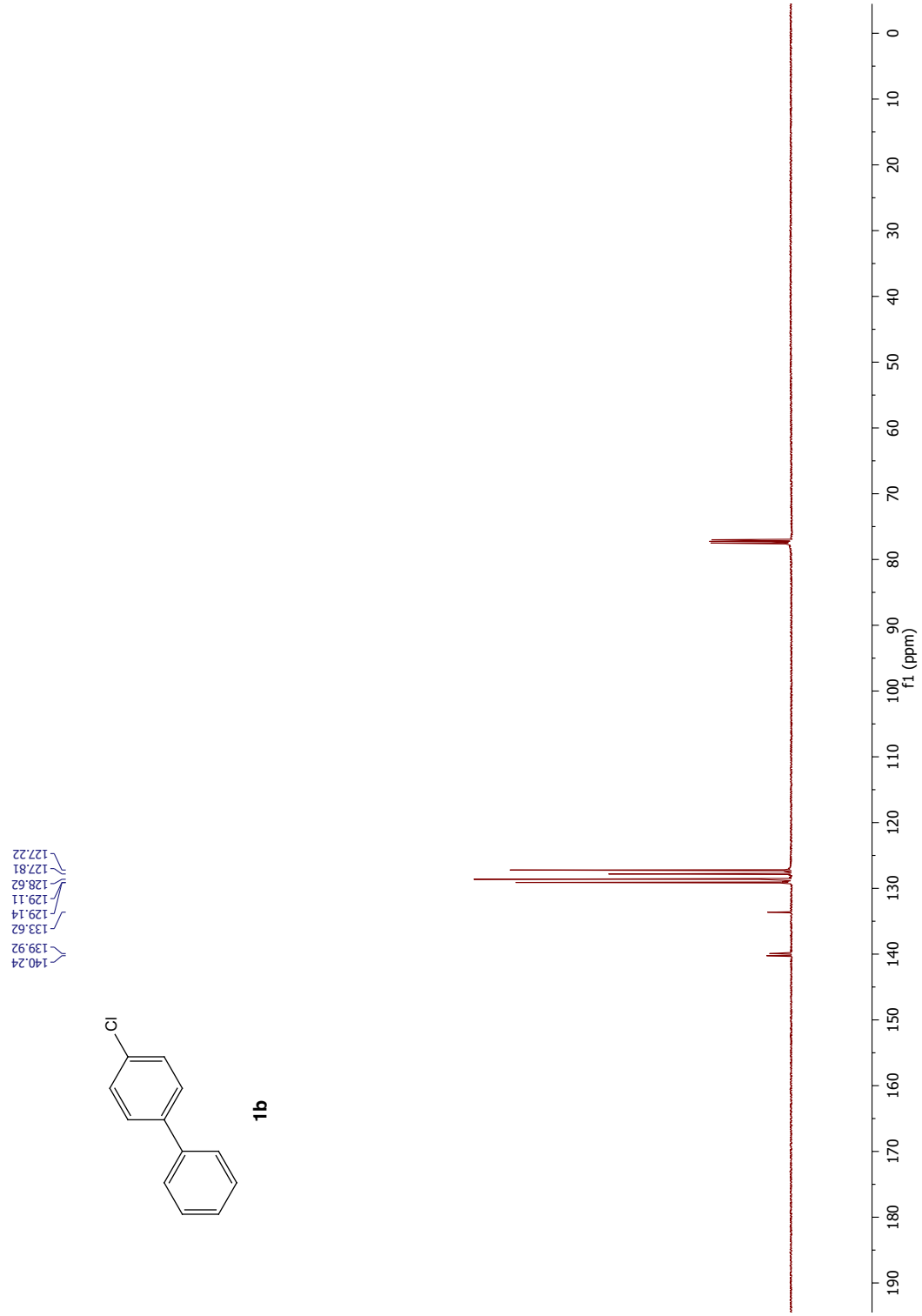


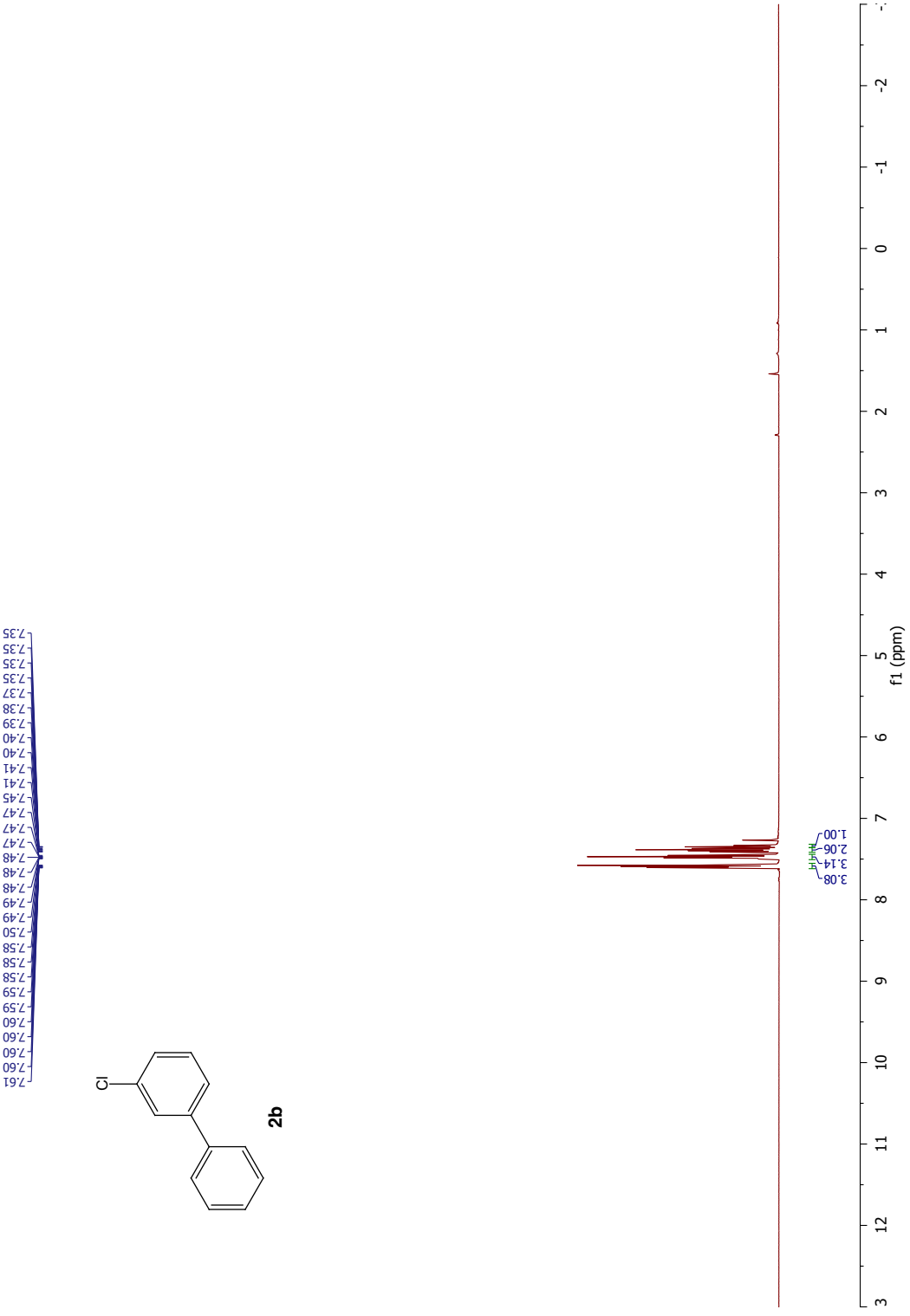

7.58
7.58
7.58
7.58
7.57
7.57
7.57
7.56
7.56
7.55
7.55
7.54
7.53
7.53
7.52
7.48
7.48
7.48
7.48
7.47
7.47
7.46
7.46
7.46
7.45
7.45
7.44
7.44
7.44
7.43
7.42
7.42
7.41
7.40
7.40
7.39
7.38
7.38
7.38
7.37
7.37
7.37
7.36

