University of Pennsylvania
ScholarlyCommons

Publicly Accessible Penn Dissertations

2017

Functionalization Of 2-Azaallyl Anions, Radicals And Benzylic Chloromethyl-Coupling Polymerization

Minyan Li
University of Pennsylvania, liminyan@sas.upenn.edu

Follow this and additional works at: https://repository.upenn.edu/edissertations

 Part of the Organic Chemistry Commons

Recommended Citation
Li, Minyan, "Functionalization Of 2-Azaallyl Anions, Radicals And Benzylic Chloromethyl-Coupling Polymerization" (2017). *Publicly Accessible Penn Dissertations*. 2929.
https://repository.upenn.edu/edissertations/2929

This paper is posted at ScholarlyCommons. https://repository.upenn.edu/edissertations/2929
For more information, please contact repository@pobox.upenn.edu.

Functionalization Of 2-Azaallyl Anions, Radicals And Benzylic Chloromethyl-Coupling Polymerization

Abstract
C-C bond forming reactions, under either metal catalyzed or metal free conditions, are mainstay in the construction of functionalized molecules in organic synthesis. Disubstituted methylamines are highly valuable small molecule pharmaceuticals which are widely applied in the treatment of human disease. To date, traditional synthesis of such amines requires significant effort of synthesizing pre-functionalized reagents. This dissertation describes an innovation in the construction of disubstituted methylamines via the umpolung functionalization of 2-azaallyl anions and radicals.

In chapter 1, umpolung synthesis of diarylmethylamines via palladium-catalyzed arylation of 2-azaallyl anion intermediates is introduced. 2-Azaallyl anion coupling partners include 1,1,3-triaryl-2-azaallyl anions and 1,3-diaryl-2-azaallyl anions. The key to success is the advancement of NIXANTPHOS-based catalysts that enabled the arylation of aryl bromides and more challenging aryl chlorides to be conducted under mild conditions. Moreover, the identification of hindered silylamide bases ensures that products of the arylation were not deprotonated or isomerized.

In chapter 2, we address the regioselectivities in the α- and γ-arylation of azapentadienyl anions. The regioselectivity was achieved by controlling the reductive elimination of the Pd-azapentadienyl intermediates using two distinct catalysts. These methods provide the first divergent synthesis of allylic amine and enamine derivatives.

In chapter 3, we presented an innovative concept that 2-azaallyl anions could behave as organic super-electron-donors. Such unique behavior was illustrated in (i) generation of 2-azaallyl radicals from single-electron-transfer (SET) between 2-azaallyl anions and neutral ketimines, which then coupled with vinyl bromides; (ii) generation of 2-azaallyl radicals from SET of 2-azaallyl anions with aryl and alkyl electrophiles, which then captured aryl and alkyl radicals to form C–C bonds. The transition-metal-free vinylation, arylation and alkylation of 2-azaallyls make possible the synthesis of high-value functionalized amine derivatives in good to excellent yields.

In chapter 4, a new polymerization method named benzylic-chloromethyl-coupling polymerization (BCCP) is introduced. BCCP is catalyzed by sulfenate anions, which promote an umpolung polycondensation via step-growth propagation cycles involving sulfoxide intermediates. This protocol represents a very rare example of an organocatalyst that links monomers by C=C double bonds after each enchainment.

Degree Type
Dissertation

Degree Name
Doctor of Philosophy (PhD)

Graduate Group
Chemistry

This dissertation is available at ScholarlyCommons: https://repository.upenn.edu/edissertations/2929

First Advisor
Patrick J. Walsh

Second Advisor
Madeleine M. Joullie

Subject Categories
Organic Chemistry

This dissertation is available at ScholarlyCommons: https://repository.upenn.edu/edissertations/2929

FUNCTIONALIZATION OF 2-AZAALLYL ANIONS, RADICALS AND BENZYLIC CHLOROMETHYL-COUPLING POLYMERIZATION

Minyan Li

A DISSERTATION

in

Chemistry

Presented to the Faculties of the University of Pennsylvania

in

Partial Fulfillment of the Requirements for the

Degree of Doctor of Philosophy

2017

Supervisor of Dissertation

_____

Professor Patrick J. Walsh, Alan G. MacDiarmid Professor of Chemistry

Graduate Group Chairperson

_____

Dr. Gary A. Molander, Hirschmann-Makineni Professor of Chemistry

Dissertation Committee

Professor Madeleine M. Joullie, Professor of Chemistry

Professor William P. Dailey, Associate Professor of Chemistry

Professor Christopher B. Murray, Richard Perry University Professor of Chemistry

FUNCTIONALIZATION OF 2-AZAALLYL ANIONS, RADICALS AND BENZYLIC CHLOROMETHYL-COUPLING POLYMERIZATION

COPYRIGHT

2017

Minyan Li

This work is licensed under the

Creative Commons Attribution-

NonCommercial-ShareAlike 3.0

License

To view a copy of this license, visit

https://creativecommons.org/licenses/by-nc-sa/3.0/us/

Dedicated to My Family

Acknowledgements

I would like to firstly express my gratitude to my advisor, Prof. Walsh, who enrolled me to Penn from Nankai, guided me and supported me over my entire graduate school life. I cannot express how grateful I am to him. I sincerely appreciate his guide of how to think chemistry, how to design and do research and how to improve the writing of papers to hit higher impact journals. I want to thank his kindness of giving me freedom in my research. Moreover, I sincerely thank him for letting me conduct collaboration projects with researchers at Autonomous University of Madrid, Chinese Agricultural University, Sichuan University and Yunnan University. Thank him for giving me extremely valuable opportunities of collaborating with visiting scholars, visiting students, new graduate students and undergraduate students. I have learned so much of teamwork from these collaborations in and out of our research group. It is such a wonderful and pleasant experience to work with him and work in our research team, I feel I never waste one day in my graduate school life. With him, i still have 6 first & co-author papers waiting for him to revise. I feel so lucky to have the best boss of the world guiding me, supporting me in the past 5 years.

I would like to give thanks to my committee members: Professor Joullie, Professor Dailey, and Professor Murray for their guide and suggestions in my graduate career. I could feel my growing in understanding of my research every year. I also want to thank them for nominating me for the graduate award. Besides my committee members, I would like to specifically thank Professor Marisa Kozlowski for her help in my job and postdoc searching process. I feel so sorry for bothering her so many times asking for letters. I would like to thank the great supporting facility at Penn Chemistry. Thanks Dr. George Furst, Dr. Jun Gu for their help on NMR. Dr. Rakesh Kohli and Dr. Chuck Ross for help on MS spectroscopy, Judith Currano for help on literature. Ms. Yvonne for help on ordering chemicals.

Just like peeling an onion, I kept deepening my understanding of the 2-azaallyl chemistry in my five years' research. From initial work of turning on the arylation of the 2-azaallyl anion, to exploring the regioselectivity of a very complicated azapentadienyl anion system, to recognizing the reducing feature of this magic anionic system and designing special transition-metal-free radical coupling methodologies out of that. I will never be able to completely peel the "azaallyl **onion**" without the guide of my advisor as well as the help of so many co-workers.

I would like to specifically thank Dr. Simon Berritt and Dr. Sonia Montel. Thanks for teaching me High-Throughput-Screening which is the core foundation of everything! Thanks for teaching me how to behave professionally in a team and how to lead a small team.

I would like to thank Professor Javier Adrio and Dr. Ana Bellomo for his pioneering work of azaallyl arylation chemistry, Professor Baris Yucel, Dr. Jacqueline Jiménez for their contribution in the arylation of *N*-benzyl aldimine project. Dr. María González-Esguevillas, Dr. Ana Bellomo for their input at the beginning of the azapentadienyl anion functionalization project. In the transition-metal-free vinylation, arylation and alkylation projects which are the most challenging but exciting projects in my graduate research, I would like to thank Professor Osvaldo Gutierrez and Professor Marisa Kozlowski for their help and collaboration on DFT calculation, Dr. Ana Pascual-Escudero, Lucas Matuszewski and Professor Xiaodong Yang for their help on the starting material synthesis. Also it is my great pleasure to work with a lot of exceptionally smart undergraduate students, Georgia Huang, Carol Wang and Ahmet Yeşilçimen thanks for their help on column chromatography.

In the collaboration projects that I am contributing author, I would like to thank Yvette (Yuying) He, Dr. Bing Zheng, Henry Sha and Byeong-Seon Kim for the pleasant collaboration and teamwork. I would like to specifically thank Professor Xiaodong Yang at Yunnan University, thanks for his

trust and let me lead a team of four graduate students in our collaboration and exploration of **6** new projects. It is such a great opportunity for me to learn how to lead a small group, how to mentor a team that never ever conducted cross-coupling chemistry before, how to effectively communicate with them, learn lessons from our mistakes, and grow up together. I would like to thank Guogang Deng, Zhengfen Liu, Xueqiong Ma and Bijun Wang for their exciting and outstanding teamwork.

I would like to thank all present and past group members in Walsh Group. I want to thank many wonderful friends in the past years. Dr. Rong Shen, Dr. Na Zhang, Dr. Shaodong Zhang, Dr. Yanran Ai, Dr. Boying Guo, Yike Zou, Nan Zhang, Qi Liu, Frank Zhang thanks for their kindness and friendship.

Finally, I would like to thank all Buddhas of the past, present and future for their bless. I would like to sincerely thank my mom and dad, thank you for your love, understanding, devotion, encouragement and support. I would like to thank my godmother “Maman Chiang”. There’s nothing comparable to the love and devotion that you all have given to me. Thank you.

ABSTRACT

FUNCTIONALIZATION OF 2-AZAALLYL ANIONS, RADICALS AND BENZYLIC CHLOROMETHYL-COUPLING POLYMERIZATION

Minyan Li

Patrick J. Walsh

C-C bond forming reactions, under either metal catalyzed or metal free conditions, are mainstay in the construction of functionalized molecules in organic synthesis. Disubstituted methylamines are highly valuable small molecule pharmaceuticals which are widely applied in the treatment of human disease. To date, traditional synthesis of such amines requires significant effort of synthesizing pre-functionalized reagents. This dissertation describes an innovation in the construction of disubstituted methylamines via the umpolung functionalization of 2-azaallyl anions and radicals.

In chapter 1, umpolung synthesis of diarylmethylamines via palladium-catalyzed arylation of 2-azaallyl anion intermediates is introduced. 2-Azaallyl anion coupling partners include 1,1,3-triaryl-2-azaallyl anions and 1,3-diaryl-2-azaallyl anions. The key to success is the advancement of NIXANTPHOS-based catalysts that enabled the arylation of aryl bromides and more challenging aryl chlorides to be conducted under mild conditions. Moreover, the identification of hindered silylamide bases ensures that products of the arylation were not deprotonated or isomerized.

In chapter 2, we address the regioselectivities in the α- and γ-arylation of azapentadienyl anions. The regioselectivity was achieved by controlling the reductive elimination of the Pd-azapentadienyl intermediates using two distinct catalysts. These methods provide the first divergent synthesis of allylic amine and enamine derivatives.

In chapter 3, we presented an innovative concept that 2-azaallyl anions could behave as organic super-electron-donors. Such unique behavior was illustrated in (i) generation of 2-azaallyl radicals

from single-electron-transfer (SET) between 2-azaallyl anions and neutral ketimines, which then coupled with vinyl bromides; (ii) generation of 2-azaallyl radicals from SET of 2-azaallyl anions with aryl and alkyl electrophiles, which then captured aryl and alkyl radicals to form C–C bonds. The transition-metal-free vinylation, arylation and alkylation of 2-azaallyls make possible the synthesis of high-value functionalized amine derivatives in good to excellent yields.

In chapter 4, a new polymerization method named benzylic-chloromethyl-coupling polymerization (BCCP) is introduced. BCCP is catalyzed by sulfenate anions, which promote an umpolung polycondensation via step-growth propagation cycles involving sulfoxide intermediates. This protocol represents a very rare example of an organocatalyst that links monomers by C=C double bonds after each enchainment.

TABLE OF CONTENTS

List of Tables

List of Schemes

List of Figures

Chapter 1. Umpolung Synthesis of Diarylmethylamines via Palladium-Catalyzed Arylation of 2-Azaallyl Anions.

1.1. Introduction

In the past decade, considerable effort has been devoted to the synthesis of diarylmethylamines due to their common occurrence in biological and pharmaceutical sciences. Examples include Zyrtec,[1] Levocetirizine,[2] Meclozine,[3] Solifenacin,[4] BDF9148,[5] SNC80,[6] and ARM434[7] (Figure 1.1).

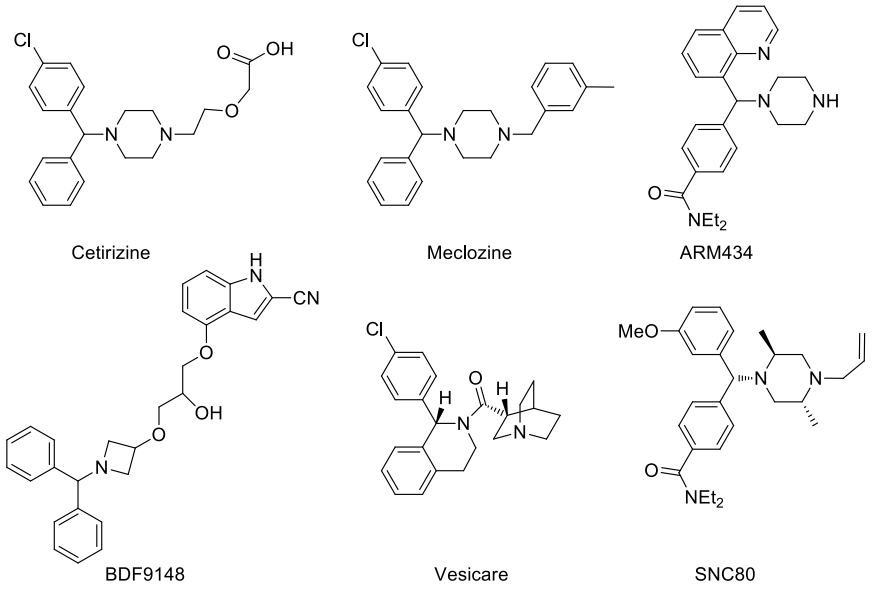
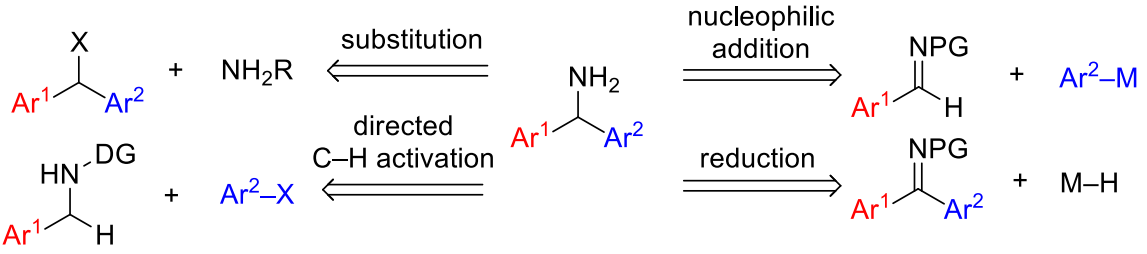


Figure 1.1. Important Diarylmethylamine Containing Molecules.

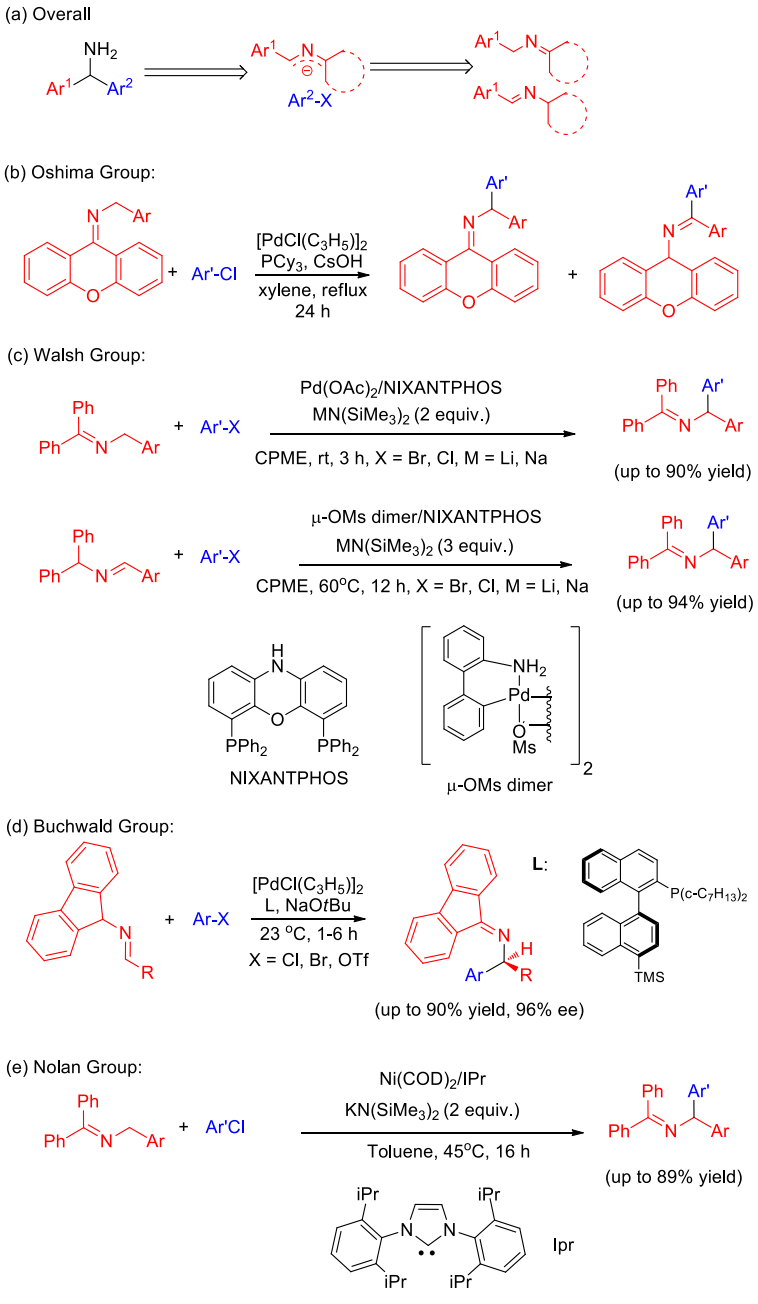
Traditional approaches for the synthesis of diarylmethylamines include addition of aryl organometallic reagents to benzaldimines,[8] reduction of benzophenone imines,[9] substitution reactions[10] and directing group facilitated C–H activation[11] (Scheme 1.1). Given the widespread utility of diarylmethylamines in medicinal chemistry, new approaches to access this class of pharmacophores have immediate potential applications and are in high demand.



Scheme 1.1. Retrosynthetic Disconnections of Diarylmethyl Amines.

One appealing strategy for the synthesis of diarylmethylamines relies on the efficient generation and regioselective couplings of 2-azaallyl anions. These semi-stabilized 2-azaallyl anions are derived from either ketimines or aldimines. Retrosynthetically, such an approach represents an umpolung disconnection (Scheme 1.2, a). The use of 2-azaallyl anions to prepare diarylmethylamines was demonstrated by Oshima, Buchwald, Nolan and us. Oshima and co-workers in 2008[12] and 2009,[13] generated 2-azaallyl anions from *N*-benzyl benzophenone ketimines with CsOH as base at 140 ^{o}C. In the presence of catalytic palladium and PCy_3, cross-coupling of the 2-azaallyl anions with aryl chlorides was achieved in moderate yields. Unfortunately, the harsh reaction conditions resulted in isomeric mixtures in every case, undermining the utility of this chemistry (Scheme 1.2, b). Our approach, is to study the regioselective arylation of 1,1,3-triaryl-2-azaallyl anions and 1,3-diaryl-2-azaallyl anions generated from the corresponding ketimines and aldimines (Scheme 1.2, c). We hypothesized that two intertwined problems would need to be surmounted. Firstly, a catalyst for the coupling that operates under mild conditions must be identified. Secondly, bases and other conditions must be introduced that avoid the undesirable deprotonation and isomerization of the product that was observed by Oshima (Scheme 1.2, b). To our delight, we observed that in the presence of a Pd(NIXANTPHOS)-based catalyst and hindered silylamide bases, 2-azaallyl anions could be readily coupled with both aryl bromides and more challenging aryl chlorides to afford diarylmethylamine derivatives in good to excellent yields.[14]

During our study, in early 2014, Buchwald and Zhu reported an elegant enantioselective arylation of 9-aminofluorene-derived aldimines with aryl halides at room temperature. The reaction worked very well for aryl bromides, but chlorobenzene underwent coupling in only 38% yield (Scheme 1.2, d).[15] In 2015, Nolan and coworkers reported that the coupling of 2-azaallyl anions with aryl chlorides could also be performed with Ni(NHC)-based catalysts (Scheme 1.2, e).[16]



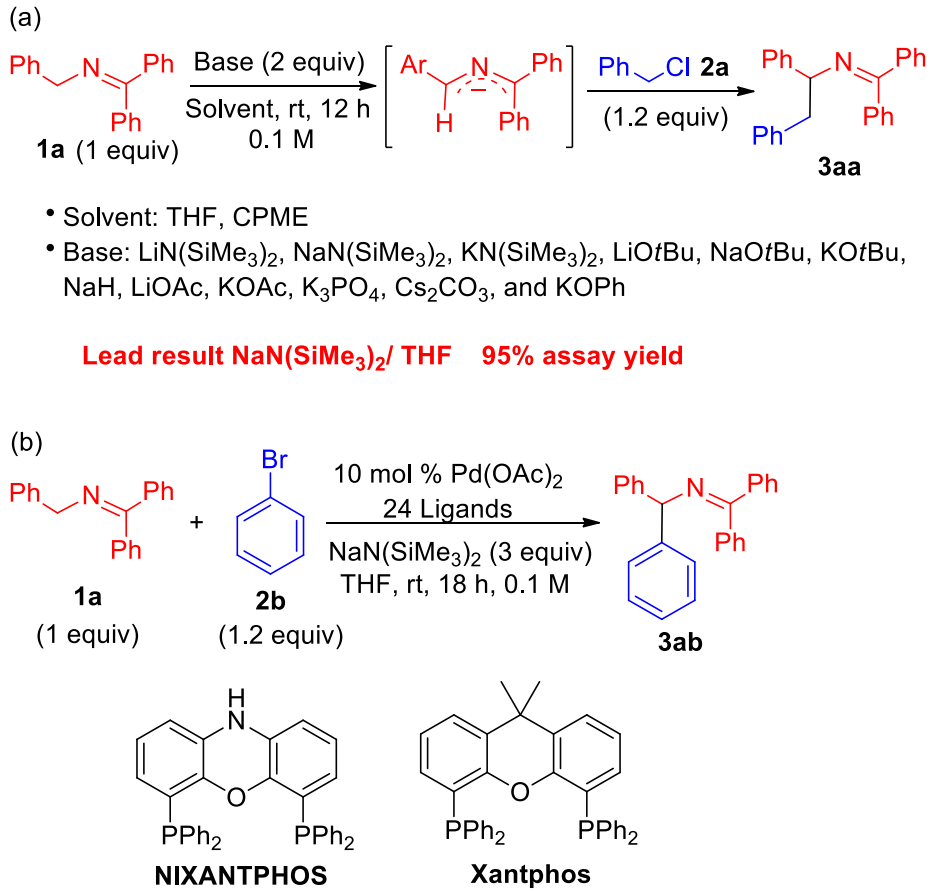
Scheme 1.2. Synthesis of Diarylmethylamine Derivatives from Arylation of 2-Azaallyl Anions.

1.2. Results and Discussion

1.2.1. Palladium-Catalyzed Arylation of 1,1,3-Triaryl-2-Azaallyl Anions.

1.2.1.1. Development and Optimization of Palladium-Catalyzed Arylation of 1,1,3-Triaryl-2-Azaallyl Anions.

To avoid simultaneous optimization of base, solvent, palladium source and ligand, we first focused on the deprotonation step. We had found that trapping the resulting anion by benzylation allowed us to determine which bases are capable of deprotonation of the substrates and served as a starting point for optimization of the deprotonation step.[17] The reaction of *N*-benzyl ketimine **1a** and benzyl chloride **2a** was examined in the presence of 12 bases [$LiN(SiMe_3)_2$, $NaN(SiMe_3)_2$, $KN(SiMe_3)_2$, Li*O*t*Bu*, Na*O*t*Bu*, K*O*t*Bu*, NaH, LiOAc, KOAc, K_3PO_4, Cs_2CO_3, and KOPh]. Reactions were conducted in THF and CPME (cyclopentyl methyl ether) on microscale (10 μmol) at rt for 12 h. $NaN(SiMe_3)_2$, $KN(SiMe_3)_2$ and K*O*t*Bu* generated the benzylated product. At laboratory scale, the most promising result was obtained with $NaN(SiMe_3)_2$ in THF (95% assay yield, Scheme 1.3, a). With the base/solvent combination outlined above, we conducted a room temperature screen of 24 electronically diverse, mono- and bidentate phosphine ligands with $Pd(OAc)_2$ (Scheme 1.3, b). The top ligand (product: internal standard ratio) was NIXANTPHOS (3.65). Notably, the product: internal standard ratio of XANTPHOS is 0.77. It is particularly interesting that NIXANTPHOS was much more efficient than the structurally similar XANTPHOS.

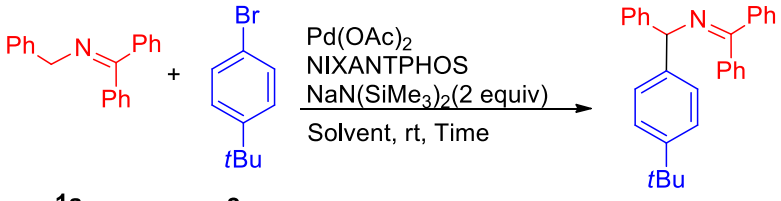


Scheme 1.3. Microscale Reaction Optimization of Base/Solvent Effect and Ligand Effect.

Based on the initial screening hits, we continued our optimization on laboratory scale with ketimine **1a**, 1-bromo-4-*tert*-butylbenzene **2c**, CPME and THF solvents, silylamide and alkoxide bases, NIXANTPHOS and $Pd(OAc)_2$. Selected optimization data were listed in Table 1.1. Direct lab-scale repeat of the top hit from the ligand screening (Scheme 1.3, b) led to product **4ac** in 67% assay yield (Table 1.1, entry 1). We also observed isomerized aldimine **1a'** and the diastereomeric di-ketimines products **4** and **4'** (Later we found out that di-ketimines were derived from homocoupling of 2-azaallyl radicals. See Chapter 3 for further discussion). The assignment of aldimine **1a'**, di-ketimines **4** and **4'** were confirmed by independent synthesis. With ketimine **1a** as the limiting reagent, attempts to eliminate the formation of less reactive isomerized aldimine

1a' or the di-ketimines products **4** and **4'** were unsuccessful. We hypothesized that the impact of the byproducts on the arylation yield could be minimized by employing 2 equivalents of the ketimine **1a** with 1 equivalent of **2c** in the coupling reaction (Table 1.1, entries 1–6). Consistent with HTE screening results, $NaN(SiMe_3)_2$ in THF and CPME were the most promising combination, with up to 80% assay yield. Furthermore, we thought that conversion to the desired arylation product, vs. the byproducts, could be improved by reducing the concentration of the azaallyl anion. We envisioned that this could be accomplished by slow addition of base to the reaction mixture. Indeed, portion-wise addition of the base led to 99% assay yield of the arylation product in CPME (Table 1.1, entry 8) and 94% yield in THF (Table 1.1, entry 9). Further optimization of the catalyst loading indicated that the yield remained above 90% at 5 and 2.5 mol % Pd (entries 10 and 11), but dropped to 78% at 1 mol % Pd (entry 12).

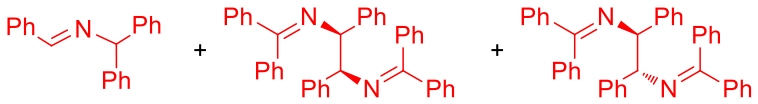
Table 1.1. Selected Optimization of Pd-Catalyzed Arylation of 1a with 2c.[a]



1a **2c** **3ac**

Entry	Pd/L (%)	Solvent	Base	Time (h)	Yield (%)
1	10/15	THF	$NaN(SiMe_3)_2$	18	67[b]
2	10/15	CPME	$NaN(SiMe_3)_2$	1	80[c]
3	10/15	CPME	$KN(SiMe_3)_2$	1	41[c]
4	10/15	CPME	KO*t*Bu	1	77[c]
5	10/15	THF	$NaN(SiMe_3)_2$	1	71[c]
6	10/15	THF	$KN(SiMe_3)_2$	1	45[c]
7	10/15	THF	KO*t*Bu	1	64[c]
8	10/15	CPME	$NaN(SiMe_3)_2$	3	99[d]
9	10/15	THF	$NaN(SiMe_3)_2$	3	94[d]
10	5/7.5	CPME	$NaN(SiMe_3)_2$	3	95[d]
11	2.5/3.75	CPME	$NaN(SiMe_3)_2$	3	92[d], (90)[e]
12	1/1.5	CPME	$NaN(SiMe_3)_2$	3	78[d]

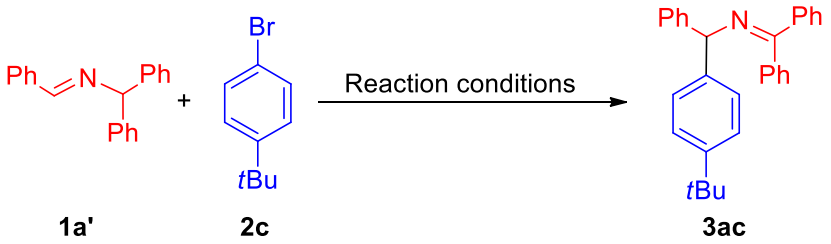
Side products observed in the optimizaiton:



Aldimine **1a'** *Rac*-di-ketimine **4** *Meso*-di-ketimine **4'**

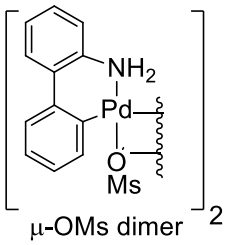
[a]Yield determined by ^{1}H NMR spectroscopy of the crude reaction mixture on a 0.1 mmol scale. [b]Reactions conducted on a 0.1 mmol scale using 1 equiv of **1a**, 3 equiv of $NaN(SiMe_3)_2$, and 1.2 equiv of **2c** at 0.1 M. [c]Reactions conducted on a 0.1 mmol scale using 2 equiv of **1a**, 2 equiv of $NaN(SiMe_3)_2$, and 1 equiv of **2c** at 0.1 M. [d]Reactions conducted on a 0.1 mmol scale using 2 equiv of **1a**, 2 equiv of $NaN(SiMe_3)_2$, and 1 equiv of **2c** at 0.1 M. Base was added portionwise at 0.1 mL/30 min. [e]Isolated yield after chromatographic purification.

In addition, a wide variety of benzaldehyde derivatives are commercially available and inexpensive, inspiring us to explore the arylation of aldimines **1a'**. Given that the aldimine precursors **1a'** and the isomeric ketimine **1a** generate the same azaallyl anion, we examined coupling with aldimines **1a'** under the standard conditions employed in Table 1.1 (entry 11). However, only 67% yield was obtained. Considering that Buchwald type precatalysts facilitate catalyst generation, often lead to increased activity, and allow lower ligand loading,[18] we employed Buchwald-type precatalysts (with L=NIXANTPHOS) *in-situ* generated from 2.5 mol % of Buchwald's μ-OMs Pd dimer **5** with 5 mol % NIXANTPHOS at 60 °C. As listed in Scheme 1.4, yield of **3ac** increased to 94% yield.



Reaction conditions 1: **3ac** 67% yield
2.5 mol % $Pd(OAc)_2$, 3.75 mol % NIXANTPHOS,
$NaN(SiMe_3)_2$ (3 equiv), CPME, rt, 0.1 M, 3 h.

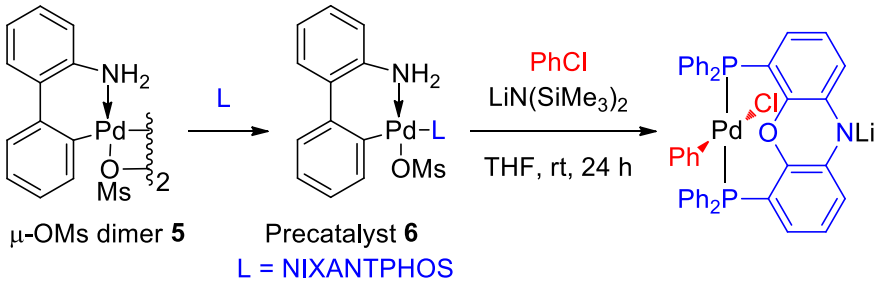
Reaction conditions 2: **3ac** 94% yield
2.5 mol % μ-OMs dimer, 5 mol % NIXANTPHOS,
$NaN(SiMe_3)_2$ (3 equiv), CPME, 60 °C, 0.1 M, 12 h.



μ-OMs dimer

Scheme 1.4. Reaction Optimization of Arylation of Aldimine 1a' with 2c.

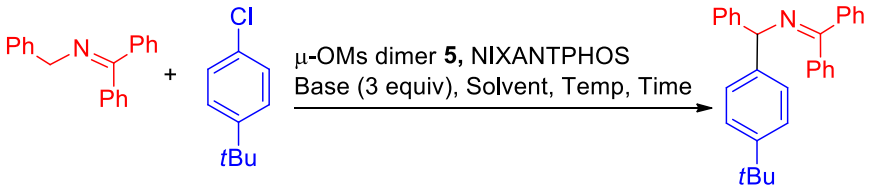
Aryl chlorides are more challenging coupling partners. It is well known that oxidative addition of aryl chlorides to palladium complexes with bidentate phosphines requires temperatures of ~100 ^{o}C, at which temperature isomerization of the type observed by Oshima (Scheme 1.1, b) would likely be problematic. However, our group subsequently discovered that the Pd(NIXANTPHOS)-based catalyst will oxidatively add aryl chlorides at room temperature (Scheme 1.5).[19] This success inspired us to revisit the arylation of 2-azaallyl anions with more abundant and economical aryl chlorides.



Scheme 1.5. Oxidative Addition using NIXANTPHOS Precatalyst at Room Temperature.

We initiated our studies with a 2:1 ratio of ketimine **1a** and aryl chloride **2c'**, 3 equiv. of $LiN(SiMe_3)_2$, 5 mol % Buchwald's μ-OMs **5** and 10 mol % NIXANTPHOS. We tested 5 solvents [CPME (cyclopentyl methyl ether), THF, toluene, DME (dimethoxyethane) and DCE (1,2-dichloroethane)] at 23 ^{o}C (Table 1.2, entries 1–5). THF was the best of these with a 68% assay yield (entry 2). With THF as solvent, a screen of bases $MN(SiMe_3)_2$ (M=Na K, Li, entries 6–8) indicated that the reaction with $LiN(SiMe_3)_2$ outperformed the others. Raising the temperature to 60 °C resulted in an increase in the yield with shorter reaction times (entry 8 and 9). Reducing Pd loading from 10 to 5 mol % at 60 ^{o}C resulted in a slight drop in the yield from 92% to 86% (entry 10).

Table 1.2. Selected Optimization of Pd-Catalyzed Arylation of 1a with 2c'.[a,b]



1a **2c'** **3ac**

Entry	5/L (%)	Solvent	Base	Temp (°C)	Time (h)	Yield (%)
1	5/10	CPME	$LiN(SiMe_3)_2$	23	12	N.R.
2	5/10	THF	$LiN(SiMe_3)_2$	23	12	68
3	5/10	Tol.	$LiN(SiMe_3)_2$	23	12	N.R.
4	5/10	DME	$LiN(SiMe_3)_2$	23	12	62
5	5/10	DCE	$LiN(SiMe_3)_2$	23	12	N.R.
6	5/10	THF	$NaN(SiMe_3)_2$	23	12	50
7	5/10	THF	$KN(SiMe_3)_2$	23	12	37
8	5/10	THF	$LiN(SiMe_3)_2$	60	12	92
9	5/10	THF	$LiN(SiMe_3)_2$	60	6	92
10	2.5/5	THF	$LiN(SiMe_3)_2$	60	6	86[c]

[a]Reactions conducted on a 0.1 mmol scale using 2 equiv of ketimine **1a**, 3 equiv of Base, and 1 equiv of **2c'** at 0.1 M. Base was added portionwise with speed 0.05 mL/30 min. N.R. is no reaction. [b]Yield determined by ^{1}H NMR spectroscopy of the crude reaction mixture on a 0.1 mmol scale. [c]Isolated yield after chromatographic purification.

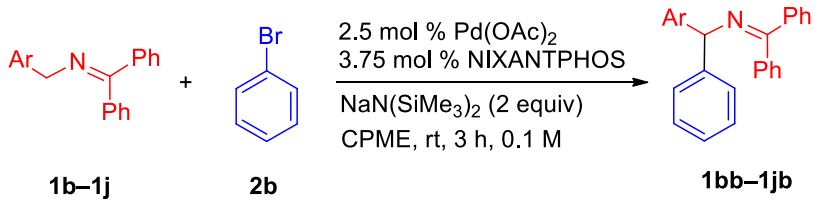
1.2.1.2. Scope of Ketimines and Aldimines in Palladium-Catalyzed Arylation of 1,1,3-Triaryl-2-azaallyl Anions with Bromobenzene 2b.

The scope of the ketimines was described in Table 1.3. Ketimine substrates bearing electron-donating, electron-withdrawing and heterocyclic *N*-benzyl derived groups furnished the coupling products with bromobenzene in moderate to excellent yields with catalyst loadings of 2.5–10 mol %. Coupling of 4-methyl benzyl ketimine **1b** furnished the product in 89% yield. 4-Methoxy benzyl amine derivative (**1c**) reacted sluggishly under our standard conditions, probably because of the increased pK_a. Replacement of $NaN(SiMe_3)_2$ with a more reactive $KN(SiMe_3)_2$ resulted in 71% yield. Ketimines containing halogens (**1d**, **1e**, **1f**) smoothly reacted with **2b** (2.5 mol % catalyst loading), generating the desired products in 83–91% yield. The sterically more

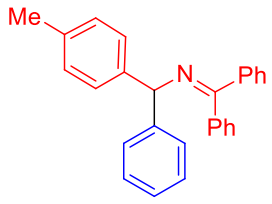
demanding 1-naphthyl substituted ketimine (**1g**) exhibited no reaction under the standard conditions. Optimization of this substrate led to **3gb** in 71% yield at 80 ^{o}C after 12 h with 10 mol % palladium in THF and LiO*t*Bu. Pyridyl-containing ketimines also participated in the arylation reaction. 3-Pyridyl derivative **1h** furnished the arylation product in 87% yield with 5 mol % catalyst loading. With the 4-pyridyl substrate **1i**, modification of the standard protocol by using $LiN(SiMe_3)_2$ at 50 ^{o}C was necessary, ultimately leading to 90% yield of the arylation product **3ib**. The 2-furyl-based substrate **1j** underwent cross coupling with 10 mol % catalyst loading in 60% yield.

As for the scope of aldimines, heterocyclic aldimine **1h'**, **1i'** and **1l'** were selected (Table 1.4). Both 3- and 4-pyridyl derived aldimines (**1h'** and **1i'**) furnished products in 77 and 91% yield with 10 and 5 mol % catalyst loading, respectively. Notably, the 3-furyl-based substrate **1l'** underwent cross-coupling at 5 mol % catalyst loading and furnished the product in 85% yield. Considering the price difference between 3-furylmethylamine ($750/g) and 3-furancarboxaldehyde ($7.94/g), the arylation with aldimine proved to be much more cost-effective.

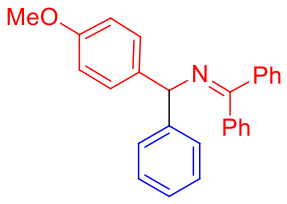
Table 1.3. Scope of Ketimine in Arylation of 1,1,3-Triaryl-2-azaallyl Anions with Bromobenzene 2b.[a,b]



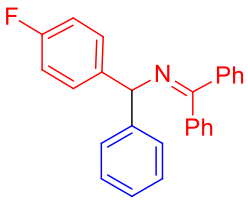
1b–1j **2b** **1bb–1jb**



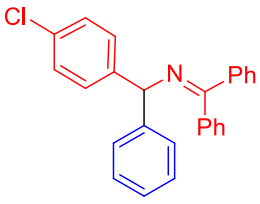
3bb, 89%[c]



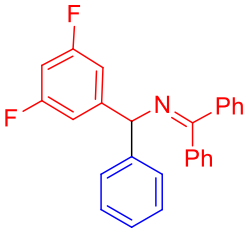
3cb, 71%[d]



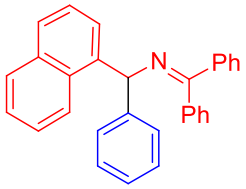
3db, 83%



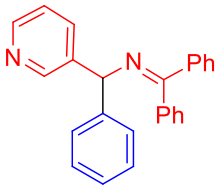
3eb, 89%



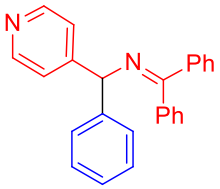
3fb, 91%



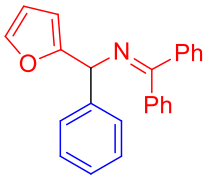
3gb, 71%[e]



3hb, 87%[c]



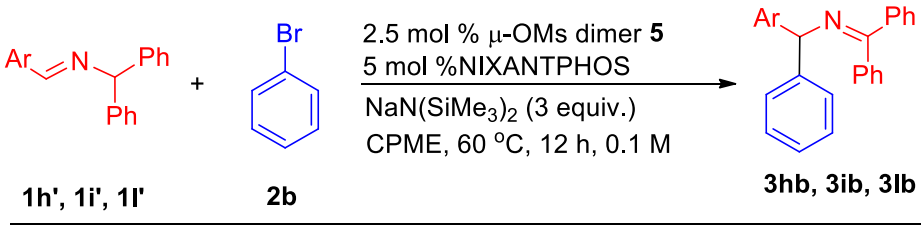
3ib, 90%[f]



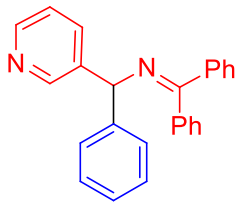
3jb, 60%[g]

[a]Reactions conducted on a 0.1 mmol scale using 2 equiv. of ketimine, 2 equiv. of $NaN(SiMe_3)_2$, and 1 equiv. of bromobenzene **2b** at 0.1 M. Base was added portionwise at 0.1 mL/30 min. [b]Isolated yield after chromatographic purification. [c]5 mol % Pd loading. [d]5 mol % Pd loading, 3 equiv. of **1c** and 3 equiv. of $KN(SiMe_3)_2$. [e]10 mol % Pd loading, 3 equiv. of Li*O*tBu at 80°C in 3 mL THF for 12 h. [f]10 mol % Pd loading, 2 equiv. $LiN(SiMe_3)_2$, 50 °C. [f]10 mol % Pd loading, 50 °C.

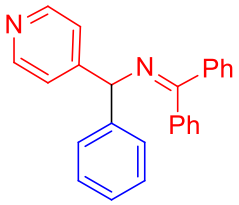
Table 1.4. Scope of Aldimine in Arylation of 1,1,3-Triaryl-2-azaallyl Anions with Bromobenzene 2b.[a,b]



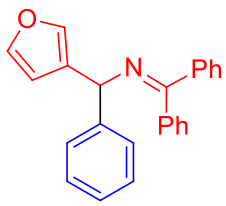
1h', 1i', 1l' **2b** **3hb, 3ib, 3lb**



3hb, 77%[c]



3ib, 91%



3lb, 85%[d]

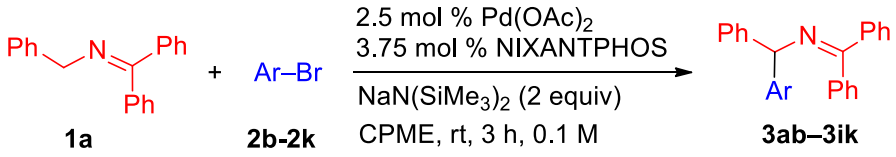
[a]Reactions conducted on a 0.1 mmol scale using 2 equiv. of aldimine, 3 equiv. of $NaN(SiMe_3)_2$, and 1 equiv. of bromobenzene **2b** at 0.1 M. Base was added portionwise at 0.1 mL/30 min. [b]Isolated yield after chromatographic purification. [c]10 mol % Pd loading. [d]THF, 3 h.

1.2.1.3. Scope of Aryl Bromides in Palladium-Catalyzed Arylation of 1,1,3-Triaryl-2-azaallyl Anions.

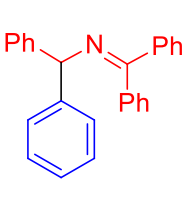
Scope of aryl bromides in the Pd-catalyzed arylation of **1a** is summarized in Table 1.5. Bromobenzene **2b** and aryl bromides bearing electron donating alkyl substituents at *para*- and *meta*-positions **2c**, **2d**, **2e** furnished coupling products **3ab**, **3ac**, **3ad** and **3ae** in 83–90% yield. Aryl bromides possessing electron-donating 4-*N,N*-dimethylamino (**2f**) and 4-methoxy (**2g**) groups furnished coupling products (**3af**, **3cb**) in 93 and 90% yield, respectively (10 mol % Pd loading). Aryl bromides with electron-withdrawing substituents were also suitable coupling partners. In particular, 4-chloro bromobenzene (**2h**) was transformed into the coupled product **3eb** in 90% yield with the carbon-chloride bond remaining intact. 4-Fluoro- (**2i**) and 4-trifluoromethyl bromobenzene (**2j**) afforded the coupled products **3db** and **3aj** in 86 and 75% yields, respectively. Heterocyclic 3-bromopyridine **2k** also coupled with **1a** to give product in 60%

yield at 5 mol % catalyst loading. Aryl bromides bearing 4-cyano (**2l**) and 4-ethyl ester (**2m**) substituents provided arylation products **3al** and **3am** in 64 and 63% yield with 10 mol % catalyst. Coupling with *N*-(4-bromophenyl) acetamide (**2n**), which possesses an acidic N-H, proved to be more challenging under these conditions. Using μ-OMs dimer **5** as Pd source enabled this coupling to proceed in 75% yield to afforded desire product **3an**. No byproduct derived from Buchwald-Hartwig coupling was observed. In the case of the sterically hindered aryl bromide, 2-bromo toluene (**2o**), a synthetically useful 56% yield was obtained**.** It is noteworthy that precatalyst **6**, in the presence of NIXANTPHOS, afforded bis-heterocyclic product **3ik** in excellent yield (90%).

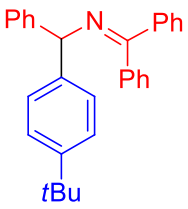
Table 1.5. Scope of Aryl Bromides in Arylations of 1,1,3-Triaryl-2-azaallyl Anions.[a,b]



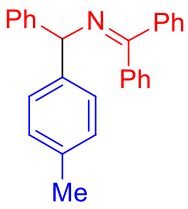
1a **2b-2k** **3ab–3ik**



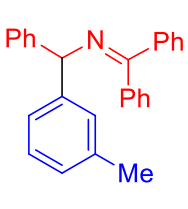
3ab, 90%



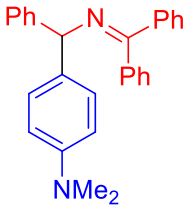
3ac, 90%



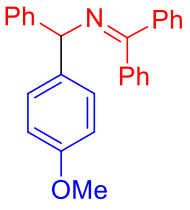
3bb, 87%



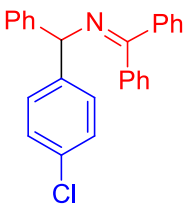
3ae, 83%



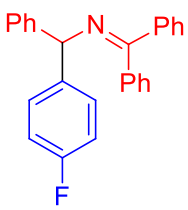
3af, 93%[c]



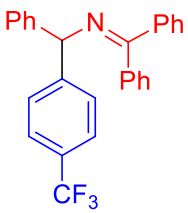
3cb, 90%[c]



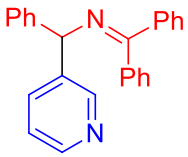
3eb, 90%



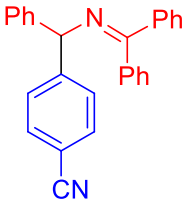
3db, 86%



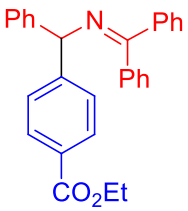
3aj, 75%



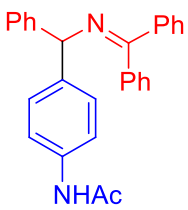
3hb, 60%[d]



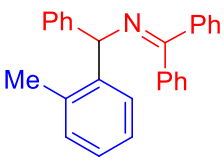
3al, 64%[c]



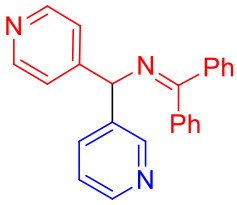
3am, 63%[c]



3an, 75%[e]



3ao, 56%[f]



3ik, 90%[f]

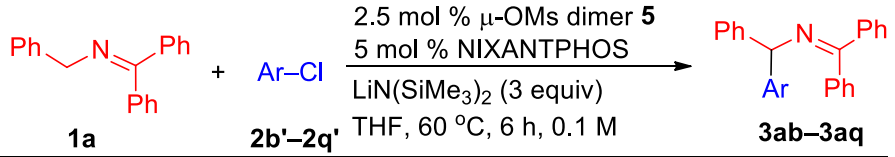
[a]Reactions conducted on a 0.1 mmol scale using 2 equiv. of ketimine, 2 equiv. of $NaN(SiMe_3)_2$, and 1 equiv. of bromobenzene at 0.1 M. Base was added portionwise at 0.1 mL/30 min. [b]Isolated yield after chromatographic purification. [c]10 mol % Pd loading. [d]5 mol % Pd loading. [e]5 mol % Buchwald's μ-OMs **5** and 10 mol % NIXANTPHOS, 3 equiv. of $NaN(SiMe_3)_2$, 60 °C, 12 h. [f]10 mol % precatalyst **6**, 3 equiv. of $LiN(SiMe_3)_2$, 60 °C, 8 h.

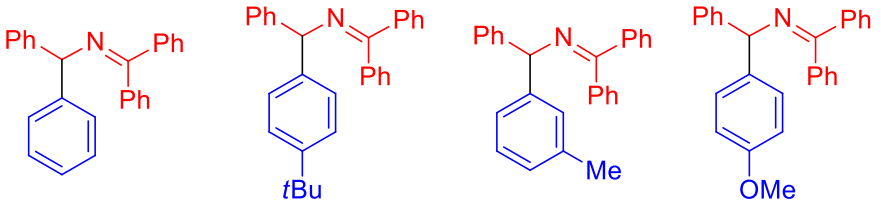
1.2.1.4. Scope of Palladium-Catalyzed Arylation of 1,1,3-Triaryl-2-azaallyl Anions with Aryl Chlorides.

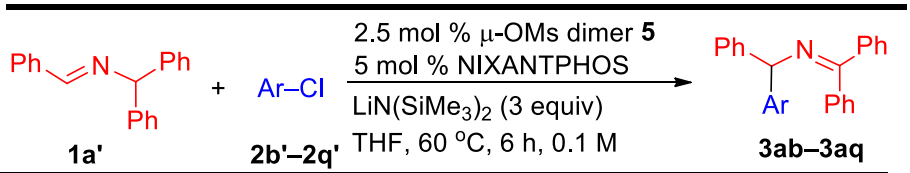
The scope of the aryl chloride-ketamine cross-coupling was determined (Table 1.6) at 60 ^{o}C (5 mol % Pd loading). Chlorobenzene **2b'** gave **3ab** in 90% yield. Aryl chlorides bearing alkyl groups (4-^{t}Bu **2c'**, 3-Me, **2e')** provided products **3ac** and **3ae** in 86% and 77% yield, respectively. Electron-rich 4-chloroanisole (**2g'**) was coupled with **1a** in 60% yield at 10 mol % Pd loading. Aryl chlorides with electron-withdrawing 4-F (**2i'**), 4-CF_3 (**2j'**) and 3-CN (**2p'**) groups were also well tolerated, providing products in 77% (**3db**), 87% (**3aj**), and 91% (**3ap**) yield, respectively. It is notable that the base-sensitive nitrile-bearing substrate gave excellent yield. 3-Chloro-*N,N*-dimethylaniline **2q'** reacted with **1a** in 61% (**3aq**) at 10 mol % catalyst loading.

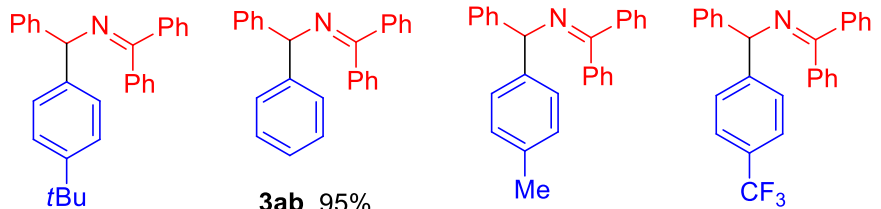
Encouraged by the results of the ketimine arylation with aryl chlorides, we next investigated translation of the optimized conditions from Table 1.2 to the arylation of aldimine **1a'** (Table 1.6). Coupling reactions at 60 °C with 5 mol % catalyst loading and 4-*tert*-butyl chloro benzene (**2c'**) gave **3ac** in 91% yield. Chlorobenzene (**2b'**) as well as alkyl substituted 4-methyl chlorobenzene (**2d'**) gave product **3ab** and **3ad** in 95% and 86% yield, respectively. Coupling of **1a'** with 4-trifluoromethyl chlorobenzene **2j'** provided **3aj** in 85% yield. 4-Fluoro chlorobenzene **2i'** reacted smoothly with aldimine **1a'** to give the product **3db** in 84% yield. 1-Chloro-3,5-difluorobenzene (**2r'**) coupled in 81% yield at 10 mol % catalyst loading.

Table 1.6. Scope of Aryl Chlorides in the Arylation of Ketimine 1a and Aldimine 1a'[a, b]





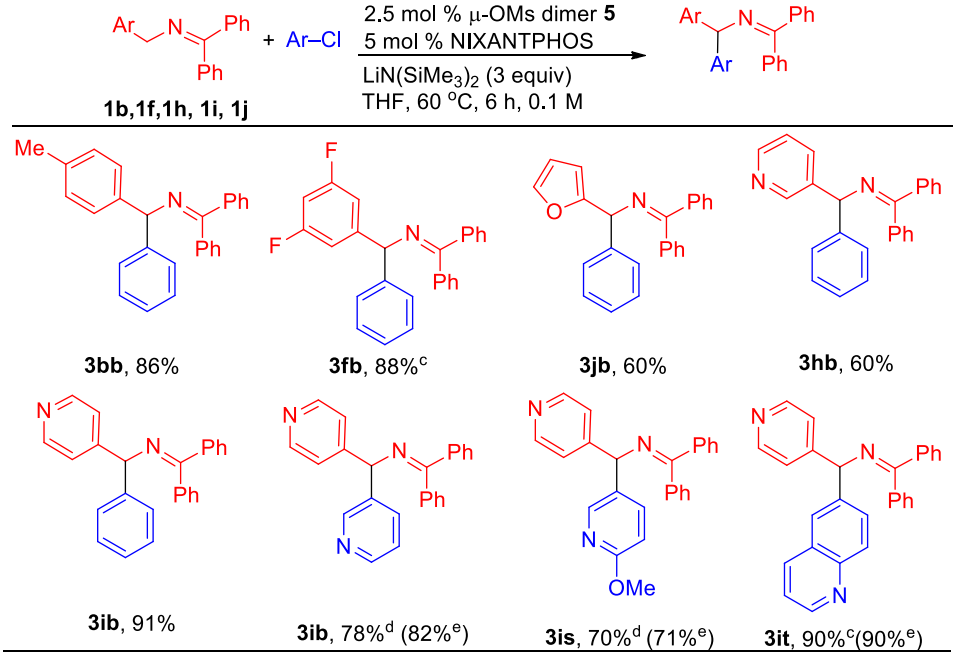




[a]Reactions conducted on a 0.1 mmol scale using 2 equiv. of **1a**, 3 equiv. of $LiN(SiMe_3)_2$, and 1 equiv. of ArCl at 0.1 M. Base was added portionwise with speed 0.05 mL/30 min. [b]Isolated yield after chromatographic purification. [c]DME as solvent. [d]DME 10 mol % Pd loading.

The substrate scope of ketimines was then studied (Table 1.7). The reaction of 4-methyl benzyl ketimine derivative (**1b**) proceeded efficiently under 10 mol % loading in 86% yield. Coupling of 3,5-difluoro benzyl ketimine derivative (**1f**) furnished the product in 88% yield at 5 mol % catalyst loading. The 2-furyl ketimine derivative led to a satisfactory yield of product **3jb** (61% yield). 3-pyridyl and 4-pyridyl ketimine derivatives coupled with chlorobenzene (**2b'**) in 60% (**3hb**) and 91% (**3ib**) yield. Synthesis of bis-heterocyclic diarylmethylamine derivatives via coupling of 4-pyridyl ketimine and aldimine with heterocyclic aryl chlorides was next investigated. Good-to-excellent yields were observed with ketimine and aldimine isomers. Employing 3-chloro pyridine (**2k'**) led to 78% yield with ketimine **1i** and 82% yield with aldimine **1i'**. At 10 mol % catalyst loading, electron-rich 5-chloro-2-methoxypyridine (**2s'**) exhibited good reactivity with **3is** generated in 71% yield from ketimine **1i** and 70% yield from aldimine **1i'**. Excellent yields were achieved with 6-chloroquinoline (**2t'**) at 5 mol % catalyst loading. Product **3it** was obtained in 90% yield from couplings with both **1i** and **1i**'.

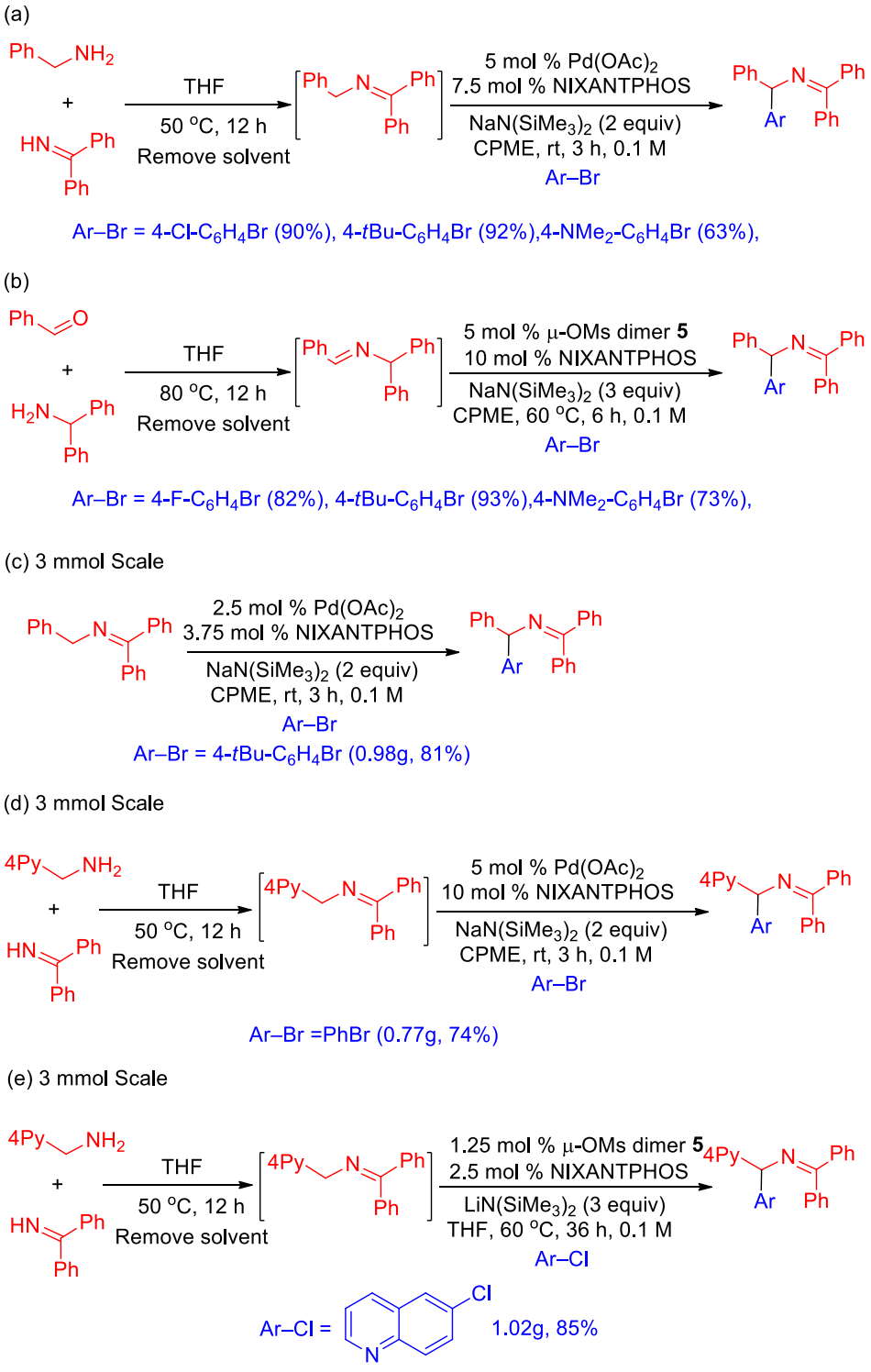
Table 1.7. Scope of Ketimine and Aldimine in the Arylation of 1,1,3-Triaryl-2-azaallyl Anions with Aryl Chlorides.[a,b]



[a]Reactions conducted on a 0.1 mmol scale using 2 equiv. of imine, 3 equiv. of $LiN(SiMe_3)_2$, and 1 equiv. of ArCl at 0.1 M. Base was added portionwise with speed 0.05 mL/30 min. [b]Isolated yield after chromatographic purification. [c]5 mol % Pd loading. [d]Base was added portionwise with speed 0.1 mL/30 min. [e]Yields from aldimine **1i'**.

1.2.1.6. One-Pot Synthesis of Diarylmethylamine Derivatives.

To further increase the synthetic utility and efficiency of our arylation of 1,1,3-triaryl-2-azaallyl anions, we set out to develop a protocol for the *in-situ* imine generation followed by cross-coupling. Subjecting the commercially available benzophenone imine $Ph_2C{=}NH$ to 1 equiv. of benzyl amine in THF at 50 ^oC for 12 h in a sealed microwave vial under nitrogen led to ketimine **1a** (Scheme 1.6, a). Complete removal of the THF solvent under vacuum was followed by addition of 5 mol % $Pd(OAc)_2$ and 7.5 mol % NIXANTPHOS. Next, aryl bromide was added followed by portionwise addition of $NaN(SiMe_3)_2$ in CPME. As illustrated in Table 1.8, aryl bromides bearing electron-withdrawing, neutral and electron-donating groups furnished the desired arylation products in 63–92% yields. In a similar fashion, a telescoped aldimine synthesis/cross-coupling procedure was conducted (Scheme 1.6, b). Aryl bromides bearing electron-withdrawing, neutral and electron-donating substituents furnished the desired arylation products in 73–93% yields. We then scaled up the ketimine arylation using ketimine **1a** with bromobenzene **2b** on a 3 mmol scale with catalyst loading of 2.5 mol %. The desired coupling product was isolated in 81% yield (0.98 g, Scheme 1.6, c). We also scaled up the telescoped synthesis with 4-pyridyl imine **1i** and cross-coupling with bromobenzene **2b**. Again, the reaction was conducted with 3 mmol **1i**. The desired product **3ib** was isolated in 74% yield (0.77 g, Scheme 1.6, d). The arylation of aryl chloride was also amenable to a sequential one-pot imine synthesis/arylation protocol. We conducted a 3 mmol scale sequential one-pot synthesis of 4-pyridyl ketimine **1i**, followed by arylation with 6-chloroquinoline **2t'** at 2.5 mol % catalyst loading. The bis-heterocylic product **3it** was isolated in 85% yield (1.02 g, Scheme 1.6, e).

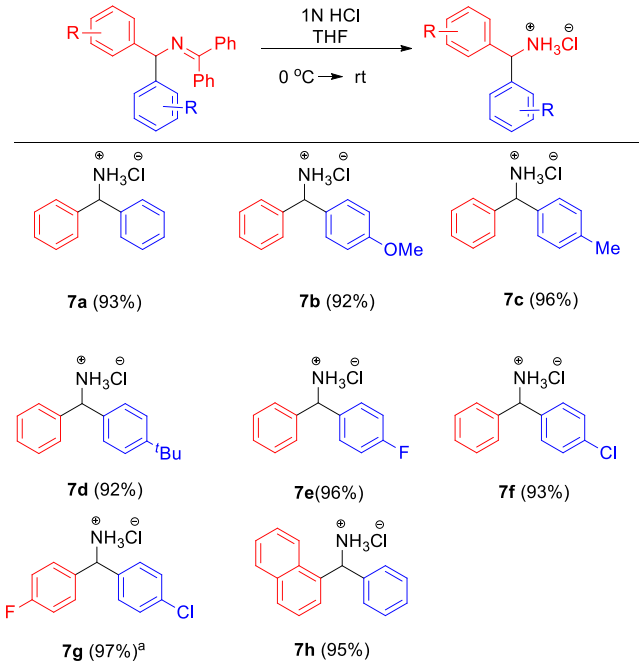


Scheme 1.6. One-Pot Synthesis of Diarylmethylamine Derivatives.

1.2.1.7 Product Functionalization

Hydrolysis of several ketimine products afforded diarylmethylamines **7a**–**7h** as crystalline hydrochloride salts in 92–97% yield (Table 1.8). In each case, only a single diarylmethylamine product was isolated in high yield, indicating that isomerization of the arylated ketimines during their formation and hydrolysis did not take place. In contrast, hydrolysis of the products from the Oshima procedure would give a mixture of diarylmethylamines.

Table 1.8. Hydrolysis of Product Ketimines.



7a (93%) **7b** (92%) **7c** (96%)

7d (92%) **7e**(96%) **7f** (93%)

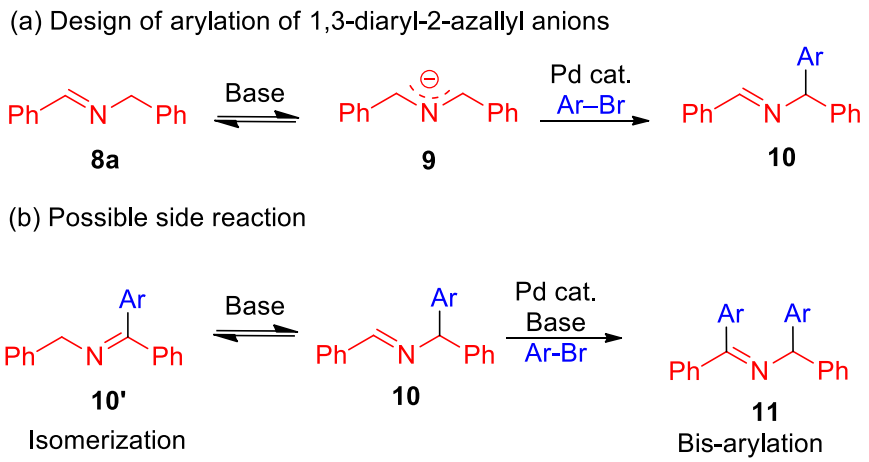
7g (97%)[a] **7h** (95%)

1.2.2 Palladium-Catalyzed Arylation of 1,3-Diaryl-2-azaallyl Anions with Aryl Bromides

1.2.2.1 Design of the 1,3-Diaryl-2-azaallyl Anions.

Despite the broad scope and high yields of the arylated products, the arylation of 1,1,3-triaryl-2-azaallyl anions leaves room for improvement. First, ketimines undergo deprotonation and isomerization to the aldimine, which requires more forcing conditions to deprotonate and regenerate the 2-azaallyl anion. Second, the formation of di-ketimines consumes two equivalents of the starting material and an excess of the 2-azaallyl anion precursor was necessary as we mentioned in Table 1.1.

To improve our method for preparing diarylmethylamine derivatives, we envisioned an improved approach for the umpolung synthesis of diarylmethylamines through Pd-catalyzed arylation of 1,3-diaryl-2-azaallyl anions (Schemes 1.7, a). The challenge of this approach is that the product **10** also readily undergoes deprotonation/isomerization or arylation (Schemes 1.7, b). Therefore, it is important that the catalyst promotes the selective formation of the mono-arylation product. Moreover, the conditions must be sufficiently mild such that the product does not undergo deprotonation.



Scheme 1.7. Palladium-Catalyzed Arylation of 1,3-Diaryl-2-azaallyl Anions 9.

1.2.2.2 Reaction Scope.

Based on the previous experience of catalyst and base identifiation, we studied the reaction of 1.0 equivalent of aldimine **8a** with 1.5 equivalents of 1-bromo-4-*tert*-butylbenzene (**2c**) using the 5 mol % $Pd(OAc)_2$ and 10 mol % NIXANTPHOS. To prevent the bis-arylation and achieve this high yield, it was necessary to add the 1.5 equivalents of $LiN(SiMe_3)_2$ over 1 h in THF at room temperature, leading to **10ac** in 93% isolated yield in Table 1.9. The reactions of the parent aldimine **8** with bromobenzene **2b** and 3-bromotoluene **2e** furnished the corresponding products **10ab** and **10ae** in 75% and 88% yield, respectively. Aryl bromides bearing electron-donating 4-methoxy (**2g**) and 4-bromo-*N,N*-dimethylaniline (**2f**) groups produced the desired imines **10ag**

and **10af** in excellent yields (85 and 93%, respectively). The reaction of imine **8a** with 1-bromo-4-fluorobenzene (**2i**) gave 52% yield of the mono-arylation product **10ai** with 16% bis-arylated product **11ai**. Although the yield of **10ai** was diminished due to bis-arylation, it is surprising that no isomerization or dimerization was observed.

