2009

The use of proazaphosphatranes and a tricyclic aluminum alkoxide in organic transformations and the use of bulky phosphines in palladium-catalyzed reactions

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Recommended Citation

Raders, Steven Michael, "The use of proazaphosphatranes and a tricyclic aluminum alkoxide in organic transformations and the use of bulky phosphines in palladium-catalyzed reactions" (2009). *Graduate Theses and Dissertations*. 10962.
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The use of proazaphosphatranes and a tricyclic aluminum alkoxide in organic transformations and the use of bulky phosphines in palladium-catalyzed reactions

by

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A dissertation submitted to the graduate faculty

in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

Major: Organic Chemistry

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Ames, Iowa

2009

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LIST OF ABBREVIATIONS

Ac	acetyl
α	alpha
aq	aqueous
atm	atmospheric pressure
BINAP	2,2’-bis(diphenylphosphino)-1,1’-binaphthyl
Bn	benzyl
β	beta
Boc	*t*-butoxycarbonyl
br	broad
s	singlet
^{i}Bu	*iso*-butyl
^{n}Bu	butyl
°C	degrees Celsius
cat.	catalytic
Cy	cyclohexyl
d	doublet
DABCO	1,4-diazabicyclo[2.2.2]octane
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
dd	doublet of doublets
DME	1,2-dimethoxyethane

DMF	*N*,*N*-dimethylformamide
DPPB	1,2-bis(diphenylphosphino)butane
DPPE	1,2-bis(diphenylphosphino)ethane
DPPF	1,2-bis(diphenylphosphino)ferrocene
DPPP	1,2-bis(diphenylphosphino)propane
DMSO	dimethyl sulfoxide
eq	equation
equiv	equivalent
Et	ethyl
h	hour(s)
HMPA	hexamethylphosphorus amide
HMPT	hexamethylphosphorus triamide
HMRS	high resolution mass spectrometry
Hz	Hertz
LDA	lithium diisopropylamide
m	multiplet
Me	methyl
min	minute(s)
mL	milliliters
mmol	millimole(s)
m.p.	melting point
n	normal
NMP	*N*-methylpyrrolidone

NMR	nuclear magnetic resonance
Nu	nucleophile
OAc	acetate
o	ortho
OTf	triflate
p	para
Neo-Pent	*neo*-pentyl
NHC	*N*-heterocyclic carbene
ppm	parts per million
Piv	pivalyl
Ph	phenyl
i-Pr	*iso*-propyl
n-Pr	propyl
Q-phos	di-*tert*-butylphosphinopentaphenylferrocene
rt (RT)	room temperature
s	singlet
S_NAr	nucleophilic aromatic substitution
t	triplet
TBAF	tetrabutylammonium fluoride
TBDMS	*tert*-butyldimethylsilyl
tert	tertiary
^{t}Bu	*tert*-butyl
THF	tetrahydrofuran

TLC	thin layer chromatography
TMS	trimethylsilyl
o-tol	*ortho*-tolyl
TON	turnover number
Xantphos	9,9-dimethyl-4,6-bis(diphenylphosphino)xanthene

ACKNOWLEDMENTS

I would like to, first and foremost, sincerely express my gratitude to my Ph. D. supervisor, Professor John G. Verkade, for his guidance, support, and encouragement throughout my graduate career. I am very grateful to him for his patience during my first couple of years when my research results came slowly and for giving me the freedom to pursue research topics that were interesting to me. I would also like to thank him for teaching me how to write scientific papers and for polishing my research presentations and this thesis and for allowing me to take vacations throughout my five years of graduate school to be with family. I would also like to thank him for listening to me and giving me advice about subjects that were important to everyday life and for being someone to talk with about problems that arose during my graduate career.

I would also like to acknowledge my committee members: Professors George Kraus, Victor Lin, Richard Larock, and Gordie Miller for their time, suggestions, and letters of support. I would also like to thank Professor Malika Jeffries-EL for giving suggestions during my Prelim Oral Examination. I would also like to thank Professor Keith Woo for acting as a substitute during my final defense.

I would especially like to thank my family members for their continued support and for trying to calm my nerves when my research was not going well.

I would now like to thank all of Dr. Verkade's group members, past and present. I would especially like to thank Dr. Weiping Su who invited me to be on my first published manuscript and who taught me how to carry out many techniques in the laboratory. I would also like to thank my graduate colleagues, Reed Oshel and Kuldeep Wadhwa, for their

suggestions during my research. I would also like to thank Dr. Jesudoss Kingston for his conversations about research and life. I would also like to acknowledge Dr. Yibo Zhou for having the patience to listen to me complain when research was not working well. I would also like to thank Dr. Nandakumar, Dr. Young-Jo Kim, and Dr. Chinta Reddy Venkat Reddy for their advice and help.

Finally, I would like to gratefully acknowledge my wonderful fiancée Gisun Park. Without her, I would have had overwhelming difficulties in my graduate courses. I thank her for being patient with me when research was not going well and just being there for me whenever I needed her to be.

ABSTRACT

In recent years, proazaphosphatranes [$P(RNCH_2CH_2)_3N$] have proven to be very useful ligands in cross-coupling reactions such as Buchwald-Hartwig aminations, Suzuki-Miyaura couplings, and Stille couplings. In this thesis is described the use of proazaphosphatranes in Lewis base catalyzed reactions such as the synthesis of biaryl ethers by S_nAr reactions and the cyclotrimerization of isocyanates to isocyanurates. Recently, our group published the synthesis of a tricyclic aluminum alkoxide Lewis acid. This thesis describes the use of this novel aluminum alkoxide in the catalyzed trimethylsilylcyanation of aldehydes and the Mukaiyama Aldol reaction. The use of ^{t}Bu_3P and the bulky phosphine ^{t}Bu_2P-N=P(^{i}$BuNCH_2CH_2)_3N$ (recently synthesized in our group) in the palladium catalyzed α-arylation of enol silyl ethers and in the Hiyama coupling, respectively, is also described.

This thesis shows that the synthesis of biaryl ethers using P(^{i}$BuNCH_2CH_2)_3N$ as a catalyst under microwave conditions is facilitated at the lowest mole percentage of promoter published in the literature for this S_nAr reaction. Herein, it is also shown experimentally that $P(BnNCH_2CH_2)_3N$ is the least basic proazaphosphatrane developed to date, but that the installation of methoxy groups on the phenyl ring markedly increases its basicity. This rise in basicity is shown to increase the rate of cyclotrimerization of isocyanates to isocyanurates.

Lewis acid catalyzed reactions using aluminum as the metal center has advantages (such as low toxicity to the environment and low cost). The chief disadvantage of such catalysts described in the literature is the large concentrations required. The use of a novel tricyclic aluminum alkoxide Lewis acid first synthesized by our group is shown to maintain such advantages while also functioning as an efficient catalyst at unusually low concentrations.

Finally, the efficiency of the palladium/ ${}^{t}Bu_3P$ catalyst system for the reaction of enol silyl ethers with aryl bromides and chlorides is found to be drastically increased in the presence of two metal fluoride additives which were found to behave synergistically. In addition, a general method for the Hiyama coupling of aryl bromides and notoriously difficult aryl chloride substrates has been developed using a new bulky phosphine recently synthesized in our group.

CHAPTER 1. GENERAL INTRODUCTION

Thesis Organization

This thesis consists of eight chapters (including the present chapter). Chapters 2 - 7 are papers that have been submitted for publication, accepted for publication or have been published in scientific journals. ^{1}H, ^{13}C, ^{31}P, ^{11}B, and ^{19}F spectra (where appropriate) for reaction products have been compiled at the end of the thesis as appendices.

The first chapter titled “**GENERAL INTRODUCTION**” introduces various Lewis base catalyzed reactions with two examples: diaryl ether synthesis and isocyanurate formation. Lewis acid catalyzed reactions are then introduced with two examples: trimethylsilylcyanation of aldehydes and the Mukaiyama aldol reaction. Lastly, palladium catalyzed reactions are introduced with two examples: α-arylation of enol silyl ethers and Hiyama coupling. The present section also includes a literature review of the aforementioned reactions. Finally, the first chapter also contains a brief description of our motivation for carrying out the research described in the thesis.

The second chapter titled “**$P(i\text{-}BuNCH_2CH_2)_3N$: AN EFFICIENT PROMOTER FOR THE MICROWAVE SYNTHESIS OF DIARYL ETHERS**” describes our efforts in finding a suitable proazaphosphatrane for the Lewis base promoted reaction of aryl TBDMS ethers with aryl fluorides under microwave conditions. Screening of a variety of electron deficient aryl fluorides and a variety of aryl TBDMS ethers constitute this chapter.

The third chapter titled “**A NEW ELECTRON RICH PROAZAPHOSPHATRANE AND ITS USE IN THE SYNTHESIS OF ISOCYANURATES**” describes the synthesis of methoxy benzyl proazaphosphatranes and a comparison of their pKa’s to other proazaphosphatranes. The synthesis of a variety of aryl isocyanurates and the recycling of proazaphosphatranes for this synthesis is also included in this chapter.

The fourth chapter titled "**THE USE OF A TRICYCLIC ALUMINUM ALKOXIDE IN THE TRIMETHYLSILYLCYANATION OF ALDEHYDES**" describes our use of the first example of a tricyclic aluminum alkoxide in the Lewis acid catalyzed reaction of aryl, alkyl, and heterocyclic aldehydes with trimethylsilylcyanide. Recycling properties of the tricyclic aluminum alkoxide in this reaction are also reported.

The fifth chapter titled "**CATALYSIS OF MUKAIYAMA ALDOL REACTIONS BY A TRICYCLIC ALUMINUM ALKOXIDE LEWIS ACID**" expands upon the use of our new tricyclic aluminum alkoxide in catalyzing the reaction of a variety of aryl, alkyl, and heterocyclic aldehydes with various TMS or TBDMS enol ethers. A mechanism is suggested which is supported by isolation of an intermediate. This chapter also records evidence that the tricyclic aluminum alkoxide is more Lewis acidic than boron trifluoride.

The sixth chapter titled "**Pd-CATALYZED α-ARYLATION OF TRIMETHYLSILYL ENOL ETHERS WITH ARYL BROMIDES AND CHLORIDES: A SYNERGISTIC EFFECT OF TWO METAL FLUORIDES AS ADDITIVES**" details our exploration of the palladium-catalyzed α-arylation of a variety of aryl bromides and chlorides with trimethylsilyl enol ethers in the presence of tri-*t*-butylphosphine as a ligand. An investigation into the simultaneous use of two metal fluorides as synergistic additives on the coupling efficiency is described.

The seventh chapter titled "**ADVANTAGEOUS USE OF $^{t}Bu_2P\text{-}N{=}P(^{i}BuNCH_2CH_2)_3N$ IN THE HIYAMA COUPLING OF ARYL BROMIDES AND CHLORIDES**" focuses on the application of a new bulky phosphine ligand in the cross-coupling of aryl bromides and chlorides with trimethoxysilanes. Optimization of reactions parameters (ligand, base, solvent, temperature) and several examples of the coupling reaction are presented in this chapter. Notably, this catalyst system facilitates the first general method developed to date for the Hiyama coupling of aryl chlorides.

This thesis ends with the eighth chapter titled "**GENERAL CONCLUSIONS**" which summarizes the findings in Chapters 2-7. This chapter ends with a new idea for the synthesis of bulky ligands of the type R'R"P-N=P(^{i}BuNCH$_2$CH$_2$)$_3$N, and some new research ideas for the exploration of proazaphosphatranes, the tricyclic aluminum alkoxide and the ^{t}Bu$_2$P-N=P(^{i}BuNCH$_2$CH$_2$)$_3$N ligand as catalysts for important organic reactions.

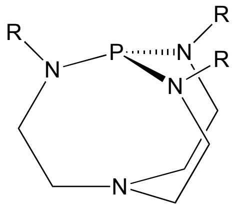
Introduction to Lewis Base Catalysis

The importance of Lewis base reactions in modern organic synthesis is well known and evident from the volume of review articles published in the literature.[1] Among the Lewis bases employed, trivalent group 5 elements such as nitrogen and phosphorus atoms have been widely used owing to their electron lone pairs available for Lewis base activation of appropriate functional groups, and their overall neutral charge.

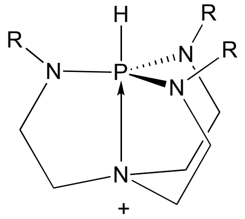
1. Proazaphosphatranes

Since 1989 when the first proazaphosphatrane was first synthesized in our laboratory,[2] a variety of proazaphosphatranes have been developed,[3] some of which have been commercially available from Strem and Aldrich for many years. A growing number of proazaphosphatranes are proving to be useful in promoting an increasing number of organic transformations.[3,4]

Proazaphosphatranes (**1**) are nonionic, bicyclic strong Lewis bases, which, upon treatment with acids become protonated at the phosphorus center to form corresponding azaphosphatranium ions (**2**) rather than on the nitrogen atoms to form ammonium ions. Proazaphosphatrane pKa's are typically 32-34 in acetonitrile.[5] An important feature of proazaphosphatranes, which contributes to their strong basicity, is their ability to undergo transannulation from the bridgehead nitrogen to the phosphorus center. This has been established by X-ray crystallography.[6]

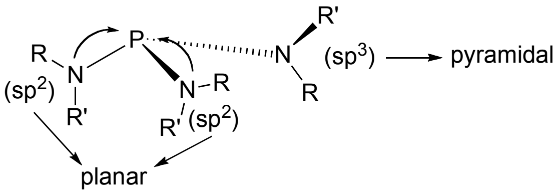


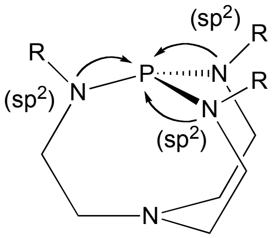
1
Prozaphosphatrane



2
Azaphosphatranium Ion

It is important to appreciate the significance of some structural differences between acyclic triaminophosphines, such as $P(NMe)_3$ (HMPT), and bicyclic proazaphosphatranes. X-ray crystallographic studies have shown that acyclic triaminophosphines have one long P-N bond with a pyramidal nitrogen and two shorter P-N bonds with planar nitrogens.[7] The two sp^2 nitrogens are better suited in terms of distance to the phosphorus and in hybridizational character than the sp^3 nitrogen for donating electron density to the phosphorus. Thus the unhybridized p lone pair orbital on an sp^2 nitrogen is better able to overlap empty π-type orbitals on the phosphorus than an sp^3 lone pair nitrogen (owing to more s character in the latter). As a consequence, an sp^3 nitrogen behaves as an electron-withdrawing group which reduces the basicity of the triaminophosphine.[8]



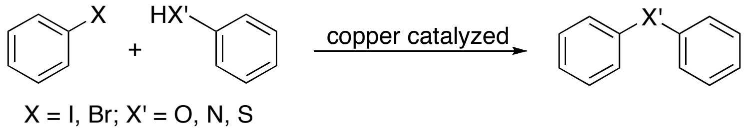


Unlike acyclic triaminophosphines, all three nitrogens adjacent to the phosphorus are planar in proazaphosphatranes as shown by X-ray crystallography.[6] The unhybridized p orbital on all three nitrogens is thus able to donate electron-density to the phosphorus, thereby increasing the phosphorus basicity. The somewhat surprising planarity of the basal nitrogen in proazaphosphatranes has been attributed to the van der Waals interactions among the methylene group hydrogens in the $N(CH_2)_3$ moiety. Another important structural feature of proazaphosphatranes is their ability to undergo transannulation from the axial nitrogen, as mentioned earlier, thereby further increasing their basicity.

2. Synthesis of Diaryl Ethers

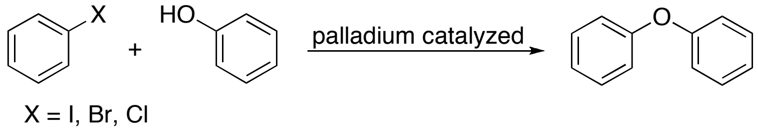
The synthesis of diaryl ethers has attracted significant interest due to the frequent presence of this structural moiety in a variety of natural products.[9] Poly(aryl ethers) have also been found to have applications in thermoplastic materials.[10] Current procedures for the synthesis of diaryl ethers include 1) the copper-catalyzed Ullmann coupling (eq 1),[11] 2) the palladium catalyzed reaction of aryl halides with phenols (eq. 2),[12] and 3) nucleophilic aromatic substitution (S_nAr) reactions between aryl halides (order of reactivity F > Cl > Br > I) and phenols (eq 3).[13]

Ullmann Coupling



(1)

Palladium Catalyzed Coupling

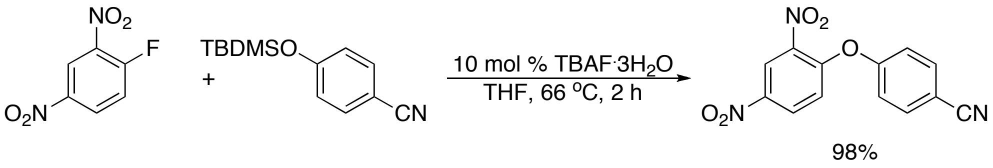


(2)

Nucleophilic Aromatic Substitution (S_nAr)

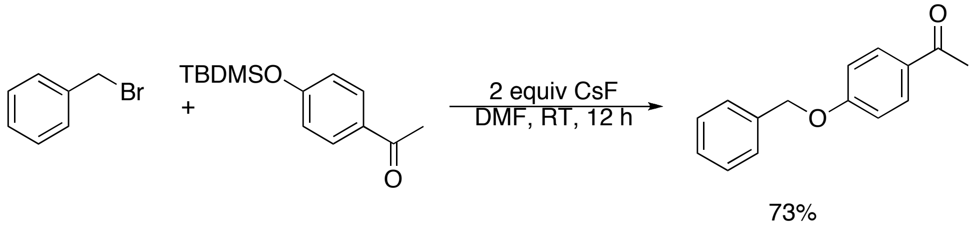
(3)

Of the methods that were previously mentioned, the S_nAr reaction between aryl halides and phenols is more environmentally friendly (since the promoter usually lacks a metal) and requires much milder conditions. Since the S_nAr method was first introduced for the synthesis of diaryl ethers,[14] progress has been made on increasing the reactivity of the phenolic moiety. In 1988, Saunders found that activated aryl fluorides react directly with aryl TBMDS ethers in the presence of TBAF in THF to give diaryl ethers (eq 4).[15] Unfortunately, this method was found to be viable only for the highly activated aryl fluoride 2,4-dinitrofluorobenzene.



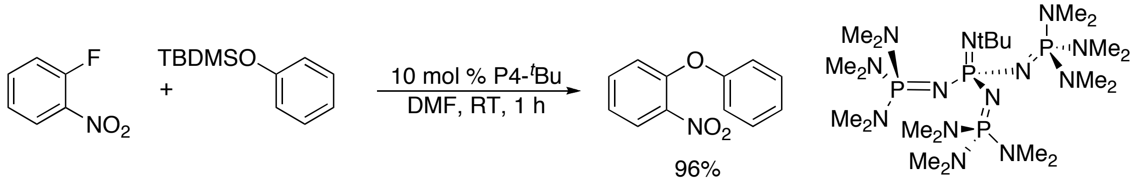
(4)

In 1997, Oriyama and co-workers described the conversion of aryl TBDMS ethers to aryl alkyl ethers by reactions of alkyl halides in DMF using CsF as the source of the silyl activation (eq 5).[16]



(5)

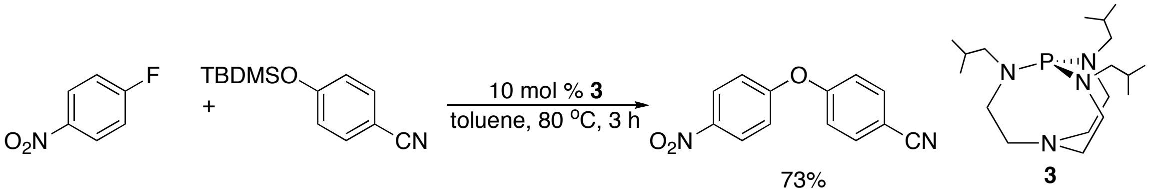
In 2005, Kondo and co-workers coupled aryl fluorides with aryl TBDMS and TMS ethers using the phosphazene base P4-^{t}Bu (eq 6) as a catalyst.[17] In their study, they noted that weak bases such as DBU were completely ineffective for this reaction. Since the phosphazene base is one of the most basic nonionic bases known (pKa 42.1 in CH_3CN), it significantly improved the general method for the synthesis of diaryl ethers, though highly polar solvents such as DMF and DMSO are needed even in the presence of activated fluoronitrobenzenes. Another drawback to using the phosphazene base is that only electron-rich TBDMS aryl ethers can be employed.



P4-^{t}Bu

(6)

The same year that Kondo published his work, our group published the synthesis of diaryl ethers in the presence of proazaphosphatranes (eq 7).[18] This protocol is an improvement to previous methods in that activated fluoronitrobenzenes undergo reaction with aryl TBDMS or TMS ethers in toluene either at room temperature or at 80 °C. Also, aryl TBDMS ethers containing electron-deficient groups such as cyano, esters, and aldehydes can be used in the reaction in DMF at 80 °C. Even sterically hindered TBDMS aryl ethers undergo this reaction. Although this method provides a more general procedure for the synthesis of diaryl ethers, high mole percentages of promoter are needed for complete conversions.

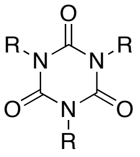


(7)

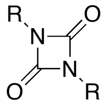
3. Synthesis of Isocyanurates

The cyclotrimerization of isocyanates to isocyanurates (perhydro-1,3,5-triazine-2,4,6-triones) (**4**) has been studied extensively owing in large part to the uses of the trimers in enhancing the physical properties of coating materials,[19] in flame resistance of polyurethanes,[20] and in the copolymerization of ε-caprolactam to nylon-6.[21] Problems with known procedures are long reaction times, product separation, by-product formation such as the 1,3-diazetidine-2,4-dione **5**, and the use of toxic solvents such as DMF or DMSO.[19,22] The cyclotrimerization of isocyanates typically occurs in the presence of Lewis acids,[23] Lewis bases,[24] and palladium complexes.[25]

Because my research focused mainly on the use of proazaphosphatranes for the cyclotrimerization of isocyanates, only literature focused on Lewis base catalysis will be discussed here.



4

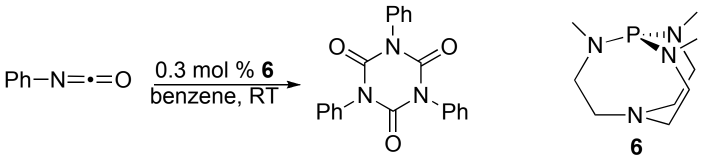


5

R = aryl and alkyl

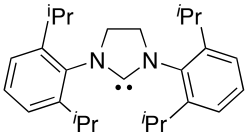
Since one of the earliest reports (1956) using amines as a Lewis base catalyst for the aforementioned cyclotrimerization,[26] there have been similar studies extensively reported in the literature. More recently (1990) Taguchi reported the use of 1 mol % of Et_3N in benzene under 800 MPa of pressure for 20 hours at 100 °C for the trimerization of a variety of isocyanates to isocyanurates including alkyl (Me, Et, *n*-Pr, and *n*-Bu) and aryl (chlorophenyl and naphthyl) derivatives.[24g]

In 1993, our group published the use of proazaphosphatrane (**6**) in the cyclotrimerization of isocyanates using only 0.3 mol % promoter in the nonpolar solvent toluene in 3 minutes at room temperature (eq 8).[24b] This was the fastest reaction time prior to the work to be described in this thesis, and since the product is insoluble in toluene and the promoter is soluble, separation of the isocyanurate from the proazaphosphatrane is easy. In that same year, Endo reported the use of 2 mol % TBAF in THF in the formation of isocyanurates.[24e] Their reaction was complete in 5 minutes with a 99% isolated yield.

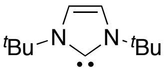


(8)

More recently (2004) Louie and co-workers reported the use of *N*-heterocyclic carbenes (NHC) in the cyclotrimerization of isocyanates to isocyanurates using only 0.1 mol % of promoter. These reactions were carried out for 1 hour in THF as the solvent. Not only were they able to obtain the trimerized product, but they found that by changing the base from **7** to **8**, they selectively obtained the carbodiimide **5**.[19] In 2005, Moghaddam reported the use of 0.08 mol % of potassium phthalimide under solvent free conditions at 140 °C for 24 hours to obtain 72-97% of the desired isocyanurates.[24h]



7



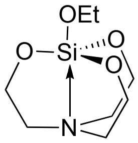
8

Introduction of Lewis Acid Catalysis

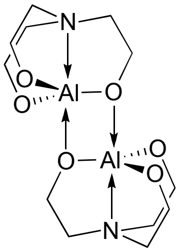
The use of multidentate ligands for the complexation of metal Lewis acid centers offers advantages such as: 1) higher stability of the metal complex which often allows a low catalyst loading without loss of catalyst integrity and 2) a nearly complete occupation of all coordination sites of the metal by a single ligand which reduces the chances for the formation of multimeric and often undefined metal complexes.[27] While C_2-symmetrical bidentate ligands have been commonly used for organic transformations, C_3-symmetrical ligands have attracted attention only recently.[28] When the ligands for the metal centers are tripodal tetradentates, structures known as atranes are formed. These species possess a pseudo-threefold symmetric environment around the metal center.

1. Alumatranes

The first known example of an atrane (1961) was silatrane **9** which possessed five-member rings in the atrane framework.[29] The particular ligand in this silatrane has been used extensively to form atranes with various atoms across the periodic table. When tris-2-hydroxyethyl amine (the precursor of this ligand) was combined with aluminum isopropoxide, however, a variety of atrane structures were formed including the dimeric alumatrane **10**, for example. Investigations of the structural features of this system (some of which were controversial)[30] revealed a variety of behaviors: 1) a dimeric structure in gas phase, 2) monomeric, hexameric, and octameric oligomers in solution, and 3) a tetrameric structure in solid state (as determined by X-ray crystallography).[31]

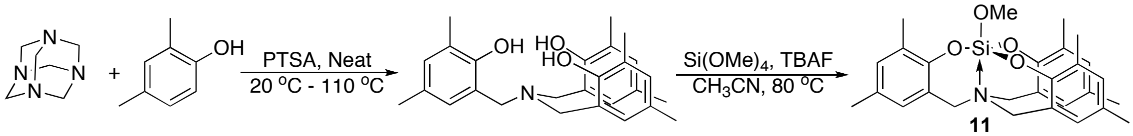


9
Silatrane



10
Alumatrane

In 2000, Holmes and co-workers described the first silatrane (**11**) possessing six-member rings in the atrane structure.[32] The first synthesis of the triphenol precursor to this ligand (eq 9) was published by the same group.[35] A variety of metal atrane analoues have been described incorporating, for example, titanium,[27,33] vanadium,[34] zirconium,[35] indium,[36] gallium,[36] iron,[37] and tantalum.[38]



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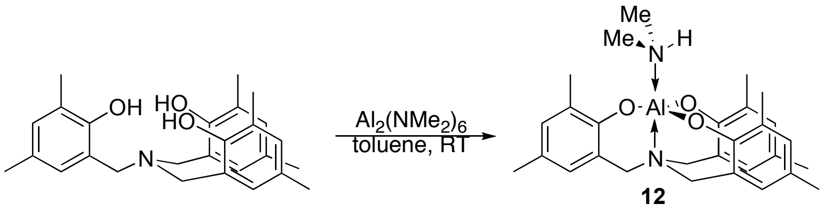
In 2003, our group utilized the ligand precursor developed by Holmes for the synthesis of the first momomeric alumatrane **12** (eq 10).[39] A unique feature of **12** is that it has a penta-coordinate aluminum center (as shown by X-ray crystallography). We thought that a four-coordinate aluminum species could be obtained with sufficiently large alkyl groups in the 3 position on the rings, which would form a type of "picket fence" that would inhibit metal oligomer formation. Somewhat surprisingly, **12** was obtained even though dimethylamine is very volatile and it had been anticipated that it would be easily driven off. Further attempts to displace the dimethylamine with acetone, water, and even more bulky amines (such as triethylamine) were unsuccessful and only starting material **12** was obtained.[39] Drying the compound under reduced pressure at elevated temperatures to obtain the free alumatrane by releasing the dimethylamine was also unsuccessful.



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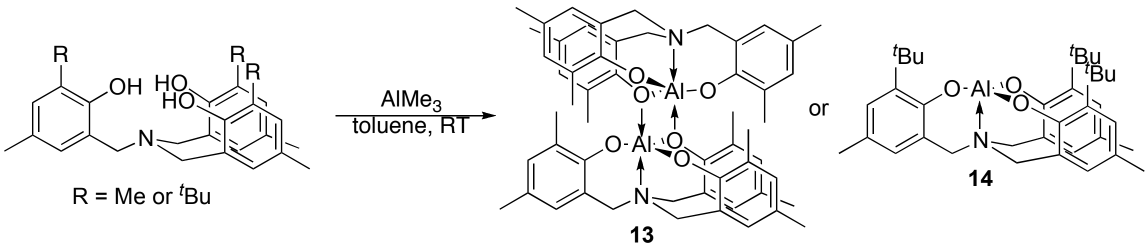
Since efforts to displace the dimethylamine were unsuccessful, a method was sought to make an alumatrane containing a four-coordinate aluminum. In 2006, our group developed a procedure that led to the penta-coordinate dimeric alumatrane **13** (eq 11) which was characterized by X-ray crystallography.[40] Alumatrane **13** is dimeric in both the solution and the solid state. It was shown in our paper, however, that dimeric **13** could be split to form monomeric alumatranes in the presence of water, benzaldehyde, ethylenediamine, THF, and



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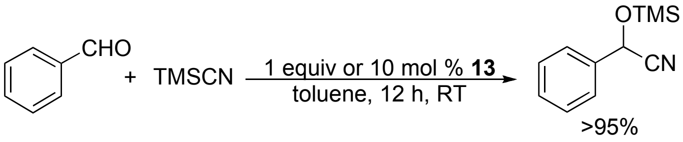
phenoxide anion. To demonstrate the usefulness of the dimeric alumatrane, its benzaldehyde alumatrane adduct was subjected to trimethylsilylcyanation in toluene to obtain >95% of the desired α-trimethylsiloxyphenylacetonitrile by using an equivalent of the adduct or via eq 12 using catalytic amounts of **13**. A four-coordinate monomeric alumatrane (**14**) was finally realized in 2007 by placing *t*-butyl groups in the 3 position of the phenyl rings, and its molecular structure determined by X-ray means was determined in our group.[41]



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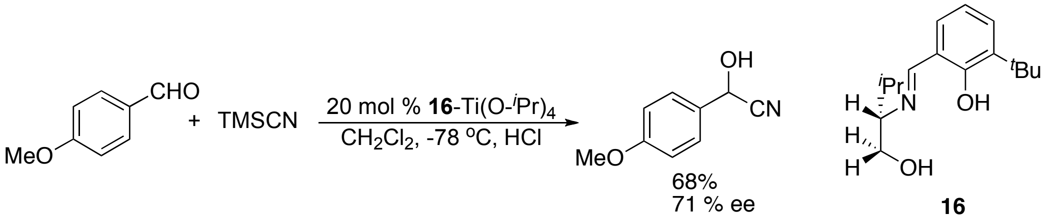
2. TMSCN of Aldehydes

First reported in 1832 by Winkler,[42] the trimethylsilylcyanation of aldehydes to form cyanohydrins became the foundation of the Kiliani-Fisher carbohydrate synthesis.[43] It also represents one of the first examples of a stereoselective reaction.[43] Both the hydroxyl and nitrile groups may be further transformed to other useful functional units. After activation, the hydroxy group can be displaced to form other functionalized nitriles. The nitrile group tolerates conversion to other useful key intermediates in natural product synthesis such as α-hydroxy acids, α-amino acids, and β-amino alcohols.[44] The utility of these intermediates has led to many literature reports of their uses during the intervening years. Since the discovery of the trimethylsilylcyanation of aldehydes, Lewis acids[45] and Lewis bases[28g,46] have been the most widely studied catalysts for this reaction. Some groups have even synthesized Lewis acid – Lewis base bifunctional catalysts that give rise to chiral induced reactions, thereby providing products in high enantioselectivity.[47] Because my research focused on the use of alumatranes for trimethylsilylcyanation, only Lewis acid catalyzed reactions for this transformation involving aldehydes and ketones will be discussed here.

Reetz and co-workers reported in 1986 the first catalytic reaction of trimethylsilylcyanide with isovaleraldehyde in the presence of either a boron- or titanium-binaphthol Lewis acid.[48] Of the Lewis acids that have been reported for this transformation, titanium promoters are the most widely studied. In 1993, Oguni reported the first use of a chiral Schiff base-titanium alkoxide (**16**) in the trimethylsilylcyanation of aldehydes (eq 13).[49] Since the use of this



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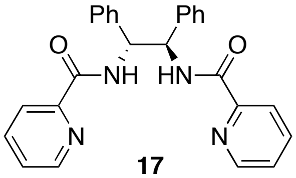
Schiff base-titanium alkoxide was successful, different variations of the Schiff base were used with titanium alkoxide. In 2000 Walsh developed different variations of substituted Schiff bases for the use in the trimethylsilylcyanation of benzaldehyde.[50] In 2002, he expanded this chemistry using the Schiff bases with titanium isopropoxide in the trimethylsilylcyanation of various aldehydes in which high yields and high enantioselectivities were obtained.[51]

Other bidentate ligands have also been used in the presence of titanium isopropoxide for the trimethylsilylcyanation of aldehydes. In 2004, Belda and co-workers used 5 mol % of a bispyridylamide ligand (**17**) in the presence of 5 mol % titanium isopropoxide in methylene chloride at room temperature to obtain >95% isolated yield with 60% ee of the desired cyanohydrin trimethylsilylether.[52] In 2005, Chen and Lee made the bipyridyl-diol (**18**) for the production of cyanohydrins using titanium isopropoxide. In the presence of 5 mol % of **18** and 5 mol % titanium isopropoxide, high product yields with moderate enantioselectivities were obtained at -78 °C.[53]



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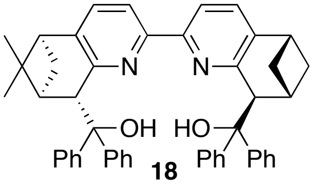

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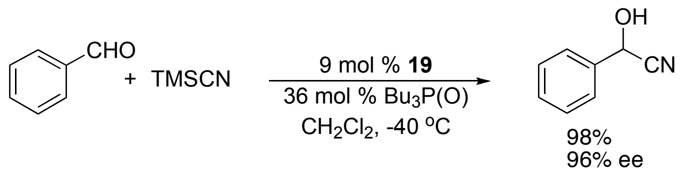
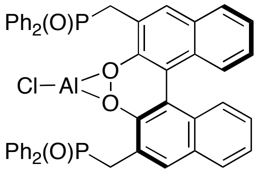
To date, however, only a handful of literature references reporting the use of aluminum Lewis acids as promoters have appeared. Most of these papers involve the use of a Lewis base-Lewis acid bifunctional catalyst with aluminum as the metal center and phosphorus or sulfur moieties as the Lewis base. In 1999, Shibasaki developed Lewis base-Lewis acid catalyst **19** for the trimethylsilylcyanation of aldehydes. In the presence of 9 mol % of **19** with 36 mol % of tributylphosphine oxide as an additive, the desired cyanohydrins were produced in high yields with high enantioselectivities (eq 14).[47a] A drawback to these reactions was the poor performance of aliphatic aldehydes. In 2001, Shibasaki was able to promote the reaction by adding the ligand and metal separately to make the active catalyst in situ.[47b] In 2005, Pu and co-workers developed a BINOL ligand (**20**) that effected not only the conversion of aryl aldehydes to cyanohydrins in high yields and enantioselectivity, but also permitted aliphatic aldehydes to function under their conditions. They also found that replacing the tributylphosphine oxide with HMPA (hexamethylphosphorus amide) increased the reaction rate while still maintaining high selectivity (eq 15).[47c]





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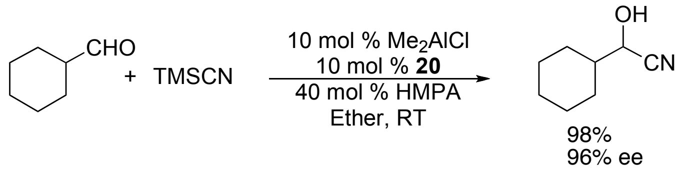

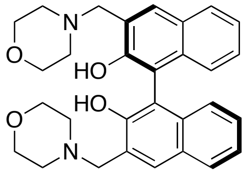

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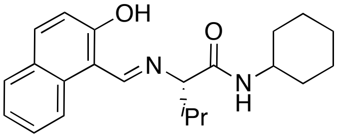
Only two literature references utilize an aluminum Lewis acid in the absence of a Lewis base. In 1992, Inoue used 1 equivalent of a chiral peptide (**21**) in the presence of 1 equivalent of trimethylaluminum to promote the production of cyanohydrins from various aldehydes.[54] Snapper (in 2002) synthesized peptide **22** to be used as a ligand in Lewis acid catalyzed reactions in the presence of aluminum isopropoxide. Using 10 mol % aluminum isopropoxide and 10 mol % **22**, high yields of desired cyanohydrins were obtained with high enantioselectivity.[55]



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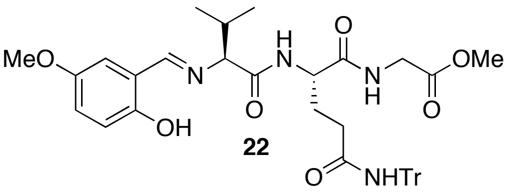
+ $AlMe_3$

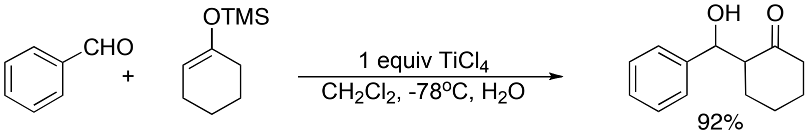


22

+ $Al(O\text{-}{}^{i}Pr)_3$

3. Mukaiyama Aldol Reactions

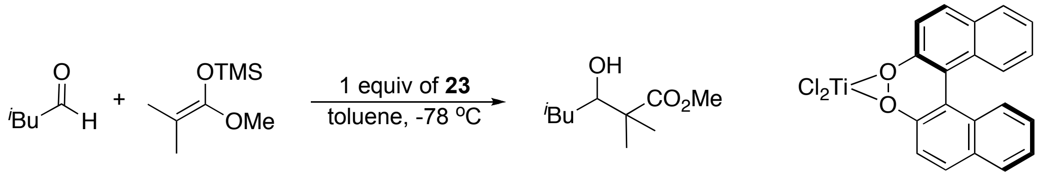
The aldol reaction is widely regarded as one of the most important carbon-carbon bond forming reactions in which β-hydroxy carbonyl compounds are produced. However, typical aldol reactions between an aldehyde and a ketone are plagued with disadvantages such as: 1) the formation of di-, poly-, or self condensation products,[56] 2) the necessity for using only highly electron withdrawing groups on the aryl carbonyl,[57] and 3) the requirement of harsh reaction conditions such as high temperatures and the use of DMF or DMSO as solvent.[57a,b] To counteract these disadvantages, Mukaiyama in 1974 developed the use of enol silyl ethers as the nucleophile in aldol reactions in the presence of titanium tetrachloride



(16)

in methylene chloride at -78 °C (eq 16).[56] Since this discovery, many literature reports on improving the effectiveness of the Mukaiyama aldol reaction have appeared. Typically, Lewis bases are used to activate the enol silyl moiety, and Lewis acids are used to activate the carbonyl moiety to facilitate these reactions. Since my research involved the use of a Lewis acidic alumatrane, only Lewis acid catalyzed reactions will be discussed here.

In 1986, Reetz developed a titanium-BINOL catalyst (**23**) which produced a high isolated yield but low enantioselectivity in the Mukaiyama aldol reaction in eq 17.[48b] To increase the selectivity of the final products, Carreira and co-workers in 1994 developed a titanium-Schiff base (**24**) catalyst for the Mukaiyama aldol reaction (eq 18).[58] Using 2 or 5 mol % of **24**, high yields (72-98%) and high enantioselectivities were obtained for the desired β-hydroxy carbonyl products.



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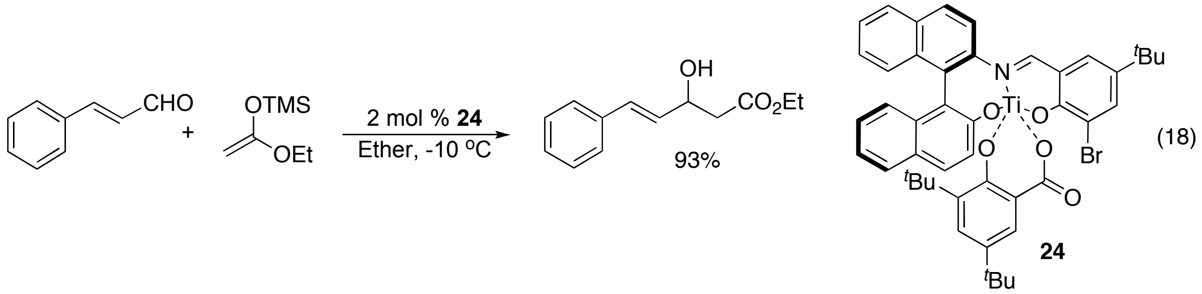

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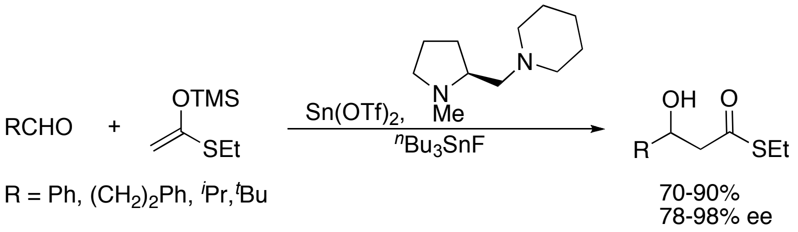
Some examples of other Lewis acids useful in the Mukaiyama reaction will now be briefly discussed. In 1988, Mukaiyama showed that the use of stoichiometric amounts of tin(II) triflate and chelating diamines in the presence of a Lewis acid co-catalyst [typically a tin (IV) salt] led to moderate to excellent yields of products obtained from the addition of enol silyl ethers to aldehydes (eq 19).[59] In 2002, Li and co-workers used magnesium iodide diethyl etherate in the catalytic Mukaiyama aldol reaction in which 5 mol % of promoter was used to obtain high product yields (eq 20).[60] This was the first example of a Mukaiyama aldol reaction catalyzed by a magnesium halide. In 1991, Yamamoto showed that in the presence of 20 mol % of a boron catalyst (**25**) the Mukaiyama aldol reaction of aryl and alkyl aldehydes with enol silyl ethers took place with high product yields (eq 21).[61] That same year, Kiyooka also developed a boron catalyst (**26**) capable of permitting high yields of the desired products.[62] A downfall of this particular boron compound is that stoichiometric amounts of promoter are needed for complete conversion to the final product. In 1991, Masamune and co-workers developed a new boron catalyst (**27**) based on **26** that was able to



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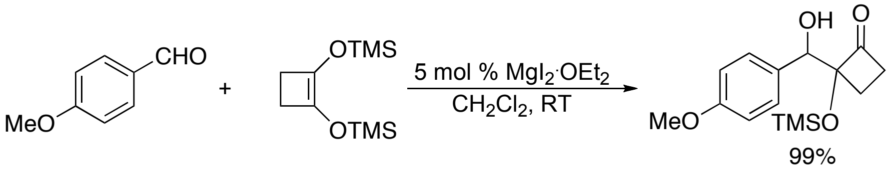

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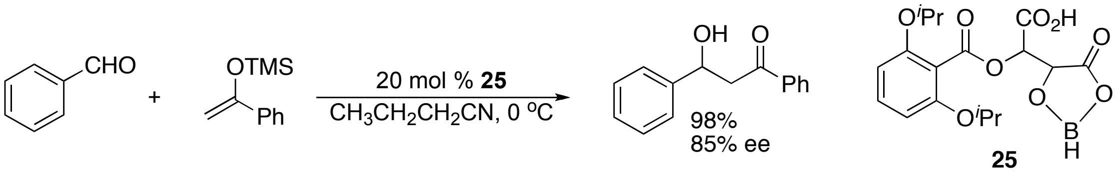

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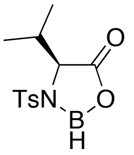

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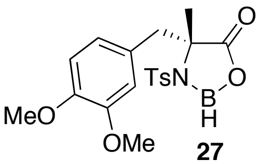

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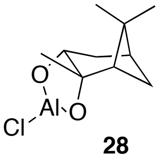
promote the Mukaiyama aldol reaction using 20 mol % of **27**.[6] The use of aluminum compounds as promoters in the Mukaiyama aldol reaction has been quite limited. The earliest report of an aluminum catalyzed Mukaiyama aldol reaction was by Reetz in 1986 in which **28** and **29** were used as catalysts for the reaction of 1-methoxy-1-trimethylsiloxy-3-methylpropene and aliphatic aldehydes. Here, 20 mol % of promoter was used to obtain high yields.[48b] Since the aforementioned reports describing the use of these aluminum catalysts in the Mukaiyama aldol reaction, there has been only one additional literature report describing such a catalyst. In 1997, Maruoka developed a bidentate aluminum catalyst (**30**)[64] whose purpose was to determine the selectivity of the Mukaiyama aldol reaction in a mixture of an aldehyde and an acetal compound. The authors found that **30** is selective for the Mukaiyama aldol reaction of aldehydes compared with acetals. TMSOTf, used in a comparison reaction with **30**, showed that the former compound displayed no selectivity in aldehyde/acetal mixtures. For such reactions to take place, however, an equivalent amount of **30** (R = Me) was needed for complete conversion. Later in 2004, different variations of **30** were made (R = Ph, *ⁿ*Oct, *ⁱ*Pr, *ᶜ*Hex, and H) and tested. However, the original aluminum catalyst (R = Me) showed the greatest catalytic activity.[65]



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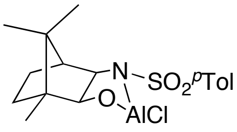

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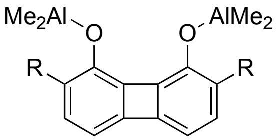


R = Me, Ph, ^{n}Oct,
^{i}Pr, ^{c}Hex, and H
30

Introduction to Palladium Catalyzed Reactions

The importance of transition metal-catalyzed reactions in organic synthesis is strongly supported by the abundance of published reviews.[66] Among the transition metals used, palladium has been extensively studied for facilitating the formation of new carbon-carbon and carbon-heteroatom bonds.[67] The favored use of palladium catalysts is largely due to their high functional group tolerance, their air and moisture stability, and their wide availability. Palladium-catalyzed reactions typically involve the reaction between an aryl or vinylic halide and a suitable organometallic nucleophile.

Suzuki-Miyaura

$$\text{R-X} + \underset{\text{M = B}}{\text{M-R'}} \xrightarrow{\text{palladium catalyst}} \text{R-R'} \qquad (22)$$

Stille

$$\text{R-X} + \underset{\text{M = Sn}}{\text{M-R'}} \xrightarrow{\text{palladium catalyst}} \text{R-R'} \qquad (23)$$

Kumada

$$\text{R-X} + \underset{\text{M = Mg}}{\text{M-R'}} \xrightarrow{\text{palladium catalyst}} \text{R-R'} \qquad (24)$$

Negishi

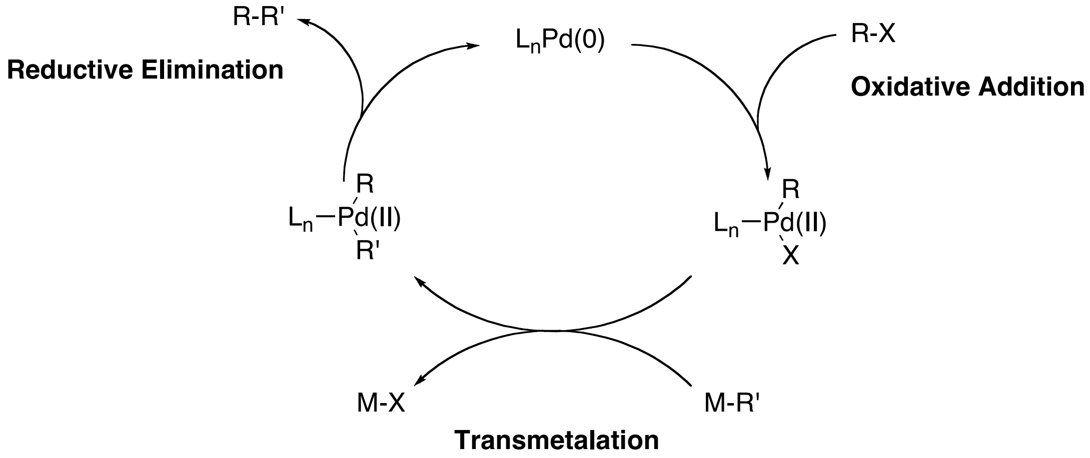
$$\text{R-X} + \underset{\text{M = Zn}}{\text{M-R'}} \xrightarrow{\text{palladium catalyst}} \text{R-R'} \qquad (25)$$

Hiyama

$$\text{R-X} + \underset{\text{M = Si}}{\text{M-R'}} \xrightarrow{\text{palladium catalyst}} \text{R-R'} \qquad (26)$$

The synthesis of biaryls has been the focus of many palladium-catalyzed chemical transformations such as: 1.) the Suzuki-Miyaura[68] cross-coupling of organoboron compounds (eq 22), 2.) the Stille[69] cross-coupling of organostannanes (eq 23), 3.) the Kumada[70] reaction of organomagnesium compounds (eq 24), 4.) the Negishi[71] coupling of organozinc compounds (eq 25), and 5.) the Hiyama[72] coupling of organosilicon compounds (eq 26). The common feature among these types of palladium-catalyzed reactions is that they follow a general mechanistic pathway as depicted in Scheme 1.[73]

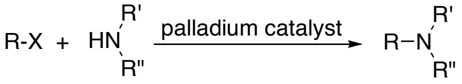
Scheme 1. General Mechanism for Palladium-Catalyzed Cross-Coupling Reactions



The first step in the catalytic cycle is the oxidative addition of an organic halide to the Pd(0) complex, which then undergoes transmetalation with an organometallic nucleophile. Reductive elimination to provide the desired coupled product is followed by regeneration of the Pd(0) catalyst. The ancillary ligand (depicted as L in Scheme 1) plays an important role at the palladium center by increasing the stability, activity, and selectivity of the palladium catalyst.

In addition to the palladium-catalyzed reactions listed in eqs 22-26 which produce biaryls, other known palladium-catalyzed reactions include the Buchwald-Hartwig amination of aryl halides with amines[74] (eq 27) and the Sonogashira coupling of acetylenes[75] (eq 28). These two reactions also follow the general mechanistic pathway shown in Scheme 1. A palladium-catalyzed reaction involving the coupling of aryl or vinyl halides and triflates with olefins is known as Heck[76] coupling (eq 29). The mechanism of this reaction differs from that of the aforementioned examples and is depicted in Scheme 2.[76b,77]

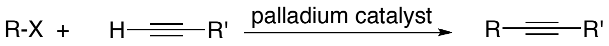
Buchwald-Hartwig Amination



$$R\text{-}X + HNR'R'' \xrightarrow{\text{palladium catalyst}} R\text{-}NR'R''$$

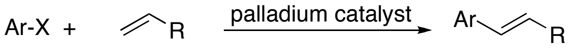
(27)

Sonogashira



(28)

Heck



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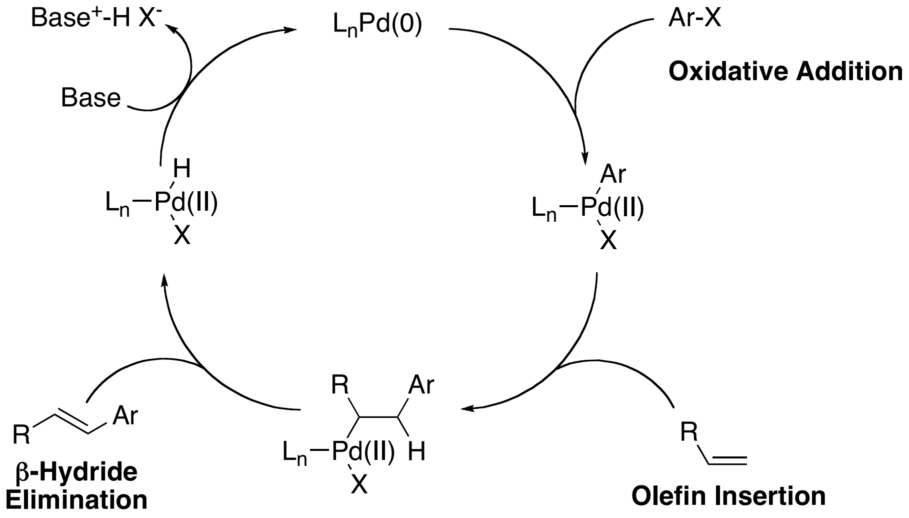
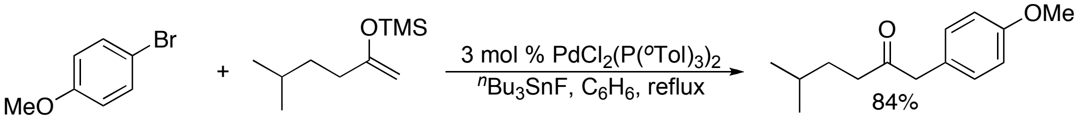
Scheme 2. Mechanistic Pathway for the Heck Cross-Coupling Reaction



1. α-Arylation of Enol Silyl Ethers

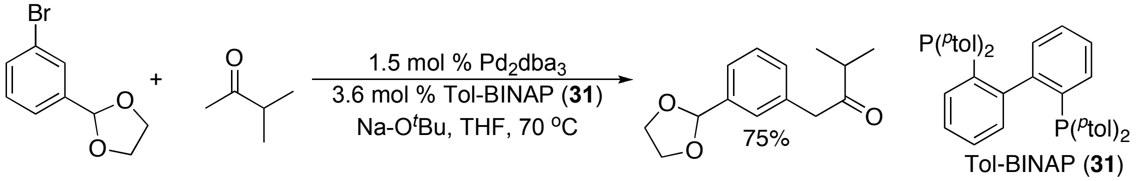
Enol silyl ethers are among the most common nucleophiles utilized in organic chemistry and palladium-catalyzed cross-coupling reactions (as previously mentioned) are among the most commonly used coupling procedures. Taking advantage of these two types of reactions simultaneously is still a relatively underdeveloped area. Kuwajima was the first to develop such a reaction in 1982 in which an aryl iodide or bromide was coupled with an enol silyl ether in the presence of 1.05 equiv of ${}^{n}Bu_3SnF$ and 3 mol % $PdCl_2[P({}^{o}MeC_6H_4)_3]_2$ in refluxing benzene to obtain moderate yields of desired products (eq



(30)

30).[78] It was postulated that the trimethylsilyl group is replaced by a tributyltin for the reaction to progress. Kuwajima observed low functional group tolerance when base sensitive groups such as nitro and cyano were employed. In 1984, Migita expanded upon this methodology by using enol acetates as starting materials instead of enol silyl ethers.[79] However, Migita also observed low functional group tolerance in the presence of nitro and cyano groups.

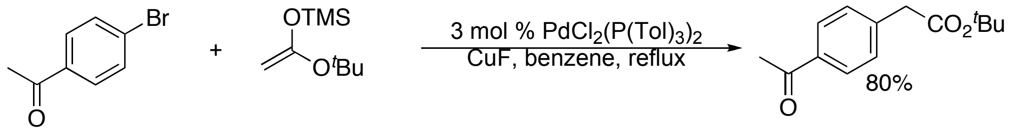
In 1997, Buchwald showed that aryl bromides undergo coupling with ketones in the presence of 1.5 mol Pd_2dba_3 and 3.6 mol % Tol-BINAP (**31**) with sodium *t*-butoxide as the base (eq 31).[80] This procedure tolerates a variety of functional groups, although only aryl bromides



Tol-BINAP (**31**)

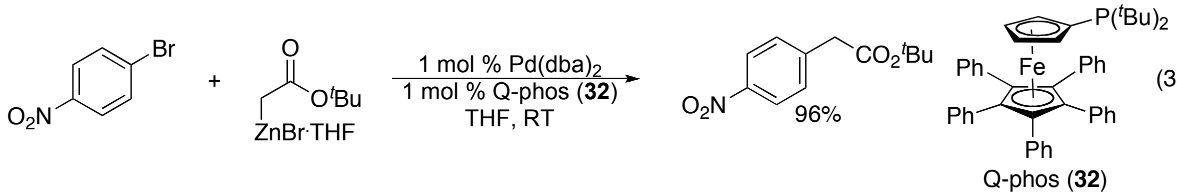
(31)

undergo coupling, and diarylation does sometimes occur. In 1998, Sulikowski and co-workers used copper(II) fluoride in place of tributyltin fluoride in the reaction of aryl bromides and enol silyl ethers (eq 32).[81] Moderate yields were obtained for the desired products.



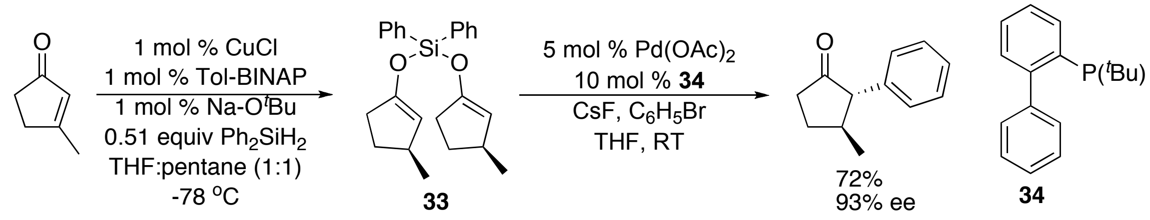
(32)

In 2003, Hartwig and co-workers developed an efficient procedure for α-arylation by using Reformatsky reagents prepared from activated zinc and α-bromo esters (eq 33).[82] In this reaction, aryl bromides undergo the reaction smoothly in the presence of 1 mol % Pd(dba)$_2$ and 1 mol % Q-phos (**32**) in THF or dioxane at room temperature. The advance in this methodology is that aryl bromides bearing a nitro or cyano group couple efficiently. However, aryl chlorides did not undergo coupling. In the same paper, Hartwig showed that aryl bromides undergo coupling with enol silyl ethers in the presence of 1 mol % Pd(dba)$_2$ and 2 mol % P(^{t}Bu)$_3$ in DMF at 80 °C. This procedure used zinc fluoride to facilitate the reaction.



(33)

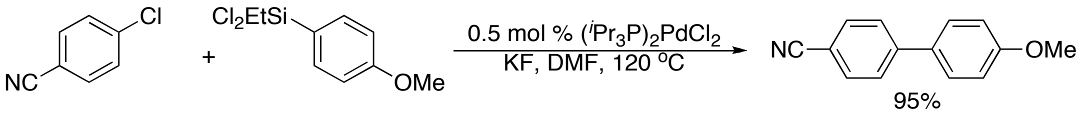
In 2004, Buchwald was able to change the type of enol silyl ether from the traditional trimethylsilyl group to a diphenylsilyl enol ether. Aryl bromides were coupled with the diphenylsilyl enol ether (**33**) in the presence of 5 mol % Pd(OAc)$_2$ and 10 mol % **34** in THF at room temperature with CsF as the fluoride source (eq 34).[83] This particular enol ether was not commercially available so they also developed a procedure to synthesize and use it in the reaction in a one pot reaction.



(33)

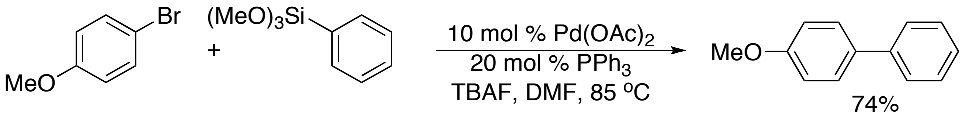
2. Hiyama Coupling

Of the previously mentioned methods for making biaryl compounds via palladium-catalyzed reactions, the Hiyama coupling is the least studied. This is mainly because organosilanes are relatively poor nucleophiles. The first coupling of aryl halides with organosilanes was developed by Hiyama in 1996. In that reaction, activated aryl chlorides were coupled with aryl(ethyl)dichlorosilanes in the presence of 0.5 mol % (^{i}Pr$_3$P)$_2$PdCl$_2$ in DMF at 120 °C, giving moderate to high product yields after 24 hours (eq 35).[84]



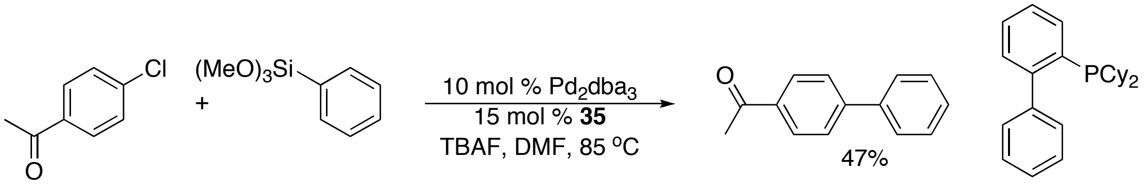
(35)

Since 1996, advances in the efficiency of Hiyama coupling have been developed. In 1999 DeShong and co-workers coupled aryl bromides with a phenylsiloxane using 10 mol % Pd(OAc)$_2$ and 20 mol % PPh$_3$ in DMF at 85 °C to obtain moderate to good yields of desired biaryl products (eq 36).[85] The use of aryl chlorides with this particular protocol gave low



(36)

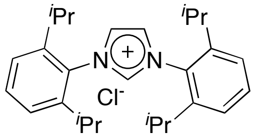
yields. DeShong also showed that the use of 15 mol % of Buchwald's ligand (**35**) provided only moderate yields when aryl chlorides were reacted in the presence of 10 mol % Pd_2dba_3 in DMF at 85 °C (eq 37).



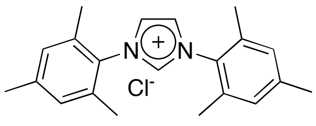
35

(37)

In 2000, Nolan used 3 mol % of imidazolium chlorides **36** and **37** with 3 mol % Pd(OAc_2) in the Hiyama coupling of aryl bromides and chlorides.[86] High yields were obtained for aryl bromides and deactivated aryl chlorides, but activated aryl chlorides provided poor yields. In 2006, Li and co-workers used 1 mol % of $PdCl_2(CH_3CN)_2$ and 2 mol % of P(^{o}Tol)$_3$ under solventless conditions at 80 °C to obtain high yields of biaryl products from aryl bromides.[87] However, activated aryl chlorides only gave low isolated yields.

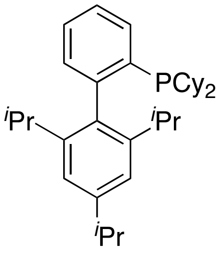


36

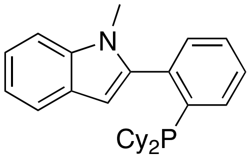


37

In 2008, Wu developed the first methodology using aryl arenesulfonates in the Hiyama coupling. This was done in the presence of 4 mol % $Pd(OAc)_2$ and 10 mol % XPhos (**38**) in THF at 80 °C.[88] A variety of aryl arenesulfonates such as electron rich, neutral, deficient, and heterocyclic substituents underwent coupling with a variety arylsiloxanes. In 2009, Kwong and co-workers were the first to use aryl mesylates in the Hiyama cross-coupling reaction.[89] Using 2 mol % $Pd(OAc)_2$ and 8 mol % CM-phos (**39**) in ^{t}BuOH at 90 °C, a variety of aryl mesylates were coupled with a variety of arylsiloxanes. However, electron deficient aryl mesylates reacted poorly under these conditions.



XPhos (**38**)



CM-phos (**39**)

Conclusions

This introduction chapter briefly summarizes important Lewis base, Lewis acid, and palladium-catalyzed reactions. As seen for each of these reactions, the optimization of various reaction parameters is of the utmost importance for achieving good success. The following chapters illustrate our approaches for enhancing the outcome of Lewis acid and base catalyzed organic transformations and palladium-catalyzed cross-coupling reactions.

References

1. A few examples of Lewis base catalyzed reported are: (a) Kim, S. S.; Song, D. H. *Letters in Organic Chemistry* **2004**, *1*, 264. (b) Song, J. J.; Gallou, F.; Reeves, J. T.; Tan, Z.; Yee, N. K.; Senanayake, C. H. *J. Org. Chem.* **2006**, *71*, 1273. (c) Hagiwara, H.; Inoguchi, H.; Fukushima, M.; Hoshi, T.; Suzuki, T. *Tetrahedron Lett.* **2006**, *47*, 5371. (d) Song, J. J.; Reeves, J. T.; Tan, Z.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013. (e) Hiraiwa, Y.; Ishihara, K.; Yamamoto, H. *Eur. J. Org. Chem.* **2006**, 1837.

2. Lensink, C.; Xi, S. K.; Danields, L. M.; Verkade, J. G. *J. Am. Chem. Soc.* **2002**, *124*, 1261.

3. For reviews, see: (a) Verkade, J. G.; Kisanga, P. B. *Tetrahedron* **2003**, *59*, 7819. (b) Verkade, J. G.; Kisanga, P. B. *Aldrichimica Acta* **2004**, *37*, 3. (c) Verkade, J. G. *Top. Curr. Chem.* **2003**, *223*, 1. (d) Verkade, J. G. *Corrd. Chem. Rev.* **1994**, *137*, 233. (e) Verkade, J. G. *Acc. Chem. Res.* **1993**, *26*, 483.

4. (a) Nandakumar, M. V.; Verkade, J. G. *Tetrahedron* **2005**, *61*, 9775. (b) Nandakumar, M. V.; Verkade, J. G. *Angew. Chem. Int. Ed.* **2005**, *44*, 2. (c) Urganokar, S.; Nagarajan, M.; Verkade, J. G. *J. Org. Chem.* **2003**, *68*, 452. (d) Urganokar, S.; Nagarajan, M.; Verkade, J. G. *Org. Lett.* **2003**, *5*, 815. (d) Urganokar, S.; Xu, J.; Verkade, J. G. *J. Org. Chem.* **2003**, *68*, 8416. (e) Urgaonkar, S.; Verkade, J. G. *J. Org. Chem.* **2004**, *69*, 9135. (f) Su, W.; Urgaonkar, S.; McLaughlin, P.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433.

5. Kisanga, P. B.; Verkade, J. G.; Schwesinger, R. *J. Org. Chem.* **2000**, *65*, 5431.

6. (a) Wroblewski, A. E.; Pinkas, J.; Verkade, J. G. *Main Group Chem.* **1995**, *1*, 69. (b) Kisanga, P. B.; Verkade, J. G. *Tetrahedron* **2001**, *57*, 467.

7. (a) Molloy, K. G.; Petersen J. L. *J. Am. Chem. Soc.* **1995**, *117*, 7696. (b) Cowley, A. H.; Lattman, M.; Stricklen, P. M.; Verkade, J. G. *Inorg. Chem.* **1982**, *21*, 543. (c) Romming, C.;

Songstad, J. *Acta Chem. Scand., Ser. A* **1980**, *34*, 365. (d) Romming, S.; Songstad, J. *Acta Chem. Scand., Ser. A* **1979**, *33*, 187.

8. Kárpáti, T.; Veszprémi, T.; Thirupathi, N.; Liu, X.; Wang, Z.; Ellern, A.; Nyulászi, L.; Verkade, J. G. *J. Am. Chem. Soc.* **2006**, *128*, 1500.

9. (a) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400. (b) Pantane, M. A.; Zhou, J.; Boger, D. L. *J. Am. Chem. Soc.* **1994**, *116*, 8544. (c) Boddy, C. N. C.; Nicolaou, K. C. *J. Am. Chem. Soc.* **2002**, *124*, 10451. (d) Crowley, B. M.; Mori, Y.; McComas, C. C.; Tang, D.; Boger, D. L. *J. Am. Chem. Soc.* **2004**, *126,* 4310. (e) Deng, H.; Jung, J.; Liu, T.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125,* 9032.

10. Cotton, R. J. *Engineering Plastics: A Handbook of Polyarylethers*; Gordon and Breach: Langhorne, PA, 1995.

11. (a) Ullmann, F. Chem. Ber. **1904**, *37,* 853. (b) Thomas, A. W.; Ley, S. V. *Angew. Chem. Int. Ed.* **2003**, *42,* 5400. (c) Cristau, H.; Cellier, P. P.; Hamada, S.; Spindler, J.; Taillefer, M. *Org. Lett.* **2004**, *6,* 913. (d) Marcoux, J.; Doye, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119,* 10539. (e) Ma, D.; Cai, Q. *Org. Lett.* **2003**, *5,* 3799.

12. (a) Mann, G.; Hartwig, J. F. *Tetrahedron Letters* **1997**, *38,* 8005. (b) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121,* 4369. (c) Mann, G.; Incarvito, C.; Rheingold, A. L.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121,* 3224. (d) Anderson, K. W.; Ikawa, T.; Tundel, R. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128,* 10694.

13. (a) Sawyer, J. S. *Tetrahedron* **2000**, *56,* 5045. (b) Wipf, P.; Lynch, S. M. *Org. Lett.* **2003**, *5,* 1155. (c) Saitoh, T.; Ichikawa, J. *J. Am. Chem. Soc.* **2005**, *127,* 9696.

14. Edwards, L. H.; Turner, C. E.; Lane, C. E.; Thames, S. F. *Tetrahedron Lett.* **1969**, *10*, 4225.

15. Saunders, D. G. *Synthesis* **1988**, 377.

16. Oriyama, T.; Noda, K.; Yatabe, K. *Synlett* **1997**, 701.

17. Ueno, M.; Hori, C.; Suzawa, K.; Ebisawa, M.; Kondo, Y. Eur. J. Org. Chem. **2005**, 1965.

18. Urgaonkar, S.; Verkade, J. G. Org. Lett. **2005**, *7,* 3319.

19. Duong, H. A.; Cross, M. J.; Louie, J. *Org. Lett.* **2004**, *6*, 4647.

20. (a) Wirpsza, Z. *Polyurethanes: Chemistry, Technology and Application*, Ellis Horwood: London, 1993. (b) Zitinkina, A. K.; Sibanova, N. A.; Tarakanov, O. G. Russ. Chem. ReV. **1985**, *54*, 1866. (c) Nawata, T.; Kresta, J. E.; Frisch, K. C. *J. Cell. Plast.* **1975**, 267. (d) Nicholas, L.; Gmitter, G. R. *J. Cell. Plast.* **1965**, 85.

21. (a) Bukac, Z.; Sebenda, J. *Chem. Prum.* **1985**, *35*, 361. (b) Horsky, J.; Kubanek, U.; Marick, J.; Kralicek, J. *Chem. Prum.* **1982**, *32*, 599.

22. (a) Wegener, G.; Brandt, M.; Duda, L.; Hofmann, J.; Klesczewski, B.; Koch, D.; Kumpf, R.-J.; Orzesek, H.; Pirkl, H.-G.; Six, C.; Steinlein, C.; Weisbeck, M. *Appl. Cat. A: Gen.* **2001**, *221*, 303. (b) Silva, A. L.; Bordado, J. C. *Catal. Rev.* **2004**, *46*, 31.

23. (a) Bloodworth, A. J.; Davies, A. G. *J. Chem. Soc.* **1965**, 6858. (b) Foley, S. R.; Yap, G. P. A.; Richeson, D. S. *Organometallics* **1999**, *18*, 4700. (c) Noltes, J. G.; Boersma, J. *J. Organomet. Chem.* **1967**, *7*, 6. (d) Li, Y.; Matsumura, H.; Yamanaka, M.; Takahashi, T. *Tetrahedron* **2004**, *60*, 1393. (e) Villa, J. F.; Powell, H. B. *Synth. React. Metal-Org. Chem.* **1976**, *6*, 59.

24. (a) Tang, J.; Mohan, T.; Verkade; J. G. *J. Org. Chem.* **1994**, *59*, 4931. (b) Tang, J.; Verkade, J. G. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 896. (c) Wroblewski, A. E.; Pinkas,

J.; Verkade, J. G. *Main Group Chem.* **1995**, *1*, 69. (d) Villa, J. F.; Powell, H. B. *Synth. React. Metal-Org. Chem.* **1976**, *6*, 59. (e) Nambu, Y.; Endo, T. *J. Org. Chem.* **1993**, *58*, 1932. (f) Mizuya, J.; Yokozawa, T.; Endo, T. *J. Polym. Sci., Polym. Chem.* **1991**, *29*, 1544. (g) Tagachi, Y.; Shibaya, I.; Yasumoto, Y.; Ynoemoto, K. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3486. (h) Moghaddam, F. M.; Dekamin, M. G.; Koozehgari, G. R. *Letters in Organic Chemistry* **2005**, *2*, 734.

25. Paul, F.; Moulin, S.; Piechaczyk, O.; Le Floch, P.; Osborn, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 7294.

26. Kogon, I. C. *J. Am. Chem. Soc.* **1956**, *78*, 4911.

27. Mba, M.; Prins, L. J.; Licini, G. *Org. Lett.* **2007**, *9*, 21.

28. (a) Bolm, C.; Sharpless, B. K. *Tetrahedron Lett.* **1988**, *29*, 5101. (b) Di Furia, F.; Licini, G.; Modena, G.; Motterle, R.; Nugent, W. A. *J. Org. Chem.* **1996**, *61*, 5175. (c) Bonchio, M.; Licini, G.; Di Furia, F.; Mantovani, S.; Modena, G.; Nugent, W. A. *J. Org. Chem.* **1999**, *64*, 1326. (d) Gade, L. H.; Renner, P.; Memmler, H.; Fecher, F.; Galka, C. H.; Laibender, M.; Radojevic, S.; McPartlin, M.; Lauher, M. J. W. *Chem. Eur. J.* **2001**, *7*, 2563. (e) Forcato, M.; Nugent, W. A.; Licini, G. *Tetrahedron Lett.* **2003**, *44*, 49. (f) Bringmann, G.; Pfeifer, R.; Rummey, C.; Hartner, K.; Breuning, M. *J. Org. Chem.* **2003**, *68*, 6859. (g) Fetterly, B. M.; Verkade, J. G. *Tetrahedron Lett.* **2005**, *46*, 8061. (h) Foltz, C.; Stecker, B.; Marconi, G.; Bellemin-Laponnaz, S.; Wadepohl, H.; Gade. L. H. *Chem. Commun.* **2005**, 5115. (i) Pei, Y.; Brulé, E.; Moberg, C. *Org. Biomol. Chem.* **2006**, *4*, 544.

29. Frye, C. L.; Vogel, G. E.; Hall, J. A. *J. Am. Chem. Soc.* **1961**, *83*, 996.

30. (a) Mehrotra, R. C.; Mehrotra, R. K. *J. Indian Chem. Soc.* **1962**, *39*, 677. (b) Lacey, M. J.; McDonald, C. G. *Aust. J. Chem.* **1976**, *29*, 1119. (c) Voronkov, M. G.; Baryshok, V. P. *J.*

Organomet. Chem. **1982**, *239*, 199. (d) Mehrotra, R. C.; Rai, A. K. *Polyhedron* **1991**, *10*, 1967. (e) Pinkas, J.; Verkade, J. G. *Inorg. Chem.* **1993**, *32*, 2711.

31. (a) Shklover, V. E.; Struchkov, Yu. T.; Voronkov, M. G.; Ovchinni-kova, Z. A.; Baryshok, V. P. *Dokl. Akad. Nauk SSSR (Engl. Transl.)* **1984**, *277*, 723. (b) Paz-Sandoval, M. A.; Fernandez-Vincent, C.; Uribe, G.; Contreras, R.; Klaebe, A. *Polyhedron* **1988**, *7*, 679. (c) Healy, M. D.; Barron, A. R. *J. Am. Chem. Soc.* **1989**, *111*, 398. (d) Pinkas, J.; Gaul, B.; Verkade, J. G. *J. Am. Chem. Soc.* **1993**, *115*, 3925. (e) Narayanan, R.; Laine, R. M. *Appl. Organomet. Chem.* **1997***, 11*, 919. (f) Opornsawad, Y.; Ksapabutr, B.; Wongkasemjit, S.; Laine, R. M. *Eur. Polym. J.* **2001***, 37*, 1877.

32. Chandrasekaran, A.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.* **2000**, *122*, 1066.

33. (a) Kol, M.; Shamis, M.; Goldberg, I.; Goldschmidt, Z.; Alfi, S.; Hayut-Salant, E. *Inorg. Chem. Comm* **2001**, *4*, 177. (b) Michalczyk, L.; de Gala, S.; Bruno, J. W. *Organometallics* **2001**, *20*, 5547. (c) Kim, Y.; Verkade, J. G. *Organometallics* **2002**, *21*, 2395. (d) Bull, S. D.; Davidson, M. G.; Johnson, A. L.; Robinson, D.; Mahon, M. F. *Chem. Commun.* **2003**, 1750. (e) Kim, Y.; Jnaneshwara, G. K.; Verkade, J. G. *Inorg. Chem.* **2003**, *42*, 1437. (f) Wang, W.; Fujiki, M.; Nomura, K. *Macromol. Rapid Commun.* **2004**, *25*, 504. (g) Ugrinova, V.; Ellis, G. A.; Brown, S. N. *Chem. Commun.* **2004**, 468. (h) Fortner, K. C.; Bigi, J. P.; Brown, S. N. *Inorg. Chem.* **2005**, *44*, 2803. (i) Cortes, S. A.; Muñoz Hernández, M. A.; Nakai, H.; Castro-Rodriguez, I.; Meyer, K.; Fout, A. R.; Miller, D. L.; Huffman, J. C.; Mindiola, D. J. *Inorg. Chem. Commun.* **2005**, *8*, 903. (j) Gendler, S.; Segal, S.; Goldberg, I.; Goldschmidt, Z.; Kol, M. *Inorg. Chem.* **2006**, *45*, 4783-4790.

34. Groysman, S.; Goldberg, I.; Goldschmidt, Z.; Kol, M. *Inorg. Chem.* **2005**, *44*, 5073.

35. Davidson, M. G.; Doherty, C. L.; Johnson, A. L.; Mahon, M. F. *Chem. Commun.* **2003**,

1832.

36. Motekaitis, R. J.; Martell, A. E.; Koch, S. A.; Hwang, J. W.; Quarless, D. A.; Welch, M. J. *Inorg. Chem.* **1998**, *37*, 5902.

37. Hwang, J.; Govindaswamy, K.; Koch, S. A. *Chem. Commun.* **1998**, 1667.

38. (a) Groysman, S.; Segal, S.; Shamis, M.; Goldberg, I.; Kol, M.; Goldschmidt, Z.; Hayut-Salant, E. *J. Chem. Soc., Dalton Trans.* **2002**, 3425. (b) Kim, Y. J.; Kapoor, P. N.; Verkade, J. G. *Inorg. Chem.* **2002**, *41*, 4834. (c) Groysman, S.; Goldberg, I.; Kol, M. *Organometallics* **2003**, *22*, 3793. (d) Groysman, S.; Segal, S.; Goldberg, I.; Kol, M.; Goldschmidt, Z. *Inorg. Chem. Commun.* **2004**, *7*, 938. (e) Groysman, S.; Goldberg, I.; Kol, M.; Genizi, E.; Goldschmidt, Z. *Adv. Synth. Catal.* **2005**, *347*, 409.

39. Kim, Y.; Verkade, J. G. *Inorg. Chem.* **2003**, *42*, 4804.

40. Su, W.; Kim, Y.; Ellern, A.; Guzei, I. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2006**, *128*, 13727.

41. Su, W.; Kobayashi, J.; Ellern, A.; Kawashima, Y.; Verkade, J. G. *Inorg. Chem.* **2007**, *46*, 7953.

42. Winkler, F. W. *Liebigs Ann. Chem.* **1832**, *4*, 246.

43. Kiliani, H. *Chem. Ber.* **1888**, *21*, 915.

44. (a) Tanaka, K.; Mori, A.; Inoue, S. *J. Org. Chem.* **1990**, *55*, 181. (b) Brown, R. F. C.; Donohue, A. C.; Jackson, W. R.; McCarthy, T. D. *Tetrahedron* **1994**, *50*, 13739. (c) Ziegler, T.; Hörsch, B.; Effenberger, F. *Synthesis* **1990**, 575. (d) Kanerva, L. T. *Acta Chem. Scand.* **1996**, *50*, 234.

45. (a) Rodriguez, B.; Pasto, M.; Jimeno, C.; Pericas, M. A. *Tetrahedron Asymmetry* **2006**, *17*, 151. (b) Khan, N. H.; Agrawal, S.; Kureshy, R.; Abdi, S. H. R.; Mayani, V. J.; Jasra, R.

V. *Eur. J. Org. Chem.* **2006**, 3175. (c) Mei, L. *Journal of Molecular Catalysis A: Chemical* **2005**, 227, 183. (d) Yang, W.; Fang, J. *J. Org. Chem.* **1998**, *63,* 1356. (e) Norsikian, S.; Holmes, I.; Lagasse, F.; Kagan, H. B. *Tetrahedron Lett.* **2002**, *43,* 5715. (f) Bandini, M.; Cozzi, P. G.; Garelli, A.; Melchiorre, P.; Unami-Ronchi, A. *Eur. J. Org. Chem.* **2002**, 3243. (g) Durini, M.; Epifan, F.; Marcotullio, M. C.; Rosati, O.; Rossi, M. *Synlett* **1999**, *3,* 315.

46. (a) Kim, S. S.; Song, D. H. *Letters in Organic Chemistry* **2004**, *1,* 264. (b) Suzuki, Y.; Bakar, A.; Muramatsu, K.; Sato, M. *Tetrahedron* **2006**, *62,* 4227. (c) Song, J. J.; Gallou, F.; Reeves, J. T.; Tan, Z.; Yee, N. K.; Senanayake, C. H. *J. Org. Chem.* **2006**, *71*, 1273. (d) Fukuda, Y.; Maeda, Y.; Ishii, S.; Kondo, K.; Aoyama, T. *Synthesis* **2006**, 589. (e) Denmark, S. E.; Chung, W. *J. Org. Chem.* **2006**, *71,* 4002.

47. (a) Hamashima, Y.; Sawada, D.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **1999**, *121*, 2641. (b) Hamashima, Y.; Sawada, D.; Nagomi, H.; Kanai, M.; Shibasaki, M. *Tetrahedron* **2001**, *57*, 805. (c) Qin, Y.; Liu, L.; Pu, L. *Org. Lett.* **2005**, *7*, 2381.

48. (a) Reetz, M. T.; Kunisch, F.; Heitmann, P. *Tetrahedron Lett.* **1986**, *39*, 4721. (b) Reetz, M.T.; Kyung, S.; Bolm, C.; Zierke, T. *Chem. Ind.* **1986**, 824.

49. Hayashi, M.; Miyamoto, Y.; Inoue, T.; Oguni, N. *J. Org. Chem.* **1993**, *58*, 1515.

50. Flores-Lopéz, L. Z.; Parra-Hake, M.; Somanathan, R.; Walsh, P. J. *Organometallics* **2000**, *19*, 2153.

51. Gama, A.; Flores-Lopéz, L. Z.; Aguirre, G.; Parra-Hake, M.; Somanathan, R.; Walsh, P. J. *Tetrahedron: Asymmetry* **2002**, *13*, 149.

52. Belda, O.; Duquesne, S.; Fischer, A.; Moberg, C. *J. Organomet. Chem.* **2004**, *689*, 3750.

53. Lee, P.; Chen, C. *Tetrahedron: Asymmetry* **2005**, *16*, 2704.

54. Ohno, H.; Nitta, H.; Tanaka, K.; Mori, A.; Inoue, S. *J. Org. Chem.* **1992**, *57*, 6778.

55. Deng, H.; Isler, M. P.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2002**, *41*, 1009.

56. Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503.

57. (a) Sakthivel, K.; Notz, W.; Bui, T.; Barbas, C. F. *J. Am. Chem. Soc.* **2001**, *123*, 5260. (b) Mase, N.; Nakai, Y.; Ohara, N.; Yoda, H.; Takabe, K.; Tanaka, F.; Barbas, C. F. *J. Am. Chem. Soc.* **2006**, *128*, 734. (c) He, L.; Jiang, J.; Tang, Z.; Cui, X.; Mi, A.; Jiang, Y.; Gong, L. *Tetrahedron: Asymmetry* **2007**, *18*, 265. (d) Chen, J.; Lu, H.; Li, X.; Cheng, L.; Wan, J.; Xiao, W. *Org. Lett.* **2005**, *7*, 4543.

58. Carreira, E. M.; Singer, R. A.; Lee, W. *J. Am. Chem. Soc.* **1994**, *116*, 8837.

59. (a) Iwasawa, N.; Mukaiyama, T. *Chem. Lett.* **1987**, 463. (b) Mukaiyama, T.; Kobayashi, S.; Tamura, M.; Sagawa, Y. *Chem. Lett.* **1987**, 491.

60. Li, W. Z.; Zhang, X. *Org. Lett.* **2002**, *4*, 3485.

61. Furuta, K.; Maruyama, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1991**, *113*, 1042.

62. Kiyooka, S.; Kaneko, Y.; Komura, M.; Matsuo, H.; Nakano, M. *J. Org. Chem.* **1991**, *56*, 2276.

63. Parmee, E. R.; Tempkin, O.; Masamune, S. *J. Am. Chem. Soc.* **1991**, *113*, 9365.

64. Ooi, T.; Tayama, E.; Takahashi, M.; Maruoka, K. *Tetrahedron Lett.* **1997**, *38*, 7403.

65. Ooi, T.; Takahashi, M.; Yamada, M.; Tayama, E.; Omoto, K.; Maruoka, K. *J. Am. Chem. Soc.* **2004**, *126*, 1150.

66. For recent reviews on transition-metal catalyzed reactions, see: (a) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (b) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (c) Fairlamb, I. J. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 1048. (d) Skoda-Foldes, R.; Kollar, L. *Chem. Rev.* **2003**, *103*, 4095. (e) Trost, B. M.; Crawley, M.

L. *Chem. Rev.* **2003**, *103*, 2921.

67. For reviews on organopalladium chemistry, see: (a) Negishi, E. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley and Sons: NewYork, 2002; Vols 1 and 2. (b) Hegedus, L. S. *Coord. Chem. Rev.* **1996**, *161*, 129. (c) Tsuji, J. *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley and Sons: New York, 1995. (d) Tsuji, J. *J. Organomet. Chem.* **1986**, *300*, 281.

68. For reviews on the Suzuki reaction, see: (a) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147. (b) Suzuki, A. In *Metal-Catalyzed Cross Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998.

69. For reviews on the Stille reaction, see: (a) Fugami, K.; Kosugi, M. *Top. Curr. Chem.* **2002**, *219*, 87. (b) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

70. For reviews on the Kumada reaction, see: (a) Yamamura, M.; Moritani, I. Murahashi, S. *J. Organomet. Chem.* **1975**, *91*, C39. (b) Negishi, E. In *Metal-Catalyzed Cross Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998.

71. Erdik, E. *Tetrahedron* **1992**, *48*, 9577.

72. For reviews on the Hiyama reaction, see: (a) Hiyama, T. In *Metal-Catalyzed Cross Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998. (b) Hiyama, T.; Hatanaka, Y. *Pure Appl. Chem.* **1994**, *66*, 1471.

73. Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, *33*, 314.

74. For reviews on the Buchwald-Hartwig amination reaction, see: (a) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131. (b) Hartwig, J. F. In *Modern Amination Methods*; Ricci, A., Ed.; Wiley-VCH: Weinheim, Germany, 2000.

75. For reviews on the Sonogashira reaction, see: (a) Negishi, E.; Anastasia, L. *Chem. Rev.*

2003, *103*, 1979. (b) Sonogashira, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley-Interscience: New York, 2002.

76. For reviews on the Heck reaction, see: (a) Heck, R. F.; Nolley, J. P. *J. Org. Chem.* **1972**, *37*, 2320. (b) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.

77. Whitecombe, N. J.; Hii, K. K.; Gibson, S. E. *Tetrahedron* **2001**, *57*, 7449.

78. Kuwajima, I.; Urabe, H. *J. Am. Chem. Soc.* **1982**, *104*, 6831.

79. Kosugi, M.; Hagiwara, I.; Sumiya, T.; Migita, T. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 242.

80. Palucki, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 11108.

81. Angelli, F.; Sulikowski, G. A. *Tetrahedron Lett.* **1998**, *39*, 8807.

82. Hama, T.; Liu, X.; Culkin, D. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 11176.

83. Chae, J.; Yun, J.; Buchwald, S. L. *Org. Lett.* **2004**, *6*, 4809.

84. Gouda, K.; Hagiwara, E.; Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1996**, *61*, 7232.

85. Mowery, M. E.; DeShong, P. *Org. Lett.* **1999**, *1*, 2137.

86. Lee, H. M.; Nolan, S. P. *Org. Lett* **2000**, *2*, 2053.

87. Li, J.; Deng, C.; Xie, Y. *Synthesis* **2006**, 969.

88. Zhang, L.; Wu, J. *J. Am. Chem. Soc.* **2008**, *130*, 12250.

89. So, C. M.; Lee, H. W. Lau, C. P.; Kwong, F. Y. *Org. Lett.* **2009**, *11*, 317.

CHAPTER 2. P(*i*-BuNCH$_2$CH$_2$)$_3$N: AN EFFICIENT PROMOTER FOR THE MICROWAVE SYNTHESIS OF DIARYL ETHERS

A paper published in *Tetrahedron Letters* **2008**, *49*, 3507

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Abstract

With the title proazaphosphatrane as a promoter, the coupling of aryl fluorides with aryl TBDMS ethers under microwave conditions gave moderate to high yields of the desired products at low catalyst loadings and in short times. In this methodology, electron deficient aryl fluorides possessing substituents, such as nitro, cyano, and ester, were coupled with sterically demanding aryl TBDMS ethers as well as with aryl TBDMS ethers bearing a variety of functionalities such as methoxy, halo, and cyano groups.

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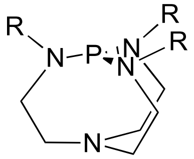
The synthesis of diaryl ethers has been intensely studied owing primarily to the presence of diaryl ether moieties in many biologically active natural products such as Piperaz-inomycin, Bouvardin, Vancomycin, Ristocetin A, and the anti-HIV agent Chloropeptin I.[1] Three general methods developed for the synthesis of diaryl ethers are (1) S$_N$Ar reactions between aryl halides (order of reactivity F > Cl > Br > I)[2] and phenols,[3] (2) copper-catalyzed Ullmann reactions between aryl halides and phenols,[4] and (3) palladium-catalyzed reactions of aryl halides with phenols.[5]

Disadvantages of the Ullmann coupling are its requirements for harsh reaction conditions and environmentally unfriendly copper. Palladium-mediated syntheses suffer from the expense of the metal. Because of these issues, investigators have focused on seeking superior S_NAr routes owing to their generally milder reaction conditions. Ways have also been sought to employ the nucleophilic phenolic coupling partner more efficiently by, for example, deprotection of a trimethylsilyl-(TMS)-protected or a tert-butyldimethylsilyl-(TBDMS)-protected phenol in the presence of a strong base. Thus, Kondo and co-workers found that by using the phosphazene base P4-*t*-Bu, diaryl ethers could be synthesized in a highly polar solvent such as DMSO or DMF using electron deficient aryl fluorides and electron rich TBDMS-protected phenols.[6]

Figure 1. Proazaphosphatranes



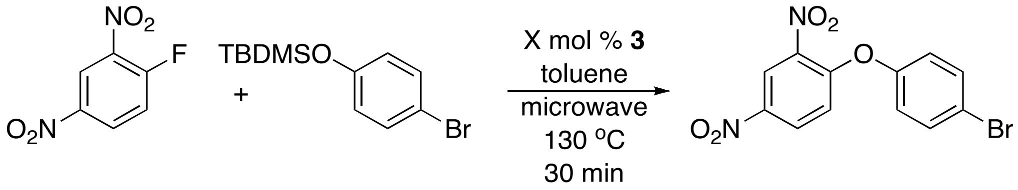
1: R = Me
2: R = *i*-Pr
3: R = *i*-Bu
5: R = Bn

About the time Kondo's work was published, our group reported that proazaphosphatrane **3** in Figure 1 also efficiently promoted such diaryl ether syntheses;[7] a finding that was based on our earlier report of the first observation of the efficient deprotection of TBDMS-protected alcohols and phenols with **1**.[8] Proazaphosphatranes are strong non-ionic bases (pKa 32–34[9]), although these are much weaker than P4-*t*-Bu (pKa 41.4[10]). However, the former may be more nucleophilic, perhaps in part because of the possible transannulation of the basal nitrogen to the phosphorus during the reaction.

To obtain diaryl ethers in high yields using our reported thermal protocol with **3**, high mole percentages of this base were needed (10–50 mol %) even with highly electron deficient aryl fluorides.[7] To avoid using large molar percentages of promoters for a variety of S_NAr reactions, several groups have resorted to microwave techniques.[11] For example, Wang and co-workers used a microwave for the S_NAr reaction involving 2 equiv of K_2CO_3 in the highly polar solvent DMSO in the absence of catalyst.[12]

In this report, we describe the utility of **3** at low loading in the synthesis of diaryl ethers under microwave conditions. Since we previously reported using **3** under thermal conditions for such syntheses,[7] we began our study by determining the lowest loading of **3** which can be usefully employed for this reaction under microwave conditions to achieve high product yields. Using the same model reaction given in our previous report, we found that only 1 mol % of **3** was necessary to obtain a 99% isolated yield of the desired product under microwave conditions in the nonpolar solvent toluene (Table 1).

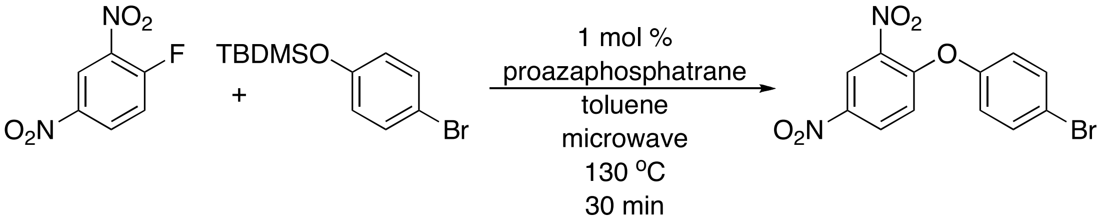
Table 1. Optimization Study on Amount of Proazaphosphatrane



Entry	mol % **3**	Yield (%)
1	10	99
2	5	99
3	1	99
4	0.5	76

[a] Average of two runs. [b] Thermal reaction required 1 hour (Ref. 7).

Table 2. Optimization Study for Proazaphosphatranes using 1 mol % Catalyst



Entry	Proazaphosphatrane	Yield (%)[a,b]
1	**1**	90 (98)
2	**2**	91 (98)
3	**3**	99 (98)
4	**4**	99
5	None	45 (0)

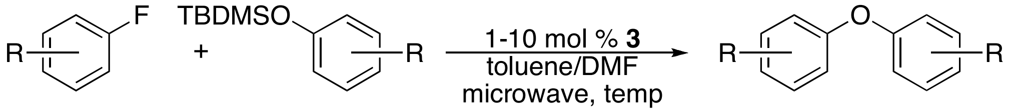
[a]Average of two runs. [b]Yields in parenthesis are under thermal conditions with 10 mol % **3** (Ref. 7).

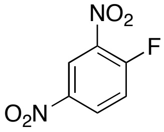
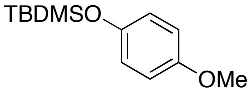
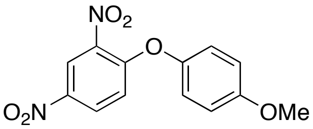
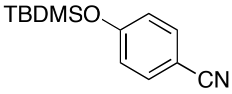
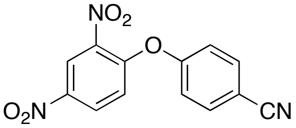
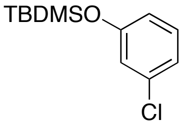
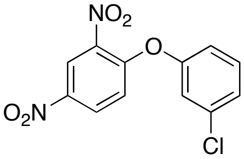
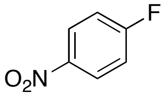
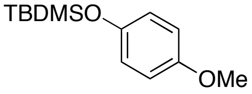
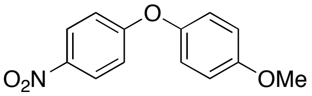
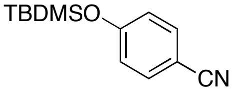
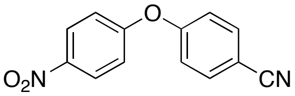
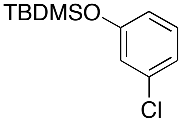
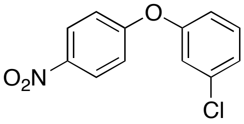
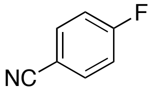
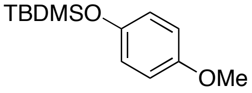
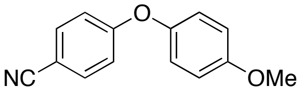
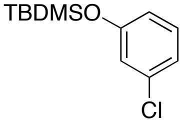
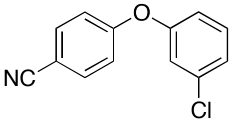
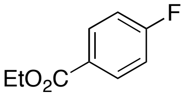
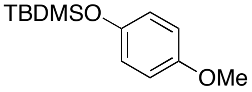
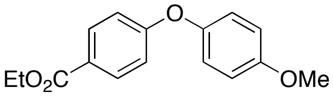
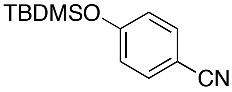
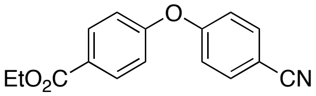
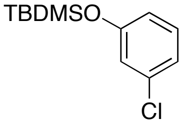
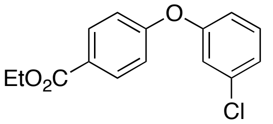
In determining the best proazaphosphatrane for diaryl ether synthesis using the present protocol, we standardized on employing 1 mol % each of 1–4 (Table 2). As shown in entry 1 of this table, 90% of the desired product was achieved using **1**. Earlier we showed that proazaphosphatrane basicity rises with the steric bulk of the substituent on its P–N nitrogens.[9] Herein, a parallel trend is seen for the product yield in Table 2. Because **4** is apparently less basic than **3**,[13] it was surprising to observe that proazaphosphatrane **4** (as well as **3**) gave a quantitative yield of the desired product (Table 2, entry 4).

It was previously shown by our group that the reaction in Table 1 fails under thermal conditions in the absence of a proazaphosphatrane.[8] However, in the same experiment carried out under microwave conditions, 45% of desired product was obtained (Table 2, entry 5). When the same model compounds were used with no catalyst in DMF at 180 °C for 5 h, the yields of the desired products did not increase. With these results in hand, the scope of our microwave approach was explored with a variety of aryl fluorides and TBDMS aryl ethers

(Table 3) using **3** because of its ease of handling and its commercial availability. Two solvents (toluene and DMF) were used for the S_NAr reactions in this table. Nitro-substituted aryl fluorides functioned better in the relatively non-polar solvent toluene, while other aryl fluorides required highly polar DMF, apparently to stabilize the Meisenheimer complex.[14] Thus, the coupling of highly activated 2,4-dinitrofluorobenzene with 4-methoxyphenyl and 3-chlorophenyl TBDMS ethers proceeded well with only 1 mol % of **3** in toluene (Table 3, entries 1 and 3). S_NAr reactions have been observed to proceed smoothly with electron rich phenols but are sluggish with electron deficient analogues.[7] Even coupling between 2,4-dinitrofluorobenzene and electron deficient 4-cyanophenyl TBDMS ether proceeded in 45 min with a 93% isolated yield in the presence of 1 mol % **3** in toluene (Table 3, entry 2).

Table 3. S_NAr Reaction of Aryl Fluorides with TBDMS Ethers



Entry	Aryl Fluoride	TBDMS Ether	mol %/time	Product	Yield (%)[a,b]
1			1/30 min		97 (88)[c,d]
2			1/45 min		93 (88)[c,e]
3			1/30 min		95 (96)[c,e]
4			2/1 h		97 (92)[f,g]
5			2/3 h		96 (95)[f,h]
6			2/90 min		95 (90)[e,f]
7			1/3 h		94 (85)[f,i]
8			1/5 h		90 (95)[e,f]
9			2/5 h		92 (92)[f,j]
10			10/5 h		61 (84)[f,k]
11			5/5 h		73 (96)[e,f]

[a] Isolated yield (average of two runs). [b] Yields in parenthesis are literature values. [c] Reaction temperature is 130 °C. [d] See Ref. 16. [e] See Ref. 7. [f] Reaction temperature is 180 °C. [g] See

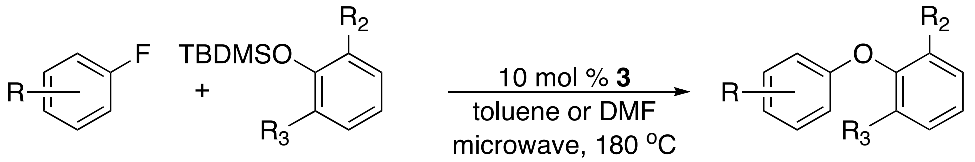
Ref. 17. [h]See Ref. 12. [i]See Ref. 11c. [j]See Ref. 6. [k]See Ref. 18.

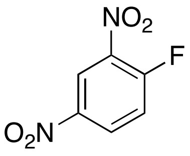
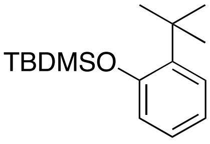
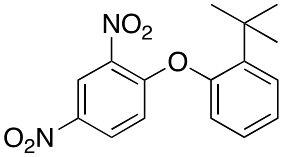
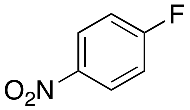
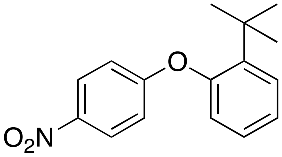
For 4-nitrofluorobenzene in toluene, the catalyst loading required for **3** for timely completion of the reaction was 2 mol % and the temperature had to be raised to 180 °C for complete conversion of the starting material. Under these conditions, 4-nitrofluorobenzene reacted readily with 4-methoxyphenyl and 3-chlorophenyl TBDMS ethers affording product yields of 97% and 95%, respectively (Table 3, entries 4 and 6). With this increased catalyst loading, 4-cyanophenyl TBDMS ether as a coupling partner provided an excellent product yield of 96% (Table 3, entry 5). Under thermal conditions, we obtained only a moderate yield of this product (73%) using 20 mol % of 3.[7] Although Wang and co-workers reported a 95% yield of the same product in 5 min using microwave conditions, 2 equiv of K_2CO_3 in DMSO was required.[12]

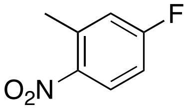
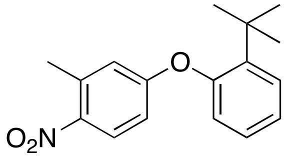
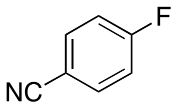
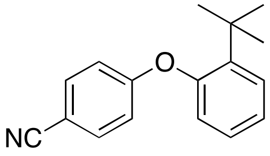
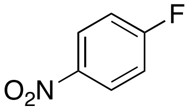
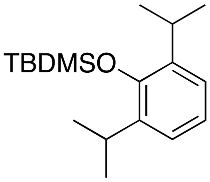
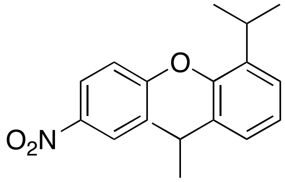
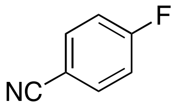
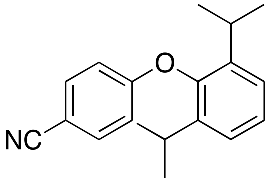
We then screened aryl fluorides bearing a nitrile or an ester functional group (Table 3, entries 7–12). These substrates required DMF as a solvent to avoid the sluggishness we observed for their reactions in toluene. Although longer reaction times were needed, the reactions in Table 3, entries 7–12 were amenable to lower loadings of **3** than we had reported under thermal conditions,[7] particularly for the reaction of 4-cyanofluorobenzene with 3-chlorophenyl TBDMS ether (Table 3, entry 8). The 90% product yield for this reaction was obtained with only 1 mol % of **3**, in contrast to the 50 mol % of this catalyst that was necessary to obtain a 95% product yield thermally.[7] For the fluoro-aryl ester (Table 3, entries 8–11) higher loadings of **3** were required to obtain reasonable to high product yields. Although the reaction between ethyl-4-fluorobenzoate and 4-cyanophenyl TBDMS ether required 10 mol % of **3** to obtain a 61% product yield, 20 mol % of this catalyst was required to obtain only a 39% product yield thermally.[7]

Finally, we examined two sterically hindered aryl TBDMS ethers in our protocol (Table 4). Under the thermal conditions used in our previous work,[7] 50 mol % of **3** was needed to obtain high yields, whereas under microwave conditions, the same products were made in excellent yields by employing only 10 mol % of **3** (Table 4, entries 1–6). However, the new compound made from 2-nitro-4-fluorotoluene generated only a moderate product yield of 56% (Table 4, entry 3). With 4-fluorobenzonitrile, the reaction failed in toluene, but when DMF was used as the solvent, a 95% yield of the desired product was achieved (Table 4, entry 4). Surprisingly, 4-nitrofluorobenzene also reacted with the sterically demanding 2,6-di-isopropylphenyl TBDMS ether to give a 92% product yield using 10 mol % of **3** (Table 4, entry 5). A previous method for making this compound involved the use of a 4-nitrophenoxide anion and 1,4-dinitrobenzene in DMSO to obtain a 76% product yield.[15] 4-Fluorobenzonitrile reacted with 2,6-di-isopropylphenyl TBDMS ether to afford a 98% yield of the new compound in Table 4, entry 6.

Table 4. S_NAr Reactions of Aryl Fluorides with Sterically Hindered TBDMS Ethers



Entry	Aryl Fluoride	TBDMS Ether	mol %/time	Product	Yield (%)[a,b]
1			10/3 h		92
2			10/3 h		95 (90)[c]

3			10/3 h		56
4			10/3 h		95 (77)[d]
5			10/3 h		92 (76)[e]
6			10/3 h		98

[a]Isolated yield (average of two runs). [b]Yields in parenthesis are literature values. [d]See Ref. 17. [e]See Ref. 11c. [e]See Ref. 15.

In summary, we have demonstrated the utility of proazaphosphatrane **3** under the microwave conditions for synthesizing diaryl ethers from electron poor aryl fluorides and a variety of TBDMS-protected phenols, including sterically hindered ones. As in our previous work under the thermal conditions,[7] the reaction of 2,4-dinitrofluorobenzene with 4-methoxyphenol also failed in our microwave protocol. This result is consistent with our earlier finding that the phosphorus of **3** can activate the silicon atom by weakening the Si–O bond.[8] Thermal[7] as well as microwave conditions require the use of an electron deficient aryl fluoride with a TBDMS aryl ether. Thus, the reaction of 4-fluoroanisole with 3-chlorophenyl TBDMS ether failed in both protocols.

General procedure: To a 10 mL microwave tube was charged 1.2 mmol of aryl TBDMS ether to which was added 1 mmol of aryl fluoride. Proazaphosphatrane **3** (from a stock solution prepared in the appropriate solvent) was then added to the tube under inert atmosphere. The tube was capped and placed in the microwave for the times given in Tables 1–3 and in entries 1–3 in Table 4, after which the solvent was removed in vacuo to produce the crude product that was purified by column chromatography (0–10% EtOAc/hexanes).

Acknowledgment

We thank the SQM Corporation for support of this work.

Supporting Information

Supplementary data (complete experimental procedures and characterizational data for all compounds.) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.03.089. This is also available in the appendix A in this thesis.

References and Notes

1. (a) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400; (b) Pantane, M. A.; Zhou, J.; Boger, D. L. *J. Am. Chem. Soc.* **1994**, *116*, 8544; (c) Boddy, C. N. C.; Nicolaou, K. C. *J. Am. Chem. Soc.* **2002**, *124*, 10451; (d) Crowley, B. M.; Mori, Y.; McComas, C. C.; Tang, D.; Boger, D. L. *J. Am. Chem. Soc.* **2004**, *126*, 4310; (e) Deng, H.; Jung, J.; Liu, T.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 9032.

2. Parker, A. J. *Chem. Rev.* **1969**, *69*, 1.

3. (a) Sawyer, J. S. *Tetrahedron* **2000**, *56*, 5045; (b) Wipf, P.; Lynch, S. M. *Org. Lett.* **2003**, *5*, 1155; (c) Saitoh, T.; Ichikawa, J. *J. Am. Chem. Soc.* **2005**, *127*, 9696.

4. (a) Ullmann, F. *Chem. Ber.* **1904**, *37*, 853; (b) Thomas, A. W.; Ley, S. V. *Angew. Chem.,*

Int. Ed. **2003**, *42*, 5400; (c) Cristau, H.; Cellier, P. P.; Hamada, S.; Spindler, J.; Taillefer, M. *Org. Lett.* **2004**, *6*, 913; (d) Marcoux, J.; Doye, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 10539; (e) Ma, D.; Cai, Q. *Org. Lett.* **2003**, *5*, 3799.

5. (a) Mann, G.; Hartwig, J. F. *Tetrahedron Lett.* **1997**, *38*, 8005; (b) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369; (c) Mann, G.; Incarvito, C.; Rheingold, A. L.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 3224; (d) Anderson, K. W.; Ikawa, T.; Tundel, R. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 10694.

6. Ueno, M.; Hori, C.; Suzawa, K.; Ebisawa, M.; Kondo, Y. *Eur. J. Org. Chem.* **2005**, 1965.

7. Urgaonkar, S.; Verkade, J. G. *Org. Lett.* **2005**, *7*, 3319.

8. Yu, Z.; Verkade, J. G. *J. Org. Chem.* **2000**, *65*, 2065.

9. Kisanga, P. B.; Verkade, J. G. *J. Org. Chem.* **2000**, *65*, 5431.

10. Schwesinger, R.; Schlemper, H.; Hasenfratz, C.; Willaredt, J.; Dambacher, T.; Breuer, T.; Ottaway, C.; Fletchinger, M.; Boele, J.; Fritz, H.; Putzas, D.; Rotter, H. W.; Bordwell, F. G.; Statish, A. V.; Ji, G. Z.; Peters, E. M.; Peters, K.; von Schnering, H. G.; Walz, L. *Liebigs* **1996**, 1055.

11. For examples see: (a) D'Angelo, N. D.; Peterson, J. J.; Booker, S. K.; Fellows, I.; Dominguez, C.; Hungate, R.; Reider, P. J.; Kim, T. *Tetrahedron Lett.* **2006**, *47*, 5045; (b) Chauochi, M.; Loupy, A.; Marque, S.; Petit, A. *Eur. J. Org. Chem.* **2002**, 1278; (c) Li, F.; Meng, Q.; Chen, H.; Li, Z.; Wang, Q.; Tao, F. *Synthesis* **2005**, *8*, 1305; (d) Lipshutz, B. H.; Unger, J. B.; Taft, B. R. *Org. Lett.* **2007**, *9*, 1089; (e) Kumar, S.; Kapoor, M.; Surolia, N. Synth. Commun. 2004, 34, 413; (f) Rebeiro, G.; Khadilkar, B. M. *Synth. Commun.* **2003**, *33*, 1405.

12. Li, F.; Wang, Q.; Ding, Z.; Tao, F. *Org. Lett.* **2003**, *5*, 2169.

13. Laramay, M. A. H.; Verkade, J. G. *J. Am. Chem. Soc.* **1990**, *112*, 9421.

14. (a) Acevedo, O.; Jorgensen, W. L. *Org. Lett.* **2004**, *6*, 2881; (b) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*, 4th ed.; Plenum Publishing: New York, 2001.

15. (a) Sammes, P. G.; Thetford, D.; Voyle, M. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1373; (b) Sammes, P. G.; Thetford, D.; Voyle, M. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3229.

16. Yeom, C.; Kim, H. W.; Lee, S. Y.; Kim, B. M. *Synlett* **2007**, *1*, 146.

17. Lee, J. C.; Choi, J.; Lee, J. S. *Bull. Korean Chem. Soc.* **2004**, *25*, 1117.

18. Lee, K.; Jung, J. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1799.

CHAPTER 3: A NEW ELECTRON RICH PROAZAPHOSPHATRANE FOR ISOCYANATE TRIMERIZATION TO ISOCYANURATES

A paper submitted to the *Journal of Organic Chemistry*

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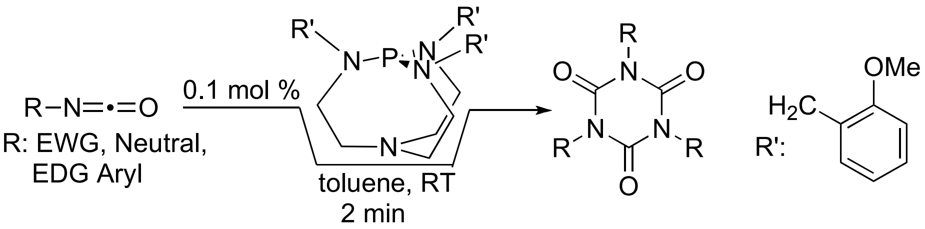
Abstract

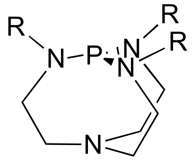


The synthesis and characterization of the new electron rich, sterically hindered proazaphosphatrane shown above (R' = *o*-methoxybenzyl) is described herein. This proazaphosphatrane catalyzes the cyclotrimerization of a wide variety of isocyanates to isocyanurates under mild conditions with unprecedentedly fast reaction times, giving moderate to high product yields.

Submitted Manuscript

Isocyanurates (perhydro-1,3,5-triazine-2,4,6-triones), typically produced by cyclotrimerizing isocyanates, enhance the physical properties of polyurethanes and coating materials.[1] Incorporation of isocyanurates into the framework of polyurethanes confers enhanced flame retardation and filming characteristics on these polymers, and property enhancements of commercial products made with polymeric isocyanurates include increased thermal and chemical resistance.[2] Isocyanurates are also employed in the preparation of copolymer resins whose requirements include water-resistance, transparency, and impact resistance,[3] and a novel optically active isocyanurate has been used for chiral discrimination of enantiomeric amino acid units.[4] Selective bonding of chloride anions via a *p*-nitrophenylsulfonamide group connected to an isocyanurate by an ethylene moiety has been reported,[5] and low-toxicity drug delivery has been achieved by tethering drug molecules to an isocyanurate backbone via an amide linker for facilitating subsequent release.[6] Triaryl isocyanurates are employed as activators in the continuous anionic copolymerization of ε-caprolactam to nylon-6,[7] and triallyl isocyanurates are useful in the preparation of flame-retardant laminating materials for electrical devices.[1]

The commercial importance of isocyanurates has generated numerous efforts aimed at the development of more effective methods for cyclotrimerizing isocyanates.[8] Problems with some of the known cyclotrimerization procedures include low catalyst activity, dimer formation, carbodiimide byproduct formation, lengthy reaction times, product separation difficulties, and the use of toxic solvents.[1,9] Examples of Lewis base cyclotrimerization catalysts that have been reported include phosphines,[3,10] N-heterocyclic carbenes,[1] amines,[11] NO,[12] fluoride anions,[13] and alkoxyalkenes.[14] Metal-containing cyclotrimerization catalysts include organotin,[15] organozinc halides and alkoxides,[16] copper and nickel halides,[12] and zirconium compounds,[17] and palladium(0) catalysts.[18]



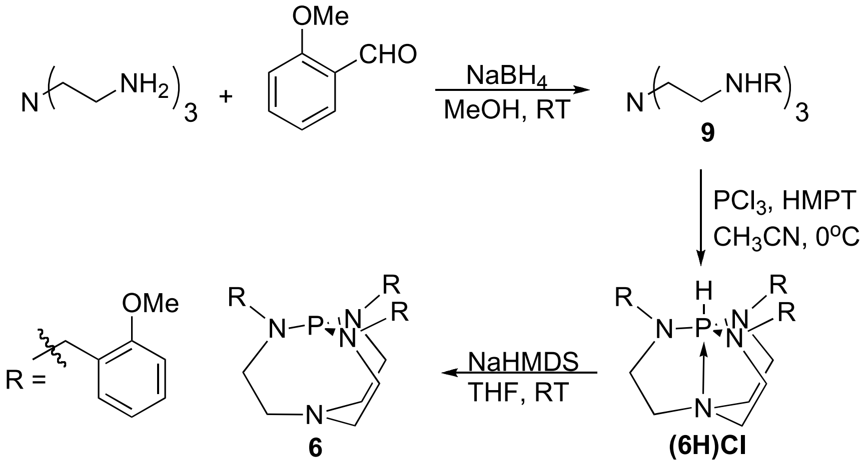
1: R = Me
2: R = *i*-Pr
3: R = *i*-Bu
4: R = Piv
5: R = Bn
6: R = 2-OMeBn
7: R = 2,4-DiOMeBn
8: R = 2,4,6-TriOMeBn

Proazaphosphatranes such as **1-5** are strong nonionic bases owing to transannulation of the basal nitrogen to the phosphorus atom upon its protonation, and to the donation of electron density from all three of the P-N nitrogens.[19] In terms of low catalyst loading, fast reaction times, ease of product purification, and optional use of a nontoxic solvent such as toluene, proazaphosphatranes have thus far been shown to be the most effective catalysts so far reported for the cyclotrimerization of isocyanates.[10]

Previously, we showed that with no attempt at temperature control of the reaction, proazaphosphatrane **1** at 0.3 mole % loading promoted the exothermic cyclotrimerization of phenyl isocyanate to the corresponding isocyanurate in benzene to give a product yield of 99% in 3 minutes[10a] and that at a loading of 0.39 mole %, **2** catalyzes this reaction under the same conditions in 1 minute in 97% isolated product yield.[10b] The basicity (pKa) of the phosphorus appears to increase as electron induction of the alkyl substituent on the P-N nitrogens increases from **1** to **2**, but this trend in pKa values is apparently reversed in the series **2** to **5** (Table 1). Thus the size increase in the alkyl substituents on these proazaphosphatranes may be interfering with the bonding of the apical proton and perhaps also with nucleophilic attack of phosphorus on an isocyanate carbon. Proazaphosphatrane **5** is less basic than **3**[20] presumably due to the electron withdrawing nature of the phenyl rings. As expected, the presence of electron donating groups on these rings in **6** to **8** (whose syntheses we report here) increases the pKa of these compounds. Here we report the pKa values of **5** to **8** in acetonitrile (Table 1) and the use of **6** as a superior catalyst for the cyclotrimerization of isocyanates to isocyanurates.

Following a known procedure,[20] **6** was synthesized in three steps in 61% overall yield (Scheme 1). This procedure was modified, however, by using NaHMDS for the deprotonation step instead of K-O^{t}Bu has the advantage of effecting full rather than partial conversion to the desired deprotonated product. The syntheses of proazaphosphatranes **7** and **8** were carried out analogously. The molecular structure of **5** (determined by X-ray means and depicted in Figure 2) confirms its formulation as proposed in Scheme 1. Following a procedure we developed earlier[21] for determining pKa values in acetonitrile of proazaphosphatranes, these values in the same solvent are shown for the new proazaphosphatranes **6**, **7**, and **8** in Table 1.

Scheme 1. Synthesis of Proazaphosphatrane **6**



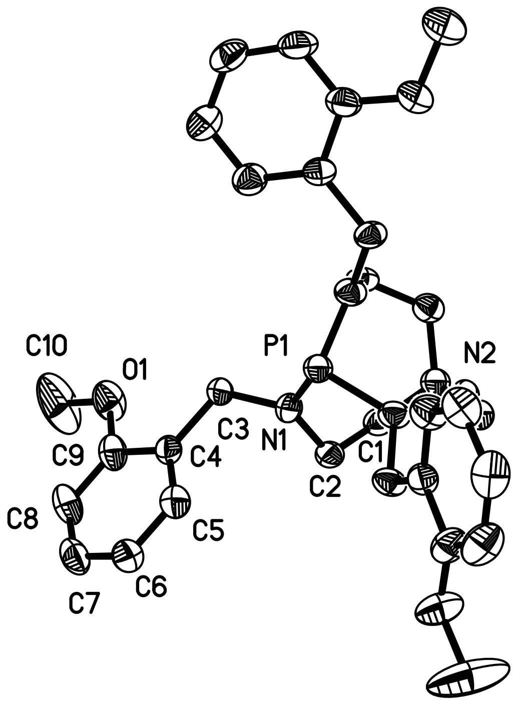
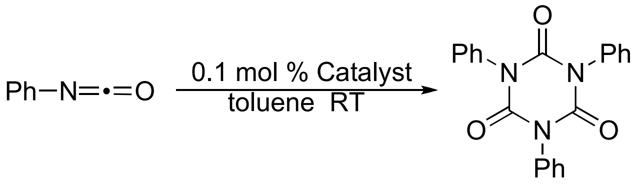


Figure 1. Computer drawing of the molecular structure of **6** at a 50% probability level. Hydrogen atoms are omitted for clarity.

For determining the catalytic activity of proazaphosphatrane **6** for isocyanate cyclotrimerization relative to analogues **1-5**, 0.1 mole % of catalyst in toluene was used to cyclotrimerize phenyl isocyanate in a room temperature water bath (Table 1). As shown in this table, excellent yields of product were obtained for **1-8** in short times in these exothermic reactions. There does not seem to be any straightforward correlation of reaction times with steric bulk or electron inductive effects from the P-N nitrogen alkyl substituents in **1-4**.

There is an increasing trend in pKa values from **6** to **8**, suggesting that steric crowding of an axial proton by the increasing number of methoxy groups is not occurring. In fact, axial proton stabilization by hydrogen bonding via six-membered ring chelation by the oxygens of three *o*-methoxy groups can be envisioned, resulting in an increased pK_a value.

Table 1. Comparison of Catalytic Activity of Various Lewis Bases for the Cyclotrimerization of Phenyl Isocyanate[a]



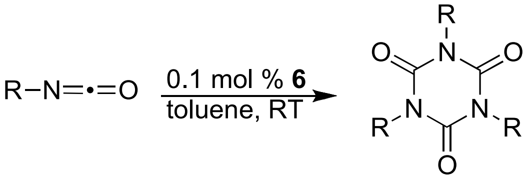
10

Entry	Cmpd	R	pKa	Time[c]	Yield (%)[d]
1	**5**	Bn	31.60	169	97
2	**4**	Piv	32.84[b]	135	97
3	**1**	Me	32.90[b]	121	95
4	**3**	^{i}Bu	33.53[b]	117	99
5	**2**	^{i}Pr	33.63[b]	110	97
6	**6**	2-OMeBn	33.70	96	99
7	**7**	2,4-DiOMeBn	34.16	92	98
8	**8**	2,4,6-TriOMeBn	34.25	84	96
9	$P(NMe)_2$			5 d	4[e,f]
10	P^tBu_3			24 h	2[f]
11	NEt_3			5 d	3[f]

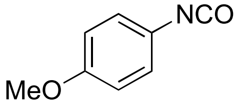
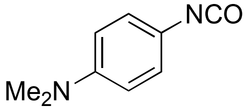
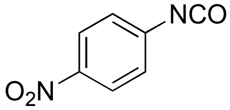
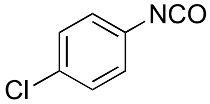
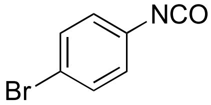
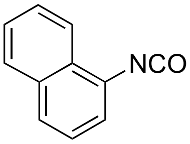
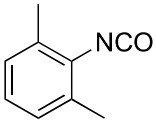
[a]Reaction conditions: 15 mmol of phenyl isocyanate, 2 mL toluene, RT. [b]Ref 21. [c]Seconds except were noted. [d]Average of three runs. [e]Heated to 70 °C. [f]1 mole % promoter used.

Tri-*tert*-butylphosphine used in our protocol met with poor results in which only a 2% yield of the desired product with a catalyst loading of 1 mole % (Table 1) was achieved after 24 h. Hexamethylphosphorous triamide (HMPT) and triethylamine were also used as catalysts (Table 1) but despite heating the HMPT reaction at 70 °C for 5 days, only 4% of the desired product was observed, and the use of triethylamine led to only 3% of the desired product. The contrasting catalyst performances of proazaphosphatranes **1**-**4**, for example, compared with HMPT demonstrate the advantageous stereoelectronic features[19a] of the proazaphosphatrane framework for catalytic purposes.

Table 2. Substrate Scope of Aryl Isocyanates



11-17

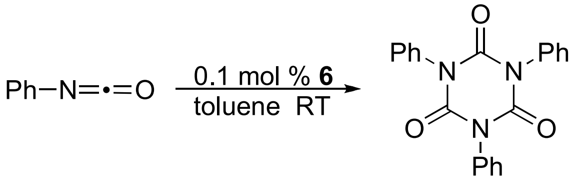
Entry	Isocyanate	Time	Product	Yield (%)[a,b]
1		7 min	**11**	96 (Lit: 56-96)
2		6 min	**12**	97
3		5 min	**13**	93 (Lit: 85-96)
4		5 min	**14**	91 (Lit: 78-99)
5		5 min	**15**	95
6		6 min	**16**	94 (Lit: 20-91)
7		30 min	**17**	53

[a]Reaction conditions: 15 mmol of isocyanate, 0.1 mole % proazaphosphatrane **6**, 2 mL toluene, RT. [b]Average of two runs.

With these results in hand, the scope of cyclotrimerization using a variety of isocyanates was explored as shown in Table 2. These reactions were carried out with 0.1 mole % of proazaphosphatrane **6** as the promoter in toluene at room temperature. The electron rich aryl isocyanate 4-methoxyphenylisocyante was trimerized in seven minutes in 96% isolated yield (Table 2, entry 1). Such electron rich substrates typically show low reactivity towards cyclotrimerization using other catalyst systems.[14] 4-Dimethylphenylisocyanate was similarly cyclotrimerized, providing a 97% isolated yield of a new isocyanurate (Table 2, entry 2) in 6 minutes. Electron deficient 4-nitrophenylisocyanate was cyclotrimerized in five minutes in 93% yield (entry 3). Isocyanates such as 4-chlorophenylisocyanate and 4-bromophenylisocyanate also cyclotrimerized in low reaction times giving 91% and 95% isolated yields of product, respectively (Table 2, entries 4 and 5). Our protocol is also effective for sterically hindered isocyanates such as 1-naphthylisocyanate that provided a 94% isolated product yield (entry 6). In the presence of catalyst **6**, sterically bulky 2,6-dimethylphenylisocyanate required 30 minutes to cyclotrimerize in 53% isolated product yield (Table 2, entry 7).

Previously, we proposed a mechanism in which a proazaphosphatrane attacks the carbon atom on phenyl isocyanate producing an anionic charge on the isocyanate nitrogen and a cationic charge on phosphorus. The anionic site then attacks a second phenyl isocyanate molecule to generate an analogous zwitterion which similarly attacks a third isocyanate. Then follows cyclotrimerization to form product and regenerated catalyst.[10b] In the present work we also demonstrate that the catalyst is indeed regenerated and can be re-used. Using 0.1 mole % of proazaphosphatrane **6** in 5 mL of toluene for the cyclotrimerization of phenyl isocyanate, the reaction was complete in 2 minutes and a white solid was formed (Table 3, entry 1). The resulting solution was filtered under inert atmosphere and the toluene filtrate (which contained only **6** was subjected to a second cyclotrimerization cycle. Pleasingly, the reaction completed in minutes with a 97% isolated yield of the phenyl isocyanurate (Table 3, entry 2). The proazaphosphatrane could then be recycled up to 3 more times in which the phenyl isocyanurate was isolated in high yields, but with longer reaction times (Table 3, entries 3-5). We believe that adventitious moisture present in the reaction mixture restricts the number of catalytic cycles of **6**.

Table 3. Recyclability of Proazaphosphatrane **6**



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Entry	Cycle	Time	Yield (%)[a,b]
1	**1**	2 min	99
2	**2**	2 min	97
3	**3**	3.5 min	98
4	**4**	8 min	98
5	**5**	15 min	95

[a] Reaction conditions: 15 mmol of phenyl isocyanate, 0.1 mole % proazaphosphatrane **6**, 5 mL toluene, RT. [b] Average of two runs.

By performing the above trimerization with 1 mole % of proazaphosphatrane **6** under the same recycling conditions, we observed a small peak in the ^{31}P NMR forming at -10 ppm in the filtrate corresponding to the phosphorus peak of **6**H$^+$ cation as well as the original +128 ppm peak corresponding to free **6**. Subsequent reaction recycles reveal that the -10 ppm ^{31}P NMR peak grows in intensity. This could be due to adventitious moisture. Attempts to remove the moisture source by distilling phenyl isocyanate onto activated molecular sieves and by using dry solvents under Schlenk techniques did not help. More rigorous experiments are underway to eliminate the moisture problem.

In conclusion, we have demonstrated that the new proazaphosphatrane **6** is a superior catalyst for the synthesis of isocyanurates from a wide variety of aryl isocyanates. We have also shown that proazaphosphatrane **6** can be recycled up to 5 times with high product yields but with successively slower reaction times. Further exploration of catalytic applications of **6** are underway.

Experimental Section

Synthesis of Compound 9. To 1.0 equivalent of freshly distilled tris(2-aminoethyl)amine in 100 mL MeOH was added (3.1 equiv) of *o*-anisaldehyde. The mixture was allowed to stir at room temperature overnight and then another 100 mL MeOH was added. The reaction mixture was cooled 0-5 ºC in an ice bath and $NaBH_4$ (1.5 equiv) was added slowly portion-wise over 1 h. The reaction mixture was stirred overnight and then the MeOH was removed by rotovap. The addition of 50 mL of water was followed by extraction with 3×100 mL toluene. The toluene extracts were combined and dried over Na_2SO_4 and then the toluene extract was filtered and removed on a rotovap. The crude dark yellow oil was purified by column chromatography (1% MeOH in CH_2Cl_2) to obtain 92% of the desired product as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.57-2.58 (d, 6H, J = 5.2 Hz), 2.62-2.63 (d, 6H, J = 4.8 Hz), 3.71 (s, 15H), 4.39 (br, 3H), 6.76-6.78 (d, 3H, J = 8 Hz), 6.80-6.84 (t, 3H, J = 14.8 Hz), and 7.15-7.27 ppm (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4, 130.1, 128.6, 126.3, 120.4, 110.1, 55.1, 53.5, 47.9, and 46.5 ppm. HRMS m/z 506.32700 (calc for $C_{30}H_{42}N_4O_3$, 506.32569).

Synthesis of Compound (6H)Cl. Dry CH_3CN (50 mL) was charged to a round bottom Schlenk flask and the flask was cooled to 0-5 ºC. HMPT ($P(NMe_2)_3$, 10.05 g, 2.0 equiv) was added under an argon flow followed by slow addition of PCl_3 (4.19 g, 1 equiv) via syringe. After stirring the reaction mixture at 0-5 ºC for 15 minutes, **9** (46.53 g, 3.0 equiv) dissolved in 50 mL dry CH_3CN was added. The reaction mixture was stirred overnight at rt and then solvent was removed using rotary evaporator, leaving a sticky yellow solid. Addition of 5-10 mL THF to this solid precipitated a free flowing solid and addition of ethyl ether (250 mL) to the THF to this mixture formed additional solids. Placing the reaction flask in a freezer for 3 days formed more solids. Filtration of the solids followed by drying on a vacuum line produced a free flowing light yellow powder (85% isolated yield). ^{1}H NMR (400 MHz, CD_3CN): δ = 3.04-3.10 (m, 6H), 3.20-3.25 (m, 6H), 3.76 (s, 9H), 4.07-4.11 (d, 6H, *J* = 16.8 Hz), 5.09-6.37 (d, 1H, *J* = 509.2 Hz), 6.9-6.95 (m, 6H), 7.16-7.18(d, 3H, *J* = 7.2 Hz), and 7.25-7.29 ppm (t, 3H, *J* = 15.6 Hz). ^{13}C NMR (400 MHz, CD_3CN): δ = 125.4, 129.7, 129.5, 127.0, 121.3, 118.3, 111.6, 56.0, 47.9, 46.8, and 40.0 ppm. ^{31}P NMR (168 MHz, CD_3CN) δ = -9.97 ppm.

Synthesis of Compound 6. To a 25 mL round bottom flask containing compound **(6H)Cl** (44.54 g, 1 equiv), was added 150 mL of THF followed by stirring for 10 min. NaHMDS (28.6 g, 2 equiv) was added to the slurry and then the reaction mixture was stirred overnight. The THF was then evaporated under inert atmosphere and then ether (100 mL) was added to extract the proazaphosphatrane. After filtration of the extract, the ether was evaporated under reduced pressure and 10 mL of toluene was added followed by 40 mL of pentane resulting in precipitation of **6**. Evaporation of the solvent under reduced pressure left 30.46 g of **6** (73% isolated yield). Crystals suitable for X-ray analysis were obtained by placing a concentrated solution of **6** in acetonitrile in a freezer for 2 days. ^{1}H NMR (400 MHz, C_6D_6): δ = 2.69-2.70 (m, 6H), 2.86 (br, 6H), 3.35 (s, 9H), 4.52-4.54 (d, 6H, *J* = 10 Hz), 6.57-6.59 (d, 3H, *J* = 8 Hz), 6.93-6.97 (t, 3H, *J* = 14.8 Hz), 7.11-7.16 (t, 3H, *J* = 14 Hz), and 7.65-7.67 (d, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, C_6D_6): δ = 158.3, 130.2 (d, *J* = 5.7 Hz), 130.0, 128.1, 55.1, 51.9, 48.0 (d, $J = 41.1$ Hz), and 46.8 (d, $J = 6.6$ Hz). ^{31}P NMR (186 MHz, C_6D_6): $\delta = 127.90$ ppm. HRMS m/z 534.27714 (calc for $C_{30}H_{39}N_4O_3P$, 534.27596).

General Procedure for the Synthesis of Isocyanurates using 6. To a 100 mL round bottom flask with a side arm, 8 mg (0.1 mole %) of proazaphosphatrane **6** was added in a glove box. The flask was capped with a rubber septum and then it was taken out of the glove box and charged with 2 mL of toluene. The isocyanate (1.78 g, 15 mmol) was added and stirred for the allotted time until the isocyanurate had precipitated. The solids were washed with 5 mL toluene to extract any impurities and the mixture was then filtered. The solids were dried under vacuum and weighed to determine the yield.

Procedure for Recycling Proazaphosphatrane 6. To a 100 mL round bottom flask with a side arm, 8 mg (0.1 mole %) of proazaphosphatrane **6** was added in a glove box. The flask was capped with a rubber septum and then it was taken out of the glove box and charged with 2 mL of toluene. Phenyl isocyanate (1.78 g, 15 mmol) was added to the flask under an argon flow and then the mixture was stirred for the allotted time. After completion of the reaction, 5 mL of toluene was added followed by stirring for an additional 30 minutes after which the solution was filtered under an inert atmosphere through a glass fritted filter tube, and then the solution was dried under reduced pressure. This procedure was repeated four more times.

Acknowledgement

The authors would like to thank the National Science Foundation for supporting this work through a grant (0750463).

Supporting Information

References to known compounds, copies of ^{1}H and ^{13}C NMR spectra for all isocyanurate products, data for unknown compounds, and ^{31}P NMR spectra for proazaphosphatranes **6**, **7**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org. This is also available in Appendix B of this thesis.

References

1. Duong, H. A.; Cross, M. J.; Louie, J. *Org. Lett.* **2004**, *6*, 4647.

2. (a) Wirpsza, Z. *Polyurethanes: Chemistry, Technology and Application*, Ellis Horwood: London, 1993. (b) Zitinkina, A. K.; Sibanova, N. A.; Tarakanov, O. G. Russ. Chem. ReV. **1985**, *54*, 1866. (c) Nawata, T.; Kresta, J. E.; Frisch, K. C. *J. Cell. Plast.* **1975**, 267. (d) Nicholas, L.; Gmitter, G. R. *J. Cell. Plast.* **1965**, 85.

3. Tang, J.; Mohan, T.; Verkade; J. G. *J. Org. Chem.* **1994**, *59*, 4931.

4. Sugimoto, H.; Yamane, Y.; Inoue, S. *Tetrahedron: Asymmetry* **2000**, *11*, 2067.

5. Hettche, F.; Hoffman, R. W. *New J. Chem.* **2003**, *27*, 172.

6. Murray, A. P.; Miller, M. J. *J. Org. Chem.* **2003**, *68*, 191.

7. (a) Bukac, Z.; Sebenda, J. *Chem. Prum.* **1985**, *35*, 361. (b) Horsky, J.; Kubanek, U.; Marick, J.; Kralicek, J. *Chem. Prum.* **1982**, *32*, 599.

8. For additional information regarding isocyanate trimerization, see Supporting Information

9. (a) Wegener, G.; Brandt, M.; Duda, L.; Hofmann, J.; Klesczewski, B.; Koch, D.; Kumpf, R.-J.; Orzesek, H.; Pirkl, H.-G.; Six, C.; Steinlein, C.; Weisbeck, M. *Appl. Cat. A: Gen.* **2001**, *221*, 303. (b) Silva, A. L.; Bordado, J. C. *Catal. Rev.* **2004**, *46*, 31.

10. (a) Tang, J.; Verkade, J. G. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 896. (b) Liu, X.; Bai, Y.; Verkade, J. G. *J. Organomet Chem.* **1999**, *582*, 16.

11. (a) Tagachi, Y.; Shibaya, I.; Yasumoto, Y.; Ynoemoto, K. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3486. (b) Moghaddam, F. M.; Dekamin, M. G.; Koozehgari, G. R. *Letters in Organic Chemistry* **2005**, *2*, 734.

12. Villa, J. F.; Powell, H. B. *Synth. React. Metal-Org. Chem.* **1976**, *6*, 59.

13. Nambu, Y.; Endo, T. *J. Org. Chem.* **1993**, *58*, 1932.

14. Mizuya, J.; Yokozawa, T.; Endo, T. *J. Polym. Sci., Polym. Chem.***1991**, *29*, 1544.

15. (a) Bloodworth, A. J.; Davies, A. G. *J. Chem. Soc.* **1965**, 6858. (b) Foley, S. R.; Yap, G. P. A.; Richeson, D. S. *Organometallics* **1999**, *18*, 4700.

16. Noltes, J. G.; Boersma, J. *J. Organomet. Chem.* **1967**, *7*, 6.

17. Li, Y.; Matsumura, H.; Yamanaka, M.; Takahashi, T. *Tetrahedron* **2004**, *60*, 1393.

18. Paul, F.; Moulin, S.; Piechaczyk, O.; Le Floch, P.; Osborn, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 7294.

19. (a) Verkade, J. G. in, “$P(RNCH_2CH_2)_3N$: very strong non-ionic bases useful in organic synthesis. New Aspects of Phosphorus Chemistry II”, J. P. Majoral, Editor, *Topics in Current Chemistry* **2003,** *223,* 1 – 44. (b) Verkade, J.G.; Kisanga, P. “Proazaphosphatranes: A Synthesis Methodology Trip From Their Discovery to Vitamin A”, *Tetrahedron* **2003**, *59*, 7819-7858. (c) Verkade, J. G.; Kisanga, P. B. “Recent Applications of Proazaphosphatranes in Organic Synthesis”, *Aldrichimica Acta* **2004**, *37*, 3-14.

20. Laramay, M. A. H.; Verkade, J. G. *J. Am. Chem. Soc.* **1990**, *112*, 9421.

21. Kisanga, P. B.; Verkade, J. G.; Schwesinger, R. *J. Org. Chem.* **2000**, *65*, 5431.

CHAPTER 4. A TRICYCLIC ALUMINUM ALKOXIDE FOR ALDEHYDE TRIMETHYLSILYLCYANATION

A paper accepted by *Tetrahedron Letters*

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Abstract

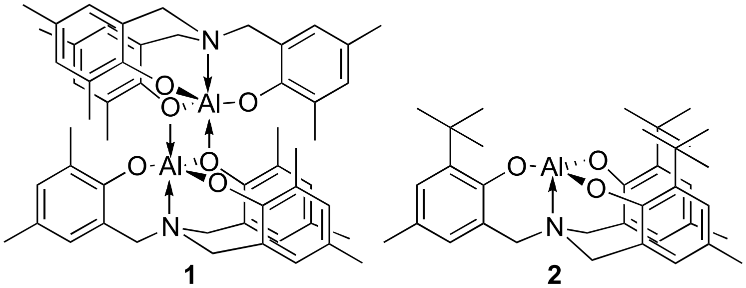
Trimethylsilylcyanation of aldehydes is efficiently accomplished with a low concentration of catalyst **1** under mild conditions in acetonitrile. This protocol tolerates a variety of electron rich, neutral, and deficient aryl, heterocyclic, and alkyl aldehydes. At the end of the reaction, catalyst **1** precipitates from solution, allowing it to be recycled three times.

Submitted Manuscript

Cyanohydrins and cyanohydrin trialkylsilylethers are intermediates in the synthesis of natural products such as L-Biotin[1] and 20S-Amoptothecin.[2] Because of the utility of such intermediates, investigations aimed at the development of improved Lewis acid and Lewis base catalysts for the reaction of trimethylsilylcyanide with aldehydes and ketones have been extensively reported. Lewis acid catalysts include a titanium isopropoxide Schiff base complex,[3] titanium complexes,[4] aluminum complexes,[5] aluminum compounds bearing chiral ligands,[6] complexes of lanthanide(III),[7] samarium(III) chloride,[8] scandium(III) triflate,[9] indium(III) bromide,[10] and potassium-exchanged zirconium hydrogen phosphate.[11] Useful Lewis base catalysts include proazaphosphatranes,[12] cesium fluoride,[13] *N*-heterocyclic carbenes,[14] and trialkylamines.[15] The aforementioned monofunctional catalysts generally lead to high product yields from both aldehydes and ketones. In addition, chiral Lewis acid – Lewis base bifunctional catalysts have been reported that give rise to chirally induced reactions of trimethylsilylcyanide with aldehydes and ketones, providing products in moderate to excellent enantiomeric excesses.[16] Typically such bifunctional chiral catalysts contain a Lewis basic phosphine, phosphine oxide, or a sulfur group; and a Lewis acidic aluminum, titanium, or zirconium functionality. Zerovalent metals such as palladium and platinum have also been shown to promote the trimethylsilylcyanation of aldehydes and ketones.[17]

Lewis acid trimethylsilylcyanation catalysts are frequently aluminum species owing to the relatively low cost and toxicity of this metal. A drawback, however, is the frequent requirement of high mole percentages and even molar excesses of such catalysts.[5,6]

Figure 1. Alumatranes



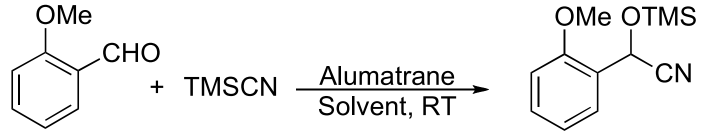
1 2

In 2006 we reported the synthesis of a novel tricyclic aluminum alkoxide (alumatrane dimer **1** in Figure 1**)** and demonstrated its ability to form monomeric alumatranes in the presence of an oxygen or nitrogen donor.[18] In that paper it was also shown that alumatrane **1** in the presence of benzaldehyde and trimethylsilylcyanide in toluene at room temperature formed the corresponding cyanohydrin trialkylsilylether in quantitative yield.[18] Recently we described the first example of a trivalent alumatrane (**2** in Figure 1) wherein the aluminum center possesses an empty (axial) coordination site.[19]

Herein we report the utility of alumatrane dimer **1** as a Lewis acid, low-concentration trimethylsilylcyanation catalyst for aryl, alkyl and heteroaryl aldehydes. Initially, we determined the minimum concentration of **1** required for completion of such a reaction under mild conditions. Because of the unstable nature of the cyanohydrins, all products were isolated as their trimethylsilyl ethers.

As shown in Table 1, entries 1 and 2, only 72 and 49% yields, respectively, of the desired products were achieved in toluene in the presence of 5 and 2.5 mole % of dimer **1**. For this type of reaction, a polar solvent is generally needed to obtain high yields with low mole percentages of catalyst.[3,4,5b,6,16] The reaction in Table 1 failed in THF, however. As we have previously shown, dimer **1** is symmetrically cleaved in THF to form the corresponding monomeric alumatrane-THF adduct in high yield.[18]

Table 1. Optimization Study

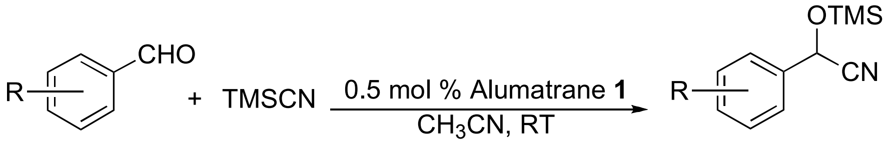


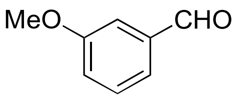
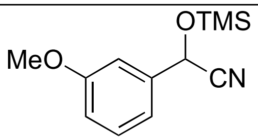
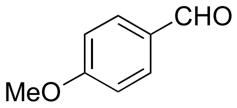
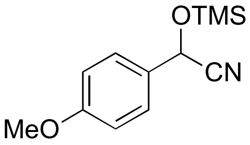
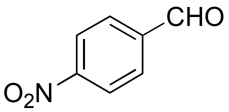
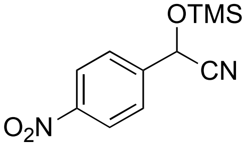
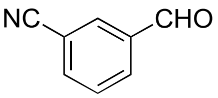
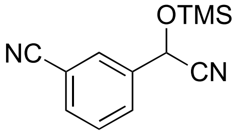
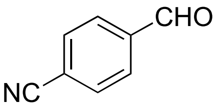
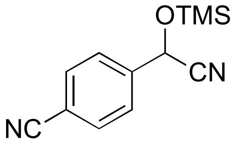
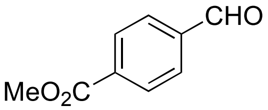
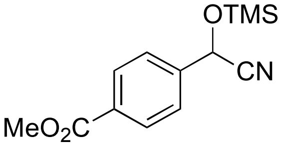
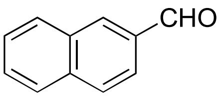
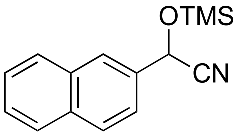
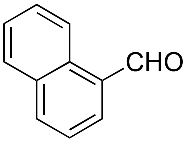
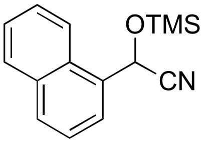
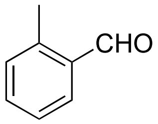
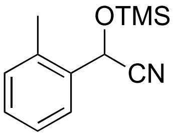
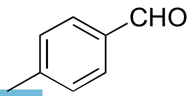
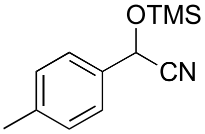
Entry	Alumatrane[a] (mole %)	Solvent	Yield (%)[b]
1	5	toluene	72
2	2.5	toluene	49
3	5	CH_3CN	98
4	2.5	CH_3CN	96
5	0.5	CH_3CN	94
6	0.5	CH_3CN	67[b]
7	none	CH_3CN	24

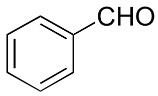
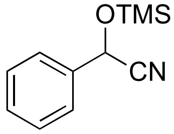
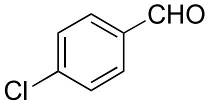
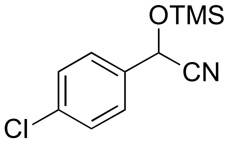
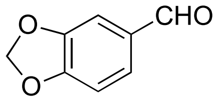
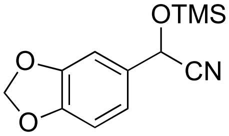
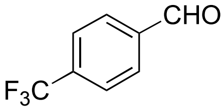
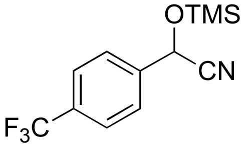
[a] Alumatrane **1** was present in all cases except where noted otherwise. [b] Reaction conditions: 2 mmol *o*-anisaldehyde, 3.5 mmol TMSCN, 5 mL solvent, 12 h, RT. [c] Average of two runs. [d] Alumatrane **2** was used at 70 °C

Compound **1** is quite insoluble in acetonitrile. We have observed that adduct formation of **1** is characterized by splitting of the dimer and increased solubility of the adduct in organic solvents as in the case of the benzaldehyde adduct in acetonitrile or toluene, and of the THF adduct in pentane.[18] A ^{13}C NMR spectrum of the supernatant liquid above a suspension of **1** in acetonitrile that had been stirred for two days at room temperature revealed no new nitrile carbon peak as would be expected for the acetonitrile adduct, assuming acetonitrile exchange was slow on the NMR time scale. The reaction between *o*-anisaldehyde and trimethylsilylcyanide in the presence of 5 mole % of dimer **1** in acetonitrile gave a nearly quantitative yield of desired product (Table 1, entry 3) and when 2.5 mole % of alumatrane dimer **1** was employed, the yield decreased only slightly to 96% (Table 1, entry 4). Even at 0.5 mole % catalyst loading, the product yield was very high (Table 1, entry 5). The highest reported yield of this trimethylsilylcyanohydrin is 99% which was achieved in the presence of 2.8 mol % of a silica supported imadazolium hydroxide in methylene chloride in 30 minutes.[20] Interestingly, despite the monomeric nature of **2** (which unlike **1** does not require dissociation to act as a catalyst) 1 mole % of **2** provided only a 67% yield of product in provided by the three *t*-Bu groups in **2**. In contrast to alumatrane **1**, **2** is soluble in a wide range of solvents including toluene, acetonitrile, and tetrahydrofuran. It may be noted that the reaction of *o*-anisaldehyde with trimethylsilylcyanide does proceed in acetonitrile in the absence of catalyst, but the product yield is only 24%. For the remainder of this report, 0.5 mole % of dimer **1** was used unless noted otherwise.

Table 2. Trimethylsilylcyanation of Aryl Aldehydes



Entry	Aldehyde	Product	Yield (%)[a,b]
1			98 (Lit: 78-100)
2			94 (Lit: 33-100)
3			94 (Lit: 22-98)
4			89
5			93 (Lit: 70-72)
6			92 (Lit: 90)
7			91 (Lit: 78-100)
8			81 (Lit: 76-98)
9			89 (Lit: 80-100)
10			85 (Lit: 62-100)

11			92 (Lit: 16-100)
12			45 82[c] (Lit: 63-100)
13			30 83[c] (Lit: 55-99)
14			52 96[c] (Lit: 95-100)

[a]Reaction conditions: 2 mmol aldehyde, 3.5 mmol TMSCN, 5 mL CH_3CN, RT. 0.5 mol % **1** was used in all cases except where noted otherwise. [b]Average of two runs.

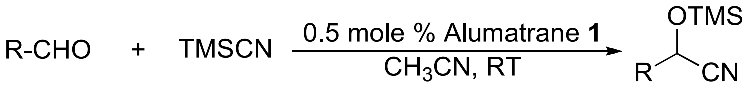
The wide variety of aryl aldehydes amenable to our protocol (Table 2) demonstrates the excellent substrate functional group tolerance of dimer **1**. The coupling of the electron donating *m*- and *p*-anisaldehyde with trimethylsilylcyanide proceeded smoothly to achieve 98% and 94% isolated yields of the desired products, respectively (Table 2, entries 1 and 2). Electron deficient aldehydes are also effective in our protocol. Thus, 4-nitrobenzaldehyde in the presence of trimethylsilylcyanide gave the corresponding cyanohydrin trimethylsilylether in 94% yield (Table 2, entry 3). Furthermore, 3- and 4-cyanobenzaldehyde gave 89% and 93% yields of the corresponding desired products (Table 2, entries 4 and 5, respectively). In a previous literature report, the reaction of 4-cyanobenzaldehyde with trimethylsilylcyanide gave a product yield of only 72% using 0.5 mole % of an ammonium salt of DBU in methylene chloride in which the DBU moiety acts as a base catalyst.[21] In the presence of methyl 4-formylbenzoate, trimethylsilylcyanide gave a 92% yield of the desired product (Table 2, entry 6). This result is consistent with the notion that dimer **1** prefers to form a carbonyl adduct with the aldehyde oxygen rather than with the ester oxygen. In the presence of methyl benzoate, no adduct formation with dimer **1** was detected by NMR spectroscopy (see Supporting Information).

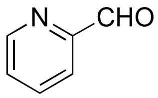
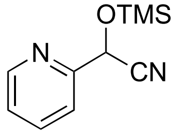
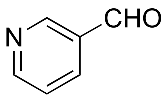
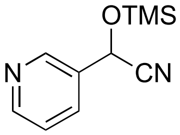
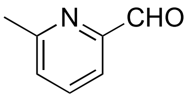
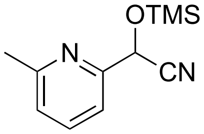
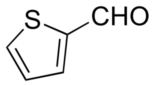
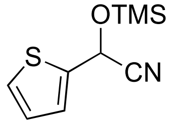
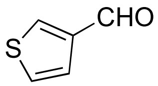
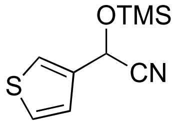
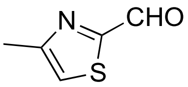
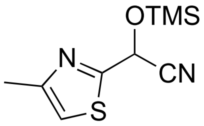
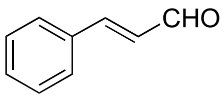
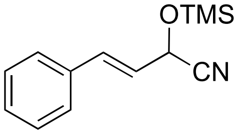
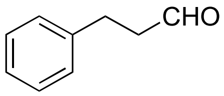
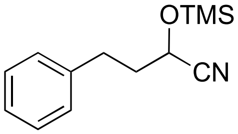
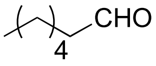
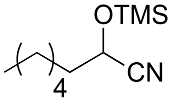
A variety of electron-neutral aryl aldehydes also worked well in our methodology. Thus, 2-naphthaldehyde reacted with trimethylsilylcyanide to produce 91% of the desired product (Table 2, entry 7). *p*-Tolualdehyde and benzaldehyde led to 85% and 92% yields, respectively, of their corresponding cyanohydrin trimethylsilylethers (Table 2, entries 10 and 11, respectively). Sterically hindered electron neutral aryl aldehydes, such as 1-naphthaldehyde and *o*-tolualdehyde, reacted smoothly to give 81% and 89% of their respective desired products (Table 2, entries 8 and 9, respectively).

With 4-chlorobenzaldehyde, a poor product yield of 45% was obtained when 0.5 mole % of dimeric **1** was employed in the presence of trimethylsilylcyanide. However, the use of 1.25 mole % of **1** afforded an 82% yield of the desired product (Table 2, entry 12). Similarly, 1.25 mole % of dimer **1** led to improved yields in the reactions of piperonal and α,α,α-trifluorotolualdehyde with trimethylsilylcyanide (Table 2, entries 13 and 14, respectively).

We also screened a variety of heterocyclic and alkyl aldehydes using catalyst **1** as shown in Table 3. Somewhat surprisingly, these reactions also proceeded well employing only 0.5 mole % of dimer **1**. Thus 2-pyridine-carboxaldehyde and 3-pyridine-carboxaldehyde afforded 91% and 86% yields of the desired products (Table 3, entries 1 and 2, respectively). The reaction between 6-methyl-2-pyridine-carboxaldehyde and trimethylsilylcyanide afforded the new product shown in Table 3, entry 3 in 94% isolated yield. 2-Thiophene- and 3-thiophenecarboxaldehyde also functioned well in our protocol, giving 90 and 77% yields of the corresponding products (Table 3, entries 4 and 5, respectively). It might have been expected that a thiophene-aluminum adduct would form, as was produced with tetrahydrofuran and **1**.[18] Using catalyst **1** in the reaction of 4-methyl-2-thiazolecarboxaldehyde with trimethylsilylcyanide, a new product was synthesized in 91% yield (Table 3, entry 6).

Table 3. Trimethylsilylcyanation of Hetero and Alkyl Aldehydes

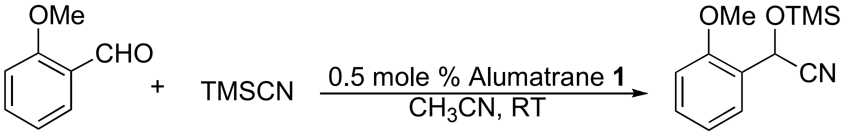


Entry	Aldehyde	Product	Yield (%)[a,b]
1			91 (Lit: 88-92)
2			86 (Lit: 90-99)
3			94
4			90 (Lit: 90-99)
5			77 (Lit: 82)
6			91
7			80 (Lit: 81-100)
8			85 (Lit: 81-100)
9			81 (Lit: 89-99)

[a]Reaction conditions: 2 mmol aldehyde, 3.5 mmol TMSCN, 5 mL CH_3CN, RT. [b]Average of two runs.

Alkyl aldehydes also provided corresponding cyanohydrin trialkylsilylethers in our procedure. When *trans*-cinnamaldehyde was used in the reaction, 80% of the desired product was obtained (Table 3, entry 7). Straight-chain alkyl aldehydes are also amenable to our approach, providing 85% and 81% of the desired products (Table 3, entries 8 and 9, respectively).

Table 4. Recyclability of Alumatrane Dimer **1**



Entry	Cycle	Time	Yield (%)[a,b]
1	1	2 h	94
2	2	3 h	93
3	3	7 h	90
4	4	10 h	85

[a]Reaction conditions: 2 mmol aldehyde, 3.5 mmol TMSCN, 5 mL CH_3CN, RT. [b]Average of two runs.

During our trimethylsilylcyanation reactions, a white precipitate consisting of the acetonitrile-insoluble dimer **1** was observed upon reaction completion. Pleasingly, the precipitated material in the reaction shown in Table 4 was successfully recycled three times, although the yield decreased significantly in the fourth cycle. The decrease in catalytic activity is attributable to the presence of adventitious moisture, mechanical loss of some of the 8.8 mg of **1** used, or the slight solubility of **1** in pentane and acetonitrile; or some combination of these factors.

Since all the products in Tables 2 and 3 possess a chiral carbon center, the issue of synthesizing a chiral alumatrane arises. Of the Lewis acid catalyst systems for carbonyl trimethylsilylcyanation published in the literature, those based on titanium complexes of chiral Schiff bases appear to be widely used[3,4] and since the first publication on such a catalyst by Oguni,[3c] more efficient chiral Schiff bases have been developed for this purpose.[3a,b,d] Literature reports of aluminum Lewis acid catalysts for carbonyl trimethylsilylcyanation[4,5,16] have also appeared. Thus Pu et al. developed a catalyst system in which 10 mol % of Me_2AlCl and 20 mol % of a chiral BINOL ligand in the presence of 40 mol % HMPA successfully converted aryl aldehydes to cyanohydrin trimethylsilylethers in moderate to high yields with enantioselectivities >90%.[5] Hoveda and co-workers reported asymmetric trimethylsilylcyanation of ketones using 1 mol % $Al(O^iPr)_3$ in the presence of 1 mol % of a peptide as an external ligand to obtain moderate to high yields of products with >80% enantioselectivities.[6a] An advantage of a chiral alumatrane (on which work is underway in our laboratories) is that no external ligand or base is required for catalyst function.

In summary, we have demonstrated the usefulness of low concentrations of alumatrane dimer **1** for the room-temperature trimethylsilylcyanation of aldehydes. Our protocol tolerates a variety of electron rich, neutral, and deficient aryl aldehydes; heterocyclic aldehydes; and alkyl aldehydes. Relative to the highest product yields recorded in the literature (see Supporting Information) two compounds were achieved in higher yield. Lower yields than the highest previously reported were obtained for nineteen compounds and of those, six were at or within 5%, four compounds were within 10%, four compounds were at or within 15%, and five compounds were within 20% of the highest yield reported. Three products are new.

As demonstrated in entries 12-14 in Table 2, product yields achieved by our methodology that poorly compete with maximum literature yields can be significantly enhanced with higher (but still catalytic) concentrations of **1.** We have also shown that the alumatrane can be recovered for recycling. Our alumatranes are the first aluminum catalysts for trimethylsilylcyanation that require no added ligand or base. Ketones did not trimethylsilylate under our conditions. Further explorations of the synthetic usefulness of alumatranes, including chiral ones, are in progress.

Acknowledgement

We gratefully thank the National Science Foundation for support of this research in the form of a grant (0750463).

Supporting Information

Complete experimental procedures and characterizational data for all known and unknown compounds are provided in the supplementary information. This is also available in appendix C of this thesis.

References

1. Yabu, K.; Masumoto, S.; Kanai, M.; Curran, D. P.; Shibasaki, M. *Tetrahedron Lett.* **2002**, *43,* 2923.

2. Masumoto, S.; Suzuki, M.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2002**, *43,* 8647.

3. (a) Gama, A.; Flores-Lopez, L. Z.; Aguirre, G.; Parra-Hake, M.; Somanathan, R.; Walsh, P. J. *Tetrahedron Asymmetry* **2002**, *13*, 149. (b) Rodriguez, B.; Pasto, M.; Jimeno, C.; Pericas, M. A. *Tetrahedron Asymmetry* **2006**, *17*, 151.

4. (a) Lee, P.; Chen, C. *Tetrahedron Asymmetry* **2005**, *16*, 2704. (b) Belda, O.; Duquesne, S.; Fischer, A.; Moberg, C. *Journal of Organometallic Chemistry* **2004**, *689*, 3750. (c) Khan, N. H.; Agrawal, S.; Kureshy, R.; Abdi, S. H. R.; Mayani, V. J.; Jasra, R. V. *Eur. J. Org. Chem.* **2006**, 3175.

5. (a) Ohno, H.; Hideaki, N.; Tanaka, K.; Mori, A.; Inoue, S. *J. Org. Chem.* **1992**, *57,* 6778. (b) Qin, Y.; Liu, L.; Pu, L. *Org. Lett.* **2005**, *7,* 2381.

6. Deng, H.; Isler, M. P.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2002**, *41,* 1009.

7. Mei, L. *Journal of Molecular Catalysis A: Chemical* **2005**, 227, 183.

8. Yang, W.; Fang, J. *J. Org. Chem.* **1998**, *63,* 1356.

9. Norsikian, S.; Holmes, I.; Lagasse, F.; Kagan, H. B. *Tetrahedron Lett.* **2002**, *43,* 5715.

10. Bandini, M.; Cozzi, P. G.; Garelli, A.; Melchiorre, P.; Unami-Ronchi, A. *Eur. J. Org. Chem.* **2002**, 3243.

11. Durini, M.; Epifan, F.; Marcotullio, M. C.; Rosati, O.; Rossi, M. *Synlett* **1999**, *3,* 315.

12. Fetterly, B. M.; Verkade, J. G. *Tetrahedron Lett.* **2005**, *46,* 8061.

13. Kim, S. S.; Song, D. H. *Letters in Organic Chemistry* **2004**, *1,* 264.

14. (a) Suzuki, Y.; Bakar, A.; Muramatsu, K.; Sato, M. *Tetrahedron* **2006**, *62,* 4227. (b) Song, J. J.; Gallou, F.; Reeves, J. T.; Tan, Z.; Yee, N. K.; Senanayake, C. H. *J. Org. Chem.* **2006**, *71*, 1273. (c) Fukuda, Y.; Maeda, Y.; Ishii, S.; Kondo, K.; Aoyama, T. *Synthesis* **2006**, 589.

15. Denmark, S. E.; Chung, W. *J. Org. Chem.* **2006**, *71,* 4002.

16. (a) Hamashima, Y.; Sawada, D.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc*. **1999**, *121,* 2641. (b) Hamashima, Y.; Sawada, D.; Nogami, H.; Kanai, M.; Shibasaki, M. *Tetrahedron* **2001**, *57,* 805-814.

17. Fossey, J. S.; Richards, C. J. *Tetrahedron Lett.* **2003**, *44,* 8773.

18. Su, W.; Kim, Y.; Ellern, A.; Guzei, I. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2006**, *128,* 13727.

19. Su, W.; Kobayashi, J.; Ellern, A.; Kawashima, T.; Verkade, J. G. *Inorg. Chem.* **2007**, *46*, 7953.

20. Yamaguchi, K.; Imago, T.; Ogasawara, Y.; Kasai, J.; Kotani, M.; Mizuno, N. *Adv. Synth. Catal.* **2006**, *348*, 1516.

21. Raj, V. P.; Suryavanshi, G.; Sudalai, A. *Tetrahedron Lett* **2007**, *48*, 7211.

CHAPTER 5: CATALYSIS OF MUKAIYAMA ALDOL REACTIONS BY A TRICYCLIC ALUMINUM ALKOXIDE LEWIS ACID

A paper published in the *Journal of Organic Chemistry* **2009**, *74*, 5417

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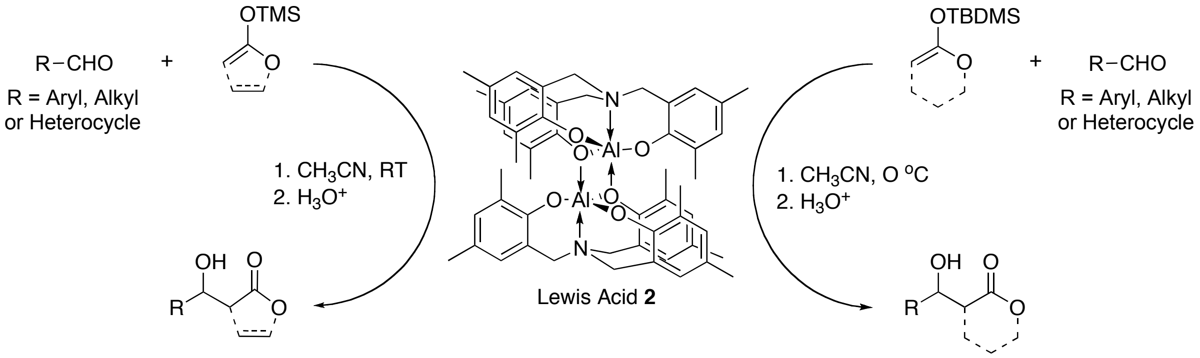
Abstract



The Mukayiama Aldol reaction of aldehydes is efficiently accomplished with a low concentration of the dimeric alumatrane catalyst **2** at mild or sub-ambient temperatures. Our protocol tolerates a wide variety of electron rich, neutral, and deficient aryl; alkyl; and heterocyclic aldehydes. A wide variety of enol silyl ethers are also tolerated. An intermediate which was isolated provides mechanistic information regarding the role of dimeric **2** in the Mukaiyama Aldol reaction. Experimental evidence is presented for the stronger Lewis acidity of **5** compared with F_3B.

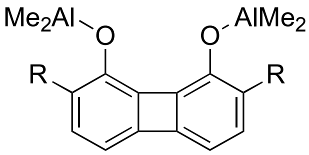
Introduction

Aldol reactions usually require electron deficient aldehydes and are often plagued by the formation of side products such as α,β-unsaturated esters. Despite these deficiencies, the Mukaiyama aldol reaction is one of the most versatile carbon-carbon bond forming reactions allowing access to synthetically challenging β-hydroxy carbonyl compounds.[1] Intensive efforts have been made to synthesize such compounds owing to the pivotal nature of the Mukaiyama aldol reaction in the synthesis of a variety of natural products.[2] Utilization of this transformation for the synthesis of β-hydroxy carbonyl compounds was a notable achievement attained through the development of the addition of a silyl enol ether to aldehydes and ketones. It may be noted that very few methodologies for catalytic aldol reactions of ketones have been developed compared with those for aldehydes.[3]

Because of the utility of β-hydroxy carbonyl compounds, many Lewis acid and Lewis base catalysts for their synthesis have been investigated. Lewis acids that activate the carbonyl moiety of an aldehyde or ketone in the Mukaiyama aldol reaction include bismuth(III) triflate,[2] lanthanum(III) bromide,[4] copper(I) fluoride,[5] $MgI_2 \bullet (OEt_2)_n$,[5] iron(II) chloride,[7] Me_3SiNTf_2,[8] and Zr(IV) compounds.[9] Common Lewis bases that activate the silicon atom of silyl enol ethers utilized in the Mukaiyama aldol reaction of aldehydes include N-heterocyclic carbenes,[10] 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU),[11] N-methylimidazole,[12] lithium benzylate,[13] and amines.[14] There are also reports describing Lewis acids that have been grafted onto polymer supports for recyclability in Mukaiyama aldol reactions of aldehydes.[15] Lewis basic ionic liquids have also been shown to facilitate the synthesis of β-hydroxy carbonyl products from aldehydes,[16] and there are a few reports in which photochemistry has been employed in the Mukaiyama aldol reaction of aldehydes (although with the formation of oxetene as a byproduct[3d, 17]).

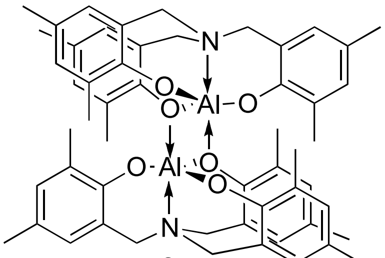
Recent studies have centered on enolate substrates that supply Mukaiyama aldol products similar to those provided by the use of enol substrates. In 2006, Knochel and co-workers developed an elegant route to β-hydroxy esters via a Reformatsky reaction involving organozinc reagents instead of silyl groups. Advantages of organozinc reagents include their functional group tolerance, their stability in various solvents, and the ease with which they are synthesized.[18] β-Hydroxy esters are also obtainable by selectively opening epoxides in the presence of a cobalt catalyst under an atmosphere of carbon monoxide in methanol.[19] Instead of trimethylsilyl enol ethers, Nakajima and co-workers used trichlorosilyl enol ethers in asymmetric aldol reactions carried out in the presence of a chiral phosphine oxide (*S*-BINAPO) to achieve high yields of the desired β-hydroxy esters with high functional group tolerance.[20] Scheeren and co-workers developed a method for synthesizing β-hydroxy esters from ketene acetals in the presence of 1 mole % of readily available inexpensive zinc chloride.[21] However, a drawback of this procedure is that ketene acetals are not commercially available and must be made from ortho esters in the presence of a sterically hindered aluminum alkoxide.[22]

Reports of the use of aluminum Lewis acids in the Mukaiyama aldol reaction are quite limited. Maruoka et al. developed a bidentate organoaluminum Lewis acid **1** (R = Me) which, at the one equivalent level, facilitated Mukaiyama aldol reactions in methylene chloride at low temperatures to produce high product yields.[23] Maruoka et al. expanded their methodology in 2007 by synthesizing several analogs of the bidentate aluminum Lewis acid analogs of **1** (R = Me), namely, R = Ph, ^{n}Oct, ^{i}Pr, ^{c}Hex, and H in order to evaluate the reactivity of different substituents in the position ortho to the $OAlMe_2$ groups.[24] In that paper, it was postulated that the use of the bidentate Lewis acid **1** (R = Me) doubly activates substrate carbonyls to augment their reactivity and hence the selectivity of the carbonyl-Lewis acid complexes for formation of the aldol product. Again, however, one or more equivalents of **1** (R = Me) were required to obtain high yields of the desired product.[24]

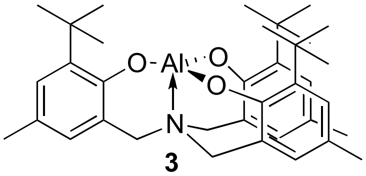


R = Me, Ph, ^{n}Oct, ^{i}Pr, ^{c}Hex, and H

1



2



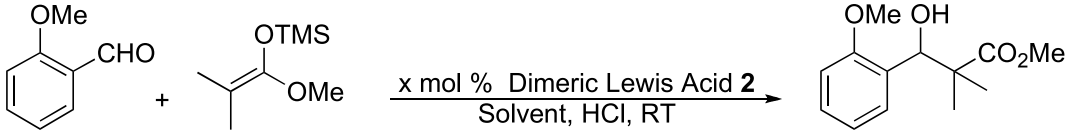
3

Aluminum compounds that function as efficient promoters for the Mukaiyama aldol reaction would be advantageous owing to their relatively low cost and toxicity. Thus in view of the high concentrations required for **1** (R = Me), efforts to develop an aluminum Lewis acid able to operate in catalytic amounts are worthwhile. In 2006, we reported the synthesis of a novel tricyclic aluminum alkoxide (alumatrane dimer **2**) and showed that oxygen donor compounds and amines can split this dimer to form monomeric alumatranes.[25] Of particular interest in the present context is our observation that aldehydes rapidly split dimeric **2** to form monomeric alumatrane•aldehyde adducts. It was therefore speculated that **2** might serve as an advantageous catalyst in various Lewis acid-catalyzed reactions, and herein we explore this application of this novel catalyst in Mukaiyama aldol transformations.

Results and Discussion

Optimization Study of a Mukaiyama Aldol Reaction. The coupling of *o*-anisaldehyde with methyl trimethylsilyl dimethylketene acetal was conducted as a model screening reaction and the results are summarized in Table 1. The desired product was isolated after hydrolysis with 2N aq HCl after 24 hours. Using 10 mole % of **2** in toluene at room temperature, 40% of the desired product was obtained (Table 1, entry 1). Interestingly, when the mole percentage of alumatrane dimer **2** in toluene was decreased, the yield of the desired products increased from 52 to 68% (Table 1, entries 2-4). When the temperature was decreased from room temperature to 0 °C, using 5 mol % of **2**, the product yield increased from 52% (entry 2) to 63% (entry 5).

Table 1. Optimization of **2**-Catalyzed Mukaiyama Aldol Reaction



Entry	Alumatrane (mol %)	Solvent	Yield (%)^{a,b}
1	10	toluene	40
2	5	toluene	52
3	5	toluene	63^{c}
4	2.5	toluene	60
5	0.5	toluene	68
6	5	CH_3CN	99
7	2.5	CH_3CN	94
8	0.5	CH_3CN	84
9	0.5	toluene/CH_3CN	86
10	5	CH_3CN	74^{e}

[a] Reaction conditions: 1 mmol of *o*-anisaldehyde, 1.2 mmol of enol silyl ether, 5 mL of solvent, RT, time: 24 h, then H_3O^+ treatment. [b] Average of two runs. [c] Reaction carried out at 0 °C for 3 days. [d] 50/50 toluene/CH_3CN. [e] Alumatrane **3**[26] was used for this reaction.

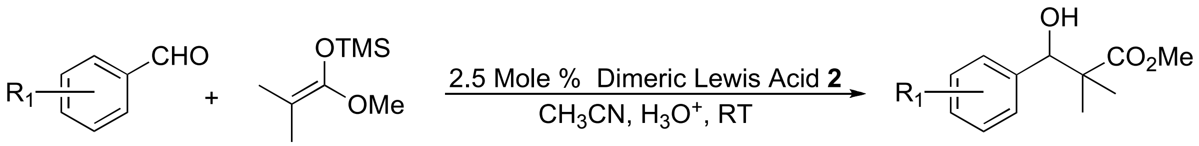
Typically, Mukaiyama aldol reactions require a polar solvent to obtain high yields. However, **2** in polar solvents such as tetrahydrofuran or diethyl ether, form soluble adducts whose ligands are quite stable to further reactions such as ether displacement by an aldehyde. On the other hand, when dimer **2** is stirred in acetonitrile for 24 hours, no adduct formation is observed as shown by ^{1}H NMR spectroscopy and by visually observing that the alumatrane dimer **2** remains insoluble in this solvent as well as other solvents that do not form adducts with **2**.

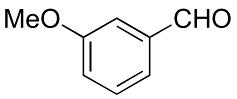
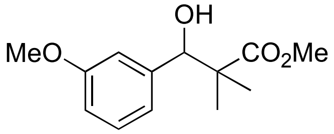
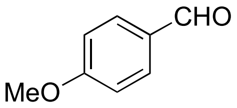
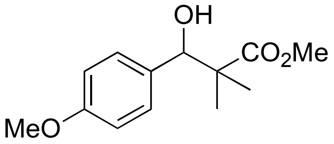
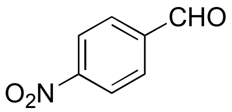
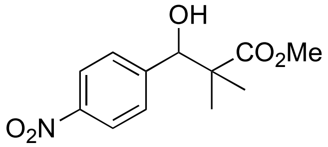
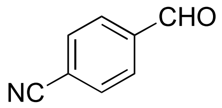
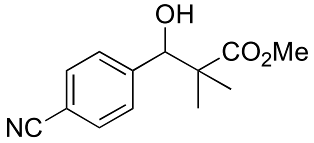
When acetonitrile is used as the solvent for the screening reaction in Table 1, a 5 mole % catalyst loading of **2** leads to a nearly quantitative yield of product (entry 6). Upon lowering the loading of dimeric **2** to 2.5 mole % and 0.5 mole %, 94% and 84% yields of desired product, respectively, were obtained (Table 1, entries 7 and 8). Since we observed higher product yields at lower loadings of **2** in toluene (entries 2-4), the screening reaction was carried out with a 50/50 mixture of acetonitrile/toluene containing 0.5 mole % of **2** in hopes of substantially increasing the product yield over 84% in acetonitrile alone (entry 8) and 68% in toluene by itself (entry 4). However, the product yield rose to only 86%. The sterically more congested alumatrane monomer **3**[26] at 5 mole % loading was also screened, but the product yield was only moderate (Table 1, entry 10). For the scoping reactions discussed below, 2.5 mole % of **2** in acetonitrile was employed unless noted otherwise.

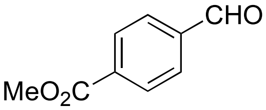
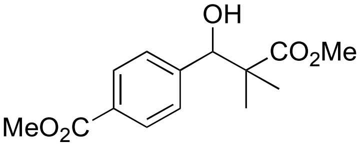
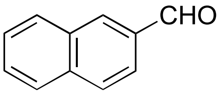
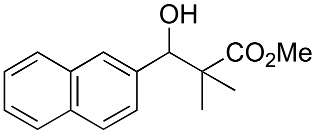
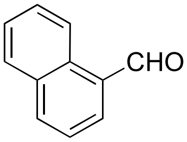
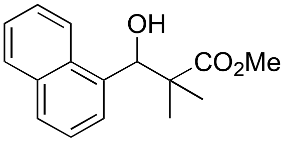
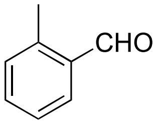
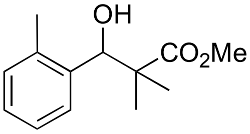
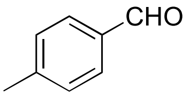
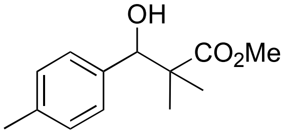
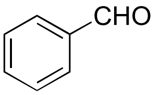
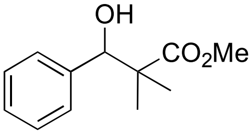
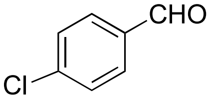
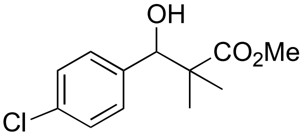
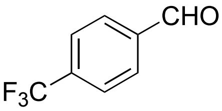
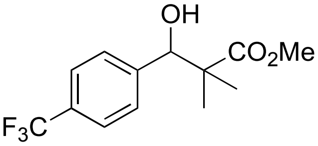
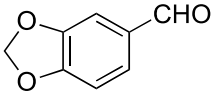
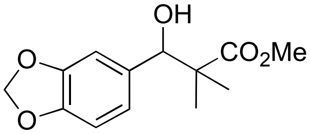
Mukaiyama Aldol Reactions of Aryl Aldehydes with Methyl Trimethylsilyl Dimethylketene Acetal. Using the optimized conditions in entry 7 of Table 1, the scope of our methodology was explored with a variety of aryl aldehydes (Table 2), including examples possessing activating or deactivating functionalities. *m*-Anisaldehyde and *p*-anisaldehyde when subjected to our protocol with methyl trimethylsilyl dimethylketene acetal, resulted in 92% and 90% yields of the desired product (Table 2, entries 1 and 2, respectively) in relatively short reaction times. A previous description of this reaction using

5 mole % of $MgI_2 \bullet (OEt)_n$ in CH_2Cl_2 for 30 minutes resulted in only a 30% product yield.[6] Deactivating groups such as nitro, cyano, and ester functionalities were also compatible with our protocol (entries 3 - 5, respectively). Interestingly, dimer **2** prefers to cleave to form an adduct with an aldehyde carbonyl rather than an ester carbonyl as shown in entry 5, wherein a 92% isolated yield of the desired β-hydroxy ester is recorded. Sterically hindered aldehydes such as 1-naphthaldehyde and *o*-tolualdehyde provide the corresponding products in 88% and 91% isolated yield, respectively (Table 2, entries 7 and 8). Pleasingly, halogen-substituted aryl aldehydes are stable to hydrodehalogenation under our conditions (entry 11). *p*-Trifluorotolualdehyde reacted with methyl trimethylsilyl dimethylketene acetal in the presence of **2**, affording a 92% yield of the desired β-hydroxy ester (entry 12). The highest yield of this compound reported in the literature is 68%.[3]

Table 2. Reactions of Aryl Aldehydes with Methyl Trimethylsilyl Dimethylketene Acetal



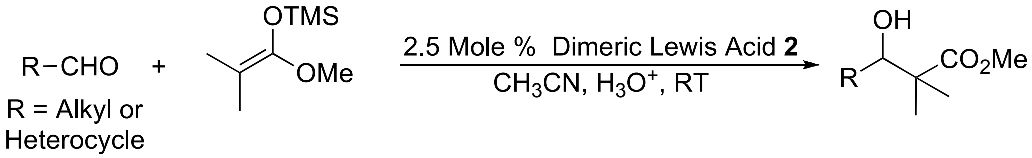
Entry	Aldehyde	Product	Time	Yield (%)^{a,b}
1			2 h	92 (Lit: 30)
2			1 h	90 (Lit: 44-98)
3			7 h	95 (Lit: 32-100)
4			6 h	98 (Lit: 68-90)

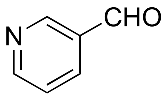
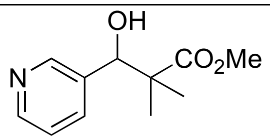
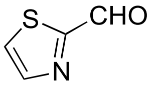
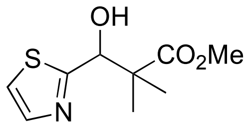
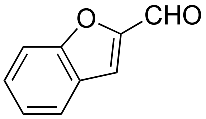
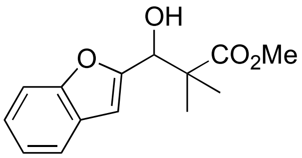
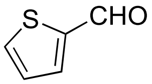
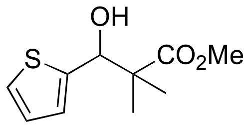
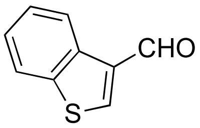
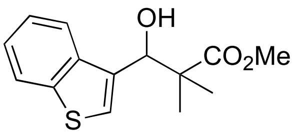
5			6 h	92 (Lit: 99)
6			2 h	92 (Lit: 77-81)
7			2 h	88 (Lit: 82-97)
8			3 h	91 (Lit: 83)
9			3 h	85 (Lit: 79-99)
10			1 h	95 (Lit: 18-100)
11			4 h	93 (Lit: 60-94)
12			10 h	92 (Lit: 33-68)
13			2 h	98 (Lit: 98)

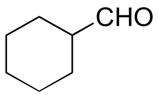
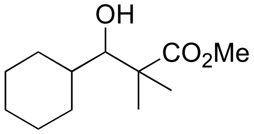
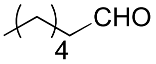
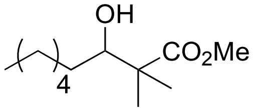
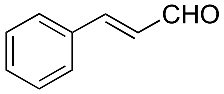
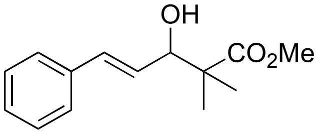
[a] Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric **2**, 5 mL of CH_3CN, RT, 1-10 h, then H_3O^+ treatment. [b] Average of two runs. Yields in parentheses are literature yields (see Supporting Information for references).

Mukaiyama Aldol Reaction of Heterocyclic and Alkyl Aldehydes with Methyl Trimethylsilyl Dimethylketene Acetal. Using the optimized conditions in entry 7 of Table 1, 3-pyridinecarboxaldehyde was subjected to our protocol with 2.5 mole % of **2**. With methyl trimethylsilyl dimethylketene acetal in acetonitrile at room temperature, a 96% yield of the desired β-hydroxy ester was achieved (Table 3, entry 1). This yield is somewhat higher than the highest yield found in the literature for this compound, which was synthesized by combining 3-pyridinecarboxaldehyde and the appropriate enol silyl ether in water after stirring for 24 hours.[27] A compound containing two hetero atoms (Table 3, entry 2) provided a 95% yield of the desired product. This compound was previously synthesized only once according to the literature, in a reaction using a PEG-supported ligand in the presence of 30 mole percent of $Cu(OTf)_2$,[28] resulting in only a moderate yield (75%) of the desired product.

Table 3. Hetero- and Alkyl- Aldehydes with Methyl Trimethylsilyl Dimethylketene Acetal



Entry	Aldehyde	Product	Time	Yield (%)[a,b]
1			7 h	96 (Lit: 47-95)
2			5 h	95 (Lit: 75)
3			5 h	91
4			6 h	96 (Lit: 57)
5			6 h	73 87[c]

6			2 h	86 (Lit: 48-89)
7			1 h	89 (Lit: 62-89)
8			12 h	52 (Lit: 55-99)

[a]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric **2**, 5 mL of CH_3CN, RT, 1-12 h, then H_3O^+ treatment. [b]Average of two runs. Yields in parentheses refer to literature yields (see Supporting Information for references). [c]5 mole % of **2** was used.

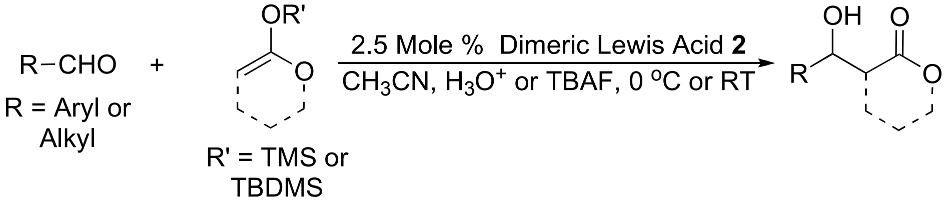
Oxygenated heterocycles are also amenable to our protocol and are apparently not vulnerable to adduct formation with **2** as is the case with THF.[25] Thus when 2-benzofurancarboxaldehyde was subjected to our protocol, 91% of the desired (but previously unreported) β-hydroxy ester in entry 3 was realized. 2-Furaldehyde when subjected to our protocol underwent >95% conversion to the trimethylsilyl-protected product as revealed by ^1H NMR spectroscopy. However, after hydrolysis, the desired product (which was shown to be present in the ^1H NMR spectrum of the crude product) decomposed to an intractable material upon attempted purification by column chromatography. Column chromatographic purification of the trimethylsilyl-protected product failed, owing to desilylation and subsequent decomposition.

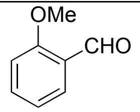
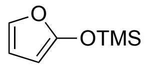
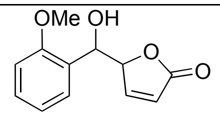
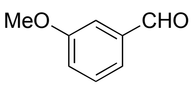
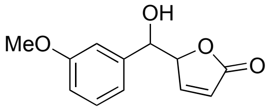
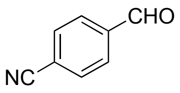
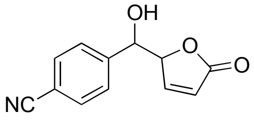
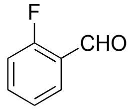
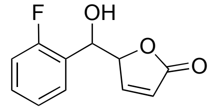
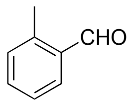
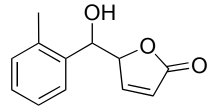
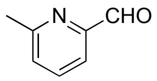
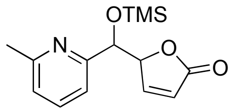
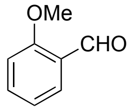
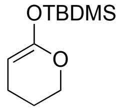
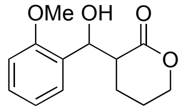
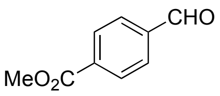
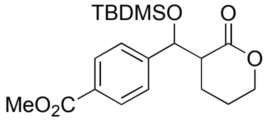
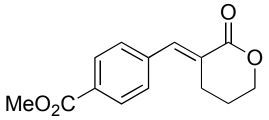
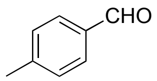
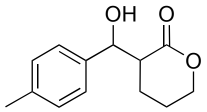
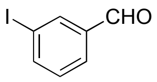
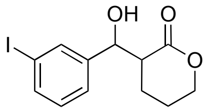
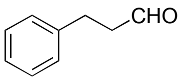
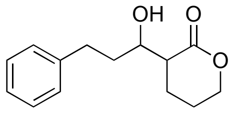
The sulfur-containing heterocycles 2-thiophenecarboxaldehyde and thianaphthene-3-carboxaldehyde upon reaction with methyl trimethylsilyl dimethylketene acetal produced 96% and 73%, respectively, of the desired products (entries 4 and 5 in Table 2). However, the latter reaction in the presence of 5 mole % of dimer **2** increased the product yield to 87%

(entry 5). Alkyl aldehydes in our protocol gave good product yields of 86% and 89% (entries 6 and 7, respectively). The vinylic aldehyde in entry 8 can be used in our procedure, but only a 52% yield of desired product was realized owing to the Michael addition product that also formed, as shown by the ^{1}H NMR spectrum of the crude reaction mixture. A higher loading of dimer **2** or a change of solvent did not improve the yield of desired product.

Mukaiyama Aldol Reaction of Various Aldehydes with 6-(tert-Butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran and 2-(Trimethylsiloxy)furan. 2-(Trimethylsiloxy)furan operates well in our protocol, undergoing coupling with *o*-anisaldehyde using the optimized conditions in Table 1, entry 7 to give 86% of the desired product (Table 4, entry 1). Although there is an opportunity for 1,2 addition to the aldehyde with this enol silyl ether, the only products obtained stemmed from the desired 1,4 addition process. During the course of our study, we discovered that for this reaction to occur, only aryl aldehydes with ortho substituents or aryl aldehydes with electron withdrawing substituents anywhere on the ring functioned satisfactorily in our procedure. When *m*-anisaldehyde was employed, 5 mole % of **2** was required to obtain a 51% yield of the desired product (Table 4, entry 2). However, when 4-cyanobenzaldehyde was used, 84% of the desired product was obtained in a 1/2 syn/anti ratio (Table 4, entry 3). 2-Fluorobenzaldehyde in our procedure gave a 93% product yield in a 1:1 syn:anti ratio (Table 4, entry 4) but the use of *o*-tolualdehyde provided only a 61% yield. However, when 5 mole % of dimeric **2** was used for the reaction of the latter aldehyde, the yield increased to 72% with a 1:4 syn:anti ratio (Table 4, entry 5).

Table 4. Various Aldehydes with 6-(*tert*-Butyldimethylsiloxy)-3,4-dihydro-2*H*-pyran and 2-(Trimethylsiloxy)furan



Entry	Aldehyde	Enol Ether	Product	Time	Yield (%)^a	Syn/Anti^d
1				2 h	86^b (Lit: 87)	1/6
2				3 h	35^b 51^c (Lit: 73-81)	1/2
3				1 h	84^b (Lit: 48)	1/2
4				2 h	93^b	1/1
5				3 h	61^b 72^e (Lit: 90)	1/4
6				1 h	82^b	Single Isomer
7				7 h	88^c	1/1
8				6 h	91^c	1/1
9				6 h	93^c	
10				8 h	92^c	1/1
11				13 h	83^c	1/1
12				15 h	87^c (Lit: 87)	1/2

[a]Average of two runs. [b]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric **2**, 5 mL of CH_3CN, RT, time: 1-3 h, H_3O^+ treatment. [c]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric **2**, 5 mL of CH_3CN, 0 °C, 6-15 h, then treatment with TBAF. Yields in parentheses are literature yields (see Supporting Information for references). [d]Syn/Anti ratio determined by either ^1H NMR spectroscopy or weight of separated isomer. [e]5 mole % of dimeric **2** used.

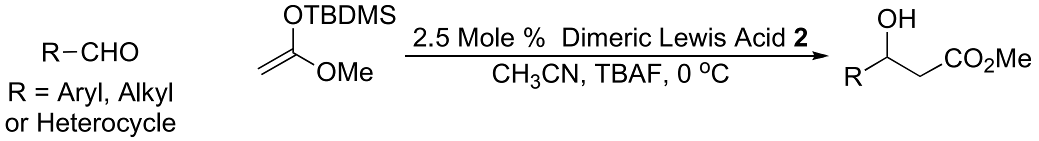
The heterocyclic aldehyde 6-methylpyridinecarboxaldehyde is compatible with 2-(trimethylsiloxy)furan. However, the desired product was isolated as the trimethysilyl-protected analogue because the hydrolyzed product decomposed on the chromatography column (Table 4, entry 6). The isomeric selectivity of the reactions with 2-(trimethylsiloxy)furan was not appreciably changed upon increasing the temperature from 0 °C to 70 °C.

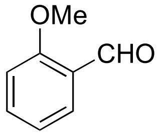
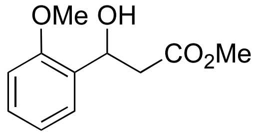
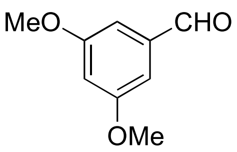
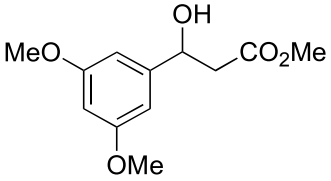
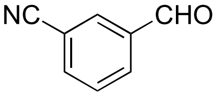
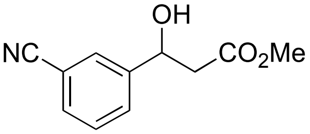
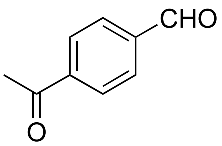
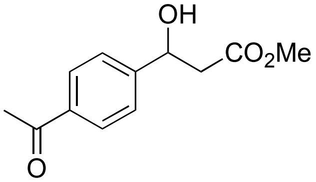
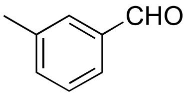
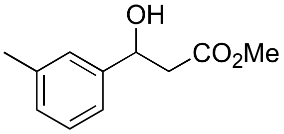
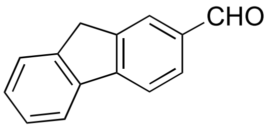
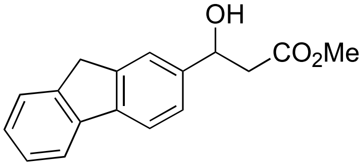
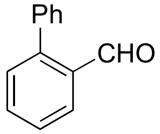
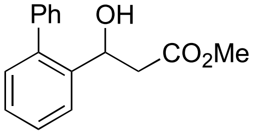
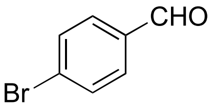
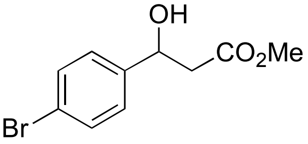
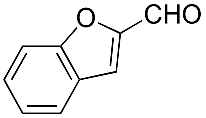
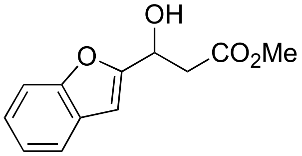
Mukaiyama aldol reactions in which the β-hydroxy ester product possesses acidic protons are plagued by dehydration under basic conditions to produce the corresponding α,β unsaturated esters.[10,14] In an effort to expand the scope of our methodology, a variety of aldehydes were coupled with different silyl enol ethers to produce products with acidic protons. To this end, 6-(tert-butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran was coupled with *o*-anisaldehyde using the optimized conditions in Table 1, entry 7. When the reaction was carried out at room temperature, the major product was the α,β unsaturated ester. Pleasingly, however, lowering the temperature to 0 °C afforded the desired β-hydroxy ester in 88% isolated yield after 7 hours (Table 4, entry 7) with no dehydration product observed by ^1H NMR spectroscopy. ^1H NMR spectroscopy also revealed that the final product was obtained in a 1:1 syn:anti ratio. This result demonstrates that our protocol not only tolerates trimethylsilyl-protected silyl enol ethers, but also tert-butyldimethylsilyl-protected silyl enol ethers which are more stable to normal hydrolytic work-up.

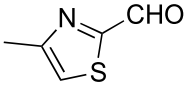
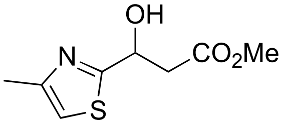
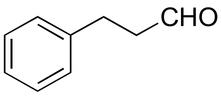
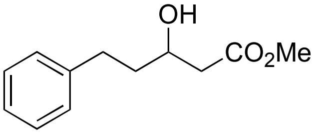
Methyl 4-formylbenzoate, *p*-tolualdehyde and 3-iodobenzaldehdye reacted with 6-(tert-butyldimethylsilyloxy)-3,4-dihydro-2H-pyran affording 91, 92% and 83% yields, respectively, of the desired products, each in a 1:1 syn:anti ratio (Table 4, entries 8-11). However, when 4-formylbenzoate was used, the silyl-protected product was isolated because on TBAF treatment, this product produced only the α,β-unsaturated ester (Table 4, entries 8 & 9). Enolizable hydrocinnamaldehyde gave an 87% isolated yield of product in a 1:2 syn:anti ratio (Table 4, entry 12).

Mukaiyama Aldol Reaction of Various Aldehydes with 1-(*tert*-Butyldimethylsilyloxy)-1-methoxyethene. Since the use of mono-substituted silyl enol ethers produced satisfying results, we investigated a silyl enol ether lacking olefinic substitution, namely, 1-(*tert*-butyldimethylsilyloxy)-1-methoxyethene. At 0 °C, a variety of aldehydes reacted with this silyl enol ether in the presence of 2.5 mole % of dimer **2**, giving the corresponding β-hydroxy ester products in high yields with no dehydration products observable by ^{1}H NMR spectroscopy. Thus, *o*-anisaldehyde reacted with 1-(*tert*-butyldimethylsilyloxy)-1-methoxyethene, leading to the desired β-hydroxy ester in 90% yield (Table 5, entry 1). We were able to find only one previous report of the synthesis of this compound, and its low yield (33%) emanated from a reaction using 10 mole % of DBU in THF at room temperature for 24 hours.[11] 3,5-Dimethoxybenzaldehyde is also a viable substrate for our procedure, producing the expected (but heretofore unreported) product in 96% isolated yield (Table 5, entry 2).

Table 5. Various Aldehydes with 1-(*tert*-Butyldimethylsiloxy)-1-methoxyethene



Entry	Aldehyde	Product	Time	Yield (%)^{a,b}
1			14 h	90 (Lit: 33)
2			15 h	96
3			10 h	93
4			11 h	57 89^{c}
5			8 h	92
6			6 h	93
7			10 h	94
8			16 h	83 (Lit: 87)
9			12 h	95 (Lit: 100)

10			10 h	81
11			13 h	90 (Lit: 16-87)

[a]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric **2**, 5 mL CH_3CN, 0 °C, 6-16 h, then treatment with TBAF. [b]Average of two runs. Yields in parenthesis refer to literature yields (see Supporting Information for references). [c]5 mole % of **2** was used.

Electron deficient aryl aldehydes bearing a cyano or acetyl group also function in our protocol (Table 5, entries 3 and 4, respectively) producing the desired (but unreported) products in both cases. Although the product yield was only 57% in the latter case, 5 mole % of **2** raised this yield to 89% (Table 5, entry 4). Electron neutral aryl aldehydes also provided high yields of the desired β-hydroxy ester (Table 5, entries 5, 6, and 8).

Use of the sterically hindered aryl aldehyde 2-biphenylcarboxaldehyde, facilitated a 94% product yield (Table 5, entry 7) and heterocyclic 2-benzofurancarboxaldehyde also led to an excellent product yield (95%, entry 9). The only reported method we were able to find for synthesizing the latter product was one in which the corresponding ketone was pre-synthesized by reacting 2-acetylbenzofuran with dimethyl carbonate in the presence of sodium hydride, affording an 87% yield of the α-ketone, which upon subsequent reduction with tartaric acid-modified Raney nickel in the presence of hydrogen gave 100% of the β-hydroxy ester.[29] Reaction of 4-methyl-2-thiazolecarboxaldehyde with 1-(*tert*-butyldimethylsilyloxy)-1-methoxyethene gave the desired (but unreported) product in 81% isolated yield (Table 5, entry 10).

The alkyl aldehyde hydrocinnamaldehyde when reacted with 1-(*tert*-butyldimethylsilyloxy)-1-methoxyethene in the presence of 2.5 mole % of dimer **2** afforded a 90% yield of the desired product (Table 5, entry 11). Literature methods for synthesizing this product include alkylation of the dianion of methylacetoacetate with benzyl bromide,[30] and a seven-step synthesis beginning with a sulfinate which was allowed to react sequentially with carbon dioxide, benzyl bromide, and diazomethane in the presence of aluminum amalgam to desulfinate the final product, resulting in an overall 80% isolated yield.[31] Product yields in the literature for this compound ranged from 16 – 87%.

Structural and Mechanistic Considerations. Earlier we reported that alumatrane dimer **2** is insoluble in acetonitrile, but upon addition of benzaldehyde to the mixture, a light yellow solution is formed. The same observation for the various aldehydes employed in the present study is consistent with splitting of dimeric **2** by the aldehydic oxygen to form adducts such as **4** in Scheme 1. Adduct **4** was synthesized and crystals suitable for X-ray analysis were grown from a 10:1 mixture of pentane:toluene (Figure 1). As shown in this figure, the methoxy group appears to be quite free of steric encumbrance by any of the three neighboring methyl groups on the alumatrane moiety.

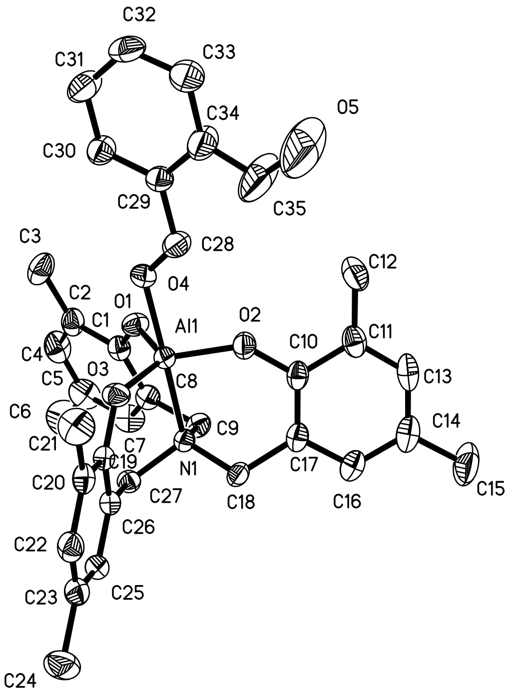
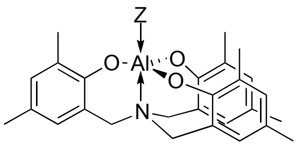
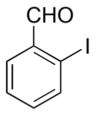


Figure 1. Computer drawing of the molecular structure of **4** at the 50% probability level. Hydrogen atoms are omitted for clarity. Major bond distances: Al-N, 2.101(3); avg Al-O_{eq}, 1.751(3); Al-O_{ax}, 1.986(3); C=O, 1.216(3) Å. Major bond angles: avg N-Al-O_{eq}, 92.76(13); avg O_{eq}-Al-O_{eq}, 119.77(12); avg O_{eq}-Al-O_{ax}, 87.26(13)^{o}.

A comparison of some of the major X-ray crystallographic structural parameters of **4** with the corresponding ones in **5** – **12** is of interest. Because such a comparison is not of particular relevance to the thrust of the present work, however this discussion can be found in the Supporting Information.



5: Z = $O(CH_2CH_2)_2$
6: Z = $O{=}CHC_6H_5$
7: Z = $^{-}OC_6H_5$
$HP(iPrNCH_2CH_2)_3N^+$
8: Z = OH_2



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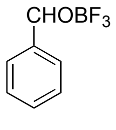

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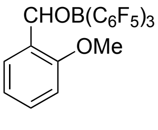

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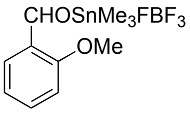

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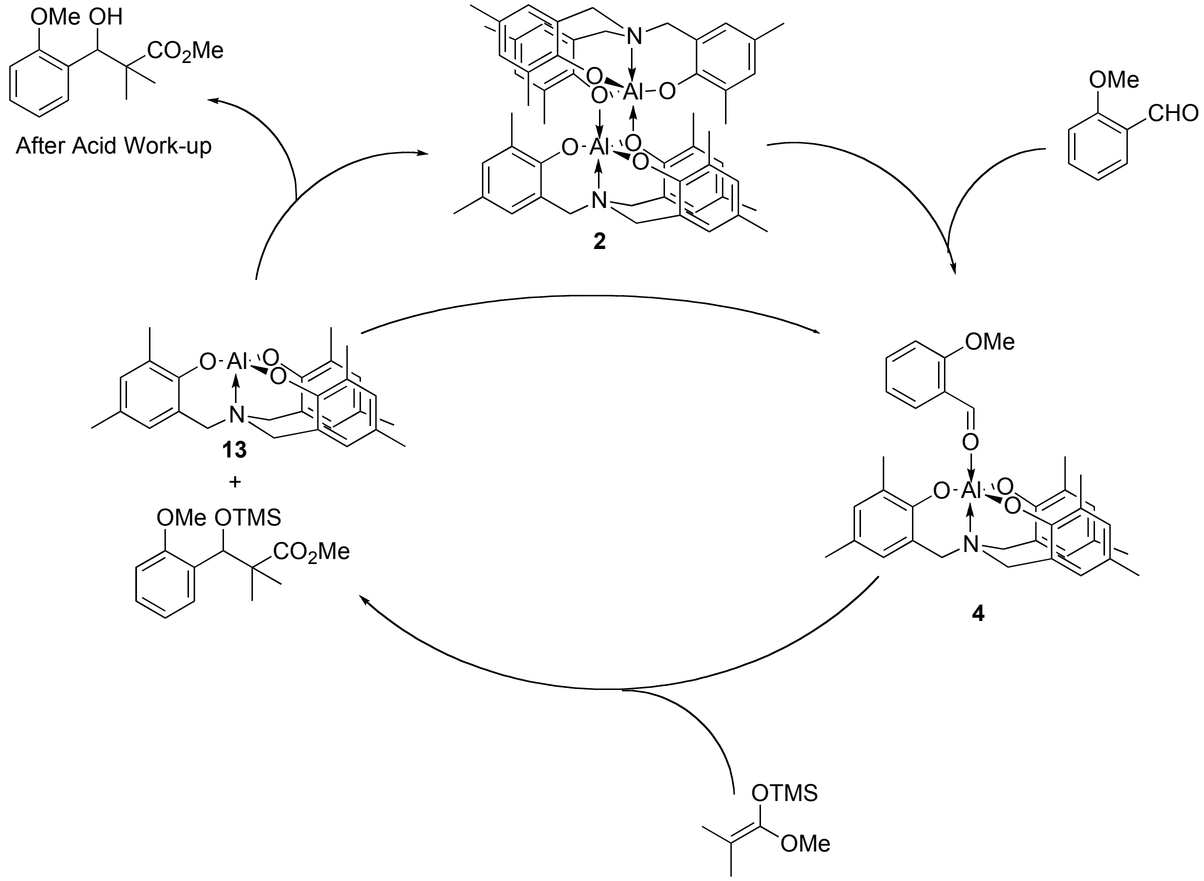
Earlier in this paper it was noted that although 2-substituted aryl aldehydes functioned well in our protocol, 2,6-dimethylbenzaldehdye and 2,6-dimethoxybenzaldehdye failed to produce detectable amounts of product (as shown by ^{1}H NMR spectroscopy) even though adduct formation was indicated by the solubility of dimer **2** in acetonitrile when either of these aldehydes was added. It would thus appear that the bulk of the second *ortho* substituent in combination with that of the alumatrane moiety increases the steric shielding of the carbonyl carbon to the point where nucleophilic attack by the double bond of the silyl enol ether is prevented, even though coordination of the aldehyde oxygen to the aluminum might render the aldehyde carbon sufficiently electrophilic.

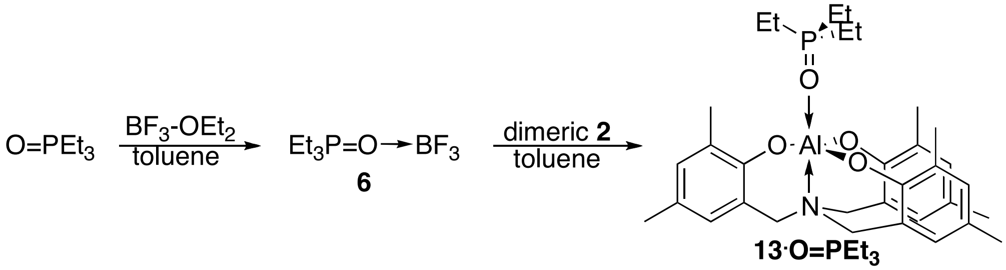
Scheme 1. Suggested Pathway of the Mukaiyama Aldol Reaction of *o*-Anisaldehyde with Alumatrane Dimer **2**



If attack of **4** by an enol silyl ether is able to occur (Scheme 1) it appears that the alumatrane monomer moiety **13** is then released from the adduct to immediately form an adduct with another aldehyde before reforming dimer **2**. This assumption is based on our observation that no solids were formed during the reaction until all of the aldehyde is consumed. At the point in the reaction where insoluble dimer **2** began to form, a 2M solution of aq HCl was added to the reaction mixture to hydrolyze the silylated penultimate product to the final aldol product. In order to demonstrate that the precipitate was indeed **2**, it was filtered under inert atmosphere immediately after its formation (before hydrolytic work up) and re-used successfully in a duplicate reaction. Additional evidence that the precipitate is **2** came from our observation of similar recyclability of precipitated **2** in experiments involving the addition of TMSCN to aldehydes.[32]

Lewis Acidity of 13. The existence of a N→Al dative bond in monomeric **2** (as represented by **13**) might be expected to diminish its Lewis acidity sufficiently to preclude its usefulness in transformations such as the Mukaiyama aldol reaction. In a previous publication we reported calculational results indicating that **13** is more Lewis acidic than BF_3.[26] In the present work we provide experimental support for this conclusion. Herein we measured the ^{31}P NMR chemical shifts of **13**•O=PEt_3 (61 ppm) and F_3B•O=PEt_3 (78 ppm) in C_6D_6, and we also characterized the former compound by single crystal X-ray crystallography (Figure 3). (Crystals of **13**•O=PEt_3 were grown from a concentrated solution of toluene in a freezer for 2 days.) Both of the aforementioned ^{31}P chemical shifts are downfield of the 55 ppm we measured for O=PEt_3 in the same solvent. However, the relative magnitudes of these deshieldings can not taken to be indicative of the relative Lewis acidities of **13** and BF_3, owing to differences in paramagnetic effects of the boron and aluminum nuclei. We then added 1 equivalent of triethyl phosphine oxide to a mixture of 1.1 equivalents of BF_3•OEt_2 in toluene to form the BF_3•O=PEt_3 adduct whose ^{31}P NMR spectrum was then taken (Scheme 2). The BF_3•O=PEt_3 adduct was then dried under reduced pressure leaving a white solid to which a 0.5 molar equivalent of the alumatrane dimer **2** was added to determine if the dimer was capable of removing $OPEt_3$ from the BF_3•O=PEt_3 adduct. Consistent with the greater Lewis acidity of **13**, the ^{31}P NMR spectrum of the reaction mixture revealed only the ^{31}P chemical shift of **13**•O=PEt_3 (Figure 2).

Scheme 2. Reactions of Triethylphosphine Oxide with BF_3•OEt_2 and Alumatrane Dimer **2**



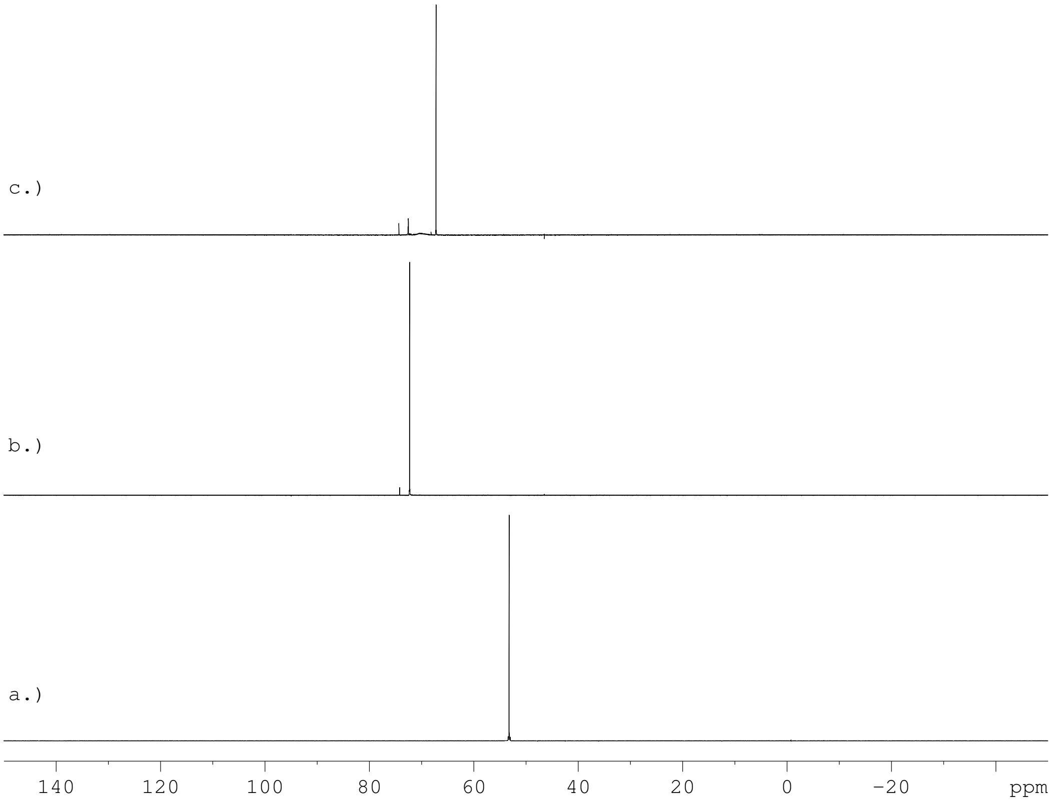


Figure 2. a) ^{31}P NMR of O=PEt$_3$ in C$_6$D$_6$. b) ^{31}P NMR of BF$_3$•O=PEt$_3$ in C$_6$D$_6$. c) ^{31}P NMR after addition of alumatrane dimer **2** to BF$_3$•O=PEt$_3$.

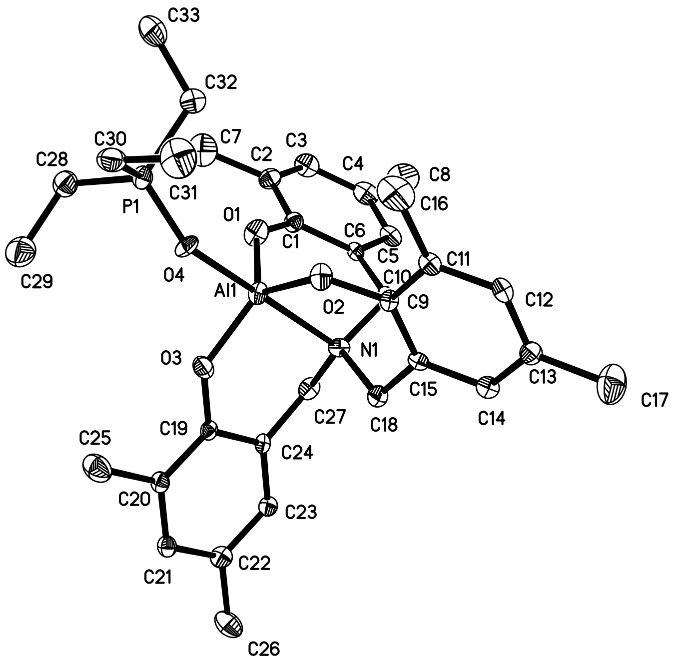
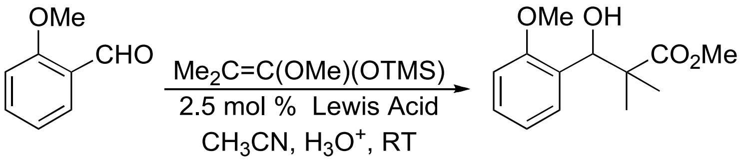


Figure 3. Computer drawing of the molecular structure of **13**•O=PEt$_3$ at the 50% probability level. Hydrogen atoms are omitted for clarity.

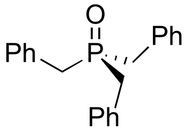
In a further effort to substantiate these results, the product yields of the reaction of *o*-anisaldehyde and methyl trimethylsilyl dimethylketene acetal in the presence of dimer **2** and BF$_3$•OEt$_2$ were compared (Table 6). The reactions were carried out in acetonitrile with 2.5 mole % of dimeric **2** and 5 mole % of BF$_3$•OEt$_2$, and after one hour, the reactions were quenched with 2N aq HCl. As depicted in Table 6, the alumatrane dimer **2** provided a 97% yield of the desired product (entry 1), whereas BF$_3$•OEt$_2$ led to only a 35% product yield (entry 2). This contrast in efficacy of **2** compared with BF$_3$•OEt$_2$ is made the more striking because energy is required to split dimer **2** into **13**, the Lewis acidic species needed for carbonyl activation. These results are supportive of our earlier calculational results indicating that **13** is more Lewis acidic than BF$_3$.[26] Another experiment was carried out with 2.5 mole % of alumatrane dimer **2** and 5 mole % diethyl ether in order to demonstrate that the presence of diethyl ether does not materially affect the outcome of the reaction. Pleasingly, 92% of the desired product was obtained (entry 3). Since energy is also required to dissociate the ether moiety from BF_3•OEt_2, we carried out a reaction using 5 mole % of BF_3 obtained from a commercially available stock solution containing 15% BF_3 in acetonitrile. Only 24% of the desired product was obtained in this reaction (entry 4).

Table 4. Comparison Reactions Between Alumatrane Dimer **2** and BF_3•OEt_2



Entry	Lewis Acid	Yield (%)[a,b]
1	**2**	97
2	BF_3•OEt_2	35
3	**2**[c]	92
4	BF_3	24

[a] Reaction conditions: 1 mmol of *o*-anisaldehyde, 1.2 mmol of methyl trimethylsilyl dimethylketene acetal, 2.5 mole % alumatrane dimer **2**, 5 mL of CH_3CN, RT, 1 h, then H_3O^+ treatment. [b] Average of two runs. [c] 5 mole % of diethyl ether added to the reaction mixture. [d] 5 mole % as a 15% solution in CH_3CN.



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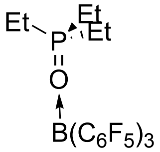


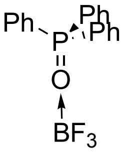
15

$Et_3P=O(GeF_4)O=PEt_3$

16

$Ph_3P=OAlCl_3$

17



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Since **13**•O=PEt_3 represents only the second example of an Al•O=PEt_3 adduct and, more particularly, the first example of an alumatrane•O=PEt_3 adduct whose molecular structures have been determined by X-ray means, it is of interest to compare some structural parameters of **13**•O=PEt_3 with analogous metrics in phosphine oxide **14** and in selected Lewis acid phosphine oxide complexes **15-18** (Table 7). The P=O bond in **13**•O=PEt_3 is within 3x the esds for this link in **14-18**. Thus, there appears to be no significant effect of the Lewis acids considered here on the P=O bond distances in their phosphine oxide adducts **15-18**. The LA-O bond length in **13**•O=PEt$_3$ is longer than in **17**, an observation that can be rationalized by the higher coordination number of the aluminum in **13**•O=PEt$_3$ in which the transannular N enriches the electron density on the metal as do the three equatorial phenoxy oxygens. On the other hand the LA-O bond length in **13**•O=PEt$_3$ is shorter than in **16** wherein the lower electronegativity/electron withdrawing effect of Ge compared with Al and the higher coordination number of **16** lengthens the LA-O bond length. The longer LA-O bond length in **13**•O=PEt$_3$ than in **15** and **18** can be attributed to the smaller size and greater electronegativity of B relative to Al as well as the expanded coordination number of Al in **13**•O=PEt$_3$. Unlike **17** (which exhibits a 180° bond angle between the phosphorus and the Lewis acid atom) **13**•O=PEt$_3$ displays a bond angle of 146.2°. The origin of this difference is not readily apparent.

Table 7. Comparison of Bond Lengths and Angles of Phosphine Oxide Lewis Acid Adducts

Entry	Compd	P=O	LA[a]-O	LA[a]-O-P
1	**13**•O=PEt$_3$	1.499(6)	1.850(6)	146.2(4)
2	**14**[b]	1.488(4)		
3	**15**[c]	1.497(17)	1.533(3)	161.04(16)
4	**16**[d]	1.522(2)	1.925(2)	142.5(1)
5	**17**[e]	1.519(4)	1.733(4)	180
6	**18**[f]	1.522(3)	1.526(6)	134.5(2)

[a] LA = Lewis Acid. [b] See reference 33. [c] See reference 34. [d] See reference 35. [e] See reference 36. [f] See reference 37.

Conclusions

We have demonstrated the utility of alumatrane dimer **2** in the Mukaiyama aldol reaction. Our protocol tolerates a wide variety of aryl, heterocyclic, and alkyl aldehydes and has high functional group tolerance. Ketone substrates failed in our protocol, however. It should be noted that our protocol requires the presence of an electron donating OR group on the olefin of the silyl enol ether. Other silyl enol ethers [such as 1-phenyl-1-trimethylsiloxyethylene and 1-(trimethylsiloxy)cyclohexene] in the presence of *o*-anisaldehyde produced no desired products. But when 6-(tert-butyldimethylsilyloxy)-3,4-dihydro-2H-pyran was employed in this reaction, the desired product was obtained in high yield (88%). It is reasonable to suggest that the presence of the electron inducting OR substituent on the olefinic moiety provides the latter with sufficient nucleophilicity for attack of the Lewis acid-activated carbonyl group. Our proposed mechanism receives support from the isolation and structural characterization of intermediate **4**. Evidence supporting our postulate that monomeric **2** (i.e., **13**) is more Lewis acidic than BF_3 has also been presented. Comparisons of structural parameters obtained from single-crystal X-ray experiments for **4** and **13**•$O{=}PEt_3$ and for related compounds in the literature are rationalized in terms of central atom electronegativity and coordination number expansion effects. Further investigations illustrating the usefulness of dimer **2** in Lewis acid-catalyzed organic reactions are underway.

Experimental Section

General Procedure for Mukaiyama Aldol Reaction of Methyl Trimethylsilyl Dimethylketene Acetal and 2-(Trimethylsiloxy)furan. To a 10 mL vial equipped with a stir bar, 22.15 mg (2.5 mole %) of alumatrane dimer **2** was added in a glove box.

Acetonitrile (5 mL) followed by 1 mmol of the corresponding aldehyde were added to the vial, and then the reaction mixture was stirred for 30 min at room temperature to form the aldehyde-alumatrane adduct. The corresponding silyl enol ether (1.2 mmol) was added under inert atmosphere and then the reaction was continued for the allotted time as recorded in the tables. Then 3 mL of 2 N hydrochloric acid solution was added and the reaction mixture was stirred for an additional 3 hours at room temperature. The reaction mixture was extracted with methylene chloride and dried over Na_2SO_4, the solution was filtered and dried on a rotovap apparatus, and then the crude product was purified by column chromatography (EtOAc:Hexanes = 1:9).

Methyl 3-Hydroxy-2,2-dimethyl-3-(2-benzofuran)propionate (Table 3, entry 3) White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55-7.57 (d, 1H), 7.45-7.47 (d, 1H), 7.22-7.30 (m, 2H), 6.67 (s, 1H), 4.96 (s, 1H), 3.77 (s, 3H), 3.73 (br, 1H), and 1.30-1.31 (d, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.8, 156.8, 154.7, 128.1, 124.3, 123.0, 121.2, 111.4, 104.9, 73.9, 52.5, 47.3, 23.0, and 20.4 ppm. HRMS *m/z*: Calcd for $C_{14}H_{16}O_4$ (M^+) 248.10485, found 248.10512.

Methyl 3-Hydroxy-2,2-dimethyl-3-(3-thianaphthene)propionate (Table 3, entry 5) Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84-7.90 (dd, 2H), 7.31-7.39 (m, 3H), 5.38 (s, 1H), 3.71 (s, 3H), 3.42 (br, 1H), 1.28 (s, 3H), and 1.16 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.3, 140.2, 138.7, 136.1, 124.7, 124.3, 124.1, 123.0, 122.8, 73.7, 52.4, 48.5, 23.5, and 19.6 ppm. HRMS *m/z*: Calcd for $C_{14}H_{16}O_3S$ (M^+) 264.08202, found 264.08256.

5-(Hydroxy(2-fluorophenyl)methyl)furan-2(5*H*)-one (Table 4, entry 4) Clear, colorless oil. (*syn/anti*:1/1) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49-7.56(m, 2H), 7.26-730 (m, 4H), 7.16-7.19(t, 2H, *J* = 7.6 Hz), 7.02-7.06 (t, 2H, *J* = 8.4 Hz), 6.10-6.14 (t, 2H, *J* = 7.6 Hz), 5.40-5.41

(d, 1H, *J* = 4 Hz), 5.28-5.29 (d, 1H, *J* = 4 Hz), 5.19-5.20 (d, 1H, *J* = 4 Hz), 5.07-5.08 (d, 1H, *J* = 4 Hz), and 3.82 (br, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.6, 173.2, 160.9, 160.8, 158.5, 158.4, 153.5, 153.0, 130.4 (d, *J* = 8.3 Hz), 130.1 (d, *J* = 8.2 Hz), 128.6 (d, *J* = 3.6 Hz), 128.1 (d, *J* = 3.8 Hz), 125.7 (d, *J* = 13 Hz), 125.5 (d, *J* = 13.2 Hz), 124.8, 123.5 (d, *J* = 5 Hz), 123.1 (d, *J* = 4.9 Hz), 115.7 (d, *J* = 15.9 Hz), 115.4 (d, *J* = 15.7 Hz), 86.7, 85.6, 68.8, and 67.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -118.07 and -118.41 ppm. HRMS *m/z*: Calcd for $C_{11}H_9FO_3$ (M^+) 208.05357, found 208.05393.

Synthesis of 5-(Trimethylsiloxy(2-(6-methylpyridine))methyl)furan-2(5*H*)-one (Table 4, entry 6). To a 10 mL vial equipped with a stir bar, 22.15 mg (2.5 mole %) of alumatrane dimer **2** was added in a glove box. Acetonitrile (5 mL) was added to the vial, followed by 1 mmol of 6-methylpyridine-2-carboxaldehyde. The reaction mixture was stirred for 30 min at room temperature to form the aldehyde-alumatrane adduct and then 2-(trimethylsiloxy)furan (1.2 mmol) was added under inert atmosphere. The reaction was allowed to proceed for 1 hour at room temperature and then the solid alumatrane dimer was filtered. The reaction mixture was concentrated on a rotovap and the crude product was purified by column chromatography (EtOAc:Hexanes = 1:9). Clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61-7.65 (t, 1H, *J* = 7.6 Hz), 7.25-7.27 (d, 1H, *J* = 8 Hz), 7.08-7.13 (m, 2H), 6.10-6.11 (d, 1H, *J* = 5.6 Hz), 5.58-5.59 (d, 1H, *J* = 1.2 Hz), 5.1-5.19 (d, 1H, *J* = 2.8 Hz), 2.55 (s, 3H), and 0.11 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 158.7, 158.1, 152.8, 137.4, 123.2, 122.7, 117.7, 86.4, 74.7, 24.6, and 0.1 ppm. HRMS *m/z*: Calcd for $C_{14}H_{19}NO_3Si$ (M^+) 277.11341, found 277.11402.

General Procedure for Mukaiyama Aldol Reaction of 6-(tert-Butyldimethylsilyloxy)-3,4-dihydro-2H-pyran and 1-(*tert*-Butyldimethylsilyloxy)-1-methoxyethene. To a 10 mL vial equipped with a stir bar, 22.15 mg (2.5 mole %) of alumatrane dimer **2** was added in a glove box. Acetonitrile (5 mL) was added to the vial followed by 1 mmol of the corresponding aldehyde, and then the reaction mixture was stirred for 30 min at room temperature to form the aldehyde-alumatrane adduct. The reaction mixture was then cooled to 0 °C and 1.2 mmol of the corresponding silyl enol ether was added under inert atmosphere. The reaction was allowed to proceed for the allotted time as specified in the tables and then a 0 °C solution of 3 mmol of a 1M TBAF/THF solution was added. The mixture was stirred at 0 °C for 1 hour after which 3 mL of water was added and stirred for an additional hour at 0 °C. The reaction mixture was extracted with methylene chloride (2 x 100 mL portions) and dried over Na_2SO_4. The solution was filtered and dried on a rotovap followed by purification of the crude product via column chromatography (EtOAc:Hexanes = 1:9). Because the products synthesized from 6-(tert-butyldimethylsilyloxy)-3,4-dihydro-2H-pyran were new compounds and attempts to separate them failed, we were unable to determine which peaks in the ^{1}H and ^{13}C NMR spectra corresponded to the *syn* and *anti* isomers.

3-(Hydroxy(2-methoxyphenyl)methyl)-tetrahydro-2*H*-pyran-2-one (Table 4, entry 7) White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45-7.51 (dd, 2H, J = 18 Hz, J = 7.6 Hz), 7.23-7.29 (q, 2H, J = 7.6 Hz), 6.96-7.01 (m, 2H), 6.84-6.88 (t, 2H, J = 8.4 Hz), 5.73 (s, 1H), 5.28-5.30 (d, 1H, J = 8.4 Hz), 4.49-4.50 (d, 1H, J = 2 Hz), 4.26-4.31 (m, 4H), 3.82 (s, 6H), 3.12-3.13 (d, 1H, J = 3.6 Hz), 3.00-3.05 (dt, 1H, J = 7.6 Hz, J = 2.4 Hz), 2.79-2.84 (q, 1H, J = 9.2 Hz), 1.75-1.88 (m, 5H), 1.53-1.58 (m, 2H), and 1.44-1.46 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.2, 174.9, 156.8, 155.5, 129.1, 129.1, 128.8, 128.3, 127.8, 127.3, 121.2, 120.6, 110.7, 110.0, 68.9, 68.6, 68.5, 67.1, 55.6, 55.4, 46.6, 44.2, 22.3, 21.9, 21.0, and 17.9 ppm. HRMS *m/z*: Calcd for $C_{13}H_{16}O_4$ (M^+) 236.10486, found 236.10533.