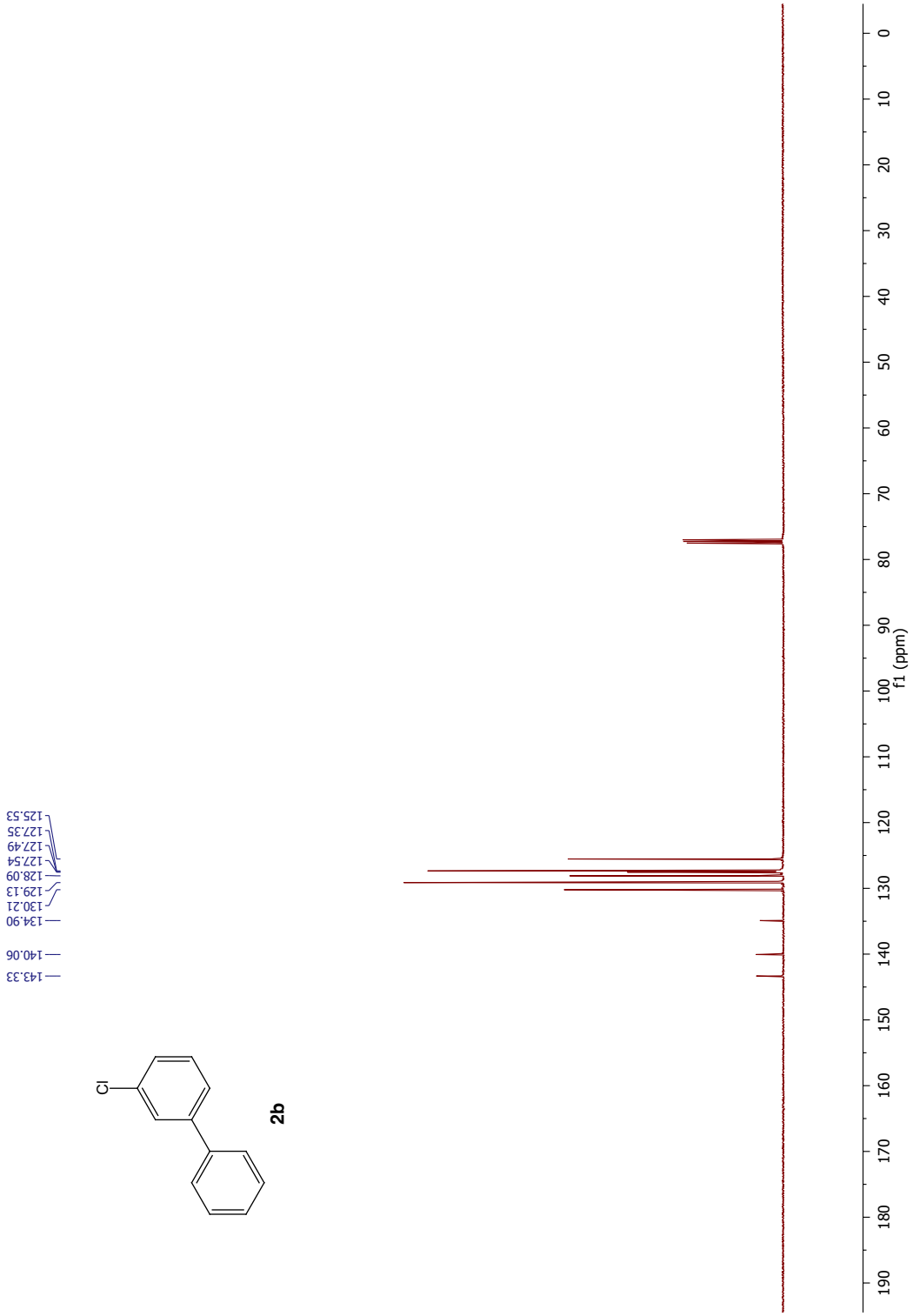

Cl

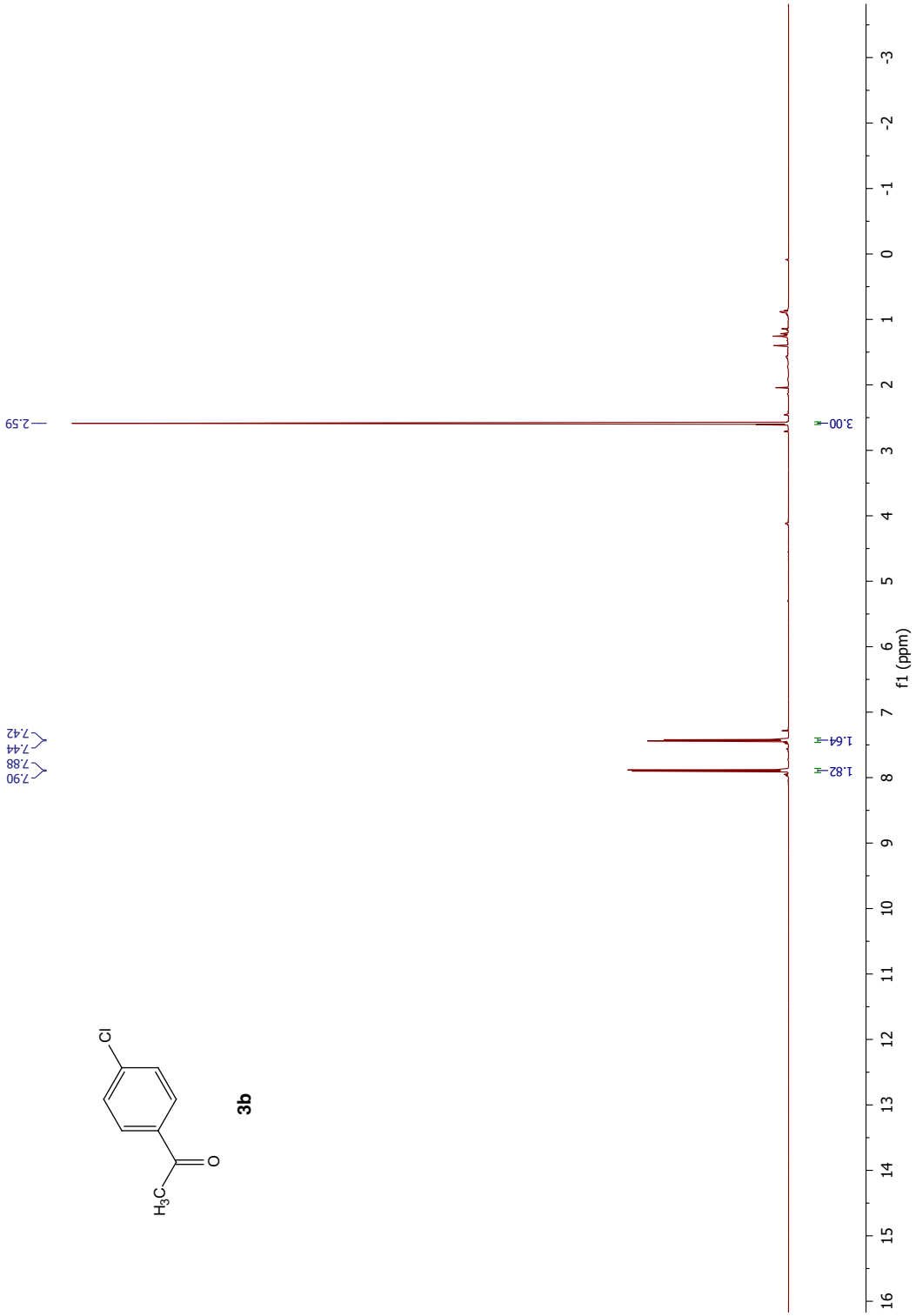
1b

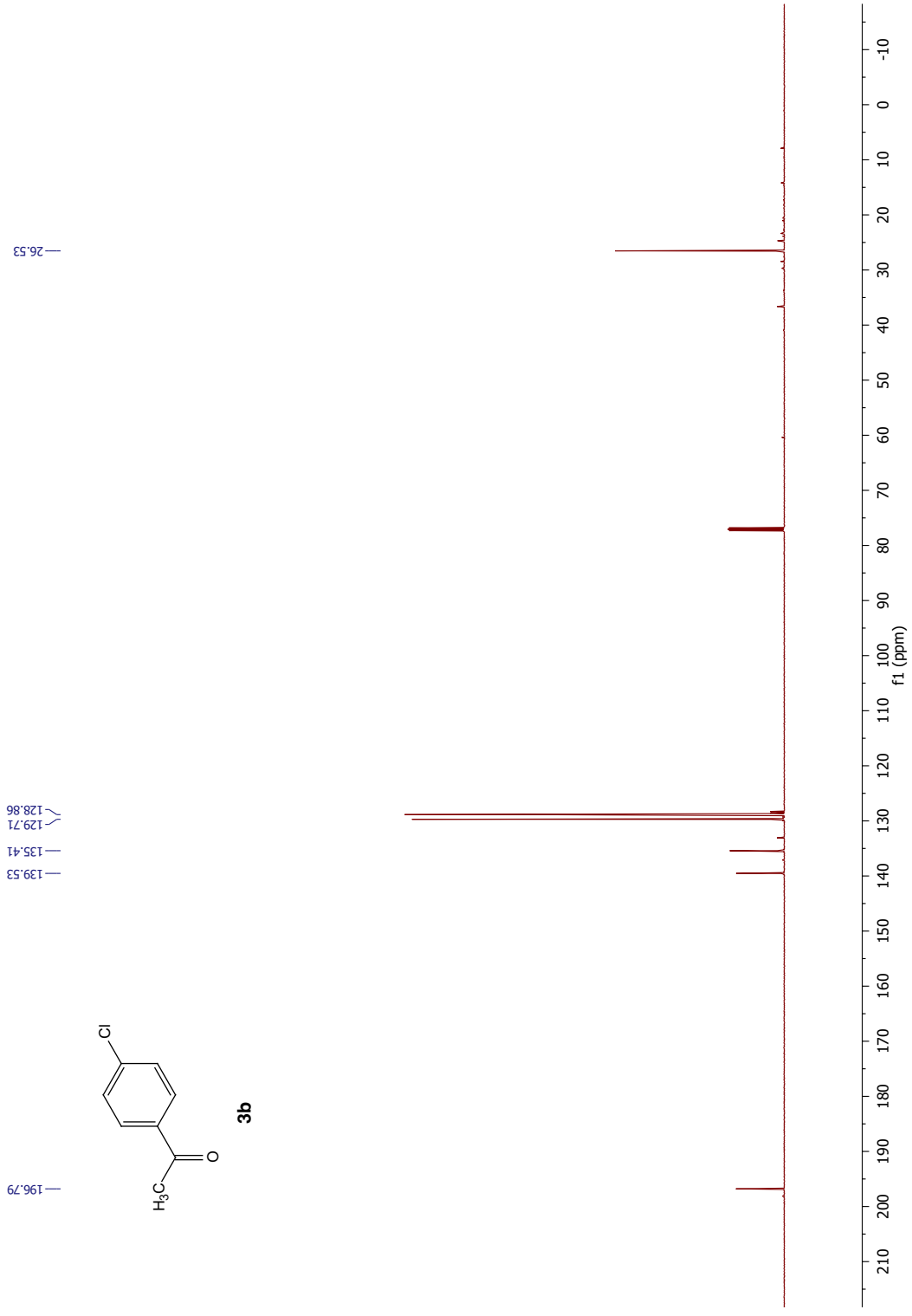

4.38
4.25
1.00
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f1 (ppm)

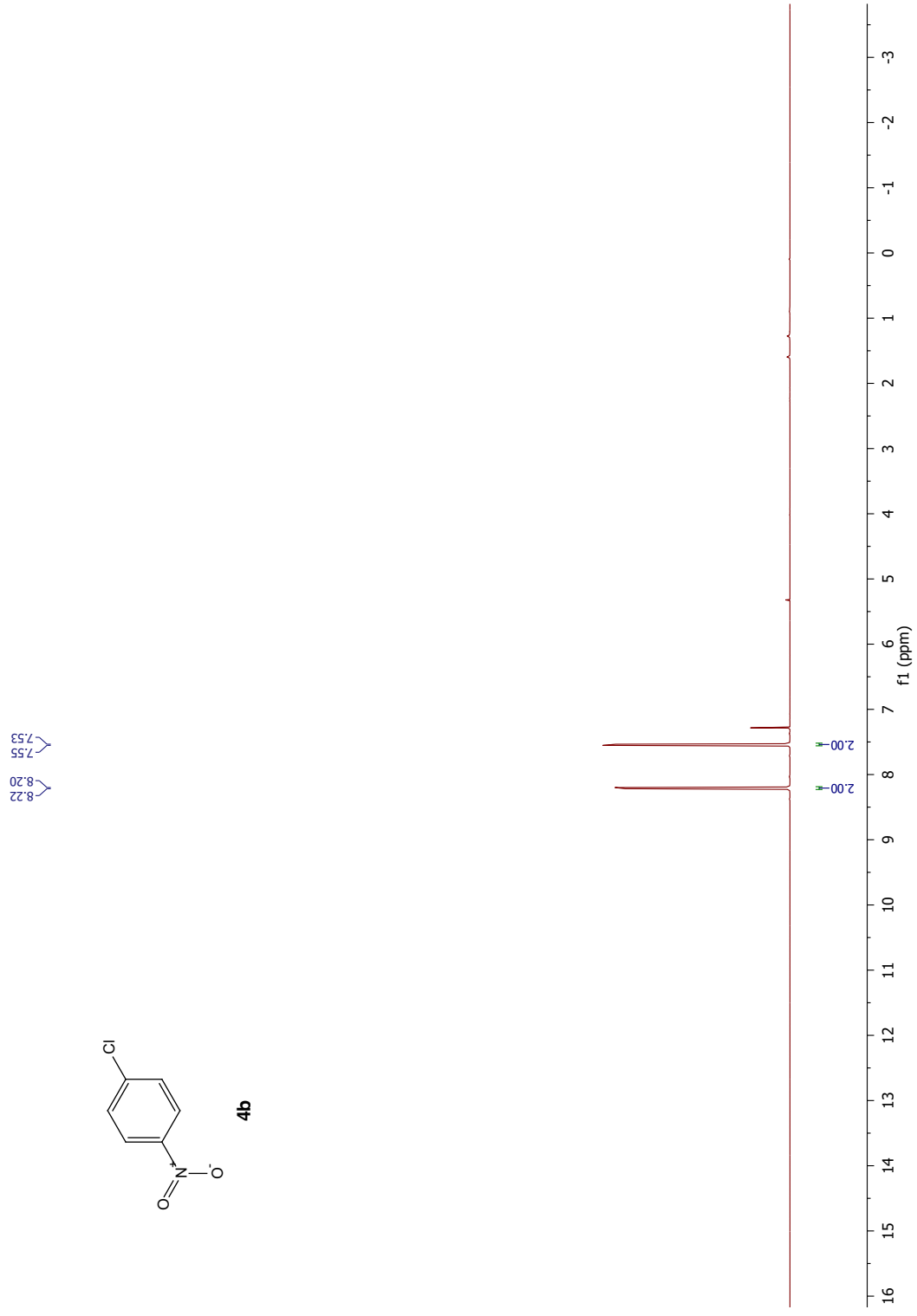

140.24
139.92
133.62
129.14
129.11
128.62
127.81
127.22
Cl
1b
f1 (ppm)

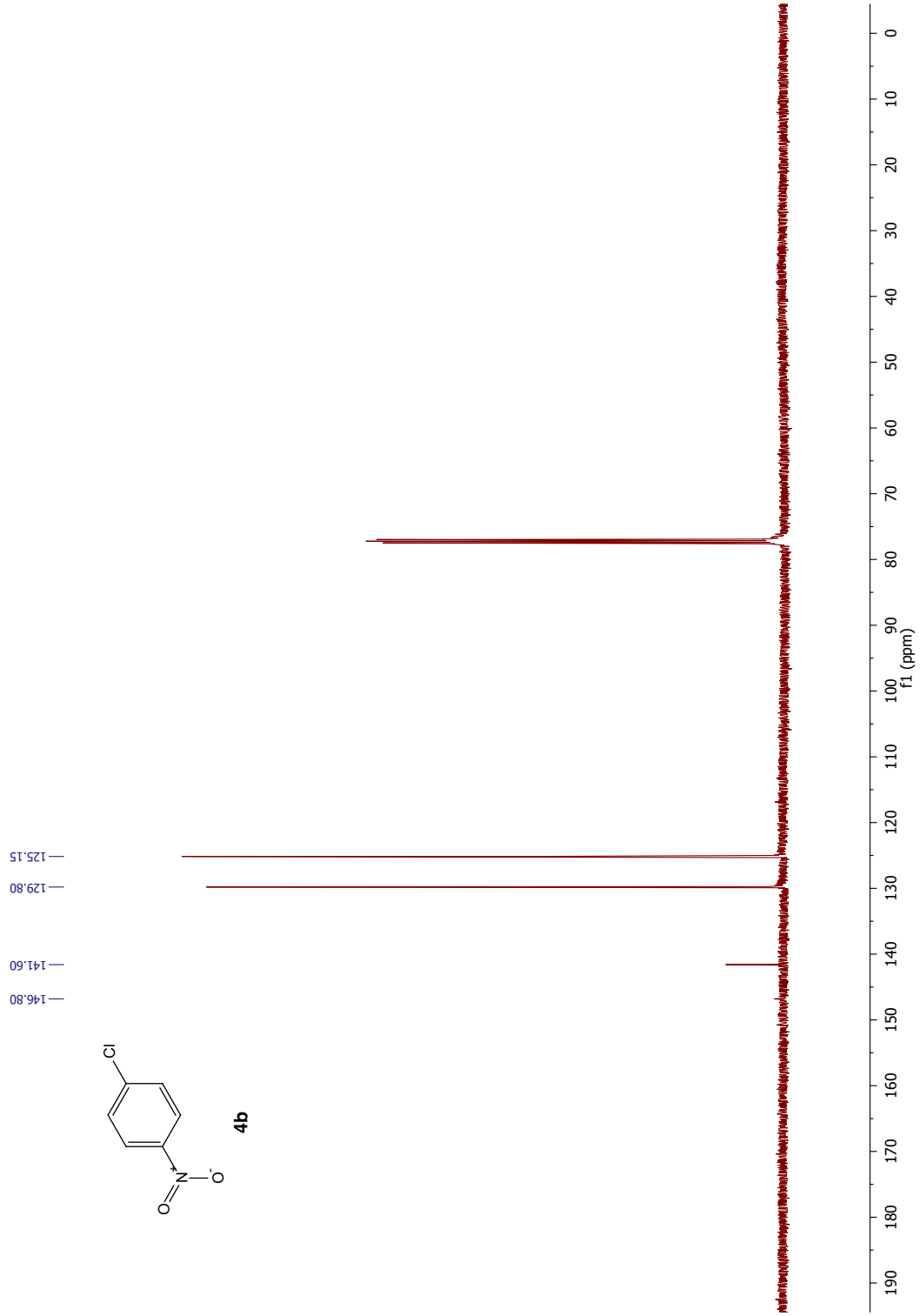

7.61
7.60
7.60
7.60
7.59
7.59
7.58
7.58
7.58
7.50
7.49
7.49
7.48
7.48
7.48
7.47
7.47
7.47
7.45
7.41
7.41
7.40
7.40
7.39
7.38
7.37
7.35
7.35
7.35
Cl
2b
3.08
3.14
2.06
1.00
f1 (ppm)

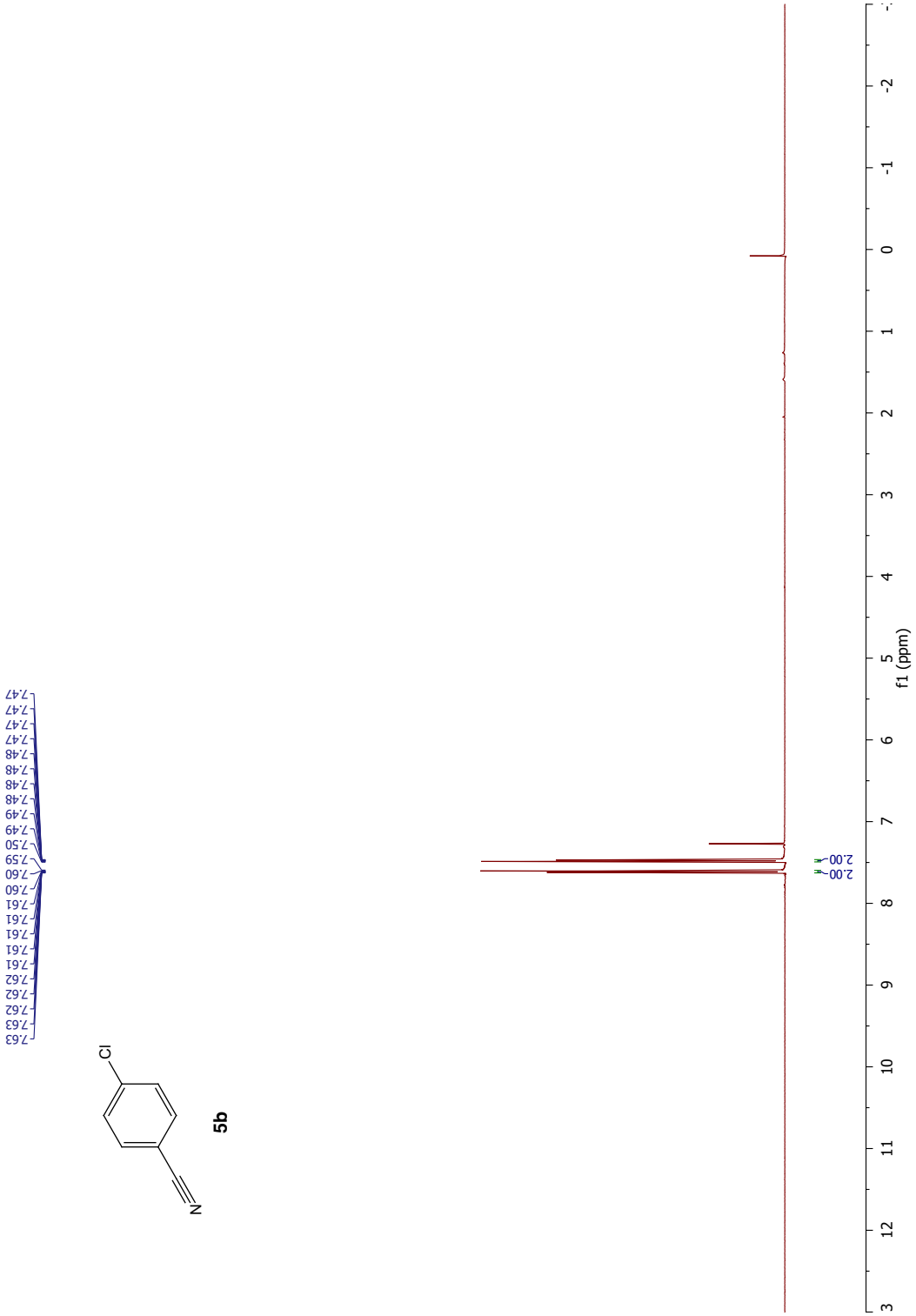

143.33
140.06
134.90
130.21
129.13
128.09
127.54
127.49
127.35
125.53
Cl
2b
f1 (ppm)