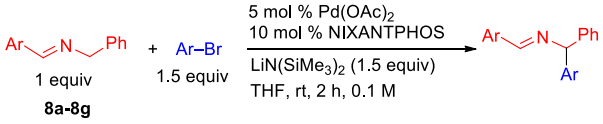
We then turned our attention to unsymmetrical 1,3-diaryl-2-azaallyl anions. In order to develop the arylation of unsymmetrical 1,3-diaryl-2-azaallyl anions into a synthetically useful method, we hypothesize that increasing steric hindrance of one aryl would enhance the regioselectivity. Hence, we studied the arylation of *o*-anisyl substituted imine **8b** with 1-bromo-4-*tert*-butylbenzene (**2c**). Results showed that arylation mainly occurred at the less sterically hindered position with a 4:1 ratio of isomers **10bc** and **10bc'** in 76% overall yield.

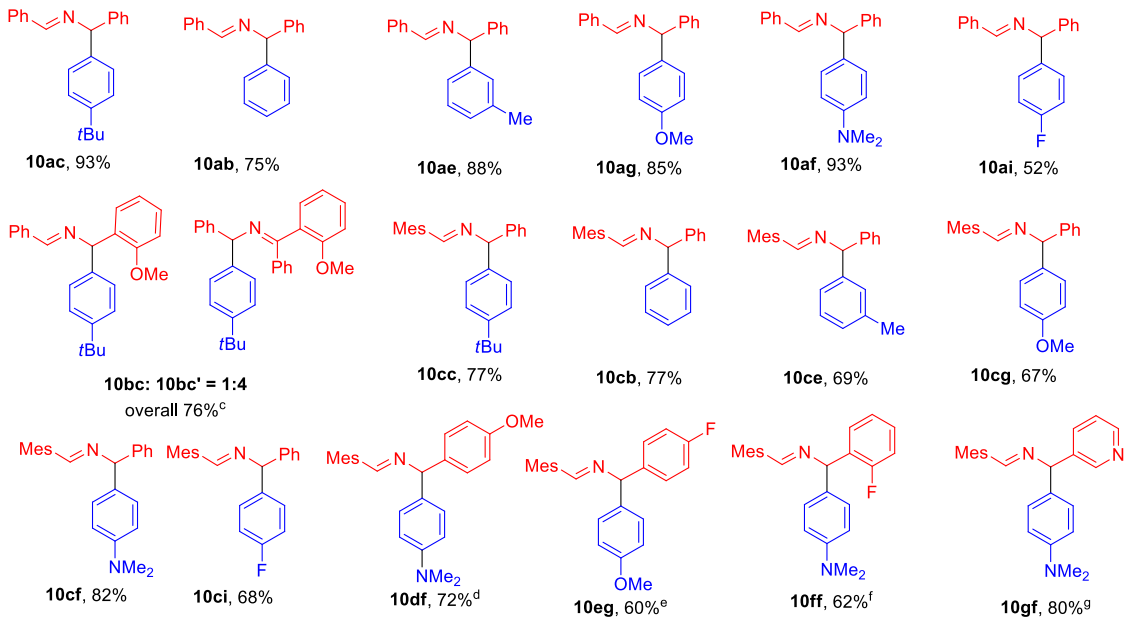
Moreover, the moderate selectivity in the arylation of **8b** led us to examine the more sterically demanding mesityl substituted aldimine **8c**. Under the reaction conditions listed in Table 2, coupling of **8c** with 1-bromo-4-*tert*-butylbenzene (**2c**) afforded product **10cc** as a single isomer in 77% yield. We therefore examined the substrate scope based on mesityl substituted aldimine nucleophiles. Arylation of **8c** with aryl bromides containing alkyl (4-C_6H_4-*t*Bu, Ph, 3-C_6H_4-Me), electron donating (4-C_6H_4-OMe, 4-C_6H_4-NMe_2) and withdrawing (4-C_6H_4-F) groups produced the desired products **8cc**–**8ci** in good yields (67–82%), demonstrating the synthetic usage of unsymmetrical 1,3-diaryl-2-azaallyl anions.

Next, the substituents on the aldimine were varied. Coupling of 4-methoxy substituted aldimine **8d** with 1-bromo-4-*N,N*-dimethylaniline (**2f**) was accomplished by slow addition (1.5 h) of $LiN(SiMe_3)_2$ to the reaction mixture at room temperature followed by heating to 50 ^oC for 5 h (**10df**, 72% yield). The arylation of fluoro substituted aldimines bearing either 4-fluoro (**8e**) or 2-fluoro (**8f**) substituents with 4-bromoanisole (**2g**) and 4-bromo-*N,N*-dimethylaniline (**2f**) required longer reaction times (6 h) at room temperature for complete consumption of aldimines and gave the products **10eg** and **10ff** in 60% and 62% yield. To access heteroaryl substituted

diarylmethylamines, we performed the reaction of 3-pyridyl substituted aldimine **8g** with 4-bromo-*N,N*-dimethylaniline **2f**. The product **10gf** was obtained in 80% yield with aryl bromide **2f** as limiting reagent.

Table 1.9. Scope of arylation of 1,3-diaryl-2-azaallyl anions.[a,b]



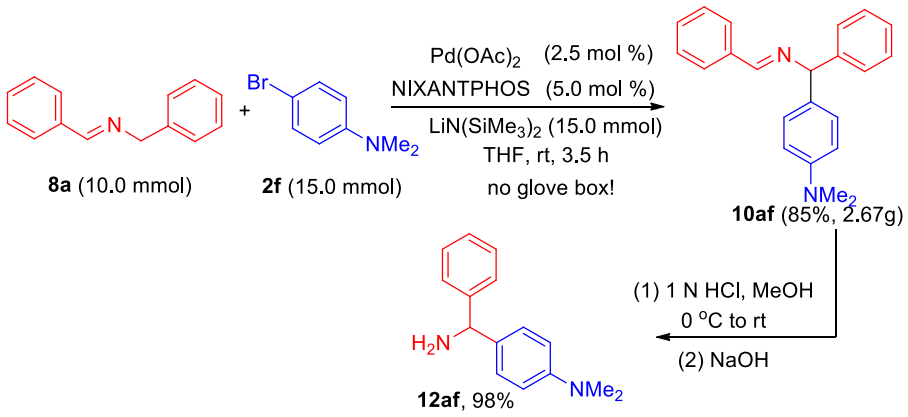


[a]Reactions conducted on 0.2 mmol scale by using 1.0 equiv. aldimine, 1.5 equiv. aryl bromide and 1.5 equiv. $LiN(SiMe_3)_2$ at 0.1 M. Slow addition of $LiN(SiMe_3)_2$ over 1 h followed by 4 h stirring. [b]Isolated yield after chromatographic purification. [c]4h. [d]2.0 equiv. aryl bromide, 6 h, 50 °C. [e]2.0 equiv. aryl bromide, 6 h. [f]2.0 equiv. aryl bromide, slow addition of $LiN(SiMe_3)_2$ in 1.5 h followed by 6 h reaction time. [g]2.0 equiv. aldimine, 1.0 equiv. aryl bromide and 2.0 equiv. $LiN(SiMe_3)_2$ at 0.05 M.

1.2.2.3 Gram Scale Synthesis.

The scalability of this approach was also studied. We performed a 10.0 mmol scale reaction of imine **8a** with 15.0 mmol 4-bromo-*N,N*-dimethylaniline (**2f**) in the presence of 2.5 mol % $Pd(OAc)_2$

and 5.0 mol % NIXANTPHOS at room temperature (Scheme 1.8). The reaction was conducted without use of a glovebox and employed a commercially available 1.0 M solution of $LiN(SiMe_3)_2$ (15.0 mmol) in THF. After slow addition of the base by syringe over 1.5 h, the reaction was stirred for an additional 2 h. After workup, 85% yield (2.67 g) of product **10af** was obtained. The imine **10af** was then hydrolyzed to give **12af** was isolated in 98% yield.



Scheme 1.9. Gram Scale Synthesis of 10af and its Hydrolysis to Produce Diarylmethylamine 12af.

1.3 Summary and Outlook

Diarylmethylamines have played a significant role in the betterment of human health and well-being. In this chapter, we have developed highly efficient approaches to the synthesis of this important class of compounds based on both 1,1,3-triaryl-2-azaallyl anions and 1,3-diaryl-2-azaallyl anions as anionic coupling partners. Over 100 examples of diarylmethylamine derivatives have been prepared from ketimines, aldimines, aryl bromides and aryl chlorides demonstrating the value of this method. These protocols are amenable to one-pot synthesis and gram-scale synthesis. The key to this chemistry is the NIXANTPHOS-based catalyst and precatalyst. It enables the arylation of aryl halides to proceed in a regioselective fashion under mild conditions. Moreover, identification of a hindered silylamide bases assured that products of the reaction were not deprotonated or isomerized.

Even though three publications[14] with diverse substrate scope have been achieved, there is still room of improvement. These include the asymmetric arylation of 2-azaallyl anions, base-free arylation protocol via *in-situ* generation of the 2-azaallyl anions from their carboxylic acid salts and introducing other transition-metals to catalyze these reactions. Expanding the substrates scope to challenging vinyl halides is also under investigation.

1.4. Experimental Section

1.4.1 Experimental Section For Arylation of 1,1,3-Triaryl-2-Azaallyl Anions With Aryl Bromides.

General Methods. All reactions were conducted under a nitrogen atmosphere with oven-dried glassware and standard Schlenk or vacuum line techniques. All solutions were handled under nitrogen and transferred via syringe. Anhydrous solvents, including CPME (cyclopentyl methyl ether), 1,4-Dioxane, and 2-MeTHF were purchased from Sigma-Aldrich and directly used without further purification. Toluene and THF were dried through activated alumina columns. Unless otherwise stated, reagents were commercially available and used as purchased without further purification. Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar or Matrix Scientific, and solvents were purchased from Fisher Scientific. Progress of reactions was monitored by thin-layer chromatography using Whatman Partisil K6F 250 µm precoated 60 Å silica gel plates and visualized by short-wave ultraviolet light as well as by treatment with iodine or ceric ammonium molybdate (CAM) stain. Flash chromatography was performed with silica gel (230–400 mesh, Silicycle). ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were obtained using a Brüker AM-500 Fourier-transform NMR spectrometer at 500 and 125 MHz, respectively. Chemical shifts were reported in units of parts per million (ppm) downfield from tetramethylsilane (TMS), and all coupling constants were reported in Hertz. The infrared spectra were taken with KBr plates with a Perkin-Elmer Spectrum 100 Series spectrometer. High resolution mass spectrometry (HRMS) data were obtained on a Waters LC-TOF mass spectrometer (model LCT-XE Premier) using chemical ionization (CI) or electrospray ionization (ESI) in positive or negative mode, depending on the analyte. Melting

points were determined on a Unimelt Thomas-Hoover melting point apparatus and were uncorrected. Deactivated silica gel was prepared by addition of 15 mL of Et_3N to 1 L of silica gel. Note that in some cases, due to the large number of inequivalent aromatic carbons in the products, coincidental overlap of resonances prevented observation of all the expected resonances.

Preparation of Imines : Imines(**1a-1j**) were prepared according to literature procedures.[20]

Preparation of Aldimines : Aldimines (**1a'**, **1i'**, **1h'**, and **1l'** in Table 4) were prepared according to literature procedures.[21]

Preparation of Buchwald's 3rd Generation Pre-catalyst: Palladium μ-OMs dimer and 3rd generation precatalyst was prepared according to literature procedure.[18]

Procedure and Characterization for the Deprotonation/Benzylation of Benzophenone Imine

General Procedure A: An oven-dried microwave vial equipped with a stir bar was charged with imine **1a** (27.2 mg, 0.10 mmol) and $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol) under a nitrogen atmosphere. Next, 1 mL of dry THF was added under nitrogen via syringe, the vial was sealed and benzyl chloride **2a** (13.8 μL, 0.12 mmol) was added to the reaction mixture via syringe through the rubber septum. The reaction mixture was next stirred for 12 h at 24 ºC, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate, and the combined solutions were concentrated in vacuo. The assay yield was determined by ^1H NMR spectroscopy of the crude reaction mixture by integration using 1,4-dimethylbenzene as internal standard in accordance to literature procedures.[22]

Procedure and Characterization for the Pd Catalyzed Arylation of Ketimines and Aldimines

General Procedure B (Pd-Catalyzed Arylation of Ketimines): An oven-dried microwave vial equipped with a stir bar was charged with imine **1a** (54.3 mg, 0.20 mmol) under a nitrogen atmosphere. A stock solution of $Pd(OAc)_2$ (0.55 mg, 0.0025 mmol) and NiXantPhos (2.1 mg, 0.00375 mmol) under nitrogen in 0.5 mL dry CPME was taken up by syringe and added to the reaction vial. The vial was sealed, and 1-bromo-4-*tert*-butylbenzene **2c** (17.3 μL, 0.10 mmol) was added dropwise by syringe to this solution through the rubber septum. A solution of $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol) in 0.5 mL CPME was added portionwise by syringe at 0.1 mL/30 min at 24 $^{\circ}$C. The reaction mixture was stirred for 3 h at 24 $^{\circ}$C, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate, and the combined solutions were concentrated in vacuo. The crude material was loaded onto a silica gel column via pipette and purified by flash chromatography. (hexanes to diethyl ether:hexanes = 1:50).

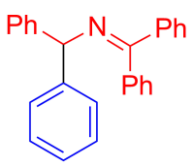
General Procedure C (Pd-Catalyzed Arylation of Aldimines): An oven-dried microwave vial equipped with a stir bar was charged with aldimine **1a'** (54.3 mg, 0.20 mmol) under a nitrogen atmosphere. A stock solution of Buchwald's 3rd generation pre-catalyst Pd dimer (1.8 mg, 0.0025 mmol) and NiXantphos (2.8 mg, 0.0050 mmol) under nitrogen in 0.5 mL dry CPME was taken up by syringe and added to the reaction vial. The vial was sealed, and 1-bromo-4-*tert*-butylbenzene **2c** (17.3 μL, 0.10 mmol) was added dropwise by syringe to this solution through the rubber septum. A solution of $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol) in 0.5 mL CPME was added portionwise by syringe at 0.1 mL/30 min at 60 $^{\circ}$C. The reaction mixture was stirred for 12 h at 60 $^{\circ}$C, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate, and the combined solutions were concentrated in vacuo. The crude material was loaded onto a silica gel column via pipette and purified by flash chromatography. (hexanes to diethyl ether:hexanes = 1:50).

General Procedure D: One-pot Ketimine Synthesis/Pd-Catalyzed arylation

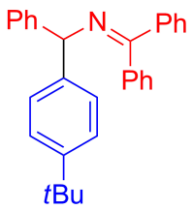
An oven-dried microwave vial equipped with a stir bar was charged with benzylamine (32.1 mg, 0.30 mmol) and benzophenone imine (54.4 mg, 0.30 mmol) under a nitrogen atmosphere. Next, 1 mL of dry THF was added under nitrogen via syringe and the vial was sealed. The reaction was then placed in an oil bath at 50 °C. After the reaction mixture was stirred for 12 h at 50 °C, the solvent was completely removed in vacuo and the vial was refilled with nitrogen. A stock solution of $Pd(OAc)_2$ (0.55 mg, 0.0025 mmol) and NiXantphos (2.1 mg, 0.00375 mmol) under nitrogen in 0.5 mL dry CPME was taken up by syringe and added to the same reaction vial through the rubber septum. 1-Bromo-4-*tert*-butylbenzene **2c** (17.3 μL, 0.10 mmol) was added dropwise. A solution of $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol) in 0.5 mL CPME was added portionwise at 0.1 mL/30 min at 24 °C. The reaction mixture was stirred for 3 h at 24 °C, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate, and the combined solutions were concentrated in vacuo. The crude material was loaded onto a silica gel column via pipette and purified by flash chromatography. (hexanes to diethyl ether:hexanes = 1:50).

General Procedure E: One-pot Aldimine Synthesis/Pd-Catalyzed aryation: An oven-dried microwave vial equipped with a stir bar was charged with benzaldehyde (21.2 mg, 0.20 mmol) and diphenylmethylamine (36.6 mg, 0.20 mmol) under a nitrogen atmosphere. Dry THF (1 mL) was then added under nitrogen via syringe and the vial was sealed. The reaction was then placed in an oil bath at 80 °C and stirred for 12 h. Next, the volatile materials were completely removed at rt and the remaining solid was dried under reduced pressure at 60 °C for 2 h. The vial was then backfilled with nitrogen and a stock solution of Buchwald's 3rd generation pre-catalyst Pd dimer (3.7 mg, 0.005 mmol) and NIXANTPHOS (5.6 mg, 0.010 mmol) in 0.5 mL dry CPME was added by syringe through the rubber septum. Next, 1-bromo-4-*tert*-butylbenzene **2c** (17.3 μL, 0.10 mmol) was added dropwise by syringe through the rubber septum. A solution of

$NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol) in 0.5 mL CPME was added portionwise at 0.05 mL/30 min at 60 °C. The reaction mixture was stirred for 6 h at 60 °C, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate, and the combined solutions were concentrated under reduced pressure. The crude material was loaded onto a silica gel column via pipette and purified by flash chromatography (hexanes to diethyl ether:hexanes = 1:50).

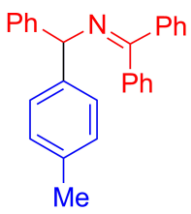


***N*-(Diphenylmethylene)-1,1-diphenylmethanamine (3ab)**: The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.2 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (31.3 mg, 90% yield) as a white solid. R_f = 0.70 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data.[23]



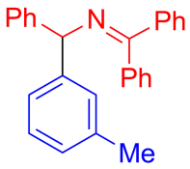
1-(4-(*tert*-Butyl)phenyl)-*N*-(diphenylmethylene)-1-phenylmethanamine (3ac):The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2c** (17.3 μL, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (36.4 mg, 90% yield) as a white solid. Compound **3ac** was also synthesized following General Procedure C with aldimine **1a'** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol), aryl bromide (17.3 μL, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (37.9 mg, 94% yield) as a white solid. The one pot synthesis of **3ac** was performed following General Procedure D with benzylamine (32.1 mg, 0.30 mmol), benzophenone imine (54.4 mg, 0.30 mmol), $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol), aryl

bromide **2b** (17.3 μL, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (37.1 mg, 92% yield) as a white solid. The one pot synthesis of **3ac** from aldimine was performed following General Procedure E with benzaldehyde (21.2 mg, 0.20 mmol) and diphenylmethanamine (36.6 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2c** (17.3 μL, 0.1 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (37.5 mg, 93% yield) as a white solid. m.p. = 50−52 °C, R_f = 0.75 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77–7.74 (m, 2H), 7.44–7.41 (m, 3H), 7.37–7.31 (m, 5H), 7.29–7.23 (m, 6H), 7.20–7.17 (m, 1H), 7.10–7.07 (m, 2H), 5.53 (s, 1H), 1.27 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.8, 149.5, 145.2, 142.0, 140.1, 136.9, 130.1, 128.9, 128.7, 128.6, 128.5, 128.1, 128.0, 127.8, 127.3, 126.8, 125.4, 69.8, 34.6, 31.6 ppm; IR (thin film): 3058, 2962, 1623, 1597, 1577, 1490, 1446, 1314, 1290, 1027, 779, 728, 700 cm^{-1}; HRMS calc'd for $C_{30}H_{30}N^+$ 404.2378, observed 404.2374 $[M+H]^+$.

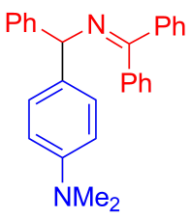


***N*-(Diphenylmethylene)-1-phenyl-1-(*p*-tolyl)methanamine(3bb):** The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2d** (12.3 µL, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (31.5 mg, 87% yield) as a white solid. Compound **3ad** was also synthesized following General Procedure B with ketamine **1b** (57.1 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (32.2 mg, 89% yield) as a white solid. m.p. = 110−112 °C, R_f = 0.77 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, J = 7.0 Hz, 2H), 7.43–7.42 (m, 3H), 7.37–7.31 (m, 5H), 7.27–7.24 (m, 2H), 7.21–7.16 (m, 3H), 7.08–7.07 (m, 4H), 5.52 (s, 1H), 2.29

(s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.9, 145.3, 142.1, 140.1, 137.0, 136.4, 130.2, 129.2, 128.9, 128.7, 128.6, 128.5, 128.1, 128.0, 127.7, 127.6, 126.8, 69.8, 21.2 ppm; IR (thin film): 3070, 1622, 1590, 1575, 1490, 1440, 1315, 1290, 1015, 780, 718, 700 cm^{-1}; HRMS calc'd for $C_{27}H_{24}N^+$ 362.1909, observed 362.1909 $[M+H]^+$.

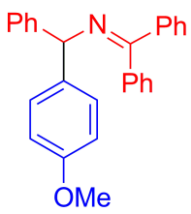


***N*-(Diphenylmethylene)-1-phenyl-1-(*m*-tolyl)methanamine (3ae)**: The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2e** (12.2 µL, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (30.1 mg, 83% yield) as a white solid. m.p. = 88−90 °C, R_f = 0.75 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75–7.74 (m, 2H), 7.42–7.39 (m, 3H), 7.36–7.30 (m, 5H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.20–7.11 (m, 4H), 7.07–7.06 (m, 2H), 7.00 (d, *J* = 7.5 Hz, 1H), 5.52 (s, 1H), 2.28 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.9, 145.2, 145.0, 140.1, 138.0, 136.9, 130.2, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 126.8, 124.8, 70.1, 21.7 ppm; IR (thin film): 3058, 1622, 1598, 1578, 1490, 1446, 1314, 1289, 1000, 780, 723, 696 cm^{-1}; HRMS calc'd for $C_{27}H_{24}N^+$ 362.1909, observed 362.1908 $[M+H]^+$.



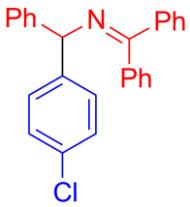
4-(((Diphenylmethylene)amino)(phenyl)methyl)-*N*,*N*-dimethylaniline (3af): The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2f** (20.2 mg, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:10) to give the product (36.2 mg, 93% yield) as a colorless oil. Compound **3af** was also synthesized following General Procedure C with aldimine **1a'** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol), and aryl bromide **2f** (20.2 mg, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted

with hexanes to diethyl ether:hexanes = 1:10) to give the product (31.2 mg, 80% yield) as a colorless oil. One pot synthesis of **3af** was performed following General Procedure D with benzylamine (32.1 mg, 0.30 mmol), benzophenone imine (54.4 mg, 0.30 mmol), $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol), aryl bromide **2f** (20.2 mg, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:10) to give the product (24.6 mg, 63% yield) as a colorless oil. The one pot synthesis of **3af** from aldimine was performed following General Procedure E with benzaldehyde (21.2 mg, 0.20 mmol) and diphenylmethanamine (36.6 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol)， aryl bromide **2f** (20.2 mg, 0.1 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:10) to give the product (28.5 mg, 73% yield) as a colorless oil. R_f = 0.44 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.5 Hz, 2H), 7.43–7.40 (m, 3H), 7.35–7.29 (m, 5H), 7.25 (t, *J* = 7.0 Hz, 1H), 7.17–7.14 (m, 3H), 7.10–7.08 (m, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 5.48 (s, 1H), 2.88 (s, 6H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.3, 149.7, 145.7, 140.2, 137.1, 133.2, 130.1, 128.9, 128.6, 128.5, 128.4, 128.1, 128.0, 127.7, 126.5, 112.8, 69.5, 40.8 ppm; IR (thin film): 3058, 1611, 1577, 1518, 1490, 1445, 1315, 1276, 1028, 780, 717, 696 cm^{-1}; HRMS calc'd for $C_{28}H_{27}N_2^+$ 391.2174, observed 391.2177 $[M+H]^+$



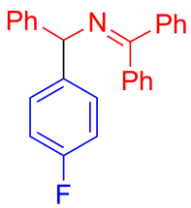
***N*-(Diphenylmethylene)-1-(*p*-methoxyphenyl)-1-phenylmethanamine (3cb)**: The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2g** (12.5 μL, 0.1 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (33.9 mg, 90% yield) as a thick oil. Compound **3cb** was also synthesized following General Procedure B with ketamine **1c** (90.4 mg, 0.30 mmol), $KN(SiMe_3)_2$ (59.8 mg, 0.30 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 5 mol % catalyst

loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (26.8 mg, 71% yield). R_f = 0.55 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.42–7.39 (m, 3H), 7.37–7.30 (m, 5H), 7.27–7.20 (m, 4H), 7.18–7.15 (m, 1H), 7.08–7.06 (m, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.51 (s, 1H), 3.74 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.8, 158.6, 145.4, 140.1, 137.4, 136.9, 130.2, 128.9, 128.8, 128.7, 128.6, 128.5, 128.2, 127.9, 127.7, 126.8, 113.9, 69.4, 55.4 ppm; IR (thin film): 3059, 1609, 1578, 1508, 1490, 1445, 1314, 1276, 1030, 781, 725, 696 cm^{-1}; HRMS calc'd for $C_{27}H_{24}NO^+$ 378.1858, observed 378.1863 $[M+H]^+$.

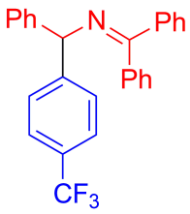


1-(*p*-Chlorophenyl)-*N*-(diphenylmethylene)-1-phenylmethanamine (3eb): The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2h** (19.1 mg, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (34.3 mg, 90% yield) as a colorless oil. **3eb** was also synthesized following General Procedure B with ketamine **1e** (61.2 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (34.0 mg, 89% yield) as a colorless oil. One pot synthesis of **3ag** was performed following General Procedure D with benzylamine (32.1 mg, 0.30 mmol), benzophenone imine (54.4 mg, 0.30 mmol, 3 equiv), $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol), aryl bromide **2h** (19.1 mg, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (34.3 mg, 90% yield) as a colorless oil. R_f = 0.78 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (dd, *J* = 7.5, 1.0 Hz, 2H)，7.42–7.40 (m, 3H), 7.37–7.31 (m, 3H), 7.29–7.22 (m, 8H), 7.20–7.17 (m, 1H), 7.05–7.04 (m, 2H), 5.51 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.5, 144.6, 143.6, 139.8, 136.7, 132.6, 130.4, 129.1, 128.9, 128.8, 128.69,

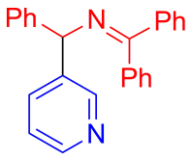
128.68, 128.65, 128.2, 127.8, 127.6, 127.1, 69.3 ppm; IR (thin film): 3060, 1622, 1598, 1576, 1488, 1446, 1315, 1282, 1014, 780, 715, 697 cm^{-1}; HRMS calc'd for $C_{26}H_{21}ClN^{+}$ 382.1363, observed 382.1350 $[M+H]^{+}$.



***N*-(diphenylmethylene)-1-(*p*-fluorophenyl)-1-phenylmethanamine (3db)**: The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2i** (11.0 µL, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (31.4 mg, 86% yield) as a white solid. **3db** was also synthesized following General Procedure B with ketamine **1d** (57.9 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2b** (10.7 µL, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (30.3 mg, 83% yield) as a white solid. One pot synthesis of **3db** was also performed following General Procedure E with benzaldehyde (21.2 mg, 0.20 mmol) and diphenylmethanamine (36.6 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol)，aryl bromide **2i** (11.0 µL, 0.1 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (30.0 mg, 82% yield) as a white solid. m.p. = 92−96 °C, R_f = 0.70 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75–7.74 (m, 2H), 7.44–7.43 (m, 3H), 7.39–7.32 (m, 3H), 7.29–7.26 (m, 6H), 7.21–7.18 (m, 1H), 7.07–7.05 (m, 2H), 6.97–6.94 (m, 2H), 5.53 (s, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 167.3, 161.8 (d, $^{1}J_{C\text{-}F}$= 243.3 Hz), 144.9, 140.8 (d, $^{4}J_{C\text{-}F}$= 3.1 Hz), 139.9, 136.8, 130.3, 129.2 (d, $^{3}J_{C\text{-}F}$= 7.9 Hz), 128.9, 128.8, 128.7, 128.6, 128.2, 127.8, 127.6, 127.0, 115.3 (d, $^{2}J_{C\text{-}F}$= 21.2 Hz), 69.3 ppm; IR (thin film): 3059, 1623, 1601, 1577, 1491, 1446, 1314, 1222, 1027, 779, 725, 696 cm^{-1}; HRMS calc'd for $C_{26}H_{21}FN^{+}$ 366.1655, observed 366.1656 $[M+H]^{+}$.

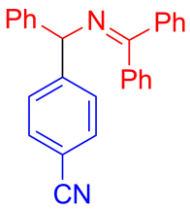


***N*-(Diphenylmethylene)-1-phenyl-1-(*p*-(trifluoromethyl)phenyl) methanamine (3aj)** : The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2j** (14.0 µL, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (31.1 mg, 75% yield) as a colorless oil. R_f = 0.77 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76–7.74 (m, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.47–7.43 (m, 5H), 7.38–7.26 (m, 7H), 7.21–7.18 (m, 1H), 7.06–7.04 (m, 2H), 5.59 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.9, 149.0, 144.2, 139.7, 136.7, 130.5, 129.2, 129.0, 128.9, 128.7, 128.3, 128.0, 127.8, 127.7, 127.2, 125.5 (q, $J_{C\text{-}F}$= 3.8 Hz), 123.4 (q, $J_{C\text{-}F}$= 270.4 Hz), 69.7 ppm; IR (thin film): 3060, 1618, 1598, 1577, 1491, 1446, 1325, 1123, 1066, 1018, 779, 726, 697 cm^{-1}; HRMS calc'd for $C_{27}H_{21}F_3N^+$ 415.1626, observed 415.1627 $[M+H]^+$.

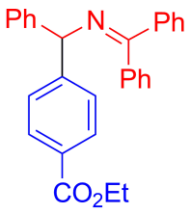


***N*-(Diphenylmethylene)-1-phenyl-1-(pyridin-3-yl)methanamine (3hb)**: The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2k** (9.6 µL, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:10 to diethyl ether:hexanes = 2.5:1) to give the product (21.1 mg, 60% yield) as a white solid. **3hb** was also synthesized following General Procedure B with ketamine **1h** (54.5 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2b** (10.7 µL, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:10 to diethyl ether:hexanes = 2.5:1) to give the product (30.3 mg, 87% yield). Synthesis of **3hb** from aldimine was performed following General Procedure C with aldimine **1h'** (54.5 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol), aryl bromide **2b** (10.7 µL, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:10 to diethyl ether:hexanes = 2.5:1) to give the product (26.8 mg,

77% yield) as a white solid. m.p. = 96−98 °C, R_f = 0.30 (diethyl ether:hexanes = 2.5:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51 (d, *J* = 2.1 Hz, 1H), 8.44 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.75–7.73 (m, 2H), 7.71 (m, 1H), 7.45–7.40 (m, 3H), 7.39–7.36 (m, 1H), 7.34–7.31 (m, 4H), 7.29–7.26 (m, 2H), 7.21–7.17 (m, 2H), 7.06–7.04 (m, 2H), 5.59 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 168.0, 149.2, 148.3, 143.9, 140.4, 139.6, 136.5, 135.3, 130.5, 128.9, 128.8, 128.7, 128.6, 128.2, 127.6, 127.5, 127.2, 123.6, 67.7 ppm; IR (thin film): 3027, 1623, 1597, 1574, 1476, 1440, 1316, 1281, 1049, 782, 704, 695 cm^{-1}; HRMS calc'd for $C_{25}H_{21}N_2^+$ 349.1705, observed 349.1692 $[M+H]^+$.

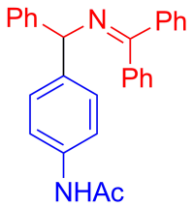


***p*-(((Diphenylmethylene)amino)(phenyl)methyl)benzonitrile (3al)**: The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2l** (18.2 mg, 0.1 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:50 to diethyl ether:hexanes = 1:10) to give the product (23.8 mg, 64% yield) as a colorless oil. R_f = 0.38 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.73 (m, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.46–7.32 (m, 8H), 7.27 (d, *J* = 4.0 Hz, 4H), 7.22–7.18 (m, 1H), 7.03–7.01 (m, 2H), 5.57 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$):168.3, 150.4, 143.7, 139.5, 136.5, 132.4, 130.6, 130.2, 128.9, 128.8, 128.7, 128.3, 128.2, 127.7, 127.6, 127.4, 119.1, 110.6, 69.6 ppm; IR (thin film): 3059, 2228, 1622, 1607, 1577, 1490, 1446, 1315, 1276, 1027, 781, 727, 697 cm^{-1}; HRMS calc'd for $C_{27}H_{21}N_2^+$ 373.1705, observed 373.1702 $[M+H]^+$.

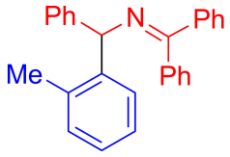


Ethyl *p*-(((Diphenylmethylene)amino)(phenyl)methyl)benzoate (3am): The reaction was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2m** (16.3 μL, 0.1 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:50 to diethyl ether:hexanes = 1:20) to give the product (26.4 mg, 63% yield) as a colorless oil. R_f = 0.45

(diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.76–7.74 (m, 2H), 7.44–7.40 (m, 5H), 7.38–7.30 (m, 5H), 7.28–7.25 (m, 2H), 7.21–7.17 (m, 1H), 7.05–7.04 (m, 2H), 5.59 (s, 1H), 4.3 (q, *J* = 7.0 Hz, 2H), 1.35 (t, *J* = 7.0 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 167.8, 166.7, 150.1, 144.3, 139.8, 136.7, 130.4, 129.8, 129.1, 128.9, 128.8, 128.7, 128.6, 128.2, 127.8, 127.7, 127.6, 127.1, 69.8, 60.9, 14.5 ppm; IR (thin film): 3059, 1716, 1622, 1599, 1576, 1490, 1446, 1314, 1274, 1021, 780, 730, 698 cm^{-1}; HRMS calc'd for $C_{29}H_{26}NO_2^+$ 420.1964, observed 420.1944 $[M+H]^+$.

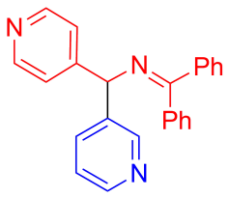


***N*-(*p*-(((Diphenylmethylene)amino)(phenyl)methyl)phenyl)acetamide (3an)**: The reaction was performed following General Procedure C with ketamine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol), aryl bromide **2n** (21.4 mg, 0.1 mmol) at 5 mol % Buchwald's 3rd generation pre-catalyst Pd dimer (3.7 mg, 0.005 mmol) and 10 mol % NiXANTPHOS (5.6 mg, 0.010 mmol) catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:10 to diethyl ether:hexanes = 3:1) to give the product (30.4 mg, 75% yield) as a white solid. R_f = 0.33 (diethyl ether:hexanes = 2.5:1); m.p. = 80−82 °C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (br s, 1H, NH), 7.72 (d, *J* = 8.0 Hz, 2H), 7.41–7.38 (m, 4H), 7.34–7.28 (m, 5H), 7.24–7.21 (m, 4H), 7.17–7.13 (m, 2H), 7.04–7.03 (m, 2H), 5.52 (s, 1H), 2.02 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 169.0, 167.1, 144.8, 140.8, 139.8, 136.7, 136.6, 130.2, 128.9, 128.8, 128.6, 128.5, 128.4, 128.1, 127.7, 127.5, 126.8, 120.2, 69.4, 24.3 ppm; IR (thin film): 3300, 3059, 1665, 1601, 1577, 1491, 1446, 1371, 1276, 1028, 780, 718, 698 cm^{-1}; HRMS calc'd for $C_{28}H_{25}N_2O^+$ 405.1967, observed 405.1980 $[M+H]^+$.



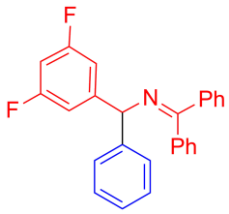
***N*-(diphenylmethylene)-1-phenyl-1-(*o*-tolyl)methanamine (3ao)**: An oven-dried microwave vial equipped with a stir bar was charged with aldimine ketamine **1a** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol) and Buchwald's 3rd generation pre-catalyst (9.3 mg, 0.010 mmol) under a nitrogen

atmosphere. The vial was sealed, and 1 mL dry CPME was taken up by syringe and added to the reaction vial. aryl bromide **2o** (12.0 μL, 0.10 mmol)) was added dropwise by syringe to this solution through the rubber septum. The reaction mixture was stirred for 8 h at 60 °C, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate, and the combined solutions were concentrated in vacuo. The crude material was loaded onto a deactivated silica gel column via pipette and purified by flash chromatography (eluted with diethyl ether:hexanes = 1:100 to diethyl ether:hexanes = 1:50) to give the product (20.3 mg, 56% yield) as a colorless thick oil. R_f = 0.71 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.69 (d, *J* = 7.5 Hz, 1H), 7.41–7.39 (m, 3H), 7.35–7.29 (m, 3H), 7.24–7.14 (m, 6H), 7.11 (td, *J* = 7.0 Hz, 1.5 Hz 1H), 7.05–7.03 (m, 3H), 5.74 (s, 1H), 1.95 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.0, 144.3, 142.9, 140.0, 137.3, 135.6, 130.6, 130.2, 128.9, 128.8, 128.7, 128.6, 128.4, 128.2, 127.9, 127.8, 126.8, 126.7, 126.3, 66.9, 19.7 ppm; IR (thin film): 3059, 3024, 1621, 1577, 1490, 1446, 1380, 1290, 1028, 778, 697 cm^{-1}; HRMS calc'd for $C_{27}H_{24}N^+$ 362.1909, observed 362.1912 $[MH]^+$.

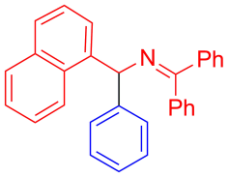


***N*-(Diphenylmethylene)-1-(pyridin-3-yl)-1-(pyridin-4-yl)methanamine (3ik)**: An oven-dried microwave vial equipped with a stir bar was charged with aldimine ketamine **1i** (54.4 mg, 0.20 mmol) and Buchwald's 3rd generation pre-catalyst (9.3 mg, 0.010 mmol) under a nitrogen atmosphere. The vial was sealed, and 0.5 mL dry CPME was taken up by syringe and added to the reaction vial. aryl bromide **2k** (10.7 μL, 0.1 mmol) was added dropwise by syringe to this solution through the rubber septum. A solution of $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol) in 0.5 mL CPME was added portionwise by syringe at 0.1 mL/30 min at 60 °C. The reaction mixture was stirred for 4 h at 60 °C, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate, and the combined solutions were concentrated in vacuo. The crude material was loaded onto a

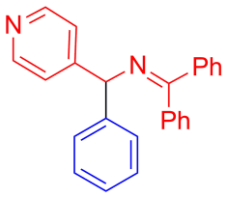
deactivated silica gel column via pipette and purified by flash chromatography (eluted with Ethyl Acetate:Hexane = 1:5 to Ethyl Acetate:Methanol = 120:1) to give the product (31.4 mg, 90% yield) as a colorless thick oil. R_f = 0.31 (Ethyl Acetate:Methanol = 100:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (dd, *J* = 4.5 Hz, 2.0 Hz, 2H), 8.49 (dd, *J* = 4.5, 1.5 Hz, 1H), 8.47 (d, *J* = 2.0 Hz, 1H), 7.75–7.73 (m, 2H), 7.70–7.67 (m, 1H), 7.49–7.44 (m, 3H), 7.42–7.41 (m, 1H), 7.38–7.35 (m, 2H), 7.27–7.22 (m, 3H), 7.03 (dd, *J* = 7.0 Hz, 2.0 Hz, 2H), 5.54 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 169.5, 152.6, 150.2, 149.2, 149.0, 139.2, 139.0, 136.3, 135.5, 130.9, 129.2, 128.9, 128.9, 128.4, 127.5, 123.9, 122.5, 66.8 ppm; IR (thin film): 3027, 1622, 1595, 1575, 1445, 1317, 1282, 1024, 783, 704, 697 cm^{-1}; HRMS calc'd for $C_{24}H_{20}N_3^+$ 350.1657, observed 350.1650 $[MH]^+$.



1-(3,5-Difluorophenyl)-*N*-(diphenylmethylene)-1-phenylmethanamine (3fb) : The reaction was performed following General Procedure B with ketamine **1f** (61.5 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 2.5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (34.9 mg, 91% yield) as a white solid. m.p. = 106−108 °C, R_f = 0.80 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75–7.73 (m, 2H), 7.45–7.41 (m, 3H), 7.39–7.32 (m, 3H), 7.28–7.25 (m, 4H), 7.23–7.19 (m, 1H), 7.05–7.03 (m, 2H), 6.91–6.87 (m, 2H), 6.61 (m, 1H), 5.48 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 168.1, 164.2 (d, $^1J_{C\text{-}F}$ = 247 Hz), 162.2 (d, $^1J_{C\text{-}F}$ = 247 Hz), 149.1 (t, $^3J_{C\text{-}F}$ = 8.5 Hz), 143.8, 139.6, 136.5, 130.6, 129.0, 128.9, 128.8(d, $^4J_{C\text{-}F}$ = 3.3 Hz), 128.3, 127.8, 127.7, 127.4, 110.5 (dd, $^2J_{C\text{-}F}$ = 20 Hz, $^3J_{C\text{-}F}$ = 5.9 Hz), 102.2 (t, $^2J_{C\text{-}F}$ = 25 Hz), 69.3 ppm; IR (thin film): 3435, 1622, 1597, 1491, 1446, 1313, 1290, 1115, 976, 780, 696 cm^{-1}; HRMS calc'd for $C_{26}H_{20}F_2N^+$ 384.1564, observed 384.1564 $[M+H]^+$.

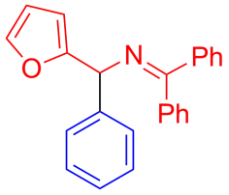


***N*-(diphenylmethylene)-1-(naphthalen-1-yl)-1-phenylmethanamine (3gb)**: The reaction was performed following General Procedure B with ketamine **1g** (64.3 mg, 0.20 mmol), LiO-*t*-Bu (24.0 mg, 0.30 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (28.3 mg, 71% yield) as a thick oil. We observed that grease co-elute with the product as only impurity shown in NMR spectra. Due to this reason, we hydrolyzed the product following the General Procedure of imine product hydrolysis to its ammonium salt **7h** depicted below. Overall yield of arylation/hydrolysis was 68%. R_f = 0.71 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.75–7.73 (m, 4H), 7.46–7.35 (m, 6H), 7.33–7.28 (m, 5H), 7.22–7.20 (m, 2H), 7.16–7.13 (m, 1H), 7.06 (d, *J* = 7.0 Hz, 2H), 6.26 (s, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 167.2, 144.6, 140.2, 140.0, 137.8, 136.8, 134.3, 132.6, 131.2, 130.3, 130.2, 129.0, 128.8, 128.7, 128.6, 128.4, 128.2, 128.0, 127.8, 127.6, 126.7, 126.5, 125.8, 125.7, 125.4, 125.0, 67.2 ppm; IR (thin film): 3057, 1618, 1596, 1576, 1491, 1393, 1315, 1283, 1028, 798, 718, 696 cm^{-1}; HRMS calc'd for $C_{30}H_{24}N^+$ 398.1909, observed 398.1905 $[M+H]^+$.

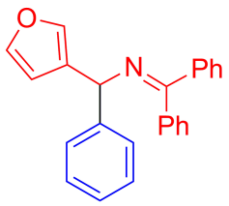


***N*-(Diphenylmethylene)-1-phenyl-1-(pyridin-4-yl)methanamine (3ib)**: The reaction was performed following General Procedure B with ketamine **1i** (54.4 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (33.5 mg, 0.20 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:10 to diethyl ether:hexanes = 2:1) to give the product (31.4 mg, 90% yield) as a white solid. **3ia** was also synthesized following General Procedure C with aldimine **1i'** (54.4 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:10 to diethyl ether:hexanes = 2:1) to give the product (31.7 mg, 91% yield) as a white solid. m.p. = 118−120 °C, R_f = 0.33 (diethyl ether:hexanes = 2:1); ^{1}H NMR

(500 MHz, $CDCl_3$): δ 8.53 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.80–7.78 (m, 2H), 7.50–7.43 (m, 4H), 7.40–7.37 (m, 2H), 7.33–7.30 (m, 6H), 7.27–7.24 (m, 1H), 7.09–7.07 (m, 2H), 5.54 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 168.3, 153.4, 149.8, 143.3, 139.4, 136.3, 130.4, 128.8, 128.7, 128.6, 128.5, 128.1, 127.6, 127.5, 127.3, 122.5, 68.9 ppm; IR (thin film): 3026, 1623, 1593, 1560, 1490, 1446, 1316, 1280, 1027, 780, 727, 697 cm^{-1}; HRMS calc'd for $C_{25}H_{21}N_2^+$ 349.1705, observed 349.1694 $[MH]^+$.



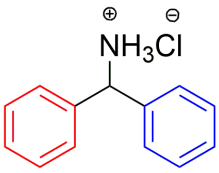
***N*-(Diphenylmethylene)-1-(furan-2-yl)-1-phenylmethanamine (3jb)**: The reaction was performed following General Procedure B with ketamine **1j** (52.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (36.7 mg, 0.20 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (20.3 mg, 60% yield) as a white solid. m.p. = 90−92 °C, R_f = 0.70 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.44–7.43 (m, 3H), 7.38–7.36 (m, 3H), 7.33–7.29 (m, 5H), 7.25–7.23 (m, 1H), 7.16–7.15 (m, 2H), 6.28–6.27 (m, 1H), 6.09 (dd, *J* = 3.0, 0.5 Hz, 1H), 5.62 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 168.7, 156.8, 142.0, 141.9, 139.9, 136.6, 130.4, 129.0, 128.8, 128.6, 128.5, 128.2, 128.0, 127.9, 127.4, 110.2, 106.6, 64.7 ppm; IR (thin film): 3059, 1622, 1597, 1576, 1490, 1446, 1316, 1286, 1009, 779, 718, 696 cm^{-1}; HRMS calc'd for $C_{24}H_{20}NO^+$ 338.1545, observed 338.1550 $[M+H]^+$.



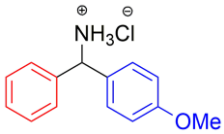
***N*-(Diphenylmethylene)-1-(furan-3-yl)-1-phenylmethanamine (3lb)**: The reaction was performed following General Procedure C with aldimine **1l'** (52.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.0 mg, 0.30 mmol), aryl bromide **2b** (10.7 μL, 0.1 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (28.7 mg, 85% yield) as a white solid. m.p. = 64−66 °C,

R_f = 0.70 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72–7.70 (m, 2H), 7.41–7.40 (m, 3H), 7.34–7.26 (m, 9H), 7.19 (t, *J* = 7.0 Hz, 1H), 7.11–7.09 (m, 2H), 6.25 (s, 1H), 5.49 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.4, 143.9, 143.1, 139.9, 139.4, 136.7, 130.3, 129.3, 128.9, 128.7, 128.6, 128.5, 128.2, 127.8, 127.6, 127.1, 109.9, 62.8 ppm; IR (thin film): 3059, 1622, 1597, 1576, 1490, 1446, 1315, 1285, 1018, 781, 716, 696 cm^{-1}; HRMS calc'd for $C_{24}H_{20}NO^+$ 338.1542, observed 338.1547 $[M+H]^+$.

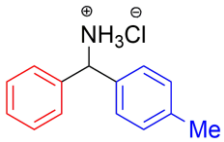
General Procedure F: Imine Product Hydrolysis. HCl 1N (1 mL) was added to the solution of imine **3ab** (40.4 mg 0.1 mmol) in THF (1 mL) at 0°C. The solution was warmed to room temperature, stirred at room temperature and monitored by TLC until all the imine was consumed. The THF was evaporated under vacuum. Another 1 mL HCl (1N) was added and a white precipitate was observed. The white solid was filtered and washed with cold Et_2O (1.0 mL×3). After drying under vacuum for 12 h, the hydrochloride salt was obtained as a white solid (25.4 mg, 92% yield).



Diphenylmethanaminium chloride salt (7a) : The reaction was performed following General Procedure F with imine **3ab** (38.2 mg, 0.10 mmol) gave its ammonium salt **7a** as white solid in 93% yield (20.4 mg). The NMR spectral data match the previously published data.[24]

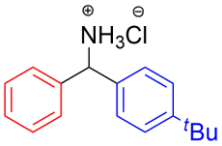


(*p*-Methoxyphenyl)(phenyl)methanaminium chloride salt (7b) : The reaction was performed following General Procedure E with imine **3cb** (37.7 mg, 0.10 mmol) gave its ammonium salt **7b** as white solid in 92% yield (22.9 mg). The NMR spectral data match the previously published data.[24]

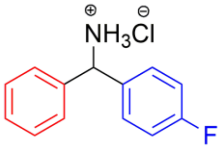


Phenyl(p-tolyl)methanaminium chloride salt (7c) : The reaction was performed following General Procedure F with imine **3ad** (36.1 mg, 0.10 mmol) gave its ammonium salt **7c** as white solid in 96% yield (22.4 mg). The

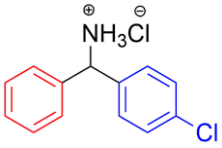
NMR spectral data match the previously published data.[24]



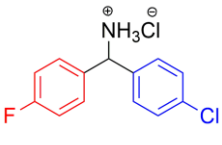
(4-(*tert*-Butyl)phenyl)(phenyl)methanamine ammounium salt (7d): The reaction was performed following General Procedure F with imine **3ac** (40.3 mg, 0.10 mmol) gave its ammonium salt **7d** as white solid in 92% yield (25.4 mg), m.p. = 272−274 ^{o}C; ^{1}H NMR (500 MHz, MeOD) δ 7.51–7.49 (m, 2H), 7.47–7.44 (m, 2H), 7.42–7.39 (m, 3H), 7.35–7.33 (m, 2H), 5.61 (s, 1H), 1.31 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, MeOD): 153.5, 138.8, 135.7, 130.4, 130.1, 128.4, 128.2, 127.3, 59.2, 35.6, 31.7 ppm; IR (thin film): 3010, 2955, 1590, 1508, 1456, 1417, 1358, 1264, 1195, 1107, 1018, 784, 738, 698 cm^{-1}; HRMS calc'd for $C_{17}H_{19}^{+}$ 223.1487, observed 223.1480 [M-(NH_2Cl)]$^{+}$.



(4-Fluorophenyl)(phenyl)methanaminium chloride salt (7e): The reaction was performed following General Procedure F with imine **3db** (36.5 mg, 0.10 mmol) gave its ammonium salt **7e** as white solid in 96% yield (22.8 mg). The NMR spectral data match the previously published data.[24]

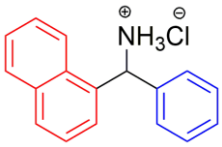


(4-Chlorophenyl)(phenyl)methanaminium chloride salt (7f) : The reaction was performed following General Procedure F with imine **3eb** (38.2 mg, 0.10 mmol) gave its ammonium salt **7f** as white solid in 93% yield (23.6 mg). The NMR spectral data match the previously published data.[24]



(4-Chlorophenyl)(4-fluorophenyl)methanaminium chloride salt (7g) : Arylation of **1d** and **2g** was conducted following General Procedure B on a 0.1 mmol scale using 1 equiv of **1d**, 2 equiv of $NaN(SiMe_3)_2$, and 2 equiv of **2g**. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:100 to diethyl ether:hexanes = 1:50) to give the product (32.4 mg, 81% yield). Imine product was then hydrolyzed following General Procedure F gave its ammonium salt **14** as white solid in 79% overall yield (21.5 mg). m.p. = 268−270 ^{o}C; ^{1}H NMR (500 MHz, MeOD) δ

7.51–7.46 (m, 6H), 7.19 (t, J = 8.0 Hz, 2H), 5.73 (s, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, MeOD): 164.3 (d, $^{1}J_{CF}$ = 246.3 Hz), 137.1, 135.9, 134.2 (d, $^{4}J_{CF}$ = 3.3 Hz), 130.8 (d, $^{3}J_{CF}$ = 8.5 Hz), 130.4, 130.1, 117.1 (d, $^{2}J_{CF}$ = 22.0 Hz), 58.0 ppm; IR (thin film): 2928, 1598, 1515, 1238, 1015, 829 cm^{-1}; HRMS calc'd for $C_{13}H_9ClF^{+}$ 219.0377, observed 219.0381 $[M-(NH_2)]^{+}$.



Naphthalen-1-yl(phenyl)methanaminium chloride salt (7h) : As described in Section 2.6. Table 3, entry2. Imine **3gb** was hydrolyzed directly after purification. The reaction was performed following General Procedure F with imine **3ca** (28.3 mg, 0.071 mmol) gave its ammonium salt **7h** as white solid in 95% yield, Overal 68% yield (18.1 mg). The NMR spectral data match the previously published data.[24]

Representative Microscale High-Throughput Experimentation for Ligand Identification

General Experimental:

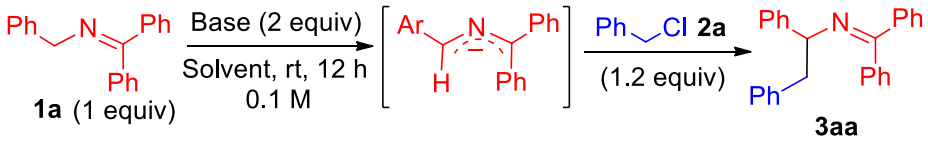
Set up:

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials was predosed with $Pd(OAc)_2$ (1 µmol) and the phosphine ligands (2 µmol for monodentate ligands and 1 µmol for bidentate ligands) in THF. The solvent was removed to dryness using a GeneVac and $NaN(SiMe_3)_2$ (30 µmol) in THF was added to the ligand/catalyst mixture. The solvent was removed on the GeneVac and a parylene stir bar was then added to each reaction vial. Imine **1a** (10 µmol/reaction), bromobenzene (12 µmol) and 4,4′-di-*tert*-butylbiphenyl (1 µmol/reaction) (used as an internal standard to measure HPLC yields) were then dosed together into each reaction vial as a solution in THF (100 µL, 0.1 M). The 24-well plate was then sealed and stirred for 18 h at room temperature.

Work up:

Upon opening the plate to air, 500 µL of acetonitrile was added into each vial. The plate was covered again and the vials stirred for 10 min. to ensure good homogenization. Into a separate 24-well LC block was added 700 µL of acetonitrile, followed by 40 µL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated HPLC instrument for analysis.

(1) Base and Solvent Screening for Deprotonation/Benzylation Studies:



- Solvent: THF, CPME
- Base: $LiN(SiMe_3)_2$, $NaN(SiMe_3)_2$, $KN(SiMe_3)_2$, LiO*t*Bu, NaO*t*Bu, KO*t*Bu, NaH, LiOAc, KOAc, K_3PO_4, Cs_2CO_3, and KOPh

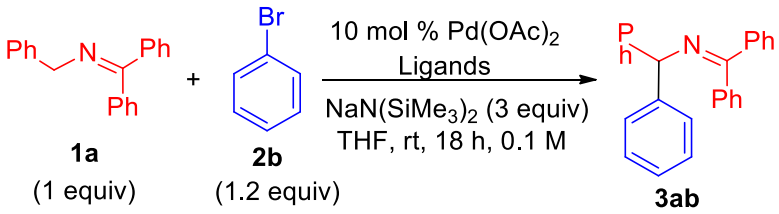
Lead result $NaN(SiMe_3)_2$/ THF 95% assay yield

Well	Base	Solvent	Prod/IS[a]
A01	LiO*t*Bu	CPME	0.00
B01		THF	0.16
A02	KO*t*Bu	CPME	5.22
B02		THF	5.79
A03	NaO*t*Bu	CPME	0.00
B03		THF	1.99
A04	$LiN(SiMe_3)_2$	CPME	0.16
B04		THF	3.59
A05	$NaN(SiMe_3)_2$	CPME	3.09
B05		THF	7.46
A06	$KN(SiMe_3)_2$	CPME	6.02
B06		THF	6.83

C01	NaH	CPME	0.10
D01		THF	0.89
C02	KOAc	CPME	0.00
D02		THF	0.00
C03	LiOAc	CPME	0.00
D03		THF	0.00
C04	K_3PO_4	CPME	0.00
D04		THF	0.00
C05	Cs_2CO_3	CPME	0.00
D05		THF	0.08
C06	KOPh	CPME	0.00
D06		THF	0.00

[a]Product/Internal standard ratio. The lead hit from the screening was **$NaN(SiMe_3)_2$** in **THF** (highest product/internal standard ratio). A scale-up reaction on a 0.1 mmol scale proved successful with isolation of the benzylation product in 95% yield.

(2) Ligand Screening:



$Pd(OAc)_2$ (10 mol %) was used to test 23 sterically and electronically diverse, mono- and bidentate phosphine ligands (ligands 1-23 from the Table below).

	Ligand libraries
1	2-(Di-*t*-butylphosphino)biphenyl (JohnPhos)
2	2-(Di-t-butylphosphino)-3-methoxy-6-methyl-2',4',6'-tri-i-propyl-1,1'-biphenyl (RockPhos)
3	1,1'-Bis(di-*t*-butylphosphino)ferrocene (dtbpf)
4	2-Dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (SPhos)
5	Tri-*o*-tolylphosphine
6	2-(Di-1-adamantylphosphino)-*N*,*N*-dimethylaniline (Me-DalPhos)
7	1,1'-Bis(diisopropylphosphino)ferrocene (dippf)
8	5-(Di-*t*-butylphosphino)-1', 3', 5'-triphenyl-1'H-[1,4']bipyrazole (BippyPhos)
9	9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (XantPhos)
10	2-(Dicyclohexylphosphino)biphenyl (Cy-JohnPhos)
11	*N*-phenyl-2-(di-*t*-butylphosphino)pyrrole (cataCXium PtB)
12	*N*-phenyl-2-(dicyclohexylphosphino)pyrrole (cataCXium PCy)
13	racemic-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl (BINAP)
14	2-Dicyclohexylphosphino-2'-(*N*,*N*-dimethylamino)biphenyl (DavePhos)
15	Butyldi-1-adamantylphosphine (cataCXium A)
16	Tricyclohexylphosphonium tetrafluoroborate
17	Tri-*t*-butylphosphonium tetrafluoroborate
18	1,2,3,4,5-Pentaphenyl-1'-(di-*t*-butylphosphino)ferrocene (QPhos)
19	2-Di-*tert*-butylphosphino-2',4',6'-triisopropylbiphenyl (*t*Bu-XPhos)
20	Dicyclohexyl-[3,6-dimethoxy-2-(2,4,6-triisopropylphenyl)phenyl]phosphane (BrettPhos)
21	1-[2-[Bis(*t*-butyl)phosphino]phenyl]-3,5-diphenyl-1H-pyrazole (TrippyPhos)
22	1,1'-Bis(diphenylphosphino)ferrocene (dppf)
23	4,6-Bis(diphenylphosphino)phenoxazine (NiXantPhos)

Well	Ligand	Prod/IS
A01	-	0.12
B01	JohnPhos	0.06
C01	RockPhos	0.07
D01	dtbpf	0.26
A02	SPhos	0.88
B02	*o*-Tolphosphine	0.37
C02	Me-DalPhos	0.12
D02	dippf	1.10
A03	BippyPhos	0.11
B03	XantPhos	0.77
C03	CyJohnPhos	0.54
D03	CataCXium PtB	0.10
A04	BINAP	0.14
B04	DavePhos	0.30
C04	CataCXium A	2.96
D04	CataCXium PCy	0.49
A05	PCy_3HBF_4	1.22
B05	*t*-Bu_3PHBF_4	0.60
C05	QPhos	0.20
D05	*t*-BuXPhos	0.07
A06	BrettPhos	0.14
B06	TrippyPhos	0.18
C06	dppf	0.47
D06	NIXANTPHOS	3.65

The lead hit from the screening was the combination of $Pd(OAc)_2$ (10 mol %) and **NIXANTPHOS** (10 mol %) (well D06). A scale-up reaction on a 0.1 mmol scale using the same procedure as HTE proved successful with product in 67% assay yield.

1.4.2 Experimental Section For Arylation of 1,1,3-Triaryl-2-Azaallyl Anions With Aryl Chlorides.

Preparation of μ-OMs dimer 5 and NIXANTPHOS precatalyst 6: μ-OMs dimer **5** and NIXANTPHOS precatalyst **6** was prepared according to literature procedure.[18]

Procedure and Characterization for the Pd Catalyzed Arylation of 1,1,3-Triaryl-2-Azaallyl Anions With Aryl Chlorides.

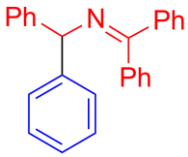
General Procedure A: An oven-dried microwave vial equipped with a stir bar was charged with ketimine **1a** (54.3 mg, 0.20 mmol) under a nitrogen atmosphere in a glove box. A stock solution (prepared in the glove box) of μ-OMs dimer **5** (1.8 mg, 0.0025 mmol) and NIXANTPHOS (2.8 mg, 0.0050 mmol) in 0.5 mL anhydrous THF was added to the reaction vial via syringe. The vial was sealed with cap (with rubber septum) and removed from the glove box. 1-*tert*-Butyl-4-chlorobenzene **2c'** (16.7 *μ*L, 0.10 mmol)) was added dropwise by syringe to this solution through the rubber septum. While the reaction mixture was stirred at 60 $^{\circ}$C in an oil bath, a solution of $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol) in 0.5 mL anhydrous THF was added portionwise by syringe (0.05 mL every 30 min) through the rubber septum. The reaction mixture was stirred for 6 h in total, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate, and the combined solutions were concentrated in *vacuo*. The crude material was loaded onto a silica gel column via pipette and purified by flash chromatography (hexanes to diethyl ether: hexanes = 1:50) to give the product (34.7 mg, 86% yield) as a white solid.

General Procedure B: An oven-dried microwave vial equipped with a stir bar was charged with ketimine **1a** (54.3 mg, 0.20 mmol) and NIXANTPHOS precatalyst **6** (9.3 mg, 0.010 mmol) under a nitrogen atmosphere in a glove box. Anhydrous THF (0.5 mL) was added to the reaction vial via syringe. The vial was sealed with cap (with rubber septum) and removed from the glove box. 1-*tert*-Butyl-4-chlorobenzene **2c'** (16.7 μL, 0.10 mmol) was added dropwise by syringe to this solution through the rubber septum. While the reaction mixture was stirred at 23 °C, a solution of $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol) in 0.5 mL anhydrous THF was added portionwise by syringe (0.1 mL every 30 min) through the rubber septum. The reaction mixture was stirred for 14 h in total, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate, and the combined solutions were concentrated in *vacuo*. The crude material was loaded onto a silica gel column via pipette and purified by flash chromatography (hexanes to diethyl ether: hexanes = 1:50) to give the product (32.6 mg, 81% yield) as a white solid.

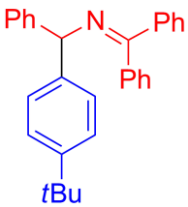
General Procedure C: Sequential One-Pot Ketimine Synthesis/Arylation

An oven-dried 50 mL Schlenk tube equipped with a stir bar was sealed with a rubber septum and was connected to a Schlenk line, evacuated, and refilled with nitrogen (repeated three times). Anhydrous THF (10 mL) was added under nitrogen via syringe through the rubber septum. 4-(Aminomethyl)pyridine (0.65 g, 6.0 mmol) and benzophenone imine (1.09 g, 6.0 mmol) were added under nitrogen via syringe through the rubber septum. The reaction was placed in an oil bath at 50 °C. After stirring for 12 h at 50 °C, the solvent was completely removed in *vacuo* and the tube was filled with nitrogen. A stock solution (prepared in the glove box) of μ-OMs dimer **5** (27 mg, 0.0375 mmol) and NIXANTPHOS (42 mg, 0.0750 mmol) under nitrogen in 10 mL anhydrous THF was taken up by syringe and added to the Schlenk tube through the rubber septum. A stock solution (prepared in the glove box) of 6-chloroquinoline (0.49 g, 3 mmol) in 5 mL anhydrous THF was added to the Schlenk tube via syringe through the rubber septum. While the

reaction mixture was stirred at 60 °C in an oil bath, a solution of $LiN(SiMe_3)_2$ (1.51 g, 9 mmol) in 15 mL anhydrous THF was added portionwise by syringe (3 mL every 30 min) through the rubber septum. The reaction mixture was stirred for 6 h in total, opened to air, and quenched with 10 mL of H_2O. The layers were separated and the aqueous layer was extracted with DCM (3X5 mL). The combined organic layers were concentrated in *vacuo*. The crude material was loaded onto a deactivated silica gel column via pipette and purified by flash chromatography (eluted with ethyl acetate: hexanes = 1:5 to ethyl acetate: methanol = 120:1) to give the product **3it** (1.02 g, 85% yield) as thick colorless oil.

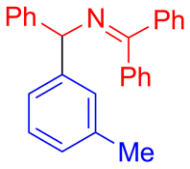


***N*-(Diphenylmethylene)-1,1-diphenylmethanamine (3ab)**: The reaction was performed following General Procedure A with ketamine **1a** (54.3 mg, 0.20 mmol) or aldimine **1a'** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2b'** (10.2 μL, 0.10 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3ab** (31.3 mg, 90% yield, arylation of **1a**) or (33.0 mg, 95% yield, arylation of **1a'**) as a white solid. Room temperature synthesis of **3ab** was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol) or aldimine **1a'** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2b'** (10.2 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3ab** (28.8 mg, 83% yield, arylation of **1a**) or (29.2 mg, 84% yield, arylation of **1a'**) as a white solid. R_f = 0.70 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data in 1.4.1.

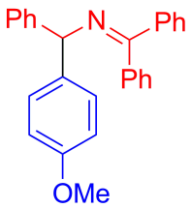


1-(4-(*tert*-Butyl)phenyl)-*N*-(diphenylmethylene)-1-phenylmethanamine (3ac): The reaction was performed following General Procedure A with ketamine **1a** (54.3 mg, 0.20 mmol) or aldimine **1a'** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2c'** (16.7 μL, 0.10 mmol) at 5

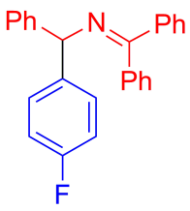
mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3ac** (34.7 mg, 86% yield, arylation of **1a**) or (36.7 mg, 91% yield, arylation of **1a'**) as a white solid. Room temperature synthesis of **3ac** was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol) or aldimine **1a'** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2c'** (16.7 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3ac** (32.6 mg, 81% yield, arylation of **1a**) or (34.3 mg, 85% yield, arylation of **1a'**) as a white solid. R_f = 0.75 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data in 1.4.1.



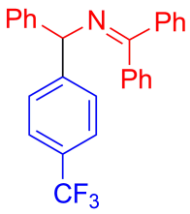
***N*-(Diphenylmethylene)-1-phenyl-1-(*m*-tolyl)methanamine (3ae)**: The reaction was performed following General Procedure A with ketamine **1a** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2e'** (11.8 μL, 0.10 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3ae** (27.8 mg, 77% yield) as a white solid. R_f = 0.75 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data in 1.4.1.



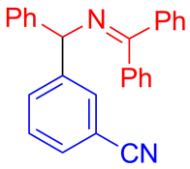
***N*-(Diphenylmethylene)-1-(*p*-methoxyphenyl)-1-phenylmethanamine (3cb)**: The reaction was performed following General Procedure A with ketamine **1a** (54.3 mg, 0.2 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2g'** (12.3 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product **3cb** (22.6 mg, 60% yield) as a thick oil. R_f = 0.55 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data in 1.4.1.



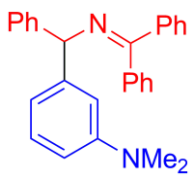
***N*-(diphenylmethylene)-1-(*p*-fluorophenyl)-1-phenylmethanamine (3db)**: The reaction was performed following General Procedure A with ketamine **1a** (54.3 mg, 0.20 mmol) or aldimine **1a'** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2i'** (10.7 μL, 0.10 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3db** (28.1 mg, 77% yield, arylation of **1a**) or (30.7 mg, 84% yield, arylation of **1a'**) as a white solid. Room temperature synthesis of **3db** was performed following General Procedure B with ketamine **1a**, $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2i'** (10.7 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3db** (25.9 mg, 71% yield) as a white solid. R_f = 0.70 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data in 1.4.1.



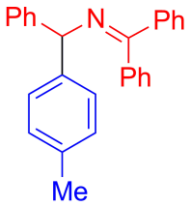
***N*-(Diphenylmethylene)-1-phenyl-1-(*p*-(trifluoromethyl)phenyl) methanamine (3aj)** : The reaction was performed following General Procedure A with ketamine **1a** (54.3 mg, 0.20 mmol) or aldimine **1a'** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2j'** (14.0 μL, 0.10 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3aj** (36.1 mg, 87% yield, arylation of **1a**) or (35.2 mg, 85% yield, arylation of **1a'**) as a colorless oil. Room temperature synthesis of **3aj** was performed following General Procedure B with ketamine **1a** (54.3 mg, 0.20 mmol) or aldimine **1a'** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2j'** (14.0 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3aj** (35.2 mg, 85% yield, arylation of **1a**) or (36.9 mg, 89% yield, arylation of **1a'**) as a colorless oil. R_f = 0.77 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data in 1.4.1.