3-(*t*-Butyldimethylsiloxy(methyl 4-benzoate)methyl)-tetrahydro-2*H*-pyran-2-one (Table 4, entry 8) Clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93-7.98 (m, 4H), 7.38-7.43 (m, 4H), 5.63 (s, 1H), 5.53-5.54 (d, 1H, *J* = 4 Hz), 4.31-4.34 (m, 1H), 4.16-4.26 (m, 2H), 3.86 (s, 6H), 2.91-2.94 (m, 1H), 2.61-2.65 (t, 1H, *J* = 9.2 Hz), 1.83-1.99 (m, 3H), 1.66-1.70 (m, 2H), 1.38-1.59 (m, 3H), 0.86-0.88 (d, 18H, *J* = 8 Hz), 0.03-0.06 (d, 6H, *J* = 7.6 Hz), -0.11 (s, 3H), and -0.18 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 171.1, 167.0, 166.9, 147.8, 146.7, 129.6, 129.4, 127.1, 126.1, 74.0, 73.5, 70.0, 69.3, 52.2, 52.2, 49.5, 49.1, 26.0, 25.0, 22.8, 22.3, 19.8, 18.8, 18.3, 18.3, -4.5, -4.8, -5.0, and -5.2 ppm. ESI$^+$ *m/z*: Calcd for $C_{20}H_{30}O_5Si$ (M^+) 378.19, found 379.

3-((Methyl 4-benzoate)2-methylene)-trihydro-2*H*-pyran-2-one (Table 4, entry 9) White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05-8.07 (d, 2H, *J* = 8 Hz), 7.91 (s, 1H), 7.47-7.49 (d, 2H, *J* = 8 Hz), 4.40-4.42 (t, 2H, *J* = 5.2 Hz), 3.92 (s, 3H), 2.86-2.89 (t, 2H, *J* = 6.4 Hz), and 1.96-2.01 (sep, 2H, *J* = 6 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.7, 166.6, 140.4, 139.5, 130.5, 130.1, 129.9, 128.1, 69.0, 52.5, 26.2, and 23.2 ppm. HRMS *m/z*: Calcd for $C_{14}H_{14}O_4$ (M^+) 246.0892, found 246.0892.

3-(Hydroxy(4-methylphenyl)methyl)-tetrahydro-2*H*-pyran-2-one (Table 4, entry 10) Clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22-7.25 (m, 4H), 7.15-7.16 (m, 4H), 5.46 (s, 1H), 4.77-4.79 (d, 1H, *J* = 8.8 Hz), 4.61 (br, 1H), 4.24-4.30 (m, 4H), 3.30 (br, 1H), 2.68-2.80 (m, 2H), 2.34 (s, 6H), 1.75-1.85 (m, 5H), 1.55-1.60 (m, 2H), and 1.49-1.53 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.9, 174.2, 138.1, 138.0, 137.2, 137.0, 129.3, 129.1, 127.0, 125.8, 75.0, 71.8, 69.2, 68.7, 47.4, 46.6, 22.3, 21.8, 21.7, 21.3, 21.2, and 18.1 ppm. HRMS *m/z*: Calcd for $C_{13}H_{16}O_3$ (M^+) 220.10994, found 220.11016.

3-(Hydroxy(3-iodophenyl)methyl)-tetrahydro-2*H*-pyran-2-one (Table 4, entry 11) Clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, 2H, *J* = 1 Hz), 7.57-7.64 (dd, 2H, *J* = 18 Hz, *J* = 8 Hz), 7.28-7.30 (d, 2H, *J* = 7.2 Hz), 7.05-7.09 (dt, 2H, *J* = 7.6 Hz, *J* = 2.4 Hz), 5.45 (s, 1H), 4.73-4.75 (d, 1H, *J* = 8.8 Hz), 4.67 (br, 1H), 4.26-4.31 (m, 4H), 3.44 (br, 1H), 2.72-2.77 (m, 1H), 2.65-2.70 (m, 1H), 1.75-1.87 (m, 5H), 1.45-1.53 (m, 2H), and 1.34-1.43 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.5, 173.9, 143.6, 142.6, 137.4, 136.5, 136.0, 134.9, 130.4, 130.2, 126.6, 125.1, 94.7, 94.6, 74.3, 71.0, 69.3, 68.7, 47.3, 46.5, 22.3, 21.7, 21.6, and 17.8 ppm. HRMS *m/z*: Calcd for $C_{12}H_{13}IO_3$ (M^+) 331.99095, found 331.99164.

Methyl 3-Hydroxy-3-(3,5-dimethoxyphenyl)-propionate (Table 5, entry 2) Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.51 (s, 2H), 6.35, (s, 1H), 5.02-5.06 (dd, 1H, *J* = 9.2 Hz, *J* = 4 Hz), 3.70-3.76 (d, 6H, *J* = 72.8 Hz), 3.70 (s, 1H), 3.67 (br, 1H), and 2.64-2.76 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.8, 161.0, 145.3, 103.6, 99.8, 70.4, 55.4, 52.0, and 43.4 ppm. HRMS *m/z*: Calcd for $C_{12}H_{16}O_5$ (M^+) 240.09977, found 240.10006.

Methyl 3-Hydroxy-3-(3-cyanophenyl)-propionate (Table 5, entry 3) Clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (s, 1H), 7.54-7.60 (m, 2H), 7.42-7.46 (m, 1H), 5.12-5.16 (t, 1H, *J* = 6.4 Hz), 3.78 (br, 1H), 3.70 (s, 3H), and 2.69-2.70 (d, 2H, *J* = 6.4 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 144.3, 131.5, 130.4, 129.5, 129.5, 118.8, 112.6, 69.3, 52.3, and 43.1 ppm. HRMS *m/z*: Calcd for $C_{11}H_{11}NO_3$ (M^+) 205.07389, found 205.07416.

Methyl 3-Hydroxy-3-(4-acetylphenyl)-propionate (Table 5, entry 4) White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88-7.90 (d, 2H, J = 8.4 Hz), 7.43-7.45 (d, 2H, J = 8 Hz), 5.15-5.18 (t, 1H, J = 5.2 Hz), 3.68 (s, 4H), 2.67-2.76 (m, 2H), and 2.55 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.1, 172.6, 148.1, 136.6, 128.8, 126.0, 70.0, 52.2, 43.2, and 26.8 ppm. HRMS *m/z*: Calcd for $C_{12}H_{14}O_4$ (M^+) 222.08921, found 222.08954.

Methyl 3-Hydroxy-3-(3-methylphenyl)-propionate (Table 5, entry 5) Clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23-7.27 (m, 1H), 7.20 (s, 1H), 7.15-7.17 (d, 1H, J = 7.2 Hz), 7.10-7.12 (d, 1H, J = 7.2 Hz), 5.08-5.12 (m, 1H, J = 9.2 Hz, J = 3.6 Hz), 3.72 (s, 3H), 3.40 (br, 1H), 2.67-2.80 (m, 2H), and 2.37 (s, 3H) ppm. ^{13}C NMR (110 MHz, $CDCl_3$): δ = 172.9, 142.6, 138.3, 128.6, 128.5, 126.4, 122.8, 70.4, 52.0, 43.4, and 21.6 ppm. HMRS *m/z*: Calcd for $C_{11}H_{14}O_3$ (M^+) 194.09429, found 194.09467.

Methyl 3-Hydroxy-3-(2-fluorene)-propionate (Table 5, entry 6) White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74-7.79 (m, 2H), 7.54-7.58 (m, 2H), 7.30-7.41 (m, 3H), 5.20-5.24 (dd, 1H, J = 9.2 Hz, J = 3.6 Hz), 3.88 (s, 2H), 3.75 (s, 3H), 3.38 (br, 1H), and 2.74-2.88 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0, 143.8, 143.6, 141.7, 141.5, 141.3, 127.0, 125.2, 124.6, 122.6, 120.1, 120.1, 70.8, 52.2, 43.7, and 37.1 ppm. HMRS *m/z*: Calcd for $C_{17}H_{16}O_3$ (M^+) 268.10994, found 268.11063.

Methyl 3-Hydroxy-3-(2-biphenyl)-propionate (Table 5, entry 7) Clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.70 (d, 1H, J = 7.6 Hz), 7.41-7.48 (m, 4H), 7.27-7.39 (m, 3H), 7.24-7.25 (d, 1H, J = 1.2 Hz), 5.28-5.31 (d, 1H, J = 9.6 Hz, J = 2.8 Hz), 3.65 (s, 3H), 3.48 (br, 1H), and 2.70-2.60 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.8, 140.7, 140.6, 139.8, 130.2, 129.3, 128.5, 128.1, 127.7, 127.4, 126.0, 66.7, 51.9, and 42.5 ppm. HRMS *m/z*: Calcd for $C_{16}H_{16}O_3$ (M^+) 256.10994, found 256.11029.

Methyl 3-Hydroxy-3-(4-methyl-2-thiazole)-propionate (Table 5, entry 10) Clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (s, 1H), 5.32-5.35 (dd, 1H, *J* = 8.4 Hz, *J* = 3.2 Hz), 4.48 (br, 1H), 3.71 (s, 3H), 2.85-3.09 (m, 2H), and 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.7, 172.5, 152.8, 114.0, 68.6, 52.2, 41.6, 17.3 ppm. HRMS *m/z*: Calcd for $C_8H_{11}NO_3S$ (M^+) 201.14596, found 201.04619.

Synthesis of Alumatrane-Aldehyde adduct 4. To a suspension of dimer **2** (0.5 mmol) in 20 mL of toluene was added 2 mmol of *o*-anisaldehyde. The reaction was stirred at room temperature for 1 hour to generate a yellowish solution that was concentrated under reduced pressure to form a yellow solid. The yellow solid was dissolved in 5 mL of toluene followed by the addition of 20 mL of pentane. The solution was placed in a freezer for 2 days to form yellow crystals that were suitable for X-ray analysis. ^{1}H NMR (400 MHz, C_6D_6): δ = 10.95 (s, 1H), 8.19-8.21 (d, 1H, *J* = 7.6 Hz), 7.00-7.16 (m, 4H), 6.56-6.58 (m, 4H), 6.11-6.13 (d, 1H, *J* = 8.4 Hz), 4.45 (br, 3H), 3.00 (s, 3H), 2.60 (br, 3H), 2.42 (s, 9H), and 2.28 (s, 9H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 196.8, 164.5, 155.7, 139.6, 132.0, 131.9, 130.5, 128.2, 128.1, 127.7, 126.1, 121.6, 121.5, 112.3, 59.5, 55.5, 21.2, and 17.3 ppm.

Lewis Acidity Test of Alumatrane Dimer 2. To an argon-filled 100 mL flask was added 1 mmol (134.16 mg) of triethyl phosphine oxide in 5 mL of toluene. To this solution, 1.2 equivalents of BF_3•OEt_2 (1.2 mmol, 170.32 mg) was added and then the mixture was stirred for 2 hours. Two layers (toluene and ether) formed during this period. After drying under reduced pressure, a ^{31}P NMR spectrum of the solid residue in C_6D_6 revealed a phosphorus shift at +78 ppm corresponding to the BF_3•O=PEt_3. The solid was taken into a glove box and weighed to determine the yield of BF_3•O=PEt_3 (97% based on the triethyl phosphine oxide). To this solid was added ½ an equivalent of alumatrane dimer **2** (0.48 mmol, 430.20

mg). After addition of 5 mL of toluene to the reaction mixture, the suspension was stirred for 2 hours after which a ^{31}P NMR spectrum revealed that all of the F_3B•O=PEt_3 compound disappeared. Thus only **13**•O=PEt_3 remained and no insoluble dimer **2** was observed in the solution.

Synthesis of the Boron Trifluoride Triethyl Phosphine Oxide Adduct F_3B•O=PEt_3. To a 50 mL round bottom flask in a glove box was charged 150 mg (1.12 mmol) of triethyl phosphine oxide. The reaction flask was removed from the glove box, 5 mL of toluene was added and then 190.2 mg (1.2 equiv, 1.34 mmol) of boron trifluoride diethyl ether was added under inert atmosphere. After 2 hours of stirring, the solution was dried under reduced pressure to produce analytically pure desired product in 98% isolated yield. White solid. ^{1}H NMR (400 MHz, C_6D_6): δ = 1.52-1.60 (dq, 6H, *J* = 12 Hz, *J* = 7.6 Hz) and 0.81-0.89 (dt, 9H, *J* = 18, *J* = 15.6) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 17.2 (d, *J* = 65 Hz) and 5.2 (d, *J* = 5.1 Hz) ppm. ^{31}P NMR (168 MHz, C_6D_6): δ = 78.855 ppm. ^{11}B NMR (128 MHz, C_6D_6): δ = -0.42 ppm. ^{19}F NMR (376 MHz, C_6D_6): δ = -146.43 ppm.

Synthesis of Triethylphosphine Oxide Alumatrane Adduct 13•O=PEt_3. To a 100 mL round bottom flask in a glove box was added 150 mg (1 equiv, 0.17 mmol) of alumatrane dimer **2** and 54.45 mg (2.4 equiv, 0.41 mmol) of triethyl phosphine oxide. The reaction flask was removed from the glove box and 10 mL of toluene was added. After stirring for 30 min, the solution became clear and colorless. During stirring for an additional 4 h, a white precipitate formed. The solids were filtered under inert atmosphere providing 75 mg of the desired product in 78% yield. Crystals suitable for X-ray analysis were obtained by placing the toluene extract in a freezer for two days. White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 (s, 3H), 6.67 (s, 3H), 4.32-4.36 (d, 3H, *J* = 13.6 Hz), 2.81-2.85 (d, 3H, *J* = 13.6 Hz), 2.28 (s, 18H), 2.20-2.11 (dq, 6H, *J* = 12 Hz, *J* = 7.6 Hz), and 1.45-1.37 (dt, 9H, *J* = 17.2 Hz, *J* = 16.8 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5, 130.8, 130.7, 129.3, 128.4, 127.1, 127.0, 126.6, 125.5, 124.9, 121.6, 59.2, 20.6, 18.6 (d, *J* = 68.2 Hz), 17.4, and 5.9 (d, *J* = 4.6 Hz) ppm. ^{31}P NMR (168 MHz, $CDCl_3$): δ = 63.166 ppm. APCI$^+$ found 580 (calc for $C_{35}H_{38}AlNO_5$, 579.26).

Acknowledgement

We thank the National Science Foundation for financial support in the form of grant 0750463, and we thank Dr. Arkady Ellern of the Iowa State University Molecular Structure Laboratory for the single-crystal X-ray results.

Supporting Information

Tables of detailed structural and refinement data, CIF files, references to known compounds, ^{1}H and ^{13}C NMR spectra for coupled products. This material is available free of charge via the Internet at http://pubs.acs.org. This is also available in Appendix D of this thesis.

References

1. For a referenced list of known Mukaiyama Aldol products, see supporting information.
2. Ollevier, T.; Bouchard, J.; Desyroy, V. *J. Org. Chem.* **2008**, *73*, 331-334.
3. (a) Kobayashi, S.; Matsui, S.; Mukaiyama T. *Chem. Lett.* **1988**, 1491-1494. (b) Chen, J.; Sakamoto, K.; Orita, A.; Otera, J. *J. Org. Chem.* **1998**, *63*, 9739-9745. (c) Denmark, S. E.; Fan, Y. *J. Am. Chem. Soc.* **2002**, *124*, 4233-4235. (d) Oisaki, K.; Suto, Y.; Kanai, M.;

Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 5644-5645. (d) Abe, M.; Shirodai, Y.; Nojima, M. *J. Chem. Soc., Perkin Trans I* **1998**, 3253-3260.

4. Lannou, M.; Helion, F.; Namy, J. *Tetrahedron* **2003**, *59*, 10551-10565.
5. Oisaki, K.; Suto, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 5644-5645.
6. Li, W. Z.; Zhang, X. *Org. Lett.* **2002**, *4*, 3485-3488.
7. Jankowska, J.; Paradowska, J.; Rakiel, B.; Mlynarski, J. *J. Org. Chem.* **2007**, *72*, 2228-2231.
8. Hiraiwa, Y.; Ishihara, K.; Yamamoto, H. *Eur. J. Org. Chem.* **2006**, 1837-1844.
9. Ishitani, H.; Ueno, M.; Kobayashi, S. *J. Am. Chem. Soc.* **1997**, *119*, 7153-7154.
10. Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.
11. Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.
12. Hagiwara, H.; Inoguchi, H.; Fukushima, M.; Hoshi, T.; Suzuki, T. *Tetrahedron Lett.* **2006**, *47*, 5371-5373.
13. Fujisawa, H.; Nakagawa, T.; Mukaiyama, T. *Adv. Synth. Catal.* **2004**, *346*, 1241-1246.
14. (a) Zhuang, W.; Poulsen, T. B.; Jorgensen, K. A. *Org. Biomol. Chem.* **2005**, *3*, 3284-3289. (b) Mukaiyama, T.; Fujisawa, H.; Nakagawa, T. *Helvetica Chimica Acta* **2002**, *85*, 4518-4531.
15. (a) Itsuno, S.; Arima, S.; Harauchi, N. *Tetrahedron* **2005**, *61*, 12074-12080. (b) Takeuchi, M.; Akiyama, R.; Kobayashi, S. *J. Am. Chem. Soc.* **2005**, *127*, 13096-13097.
16. Chen, S.; Ji, S. Loh, T. *Tetrahedron Lett.* **2004**, *45*, 375-377.
17. Abe, M.; Ikeda, M.; Shirodai, Y.; Nojima, M. *Tetrahedron Lett.* **1996**, *37*, 5901-5904.

18. Kloetzing, R. J.; Thaler, T.; Knochel, P. *Org. Lett.* **2006**, *8*, 1125-1128.

19. Denmark, S. E.; Ahmad, M. *J. Org. Chem.* **2007**, *72*, 9630-9634.

20. Kotani, S.; Hasimoto, S.; Nakajima, M. *Tetrahedron* **2007**, *63*, 3122-3132.

21. Aben, R. W.; Scheeren, J. W. *Synthesis* **1978**, 400-402.

22. McElvain, S. M.; Davie, W. R. *J. Am. Chem. Soc.* **1951**, *73*, 1400-1402.Ooi, T.; Tayama, E.; Takahasi, M.; Maruoka, K. *Tetrahedron Lett.* **1997**, *38*, 7403-7406.

23. Ooi, T.; Tayama, E.; Takahashi, M.; Maruoka, K. *Tetrahedron Lett.* **1997**, *38*, 7403-7406.

24. Ooi, T.; Takahashi, M.; Yamada, M.; Tayama, E.; Omoto, K.; Maruoka, K. *J. Am. Chem. Soc.* **2004**, *126*, 1150-1160.

25. Su, W.; Kim, Y.; Ellern, A.; Guzei, I. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2006**, *128*, 13727-13735.

26. Su, W.; Kobayashi, J.; Ellern, A.; Kawashima, T.; Verkade, J. G. *Inorg. Chem.* **2007**, *46*, 7953-7959.

27. Loh, T.; Feng, L.; Wei, L. *Tetrahedron* **2000**, *56*, 7309-7312.

28. Maurizio, B.; Cinquini, M.; Franco, C.; Giuseppe, C. *Organic & Biomolecular Chemistry* **2004**, *2*, 3401-3407.

29. Haruna, N.; Acosta, D. E.; Nakagawa, S.; Yamaguchi, K.; Tai, A.; Okuyama, T.; Sugimura, T. *Heterocycles* **2004**, *62*, 375-386.

30. Kamal, A.; Krishnaji, T.; Khanna, G. B. R. *Tetrahedron Lett.* **2006**, *47*, 8657-8660.

31. Fujisawa, T.; Fujimura, A.; Sato, T. *Bulletin of the Chemical Society of Japan* **1988**, *61*, 1273-1279.

32. Raders, S. M.; Verkade, J. G., manuscript in progress.

33. Novoa de Armas, Héctor; Pérez, H.; Peeters, O. M.; Balton, N. M.; de Ranter, C. J.; López, J. M. *Acta Cyrstallographica Section C* **2000**, *C56*, e98-e99.

34. Beckett, M. A.; Brassington, D. S.; Coles, S. J.; Hursthouse, M. B. *Inorganic Chemistry Communications* **2000**, *3*, 530-533.

35. Cheng, F.; Davis, M. F.; Hector, A. L.; Levason, W.; Reid, G.; Webster M.; Zheng, W. *Eur. J. Inorg. Chem.* **2007**, 2488-2495.

36. Burford, N.; Royan, B. W.; Spence, R.; Cameron, S.; Linden, A.; Rogers, R. D. *J. Chem. Soc. Dalton Trans.* **1990**, 1521-1528.

37. Burford, N.; Spence, R.; Linden, A.; Cameron, S. *Acta. Cryst.* **1990**, *C46*, 92-95.

CHAPTER 6. Pd-CATALYZED α-ARYLATION OF TRIMETHYLSILYL ENOL ETHERS WITH ARYL BROMIDES AND CHLORIDES: A SYNERGISTIC EFFECT OF TWO METAL FLUORIDES AS ADDITIVES

A paper published in *Angew. Chem. Int. Ed.* **2006**, *45*, 5852

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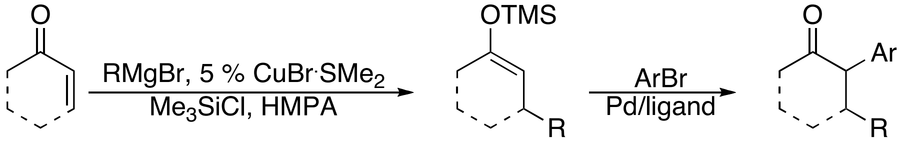
Published Manuscript

Ketone enolates are among the most common nucleophiles in organic chemistry, and transition-metal-catalyzed cross-coupling reactions are among the most commonly used catalytic processes.[1] However, the combination of these two chemistries—cross-coupling of enolate nucleophiles—has been developed only recently.[2–6] Moreover, coupling of silyl enol ethers, which temper the high basicity and nucleophilicity of alkali metal enolates,[7] is undeveloped.[8–11] The first example of the cross-coupling of silyl enol ethers was reported in 1982 by Kuwajima and Urabe, and the reactions of related tin enolates were reported by Kosugi and co-workers in 1984.[9] The reactions of silyl enol ethers were limited to the enolates of methyl ketones, and the activation of the silyl enol ether was conducted with stoichiometric tributyltin fluoride. Over the next twenty years, the scope and utility of the coupling of silyl or stannyl enol ethers has advanced only slightly.[10–12]

The cross-coupling of silyl enol ethers offers several advantages over the coupling of alkali-metal enolates of ketones. The reduced basicity should improve functional group compatibility; the defined structure of the main-group enolate could allow coupling at the more hindered site of a ketone with two enolizable positions; and conditions for the coupling of silyl enol ethers could ultimately allow the development of enantioselective processes to form acidic tertiary stereocenters.

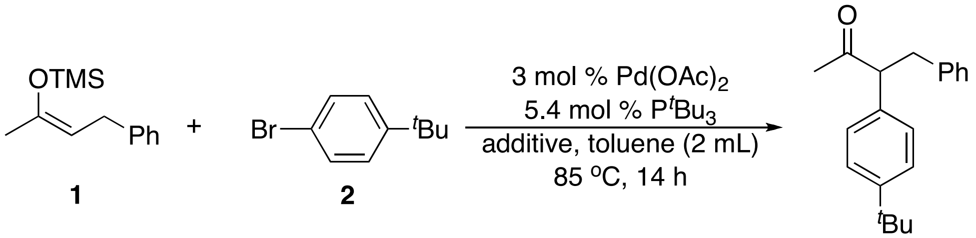
We report two protocols for the coupling of several classes of ketones with aryl bromides catalyzed by palladium and P^tBu_3. These reactions are conducted in toluene as the solvent with a combination of tributyltin fluoride and cesium fluoride as additives, or in *N*,*N*-dimethylformamide (DMF) with a combination of cesium fluoride and zinc fluoride as additives. The success of these procedures, which tolerate a variety of electrophilic functionalities and allow arylations at the more hindered position of dialkyl ketones, results from a synergistic effect[13] of two fluoride activators.

Scheme 1. One Approach to α-Arylated Carbonyl Compounds



One set of studies focused on the arylation of silyl enol ethers formed by the addition of Grignard regents to α,β-unsaturated ketones in the presence of CuBr•Me_2S, chlorotrimethylsilane, and hexamethylphosphoramide (HMPA; Scheme 1).[14] Studies of the model reaction of 2-trimethyl-siloxy-4-phenyl-2-butene (**1**) with 1-bromo-4-tert-butylbenzene (**2**) were examined with a variety of additives, ligands, solvents, and palladium sources (Table 1). In the presence of catalytic amounts of $Pd(OAc)_2$ and P^tBu_3, the reaction between 1.2 equivalents of **1** with limiting **2** in toluene in the absence of an additive did not afford the desired product in appreciable amounts (entry 1). The same reactions conducted with added Bu_3SnF formed some arylated product, but the yields were poor (entry 2). These reactions with added CsF or ZnF_2 (entries 3 and 4) formed the product in low yield, and reactions conducted with the more soluble Me_4NF apparently caused only decomposition of silyl enol ether **1** (entry 6).

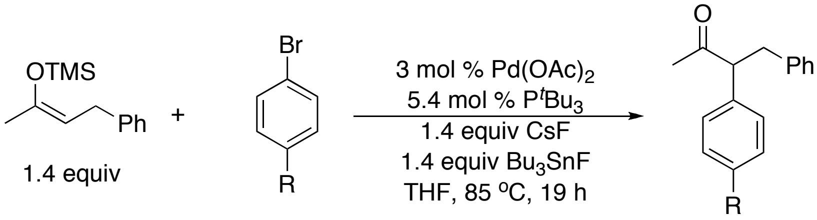
Table 1. Coupling of **1** with **2**[a]



Entry	Additive (equiv)	Ratio of **1**/**2**	Yield (%)[b]
1		1.2:1	0
2	Bu_3SnF (1.2)	1.2:1	34
3	CsF (1.2)	1.2:1	18
4	Bu_3SnF (1.2), CsF (1.2)	1.2:1	81
5	ZnF_2	1.2:1	38[c]
6	Me_4NF (1.2)	1.2:1	0
7	Bu_3SnF (1.2), CsF (1.2)	1:1.2	65
8	Bu_3SnF (1.4), CsF (1.4)	1.4:1	98
9	Bu_3SnF (0.14), CsF (1.4)	1.4:1	67
10	CsF (1.4)	1.4:1	81[d]
11	Bu_3SnF (1.4), CsF (1.4)	1.4:1	93[d]

[a] Reactions were run at 85 °C with 0.5 mmol **2** (0.25 M). [b] Yield of the isolated product (average of two runs). [c] DMF was used as the solvent. [d] THF was used as the solvent.

The reaction of 1.4 equivalents of **1** with **2** in THF containing CsF as the additive afforded the desired product in a high yield of 81 % (entry 10), but the functional-group tolerance of reactions with CsF alone was similar to that of reactions of alkali-metal enolates. For example, reactions of **1** with 1-bromo-4-nitrobenzene and 4'-bromoacetophenone in THF afforded only 40 and 10 % yields, respectively [Eq. (1)].



(1)

Values in parenthesis are yields obtained without Bu_3SnF

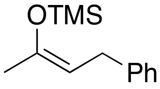
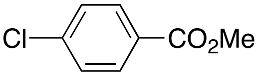
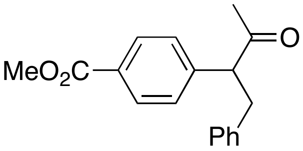
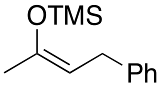
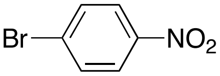
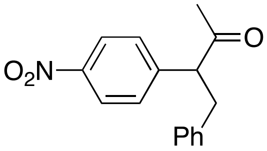
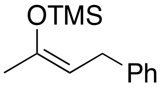
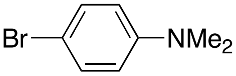
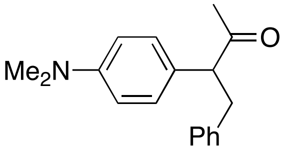
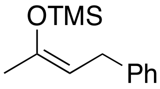
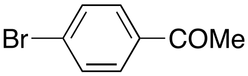
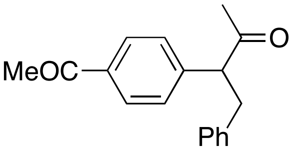
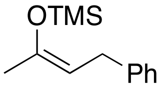
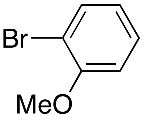
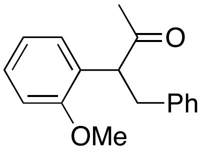
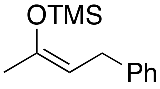
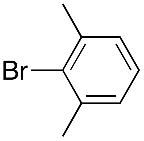
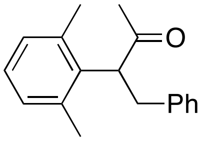
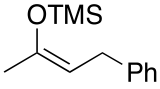
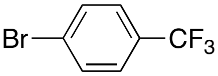
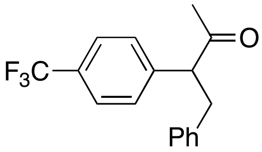
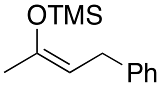
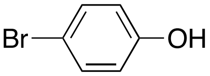
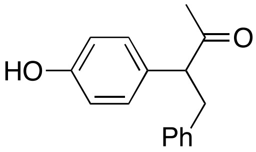
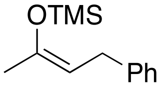
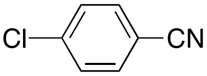
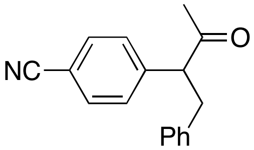
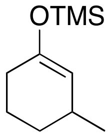
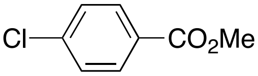
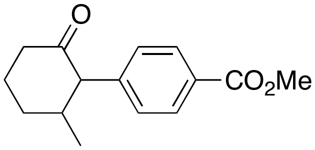
R = NO_2: yield: 87% (40%)

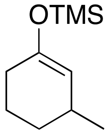
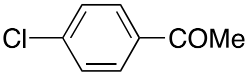
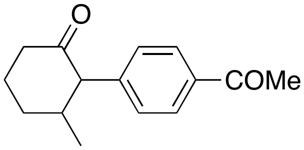
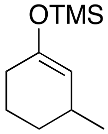
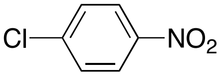
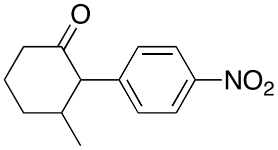
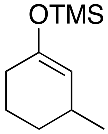
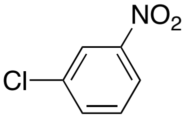
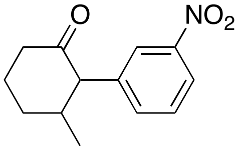
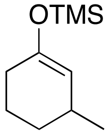
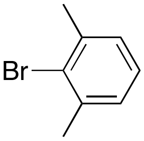
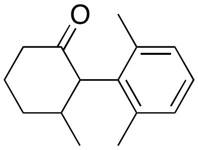
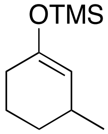
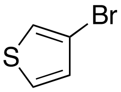
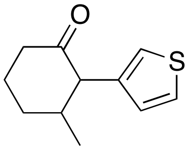
R = COMe: yield: 60% (10%)

In contrast, reactions conducted with a combination of Bu_3SnF and CsF as additives occurred in high yields (entry 4) and with a broad scope (see below). Reactions conducted with a catalytic amount of Bu_3SnF (10 mol % based on the silyl enol ether) and 1 equivalent of CsF afforded the desired product in 67 % yield (entry 9). Altering the ligand, palladium precursor, and solvent did not further improve the reaction (reactions in toluene and THF occurred in comparable yields), but increasing the amount of the silyl enol ether and additive (1.4:1.4:1.4:1 ratio of the two additives, enol **1**, and aryl halide **2**) led to formation of the coupled product in 98 % yield (entry 8).

Table 2 illustrates the scope of the reactions under the conditions of entry 8 in Table 1 with Bu_3SnF and CsF as the additives. Both acyclic and cyclic silyl enol ethers smoothly underwent coupling at 85–90 °C with a wide variety of aryl bromides and chlorides to form α-arylated ketones in good-to-excellent yields. These weakly basic conditions were compatible with ester, nitro, cyano, and keto substituents. Both sterically hindered aryl bromides and heterocyclic aryl bromides, such as 3-bromothiophene, served as coupling partners.

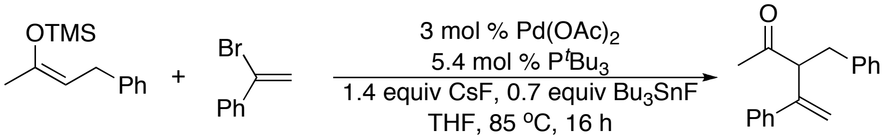
Table 2. Scope of the Arylation of a Trimethylsilyl Enol Ether[a]

Entry	Silyl Enol Ether	Halide	Products	Yield (%)[b]
1				89[c]
2				84
3				96
4				97
5				97
6				93
7				91
8				55
9				80[c]
10				80[c]

11				70^{c}
12				84
13				77^{c}
14				85
15				78

[a] Reactions were run under the conditions of entry 8 in Table 1 for 12 – 20 h. [b] Yield of the isolated product (average to two runs). [c] Reaction run at 90 °C

The coupling between a vinyl bromide and a silyl enol ether under these conditions was tested briefly [Eq. (2)].[15] The combination of 3 mol % $Pd(OAc)_2$ and 5.4 mol % P^tBu_3 catalyzed the coupling of α-bromostyrene with **1** in THF in the presence of 1.4 equivalents of CsF and 0.7 equivalents of Bu_3SnF (based on the amount of silyl enol ether) in 66 % yield. Considering the stoichiometric amounts of tin reagent in the couplings of Table 2 and the toxicity of tin, other combinations of metal fluorides were examined to promote the couplings of silyl enol ethers. One of us recently reported that the combination of CsF and ZnF_2 promotes the asymmetric iridium-catalyzed allylation of silyl enol ethers with allylic carbonates.[16] Thus, we investigated the combination of ZnF_2 with other metal fluorides as promoters for the palladium-catalyzed coupling of silyl enol ethers with bromoarenes.

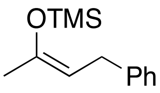
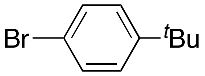
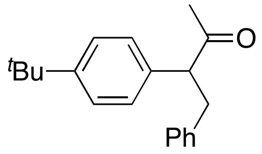
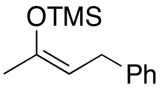
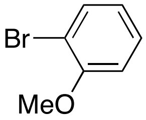
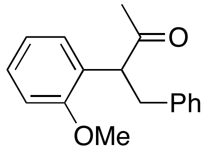
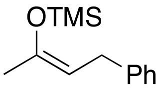
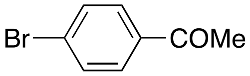
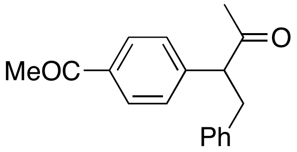
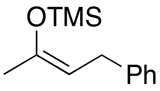
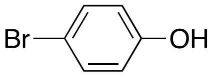
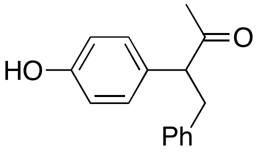
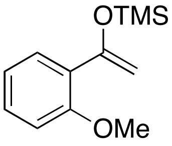
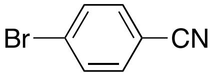
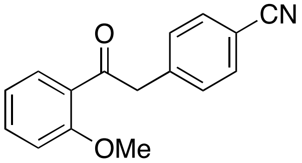
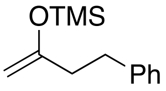
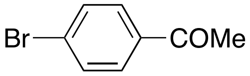
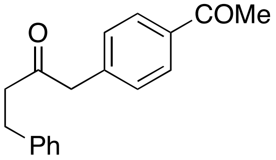
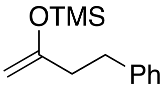
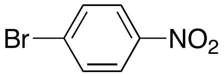
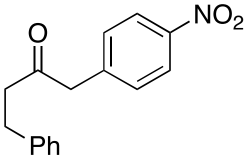
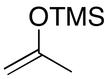
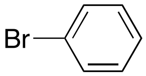
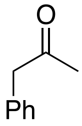


(2)

The results of experiments to develop reaction conditions with the metal fluoride additives are provided in the Supporting Information. Experiments on the coupling of **1** with 4-bromoacetophenone showed that conditions could be developed for the coupling of silyl enol ethers with aryl bromides in high yield and in the presence of the combination of stoichiometric amounts of ZnF_2 and either CsF or MnF_2 as additives. These reactions occurred in much higher yield in the polar DMF than the less polar toluene and with $Pd(dba)_2$ (dba = dibenzylideneacetone) as the precursor than $Pd(OAc)_2$. Reactions carried out in DMF with $Pd(dba)_2$ and $P^{t}Bu_3$ as the catalyst with stoichiometric amounts of ZnF_2 and CsF occurred in lower yields than reactions with stoichiometric amounts of ZnF_2 and 0.4 equivalents of CsF. Reactions with stoichiometric ZnF_2 and substoichiometric CsF as additives occurred with high functional-group tolerance (see below). However, this combination of metal fluorides led to diarylation of the silyl enol ethers of methyl ketones. Selective monoarylation of silyl enol ethers of ketones was achieved instead when the reactions were carried out with the combination of ZnF_2 and MnF_2 as additives.

Several examples of the $Pd(dba)_2/P^{t}Bu_3$-catalyzed reactions of silyl enol ethers promoted by catalytic CsF or MnF_2 and stoichiometric ZnF_2 are shown in Table 3. Most generally, these data illustrate the same two beneficial effects of conducting the coupling of silyl enol ethers in the presence of these fluoride activators, as was observed from the use of Bu_3SnF and CsF as additives: The product from the reaction of the silyl enol ether 2-siloxy-1-butene was formed by monoarylation of the methyl group with aryl halides that contained functionalities intolerant of the basic conditions of the couplings of alkali-metal enolates, and reactions of the more substituted silyl enol ethers of an alkyl ketone regioselectively formed the product from arylation at the more hindered enolizable position.

Table 3. Scope of the Palladium-Catalyzed Arylation of Trimethylsilyl Enol Ethers in the Presence of ZnF_2 and CsF or MnF_2

Entry	Silyl Enol Ether	Halide	Product	Yield (%)
1				89^{a}
2				87^{a}
3				90^{a}
4				53^{a}
5				78^{b}
6				$71^{b,c}$
7				$64^{d,e}$
8				$68^{f,g}$

[a]Reaction conditions: aryl halide (1.0 equiv), silyl enol ether (1.4 equiv), zinc fluoride (1.4

equiv), cesium fluoride (0.4 equiv), $Pd(dba)_2$ (3 mol %), and P^tBu_3 (5.4 mol %), 85 °C; DMF (1 mL) was added per 0.2 mmol of aryl halide. [b]Reaction conditions: aryl halide (1.0 equiv), silyl enol ether (1.5 equiv), zinc fluoride (1.0 equiv), manganese fluoride (0.4 equiv), $Pd(dba)_2$ (2 mol %), and P^tBu_3 (4 mol %), 70 °C; DMF (1 mL) was added per 0.2 mmol of aryl halide. [c]The ratio of mono/diarylation was 5.5:1. [d]Reaction conditions: aryl halide (1.0 equiv), silyl enol ether (1.5 equiv), zinc fluoride (1.4 equiv), manganese fluoride (1.4 equiv), $Pd(dba)_2$ (3 mol %), and P^tBu_3 (5.4 mol %), 60 °C; DMF (1 mL) was added per 0.2 mmol of aryl halide. [e]The ratio of mono/diarylation was 4:1. [f]Reaction conditions: aryl halide (1.0 equiv), silyl enol ether (5.0 equiv), zinc fluoride (1.4 equiv), manganese fluoride (1.4 equiv), $Pd(dba)_2$ (3 mol %), and P^tBu_3 (5.4 mol %), 70 °C; DMF (2 mL) was added per 0.2 mmol of aryl halide. [g]The ratio of mono/diarylation was 5.5:1.

The first two examples (Table 3, entries 1 and 2) show that similar yields for reactions of electron-neutral and ortho-substituted bromoarenes are obtained for reactions containing tin fluoride as an additive. Entries 3 and 4 show that these conditions allow the coupling of bromoarenes with functionalities that are not tolerated by the basic alkali-metal enolates. Hydrolysis of the silyl enol ether during the reaction of bromophenol did limit the yield of entry 4, but substantial quantities of coupled product were formed. Entries 5–7 show examples of the selective monoarylation of the silyl enol ether of 4-phenyl-2-butanone with bromoarenes that are intolerant of alkali-metal enolates. Finally, entry 8 (Table 3) shows the first coupling of an enolate of acetone without tin reagents. Diarylation to form 1,1-diphenylacetone competed with the monoarylation in this case, but the use of excess silyl enol ether led to the formation of a-aryl acetone in good yield.

In summary, the combination of two metal fluorides synergistically promotes the coupling of silyl enol ethers with aryl bromides and chlorides. Two procedures are presented, each with certain advantages: reactions containing CsF and tributyltin fluoride occur in nonpolar solvents, whereas the reactions containing either ZnF_2/MnF_2 or ZnF_2/CsF occur without tin. All the reactions appear to occur without cleavage to form alkali-metal enolates, thus providing a mild and selective methodology for the preparation of α-aryl ketones. Studies to determine the origin of the synergistic effect, which remains unclear at this time, will be the subject of future studies.

Acknowledgement

J.G.V. gratefully acknowledges the National Science Foundation for financial support of this investigation, and J.F.H. thanks the NIH (NIGMS GM-58108). The authors thank Professor Robert Angelici for helpful discussions.

Supporting Information

Supporting information for this article is available on the WWW under http ://www.angewandte.org or from the author. This is also available in the appendix E in this thesis.

References

[1] a) A. de Meijere, F. Diederich, *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH, Weinheim, **2004**; b) E. Negishi, *Handbook of Organopalladium Chemistry for Organic Synthesis,* Wiley, Hoboken, **2002**.

[2] a) D. Culkin, J. F. Hartwig, *Acc. Chem. Res.* **2003**, *36*, 234 ; b) M. Miura, M. Nomura, *Top. Curr. Chem.* **2002**, *219*, 211.

[3] a) M. Palucki, S. L. Buchwald, *J. Am. Chem. Soc.* **1997**, *119*, 11108; b) B. C. Hamann, J. F. Hartwig, *J. Am. Chem. Soc.* **1997**, *119*, 12382; c) M. Kawatsura, J. F. Hartwig, *J. Am. Chem. Soc.* **1999**, *121*, 1473; d) J. M. Fox, X. H. Huang, A. Chieffi, S. L. Buchwald, *J. Am.*

Chem. Soc. **2000**, *122*, 1360; e) T. Satoh, Y. Kawamura, M. Miura, M. Nomura, *Angew. Chem.* **1997**, *109*, 1820; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1740; f) J. L. Rutherford, M. P. Rainka, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 15168; g) M. S. Viciu, R. F. Germaneau, S. P. Nolan, *Org. Lett.* **2002**, *4*, 4053; h) D. SolØ, L. Vallverdﬄ, X. Solans, M. Font-Bardia, J. Bonjoch, *J. Am. Chem. Soc.* **2003**, *125*, 1587; i) A. Ehrentraut, A. Zapf, M. Beller, *Adv. Synth. Catal.* **2002**, *344*, 209; j) T. Satoh, Y. Kametani, Y. Terao, M. Miura, M Nomura, *Tetrahedron Lett.* **1999**, *40*, 5345; k) Y. Terao, Y. Kametani, H. Wahui, T. Satoh, M. Miura, M Momura, *Tetrahedron* **2001**, *57*, 5967.

[4] a) M. Jørgensen, S. Lee, X. Liu, J. P. Wolkowski, J. F. Hartwig, *J. Am. Chem. Soc.* **2002**, *124*, 12 557; b) W. A. Moradi, S. L. Buchwald, *J. Am. Chem. Soc.* **2001**, *123*, 7996; c) S. Lee, N. A. Beare, J. F. Hartwig, *J. Am. Chem. Soc.* **2001**, *123*, 8410.

[5] a) N. A. Beare, J. F. Hartwig, *J. Org. Chem.* **2002**, *67*, 541; b) S. Lee, J. F. Hartwig, *J. Org. Chem.* **2001**, *66*, 3402 ; c) J. Cossy, A. Filippis, D. G. Pardo, *Org. Lett.* **2003**, *5*, 3037.

[6] T. Hamada, A. Chieffi, J. Ahman, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 1261.

[7] I. Fleming, A. Barbero, D. Walter, *Chem. Rev.* **1997**, *97*, 2063.

[8] I. Kuwajima, H. Urabe, *J. Am. Chem. Soc.* **1982**, *104*, 6831.

[9] M. Kosugi, I. Hagiwara, T. Sumiya, T. Migita, *Bull. Chem. Soc. Jpn.* **1984**, *57*, 242.

[10] For a recent coupling of a diphenyl bisenol ether, see : J. Chae, J. Yun, S. L. Buchwald, *Org. Lett.* **2004**, *6*, 4809.

[11] For coupling of silyl ketene acetals, see : a) T. Hama, X. Liu, D. A. Culkin, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 11176; b) X. Liu, J. F. Hartwig, *J. Am. Chem. Soc.* **2004**, *126*, 5182.

[12] For activation of silyl ketene acetals of an acetate, see : F. Agnelli, G. A. Sulikowski,

Tetrahedron Lett. **1998**, *39*, 8807.

[13] A synergistic effect of the combination of CsF and CuI as additives has been observed in the promotion of Stille coupling reactions ; see : S. P. H. Mee, V. Lee, J. E. Baldwin, *Angew. Chem.* **2004**, *116*, 1152; *Angew. Chem. Int. Ed.* **2004**, *43*, 1132.

[14] S. Matsuzawa, Y. Horiguchi, E. Nakamura, I. Kuwajima, *Tetrahedron* **1989**, *45*, 349.

[15] For the palladium-catalyzed intermolecular vinylation of ketones, see: Ref. [6]; A. Chieffi, K. Kamikawa, J. Ahman, J. M. Fox, S. L. Buchwald, *Org. Lett.* **2001**, *3*, 1897; for the palladium-catalyzed intramolecular vinylation of ketones, see: a) T. Wang, J. M. Cook, *Org. Lett.* **2000**, 2057; b) D. SolØ, E. Peidró, J. Bonjoch, *Org. Lett.* **2000**, *2*, 2225 ; c) D. SolØ, F. Diaba, J. Bonjoch, *J. Org. Chem.* **2003**, *68*, 5746; d) D. SolØ, X. Urbaneja, J. Bonjoch, *Adv. Synth. Catal.* **2004**, *346*, 1646.

[16] T. Graening, J. F. Hartwig, *J. Am. Chem. Soc.* **2005**, *127*, 17192.

CHAPTER 7. ADVANTAGEOUS USE OF $^{t}\mathrm{Bu_2P\text{-}N{=}P(^{i}BuNCH_2CH_2)_3N}$ IN THE HIYAMA COUPLING OF ARYL BROMIDES AND CHLORIDES

A manuscript submitted to the *Journal of Organic Chemistry*

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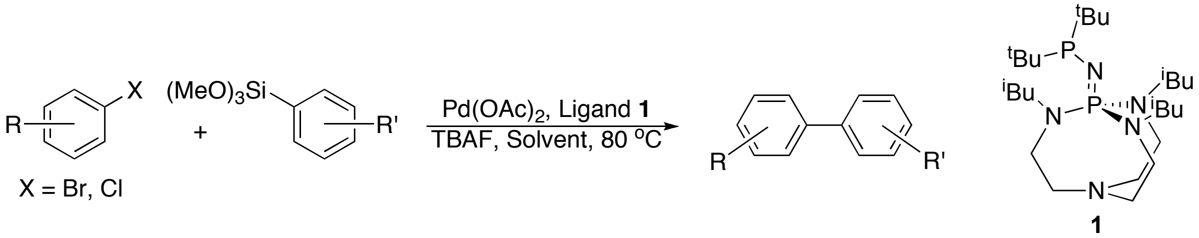
Abstract



An efficient catalytic route to biaryls employing (generally) only 0.25 mole % $Pd(OAc)_2$ and 0.5 mole % 1 in the Hiyama coupling is reported (see scheme). The reaction proceeds in high yields for electron rich, neutral, and deficient aryl chlorides. A variety of phenylsiloxanes also undergo coupling with aryl bromides at the above low $Pd(OAc)_2$ /1 loadings.

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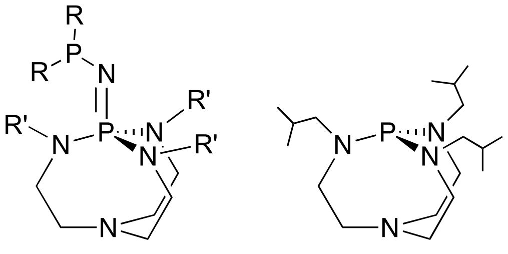
Palladium-catalyzed C-C bond-forming reactions are exceedingly useful in modern organic synthesis. Biaryls (constituents of aromatic polymers, liquid crystals, natural products and pharmaceuticals) can be synthesized using, e.g., Pd-catalyzed Suzuki,[1] Negishi,[2] Kumada,[3] Hiyama[4] and Stille[5] reactions. Despite the toxicity and relatively expensive organotin reagents, the Stille reaction remains popular especially because of its utility in the stereoselective coupling of vinyl- and alkenylstannanes.[6]

The potentially most attractive of the aforementioned methodologies is Hiyama cross coupling because organosilicon reagents are commercially available at relatively low cost or can be easily prepared. These reagents also are non-toxic, and quite stable to the presence of other functionalities and to a variety of reaction conditions. However, because organosilanes are comparatively unreactive nucleophiles, Hiyama coupling has not yet replaced Stille and Suzuki methodologies.[1,4,5] For example, in contrast to Suzuki, Kumada and Stille methodologies, there is presently no general method for cross-coupling considerably cheaper, more widely available aryl chlorides with organosilicon compounds.

Hiyama and co-workers showed that aryl(ethyl)dichlorosilanes could be coupled with activated aryl chlorides to give good yields of coupled product after 24 – 48 hours at 120ºC in DMF.[4b] Deshong and Mowery developed a useful protocol for coupling aryl bromides and iodides with siloxane derivatives, which have been touted as the most convenient organosilanes for Hiyama cross-coupling.[4c] However, challenges with aryl chlorides were encountered in that work. Recently, an efficient method for producing biaryls from mesityl-protected aryl alcohols and aryl siloxanes using 2 mole % $Pd(OAc)_2$ and 8 mole % CM-phos.[7] Ligands such as PPh_3, $(^tBu)_3P$ and $^tBu_2P$-biphenyl, were completely ineffective. Even Cy_2P-biphenyl/Pd_2dba_3 (the most effective catalyst utilized by Buchwald for a range of aryl chloride cross-couplings[4c]) produced only a 47% yield of product in the cross-coupling of $PhSi(OMe)_3$ with 4-chloroacetophenone using 10 mol % Pd_2dba_3.[4c] It has been reported that an imidazolium chloride/$Pd(OAc)_2$ catalyst was more useful than Cy_2P-biphenyl/Pd_2dba_3 for three activated aryl chlorides, but unactivated substrates such as 4-chloroanisole gave poor yields.[4f] $PdCl_2(CH_3CN)_2$ in the presence of β-diimine ligands for the coupling of 4-chloroacetophenone with $PhSi(OMe)_3$ afforded only a 62% yield of product.[8]

Figure 1. Some phosphines Synthesized in our Laboratory



1: R = ^{t}Bu, R' = ^{i}Bu
2: R = Ph, R' = ^{i}Bu
3: R = ^{t}Bu, R' = Me

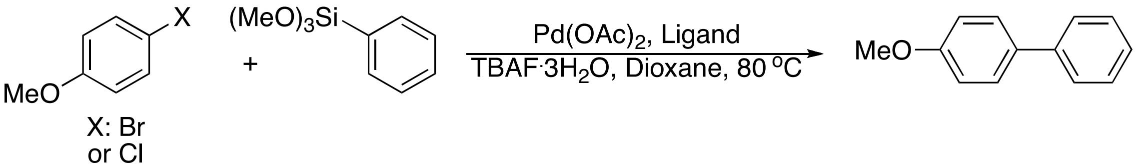
4

Recently we reported the synthesis of the bulky phosphine **1** (Figure 1) and showed it to be effective in Suzuki-Miyaura cross-coupling reactions, giving high yields of desired biaryls in the presence of 1 mole % $Pd(OAc)_2$ and 2 mole % **1**.[9] Ligand **1** features a bulky imino-proazaphosphatrane moiety that provides electron richness to the ^{t}Bu$_2$P via donation from the "equatorial" ^{i}BuN and from potential transannulation from the basal planar N.[9] Here we show the usefulness of **1** in the Hiyama coupling of a variety of aryl bromides and chlorides to obtain high yields of biaryls with low loadings of Pd (0.25-1.0 mol %) and **1** (0.5-2.0 mol%).

4-Chloroanisole is the most recalcitrant aryl halide substrate in Hiyama coupling with $PhSi(OMe)_3$. A 40% product yield was obtained using 10 mole % $PdCl_2(CH_3CN)_2$ and 20 mole % P(*o*-tol)$_3$ in toluene at 80 °C.[10] In the presence of 3 mole % $Pd(OAc)_2$ and 6 mole % DABCO, only 20% of the desired product was obtained after 24 hours at 80 °C.[11] The highest reported yield (93%) was achieved using microwaves at 120 °C for 10 minutes in the presence of 1 mole % of an oxime-derived palladacycle.[12] Under the conditions in entry 1 of

Table 1, we received an 87% yield of product using ligand **1**. Using Pd_2dba_3 or $Pd(dba)_2$ decreased the product yield, owing to the formation of Pd black. Increasing the temperature accelerated the formation of Pd black and also decreased product yield. Lower temperatures decreased the amount of Pd black, but decreased product yields were also observed.

Table 1. Optimization Study

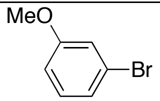
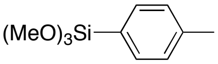
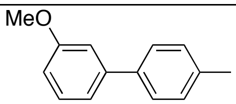
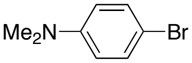
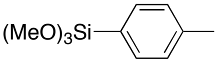
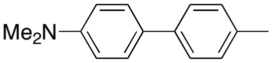
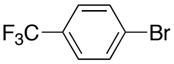
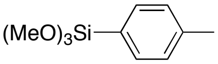
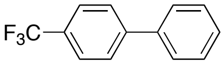
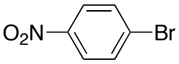
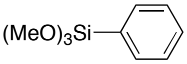
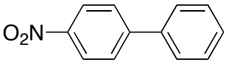
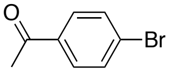
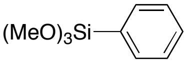
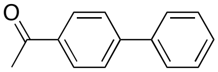
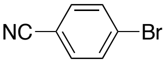
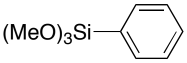
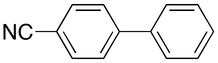
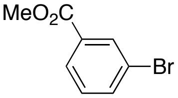
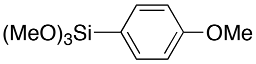
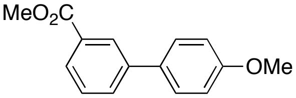
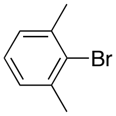
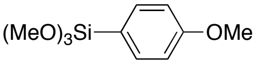
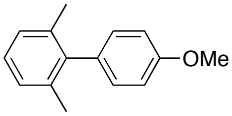
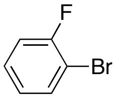
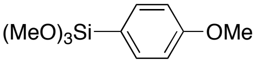
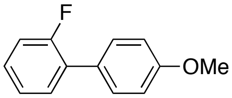
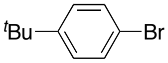
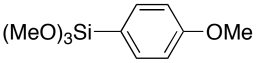
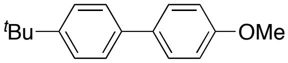
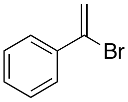
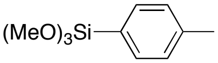
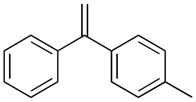


Entry	Aryl Halide	Solvent	$Pd(OAc)_2$ (mole %)	Ligand (mole %)	Yield (%)[a]
1	Cl	Dioxane	1.0	**1** (2.0)	86
2	Cl	THF	1.0	**1** (2.0)	64
3	Cl	Dioxane	0.5	**1** (1.0)	81
4	Cl	Dioxane	0.25	**1** (0.5)	56
5	Cl	Dioxane	0.5	**2** (2.0)	6
6	Cl	Dioxane	0.5	**3** (2.0)	42
7	Cl	Dioxane	0.5	**4** (2.0)	0
8	Cl	Dioxane	0.5	**1** (0.5)	70
9	Cl	Neat	0.5	**1** (1.0)	81
10	Br	Neat	0.5	**1** (1.0)	93
11	Br	Neat	0.25	**1** (0.5)	87

[a] Reaction conditions: 2 mmol 4-chloroanisole, 4 mmol trimethoxyphenylsilane, 3.5 mmol base, 5 mL solvent, time: 2.5 h.

Other fluoride sources (e.g., CsF and Bu_3SnF) were ineffective in our protocol. Only low product yields were obtained with phosphine analogues **2** and **3** (Table 1, entries 5 and 6) and **4** was completely ineffective (entry 7). Changing the Pd:L ratio from 1:2 to 1:1, gave a moderate product yield of 70% (Table 1, entry 8). When both reactants are liquids, the reaction could be carried out in the absence of solvent to achieve the same yield as in entry 3 (entry 9). When 4-bromoanisole was coupled, an excellent yield of desired biaryl was achieved (entry 10). Decreasing the palladium loading to 0.25 mole % decreased product yield by only 6% (entry 11).

Table 2. Scope of Aryl Bromides

Entry	Aryl Bromide	Siloxane	Time	Product	Yield (%)[a,b]
1			3 h		91[c] (Lit: 80)
2			5 h		71[d]
3			2 h		93[e] (Lit:87-99)
4			2 h		91[e] (Lit: 51-93)
5			2 h		91[e] (Lit: 55-99)
6			2 h		84[e] (Lit: 85)
7			1.5 h		87[f]
8			2 h		89[g]
9			0.5 h		83[c]
10			0.5 h		85[c]
11			1 h		78[c]

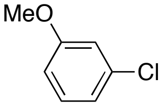
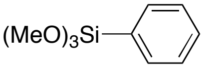
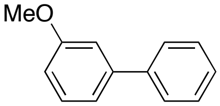
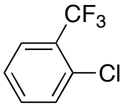
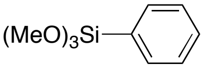
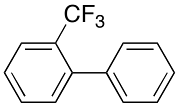
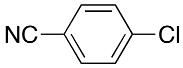
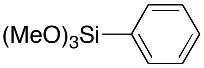
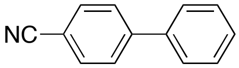
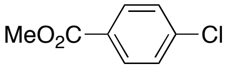
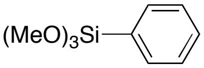
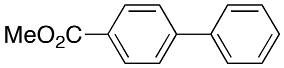
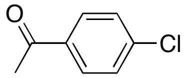
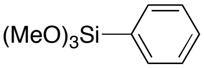
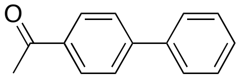
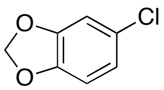
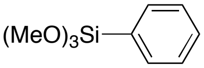
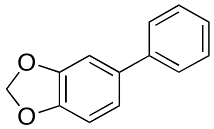
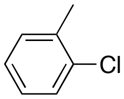
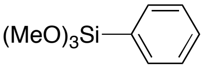
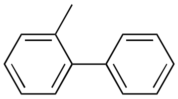
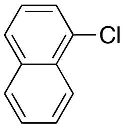
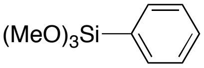
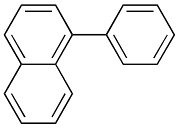
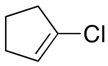
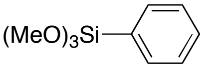
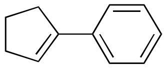
[a] Average of two runs. Yields in parenthesis correspond to isolated yields. [b] Reaction conditions: 2 mmol aryl bromide, 4 mmol siloxane, 3 mmol TBAF-3H_2O. [c] 0.5 mole % Pd$(OAc)_2$, 1 mole % **1**, neat. [d] 1 mole % Pd$(OAc)_2$, 2 mole % **1**, 5 mL dioxane. [e] 0.5 mole % Pd$(OAc)_2$, 1 mole % **1**, 5 mL dioxane. [f] 0.25 mole % Pd$(OAc)_2$, 0.5 mole % **1**, 5 mL dioxane. [g] 1 mole % Pd$(OAc)_2$, 2 mole % **1**, neat.

With the low catalyst loading in Table 1, entry 11, we investigated a variety of aryl bromides (Table 2). All the products in Table 2 have been reported previously using other coupling approaches, although the products in Table 2, entries 1, 3-6 and 8; those in Table 3, entries 1, 2 and 5; and the product in Table 4, entry 2 have also been reported earlier via Hiyama coupling (see corresponding references in the last column of these tables). Pleasingly, a wide range of aryl bromides can be coupled with a variety of siloxanes. For example, electron rich aryl bromides bearing OMe or NMe_2 substituents are coupled with *p*-tolyltrimethoxysilane in moderate to excellent product yields (Table 2, entries 1 and 2), Electron deficient aryl bromides containing CF_3, NO_2, COMe, or CN substituents are also easily coupled with $PhSi(OMe)_3$ in good to excellent yields (Table 2, entries 3-6). Surprisingly, methyl 3-bromobenzoate was coupled to *p*-methoxyphenyltrimethoxysilane in 87% yield in the presence of only 0.25 mole % $Pd(OAc)_2$ and 0.50 mole % of **1** (Table 2, entry 7).

With some Hiyama catalyst systems, aryl bromides bearing an ortho methyl or phenyl group have provided only low to moderate yields of products.[7,8,10,11,13] Here, sterically hindered 2-bromo-*m*-xylene coupled with *p*-methoxyphenyltrimethoxysilane to give an 89% product yield (Table 2, entry 8). α-Bromostyrene coupled well with *p*-tolyltrimethoxysilane in the absence of solvent to produce a 78% product yield (Table 2, entry 12).

We next focused on aryl chloride substrates (Table 3). Aryl chlorides are generally quite refractory in palladium-assisted coupling reactions owing to their reluctance to oxidatively add to Pd(0).[14] Hence, only aryl chlorides with highly deactivating substituents tend to undergo coupling with aryl siloxanes.[8,10,11,13,15] Activated aryl chlorides generally lead to low to moderate yields.[10,11,13,15a-b] Here, ligand **1** effectively facilitates coupling of not only electron deficient aryl chlorides under low catalyst loadings, but also electron rich and sterically hindered aryl chlorides. Aryl chlorides with electron withdrawing groups such as CF_3, CN, C(O)OMe, and C(O)Me are efficiently coupled to $PhSi(OMe)_3$ in excellent yields in the presence of only 0.5 mole % $Pd(OAc)_2$ and 1 mole % **1** (Table 3, entries 3-5). The coupling of 2-chlorotrifluorotoluene with $PhSi(OMe)_3$ proceeded smoothly with 1 mol % $Pd(OAc)_2$ and 2 mole % **1** to provide 82% of the desired product (entry 2). This is the first time that the products in entries 2-4 have been made from an aryl chloride via Hiyama coupling.

Table 3. Scope of Aryl Chlorides

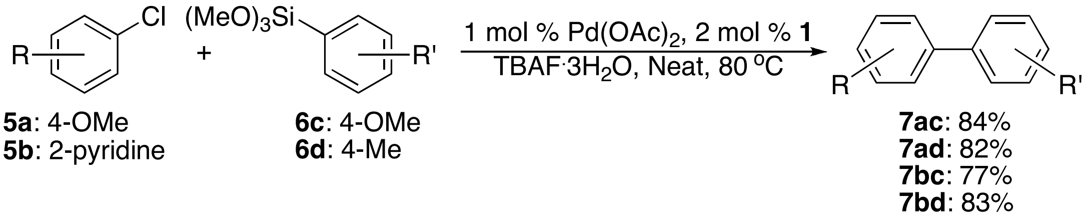
Entry	Aryl Chloride	Siloxane	Time	Product	Yield (%)[a,b]
1			1.5 h		87[c] (Lit: 25)
2			3 h		82[d]
3			2 h		93[e]
4			2 h		95[e]
5			1.5 h		95[e] (Lit: 62-99)
6			2 h		90[c]
7			2 h		87[d]
8			1 h		83[d]
9			0.5 h		91[c]

[a] Average of two runs. Yields correspond to isolated yields. [b] Reaction conditions: 2 mmol aryl chloride, 4 mmol siloxane, 3 mmol TBAF-$3H_2O$, neat, time: 0.5-2 h. [c] 0.5 mole % $Pd(OAc)_2$, 1 mole % **1**, neat. [d] 1 mole % $Pd(OAc)_2$, 2 mole % **1**, neat. [e] 0.5 mole % $Pd(OAc)_2$, 1.0 mole % **1**, 5 mL dioxane.

Electron rich aryl chlorides were coupled with $PhSi(OMe)_3$ with surprising efficiency. Thus 3-chloroanisole underwent coupling to give 87% of the biaryl product in 1.5 hours (Table 3, entry 1). This biaryl was made only once previously in a Hiyama coupling in which only 25% of the desired product was obtained via the reaction of 3-chloroanisole with $PhSi(OMe)_3$ in the presence of 5 mole % $Pd(acac)_2$ and 5 mole % of a phosphite [3-Me-2,6-$t$$Bu_2C_6H_2OP(OCH_2)_2]_2C$ in *p*-xylene at 120 °C.[13a] The electron rich aryl chloride 5-chloro-1,3-benzodioxole underwent coupling in 90% isolated yield (Table 3, entry 6).

Sterically demanding aryl bromides are difficult substrates in some catalytic Hiyama approaches, leading to only moderate yields of the corresponding coupled products.[7,8,10,11,13] Thus sterically encumbered aryl chlorides might be predicted to be even more problematic in this respect. However, using only 1 mole % $Pd(OAc)_2$/2 mole % **1**, 2-chlorotoluene and 1-chloronaphthalene were coupled with $PhSi(OMe)_3$ in good yields (87% and 83%, respectively, Table 3, entries 7 and 8). Even 1-chlorocyclopentene was coupled with $PhSi(OMe)_3$ using only 0.5 mole % $Pd(OAc)_2$/1 mole % **1**, producing a 91% product yield (entry 9). To the best of our knowledge, this is the first time 1-chlorocyclopentene has been used for Hiyama coupling.

Scheme 1.

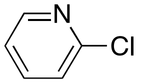
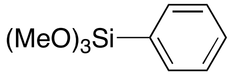
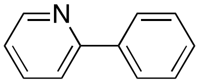
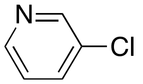
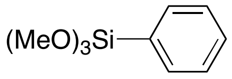
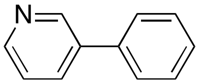
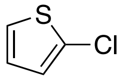
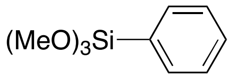
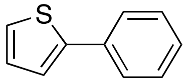


Reaction conditions: 2 mmol aryl chloride, 4 mmol siloxane, 3 mmol $TBAF\cdot 3H_2O$, time: 2 h.

The usefulness of our catalytic system also applies to the coupling of 4-chloroanisole and 2-chloropyridine which were coupled with *p*-methoxyphenyltrimethoxysilane and *p*-

tolyltrimethoxysilane in the presence of 1 mole % Pd(OAc)$_2$ and 2 mole % **2** to give moderate to good product yields (Scheme 1).

Table 4. Scope of Heterocyclic Chlorides

Entry	Aryl Chloride	Siloxane	Time	Product	Yield (%)^{a,b}
1			2 h		81^{c}
2			1.5 h		82^{d} (Lit: 63-92)
3			1 h		95^{c}

^{a}Average of two runs. Yields correspond to isolated yields. ^{a}Reaction conditions: 2 mmol aryl chloride, 4 mmol siloxane, 0.5 mole % Pd(OAc)$_2$, 1 mole % **1**, 3 mmol TBAF, time: 0.5-2 h. ^{c}Neat conditions. ^{d}5 mL dioxane.

Next, we turned our focus to heterocyclic aryl chlorides (Table 4). Only a few literature reports on the use of heterocyclic aryl chlorides in Hiyama coupling have appeared.[12,15c] Here, we show that such substrates couple well with PhSi(OMe)$_3$, in the presence of 0.5 mole % Pd(OAc)$_2$/1 mole % **1**. Thus, 2-chloropyridine and 2-chlorothiophene underwent coupling to give 81 and 95% isolated product yield, respectively, in the absence of solvent (Table 3, entries 1 and 3). When dioxane was used as solvent, GC revealed very low conversion to product. To the best of our knowledge, this is the first time these products have been made from a heterocyclic aryl chloride via Hiyama coupling. When 3-chloropyridine was coupled with PhSi(OMe)$_3$, dioxane was required to suppress the rate of Pd black production until the starting material was consumed. After 1.5 hours, an 82% yield of the desired biaryl was isolated (Table 3, entry 2). The highest reported literature yield for this reaction was 92% which was obtained using 1 mole % of an oxime-derived palladcycle under microwave conditions at 120 °C.[12]

Herein we have demonstrated the wide utility of low loadings of $Pd(OAc)_2$/**1** (generally 0.25 mole % $Pd(OAc)_2$ and 0.5 mole % **1**) and relatively mild conditions (generally 80° C for 0.5-3 hours) for coupling a wide range of aryl bromides and chlorides with phenylsiloxanes. These reactions are characterized by generally good to excellent product yields. Further work directed at expanding the substrate scope is currently underway.

Acknowledgement

We thank the National Science Foundation for a grant (0750463) in support of this work.

Supporting Information

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author. This is also available in appendix F of this thesis.

References

1. a) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979,** 3437; b) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263; c) Suzuki, A. *Pure Appl. Chem.* **1991**, *63*, 419; d) Wolfe, J. P.; Buchwald, S. P. *Angew. Chem. Int. Ed.* **1999**, *38*, 2413; e) Zapf, A.; Beller, M. *Chem. Eur. J.* **2000**, 6, 1830; f) Bedford, R. B.; Cazin, C. S. J.; Coles, S. J.; Gelbrich, T.; Horton, P. N.; Hursthouse, M. B.; Light, M. E. *Organometallics* **2003**, *22*, 987.

2. a) Baba, S.; Negishi, E. *J. Am. Chem. Soc.* **1976**, *98*, 6729; b) Dai, C.; Fu. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719.

3. a) Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 4374; b) Herrmann, W. A.; Bohm, V. P. W.; Reisinger, C. *J. Organomet. Chem.* **1999**, *576*, 23.

4. a) Hatanaka, Y.; Hiyama T. *J. Org. Chem.* **1988**, *53*, 920; b) Gouda, K.; Hagiwara, E.; Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1996**, *61*, 7232; c) Mowery, M. E.; DeShong, P. *Org. Lett.* **1999**, *1*, 2137; d) Lee, J.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 5616; e) Riggleman, S.; DeShong, P. *J. Org. Chem.* **2003**, *68*, 8106; f) Lee, H. M.; Nolan, S. P. *Org. Lett.* **2000**, *2*, 2053.

5. a) Stille, J. K. *Pure Appl. Chem.* **1985**, *57*, 1771; b) Stille, J. K. *Angew. Chem. Int. Ed.* **1986**, *25*, 508; c) Farina, V.; Krishnamurthy, V.; Scott, W. *J. Org. React.* **1997**, *50*, 1; d) Hassa, J.; Svignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359; e) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176.

6. a) Nakao, N.; Satoh, J.; Shirakawa, E.; Hiyama, T. *Angew. Chem. Int. Ed.* **2006**, *45*, 2271; b) von Zezschwitz, P.; Petry, F.; de Meijere, A. *Chemistry-A European Journal* **2001**, *7*, 4035; c) Paley, R. S.; de Dios, A.; Estroff, L. A.; Lafontaine, J. A.; Montero, C.; McCulley, D. J.; Rubio, M. B.; Ventura, M. P.; Weers, H. L.; Fernandez de la Pradilla, R.; Castro, S.; Dorado, R.; Morente, M. *J. Org. Chem.* **1997**, *62*, 6326; d) Chu, K. H.; Wang, K. K. *J. Org. Chem.* **1986**, *51*, 767.

7. So, C. M.; Lee, H. W.; Lau, C. P.; Kwong, F. Y. *Org. Lett.* **2009**, *11*, 317.

8. Domin, D.; Benito-Garagorri, D.; Mereiter, K.; Fröhlich, J.; Kirchner, K. *Organometallics* **2005**, *24*, 3957.

9. Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816.

10. Alacid, E.; Nájera, C. *Adv. Synth. Catal.* **2006**, *348*, 945.

11. Li, J.; Deng, C.; Xie, Y. *Synthesis* **2006**, 969.

12. Li, J.; Deng, C.; Liu, W.; Xie, Y. *Synthesis* **2005**, 3039.

13. a) Ju, J.; Nam, H.; Jung, H.; Lee, S. *Tetrahedron Lett.* **2006**, *47*, 8673; b) Shi, S.; Zhang, Y. *J. Org. Chem.* **2007**, *72*, 5927; c) Murata, M.; Yoshida, S.; Nirei, S.; Watanabe, S.; Masuda, Y. *Synlett* **2006**, 118.

14. a) Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 1047; b) Grushin, V. V.; Alper, H. *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S. Ed.; Springer, Berlin, **1999**, p 193; c) Herrmann, W. A. *Applied Homogenous Catalysis With Organometallic Compounds, A Comprehensive Handbook*; Cornils, B., Herrmann, W. A., Eds.; VCH: Weinheim, **1996**; Vol. *1*, p 722.

15. a) Wu, Z.; Yang, M.; Li, H.; Qi, Y. *Synthesis* **2008**, 1415; b) Pan, C.; Liu, M.; Zhao, L.; Wu, H.; Ding, J.; Cheng, J. *Catalysis Comm.* **2008**, *9*, 1685; c) Ackermann, L.; Gschrei, C. J.; Althammer, A.; Reiderer, M. *Chem. Comm.* **2006**, 1419.

CHAPTER 8. GENERAL CONCLUSIONS AND FUTURE PROSPECTS

General Conclusions

In this thesis are described our efforts to utilize proazaphosphatranes as catalysts for diaryl ether synthesis under microwave conditions, the synthesis of new proazaphosphatranes and their use in the synthesis of isocyanurates, the use of a novel aluminum Lewis acid in organic transformations, advances in the palladium-catalyzed α-arylation of enol silyl ethers, and the use of a novel bulky phosphine in Hiyama coupling. The following conclusions have been reached:

1. Proazaphosphatranes are stable under microwave conditions in which the synthesis of diaryl ethers is achieved. The use of a microwave allowed the coupling to proceed under low mole percentages of proazaphosphatrane. However, these couplings are limited to the use of electron deficient aryl fluorides. In the presence of a nitro group on the aryl fluoride, toluene is used as the solvent instead of DMF, thereby decreasing the number of steps needed to obtain pure products. Even electron deficient aryl TBDMS ethers undergo coupling at low mole percentages of catalyst. Sterically hindered aryl TBDMS ethers under microwave conditions can be used in the presence of 10 mol % proazaphosphatrane.

2. Increasing the number of methoxy groups on the benzene ring in tribenzyl proazaphosphatrane increases their pKa values. The reaction time for the trimerization of isocyanates shortens as the basicity of the proazaphosphatrane increases. Different types of isocyanates are timerized under very low mole percentages of proazaphosphatrane with fast reaction times. The proazaphosphatrane can be recycled to a modest extent.

3. The use of a novel tricyclic aluminum alkoxide in the trimethylsilylcyanation of aldehydes proceeded smoothly in low mole percentages of promoter in acetonitrile. It was shown that the tricyclic aluminum alkoxide could be recycled up to four times with minor decreases in product yield. The tricyclic aluminum alkoxide also efficiently catalyzed the Mukaiyama aldol reaction. Of the three aluminum catalysts (including ours) used for this reaction, the mole percentage used in our methodology is the lowest reported. A variety of electron rich, neutral, and deficient, heterocyclic, and alkyl aldehydes were successfully utilized in both the trimethylsilylcyanation and the Mukaiyama aldol reaction. Isolation of a reaction intermediate in the latter reaction supports the proposed mechanism. Lewis acidity determinations show that the tricyclic aluminum alkoxide is more Lewis acidic than $BF_3 \bullet OEt_2$.

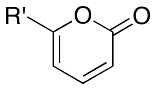
4. The use of two metal fluorides as synergistic additives in the $Pd/P(^tBu)_3$ catalyzed α-arylation of enol silyl ethers significantly accelerates the cross-coupling reaction of difficult substrates such as aryl halides with nitro and cyano substituents. Noteworthy is that this methodology is also efficient in the cross-coupling of aryl chlorides in α-arylation reactions. The mechanism of this reaction remains obscure.

5. The use of $^tBu_2P\text{-}N{=}P(^iBuNCH_2CH_2)_3N$ in the Hiyama cross-coupling reaction has proven to be the most effective ligand reported to date for this transformation. A variety of aryl bromides are coupled with a range of arylsiloxanes under low palladium loadings in high yields. Aryl chlorides (which are believed to be the most difficult substrates for the Hiyama reaction) are also coupled with phenylsiloxanes in high yields using the lowest palladium and ligand loading reported in the literature.

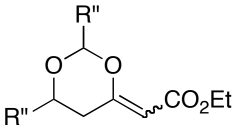
Future Prospects

There are numerous possibilities for new research areas to be explored based on the results reported in this thesis including:

1. The use of proazaphosphatranes in the phosphine-catalyzed synthesis of pyrones[1] (**1**) and 1,3-dioxan-4-ylidenes (**2**):[2] These compounds are synthesized in the reaction of aldehydes with allenes in the presence of catalytic amounts of phosphines. Interestingly, depending on the steric bulk of the phosphine, one product dominates the other. In the presence of bulky phosphines, the synthesis of pyrones dominates while a non-bulky phosphine, such as PMe_3, promotes the formation of dioxan-4-ylidines. Such selectivity could be accentuated in the case of proazaphosphatranes since their steric bulk and basicity can be so widely varied by the stereoelectronic nature of the exocyclic substituents on the PN nitrogens. It would be interesting to see whether proazaphosphatrane steric bulk or basicity dominates any selectivity observed.



1



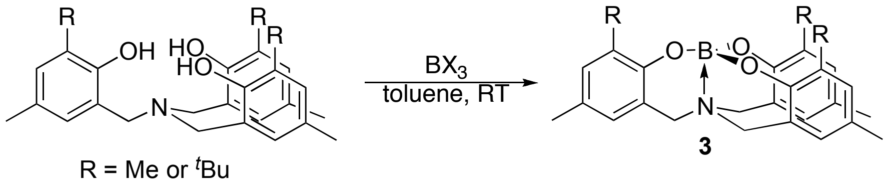
2

2. Use of our tricyclic aluminum alkoxide as a catalyst in the allylation of aldehydes and ketones: This could be achieved by the use of a potassium organotrifluoroborate salt. Recently, Batey and co-workers showed that 5 mol % BF_3•OEt_2 catalyzes this reaction.[3] Since it was previously shown that the tricyclic aluminum alkoxide is more Lewis acidic than BF_3•OEt_2, this reaction may proceed well with even lower mole percentages of our promoter.

3. The synthesis of a new boratrane Lewis acid: Following literature procedures, the synthesis of a tricyclic boron alkoxide could be envisioned as shown in Scheme 1.[4] The use

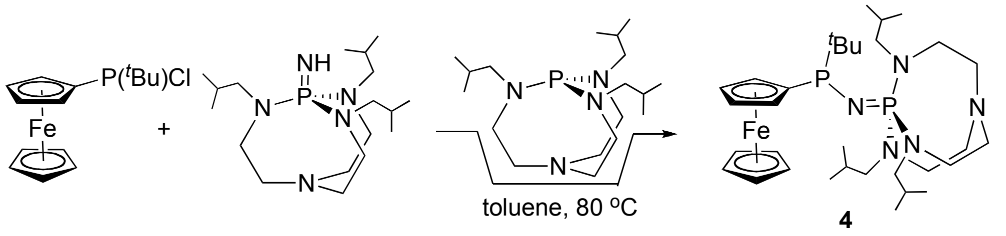
of either BX_3 (X = Br, Cl, OEt, OH, Me, or Et) could produce the corresponding boratrane **3**. The structure of **3** may or may not be dimeric. If it is dimeric, however, the linear N-B-O linkage would best be interpreted in terms of a 3-center-4–electron bond. In any case, the catalytic properties (if any) of **3** will be of interest to determine.

Scheme 1. Synthetic approach to a tricyclic boron alkoxide (boratrane)

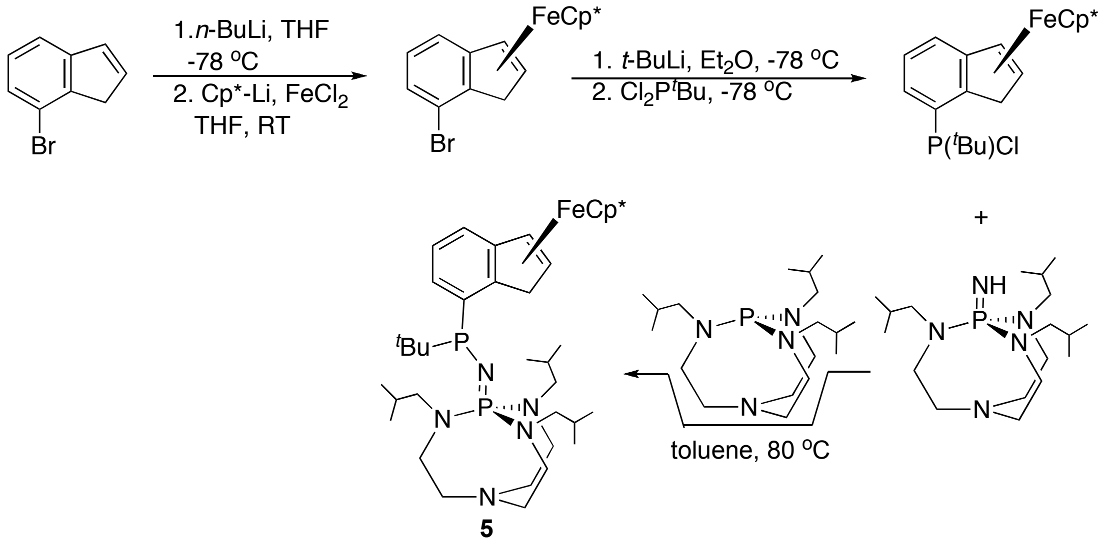


4. The synthesis of a new derivatives of R'R"P-N=P(^{i}BuNCH$_2$CH$_2$)$_3$N: This could result in the formation of additional bulky phosphine candidates for palladium-catalyzed reactions and could also be useful in asymmetric catalysis. The latter goal might be achieved by replacing one of the *tert*-butyl groups in ^{t}Bu$_2$P-N=P(^{i}BuNCH$_2$CH$_2$)$_3$N with a ferrocenyl substituent. Ferrocenyl groups have been known to increase the steric bulk and reactivity of phosphines.[5] A method of producing such a phosphine is shown in Scheme 2. The FcP(^{t}Bu)Cl is made following known procedures.[5a] Then, following a method recently published by our group,[6] phosphine **4** could be synthesized. Another type of ferrocenyl phosphine is shown in Scheme 3 in which phosphine **5** could be synthesized by following known literature procedures.[6,7] Either phosphine **4** or **5** could potentially be a useful ligand in palladium-catalyzed reactions or, in enantiomerically resolved form, they could be useful in appropriate palladium-catalyzed asymmetric catalysis reactions.

Scheme 2. Synthetic approach to phosphine **4**.



Scheme 3. Synthetic approach to **5**.



References

1. (a) Zhu, X.; Schaffner, A.; Li, R. C.; Kwon, O. *Org. Lett.* **2005**, *7*, 2977. (b) Komiyama, T.; Takaguchi, Y.; Tsuboi, S. *Tetrahedron Lett.* **2004**, *45*, 6299. (c) Sheibani, H.; Islami, M. R.; Khabazzadeh, H.; Saidi, K. *Tetrahedron* **2004**, *60*, 5931. (d) Ma, S.; Yu, S.; Yin, S. *J. Org. Chem.* **2003**, *68*, 8996. (e) Yao, T.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 5936. (f) Biagetti, M.; Bellina, F.; Carpita, A.; Rossi, R. *Tetrahedron Lett.* **2003**, *44*, 607. (g) Anastasia, L.; Xu, C.; Negishi, E. *Tetrahedron Lett.* **2002**, *43*, 5673. (h) Kotretsou, S. I.;

Georgiadis, M. P. *Org. Prep. Proc. Int.* **2000**, *32*, 161.

2. Zhu, X.; Henry, C. E.; Wang, J.; Dudding, T.; Kwon, O. *Org. Lett.* **2005**, *7*, 1387.

3. (a) Nowrouzi, F.; Thadani, A. N.; Batey, R. A. *Org. Lett.* **2009**, *11*, 2631. (b) Aoyama, N.; Hamada, T.; Manabe, K.; Kobayashi, S. *Chem. Commun.* **2003**, 676. (c) Wadamoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 14556. (d) Waltz, K. M.; Gavenonis, J.; Walsh, P. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3697. (e) Lu, J.; Hong, M.; Ji, S.; Teo, Y.; Loh, T. *Chem. Commun.* **2005**, 4217.

4. (a) Su, W.; Kim, Y.; Ellern, A.; Guzei, I. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2006**, *128*, 13727. (b) Su, W.; Kobayashi, J.; Ellern, A.; Kawashima, Y.; Verkade, J. G. *Inorg. Chem.* **2007**, *46*, 7953.

5. (a) Stambuli, J. P.; Stauffer, S. R.; Shaugnessy, K. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 2677. (b) Shen, Q.; Ogata, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 6586. (c) Guillaneux, D.; Kagan, H. B. *J. Org. Chem.* **1995**, *60*, 2502.

6. Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816.

7. (a) Adamczyk, M.; Watt, D. S. *J. Org. Chem.* **1984**, *49*, 4226. (b) Thimmaiah, M.; Luck, R. L.; Fang, S. *Tetrahedron Lett.* **2007**, *692*, 1956.

APPENDIX A

CHAPTER 2. Supplementary Information

Experimental Procedures

References for known compounds

Data for unknown compounds

^{1}H and ^{13}C NMR spectra for reaction products

General Considerations

All reactions were run under argon and all glassware was oven dried prior to use. Toluene was dried with sodium in a solvent still. DMF was refluxed over 4 Å molecular sieves, distilled under vacuum and stored over 4 Å molecular sieves. Aryl fluorides were purchased from Aldrich Chemical and used without further purification. Proazaphosphatranes **1**[1], **3**[2], and **4**[3] were synthesized according to literature procedures. Proazaphosphatrane **2** was kindly donated by Aldrich Chemical. Stock solutions of proazaphosphatranes **1**, **2**, **3**, and **4** were made using either toluene or DMF as the solvent. Phenyl TBDMS ethers were made according to literature procedures[4] from the corresponding phenol with *tert*-butyldimethylsilyl chloride and imidazole in DMF as the solvent. Products were purified by column chromatography. The microwave reactions were run on a CEM Discover microwave apparatus with 300 watts power and a temperature of 180 °C for the times given in the manuscript. When the reactions were run in toluene, the temperature reached in the microwave was 170 °C with 300 watts of power. When DMF was used as the solvent, the maximum temperature was 180 °C with 100 watts of power. ^{1}H and ^{13}C NMR spectra were obtained on a VXR-400 Varian NMR spectrometer. All NMR spectra were taken in $CDCl_3$. Thin layer chromatography was used to monitor reaction progress. Yields are isolated yields and are an average of two runs.

Experimental Procedure

Reactions carried out in toluene: To a 10 mL microwave tube was charged 1.2 mmol of aryl TBDMS ether to which was added 1 mmol of aryl fluoride. Proazaphosphatrane **3** (from a stock solution prepared in toluene) was then added to the tube under inert atmosphere. The tube was capped and placed in the microwave for the time given in Tables 1-3 and in entries 1-3 in Table 4, after which the solvent was removed in vacuo to produce the crude product that was purified by column chromatography (0-10% EtOAc/hexanes).

Reactions carried out in DMF: To a 10 mL microwave tube was charged 1.2 mmol of aryl TBDMS ether to which was added 1 mmol of aryl fluoride. Proazaphosphatrane **3** (from a stock solution prepared in DMF) was then added to the tube under inert atmosphere. The tube was capped and placed in the microwave for the times mentioned in Tables 3 and in entries 4-6 in Table 4. Thereafter the reaction mixture was dissolved in 5 mL of water and extracted with diethyl ether followed by drying over magnesium sulfate. The solvent was removed in vacuo leaving the crude product, which was purified by column chromatography (0-10% EtOAc/hexanes).

[1] Schmidt, H.; Lensink, C.; Xi, S. K.; Verkade, J. G. *Z. Anorg. Allg. Chem.* **1989**, *578*, 75.

[2] Kisanga, P. B.; Verkade, J. G. *Tetrahedron* **2001**, *57*, 467.

[3] Su, W.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433.

[4] Anemian, R.; Cupertino, D. C.; Mackie, P. R.; Yeates, S. G. *Tetrahedron Letters* **2005**, *46*, 6717.

References for Known Compounds

4-Bromo-2’,4’-dinitro-diphenylether (Product in Table 1 and 2). Urgaonkar, S.; Verkade, J. G. *Org. Lett.* **2005**, *7*, 3319.

4-Methoxy-2',4'-dinitro-diphenylether (Table 3, entry 1). Yeom, C.; Kim, H. W.; Lee, S. Y.; Kim, B. M. *Synlett* **2007**, *1*, 146.

4-Cyano-2',4'-dinitro-diphenylether (Table 3, entry 2). Saunders, D. G. *Synthesis* **1988**, 377.

3-Chloro-2',4'-dinitro-diphenylether (Table 3, entry 3). Bartoli, G.; Todesco, P. E.; Ciminale, F.; Fiorentino, M. *J. Org. Chem.* **1975**, *40*, 3777.

4-Methoxy-4'-nitro-diphenylether (Table 3, entry 4). Sawyer, J. S.; Schmittling, E. A.; Palkowitz, J. A.; Smith, W. J., III. *J. Org. Chem.* **1998**, *63*, 6338.

4-Cyano-4'-nitro-diphenylether (Table 3, entry 5). Wilcox, C. S. *Tetrahedron Lett.* **1985**, *26*, 5749.

3-Chloro-4'-nitro-diphenylether (Table 3, entry 6). Steller, K. E.; Letsinger, R. L. *J. Org. Chem.* **1970**, *35*, 308.

4-Methoxy-4'-cyano-diphenylether (Table 3, entry 7). Sawyer, J. S.; Schmittling, E. A.; Palkowitz, J. A.; Smith, W. J., III. *J. Org. Chem.* **1998**, *63*, 6338.

3-Chloro-4'-cyano-diphenylether (Table 3, entry 8). Urgaonkar, S.; Verkade, J. G. *Org. Lett.* **2005**, *7*, 3319.

4-Methoxy-4'-ethxoycarbonyl-diphenylether (Table 3, entry 9). Ueno, M.; Hori, C.; Suzawa, K.; Ebisawa, M.; Kondo, Y. Eur. J. Org. Chem. **2005**, 1965.

4-Cyano-4'-ethoxycarbonyl-diphenylether (Table 3, entry 10). Lee, K.; Jung, J. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1799.

3-Chloro-4'-ethoxycarbonyl-diphenylether (Table 3, entry 11). Urgaonkar, S.; Verkade, J. G. *Org. Lett.* **2005**, *7*, 3319.

2-*tert*-Butyl-2'-nitro-diphenylether (Table 4, entry 2). Sawyer, J. S.; Schmittling, E.

A.; Palkowitz, J. A.; Smith, W. J. *J. Org. Chem.* **1998**, *63*, 6338.

2-*tert*-Butyl-2'-cyano-diphenylether (Table 4, entry 4). Sawyer, J. S.; Schmittling, E. A.; Palkowitz, J. A.; Smith, W. J. *J. Org. Chem.* **1998**, *63*, 6338.

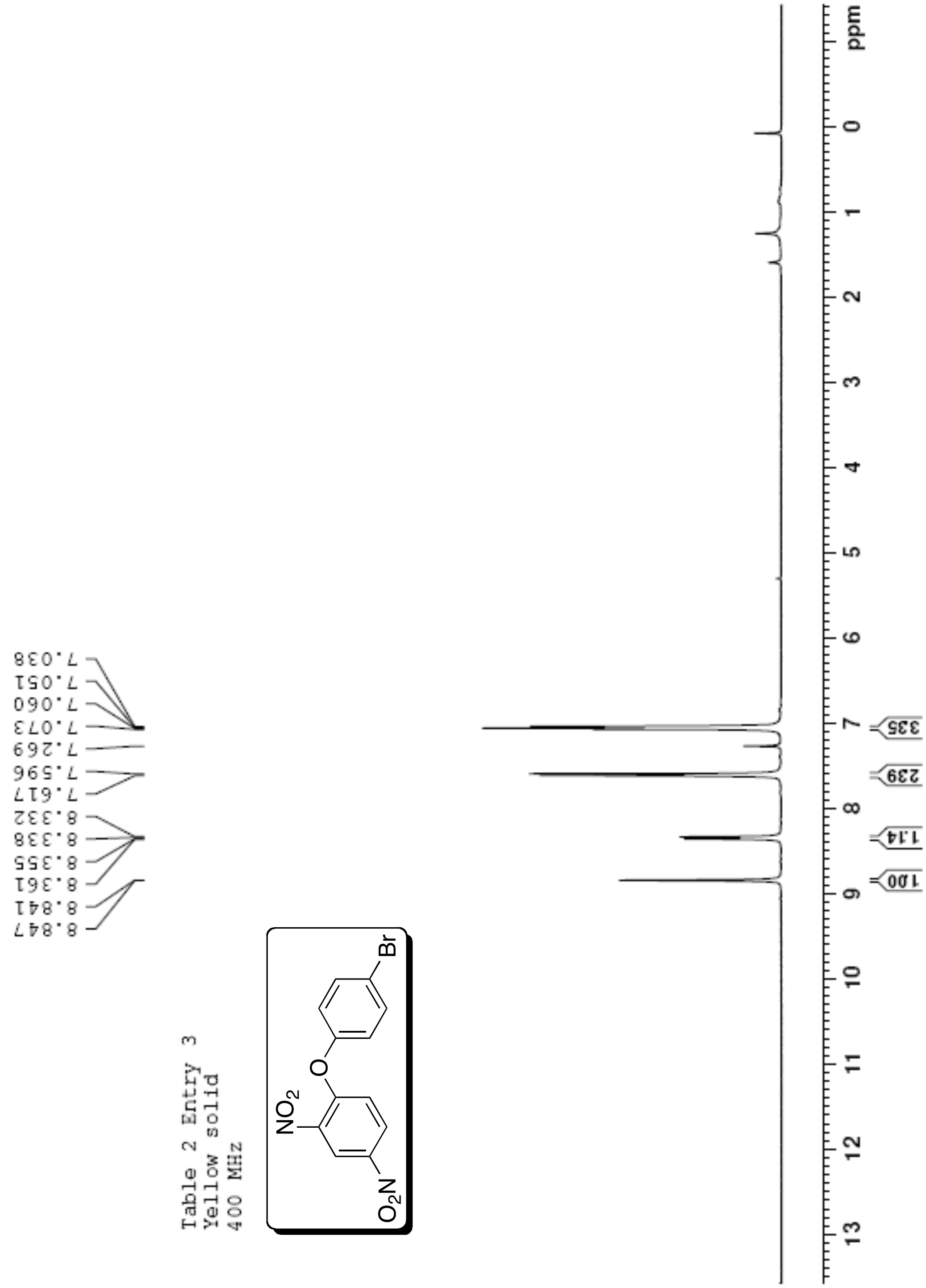
2,6-diisopropyl-4'-nitro-diphenylether (Table 4, entry 5). Sammes, P. G.; Thetford, D.; Voyle, M. J. J. Chem. Soc., Chem. Commun. **1987**, 1373.

Spectroscopic Data for Previously Unknown Compounds

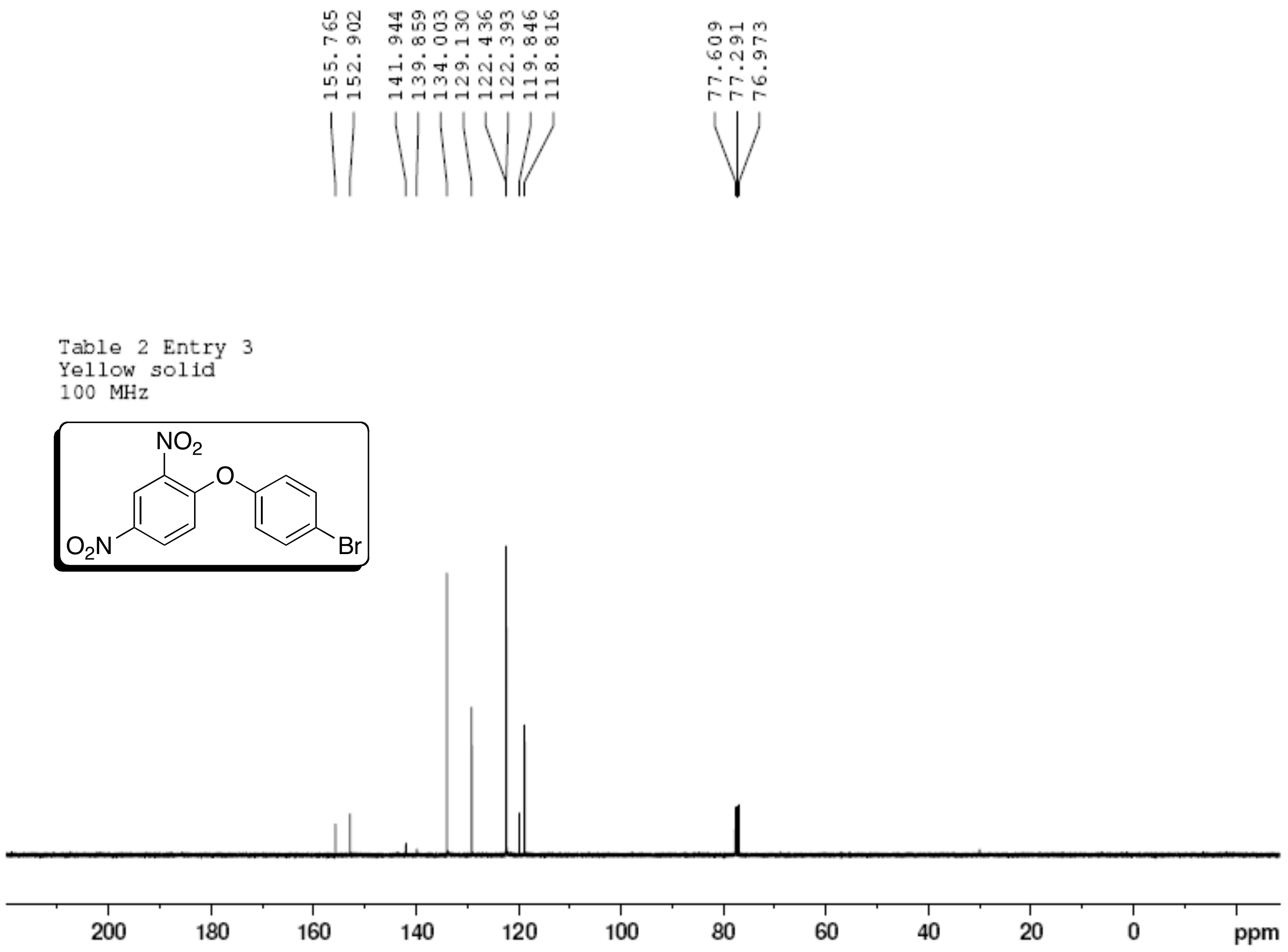
2-*tert*-Butyl-2',4'-dinitro-diphenylether (Table 4, entry 1). Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91-8.90 (d, 1H), 8.37-8.33 (m, 1H), 7.57-7.54 (m, 1H), 7.32-7.29 (m, 2H), 7.06-7.03(d, 1H), 6.95-6.91 (m, 1H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 152.4, 142.3, 141.1, 139.7, 128.9, 128.5, 128.0 126.6, 122.2, 121.5, 118.8, 34.9, 30.3. HRMS m/z 316.10660 (calc for $C_{16}H_{16}N_2O_5$, 316.10592)

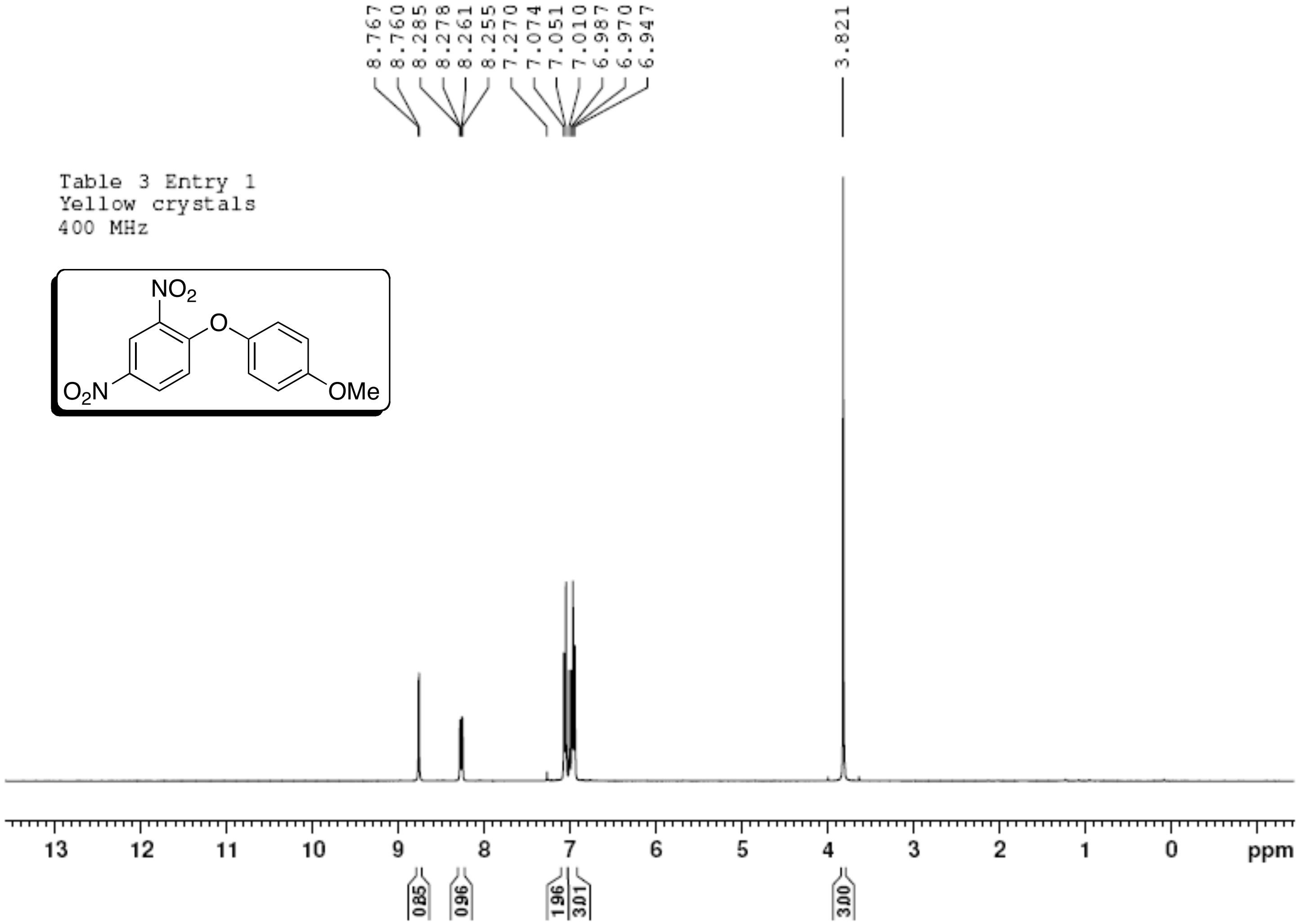
2-*tert*-Butyl-2'-methyl-4'-nitro-diphenylether (Table 4, entry 3). Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08-8.06 (d, 1H), 7.49-7.46 (m, 1H), 7.27-7.16 (m, 2H), 6.91-6.89 (m, 2H), 6.85-6.82 (m, 1H), 2.63 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 153.8, 143.4, 141.9, 137.3, 127.9, 127.6, 125.2, 121.8, 120.9, 115.3, 34.9, 30.4, 21.7. HRMS m/z 285.13686 (calc for $C_{17}H_{19}NO_3$, 285.13649)

2,6-diisopropyl-4'-cyano-diphenylether (Table 4, entry 6). White solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.56 (d, 2H), 7.31-7.21 (m, 3H), 6.87-6.84 (d, 2H), 3.00-2.87 (m, 2H), 1.15-1.12 (d, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): 162.6, 147.7, 141.4, 134.4, 126.8, 124.9, 119.2, 115.8, 105.0, 27.2, 23.5. HRMS m/z 279.16267 (calc for $C_{19}H_{21}NO$, 279.16231)



7.038
7.051
7.060
7.073
7.269
7.596
7.617
8.332
8.338
8.355
8.361
8.841
8.847
Table 2 Entry 3
Yellow solid
400 MHz
NO_2
O
Br
O_2N
3.35
2.39
1.14
1.00
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


155.765
152.902
141.944
139.859
134.003
129.130
122.436
122.393
119.846
118.816
77.609
77.291
76.973
Table 2 Entry 3
Yellow solid
100 MHz
NO2
O
O2N
Br
200
180
160
140
120
100
80
60
40
20
0
ppm


8.767
8.760
8.285
8.278
8.261
8.255
7.270
7.074
7.051
7.010
6.987
6.970
6.947
3.821
Table 3 Entry 1
Yellow crystals
400 MHz
NO2
O
O2N
OMe
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.85
0.96
1.96
3.01
3.00

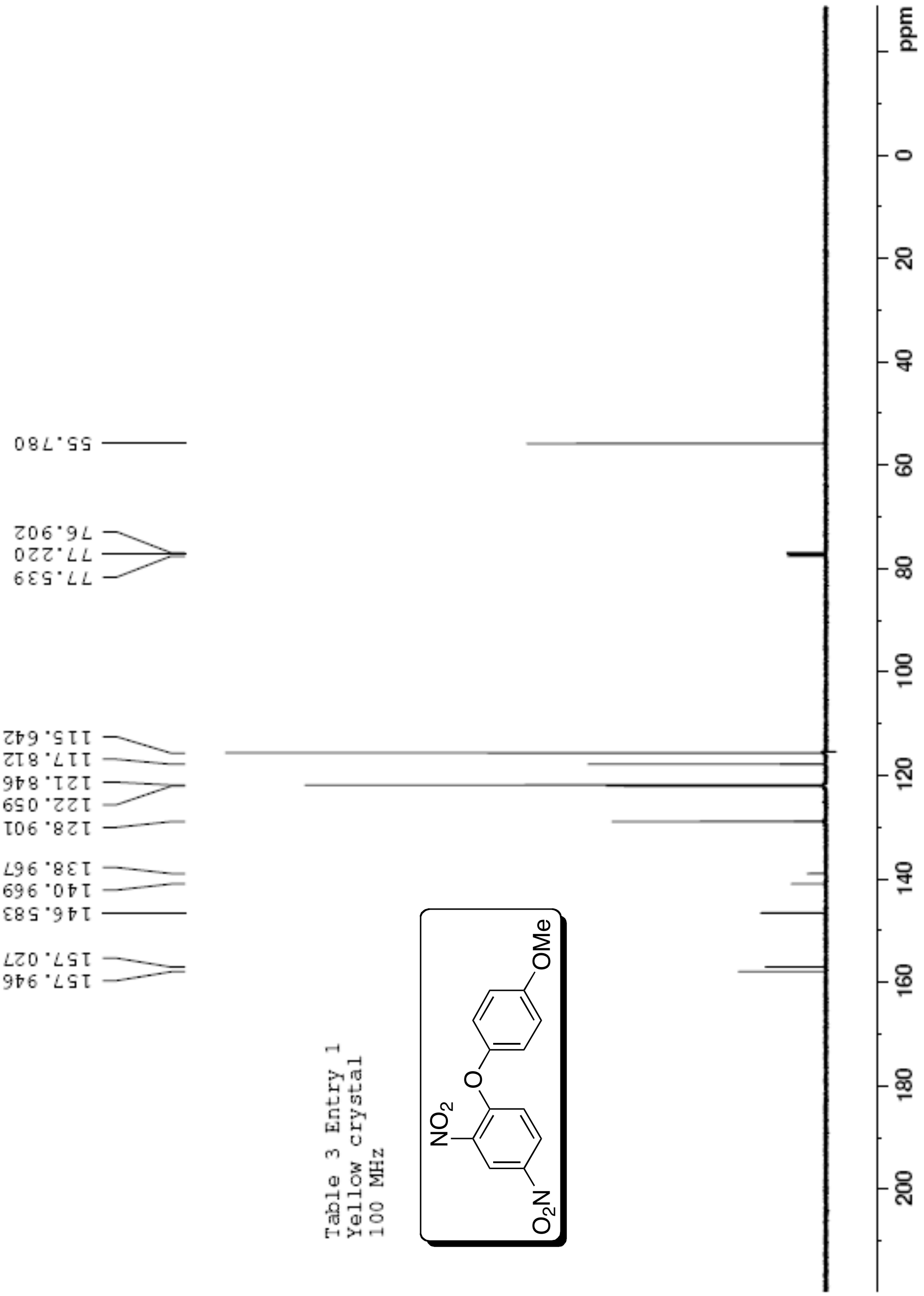


Table 3 Entry 1
Yellow crystal
100 MHz

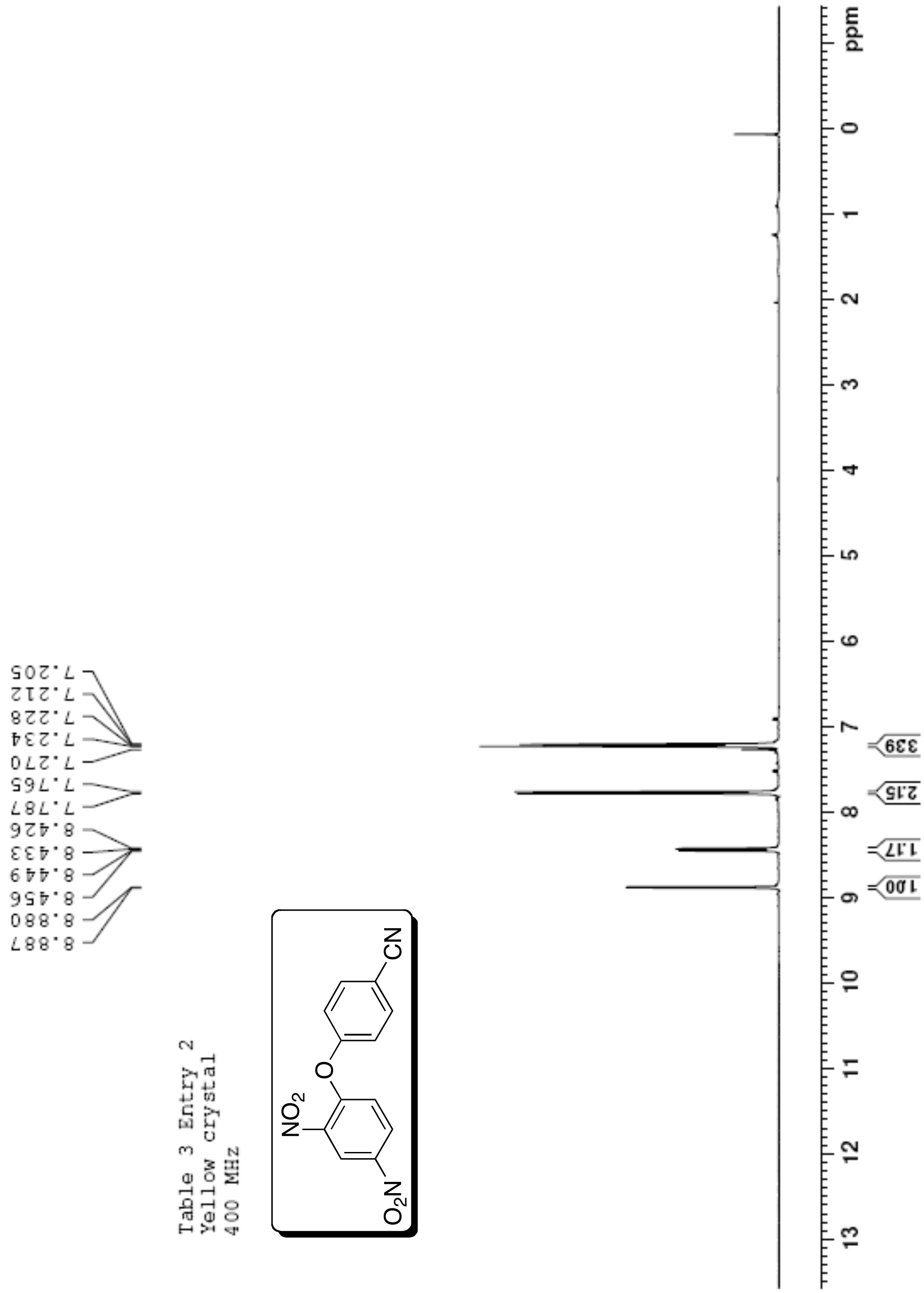
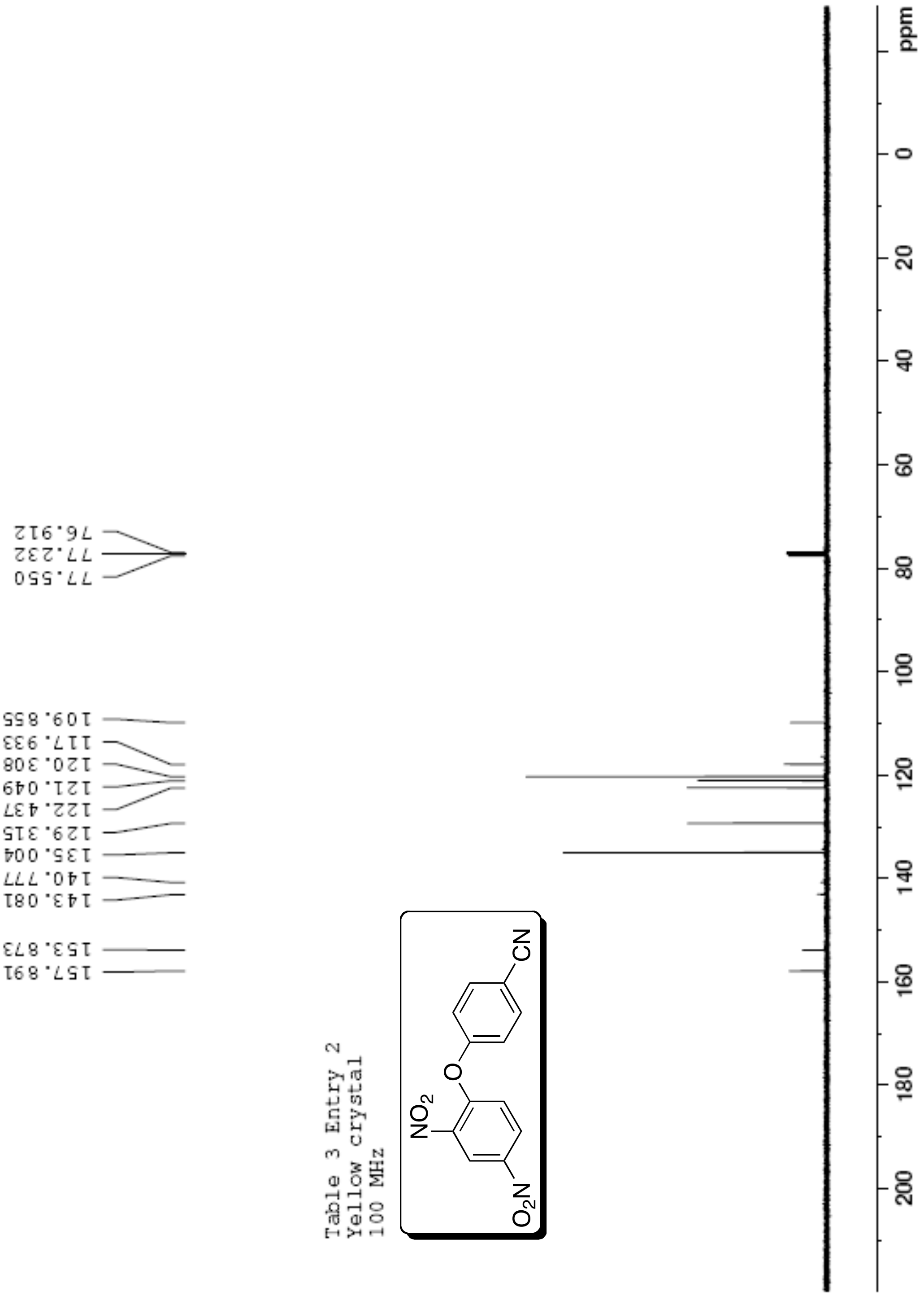
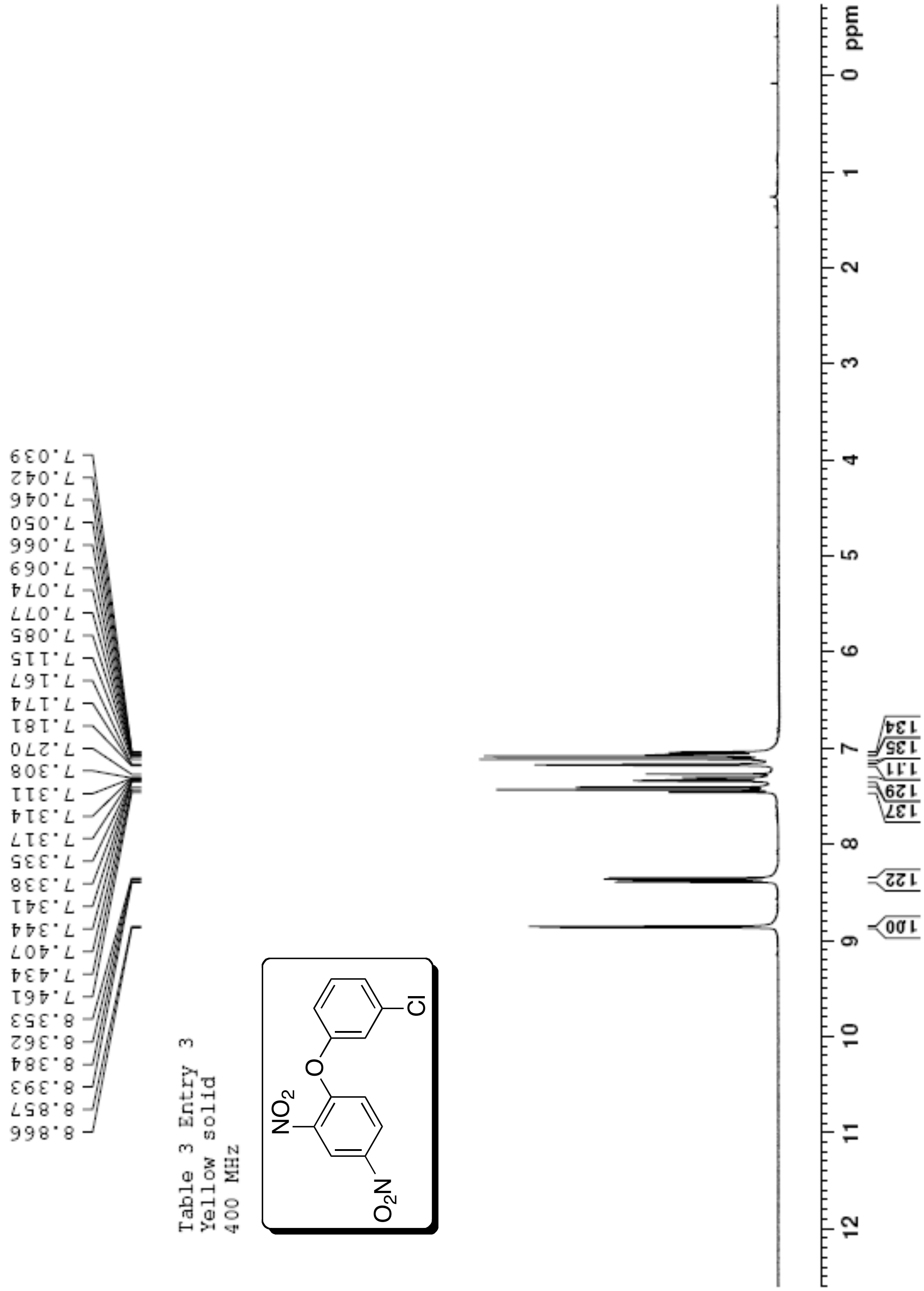
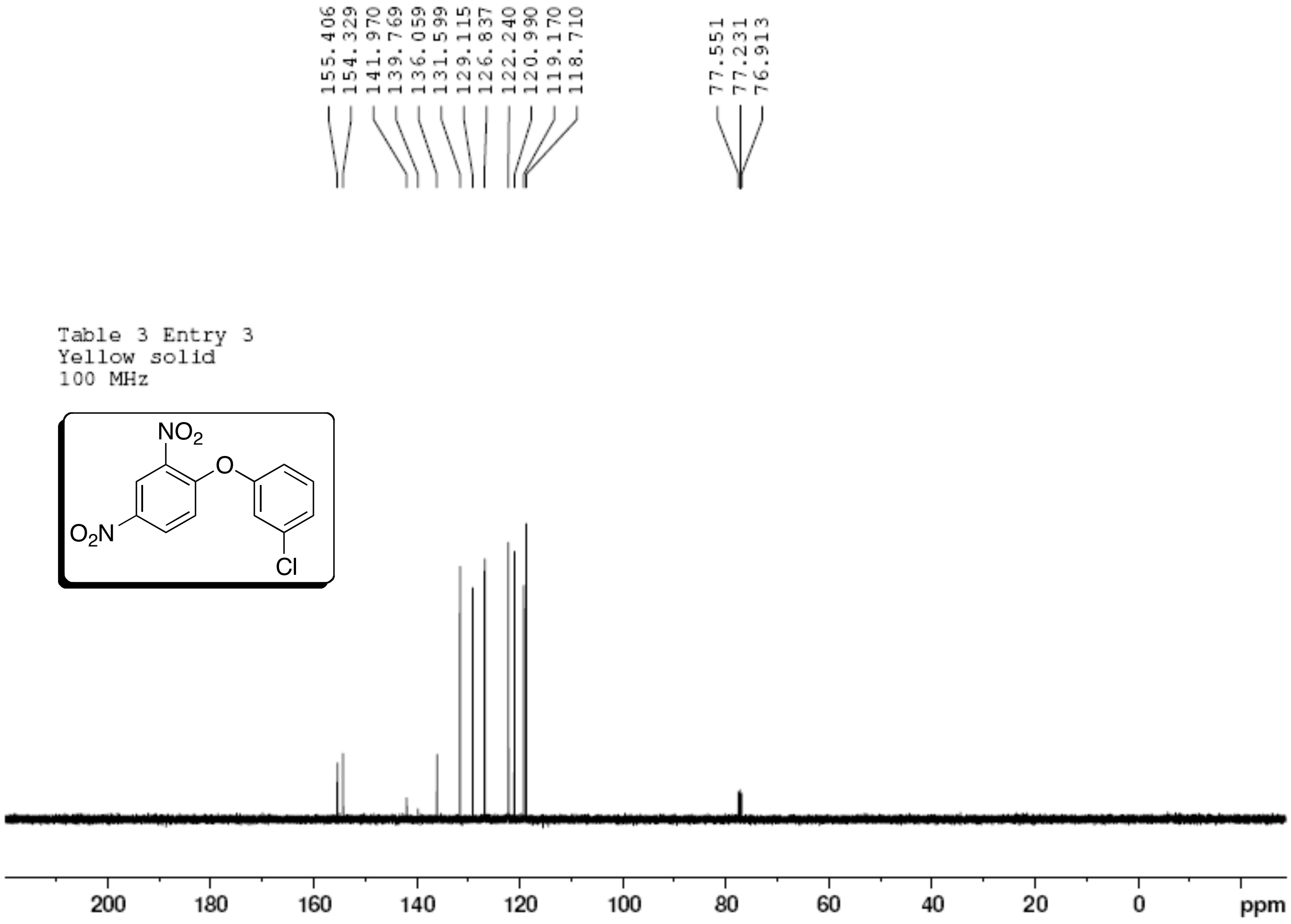


Table 3 Entry 2
Yellow crystal
400 MHz
O2N
NO2
O
CN
7.205
7.212
7.228
7.234
7.270
7.765
7.787
8.426
8.433
8.449
8.456
8.880
8.887
3.39
2.15
1.17
1.00
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


76.912
77.232
77.550
109.855
117.933
120.308
121.049
122.437
129.315
135.004
140.777
143.081
153.873
157.891
Table 3 Entry 2
Yellow crystal
100 MHz
O_2N
NO_2
O
CN
ppm
0
20
40
60
80
100
120
140
160
180
200


8.866
8.857
8.393
8.384
8.362
8.353
7.461
7.434
7.407
7.344
7.341
7.338
7.335
7.317
7.314
7.311
7.308
7.270
7.181
7.174
7.167
7.115
7.085
7.077
7.074
7.069
7.066
7.050
7.046
7.042
7.039
Table 3 Entry 3
Yellow solid
400 MHz
NO$_2$
O
Cl
O$_2$N
1.00
1.22
1.37
1.29
1.11
1.35
1.34
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm


155.406
154.329
141.970
139.769
136.059
131.599
129.115
126.837
122.240
120.990
119.170
118.710
77.551
77.231
76.913
Table 3 Entry 3
Yellow solid
100 MHz
NO2
O
O2N
Cl
200
180
160
140
120
100
80
60
40
20
0
ppm

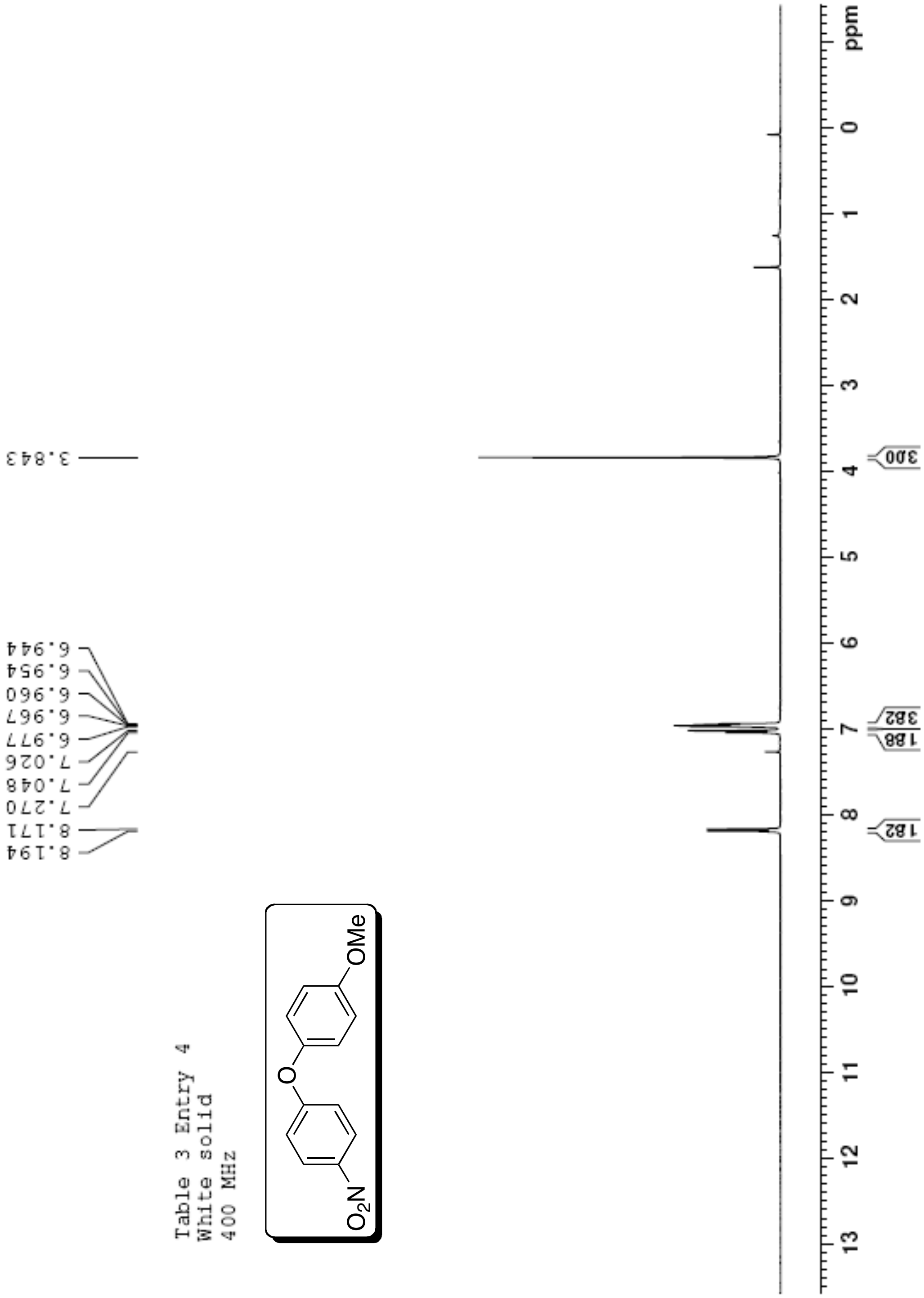


Table 3 Entry 4
White solid
400 MHz

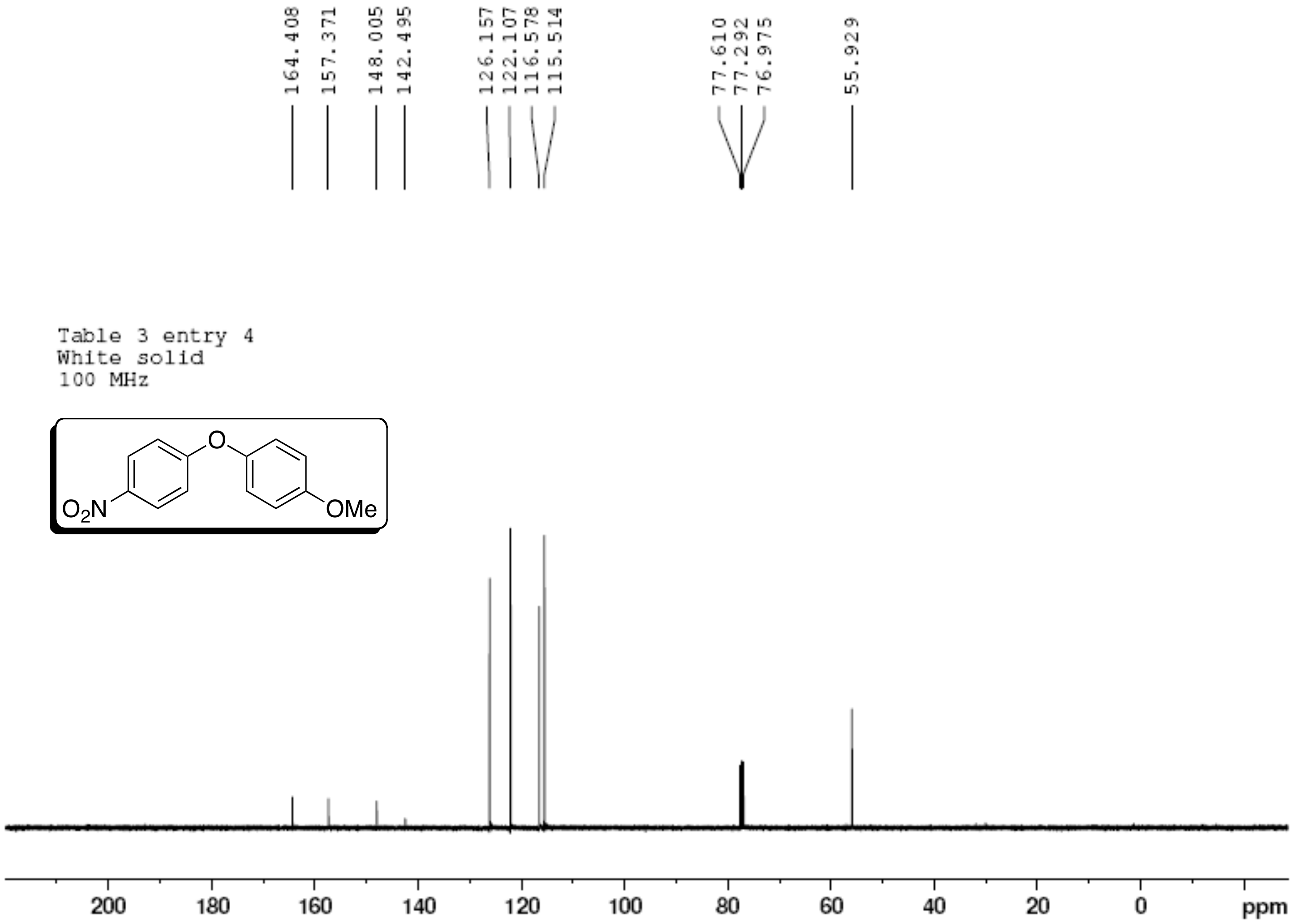


Table 3 entry 4
White solid
100 MHz

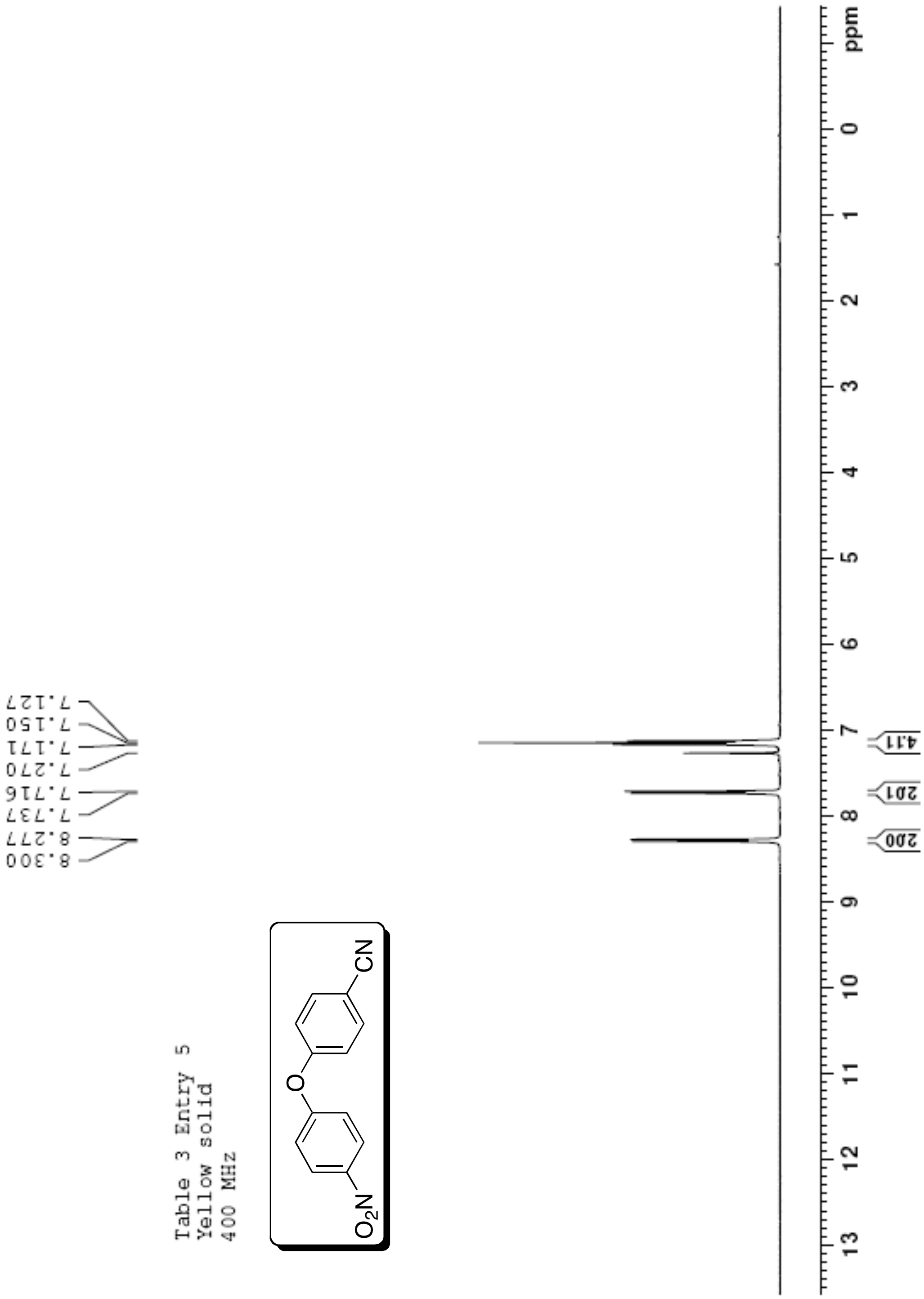
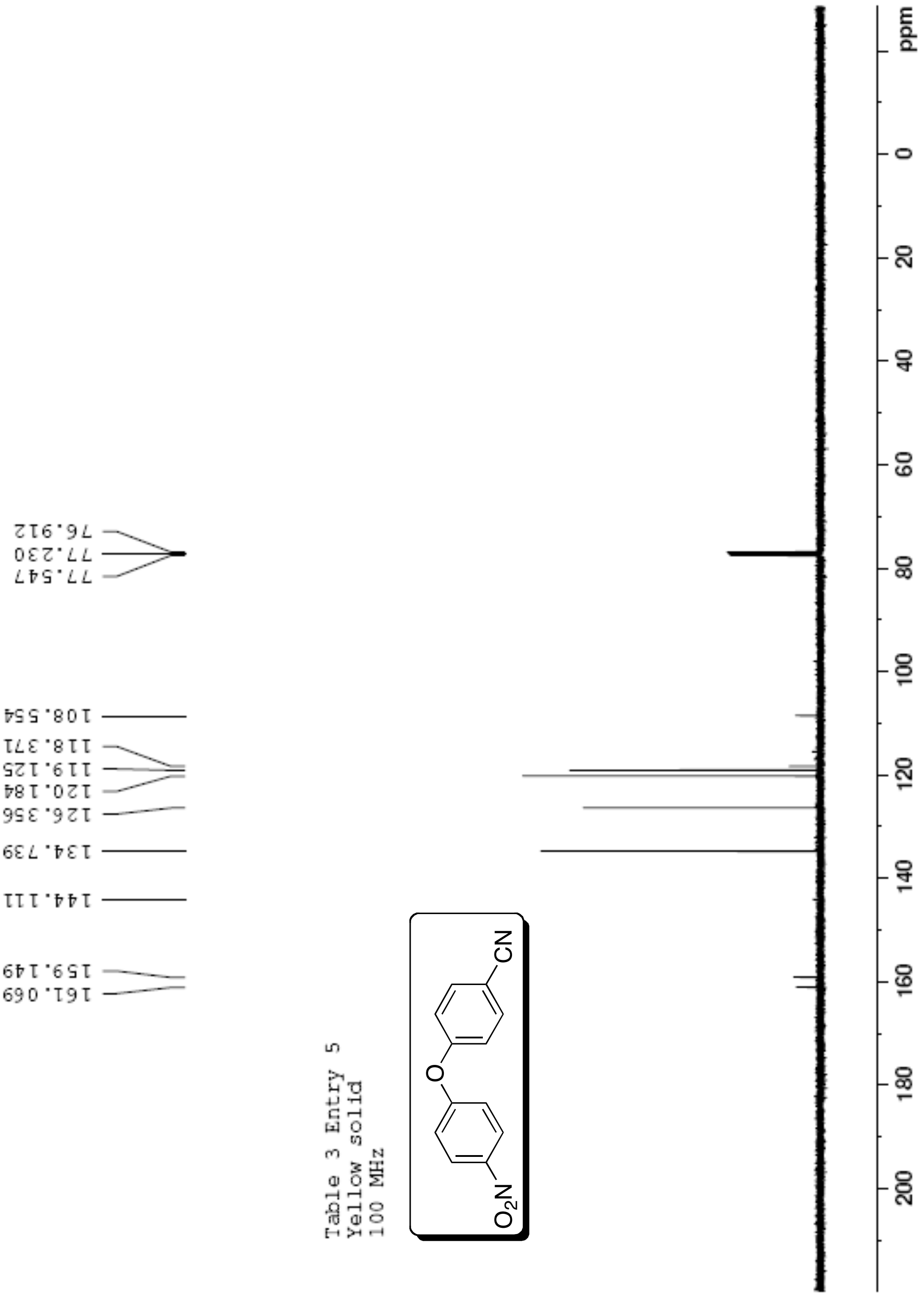
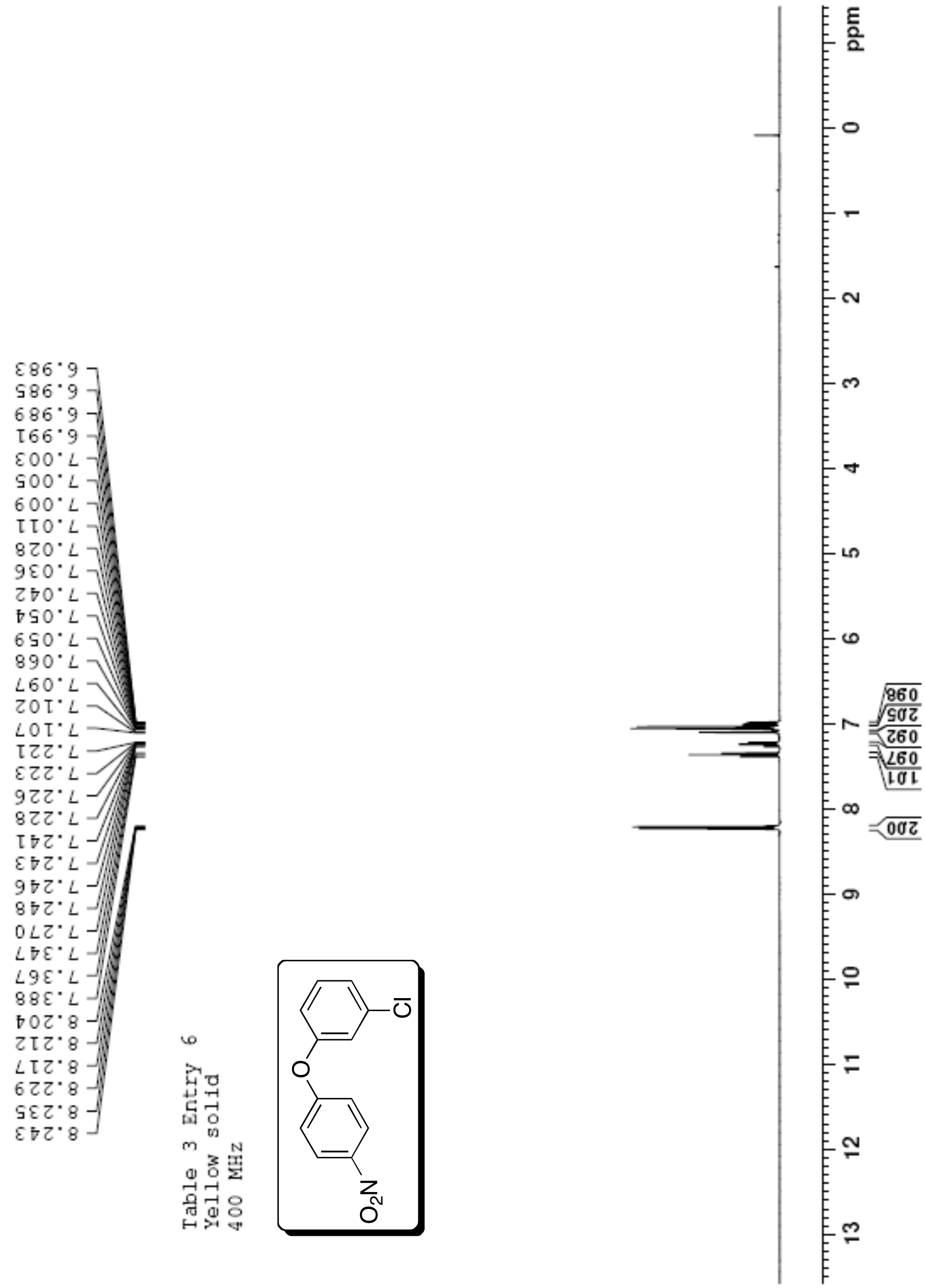


Table 3 Entry 5
Yellow solid
400 MHz
O
O$_2$N
CN
8.300
8.277
7.737
7.716
7.270
7.171
7.150
7.127
2.00
2.01
4.11
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm


76.912
77.230
77.547
108.554
118.371
119.125
120.184
126.356
134.739
144.111
159.149
161.069
Table 3 Entry 5
Yellow solid
100 MHz
O$_2$N
O
CN
ppm
0
20
40
60
80
100
120
140
160
180
200


6.983
6.985
6.989
6.991
7.003
7.005
7.009
7.011
7.028
7.036
7.042
7.054
7.059
7.068
7.097
7.102
7.107
7.221
7.223
7.226
7.228
7.241
7.243
7.246
7.248
7.270
7.347
7.367
7.388
8.204
8.212
8.217
8.229
8.235
8.243
Table 3 Entry 6
Yellow solid
400 MHz
O
Cl
O2N
200
101
097
092
205
098
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm

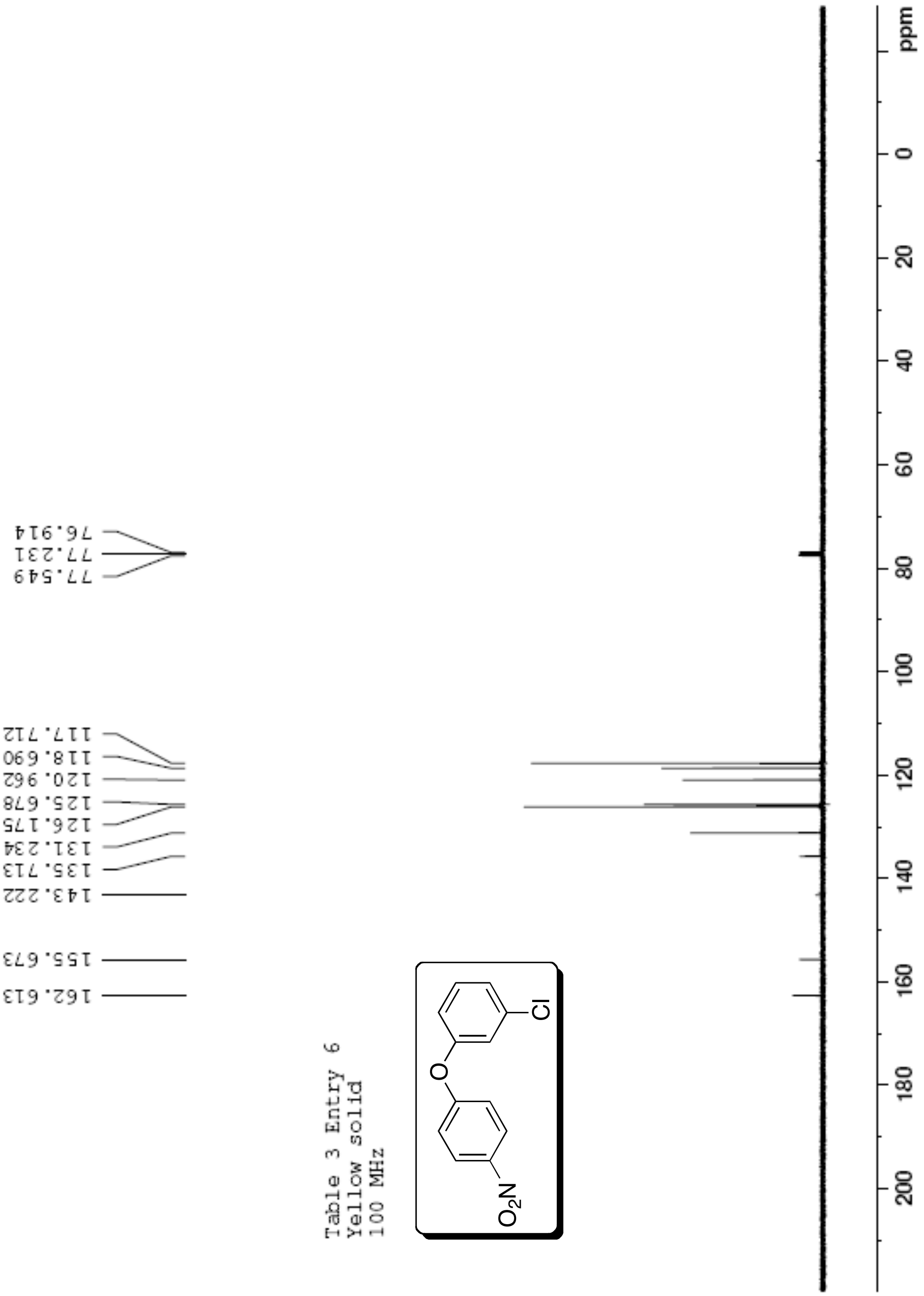


Table 3 Entry 6
Yellow solid
100 MHz
O2N
O
Cl
162.613
155.673
143.222
135.713
131.234
126.175
125.678
120.962
118.690
117.712
77.549
77.231
76.914
ppm
200
180
160
140
120
100
80
60
40
20
0

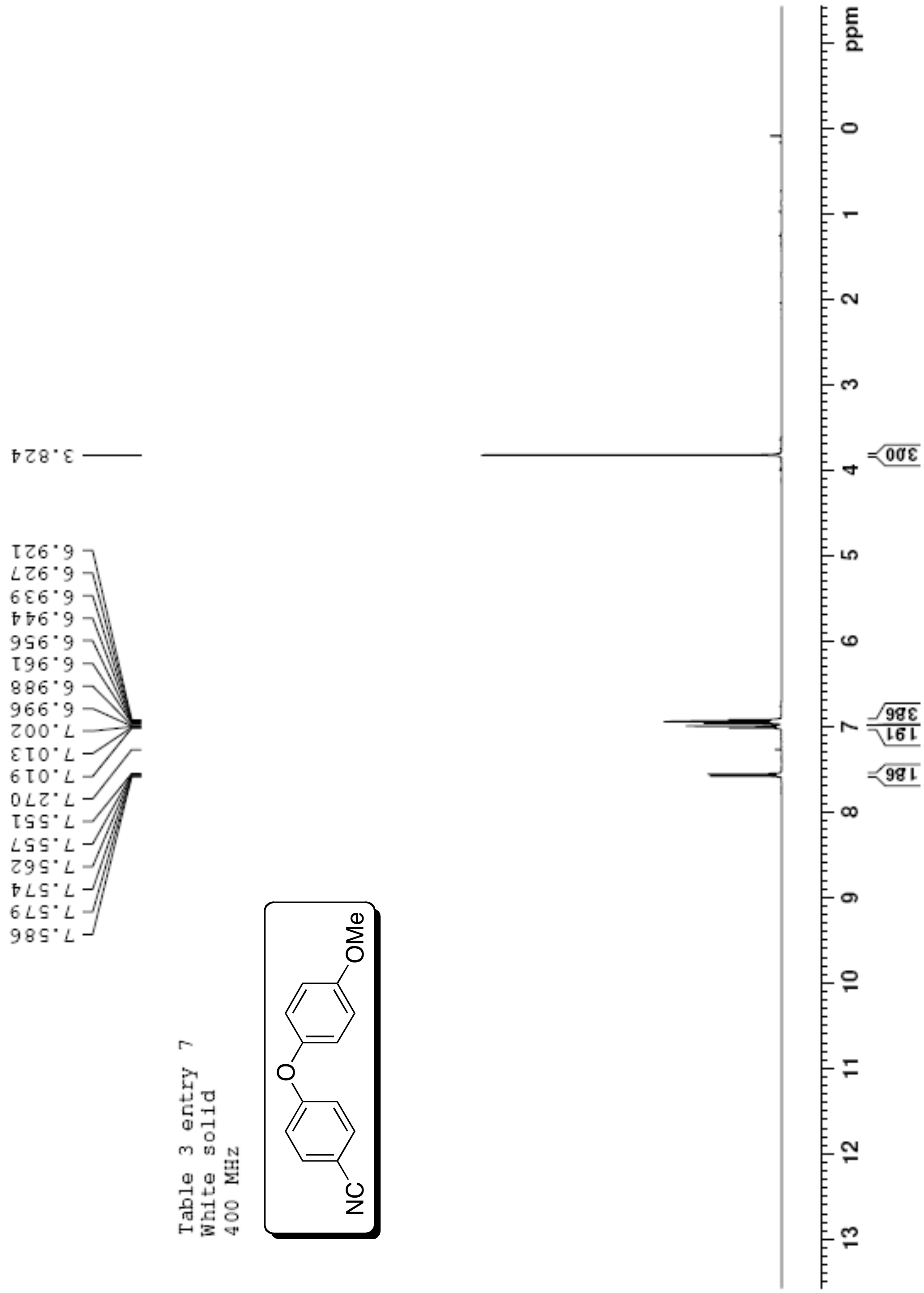
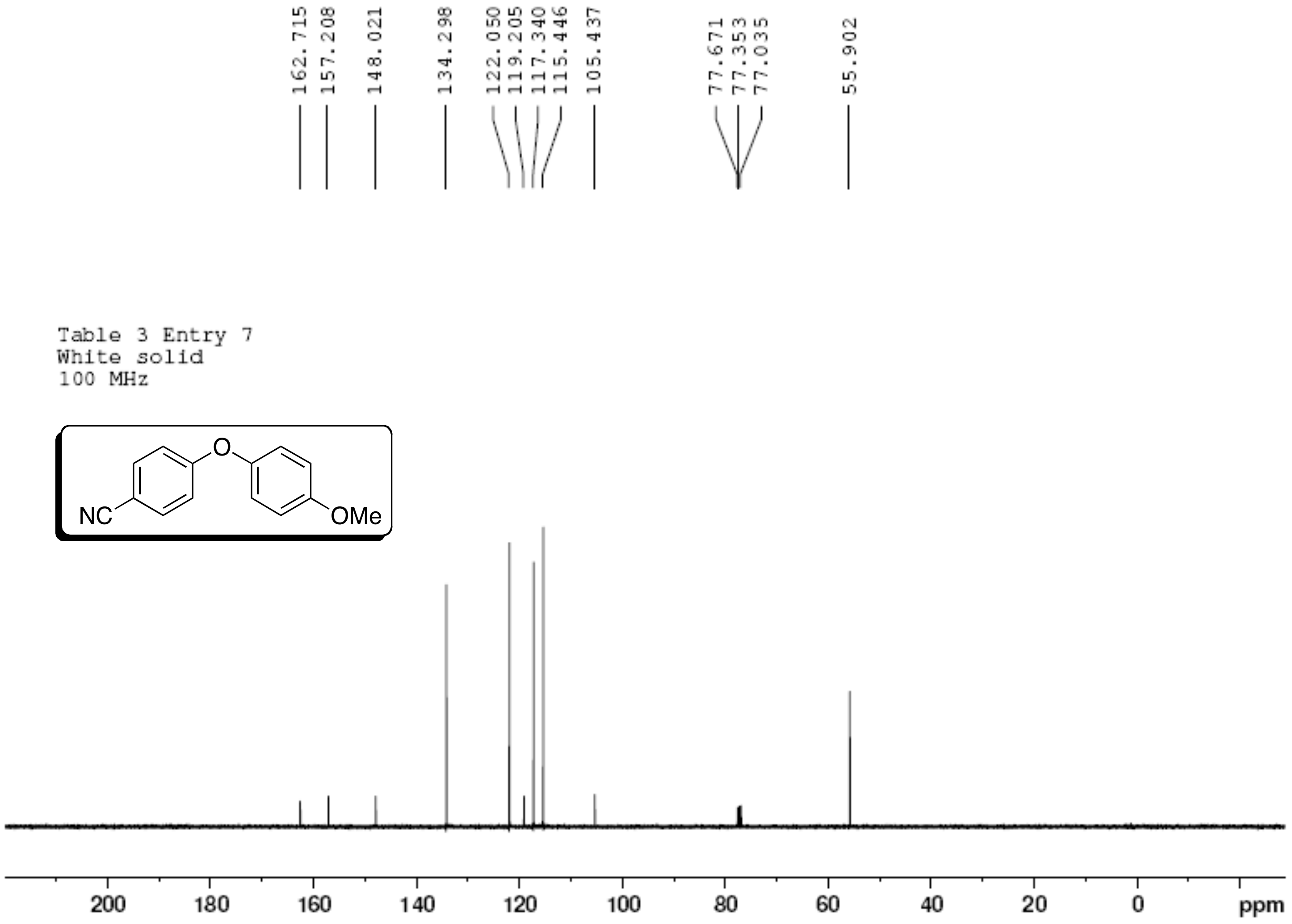
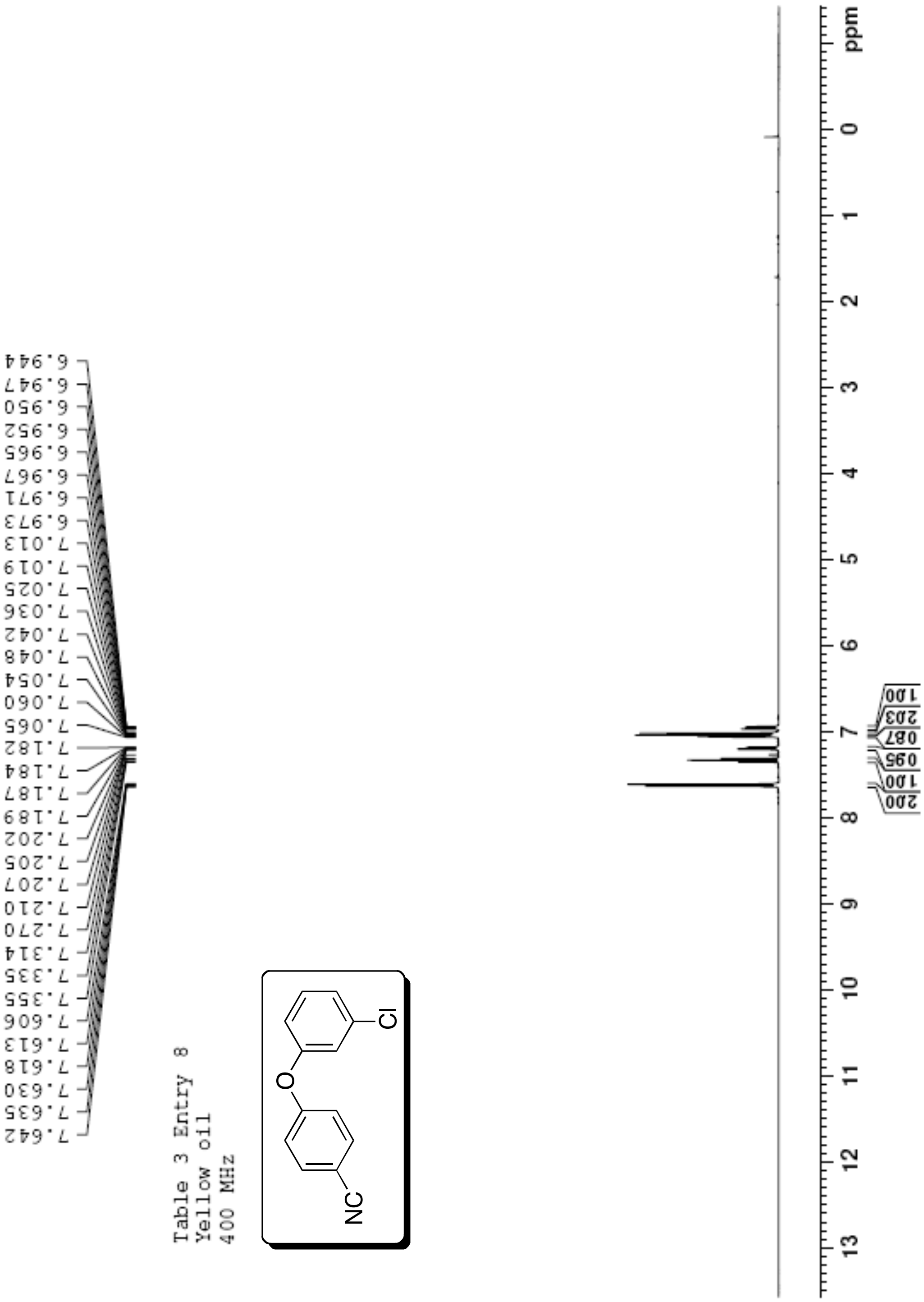


Table 3 entry 7
White solid
400 MHz
NC
O
OMe
3.824
6.921
6.927
6.939
6.944
6.956
6.961
6.988
6.996
7.002
7.013
7.019
7.270
7.551
7.557
7.562
7.574
7.579
7.586
3.00
3.86
1.91
1.86
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


162.715
157.208
148.021
134.298
122.050
119.205
117.340
115.446
105.437
77.671
77.353
77.035
55.902
Table 3 Entry 7
White solid
100 MHz
NC
O
OMe
200
180
160
140
120
100
80
60
40
20
0
ppm


7.642
7.635
7.630
7.618
7.613
7.606
7.355
7.335
7.314
7.270
7.210
7.207
7.205
7.202
7.189
7.187
7.184
7.182
7.065
7.060
7.054
7.048
7.042
7.036
7.025
7.019
7.013
6.973
6.971
6.967
6.965
6.952
6.950
6.947
6.944
Table 3 Entry 8
Yellow oil
400 MHz
NC
O
Cl
2.00
1.00
0.95
0.87
2.03
1.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm

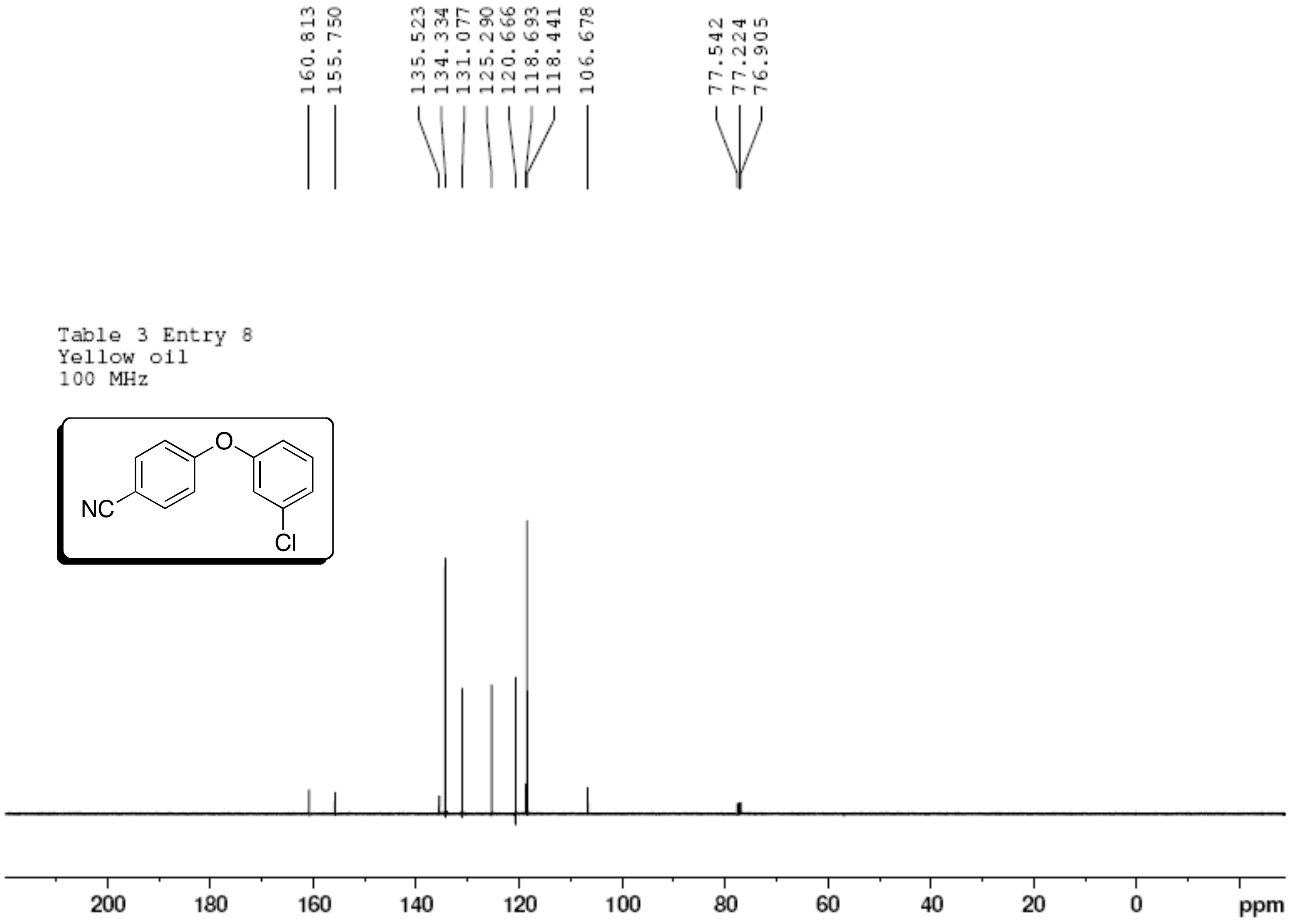
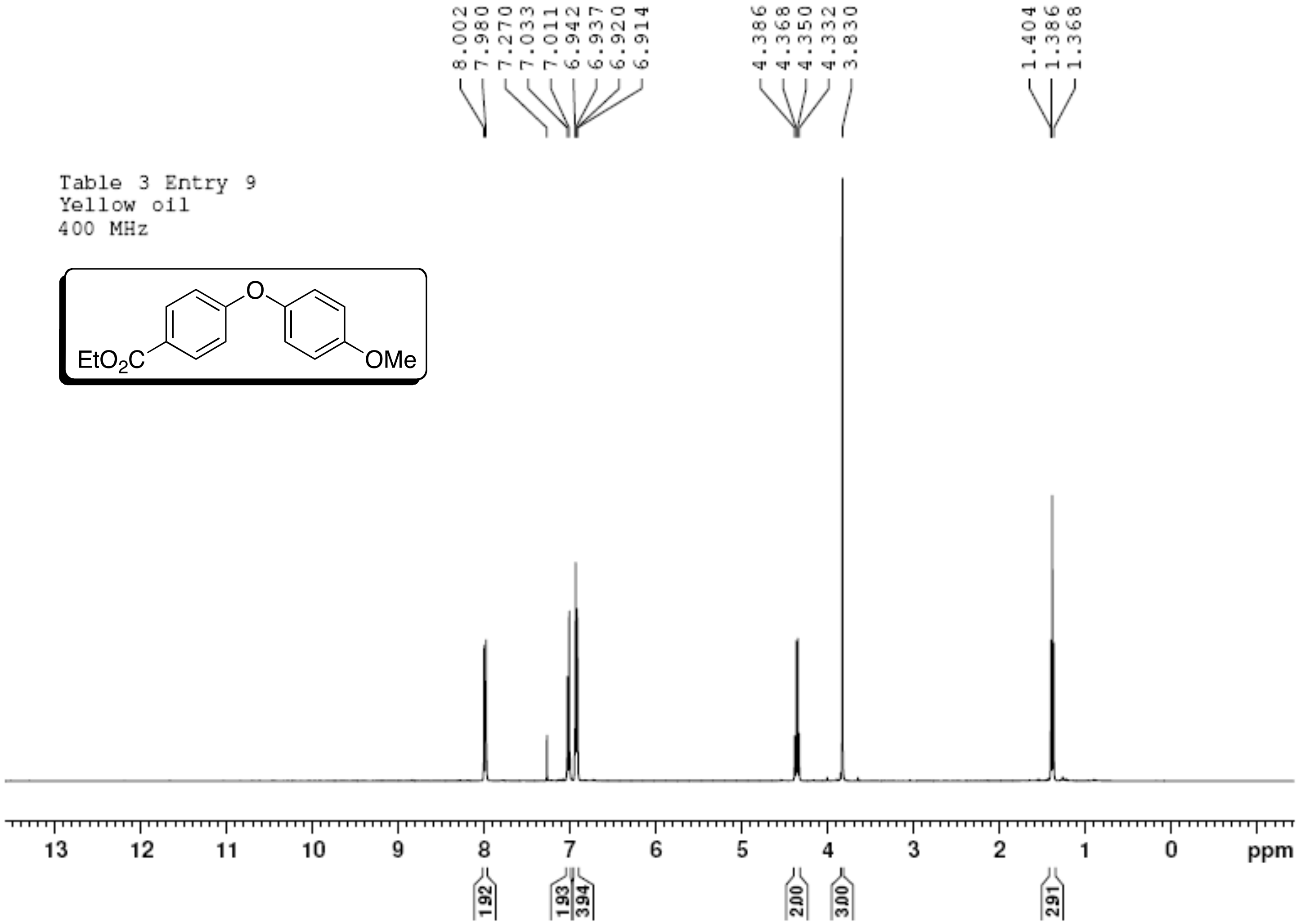
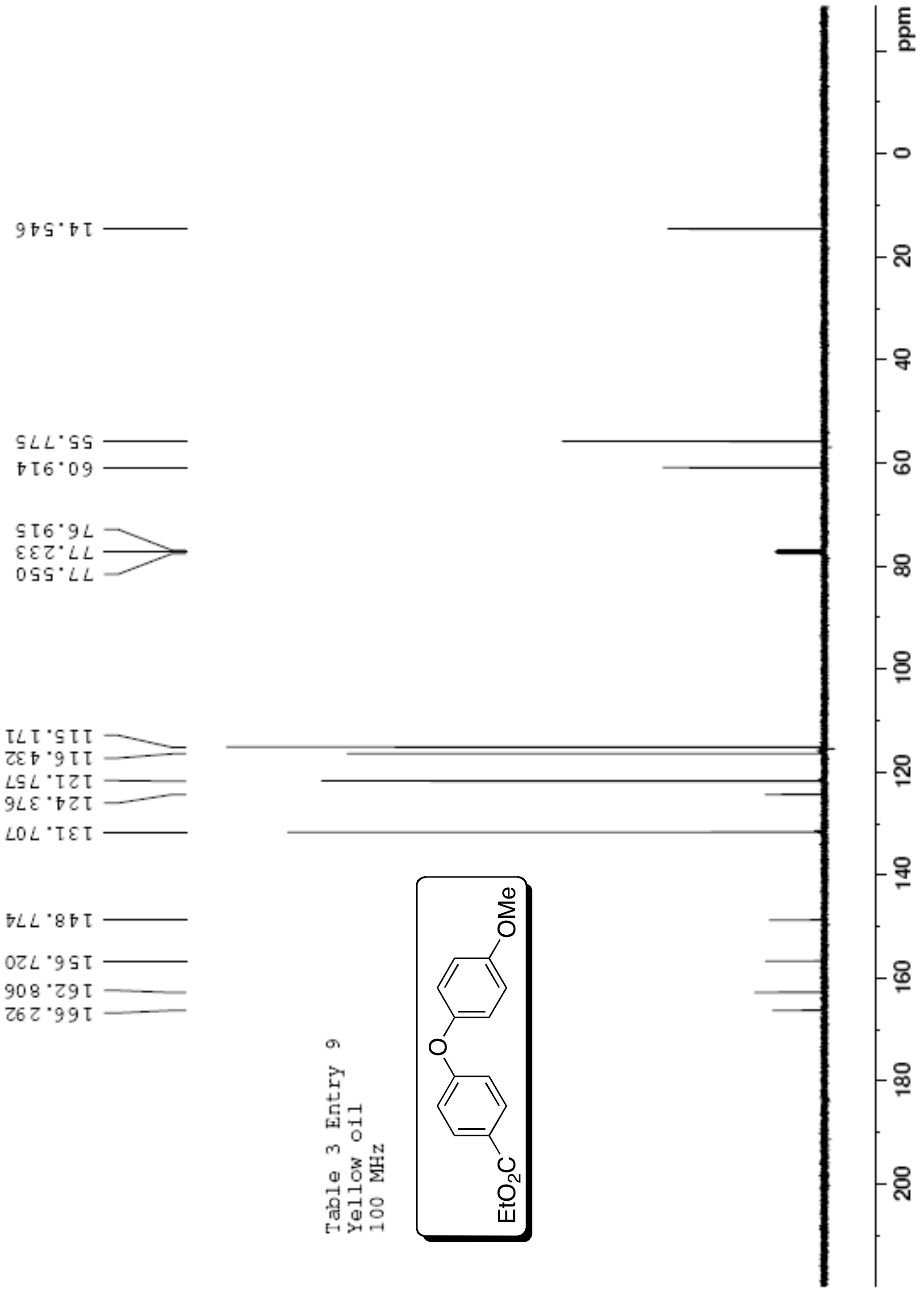
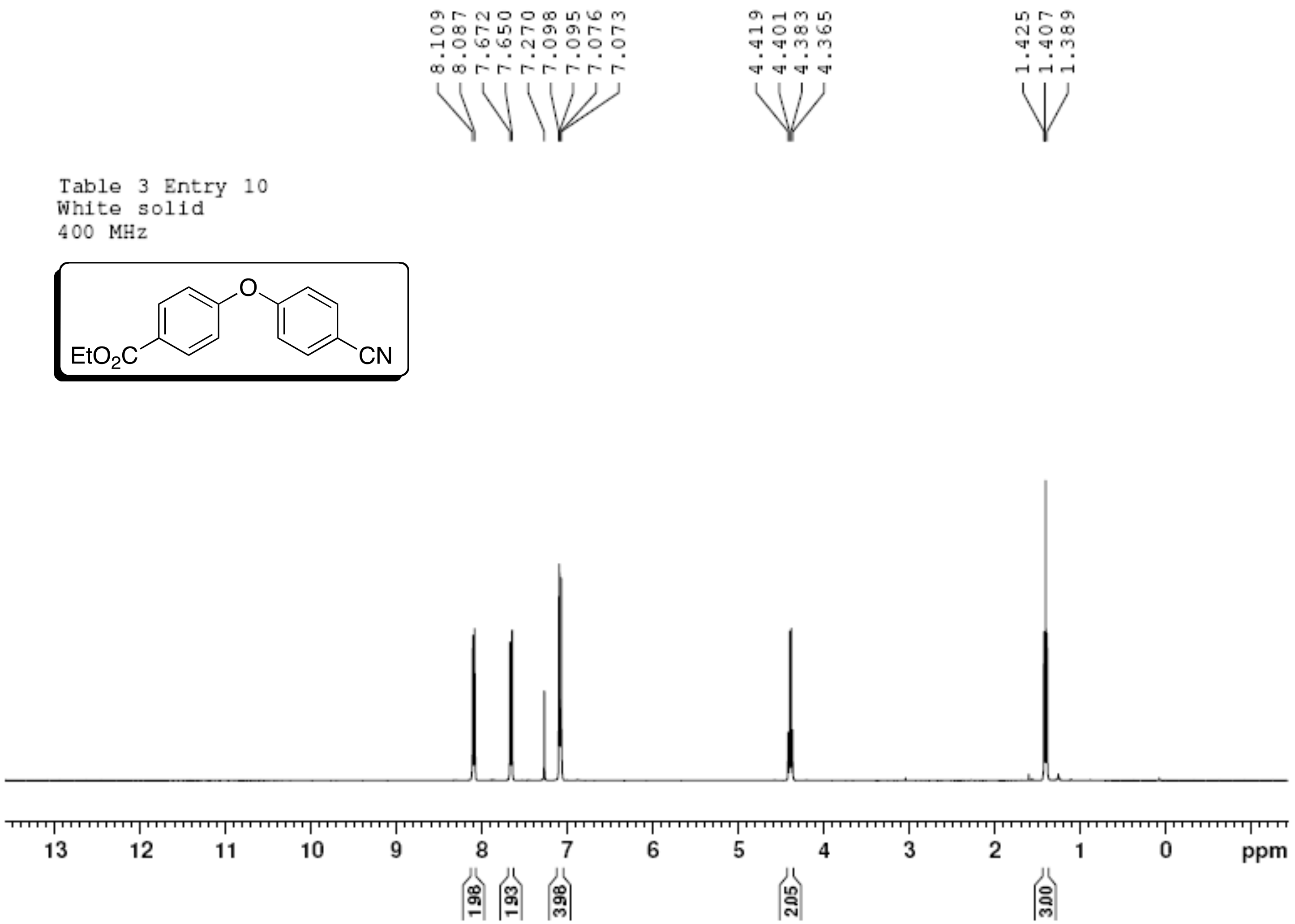
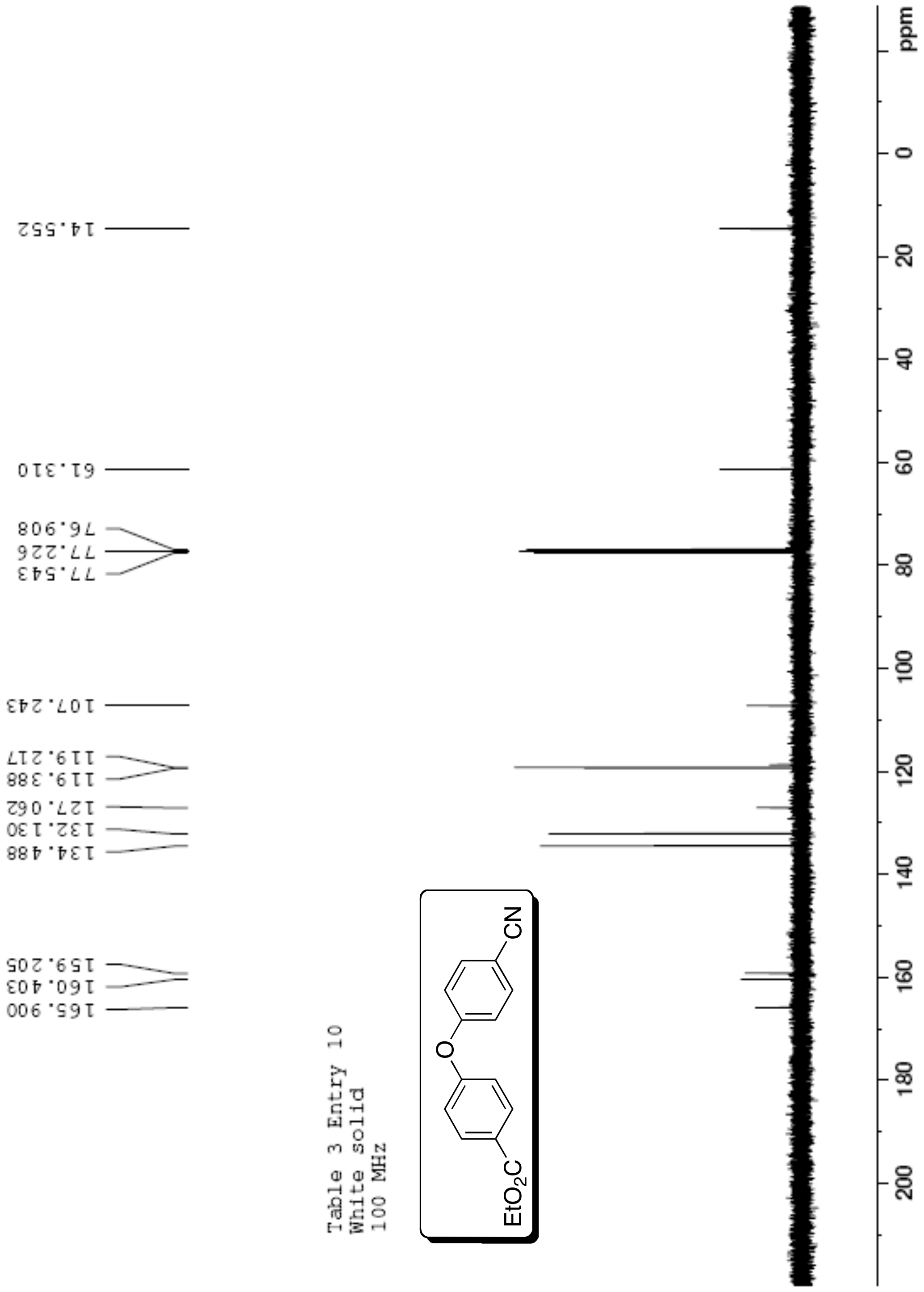


Table 3 Entry 8
Yellow oil
100 MHz


8.002
7.980
7.270
7.033
7.011
6.942
6.937
6.920
6.914
4.386
4.368
4.350
4.332
3.830
1.404
1.386
1.368
Table 3 Entry 9
Yellow oil
400 MHz
EtO2C
O
OMe
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.92
1.93
3.94
2.00
3.00
2.91


14.546
55.775
60.914
76.915
77.233
77.550
115.171
116.432
121.757
124.376
131.707
148.774
156.720
162.806
166.292
Table 3 Entry 9
Yellow oil
100 MHz
EtO$_2$C
O
OMe
ppm
0
20
40
60
80
100
120
140
160
180
200


8.109
8.087
7.672
7.650
7.270
7.098
7.095
7.076
7.073
4.419
4.401
4.383
4.365
1.425
1.407
1.389
Table 3 Entry 10
White solid
400 MHz
EtO2C
O
CN
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.98
1.93
3.98
2.05
3.00


14.552
61.310
76.908
77.226
77.543
107.243
119.217
119.388
127.062
132.130
134.488
159.205
160.403
165.900
Table 3 Entry 10
White solid
100 MHz
EtO2C
O
CN
ppm
0
20
40
60
80
100
120
140
160
180
200

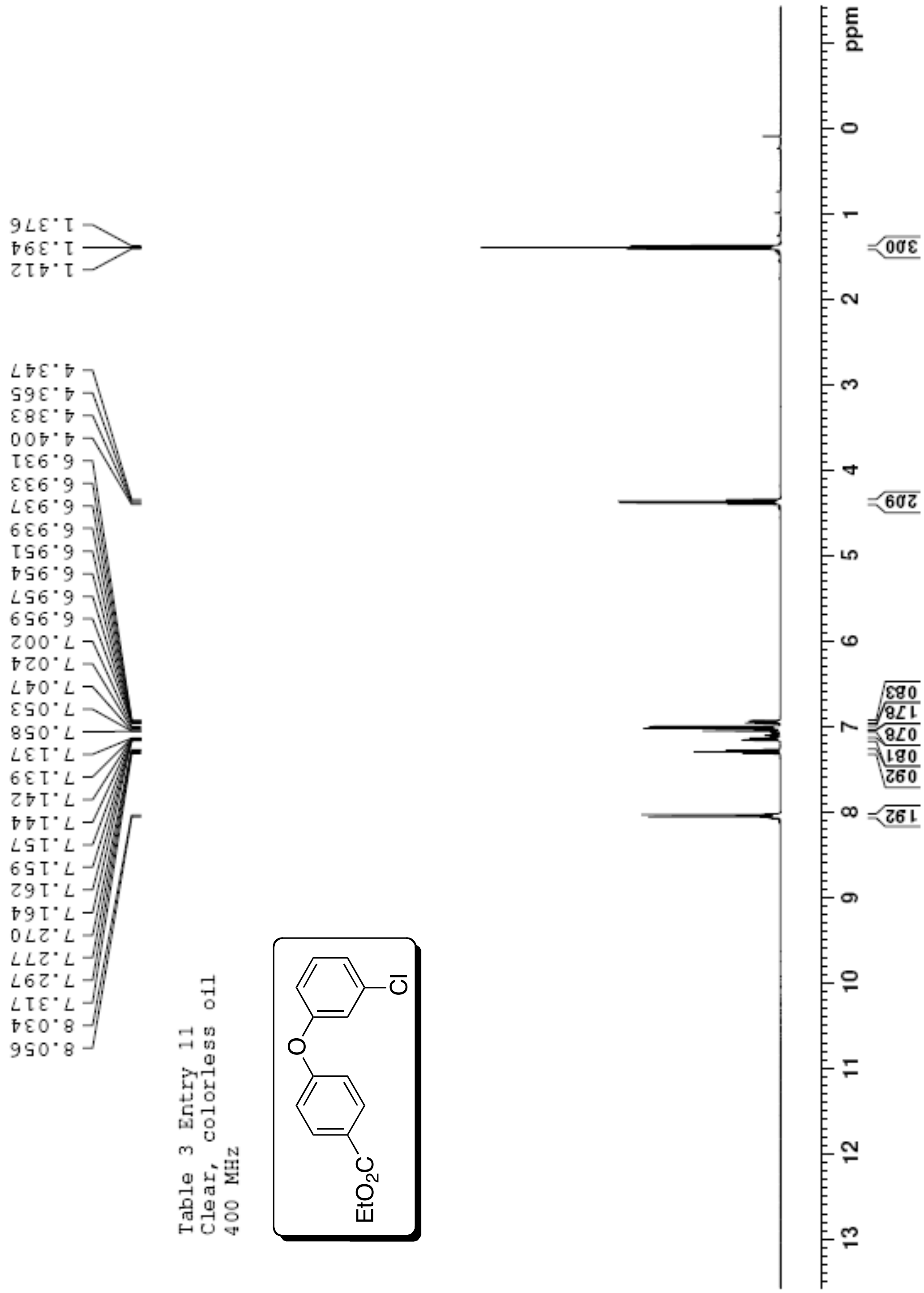
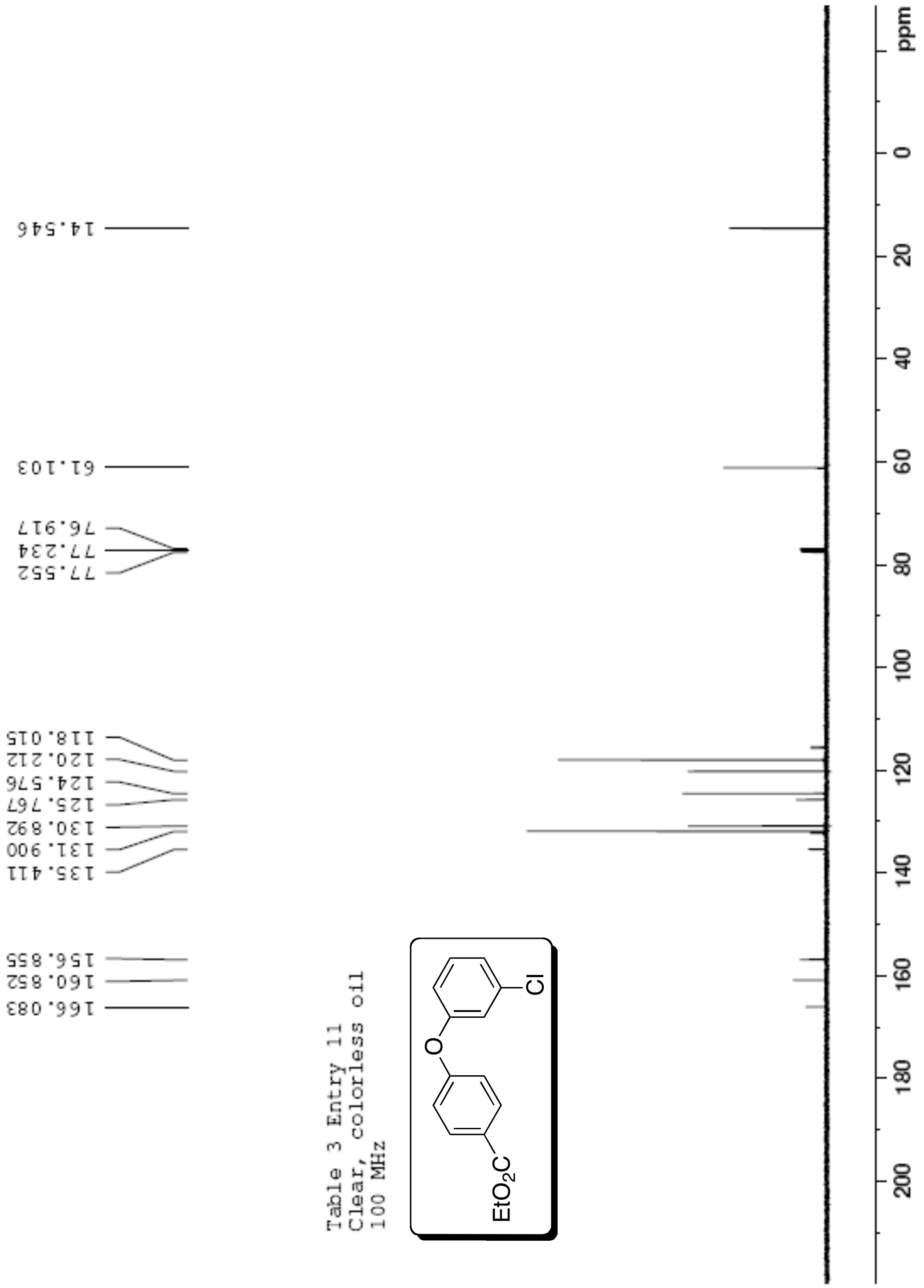
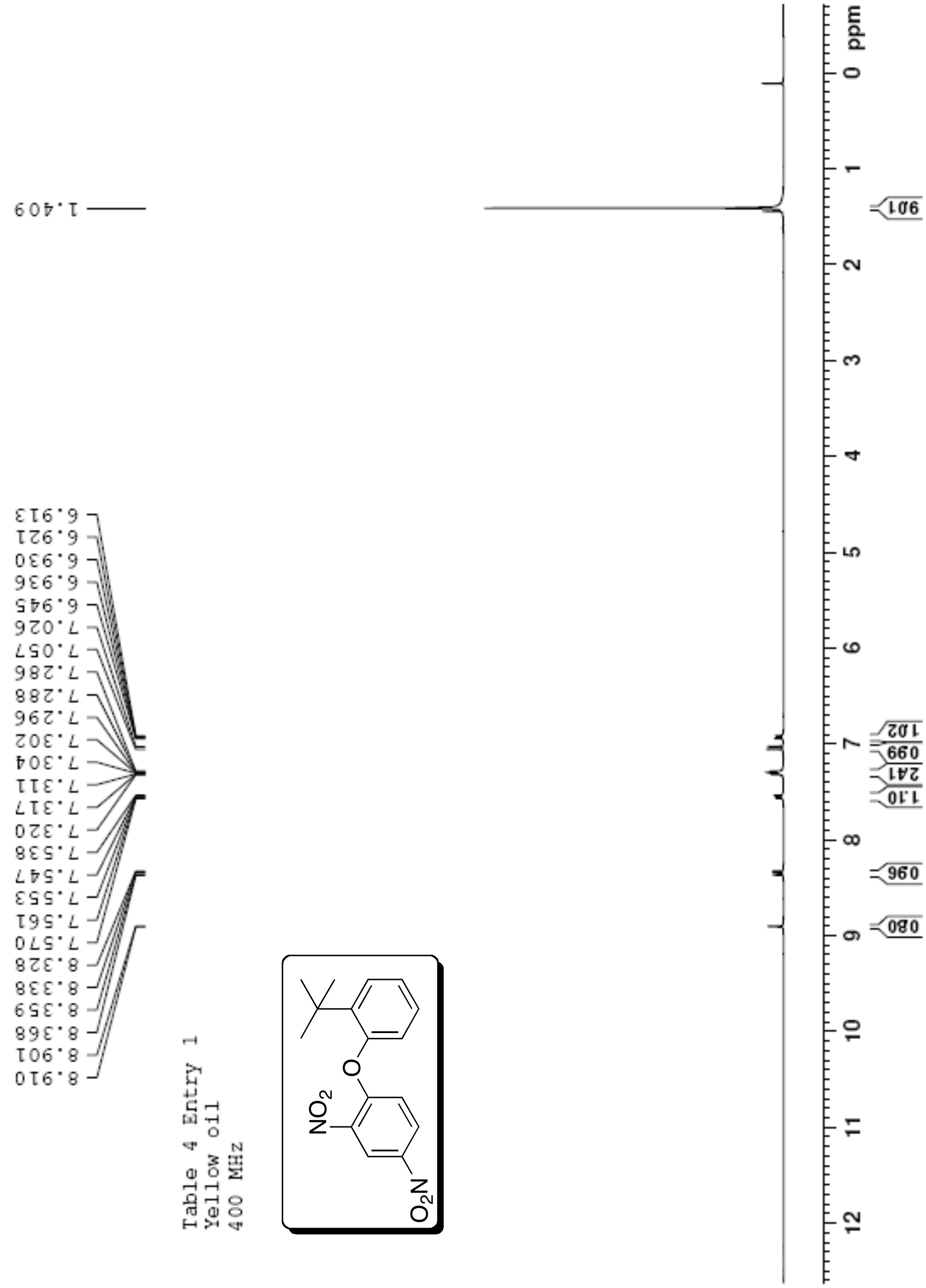
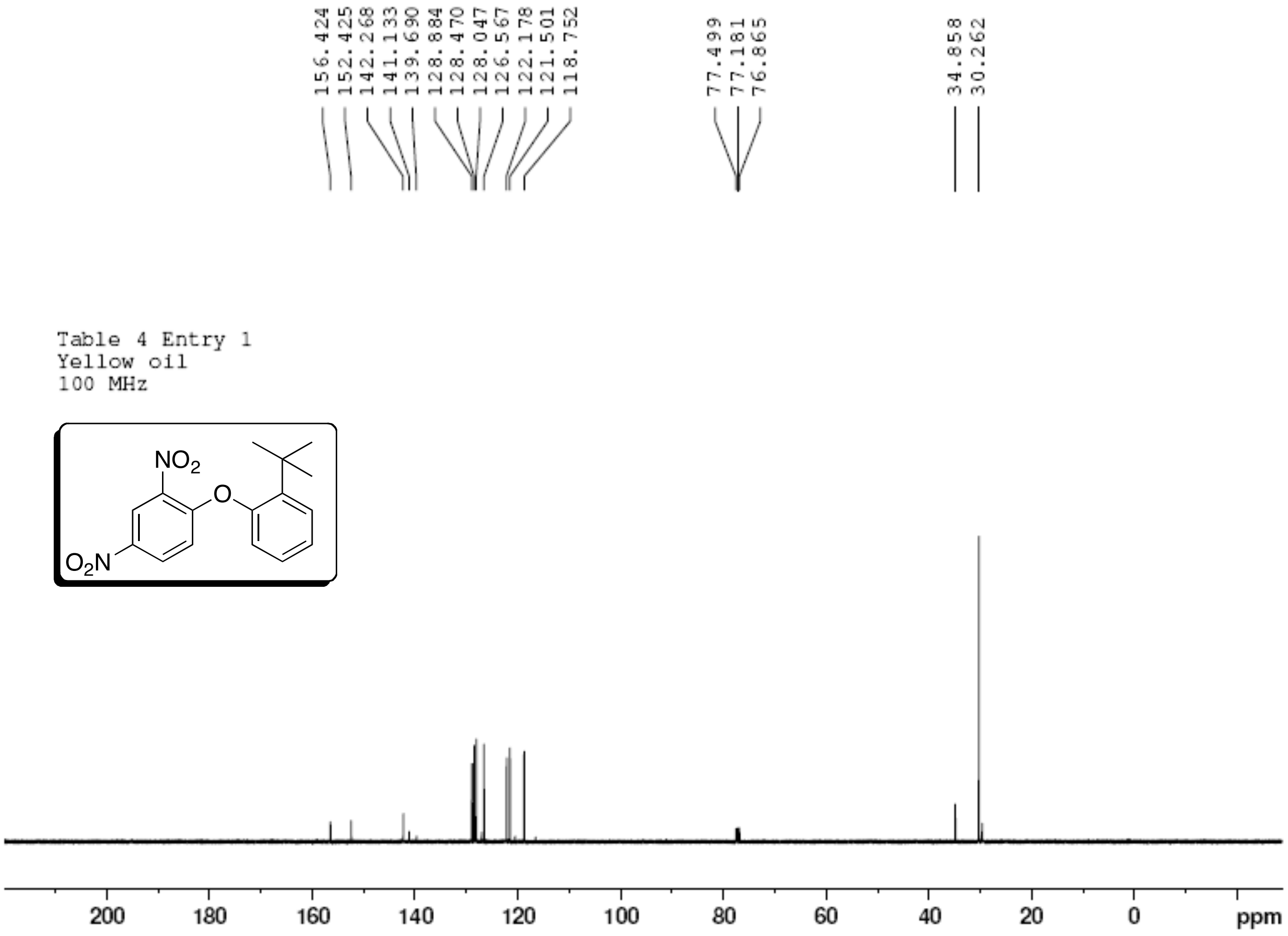
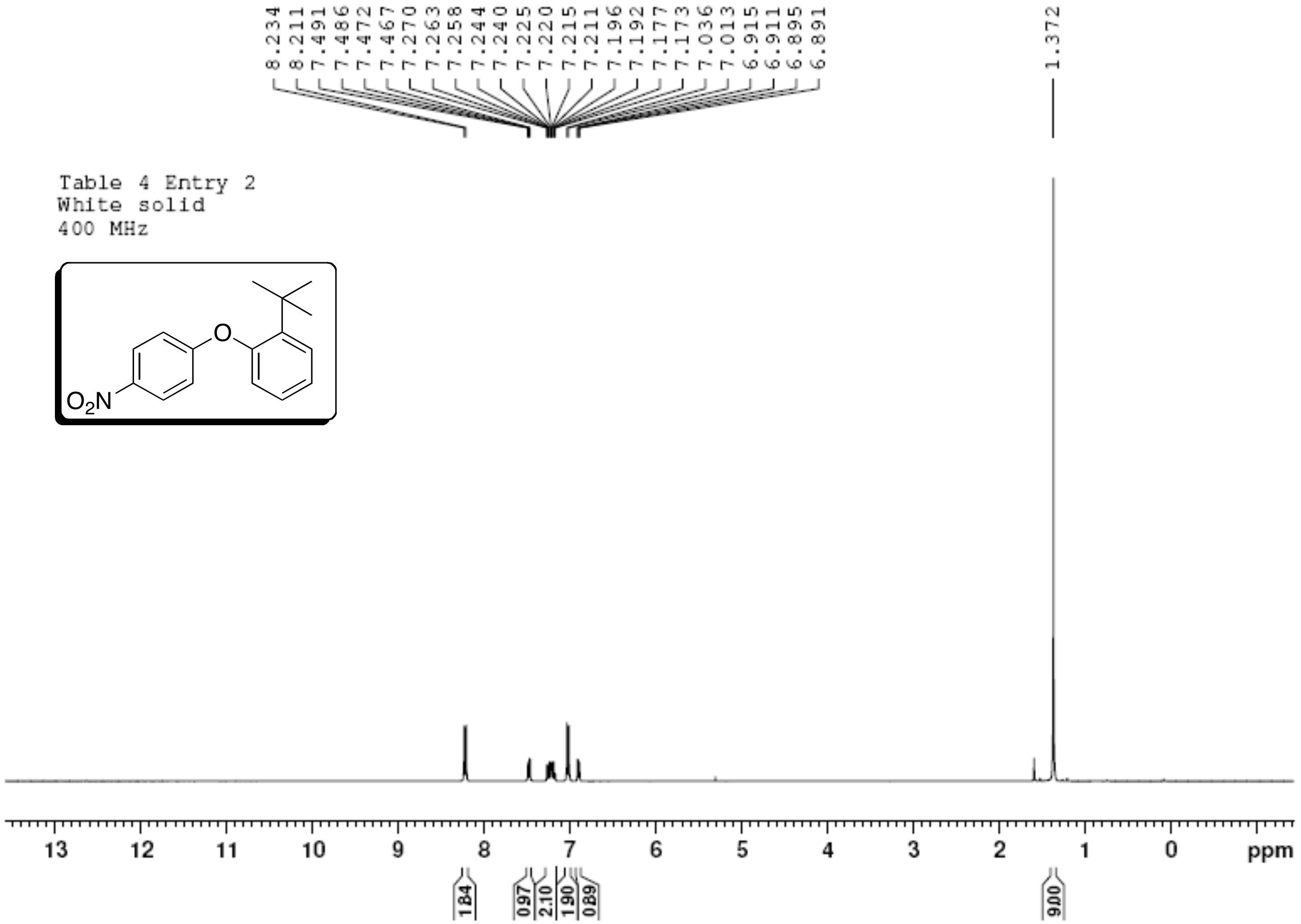


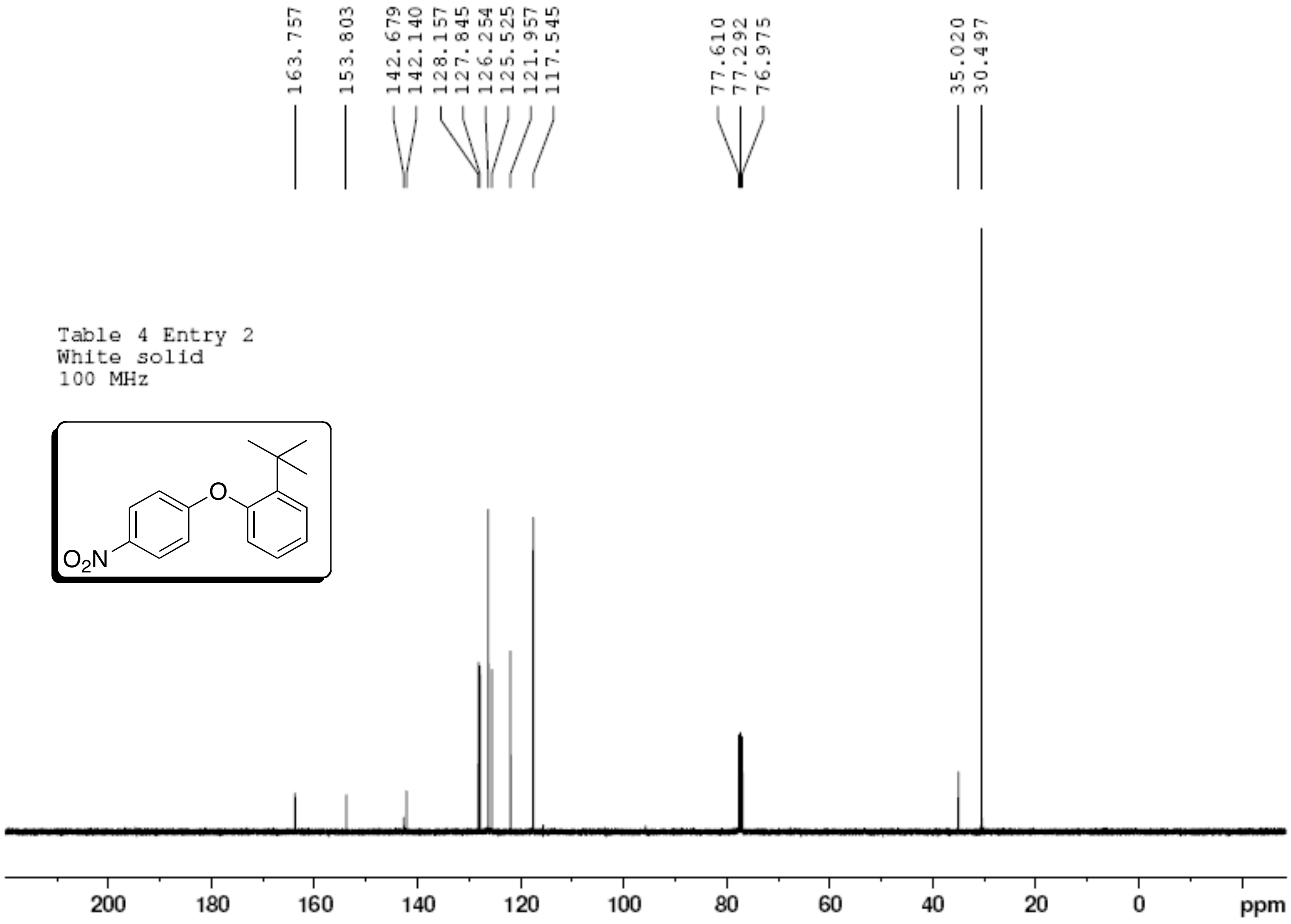
Table 3 Entry 11
Clear, colorless oil
400 MHz
EtO$_2$C
O
Cl
1.376
1.394
1.412
4.347
4.365
4.383
4.400
6.931
6.933
6.937
6.939
6.951
6.954
6.957
6.959
7.002
7.024
7.047
7.053
7.058
7.137
7.139
7.142
7.144
7.157
7.159
7.162
7.164
7.270
7.277
7.297
7.317
8.034
8.056
3.00
2.09
0.83
1.78
0.78
0.81
0.92
1.92
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

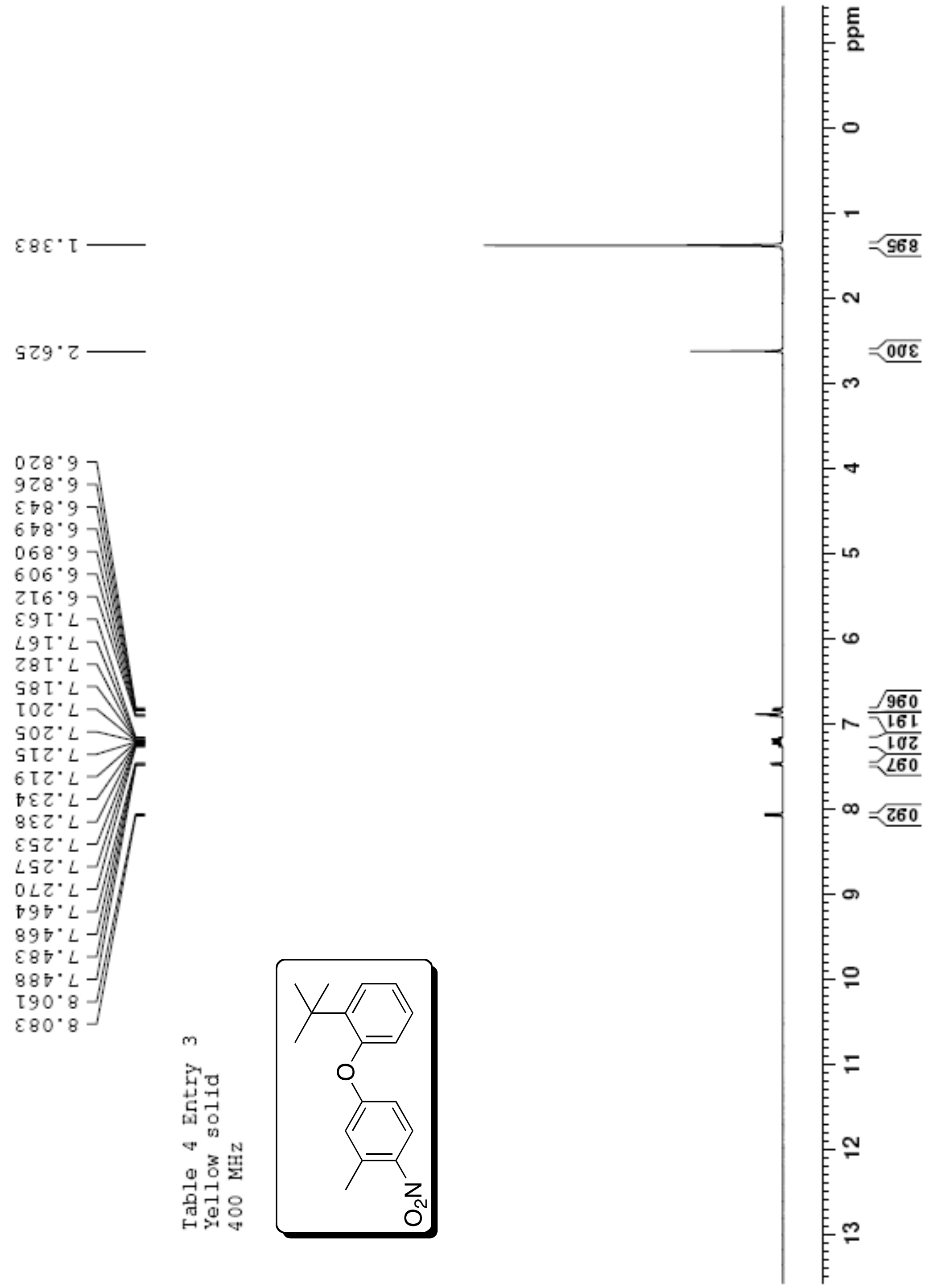

14.546
61.103
76.917
77.234
77.552
118.015
120.212
124.576
125.767
130.892
131.900
135.411
156.855
160.852
166.083
Table 3 Entry 11
Clear, colorless oil
100 MHz
EtO2C
O
Cl
ppm
0
20
40
60
80
100
120
140
160
180
200

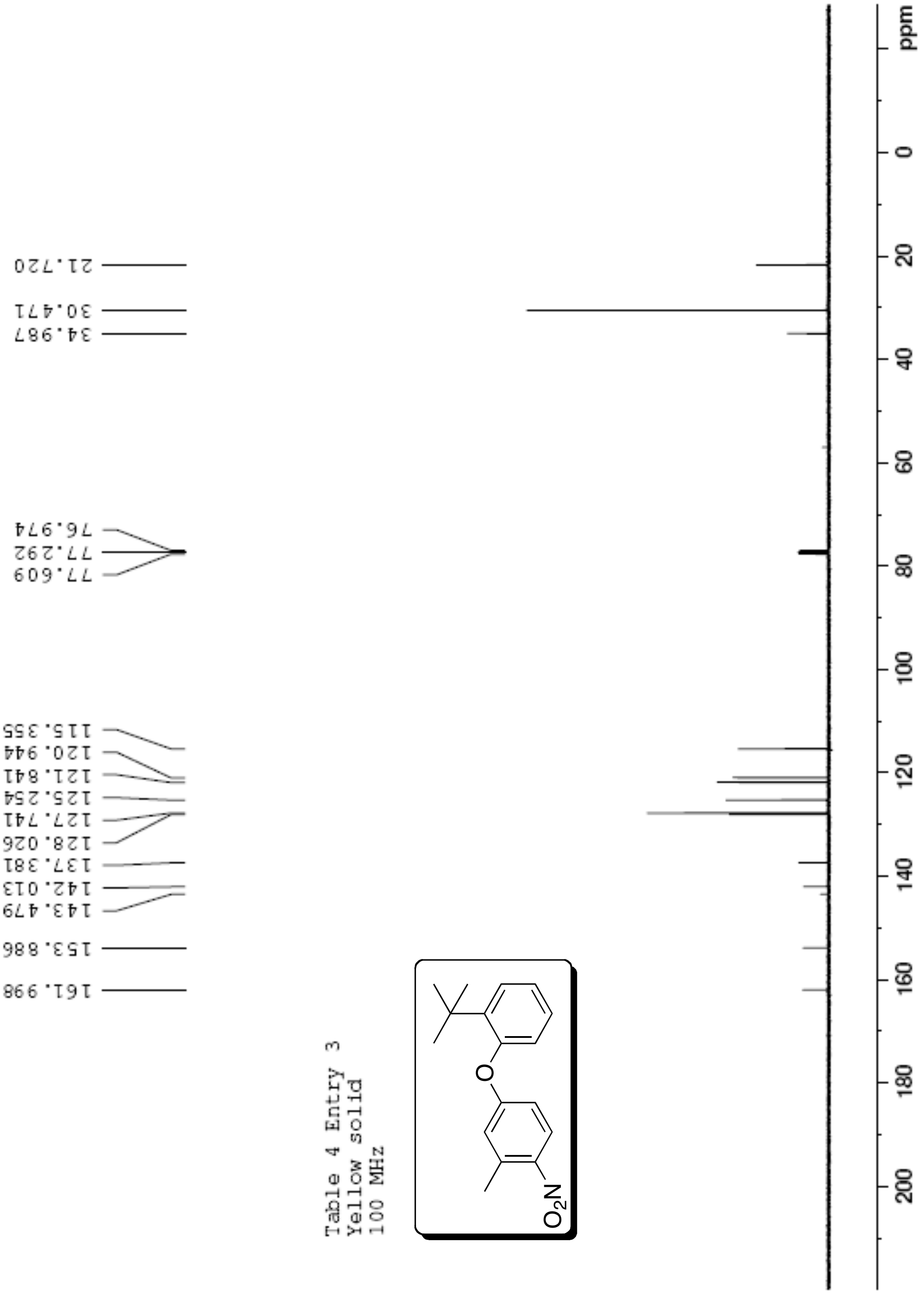

1.409
6.913
6.921
6.930
6.936
6.945
7.026
7.057
7.286
7.288
7.296
7.302
7.304
7.311
7.317
7.320
7.538
7.547
7.553
7.561
7.570
8.328
8.338
8.359
8.368
8.901
8.910
Table 4 Entry 1
Yellow oil
400 MHz
NO2
O
O2N
9.01
1.02
0.99
2.41
1.10
0.96
0.80
0
1
2
3
4
5
6
7
8
9
10
11
12
ppm


156.424
152.425
142.268
141.133
139.690
128.884
128.470
128.047
126.567
122.178
121.501
118.752
77.499
77.181
76.865
34.858
30.262
Table 4 Entry 1
Yellow oil
100 MHz
NO2
O
O2N
200
180
160
140
120
100
80
60
40
20
0
ppm


8.234
8.211
7.491
7.486
7.472
7.467
7.270
7.263
7.258
7.244
7.240
7.225
7.220
7.215
7.211
7.196
7.192
7.177
7.173
7.036
7.013
6.915
6.911
6.895
6.891
1.372
Table 4 Entry 2
White solid
400 MHz
O2N
O
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.84
0.97
2.10
1.90
0.89
9.00


163.757
153.803
142.679
142.140
128.157
127.845
126.254
125.525
121.957
117.545
77.610
77.292
76.975
35.020
30.497
Table 4 Entry 2
White solid
100 MHz
O
O_2N
200
180
160
140
120
100
80
60
40
20
0
ppm


1.383
2.625
6.820
6.826
6.843
6.849
6.890
6.909
6.912
7.163
7.167
7.182
7.185
7.201
7.205
7.215
7.219
7.234
7.238
7.253
7.257
7.270
7.464
7.468
7.483
7.488
8.061
8.083
Table 4 Entry 3
Yellow solid
400 MHz
O
O2N
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
895
300
096
191
201
097
092


21.720
30.471
34.987
76.974
77.292
77.609
115.355
120.944
121.841
125.254
127.741
128.026
137.381
142.013
143.479
153.886
161.998
Table 4 Entry 3
Yellow solid
100 MHz
O
O_2N
ppm
0
20
40
60
80
100
120
140
160
180
200

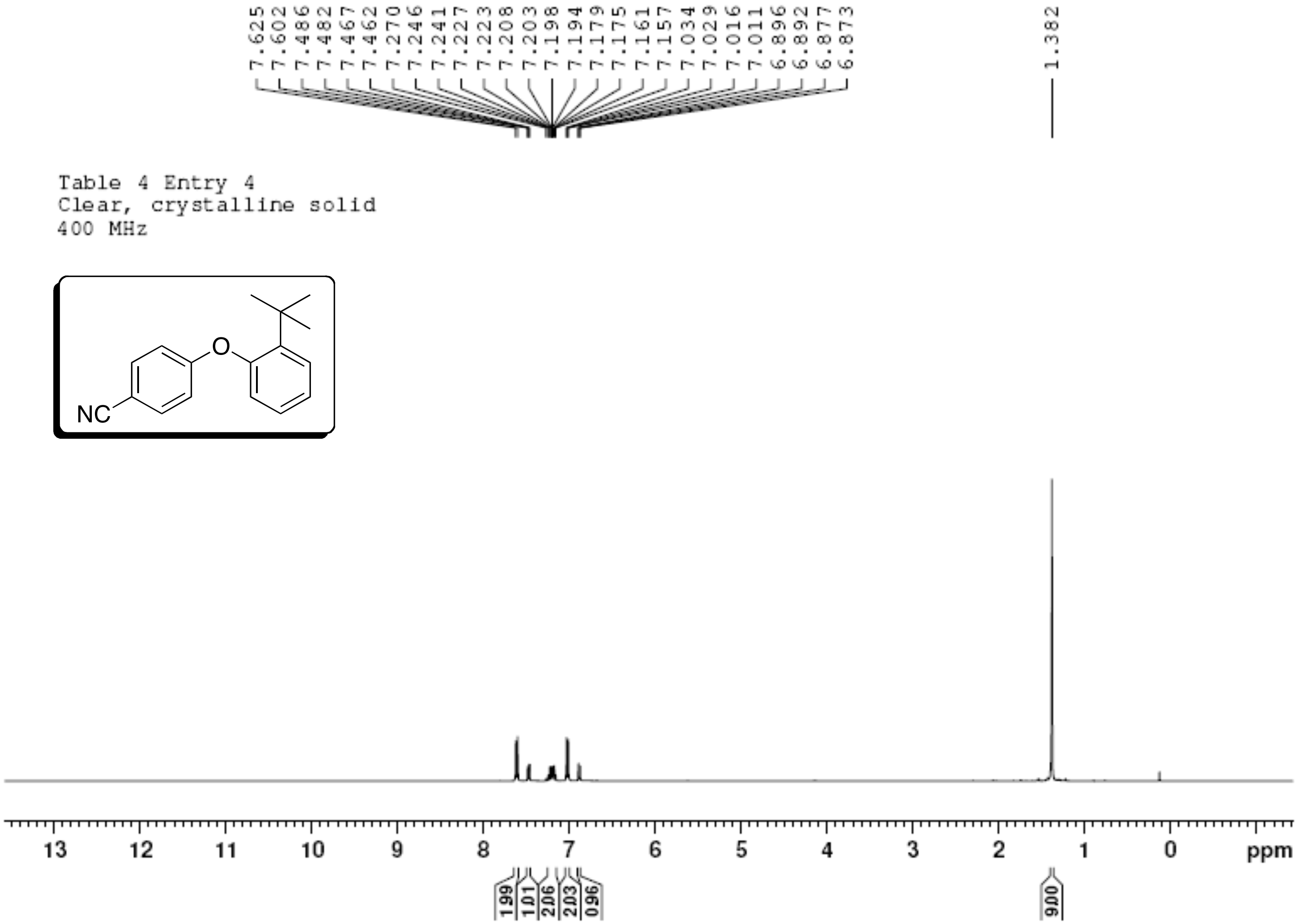
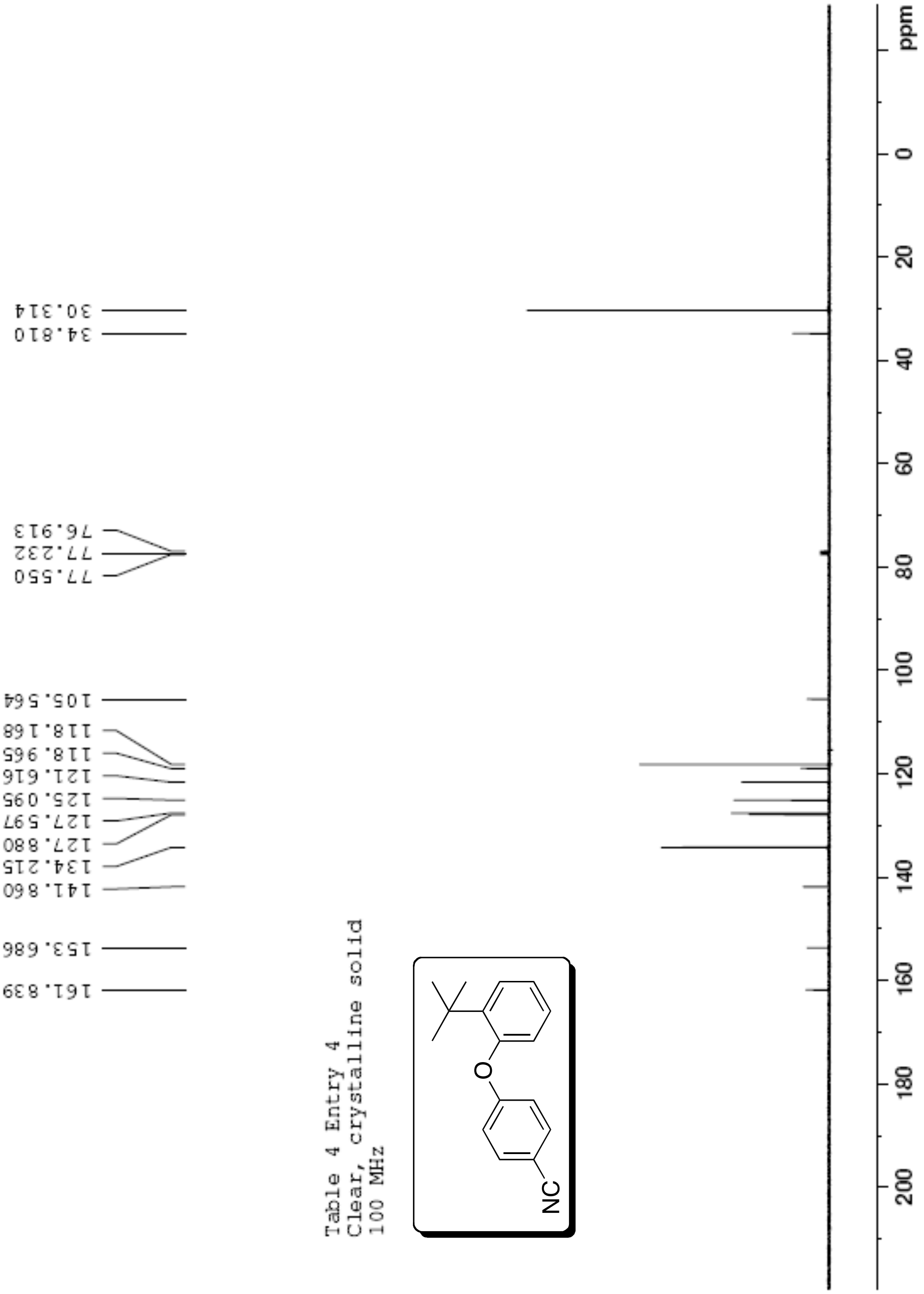


Table 4 Entry 4
Clear, crystalline solid
400 MHz



30.314
34.810
76.913
77.232
77.550
105.564
118.168
118.965
121.616
125.095
127.597
127.880
134.215
141.860
153.686
161.839
Table 4 Entry 4
Clear, crystalline solid
100 MHz
O
NC
ppm
0
20
40
60
80
100
120
140
160
180
200

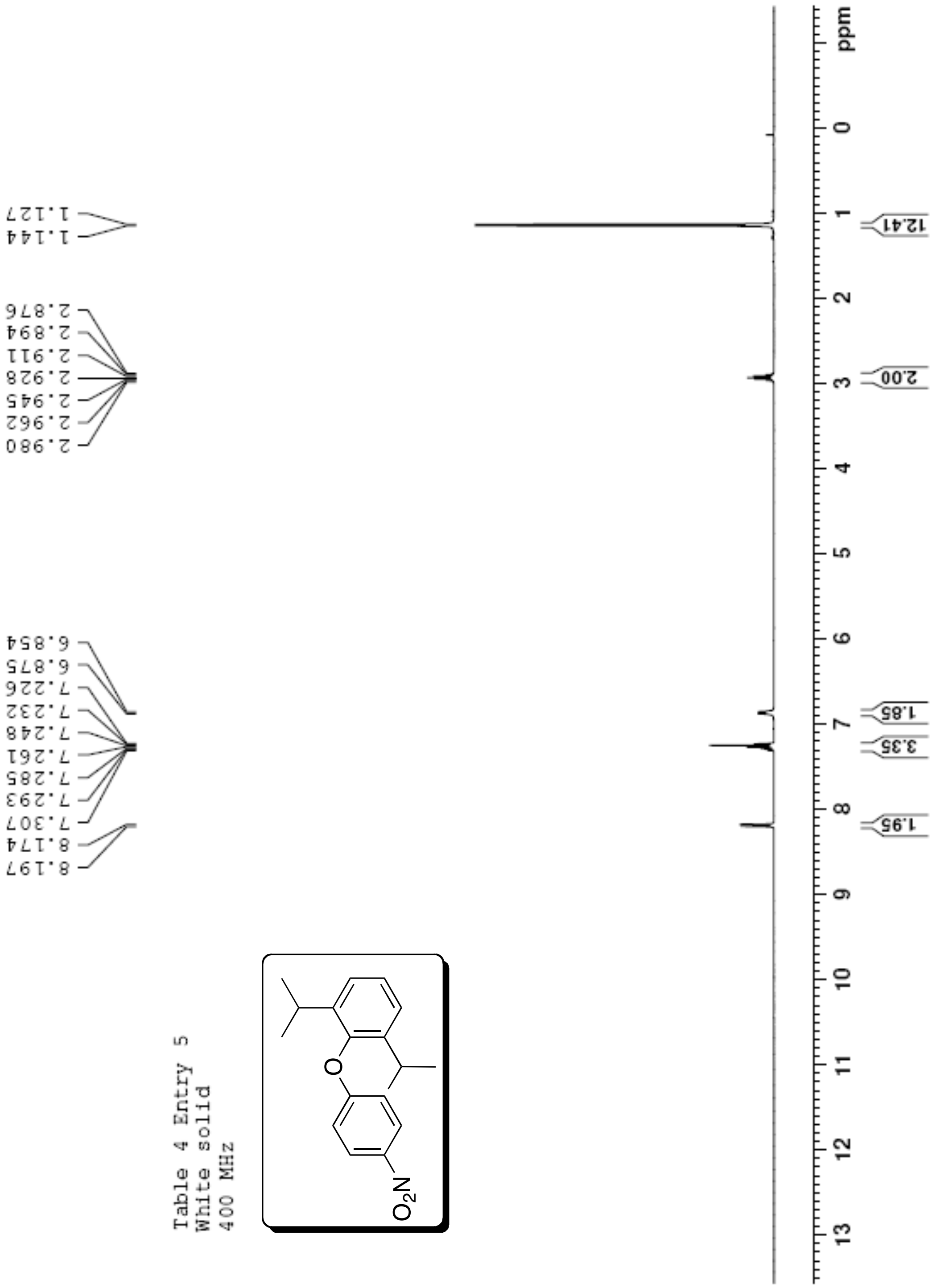
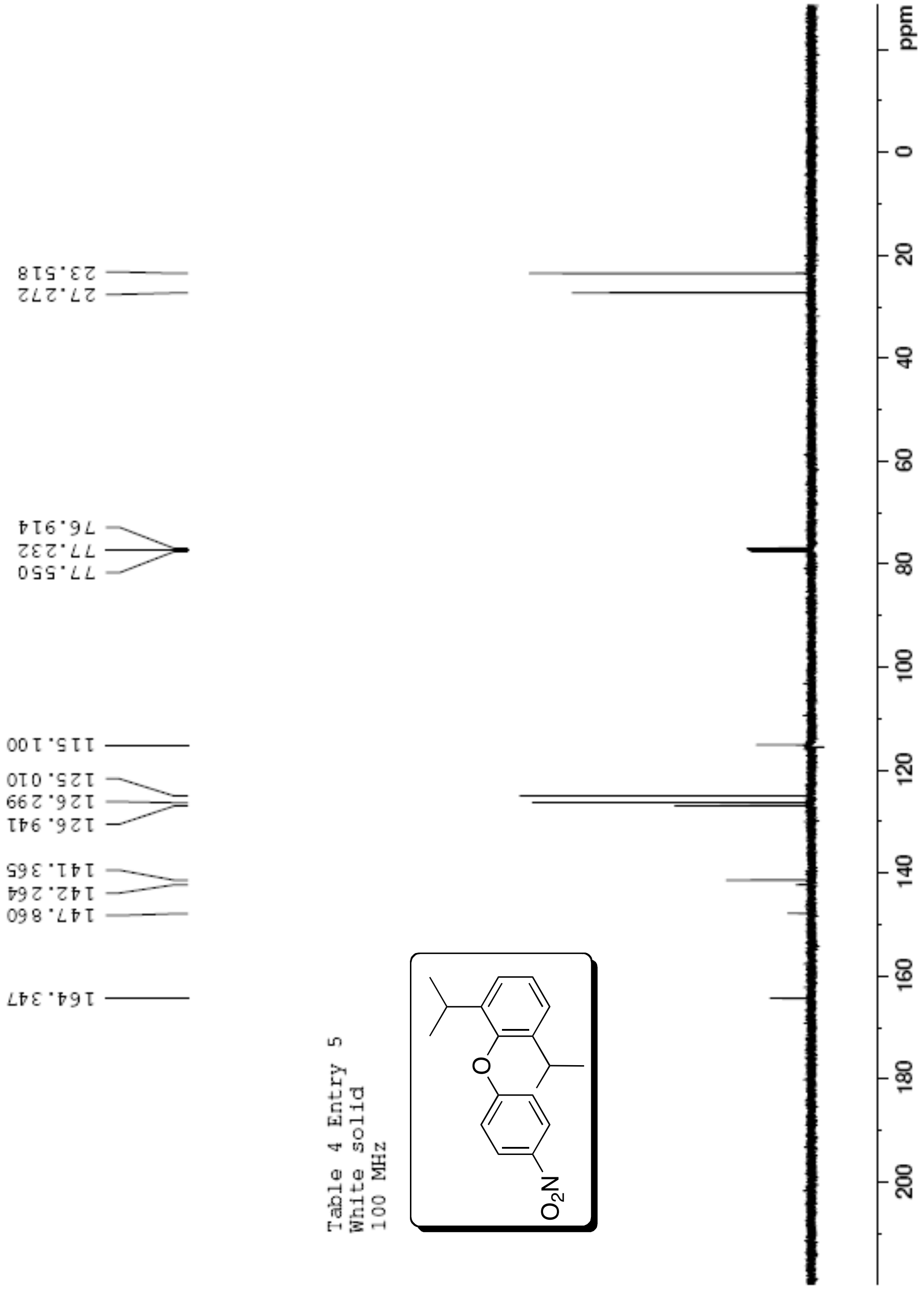


Table 4 Entry 5
White solid
400 MHz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27.272
76.914
77.232
77.550
115.100
125.010
126.299
126.941
141.365
142.264
147.860
164.347
Table 4 Entry 5
White solid
100 MHz
O2N
O
ppm
0
20
40
60
80
100
120
140
160
180
200

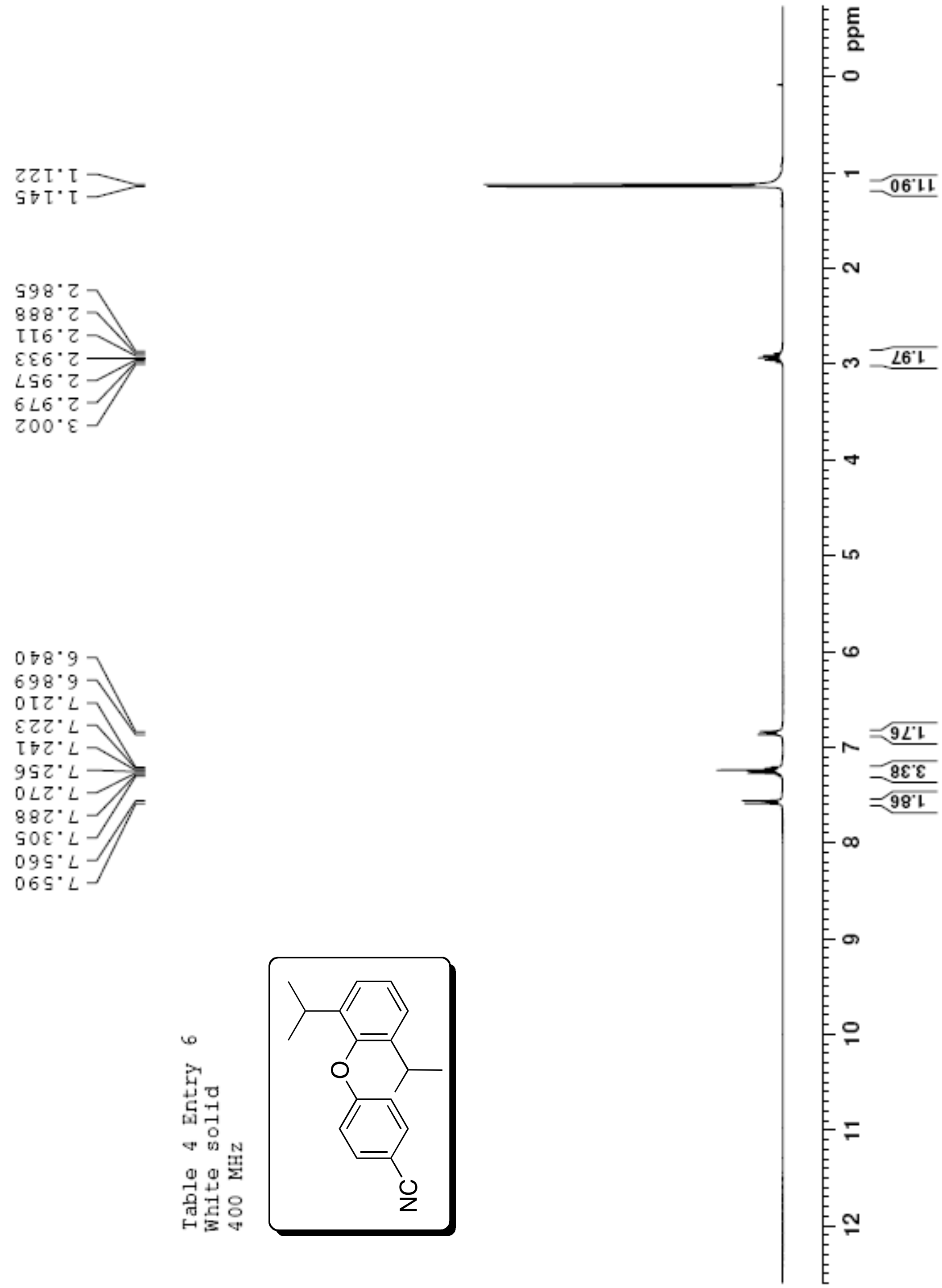
Table 4 Entry 6
White solid
400 MHz
NC
O
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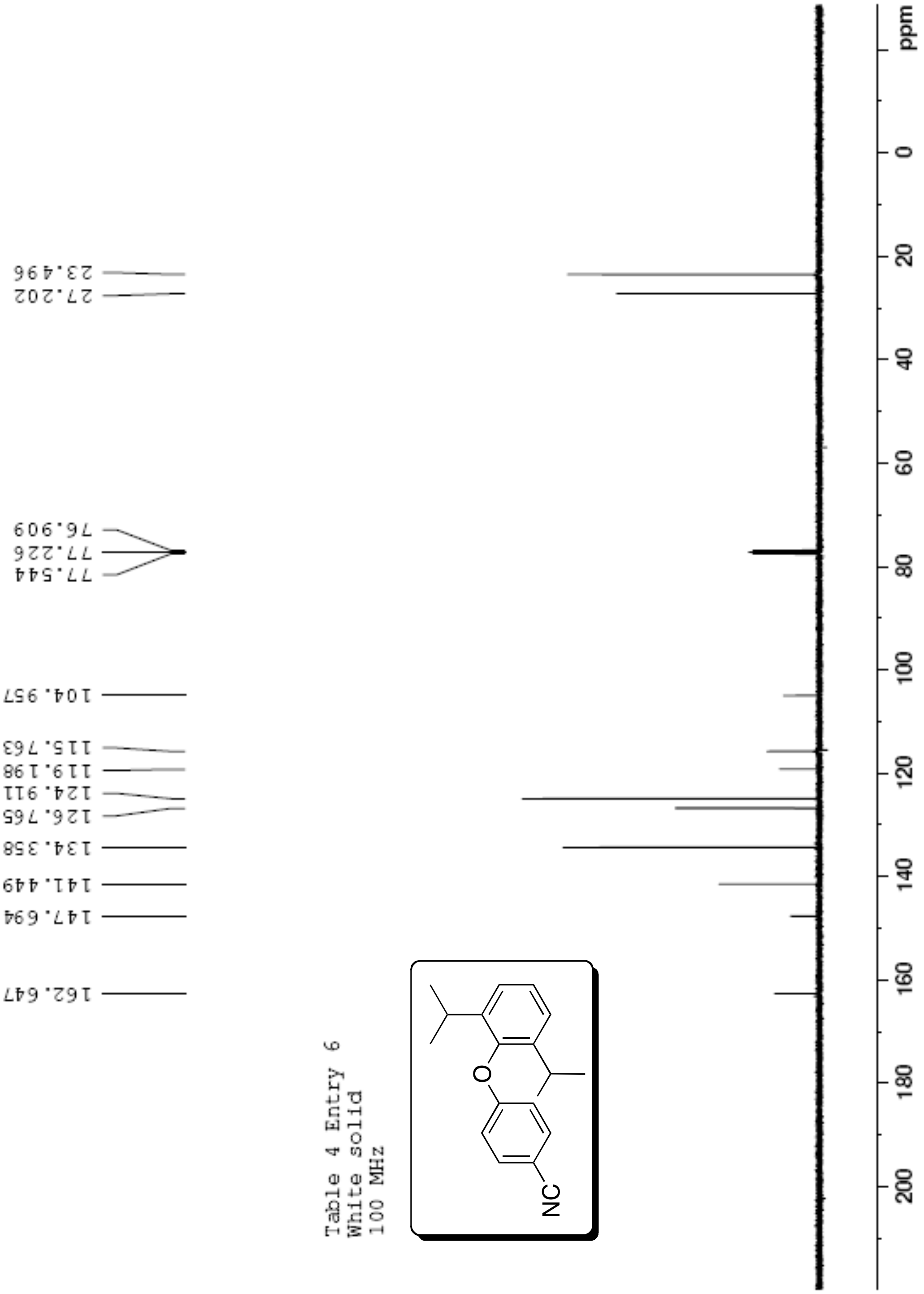
1.145
2.865
2.888
2.911
2.933
2.957
2.979
3.002
6.840
6.869
7.210
7.223
7.241
7.256
7.270
7.288
7.305
7.560
7.590
11.90
1.97
1.76
3.38
1.86
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12


23.496
27.202
76.909
77.226
77.544
104.957
115.763
119.198
124.911
126.765
134.358
141.449
147.694
162.647
Table 4 Entry 6
White solid
100 MHz
O
NC
ppm
0
20
40
60
80
100
120
140
160
180
200

APPENDIX B

CHAPTER 3. Supplementary Information

Experimental Procedures

References for known compounds

Data for unknown compounds

^{1}H, ^{13}C, and ^{31}P NMR spectra for proazaphosphatranes

^{1}H and ^{13}C NMR spectra for reaction products

X-ray data for Proazaphosphatrane 6

General Considerations: All reactions were carried out under dry argon using standard Schlenk procedures. All solvents were dried with sodium in a solvent still and distilled prior to use. Chemicals used in the sythensis of proazaphosphatrane **5** and chemicals used in the cyclotrimerization of isocyanates were purchased from Aldrich chemical company and used without any further purification. Proazaphosphatranes **1**[1], **3**[2], **4**[2] and **5**[3] were prepared according to literature procedures. Proazaphosphatrane **2** was kindly donated from Aldrich chemical. ^{1}H, ^{13}C, and ^{31}P NMR were recorded using a VXR-400 Varian spectrometer. Reactions were run until the production of solids formed in the reaction. All reaction yields are an average to two runs.