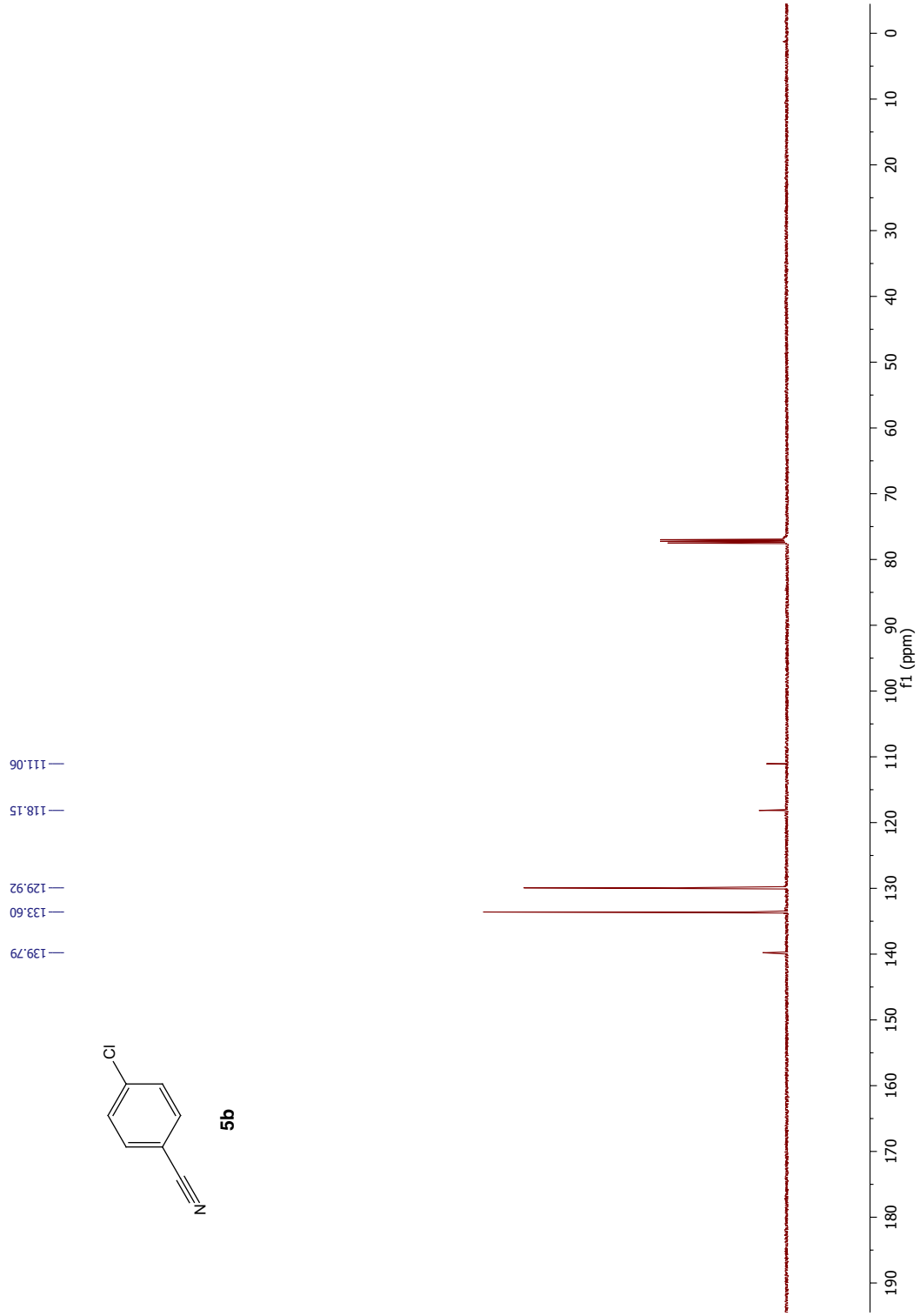

2.59
7.90
7.88
7.44
7.42
3.00
1.64
1.82
f1 (ppm)
Cl
O
H3C
3b

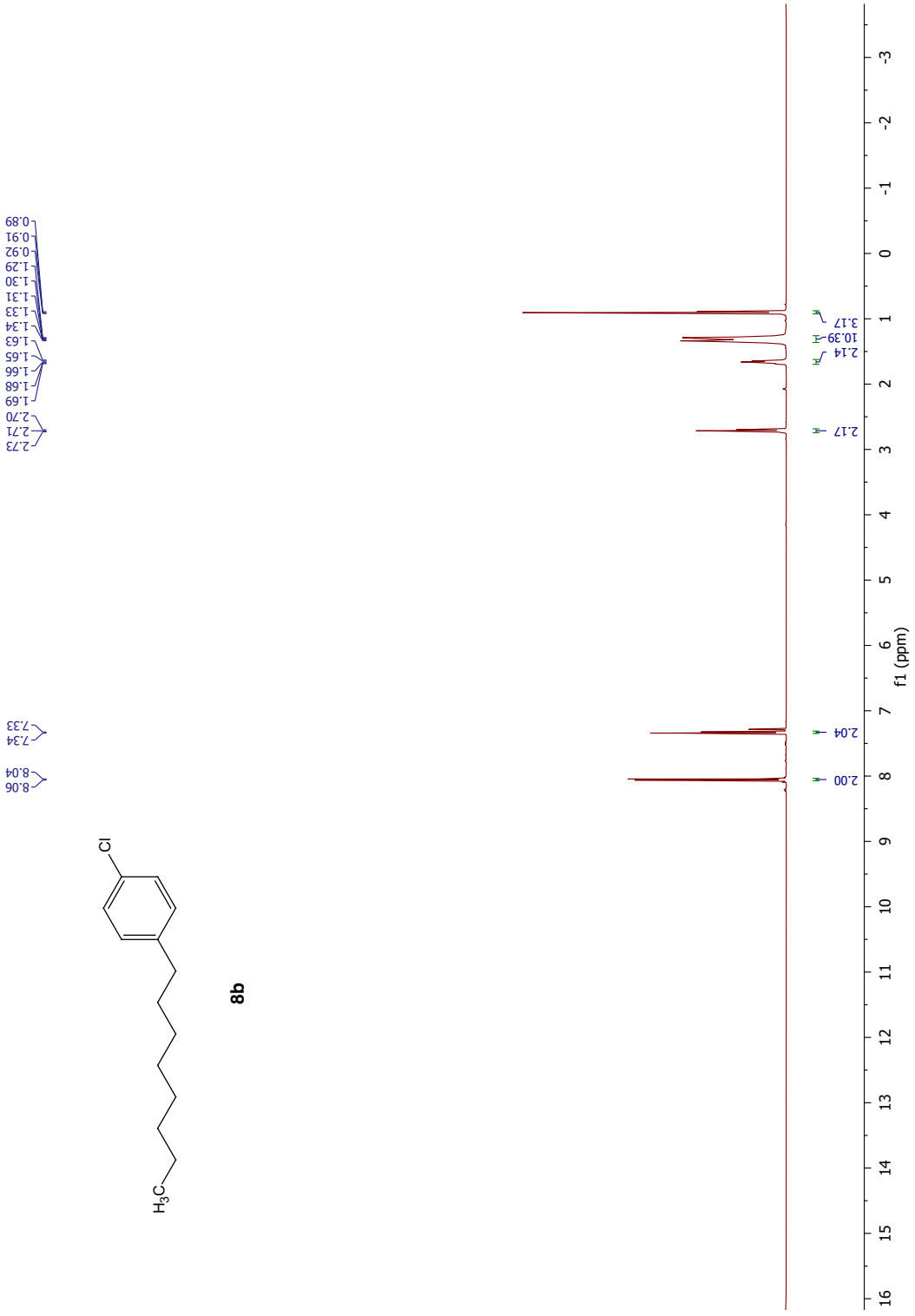

196.79
139.53
135.41
129.71
128.86
26.53
Cl
O
H3C
3b
f1 (ppm)

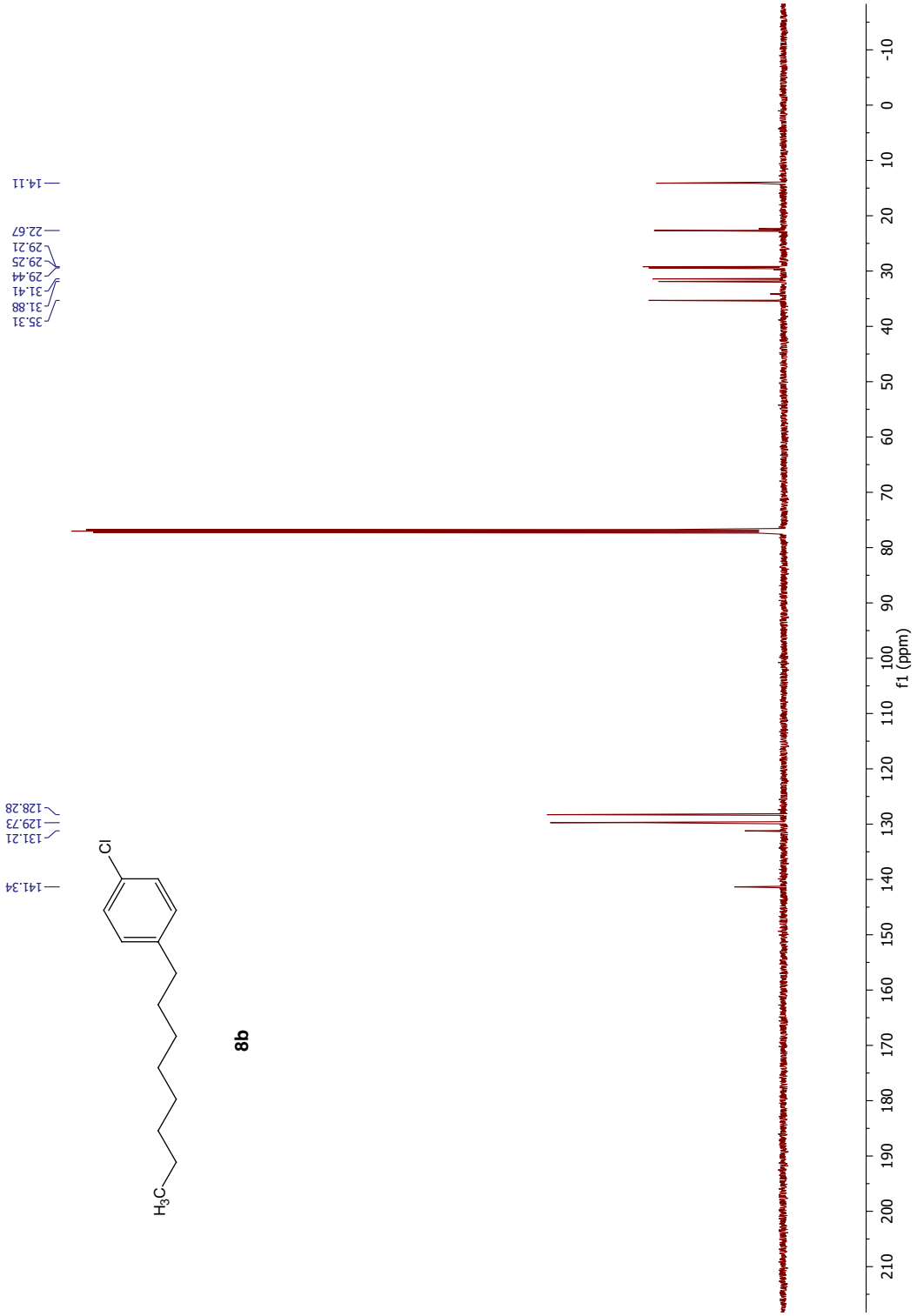

8.22
8.20
7.55
7.53
Cl
O
N
O
4b
2.00
2.00
f1 (ppm)

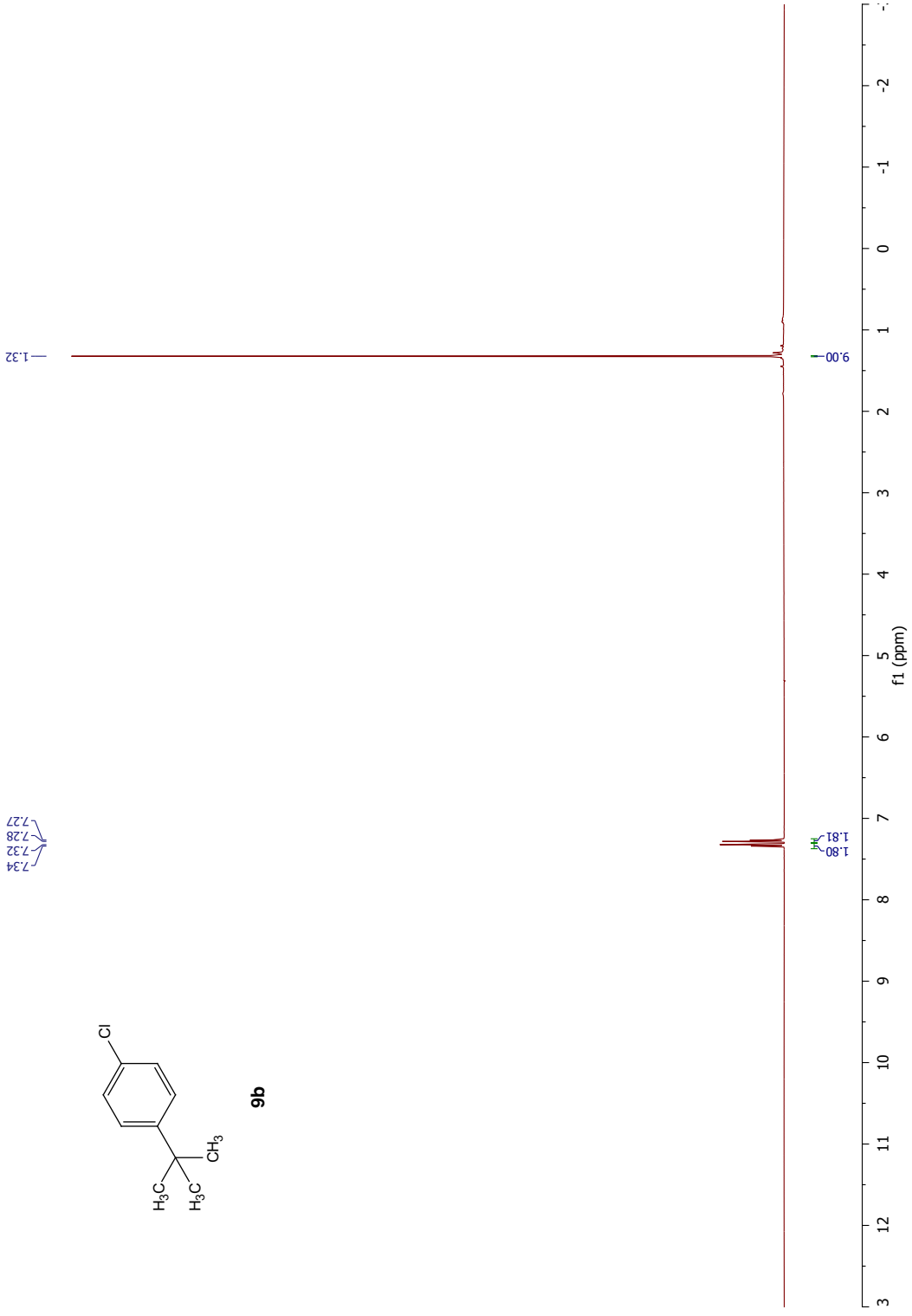

125.15
129.80
141.60
146.80
Cl
O
N
O
4b
f1 (ppm)