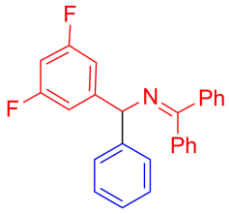
3-(((Diphenylmethylene)amino)(phenyl)methyl)benzonitrile (3ap): The reaction was performed following General Procedure A with ketamine **1a** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2p'** (13.8 mg, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:5) to give the product **3ap** (33.9 mg, 91% yield) as colorless oil. R_f = 0.39 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75–7.73 (m, 2H), 7.67 (s, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.48–7.39 (m, 5H), 7.35 (t, *J* = 8.0 Hz, 3H), 7.29–7.27 (m, 4H), 7.23–7.10 (m, 1H), 7.03 (dd, *J* = 7.0, 1.5 Hz, 2H), 5.55 (s, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 168.3, 146.6, 143.9, 139.5, 136.5, 132.2, 131.4, 130.7, 130.6, 129.3, 128.9, 128.8, 128.7, 128.3, 127.7, 127.6, 127.4, 119.3, 112.5, 69.3 ppm; IR (thin film): 3060, 2229, 1623, 1597, 1578, 1490, 1446, 1315, 1289, 1028, 781, 697 cm^{-1}; HRMS calc'd for $C_{27}H_{21}N_2^+$ 373.1705, observed 373.1701 $[M+H]^+$.



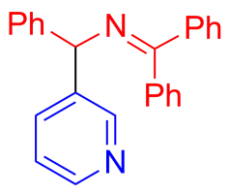
3-(((Diphenylmethylene)amino)(phenyl)methyl)-*N*,*N*-dimethylaniline (3aq): The reaction was performed following General Procedure A with ketamine **1a** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2q'** (14.0 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:10) to give the product **3aq** (23.8 mg, 61% yield) as colorless oil. R_f = 0.42 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ7.75–7.74 (m, 2H), 7.41–7.39 (m, 3H), 7.35–7.30 (m, 5H), 7.25 (t, *J* = 8.0 Hz, 2H), 7.17–7.13 (m, 2H), 7.10–7.08 (m, 2H), 6.73 (d, *J* = 2.0 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.58 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.51 (s, 1H), 2.87 (s, 6H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.8, 150.9, 145.8, 145.3, 140.2, 137.0, 130.1, 129.2, 129.0, 128.6, 128.5, 128.4, 128.2, 128.1, 127.7, 126.7, 116.5, 112.3, 111.3, 70.5, 40.9 ppm; IR (thin film): 3058, 1600, 1577, 1492, 1445, 780, 696 cm^{-1}; HRMS calc'd for $C_{26}H_{26}N_2Na^+$ 391.2150, observed 391.2155 $[M+Na]^+$.



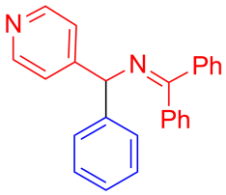
***N*-(Diphenylmethylene)-1-phenyl-1-(*p*-tolyl)methanamine(3bb):** The reaction was performed following General Procedure A with ketamine **1a** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2d'** (11.8 μL, 0.10 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3bb** (31.1 mg, 86% yield) as a white solid. Compound **3bb** was also synthesized following General Procedure A with ketamine **1b** (57.1 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2b'** (10.2 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3bb** (31.1 mg, 86% yield) as a white solid. R_f = 0.77 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data in 1.4.1.



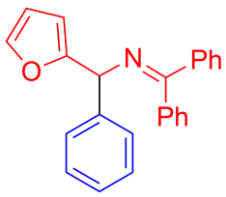
1-(3,5-Difluorophenyl)-*N*-(diphenylmethylene)-1-phenylmethanamine (3fb) : The reaction was performed following General Procedure A with aldimine **1a'** (54.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2r'** (11.2 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3fb** (31.1 mg, 81% yield) as a white solid. Compound **3aj** was also synthesized following General Procedure A with ketamine **1f** (61.4 mg, 0.2 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2b'** (10.2 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **3fb** (33.7 mg, 88% yield) as a white solid. R_f = 0.80 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data in 1.4.1.



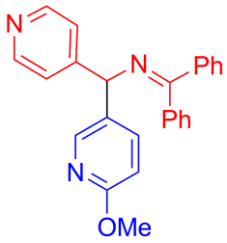
***N*-(Diphenylmethylene)-1-phenyl-1-(pyridin-3-yl)methanamine (3hb)**: The reaction was performed following General Procedure A with ketamine **1h** (54.5 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2b'** (10.2 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:10 to diethyl ether:hexanes = 2.5:1) to give the product **3hb** (20.9 mg, 60% yield) as a white solid. R_f = 0.30 (diethyl ether:hexanes = 2.5:1). The NMR spectral data match the previously published data in 1.4.1.



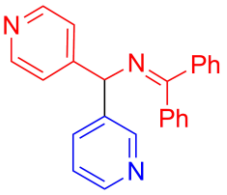
***N*-(Diphenylmethylene)-1-phenyl-1-(pyridin-4-yl)methanamine (3ib)**: The reaction was performed following General Procedure A with ketamine **1i** (54.5 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2b'** (10.2 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with diethyl ether:hexanes = 1:10 to diethyl ether:hexanes = 2:1) to give the product **3ib** (31.7 mg, 91% yield) as a white solid. R_f = 0.33 (diethyl ether:hexanes = 2:1). The NMR spectral data match the previously published data in 1.4.1.



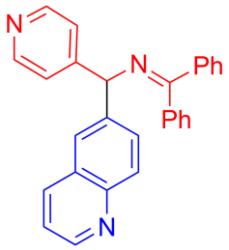
***N*-(Diphenylmethylene)-1-(furan-2-yl)-1-phenylmethanamine (3jb)**: The reaction was performed following General Procedure A with ketamine **1j** (52.3 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2b'** (10.2 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product **3jb** (20.3 mg, 60% yield) as a white solid. R_f = 0.70 (diethyl ether:hexanes = 1:5). The NMR spectral data match the previously published data in 1.4.1.



***N*-(Diphenylmethylene)-1-(6-methoxypyridin-3-yl)-1-(pyridin-4-yl)methanamine (3is)** : The reaction was performed following General Procedure A with ketamine **1i** (54.5 mg, 0.20 mmol) or aldimine **1i'** (54.5 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2s'** (12.0 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with ethyl acetate: hexanes = 1:5 to ethyl acetate: methanol = 120:1) to give the product **3is** (26.5 mg, 70% yield, arylation of **1i**) or (26.9 mg, 71% yield, arylation of **1i'**) as thick colorless oil. R_f = 0.26 (ethyl acetate:methanol = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (dd, *J* = 4.5, 1.5 Hz, 2H), 7.98 (d, *J* = 1.5 Hz, 1H), 7.74–7.72 (m, 2H), 7.56 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.48–7.40 (m, 4H), 7.36 (t, *J* = 7.0 Hz, 3H), 7.26–7.24 (m, 2H), 7.07–7.04 (m, 2H), 6.69 (d, *J* = 8.5 Hz, 1H), 5.47 (s, 1H), 3.91 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 168.9, 163.7, 153.1, 150.1, 145.6, 139.3, 138.6, 136.4, 131.9, 130.8, 129.1, 128.9, 128.4, 127.6, 122.5, 111.4, 66.2, 53.6 ppm; IR (thin film): 3021, 1604, 1571, 1490, 1291, 1026, 783, 696 cm^{-1}; HRMS calc'd for $C_{25}H_{22}N_3O^+$ 380.1763, observed 380.1769 $[M+H]^+$.



***N*-(Diphenylmethylene)-1-(pyridin-3-yl)-1-(pyridin-4-yl)methanamine (3ik)** : The reaction was performed following General Procedure A with ketamine **1i** (54.5 mg, 0.20 mmol) or aldimine **1i'** (54.5 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2k'** (9.6 μL, 0.10 mmol) at 10 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with ethyl acetate: hexanes = 1:5 to ethyl acetate:methanol = 120:1) to give the product **3ik** (27.2 mg, 78% yield, arylation of **1i**) or (28.6 mg, 82% yield, arylation of **1i'**) as thick colorless oil. R_f = 0.31 (ethyl acetate:methanol = 20:1). The NMR spectral data match the previously published data in 1.4.1.



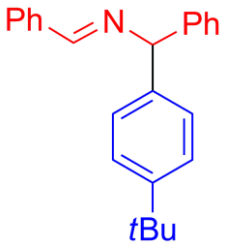
***N*-(Diphenylmethylene)-1-(pyridin-4-yl)-1-(quinolin-6-yl)methanamine (3it)** : The reaction was performed following General Procedure A with ketamine **1i** (54.5 mg, 0.20 mmol) or aldimine **1i'** (54.5 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol), aryl chloride **2t'** (16.4 mg, 0.10 mmol) at 5 mol % catalyst loading. The crude material was purified by flash chromatography on deactivated silica gel (eluted with ethyl acetate: hexanes = 1:5 to ethyl acetate:methanol = 120:1) to give the product **3it** (35.9 mg, 90% yield, arylation of **1i**) or (35.9 mg, 90% yield, arylation of **1i'**) as thick colorless oil. Sequential One-Pot Synthesis of **3it** is described in General Procedure C. R_f = 0.38 (ethyl acetate:methanol = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.88 (dd, *J* = 4.0, 1.5 Hz, 2H), 8.52 (d, *J* = 6.0 Hz, 1H), 8.11 (d, *J* = 7.5 Hz, 1H), 8.04 (d, *J* = 7.5 Hz, 1H), 7.79–7.77 (m, 2H), 7.72 (s, 1H), 7.67 (dd, *J* = 9.0, 1.5 Hz, 1H),7.50–7.42 (m, 4H), 7.39–7.36 (m, 3H), 7.31 (d, *J* = 6.0 Hz, 2H), 7.06–7.05 (m, 2H), 5.70 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 169.0, 152.9, 150. 5, 150.0, 147.7, 141.5, 139.3, 136.3, 136.1, 130.7, 129.9, 129.5, 128.9, 128.8, 128.7, 128.3, 128.2, 127.5, 125.9, 122.6, 121.3, 68.8 ppm; IR (thin film): 3055, 1622, 1595, 1498, 1319, 1281, 697 cm^{-1}; HRMS calc'd for $C_{28}H_{22}N_3^+$ 400.1814, observed 400.1814 $[M+H]^+$.

1.4.3 Experimental Section For Arylation of 1,3-Diaryl-2-Azaallyl Anions.

Synthesis of aldimines Amine (5.0 mmol), aldehyde (5.0 mmol) and $MgSO_4$ (1.4 g) were combined in CH_2Cl_2 (20 mL) at room temperature and the flask capped. The resulting mixture was stirred for 24 h at room temperature. The solution was then filtered through a pad of Celite and the pad was rinsed with additional CH_2Cl_2 (3 X 2 mL). The CH_2Cl_2 solutions was combined and concentrated under reduce pressure to yield an oil. The aldimine was used as an oil without further purification.

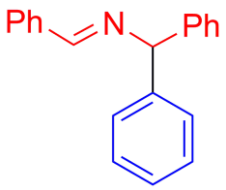
General Procedure and Characterization for Pd Catalyzed reactions of Aldimines

An oven-dried microwave vial equipped with a stir bar was charged with aldimine **8a** (39.0 mg, 0.20 mmol) and 1-bromo-4-*tert*-butylbenzene **2c** (51.9 *μ*L, 0.30 mmol) under a nitrogen atmosphere in a glove box. A stock solution of $Pd(OAc)_2$ (2.25 mg, 0.010 mmol, 5 mol %) and NIXANTPHOS (11.10 mg, 0.020 mmol, 10 mol %) in 0.5 mL of dry THF was taken up by syringe and added to the reaction vial under nitrogen. The vial was sealed with cap (with rubber septum) and removed from the glovebox. A solution of $LiN(SiMe_3)_2$ (50.2 mg, 0.30 mmol) in 1.5 mL THF was added portionwise by syringe at 23 ºC over 1 h. The reaction mixture was stirred for 1 h after the addition (2 h in total) at 23 °C then opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad (a 6mL Syringe) of $MgSO_4$ and silica. The pad was rinsed with ethyl acetate (3 X 2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was loaded onto a deactivated silica gel column and purified by flash chromatography using 20:1 hexanes/ethyl acetate as eluent to yield the product **10ac** (61 mg, 0.19 mmol, 93%) as a white solid.

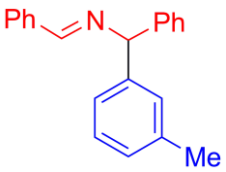


***N*-Benzylidine-1-(4-*tert*-butylphenyl)-1-phenylmethanamine** (**10ac**): The reaction was performed following the General Procedure with **8a** (0.2 mmol, 39 mg), 1-bromo-4-*tert*-butylbenzene (**2c**, 0.3 mmol, 51.9 μL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 1 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10ac** (61 mg, 0.19 mmol, 93%) as a white solid. Mp 108−110 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (s, 1H), 7.85−7.83 (m, 2H), 7.43−7.38 (m, 5H), 7.34−7.32 (m, 6H), 7.24−7.21 (m, 1H), 5.57 (s, 1H), 1.29 (s, 9H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.59, 149.74, 144.06, 140.88, 136.40, 130.68, 128.50, 128.46, 128.39, 127.66, 127.25, 126.90, 125.34, 77.76, 34.43, 31.36 ppm; IR (thin film): 3084, 3060, 3026, 2962, 2867, 1643, 1601, 1581, 1509, 1492, 1451,

1378, 1363, 1269, 1109, 1025, 842, 830, 800 cm^{-1}; HRMS calcd. for $C_{24}H_{26}N$ 328.2065, observed 328.2065 $[M+H]^+$.

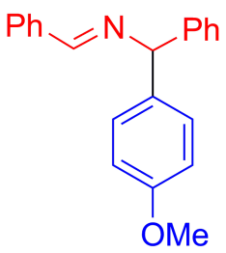


***N*-Benzylidine-1,1-diphenylmethanamine** (**10ab**): The reaction was performed following the General Procedure with **8a** (0.2 mmol, 39 mg), bromobenzene (**2b**, 0.3 mmol, 31.5 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 1 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10ab** (41 mg, 0.15 mmol, 75%) as a white solid. Mp 90−92 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.84−7.82 (m, 2H), 7.41−7.39 (m, 7H), 7.32−7.29 (m, 4H), 7.23−7.20 (m, 2H), 5.59 (s, 1H) ppm; ^{13}C $\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 160.76, 143.90, 136.33, 130.74, 128.51, 128.45, 128.42, 127.67, 126.96, 77.89 ppm; IR (thin film): 3060, 3025, 2925, 2848, 1642, 1599, 1580, 1492, 1451, 1378, 1025 cm^{-1}; HRMS calcd. for $C_{20}H_{18}N$ 272.1439, observed 272.1441 $[M+H]^+$.

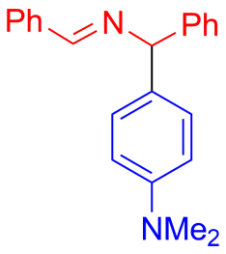


***N*-Benzylidine-1-phenyl-1-(3-tolyl)methanamine** (**10ae**): The reaction was performed following the General Procedure with **8a** (0.2 mmol, 39 mg), 3-bromotoluene (**2e**, 0.3 mmol, 36.0 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 1 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10ae** (50 mg, 0.18 mmol, 88%) as a white solid. Mp 62−64 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.85−7.83 (m, 2H), 7.42−7.39 (m, 5H), 7.33−7.30 (m, 2H), 7.22−7.19 (m, 4H), 7.05−7.03 (m, 1H), 5.56 (s, 1H), 2.32 (s, 3H) ppm; ^{13}C $\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 160.67, 143.99, 143.81, 138.00, 136.37, 130.69, 128.49, 128.46, 128.39, 128.33, 128.30, 127.75, 127.64, 126.89, 124.77, 77.95, 21.50 ppm; IR (thin film): 3060, 3028,

2921, 2844, 1641, 1601, 1580, 1492, 1451, 1379, 1217, 1026 cm^{-1}; HRMS calcd. for $C_{21}H_{20}N$ 286.1596, observed 286.1596 $[M+H]^+$.

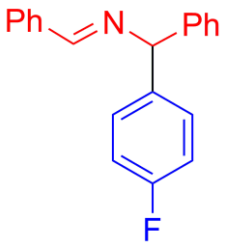


***N*-Benzylidine-1-(4-methoxyphenyl)-1-phenylmethanamine** (**10ag**): The reaction was performed following the General Procedure with **8a** (0.2 mmol, 39 mg), 4-bromoanisole (**2g**, 0.3 mmol, 37.5 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 1 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10ag** (51 mg, 0.17 mmol, 85%) as a white solid. Mp 60−62 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ 8.40 (s, 1H), 7.84−7.82 (m, 2H), 7.41−7.38 (m, 5H), 7.33−7.29 (m, 4H), 7.24−7.21 (m, 1H), 6.86 (d, *J* = 8.1 Hz, 2H), 5.57 (s, 1H), 3.78 (s, 3H) ppm; ^{13}C {^1H} NMR (125 MHz, $CDCl_3$): δ 160.48, 158.55, 144.11, 136.34, 136.11, 130.65, 128.73, 128.46, 128.40, 128.35, 127.56, 126.84, 113.80, 77.19, 55.17 ppm; IR (thin film): 2918, 2851, 1640, 1607, 1580, 1509, 1492, 1451, 1378, 1246, 1171, 1033, 833, 805 cm^{-1}; HRMS calcd. for $C_{21}H_{20}NO$ 302.1545, observed 302.1548 $[M+H]^+$.



***N*-Benzylidine-1-(4-dimethylaminophenyl)-1-phenylmethanamine (10af):** The reaction was performed following the General Procedure with **8a** (0.2 mmol, 39 mg), 4-bromo-*N*,*N*-dimethylaniline (**2f**, 0.3 mmol, 60 mg) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 1 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10af** (58 mg, 0.19 mmol, 93%) as a white solid. Mp 114−116 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ 8.40 (s, 1H), 7.84−7.82 (m, 2H), 7.41−7.39 (m, 5H), 7.32−7.29 (m, 2H), 7.23−7.21 (m, 3H), 6.69 (d, *J* = 9.1 Hz, 2H), 5.55 (s, 1H), 2.91 (s, 6H) ppm; ^{13}C {^1H} NMR (125

MHz, $CDCl_3$): δ 160.18, 149.70, 144.43, 136.53, 131.89, 130.52, 128.49, 128.49, 128.43, 128.41, 128.26, 127.61, 126.66, 112.62, 77.26, 40.65 ppm; IR (thin film): 3023, 2919, 2852, 1637, 1612, 1519, 1491, 1447, 1348, 1162, 947, 815 cm^{-1}; HRMS calcd. for $C_{22}H_{23}N_2$ 315.1861, observed 315.1852 $[M+H]^+$.

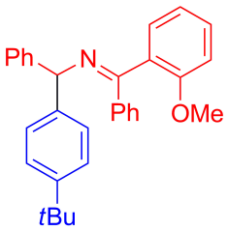


***N*-Benzylidine-1-(4-fluorophenyl)-1-phenylmethanamine (10ai):** The reaction was performed following the General Procedure with **8a** (0.2 mmol, 39 mg), 1-bromo-4-fluorobenzene (**2i**, 0.3 mmol, 33 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 1 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10ai** (29 mg, 0.10 mmol, 50%) as a white solid. Mp 40−42 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.84−7.83 (m, 1H), 7.43−7.40 (m, 3H), 7.38−7.30 (m, 6H), 7.25−7.24 (m, 1H), 7.00 (t, *J* = 8.5 Hz, 2H), 5.57 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.85 (d, *J* = 243 Hz), 160.88, 143.72, 139.70 (d, *J* = 3.6 Hz), 136.19, 130.86, 129.16 (d, *J* = 7.4 Hz), 128.55, 128.49, 128.46, 127.57, 127.10, 115.19 (d, *J* = 21.2 Hz), 77.10 ppm; IR (thin film): 3083, 3060, 3027, 2845, 1642, 1601, 1580, 1506, 1493, 1451, 1220, 1156, 1026, 840, 812 cm^{-1}; HRMS calcd. for $C_{20}H_{17}FN$ 290.1345, observed 290.1343 $[M+H]^+$.

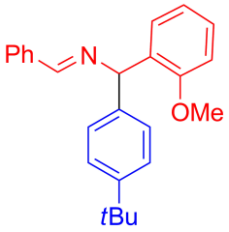
***N*-(2-Methoxybenzylidine)-1-(4-*tert*-butylphenyl)-1-phenylmethanamine (10bc)** and ***N*-Benzylidine-1-(4-*tert*-butylphenyl)-1-(2-methoxyphenyl)methanamine (10bc'):**

The reaction was performed following the General Procedure with **8b** (0.2 mmol, 47 mg), 1-bromo-4-*tert*-butylbenzene (**2c**, 0.3 mmol, 51.9 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 3 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl

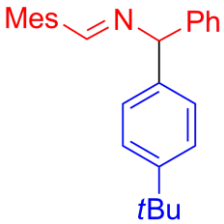
acetate as eluent to yield the regioisomers **10bc** and **10bc'** (54 mg, 0.15 mmol, 76%, ratio 4:1 according to ^{1}H NMR of the isolated mixture) as an white solid and colorless oil, respectively.



(**10ba**) Mp 126−128 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.89 (s, 1H), 8.16 (dd, *J* = 1.6, 7.5 Hz, 1H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.38−7.35 (m, 1H), 7.32−7.29 (m, 6H), 7.23−7.19 (m, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 8.5 Hz, 1H), 5.56 (s, 1H), 3.85 (s, 3H), 1.28 (s, 9H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 158.86, 156.46, 149.55, 144.41, 141.26, 131.85, 128.31, 127.79, 127.66, 127.23, 126.74, 125.26, 124.86, 120.70, 110.91, 78.31, 55.46, 34.40, 31.36 ppm; IR (thin film): 2959, 1634, 1600, 1487, 1465, 1437, 1376, 1287, 1246, 1159, 1109, 1025 cm^{-1}; HRMS calcd. for $C_{25}H_{28}NO$ 358.2171, observed 358.2171 $[M+H]^{+}$.

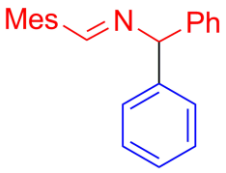


(**10ba'**): ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.83−7.81 (m, 2H), 7.57 (dd, *J* = 1.8, 7.6 Hz, 1H), 7.40−7.38 (m, 3H), 7.34−7.29 (m, 4H), 7.22−7.19 (m, 1H), 6.94 (td, *J* = 1.0, 8.0 Hz, 1H), 6.87 (dd, *J* = 1.0, 8.0 Hz, 1H), 6.05 (s, 1H), 3.82 (s, 3H), 1.28 (s, 9H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.62, 156.45, 149.28, 140.76, 136.71, 132.44, 130.48, 128.89, 128.43, 128.41, 127.82, 127.30, 125.10, 120.75, 110.58, 69.96, 55.50, 34.40, 31.40 ppm; IR (thin film): 3060, 3028, 2961, 2903, 2867, 1642, 1599, 1586, 1489, 1463, 1379, 1288, 1242, 1107, 1050, 1030, 829 cm^{-1}; HRMS calcd. for $C_{25}H_{28}NO$ 358.2171, observed 358.2178 $[M+H]^{+}$.

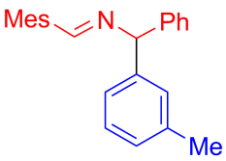


***N*-(2,4,6-Methylbenzylidine)-1-(4-*tert*-butylphenyl)-1-phenylmethanamine** (**10cc**): The reaction was performed following the General Procedure with **8c** (0.2 mmol, 47 mg), 1-bromo-4-*tert*-butylbenzene (**2c**, 0.3 mmol, 51.9 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 3 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to

yield the product **10cc** (55 mg, 0.15 mmol, 75%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.79 (s, 1H), 7.45−7.44 (m, 2H), 7.33−7.29 (m, 6H), 7.23−7.20 (m, 1H), 6.85 (s, 2H), 5.50 (s, 1H), 2.44 (s, 6H), 2.26 (s, 3H), 1.29 (s, 9H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.63, 149.58, 144.47, 141.26, 138.92, 137.99, 130.69, 129.48, 128.36, 127.60, 127.09, 126.77, 125.28, 79.85, 34.41, 31.36, 21.09 ppm; IR (thin film): 3028, 2963, 2922, 2866, 1638, 1611, 1452, 1375, 1269, 1018, 851, 827 cm^{-1}; HRMS calcd. for $C_{27}H_{32}N$ 370.2535, observed 370.2536 $[M+H]^+$.

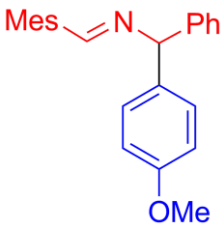


***N*-(2,4,6-Methylbenzylidine)-1,1-diphenylmethanamine** (**10cb**): The reaction was performed following the General Procedure with **8c** (0.2 mmol, 47 mg), bromobenzene (**2b**, 0.3 mmol, 31.5 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 3 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10cb** (48 mg, 0.15 mmol, 77%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.81 (s, 1H), 7.42 (d, *J* = 7.5 Hz, 4H), 7.31 (t, *J* = 7.8 Hz, 4H), 7.24−7.20 (m, 2H), 6.85 (s, 1H), 5.53 (s, 1H), 2.42 (s, 6H), 2.27 (s, 3H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.83, 144.27, 138.95, 137.92, 130.67, 129.47, 128.37, 127.54, 126.82, 79.99, 21.08, 21.02 ppm; IR (thin film): 3061, 3027, 2918, 2855, 1641, 1610, 1495, 1452, 1432, 1374, 1343, 1029, 851 cm^{-1}; HRMS calcd. for $C_{23}H_{24}N$ 314.1909, observed 314.1908 $[M+H]^+$.

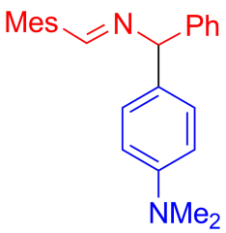


***N*-(2,4,6-Methylbenzylidine)-1-phenyl-1-(3-tolyl)methanamine** (**10ce**): The reaction was performed following the General Procedure with **8c** (0.2 mmol, 47 mg), 3-bromotoluene (**2e**, 0.3 mmol, 36.0 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 3 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1

hexanes/ethyl acetate as eluent to yield the product **10ce** (45 mg, 0.14 mmol, 69%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.79 (s, 1H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.23−7.19 (m, 4H), 7.03 (d, *J* = 6.6 Hz, 1H), 6.85 (s, 2H), 5.49 (s, 1H), 2.42 (s, 6H), 2.31 (s, 3H), 2.26 (s, 3H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.76, 144.36, 144.21, 138.91, 137.92, 137.90, 130.76, 129.45, 128.36, 128.26, 128.22, 127.59, 127.54, 126.78, 124.62, 80.03, 21.48, 21.08, 21.00 ppm; IR (thin film): 3025, 2918, 2854, 1637, 1610, 1487, 1451, 1375, 1292, 1030, 851 cm^{-1}; HRMS calcd. for $C_{24}H_{26}N$ 328.2065, observed 328.2062 $[M+H]^+$.

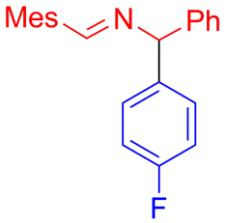


***N*-(2,4,6-Methylbenzylidine)-1-(4-methoxyphenyl)-1-phenylmethanamine** (**10cg**): The reaction was performed following the General Procedure with **8c** (0.2 mmol, 47 mg), 4-bromoanisole (**2g**, 0.3 mmol, 37.5 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 3 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10cg** (46 mg, 0.13 mmol, 67%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.79 (s, 1H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.32−7.29 (m, 4H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.86−6.84 (m, 4H), 5.49 (s, 1H), 3.77 (s, 3H), 2.41 (s, 6H), 2.27 (s, 3H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.60, 158.47, 144.50, 138.89, 137.87, 136.57, 130.77, 129.43, 128.60, 128.34, 127.48, 126.74, 113.77, 79.32, 55.19, 21.08, 20.99 ppm; IR (thin film): 3059, 3024, 2954, 2918, 2834, 1637, 1610, 1509, 1451, 1374, 1301, 1246, 1172, 1034, 851, 827 cm^{-1}; HRMS calcd. for $C_{24}H_{26}NO$ 344.2014, observed 344.2012 $[M+H]^+$.

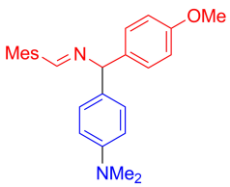


***N*-(2,4,6-methylbenzylidine)-1-(4-dimethylaminophenyl)-1-phenyl-methanamine (10cf):** The reaction was performed following the General Procedure with **8c** (0.2 mmol, 47 mg), 4-bromo-*N*,*N*-dimethylaniline (**2f**, 0.3 mmol, 60 mg) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was

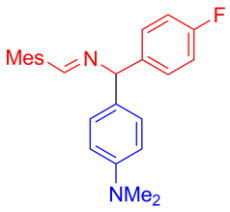
stirred for 3 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10cf** (58 mg, 0.16 mmol, 82%) as a white solid. Mp 90−92 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.78 (s, 1H), 7.42 (d, *J* = 7.5 Hz, 2H), 7.31−7.28 (m, 2H), 7.25−7.23 (m, 2H), 7.21−7.18 (m, 1H), 6.84 (s, 2H), 6.69 (d, *J* = 8.8 Hz, 2H), 5.47 (s, 1H), 2.91 (s, 6H), 2.42 (s, 6H), 2.26 (s, 3H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.26, 149.60, 144.83, 138.72, 137.84, 132.44, 130.97, 129.38, 128.29, 128.26, 127.54, 126.55, 112.61, 79.41, 40.67, 21.09, 21.00 ppm; IR (thin film): 3027, 2920, 2849, 1637, 1611, 1567, 1519, 1449, 1349, 1162, 1048, 947, 855 cm^{-1}; HRMS calcd. for $C_{25}H_{29}N_2$ 357.2331, observed 357.2343 $[M+H]^+$.



***N*-(2,4,6-methylbenzylidine)-1-(4-fluorophenyl)-1-phenylmethanamine (10ci):** The reaction was performed following the General Procedure with **8c** (0.2 mmol, 47 mg), 1-bromo-4-fluorobenzene (**2i**, 0.3 mmol, 33 μL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 3 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10ci** (45 mg, 0.14 mmol, 68%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.79 (s, 1H), 7.39−7.36 (m, 4H), 7.33−7.30 (m, 2H), 7.24−7.21 (m, 1H), 7.01−6.98 (m, 2H), 6.86 (s, 2H), 5.51 (s, 1H), 2.42 (s, 6H), 2.27 (s, 3H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.85 (d, *J* = 245 Hz), 161.05, 144.17, 140.16 (d, *J* = 2.8 Hz), 139.18, 138.01, 130.62, 129.59, 129.10 (d, *J* = 8.5 Hz), 128.53, 127.51, 127.04, 115.23 (d, *J* = 21.2 Hz), 79.26, 21.15, 21.08 ppm; IR (thin film): 3060, 3028, 2959, 1918, 2853, 1638, 1609, 1506, 1451, 1432, 1375, 1292, 1221, 1155, 1015, 851, 830, 807, 784 cm^{-1}; HRMS calcd. for $C_{23}H_{23}FN$ 332.1815, observed 332.1817 $[M+H]^+$.

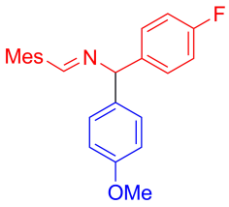


***N*-(2,4,6-Methylbenzylidine)-1-(4-methoxyphenyl)-1-(4-methylaminophenyl)methan-amine (10df) :** The reaction was performed following the General Procedure with **8d** (0.2 mmol, 53 mg), 4-bromo-*N*,*N*-dimethylaniline (**2f**, 0.4 mmol, 80 mg) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 5 h at 50 ^oC after portionwise addition of the $LiN(SiMe_3)_2$ solution was completed. The workup was performed following General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10df** (56 mg, 0.14 mmol, 72%) as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ 8.76 (s, 1H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 6.85−6.83 (m, 4H), 6.69 (d, *J* = 8.6 Hz, 2H), 5.43 (s, 1H), 3.77 (s, 3H), 2.91 (s, 6H), 2.41 (s, 6H), 2.26 (s, 3H) ppm; ^{13}C {^1H} NMR (125 MHz, $CDCl_3$): δ 159.98, 158.25, 149.52, 138.64, 137.76, 137.10, 132.62, 130.99, 129.33, 128.54, 128.18, 113.62, 112.58, 78.73, 55.19, 40.66, 21.07, 20.98 ppm; IR (thin film): 2953, 2918, 2853, 1637, 1611, 1519, 1510, 1443, 1349, 1246, 1171, 1035, 947, 827, 817, 800 cm^{-1}; HRMS calcd. for $C_{26}H_{31}N_2O$ 387.2436, observed 387.2440 $[M+H]^+$.

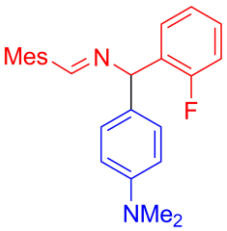


***N*-(2,4,6-methylbenzylidine)-1-(4-fluorophenyl)-1-(4-methoxyphenyl)-methanamine (10ef):** The reaction was performed following the General Procedure with **8e** (0.2 mmol, 51 mg), 4-bromoanisole (**2f**, 0.4 mmol, 50.0 µL) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 5 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10ef** (43 mg, 0.12 mmol, 60%) as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ 8.81 (s, 1H), 7.44 (dd, *J* = 5.5, 7.6 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.03 (t, *J* = 8.5 Hz, 2H), 6.89−6.90 (m, 4H), 5.50 (s, 1H), 3.81 (s, 3H), 2.45 (s, 6H), 2.31 (s, 3H) ppm; ^{13}C {^1H} NMR (125 MHz, $CDCl_3$): δ 161.70 (d, *J* = 245 Hz), 160.71, 158.53, 140.30 (d, *J* = 2.9 Hz), 139.03, 137.85, 136.86, 130.60, 129.47, 128.94 (d, *J* = 8.2 Hz), 128.40, 115.10 (d, *J* = 21.1 Hz), 113.82, 78.52, 55.18, 21.07,

20.99 ppm; IR (thin film): 3000, 2956, 2919, 2838, 1638, 1610, 1506, 1481, 1442, 1302, 1247, 1222, 1173, 1155, 1038, 831, 813, 780 cm^{-1}; HRMS calcd. for $C_{24}H_{25}NOF$ 362.1920, observed 362.1918 $[M+H]^+$.

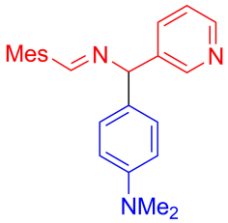


***N*-(2,4,6-methylbenzylidine)-1-(4-fluorophenyl)-1-(4-methylamino-phenyl)methanamine (8eg):** The reaction was performed following the General Procedure with **8e** (0.2 mmol, 51 mg), 4-bromo-*N*,*N*-dimethylaniline (**2g**, 0.4 mmol, 80 mg) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 4.5 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10eg** (45 mg, 0.12 mmol, 60%) as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ 8.77 (s, 1H), 7.39−7.36 (m, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 6.98 (t, *J* = 8.8 Hz, 2H), 6.85 (s, 2H), 6.69 (d, *J* = 8.8 Hz, 2H), 5.41 (s, 1H), 2.91 (s, 6H), 2.41 (s, 6H), 2.27 (s, 3H) ppm; ^{13}C $\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.61 (d, *J* = 245 Hz), 160.35, 149.61, 140.62 (d, *J* = 2.9 Hz), 138.83, 137.80, 132.12, 130.78, 129.41, 128.96 (d, *J* = 7.0 Hz), 128.16, 114.97 (d, *J* = 21.0 Hz), 112.54, 78.59, 40.58, 21.07, 20.98 ppm; IR (thin film): 2918, 2855, 1637, 1612, 1520, 1505, 1351, 1220, 1155, 831, 817 cm^{-1}; HRMS calcd. for $C_{25}H_{28}N_2F$ 375.2237, observed 375.2225 $[M+H]^+$.



***N*-(2,4,6-methylbenzylidine)-1-(2-fluorophenyl)-1-(4-methylamino-phenyl)methanamine (10ff):** The reaction was performed following the General Procedure with **8f** (0.2 mmol, 51 mg), 4-bromo-*N*,*N*-dimethylaniline (**2f**, 0.4 mmol, 80 mg) and $LiN(SiMe_3)_2$ (0.3 mmol, 50.2 mg). The reaction was stirred for 4.5 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10ff** (46 mg, 0.124 mmol, 62%) as a white solid. Mp 106−108 ^oC; ^1H

NMR (500 MHz, $CDCl_3$): δ 8.81 (s, 1H), 7.59 (dt, *J* = 1.7, 7.6 Hz, 1H), 7.29 (d, *J* = 8.9 Hz, 2H), 7.20−7.15 (m, 1H), 7.09 (dt, *J* = 0.9, 7.6 Hz, 1H), 7.02−6.98 (m, 1H), 6.84 (s, 2H), 6.70 (d, *J* = 8.9 Hz, 2H), 5.84 (s, 1H), 2.91 (s, 6H), 2.42 (s, 6H), 2.26 (s, 3H) ppm; ^{13}C {^1H} NMR (125 MHz, $CDCl_3$): δ 161.14, 160.0 (d, *J* = 246 Hz), 149.62, 138.82, 137.85, 131.85 (d, *J* = 13.1 Hz), 131.00 (d, *J* = 30.0 Hz), 129.42, 129.38, 128.18, 128.05 (d, *J* = 9.3 Hz), 124.07 (d, *J* = 2.5 Hz), 115.14 (d, *J* = 22.0 Hz), 112.54, 71.57, 40.62, 21.09, 20.96 ppm; IR (thin film): 2953, 2917, 2857, 1637, 1612, 1519, 1485, 1455, 1350, 1226, 1162, 1032, 947, 852, 818, 758 cm^{-1}; HRMS calcd. for $C_{25}H_{28}N_2F$ 375.2237, observed 375.2239 $[M+H]^+$.



***N*,*N*-dimethyl-4-(pyridin-3-yl((2,4,6-trimethylbenzylidene)amino)methyl)aniline (10gf):** The reaction was performed following the General Procedure with **8g** (0.2 mmol, 48 mg), 4-bromo-*N*,*N*-dimethylaniline (**2f,** 0.1 mmol, 2mg) and $LiN(SiMe_3)_2$ (0.2 mmol, 34.0 mg). The reaction was stirred for 4 h at room temperature after portionwise addition of the $LiN(SiMe_3)_2$ solution was complete. The workup was performed following the General Procedure and the crude material was purified by flash chromatography on silica gel using 20:1 hexanes/ethyl acetate as eluent to yield the product **10gf** (29 mg, 0.08 mmol, 80%) as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ 8.80 (s, 1H), 8.68 (d, *J* = 2.0 Hz, 1H), 8.46 (dd, *J* = 2.0, 4.9 Hz, 1H), 7.77−7.74 (m, 1H), 7.24−7.20 (m, 2H), 6.85 (s, 2H), 6.69 (d, *J* = 8.8 Hz, 2H), 5.49 (s, 1H), 2.91 (s, 6H), 2.42 (s, 6H), 2.26 (s, 3H) ppm; ^{13}C {^1H} NMR (125 MHz, $CDCl_3$): δ 161.02, 149.73, 148.92, 147.97, 140.29, 139.04, 137.90, 135.15, 131.18, 130.47, 129.46, 128.12, 123.30, 112.57, 40.53, 21.06, 21.03 ppm (one signal not observed or co-incident); IR (thin film): 3028, 2954, 2919, 2854, 1636, 1612, 1520, 1477, 1351, 816, 713 cm^{-1}; HRMS calcd. for $C_{24}H_{28}N_3$ 358.2283, observed 358.2279 $[M+H]^+$.

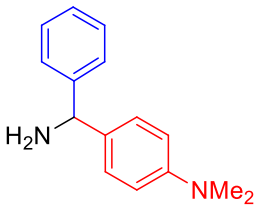
One-pot, gram scale preparation of *N*-benzylidine-1-(4-dimethylaminophenyl)-1-phenylmethanamine (10af):

An oven-dried 250 mL two-neck round-bottomed reaction flask equipped with a stirring bar and a glass stopcock adapter connected to a Schlenk line was charged with **8a** (10 mmol, 1.95 g), 4-bromo-*N*,*N*-dimethylaniline **2f** (15 mmol, 3.0 g), NIXANTPHOS (5.0 mol %, 276 mg) and $Pd(OAc)_2$ (2.5 mol %, 56 mg), respectively. The open neck was closed with a rubber septum and sealed with a strip of Parafilm. The flask was evacuated by vacuum and then refilled with nitrogen gas. This process was repeated 3 times and 85 mL dry THF was added through the septum by syringe. The resulting solution was stirred at room temperature for 3 min and a solution of $LiN(SiMe_3)_2$ (15 mmol, 15 mL of a 1.0 M of THF solution) was added by syringe over 1.5 h under a nitrogen atmosphere. The flask was removed from the Schlenk line and the reaction mixture was stirred under a nitrogen atmosphere at room temperature. After complete consumption (2 hours) of **8a**, 25 mL H_2O was added and the mixture was transferred to a separatory funnel with 250 mL diethyl ether. The organic phase was separated and washed with water (2 × 50 mL). The aqueous phase was washed with 100 mL diethyl ether, and combined organic phases were dried ($MgSO_4$) and filtered. During the evaporation of the solvent in a rotatory evaporator under vacuum, precipitation of the product **10af** together with some amount of remaining **2f** as a white solid (determined by NMR spectroscopy) was observed. The white solid was filtered and washed several times by small portions (20 mL) of cold diethyl ether to get rid of the remaining **2f**. By this way 2.17 g (69%) the product **10af** was isolated in a pure form. The ether washings were combined and evaporated in a rotatory evaporator. The remaining white solid residue was loaded onto a deactivated silica gel column and purified by flash chromatography using 20:1 hexanes/ethyl acetate as eluent to yield the product **10af** (0.5 g, 16%) as a white solid. The silica gel was deactivated by flushing with 5% triethylamine/hexanes solution (3 times) followed by 20:1 hexanes/ethyl acetate solution (3 times) to remove excess triethylamine.

Hydrolysis of Product 10af: An oven-dried microwave vial equipped with a stir bar was charged with **10af** (125.6 mg, 0.4 mmol). HCl 1N (4 mL) and MeOH (4 mL) were added to the reaction vial via syringe in a water-ice bath. The solution was warmed to room temperature and stirred at room

temperature. After 6 h the reaction was judged complete by TLC. The reaction mixture was transferred to a 10 mL seperatory funnel via pipette and was extracted with dichloromethane (3X2 mL). The aqueous layer was then treated with 1N NaOH utill the pH reached 10, as judged using pH paper. The aqueous layer was extracted with dichloromethane (3X2 mL) and the combined organic layers were dried by $MgSO_4$ and concentrated in *vacuo*. After drying under vacuum for 12 h, the amine product **12af** was obtained as a white solid (88.6 mg, 98% yield).

4-(Amino(phenyl)methyl)-*N,N*-dimethylaniline 12af:



Mp. 82−84 ^{o}C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38−7.36 (m, 2H), 7.29 (t, *J* = 8.0 Hz, 2H), 7.23−7.18 (m, 3H), 6.68 (d, *J* = 8.5 Hz, 2H), 5.13 (s, 1H), 2.90 (s, 6H), 1.75 (s, 2H) ppm; ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.63, 146.22, 133.79, 128.29, 127.59, 126.76, 126.58, 112.58, 59.06, 40.64 ppm; IR (thin film): 3304, 3023, 2885, 2828, 1614, 1521, 1452, 1343, 829, 789 cm^{-1}; HRMS calcd. for $C_{15}H_{17}N$ 211.1271, observed 211.1278 $[M\text{-}NH2]^{+}$.

1.5. Acknowledgement

I would like to thank Professor Javier Adrio, Dr. Ana Bellomo, Professor Baris Yucel, Dr. Jacqueline Jiménez for their collaboration and contribution. Prof. Javier and Ana conducted the HTE screening of benzylation study and ligand study as shown in Scheme 1.3. Prof. Baris and Jacqueline worked with me together on the chromatographic purification of substrates in Table 1.9 and Scheme 1.9.

1.6. References

1. Li, J. J. *In Contemporary Drug Synthesis*; Wiley-Interscience: **2004**, 221.

2. Grant, J. A.; Riethuisen, J.-M.; Moulaert, B.; DeVos, C. *Ann. Allergy. Asthma. Immunol.* **2002**, *88*, 190.

3. Fuhrkop, J. H.; Li, G. *Organic Synthesis. Concepts and Methods*;Wiley-Interscience: **2003**, 237.

4. Ko, Y.; Malone, D. C.; Armstrong, E. P. *Pharmacotherapy* **2006**, *26*, 1694.

5. Doggrell, S. A.; Liang, L. C., *N-S Arch. Pharmacol.* **1998,** *357*, 126.

6. Plobeck, N.; Delorme, D.; Wei, Z.-Y.; Yang, H.; Zhou, F.; Schwarz, P.; Gawell, L.; Gagnon, H.; Pelcman, B.; Schmidt, R.; Yue, S. Y.; Walpole, C.; Brown, W.; Zhou, E.; Labarre, M.; Payza, K.; St-Onge, S.; Kamassah, A.; Morin, P.-E.; Projean, D.; Ducharme, J.; Roberts, E., *J. Med. Chem.* **2000,** *43*, 3878.

7. Wei, Z.-Y.; Brown, W.; Takasaki, B.; Plobeck, N.; Delorme, D.; Zhou, F.; Yang, H.; Jones, P.; Gawell, L.; Gagnon, H.; Schmidt, R.; Yue, S.-Y.; Walpole, C.; Payza, K.; St-Onge, S.; Labarre, M.; Godbout, C.; Jakob, A.; Butterworth, J.; Kamassah, A.; Morin, P.-E.; Projean, D.; Ducharme, J.; Roberts, E., *J. Med. Chem.* **2000,** *43*, 3895.

8. (a) Kobayashi, S.; Ishitani, H. Chem. Rev. 1999, 99, 1069. (b) Plobeck, N.; Powell, D. *Tetrahedron: Asymmetry* **2002**, *13*, 303. (c) Kauffman, M. C.; Walsh, P. J. *Science of Synthesis, Stereoselective Synthesis.* Molander, G. A., Ed.; Thieme: Stuttgart, **2011**, 449.

9. (a) Liu, Y.; Du, H. *J. Am. Chem. Soc.* **2013**, *135*, 6810. (b) Boone, M. P.; Stephan, D. W. *J. Am. Chem. Soc.* **2013**, *135*, 8508.

10. Das, B. G.; Nallagonda, R.; Ghorai, P. *J. Org. Chem.* **2012**, *77*, 5577.

11. (a) Dastbaravardeh, N.; Schnürch, M.; Mihovilovic, M. D. *Org. Lett.* **2012**, *14*, 1930. (b) Dastbaravardeh, N.; Schnürch, M.; Mihovilovic, M. D. *Org. Lett.* **2012**, *14*, 3792.

12. Niwa, T.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2008**, *10*, 4689.

13. Niwa, T.; Suehiro, T.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2009**, *65*, 5125.

14. (a) Li, M.; Berritt, S.; Walsh, P. J., *Org. Lett.* **2014,** *16*, 4312; (b) Li, M.; Yucel, B.; Adrio, J.; Bellomo, A.; Walsh, P. J., *Chem. Sci.* **2014,** *5*, 2383; (c) Li, M.; Yucel, B.; Jiménez, J.; Rotella, M.; Fu, Y.; Walsh, P. J., *Adv. Syn. Catal*. **2016,** *358*, 1910.

15. Zhu, Y.; Buchwald, S. L., *J. Am. Chem. Soc.* **2014,** *136*, 4500.

16. Fernandez-Salas, J. A.; Marelli, E.; Nolan, S. P., *Chem. Sci.* **2015,** *6*, 4973.

17. Zhang, J.; Bellomo, A.; Creamer, A. D.; Dreher, S. D.; Walsh, P. J. *J. Am. Chem. Soc.* **2012**, *134*, 13765.

18. (a) Bruno, N. C.; Niljianskul, N.; Buchwald, S. L., *J. Org. Chem.* **2014,** *79*, 4161; (b) Bruno, N. C.; Tudge, M. T.; Buchwald, S. L., *Chem. Sci.* **2013,** *4*, 916.

19. Zhang, J.; Bellomo, A.; Trongsiriwat, N.; Jia, T.; Carroll, P. J.; Dreher, S. D.; Tudge, M. T.; Yin, H.; Robinson, J. R.; Schelter, E. J.; Walsh, P. J., *J. Am. Chem. Soc.* **2014,** *136*, 6276.

20. J. O'Donnell, W. D. Bennett, W. A. Bruder, W. N. Jacobsen, K. Knuth, B. LeClef, R. L. Polt, F. G. Bordwell, S. R. Mrozack and T. A. Cripe, *J. Am. Chem. Soc.*, **1988**, *110*, 8520.

21. M. Hatano, Y. Hattori and Y. Furuya, K. Ishihara, *Org. Lett.*, **2009**, *11*, 2321.

22. W. H. Fields and J. J. Chruma, *Org. Lett.*, **2010**, *12*, 316.

23. D. Armesto, M. J. Ortiz and R. Perez-Ossorio, *J. Chem. Soc., Perkin Trans.*, **1986**, *1*, 2021.

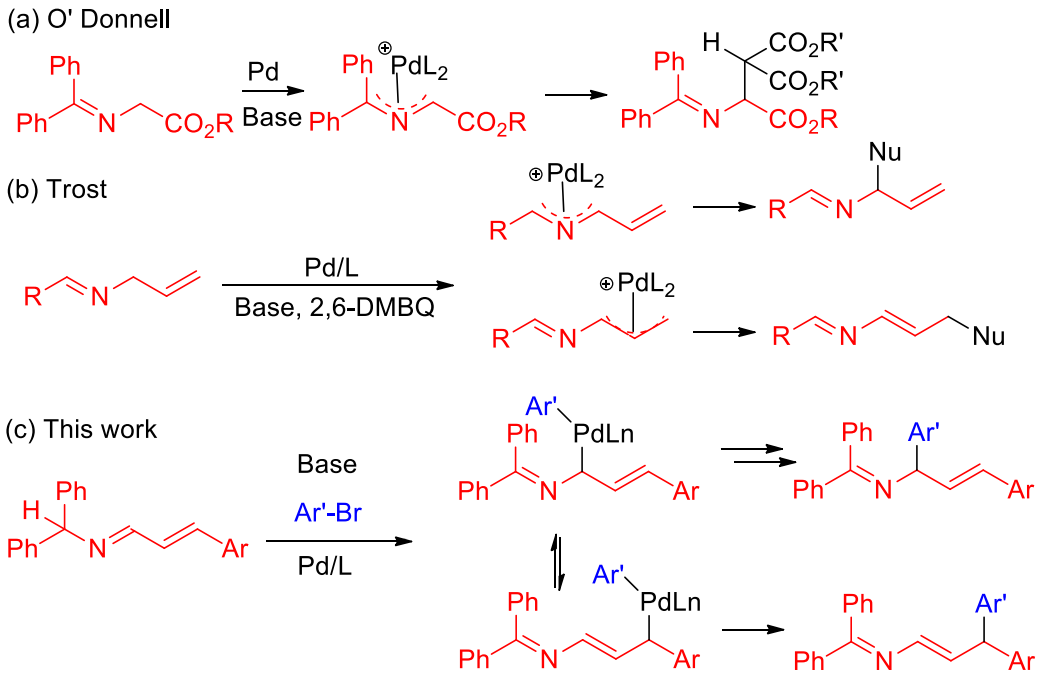
24. (a) N. Plobeck and D. Powell, *Tetrahedron: Asymmetry*, **2002**, *13*, 303; (b) T. Niwa, H. Yorimitsu and K. Oshima, *Org. Lett.*, **2008**, *10*, 4689.

Chapter 2. Divergent Synthesis of Allylic Amine and Enamine Derivatives via Palladium-Catalyzed Chemo- and Regioselective Arylation of Azapentadienyl Anions.

2.1. Introduction.

Allylic amines are prevalent in bioactive compounds[1] such as Naftifine[1d] and Flunarizine.[1e] They are also valuable building blocks in the synthesis of nitrogen-containing molecules, including amino acids, alkaloids and carbohydrate derivatives.[2] Likewise, their enamine isomers are utilized as intermediates for the synthesis of natural products and bioactive molecules.[3] Approaches for the synthesis of allylic amine and enamine derivatives include allylic amination reactions,[4] nucleophilic addition of aryl organometallic reagents to imines[5] and other transformations[6] such as the Overman rearrangement,[7] aza-Morita-Baylis-Hillman reaction,[8] and reductive amination.[9]

Chemo- and regioselective allylic C–H functionalization of organic compounds by transition metal-based catalysts has attracted considerable attention.[10] Beautiful applications of this work to organic synthesis continue to emerge.[11] In contrast, analogous C–H functionalizations of azaallyl derivatives remain largely unexplored. Early studies with azaallyl palladium intermediates were reported by O'Donnell and coworkers[12] and involved relatively sensitive hemiaminal precursors (Scheme 2.1，a). In 2015, Trost and coworkers[13] reported use of readily available *N*-allyl imines in oxidative C–H functionalization reactions in the presence of 2,6-dimethylbenzoquinone (Scheme 2.1，b). This groundbreaking chemistry appears to generate equilibrating π-allyl intermediates that can be regioselectively trapped with nucleophiles of differing steric demands. Herein, we report the first chemo- and regioselective arylation of azapentadienyl with aryl bromides (Scheme 2.1，c). Two distinct catalysts and sets of conditions were successfully identified to control the regioselectivity of the reductive elimination and thus achieve the divergent synthesis of allylic amine and enamine derivatives.

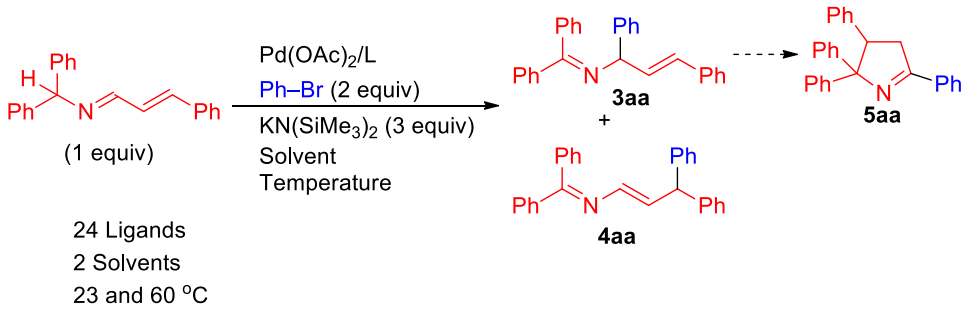


Scheme 2.1. Regioselectivity in Functionalization of Azaallyl Anions.

2.2. Results and Discussion.

2.2.1. Development and Optimization of Palladium-Catalyzed Arylation of Azapentadienyl Anions.

We initiated our studies with aldimine **1a** and bromobenzene **2a** using microscale screening (10 μmol) with 24 electronically diverse mono- and bidentate phosphine ligands, two solvents [CPME (cyclopentyl methyl ether) and THF], and two temperatures [23 ^{o}C and 60 ^{o}C] using $Pd(OAc)_2$ and $KN(SiMe_3)_2$ (Scheme 2.2). We were pleased to find that $P^tBu_3HBF_4$ and XANTPHOS were identified as ligands favoring α-arylation, generating allylic amine derivative **3aa**. In sharp contrast, van Leeuwen's NIXANTPHOS[14] generated the γ-arylation product, enamine **4aa**. A byproduct was observed arising from cyclization of the α-arylation product to give up to 50% **5aa**.



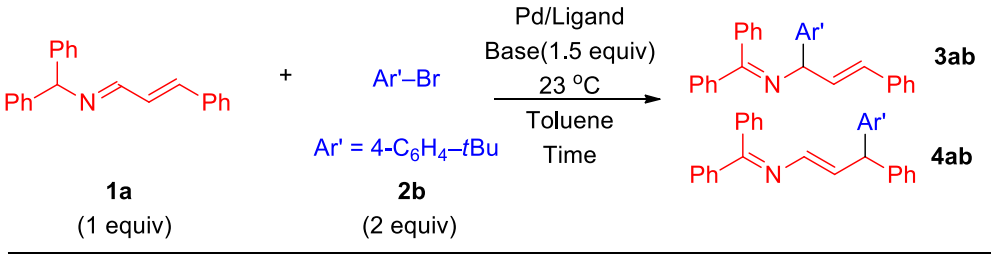
Scheme 2.2. Initial Screening of ligands, Solvents and Temperatures.

We suspected we could minimize cyclic byproduct **5aa** by reducing the equivalents of base at the lower temperature (23 ^{o}C). With this in mind, a series of microscale experiments (20 µmol) were performed using 1.5 equiv base with P^{t}Bu$_3$HBF$_4$, XANTPHOS, and NIXANTPHOS, with Pd(dba)$_2$, Pd(OAc)$_2$, [ClPd(2-methallyl)]$_2$, [ClPd(allyl)]$_2$, four solvents [THF, CPME, DME, toluene] and two bases [NaN(SiMe$_3$)$_2$ and KN(SiMe$_3$)$_2$]. The most promising α-arylation screening result was obtained with [ClPd(2-methallyl)]$_2$, P^{t}Bu$_3$HBF$_4$, and KN(SiMe$_3$)$_2$ in toluene. Laboratory scale optimization (0.1 mmol) led to α-arylation (**3ab**) in 84% assay yield (AY) (Table 2.1, entry 1). The optimal concentration was 0.05 M and resulted in excellent selectivity (>20 : 1) and 90% isolated yield (entry 2).

The leading screening result for the γ-arylation was Pd(dba)$_2$, NIXANTPHOS, and NaN(SiMe$_3$)$_2$ in toluene, which gave 72% on laboratory scale (0.1 mmol) (entry 3). A slight increase in AY was observed at 0.05 M (75% AY, entry 4). Buchwald precatalysts[15] facilitate catalyst generation, often led to increased activity, and allow lower ligand loading. Therefore, we employed Buchwald-type[16] precatalysts **6** and **7** (with L=NIXANTPHOS, entries 5–6). Precatalyst **7** led to γ-arylated product **4ab** in 85% AY with high selectivity (>20 : 1). Reducing the reaction time to 6 h led to **4ab** in 88% isolated yield (entry 7). The yield dropped to 67% when changing from NaN(SiMe$_3$)$_2$ to KN(SiMe$_3$)$_2$, but the regioselectivity was >20:1 (entry 8). No reaction was observed with

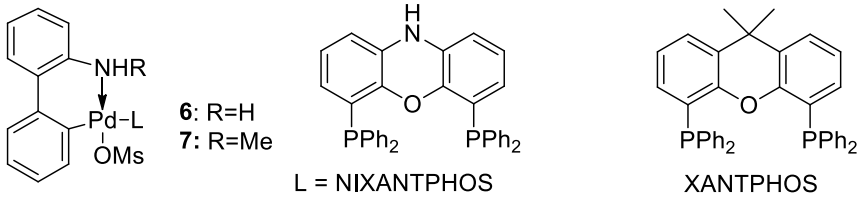
$LiN(SiMe_3)_2$ at rt, but at 60 °C γ-arylation predominated and afforded the product in 63% yield with 16:1 selectivity (entry 9).

Table 2.1. Optimization of Arylation α and γ to Nitrogen of 1a with 2b.[a,b]



1a (1 equiv) **2b** (2 equiv)

Entry	Pd(mol %)/L(mol %)	$MN(SiMe_3)_2$ M =	Time (h)	Conc. (M)	**3ab** (%)	**4ab** (%)
1	$[ClPd(2\text{-methallyl})]_2$ (5) $PtBu_3$(15%)	K	10	0.1	84	trace
2	same with 1	K	10	0.05	93 (90)[c]	trace
3	$Pd(dba)_2$ (10) NIXANTPHOS (20)	Na	10	0.1	trace	72
4	same with 2	Na	10	0.05	trace	75
5	Precatalyst **6** (10)	Na	10	0.05	trace	82
6	Precatalyst **7** (10)	Na	10	0.05	trace	85
7	same with 6	Na	6	0.05	trace	89(88)[c]
8	same with 7	K	6	0.05	trace	67
9	same with 7	Li	6	0.05	4	63[d]



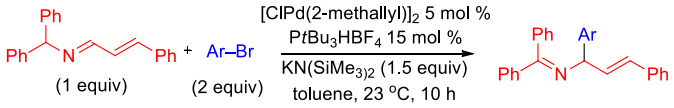
[a]Reactions conducted on a 0.1 mmol scale. [b]Assay yield determined by ^1H NMR of the crude reaction mixture. [c]Isolated yield after chromatographic purification. [d]60 °C.

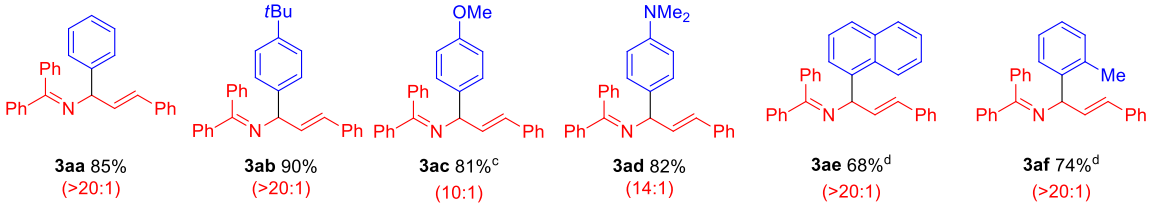
2.2.2. Substrate Scope of Palladium-Catalyzed Arylation of Azapentadienyl Anions.

With the optimized conditions in hand, we investigated the substrate scope of aryl bromides in the α-arylation (Table 2.2). It is noteworthy that high regioselectivities (α : γ= 9:1 to >20:1) were

observed in all cases. Bromobenzene **2a** and 4-*tert*-butyl-bromobenzene **2b** underwent coupling in excellent yield (85 and 90%, respectively). Efficient coupling of electron-donating 4-bromo anisole **2c** and 4-bromo-*N*,*N*-dimethylaniline **2d** afforded allylic amine derivatives **3ac** and **3ad** in 81 and 82% yield with 10:1 and 14:1 selectivity, respectively. Coupling reactions with sterically hindered 1-bromonaphthylene **2e** and 2-bromotoluene **2f** afforded better yields with $NaN(SiMe_3)_2$ in CPME, ultimately furnishing the products **3ae** and **3af** in 68 and 74% yield, respectively. Heterocyclic 5-bromo benzofuran **2g** and 5-bromo *N*-methyl indole **2h** were also good substrates, leading to products **3ag** and **3ah** in 70 and 80% yield, respectively, both with excellent regioselectivity. In the case of *meta*-substituted aryl bromides, 3-bromotoluene **2i** and 3-bromo-*N*,*N*-dimethylaniline **2j** coupled with **1a** both in 80% yield with 9:1 and 10:1 selectivity, respectively. With CPME as solvent, coupling of 3-bromoanisole afforded product **3ak** in 71% yield. 2-Bromonaphthalene afforded product **3al** in 72% yield with 20:1 regioselectivity. Unfortunately, reaction with electron-withdrawing 1-bromo-4-fluorobenzene exhibited low selectivity.

Table 2.2. Scope of Aryl Bromides in α-Arylation.[a,b]



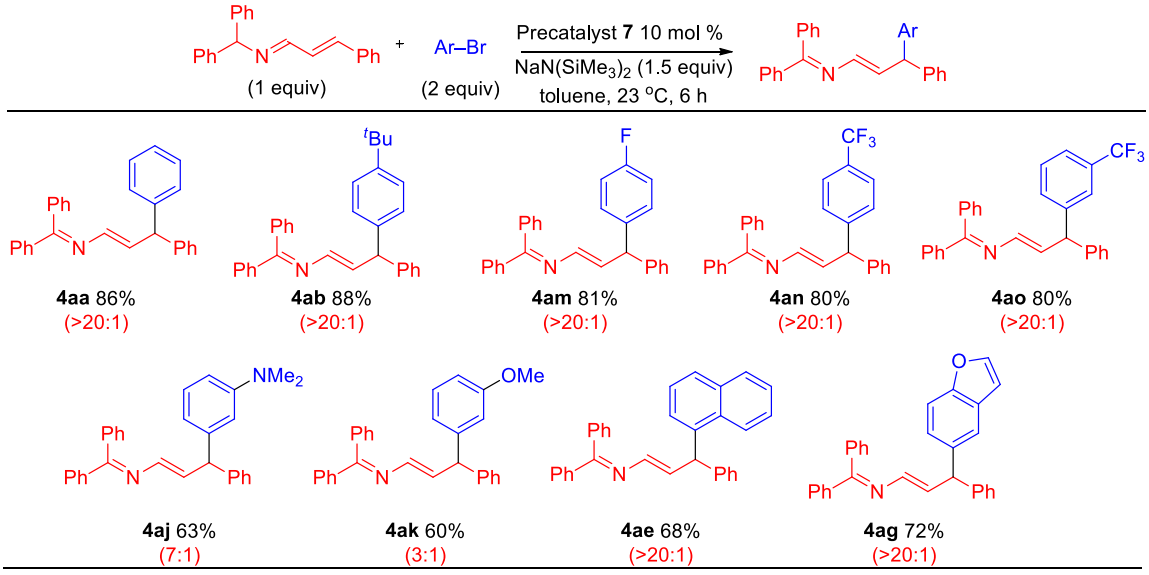


[a]Reactions conducted on a 0.1 mmol at 0.05 M. [b]Isolated yield after chromatographic purification,

ratio of **3:4** determined by ^{1}H NMR spectroscopy of the crude reaction mixture. [c]CPME. [d]$NaN(SiMe_3)_2$, CPME.

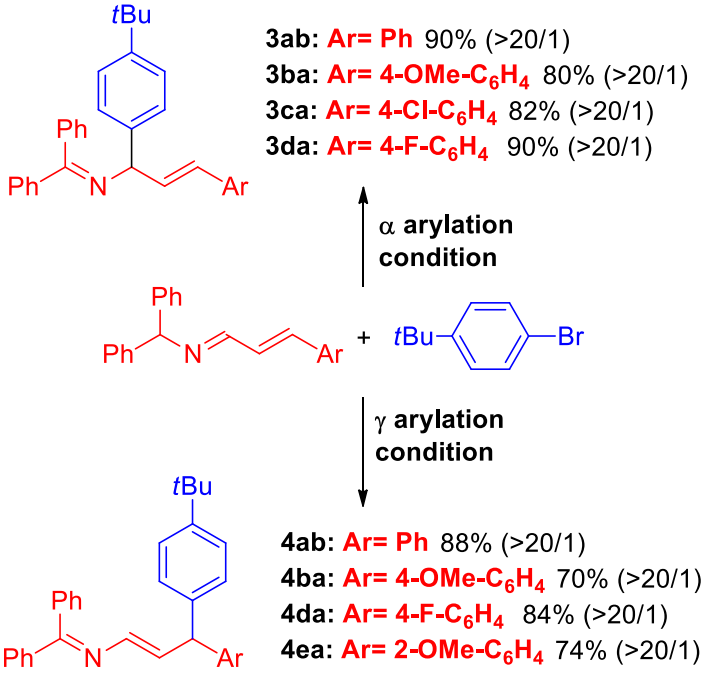
Having demonstrated the scope of aryl bromides in the α-selective arylation, we next turned to the γ-arylation. As outlined in Table 2.3, high regioselectivity (>20 : 1) was achieved in most cases with the NIXANTPHOS-based catalyst. Bromobenzene **2a** and 4-*tert*-butyl bromobenzene **2b** provided products **4aa** and **4ab** in 86 and 88% yield, respectively. Aryl bromides with electron-withdrawing substituents such as 4-F (**2m**), 4-CF_3 (**2n**) and 3-CF_3 (**2o**) all underwent coupling in 80–81% yield and >20:1 regioselectivity. Coupling of **1a** with aryl bromides having electron-donating groups at the 3-position resulted in decreased yields (60–63%), partially due to the moderate selectivity (7 : 1 and 3 : 1, respectively). Sterically more demanding 1-bromonaphthalene **2e** also exhibited catalyst controlled reactivity and afforded the γ-arylated product in 68% yield with excellent regioselectivity. Coupling **1a** with heterocyclic 5-bromo benzofuran **2g** resulted in 72% yield.

Table 2.3. Scope of Aryl Bromides in γ-Arylation.[a,b]



[a]Reactions conducted on a 0.1 mmol scale at 0.05 M. [b]Isolated yield after chromatographic purification, ratio of **4**:**3** was determined by ^{1}H NMR spectroscopy of the crude reaction mixture.

We next surveyed a few cinnamaldehyde derived aldimines (Scheme 2.3). The α-arylation of aldimines **1b** (Ar = 4-C_6H_4-OMe), **1c** (Ar = 4-C_6H_4-Cl), **1d** (Ar = 4-C_6H_4-F) with 4-*tert*-butyl bromobenzene **2b** and the P^{t}Bu$_3$-based catalyst afforded products in 80–90% yield with regioselectivities unaffected by the different electronic properties of the substrates. Likewise, high regioselectivities (>20:1) and good yields (70–88%) were achieved in the γ-arylation with the NIXANTPHOS-based catalyst.