Experimental Section:

Synthesis of $N[CH_2CH_2NH(2,4\text{-}OMeC_6H_3CH_2)]_3$ (Compound 18). To 1.0 equivalent of freshly distilled tris(2-aminoethyl)amine in 100 mL MeOH was added (3.1 equiv) of 2,4-dimethoxybenzaldehyde. The mixture was allowed to stir at room temperature overnight and another 100 mL MeOH was added and the reaction mixture was cooled 0-5 ºC in an ice bath and $NaBH_4$ (1.5 equiv) was added slowly portion-wise over 1 h. The reaction was stirred overnight and the MeOH was removed by rotovap. Sufficient amount of water was added and extracted with 3×100 mL toluene. The toluene extracts were combined and dried over Na_2SO_4. The toluene was filtered and removed by rotovap. The crude dark yellow oil was purified by column chromatography (1% MeOH in CH_2Cl_2) to obtain 94% of the desired product. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 1.69$ (br, 3H), 2.57-2.58 (d, 6H, $J = 5.6$ Hz), 2.62-2.64 (d, 6H, $J = 5.6$), 3.68 (s, 6H), 3.74 (s, 9H), 3.78 (s, 9H), 6.37-6.41 (m, 3H), 6.46 (s, 3H), and 7.09-7.11 (d, 3H, $J = 8$ Hz) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 160.1$, 158.7, 130.4, 121.4, 103.9, 98.7, 55.6, 55.4, 55.0, 49.0, 47.4 ppm. APCI$^+$ found 597 (calc for $C_{33}H_{48}N_4O_6$, 596.36).

Synthesis of (7H)Cl. Add 50 mL of dry CH_3CN in a RB (preferably Schlenk flask). The RB flask was cooled to 0-5 ºC and HMPT {$P(NMe_2)_3$} (2.0 equiv) was added under an argon flow. Phosphorus trichloride (PCl_3) was added slowly through syringe. After stirring at 0-5 ºC for 15 minutes, compound 20 (3.0 equiv) dissolved in 50 mL dry CH_3CN wad added. The reaction mixture was stirred overnight at rt. Removal the solvent using rotary evaporator left a light yellow solid. Addition of diethyl ether and stirring overnight afforded a free flowing white powder in 88% isolated yield. ^{1}H NMR (CD_3CN, 400 MHz): δ = 2.62-2.64 (m, 6H), 2.83-2.84 (d, 6H, J = 4.8 Hz), 3.36 (s, 9H), 3.38 (s, 9H), 3.59-3.63 (d, 6H, J = 16.4 Hz), 4.71-5.98 (d, 1H, J = 508 Hz), and 6.04-6.07 (d, 3H, J = 8.4 Hz), 6.11 (s, 3H), 6.64-6.66 (d, 3H, J = 8 Hz) ppm. ^{13}C NMR (CD_3CN, 100 MHz): δ = 161.5, 159.5, 130.6, 119.3, 105.4, 99.4, 66.3, 56.2, 56.1, 48.0, 47.9 (d, J = 7.6 Hz), 46.4 (d, J = 17.1 Hz), 40.04 (d, J = 5.5 Hz). ^{31}P NMR (168 MHz, CD_3CN) δ = -10.88 ppm.

Synthesis of Compound 7. To a 25 mL round bottom flask containing compound 21 (1 equiv), 150 mL of THF was added. The salt was stirred for 10 minutes and NaHMDS (2 equiv) was added to the slurry. The reaction was stirred overnight and the THF was evaporated under inert atmosphere. Toluene was added to extract the proazaphosphatrane and the solids were filtered off. The toluene extract is then evaporated and 100 mL of pentane is added and the flask was placed in the freezer for 1 day in which a yellow oil formed on the bottom of the flask. The pentane was withdrawn and the resulting liquid was dried under vacuum (67% isolated yield). ^{1}H NMR (400 MHz, C_6D_6): δ = 2.73(s, 6H), 2.91 (s, 6H), 3.38 (s, 9H), 3.44 (s, 9H), 4.47-4.49 (d, 6H, J = 9.6 Hz), 6.40-6.2 (m, 3H), 6.46-6.47

(d, 3H, *J* = 2 Hz), and 7.50-7.52 (d, 3H, *J* = 8.4 Hz) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 160.6, 159.2, 130.7, 122.6, 122.6, 104.6, 99.1, 99.1, 55.4, 55.2, 52.1, 47.7 (d, *J* = 41.5 Hz), and 46.7 (d, *J* = 6.1 Hz) ppm. ^{31}P NMR (186 MHz, C_6D_6): δ = 127.18 ppm. APCI$^+$ found 625 (calc for $C_{32}H_{45}N_4O_6P$, 624.31).

Synthesis of N[CH$_2$CH$_2$NH(2,4,6-OMeC$_6$H$_2$CH$_2$)]$_3$ (Compound 19). To 1.0 equivalent of freshly distilled tris(2-aminoethyl)amine in 100 mL MeOH was added (3.1 equiv) of 2,4,6-trimethoxybenzaldehyde. The mixture was allowed to stir at room temperature overnight and another 100 mL MeOH was added and the reaction mixture was cooled 0-5 ºC in an ice bath and $NaBH_4$ (1.5 equiv) was added slowly portion-wise over 1 h. The reaction was stirred overnight and the MeOH was removed by rotovap. Sufficient amount of water was added and extracted with 3×100 mL toluene. The toluene extracts were combined and dried over Na_2SO_4. The toluene was filtered and removed by rotovap. The crude dark yellow oil was purified by the addition of diethyl ether to obain 94% of the desired product as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.52-2.53 (d, 6H, *J* = 5.6 Hz), 2.57-2.59 (d, 6H, *J* = 5.6 Hz), 3.70 (s, 6H), 3.72 (2, 18H), 3.75 (s, 9H), and 6.06 (s, 6H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 160.2, 159.4, 109.5, 90.4, 55.6, 55.3, 55.0, 47.1, and 41.5 ppm. APCI$^+$ found 687 (calc for $C_{36}H_{54}N_4O_9$, 686.39).

Synthesis of (8H)Cl. Add 50 mL of dry CH_3CN in a RB (preferably Schlenk flask). The RB flask was cooled to 0-5 ºC and HMPT {P(NMe$_2$)$_3$} (2.0 equiv) was added under an argon flow. Phosphorus trichloride (PCl_3) was added slowly through syringe. After stirring at 0-5 ºC for 15 minutes, compound 20 (3.0 equiv) dissolved in 50 mL dry CH_3CN wad added. The reaction mixture was stirred overnight at rt. Removal the solvent using rotary evaporator left a light yellow solid. Addition of diethyl ether and stirring overnight afforded a free flowing white powder in 91% isolated yield. ^{1}H NMR (CD_3CN, 400 MHz): δ = 2.39 (s, 6H), 2.48 (s, 6H), 3.29 (s, 27H), 3.50-3.54 (d, 6H, *J* = 12.8 Hz), 5.02-6.33 (d, 1H, *J* = 525.2 Hz), and 5.72 (s, 6H) ppm. ^{13}C NMR (CD_3CN, 100 MHz): δ = 162.2, 160.7, 107.7, 107.6, 91.6, 56.4, 56.1, 47.4 (d, *J* = 7.5 Hz), 39.7 (d, *J* = 4.3 Hz), and 39.6 (d, *J* = 18 Hz) ppm. ^{31}P NMR (168 MHz, CD_3CN) δ = -9.74 ppm.

Synthesis of Compound 8. To a 25 mL round bottom flask containing compound 21 (1 equiv), 150 mL of THF was added. The salt was stirred for 10 minutes and NaHMDS (2 equiv) was added to the slurry. The reaction was stirred overnight and the THF was evaporated under inert atmosphere. Toluene was added to extract the proazaphosphatrane and the solids were filtered off. The toluene extract is then evaporated and 10 mL of acetonitrile was added. The proazaphosphatrane precipitates from the acetonitrile as a white solid and was filtered (82% isolated yield). ^{1}H NMR (400 MHz, C_6D_6): δ = 2.86 (s, 6H), 3.15 (s, 6H), 3.42 (s, 9H), 3.47 (s, 18H), 4.64-4.66 (d, 6H, *J* = 8 Hz), and 6.16 (s, 6H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 161.0, 160.8, 112.5, 112.4, 91.3, 55.7, 55.2, 53.6, 46.4 (d, *J* = 5.5 Hz), and 43.7 (d, *J* = 51.6 Hz) ppm. ^{31}P NMR (186 MHz, C_6D_6): δ = 131.96 ppm. APCI$^+$ found 715 (calc for $C_{36}H_{51}N_4O_9P$, 714.34).

References:

1. Schmidt, H.; Lensink, C.; Xi, S. K.; Verkade, J. G. *Z. Anorg. Allg. Chem.* **1989**, *578*, 75.
2. Kisanga, P. B.; Verkade, J. G. *Tetrahedron* **2001**, *57*, 467.
3. Su, W.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433.
4. For reports on the cyclotrimerization of isocyanates to isocyanurates, see: (a) Montilla, F.; Clara, E.; Aviles, T.; Casimiro, T.; Ricardo, A. A.; da Ponte, M. N. *J. of Organomet. Chem.* **2001**, 626, 227. (b) Moghaddam, F. M.; Dekamin, M. G.; Koozehgari, G. R. *Letters in Organic Chemistry* **2005**, *2*, 734. (c) Dekamin, M. G.; Moghaddam, F. M.; Saeidian, H.; Mallakpour, S. *Monatshefte fur Chemie* **2006**, *137*, 1591. (d) Moghaddam, F. M.; Koozehgiri, G. R.; Dekamin, M. G. *Monatshefte fur Chemie* **2004**, *135*, 849. (e) Duong, H. A.; Cross, M. J.; Louie, J. *Org. Lett.* **2004**, *6*, 4647. (f) Dekamin, M.; Mallakpour, S.; Ghassemi, M. *J Chem. Research* **2005**, *3*, 177. (g) Khajavi, M. S.; Dakamin, M. G.; Hazarkhani, H. *J. Chem. Research* **2000**, 145. (h) Zhou, A.; Cao, L.; Li, H.; Liu, Z.; Cho, H.; Henry, W. P.; Pittman, C. U. *Tetrahedron* **2006**, *62*, 4188. (i) Dekamin, M. G.; Mallakpour, S.; Ghassemi, M. *Synthetic Comm.* **2005**, *35*, 427. (j) Sarkar, A.; Ilankumaran, P.; Kisanga, P.; Verkade, J. G. *Advance Synthesis and Catalysis* **2004**, *346*, 1093. (k) Li, Y.; Matsumura, H.; Yamanaka, M.; Takahashi, T. *Tetrahedron* **2004**, *60*, 1393. (l) Moghaddam, F. M.; Dekamin, M. G.; Khajavi, M. S.; Jalili, S. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 851. (m) Tagachi, Y.; Shibaya, I.; Yasumoto, Y.; Ynoemoto, K *Bull.*

Chem. Soc. Jpn. **1990**, *63*, 3486. (n) Carelli, V.; Liberatore, F.; Moracci, F. M.; Tortorella, S.; Carelli, I.; Inesi, A. *Synthetic Comm.* **1985**, *15*, 249.

Literature references for known compounds

1,3,5-Trisphenyl-1,3,5-triazinane-2,4,6-trione (Table 1): Duong, H. A.; Cross, M. J.; Louie, J. *Org. Lett.* **2004**, *6*, 4647.

1,3,5-Tris(4-methoxyphenyl)-1,3,5-triazinane-2,4,6-trione (Table 2, entry 1): Duong, H. A.; Cross, M. J.; Louie, J. *Org. Lett.* **2004**, *6*, 4647.

1,3,5-Tris(4-nitrophenyl)-1,3,5-triazinane-2,4,6-trione (Table 2, entry 3): Zhou, A.; Cao, L.; Li, H.; Liu, Z.; Cho, H.; Henry, W. P.; Pittman, C. U. *Tetrahedron* **2006**, *62*, 4188.

1,3,5-Tris(4-chlorophenyl)-1,3,5-triazinane-2,4,6-trione (Table 2, entry 4): Moghaddam, F. M.; Dekamin, M. G.; Koozehgari, G. R. *Letters in Organic Chemistry* **2005**, *2*, 734.

1,3,5-Tris(1-naphthyl)-1,3,5-triazinane-2,4,6-trione (Table 2, entry 6): Moghaddam, F. M.; Dekamin, M. G.; Koozehgari, G. R. *Letters in Organic Chemistry* **2005**, *2*, 734.

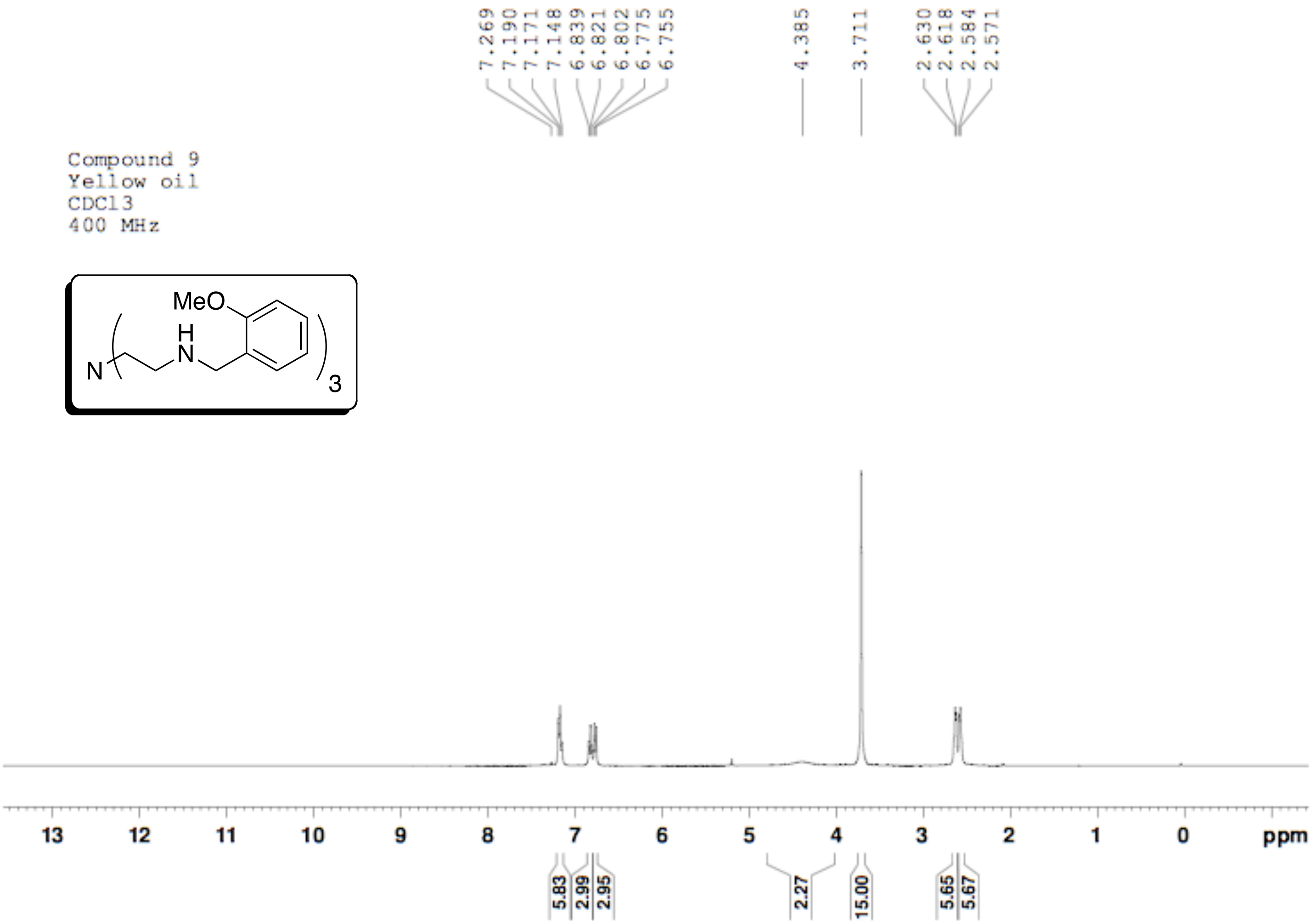
Data for unknown compounds

1,3,5-Tris(4-dimethylamino)-1,3,5-triazinane-2,4,6-trione *White solid* (Table 2, entry 2): ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.15-7.12 (d, 6H), 6.74-6.71 (d, 6H), 2.95 (s, 18H). ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 150.9, 150.1, 129.2, 123.1, 112.4, 40.6. HRMS m/z 486.23873 (calc for $C_{27}H_{30}N_6O_3$, 486.23794).

1,3,5-Tris(4-bromophenyl)-1,3,5-triazinane-2,4,6-trione *White solid* (Table 2, entry 5): ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.69-7.67 (d, 6H), 7.30-7.28 (d, 6H). ^{13}C NMR (100 MHz,

CD_2Cl_2): δ = 148.5, 133.2, 133.1, 130.7, 124.0. HRMS m/z 594.84028 (calc for $C_{21}H_{12}Br_3N_3O_3$, 594.83878).

1,3,5-Tris(2,6-dimethylphenyl)-1,3,5-triazinane-2,4,6-trione *White solid* (Table 2, entry 7): ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.35-7.31 (m, 3H), 7.26-7.24 (d, 6H), 2.30 (s, 18H). ^{13}C NMR (100 MHz): δ = 147.7, 136.4, 132.6, 130.1, 129.3, 17.9. HRMS m/z 441.20617 (calc for $C_{27}H_{27}N_3O_3$, 441.20524).


Compound 9
Yellow oil
CDCl3
400 MHz
MeO
H
N
N
3
7.269
7.190
7.171
7.148
6.839
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6.802
6.775
6.755
4.385
3.711
2.630
2.618
2.584
2.571
13
12
11
10
9
8
7
6
5
4
3
2
1
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ppm
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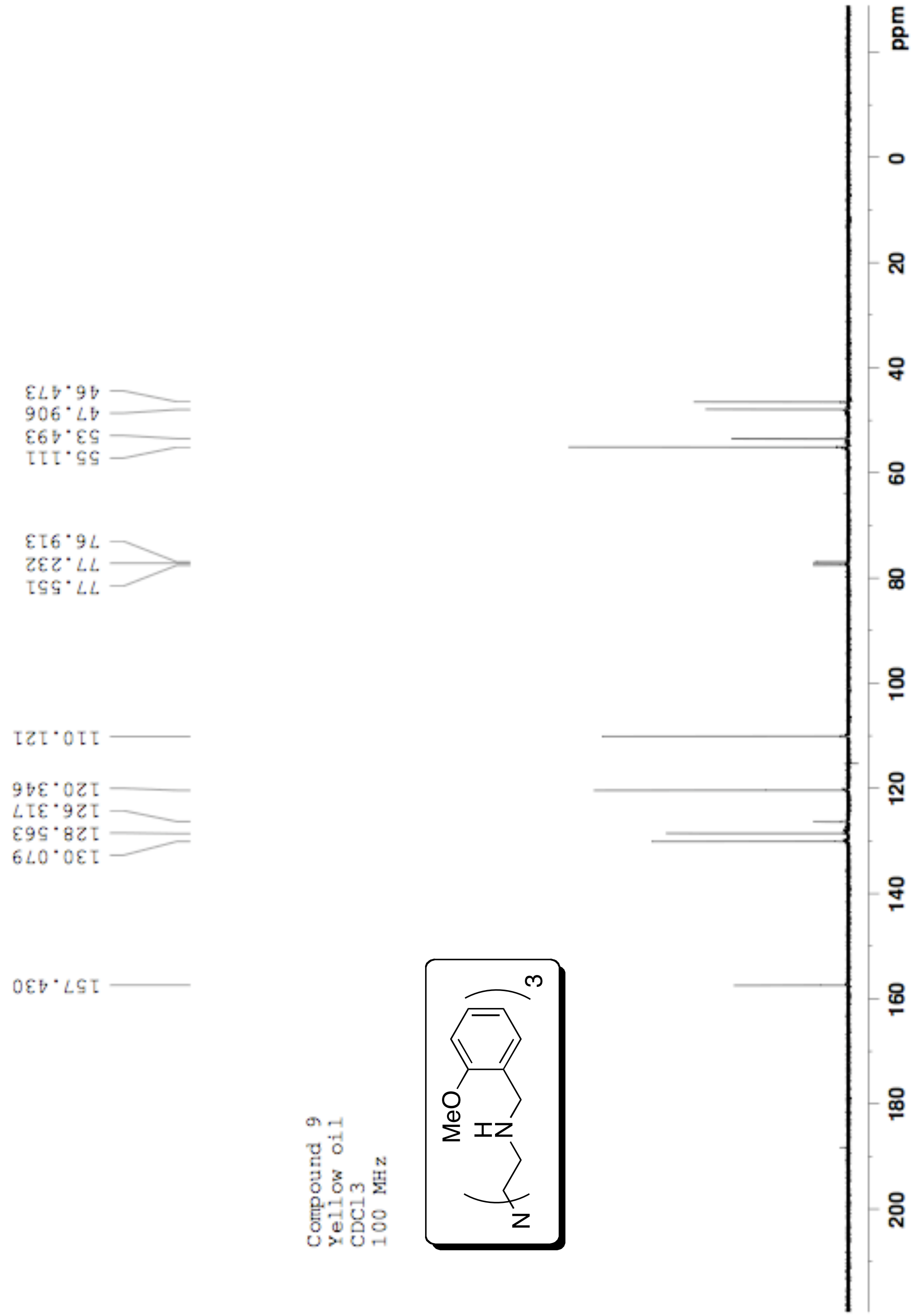
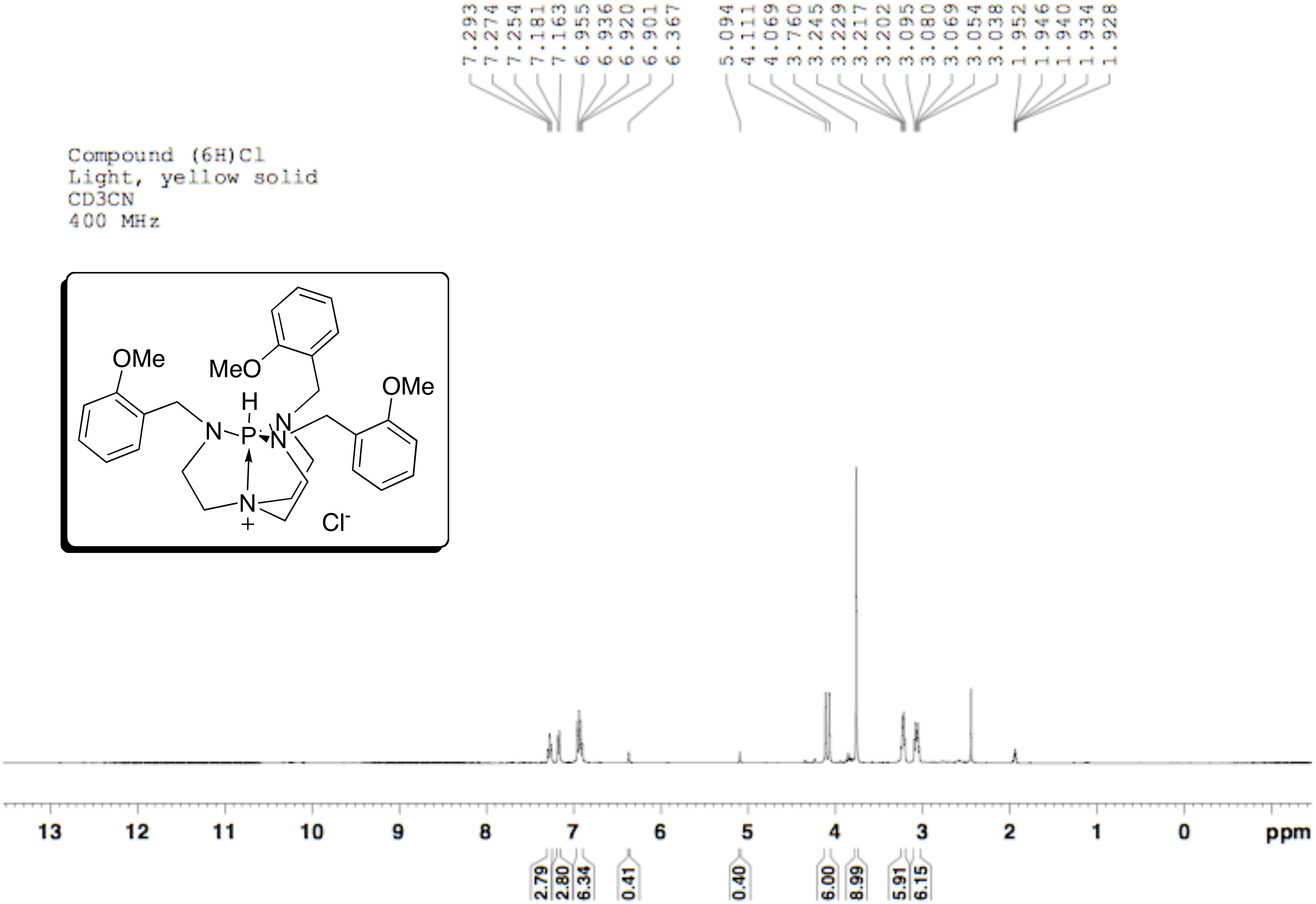
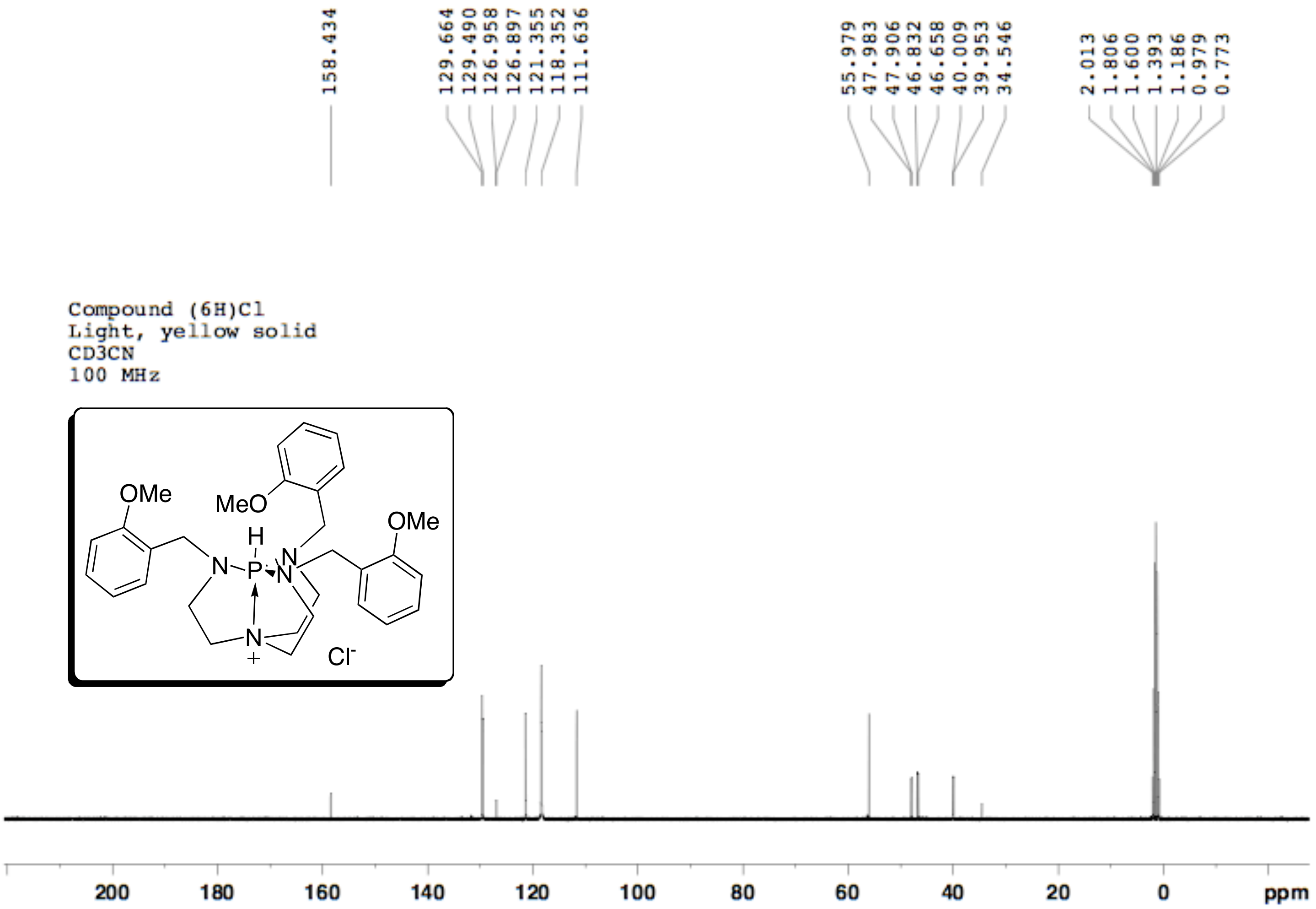
2.99
2.95
2.27
15.00
5.65
5.67



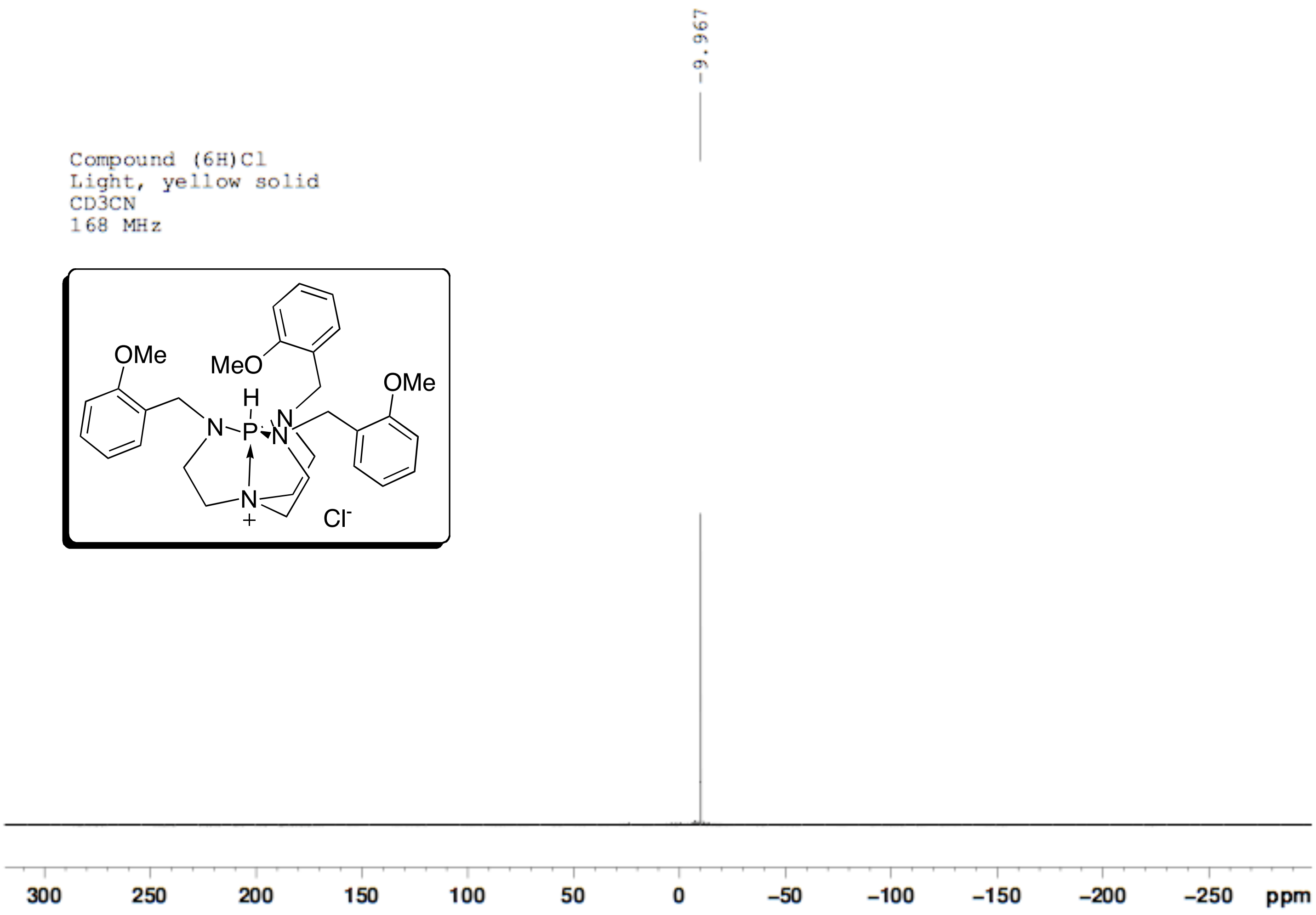
Compound 9
Yellow oil
CDCl3
100 MHz



Compound (6H)Cl
Light, yellow solid
CD3CN
400 MHz



Compound (6H)Cl
Light, yellow solid
CD3CN
100 MHz


-9.967
Compound (6H)Cl
Light, yellow solid
CD3CN
168 MHz
OMe
MeO
OMe
H
N
P
N
N
N
+
Cl-
300
250
200
150
100
50
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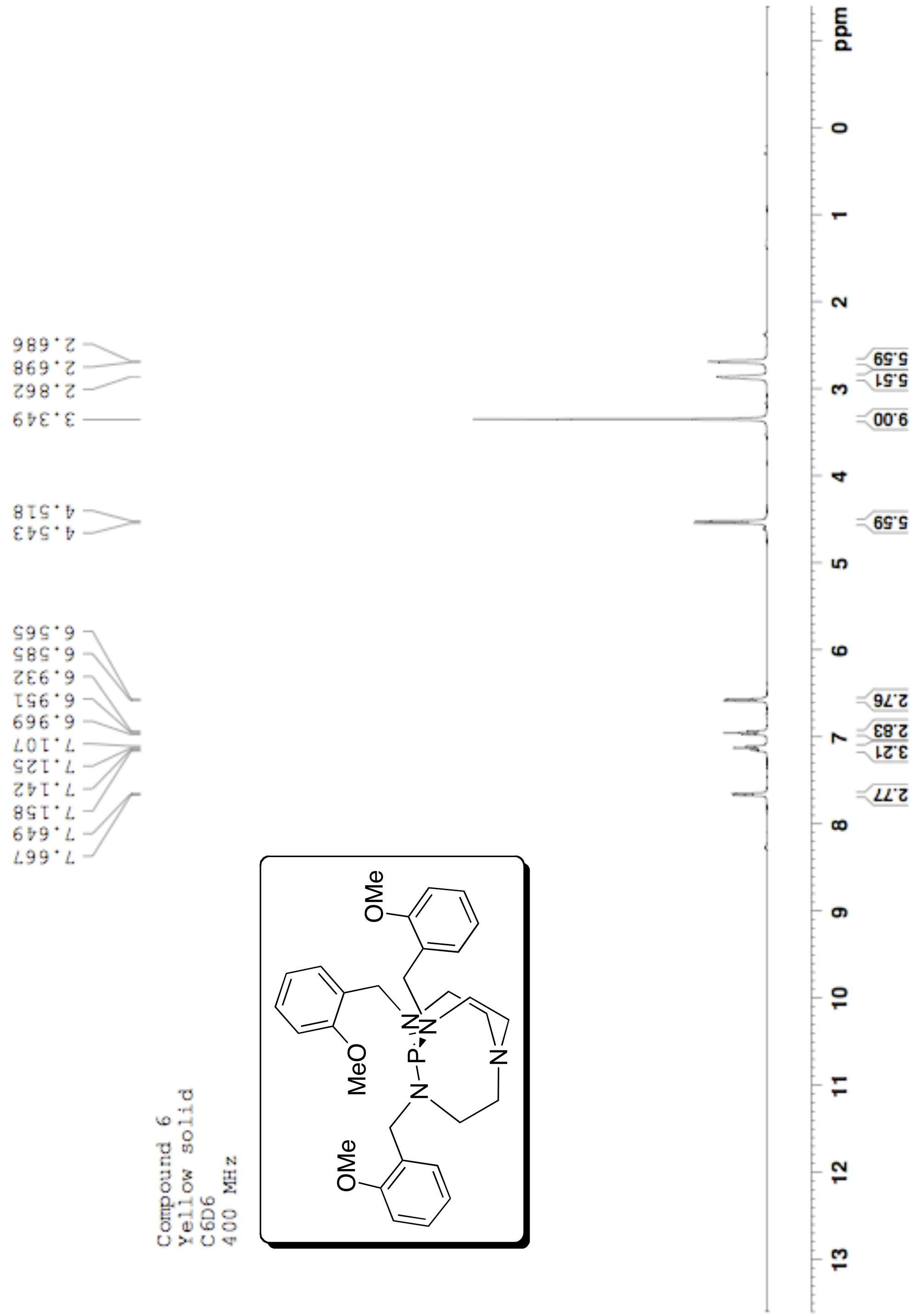
-200
-250
ppm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6.951
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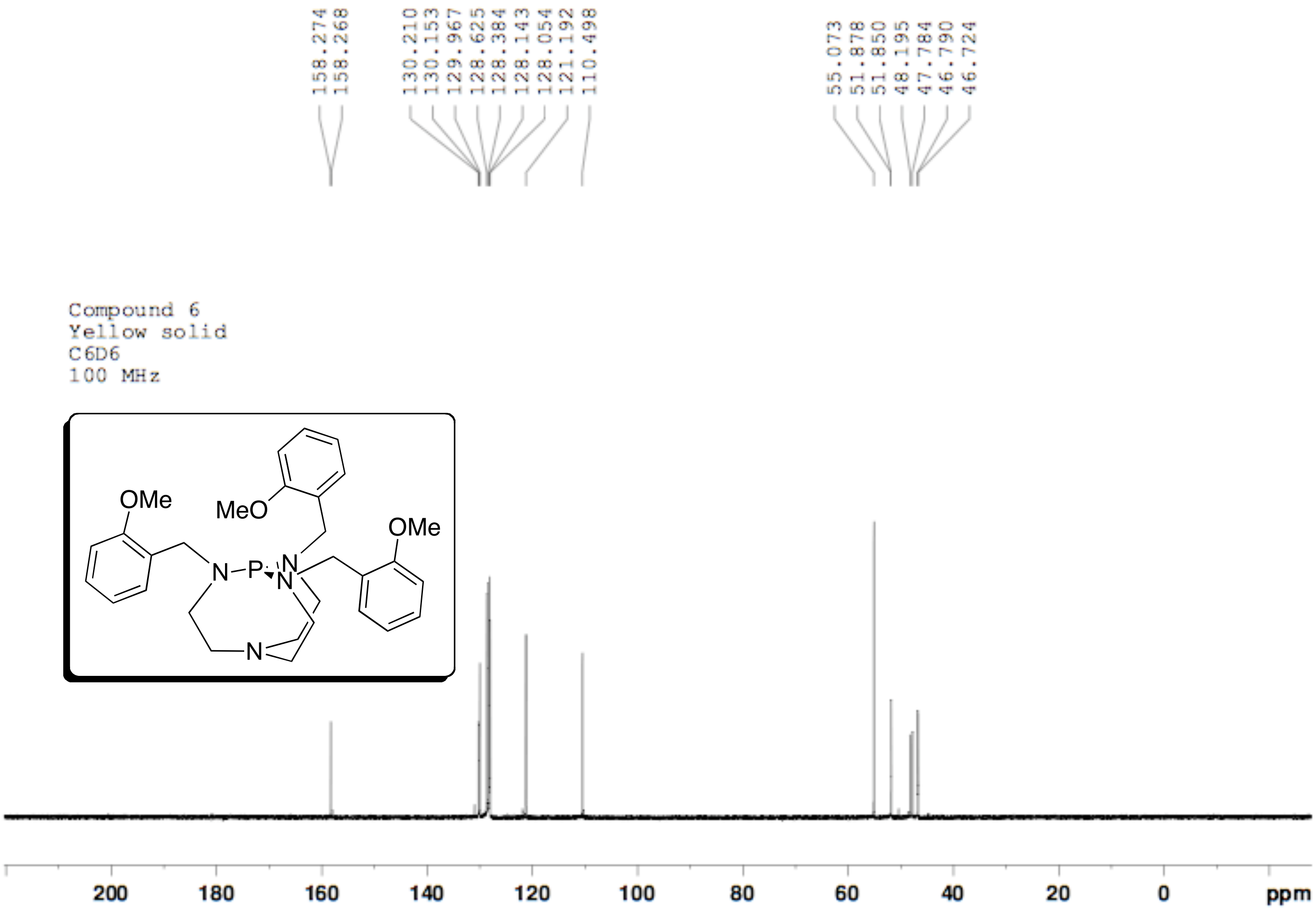
7.107
7.125
7.142
7.158
7.649
7.667
5.59
5.51
9.00
5.59
2.76
2.83
3.21
2.77
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
OMe
MeO
OMe
N
P
N
N
N


158.274
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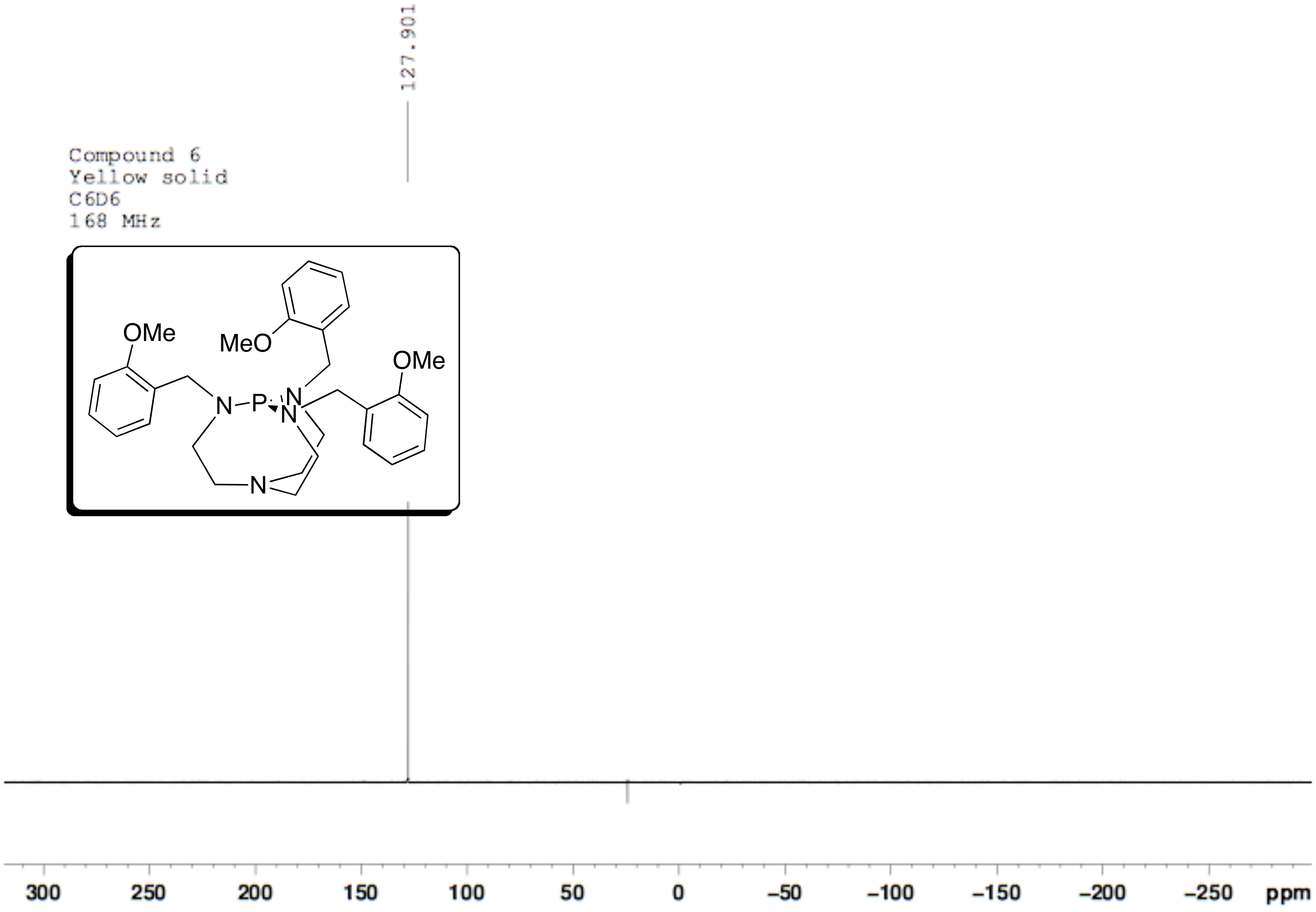
130.153
129.967
128.625
128.384
128.143
128.054
121.192
110.498
55.073
51.878
51.850
48.195
47.784
46.790
46.724
Compound 6
Yellow solid
C6D6
100 MHz
OMe
MeO
OMe
N
P
N
N
N
200
180
160
140
120
100
80
60
40
20
0
ppm


Compound 6
Yellow solid
C6D6
168 MHz
127.901
OMe
MeO
OMe
N
P
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N
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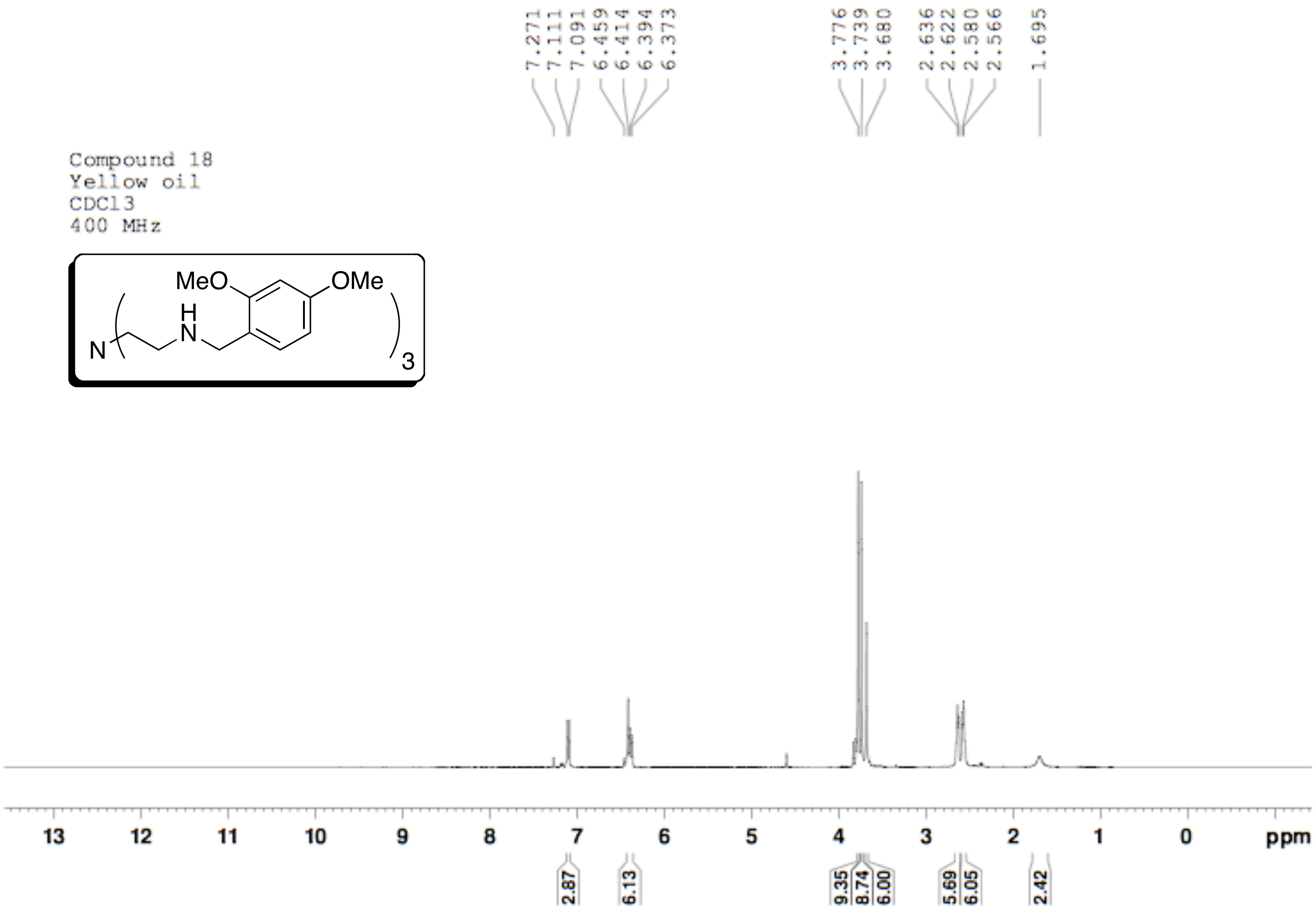
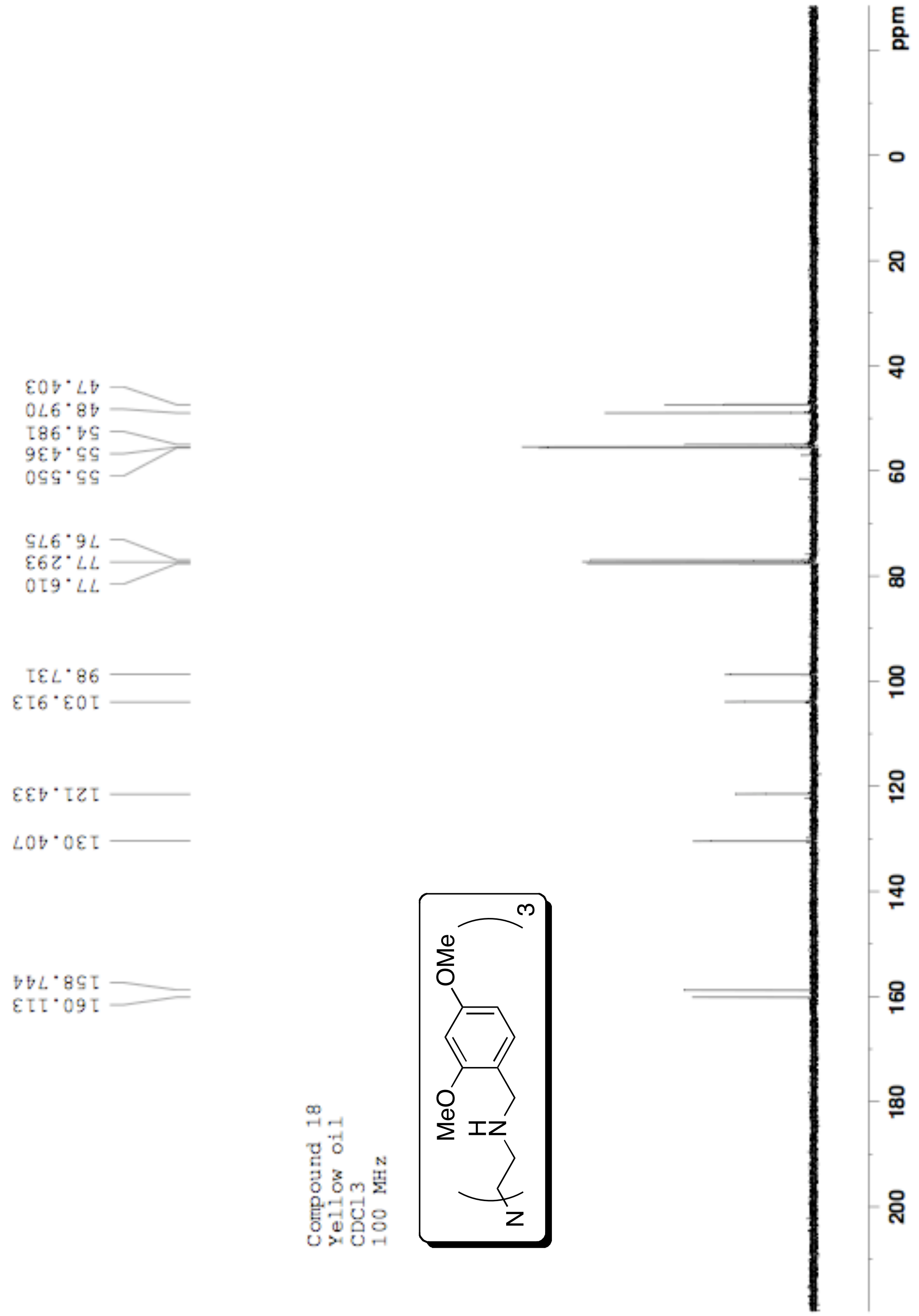
150
100
50
0
−50
−100
−150
−200
−250
ppm



Compound 18
Yellow oil
CDCl3
400 MHz


Compound 18
Yellow oil
CDCl3
100 MHz
MeO
OMe
H
N
N
3
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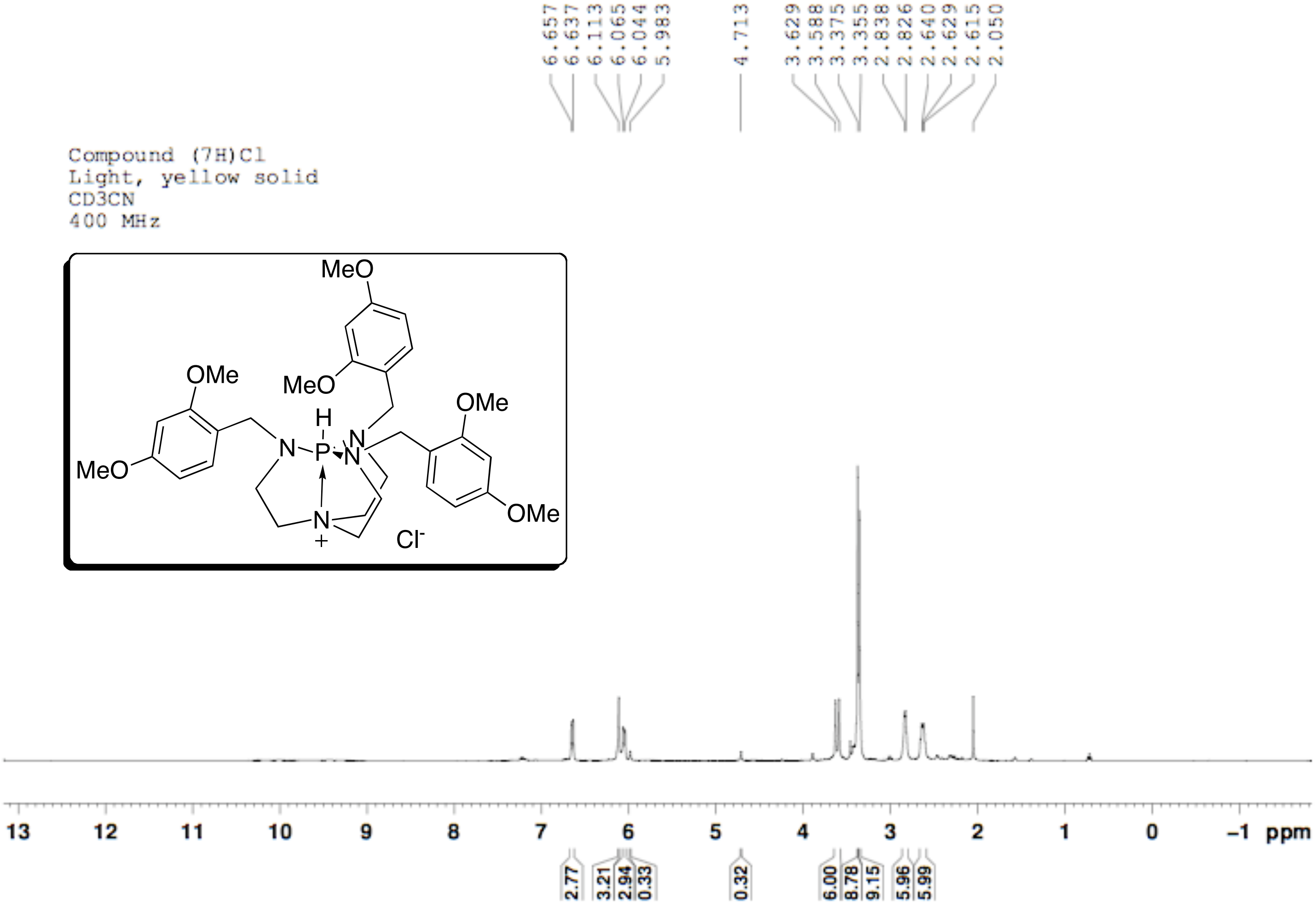
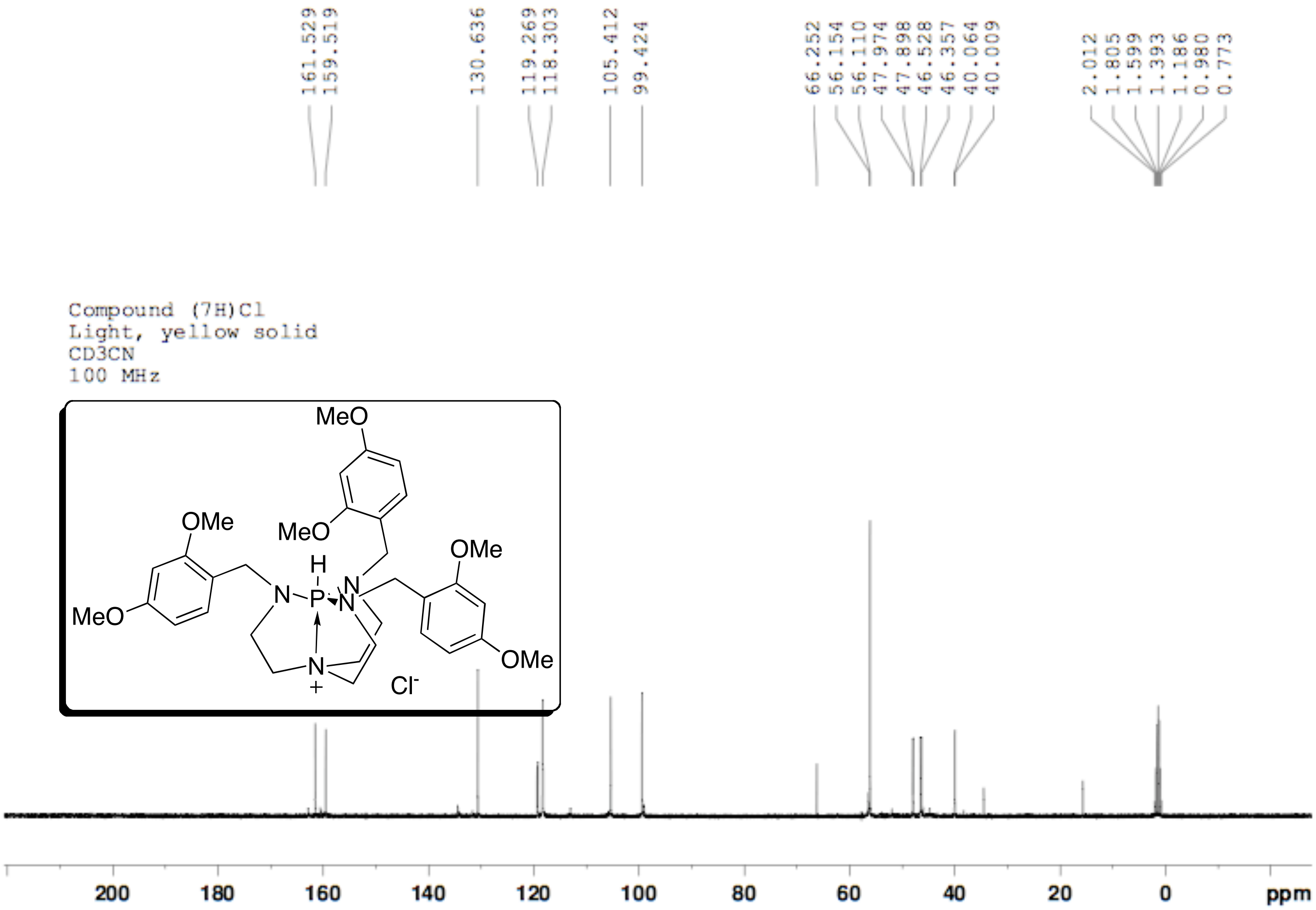
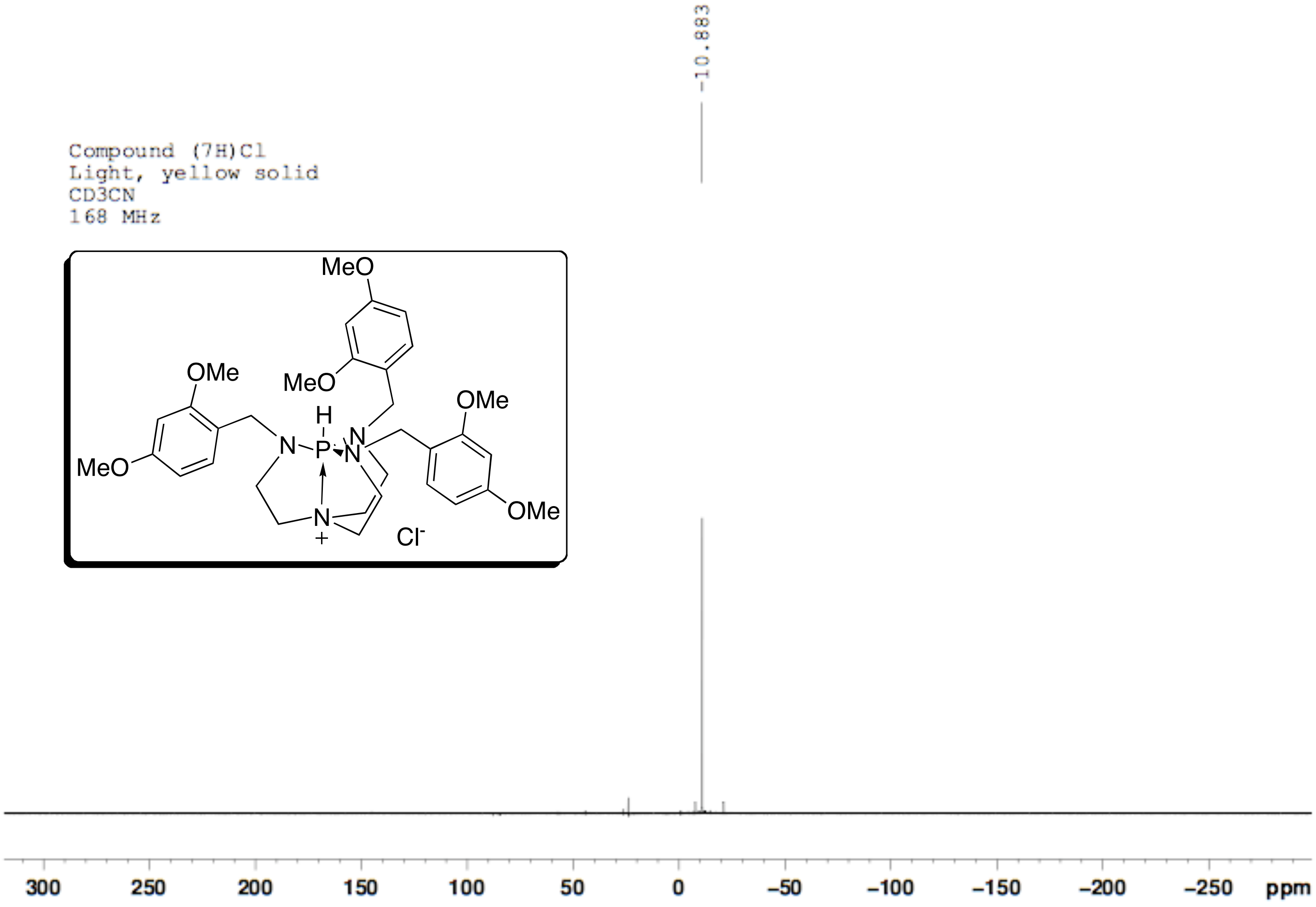
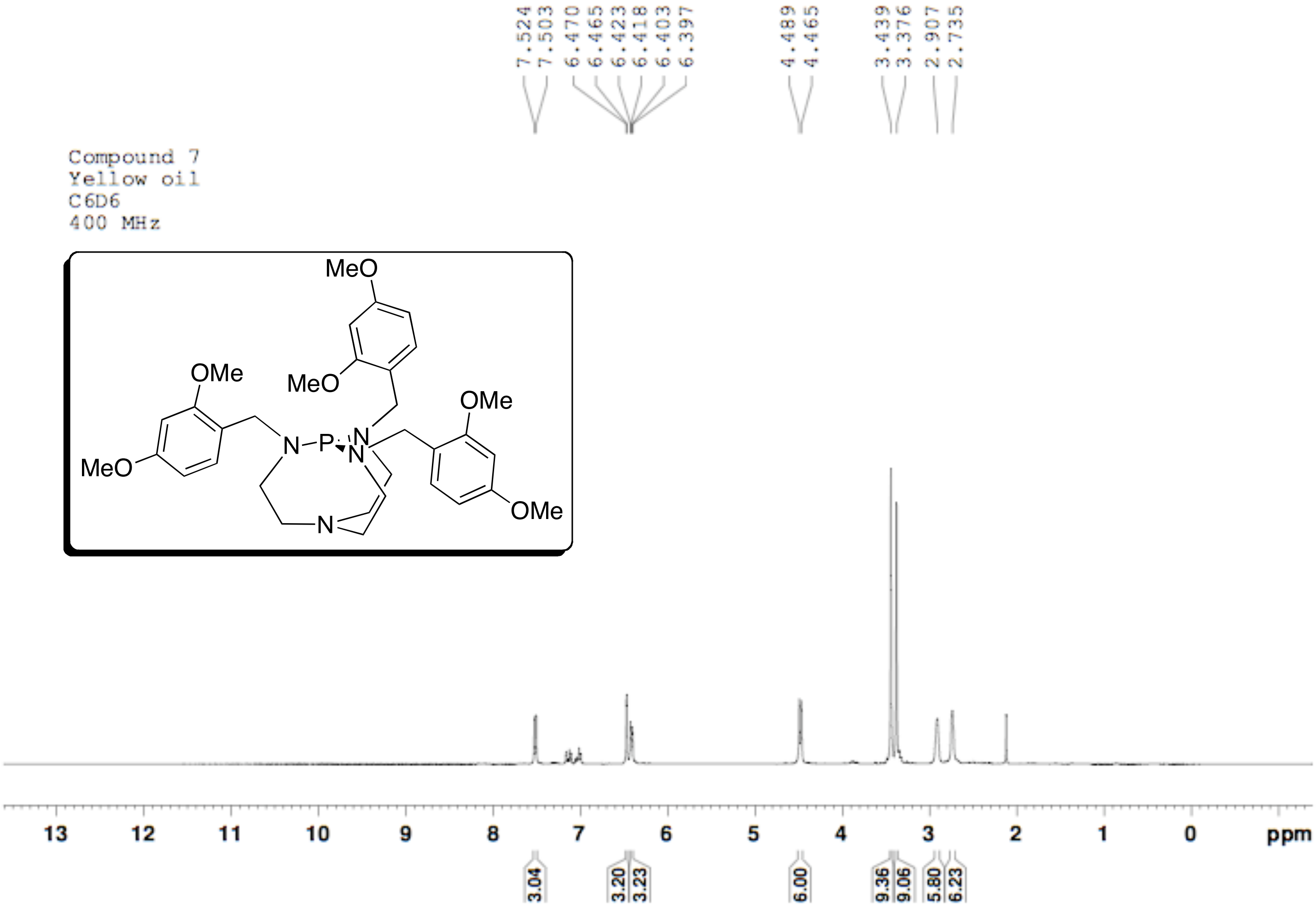
55.436
55.550
76.975
77.293
77.610
98.731
103.913
121.433
130.407
158.744
160.113
ppm
0
20
40
60
80
100
120
140
160
180
200

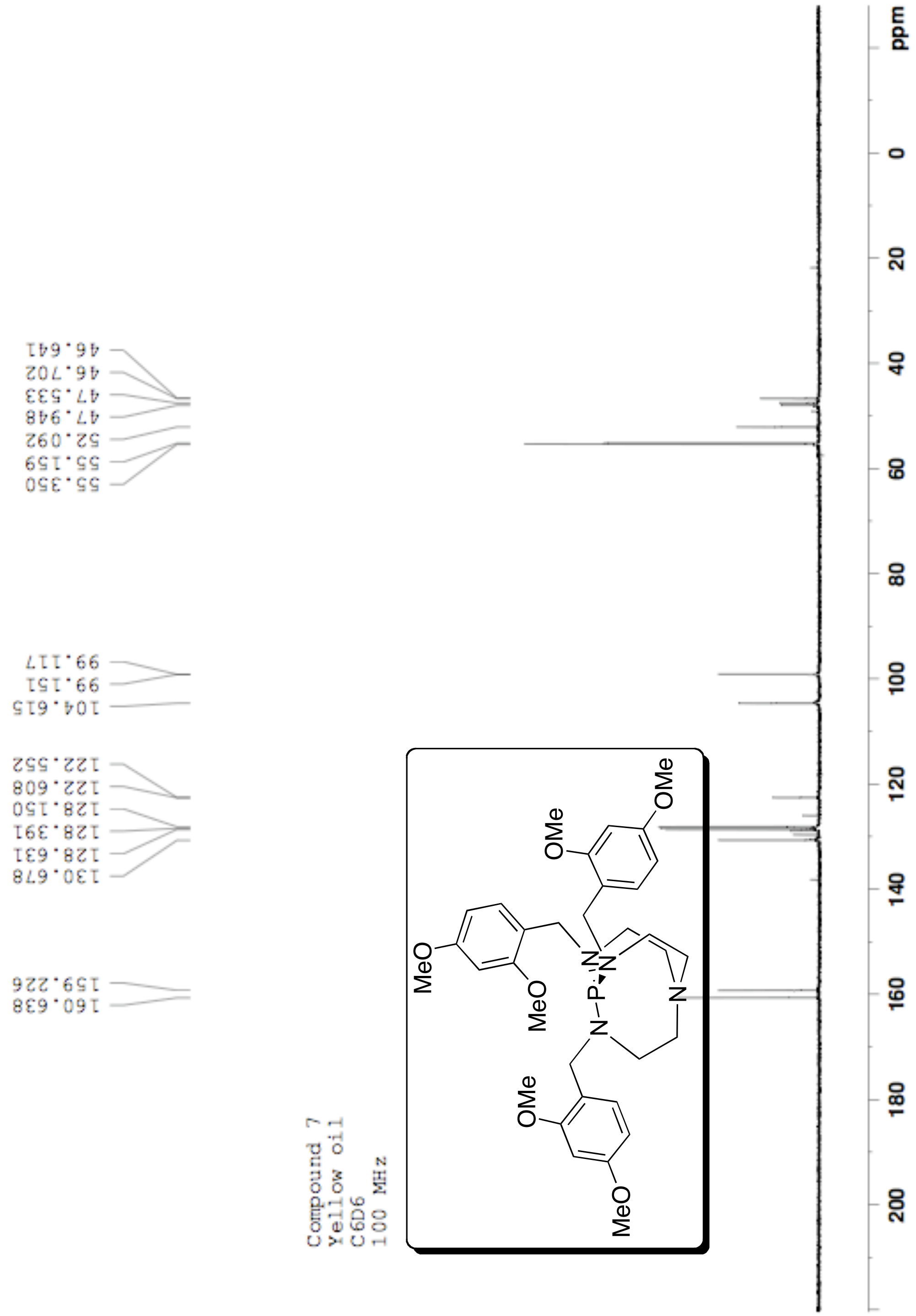

Compound (7H)Cl
Light, yellow solid
CD3CN
400 MHz
6.657
6.637
6.113
6.065
6.044
5.983
4.713
3.629
3.588
3.375
3.355
2.838
2.826
2.640
2.629
2.615
2.050
MeO
OMe
MeO
MeO
OMe
OMe
H
N
P
N
N
N
+
Cl-
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
ppm
2.77
3.21
2.94
0.33
0.32
6.00
8.78
9.15
5.96
5.99

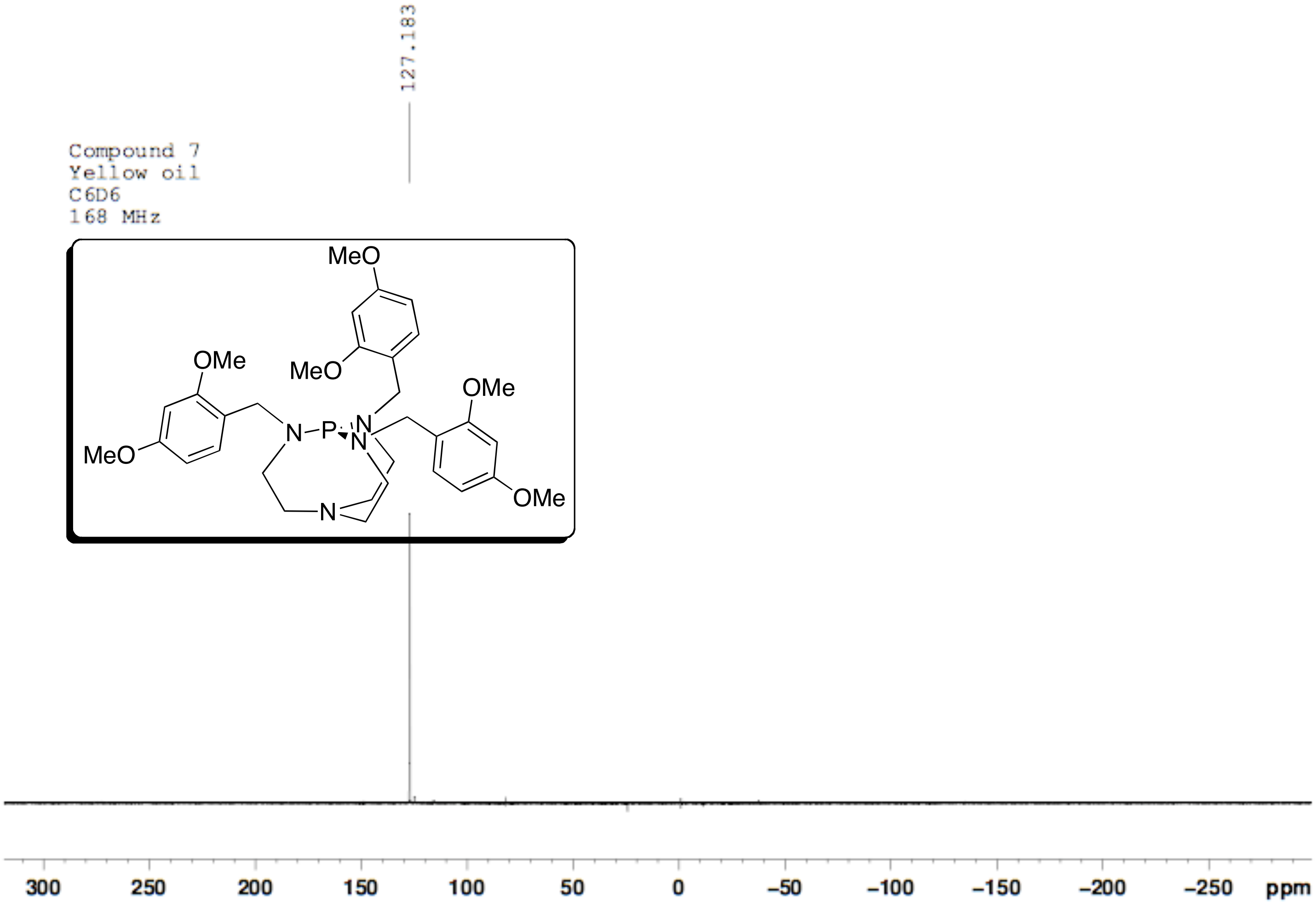


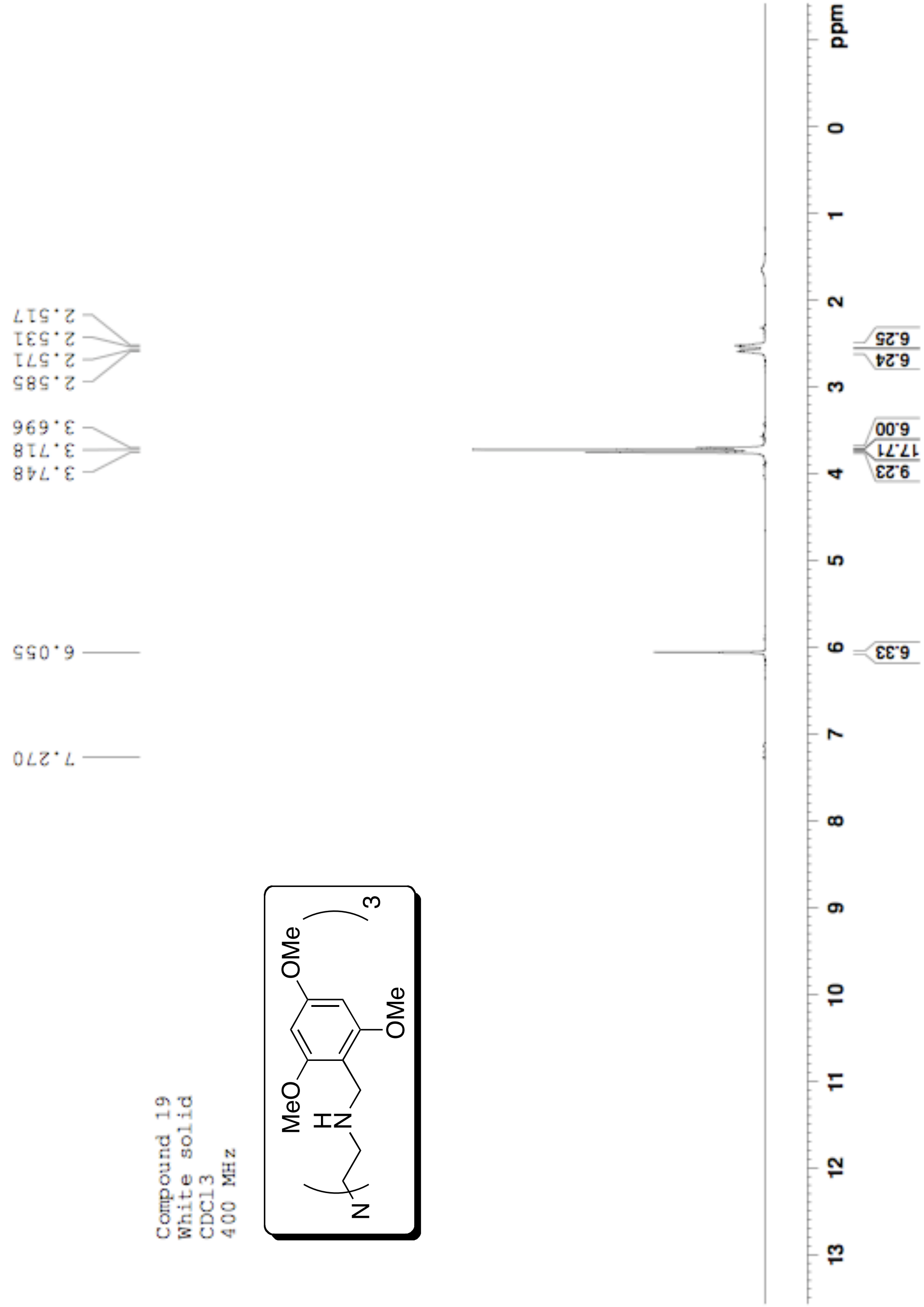
Compound (7H)Cl
Light, yellow solid
CD3CN
100 MHz

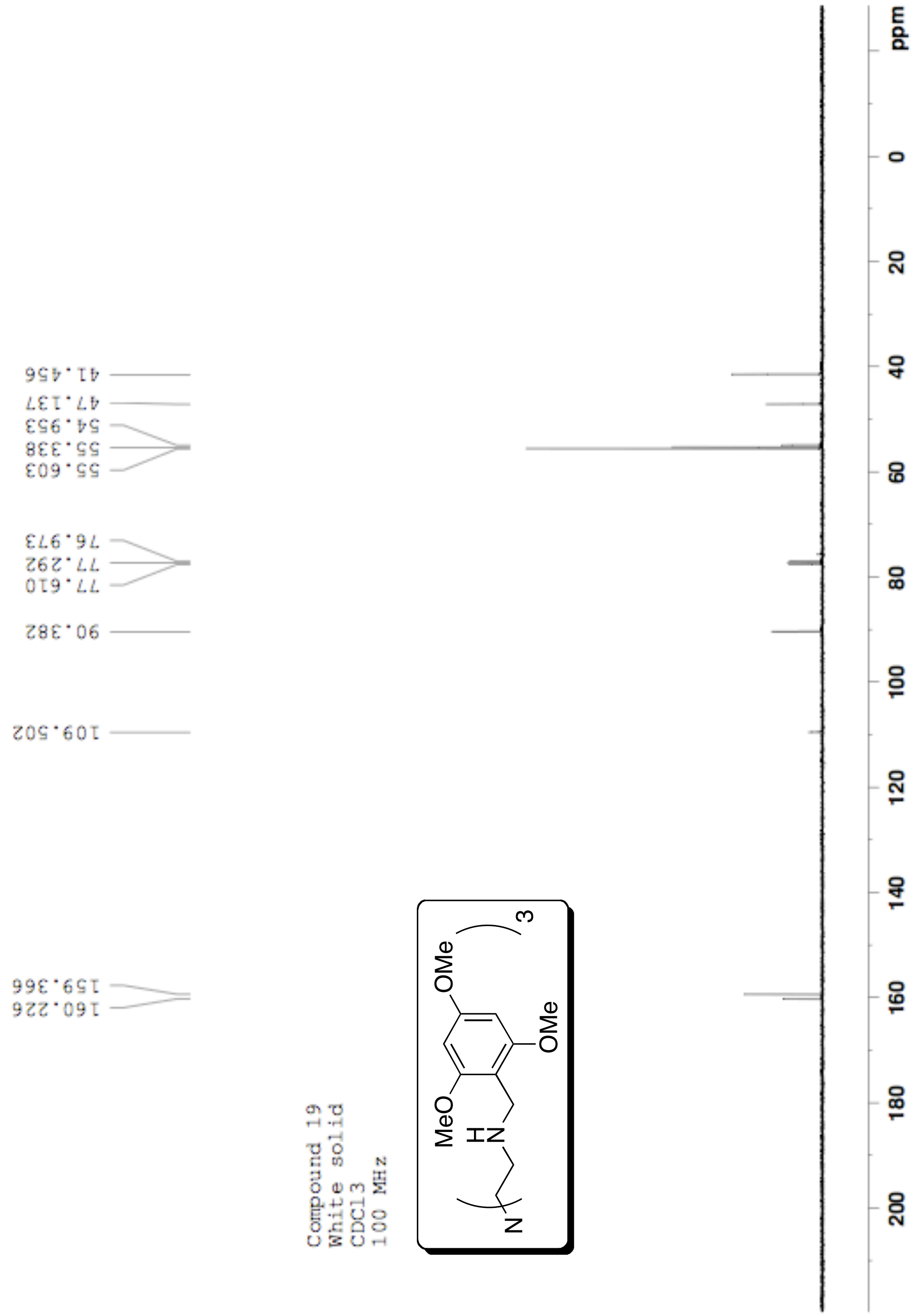

Compound (7H)Cl
Light, yellow solid
CD3CN
168 MHz


Compound 7
Yellow oil
C6D6
400 MHz
7.524
7.503
6.470
6.465
6.423
6.418
6.403
6.397
4.489
4.465
3.439
3.376
2.907
2.735
MeO
OMe
MeO
OMe
OMe
MeO
N
P
N
N
N
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
3.04
3.20
3.23
6.00
9.36
9.06
5.80
6.23

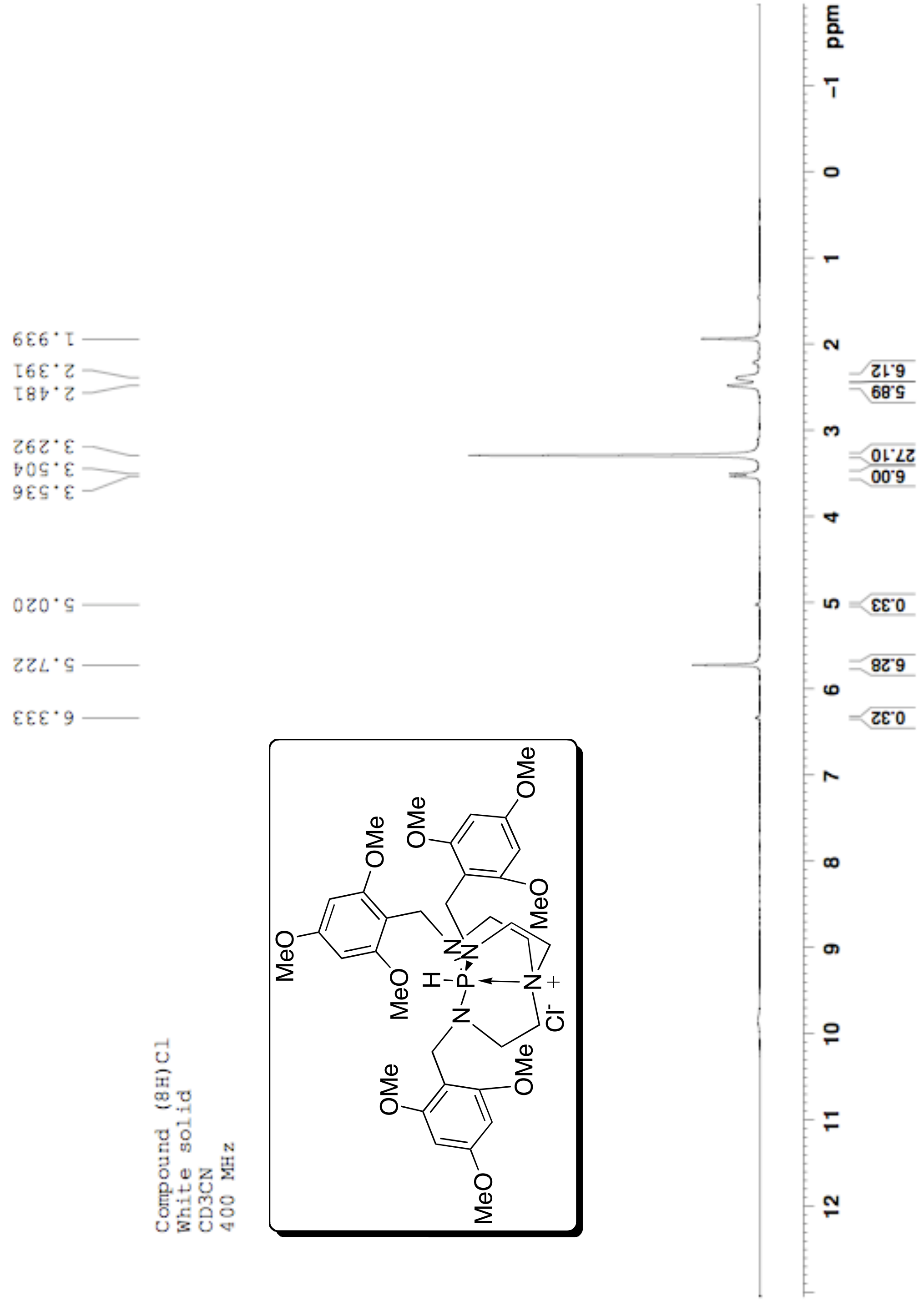

46.641
46.702
47.533
47.948
52.092
55.159
55.350
99.117
99.151
104.615
122.552
122.608
128.150
128.391
128.631
130.678
159.226
160.638
Compound 7
Yellow oil
C6D6
100 MHz
MeO
OMe
MeO
OMe
MeO
OMe
N
P
N
N
N
ppm
0
20
40
60
80
100
120
140
160
180
200

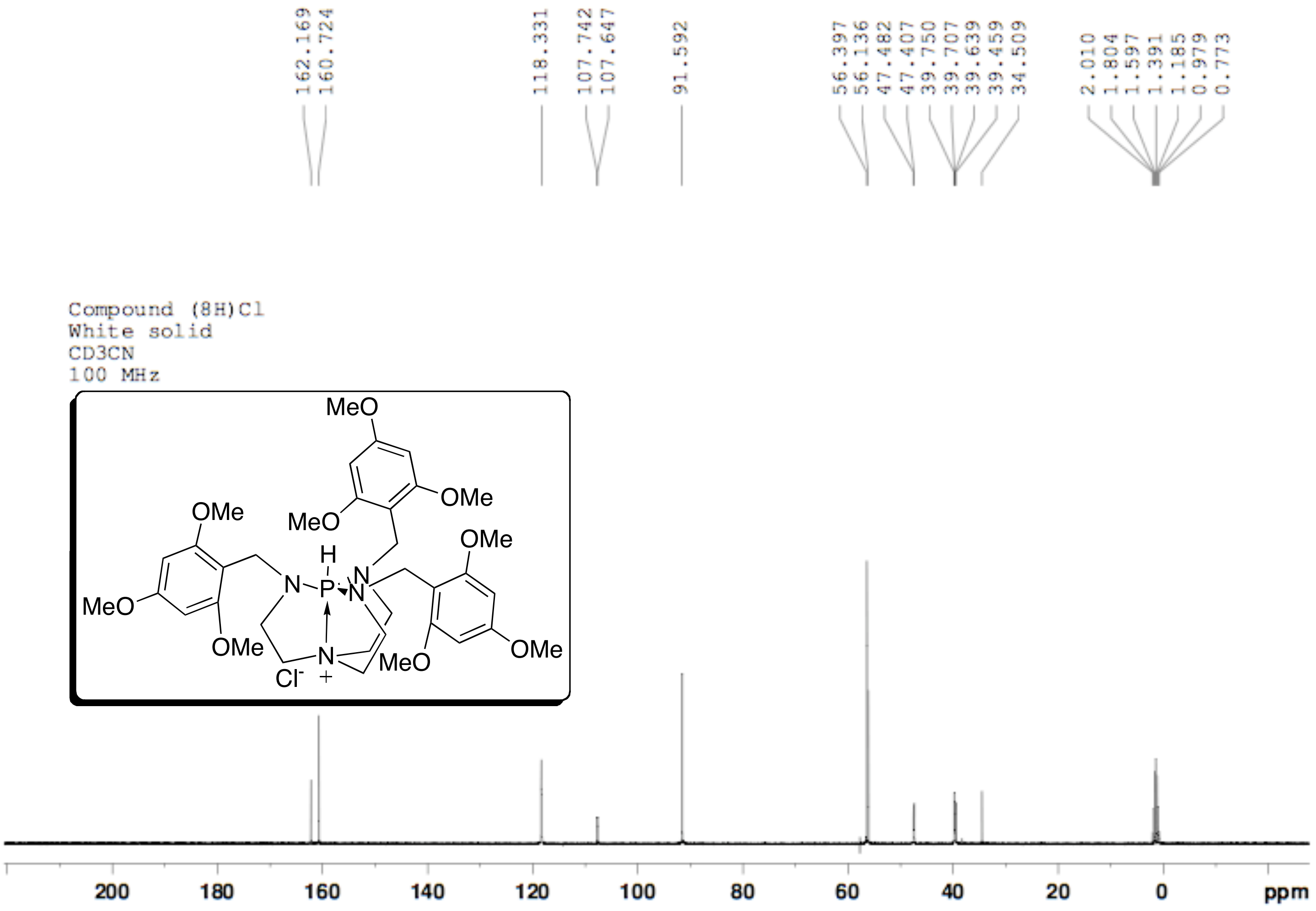

127.183
Compound 7
Yellow oil
C6D6
168 MHz
MeO
OMe
MeO
MeO
OMe
OMe
N
P
N
N
N
300
250
200
150
100
50
0
−50
−100
−150
−200
−250
ppm

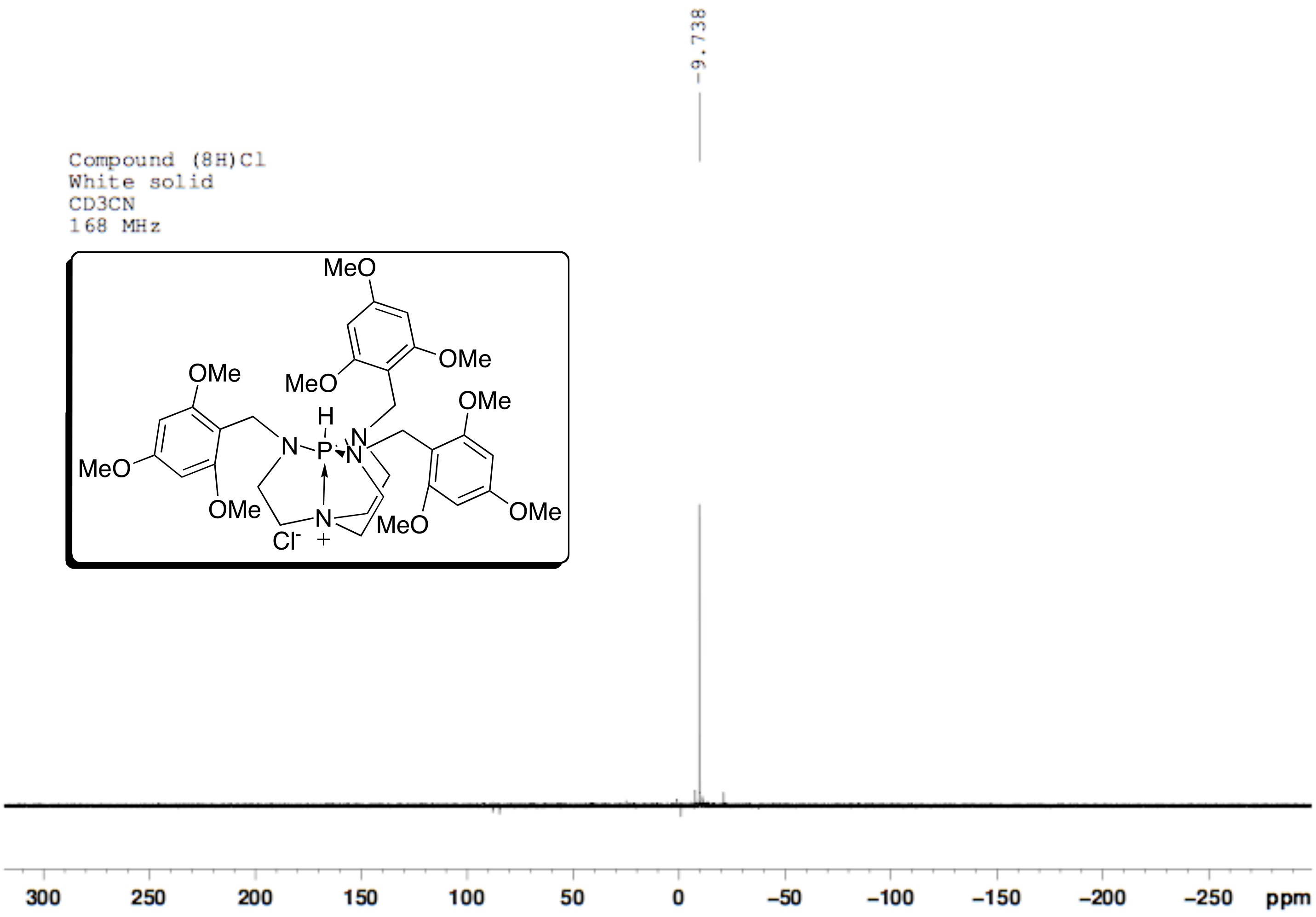

Compound 19
White solid
CDCl3
400 MHz
MeO
OMe
OMe
N
H
N
3
2.517
2.531
2.571
2.585
3.696
3.718
3.748
6.055
7.270
6.25
6.24
6.00
17.71
9.23
6.33
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

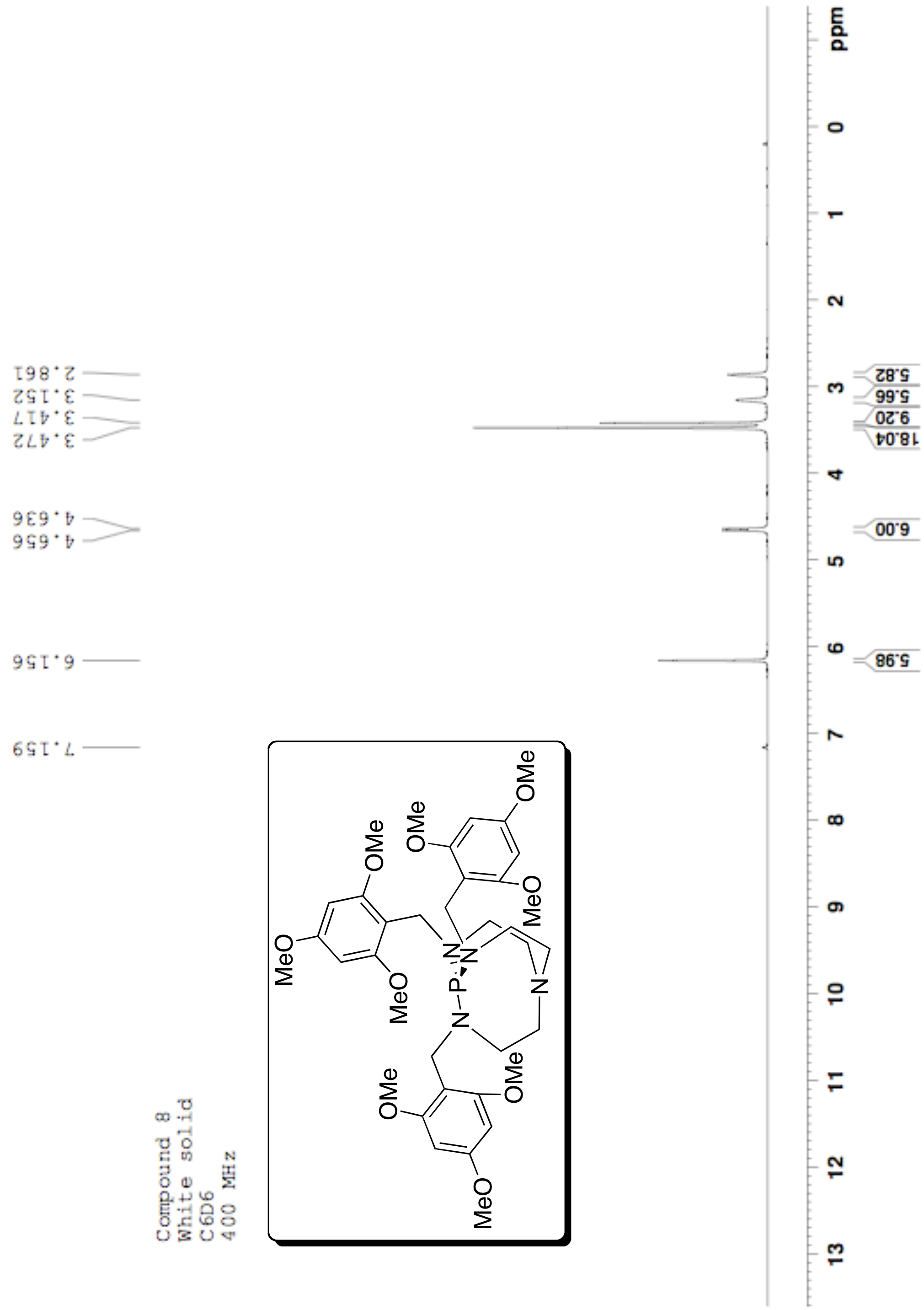


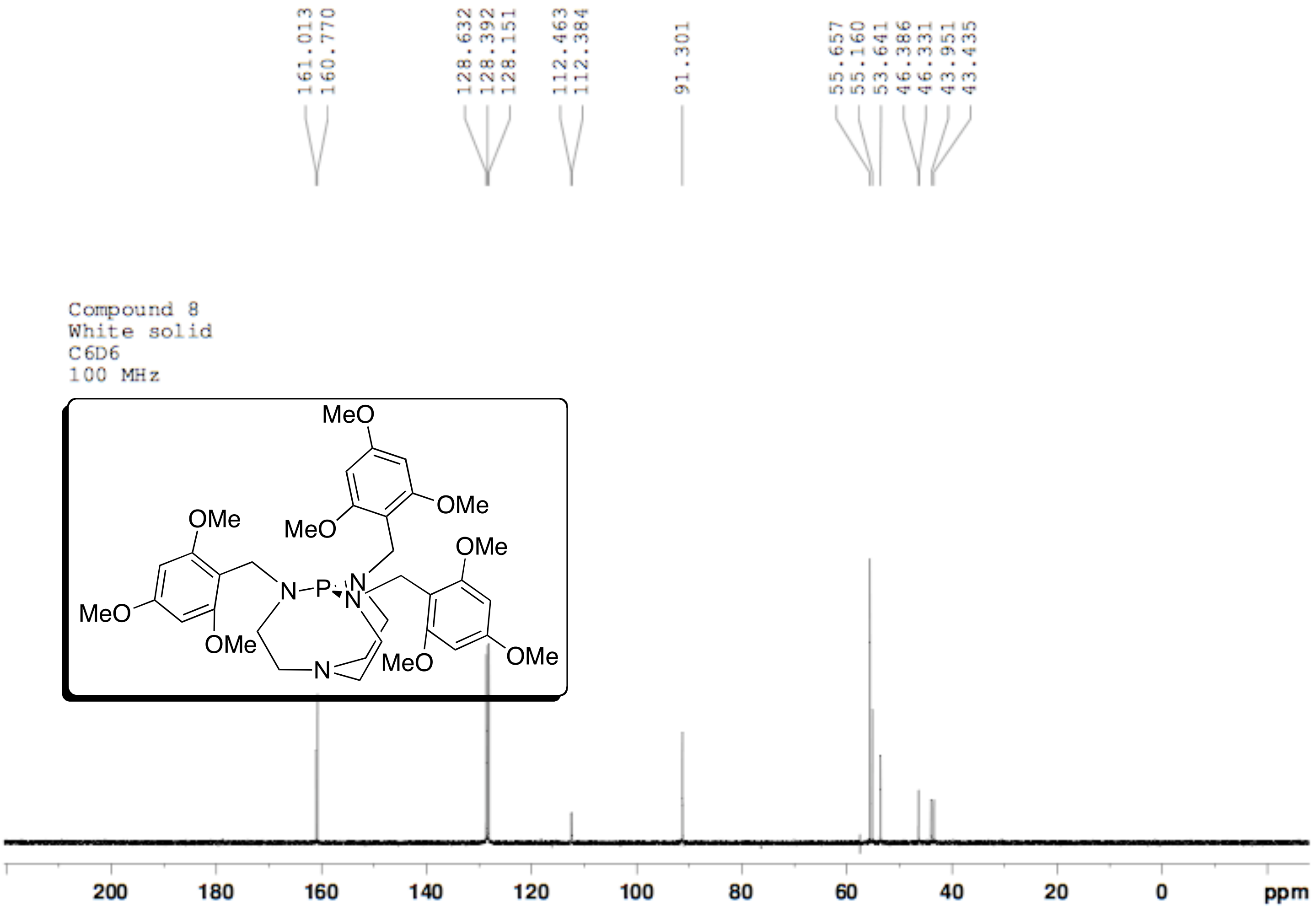
Compound 19
White solid
CDCl3
100 MHz

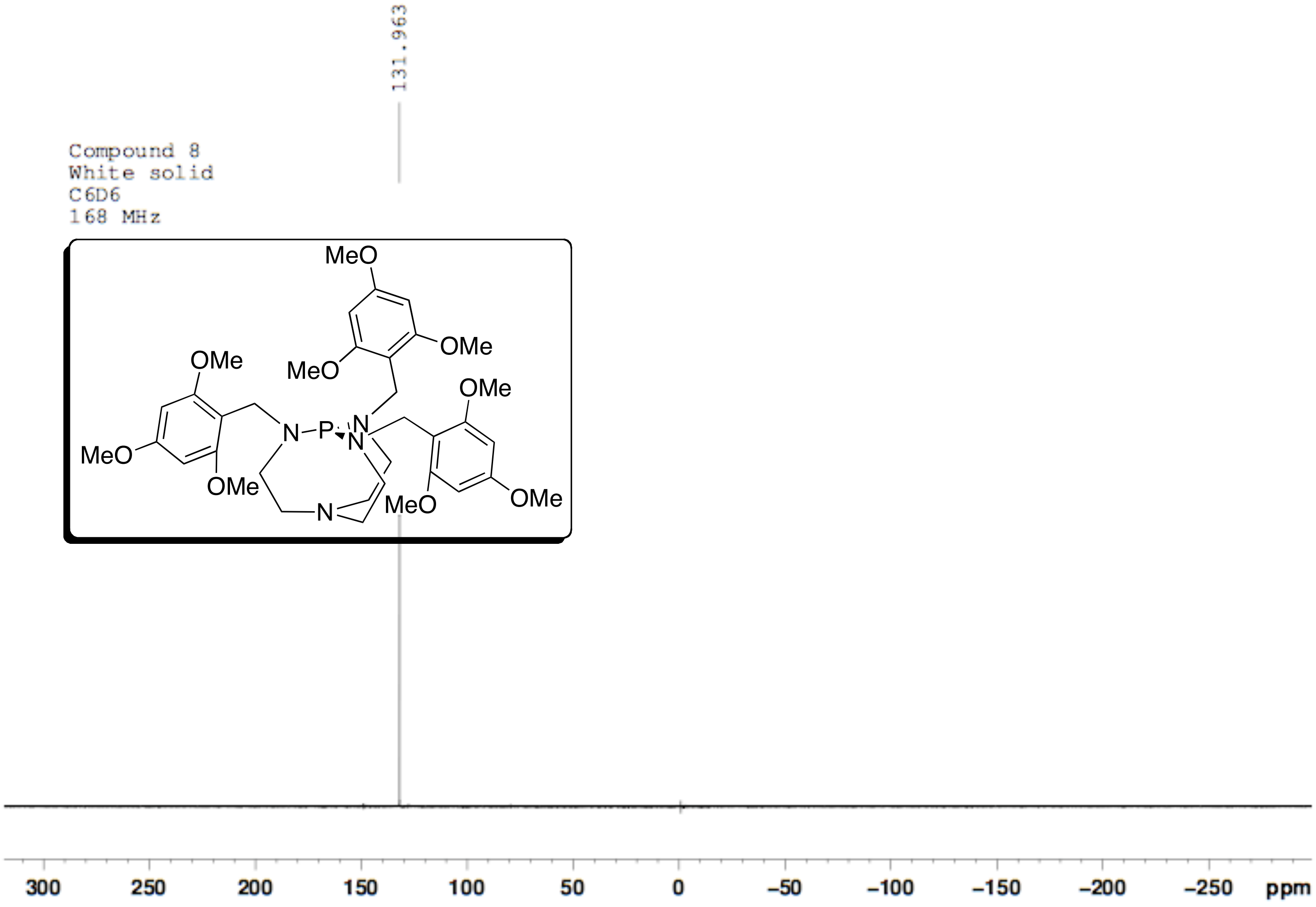

Compound (8H)Cl
White solid
CD3CN
400 MHz
1.939
2.391
2.481
3.292
3.504
3.536
5.020
5.722
6.333
6.12
5.89
27.10
6.00
0.33
6.28
0.32
ppm
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
OMe
MeO
OMe
MeO
OMe
MeO
OMe
MeO
OMe
H
P
N
N
N
N
Cl-
+


162.169
160.724
118.331
107.742
107.647
91.592
56.397
56.136
47.482
47.407
39.750
39.707
39.639
39.459
34.509
2.010
1.804
1.597
1.391
1.185
0.979
0.773
Compound (8H)Cl
White solid
CD3CN
100 MHz
MeO
OMe
MeO
OMe
OMe
MeO
H
N
P
N
N
OMe
OMe
MeO
N
Cl⁻
+
MeO
OMe
200
180
160
140
120
100
80
60
40
20
0
ppm


-9.738
Compound (8H)Cl
White solid
CD3CN
168 MHz
MeO
OMe
MeO
OMe
OMe
MeO
OMe
H
N
P
N
N
N
Cl-
+
MeO
OMe
MeO
OMe
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
ppm


Compound 8
White solid
C6D6
400 MHz
7.159
6.156
4.656
4.636
3.472
3.417
3.152
2.861
5.98
6.00
18.04
9.20
5.66
5.82
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
MeO
OMe
MeO
OMe
MeO
OMe
MeO
OMe
MeO
N
P
N
N
N


161.013
160.770
128.632
128.392
128.151
112.463
112.384
91.301
55.657
55.160
53.641
46.386
46.331
43.951
43.435
Compound 8
White solid
C6D6
100 MHz
MeO
OMe
MeO
OMe
OMe
MeO
N
P
N
N
N
OMe
MeO
OMe
200
180
160
140
120
100
80
60
40
20
0
ppm


131.963
Compound 8
White solid
C6D6
168 MHz
MeO
OMe
MeO
OMe
MeO
OMe
N
P
N
N
N
OMe
MeO
OMe
300
250
200
150
100
50
0
−50
−100
−150
−200
−250
ppm

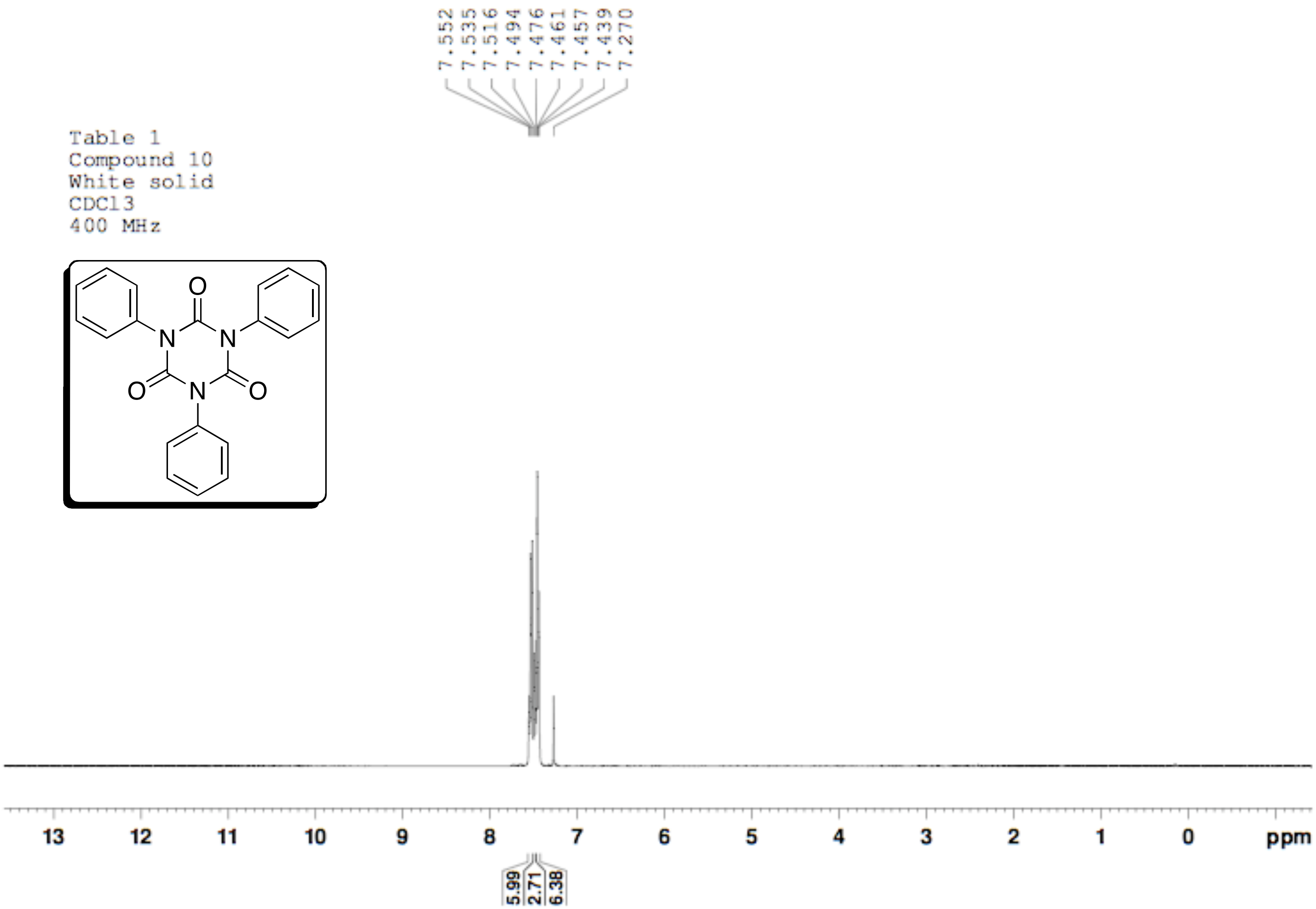


Table 1
Compound 10
White solid
CDCl3
400 MHz
7.552
7.535
7.516
7.494
7.476
7.461
7.457
7.439
7.270
O
N
N
O
N
O
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
5.99
2.71
6.38

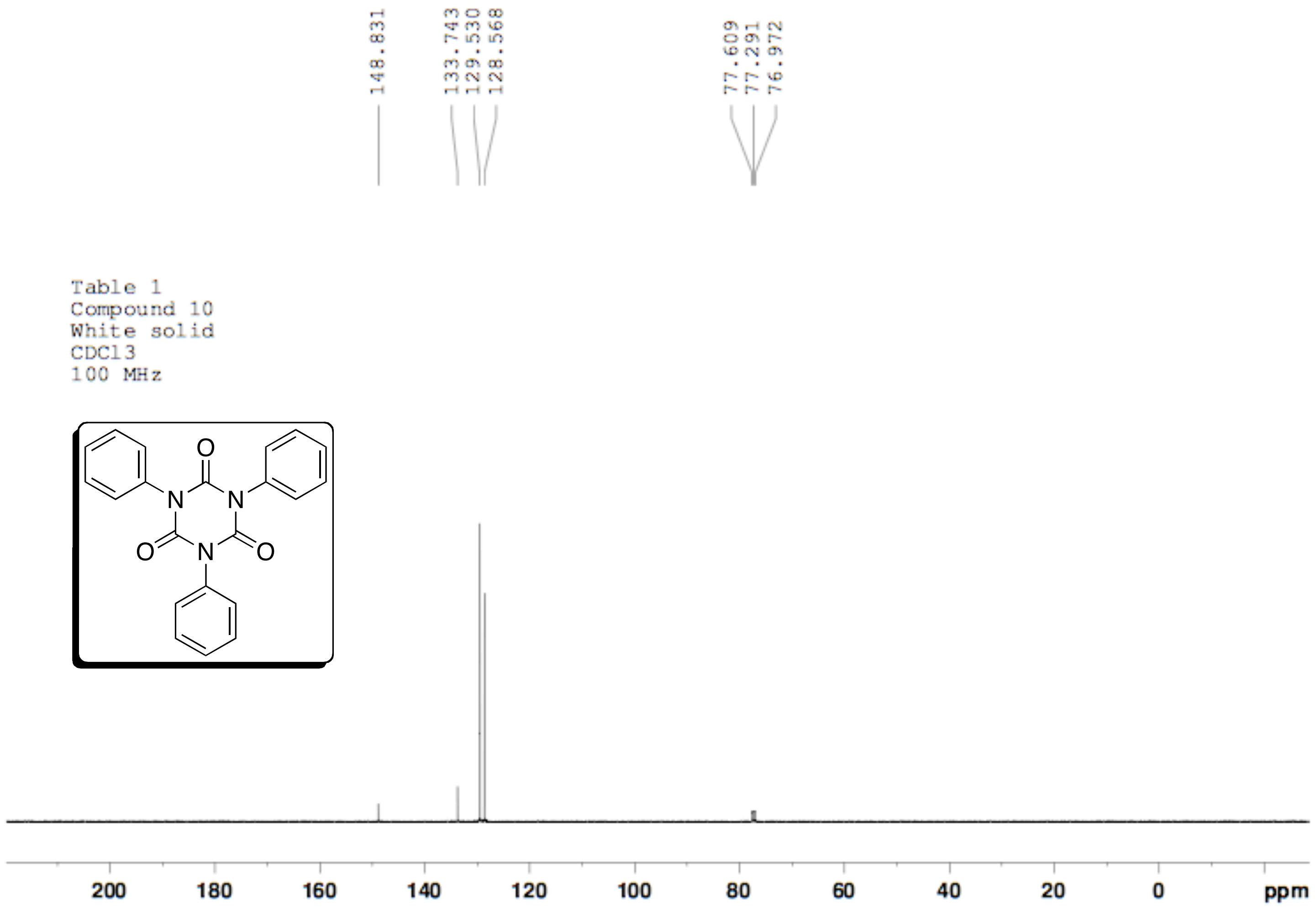
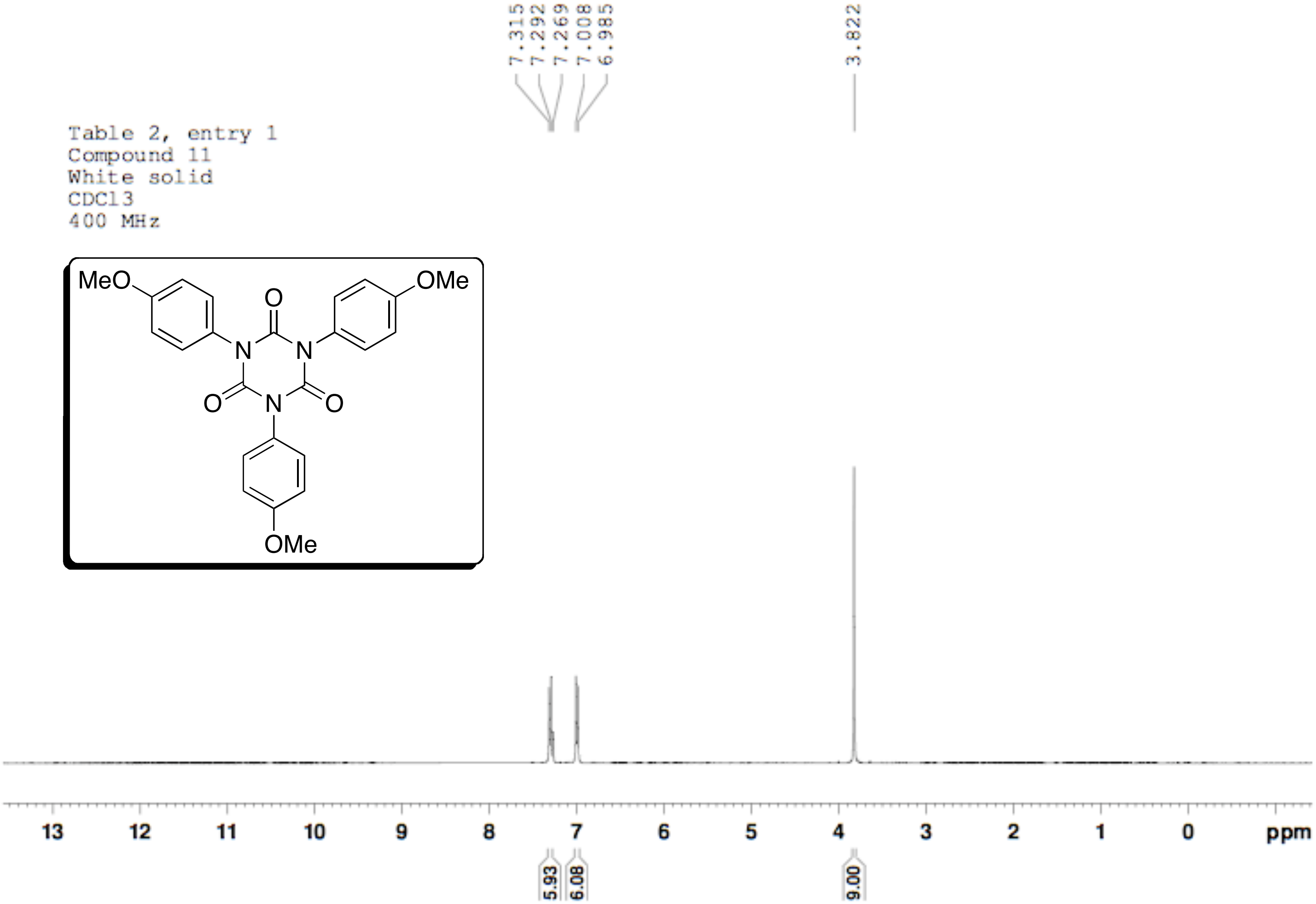


Table 1
Compound 10
White solid
CDCl3
100 MHz


7.315
7.292
7.269
7.008
6.985
3.822
Table 2, entry 1
Compound 11
White solid
CDCl3
400 MHz
MeO
OMe
OMe
O
O
O
N
N
N
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
5.93
6.08
9.00

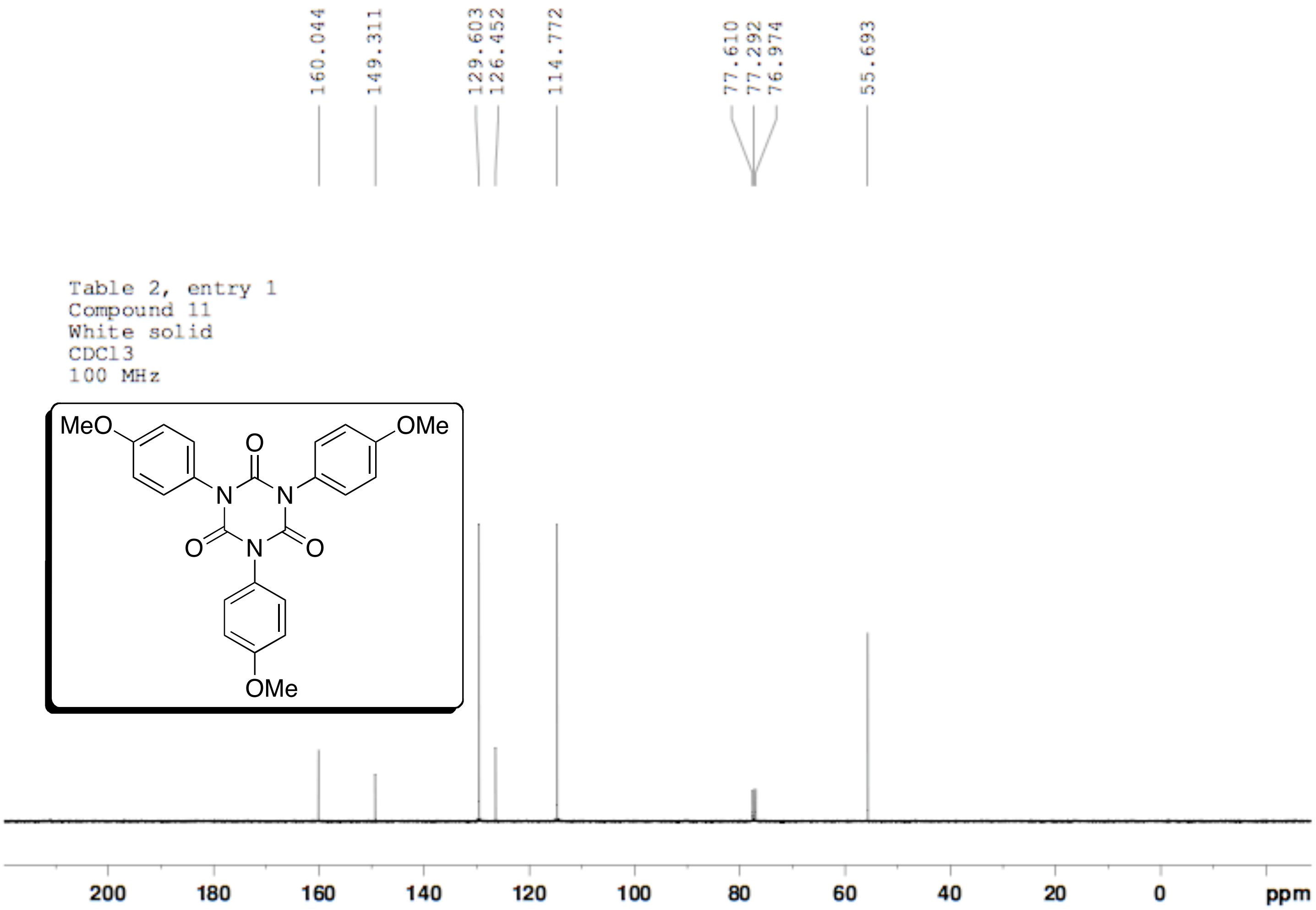


Table 2, entry 1
Compound 11
White solid
CDCl3
100 MHz

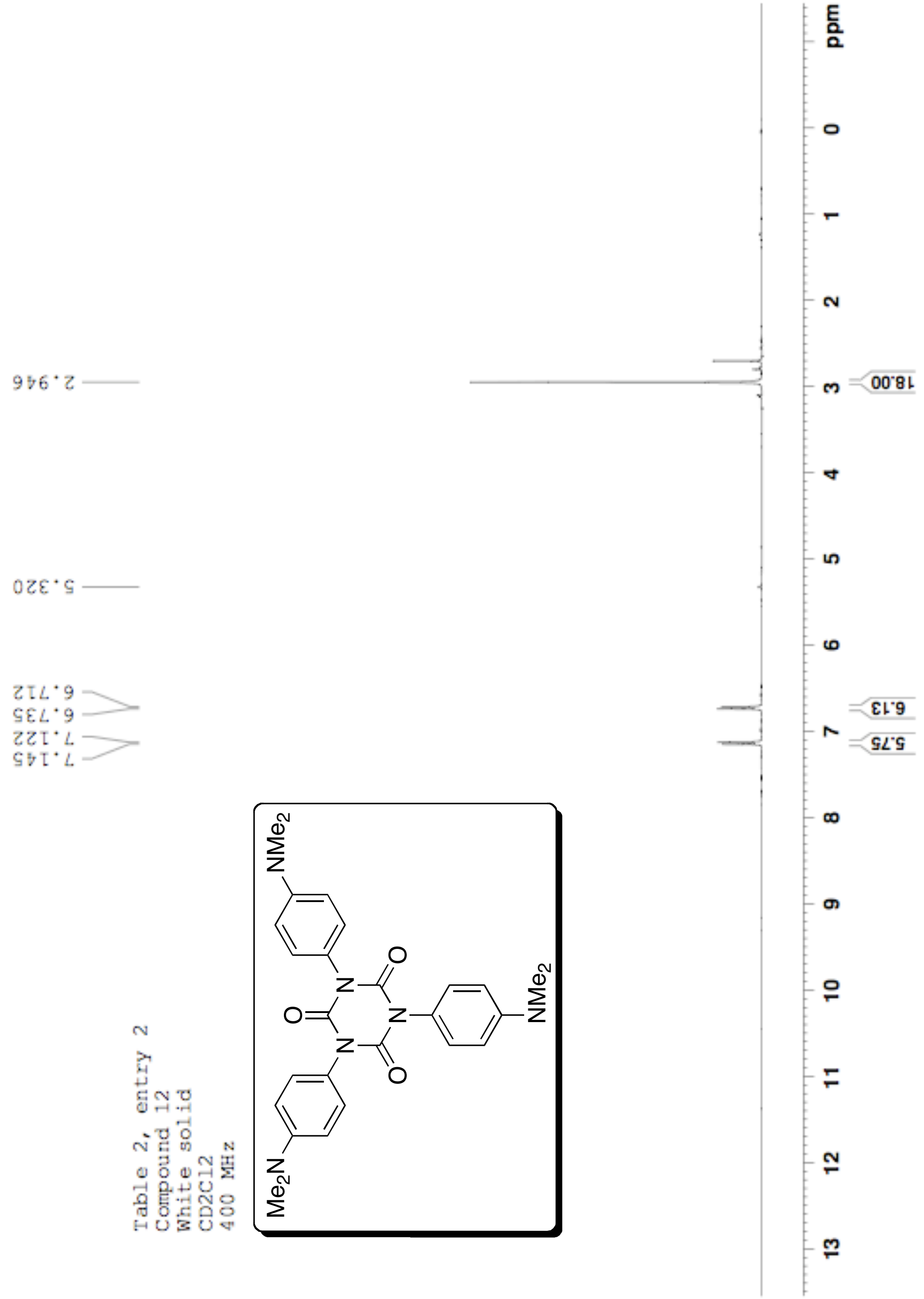
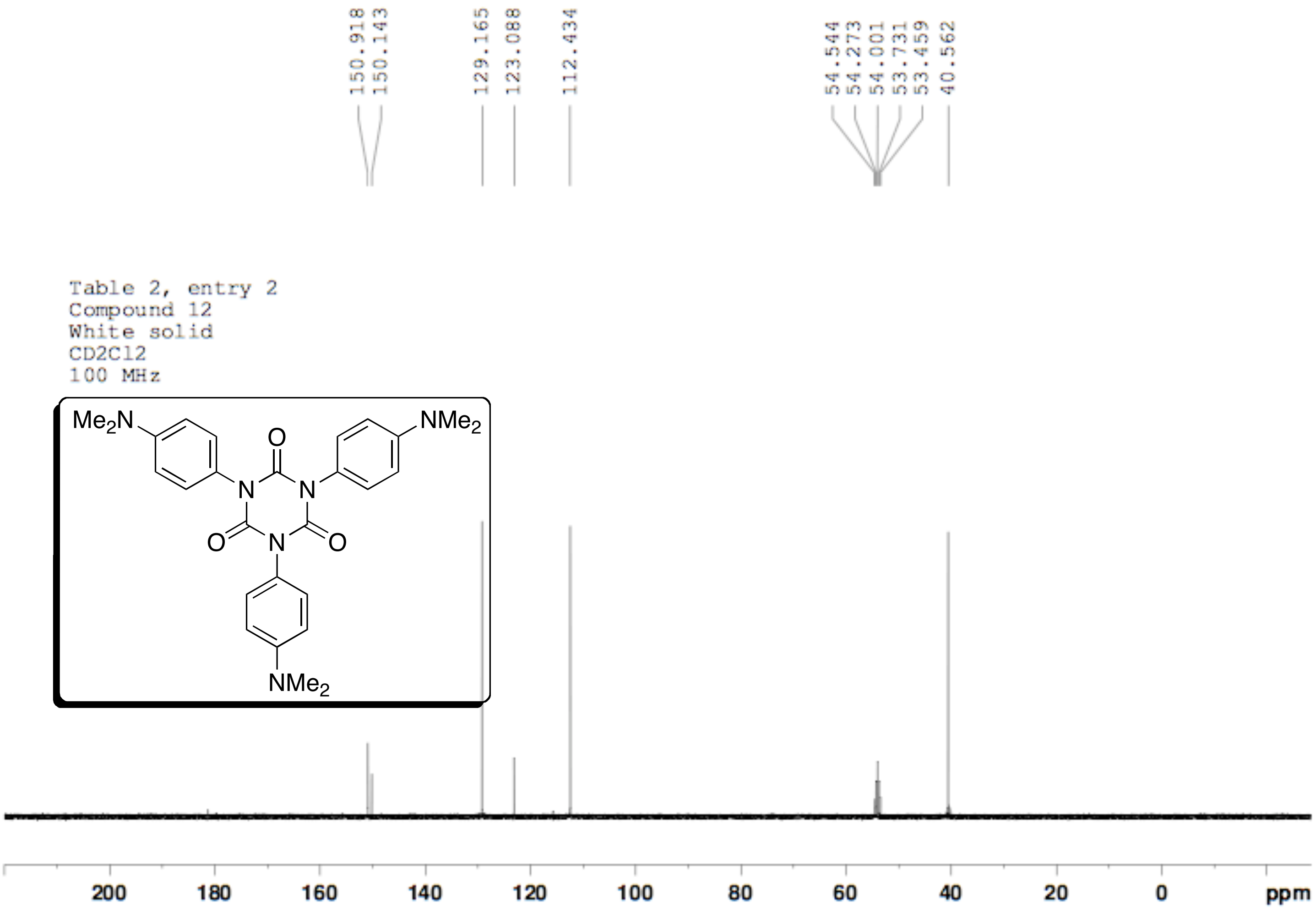
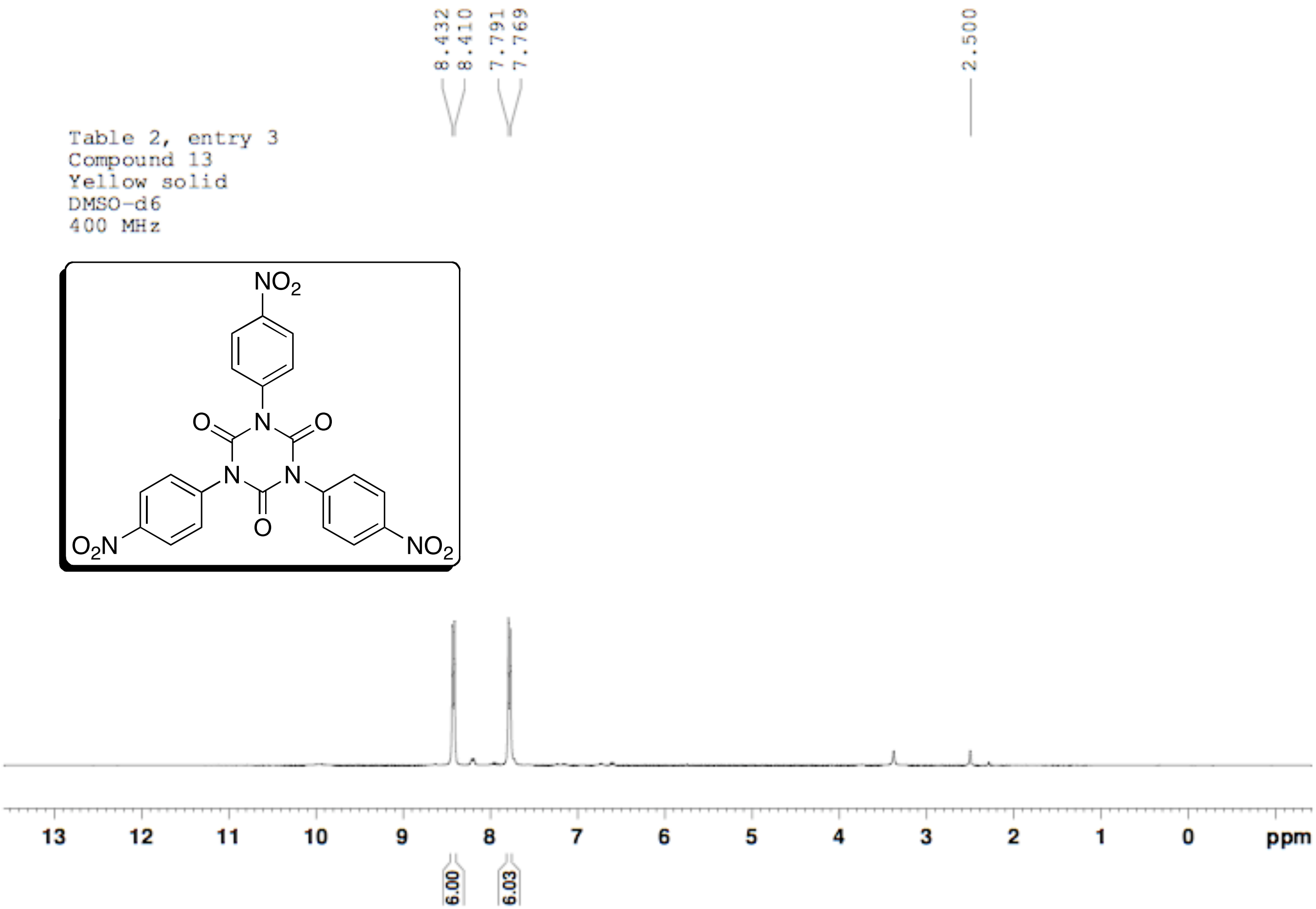
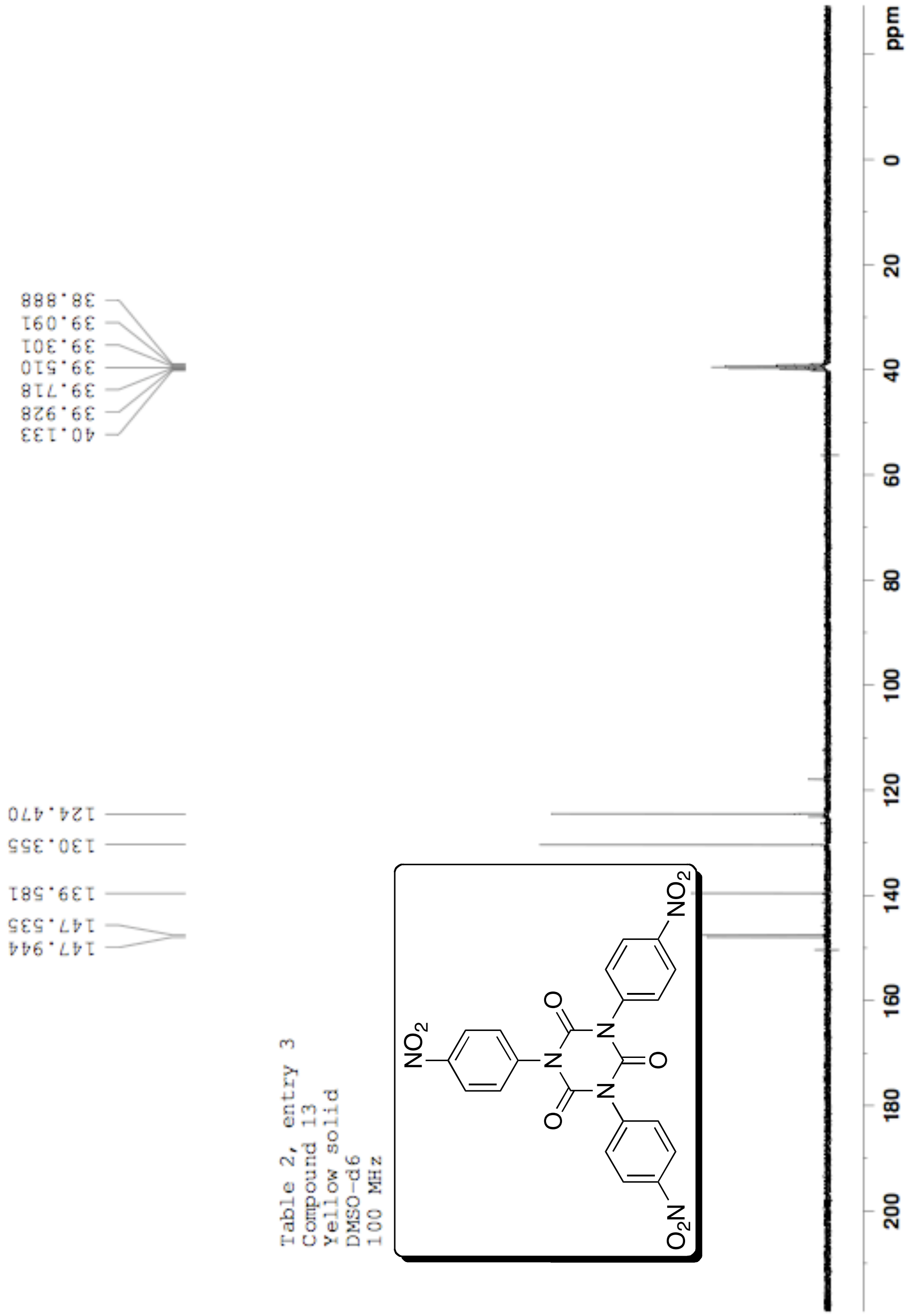


Table 2, entry 2
Compound 12
White solid
CD2Cl2
400 MHz
2.946
5.320
6.712
6.735
7.122
7.145
18.00
6.13
5.75
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
Me2N
NMe2
NMe2
N
N
N
O
O
O


150.918
150.143
129.165
123.088
112.434
54.544
54.273
54.001
53.731
53.459
40.562
Table 2, entry 2
Compound 12
White solid
CD2Cl2
100 MHz
Me2N
NMe2
NMe2
O
O
O
N
N
N
200
180
160
140
120
100
80
60
40
20
0
ppm


8.432
8.410
7.791
7.769
2.500
Table 2, entry 3
Compound 13
Yellow solid
DMSO-d6
400 MHz
NO2
O
O
N
N
N
O
O2N
NO2
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
6.00
6.03


38.888
39.091
39.301
39.510
39.718
39.928
40.133
124.470
130.355
139.581
147.535
147.944
Table 2, entry 3
Compound 13
Yellow solid
DMSO-d6
100 MHz
NO_2
NO_2
O_2N
N
N
N
O
O
O
ppm
0
20
40
60
80
100
120
140
160
180
200

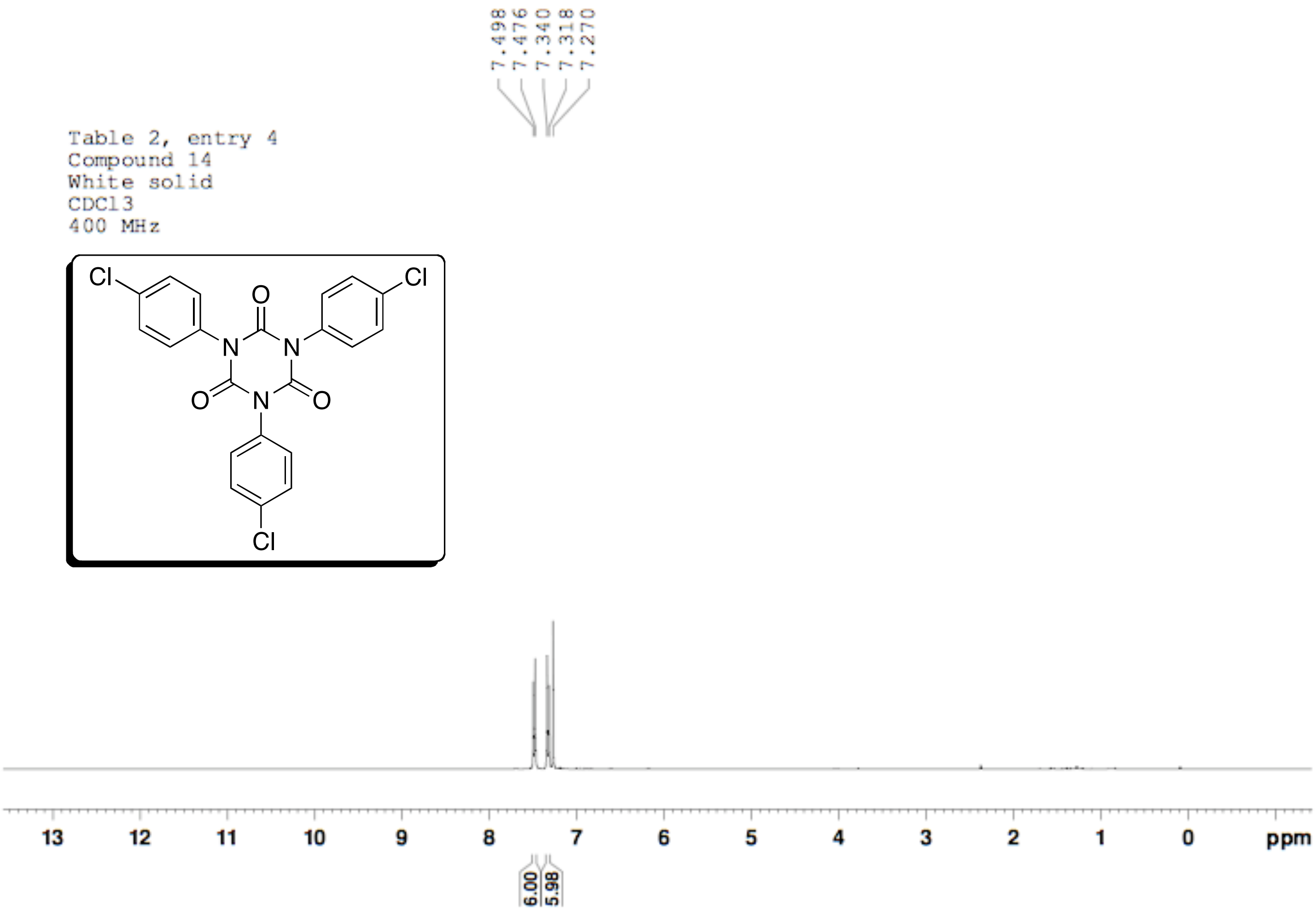
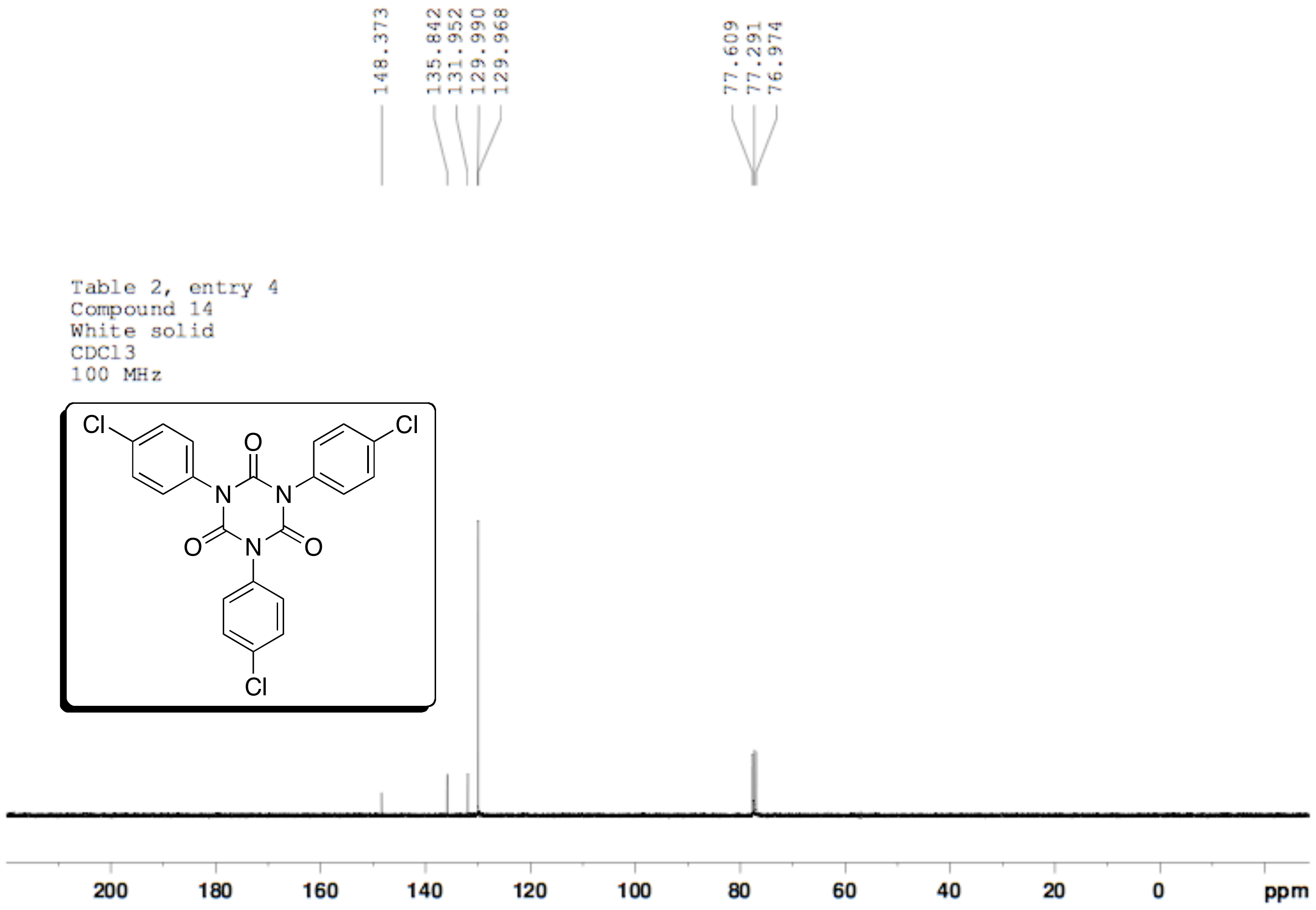


Table 2, entry 4
Compound 14
White solid
CDCl3
400 MHz
Cl
Cl
Cl
N
N
N
O
O
O
7.498
7.476
7.340
7.318
7.270
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
6.00
5.98


148.373
135.842
131.952
129.990
129.968
77.609
77.291
76.974
Table 2, entry 4
Compound 14
White solid
CDCl3
100 MHz
Cl
Cl
Cl
O
O
O
N
N
N
200
180
160
140
120
100
80
60
40
20
0
ppm

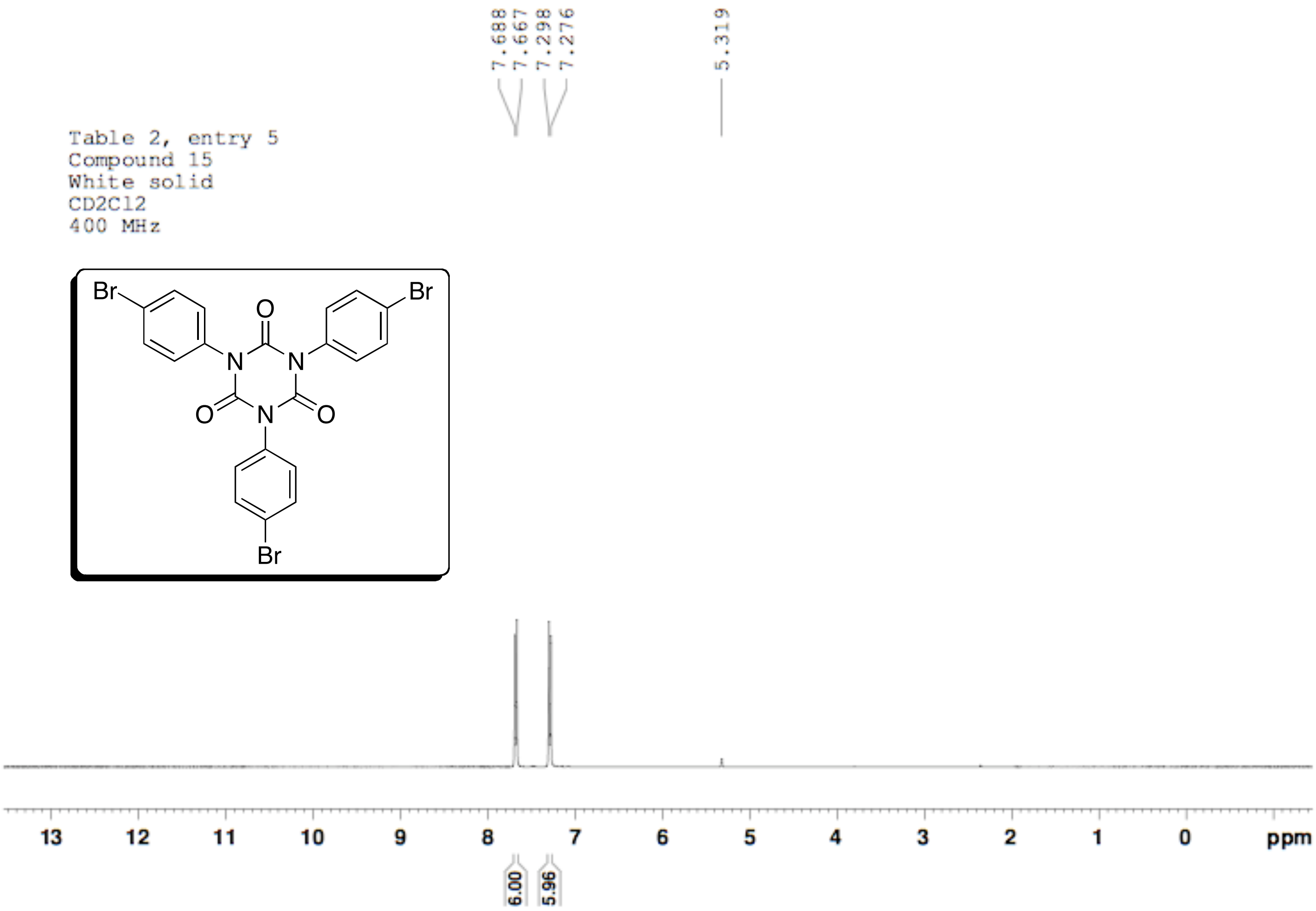


Table 2, entry 5
Compound 15
White solid
CD2Cl2
400 MHz

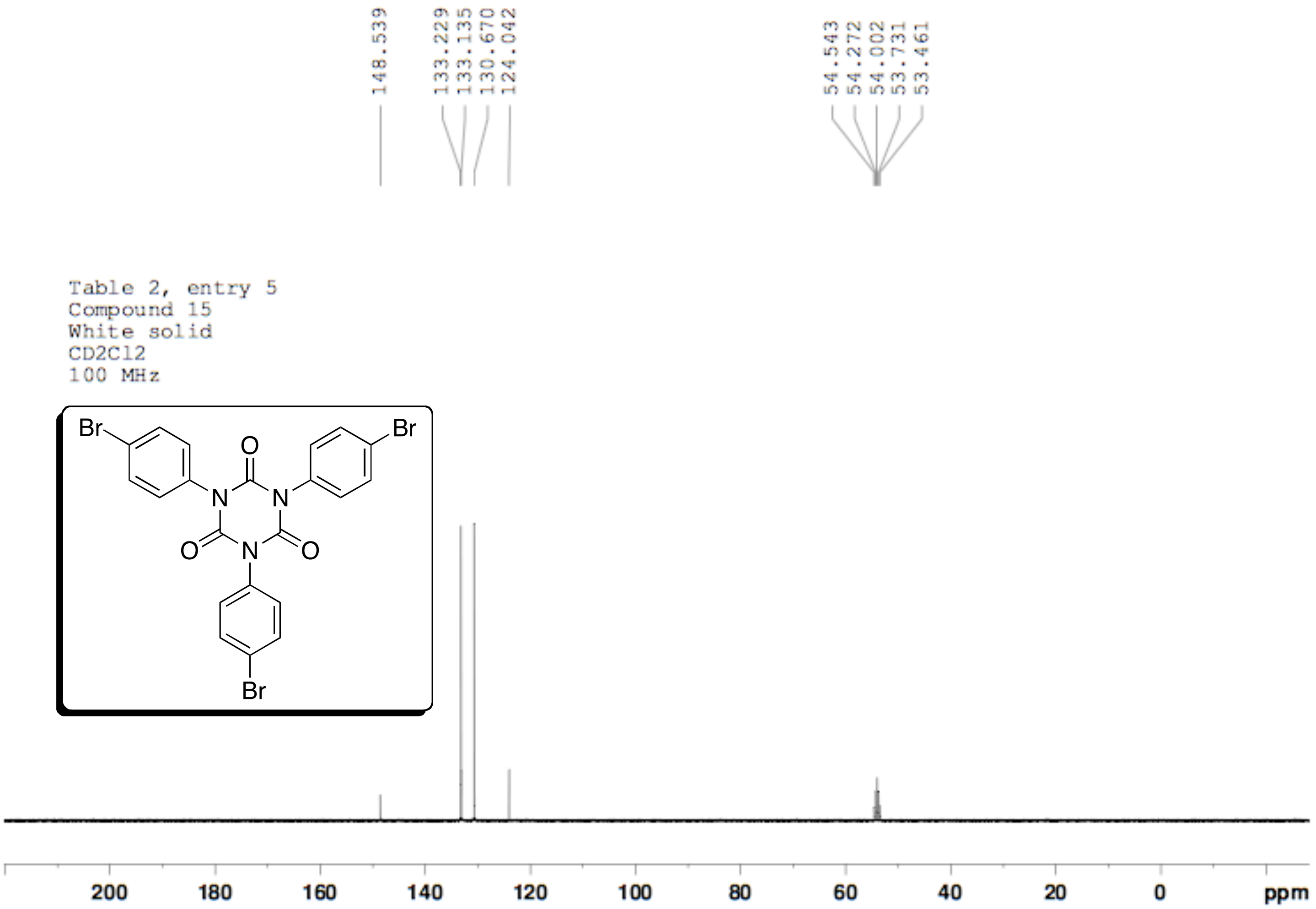


Table 2, entry 5
Compound 15
White solid
CD2Cl2
100 MHz

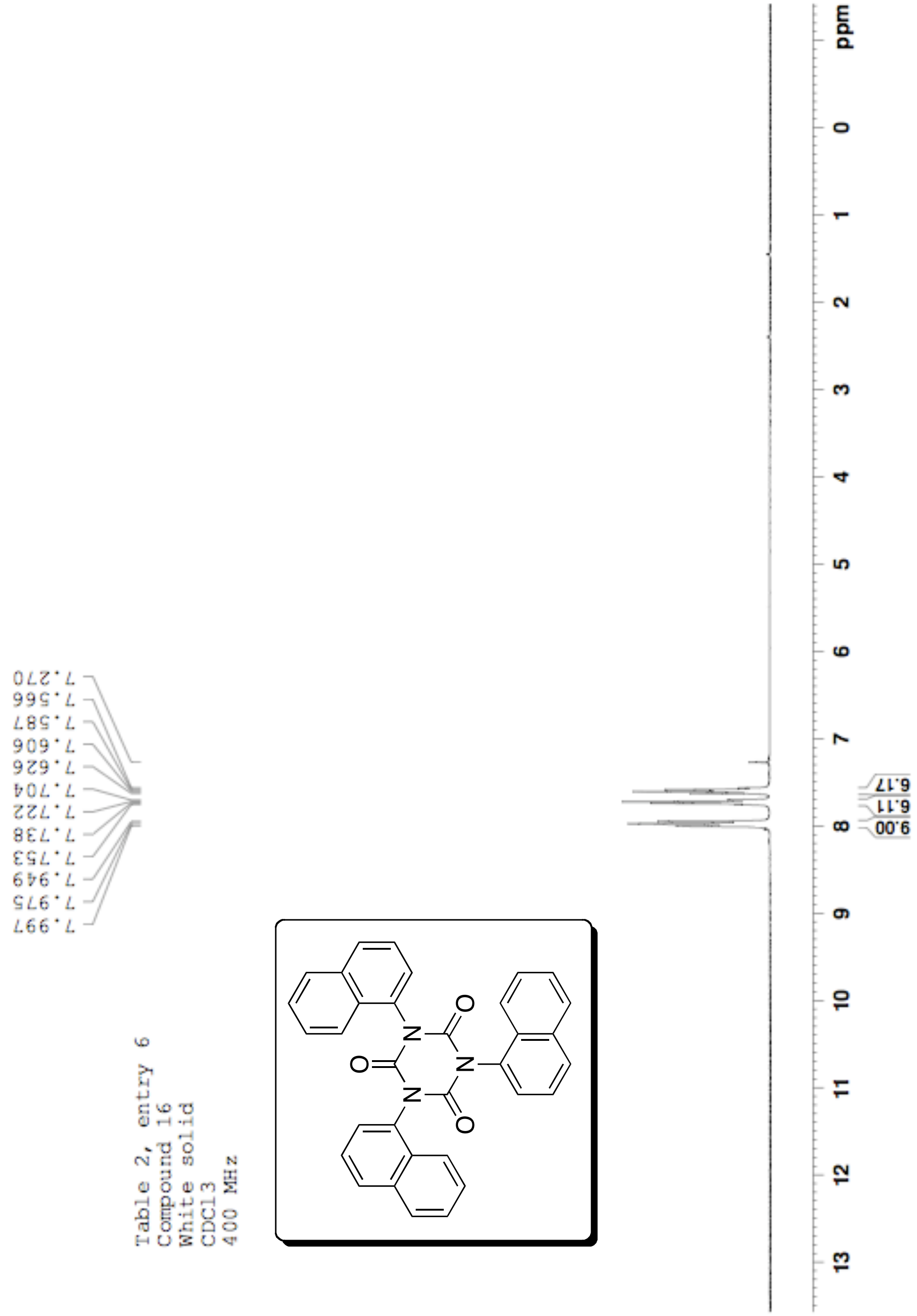


Table 2, entry 6
Compound 16
White solid
CDCl3
400 MHz
7.270
7.566
7.587
7.606
7.626
7.704
7.722
7.738
7.753
7.949
7.975
7.997
9.00
6.11
6.17
ppm
13
12
11
10
9
8
7
6
5
4
3
2
1
0
N
O

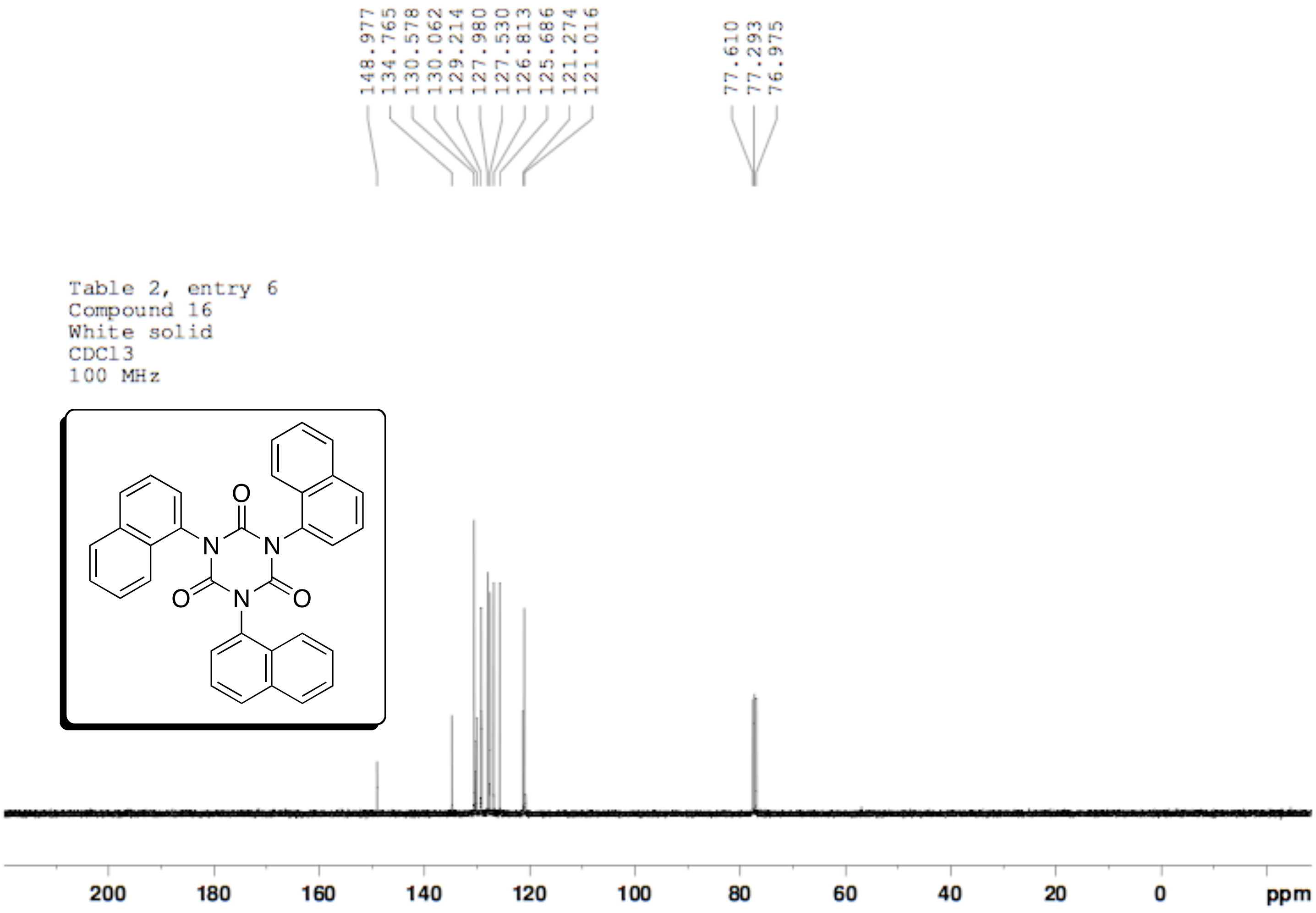


Table 2, entry 6
Compound 16
White solid
CDCl3
100 MHz

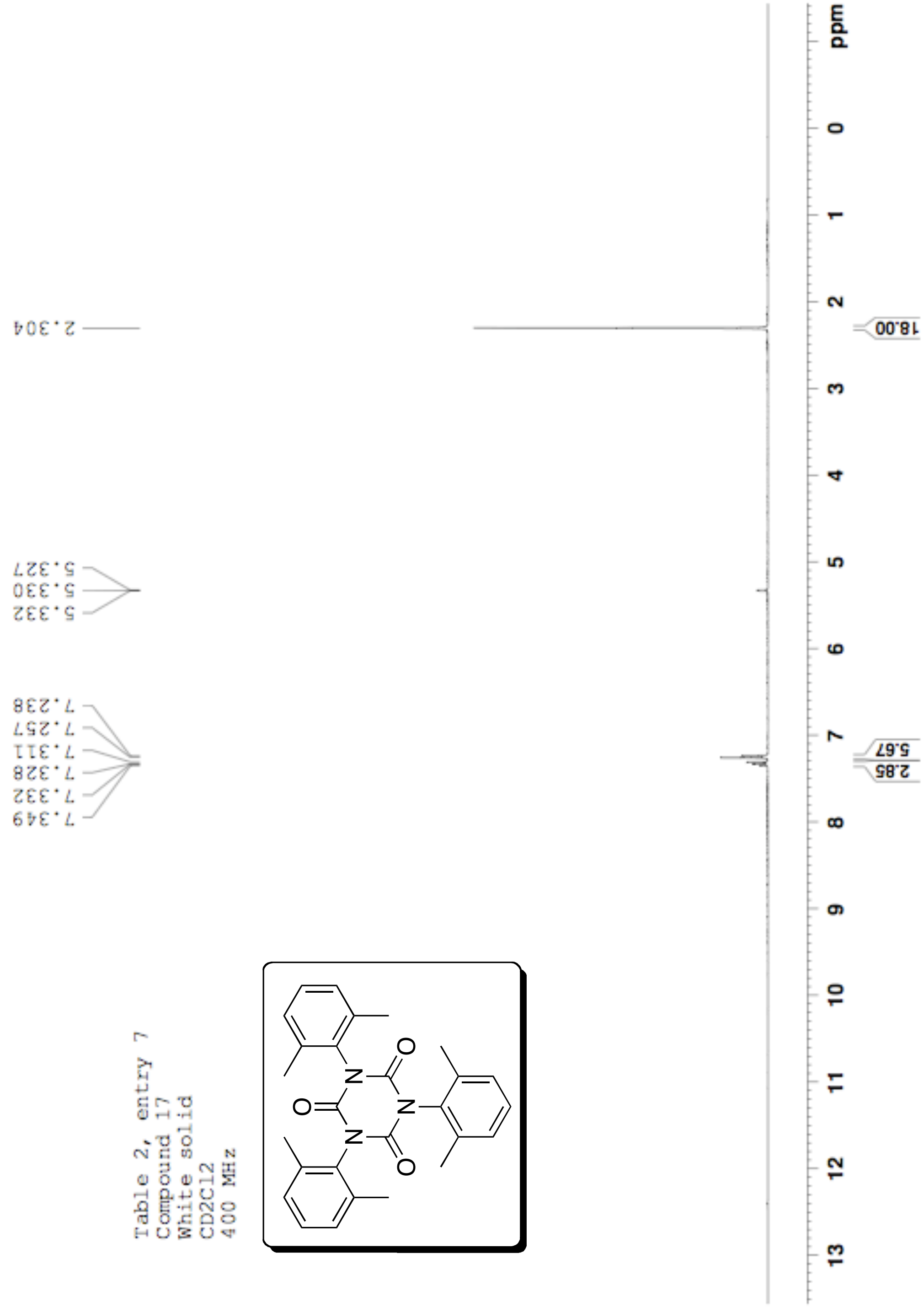


Table 2, entry 7
Compound 17
White solid
CD2Cl2
400 MHz

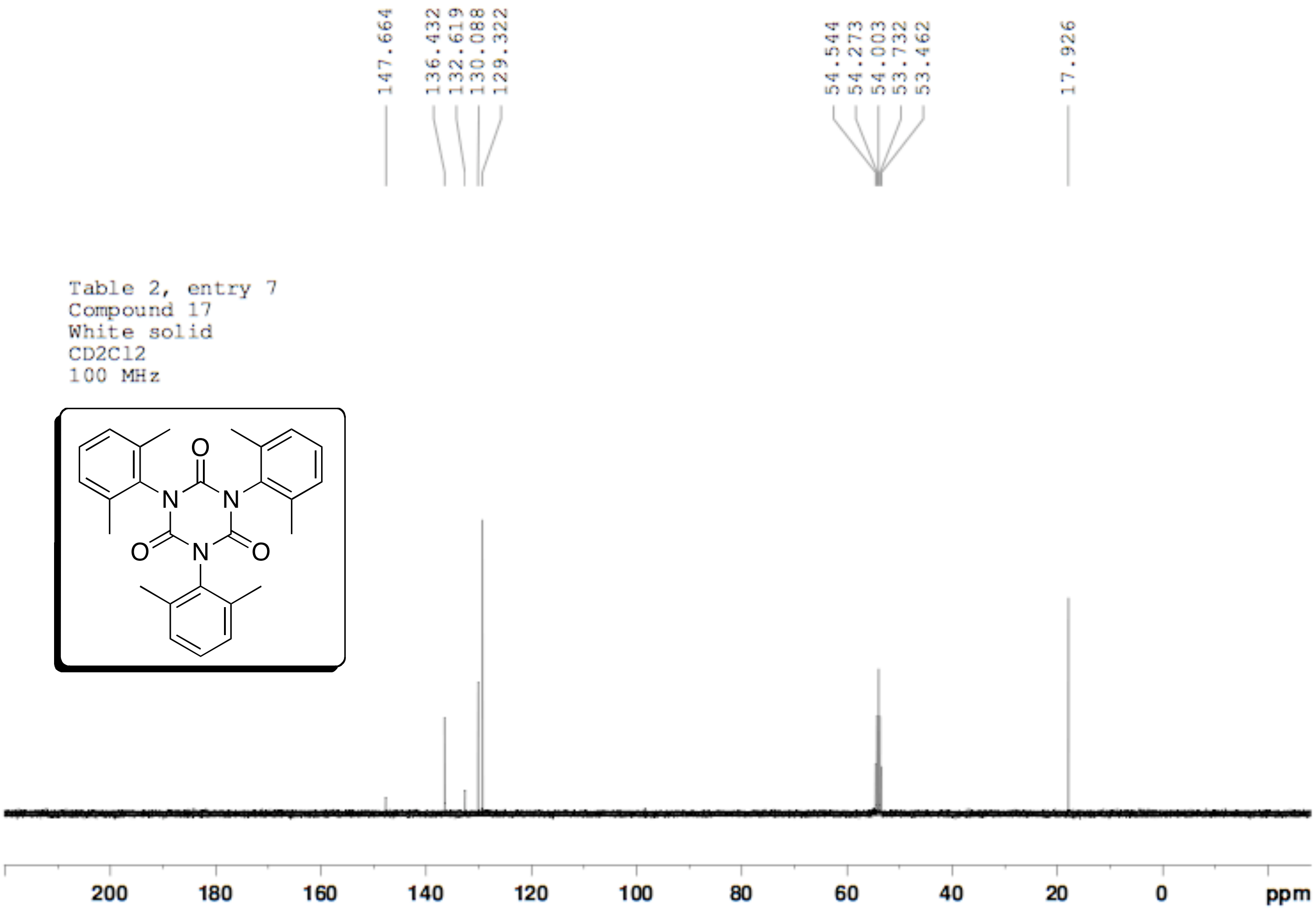


Table 2, entry 7
Compound 17
White solid
CD2Cl2
100 MHz

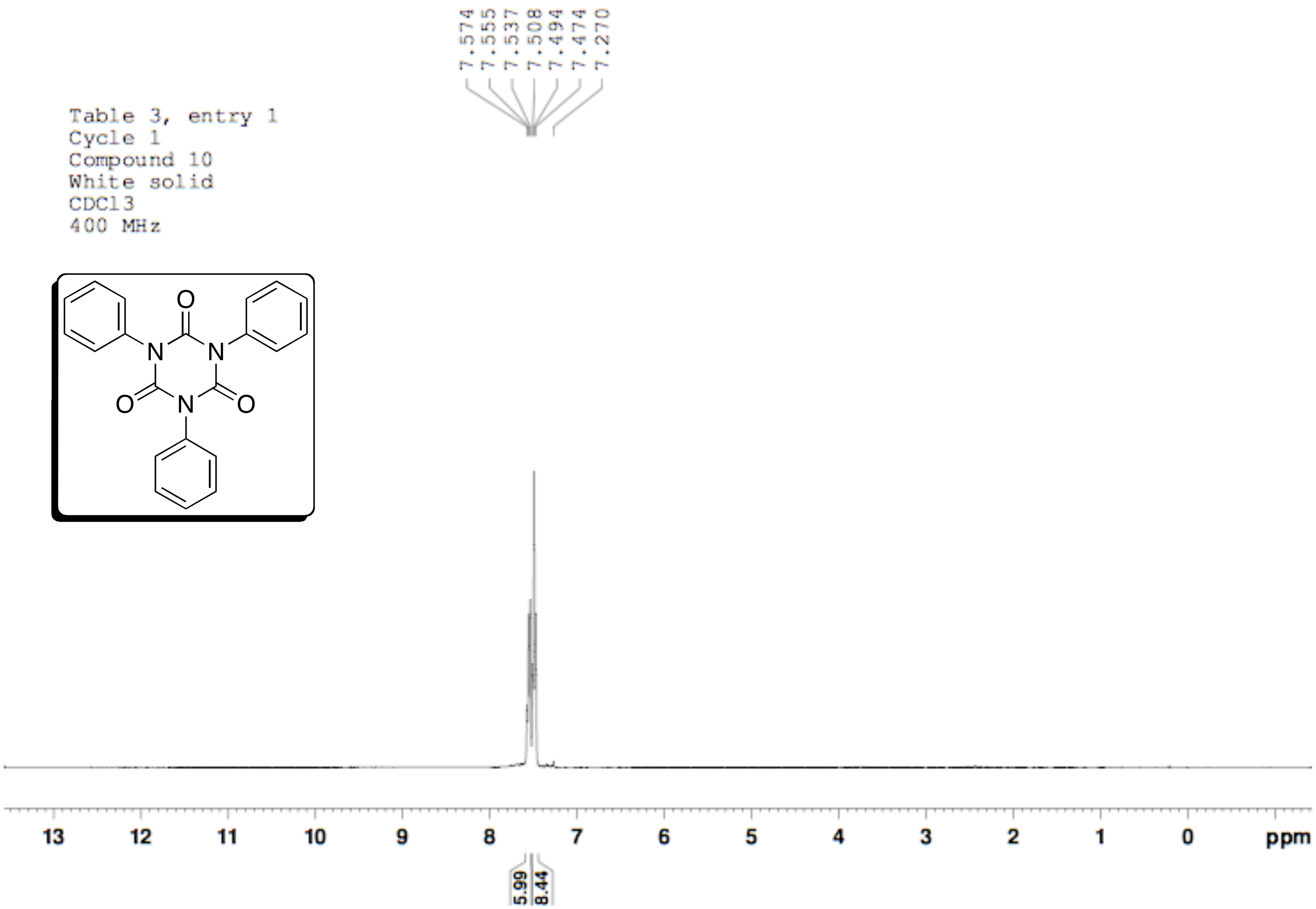


Table 3, entry 1
Cycle 1
Compound 10
White solid
CDCl3
400 MHz

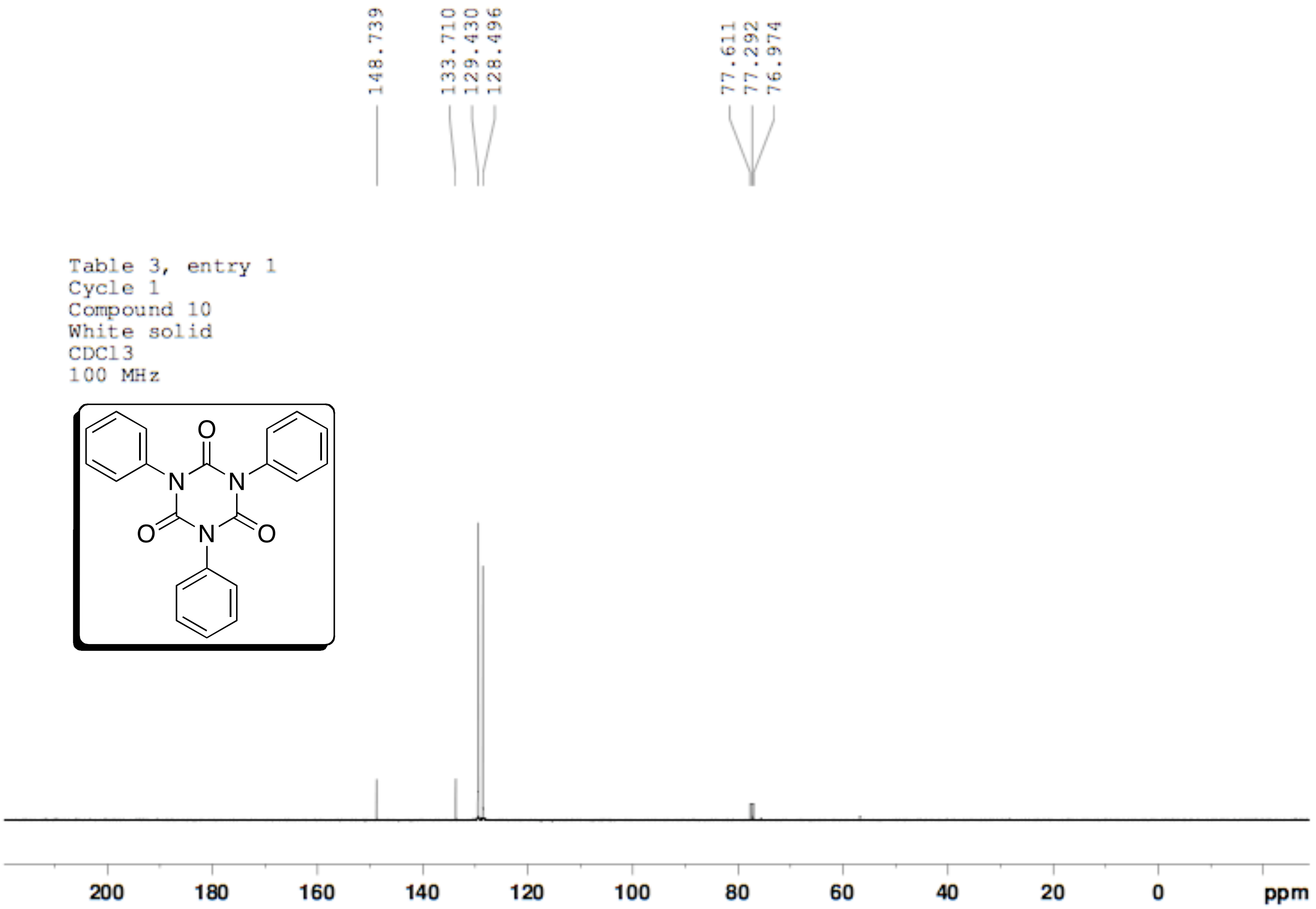


Table 3, entry 1
Cycle 1
Compound 10
White solid
CDCl3
100 MHz

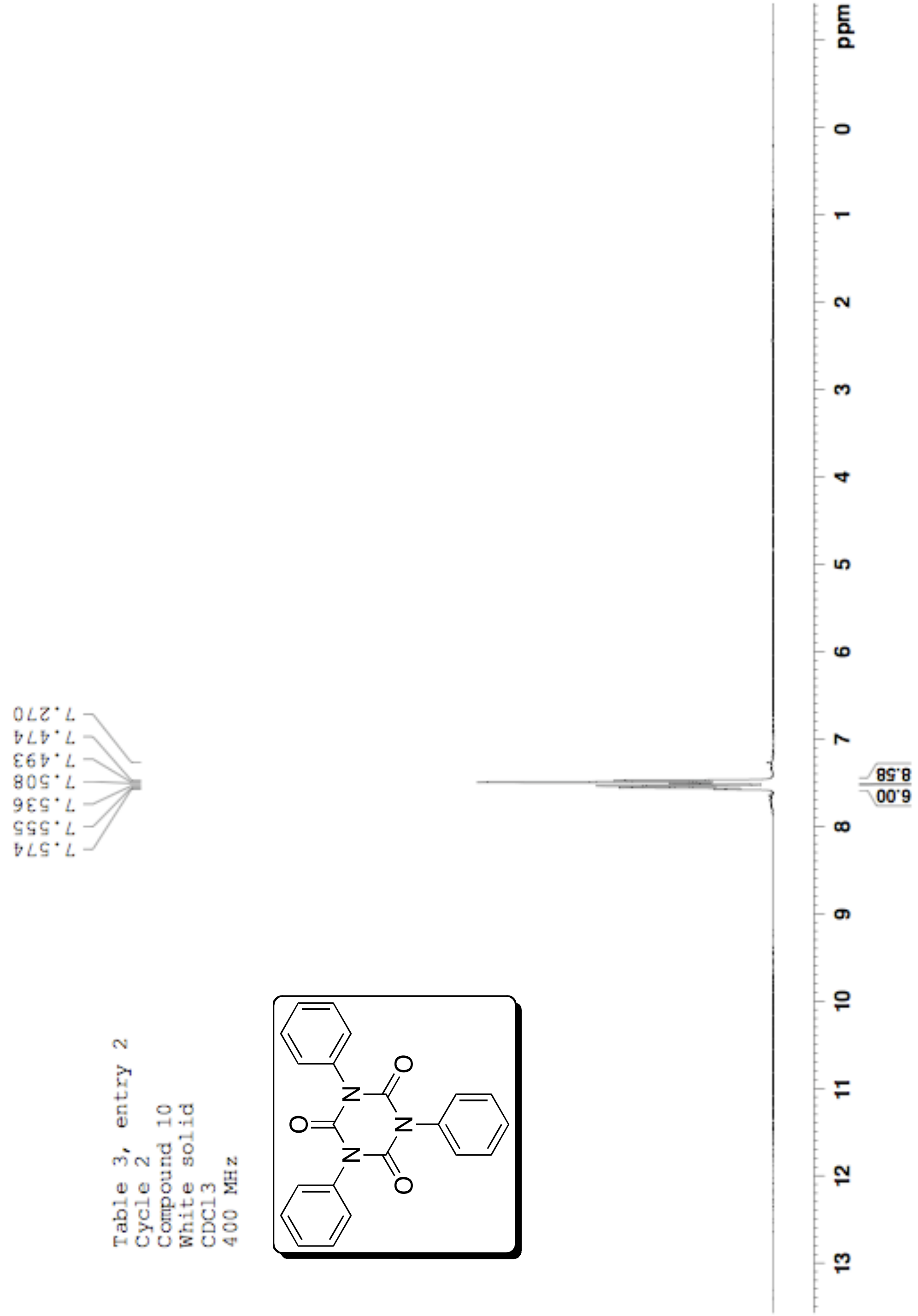


Table 3, entry 2
Cycle 2
Compound 10
White solid
CDCl3
400 MHz

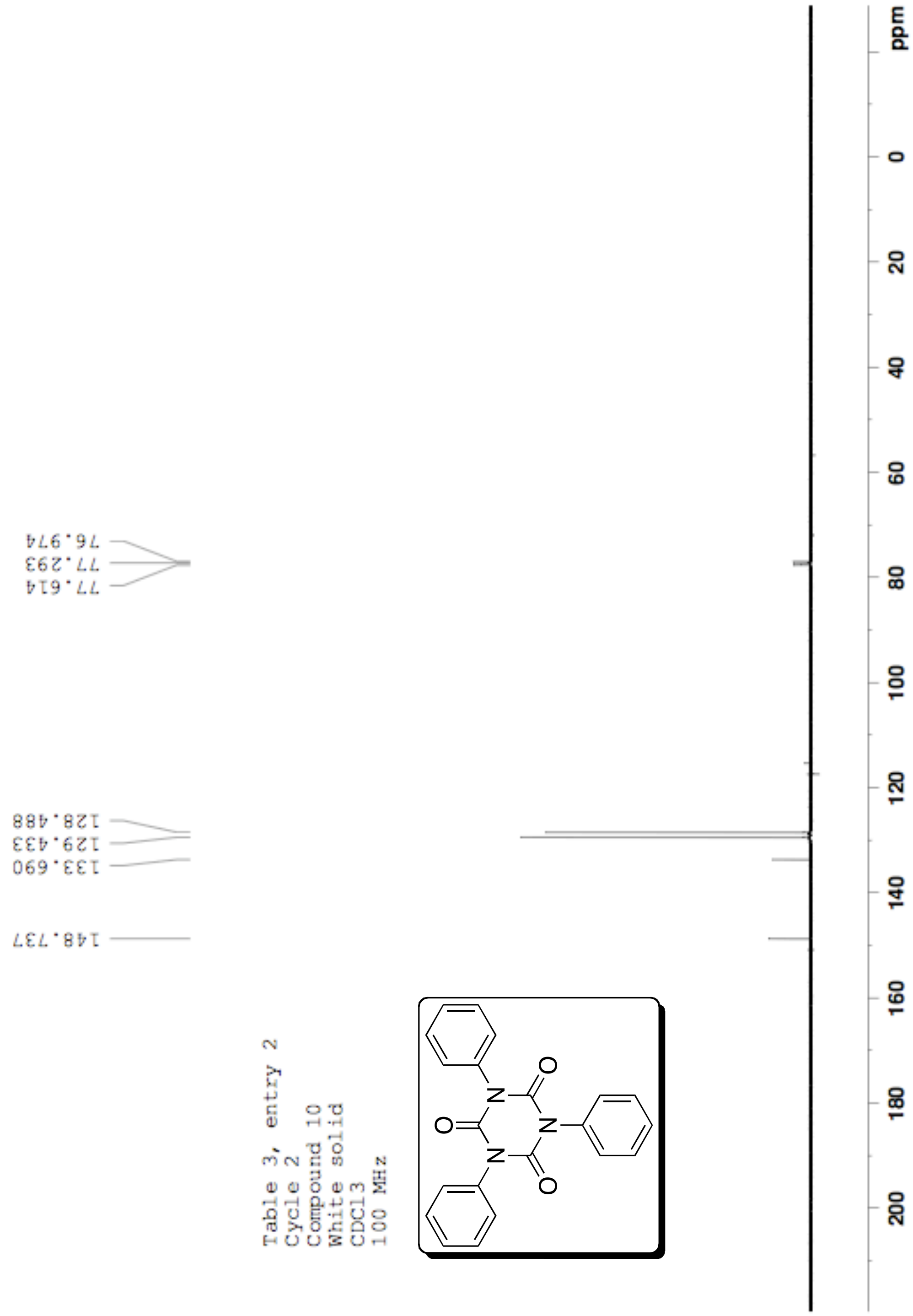


Table 3, entry 2
Cycle 2
Compound 10
White solid
CDCl3
100 MHz
148.737
133.690
129.433
128.488
77.614
77.293
76.974
N
N
N
O
O
O
ppm
200
180
160
140
120
100
80
60
40
20
0

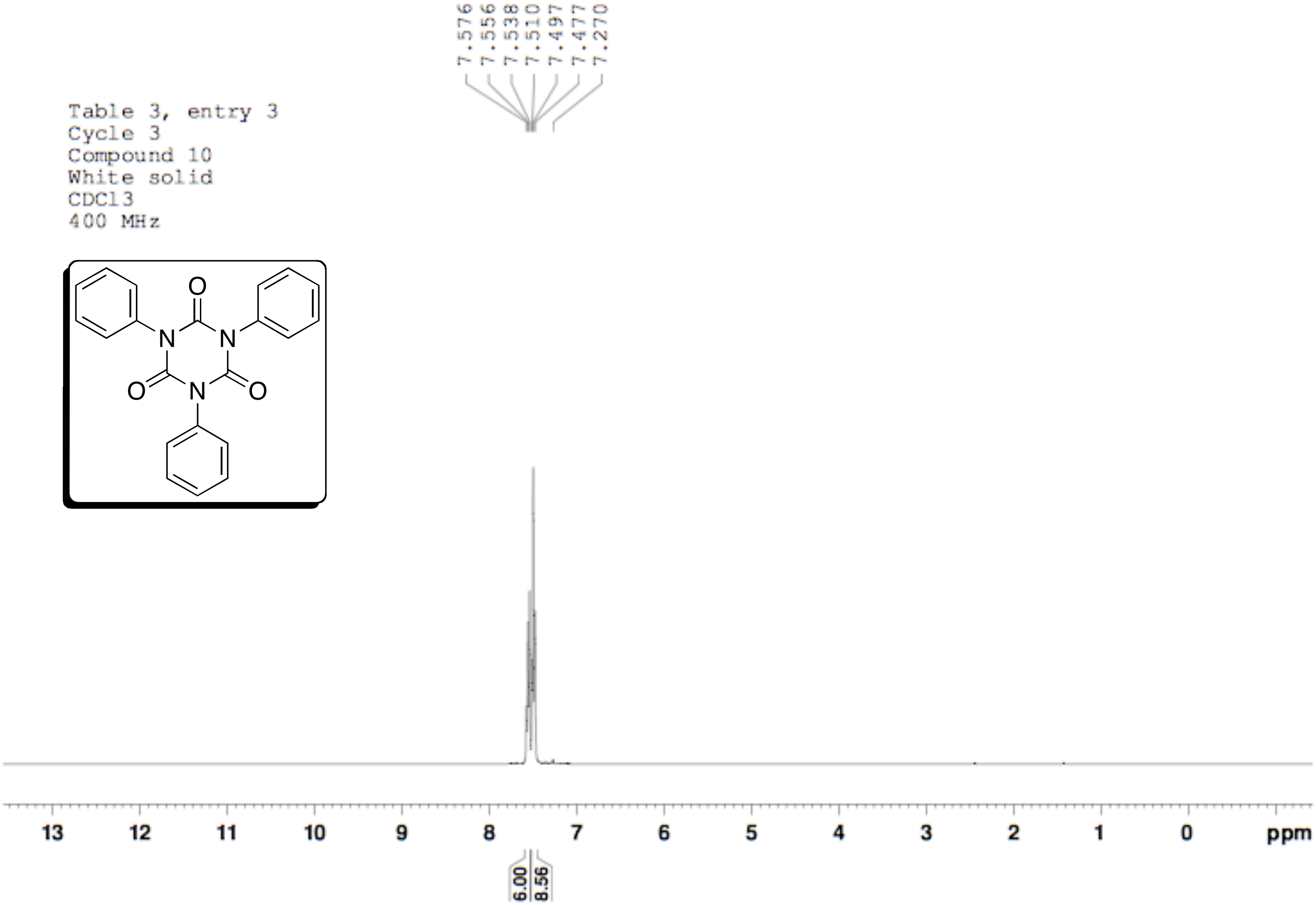


Table 3, entry 3
Cycle 3
Compound 10
White solid
CDCl3
400 MHz
7.576
7.556
7.538
7.510
7.497
7.477
7.270
6.00
8.56
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
O
N
N
O
N
O


148.725
133.675
129.425
128.474
77.612
77.292
76.974
Table 3, entry 3
Cycle 3
Compound 10
White solid
CDCl3
100 MHz
O
N
N
O
N
O
200
180
160
140
120
100
80
60
40
20
0
ppm

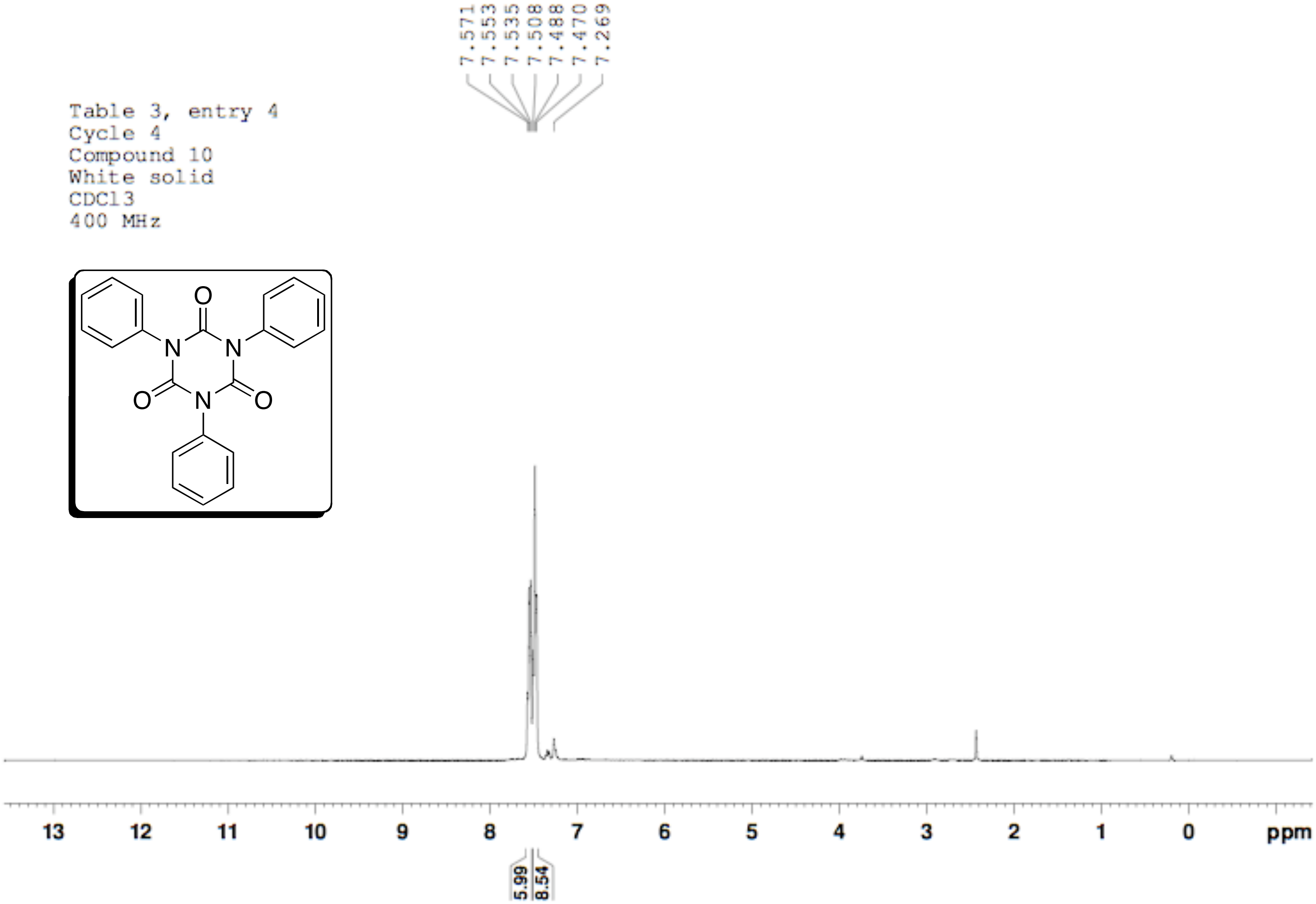
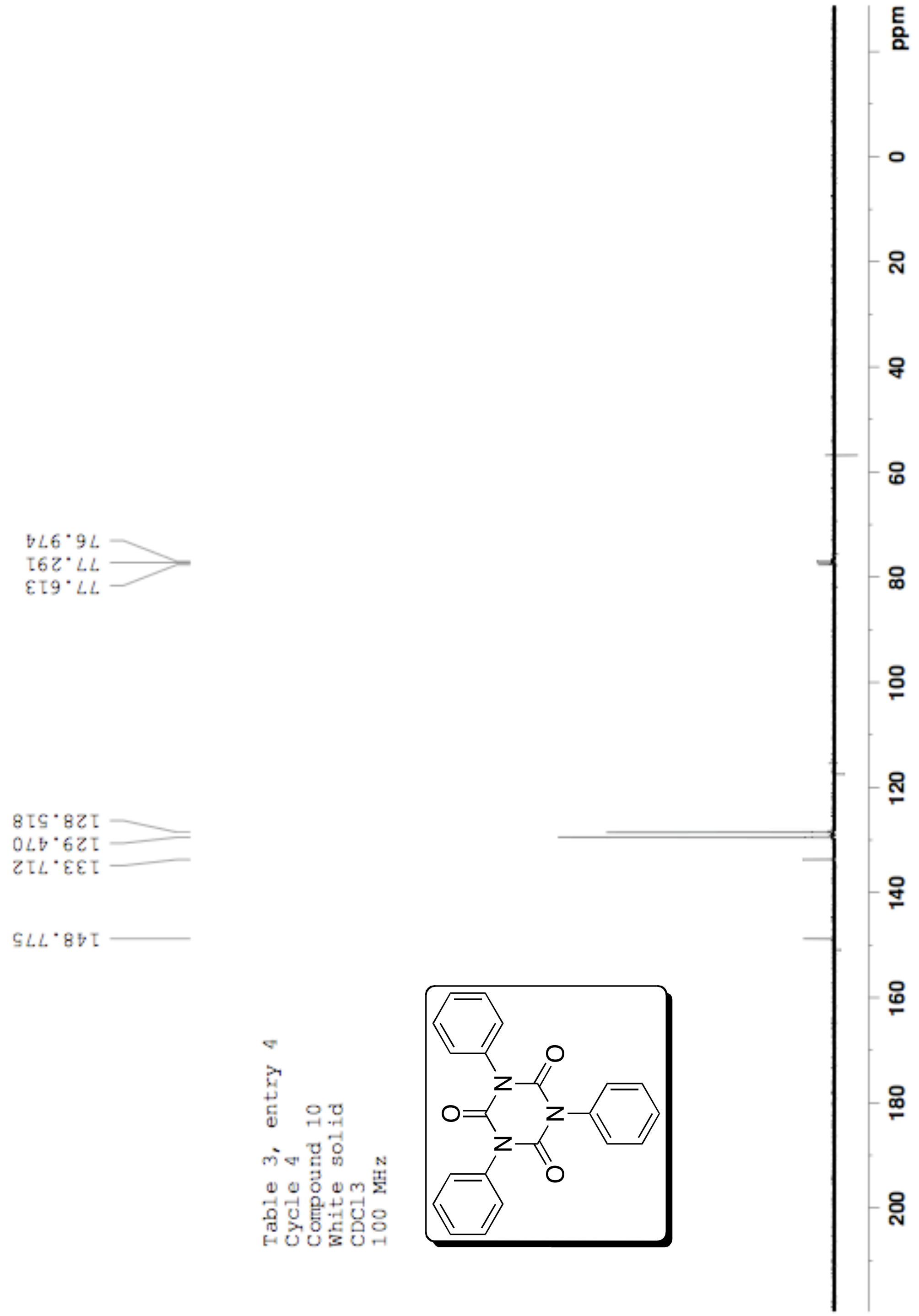


Table 3, entry 4
Cycle 4
Compound 10
White solid
CDCl3
400 MHz


76.974
77.291
77.613
128.518
129.470
133.712
148.775
Table 3, entry 4
Cycle 4
Compound 10
White solid
CDCl3
100 MHz
ppm
0
20
40
60
80
100
120
140
160
180
200

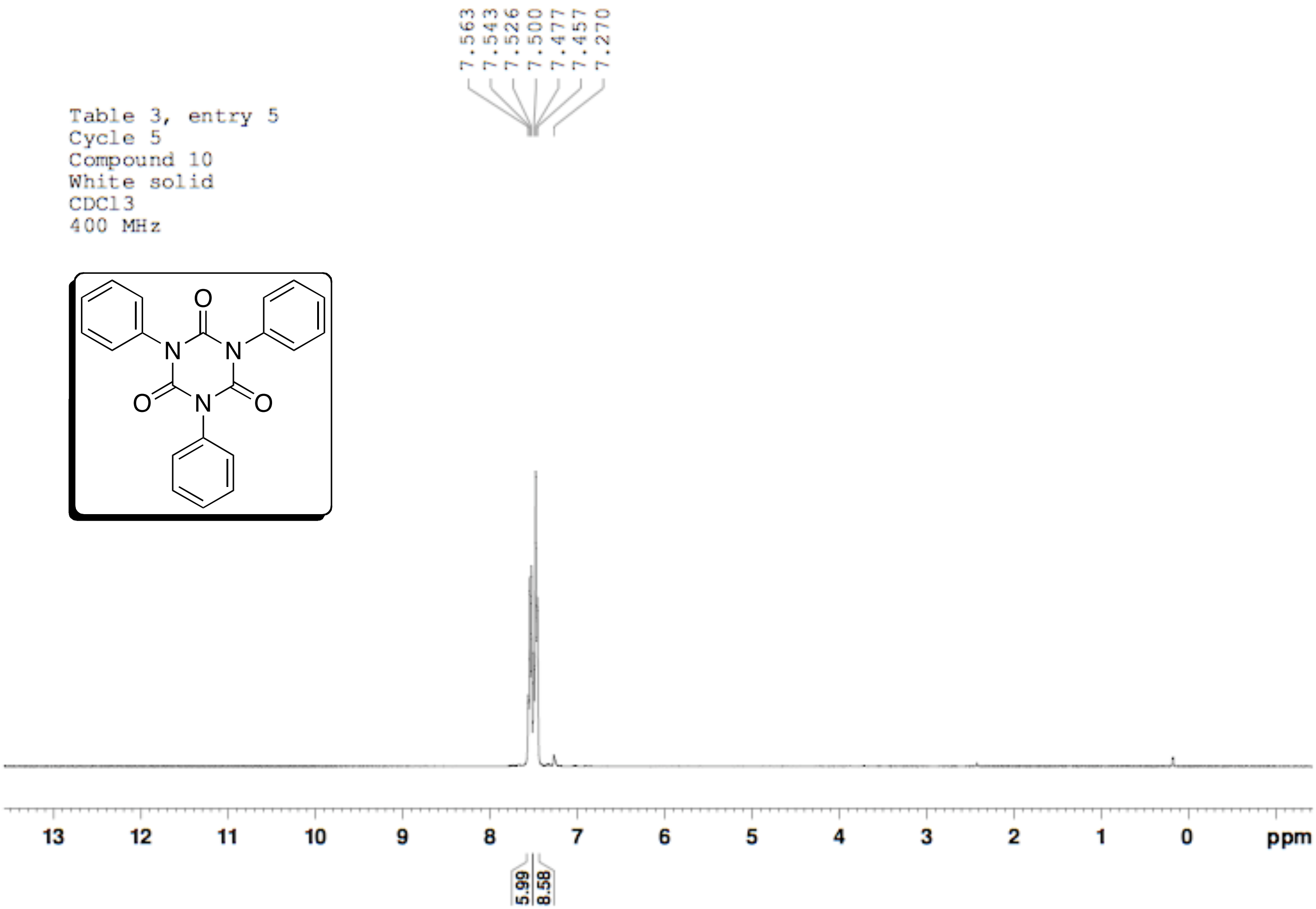


Table 3, entry 5
Cycle 5
Compound 10
White solid
CDCl3
400 MHz

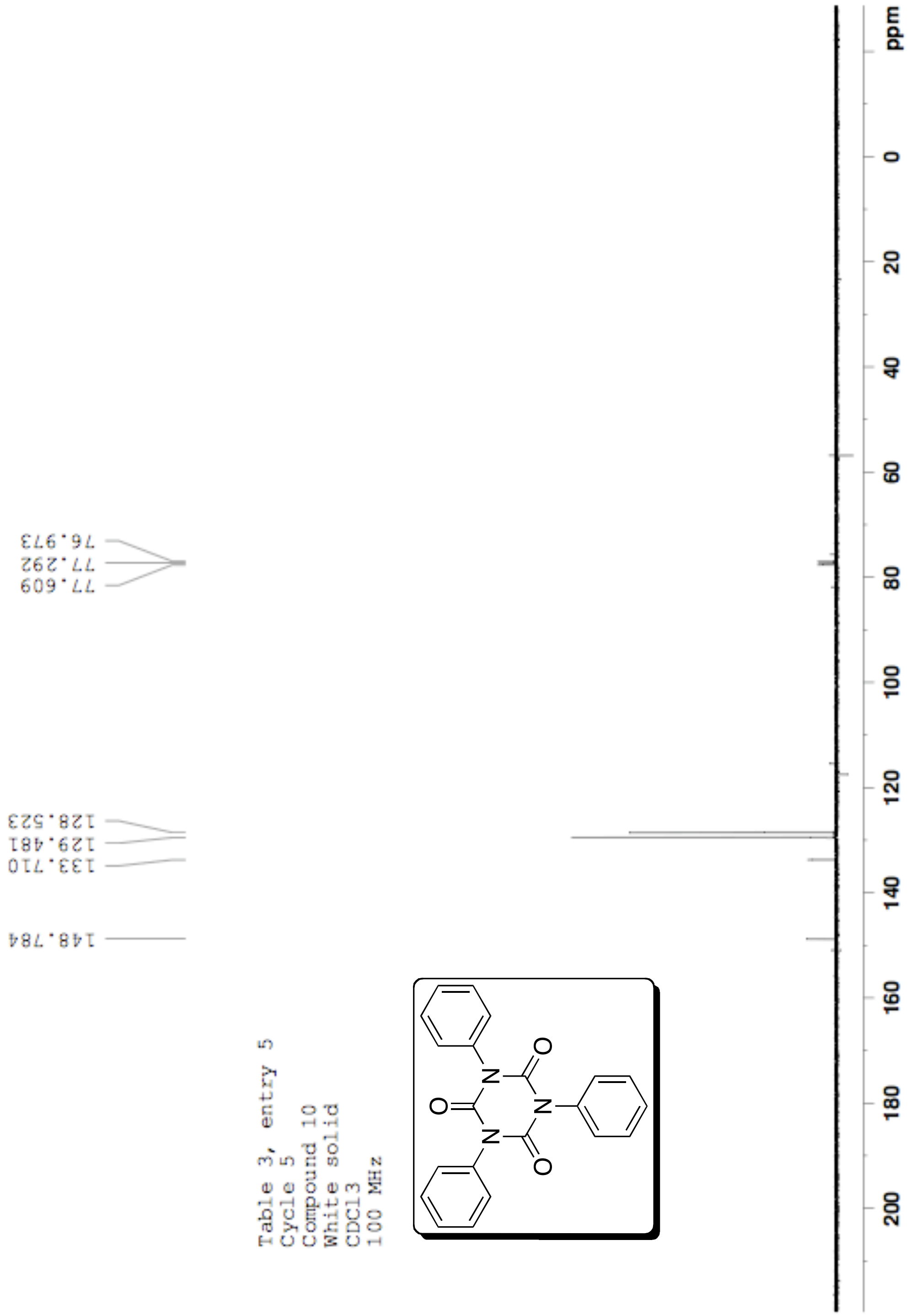


Table 3, entry 5
Cycle 5
Compound 10
White solid
CDCl3
100 MHz
148.784
133.710
129.481
128.523
77.609
77.292
76.973
ppm
0
20
40
60
80
100
120
140
160
180
200
O
N
N
N
O
O

Crystallographic Experimental Section

Data Collection

A colorless crystal was selected under ambient conditions. The crystal was mounted and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed at 173 K on a Bruker CCD-1000 diffractometer with Mo K_α (λ = 0.71073 Å) radiation and the detector to crystal distance of 5.03 cm.

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 30 frames collected at intervals of 0.3º in a 10º range about ω with the exposure time of 15 seconds per frame. The obtained reflections were successfully indexed by an automated indexing routine built in the SMART program. The final cell constants were calculated from a set of strong reflections from the actual data collection.

The data were collected using the full sphere routine by collecting four sets of frames with 0.3º scans in ω with an exposure time 15 sec per frame. This dataset was corrected for Lorentz and polarization effects. The absorption correction was based on a fit of a spherical harmonic function to the empirical transmission surface as sampled by multiple equivalent measurements [1] using SADABS software [2].

Structure Solution and Refinement

The systematic absences in the diffraction data were consistent for the space groups $P4_332$ [2] yielded chemically reasonable and computationally stable results of refinement. The position of almost all non-hydrogen atoms were found by direct methods. The remaining atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined in full-matrix anisotropic approximation. All hydrogen atoms were placed in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.

The unreasonably high final R-factor (R1 = 0.197) for this space group and non-realistic shape of thermal ellipsoids for all atoms clearly indicated the wrong assignment. Automatic test for merohedral twinning in XPREP software did not indicate the existence of twinning. The molecule was expected to lay on a 3-fold axis, so it was suggested, that 4-fold axis in a crystal lattice is a pseudo-axis and structure was solved in a $P2_13$ space group with twinning law (0 1 0 1 0 0 0 0 -1) emulationg pseudo-4 fold axis. Structure was successfully resolved and refined to R1=0.0428.

The ORTEP diagram was drawn at 50% probability level. H-atoms were omitted for clarity. The resulting CIF file has been tested with PLATON [3] software. The results and comments have been included to output package (Platon_Lar15.doc.). The X-Ray structure determination description from this report may be also added to correspondent fields of CIF file.

References

[1] Blessing, R.H. *Acta Cryst*. **1995**, *A51*, 33-38.

[2] Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112-122

[3] A.L.Spek, J.Appl.Cryst. 36, 7-13.

Table 1. Crystal data and structure refinement for Proazaphosphatrane **6**.

Identification code	Proazaphosphatrane **6**	
Empirical formula	C30 H39 N4 O3 P	
Formula weight	534.62	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Cubic	
Space group	P2(1)3	
Unit cell dimensions	a = 18.1117(11) Å	a= 90°.
	b = 18.1117(11) Å	b= 90°.
	c = 18.1117(11) Å	g = 90°.
Volume	5941.2(6) Å^3	
Z	8	
Density (calculated)	1.195 Mg/m^3	
Absorption coefficient	0.129 mm^{-1}	
F(000)	2288	
Crystal size	0.52 x 0.48 x 0.32 mm^3	
Theta range for data collection	1.12 to 28.25°.	
Index ranges	-24<=h<=24, -24<=k<=24, -23<=l<=23	
Reflections collected	53616	
Independent reflections	4889 [R(int) = 0.0746]	
Completeness to theta = 28.25°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1 and 0.77	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4889 / 0 / 245	
Goodness-of-fit on F^2	1.113	
Final R indices [I>2sigma(I)]	R1 = 0.0428, wR2 = 0.1047	
R indices (all data)	R1 = 0.0646, wR2 = 0.1236	
Absolute structure parameter	0.12(14)	
Largest diff. peak and hole	0.475 and -0.186 e.Å^{-3}	

$R1 = \Sigma \,||F_o| - |F_c|| \,/\, \Sigma |F_o|$ and $wR2 = \{ \Sigma [w(F_o^2 - F_c^2)^2] \,/\, \Sigma [w(F_o^2)^2] \}^{1/2}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for Proazaphosphatrane **6**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
P(1)	9770(1)	-231(1)	-231(1)	31(1)
P(2)	7371(1)	7630(1)	2371(1)	34(1)
C(1)	8072(2)	-939(2)	-960(2)	36(1)
C(2)	8275(2)	-620(2)	-210(2)	34(1)
C(3)	8609(2)	711(2)	-199(2)	34(1)
C(4)	8291(2)	964(2)	542(2)	33(1)
C(5)	8482(2)	628(2)	1199(2)	42(1)
C(6)	8192(2)	855(2)	1870(2)	45(1)
C(7)	7690(2)	1424(2)	1877(2)	48(1)
C(8)	7502(2)	1782(2)	1234(2)	51(1)
C(9)	7794(2)	1560(2)	569(2)	41(1)
C(10)	7119(4)	2461(4)	-105(3)	117(3)
C(11)	6703(2)	9323(2)	1595(2)	38(1)
C(12)	7052(2)	9142(2)	2337(2)	36(1)
C(13)	8367(2)	8747(2)	2314(2)	38(1)
C(14)	8649(2)	9147(2)	2998(2)	37(1)
C(15)	8273(2)	9117(2)	3655(2)	43(1)
C(16)	8506(2)	9525(2)	4270(2)	52(1)
C(17)	9120(2)	9957(2)	4221(2)	56(1)
C(18)	9534(2)	9965(2)	3565(2)	59(1)
C(19)	9295(2)	9559(2)	2962(2)	44(1)
C(20)	10368(3)	9885(4)	2240(4)	111(3)
N(1)	8852(1)	-55(1)	-202(1)	34(1)
N(2)	8657(1)	-1343(1)	-1343(1)	34(1)
N(3)	7590(1)	8545(1)	2348(1)	36(1)
N(4)	6255(2)	8745(2)	1255(2)	36(1)
O(1)	7641(2)	1884(1)	-99(1)	55(1)
O(2)	9660(1)	9542(2)	2297(2)	60(1)

Table 3. Bond lengths [Å] and angles [°] for Proazaphosphatrane **6**.

P(1)-N(1)	1.694(2)	C(6)-C(7)	1.374(5)	C(13)-H(13B)	0.9900
P(1)-N(1)#1	1.694(2)	C(6)-H(6)	0.9500	C(14)-C(15)	1.372(5)
P(1)-N(1)#2	1.694(2)	C(7)-C(8)	1.376(5)	C(14)-C(19)	1.390(4)
P(2)-N(3)	1.705(2)	C(7)-H(7)	0.9500	C(15)-C(16)	1.403(5)
P(2)-N(3)#3	1.705(2)	C(8)-C(9)	1.375(5)	C(15)-H(15)	0.9500
P(2)-N(3)#4	1.705(2)	C(8)-H(8)	0.9500	C(16)-C(17)	1.363(6)
C(1)-N(2)	1.464(3)	C(9)-O(1)	1.373(4)	C(16)-H(16)	0.9500
C(1)-C(2)	1.521(4)	C(10)-O(1)	1.409(4)	C(17)-C(18)	1.405(6)
C(1)-H(1A)	0.9900	C(10)-H(10A)	0.9800	C(17)-H(17)	0.9500
C(1)-H(1B)	0.9900	C(10)-H(10B)	0.9800	C(18)-C(19)	1.386(5)
C(2)-N(1)	1.463(4)	C(10)-H(10C)	0.9800	C(18)-H(18)	0.9500
C(2)-H(2A)	0.9900	C(11)-N(4)	1.460(3)	C(19)-O(2)	1.375(4)
C(2)-H(2B)	0.9900	C(11)-C(12)	1.521(5)	C(20)-O(2)	1.427(5)
C(3)-N(1)	1.455(3)	C(11)-H(11A)	0.9900	C(20)-H(20A)	0.9800
C(3)-C(4)	1.529(4)	C(11)-H(11B)	0.9900	C(20)-H(20B)	0.9800
C(3)-H(3A)	0.9900	C(12)-N(3)	1.456(4)	C(20)-H(20C)	0.9800
C(3)-H(3B)	0.9900	C(12)-H(12A)	0.9900	N(2)-C(1)#1	1.464(3)
C(4)-C(5)	1.380(4)	C(12)-H(12B)	0.9900	N(2)-C(1)#2	1.464(3)
C(4)-C(9)	1.407(4)	C(13)-N(3)	1.455(4)	N(4)-C(11)#3	1.460(3)
C(5)-C(6)	1.386(5)	C(13)-C(14)	1.522(4)	N(4)-C(11)#4	1.460(3)
C(5)-H(5)	0.9500	C(13)-H(13A)	0.9900		

N(1)-P(1)-N(1)#1	102.06(11)	C(1)-C(2)-H(2B)	108.2	C(4)-C(5)-C(6)	122.0(3)
N(3)-P(2)-N(3)#3	102.07(11)	H(2A)-C(2)-H(2B)	107.3	C(4)-C(5)-H(5)	119.0
N(3)-P(2)-N(3)#4	102.07(11)	N(1)-C(3)-C(4)	113.8(2)	C(6)-C(5)-H(5)	119.0
N(2)-C(1)-C(2)	116.0(3)	N(1)-C(3)-H(3A)	108.8	C(7)-C(6)-C(5)	118.8(3)
N(2)-C(1)-H(1A)	108.3	C(4)-C(3)-H(3A)	108.8	C(7)-C(6)-H(6)	120.6
C(2)-C(1)-H(1B)	108.3	N(1)-C(3)-H(3B)	108.8	C(5)-C(6)-H(6)	120.6
H(1A)-C(1)-H(1B)	107.4	C(4)-C(3)-H(3B)	108.8	C(6)-C(7)-C(8)	120.6(3)
N(1)-C(2)-C(1)	116.5(2)	H(3A)-C(3)-H(3B)	107.7	C(6)-C(7)-H(7)	119.7
N(1)-C(2)-H(2A)	108.2	C(5)-C(4)-C(9)	117.9(3)	C(8)-C(7)-H(7)	119.7
C(1)-C(2)-H(2A)	108.2	C(5)-C(4)-C(3)	122.0(3)	C(9)-C(8)-C(7)	120.6(3)
N(1)-C(2)-H(2B)	108.2	C(9)-C(4)-C(3)	120.1(3)	C(9)-C(8)-H(8)	119.7

C(7)-C(8)-H(8)	119.7
O(1)-C(9)-C(8)	124.7(3)
O(1)-C(9)-C(4)	115.2(3)
C(8)-C(9)-C(4)	120.0(3)
O(1)-C(10)-H(10A)	109.5
O(1)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
O(1)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
N(4)-C(11)-C(12)	116.8(3)
N(4)-C(11)-H(11A)	108.1
C(12)-C(11)-H(11A)	108.1
N(4)-C(11)-H(11B)	108.1
C(12)-C(11)-H(11B)	108.1
H(11A)-C(11)-H(11B)	107.3
N(3)-C(12)-C(11)	116.7(3)
N(3)-C(12)-H(12A)	108.1
C(11)-C(12)-H(12A)	108.1
N(3)-C(12)-H(12B)	108.1
C(11)-C(12)-H(12B)	108.1
H(12A)-C(12)-H(12B)	107.3
N(3)-C(13)-C(14)	114.2(2)
N(3)-C(13)-H(13A)	108.7
C(14)-C(13)-H(13A)	108.7
N(3)-C(13)-H(13B)	108.7
C(14)-C(13)-H(13B)	108.7
H(13A)-C(13)-H(13B)	107.6
C(15)-C(14)-C(19)	118.6(3)
C(15)-C(14)-C(13)	121.3(3)
C(19)-C(14)-C(13)	120.1(3)
C(14)-C(15)-C(16)	121.3(3)
C(14)-C(15)-H(15)	119.4
C(16)-C(15)-H(15)	119.4
C(17)-C(16)-C(15)	119.8(3)
C(17)-C(16)-H(16)	120.1
C(15)-C(16)-H(16)	120.1
C(16)-C(17)-C(18)	119.8(3)
C(16)-C(17)-H(17)	120.1
C(18)-C(17)-H(17)	120.1
C(19)-C(18)-C(17)	119.6(3)
C(19)-C(18)-H(18)	120.2
C(17)-C(18)-H(18)	120.2
O(2)-C(19)-C(18)	123.5(3)
O(2)-C(19)-C(14)	115.7(3)
C(18)-C(19)-C(14)	120.8(3)
O(2)-C(20)-H(20A)	109.5
O(2)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
O(2)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(3)-N(1)-C(2)	116.9(2)
C(3)-N(1)-P(1)	118.41(19)
C(2)-N(1)-P(1)	124.68(18)
C(1)-N(2)-C(1)#1	117.95(10)
C(1)-N(2)-C(1)#2	117.96(10)
C(1)#1-N(2)-C(1)#2	117.96(10)
C(13)-N(3)-C(12)	117.3(2)
C(13)-N(3)-P(2)	118.1(2)
C(12)-N(3)-P(2)	124.52(18)
C(11)#3-N(4)-C(11)	117.75(11)
C(11)#3-N(4)-C(11)#4	117.75(11)
C(11)-N(4)-C(11)#4	117.74(11)
C(9)-O(1)-C(10)	117.3(3)
C(19)-O(2)-C(20)	119.0(3)

Symmetry transformations used to generate equivalent atoms:

#1 y+1,z,x-1 #2 z+1,x-1,y #3 z+1/2,-x+3/2,-y+1

#4 -y+3/2,-z+1,x-1/2

Table 4. Anisotropic displacement parameters (Å^{2}x 10^3)for Proazaphosphatrane **6**. The anisotropic displacement factor exponent takes the form: -2p^2[h^{2}a*^{2}U^{11} + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	31(1)	31(1)	31(1)	2(1)	2(1)	2(1)
P(2)	34(1)	34(1)	34(1)	-5(1)	5(1)	-5(1)
C(1)	31(1)	36(2)	40(2)	5(1)	4(1)	0(1)
C(2)	29(1)	32(1)	40(2)	3(1)	11(1)	3(1)
C(3)	42(2)	26(1)	34(1)	3(1)	9(1)	7(1)
C(4)	33(1)	28(1)	37(1)	-2(1)	5(1)	1(1)
C(5)	48(2)	36(2)	42(2)	-2(1)	4(1)	3(1)
C(6)	53(2)	42(2)	40(2)	-5(1)	5(1)	-5(1)
C(7)	48(2)	51(2)	44(2)	-21(2)	5(1)	-5(2)
C(8)	46(2)	52(2)	55(2)	-18(2)	4(2)	15(2)
C(9)	36(2)	38(2)	48(2)	-8(1)	-2(1)	8(1)
C(10)	164(7)	112(5)	75(3)	-11(3)	-17(4)	105(5)
C(11)	37(2)	30(1)	48(2)	-5(1)	4(1)	-4(1)
C(12)	34(1)	33(1)	43(2)	-14(1)	4(1)	-6(1)
C(13)	30(1)	44(2)	40(2)	-10(1)	6(1)	-10(1)
C(14)	32(1)	36(2)	42(2)	-1(1)	-1(1)	1(1)
C(15)	38(2)	50(2)	41(2)	-1(1)	-3(1)	-1(1)
C(16)	51(2)	67(2)	36(2)	-4(2)	-8(1)	6(2)
C(17)	58(2)	63(2)	48(2)	-8(2)	-20(2)	-2(2)
C(18)	52(2)	68(2)	57(2)	2(2)	-16(2)	-20(2)
C(19)	42(2)	46(2)	44(2)	-2(1)	-4(1)	-9(1)
C(20)	78(3)	135(5)	119(5)	-55(4)	45(3)	-66(4)
N(1)	37(1)	26(1)	38(1)	3(1)	5(1)	6(1)
N(2)	34(1)	34(1)	34(1)	4(1)	4(1)	4(1)
N(3)	30(1)	35(1)	42(1)	-10(1)	4(1)	-5(1)
N(4)	36(1)	36(1)	36(1)	-8(1)	8(1)	-8(1)
O(1)	61(2)	53(1)	51(1)	-2(1)	-6(1)	27(1)
O(2)	50(1)	72(2)	58(2)	-9(1)	9(1)	-30(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Proazaphosphatrane **6**.