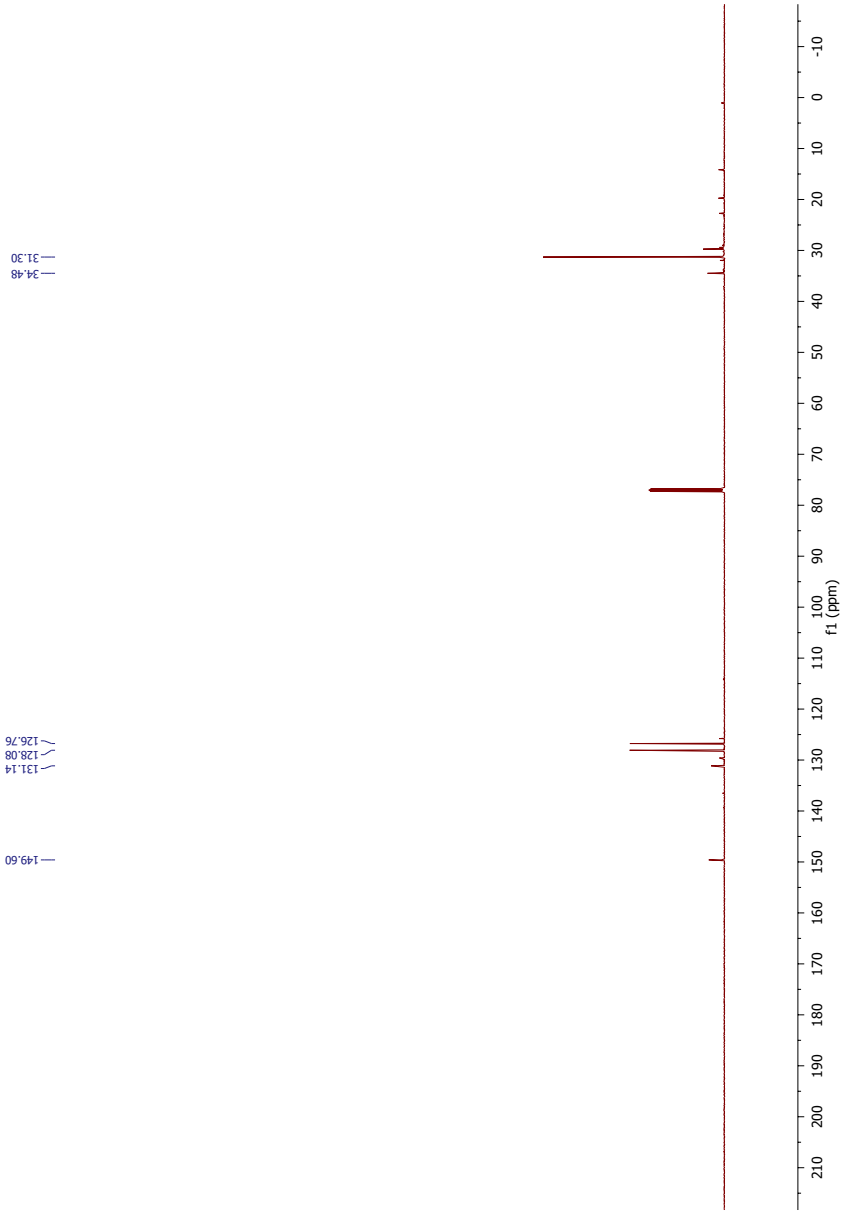

7.63
7.62
7.62
7.62
7.61
7.61
7.61
7.61
7.61
7.60
7.60
7.59
7.50
7.49
7.49
7.48
7.48
7.48
7.48
7.47
7.47
7.47
7.47
Cl
N
5b
2.00
2.00
f1 (ppm)

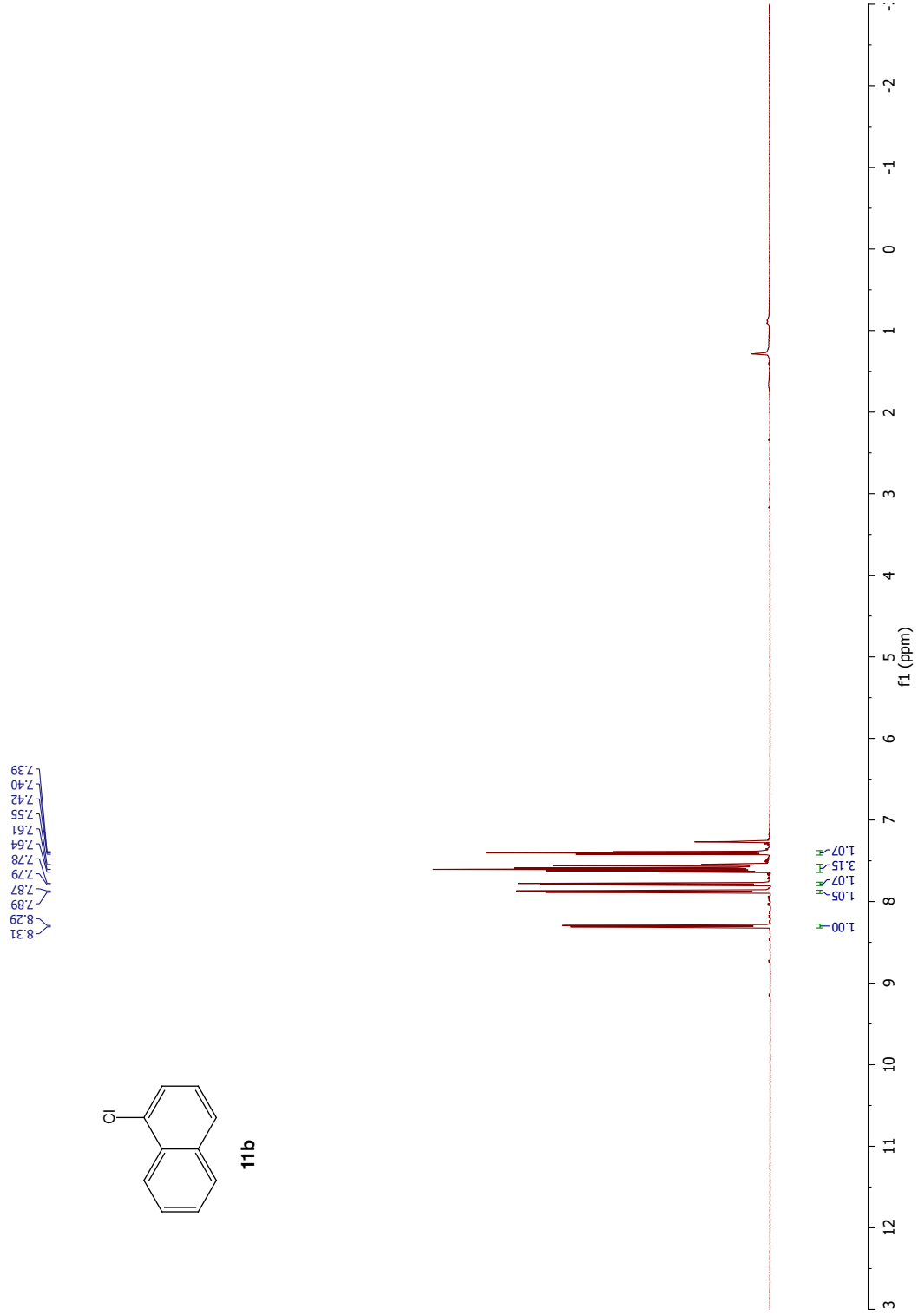

111.06
118.15
129.92
133.60
139.79
Cl
N
5b
f1 (ppm)

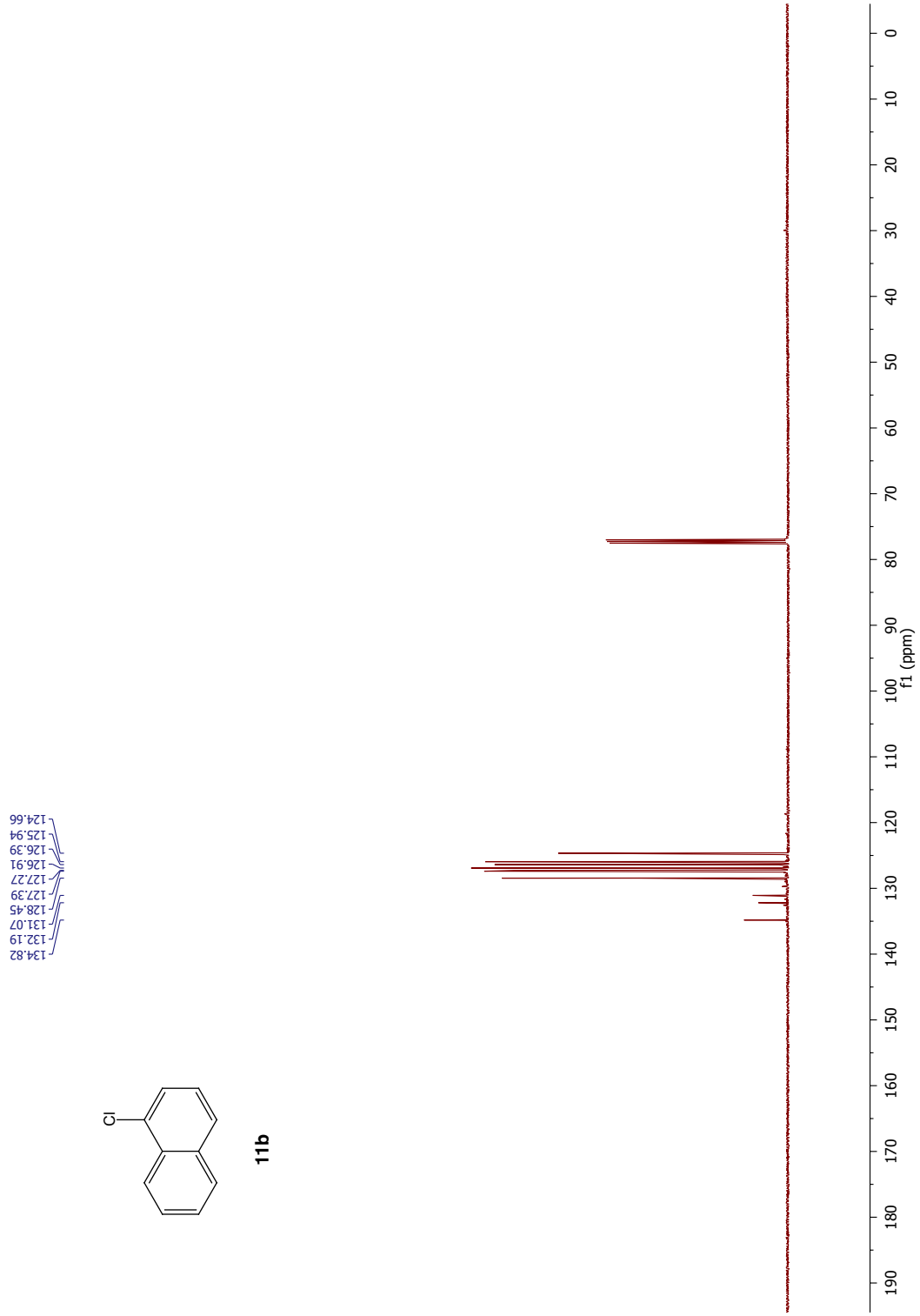

8.06
8.04
7.34
7.33
2.73
2.71
2.70
1.69
1.68
1.66
1.65
1.63
1.34
1.33
1.31
1.30
1.29
0.92
0.91
0.89
Cl
H3C
8b
2.00
2.04
2.17
3.17
10.39
2.14
f1 (ppm)

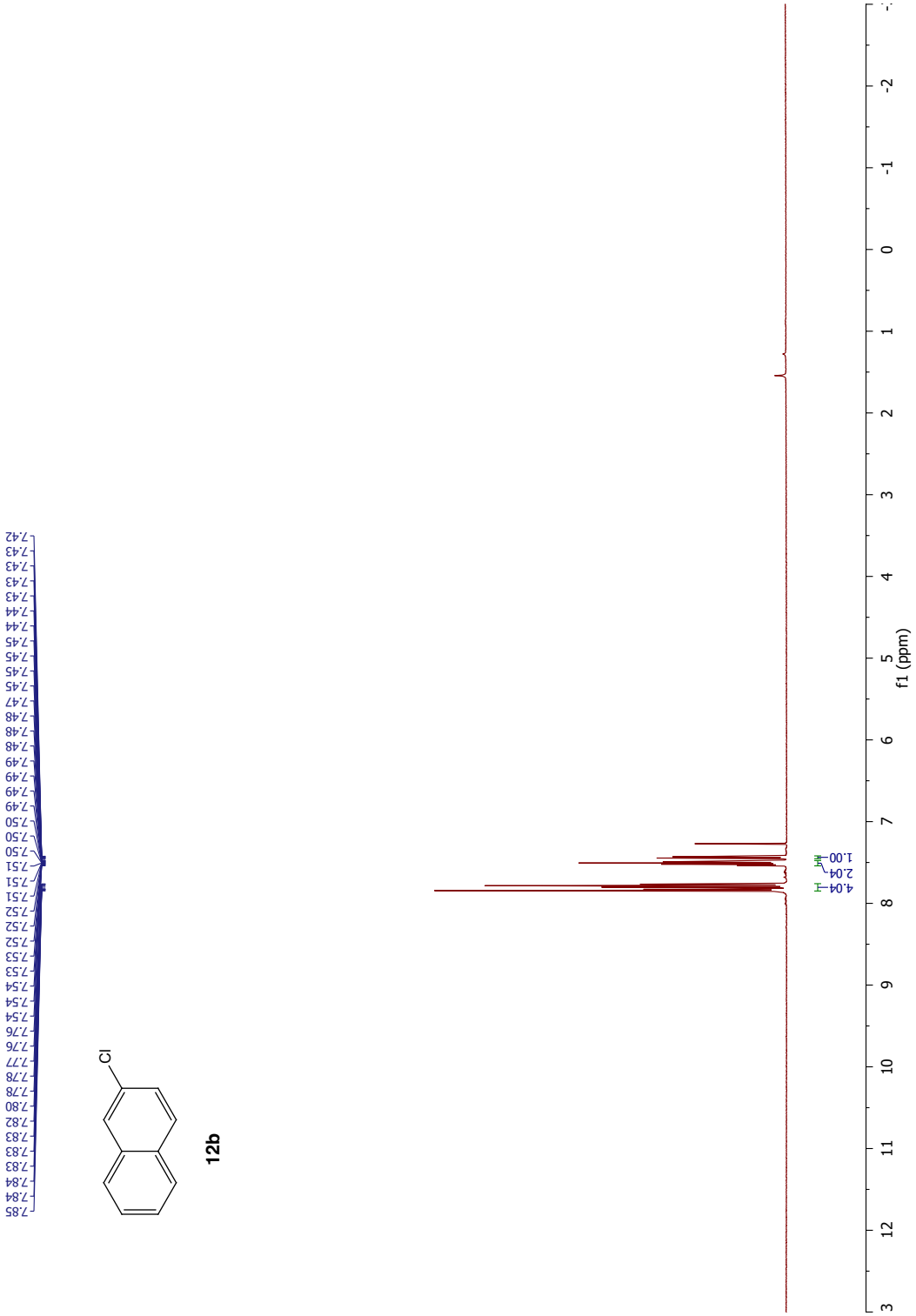

141.34
131.21
129.73
128.28
35.31
31.88
31.41
29.44
29.25
29.21
22.67
14.11
Cl
H3C
8b
f1 (ppm)