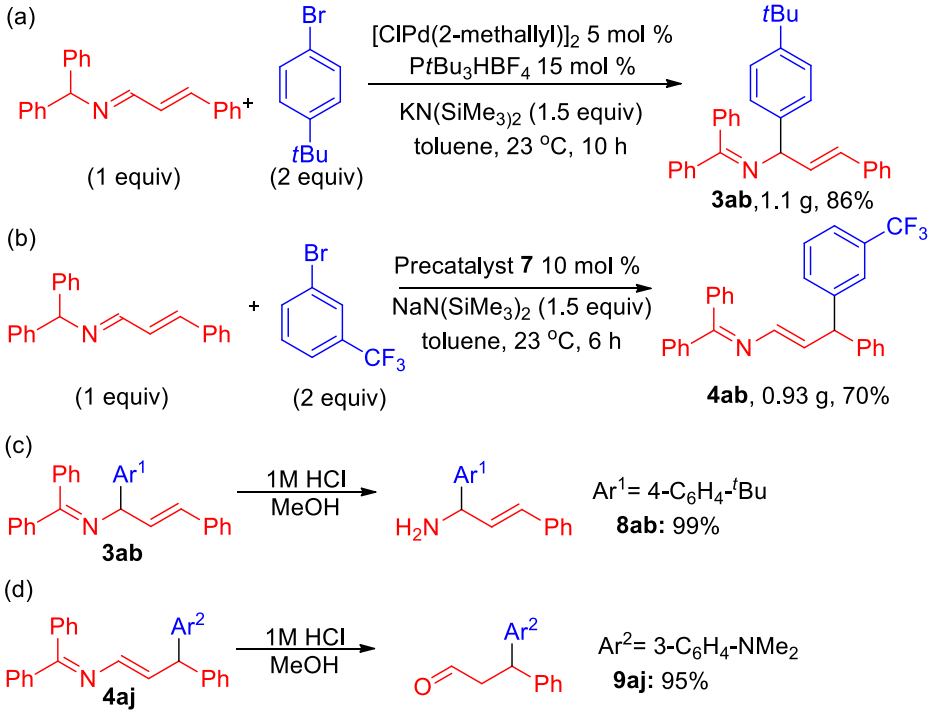


Scheme 2.3. Scope of Aldimines in Regioselective Arylation α and γ to Nitrogen.

2.2.3. Gram Scale Synthesis and Product Hydrolysis.

To probe the scalability and to study the regioslectivity at large scale reactions, we conducted 3 mmol gram sacle reactions. For α-aryatlion, the synthesis of **3ab** was performed with 5 mol % catalyst loading, leading to an isolated yield of 86% (1.1 g, >20 : 1 regioselectivity, Scheme 2.4, a). For γ-aryatlion, the reaction with 3-trifluoromethy bromobenzene **2o** was performed with 5 mol % catalyst loading. The product was isolated in 70% yield (0.93 g, >20 : 1 regioselectivity,

Scheme 2.4, b). Hydrolysis of the α-arylated product **3ab** was performed to isolate the allylic amine (99% yield, Scheme 2.4, c). Similarly, the enamine derivative **4aj** was hydrolyzed to the aldehyde in 95% yield (Scheme 2.4, d).

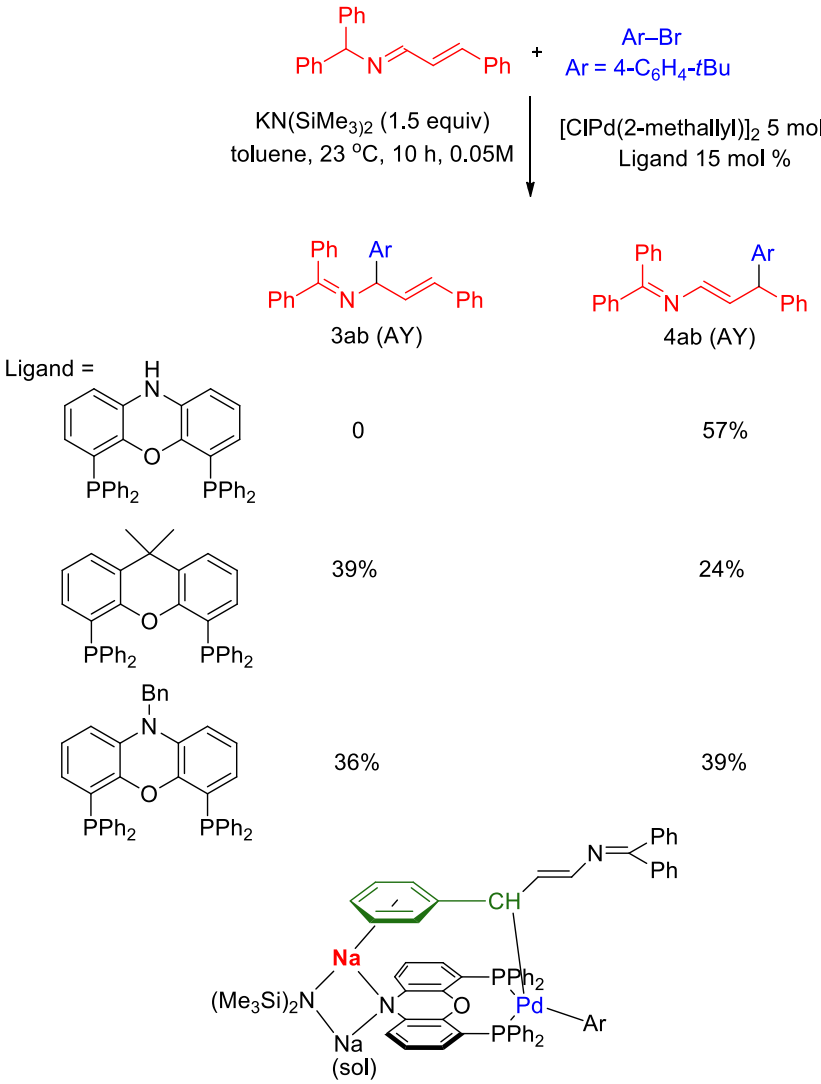


Scheme 2.4. Gram Scale Synthesis and Product Hydrolysis.

2.2.4. Mechanistic Insight of the Regioselectivity.

Although a mechanistic study has not yet been performed, the ligand screening results provide some food for thought. In particular, of the 24 ligands screened, 22 favor α-arylation, establishing as the substrate-controlled arylation site. Only NIXANTPHOS and bulky P(2-tolyl)$_3$ give γ-arylation. Additionally, there is an intriguing difference in selectivity between the XANTPHOS- and NIXANTPHOS-based catalysts in this arylation reaction. Although both ligands are structurally similar (see Table 2.1 for structures), NIXANTPHOS possess an acidic N–H (pK$_a$ ~ 21), which we have shown to be deprotonated in other catalytic reactions[17] in the presence of silylamide bases, MN(SiMe$_3$)$_2$, to give rise to a heterobimetallic catalyst. When the Pd(XANTPHOS) system was

employed, the α-arylation product was favored over the γ-product (1.6 : 1, Scheme 2.5). In contrast, the NIXANTPHOS-based catalyst provided exclusively the γ-arylation. Moreover, with the NIXANTPHOS N-H replaced with *N*-Bn, the resulting catalyst is unselective (Scheme 2.5). To rationalize this surprising shift in selectivity, we propose that the cation of the bimetallic NIXANTPHOS-based catalyst forms a cation-π interaction with the aryl ring of the substrate (Scheme 2.5),[18] forcing reductive elimination at the γ-position to form the enamine product with high selectivity. Our working model has a bridging $NaN(SiMe_3)_2$, similar to related crystal structures of deprotonated NIXANTPHOS complexes.[19]



Scheme 2.5. Comparison of Pd Complexes of NIXANTPHOS, XANTPHOS, and N-Bn-NIXANTPHOS. Proposed Cation-π Interaction Guiding Regioselectivity.

2.3. Summary and Outlook.

In summary, we have developed a remarkable catalyst controlled chemo- and regioselective α- and γ-arylation of azapentadienyl anions. This work represents the first umpolung C–H functionalizations of azapentadienyl palladium intermediates and enables the synthesis of allylic amine and enamine derivatives from common, readily accessible precursors. We propose that the high selectivity observed for the α-arylation is the result of a cation-π interaction between the heterobimetallic Pd/Na NIXANTPHOS-based catalyst and substrate.

2.4. Experimental Section.

General methods. All reactions were conducted under a nitrogen atmosphere with oven-dried glassware and standard Schlenk or vacuum line techniques. All solutions were handled under nitrogen and transferred via syringe. Anhydrous solvents, including CPME (cyclopentyl methyl ether) were purchased from Sigma-Aldrich and directly used without further purification. Toluene and THF were dried through activated alumina columns. Unless otherwise stated, reagents were commercially available and used as purchased without further purification. Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar or Matrix Scientific, and solvents were purchased from Fisher Scientific. Progress of reactions was monitored by thin-layer chromatography using Whatman Partisil K6F 250 μm precoated 60 Å silica gel plates and visualized by short-wave ultraviolet light as well as by treatment with iodine or ceric ammonium molybdate (CAM) stain. Flash chromatography was performed with silica gel (230–400 mesh, Silicycle). ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were obtained using a Brüker AM-500 Fourier-transform NMR spectrometer at 500 and 125 MHz, respectively. Chemical shifts were reported in units of parts per million (ppm) downfield from tetramethylsilane (TMS), and all coupling constants were reported in hertz. The infrared spectra were taken with KBr plates with a Perkin-Elmer Spectrum 100 Series spectrometer. High resolution mass spectrometry (HRMS) data were obtained on a

Waters LC-TOF mass spectrometer (model LCT-XE Premier) using chemical ionization (CI) or electrospray ionization (ESI) in positive or negative mode, depending on the analyte. Deactivated silica gel was prepared by addition of 15 mL of Et_3N to 1 L of silica gel.

Preparation of aldimines : Aldimines were prepared according to literature procedures.[20]

Preparation of NIXANTPHOS precatalyst 6 and 7: NIXANTPHOS precatalyst 6 and 7 were prepared according to literature procedure.[16]

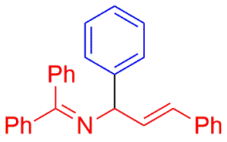
Preparation of N-Bn-NIXANTPHOS: N-Bn-NIXANTPHOS was prepared according to literature procedure.[14]

Procedure and characterization for the Pd-catalyzed chemo- and regioselective arylation:

General Procedure A (α-arylation): An oven-dried microwave vial equipped with a stir bar was charged with aldimine **1a** (29.7 mg, 0.10 mmol) and (2-methylallyl) palladium(II) chloride dimer (1.97 mg, 0.005 mmol) and tri-*tert*-butylphosphonium tetrafluoroborate (4.35 mg, 0.015 mmol) under a nitrogen atmosphere in a glove box. Anhydrous toluene (1.0 mL) was added to the reaction vial via syringe. The vial was sealed with cap (with rubber septum) and removed from the glove box. 1-Bromo-4-*tert*-butylbenzene **2b** (34.6 μL, 0.20 mmol) was added dropwise by syringe to this solution through the rubber septum. While the reaction mixture was stirred at 23 $^{\circ}$C, a solution of $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol) in 1.0 mL anhydrous toluene was added by syringe through the rubber septum. The reaction mixture was stirred for 10 h in total at 23 $^{\circ}$C, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate (3X2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was taken up in $CDCl_3$ and ratio of **3ab**:**4ab** (>20:1) was determined by ^{1}H NMR spectroscopy. Finally, the entire crude material was transfer into a 20 mL vial with NMR tube rinsed by additional 6 mL of ethyl acetate (3X2 mL), concentrated *in vacuo* and loaded onto a deactivated silica gel column via pipette and

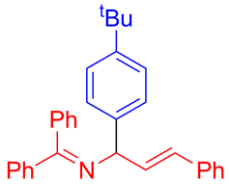
purified by flash chromatography (hexanes to diethyl ether: hexanes = 1:50) to give the product (38.8 mg, 90% yield) as a thick colorless oil.

General Procedure B (γ-arylation): An oven-dried microwave vial equipped with a stir bar was charged with aldimine **1a** (29.7 mg, 0.10 mmol) and NIXANTPHOS precatalyst **7** (9.5 mg, 0.010 mmol) under a nitrogen atmosphere in a glove box. Anhydrous toluene (1.0 mL) was added to the reaction vial via syringe. The vial was sealed with cap (with rubber septum) and removed from the glove box. 1-Bromo-4-*tert*-butylbenzene **2b** (34.6 μL, 0.20 mmol) was added dropwise by syringe to this solution through the rubber septum. While the reaction mixture was stirred at 23 °C, a solution of $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol) in 1.0 mL anhydrous toluene was added by syringe through the rubber septum. The reaction mixture was stirred for 6 h in total at 23 °C, opened to air, quenched with two drops of H_2O, diluted with 3 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate (3X2 mL), and the combined solutions were concentrated *in vacuo*. The crude material was taken up in $CDCl_3$ and ratio of **4ab**:**3ab** (>20:1) was determined by ^1H NMR spectroscopy. Finally, the entire crude material was transfer into a 20 mL vial with NMR tube rinsed by additional 6 mL of ethyl acetate (3X2 mL), concentrated *in vacuo* and loaded onto a deactivated silica gel column via pipette and purified by flash chromatography (hexanes to diethyl ether: hexanes = 1:50) to give the product (37.8 mg, 88% yield) as a thick colorless oil.

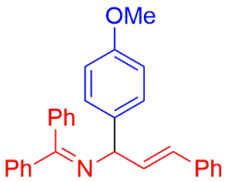


(*E*)-*N*-(Diphenylmethylene)-1,3-diphenylprop-2-en-1-amine (3aa): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2a** (21.4 μL, 0.20 mmol). Ratio of **3aa**:**4aa** (>20:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (31.7 mg, 85% yield) as a thick colorless oil. R_f = 0.55 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.73–7.71 (m,

2H), 7.46–7.44 (m, 3H), 7.40–7.28 (m, 10H), 7.25–7.18 (m, 5H), 6.52 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.39 (d, *J* = 16.0 Hz, 1H), 5.15 (d, *J* = 6.5 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.7, 143.6, 140.1, 137.4, 137.0, 132.7, 130.3, 129.6, 128.9, 128.7, 128.6, 128.3, 127.9, 127.6, 127.5, 127.1, 126.6, 68.7 ppm; IR (thin film): 3024, 2924, 1597, 1554, 1490, 1395, 1316, 1069, 746, 696 cm^{-1}; HRMS calc'd for $C_{28}H_{24}N^+$ 374.1909, observed 374.1904 $[M+H]^+$.

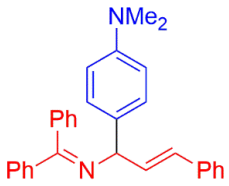


(*E*)-1-(4-(*tert*-Butyl)phenyl)-*N*-(diphenylmethylene)-3-phenylprop-2-en-1-amine (3ab): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2b** (34.6 *μ*L, 0.20 mmol). Ratio of **3ab**:**4ab** (>20:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (38.8 mg, 90% yield) as a thick colorless oil. R_f = 0.57 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.73–7.71 (m, 2H), 7.46–7.45 (m, 3H), 7.38–7.32 (m, 9H), 7.28–7.25 (m, 2H), 7.20–7.18 (m, 3H), 6.52 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.38 (d, *J* = 16.0 Hz, 1H), 5.13 (d, *J* = 6.5 Hz, 1H), 1.30 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.5, 149.9, 140.6, 140.2, 137.5, 137.1, 132.8, 130.2, 129.4, 128.9, 128.7, 128.65, 128.62, 128.2, 128.0, 127.5, 127.2, 126.6, 125.6, 68.5, 44.9, 34.7, 31.6 ppm; IR (thin film): 3026, 2962, 1621, 1576, 1446, 1314, 1269, 1028, 964, 751, 694 cm^{-1}; HRMS calc'd for $C_{32}H_{32}N^+$ 430.2535, observed 430.2541 $[M+H]^+$.

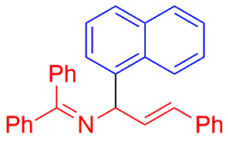


(*E*)-*N*-(Diphenylmethylene)-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-amine (3ac): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2c** (25.0 *μ*L, 0.20 mmol) with CPME as solvent. Ratio of **3ac**:**4ac** (10:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (32.7 mg, 81% yield) as a thick colorless oil. R_f = 0.39 (diethyl ether:hexanes = 1:5); ^1H NMR (500

MHz, $CDCl_3$): δ 7.72–7.70 (m, 2H), 7.46–7.45 (m, 3H), 7.38–7.25 (m, 9H), 7.20–7.16 (m, 3H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.50 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.38 (d, *J* = 16.0 Hz, 1H), 5.10 (d, *J* = 6.5 Hz, 1H), 3.78 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.4, 158.8, 140.1, 137.5, 137.1, 135.8, 132.9, 130.3, 129.3, 128.9, 128.7, 128.7, 128.64, 128.60, 128.2, 127.9, 127.5, 126.6, 114.1, 68.1, 55.5 ppm; IR (thin film): 3025, 2953, 1610, 1576, 1508, 1247, 1034, 747, 695 cm^{-1}; HRMS calc'd for $C_{29}H_{26}NO^+$ 404.2000, observed 404.2014 $[M+H]^+$.

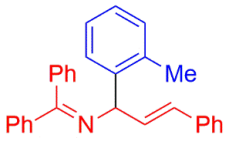


(*E*)-4-(1-((Diphenylmethylene)amino)-3-phenylallyl)-*N*,*N*-dimethylaniline (3ad): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2d** (40.4 mg, 0.20 mmol). Ratio of **3ad**:**4ad** (14:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:20) to give the product (34.2 mg, 82% yield) as a thick colorless oil. R_f = 0.29 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.72–7.70 (m, 2H), 7.46–7.44 (m, 3H), 7.36–7.31 (m, 5H), 7.27–7.24 (m, 4H), 7.19–7.17 (m, 3H), 6.70 (d, *J* = 9.0 Hz, 2H), 6.53 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.38 (d, *J* = 16.0 Hz, 1H), 5.07 (d, *J* = 6.5 Hz, 1H), 2.91 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 166.9, 149.9, 140.3, 137.7, 137.2, 133.3, 131.6, 130.1, 128.9, 128.60, 128.57, 128.3, 128.2, 128.0, 127.3, 126.6, 112.9, 68.2, 40.9 ppm; IR (thin film): 3025, 2882, 1612, 1576, 1490, 1445, 1348, 1162, 964, 695 cm^{-1}; HRMS calc'd for $C_{30}H_{29}N_2^+$ 417.2331, observed 417.2344 $[M+H]^+$.

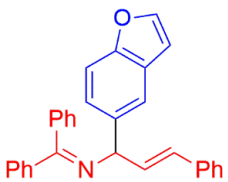


(*E*)-*N*-(Diphenylmethylene)-1-(naphthalen-1-yl)-3-phenylprop-2-en-1-amine (3ae): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2e** (28.0 μL, 0.20 mmol) with CPME as solvent. Ratio of **3ae**:**4ae** (>20:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product

(28.8 mg, 68% yield) as a thick colorless oil. R_f = 0.50 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.0 Hz, 1H), 7.81 (dd, *J* = 17.0, 8.0 Hz, 2H), 7.76–7.73 (m, 3H), 7.47–7.30 (m, 12H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.16–7.14 (m, 3H), 6.64 (dd, *J* = 16.0, 5.5 Hz, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 5.86 (d, *J* = 5.5 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 167.8, 140.1, 139.5, 137.4, 136.9, 134.3, 132.9, 131.1, 130.3, 129.7, 129.0, 128.9, 128.8, 128.7, 128.6, 128.3, 128.0, 127.8, 127.5, 126.6, 125.94, 125.93, 125.8, 125.5, 124.5, 65.7 ppm; IR (thin film): 3057, 3025, 1617, 1596, 1492, 1445, 1284, 1173, 964, 778, 754, 695 cm^{-1}; HRMS calc'd for $C_{32}H_{26}N^+$ 424.2065, observed 424.2059 $[M+H]^+$.

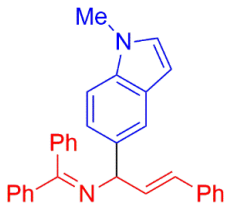


(*E*)-*N*-(Diphenylmethylene)-3-phenyl-1-(o-tolyl)prop-2-en-1-amine (3af): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2f** (24.1 μL, 0.20 mmol) with CPME as solvent. Ratio of **3af**:**4af** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (28.7 mg, 74% yield) as a thick colorless oil. R_f = 0.58 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.73–7.71 (m, 2H), 7.44–7.42 (m, 3H), 7.37–7.35 (m, 1H), 7.34–7.32 (m, 4H), 7.26–7.21 (m, 3H), 7.17 (d, *J* = 7.5 Hz, 1H), 7.13–7.11 (m, 3H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.47 (dd, *J* = 16.0, 7.0 Hz, 1H), 6.34 (d, *J* = 16.0 Hz, 1H), 5.31 (d, *J* = 7.0 Hz, 1H), 2.04 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 167.4, 141.8, 139.9, 137.3, 137.2, 135.2, 132.3, 130.4, 130.1, 129.2, 128.8, 128.54, 128.48, 128.2, 128.1, 127.7, 127.3, 126.7, 126.5, 126.4, 65.3, 19.4 ppm; IR (thin film): 3058, 3024, 1618, 1597, 1576, 1489, 1446, 1314, 1287, 1028, 965, 748, 694 cm^{-1}; HRMS calc'd for $C_{29}H_{26}N^+$ 388.2065, observed 388.2050 $[M+H]^+$.

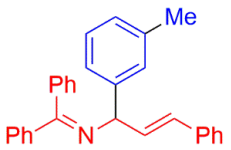


(*E*)-1-(Benzofuran-5-yl)-*N*-(diphenylmethylene)-3-phenylprop-2-en-1-amine(3ag): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol),

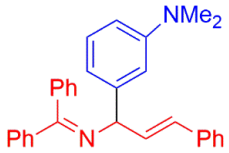
aryl bromide **2g** (25.1 μL, 0.20 mmol). Ratio of **3ag**:**4ag** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (29.0 mg, 70% yield) as a thick colorless oil. R_f = 0.44 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75–7.73 (m, 2H), 7.63 (d, *J* = 1.0 Hz, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.45–7.43 (m, 4H), 7.37–7.32 (m, 6H), 7.26 (t, *J* = 7.0 Hz, 2H), 7.19–7.17 (m, 3H), 6.71 (dd, *J* = 2.0, 1.0 Hz, 1H), 6.56 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.25 (d, *J* = 6.5 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 167.4, 154.2, 145.3, 139.9, 138.2, 137.3, 136.9, 133.0, 130.2, 129.2, 128.8, 128.6, 128.5, 128.2, 127.8, 127.6, 127.4, 126.5, 124.0, 119.8, 111.3, 106.8, 68.6 ppm; IR (thin film): 3025, 1621, 1597, 1464, 1445, 1262, 1030, 965, 748, 695 cm^{-1}; HRMS calc'd for $C_{30}H_{24}NO^+$ 414.1858, observed 414.1846 $[M+H]^+$.



(*E*)-*N*-(Diphenylmethylene)-1-(1-methyl-1H-indol-5-yl)-3-phenylprop-2-en-1-amine (3ah): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2h** (40.2 mg, 0.20 mmol). Ratio of **3ah**:**4ah** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:20) to give the product (34.0 mg, 80% yield) as a thick colorless oil. R_f = 0.24 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75–7.73 (m, 2H), 7.60 (s, 1H), 7.45–7.44 (m, 3H), 7.37–7.31 (m, 5H), 7.30–7.24 (m, 4H), 7.20–7.15 (m, 3H), 6.99 (d, *J* = 3.0 Hz, 1H), 6.61 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.44–6.41 (m, 2H), 5.26 (d, *J* = 6.5 Hz, 1H), 3.73 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 166.9, 140.3, 137.7, 137.2, 136.2, 134.6, 133.8, 130.1, 129.2, 129.0, 128.9, 128.8, 128.6, 128.5, 128.2, 128.1, 127.3, 126.6, 121.7, 119.5, 109.4, 101.2, 69.1, 33.1 ppm; IR (thin film): 3024, 1618, 1575, 1489, 1446, 1288, 1244, 1075, 965, 751, 695 cm^{-1}; HRMS calc'd for $C_{31}H_{27}N_2^+$ 427.2174, observed 427.2172 $[M+H]^+$.

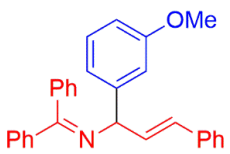


(*E*)-*N*-(Diphenylmethylene)-3-phenyl-1-(m-tolyl)prop-2-en-1-amine (3ai): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2i** (24.4 μL, 0.20 mmol). Ratio of **3ai**:**4ai** (9:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (31.0 mg, 80% yield) as a thick colorless oil. R_f = 0.70 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.73–7.72 (m, 2H), 7.44–7.43 (m, 3H), 7.37–7.31 (m, 5H), 7.27–7.24 (m, 2H), 7.21 (s, 1H), 7.19–7.16 (m, 5H), 7.03 (d, *J* = 6.5 Hz, 1H), 6.52 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.38 (d, *J* = 16.0 Hz, 1H), 5.12 (d, *J* = 6.5 Hz, 1H), 2.32 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.5, 143.4, 140.0, 138.1, 137.3, 136.9, 132.7, 130.2, 129.3, 128.8, 128.60, 128.55, 128.5, 128.4, 128.14, 128.12, 127.9, 127.8, 127.4, 126.5, 124.5, 68.7, 21.6 ppm; IR (thin film): 3025, 1621, 1598, 1489, 1446, 1279, 1028, 965, 761, 695 cm^{-1}; HRMS calc'd for $C_{29}H_{26}N^+$ 388.2065, observed 388.2070 $[M+H]^+$.

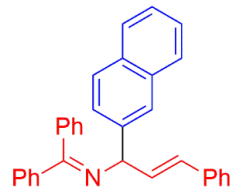


(*E*)-3-(1-((Diphenylmethylene)amino)-3-phenylallyl)-*N*,*N*-dimethylaniline (3aj): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2j** (28.5 μL, 0.20 mmol) with CPME as solvent. Ratio of **3aj**:**4aj** (10:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:20) to give the product (33.3 mg, 80% yield) as a thick colorless oil. R_f = 0.23 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.72–7.71 (m, 2H), 7.45–7.44 (m, 3H), 7.37–7.31 (m, 5H), 7.26–7.23 (m, 2H), 7.20–7.17 (m, 4H), 6.80 (s, 1H), 6.77 (d, *J* = 8.5 Hz, 1H), 6.62 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.55 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.39 (d, *J* = 16.0 Hz, 1H), 5.10 (d, *J* = 6.5 Hz, 1H), 2.92 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.4, 151.0, 144.5, 140.3, 137.6, 137.1, 133.1, 130.2, 129.3, 129.3, 128.9, 128.7, 128.61, 128.57, 128.2, 128.1, 127.4, 126.6, 116.1, 111.9, 111.6, 69.2, 40.9 ppm; IR (thin film):

3025, 2877, 2802, 1599, 1577, 1495, 1445, 1351, 997, 966, 755, 695 cm^{-1}; HRMS calc'd for $C_{30}H_{29}N_2^+$ 417.2331, observed 417.2327 $[M+H]^+$.

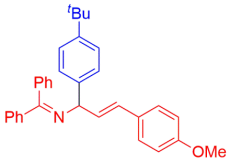


(*E*)-*N*-(Diphenylmethylene)-1-(3-methoxyphenyl)-3-phenylprop-2-en-1-amine (3ak): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2k** (25.3 μL, 0.20 mmol). Ratio of **3ak**:**4ak** (>20:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (28.7 mg, 71% yield) as a thick colorless oil. R_f = 0.28 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.73–7.71 (m, 2H), 7.46–7.45 (m, 3H), 7.39–7.32 (m, 5H), 7.29–7.23 (m, 3H), 7.20–7.17 (m, 3H), 7.00 (s, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.78 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.51 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.38 (d, *J* = 16.0 Hz, 1H), 5.11 (d, *J* = 6.5 Hz, 1H), 3.79 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.8, 159.9, 145.3, 140.1, 137.4, 136.9, 132.6, 130.3, 129.7, 129.6, 128.9, 128.8, 128.66, 128.65, 128.3, 127.9, 127.6, 126.7, 119.9, 113.3, 112.4, 68.7, 55.4 ppm; IR (thin film): 3025, 1937, 1597, 1584, 1486, 1446, 1257, 1048, 965, 746, 695 cm^{-1}; HRMS calc'd for $C_{29}H_{26}NO^+$ 404.2014, observed 404.2017 $[M+H]^+$.

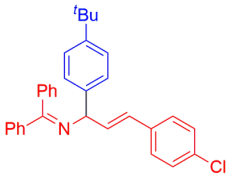


(*E*)-N-(Diphenylmethylene)-1-(naphthalen-2-yl)-3-phenylprop-2-en-1-amine (3al): The reaction was performed following General Procedure A with aldimine **1a** (29.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2l** (41.4 mg, 0.20 mmol). Ratio of **3al**:**4al** (>20:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (30.5 mg, 72% yield) as a thick colorless oil. R_f = 0.47 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.80–7.75 (m, 6H), 7.58–7.56 (m, 1H), 7.46–7.44 (m, 3H), 7.43–7.39 (m, 2H), 7.39–7.33 (m, 5H), 7.28–7.25 (m, 2H), 7.19–7.18 (m, 3H), 6.59 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.46 (d,

J = 16.0 Hz, 1H), 5.31 (d, J = 6.5 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.9, 141.1, 140.1, 137.4, 137.0, 133.8, 132.9, 132.6, 130.4, 129.8, 128.9, 128.8, 128.7, 128.3, 128.1, 127.9, 127.8, 127.6, 126.7, 126.2, 126.1, 125.8, 68.9 ppm; IR (thin film): 3056, 3024, 1620, 1597, 1491, 1446, 1281, 964, 749, 695 cm^{-1}; HRMS calc'd for $C_{32}H_{26}N^+$ 424.2065, observed 424.2066 $[M+H]^+$.

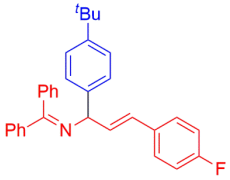


(*E*)-1-(4-(*tert*-Butyl)phenyl)-*N*-(diphenylmethylene)-3-(4-methoxyphenyl)prop-2-en-1-amine (3bb): The reaction was performed following General Procedure A with aldimine **1b** (32.7 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2b** (34.6 μL, 0.20 mmol). Ratio of **3bb**:**4bb** (>20:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (36.8 mg, 80% yield) as a thick colorless oil. R_f = 0.37 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.72–7.71 (m, 2H), 7.45–7.44 (m, 3H), 7.37–7.31 (m, 7H), 7.28 (d, J = 9.0 Hz, 2H), 7.20–7.18 (m, 2H), 6.80 (d, J = 9.0 Hz, 2H), 6.39 (dd, J = 16.0, 6.5 Hz, 1H), 6.31 (d, J = 16.0 Hz, 1H), 5.11 (d, J = 6.5 Hz, 1H), 3.75 (s, 3H), 1.30 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.3, 159.2, 149.8, 140.8, 140.2, 137.1, 130.7, 130.3, 130.2, 128.9, 128.8, 128.6, 128.6, 128.2, 128.0, 127.8, 127.2, 125.5, 114.1, 68.5, 55.5, 34.6, 31.6 ppm; IR (thin film): 3057, 3027, 2961, 1607, 1576, 1510, 1444, 1250, 1174, 1035, 965, 832, 757, 699 cm^{-1}; HRMS calc'd for $C_{33}H_{34}NO^+$ 460.2640, observed 460.2634 $[M+H]^+$.

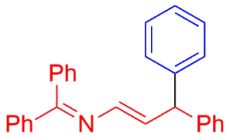


(*E*)-1-(4-(*tert*-Butyl)phenyl)-3-(4-chlorophenyl)-*N*-(diphenylmethylene)prop-2-en-1-amine (3cb): The reaction was performed following General Procedure A with aldimine **1c** (33.1 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2b** (34.6 μL, 0.20 mmol). Ratio of **3cb**:**4cb** (>20:1) was determined by ^1H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl

ether:hexanes = 1:50) to give the product (38.1 mg, 82% yield) as a thick colorless oil. R_f = 0.54 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72–7.71 (m, 2H), 7.46–7.45 (m, 3H), 7.38–7.30 (m, 7H), 7.28–7.24 (m, 4H), 7.18–7.16 (m, 2H), 6.50 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.34 (d, *J* = 16.0 Hz, 1H), 5.11 (d, *J* = 6.5 Hz, 1H), 1.30 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.6, 150.0, 140.3, 140.0, 136.7, 136.0, 133.6, 133.0, 130.3, 128.9, 128.8, 128.7, 128.6, 128.3, 128.1, 127.9, 127.8, 127.2, 125.6, 68.3, 34.7, 31.6 ppm; IR (thin film): 2962, 1621, 1576, 1490, 1445, 1290, 1090, 757, 696 cm^{-1}; HRMS calc'd for $C_{32}H_{31}NCl^+$ 464.2145, observed 464.2149 $[M+H]^+$.

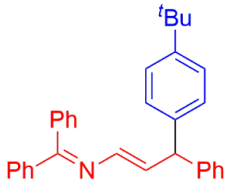


(*E*)-1-(4-(*tert*-Butyl)phenyl)-*N*-(diphenylmethylene)-3-(4-fluorophenyl)prop-2-en-1-amine (3db): The reaction was performed following General Procedure A with aldimine **1d** (31.5 mg, 0.10 mmol), $KN(SiMe_3)_2$ (30.0 mg, 0.15 mmol), aryl bromide **2b** (34.6 *μ*L, 0.20 mmol). Ratio of **3db**:**4db** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (40.3 mg, 90% yield) as a thick colorless oil. R_f = 0.79 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73–7.71 (m, 2H), 7.44–7.43 (m, 3H), 7.35–7.27 (m, 9H), 7.16 (s, 2H), 6.94 (t, *J* = 9.0 Hz, 2H), 6.45 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.34 (d, *J* = 16.0 Hz, 1H), 5.12 (d, *J* = 6.5 Hz, 1H), 1.30 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.5, 162.3 (d, $^1J_{C-F}$= 245.0 Hz), 149.9, 140.5, 140.1, 137.0, 133.6 (d, $^4J_{C-F}$= 2.5 Hz), 132.7, 130.3, 128.9, 128.7, 128.6, 128.2, 128.12, 128.11, 128.0, 127.9, 127.2, 125.6, 115.5 (d, $^2J_{C-F}$= 21.3 Hz), 68.4, 34.7, 31.6 ppm; IR (thin film): 2962, 1618, 1600, 1576, 1508, 1445, 1227, 1157, 835, 758, 697 cm^{-1}; HRMS calc'd for $C_{32}H_{31}NF^+$ 448.2441, observed 448.2436 $[M+H]^+$.

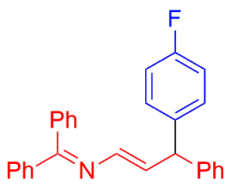


(*E*)-*N*-(Diphenylmethylene)-3, 3-diphenylprop-1-en-1-amine (4aa): The reaction was performed following General Procedure B with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2a**

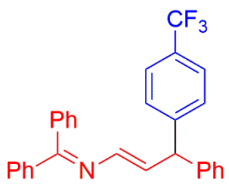
(21.4 μL, 0.20 mmol). Ratio of **4aa**:**3aa** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (32.1 mg, 86% yield) as a thick colorless oil. R_f = 0.64 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67–7.65 (m, 2H), 7.41–7.40 (m, 3H), 7.38–7.33 (m, 1H), 7.33–7.30 (m, 2H), 7.26–7.23 (m, 4H), 7.18–7.14 (m, 8H), 6.79 (d, *J* = 13.0 Hz, 1H), 6.64 (dd, *J* = 13.0, 9.0 Hz, 1H), 4.72 (d, *J* = 9.0 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 166.5, 143.9, 139.6, 139.2, 136.3, 134.7, 130.3, 128.9, 128.9, 128.8, 128.5, 128.4, 128.2, 126.4, 52.1 ppm; IR (thin film): 3059, 3025, 2962, 1596, 1553, 1492, 1445, 1318, 948, 758, 697 cm^{-1}; HRMS calc'd for $C_{28}H_{24}N^+$ 374.1909, observed 374.1910 $[M+H]^+$.



(*E*)-3-(4-(*tert*-Butyl)phenyl)-*N*-(diphenylmethylene)-3-phenylprop-1-en-1-amine (4ab): The reaction was performed following General Procedure B with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2b** (34.6 μL, 0.20 mmol). Ratio of **4ab**:**3ab** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (37.8 mg, 88% yield) as a thick colorless oil. R_f = 0.61 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67–7.65 (m, 2H), 7.41–7.35 (m, 4H), 7.33–7.30 (m, 2H), 7.27–7.24 (m, 4H), 7.20–7.15 (m, 5H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.76 (d, *J* = 13.0 Hz, 1H), 6.66 (dd, *J* = 13.0, 9.0 Hz, 1H), 4.70 (d, *J* = 9.0 Hz, 1H), 1.28 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 166.5, 149.3, 144.1, 140.9, 139.8, 139.2, 136.5, 135.2, 130.4, 129.04, 129.01, 128.9, 128.6, 128.6, 128.6, 128.3, 128.2, 126.5, 125.5, 51.9, 34.6, 31.6 ppm; IR (thin film): 2962, 1599, 1553, 1492, 1445, 1318, 1090, 947, 757, 699 cm^{-1}; HRMS calc'd for $C_{32}H_{32}N^+$ 430.2535, observed 430.2535 $[M+H]^+$.

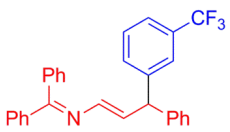


(*E*)-*N*-(Diphenylmethylene)-3-(4-fluorophenyl)-3-phenylprop-1-en-1-amine (4am): The reaction was performed following General Procedure B with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2m** (22.0 μL, 0.20 mmol). Ratio of **4am**:**3am** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (31.7 mg, 81% yield) as a thick colorless oil. R_f = 0.72 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67–7.65 (m, 2H), 7.42–7.41 (m, 3H), 7.39–7.35 (m, 1H), 7.33–7.30 (m, 2H), 7.27–7.24 (m, 2H), 7.19–7.14 (m, 5H), 7.12–7.10 (m, 2H), 6.91–6.94 (m, 2H), 6.75 (d, *J* = 13.0 Hz, 1H), 6.60 (dd, *J* = 13.0, 9.0 Hz, 1H), 4.70 (d, *J* = 9.0 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 166.9, 161.6 (d, $^1J_{C\text{-}F}$= 243.2 Hz), 143.7, 133.7 (d, $^4J_{C\text{-}F}$= 3.1 Hz), 139.6, 139.5, 136.4, 134.5, 130.5, 130.0 (d, $^3J_{C\text{-}F}$= 7.9 Hz), 129.0, 128.95, 128.93, 128.7, 128.6, 128.5, 128.3, 126.7, 115.3 (d, $^2J_{C\text{-}F}$= 21.1 Hz), 51.5 ppm; IR (thin film): 3059, 3026, 1601, 1553, 1506, 1445, 1318, 1223, 1157, 947, 7808, 697 cm^{-1}; HRMS calc'd for $C_{28}H_{23}NF^+$ 392.1815, observed 392.1817 $[M+H]^+$.

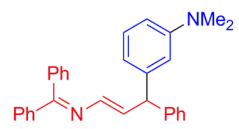


(*E*)-*N*-(Diphenylmethylene)-3-phenyl-3-(4-(trifluoromethyl)phenyl)prop-1-en-1-amine (4an): The reaction was performed following General Procedure B with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2n** (28.0 μL, 0.20 mmol). Ratio of **4an**:**3an** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (35.4 mg, 80% yield) as a thick colorless oil. R_f = 0.55 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68–7.66 (m, 2H), 7.50 (d, *J* = 8.5 Hz, 1H), 7.42–7.40 (m, 3H), 7.38–7.37 (m, 1H), 7.34–7.31 (m, 2H), 7.29–7.26 (m, 4H), 7.21–7.14 (m, 5H), 6.73 (d, *J* = 13.0 Hz, 1H), 6.60 (dd, *J* = 13.0, 9.0 Hz, 1H), 4.78 (d, *J* = 9.0 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 167.4, 148.1, 142.9, 140.1, 139.6, 136.4, 133.6, 130.7, 129.1, 129.0, 128.95, 128.91,

128.8, 128.6, 128.5, 128.4, 126.9, 125.5 (q, $J_{C\text{-}F}$= 3.7 Hz), 52.0 ppm; IR (thin film): 3060, 6027, 1617, 1600, 1553, 1493, 1445, 1325, 1165, 1123, 1067, 1018, 756, 698 cm^{-1}; HRMS calc'd for $C_{29}H_{23}NF_3^+$ 442.1783, observed 442.1784 $[M+H]^+$.

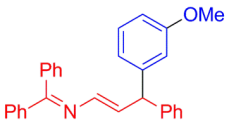


(*E*)-*N*-(Diphenylmethylene)-3-phenyl-3-(3-(trifluoromethyl)phenyl)prop-1-en-1-amine (4ao): The reaction was performed following General Procedure B with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2o** (28.0 μL, 0.20 mmol). Ratio of **4ao**:**3ao** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (35.3 mg, 80% yield) as a thick colorless oil. R_f = 0.55 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68–7.66 (m, 2H), 7.45–7.40 (m, 5H), 7.38–7.37 (m, 1H), 7.35–7.26 (m, 6H), 7.21–7.20 (m, 1H), 7.17–7.15 (m, 4H), 6.75 (d, J = 13.0 Hz, 1H), 6.60 (dd, J = 13.0, 9.0 Hz, 1H), 4.78 (d, J = 9.0 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.2, 144.8, 142.8, 139.8, 139.4, 136.2, 133.5, 131.9, 130.5, 128.95, 128.88, 128.84, 128.8, 128.7, 128.5, 128.4, 128.2, 126.8, 125.1(q, $J_{C\text{-}F}$= 3.6 Hz), 123.2(q, $J_{C\text{-}F}$= 3.9 Hz), 51.9. ppm; IR (thin film): 3060, 3026, 2962, 1596, 1554, 1493, 1445, 1329, 1165, 1125, 1074, 947, 771, 699 cm^{-1}; HRMS calc'd for $C_{29}H_{23}NF_3^+$ 442.1783, observed 442.1784 $[M+H]^+$.

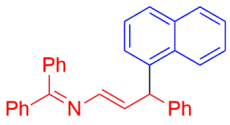


(*E*)-3-(3-((Diphenylmethylene)amino)-1-phenylallyl)-*N*,*N*-dimethylaniline (4aj): The reaction was performed following General Procedure B with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2j** (28.5 μL, 0.20 mmol). Ratio of **4aj**:**3aj** (7:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (26.2 mg, 63% yield) as a thick colorless oil. R_f = 0.42 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66–7.65 (m, 2H), 7.41–7.40 (m, 3H), 7.36–7.30 (m, 3H), 7.24–7.11 (m, 8H), 6.81 (d, J = 13.0

Hz, 1H), 6.68 (dd, *J* = 13.0, 9.0 Hz, 1H), 6.56 (d, *J* = 3.0 Hz, 3H), 4.66 (d, *J* = 9.0 Hz, 1H), 2.88 (s, 6H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 166.4, 150.9, 144.8, 144.3, 139.9, 139.2, 136.5, 135.2, 130.4, 129.3, 129.1, 129.0, 128.9, 128.6, 128.5, 128.4, 128.3, 126.3, 117.1, 112.9, 110.9, 52.7, 40.8 ppm; IR (thin film): 3057, 3024, 1599, 1577, 1493, 1444, 1318, 996, 774, 695 cm^{-1}; HRMS calc'd for $C_{30}H_{29}N_2^+$ 417.2318, observed 417.2331 $[M+H]^+$.

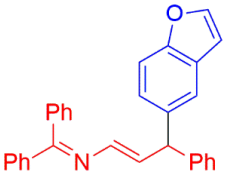


(*E*)-*N*-(Diphenylmethylene)-3-(3-methoxyphenyl)-3-phenylprop-1-en-1-amine (4ak): The reaction was performed following General Procedure B with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2k** (25.3 μL, 0.20 mmol). Ratio of **4ak**:**3ak** (3:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (24.2 mg, 60% yield) as a thick colorless oil. R_f = 0.39 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67–7.65 (m, 2H), 7.43–7.41 (m, 3H), 7.39–7.36 (m, 1H), 7.34–7.31 (m, 2H), 7.27–7.24 (m, 2H), 7.19–7.16 (m, 6H), 6.80–6.77 (m, 2H), 6.73–6.71 (m, 2H), 6.64 (dd, *J* = 13.0, 9.0 Hz, 1H), 4.69 (d, *J* = 9.0 Hz, 1H), 3.74 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 166.7, 159.9, 145.6, 143.8, 139.8, 139.41, 136.5, 134.7, 130.5, 129.6, 129.1, 129.0, 128.9, 128.6, 128.6, 128.5, 128.3, 126.6, 121.1, 114.6, 111.7, 55.4, 52.3 ppm; IR (thin film): 3058, 3025, 1597, 1583, 1489, 1445, 1260, 947, 776, 695 cm^{-1}; HRMS calc'd for $C_{30}H_{26}NO^+$ 404.2014, observed 404.2014 $[M+H]^+$.

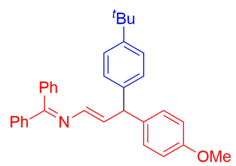


(*E*)-*N*-(Diphenylmethylene)-3-(naphthalen-1-yl)-3-phenylprop-1-en-1-amine (4ae): The reaction was performed following General Procedure B with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2e** (28.0 μL, 0.20 mmol). Ratio of **4ae**:**3ae** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (28.8 mg, 68% yield) as a thick colorless oil. R_f = 0.41 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (d,

J = 9.0 Hz, 1H), 7.81 (d, *J* = 9.0 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.65 (d, *J* = 7.5 Hz, 2H), 7.42–7.27 (m, 10H), 7.14–7.11 (m, 4H), 7.04 (d, *J* = 7.0 Hz, 1H), 6.77 (d, *J* = 13.0 Hz, 1H), 6.68 (dd, *J* = 13.0, 8.0 Hz, 1H), 5.50 (d, *J* = 8.0 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 166.7, 143.5, 140.0, 139.7, 139.4, 136.2, 134.7, 134.2, 131.7, 130.5, 129.1, 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 127.53, 126.51, 126.50, 126.1, 125.58, 125.56, 124.4, 48.6 ppm; IR (thin film): 3058, 3025, 1597, 1583, 1491, 1444, 1318, 1298, 1216, 953, 778, 698 cm^{-1}; HRMS calc'd for $C_{32}H_{26}N^{+}$ 424.2065, observed 424.2058 $[M+H]^{+}$.

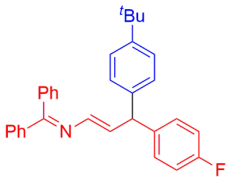


(*E*)-3-(Benzofuran-5-yl)-*N*-(diphenylmethylene)-3-phenylprop-1-en-1-amine (4ag): The reaction was performed following General Procedure B with aldimine **1a** (29.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2g** (25.1 μL, 0.20 mmol). Ratio of **4ag**:**3ag** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (29.7 mg, 72% yield) as a thick colorless oil. R_f = 0.40 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.0 Hz, 1H), 7.58 (d, *J* = 2.0 Hz, 1H) , 7.41–7.37 (m, 6H), 7.34–7.31 (m, 2H), 7.28–7.25 (m, 2H), 7.20–7.15 (m, 5H), 7.10 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.79 (d, *J* = 13.0 Hz, 1H), 6.71–6.67 (m, 2H), 4.83 (d, *J* = 9.0 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 166.7, 153.9, 145.4, 144.4, 139.8, 139.4, 138.7, 136.5, 135.2, 130.5, 129.1, 129.0, 128.9, 128.61, 128.57, 128.3, 127.7, 126.5, 125.2, 120.8, 111.4, 106.8, 52.1 ppm; IR (thin film): 3058, 3024, 1599, 1553, 1464, 1444, 1318, 1298, 1126, 947, 768, 698 cm^{-1}; HRMS calc'd for $C_{30}H_{24}NO^{+}$ 414.1858, observed 414.1864 $[M+H]^{+}$.

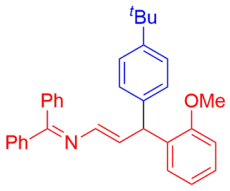


(*E*)-1-(4-(*tert*-Butyl)phenyl)-*N*-(diphenylmethylene)-3-(4-methoxyphenyl)prop-2-en-1-amine (4bb): The reaction was performed following General Procedure B with aldimine **1b** (32.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2b** (34.6 μL, 0.20 mmol). Ratio of **4bb**:**3bb**

(>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (32.1 mg, 70% yield) as a thick colorless oil. R_f = 0.40 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66–7.65 (m, 2H), 7.42–7.39 (m, 3H), 7.37–7.34 (m, 1H), 7.32–7.29 (m, 2H), 7.27–7.25 (m, 2H), 7.16–7.14 (m, 2H), 7.09 (t, *J* = 8.5 Hz, 4H), 6.80 (d, *J* = 8.5 Hz, 2H), 6.74 (d, *J* = 13.0 Hz, 1H), 6.63 (dd, *J* = 13.0, 9.0 Hz, 1H), 4.64 (d, *J* = 9.0 Hz, 1H), 3.75 (s, 3H), 1.27 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 166.4, 158.2, 149.2, 141.1, 139.8, 139.0, 136.5, 136.3, 135.5, 130.4, 129.5, 129.01, 129.00, 128.8, 128.6, 128.3, 128.1, 125.4, 113.9, 55.4, 51.0, 34.5, 31.6 ppm; IR (thin film): 3057, 3024, 2961, 1608, 1583, 1553, 1509, 1462, 1444, 1318, 1249, 1177, 1035, 946, 757, 694 cm^{-1}; HRMS calc'd for $C_{33}H_{34}NO^{+}$ 460.2640, observed 460.2626 $[M+H]^{+}$.



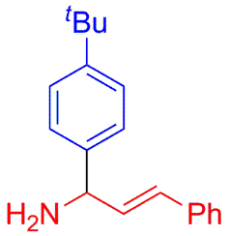
(*E*)-3-(4-(tert-Butyl)phenyl)-*N*-(diphenylmethylene)-3-(4-fluorophenyl)prop-1-en-1-amine (4db): The reaction was performed following General Procedure B with aldimine **1d** (31.5 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2b** (34.6 μL, 0.20 mmol). Ratio of **4db**:**3db** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (37.5 mg, 84% yield) as a thick colorless oil. R_f = 0.80 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67–7.65 (m, 2H), 7.42–7.36 (m, 4H), 7.33–7.31 (m, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.16–7.12 (m, 4H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.93 (t, *J* = 9.0 Hz, 2H), 6.72 (d, *J* = 13.0 Hz, 1H), 6.60 (dd, *J* = 13.0, 9.0 Hz, 1H), 4.69 (d, *J* = 9.0 Hz, 1H), 1.28 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 166.6, 161.5 (d, $^{1}J_{C\text{-}F}$= 243.1 Hz), 149.3, 140.4, 139.7 (d, $^{4}J_{C\text{-}F}$= 3.1 Hz), 139.5, 139.2, 136.3, 134.8, 130.3, 129.9 (d, $^{3}J_{C\text{-}F}$= 7.9 Hz), 128.9, 128.8, 128.7, 128.4, 128.2, 127.9, 125.4, 115.1 (d, $^{2}J_{C\text{-}F}$= 21.0 Hz), 50.9, 34.4, 31.4 ppm; IR (thin film): 2962, 1602, 1553, 1506, 1445, 1222, 1157, 832, 702, 694 cm^{-1}; HRMS calc'd for $C_{32}H_{31}NF^{+}$ 448.2441, observed 448.2436 $[M+H]^{+}$.



(*E*)-3-(4-(*tert*-Butyl)phenyl)-*N*-(diphenylmethylene)-3-(2-methoxyphenyl)prop-1-en-1-amine (4eb): The reaction was performed following General Procedure B with aldimine **1e** (32.7 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (27.5 mg, 0.15 mmol), aryl bromide **2b** (34.6 μL, 0.20 mmol). Ratio of **4eb**:**3eb** (>20:1) was determined by ^{1}H NMR spectroscopy. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (34.0 mg, 74% yield) as a thick colorless oil. R_f = 0.48 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66–7.64 (m, 2H), 7.39–7.38 (m, 3H), 7.35–7.34 (m, 1H), 7.32–7.29 (m, 2H), 7.22–7.14 (m, 6H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.89 (td, *J* = 7.5, 1.0 Hz, 1H), 6.80 (d, *J* = 6.5 Hz, 1H), 6.73 (d, *J* = 13.0 Hz, 1H), 6.66 (dd, *J* = 13.0, 9.0 Hz, 1H), 5.12 (d, *J* = 9.0 Hz, 1H), 3.69 (s, 3H), 1.26 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 166.0, 156.9, 148.8, 140.7, 139.9, 139.3, 136.6, 135.2, 132.5, 130.3, 129.3, 129.0, 129.0, 128.7, 128.5, 128.3, 128.1, 127.6, 125.2, 120.7, 110.9, 55.6, 44.7, 34.5, 31.6 ppm; IR (thin film): 2961, 1597, 1584, 1553, 1490, 1444, 1318, 1244, 1029, 948, 753, 695 cm^{-1}; HRMS calc'd for $C_{33}H_{34}NO^+$ 460.2640, observed 460.2635 $[M+H]^+$.

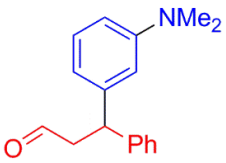
Product hydrolysis:

Hydrolysis of Product 3ab: An oven-dried microwave vial equipped with a stir bar was charged with **3ab** (43.0 mg 0.1 mmol). HCl 1N (1 mL) and MeOH (1 mL) were added to the reaction vial via syringe at 0 °C. The solution was warmed to room temperature, stirred at room temperature and was monitored by TLC until all **4ab** was consumed (Reaction completed in 3 h). The reaction mixture was transferred to a 10 mL seperatory funnel via pipette and was extracted with dichloromethane (3X2 mL). The aqueous layer was then basified with 1N NaOH till pH=10 and was extracted with dichloromethane (3X2 mL). The combined organic layers were concentrated in *vacuo*. After drying under vacuum for 12 h, the amine product **8ab** was obtained as a yellow oil (26.3 mg, 99% yield).



8ab-(E)-1-(4-(*tert*-butyl)phenyl)-3-phenylprop-2-en-1-amine: R_f = 0.20 (ethyl acetate:methanol = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38–7.37 (m, 4H), 7.34–7.33 (m, 2H), 7.23–7.27 (m, 2H), 7.22–7.19 (m, 1H), 6.60 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 4.69 (d, *J* = 6.5 Hz, 1H), 1.77 (s, br, 2H), 1.32 (s, 9H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.4, 141.7, 137.2, 134.1, 129.2, 128.7, 127.60, 126.62, 126.55, 125.8, 57.9, 34.7, 31.6. ppm; IR (thin film): 3293, 3057, 2962, 2866, 1676, 1599, 1508, 1494, 1462, 1448, 1363, 1269, 1109, 965, 830, 751, 694 cm^{-1}; HRMS calc'd for $C_{19}H_{21}$ 249.1643, observed 249.1643 $[M\text{-}NH_2]^+$.

Hydrolysis of Product 4aj: An oven-dried microwave vial equipped with a stir bar was charged with **4aj** (41.7 mg 0.1 mmol). HCl 1N (1 mL) and MeOH (1 mL) was added to the reaction vial via syringe at 0°C. The solution was stirred at 0 °C and was monitored by TLC until all **4aj** was consumed (Reaction completed in 15 min). The reaction mixture was transferred to a 10ml seperatory funnel via pipette and was extracted with dichloromethane (3X2 mL). The aqueous layer was then basified with 1N NaOH till pH=10 and was extracted with dichloromethane (3X2 mL). The combined organic layers were concentrated in *vacuo*. After drying under vacuum for 12 h, the aldehyde product **9aj** was obtained as a colorless oil (24.1 mg, 95%yield).



9aj-3-(3-(dimethylamino)phenyl)-3-phenylpropanal: R_f = 0.15 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.73 (t, *J* = 2.0 Hz, 1H), 7.29–7.27 (m, 2H), 7.25–7.24 (m, 1H), 7.20–7.14 (m, 3H), 6.59–6.57 (m, 3H), 4.55 (t, *J* = 8.0 Hz, 1H), 3.14 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 2H), 2.91 (s, 6H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 201.7, 151.0, 144.2, 143.7, 129.6, 128.8, 127.9, 126.8, 115.9, 112.3, 111.1, 49.7, 45.7, 40.7 ppm; IR (thin film): 3058, 3026, 2884，2807，2726， 1723， 1600，1578, 1497, 1438, 1353, 996, 701 cm^{-1}; HRMS calc'd for $C_{17}H_{20}NO^+$ 254.1545, observed 254.1540 $[M+H]^+$.

High-throughput experimentation screenings for Pd-catalyzed chemo- and regioselective arylation:

(1) Screening of ligand, solvent and temperature:

Set up:

24-Well Plate A (24 ligand, THF, room temperature):

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials was predosed with $Pd(OAc)_2$ (1 μmol) and the phosphine ligands (2 μmol for monodentate ligands and 1 μmol for bidentate ligands) in THF. The solvent was removed to dryness using a GeneVac and $KN(SiMe_3)_2$ (30 μmol) in THF was added to the ligand/catalyst mixture. The solvent was removed on the GeneVac and a parylene stir bar was then added to each reaction vial. Aldimine 1a (10 μmol/reaction) and bromobenzene (20 μmol) were then dosed together into each reaction vial as a solution in THF (100 μL, 0.1 M). The 24-well plate was then sealed and stirred for 12 h at room temperature.

24-Well Plate B (24 Ligand, THF, 60 ^{o}C):

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials was predosed with $Pd(OAc)_2$ (1 μmol) and the phosphine ligands (2 μmol for monodentate ligands and 1 μmol for bidentate ligands) in THF. The solvent was removed to dryness using a GeneVac and $KN(SiMe_3)_2$ (30 μmol) in THF was added to the ligand/catalyst mixture. The solvent was removed on the GeneVac and a parylene stir bar was then added to each reaction vial. Aldimine 1a (10 μmol/reaction), bromobenzene (20 μmol) were then dosed together into each reaction vial as a solution in THF (100 μL, 0.1 M). The 24-well plate was then sealed and stirred for 12 h at 60 ^{o}C.

24-Well Plate C (24 Ligand, CPME, Room Temperature):

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials was predosed with $Pd(OAc)_2$ (1 μmol) and the phosphine

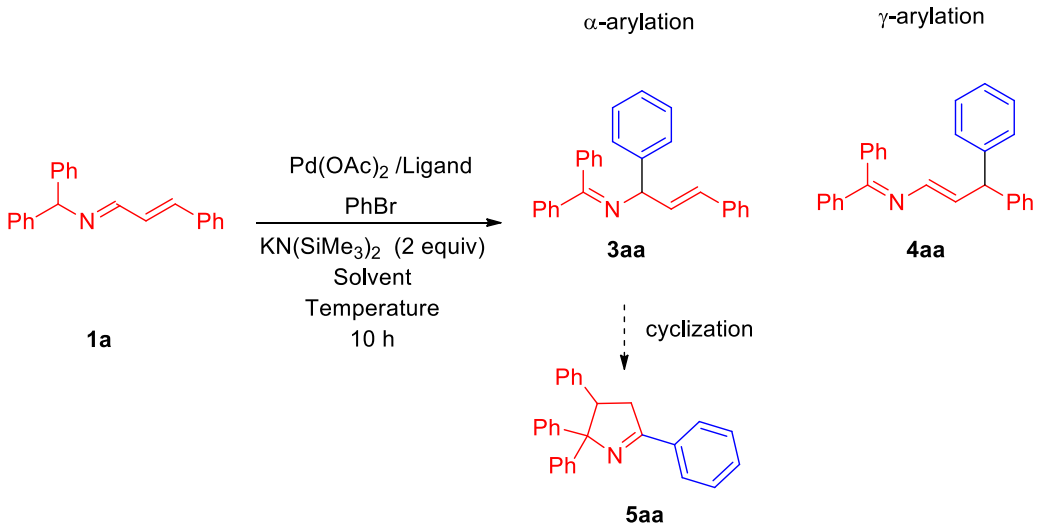
ligands (2 μmol for monodentate ligands and 1 μmol for bidentate ligands) in THF. The solvent was removed to dryness using a GeneVac and $KN(SiMe_3)_2$ (30 μmol) in THF was added to the ligand/catalyst mixture. The solvent was removed on the GeneVac and a parylene stir bar was then added to each reaction vial. Aldimine **1a** (10 μmol/reaction), bromobenzene (20 μmol) were then dosed together into each reaction vial as a solution in CPME (100 μL, 0.1 M). The 24-well plate was then sealed and stirred for 12 h at room temperature.

24-Well Plate D (24 Ligand, CPME, 60 ^{o}C):

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials was predosed with $Pd(OAc)_2$ (1 μmol) and the phosphine ligands (2 μmol for monodentate ligands and 1 μmol for bidentate ligands) in THF. The solvent was removed to dryness using a GeneVac and $KN(SiMe_3)_2$ (30 μmol) in THF was added to the ligand/catalyst mixture. The solvent was removed on the GeneVac and a parylene stir bar was then added to each reaction vial. Aldimine **1a** (10 μmol/reaction), bromobenzene (20 μmol) were then dosed together into each reaction vial as a solution in CPME (100 μL, 0.1 M). The 24-well plate was then sealed and stirred for 12 h at 60 ^{o}C.

Work up:

Upon opening the plate to air, 500 μL of a solution of 4,4'-di-*tert*-butyl diphenyl (used as internal standard to measure HPLC yields) in acetonitrile (0.002 mol/L) was added into each vial. The plate was covered again and the vials stirred for 10 min. to ensure good homogenization. Into a separate 96-well LC block was added 700 μL of acetonitrile, followed by 25 μL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated HPLC instrument for analysis.



THF, 60 °C

Ligand	5aa/IS	3aa/IS	3aa+5aa/IS	4aa/IS
2-(Di-*tert*-butylphosphino)biphenyl (JohnPhos)	1.38	0.83	2.21	0.09
4-(Di-*tert*-butylphosphino)-N,N-dimethylaniline (Ataphos)	5.52	0.30	5.83	1.69
2-Dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (Dave Phos)	3.40	0.52	3.92	0.62
2-Di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropyl-1,1'-biphenyl (Me4tBuXPhos)	0.35	1.02	1.37	0.00
Dicyclohexyl-[3,6-dimethoxy-2-(2,4,6-triisopropylphenyl)phenyl]phosphane (BrettPhos)	0.15	0.03	0.19	0.02
1,1'-Bis(diphenylphosphino)ferrocene (Dppf)	0.08	0.05	0.13	0.11
9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (XantPhos)	0.49	0.45	0.94	0.92
2-Dicyclohexylphosphino-2′-methylbiphenyl (MePhos)	3.92	0.69	4.61	0.12
N-(dicyclohexylphosphino)-2-2'-tolylindole (Indole ligand)	1.94	0.67	2.61	0.50
P(O-Tol)3	0.69	0.10	0.79	1.05
$P^tBu_3HBF_4$	5.15	0.55	5.69	0.36

2-(Dicyclohexylphosphino)-1-phenyl-1H-pyrrole (CataCXium Pcy)	4.04	0.64	4.67	0.60
4,6-Bis(diphenylphosphino)phenoxazine (NIXANTPHOS)	0.63	0.52	1.15	2.48
Di(1-adamantyl)-2-dimethylaminophenylphosphine (Me-Dalphos)	0.09	0.10	0.19	0.00
2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (Sphos)	0.37	0.03	0.41	0.04
Butyldi-1-adamantylphosphine (CataCXium A)	4.39	0.47	4.86	1.87
PCy_3HBF_4	3.37	0.42	3.79	1.32
2-Di-*tert*-butylphosphino-3-Methoxy-6-Methyl-2'-4'-6'-triisopropylbiphenyl (RockPhos)	0.05	0.02	0.08	0.00
1,2,3,4,5-Pentaphenyl-1'-(di-t-butylphosphino)ferrocene (Qphos)	2.04	0.63	2.67	0.42
PPh_3	0.67	0.90	1.56	0.38
1-[2-[Bis(tert-butyl)phosphino]phenyl]-3,5-diphenyl-1H-pyrazole (Trippy Phos)	0.85	0.98	1.83	0.17
2-(Dicyclohexylphosphino)biphenyl (CyJohnPhos)	3.85	0.50	4.34	0.65
2-Dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl (Xphos)	1.81	0.23	2.04	1.96
Di(1-adamantyl)-2-morpholinophenylphosphine (Mor-DalPhos)	1.61	0.51	2.12	0.41

THF, rt

Ligand	5aa/IS	3aa/IS	3aa+5aa/IS	4aa/IS
2-(Di-*tert*-butylphosphino)biphenyl (JohnPhos)	2.06	0.33	2.40	0.00
4-(Di-*tert*-butylphosphino)-N,N-dimethylaniline (Ataphos)	3.12	0.42	3.54	0.15
2-Dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (Dave Phos)	3.96	0.40	4.36	0.00
2-Di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropyl-1,1'-biphenyl (Me4tBuXPhos)	0.27	0.59	0.86	0.00
Dicyclohexyl-[3,6-dimethoxy-2-(2,4,6-	0.20	0.82	1.02	0.30

triisopropylphenyl)phenyl]phosphane (BrettPhos)				
1,1'-Bis(diphenylphosphino)ferrocene (Dppf)	0.21	0.33	0.55	0.00
9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (XantPhos)	3.65	1.12	4.77	1.09
2-Dicyclohexylphosphino-2′-methylbiphenyl (MePhos)	3.55	0.35	3.91	0.06
N-(dicyclohexylphosphino)-2-2'-tolylindole (Indole ligand)	0.70	0.27	0.97	0.00
P(O-Tol)3	0.23	0.27	0.49	0.78
$P^tBu_3HBF_4$	5.08	0.60	5.68	0.33
2-(Dicyclohexylphosphino)-1-phenyl-1H-pyrrole (CataCXium Pcy)	1.01	0.27	1.28	0.00
4,6-Bis(diphenylphosphino)phenoxazine (NIXANTPHOS)	0.51	0.00	0.51	2.77
Di(1-adamantyl)-2-dimethylaminophenylphosphine (Me-Dalphos)	0.04	0.92	0.96	0.10
2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (Sphos)	0.85	0.27	1.13	0.05
Butyldi-1-adamantylphosphine (CataCXium A)	3.72	0.35	4.07	0.29
PCy_3HBF_4	0.42	0.26	0.68	0.00
2-Di-*tert*-butylphosphino-3-Methoxy-6-Methyl-2'-4'-6'-triisopropylbiphenyl (RockPhos)	0.27	0.48	0.75	0.00
1,2,3,4,5-Pentaphenyl-1'-(di-t-butylphosphino)ferrocene (Qphos)	2.69	0.42	3.11	0.68
PPh_3	0.21	0.42	0.64	0.00
1-[2-[Bis(tert-butyl)phosphino]phenyl]-3,5-diphenyl-1H-pyrazole (Trippy Phos)	0.51	0.31	0.81	0.00
2-(Dicyclohexylphosphino)biphenyl (CyJohnPhos)	1.15	0.25	1.40	0.00
2-Dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl (Xphos)	0.91	0.34	1.24	0.23
Di(1-adamantyl)-2-morpholinophenylphosphine (Mor-DalPhos)	0.90	0.41	1.31	0.00

CPME, 60 ^{o}C

Ligand	5aa/IS	3aa/IS	3aa+5aa/IS	4aa/IS
2-(Di-*tert*-butylphosphino)biphenyl (JohnPhos)	0.81	0.38	1.19	0.00
4-(Di-*tert*-butylphosphino)-N,N-dimethylaniline (Ataphos)	4.24	0.23	4.46	1.39
2-Dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (Dave Phos)	3.51	0.40	3.91	0.49
2-Di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropyl-1,1'-biphenyl (Me4tBuXPhos)	0.13	0.56	0.69	0.07
Dicyclohexyl-[3,6-dimethoxy-2-(2,4,6-triisopropylphenyl)phenyl]phosphane (BrettPhos)	0.07	0.58	0.65	0.00
1,1'-Bis(diphenylphosphino)ferrocene (Dppf)	0.37	0.49	0.86	0.13
9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (XantPhos)	5.08	0.70	5.78	1.16
2-Dicyclohexylphosphino-2′-methylbiphenyl (MePhos)	3.98	0.40	4.39	0.68
N-(dicyclohexylphosphino)-2-2'-tolylindole (Indole ligand)	1.73	0.32	2.05	0.82
P(O-Tol)3	0.38	0.41	0.78	1.02
$P^tBu_3HBF_4$	6.49	0.37	6.86	0.88
2-(Dicyclohexylphosphino)-1-phenyl-1H-pyrrole (CataCXium Pcy)	3.30	0.46	3.76	0.53
4,6-Bis(diphenylphosphino)phenoxazine (NIXANTPHOS)	0.25	0.46	0.71	1.08
Di(1-adamantyl)-2-dimethylaminophenylphosphine (Me-Dalphos)	1.08	0.20	1.29	0.16
2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (Sphos)	1.43	0.30	1.73	1.02
Butyldi-1-adamantylphosphine (CataCXium A)	3.82	0.23	4.05	1.64
PCy_3HBF_4	2.83	0.10	2.93	0.62
2-Di-*tert*-butylphosphino-3-Methoxy-6-Methyl-2'-4'-6'-triisopropylbiphenyl (RockPhos)	0.10	0.49	0.59	0.00
1,2,3,4,5-Pentaphenyl-1'-(di-t-	2.77	0.34	3.11	0.43

butylphosphino)ferrocene (Qphos)				
PPh_3	0.49	0.57	1.06	0.12
1-[2-[Bis(tert-butyl)phosphino]phenyl]-3,5-diphenyl-1H-pyrazole (Trippy Phos)	0.57	0.41	0.98	0.27
2-(Dicyclohexylphosphino)biphenyl (CyJohnPhos)	3.20	0.35	3.55	0.59
2-Dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl (Xphos)	0.60	0.34	0.94	0.41
Di(1-adamantyl)-2-morpholinophenylphosphine (Mor-DalPhos)	0.94	0.51	1.45	0.25

CPME, rt

Ligand	5aa/IS	3aa/IS	3aa+5aa/IS	4aa/IS
2-(Di-*tert*-butylphosphino)biphenyl (JohnPhos)	1.25	0.43	1.68	0.00
4-(Di-*tert*-butylphosphino)-N,N-dimethylaniline (Ataphos)	1.21	0.16	1.38	0.00
2-Dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (Dave Phos)	4.34	0.50	4.83	0.00
2-Di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropyl-1,1'-biphenyl (Me4tBuXPhos)	0.08	0.49	0.57	0.00
Dicyclohexyl-[3,6-dimethoxy-2-(2,4,6-triisopropylphenyl)phenyl]phosphane (BrettPhos)	0.00	0.41	0.41	0.00
1,1'-Bis(diphenylphosphino)ferrocene (Dppf)	0.21	0.18	0.39	0.00
9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (XantPhos)	4.43	0.60	5.03	0.12
2-Dicyclohexylphosphino-2′-methylbiphenyl (MePhos)	3.63	0.34	3.96	0.00
N-(dicyclohexylphosphino)-2-2'-tolylindole (Indole ligand)	0.31	0.00	0.31	0.00
P(O-Tol)3	0.24	0.41	0.65	0.76
$P^tBu_3HBF_4$	6.22	0.42	6.64	0.06
2-(Dicyclohexylphosphino)-1-phenyl-1H-pyrrole (CataCXium Pcy)	0.67	0.16	0.83	0.00

4,6-Bis(diphenylphosphino)phenoxazine (NIXANTPHOS)	0.00	2.00	2.00	0.00
Di(1-adamantyl)-2-dimethylaminophenylphosphine (Me-Dalphos)	0.08	0.40	0.48	0.00
2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (Sphos)	0.88	0.31	1.18	0.04
Butyldi-1-adamantylphosphine (CataCXium A)	1.19	0.18	1.37	0.00
PCy_3HBF_4	0.55	0.06	0.61	0.00
2-Di-*tert*-butylphosphino-3-Methoxy-6-Methyl-2'-4'-6'-triisopropylbiphenyl (RockPhos)	0.00	0.34	0.34	0.00
1,2,3,4,5-Pentaphenyl-1'-(di-t-butylphosphino)ferrocene (Qphos)	4.20	0.35	4.55	0.45
PPh_3	0.29	0.37	0.66	0.00
1-[2-[Bis(tert-butyl)phosphino]phenyl]-3,5-diphenyl-1H-pyrazole (Trippy Phos)	0.43	0.45	0.88	0.00
2-(Dicyclohexylphosphino)biphenyl (CyJohnPhos)	1.04	0.14	1.18	0.32
2-Dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl (Xphos)	0.50	0.53	1.04	0.14
Di(1-adamantyl)-2-morpholinophenylphosphine (Mor-DalPhos)	0.78	0.38	1.16	0.44

(2) Screening of Palladium, Ligand, Solvent and Base:

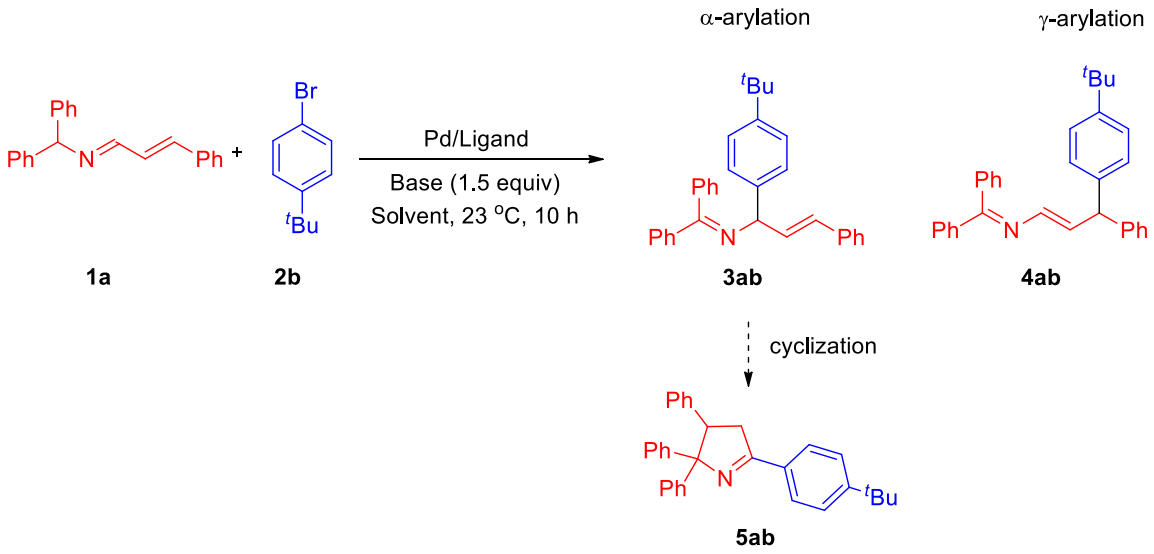
Set up:

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 96-well aluminum block containing 1 mL glass vials was predosed with $Pd(OAc)_2$ (2μmol), $Pd(dba)_2$ (2 μmol), Allylpalladium(II) chloride dimer (1 μmol), (2-Methylallyl)palladium(II) chloride dimer (1 μmol) and three phosphine ligands: Tri-*tert*-butylphosphonium tetrafluoroborate (3 μmol), XantPhos (3μmol), NIXANTPHOS (3 μmol) in THF. The solvent was removed to dryness using a GeneVac and aldimine **1a** (20 μmol) in THF was added to the ligand/catalyst mixture. The solvent was

removed on the GeneVac and a parylene stir bar was then added to each reaction vial. 4-*tert*-butyl bromobenzene (40 μmol) was then dosed into each reaction vial as a solution in 4 different solvents (CPME, DME, THF, toluene, 100 μL, 0.2 M). $NaN(SiMe_3)_2$ (30 μmol) and $KN(SiMe_3)_2$ (30 μmol) were finally dosed into each reaction vial as a solution in 4 different solvents (CPME, DME, THF, toluene, 100 μL, 0.2 M). Total reaction concentration is 0.1 M (200 μL). The 24-well plate was then sealed and stirred for 12 h at room temperature.