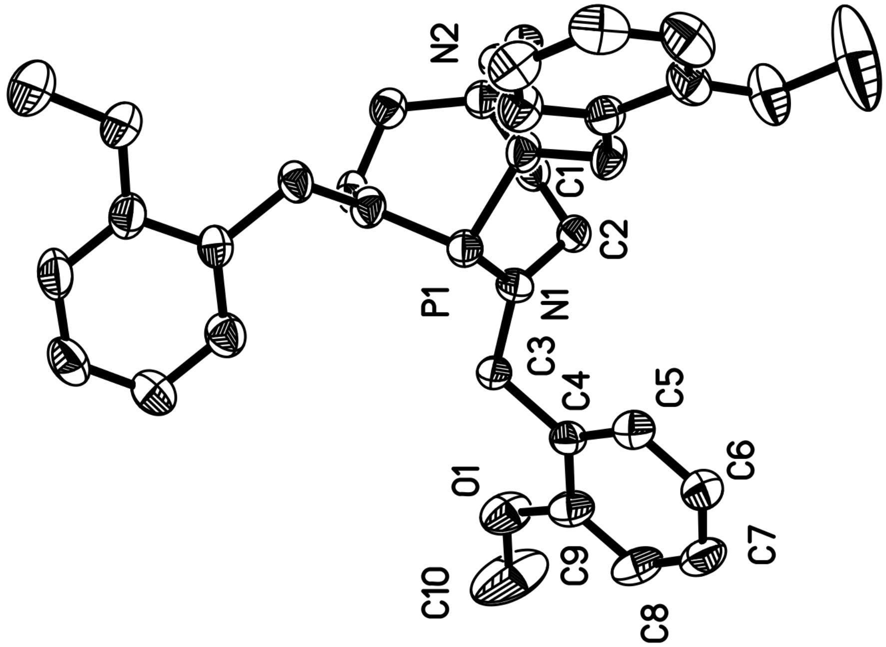
	x	y	z	U(eq)
H(1A)	7646	-1275	-894	59(11)
H(1B)	7908	-528	-1281	41(9)
H(2A)	7823	-406	12	30(8)
H(2B)	8435	-1032	112	54(10)
H(3A)	8229	778	-585	56(11)
H(3B)	9033	1031	-327	50(10)
H(5)	8822	229	1191	67(12)
H(6)	8338	622	2316	58(11)
H(7)	7470	1571	2330	63(11)
H(8)	7169	2187	1250	62(11)
H(10A)	6682	2313	179	260(60)
H(10B)	6974	2569	-615	150(30)
H(10C)	7336	2904	117	66(13)
H(11A)	6389	9766	1658	46
H(11B)	7103	9455	1247	46
H(12A)	7296	9594	2525	44
H(12B)	6651	9016	2687	44
H(13A)	8446	9067	1879	46
H(13B)	8663	8293	2242	46
H(15)	7847	8814	3694	52
H(16)	8237	9500	4720	62
H(17)	9268	10252	4629	68
H(18)	9976	10247	3535	71
H(20A)	10321	10413	2344	166
H(20B)	10561	9816	1739	166
H(20C)	10706	9660	2597	166

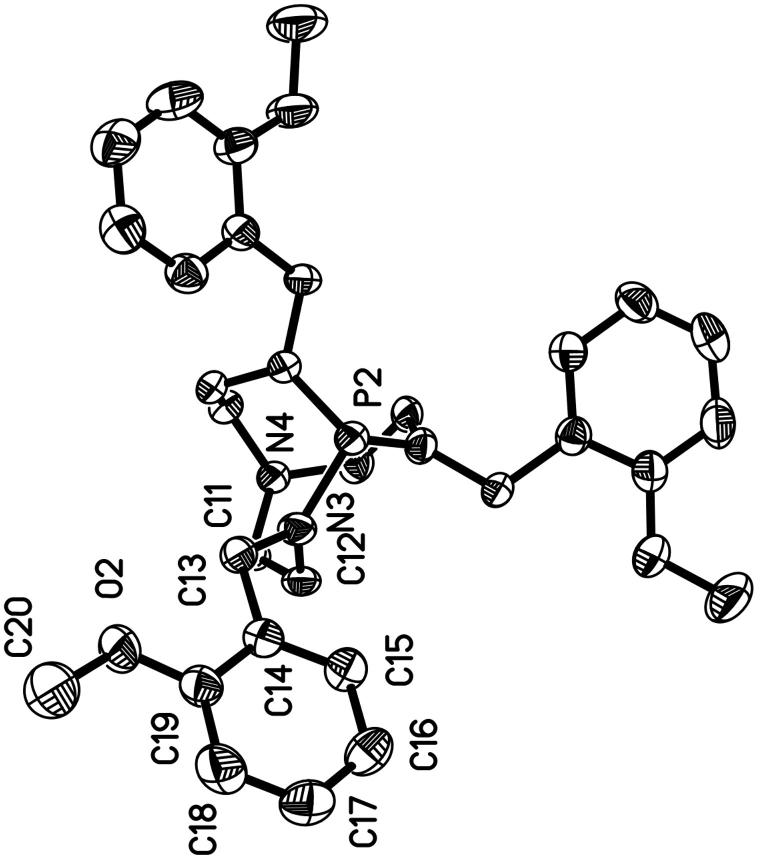
Table 4. Anisotropic displacement parameters (Å^{2}x 10^3)for Proazaphosphatrane 6. The anisotropic displacement factor exponent takes the form: -2p^2[h^{2}a*^{2}U^{11} + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
P(1)	31(1)	31(1)	31(1)	2(1)	2(1)	2(1)
P(2)	34(1)	34(1)	34(1)	-5(1)	5(1)	-5(1)
C(1)	31(1)	36(2)	40(2)	5(1)	4(1)	0(1)
C(2)	29(1)	32(1)	40(2)	3(1)	11(1)	3(1)
C(3)	42(2)	26(1)	34(1)	3(1)	9(1)	7(1)
C(4)	33(1)	28(1)	37(1)	-2(1)	5(1)	1(1)
C(5)	48(2)	36(2)	42(2)	-2(1)	4(1)	3(1)
C(6)	53(2)	42(2)	40(2)	-5(1)	5(1)	-5(1)
C(7)	48(2)	51(2)	44(2)	-21(2)	5(1)	-5(2)
C(8)	46(2)	52(2)	55(2)	-18(2)	4(2)	15(2)
C(9)	36(2)	38(2)	48(2)	-8(1)	-2(1)	8(1)
C(10)	164(7)	112(5)	75(3)	-11(3)	-17(4)	105(5)
C(11)	37(2)	30(1)	48(2)	-5(1)	4(1)	-4(1)
C(12)	34(1)	33(1)	43(2)	-14(1)	4(1)	-6(1)
C(13)	30(1)	44(2)	40(2)	-10(1)	6(1)	-10(1)
C(14)	32(1)	36(2)	42(2)	-1(1)	-1(1)	1(1)
C(15)	38(2)	50(2)	41(2)	-1(1)	-3(1)	-1(1)
C(16)	51(2)	67(2)	36(2)	-4(2)	-8(1)	6(2)
C(17)	58(2)	63(2)	48(2)	-8(2)	-20(2)	-2(2)
C(18)	52(2)	68(2)	57(2)	2(2)	-16(2)	-20(2)
C(19)	42(2)	46(2)	44(2)	-2(1)	-4(1)	-9(1)
C(20)	78(3)	135(5)	119(5)	-55(4)	45(3)	-66(4)
N(1)	37(1)	26(1)	38(1)	3(1)	5(1)	6(1)
N(2)	34(1)	34(1)	34(1)	4(1)	4(1)	4(1)
N(3)	30(1)	35(1)	42(1)	-10(1)	4(1)	-5(1)
N(4)	36(1)	36(1)	36(1)	-8(1)	8(1)	-8(1)
O(1)	61(2)	53(1)	51(1)	-2(1)	-6(1)	27(1)
O(2)	50(1)	72(2)	58(2)	-9(1)	9(1)	-30(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for Proazaphosphatrane **6**.

	x	y	z	U(eq)
H(1A)	7646	-1275	-894	59(11)
H(1B)	7908	-528	-1281	41(9)
H(2A)	7823	-406	12	30(8)
H(2B)	8435	-1032	112	54(10)
H(3A)	8229	778	-585	56(11)
H(3B)	9033	1031	-327	50(10)
H(5)	8822	229	1191	67(12)
H(6)	8338	622	2316	58(11)
H(7)	7470	1571	2330	63(11)
H(8)	7169	2187	1250	62(11)
H(10A)	6682	2313	179	260(60)
H(10B)	6974	2569	-615	150(30)
H(10C)	7336	2904	117	66(13)
H(11A)	6389	9766	1658	46
H(11B)	7103	9455	1247	46
H(12A)	7296	9594	2525	44
H(12B)	6651	9016	2687	44
H(13A)	8446	9067	1879	46
H(13B)	8663	8293	2242	46
H(15)	7847	8814	3694	52
H(16)	8237	9500	4720	62
H(17)	9268	10252	4629	68
H(18)	9976	10247	3535	71
H(20A)	10321	10413	2344	166
H(20B)	10561	9816	1739	166
H(20C)	10706	9660	2597	166


N2
C1
C2
P1
N1
C3
C4
C5
O1
C6
C7
C9
C10
C8


P2
N4
C11
N3
C12
C13
O2
C20
C15
C14
C19
C16
C18
C17

APPENDIX C

CHAPTER 4. Supplementary Information

Experimental Procedures

References for known compounds

Data for unknown compounds

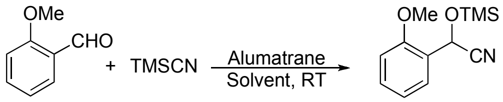
^{1}H and ^{13}C NMR spectra for reaction products

General Considerations: All reactions were carried out under dry argon using standard Schlenk procedures. Acetonitrile was dried with calcium hydride and distilled prior to use. Aldehydes were purchased from Aldrich. Trimethylsilylcyanide was purchased from Aldrich and distilled at 110 °C under atmospheric pressure to afford a clear, colorless liquid which was stored in a refrigerator under argon. Dimeric **1** was synthesized according to a literature procedure[1] and stored in a glove box. ^{1}H and ^{13}C NMR spectra were recorded using a VXR-400 Varian spectrometer. All NMR spectra were recorded in dry $CDCl_3$.

General procedure for the synthesis of cyanohydrin trialkylsilylethers: In a glove box, a 10 mL vial was charged with 1 mole % (8.87 mg) of **1** and then 5 mL of freshly distilled acetonitrile was added via syringe outside the glove box, resulting in a white suspension of **1**. Aldehyde (2 mmol) was added under argon and the resulting mixture was stirred for 20 - 30 minutes. During this time, the white suspension of **1** disappeared into the solution. Trimethylsilylcyanide (3 mmol) was added and the reaction mixture was stirred for 12 hours. During this time, the catalyst precipitated. The solvent and excess TMSCN were evaporated at reduced pressure on a Schlenk line at 70 ºC and then 10 mL of hexanes was added. The precipitated catalyst was filtered and the crude product was purified by column chromatography (5% EtOAc).

Procedure for recycling: The above procedure was carried out with *o*-anisaldehyde (2 mmol) through the step in which the solvent and excess TMSCN were evaporated at reduced pressure at 70 ºC. Then 10 mL of dry pentane was added to extract the product. After the solid settled to the bottom of the flask, the solvent was withdrawn with a syringe under a flow of argon. Dry acetonitrile (5 mL) and *o*-anisaldehyde (2 mmol) was added as in the preceding procedure, the reaction mixture was stirred for 30 minutes, and then trimethylsilylcyanide (3 mmol) was added. The reaction mixture was stirred for 12 hours after the solvent and excess TMSCN were evaporated. 10 mL of pentane was added to extract the product. Then the reaction was carried out two more times. Purification of the crude product was carried out as before by column chromatography (5% EtOAc).

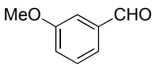
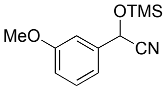
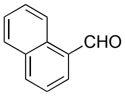
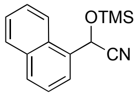
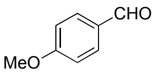
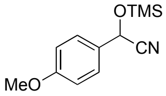
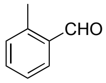
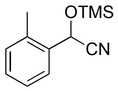
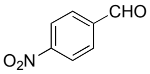
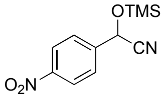
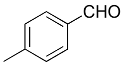
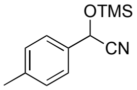
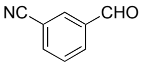
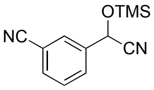
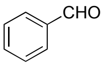
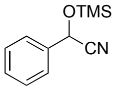
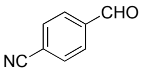
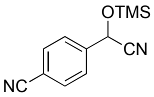
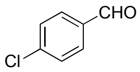
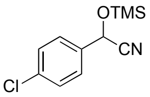
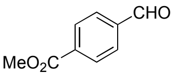
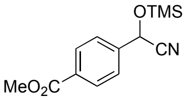
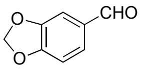
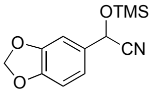
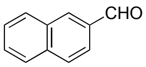
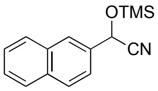
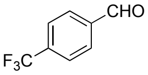
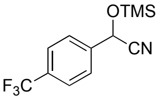
Table 1. Optimization Study



Entry	Alumatrane[a] (mole %)	Solvent	Yield (%)[b,c,d]
1	10	toluene	72
2	5	toluene	49
3	10	CH_3CN	98
4	5	CH_3CN	96
5	1	CH_3CN	94
6	1	CH_3CN	67[e]
7	none	CH_3CN	24

[a] Alumatrane **1** was present in all cases except where noted otherwise. [b] Reaction conditions: 2 mmol *o*-anisaldehyde, 3.5 mmol TMSCN, 5 mL solvent, 12 h, RT. [c] Average of two runs. [d] Literature Yields (91-99%) Refs 2a-2c, 3c, 3p, 3s, 3u. [e] Alumatrane **2** was used at 70 C.

Table 2. Trimethylsilylcyanation of Aryl Aldehdyes

Entry	Aldehyde	Product	Yield (%)[a,b]	Entry	Aldehyde	Product	Yield (%)[a,b]
1			98 (Lit: 78-100)[d]	8			81 (Lit: 76-98)[j]
2			94 (Lit 33-100)[e]	9			89 (Lit: 80-100)[k]
3			94 (Lit: 22-98)[f]	10			85 (Lit: 62-100)[l]
4			89	11			92 (Lit: 16-100)[m]
5			93 (Lit: 70-72)[g]	12			45 82[c] (Lit: 63-100)[n]
6			92 (Lit: 90)[h]	13			30 83[c] (Lit: 55-99)[o]
7			91 (Lit: 78-100)[i]	14			52 96[c] (Lit: 95-100)[p]

[a] Reaction conditions: 2 mmol aldehyde, 3.5 mmol TMSCN, 1 mole % **1**, 5 mL CH_3CN, time: 9 h, RT. [b] Average of two runs. [c] 2.5 mole % of **1** used. [d] Ref 3a-3e. [e] Refs 3a-3c, 3f-3n. [f] Refs 3a, 3f, 3m, 3o-3s. [g] Refs 3e-3f, 3q. [h] Refs 3e, 3s. [i] Refs 3g, 3q, 3t-3v. [j] Refs 3m, 3p-3q, 3s-3u, 3w-3x. [k] Refs 3s, 3u-3v, 3y-3aa. [l] Refs 3e-

3g, 3k, 3o, 3q, 3t-3u, 3ab-3ag. [m]Refs 3a-3ah. [n]Refs 3e, 3g-3h, 3k, 3o-3p, 3s-3t, 3v, 3x-3y, 3ab-3ag, 3ai. [o]Refs 3y, 3ak. [p]Refs 3g, 3al.

Table 3. Trimethylsilylcyanation of Hetero and Alkyl Aldehydes

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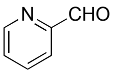
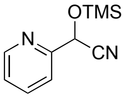
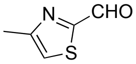
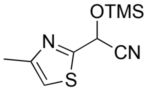
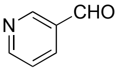
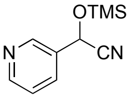
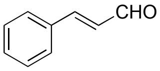
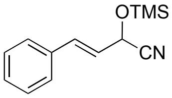
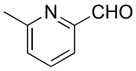
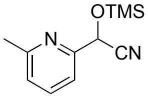
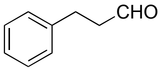
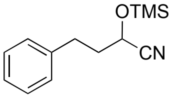
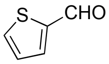
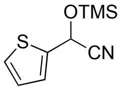
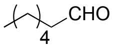
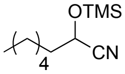
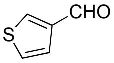
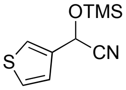
1			91 (Lit: 88-92)[c]	6			91
2			86 (Lit: 90-99)[d]	7			80 (Lit: 81-100)[g]
3			94	8			85 (Lit: 81-100)[h]
4			90 (Lit: 90-99)[e]	9			81 (Lit: 89-99)[i]
5			77 (Lit: 82)[f]				

[a]Reaction conditions: 2 mmol aldehyde, 3.5 mmol TMSCN, 1 mole % **1**, 5 mL CH_3CN, time: 9h, RT. [b]Average of two runs. [c]Refs 3m, 4a-4b. [d]Refs 3h, 3m, 3o, 3v, 3y, 4b. [e]Refs 3o, 3e, 3v. [f]Refs 4a. [g]Refs 3h, 3m-3o, 3q, 3v, 3ai, 3ak, 4c, 4d. [h]Refs 3f, 3o, 3v, 3y, 3ai, 4d-4g. [i]Refs 3e, 3h, 3n, 3q, 3y, 3ab.

References:

1. Su, W.; Kim, Y.; Ellern, A.; Guzei, I. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2006**, *128*, 13727.

2. (a) Dekamin, M. G.; Farahmand, M.; Reza, N. M.; Javanshir, S. *Catalysis Comm.* **2008**, *9*, 1352. (b) Khan, N. H.; Agrawal, S.; Kureshy, R. I.; Abdi, S. H. R.; Singh, S.; Jasra, R. V. *J. Organomet. Chem.* **2007**, *692*, 4361. (c) Yamaguchi, K.; Imago, T.; Ogasawara, Y.; Kasai, J.; Kotani, M.; Mizuno, N. *Adv. Synth. Catal.* **2006**, *348*, 1516.

3. For reports on synthesis of cyanohydrin trialkylsilylethers, see: (a) Cho, W. K.; Lee, J. K.; Kang, S. M.; Chi, Y. S.; Lee, H.; Choi, I. S. *Chemistry-A European Journal* **2007**, *13*, 6351. (b) Wen, Y.; Huang, X.; Huang, J.; Xiong, Y.; Qin, B.; Feng, X. *Synlett* **2005**, *16*, 2445. (c) Jiang, W.; Yao, X.; Song, Y.; Hu, X.; Chen, H.; Bai, C.; Zheng, Z. *Cuihua Xuebao* **2003**, *24*, 57. (d) Dunnwald, T.; Demir, A. S.; Seigert, P.; Pohl, M.; Muller, M. *European Journal of Organic Chemistry* **2000**, *11*, 2161. (e) Mai, K.; Patil, G. *Tetrahedron Letters* **1984**, *25*, 4583. (f) Raj, V. P.; Suryavanshi, G.; Sudalai, A. *Tetrahedron Letters* **2007**, *48*, 7211. (g) Kurono, N.; Yamaguchi, M.; Suzuki, K.; Ohkuma, T. *J. Org. Chem.* **2005**, *70*, 6530. (h) Karimi, B.; Ma'Mani, L. *Org. Lett.* **2004**, *6*, 4813. (i) Baleizao, C.; Gigante, B.; Garcia, H.; Corma, A. *Tetrahedron* **2004**, *60*, 10461. (j) He, K.; Zhou, Z.; Wang, L.; Li, K.; Zhao, G.; Zhou, Q.; Tang, C. *Tetrahedron* **2004**, *60*, 10505. (k) Kim, S. S.; Song, D. H. *Letters in Organic Chemistry* **2004**, *1*, 264. (l) Baleizao, C.; Gigante, B.; Garcia, H.; Corma, A. *Tetrahedron Letters* **2003**, *44*, 6813. (m) Cordoba, R.; Plumet, J. *Tetrahedron Letters* **2003**, *44*, 6157. (n) Manja, K.; Trehan, S. *Journal of Chemical Society, Perkin Transaction 1: Organic and Bio-Organic*

Chemistry **1995**, 2383. (o) Choudary, B. M.; Roy, M.; Roy, S.; Kantam, M. L.; Sreedhar, B; Kumar, K. V. *Advanced Synthesis & Catalysis* **2006**, *348*, 1734. (p) Mei, L.; Ping, K. Y.; Xuan, L. X.; Hao, Y.; Liang, H. K.; Ying, J. *Synthetic Communications* **2006**, *36*, 2483. (q) Rafiee, E.; Tangestaninejad, S.; Habibi, M. H.; Mirkhani, V. *Bulletin of the Korean Chemical Society* **2005**, *26*, 1585. (r) Huh, S.; Chen, H. T.; Wiench, J. W.; Pruski, M.; Lin, V. S. *Angew. Chem. Int. Ed.* **2005**, *44*, 1826. (s) Azizi, N.; Saidi, M. R. *Phosphorus, Sulfur, and Silicon and the Related Elements* **2003**, *178*, 2111. (t) Wen, Y.; Huang, X; Huang, J.; Xiong, Y.; Qin, B.; Feng, X. *Synlett* **2005**, *16*, 2445. (u) Blanrue, A.; Wilhelm, R. *Synlett* **2004**, *14*, 2621. (v) Azizi, N.; Saidi, M. R. *Journal of Organometallic Chemistry* **2003**, *688*, 283. (w) Kim, S. R.; Rajagopal, G. *Synthesis* **2007**, 215. (x) Mei, L. *Journal of Molecular Catalysis A: Chemical* **2005**, *227*, 183. (y) Braeza, A.; Najera, C.; de Garcia Retamosa, M.; Sansano, J. M. *Synthesis* **2005**, 2787. (z) Wessig, P.; Glomblitza, C.; Mueller, G.; Teubner, J. *J. Org. Chem.* **2004**, *69*, 7582. (aa) Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O.; Rossi, M. *Synlett* **1999**, *3*, 315. (ab) Yamaguchi, K.; Imago, T.; Ogasawara, Y.; Kasai, J.; Kotani, M.; Mizuno, N. *Advanced Synthesis & Catalysis* **2006**, *348*, 1516. (ac) Kim, S. S.; Lee, J. T.; Song, D. H.; Lee, I.; Park, S. Y. *Bulletin of the Korean Chemical Society* **2005**, *26*, 265. (ad) Kim, S. S.; Lee, J. T.; Lee, S. H. *Bulletin of the Korean Chemical Society* **2005**, *26*, 993. (ae) He, B.; Li, Y.; Feng, X.; Zhang, G. *Synlett* **2004**, *10*, 1776. (af) Kim, S. S.; Rajagopal, G.; Kim, D. W.; Song, D. H. *Synthetic Comm.* **2004**, *34*, 2973. (ag) Jiang, W.; Yao, X.; Song, Y.; Hu, X,.; Chen, H.; Bai, C.; Zheng, Z. *Cuihua Xuebao* **2003**, *24*, 57. (ah) Kumamoto, K.; Iida, H.; Hamana, H.; Kotsuki, H.; Matsumoto, K. *Heterocycles* **2005**, *66*, 675. (ai) Wang, X.; Tian, S. *Synlett* **2007**, *9*, 1416. (aj) Bantu, B.; Wang, D.; Wurst, K.; Buchmeiser, M. R.

Tetrahedron Letters **2005**, *61*, 12145. (ak) Yang, Y.; Wang D. *Synlett* **1997**, *12*, 1379. (al) Belda, O.; Duquesne, S.; Fischer, A.; Moberg, C. *Journal of Organometallic Chemistry* **2004**, *689*, 3750.

4. (a) Haerle, H.; Jochims, J. C. *Chemische Berichte* **1986**, *119*, 1400. (b) Deuchert, K.; Hertenstein, U.; Huenig, S.; Wehner, G. *Chemische Berichte* **1979**, *112*, 2045. (c) Firouzabadi, H.; Iranpoor, N.; Jafari, A. A. *Journal of Organometallic Chemistry* **2005**, *690*, 1556. (d) Kano, T.; Sasaki, K.; Kouji, T.; Mii, H.; Maruoka, K. *Tetrahedron Letters* **2006**, *47*, 4615. (e) Denmark, S. E.; Chung, W. *J. Org. Chem.* **2006**, *71*, 4002. (f) Sasai, H.; Suzuki, T.; Arai, S.; Takayoshi, S. M. *J. Am. Chem. Soc* **1992**, *114*, 4418. (g) Ichikawa, E.; Suzuki, M.; Yabu, K.; Albert, M.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 11808.

References for known compounds:

2-(o-Methoxyphenyl)-2-trimethylsiloxyacetonitrile (Table 1) Yang, W.; Fang, J. *J. Org. Chem.* **1998**, *63*, 1356.

2-(m-Methoxyphenyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 1) Yang, W.; Fang, J. *J. Org. Chem.* **1998**, *63*, 1356.

2-(p-Methoxyphenyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 2) Yang, W.; Fang, J. *J. Org. Chem.* **1998**, *63*, 1356.

2-(p-Nitrophenyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 3) Yang, W.; Fang, J. *J. Org. Chem.* **1998**, *63*, 1356.

2-(p-Cyanophenyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 5) Yang, W.; Fang, J. *J. Org. Chem.* **1998**, *63*, 1356.

2-(Methyl p-benzoate)-2-trimethylsiloxyacetonitrile (Table 2, Entry 6) Mai, K.; Patil, G. *Tetrahedron Letters* **1984**, *25*, 4583.

2-(2-Naphthyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 7) Kurono, N.; Yamaguchi, M.; Suzuki, K.; Ohkuma, T. *J. Org. Chem.* **2005**, *70*, 6530.

2-(1-Naphthyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 8) Mei, L. *Journal of Molecular Catalysis A: Chemical* **2005**, *227*, 183.

2-(o-Methylphenyl)-2-trimethylsiloxyacetonitirle (Table 2, Entry 9) Wessig, P.; Glomblitza, C.; Mueller, G.; Teubner, J. *J. Org. Chem.* **2004**, *69*, 7582.

2-(p-Methylphenyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 10) Yang, W.; Fang, J. *J. Org. Chem.* **1998**, *63*, 1356.

2-(Phenyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 11) Yang, W.; Fang, J. *J. Org. Chem.* **1998**, *63*, 1356.

2(p-Chlorophenyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 12) Kurono, N.; Yamaguchi, M.; Suzuki, K.; Ohkuma, T. *J. Org. Chem.* **2005**, *70*, 6530.

2-(3,4-Methylenedioxyphenyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 13) Braeza, A.; Najera, C.; de Garcia Retamosa, M.; Sansano, J. M. *Synthesis* **2005**, 2787.

2(p-α,α,α-Trifluorophenyl)-2-trimethylsiloxyacetonitrile (Table 2, Entry 14) Kurono, N.; Yamaguchi, M.; Suzuki, K.; Ohkuma, T. *J. Org. Chem.* **2005**, *70*, 6530.

2-(2-Pyridyl)-2-trimethylsiloxyacetonitrile (Table 3, Entry 1) Cordoba, R.; Plumet, J. *Tetrahedron Letters* **2003**, *44*, 6157.

2-(3-Pyridyl)-2-trimethylsiloxyacetonitrile (Table 3, Entry 2) Cordoba, R.; Plumet, J. *Tetrahedron Letters* **2003**, *44*, 6157.

2-(2-Thiophene)-2-trimethylsiloxyacetonitrile (Table 3, Entry 4) Mai, K.; Patil, G. *Tetrahedron Letters* **1984**, *25*, 4583.

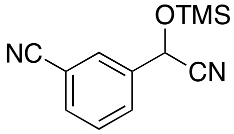
2-(3-Thiophene)-2-trimethylsiloxyacetonitrile (Table 3, Entry 5) Haerle, H.; Jochims, J. C. *Chemische Berichte* **1986**, *119*, 1400.

(E)-4-Phenyl-2-(trimethylsiloxy)-but-3-enenitrile (Table 3, Entry 6) Braeza, A.; Najera, C.; de Garcia Retamosa, M.; Sansano, J. M. *Synthesis* **2005**, 2787.

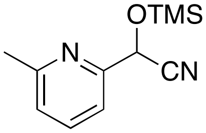
4-Phenyl-2-(trimethylsiloxy)-butanenitrile (Table 3, Entry 7) Braeza, A.; Najera, C.; de Garcia Retamosa, M.; Sansano, J. M. *Synthesis* **2005**, 2787.

2-(Trimethysiloxy)-octanenitrile (Table 3, Entry 8) Braeza, A.; Najera, C.; de Garcia Retamosa, M.; Sansano, J. M. *Synthesis* **2005**, 2787.

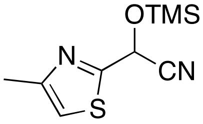
Data for unknown compounds:



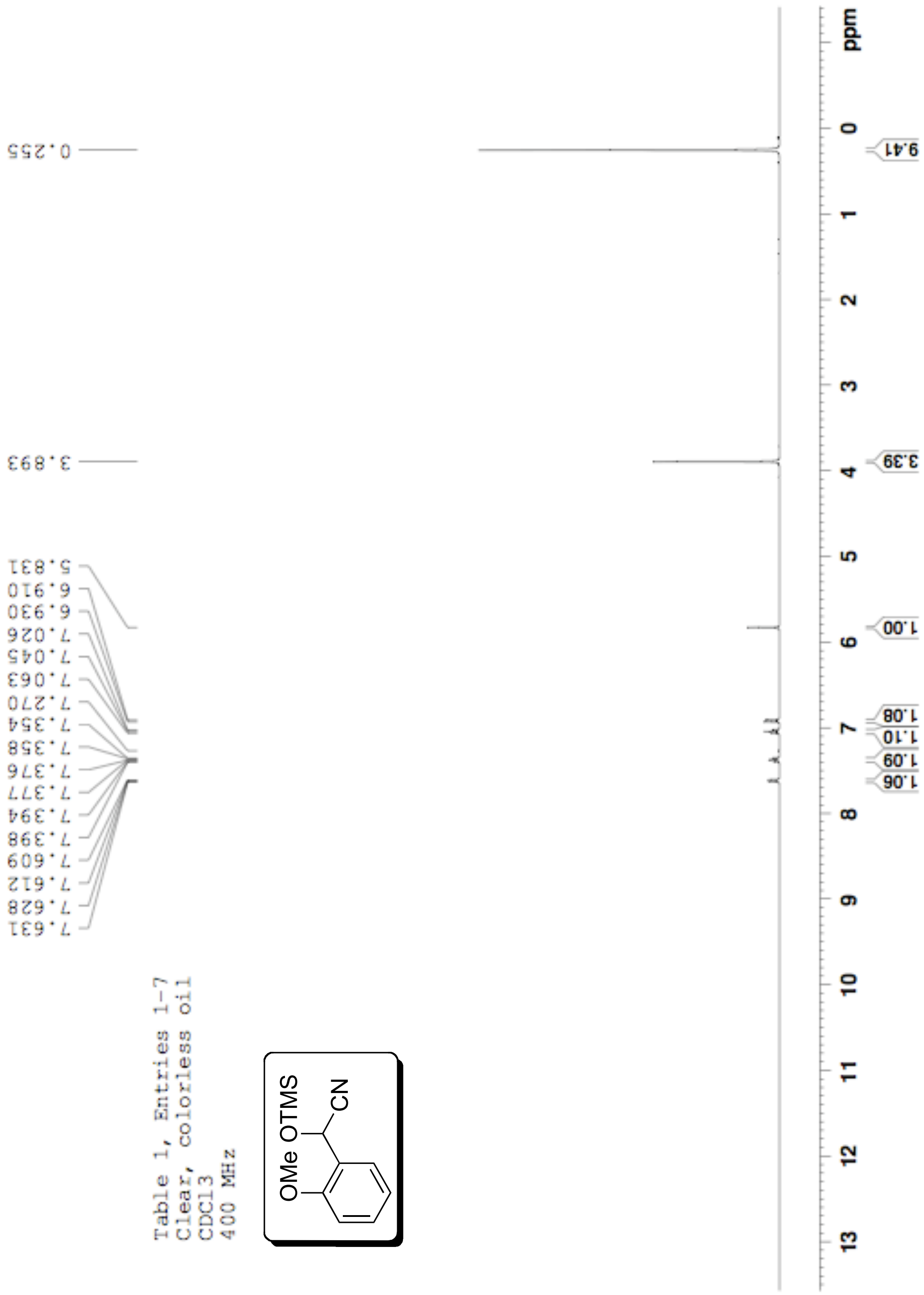
2-(3-Cyanophenyl)-2-trimethylsiloxyacetonitrile Clear, colorless oil (Table 2, entry 4): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (s, 1H), 7.33-7.68 (m, 2H), 7.58-7.54 (m, 1H), 5.55 (s, 1H), 0.27 (s, 9H). ^{13}C NMR (100MHz, $CDCl_3$): δ = 138.06, 133.04, 130.62, 130.04, 129.85, 118.52, 118.26, 113.34, 62.70, -0.15. HRMS m/z 230.08782 (calc for $C_{12}H_{14}N_2OSi$ 230.08754).

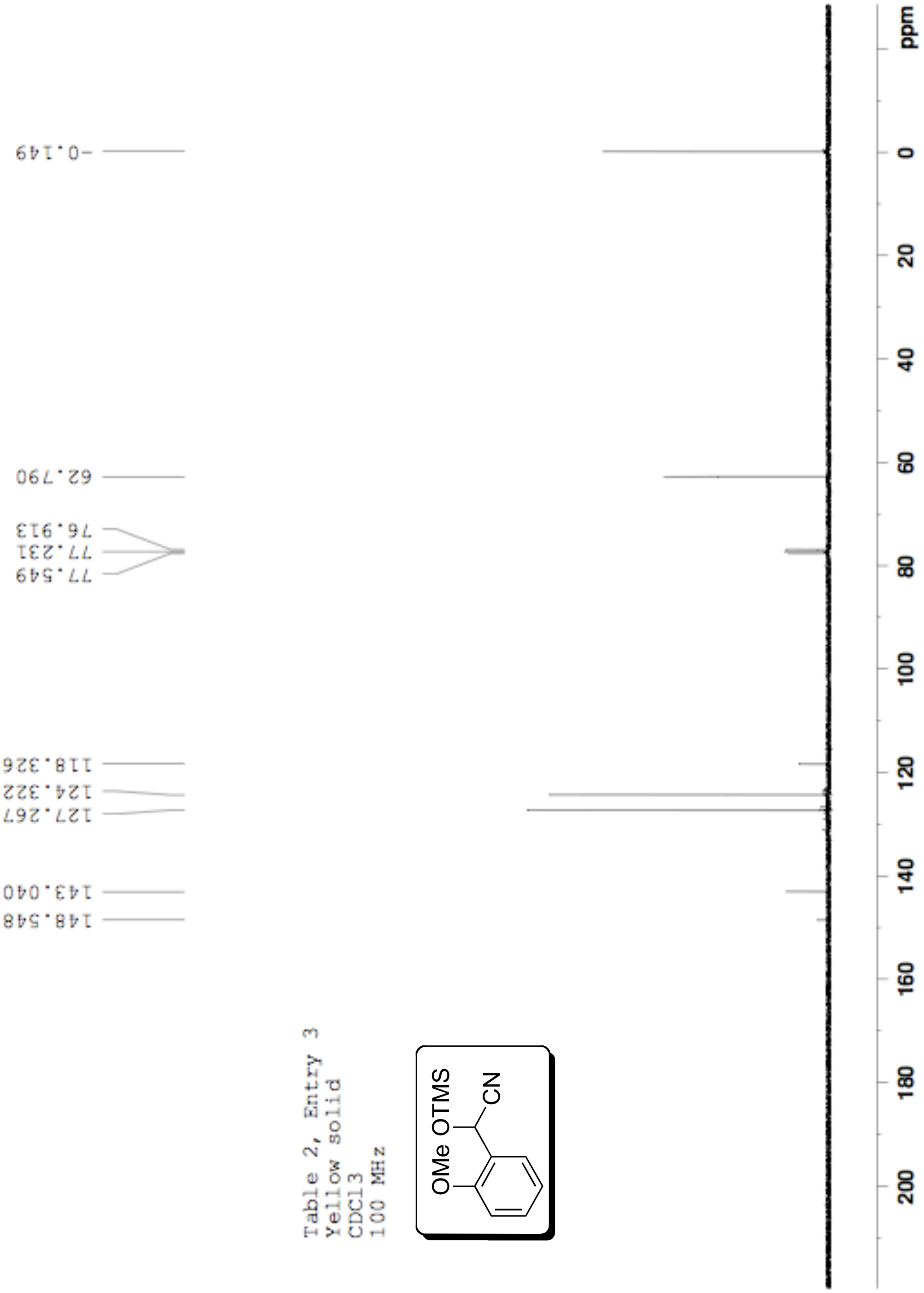


2-(3-Methyl-2-pyridyl)-2-trimethylsiloxyacetonitrile Light, yellow oil (Table 3, entry 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65-7.61 (t, 1H), 7.38-7.36 (d, 1H), 7.13-7.11 (d, 1H), 5.52 (s, 1H), 2.52 (s, 3H), 0.23 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.53, 154.85, 137.71, 123.73, 119.01, 117.43, 65.29, 24.35, -0.18. HRMS m/z 220.10352 (calc for $C_{11}H_{16}N_2OSi$ 220.10319).



2-(4-Methyl-2-thiazole)-2-trimethylsiloxyacetonitrile Orange liquid (Table 3, entry 6): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 (s, 1H), 5.73 (s, 1H), 2.43 (s, 3H), 0.25 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.97, 153.72, 117.29, 115.66, 61.76, 17.20, -0.23. HRMS m/z 226.05994 (calc for $C_9H_{14}N_2OSSi$ 226.05961).


0.255
3.893
5.831
6.910
6.930
7.026
7.045
7.063
7.270
7.354
7.358
7.376
7.377
7.394
7.398
7.609
7.612
7.628
7.631
Table 1, Entries 1-7
Clear, colorless oil
CDCl3
400 MHz
OMe OTMS
CN
9.41
3.39
1.00
1.08
1.10
1.09
1.06
0
1
2
3
4
5
6
7
8
9
10
11
12
13
ppm


-0.149
62.790
76.913
77.231
77.549
118.326
124.322
127.267
143.040
148.548
Table 2, Entry 3
Yellow solid
CDCl3
100 MHz
OMe
OTMS
CN
ppm
0
20
40
60
80
100
120
140
160
180
200

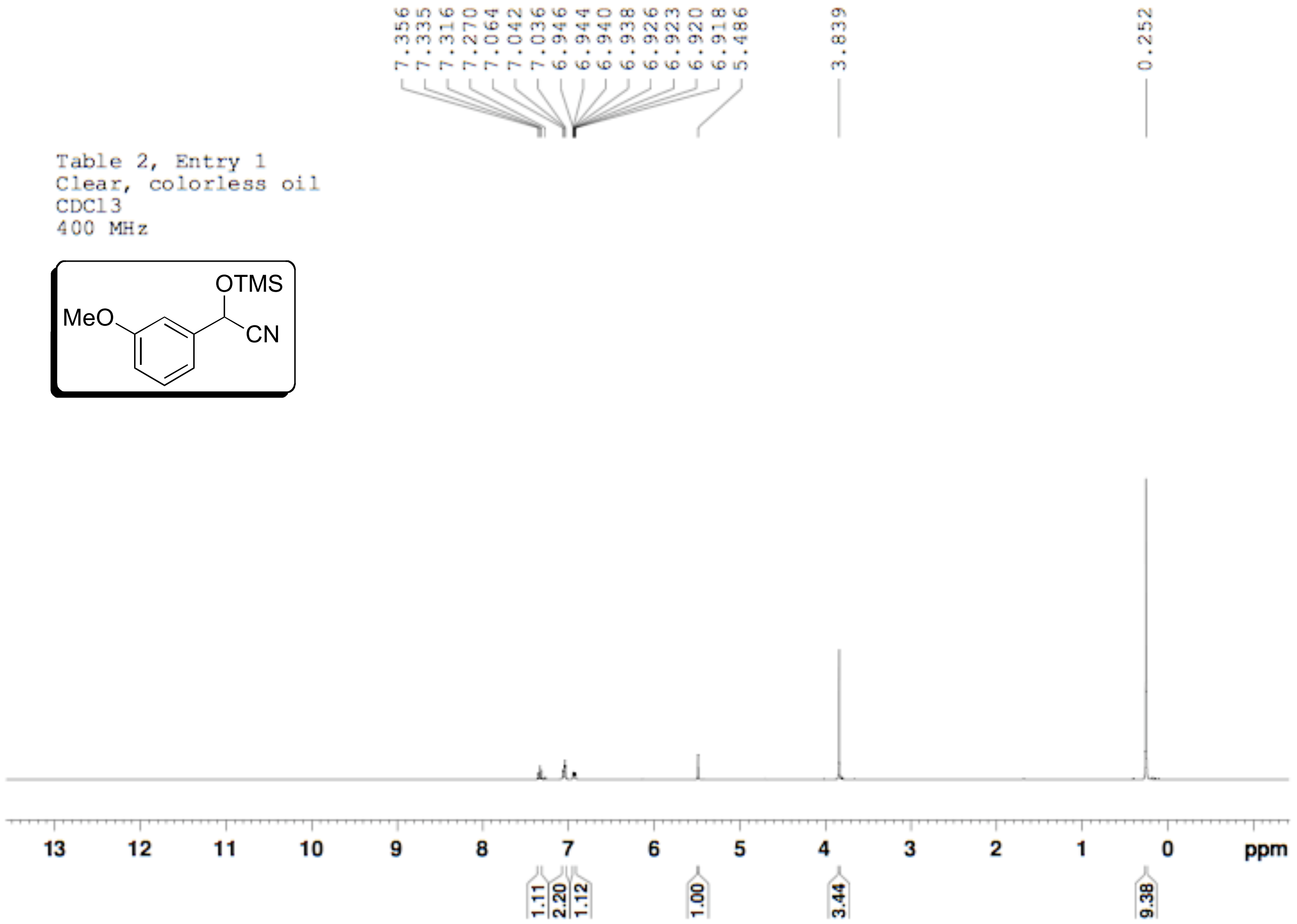


Table 2, Entry 1
Clear, colorless oil
CDCl3
400 MHz

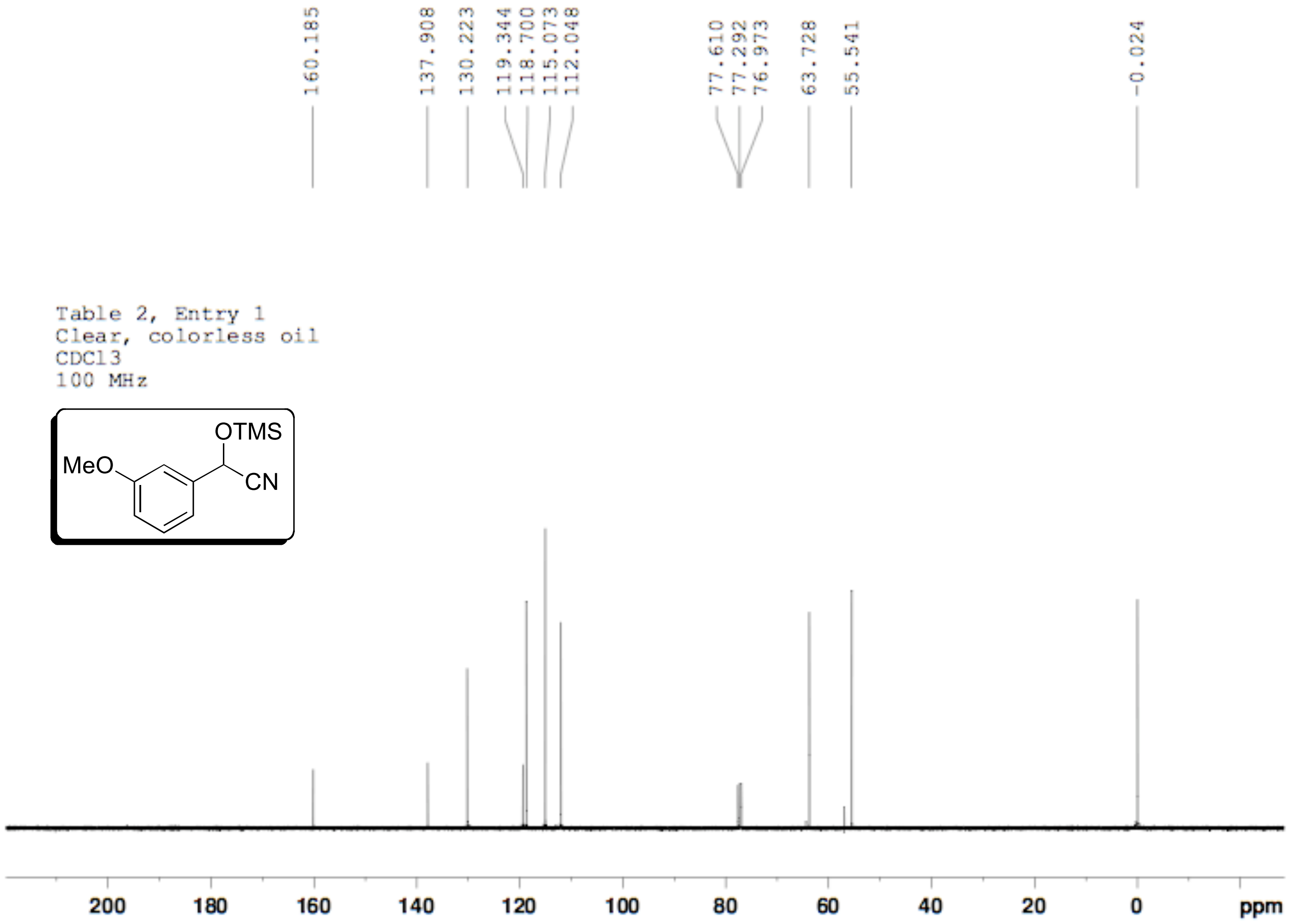


Table 2, Entry 1
Clear, colorless oil
CDCl3
100 MHz

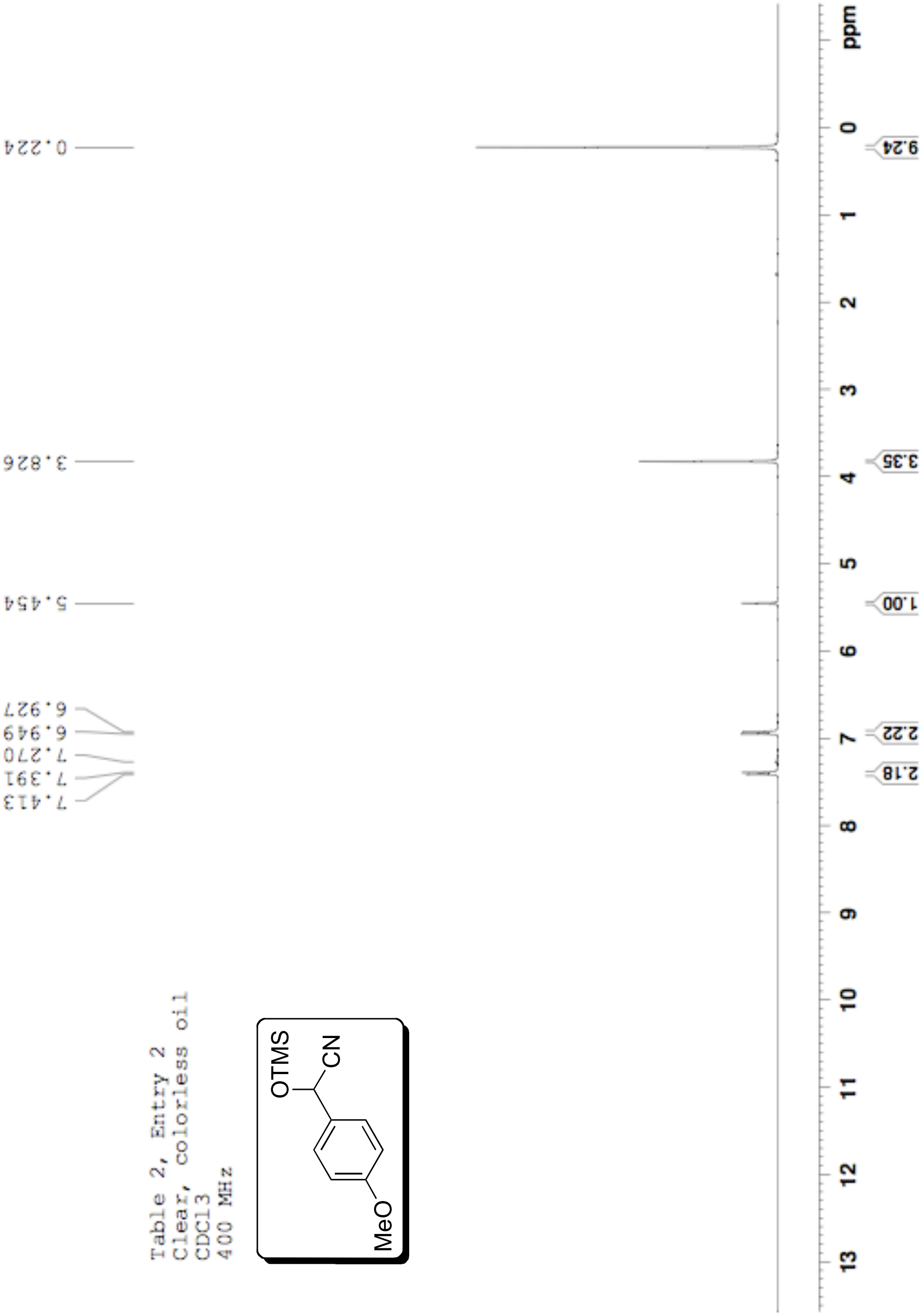


Table 2, Entry 2
Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
MeO
0.224
3.826
5.454
6.927
6.949
7.270
7.391
7.413
9.24
3.35
1.00
2.22
2.18
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

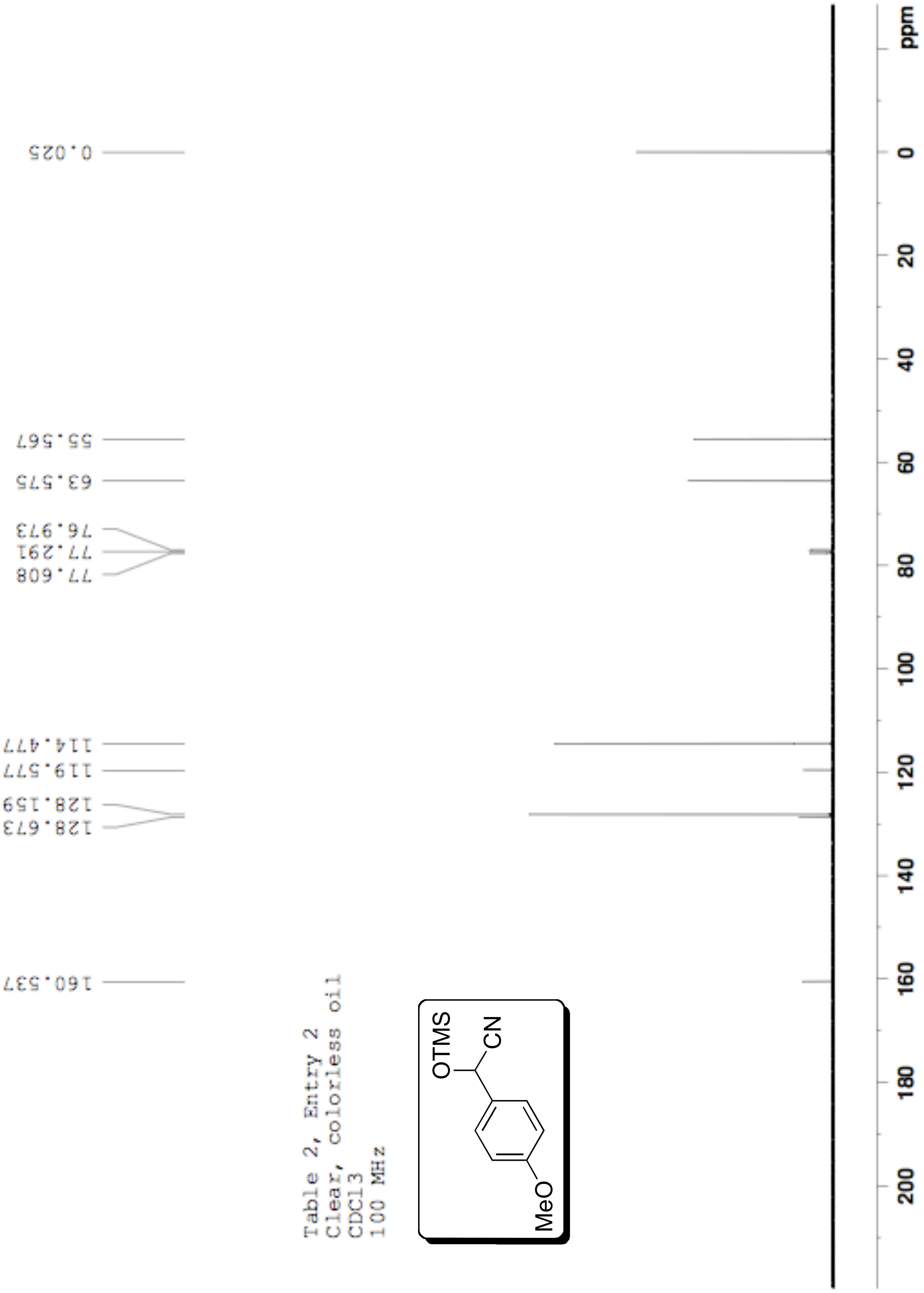
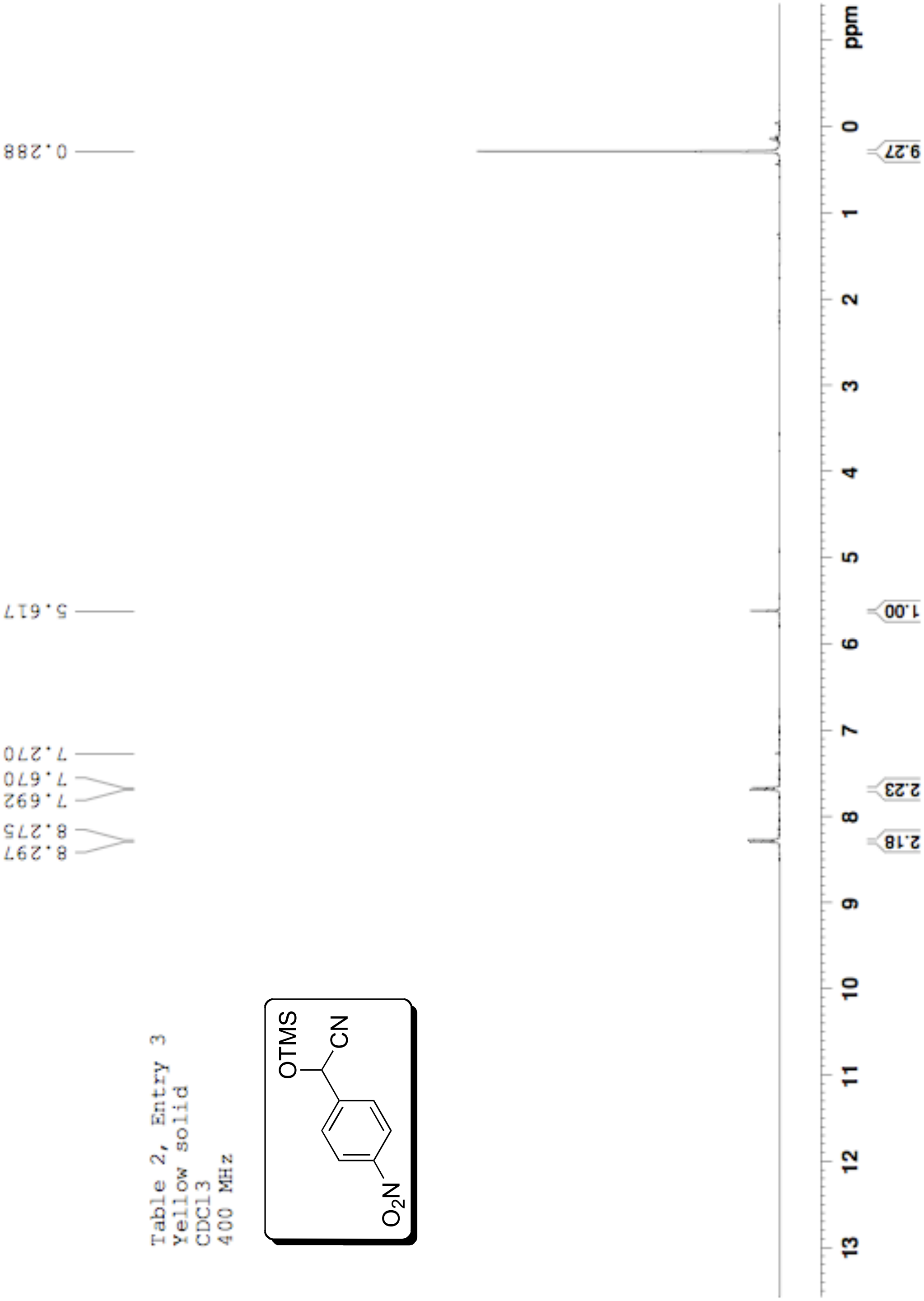
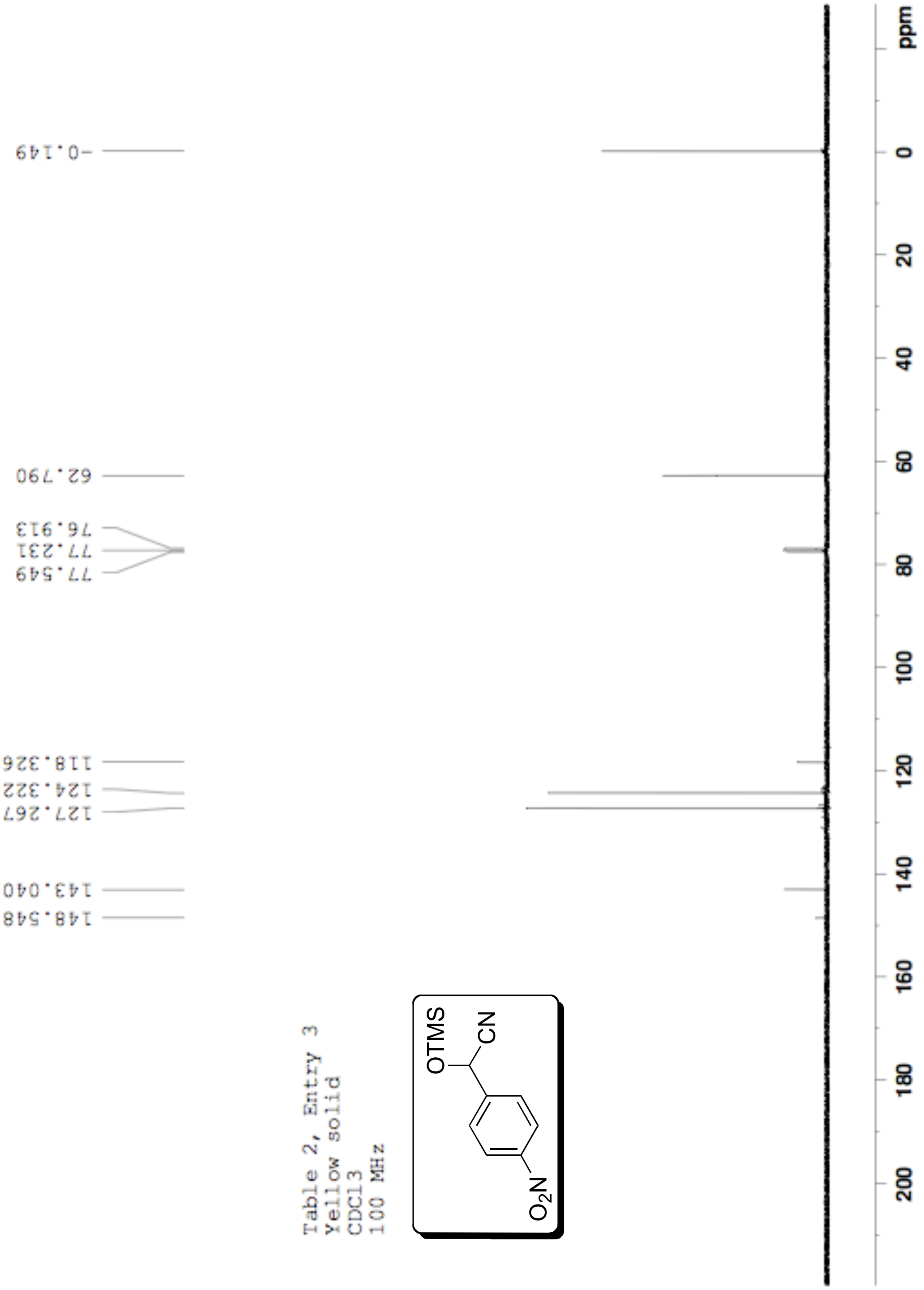


Table 2, Entry 2
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
MeO
0.025
55.567
63.575
76.973
77.291
77.608
114.477
119.577
128.159
128.673
160.537
ppm
0
20
40
60
80
100
120
140
160
180
200


0.288
5.617
7.270
7.670
7.692
8.275
8.297
Table 2, Entry 3
Yellow solid
CDCl3
400 MHz
OTMS
CN
O_2N
9.27
1.00
2.23
2.18
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


-0.149
62.790
76.913
77.231
77.549
118.326
124.322
127.267
143.040
148.548
Table 2, Entry 3
Yellow solid
CDCl3
100 MHz
OTMS
CN
O2N
ppm
0
20
40
60
80
100
120
140
160
180
200

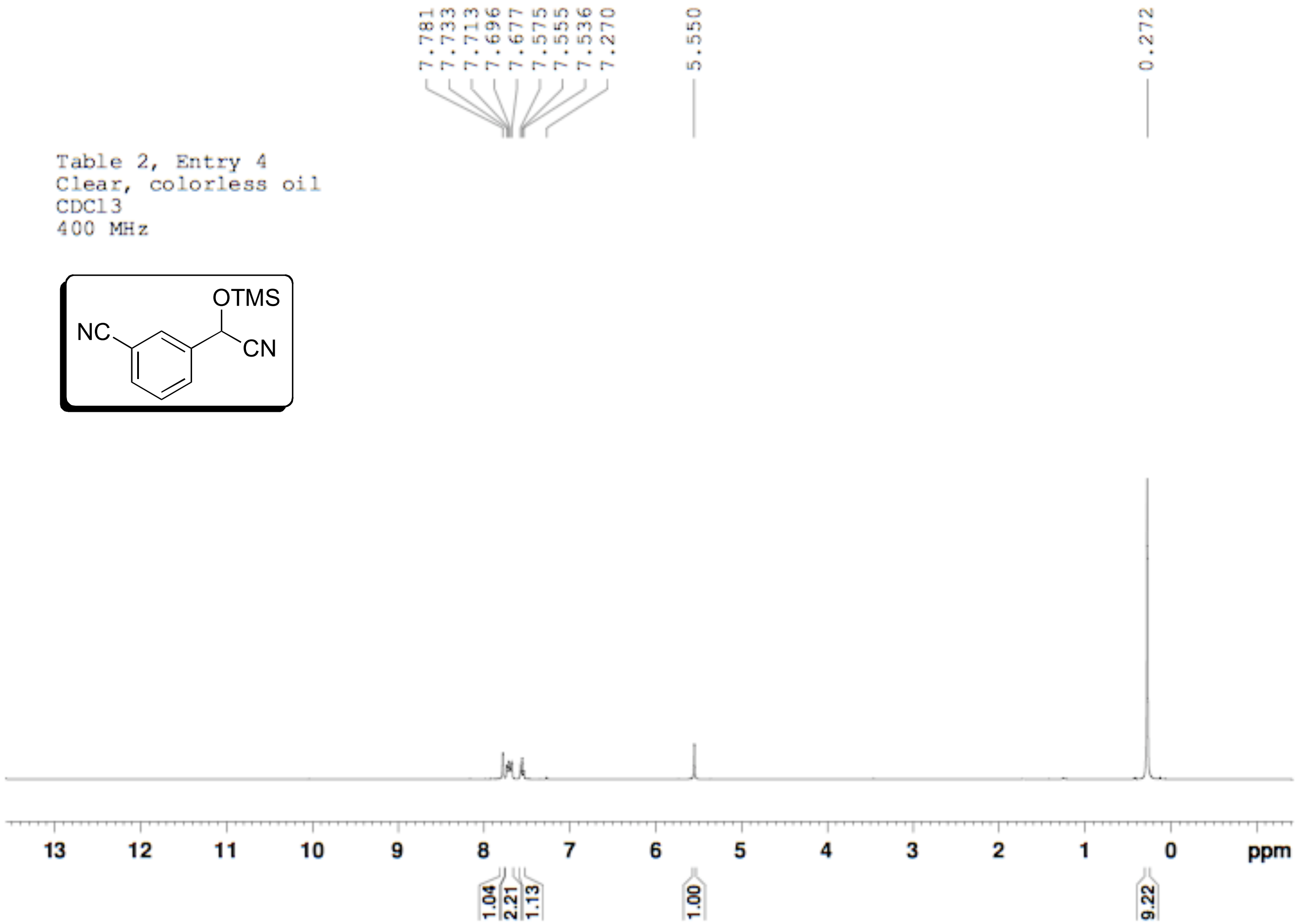
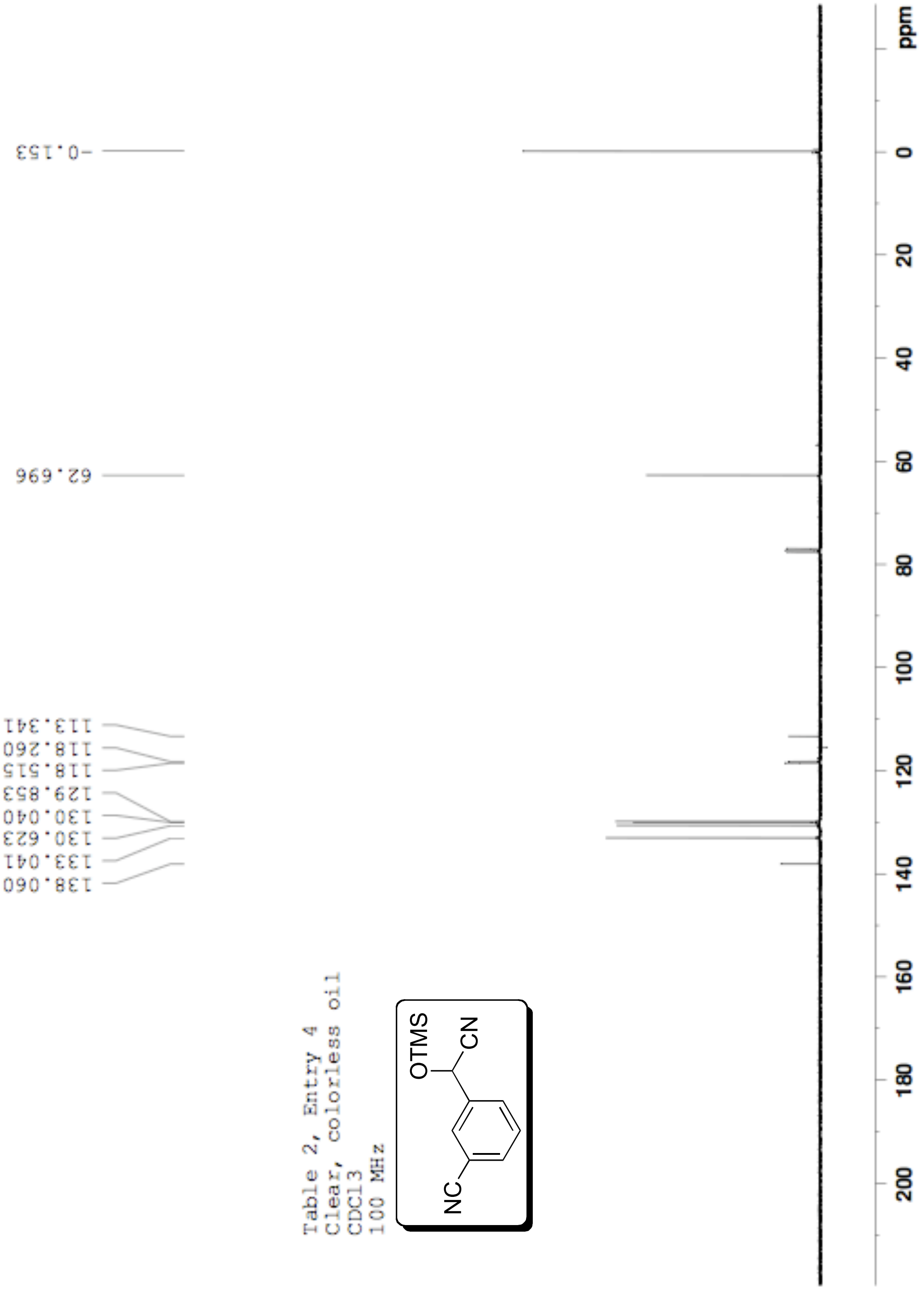
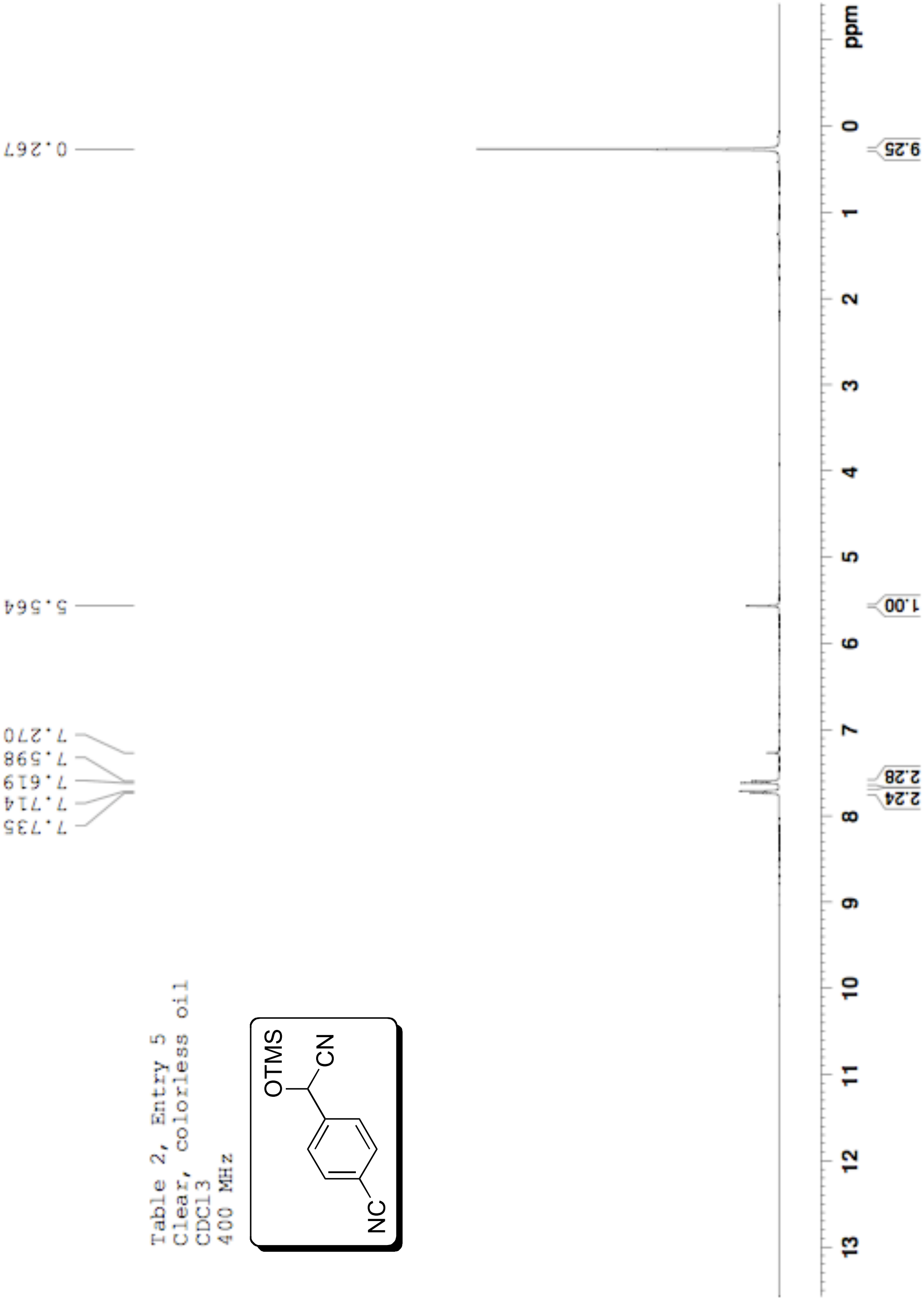
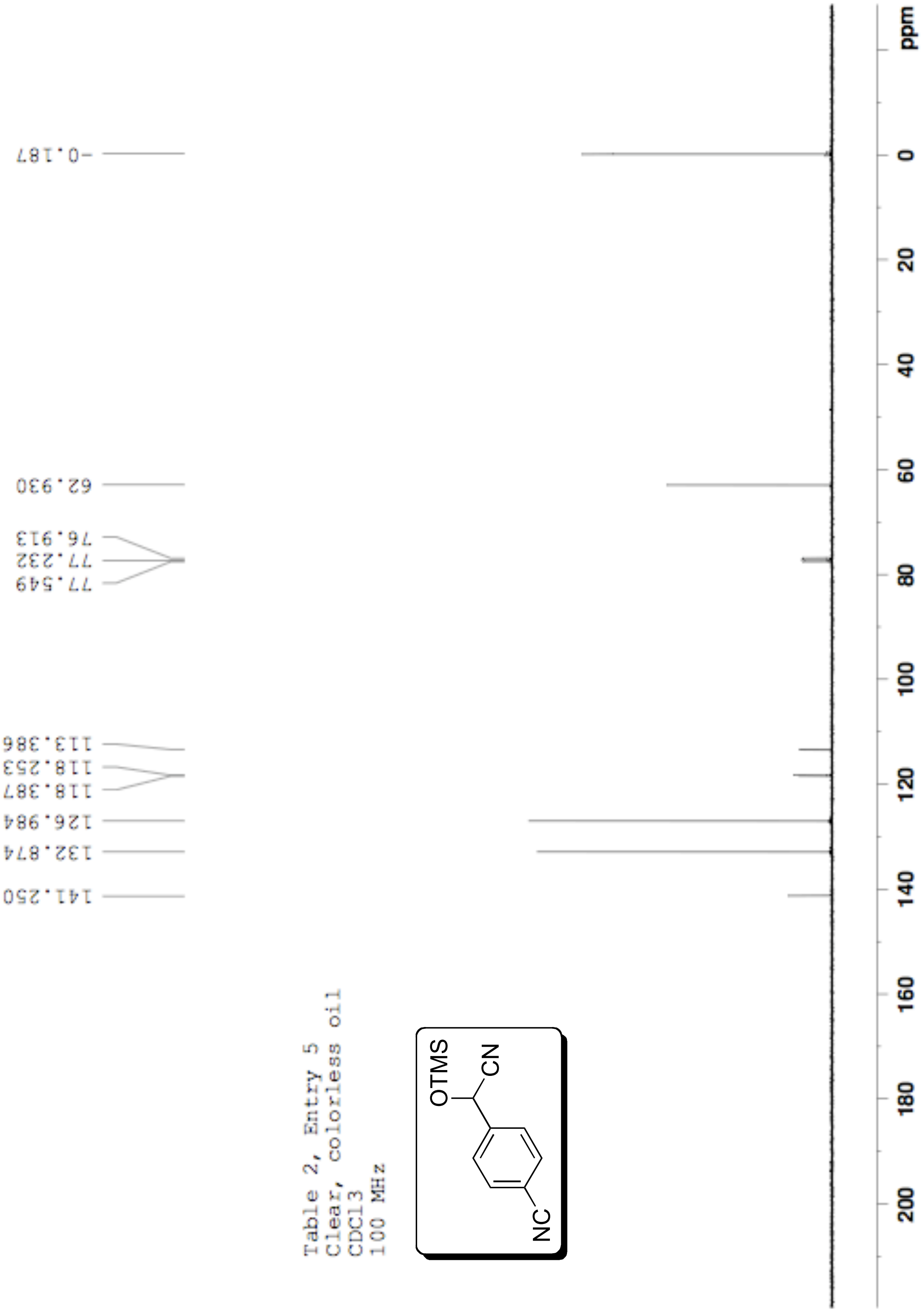


Table 2, Entry 4
Clear, colorless oil
CDCl3
400 MHz


-0.153
62.696
113.341
118.260
118.515
129.853
130.040
130.623
133.041
138.060
Table 2, Entry 4
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
NC
ppm
0
20
40
60
80
100
120
140
160
180
200


0.267
5.564
7.270
7.598
7.619
7.714
7.735
Table 2, Entry 5
Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
NC
9.25
1.00
2.28
2.24
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13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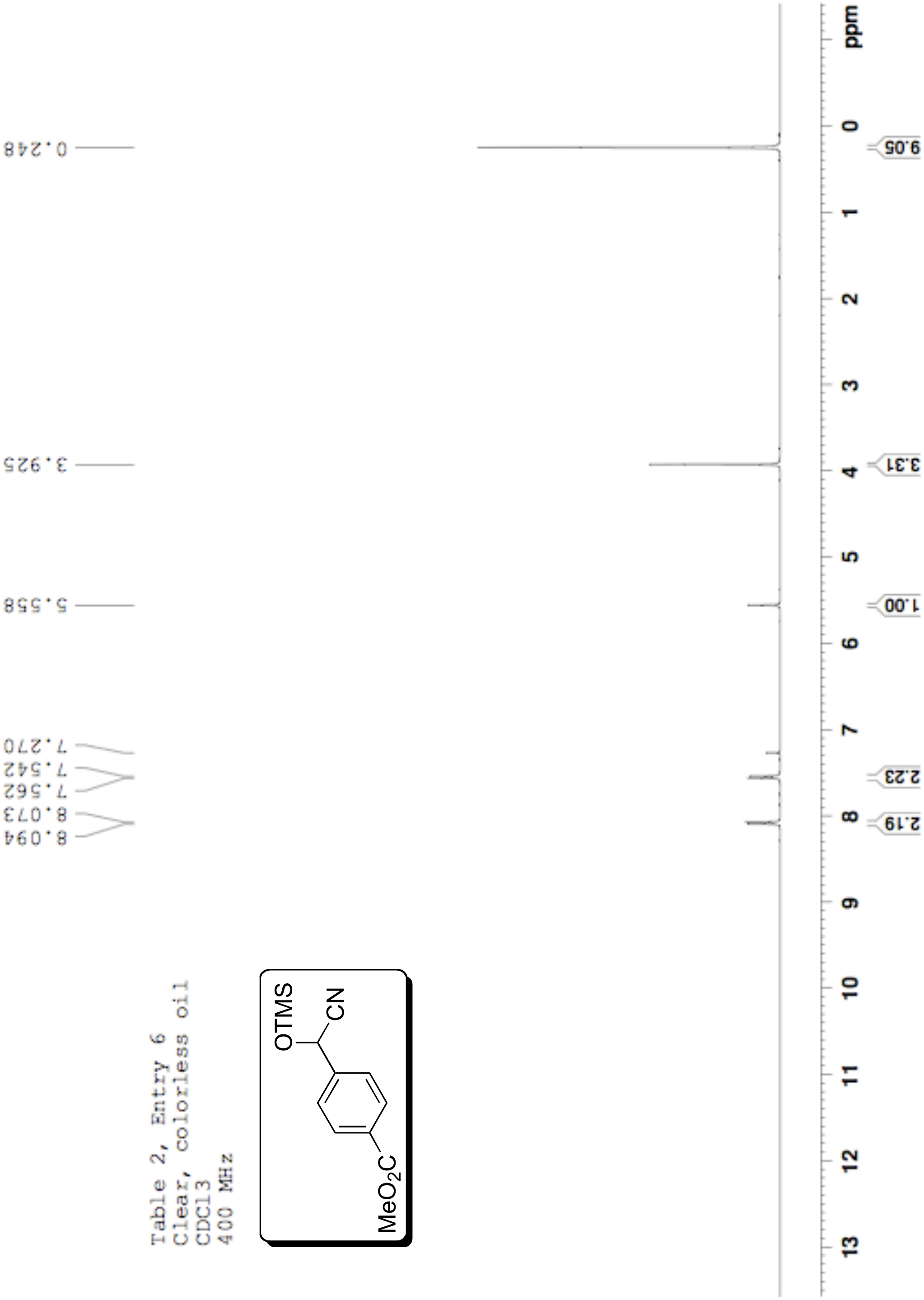
62.930
76.913
77.232
77.549
113.386
118.253
118.387
126.984
132.874
141.250
Table 2, Entry 5
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
NC
ppm
0
20
40
60
80
100
120
140
160
180
200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Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
MeO2C
0.248
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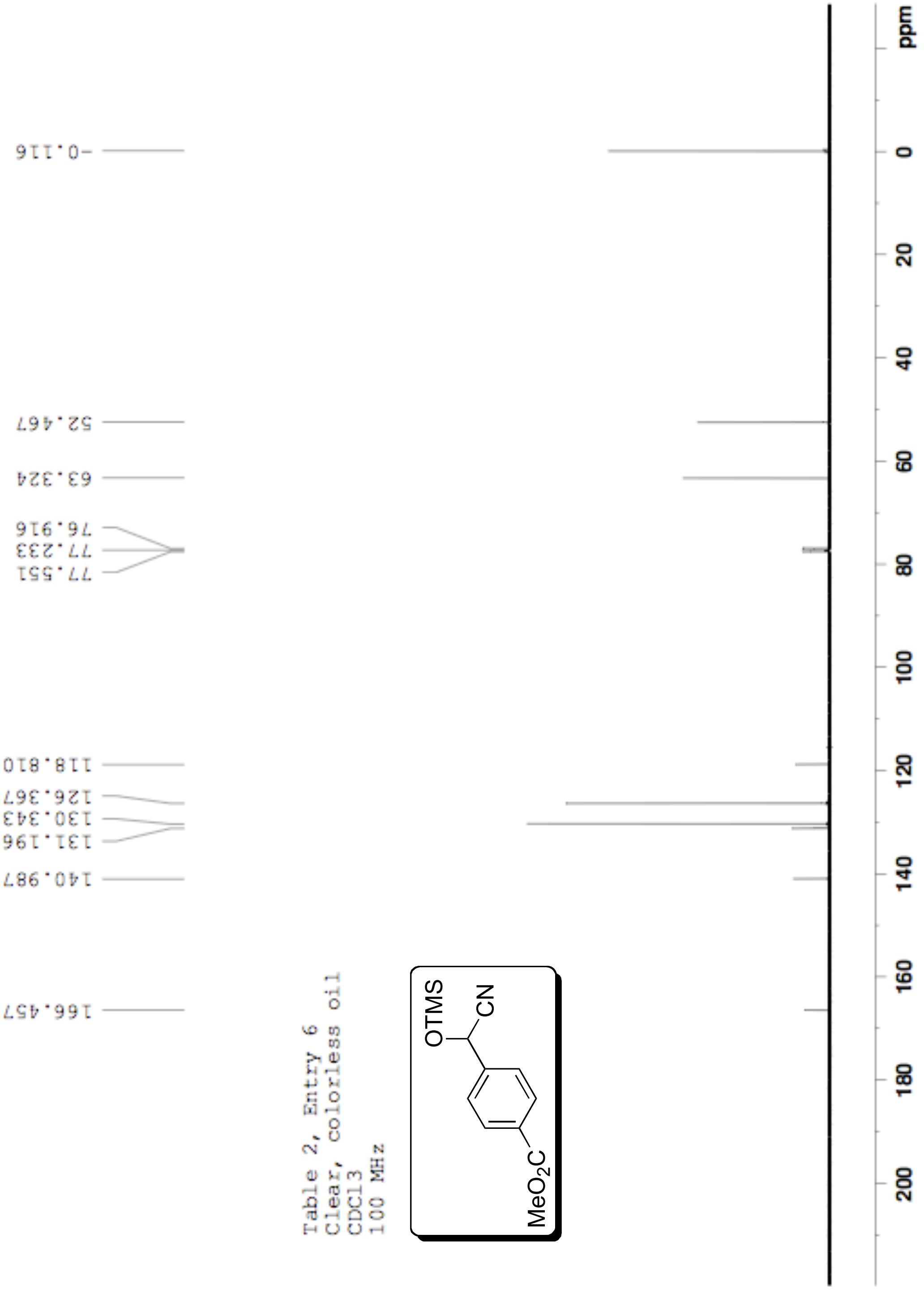
5.558
7.270
7.542
7.562
8.073
8.094
9.05
3.31
1.00
2.23
2.19
0
1
2
3
4
5
6
7
8
9
10
11
12
13
ppm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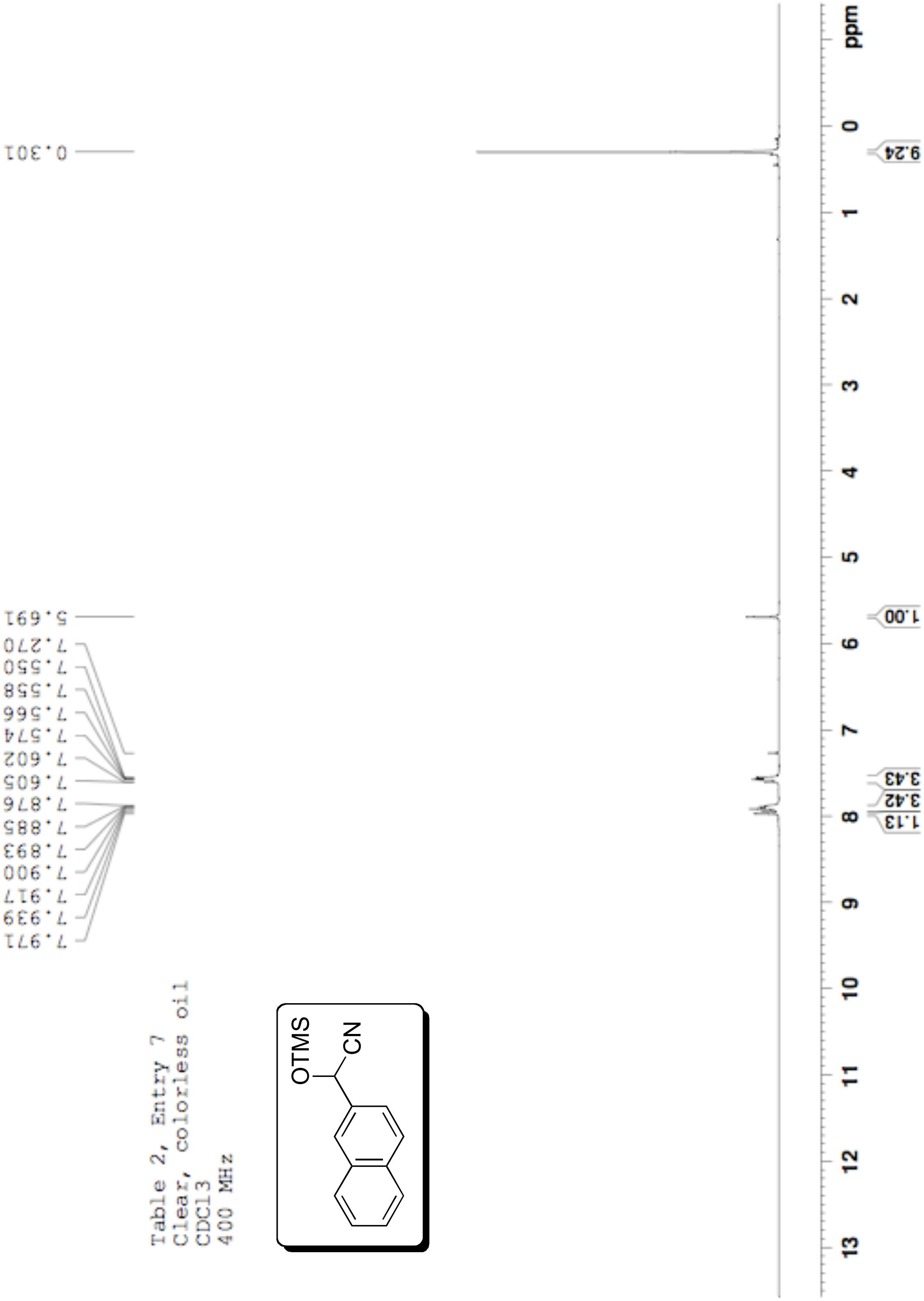
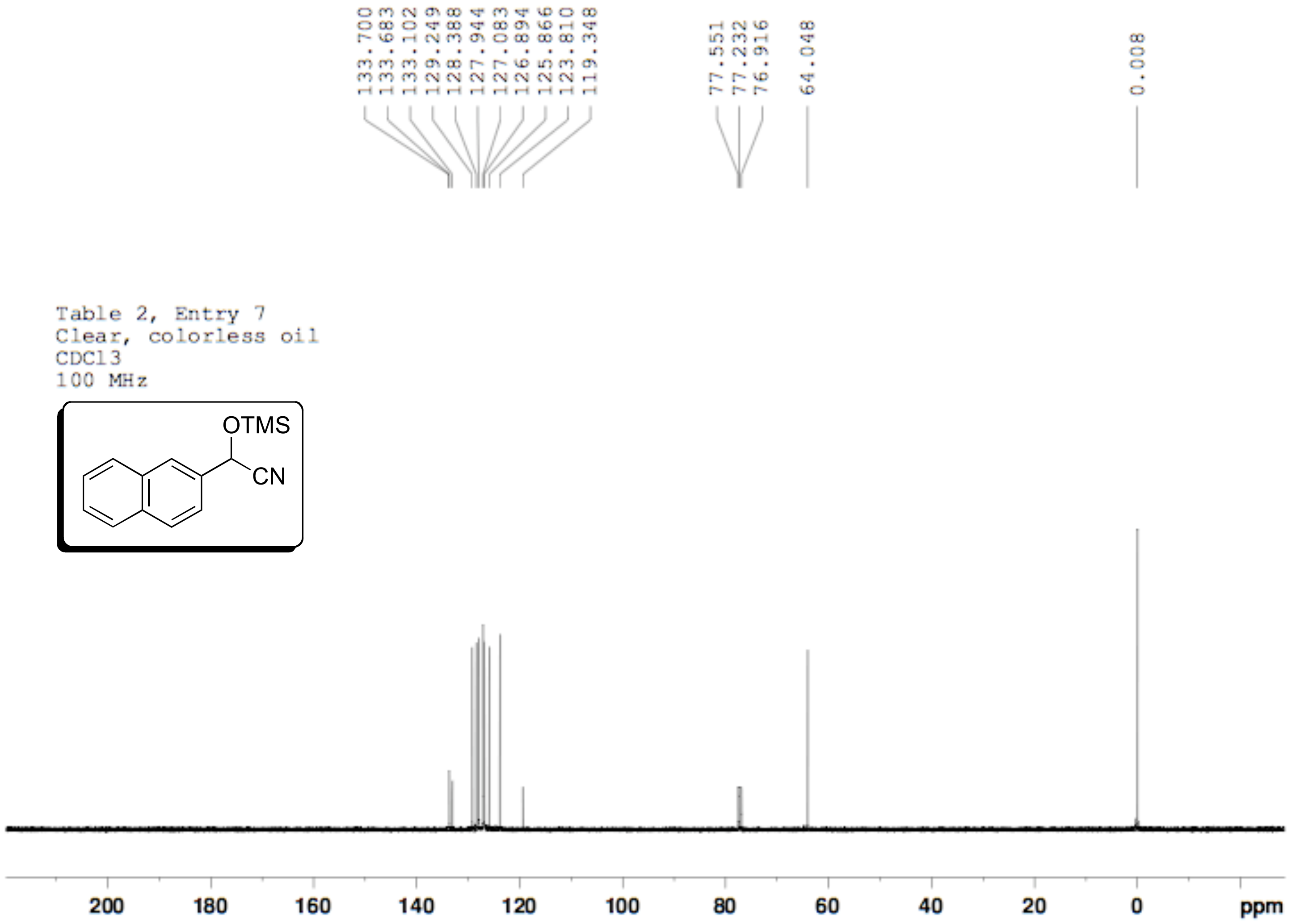
52.467
63.324
76.916
77.233
77.551
118.810
126.367
130.343
131.196
140.987
166.457
Table 2, Entry 6
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
MeO2C
ppm
0
20
40
60
80
100
120
140
160
180
200


0.301
5.691
7.270
7.550
7.558
7.566
7.574
7.602
7.605
7.876
7.885
7.893
7.900
7.917
7.939
7.971
Table 2, Entry 7
Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
9.24
1.00
3.43
3.42
1.13
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


133.700
133.683
133.102
129.249
128.388
127.944
127.083
126.894
125.866
123.810
119.348
77.551
77.232
76.916
64.048
0.008
Table 2, Entry 7
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
200
180
160
140
120
100
80
60
40
20
0
ppm

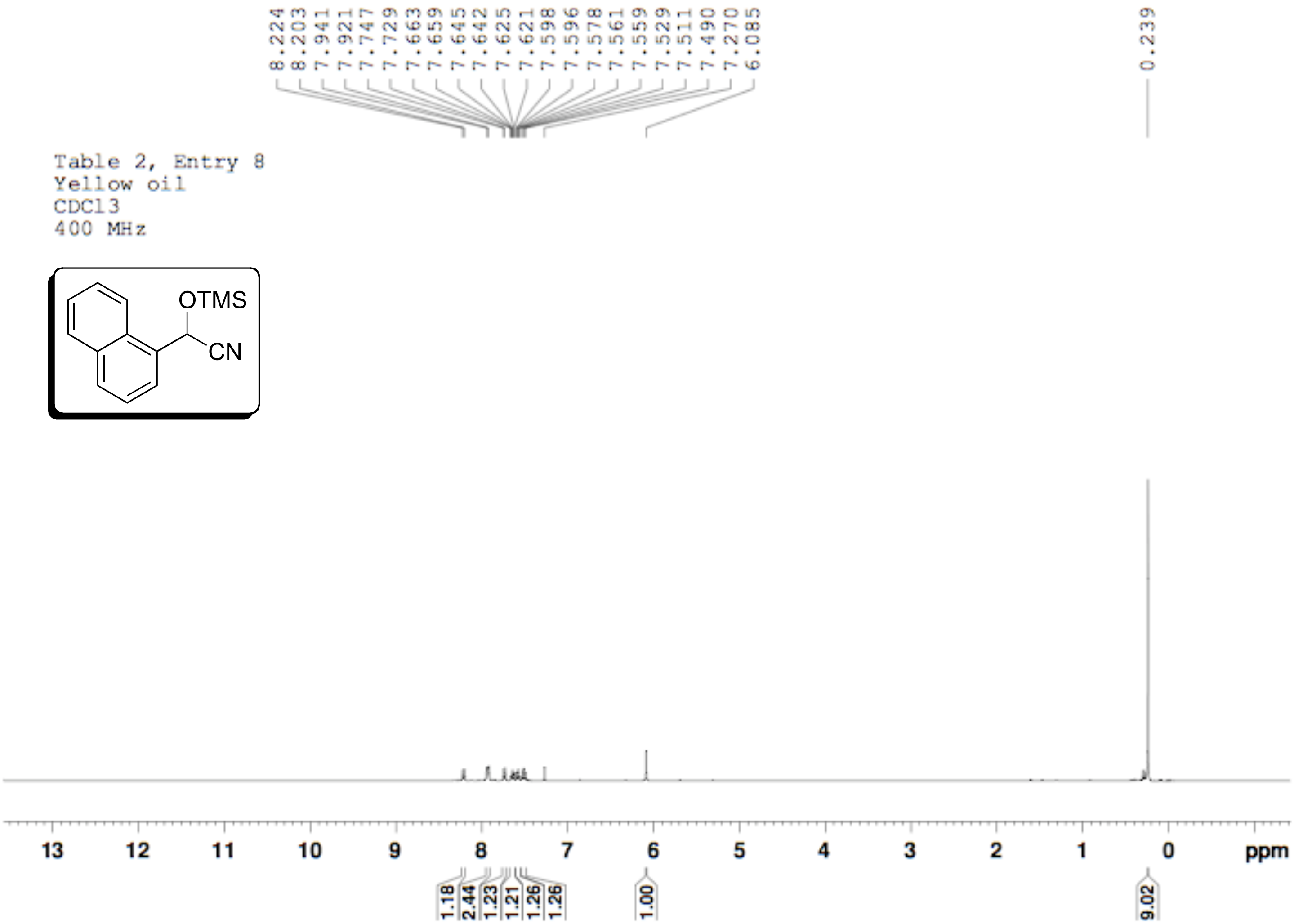


Table 2, Entry 8
Yellow oil
CDCl3
400 MHz

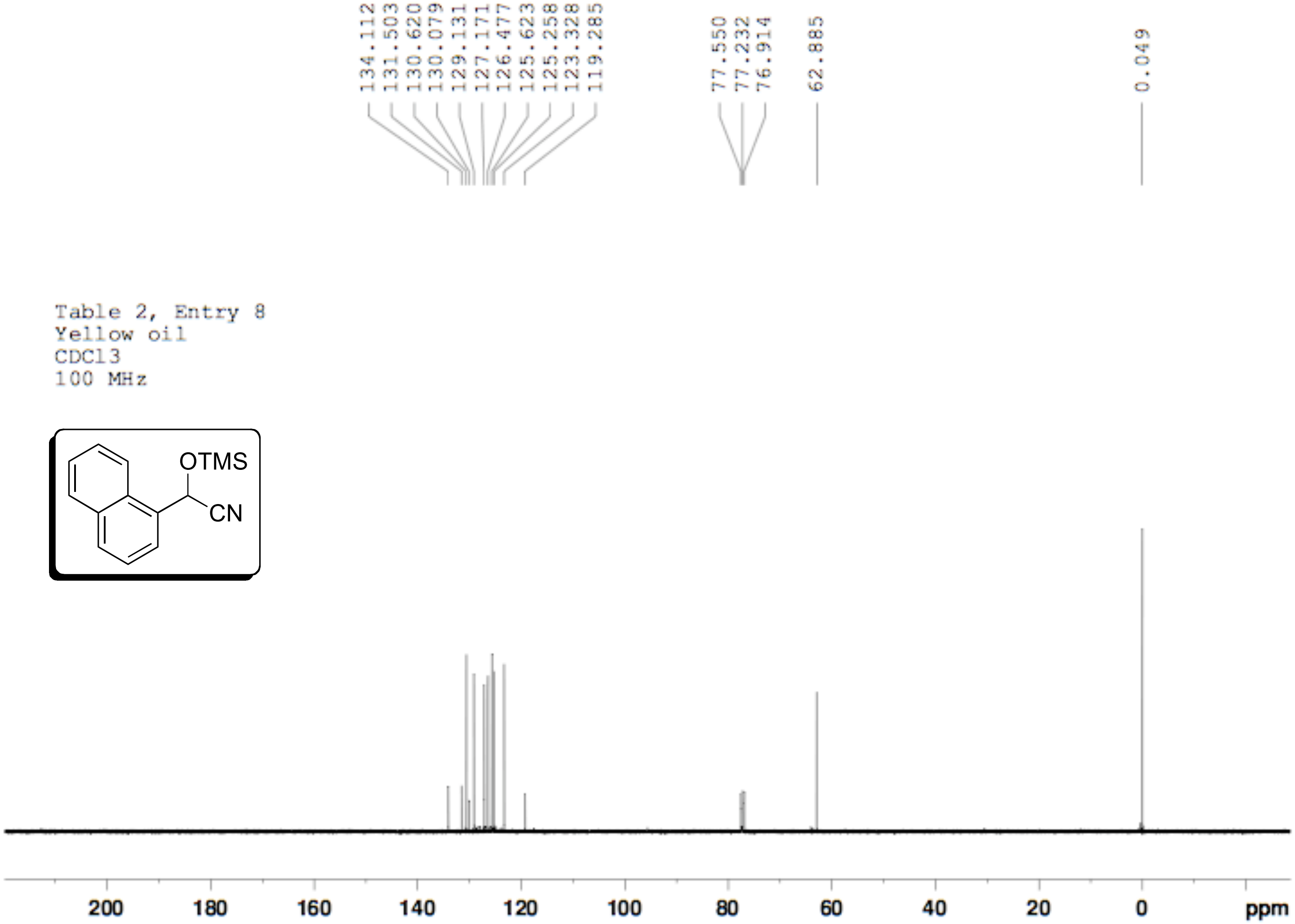


Table 2, Entry 8
Yellow oil
CDCl3
100 MHz

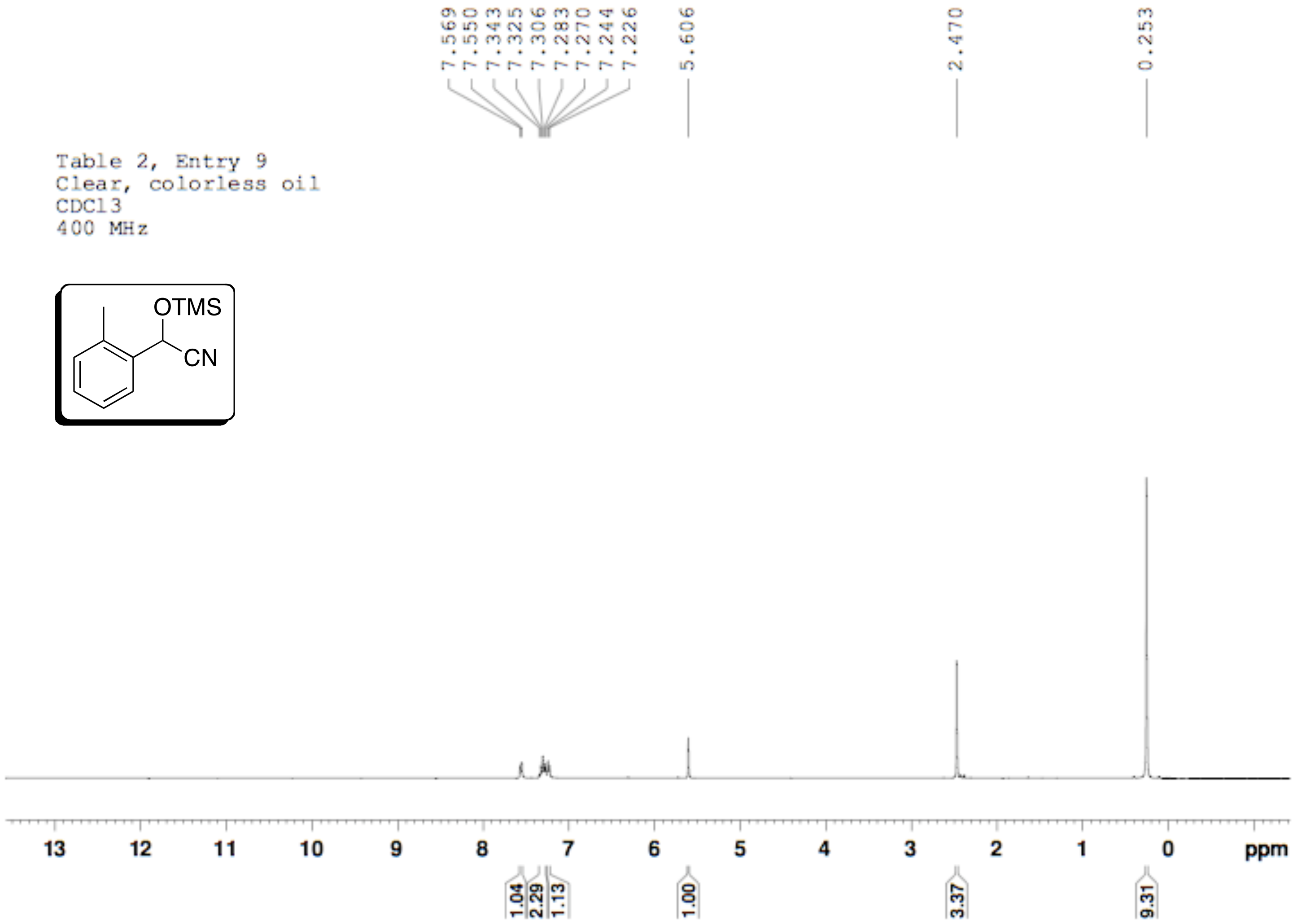


Table 2, Entry 9
Clear, colorless oil
CDCl3
400 MHz

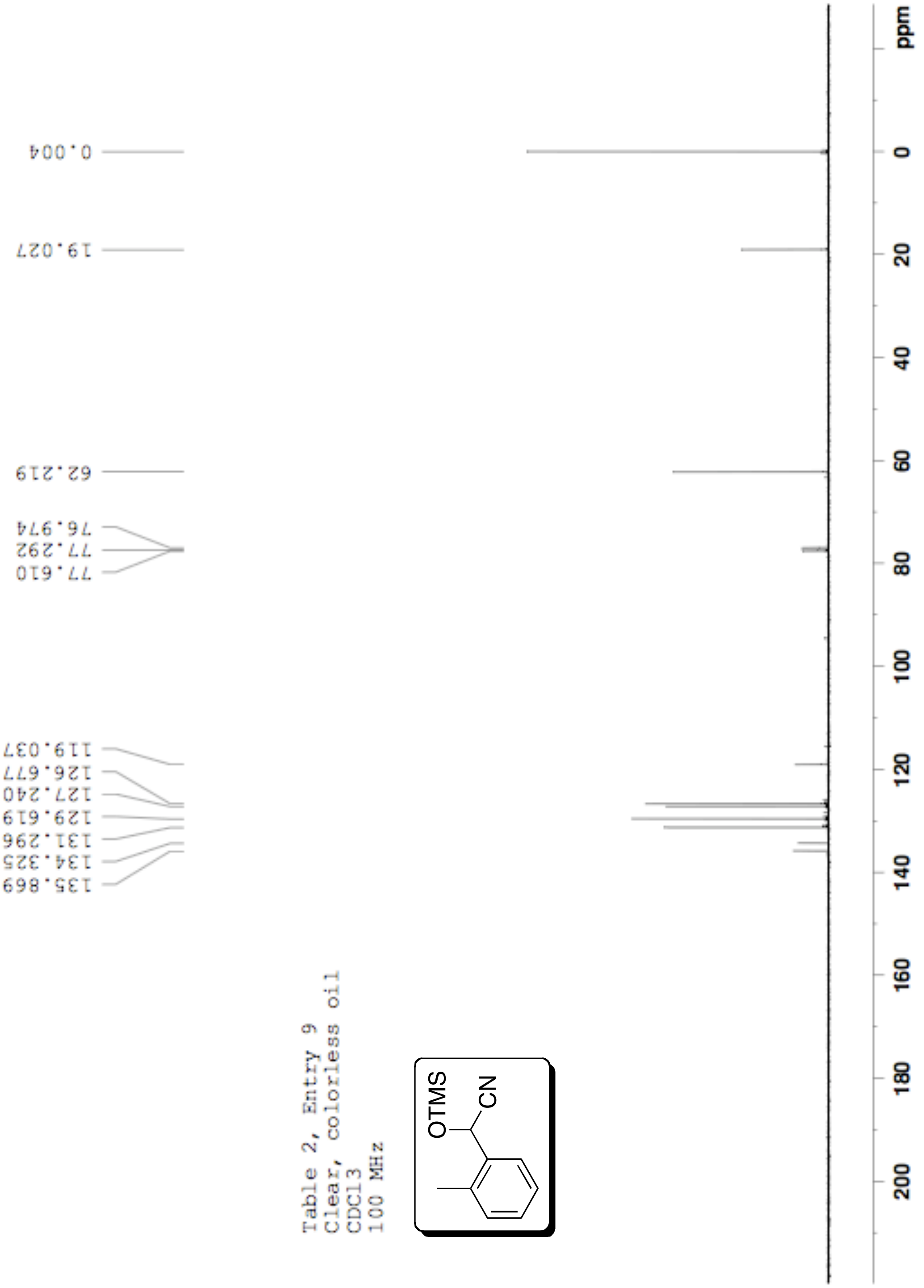


Table 2, Entry 9
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
0.004
19.027
62.219
76.974
77.292
77.610
119.037
126.677
127.240
129.619
131.296
134.325
135.869
ppm
0
20
40
60
80
100
120
140
160
180
200

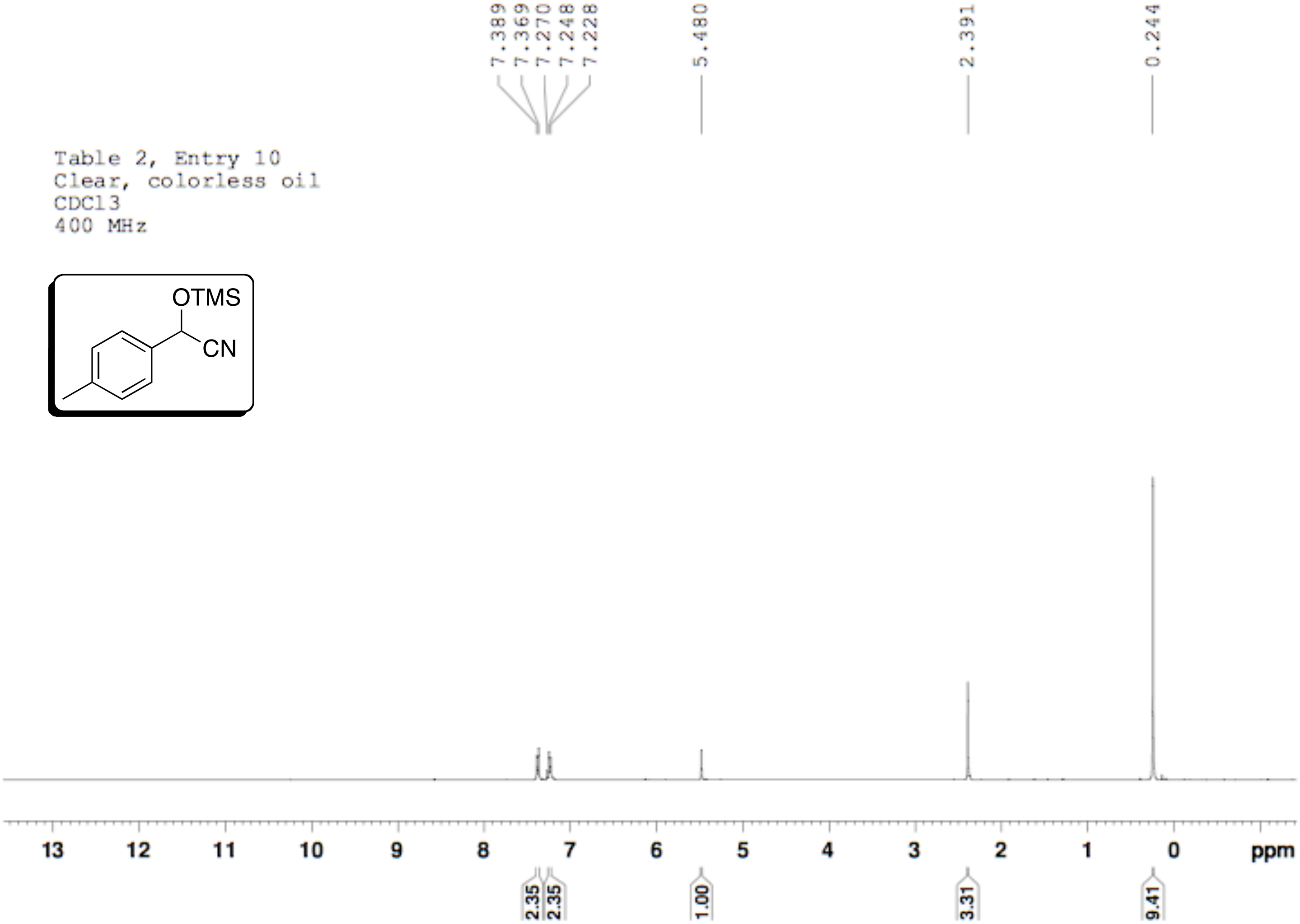
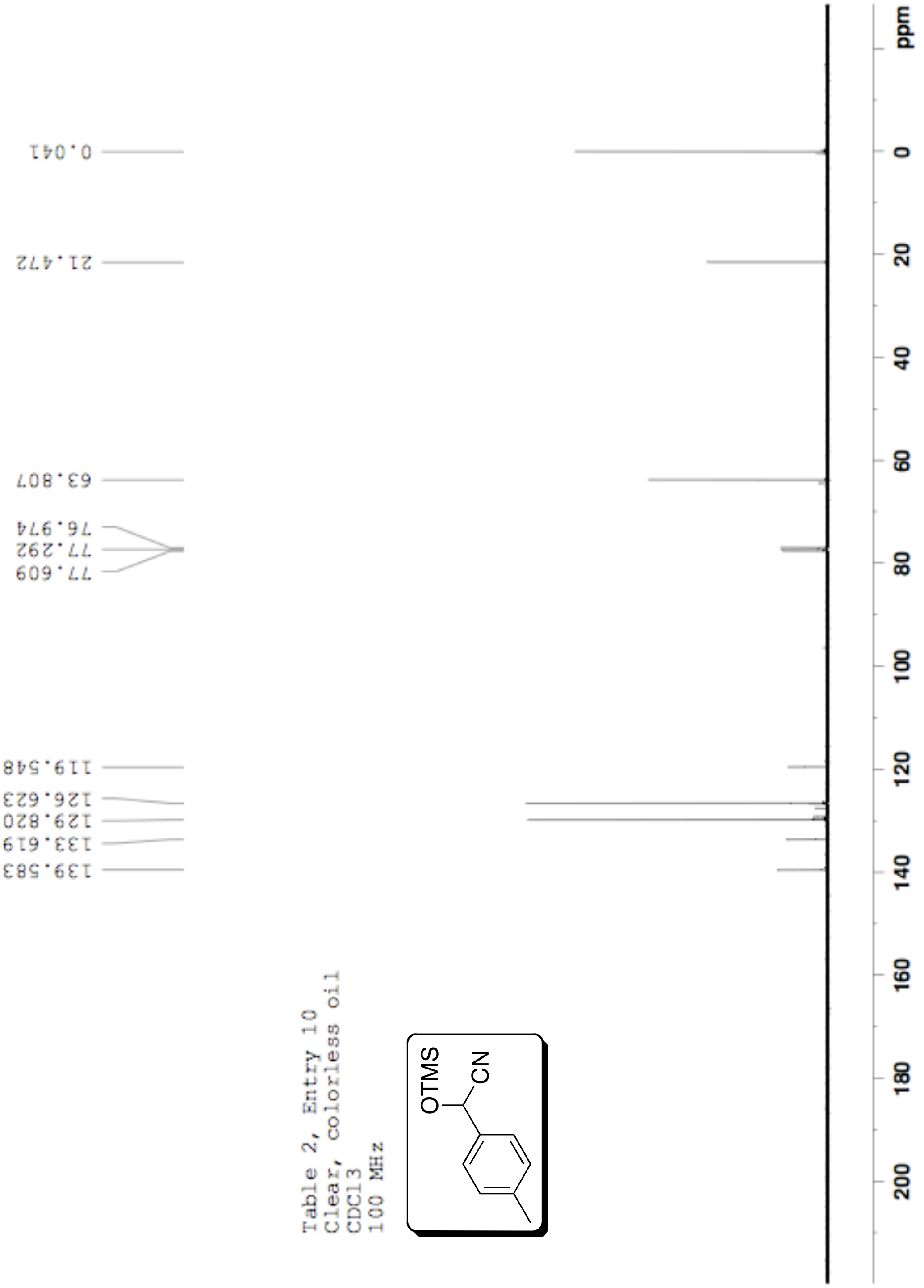


Table 2, Entry 10
Clear, colorless oil
CDCl3
400 MHz


0.041
21.472
63.807
76.974
77.292
77.609
119.548
126.623
129.820
133.619
139.583
Table 2, Entry 10
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
ppm
0
20
40
60
80
100
120
140
160
180
200

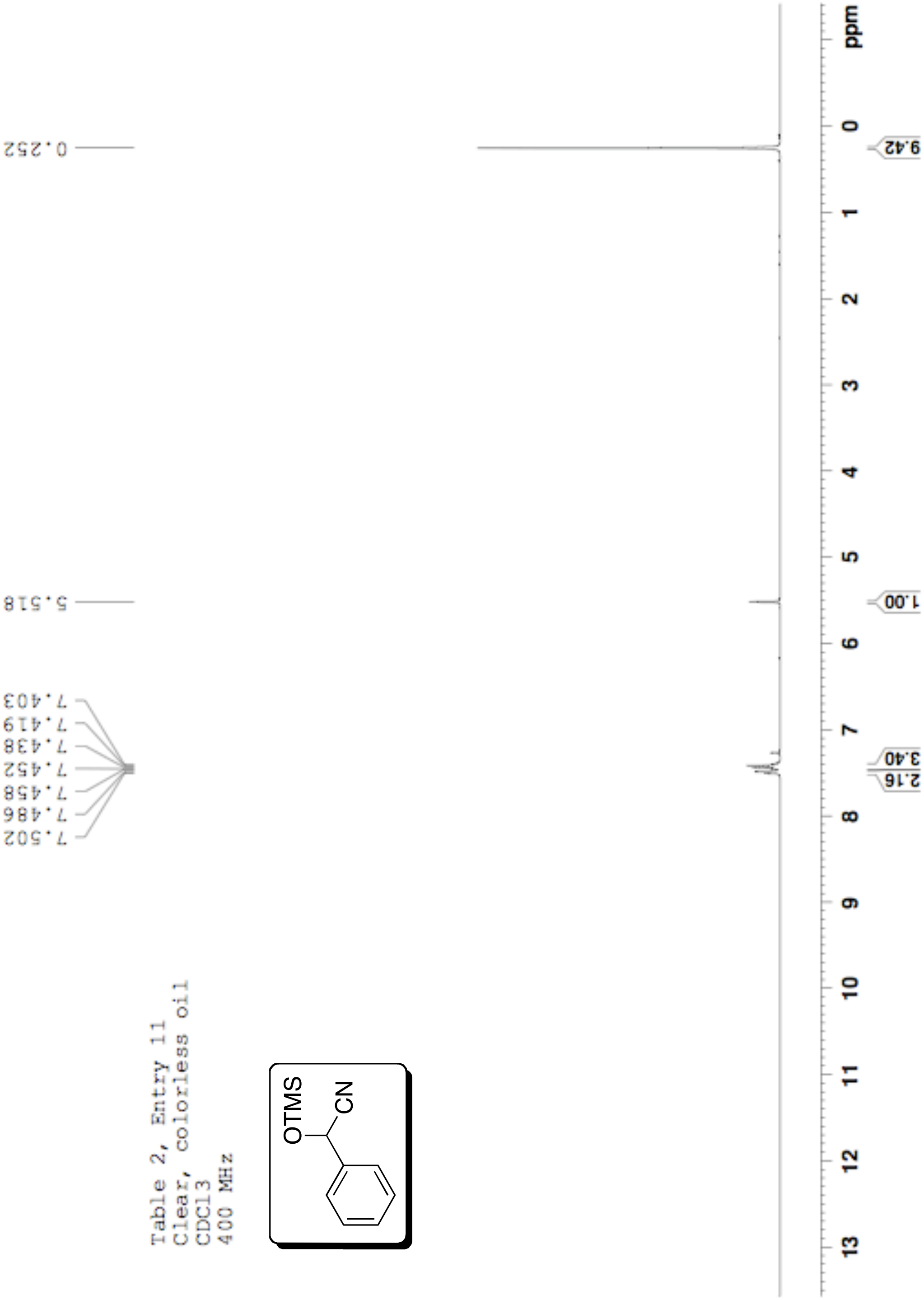
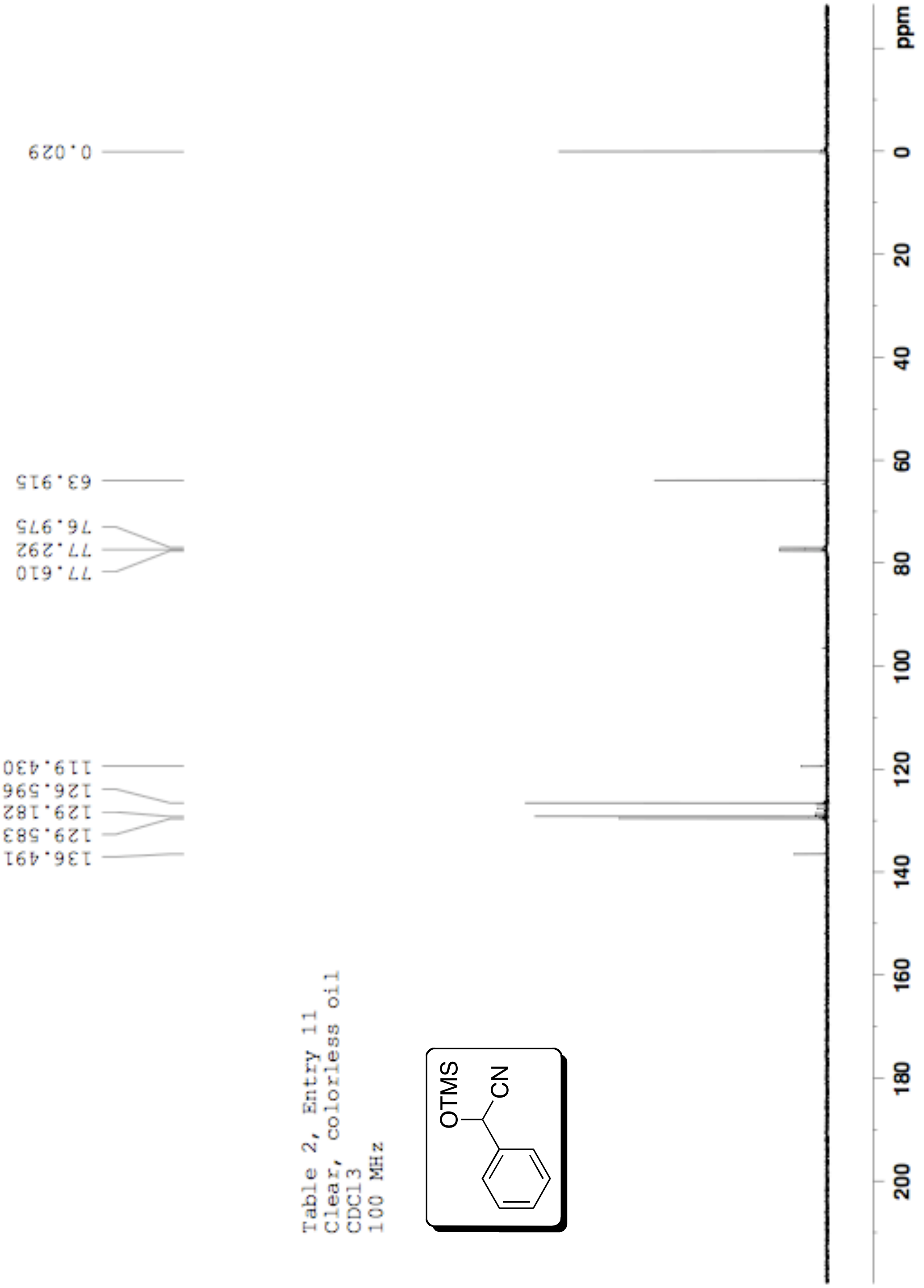


Table 2, Entry 11
Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
0.252
5.518
7.403
7.419
7.438
7.452
7.458
7.486
7.502
9.42
1.00
3.40
2.16
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


0.029
63.915
76.975
77.292
77.610
119.430
126.596
129.182
129.583
136.491
Table 2, Entry 11
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
ppm
0
20
40
60
80
100
120
140
160
180
200

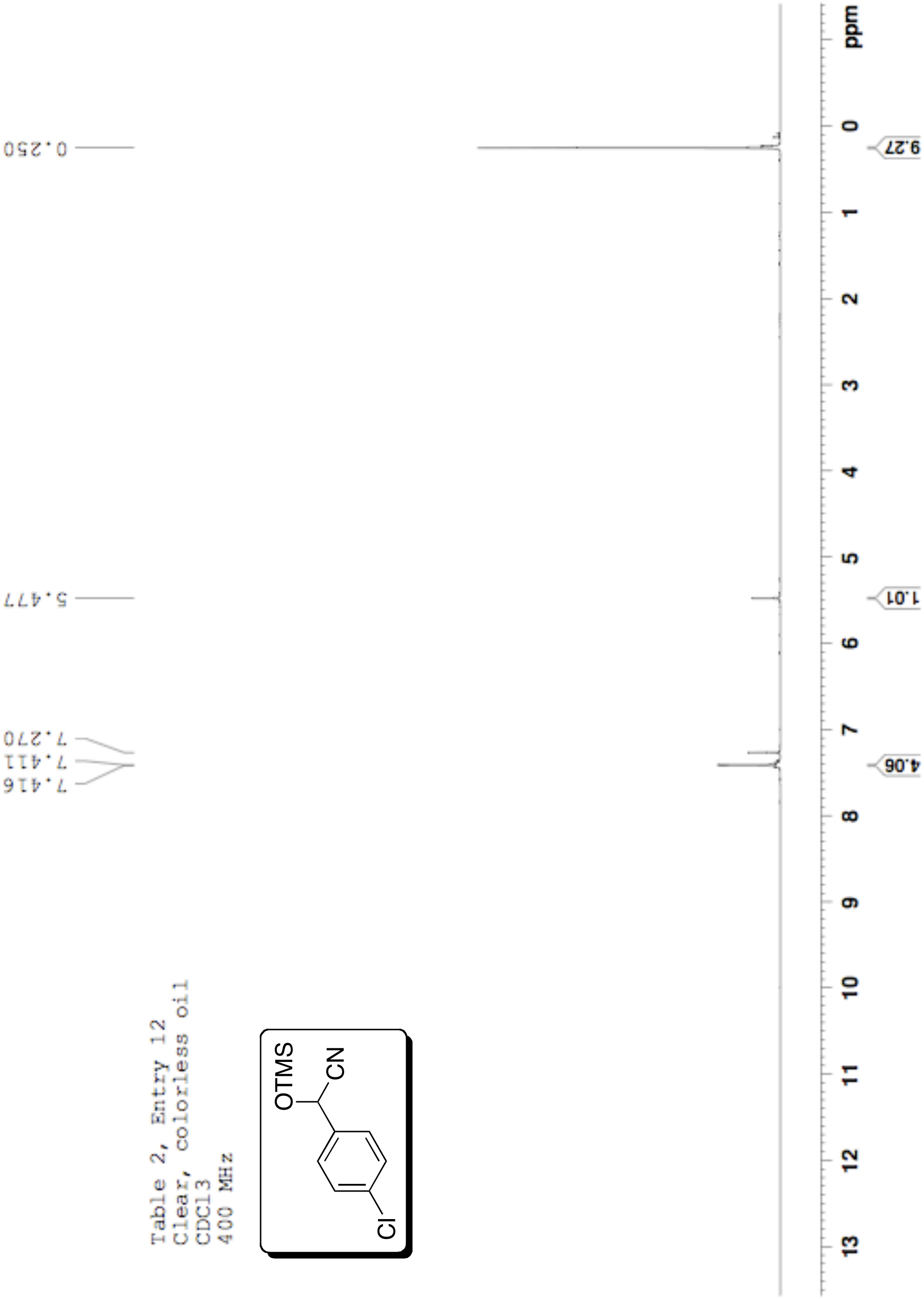


Table 2, Entry 12
Clear, colorless oil
CDCl3
400 MHz

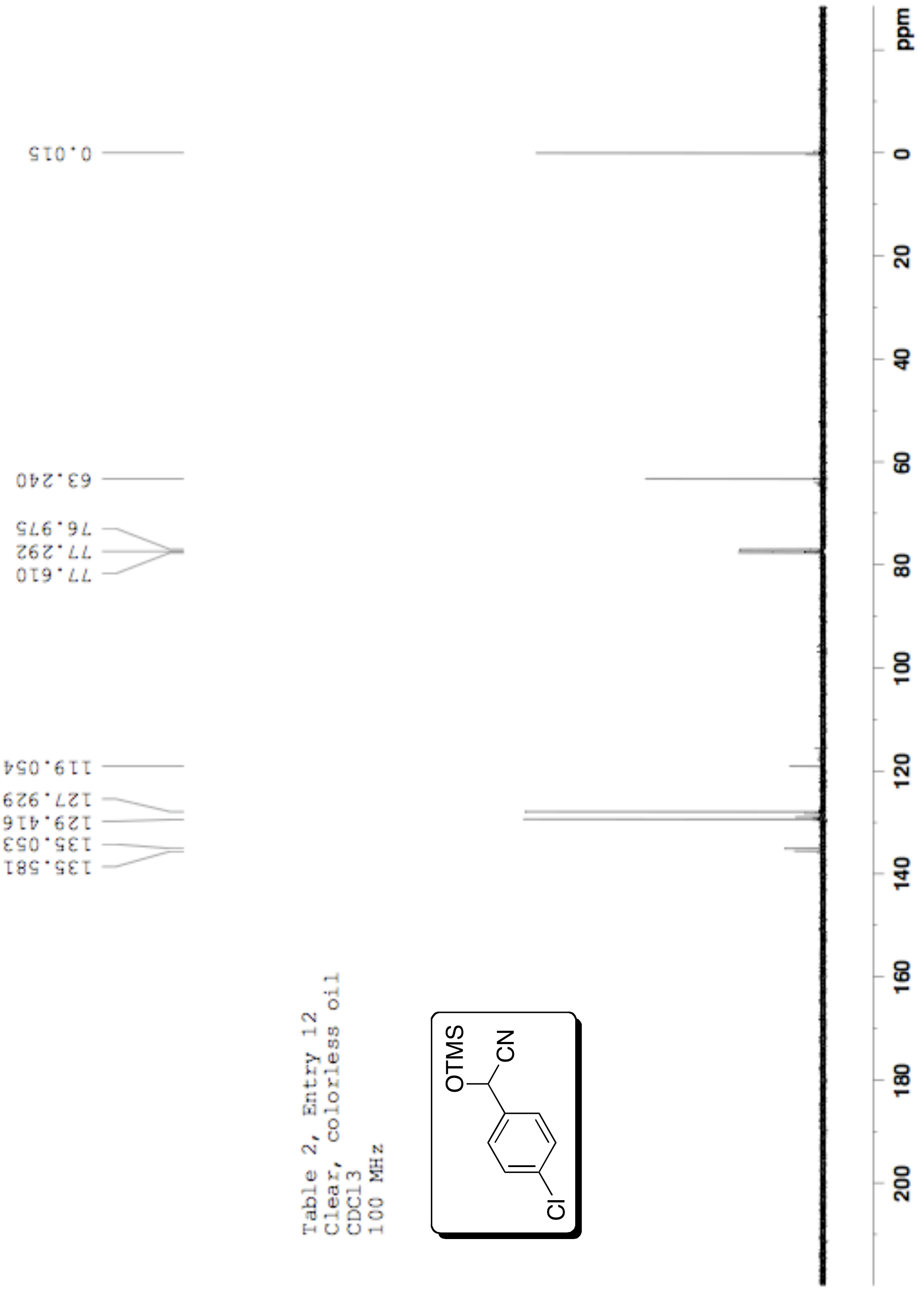


Table 2, Entry 12
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
Cl
0.015
63.240
76.975
77.292
77.610
119.054
127.929
129.416
135.053
135.581
ppm
0
20
40
60
80
100
120
140
160
180
200

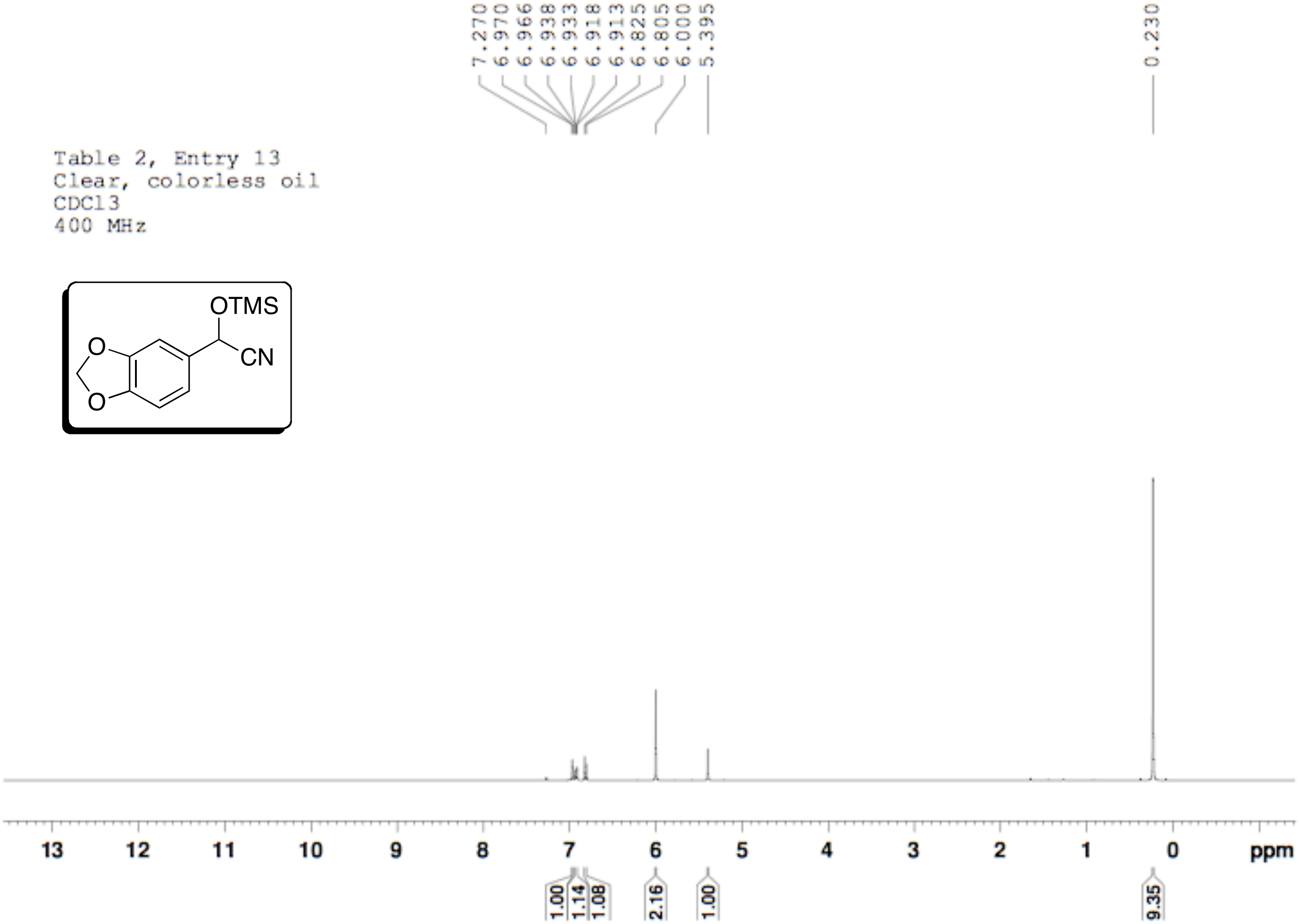


Table 2, Entry 13
Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
O
O
7.270
6.970
6.966
6.938
6.933
6.918
6.913
6.825
6.805
6.000
5.395
0.230
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.14
1.08
2.16
1.00
9.35

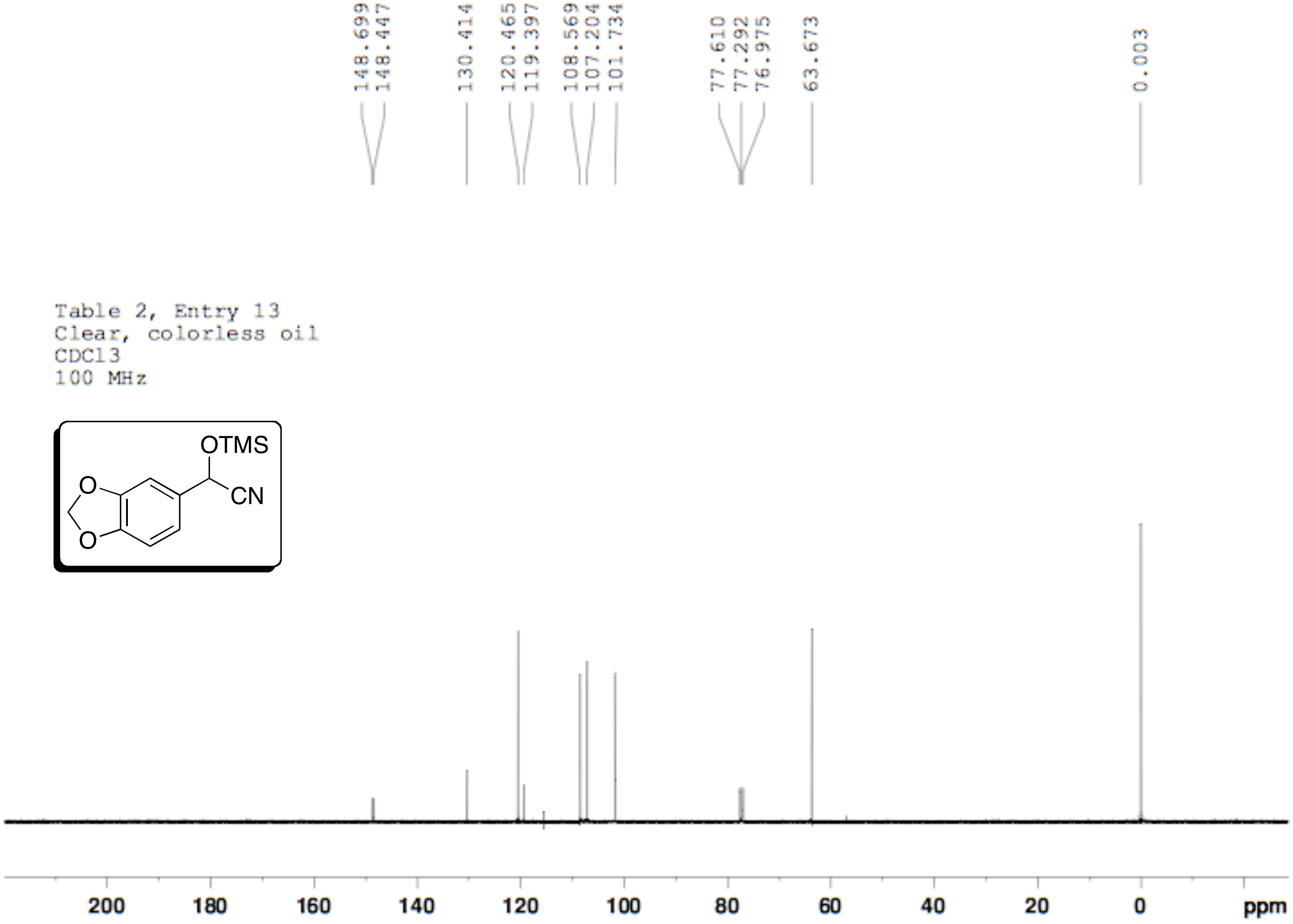
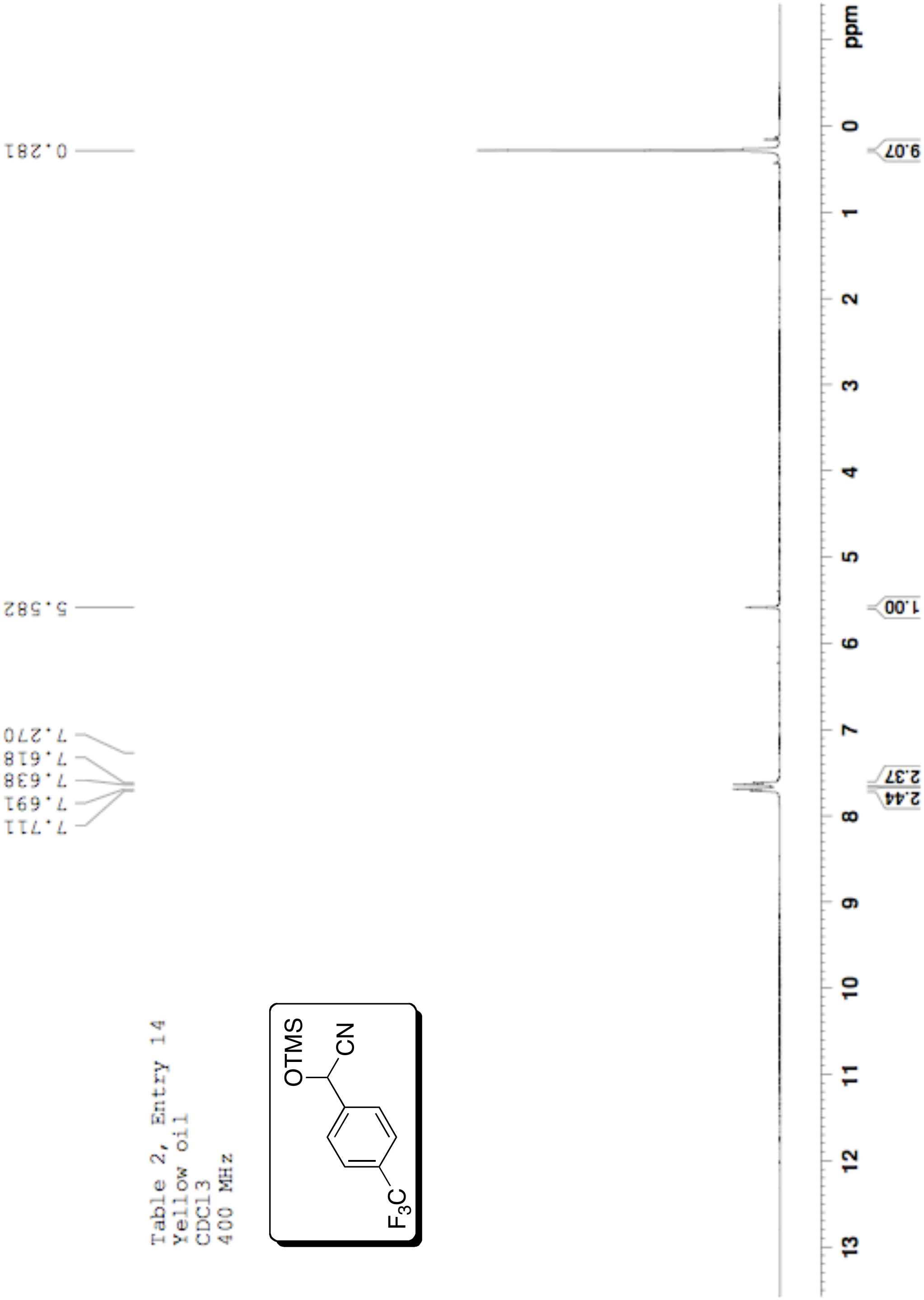
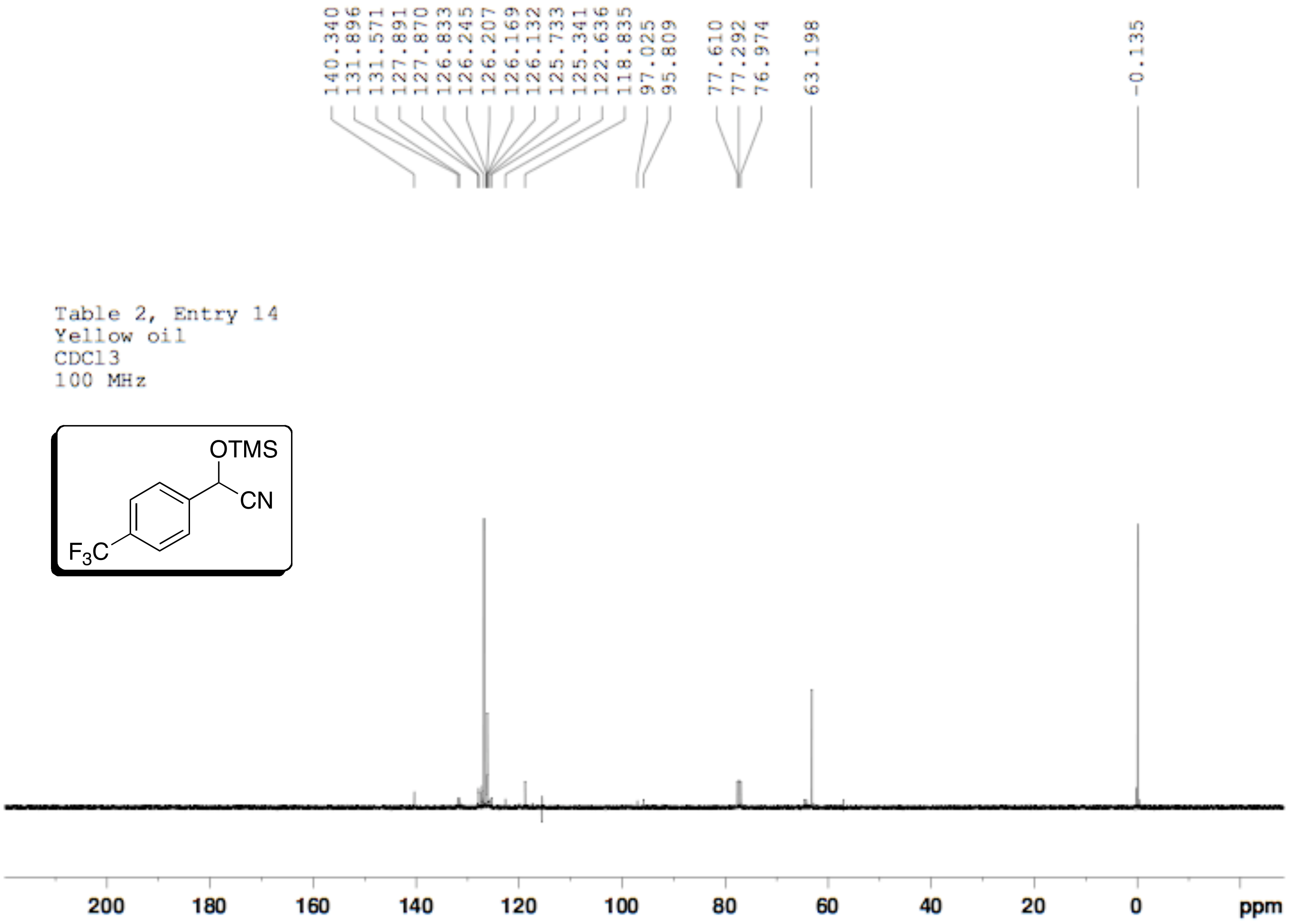


Table 2, Entry 13
Clear, colorless oil
CDCl3
100 MHz


0.281
5.582
7.270
7.618
7.638
7.691
7.711
Table 2, Entry 14
Yellow oil
CDCl3
400 MHz
OTMS
CN
F3C
9.07
1.00
2.37
2.44
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


140.340
131.896
131.571
127.891
127.870
126.833
126.245
126.207
126.169
126.132
125.733
125.341
122.636
118.835
97.025
95.809
77.610
77.292
76.974
63.198
-0.135
Table 2, Entry 14
Yellow oil
CDCl3
100 MHz
OTMS
CN
F3C
200
180
160
140
120
100
80
60
40
20
0
ppm

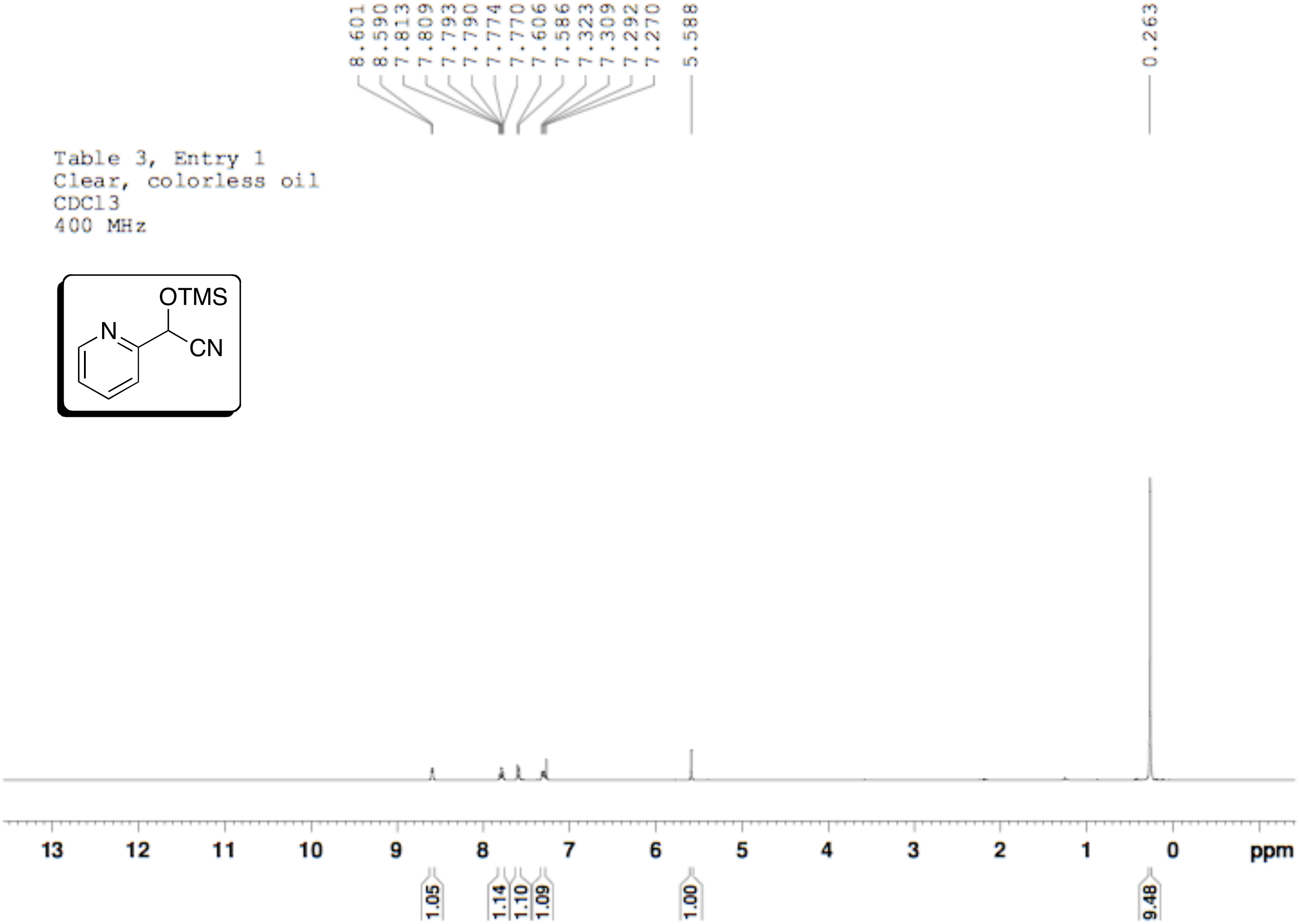


Table 3, Entry 1
Clear, colorless oil
CDCl3
400 MHz

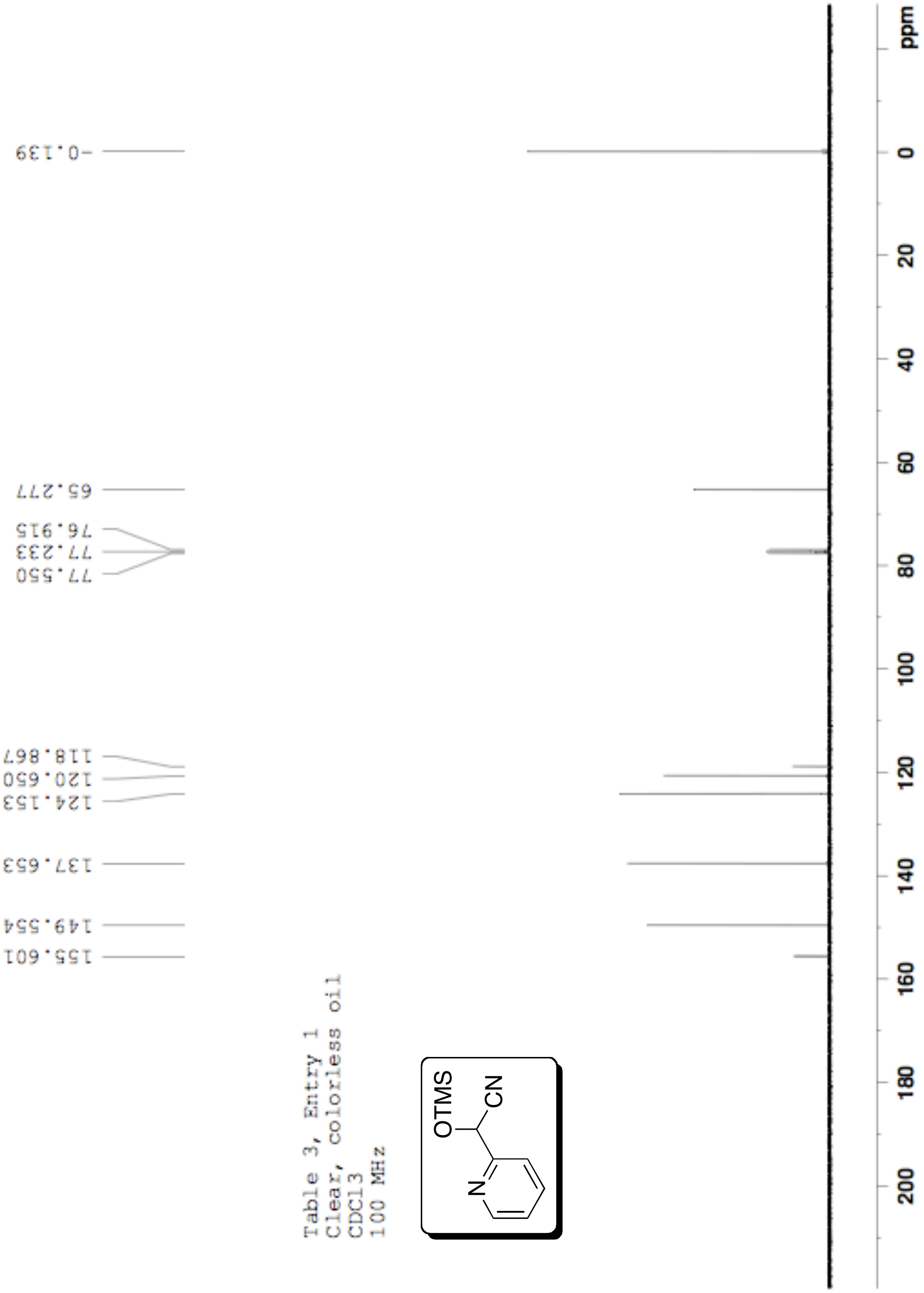
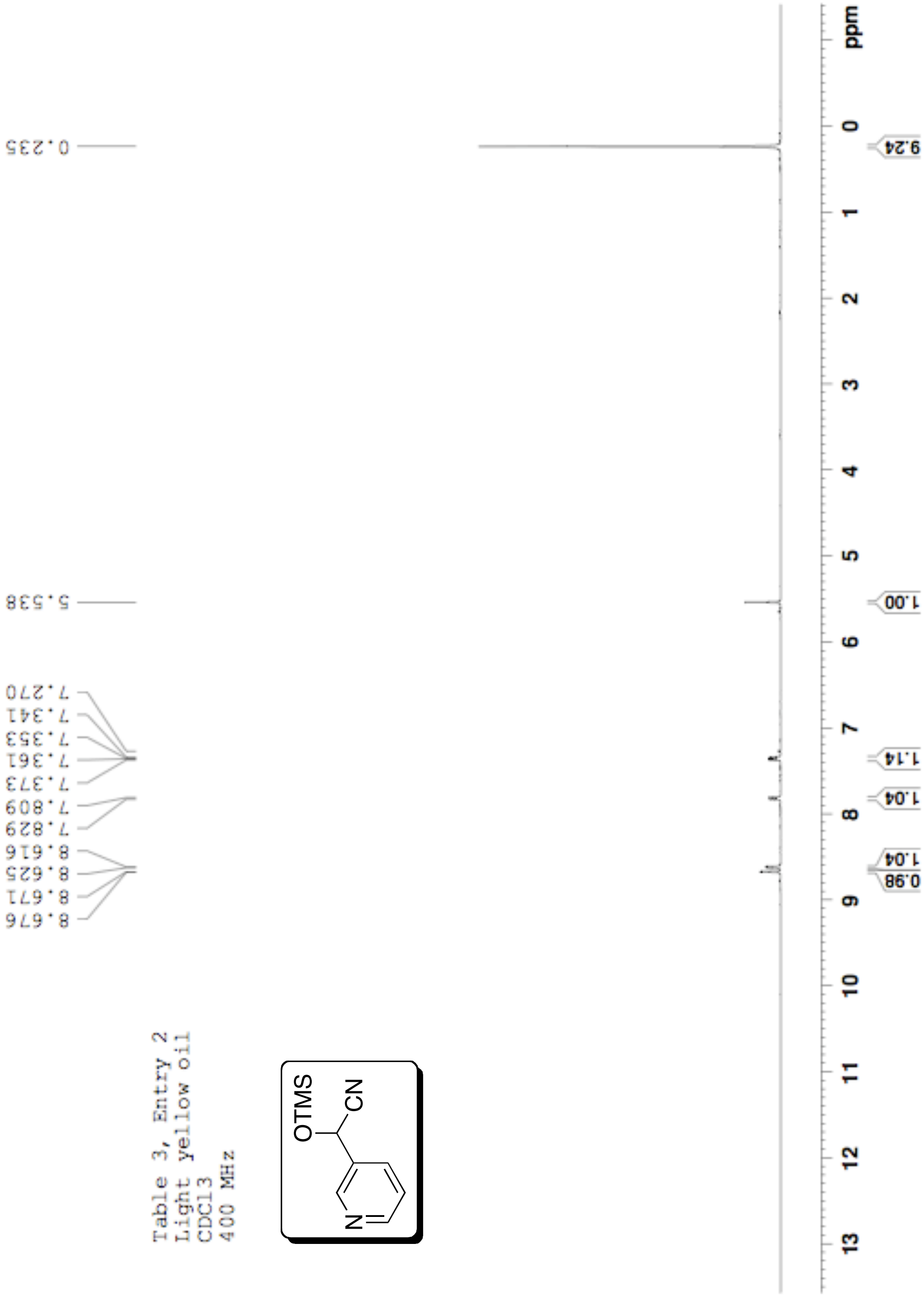
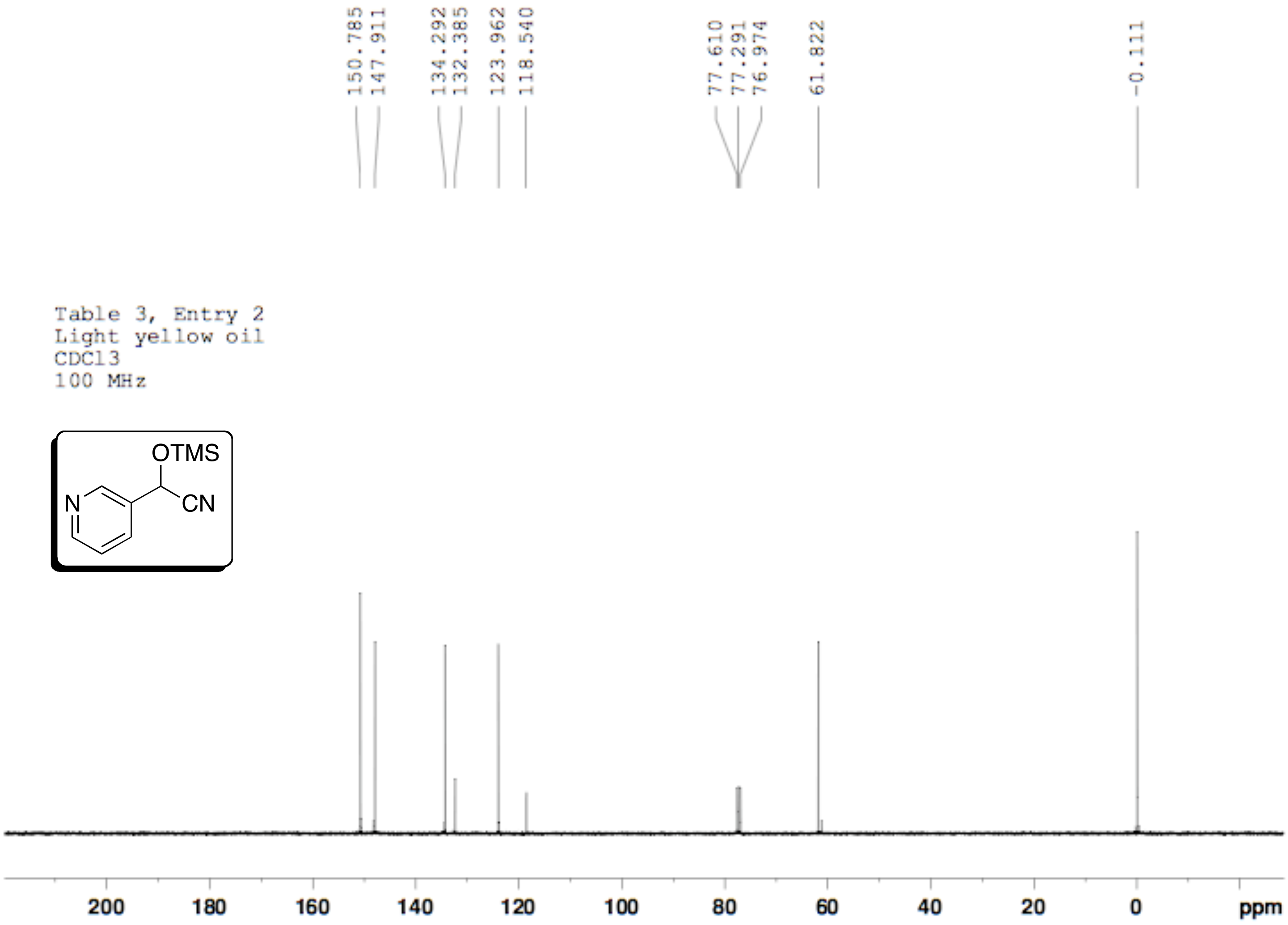
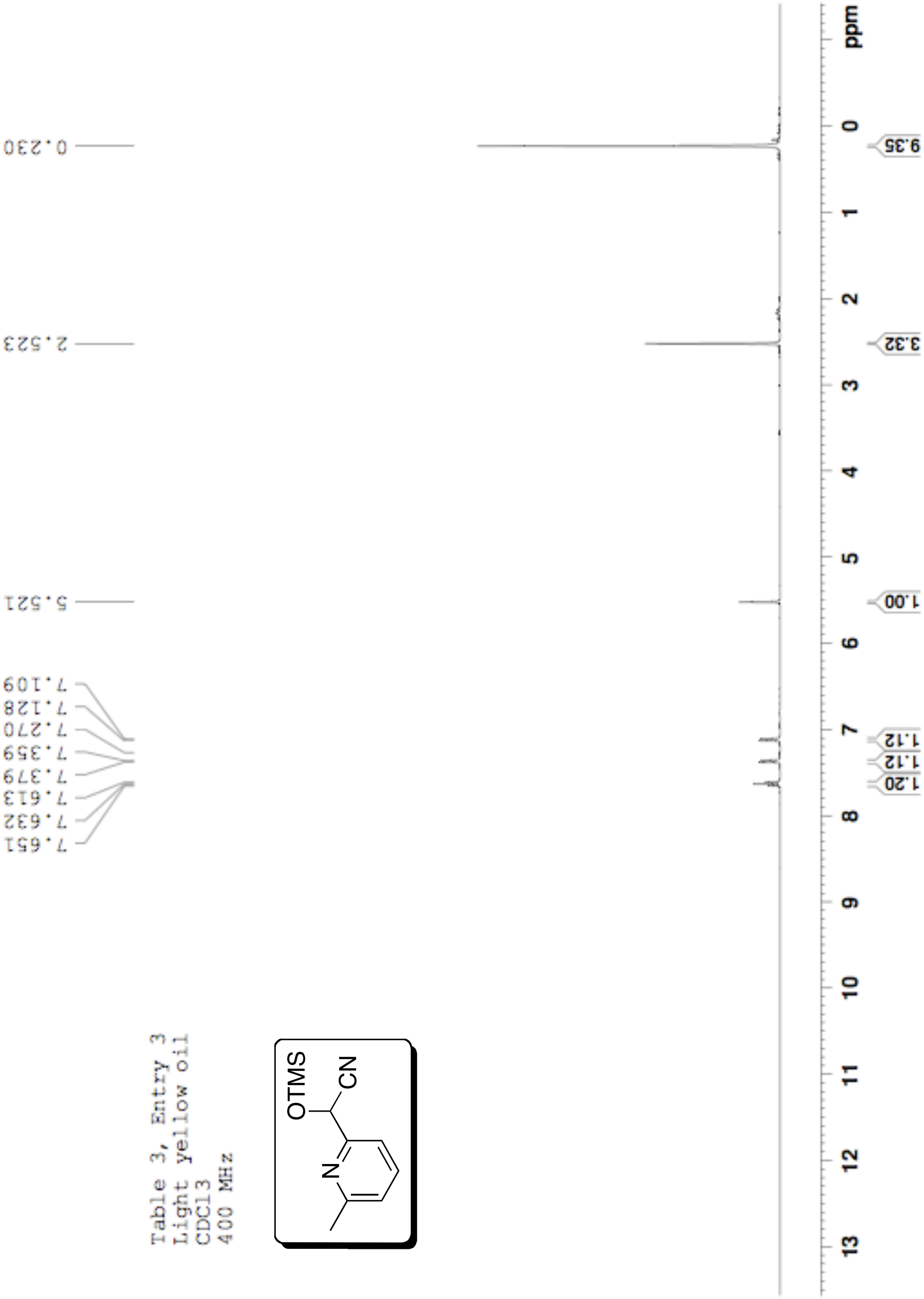
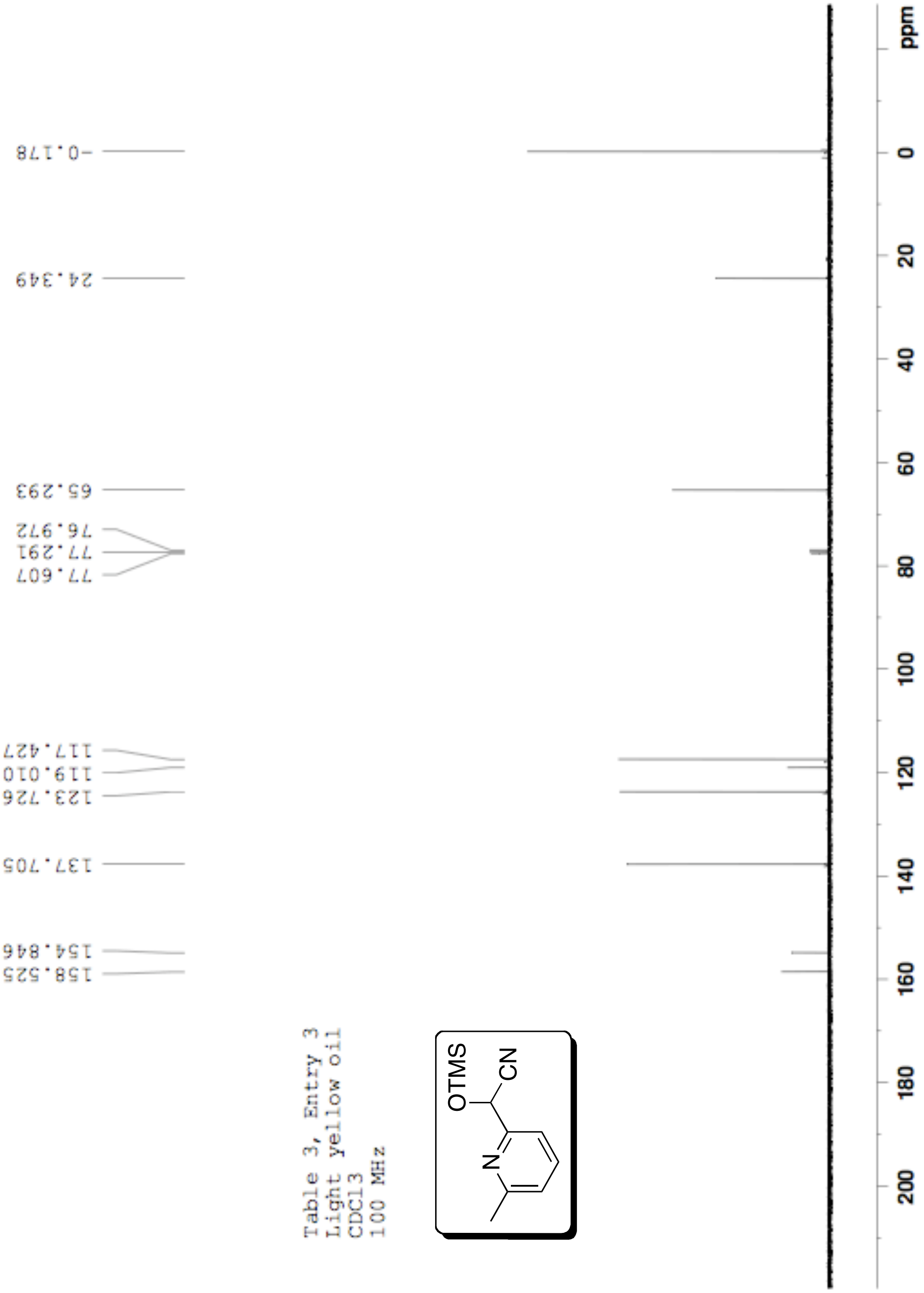


Table 3, Entry 1
Clear, colorless oil
CDCl3
100 MHz


0.235
5.538
7.270
7.341
7.353
7.361
7.373
7.809
7.829
8.616
8.625
8.671
8.676
Table 3, Entry 2
Light yellow oil
CDCl3
400 MHz
OTMS
CN
N
9.24
1.00
1.14
1.04
1.04
0.98
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


150.785
147.911
134.292
132.385
123.962
118.540
77.610
77.291
76.974
61.822
-0.111
Table 3, Entry 2
Light yellow oil
CDCl3
100 MHz
OTMS
N
CN
200
180
160
140
120
100
80
60
40
20
0
ppm


0.230
2.523
5.521
7.109
7.128
7.270
7.359
7.379
7.613
7.632
7.651
Table 3, Entry 3
Light yellow oil
CDCl3
400 MHz
OTMS
CN
N
9.35
3.32
1.00
1.12
1.12
1.20
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


-0.178
24.349
65.293
76.972
77.291
77.607
117.427
119.010
123.726
137.705
154.846
158.525
Table 3, Entry 3
Light yellow oil
CDCl3
100 MHz
OTMS
CN
N
ppm
0
20
40
60
80
100
120
140
160
180
200

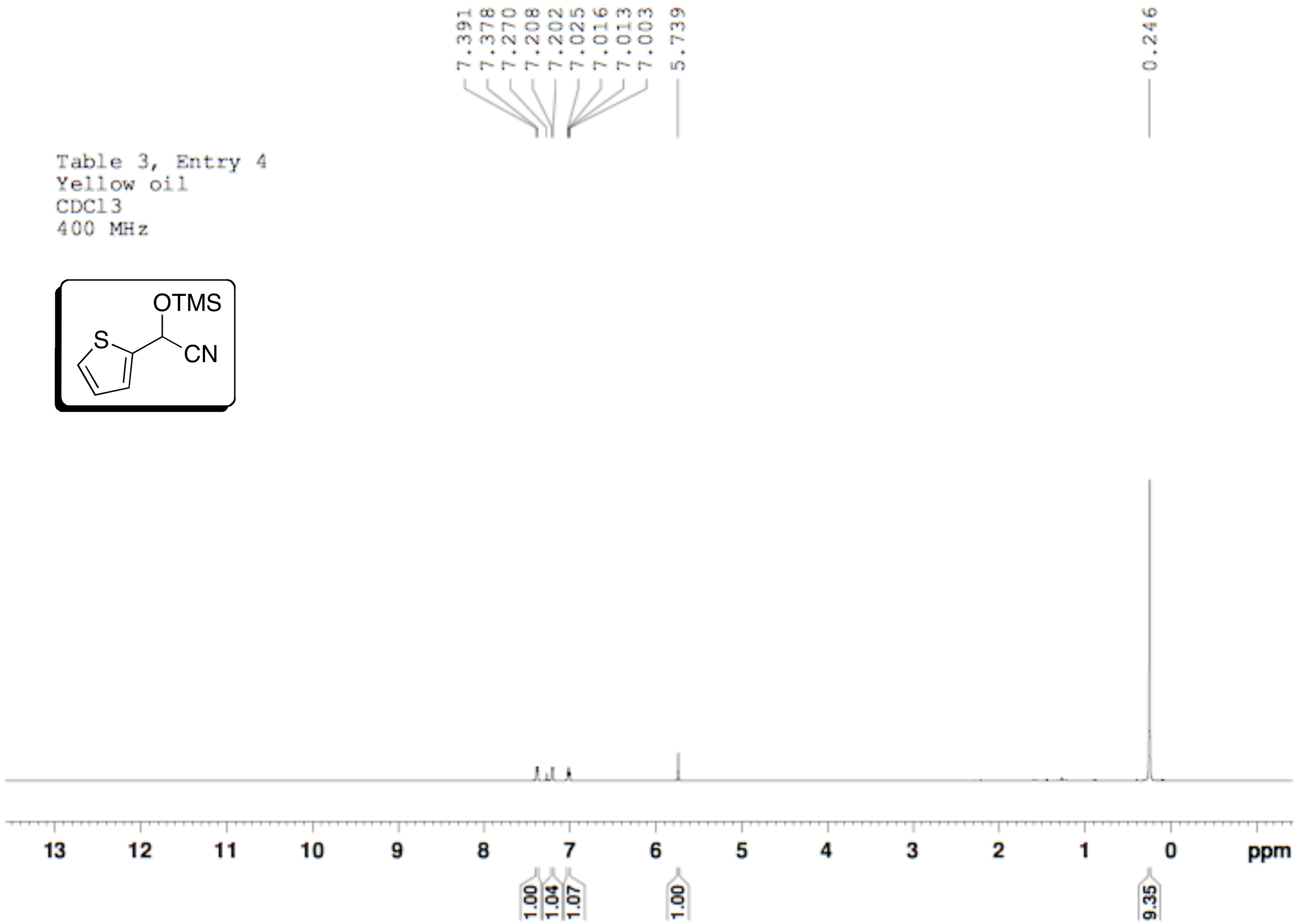


Table 3, Entry 4
Yellow oil
CDCl3
400 MHz

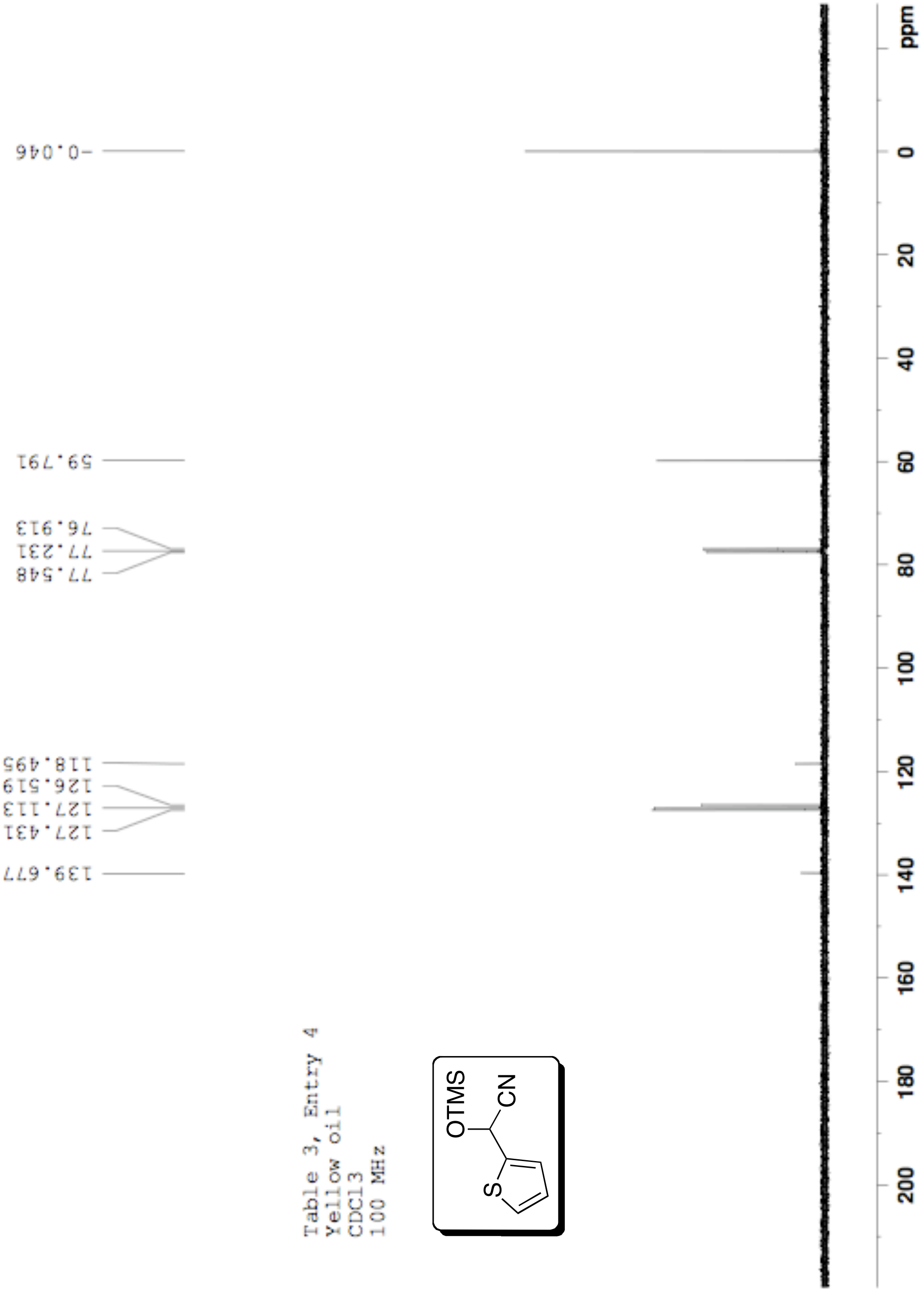


Table 3, Entry 4
Yellow oil
CDCl3
100 MHz

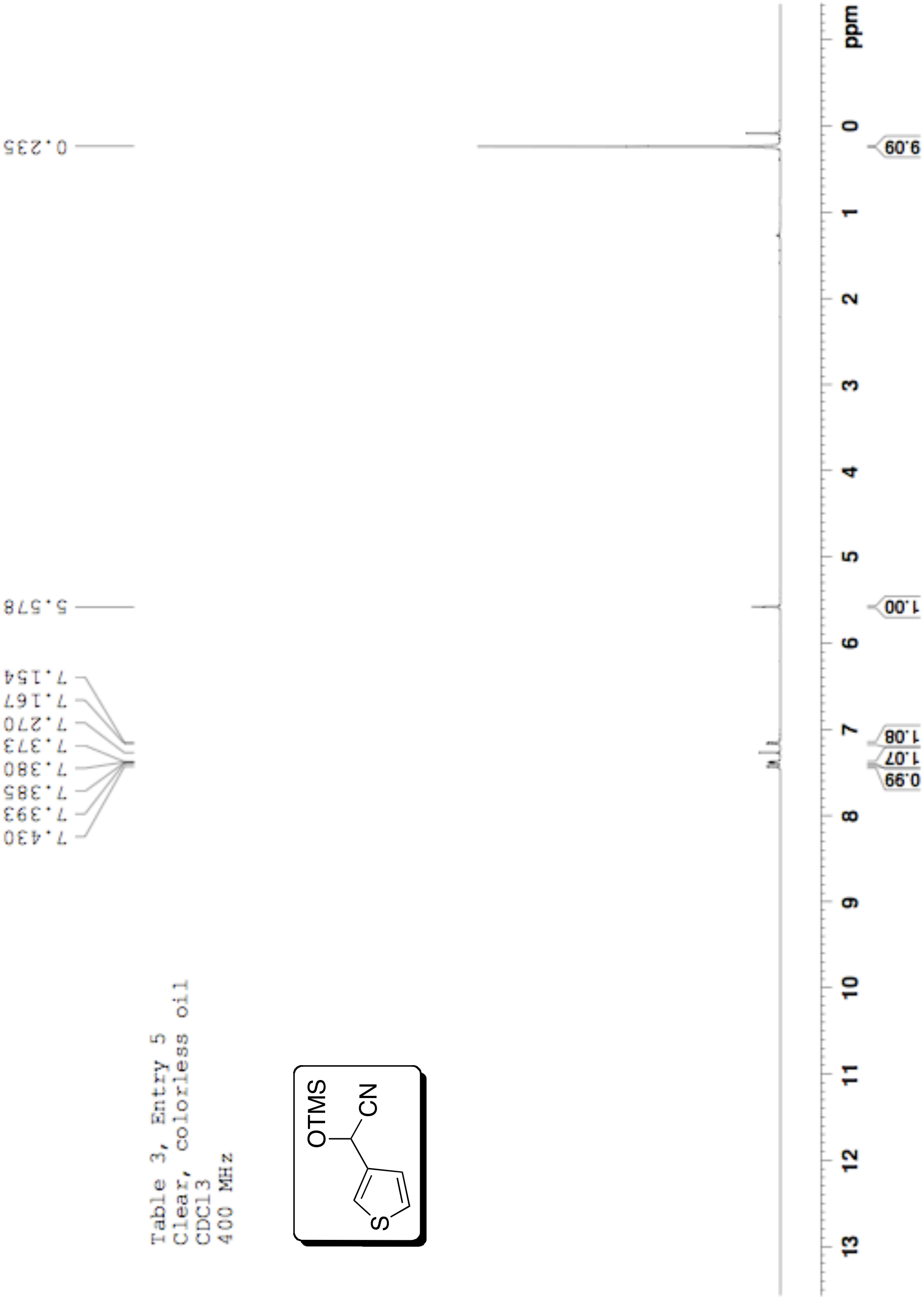


Table 3, Entry 5
Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
S
0.235
5.578
7.154
7.167
7.270
7.373
7.380
7.385
7.393
7.430
9.09
1.00
1.08
1.07
0.99
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

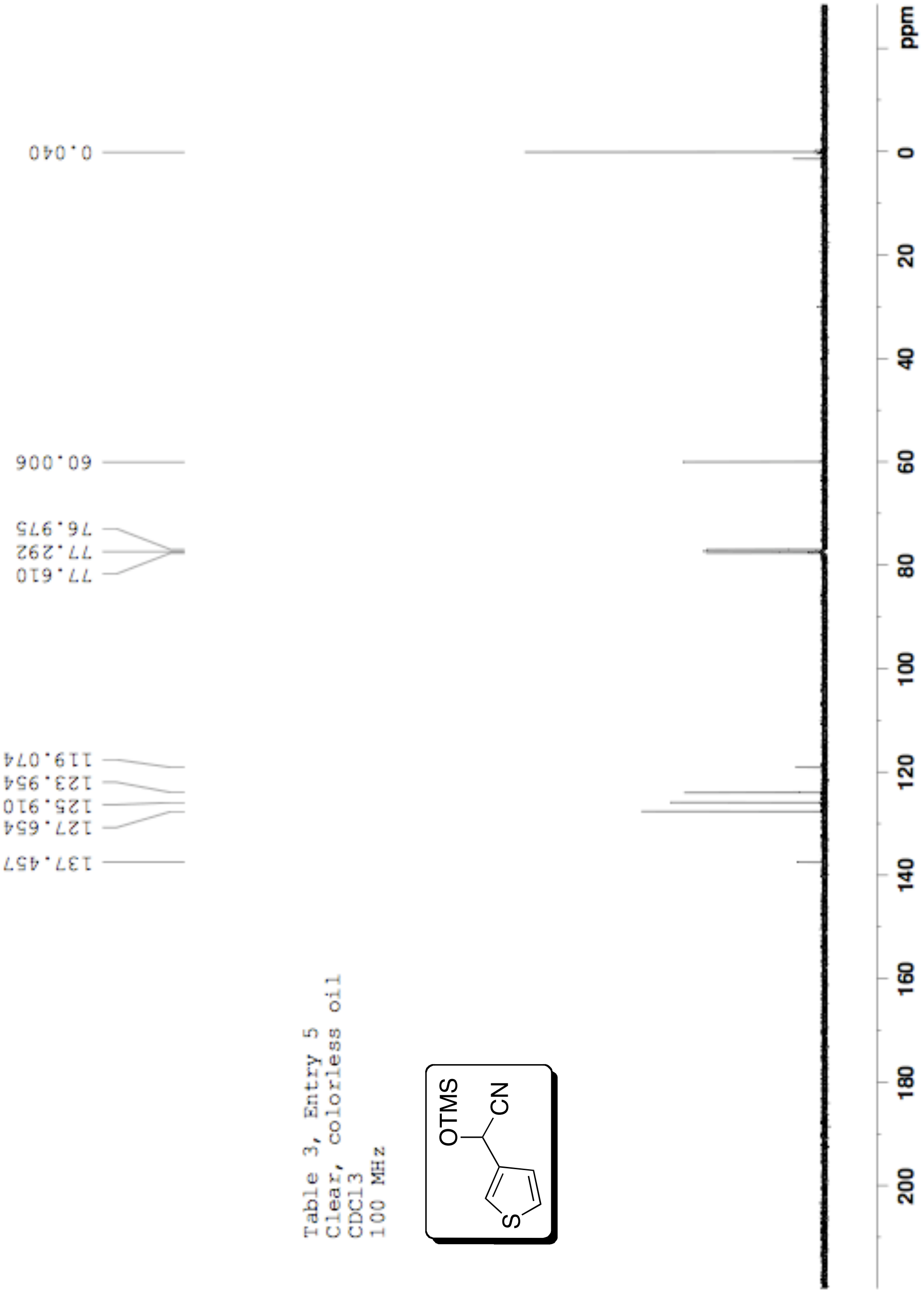
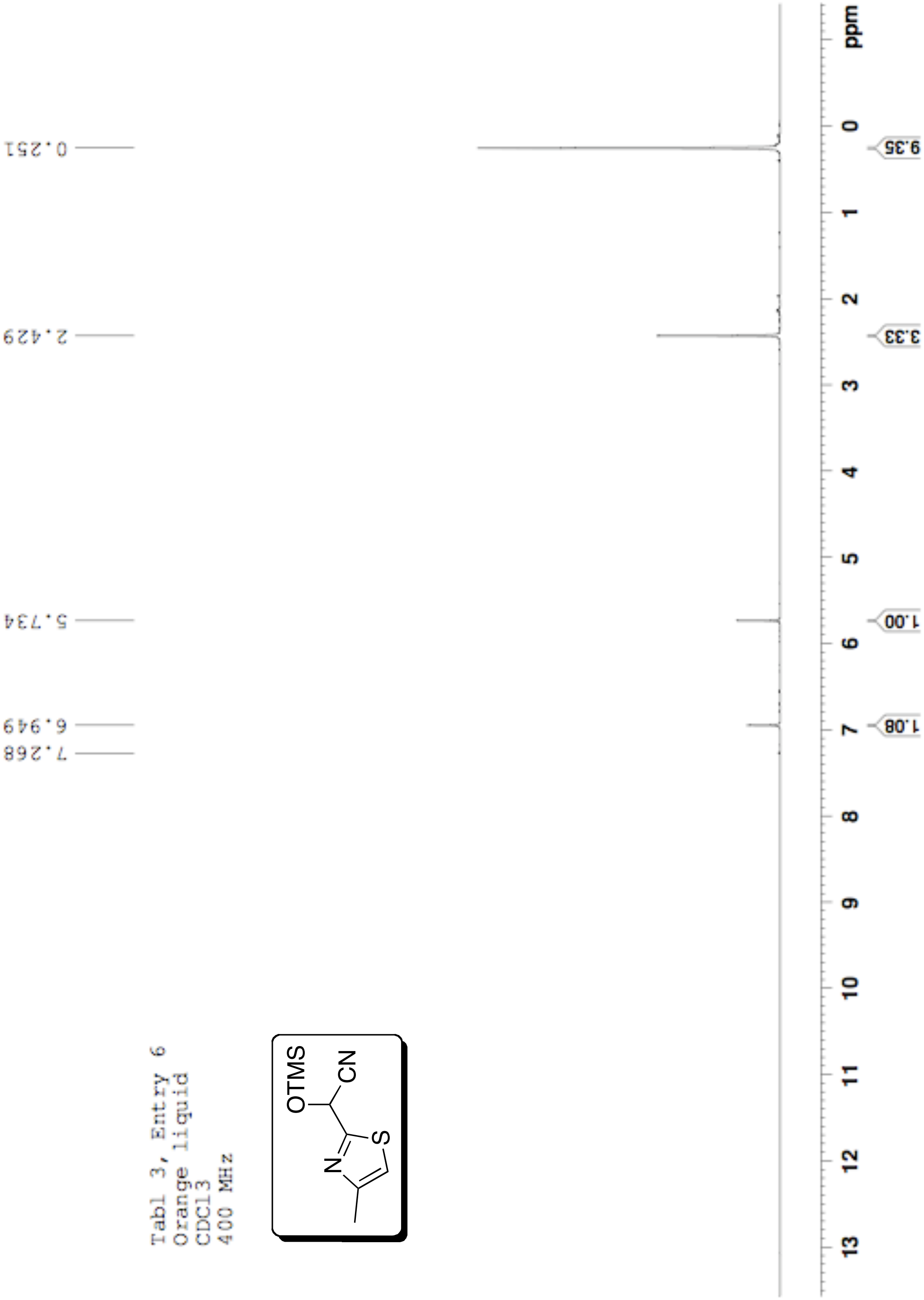
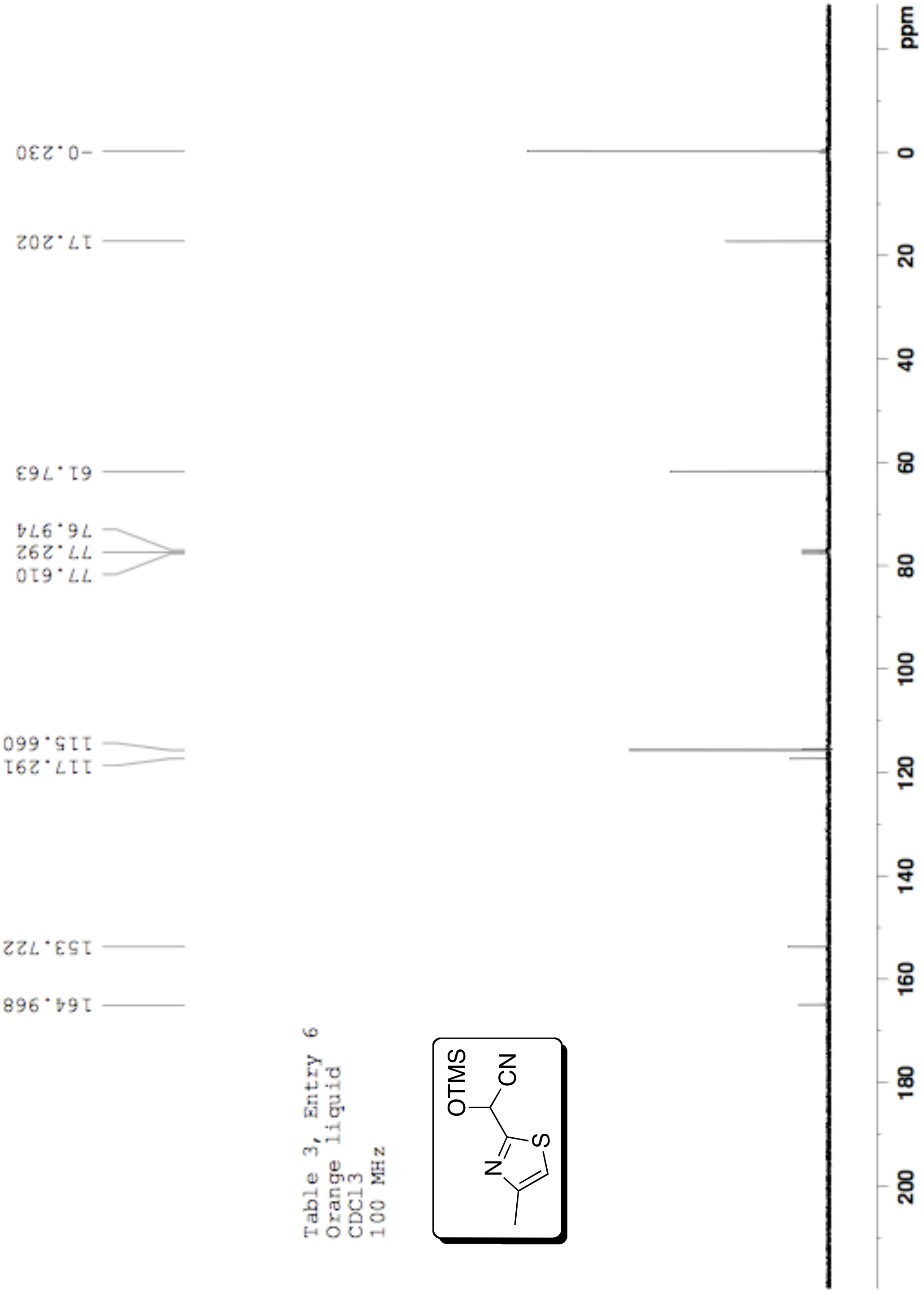
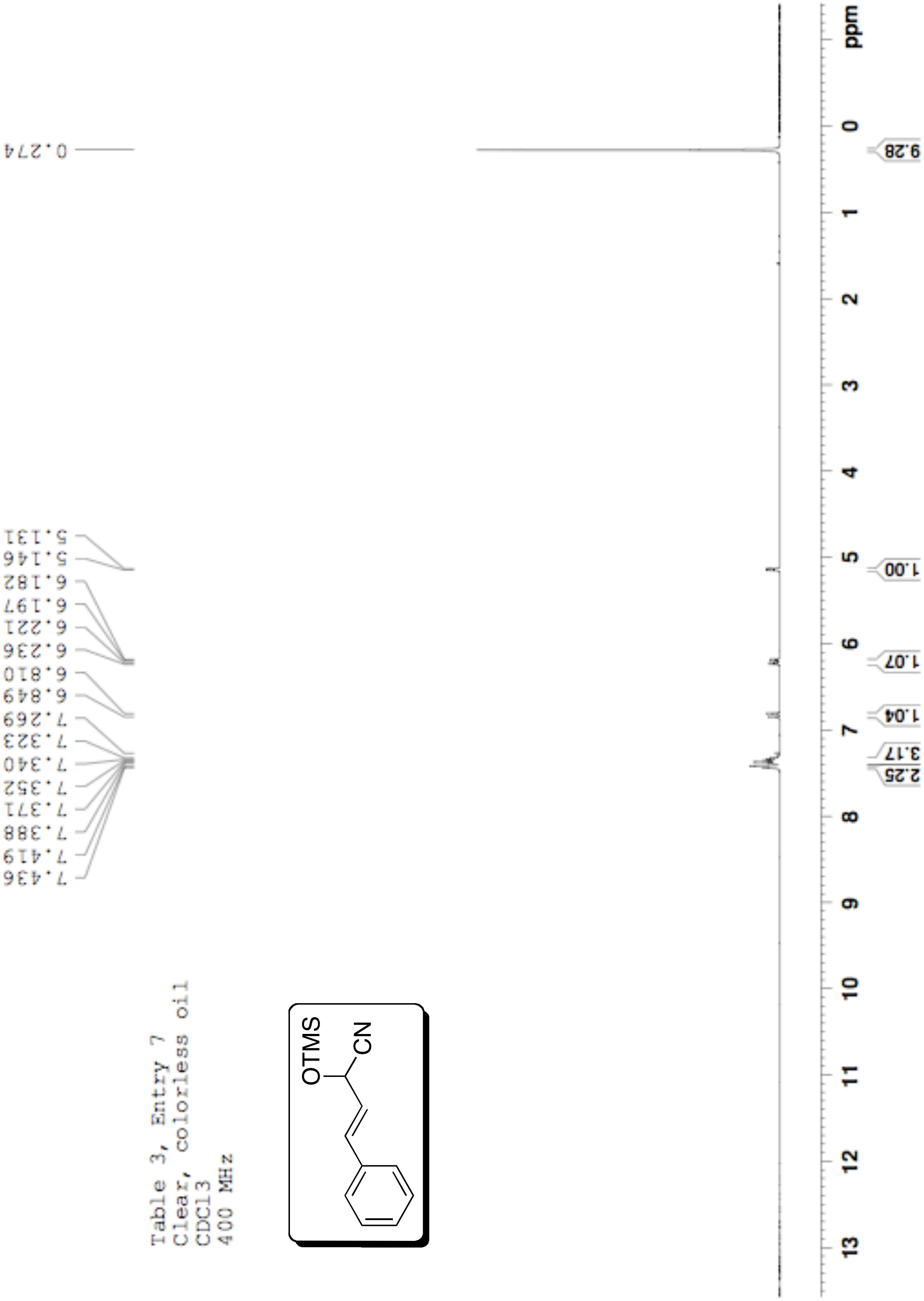


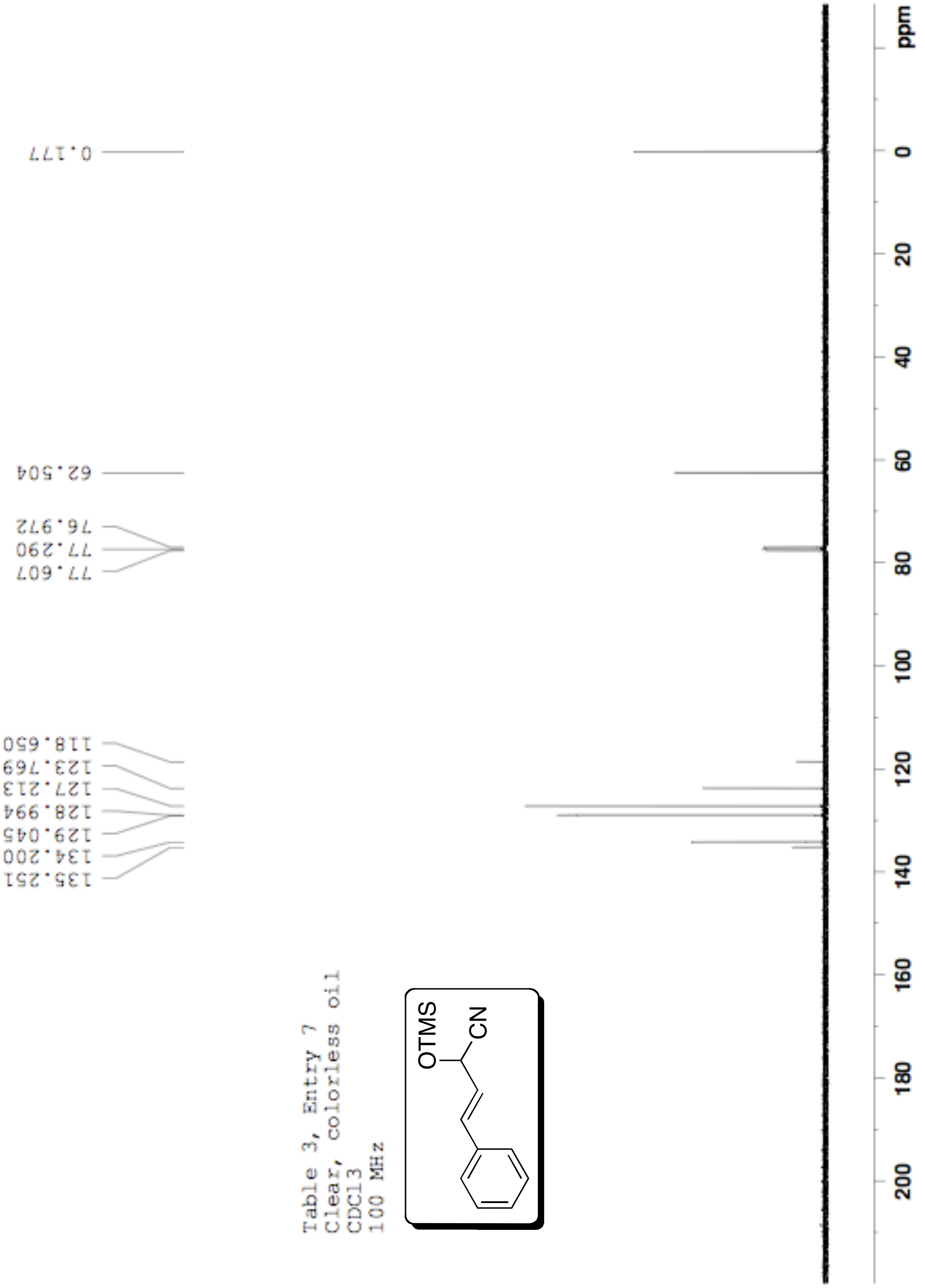
Table 3, Entry 5
Clear, colorless oil
CDCl3
100 MHz



Tabl 3, Entry 6
Orange liquid
CDCl3
400 MHz


-0.230
17.202
61.763
76.974
77.292
77.610
115.660
117.291
153.722
164.968
Table 3, Entry 6
Orange liquid
CDCl3
100 MHz
OTMS
CN
N
S
ppm
0
20
40
60
80
100
120
140
160
180
200


0.274
5.131
5.146
6.182
6.197
6.221
6.236
6.810
6.849
7.269
7.323
7.340
7.352
7.371
7.388
7.419
7.436
Table 3, Entry 7
Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
9.28
1.00
1.07
1.04
3.17
2.25
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


0.177
62.504
76.972
77.290
77.607
118.650
123.769
127.213
128.994
129.045
134.200
135.251
Table 3, Entry 7
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
ppm
0
20
40
60
80
100
120
140
160
180
200

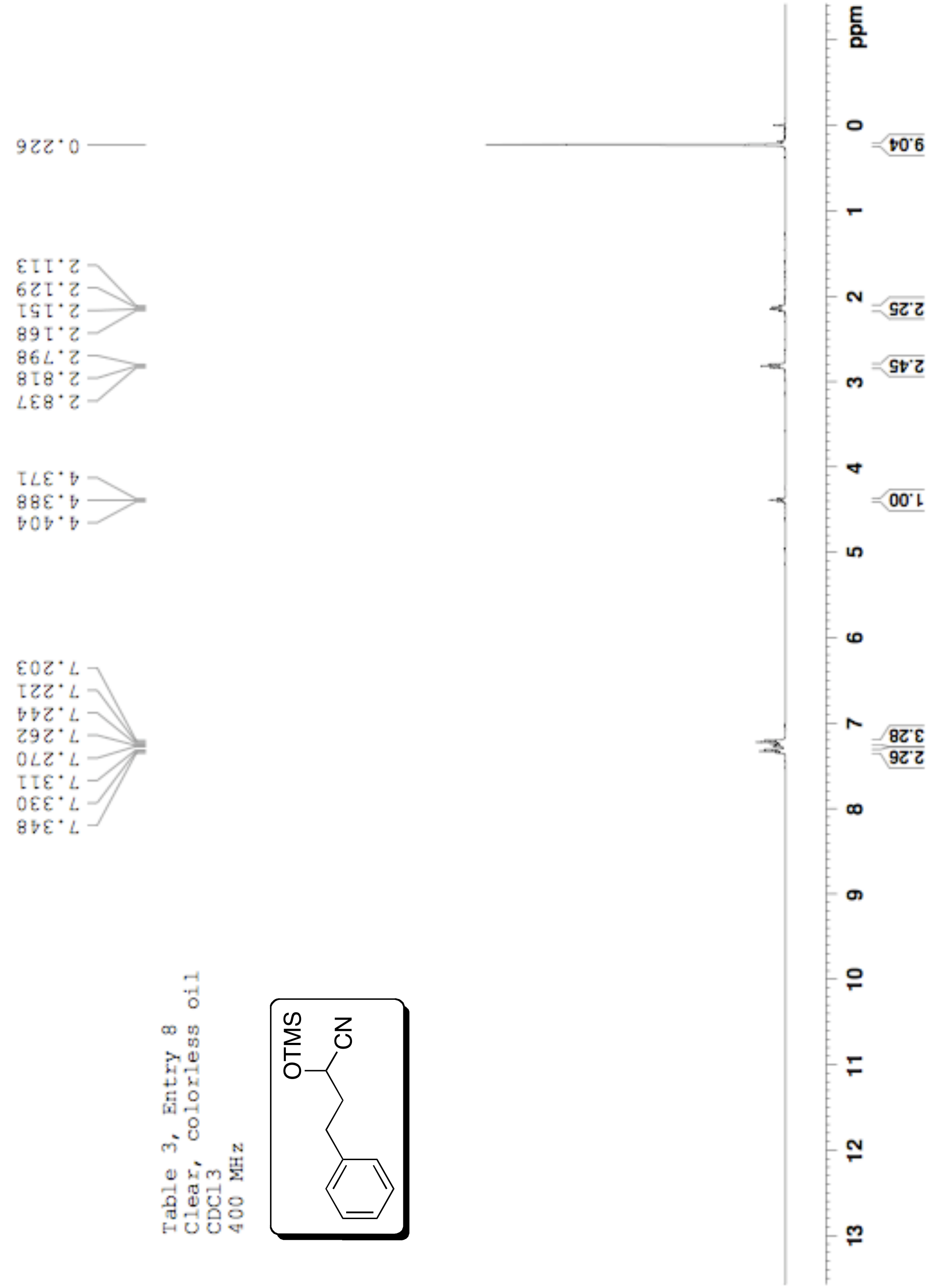
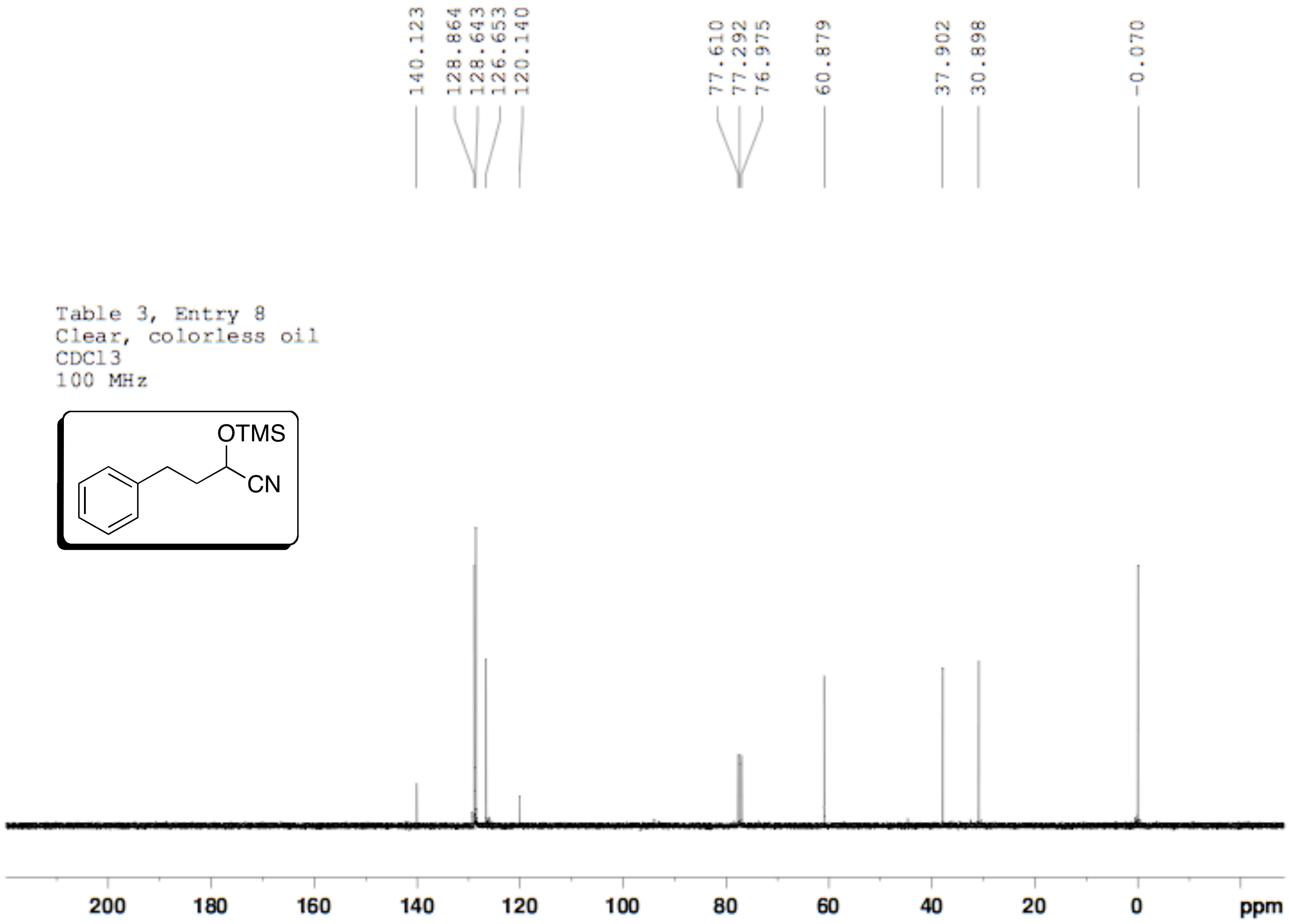


Table 3, Entry 8
Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
0.226
2.113
2.129
2.151
2.168
2.798
2.818
2.837
4.371
4.388
4.404
7.203
7.221
7.244
7.262
7.270
7.311
7.330
7.348
9.04
2.25
2.45
1.00
3.28
2.26
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


140.123
128.864
128.643
126.653
120.140
77.610
77.292
76.975
60.879
37.902
30.898
-0.070
Table 3, Entry 8
Clear, colorless oil
CDCl3
100 MHz
OTMS
CN
200
180
160
140
120
100
80
60
40
20
0
ppm

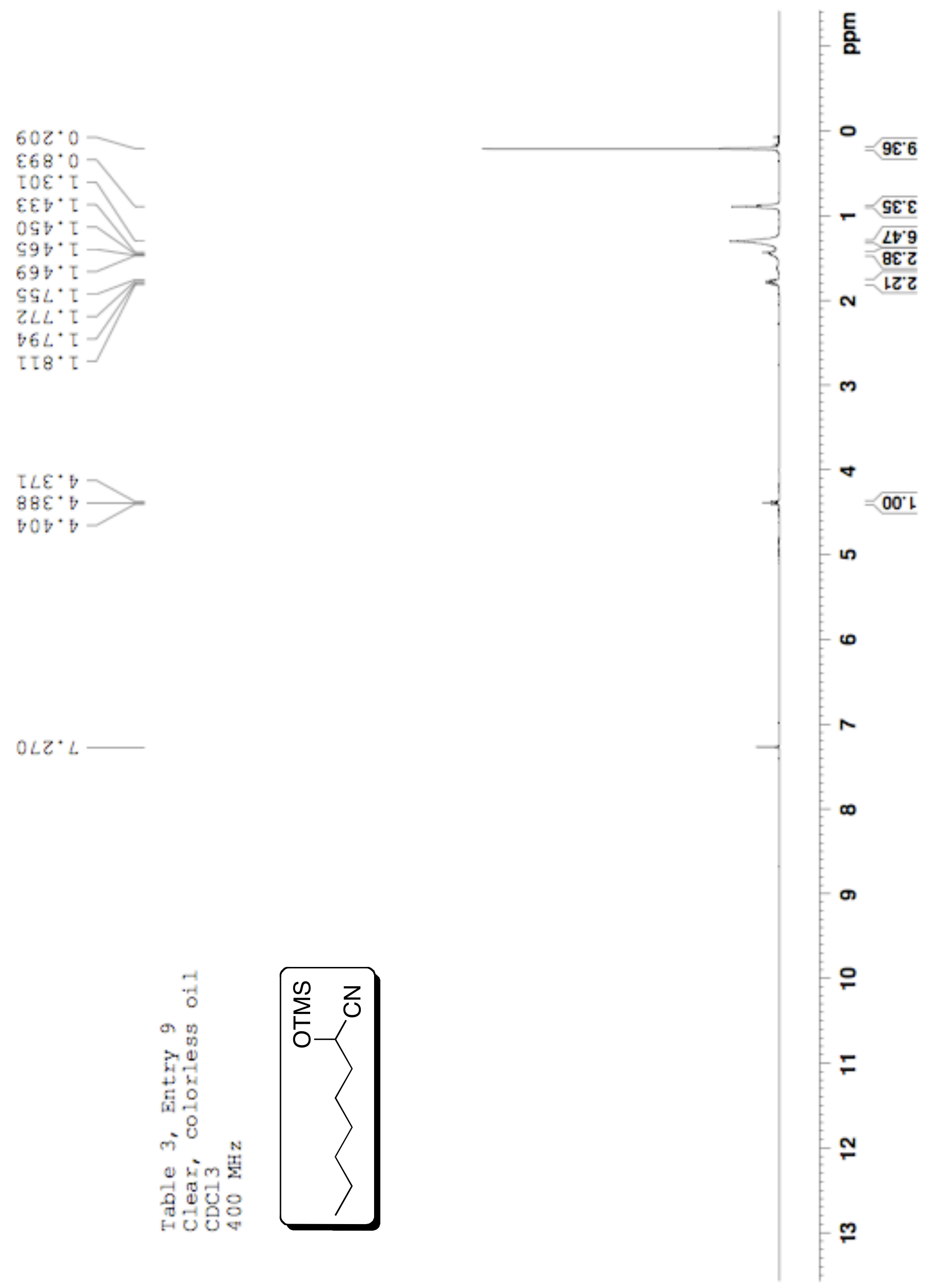


Table 3, Entry 9
Clear, colorless oil
CDCl3
400 MHz
OTMS
CN
0.209
0.893
1.301
1.433
1.450
1.465
1.469
1.755
1.772
1.794
1.811
4.371
4.388
4.404
7.270
9.36
3.35
6.47
2.38
2.21
1.00
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

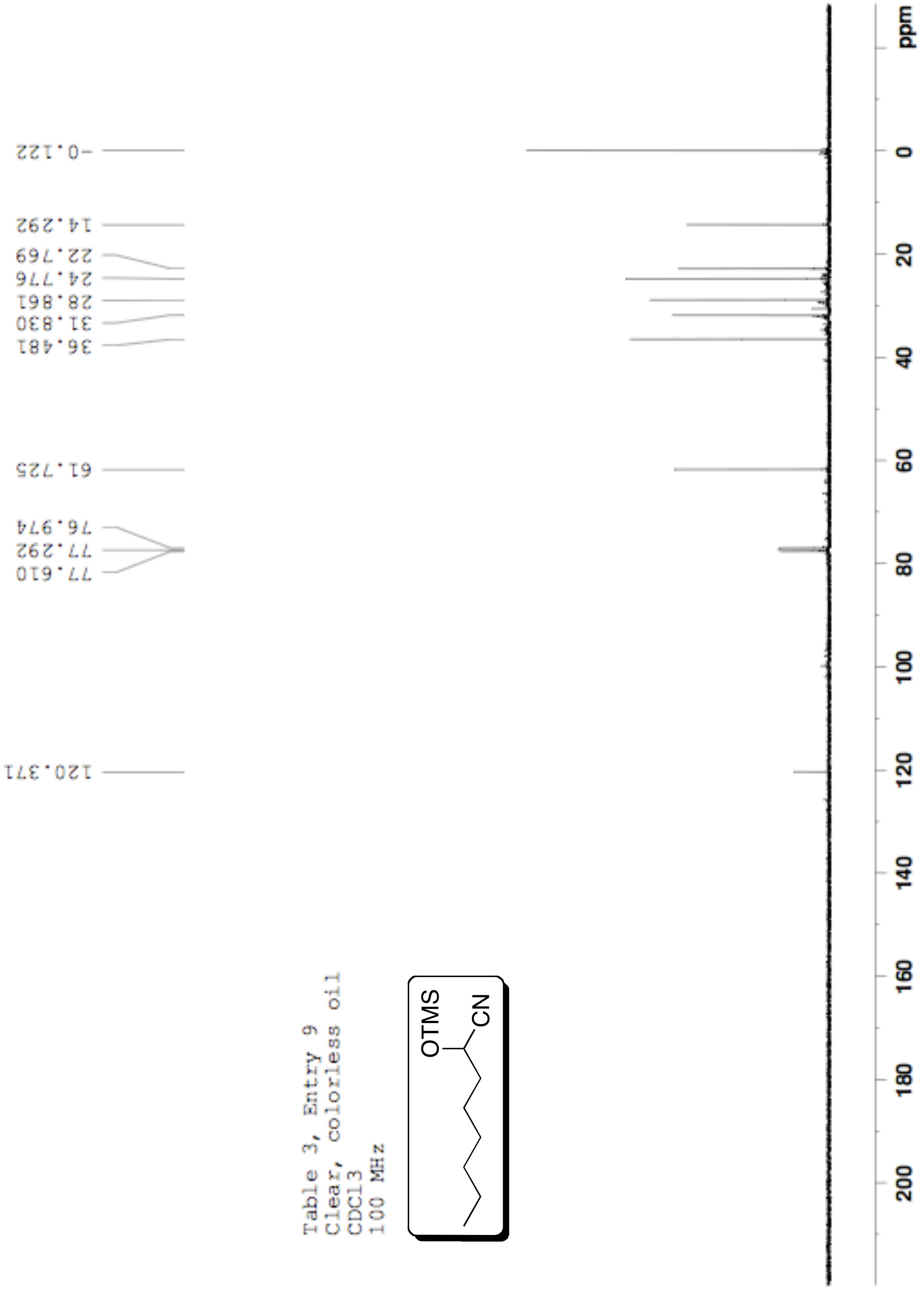
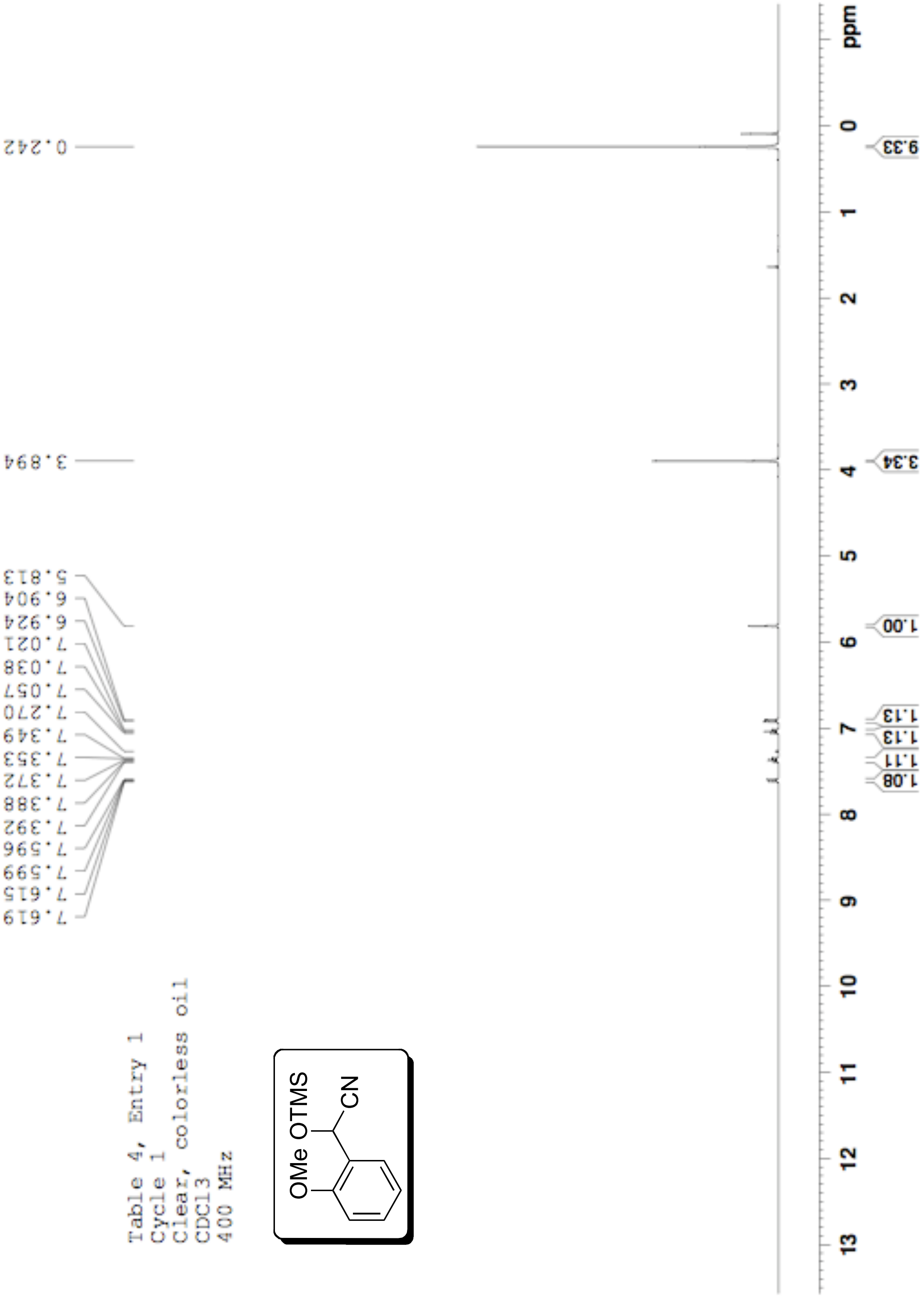
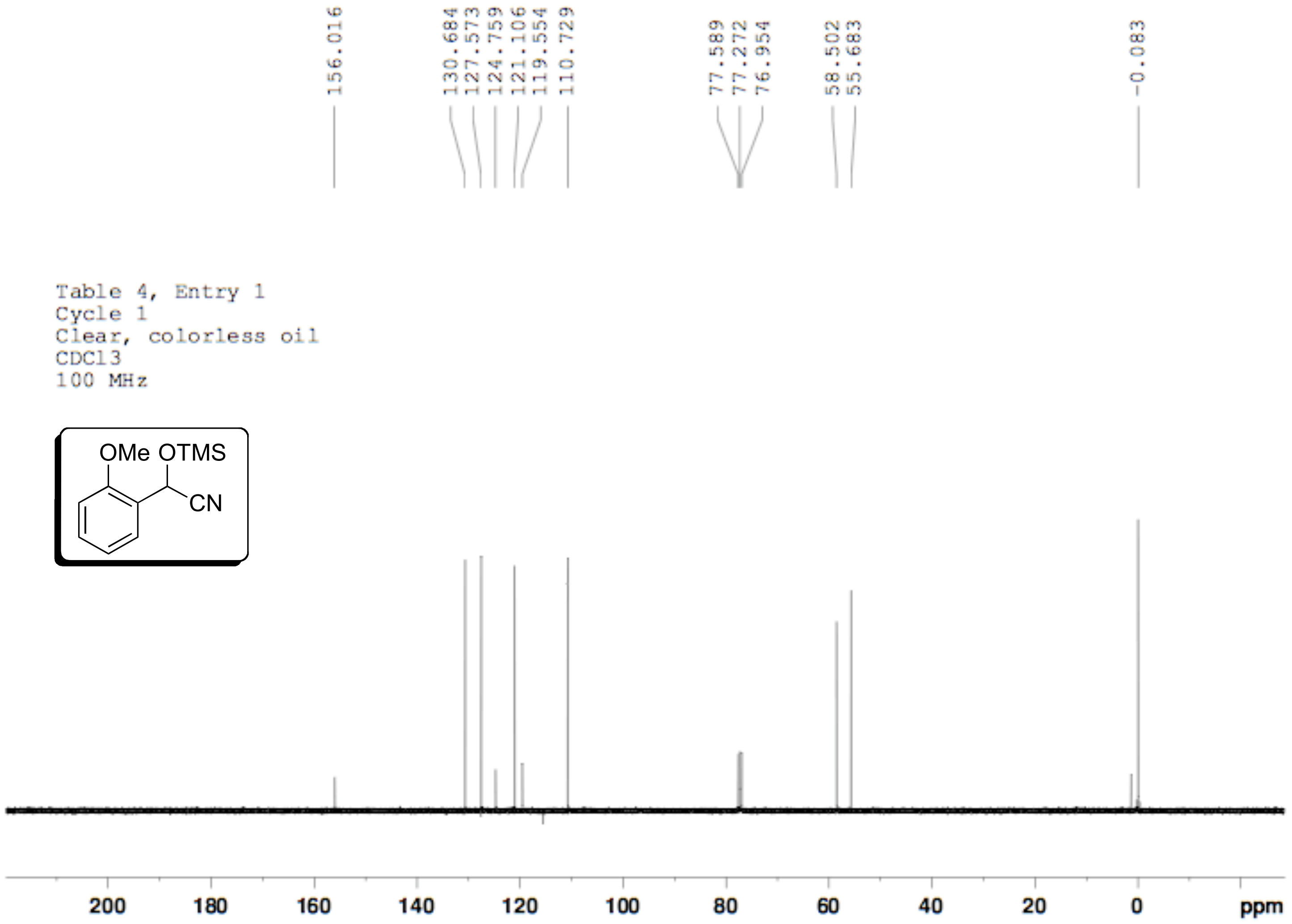
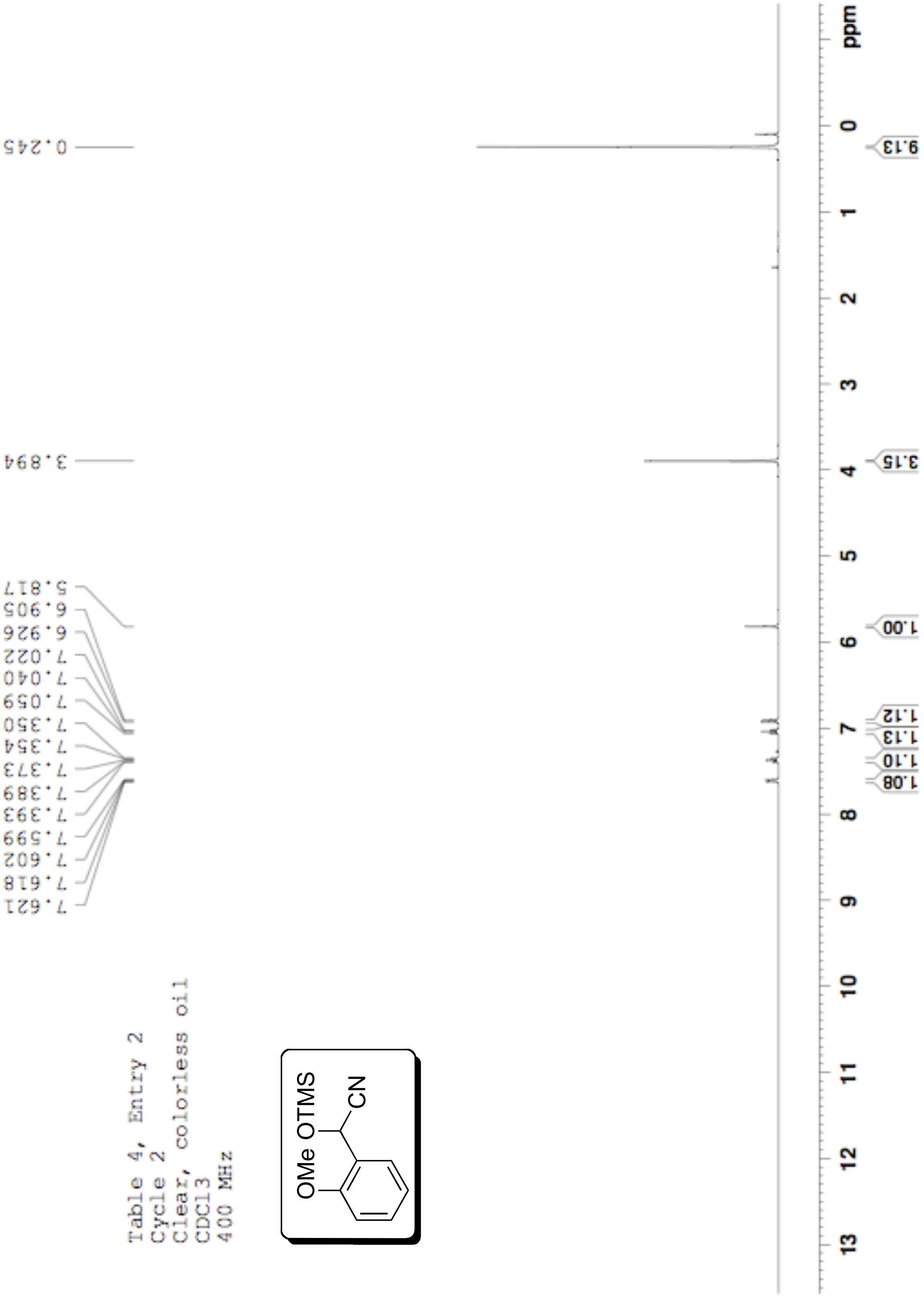


Table 3, Entry 9
Clear, colorless oil
CDCl3
100 MHz


0.242
3.894
5.813
6.904
6.924
7.021
7.038
7.057
7.270
7.349
7.353
7.372
7.388
7.392
7.596
7.599
7.615
7.619
Table 4, Entry 1
Cycle 1
Clear, colorless oil
CDCl3
400 MHz
OMe
OTMS
CN
9.33
3.34
1.00
1.13
1.13
1.11
1.08
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


156.016
130.684
127.573
124.759
121.106
119.554
110.729
77.589
77.272
76.954
58.502
55.683
-0.083
Table 4, Entry 1
Cycle 1
Clear, colorless oil
CDCl3
100 MHz
OMe OTMS
CN
200
180
160
140
120
100
80
60
40
20
0
ppm


0.245
3.894
5.817
6.905
6.926
7.022
7.040
7.059
7.350
7.354
7.373
7.389
7.393
7.599
7.602
7.618
7.621
Table 4, Entry 2
Cycle 2
Clear, colorless oil
CDCl3
400 MHz
OMe OTMS
CN
9.13
3.15
1.00
1.12
1.13
1.10
1.08
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

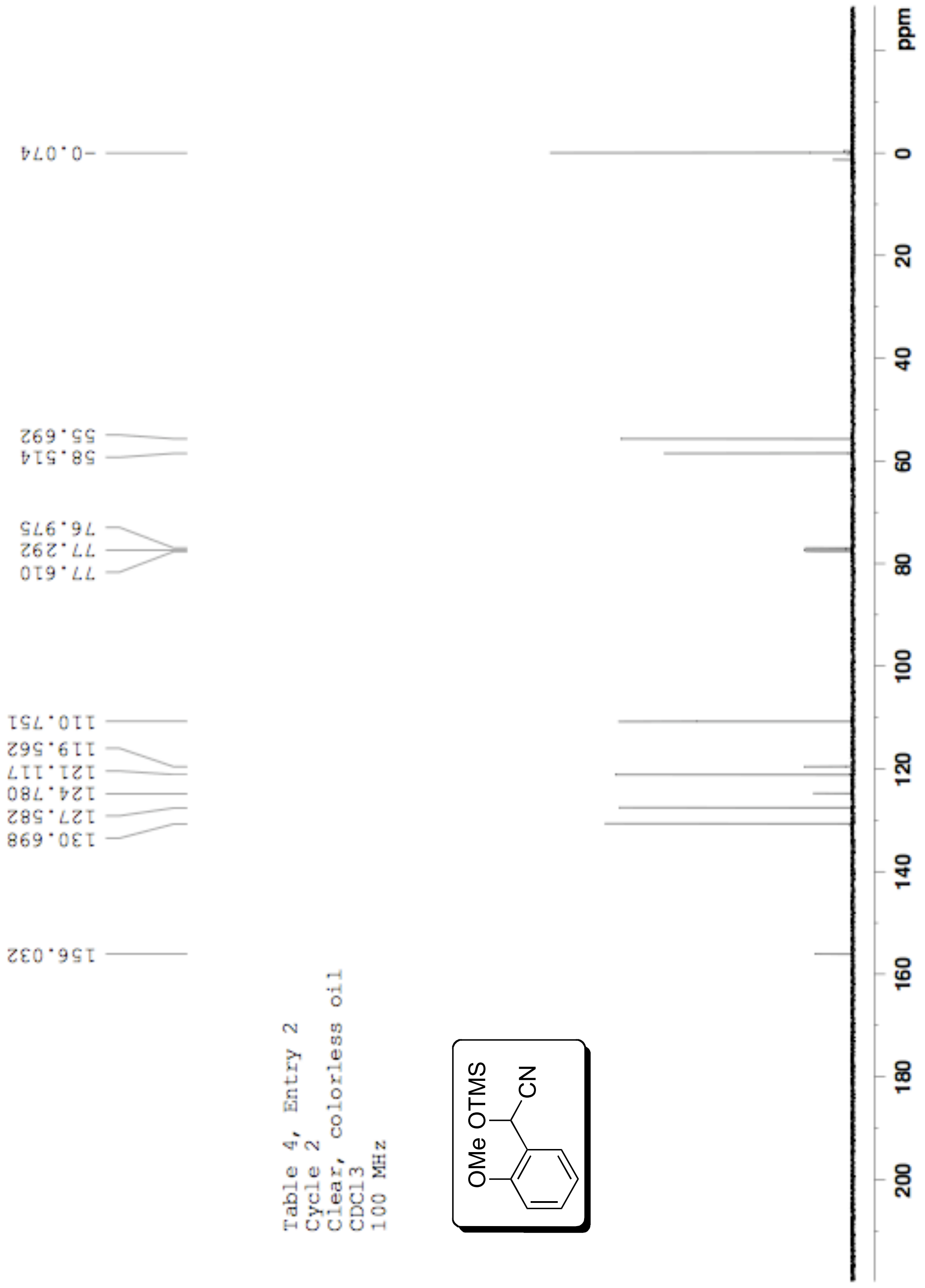
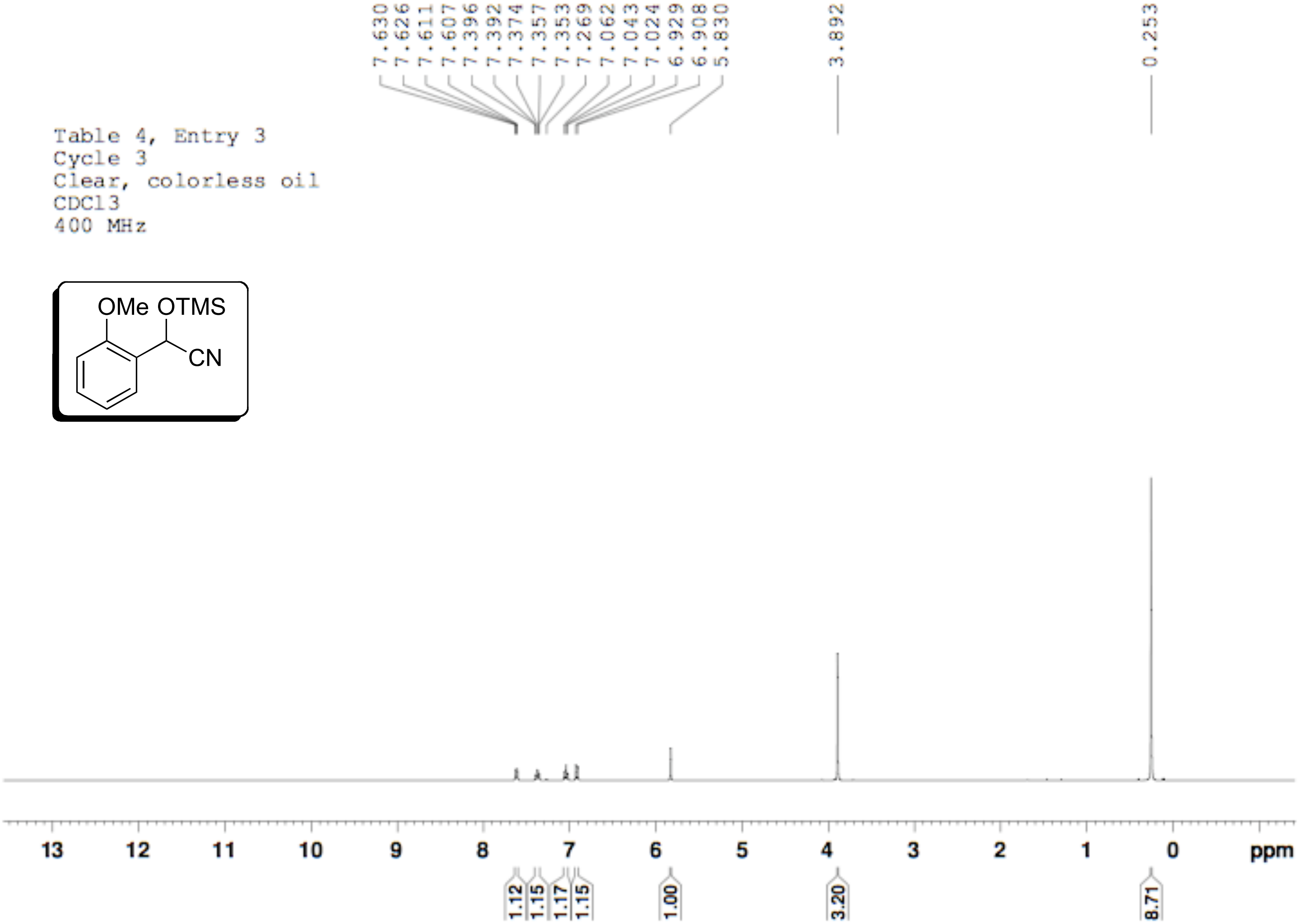


Table 4, Entry 2
Cycle 2
Clear, colorless oil
CDCl3
100 MHz

Table 4, Entry 3
Cycle 3
Clear, colorless oil
CDCl3
400 MHz



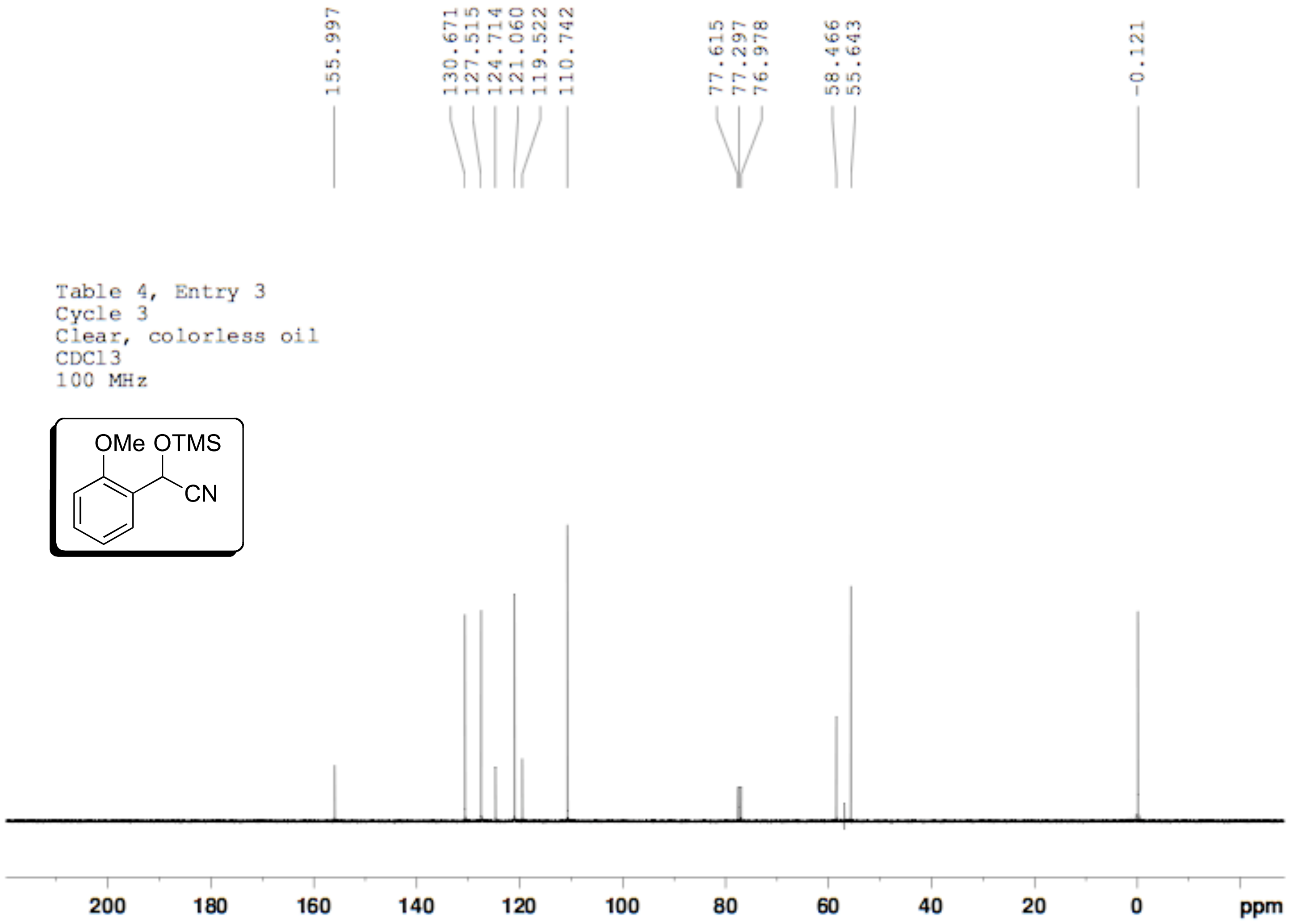


Table 4, Entry 3
Cycle 3
Clear, colorless oil
CDCl3
100 MHz

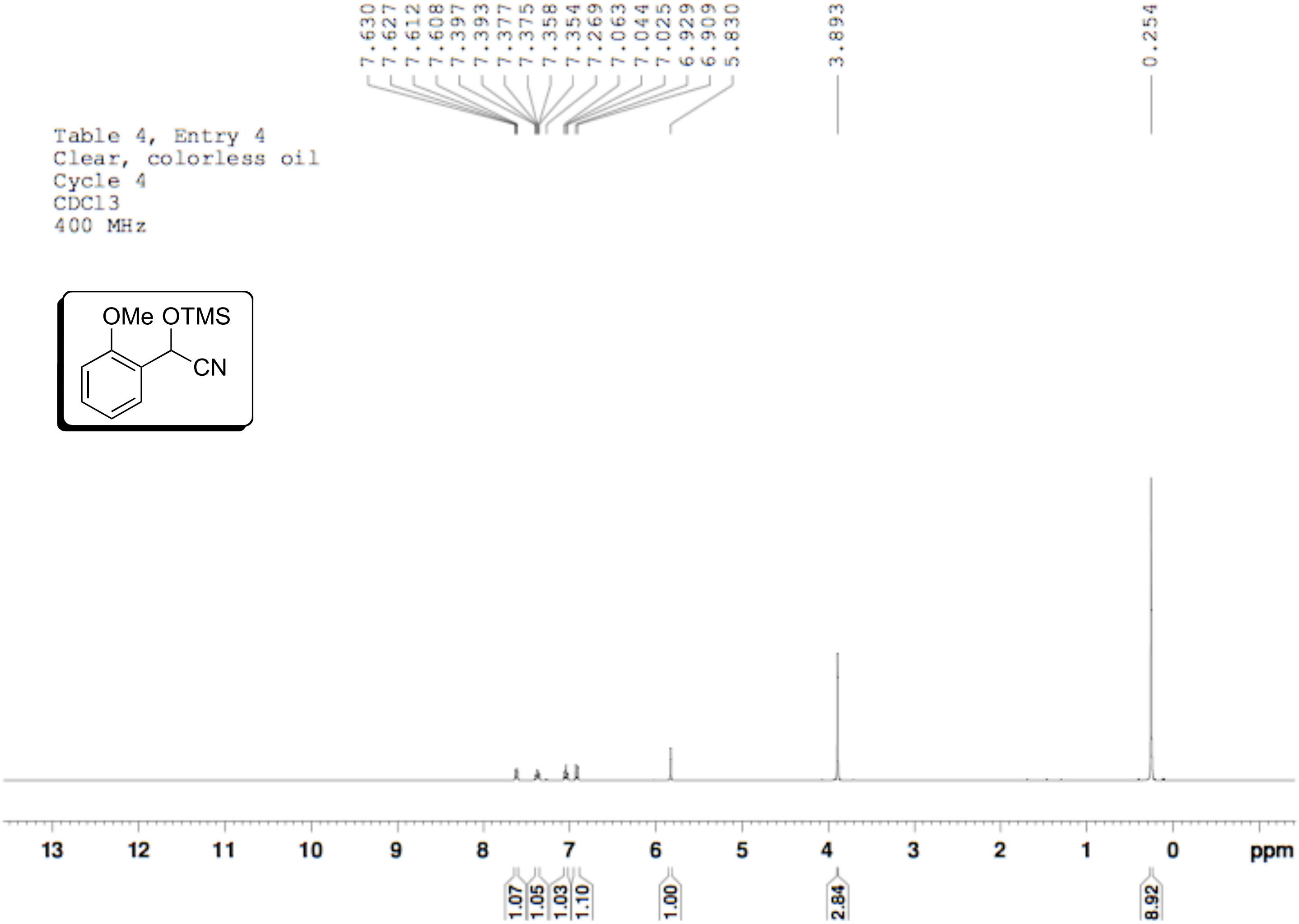


Table 4, Entry 4
Clear, colorless oil
Cycle 4
CDCl3
400 MHz

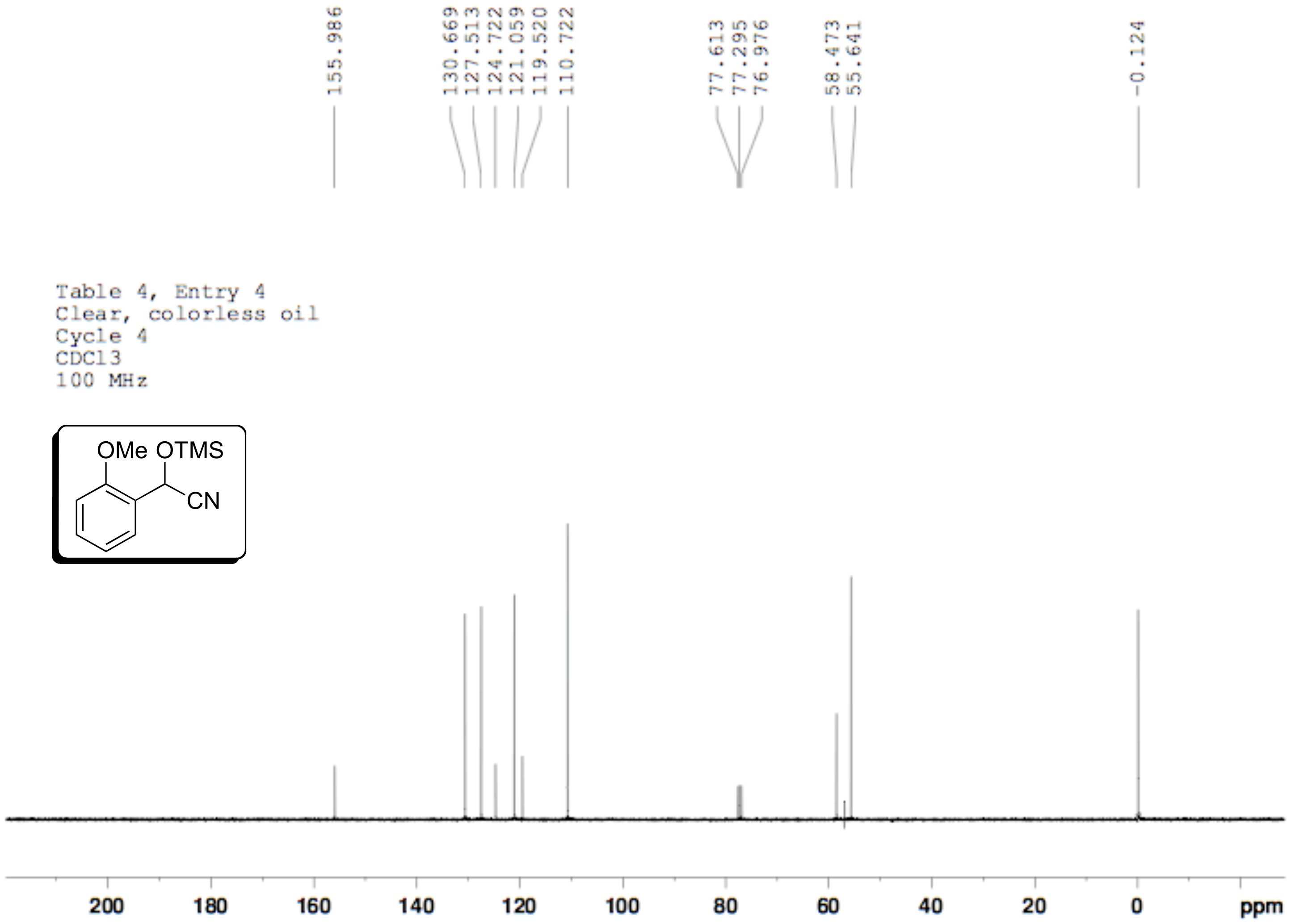
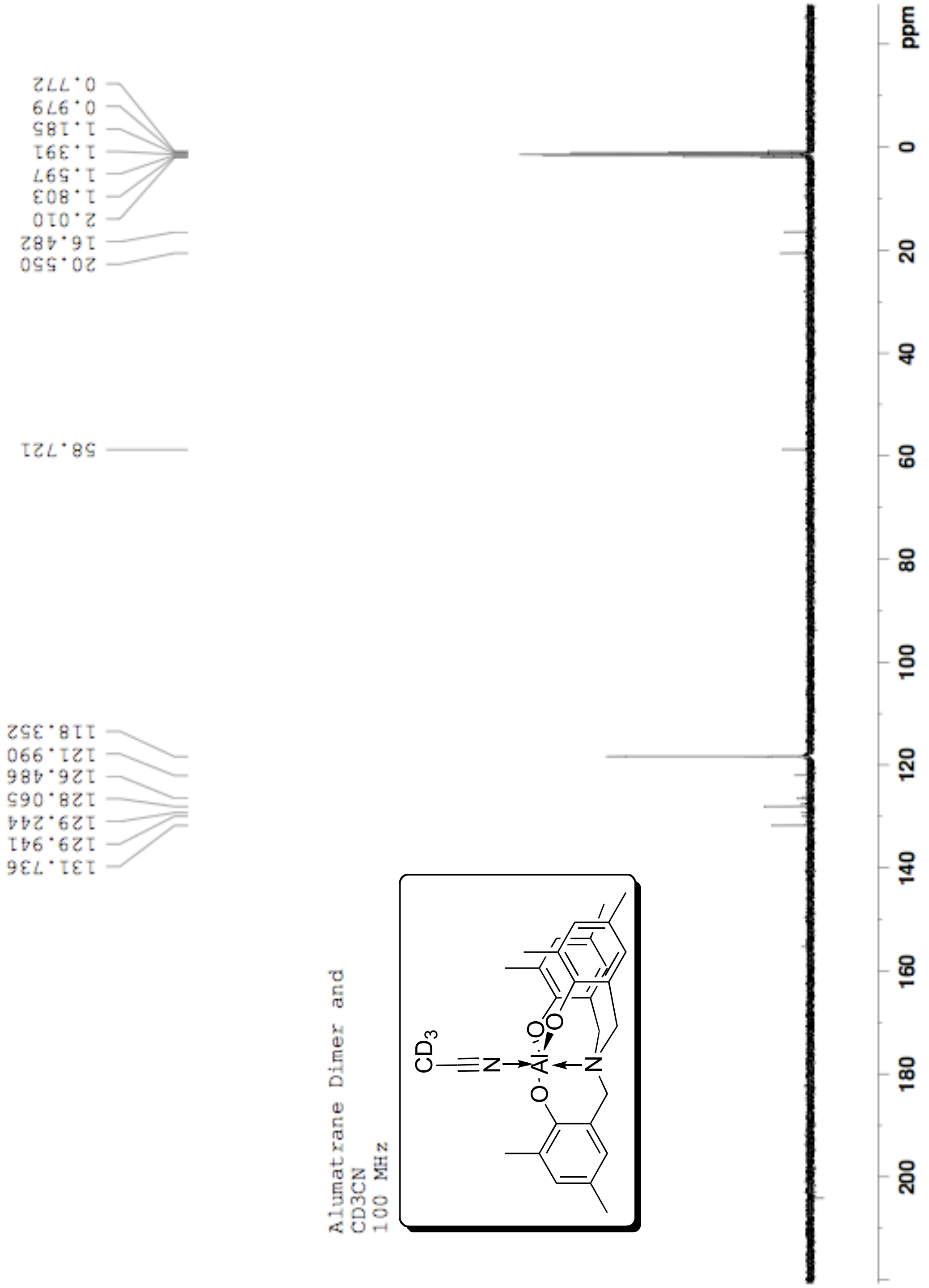
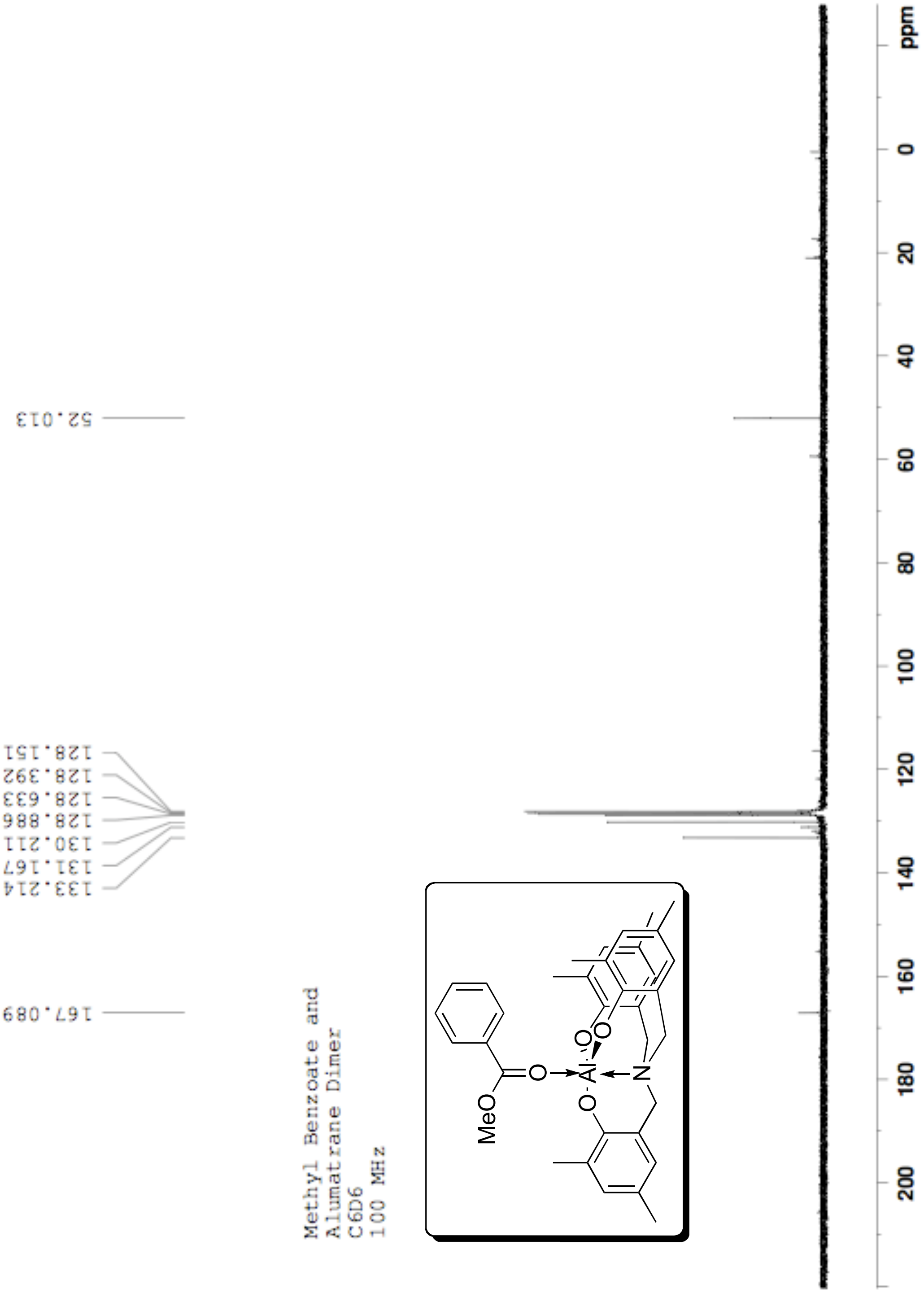


Table 4, Entry 4
Clear, colorless oil
Cycle 4
CDCl3
100 MHz


Alumatrane Dimer and
CD3CN
100 MHz
CD3
N
Al
O
O
O
N
0.772
0.979
1.185
1.391
1.597
1.803
2.010
16.482
20.550
58.721
118.352
121.990
126.486
128.065
129.244
129.941
131.736
ppm
0
20
40
60
80
100
120
140
160
180
200


167.089
133.214
131.167
130.211
128.886
128.633
128.392
128.151
52.013
Methyl Benzoate and
Alumatrane Dimer
C6D6
100 MHz
MeO
O
O
Al
O
O
N
ppm
0
20
40
60
80
100
120
140
160
180
200

APPENDIX D

CHAPTER 5. Supplementary Information

References for known compounds

X-ray data comparison for alumatranes

Data for unknown compounds

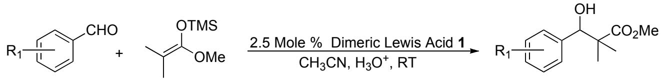
X-ray data for compounds 4 and 13•O=PEt$_3$

^{1}H, ^{13}C, ^{31}P, ^{11}B, and ^{19}F NMR spectra for reaction products

Experimental Section

Reagents and General Procedures. All reactions were carried under inert atmosphere using standard Schlenk procedures. Solvents were purified by standard procedures and distilled prior to use. Alumatrane dimer **1** and alumatrane monomer **2** were prepared according to literature procedures.[1a,b] Aldehydes and enol silyl ethers were purchased from Aldrich Chemical and used without further purification. ^1H and ^{13}C NMR were recorded on a 400 MHz Varian VXR and d-chloroform ($CDCl_3$) was used unless otherwise noted. Peaks shown at 57 and 115 ppm in the ^{13}C NMR are considered noise peaks unless they are picked. ^{31}P NMR spectra were recorded on a 162 MHz NMR spectrometer. Thin layer chromatography (TLC) was performed using commercial 60 mesh silica gel plates visualized with short-wavelength UV (254 nm) light. X-ray data collection and structure were conducted at the Iowa State Molecular Structure Laboratory.