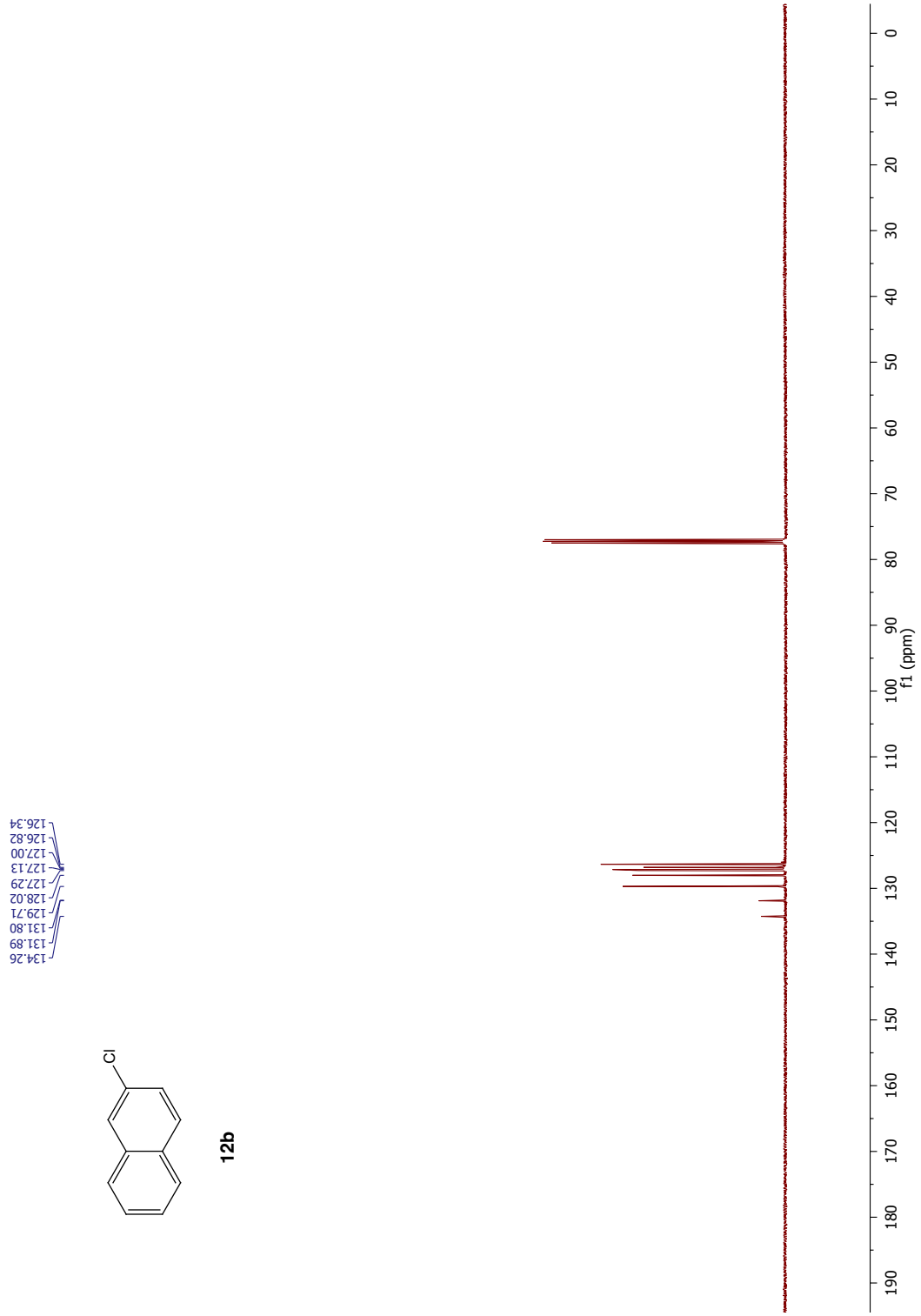

Cl
H3C
H3C
CH3
9b
7.34
7.32
7.28
7.27
1.32
1.80
1.81
9.00
f1 (ppm)

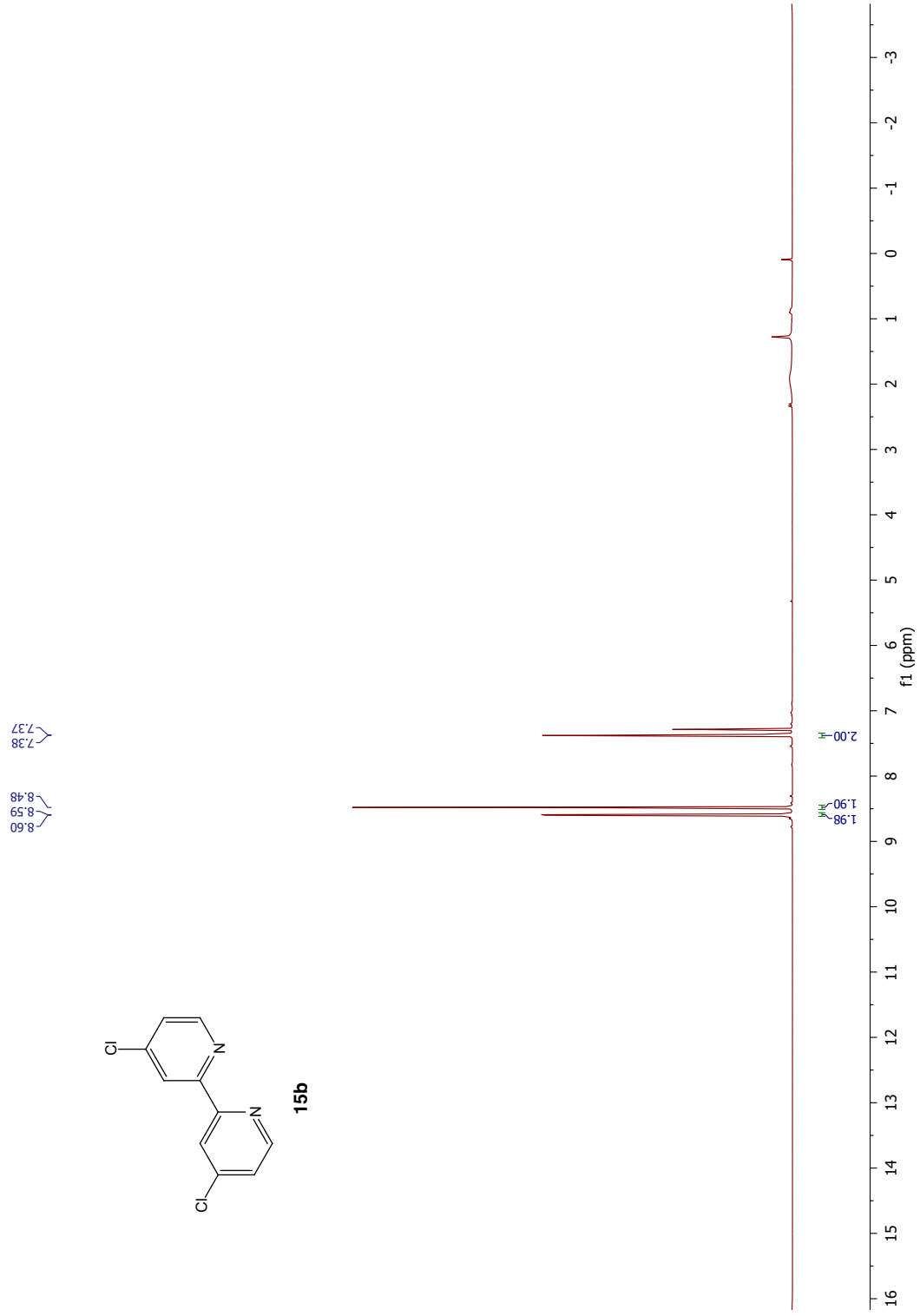

31.30
34.48
126.76
128.08
131.14
149.60
f1 (ppm)

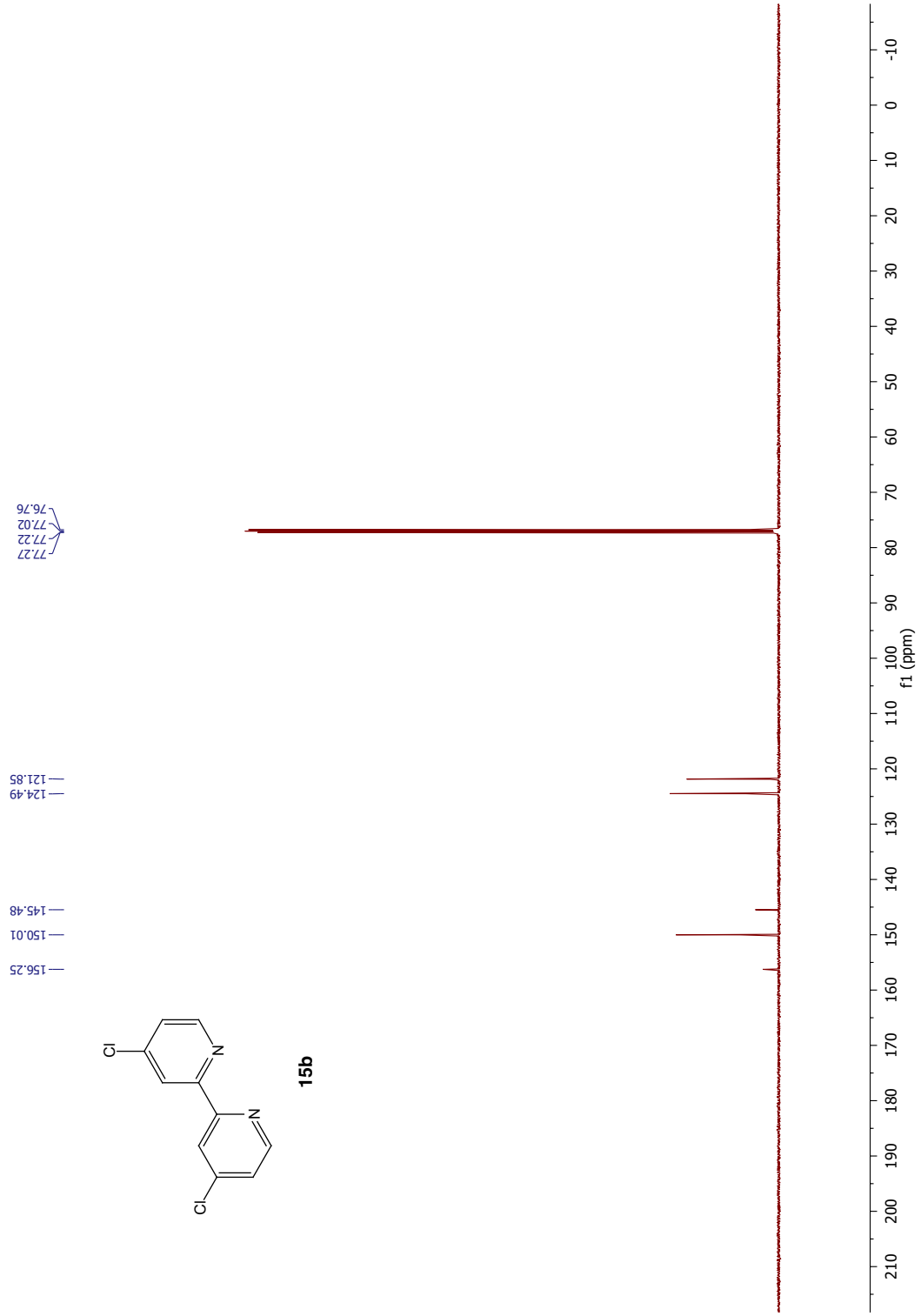

8.31
8.29
7.89
7.87
7.79
7.78
7.64
7.61
7.55
7.42
7.40
7.39
1.00
1.05
1.07
3.15
1.07
f1 (ppm)
Cl
11b

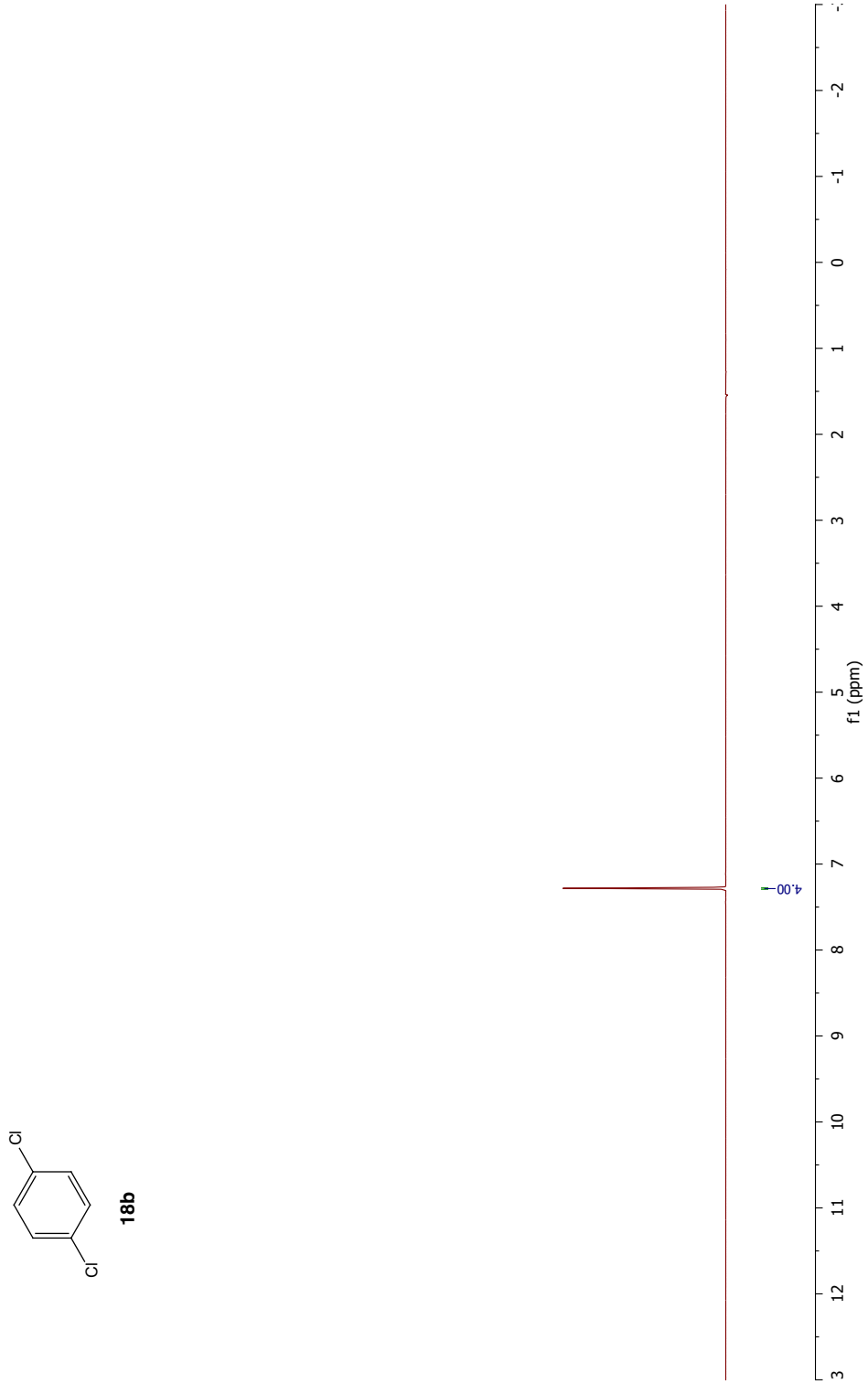

Cl
11b
134.82
132.19
131.07
128.45
127.39
127.27
126.91
126.39
125.94
124.66
f1 (ppm)