Work up:

Upon opening the plate to air, 500 μL of a solution of biphenyl (used as internal standard to measure HPLC yields) in acetonitrile (0.001 mol/L) was added into each vial. The plate was covered again and the vials stirred for 10 min. to ensure good homogenization. Into a separate 96-well LC block was added 700 μL of acetonitrile, followed by 25 μL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated HPLC instrument for analysis.



THF

Ligand	Pd	Base	3ab/IS	4ab/IS	5ab/ IS
$P^tBu_3HBF_4$	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	0.00	0.00	0.00
$P^tBu_3HBF_4$	$Pd(dba)_2$	$NaN(SiMe_3)_2$	2.85	0.00	1.30
$P^tBu_3HBF_4$	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	2.90	0.00	1.61
$P^tBu_3HBF_4$	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	17.53	5.38	1.83
XantPhos	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	2.78	0.00	0.00
XantPhos	$Pd(dba)_2$	$NaN(SiMe_3)_2$	2.61	0.00	0.00
XantPhos	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	1.67	0.00	1.41
XantPhos	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	15.19	8.62	0.00
NIXANTPHOS	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	3.20	1.68	0.00
NIXANTPHOS	$Pd(dba)_2$	$NaN(SiMe_3)_2$	3.08	1.48	0.00
NIXANTPHOS	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	3.80	0.51	0.00
NIXANTPHOS	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	2.86	3.45	0.00
$P^tBu_3HBF_4$	$Pd(OAc)_2$	$KN(SiMe_3)_2$	3.53	0.00	2.10
$P^tBu_3HBF_4$	$Pd(dba)_2$	$KN(SiMe_3)_2$	1.72	0.00	1.36
$P^tBu_3HBF_4$	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	1.77	0.00	13.36
$P^tBu_3HBF_4$	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	8.99	0.00	15.64
XantPhos	$Pd(OAc)_2$	$KN(SiMe_3)_2$	2.47	0.00	3.43
XantPhos	$Pd(dba)_2$	$KN(SiMe_3)_2$	1.62	0.00	1.54
XantPhos	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	1.94	0.00	2.14
XantPhos	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	10.22	0.00	2.61
NIXANTPHOS	$Pd(OAc)_2$	$KN(SiMe_3)_2$	0.00	2.51	1.59
NIXANTPHOS	$Pd(dba)_2$	$KN(SiMe_3)_2$	0.51	0.00	0.00
NIXANTPHOS	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	0.00	1.63	1.39
NIXANTPHOS	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	1.29	0.00	0.19

CPME

Ligand	Pd	Base	3ab/IS	4ab/IS	5ab/ IS
$P^tBu_3HBF_4$	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	0.29	0.00	0.14
$P^tBu_3HBF_4$	$Pd(dba)_2$	$NaN(SiMe_3)_2$	1.15	0.21	0.11
$P^tBu_3HBF_4$	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	0.72	0.00	0.17
$P^tBu_3HBF_4$	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	16.03	5.84	0.96
XantPhos	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	10.37	10.45	0.60
XantPhos	$Pd(dba)_2$	$NaN(SiMe_3)_2$	9.41	7.44	0.00
XantPhos	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	3.51	0.00	0.00
XantPhos	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	4.41	0.00	0.00
NIXANTPHOS	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	2.46	26.44	0.00
NIXANTPHOS	$Pd(dba)_2$	$NaN(SiMe_3)_2$	22.04	16.54	0.00
NIXANTPHOS	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	0.00	15.50	0.00
NIXANTPHOS	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	0.00	23.76	0.00
$P^tBu_3HBF_4$	$Pd(OAc)_2$	$KN(SiMe_3)_2$	0.00	0.00	5.03
$P^tBu_3HBF_4$	$Pd(dba)_2$	$KN(SiMe_3)_2$	3.92	0.00	10.78
$P^tBu_3HBF_4$	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	3.51	0.00	16.57
$P^tBu_3HBF_4$	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	5.19	0.00	14.20
XantPhos	$Pd(OAc)_2$	$KN(SiMe_3)_2$	2.44	0.00	3.37
XantPhos	$Pd(dba)_2$	$KN(SiMe_3)_2$	2.47	0.00	0.97
XantPhos	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	2.31	0.00	1.40
XantPhos	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	17.98	1.59	3.90
NIXANTPHOS	$Pd(OAc)_2$	$KN(SiMe_3)_2$	0.00	2.89	0.00
NIXANTPHOS	$Pd(dba)_2$	$KN(SiMe_3)_2$	0.00	6.26	0.00
NIXANTPHOS	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	0.53	4.99	0.00
NIXANTPHOS	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	0.00	6.49	0.00

DME

Ligand	Pd	Base	3ab/IS	4ab/IS	5ab/ IS
$P^tBu_3HBF_4$	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	0.00	0.00	1.70
$P^tBu_3HBF_4$	$Pd(dba)_2$	$NaN(SiMe_3)_2$	2.92	0.00	2.05
$P^tBu_3HBF_4$	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	2.43	0.00	1.93
$P^tBu_3HBF_4$	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	5.88	0.00	0.00
XantPhos	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	4.12	0.00	0.00
XantPhos	$Pd(dba)_2$	$NaN(SiMe_3)_2$	2.47	0.00	0.00
XantPhos	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	3.83	0.00	0.00
XantPhos	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	15.14	1.69	1.50
NIXANTPHOS	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	4.21	0.00	0.00
NIXANTPHOS	$Pd(dba)_2$	$NaN(SiMe_3)_2$	3.28	0.00	0.00
NIXANTPHOS	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	0.00	6.19	0.68
NIXANTPHOS	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	0.00	0.43	0.00
$P^tBu_3HBF_4$	$Pd(OAc)_2$	$KN(SiMe_3)_2$	2.59	0.00	2.51
$P^tBu_3HBF_4$	$Pd(dba)_2$	$KN(SiMe_3)_2$	2.07	0.00	2.98
$P^tBu_3HBF_4$	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	1.09	0.00	0.75
$P^tBu_3HBF_4$	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	1.38	0.00	2.55
XantPhos	$Pd(OAc)_2$	$KN(SiMe_3)_2$	2.06	0.00	2.45
XantPhos	$Pd(dba)_2$	$KN(SiMe_3)_2$	1.69	0.00	2.27
XantPhos	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	1.76	0.00	0.92
XantPhos	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	0.72	0.00	4.02
NIXANTPHOS	$Pd(OAc)_2$	$KN(SiMe_3)_2$	0.00	0.00	0.93
NIXANTPHOS	$Pd(dba)_2$	$KN(SiMe_3)_2$	0.00	1.57	0.73
NIXANTPHOS	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	0.00	1.35	0.00
NIXANTPHOS	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	0.00	2.30	0.00

Toluene

Ligand	Pd	Base	3ab/IS	4ab/IS	5ab/ IS
$P^tBu_3HBF_4$	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	9.58	5.82	0.00
$P^tBu_3HBF_4$	$Pd(dba)_2$	$NaN(SiMe_3)_2$	18.57	12.16	0.00
$P^tBu_3HBF_4$	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	14.10	8.90	0.00
$P^tBu_3HBF_4$	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	9.85	4.45	0.00
XantPhos	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	1.99	0.00	0.00
XantPhos	$Pd(dba)_2$	$NaN(SiMe_3)_2$	0.65	0.00	0.00
XantPhos	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	0.00	0.00	0.00
XantPhos	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	17.93	10.21	0.00
NIXANTPHOS	$Pd(OAc)_2$	$NaN(SiMe_3)_2$	0.00	22.10	0.00
NIXANTPHOS	$Pd(dba)_2$	$NaN(SiMe_3)_2$	0.00	30.33	0.00
NIXANTPHOS	$[ClPd(allyl)]_2$	$NaN(SiMe_3)_2$	0.00	23.63	0.00
NIXANTPHOS	$[ClPd(2\text{-methallyl})]_2$	$NaN(SiMe_3)_2$	0.00	27.08	0.00
$P^tBu_3HBF_4$	$Pd(OAc)_2$	$KN(SiMe_3)_2$	15.97	0.43	5.01
$P^tBu_3HBF_4$	$Pd(dba)_2$	$KN(SiMe_3)_2$	20.50	0.00	2.45
$P^tBu_3HBF_4$	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	15.46	0.00	0.00
$P^tBu_3HBF_4$	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	28.38	0.46	0.00
XantPhos	$Pd(OAc)_2$	$KN(SiMe_3)_2$	13.13	0.00	5.43
XantPhos	$Pd(dba)_2$	$KN(SiMe_3)_2$	2.39	0.00	1.52
XantPhos	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	0.00	0.00	0.00
XantPhos	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	3.87	0.00	0.00
NIXANTPHOS	$Pd(OAc)_2$	$KN(SiMe_3)_2$	2.24	0.00	0.00
NIXANTPHOS	$Pd(dba)_2$	$KN(SiMe_3)_2$	0.00	5.34	0.00
NIXANTPHOS	$[ClPd(allyl)]_2$	$KN(SiMe_3)_2$	1.27	0.00	0.00
NIXANTPHOS	$[ClPd(2\text{-methallyl})]_2$	$KN(SiMe_3)_2$	1.55	0.91	0.00

2.5. Acknowledgement

I would like to thank Dr. María González-Esguevillas, Dr. Ana Bellomo, Prof. Xiaodong Yang for their collaboration and contribution. María and Ana conducted the HTE screening of Scheme 2.2. Prof. Xiaodong synthesized the *N*-Bn-NIXANTPHOS listed in Scheme 2.5.

2.6. References

1. (a) Stütz, A., *Angew. Chem. Int. Ed.* **1987,** *26*, 320; (b) Stutz, A.; Georgopoulos, A.; Granitzer, W.; Petranyi, G.; Berney, D., *J. Med. Chem.* **1986,** *29*, 112; (c) Nanavati, S. M.; Silverman, R. B., *J. Am. Chem. Soc.* **1991,** *113*, 9341; (d) Petranyi, G.; Ryder, N. S.; Stutz, A., *Science* **1984,** *224*, 1239; (e) *Olesen, J. J Neurol* ***1991****, 238, S23.*

2. (a) Burgess, K.; Liu, L. T.; Pal, B., *J. Org. Chem.* **1993,** *58*, 4758; (b) Trost, B. M.; Vanvranken, D. L., *J. Am. Chem. Soc.* **1993,** *115*, 444; (c) Paquette, L. A.; Leit, S. M., *J. Am. Chem. Soc.* **1999,** *121*, 8126; (d) Nagashima, H.; Isono, Y.; Iwamatsu, S.-i., *J. Org. Chem.* **2000,** *66*, 315; (e) Liu, H. Z.; Liang, X. F.; Sohoel, H.; Bulow, A.; Bols, M., *J. Am. Chem. Soc.* **2001,** *123*, 5116; (f) Welter, C.; Moreno, R. M.; Streiff, S.; Helmchen, G., *Org. Biomol. Chem.* **2005,** *3*, 3266; (g) Ghorai, M. K.; Kumar, A.; Das, K., *Org. Lett.* **2007,** *9*, 5441; (h) Gnamm, C.; Franck, G.; Miller, N.; Stork, T.; Brödner, K.; Helmchen, G., *Synthesis* **2008,** *2008*, 3331; (i) Hayashi, S.; Yorimitsu, H.; Oshima, K., *Angew. Chem. Int. Ed.* **2009,** *121*, 7360; (j) Ichikawa, Y.; Yamamoto, S.-I.; Kotsuki, H.; Nakano, K., *Synlett.* **2009,** *2009*, 2281; (k) Farwick, A.; Helmchen, G., *Org. Lett.* **2010,** *12*, 1108; (l) Gärtner, M.; Weihofen, R.; Helmchen, G., *Chem. Eur. J.* **2011,** *17*, 7605.

3. (a) Negri, G.; Kascheres, C.; Kascheres, A. J., *J. Heterocycl. Chem.* **2004**, *41*, 461; (b) Liu, D.; Xie, F.; Zhang, W., *Tetrahedron Lett.* **2007,** *48*, 7591; (c) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B., *Chem. Rev.* **2007,** *107*, 5471; (d) Maji, B.; Lakhdar, S.; Mayr, H., *Chem. Eur. J.* **2012,** *18*, 5732; (e) Xiao, J., *ChemCatChem* **2012,** *4*, 612; (f) Gigant, N.; Chausset-Boissarie, L.; Gillaizeau, I., *Chem. Eur. J.* **2014,** *20*, 7548.

4. (a) Stanley, L. M.; Hartwig, J. F., *Angew. Chem. Int. Ed.* **2009,** *121*, 7981; (b) Shu, C.; Leitner, A.; Hartwig, J. F., *Angew. Chem. Int. Ed.* **2004,** *43*, 4797; (c) Leitner, A.; Shekhar, S.; Pouy, M. J.; Hartwig, J. F., *J. Am. Chem. Soc.* **2005,** *127*, 15506; (d) Ohmura, T.; Hartwig, J. F., *J. Am. Chem. Soc.* **2002,** *124*, 15164; (e) Pouy, M. J.; Stanley, L. M.; Hartwig, J. F., *J. Am. Chem. Soc.* **2009,** *131*, 11312; (f) Shekhar, S.; Trantow, B.; Leitner, A.; Hartwig, J. F., *J. Am. Chem. Soc.* **2006,** *128*, 11770; (g) Defieber, C.; Ariger, M. A.; Moriel, P.; Carreira, E. M., *Angew. Chem. Int. Ed.* **2007,** *46*, 3139; (h) Roggen, M.; Carreira, E. M., *J. Am. Chem. Soc.* **2010,** *132*, 11917; (i) Johannsen, M.; Jørgensen, K. A., *Chem. Rev.* **1998,** *98*, 1689; (j) Mancheño, O. G.; Priego, J.; Cabrera, S.; Arrayás, R. G.; Llamas, T.; Carretero, J. C., *J. Org. Chem.* **2003,** *68*, 3679; (k) Nagano, T.; Kobayashi, S., *J. Am. Chem. Soc.* **2009,** *131*, 4200; (l) Ohshima, T.; Miyamoto, Y.; Ipposhi, J.; Nakahara, Y.; Utsunomiya, M.; Mashima, K., *J. Am. Chem. Soc.* **2009,** *131*, 14317; (m) Tonogaki, K.; Itami, K.; Yoshida, J.-i., *J. Am. Chem. Soc.* **2006,** *128*, 1464.

5. (a) Patel, S. J.; Jamison, T. F., *Angew. Chem. Int. Ed.* **2004,** *43*, 3941; (b) Boezio, A. A.; Solberghe, G.; Lauzon, C.; Charette, A. B., *J. Org. Chem.* **2003,** *68*, 3241; (c) Shi, X.; Kiesman, W. F.; Levina, A.; Xin, Z., *J. Org. Chem.* **2013,** *78*, 9415; (d) Concellon, J. M.; Suarez, J. R.; Del Solar, V., *Org. Lett.* **2006,** *8*, 349.

6. (a) Wang, Q. S.; Xie, J. H.; Li, W.; Zhu, S. F.; Wang, L. X.; Zhou, Q. L., *Org. Lett.* **2011,** *13*, 3388; (b) Barchuk, A.; Ngai, M.-Y.; Krische, M. J., *J. Am. Chem. Soc.* **2007,** *129*, 8432; (c) Ngai, M.-Y.; Barchuk, A.; Krische, M. J., *J. Am. Chem. Soc.* **2007,** *129*, 12644; (d) Skucas, E.; Kong, J. R.; Krische, M. J., *J. Am. Chem. Soc.* **2007,** *129*, 7242; (e) Ahmed, M.; Seayad, A. M.; Jackstell, R.; Beller, M., *Angew. Chem. Int. Ed.* **2003,** *42*, 5615; (f) Meng, L. G.; Wang, L., *Chem. Commun.* **2012,** *48*, 3242; (g) Zhang, Z.; Wei, Y.; Shi, M., *Chem. Commun.* **2012,** *48*, 5334; (h) Kim, D. D.; Lee, S. J.; Beak, P., *J. Org. Chem.* **2005,** *70*, 5376; (i) Hesp, K. D.; Bergman, R. G.; Ellman, J. A., *J. Am. Chem. Soc.* **2011,** *133*, 11430; (j) Park, Y. S.; Weisenburger, G. A.; Beak, P., *J. Am. Chem. Soc.* **1997,** *119*, 10537; (k) Wallace, D. J.; Klauber, D. J.; Chen, C. Y.; Volante, R. P., *Org. Lett.*

2003, *5*, 4749; (l) Andappan, M. M. S.; Nilsson, P.; von Schenck, H.; Larhed, M., *J. Org. Chem.* **2004,** *69*, 5212; (m) Selander, N.; Worrell, B. T.; Chuprakov, S.; Velaparthi, S.; Fokin, V. V., *J. Am. Chem. Soc.* **2012,** *134*, 14670; (n) Ramtohul, Y. K.; Chartrand, A., *Org. Lett.* **2007,** *9*, 1029.

7. (a) Overman, L. E., *Acc. Chem. Res.* **1980,** *13*, 218; (b) Anderson, C. E.; Overman, L. E., *J. Am. Chem. Soc.* **2003,** *125*, 12412; (c) Overman, L. E., *J. Am. Chem. Soc.* **1976,** *98*, 2901.

8. (a) Matsui, K.; Takizawa, S.; Sasai, H., *J. Am. Chem. Soc.* **2005,** *127*, 3680; (b) Yukawa, T.; Seelig, B.; Xu, Y.; Morimoto, H.; Matsunaga, S.; Berkessel, A.; Shibasaki, M., *J. Am. Chem. Soc.* **2010,** *132*, 11988; (c) Matsui, K.; Takizawa, S.; Sasai, H., *Synlett* **2006,** *2006*, 0761.

9. Shi, S. L.; Buchwald, S. L., *Nat. Chem.* **2015,** *7*, 38.

10. (a) Hansson, S.; Heumann, A.; Rein, T.; Aakermark, B., *J. Org. Chem.* **1990,** *55*, 975; (b) Grennberg, H.; Simon, V.; Backvall, J.-E., *J. Am. Chem. Soc., Chem. Commun.* **1994**, 265; (c) Chen, M. S.; White, M. C., *J. Am. Chem. Soc.* **2004,** *126*, 1346; (d) Chen, M. S.; Prabagaran, N.; Labenz, N. A.; White, M. C., *J. Am. Chem. Soc.* **2005,** *127*, 6970; (e) Liron, F.; Oble, J.; Lorion, M. M.; Poli, G., *Eur. J. Org. Chem.* **2014,** *2014*, 5863.

11. (a) Stang, E. M.; White, M. C., *Nat. Chem.* **2009,** *1*, 547; (b) Stang, E. M.; White, M. C., *Angew. Chem. Int. Ed.* **2011,** *50*, 2094; (c) Luzung, M. R.; Lewis, C. A.; Baran, P. S., *Angew. Chem. Int. Ed.* **2009,** *48*, 7025.

12. O'Donnell, M. J.; Yang, X.; Li, M., *Tetrahedron Lett.* **1990,** *31*, 5135.

13. (a) Trost, B. M.; Mahapatra, S.; Hansen, M., *Angew. Chem. Int. Ed.* **2015,** *54*, 6032; (b) Trost, B. M.; Mahapatra, S.; Hansen, M., *Angew. Chem. Int. Ed.* **2015,** *127*, 6130.

14. van der Veen, L. A.; Keeven, P. H.; Schoemaker, G. C.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Lutz, M.; Spek, A. L., *Organometallics* **2000,** *19*, 872.

15. Li, M.; Berritt, S.; Walsh, P. J., *Org. Lett.* **2014,** *16*, 4312.

16. (a) Bruno, N. C.; Tudge, M. T.; Buchwald, S. L., *Chem. Sci.* **2013,** *4*, 916; (b) Bruno, N. C.; Niljianskul, N.; Buchwald, S. L., *J. Org. Chem.* **2014,** *79*, 4161.

17. Zhang, J.; Bellomo, A.; Trongsiriwat, N.; Jia, T.; Carroll, P. J.; Dreher, S. D.; Tudge, M. T.; Yin, H.; Robinson, J. R.; Schelter, E. J.; Walsh, P. J., *J. Am. Chem. Soc.* **2014,** *136*, 6276.

18. Meyer, E. A.; Castellano, R. K.; Diederich, F., *Angew. Chem. Int. Ed.* **2003,** *42*, 1210.

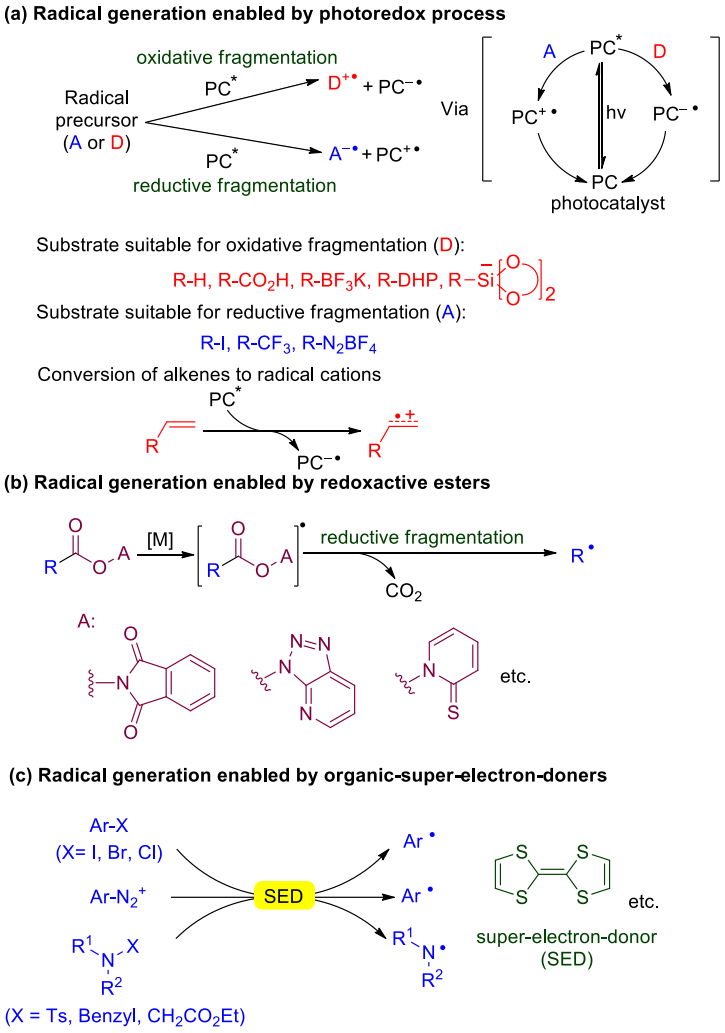
19. Zhang, J.; Bellomo, A.; Trongsiriwat, N.; Jia, T.; Carroll, P. J.; Dreher, S. D.; Tudge, M. T.; Yin, H.; Robinson, J. R.; Schelter, E. J.; Walsh, P. J., *J. Am. Chem. Soc.* **2014,** *136*, 6276.

20. Hatano, M.; Hattori, Y.; Furuya, Y.; Ishihara, K. *Org. Lett.*, **2009**, *11*, 2321.

Chapter 3. Transition-Metal-Free Vinyaltion, Arylation and Alkylation of 2-Azaallyls.

3.1. Introduction.

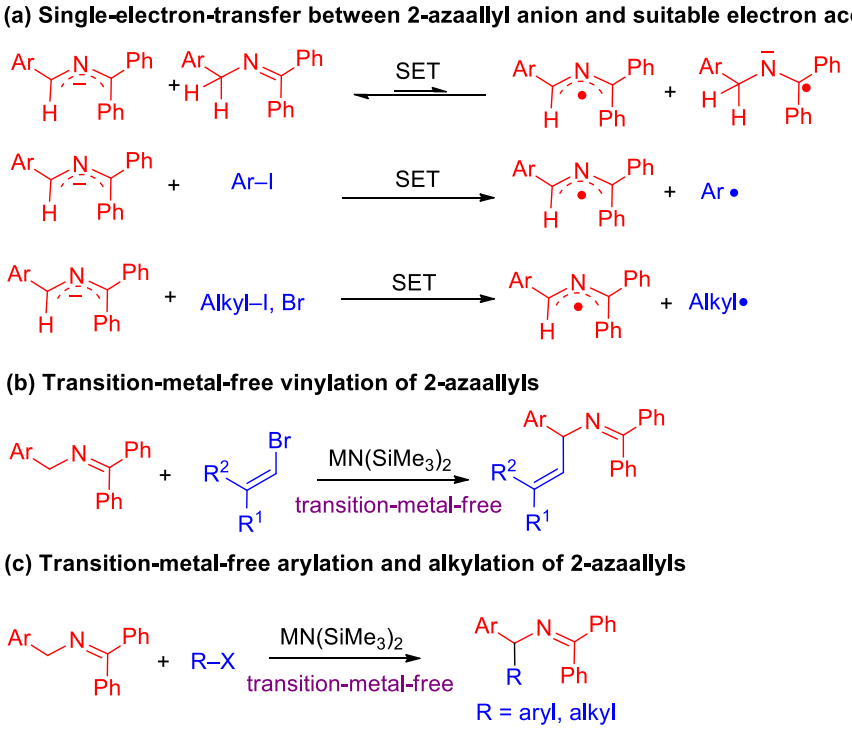
C–C bond forming reactions under transition-metal-free conditions offers an atom-economical, inexpensive, and environmentally benign alternative to traditional transition metal-catalyzed cross-coupling reactions. They have received tremendous attention due to their value in synthetic organic chemistry and drug discovery.[1] Of these, the formation of C–C bonds via radical intermediates has witnessed increasing popularity due to the mild nature of many of these processes.[1h, 2] Over the past few decades, a series of groundbreaking radical-based coupling strategies have been developed that enable a wide variety of bonds to be formed. Among these, use of visible-light activated transition metal and organo-photocatalysts to generate organic radicals has found tremendous applications in novel C–C bond-forming methods.[3] A key feature of such photocatalysts (PC*) is their ability to behave as both reductants and oxidants, as shown in Scheme 3.1, a. Under photocatalytic conditions, a wide variety of reagents undergo oxidative or reductive fragmentation to organic radicals. Another beautiful strategy for radical generation is through redox-active esters, which are converted efficiently to radicals by reductive fragmentation using transition-metals as electron donors (Scheme 3.1, b).[4] Finally, a metal-free strategy to generate radicals involves the use of organic super-electron-donors (SEDs).[5] SEDs possess reduction potentials as high as –1.50 V (versus SCE)[6] and reduce a range of substrates to generate radicals (Scheme 3.1, c). The reducing features of SEDs have been demonstrated in intramolecular radical cyclization experiments.[7] In contrast, kinetically slower intermolecular (bimolecular)[8] C–C bond formations enabled by excess amounts of SEDs are far less developed.



Scheme 3.1. Representative Strategies for Radical Generation.

We discovered a unique strategy to generate 2-azaallyl radicals in transition-metal-free fashion. As shown in Scheme 3.2, a, 2-azaallyl anions behaved as organic “super electron donors” which could reduce neutral ketimine to give 2-azaallyl radicals and ketimine radical anions. They could also reduce aryl halides and alkyl halides to generate 2-azaallyl radicals together with aryl and alkyl radicals. These unprecedented single-electron-transfer (SET) processes were employed in the transition-metal-free vinylation, arylation and alkylation of 2-azaallyls. In the vinylation reaction (Scheme 3.2, b), coupling of 2-azaallyl anions and 2-azaallyl radicals with vinyl halides afforded the *E* vinylation products in high yields with excellent chemo- and regioselectivity. The

vinylation outperformed a rapid background reaction arising from the base promoted elimination of the vinyl bromide to form a terminal alkyne. In addition, the base/solvent combination efficiently promoted the metal-free vinylation but does not deprotonate the product. Thus, neither product deprotonation/isomerization, which will form a more stable conjugated byproduct, nor product deprotonation/cyclization, is observed. The arylation protocol enables the synthesis of diarylmethylamine derivatives, which are of great importance in medicinal and pharmaceutical chemistry.[9] Arylation at the benzhydryl carbon (side-reaction) was also observed which afforded pharmaceutically valuable triarylmethylamine derivatives.[10] The alkylation protocol overcomes limitations of hindered alkyl halide electrophiles that show little or no reactivity in classic nucleophilic substitution reactions[11] and provides efficient synthesis of challenging alkyl amine derivatives. Moreover, EPR studies, calculations and additional experiments provided preliminary pictures of the mechanistic landscape of these C–C bond-forming reactions.



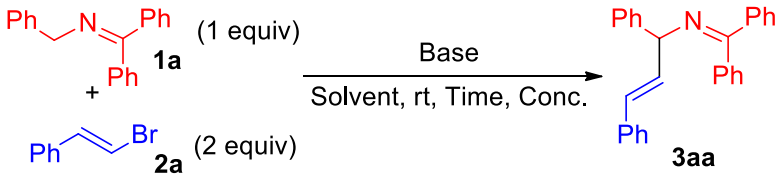
Scheme 3.2. 2-Azaallyl Anions as Super-electron Donor and Radical Coupling Partners in Transition-Metal-Free C–C Bond Formation.

3.2. Transition-Metal-Free Vinylation of 2-Azaallyl Anions and 2-Azaallyl Radicals.

3.2.1. Development of Optimization of Transition-Metal-Free Vinylation.

In chapter 1, we reported the arylation of 1,1,3-triaryl-2-azaallyl anions and 1,3-diaryl-2-azaallyl anions via *in situ* deprotonation of ketimines and aldimines followed by palladium-catalyzed arylation with Ar'–X.[12] Key to preventing product deprotonation and isomerization was the use of hindered bases [$MN(SiMe_3)_2$ (M = Li, Na)] at room temperature. To explore the analogous vinylation reaction, we investigated the deprotonative cross-coupling of ketimine **1a** and β-bromostyrene **2a** using microscale high-throughput screening (10 μmol) of 23 electronically diverse mono- and bidentate phosphine ligands in the presence of $Pd(OAc)_2$, $NaN(SiMe_3)_2$ and THF at room temperature for three hours. To our surprise, a considerable amount of the targeted vinylated product (**3aa**) was found in the control vial, which contained no added transition-metal or ligand. Validation on a larger scale (0.1 mmol) provided further support for a transition-metal-free process; specifically, reactions conducted without addition of catalyst led to the vinylation product **3aa** in 51% assay yield (AY) in THF as determined by ^{1}H NMR spectroscopy (Table 3.1, entry 1). Increasing the concentration from 0.1 M to 0.2 M (entry 2) resulted in an increase to 65% AY. We next tested 5 solvents [CPME (cyclopentyl methyl ether), THF, 2-Me-THF, DME (dimethoxyethane) and 1,4-dioxane, entries 3–7]. Surprisingly, the reaction was complete in just 10 min in DME, giving 98% AY of **3aa** (entry 6). Further optimization of the base ratio revealed that 2 equiv of $LiN(SiMe_3)_2$ and a 30 min reaction time resulted in 98% isolated yield (entry 9).

Table 3.1 Optimization of the Transition-Metal-Free Vinylation.[a,b]



Entry	Base (equiv)	Solvent	Time (min)	Conc.	**3aa** (%)
1	$NaN(SiMe_3)_2$ (3)	THF	180	0.1 M	51
2	$NaN(SiMe_3)_2$ (3)	THF	180	0.2 M	65
3	$NaN(SiMe_3)_2$ (3)	CPME	10	0.2 M	0
4	$NaN(SiMe_3)_2$ (3)	THF	10	0.2 M	32
5	$NaN(SiMe_3)_2$ (3)	2-Me THF	10	0.2 M	0
6	$NaN(SiMe_3)_2$ (3)	DME	10	0.2 M	98
7	$NaN(SiMe_3)_2$ (3)	Dioxane	10	0.2 M	0
8	$LiN(SiMe_3)_2$ (3)	DME	10	0.2 M	99
9	$LiN(SiMe_3)_2$ (2)	DME	30	0.2 M	98[c]
10	$LiN(SiMe_3)_2$ (1.5)	DME	30	0.2 M	54
11	$LiN(SiMe_3)_2$ (1)	DME	30	0.2 M	21

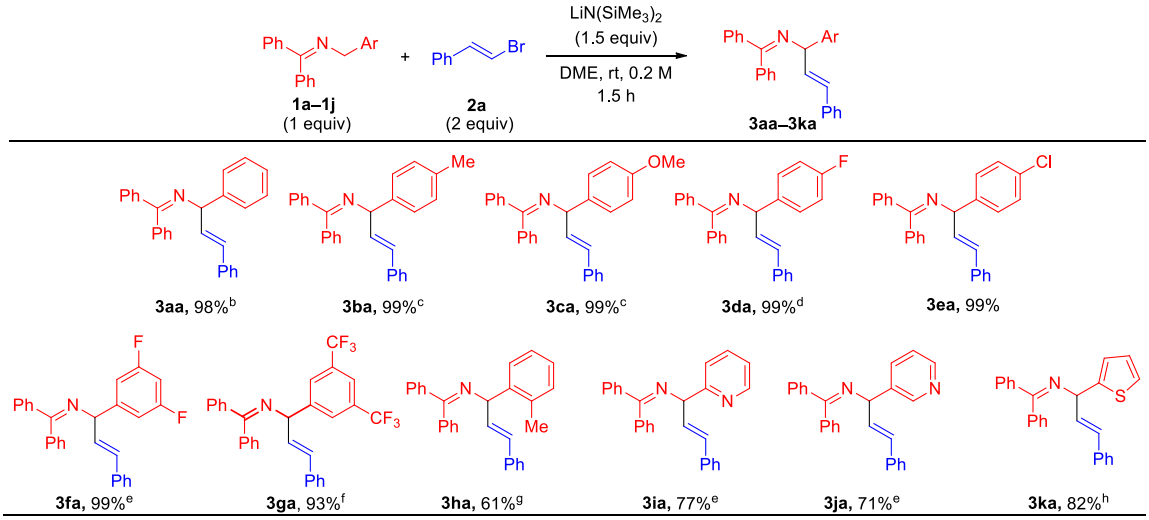
[a]Reactions conducted on a 0.1 mmol scale. [b]Assay yields determined by ^{1}H NMR spectroscopy of the reaction mixture on a 0.1 mmol scale using an internal standard. [c]Isolated yield after chromatographic purification.

3.2.2. Scope of Transition-Metal-Free Vinyaltion.

With the optimized reaction conditions (entry 9, Table 3.1), the scope of the *N*-benzyl group on the ketimine was examined (Table 3.2). Overall, some tuning of the reaction parameters, such as the base, reagent ratios, concentration and reaction times, was necessary for certain substrates. Nonetheless, vinylation of ketimine substrates bearing electron-donating (4-Me, **1b**

and 4-OMe **1c**) and electron-withdrawing [4-F (**1d**), 4-Cl (**1e**), 3,5-di-F (**1f**) and 3,5-di-CF_3 (**1g**)] *N*-benzyl derived groups with β-bromostyrene (**2a**) proceeded in excellent yields. The sterically demanding 2-tolyl substituted ketimine (**1h**) underwent coupling, albeit in lower yield (61%), even when performed with 3 equiv $LiN(SiMe_3)_2$ and an extended reaction time (8 h). More acidic heterocyclic substrates underwent coupling, including 2-pyridyl **1i** (77%), 3-pyridyl **1j** (71%) and 2-thiophenyl **1k** (82%) ketimine substrates, 0.05 M concentration was optimal with 1.5 equivalent of $LiN(SiMe_3)_2$ to prevent deprotonation, isomerization and cyclization.

Table 3.2 Scope of Ketimines in the Vinylation Reaction.[a]

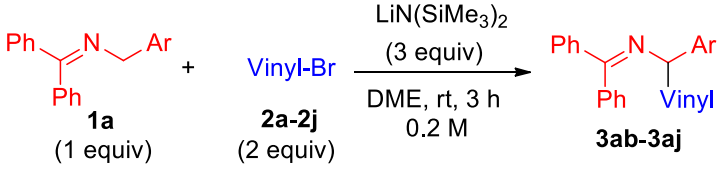


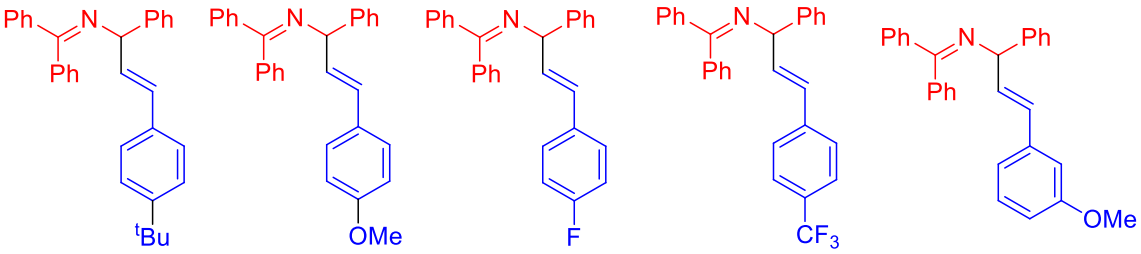
[a]Reactions were conducted on a 0.1 mmol scale using 1 equiv of ketimine **1** and 2 equiv of **2a** at 0.2 M. Isolated yields after chromatographic purification. [b]2 equiv of $LiN(SiMe_3)_2$, 30 min. [c]3 equiv of $LiN(SiMe_3)_2$, 3 h. [d]2 equiv of $LiN(SiMe_3)_2$, 6 h. [e]0.05 M. [f]1.2 equiv of $LiN(SiMe_3)_2$, 0.05 M, 15 min. [g]2 equiv of $LiN(SiMe_3)_2$, 8 h. [h]0.05 M, 3 h.

We next determined the scope in the vinyl bromide component and found it to be broad (Table 3.3). *trans*-β-Aryl vinyl bromides bearing neutral (4-C_6H_4-*t*Bu) and electron donating (4-C_6H_4-OMe) groups furnished coupling products **3ab** and **3ac** in 92 and 98% yield, respectively. 4-Fluoro- (**2d**) and 4-trifluoromethyl-substituted vinyl bromides (**2e**) afforded the coupled products **3ad** and **3ae** in 96 and 70% yield. The reactions also proceeded well with substitution at the 3-

position of the β-bromostyrene, such as 3-OMe (**2f**) and 3-CF_3 (**2g**), giving the products in 98 and 75% yield, respectively. *trans*-β-2-Tolyl vinyl bromide (**2h**) was an excellent substrate, affording the product in 96% yield. Surprisingly, the aliphatic vinyl bromides 1-bromo-2-methylprop-1-ene (**2i**) and (bromomethylene)cyclohexane (**2j**) were successfully coupled with **1a** to afford **3ai** and **3aj** in 54–55% yield.

Table 3.3 Scope of Vinyl Bromides in Transition-Metal-Free Vinylation.[a]





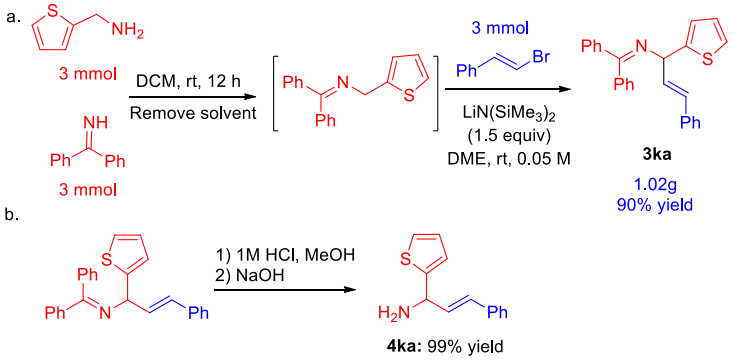
3ab, 92%[b] **3ac,** 98% **3ad,** 96%[b] **3ae,** 70%[c] **3af,** 98%[b]

3ag, 75%[c] **3ah,** 96% **3ai,** 54%[d] **3aj,** 55%[e]

[a]Reactions conducted on a 0.1 mmol scale using 1 equiv **1a** (0.2 M), 2 equiv $LiN(SiMe_3)_2$, and 2 equiv vinyl bromides at 0.2 M. Isolated yields after chromatographic purification. [b]2 equiv $LiN(SiMe_3)_2$ [c]0.1 M. [d]3 equiv $NaN(SiMe_3)_2$, 12 h, 0.1 M. [e]3 equiv $NaN(SiMe_3)_2$, 15 min, 60 °C.

The vinylation is amenable to a telescoped imine synthesis/vinylation protocol on gram-scale (Scheme 3.3, a). For example, the sequential one-pot synthesis of 2-thiophenyl ketimine **1k**, followed by vinylation with **2a** successfully afforded product **3ka** in 90% yield (1.02 g). Finally,

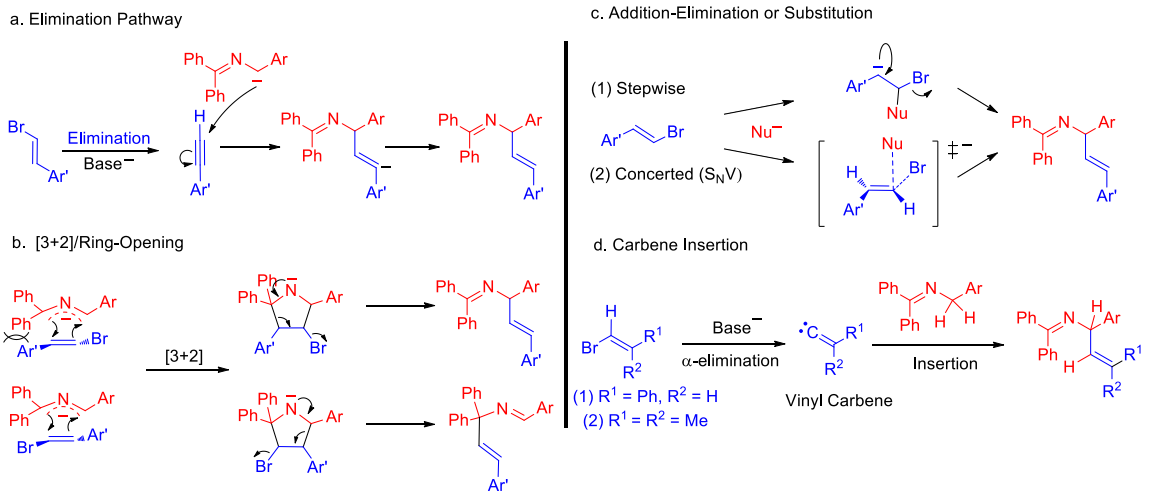
hydrolysis of the vinylated product **3ka** was performed to isolate the allylic amine **5ka** in 99% yield (Scheme 3.3, b).



Scheme 3.3. One-pot Gram Scale Synthesis and Imine Hydrolysis.

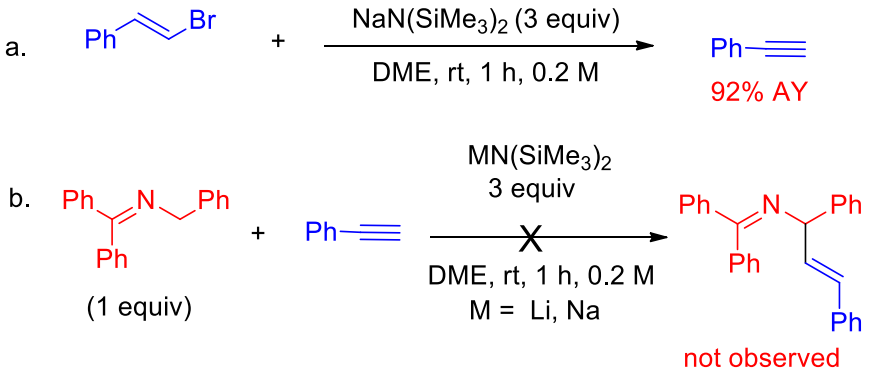
3.2.3. Mechanistic Study of Transition-Metal-Free Vinylation.

Given the unexpected and unusual coupling of ketimines with vinyl bromides in the absence of added catalyst, a synergistic computational and experimental study was undertaken to gain insight into the mechanistic possibilities. Several reasonable mechanisms can be envisioned (Scheme 3.4), including those involving alkyne intermediates, cycloadditions, addition/eliminations, substitutions and carbene insertions.



Scheme 3.4. Possible Mechanisms for Vinylation of Benzyl Ketimines.

Of relevance to Scheme 3.4, a, in the absence of ketimine the vinyl bromide undergoes rapid (1 h at rt) $NaN(SiMe_3)_2$ promoted background elimination to yield the corresponding alkyne (Scheme 3.5, a). Submission of the terminal alkyne to imine **1a** under the same conditions used in the vinylation (Scheme 3.5) did not result in formation of the vinylated product **3aa**. These results indicate that the alkyne is not an intermediate en route to the vinylation product, discounting the pathway in Scheme 3.4, a.

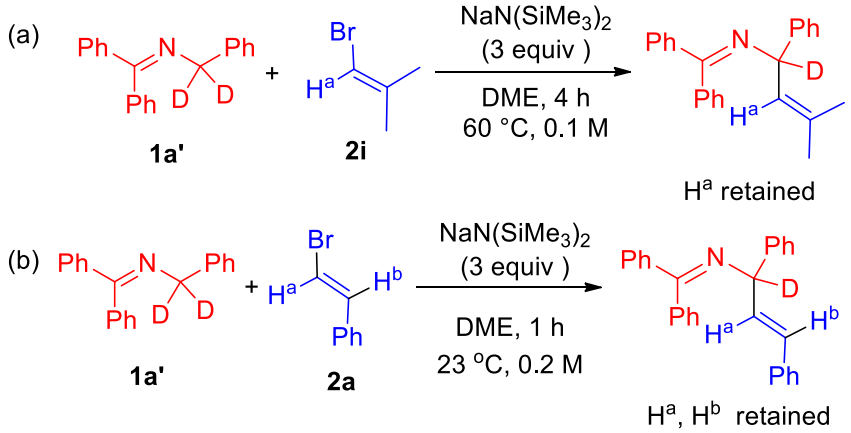


Scheme 3.5. Probing the Intermediacy of An Alkyne.

Addition of the silylamide base is expected to cause rapid deprotonation of the *N*-benzyl ketimine giving rise to an azaallyl anion ***A1*** (Figure 3.1).[13] It is known that azaallyl anions undergo cycloadditions with styrene and, therefore, this pathway was explored with β-bromostyrene.[14] Two isomeric [3+2] reactions are possible from this intermediate (Scheme 3.4, b), with the first leading to the observed product after elimination of bromide. However, significant steric interactions arise in this pathway between the vinyl aryl group and the diphenyl moiety of the azaallyl anion. The alternate cyclization pathway gives rise to the regioisomeric product, which was not observed. Computations undertaken on the azaallyl anion found the concerted [3+2] cyclization pathway to be higher in energy than a step-wise substitution mechanism (Scheme 3.4, c1).

Another possibility is the α-elimination of vinyl halides in the presence of $MN(SiMe_3)_2$ (M = Na, K) to form vinylidenes.[15] A highly reactive vinylidene could then insert into the benzylic C–H bond of

the ketimine. If this mechanism is operative in our system, the hydrogen of the vinyl motif would originate from a benzylic hydrogen of the ketimine **1a**. With this in mind, the deuterated ketimine **1a'** was prepared and investigated in the coupling with vinyl bromides **2i** and **2a.** The results (Scheme 3.6) indicate that vinyl hydrogens of the products are not deuterated, which excludes the α-elimination mechanism in Scheme 3.4, d.



Scheme 3.6. Probing the Vinylidine Insertion Mechanism.

Our attention next turned to possible substitution pathways.[16] Both stepwise and concerted (S_NV)[17] substitutions have been reported for vinyl halides, but not with carbon-derived anions. Mechanisms are case-dependent with the nature of the nucleophile, the leaving group, and the electrophile substitution pattern all playing a role.[18] All attempts to calculate intermediates for the corresponding stepwise process (Scheme 3.4, c1) using functionals previously used to study S_NV reactions (B3LYP and OPBE) led directly to dissociation back to starting materials or formation of vinylated product and bromide.[19] DFT calculations did, however, reveal a concerted displacement with a low energetic barrier (11.7 kcal/mol) to deliver the vinylated product ***B1*** with concomitant release of bromide (Figure 3.1). A strong kinetic preference ($\Delta\Delta G^{\ddagger}$ > 7 kcal/mol) for nucleophilic attack perpendicular to the carbon-carbon double bond (S_NV)[17] at the less sterically encumbered β-position (**A1-B1-TS** vs **A1-C1-TS**) was found. Notably, both product regioisomers (***B1*** and ***C1***) are nearly isoenergetic.

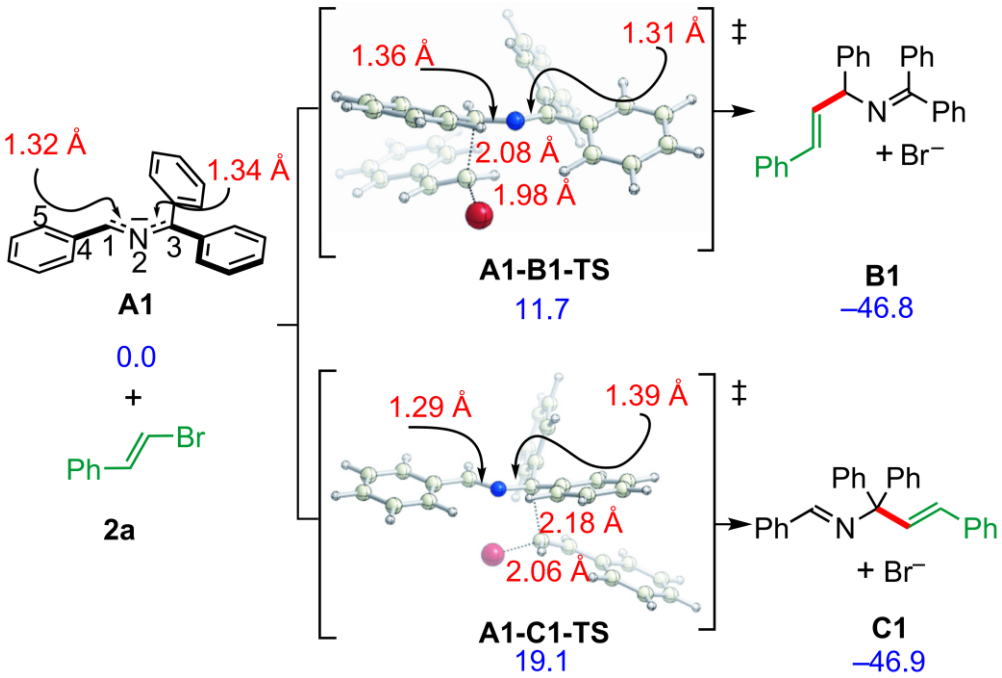


Figure 3.1. Computed Free-Energy Profile for Nucleophilic Vinyl Substitution of Azaallyl Anion A1 and Vinyl Bromide 2a.

These computational results are in accord with both the experimentally observed reactivity (20 min – 3 h at room temperature) and regioselectivity (> 20:1 dr) using bromostyrene. However, experiments with the *Z*-bromostyrene **2a'**[20] at room temperature yield a near 2:1 ratio of *E*- and *Z*-products, albeit in low yield (14%) due to rapid competing elimination of *Z*-bromostyrene **2a'** to form alkyne. The anionic-pathway S_NV shown in Figure 3.1 is a concerted and stereospecific process,[16] which is inconsistent with the stereochemical scrambling observed. These results motivated us to examine alternative pathways.

We speculated that an azaallyl radical **A0** (Figure 3.2, a)[21] could participate in the process. This azaallyl radical could form by electron transfer from the azaallyl anion (**A1**) to a molecule of ketimine **1a** (Figure 3.2, a).[22] DFT calculations for azaallyl radical recombination with a putative vinyl radical[21b, 23] showed very small energetic barriers (ca. 11 kcal/mol), indicating that such a

process is facile. The energy difference between the competing transition states, however, indicates negligible levels of E/Z product regioselectivity, which is inconsistent with experiments.

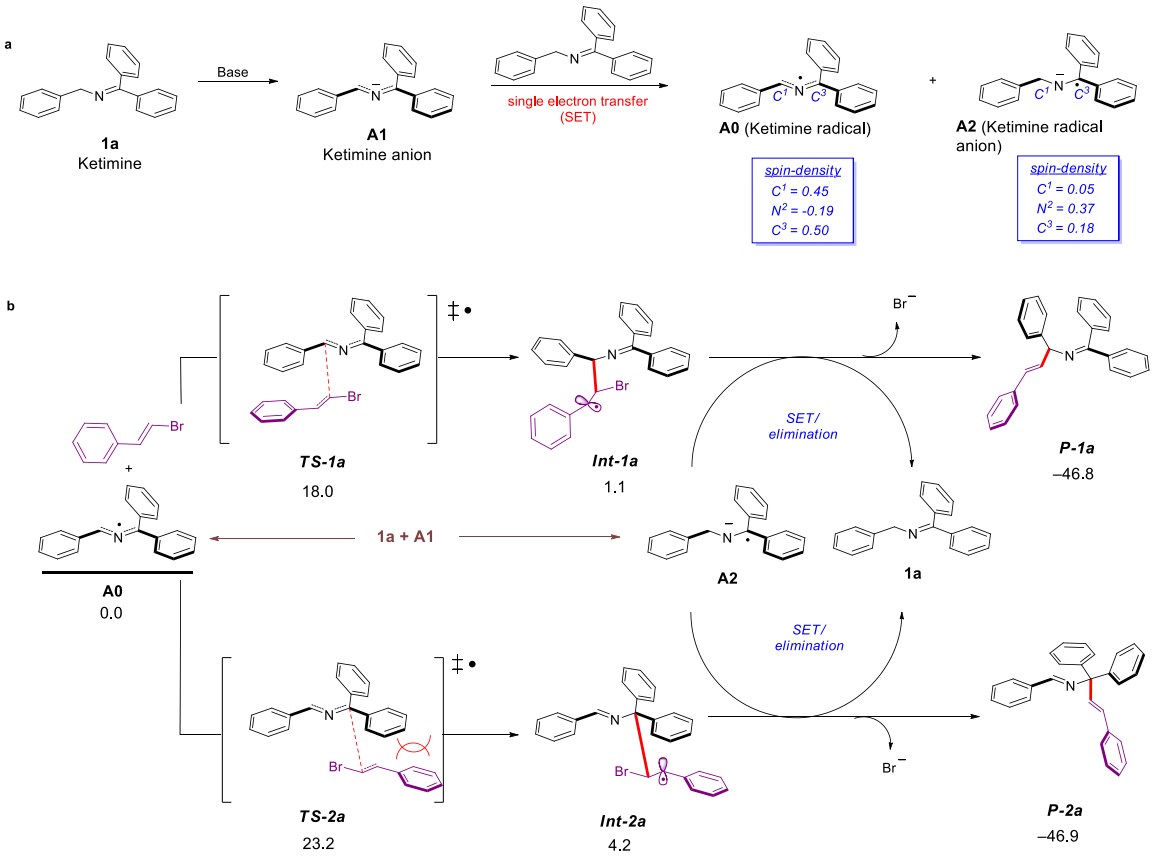


Figure 3.2. Proposed Formation of 2-Aazallyl Radical A0 and Ketimine Radical Anion A2 via a SET process. b. Gibbs Gree Energy Profile for the Azaallyl Radical Addition Mechanism.

Transition states could also be located for the addition of azaallyl radical **A0** to *trans*-bromostyrene (Figure 3.2, b), which proceeds in a stepwise manner with an overall barrier of 18.0 kcal/mol (via ***TS-1a***) to yield radical intermediate ***Int-1a***, and eventually to the observed regioisomer (Figure 5b). The transition state ***TS-2a***, which leads to the unobserved regioisomer is much higher in energy (23.2 kcal/mol) due to increased steric interactions between the diaryl moiety of the azaallyl radical and β-bromostyrene.

From ***Int-1a***, a scan for dissociation of Br• and formation of observed product ***P-1a*** was computed to be prohibitively high in energy (>35 kcal/mol). Alternatively, radical intermediate ***Int-1a*** can undergo single electron reduction to generate a negatively charged species, which facilitates the heterolytic cleavage of the C–Br bond to generate Br^- and the observed product **P-*1a***. In support of this hypothesis, all optimizations of anionic version of ***Int-1a*** led directly to dissociation of Br^- and formation of **P-*1a***. This result implies that once radical ***Int-1a*** undergoes single electron reduction, it quickly dissociates bromide leading to the observed product, consistent with the highly exergonic (–47 kcal/mol) nature of the net process. This process also converts radical anion **A2** back to ketimine **1a**. The product regioisomers ***P-1a*** and ***P-2a*** are nearly isoenergetic, and hence the regioselectivity derives from the kinetic preference of ***TS-1a*** over ***TS-2a***. In contrast to the azaallyl anion pathway, the pathway involving the radical intermediates ***Int-1a*** accounts for the stereochemical scrambling from *Z*-bromostyrene **2a'** (bond rotation more rapid than reduction/elimination).

The mechanism in Figure 3.2 proposes radical intermediates (**A0** and **A2**). To probe for the presence of radicals, an electron paramagnetic resonance (EPR) study was undertaken. In these experiments, DME solutions of $NaN(SiMe_3)_2$ were added to DME solutions of ketimine **1a** and the samples were allowed to react for ~5 min at rt before freezing in liquid nitrogen. The EPR spectra were acquired in DME glass at 190 K and microwave power of 1 mW. No signal was detected in samples with only base in DME or DME alone. In contrast, for the deprotonations of **1a**, EPR spectra showed clear signals for the presence of radical species (Figure 3.3). The observation of an EPR signal is supportive of one or more radicals, but definitive conclusions concerning the nature of the radical species must await future investigations. Despite numerous studies of azaallyl anions in the literature, to the best of our knowledge this is the first evidence of radical formation upon deprotonation of ketimines.

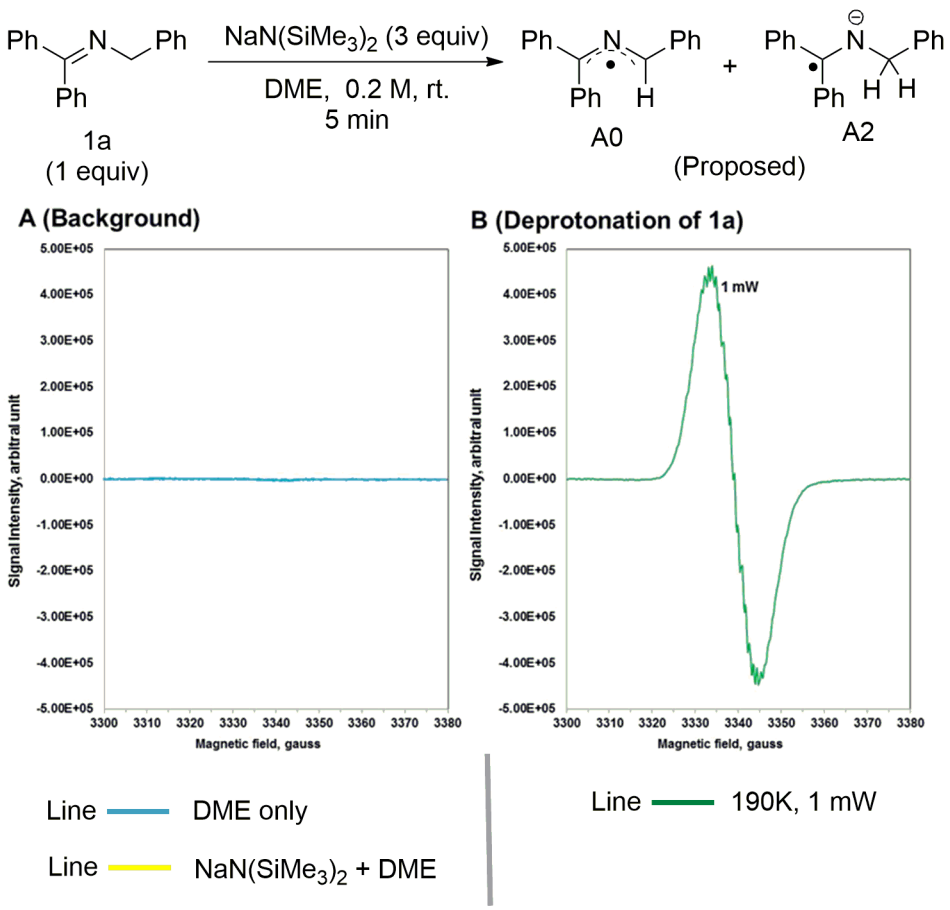
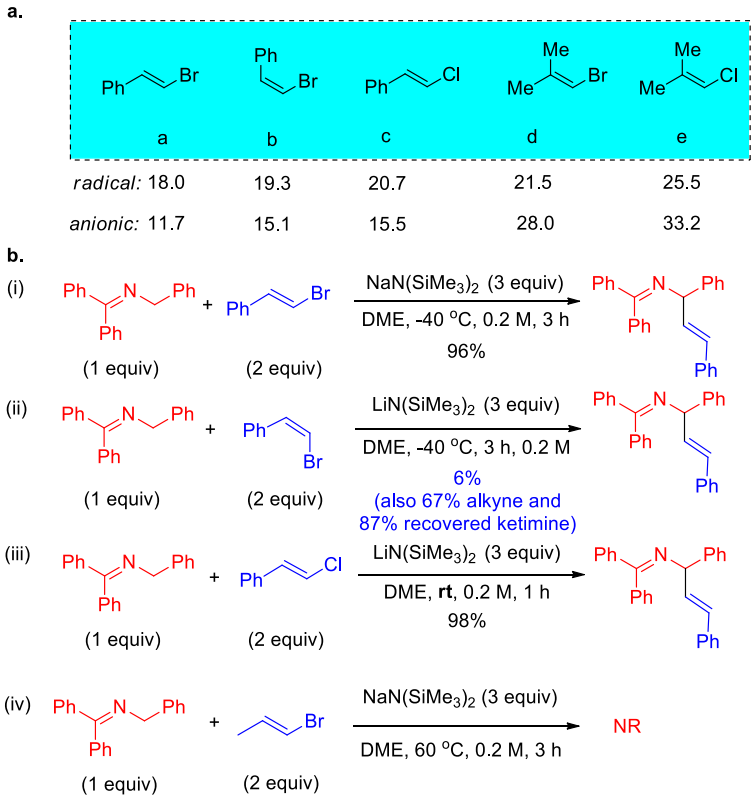


Figure 3.3. EPR Spectra of Deprotonation of 1a.