Table 2. Reactions of Aryl Aldehydes with Methyl Trimethylsilyl Dimethylketene Acetal.



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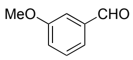
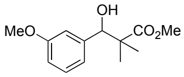
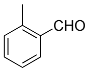
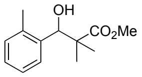
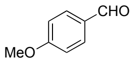
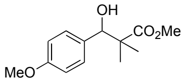
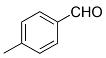
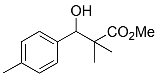
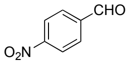
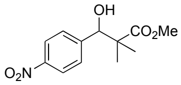
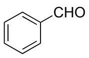
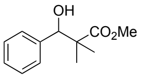
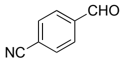
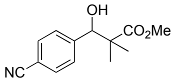
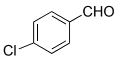
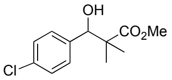
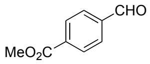
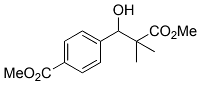
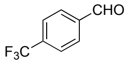
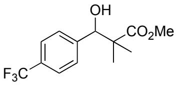
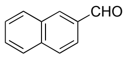
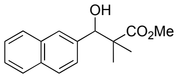
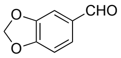
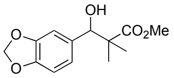
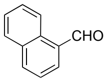
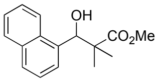
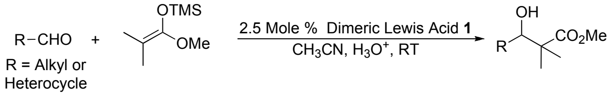
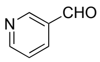
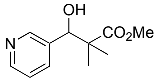
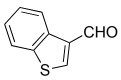
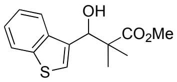
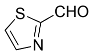
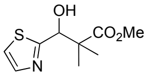
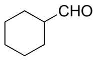
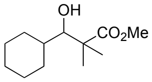
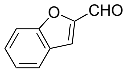
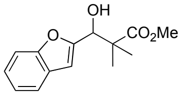
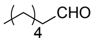
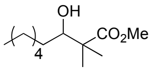
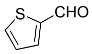
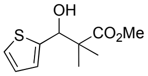
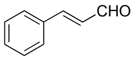
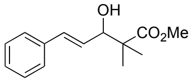
1			2 h	92 (Lit: 30)[c]	8			3 h	91 (Lit: 83)[j]
2			1 h	90 (Lit: 44-98)[d]	9			3 h	85 (Lit: 79-99)[k]
3			7 h	95 (Lit: 32-100)[e]	10			1 h	95 (Lit: 18-100)[l]
4			6 h	98 (Lit: 68-90)[f]	11			4 h	93 (Lit: 60-94)[m]
5			6 h	92 (Lit: 99)[g]	12			10 h	92 (Lit: 33-68)[n]
6			2 h	92 (Lit: 77-81)[h]	13			2 h	98 (Lit: 98)[o]
7			2 h	88 (Lit: 82-97)[i]					

[a]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric **2**, 5 mL of CH_3CN, RT, 1-10 h, then H_3O^+ treatment. [b]Average of two runs. Yields in parenthesis refer to literature yields. [c]Ref 2a. [d]Ref 2b-2p. [e]Refs 2b-2h, 2j-2n, 2q-2s. [f]Refs 2c, 2e, 2l-2m, 2s. [g]Refs 2h, 2k. [i]Refs 2c, 2e, 2g, 2l-2m. [j]Ref 2t. [k]Refs 2b-2c, 2e, 2h, 2j-2o, 2t-2w.[l]Refs 2a-2l, 2n-2af. [m]Refs 2c-2m, 2o,2t, 2v-2w, 2ai. [n]Ref 2g. [o]Ref 2q.

Table 3: Hetero- and Alkyl- Aldehydes with Methyl Trimethylsilyl Dimethylketene.

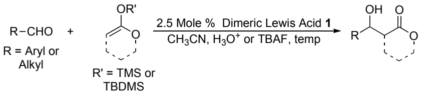


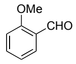
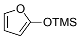
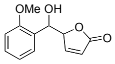
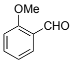
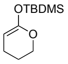
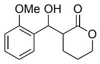
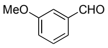
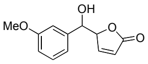
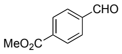
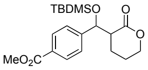
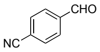
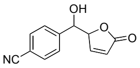
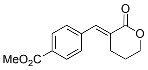
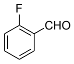
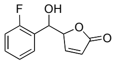
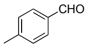
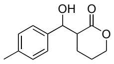
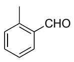
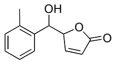
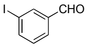
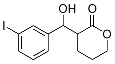
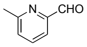
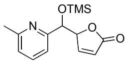
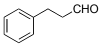
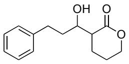
Entry	Aldehyde	Product	Time	Yield (%)[a,b]	Entry	Aldehyde	Product	Time	Yield (%)[a,b]
1			7 h	96 (Lit: 47-95)[d]	5			6 h	73 87[c]
2			5 h	95 (Lit: 75)[e]	6			2 h	86 (Lit: 48-89)[g]
3			5 h	91	7			1 h	89 (Lit: 62-89)[h]
4			6 h	96 (Lit: 57)[f]	8			12 h	52 (Lit: 55-99)[i]

[a]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric **1**, 5 mL of

CH_3CN, RT, 1-12 h, then H_3O^+ treatment. [b]Average of two runs. Yields in parenthesis refer to literature yields. [c]5 mole % of **2** was used. [d]Refs 2a, 2i, 2v, 2ah. [e]Ref 3a. [f]Ref 2t. [g]Refs 2w, 2ab. [h]Refs 2b, 3b-3c. [i]Refs 2n, 2p, 2v, 3d-3f.

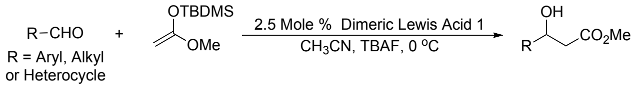
Table 4. Various Aldehydes with 6-(tert-Butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran and 2-(Trimethylsiloxy)furan.

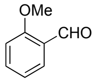
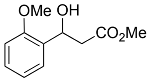
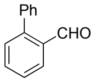
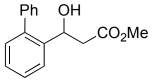
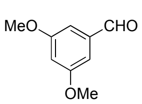
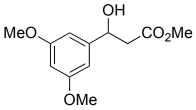
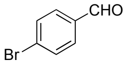
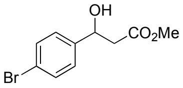
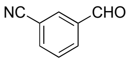
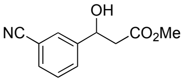
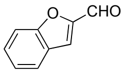
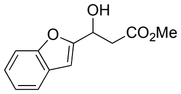
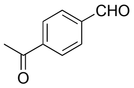
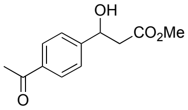
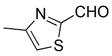
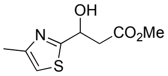
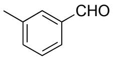
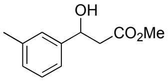
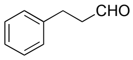
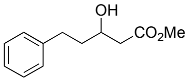
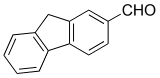
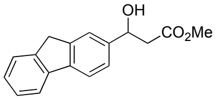


Entry	Aldehdye	Enol Ether	Product	Time	Yield (%)^{a,b}	Syn/Anti^{d}	Entry	Aldehyde	Enol Ether	Product	Time	Yield (%)^{a,c}	Syn/Anti^{d}
1				2 h	86 (Lit: 87)^{f}	1/6	7				7 h	88	1/1
2				3 h	35 51^{e} (Lit: 73-81)^{g}	1/2	8				6 h	91	1/1
3				1 h	84 (Lit 48)^{h}	1/2	9				6 h	93	
4				2 h	93	1/1	10				8 h	92	1/1
5				3 h	61 72^{e} (Lit: 90)^{i}	1/4	11				13 h	83	1/1
6				1 h	82	Single Isomer	12				15 h	87 (Lit: 87)^{j}	1/2

[a]Average of two runs. [b]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric **2**, 5 mL of CH_3CN, RT, time: 1-3 h, the H_3O^+ treatment. [c]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric **2**, 5 mL of CH_3CN, 0 C, 6-15 h, then TBAF treatment. Yields in parenthesis refer to literature yields (see Supporting Information). [d]Syn/Anti ratio determined by either ^1H NMR spectroscopy or weight of separated isomer. [e]5 mole % of dimeric **2** used. [f]Ref 4a. [g]Refs 4b-4c. [h]Ref 4d. [i]Ref 4b. [j]Ref 4e.

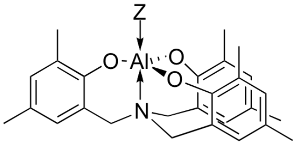
Table 5. Various Aldehydes with 1-(*tert*-Butydimethylsilyloxy)-1-methoxyethene.



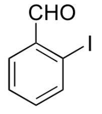
Entry	Aldehyde	Product	Time	Yield (%)[a,b]	Entry	Aldedhyde	Product	Time	Yield (%)[a,b]
1			14 h	90 (Lit: 33)[d]	7			10 h	94
2			15 h	96	8			16 h	83 (Lit: 87)[e]
3			10 h	93	9			12 h	95 (Lit: 100)[f]
4			11 h	57 89[c]	10			10 h	81
5			8 h	92	11			13 h	90 (Lit: 16-87)[g]
6			6 h	93					

[a]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mole % of dimeric 2, 5 mL CH_3CN, 0 C, 6-16 h, then TBAF treatment. [b]Average of two runs. Yields in parenthesis refer to literature yields. [c]5 mole % of 2 used. [d]Ref 2v. [e]Ref 5a. [f]Ref 5b. [g]Refs 5c-5g.

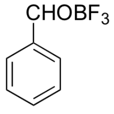
Comparison of major structural parameters in 4 with those in with the corresponding ones in 5 – 12.



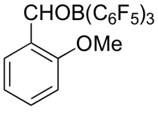
5: Z = $O(CH_2CH_2)_2$
6: Z = $O{=}CHC_6H_5$
7: Z = $^{-}OC_6H_5$
$HP(i\text{BuNCH}_2CH_2)_3N^+$
8: Z = OH_2



9



10



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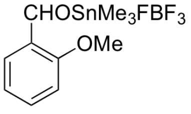


12

These parameters, obtained by X-ray crystallographic means, are collected in Tables 1 and 2. Comparisons of the same structural parameters will be considered valid only if they lie outside 3x the esd values. The LA-O_{ax} (LA = Lewis acid) bond length in **4** is longer than that in **7**,[6] which is consistent with the lack of an anionic charge on the LA-O oxygen in **4** and perhaps some steric crowding by its 2-methoxy group. To compensate for the greater LA-O_{ax} distance in **4**, the transannular N→Al distance in **4** is shorter than in **7**. These results can be rationalized on the reasonable assumption that electron donation from the aldehyde oxygen in **4** is expected to be considerably weaker than that from the anionic phenolate oxygen in **7**, thus allowing increased electron pair donation from the transannular nitrogen in **4**. Because the esd's for the The LA-O_{ax}, N→Al, and the averages of the equatorial Al-O_{eq} distances are relatively large in alumatranes **5** and **6**, we will exclude these parameters from further comparisons. Assuming that an sp^3 lone pair on a water oxygen in **8** is more Lewis basic (because of more p character) than an sp^2 counterpart on an aldehyde oxygen in **4**, the longer LA-O_{ax} and shorter N→Al distance in **4** than in **8** is reasonable. The averages of the equatorial Al-O_{eq} bond lengths in **5** and **6** are within 3x the esd's of those in **4**.

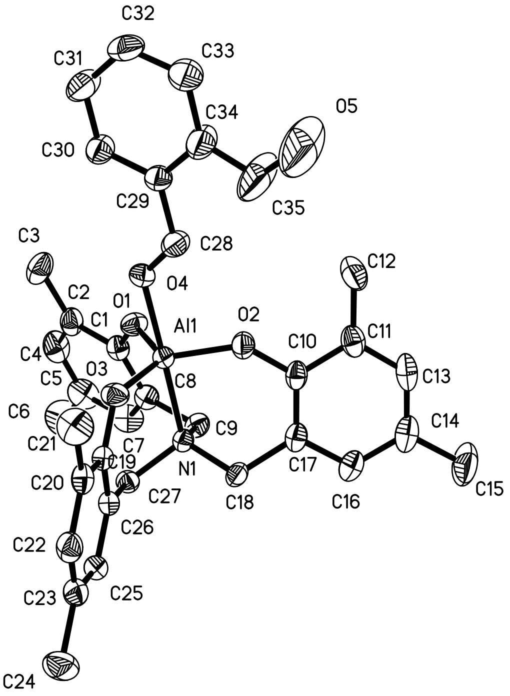


Figure 1. Computer drawing of the molecular structure of **4** at the 50% probability level. Hydrogen atoms are omitted for clarity.

The C=O bond lengths in **9-12** are all within 3x their corresponding esd's, even though this distance in **10-12** might have been expected to be longer than in **9** owing to the electron withdrawing power of their Lewis acid moieties. Thus the C=O length in **9** may be taken as representative of the length in free benzaldehyde in view of the weakly deactivating action of the iodo substituent in this compound. Despite the stronger electron withdrawing power of the alumatrane moiety than a BF_3 group (see below) the C=O bond distance in **4** is the same as in **9**. The very short C=O bond length in **6** is puzzling.

Table 1. Bond distances in Alumatranes and Boron Lewis Acids with Oxygen Donors.

Entry	Cmpd	Al-N	Al-O(1)	Al-O(2)	Al-O(3)	LA[a]-O	C=O
1	**4**	2.101(3)	1.747(3)	1.757(3)	1.750(3)	1.986(3)	1.216(3)
2	**5**[b]	2.068(18)	1.748(16)	1.762(18)	1.750(17)	1.961(16)	
3	**6**[b]	2.098(15)	1.745(4)			1.982(15)	1.101(6)
4	**7**[b]	2.233(6)	1.739(6)	1.757(6)	1.771(6)	1.768(6)	
5	**8**[b]	2.058(4)	1.736(3)	1.752(4)	1.782(3)	1.926(4)	
6	**9**[c]						1.215(5)
7	**10**[d]					1.591(6)	1.244(5)
8	**11**[e]					1.589(5)	1.262(4)
9	**12**[f]					2.231(3)	1.233(5)

[a]LA = Lewis Acid atom. [b]See reference 6. [c]See reference 7. [d]See reference 8. [e]See reference 9. [f]See reference 10.

Table 7. Bond Angles in Some Alumatranes

Entry	Cmpd	N-Al-O_{eq}[a]	O_{eq}-Al-O_{eq}[a]	O_{eq}-Al-O_{ax}[a]
1	**4**	92.76	119.77	87.26
2	**5**[b]	92.17	119.88	87.98
3	**6**[b]	92.95	119.74	87.05
4	**7**[b]	85.76	119.49	94.30
5	**8**[b]	92.22	119.83	87.66

[a]Average of bond angles. [b]See reference 6.

The bond angles recorded in Table 7 are unremarkable except for the N-Al-O_{eq} and O_{eq}-Al-O_{ax} values for **7**. Here the larger O_{eq}-Al-O_{ax} and smaller N-Al-O_{eq} angles reflect the distortion of the Al geometry toward tetrahedral by the strong donation of the phenolate anionic ligand.

References:

1. a.) Su, W.; Kim, Y.; Ellern, A.; Guzei, I. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2006**, *128*, 13727-13735. b.) Su, W.; Kobayashi, J.; Ellern, A.; Kawashima, T.; Verkade, J. G. *Inorg. Chem.* **2007**, *46*, 7953- 7959.
2. a.) Li, W. Z.; Zhang, X. *Org. Lett.* **2002**, *4*, 3485-3488. b.) Rajendra, S. *Journal of Molecular Catalysis A:Chemical* **2007**, *264*, 146-152. c.) Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016. d.) Hagiwara, H.; Inoguchi, H.; Fukushima, M.; Hoshi, T.; Suzuki, T. *Tetrahedron Lett.* **2006**, *47*, 5371-5373. e.) Fujisawa, H.; Nakagawa, T.; Mukaiyama, T. *Advanced Synthesis & Catalysis* **2004**, *346*, 1241-1246. f.) Hagiwara, H.; Inoguchi, H.; Fukushima, M.; Hoshi, T.; Suzuki, T. *Synlett* **2005**, 2388-2390. g.) Lannou, M.; Helion, F.; Namy, J. *Tetrahedron* **2003**, *59*, 10551-10565. h.) Fujisawa, H.; Nakagawa, T.; Nagata, Y.; Mukaiyama, T. *Bulletin of Chemical Society of Japan* **2004**, *77*, 1555-1567. i.) Chen, S.; Ji, S.; Loh, T. *Tetrahedron Lett.* **2004**, *45*, 375-377. j.) Nakagawa, T.; Fujisawa, H.; Mukaiyama, T. *Chemistry Letters* **2003**, *32*, 462-463. k.) Nakagawa, T.; Fujisawa, H.; Mukaiyama, T. *Chemistry Letters* **2003**, *32*, 696-697. l.) Mukaiyama, T.; Fujisawa, H.; Nakagawa, T. *Helvetica Chimica Acta* **2002**, *85*, 4518-4531. m.) Fujisawa, H.; Mukaiyama, T. *Chemistry Letters* **2002**, 858-859. n.) Fujisawa, H.; Mukaiyama, T. *Chemistry Letters* **2002**, 182-183. o.) Doucet, H.; Parrain, J.; Santelli, M. *Synlett* **2000**, 871-873. p.) Genisson, Y.; Gorrichon, L. *Tetrahedron Lett.* **2000**, *41*, 4881-4884. q.) Zhung, W.; Poulsen, T.; Jorgensen, K. A. *Organic & Biomolecular Chemistry* **2005**, *3*, 3284-3289. r.) Phukan, P. *Synthetic Comm.* **2004**, *34*, 1065-1070. s.) Sasidharan, M.; Kumar, R. *Journal of Catalysis* **2003**, *220*, 326-

332. t.) Takeuchi, M.; Akiyama, R.; Kobayashi, S. *J. Am. Chem. Soc.* **2005**, *127*, 13096-13097. u.) Li, X.; Kurita, A.; Man-E, S.; Orita, A. Otera, J. *Organometallics* **2005**, *24*, 2567-2569. v.) Shen, Z.; Ji, S.; Loh, T. *Tetrahedron Lett.* **2005**, *46*, 507-508. w.) Matsukawa, S.; Okano, N.; Imamoto, T. *Tetrahedron Lett.* **2000**, *41*, 103-107. x.) Gaydhankar, T. R.; Joshi, P. N.; Kumar, R. *Journal of Molecular Catalysis A: Chemical* **2007**, *265*, 306-315. y.) Fujisawa, H.; Takahashi, E.; Mukaiyama, T. *Chemistry-A European Journal* **2006**, *12*, 5082-5093. z.) Yamashita, Y.; Salter, M. M.; Aoyama, K.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2006**, *45*, 3816-3819. aa.) An, D.; Peng, Z.; Orita, A.; Kurita, A.; Man-e, S.; Ohkubo, K.; Li, X.; Fukuzumi, S.; Otera, J. *Chemistry-A European Journal* **2006**, *12*, 1642-1647. ab.) Ooi, T.; Takahashi, M.; Yamada, M.; Tayama, E.; Omoto, K.; Maruoka, K. *J. Am. Chem. Soc.* **2004**, *126*, 1150-1160. ac.) Iimura, S.; Manabe, K.; Kobayashi, S. *Tetrahedron* **2004**, *60*, 7673-7678. ad.) Mikami, K.; Yamanaka, M.; Islam, M. N.; Kudo, K.; Seino, N.; Shinoda, M. *Tetrahedron Lett.* **2003**, *44*, 7545-7548. ae.) Yoon, U. C.; Kim, M. J.; Moon, J. J.; Oh, S. W.; Kim, H. J.: Mariano, P. S. *Bulletin of the Korean Chemical Society* **2002**, *23*, 1218-1228. af.) Nishikido, J.; Nanbo, M.; Yoshida, A.; Nakajima, H.; Matsumoto, Y.; Mikami, K. *Synlett* **2002**, 1613-1616. ag.) Ohkouchi, M.; Masui, D.; Yamaguchi, M.; Yamagishi, T. *Journal of Molecular Catalysis A: Chemical* **2001**, *170*, 1-15. ah) Loh, T.; Feng, L.; Wei, L. *Tetrahedron* **2000**, *56*, 7309-7312. ai.) Chen, S.; Ji, S.; Loh, T. *Tetrahedron Lett.* **2003**, *44*, 2405-2408.

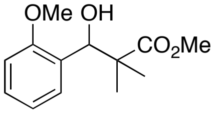
3. a.) Maurizio, B.; Cinquini, M.; Franco, C.; Giuseppe, C. *Organic & Biomolecular Chemistry* **2004**, *2*, 3401-3407. b.) Ooi, T.; Tayama, E.; Takahashi, M.; Maruoka, K. *Tetrahedron Lett.* **1997**, *38*, 7403-7406. c.) Reetz, M. T.; Vougioukas, A. E.

Tetrahedron Lett. **1987**, *28*, 793-796. d.) Cozzi, P. G.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *Synlett* **1994**, 857-858. e.) Maruoka, K.; Imoto, H.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 4131-4132. f.) Aben, R. W.; Scheeren, J. W. *Synthesis* **1978**, 400-402.

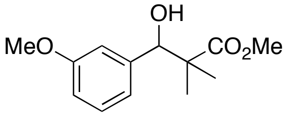
4. a.) Yadav, J. S.; Reddy, B. V. S.; Narasimhula, G. Satheesh, G. *Tetrahedron Lett.* **2008**, *49*, 5683-5686. b.) Ollevier, T.; Bouchard, J.; Desyroy, V. *J. Org. Chem.* **2008**, *73*, 331-334. c.) Pohmakotr, M.; Tuchinda, P.; Premkaisorn, P.; Reutrakul, V. *Tetrahedron* **1998**, *54*, 11297-11304. d.) Acocella, M. R.; Rosa, M. D.; Massa, A.; Palombi, L.; Villano, R.; Scettri, A. *Tetrahedron* **2005**, *61*, 4091-4097. e.) Kuwajima, I.; Minami, N.; Sato, T. *Tetrahedron Lett.* **1976**, 2253-2256.
5. a.) Kloetzing, R. J.; Thaler, T.; Knochel, P. *Org. Lett.* **2006**, *8*, 1125-1128. b.) Haruna, N.; Acosta, D. E.; Nakagawa, S.; Yamaguchi, K.; Tai, A.; Okuyama, T.; Sugimura, T. *Heterocycles* **2004**, *62*, 375-386. c.) Kamal, A.; Krishnaji, T.; Khanna, G. B. R. *Tetrahedron Lett.* **2006**, *47*, 8657-8660. d.) Denmark, S. E.; Wynn, T.; Beutner, G. L. *J. Am. Chem. Soc.* **2002**, *124*, 13405-13407. e.) Ema, T.; Moriya, H.; Kofukuda, T.; Ishida, T.; Maehara, K.; Utaka, M.; Sakai, T. *J. Org. Chem.* **2001**, *66*, 8682-8684. f.) Rho, H. *Synthetic Comm.* **1997**, *27*, 3887-3893. g.) Fujisawa, T.; Fujimura, A.; Sato, T. *Bulletin of the Chemical Society of Japan* **1988**, *61*, 1273-1279.
6. Su, W.; Kim, Y.; Eller, A.; Guzei, I. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2006**, *128*, 13727-13735.
7. Betz, R.; Klüfers, P. *Acta. Cryst.* **2007**, *63*, 4879.
8. Reetz, M. T.; Hüllman, M.; Massa, W.; Berger, S.; Rademacher, P.; Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405-2408.

9. Blackwell, J. M.; Piers, W. E.; Parvez, M. *Org. Lett.* **2000**, *2*, 695-698.
10. Blackwell, J. M.; Piers, W. E.; McDonald, R. *J. Am. Chem. Soc.* **2002**, *124*, 1295-1306.

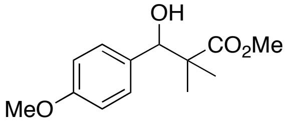
Literature References for Known Compounds



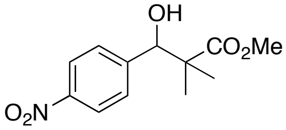
(Table 1, entry 1-10): Li, W. Z.; Zhang, X. *Org. Lett.* **2002**, *4*, 3485-3488.



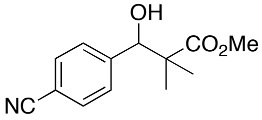
(Table 2, entry 1): Li, W. Z.; Zhang, X. *Org. Lett.* **2002**, *4*, 3485-3488.



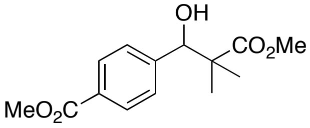
(Table 2, entry 2): Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.



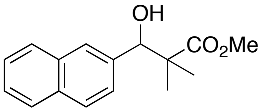
(Table 2, entry 3): Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.



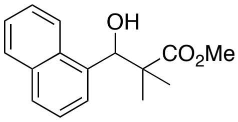
(Table 2, entry 4): Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.



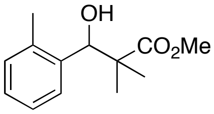
(Table 2, entry 5): Nakagawa, T.; Fujisawa, H.; Mukaiyama, T. *Chemistry Letters* **2003**, *32*, 696-697.



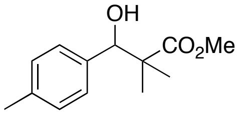
(Table 2, entry 6): Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.



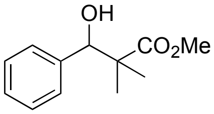
(Table 2, entry 7): Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.



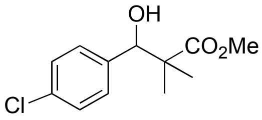
(Table 2, entry 8): Takeuchi, M.; Akiyama, R.; Kobayashi, S. *J. Am. Chem. Soc.* **2005**, *127*, 13096-13097.



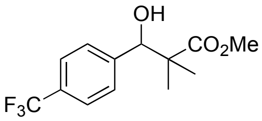
(Table 2, entry 9): Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.



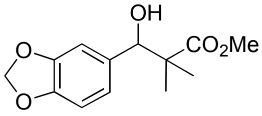
(Table 2, entry 10): Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.



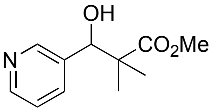
(Table 2, entry 11): Song, J. J.; Tan, Z.; Reeves, J. T.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2007**, *9*, 1013-1016.

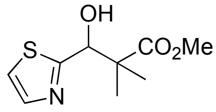


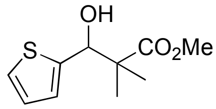
(Table 2, entry 12): Lannou, M.; Helion, F.; Namy, J. *Tetrahedron* **2003**, *59*, 10551-10565.

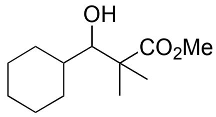


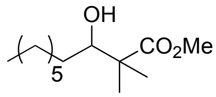
(Table 2, entry 13): Li, W. Z.; Zhang, X. *Org. Lett.* **2002**, *4*, 3485-3488.

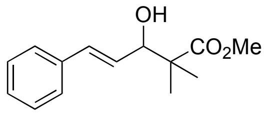

(Table 3, entry 1): Shen, Z.; Ji, S.; Loh, T. *Tetrahedron Lett.* **2005**, *46*, 507-508.

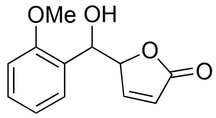

(Table 3, entry 2): Maurizio, B.; Cinquini, M.; Franco, C.; Giuseppe, C. *Organic & Biomolecular Chemistry* **2004**, *2*, 3401-3407.

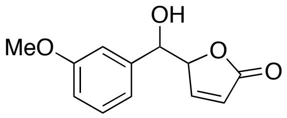

(Table 3, entry 4): Takeuchi, M.; Akiyama, R.; Kobayashi, S. *J. Am. Chem. Soc.* **2005**, *127*, 13096-13097.


(Table 3, entry 6): Ooi, T.; Takahashi, M.; Yamada, M.; Tayama, E.; Omoto, K.; Maruoka, K. *J. Am. Chem. Soc.* **2004**, *126*, 1150-1160.

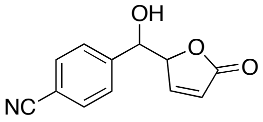

(Table 3, entry 7): Li, W. Z.; Zhang, X. *Org. Lett.* **2002**, *4*, 3485-3488.


(Table 3, entry 8): Li, W. Z.; Zhang, X. *Org. Lett.* **2002**, *4*, 3485-3488.

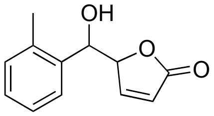

(Table 4, entry 1): Yadav, J. S.; Reddy, B. V. S.; Narasimhula, G. Satheesh, G. *Tetrahedron Lett.* **2008**, *49*, 5683-5686.



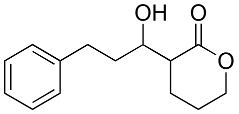
(Table 4, entry 2): Ollevier, T.; Bouchard, J.; Desyroy, V. *J. Org. Chem.* **2008**, *73*, 331-334.



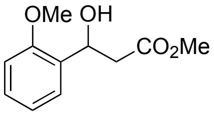
(Table 4, entry 3): Acocella, M. R.; Rosa, M. D.; Massa, A.; Palombi, L.; Villano, R.; Scettri, A. *Tetrahedron* **2005**, *61*, 4091-4097.



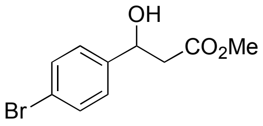
(Table 4, entry 5): Ollevier, T.; Bouchard, J.; Desyroy, V. *J. Org. Chem.* **2008**, *73*, 331-334.



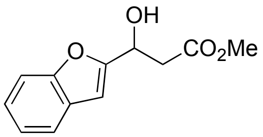
(Table 4, entry 12): Kuwajima, I.; Minami, N.; Sato, T. *Tetrahedron Lett.* **1976**, 2253-2256.



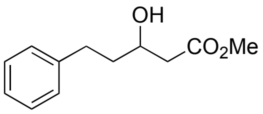
(Table 5, entry 1): Shen, Z.; Ji, S.; Loh, T. *Tetrahedron Lett.* **2005**, *46*, 507-508.



(Table 5, entry 8): Kloetzing, R. J.; Thaler, T.; Knochel, P. *Org. Lett.* **2006**, *8*, 1125-1128.



(Table 5, entry 9): Haruna, N.; Acosta, D. E.; Nakagawa, S.; Yamaguchi, K.; Tai, A.; Okuyama, T.; Sugimura, T. *Heterocycles* **2004**, *62*, 375-386.



(Table 5, entry 11): Denmark, S. E.; Wynn, T.; Beutner, G. L. *J. Am. Chem. Soc.* **2002**, *124*, 13405-13407.

Crystallographic Experimental Section

Data Collection

A small yellow crystal with visual breaks inside was selected under ambient conditions. The crystal was mounted and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed at 173 K on a Bruker CCD-1000 diffractometer with Mo K_α ($\lambda = 0.71073$ Å) radiation and the detector to crystal distance of 5.03 cm.

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 30 frames collected at intervals of 0.3º in a 10º range about ω with the exposure time of 20 seconds per frame. The obtained reflections were successfully indexed by an automated indexing routine built in the SMART program. The final cell constants were calculated from a set of strong reflections from the actual data collection.

The data were collected using the full sphere routine by collecting four sets of frames with 0.3º scans in ω with an exposure time 20 sec per frame. This dataset was corrected for Lorentz and polarization effects. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiple equivalent measurements [1] using SADABS software [2].

Structure Solution and Refinement

The systematic absences in the diffraction data were consistent for the space groups $P2_1/c$ yielded chemically reasonable and computationally stable results of refinement. The positions of almost all non-hydrogen atoms were found by direct methods. The remaining atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined in full-matrix anisotropic approximation. All hydrogen atoms were placed in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients. PhOMe group was found slightly disordered because of librations.

The ORTEP diagram was drawn at 50% probability level. H-atoms were omitted for clarity. The resulting CIF file has been tested with PLATON [3] software. The results and comments have been included to output package (Platon.txt file in ACSII format).

References

[1] Blessing, R.H. *Acta Cryst*. **1995**, *A51*, 33-38.

[2] All software and sources of the scattering factors are contained in the SHELXTL (version 5.1) program library (G. Sheldrick, Bruker Analytical X-Ray Systems, Madison, WI).

[3] A.L.Spek, J.Appl.Cryst. 36, 7-13.

Table 1. Crystal data and structure refinement for **4**.

Empirical formula	C35 H38 Al N O5	
Formula weight	579.64	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 12.99(2) Å	a= 90°.
	b = 11.142(17) Å	b= 97.03(2)°.
	c = 22.53(3) Å	g = 90°.
Volume	3235(9) Å^3	
Z	4	
Density (calculated)	1.190 Mg/m^3	
Absorption coefficient	0.104 mm^{-1}	
F(000)	1232	
Crystal size	0.45 x 0.28 x 0.22 mm^3	
Theta range for data collection	2.04 to 26.38°.	
Index ranges	-15<=h<=16, -13<=k<=13, -27<=l<=28	
Reflections collected	26414	
Independent reflections	6614 [R(int) = 0.0496]	
Completeness to theta = 26.38°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9776 and 0.9549	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6614 / 0 / 379	
Goodness-of-fit on F^2	1.050	
Final R indices [I>2sigma(I)]	R1 = 0.0600, wR2 = 0.1671	
R indices (all data)	R1 = 0.0914, wR2 = 0.1953	
Largest diff. peak and hole	0.856 and -0.650 e.Å^{-3}	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **4**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Al(1)	6694(1)	5102(1)	1570(1)	24(1)
C(1)	4680(2)	4335(2)	1086(1)	28(1)
C(2)	4163(2)	3879(3)	548(1)	36(1)
C(3)	4778(3)	3267(3)	110(1)	47(1)
C(4)	3085(2)	4047(3)	431(1)	46(1)
C(5)	2519(2)	4634(3)	827(2)	47(1)
C(6)	1353(3)	4841(4)	676(2)	72(1)
C(7)	3049(2)	5059(3)	1359(2)	41(1)
C(8)	4125(2)	4922(2)	1494(1)	30(1)
C(9)	4702(2)	5400(2)	2065(1)	30(1)
C(10)	7111(2)	4787(2)	2839(1)	29(1)
C(11)	7535(2)	3950(3)	3272(1)	35(1)
C(12)	8201(3)	2948(3)	3094(2)	51(1)
C(13)	7325(2)	4110(3)	3862(1)	42(1)
C(14)	6757(2)	5072(3)	4039(1)	44(1)
C(15)	6546(4)	5205(4)	4686(2)	71(1)
C(16)	6361(2)	5887(3)	3603(1)	38(1)
C(17)	6521(2)	5743(3)	3005(1)	30(1)
C(18)	6093(2)	6666(2)	2551(1)	29(1)
C(19)	7082(2)	7533(2)	1287(1)	26(1)
C(20)	7887(2)	8311(3)	1179(1)	31(1)
C(21)	8887(2)	7799(3)	1011(2)	46(1)
C(22)	7739(2)	9543(3)	1234(1)	35(1)
C(23)	6827(2)	10031(2)	1384(1)	36(1)
C(24)	6683(3)	11368(3)	1436(2)	53(1)
C(25)	6035(2)	9239(2)	1491(1)	31(1)
C(26)	6148(2)	8003(2)	1444(1)	26(1)
C(27)	5270(2)	7172(2)	1552(1)	26(1)
C(28)	8503(2)	3692(3)	1405(1)	37(1)
C(29)	9141(2)	2886(3)	1101(1)	34(1)
C(30)	8859(2)	2560(3)	514(1)	37(1)

C(31)	9470(3)	1795(3)	228(2)	51(1)
C(32)	10379(3)	1349(3)	533(2)	49(1)
C(33)	10691(3)	1662(4)	1113(2)	66(1)
C(34)	10075(3)	2451(4)	1400(2)	65(1)
C(35)	11375(5)	2664(8)	2256(2)	162(4)
O(5)	10329(3)	2889(4)	1961(1)	129(2)
N(1)	5622(2)	6155(2)	1966(1)	24(1)
O(1)	5720(1)	4206(2)	1195(1)	32(1)
O(2)	7316(1)	4637(2)	2269(1)	33(1)
O(3)	7225(1)	6338(2)	1236(1)	31(1)
O(4)	7682(1)	4104(2)	1176(1)	30(1)

Table 3. Bond lengths [Å] and angles [°] for **4**.

Al(1)-O(1)	1.747(3)	C(7)-H(7A)	0.9500	C(16)-H(16A)	0.9500
Al(1)-O(3)	1.750(3)	C(8)-C(9)	1.503(4)	C(17)-C(18)	1.508(4)
Al(1)-O(2)	1.757(3)	C(9)-N(1)	1.500(4)	C(18)-N(1)	1.496(3)
Al(1)-O(4)	1.986(3)	C(9)-H(9A)	0.9900	C(18)-H(18A)	0.9900
Al(1)-N(1)	2.101(3)	C(9)-H(9B)	0.9900	C(18)-H(18B)	0.9900
C(1)-O(1)	1.350(4)	C(10)-O(2)	1.354(4)	C(19)-O(3)	1.351(4)
C(1)-C(8)	1.398(4)	C(10)-C(17)	1.390(4)	C(19)-C(20)	1.402(4)
C(1)-C(2)	1.407(4)	C(10)-C(11)	1.412(4)	C(19)-C(26)	1.405(4)
C(2)-C(4)	1.405(5)	C(11)-C(13)	1.400(5)	C(20)-C(22)	1.394(5)
C(2)-C(3)	1.506(4)	C(11)-C(12)	1.498(5)	C(20)-C(21)	1.507(4)
C(3)-H(3A)	0.9800	C(12)-H(12A)	0.9800	C(21)-H(21A)	0.9800
C(3)-H(3B)	0.9800	C(12)-H(12B)	0.9800	C(21)-H(21B)	0.9800
C(3)-H(3C)	0.9800	C(12)-H(12C)	0.9800	C(21)-H(21C)	0.9800
C(4)-C(5)	1.387(5)	C(13)-C(14)	1.387(5)	C(22)-C(23)	1.383(5)
C(4)-H(4A)	0.9500	C(13)-H(13A)	0.9500	C(22)-H(22A)	0.9500
C(5)-C(7)	1.390(5)	C(14)-C(16)	1.389(5)	C(23)-C(25)	1.398(4)
C(5)-C(6)	1.528(5)	C(14)-C(15)	1.521(5)	C(23)-C(24)	1.507(5)
C(6)-H(6A)	0.9800	C(15)-H(15A)	0.9800	C(24)-H(24A)	0.9800
C(6)-H(6B)	0.9800	C(15)-H(15B)	0.9800	C(24)-H(24B)	0.9800
C(6)-H(6C)	0.9800	C(15)-H(15C)	0.9800	C(24)-H(24C)	0.9800
C(7)-C(8)	1.401(4)	C(16)-C(17)	1.398(4)	C(25)-C(26)	1.390(4)

C(25)-H(25A)	0.9500	C(29)-C(30)	1.378(4)	C(33)-C(34)	1.400(5)
C(26)-C(27)	1.512(4)	C(29)-C(34)	1.400(4)	C(33)-H(33A)	0.9500
C(27)-N(1)	1.503(4)	C(30)-C(31)	1.377(4)	C(34)-O(5)	1.356(5)
C(27)-H(27A)	0.9900	C(30)-H(30A)	0.9500	C(35)-O(5)	1.459(6)
C(27)-H(27B)	0.9900	C(31)-C(32)	1.383(5)	C(35)-H(35A)	0.9800
C(28)-O(4)	1.216(3)	C(31)-H(31A)	0.9500	C(35)-H(35B)	0.9800
C(28)-C(29)	1.449(4)	C(32)-C(33)	1.365(5)	C(35)-H(35C)	0.9800
C(28)-H(28A)	0.9500	C(32)-H(32A)	0.9500		

O(1)-Al(1)-O(3)	122.84(12)	C(4)-C(5)-C(6)	121.1(3)	C(11)-C(12)-H(12A)	109.5
O(1)-Al(1)-O(2)	119.37(12)	C(7)-C(5)-C(6)	120.9(3)	C(11)-C(12)-H(12B)	109.5
O(3)-Al(1)-O(2)	117.09(12)	C(5)-C(6)-H(6A)	109.5	H(12A)-C(12)-H(12B)	109.5
O(1)-Al(1)-O(4)	86.16(14)	C(5)-C(6)-H(6B)	109.5	C(11)-C(12)-H(12C)	109.5
O(3)-Al(1)-O(4)	86.54(13)	H(6A)-C(6)-H(6B)	109.5	H(12A)-C(12)-H(12C)	109.5
O(2)-Al(1)-O(4)	89.08(13)	C(5)-C(6)-H(6C)	109.5	H(12B)-C(12)-H(12C)	109.5
O(1)-Al(1)-N(1)	92.62(14)	H(6A)-C(6)-H(6C)	109.5	C(14)-C(13)-C(11)	122.9(3)
O(3)-Al(1)-N(1)	93.37(13)	H(6B)-C(6)-H(6C)	109.5	C(14)-C(13)-H(13A)	118.6
O(2)-Al(1)-N(1)	92.30(13)	C(5)-C(7)-C(8)	121.8(3)	C(11)-C(13)-H(13A)	118.6
O(4)-Al(1)-N(1)	178.49(9)	C(5)-C(7)-H(7A)	119.1	C(13)-C(14)-C(16)	117.8(3)
O(1)-C(1)-C(8)	121.0(2)	C(8)-C(7)-H(7A)	119.1	C(13)-C(14)-C(15)	121.0(3)
O(1)-C(1)-C(2)	118.6(2)	C(1)-C(8)-C(7)	119.2(3)	C(16)-C(14)-C(15)	121.3(3)
C(8)-C(1)-C(2)	120.4(3)	C(1)-C(8)-C(9)	119.0(3)	C(14)-C(15)-H(15A)	109.5
C(4)-C(2)-C(1)	118.2(3)	C(7)-C(8)-C(9)	121.8(3)	C(14)-C(15)-H(15B)	109.5
C(4)-C(2)-C(3)	122.3(3)	N(1)-C(9)-C(8)	113.2(2)	H(15A)-C(15)-H(15B)	109.5
C(1)-C(2)-C(3)	119.5(3)	N(1)-C(9)-H(9A)	108.9	C(14)-C(15)-H(15C)	109.5
C(2)-C(3)-H(3A)	109.5	C(8)-C(9)-H(9A)	108.9	H(15A)-C(15)-H(15C)	109.5
C(2)-C(3)-H(3B)	109.5	N(1)-C(9)-H(9B)	108.9	H(15B)-C(15)-H(15C)	109.5
H(3A)-C(3)-H(3B)	109.5	C(8)-C(9)-H(9B)	108.9	C(14)-C(16)-C(17)	121.4(3)
C(2)-C(3)-H(3C)	109.5	H(9A)-C(9)-H(9B)	107.7	C(14)-C(16)-H(16A)	119.3
H(3A)-C(3)-H(3C)	109.5	O(2)-C(10)-C(17)	121.9(2)	C(17)-C(16)-H(16A)	119.3
H(3B)-C(3)-H(3C)	109.5	O(2)-C(10)-C(11)	118.0(3)	C(10)-C(17)-C(16)	119.9(3)
C(5)-C(4)-C(2)	122.5(3)	C(17)-C(10)-C(11)	120.1(3)	C(10)-C(17)-C(18)	120.6(2)
C(5)-C(4)-H(4A)	118.7	C(13)-C(11)-C(10)	117.9(3)	C(16)-C(17)-C(18)	119.3(3)
C(2)-C(4)-H(4A)	118.7	C(13)-C(11)-C(12)	122.4(3)	N(1)-C(18)-C(17)	114.5(2)
C(4)-C(5)-C(7)	118.0(3)	C(10)-C(11)-C(12)	119.7(3)	N(1)-C(18)-H(18A)	108.6

C(17)-C(18)-H(18A)	108.6	N(1)-C(27)-H(27A)	109.1	C(9)-N(1)-C(27)	109.1(2)
N(1)-C(18)-H(18B)	108.6	C(26)-C(27)-H(27A)	109.1	C(18)-N(1)-Al(1)	111.41(17)
C(17)-C(18)-H(18B)	108.6	N(1)-C(27)-H(27B)	109.1	C(9)-N(1)-Al(1)	109.35(19)
H(18A)-C(18)-H(18B)	107.6	C(26)-C(27)-H(27B)	109.1	C(27)-N(1)-Al(1)	108.96(17)
O(3)-C(19)-C(20)	118.8(2)	H(27A)-C(27)-H(27B)	107.8	C(1)-O(1)-Al(1)	132.52(18)
O(3)-C(19)-C(26)	121.3(2)	O(4)-C(28)-C(29)	123.8(3)	C(10)-O(2)-Al(1)	133.79(19)
C(20)-C(19)-C(26)	119.9(3)	O(4)-C(28)-H(28A)	118.1	C(19)-O(3)-Al(1)	132.39(18)
C(22)-C(20)-C(19)	118.6(3)	C(29)-C(28)-H(28A)	118.1	C(28)-O(4)-Al(1)	127.1(2)
C(22)-C(20)-C(21)	121.8(3)	C(30)-C(29)-C(34)	119.0(3)		
C(19)-C(20)-C(21)	119.5(3)	C(30)-C(29)-C(28)	121.2(3)		
C(20)-C(21)-H(21A)	109.5	C(34)-C(29)-C(28)	119.9(3)		
C(20)-C(21)-H(21B)	109.5	C(31)-C(30)-C(29)	120.8(3)		
H(21A)-C(21)-H(21B)	109.5	C(31)-C(30)-H(30A)	119.6		
C(20)-C(21)-H(21C)	109.5	C(29)-C(30)-H(30A)	119.6		
H(21A)-C(21)-H(21C)	109.5	C(30)-C(31)-C(32)	119.7(3)		
H(21B)-C(21)-H(21C)	109.5	C(30)-C(31)-H(31A)	120.2		
C(23)-C(22)-C(20)	122.7(3)	C(32)-C(31)-H(31A)	120.2		
C(23)-C(22)-H(22A)	118.6	C(33)-C(32)-C(31)	121.3(3)		
C(20)-C(22)-H(22A)	118.6	C(33)-C(32)-H(32A)	119.3		
C(22)-C(23)-C(25)	117.7(3)	C(31)-C(32)-H(32A)	119.3		
C(22)-C(23)-C(24)	121.7(3)	C(32)-C(33)-C(34)	118.9(3)		
C(25)-C(23)-C(24)	120.6(3)	C(32)-C(33)-H(33A)	120.5		
C(23)-C(24)-H(24A)	109.5	C(34)-C(33)-H(33A)	120.5		
C(23)-C(24)-H(24B)	109.5	O(5)-C(34)-C(29)	114.9(3)		
H(24A)-C(24)-H(24B)	109.5	O(5)-C(34)-C(33)	124.7(3)		
C(23)-C(24)-H(24C)	109.5	C(29)-C(34)-C(33)	120.3(3)		
H(24A)-C(24)-H(24C)	109.5	O(5)-C(35)-H(35A)	109.5		
H(24B)-C(24)-H(24C)	109.5	O(5)-C(35)-H(35B)	109.5		
C(26)-C(25)-C(23)	121.7(3)	H(35A)-C(35)-H(35B)	109.5		
C(26)-C(25)-H(25A)	119.2	O(5)-C(35)-H(35C)	109.5		
C(23)-C(25)-H(25A)	119.2	H(35A)-C(35)-H(35C)	109.5		
C(25)-C(26)-C(19)	119.4(2)	H(35B)-C(35)-H(35C)	109.5		
C(25)-C(26)-C(27)	120.4(2)	C(34)-O(5)-C(35)	117.9(3)		
C(19)-C(26)-C(27)	120.2(2)	C(18)-N(1)-C(9)	109.3(2)		
N(1)-C(27)-C(26)	112.5(2)	C(18)-N(1)-C(27)	108.7(2)		

Table 4. Anisotropic displacement parameters (Å^{2}x 10^3)for **4**. The anisotropic displacement factor exponent takes the form: -2p^2[h^{2}a*^{2}U^{11} + ... + 2 h k a* b* U^{12}]

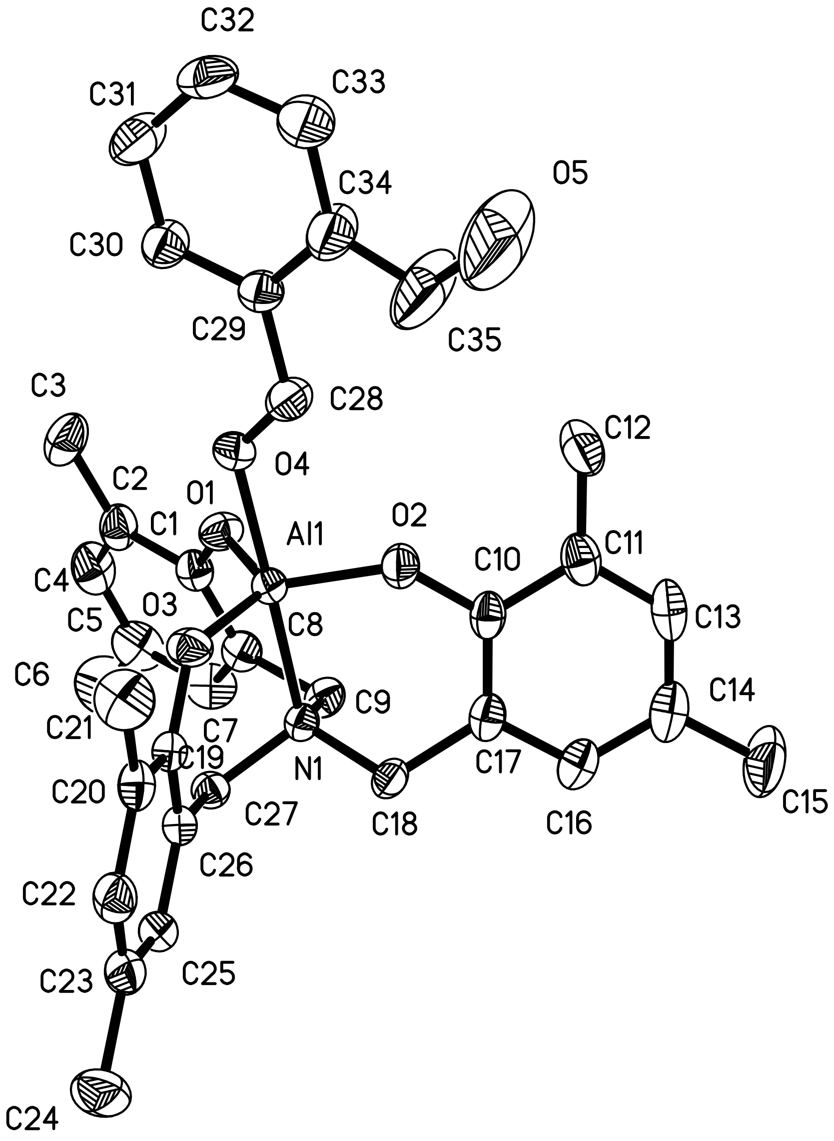
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Al(1)	25(1)	24(1)	23(1)	0(1)	3(1)	2(1)
C(1)	29(1)	27(1)	29(1)	3(1)	1(1)	-6(1)
C(2)	43(2)	34(2)	29(1)	2(1)	-2(1)	-10(1)
C(3)	58(2)	52(2)	31(2)	-10(1)	3(1)	-12(2)
C(4)	45(2)	46(2)	43(2)	2(1)	-13(1)	-13(2)
C(5)	32(2)	44(2)	63(2)	1(2)	-6(2)	-9(1)
C(6)	36(2)	78(3)	98(3)	-3(2)	-13(2)	-8(2)
C(7)	29(2)	42(2)	54(2)	-2(1)	8(1)	-5(1)
C(8)	30(1)	28(1)	33(1)	1(1)	6(1)	-8(1)
C(9)	31(1)	31(1)	30(1)	-2(1)	11(1)	-5(1)
C(10)	28(1)	35(2)	23(1)	2(1)	-2(1)	-7(1)
C(11)	31(1)	40(2)	33(2)	6(1)	-6(1)	-7(1)
C(12)	57(2)	49(2)	43(2)	12(2)	-7(2)	9(2)
C(13)	41(2)	55(2)	29(2)	14(1)	-6(1)	-12(2)
C(14)	42(2)	64(2)	26(2)	4(1)	2(1)	-9(2)
C(15)	85(3)	101(3)	28(2)	6(2)	9(2)	6(3)
C(16)	39(2)	48(2)	27(1)	-3(1)	7(1)	-6(1)
C(17)	29(1)	37(2)	23(1)	1(1)	2(1)	-8(1)
C(18)	35(1)	30(1)	21(1)	-3(1)	5(1)	-2(1)
C(19)	30(1)	26(1)	21(1)	1(1)	4(1)	1(1)
C(20)	32(1)	38(2)	22(1)	5(1)	5(1)	-2(1)
C(21)	32(2)	54(2)	56(2)	5(2)	18(1)	-4(1)
C(22)	41(2)	33(2)	30(1)	3(1)	5(1)	-10(1)
C(23)	49(2)	29(2)	28(1)	2(1)	5(1)	-3(1)
C(24)	72(2)	30(2)	60(2)	2(2)	18(2)	-6(2)
C(25)	38(2)	28(1)	27(1)	1(1)	5(1)	5(1)
C(26)	30(1)	26(1)	21(1)	2(1)	2(1)	1(1)
C(27)	25(1)	26(1)	27(1)	0(1)	5(1)	2(1)

C(28)	35(2)	43(2)	32(2)	-9(1)	-1(1)	9(1)
C(29)	31(2)	37(2)	33(1)	-2(1)	4(1)	9(1)
C(30)	31(2)	47(2)	34(2)	-4(1)	3(1)	5(1)
C(31)	45(2)	67(2)	40(2)	-18(2)	4(1)	10(2)
C(32)	49(2)	48(2)	51(2)	-11(2)	14(2)	15(2)
C(33)	60(2)	87(3)	49(2)	-2(2)	3(2)	46(2)
C(34)	58(2)	99(3)	35(2)	-10(2)	-2(2)	45(2)
C(35)	106(4)	300(10)	67(3)	-54(5)	-42(3)	117(6)
O(5)	93(2)	237(5)	48(2)	-52(2)	-31(2)	114(3)
N(1)	25(1)	26(1)	21(1)	-1(1)	2(1)	-2(1)
O(1)	31(1)	30(1)	34(1)	-7(1)	2(1)	0(1)
O(2)	34(1)	41(1)	25(1)	2(1)	2(1)	8(1)
O(3)	33(1)	27(1)	36(1)	1(1)	14(1)	3(1)
O(4)	31(1)	29(1)	31(1)	1(1)	5(1)	7(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **4**.

	x	y	z	U(eq)
H(3A)	5511	3234	277	71
H(3B)	4709	3720	-266	71
H(3C)	4515	2450	34	71
H(4A)	2731	3747	68	55
H(6A)	1116	4485	285	109
H(6B)	1210	5704	663	109
H(6C)	986	4464	982	109
H(7A)	2672	5452	1638	50
H(9A)	4221	5887	2274	36
H(9B)	4939	4717	2327	36
H(12A)	8433	2454	3445	76
H(12B)	8806	3281	2931	76
H(12C)	7799	2452	2789	76

H(13A)	7584	3534	4154	51
H(15A)	6880	4545	4924	107
H(15B)	5796	5183	4703	107
H(15C)	6827	5972	4845	107
H(16A)	5973	6556	3714	45
H(18A)	5560	7145	2723	34
H(18B)	6660	7219	2476	34
H(21A)	9367	8454	952	69
H(21B)	8743	7337	640	69
H(21C)	9199	7272	1332	69
H(22A)	8288	10069	1165	42
H(24A)	7313	11780	1347	79
H(24B)	6550	11566	1844	79
H(24C)	6093	11626	1152	79
H(25A)	5404	9554	1599	37
H(27A)	4730	7638	1725	31
H(27B)	4954	6840	1164	31
H(28A)	8740	3910	1806	44
H(30A)	8235	2866	303	45
H(31A)	9268	1574	-177	61
H(32A)	10794	815	335	58
H(33A)	11317	1349	1318	79
H(35A)	11455	3033	2654	243
H(35B)	11882	3012	2017	243
H(35C)	11490	1797	2295	243


C32
C31
C33
C34
O5
C30
C29
C35
C28
C3
O4
C12
C2
O1
C1
Al1
O2
C10
C11
C4
C13
C5
O3
C8
C6
C14
C9
C21
C7
C19
N1
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Crystallographic Experimental Section

Data Collection

A colorless crystal was selected under ambient conditions under the layer of Paratone oil. The covered by oil crystal was mounted and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed at 173K on a Bruker CCD-1000 diffractometer with Mo K_α (λ = 0.71073 Å) radiation and the detector to crystal distance of 5.03 cm.

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 30 frames collected at intervals of 0.3° in a 10° range about ω with the exposure time of 20 seconds per frame. The obtained reflections were successfully indexed by an automated indexing routine built in the SMART program. The final cell constants were calculated from a set of strong reflections from the actual data collection.

The data were collected using the full sphere routine by collecting four sets of frames with 0.3° scans in ω with an exposure time 20 sec per frame. This dataset was corrected for Lorentz and polarization effects. The absorption correction was based on a fit of a spherical harmonic function to the empirical transmission surface as sampled by multiple equivalent measurements [1] using SADABS software [2].

Structure Solution and Refinement

The systematic absences in the diffraction data were consistent for the space groups $P1$ and $P\bar{1}$ [2]. The *E*-statistics strongly suggested the centrosymmetric space group *P-1* yielded chemically reasonable and computationally stable results of refinement. The positions of Br atoms were found by the direct methods. The position of almost all non-hydrogen atoms were found by direct methods. The remaining atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined in full-matrix anisotropic approximation. All hydrogen atoms were placed in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.

Two chemically equivalent, but structurally independent cluster molecules and two toluene solvent molecules were found in an asymmetric unit of triclinic cell (Z = 4). A crystal had a very strong diffraction at low Bragg angles and no significant reflections above 19 degrees of THETA. Data were truncated to statistically relevant resolution. The low resolution data lead to a low data-to-parameter ration, however, structure refinement converged well. To increase the data-to-parameter ration all benzene rings were refined with AFIX 66 constrain. Rigid body restraines were applied to some C atoms to avoid NPD temperature displacement coefficients.

The ORTEP diagram was drawn at 50% probability level. H-atoms were omitted for clarity. The resulting CIF file has been tested with PLATON [3] software. The results and comments have been included to output package (Platon_Ver130.doc.). The X-Ray structure determination description from this report may be also added to correspondent fields of CIF file.

All instructions for correct editing of CIF file could be found at www.iucr.org .

References

[1] Blessing, R.H. *Acta Cryst.* **1995**, *A51*, 33-38.

[2] Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112-122

[3] A.L.Spek, J.Appl.Cryst. 36, 7-13.

Table 1. Crystal data and structure refinement for **13**•O=PEt$_3$.

Empirical formula	C40 H53 Al N O4 P	
Formula weight	669.78	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 11.159(4) Å	a= 80.131(6)°.
	b = 15.333(6) Å	b= 89.476(7)°.
	c = 21.909(8) Å	g = 85.057(7)°.
Volume	3679(2) Å^3	
Z	4	
Density (calculated)	1.209 Mg/m^3	
Absorption coefficient	0.139 mm^{-1}	
F(000)	1440	
Crystal size	0.40 x 0.30 x 0.20 mm^3	
Theta range for data collection	1.51 to 18.84°.	
Index ranges	-10<=h<=10, -13<=k<=13, -19<=l<=19	
Reflections collected	15122	
Independent reflections	5776 [R(int) = 0.1087]	
Completeness to theta = 18.84°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9727 and 0.9464	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5776 / 835 / 771	
Goodness-of-fit on F^2	1.027	
Final R indices [I>2sigma(I)]	R1 = 0.0753, wR2 = 0.1822	
R indices (all data)	R1 = 0.1370, wR2 = 0.2244	
Largest diff. peak and hole	0.653 and -0.410 e.Å^{-3}	

$R1 = \Sigma \, ||F_o| - |F_c|| \, / \, \Sigma |F_o|$ and $wR2 = \{ \Sigma [w(F_o^2 - F_c^2)^2] \, / \, \Sigma [w(F_o^2)^2] \}^{1/2}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **13**•O=PEt$_3$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Al(1)	1918(2)	1565(2)	518(1)	14(1)
Al(2)	2917(2)	8785(2)	4176(1)	15(1)
C(1)	4275(4)	2204(3)	581(3)	16(2)
C(2)	5388(5)	2012(3)	875(2)	19(2)
C(3)	6274(4)	2600(4)	744(3)	24(2)
C(4)	6047(4)	3380(3)	319(3)	23(2)
C(5)	4933(5)	3572(3)	26(2)	16(2)
C(6)	4047(4)	2985(4)	156(2)	11(2)
C(7)	5620(9)	1202(6)	1357(4)	34(3)
C(8)	7036(8)	4038(6)	178(5)	34(3)
C(9)	2889(8)	3188(6)	-203(4)	18(2)
C(10)	1153(5)	1926(3)	-777(2)	11(2)
C(11)	1147(5)	1548(3)	-1310(2)	14(2)
C(12)	683(5)	2046(3)	-1860(2)	14(2)
C(13)	224(5)	2922(3)	-1877(2)	17(2)
C(14)	229(5)	3300(3)	-1344(2)	16(2)
C(15)	694(5)	2802(3)	-794(2)	11(2)
C(16)	1632(9)	583(6)	-1284(4)	32(3)
C(17)	-312(9)	3467(6)	-2483(4)	40(3)
C(18)	719(8)	3231(6)	-220(4)	19(3)
C(19)	301(5)	2487(3)	1295(2)	13(2)
C(20)	-675(5)	2354(3)	1689(2)	14(2)
C(21)	-1346(4)	3079(4)	1861(2)	15(2)
C(22)	-1041(5)	3936(3)	1640(3)	17(2)
C(23)	-65(5)	4068(3)	1246(2)	14(2)
C(24)	606(4)	3343(4)	1074(2)	11(2)
C(25)	-1003(8)	1424(6)	1930(4)	29(3)
C(26)	-1793(8)	4726(6)	1816(4)	28(3)
C(27)	1711(8)	3481(6)	693(4)	17(2)
C(28)	3014(8)	-713(6)	1776(4)	24(3)

C(29)	1890(9)	-633(6)	2178(4)	34(3)
C(30)	1919(8)	-1405(6)	786(4)	25(3)
C(31)	1526(9)	-1263(6)	115(4)	39(3)
C(32)	4087(8)	-515(6)	563(4)	21(3)
C(33)	4983(8)	-1293(6)	756(4)	32(3)
C(34)	4471(5)	8411(3)	3167(2)	13(2)
C(35)	5455(5)	8716(3)	2828(3)	16(2)
C(36)	6058(4)	8195(4)	2442(2)	17(2)
C(37)	5677(5)	7370(3)	2396(2)	17(2)
C(38)	4693(5)	7064(3)	2735(3)	16(2)
C(39)	4090(4)	7585(4)	3121(2)	11(2)
C(40)	5841(8)	9626(5)	2872(4)	17(2)
C(41)	6341(8)	6785(6)	1989(4)	31(3)
C(42)	2980(8)	7283(6)	3463(4)	15(2)
C(43)	3755(5)	7726(3)	5349(2)	16(2)
C(44)	3796(5)	7737(3)	5981(3)	20(2)
C(45)	4133(5)	6961(4)	6392(2)	24(2)
C(46)	4429(5)	6173(3)	6171(2)	25(2)
C(47)	4388(5)	6162(3)	5539(3)	21(2)
C(48)	4051(5)	6938(4)	5128(2)	16(2)
C(49)	3467(9)	8595(6)	6209(4)	35(3)
C(50)	4768(10)	5311(6)	6635(4)	49(3)
C(51)	4052(8)	6927(6)	4442(4)	15(2)
C(52)	507(5)	8332(4)	3926(3)	18(2)
C(53)	-595(5)	8684(3)	3660(3)	17(2)
C(54)	-1486(4)	8126(4)	3595(3)	24(2)
C(55)	-1275(5)	7216(4)	3796(3)	27(2)
C(56)	-174(5)	6864(3)	4062(3)	21(2)
C(57)	717(4)	7422(4)	4127(3)	17(2)
C(58)	-795(9)	9658(6)	3402(4)	38(3)
C(59)	-2282(8)	6603(6)	3724(5)	38(3)
C(60)	1881(8)	7026(6)	4433(4)	18(2)
C(61)	1880(9)	11309(7)	3374(5)	42(3)
C(62)	2933(11)	11297(7)	2947(5)	63(4)
C(63)	873(8)	10811(6)	4582(4)	25(3)

C(64)	-21(9)	11630(7)	4461(5)	50(3)
C(65)	3091(10)	11635(7)	4464(5)	50(3)
C(66)	3491(10)	11310(9)	5119(6)	75(4)
C(67)	3194(9)	6174(6)	1470(5)	40(3)
C(68)	3551(6)	5204(3)	1652(3)	28(3)
C(69)	2709(4)	4635(4)	1914(3)	33(3)
C(70)	3034(5)	3729(4)	2072(3)	33(3)
C(71)	4200(6)	3391(3)	1968(3)	40(3)
C(72)	5042(4)	3960(4)	1706(3)	36(3)
C(73)	4718(5)	4867(4)	1549(3)	23(3)
C(74)	7905(13)	5741(7)	5566(6)	92(5)
C(75)	8885(7)	5856(5)	5925(4)	85(5)
C(76)	8702(6)	6070(5)	6512(4)	59(4)
C(77)	9672(9)	6236(5)	6856(3)	79(4)
C(78)	10826(7)	6188(5)	6612(4)	80(4)
C(79)	11009(6)	5974(5)	6025(4)	94(5)
C(80)	10038(8)	5808(5)	5682(3)	48(3)
N(1)	1808(6)	2966(4)	173(3)	12(2)
N(2)	2958(6)	7404(4)	4124(3)	10(2)
O(1)	3459(5)	1591(4)	689(3)	22(2)
O(2)	1554(5)	1412(4)	-242(3)	18(2)
O(3)	898(5)	1762(4)	1108(3)	20(2)
O(4)	1933(5)	352(4)	785(3)	17(2)
O(5)	3911(5)	8928(4)	3546(2)	18(2)
O(6)	3409(5)	8472(4)	4957(2)	19(2)
O(7)	1357(5)	8899(4)	4004(3)	19(2)
O(8)	2937(5)	9972(4)	4243(3)	18(2)
P(1)	2694(2)	-507(2)	967(1)	16(1)
P(2)	2248(2)	10874(2)	4171(1)	26(1)

Table 3. Bond lengths [Å] and angles [°] for **13**•O=PEt$_3$.

Al(1)-O(3)	1.762(6)	Al(1)-O(2)	1.777(6)	Al(1)-N(1)	2.145(7)
Al(1)-O(1)	1.768(6)	Al(1)-O(4)	1.850(6)	Al(2)-O(5)	1.760(6)

Al(2)-O(7)	1.772(6)	C(14)-H(14)	0.9500	C(28)-H(28B)	0.9900
Al(2)-O(6)	1.773(6)	C(15)-C(18)	1.517(9)	C(29)-H(29A)	0.9800
Al(2)-O(8)	1.853(6)	C(16)-H(16A)	0.9800	C(29)-H(29B)	0.9800
Al(2)-N(2)	2.136(7)	C(16)-H(16B)	0.9800	C(29)-H(29C)	0.9800
C(1)-O(1)	1.355(7)	C(16)-H(16C)	0.9800	C(30)-C(31)	1.511(12)
C(1)-C(2)	1.3900	C(17)-H(17A)	0.9800	C(30)-P(1)	1.790(9)
C(1)-C(6)	1.3900	C(17)-H(17B)	0.9800	C(30)-H(30A)	0.9900
C(2)-C(3)	1.3900	C(17)-H(17C)	0.9800	C(30)-H(30B)	0.9900
C(2)-C(7)	1.492(10)	C(18)-N(1)	1.481(10)	C(31)-H(31A)	0.9800
C(3)-C(4)	1.3900	C(18)-H(18A)	0.9900	C(31)-H(31B)	0.9800
C(3)-H(3)	0.9500	C(18)-H(18B)	0.9900	C(31)-H(31C)	0.9800
C(4)-C(5)	1.3900	C(19)-O(3)	1.368(6)	C(32)-C(33)	1.493(11)
C(4)-C(8)	1.553(9)	C(19)-C(20)	1.3900	C(32)-P(1)	1.782(9)
C(5)-C(6)	1.3900	C(19)-C(24)	1.3900	C(32)-H(32A)	0.9900
C(5)-H(5)	0.9500	C(20)-C(21)	1.3900	C(32)-H(32B)	0.9900
C(6)-C(9)	1.501(9)	C(20)-C(25)	1.508(9)	C(33)-H(33A)	0.9800
C(7)-H(7A)	0.9800	C(21)-C(22)	1.3900	C(33)-H(33B)	0.9800
C(7)-H(7B)	0.9800	C(21)-H(21)	0.9500	C(33)-H(33C)	0.9800
C(7)-H(7C)	0.9800	C(22)-C(23)	1.3900	C(34)-O(5)	1.357(6)
C(8)-H(8A)	0.9800	C(22)-C(26)	1.517(9)	C(34)-C(35)	1.3900
C(8)-H(8B)	0.9800	C(23)-C(24)	1.3900	C(34)-C(39)	1.3900
C(8)-H(8C)	0.9800	C(23)-H(23)	0.9500	C(35)-C(36)	1.3900
C(9)-N(1)	1.485(10)	C(24)-C(27)	1.492(9)	C(35)-C(40)	1.515(9)
C(9)-H(9A)	0.9900	C(25)-H(25A)	0.9800	C(36)-C(37)	1.3900
C(9)-H(9B)	0.9900	C(25)-H(25B)	0.9800	C(36)-H(36)	0.9500
C(10)-O(2)	1.351(6)	C(25)-H(25C)	0.9800	C(37)-C(38)	1.3900
C(10)-C(11)	1.3900	C(26)-H(26A)	0.9800	C(37)-C(41)	1.514(9)
C(10)-C(15)	1.3900	C(26)-H(26B)	0.9800	C(38)-C(39)	1.3900
C(11)-C(12)	1.3900	C(26)-H(26C)	0.9800	C(38)-H(38)	0.9500
C(11)-C(16)	1.522(9)	C(27)-N(1)	1.492(10)	C(39)-C(42)	1.507(9)
C(12)-C(13)	1.3900	C(27)-H(27A)	0.9900	C(40)-H(40A)	0.9800
C(12)-H(12)	0.9500	C(27)-H(27B)	0.9900	C(40)-H(40B)	0.9800
C(13)-C(14)	1.3900	C(28)-C(29)	1.533(12)	C(40)-H(40C)	0.9800
C(13)-C(17)	1.539(10)	C(28)-P(1)	1.780(9)	C(41)-H(41A)	0.9800
C(14)-C(15)	1.3900	C(28)-H(28A)	0.9900	C(41)-H(41B)	0.9800

C(41)-H(41C)	0.9800	C(55)-C(59)	1.551(9)	C(66)-H(66C)	0.9800
C(42)-N(2)	1.491(10)	C(56)-C(57)	1.3900	C(67)-C(68)	1.493(10)
C(42)-H(42A)	0.9900	C(56)-H(56)	0.9500	C(67)-H(67A)	0.9800
C(42)-H(42B)	0.9900	C(57)-C(60)	1.499(9)	C(67)-H(67B)	0.9800
C(43)-O(6)	1.338(6)	C(58)-H(58A)	0.9800	C(67)-H(67C)	0.9800
C(43)-C(44)	1.3900	C(58)-H(58B)	0.9800	C(68)-C(69)	1.3900
C(43)-C(48)	1.3900	C(58)-H(58C)	0.9800	C(68)-C(73)	1.3900
C(44)-C(45)	1.3900	C(59)-H(59A)	0.9800	C(69)-C(70)	1.3900
C(44)-C(49)	1.501(9)	C(59)-H(59B)	0.9800	C(69)-H(69)	0.9500
C(45)-C(46)	1.3900	C(59)-H(59C)	0.9800	C(70)-C(71)	1.3900
C(45)-H(45)	0.9500	C(60)-N(2)	1.487(10)	C(70)-H(70)	0.9500
C(46)-C(47)	1.3900	C(60)-H(60A)	0.9900	C(71)-C(72)	1.3900
C(46)-C(50)	1.544(10)	C(60)-H(60B)	0.9900	C(71)-H(71)	0.9500
C(47)-C(48)	1.3900	C(61)-C(62)	1.496(13)	C(72)-C(73)	1.3900
C(47)-H(47)	0.9500	C(61)-P(2)	1.798(10)	C(72)-H(72)	0.9500
C(48)-C(51)	1.505(9)	C(61)-H(61A)	0.9900	C(73)-H(73)	0.9500
C(49)-H(49A)	0.9800	C(61)-H(61B)	0.9900	C(74)-C(75)	1.394(12)
C(49)-H(49B)	0.9800	C(62)-H(62A)	0.9800	C(74)-H(74A)	0.9800
C(49)-H(49C)	0.9800	C(62)-H(62B)	0.9800	C(74)-H(74B)	0.9800
C(50)-H(50A)	0.9800	C(62)-H(62C)	0.9800	C(74)-H(74C)	0.9800
C(50)-H(50B)	0.9800	C(63)-C(64)	1.522(12)	C(75)-C(76)	1.3900
C(50)-H(50C)	0.9800	C(63)-P(2)	1.774(9)	C(75)-C(80)	1.3900
C(51)-N(2)	1.483(10)	C(63)-H(63A)	0.9900	C(76)-C(77)	1.3900
C(51)-H(51A)	0.9900	C(63)-H(63B)	0.9900	C(76)-H(76)	0.9500
C(51)-H(51B)	0.9900	C(64)-H(64A)	0.9800	C(77)-C(78)	1.3900
C(52)-O(7)	1.370(7)	C(64)-H(64B)	0.9800	C(77)-H(77)	0.9500
C(52)-C(53)	1.3900	C(64)-H(64C)	0.9800	C(78)-C(79)	1.3900
C(52)-C(57)	1.3900	C(65)-C(66)	1.495(14)	C(78)-H(78)	0.9500
C(53)-C(54)	1.3900	C(65)-P(2)	1.764(11)	C(79)-C(80)	1.3900
C(53)-C(58)	1.501(10)	C(65)-H(65A)	0.9900	C(79)-H(79)	0.9500
C(54)-C(55)	1.3900	C(65)-H(65B)	0.9900	C(80)-H(80)	0.9500
C(54)-H(54)	0.9500	C(66)-H(66A)	0.9800	O(4)-P(1)	1.499(6)
C(55)-C(56)	1.3900	C(66)-H(66B)	0.9800	O(8)-P(2)	1.508(6)

O(3)-Al(1)-O(1)	116.2(3)	O(3)-Al(1)-O(2)	126.8(3)	O(1)-Al(1)-O(2)	116.9(3)

O(3)-Al(1)-O(4)	90.5(3)	C(2)-C(7)-H(7A)	109.5	C(10)-C(15)-C(18)	120.6(5)
O(1)-Al(1)-O(4)	93.6(3)	C(2)-C(7)-H(7B)	109.5	C(11)-C(16)-H(16A)	109.5
O(2)-Al(1)-O(4)	89.6(3)	H(7A)-C(7)-H(7B)	109.5	C(11)-C(16)-H(16B)	109.5
O(3)-Al(1)-N(1)	89.4(3)	C(2)-C(7)-H(7C)	109.5	H(16A)-C(16)-H(16B)	109.5
O(1)-Al(1)-N(1)	89.6(3)	H(7A)-C(7)-H(7C)	109.5	C(11)-C(16)-H(16C)	109.5
O(2)-Al(1)-N(1)	87.7(3)	H(7B)-C(7)-H(7C)	109.5	H(16A)-C(16)-H(16C)	109.5
O(4)-Al(1)-N(1)	176.5(3)	C(4)-C(8)-H(8A)	109.5	H(16B)-C(16)-H(16C)	109.5
O(5)-Al(2)-O(7)	117.2(3)	C(4)-C(8)-H(8B)	109.5	C(13)-C(17)-H(17A)	109.5
O(5)-Al(2)-O(6)	123.1(3)	H(8A)-C(8)-H(8B)	109.5	C(13)-C(17)-H(17B)	109.5
O(7)-Al(2)-O(6)	119.6(3)	C(4)-C(8)-H(8C)	109.5	H(17A)-C(17)-H(17B)	109.5
O(5)-Al(2)-O(8)	90.4(3)	H(8A)-C(8)-H(8C)	109.5	C(13)-C(17)-H(17C)	109.5
O(7)-Al(2)-O(8)	92.9(3)	H(8B)-C(8)-H(8C)	109.5	H(17A)-C(17)-H(17C)	109.5
O(6)-Al(2)-O(8)	90.1(3)	N(1)-C(9)-C(6)	113.8(6)	H(17B)-C(17)-H(17C)	109.5
O(5)-Al(2)-N(2)	89.4(3)	N(1)-C(9)-H(9A)	108.8	N(1)-C(18)-C(15)	114.8(6)
O(7)-Al(2)-N(2)	89.3(3)	C(6)-C(9)-H(9A)	108.8	N(1)-C(18)-H(18A)	108.6
O(6)-Al(2)-N(2)	88.0(3)	N(1)-C(9)-H(9B)	108.8	C(15)-C(18)-H(18A)	108.6
O(8)-Al(2)-N(2)	177.6(3)	C(6)-C(9)-H(9B)	108.8	N(1)-C(18)-H(18B)	108.6
O(1)-C(1)-C(2)	118.5(4)	H(9A)-C(9)-H(9B)	107.7	C(15)-C(18)-H(18B)	108.6
O(1)-C(1)-C(6)	121.4(4)	O(2)-C(10)-C(11)	118.6(4)	H(18A)-C(18)-H(18B)	107.5
C(2)-C(1)-C(6)	120.0	O(2)-C(10)-C(15)	121.3(4)	O(3)-C(19)-C(20)	118.3(4)
C(1)-C(2)-C(3)	120.0	C(11)-C(10)-C(15)	120.0	O(3)-C(19)-C(24)	121.6(4)
C(1)-C(2)-C(7)	120.5(5)	C(12)-C(11)-C(10)	120.0	C(20)-C(19)-C(24)	120.0
C(3)-C(2)-C(7)	119.5(5)	C(12)-C(11)-C(16)	120.3(5)	C(19)-C(20)-C(21)	120.0
C(4)-C(3)-C(2)	120.0	C(10)-C(11)-C(16)	119.7(5)	C(19)-C(20)-C(25)	119.9(5)
C(4)-C(3)-H(3)	120.0	C(11)-C(12)-C(13)	120.0	C(21)-C(20)-C(25)	120.1(5)
C(2)-C(3)-H(3)	120.0	C(11)-C(12)-H(12)	120.0	C(20)-C(21)-C(22)	120.0
C(3)-C(4)-C(5)	120.0	C(13)-C(12)-H(12)	120.0	C(20)-C(21)-H(21)	120.0
C(3)-C(4)-C(8)	119.8(5)	C(12)-C(13)-C(14)	120.0	C(22)-C(21)-H(21)	120.0
C(5)-C(4)-C(8)	120.2(5)	C(12)-C(13)-C(17)	120.0(5)	C(23)-C(22)-C(21)	120.0
C(6)-C(5)-C(4)	120.0	C(14)-C(13)-C(17)	120.0(5)	C(23)-C(22)-C(26)	120.1(5)
C(6)-C(5)-H(5)	120.0	C(15)-C(14)-C(13)	120.0	C(21)-C(22)-C(26)	119.9(5)
C(4)-C(5)-H(5)	120.0	C(15)-C(14)-H(14)	120.0	C(22)-C(23)-C(24)	120.0
C(5)-C(6)-C(1)	120.0	C(13)-C(14)-H(14)	120.0	C(22)-C(23)-H(23)	120.0
C(5)-C(6)-C(9)	118.2(5)	C(14)-C(15)-C(10)	120.0	C(24)-C(23)-H(23)	120.0
C(1)-C(6)-C(9)	121.7(5)	C(14)-C(15)-C(18)	119.4(5)	C(23)-C(24)-C(19)	120.0

C(23)-C(24)-C(27)	119.9(5)
C(19)-C(24)-C(27)	119.9(5)
C(20)-C(25)-H(25A)	109.5
C(20)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
C(20)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
C(22)-C(26)-H(26A)	109.5
C(22)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
C(22)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
C(24)-C(27)-N(1)	113.7(6)
C(24)-C(27)-H(27A)	108.8
N(1)-C(27)-H(27A)	108.8
C(24)-C(27)-H(27B)	108.8
N(1)-C(27)-H(27B)	108.8
H(27A)-C(27)-H(27B)	107.7
C(29)-C(28)-P(1)	113.4(6)
C(29)-C(28)-H(28A)	108.9
P(1)-C(28)-H(28A)	108.9
C(29)-C(28)-H(28B)	108.9
P(1)-C(28)-H(28B)	108.9
H(28A)-C(28)-H(28B)	107.7
C(28)-C(29)-H(29A)	109.5
C(28)-C(29)-H(29B)	109.5
H(29A)-C(29)-H(29B)	109.5
C(28)-C(29)-H(29C)	109.5
H(29A)-C(29)-H(29C)	109.5
H(29B)-C(29)-H(29C)	109.5
C(31)-C(30)-P(1)	112.8(6)
C(31)-C(30)-H(30A)	109.0
P(1)-C(30)-H(30A)	109.0
C(31)-C(30)-H(30B)	109.0
P(1)-C(30)-H(30B)	109.0
H(30A)-C(30)-H(30B)	107.8
C(30)-C(31)-H(31A)	109.5
C(30)-C(31)-H(31B)	109.5
H(31A)-C(31)-H(31B)	109.5
C(30)-C(31)-H(31C)	109.5
H(31A)-C(31)-H(31C)	109.5
H(31B)-C(31)-H(31C)	109.5
C(33)-C(32)-P(1)	117.1(6)
C(33)-C(32)-H(32A)	108.0
P(1)-C(32)-H(32A)	108.0
C(33)-C(32)-H(32B)	108.0
P(1)-C(32)-H(32B)	108.0
H(32A)-C(32)-H(32B)	107.3
C(32)-C(33)-H(33A)	109.5
C(32)-C(33)-H(33B)	109.5
H(33A)-C(33)-H(33B)	109.5
C(32)-C(33)-H(33C)	109.5
H(33A)-C(33)-H(33C)	109.5
H(33B)-C(33)-H(33C)	109.5
O(5)-C(34)-C(35)	118.7(4)
O(5)-C(34)-C(39)	121.3(4)
C(35)-C(34)-C(39)	120.0
C(34)-C(35)-C(36)	120.0
C(34)-C(35)-C(40)	119.3(5)
C(36)-C(35)-C(40)	120.7(5)
C(35)-C(36)-C(37)	120.0
C(35)-C(36)-H(36)	120.0
C(37)-C(36)-H(36)	120.0
C(38)-C(37)-C(36)	120.0
C(38)-C(37)-C(41)	119.3(5)
C(36)-C(37)-C(41)	120.7(5)
C(37)-C(38)-C(39)	120.0
C(37)-C(38)-H(38)	120.0
C(39)-C(38)-H(38)	120.0
C(38)-C(39)-C(34)	120.0
C(38)-C(39)-C(42)	120.4(5)
C(34)-C(39)-C(42)	119.5(5)
C(35)-C(40)-H(40A)	109.5
C(35)-C(40)-H(40B)	109.5
H(40A)-C(40)-H(40B)	109.5
C(35)-C(40)-H(40C)	109.5
H(40A)-C(40)-H(40C)	109.5
H(40B)-C(40)-H(40C)	109.5
C(37)-C(41)-H(41A)	109.5
C(37)-C(41)-H(41B)	109.5
H(41A)-C(41)-H(41B)	109.5
C(37)-C(41)-H(41C)	109.5
H(41A)-C(41)-H(41C)	109.5
H(41B)-C(41)-H(41C)	109.5
N(2)-C(42)-C(39)	113.7(6)
N(2)-C(42)-H(42A)	108.8
C(39)-C(42)-H(42A)	108.8
N(2)-C(42)-H(42B)	108.8
C(39)-C(42)-H(42B)	108.8
H(42A)-C(42)-H(42B)	107.7
O(6)-C(43)-C(44)	119.6(4)
O(6)-C(43)-C(48)	120.4(4)
C(44)-C(43)-C(48)	120.0
C(43)-C(44)-C(45)	120.0
C(43)-C(44)-C(49)	119.1(5)
C(45)-C(44)-C(49)	120.9(5)
C(46)-C(45)-C(44)	120.0
C(46)-C(45)-H(45)	120.0
C(44)-C(45)-H(45)	120.0
C(47)-C(46)-C(45)	120.0
C(47)-C(46)-C(50)	120.5(5)
C(45)-C(46)-C(50)	119.4(5)
C(46)-C(47)-C(48)	120.0

C(46)-C(47)-H(47)	120.0
C(48)-C(47)-H(47)	120.0
C(47)-C(48)-C(43)	120.0
C(47)-C(48)-C(51)	119.7(5)
C(43)-C(48)-C(51)	120.3(5)
C(44)-C(49)-H(49A)	109.5
C(44)-C(49)-H(49B)	109.5
H(49A)-C(49)-H(49B)	109.5
C(44)-C(49)-H(49C)	109.5
H(49A)-C(49)-H(49C)	109.5
H(49B)-C(49)-H(49C)	109.5
C(46)-C(50)-H(50A)	109.5
C(46)-C(50)-H(50B)	109.5
H(50A)-C(50)-H(50B)	109.5
C(46)-C(50)-H(50C)	109.5
H(50A)-C(50)-H(50C)	109.5
H(50B)-C(50)-H(50C)	109.5
N(2)-C(51)-C(48)	112.8(6)
N(2)-C(51)-H(51A)	109.0
C(48)-C(51)-H(51A)	109.0
N(2)-C(51)-H(51B)	109.0
C(48)-C(51)-H(51B)	109.0
H(51A)-C(51)-H(51B)	107.8
O(7)-C(52)-C(53)	118.9(5)
O(7)-C(52)-C(57)	121.0(5)
C(53)-C(52)-C(57)	120.0
C(52)-C(53)-C(54)	120.0
C(52)-C(53)-C(58)	120.1(5)
C(54)-C(53)-C(58)	119.7(5)
C(55)-C(54)-C(53)	120.0
C(55)-C(54)-H(54)	120.0
C(53)-C(54)-H(54)	120.0
C(56)-C(55)-C(54)	120.0
C(56)-C(55)-C(59)	120.7(5)
C(54)-C(55)-C(59)	119.3(5)
C(55)-C(56)-C(57)	120.0
C(55)-C(56)-H(56)	120.0
C(57)-C(56)-H(56)	120.0
C(56)-C(57)-C(52)	120.0
C(56)-C(57)-C(60)	118.7(5)
C(52)-C(57)-C(60)	121.2(5)
C(53)-C(58)-H(58A)	109.5
C(53)-C(58)-H(58B)	109.5
H(58A)-C(58)-H(58B)	109.5
C(53)-C(58)-H(58C)	109.5
H(58A)-C(58)-H(58C)	109.5
H(58B)-C(58)-H(58C)	109.5
C(55)-C(59)-H(59A)	109.5
C(55)-C(59)-H(59B)	109.5
H(59A)-C(59)-H(59B)	109.5
C(55)-C(59)-H(59C)	109.5
H(59A)-C(59)-H(59C)	109.5
H(59B)-C(59)-H(59C)	109.5
N(2)-C(60)-C(57)	113.6(6)
N(2)-C(60)-H(60A)	108.8
C(57)-C(60)-H(60A)	108.8
N(2)-C(60)-H(60B)	108.8
C(57)-C(60)-H(60B)	108.8
H(60A)-C(60)-H(60B)	107.7
C(62)-C(61)-P(2)	113.9(8)
C(62)-C(61)-H(61A)	108.8
P(2)-C(61)-H(61A)	108.8
C(62)-C(61)-H(61B)	108.8
P(2)-C(61)-H(61B)	108.8
H(61A)-C(61)-H(61B)	107.7
C(61)-C(62)-H(62A)	109.5
C(61)-C(62)-H(62B)	109.5
H(62A)-C(62)-H(62B)	109.5
C(61)-C(62)-H(62C)	109.5
H(62A)-C(62)-H(62C)	109.5
H(62B)-C(62)-H(62C)	109.5
C(64)-C(63)-P(2)	116.5(7)
C(64)-C(63)-H(63A)	108.2
P(2)-C(63)-H(63A)	108.2
C(64)-C(63)-H(63B)	108.2
P(2)-C(63)-H(63B)	108.2
H(63A)-C(63)-H(63B)	107.3
C(63)-C(64)-H(64A)	109.5
C(63)-C(64)-H(64B)	109.5
H(64A)-C(64)-H(64B)	109.5
C(63)-C(64)-H(64C)	109.5
H(64A)-C(64)-H(64C)	109.5
H(64B)-C(64)-H(64C)	109.5
C(66)-C(65)-P(2)	112.6(8)
C(66)-C(65)-H(65A)	109.1
P(2)-C(65)-H(65A)	109.1
C(66)-C(65)-H(65B)	109.1
P(2)-C(65)-H(65B)	109.1
H(65A)-C(65)-H(65B)	107.8
C(65)-C(66)-H(66A)	109.5
C(65)-C(66)-H(66B)	109.5
H(66A)-C(66)-H(66B)	109.5
C(65)-C(66)-H(66C)	109.5
H(66A)-C(66)-H(66C)	109.5
H(66B)-C(66)-H(66C)	109.5
C(68)-C(67)-H(67A)	109.5
C(68)-C(67)-H(67B)	109.5
H(67A)-C(67)-H(67B)	109.5
C(68)-C(67)-H(67C)	109.5
H(67A)-C(67)-H(67C)	109.5
H(67B)-C(67)-H(67C)	109.5
C(69)-C(68)-C(73)	120.0
C(69)-C(68)-C(67)	119.9(6)
C(73)-C(68)-C(67)	120.0(6)
C(68)-C(69)-C(70)	120.0

C(68)-C(69)-H(69)	120.0	C(79)-C(80)-C(75)	120.0
C(70)-C(69)-H(69)	120.0	C(79)-C(80)-H(80)	120.0
C(71)-C(70)-C(69)	120.0	C(75)-C(80)-H(80)	120.0
C(71)-C(70)-H(70)	120.0	C(18)-N(1)-C(9)	109.1(6)
C(69)-C(70)-H(70)	120.0	C(18)-N(1)-C(27)	107.5(6)
C(72)-C(71)-C(70)	120.0	C(9)-N(1)-C(27)	109.9(6)
C(72)-C(71)-H(71)	120.0	C(18)-N(1)-Al(1)	109.9(5)
C(70)-C(71)-H(71)	120.0	C(9)-N(1)-Al(1)	109.6(5)
C(73)-C(72)-C(71)	120.0	C(27)-N(1)-Al(1)	110.7(5)
C(73)-C(72)-H(72)	120.0	C(51)-N(2)-C(60)	108.8(6)
C(71)-C(72)-H(72)	120.0	C(51)-N(2)-C(42)	109.1(6)
C(72)-C(73)-C(68)	120.0	C(60)-N(2)-C(42)	109.7(6)
C(72)-C(73)-H(73)	120.0	C(51)-N(2)-Al(2)	109.5(5)
C(68)-C(73)-H(73)	120.0	C(60)-N(2)-Al(2)	109.8(5)
C(75)-C(74)-H(74A)	109.5	C(42)-N(2)-Al(2)	109.9(5)
C(75)-C(74)-H(74B)	109.5	C(1)-O(1)-Al(1)	135.7(5)
H(74A)-C(74)-H(74B)	109.5	C(10)-O(2)-Al(1)	137.2(4)
C(75)-C(74)-H(74C)	109.5	C(19)-O(3)-Al(1)	136.6(4)
H(74A)-C(74)-H(74C)	109.5	P(1)-O(4)-Al(1)	146.2(4)
H(74B)-C(74)-H(74C)	109.5	C(34)-O(5)-Al(2)	136.9(5)
C(76)-C(75)-C(80)	120.0	C(43)-O(6)-Al(2)	138.0(5)
C(76)-C(75)-C(74)	120.0(9)	C(52)-O(7)-Al(2)	135.7(5)
C(80)-C(75)-C(74)	119.9(9)	P(2)-O(8)-Al(2)	147.1(4)
C(77)-C(76)-C(75)	120.0	O(4)-P(1)-C(28)	111.0(4)
C(77)-C(76)-H(76)	120.0	O(4)-P(1)-C(32)	112.1(4)
C(75)-C(76)-H(76)	120.0	C(28)-P(1)-C(32)	108.1(4)
C(76)-C(77)-C(78)	120.0	O(4)-P(1)-C(30)	109.8(4)
C(76)-C(77)-H(77)	120.0	C(28)-P(1)-C(30)	108.5(4)
C(78)-C(77)-H(77)	120.0	C(32)-P(1)-C(30)	107.2(4)
C(79)-C(78)-C(77)	120.0	O(8)-P(2)-C(65)	110.7(5)
C(79)-C(78)-H(78)	120.0	O(8)-P(2)-C(63)	110.6(4)
C(77)-C(78)-H(78)	120.0	C(65)-P(2)-C(63)	108.1(5)
C(78)-C(79)-C(80)	120.0	O(8)-P(2)-C(61)	111.6(4)
C(78)-C(79)-H(79)	120.0	C(65)-P(2)-C(61)	108.6(5)
C(80)-C(79)-H(79)	120.0	C(63)-P(2)-C(61)	107.1(5)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **13**•O=PEt$_3$. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Al(1)	17(2)	9(2)	16(2)	-3(1)	-1(1)	-6(1)
Al(2)	18(2)	12(2)	16(2)	-4(1)	-2(1)	-4(1)
C(1)	16(3)	14(4)	17(4)	-1(3)	0(3)	-2(3)
C(2)	18(3)	18(3)	20(3)	-4(3)	-2(3)	-1(3)
C(3)	21(3)	28(3)	24(3)	-7(3)	-1(3)	-4(3)
C(4)	23(3)	25(3)	24(3)	-12(3)	3(3)	-7(3)
C(5)	18(3)	16(4)	18(4)	-9(3)	4(3)	-8(3)
C(6)	12(4)	9(4)	13(4)	-2(3)	3(3)	-6(3)
C(7)	32(7)	36(7)	38(7)	-7(6)	-4(6)	-15(6)
C(8)	26(6)	32(6)	50(7)	-16(5)	-9(5)	-17(5)
C(9)	23(4)	17(4)	15(4)	-6(3)	5(4)	-5(4)
C(10)	11(3)	12(3)	11(3)	-2(3)	-3(3)	-5(3)
C(11)	16(3)	14(3)	15(3)	-6(3)	2(3)	-5(3)
C(12)	16(3)	16(3)	12(3)	-5(3)	1(3)	-7(3)
C(13)	15(3)	21(3)	15(3)	-4(3)	-2(3)	-2(3)
C(14)	15(3)	17(3)	17(3)	-5(3)	-1(3)	-3(3)
C(15)	8(3)	12(3)	14(3)	-5(3)	1(3)	-4(3)
C(16)	45(7)	23(7)	37(7)	-22(5)	5(6)	-14(6)
C(17)	54(8)	39(7)	26(7)	-3(6)	-8(6)	-4(6)
C(18)	22(4)	17(4)	17(4)	-1(3)	2(4)	1(4)
C(19)	16(3)	13(3)	9(3)	-2(3)	-2(3)	0(3)
C(20)	12(3)	14(3)	16(3)	0(3)	-1(3)	-5(3)
C(21)	16(3)	14(3)	16(3)	-2(3)	1(3)	-5(3)
C(22)	22(3)	14(3)	17(3)	-7(3)	-1(3)	-1(3)
C(23)	18(3)	11(3)	14(3)	-4(3)	-1(3)	-2(3)
C(24)	16(3)	9(3)	8(3)	-3(3)	-2(3)	-3(3)
C(25)	28(7)	26(7)	36(7)	-8(5)	10(5)	-9(5)
C(26)	30(7)	33(7)	26(6)	-14(5)	8(5)	-7(6)

C(27)	22(4)	14(4)	15(4)	-6(3)	-6(3)	-1(3)
C(28)	20(4)	23(4)	27(4)	-1(4)	0(4)	-4(4)
C(29)	45(8)	28(7)	31(7)	-7(5)	1(6)	2(6)
C(30)	21(4)	23(4)	32(4)	-5(4)	5(4)	0(4)
C(31)	47(8)	31(7)	43(8)	-11(6)	1(6)	-16(6)
C(32)	21(4)	21(4)	21(4)	-6(4)	-2(4)	-3(4)
C(33)	27(7)	36(7)	32(7)	-4(5)	9(5)	-9(6)
C(34)	13(3)	15(3)	9(3)	1(3)	-2(3)	-1(3)
C(35)	14(3)	17(3)	18(3)	1(3)	-2(3)	-4(3)
C(36)	15(3)	19(3)	15(3)	0(3)	-1(3)	-4(3)
C(37)	17(3)	21(3)	14(3)	-4(3)	-1(3)	-2(3)
C(38)	17(3)	18(3)	15(3)	-1(3)	0(3)	-3(3)
C(39)	12(3)	12(3)	9(3)	0(3)	-3(3)	0(3)
C(40)	13(6)	17(6)	23(6)	-6(5)	3(5)	-7(5)
C(41)	29(7)	26(7)	37(7)	-3(5)	12(6)	-1(5)
C(42)	19(4)	12(4)	13(4)	-3(3)	-1(3)	-4(3)
C(43)	15(3)	18(3)	15(3)	-4(3)	-5(3)	-3(3)
C(44)	21(4)	22(3)	19(3)	-8(3)	-1(3)	0(3)
C(45)	27(4)	27(3)	17(3)	-4(3)	-3(3)	0(3)
C(46)	27(4)	24(3)	21(3)	-1(3)	-4(3)	3(3)
C(47)	23(4)	20(3)	19(3)	-1(3)	0(3)	1(3)
C(48)	17(3)	16(3)	14(3)	-3(3)	-3(3)	-2(3)
C(49)	54(8)	33(7)	18(6)	-12(5)	1(6)	5(6)
C(50)	86(10)	40(8)	18(7)	2(6)	-2(6)	-3(7)
C(51)	16(4)	14(4)	16(3)	-5(3)	0(3)	-7(3)
C(52)	17(4)	20(4)	18(4)	-3(3)	1(3)	-4(3)
C(53)	18(3)	18(3)	16(3)	-4(3)	3(3)	0(3)
C(54)	23(3)	29(3)	22(4)	-3(3)	1(3)	-5(3)
C(55)	24(4)	31(4)	28(4)	-5(3)	2(3)	-10(3)
C(56)	21(4)	24(4)	19(4)	-4(3)	-1(3)	-4(3)
C(57)	18(4)	20(4)	15(4)	-7(3)	1(3)	-4(3)
C(58)	36(7)	41(8)	35(7)	-1(6)	-17(6)	-4(6)
C(59)	29(7)	35(7)	53(8)	-10(6)	-10(6)	-20(6)
C(60)	23(4)	17(4)	16(4)	-4(3)	0(4)	-4(4)
C(61)	44(5)	34(5)	43(5)	1(4)	12(4)	1(4)

C(62)	98(11)	38(8)	48(8)	7(6)	23(8)	2(7)
C(63)	25(4)	24(4)	27(4)	-8(4)	4(4)	-4(4)
C(64)	44(8)	49(8)	57(8)	-14(7)	15(7)	-2(7)
C(65)	49(5)	46(5)	58(5)	-13(4)	5(4)	-10(4)
C(66)	51(9)	114(12)	84(11)	-62(9)	18(8)	-49(9)
C(67)	28(7)	52(8)	43(7)	-14(6)	1(6)	0(6)
C(68)	30(5)	26(4)	28(4)	-6(4)	-8(4)	-4(4)
C(69)	33(5)	36(5)	31(4)	-9(4)	2(4)	-8(4)
C(70)	35(5)	38(5)	28(4)	-9(4)	1(4)	-10(4)
C(71)	49(5)	38(5)	35(5)	-14(4)	-3(4)	-2(4)
C(72)	34(5)	40(5)	36(5)	-8(4)	-1(4)	-4(4)
C(73)	22(4)	23(4)	24(4)	-6(4)	2(4)	-2(4)
C(74)	143(14)	19(8)	116(12)	-13(8)	-82(11)	-7(8)
C(75)	90(6)	76(6)	88(6)	-14(4)	0(5)	-8(4)
C(76)	71(5)	57(5)	50(5)	-15(4)	7(4)	-3(4)
C(77)	77(6)	81(6)	75(6)	-10(4)	6(4)	-1(4)
C(78)	84(6)	78(6)	75(6)	-5(4)	-6(4)	-6(4)
C(79)	100(6)	87(6)	92(6)	-9(4)	6(5)	-4(4)
C(80)	47(5)	46(5)	53(5)	-9(4)	4(4)	-8(4)
N(1)	11(4)	14(4)	13(3)	-8(3)	-4(3)	-3(3)
N(2)	9(4)	13(3)	8(3)	0(3)	1(3)	-2(3)
O(1)	20(3)	20(3)	25(3)	-2(3)	-6(3)	-7(3)
O(2)	27(3)	12(3)	17(3)	-6(3)	-1(3)	-7(3)
O(3)	23(3)	19(3)	19(3)	-2(3)	7(3)	-2(3)
O(4)	16(3)	9(3)	24(3)	0(3)	-4(3)	0(3)
O(5)	26(3)	13(3)	16(3)	-7(3)	3(3)	-6(3)
O(6)	25(3)	14(3)	17(3)	-2(3)	-4(3)	-1(3)
O(7)	21(3)	14(3)	23(3)	-2(3)	-4(3)	-5(3)
O(8)	20(3)	13(3)	24(3)	-9(3)	4(3)	-4(3)
P(1)	18(2)	11(2)	20(2)	-1(1)	2(1)	-6(1)
P(2)	31(2)	15(2)	31(2)	-4(1)	11(1)	-5(1)

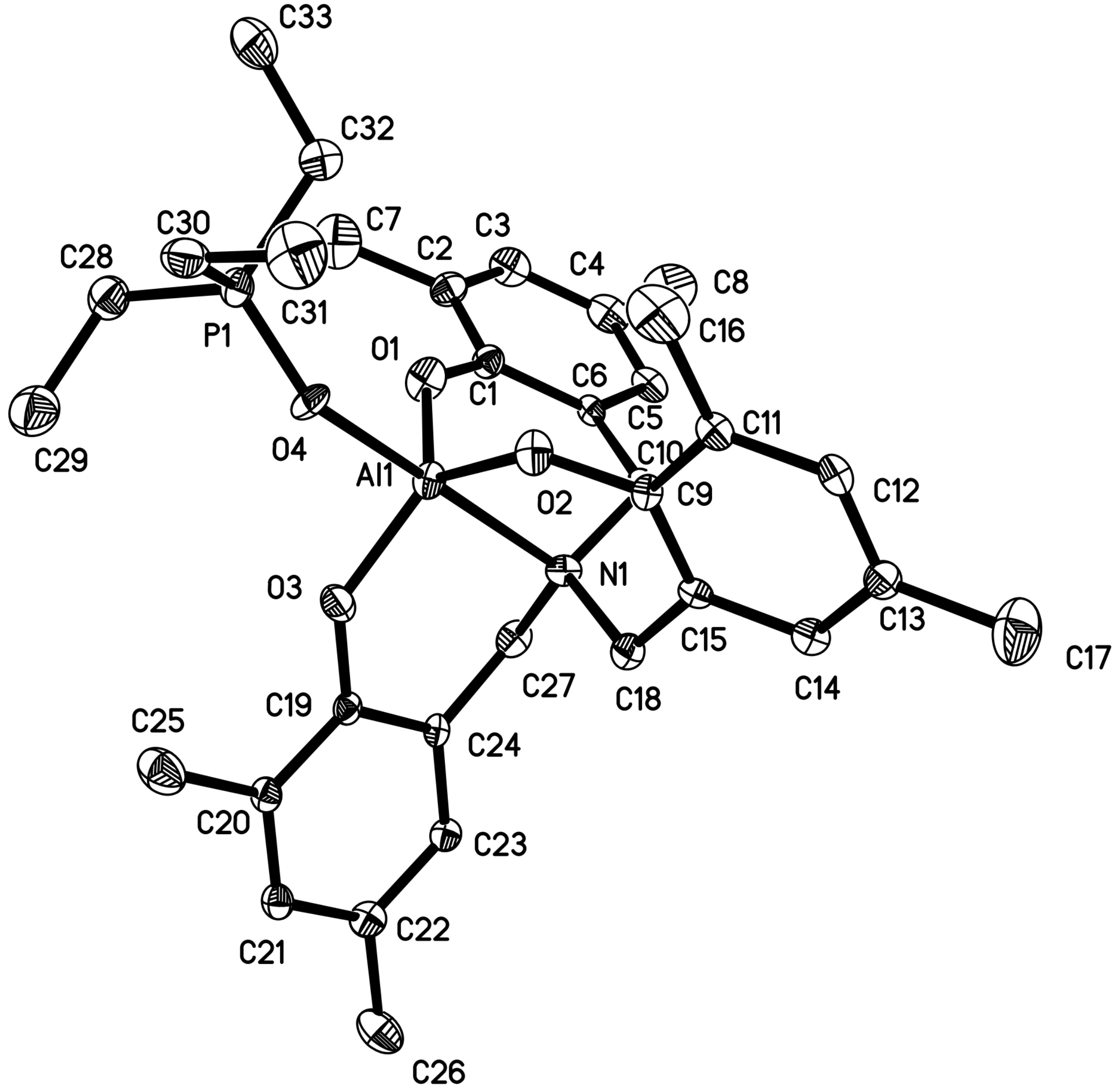
Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10 ^{3}) for **13**•O=PEt$_3$.

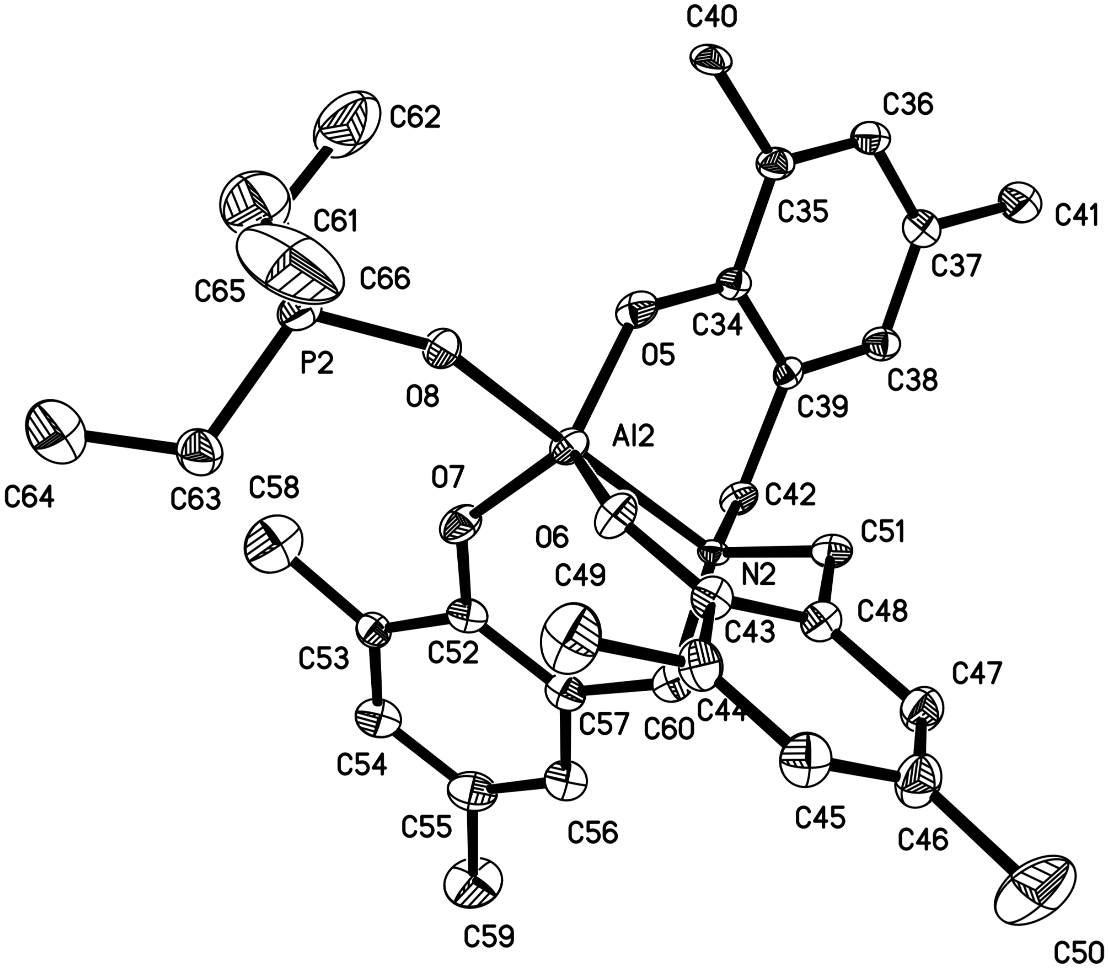
	x	y	z	U(eq)
H(3)	7035	2468	945	28
H(5)	4778	4106	-265	20
H(7A)	4910	1123	1622	51
H(7B)	6314	1269	1611	51
H(7C)	5787	680	1156	51
H(8A)	6832	4455	-205	51
H(8B)	7812	3705	129	51
H(8C)	7091	4367	521	51
H(9A)	2803	3828	-382	21
H(9B)	2929	2851	-551	21
H(12)	679	1787	-2224	17
H(14)	-84	3898	-1356	19
H(16A)	1091	193	-1038	49
H(16B)	2434	488	-1093	49
H(16C)	1684	448	-1705	49
H(17A)	-1097	3761	-2399	60
H(17B)	-413	3071	-2783	60
H(17C)	230	3916	-2654	60
H(18A)	656	3884	-350	23
H(18B)	4	3078	34	23
H(21)	-2012	2989	2130	18
H(23)	144	4653	1094	17
H(25A)	-1329	1174	1590	44
H(25B)	-1609	1441	2255	44
H(25C)	-284	1054	2100	44
H(26A)	-2555	4534	1994	43
H(26B)	-1955	5179	1446	43
H(26C)	-1354	4976	2121	43
H(27A)	2426	3307	965	20
H(27B)	1718	4121	521	20
H(28A)	3420	-1319	1891	29

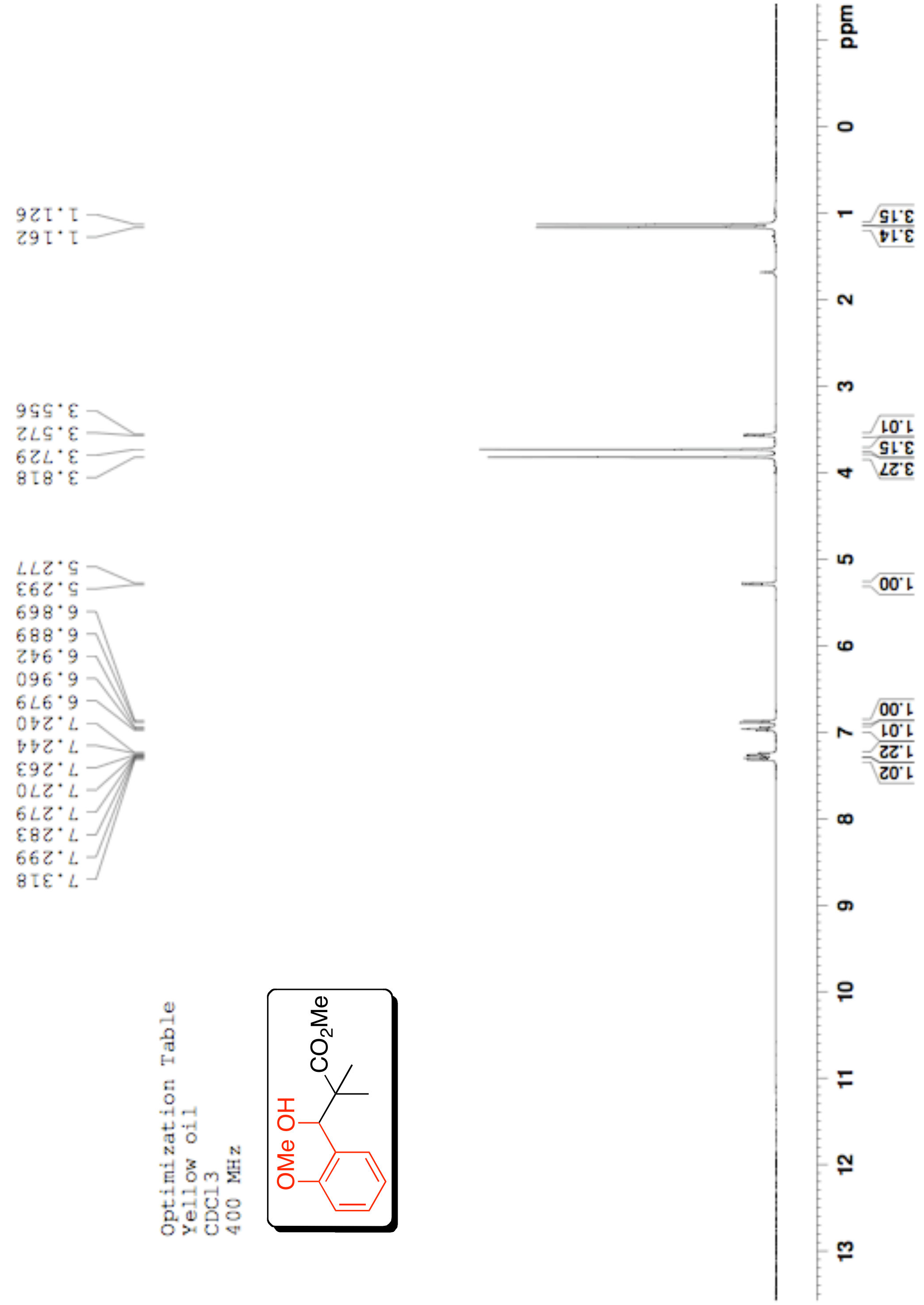
H(28B)	3577	-287	1867	29
H(29A)	1481	-35	2067	52
H(29B)	2126	-738	2616	52
H(29C)	1344	-1073	2106	52
H(30A)	2454	-1962	878	30
H(30B)	1203	-1477	1054	30
H(31A)	999	-712	20	58
H(31B)	1089	-1764	43	58
H(31C)	2234	-1222	-152	58
H(32A)	3910	-479	117	25
H(32B)	4469	29	609	25
H(33A)	5188	-1334	1194	48
H(33B)	5711	-1217	505	48
H(33C)	4639	-1838	694	48
H(36)	6730	8404	2210	20
H(38)	4433	6500	2704	20
H(40A)	5198	10081	2710	26
H(40B)	6572	9728	2629	26
H(40C)	6001	9659	3306	26
H(41A)	6347	6161	2188	46
H(41B)	7170	6947	1931	46
H(41C)	5935	6868	1586	46
H(42A)	2263	7619	3248	18
H(42B)	2927	6646	3446	18
H(45)	4161	6969	6825	28
H(47)	4591	5623	5388	25
H(49A)	4038	9027	6047	52
H(49B)	3494	8490	6663	52
H(49C)	2653	8828	6067	52
H(50A)	4112	5200	6932	73
H(50B)	5504	5373	6858	73
H(50C)	4902	4811	6410	73
H(51A)	4769	7204	4256	18
H(51B)	4114	6303	4374	18
H(54)	-2238	8367	3414	29

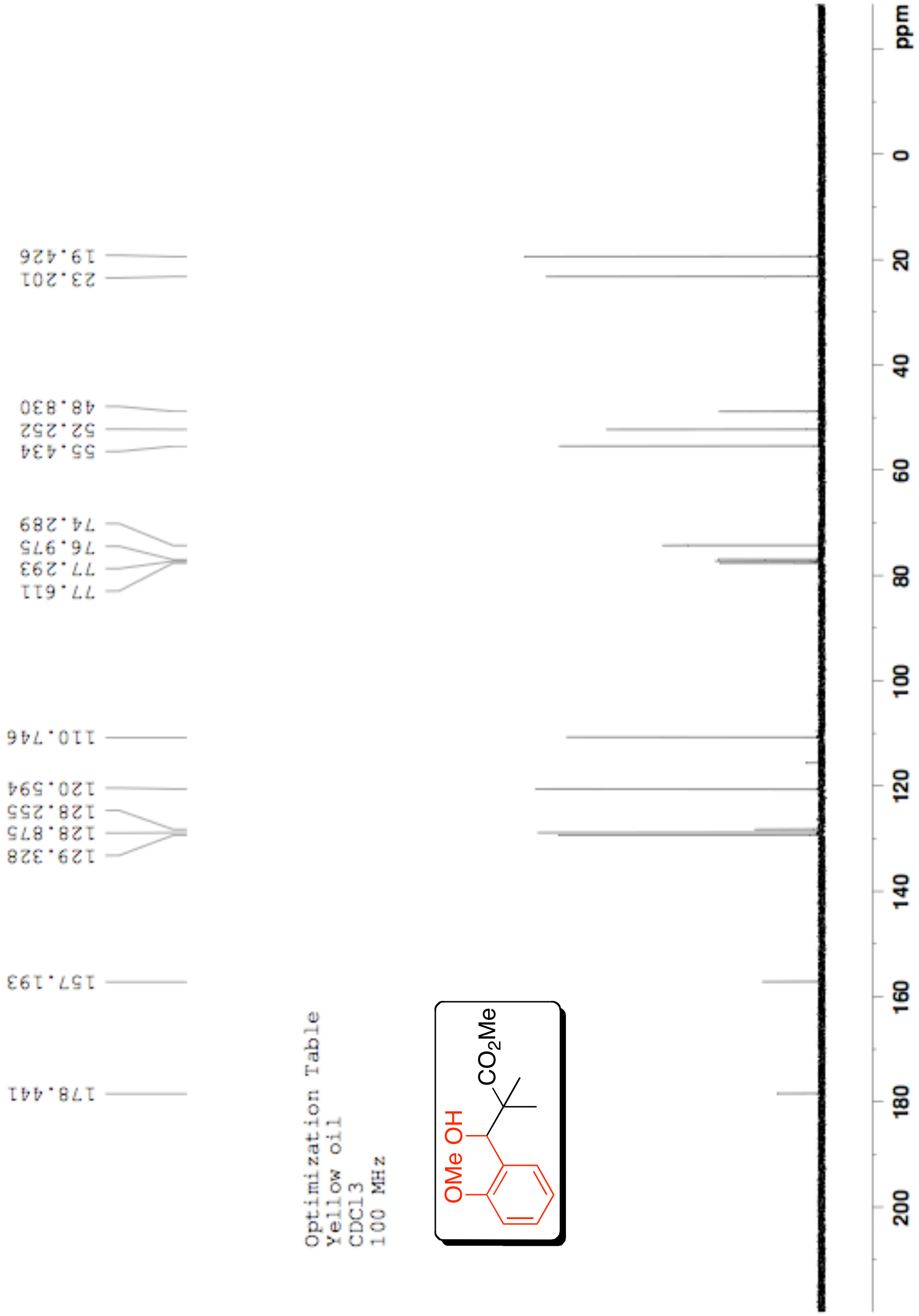
H(56)	-30	6241	4199	25
H(58A)	-1573	9780	3188	57
H(58B)	-152	9830	3110	57
H(58C)	-790	10000	3741	57
H(59A)	-1950	6103	3532	57
H(59B)	-2928	6942	3462	57
H(59C)	-2605	6377	4133	57
H(60A)	1869	7121	4869	22
H(60B)	1949	6377	4437	22
H(61A)	1264	10957	3235	50
H(61B)	1522	11929	3343	50
H(62A)	3525	11677	3062	95
H(62B)	2662	11518	2520	95
H(62C)	3303	10687	2979	95
H(63A)	475	10301	4481	30
H(63B)	1062	10682	5031	30
H(64A)	323	12128	4601	75
H(64B)	-766	11505	4687	75
H(64C)	-197	11783	4016	75
H(65A)	3808	11742	4201	60
H(65B)	2597	12207	4441	60
H(66A)	2785	11264	5389	113
H(66B)	4012	11729	5249	113
H(66C)	3936	10725	5150	113
H(67A)	2384	6259	1289	60
H(67B)	3764	6439	1165	60
H(67C)	3200	6461	1837	60
H(69)	1912	4865	1985	39
H(70)	2458	3340	2250	39
H(71)	4422	2772	2076	48
H(72)	5839	3730	1636	44
H(73)	5293	5255	1370	28
H(74A)	7331	5398	5826	138
H(74B)	8183	5422	5233	138
H(74C)	7511	6324	5386	138

H(76)	7913	6102	6679	71
H(77)	9547	6383	7257	94
H(78)	11489	6302	6847	96
H(79)	11797	5941	5858	113
H(80)	10163	5661	5281	58




C40
C62
C36
C35
C41
C61
C37
C65
C66
O5
C34
P2
C38
O8
C39
C64
C63
Al2
C58
O7
C42
O6
C51
C49
N2
C43
C48
C53
C52
C47
C57
C60
C44
C54
C55
C56
C45
C46
C59
C50


Optimization Table
Yellow oil
CDCl3
400 MHz
OMe OH
CO2Me
1.126
1.162
3.556
3.572
3.729
3.818
5.277
5.293
6.869
6.889
6.942
6.960
6.979
7.240
7.244
7.263
7.270
7.279
7.283
7.299
7.318
3.15
3.14
1.01
3.15
3.27
1.00
1.00
1.01
1.22
1.02
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13



Optimization Table
Yellow oil
CDCl3
100 MHz

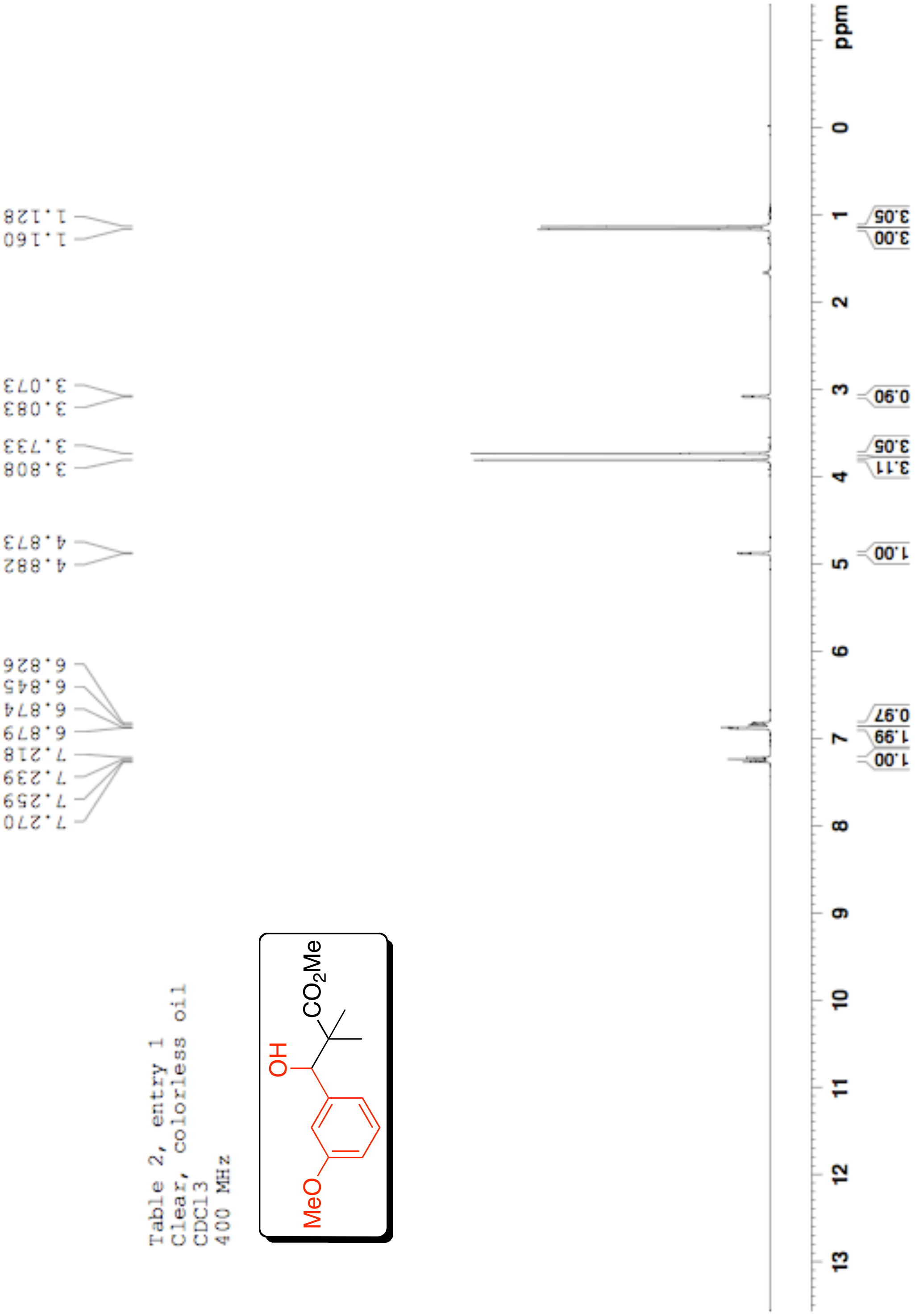


Table 2, entry 1
Clear, colorless oil
CDCl3
400 MHz
MeO
OH
CO2Me
1.128
1.160
3.073
3.083
3.733
3.808
4.873
4.882
6.826
6.845
6.874
6.879
7.218
7.239
7.259
7.270
3.05
3.00
0.90
3.05
3.11
1.00
0.97
1.99
1.00
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

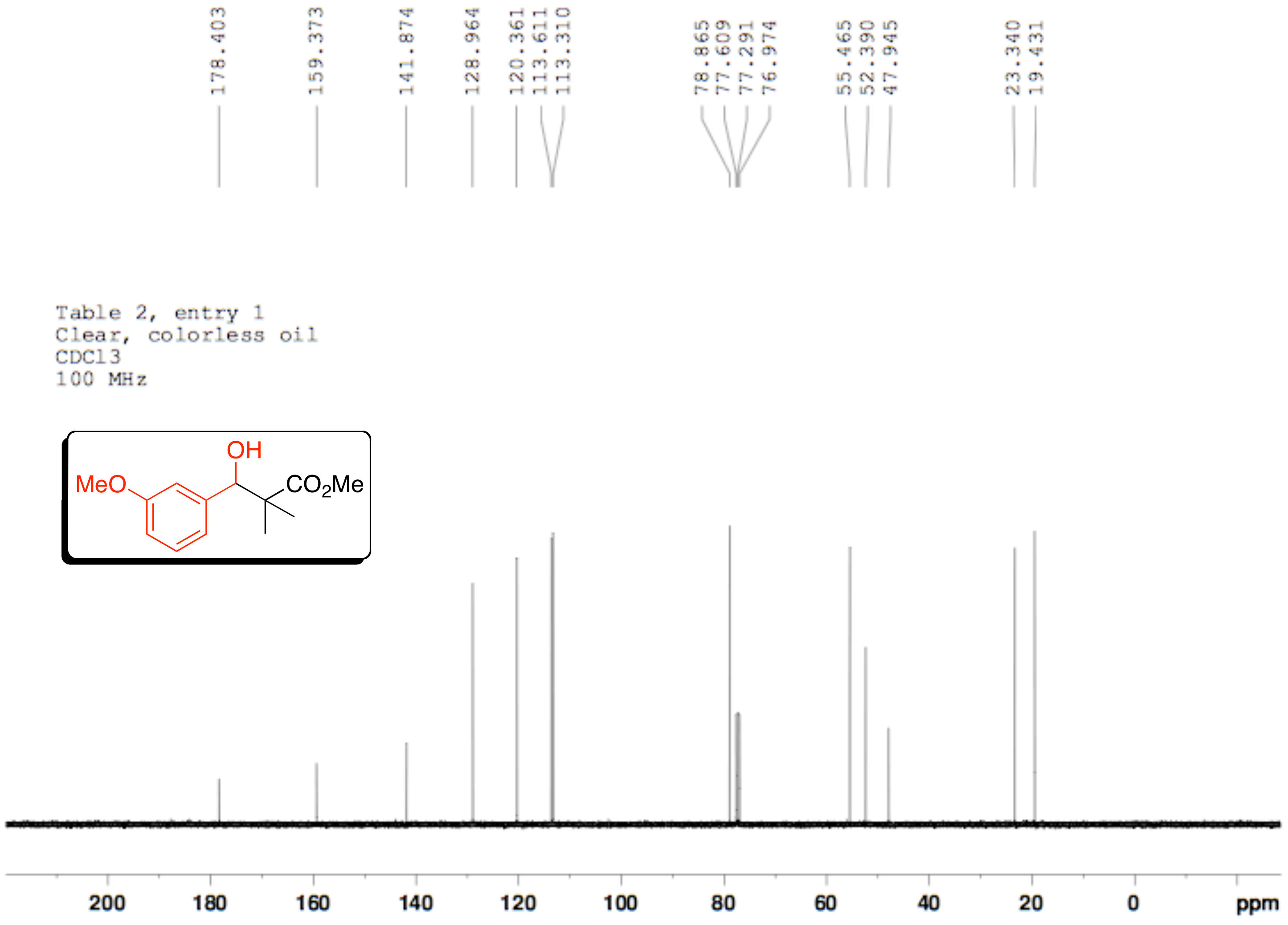


Table 2, entry 1
Clear, colorless oil
CDCl3
100 MHz

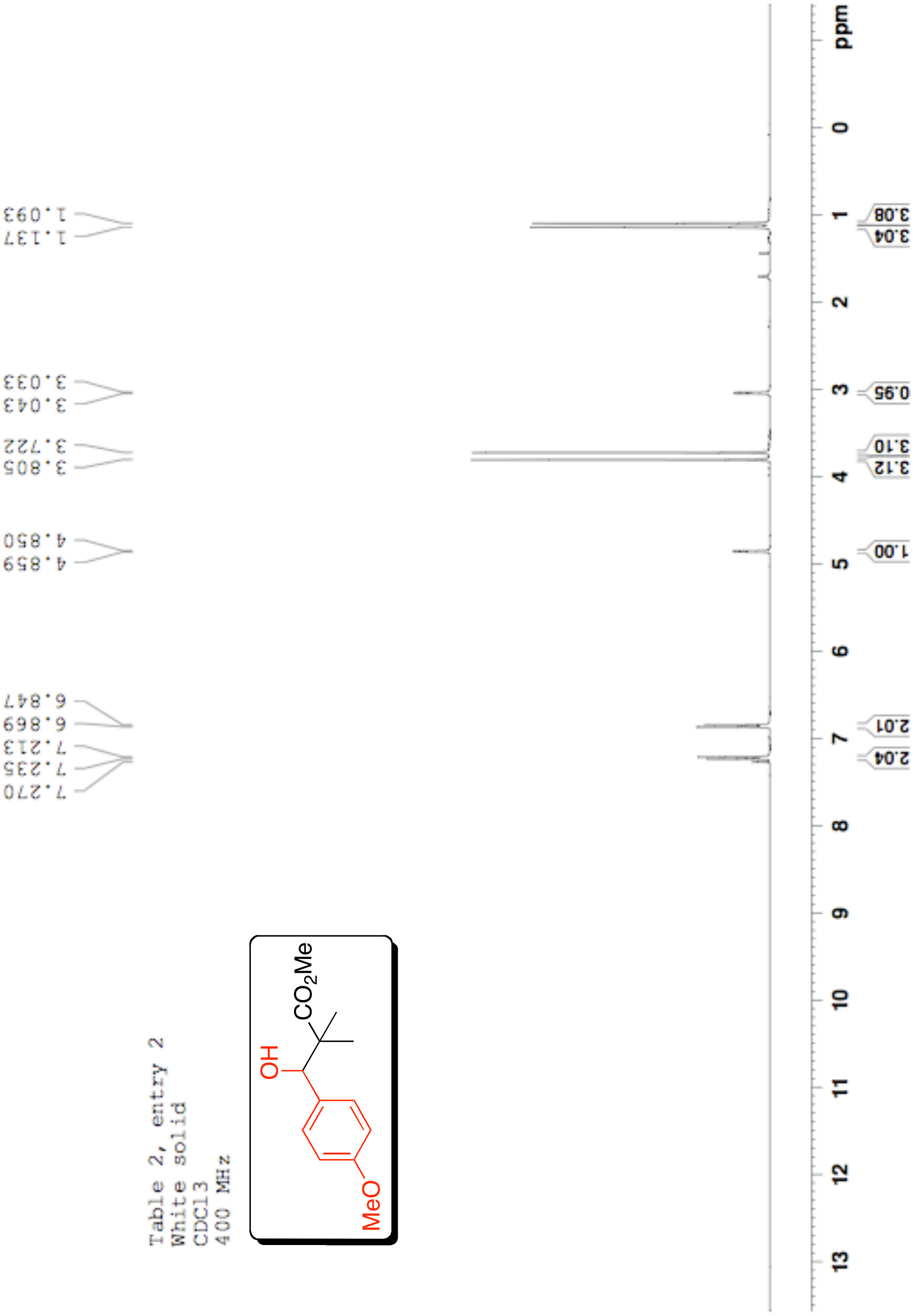


Table 2, entry 2
White solid
CDCl3
400 MHz
OH
CO_2Me
MeO
1.093
1.137
3.033
3.043
3.722
3.805
4.850
4.859
6.847
6.869
7.213
7.235
7.270
3.08
3.04
0.95
3.10
3.12
1.00
2.01
2.04
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

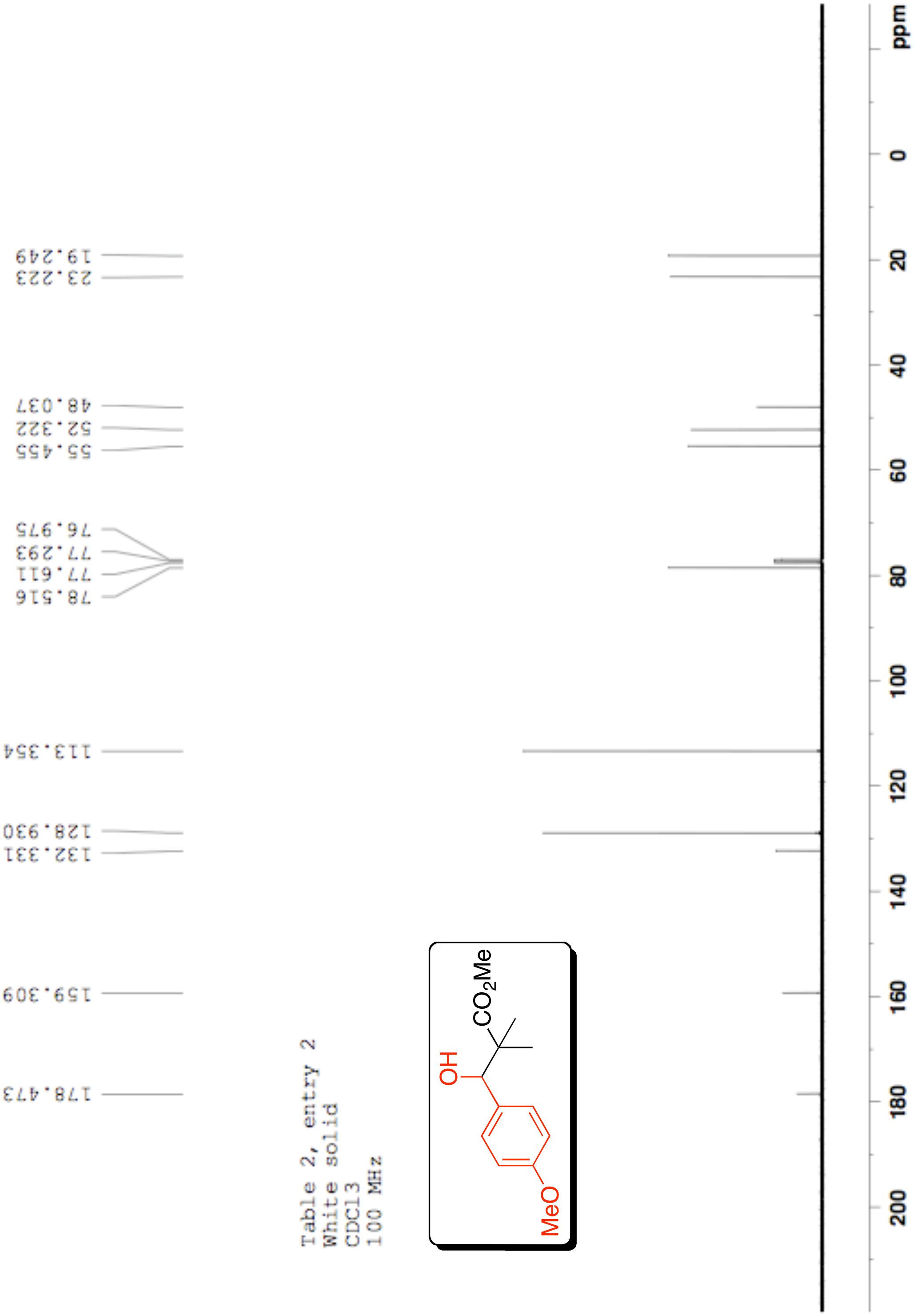


Table 2, entry 2
White solid
CDCl3
100 MHz

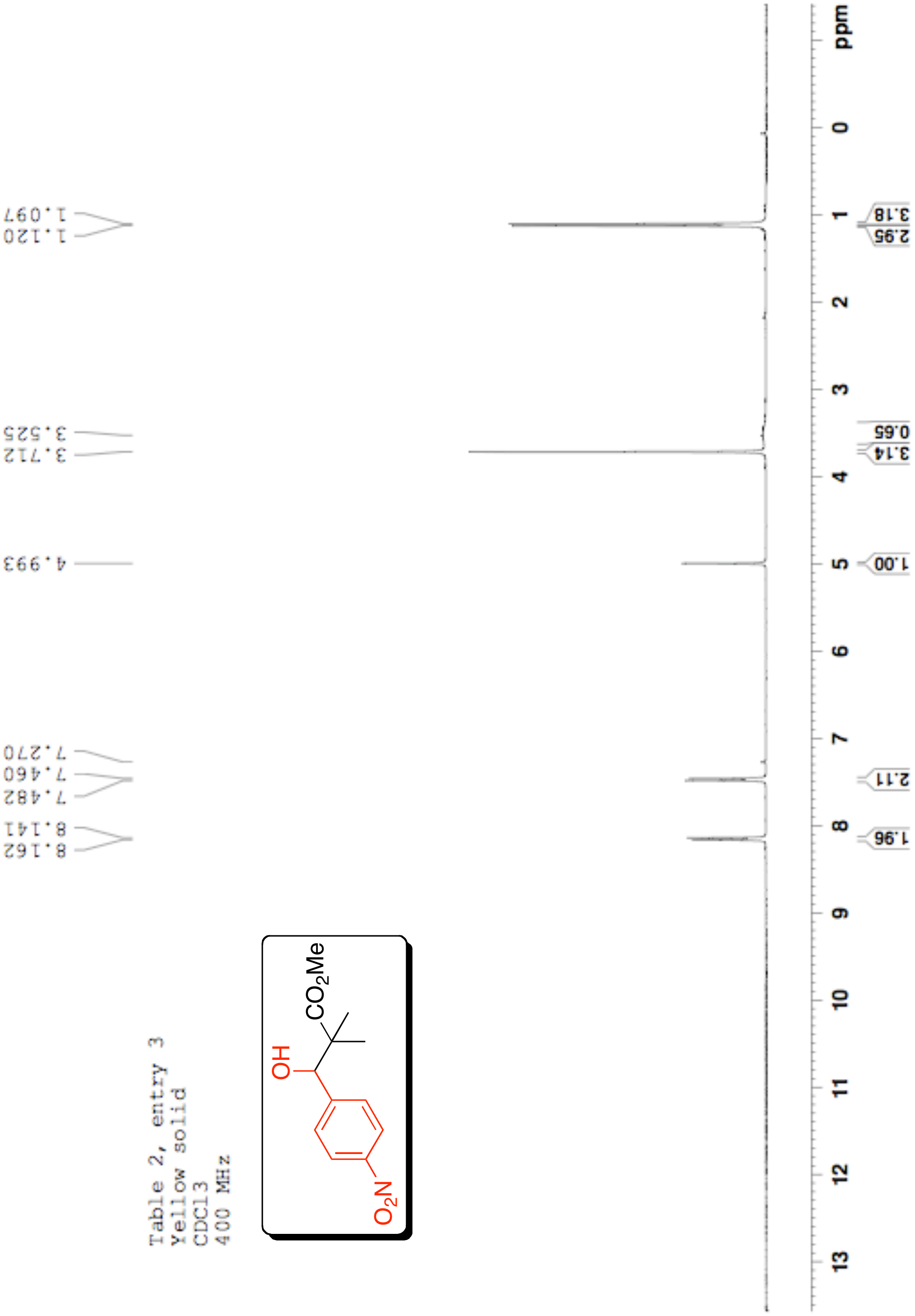


Table 2, entry 3
Yellow solid
CDCl3
400 MHz

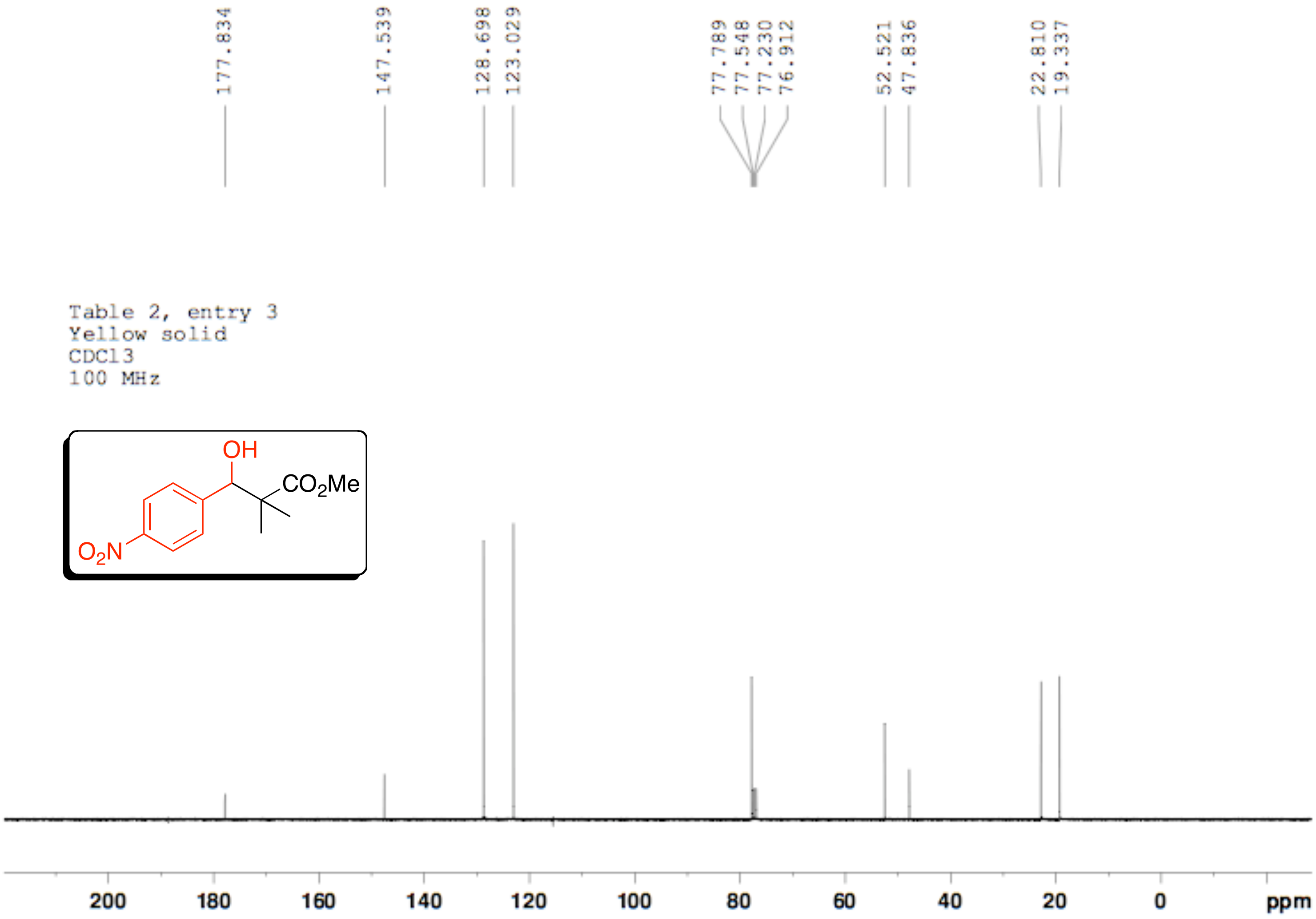


Table 2, entry 3
Yellow solid
CDCl3
100 MHz

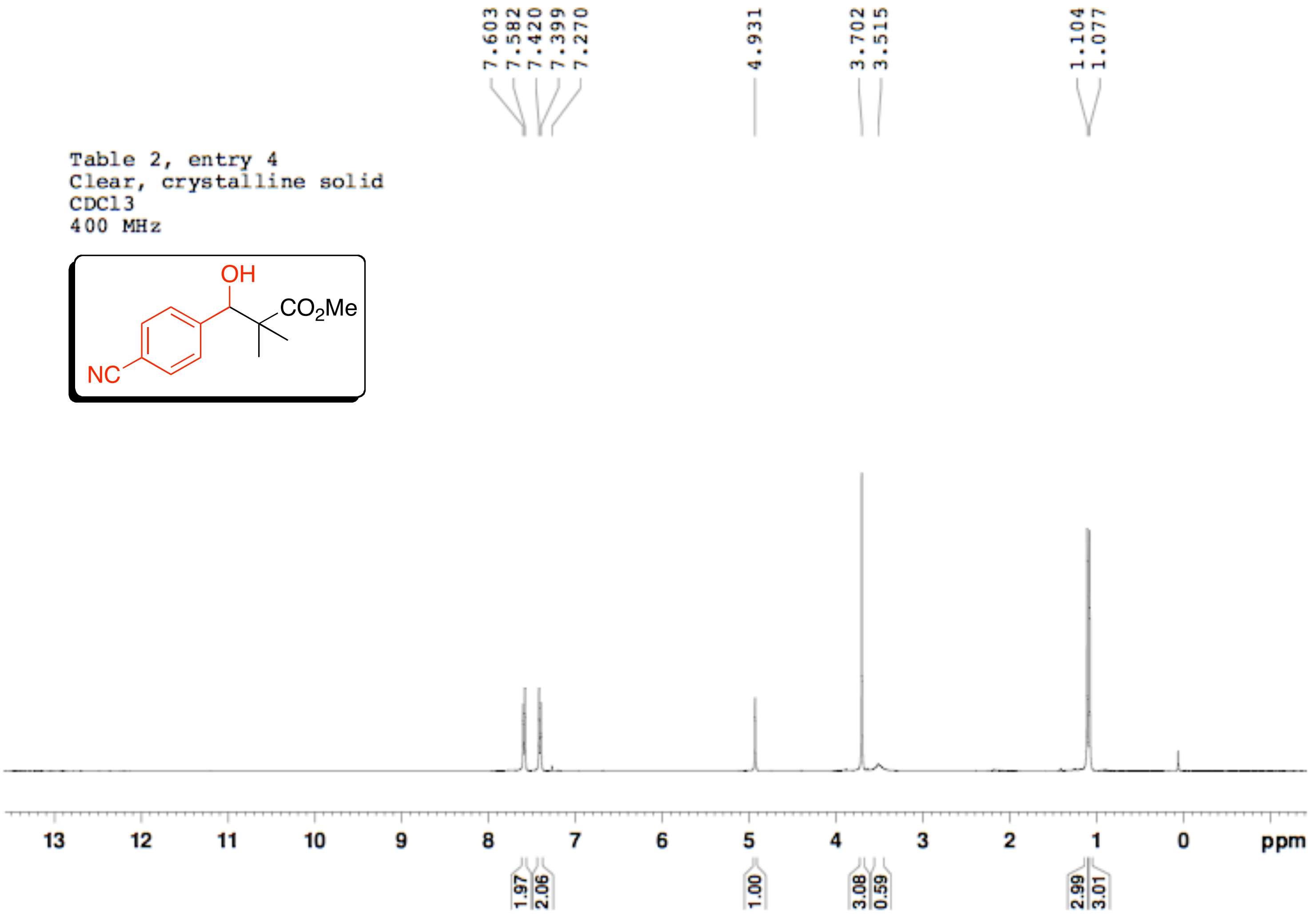
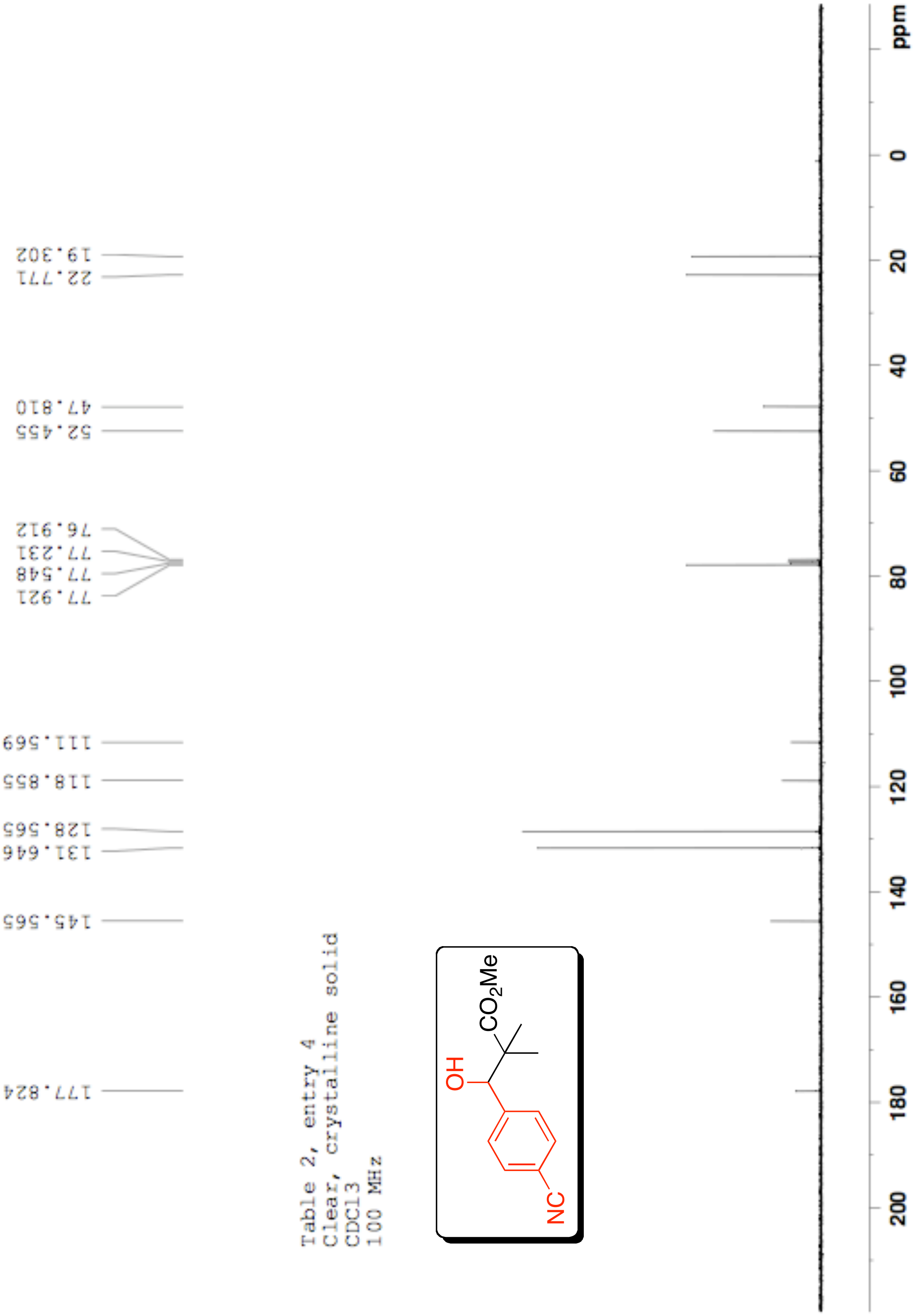
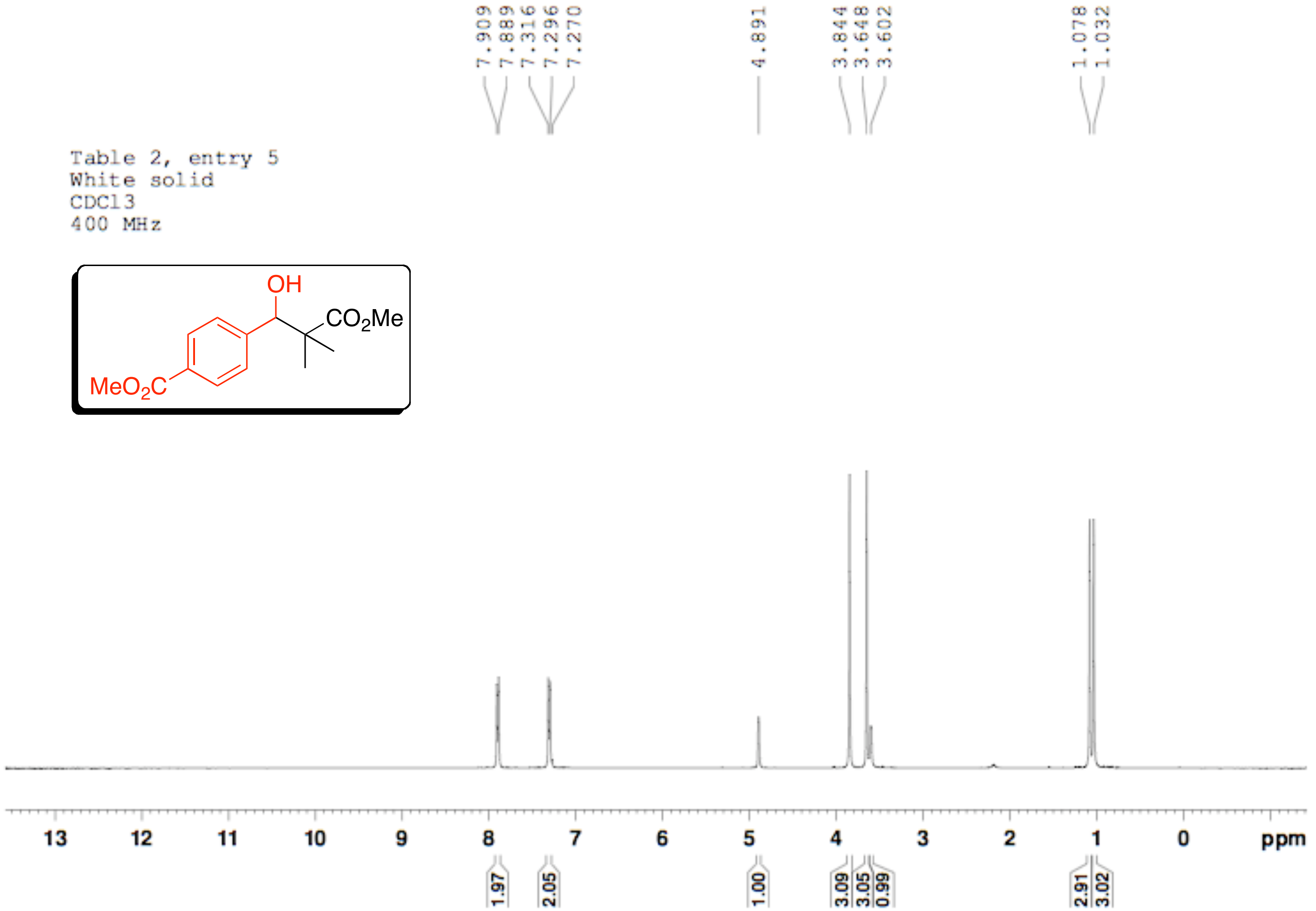
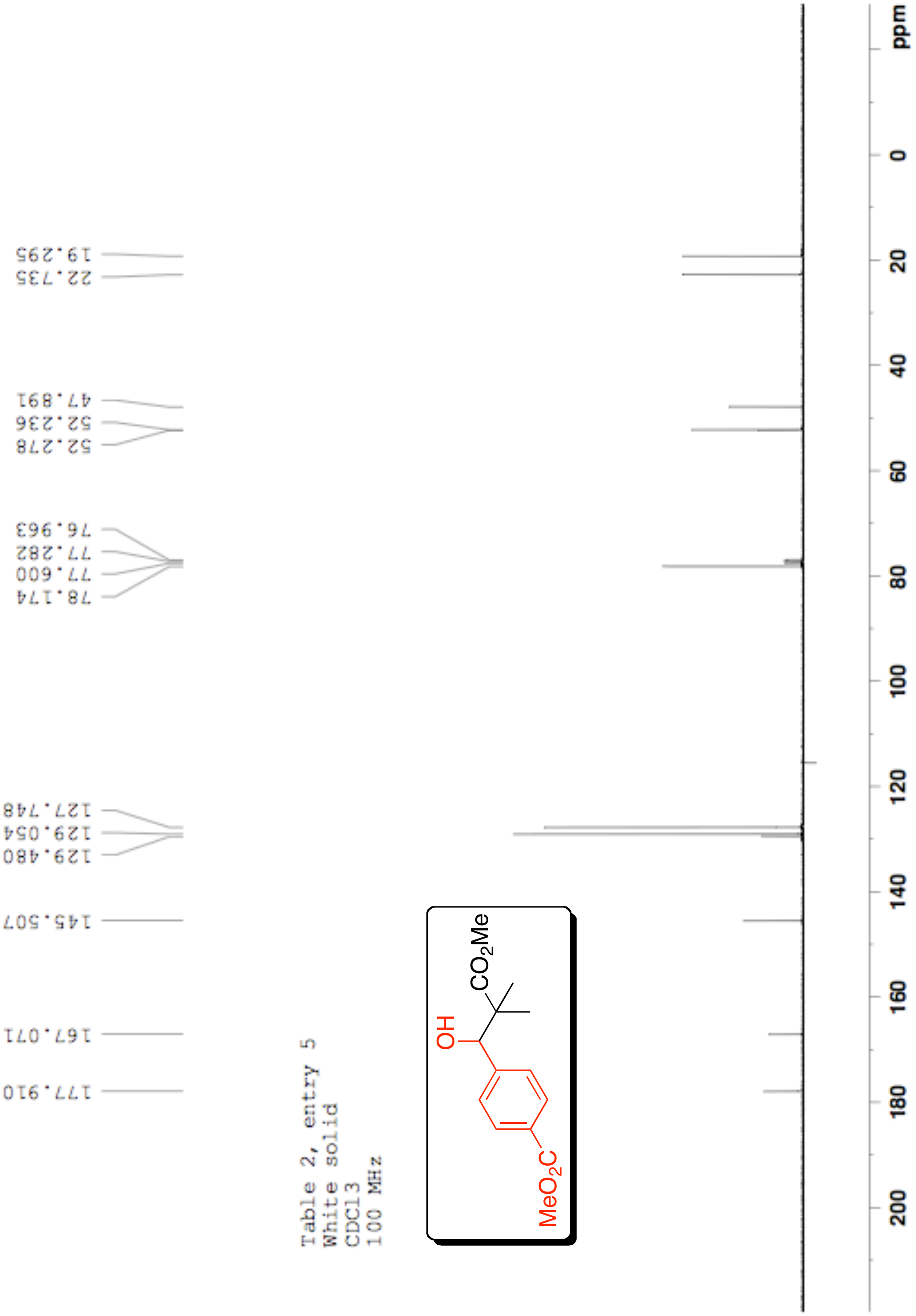


Table 2, entry 4
Clear, crystalline solid
CDCl3
400 MHz
OH
CO2Me
NC
7.603
7.582
7.420
7.399
7.270
4.931
3.702
3.515
1.104
1.077
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.97
2.06
1.00
3.08
0.59
2.99
3.01


19.302
22.771
47.810
52.455
76.912
77.231
77.548
77.921
111.569
118.855
128.565
131.646
145.565
177.824
Table 2, entry 4
Clear, crystalline solid
CDCl3
100 MHz
OH
CO2Me
NC
ppm
0
20
40
60
80
100
120
140
160
180
200


7.909
7.889
7.316
7.296
7.270
4.891
3.844
3.648
3.602
1.078
1.032
Table 2, entry 5
White solid
CDCl3
400 MHz
OH
CO_2Me
MeO_2C
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.97
2.05
1.00
3.09
3.05
0.99
2.91
3.02


19.295
22.735
47.891
52.236
52.278
76.963
77.282
77.600
78.174
127.748
129.054
129.480
145.507
167.071
177.910
Table 2, entry 5
White solid
CDCl3
100 MHz
OH
CO_2Me
MeO_2C
ppm
0
20
40
60
80
100
120
140
160
180
200

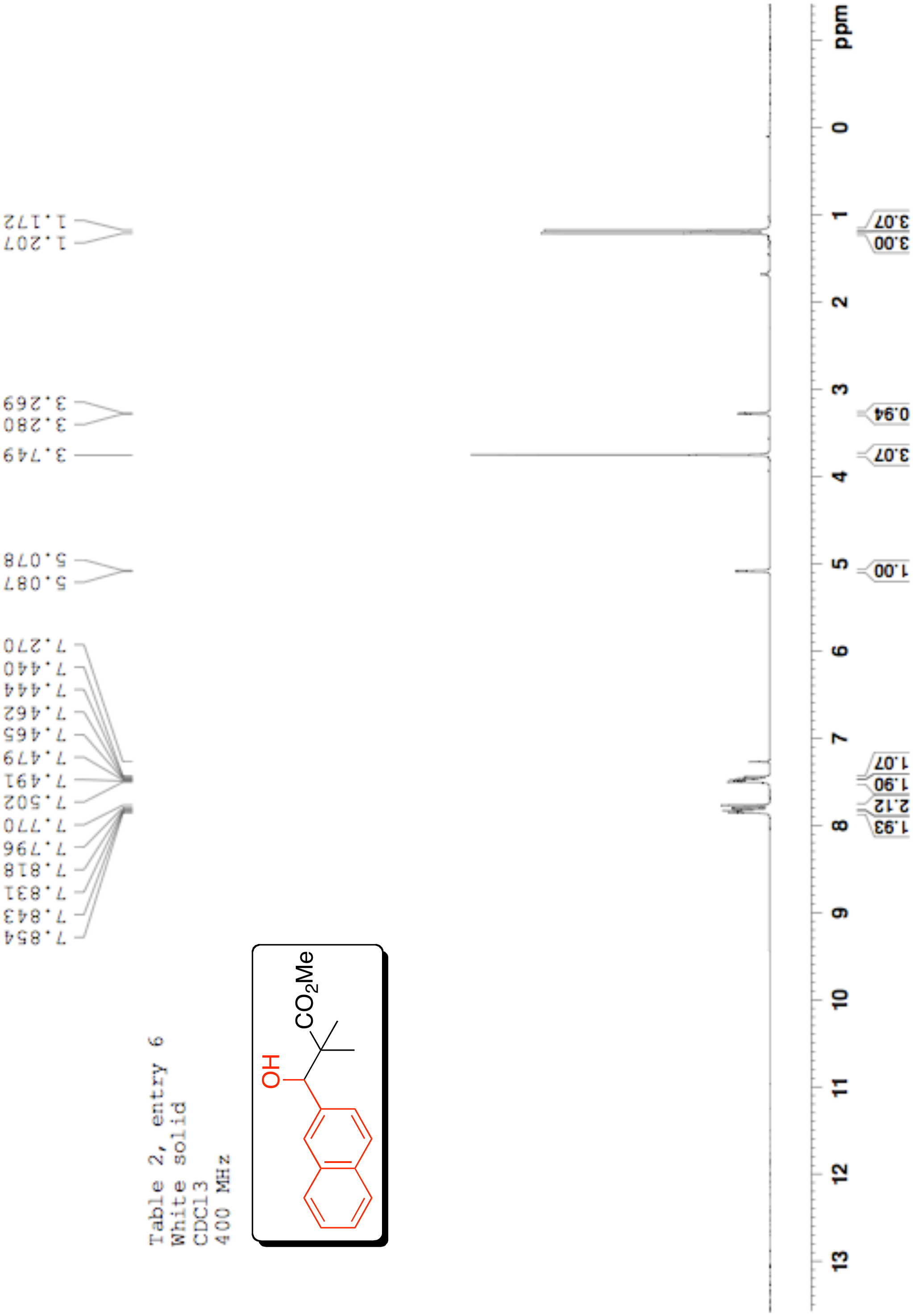


Table 2, entry 6
White solid
CDCl3
400 MHz
OH
CO2Me
1.172
1.207
3.269
3.280
3.749
5.078
5.087
7.270
7.440
7.444
7.462
7.465
7.479
7.491
7.502
7.770
7.796
7.818
7.831
7.843
7.854
3.07
3.00
0.94
3.07
1.00
1.07
1.90
2.12
1.93
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

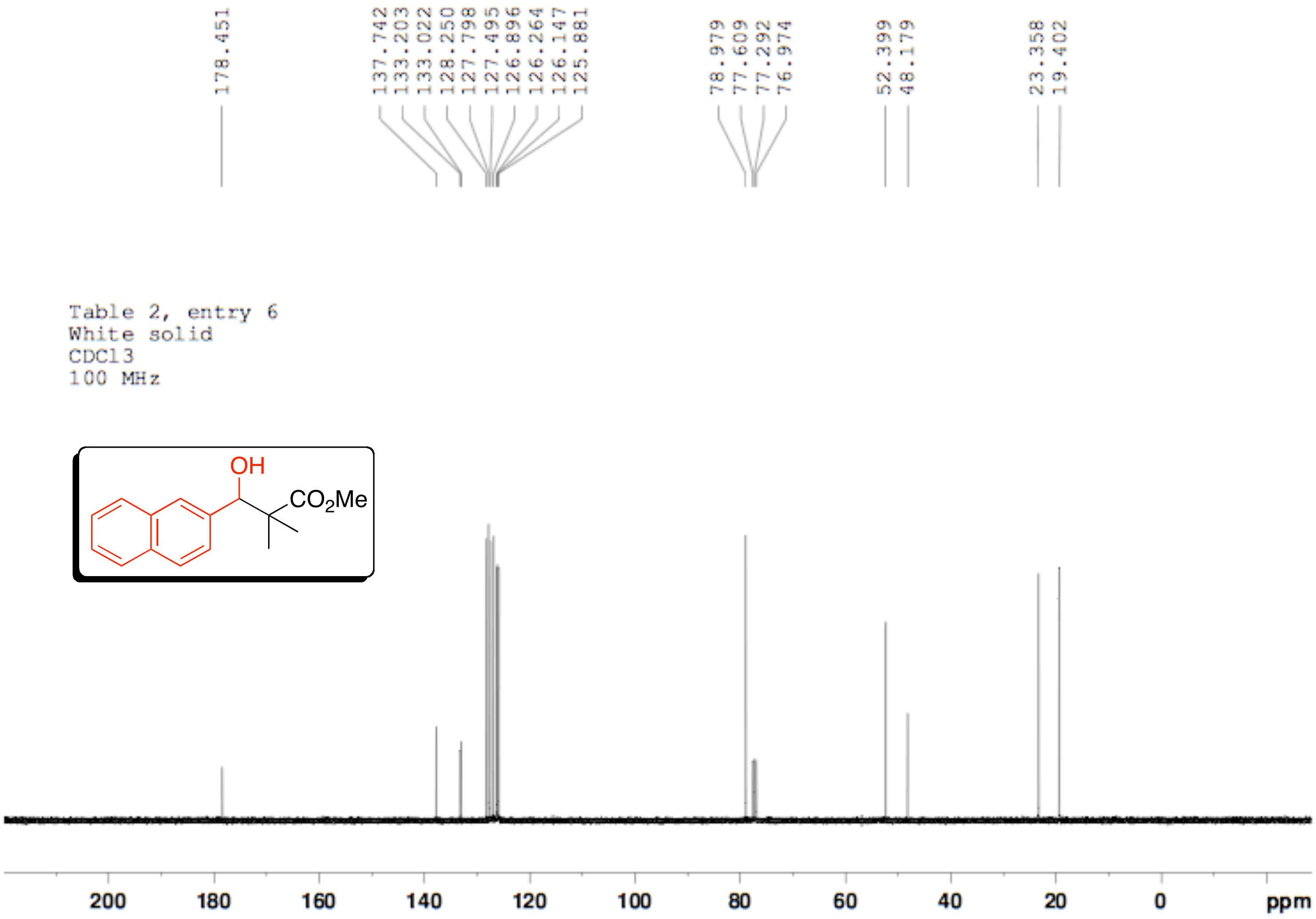


Table 2, entry 6
White solid
CDCl3
100 MHz

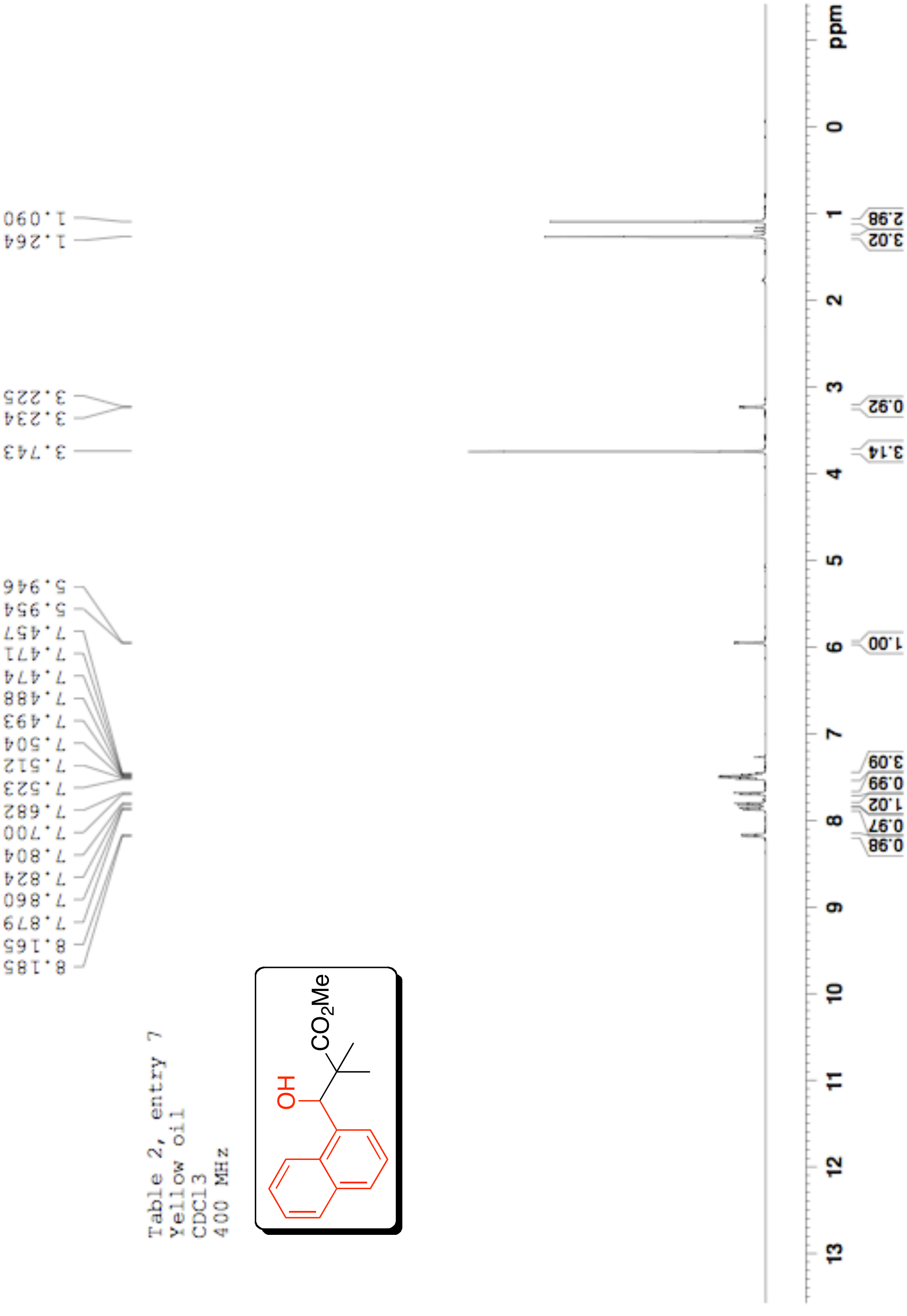
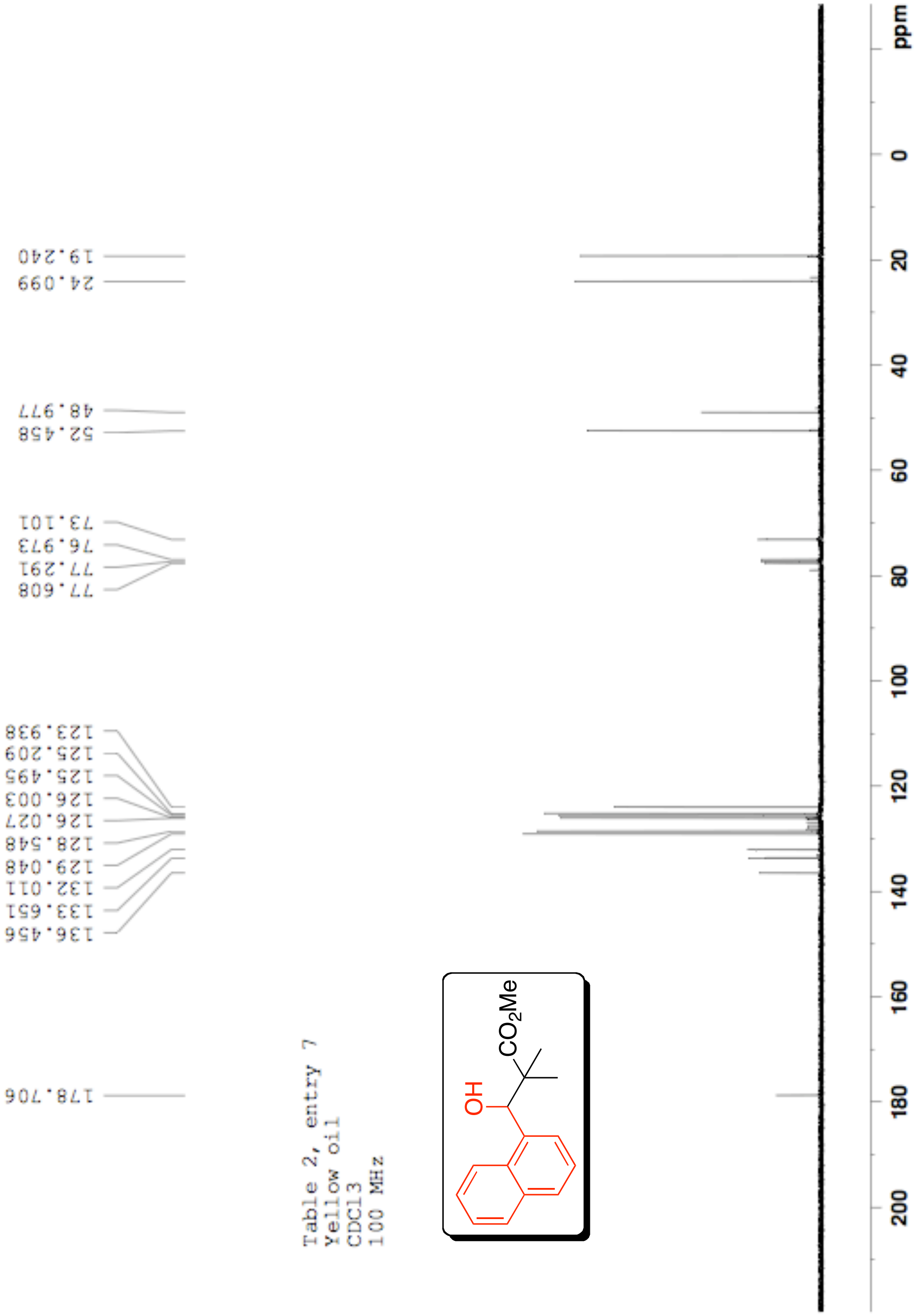


Table 2, entry 7
Yellow oil
CDCl3
400 MHz


19.240
24.099
48.977
52.458
73.101
76.973
77.291
77.608
123.938
125.209
125.495
126.003
126.027
128.548
129.048
132.011
133.651
136.456
178.706
Table 2, entry 7
Yellow oil
CDCl3
100 MHz
OH
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200

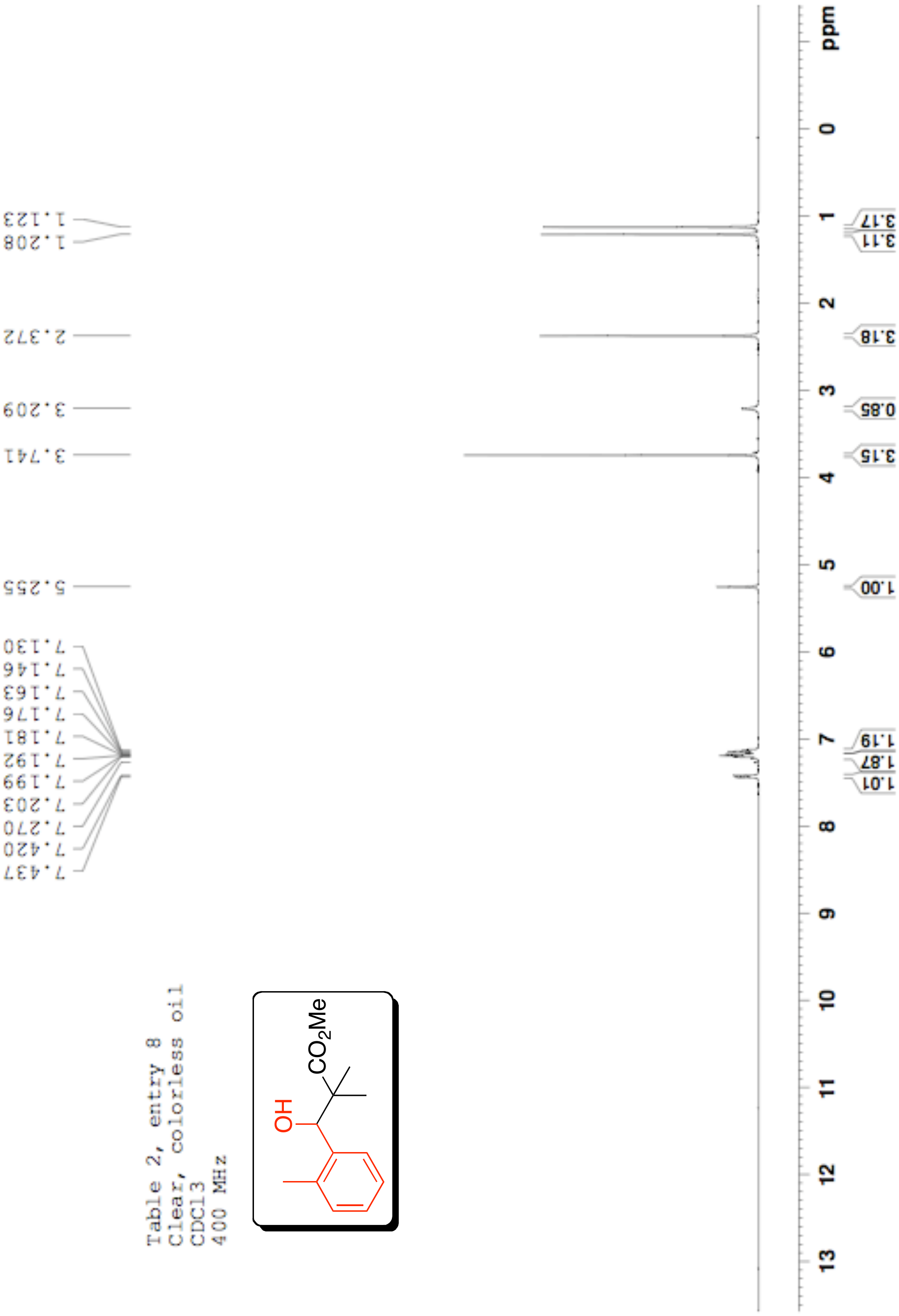
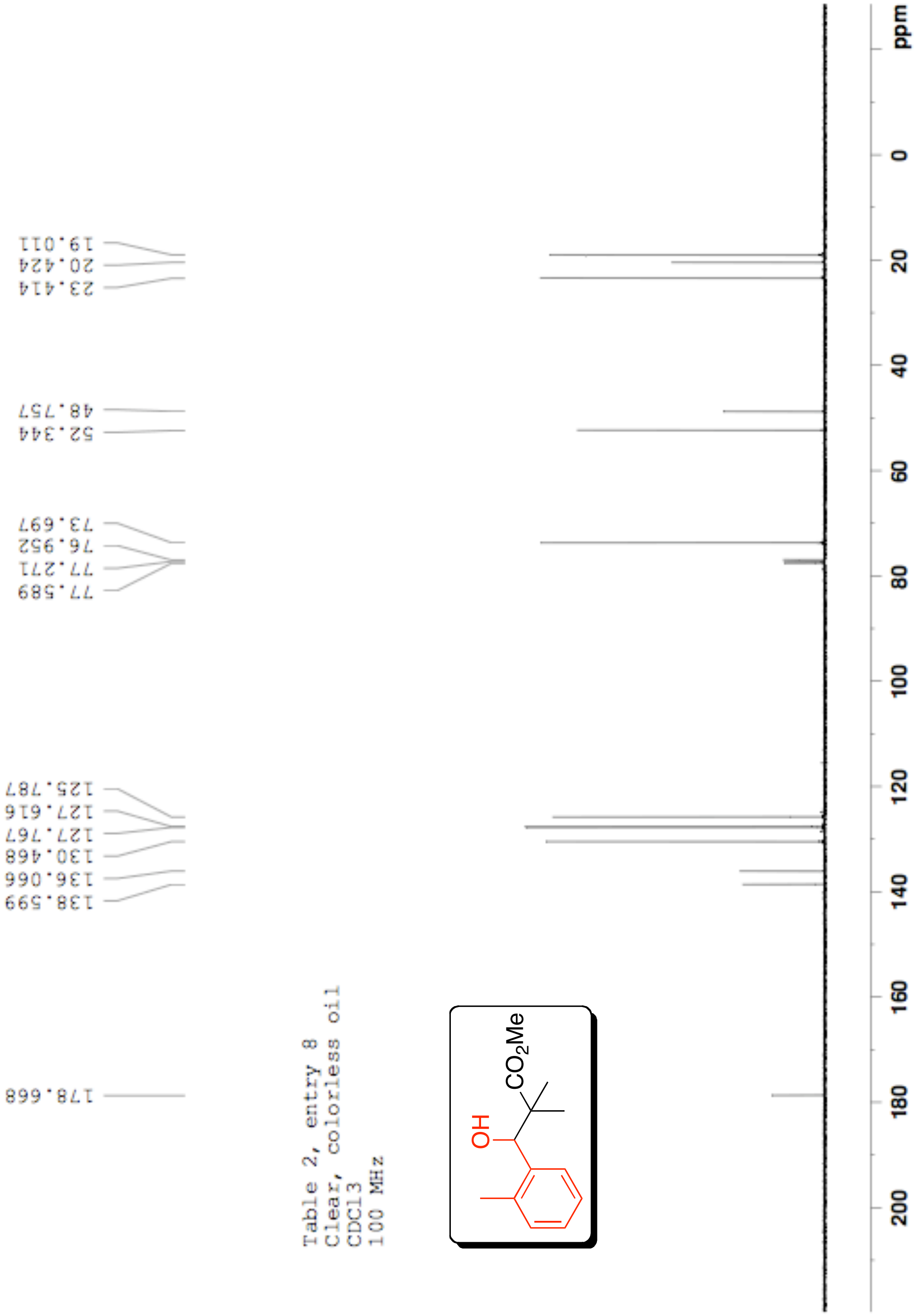
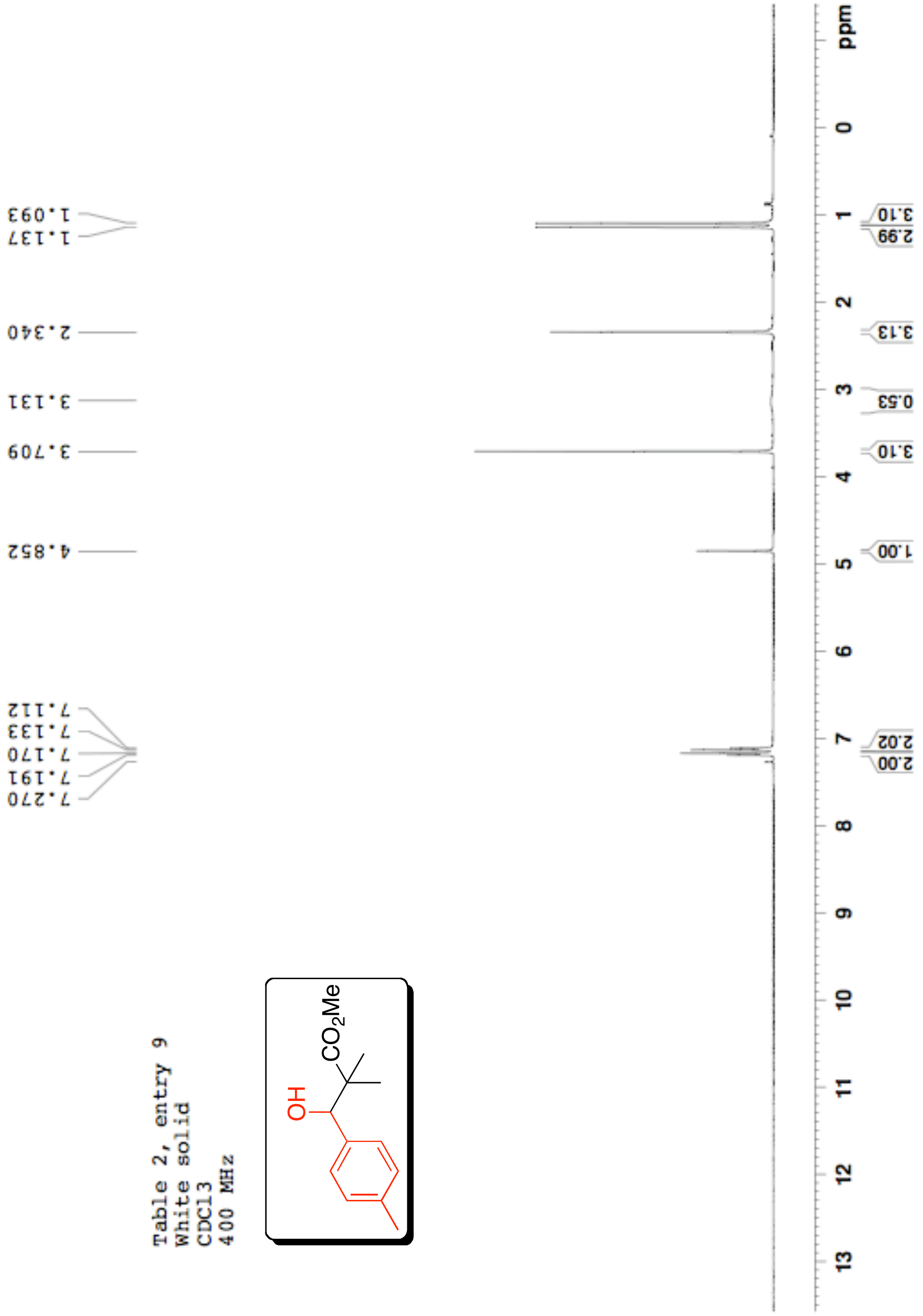
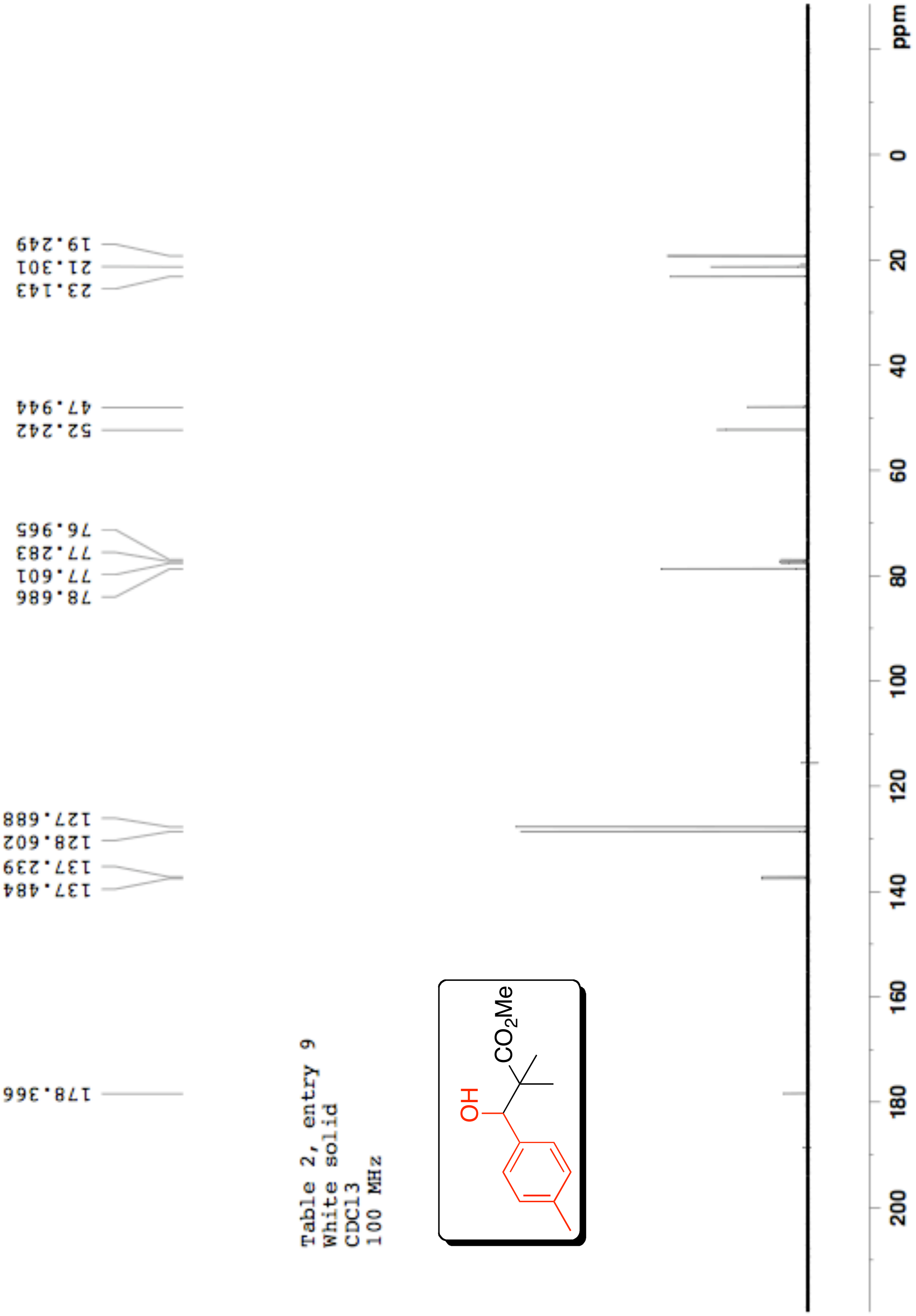
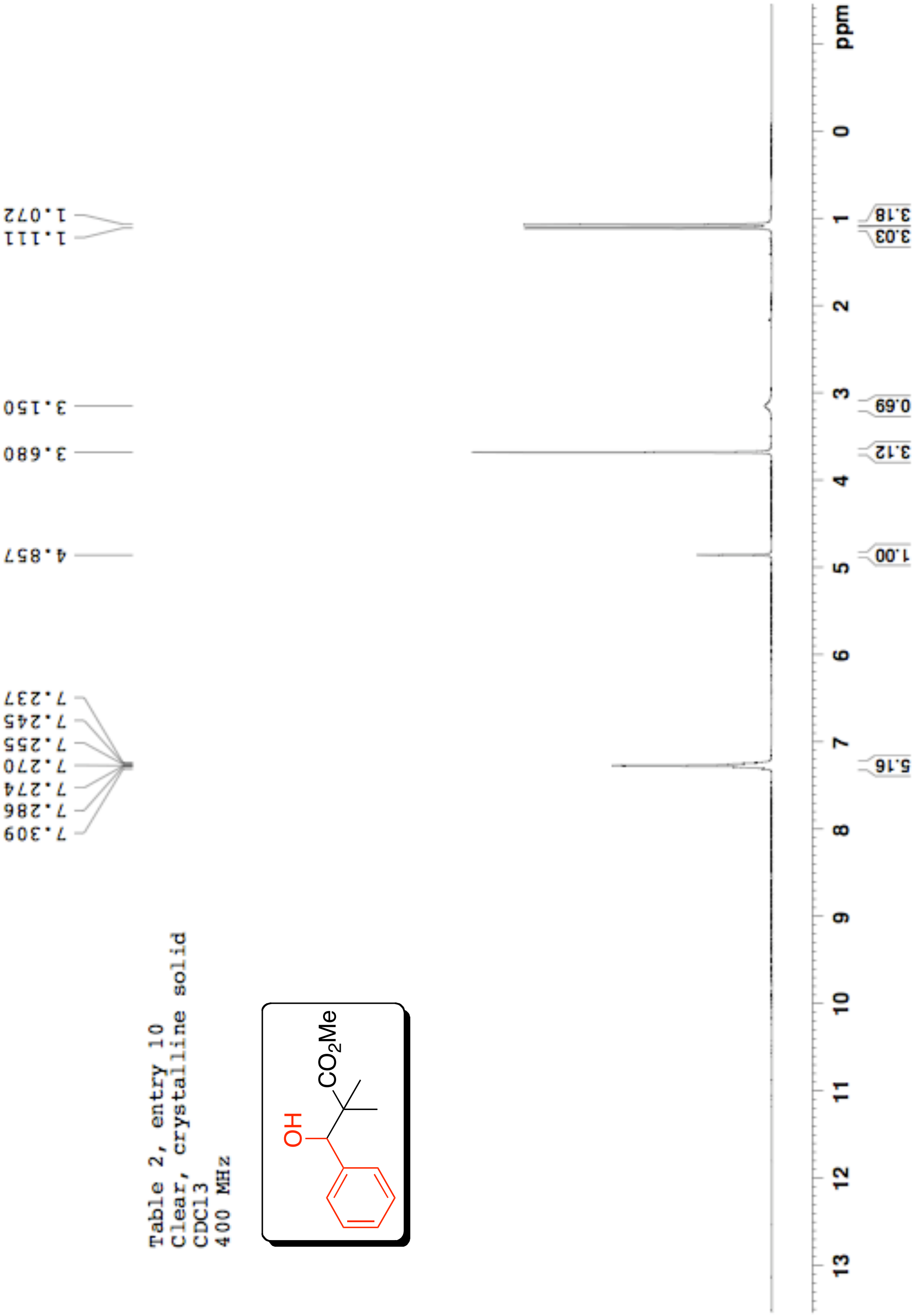


Table 2, entry 8
Clear, colorless oil
CDCl3
400 MHz
OH
CO2Me
1.123
1.208
2.372
3.209
3.741
5.255
7.130
7.146
7.163
7.176
7.181
7.192
7.199
7.203
7.270
7.420
7.437
3.17
3.11
3.18
0.85
3.15
1.00
1.19
1.87
1.01
ppm
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
13


19.011
20.424
23.414
48.757
52.344
73.697
76.952
77.271
77.589
125.787
127.616
127.767
130.468
136.066
138.599
178.668
Table 2, entry 8
Clear, colorless oil
CDCl3
100 MHz
OH
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200


1.093
1.137
2.340
3.131
3.709
4.852
7.112
7.133
7.170
7.191
7.270
Table 2, entry 9
White solid
CDCl3
400 MHz
OH
CO2Me
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
3.10
2.99
3.13
0.53
3.10
1.00
2.02
2.00


19.249
21.301
23.143
47.944
52.242
76.965
77.283
77.601
78.686
127.688
128.602
137.239
137.484
178.366
Table 2, entry 9
White solid
CDCl3
100 MHz
OH
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200


1.072
1.111
3.150
3.680
4.857
7.237
7.245
7.255
7.270
7.274
7.286
7.309
Table 2, entry 10
Clear, crystalline solid
CDCl3
400 MHz
OH
CO2Me
3.18
3.03
0.69
3.12
1.00
5.16
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

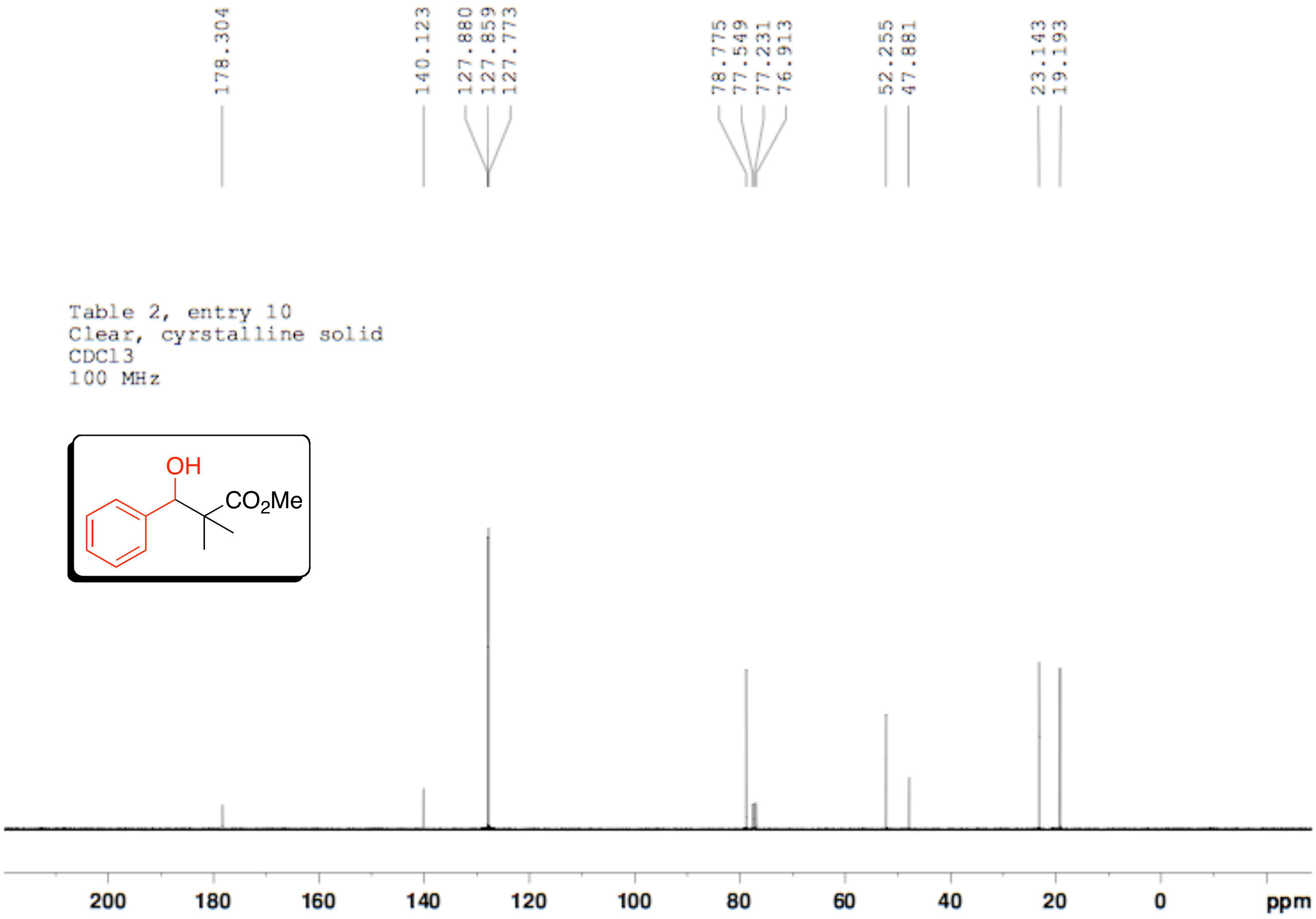


Table 2, entry 10
Clear, cyrstalline solid
CDCl3
100 MHz

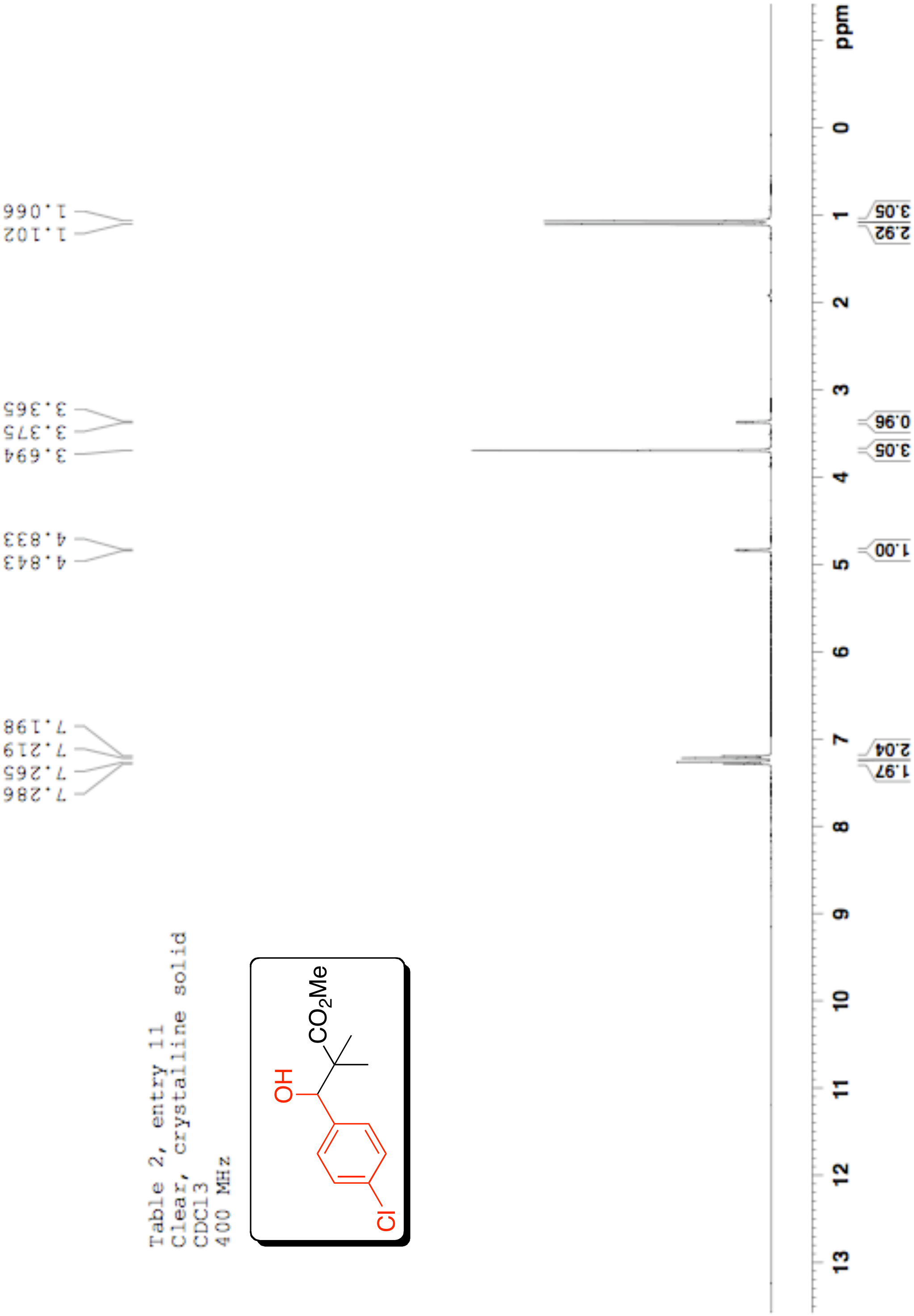
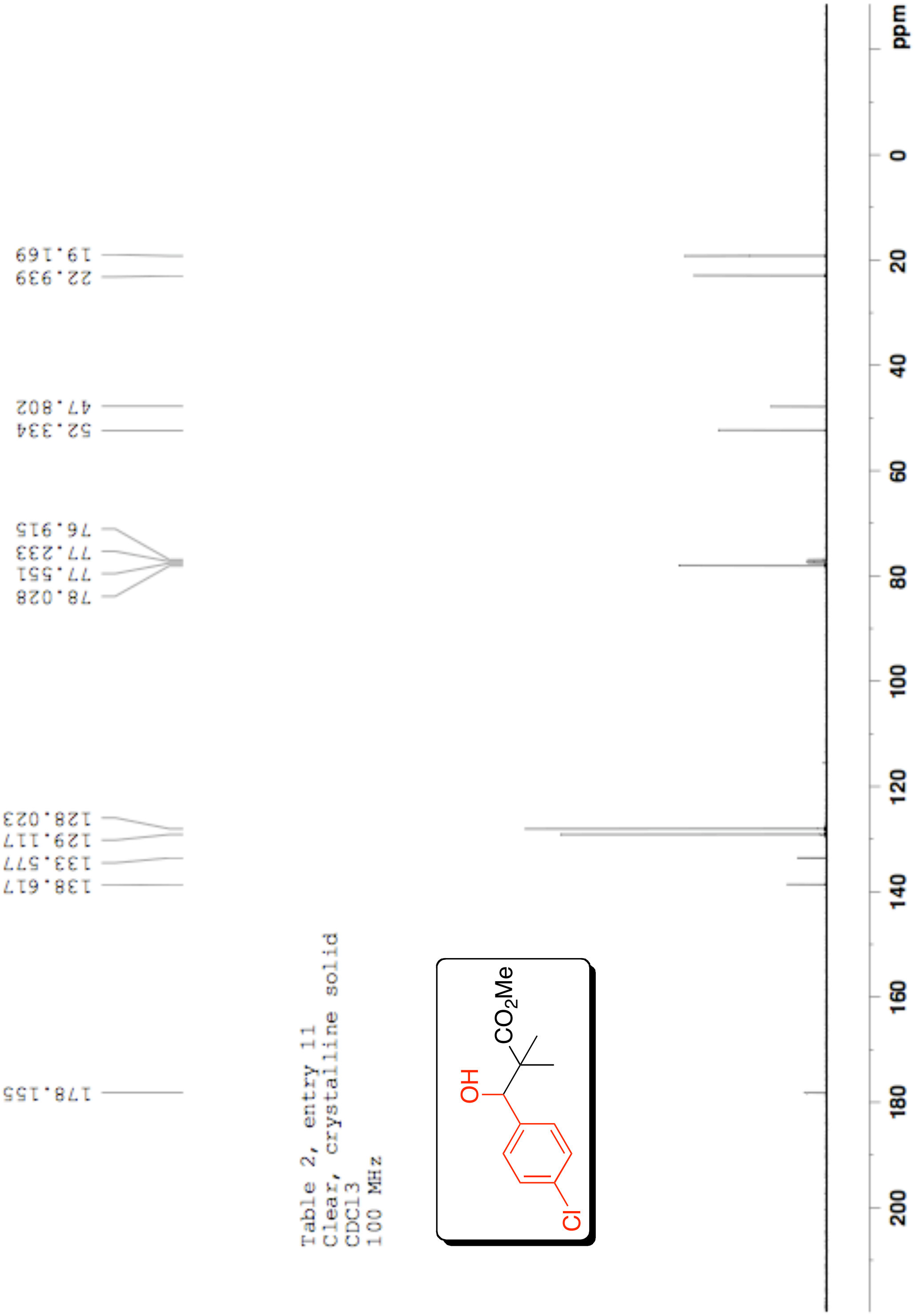