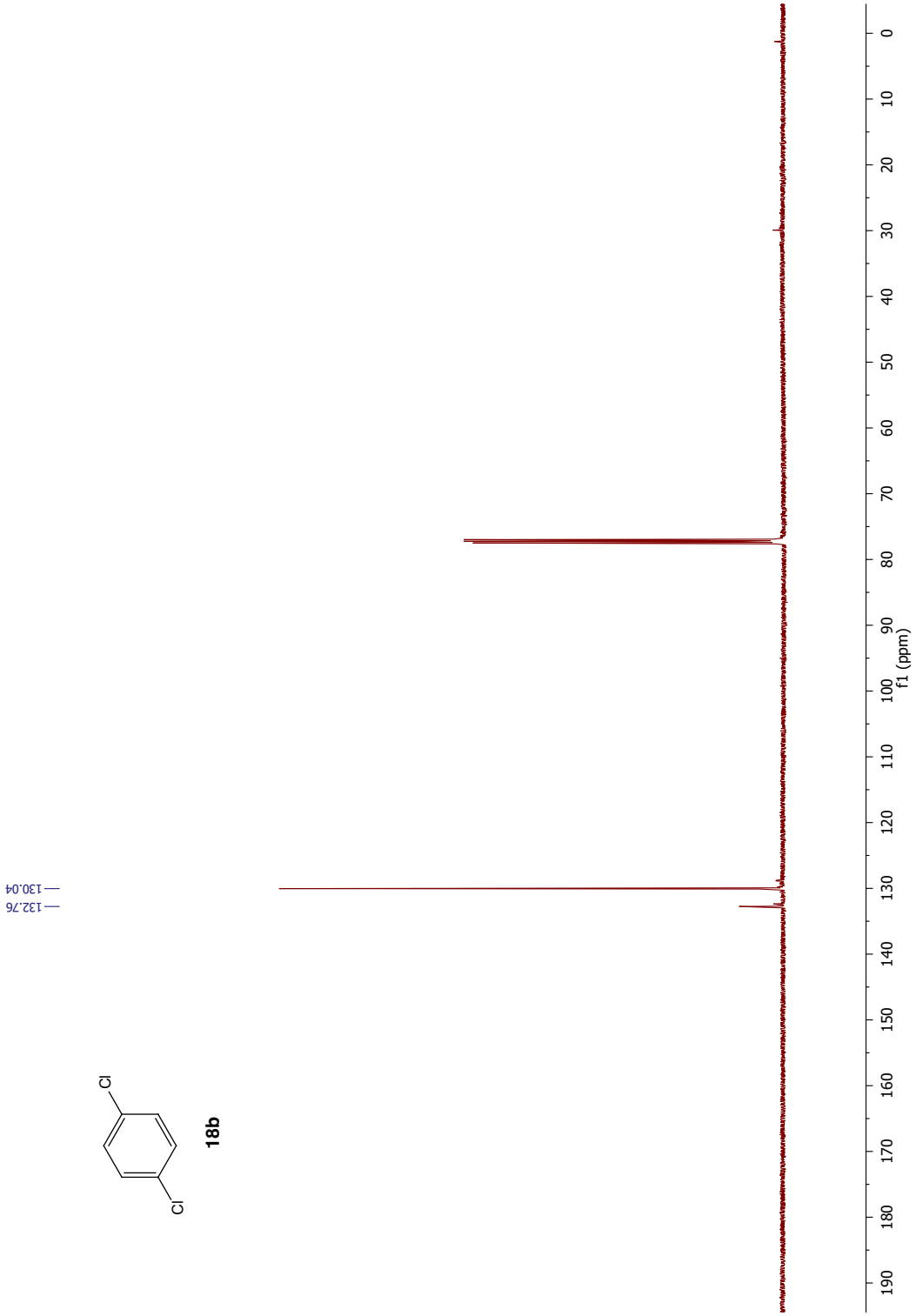

Cl
12b
4.04
2.04
1.00
f1 (ppm)


134.26
131.89
131.80
129.71
128.02
127.29
127.13
127.00
126.82
126.34
Cl
12b
f1 (ppm)


8.60
8.59
8.48
7.38
7.37
1.98
1.90
2.00
f1 (ppm)
15b


77.27
77.22
77.02
76.76
124.49
121.85
145.48
150.01
156.25
Cl
N
N
Cl
15b
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
f1 (ppm)


Cl
Cl
18b
4.00
f1 (ppm)


Cl
Cl
18b
132.76
130.04
f1 (ppm)

BIBLIOGRAPHY

1. Thayer, J. S. Cadet's Fuming Liquid: An Historical Survey. *Journal of Chemical Education* **1966**, *43*, 594–595.

2. Zeise, W. C. Gekohlenwasserstofftes Chlorplatin - Ammoniak. *Annalen der Physik* **1831**, *97*, 542–549.

3. Hunt, L. B. The First Organometallic Compounds. *Platinum Metals Review* **1984**, *28*, 76–83.

4. Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*; John Wiley & Sons, Inc., 2014.

5. Thayer, J. S. Historical Origins of Organometallic Chemistry. Part II, Edward Frankland and Diethylzinc. *Journal of Chemical Education* **1969**, *46*, 764–765.

6. Mond, L.; Langer, C.; Quincke, F. L.—Action of Carbon Monoxide on Nickel. *Journal of the Chemical Society, Transactions* **1890**, *57*, 749–753.

7. The Extraction of Nickel from Its Ores by the Mond Process. *Nature* **1898**, *59*, 63–64.

8. Kagan, H. B. Victor Grignard and Paul Sabatier: Two Showcase Laureates of the Nobel Prize for Chemistry. *Angewandte Chemie International Edition* **2012**, *51*, 7376–7382.

9. Grignard, V. Sur Quelques Nouvelles Combinaisons Organométaliques Du Magnésium Et Leur Application À Des Synthèses D'alcools Et D'hydrocabures. *Comptes rendus hebdomadaires des séances de l'Académie des sciences* **1900**, *130*, 1322–1324.

10. Klein, D. *Organic Chemistry*, Third ed.; John Wiley and Sons, Inc., 2017.

11. Hein, F. Notiz Über Chromorganoverbindungen. *Berichte der deutschen chemischen Gesellschaft (A and B Series)* **1919**, *52*, 195–196.

12. Kealy, T. J.; Pauson, P. L. A New Type of Organo–Iron Compound. *Nature* **1951**, *168*, 1039–1040.

13. Fischer, E. O.; Pfab, W. Cyclopentadien-Metallkomplexe, Ein Neuer Typ Metallorganischer Verbindungen. *Zeitschrift für Naturforschung B* **1952**, *7*, 377–379.

14. Wilkinson, G.; Rosenblum, M.; Whiting, M. C.; Woodward, R. B. The Structure of Iron Bis-Cyclopentadienyl. *Journal of the American Chemical Society* **1952**, *74*, 2125–2126.

15. Hartwig, J. F. *Organotransition Metal Chemistry: From Bonding to Catalysis*; Univeristy Science Books, 2010.

16. Ziegler, K.; Holzkamp, E.; Breil, H.; Martin, H. Polymerisation Von Äthylen Und Anderen Olefinen. *Angewandte Chemie* **1955**, *67*, 426.

17. Pino, P.; Corradini, P.; Danusso, F.; Mantica, E.; Mazzanti, G.; Moraglio, G.; Natta, G. Crystalline High Polymers of A-Olefins. *Journal of the American Chemical Society* **1955**, *77*, 1708–1710.

18. Ziegler, K. Consequences and Development of an Invention. *Rubber Chemistry and Technology* **1965**, *38*, 23–36.

19. Natta, G. Macromolecular Chemistry. *Science* **1965**, *147*, 261–272.

20. Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry: A Comprehensive Text*; Interscience Publishers, 1972.

21. Cotton, S. A. Scandium, Yttrium & the Lanthanides: Inorganic & Coordination Chemistry. In *Encyclopedia of Inorganic Chemistry*2005. https://onlinelibrary.wiley.com/doi/abs/10.1002/0470862106.ia211 DOI: https://doi.org/10.1002/0470862106.ia211

22. Neuss, G. R. H. A Problem with Explaining the Electron Configuration of Scandium. *Foundations of Chemistry* **2021**, *23*, 239–245.

23. Jana, R.; Pathak, T. P.; Sigman, M. S. Advances in Transition Metal (Pd,Ni,Fe)-Catalyzed Cross-Coupling Reactions Using Alkyl-Organometallics as Reaction Partners. *Chemical Reviews* **2011**, *111*, 1417–1492.

24. Petrone, D. A.; Ye, J.; Lautens, M. Modern Transition-Metal-Catalyzed Carbon–Halogen Bond Formation. *Chemical Reviews* **2016**, *116*, 8003–8104.

25. Colacot, T. Richard F. Heck (1931–2015). *Angewandte Chemie International Edition* **2015**, *54*, 15611–15612.

26. Negishi, E. Magical Power of Transition Metals: Past, Present, and Future (Nobel Lecture). *Angewandte Chemie International Edition* **2011**, *50*, 6738–6764.

27. Suzuki, A. Cross-Coupling Reactions of Organoboranes: An Easy Way to Construct C–C Bonds (Nobel Lecture). *Angewandte Chemie International Edition* **2011**, *50*, 6722–6737.

28. Nolley, J. P.; Heck, R. F. Palladium-Catalyzed Vinylic Hydrogen Substitution Reactions with Aryl, Benzyl, and Styryl Halides. *The Journal of Organic Chemistry* **1972**, *37*, 2320–2322.

29. Dieck, H. A.; Heck, R. F. Organophosphinepalladium Complexes as Catalysts for Vinylic Hydrogen Substitution Reactions. *Journal of the American Chemical Society* **1974**, *96*, 1133–1136.

30. Heck, R. F. Palladium-Catalyzed Vinylation of Organic Halides. In *Organic Reactions*2005; pp 345–390. https://onlinelibrary.wiley.com/doi/abs/10.1002/0471264180.or027.02 DOI: https://doi.org/10.1002/0471264180.or027.02

31. Mizoroki, T.; Mori, K.; Ozaki, A. Arylation of Olefin with Aryl Iodide Catalyzed by Palladium. *Bulletin of the Chemical Society of Japan* **1971**, *44*, 581–581.

32. Cheprakov, A. V.; Beletskaya, I. P. The Heck Reaction as a Sharpening Stone of Palladium Catalysis. *Chemical Reviews* **2000**, *100*, 3009–3066.

33. Hong, C. Y.; Kado, N.; Overman, L. E. Asymmetric Synthesis of Either Enantiomer of Opium Alkaloids and Morphinans. Total Synthesis of (-)- and (+)-Dihydrocodeinone and (-)- and (+)-Morphine. *Journal of the American Chemical Society* **1993**, *115*, 11028–11029.

34. King, A. O.; Okukado, N.; Negishi, E. Highly General Stereo-, Regio-, and Chemo-Selective Synthesis of Terminal and Internal Conjugated Enynes by the Pd-Catalysed Reaction of Alkynylzinc Reagents with Alkenyl Halides. *Journal of the Chemical Society, Chemical Communications* **1977**, 683–684.

35. King, A. O.; Okukado, N.; Negishi, E. Selective Carbon-Carbon Bond Formation Via Transition Metal Catalysis. 3. A Highly Selective Synthesis of Unsymmetrical Biaryls and Diarylmethanes by the Nickel- or Palladium-Catalyzed Reaction of Aryl- and Benzylzinc Derivatives with Aryl Halides. *The Journal of Organic Chemistry* **1977**, *42*, 1821–1823.

36. Aoyagi, S.; Kibayashi, C. A Convergent Total Synthesis of Pumiliotoxins a and B Via Palladium-Catalyzed Cross-Coupling Reaction of Homoallylic Organozinc Compounds with Vinyl Iodides. *Journal of Organometallic Chemistry* **2002**, *653*, 229–233.

37. Miyaura, N.; Yamada, K.; Suzuki, A. A New Stereospecific Cross-Coupling by the Palladium-Catalyzed Reaction of 1-Alkenylboranes with 1-Alkenyl or 1-Alkynyl Halides. *Tetrahedron Letters* **1979**, *20*, 3437–3440.

38. Miyaura, N.; Suzuki, A. Stereoselective Synthesis of Arylated (E)-Alkenes by the Reaction of Alk-1-Enylboranes with Aryl Halides in the Presence of Palladium Catalyst. *Journal of the Chemical Society, Chemical Communications* **1979**, 866–867.

39. Miyaura, N.; Suzuki, A. Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chemical Reviews* **1995**, *95*, 2457–2483.

40. Peterson, E. A.; Stephan, M. L.; Vyvyan, J. R. An Expedient Total Synthesis of (±)-Caparratriene. *Tetrahedron Letters* **1999**, *40*, 4947–4949.

41. Tamao, K.; Sumitani, K.; Kumada, M. Selective Carbon-Carbon Bond Formation by Cross-Coupling of Grignard Reagents with Organic Halides. Catalysis by Nickel-Phosphine Complexes. *Journal of the American Chemical Society* **1972**, *94*, 4374–4376.

42. Kumada, M. Nickel and Palladium Complex Catalyzed Cross-Coupling Reactions of Organometallic Reagents with Organic Halides. *Pure and Applied Chemistry* **1980**, *52*, 669–679.

43. Stille, J. K. The Palladium-Catalyzed Cross-Coupling Reactions of Organotin Reagents with Organic Electrophiles. *Angewandte Chemie International Edition in English* **1986**, *25*, 508–524.

44. Hatanaka, Y.; Hiyama, T. Cross-Coupling of Organosilanes with Organic Halides Mediated by a Palladium Catalyst and Tris(Diethylamino)Sulfonium Difluorotrimethylsilicate. *The Journal of Organic Chemistry* **1988**, *53*, 918–920.

45. Sonogashira, K. Development of Pd–Cu Catalyzed Cross-Coupling of Terminal Acetylenes with sp^2-Carbon Halides. *Journal of Organometallic Chemistry* **2002**, *653*, 46–49.

46. Albaneze-Walker, J.; Murry, J. A.; Dormer, P. G.; Hughes, D. L.; Soheili, A. Efficient and General Protocol for the Copper-Free Sonogashira Coupling of Aryl Bromides at Room Temperature. *Organic Letters* **2003**, *5*, 4191–4194.

47. Osborn, J. A.; Jardine, F. H.; Young, J. F.; Wilkinson, G. The Preparation and Properties of Tris(Triphenylphosphine)Halogeno- Rhodium(1) and Some Reactions Thereof Including Catalytic Homo- Geneous Hydrogenation of Olefins and Acetylenes and Their Derivatives. *Journal of the Chemical Society A: Inorganic, Physical, Theoretical* **1966**, 1711–1732.

48. Colby, D. A.; Bergman, R. G.; Ellman, J. A. Rhodium-Catalyzed C−C Bond Formation Via Heteroatom-Directed C−H Bond Activation. *Chemical Reviews* **2010**, *110*, 624–655.

49. Lim, Y. G.; Kim, Y. H.; Kang, J. B. Rhodium-Catalysed Regioselective Alkylation of the Phenyl Ring of 2-Phenylpyridines with Olefins. *Journal of the Chemical Society, Chemical Communications* **1994**, 2267–2268.

50. Lim, Y. G.; Kang, J. B.; Kim, Y. H. Regioselective Alkylation of 2-Phenylpyridines with Terminal Alkenes Via C–H Bond Activation by a Rhodium Catalyst. *Journal of the Chemical Society, Perkin Transactions 1* **1996**, 2201–2206.

51. Colby, D. A.; Bergman, R. G.; Ellman, J. A. Synthesis of Dihydropyridines and Pyridines from Imines and Alkynes Via C−H Activation. *Journal of the American Chemical Society* **2008**, *130*, 3645–3651.

52. Ueura, K.; Satoh, T.; Miura, M. Rhodium- and Iridium-Catalyzed Oxidative Coupling of Benzoic Acids with Alkynes Via Regioselective C−H Bond Cleavage. *The Journal of Organic Chemistry* **2007**, *72*, 5362–5367.

53. Ueura, K.; Satoh, T.; Miura, M. An Efficient Waste-Free Oxidative Coupling Via Regioselective C−H Bond Cleavage: Rh/Cu-Catalyzed Reaction of Benzoic Acids with Alkynes and Acrylates under Air. *Organic Letters* **2007**, *9*, 1407–1409.

54. Hong, J. B.; Kim, Y. H.; Chung, K. Y.; Jun, C. H. The Catalytic Alkylation of Aromatic Imines by Wilkinson's Complex: The Domino Reaction of Hydroacylation and Ortho-Alkylation. *Angewandte Chemie International Edition* **2000**, *39*, 3440–3442.

55. Kisenyi, J. M.; Sunley, G. J.; Cabeza, J. A.; Smith, A. J.; Adams, H.; Salt, N. J.; Maitlis, P. M. The Cyclometallation of Benzoic Acid to Give Rhodium, Iridium, and Osmium C,O-Benzoates. X-Ray Structure Determination of the Dibenzoate $[(C_5Me_5)Rh(OOCPh)_2(H_2O)]$. *Journal of the Chemical Society, Dalton Transactions* **1987**, 2459–2466.

56. Rayabarapu, D. K.; Tunge, J. A. Catalytic Decarboxylative sp–sp^3 Coupling. *Journal of the American Chemical Society* **2005**, *127*, 13510–13511.