Given the evidence for the presence of radicals, which we propose to be the azaallyl radical (**A0**) and the ketimine radical anion (**A2**), an effort was made to distinguish the azaallyl anion S_NV and azaallyl radical additions by calculating the reaction barriers (Scheme 3.7, a). Based on the computations, similar trends were observed for both mechanisms (Scheme 3.7, b). Thus, *E*-β-bromostyrene was predicted to react more readily than the *Z*-isomer or *E*-β-chlorostyrene. Experimentally, *E*-β-bromostyrene reacted at –40 ^{o}C to afford the vinylation product in 96% assay yield (i, Figure 5d) while *Z*-β-bromostyrene generated the *E*-product in 6% yield (no *cis*-product observed and elimination dominating the reaction, ii, Scheme 3.7, b). At room temperature, coupling of *E*-β-chlorostyrene afforded product in 98% assay yield. For substrates lacking a β-aryl group, reaction is expected to slow according to both mechanisms, but to a far

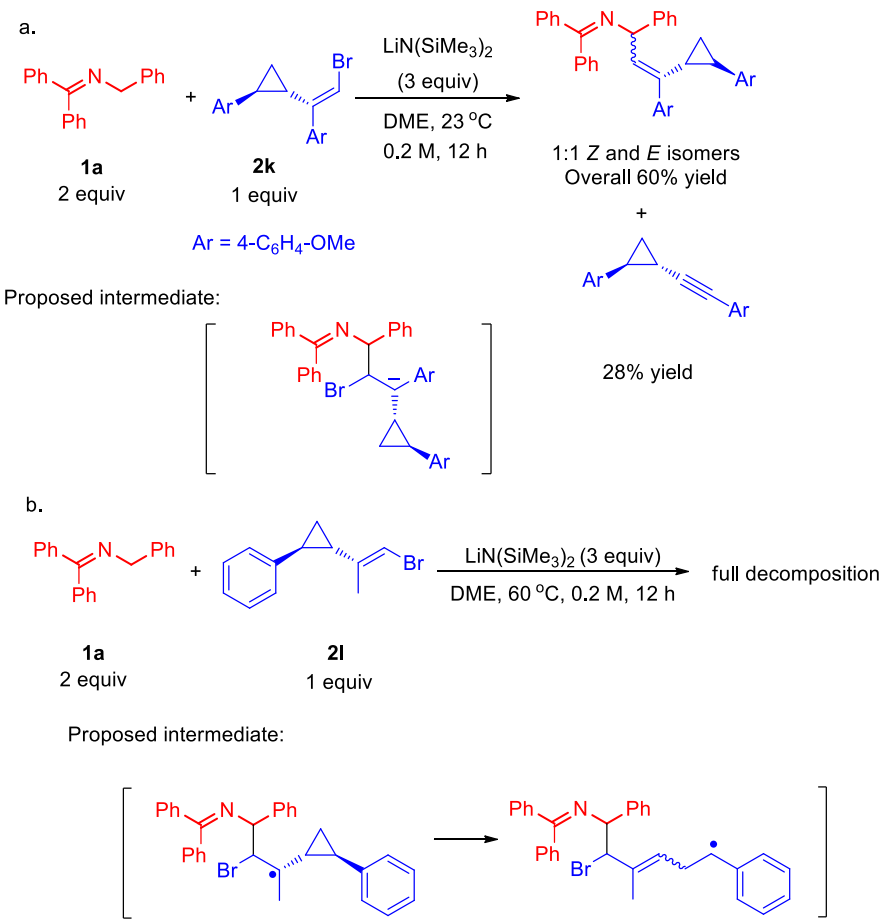
larger degree for the azaallyl anion mechanism.[17] As illustrated in Table 3.2, 1-bromo-2-methylprop-1-ene (**2i**) and (bromomethylene)cyclohexane (**2j**) underwent reaction, albeit more slowly (12 h) and with reduced yields (54 and 55%, respectively). Although there are well-documented errors associated with determining accurate quantitative barriers with charged species, computations employing the commonly used B3LYP functional, which has been used by others to study S_NV reactions, predicted prohibitively high barriers (>36 kcal/mol) for the azaallyl anion ***A1*** and 1-bromo-2-methylprop-1-ene in both gas-phase and in implicit solvent. Moreover, the greater reactivity of 1-bromo-2-methylprop-1-ene (Table 3.2, **2i**) vs *E*-1-bromo-prop-1-ene (iv, Scheme 3.7, b) also seemingly runs counter to the azaallyl anion mechanism; a build-up of negative charge would be less favorable with two methyl substituents as is the case for the former.



Scheme 3.7. Substituent Effects of Electrophile on the Radical and Anionic Addition Barriers and Substrate Study of Vinylation.

The EPR results support the presence of radicals, but do not indicate if they are involved in the vinylation reactions. To probe for the direct participation of radicals in the vinylations, we next examined the reactions of radical clock-containing styryl and non-styryl substrates. We prepared the radical clock **2k** (Scheme 3.8, a) to test for the intermediacy of radical intermediates in the reaction with β-bromostyrene derivatives. As outlined in Figure 3.2, **Int-1a** possesses a stabilized benzylic radical. Thus, a second aryl group was built into the substrate such that, in the event the benzylic radical analogous to **Int-1a** is formed, ring-opening would also give a stabilized benzylic radical. The reaction of the *E*-styryl radical clock **2k** with ketimine **1a** in the presence of $LiN(SiMe_3)_2$ furnished a mixture of *Z* and *E* vinylated products in a 1:1 ratio (overall 60% yield). An alkyne side-product was observed in 28% isolated yield, which we propose is derived from the α-elimination-migration mechanism. Thus, no cyclopropane ring-opened products were detected, suggesting that the reaction of styryl substrates does not proceed through radical intermediates. Furthermore, the scrambling of the double bond geometry is inconsistent with an anionic concerted S_NV substitution mechanism. Based on these results, the pathway favored is the addition/elimination, wherein the azaallyl anion adds to the styrene to generate a benzylic carbanion that can rotate about the single bond before elimination, giving rise to the observed products. Unfortunately, we were unable to locate such an intermediate computationally without an additional anion-stabilizing group.

To probe the participation of radicals with aliphatic vinyl bromides, radical clock **2l** was prepared and isolated as the pure *E*-isomer. Reaction with of *E*-**2l** (Scheme 3.8, b) with ketimine **1a** in the presence of $LiN(SiMe_3)_2$ led to a complex mixture, as determined by ^1H NMR. Further, no clean products could be isolated from this mixture. We propose that ring-opening occurs to give a reactive radical. These results suggest the presence of radical addition mechanism for aliphatic vinyl bromides.



Scheme 3.8. Radical Clock Study.

Based on the computational, spectroscopic (EPR), and experimental results, both azaallyl anion and radical exist under the reaction conditions. To rationalize these observations, we propose substrate dependent reactions with different electrophiles. Thus, with aliphatic vinyl bromides the azaallyl radical addition mechanism best fits with the experimental and computational results. In contrast, for the styryl vinyl bromides, the data is most consistent with the anionic pathway.

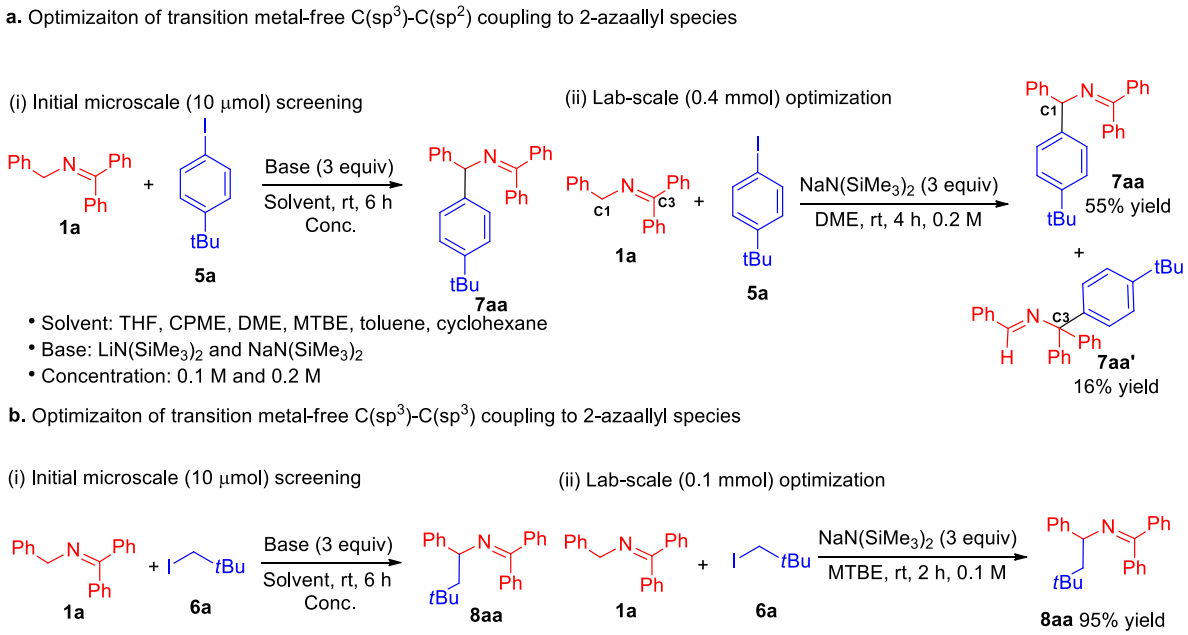
3.3. Transition-Metal-Free Arylation and Alkylation of 2-Azaallyl Radicals.

3.3.1. Development and Optimization of Transition-Metal-Free Arylation and Alkylation.

We initiated our study with aryl iodides. A focused microscale (10 μmol) high-throughput-screen (HTS) was performed for the study of arylation of ketimine **1a** with 4-*tert*-butyliodobenzene (**5a**) at room temperature for 6 h. Other parameters included six solvents (THF, CPME, DME, MTBE,

toluene, and cyclohexane), two bases [$LiN(SiMe_3)_2$ and $NaN(SiMe_3)_2$] and two concentrations (0.1 M and 0.2 M). The best conditions in this screen involved DME, $NaN(SiMe_3)_2$ at 0.2 M concentration. We next monitored the reaction of 4-*tert*-butyl iodobenzene (**5a**, 10 µmol) with ketimine **1a** and $NaN(SiMe_3)_2$ and found that the reaction reached completion in 4 h. A laboratory scale (0.4 mmol) repeat (Scheme 3.9, a) of these optimal conditions gave the C3-arylation product **7aa** in 55% isolated yield. To our surprise, the product from arylation at the benzhydryl carbon (C3-arylation, **7aa'**) was isolated in 16% yield. We propose that the C3-arylation is derived from the coupling of azaallyl radical with phenyl radical at the more substituted C3 carbon. Steric influences also affect the ratio of C1 vs. C3 arylation, leading to greater arylation at the less substituted carbon in the 2-azaallyl system.

For alkylation, we selected neopentyl iodide (**6a**) as the model alkylation electrophile because its steric hindrance precludes an S_N2 coupling pathway.[10] The same parameters employed in Scheme 3a were applied to the 10 µmol scale screening of ketimine **1a** with neopentyl iodide (**6a**; rt for 6 h, Scheme 3.9, b). We were pleased and surprised to find that the alkylation reaction proceeded. The leading result from the HTS for alkylation was with MTBE and $NaN(SiMe_3)_2$ at 0.1 M concentration. In a similar fashion, we next monitored reaction profiles of alkylation at 10 µmol scale and results revealed that coupling of neopentyl iodide **6a** with ketimine **1a** was completed in 2 h. To our delight, lab scale reaction (0.1 mmol) under the optimal conditions gave alkylation product **8aa** in 95% isolated yield (Scheme 3.9, b). Notably, C3-alkylation was not observed under these reaction conditions.



Scheme 3.9. Reaction Optimization of Alkylation. (i) Initial High-throughput-Screening Conditions, (ii) Lab-scale (0.1 mmol) Repeat.

3.3.2. Scope of Transition-Metal-Free Arylation and Alkylation.

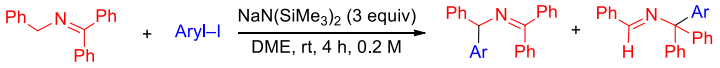
We then turned to the scope of the transition metal-free arylation with different aryl iodides (Table 3.4). Iodobenzene (**5b**) furnished C1-arylation product **7ab** in 58% yield and C3-arylated **7ab'** in 14% yield. Electron-rich 4-iodoanisole (**5c**) coupled with **1a** in 50% yield at the C1 position (**7ac**) and 13% yield at the C3 position (**7ac'**). Using MTBE as solvent, electron-withdrawing 1-bromo-4-iodobenzene (**5d**) coupled with **1a** affording product **7ad** (C1) in 43% yield and **7ad'** (C3) in 14% yield. Under the same conditions, coupling between 1-chloro-4-iodobenzene (**5e**) and **1a** led to C1-arylated product **7ae** and C3-arylated product **7ae'** in 44% and 15% yield, respectively. We observed that these aryl iodides underwent reaction with high chemoselectivity at the C–I sites, indicating that 2-azaallyl anions preferentially reduce aryl iodides over aryl chlorides or aryl bromides under these reaction conditions. It is noteworthy that aryl iodides **5d** and **5e** are Bunnett and Crearys' dihalide mechanistic probes (see the

mechanistic study section).[24] The fluoro analogue, 4-fluoroiodobenzene (**5f**), coupled with **1a** to give **7af** and **7af'** in 48% and 13% yield, respectively. The arylation also preceded with *meta*-substituted aryl iodides (3-OMe, **5g**) to give C1-arylated product **7ag** in 47% yield and its C3-arylated counterpart **7ag'** in 17% yield.

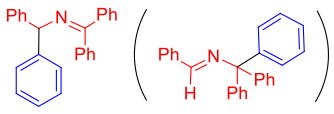
We next wanted to address the possibility of benzyne formation under the basic conditions for the arylation reaction. We therefore examined 2-iodotoluene and 2-iodo-1,3-dimethylbenzene. If benzyne intermediates were involved in the reactions in Table 3.4, the benzyne generated from 2-iodotoluene would likely undergo reaction at the less hindered position of the benzyne and generate product with a 3-tolyl group. Furthermore, 2-iodo-1,3-dimethylbenzene would be expected to be unreactive if benzyne intermediates are required for the reactions in Table 3.4. In the event, 2-iodotoluene participated in the arylation to afford the 2-tolyl product, albeit in 21% yield after 4 h. When the reaction time was extended to 9 h, product **7ah** was formed in 46% yield. Interestingly, C3 arylated **7ah'** was isolated in 15% yield. More hindered 2-iodo-1,3-dimethylbenzene (**5i**) furnished 44% yield of the coupling product **7ai**. Notably, arylation at the more hindered C3 position was not observed. These results indicate that benzyne intermediates are not necessary in these coupling reactions. Coupling of 2-iodonaphthalene (**5j**) with ketamine **1a** afforded product **7aj** in 35% yield and product **7aj'** in 11% yield. From this reaction mixture, we were also able to isolate naphthalene in 20% yield. We hypothesize that naphthalene is derived from hydrogen atom transfer (HAT) to a 2-naphthyl radical intermediate from the DME solvent. This result is significant, because it provides support for the existence of isolated aryl radical intermediates in these transformations.

Table 3.4. Scope of Arylation.[a,b]

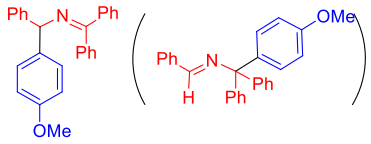
Scope of transition metal-free C(sp^3)-C(sp^2) coupling to 2-azaallyl species



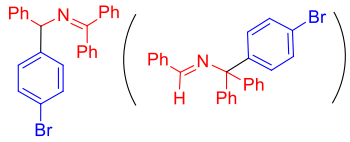
1a **5a–5i** **7aa–7ai** **7aa'–7aj'**



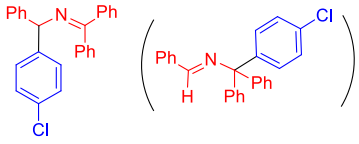
7ab, 58% yield **7ab'**, 14% yield



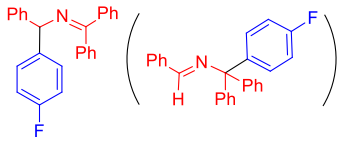
7ac, 50% yield **7ac'**, 13% yield



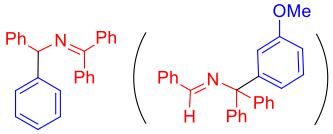
7ad, 43% yield[b] **7ad'**, 14% yield[b]



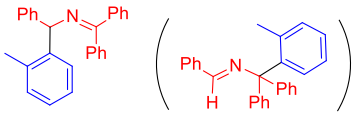
7ae, 44% yield[b] **7ae'**, 15% yield[b]



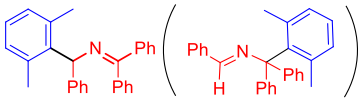
7af, 48% yield[c] **7af'**, 13% yield[c]



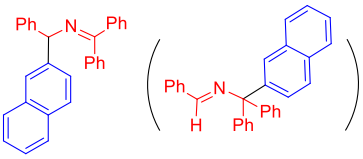
7ag, 47% yield **7ag'**, 17% yield



7ah, 46% yield[c] **7ah'**, 15% yield[c]



7ai, 44% yield[c] **7ai'**, not observed



7aj, 35% yield **7aj'**, 11% yield

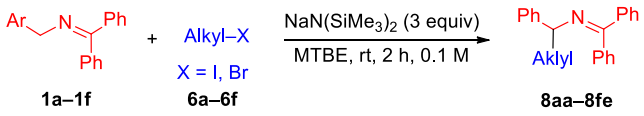
[a]Reactions were conducted on a 0.4 mmol scale using 2 equiv. ketimine, 1 equiv. aryl iodide and 3 equiv. $NaN(SiMe_3)_2$ at 0.2 M. Isolated yields after chromatographic purification. [b]MTBE. [c]Reaction time 9 h.

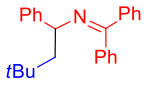
With the optimal conditions, we investigated the scope of the alkylation reaction with respect to unactivated and hindered alkyl halide electrophiles (Table 3.5). We were concerned that *tert*-butyl iodide would undergo rapid E2 elimination under the basic reaction conditions. Nevertheless, *tert*-butyl iodide reacted to afford the alkylation product **8ab** in 53% yield. Furthermore, both 1-iodo-1-methylcyclohexane **6c** and 1-bromo-1-methylcyclohexane **6d** successfully coupled with ketimine **1a**, leading to products **8ac** in 41% and 37% yield, respectively. Aminoadamantane derivatives are widely present in medications to fight Parkinson's disease,[25] antiviral agents,[26] and *N*-methyl-D-aspartate (NMDA) receptor antagonists.[27] To our delight, 1-adamantyl iodide **6e** underwent coupling with ketimine **1a** in excellent yield (93%). The same product could also be synthesized from 1-adamantyl bromide

(**6f**) in 61% yield with toluene as solvent. Considering the value of aminoadamantane derivatives, we continued surveying the coupling of 1-adamantyl iodide **6e** with a few ketimines. *tert*-Butyl substituted triaryl ketimine **1b** underwent coupling with 1-adamantyl iodide **6e** in 58% yield. The relatively electron-rich (4-C_6H_4-OMe) ketimine **1c** provided product **8ce** in 68% yield. Coupling electron-withdrawing (3-C_6H_4-CF_3) ketimine **1d** with **6e** proceeded in 80% yield. Heterocyclic 2-furyl (**1e**) and 2-thiophenyl (**1f**) ketimines were also examined and afforded products **8ee** and **8fe** in 60 and 85% yield, respectively. No C3-alkylated products were observed in the coupling of ketimines with 1-adamantyl halides, presumably due to steric effects.

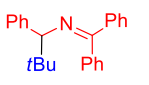
Table 3.5. Scope of Alkylation.

Scope of transition metal-free $C(sp^3)$-$C(sp^3)$ coupling to 2-azaallyl species

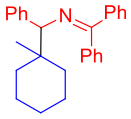




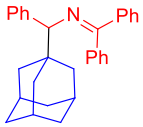
8aa, 95% yield



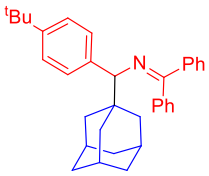
8ab, 53% yield



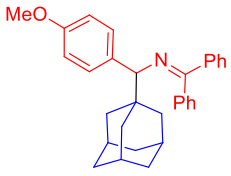
8ac
41% yield (with **6c**, X = I)
37% yield (with **6d**, X = Br)



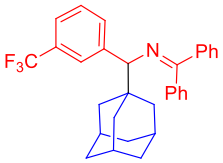
8ae
93% yield (with **6e**, X = I)
61% yield (with **6f**, X = Br)[b]



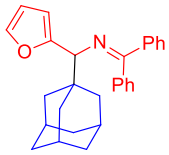
8be, 58% yield



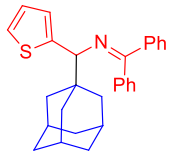
8ce, 68% yield



8de, 80% yield



8ee, 60% yield

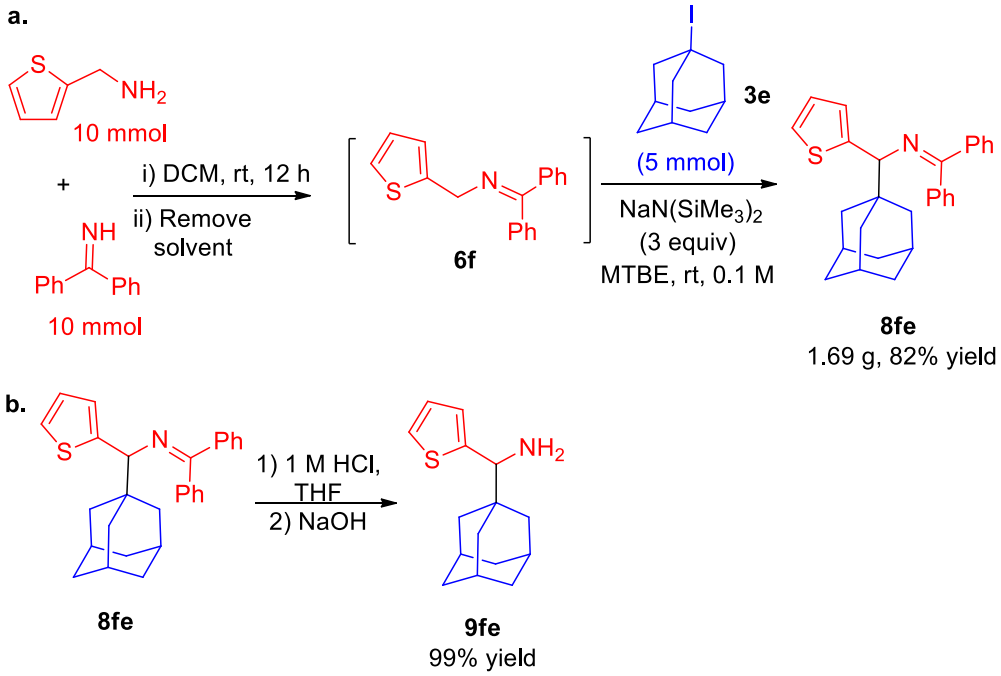


8fe, 85% yield

[a]Reactions were conducted on a 0.1 mmol scale using 2 equiv. ketimine, 1 equiv. alkyl iodide and 3 equiv. $NaN(SiMe_3)_2$ at 0.1 M. Isolated yields after chromatographic purification. [b]Toluene.

To test the scalability of our method, we conducted the gram-scale synthesis of heterocyclic product **8fe**. Thus, ketimine **1f** was synthesized from amine and benzophenone imine precursors and dried under vacuum.[28] Using the unpurified imine, the alkylation reaction was performed with 1-adamantyl iodide **6e** as described above leading to product **8fe** in 82% yield (1.69 g,

Scheme 5a). Hydrolysis of ketimine **8fe** was also performed to afford 1-adamantyl(thiophen-2-yl)methanamine (**9fe**) in 99% isolated yield (Scheme 3.10).



Scheme 3.10. a. Gram-scale One-Pot Synthesis of 5fe Through a Telescoped Imine Synthesis/Alkylation Process. b. Ketimine Hydrolysis.

3.3.3. Mechanistic Study of Transition-Metal-Free Arylation and Alkylation.

The reaction presented herein with aryl iodides and alkyl halides are most easily rationalized by SET from the 2-azaallyl anion (**A1**, Figure 3.4) to either the aryl iodide or alkyl halide to generate radical intermediates. The transient aryl/alkyl radicals can react with the 2-azaallyl radical (**A0**, proposed to be a persistent radical) to afford the coupled product (Path a, Figure 3.4). Or, they might instead react with azaallyl anion (**A1**) to give a ketiminyl radical anion (**A2**), which then reduces Ar–I or Alkyl–X to give product and Ar• /Alkyl• in an $S_{RN}1$ process (Path b, Figure 3.4).[29]

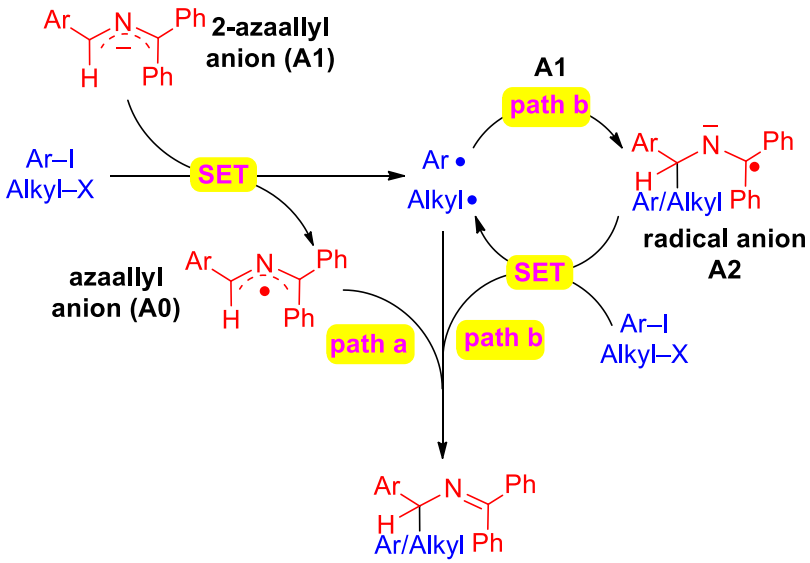
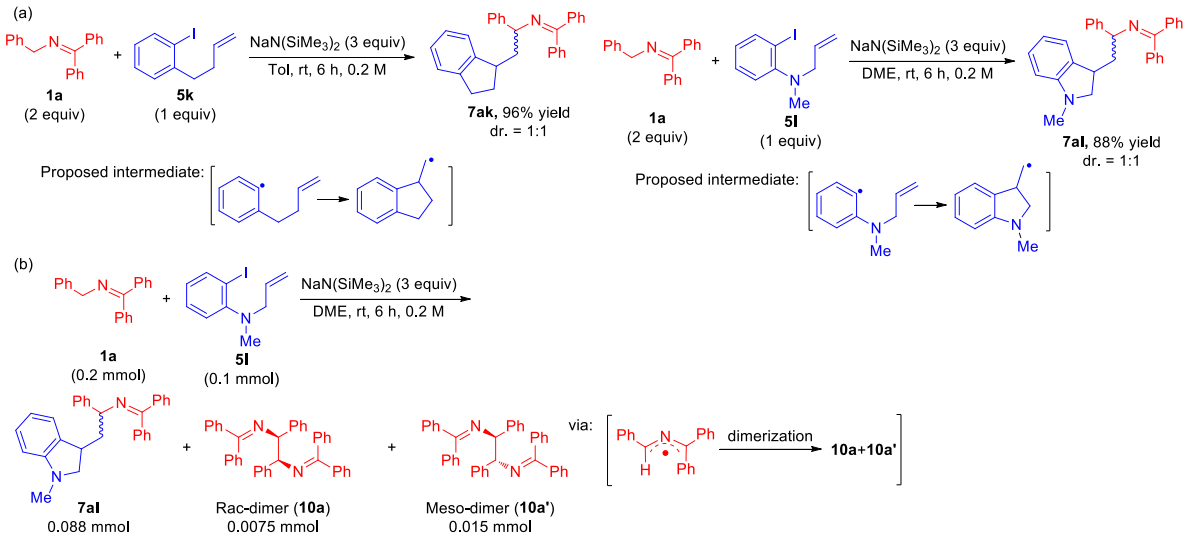


Figure 3.4. Possible Reaction Mechanisms.

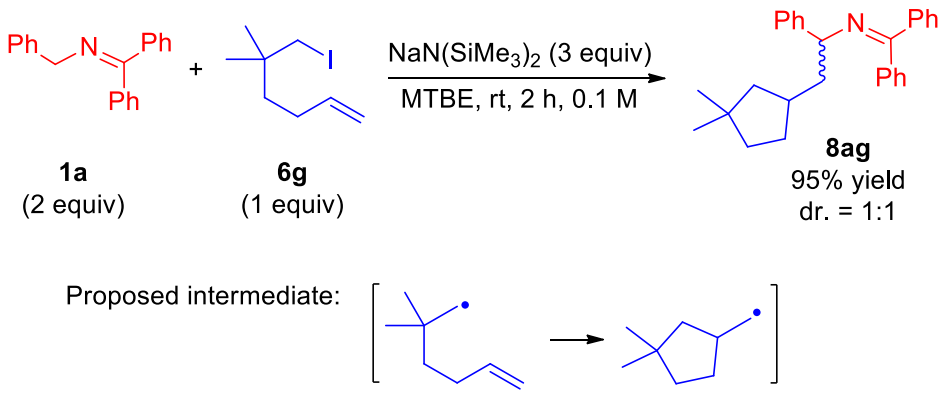
To investigate the SET process, we undertook a series of experiments with radical clock substrates that undergo rapid cyclization in the presence of radicals. In order to probe for aryl radicals in the coupling of ketimine **1a** with aryl iodides, radical clock **5k** was employed.[30] In the presence of ketimine **1a**, **5k** was treated with 3 equiv of $NaN(SiMe_3)_2$ at rt (Scheme 3.11, a). The cyclized product **7ak** was obtained in 96% yield as a 1:1 mixture of diastereomers. A second radical trap based on *N*-allyl-2-iodo-*N*-methylaniline was subjected to similar conditions and again gave rise to cyclized product in 88% yield. These results confirm the intermediacy of radicals in these reactions.

In the coupling of **1a** with *N*-allylaniline **5l**, we observed the formation of *rac*- and *meso*-di-ketimines, which we proposed to be derived from dimerization of 2-azaallyl radicals (Scheme 3.11, b). NMR spectra of the isolated di-ketimine byproducts matched with the *rac*- and *meso*-di-ketimines independently prepared by condensation of the *rac*- and *meso*-diamines with benzophenone imine. Such dimers could be observed throughout all of the arylations and alkylations of 2-azaallyl species described above and their formation supports the existence of 2-azaallyl radicals under the reaction conditions.



Scheme 3.11. Radical Clock Study in the Arylation.

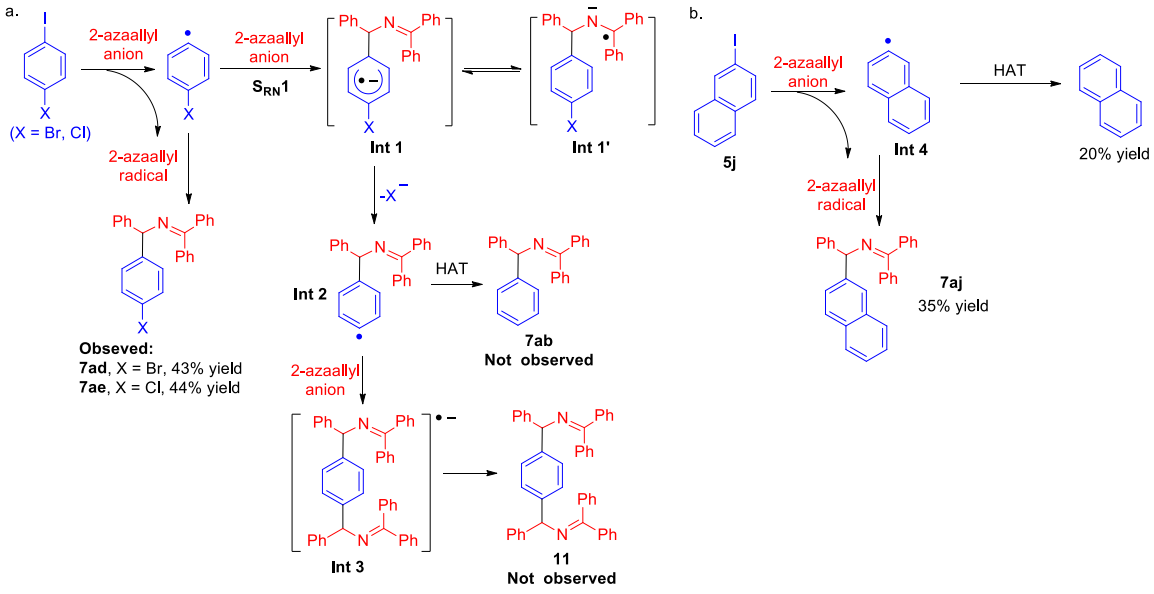
We next performed parallel mechanistic studies using an alkyl radical clock **6g**.[30] As outlined in Scheme 3.12, treatment of ketimine **1a** with $NaN(SiMe_3)_2$ in the presence of alkyl iodide **6g** with a pendent alkene resulted in formation of **8ag** in 95% yield as a 1:1 mixture of diastereomers. The formation of the cyclized product confirms that the alkylation reaction, as with the arylation process, proceeds via a radical mechanism.



Scheme 3.12. Radical Clock Study in the Alkylation.

The radical clock studies and 2-azaallyl anion coupling studies support the SET process. We next focused on two possible C–C bond forming pathways (radical-radical coupling vs. $S_{RN}1$,

paths a and b in Figure 3.4). The goal of this study was to probe the radical anion intermediate (**A2**, Figure 3.4) to determine if the reaction follows the $S_{RN}1$ mechanism. Hence, we employed Bunnett and Crearys' dihalides [1-bromo-4-iodobenzene (**5d**) and 1-chloro-4-iodobenzene (**5e**) of Table 1], which are widely used in probing $S_{RN}1$ mechanisms.[24, 31] In analogy to Kwong and Lei's work,[31a] if the reaction follows the $S_{RN}1$ mechanism, aryl radical trapping by the 2-azaallyl anion would give radical anion **Int 1** (Scheme 3.13, a). The bromo or chloro group of **Int 1** should then dissociate to radical intermediate **Int 2**, which could undergo HAT to give product **7ab** or couple with another equivalent to 2-azaallyl anion to afford bis-coupled products **11** (Scheme 3.13, a). As we reported in Table 3.2, coupling of 1-bromo-4-iodobenzene (**5d**) and 1-chloro-4-iodobenzene (**5e**) with ketimine **1a** afforded **7ad** and **7ae** in 43% and 44% yields with Br and Cl retained in the products. Neither the dehalogenation product nor the bis-ketimine adduct were observed in the reaction. We interpret this observation as evidence against an $S_{RN}1$ mechanism. Moreover, naphthalene isolated from coupling between 2-iodonaphthalene **5j** and ketimine **1a** support the existence of radical intermediate **Int 4**, which favors the radical-radical coupling pathway (Scheme 3.13, b). Overall, the data points to an SET process followed by a radical-radical coupling mechanism as accounting for the unique reactivity of arylation and alkylation of 2-azaallyl species.



Scheme 3.13. a. Probe of $S_{RN}1$ Mechanism Using Bunnett and Crearys' 1,4-Dihalobenzenes. b. Reaction of 2-Iodonaphthalene.

3.4. Summary and Outlook.

In sum, we "unlocked" a hidden feature of 2-azaallyl anion species that they could behave not only as anionic nucleophiles but also as organic "super-electron-donors". This unique feature enabled the transition-metal-free vinylation, arylation and alkylation of 2-azaallyls via substrates-dependent mechanisms that were first reported by us.

In the study of transition-metal free coupling of 2-azaallyls with vinyl bromides, high regioselectivities and yields of *E*-vinylation products were observed. The vinylation reaction outcompeted a rapid background reaction arising from the elimination of the styryl bromides to form alkynes. Several mechanistic possibilities were explored both experimentally and with DFT calculations. EPR studies indicate the presence of radicals, which we think are the 2-azaallyl radical and imino-ketyl radical anion species. We think both azaallyl anion and radical exist and participate in the reaction. Hence, we propose substrate dependent reactions with different electrophiles. With aliphatic vinyl bromides the azaallyl radical addition mechanism best fits with

the experimental and computational results. For the styryl vinyl bromides, the data is most consistent with the anionic pathway.

In the study of transition-metal free coupling of 2-azaallyls with aryl iodides and alkyl halides, we discovered that the reducing feature of 2-azaallyl anions enabled the reductive fragmentation of unactivated aryl iodides and tertiary alkyl halides to aryl and alkyl radicals. After SET from the 2-azaallyl anion, the resulting 2-azaallyl radical behaved as a persistent radical that then trapped both aryl and alkyl radicals forming C–C bonds. This radical coupling method enabled facile access to diarylmethyl and benzylalkyl amines that are of great importance in medicinal and pharmaceutical chemistry. Di-ketimine products isolated from the reaction are proposed to arise via homo-coupling of 2-azaallyl radicals. Three radical clock studies, 2-azaallyl anion coupling studies, and Bunnett and Crearys' dihalide probes confirm the intermediacy of radical intermediates and lend further support to a radical coupling mechanism.

3.5. Experimental Section.

3.5.1 Experimental Section of Transition-Metal-Free Vinylation.

General methods. All reactions were conducted under a nitrogen atmosphere with oven-dried glassware and standard Schlenk or vacuum line techniques. All solutions were handled under nitrogen and transferred via syringe. Anhydrous solvents, including CPME (cyclopentyl methyl ether) were purchased from Sigma-Aldrich and directly used without further purification. Unless otherwise stated, reagents were commercially available and used as purchased without further purification. Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar or Matrix Scientific, and solvents were purchased from Fisher Scientific. Progress of reactions was monitored by thin-layer chromatography using Whatman Partisil K6F 250 μm precoated 60 Å silica gel plates and visualized by short-wave ultraviolet light as well as by treatment with iodine or ceric ammonium molybdate (CAM) stain. Flash chromatography was performed with silica gel (230–400 mesh, Silicycle). ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were obtained using a Brüker AM-500 Fourier-transform NMR spectrometer at 500 and 125 MHz, respectively. Chemical shifts were reported in units of parts per million (ppm) downfield from tetramethylsilane (TMS), and all

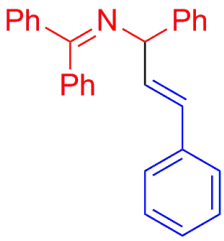
coupling constants were reported in hertz. The infrared spectra were taken with KBr plates with a Perkin-Elmer Spectrum 100 Series spectrometer. High resolution mass spectrometry (HRMS) data were obtained on a Waters LC-TOF mass spectrometer (model LCT-XE Premier) using chemical ionization (CI) or electrospray ionization (ESI) in positive or negative mode, depending on the analyte. Deactivated silica gel was prepared by addition of 15 mL of Et_3N to 1 L of silica gel.

Preparation of ketimines: ketimines were prepared according to literature procedures.

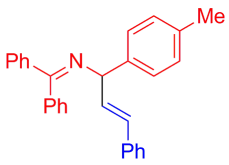
Preparation of vinyl halides: vinyl halides were prepared according to literature procedures.[32]

Procedure and characterization for the vinylation reaction:

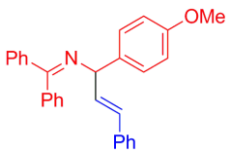
General Procedure: A brand-new oven-dried 4 mL glass vial equipped with two oven-dried glass beads was charged with ketimine **1a** (27.2 mg, 0.10 mmol) and vinyl bromide 2a (36.6 mg, 0.20 mmol) under a nitrogen atmosphere in a glove box. A solution of $LiN(SiMe_3)_2$ (33.5 mg, 0.2 mmol) in 0.5 mL anhydrous DME was added by a pipetter to the reaction vial. The vial was sealed with a cap, removed from the glove box and put in the reaction slot of a Innva 2180 platform shaker. The reaction mixture was stirred on the platform shaker for 30 min in total at 23 $^{\circ}C$, opened to air, quenched with two drops of H_2O, diluted with 2 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate (3X2 mL), and the combined solutions were concentrated *in vacuo*. The entire crude material was loaded onto a deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (36.6 mg, 98% yield) as a thick colorless oil.



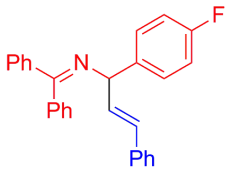
(*E*)-*N*-(Diphenylmethylene)-1,3-diphenylprop-2-en-1-amine (3aa): The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (33.5 mg, 0.2 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (36.6 mg, 98% yield) as a thick colorless oil. The ^{1}H and $^{13}C\{^{1}H\}$ NMR data for this compound match the literature data.[12b]



(*E*)-*N*-(Diphenylmethylene)-3-phenyl-1-(p-tolyl)prop-2-en-1-amine (3ba): The reaction was performed following the General Procedure with ketimine **1b** (28.5 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol) in 3 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (38.4 mg, 99% yield) as a thick colorless oil. R_f = 0.65 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 7.0 Hz, 2H), 7.45–7.44 (m, 3H), 7.39–7.32 (m, 5H), 7.29–7.24 (m, 4H), 7.19–7.16 (m, 3H), 7.13 (d, *J* = 7.5 Hz, 2H), 6.51 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.38 (d, *J* = 16.0 Hz, 1H), 5.11 (d, *J* = 6.5 Hz, 1H), 2.32 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.5, 140.6, 140.1, 137.5, 137.1, 136.7, 132.9, 130.2, 129.4, 129.3, 128.9, 128.5, 128.7, 128.64, 128.63, 128.2, 127.9, 127.5, 126.6, 68.5, 21.3 ppm; IR (thin film): 3025, 2961, 1620, 1576, 1446, 1314, 1284, 964, 694 cm^{-1}; HRMS calc'd for $C_{29}H_{26}N^+$ 288.2065, observed 388.2068 $[M+H]^+$.

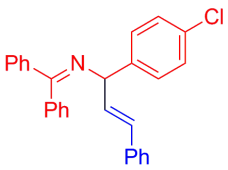


(*E*)-*N*-(Diphenylmethylene)-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-amine (3ca): The reaction was performed following the General Procedure with ketimine **1c** (30.2 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol) in 3 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:20) to give the product (39.9 mg, 81% yield) as a thick colorless oil. The ^{1}H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data.[12b]

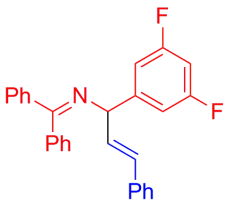


(*E*)-*N*-(Diphenylmethylene)-1-(4-fluorophenyl)-3-phenylprop-2-en-1-amine (3da): The reaction was performed following the General Procedure with ketimine **1d** (28.9 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (33.5 mg, 0.2 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol) in 6 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50)

to give the product (38.8 mg, 99% yield) as a thick colorless oil. R_f = 0.60 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.0 Hz, 2H), 7.46–7.44 (m, 3H), 7.38–7.32 (m, 7H), 7.27 (t, *J* = 7.5 Hz, 2H), 7.21–7.15 (m, 3H), 6.99 (t, *J* = 8.5 Hz, 2H), 6.47 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.12 (d, *J* = 6.5 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 167.9, 162.1 (d, $^1J_{C\text{-}F}$= 243.4 Hz), 139.9, 139.3 (d, $^4J_{C\text{-}F}$= 3.1 Hz), 137.3, 136.9, 132.5, 130.4, 129.7, 129.1, 129.0, 128.9, 128.8, 128.7, 128.3, 127.9, 127.6, 126.6, 115.4 (d, $^2J_{C\text{-}F}$= 21.1 Hz), 67.9 ppm; IR (thin film): 3026, 2866, 1621, 1599, 1506, 1446, 1221, 1155, 965, 833, 694 cm^{-1}; HRMS calc'd for $C_{28}H_{23}NF^+$ 392.1815, observed 392.1799 $[M+H]^+$.

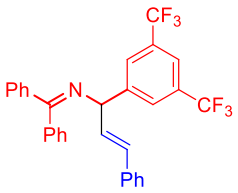


(*E*)-1-(4-Chlorophenyl)-*N*-(diphenylmethylene)-3-phenylprop-2-en-1-amine (3ea): The reaction was performed following the General Procedure with ketimine **1e** (30.6 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol) in 1.5 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (40.4 mg, 99% yield) as a thick colorless oil. R_f = 0.67 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72–7.70 (m, 2H), 7.46–7.44 (m, 3H), 7.39–7.37 (m, 1H), 7.35–7.31 (m, 6H), 7.25–7.21 (m, 4H), 7.21–7.19 (m, 1H), 7.17–7.14 (m, 2H), 6.45 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.10 (d, *J* = 6.5 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 168.1, 142.1, 139.9, 137.2, 136.9, 132.8, 132.2, 130.5, 129.9, 128.9, 128.84, 128.77, 128.72, 128.71, 128.5, 128.3, 127.8, 127.7, 126.7, 68.1 ppm; IR (thin film): 3026, 2862, 1620, 1596, 1486, 1446, 1284, 1173, 694 cm^{-1}; HRMS calc'd for $C_{28}H_{23}NCl^+$ 408.1519, observed 408.1529 $[M+H]^+$.

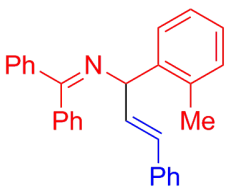


(*E*)-1-(3,5-Difluorophenyl)-*N*-(diphenylmethylene)-3-phenylprop-2-en-1-amine (3fa): The reaction was performed the General Procedure with ketimine **1f** (30.7 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol) in 1.5 h at 0.05 M. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (40.5 mg, 99% yield) as a thick colorless oil. R_f = 0.57

(diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 7.0 Hz, 2H), 7.47–7.44 (m, 3H), 7.42–7.39 (m, 1H), 7.37–7.33 (m, 4H), 7.28 (t, *J* = 7.5 Hz, 2H), 7.22–7.19 (m, 1H), 7.16–7.14 (m, 2H), 6.95 (dt, *J* = 10.0, 1.5 Hz, 2H), 6.66 (tt, *J* = 9.0, 2.5 Hz, 1H), 6.41 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.36 (d, *J* = 16.0 Hz, 1H), 5.08 (d, *J* = 6.5 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 168.8, 164.3 (d, $^{1}J_{C\text{-}F}$ = 247 Hz), 162.3 (d, $^{1}J_{C\text{-}F}$ = 247 Hz), 147.7(t, $^{3}J_{C\text{-}F}$ = 8.3 Hz), 139.7, 136.9, 136.7, 131.2, 130.6, 130.5, 128.9, 128.80, 128.76, 128.4, 127.9, 127.8, 126.7, 110.3 (dd, $^{2}J_{C\text{-}F}$ = 19.6 Hz, $^{3}J_{C\text{-}F}$ = 5.9 Hz), 102.2 (t, $^{2}J_{C\text{-}F}$ = 25 Hz), 67.9 (t, *J* = 1.9 Hz) ppm; IR (thin film): 3059, 3027, 1621, 1596, 1576, 1492, 1446, 1313, 1116, 970, 756, 694 cm^{-1}; HRMS calc'd for $C_{28}H_{22}F_2N^+$ 410.1715, observed 410.1720 $[M+H]^+$.

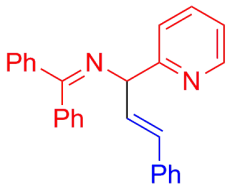


(*E*)-1-(3,5-Bis(trifluoromethyl)phenyl)-*N*-(diphenylmethylene)-3-phenylprop-2-en-1-amine (3ga): The reaction was performed the General Procedure with ketimine **1g** (40.6 mg, 0.10 mmol), LiN(SiMe3)2 (20.1 mg, 0.12 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol) in 15 min at 0.05 M. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (47.4 mg, 93% yield) as a thick colorless oil. R_f = 0.75 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.76 (s, 1H), 7.74–7.72 (m, 2H), 7.50–7.48 (m, 3H), 7.44–7.42 (m, 1H), 7.39–7.34 (m, 4H), 7.27 (t, *J* = 7.5 Hz, 2H), 7.24–7.21 (m, 1H), 7.16–7.14 (m, 2H), 6.41–6.40 (m, 2H), 5.23 (t, *J* = 3.0 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.4, 146.4, 139.5, 136.7, 136.6, 131.8 (q, *J* = 32.8 Hz), 131.0, 130.87, 130.86, 129.1, 128.99, 128.93, 128.8, 128.5, 128.1, 127.85, 127.83, 127.7, 126.8, 124.7, 122.6 (m), 67.9 ppm; IR (thin film): 3060, 3027, 1620, 1446, 1374, 1278, 1171, 996, 741, 694 cm^{-1}; HRMS calc'd for $C_{30}H_{22}F_6N^+$ 510.1656, observed 510.1646 $[M+H]^+$.

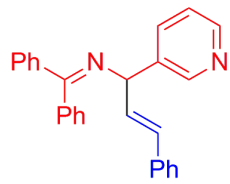


(*E*)-*N*-(Diphenylmethylene)-3-phenyl-1-(o-tolyl)prop-2-en-1-amine (3ha): The reaction was performed following the General Procedure with ketimine **1h** (28.5 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), vinyl bromide

2a (36.6 mg, 0.20 mmol) in 8 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (23.1 mg, 61% yield) as a thick colorless oil. The ^{1}H and $^{13}C\{^{1}H\}$ NMR data for this compound match the literature data.[12b]

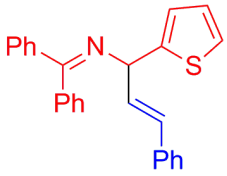


(*E*)-*N*-(Diphenylmethylene)-3-phenyl-1-(pyridin-2-yl)prop-2-en-1-amine (3ia): The reaction was performed following the General Procedure with ketimine **1i** (27.2 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol) in 1.5 h at 0.05 M. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to ethyl acetate:hexanes = 1:10) to give the product (28.8 mg, 77% yield) as a thick colorless oil. R_f = 0.30 (ethyl acetate:hexanes = 1:3); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, *J* = 5.5 Hz, 1H), 7.76 (dd, *J* = 9.0, 7.0 Hz, 3H), 7.69 (td, *J* = 7.5, 2.0 Hz, 1H), 7.44–7.40 (m, 4H), 7.38–7.34 (m, 4H), 7.26–7.24 (m, 2H), 7.19–7.16 (m, 3H), 7.14 (ddd, *J* = 7.0, 5.0 , 1.0 Hz, 1H), 6.59 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.45 (d, *J* = 16.0 Hz, 1H), 5.34 (d, *J* = 6.5 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 168.9, 162.9, 149.3, 140.1, 137.4, 136.9, 136.6, 131.8, 130.4, 129.9, 129.0, 128.9, 128.7, 128.6, 128.3, 127.9, 127.5, 126.7, 122.23, 122.19, 70.5 ppm; IR (thin film): 3026, 1622, 1587, 1490, 1446, 1289, 749, 695 cm^{-1}; HRMS calc'd for $C_{27}H_{23}N_2^+$ 375.1861, observed 375.1849 $[M+H]^+$.

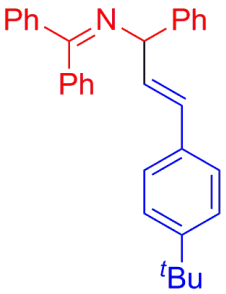


(*E*)-*N*-(Diphenylmethylene)-3-phenyl-1-(pyridin-3-yl)prop-2-en-1-amine (3ja): The reaction was performed following the General Procedure with ketimine **1j** (27.2 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol) in 1.5 h at 0.05 M. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to ethyl acetate:hexanes = 1:10) to give the product (26.6 mg, 71% yield) as a thick colorless oil. R_f = 0.30 (ethyl acetate:hexanes = 1:3); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.56 (d, *J* = 2.0 Hz, 1H), 8.49

(dd, *J* = 4.5, 1.5 Hz, 1H), 7.79 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.73–7.71 (m, 2H), 7.47–7.46 (m, 3H), 7.39–7.37 (m, 1H), 7.35–7.32 (m, 4H), 7.27–7.15 (m, 6H), 6.48 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.18 (d, *J* = 6.5 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 168.6, 149.2, 148.6, 139.6, 139.0, 136.9, 136.7, 135.2, 131.5, 130.5, 130.3, 128.9, 128.86, 128.76, 128.67, 128.3, 127.76, 127.69, 126.6, 123.6, 66.4 ppm; IR (thin film): 3027, 1621, 1596, 1474, 1446, 1282, 750, 695 cm^{-1}; HRMS calc'd for $C_{27}H_{23}N_2^+$ 375.1861, observed 375.1869 $[M+H]^+$.

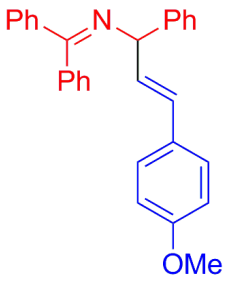


(*E*)-*N*-(Diphenylmethylene)-3-phenyl-1-(thiophen-2-yl)prop-2-en-1-amine(3ka): The reaction was performed following the General Procedure with ketimine **1k** (27.7 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (25.1 mg, 0.15 mmol), vinyl bromide **2a** (36.6 mg, 0.20 mmol) in 3 h at 0.05 M. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (31.1 mg, 82% yield) as a thick colorless oil. R_f = 0.67 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73–7.72 (m, 2H), 7.47–7.46 (m, 3H), 7.41–7.33 (m, 5H), 7.28 (t, *J* = 7.5 Hz, 2H), 7.24–7.19 (m, 4H), 6.96 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.87 (d, *J* = 3.5 Hz, 1H), 6.53 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.38 (d, *J* = 16.0 Hz, 1H), 5.39 (d, *J* = 6.5 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 168.5, 147.8, 139.8, 137.1, 136.6, 131.8, 130.5, 129.9, 129.1, 128.9, 128.72, 128.70, 128.3, 127.9, 127.7, 126.9, 126.8, 124.6, 123.3, 64.9 ppm; IR (thin film): 3025, 1621, 1596, 1496, 1446, 694 cm^{-1}; HRMS calc'd for $C_{26}H_{22}NS^+$ 380.1473, observed 380.1466 $[M+H]^+$.

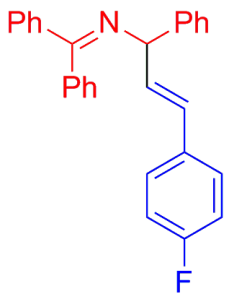


(*E*)-3-(4-(tert-Butyl)phenyl)-*N*-(diphenylmethylene)-1-phenylprop-2-en-1-amine (3ab): The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.30 mmol), vinyl bromide **2b** (47.8 mg, 0.20 mmol) in 3 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (39.5 mg, 92% yield) as a thick colorless oil. R_f = 0.63 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73–7.71 (m, 2H), 7.44–7.42 (m, 3H), 7.40–7.38 (m, 2H), 7.36–7.28 (m, 9H), 7.22–7.16 (m, 3H),

6.49 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.14 (d, *J* = 6.5 Hz, 1H), 1.28 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.6, 150.6, 143.7, 140.1, 137.1, 134.6, 131.9, 130.3, 129.3, 128.9, 128.7, 128.62, 128.60, 128.2, 127.9, 127.6, 127.0, 126.4, 125.6, 68.8, 34.7, 31.5 ppm; IR (thin film): 2962, 1622, 1576, 1446, 1314, 1269, 966, 697 cm^{-1}; HRMS calc'd for $C_{32}H_{32}N^+$ 430.2535, observed 430.2535 $[M+H]^+$.

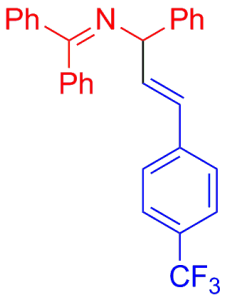


(*E*)-*N*-(Diphenylmethylene)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-amine (3ac): The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), vinyl bromide **2c** (42.6 mg, 0.20 mmol) in 3 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (39.5 mg, 98% yield) as a thick colorless oil. R_f = 0.46 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.73–7.71 (m, 2H), 7.44–7.43 (m, 3H), 7.40–7.27 (m, 9H), 7.21–7.20 (m, 1H), 7.18–7.16 (m, 2H), 6.80 (d, *J* = 9.0 Hz, 2H), 6.39 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.32 (d, *J* = 16.0 Hz, 1H), 5.13 (d, *J* = 6.5 Hz, 1H), 3.76 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.5, 159.2, 143.8, 140.1, 137.1, 130.6, 130.3, 130.1, 129.1, 128.9, 128.68, 128.61, 128.2, 127.9, 127.8, 127.5, 127.0, 114.1, 68.8, 55.5 ppm; IR (thin film): 3058, 3027, 1607, 1576, 1510, 1446, 1250, 966, 698 cm^{-1}; HRMS calc'd for $C_{29}H_{26}NO^+$ 404.2014, observed 404.2000 $[M+H]^+$.

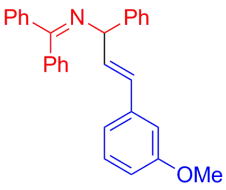


(*E*)-*N*-(Diphenylmethylene)-3-(4-fluorophenyl)-1-phenylprop-2-en-1-amine (3ad): The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (33.5 mg, 0.2 mmol), vinyl bromide **2d** (40.2 mg, 0.20 mmol) in 3 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (37.6 mg, 96% yield) as a thick colorless oil. R_f = 0.56 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.73–7.72 (m, 2H), 7.43–7.42 (m, 3H), 7.39–7.37 (m, 2H), 7.35–7.26 (m, 7H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.16–7.14 (m, 2H), 6.93 (t, *J* = 9.0 Hz, 2H), 6.48 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.35 (d, *J* = 16.0 Hz, 1H),

5.14 (d, J = 6.5 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): 167.7, 162.3 (d, $^{1}J_{C\text{-}F}$= 245.0 Hz), 143.5, 140.1, 136.9, 133.5 (d, $^{4}J_{C\text{-}F}$= 3.1 Hz), 132.5 (d, $^{4}J_{C\text{-}F}$= 2.2 Hz), 130.3, 128.9, 128.73, 128.68, 128.64, 128.3, 128.2, 128.1, 128.0, 127.9, 127.5, 127.1, 115.5 (d, $^{2}J_{C\text{-}F}$= 21.5 Hz), 68.6 ppm; IR (thin film): 3059, 3027, 1621, 1600, 1508, 1446, 1228, 1157, 966, 698 cm^{-1}; HRMS calc'd for $C_{28}H_{23}NF^{+}$ 392.1815, observed 392.1810 $[M+H]^{+}$.

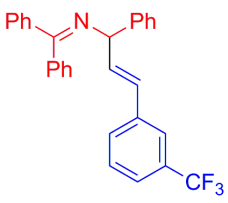


(*E*)-*N*-(Diphenylmethylene)-1-phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-amine (3ae): The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), vinyl bromide **2e** (50.2 mg, 0.20 mmol) in 3 h at 0.1 M. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (30.9 mg, 70% yield) as a thick colorless oil. R_f = 0.74 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.53–7.51 (m, 2H), 7.47–7.43 (m, 5H), 7.40–7.31 (m, 7H), 7.25–7.23 (m, 1H), 7.17–7.15 (m, 2H), 6.61 (dd, J = 16.0, 6.5 Hz, 1H), 6.45 (d, J = 16.0 Hz, 1H), 5.16 (d, J = 6.5 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 168.1, 143.1, 140.9, 139.9, 136.9, 135.5, 130.5, 129.3 (d, J = 32 Hz), 128.9, 128.84, 128.78, 128.72, 128.3, 128.2, 127.9, 127.6, 127.3, 126.8, 125.6 (q, J= 4 Hz), 124.5 (q, J = 271 Hz), 68.5 ppm; IR (thin film): 3027, 1614, 1577, 1325, 1122, 1067, 698 cm^{-1}; HRMS calc'd for $C_{29}H_{23}NF_3^{+}$ 442.1783, observed 442.1781 $[M+H]^{+}$.

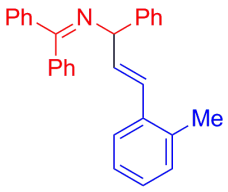


(*E*)-*N*-(Diphenylmethylene)-3-(3-methoxyphenyl)-1-phenylprop-2-en-1-amine (3af): The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (33.5 mg, 0.2 mmol), vinyl bromide **2f** (42.6 mg, 0.20 mmol) in 3 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (39.5 mg, 98% yield) as a thick colorless oil. R_f = 0.40 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.44–7.39 (m, 5H), 7.35–7.28 (m, 5H), 7.21 (t, J = 7.0 Hz, 1H), 7.17–7.13 (m, 3H), 6.93 (d, J = 7.5 Hz, 1H),

6.90 (s, 1H), 6.73 (dd, *J* = 8.0, 2.5 Hz, 1H), 6.53 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.38 (d, *J* = 16.0 Hz, 1H), 5.15 (d, *J* = 6.5 Hz, 1H), 3.73 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.7, 159.9, 143.5, 140.0, 138.8, 136.9, 132.9, 130.3, 129.6, 129.5, 128.9, 128.7, 128.64, 128.62, 128.2, 127.9, 127.5, 127.1, 119.3, 113.5, 111.6, 68.7, 55.3 ppm; IR (thin film): 3058, 3026, 1620, 1598, 1446, 1267, 967, 699 cm^{-1}; HRMS calc'd for $C_{29}H_{26}NO^+$ 404.2014, observed 404.2002 $[M+H]^+$.

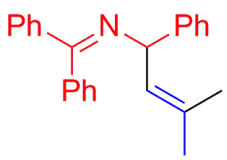


(*E*)-*N*-(Diphenylmethylene)-1-phenyl-3-(3-(trifluoromethyl)phenyl)prop-2-en-1-amine (3ag): The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), vinyl bromide **2g** (50.2 mg, 0.20 mmol) in 3 h at 0.1 M. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (33.1 mg, 75% yield) as a thick colorless oil. R_f = 0.56 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.60 (s, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.47–7.42 (m, 4H), 7.40–7.31 (m, 8H), 7.25–7.22 (m, 1H), 7.17–7.15 (m, 2H), 6.59 (dd, *J* = 16.0, 6.5 Hz, 1H), 6.45 (d, *J* = 16.0 Hz, 1H), 5.16 (d, *J* = 6.5 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.0, 143.2, 139.9, 138.2, 134.8, 131.1 (d, $J_{C\text{-}F}$= 32 Hz), 130.5, 129.7, 129.1, 128.9, 128.8, 128.78, 128.72, 128.3, 128.1, 127.9, 127.6, 127.3, 125.4, 124.0 (q, $J_{C\text{-}F}$= 4 Hz), 123.3 (q, $J_{C\text{-}F}$= 4 Hz), 68.5 ppm; IR (thin film): 3060, 3027, 1621, 1598, 1490, 1446, 1331, 1072, 964, 697 cm^{-1}; HRMS calc'd for $C_{29}H_{23}NF_3^+$ 442.1783, observed 441.1778 $[M+H]^+$.

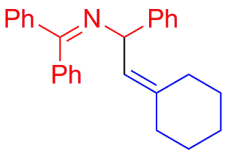


(*E*)-*N*-(Diphenylmethylene)-1-phenyl-3-(o-tolyl)prop-2-en-1-amine (3ah): The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), vinyl bromide **2h** (39.4 mg, 0.20 mmol) in 3 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (37.2 mg, 96% yield) as a thick colorless oil. R_f = 0.69 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.45–7.41 (m, 6H), 7.36–7.30 (m, 5H), 7.22–7.17 (m, 3H), 7.11–7.09 (m, 3H), 6.60 (d, *J* = 16.0 Hz, 1H), 6.41 (dd, *J* = 16.0, 6.5 Hz, 1H),

5.17 (d, J = 6.5 Hz, 1H), 2.29 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 167.6, 143.7, 140.1, 137.1, 136.4, 135.5, 133.9, 130.4, 130.3, 128.9, 128.8, 128.6, 128.3, 127.9, 127.53, 127.46, 127.1, 126.2, 125.9, 69.1, 20.0 ppm; IR (thin film): 3058, 3024, 1621, 1598, 1490, 1446, 1314, 965, 748, 698 cm^{-1}; HRMS calc'd for $C_{29}H_{26}N^+$ 388.2065, observed 388.2067 $[M+H]^+$.



***N*-(Diphenylmethylene)-3-methyl-1-phenylbut-2-en-1-amine (3ai):** The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.30 mmol), vinyl bromide **2i** (27.0 mg, 0.20 mmol) in 12 h at 0.1 M. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (17.6 mg, 54% yield) as a thick colorless oil. R_f = 0.64 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.70–7.69 (m, 2H), 7.42–7.39 (m, 3H), 7.34–7.27 (m, 7H), 7.19–7.17 (m, 1H), 7.15–7.13 (m, 2H), 5.60 (dt, J = 9.0, 1.0 Hz, 1H), 5.25 (d, J = 9.0 Hz, 1H), 1.70 (s, 3H), 1.36 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 166.9, 144.9, 140.2, 137.4, 131.7, 130.1, 128.8, 128.54, 128.50, 128.4, 128.2, 128.1, 127.4, 127.1, 126.6, 64.7, 26.01, 18.5 ppm; IR (thin film): 3059, 3023, 1971, 2912, 1621, 1599, 1446, 1314, 1279, 773, 697 cm^{-1}; HRMS calc'd for $C_{24}H_{24}N^+$ 326.1909, observed 326.1917 $[M+H]^+$.



2-Cyclohexylidene-N-(diphenylmethylene)-1-phenylethanamine (3aj): The reaction was performed following the General Procedure with ketimine **1a** (27.1 mg, 0.10 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.30 mmol), vinyl bromide **2j** (35.0 mg, 0.20 mmol) in 15 min at 60 ^oC. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (20.1 mg, 55% yield) as a thick colorless oil. R_f = 0.76 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.71–7.69 (m, 2H), 7.43–7.40 (m, 3H), 7.37–7.27 (m, 7H), 7.20–7.18 (m, 1H), 7.16–7.15 (m, 2H), 5.54 (d, J = 9.0 Hz, 1H), 5.33 (d, J = 9.0 Hz, 1H), 2.09 (t, J = 6.0 Hz, 2H), 2.85 (t, J = 6.0 Hz, 2H), 1.22–1.47 (m, 4H), 1.42–1.37 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 166.9, 145.0, 140.2, 139.6, 137.4, 130.1, 128.8, 128.50, 128.45, 128.2, 128.0, 127.0, 12635, 124.1, 63.6, 37.3, 29.6, 28.5, 27.8, 26.9 ppm; IR (thin film): 3058, 3024,

2927, 2852, 1621, 1598, 1446, 1314, 1165, 1028, 779, 696 cm^{-1}; HRMS calc'd for $C_{27}H_{28}N^+$ 366.2222, observed 366.2227 $[M+H]^+$.

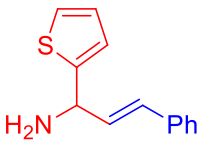
Gram scale sequential one-pot ketimine Synthesis/vinylation procedure:

An oven-dried 100 mL Schlenk tube equipped with a stir bar was sealed with a rubber septum and was connected to a Schlenk line, evacuated, and refilled with nitrogen (repeated three times). DCM (10 mL) was added under nitrogen via syringe through the rubber septum. 2-thiophenemethylamine (339.54 mg, 3.0 mmol) and benzophenone imine (543.69 mg, 3.0 mmol) were added under nitrogen via syringe through the rubber septum. The reaction was stirred at 23 $^{\circ}C$ for 12 h, the solvent was completely removed in *vacuo* and the tube was filled with nitrogen. A solution (prepared in the glove box) of vinyl bromide 2a (1.09 g, 6.0 mmol) in 10 mL anhydrous DME was added to the Schlenk tube via syringe through the rubber septum. Next, a solution of $LiN(SiMe_3)_2$ (0.76 g, 4.5 mmol) in 50 mL anhydrous DME was added by syringe through the rubber septum. The reaction mixture was stirred for 3 h in total at 23 $^{\circ}C$, opened to air, and quenched with 10 mL of H_2O. The layers were separated and the aqueous layer was extracted with DCM (3X5 mL). The combined organic layers were concentrated in *vacuo*. The crude material was loaded onto a deactivated silica gel column via pipette and purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (1.02 g, 90% yield) as a thick colorless oil.

Product hydrolysis:

Hydrolysis of Product 3ka: An oven-dried microwave vial equipped with a stir bar was charged with **3ka** (38.0 mg 0.1 mmol). HCl 1N (1 mL) and MeOH (1 mL) were added to the reaction vial via syringe at 0 $^{\circ}C$. The solution was warmed to room temperature, stirred at room temperature and was monitored by TLC until all **3ka** was consumed (Reaction completed in 3 h). The reaction mixture was transferred to a 10 mL seperatory funnel via pipette and was extracted with dichloromethane (3X2 mL). The aqueous layer was then basified with 1N NaOH till pH=10 and was extracted with dichloromethane (3X2 mL). The combined organic layers were concentrated

in *vacuo*. After drying under vacuum for 12 h, the amine product **4ka** was obtained as a yellow oil (21.3 mg, 99% yield).



4ka-(*E*)-3-phenyl-1-(thiophen-2-yl)prop-2-en-1-amine: R_f = 0.12 (ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40–7.38 (m, 2H), 7.32–7.29 (m, 2H), 7.24–7.22 (m, 2H), 6.97–6.95 (m, 2H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.28 (dd, *J* = 16.0, 6.5 Hz, 1H), 4.93 (d, *J* = 6.5 Hz, 1H), 1.88 (s, br, 2H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.5, 136.9, 133.4, 129.9, 128.8, 127.8, 127.0, 126.7, 124.5, 123.7, 55.3 ppm; IR (thin film): 3059, 3025, 2920, 2851, 1597, 1577, 1494, 1448, 1384, 1230, 1117, 954, 694 cm^{-1}; HRMS calc'd for $C_{13}H_{11}S$ 199.0581, observed 199.0565 $[M\text{-}NH_2]^+$.

High-throughput experimentation screenings for Pd-catalyzed chemo- and regioselective arylation:

(1) Screening of ligand, solvent and temperature:

Set up:

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials was predosed with $Pd(OAc)_2$ (1 μmol) **(Vial A1 contained no Pd)** and the phosphine ligands (2 μmol for monodentate ligands and 1 μmol for bidentate ligands) **(Vial A1 contained no ligand)** in THF. The solvent was removed to dryness using a GeneVac and $NaN(SiMe_3)_2$ (30 μmol) in THF was added to the ligand/Pd mixture. The solvent was removed on the GeneVac and a parylene stir bar was then added to each reaction vial. Ketimine **1a** (10 μmol/reaction) and vinyl bromide **2a** (20 μmol) were then dosed together into each reaction vial as a solution in THF (100 μL, 0.1 M). The 24-well plate was then sealed and stirred for 3 h at 23 °C.

Work up:

Upon opening the plate to air, 500 μL of a solution of biphenyl (used as internal standard to measure UPLC yields) in acetonitrile (0.002 mol/L) was added into each vial. The plate was covered again and the vials stirred for 10 min. to ensure good homogenization. Into a separate

96-well LC block was added 700 µL of acetonitrile, followed by 25 µL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated UPLC instrument for analysis.