Table 2, entry 11
Clear, crystalline solid
CDCl3
400 MHz
OH
CO2Me
Cl
1.066
1.102
3.365
3.375
3.694
4.833
4.843
7.198
7.219
7.265
7.286
3.05
2.92
0.96
3.05
1.00
2.04
1.97
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


19.169
22.939
47.802
52.334
76.915
77.233
77.551
78.028
128.023
129.117
133.577
138.617
178.155
Table 2, entry 11
Clear, crystalline solid
CDCl3
100 MHz
OH
CO2Me
Cl
ppm
0
20
40
60
80
100
120
140
160
180
200

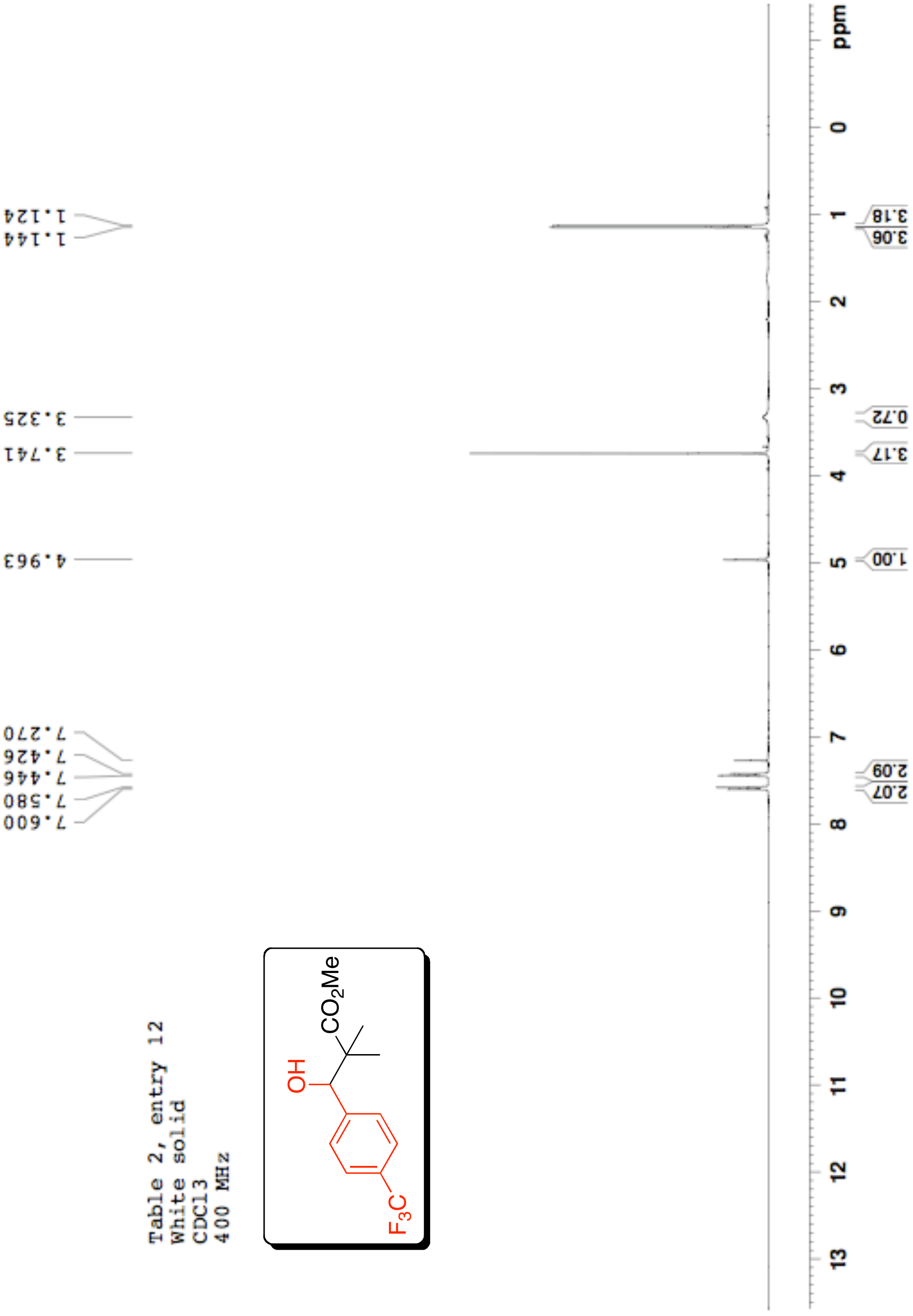


Table 2, entry 12
White solid
CDCl3
400 MHz
OH
CO2Me
F3C
1.124
1.144
3.325
3.741
4.963
7.270
7.426
7.446
7.580
7.600
3.18
3.06
0.72
3.17
1.00
2.09
2.07
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

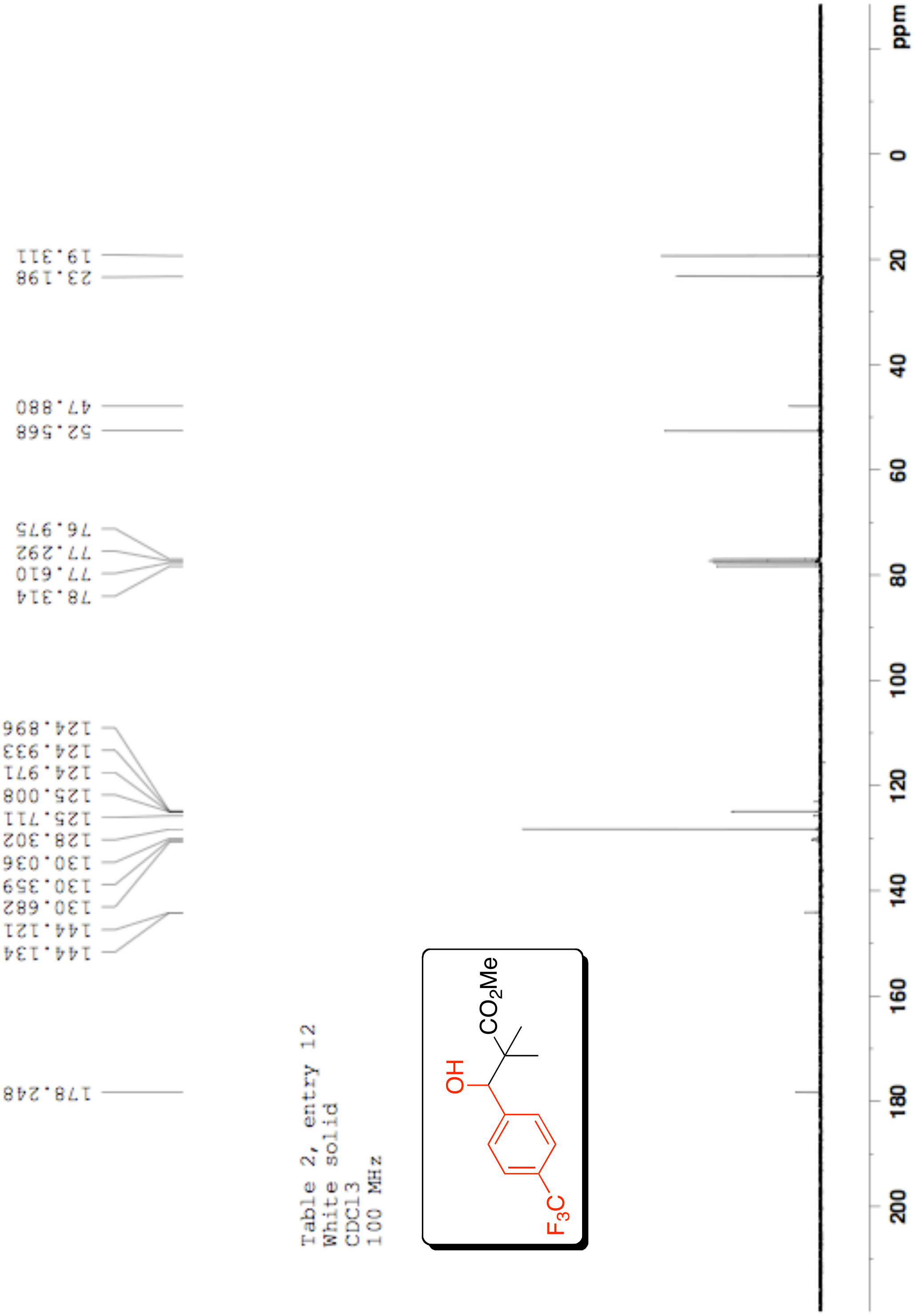


Table 2, entry 12
White solid
CDCl3
100 MHz

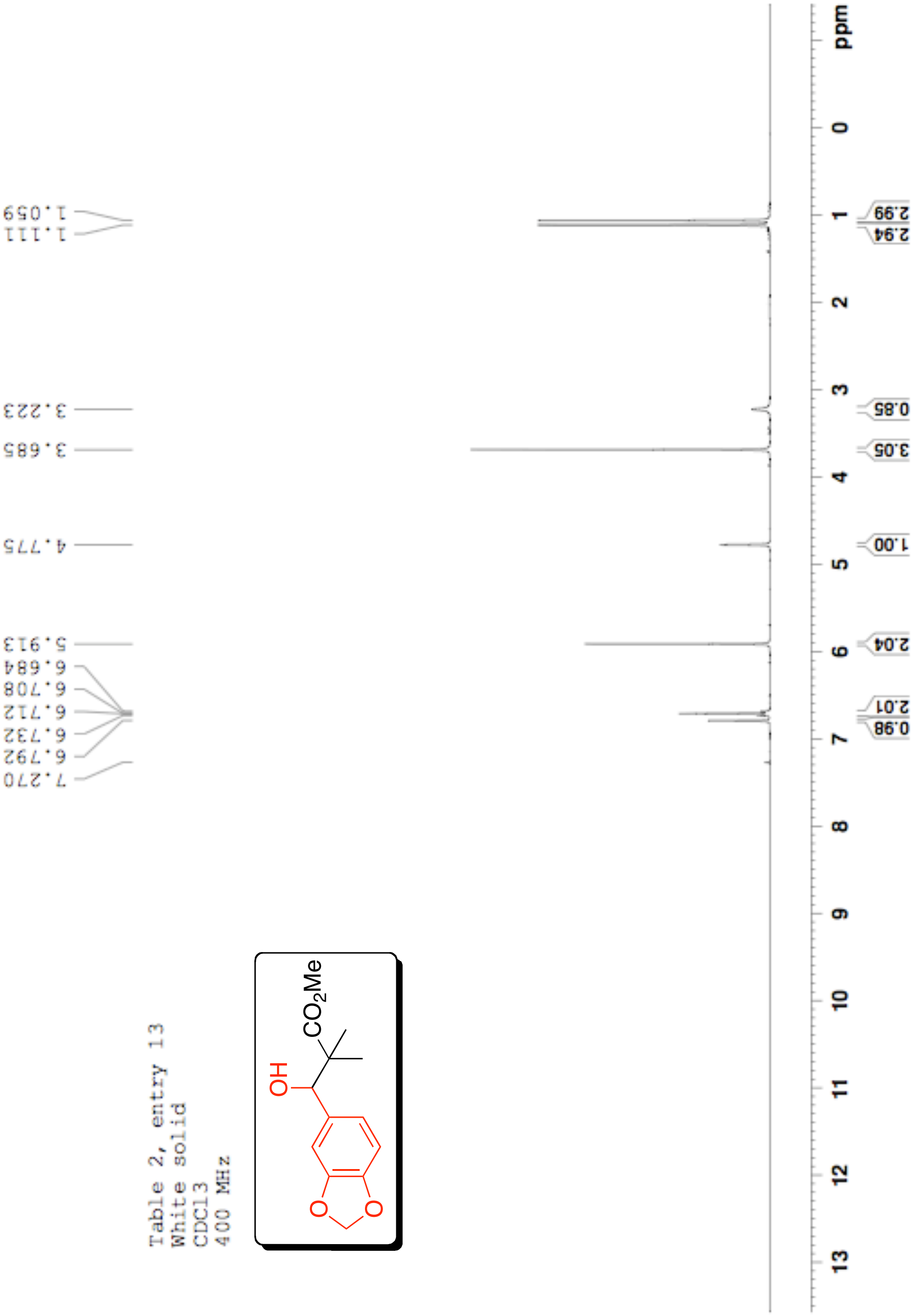
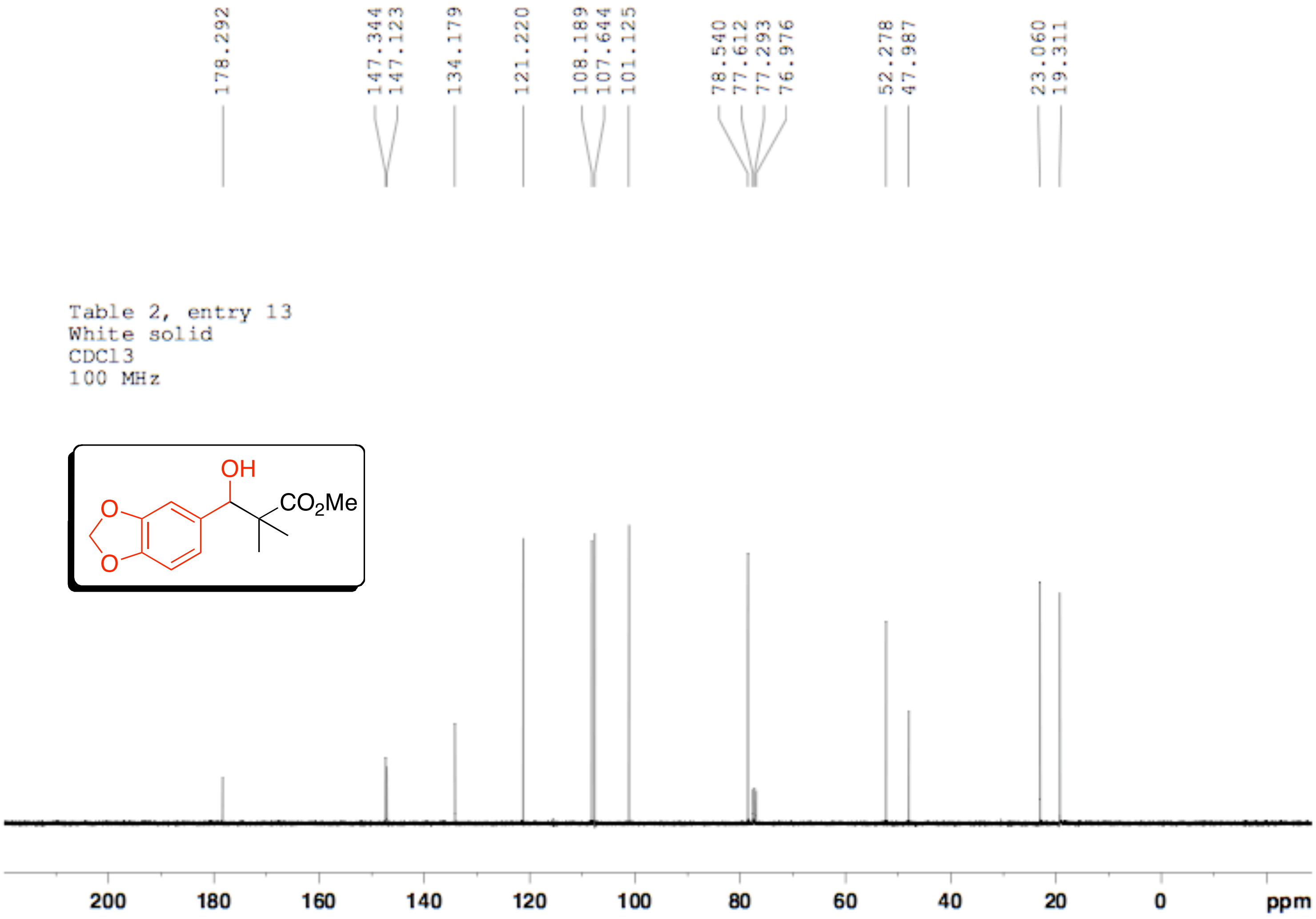


Table 2, entry 13
White solid
CDCl3
400 MHz
OH
CO2Me
O
O
1.059
1.111
3.223
3.685
4.775
5.913
6.684
6.708
6.712
6.732
6.792
7.270
2.99
2.94
0.85
3.05
1.00
2.04
2.01
0.98
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


178.292
147.344
147.123
134.179
121.220
108.189
107.644
101.125
78.540
77.612
77.293
76.976
52.278
47.987
23.060
19.311
Table 2, entry 13
White solid
CDCl3
100 MHz
OH
CO$_2$Me
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm

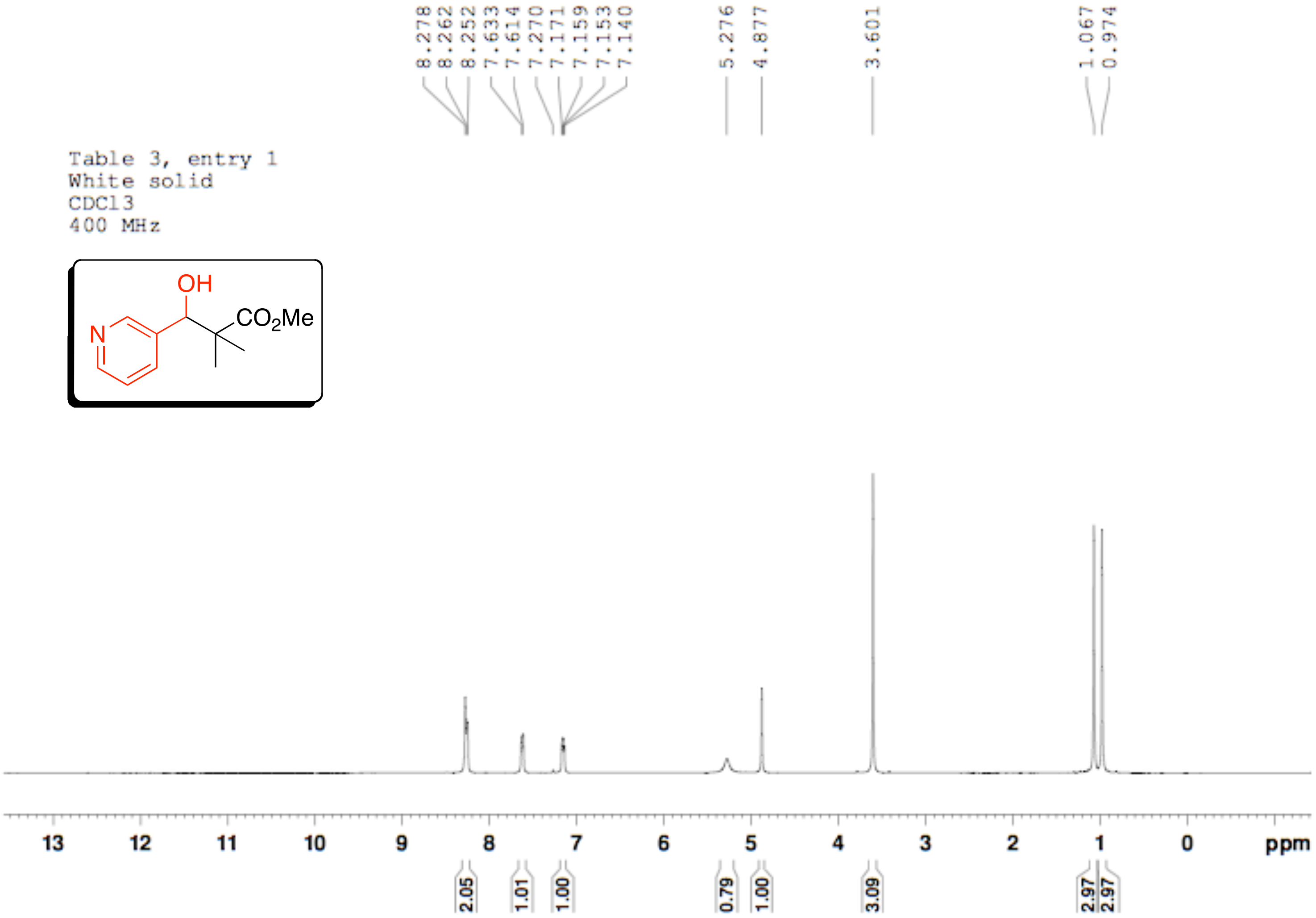
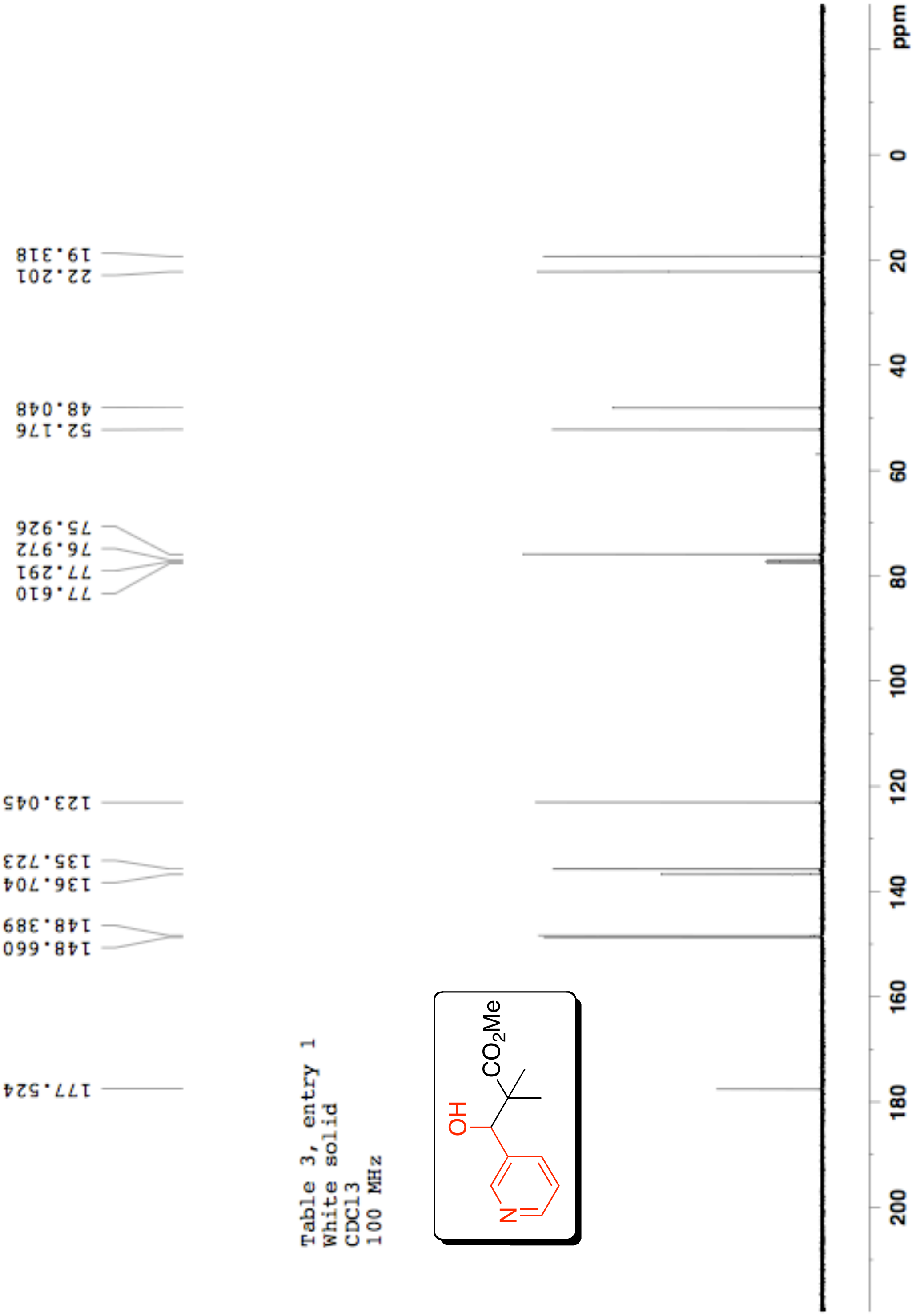


Table 3, entry 1
White solid
CDCl3
400 MHz
OH
N
CO_2Me
8.278
8.262
8.252
7.633
7.614
7.270
7.171
7.159
7.153
7.140
5.276
4.877
3.601
1.067
0.974
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
2.05
1.01
1.00
0.79
1.00
3.09
2.97
2.97


19.318
22.201
48.048
52.176
75.926
76.972
77.291
77.610
123.045
135.723
136.704
148.389
148.660
177.524
Table 3, entry 1
White solid
CDCl3
100 MHz
OH
CO2Me
N
ppm
0
20
40
60
80
100
120
140
160
180
200

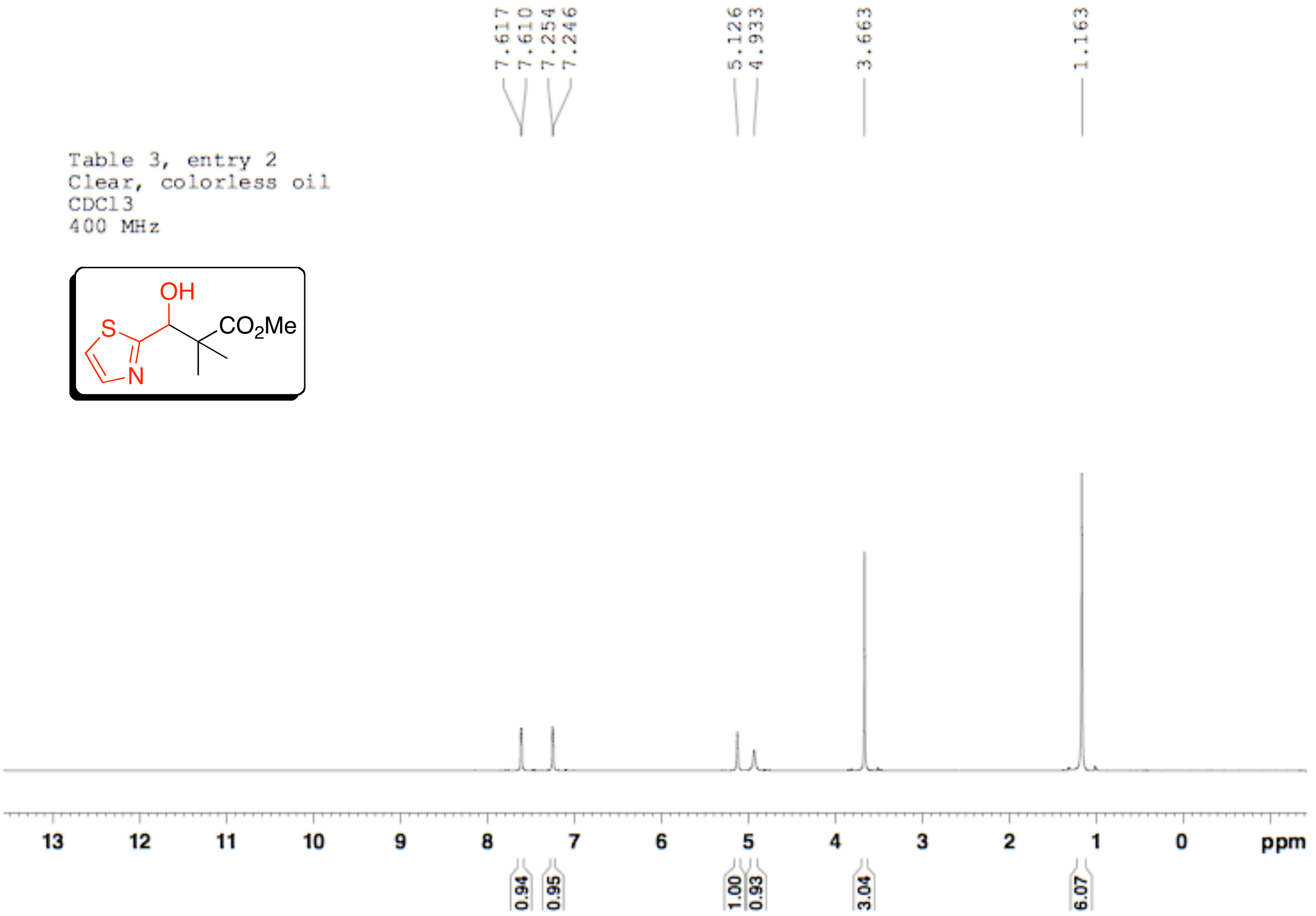
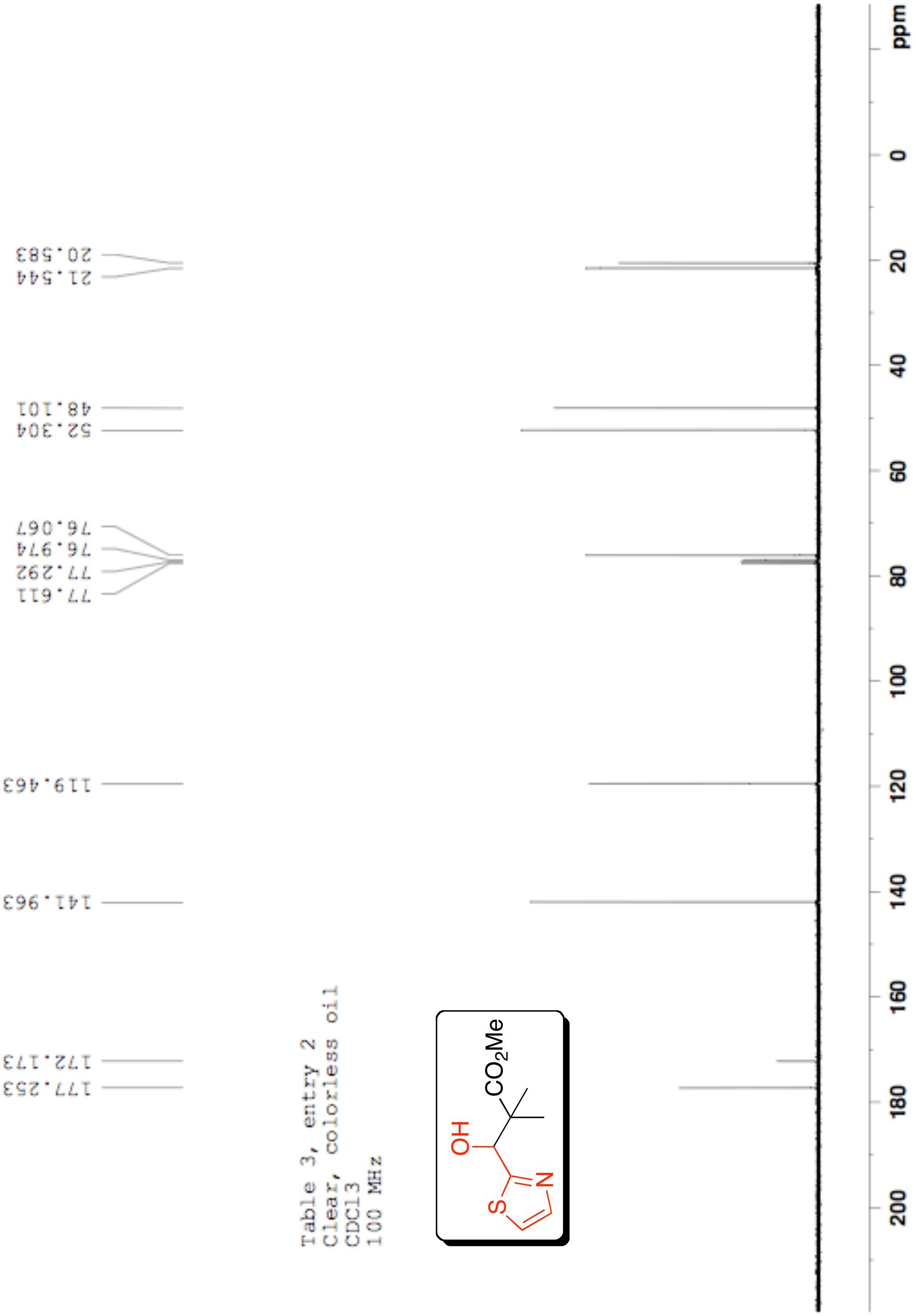


Table 3, entry 2
Clear, colorless oil
CDCl3
400 MHz


20.583
21.544
48.101
52.304
76.067
76.974
77.292
77.611
119.463
141.963
172.173
177.253
Table 3, entry 2
Clear, colorless oil
CDCl3
100 MHz
OH
CO2Me
S
N
ppm
0
20
40
60
80
100
120
140
160
180
200

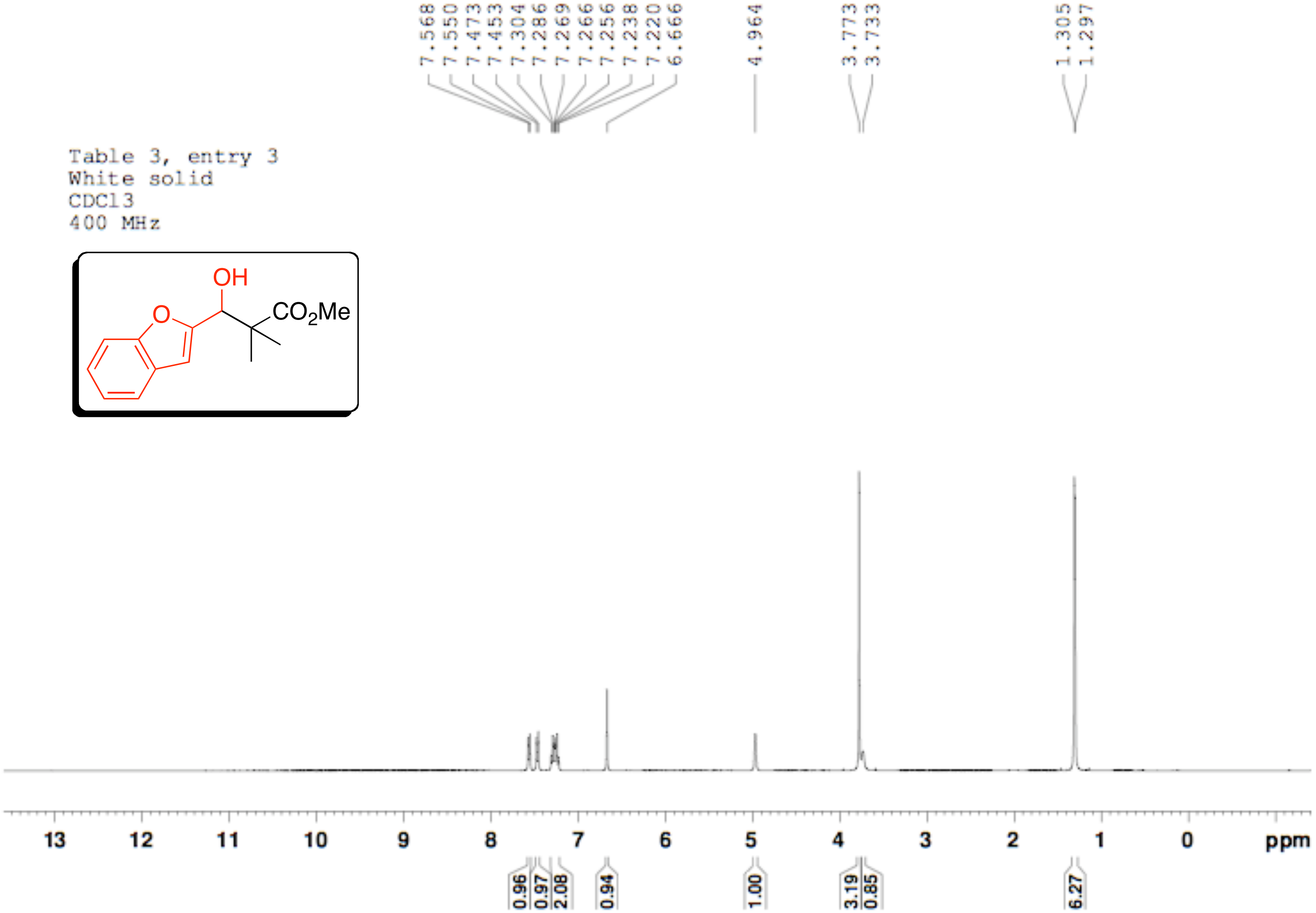
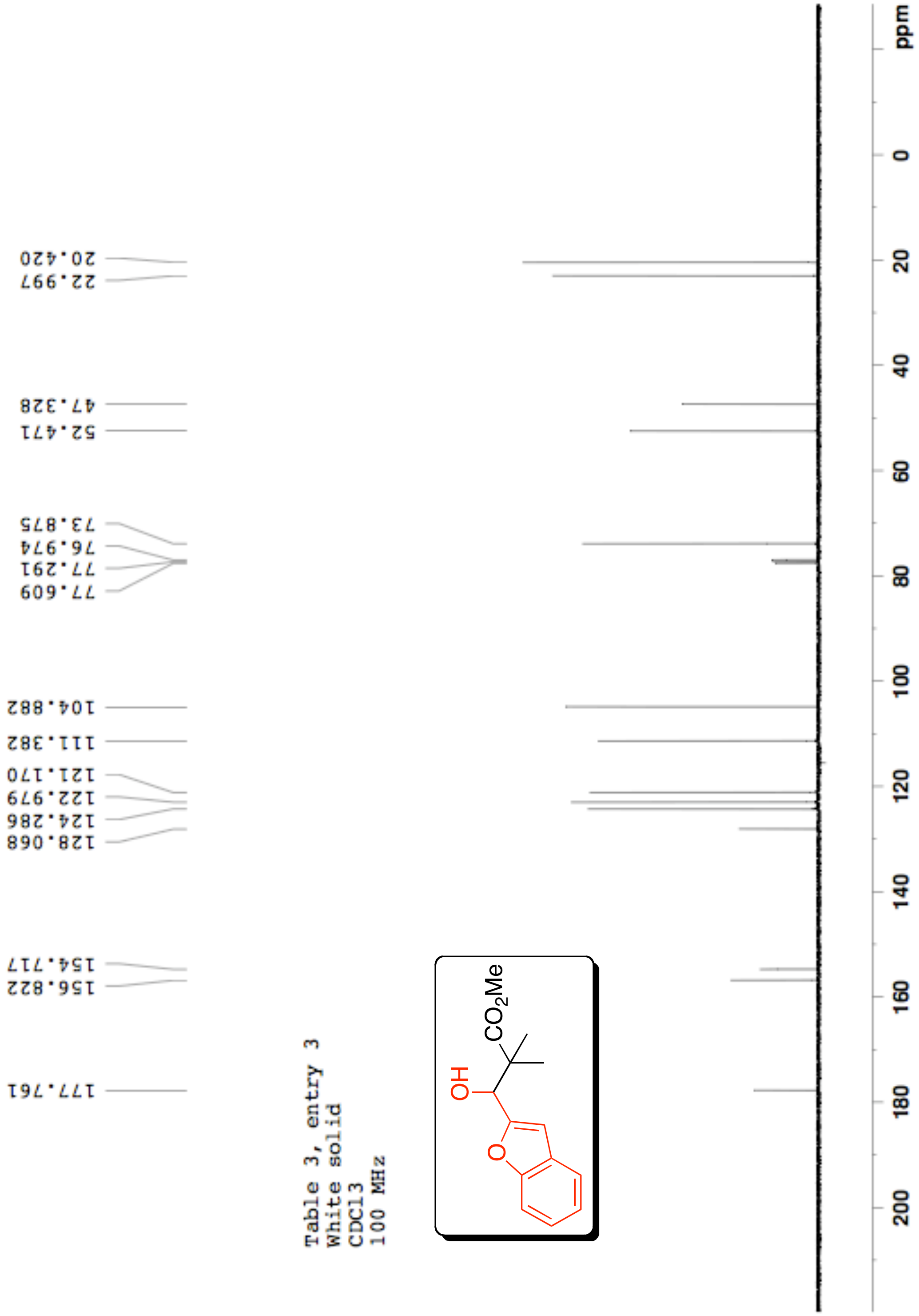
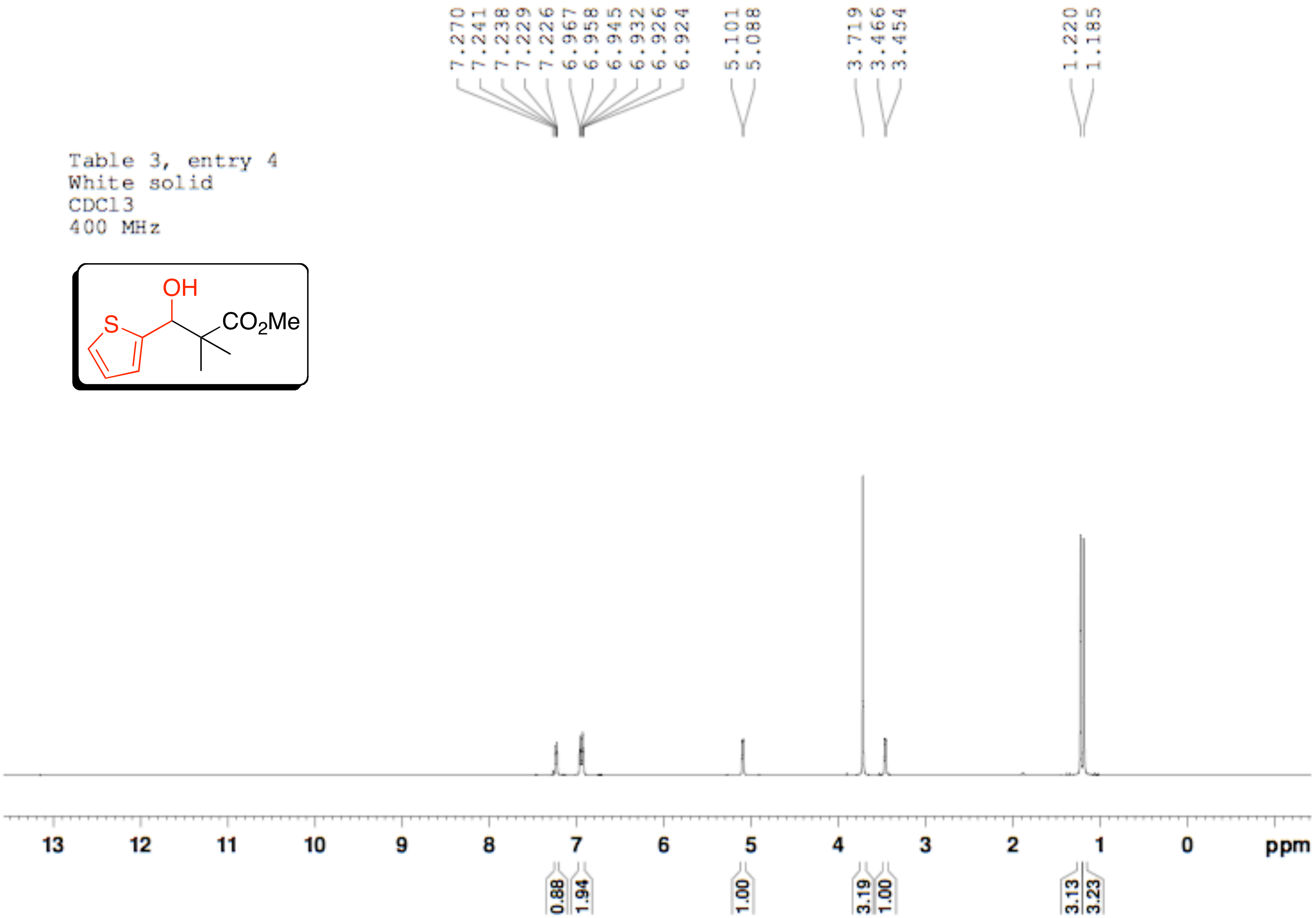


Table 3, entry 3
White solid
CDCl3
400 MHz
OH
O
CO2Me
7.568
7.550
7.473
7.453
7.304
7.286
7.269
7.266
7.256
7.238
7.220
6.666
4.964
3.773
3.733
1.305
1.297
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.96
0.97
2.08
0.94
1.00
3.19
0.85
6.27


20.420
22.997
47.328
52.471
73.875
76.974
77.291
77.609
104.882
111.382
121.170
122.979
124.286
128.068
154.717
156.822
177.761
Table 3, entry 3
White solid
CDCl3
100 MHz
OH
O
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200


7.270
7.241
7.238
7.229
7.226
6.967
6.958
6.945
6.932
6.926
6.924
5.101
5.088
3.719
3.466
3.454
1.220
1.185
Table 3, entry 4
White solid
CDCl3
400 MHz
OH
S
CO2Me
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.88
1.94
1.00
3.19
1.00
3.13
3.23

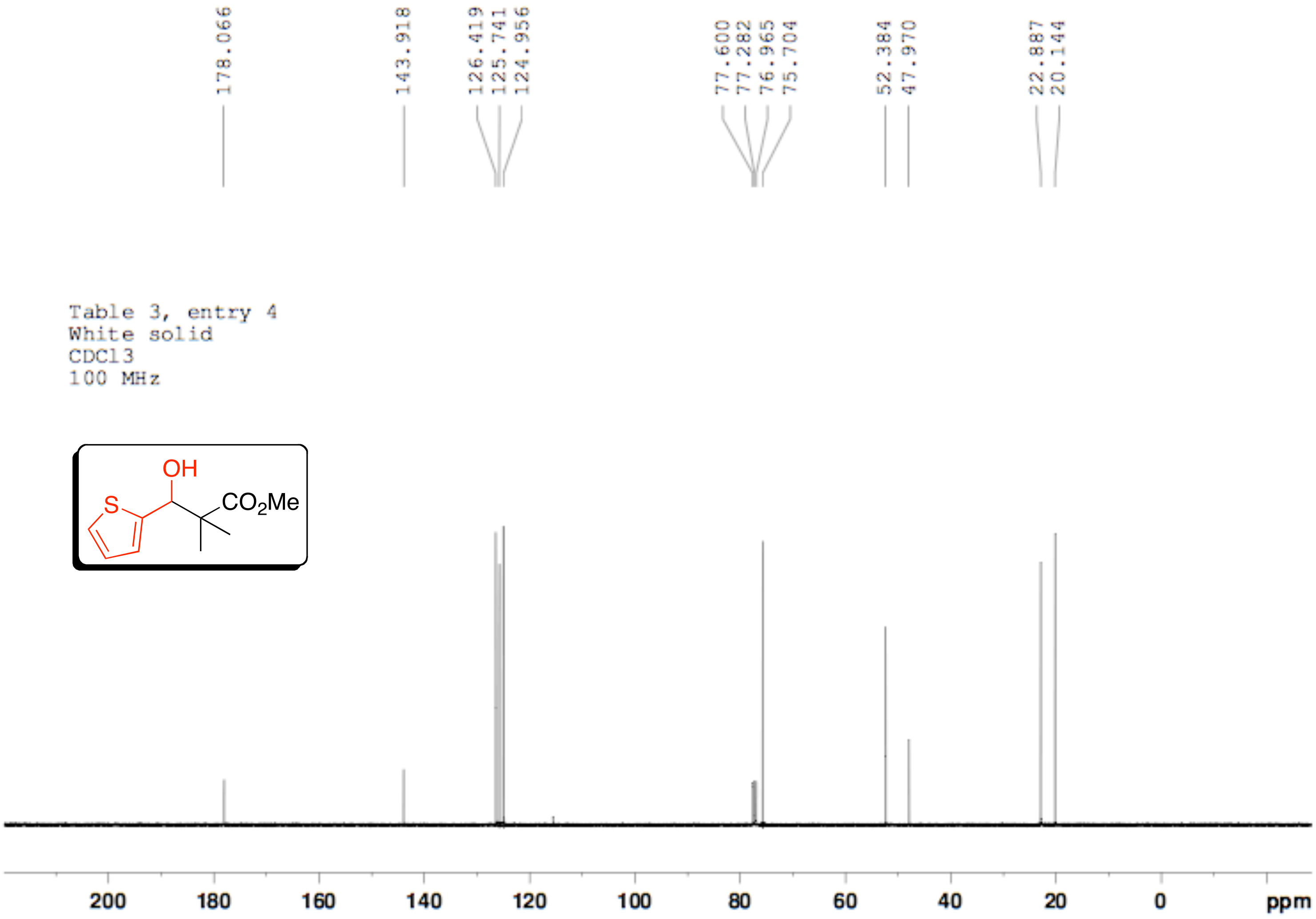


Table 3, entry 4
White solid
CDCl3
100 MHz

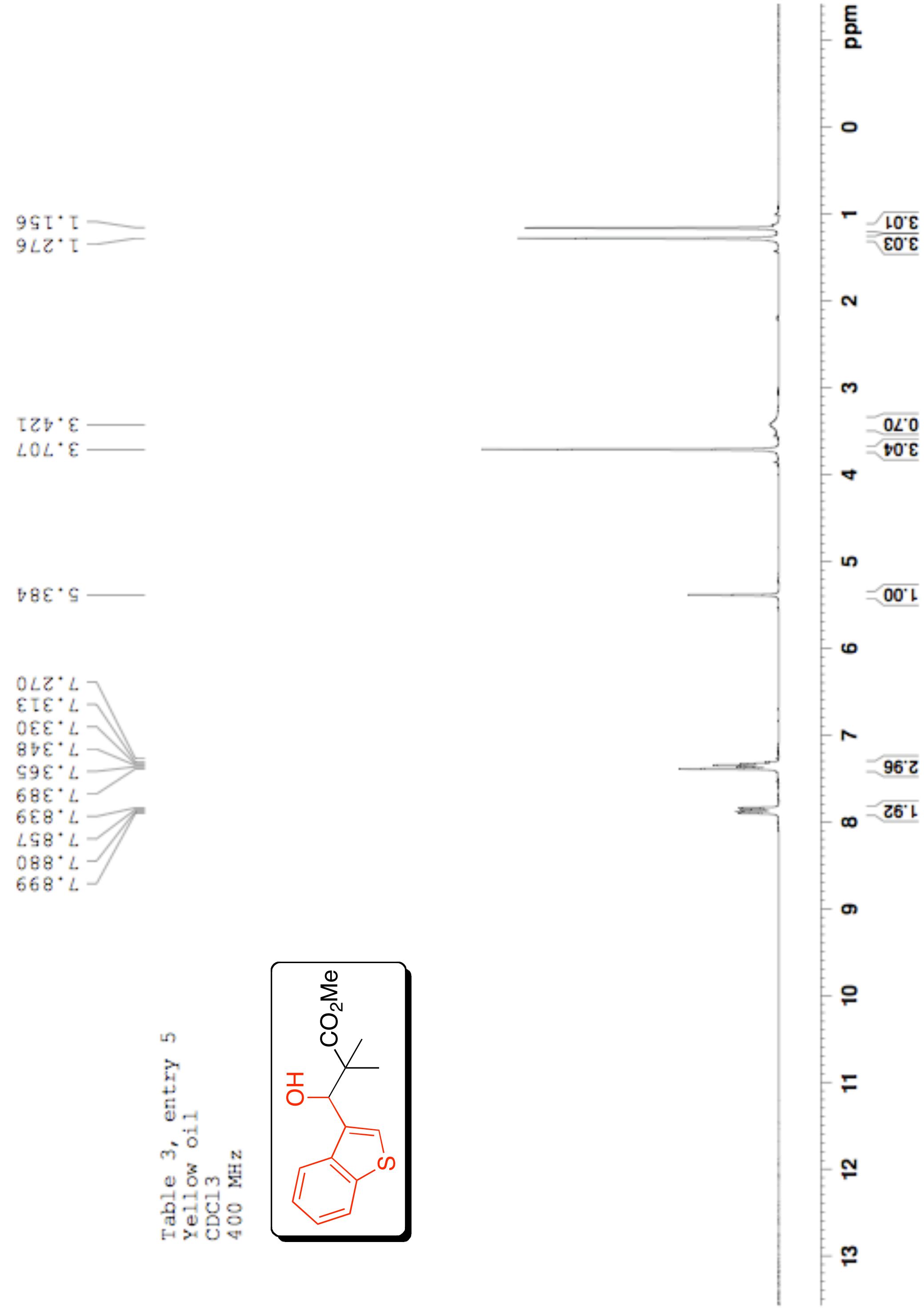
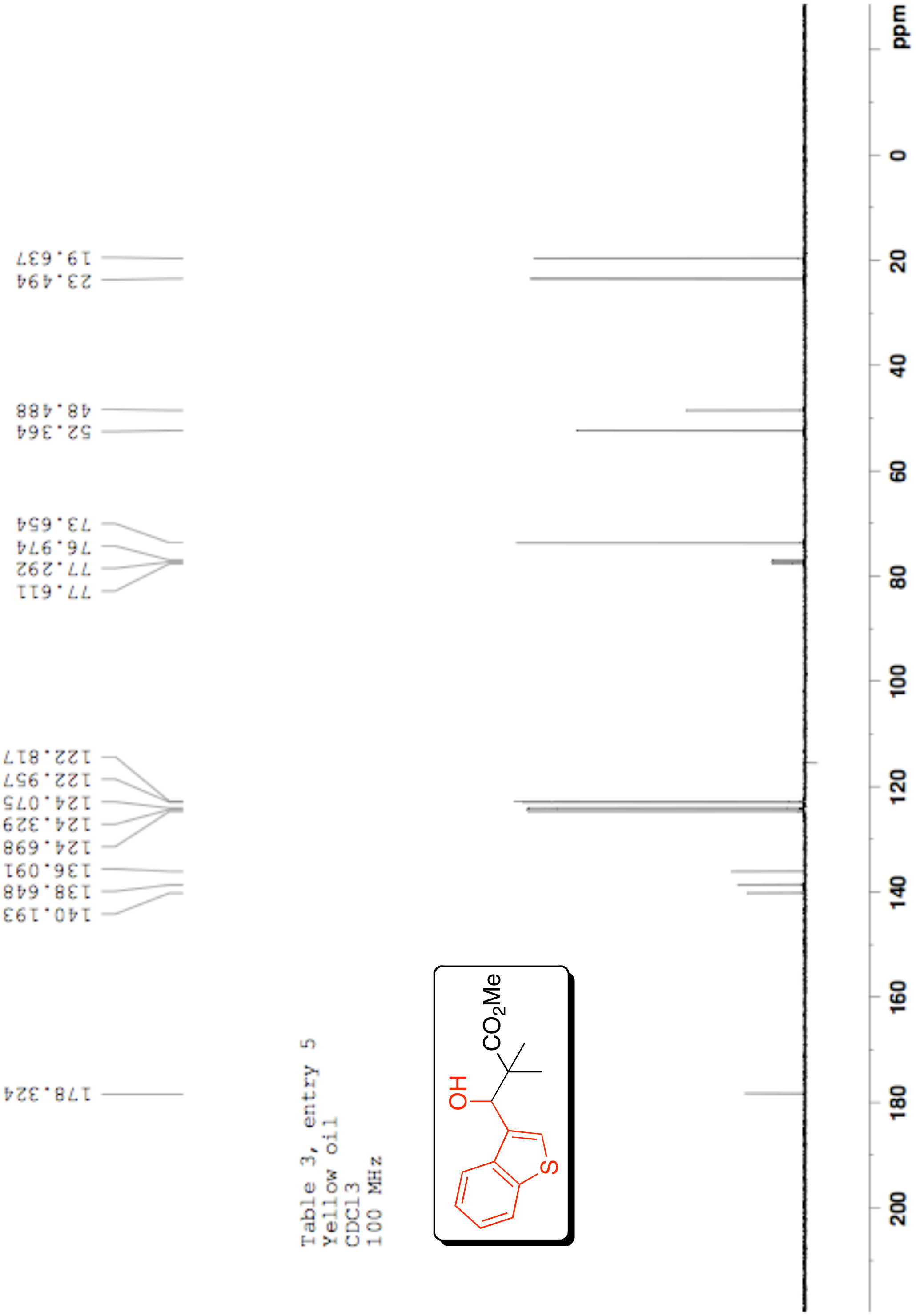


Table 3, entry 5
Yellow oil
CDCl3
400 MHz
OH
CO2Me
S
1.156
1.276
3.421
3.707
5.384
7.270
7.313
7.330
7.348
7.365
7.389
7.839
7.857
7.880
7.899
3.01
3.03
0.70
3.04
1.00
2.96
1.92
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


19.637
23.494
48.488
52.364
73.654
76.974
77.292
77.611
122.817
122.957
124.075
124.329
124.698
136.091
138.648
140.193
178.324
Table 3, entry 5
Yellow oil
CDCl3
100 MHz
OH
CO2Me
S
ppm
0
20
40
60
80
100
120
140
160
180
200

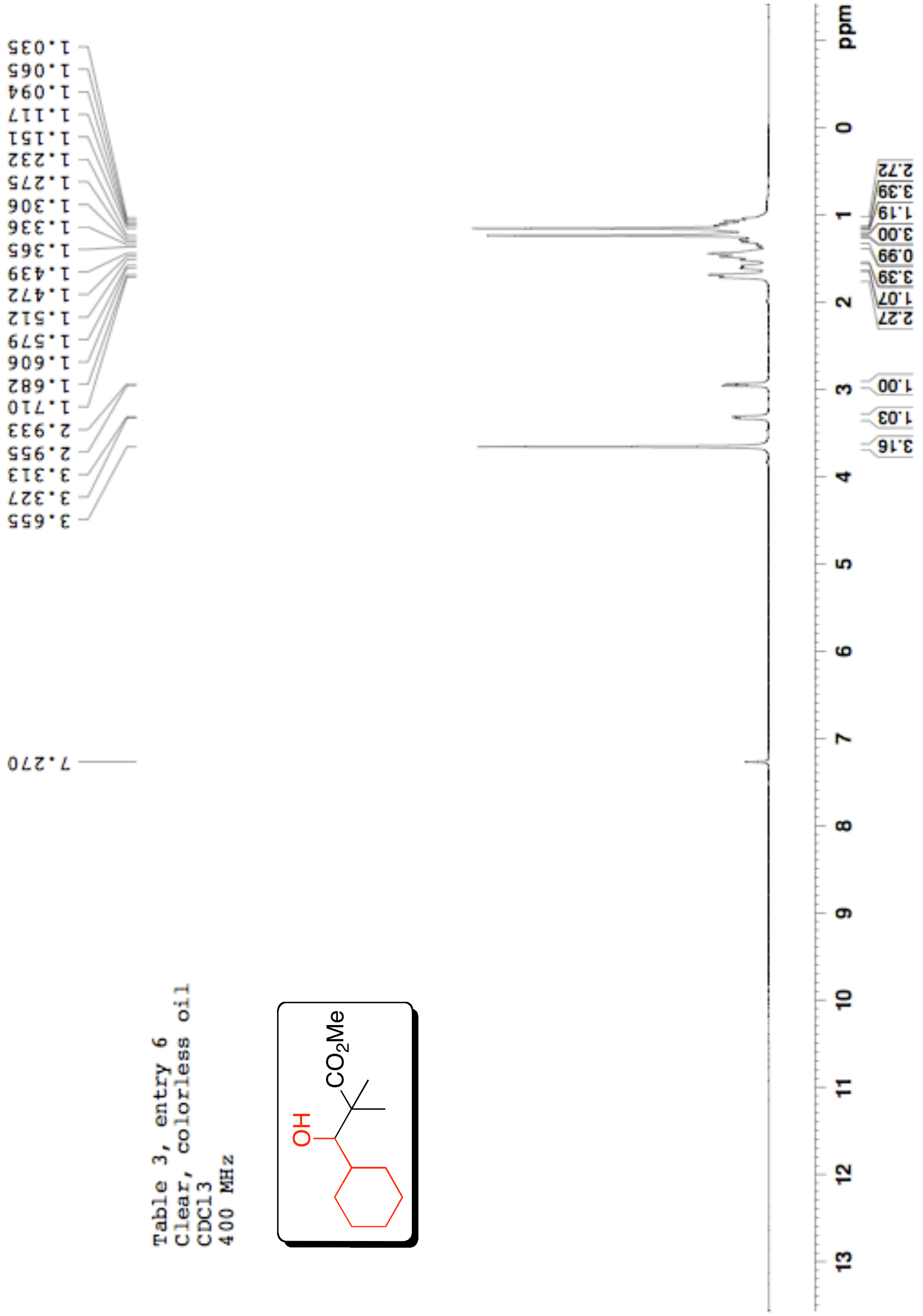
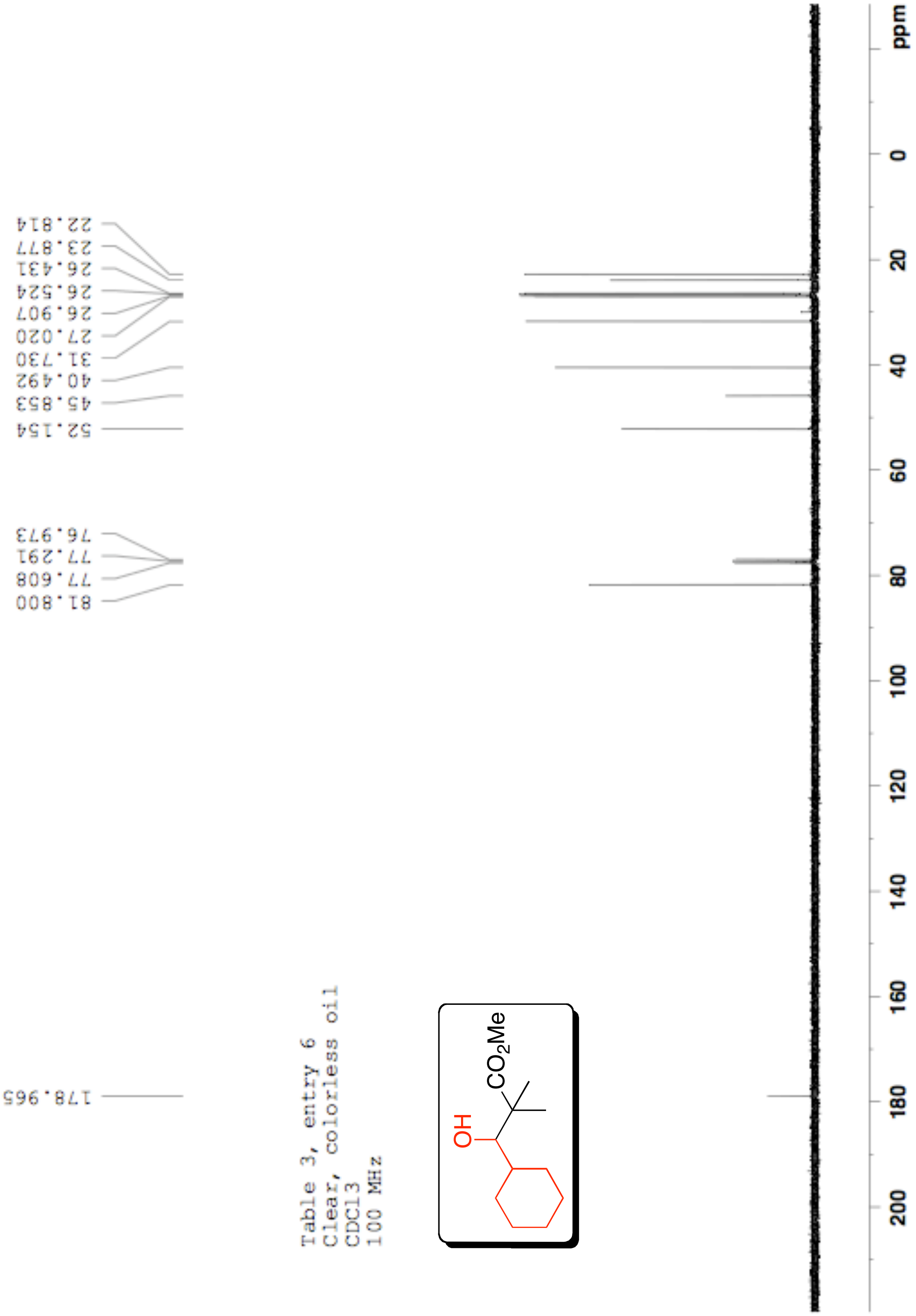


Table 3, entry 6
Clear, colorless oil
CDCl3
400 MHz
OH
CO2Me
1.035
1.065
1.094
1.117
1.151
1.232
1.275
1.306
1.336
1.365
1.439
1.472
1.512
1.579
1.606
1.682
1.710
2.933
2.955
3.313
3.327
3.655
7.270
2.72
3.39
1.19
3.00
0.99
3.39
1.07
2.27
1.00
1.03
3.16
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


22.814
23.877
26.431
26.524
26.907
27.020
31.730
40.492
45.853
52.154
76.973
77.291
77.608
81.800
178.965
Table 3, entry 6
Clear, colorless oil
CDCl3
100 MHz
OH
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200

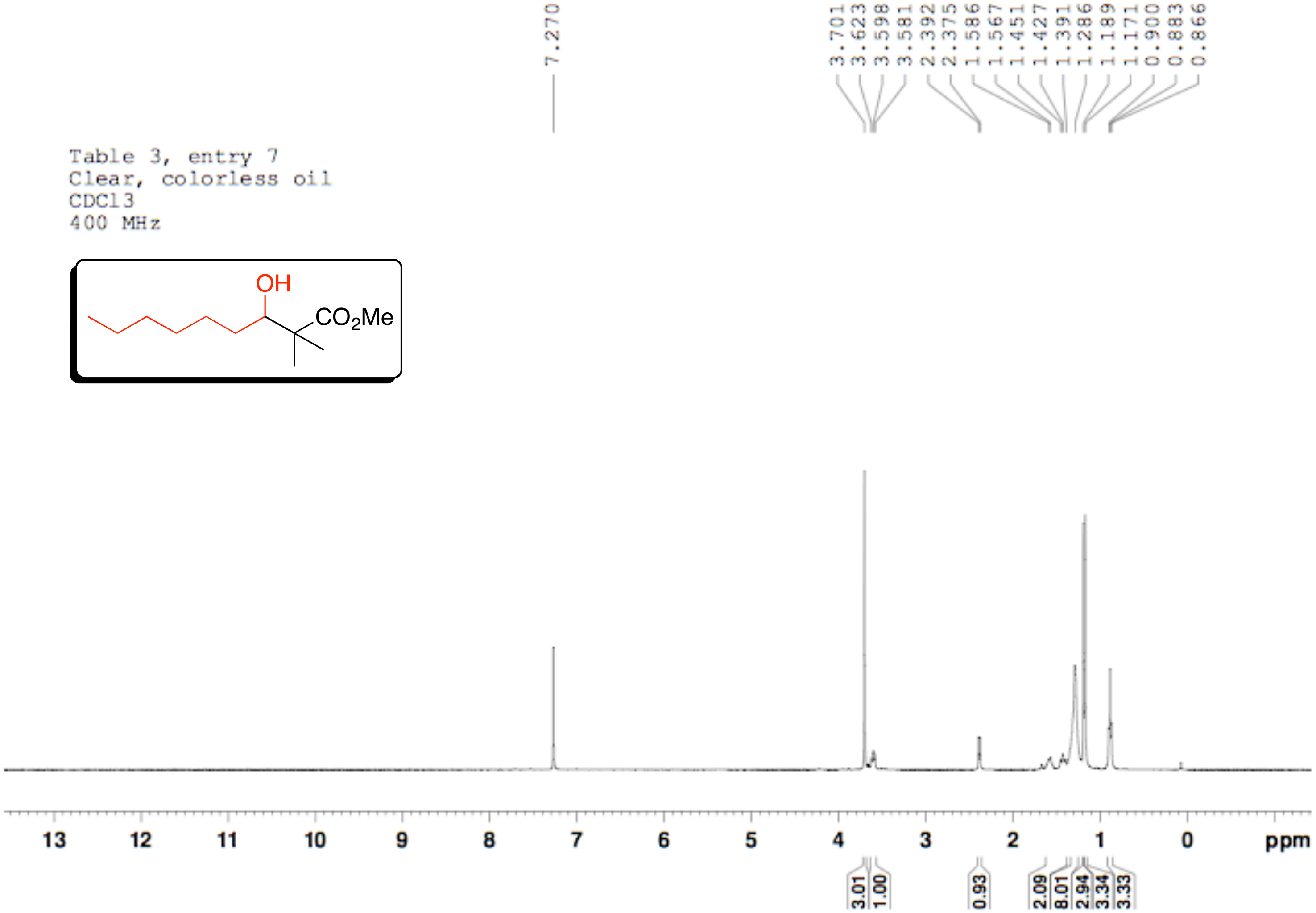
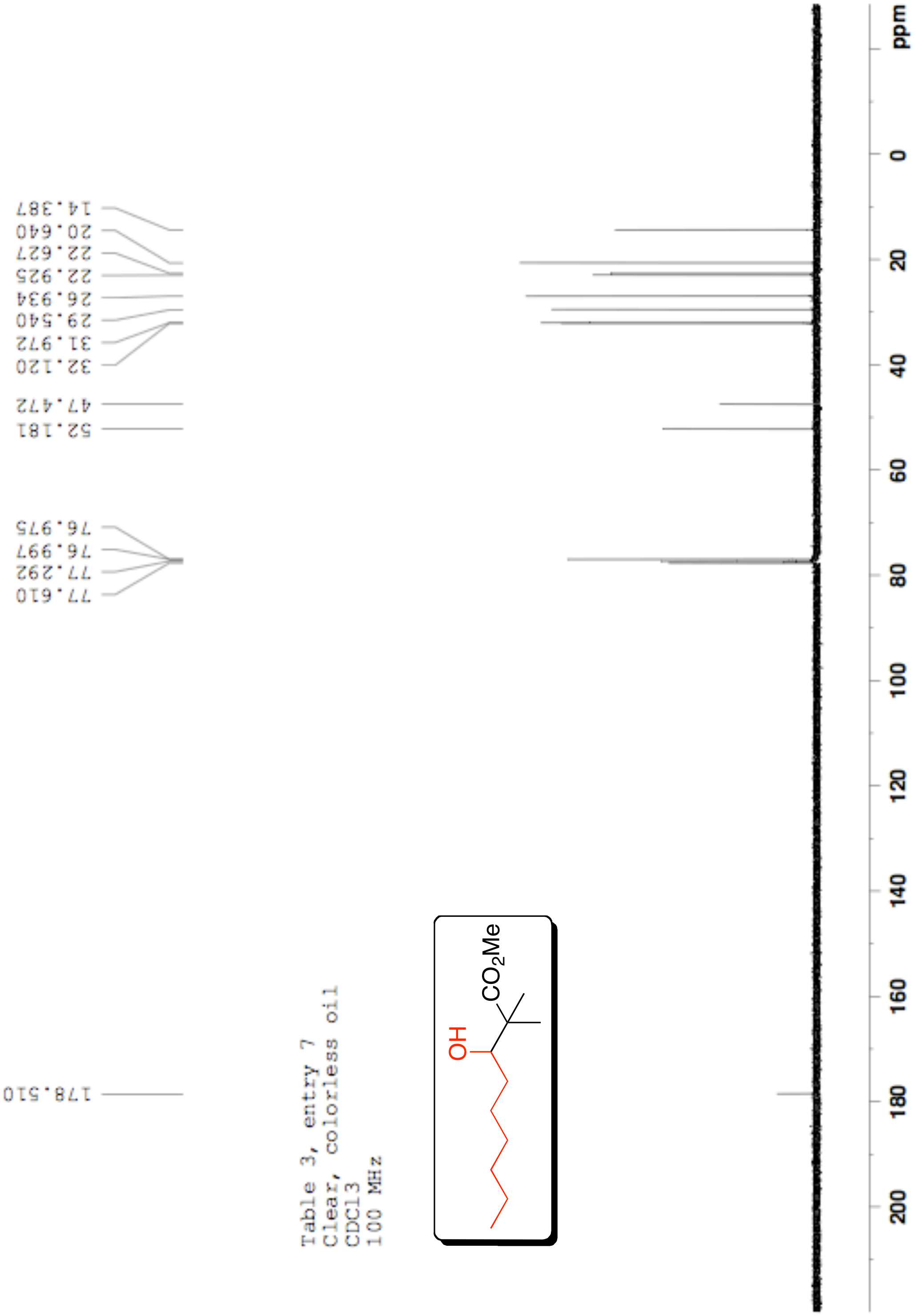


Table 3, entry 7
Clear, colorless oil
CDCl3
400 MHz


14.387
20.640
22.627
22.925
26.934
29.540
31.972
32.120
47.472
52.181
76.975
76.997
77.292
77.610
178.510
Table 3, entry 7
Clear, colorless oil
CDCl3
100 MHz
OH
CO_2Me
ppm
0
20
40
60
80
100
120
140
160
180
200

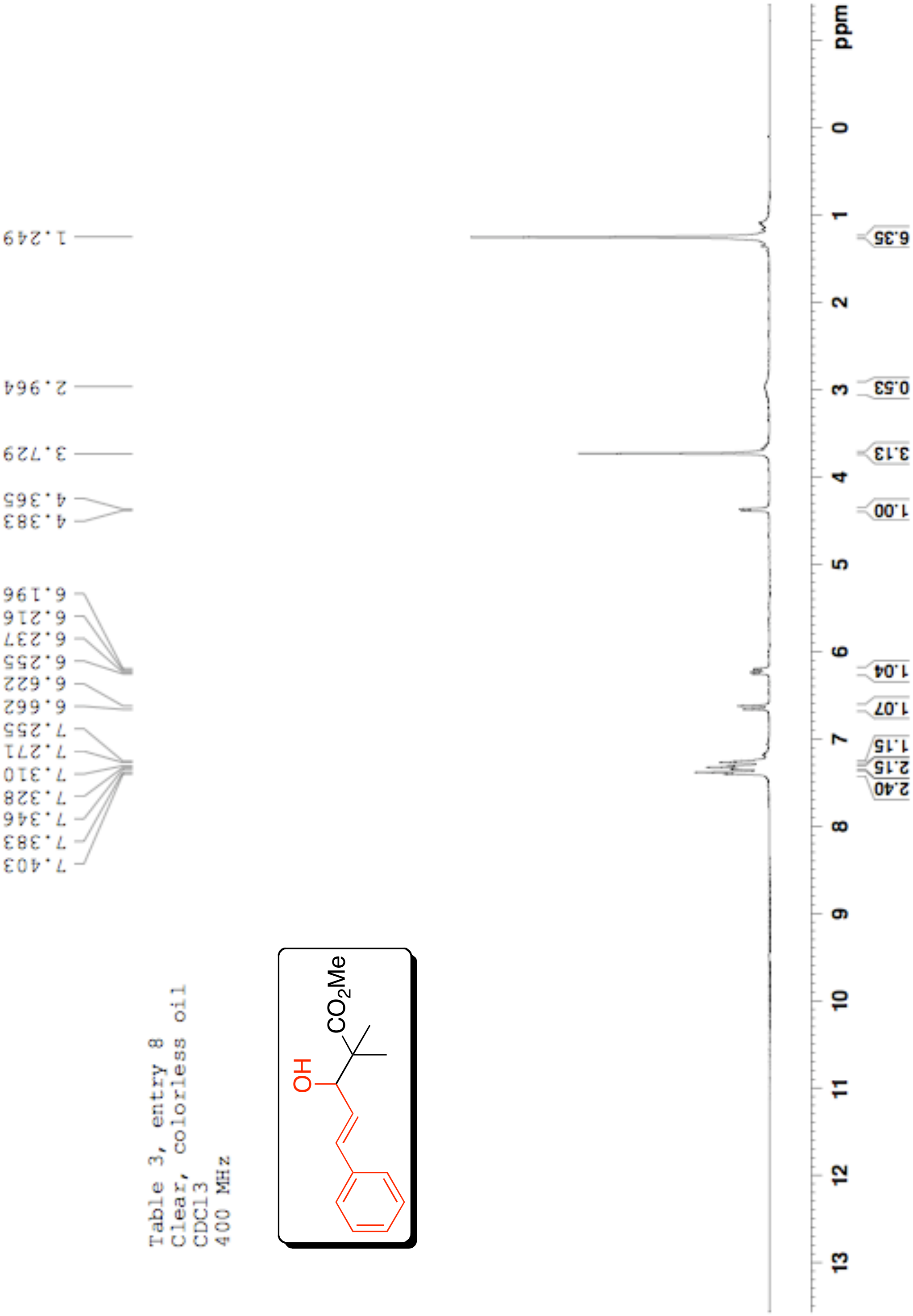
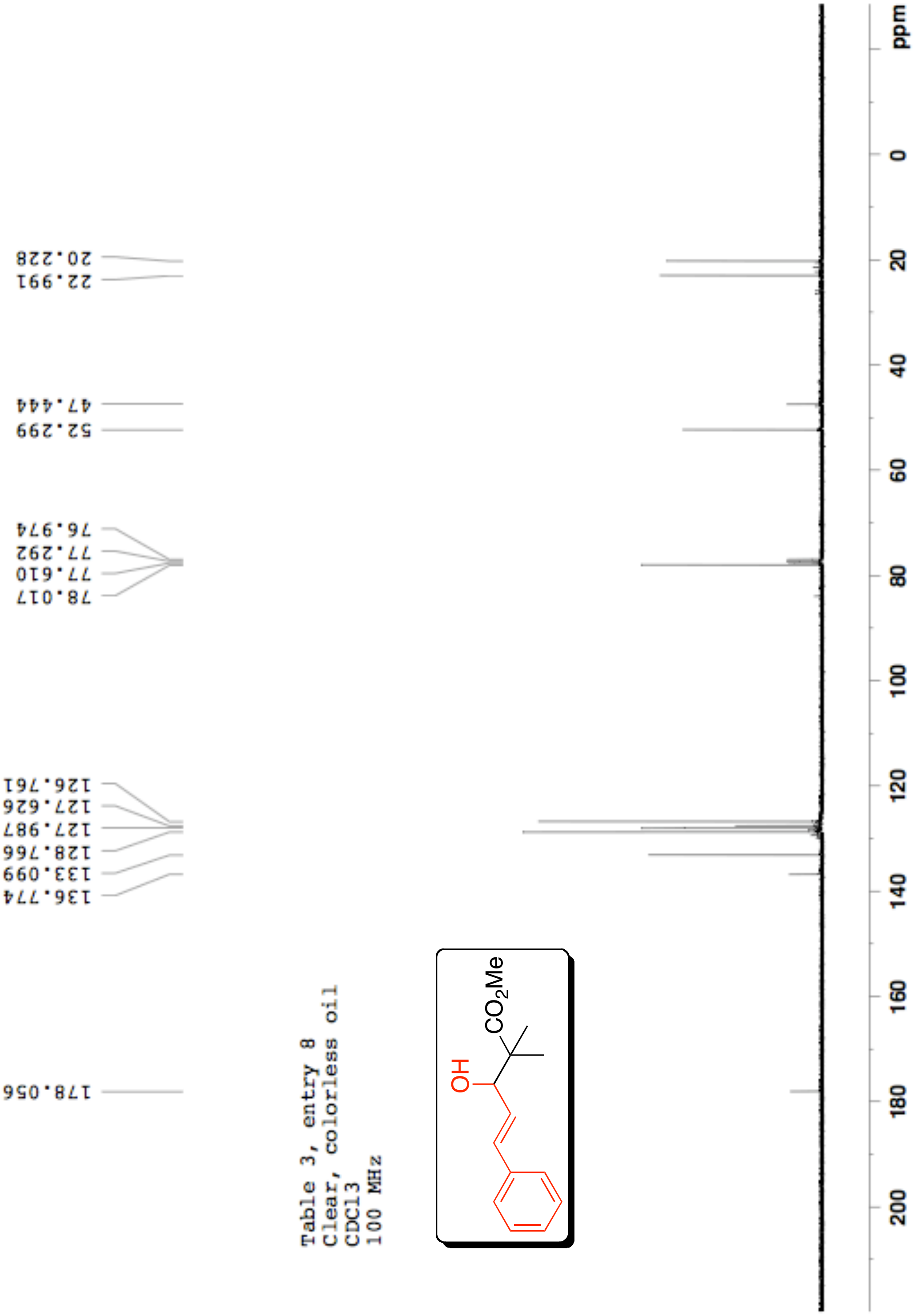


Table 3, entry 8
Clear, colorless oil
CDCl3
400 MHz
OH
CO2Me
1.249
2.964
3.729
4.365
4.383
6.196
6.216
6.237
6.255
6.622
6.662
7.255
7.271
7.310
7.328
7.346
7.383
7.403
6.35
0.53
3.13
1.00
1.04
1.07
1.15
2.15
2.40
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


20.228
22.991
47.444
52.299
76.974
77.292
77.610
78.017
126.761
127.626
127.987
128.766
133.099
136.774
178.056
Table 3, entry 8
Clear, colorless oil
CDCl3
100 MHz
OH
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200

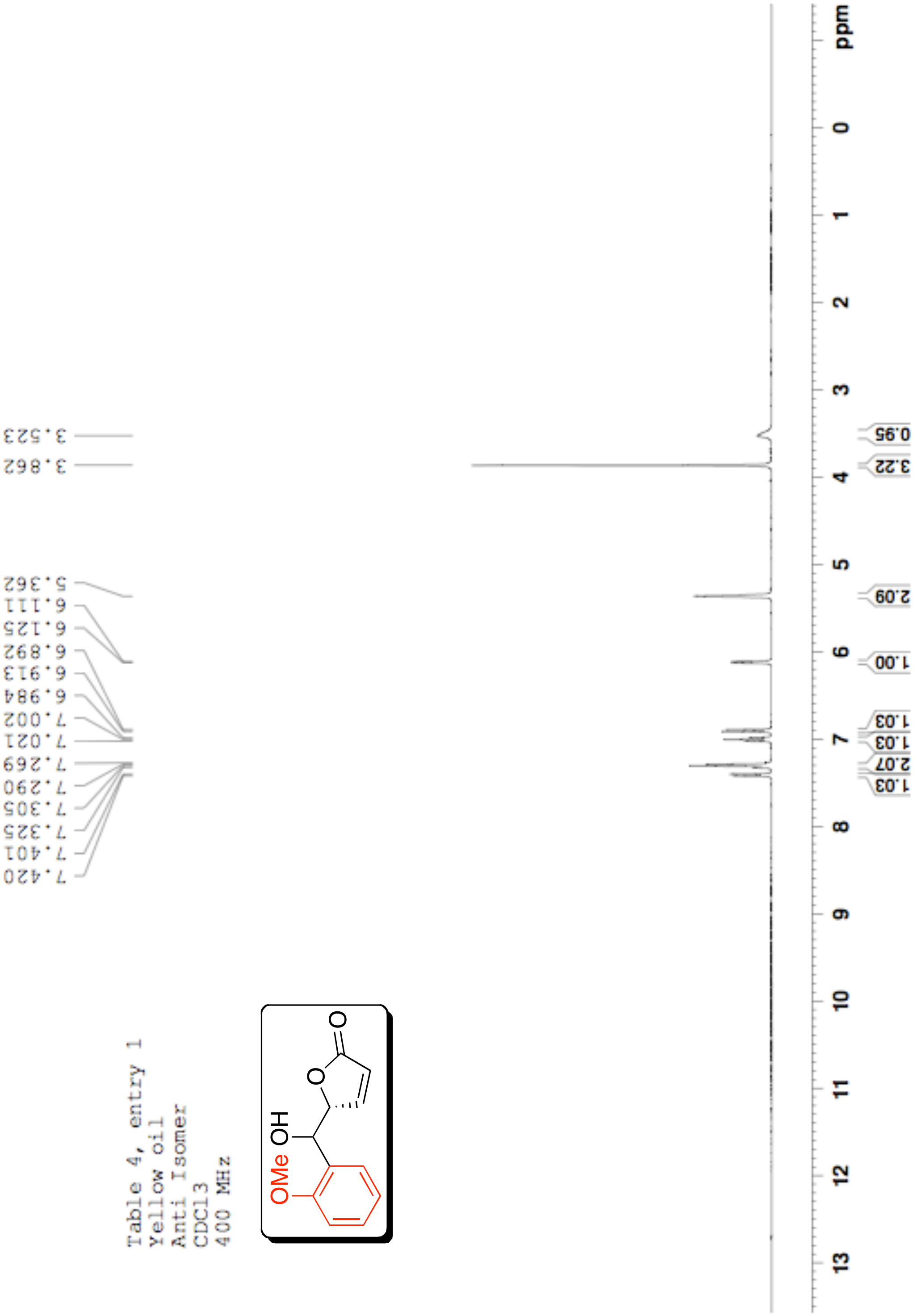
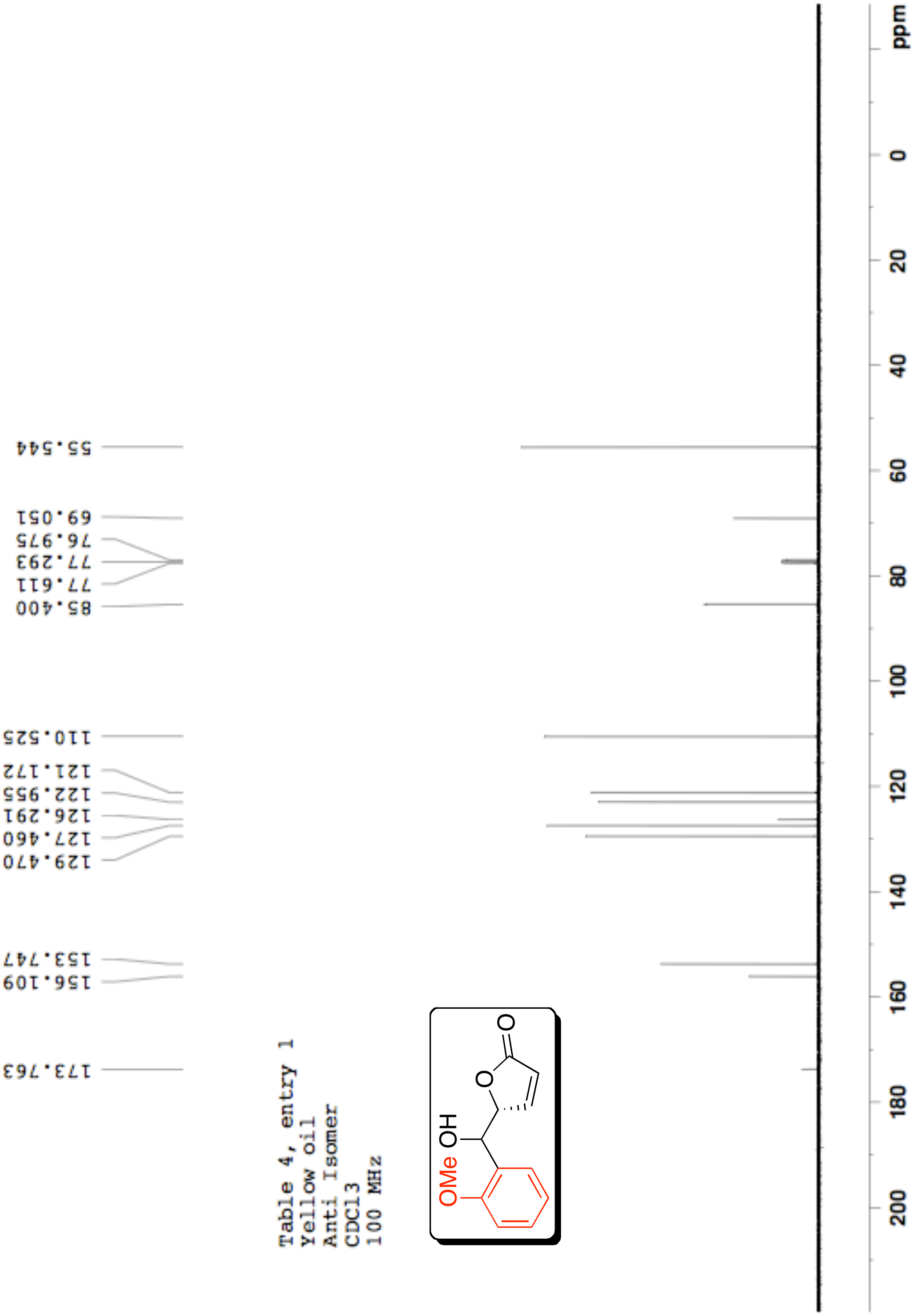


Table 4, entry 1
Yellow oil
Anti Isomer
CDCl3
400 MHz
OMe
OH
O
O
3.523
3.862
5.362
6.111
6.125
6.892
6.913
6.984
7.002
7.021
7.269
7.290
7.305
7.325
7.401
7.420
0.95
3.22
2.09
1.00
1.03
1.03
2.07
1.03
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


55.544
69.051
76.975
77.293
77.611
85.400
110.525
121.172
122.955
126.291
127.460
129.470
153.747
156.109
173.763
Table 4, entry 1
Yellow oil
Anti Isomer
CDCl3
100 MHz
OMe
OH
O
O
ppm
0
20
40
60
80
100
120
140
160
180
200

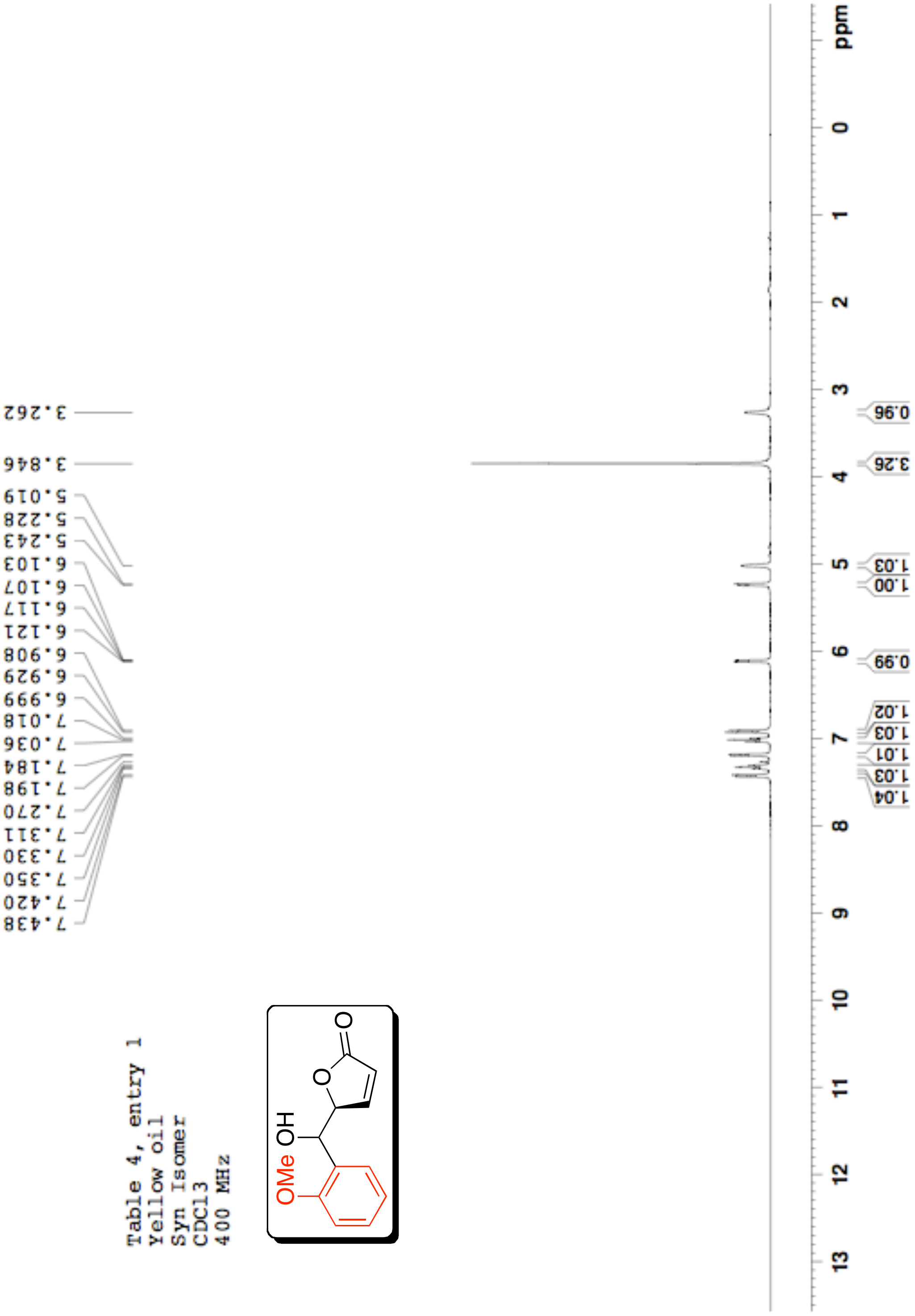


Table 4, entry 1
Yellow oil
Syn Isomer
CDCl3
400 MHz
OMe
OH
O
O
3.262
3.846
5.019
5.228
5.243
6.103
6.107
6.117
6.121
6.908
6.929
6.999
7.018
7.036
7.184
7.198
7.270
7.311
7.330
7.350
7.420
7.438
0.96
3.26
1.03
1.00
0.99
1.02
1.03
1.01
1.03
1.04
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

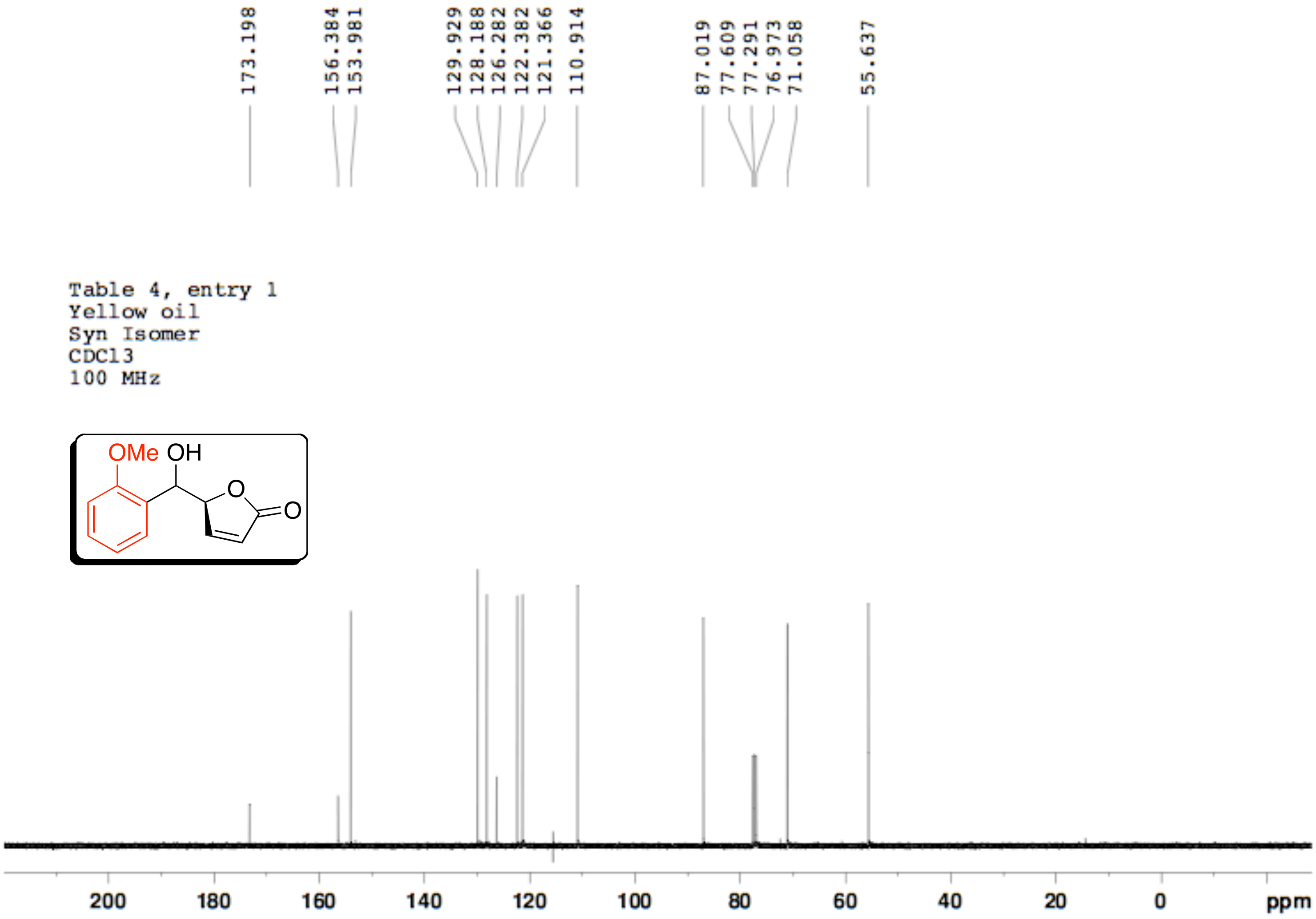
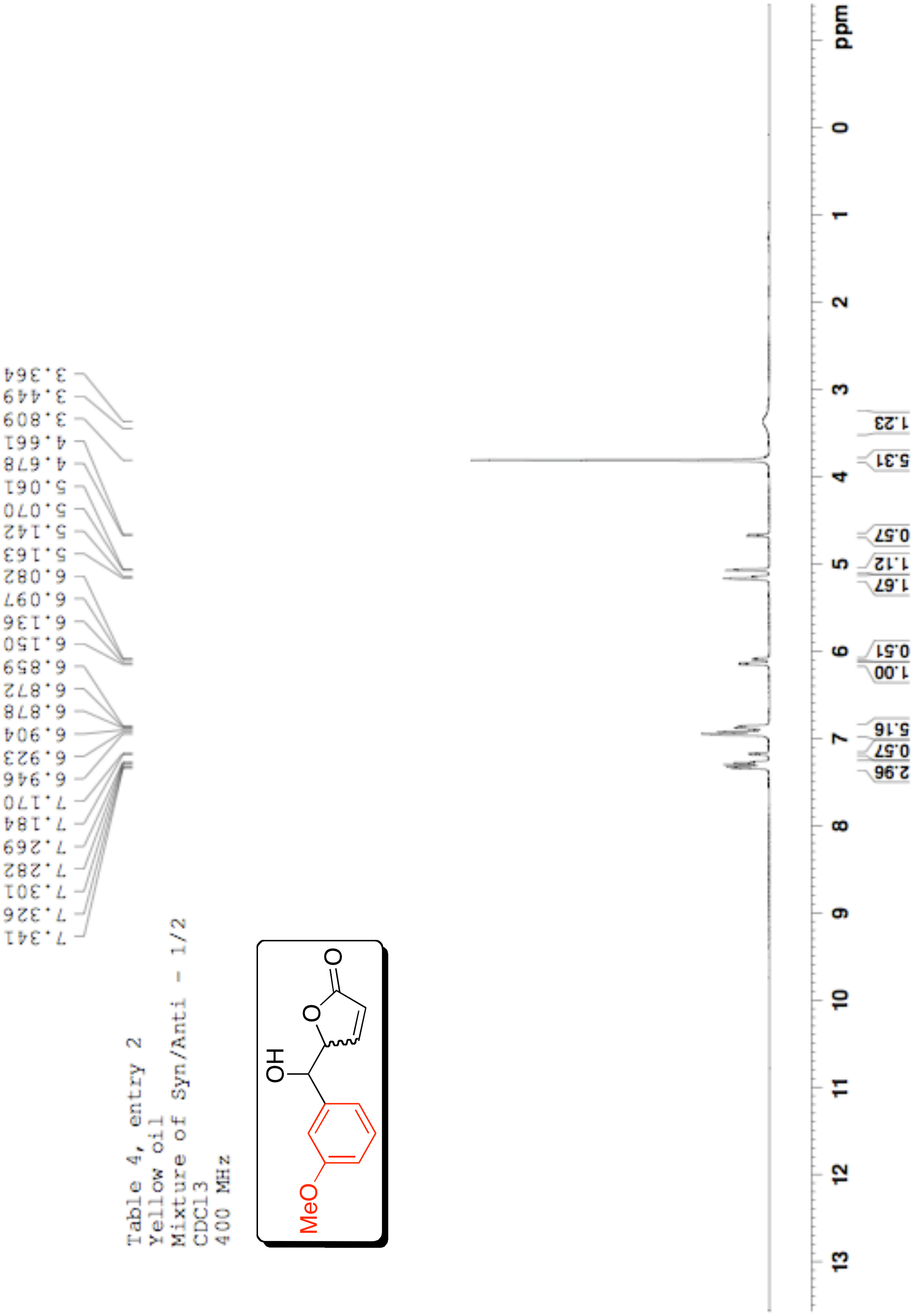


Table 4, entry 1
Yellow oil
Syn Isomer
CDCl3
100 MHz


3.364
3.449
3.809
4.661
4.678
5.061
5.070
5.142
5.163
6.082
6.097
6.136
6.150
6.859
6.872
6.878
6.904
6.923
6.946
7.170
7.184
7.269
7.282
7.301
7.326
7.341
Table 4, entry 2
Yellow oil
Mixture of Syn/Anti - 1/2
CDCl3
400 MHz
MeO
OH
O
O
1.23
5.31
0.57
1.12
1.67
0.51
1.00
5.16
0.57
2.96
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

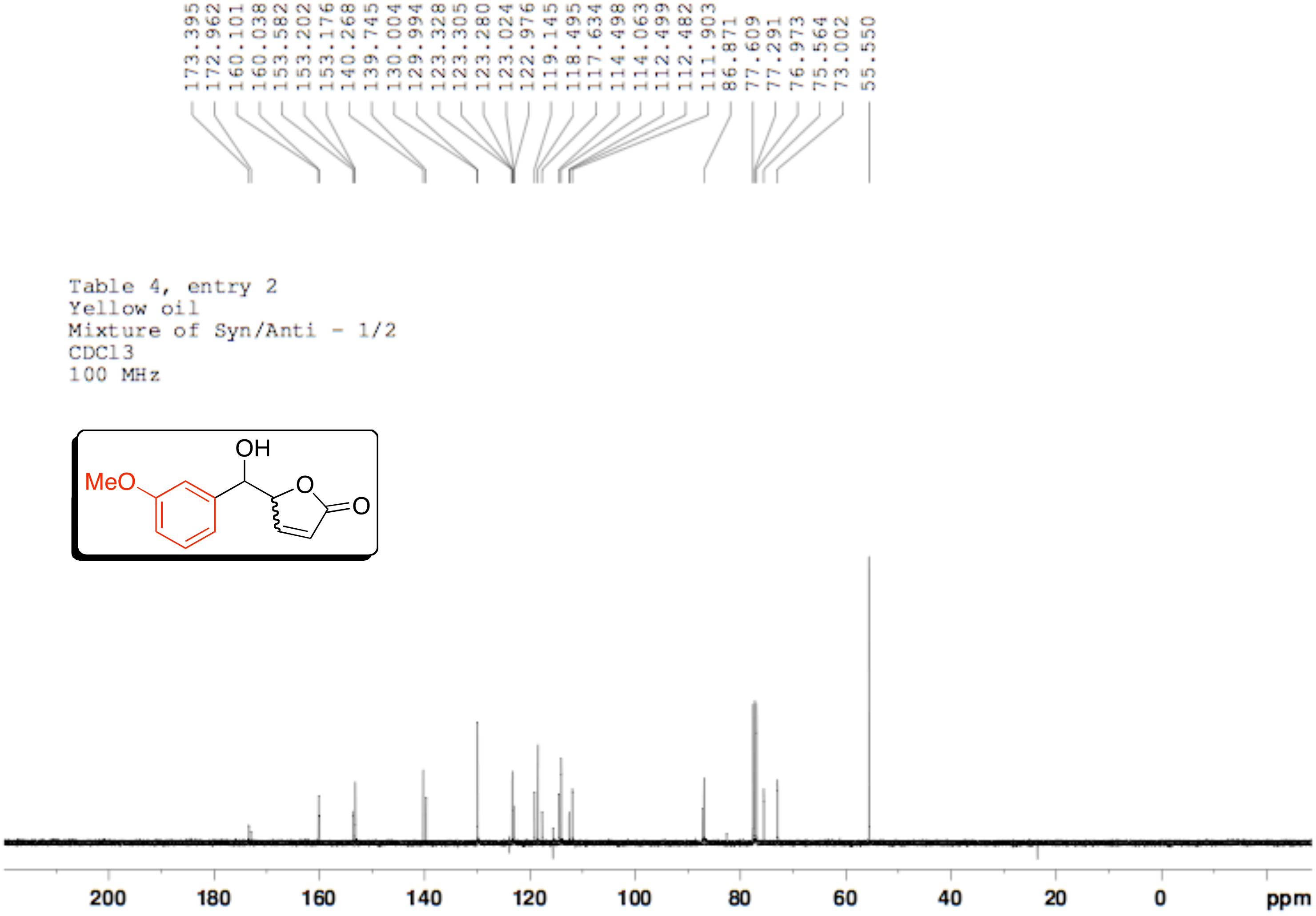


Table 4, entry 2
Yellow oil
Mixture of Syn/Anti - 1/2
CDCl3
100 MHz

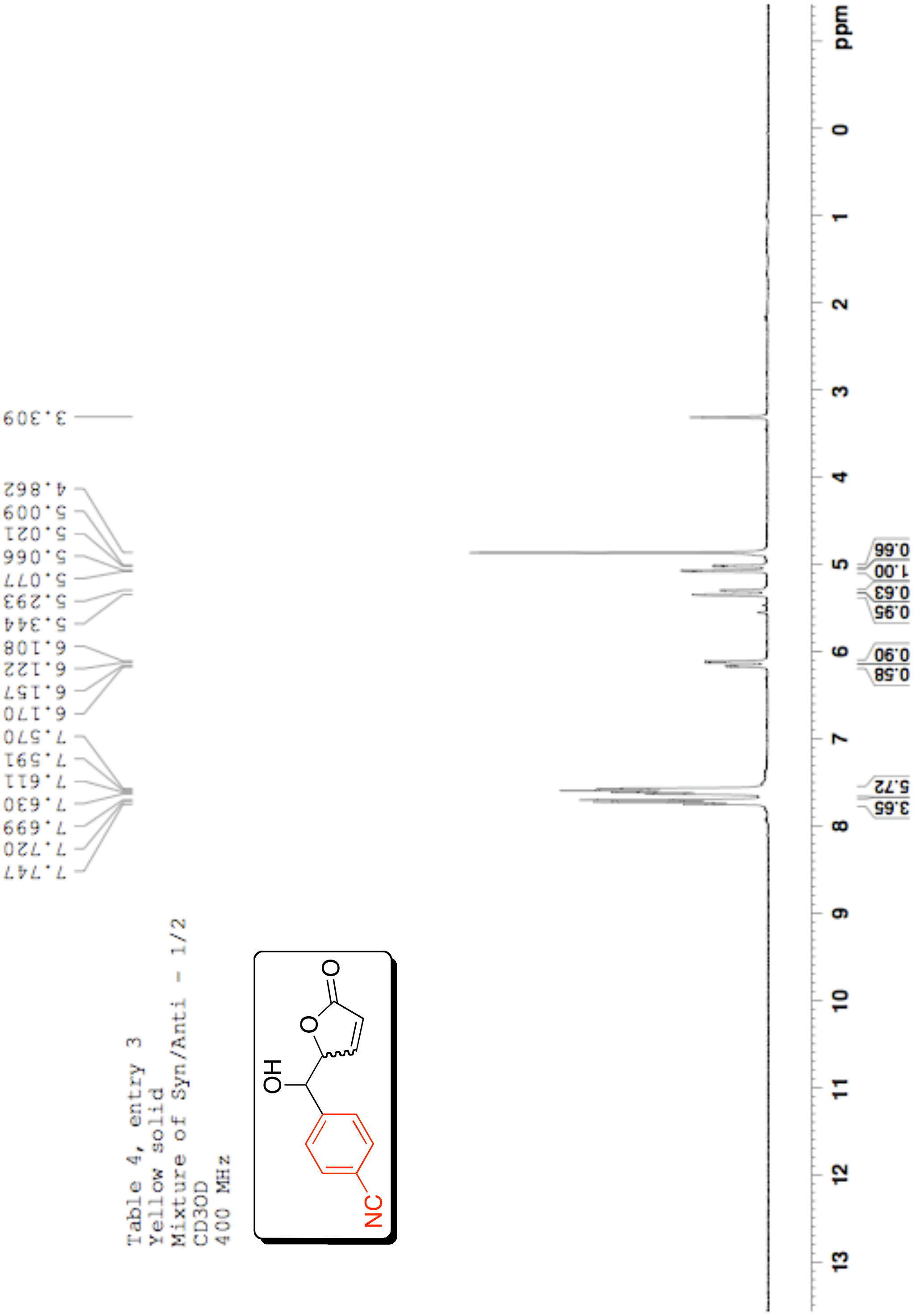


Table 4, entry 3
Yellow solid
Mixture of Syn/Anti - 1/2
CD3OD
400 MHz

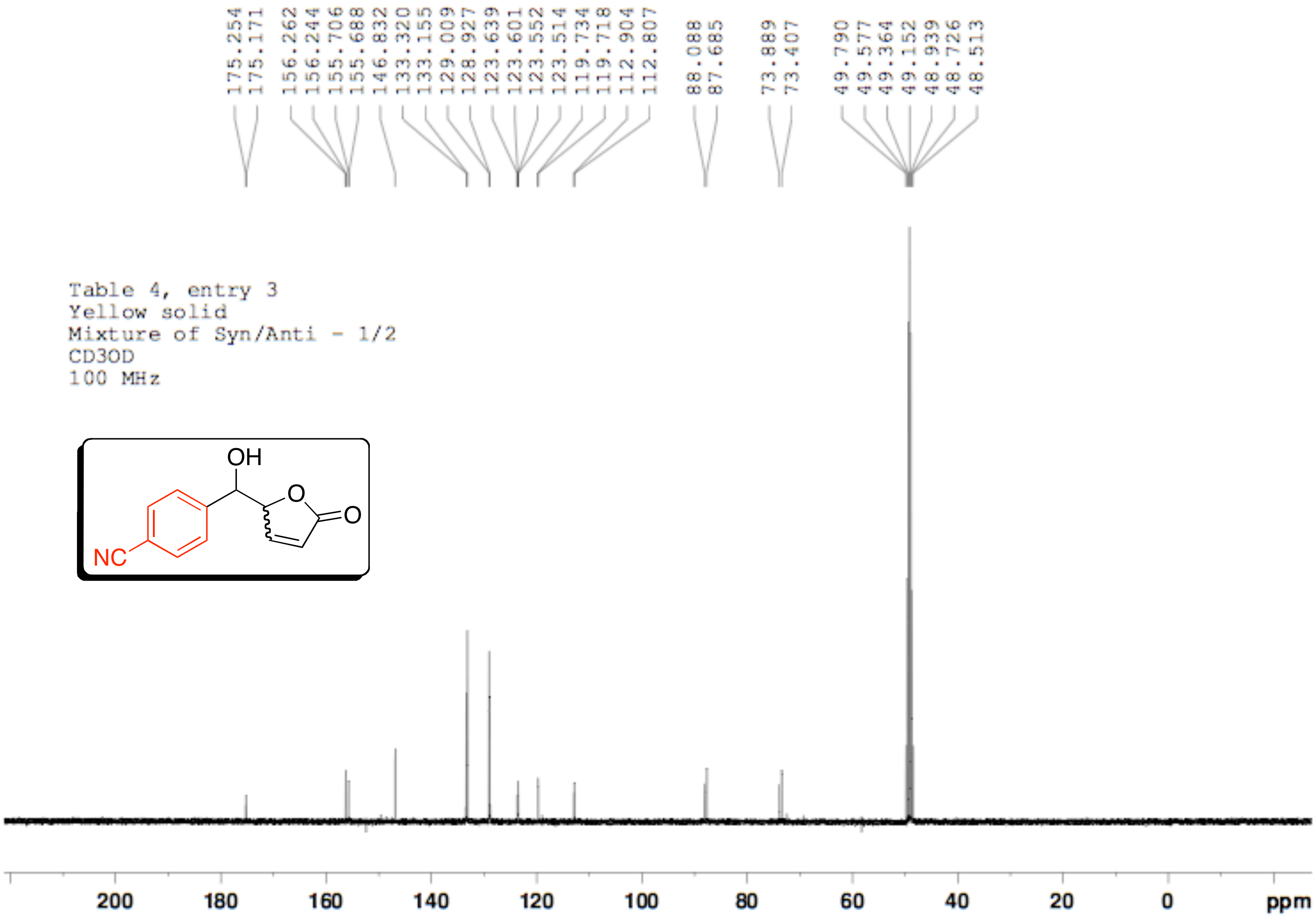


Table 4, entry 3
Yellow solid
Mixture of Syn/Anti - 1/2
CD3OD
100 MHz

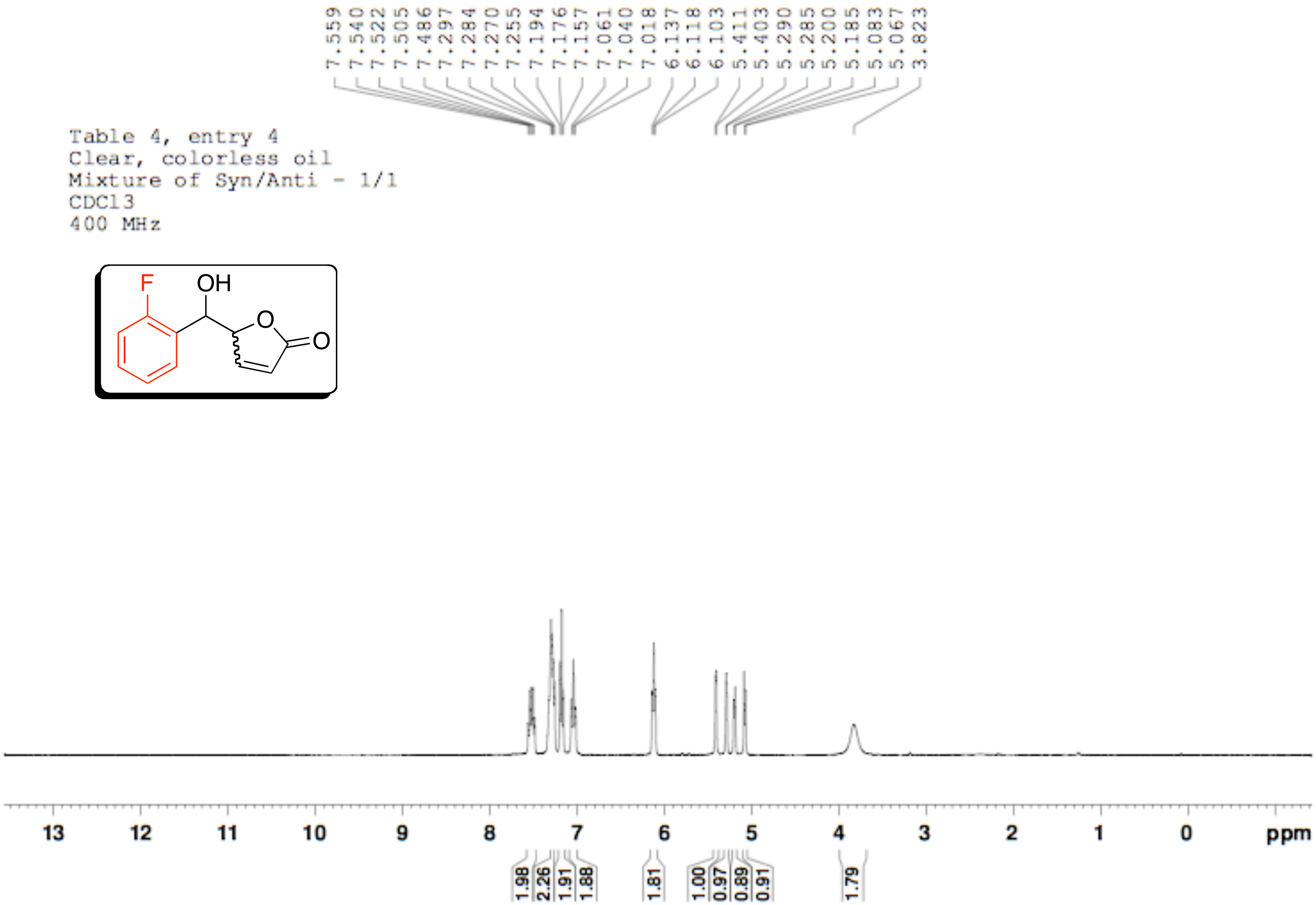
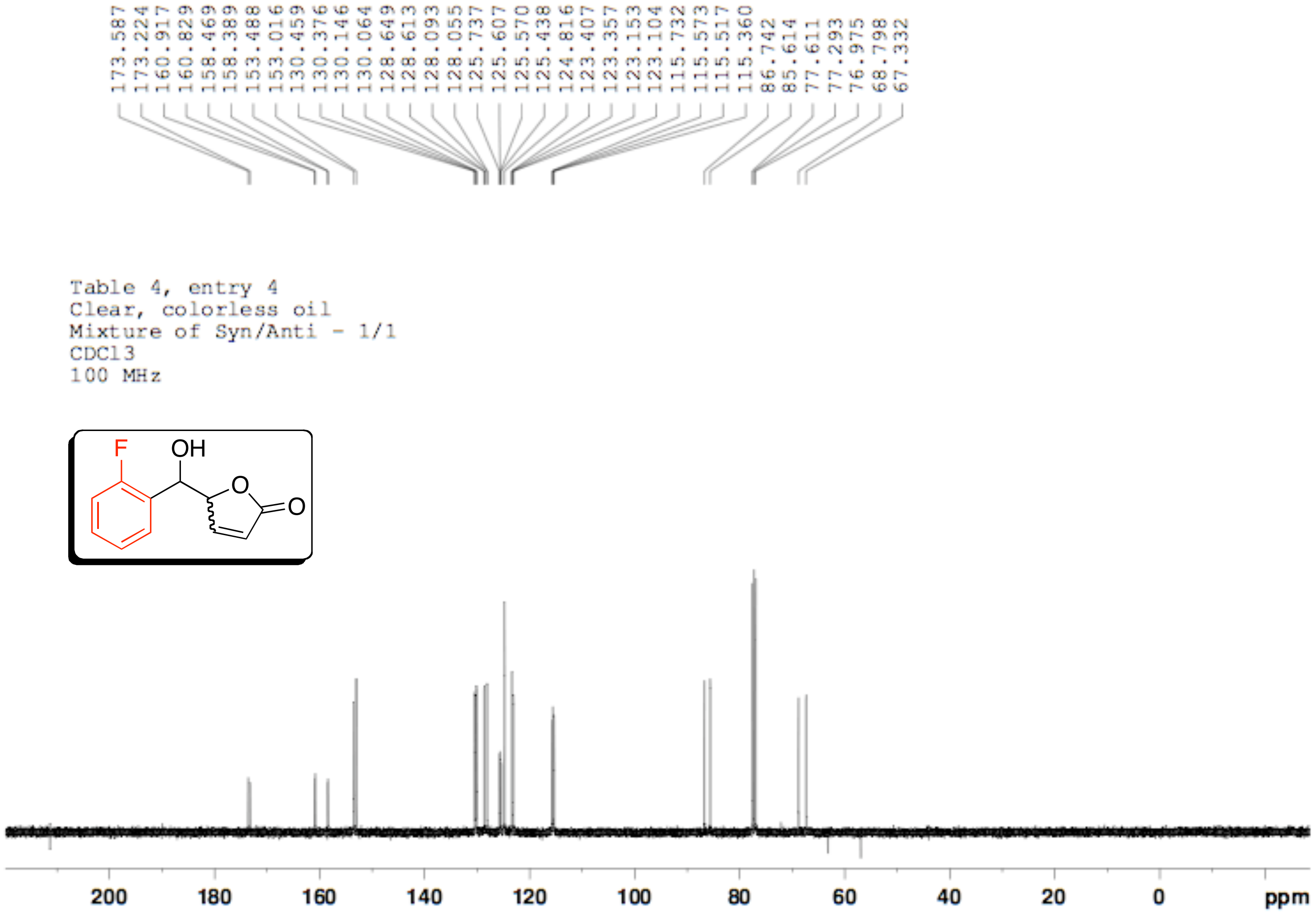
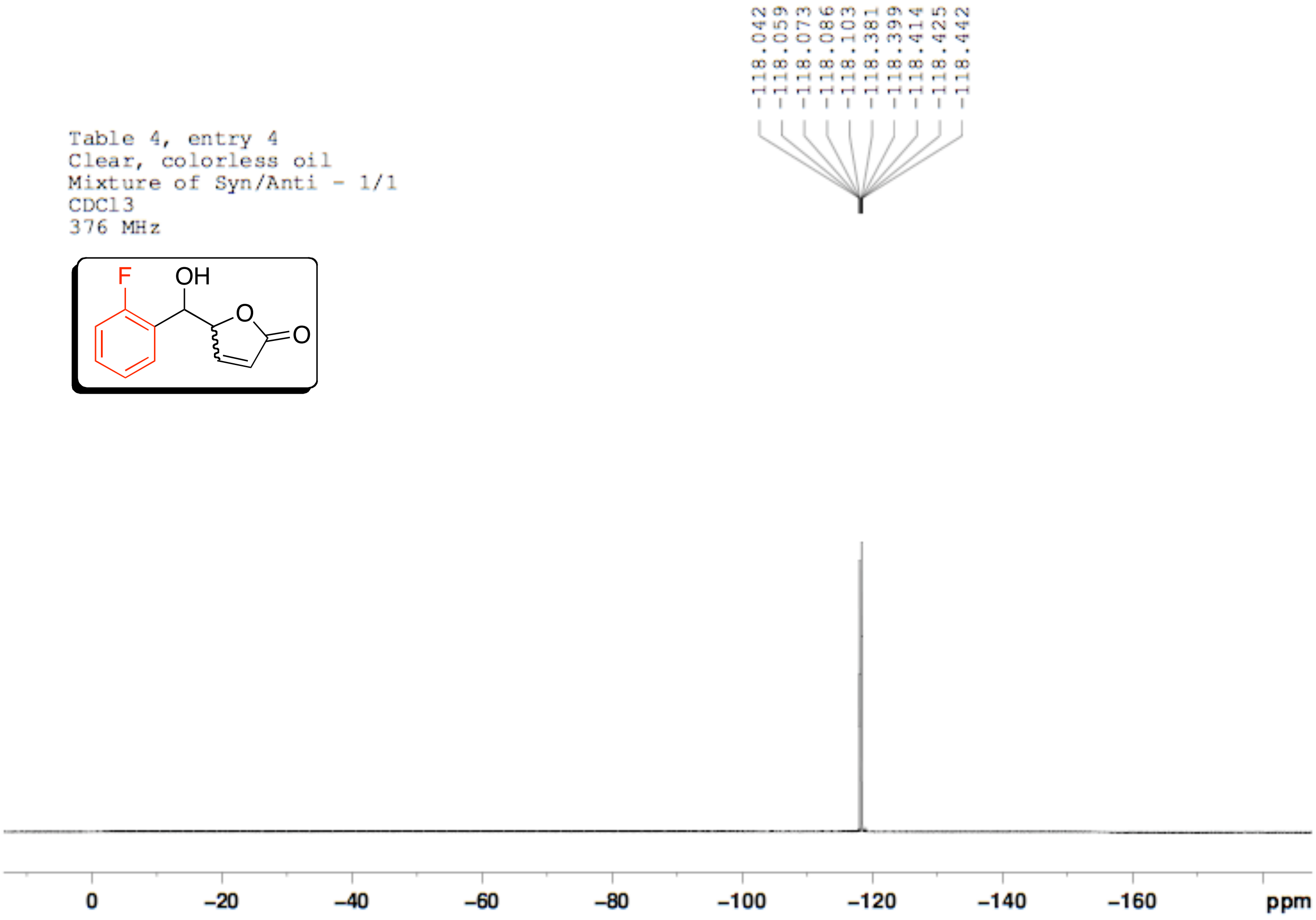


Table 4, entry 4
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
400 MHz


173.587
173.224
160.917
160.829
158.469
158.389
153.488
153.016
130.459
130.376
130.146
130.064
128.649
128.613
128.093
128.055
125.737
125.607
125.570
125.438
124.816
123.407
123.357
123.153
123.104
115.732
115.573
115.517
115.360
86.742
85.614
77.611
77.293
76.975
68.798
67.332
Table 4, entry 4
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
100 MHz
F
OH
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm


-118.042
-118.059
-118.073
-118.086
-118.103
-118.381
-118.399
-118.414
-118.425
-118.442
Table 4, entry 4
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
376 MHz
F
OH
O
O
0
-20
-40
-60
-80
-100
-120
-140
-160
ppm

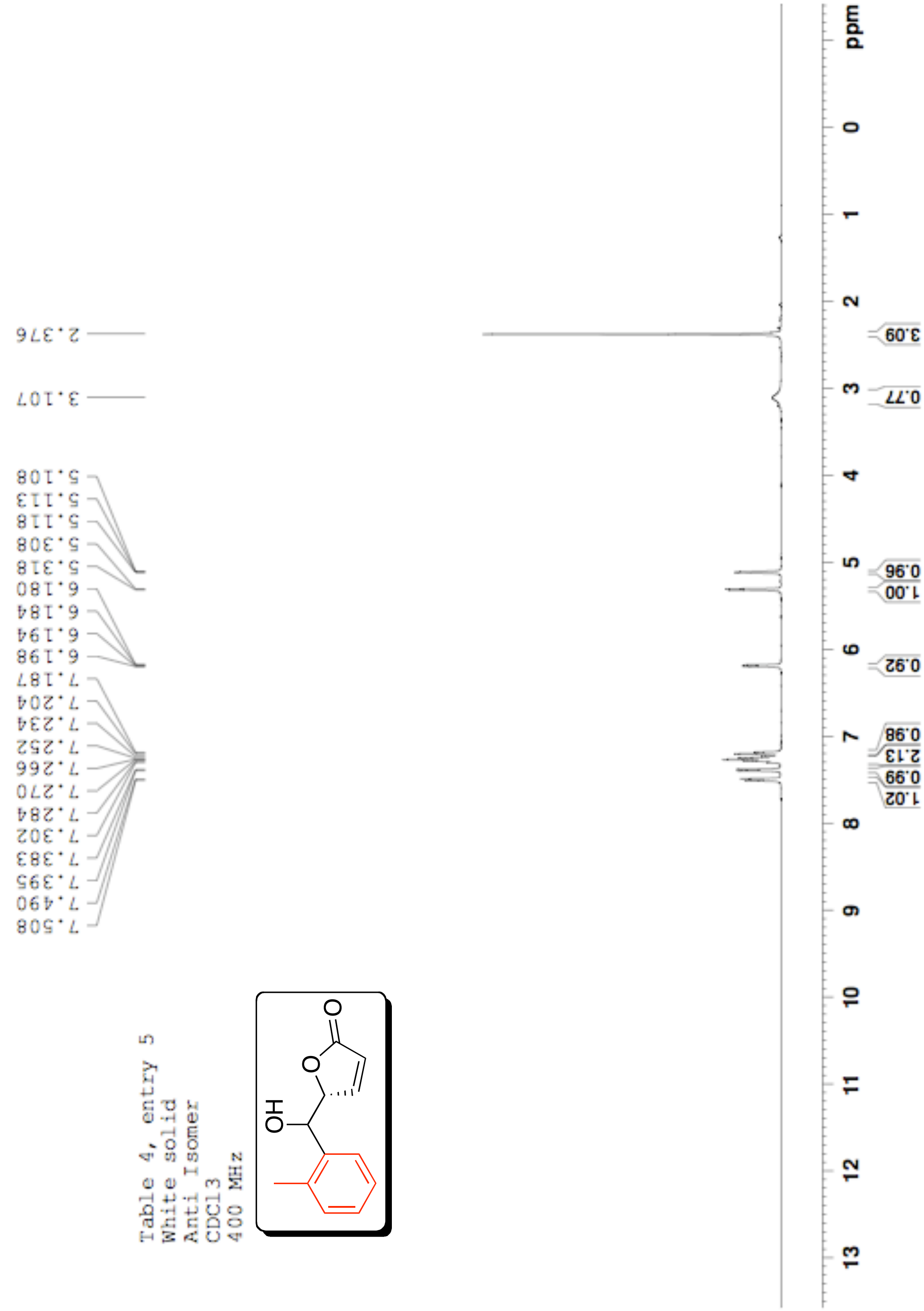
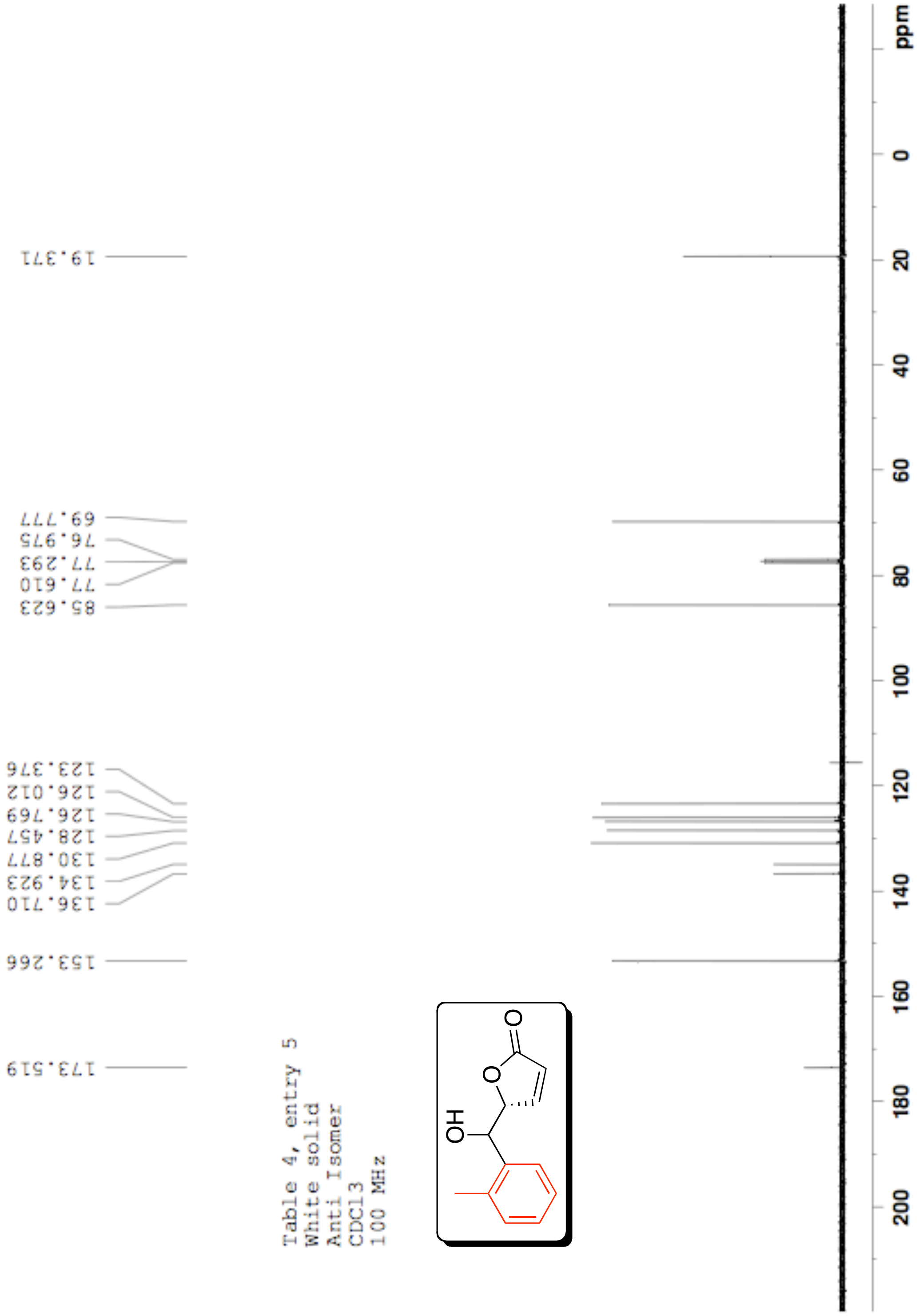


Table 4, entry 5
White solid
Anti Isomer
CDCl3
400 MHz
OH
O
O
2.376
3.107
5.108
5.113
5.118
5.308
5.318
6.180
6.184
6.194
6.198
7.187
7.204
7.234
7.252
7.266
7.270
7.284
7.302
7.383
7.395
7.490
7.508
3.09
0.77
0.96
1.00
0.92
0.98
2.13
0.99
1.02
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


19.371
69.777
76.975
77.293
77.610
85.623
123.376
126.012
126.769
128.457
130.877
134.923
136.710
153.266
173.519
Table 4, entry 5
White solid
Anti Isomer
CDCl3
100 MHz
OH
O
O
ppm
0
20
40
60
80
100
120
140
160
180
200

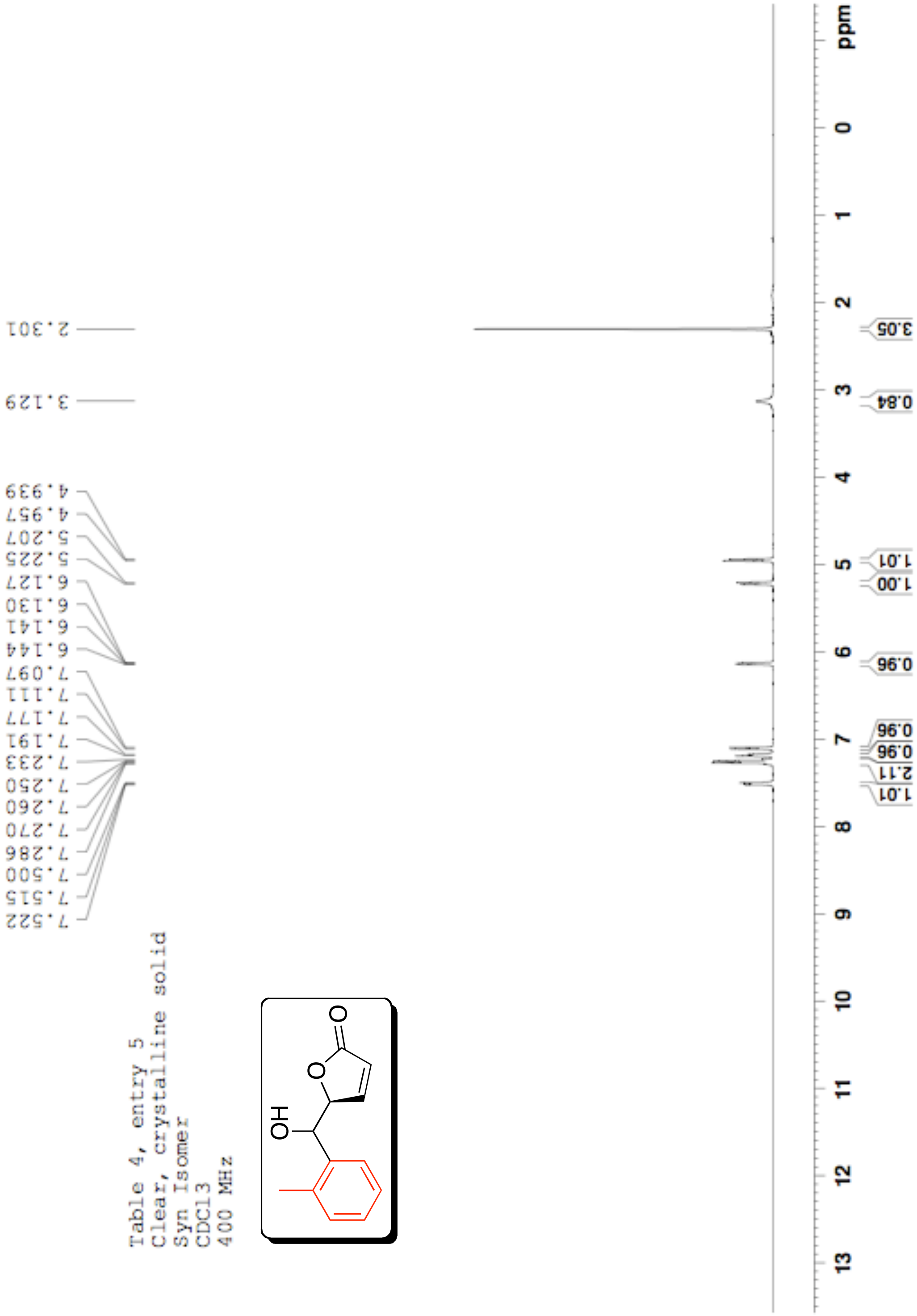


Table 4, entry 5
Clear, crystalline solid
Syn Isomer
CDCl3
400 MHz
2.301
3.129
4.939
4.957
5.207
5.225
6.127
6.130
6.141
6.144
7.097
7.111
7.177
7.191
7.233
7.250
7.260
7.270
7.286
7.500
7.515
7.522
OH
O
O
3.05
0.84
1.01
1.00
0.96
0.96
0.96
2.11
1.01
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

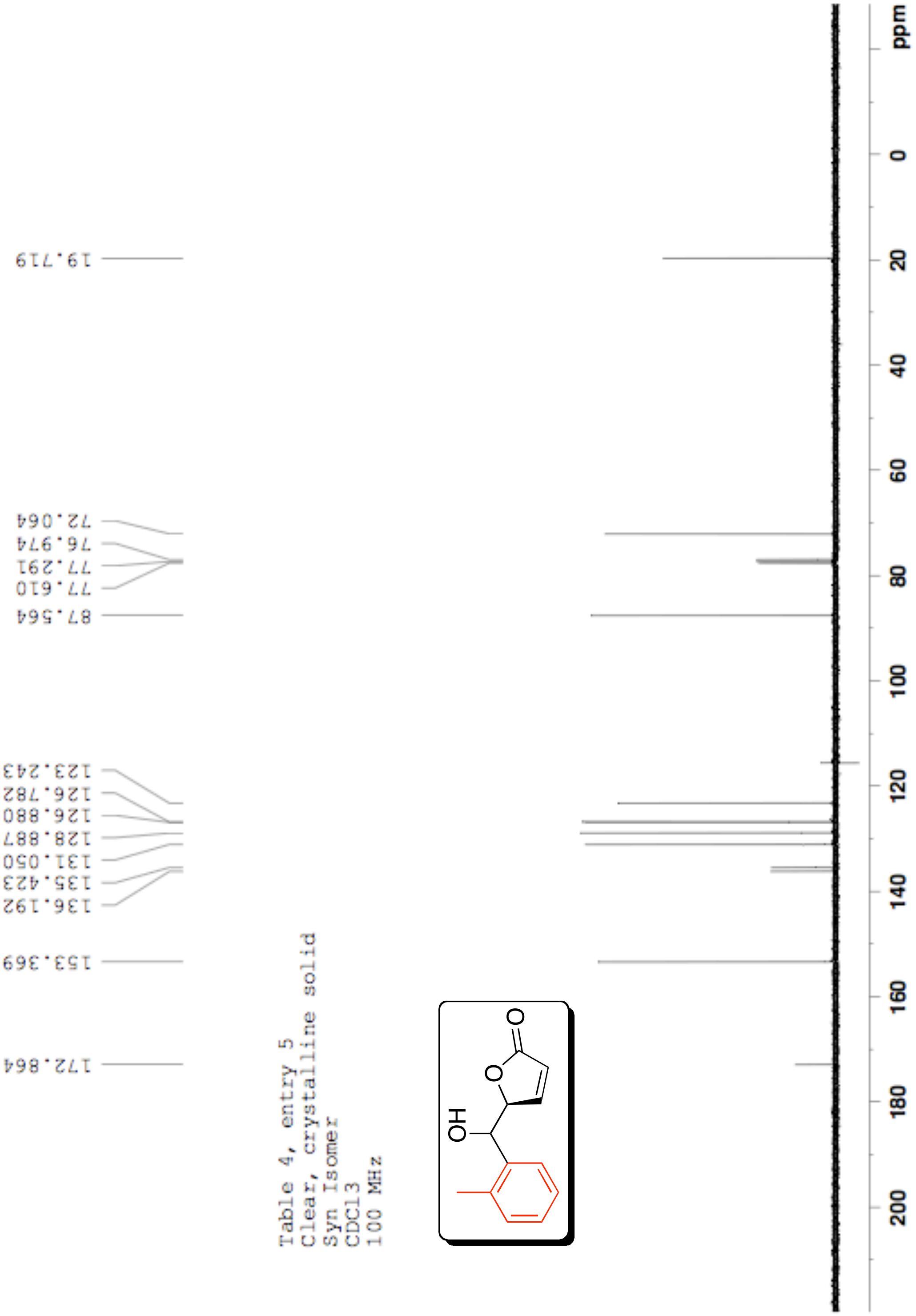
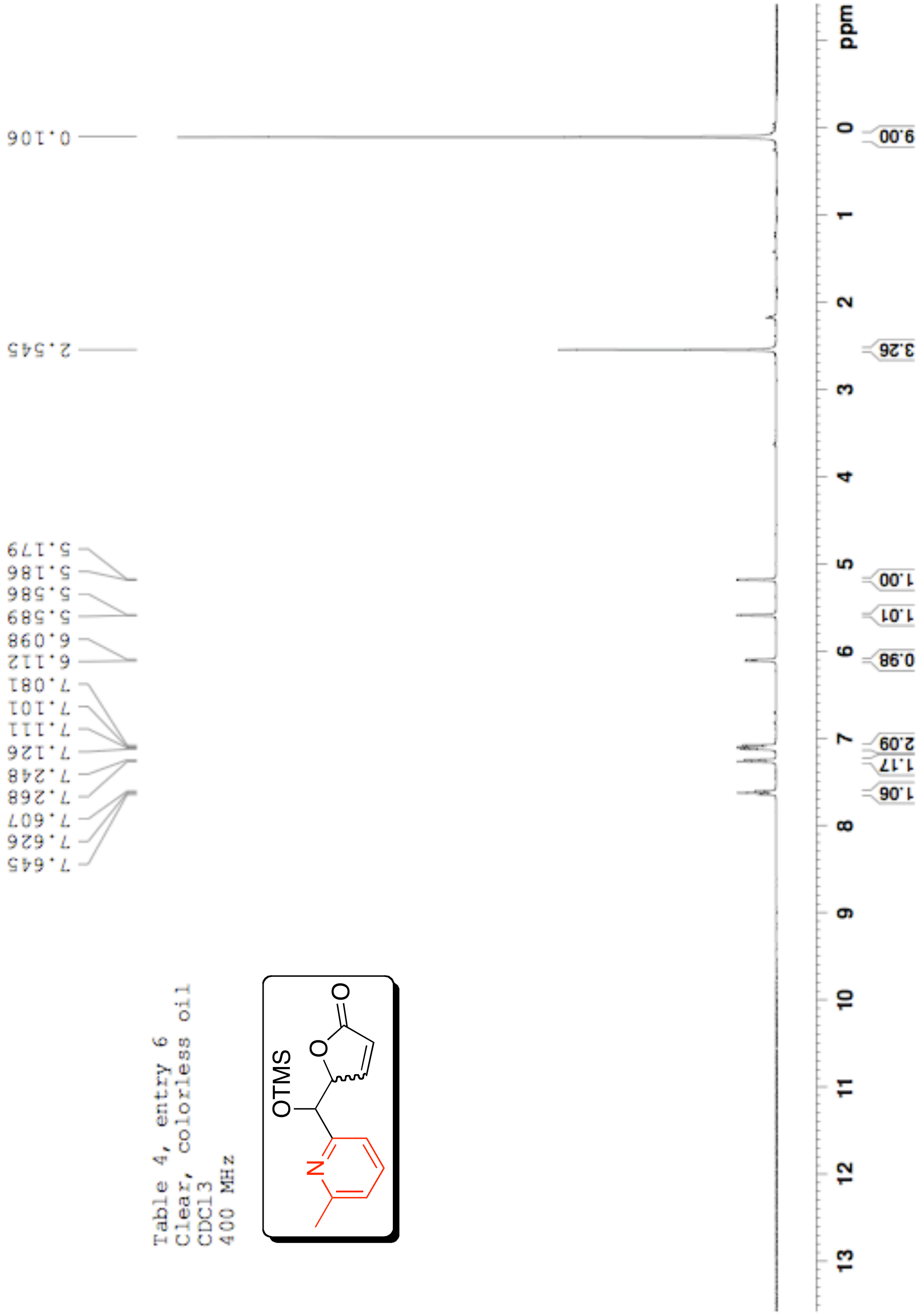


Table 4, entry 5
Clear, crystalline solid
Syn Isomer
CDCl3
100 MHz


0.106
2.545
5.179
5.186
5.586
5.589
6.098
6.112
7.081
7.101
7.111
7.126
7.248
7.268
7.607
7.626
7.645
Table 4, entry 6
Clear, colorless oil
CDCl3
400 MHz
OTMS
O
O
N
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
9.00
3.26
1.00
1.01
0.98
2.09
1.17
1.06

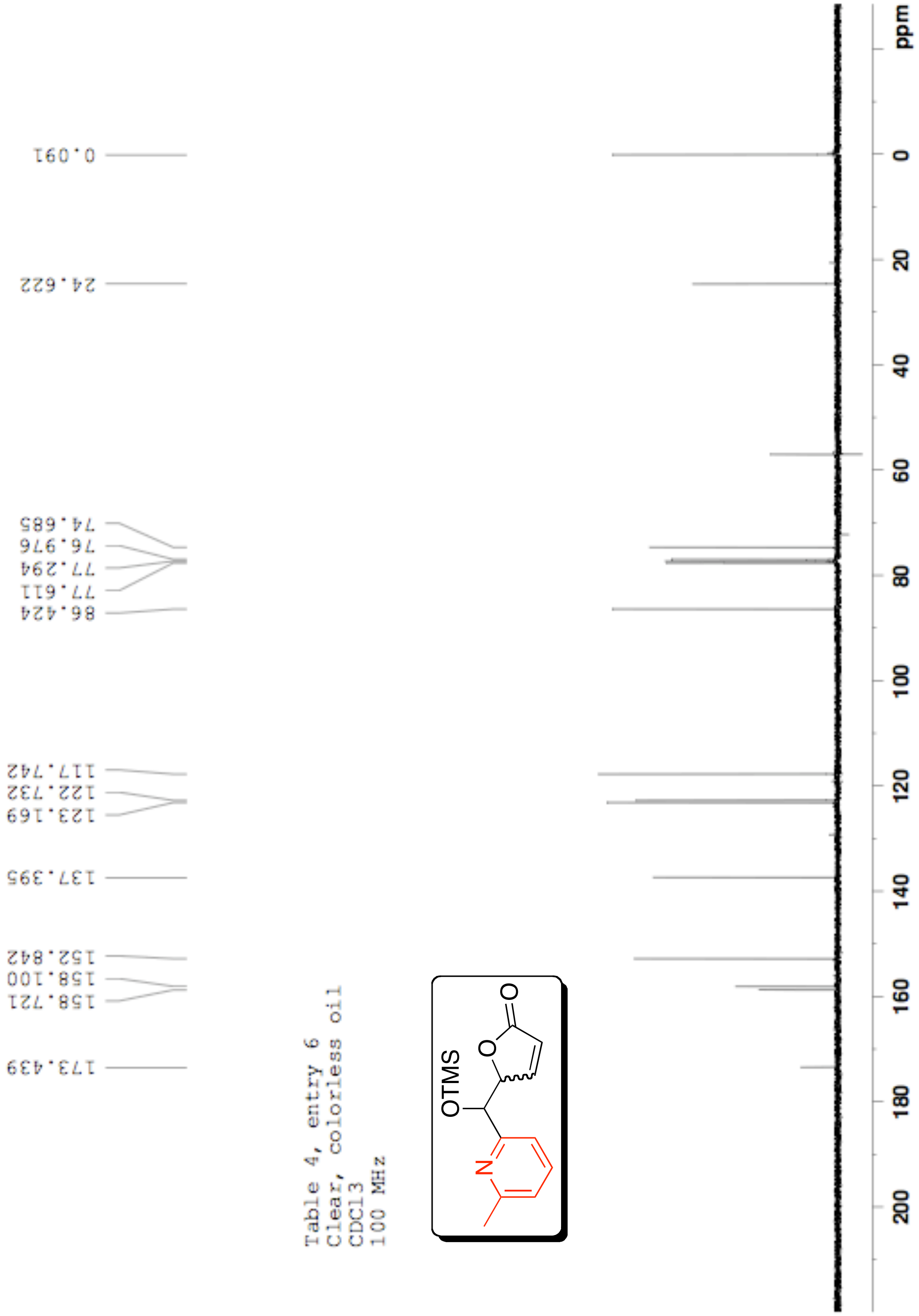
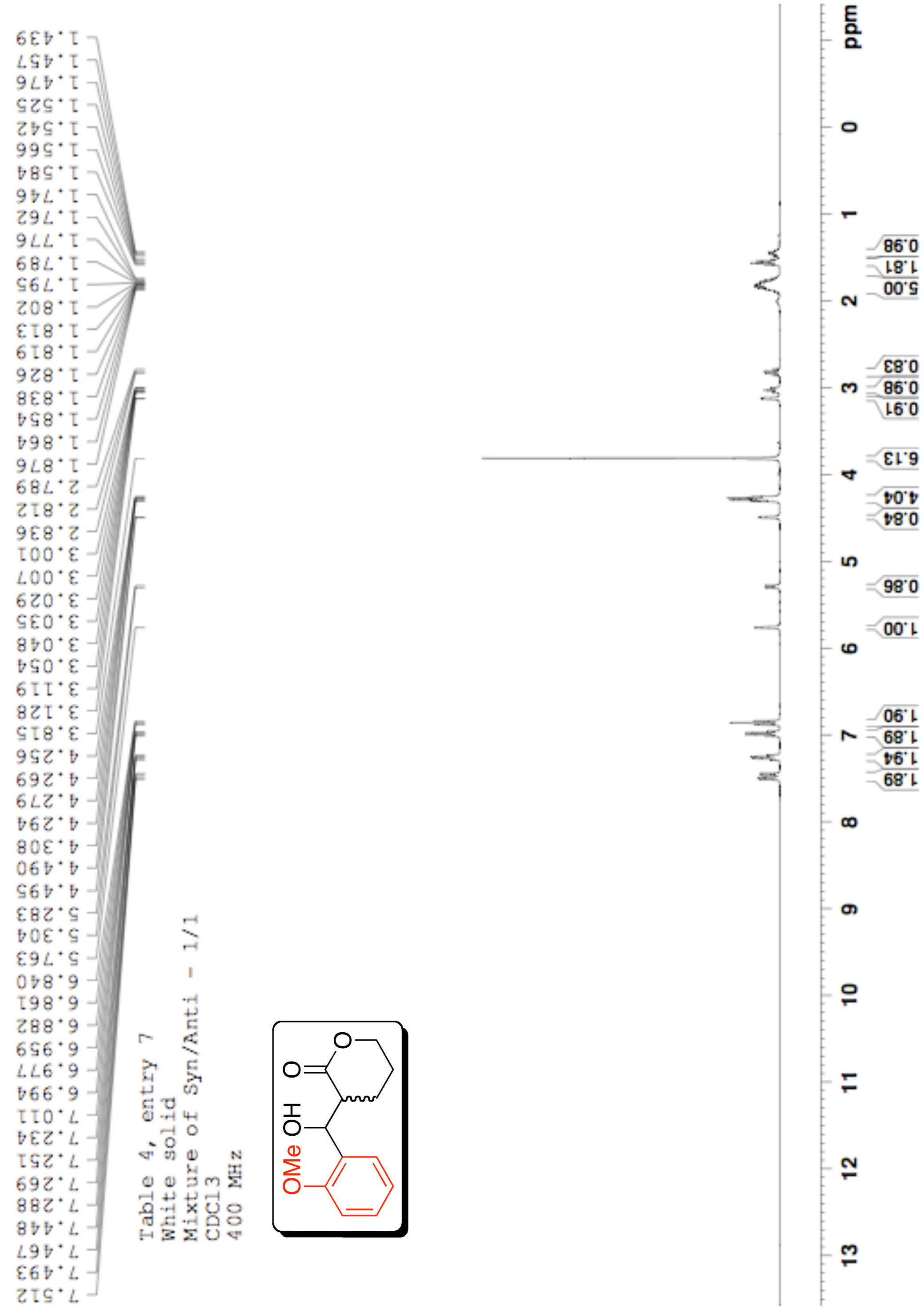
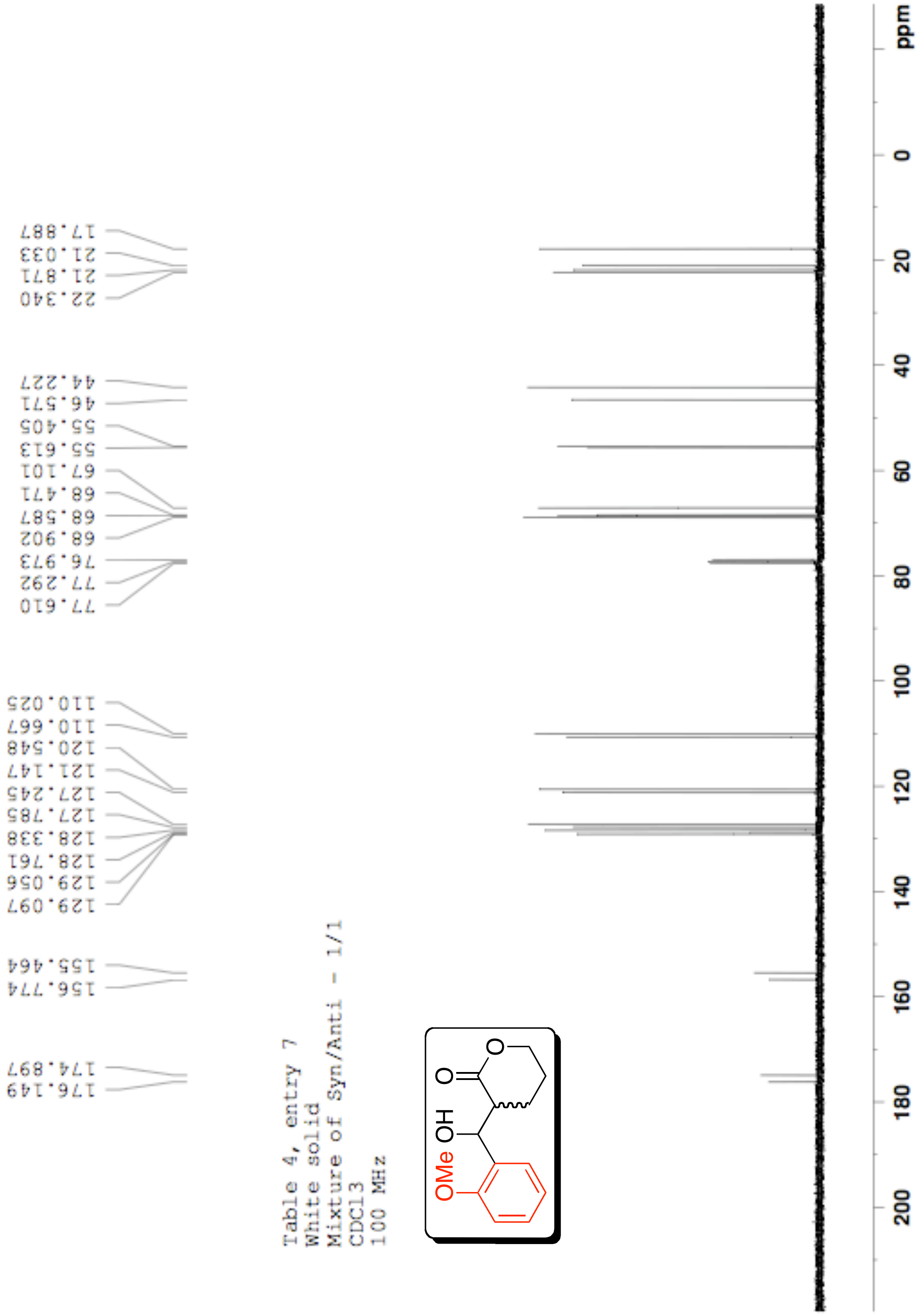


Table 4, entry 6
Clear, colorless oil
$CDCl_3$
100 MHz


1.439
1.457
1.476
1.525
1.542
1.566
1.584
1.746
1.762
1.776
1.789
1.795
1.802
1.813
1.819
1.826
1.838
1.854
1.864
1.876
2.789
2.812
2.836
3.001
3.007
3.029
3.035
3.048
3.054
3.119
3.128
3.815
4.256
4.269
4.279
4.294
4.308
4.490
4.495
5.283
5.304
5.763
6.840
6.861
6.882
6.959
6.977
6.994
7.011
7.234
7.251
7.269
7.288
7.448
7.467
7.493
7.512
Table 4, entry 7
White solid
Mixture of Syn/Anti - 1/1
CDCl3
400 MHz
OMe
OH
O
O
0.98
1.81
5.00
0.83
0.98
0.91
6.13
4.04
0.84
0.86
1.00
1.90
1.89
1.94
1.89
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


17.887
21.033
21.871
22.340
44.227
46.571
55.405
55.613
67.101
68.471
68.587
68.902
76.973
77.292
77.610
110.025
110.667
120.548
121.147
127.245
127.785
128.338
128.761
129.056
129.097
155.464
156.774
174.897
176.149
Table 4, entry 7
White solid
Mixture of Syn/Anti - 1/1
CDCl3
100 MHz
OMe
OH
O
O
ppm
0
20
40
60
80
100
120
140
160
180
200

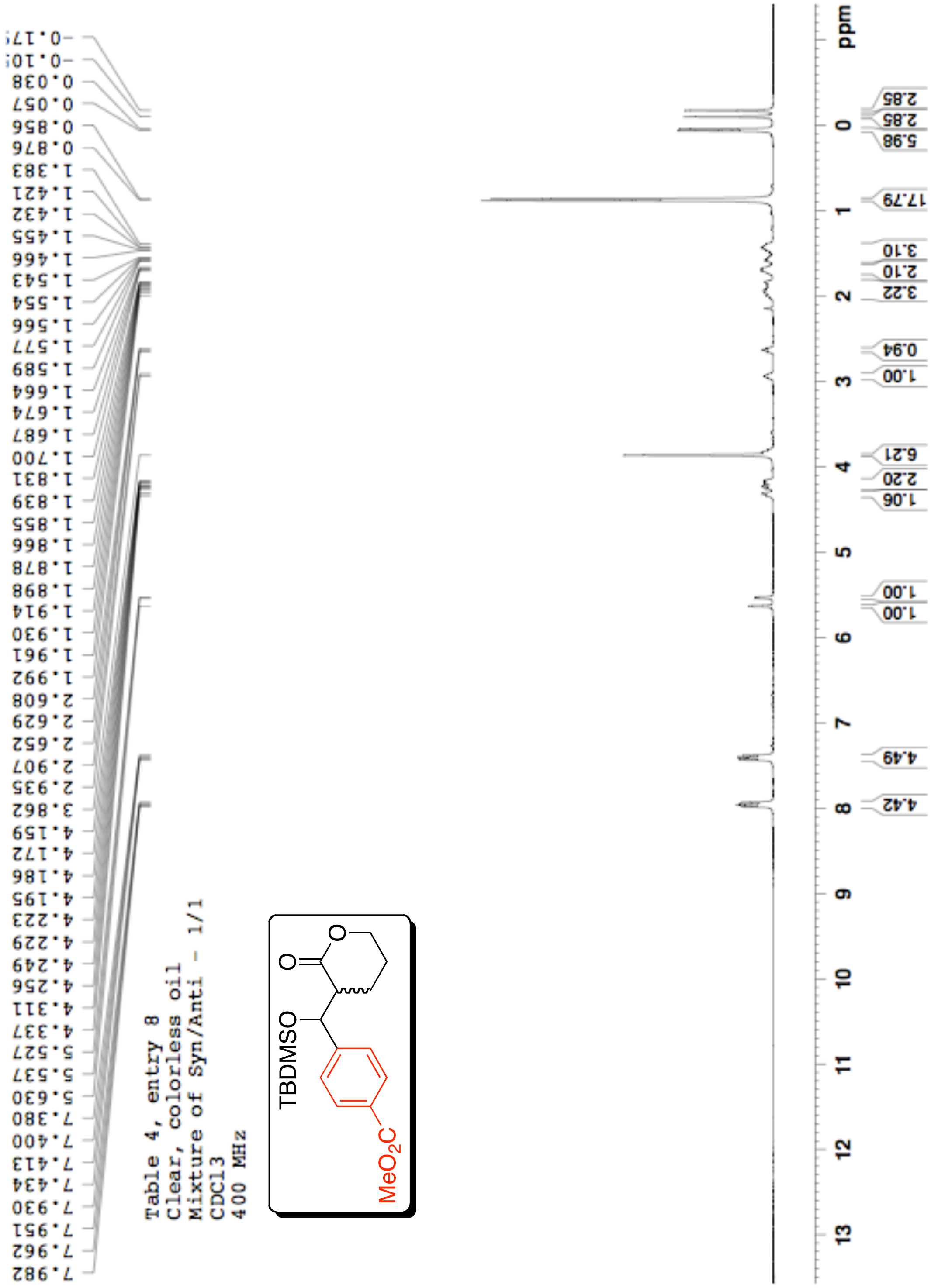
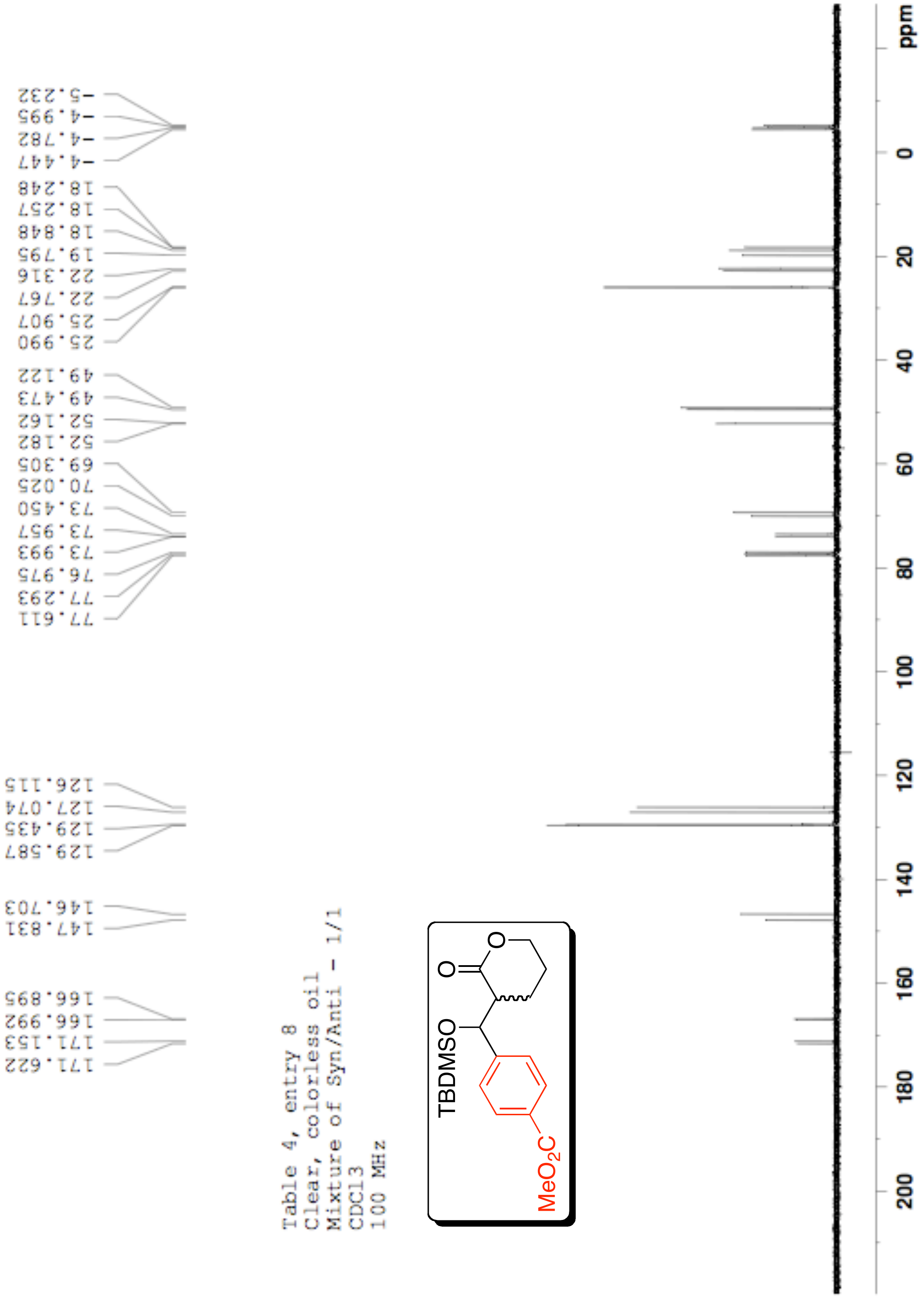


Table 4, entry 8
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
400 MHz


-5.232
-4.995
-4.782
-4.447
18.248
18.257
18.848
19.795
22.316
22.767
25.907
25.990
49.122
49.473
52.162
52.182
69.305
70.025
73.450
73.957
73.993
76.975
77.293
77.611
126.115
127.074
129.435
129.587
146.703
147.831
166.895
166.992
171.153
171.622
Table 4, entry 8
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
100 MHz
TBDMSO
O
O
MeO2C
ppm
0
20
40
60
80
100
120
140
160
180
200

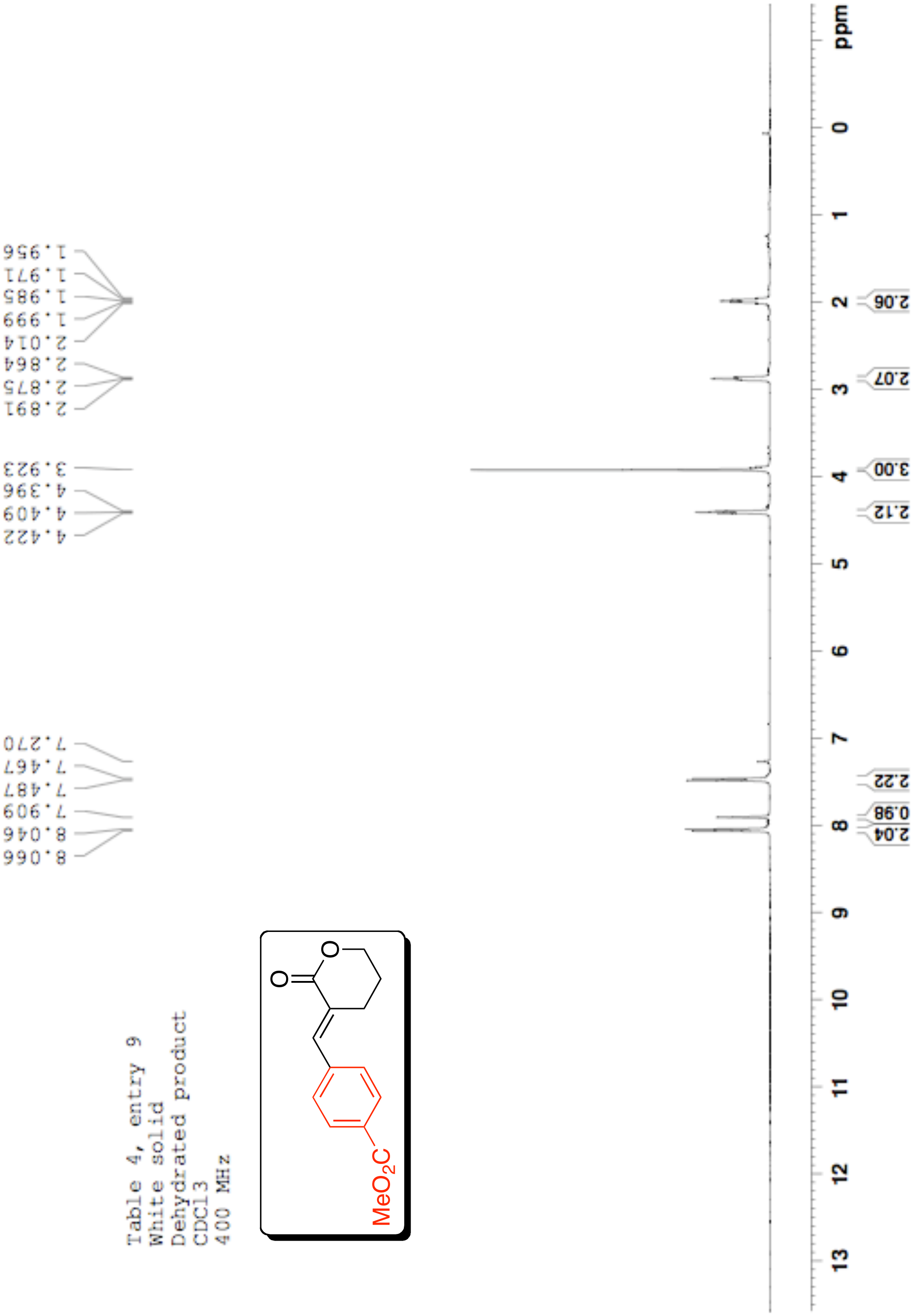
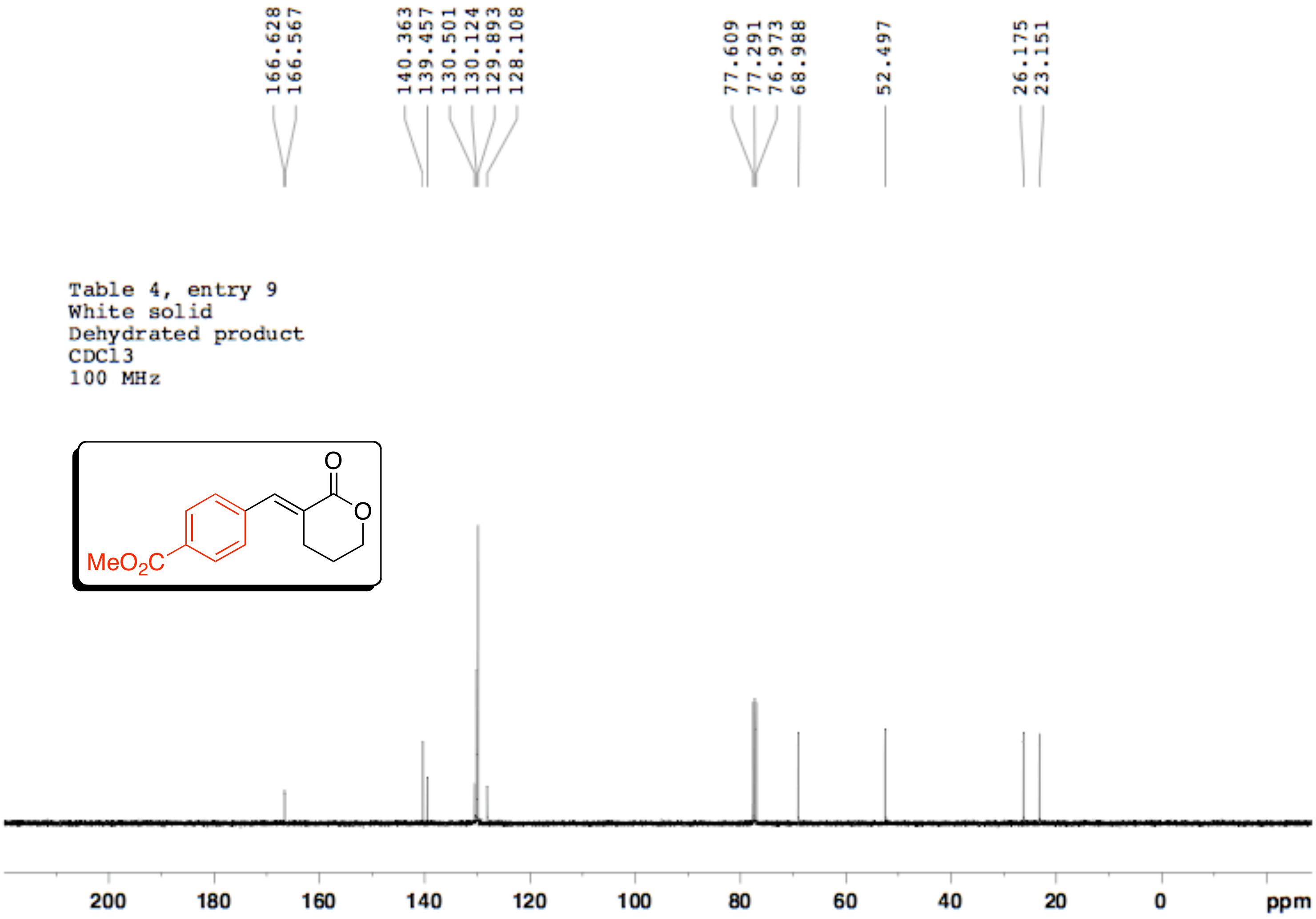
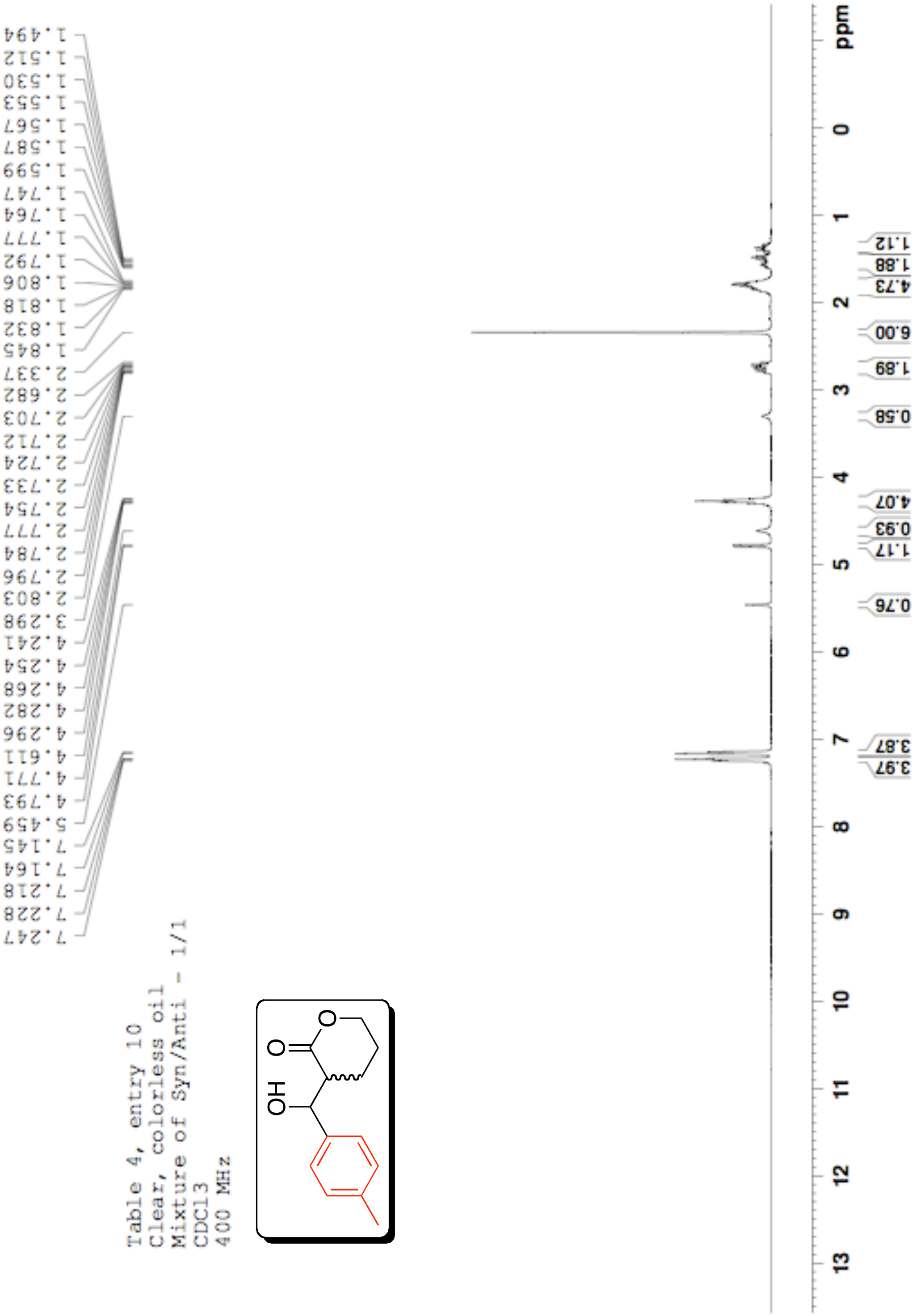


Table 4, entry 9
White solid
Dehydrated product
CDCl3
400 MHz
MeO$_2$C
O
O
1.956
1.971
1.985
1.999
2.014
2.864
2.875
2.891
3.923
4.396
4.409
4.422
7.270
7.467
7.487
7.909
8.046
8.066
2.06
2.07
3.00
2.12
2.22
0.98
2.04
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


166.628
166.567
140.363
139.457
130.501
130.124
129.893
128.108
77.609
77.291
76.973
68.988
52.497
26.175
23.151
Table 4, entry 9
White solid
Dehydrated product
CDCl3
100 MHz
MeO2C
O
O
200
180
160
140
120
100
80
60
40
20
0
ppm


1.494
1.512
1.530
1.553
1.567
1.587
1.599
1.747
1.764
1.777
1.792
1.806
1.818
1.832
1.845
2.337
2.682
2.703
2.712
2.724
2.733
2.754
2.777
2.784
2.796
2.803
3.298
4.241
4.254
4.268
4.282
4.296
4.611
4.771
4.793
5.459
7.145
7.164
7.218
7.228
7.247
Table 4, entry 10
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
400 MHz
OH
O
O
1.12
1.88
4.73
6.00
1.89
0.58
4.07
0.93
1.17
0.76
3.87
3.97
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

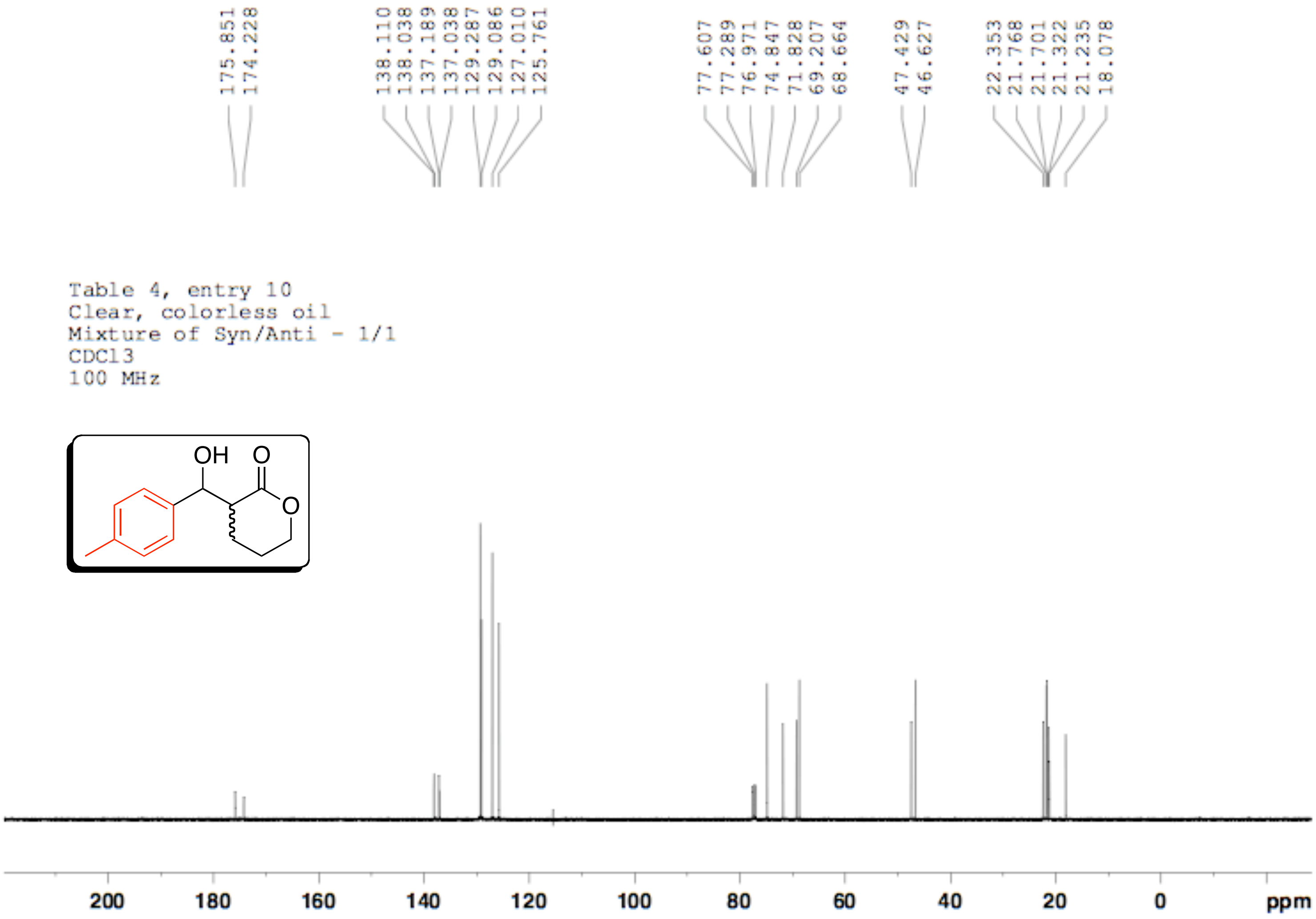


Table 4, entry 10
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
100 MHz

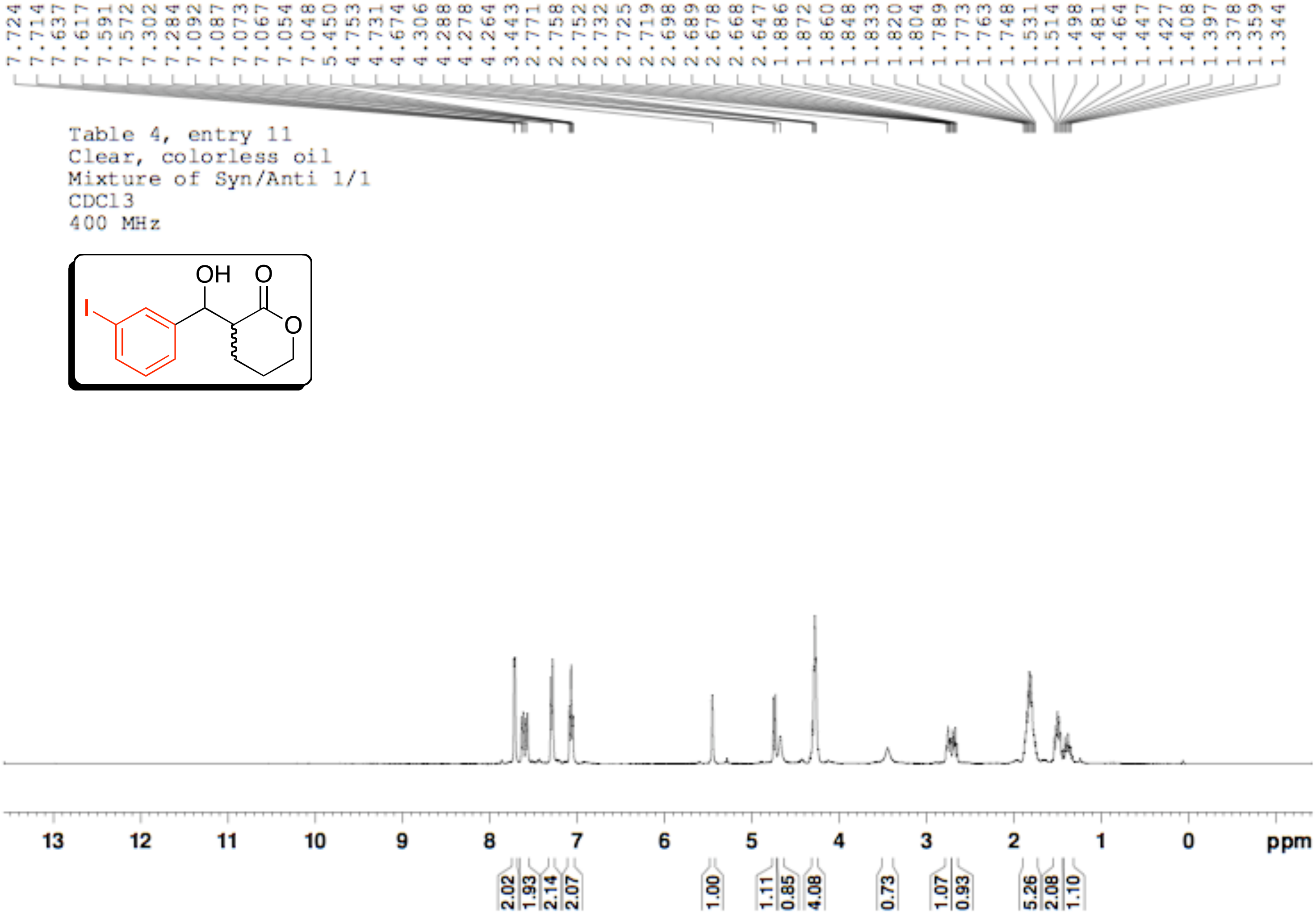
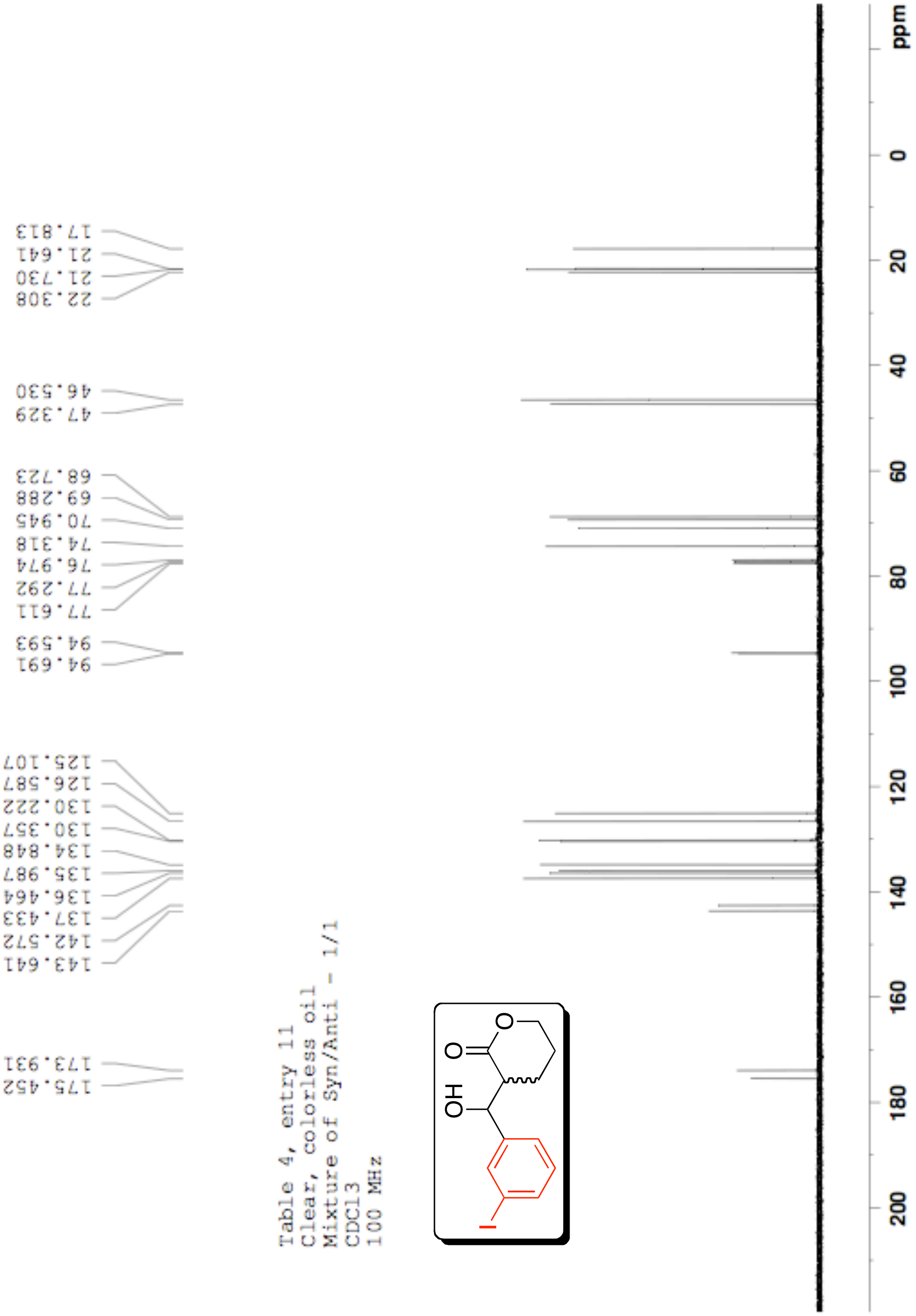


Table 4, entry 11
Clear, colorless oil
Mixture of Syn/Anti 1/1
CDCl3
400 MHz


17.813
21.641
21.730
22.308
46.530
47.329
68.723
69.288
70.945
74.318
76.974
77.292
77.611
94.593
94.691
125.107
126.587
130.222
130.357
134.848
135.987
136.464
137.433
142.572
143.641
173.931
175.452
Table 4, entry 11
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
100 MHz
OH
O
O
I
ppm
0
20
40
60
80
100
120
140
160
180
200

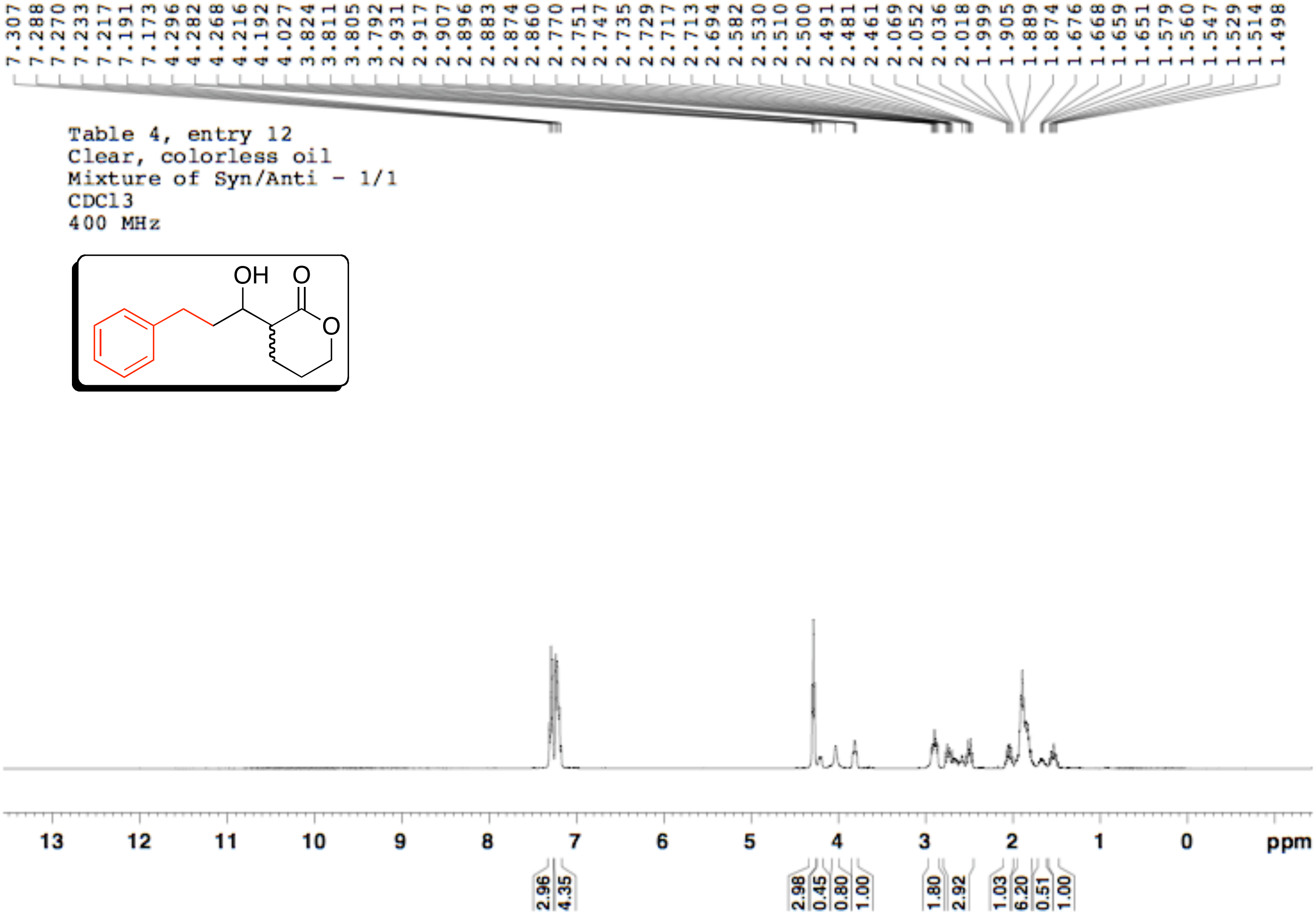


Table 4, entry 12
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
400 MHz

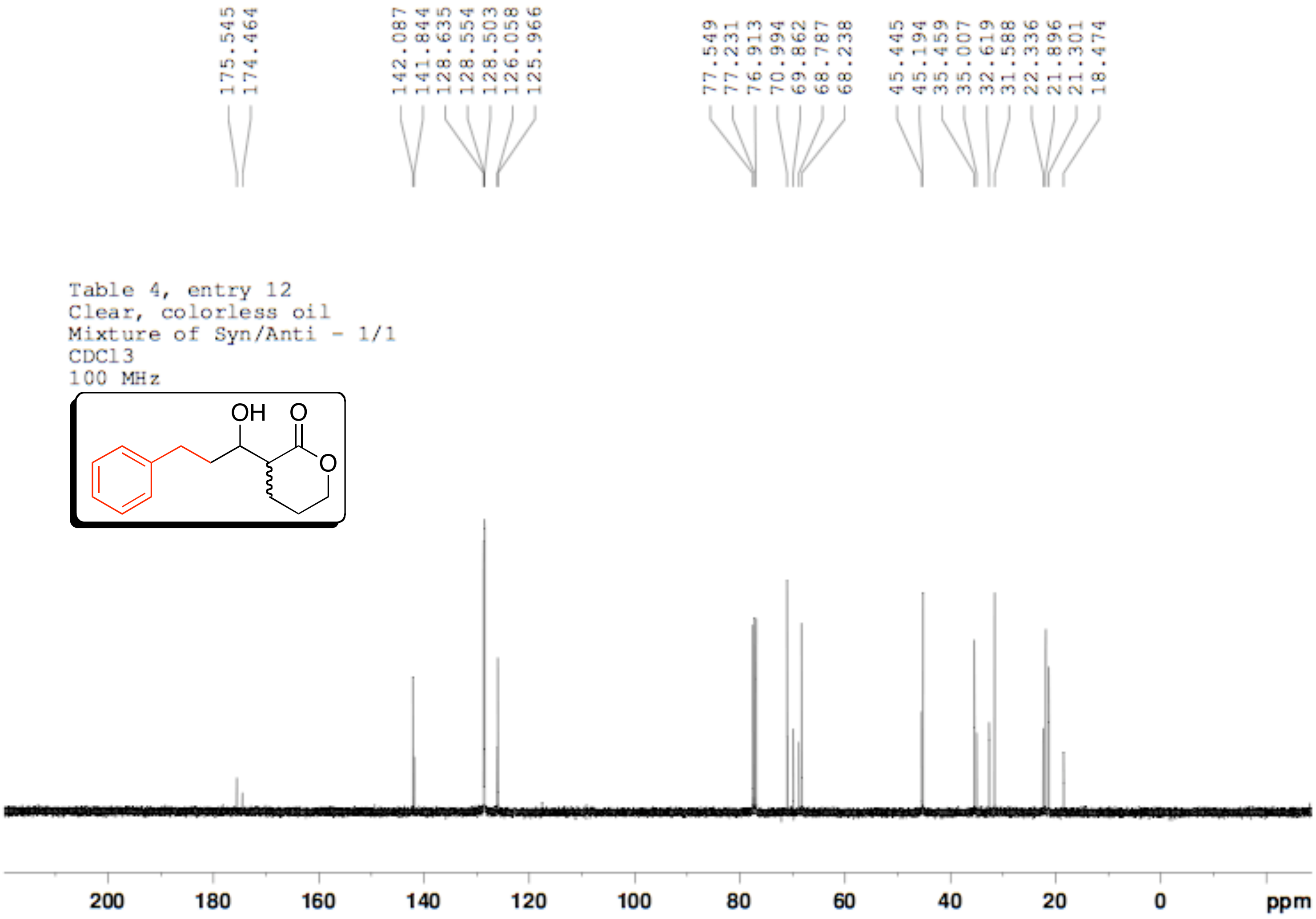


Table 4, entry 12
Clear, colorless oil
Mixture of Syn/Anti - 1/1
CDCl3
100 MHz

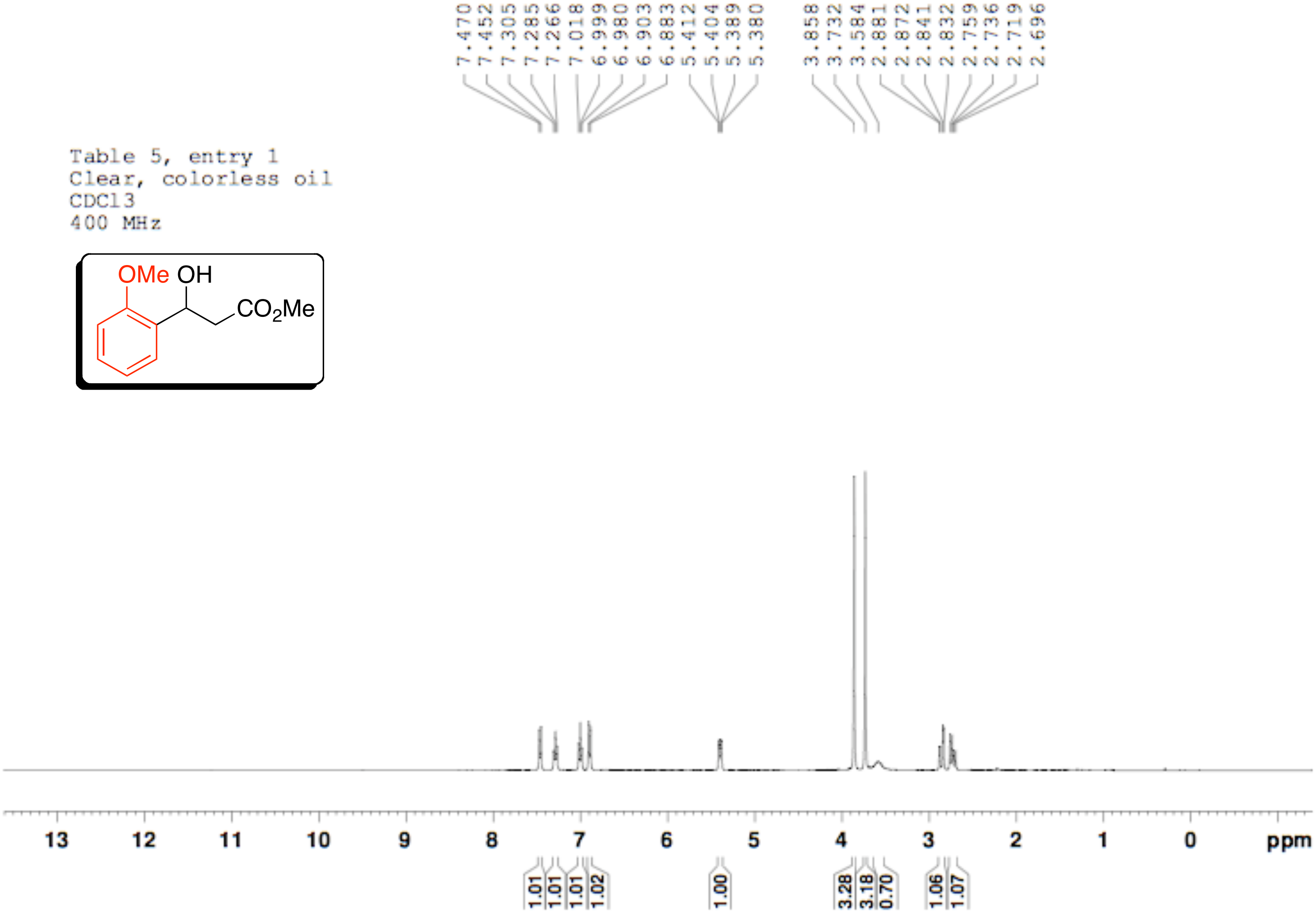
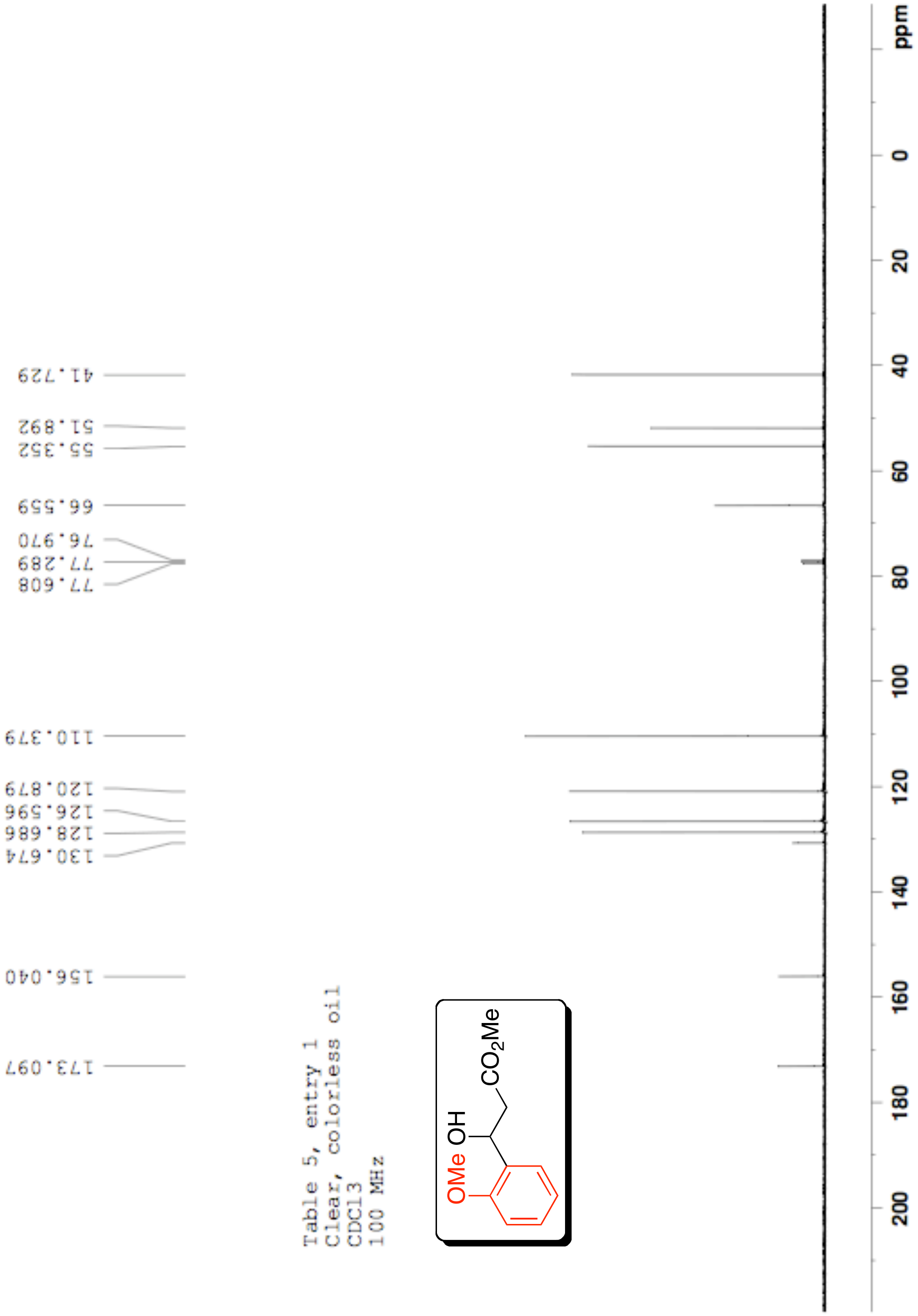


Table 5, entry 1
Clear, colorless oil
CDCl3
400 MHz


173.097
156.040
130.674
128.686
126.596
120.879
110.379
77.608
77.289
76.970
66.559
55.352
51.892
41.729
Table 5, entry 1
Clear, colorless oil
CDCl3
100 MHz
OMe
OH
CO2Me
200
180
160
140
120
100
80
60
40
20
0
ppm

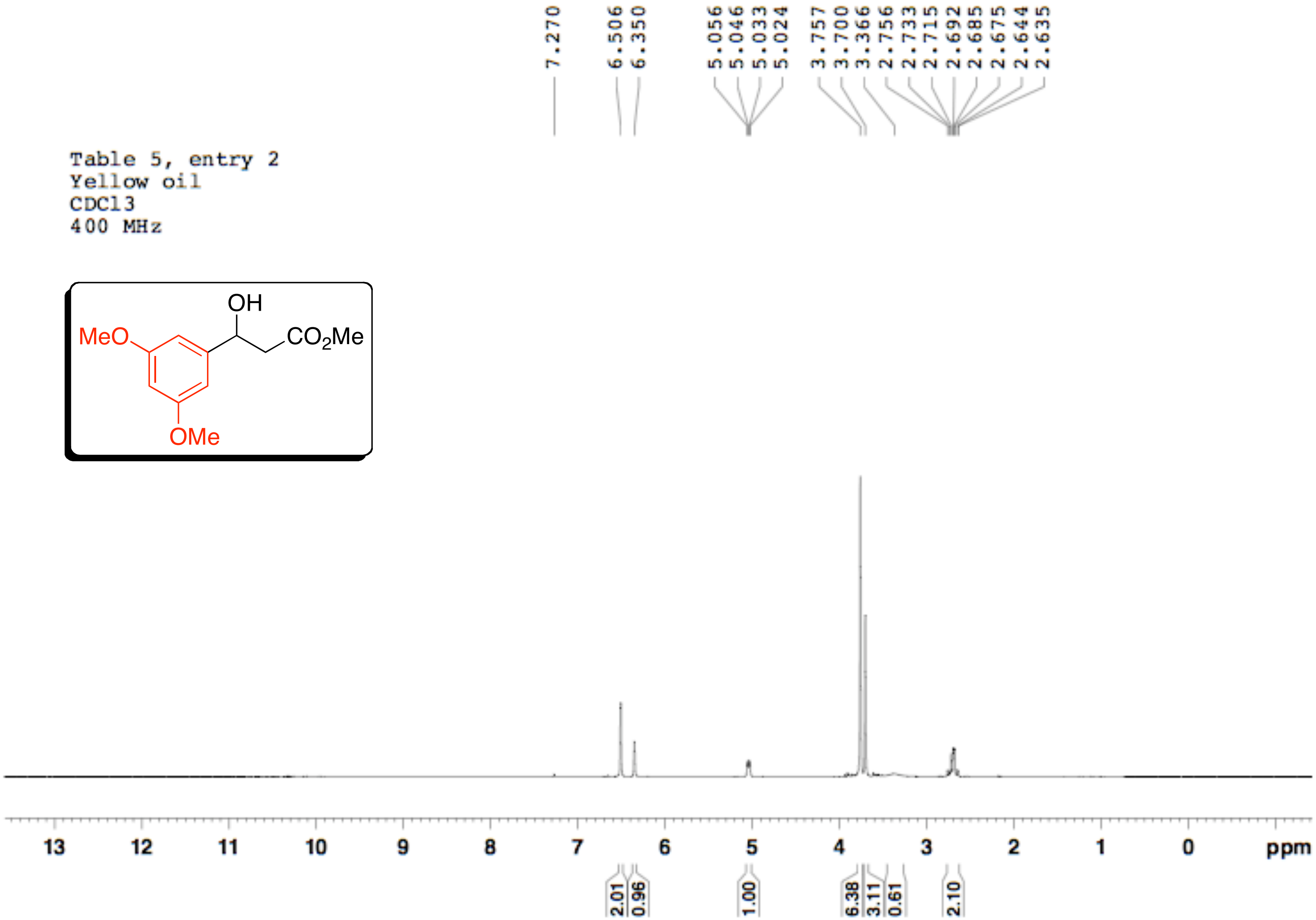


Table 5, entry 2
Yellow oil
CDCl3
400 MHz

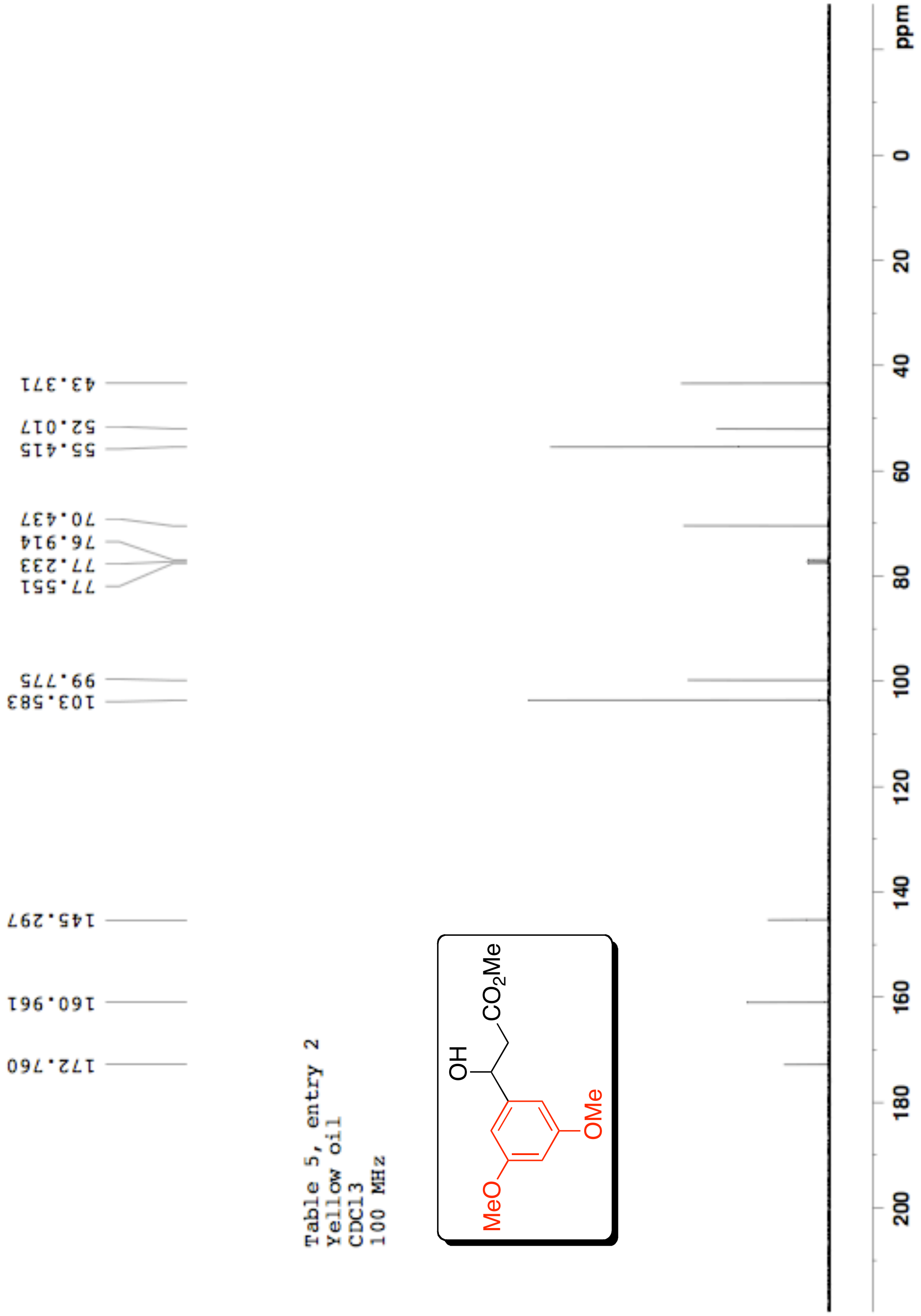
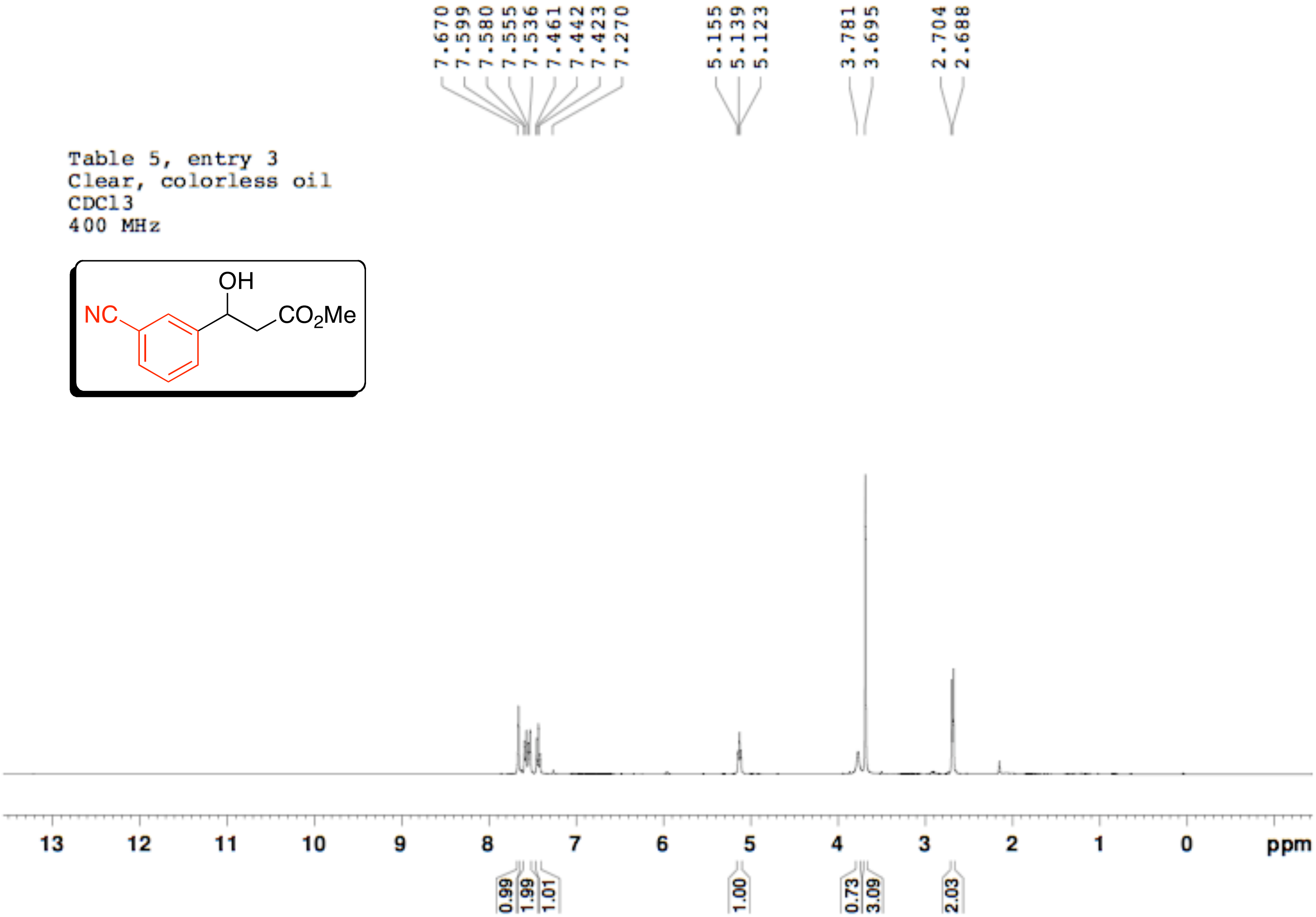
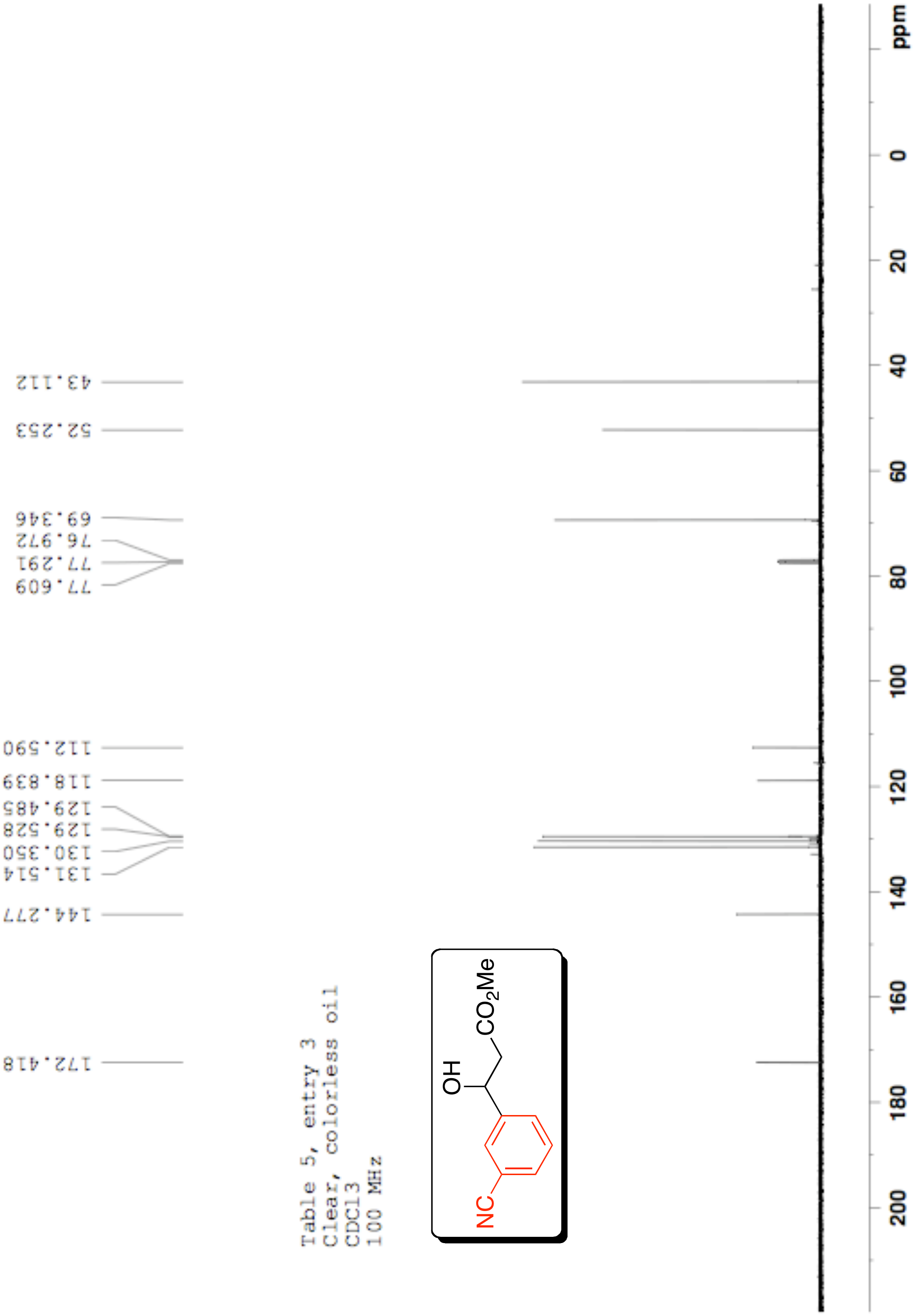

43.371
52.017
55.415
70.437
76.914
77.233
77.551
99.775
103.583
145.297
160.961
172.760
Table 5, entry 2
Yellow oil
CDCl3
100 MHz
OH
CO2Me
MeO
OMe
ppm
0
20
40
60
80
100
120
140
160
180
200

Table 5, entry 3
Clear, colorless oil
CDCl3
400 MHz




43.112
52.253
69.346
76.972
77.291
77.609
112.590
118.839
129.485
129.528
130.350
131.514
144.277
172.418
Table 5, entry 3
Clear, colorless oil
CDCl3
100 MHz
OH
CO$_2$Me
NC
ppm
0
20
40
60
80
100
120
140
160
180
200

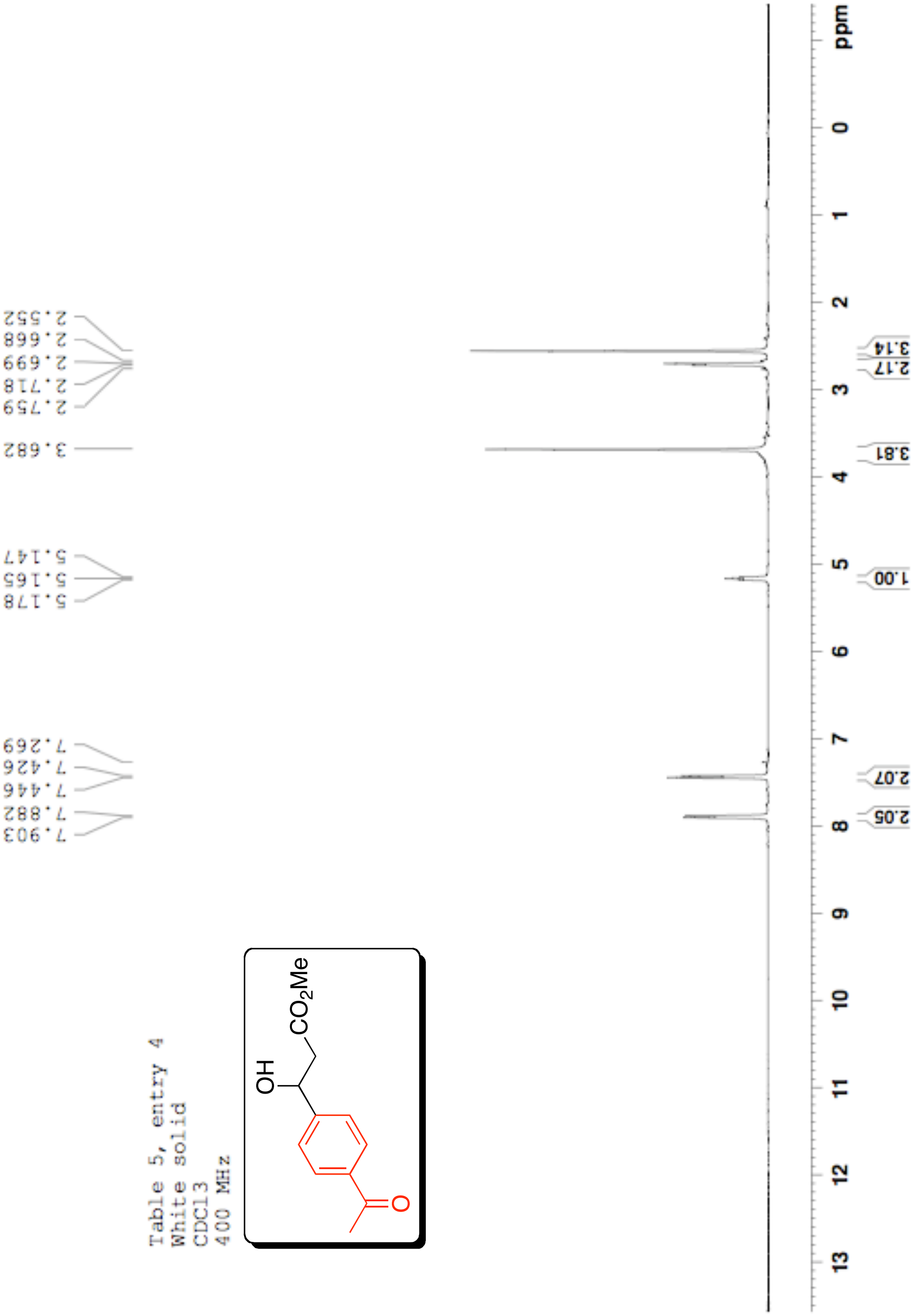
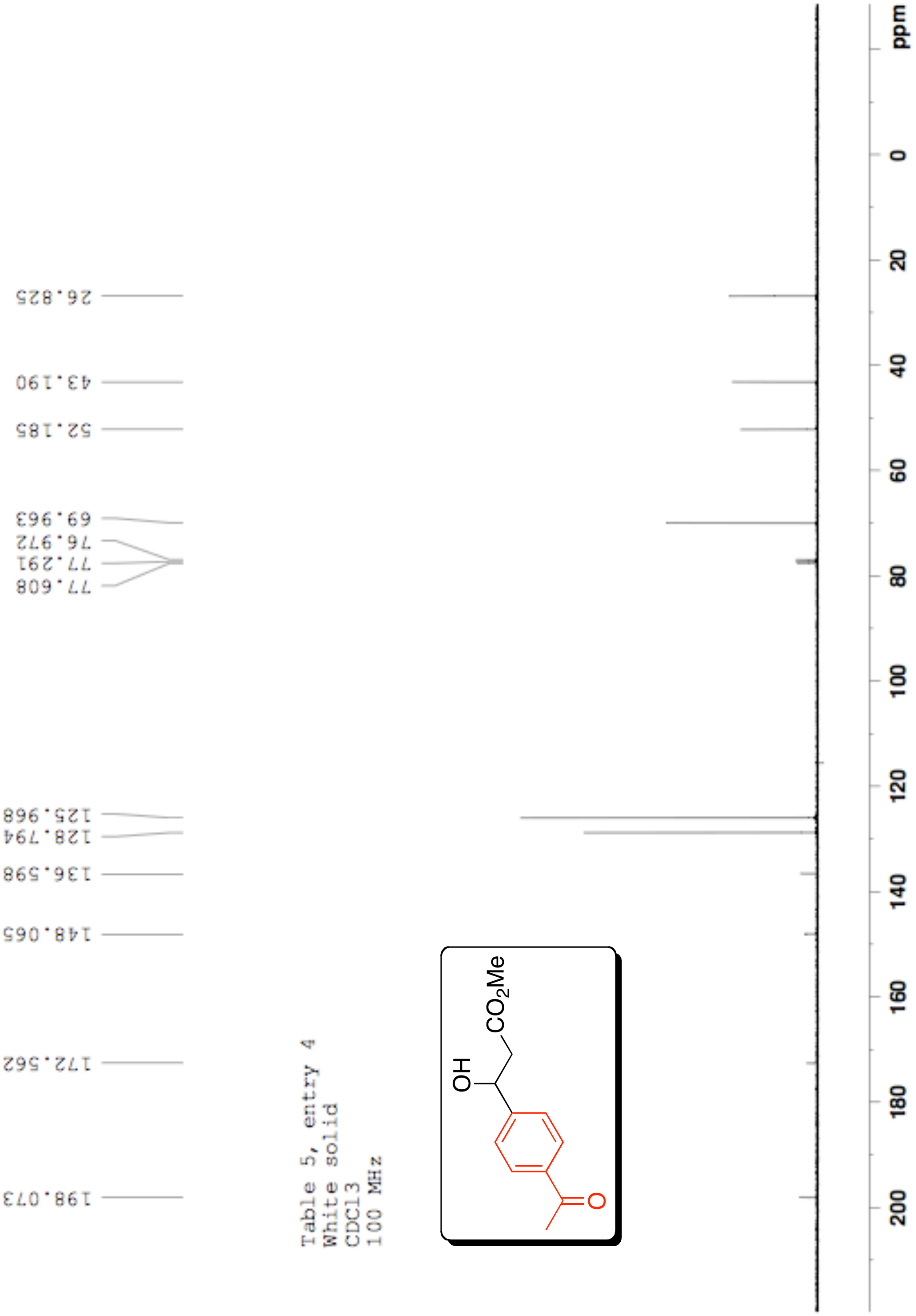


Table 5, entry 4
White solid
CDCl3
400 MHz
OH
CO2Me
O
2.552
2.668
2.699
2.718
2.759
3.682
5.147
5.165
5.178
7.269
7.426
7.446
7.882
7.903
3.14
2.17
3.81
1.00
2.07
2.05
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


26.825
43.190
52.185
69.963
76.972
77.291
77.608
125.968
128.794
136.598
148.065
172.562
198.073
Table 5, entry 4
White solid
CDCl3
100 MHz
OH
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200

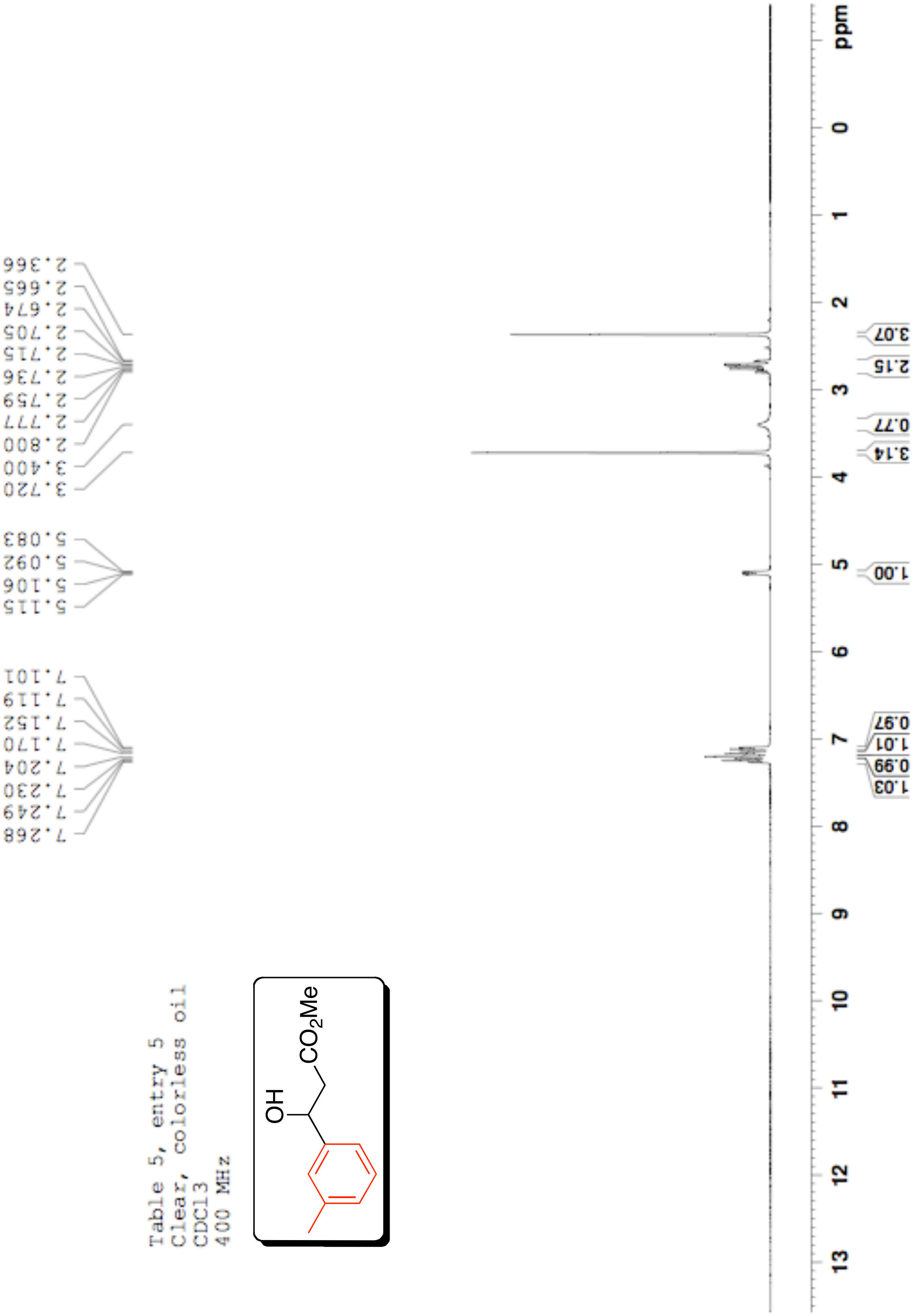


Table 5, entry 5
Clear, colorless oil
CDCl3
400 MHz
OH
CO2Me
2.366
2.665
2.674
2.705
2.715
2.736
2.759
2.777
2.800
3.400
3.720
5.083
5.092
5.106
5.115
7.101
7.119
7.152
7.170
7.204
7.230
7.249
7.268
3.07
2.15
0.77
3.14
1.00
0.97
1.01
0.99
1.03
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