57. Yang, L.; Correia, C. A.; Guo, X.; Li, C. J. A Novel Catalytic Decarbonylative Heck-Type Reaction and Conjugate Addition of Aldehydes to Unsaturated Carbonyl Compounds. *Tetrahedron Letters* **2010**, *51*, 5486–5489.

58. Kang, L.; Zhang, F.; Ding, L. T.; Yang, L. Rhodium-Catalyzed Oxidative Decarbonylative Heck-Type Coupling of Aromatic Aldehydes with Terminal Alkenes. *RSC Advances* **2015**, *5*, 100452–100456.

59. Yang, L.; Guo, X.; Li, C. J. The First Decarbonylative Coupling of Aldehydes and Norbornenes Catalyzed by Rhodium. *Advanced Synthesis & Catalysis* **2010**, *352*, 2899–2904.

60. Yang, L.; Zeng, T.; Shuai, Q.; Guo, X.; Li, C.-J. Phosphine Ligand Triggered Oxidative Decarbonylative Homocoupling of Aromatic Aldehydes: Selectively Generating Biaryls and Diarylketones. *Chemical Communications* **2011**, *47*, 2161–2163.

61. Shuai, Q.; Yang, L.; Guo, X.; Baslé, O.; Li, C. J. Rhodium-Catalyzed Oxidative C−H Arylation of 2-Arylpyridine Derivatives Via Decarbonylation of Aromatic Aldehydes. *Journal of the American Chemical Society* **2010**, *132*, 12212–12213.

62. Tomberg, A.; Kundu, S.; Zhou, F.; Li, C. J.; Moitessier, N. Revised Mechanism for a Ruthenium-Catalyzed Coupling of Aldehyde and Terminal Alkyne. *ACS Omega* **2018**, *3*, 3218–3227.

63. Guo, L.; Srimontree, W.; Zhu, C.; Maity, B.; Liu, X.; Cavallo, L.; Rueping, M. Nickel-Catalyzed Suzuki–Miyaura Cross-Couplings of Aldehydes. *Nature Communications* **2019**, *10*, 1957.

64. Pines, H.; Eschinazi, H. Notes: Study in the Terpene Series. XXXI. Synthesis of Appinene by Catalytic Decarbonylation of Myrtenal. *The Journal of Organic Chemistry* **1959**, *24*, 1369–1369.

65. Tsuji, J.; Ohno, K.; Kajimoto, T. Organic Syntheses by Means of Noble Metal Compounds Xx. Decarbonylation of Acyl Chloride and Aldehyde Catalyzed by Palladium and Its Relationship with the Rosenmund Reduction. *Tetrahedron Letters* **1965**, *6*, 4565–4568.

66. Tsuji, J.; Ohno, K. Organic Syntheses by Means of Noble Metal Compounds. XXXIV. Carbonylation and Decarbonylation Reactions Catalyzed by Palladium. *Journal of the American Chemical Society* **1968**, *90*, 94–98.

67. Tsuji, J.; Ohno, K. Organic Syntheses by Means of Noble Metal Compounds XXI. Dcarbonylation of Aldehydes Using Rhodium Complex. *Tetrahedron Letters* **1965**, *6*, 3969–3971.

68. Ohno, K.; Tsuji, J. Organic Synthesis by Means of Noble Metal Compounds. XXXV. Novel Decarbonylation Reactions of Aldehydes and Acyl Halides Using Rhodium Complexes. *Journal of the American Chemical Society* **1968**, *90*, 99–107.

69. Doughty, D. H.; Pignolet, L. H. Catalytic Decarbonylation of Aldehydes. *Journal of the American Chemical Society* **1978**, *100*, 7083–7085.

70. Beck, C. M.; Rathmill, S. E.; Park, Y. J.; Chen, J.; Liable-Sands, L. M.; Rheingold, A. L.; Crabtree, R. H. Aldehyde Decarbonylation Catalysis Under Mild Conditions. *Organometallics* **1999**, *18*, 5311–5317.

71. Fristrup, P.; Kreis, M.; Palmelund, A.; Norrby, P. O.; Madsen, R. The Mechanism for the Rhodium-Catalyzed Decarbonylation of Aldehydes: A Combined Experimental and Theoretical Study. *Journal of the American Chemical Society* **2008**, *130*, 5206–5215.

72. Wilt, J. W.; Pawlikowski, W. W. Palladium- Vs. Peroxide-Promoted Decarbonylation of Neophyl-Like Aldehydes. *The Journal of Organic Chemistry* **1975**, *40*, 3641–3644.

73. Fessard, T. C.; Andrews, S. P.; Motoyoshi, H.; Carreira, E. M. Enantioselective Preparation of 1,1-Diarylethanes: Aldehydes as Removable Steering Groups for Asymmetric Synthesis. *Angewandte Chemie International Edition* **2007**, *46*, 9331–9334.

74. Ding, K.; Xu, S.; Alotaibi, R.; Paudel, K.; Reinheimer, E. W.; Weatherly, J. Nickel-Catalyzed Decarbonylation of Aromatic Aldehydes. *The Journal of Organic Chemistry* **2017**, *82*, 4924–4929.

75. Iwai, T.; Fujihara, T.; Tsuji, Y. The Iridium-Catalyzed Decarbonylation of Aldehydes under Mild Conditions. *Chemical Communications* **2008**, 6215–6217.

76. Roa, A. E.; Salazar, V.; López-Serrano, J.; Oñate, E.; Paneque, M.; Poveda, M. L. Decarbonylation of Aliphatic Aldehydes by a TpMe2Ir(III) Metallacyclopentadiene. *Organometallics* **2012**, *31*, 716–721.

77. Domazetis, G.; Tarpey, B.; Dolphin, D.; James, B. R. Catalytic Decarbonylation of Aldehydes Using Ruthenium(II) Porphyrin Systems. *Journal of the Chemical Society, Chemical Communications* **1980**, 939–940.

78. Hernandes, Z. M.; Cavalcanti, T. S. M.; Moreira, M. D. R.; de Azevedo Junior, F. W.; Leite, L. A. C. Halogen Atoms in the Modern Medicinal Chemistry: Hints for the Drug Design. *Current Drug Targets* **2010**, *11*, 303–314.

79. Iskra, J.; A., D. *Halogenated Heterocycles : Synthesis, Application and Environment*; Springer, 2012.

80. Wilcken, R.; Zimmermann, M. O.; Lange, A.; Joerger, A. C.; Boeckler, F. M. Principles and Applications of Halogen Bonding in Medicinal Chemistry and Chemical Biology. *Journal of Medicinal Chemistry* **2013**, *56*, 1363–1388.

81. Gribble, G. W. Naturally Occurring Organohalogen Compounds. *Accounts of Chemical Research* **1998**, *31*, 141–152.

82. Blunt, J. W.; Copp, B. R.; Keyzers, R. A.; Munro, M. H. G.; Prinsep, M. R. Marine Natural Products. *Natural Product Reports* **2012**, *29*, 144–222.

83. Gribble, G. W. Natural Organohalogens: A New Frontier for Medicinal Agents? *Journal of Chemical Education* **2004**, *81*, 1441–1449.

84. Fujimori, D. G.; Walsh, C. T. What's New in Enzymatic Halogenations. *Current Opinion in Chemical Biology* **2007**, *11*, 553–560.

85. Wishar, D. S.; Knox, C.; Guo, A. C.; Shrivastava, S.; Hassanali, M.; Stothard, P.; Chang, Z.; Woolsey, J. Drugbank: A Comprehensive Resource for in Silico Drug Discovery and Exploration.

86. Liu, C.; Bayer, A.; Cosgrove, S. E.; Daum, R. S.; Fridkin, S. K.; Gorwitz, R. J.; Kaplan, S. L.; Karchmer, A. W.; Levine, D. P.; Murray, B. E.; J. Rybak, M.; Talan, D. A.; Chambers, H. F. Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant Staphylococcus Aureus Infections in Adults and Children: Executive Summary. *Clinical Infectious Diseases* **2011**, *52*, 285–292.

87. Harris, C. M.; Kannan, R.; Kopecka, H.; Harris, T. M. The Role of the Chlorine Substituents in the Antibiotic Vancomycin: Preparation and Characterization of Mono- and Didechlorovancomycin. *Journal of the American Chemical Society* **1985**, *107*, 6652–6658.

88. Jeschke, P. The Unique Role of Halogen Substituents in the Design of Modern Agrochemicals. *Pest Management Science* **2010**, *66*, 10–27.

89. Guan, A. Y.; Liu, C. L.; Huang, G.; Li, H. C.; Hao, S. L.; Xu, Y.; Li, Z. N. Design, Synthesis, and Structure-Activity Relationship of Novel Aniline Derivatives of Chlorothalonil. *Journal of Agricultural and Food Chemistry* **2013**, *61*, 11929–11936.

90. Jayaraj, R.; Megha, P.; Sreedev, P. Review Article. Organochlorine Pesticides, Their Toxic Effects on Living Organisms and Their Fate in the Environment. *Interdisciplinary Toxicology* **2016**, *9*, 90–100.

91. Baumann, M.; Baxendale, I. R. An Overview of the Synthetic Routes to the Best Selling Drugs Containing 6-Membered Heterocycles. *Beilstein Journal of Organic Chemistry* **2013**, *9*, 2265–2319.

92. Stiles, M.; Miller, R. G.; Burckhardt, U. Reactions of Benzyne Intermediates in Non-Basic Media. *Journal of the American Chemical Society* **1963**, *85*, 1792–1797.

93. Ayogu, J. I.; Onoabedje, E. A. Recent Advances in Transition Metal-Catalysed Cross-Coupling of (Hetero)Aryl Halides and Analogues under Ligand-Free Conditions. *Catalysis Science & Technology* **2019**, *9*, 5233–5255.

94. Cho, E. J.; Senecal, T. D.; Kinzel, T.; Zhang, Y.; Watson, D. A.; Buchwald, S. L. The Palladium-Catalyzed Trifluoromethylation of Aryl Chlorides. *Science* **2010**, *328*, 1679–81.

95. Lishchynskyi, A.; Novikov, M. A.; Martin, E.; Escudero-Adan, E. C.; Novak, P.; Grushin, V. V. Trifluoromethylation of Aryl and Heteroaryl Halides with Fluoroform-Derived $CuCF_3$: Scope, Limitations, and Mechanistic Features. *Journal of Organic Chemistry* **2013**, *78*, 11126–11146.

96. Nilsson, M. A New Biaryl Synthesis Illustrating a Connection between the Ullmann Biaryl Synthesis and Copper-Catalysed Decarboxylation. *Acta Chemica Scandinavica* **1966**, *20*, 423–426.

97. Hennings, D. D.; Iwama, T.; Rawal, V. H. Palladium-Catalyzed (Ullmann-Type) Homocoupling of Aryl Halides: A Convenient and General Synthesis of Symmetrical Biaryls Via Inter- and Intramolecular Coupling Reactions. *Organic Letters* **1999**, *1*, 1205–1208.

98. Sandmeyer, T. Ueber Die Ersetzung Der Amidgruppe Durch Chlor in Den Aromatischen Substanzen. *Berichte der deutschen chemischen Gesellschaft* **1884**, *17*, 1633–1635.

99. Kürti, L.; Czakó, B. *Strategic Applications of Named Reactions in Organic Synthesis*; Elsevier Inc., 2005.

100. Firth, J. D.; Fairlamb, I. J. S. A Need for Caution in the Preparation and Application of Synthetically Versatile Aryl Diazonium Tetrafluoroborate Salts. *Organic Letters* **2020**, *22*, 7057–7059.

101. Sehnal, P.; Taylor, R. J. K.; Fairlamb, I. J. S. Emergence of Palladium(Iv) Chemistry in Synthesis and Catalysis. *Chemical Reviews* **2010**, *110*, 824–889.

102. Kalyani, D.; Sanford, M. S. Chelate-Directed Oxidative Functionalization of Carbon–Hydrogen Bonds: Synthetic applications and Mechanistic Insights. In *Directed Metallation*; Chatani, N., Ed.; Springer Berlin Heidelberg, 2007; pp 85–116.

103. Racowski, J. M.; Sanford, M. S. Carbon–Heteroatom Bond-Forming Reductive Elimination from Palladium(IV) Complexes. In *Higher Oxidation State Organopalladium and Platinum Chemistry*; Canty, A. J., Ed.; Springer Berlin Heidelberg, 2011; pp 61–84.

104. Hickman, A. J.; Sanford, M. S. High-Valent Organometallic Copper and Palladium in Catalysis. *Nature* **2012**, *484*, 177–185.

105. Hull, K. L.; Anani, W. Q.; Sanford, M. S. Palladium-Catalyzed Fluorination of Carbon−Hydrogen Bonds. *Journal of the American Chemical Society* **2006**, *128*, 7134–7135.

106. Fahey, D. R. The Homogeneous Palladium-Catalysed Ortho-Chlorination of Azobenzene. *Journal of the Chemical Society D: Chemical Communications* **1970**, 417.

107. Fahey, D. R. The Coordination-Catalyzed Ortho-Halogenation of Azobenzene. *Journal of Organometallic Chemistry* **1971**, *27*, 283–292.

108. Ma, X. T.; Tian, S. K. Palladium-Catalyzed Regioselective Halogenation of Aromatic Azo Compounds. *Advanced Synthesis & Catalysis* **2013**, *355*, 337–340.

109. Andrienko, O. S.; Goncharov, V. S.; Raida, V. S. Catalytic Iodination of Aromatic Compounds Via Ortho-Palladated Complexes. *Russian Journal of Organic Chemistry* **1996**, *32*, 79–81.

110. Powers, D. C.; Ritter, T. Bimetallic Pd(III) Complexes in Palladium-Catalysed Carbon–Heteroatom Bond Formation. *Nature Chemistry* **2009**, *1*, 302–309.

111. Powers, D. C.; Xiao, D. Y.; Geibel, M. A. L.; Ritter, T. On the Mechanism of Palladium-Catalyzed Aromatic C−H Oxidation. *Journal of the American Chemical Society* **2010**, *132*, 14530–14536.

112. Casado, A. L.; Espinet, P. Mechanism of the Stille Reaction. 1. The Transmetalation Step. Coupling of RLi and R_2SnBu_3 Catalyzed by Trans-[PdR_1IL_2] ($R_1 = C_6Cl_2F_3$; R_2 = Vinyl, 4-Methoxyphenyl; L = $AsPh_3$). *Journal of the American Chemical Society* **1998**, *120*, 8978–8985.

113. Xue, L.; Lin, Z. Theoretical Aspects of Palladium-Catalysed Carbon–Carbon Cross-Coupling Reactions. *Chemical Society Reviews* **2010**, *39*, 1692–1705.

114. Roy, A. H.; Hartwig, J. F. Reductive Elimination of Aryl Halides from Palladium(II). *Journal of the American Chemical Society* **2001**, *123*, 1232–1233.

115. Stambuli, J. P.; Bühl, M.; Hartwig, J. F. Synthesis, Characterization, and Reactivity of Monomeric, Arylpalladium Halide Complexes with a Hindered Phosphine as the Only Dative Ligand. *Journal of the American Chemical Society* **2002**, *124*, 9346–9347.

116. Alcazar-Roman, L. M.; Hartwig, J. F. Mechanistic Studies on Oxidative Addition of Aryl Halides and Triflates to $Pd(Binap)_2$ and Structural Characterization of the Product from Aryl Triflate Addition in the Presence of Amine. *Organometallics* **2002**, *21*, 491–502.

117. Roy, A. H.; Hartwig, J. F. Directly Observed Reductive Elimination of Aryl Halides from Monomeric Arylpalladium(II) Halide Complexes. *Journal of the American Chemical Society* **2003**, *125*, 13944–13945.

118. Roy, A. H.; Hartwig, J. F. Reductive Elimination of Aryl Halides Upon Addition of Hindered Alkylphosphines to Dimeric Arylpalladium(II) Halide Complexes. *Organometallics* **2004**, *23*, 1533–1541.