Vial	Ligand	3aa/IS
A1	**Blank (No Pd, No ligand)**	2.30
A2	4-(Di-*tert*-butylphosphino)-N,N-dimethylaniline (Ataphos)	2.69
A3	2-Dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (Dave Phos)	1.23
A4	2-Di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropyl-1,1'-biphenyl (Me4tBuXPhos)	1.99
A5	Dicyclohexyl-[3,6-dimethoxy-2-(2,4,6-triisopropylphenyl)phenyl]phosphane (BrettPhos)	0.39
A6	1,1'-Bis(diphenylphosphino)ferrocene (Dppf)	2.63
B1	9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (XantPhos)	2.71
B2	2-Dicyclohexylphosphino-2′-methylbiphenyl (MePhos)	2.40
B3	N-(dicyclohexylphosphino)-2-2'-tolylindole (Indole ligand)	0.23
B4	P(O-Tol)3	4.34
B5	$P^tBu_3HBF_4$	1.41
B6	2-(Dicyclohexylphosphino)-1-phenyl-1H-pyrrole (CataCXium Pcy)	2.03
C1	4,6-Bis(diphenylphosphino)phenoxazine (NIXANTPHOS)	2.63
C2	Di(1-adamantyl)-2-dimethylaminophenylphosphine (Me-Dalphos)	2.69
C3	2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (Sphos)	2.60
C4	Butyldi-1-adamantylphosphine (CataCXium A)	2.36
C5	PCy_3HBF_4	2.78
C6	2-Di-*tert*-butylphosphino-3-Methoxy-6-Methyl-2'-4'-6'-triisopropylbiphenyl (RockPhos)	2.60
D1	1,2,3,4,5-Pentaphenyl-1'-(di-t-butylphosphino)ferrocene (Qphos)	2.39
D2	PPh_3	2.16
D3	1-[2-[Bis(tert-butyl)phosphino]phenyl]-3,5-diphenyl-1H-pyrazole (Trippy Phos)	2.36
D4	2-(Dicyclohexylphosphino)biphenyl (CyJohnPhos)	2.82

D5	2-Dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl (Xphos)	2.61
D6	Di(1-adamantyl)-2-morpholinophenylphosphine (Mor-DalPhos)	2.13

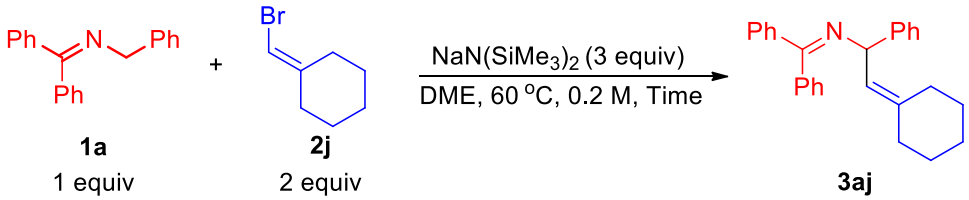
Reaction kinetics study of coupling between 1a and 2j

Set up:

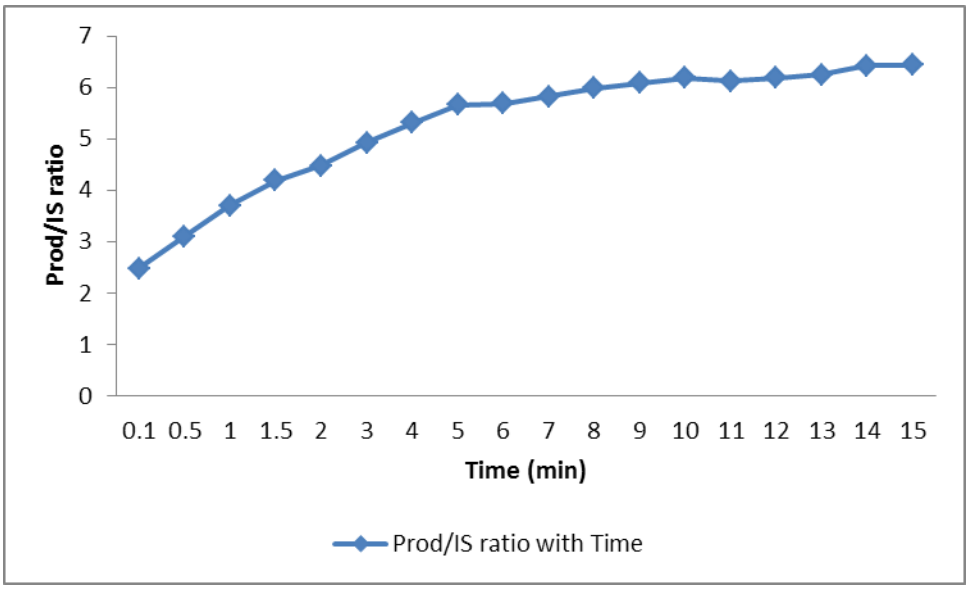
Experiments were set up inside a glovebox under a nitrogen atmosphere. Ketimine **1a** (20 µmol/reaction) and vinyl bromide **2j** (40 µmol/reaction) were dosed together into 2 mL crimp top glass vials as a solution in DME (50 µL). $NaN(SiMe_3)_2$ (60 µmol/reaction) was then dosed into the vials as a solution in DME (50 µL). Total volume of the reactions is 100 µL, 0.2 M. The vials were sealed with crimp caps, removed from the glovebox and stirred at 60 °C. Vials were sequentially quenched with 1 drop of water via syringe through the rubber septum at 10 s, 30 s, 1 min then every 1 min until 15 min.

Work up:

Upon opening the seal, 500 µL of a solution of 4,4'-di-*tert*-butylbiphenyl (used as internal standard to measure UPLC yields) in acetonitrile (0.002 mol/L) was added into each vial. The plate of vials were stirred for 10 min. to ensure good homogenization. Into a separate 96-well LC block was added 700 µL of acetonitrile, followed by 25 µL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated UPLC instrument for analysis.



1a 1 equiv + **2j** 2 equiv → **3aj**



Supplementary Figure 1. Reaction kinetics study of coupling between 1a and 2j.

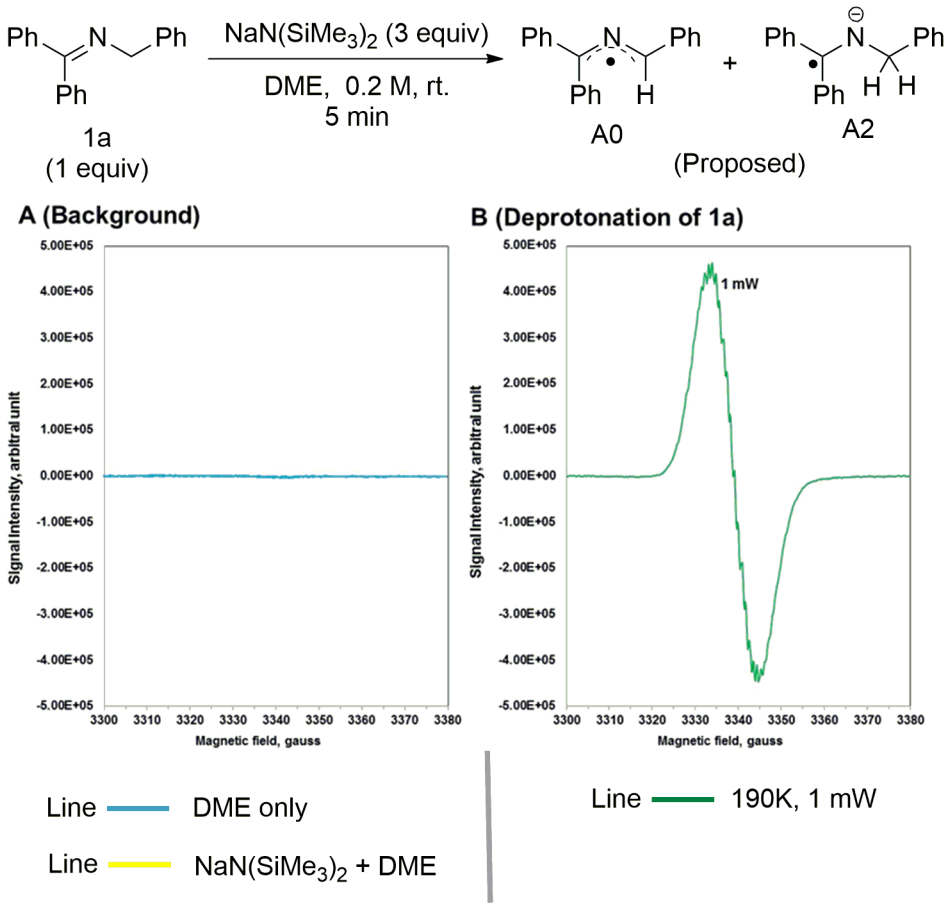
EPR experiments

Sample tube preparation:

In a thin wall quartz EPR tube (4 mm*250 mm), a solution of $NaN(SiMe_3)_2$ in DME (or Toluene) (0.10 mmol, 250 µL) and a solution of ketimine **1a** (0.10 mmol, 250 µL) were added by pipetter under a nitrogen atmosphere in a glove box. The EPR tube was sealed with a cap. The samples were allowed to react for ~5 min at rt, followed by removal from the glove box and cooling in liquid nitrogen.

EPR spectra analysis:

EPR spectra were recorded by a Bruker EMXmicro spectrometer at X-band (9.37 GHz). The temperature of the EPR experiments was held at 190 K using a Bruker liquid nitrogen flow system (ER4131VT). EPR conditions were as follow: microwave power 1 mW; modulation frequency, 100 kHz; modulation amplitude, 1 G (gauss); time constant, 82 ms.

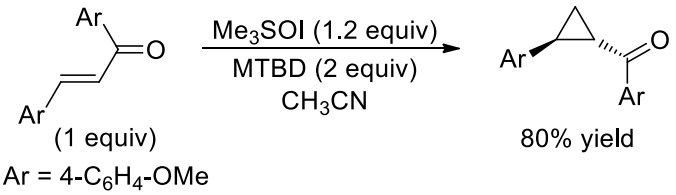


Supplementary Figure 2. EPR spectra of deprotonation of **1a**.

Radical clock experiments

Synthesis of radical clock 2k:

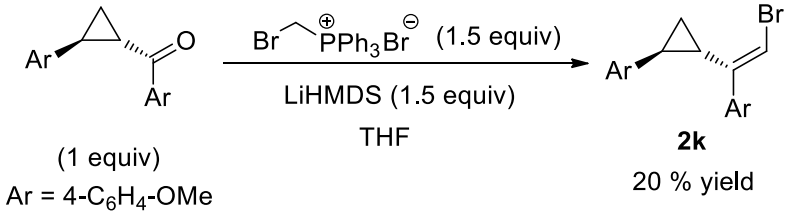
Synthesis of (4-methoxyphenyl)(2-(4-methoxyphenyl)cyclopropyl)methanone:



First, (4-methoxyphenyl)(2-(4-methoxyphenyl)cyclopropyl)methanone was prepared based on literature procedures.[4] An oven-dried 250 mL Schlenk tube equipped with a stir bar was charged

with a mixture of trimethylsulfoxonium iodide (2.64 g, 12 mmol, 1.2 equiv), 1,3,4,6,7,8-hexahydro-1-methyl-2H-pyrimido[1,2-a]pyrimidine (MTBD, 3.06 g, 20 mmol, 2 equiv) and (*E*)-1,3-bis(4-methoxyphenyl)prop-2-en-1-one (2.68 g, 10 mmol, 1 equiv). The Schlenk tube was sealed with a rubber septum and was connected to a Schlenk line, evacuated, and refilled with nitrogen (repeated three times). Anhydrous MeCN (50 mL) was added under nitrogen via syringe through the rubber septum. The reaction mixture was stirred at 60 ºC under nitrogen for 2.5 h. After cooling to room temperature, the mixture was diluted with water (50 mL) and was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with saturated brine (50 mL), then dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography (ethyl acetate:hexanes = 1:4) to the product (2.25 g , 80% yield) as a thick yellow oil. R_f = 0.15 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 3.82 (s, 3H), 3.76 (s, 3H), 2.79 – 2.74 (m, 1H), 2.64 – 2.57 (m, 1H), 1.86 – 1.83 (m, 1H), 1.46 – 1.42 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 197.0, 163.5, 158.5, 132.8, 130. 9, 130.4, 127.5, 114.1, 113.8, 55.5, 55.4, 29.2, 28.8, 18.6 ppm; IR (thin film): 3003, 2957, 2836, 1656, 1600, 1515, 1420, 1392, 1292, 1167, 1032, 989, 854 cm^{-1}.

Synthesis of radical clock 2k:



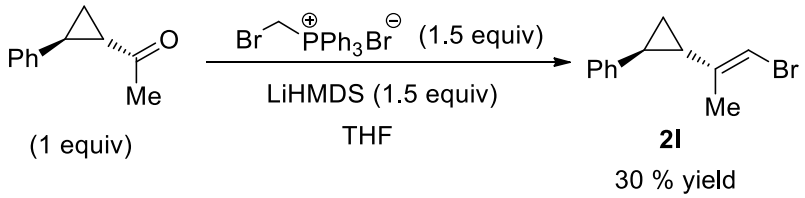
An oven-dried 100 mL Schlenk tube equipped with a stir bar was charged with a mixture of bromomethyl triphenylphosphonium bromide (3.27 g, 7.5 mmol, 1.5 equiv) and $LiN(SiMe_3)_2$ (1.26 g, 7.5 mmol, 1.5 equiv). The Schlenk tube was sealed with a rubber septum and was connected to a Schlenk line, evacuated, and refilled with nitrogen (repeated three times). Anhydrous THF (25 mL) was added under nitrogen via syringe through the rubber septum. The reaction mixture was stirred at 0 ºC under nitrogen for 30 min. Next, a solution of (4-methoxyphenyl)(2-(4-

methoxyphenyl)cyclopropyl)methanone (1.41 g, 5.0 mmol, 1.0 equiv.) in 25 mL anhydrous THF was added dropwise via syringe through the rubber septum in 10 min. The reaction mixture was wrapped with aluminum foil and stirred at room temperature for 12 h. The mixture was then diluted with water (50 mL) and extracted with EtOAc (20 mL × 3). The combined organic layers were washed with saturated brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified with a Waters autopurificaiton system (Waters SunFire Prep C18 OBD 19x100 mm; 50% acetonitrile:water to 96 % acetonitrile in 8 mins; 25 mL/min) to provide the product **2k** (359 mg , 20% yield) as a thick colorless oil. R_f = 0.50 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.26 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 2.23 – 2.19 (m, 1H), 1.88 – 1.84 (m, 1H), 1.25 – 1.20 (m, 1H), 1.01 – 0.97 (m, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.4, 158.1, 145.9, 134.1, 131.3, 129.6, 127.5, 114.1, 113.8, 105.9, 55.52, 55.50, 26.4, 23.7, 16.0 ppm; IR (thin film): 3072, 2999, 2954, 2833, 2359, 1607, 1513, 1289, 1247, 1177, 1034, 833 cm^{-1}.

Synthesis of radical clock 2l:

Synthesis of 1-(2-phenylcyclopropyl)ethanone: 1-(2-phenylcyclopropyl)ethanone was prepared according to literature procedures. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data.[33]

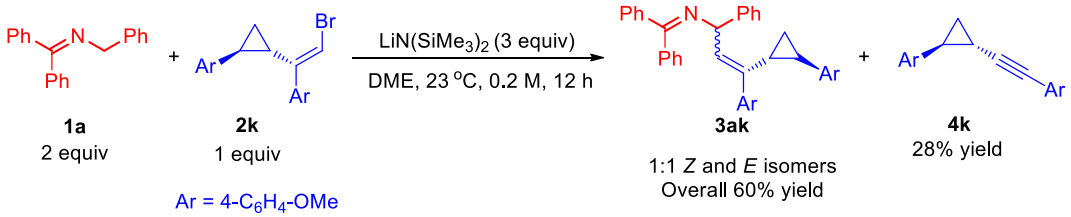
Synthesis of radical clock 2l:



An oven-dried 100 mL Schlenk tube equipped with a stir bar was charged with a mixture of bromomethyl triphenylphosphonium bromide (3.27 g, 7.5 mmol, 1.5 equiv) and $LiN(SiMe_3)_2$ (1.26 g, 7.5 mmol, 1.5 equiv). The Schlenk tube was sealed with a rubber septum and was connected to a Schlenk line, evacuated, and refilled with nitrogen (repeated three times). Anhydrous THF

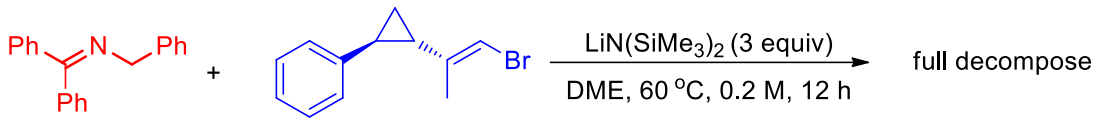
(25 mL) was added under nitrogen via syringe through the rubber septum. The reaction mixture was stirred at 0 ºC under nitrogen for 30 min. Next, a solution of 1-(2-phenylcyclopropyl)ethanone (0.8 g, 5.0 mmol, 1.0 equiv.) in 25 mL anhydrous THF was added dropwise via syringe through the rubber septum in 10 min. The reaction mixture was wrapped with aluminum foil and stirred at room temperature for 12 h. The mixture was then diluted with water (50 mL) and was extracted with EtOAc (20 mL × 3). The combined organic layers were washed with saturated brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified with a Waters autopurificaiton system (Waters SunFire Prep C18 OBD 19x100mm; 50% acetonitrile:water to 96 % acetonitrile in 8 mins; 25 mL/min) to the product **2l** (355 mg , 30% yield) as a colorless oil. R_f = 0.38 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 – 2.24 (m, 2H), 7.17 – 7.14 (m, 1H), 7.08 – 7.06 (m, 2H), 5.99 (t, *J* = 1.0 Hz, 1H), 2.02 – 1.98 (m, 1H), 1.77 (d, *J* = 1.0 Hz, 3H), 1.76 – 1.72 (m, 1H), 1.25 – 1.21 (m, 1H), 1.15 – 1.11 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 142.1, 141.4, 128.6, 126.1, 101.4, 30.2, 23.4, 17.7, 14.5 ppm; IR (thin film): 3073, 3026, 2915, 1603, 1498, 1459, 1376, 1302, 1193, 1073, 930, 742 cm^{-1}.

Coupling of ketimine 1a with radical clock 2k:



The reaction was performed following General Procedure with ketimine **1a** (54.1 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), vinyl bromide **2k** (35.9 mg, 0.1 mmol) in 12 h at 0.2 M. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:10) to give the product **3ak** (32.9 mg, mixture of 1:1 *Z* and *E* isomers, overall 60% yield) as a thick colorless oil. R_f = 0.25 (diethyl ether:hexanes = 1:5). A side product **4k** was isolated (7.8 mg, 28% yield) as a think color less oil. R_f = 0.42 (diethyl ether:hexanes = 1:5).

Coupling of ketimine 1a with radical clock 2l:



1a
2 equiv

2l
1 equiv

The reaction was performed following General Procedure with ketimine **1a** (54.1 mg, 0.20 mmol), $LiN(SiMe_3)_2$ (50.2 mg, 0.3 mmol), vinyl bromide **2l** (23.7 mg, 0.1 mmol) in 12 h at 60 °C, 0.2 M. No clean products could be isolated from this mixture.

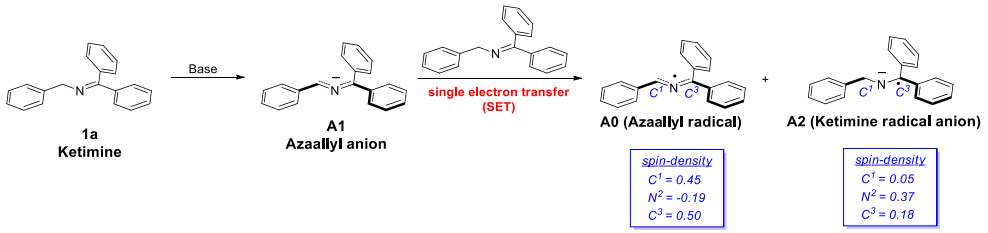
Computational Details and References

Full Reference of Gaussian09:

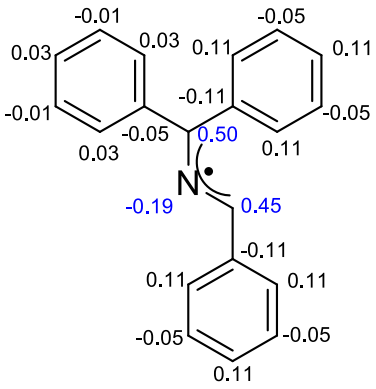
Gaussian 09, Revision B.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T.Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2010.

All optimizations were performed in Gaussian 09 using DFT using (U)UM06 with 6-31G(d) basis sets (with the guess=mix keyword as implemented in Gaussian09 for open shell calculation) in CH_2Cl_2 using CPCM[7] solvation model. Vibrational frequencies were computed at the same level to obtain thermal corrections (at 298 K; enthalpic and free energy) and to characterize the stationary points as transition states (one and only one imaginary frequency) or minima (zero

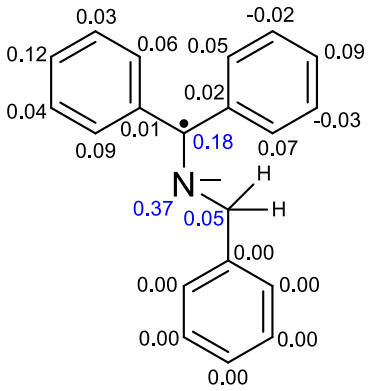
imaginary frequencies). Exhaustive conformational searches were performed for all intermediates to map out the lowest energy profile, and intrinsic reaction coordinate (IRCs) calculations were undertaken to ensure transitions states connected the illustrated ground states. Although all attempts to locate the intermediates for the corresponding stepwise process (iv, Figure 3a) led directly to dissociation back to starting materials or formation of vinylated product and bromide for this system, the anionic intermediate in the stepwise process (prior to bromide elimination) can be accessed by tuning the electronic properties of the substrate. For instance, the introduction of an electron-withdrawing group (para-NO_2) at the aryl ring or substitution of Br with weaker leaving group (F) on the styryl substrate led to a discrete anionic tetrahedral intermediate at all levels of theory. Thus, it appears that the combination of good leaving group (Br^-) and weakly stabilizing β-phenyl group is not sufficient to favor such an intermediate. Moreover, experiment with the *Z*-bromostyrene **2a'** at room temperature yield a near 2:1 ratio of *E*- and *Z*-products, albeit in low yield (14%) due to rapid competing elimination of *Z*-bromostyrene **2a'** to form alkyne (Supplementary Figure 5).



Supplementary Figure 3. Proposed formation of azaallyl radical **A0** and ketimine radical anion **A2** via a SET process.

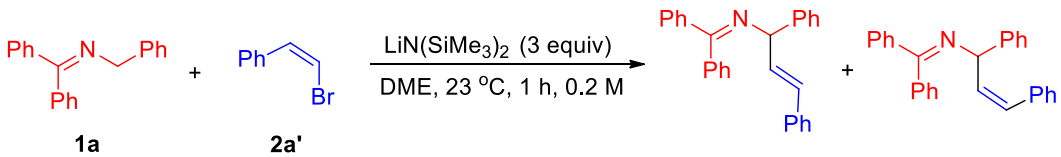


A0
(azaallyl radical)



A2
(ketimine radical anion)

Supplementary Figure 4. Mulliken charges and spin densities with hydrogens summed into heavy atoms of azaallyl radical **A0** and ketimine radical anion **A2** computed using M06-2X/6-31G(d)-CH_2Cl_2(CPCM).



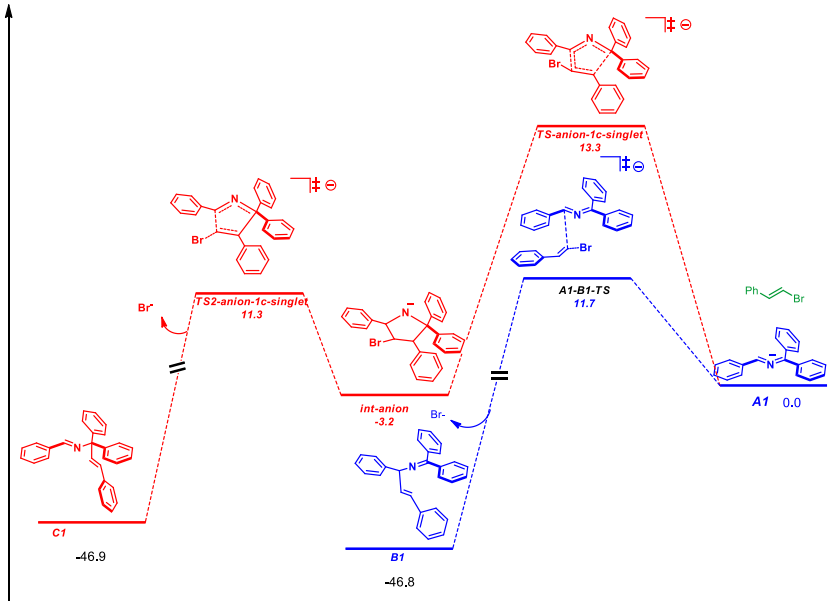
1a
(1 equiv)

2a'
(2 equiv)

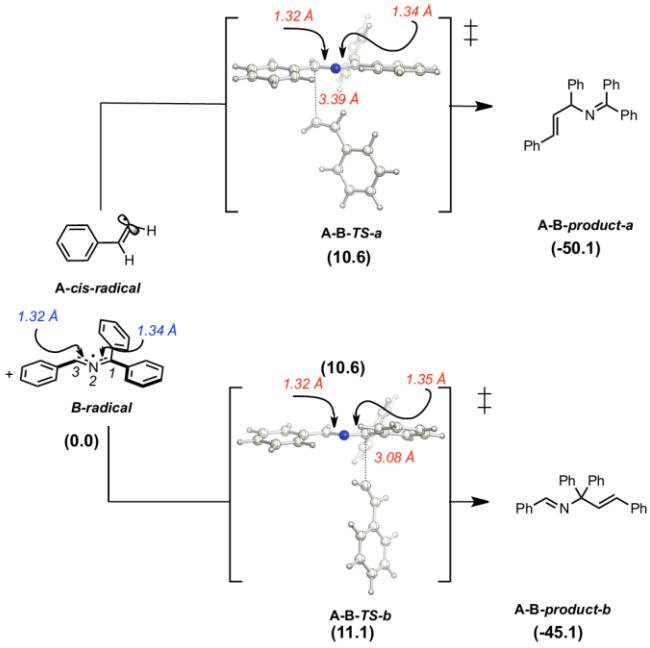
10 % AY

4 % AY

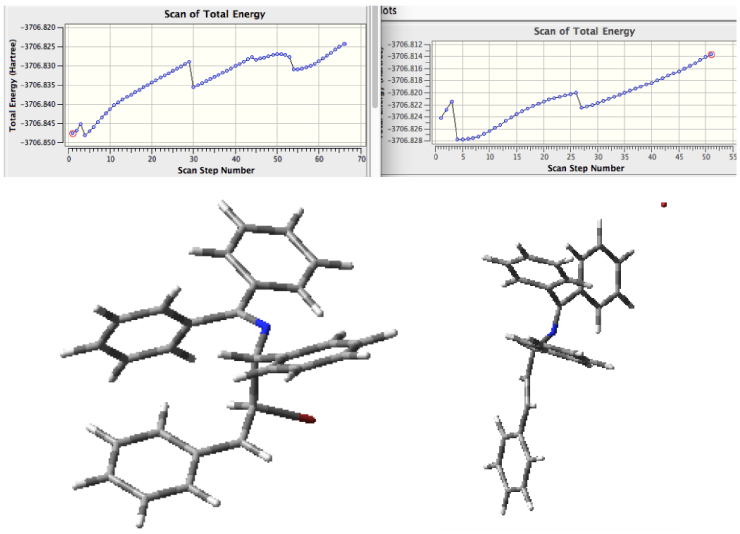
Supplementary Figure 5. Coupling of ketimine **1a** with the Z-bromostyrene **2a'**.



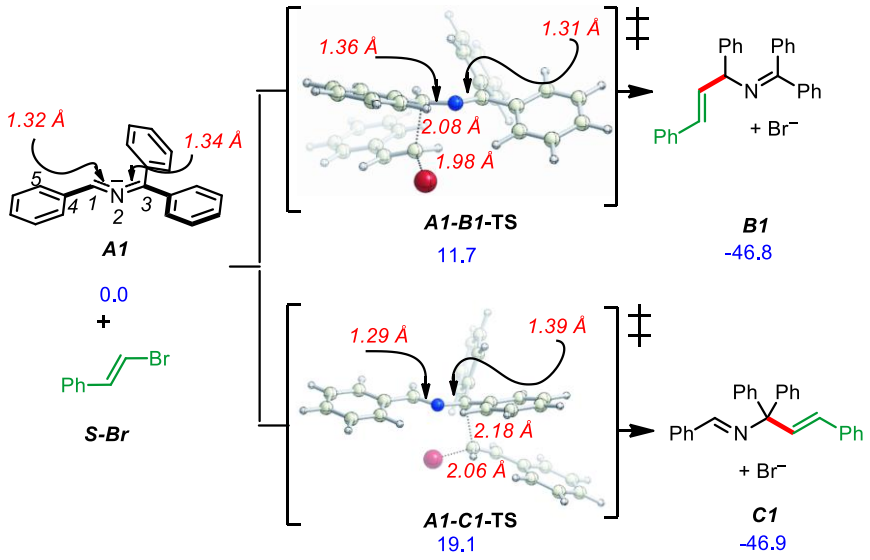
Supplementary Figure 6. M06-2X/6-31G(d)-CH2Cl2(CPCM) geometries of competing transition states for azaallyl anion S_NV reaction (blue) with styryl bromide versus stepwise cyclization path (red). Gibbs free energies are in kcal/mol relative to isolated reactants.



Supplementary Figure 7. UM06-2X/6-31G(d)-CH_2Cl_2(CPCM) geometries of competing transition states for azaallyl radical (**B-radical)** reaction with styryl radical (**A-cis-radical**). Gibbs free energies are in kcal/mol relative to isolated reactants. Selected distances (red) are in Å.



Supplementary Figure 8. M06-2X/6-31G(d)-CH2Cl2(CPCM) scan along the C-Br bond.



S-Br

Zero-point correction= 0.125531 (Hartree/Particle)

Thermal correction to Energy= 0.133512

Thermal correction to Enthalpy= 0.134456

Thermal correction to Gibbs Free Energy= 0.090756

Sum of electronic and zero-point Energies= -2880.560193

Sum of electronic and thermal Energies= -2880.552213

Sum of electronic and thermal Enthalpies= -2880.551269

Sum of electronic and thermal Free Energies= -2880.594969

C	-0.43487900	0.45038100	-0.05152800
C	0.95541600	0.49924500	-0.00632900
C	1.62935300	1.72527400	0.05010600
C	0.87400900	2.90663100	0.07693500
C	-0.51372700	2.85762200	0.03097200
C	-1.17412700	1.63018600	-0.03556600
H	-0.93935500	-0.50971800	-0.09895900
H	1.53103700	-0.42254700	-0.01956000
H	1.37027400	3.87000400	0.14801400
H	-1.08422200	3.78094300	0.05362600
H	-2.25852600	1.59618500	-0.06900800
C	3.10239600	1.71289000	0.07924600
H	3.56938100	0.74208500	0.23195000
C	3.88217100	2.77925500	-0.08602700
H	3.53654000	3.78852800	-0.26973200
Br	5.76707500	2.64972100	-0.03486100

A1

Zero-point correction= 0.301748 (Hartree/Particle)

Thermal correction to Energy= 0.318281

Thermal correction to Enthalpy= 0.319225

Thermal correction to Gibbs Free Energy= 0.255858

Sum of electronic and zero-point Energies= -825.940678

Sum of electronic and thermal Energies= -825.924146

Sum of electronic and thermal Enthalpies= -825.923201

Sum of electronic and thermal Free Energies= -825.986569

C	-1.67519700	-0.35409900	0.22594500
N	-0.34880100	-0.38475400	0.39079500
C	1.86981900	-1.29175300	0.57937100
C	2.71046700	-2.42690700	0.54851400
C	2.49416300	-0.04071300	0.79315500
C	4.08543700	-2.32021900	0.71745600
H	2.26131700	-3.40538200	0.38791400
C	3.86784800	0.05996100	0.95874400
H	1.86768100	0.84570700	0.82827900
C	4.68352000	-1.07579900	0.92424300
H	4.69834300	-3.21800400	0.68838600
H	4.31442800	1.03852400	1.12015200
H	5.75764800	-0.99160500	1.05763100
C	-2.30240000	0.96336600	0.17830800
C	-3.70006800	1.15782200	0.28609100
C	-1.51972300	2.13937900	0.06221600
C	-4.26823600	2.42701400	0.26883500
H	-4.35028400	0.29603600	0.40361200
C	-2.09204200	3.40267200	0.05279400
H	-0.44355500	2.02749600	-0.02068300
C	-3.47645700	3.56873700	0.15093800
H	-5.34789400	2.52339300	0.35955900
H	-1.44842300	4.27502800	-0.03842300
H	-3.92211200	4.55863000	0.13647700
C	-2.50070600	-1.58156200	0.12152800
C	-3.46736600	-1.74905600	-0.88725400
C	-2.34041500	-2.64206000	1.03234300
C	-4.23419400	-2.90703800	-0.97813600
H	-3.61223600	-0.95036800	-1.61082900
C	-3.10000400	-3.80394000	0.94186800

H	-1.60725100	-2.54055200	1.82804600
C	-4.05432200	-3.94603400	-0.06526000
H	-4.97079700	-3.00329300	-1.77150700
H	-2.95306000	-4.59955000	1.66749400
H	-4.64858400	-4.85208000	-0.13706700
C	0.44122100	-1.43473300	0.40548600
H	0.07033900	-2.45557100	0.26402600
Br	5.76707500	2.64972100	-0.03486100

A1-B1-TS

Imaginary frequency (cm^{-1}) = -455.56

Zero-point correction= 0.428185 (Hartree/Particle)

Thermal correction to Energy= 0.453322

Thermal correction to Enthalpy= 0.454266

Thermal correction to Gibbs Free Energy= 0.370596

Sum of electronic and zero-point Energies= -3706.505357

Sum of electronic and thermal Energies= -3706.480220

Sum of electronic and thermal Enthalpies= -3706.479275

Sum of electronic and thermal Free Energies= -3706.562946

C	-0.88521200	-0.12797100	-0.35037100
N	-1.25518800	1.07587600	-0.00804800
C	-0.92196500	3.39537500	0.62170700
C	-0.03000800	4.46306400	0.82825700
C	-2.28878800	3.62278200	0.86603800
C	-0.48290200	5.70264500	1.27409300
H	1.02946100	4.30467700	0.63761200
C	-2.73610400	4.85821700	1.31686300
H	-2.98434200	2.80604800	0.70139300
C	-1.83829800	5.90974300	1.52366200
H	0.22849600	6.50956100	1.43050500

H	-3.79585400	5.00786500	1.50800600
H	-2.19261200	6.87338500	1.87758600
C	-1.95991800	-1.10250600	-0.64885700
C	-1.77715500	-2.48679800	-0.50234200
C	-3.21685600	-0.64319700	-1.08016800
C	-2.81627500	-3.37708900	-0.75942500
H	-0.81435800	-2.86563400	-0.17040000
C	-4.25237400	-1.53346200	-1.33550600
H	-3.33963600	0.42393000	-1.23985600
C	-4.06121100	-2.90723400	-1.17368100
H	-2.65328100	-4.44341300	-0.62916900
H	-5.21290800	-1.15682600	-1.67655900
H	-4.87025500	-3.60254100	-1.37652800
C	0.53285700	-0.58311000	-0.45818400
C	0.98227700	-1.26671800	-1.59906100
C	1.45525500	-0.33711200	0.56861400
C	2.30988800	-1.66202300	-1.72338200
H	0.27585200	-1.47331200	-2.39961700
C	2.78457200	-0.73428400	0.44839200
H	1.12033300	0.17127800	1.46891100
C	3.21964400	-1.39292800	-0.70017200
H	2.63732500	-2.17742300	-2.62170300
H	3.48325300	-0.52904000	1.25448900
H	4.25754200	-1.69786400	-0.79602300
C	-0.41798300	2.14746200	0.06163400
H	0.65949200	2.00027000	0.17844200
C	4.14478500	2.15477300	-1.50346700
C	2.76845600	2.23788100	-1.68537800
C	2.14017800	3.47063300	-1.99072000
C	2.98514100	4.60349000	-2.09016600

C	4.35684000	4.51095200	-1.91019400
C	4.95677400	3.28329100	-1.61347000
H	4.58361000	1.18781900	-1.26812600
H	2.17433000	1.33172700	-1.59368000
H	2.53436400	5.56877600	-2.31190700
H	4.96759800	5.40648500	-1.99587300
H	6.03012500	3.21178400	-1.46774300
C	0.71899600	3.61437800	-2.17701900
H	0.33053600	4.61869800	-2.31797200
C	-0.17129400	2.58490000	-1.93715100
H	0.07599200	1.53754700	-2.11506000
Br	-1.99666900	2.88955400	-2.50688300

A1-C1-TS

Imaginary frequency (cm^{-1}) = -383.85

Zero-point correction= 0.427953 (Hartree/Particle)

Thermal correction to Energy= 0.453139

Thermal correction to Enthalpy= 0.454083

Thermal correction to Gibbs Free Energy= 0.370267

Sum of electronic and zero-point Energies= -3706.493367

Sum of electronic and thermal Energies= -3706.468181

Sum of electronic and thermal Enthalpies= -3706.467236

Sum of electronic and thermal Free Energies= -3706.551053

C	-0.89573800	0.26350100	-0.84250300
N	-1.11733700	-1.01371700	-1.34347600
C	-2.45837700	-2.80746000	-2.22134000
C	-3.75183900	-3.29617300	-2.45168800
C	-1.36540500	-3.58892600	-2.63116800
C	-3.95199800	-4.52527900	-3.07394800

H	-4.60624300	-2.69939800	-2.14011500
C	-1.56571400	-4.81529400	-3.25032300
H	-0.36334500	-3.20913400	-2.45575600
C	-2.85988400	-5.29176800	-3.47612800
H	-4.96234900	-4.88583000	-3.24462800
H	-0.70935500	-5.40750300	-3.56059800
H	-3.01271100	-6.25169000	-3.95985500
C	0.50571800	0.48180100	-0.40807200
C	0.92448700	1.72138500	0.10654900
C	1.48681900	-0.51333400	-0.57755200
C	2.26129900	1.96051700	0.41102500
H	0.19570800	2.50950800	0.26309200
C	2.81947500	-0.27549200	-0.26398700
H	1.18085100	-1.47959400	-0.96325500
C	3.22135900	0.96959000	0.22161900
H	2.55590100	2.93490300	0.79277900
H	3.55229200	-1.06662500	-0.40221600
H	4.26442300	1.16022700	0.45748900
C	-1.95201600	0.88761700	0.03595600
C	-2.59350600	0.09870200	1.00372300
C	-2.28983700	2.24598900	-0.01406200
C	-3.53271100	0.63662700	1.87825800
H	-2.34300100	-0.95682500	1.07123800
C	-3.22679000	2.79175500	0.86222300
H	-1.80414100	2.88510800	-0.74310700
C	-3.85766700	1.99087700	1.80998800
H	-4.00504300	-0.00147900	2.62011300
H	-3.46440400	3.85027900	0.80005000
H	-4.58790000	2.41588100	2.49228700
C	-2.28418800	-1.50568500	-1.56650700

H	-3.20831200	-0.98283900	-1.29484700
C	3.49240600	2.12117600	-3.46731100
C	2.17582700	1.80877100	-3.15705500
C	1.19507800	2.81644000	-2.99880200
C	1.64029800	4.15273600	-3.14724300
C	2.96028200	4.45904900	-3.44875500
C	3.90647700	3.44641400	-3.62065600
H	4.21415400	1.31443600	-3.57525700
H	1.90299600	0.77018600	-2.99572600
H	0.91740700	4.95703800	-3.02502100
H	3.25432300	5.50082500	-3.55423400
H	4.93985800	3.68341500	-3.85410800
C	-0.19748900	2.55992600	-2.72675500
H	-0.82695800	3.43298000	-2.57184300
C	-0.78553100	1.30698300	-2.67267400
H	-0.29034600	0.45108500	-3.12437000
Br	-2.68936100	1.27735000	-3.17153300

B1

Imaginary frequency (cm^{-1}) = none

Zero-point correction= 0.433574 (Hartree/Particle)

Thermal correction to Energy= 0.459400

Thermal correction to Enthalpy= 0.460344

Thermal correction to Gibbs Free Energy= 0.372963

Sum of electronic and zero-point Energies= -3706.595575

Sum of electronic and thermal Energies= -3706.569749

Sum of electronic and thermal Enthalpies= -3706.568805

Sum of electronic and thermal Free Energies= -3706.656185

C	-0.46061600	-1.73373600	0.70514500
N	-0.53138000	-0.48729600	0.44802500

C	-0.33101000	1.52718300	1.76906700
C	0.06267300	1.82168600	3.07371200
C	-1.42607000	2.19760200	1.21119900
C	-0.62797800	2.77551600	3.82235100
H	0.91444900	1.30161200	3.50757400
C	-2.11316400	3.14775900	1.96008700
H	-1.72531500	1.97723500	0.18661600
C	-1.71826900	3.43877100	3.26694000
H	-0.31369600	2.99699100	4.83811300
H	-2.96088700	3.66657900	1.52174000
H	-2.25844200	4.18098900	3.84714200
C	-1.42308900	-2.62162600	-0.02112500
C	-1.71456200	-3.91436400	0.42471900
C	-2.05759400	-2.13415600	-1.17338200
C	-2.62649700	-4.71030600	-0.26659900
H	-1.23516600	-4.29950600	1.31987100
C	-2.96204800	-2.93335700	-1.86122600
H	-1.83856300	-1.12414400	-1.51520400
C	-3.24944600	-4.22352900	-1.41228200
H	-2.84897700	-5.71045600	0.09288400
H	-3.44343700	-2.54845800	-2.75563800
H	-3.95530200	-4.84525700	-1.95507400
C	0.50210800	-2.36459600	1.66370600
C	1.36128000	-3.38534400	1.24574600
C	0.55120700	-1.93033600	2.99199300
C	2.26913700	-3.94910000	2.13825000
H	1.31814000	-3.73342300	0.21709900
C	1.45209000	-2.50100700	3.88706900
H	-0.12298000	-1.14188800	3.31885400
C	2.31499000	-3.50869800	3.46001400

H	2.93928800	-4.73414000	1.80182700
H	1.48014800	-2.15876000	4.91694700
H	3.02037400	-3.95114100	4.15664200
C	0.42349800	0.49571400	0.94328800
H	1.22989100	0.06694600	1.55425100
C	2.73976600	2.72705200	-3.99966800
C	2.13786500	2.16465900	-2.87991500
C	2.90848300	1.83068600	-1.75317400
C	4.28870400	2.06403000	-1.79593400
C	4.88934200	2.62654000	-2.91943600
C	4.11528400	2.96314300	-4.02667200
H	2.13068900	2.97942300	-4.86288800
H	1.06549200	1.97518300	-2.88966900
H	4.89581200	1.80206400	-0.93262900
H	5.96128900	2.80068300	-2.92858500
H	4.57773400	3.40123800	-4.90595300
C	2.31769200	1.23752000	-0.53848600
H	3.03058600	0.86867600	0.20058600
C	1.00933000	1.13296000	-0.29382300
H	0.26123500	1.47764600	-1.00841500
Br	-1.85618300	1.58182700	-2.68867500

C1

Imaginary frequency (cm^{-1}) = none

Zero-point correction= 0.432179 (Hartree/Particle)

Thermal correction to Energy= 0.458334

Thermal correction to Enthalpy= 0.459278

Thermal correction to Gibbs Free Energy= 0.370724

Sum of electronic and zero-point Energies= -3706.594885

Sum of electronic and thermal Energies= -3706.568730

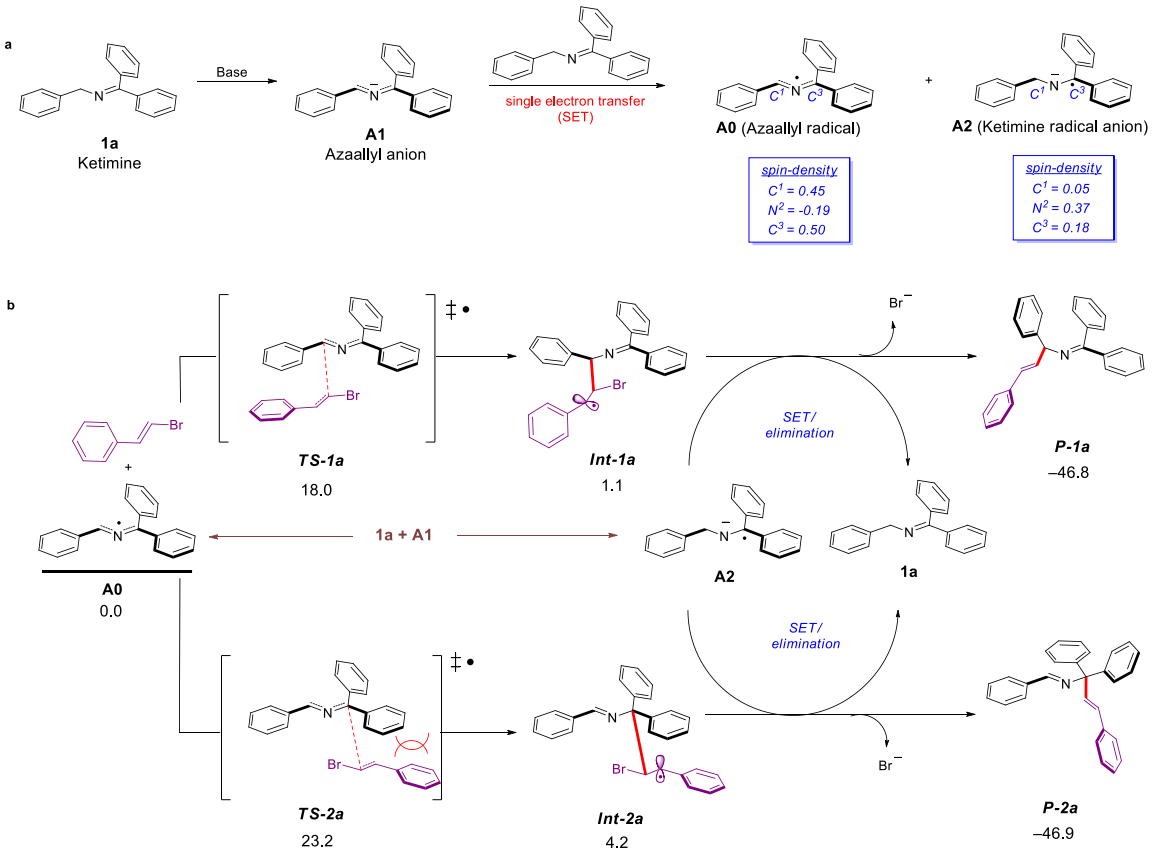
Sum of electronic and thermal Enthalpies= -3706.567786

Sum of electronic and thermal Free Energies= -3706.656340

C	-0.74198400	0.56449800	-0.94090500
N	-0.92809800	-0.83211900	-1.42345900
C	-2.28120300	-2.41515400	-2.63217300
C	-3.32971400	-2.53272600	-3.55014900
C	-1.53242800	-3.54452100	-2.28180100
C	-3.62541300	-3.77077000	-4.11589800
H	-3.88824200	-1.63881500	-3.82474700
C	-1.83454800	-4.77895400	-2.84238000
H	-0.72378300	-3.43641800	-1.56517900
C	-2.88100600	-4.89389000	-3.76070400
H	-4.43509100	-3.85968800	-4.83370900
H	-1.25751600	-5.65618200	-2.56567400
H	-3.11359500	-5.86032800	-4.19805100
C	0.58754500	0.64579700	-0.18840000
C	0.85847700	1.75620700	0.61913100
C	1.57163100	-0.33088400	-0.33690900
C	2.08163300	1.88337000	1.26913700
H	0.09925700	2.52551600	0.73772900
C	2.79786300	-0.20750200	0.31756700
H	1.36528000	-1.19128700	-0.96289500
C	3.05772800	0.89716500	1.12236600

H	2.27378100	2.75162100	1.89264600
H	3.55115900	-0.98032400	0.19497700
H	4.01191200	0.99243600	1.63189400
C	-1.90499500	0.91238800	0.00266100
C	-1.95065600	0.28870100	1.25646400
C	-2.94964400	1.76136500	-0.36256800
C	-3.00749000	0.51577600	2.12899800
H	-1.14355600	-0.37982300	1.54534200
C	-4.01383600	1.98740300	0.51392100
H	-2.97360200	2.22148600	-1.34513600
C	-4.04542300	1.37345100	1.76046900
H	-3.02343100	0.02413200	3.09733700
H	-4.82186000	2.64624200	0.20916100
H	-4.87253900	1.55416000	2.44051100
C	-1.99546000	-1.08073800	-2.07080800
H	-2.76378000	-0.32387500	-2.28067400
C	-0.66653700	3.82638000	-5.88383100
C	-0.75552400	3.07430900	-4.71815700
C	0.33823000	2.99291800	-3.84078000
C	1.50809100	3.69066300	-4.16873800
C	1.59496900	4.44359300	-5.33715600
C	0.50622200	4.51323200	-6.20174600
H	-1.52235600	3.87661300	-6.55091900
H	-1.68611600	2.55503000	-4.49575800
H	2.36162000	3.63702700	-3.49695200
H	2.51332700	4.97421700	-5.57047400
H	0.56739700	5.09756200	-7.11487500
C	0.31470200	2.19785900	-2.59743000
H	1.23206400	2.23106200	-2.01181800
C	-0.71576400	1.46124700	-2.17197200

H	-1.62682000	1.41557200	-2.76973000
Br	-4.18919700	1.38790300	-3.84124400



A0

Imaginary frequency (cm^{-1}) = none

Zero-point correction= 0.303012 (Hartree/Particle)

Thermal correction to Energy= 0.319595

Thermal correction to Enthalpy= 0.320539

Thermal correction to Gibbs Free Energy= 0.256190

Sum of electronic and zero-point Energies= -825.831429

Sum of electronic and thermal Energies= -825.814846

Sum of electronic and thermal Enthalpies= -825.813902

Sum of electronic and thermal Free Energies= -825.878251

C	-1.64546800	-0.27491400	0.23107400
N	-0.31804800	-0.25497400	0.38207300
C	1.86142400	-1.27650900	0.51379100
C	2.64247700	-2.42480700	0.29938900
C	2.48735100	-0.10939300	0.98985900
C	4.00924100	-2.40829300	0.54929000
H	2.16606600	-3.33071600	-0.06738500
C	3.85198200	-0.09824900	1.23854500
H	1.88200300	0.77553600	1.15877900
C	4.61915300	-1.24578900	1.02037700
H	4.60047900	-3.30238200	0.37680300
H	4.32494600	0.80712200	1.60695400
H	5.68642500	-1.23253500	1.21806600
C	-2.32640500	1.02238300	0.16971400
C	-3.71513600	1.14206400	0.36133700
C	-1.58304800	2.19629300	-0.06051500
C	-4.33408900	2.38632600	0.31806600
H	-4.30919900	0.25706300	0.56540800
C	-2.20595000	3.43501300	-0.10558500
H	-0.51156300	2.11176600	-0.20590900
C	-3.58573300	3.53803900	0.08168900
H	-5.40593000	2.45676500	0.47625800
H	-1.61557600	4.32713200	-0.29206500
H	-4.07167000	4.50809800	0.04453400
C	-2.43105000	-1.53242300	0.15296600
C	-3.36203400	-1.73816900	-0.87457000
C	-2.25525100	-2.53852100	1.11408200
C	-4.09184900	-2.92109800	-0.94255400
H	-3.50551500	-0.96579600	-1.62512700
C	-2.99186500	-3.71642200	1.05094000

H	-1.54398800	-2.38523500	1.92137500
C	-3.91054900	-3.91210800	0.02081100
H	-4.80410100	-3.06885700	-1.74832200
H	-2.85105500	-4.48101400	1.80843200
H	-4.48408900	-4.83233700	-0.02971800
C	0.43726600	-1.32435500	0.24640200
H	0.02845200	-2.28001400	-0.09421200

TS-1a

Imaginary frequency (cm^{-1}) = -709.42

Zero-point correction= 0.430287 (Hartree/Particle)

Thermal correction to Energy= 0.455347

Thermal correction to Enthalpy= 0.456291

Thermal correction to Gibbs Free Energy= 0.372229

Sum of electronic and zero-point Energies= -3706.386411

Sum of electronic and thermal Energies= -3706.361350

Sum of electronic and thermal Enthalpies= -3706.360406

Sum of electronic and thermal Free Energies= -3706.444468

C	-0.94749600	-0.09268300	-0.37360200
N	-1.29171800	1.12567100	-0.07422000
C	-0.84006500	3.42183600	0.56717900
C	0.10676700	4.41305200	0.86529600
C	-2.19965500	3.69550500	0.77603200
C	-0.29342800	5.64681200	1.36575300
H	1.16239700	4.20654200	0.70081200
C	-2.59609700	4.92928400	1.28073300
H	-2.92816400	2.92505600	0.54654200
C	-1.64773000	5.90904400	1.57482100
H	0.45026800	6.40413300	1.59487600

H	-3.65070500	5.12981900	1.44484000
H	-1.96264400	6.87114000	1.96725700
C	-2.03913200	-1.05563600	-0.63978000
C	-1.86392100	-2.43250500	-0.44693500
C	-3.28029000	-0.58080900	-1.09067200
C	-2.91525000	-3.31422900	-0.67902800
H	-0.90661200	-2.80952200	-0.09880200
C	-4.32403800	-1.46515200	-1.33059500
H	-3.38660600	0.48318400	-1.27975400
C	-4.14688800	-2.83374900	-1.11993200
H	-2.77268500	-4.37771400	-0.51421000
H	-5.27685200	-1.09017800	-1.69150900
H	-4.96392900	-3.52381300	-1.30699900
C	0.46139400	-0.56607700	-0.51098300
C	0.86773000	-1.20104600	-1.69241600
C	1.39630400	-0.37027900	0.51298500
C	2.19055400	-1.60142000	-1.85938100
H	0.14131700	-1.36789100	-2.48369700
C	2.71553100	-0.78263000	0.35015000
H	1.08186400	0.09955100	1.44118700
C	3.11636900	-1.39296200	-0.83794100
H	2.49717800	-2.07980800	-2.78422900
H	3.43188000	-0.62868100	1.15100600
H	4.14682000	-1.71083500	-0.96480000
C	-0.39200800	2.15824700	-0.02306800
H	0.67961700	1.95814200	0.05149400
C	4.10796700	2.09708300	-1.58336200
C	2.73785700	2.19066000	-1.79073100
C	2.12726400	3.44600400	-1.99328500
C	2.94508800	4.59396900	-1.97342500

C	4.31401200	4.49345800	-1.76891300
C	4.90344700	3.24354800	-1.57239100
H	4.55635100	1.12022300	-1.42845200
H	2.14312900	1.28035700	-1.79885500
H	2.48654800	5.56865400	-2.11944300
H	4.92457300	5.39100200	-1.75931100
H	5.97365000	3.16376500	-1.41011000
C	0.70197600	3.60897300	-2.18650800
H	0.32696300	4.62487400	-2.27765100
C	-0.21446300	2.58262400	-2.07612300
H	0.04749200	1.54703700	-2.27263700
Br	-2.01712500	2.94397900	-2.58519700

TS-2a

Imaginary frequency (cm^{-1}) = -611.27

Zero-point correction= 0.429144 (Hartree/Particle)

Thermal correction to Energy= 0.454415

Thermal correction to Enthalpy= 0.455359

Thermal correction to Gibbs Free Energy= 0.370551

Sum of electronic and zero-point Energies= -3706.377633

Sum of electronic and thermal Energies= -3706.352362

Sum of electronic and thermal Enthalpies= -3706.351417

Sum of electronic and thermal Free Energies= -3706.436226

C	-0.71665900	0.18269300	-1.21444900
N	-1.05269900	-1.09756800	-1.62772300
C	-2.65183800	-2.79458400	-2.21456900
C	-4.00024500	-3.17206300	-2.22257800
C	-1.68782400	-3.68423400	-2.71181500
C	-4.38163200	-4.41715200	-2.71307700
H	-4.74874500	-2.48248600	-1.84003700
C	-2.07007600	-4.92615600	-3.19972300
H	-0.64537800	-3.38130200	-2.70697200
C	-3.41736400	-5.29662200	-3.20118600
H	-5.42933100	-4.70120400	-2.71433700
H	-1.32024400	-5.61128500	-3.58318400
H	-3.71322400	-6.26863600	-3.58367700
C	0.69394500	0.33167400	-0.77120700
C	1.11783300	1.48776200	-0.09693400
C	1.64898100	-0.65170100	-1.07334000
C	2.44816100	1.64998000	0.27292200
H	0.39966500	2.27026000	0.12900200
C	2.97960400	-0.48433700	-0.70665000

H	1.33002000	-1.54887200	-1.59338100
C	3.38605000	0.66656100	-0.03186600
H	2.75459900	2.55594100	0.78750000
H	3.70340700	-1.25808900	-0.94599300
H	4.42637500	0.79606600	0.25120300
C	-1.73441700	0.98765100	-0.44013900
C	-1.77633100	0.76689300	0.94553800
C	-2.66467800	1.86692500	-0.99832200
C	-2.70659400	1.41483200	1.74965000
H	-1.06072100	0.08093000	1.39163600
C	-3.59590600	2.52183700	-0.19135900
H	-2.69114500	2.03132400	-2.06814300
C	-3.62021600	2.30197100	1.18159500
H	-2.71670200	1.22847300	2.81922900
H	-4.30656400	3.20562100	-0.64554600
H	-4.34619600	2.81417000	1.80545300
C	-2.28219500	-1.47734900	-1.69237200
H	-3.10961900	-0.83970400	-1.35972600
C	3.62466200	2.66097100	-2.85540100
C	2.37365500	2.11449800	-3.09526400
C	1.20629000	2.88012400	-2.90311900
C	1.35081500	4.22176700	-2.49509500
C	2.60566300	4.76456300	-2.25673800
C	3.75020500	3.98559900	-2.43094300
H	4.51142000	2.05082400	-2.99987800
H	2.29913400	1.08268300	-3.42439500
H	0.45933700	4.82739500	-2.35229300
H	2.69362800	5.79748200	-1.93376800

H	4.73239800	4.40914600	-2.24585600
C	-0.12398700	2.35626900	-3.12224000
H	-0.93555000	3.07869200	-3.16055800
C	-0.43916400	1.00881900	-3.19763500
H	0.32501500	0.26031600	-3.37145800
Br	-2.03313600	0.54633800	-4.15625500

Int-1a

Imaginary frequency (cm^{-1}) = none

Zero-point correction= 0.432557 (Hartree/Particle)

Thermal correction to Energy= 0.457128

Thermal correction to Enthalpy= 0.458072

Thermal correction to Gibbs Free Energy= 0.373730

Sum of electronic and zero-point Energies= -3706.412687

Sum of electronic and thermal Energies= -3706.388116

Sum of electronic and thermal Enthalpies= -3706.387171

Sum of electronic and thermal Free Energies= -3706.471514

C	-0.82471000	-1.69716700	0.65831400
N	-1.17375000	-0.47548100	0.78870300
C	-0.76875500	1.79431900	1.60959900
C	0.03781300	2.60724600	2.40964000
C	-2.10519000	2.14820200	1.41025500
C	-0.47651600	3.76163800	2.99560800
H	1.07708700	2.33147100	2.57685300
C	-2.62158800	3.29973800	1.99925900
H	-2.73396700	1.50725800	0.80232200
C	-1.80943700	4.11070200	2.79027000
H	0.16131100	4.38234000	3.61741000

H	-3.66300300	3.56363400	1.84092700
H	-2.21532800	5.00734300	3.24866000
C	-1.88391300	-2.67807700	0.28745500
C	-1.77779100	-4.02787400	0.63463900
C	-3.00083500	-2.23411700	-0.43058600
C	-2.79250000	-4.91881200	0.29436100
H	-0.90573500	-4.37686700	1.18087500
C	-4.00596400	-3.12785400	-0.77971400
H	-3.04132300	-1.19018200	-0.72817300
C	-3.90668400	-4.47031000	-0.41156700
H	-2.71155400	-5.96348900	0.57799800
H	-4.86514600	-2.78253700	-1.34654500
H	-4.69325600	-5.16733100	-0.68434200
C	0.57689300	-2.21832900	0.78639100
C	1.22288400	-2.74015900	-0.33925400
C	1.24914900	-2.18101200	2.01061700
C	2.53939000	-3.18568500	-0.24802900
H	0.69202600	-2.78799800	-1.28736300
C	2.56066800	-2.64164500	2.10307900
H	0.74160600	-1.79389600	2.89047300
C	3.20926400	-3.13592900	0.97347000
H	3.03859400	-3.57686600	-1.12916000
H	3.07565200	-2.61238500	3.05812300
H	4.23330500	-3.48839400	1.04586100
C	-0.17289500	0.56826700	0.95015200
H	0.68576900	0.23738300	1.55078900
C	4.53555900	0.61036700	-2.12740600
C	3.26521400	0.64151400	-1.57454200

C	2.72271600	1.85130300	-1.07335100
C	3.52997100	3.01419800	-1.14874000
C	4.79819800	2.97295500	-1.70286400
C	5.31036800	1.77085800	-2.19896600
H	4.93022900	-0.32825800	-2.50434100
H	2.69522600	-0.28122800	-1.52014700
H	3.13344000	3.95054400	-0.76535800
H	5.39437100	3.87896800	-1.75046300
H	6.30428700	1.73731700	-2.63333300
C	1.42780700	1.94990300	-0.48821900
H	1.10918000	2.91474600	-0.10425000
C	0.45159100	0.85792000	-0.43337700
H	0.84208700	-0.07666900	-0.83060600
Br	-1.03390700	1.27170200	-1.74440400

Int-2a

Imaginary frequency (cm^{-1}) = none

Zero-point correction= 0.432035 (Hartree/Particle)

Thermal correction to Energy= 0.457356

Thermal correction to Enthalpy= 0.458300

Thermal correction to Gibbs Free Energy= 0.372828

Sum of electronic and zero-point Energies= -3706.407239

Sum of electronic and thermal Energies= -3706.381918

Sum of electronic and thermal Enthalpies= -3706.380974

Sum of electronic and thermal Free Energies= -3706.466446

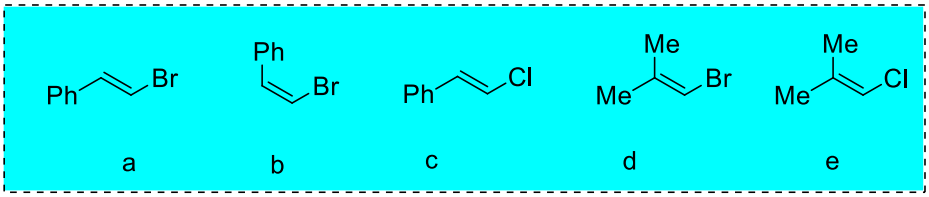
C	-0.74335300	0.35782300	-1.33292700
N	-1.05708600	-1.02194900	-1.71288200

C	-2.63396600	-2.75925100	-2.22909900
C	-3.98399000	-3.11759500	-2.26401800
C	-1.66366100	-3.68282100	-2.63594000
C	-4.36523200	-4.38430100	-2.69941400
H	-4.73643700	-2.39860500	-1.94900800
C	-2.04408300	-4.94632100	-3.06854500
H	-0.61805300	-3.39188900	-2.60842100
C	-3.39540400	-5.29918400	-3.10114000
H	-5.41587900	-4.65568000	-2.72443500
H	-1.28989800	-5.66051100	-3.38446700
H	-3.68982100	-6.28738200	-3.44092700
C	0.61888400	0.35439400	-0.60589400
C	0.99975900	1.44591300	0.18189000
C	1.53548100	-0.67814800	-0.81423400
C	2.26780800	1.50304800	0.75044800
H	0.29942300	2.26005300	0.34662900
C	2.80504500	-0.62319500	-0.23978300
H	1.24795400	-1.52550200	-1.42645400
C	3.17654600	0.46682200	0.54205800
H	2.54576200	2.35940500	1.35714300
H	3.50459800	-1.43675600	-0.40700200
H	4.16601800	0.51047400	0.98686200
C	-1.81466400	1.00515700	-0.45087300
C	-1.95441000	0.49173600	0.84729200
C	-2.68645500	2.01611100	-0.85700400
C	-2.92043300	0.98145000	1.71589100
H	-1.28877000	-0.30256200	1.17583200
C	-3.65269100	2.51773400	0.01886400

H	-2.64784900	2.41166300	-1.86431800
C	-3.77308000	2.00688700	1.30491300
H	-3.00705400	0.56603100	2.71515500
H	-4.31393300	3.30996800	-0.31841600
H	-4.52515000	2.39806900	1.98291700
C	-2.26672900	-1.40634100	-1.76898600
H	-3.10836800	-0.76181600	-1.48524300
C	3.71215700	2.61974900	-3.37189400
C	2.45043600	2.10398500	-3.11819000
C	1.35588200	2.96423200	-2.85749300
C	1.60412200	4.35941300	-2.84793400
C	2.86726000	4.86525900	-3.10495200
C	3.93105200	3.99928000	-3.37209500
H	4.53689800	1.94042900	-3.56507700
H	2.31540700	1.02729900	-3.09535000
H	0.77923300	5.03578700	-2.63967300
H	3.02927000	5.93873900	-3.09699700
H	4.92166900	4.39552800	-3.57078600
C	0.03950100	2.50153200	-2.57043600
H	-0.69637300	3.24095500	-2.27212400
C	-0.39891200	1.09435900	-2.67063700
H	0.34514700	0.47240500	-3.16595300
Br	-1.91184900	1.00343200	-3.99163800

Note : P-1a = B1 and P-2a = C1

c



radical:	18.0	19.3	20.7	21.5	25.5
anionic:	11.7	15.1	15.5	28.0	33.2

b-radical-TS

Imaginary frequency (cm^{-1}) = -712.97

Zero-point correction= 0.429452 (Hartree/Particle)

Thermal correction to Energy= 0.454666

Thermal correction to Enthalpy= 0.455611

Thermal correction to Gibbs Free Energy= 0.370188

Sum of electronic and zero-point Energies= -3706.382117

Sum of electronic and thermal Energies= -3706.356902

Sum of electronic and thermal Enthalpies= -3706.355958

Sum of electronic and thermal Free Energies= -3706.441380

C	-0.98696000	-0.13626600	-0.42092100
N	-1.40339000	1.06719900	-0.16204000
C	-1.03848400	3.37552000	0.50058500
C	-0.11807300	4.37947300	0.83417400
C	-2.40627600	3.60549500	0.71827900
C	-0.54943100	5.58864500	1.36699900
H	0.94176500	4.20624300	0.66026700
C	-2.83400700	4.81896300	1.24508600
H	-3.11443600	2.82146800	0.47292600
C	-1.91061900	5.81534300	1.56613900
H	0.17436800	6.35856200	1.61735700

H	-3.89377900	4.99045200	1.40972400
H	-2.25177400	6.76135900	1.97564000
C	-2.01558700	-1.17554800	-0.65181600
C	-1.74220100	-2.53359500	-0.43919900
C	-3.29670300	-0.79697700	-1.08191700
C	-2.73387500	-3.49045700	-0.63432400
H	-0.75452400	-2.83827100	-0.10592200
C	-4.28082000	-1.75600700	-1.28459700
H	-3.48432000	0.25303500	-1.28348900
C	-4.00461100	-3.10528700	-1.05680600
H	-2.51394200	-4.53816500	-0.45423800
H	-5.26532800	-1.45345100	-1.62818300
H	-4.77554500	-3.85330300	-1.21397900
C	0.44970400	-0.53553100	-0.50826600
C	0.93764700	-1.15343500	-1.66566300
C	1.32111400	-0.30983700	0.56384100
C	2.27805100	-1.51669000	-1.75867800
H	0.26023200	-1.34417100	-2.49426600
C	2.65776800	-0.68677600	0.47521800
H	0.94149200	0.15271700	1.47124100
C	3.13956700	-1.28546400	-0.68775800
H	2.64856200	-1.98431900	-2.66553400
H	3.32354800	-0.51429300	1.31508300
H	4.18335100	-1.57544300	-0.75707900
C	-0.55921600	2.14900900	-0.13734400
H	0.52126900	1.99776700	-0.11382000
C	0.29865900	3.70829100	-2.39703300
C	-0.55277700	2.63739800	-2.19563200

H	-0.18841000	1.64426500	-2.44079200
Br	-2.42392500	2.74257700	-2.58399600
C	0.07454100	5.13816100	-2.40844200
C	-1.13016200	5.77381300	-2.04006900
C	1.16185200	5.95700700	-2.78240200
C	-1.23269700	7.15825200	-2.06185600
H	-1.97554800	5.18670100	-1.70341500
C	1.05035400	7.33955400	-2.81064000
H	2.10277800	5.48617500	-3.05594100
C	-0.15175900	7.94993000	-2.45171100
H	-2.16550900	7.62514300	-1.75934400
H	1.90290400	7.94302900	-3.10663600
H	-0.24272800	9.03150800	-2.46692200
H	1.34432600	3.41174500	-2.48016100

b-substrate

Imaginary frequency (cm^{-1}) = none

Zero-point correction= 0.125798 (Hartree/Particle)