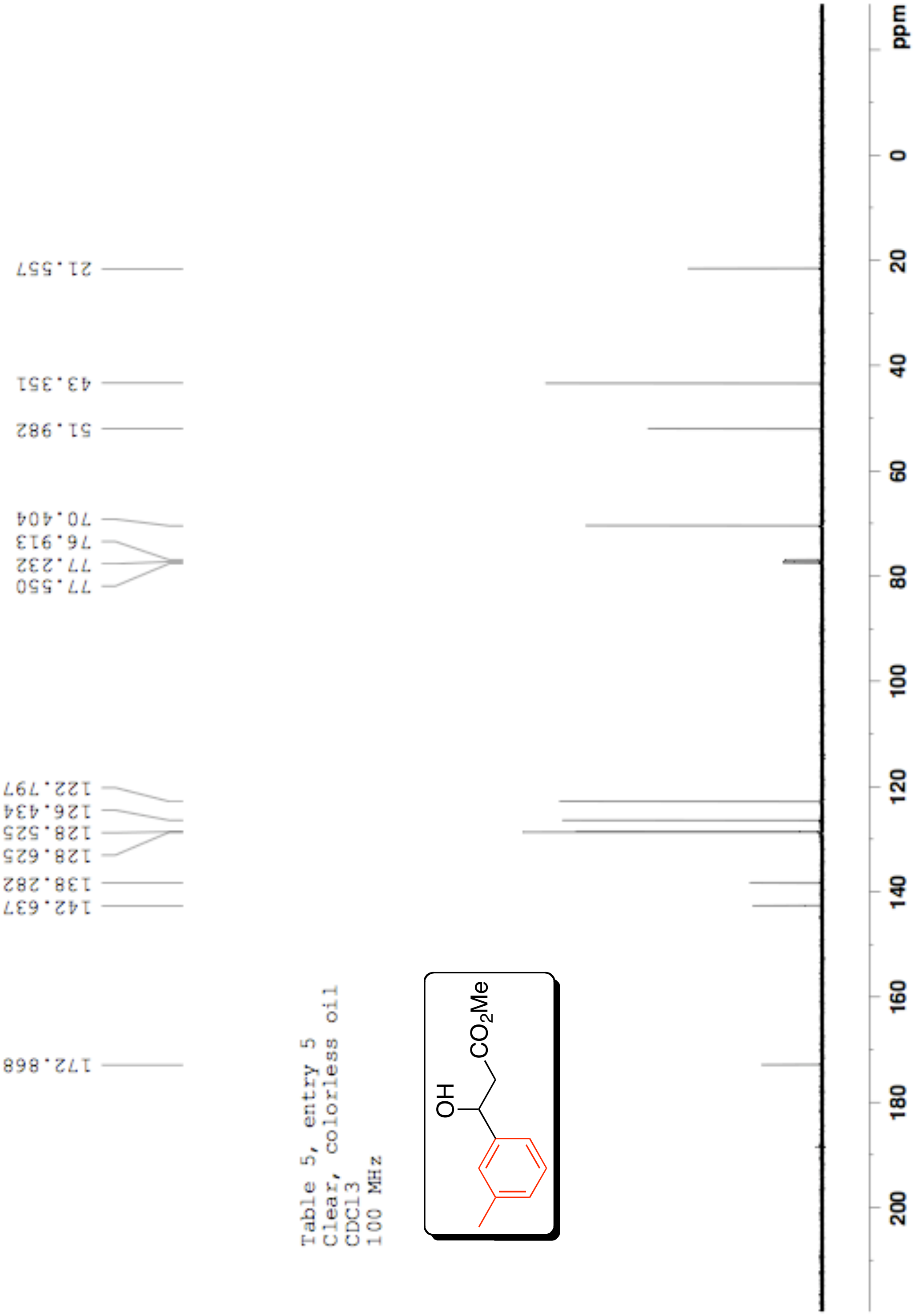


Table 5, entry 5
Clear, colorless oil
CDCl3
100 MHz

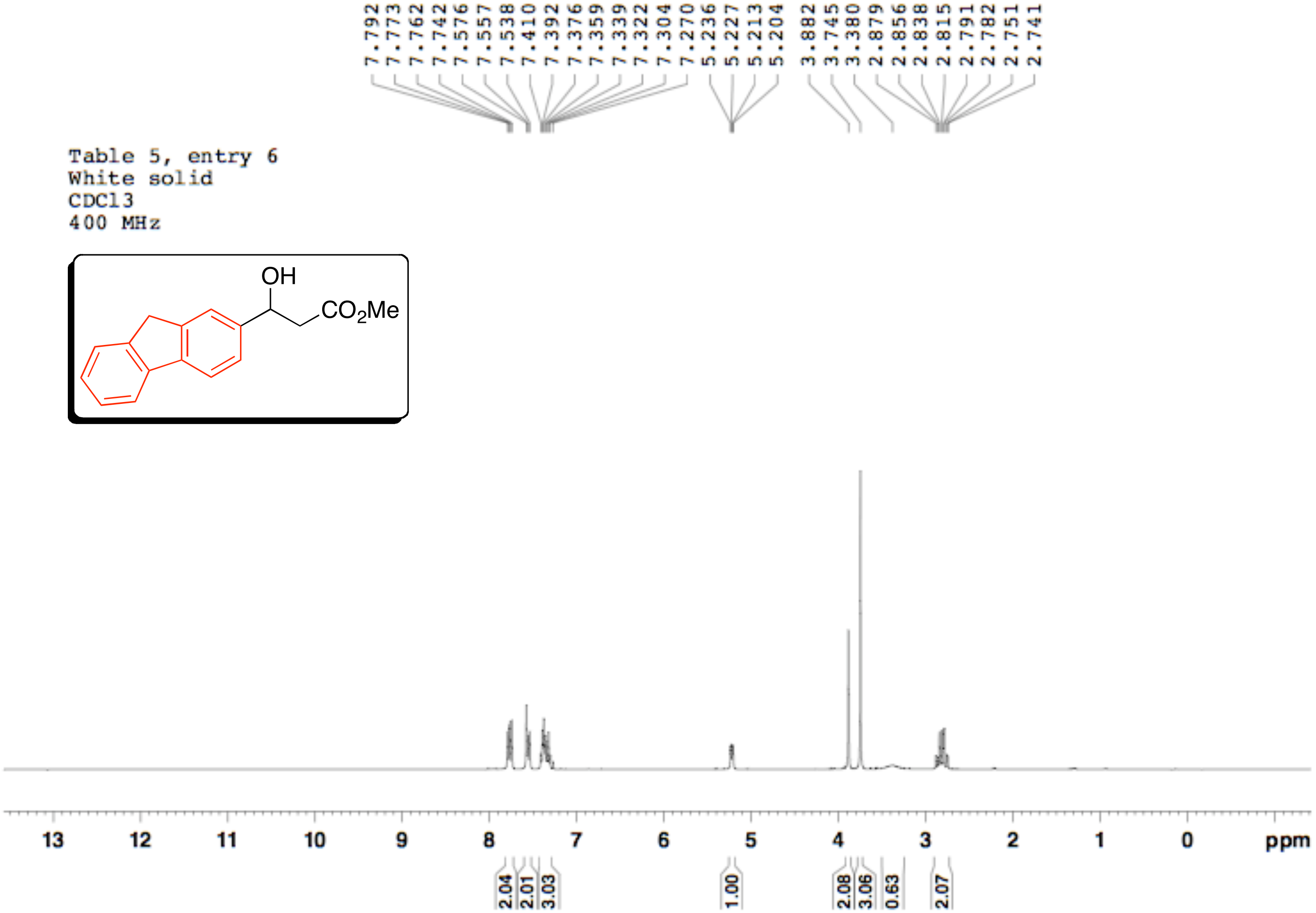


Table 5, entry 6
White solid
CDCl3
400 MHz

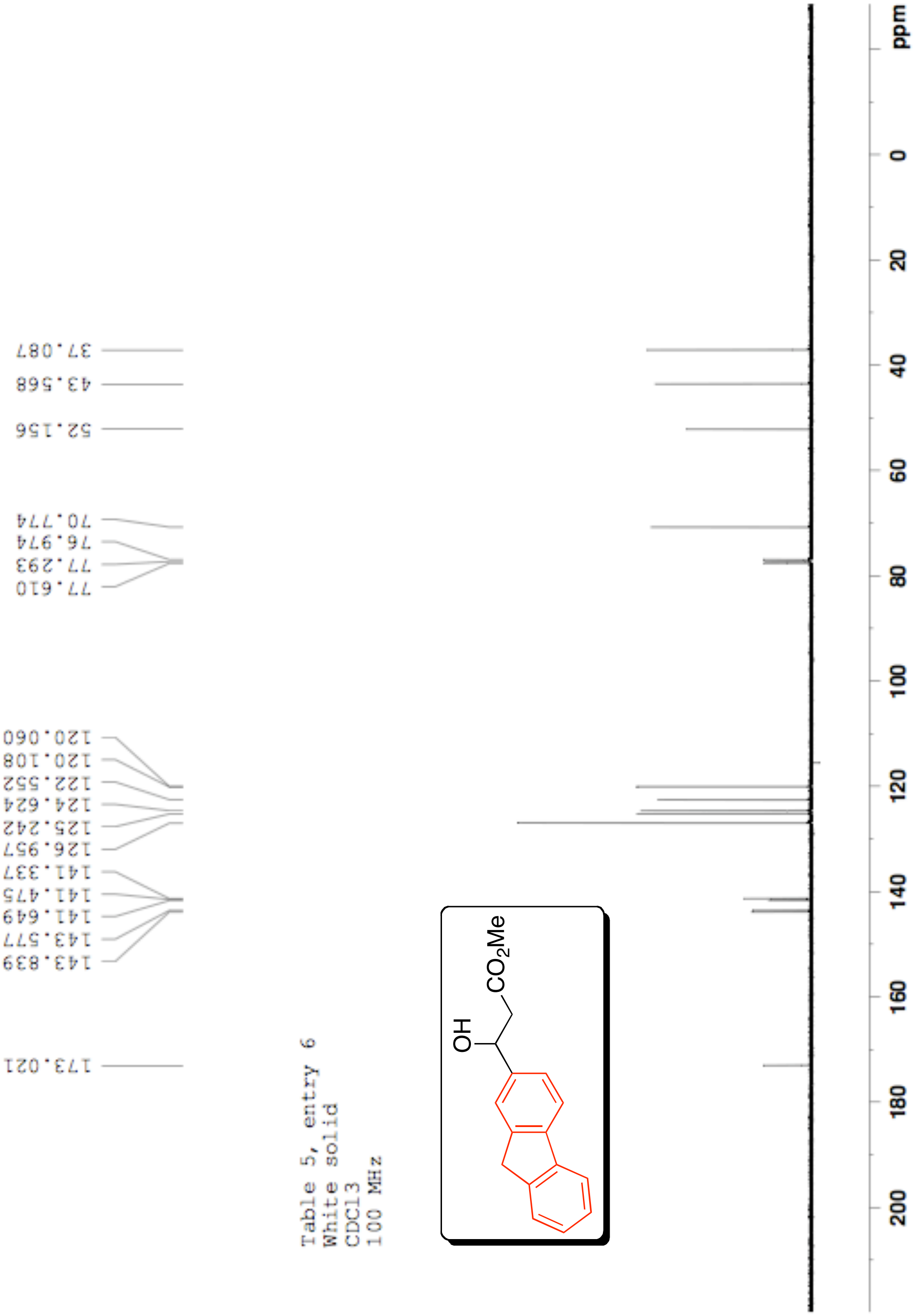
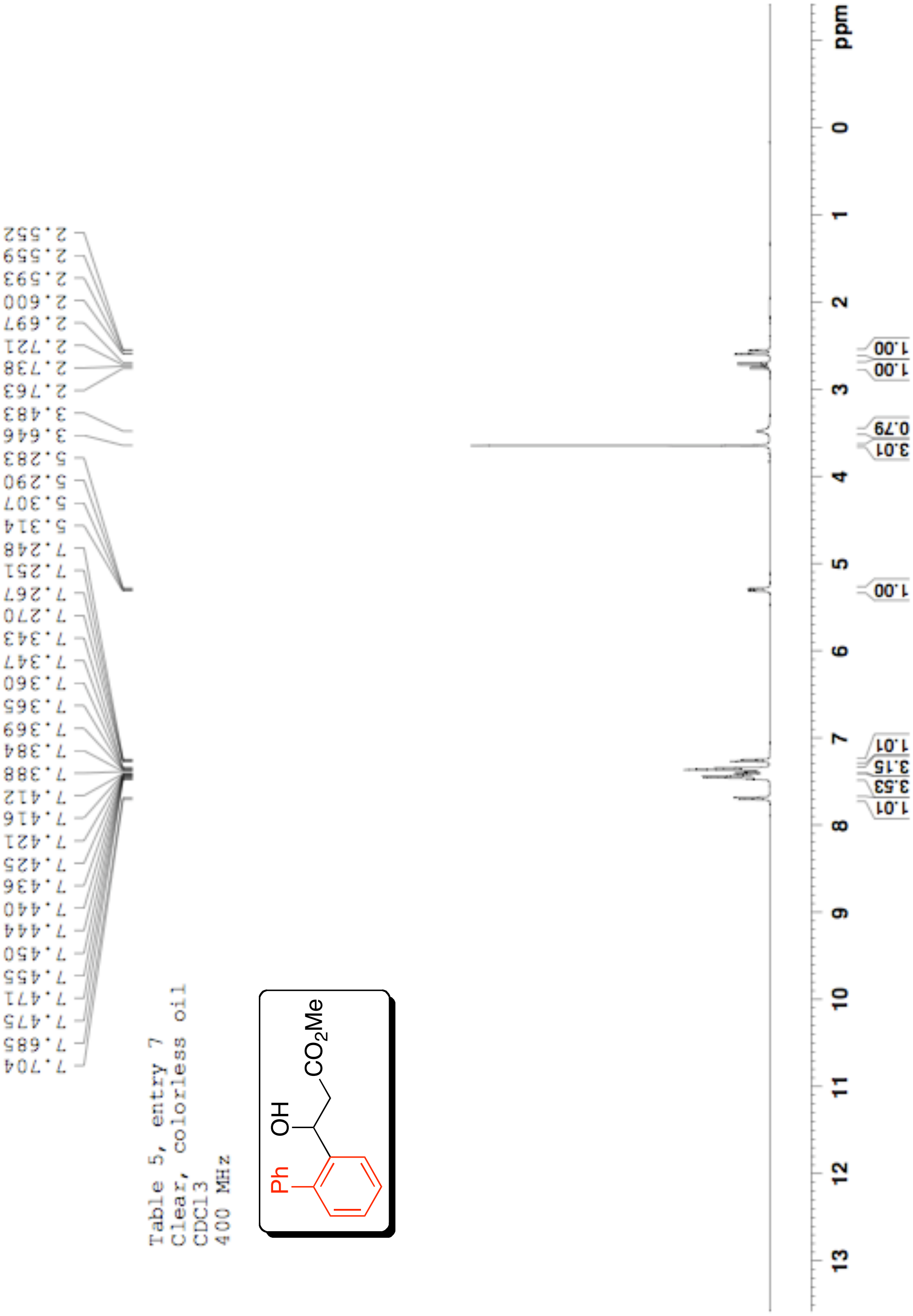


Table 5, entry 6
White solid
CDCl3
100 MHz


2.552
2.559
2.593
2.600
2.697
2.721
2.738
2.763
3.483
3.646
5.283
5.290
5.307
5.314
7.248
7.251
7.267
7.270
7.343
7.347
7.360
7.365
7.369
7.384
7.388
7.412
7.416
7.421
7.425
7.436
7.440
7.444
7.450
7.455
7.471
7.475
7.685
7.704
Table 5, entry 7
Clear, colorless oil
CDCl3
400 MHz
Ph
OH
CO2Me
1.00
1.00
0.79
3.01
1.00
1.01
3.15
3.53
1.01
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

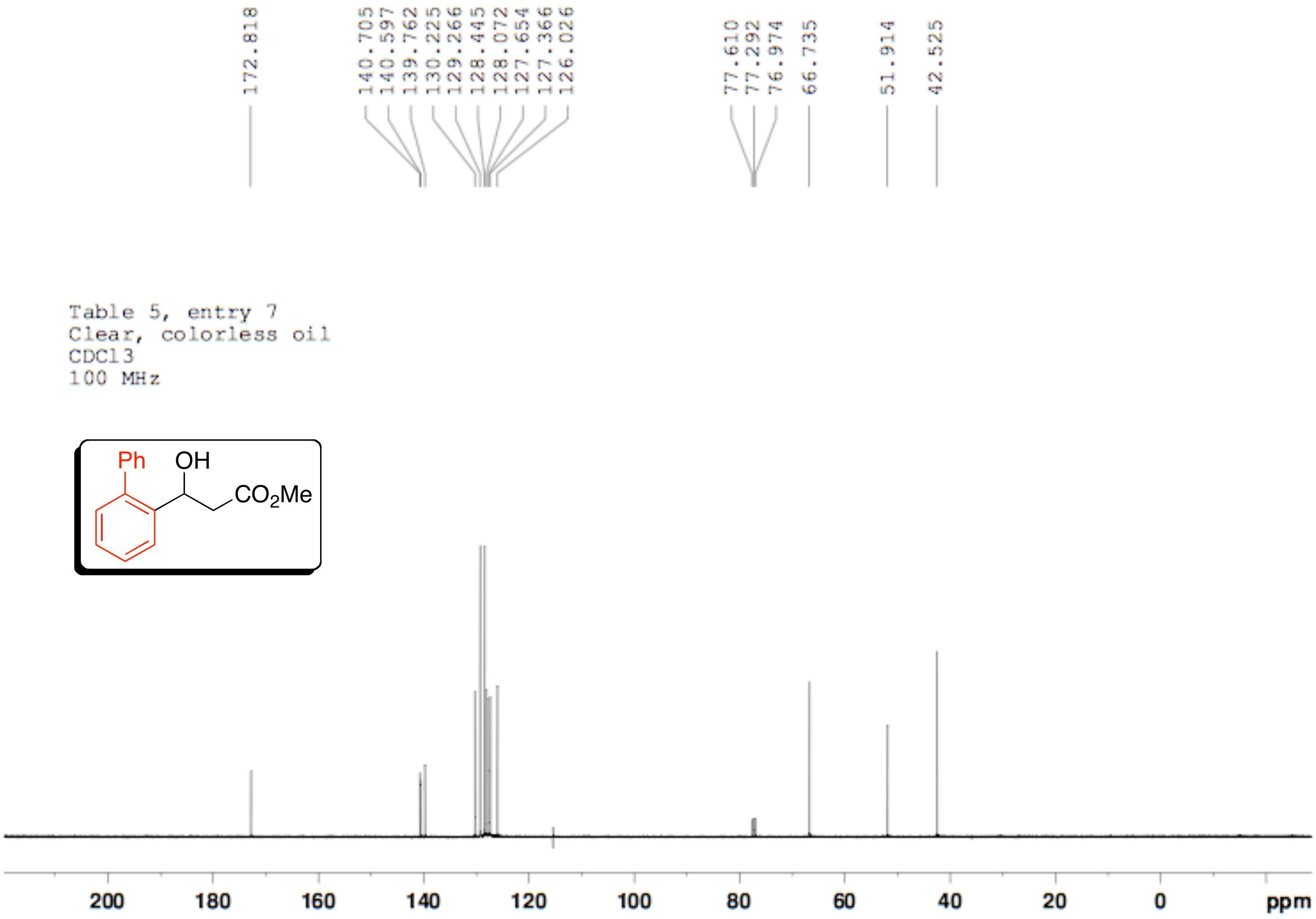


Table 5, entry 7
Clear, colorless oil
CDCl3
100 MHz

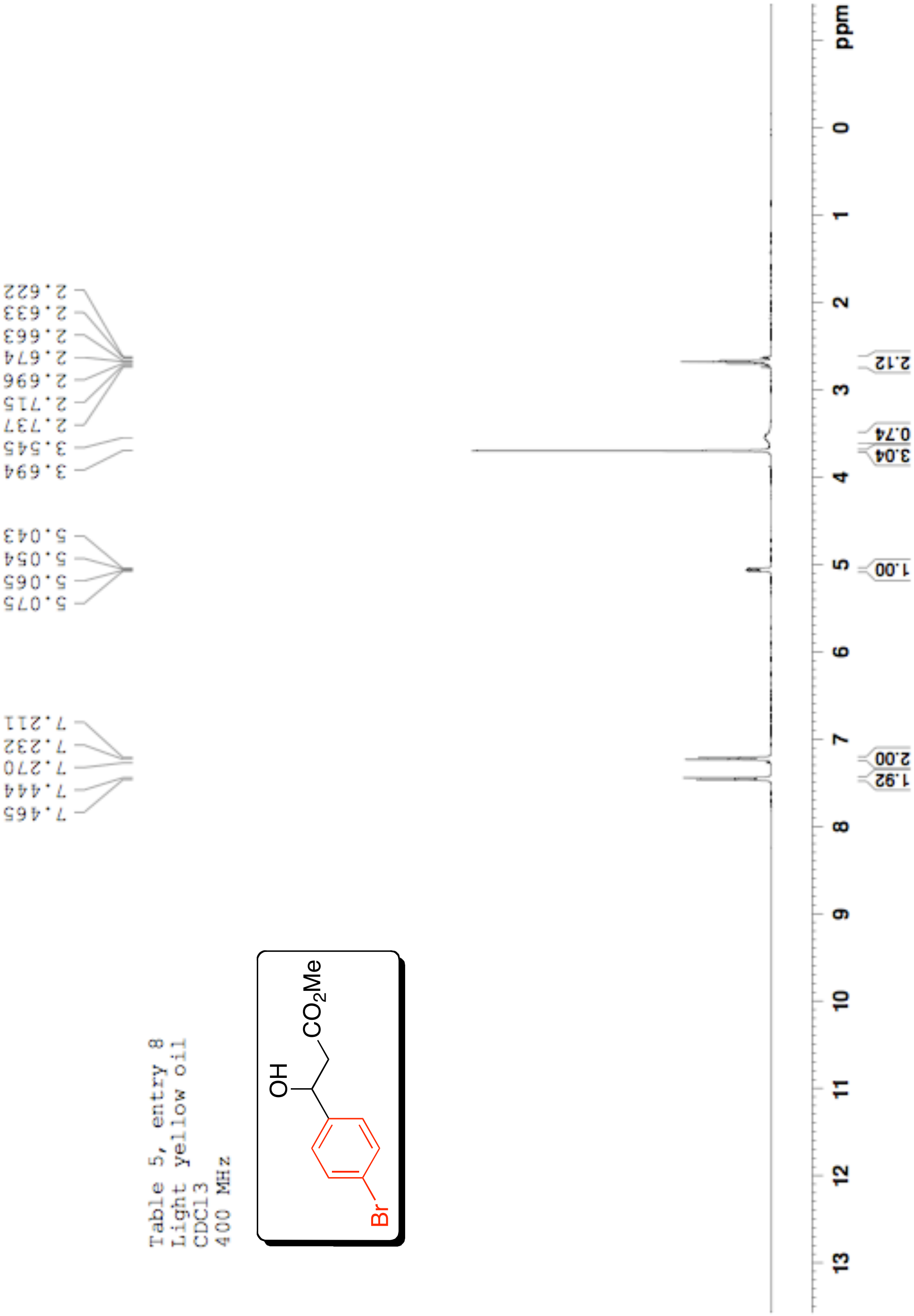
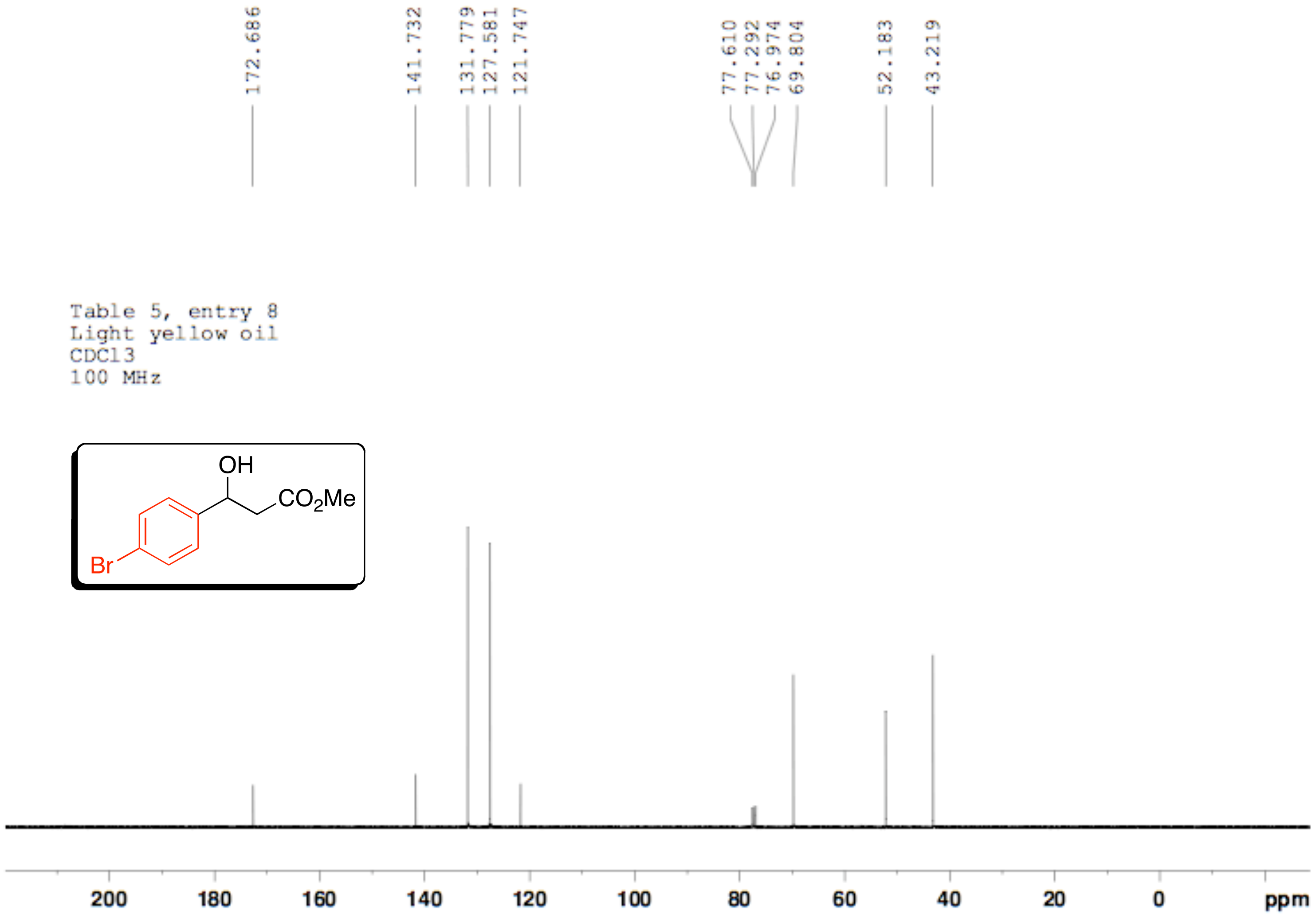


Table 5, entry 8
Light yellow oil
CDCl3
400 MHz
OH
CO2Me
Br
2.622
2.633
2.663
2.674
2.696
2.715
2.737
3.545
3.694
5.043
5.054
5.065
5.075
7.211
7.232
7.270
7.444
7.465
2.12
0.74
3.04
1.00
2.00
1.92
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


172.686
141.732
131.779
127.581
121.747
77.610
77.292
76.974
69.804
52.183
43.219
Table 5, entry 8
Light yellow oil
CDCl3
100 MHz
OH
CO2Me
Br
200
180
160
140
120
100
80
60
40
20
0
ppm

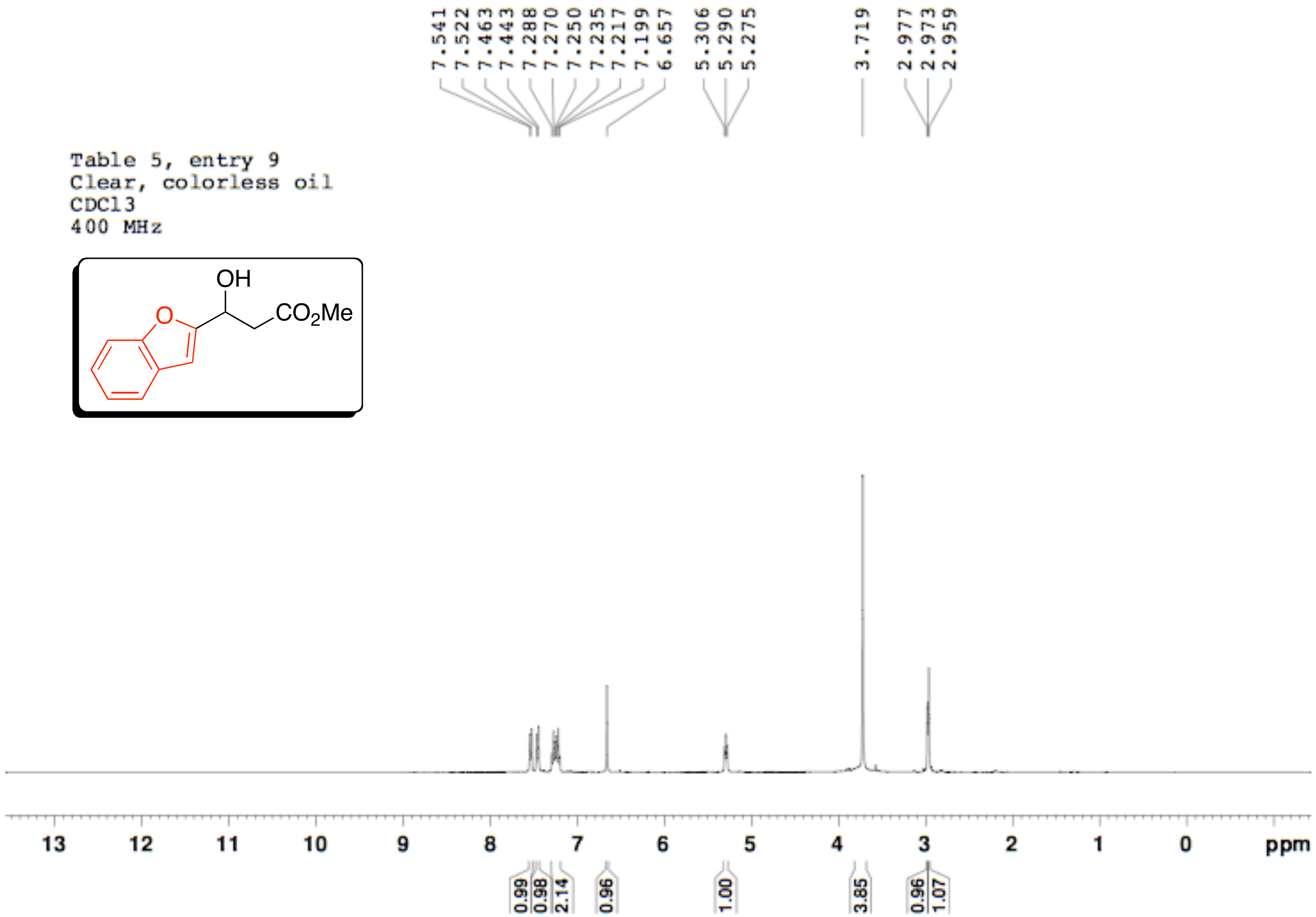
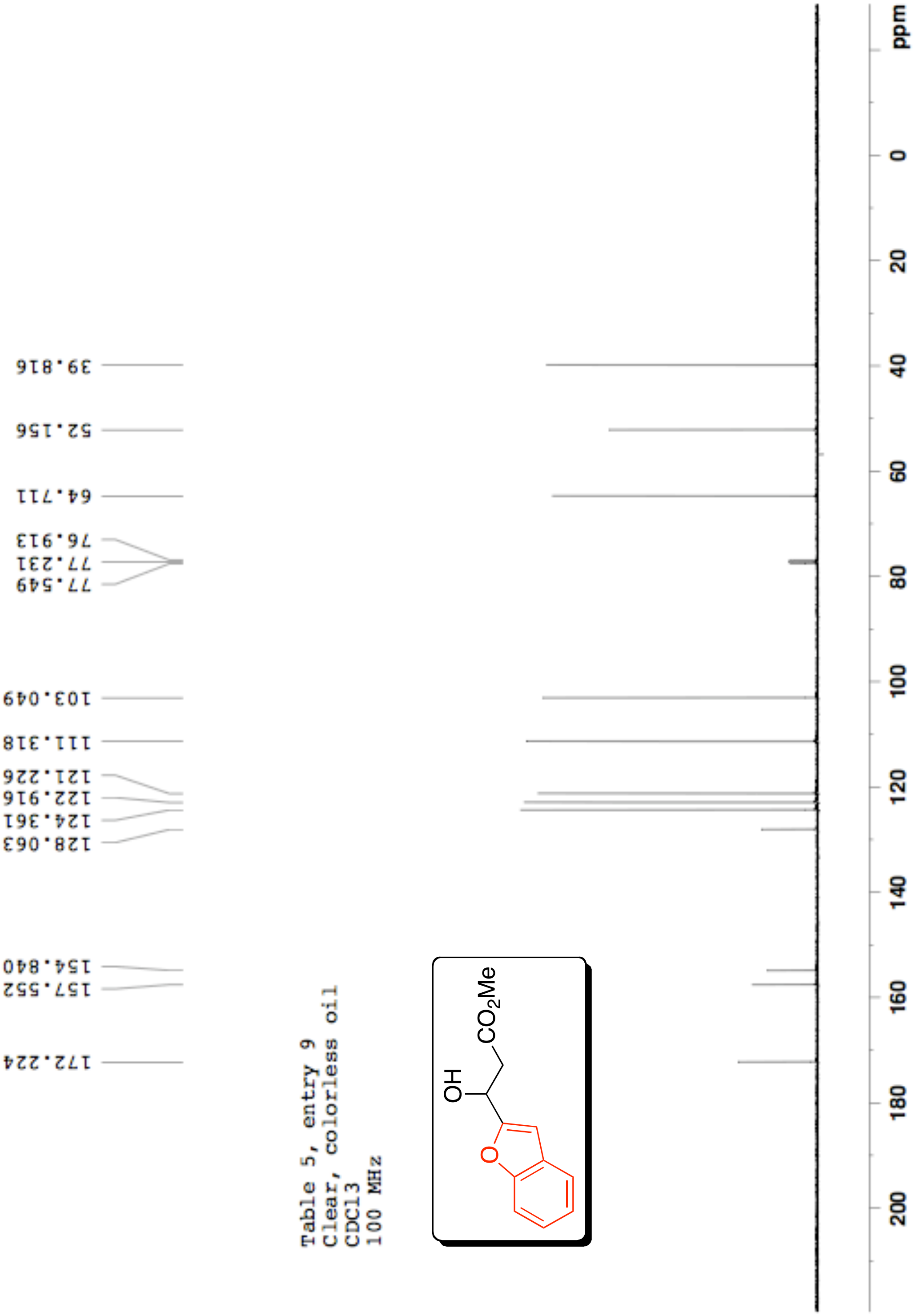
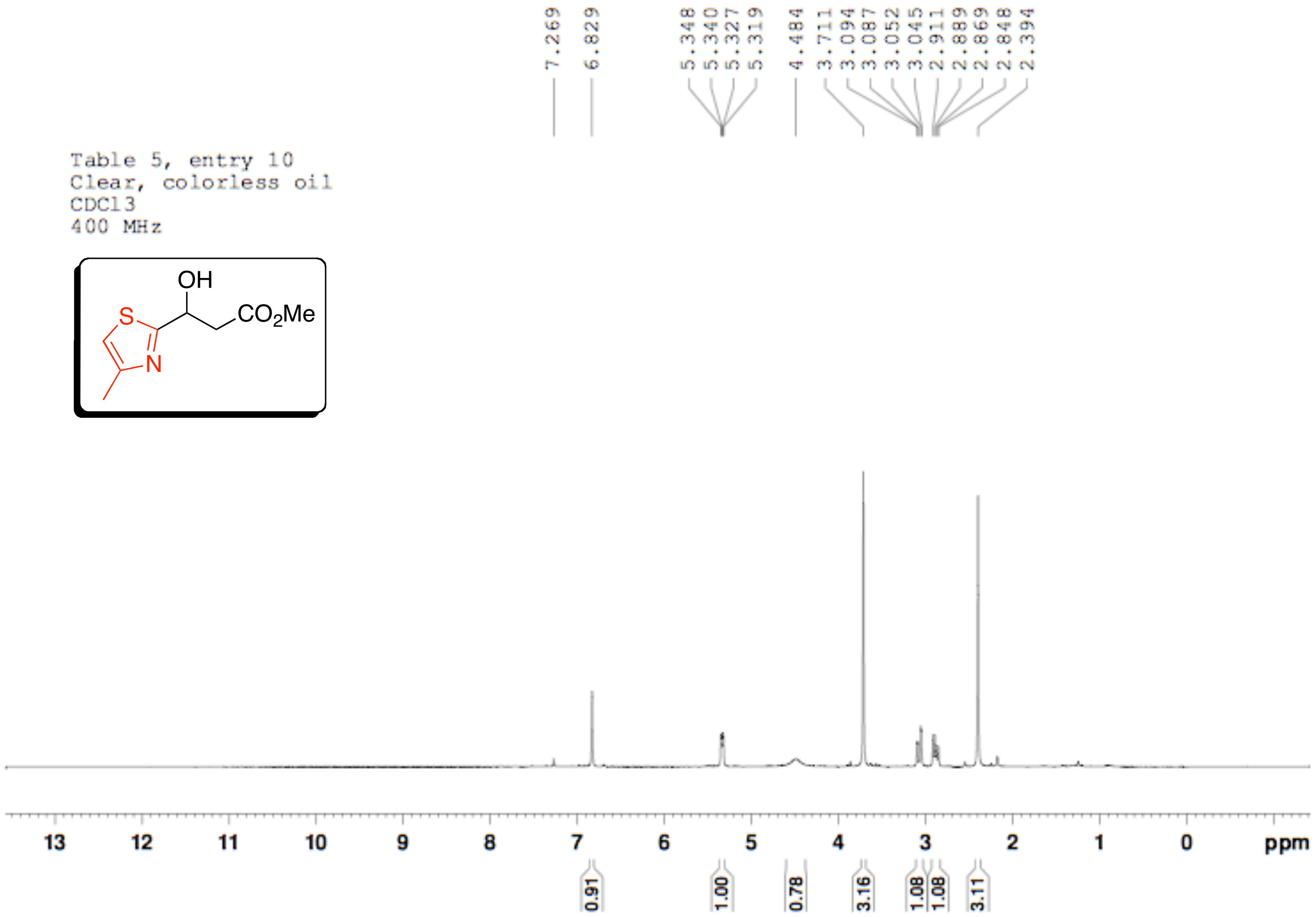
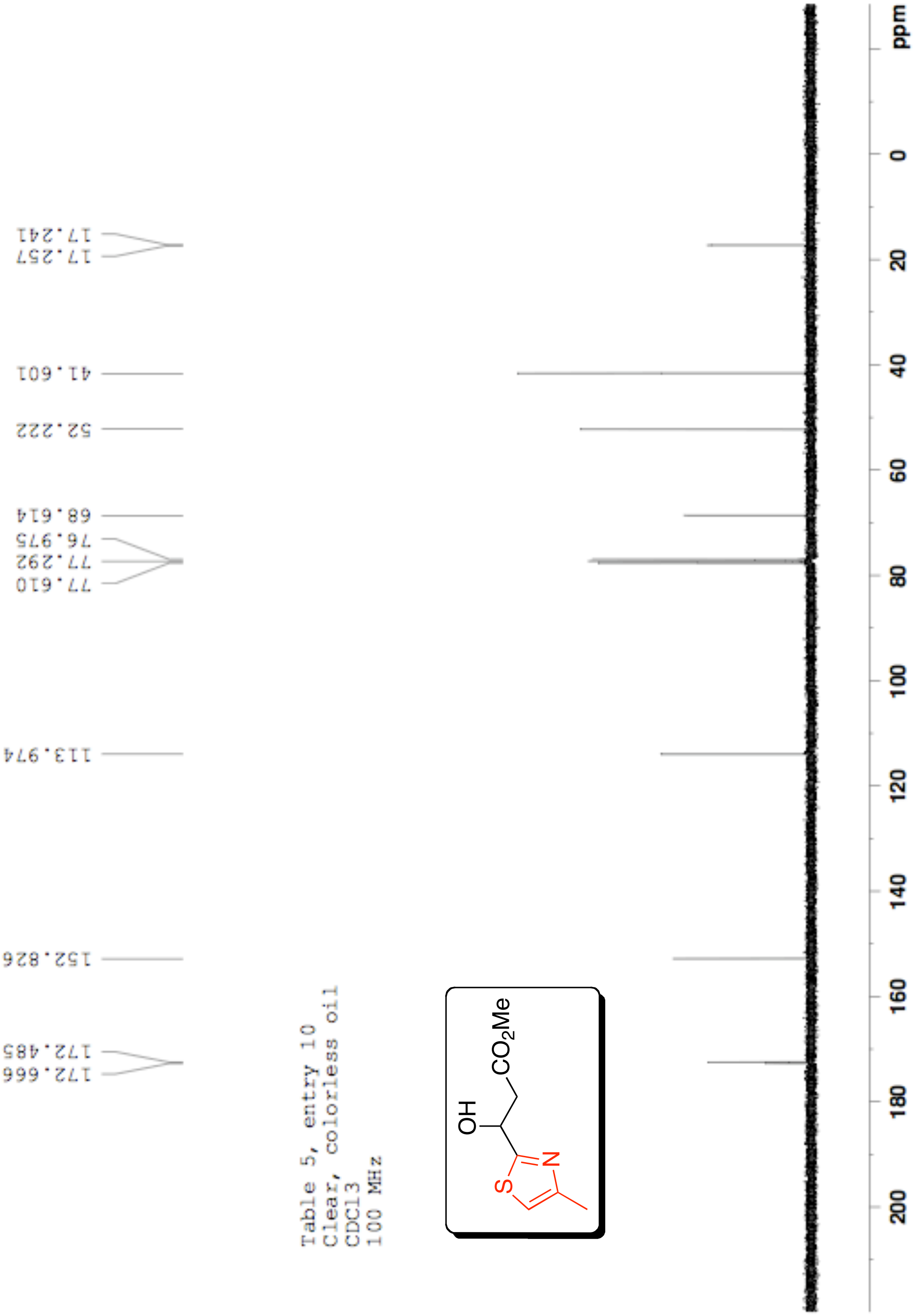
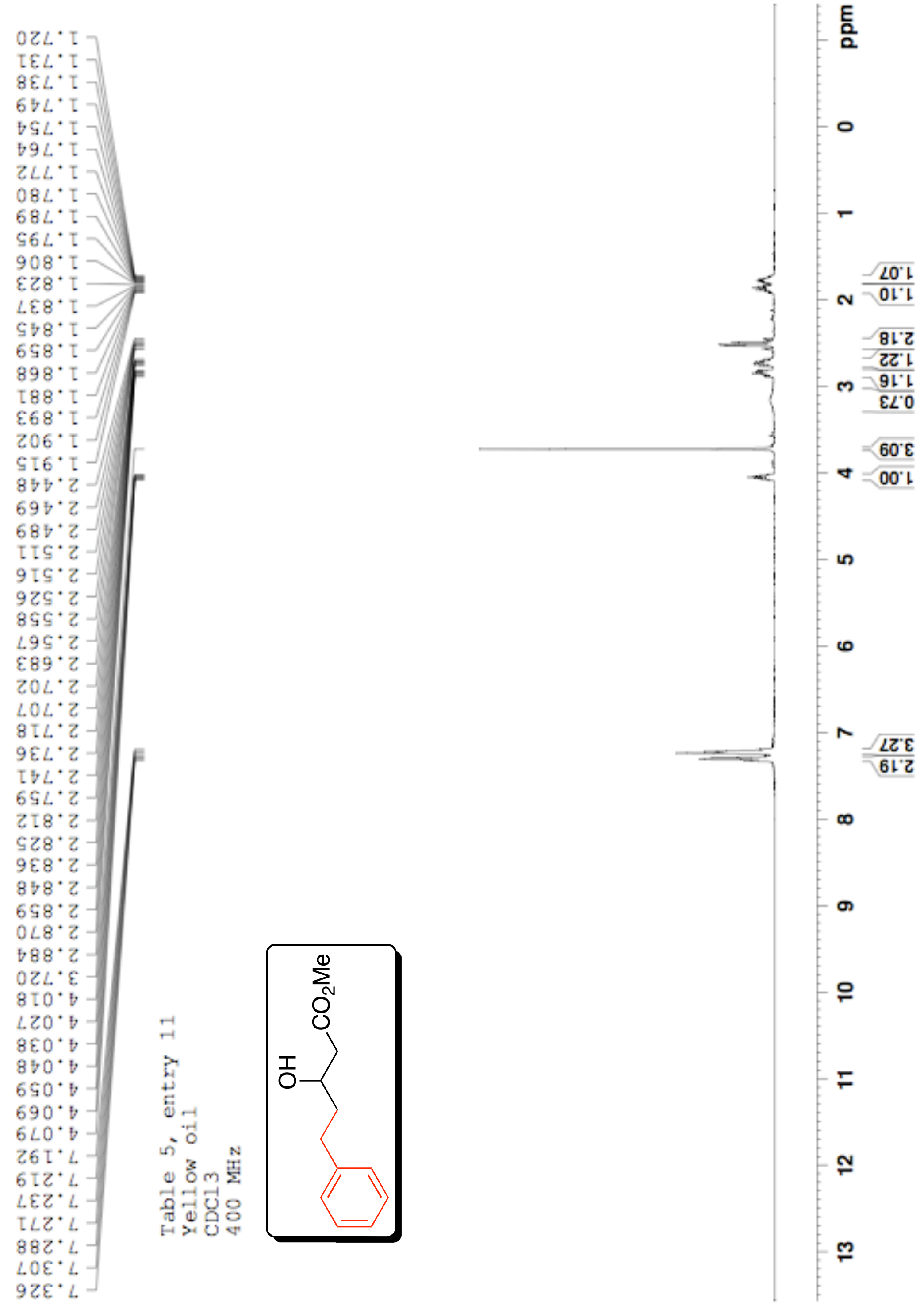


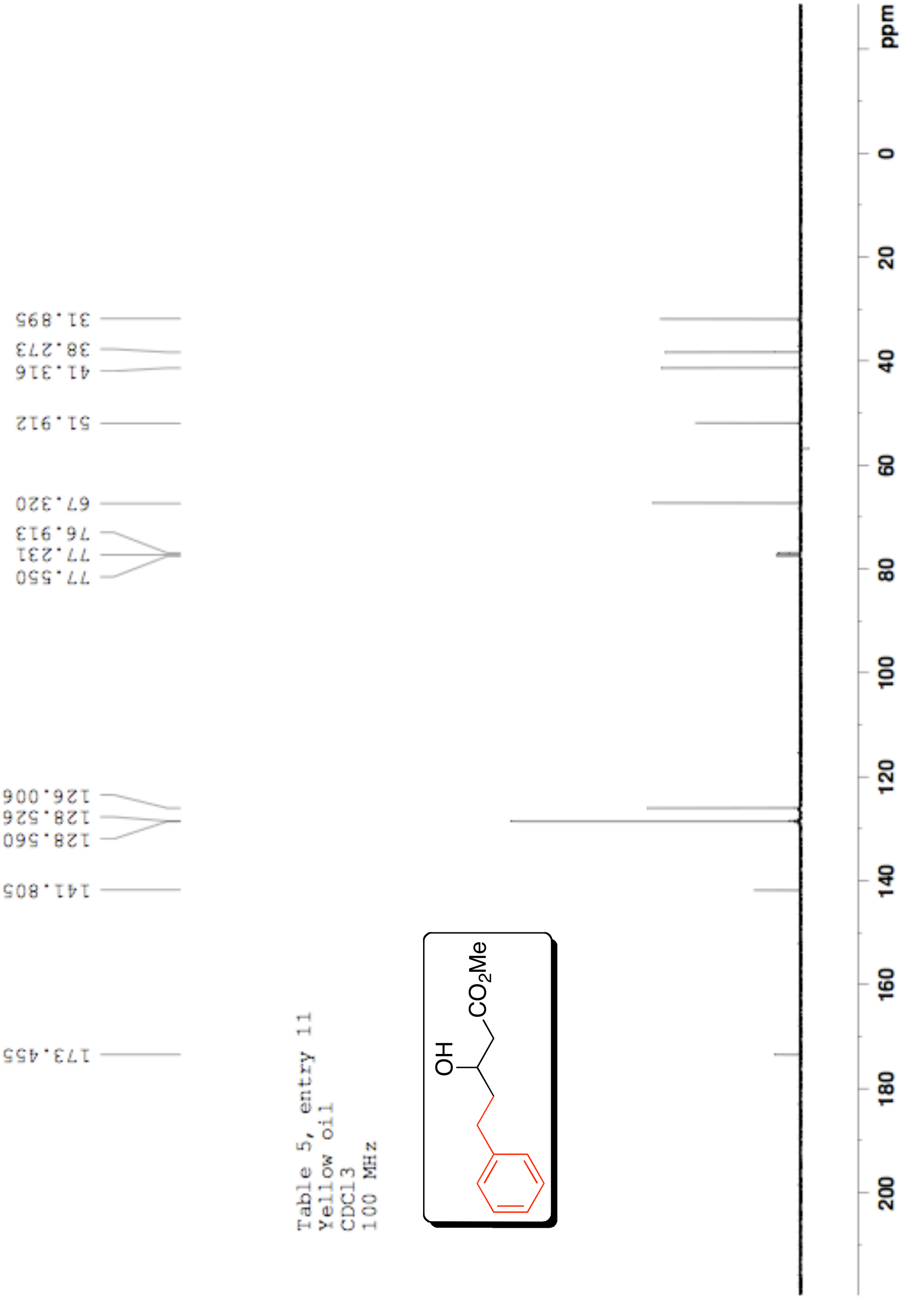
Table 5, entry 9
Clear, colorless oil
CDCl3
400 MHz

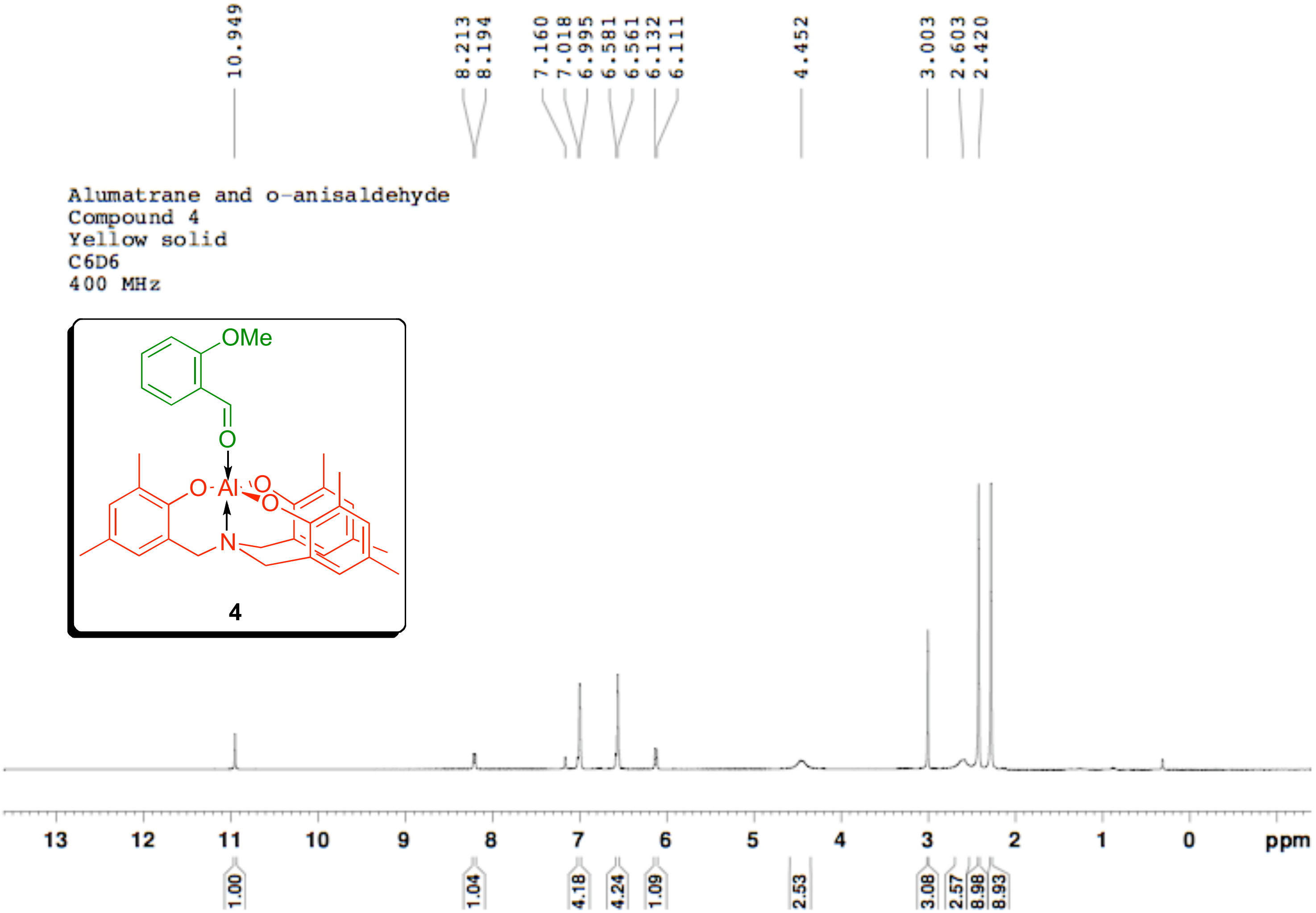

39.816
52.156
64.711
76.913
77.231
77.549
103.049
111.318
121.226
122.916
124.361
128.063
154.840
157.552
172.224
Table 5, entry 9
Clear, colorless oil
CDCl3
100 MHz
OH
CO2Me
O
ppm
0
20
40
60
80
100
120
140
160
180
200

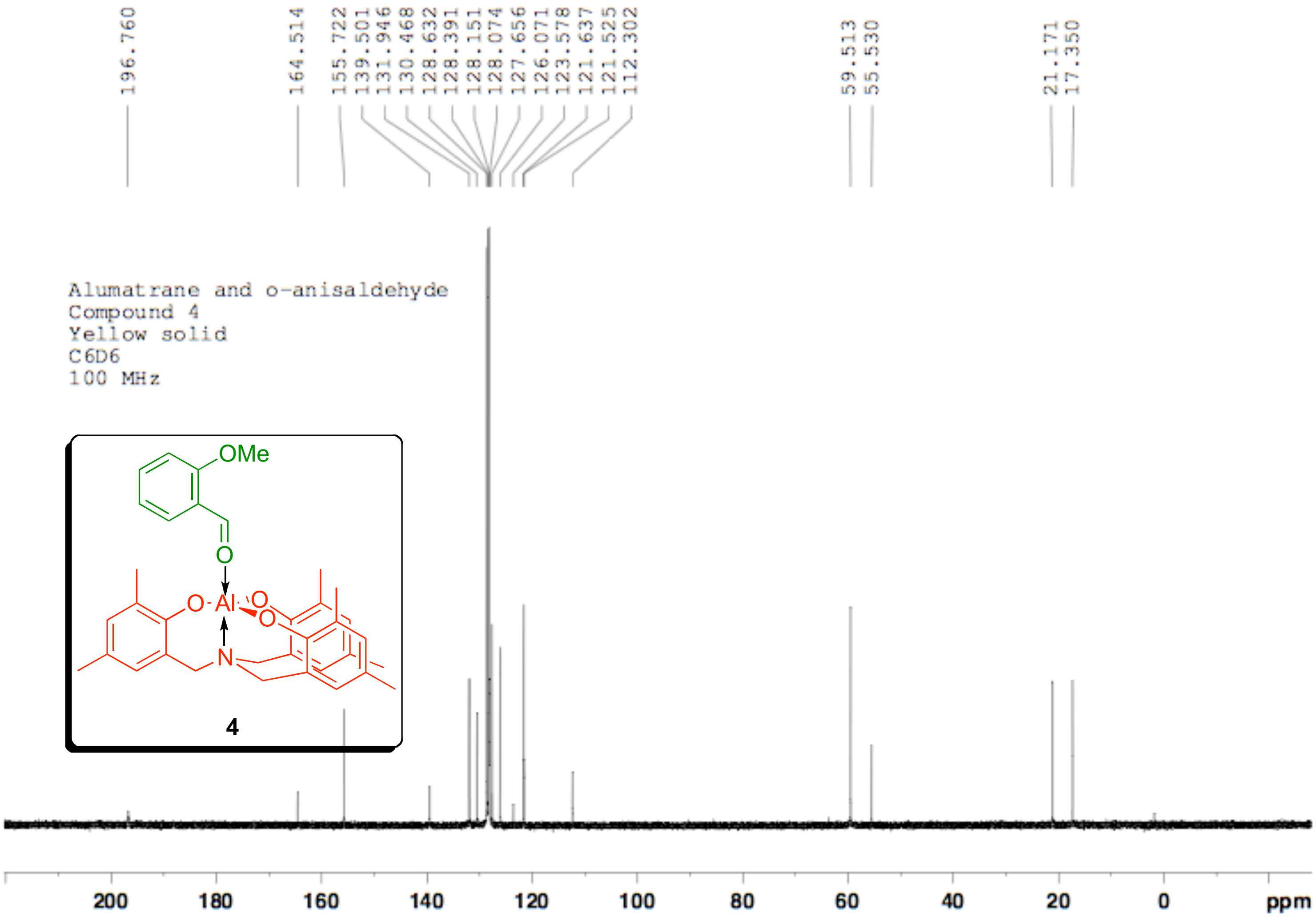

7.269
6.829
5.348
5.340
5.327
5.319
4.484
3.711
3.094
3.087
3.052
3.045
2.911
2.889
2.869
2.848
2.394
Table 5, entry 10
Clear, colorless oil
CDCl3
400 MHz
OH
CO2Me
S
N
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.91
1.00
0.78
3.16
1.08
1.08
3.11

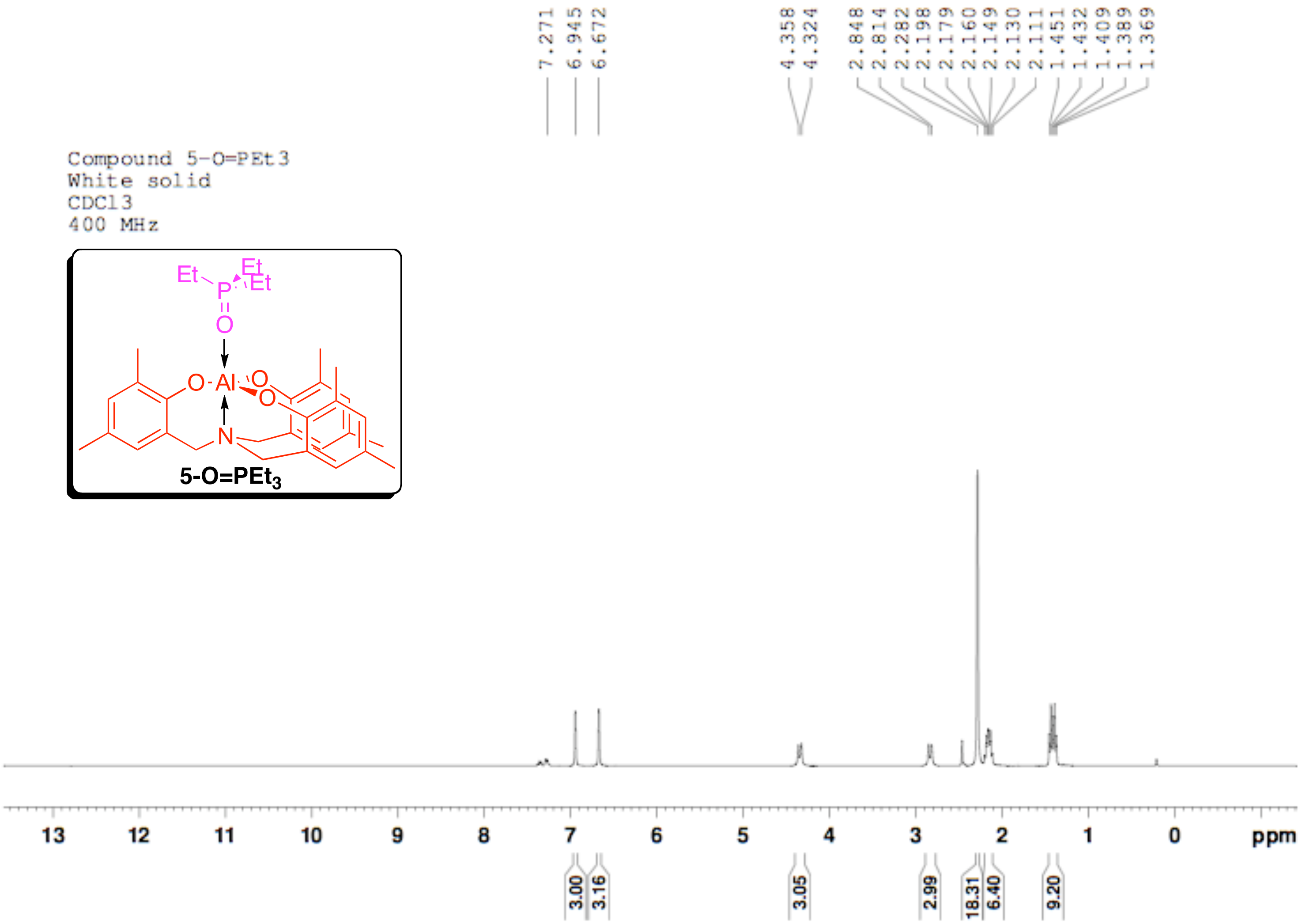

172.666
172.485
152.826
113.974
77.610
77.292
76.975
68.614
52.222
41.601
17.257
17.241
Table 5, entry 10
Clear, colorless oil
CDCl3
100 MHz
OH
CO_2Me
S
N
ppm
200
180
160
140
120
100
80
60
40
20
0

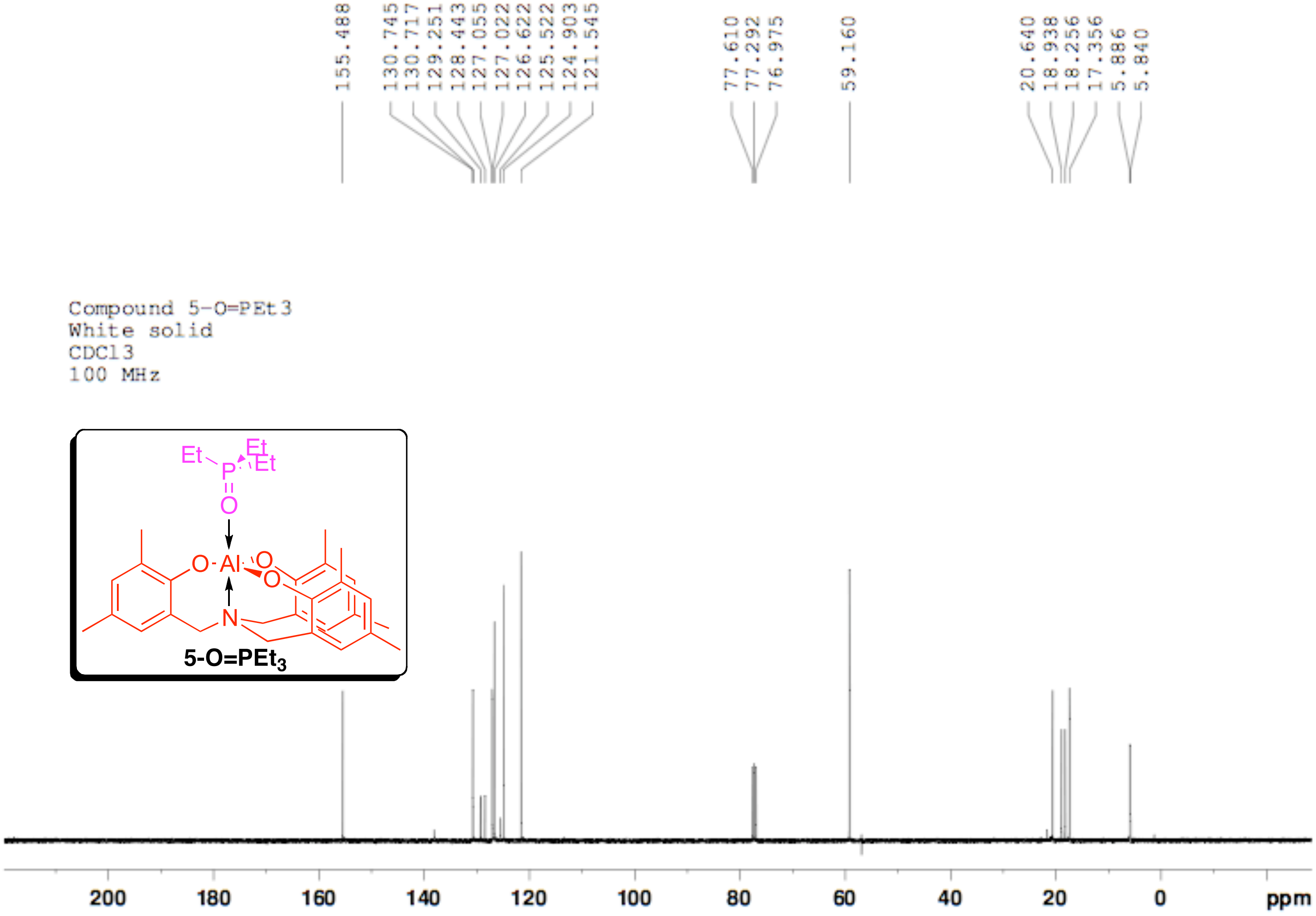

1.720
1.731
1.738
1.749
1.754
1.764
1.772
1.780
1.789
1.795
1.806
1.823
1.837
1.845
1.859
1.868
1.881
1.893
1.902
1.915
2.448
2.469
2.489
2.511
2.516
2.526
2.558
2.567
2.683
2.702
2.707
2.718
2.736
2.741
2.759
2.812
2.825
2.836
2.848
2.859
2.870
2.884
3.720
4.018
4.027
4.038
4.048
4.059
4.069
4.079
7.192
7.219
7.237
7.271
7.288
7.307
7.326
Table 5, entry 11
Yellow oil
CDCl3
400 MHz
OH
CO2Me
1.07
1.10
2.18
1.22
1.16
0.73
3.09
1.00
3.27
2.19
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

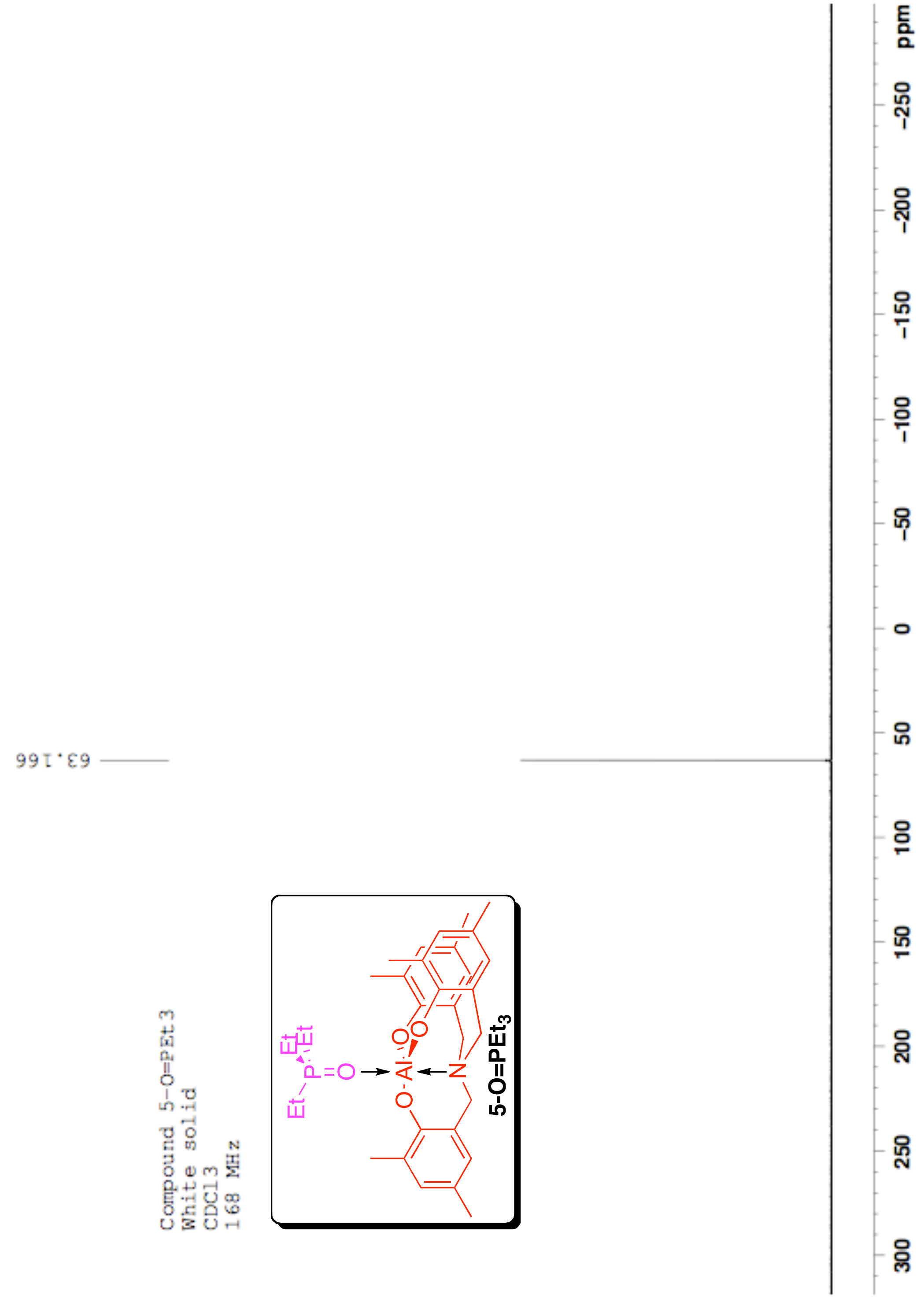

31.895
38.273
41.316
51.912
67.320
76.913
77.231
77.550
126.006
128.526
128.560
141.805
173.455
Table 5, entry 11
Yellow oil
CDCl3
100 MHz
OH
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200

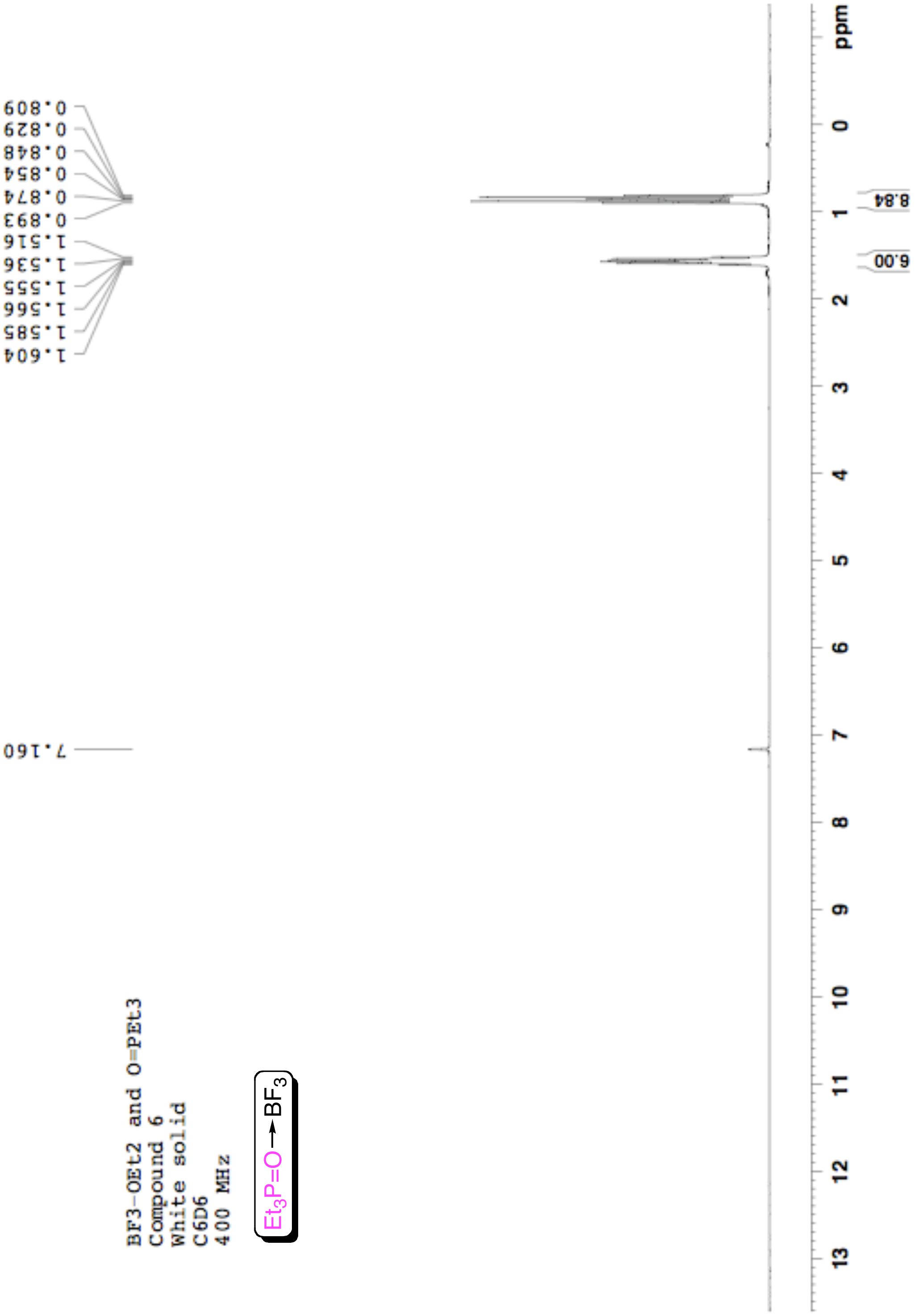

Alumatrane and o-anisaldehyde
Compound 4
Yellow solid
C6D6
400 MHz
OMe
O
O
Al
O
O
N
4
10.949
8.213
8.194
7.160
7.018
6.995
6.581
6.561
6.132
6.111
4.452
3.003
2.603
2.420
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.04
4.18
4.24
1.09
2.53
3.08
2.57
8.98
8.93

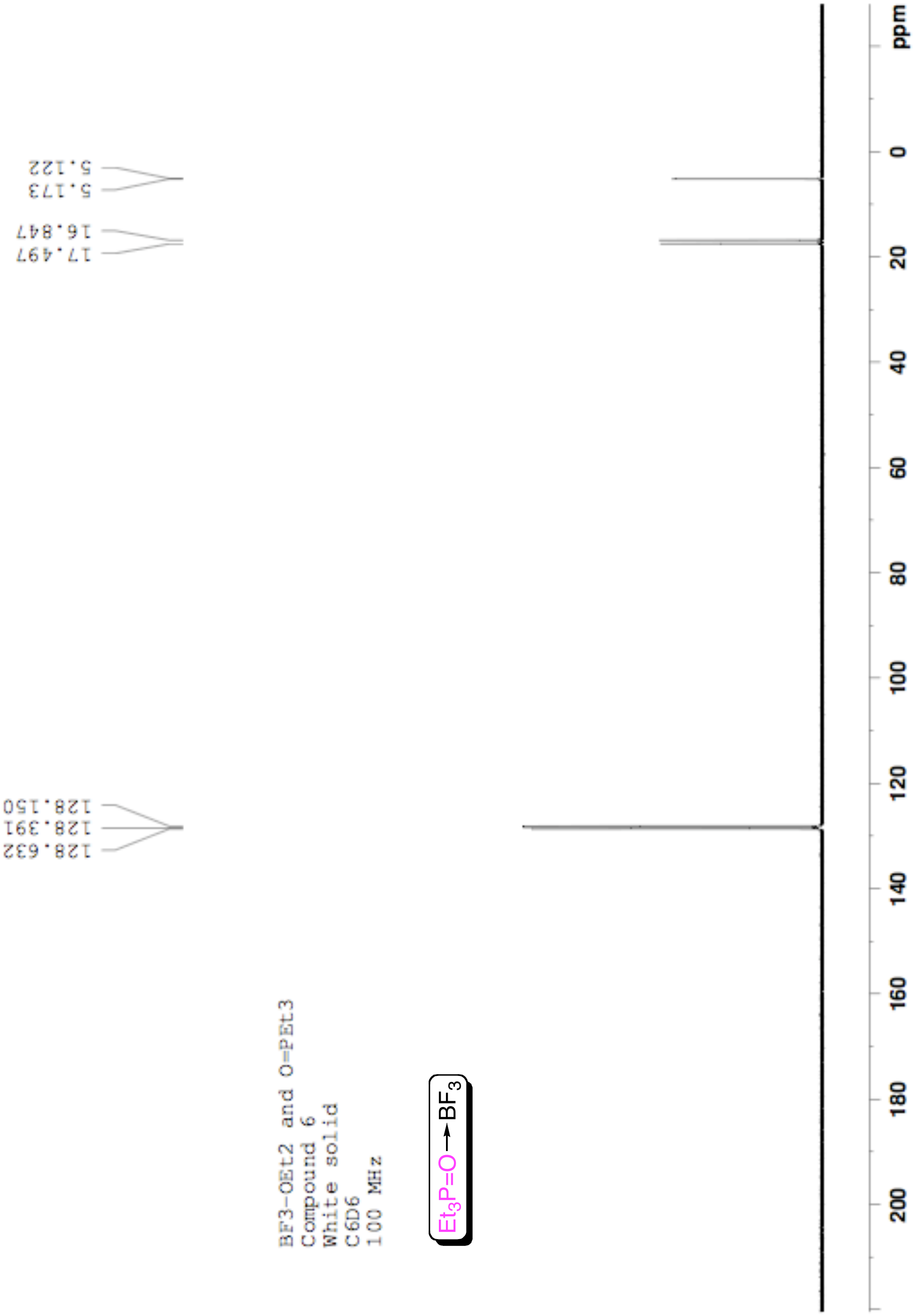

196.760
164.514
155.722
139.501
131.946
130.468
128.632
128.391
128.151
128.074
127.656
126.071
123.578
121.637
121.525
112.302
59.513
55.530
21.171
17.350
Alumatrane and o-anisaldehyde
Compound 4
Yellow solid
C6D6
100 MHz
OMe
O
O
Al
O
O
N
4
200
180
160
140
120
100
80
60
40
20
0
ppm

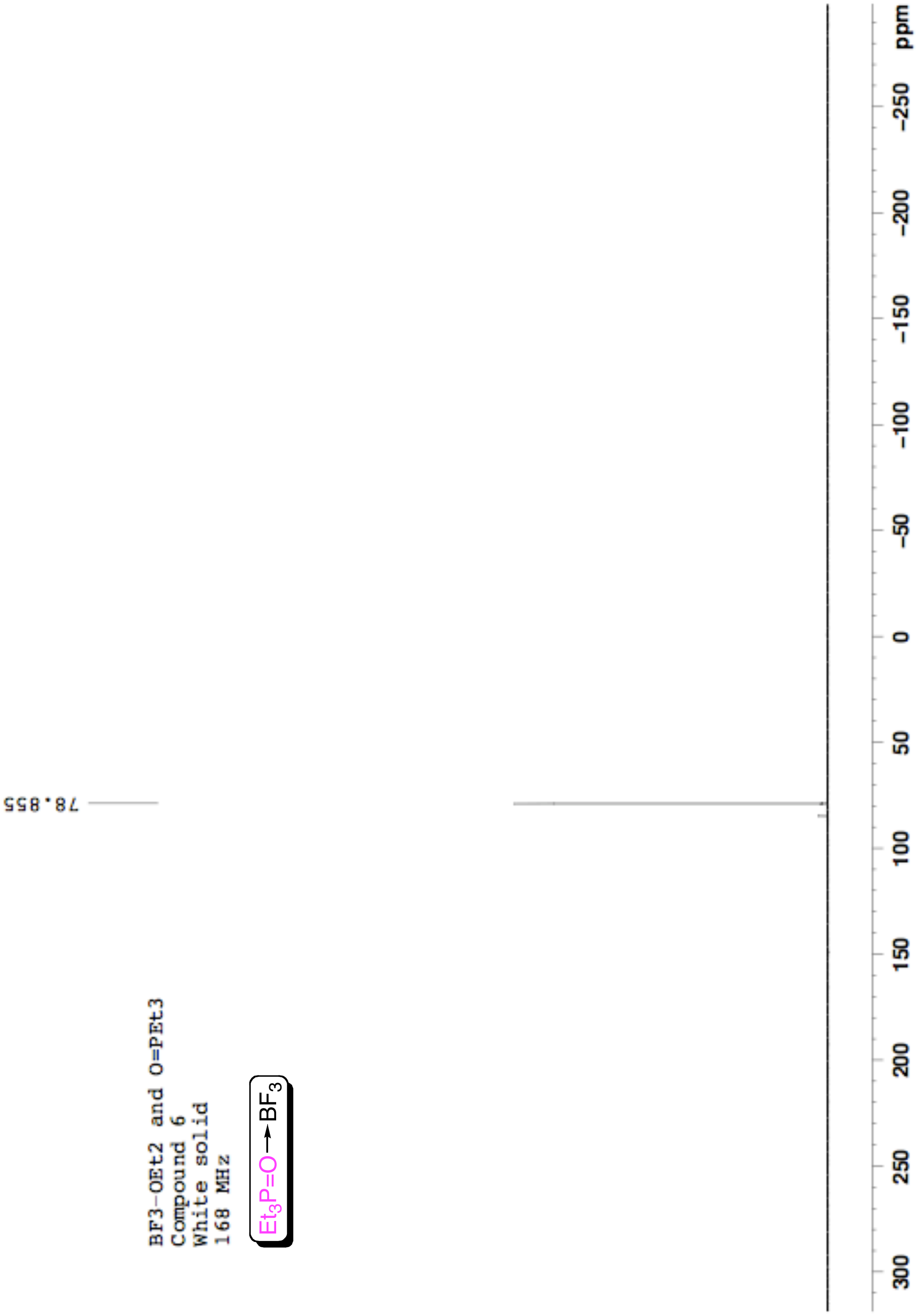

Compound 5-O=PEt3
White solid
CDCl3
400 MHz
7.271
6.945
6.672
4.358
4.324
2.848
2.814
2.282
2.198
2.179
2.160
2.149
2.130
2.111
1.451
1.432
1.409
1.389
1.369
Et
Et
Et
P
O
O
Al
O
O
N
5-O=PEt$_3$
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
3.00
3.16
3.05
2.99
18.31
6.40
9.20

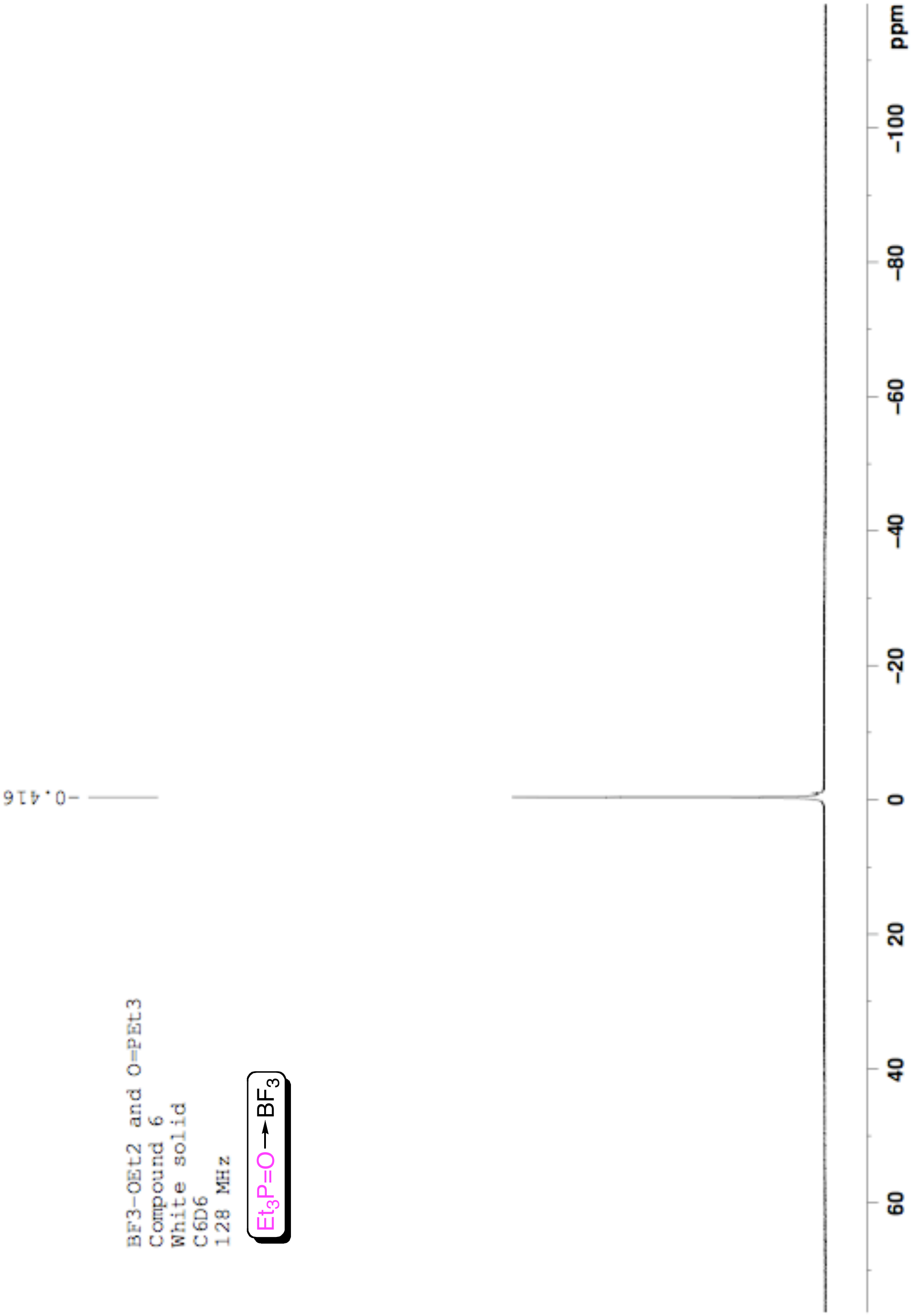

155.488
130.745
130.717
129.251
128.443
127.055
127.022
126.622
125.522
124.903
121.545
77.610
77.292
76.975
59.160
20.640
18.938
18.256
17.356
5.886
5.840
Compound 5-O=PEt3
White solid
CDCl3
100 MHz
Et
P
Et
Et
O
O
Al
O
O
N
5-O=PEt₃
200
180
160
140
120
100
80
60
40
20
0
ppm

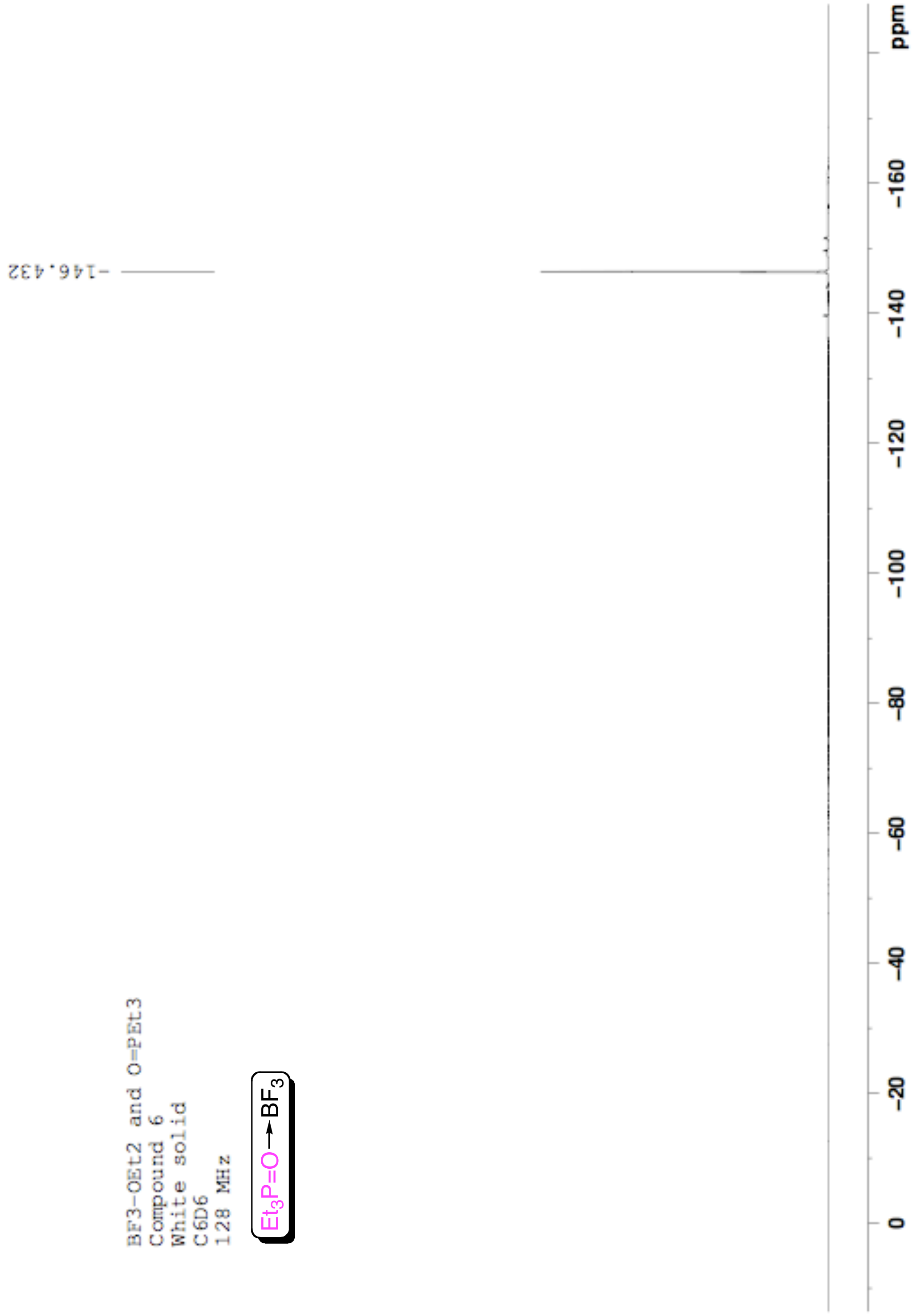

Compound 5-O=PEt3
White solid
CDCl3
168 MHz
63.166
Et
P
O
Al
N
5-O=PEt$_3$
300
250
200
150
100
50
0
−50
−100
−150
−200
−250
ppm


0.809
0.829
0.848
0.854
0.874
0.893
1.516
1.536
1.555
1.566
1.585
1.604
7.160
BF3-OEt2 and O=PEt3
Compound 6
White solid
C6D6
400 MHz
Et3P=O→BF3
8.84
6.00
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


5.122
5.173
16.847
17.497
128.150
128.391
128.632
BF3-OEt2 and O=PEt3
Compound 6
White solid
C6D6
100 MHz
Et3P=O→BF3
ppm
0
20
40
60
80
100
120
140
160
180
200


BF3-OEt2 and O=PEt3
Compound 6
White solid
168 MHz
Et3P=O→BF3
78.855
ppm
-250
-200
-150
-100
-50
0
50
100
150
200
250
300


BF3-OEt2 and O=PEt3
Compound 6
White solid
C6D6
128 MHz
$Et_3P{=}O \longrightarrow BF_3$
-0.416
ppm
-100
-80
-60
-40
-20
0
20
40
60


-146.432
BF3-OEt2 and O=PEt3
Compound 6
White solid
C6D6
128 MHz
$Et_3P=O \longrightarrow BF_3$
ppm
-160
-140
-120
-100
-80
-60
-40
-20
0

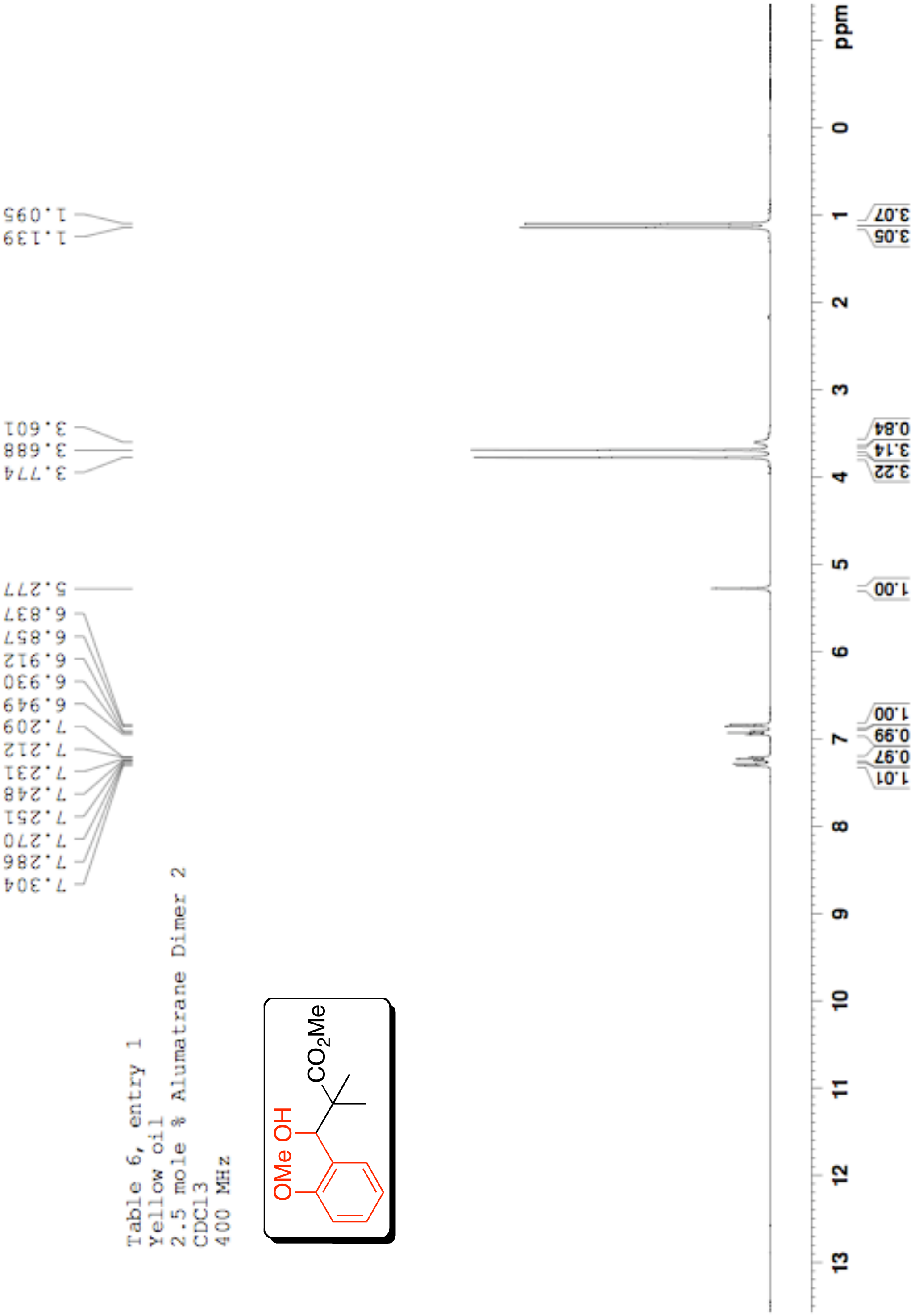


Table 6, entry 1
Yellow oil
2.5 mole % Alumatrane Dimer 2
CDCl3
400 MHz
OMe OH
CO2Me
1.095
1.139
3.601
3.688
3.774
5.277
6.837
6.857
6.912
6.930
6.949
7.209
7.212
7.231
7.248
7.251
7.270
7.286
7.304
3.07
3.05
0.84
3.14
3.22
1.00
1.00
0.99
0.97
1.01
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13

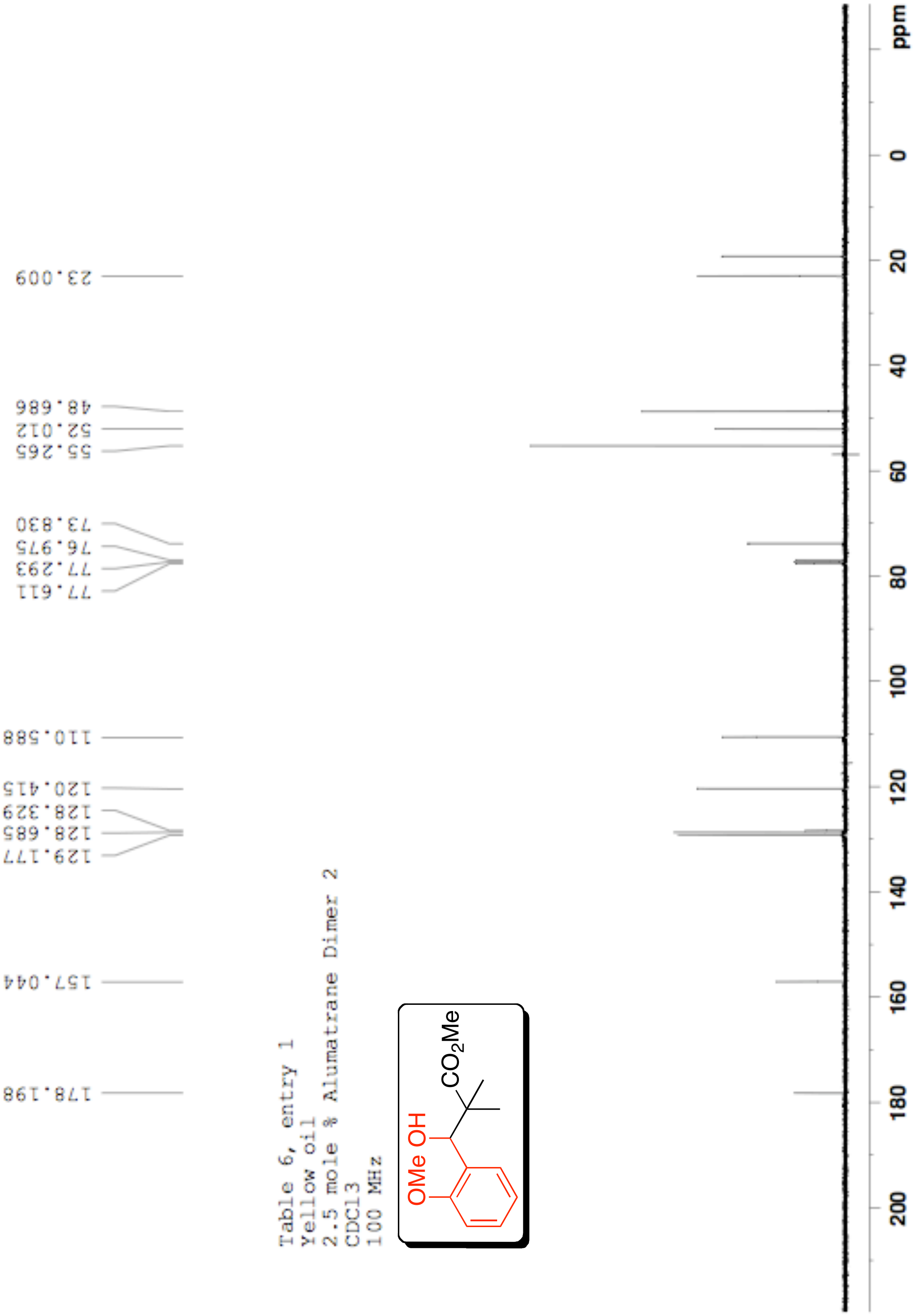
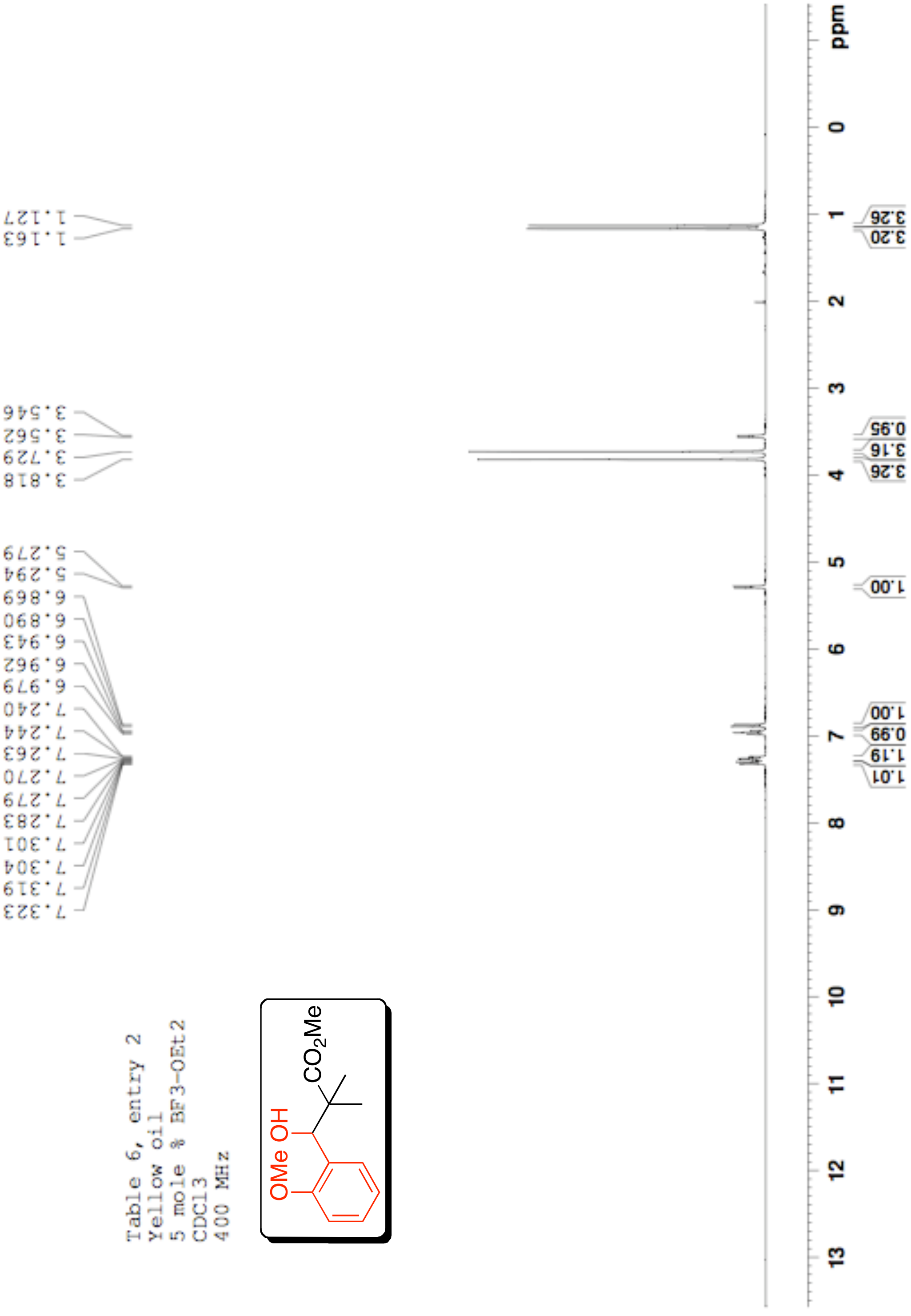
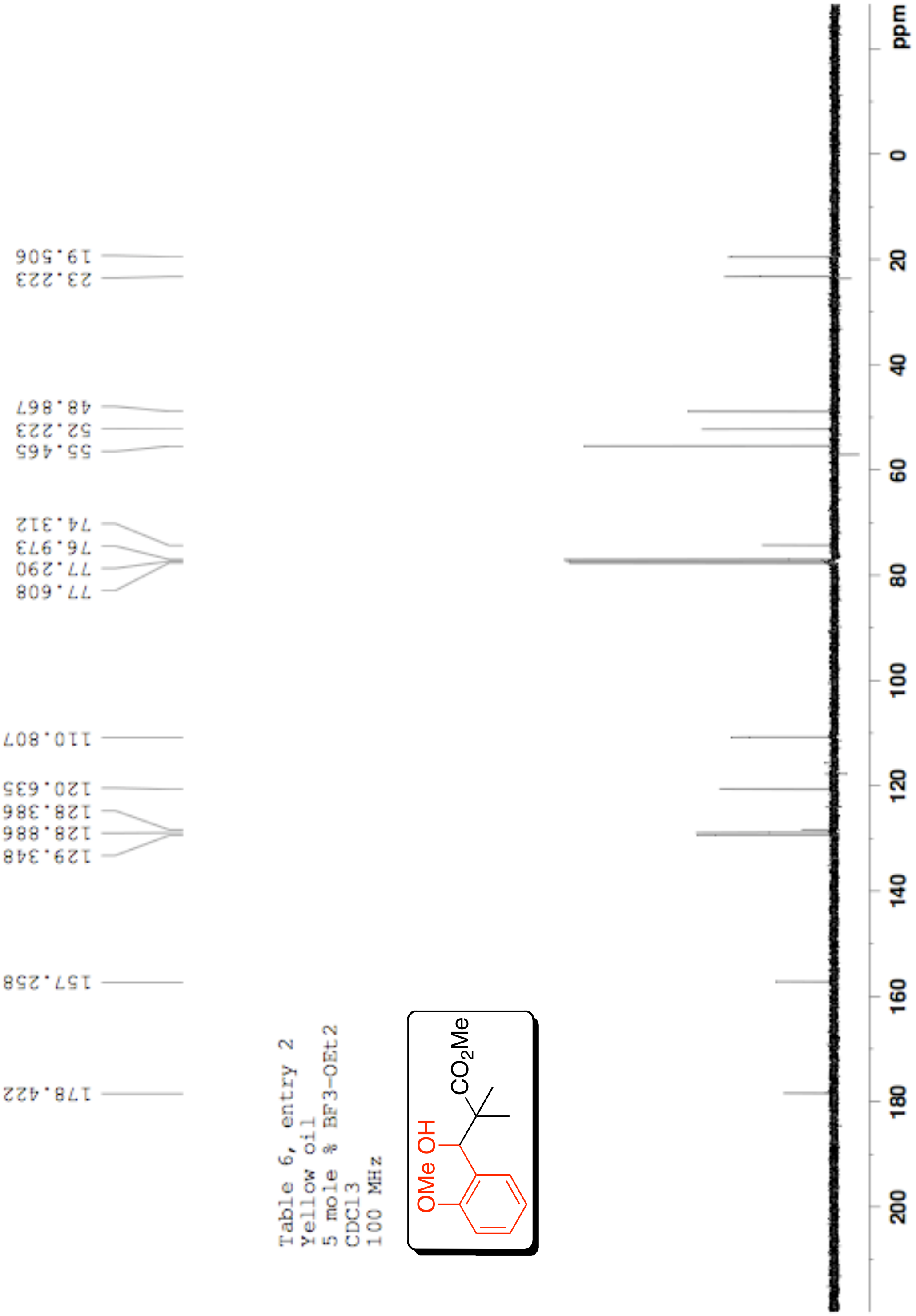


Table 6, entry 1
Yellow oil
2.5 mole % Alumatrane Dimer 2
CDCl3
100 MHz


1.127
1.163
3.546
3.562
3.729
3.818
5.279
5.294
6.869
6.890
6.943
6.962
6.979
7.240
7.244
7.263
7.270
7.279
7.283
7.301
7.304
7.319
7.323
Table 6, entry 2
Yellow oil
5 mole % BF3-OEt2
CDCl3
400 MHz
OMe OH
CO2Me
3.26
3.20
0.95
3.16
3.26
1.00
1.00
0.99
1.19
1.01
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13


19.506
23.223
48.867
52.223
55.465
74.312
76.973
77.290
77.608
110.807
120.635
128.386
128.886
129.348
157.258
178.422
Table 6, entry 2
Yellow oil
5 mole % BF3-OEt2
CDCl3
100 MHz
OMe OH
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200

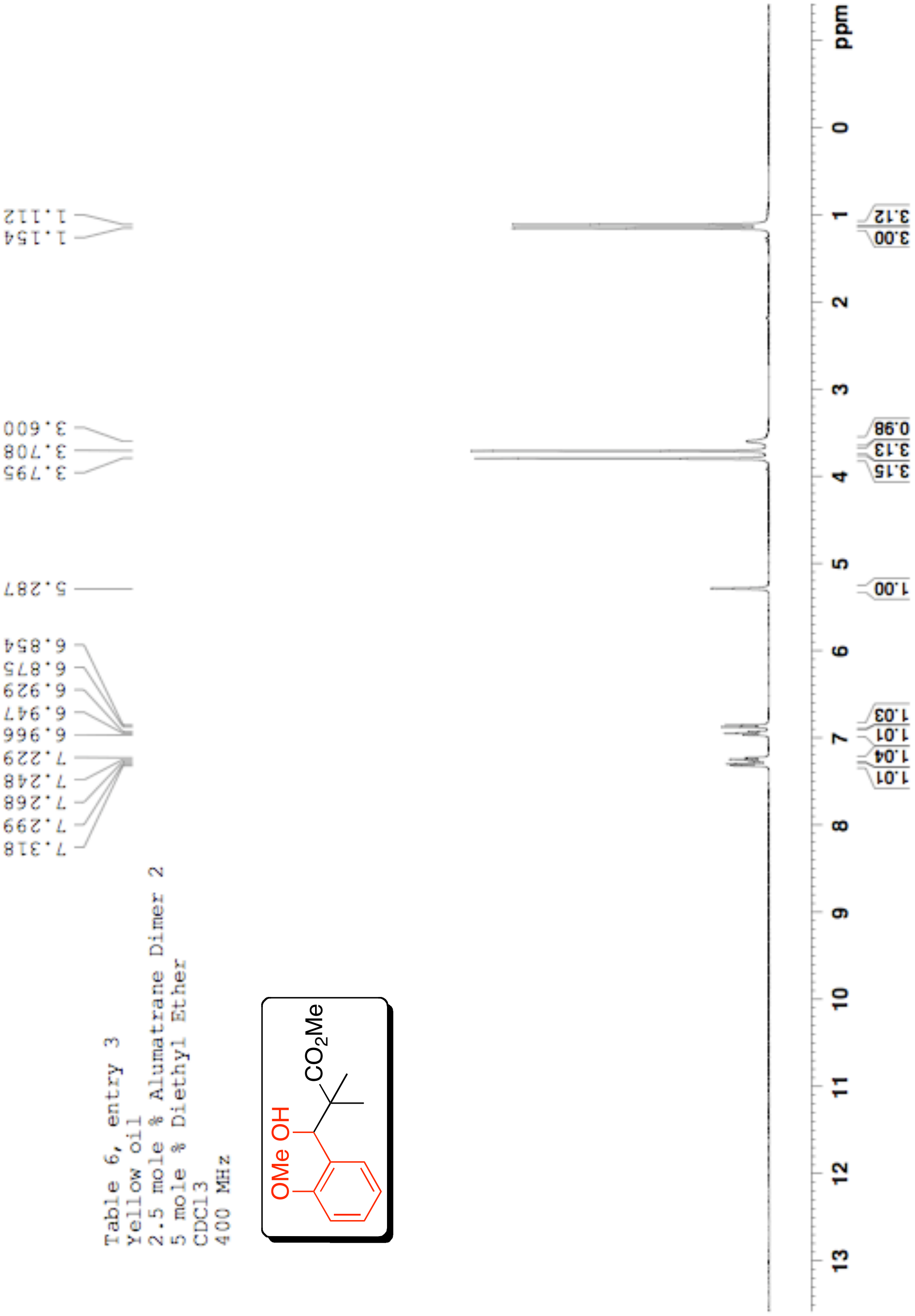


Table 6, entry 3
Yellow oil
2.5 mole % Alumatrane Dimer 2
5 mole % Diethyl Ether
CDCl3
400 MHz
OMe OH
CO2Me
7.318
7.299
7.268
7.248
7.229
6.966
6.947
6.929
6.875
6.854
5.287
3.795
3.708
3.600
1.154
1.112
1.01
1.04
1.01
1.03
1.00
3.15
3.13
0.98
3.00
3.12
ppm
13
12
11
10
9
8
7
6
5
4
3
2
1
0

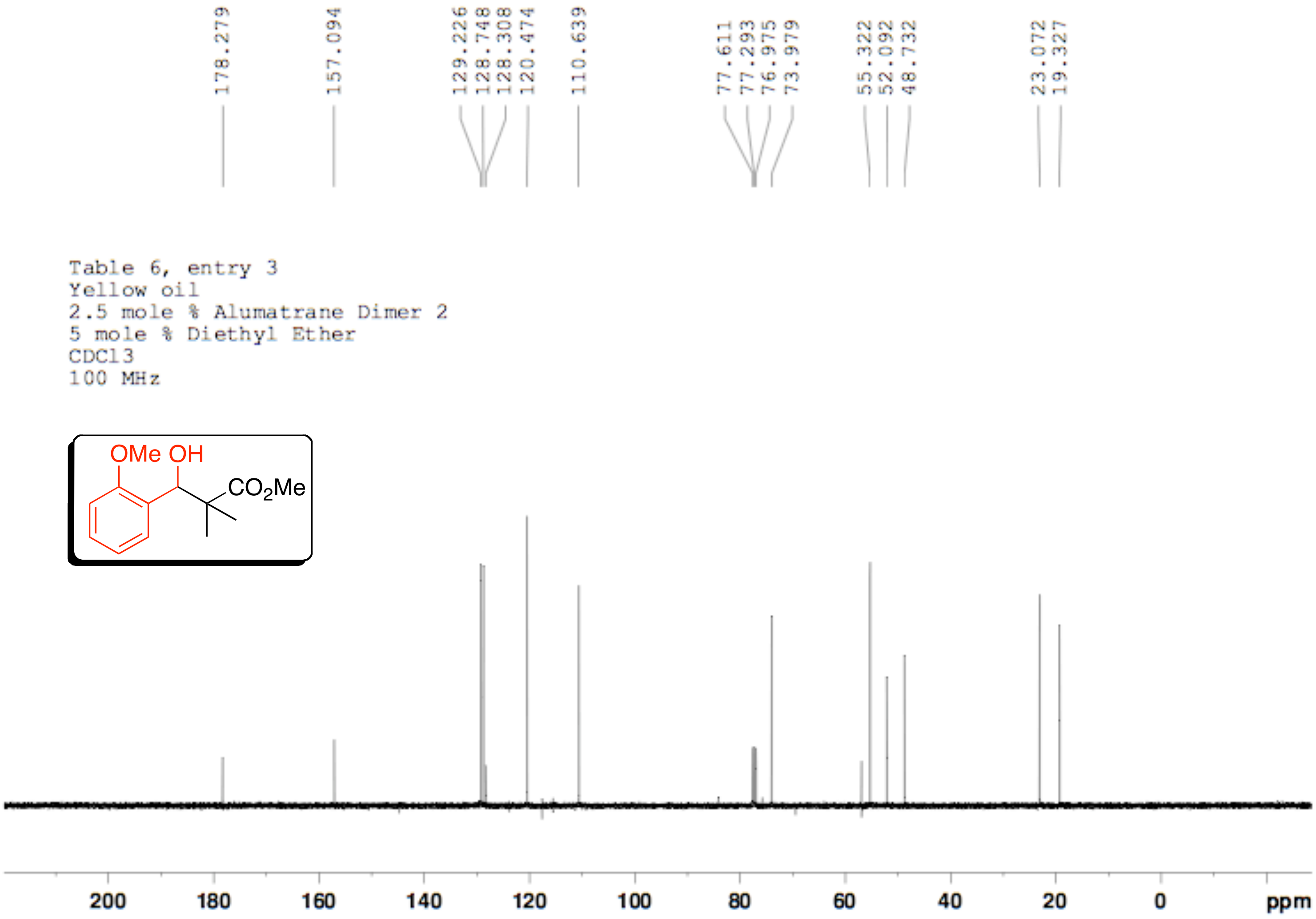
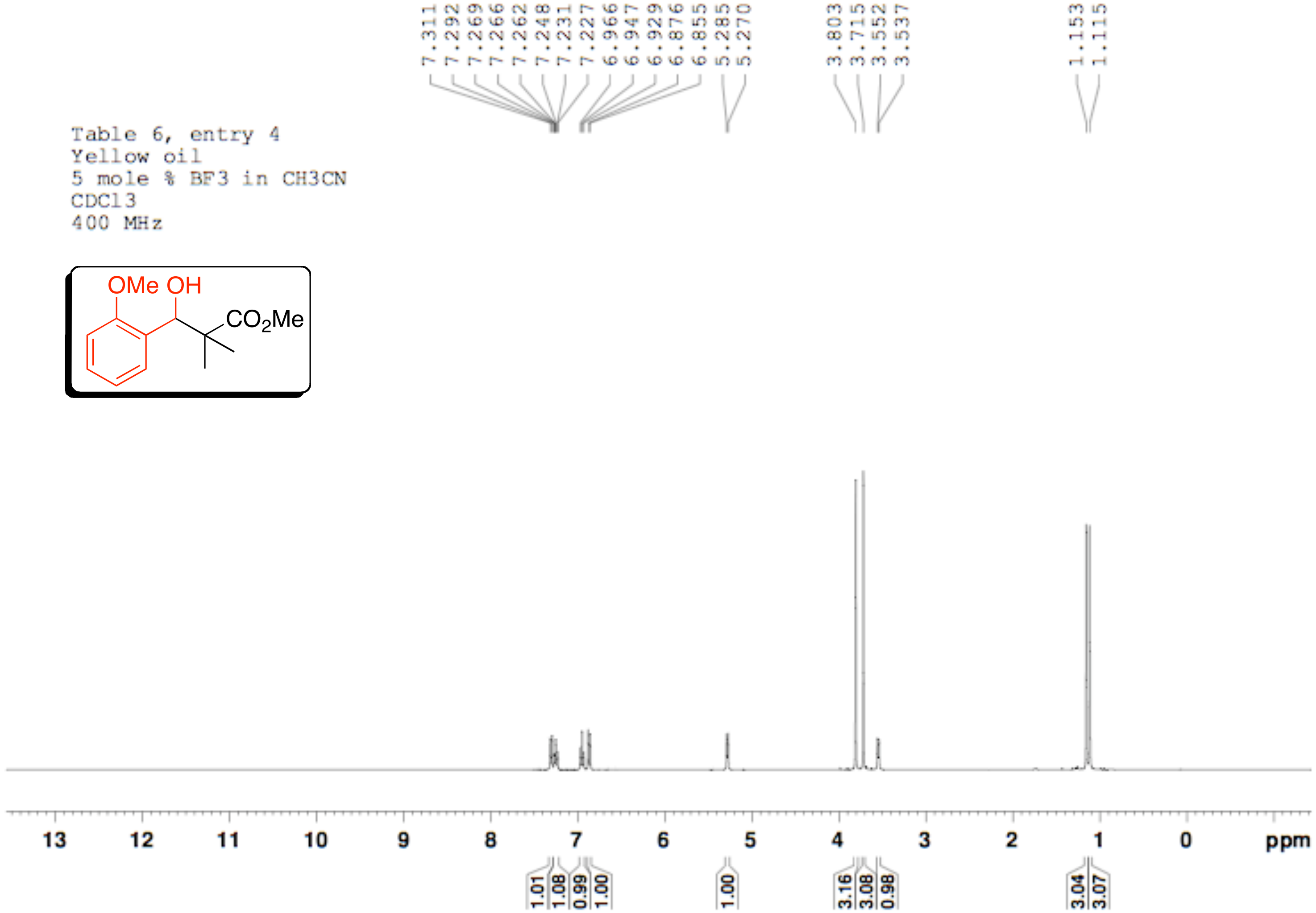
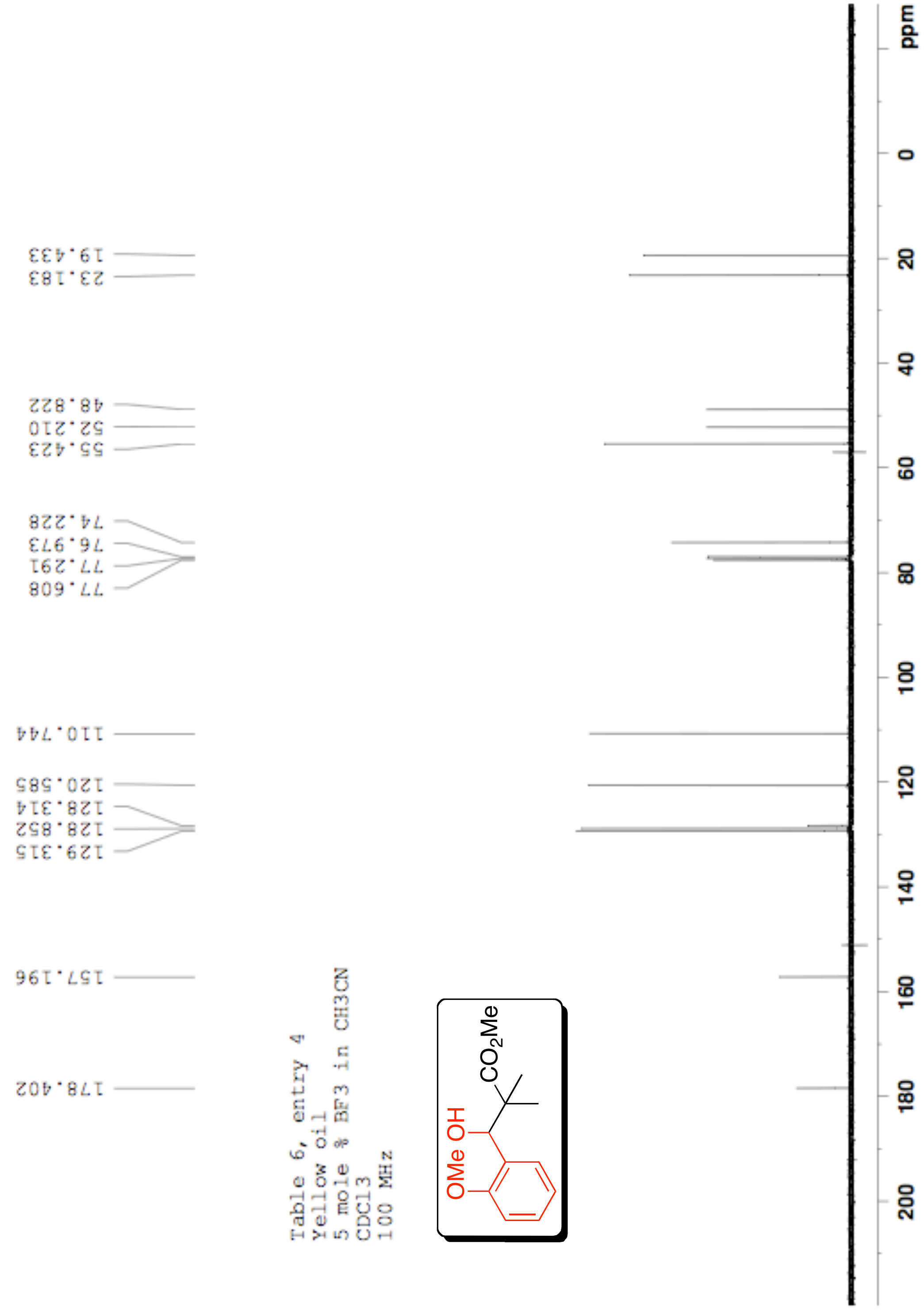


Table 6, entry 3
Yellow oil
2.5 mole % Alumatrane Dimer 2
5 mole % Diethyl Ether
CDCl3
100 MHz

Table 6, entry 4
Yellow oil
5 mole % BF3 in CH3CN
CDCl3
400 MHz




19.433
23.183
48.822
52.210
55.423
74.228
76.973
77.291
77.608
110.744
120.585
128.314
128.852
129.315
157.196
178.402
Table 6, entry 4
Yellow oil
5 mole % BF3 in CH3CN
CDCl3
100 MHz
OMe OH
CO2Me
ppm
0
20
40
60
80
100
120
140
160
180
200

APPENDIX E

CHAPTER 6. Supplementary Information

Experimental Procedures

Data for compounds

^{1}H and ^{13}C NMR spectra for reaction products

General

Trimethylsiloxy-4-phenyl-2-butene and 3-methyl-1-(trimethylsiloxy)cyclohexene were prepared as described previously [1]. Aryl bromides, aryl chlorides, tributyltin fluoride, ZnF_2, $Pd(OAc)_2$, $P(t\text{-}Bu)_3$, and DMF solvent (anhydrous, sure-seal) were purchased from Aldrich Chemical Co. and used as received. THF and toluene were distilled under argon from sodium/benzophenone prior to use. CsF (Aldrich Chemical Co.) was ground to a fine powder using a mortar and pestle and then dried under vacuum at 100 °C overnight ^{1}H NMR spectra were recorded at 300 MHz and ^{13} C NMR spectra were recorded at 75.5 MHz . The products were characterized by NMR and HRMS.

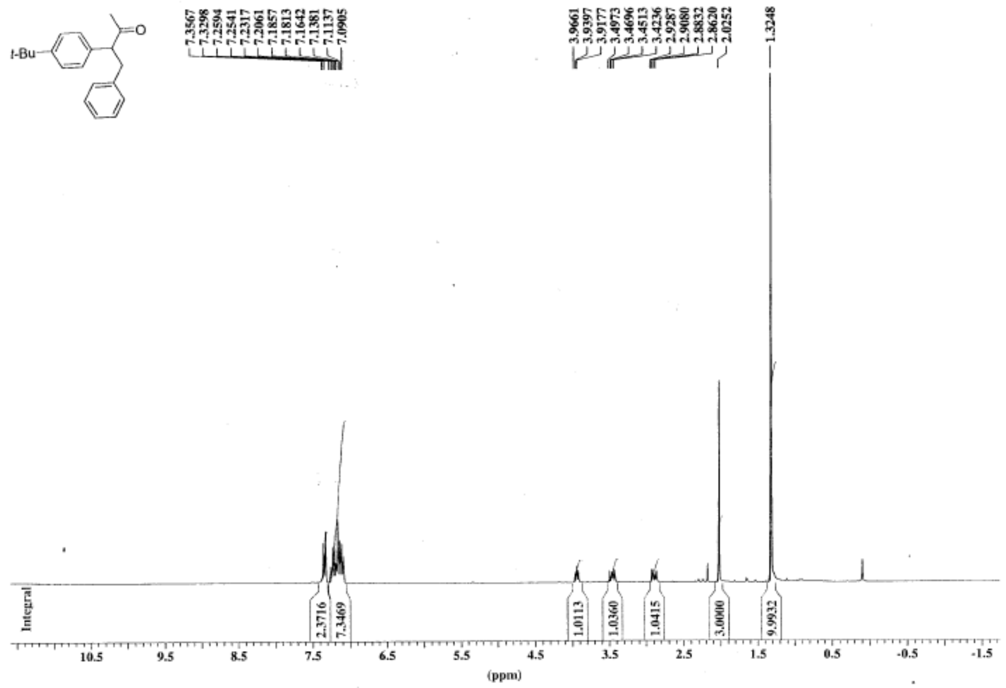
All reactions were carried out under an atmosphere of argon in a Schlenk tube equipped with a screw cap. Products were isolated by column chromatography on silica gel and isolated yields are the average of two runs.

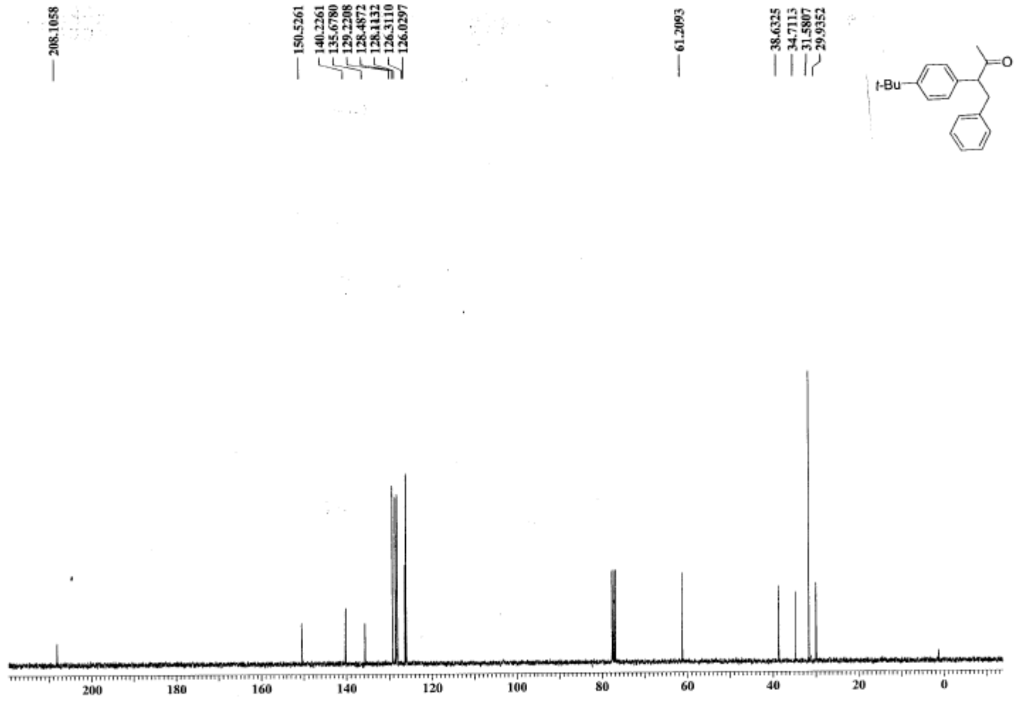
Palladium catalyzed coupling reaction of Silyl enol ethers with aryl halides

General procedure. In a glove box, a Schlenk tube equipped with a stir bar was charged with $Pd(OAc)_2$ (0.015 mmol), CsF (0.700 mmol) and Bu_3SnF (0.700 mmol). The tube was fitted with a rubber septum and removed from the glove box. Two mL of toluene, $P(t\text{-}Bu)_3$ (0.027 mmol) in a stock solution of toluene (0.3-0.4 mL), a solution of aryl halide (0.50 mmol) in a stock solution of toluene (0.5-0.6 mL) and silyl enol ether (0.700 mmol) were added in turn to the Schlenk tube through the rubber septum using syringes, and then the septum was replaced by a Teflon screw cap under an argon flow. The reaction mixture was heated to the indicated temperature over 30 minutes with stirring and allowed to stir at that temperature for the indicated time. After cooling to room temperature, the reaction mixture was diluted with 10 mL of ether or ethyl acetate, filtered through a pad of silica gel and then the filtrate was concentrated in vacuo after washing the pad of silica gel with the same solvent. The crude product was purified by column chromatography on silica gel.

3-(4-*tert*-Butylphenyl)-4-phenyl-2-butanone (Table 1, entry 8). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 1-bromo-4-*tert*-butylbenzene (109 mg, 0.501 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol). The reaction mixture was purified by column chromatography on silica gel (2 % ethyl acetate in hexanes) to afford 137 mg (98%) of the desired product as a colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34 (d, J = 8.07 Hz, 2H), 7.25-7.09 (m, 7H), 3.94 (t, J = 7.26 Hz, 1H), 3.46(dd, J = 13.8 Hz, J=8.31 Hz, 1H), 2.89 (dd, J = 13.7Hz, J=6.21 Hz, 1H), 2.02 (s, 3H) 1.32 (s, 9 H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ 208.1, 150.5, 140.2, 135.6, 129.2, 128.5, 128.1, 126.3, 126.0, 61.2, 38.6, 34.7, 31.6, 29.9. HR MS (EI) Calcd for $C_{20}H_{24}O$: 280.18272. Found m/e $(M)^+$ 280.18328.

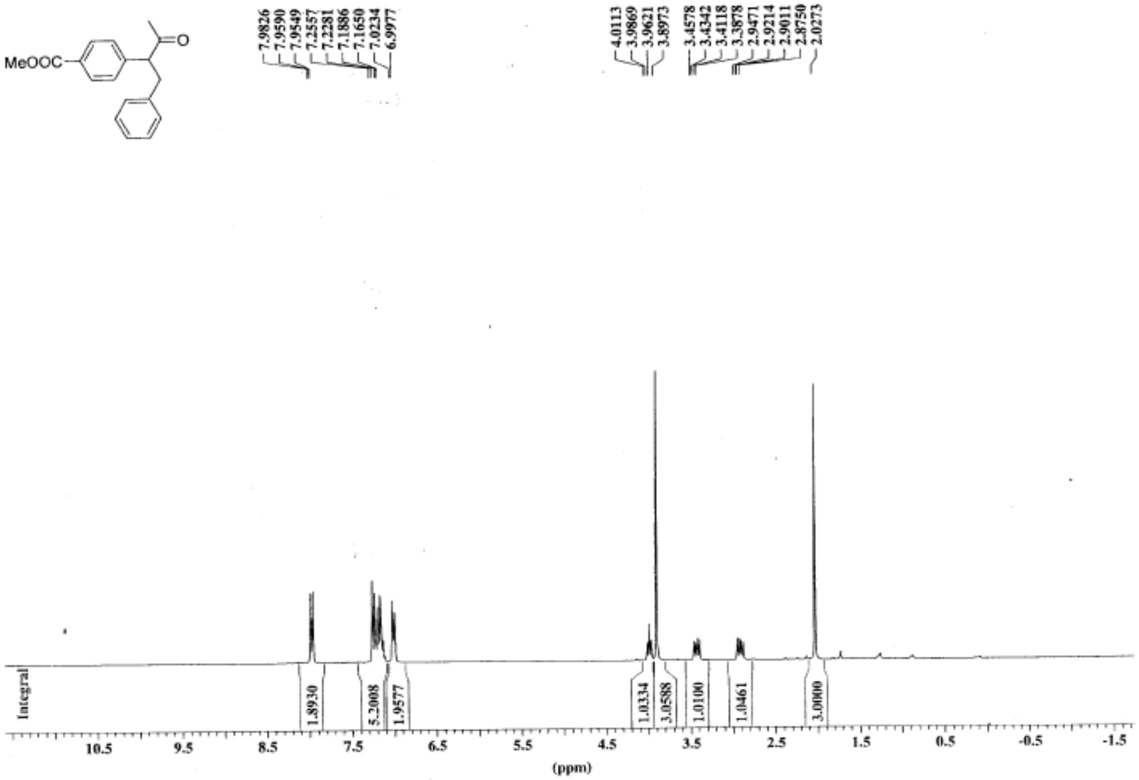


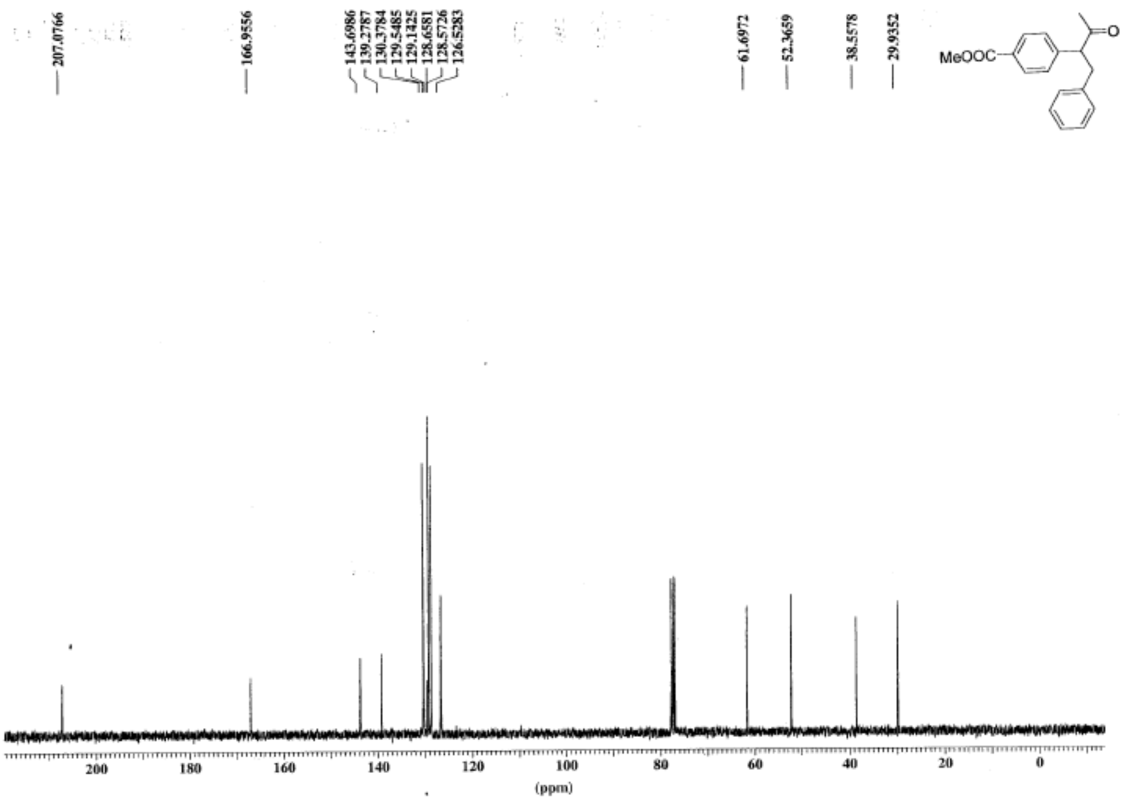


3-(4-Carboxyphenyl)-4-phenyl-2-butanone (Table 2, entry 1). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), methyl-4-

chlorobenzoate (86 mg, 0.499 mmol), CsF (107mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and $P(t\text{-}Bu)_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 90 °C for 17 h. The reaction mixture was purified by column chromatography on silica gel (5-10 % ethyl acetate in hexanes) to afford 126 mg (89%) of the desired product as a white solid.

^1H NMR (300 MHz, $CDCl_3$): δ 7.97 (d, J = 8.31 Hz, 2H), 7.25-7.16 (m, 5H), 7.01(d, J = 7.71 Hz, 2H), 3.98 (t, J = 7.44 Hz, 1H), 3.89 (s, 3H), 3.42(dd, J = 13.8 Hz, J = 7.2 Hz, 1H), 2.92 (dd, J = 13.8Hz, J = 7.71 Hz, 1H), 2.03 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 207.1, 166.9, 143.7, 139.2, 130.3, 129.5, 129.1, 128.6, 128.5, 126.5, 61.7, 52.3, 38.5, 29.9. HR MS (EI) Calcd for $C_{18}H_{18}O_3$: 282.12559. Found m/e $(M)^+$ 282.12587.

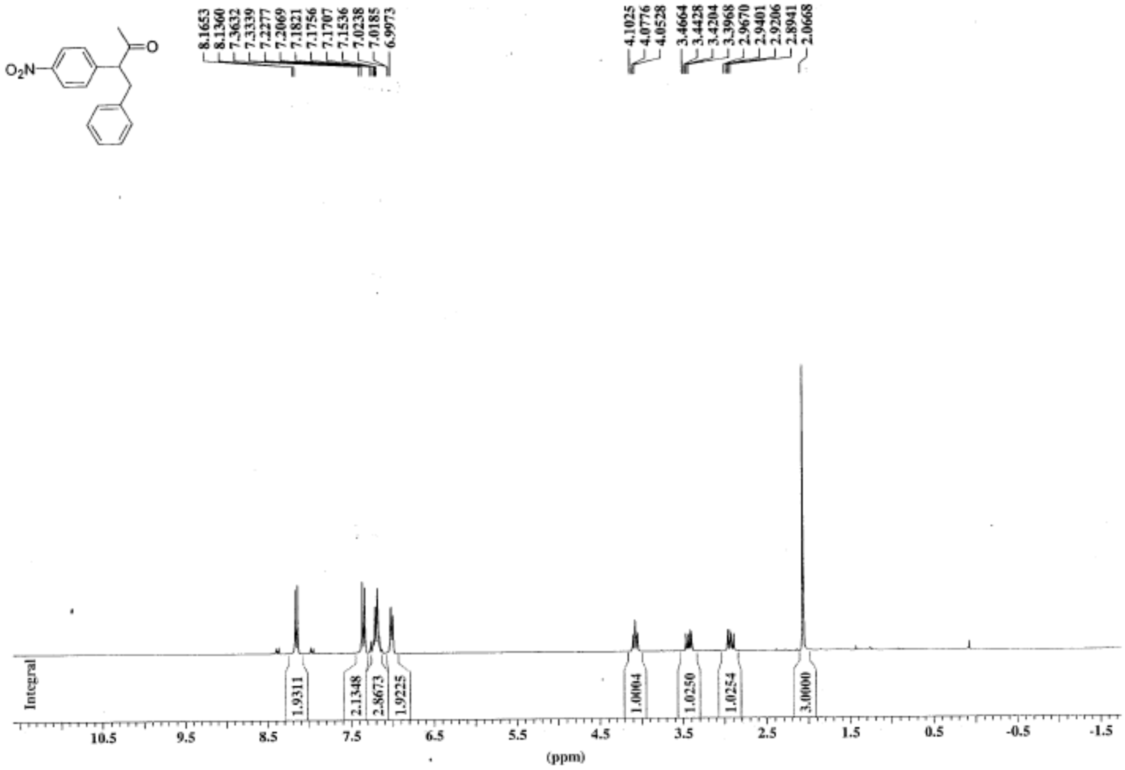


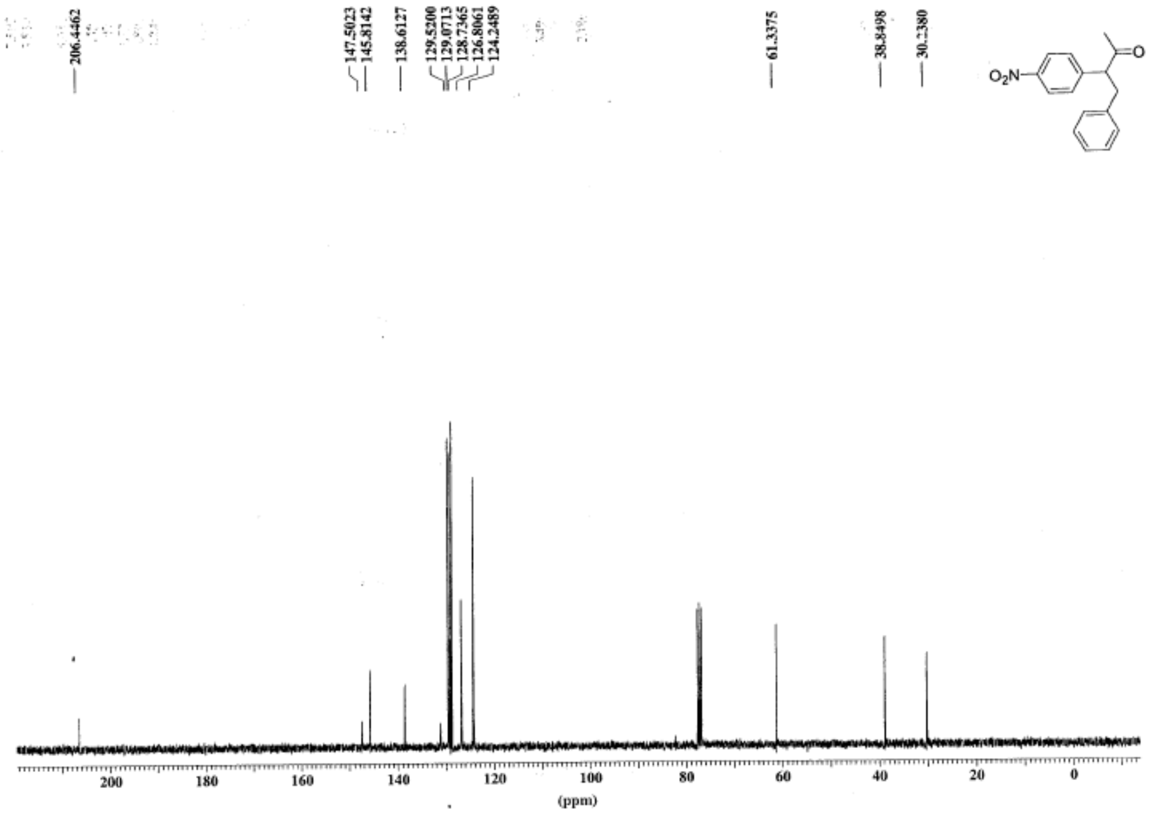


3-(4-Nitrophenyl)-4-phenyl-2-butanone (Table 2, entry 2). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 1-bromo-4-nitrobenzene (102 mg, 0.500 mmol), CsF (107mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ ((5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 14 h. The reaction mixture was purified by column chromatography on silica gel (5-10 % ethyl acetate in hexanes) to afford 113 mg (84%) of the desired product as a pale yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15 (d, J = 8.79 Hz, 2H), 7.34 (d, J = 8.79 Hz, 2H), 7.22-7.15 (m, 3H), 7.02-6.99(m, 2H), 4.07 (t, J = 7.47 Hz, 1H), 3.43 (dd, J = 13.8 Hz, J = 7.08Hz, 1H), 2.93(dd, J = 13.92 Hz, J = 8.07 Hz, 1H), 2.06 (s, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ

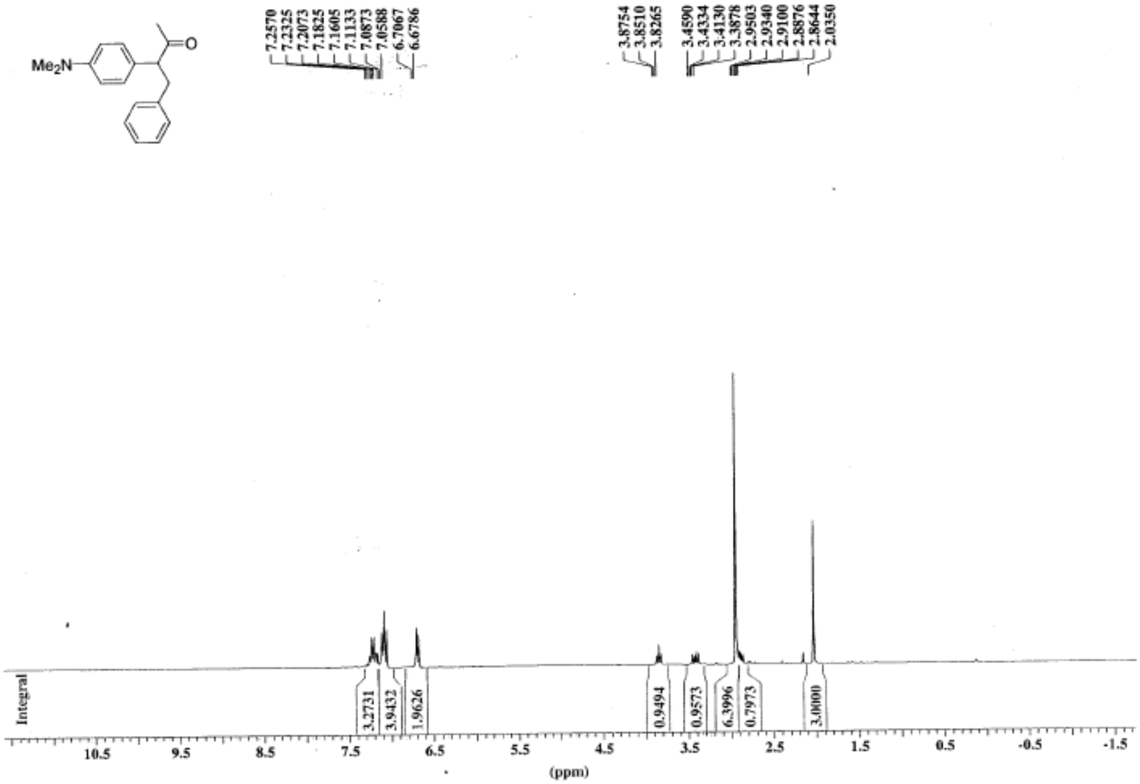
206.4, 147.5, 145.8, 138.6, 129.5, 129.0, 128.7, 126.8, 124.2, 61.3, 38.8, 30.2 HR MS (EI) Calcd for $C_{16}H_{15}NO_2$: 269.101519. Found m/e $(M)^+$ 269.10545.

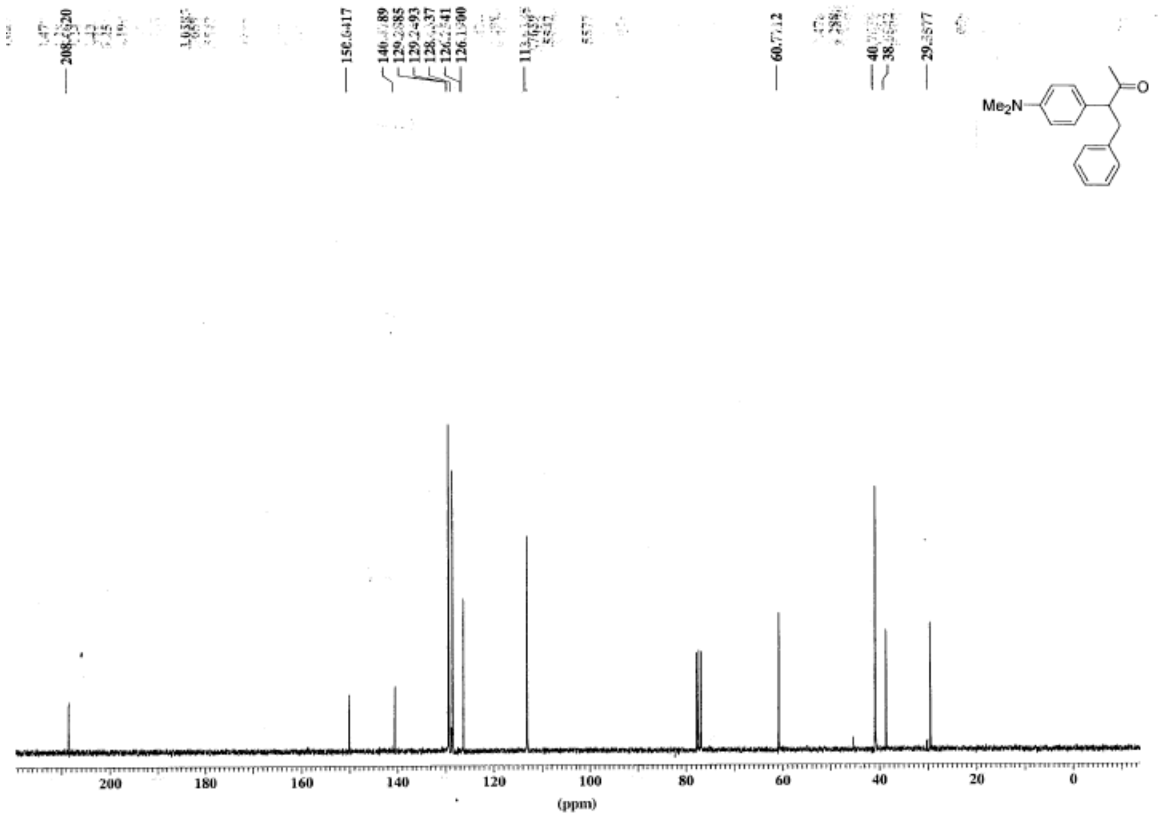




3-(4-N,N-dimethylaminophenyl)-4-phenyl-2-butanone (Table 2, entry 3). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 4-bromo-N,N-dimethylaniline (103 mg, 0.499 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and $P(t\text{-}Bu)_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 12 h. The reaction mixture was purified by column chromatography on silica gel (5 % ethyl acetate in hexanes) to afford 129 mg (96%) of the desired product as an off-white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25-7.16 (m, 3H), 7.11-7.05 (m, 4H), 6.69 (d, J = 8.43 Hz, 2H), 3.85 (t, J = 7.35 Hz, 1H), 3.42 (dd, J = 13.8 Hz, J=7.68Hz, 1H), 2.95-2.86(overlap, 7H), 2.03 (s, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ 208.4, 150.0, 140.4, 129.28, 129.24, 128.4, 126.2, 113.0, 60.7, 40.7, 38.5, 29.5. HR MS (EI) Calcd for $C_{18}H_{21}NO$: 267.16231. Found m/e $(M)^+$ 267.16265.

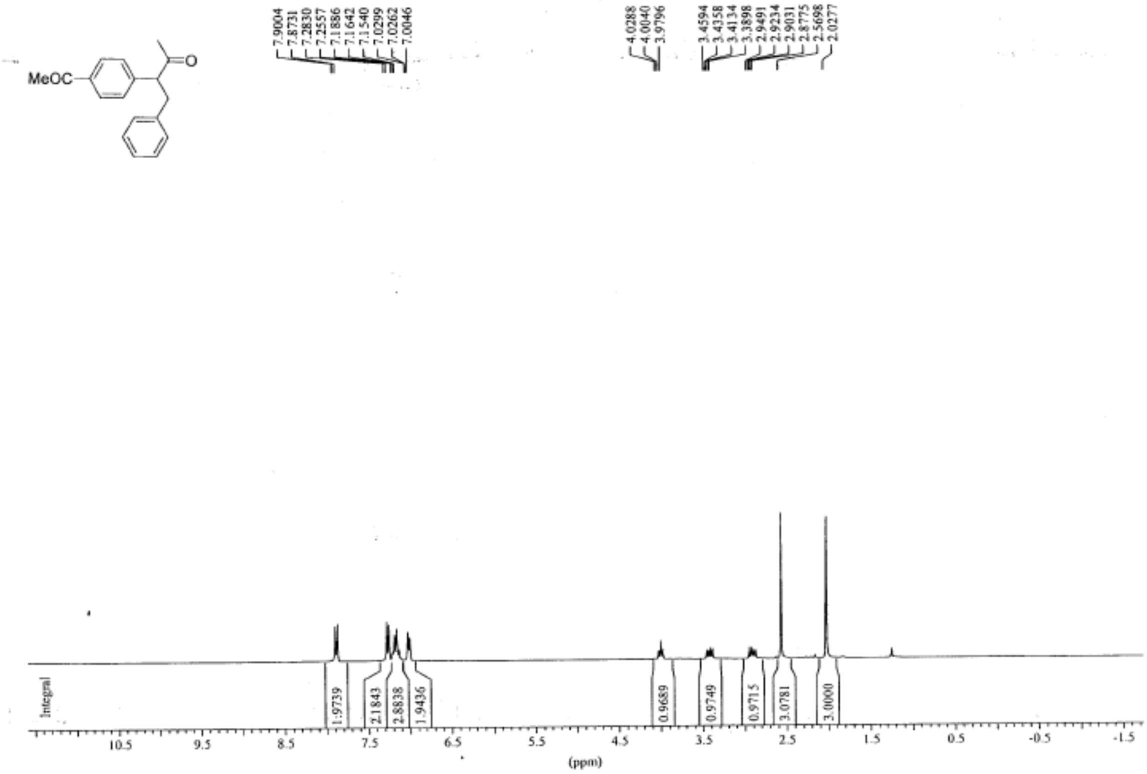


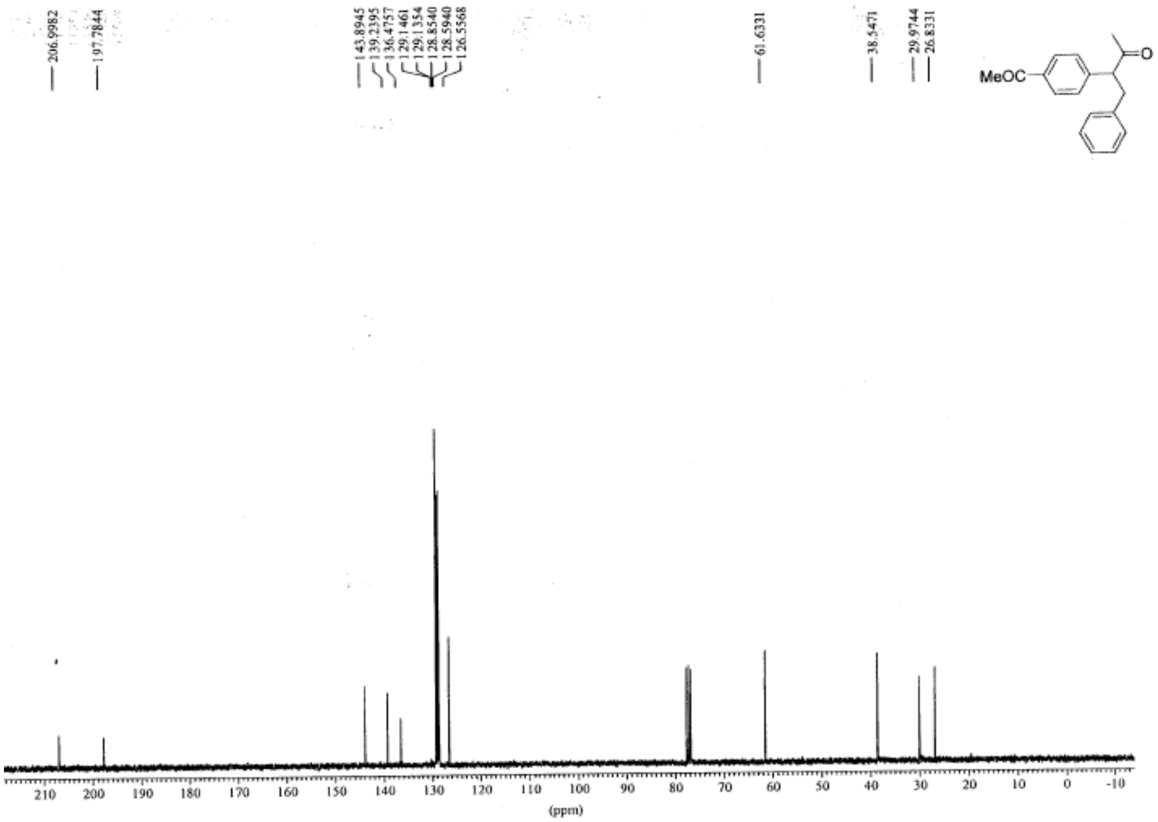


3-(4-Acetylphenyl)-4-phenyl-2-butanone (Table 2, entry 4). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 4'-bromoacetophenone (101mg, 0.497 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 12 h. The reaction mixture was purified by column chromatography on silica gel (10 % ethyl acetate in hexanes) to afford 129 mg (97%) of the desired product as a white solid.

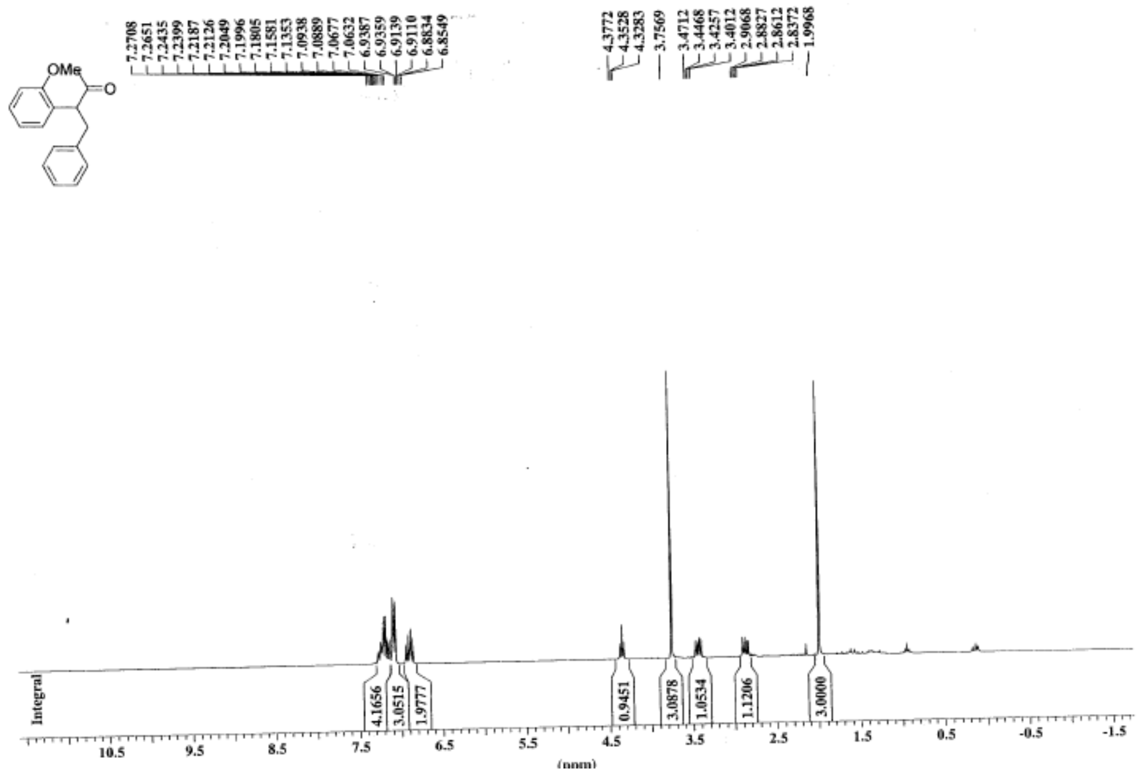
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88 (d, J = 9.27 2H), 7.27 (d, J = 8.19 Hz, 2H), 7.18-7.15 (m, 3), 7.02-7.00 (m, 2H), 4.00 (t, J = 7.44 Hz, 1H), 3.42 (dd, J = 13.8 Hz, J = 7.08Hz, 1H), 2.91 (dd, J = 13.8 Hz, J=7.71, 1H), 2.57 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$):

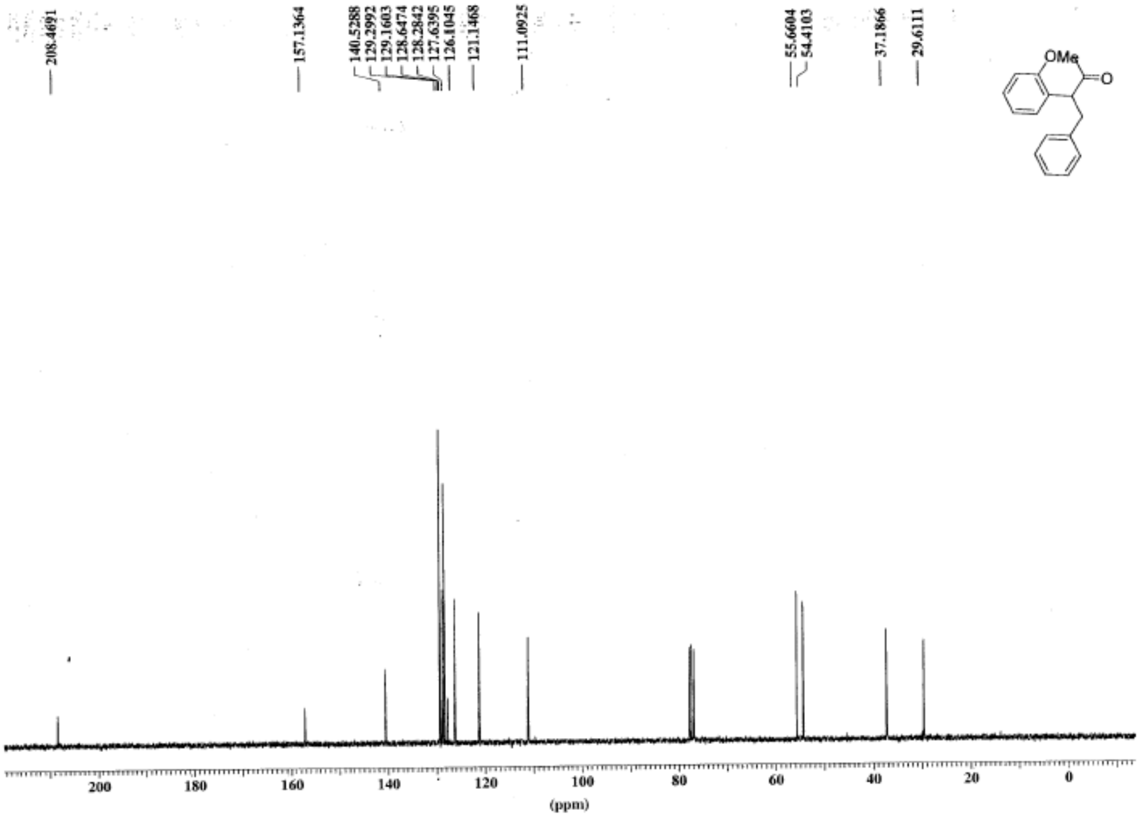
δ 206.9, 197.8, 143.9, 139.2, 136.4, 129.15, 129.13, 128.8, 128.6, 126.6 61.6, 38.5, 29.9, 26.8. HR MS (EI) Calcd for $C_{18}H_{18}O_2$: 266.13068. Found m/e $(M)^+$ 266.13117.





3-(2-Methoxyphenyl)-4-phenyl-2-butanone (Table 2, entry 5). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 2-bromoanisole (96 mg, 0.498 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 19 h. The reaction mixture was purified by column chromatography on silica gel (5 % ethyl acetate in hexanes) to afford 124 mg (97%) of the desired product as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27-7.13 (m, 4H), 7.09-7. 06 (m, 3H), 6.93-6.85 (m, 2H), 4.35 (t, J = 7.35 Hz, 1H), 3.75 (s, 3H), 3.43 (dd, J = 13.65 Hz, J = 7.32Hz, 1H), 2.87 (dd, J = 13.68 Hz, J = 7.2, 1H), 1.99 (s, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): 208.5, 157.1, 140.5, 129.3, 129.1, 128.6, 128.2, 127.6, 126.1, 121.1, 111.1, 55.6, 54.4, 37.1, 29.6. δ. . HR MS (EI) Calcd for $C_{17}H_{19}O_2$: 254.13068. Found m/e $(M)^+$ 254.13112.

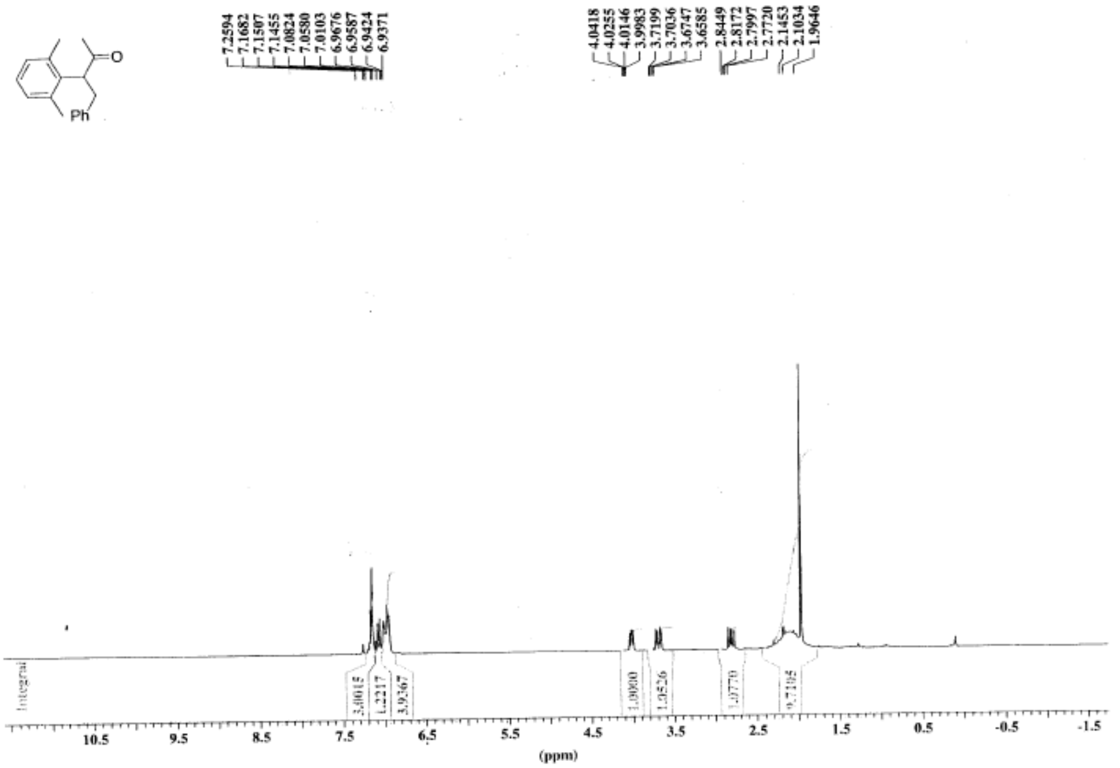


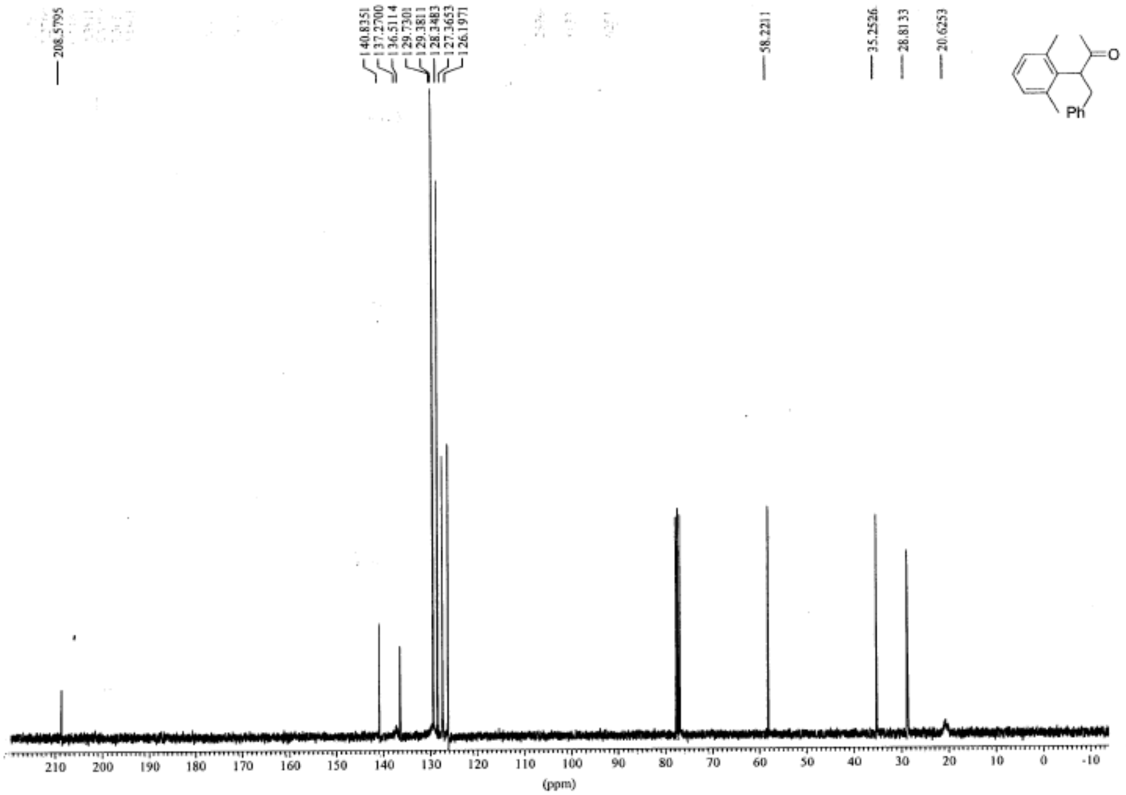


3-(2,6-Dimethylphenyl)-4-phenyl-2-butanone (Table 2, entry 6). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 2-bromo-*m*-xylene (94 mg, 0.492 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and $P(t\text{-}Bu)_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 20 h. The reaction mixture was purified by column chromatography on silica gel (3 % ethyl acetate in hexanes) to afford 117 mg (93%) of the desired product as a colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16-7.14 (m, 3H), 7.08-7. 01 (m, 1H), 6.96-6.93 (m, 4H), 4.02 (dd, J = 8.16 Hz, J = 4.89 Hz, 1H), 3.69 (dd, J = 13.56 Hz, J = 4.89 Hz, 1H), 2.80 (dd, J = 13.65 Hz, J = 8.31Hz, 1H), 2.1 (b, 6H), 1.96 (s, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ

208.5, 140.8, 136.5, 129.3, 128.3, 127.3, 126.2, 58.2, 35.2, 28.81. HR MS (EI) Calcd for $C_{18}H_{20}O$: 252.15142. Found m/e $(M)^+$ 252.15174.

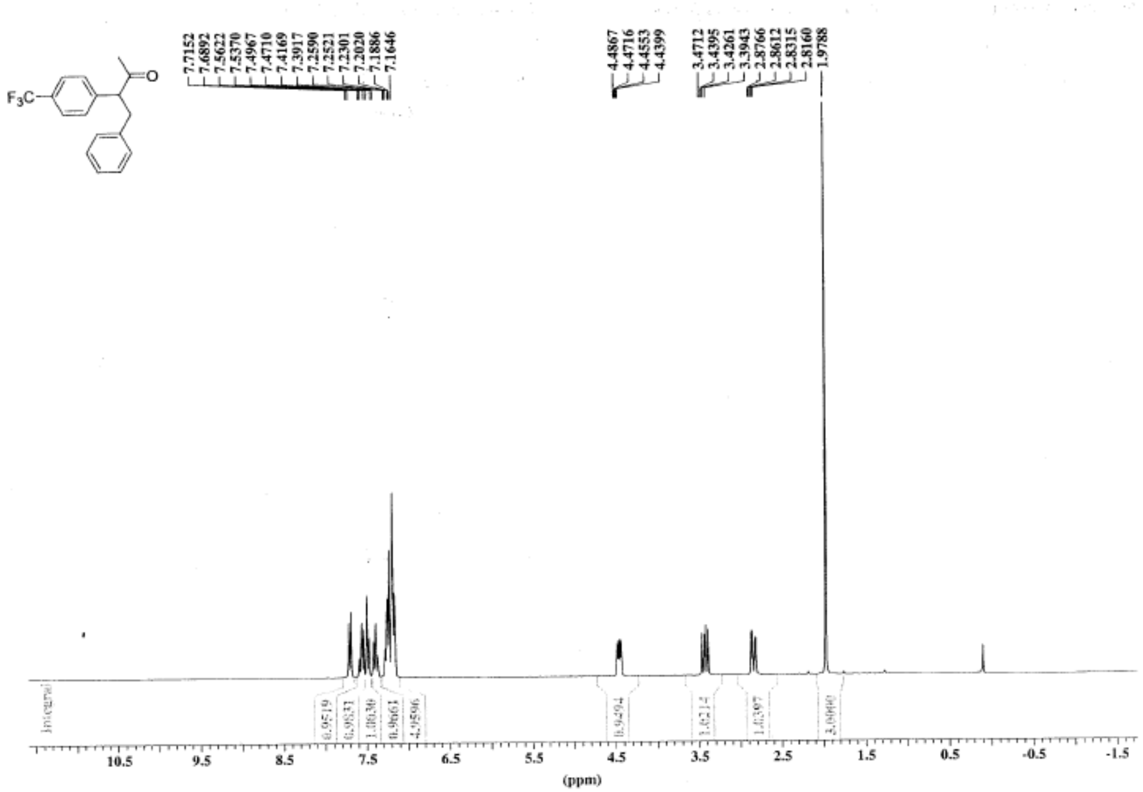


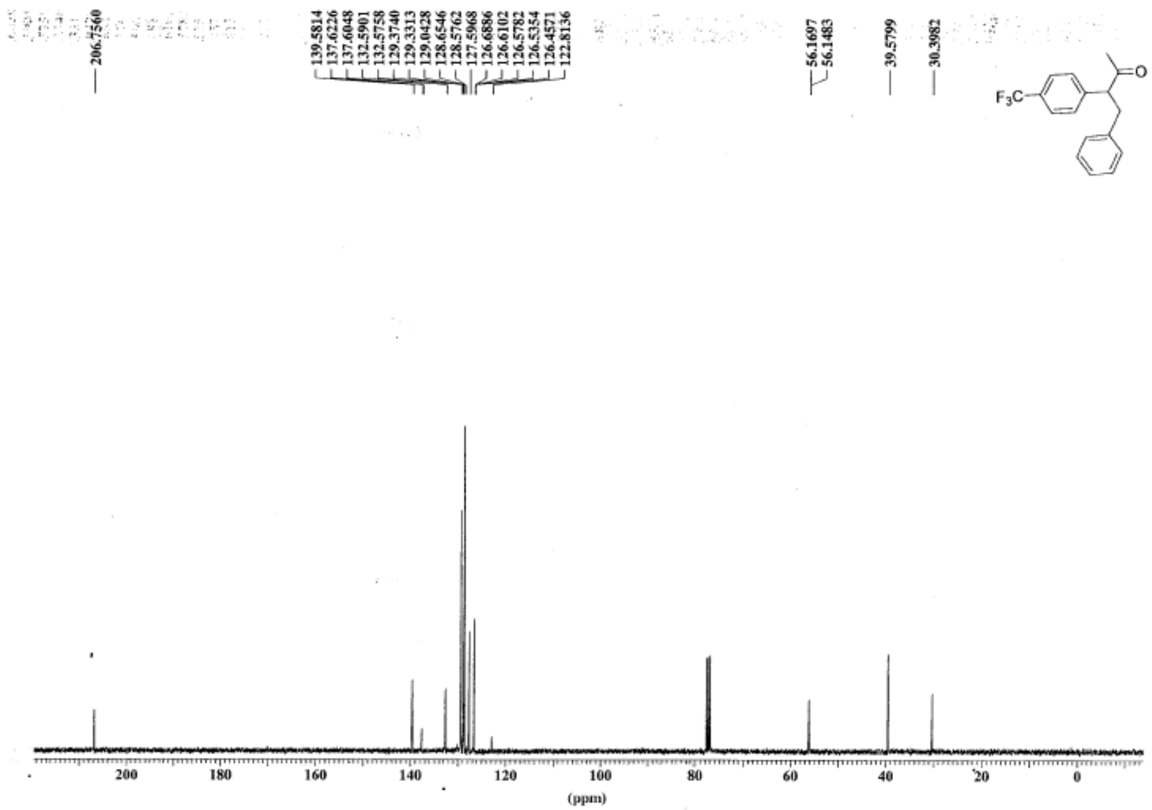


3-(4-Trifluoromethylphenyl)-4-phenyl-2-butanone (Table 2, entry 7). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 4-bromobenzotrifluoride (114 mg, 0.502 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 16 h. The reaction mixture was purified by column chromatography on silica gel (3 % ethyl acetate in hexanes) to afford 133 mg (91%) of the desired product as a pale yellow liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, J = 7.8 Hz, 1H), 7.56-7.49 (m, 1H), 7.47-7.39 (m, 3H), 7.25-7.16 (m, 5H), 4.46 (dd, J = 9.45 Hz, J = 4.89 Hz, 1H), 3.43 (dd, J = 13.53 Hz, J = 9.51 Hz, 1H), 2.84 (dd, J = 13.53 Hz, J = 4.62 Hz, 1H), 1.97 (s, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ 206.7, 139.6, 137.62, 137.60, 132.59, 132.57, 129.37, 129.33, 129.04, 128.65, 128.57, 127.59, 126.68, 126.61, 126.57, 126.53, 126.45, 122.81, 56.17, 56.14, 39.58, 30.39.

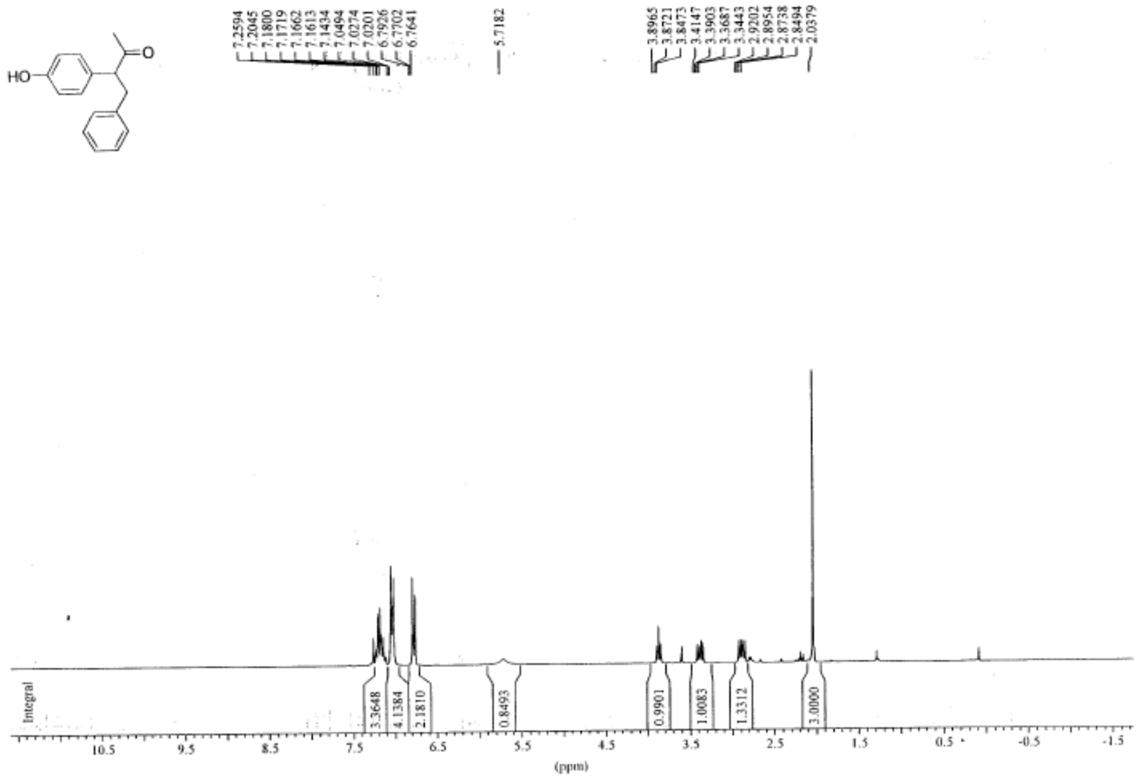
HR MS (EI) Calcd for $C_{17}H_{15}F_3O$: 292.10750. Found m/e $(M)^+$ 292.10793.

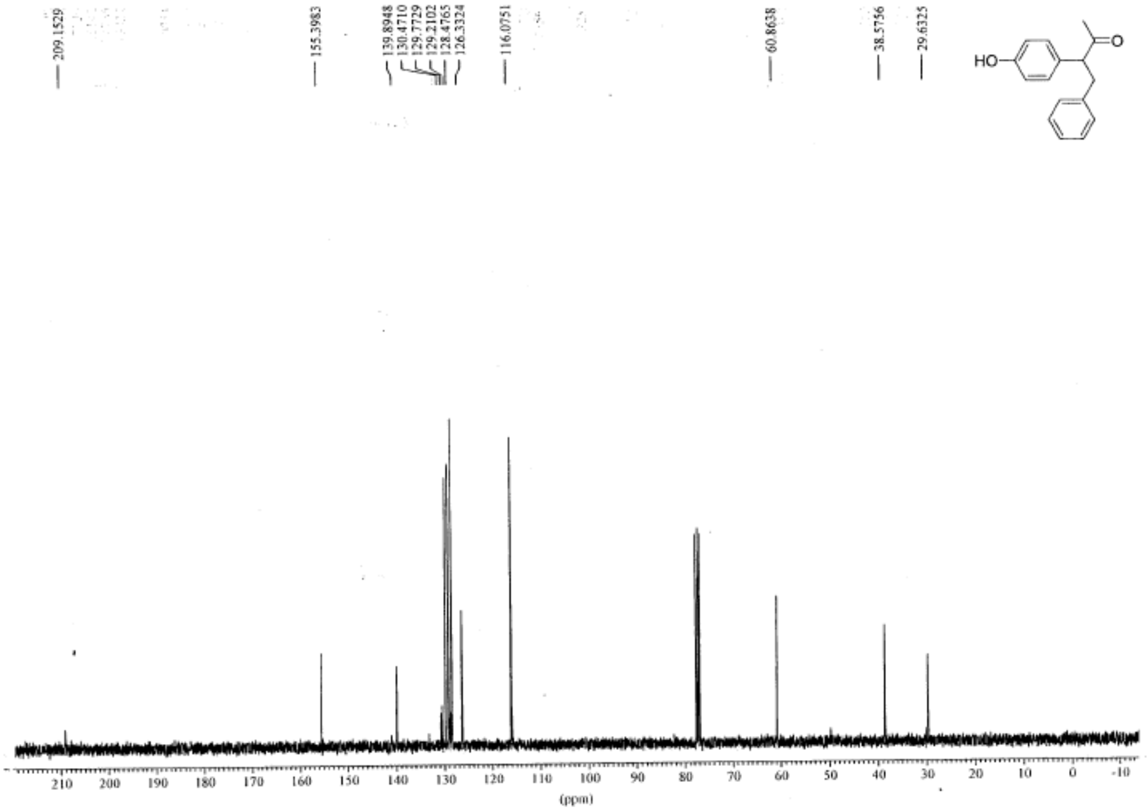




3-(4-Hydroxyphenyl)-4-phenyl-2-butanone (Table 2, entry 8). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 4-bromophenol (87 mg, 0.498 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 19 h. The reaction mixture was purified by column chromatography on silica gel (chloroform) to afford 66 mg (55 %) of the desired product as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20-7.14 (m, 3H), 7.05-7.02 (m, 4H), 6.79-6.76 (m, 2H), 5.72 (b, 1H), 3.87(t, J = 7.44 Hz, 1H), 3.38 (dd, J = 14.76 Hz, 7.32 Hz 1H), 2.88 (dd, J = 13.92 Hz, J = 7.44 Hz, 1H), 2.03 (s, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ 209.1, 155.39, 139.9, 130.4, 129.7, 129.2, 128.4, 126.3, 116.1, 60.8, 38.5, 29.6. HR MS (EI) Calcd for $C_{16}H_{16}O_2$: 240.11503. Found m/e $(M)^+$ 240.11528.

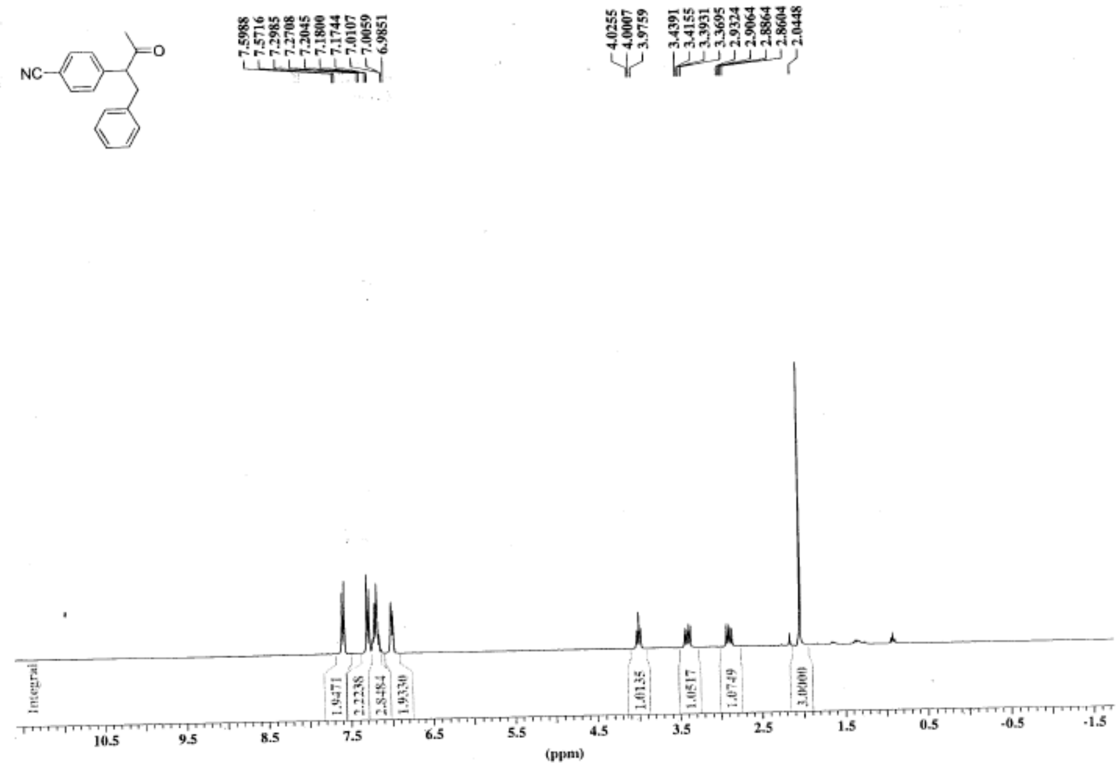


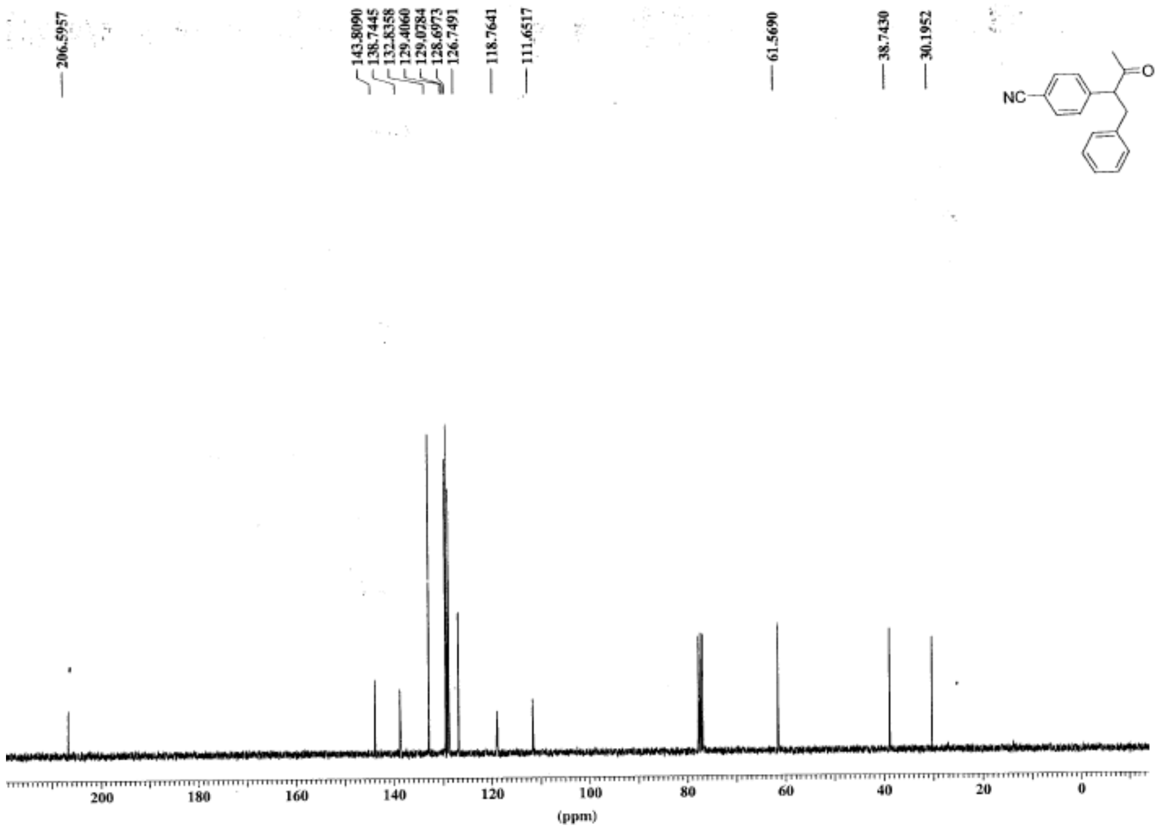


3-(4-Cyanophenyl)-4-phenyl-2-butanone (Table 2, entry 9). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 4-chlorobenzonitrile (67 mg, 0.482 mmol) , CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 90 °C for 16 h. The reaction mixture was purified by column chromatography on silica gel (5-10 % ethyl acetate in hexanes) to afford 99 mg (80 %) of the desired product as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59 (d, J = 8.19 Hz, 2H), 7.56-7.49 (m, 1H), 7.28 (d, J = 8.19, 2H), 7.20-7.17 (m, 3H), 7.01-6.98 (m, 2H), 3.99 (d, J = 7.44 Hz, 1H), 3.40 (dd, J = 13.8 Hz, J = 7.2 Hz, 1H), 2.89 (dd, J = 13.92 Hz, J = 7.92 Hz, 1H), 2.04 (s, 3H). ^{13} C NMR (75.5

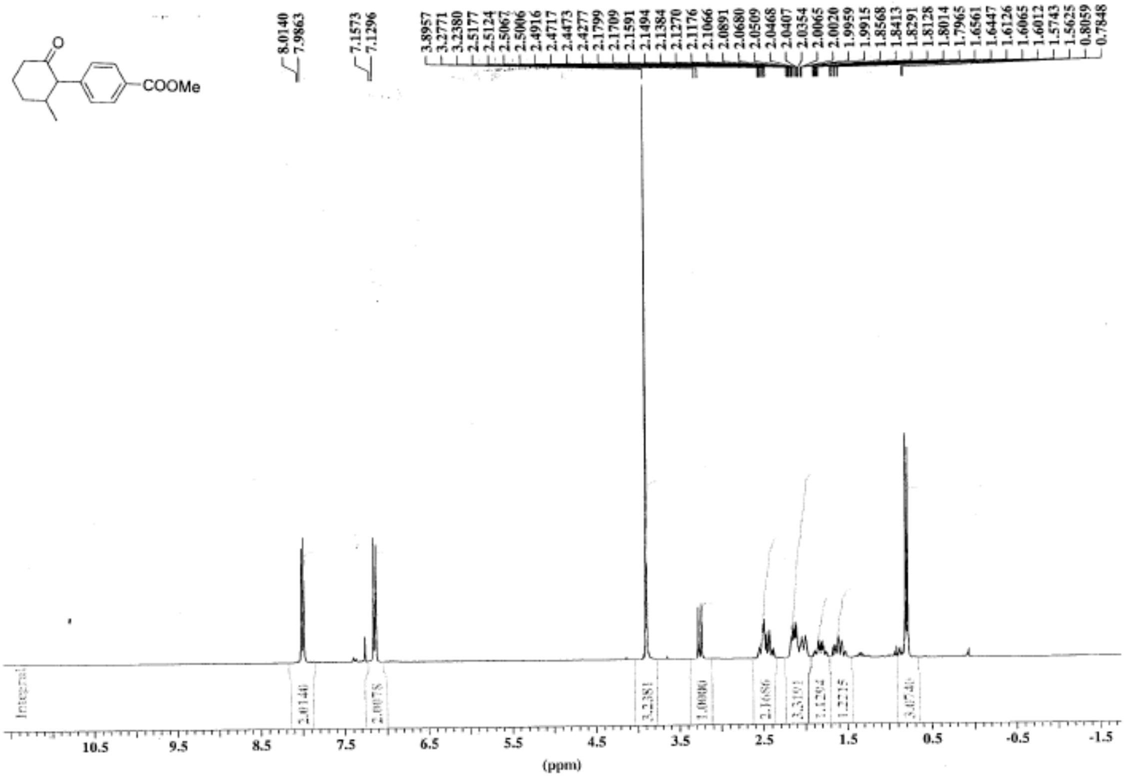
MHz, $CDCl_3$): δ 206.5, 143.8, 138.7, 132.8, 129.4, 129.0, 128.7, 126.7, 118.7, 111.6, 61.6, 38.7, 30.2. HR MS (EI) Calcd for $C_{17}H_{15}NO$: 249.11536. Found m/e $(M)^+$ 249.11576.

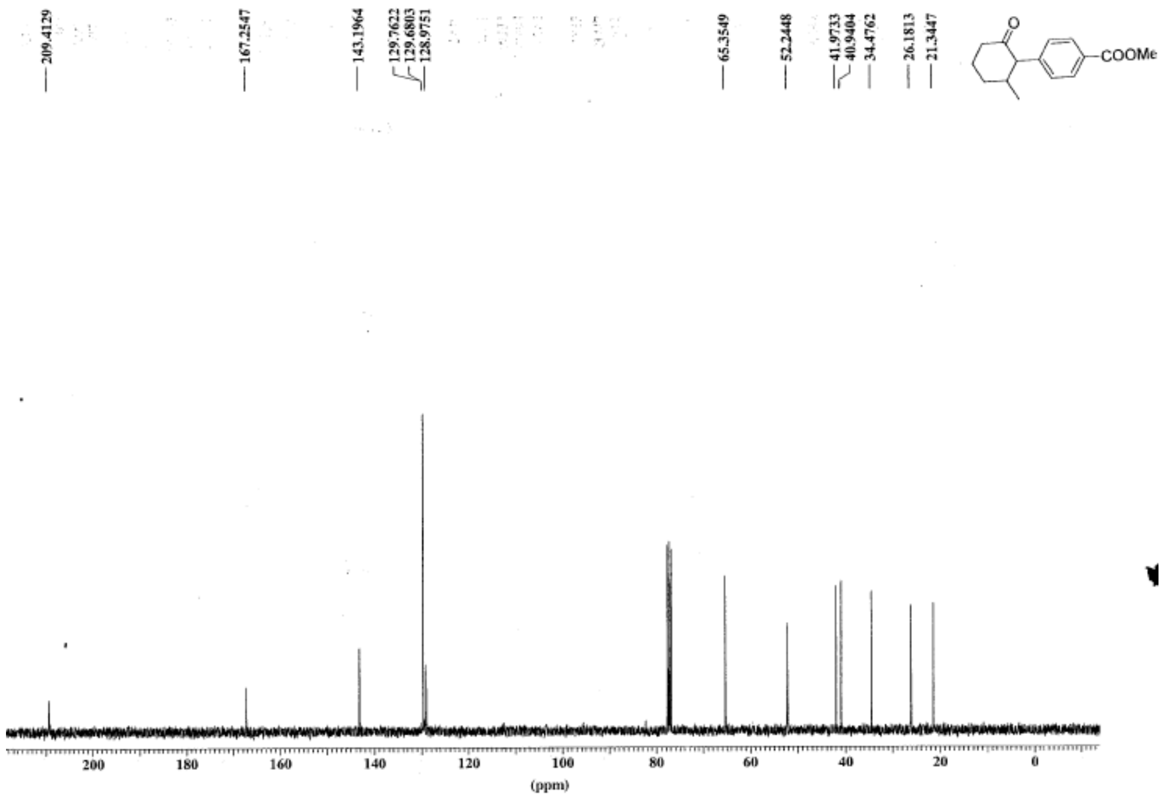




2-(4-Carboxyphenyl)-3-methyl-1-cyclohexanone (Table 2, entry 10). The general procedure was followed using 1-trimethylsiloxy-3-methyl-1-cyclohexene (129 mg, 0.700 mmol), methyl-4-chlorobenzoate (86 mg, 0.499 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and $P(t\text{-}Bu)_3$ (5.45 mg, 0.027 mmol) (5.45 mg, 0.027 mmol). The reaction was conducted at 90 °C for 16 h. The reaction mixture was purified by column chromatography on silica gel (10 % ethyl acetate in hexanes) to afford 99 mg (80 %) of the desired product as a white solid.

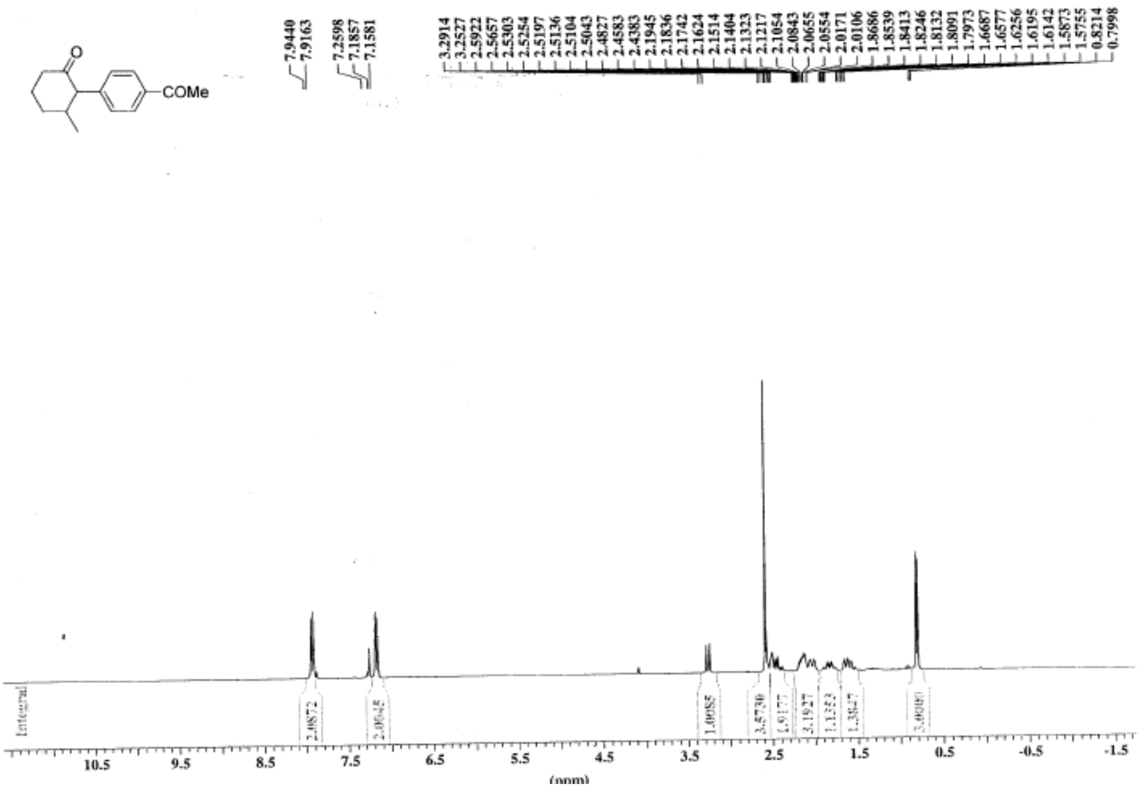
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, J = 8.31 Hz, 2H), 7.14 (d, J = 8.31, 2H), 3.89 (s, 3H), 3.25 (d, J = 11.73 Hz, 1H), 2.51-2.42 (m, 2H), 2.18-1.99 (m, 3H), 1.85-1.79 (m, 1H), 1.65-1.56 (m, 1H), 0.79 (d, J = 6.33 Hz, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ 209.4, 167.2, 143.1, 129.7, 129.6, 128.9, 65.3, 52.2, 41.9, 40.9, 34.4, 26.1, 21.3. HR MS (EI) Calcd for $C_{15}H_{18}O_3$: 246.12559. Found m/e $(M)^+$ 246.12606.

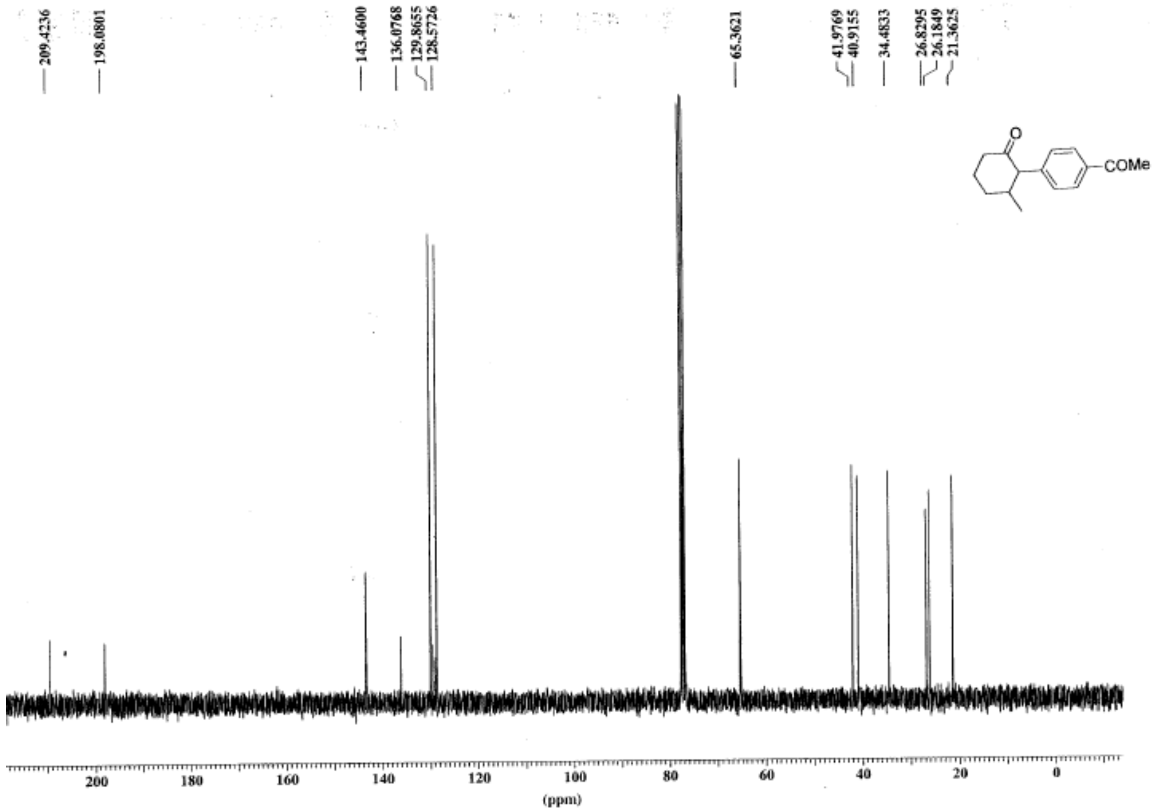




2-(4-Acetylphenyl)-3-methyl-1-cyclohexanone (Table 2, entry 11). The general procedure was followed using 1-trimethylsiloxy-3-methyl-1-cyclohexene (129 mg, 0.700 mmol), 4'-chloroacetophenone (80 mg, 0.502 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), $P(t\text{-}Bu)_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 90 °C for 17 h. The reaction mixture was purified by column chromatography on silica gel (10 % ethyl acetate in hexanes) to afford 81 mg (70 %) of the desired product as a white solid.

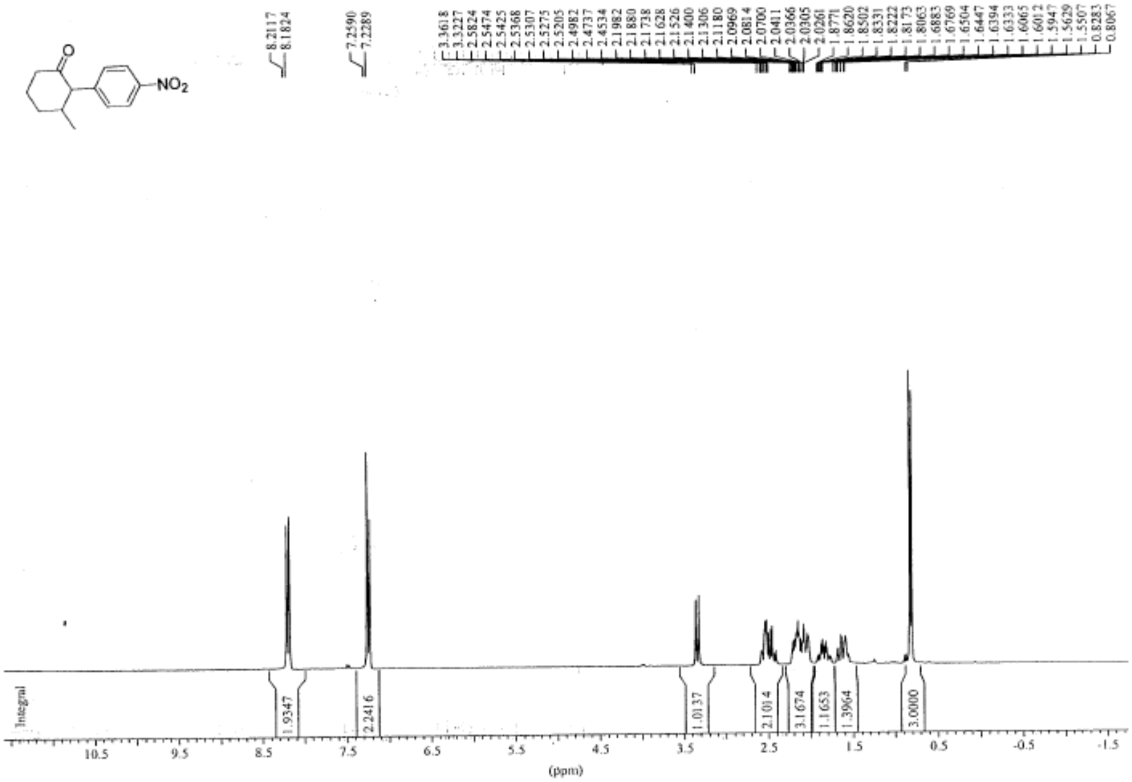
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93 (d, J = 8.31 Hz, 2H), 7.17 (d, J = 8.31, 2H), 3.27 (d, J = 11.61 Hz, 1H), 2.59 (s, 3H), 2.56-2.43 (m, 2H), 2.19-2.01 (m, 3H), 1.86-1.79 (m, 1H), 1.66-1.57 (m, 1H), 0.81 (d, J = 6.48 Hz, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 209.4, 198.1, 143.4, 136.1, 129.8, 128.6, 65.36, 41.9, 40.9, 34.4, 26.8, 26.1, 21.3. HR MS (EI) Calcd for $C_{15}H_{18}O_2$: 230.13068. Found m/e $(M)^+$ 230.13110.

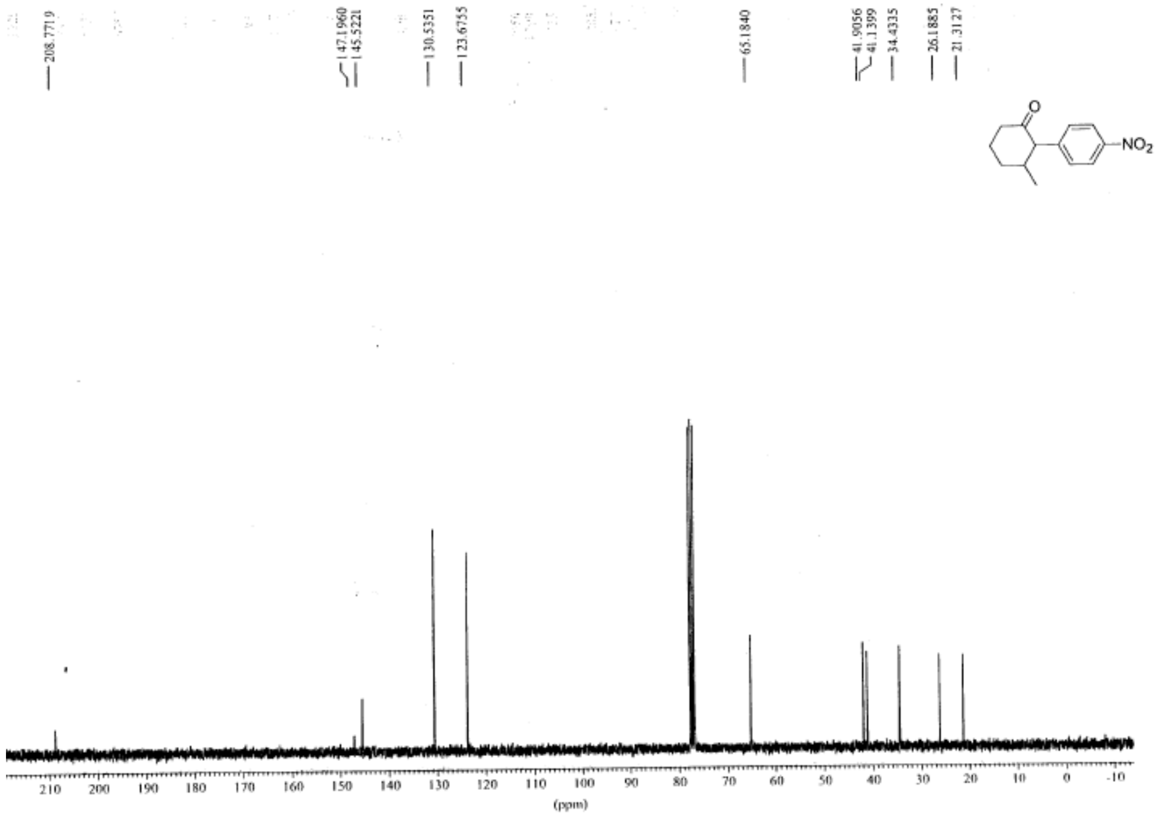




2-(4-Nitrophenyl)-3-methyl-1-cyclohexanone (Table 2, entry 12). The general procedure was followed using 1-trimethylsiloxy-3-methyl-1-cyclohexene (129 mg, 0.700 mmol), 1-chloro-4-nitrobenzene (80 mg, 0.502 mmol), CsF (107mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), $P(t\text{-}Bu)_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 90 °C for 15 h. The reaction mixture was purified by column chromatography on silica gel (10 % ethyl acetate in hexanes) to afford 98 mg (84 %) of the desired product as a white solid.

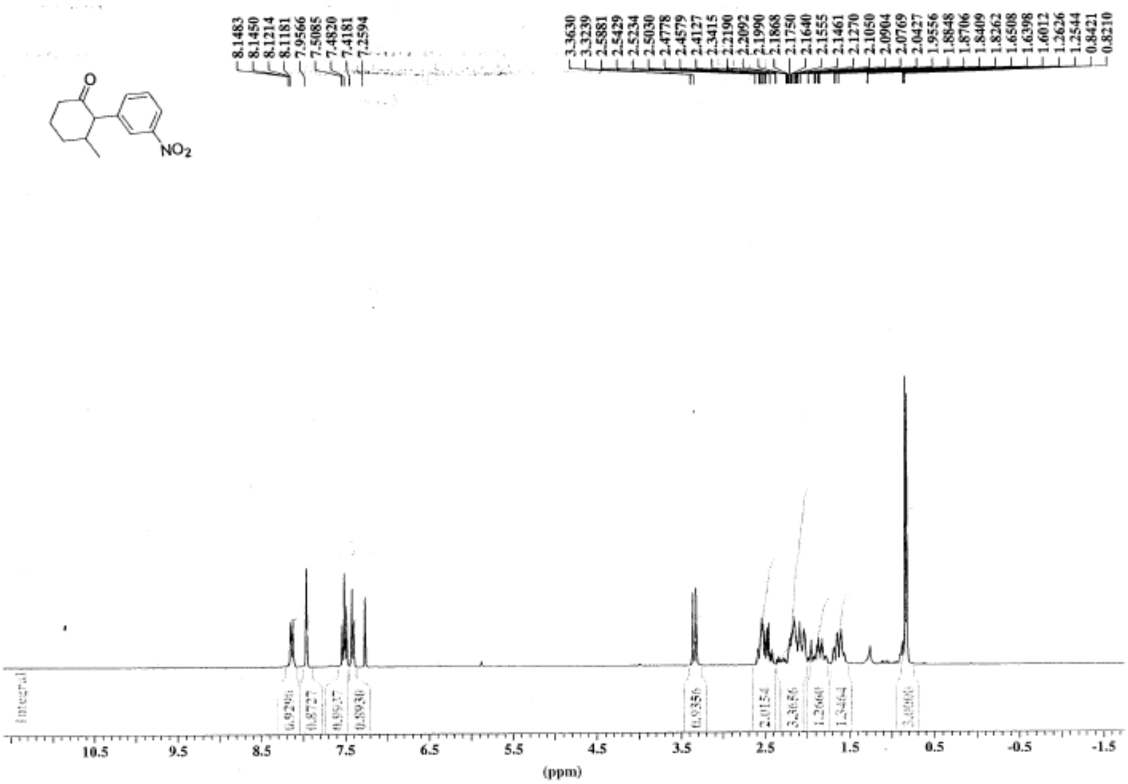
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (d, J = 8.79 Hz, 2H), 7.23 (d, J = 8.79, 2H), 3.34 (d, J = 11.73 Hz, 1H), 2.59 (s, 3H), 2.58-2.45 (m, 2H), 2.19-2.02 (m, 3H), 1.87-1.80 (m, 1H), 1.68-1.55 (m, 1H), 0.81 (d, J=6.48 Hz, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ 208.7, 147.2, 145.5, 130.5, 123.6, 65.1, 41.9, 41.1, 34.4, 26.1, 21.3. HR MS (EI) Calcd for $C_{13}H_{15}NO_3$: 233.10519. Found m/e $(M)^+$ 233.10548.

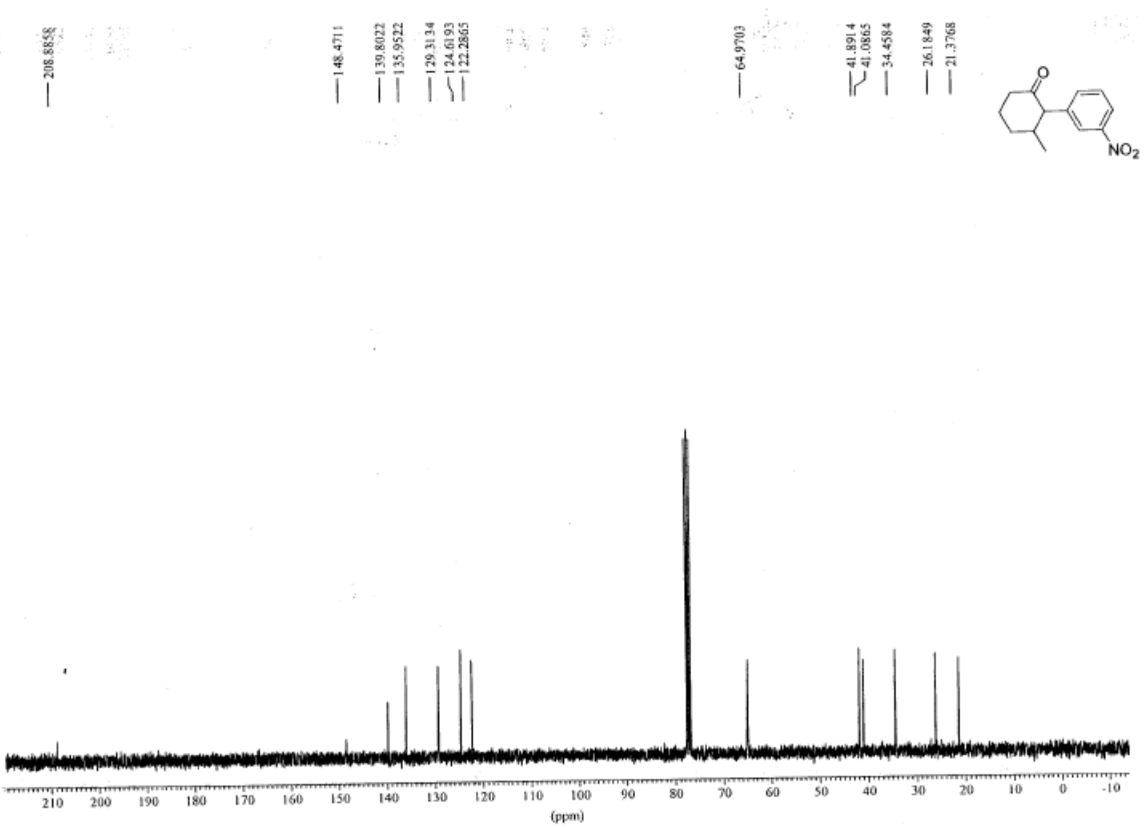




2-(3-Nitrophenyl)-3-methyl-1-cyclohexanone (Table 2, entry 13). The general procedure was followed using 1-trimethylsiloxy-3-methyl-1-cyclohexene (129 mg, 0.700 mmol), 1-chloro-3-nitrobenzene (80 mg, 0.498 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and $P(t\text{-}Bu)_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 90 °C for 17 h. The reaction mixture was purified by column chromatography on silica gel (10 % ethyl acetate in hexanes) to afford 90 mg (77 %) of the desired product as a white solid.

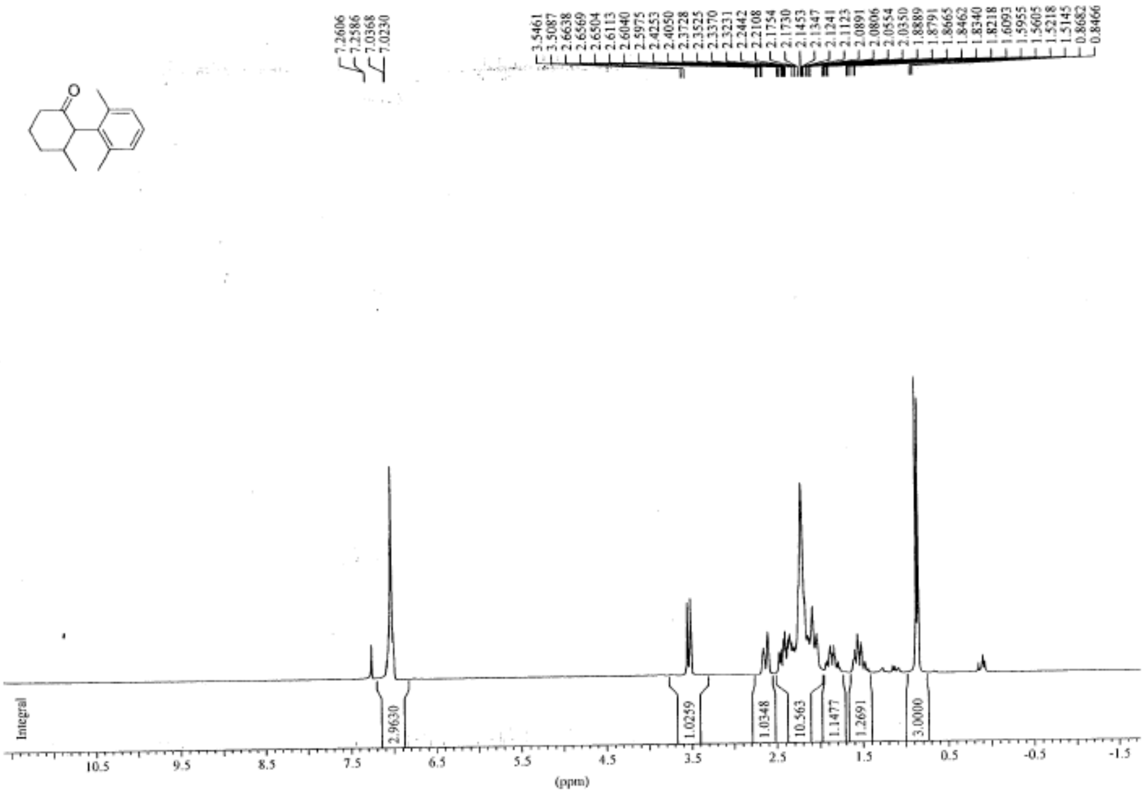
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14-8.11 (m, 1H), 7.95 (s, 1H), 7.50-7.41 (m, 2H), 3.34 (d, J = 11.73 Hz, 1H), 2.58-2.43 (m, 2H), 2.19-2.07 (m, 3H), 1.88-1.82 (m, 1H), 1.65-1.60 (m, 1H), 0.83 (d, J = 6.33 Hz, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ 208.8, 148.4, 139.8, 135.9, 129.3, 124.6, 122.2, 64.9, 41.8, 41.0, 34.4, 26.1, 21.3. HR MS (EI) Calcd for $C_{13}H_{15}NO_3$: 233.10519. Found m/e $(M)^+$ 233.10548.

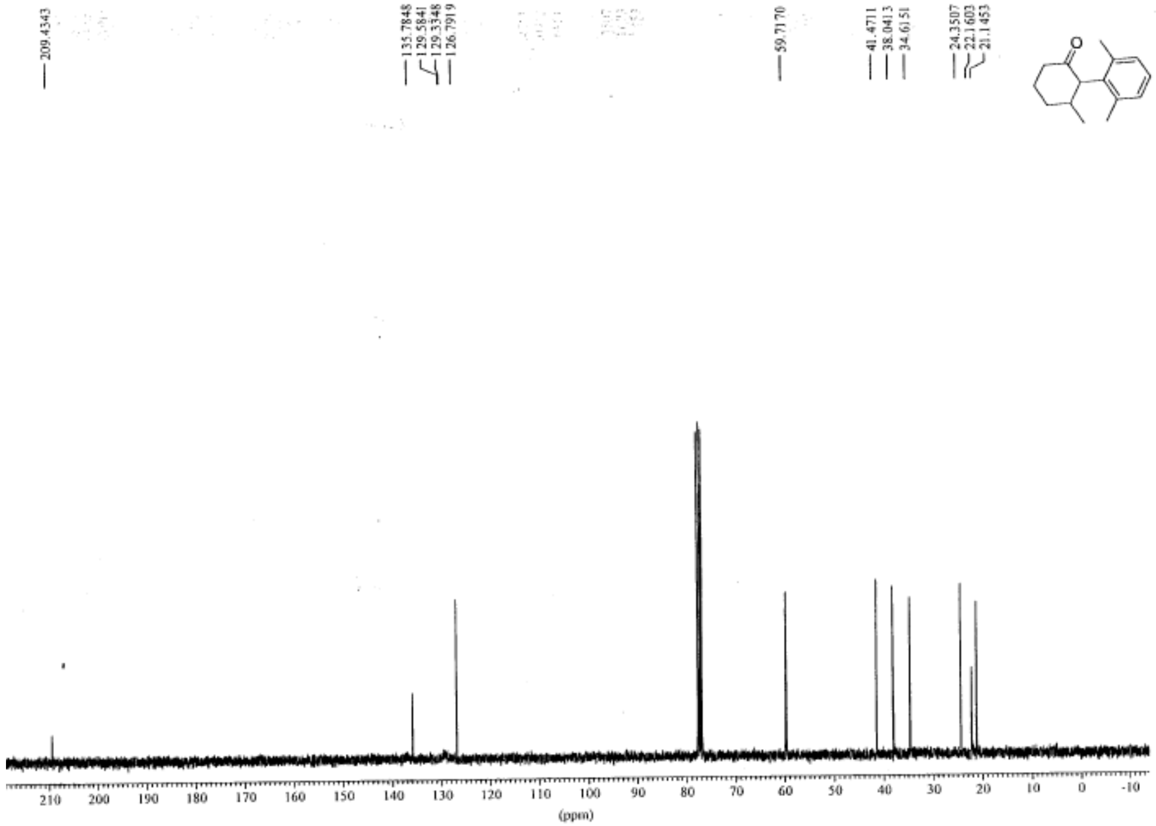




2-(2,6-Dimethylphenyl)-3-methyl-1-cyclohexanone (Table 2, entry 14). The general procedure was followed using 1-trimethylsiloxy-3-methyl-1-cyclohexene (129 mg, 0.700 mmol), 2-bromo-*m*-xylene (94 mg, 0.492 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 20 h. The reaction mixture was purified by column chromatography on silica gel (2-4 % ethyl acetate in hexanes) to afford 92 mg (85 %) of the desired product as a colorless liquid.

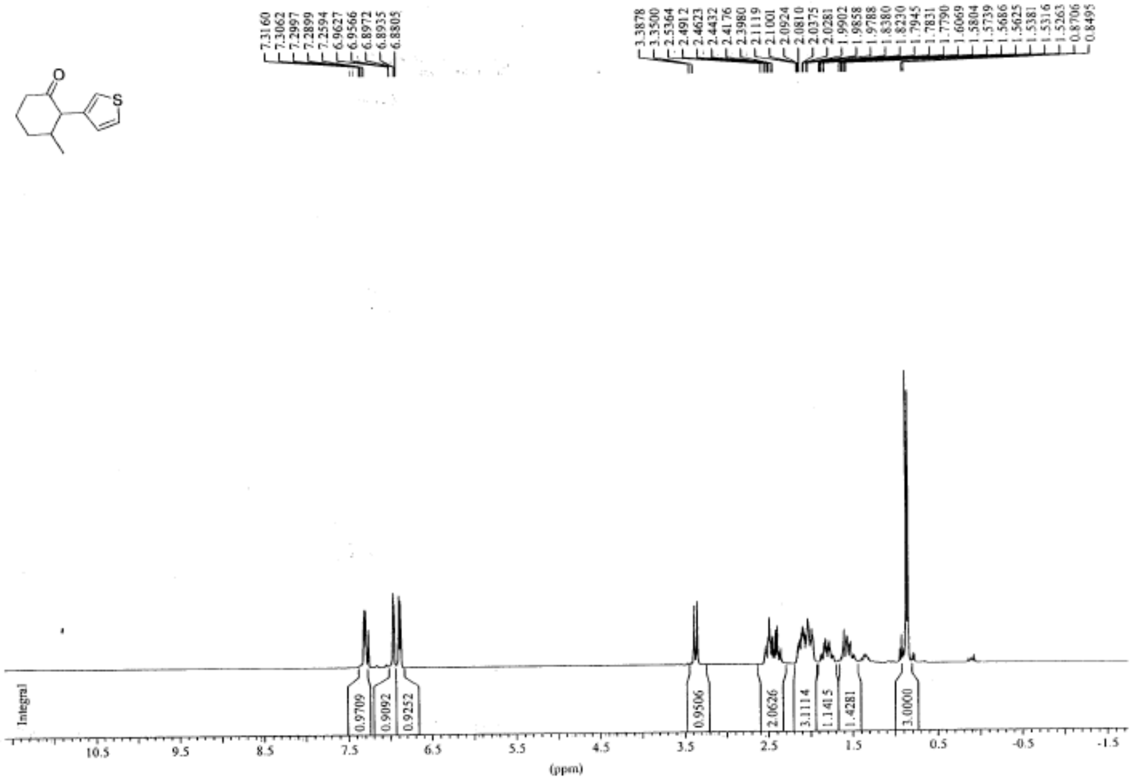
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.03-7.02 (m, 3H), 3.52 (d, J = 11.22 Hz, 1H), 2.66-2.59 (m, 1H), 2.42-2.03 (overlap, 10H), 1.88-1.82 (m, 1H), 1.60-1.51 (m, 1H), 0.85 (d, J = 6.48 Hz, 3H). ^{13} C NMR (75.5 MHz, $CDCl_3$): δ 209.4, 135.7, 129.5, 129.3, 126.8, 59.7, 41.4, 38.0, 34.6, 24.3, 22.1, 21.1. HR MS (EI) Calcd for $C_{15}H_{20}O$: 216.15142. Found m/e $(M)^+$ 216.15174.