119. Hartwig, J. F. Electronic Effects on Reductive Elimination to Form Carbon−Carbon and Carbon−Heteroatom Bonds from Palladium(II) Complexes. *Inorganic Chemistry* **2007**, *46*, 1936–1947.

120. Watson, D. A.; Su, M.; Teverovskiy, G.; Zhang, Y.; García-Fortanet, J.; Kinzel, T.; Buchwald, S. L. Formation of ArF from LPdAr(F): Catalytic Conversion of Aryl Triflates to Aryl Fluorides. *Science* **2009**, *325*, 1661–1664.

121. Schröder, N.; Wencel-Delord, J.; Glorius, F. High-Yielding, Versatile, and Practical [Rh(III)Cp*]-Catalyzed Ortho Bromination and Iodination of Arenes. *Journal of the American Chemical Society* **2012**, *134*, 8298–8301.

122. Frech, C. M.; Milstein, D. Direct Observation of Reductive Elimination of Methyl Iodide from a Rhodium(III) Pincer Complex: The Importance of Sterics. *Journal of the American Chemical Society* **2006**, *128*, 12434–12435.

123. Feller, M.; Diskin-Posner, Y.; Leitus, G.; Shimon, L. J. W.; Milstein, D. Direct Observation of Reductive Elimination of Mex (X = Cl, Br, I) from RhIII Complexes: Mechanistic Insight and the Importance of Sterics. *Journal of the American Chemical Society* **2013**, *135*, 11040–11047.

124. Vigalok, A. Metal-Mediated Formation of Carbon–Halogen Bonds. *Chemistry – A European Journal* **2008**, *14*, 5102–5108.

125. Cannon, K. A.; Geuther, M. E.; Kelly, C. K.; Lin, S.; Roy MacArthur, A. H. Hydrodehalogenation of Aryl Chlorides and Aryl Bromides Using a Microwave-Assisted, Copper-Catalyzed Concurrent Tandem Catalysis Methodology. *Organometallics* **2011**, *30*, 4067–4073.

126. Klapars, A.; Buchwald, S. L. Copper-Catalyzed Halogen Exchange in Aryl Halides: An Aromatic Finkelstein Reaction. *Journal of the American Chemical Society* **2002**, *124*, 14844–14845.

127. Chen, M.; Ichikawa, S.; Buchwald, S. L. Rapid and Efficient Copper-Catalyzed Finkelstein Reaction of (Hetero)Aromatics under Continuous-Flow Conditions. *Angewandte Chemie International Edition* **2015**, *54*, 263–266.

128. Zanon, J.; Klapars, A.; Buchwald, S. L. Copper-Catalyzed Domino Halide Exchange-Cyanation of Aryl Bromides. *Journal of the American Chemical Society* **2003**, *125*, 2890–2891.

129. Coulson, D. R.; Cramer, R. Nickel-Catalyzed Displacement Reactions of Aryl Halides. *The Journal of Organic Chemistry* **1975**, *40*, 2267–2273.

130. Takagi, K.; Hayama, N.; Okamoto, T. Synthesis of Aryl Iodides from Aryl Halides and Potassium Iodide by Means of Nickel Catalyst. *Chemistry Letters* **1978**, *7*, 191–192.

131. Takagi, K.; Hayama, N.; Inokawa, S. The in Situ-Generated Nickel(0)-Catalyzed Reaction of Aryl Halides with Potassium Iodide and Zinc Powder. *Bulletin of the Chemical Society of Japan* **1980**, *53*, 3691–3695.

132. Cant, A. A.; Bhalla, R.; Pimlott, S. L.; Sutherland, A. Nickel-Catalysed Aromatic Finkelstein Reaction of Aryl and Heteroaryl Bromides. *Chemical Communications* **2012**, *48*, 3993–3995.

133. O'Connor, K. J.; Burrows, C. J. Catalysis of Aryl-Halogen Exchange by Nickel(II) Complexes Using Sodium Hypochlorite. *The Journal of Organic Chemistry* **1991**, *56*, 1344–1346.

134. Menini, L.; Gusevskaya, E. V. Novel Highly Selective Catalytic Oxychlorination of Phenols. *Chemical Communications* **2006**, 209–211.

135. Menini, L.; Parreira, L. A.; Gusevskaya, E. V. A Practical Highly Selective Oxybromination of Phenols with Dioxygen. *Tetrahedron Letters* **2007**, *48*, 6401–6404.

136. Yang, L.; Lu, Z.; Stahl, S. S. Regioselective Copper-Catalyzed Chlorination and Bromination of Arenes with O_2 as the Oxidant. *Chemical Communications* **2009**, 6460–6462.

137. Wang, W.; Pan, C.; Chen, F.; Cheng, J. Copper(II)-Catalyzed Ortho-Functionalization of 2-Arylpyridines with Acyl Chlorides. *Chemical Communications* **2011**, *47*, 3978–3980.

138. Mo, S.; Zhu, Y.; Shen, Z. Copper-Catalyzed Aromatic C–H Bond Halogenation with Lithium Halides under Aerobic Conditions. *Organic & Biomolecular Chemistry* **2013**, *11*, 2756–2760.

139. Urones, B.; Martínez, Á. M.; Rodríguez, N.; Arrayás, R. G.; Carretero, J. C. Copper-Catalyzed Ortho-Halogenation of Protected Anilines. *Chemical Communications* **2013**, *49*, 11044–11046.

140. Yu, D. G.; Gensch, T.; de Azambuja, F.; Vásquez-Céspedes, S.; Glorius, F. Co(III)-Catalyzed C–H Activation/Formal Sn-Type Reactions: Selective and Efficient Cyanation, Halogenation, and Allylation. *Journal of the American Chemical Society* **2014**, *136*, 17722–17725.

141. Limberg, C.; Teles, Joaquim H. The Activation of O2 at Ruthenium Complexes: Catalytic Chlorination of Unsaturated Organic Substrates within the System O_2/HCl/H_2O. *Advanced Synthesis & Catalysis* **2001**, *343*, 447–449.

142. Wang, L.; Ackermann, L. Ruthenium-Catalyzed Ortho-C–H Halogenations of Benzamides. *Chemical Communications* **2014**, *50*, 1083–1085.

143. Teskey, C. J.; Lui, A. Y. W.; Greaney, M. F. Ruthenium-Catalyzed Meta-Selective C–H Bromination. *Angewandte Chemie International Edition* **2015**, *54*, 11677–11680.

144. Yu, Q.; Hu, L.; Wang, Y.; Zheng, S.; Huang, J. Directed Meta-Selective Bromination of Arenes with Ruthenium Catalysts. *Angewandte Chemie International Edition* **2015**, *54*, 15284–15288.

145. Mo, F.; Yan, J. M.; Qiu, D.; Li, F.; Zhang, Y.; Wang, J. Gold-Catalyzed Halogenation of Aromatics by N-Halosuccinimides. *Angewandte Chemie International Edition* **2010**, *49*, 2028–2032.

146. Shirakawa, E.; Imazaki, Y.; Hayashi, T. Ruthenium-Catalyzed Transformation of Alkenyl Triflates to Alkenyl Halides. *Chemical Communications* **2009**, 5088–5090.

147. Imazaki, Y.; Shirakawa, E.; Ueno, R.; Hayashi, T. Ruthenium-Catalyzed Transformation of Aryl and Alkenyl Triflates to Halides. *Journal of the American Chemical Society* **2012**, *134*, 14760–14763.

148. Lu, H.; Yu, T. Y.; Xu, P. F.; Wei, H. Selective Decarbonylation Via Transition-Metal-Catalyzed Carbon–Carbon Bond Cleavage. *Chemical Reviews* **2021**, *121*, 365–411.

149. Yue, H.; Guo, L.; Liao, H. H.; Cai, Y.; Zhu, C.; Rueping, M. Catalytic Ester and Amide to Amine Interconversion: Nickel-Catalyzed Decarbonylative Amination of Esters and Amides by C−O and C−C Bond Activation. *Angewandte Chemie International Edition* **2017**, *56*, 4282–4285.

150. Chatupheeraphat, A.; Liao, H. H.; Lee, S. C.; Rueping, M. Nickel-Catalyzed C–CN Bond Formation Via Decarbonylative Cyanation of Esters, Amides, and Intramolecular Recombination Fragment Coupling of Acyl Cyanides. *Organic Letters* **2017**, *19*, 4255–4258.

151. Lee, S. C.; Liao, H. H.; Chatupheeraphat, A.; Rueping, M. Nickel-Catalyzed C−S Bond Formation Via Decarbonylative Thioetherification of Esters, Amides and Intramolecular Recombination Fragment Coupling of Thioesters. *Chemistry – A European Journal* **2018**, *24*, 3608–3612.

152. Isshiki, R.; Muto, K.; Yamaguchi, J. Decarbonylative C–P Bond Formation Using Aromatic Esters and Organophosphorus Compounds. *Organic Letters* **2018**, *20*, 1150–1153.

153. Pu, X.; Hu, J.; Zhao, Y.; Shi, Z. Nickel-Catalyzed Decarbonylative Borylation and Silylation of Esters. *ACS Catalysis* **2016**, *6*, 6692–6698.

154. Osakada, K.; Yamamoto, T.; Yamamoto, A. Decarbonylation of Thiol Esters to Give Sulfides Promoted by Transition Metal Complexes. *Tetrahedron Letters* **1987**, *28*, 6321–6324.

155. Wenkert, E.; Chianelli, D. Nickel-Catalysed Decarbonylation of Thioesters. *Journal of the Chemical Society, Chemical Communications* **1991**, 627–628.

156. Kato, T.; Kuniyasu, H.; Kajiura, T.; Minami, Y.; Ohtaka, A.; Kinomoto, M.; Terao, J.; Kurosawa, H.; Kambe, N. "B-Cis-Sar Effect" on Decarbonylation from α,β-Unsaturated Acyl and Aroyl Complexes. *Chemical Communications* **2006**, 868–870.

157. Ichiishi, N.; Malapit, C. A.; Woźniak, Ł.; Sanford, M. S. Palladium- and Nickel-Catalyzed Decarbonylative C–S Coupling to Convert Thioesters to Thioethers. *Organic Letters* **2018**, *20*, 44–47.

158. Liu, C.; Szostak, M. Decarbonylative Thioetherification by Nickel Catalysis Using Air- and Moisture-Stable Nickel Precatalysts. *Chemical Communications* **2018**, *54*, 2130–2133.

159. Ishitobi, K.; Isshiki, R.; Asahara, K. K.; Lim, C.; Muto, K.; Yamaguchi, J. Decarbonylative Aryl Thioether Synthesis by Ni Catalysis. *Chemistry Letters* **2018**, *47*, 756–759.

160. Murahashi, S.; Naota, T.; Nakajima, N. Palladium-Catalyzed Decarbonylation of Acyl Cyanides. *The Journal of Organic Chemistry* **1986**, *51*, 898–901.

161. Srimontree, W.; Lakornwong, W.; Rueping, M. Nickel-Catalyzed Synthesis of Silanes from Silyl Ketones. *Organic Letters* **2019**, *21*, 9330–9333.

162. Takise, R.; Isshiki, R.; Muto, K.; Itami, K.; Yamaguchi, J. Decarbonylative Diaryl Ether Synthesis by Pd and Ni Catalysis. *Journal of the American Chemical Society* **2017**, *139*, 3340–3343.

163. Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. Rhodium-Catalyzed Reaction of Aroyl Chlorides with Alkynes. *The Journal of Organic Chemistry* **1996**, *61*, 6941–6946.

164. Iwai, T.; Fujihara, T.; Terao, J.; Tsuji, Y. Iridium-Catalyzed Addition of Acid Chlorides to Terminal Alkynes. *Journal of the American Chemical Society* **2009**, *131*, 6668–6669.

165. Sugihara, T.; Satoh, T.; Miura, M.; Nomura, M. Rhodium-Catalyzed Mizoroki–Heck-Type Arylation of Alkenes with Aroyl Chlorides under Phosphane- and Base-Free Conditions. *Angewandte Chemie International Edition* **2003**, *42*, 4672–4674.

166. Merkul, E.; Oeser, T.; Müller, T. J. J. Consecutive Three-Component Synthesis of Ynones by Decarbonylative Sonogashira Coupling. *Chemistry – A European Journal* **2009**, *15*, 5006–5011.

167. Gers, C. F.; Rosellen, J.; Merkul, E.; Müller, T. J. J. One-Pot Four-Component Synthesis of Pyrimidyl and Pyrazolyl Substituted Azulenes by Glyoxylation–Decarbonylative Alkynylation–Cyclocondensation Sequences. *Beilstein Journal of Organic Chemistry* **2011**, *7*, 1173–1181.

168. Verbicky, J. W.; Dellacoletta, B. A.; Williams, L. Palladium Catalyzed Decarbonylation of Aromatic Acyl Chlorides. *Tetrahedron Letters* **1982**, *23*, 371–372.

169. Malapit, C. A.; Ichiishi, N.; Sanford, M. S. Pd-Catalyzed Decarbonylative Cross-Couplings of Aroyl Chlorides. *Organic Letters* **2017**, *19*, 4142–4145.

170. Blum, J. The Decarbonylation of Aroyl to Aryl Chlorides. *Tetrahedron Letters* **1966**, *7*, 1605–1608.

171. Kampmeier, J. A.; Rodehorst, R. M.; Philip, J. B. J.; Kampmeier, J. A. Stoichiometric Decarbonylation of Benzoyl Chloride by Chiorotris(Triphenylphosphine)Rhodium(I). *Journal of the American Chemical Society* **1981**, *103*, 1847–1849.

172. Kampmeier, J. A.; Mahalingam, S. Mechanistic and Synthetic Implications of the Reactions of Aroyl Chlorides with Chlorocarbonylbis(Triphenylphosphine)Rhodium(I). A Catalytic Procedure for the Preparation of Carbonyl-Labeled Aroyl Chlorides. *Organometallics* **1984**, *3*, 489–491.

173. Stille, J. K.; Regan, M. T. Mechanism and Kinetics of the Decarbonylation of Para-Substituted Benzoyl and Phenylacetyl Chlorides by Chlorotris(Triphenylphosphine)Rhodium(I). *Journal of the American Chemical Society* **1974**, *96*, 1508–1514.

174. Lau, K. S. Y.; Becker, Y.; Huang, F.; Baenziger, N.; Stille, J. K. Mechanism of Decarbonylation of Acid Chlorides with Chlorotris(Triphenylphosphine)Rhodium(I) Structure and Stereochemistry. *Journal of the American Chemical Society* **1977**, *99*, 5664–5672.

175. Gutmann, B.; Elsner, P.; Glasnov, T.; Roberge, D. M.; Kappe, C. O. Shifting Chemical Equilibria in Flow—Efficient Decarbonylation Driven by Annular Flow Regimes. *Angewandte Chemie* **2014**, *126*, 11741–11745.

176. Zhou, D.; Gao, Y.; Liu, B.; Tan, Q.; Xu, B. Synthesis of Silicon and Germanium-Containing Heterosumanenes Via Rhodium-Catalyzed Cyclodehydrogenation of Silicon/Germanium–Hydrogen and Carbon–Hydrogen Bonds. *Organic Letters* **2017**, *19*, 4628–4631.

177. Collins, K. D.; Glorius, F. A Robustness Screen for the Rapid Assessment of Chemical Reactions. *Nature Chemistry* **2013**, *5*, 597–601.

178. Batesky, D. C.; Goldfogel, M. J.; Weix, D. J. Removal of Triphenylphosphine Oxide by Precipitation with Zinc Chloride in Polar Solvents. *The Journal of Organic Chemistry* **2017**, *82*, 9931–9936.

VITA

Wiktoria Koza received her undergraduate degree in biology from Loyola University Chicago in 2017. Dr. Koza continued her education at Loyola and pursued a Ph.D. in organometallic chemistry. She worked under the advisement of Dr. Hee Yeon Cho and Dr. James Devery. Her research focused on developing a novel method for the synthesis of aryl chlorides via transition metal catalysis.