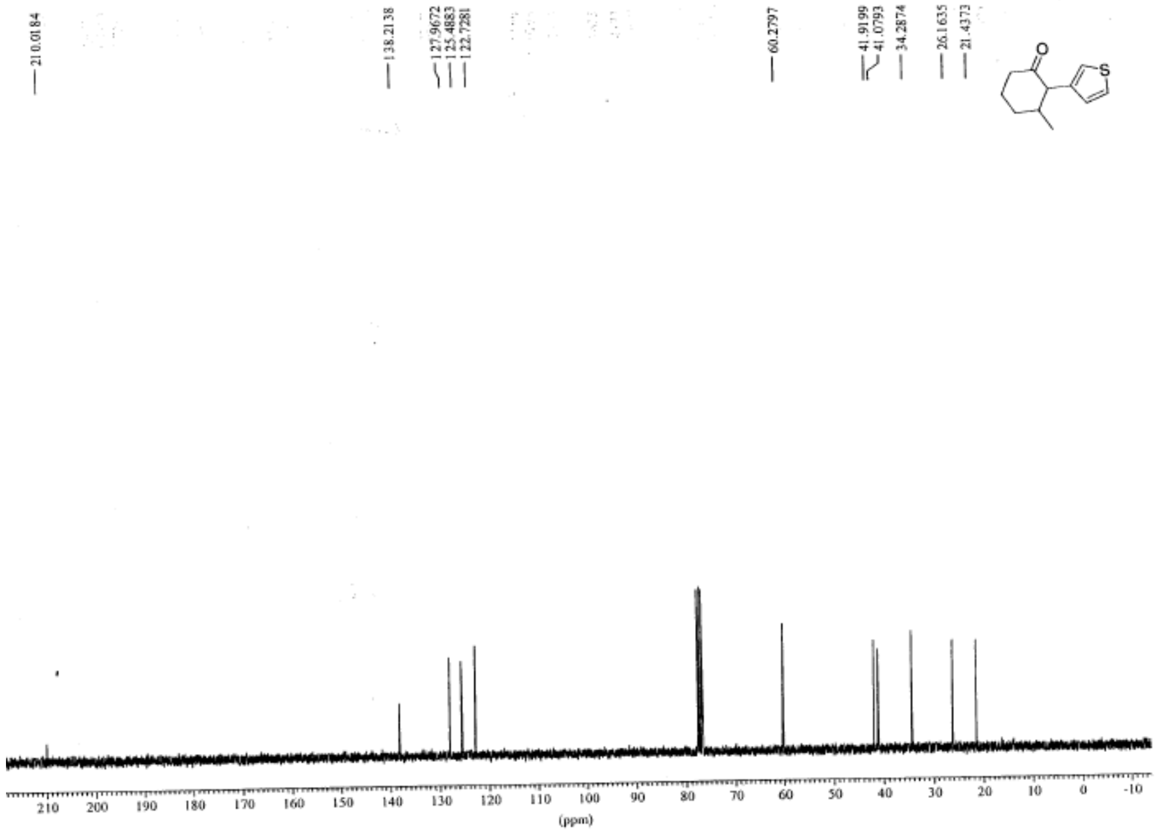




2-(3-thienyl)-3-methyl-1-cyclohexanone (Table 2, entry 15). The general procedure was followed using 1-trimethylsiloxy-3-methyl-1-cyclohexene (129 mg, 0.700 mmol), 3-bromothiophene (84 mg, 0.500 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and $P(t\text{-}Bu)_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 20 h. The reaction mixture was purified by column chromatography on silica gel (2-4 % ethyl acetate in hexanes) to afford 76 mg (78 %) of the desired product as a colorless liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31-7.28 (m, 1H), 6.96 (s, 1H), 6.89-6.88 (m, 1H), 3.37 (d, J = 11.34 Hz, 1H), 2.53-2.39 (m, 2H), 2.11-1.97 (m, 3H), 1.84-1.78 (m, 1H), 1.60-1.52 (m, 1H), 0.86 (d, J = 6.33 Hz, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 210.0, 138.2, 127.9, 125.4, 122.7, 60.2, 41.9, 41.0, 34.2, 26.1, 21.4. HR MS (EI) Calcd for $C_{11}H_{14}OS$: 194.07654. Found m/e $(M)^+$ 194.07684.





3-(4-Nitrophenyl)-4-phenyl-2-butanone (Reaction 1). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 1-bromo-4-nitrobenzene (102 mg, 0.500 mmol), CsF (107mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), $Pd(OAc)_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol) and 2 mL of THF. The reaction was conducted at 85 °C for 19 h. The reaction mixture was purified by column chromatography on silica gel (5-10 % ethyl acetate in hexanes) to afford 105 mg (78%) of the desired product as a pale yellow solid.

3-(4-Acetylphenyl)-4-phenyl-2-butanone (Reaction 1). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 4'-bromoacetophenone (101 mg, 0.497 mmol), CsF (107 mg, 0.703 mmol), Bu_3SnF (216 mg, 0.699 mmol), Pd(OAc)$_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol) and 2mL THF. The reaction was conducted at 85 °C for 12 h. The reaction mixture was purified by column chromatography on silica gel (10 % ethyl acetate in hexanes) to afford 80 mg (60%) of the desired product as a white solid.

3-(4-*tert*-Butylphenyl)-4-phenyl-2-butanone (Reaction 2). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 1-bromo-4-*tert*-butylbenzene (109 mg, 0.501 mmol), CsF (107 mg, 0.703 mmol), ZnF$_2$ (72.1 mg, 0.700 mmol), Pd(OAc)$_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol) and 2 mL DMF. The reaction mixture was purified by column chromatography on silica gel (2 % ethyl acetate in hexanes) to afford 121 mg (87%) of the desired product as a colorless liquid.

3-(4-Acetylphenyl)-4-phenyl-2-butanone (Reaction 2). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 4'-bromoacetophenone (101mg, 0.497 mmol), CsF (107 mg, 0.703 mmol), ZnF$_2$ (72.1 mg, 0.700 mmol), Pd(OAc)$_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol). The reaction was conducted at 85 °C for 12 h. The reaction mixture was purified by column chromatography on silica gel (10 % ethyl acetate in hexanes) to afford 120 mg (90%) of the desired product as a white solid.

3-(2-Methoxyphenyl)-4-phenyl-2-butanone (Reaction 2). The general procedure was followed using 2-trimethylsiloxy-4-phenyl-2-butene (154 mg, 0.699 mmol), 2-bromoanisole (96 mg, 0.498 mmol), CsF (107 mg, 0.703 mmol), ZnF$_2$ (72.1 mg, 0.700 mmol), Pd(OAc)$_2$ (3.36 mg, 0.015 mmol), and P(*t*-Bu)$_3$ (5.45 mg, 0.027 mmol) and 2 mL of DMF. The reaction was conducted at 85 °C for 19 h. The reaction mixture was purified by column chromatography on silica gel (5 % ethyl acetate in hexanes) to afford 111 mg (87%) of the desired product as a colorless liquid.

Reference

Matsuzawa, S.; Horiguchi, Y. Nakamura, E. Kuwajima, I. *Tetrahedron*, **1989**, *45*, 349.

APPENDIX F

CHAPTER 7. Supplementary Information

Experimental Procedures

References for known compounds

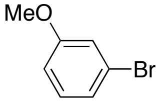
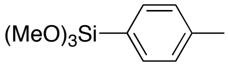
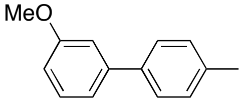
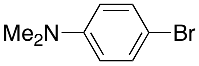
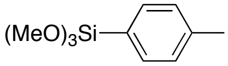
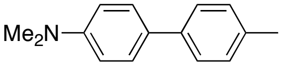
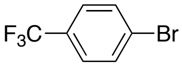
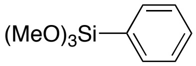
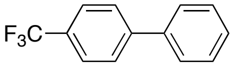
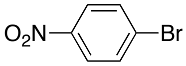
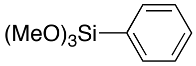
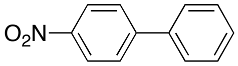
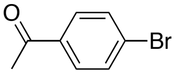
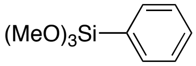
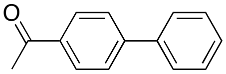
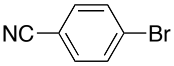
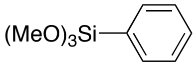
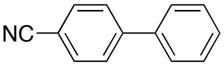
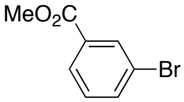
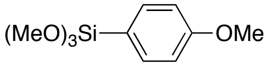
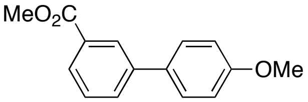
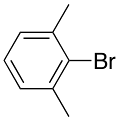
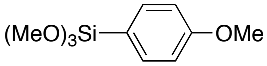
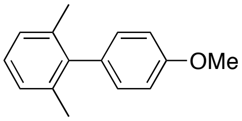
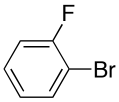
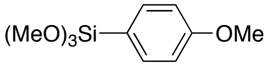
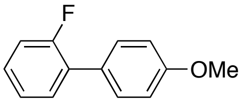
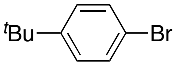
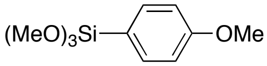
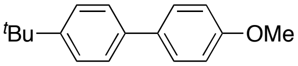
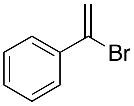
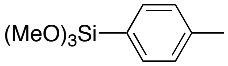
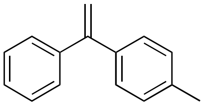
^{1}H and ^{13}C NMR spectra for reaction products

Experimental Section:

General Considerations. All reactions were carried out under inert atmosphere using standard Schlenk procedures. Dioxane was refluxed at 130 °C over activated molecular sieves and distilled and stored over activated molecular sieves under argon. Aryl bromides and chlorides were purchased from Aldrich chemical company and used without further purification. Phenylsiloxanes were purchased from Gelest and used without further purification. Palladium, ligand, and tetrabutylammonium fluoride (TBAF•3H_2O) were stored in a glove box. Ligands **1**, **2**, and **3** were prepared according to literature procedures.[1] Ligand **4** is available from Aldrich chemical company. ^{1}H and ^{13}C NMR were recorded on a 400 MHz Bruker DRX in $CDCl_3$. Thin layer chromatography (TLC) was performed using commercial 60 mesh silica gel plates visualized with short-wavelength UV (254 nm) light.

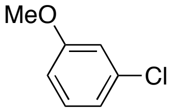
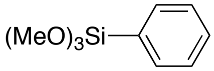
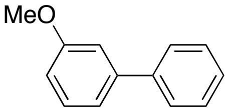
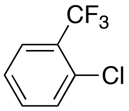
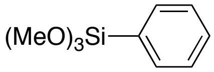
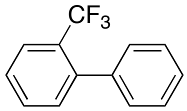
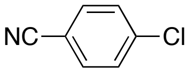
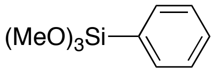
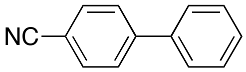
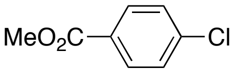
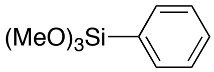
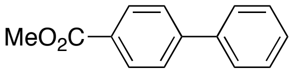
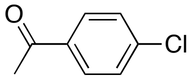
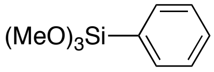
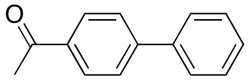
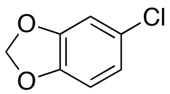
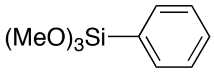
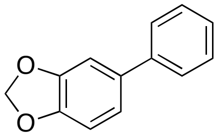
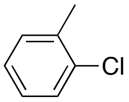
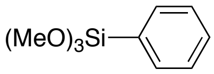
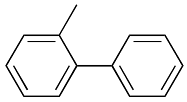
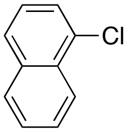
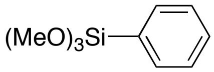
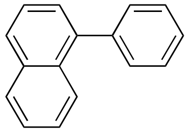
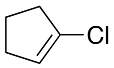
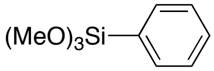
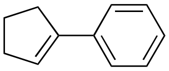
General Procedure for the Hiyama Coupling of Aryl Bromides and Chlorides. To a 10 mL vial was added 3 mmol TBAF•3H_2O (794 mg), 0.5 mole % $Pd(OAc)_2$ (2.24 mg) and 1.0 mole % ligand **1** (10.03 mg) in a glove box. The vial was capped and brought outside the glove box where 4 mmol of phenylsiloxane and 2 mmol of aryl halide was added under an argon flow. The reaction vessel was heated to 80 °C for the specified times given in the tables. The mixture was purified by column chromatography (0-5% EtOAc) to obtain pure biaryls.

Table 2. Scope of Aryl Bromides

entry	aryl bromide	siloxane	time	product	yield (%)[a,b]
1			3 h		91[c] (Lit: 80)[h]
2			5 h		71[d]
3			2 h		93[e] (Lit: 87-99)[i]
4			2 h		91[e] (Lit: 51-93)[j]
5			2 h		91[e] (Lit: 55-99)[k]
6			2 h		84[e] (Lit: 85)[l]
7			1.5 h		87[f]
8			2 h		89[g]
9			0.5 h		83[c]
10			0.5 h		85[c]
11			1 h		78[c]

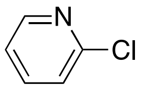
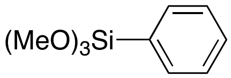
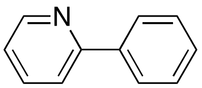
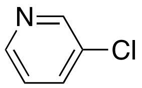
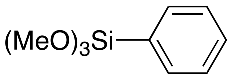
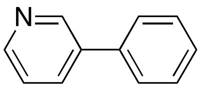
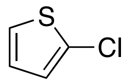
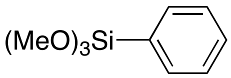
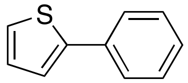
[a] Average of two runs. Yields in correspond to isolated yields. [b] Reaction conditions: 2 mmol aryl bromide, 4 mmol siloxane, 3 mmol TBAF-3H_2O. [c] 0.5 mole % Pd$(OAc)_2$, 1 mole % **1**, neat. [d] 1 mole % Pd$(OAc)_2$, 2 mole % 1, 5 mL dioxane. [e] 0.5 mole % Pd$(OAc)_2$, 1 mole % 1, 5 mL dioxane. [f] 0.25 mole % Pd$(OAc)_2$, 0.5 mole % 1, 5 mL dioxane. [g] 1 mole % Pd$(OAc)_2$, 2 mole % 1, neat. [h] Ref 2a. [i] Refs 2b-2e. [j] Refs 2e-2j. [k] Refs 2a-2d, 2f-2i, 2k, 2l-2p. [l] Ref 2c.

Table 3. Scope of Aryl Chlorides

entry	aryl chloride	siloxane	time	product	yield (%)[a,b]
1			1.5 h		87[c] (Lit: 25)[f]
2			3 h		82[d]
3			2 h		93[e]
4			2 h		95[e] (Lit: 68)[g]
5			1.5 h		95[e] (Lit: 62-99)[h]
6			2 h		90[c]
7			2 h		87[d]
8			1 h		83[d]
9			0.5 h		91[c]

[a] Average of two runs. Yields correspond to isolated yields. [b] Reaction conditions: 2 mmol aryl chloride, 4 mmol siloxane, 3 mmol TBAF-3H_2O, neat, time: 0.5-2 h. [c] 0.5 mole % $Pd(OAc)_2$, 1 mole % **1**, neat. [d] 1 mole % $Pd(OAc)_2$, 2 mole % **1**, neat. [e] 0.5 mole % $Pd(OAc)_2$, 1.0 mole % **1**, 5 mL dioxane. [f] Ref 2g. [g] Ref 3a. [h] Refs 2g-2i, 2m-2n, 3b.

Table 4. Scope of Heterocyclic Aryl Chlorides

entry	aryl chloride	siloxane	time	product	yield (%)^{a,b}
1			2 h		81^{c}
2			1.5 h		82^{d} (Lit: 63-92)^{e}
3			1 h		95^{c}

[a] Average of two runs. Yields correspond to isolated yields. [b] Reaction conditions: 2 mmol aryl chloride, 4 mmol siloxane, 0.5 mole % Pd(OAc)$_2$, 1 mole % **1**, 3 mmol TBAF, time: 0.5-2 h.
[c] Neat condition. [d] 5 mL dioxane. [e] Refs 3a-3b.

References in Tables:

1. Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816-2822.

2. a.) Ranu, B. C.; Dey, R.; Chattopadhyay *Tetrahedron Lett.* **2008**, *49*, 3430-3432. b.) Chen, S.; Wu, W.; Tsai, F. *Tetrahedron* **2008**, *64*, 8164-8168. c.) Pan, C.; Liu, M.; Zhao, L.; Wu, H.; Ding, J.; Cheng, J. *Catalysis Comm.* **2008**, *9*, 1685-1687. d.) Mino, T.; Shire, Y.; Saito, T.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2006**, *71*, 9499-9502. e.) Pachón, L. D.; Thathagar, M. B.; Hartl, F.; Rothenberg, G. *Phys. Chem. Chem. Phys.* **2006**, *8*, 151-157. f.) Srimani, D.; Sawoo, S.; Sarkar, A. *Org. Lett.* **2007**, *9*, 3639-3642. g.) Ju, J.; Nam, H.; Jung, H.; Lee, S. *Tetrahedron Lett.* **2006**, *47*, 8673-8678. h.) Li, J.; Deng, C.; Xie, Y. *Synthesis* **2006**, 969-974. i.) Wu, Z.; Yang, M.; Li, H.; Qi, Y. *Synthesis* **2008**, 1415-1419. j.) Li, J.; Deng, C.; Liu, W.; Xie, Y. *Synthesis* **2005**, 3039-3044. k.) Shi, S.; Zhang, Y. *J. Org. Chem.* **2007**, *72*, 5927-5930. l.) Gordillo, A.; de Jesús, E.; López-Mardomingo, C. *Org. Lett.* **2006**, *8*, 3517-3520. m.) Domin, D.; Benito-Garagorri, D.; Mereiter, K.; Fröhlich, J.; Kirchner, K. *Organometallics* **2005**, *24*, 3957-3965. n.) Clarke, M. L. *Adv. Synth. Catal.* **2005**, *347*, 303-307. o.) Inés, B.; SanMartin, R.; Churruca, F.; Domíguez, E.; Urtiaga, M. K.; Arriortua, M. I. *Organometallics* **2008**, *27*, 2833-2839. p.) Napier, S.; Maruccio, S. M.; Tye, H.; Whittaker, M. *Tetrahedron Lett.* **2008**, *49*, 3939-3942.

3. (a) Ackermann, L.; Gschrei, C. J.; Althammer, A.; Reiderer, M. *Chem. Comm.* **2006**, 1419-1421. (b) Alacid, E.; Nájera, C. *Adv. Synth. Catal.* **2006**, *348*, 945-952.

References for Known Compounds:

3-Methoxy-2'-methylbiphenyl (Table 2, entry 1): Ranu, B. C.; Dey, R.; Chattopadhyay *Tetrahedron Lett.* **2008**, *49*, 3430-3432.

4-Dimethylamino-4'-methylbiphenyl (Table 2, entry 2): Yamamoto, Y.; Takizawa, M.; Yu, X.; Miyaura, N. *Angew. Chem. Int. Ed.* **2008**, *47*, 928-931.

4-Trifloromethylbiphenyl (Table 2, entry 3): Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816-2822.

4-Nitrobiphenyl (Table 2, entry 4): Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816-2822.

4-Acetylbiphenyl (Table 2, entry 5, & Table 3, entry 5): Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816-2822.

4-Cyano-biphenyl (Table 2, entry 6 & Table 3, entry 3): Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816-2822.

Methyl 4'-methoxy-3-biphenylcarboxylate (Table 2, entry 7): Kitamura, Y.; Sakurai, A.; Udzu, T.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Tetrahedron* **2007**, *63*, 10596-10602.

4-Methoxy-2',6'-dimethylbiphenyl (Table 2, entry 8): Ralzer, T. M.; Hsiao, Y.; Qian, F.; Fu, R.; Khan, R. K.; Doubleday, W. *J. Org. Chem.* **2009**, *74*, 1381-1384.

4-Methoxy-2'-fluorobiphenyl (Table 2, entry 9): Simeone, J. P.; Sowa, J. R. *Tetrahedron* **2007**, *63*, 12646-12654.

4-Methoxy-4'-*tert*-butylbiphenyl (Table 2, entry 10): Zhang, L.; Qing, J.; Yang, P.; Wu, J. *Org. Lett.* **2008**, *10*, 4971-4974.

α-(4-methylphenyl)-styrene (Table 2, entry 11): Lindh, J.; Enquist, P.; Pilotti, A.; Nilsson, P.; Larhed, M. *J. Org. Chem.* **2007**, *72*, 9757-9562.

3-Methoxybiphenyl (Table 3, entry 1): Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816-2822.

2-Trifluoromethylbiphenyl (Table 3, entry 2): Demir, A. S.; Findik, H. *Tetrahedron* **2008**, *64*, 6196-6201.

Methyl-4-biphenylcarboxylate (Table 3, entry 4): Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816-2822.

3,4-Methylenedioxybiphenyl (Table 3, entry 6): Su, W.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433-16439.

2-Methylbiphenyl (Table 3, entry 7): Fujihara, T.; Yoshida, S.; Ohta, H.; Tsuji, Y. *Angew. Chem. Int. Ed.* **2008**, *47*, 8310-8314.

1-Phenylnaphthalene (Table 3, entry 8): Fujihara, T.; Yoshida, S.; Ohta, H.; Tsuji, Y. *Angew. Chem. Int. Ed.* **2008**, *47*, 8310-8314.

1-Phenylcylcopentene (Table 3, entry 9): Su, W.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433-16439.

2-Phenylpyridine (Table 4, entry 1): Su, W.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433-16439.

3-Phenylpyridine (Table 4, entry 2): Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816-2822.

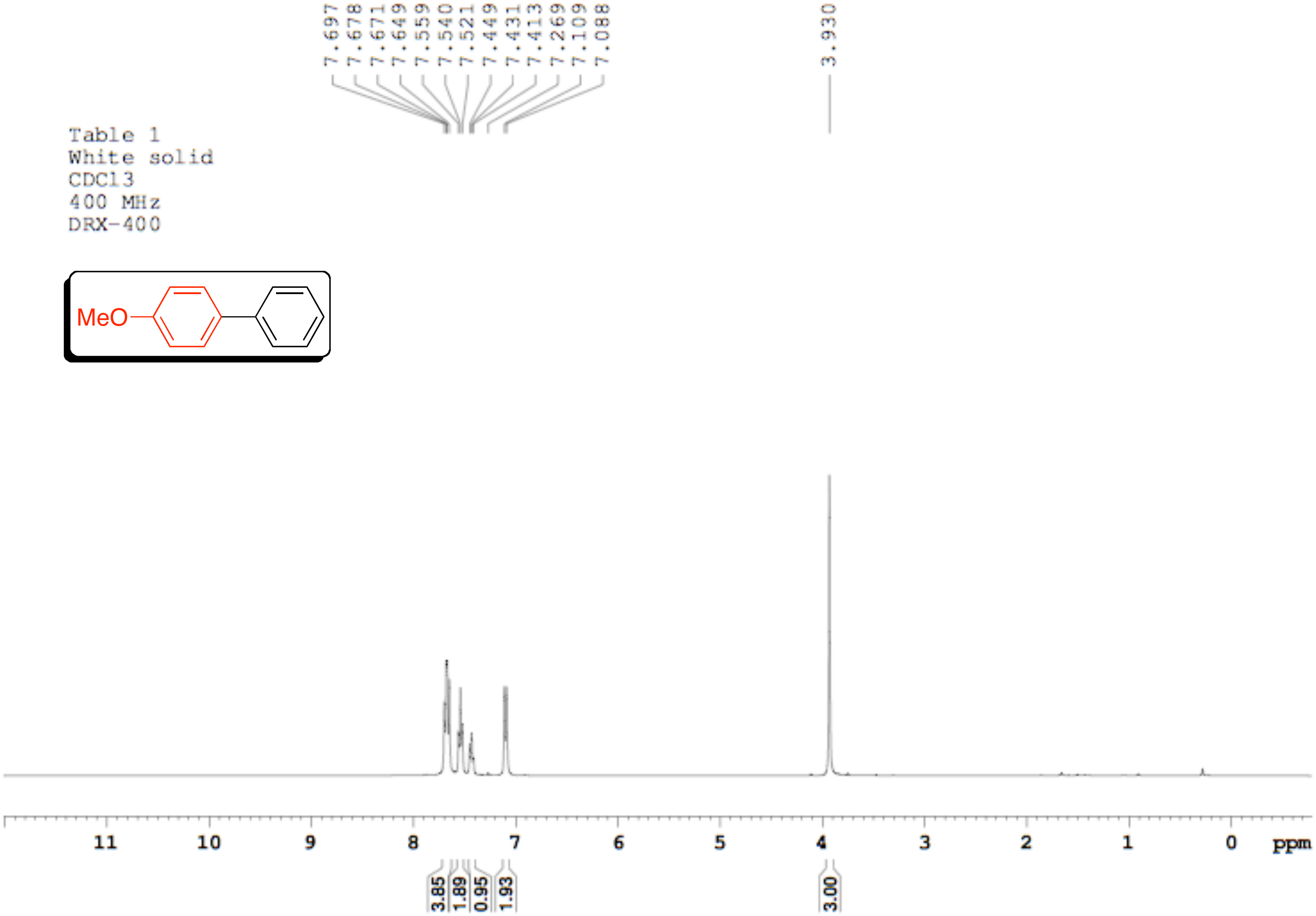
2-Phenylthiophene (Table 4, entry 3): Su, W.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433-16439.

4,4'-Dimethoxybiphenyl (Scheme 1, Compound 7ac): Alacid, E.; Nájera, C. *Adv. Synth. Catal.* **2006**, *348*, 945-952.

4-Methoxy-4’-methylbiphenyl (Scheme 1, Compound 7ad): Li, J.; Deng, C.; Liu, W.; Xie, Y. *Synthesis* **2005**, 3039.

2-(4-Methoxyphenyl)pyridine (Scheme 1, Compound 7bc): Napier, S.; Marcuccio, S. M.; Yye, H.; Whittaker, M. *Tetrahedron Lett.* **2008**, *49*, 6314-6315.

2-(4-Methylphenyl)pyridine (Scheme 1, Compound 7bd): Nishimura, M.; Ueda, M.; Miyaura, N. *Tetrahedron* **2002**, *58*, 5779-5787.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3.930
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CDCl3
400 MHz
DRX-400
MeO
11
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9
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5
4
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2
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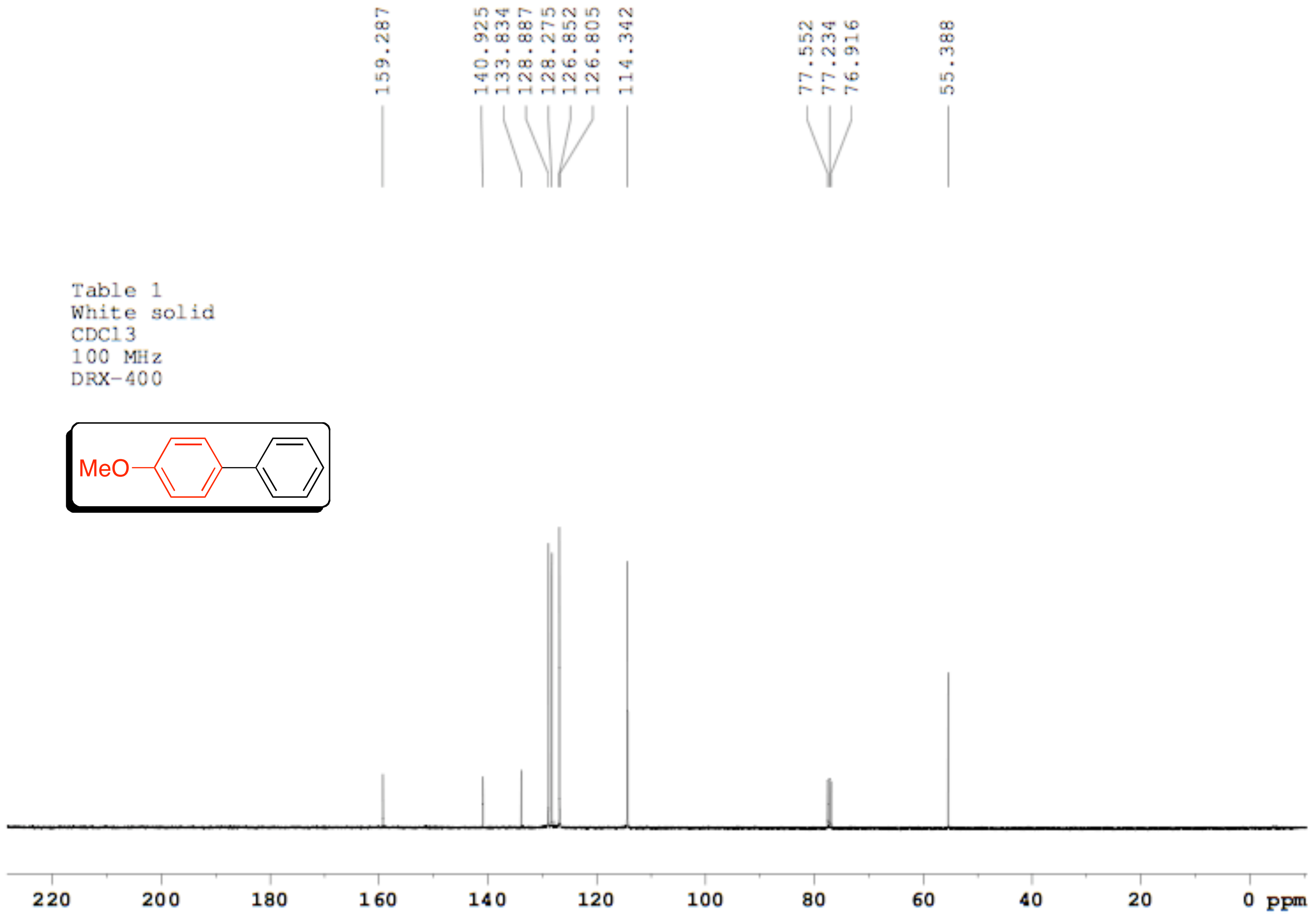
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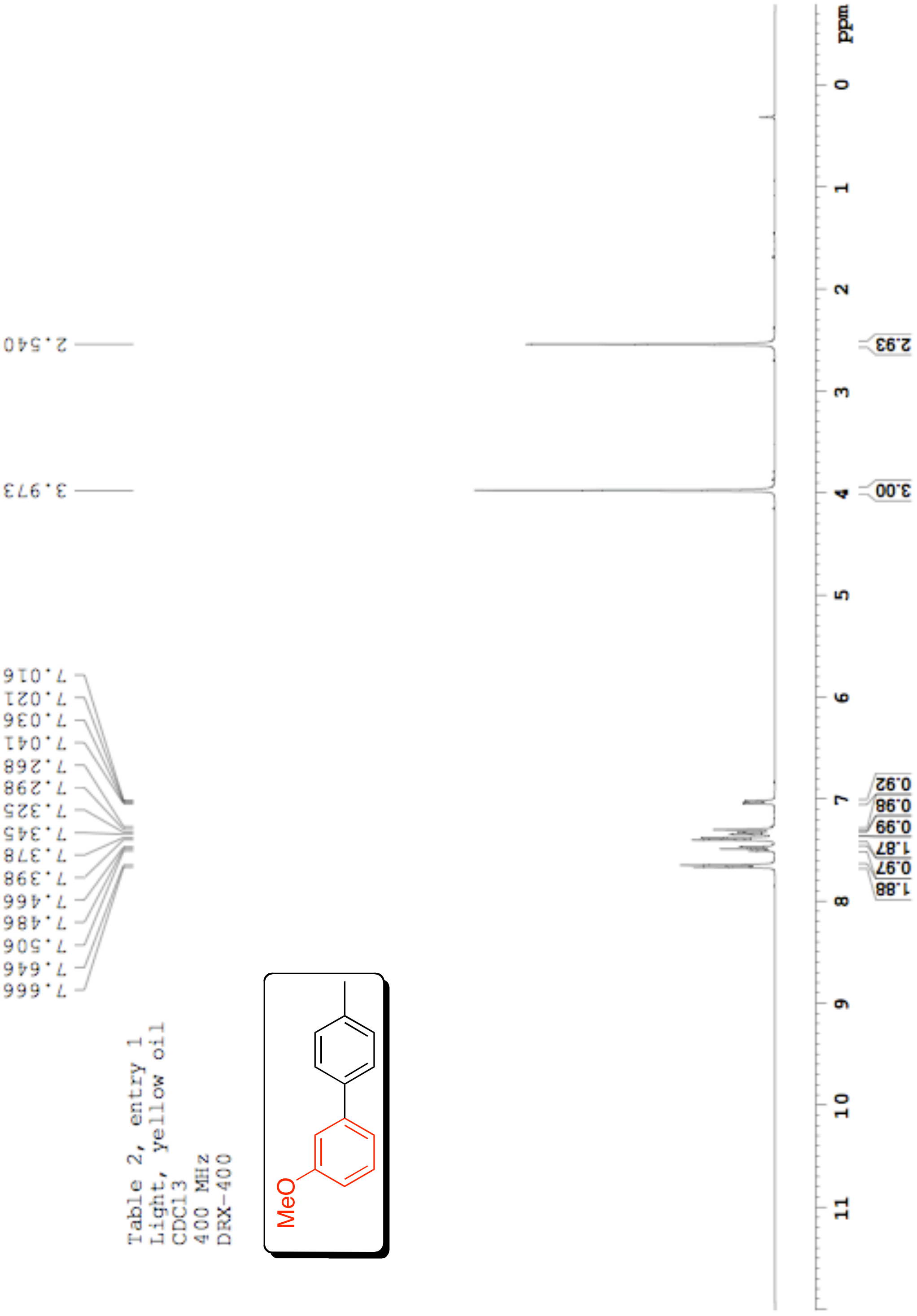
Table 1
White solid
CDCl3
100 MHz
DRX-400
MeO
220
200
180
160
140
120
100
80
60
40
20
0 ppm


2.540
3.973
7.016
7.021
7.036
7.041
7.268
7.298
7.325
7.345
7.378
7.398
7.466
7.486
7.506
7.646
7.666
Table 2, entry 1
Light, yellow oil
CDCl3
400 MHz
DRX-400
MeO
2.93
3.00
0.92
0.98
0.99
1.87
0.97
1.88
ppm
0
1
2
3
4
5
6
7
8
9
10
11

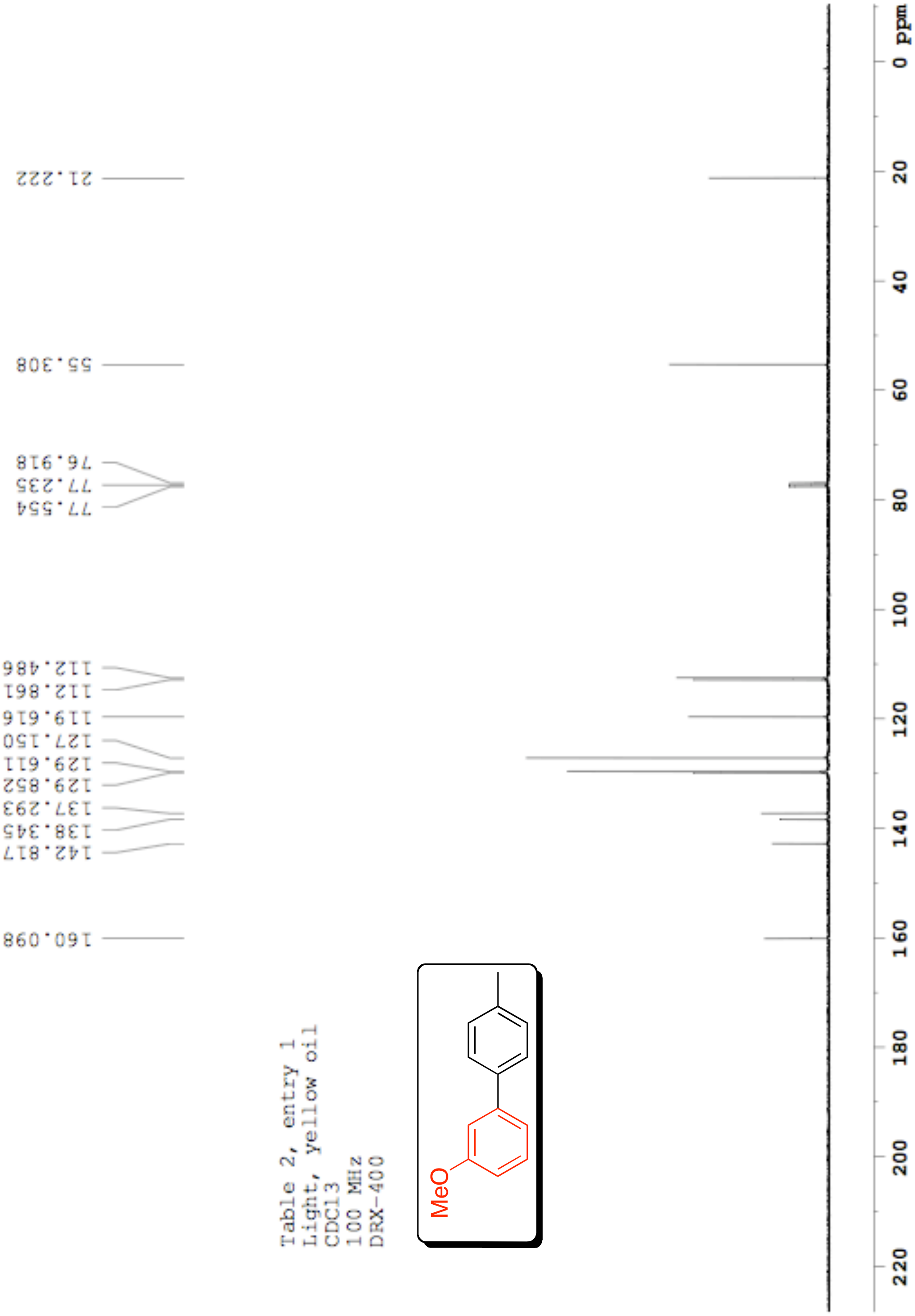
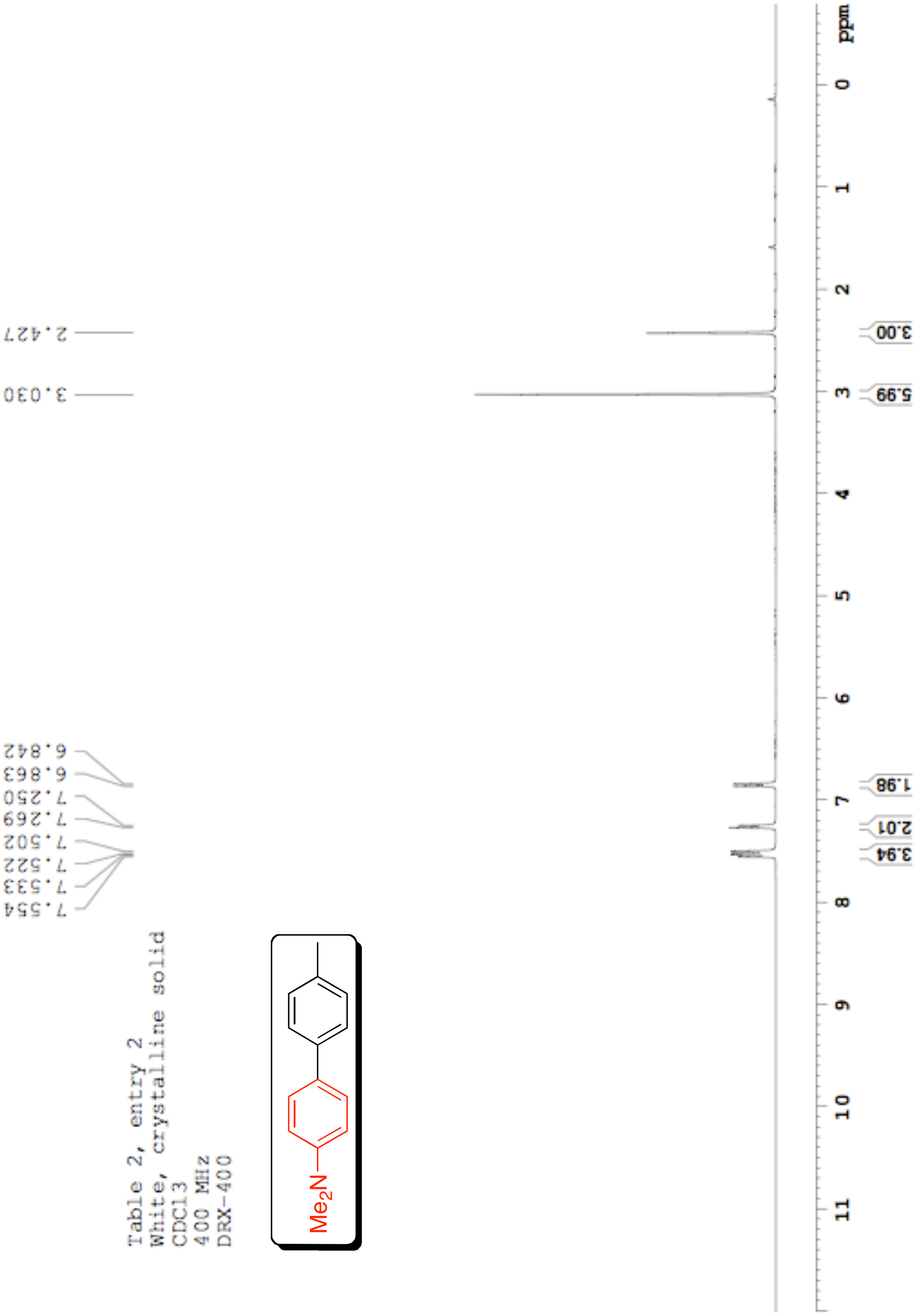
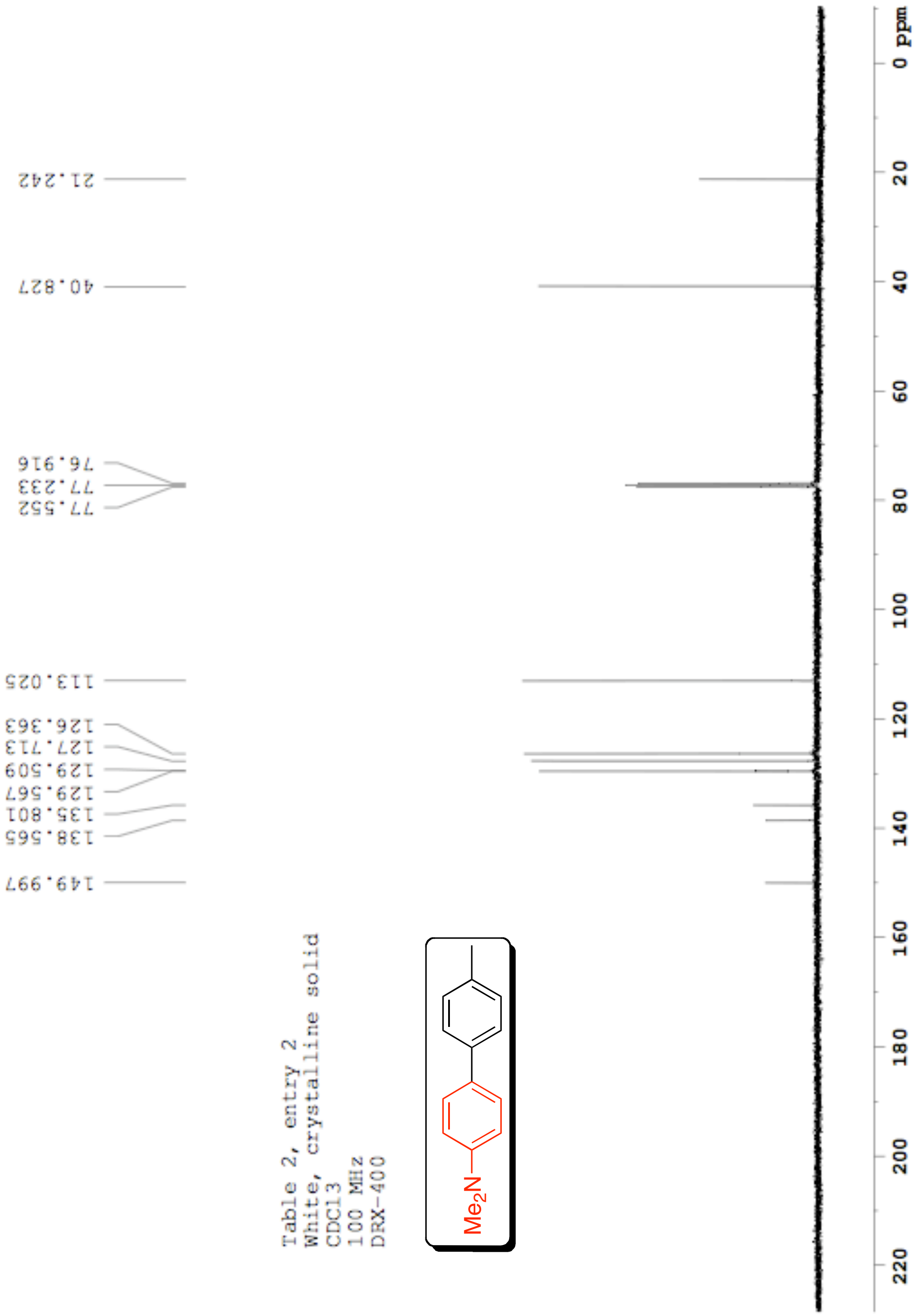
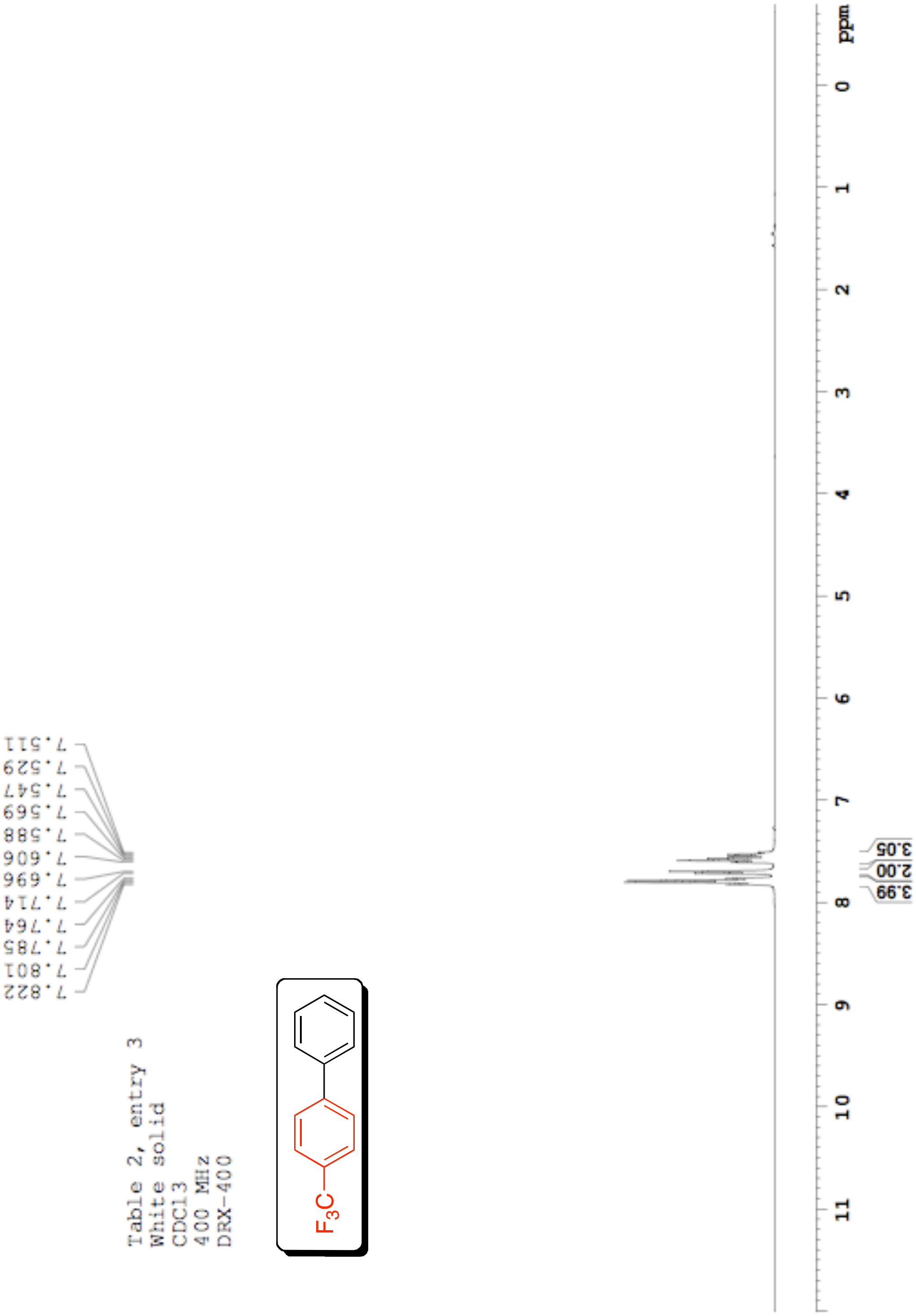
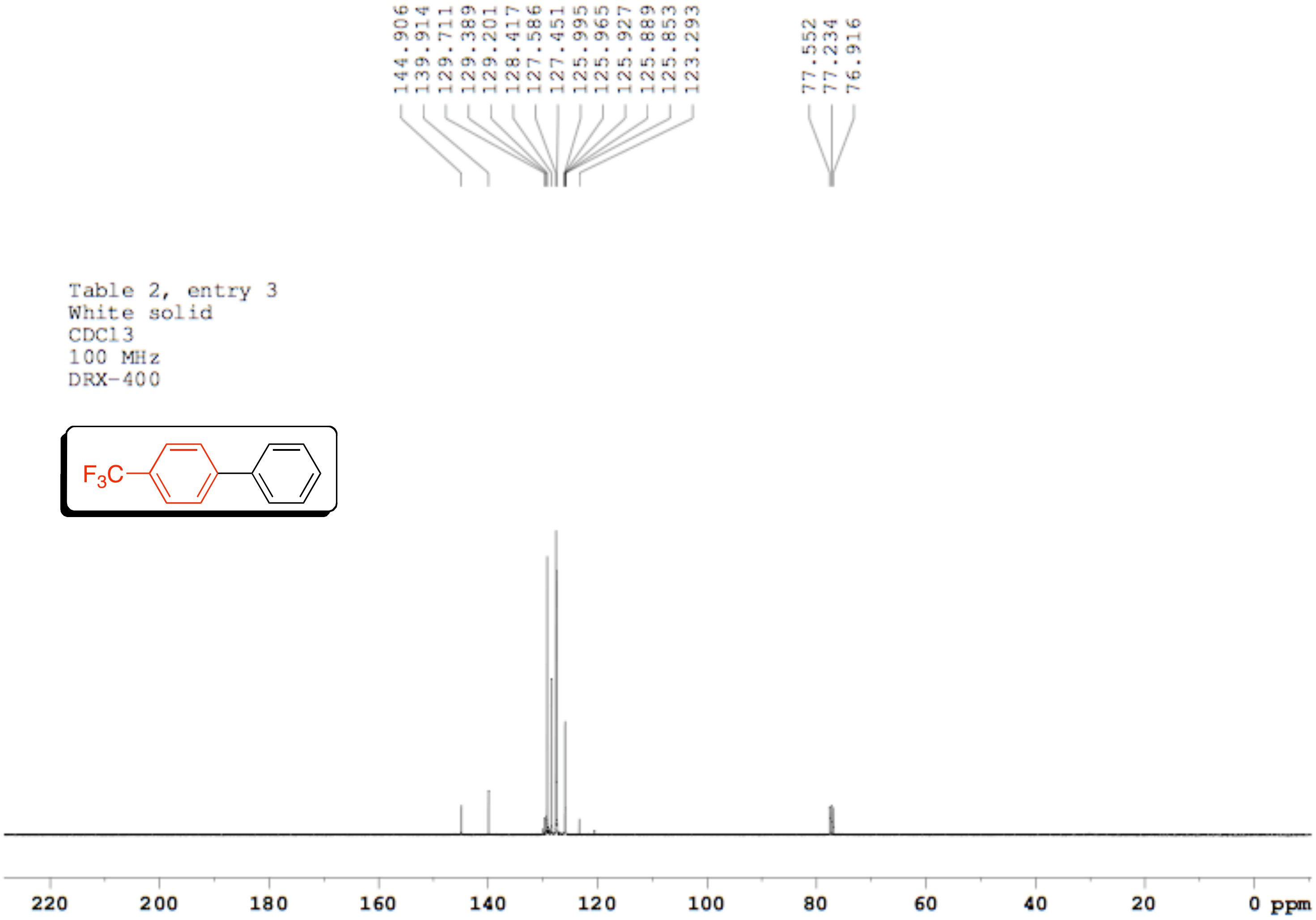


Table 2, entry 1
Light, yellow oil
CDCl3
100 MHz
DRX-400


2.427
3.030
6.842
6.863
7.250
7.269
7.502
7.522
7.533
7.554
Table 2, entry 2
White, crystalline solid
CDCl3
400 MHz
DRX-400
Me2N
3.00
5.99
1.98
2.01
3.94
ppm
0
1
2
3
4
5
6
7
8
9
10
11


21.242
40.827
76.916
77.233
77.552
113.025
126.363
127.713
129.509
129.567
135.801
138.565
149.997
Table 2, entry 2
White, crystalline solid
CDCl3
100 MHz
DRX-400
Me2N
0 ppm
20
40
60
80
100
120
140
160
180
200
220


7.511
7.529
7.547
7.569
7.588
7.606
7.696
7.714
7.764
7.785
7.801
7.822
Table 2, entry 3
White solid
CDCl3
400 MHz
DRX-400
F3C
3.05
2.00
3.99
ppm
0
1
2
3
4
5
6
7
8
9
10
11


144.906
139.914
129.711
129.389
129.201
128.417
127.586
127.451
125.995
125.965
125.927
125.889
125.853
123.293
77.552
77.234
76.916
Table 2, entry 3
White solid
CDCl3
100 MHz
DRX-400
F_3C
220
200
180
160
140
120
100
80
60
40
20
0 ppm

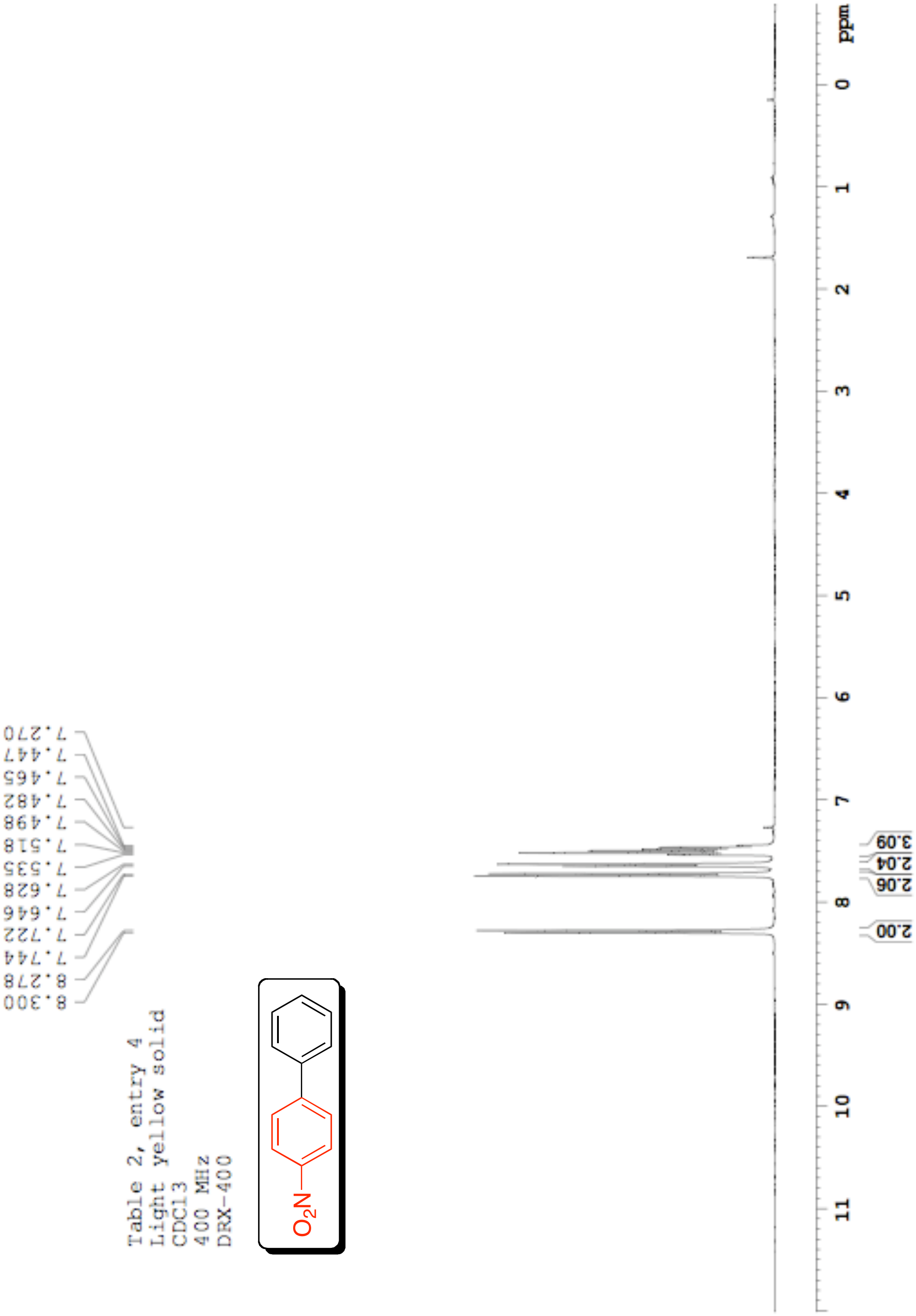


Table 2, entry 4
Light yellow solid
CDCl3
400 MHz
DRX-400
O_2N
8.300
8.278
7.744
7.722
7.646
7.628
7.535
7.518
7.498
7.482
7.465
7.447
7.270
2.00
2.06
2.04
3.09
ppm
0
1
2
3
4
5
6
7
8
9
10
11

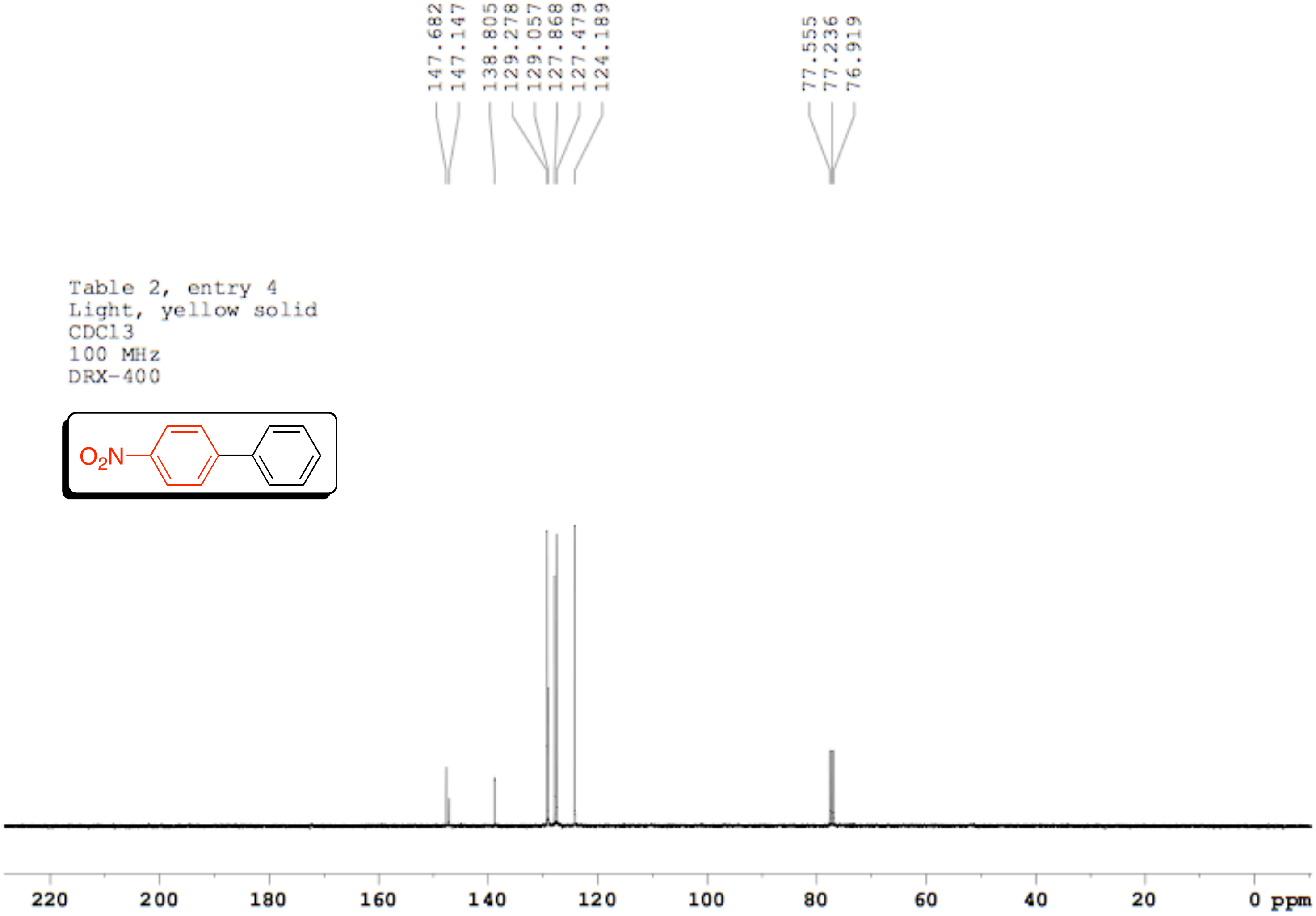
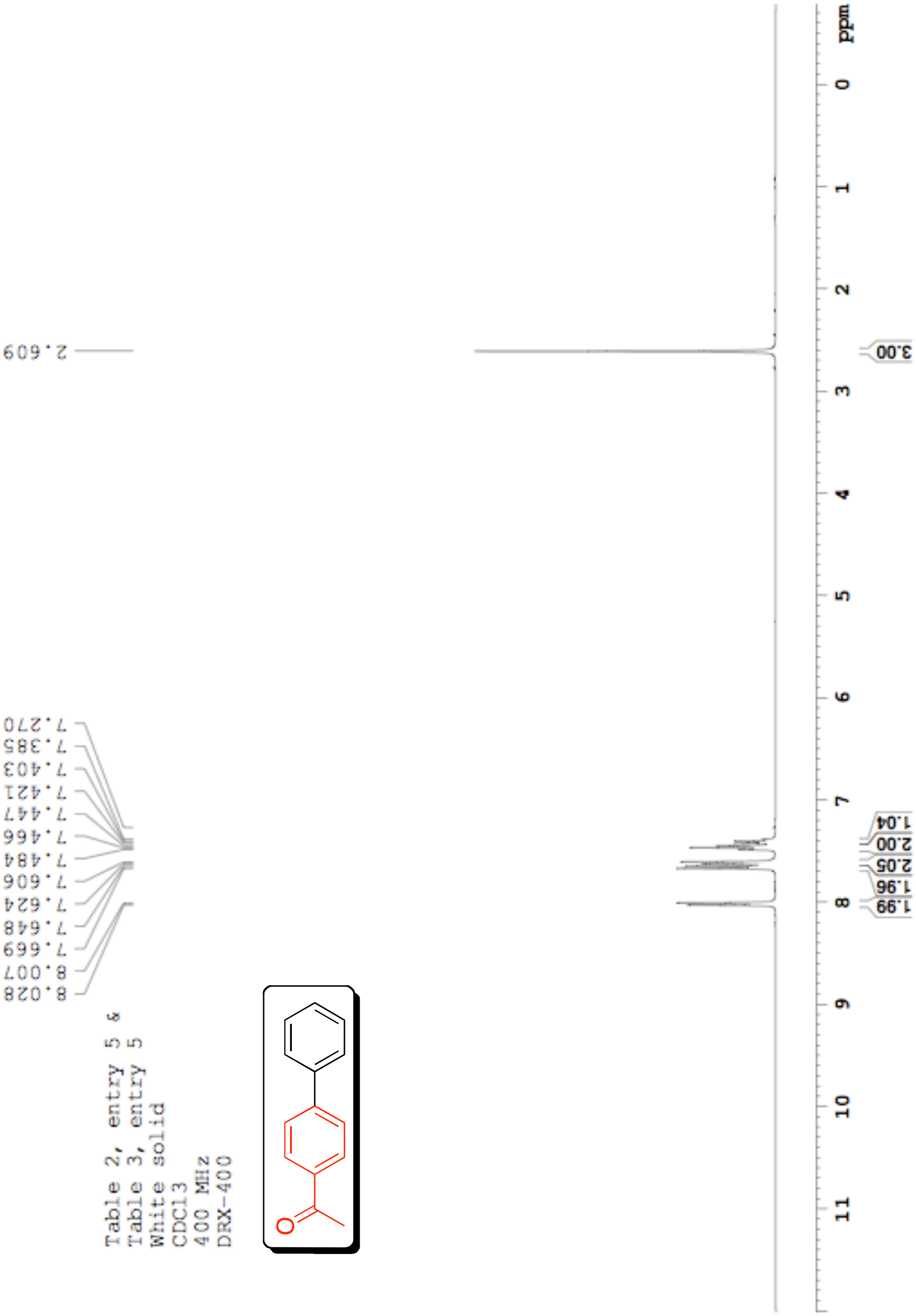
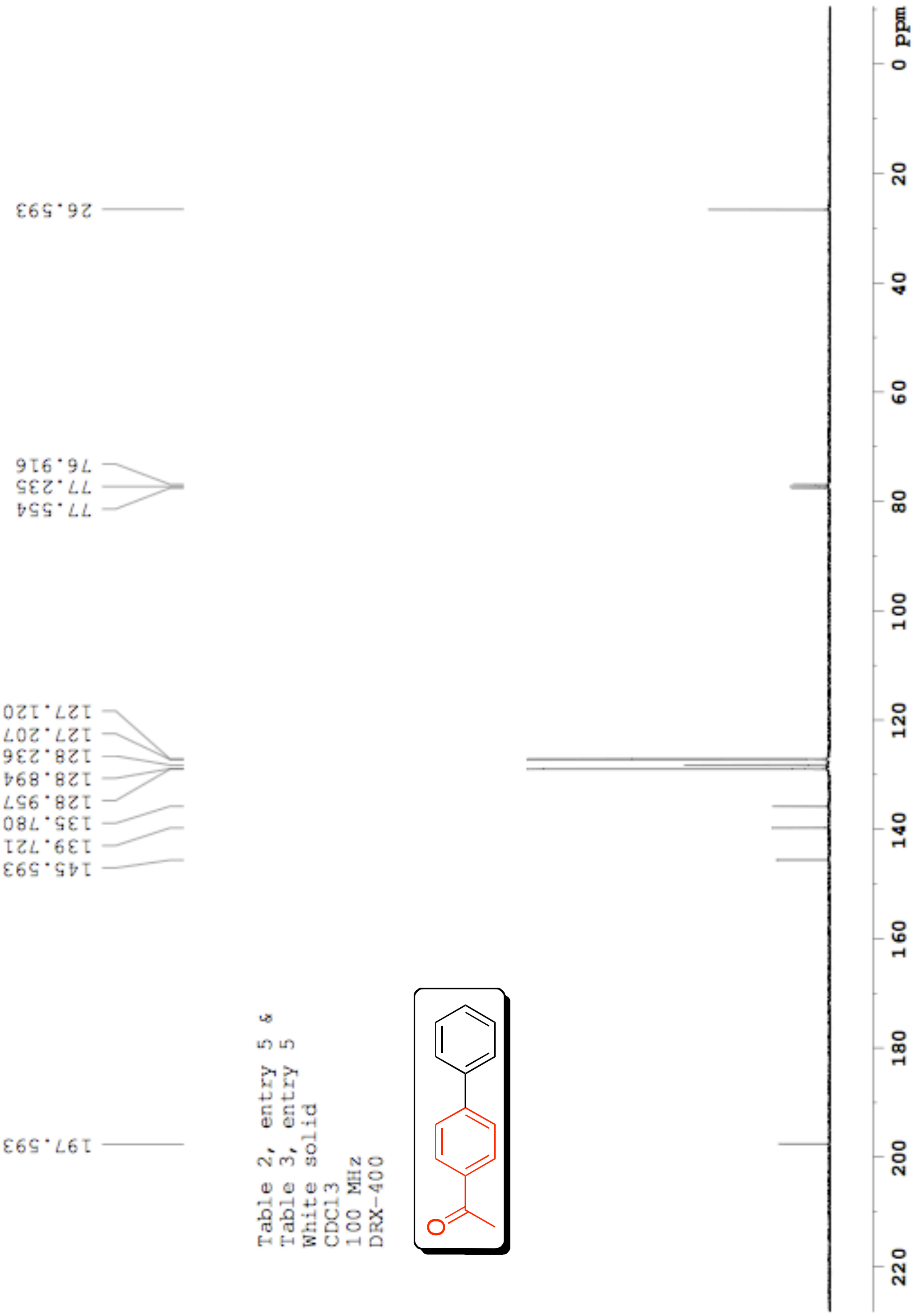
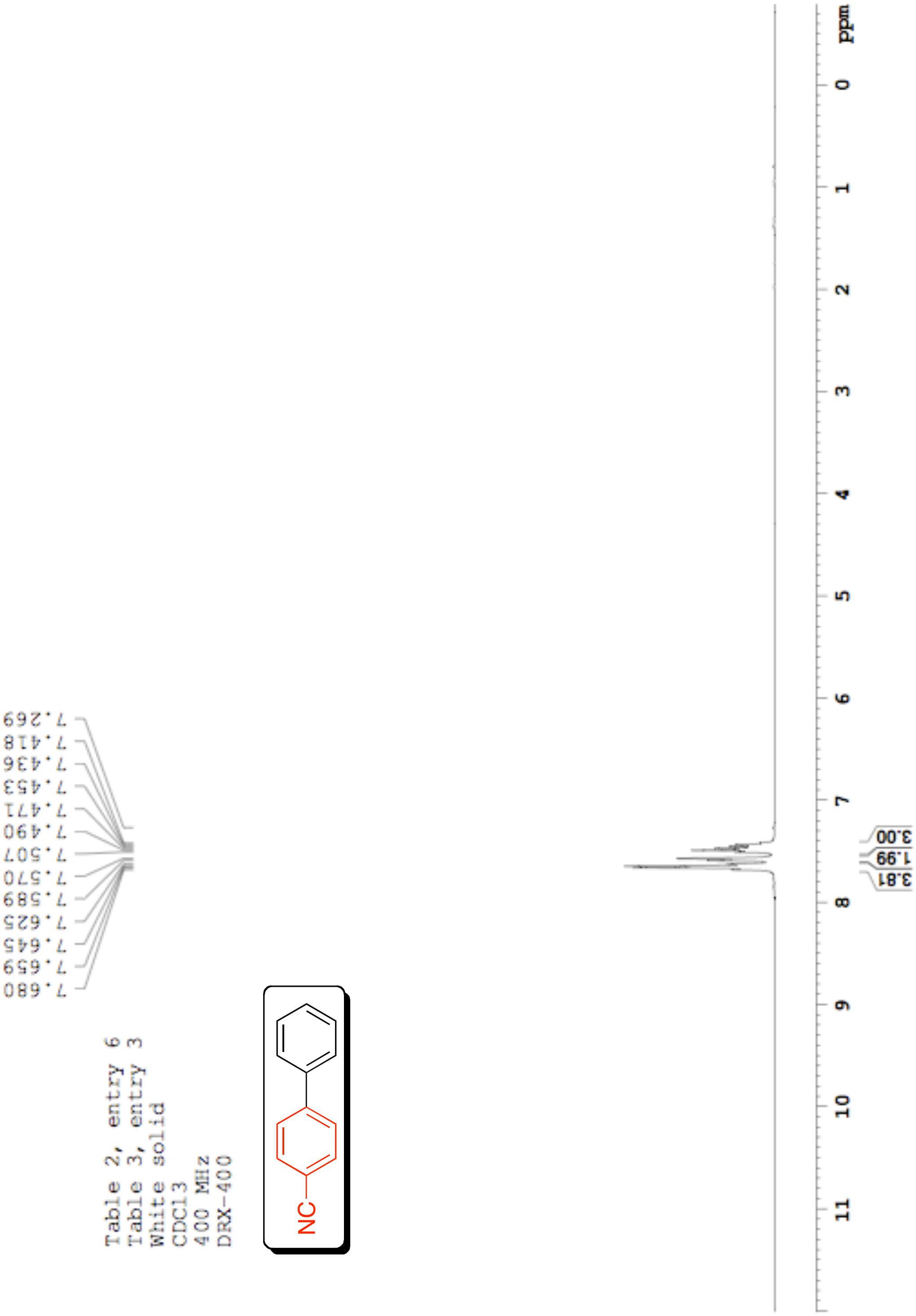
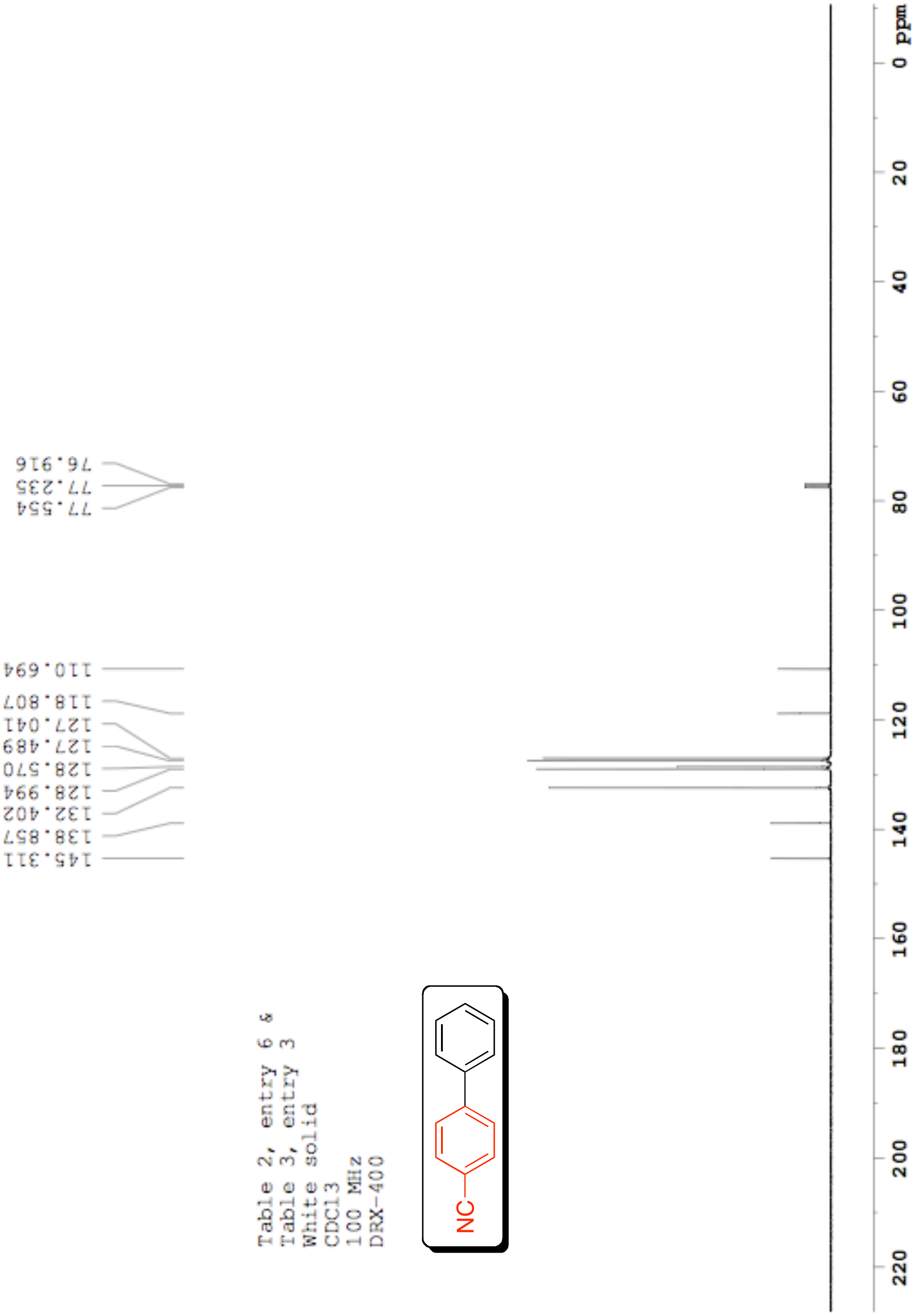


Table 2, entry 4
Light, yellow solid
CDCl3
100 MHz
DRX-400


2.609
7.270
7.385
7.403
7.421
7.447
7.466
7.484
7.606
7.624
7.648
7.669
8.007
8.028
Table 2, entry 5 &
Table 3, entry 5
White solid
CDCl3
400 MHz
DRX-400
3.00
1.04
2.00
2.05
1.96
1.99
ppm
0
1
2
3
4
5
6
7
8
9
10
11


26.593
76.916
77.235
77.554
127.120
127.207
128.236
128.894
128.957
135.780
139.721
145.593
197.593
Table 2, entry 5 &
Table 3, entry 5
White solid
CDCl3
100 MHz
DRX-400
O
0 ppm
20
40
60
80
100
120
140
160
180
200
220


7.269
7.418
7.436
7.453
7.471
7.490
7.507
7.570
7.589
7.625
7.645
7.659
7.680
Table 2, entry 6
Table 3, entry 3
White solid
CDCl3
400 MHz
DRX-400
NC
3.00
1.99
3.81
ppm
0
1
2
3
4
5
6
7
8
9
10
11



76.916
77.235
77.554
110.694
118.807
127.041
127.489
128.570
128.994
132.402
138.857
145.311
Table 2, entry 6 &
Table 3, entry 3
White solid
CDCl3
100 MHz
DRX-400
NC
0 ppm
20
40
60
80
100
120
140
160
180
200
220

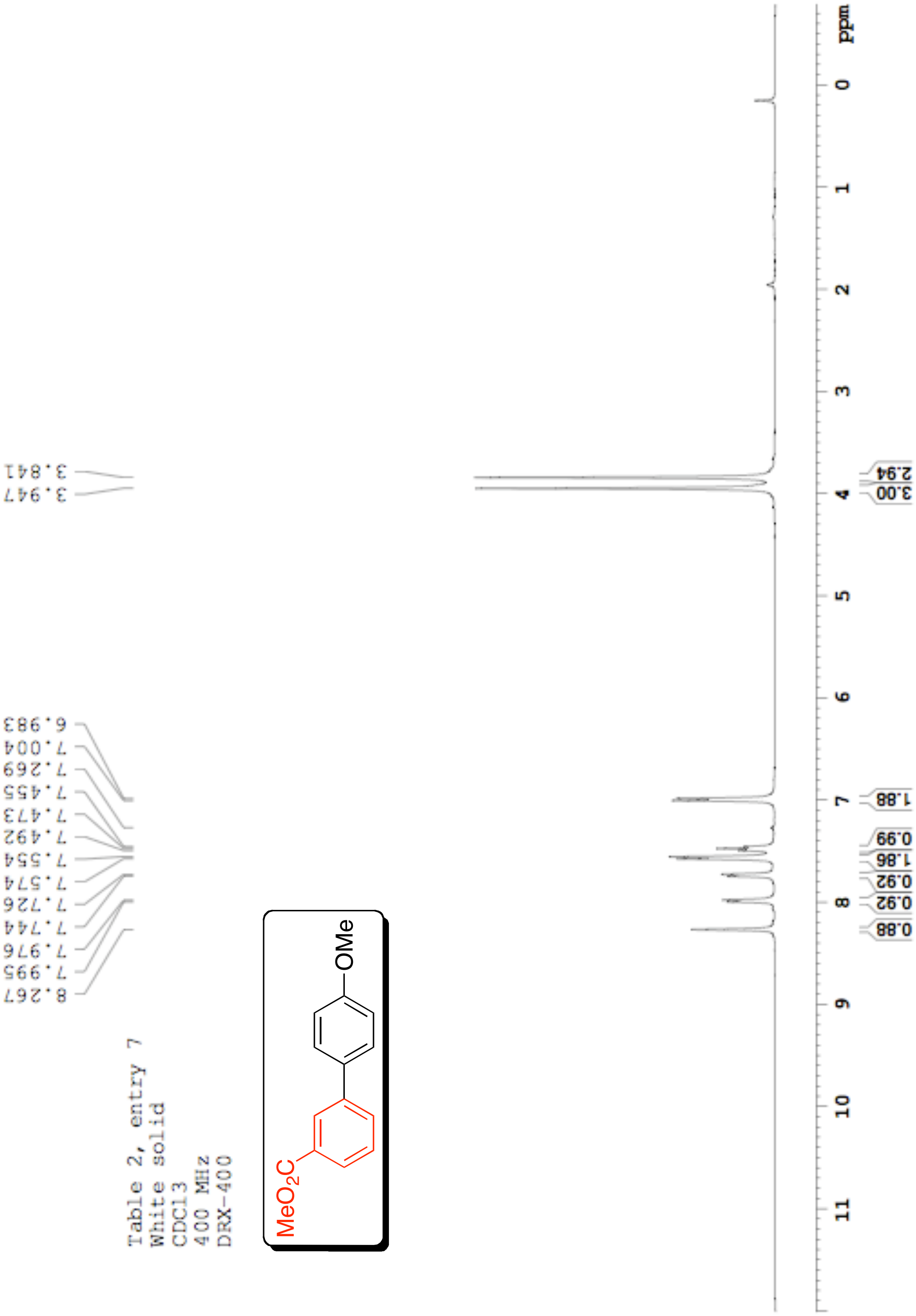


Table 2, entry 7
White solid
CDCl3
400 MHz
DRX-400
MeO2C
OMe
3.841
3.947
6.983
7.004
7.269
7.455
7.473
7.492
7.554
7.574
7.726
7.744
7.976
7.995
8.267
2.94
3.00
1.88
0.99
1.86
0.92
0.92
0.88
ppm
0
1
2
3
4
5
6
7
8
9
10
11

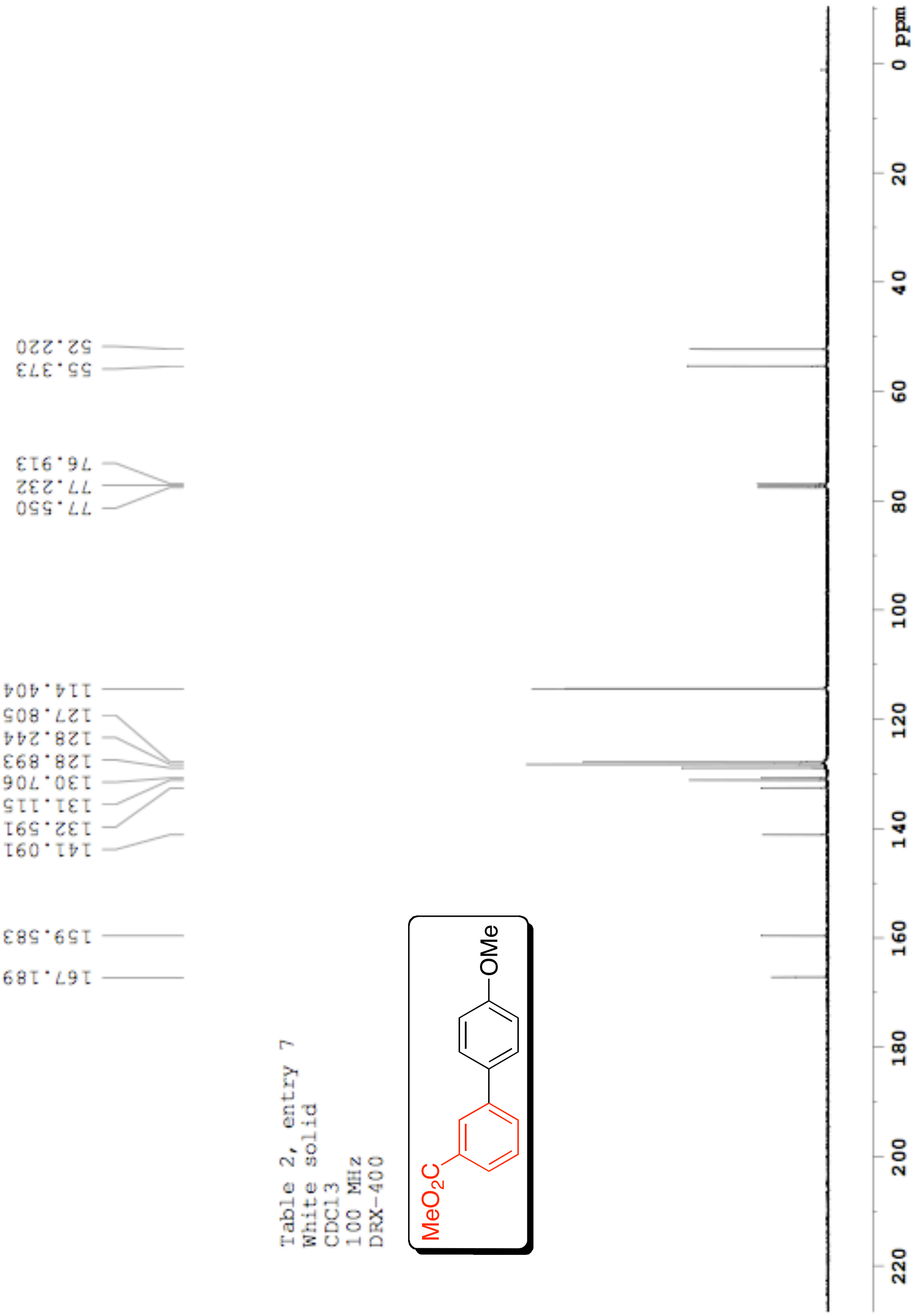
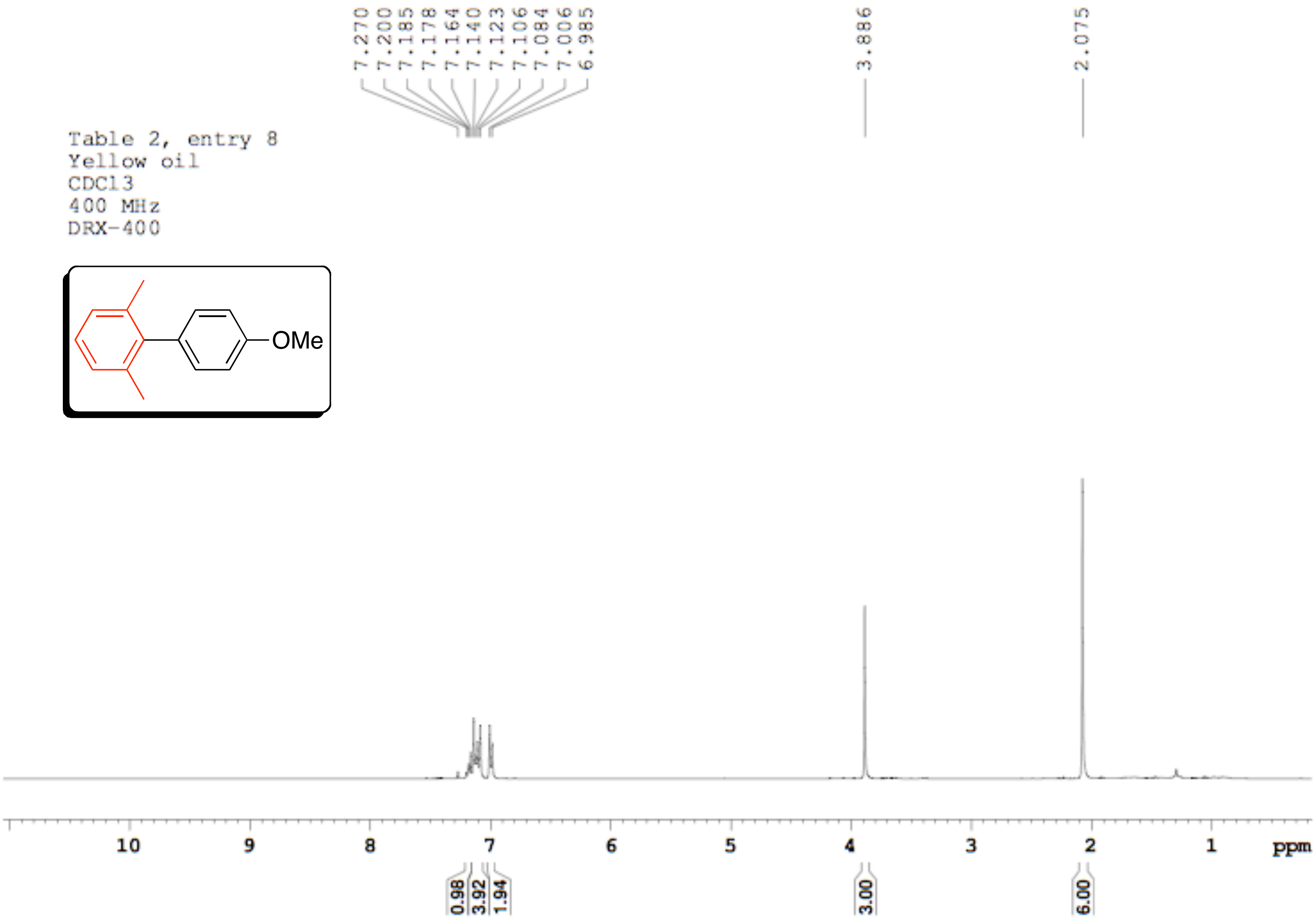
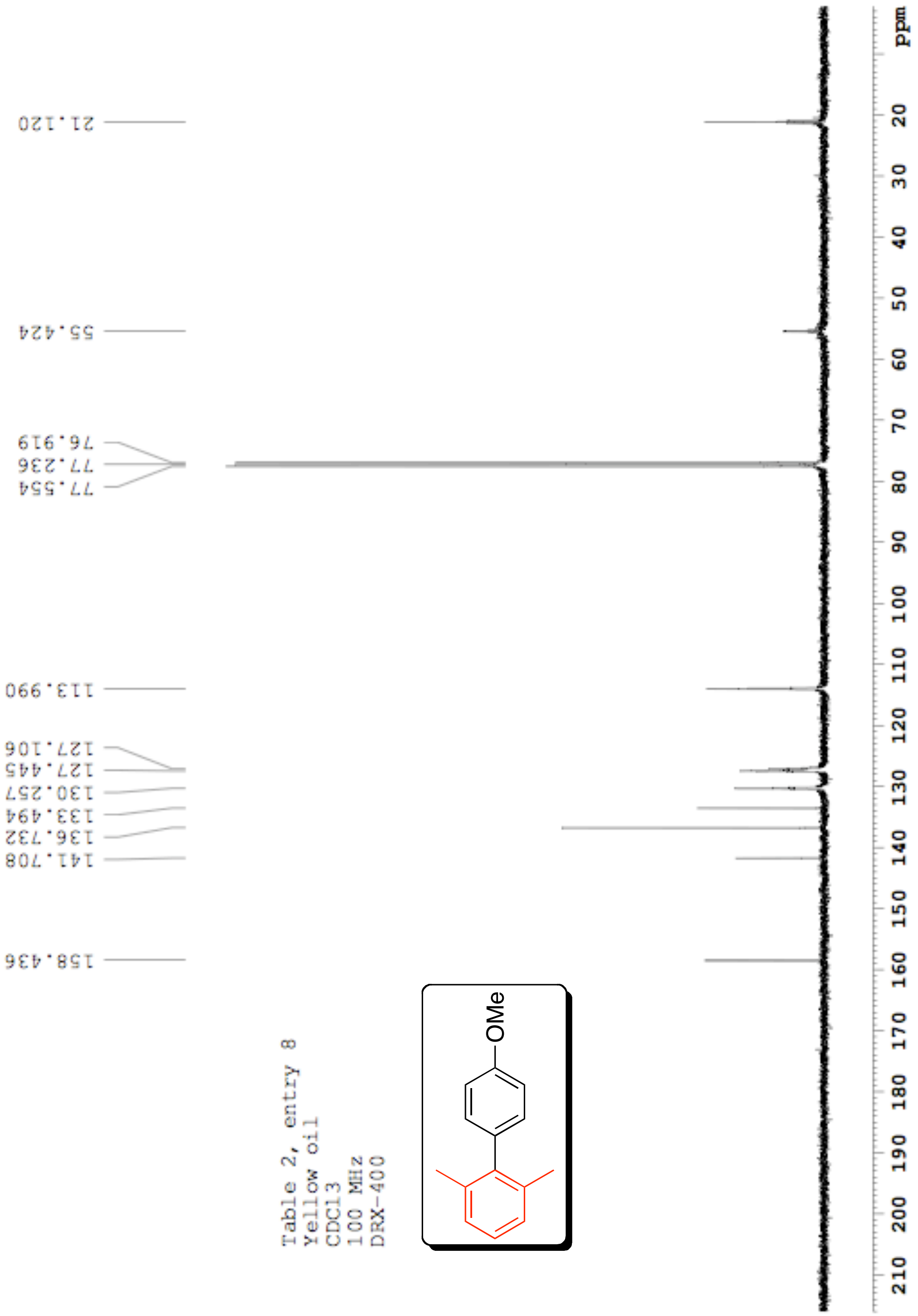
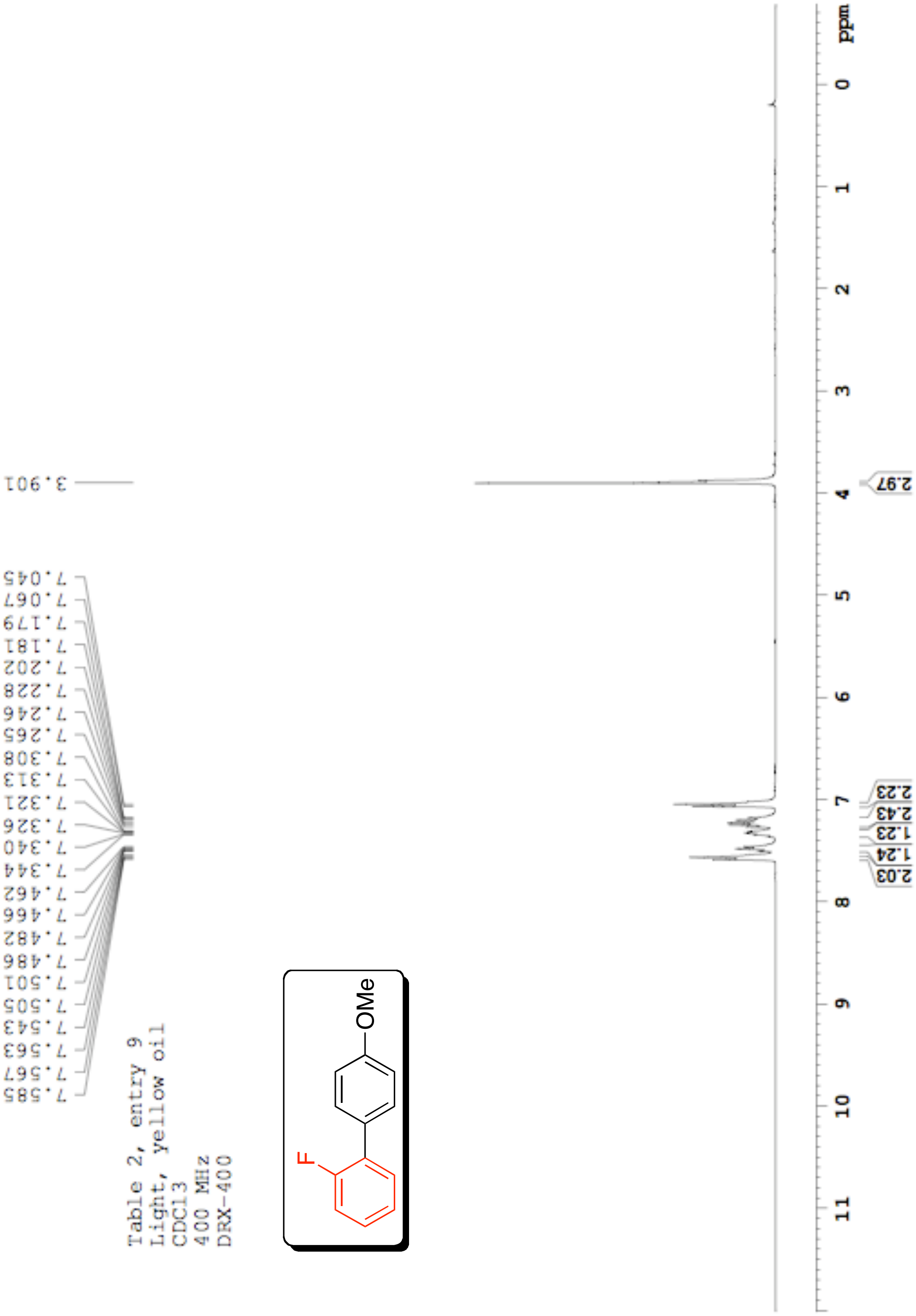
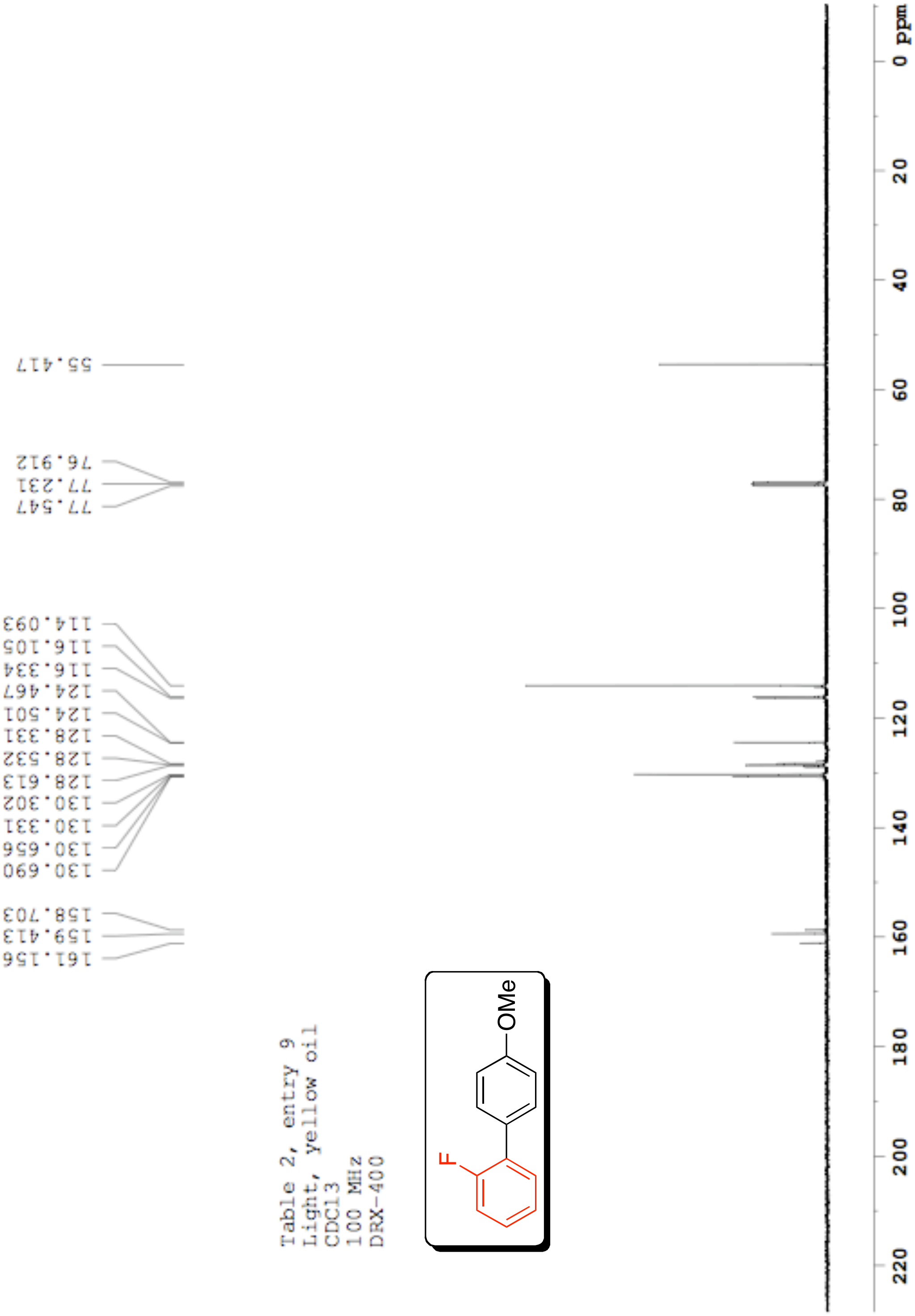


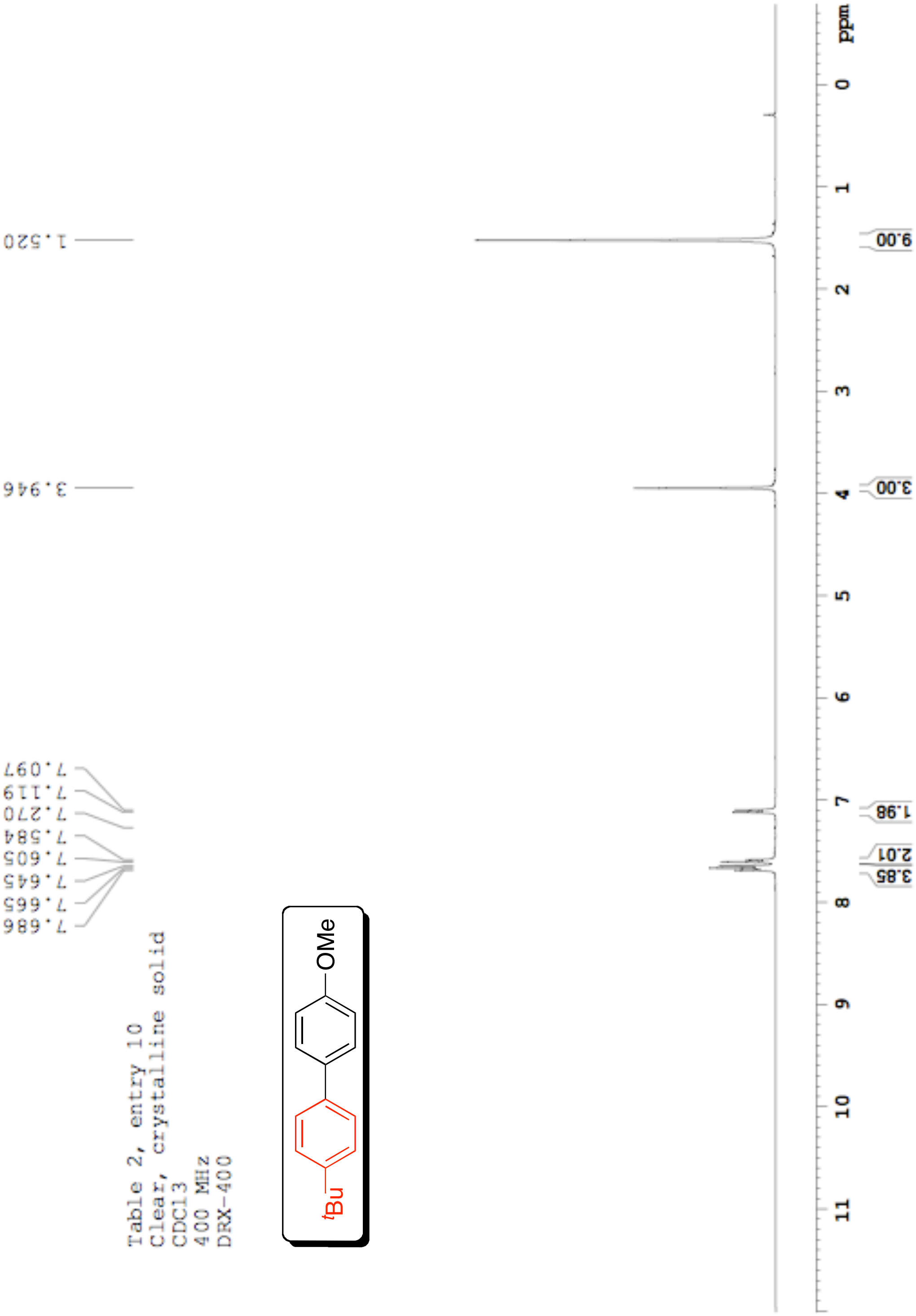
Table 2, entry 7
White solid
CDCl3
100 MHz
DRX-400
MeO2C
OMe
52.220
55.373
76.913
77.232
77.550
114.404
127.805
128.244
128.893
130.706
131.115
132.591
141.091
159.583
167.189
0 ppm
20
40
60
80
100
120
140
160
180
200
220

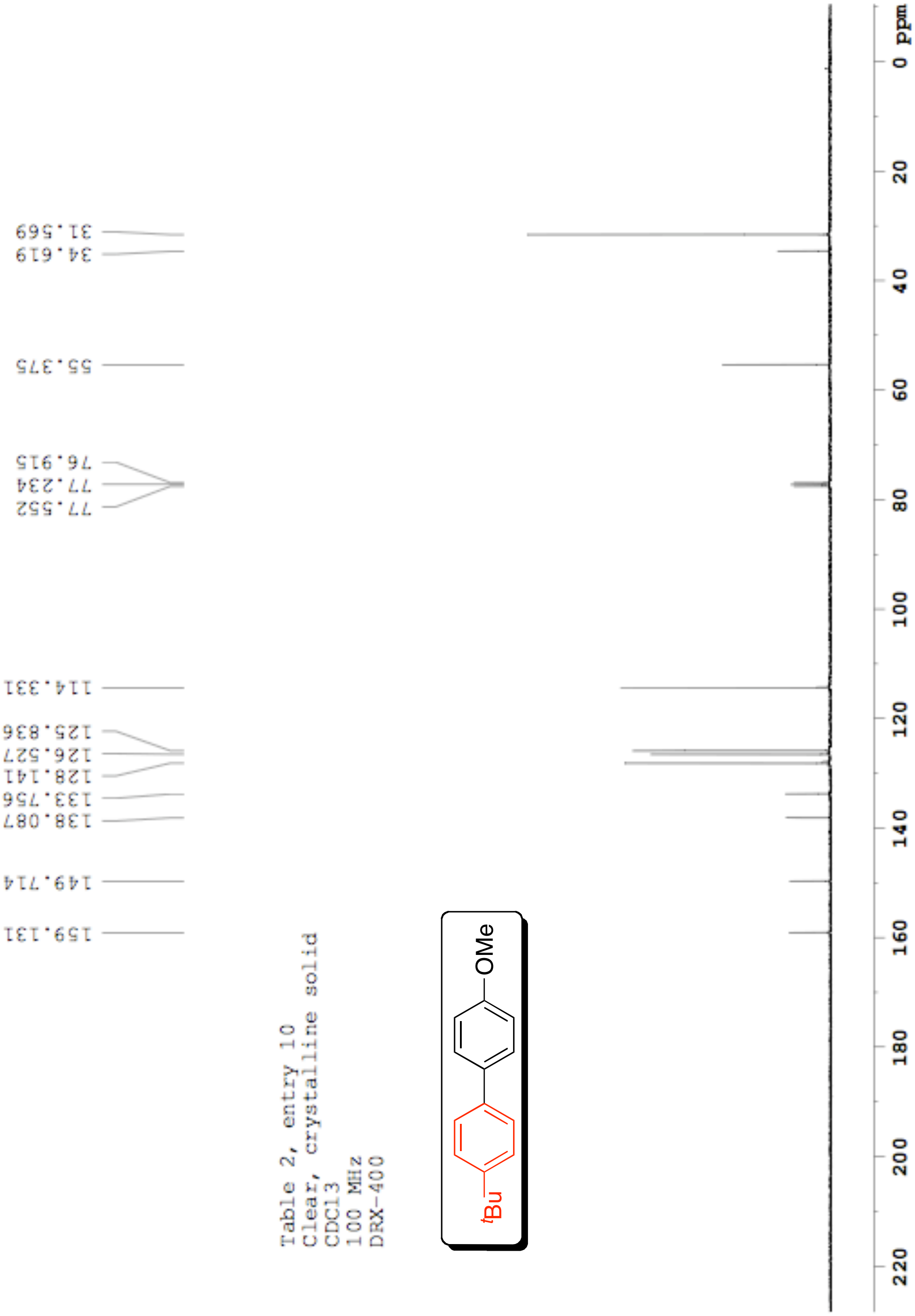

7.270
7.200
7.185
7.178
7.164
7.140
7.123
7.106
7.084
7.006
6.985
3.886
2.075
Table 2, entry 8
Yellow oil
CDCl3
400 MHz
DRX-400
OMe
10
9
8
7
6
5
4
3
2
1
ppm
0.98
3.92
1.94
3.00
6.00


21.120
55.424
76.919
77.236
77.554
113.990
127.106
127.445
130.257
133.494
136.732
141.708
158.436
Table 2, entry 8
Yellow oil
CDCl3
100 MHz
DRX-400
OMe
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210


7.585
7.567
7.563
7.543
7.505
7.501
7.486
7.482
7.466
7.462
7.344
7.340
7.326
7.321
7.313
7.308
7.265
7.246
7.228
7.202
7.181
7.179
7.067
7.045
3.901
Table 2, entry 9
Light, yellow oil
CDCl3
400 MHz
DRX-400
F
OMe
2.97
2.23
2.43
1.23
1.24
2.03
ppm
0
1
2
3
4
5
6
7
8
9
10
11


55.417
76.912
77.231
77.547
114.093
116.105
116.334
124.467
124.501
128.331
128.532
128.613
130.302
130.331
130.656
130.690
158.703
159.413
161.156
Table 2, entry 9
Light, yellow oil
CDCl3
100 MHz
DRX-400
F
OMe
0 ppm
20
40
60
80
100
120
140
160
180
200
220


1.520
3.946
7.097
7.119
7.270
7.584
7.605
7.645
7.665
7.686
Table 2, entry 10
Clear, crystalline solid
CDCl3
400 MHz
DRX-400
tBu
OMe
9.00
3.00
1.98
2.01
3.85
ppm
0
1
2
3
4
5
6
7
8
9
10
11


31.569
34.619
55.375
76.915
77.234
77.552
114.331
125.836
126.527
128.141
133.756
138.087
149.714
159.131
Table 2, entry 10
Clear, crystalline solid
CDCl3
100 MHz
DRX-400
OMe
tBu
0 ppm
20
40
60
80
100
120
140
160
180
200
220

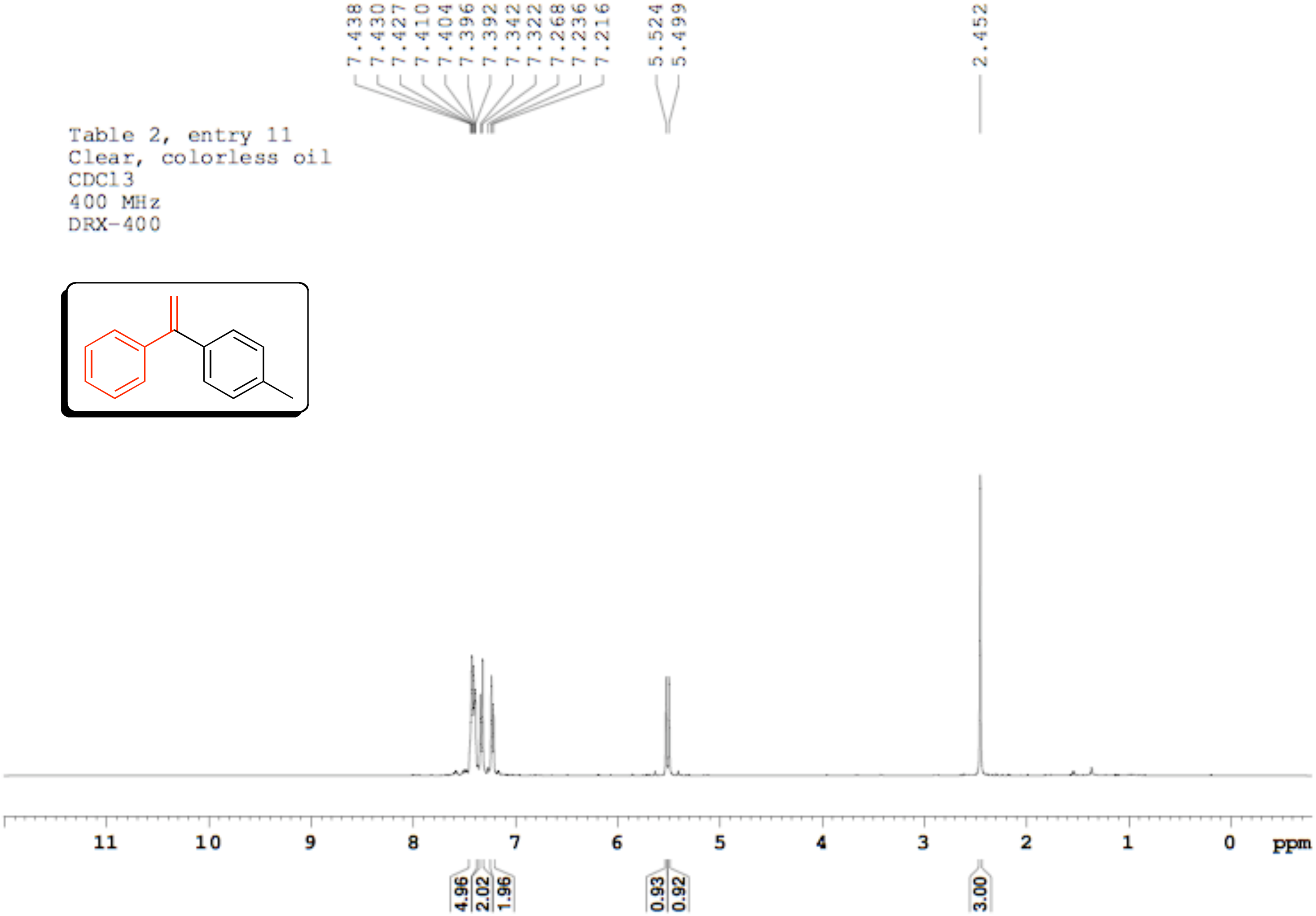


Table 2, entry 11
Clear, colorless oil
CDCl3
400 MHz
DRX-400

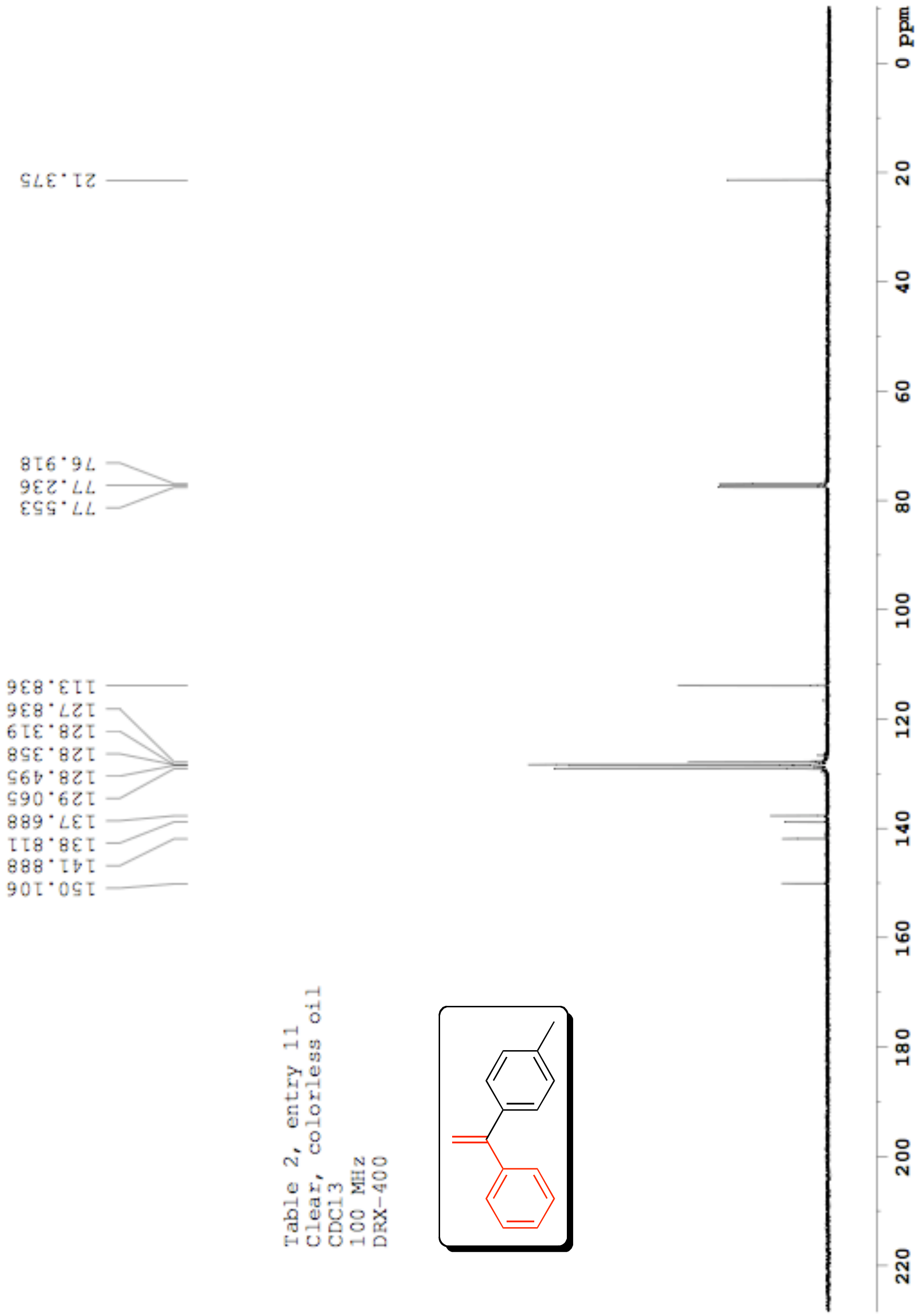
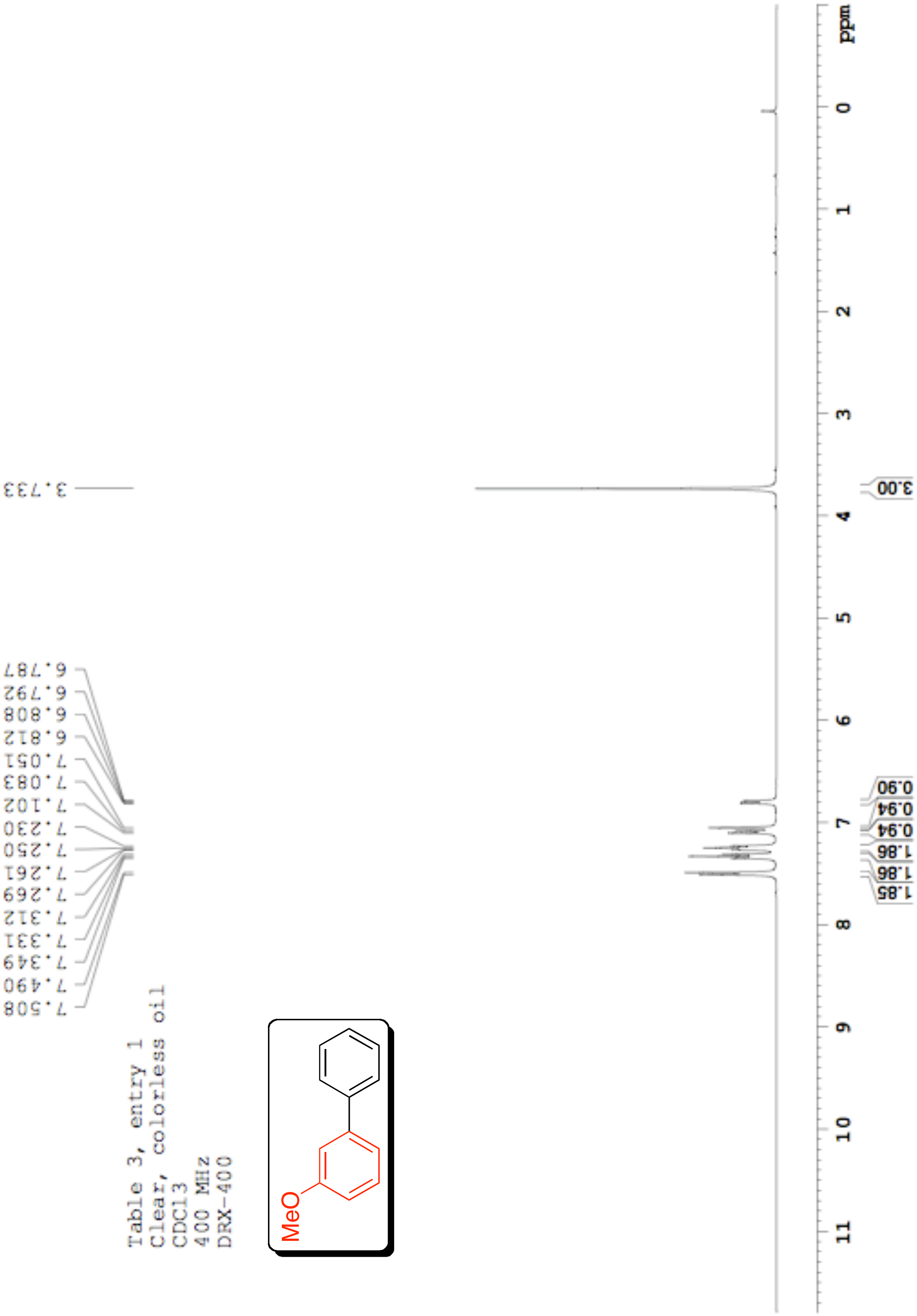
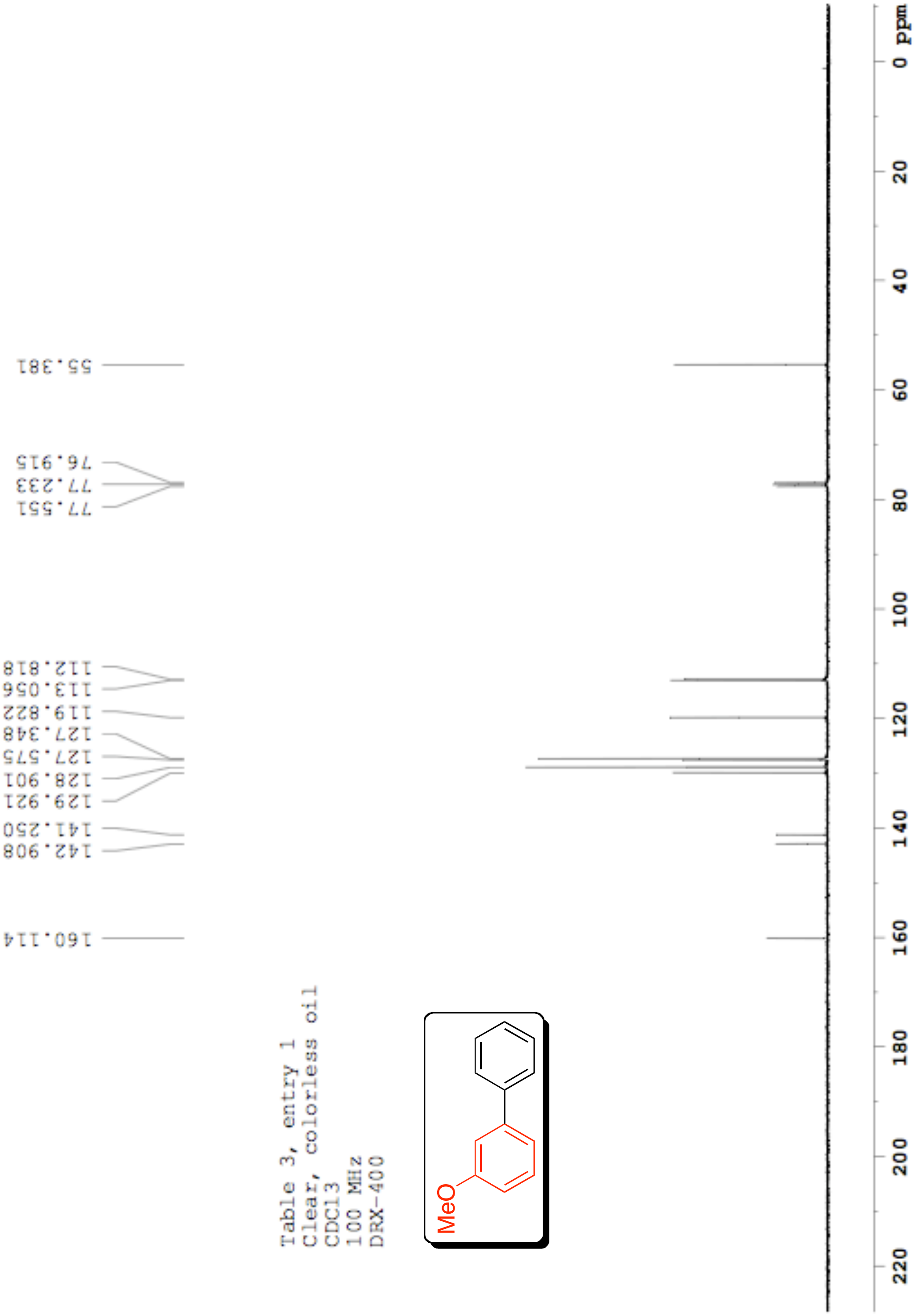
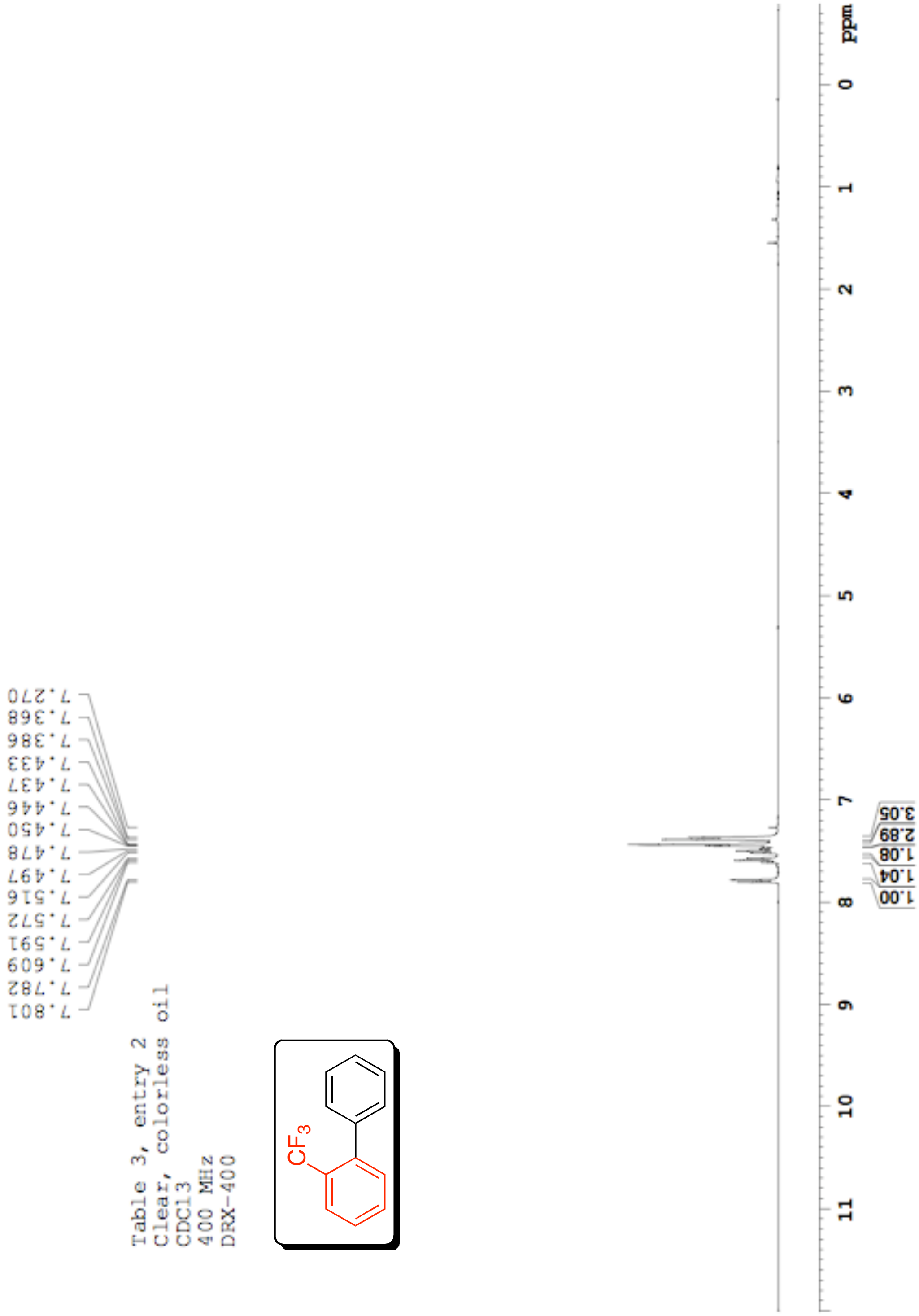
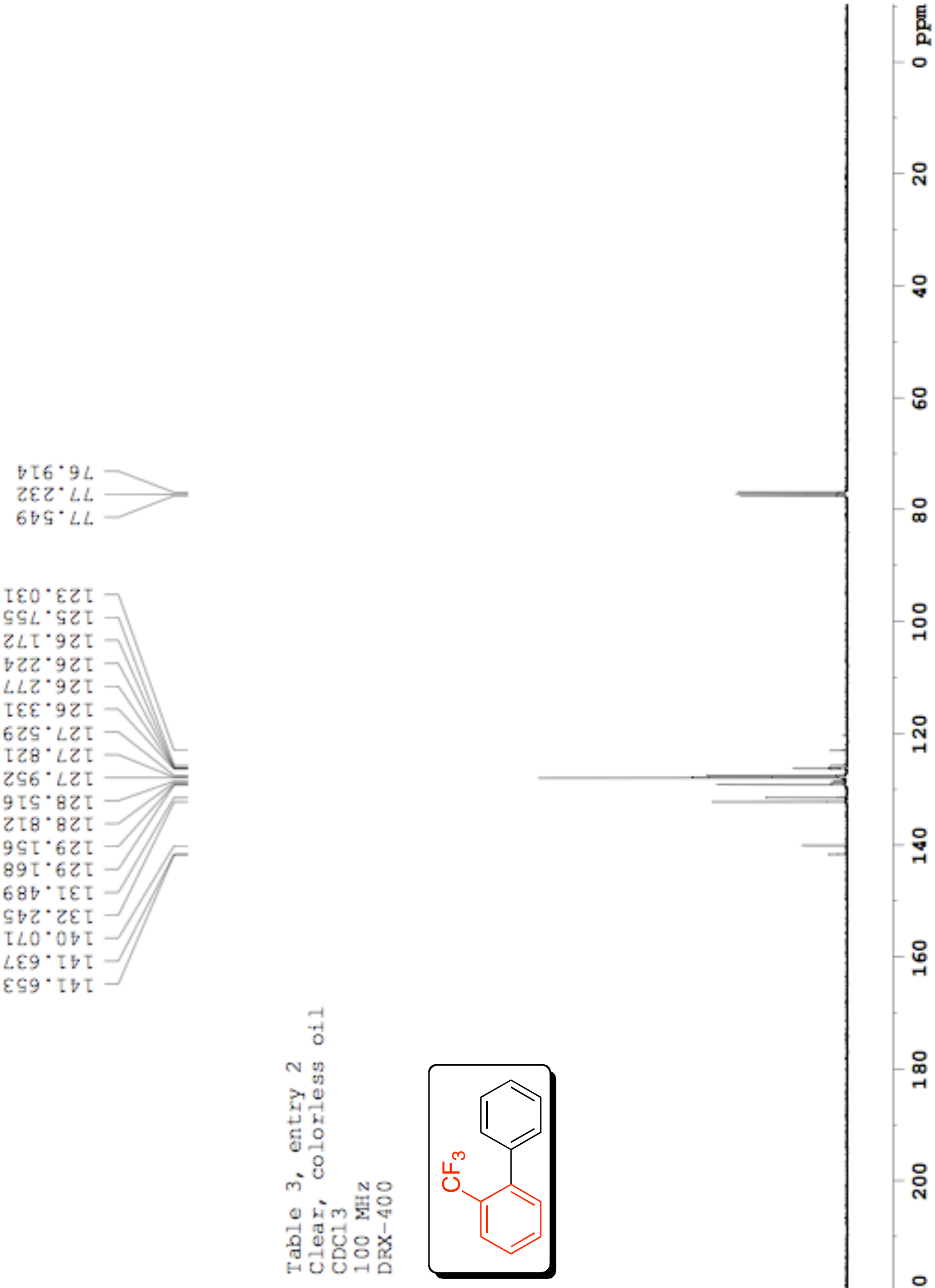


Table 2, entry 11
Clear, colorless oil
CDCl3
100 MHz
DRX-400


3.733
6.787
6.792
6.808
6.812
7.051
7.083
7.102
7.230
7.250
7.261
7.269
7.312
7.331
7.349
7.490
7.508
Table 3, entry 1
Clear, colorless oil
CDCl3
400 MHz
DRX-400
MeO
3.00
0.90
0.94
0.94
1.86
1.86
1.85
ppm
0
1
2
3
4
5
6
7
8
9
10
11


55.381
76.915
77.233
77.551
112.818
113.056
119.822
127.348
127.575
128.901
129.921
141.250
142.908
160.114
Table 3, entry 1
Clear, colorless oil
CDCl3
100 MHz
DRX-400
MeO
0 ppm
20
40
60
80
100
120
140
160
180
200
220


7.270
7.368
7.386
7.433
7.437
7.446
7.450
7.478
7.497
7.516
7.572
7.591
7.609
7.782
7.801
Table 3, entry 2
Clear, colorless oil
CDCl3
400 MHz
DRX-400
CF3
3.05
2.89
1.08
1.04
1.00
ppm
0
1
2
3
4
5
6
7
8
9
10
11


76.914
77.232
77.549
123.031
125.755
126.172
126.224
126.277
126.331
127.529
127.821
127.952
128.516
128.812
129.156
129.168
131.489
132.245
140.071
141.637
141.653
Table 3, entry 2
Clear, colorless oil
CDCl3
100 MHz
DRX-400
CF3
0 ppm
20
40
60
80
100
120
140
160
180
200
220

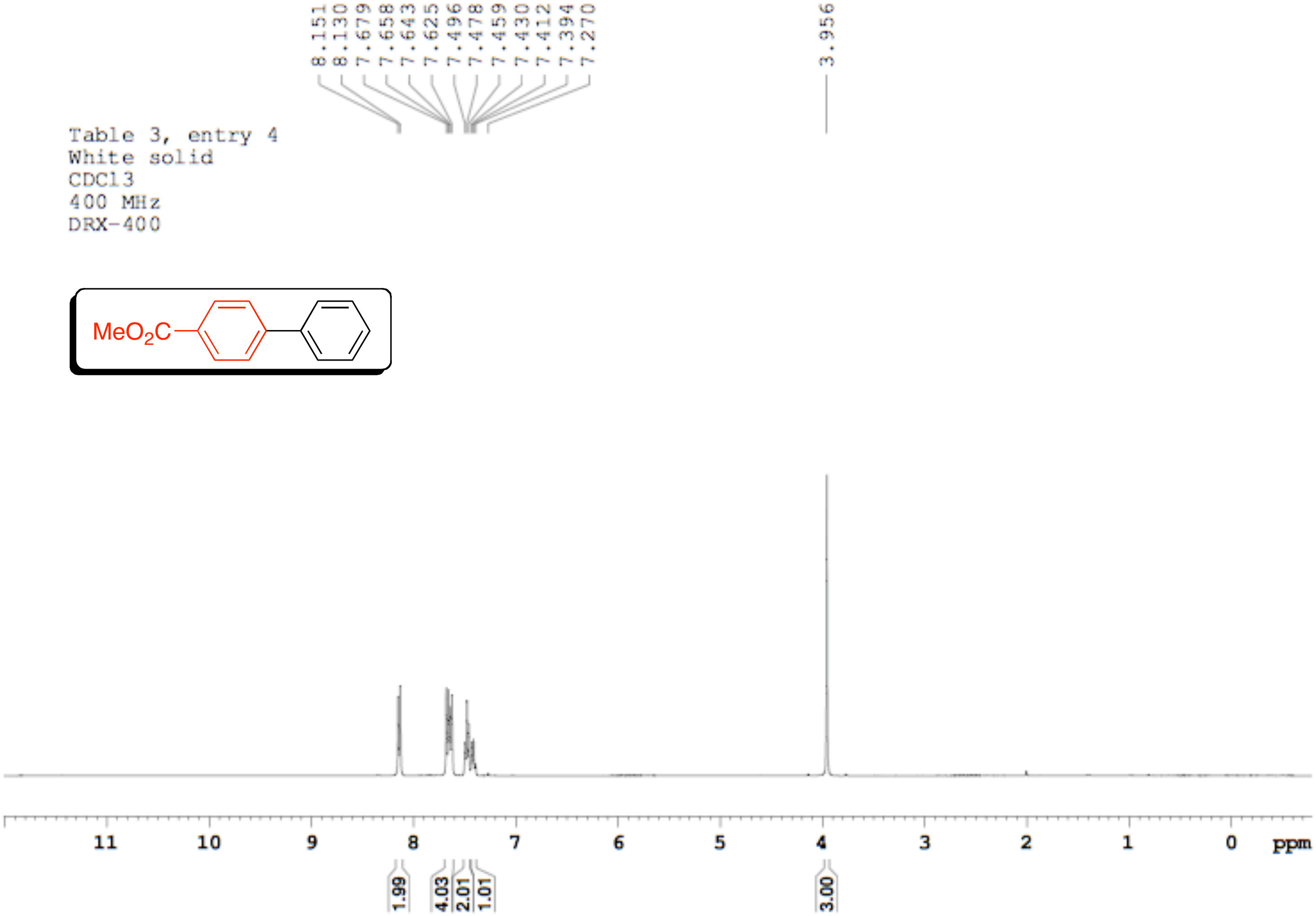
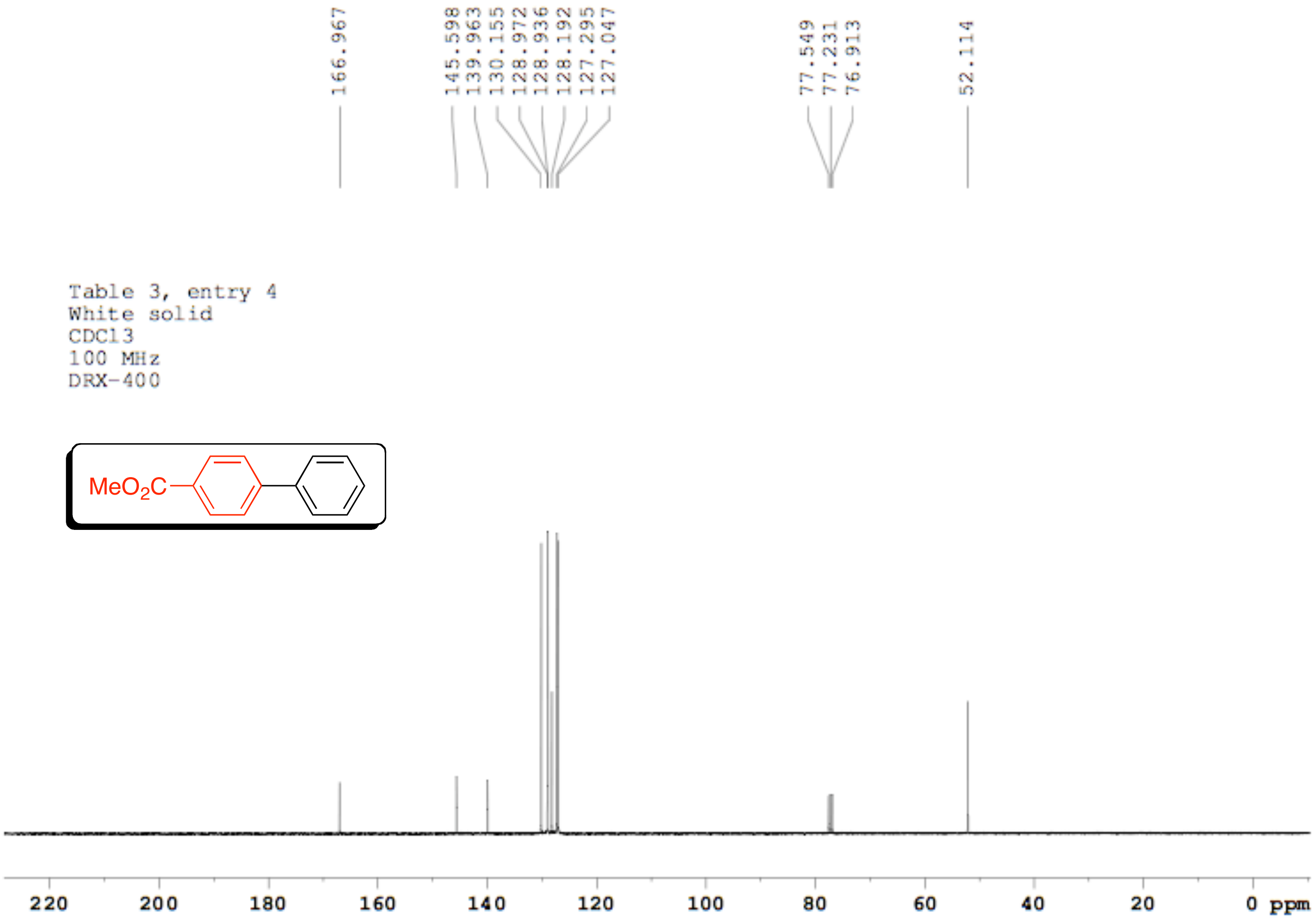


Table 3, entry 4
White solid
CDCl3
400 MHz
DRX-400
MeO2C
8.151
8.130
7.679
7.658
7.643
7.625
7.496
7.478
7.459
7.430
7.412
7.394
7.270
3.956
1.99
4.03
2.01
1.01
3.00
11
10
9
8
7
6
5
4
3
2
1
0
ppm


166.967
145.598
139.963
130.155
128.972
128.936
128.192
127.295
127.047
77.549
77.231
76.913
52.114
Table 3, entry 4
White solid
CDCl3
100 MHz
DRX-400
MeO_2C
220
200
180
160
140
120
100
80
60
40
20
0 ppm

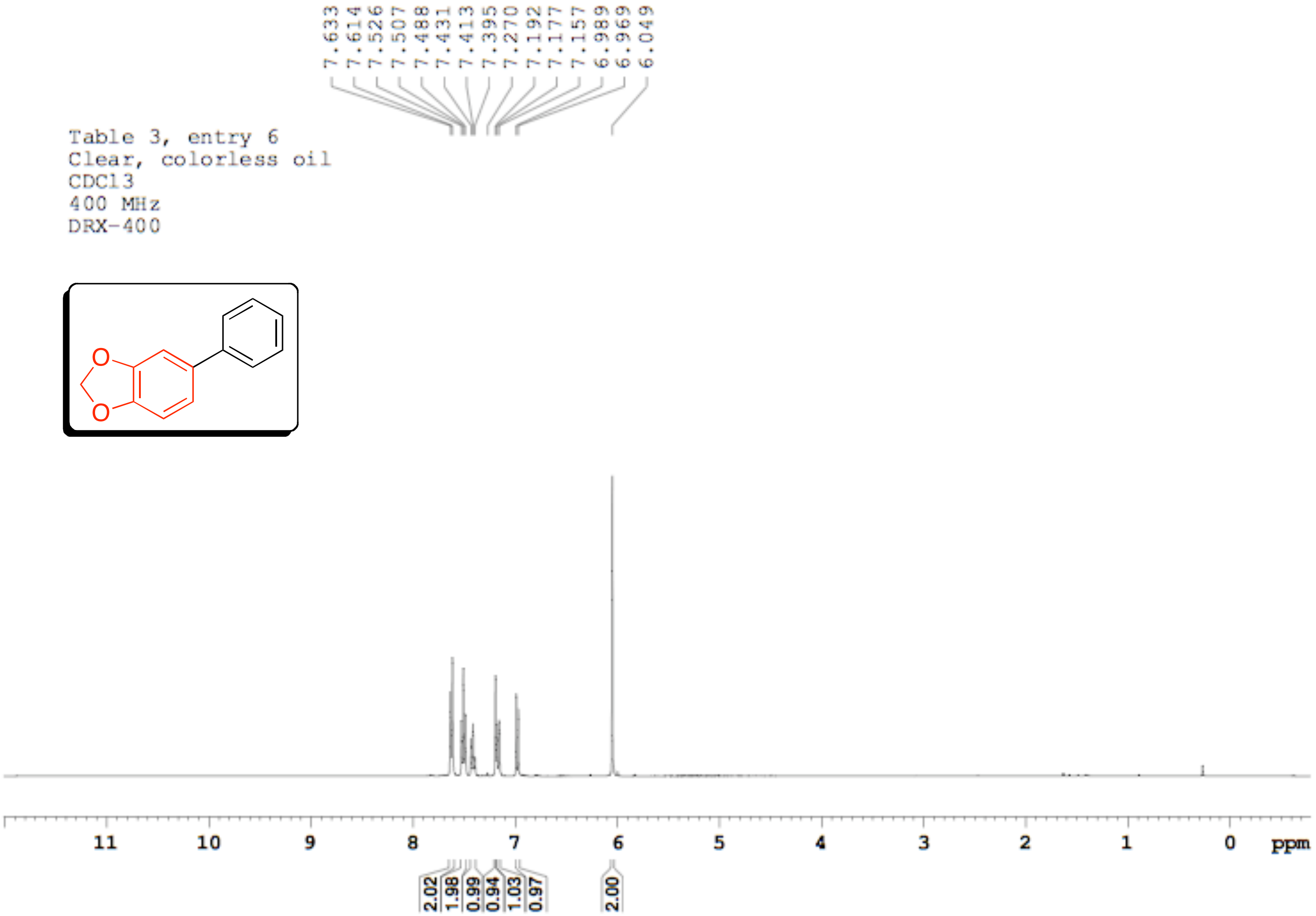


Table 3, entry 6
Clear, colorless oil
CDCl3
400 MHz
DRX-400

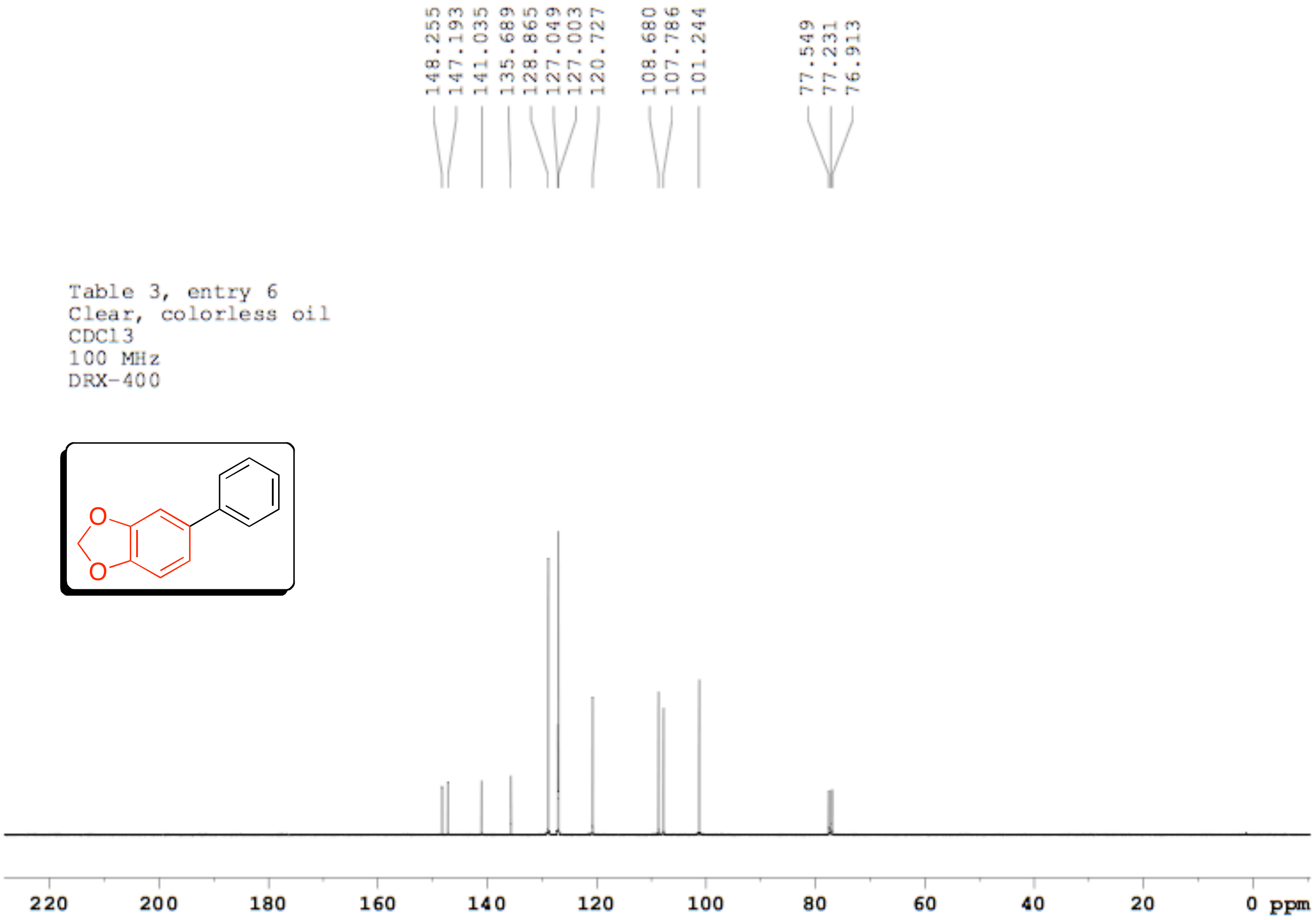
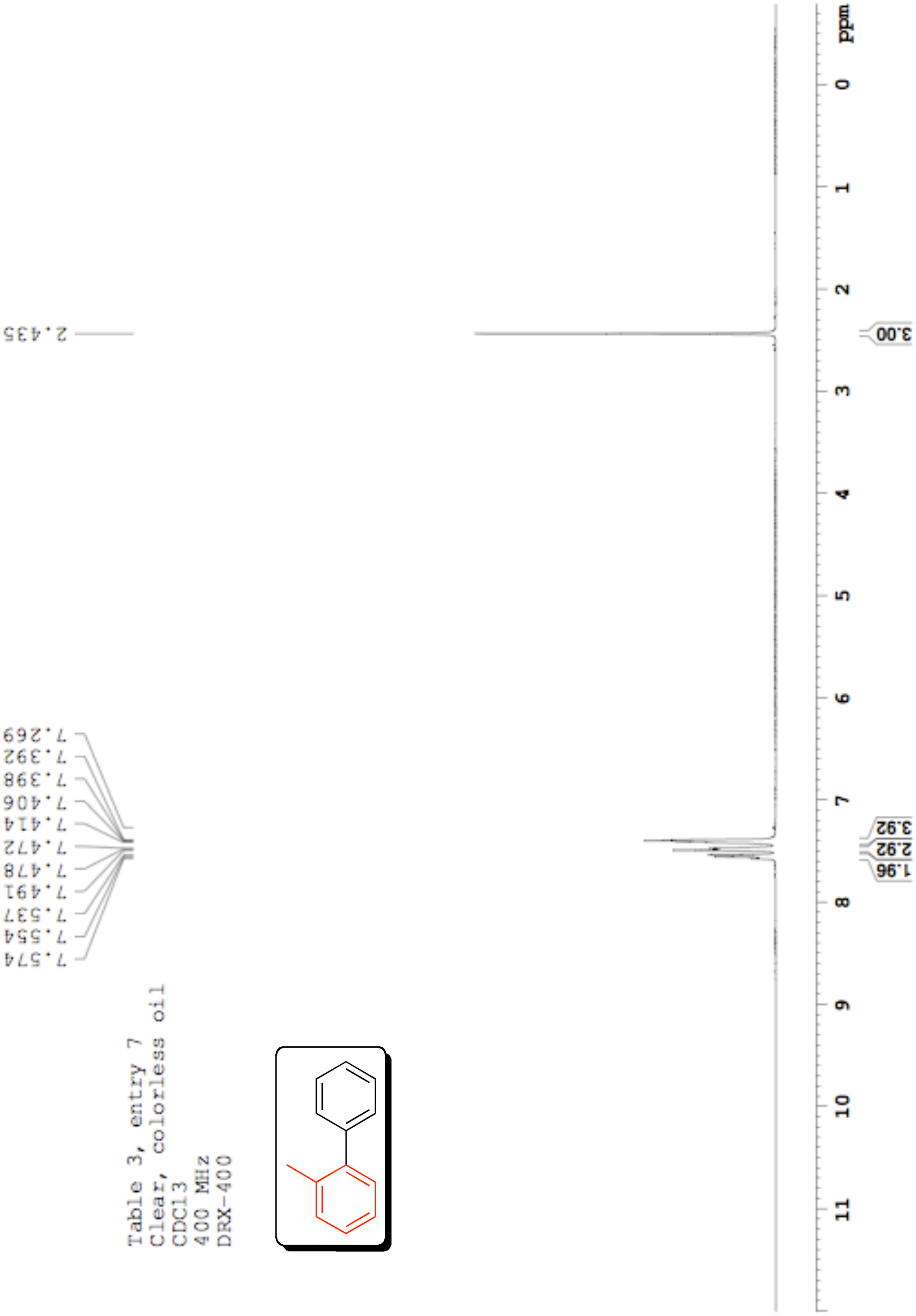
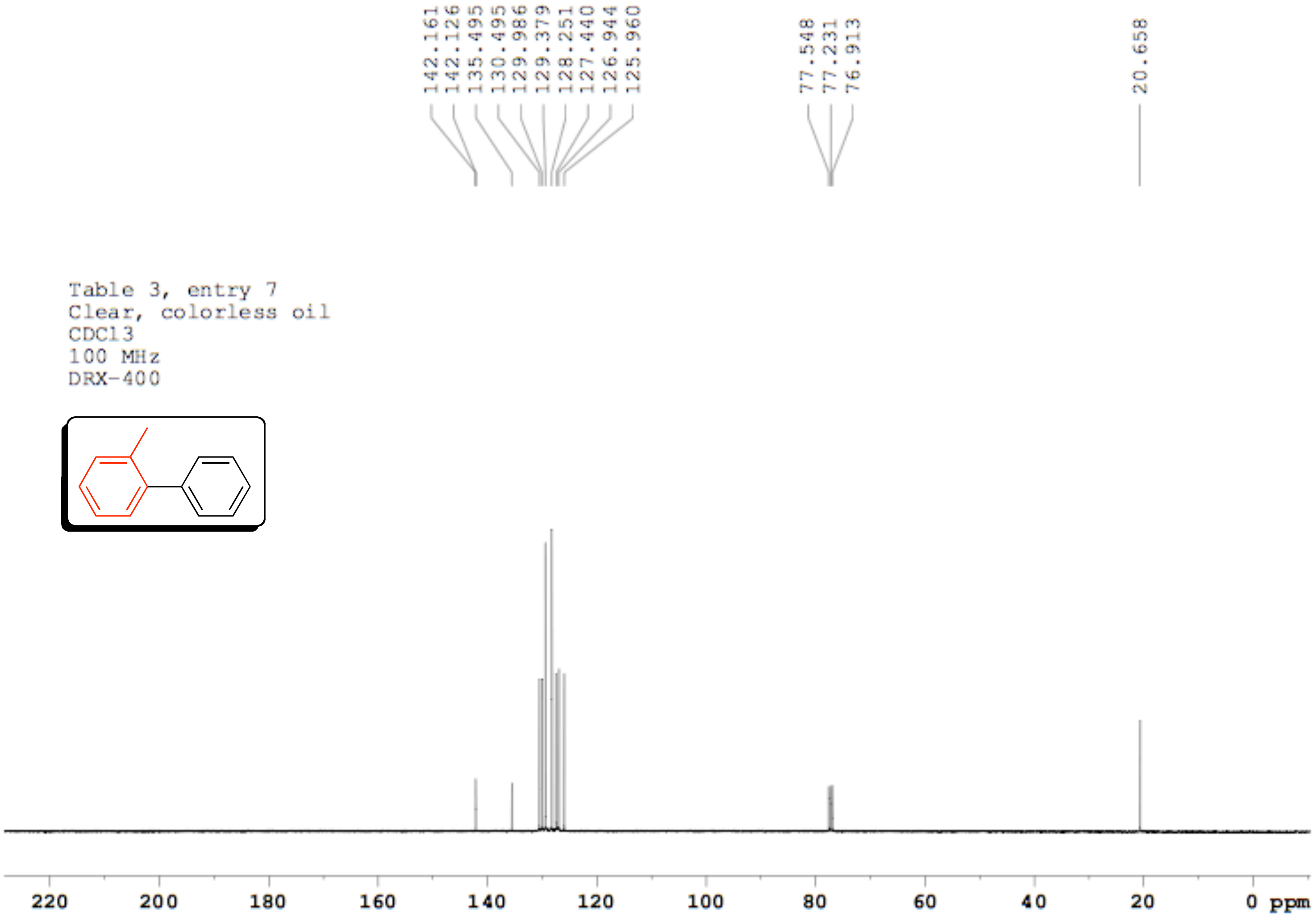


Table 3, entry 6
Clear, colorless oil
CDCl3
100 MHz
DRX-400


2.435
7.269
7.392
7.398
7.406
7.414
7.472
7.478
7.491
7.537
7.554
7.574
Table 3, entry 7
Clear, colorless oil
CDCl3
400 MHz
DRX-400
3.00
3.92
2.92
1.96
ppm
0
1
2
3
4
5
6
7
8
9
10
11


142.161
142.126
135.495
130.495
129.986
129.379
128.251
127.440
126.944
125.960
77.548
77.231
76.913
20.658
Table 3, entry 7
Clear, colorless oil
CDCl3
100 MHz
DRX-400
220
200
180
160
140
120
100
80
60
40
20
0 ppm

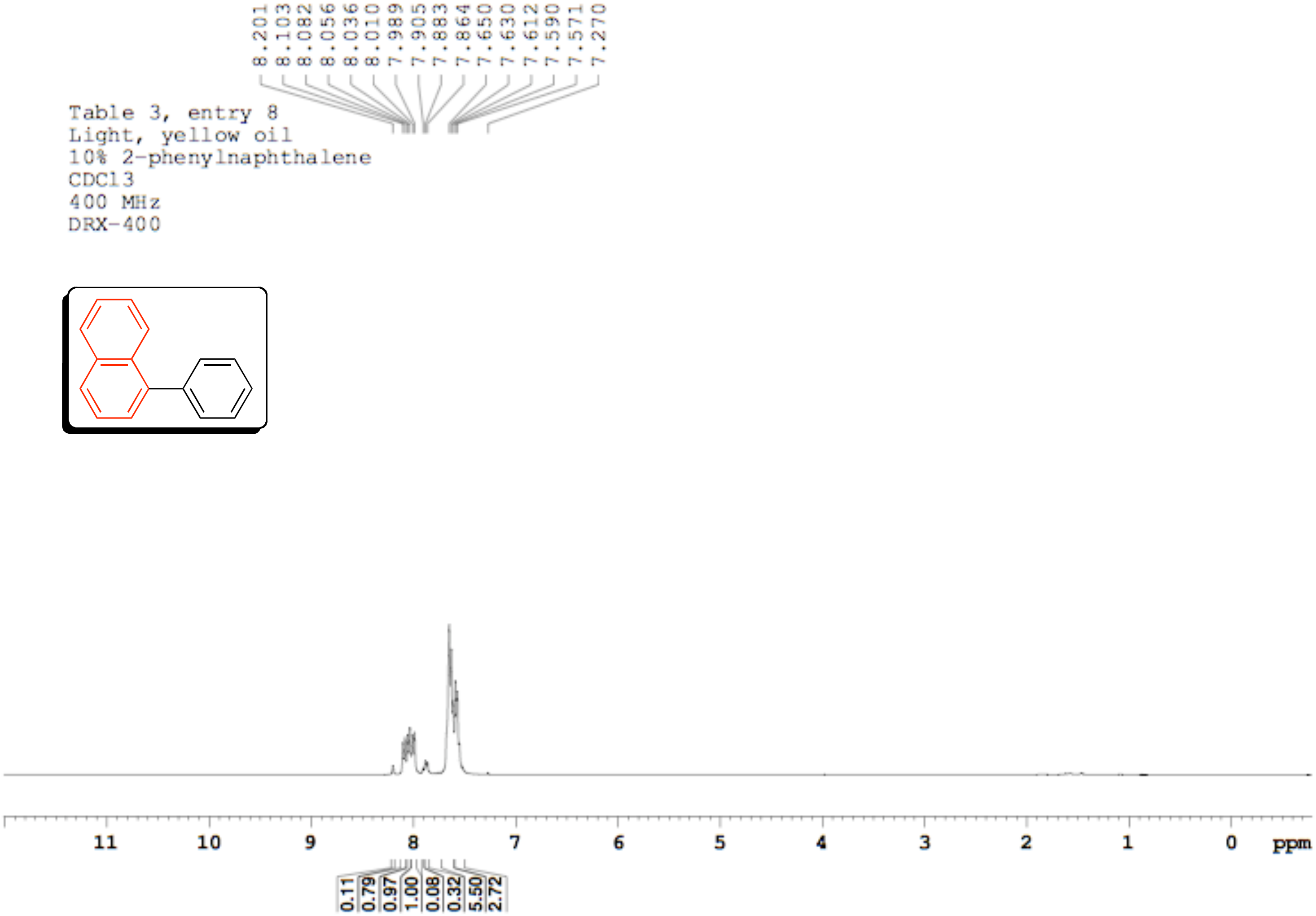


Table 3, entry 8
Light, yellow oil
10% 2-phenylnaphthalene
CDCl3
400 MHz
DRX-400
8.201
8.103
8.082
8.056
8.036
8.010
7.989
7.905
7.883
7.864
7.650
7.630
7.612
7.590
7.571
7.270
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.11
0.79
0.97
1.00
0.08
0.32
5.50
2.72

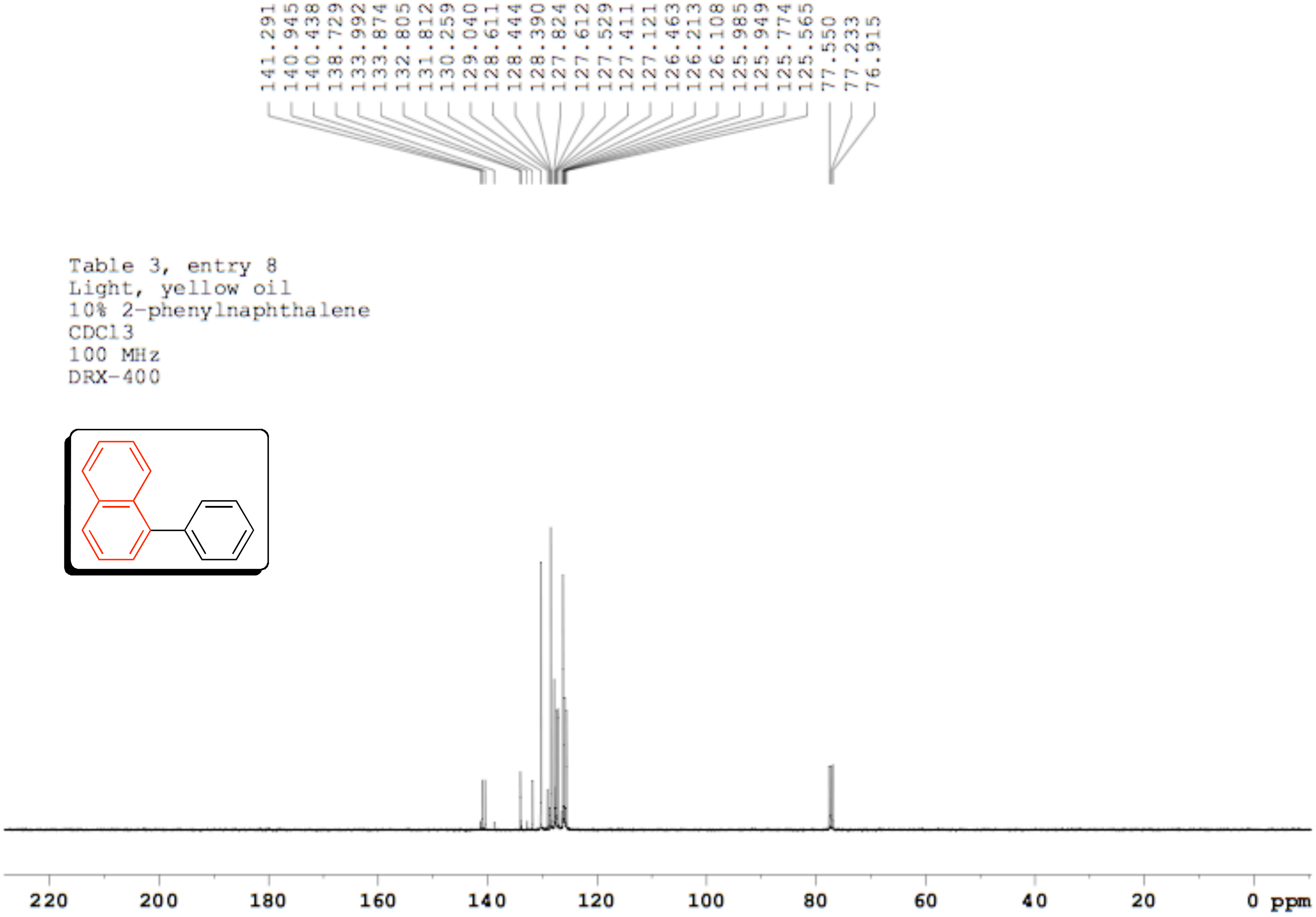
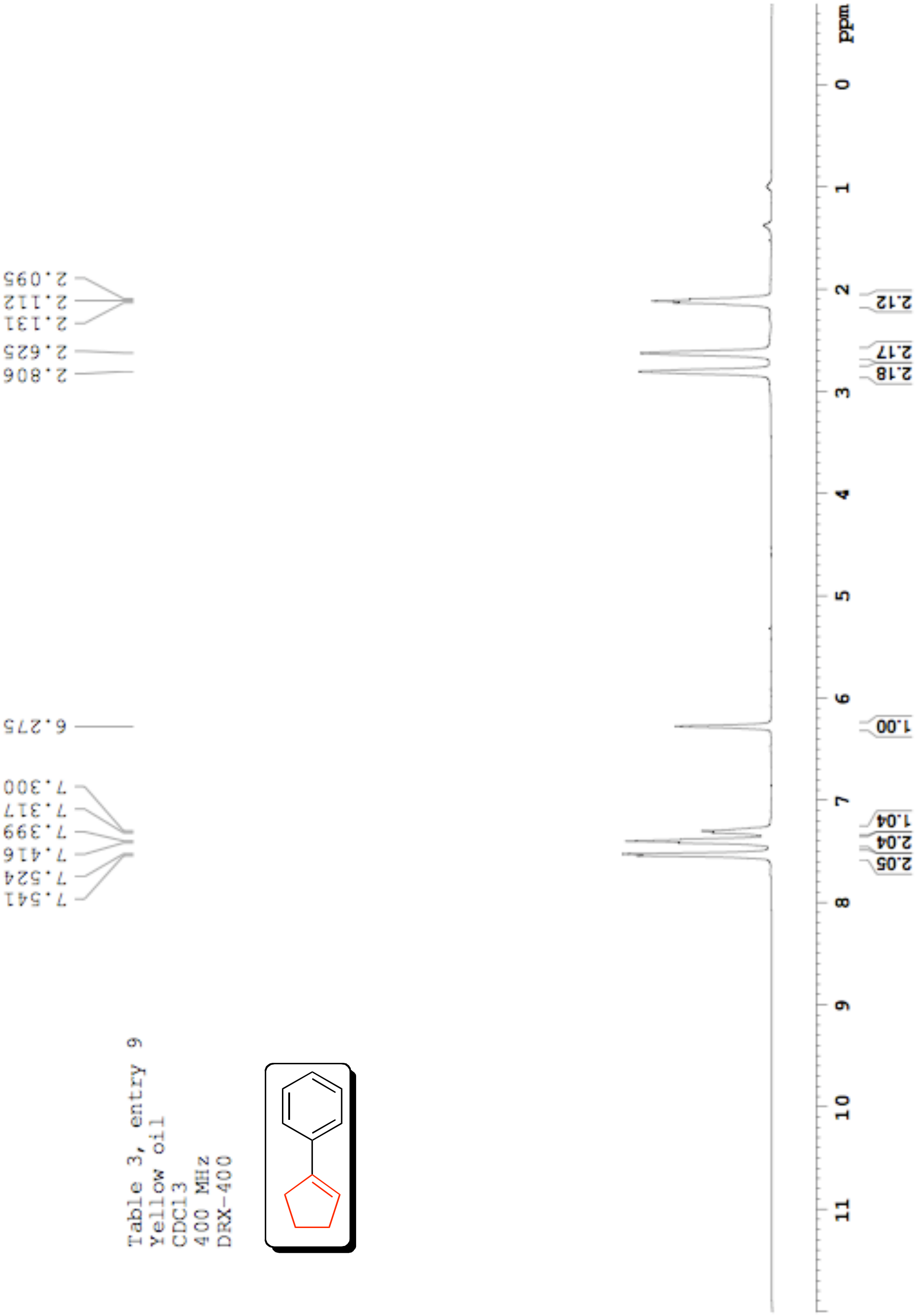
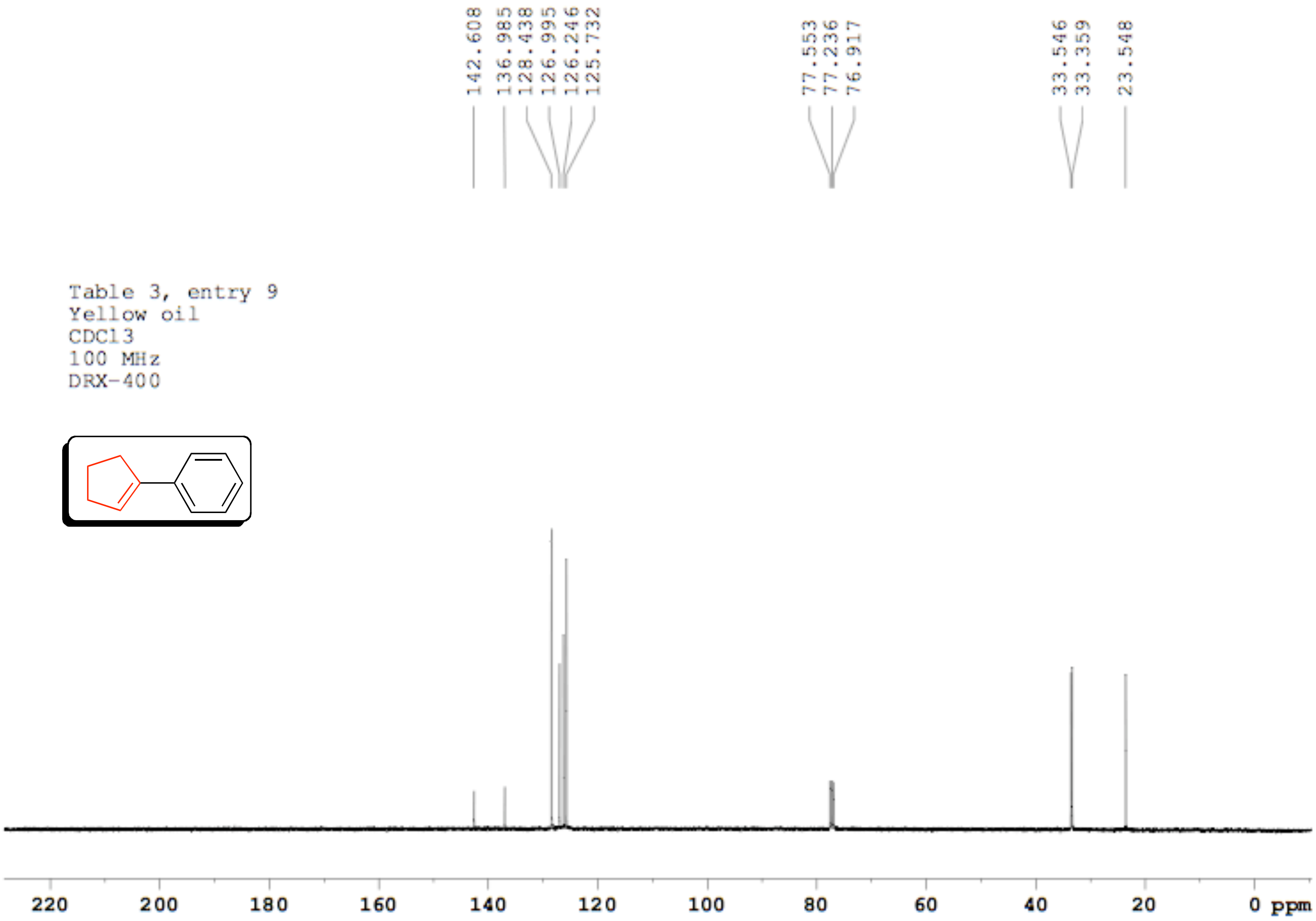


Table 3, entry 8
Light, yellow oil
10% 2-phenylnaphthalene
CDCl3
100 MHz
DRX-400


2.095
2.112
2.131
2.625
2.806
6.275
7.300
7.317
7.399
7.416
7.524
7.541
Table 3, entry 9
Yellow oil
CDCl3
400 MHz
DRX-400
2.12
2.17
2.18
1.00
1.04
2.04
2.05
ppm
0
1
2
3
4
5
6
7
8
9
10
11


142.608
136.985
128.438
126.995
126.246
125.732
77.553
77.236
76.917
33.546
33.359
23.548
Table 3, entry 9
Yellow oil
CDCl3
100 MHz
DRX-400
220
200
180
160
140
120
100
80
60
40
20
0 ppm

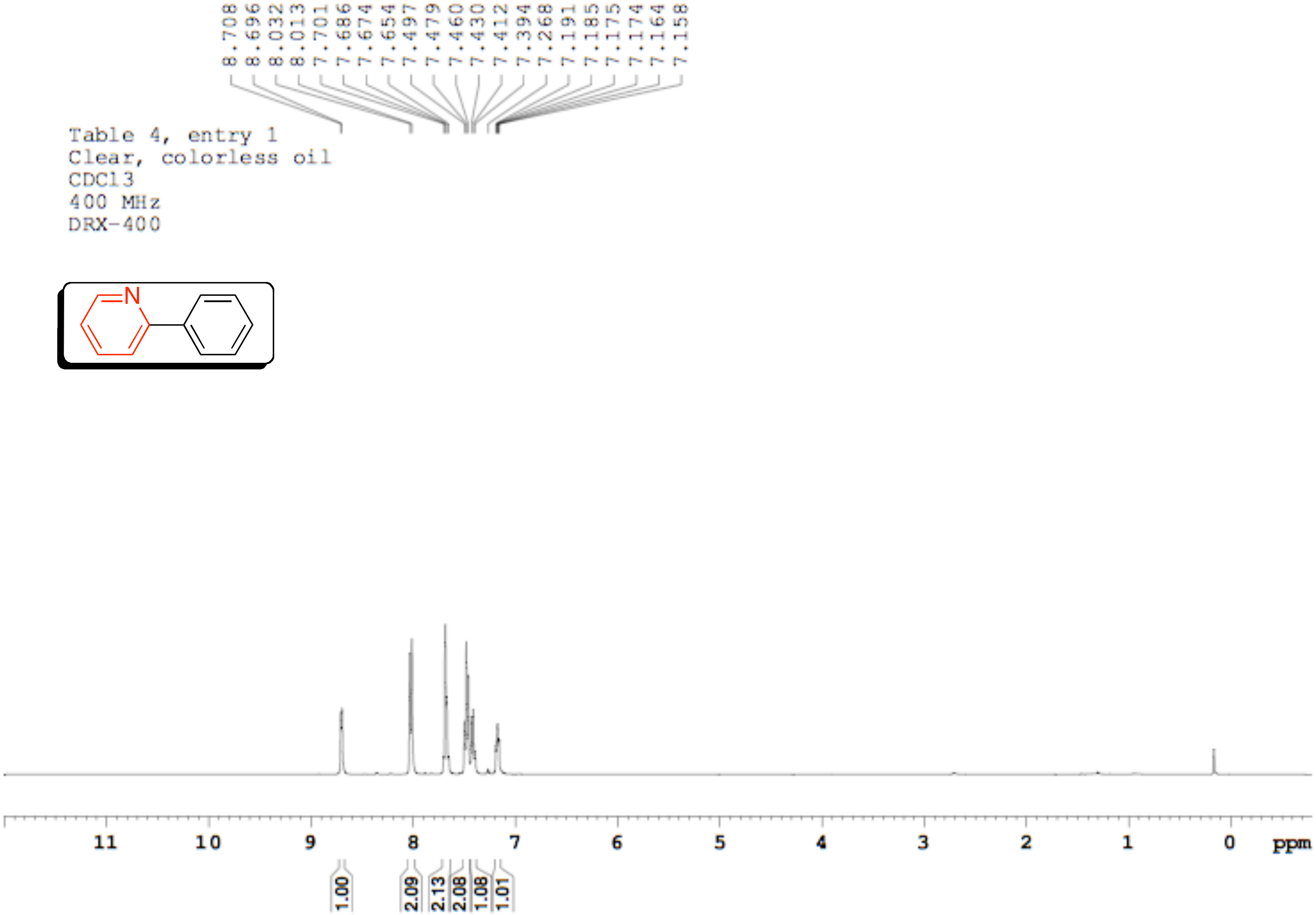
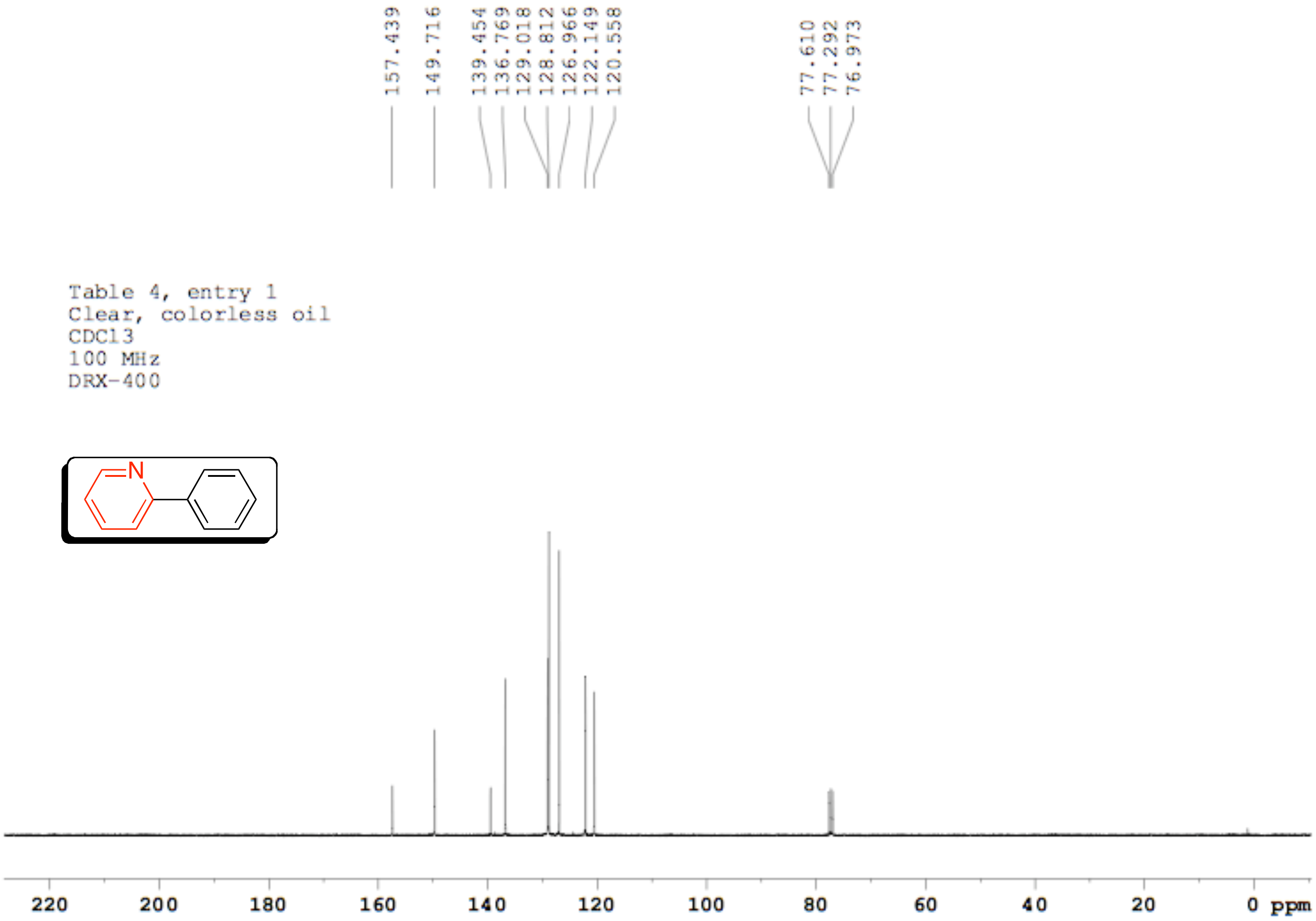
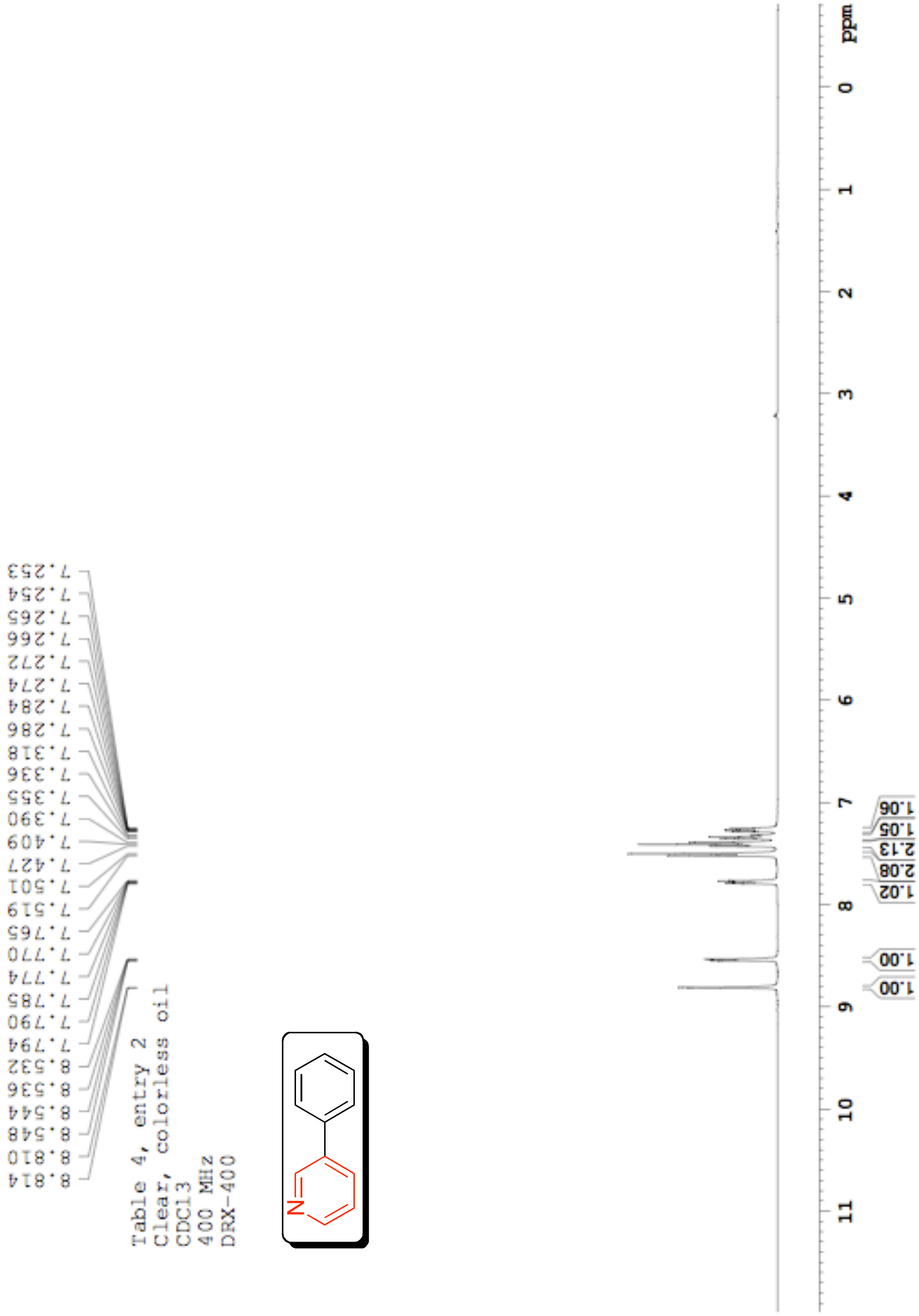


Table 4, entry 1
Clear, colorless oil
CDCl3
400 MHz
DRX-400


157.439
149.716
139.454
136.769
129.018
128.812
126.966
122.149
120.558
77.610
77.292
76.973
Table 4, entry 1
Clear, colorless oil
CDCl3
100 MHz
DRX-400
N
220
200
180
160
140
120
100
80
60
40
20
0 ppm


8.814
8.810
8.548
8.544
8.536
8.532
7.794
7.790
7.785
7.774
7.770
7.765
7.519
7.501
7.427
7.409
7.390
7.355
7.336
7.318
7.286
7.284
7.274
7.272
7.266
7.265
7.254
7.253
Table 4, entry 2
Clear, colorless oil
CDCl3
400 MHz
DRX-400
N
1.00
1.00
1.02
2.08
2.13
1.05
1.06
11
10
9
8
7
6
5
4
3
2
1
0
ppm

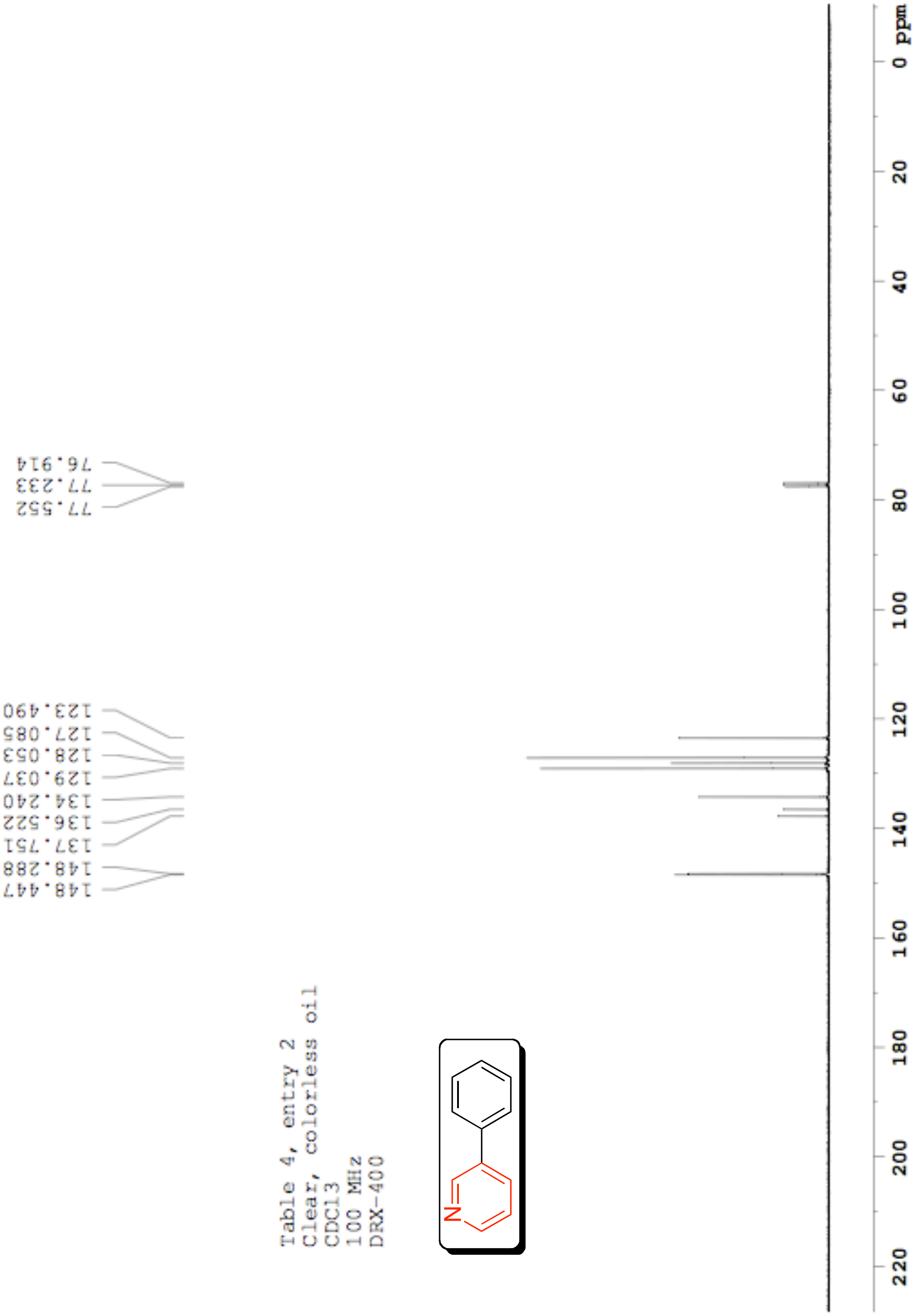
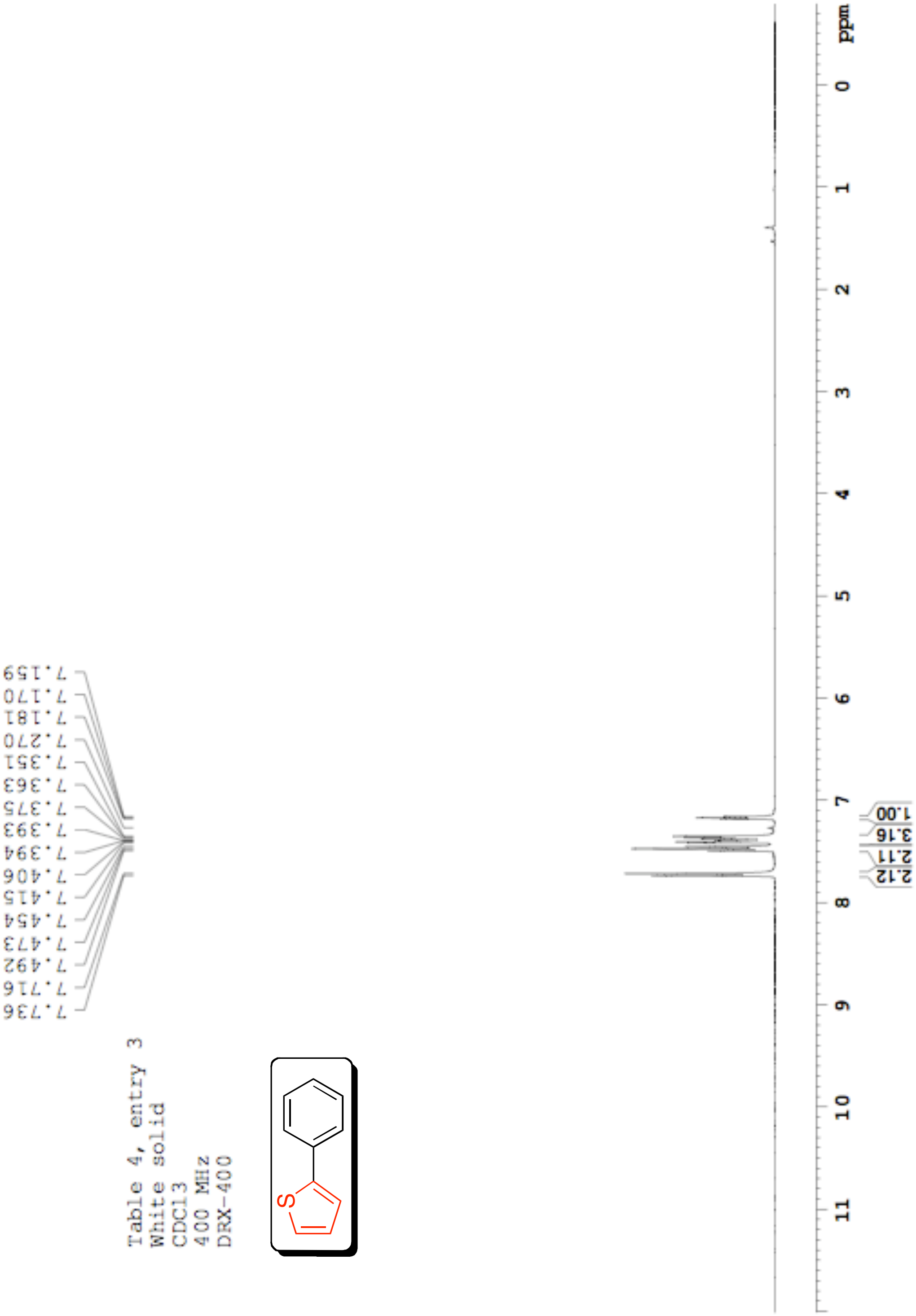
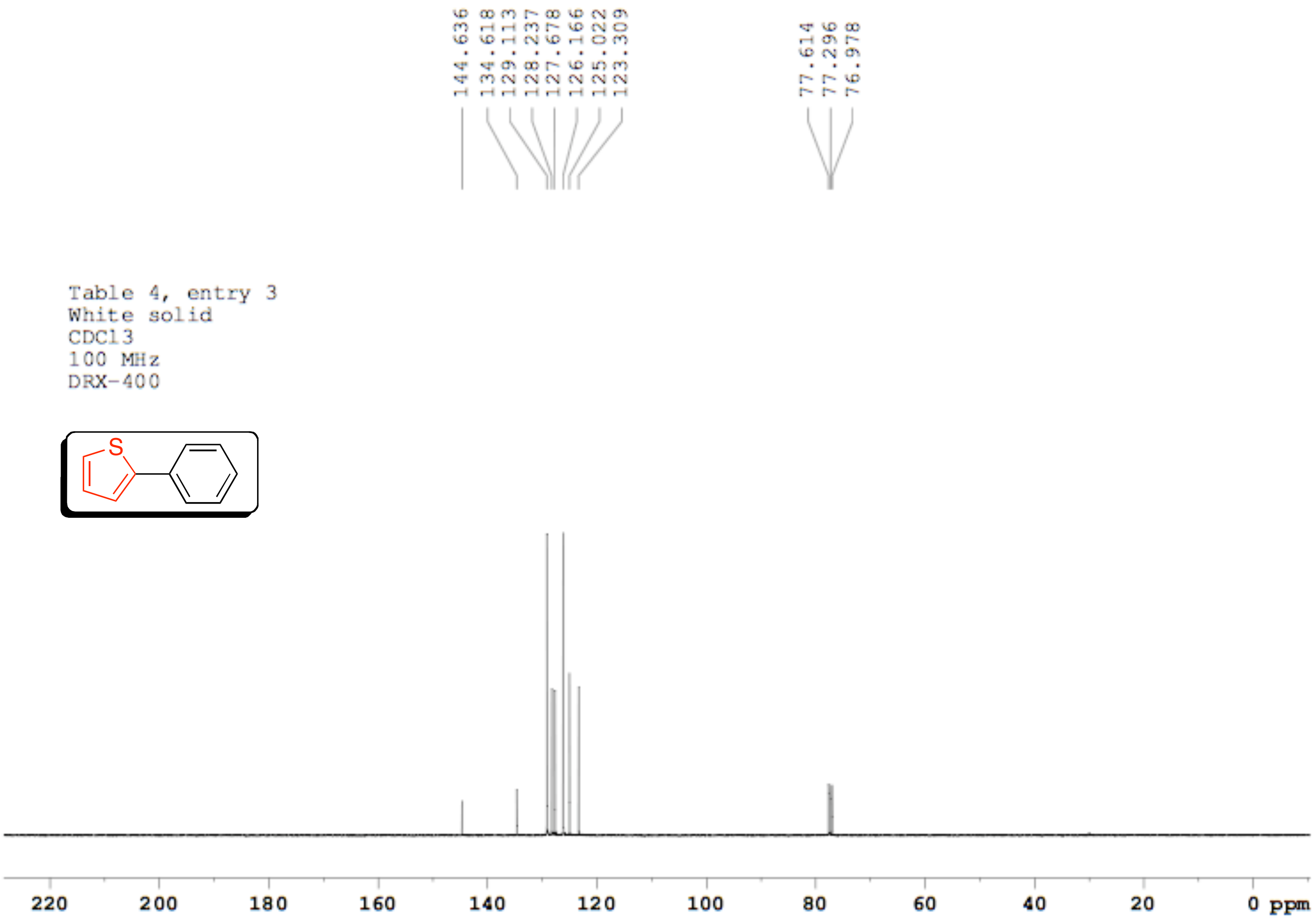
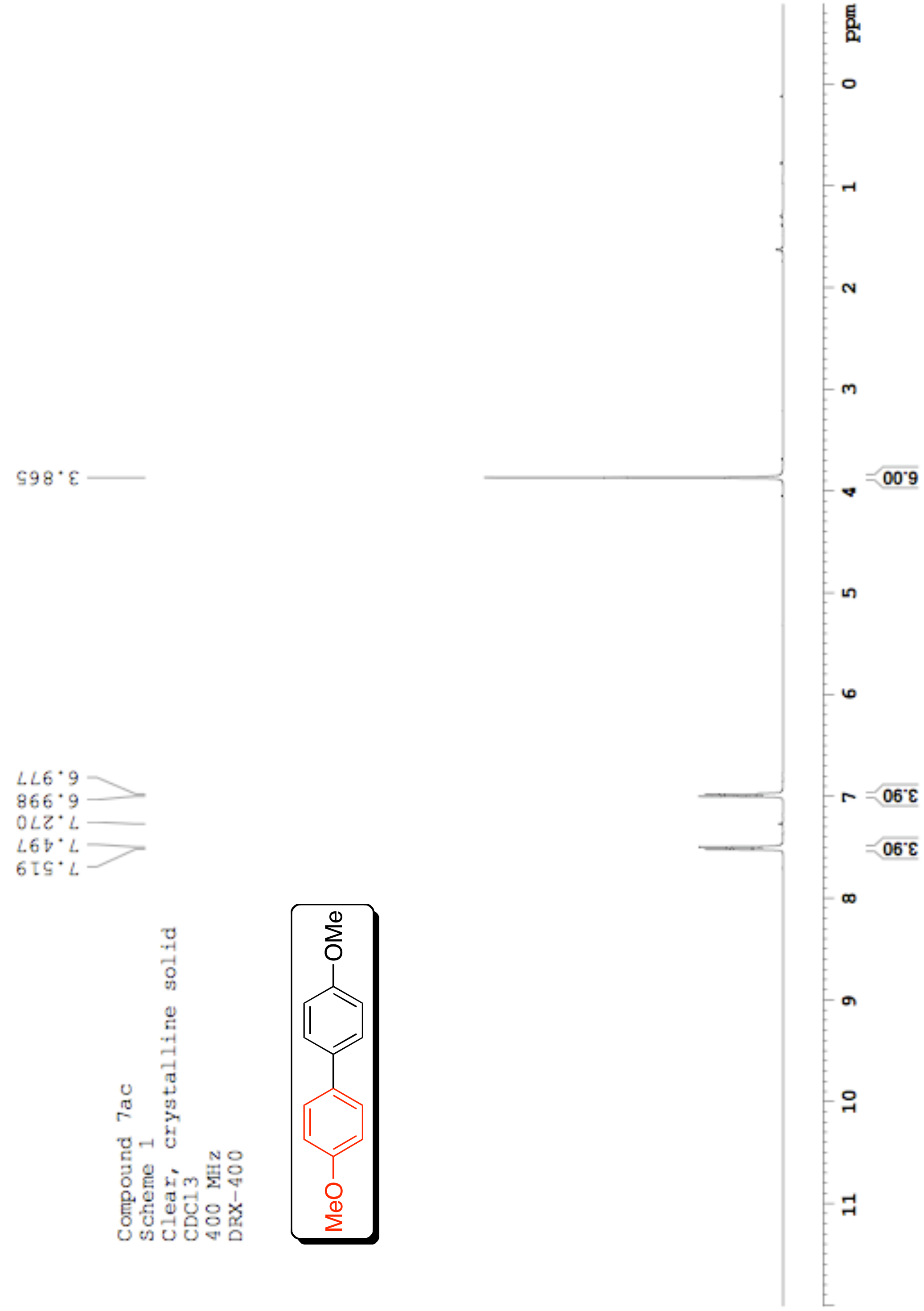


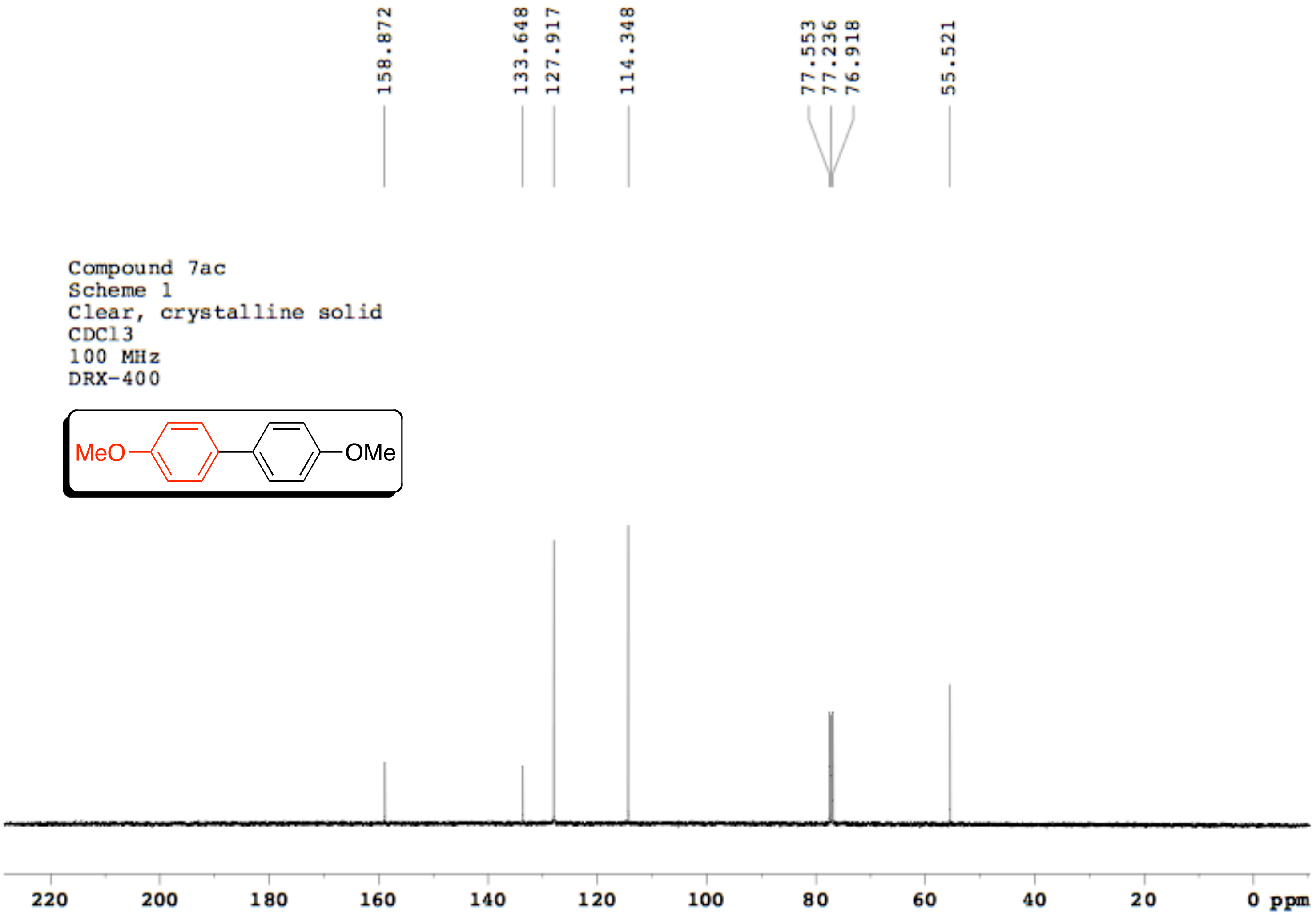
Table 4, entry 2
Clear, colorless oil
CDCl3
100 MHz
DRX-400

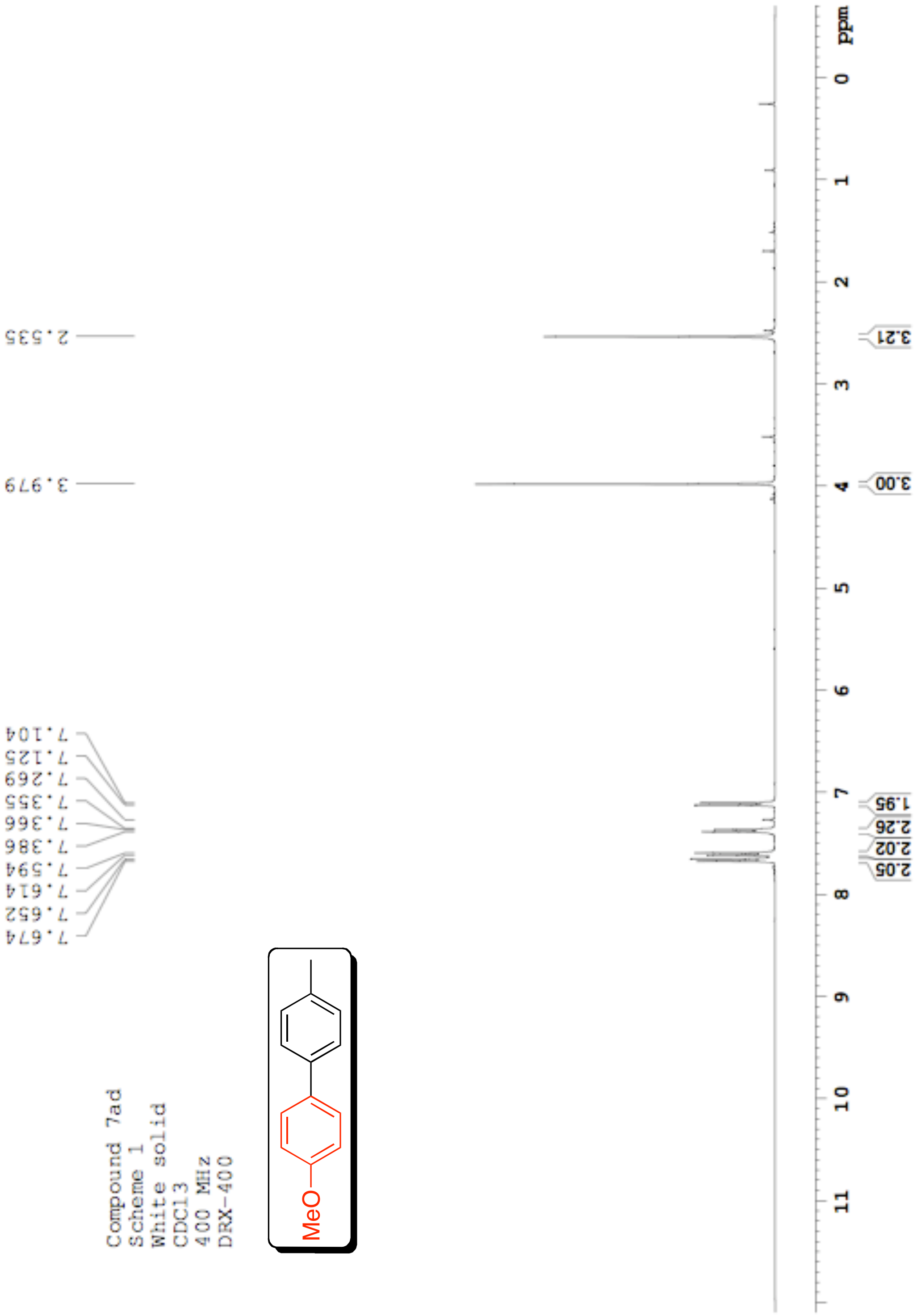

7.159
7.170
7.181
7.270
7.351
7.363
7.375
7.393
7.394
7.406
7.415
7.454
7.473
7.492
7.716
7.736
Table 4, entry 3
White solid
CDCl3
400 MHz
DRX-400
S
1.00
3.16
2.11
2.12
ppm
0
1
2
3
4
5
6
7
8
9
10
11

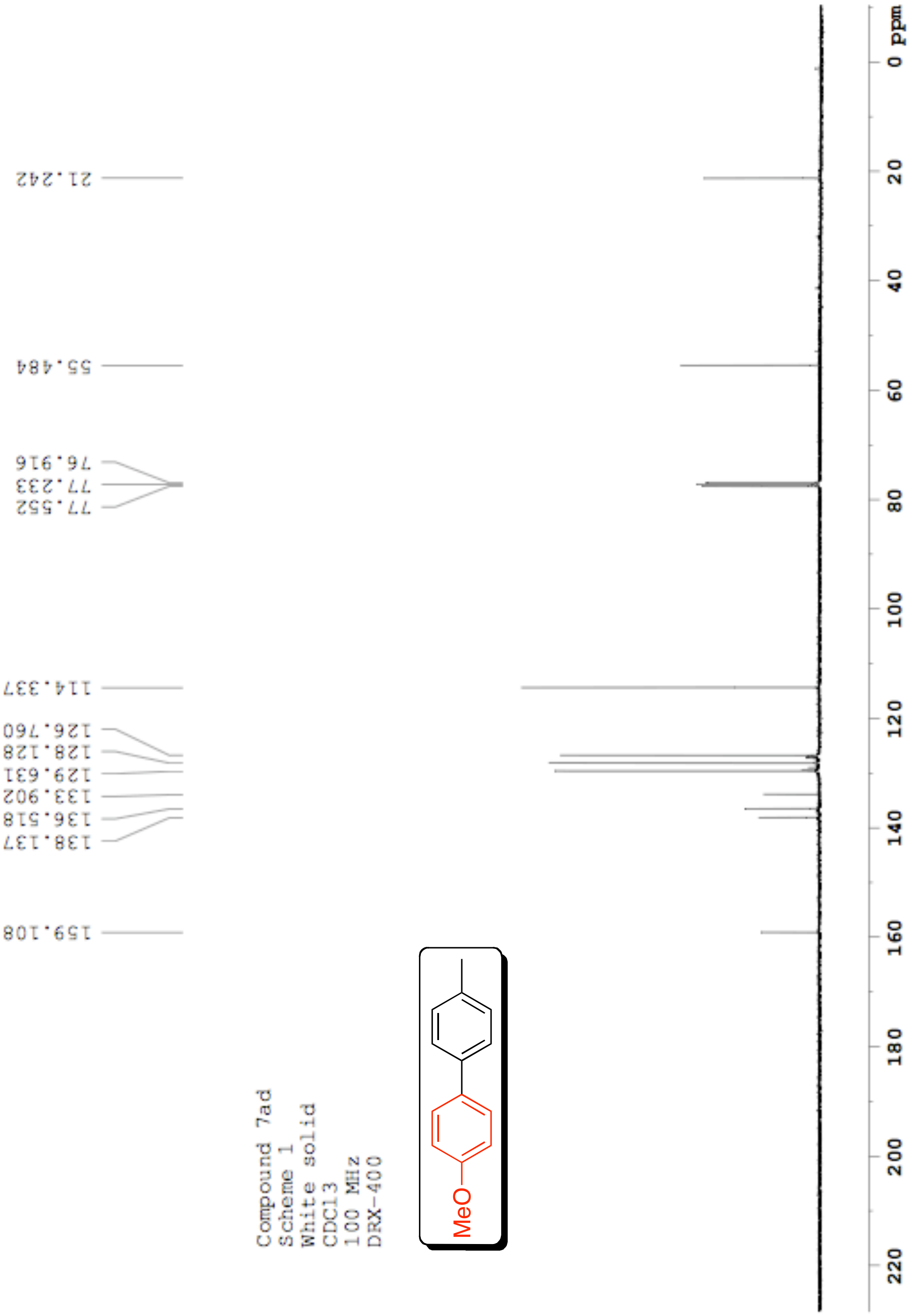

144.636
134.618
129.113
128.237
127.678
126.166
125.022
123.309
77.614
77.296
76.978
Table 4, entry 3
White solid
CDCl3
100 MHz
DRX-400
S
220
200
180
160
140
120
100
80
60
40
20
0 ppm

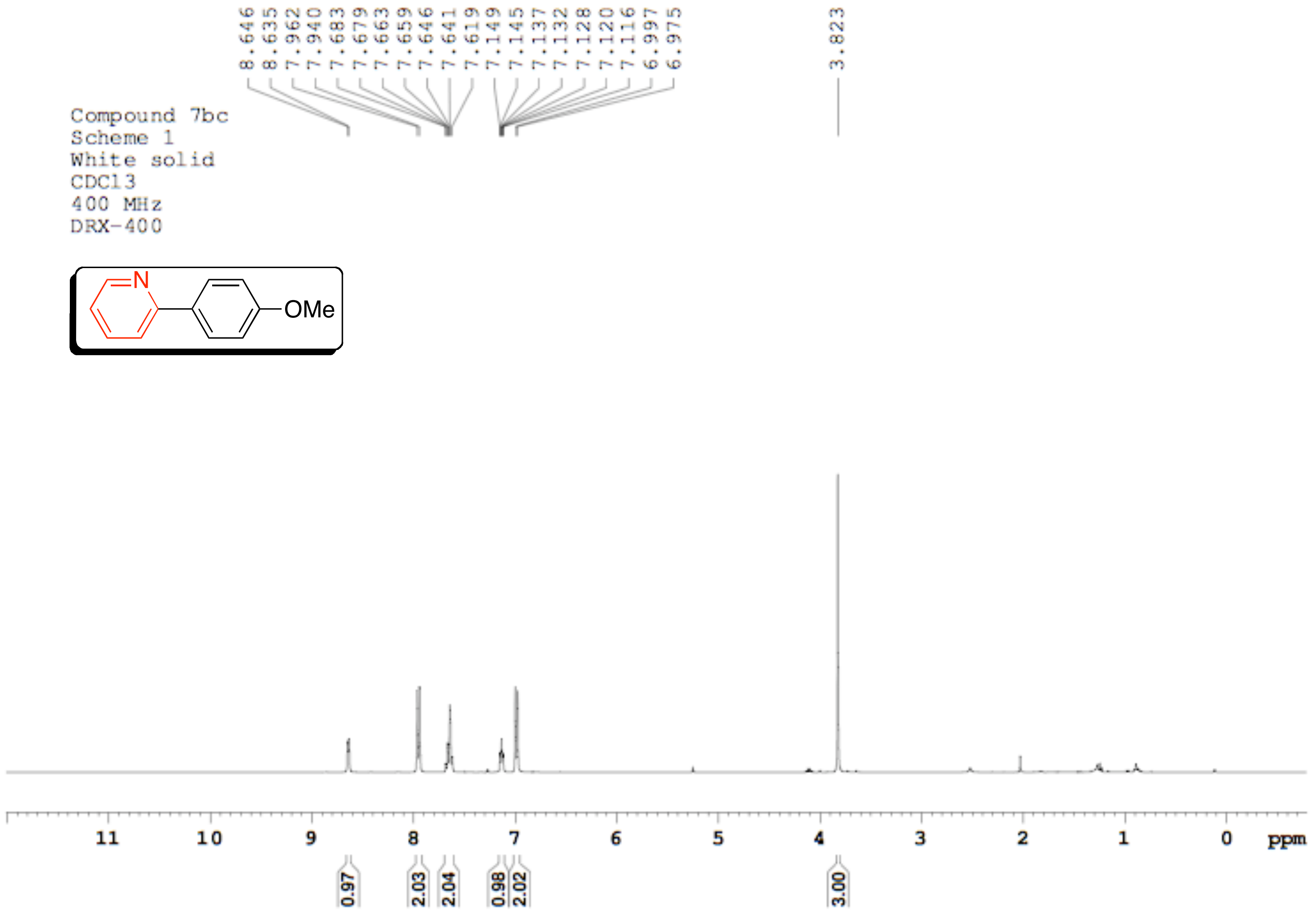


Compound 7ac
Scheme 1
Clear, crystalline solid
CDCl3
400 MHz
DRX-400

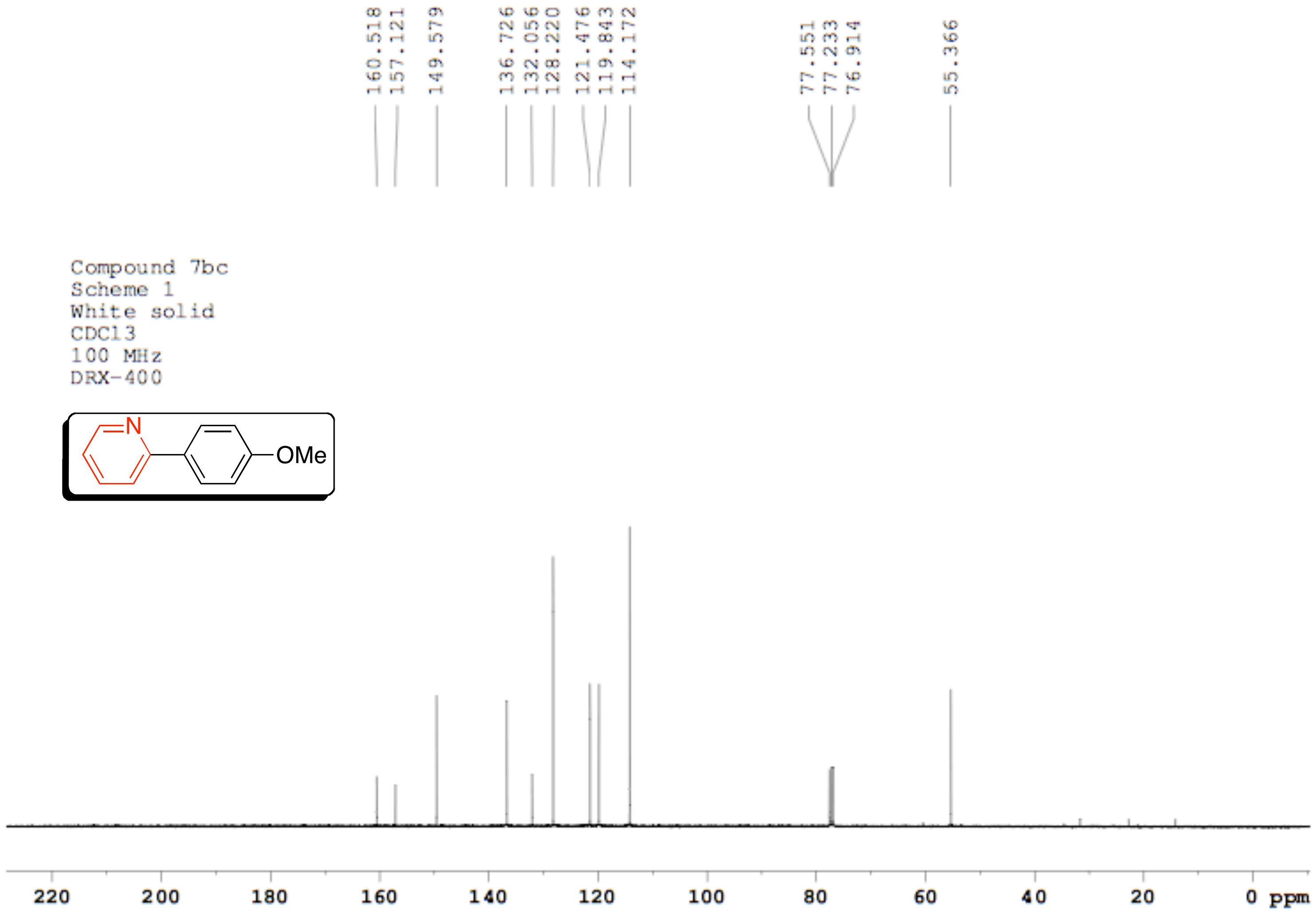

158.872
133.648
127.917
114.348
77.553
77.236
76.918
55.521
Compound 7ac
Scheme 1
Clear, crystalline solid
CDCl3
100 MHz
DRX-400
MeO
OMe
220
200
180
160
140
120
100
80
60
40
20
0 ppm

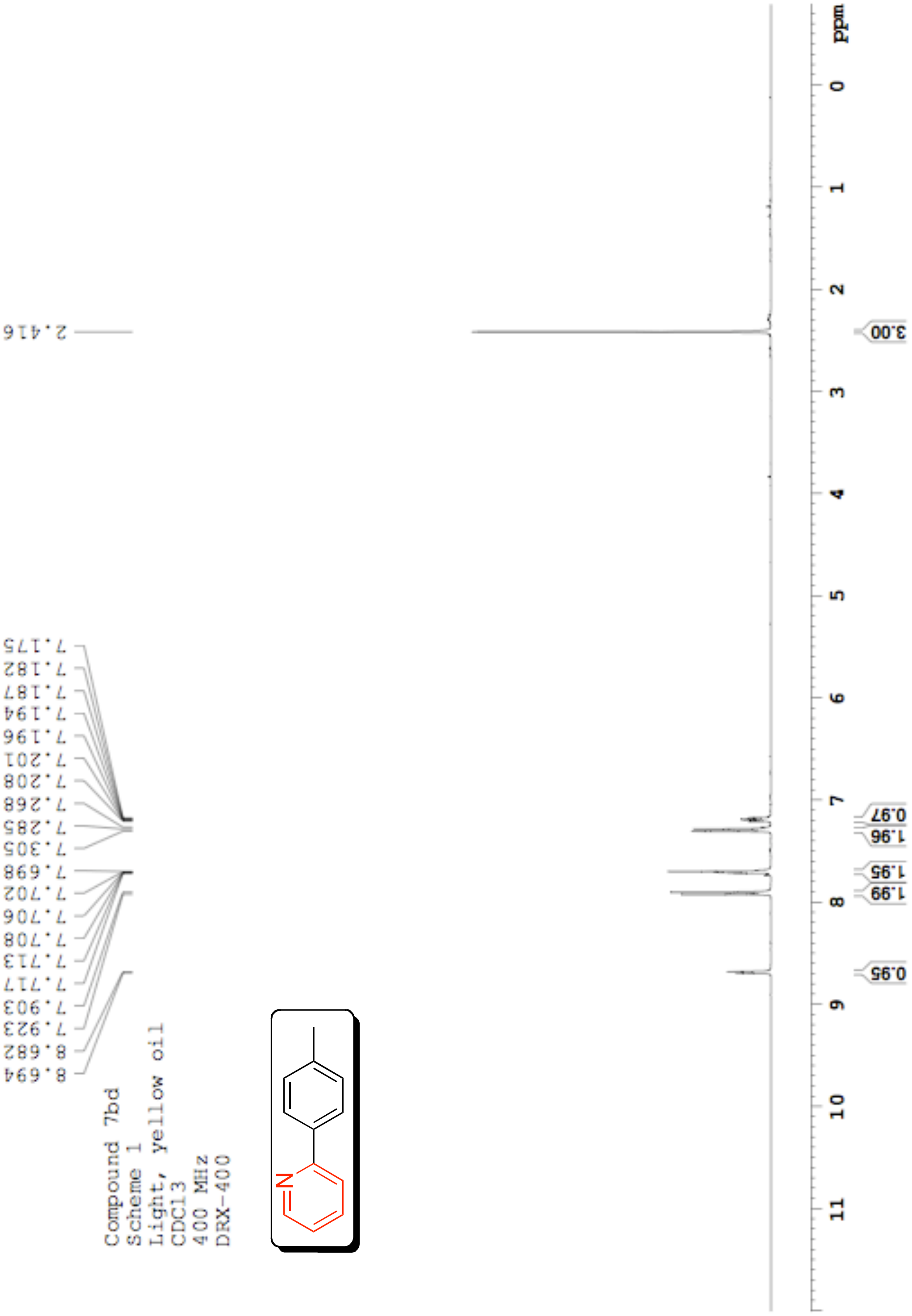

2.535
3.979
7.104
7.125
7.269
7.355
7.366
7.386
7.594
7.614
7.652
7.674
Compound 7ad
Scheme 1
White solid
CDCl3
400 MHz
DRX-400
MeO
3.21
3.00
1.95
2.26
2.02
2.05
0
1
2
3
4
5
6
7
8
9
10
11
ppm

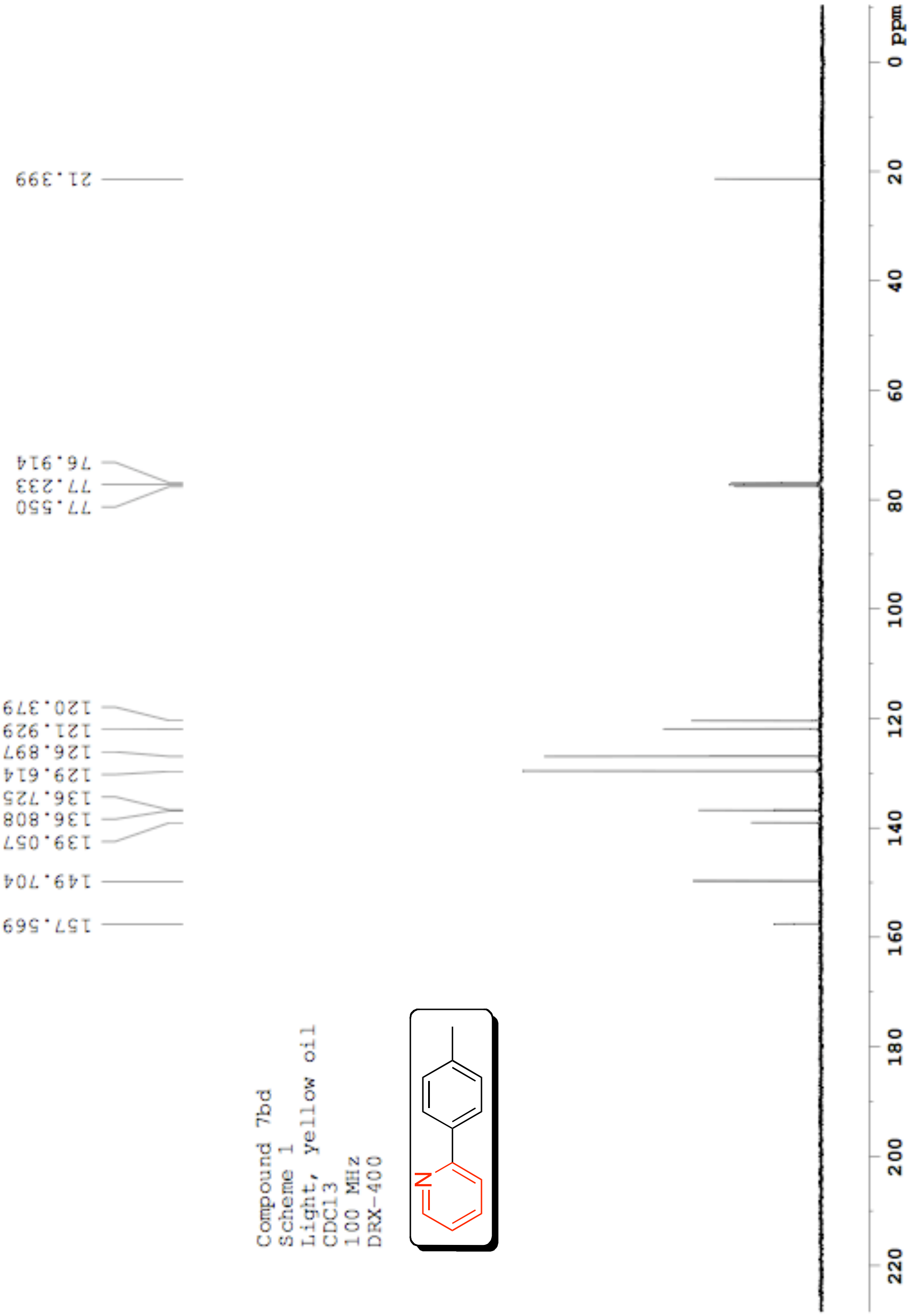

21.242
55.484
76.916
77.233
77.552
114.337
126.760
128.128
129.631
133.902
136.518
138.137
159.108
Compound 7ad
Scheme 1
White solid
CDCl3
100 MHz
DRX-400
MeO
0 ppm
20
40
60
80
100
120
140
160
180
200
220



Compound 7bc
Scheme 1
White solid
CDCl3
400 MHz
DRX-400
N
OMe
8.646
8.635
7.962
7.940
7.683
7.679
7.663
7.659
7.646
7.641
7.619
7.149
7.145
7.137
7.132
7.128
7.120
7.116
6.997
6.975
3.823
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.97
2.03
2.04
0.98
2.02
3.00


160.518
157.121
149.579
136.726
132.056
128.220
121.476
119.843
114.172
77.551
77.233
76.914
55.366
Compound 7bc
Scheme 1
White solid
CDCl3
100 MHz
DRX-400
N
OMe
220
200
180
160
140
120
100
80
60
40
20
0 ppm


2.416
7.175
7.182
7.187
7.194
7.196
7.201
7.208
7.268
7.285
7.305
7.698
7.702
7.706
7.708
7.713
7.717
7.903
7.923
8.682
8.694
Compound 7bd
Scheme 1
Light, yellow oil
CDCl3
400 MHz
DRX-400
N
3.00
0.97
1.96
1.95
1.99
0.95
ppm
0
1
2
3
4
5
6
7
8
9
10
11


21.399
76.914
77.233
77.550
120.379
121.929
126.897
129.614
136.725
136.808
139.057
149.704
157.569
Compound 7bd
Scheme 1
Light, yellow oil
CDCl3
100 MHz
DRX-400
N
0 ppm
20
40
60
80
100
120
140
160
180
200
220