Thermal correction to Energy= 0.133537

Thermal correction to Enthalpy= 0.134481

Thermal correction to Gibbs Free Energy= 0.091229

Sum of electronic and zero-point Energies= -2880.559400

Sum of electronic and thermal Energies= -2880.551661

Sum of electronic and thermal Enthalpies= -2880.550717

Sum of electronic and thermal Free Energies= -2880.593969

C	-0.42210800	0.45052300	0.15561900
C	0.96266000	0.55135000	0.08844100
C	1.58890400	1.79285100	-0.09574400

C	0.78606300	2.93196300	-0.24836900
C	-0.60059500	2.82754500	-0.19178900
C	-1.20967800	1.59182400	0.01740300
H	-0.88597000	-0.51902100	0.30789200
H	1.57503900	-0.34157900	0.18494300
H	1.24245100	3.89813100	-0.42678200
H	-1.20829500	3.71825100	-0.31920900
H	-2.29175000	1.51741900	0.06283700
C	3.06053700	1.80693500	-0.15966200
H	3.51022500	0.86976900	-0.48765900
C	3.95036200	2.75035700	0.14527700
H	5.01566700	2.58945000	0.04820600
Br	3.56320600	4.46858900	0.83823800

b-anionic-TS

Imaginary frequency (cm^{-1}) = -482.30

Zero-point correction= 0.427775 (Hartree/Particle)

Thermal correction to Energy= 0.452967

Thermal correction to Enthalpy= 0.453911

Thermal correction to Gibbs Free Energy= 0.369687

Sum of electronic and zero-point Energies= -3706.498319

Sum of electronic and thermal Energies= -3706.473127

Sum of electronic and thermal Enthalpies= -3706.472183

Sum of electronic and thermal Free Energies= -3706.556407

C	-0.90917700	-0.16999200	-0.35163100
N	-1.32227100	1.02063400	-0.02044100
C	-1.05143900	3.34015000	0.63981000
C	-0.17338100	4.39636700	0.93949200

C	-2.43071000	3.55622300	0.81759400
C	-0.65162700	5.62598100	1.37768500
H	0.89537100	4.24251900	0.80791400
C	-2.90459900	4.78603300	1.25812000
H	-3.11326200	2.74121000	0.59955500
C	-2.02168900	5.83444200	1.53135800
H	0.04756300	6.43018200	1.59285000
H	-3.97403800	4.93352300	1.38843300
H	-2.39759100	6.79438500	1.87321600
C	-1.94066700	-1.19747100	-0.61758300
C	-1.66959400	-2.57224900	-0.52308600
C	-3.24665200	-0.80393500	-0.96236100
C	-2.66784700	-3.51642700	-0.74861800
H	-0.66939900	-2.90304300	-0.25785100
C	-4.24000900	-1.74840700	-1.18708500
H	-3.44410000	0.25729300	-1.07745000
C	-3.95976300	-3.11222700	-1.07912800
H	-2.43502900	-4.57405100	-0.66010000
H	-5.23984300	-1.42130100	-1.45966100
H	-4.73709300	-3.84932700	-1.25660000
C	0.52917500	-0.56929200	-0.45109800
C	1.02957500	-1.18327800	-1.60747400
C	1.40862000	-0.35710500	0.61924600
C	2.36686200	-1.55836400	-1.69908800
H	0.35524300	-1.36284300	-2.44165800
C	2.74621000	-0.73251500	0.53181200
H	1.03075100	0.10519300	1.52766300
C	3.23166400	-1.33256200	-0.62903400

H	2.73533500	-2.02511400	-2.60800900
H	3.41077600	-0.56058800	1.37364200
H	4.27520100	-1.62447200	-0.69812600
C	-0.52468400	2.12304200	0.03746100
H	0.55919800	2.00728000	0.11422800
C	0.40983500	3.71138500	-2.30545100
C	-0.37907100	2.62843300	-1.97754600
H	-0.00343500	1.62675100	-2.18121900
Br	-2.27845700	2.63654500	-2.47090500
C	0.08908300	5.11532800	-2.44181700
C	1.03322900	5.96659600	-3.06325500
C	-1.10992600	5.72343400	-1.99898000
C	0.79244500	7.32084500	-3.25517900
H	1.97228800	5.53730200	-3.40731800
C	-1.34844500	7.07681800	-2.20297800
H	-1.84018400	5.13185500	-1.45758400
C	-0.40872000	7.89366500	-2.83498900
H	1.54814100	7.93398900	-3.74033100
H	-2.27938500	7.50526700	-1.83815900
H	-0.60201100	8.95160700	-2.98408600
H	1.45808200	3.45782700	-2.46551300

c-radical-TS

Imaginary frequency (cm^{-1}) = -723.22

Zero-point correction= 0.430177 (Hartree/Particle)

Thermal correction to Energy= 0.455155

Thermal correction to Enthalpy= 0.456099

Thermal correction to Gibbs Free Energy= 0.372229

Sum of electronic and zero-point Energies= -1594.769560

Sum of electronic and thermal Energies= -1594.744582

Sum of electronic and thermal Enthalpies= -1594.743638

Sum of electronic and thermal Free Energies= -1594.827508

C	-0.99893500	-0.09843000	-0.38573400
N	-1.33831600	1.12617300	-0.10739100
C	-0.87853800	3.41225900	0.56192400
C	0.07230900	4.37881300	0.92243200
C	-2.23975500	3.70355300	0.72924600
C	-0.32706700	5.60709200	1.43699300
H	1.13026100	4.15724100	0.79784800
C	-2.63573800	4.93247400	1.24628600
H	-2.97239300	2.95206400	0.45344800
C	-1.68366500	5.88848900	1.60010100
H	0.41965600	6.34459700	1.71591000
H	-3.69259200	5.14662500	1.37506600
H	-1.99742000	6.84640600	2.00351500
C	-2.08681200	-1.07805300	-0.60494900
C	-1.84880200	-2.45881500	-0.55209400
C	-3.39172300	-0.62572400	-0.85863500
C	-2.88953500	-3.36305900	-0.74360000
H	-0.84820200	-2.82717300	-0.34763200
C	-4.42616800	-1.53020100	-1.05485700
H	-3.56943000	0.44371700	-0.90629900
C	-4.17941300	-2.90334200	-0.99768300
H	-2.69112300	-4.42909700	-0.69232900
H	-5.42871800	-1.16636900	-1.25835400
H	-4.98872600	-3.61021500	-1.15217700

C	0.41421100	-0.56826600	-0.51746700
C	0.85119400	-1.14223900	-1.71853300
C	1.31923500	-0.43171900	0.54142100
C	2.17513600	-1.54737200	-1.86629500
H	0.14743900	-1.26280800	-2.53836900
C	2.64014400	-0.84697800	0.39646000
H	0.98111000	-0.00494400	1.48201100
C	3.07125200	-1.40119200	-0.80823900
H	2.50581500	-1.98005200	-2.80523800
H	3.33380700	-0.73823600	1.22431800
H	4.10225600	-1.72262700	-0.92055400
C	-0.42752600	2.14790700	-0.02833800
H	0.63591400	1.92847800	0.09570800
C	4.15327000	2.08219800	-1.29549800
C	2.79884500	2.18253100	-1.58650600
C	2.20585000	3.44165800	-1.81556200
C	3.02446700	4.58636000	-1.73336000
C	4.37780900	4.47913400	-1.44574100
C	4.95023500	3.22535100	-1.22497000
H	4.58834000	1.10219700	-1.12311200
H	2.20362500	1.27415200	-1.64131400
H	2.57893900	5.56411500	-1.89813800
H	4.98922800	5.37455400	-1.39123200
H	6.00828900	3.14018900	-0.99848900
C	0.79882900	3.61157700	-2.10505900
H	0.43601300	4.62944300	-2.22217600
C	-0.13010500	2.59036400	-2.06379400
H	0.14529200	1.55526800	-2.24517900

Cl	-1.74709000	2.93314900	-2.66291000

c-substrate

Imaginary frequency (cm^{-1}) = none

Zero-point correction= 0.126010 (Hartree/Particle)

Thermal correction to Energy= 0.133854

Thermal correction to Enthalpy= 0.134798

Thermal correction to Gibbs Free Energy= 0.092112

Sum of electronic and zero-point Energies= -768.948418

Sum of electronic and thermal Energies= -768.940575

Sum of electronic and thermal Enthalpies= -768.939631

Sum of electronic and thermal Free Energies= -768.982317

C	-0.43392800	0.45186100	-0.06108800
C	0.95621000	0.49901100	-0.00956900
C	1.63137200	1.72389500	0.05749100
C	0.87677800	2.90556200	0.09063200
C	-0.51093000	2.85828300	0.03778000
C	-1.17229200	1.63219300	-0.04050200
H	-0.93891900	-0.50753400	-0.11674600
H	1.53069300	-0.42344000	-0.02635000
H	1.37353700	3.86762400	0.17495600
H	-1.08048900	3.78205000	0.06595700
H	-2.25659000	1.59943600	-0.07814600
C	3.10387900	1.71144700	0.09346300
H	3.57309400	0.74693900	0.27617800
C	3.88183600	2.77382800	-0.10321300
H	3.53061200	3.77443600	-0.32306200
Cl	5.61826500	2.67000700	-0.04202300

c-anionic-TS

Imaginary frequency (cm^{-1}) = -468.87

Zero-point correction= 0.428871 (Hartree/Particle)

Thermal correction to Energy= 0.453747

Thermal correction to Enthalpy= 0.454691

Thermal correction to Gibbs Free Energy= 0.372250

Sum of electronic and zero-point Energies= -1594.887532

Sum of electronic and thermal Energies= -1594.862657

Sum of electronic and thermal Enthalpies= -1594.861713

Sum of electronic and thermal Free Energies= -1594.944154

C	-0.93262700	-0.11542200	-0.42299900
N	-1.29604600	1.09925700	-0.11810200
C	-0.94212700	3.41388800	0.51018600
C	-0.03897900	4.46773900	0.74086600
C	-2.30697000	3.65200600	0.75442500
C	-0.48162400	5.70623500	1.20013300
H	1.02039400	4.29889500	0.56010000
C	-2.74411400	4.88699800	1.21676300
H	-3.01177400	2.84536000	0.57652500
C	-1.83625200	5.92604700	1.44223600
H	0.23789400	6.50246600	1.37359000
H	-3.80320700	5.04532900	1.40447600
H	-2.18234900	6.88929100	1.80522000
C	-1.99939800	-1.12178300	-0.62890900
C	-1.73263700	-2.50133100	-0.64471100
C	-3.33646100	-0.71449400	-0.79272500
C	-2.75519600	-3.43053800	-0.81960600
H	-0.71462300	-2.85330300	-0.50851300

C	-4.35457900	-1.64254200	-0.96456100
H	-3.55207900	0.34889400	-0.78359400
C	-4.07284000	-3.01067600	-0.98209000
H	-2.51772200	-4.49081000	-0.82340200
H	-5.37709800	-1.29767300	-1.09264200
H	-4.86876200	-3.73589100	-1.12098900
C	0.49184900	-0.55856300	-0.54164600
C	0.96306800	-1.17003900	-1.71277400
C	1.39226800	-0.37117200	0.51506700
C	2.29242700	-1.56293600	-1.83242300
H	0.27247200	-1.32736200	-2.53817300
C	2.72363800	-0.76391600	0.39940200
H	1.03917400	0.08905900	1.43439400
C	3.17958900	-1.35918800	-0.77528900
H	2.63852900	-2.02459100	-2.75262000
H	3.40723900	-0.60484000	1.22846100
H	4.21824800	-1.66304600	-0.86657800
C	-0.44618000	2.16391400	-0.05701200
H	0.62422200	1.99463700	0.09429300
C	4.17928200	2.14969900	-1.37671700
C	2.81396800	2.24225200	-1.62528200
C	2.20782300	3.48093000	-1.95194300
C	3.06380800	4.60995300	-1.99692100
C	4.42424700	4.50782600	-1.75037000
C	5.00249800	3.27401300	-1.43619100
H	4.60073700	1.17813800	-1.12900100
H	2.21144300	1.33867600	-1.57323600
H	2.63044300	5.58000400	-2.23240300

H	5.04316500	5.40058900	-1.79714200
H	6.06695900	3.19444200	-1.23885300
C	0.80220700	3.63503900	-2.21446700
H	0.42952400	4.64406400	-2.36570800
C	-0.11561400	2.61363600	-2.03354800
H	0.13727300	1.56781100	-2.21126900
Cl	-1.75637600	2.92966600	-2.65950000

d-radical-TS

Imaginary frequency (cm^{-1}) = -758.00

Zero-point correction= 0.403682 (Hartree/Particle)

Thermal correction to Energy= 0.427808

Thermal correction to Enthalpy= 0.428752

Thermal correction to Gibbs Free Energy= 0.345165

Sum of electronic and zero-point Energies= -3554.037215

Sum of electronic and thermal Energies= -3554.013089

Sum of electronic and thermal Enthalpies= -3554.012145

Sum of electronic and thermal Free Energies= -3554.095732

C	-0.98184000	-0.07823200	-0.46314000
N	-1.37321400	1.12013800	-0.14975400
C	-0.99158900	3.38458800	0.65516500
C	-0.07940100	4.33231100	1.13962000
C	-2.36246100	3.67332700	0.71224400
C	-0.52145700	5.54173200	1.66571800
H	0.98579700	4.11083100	1.10372800
C	-2.80256800	4.88183800	1.24142800
H	-3.06654900	2.93558000	0.34307200
C	-1.88658900	5.82178100	1.71546000

H	0.19778600	6.26412300	2.03992000
H	-3.86679700	5.09446400	1.28367600
H	-2.23593400	6.76436200	2.12566700
C	-2.02167200	-1.04370300	-0.88561300
C	-1.83228600	-2.42626700	-0.76085900
C	-3.22769600	-0.56566900	-1.42085500
C	-2.83691000	-3.31147800	-1.14100200
H	-0.90027900	-2.80629600	-0.35234800
C	-4.22485300	-1.45234400	-1.80586000
H	-3.34075500	0.50582900	-1.55673200
C	-4.03548700	-2.82802000	-1.66208100
H	-2.68359400	-4.38044700	-1.02890800
H	-5.15065800	-1.07293500	-2.22772200
H	-4.81617000	-3.51946800	-1.96417700
C	0.44301200	-0.53037400	-0.45435000
C	1.02190600	-1.05007700	-1.61857800
C	1.21980100	-0.43267300	0.70605000
C	2.35952900	-1.43645700	-1.63005100
H	0.41800000	-1.14292800	-2.51808500
C	2.55346200	-0.83083600	0.69739500
H	0.77026700	-0.04785700	1.61778900
C	3.12770300	-1.32630000	-0.47223200
H	2.79979600	-1.82729600	-2.54205400
H	3.14422900	-0.75635900	1.60509300
H	4.16937400	-1.63167900	-0.47933200
C	-0.48530000	2.15606400	0.02951600
H	0.56450200	1.93660000	0.23655300
C	0.84143100	3.65497500	-1.95096000

C	-0.13414600	2.67234200	-1.92121900
H	0.13413700	1.64879100	-2.17234100
Br	-1.89493000	3.06676500	-2.58030300
C	2.26218300	3.22536700	-1.73668000
H	2.91145200	3.63910100	-2.51850500
H	2.64319500	3.60724200	-0.77897200
H	2.36941500	2.13596400	-1.73734600
C	0.56897500	5.12145300	-2.03623300
H	0.92350200	5.51713500	-2.99844800
H	-0.49613400	5.34414000	-1.94662600
H	1.11030600	5.66116900	-1.25019500

d-substrate

Imaginary frequency (cm^{-1}) = none

Zero-point correction= 0.099628 (Hartree/Particle)

Thermal correction to Energy= 0.106199

Thermal correction to Enthalpy= 0.107143

Thermal correction to Gibbs Free Energy= 0.068261

Sum of electronic and zero-point Energies= -2728.220386

Sum of electronic and thermal Energies= -2728.213814

Sum of electronic and thermal Enthalpies= -2728.212870

Sum of electronic and thermal Free Energies= -2728.251753

C	3.23099500	1.68426100	-0.09747200
C	3.91886300	2.80570300	-0.29872900
H	3.47230400	3.79172500	-0.31928200
Br	5.79712200	2.86642200	-0.58968200
C	1.74130300	1.76933700	0.11534500
H	1.21680900	1.19954300	-0.66004400

H	1.47129900	1.32463700	1.07982800
H	1.38011500	2.79997800	0.09340400
C	3.81780600	0.30384400	-0.06470700
H	4.89515600	0.30912100	-0.23257600
H	3.61419800	-0.16636000	0.90401800
H	3.34407600	-0.32205900	-0.82941500

d-anionic-TS

Imaginary frequency (cm^{-1}) = -551.88

Zero-point correction= 0.401949 (Hartree/Particle)

Thermal correction to Energy= 0.426166

Thermal correction to Enthalpy= 0.427110

Thermal correction to Gibbs Free Energy= 0.345352

Sum of electronic and zero-point Energies= -3554.137122

Sum of electronic and thermal Energies= -3554.112905

Sum of electronic and thermal Enthalpies= -3554.111961

Sum of electronic and thermal Free Energies= -3554.193719

C	-0.96376600	-0.07908900	-0.48973600
N	-1.35709300	1.11870300	-0.16297000
C	-1.00904300	3.36714400	0.69287600
C	-0.09649400	4.33091800	1.15067000
C	-2.38020300	3.64115100	0.82583600
C	-0.53214800	5.52669700	1.71389300
H	0.96899800	4.13273000	1.04991900
C	-2.81461500	4.83292100	1.39503100
H	-3.09078200	2.90087800	0.47355700
C	-1.89612700	5.78716700	1.83949100
H	0.19520400	6.25688000	2.05958900

H	-3.88048100	5.02335400	1.49318600
H	-2.24091200	6.71685900	2.28274600
C	-2.00262200	-1.04020400	-0.92537300
C	-1.82519600	-2.42988200	-0.82955600
C	-3.22264000	-0.56198300	-1.43740900
C	-2.83547600	-3.30840100	-1.21185800
H	-0.89088800	-2.82370700	-0.43929300
C	-4.22790800	-1.44143400	-1.81835400
H	-3.33707400	0.51137200	-1.55875900
C	-4.04458100	-2.82134500	-1.70474600
H	-2.67795600	-4.37946400	-1.11867100
H	-5.15981700	-1.05058400	-2.21806300
H	-4.83157400	-3.50673900	-2.00484800
C	0.45258300	-0.55748500	-0.40968800
C	1.07776800	-1.16963600	-1.50475200
C	1.18401900	-0.41986000	0.77762400
C	2.39577900	-1.61092600	-1.42279400
H	0.51982500	-1.29228900	-2.43018600
C	2.50155100	-0.86071900	0.86362400
H	0.70618000	0.04040900	1.63877500
C	3.11456700	-1.45507500	-0.23837500
H	2.86364800	-2.07492600	-2.28624300
H	3.04921900	-0.74404800	1.79436800
H	4.14277300	-1.79793200	-0.17365200
C	-0.50344100	2.17439600	0.00770600
H	0.54858600	1.96699300	0.22382200
C	0.80849000	3.72904000	-2.08596100
C	-0.07362800	2.72175600	-1.83979900

H	0.17533000	1.69958900	-2.13625400
Br	-2.03486100	3.03854400	-2.51466300
C	2.23254400	3.37811000	-2.42937900
H	2.55523500	3.85553600	-3.36963900
H	2.94520500	3.71688600	-1.65952600
H	2.36962100	2.29627200	-2.54224200
C	0.48730300	5.19323300	-1.99844600
H	0.67672300	5.69658700	-2.96185200
H	-0.56174300	5.35422100	-1.73539300
H	1.10170400	5.71842900	-1.25198400

e-radical-TS

Imaginary frequency (cm^{-1}) = -630.33

Zero-point correction= 0.429432 (Hartree/Particle)

Thermal correction to Energy= 0.454494

Thermal correction to Enthalpy= 0.455438

Thermal correction to Gibbs Free Energy= 0.369450

Sum of electronic and zero-point Energies= -1594.759883

Sum of electronic and thermal Energies= -1594.734821

Sum of electronic and thermal Enthalpies= -1594.733876

Sum of electronic and thermal Free Energies= -1594.819864

C	-0.73798400	0.22489000	-1.22464200
N	-1.04855900	-1.06202400	-1.64526800
C	-2.61962600	-2.79160000	-2.21529500
C	-3.96370900	-3.18398600	-2.23441700
C	-1.64084200	-3.67426300	-2.69604900
C	-4.32676500	-4.43536500	-2.72273900
H	-4.72349700	-2.50039200	-1.86358500

C	-2.00478400	-4.92268100	-3.18116300
H	-0.60153400	-3.36109900	-2.68084500
C	-3.34811100	-5.30704700	-3.19583000
H	-5.37137100	-4.73033700	-2.73384500
H	-1.24355700	-5.60230900	-3.55177200
H	-3.62940200	-6.28416900	-3.57632400
C	0.66532600	0.39639300	-0.77082400
C	1.06000700	1.56724600	-0.10503900
C	1.63654600	-0.58067700	-1.03870100
C	2.38207000	1.75519200	0.28108600
H	0.32388400	2.33982500	0.09882700
C	2.95798500	-0.39011500	-0.65018300
H	1.33755300	-1.49057100	-1.54829500
C	3.33752800	0.77856300	0.00894400
H	2.66840300	2.67249400	0.78705300
H	3.69578000	-1.15905600	-0.86049100
H	4.37101600	0.92698300	0.30753000
C	-1.76999300	0.98974100	-0.42724500
C	-1.91981200	0.59067900	0.91055400
C	-2.58542200	2.01448600	-0.90717900
C	-2.85035300	1.20020300	1.74281200
H	-1.28817200	-0.20609600	1.29602400
C	-3.51896800	2.63058700	-0.07147600
H	-2.50885700	2.33867100	-1.93686800
C	-3.65531700	2.22836900	1.25229400
H	-2.94558200	0.87485000	2.77430300
H	-4.14181400	3.42793400	-0.46540200
H	-4.38237400	2.70963800	1.89911500

C	-2.27010700	-1.46724400	-1.69637700
H	-3.10625800	-0.84552100	-1.35577800
C	3.63327600	2.53507200	-2.92251000
C	2.35738500	2.03836700	-3.13981700
C	1.22592500	2.85642100	-2.95028800
C	1.43266800	4.19859700	-2.57093400
C	2.71185400	4.69192900	-2.35687900
C	3.81996300	3.86102800	-2.52579000
H	4.49102600	1.88399000	-3.06316800
H	2.23530500	1.00573800	-3.45133500
H	0.56987900	4.84492700	-2.43056700
H	2.84758500	5.72648300	-2.05636300
H	4.82115000	4.24529900	-2.35759800
C	-0.12956600	2.39183500	-3.14242500
H	-0.90382800	3.15409300	-3.17869800
C	-0.51636100	1.06123700	-3.20190000
H	0.20282300	0.27608900	-3.40766100
Cl	-2.05964800	0.70821300	-3.98409700

e-substrate

Imaginary frequency (cm^{-1}) = none

Zero-point correction= 0.126010 (Hartree/Particle)

Thermal correction to Energy= 0.133854

Thermal correction to Enthalpy= 0.134798

Thermal correction to Gibbs Free Energy= 0.092112

Sum of electronic and zero-point Energies= -768.948418

Sum of electronic and thermal Energies= -768.940575

Sum of electronic and thermal Enthalpies= -768.939631

Sum of electronic and thermal Free Energies= -768.982317

C	-0.43488	0.45038	-0.05153
C	0.95542	0.49925	-0.00633
C	1.62935	1.72527	0.05011
C	0.87401	2.90663	0.07694
C	-0.51373	2.85762	0.03097
C	-1.17413	1.63019	-0.03557
H	-0.93936	-0.50972	-0.09896
H	1.53104	-0.42255	-0.01956
H	1.37027	3.87	0.14801
H	-1.08422	3.78094	0.05363
H	-2.25853	1.59619	-0.06901
C	3.1024	1.71289	0.07925
H	3.56938	0.74209	0.23195
C	3.88217	2.77926	-0.08603
H	3.53654	3.78853	-0.26973
Cl	5.63739	2.65863	-0.03838

e-anionic-TS

Imaginary frequency (cm^{-1}) = -539.84

Zero-point correction= 0.402286 (Hartree/Particle)

Thermal correction to Energy= 0.426233

Thermal correction to Enthalpy= 0.427177

Thermal correction to Gibbs Free Energy= 0.345927

Sum of electronic and zero-point Energies= -1442.515257

Sum of electronic and thermal Energies= -1442.491310

Sum of electronic and thermal Enthalpies= -1442.490366

Sum of electronic and thermal Free Energies= -1442.571617

C	-1.01698900	-0.05617300	-0.52918900
N	-1.41130200	1.14979200	-0.24764600
C	-1.05227100	3.40003100	0.59783900
C	-0.14023000	4.34185000	1.09788800
C	-2.42173400	3.68186500	0.71283600
C	-0.57644500	5.52802800	1.68158900
H	0.92487900	4.13531500	1.01230300
C	-2.85845100	4.86315100	1.30291800
H	-3.13274900	2.95601900	0.33072800
C	-1.94003900	5.79717200	1.78821000
H	0.15021300	6.24286200	2.05906800
H	-3.92430800	5.05996800	1.38627900
H	-2.28490000	6.71868200	2.24821000
C	-2.04881000	-1.05435300	-0.89645600
C	-1.78094200	-2.43295600	-0.91945200
C	-3.35159800	-0.63329300	-1.22051400
C	-2.77308800	-3.35163300	-1.25299500
H	-0.78754500	-2.79083000	-0.66593300
C	-4.33866400	-1.55089900	-1.55248800
H	-3.56136400	0.43125100	-1.20949800
C	-4.05780500	-2.91921000	-1.57244800
H	-2.53895500	-4.41259600	-1.25881000
H	-5.33545000	-1.19898700	-1.80436600
H	-4.83052300	-3.63565200	-1.83462500
C	0.41126400	-0.51193800	-0.46613800
C	1.05549900	-1.03958000	-1.59267300
C	1.13264300	-0.42385900	0.73066300
C	2.38541000	-1.44753400	-1.53116400

H	0.50372000	-1.12140900	-2.52637700
C	2.46345300	-0.82963200	0.79601000
H	0.64027300	-0.02714600	1.61509400
C	3.09560200	-1.34027000	-0.33594700
H	2.86863400	-1.84654200	-2.41825100
H	3.00616300	-0.74996400	1.73347000
H	4.13348700	-1.65554500	-0.28730100
C	-0.53781700	2.20684200	-0.09722600
H	0.48685500	1.96755200	0.20534000
C	0.92426100	3.68864600	-2.04233100
C	-0.02018300	2.70932800	-1.84407400
H	0.24060700	1.69055500	-2.14574100
C	2.35866400	3.27373900	-2.21890500
H	2.82072300	3.74232900	-3.10539900
H	2.99744900	3.56267300	-1.36500200
H	2.45610000	2.18676300	-2.33343300
C	0.66056300	5.16476900	-1.97880500
H	0.94814400	5.66607100	-2.92011300
H	-0.39766100	5.37693100	-1.79960900
H	1.23167900	5.66983000	-1.18307400
Cl	-1.74773000	3.04684000	-2.61641800

3.5.2. Experimental Section of Transition-Metal-Free Arylation and Alkylation.

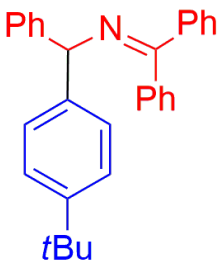
Preparation of Alkyl Halides 3c, 3d and Radical Clocks 2k, 2l, 3g:

Alkyl halides **3c**,[2a] **3d**[2b] and radical clocks **2k**,[2c] **2l**,[2d] **3g**[2e] were prepared according to literature procedures.[2]

Procedure and Characterization for the Arylation/Alkylation Reactions:

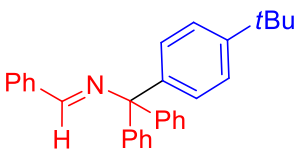
General procedure A for arylation: A brand-new oven-dried 4 mL glass vial equipped with two oven-dried glass beads was charged with ketimine **1a** (217.2 mg, 0.80 mmol) and 1-(*tert*-butyl)-4-iodobenzene **5a** (104.4 mg, 0.40 mmol) under a nitrogen atmosphere in a glove box. A solution of $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol) in 2.0 mL anhydrous DME was added by a pipetter to the reaction vial. The reaction mixture turned to a dark purple color. The vial was sealed with a cap, removed from the glove box and put in the reaction slot of a Innova 2180 platform shaker. The reaction mixture was shaken on the platform shaker for 4 h in total at 23 °C, opened to air, quenched with two drops of H_2O, diluted with 2 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate (3 x 2 mL), and the combined solutions were concentrated *in vacuo*. The entire crude material was loaded onto a deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (88.8 mg, 55% yield) as a white solid. From the flash chromatography, C3-arylated product **4aa'** was isolated in 25.8 mg, 16% yield as a colorless thick oil.

General procedure B for alkylation: A brand-new oven-dried 4 mL glass vial equipped with two oven-dried glass beads was charged with ketimine **1a** (54.3 mg, 0.20 mmol) and neopentyl iodide **6a** (19.8 mg, 0.10 mmol) under a nitrogen atmosphere in a glove box. A solution of $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol) in 1.0 mL anhydrous MTBE was added by a pipetter to the reaction vial. The reaction mixture turned to a dark purple color. The vial was sealed with a cap, removed from the glove box and put in the reaction slot of a Innova 2180 platform shaker. The reaction mixture was shaken on the platform shaker for 2 h in total at 23 °C, opened to air, quenched with two drops of H_2O, diluted with 2 mL of ethyl acetate, and filtered over a pad of $MgSO_4$ and silica. The pad was rinsed with an additional 6 mL of ethyl acetate (3 x 2 mL), and the combined solutions were concentrated *in vacuo*. The entire crude material was loaded onto a deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (32.4 mg, 95% yield) as a colorless thick oil.

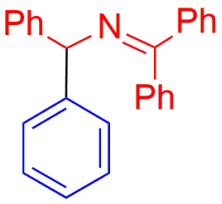


1-(4-(*tert*-Butyl)phenyl)-*N*-(diphenylmethylene)-1-phenylmethanamine (7aa): The reaction was performed following the General Procedure A with ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), 1-(*tert*-butyl)-4-iodobenzene **5a** (104.4 mg, 0.40 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product **7aa** (88.8 mg, 55% yield) as a white solid. The ^1H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data.[12c]

From the flash chromatography, C3-arylated product **7aa'** was isolated in 25.8 mg, 16% yield as colorless thick oil.

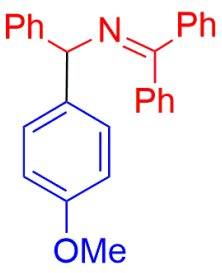


***N*-Benzylidene-1-(4-(*tert*-butyl)phenyl)-1,1-diphenylmethanamine (7aa'):** R_f = 0.85 (diethyl ether:hexanes = 1:5); ^1H NMR (500 MHz, $CDCl_3$): δ 7.86–7.83 (m, 2H), 7.83 (s, 1H), 7.43–7.41 (m, 3H), 7.30–7.29 (m, 10H), 7.25–7.24 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 1.31 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 159.7, 149.7, 146.3, 142.7, 137.0, 130.8, 130.0, 129.6, 128.8, 128.7, 127.9, 126.8, 124.8, 78.2, 34.6, 31.5 ppm; IR (thin film): 2962, 1642, 1446, 1216, 830, 755 cm^{-1}; HRMS calc'd for $C_{30}H_{30}N^+$ 404.2378, observed 404.2403 $[M+H]^+$.



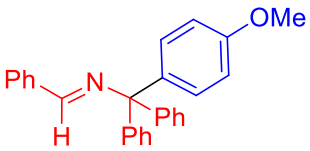
***N*-(Diphenylmethylene)-1,1-diphenylmethanamine (7ab):** The reaction was performed following the General Procedure A with ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), iodobenzene **5b** (81.6 mg, 0.40 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (80.6 mg, 58% yield) as a white solid. The ^1H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data. [12c]

From the flash chromatography, C3-arylated product **7ab'** was isolated in 19.5 mg, 14% yield as colorless thick oil. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for this compound match the literature data.[12c]

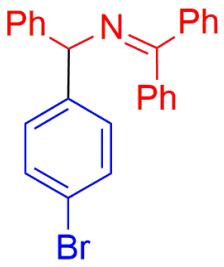


***N*-(Diphenylmethylene)-1-(4-methoxyphenyl)-1-phenylmethanamine (7ac):** The reaction was performed following the General Procedure A with ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), 1-iodo-4-methoxybenzene **5c** (93.6 mg, 0.40 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (75.5 mg, 50% yield) as a thick colorless oil. The ^{1}H and $^{13}C\{^{1}H\}$ NMR data for this compound match the literature data.[12c]

From the flash chromatography, C3-arylated product **4ac'** was isolated in 19.6 mg, 13% yield as colorless thick oil.



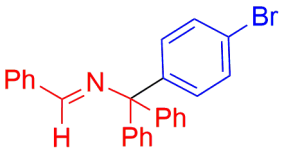
***N*-Benzylidene-1-(4-methoxyphenyl)-1,1-diphenylmethanamine (4ac'):** R_f = 0.61 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86–7.84 (m, 2H), 7.83 (s, 1H), 7.43–7.41 (m, 3H), 7.30–7.29 (m, 7H), 7.25–7.23 (m, 3H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.0 Hz, 2H), 3.80 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 159.6, 158.5, 146.4, 138.0, 136.9, 131.2, 130.9, 130.3, 129.9, 128.8, 128.7, 128.5, 127.95, 126.92, 113.2, 78.0, 55.4 ppm; IR (thin film): 3057, 2925, 1641, 1603, 1445, 1179, 998, 828, 755 cm^{-1}; HRMS calc'd for $C_{27}H_{24}NO^{+}$ 378.1858, observed 378.1875 $[M+H]^{+}$.



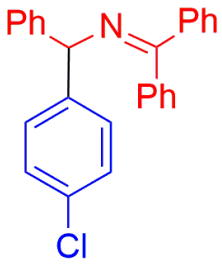
1-(4-Bromophenyl)-*N*-(diphenylmethylene)-1-phenylmethanamine (4ad): The reaction was performed following the General Procedure A with ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), 1-bromo-4-iodobenzene **5d** (113.2 mg, 0.40 mmol) in 9 h with MTBE as solvent. The crude material was purified by flash chromatography on

deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (73.3 mg, 43% yield) as a thick colorless oil. R_f = 0.53 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.44–7.37 (m, 6H), 7.35–7.32 (m, 2H), 7.29–7.25 (m, 4H), 7.20 (d, *J* = 8.5 Hz, 3H), 7.06–7.04 (m, 2H), 5.49 (s, 1H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.6, 144.6, 144.2, 139.8, 136.8, 131.6, 130.4, 129.5, 128.9, 128.8, 128.7, 128.6, 128.3, 127.9, 127.7, 127.1, 120.8, 69.5 ppm; IR (thin film): 3061, 2876, 1622, 1485, 1446, 1216, 908, 758 cm^{-1}; HRMS calc'd for $C_{26}H_{21}BrN^+$ 426.0852, observed 426.0852 $[M+H]^+$.

From the flash chromatography, C3-arylated product **7ad'** was isolated in 23.9 mg, 14% yield as colorless thick oil.

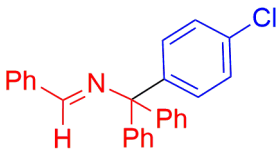


***N*-Benzylidene-1-(4-bromophenyl)-1,1-diphenylmethanamine (7ad'):** R_f = 0.78 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85–7.83 (m, 2H), 7.79 (s, 1H), 7.44–7.41 (m, 5H), 7.32–7.23 (m, 12H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.1, 145.6, 145.3, 136.7, 131.7, 131.1, 131.0, 129.9, 128.85, 128.84, 128.1, 127.2, 121.1, 78.1 ppm; IR (thin film): 3058, 2924, 1642, 1580, 1446, 1217, 818, 698 cm^{-1}; HRMS calc'd for $C_{26}H_{21}NBr^+$ 426.0857, observed 426.0869 $[M+H]^+$.

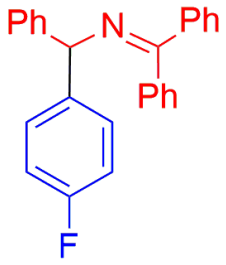


1-(4-Chlorophenyl)-*N*-(diphenylmethylene)-1-phenylmethanamine (7ae): The reaction was performed following the General Procedure A with ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), 1-chloro-4-iodobenzene **5e** (95.6 mg, 0.40 mmol) in 9 h with MTBE as solvent. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (67.2 mg, 44% yield) as a thick colorless oil. The ^{1}H and ^{13}C{^{1}H} NMR data for this compound match the literature data.[12c]

From the flash chromatography, C3-arylated product **7ae'** was isolated in 22.9 mg, 15% yield as colorless thick oil.

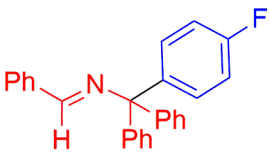


***N*-Benzylidene-1-(4-chlorophenyl)-1,1-diphenylmethanamine (7ae'):** R_f = 0.78 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85–7.83 (m, 2H), 7.80 (s, 1H), 7.43–7.41 (m, 3H), 7.31–7.23 (m, 14H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 160.0, 145.4, 145.0, 136.7, 132.8, 131.3, 131.1, 129.9, 128.84, 128.83, 128.1, 127.2, 78.0 ppm; IR (thin film): 3059, 1642, 1489, 1217, 822, 697 cm^{-1}; HRMS calc'd for $C_{26}H_{21}NCl^+$ 382.1363, observed 382.1346 $[M+H]^+$.

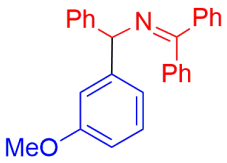


***N*-(Diphenylmethylene)-1-(4-fluorophenyl)-1-phenylmethanamine (7af):** The reaction was performed following the General Procedure A with ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), 1-fluoro-4-iodobenzene **5f** (88.8 mg, 0.40 mmol) in 9 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (70.2 mg, 48% yield) as a white solid. The ^{1}H and $^{13}C\{^1H\}$ NMR data for this compound match the literature data.[12c]

From the flash chromatography, C3-arylated product **7af'** was isolated in 19.0 mg, 13% yield as colorless thick oil.

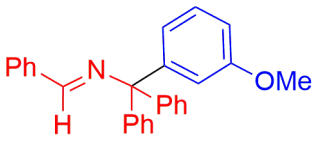


***N*-Benzylidene-1-(4-fluorophenyl)-1,1-diphenylmethanamine (7af'):** R_f = 0.78 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86–7.84 (m, 2H), 7.81 (s, 1H), 7.44–7.42 (m, 3H), 7.32–7.25 (m, 12H), 6.99 (t, J = 6.5 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.8 (d, $J_{C\text{-}F}$ = 240.0 Hz) 159.9, 145.7, 142.0, 136.8, 131.6, 131.5, 131.0, 129.92, 128.8 (d, $J_{C\text{-}F}$ = 1.9 Hz), 128.0, 127.1, 114.7 (d, $J_{C\text{-}F}$ = 21.0 Hz), 78.0 ppm; IR (thin film): 3059, 1641, 1446, 1224, 755, 696 cm^{-1}; HRMS calc'd for $C_{26}H_{21}NF^+$ 366.1658, observed 166.1673 $[M+H]^+$.

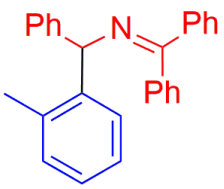


***N*-(Diphenylmethylene)-1-(3-methoxyphenyl)-1-phenylmethanamine (7ag):** The reaction was performed following the General Procedure A with ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), 1-iodo-3-methoxybenzene **5g** (93.6 mg, 0.40 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:30) to give the product (71.0 mg, 47% yield) as a thick colorless oil. R_f = 0.45 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77–7.76 (m, 2H), 7.46–7.43 (m, 3H), 7.40–7.38 (m, 1H), 7.36–7.33 (m, 4H), 7.29–7.27 (m, 2H), 7.22–7.18 (m, 2H), 6.95 (t, *J* = 2.0 Hz, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 6.75 (ddd, *J* = 8.5, 2.0, 1.0 Hz, 1H), 5.54 (s, 1H) , 3.77 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.2, 159.8, 146.7, 144.9, 140.1, 136.9, 130.3, 129.5, 128.9, 128.7, 128.6, 128.5, 128.2, 127.9, 127.8, 126.9, 120.2, 113.7, 112.1, 70.0, 55.4 ppm; IR (thin film): 3018, 2400, 1657, 1487, 1447, 1258, 908, 758 cm^{-1}; HRMS calc'd for $C_{27}H_{24}NO^+$ 378.1858, found 378.1841 $[M+H]^+$.

From the flash chromatography, C3-arylated product **7ag'** was isolated in 25.7 mg, 17% yield as colorless thick oil.

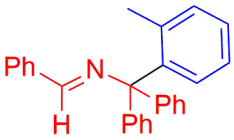


***N*-Benzylidene-1-(3-methoxyphenyl)-1,1-diphenylmethanamine (7ag')**: R_f = 0.60 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86–7.84 (m, 2H), 7.83 (s, 1H), 7.44–7.42 (m, 3H), 7.30–7.29 (m, 8H), 7.26–7.24 (m, 3H), 6.91 (t, *J* = 2.0 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 1H), 6.80 (ddd, *J* = 8.5, 2.0, 1.0 Hz, 1H), 3.72 (s, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.9, 159.3, 147.8, 145.8, 136.9, 130.9, 130.0, 128.84, 128.80, 128.7, 128.3, 128.1, 127.9, 127.0, 126.8, 122.6, 116.3, 111.8, 78.4, 55.3 ppm; IR (thin film): 3057, 1642, 1446, 755, 691 cm^{-1}; HRMS calc'd for $C_{27}H_{24}NO^+$ 378.1858, observed 378.1875 $[M+H]^+$.

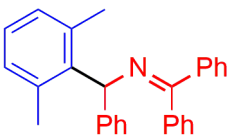


***N*-(Diphenylmethylene)-1-phenyl-1-(*o*-tolyl)methanamine (7ah):** The reaction was performed following the General Procedure A with with ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), 1-iodo-2-methylbenzene **5h** (87.2 mg, 0.40 mmol) in 9 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (66.5 mg, 46% yield) as a thick colorless oil. R_f = 0.67 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.69 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.42–7.38 (m, 3H), 7.36–7.29 (m, 3H), 7.26–7.16 (m, 6H), 7.11 (td, *J* = 7.5, 1.0 Hz, 1H), 7.05–7.03 (m, 3H), 5.74 (s, 1H), 1.95 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.0, 144.2, 142.9, 140.0, 137.3, 135.6, 130.6, 130.2, 128.9, 128.8, 128.7, 128.6, 128.4, 128.2, 127.9, 127.8, 126.8, 126.7, 126.3, 66.9, 19.7 ppm; IR (thin film): 3060, 2250, 1621, 1490, 1446, 1265, 908, 734 cm^{-1}; HRMS calc'd for $C_{27}H_{24}N^+$362.1909, found 362.1904 $[M+H]^+$.

From the flash chromatography, C3-arylated product **7ah'** was isolated in 21.7 mg, 15% yield as colorless thick oil.

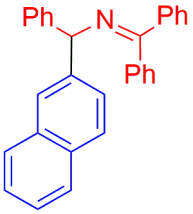


***N*-Benzylidene-1,1-diphenyl-1-(o-tolyl)methanamine (7ah'):** R_f = 0.71 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.89–7.86 (m, 2H), 7.43–7.41 (m, 3H), 7.33–7.32 (m, 4H), 7.29–7.26 (m, 4H), 7.25–7.21 (m, 3H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 7.5 Hz, 1H), 1.72 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 159.8, 146.3, 143.5, 138.6, 137.1, 132.4, 132.2, 130.9, 129.1, 128.8, 128.1, 127.2, 126.7, 125.2, 79.3, 23.1 ppm; IR (thin film): 3058, 2924, 1638, 1490, 1217, 850, 697 cm^{-1}; HRMS calc'd for $C_{27}H_{24}N^+$ 362.1909, observed 362.1919 $[M+H]^+$.



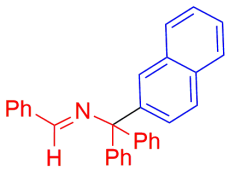
1-(2,6-Dimethylphenyl)-*N*-(diphenylmethylene)-1-phenylmethanamine (7ai): The reaction was performed following the General Procedure A with

ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), 2-iodo-1,3-dimethylbenzene **5i** (92.8 mg, 0.40 mmol) in 9 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (66.1 mg, 44% yield) as a thick colorless oil. R_f = 0.72 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75–7.73 (m, 2H), 7.40–7.31 (m, 6H), 7.27 (d, *J* = 7.5 Hz, 2H), 7.20–7.15 (m, 3H), 7.10–7.00 (m, 3H), 6.92 (d, *J* = 7.5 Hz, 2H), 6.10 (s, 1H), 2.02 (s, 6H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.1, 144.2, 140.3, 140.2, 137.9, 137.3, 130.2, 129.1, 128.9, 128.8, 128.6, 128.3, 128.2, 127.8, 127.0, 126.6, 126.2, 64.6, 21.2 ppm; IR (thin film): 3018, 2400, 1623, 1491, 1468, 1216, 950, 754 cm^{-1}; HRMS calc'd for $C_{28}H_{26}N^+$376.2065, found 376.2072 $[M+H]^+$.

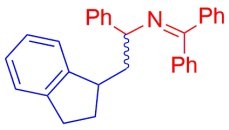


***N*-(Diphenylmethylene)-1-(naphthalen-2-yl)-1-phenylmethanamine (7aj):** The reaction was performed following the General Procedure A with ketimine **1a** (217.2 mg, 0.80 mmol), $NaN(SiMe_3)_2$ (220.4 mg, 1.2 mmol), 2-iodonaphthalene **5j** (101.6 mg, 0.40 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (55.7 mg, 35% yield) as a thick colorless oil. R_f = 0.45 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79–7.73 (m, 6H), 7.48–7.34 (m, 11H), 7.30–7.25 (m, 2H), 7.22–7.17 (m, 1H), 7.11–7.09 (m, 2H), 5.73 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.5, 144.9, 142.6, 140.1, 137.0, 133.8, 132.9, 130.4, 130.3, 129.1, 129.0, 128.7, 128.6, 128.3, 128.2, 128.02, 127.96, 127.90, 127.1, 126.9, 126.8, 126.6, 126.5, 126.2, 126.1, 125.9, 125.7, 70.3 ppm; IR (thin film): 3025, 2875, 1621, 1491, 1278, 1216, 908, 720 cm^{-1}; HRMS calc'd for $C_{30}H_{24}N^+$398.1903, found 398.1906 $[M+H]^+$.

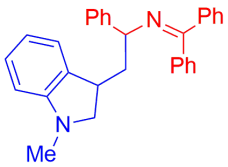
From the flash chromatography, C3-arylated product **7aj'** was isolated in 17.5 mg, 11% yield as colorless thick oil.



***N*-Benzylidene-1-(naphthalen-2-yl)-1,1-diphenylmethanamine (7aj')** R_f = 0.73 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.88–7.86 (m, 2H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 1.0 Hz, 1H), 7.49–7.41 (m, 6H), 7.36–7.27 (m, 10H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 160.2, 145.8, 143.6, 136.9, 133.0, 132.5, 131.0, 130.0, 128.88, 128.80, 128.6, 128.5, 128.0, 127.6, 127.4, 127.0, 126.2, 126.1, 78.6 ppm; IR (thin film): 3056, 1641, 1489, 1192, 817, 696 cm^{-1}; HRMS calc'd for $C_{30}H_{24}N^+$ 398.1909, observed 398.1918 $[M+H]^+$.

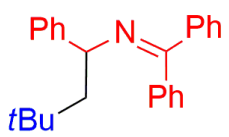


2-(2,3-Dihydro-1H-inden-1-yl)-*N*-(diphenylmethylene)-1-phenylethanamine (7ak): The reaction was performed following the General Procedure A with ketimine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 1-(but-3-en-1-yl)-2-iodobenzene **5k** (25.8 mg, 0.10 mmol) with Toluene as solvent in 6 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the **1:1** mixture of diastereomers of product **7ak** (38.5 mg, overall 96% yield) as a thick colorless oil. R_f = 0.62 (diethyl ether:hexanes = 1:5); HRMS calc'd for $C_{30}H_{28}N^+$ 402.2222, found 402.2222 $[M+H]^+$. Diastereomeric ratio was determined based on H^a (1H, ~ 4.6 ppm) and H^b (2H, ~ 7.7 ppm).

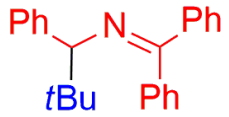


***N*-(Diphenylmethylene)-2-(1-methylindolin-3-yl)-1-phenylethanamine (7al)** :The reaction was performed following the General Procedure A with ketimine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), *N*-allyl-2-iodo-N-methylaniline **5l** (27.3 mg, 0.10 mmol) with DME as solvent in 6 h. The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:10) to give the **1:1** mixture of diastereomers of product **7al** (36.7 mg, overall 88% yield) as a thick colorless oil. R_f = 0.40 (diethyl ether:hexanes = 1:5); HRMS calc'd for

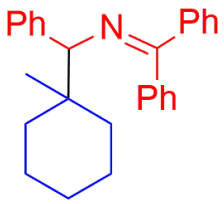
$C_{30}H_{29}N_2^+$ 417.2325, found 417.2325 $[M+H]^+$. Diastereomeric ratio was determined based on indoline methyl group (3H, ~ 2.6 ppm) and H^b (1H, ~ 6.6 ppm).



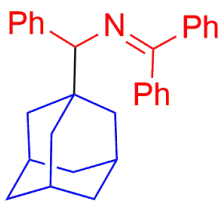
***N*-(Diphenylmethylene)-3,3-dimethyl-1-phenylbutan-1-amine (8aa):** The reaction was performed following the General Procedure B with ketimine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), neopentyl iodide **6a** (19.8 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (32.4 mg, 95% yield) as a thick colorless oil. R_f = 0.73 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69–7.67 (m, 2H), 7.44–7.41 (m, 3H), 7.37–7.32 (m, 3H), 7.30–7.25 (m, 4H), 7.21–7.18 (m, 1H), 7.04–7.02 (m, 2H), 4.52 (dd, *J* = 8.0, 4.0 Hz, 1H), 2.12 (dd, *J* = 14.0, 8.0 Hz, 1H), 1.80 (dd, *J* = 14.0, 4.0 Hz, 1H), 0.82 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 165.6, 147.2, 140.4, 137.5, 129.9, 128.8, 128.5, 128.4, 128.3, 128.2, 127.9, 127.4, 126.5, 64.7, 53.9, 31.2, 30.5 ppm; IR (thin film): 3018, 2955, 2359, 1618, 1491, 1445, 1216, 909, 769 cm^{-1}; HRMS calc'd for $C_{25}H_{28}N^+$ 342.2222, found 342.2199 $[M+H]^+$.



***N*-(Diphenylmethylene)-2,2-dimethyl-1-phenylpropan-1-amine (8ab):** The reaction was performed following the General Procedure B with ketimine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 2-iodo-2-methylpropane **3b** (18.4 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (17.4 mg, 53% yield) as a thick colorless oil. R_f = 0.82 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72–7.70 (m, 2H), 7.41–7.32 (m, 6H), 7.24–7.18 (m, 5H), 6.91 (d, *J* = 6.5 Hz, 2H), 3.99 (s, 1H), 0.91 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 165.7, 143.0, 140.4, 137.2, 129.7, 129.1, 128.5, 128.04, 128.03, 127.95, 127.94, 127.4, 126.4, 75.6, 36.3, 26.9 ppm; IR (thin film): 3019, 2968, 1625, 1489, 1374, 1215, 761, 689 cm^{-1}; HRMS calc'd for $C_{24}H_{26}N^+$ 328.2065, found 328.2039 $[M+H]^+$.

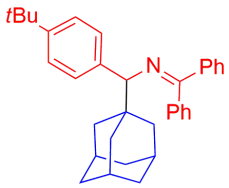


***N*-(Diphenylmethylene)-1-(1-methylcyclohexyl)-1-phenylmethanamine (8ac):** The reaction was performed following the General Procedure B with ketimine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 1-iodo-1-methylcyclohexane **6c** (22.4 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (15.1 mg, 41% yield) as a thick colorless oil. When 1-bromo-1-methylcyclohexane **6d** was used, following the same procedure, product was isolated in 13.6 mg, 37% yield. R_f = 0.78 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72–7.70 (m, 2H), 7.40–7.32 (m, 6H), 7.22–7.17 (m, 5H), 6.88 (d, *J* = 6.5 Hz, 2H), 4.00 (s, 1H), 1.54–1.51 (m, 1H), 1.32–1.44 (m, 6H), 1.25–1.19 (m, 1H), 1.16–1.06 (m, 2H), 1.03 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.0, 142.7, 140.6, 137.4, 129.9, 129.5, 128.7, 128.6, 128.24, 128.19, 128.18, 128.16, 127.5, 126.0, 126.5, 126.3, 76.1, 39.1, 35.3, 34.8, 26.6, 22.7, 22.2, 19.7 ppm; IR (thin film): 3019, 2975, 2400, 1625, 1489, 1215, 908, 769 cm^{-1}; HRMS calc'd for $C_{27}H_{30}N^+$368.2378, found 368.2368 $[M+H]^+$.

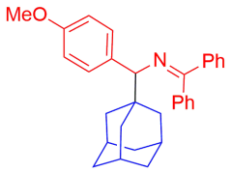


1-(Adamantan-1-yl)-*N*-(diphenylmethylene)-1-phenylmethanamine (8ae): The reaction was performed following the General Procedure B with ketimine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 1-iodoadamantane **6e** (26.2 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (37.7 mg, 93% yield) as a thick colorless oil. When 1-bromoadamantane **6f** was used, following the same procedure with toluene as solvent, product was isolated in 24.7 mg, 61% yield. R_f = 0.72 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.40–7.33 (m, 6H), 7.25–7.18 (m, 5H), 6.91 (d, *J* = 6.5 Hz, 2H), 3.83 (s, 1H), 1.93 (s, 3H), 1.66–1.64 (m, 3H), 1.57 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.1, 142.0, 140.6, 137.4, 129.8, 129.4, 128.7, 128.22, 128.20, 128.16, 127.5, 126.5, 76.7, 39.5,

38.2, 37.4, 28.9 ppm; IR (thin film): 3019, 2400, 1730, 1600, 1215, 908, 756 cm^{-1}; HRMS calc'd for $C_{30}H_{32}N^{+}$406.2535, found 406.2543 $[M+H]^{+}$.

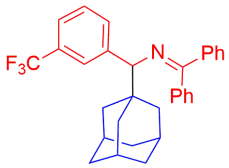


1-(Adamantan-1-yl)-1-(4-(*tert*-butyl)phenyl)-*N*-(diphenylmethylene)-methanamine (8be): The reaction was performed following the General Procedure B with ketimine **1b** (65.4 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 1-iodoadamantane **6e** (26.2 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (26.8 mg, 58% yield) as a thick colorless oil. R_f = 0.78 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70–7.68 (m, 2H), 7.37–7.30 (m, 6H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 6.5 Hz, 2H), 3.80 (s, 1H), 1.91 (s, 3H), 1.63–1.61 (m, 3H), 1.53–1.51 (m, 9H), 1.30 (s, 9H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 165.7, 149.1, 140.7, 138.8, 137.4, 129.7, 128.9, 128.7, 128.4, 128.2, 128.14, 128.12, 124.3, 76.5, 39.4, 38.3, 37.5, 34.6, 31.7, 28.9 ppm; IR (thin film): 3022, 2905, 2400, 1732, 1624, 1490, 1393, 1268, 908, 751 cm^{-1}; HRMS calc'd for $C_{34}H_{40}N^{+}$ 462.3161, found 462.3156 $[M+H]^{+}$.

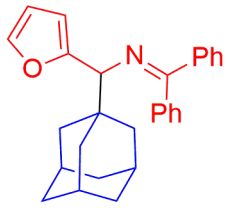


1-(Adamantan-1-yl)-*N*-(diphenylmethylene)-1-(4-methoxyphenyl)-methanamine (8ce): The reaction was performed following the General Procedure B with ketimine **1c** (60.2 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 1-iodoadamantane **6e** (26.2 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the product (29.6 mg, 68% yield) as a thick colorless oil. R_f = 0.63 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70–7.68 (m, 2H), 7.37–7.30 (m, 6H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 6.5 Hz, 2H), 6.79 (d, *J* = 8.0 Hz, 2H), 3.79 (s, 3H), 3.75 (s, 1H), 1.90 (s, 3H), 1.64–1.61 (m, 3H), 1.56–1.53 (m, 9H) ppm; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 165.8, 158.3, 140.6, 137.4, 134.3, 130.3, 129.8, 128.7, 128.22, 128.20, 128.17, 128.15, 112.8, 76.0, 55.4, 39.4, 38.2,

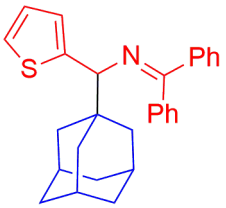
37.5, 28.9 ppm; IR (thin film): 3019, 2399, 1626, 1508, 1217, 908, 773 cm^{-1}; HRMS calc'd for $C_{31}H_{34}NO^+$ 436.2640, found 436.2646 $[M+H]^+$.



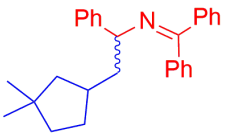
1-(Adamantan-1-yl)-*N*-(diphenylmethylene)-1-(3-(trifluoromethyl)-phenyl)methanamine (8de): The reaction was performed following the General Procedure B with ketimine **1d** (67.8 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 1-iodoadamantane **6e** (26.2 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (37.9 mg, 80% yield) as a thick colorless oil. R_f = 0.73 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72–7.70 (m, 2H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.40–7.30 (m, 9H), 6.85 (d, *J* = 6.5 Hz, 2H), 3.86 (s, 1H), 1.93 (s, 3H), 1.65–1.62 (m, 3H), 1.56–1.52 (m, 9H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.1, 142.9, 140.2, 137.2, 132.8, 130.1, 128.8, 128.4, 128.3, 128.2, 127.98, 127.90, 126.0 (q, $J_{C\text{-}F}$ = 4.0 Hz), 123.5 (q, $J_{C\text{-}F}$= 4.0 Hz), 76.4, 39.3, 38.8, 37.3, 28.8 ppm; IR (thin film): 3018, 2907, 1624, 1360, 1215, 908, 758 cm^{-1}; HRMS calc'd for $C_{31}H_{31}N_3F_3^+$ 474.2412, found 406.2535 $[M+H]^+$.



1-(Adamantan-1-yl)-*N*-(diphenylmethylene)-1-(furan-2-yl)methanamine (8ee): The reaction was performed following the General Procedure B with ketimine **1e** (52.2 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 1-iodoadamantane **6e** (26.2 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (23.7 mg, 60% yield) as a thick colorless oil. R_f = 0.74 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68–7.66 (m, 2H), 7.40–7.30 (m, 7H), 6.97–6.95 (m, 2H), 6.29–6.28 (m, 1H), 6.06–6.05 (m, 1H), 3.98 (s, 1H), 1.94 (s, 3H), 1.67–1.59 (m, 12H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.9, 155.7, 140.9, 140.5, 137.1, 130.0, 128.9, 128.42, 128.38, 128.2, 109.9, 107.2, 70.9, 39.5, 38.6, 37.4, 28.9 ppm; IR (thin film): 3018, 2904, 2846, 1614, 1314, 1215, 942, 804 cm^{-1}; HRMS calc'd for $C_{28}H_{30}NO^+$ 396.2327, found 396.2349 $[M+H]^+$.



1-(Adamantan-1-yl)-*N*-(diphenylmethylene)-1-(thiophen-2-yl)methanamine (8fe): The reaction was performed following the General Procedure B with ketimine **1f** (55.4 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 1-iodoadamantane **6e** (26.2 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (35.0 mg, 85% yield) as a thick colorless oil. R_f = 0.85 (diethyl ether:hexanes = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71–7.69 (m, 2H), 7.37–7.29 (m, 6H), 7.15 (d, *J* = 5.0 Hz, 1H), 6.95–6.94 (m, 2H), 6.91 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.68 (d, *J* = 3.5 Hz, 1H), 4.15 (s, 1H), 1.93 (s, 3H), 1.65–1.62 (m, 4H), 1.65–1.60 (m, 8H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.6, 144.6, 140.2, 136.8, 130.0, 128.8, 128.4, 128.3, 128.2, 128.1, 125.7, 124.3, 123.9, 72.7, 39.4, 38.2, 37.4, 28.9 ppm; IR (thin film): 3018, 2905, 1625, 1445, 1215, 815, 597 cm^{-1}; HRMS calc'd for $C_{28}H_{30}NS^+$ 412.2099, found 412.2073 $[M+H]^+$.



2-(3,3-Dimethylcyclopentyl)-*N*-(diphenylmethylene)-1-phenylethanamine (8ag): The reaction was performed following the General Procedure B with ketimine **1a** (54.3 mg, 0.20 mmol), $NaN(SiMe_3)_2$ (55.1 mg, 0.3 mmol), 6-iodo-5,5-dimethylhex-1-ene **6g** (23.8 mg, 0.10 mmol). The crude material was purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:50) to give the **1:1** mixture of diastereomers of product **8ag** (36.2 mg, overall 95% yield) as a thick colorless oil. R_f = 0.68 (diethyl ether:hexanes = 1:5); HRMS calc'd for $C_{28}H_{32}N^+$ 382.2535, found 382.2559 $[M+H]^+$. Diastereomeric ratio was determined based on methyl group of the cyclopentane ring (3H, ~ 1.0 ppm and 3H, ~0.9 ppm), see ^{1}H spectra (Page S53) for determination of diastereomeric ratio.

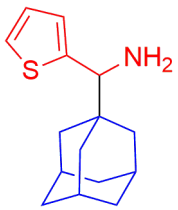
Gram Scale Sequential One-Pot Ketimine Synthesis/Alkylation Procedure:

An oven-dried 100 mL Schlenk tube equipped with a stir bar was sealed with a rubber septum and was connected to a Schlenk line, evacuated, and refilled with nitrogen (repeated three times).

DCM (10 mL) was added under nitrogen via syringe through the rubber septum. 2-Thiophenemethylamine (1.13 g, 10.0 mmol) and benzophenone imine (1.81 g, 10.0 mmol) were added under nitrogen via syringe through the rubber septum. The reaction was stirred at 23 °C for 12 h, the solvent was completely removed in *vacuo* and the tube was filled with nitrogen. A solution (prepared in the glove box) of 1-iodoadamantane **6e** (1.31 g, 5.0 mmol) in 20 mL anhydrous MTBE was added to the Schlenk tube via syringe through the rubber septum. Next, a solution of $NaN(SiMe_3)_2$ (7.6 g, 15 mmol) in 30 mL anhydrous DME was added by syringe through the rubber septum. The reaction mixture was stirred for 6 h in total at 23 °C, opened to air, and quenched with 10 mL of H_2O. The layers were separated and the aqueous layer was extracted with DCM (3X5 mL). The combined organic layers were concentrated in *vacuo*. The crude material was loaded onto a deactivated silica gel column via pipette and purified by flash chromatography on deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the product (1.69 g, 82% yield) as a thick colorless oil.

Product hydrolysis:

Hydrolysis of Product 8fe: An oven-dried microwave vial equipped with a stir bar was charged with **8fe** (41.2 mg 0.1 mmol). THF (1 mL) was added to the reaction vial via syringe and the reaction was cooled at 0 °C. HCl 1N (1 mL) was added to the reaction vial via syringe. The stirring solution was warmed to room temperature and was monitored by TLC until **8fe** was consumed (reaction completed in 3 h). The reaction mixture was basified with 1N NaOH until the pH reached 14, transferred to a 30 mL seperatory funnel via pipette and was extracted with dichloromethane (3 x 2 mL). The combined organic layers were concentrated in *vacuo*, loaded onto a deactivated silica gel column via pipette and purified by flash chromatography on deactivated silica gel (eluted with hexanes to ethyl acetate:hexanes = 1:2) to give the amine product **9fe** as a yellow oil (24.5 mg, 99% yield).



Adamantan-1-yl(thiophen-2-yl)methanamine (9fe): R_f = 0.12 (ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18 (d, *J* = 5.0 Hz, 1H), 6.95 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.85 (d, *J* = 3.5 Hz, 1H), 3.81 (s, 1H), 1.98 (s, 3H), 1.69–1.51 (m, 15H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 147.3, 126.1, 124.9, 123.5, 62.4, 38.9, 37.3, 36.7, 28.7 cm^{-1}; HRMS calc'd for $C_{15}H_{19}S$ 231.1207, observed 231.1190 $[M\text{-}NH_2]^+$.

Microscale High-throughput Experimentation:

General Information. High-throughput Experimentation Screening was accomplished in a Vacuum Atmospheres glovebox with oxygen typically <5 ppm. The experimental design was accomplished using Accelrys Library Studio. Screening reactions were carried out in 1 mL vials (30 mm height×8 mm diameter) in 24-well plate aluminum reactor block. Liquid chemicals were dosed using multi-channel or single-channel pipettors. Solid chemicals were dosed manually as solutions or slurries in appropriate solvents. Undesired additional solvent was removed using a GeneVac system located inside the glovebox. The reactions were heated and stirred on a heating block with a tumble-stirrer (V&P Scientific) using 1.98 mm diameter×4.80 mm length parylene stir bars. The tumble stirring mechanism helped to insure uniform stirring throughout the 24-well plate. The reactions were sealed in the 24-well plate during reaction. Below each reactor vial in the aluminum 24-well plate was a 0.062 mm thick silicon-rubber gasket. Directly above the glass vial reactor tops was a Teflon perfluoroalkoxy copolymer resin sealing gasket and above that, two more 0.062 mm thick silicon-rubber gaskets. The entire assembly was compressed between an aluminum top and the reactor base with 9 evenly-placed screws.

Screening of base, solvent and concentration for transition metal-free arylation:

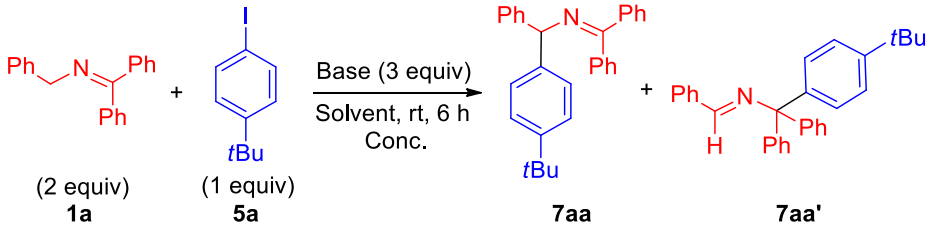
***Set up*:**

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials were firstly dosed with $NaN(SiMe_3)_2$ (30 μmol) and $LiN(SiMe_3)_2$

(30 µmol) in THF. The solvent was removed to dryness using a GeneVac. and a parylene stir bar was then added to each reaction vial. Ketimine **1a** (20 µmol/reaction) and 1-(*tert*-butyl)-4-iodobenzene **2a** (10 µmol) were then dosed together into each reaction vial as a solution in different solvents (50 µL, 0.2 M). For 0.1 M reactions, extra 50 µL solvent was added. The 24-well plate was then sealed with screws and stirred for 6 h at 23 ^{o}C.

***Work up*:**

Upon opening the plate to air, 500 µL of a solution of biphenyl (used as internal standard to measure UPLC yields) in acetonitrile (0.002 mol/L) was added into each vial. The plate was covered again and the vials stirred for 10 min. to ensure good homogenization. Into a separate 96-well LC block was added 700 µL of acetonitrile, followed by 25 µL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated UPLC instrument for analysis.



(2 equiv) **1a** (1 equiv) **5a** **7aa** **7aa'**

- Solvent: THF, CPME, DME, MTBE, Toluene, Cyclohexane
- Base: $LiN(SiMe_3)_2$ and $NaN(SiMe_3)_2$
- Concentration: 0.1 M and 0.2 M

Solvent	Base	Conc.	**4aa**/IS	**4aa'**/IS
THF	$LiN(SiMe_3)_2$	0.2	5.13	1.29
CPME	$LiN(SiMe_3)_2$	0.2	3.86	0.64
DME	$LiN(SiMe_3)_2$	0.2	7.01	1.72
MTBE	$LiN(SiMe_3)_2$	0.2	3.08	0.86
Tol	$LiN(SiMe_3)_2$	0.2	3.15	0.58

Cyclohexane	$LiN(SiMe_3)_2$	0.2	3.89	0.63
THF	$LiN(SiMe_3)_2$	0.1	5.32	1.10
CPME	$LiN(SiMe_3)_2$	0.1	3.02	0.48
DME	$LiN(SiMe_3)_2$	0.1	6.21	1.38
MTBE	$LiN(SiMe_3)_2$	0.1	4.17	0.87
Tol	$LiN(SiMe_3)_2$	0.1	2.07	0.34
Cyclohexane	$LiN(SiMe_3)_2$	0.1	3.15	0.41
THF	$NaN(SiMe_3)_2$	0.2	6.68	2.02
CPME	$NaN(SiMe_3)_2$	0.2	7.16	1.57
DME	**$NaN(SiMe_3)_2$**	**0.2**	**7.36**	**2.04**
MTBE	$NaN(SiMe_3)_2$	0.2	6.63	2.06
Tol	$NaN(SiMe_3)_2$	0.2	6.76	1.52
Cyclohexane	$NaN(SiMe_3)_2$	0.2	5.52	1.49
THF	$NaN(SiMe_3)_2$	0.1	6.05	1.36
CPME	$NaN(SiMe_3)_2$	0.1	5.87	1.08
DME	$NaN(SiMe_3)_2$	0.1	6.83	1.77
MTBE	$NaN(SiMe_3)_2$	0.1	6.13	1.70
Tol	$NaN(SiMe_3)_2$	0.1	5.33	1.02
Cyclohexane	$NaN(SiMe_3)_2$	0.1	5.33	1.31

(3) Screening of base, solvent and concentration for transition metal-free alkylation:

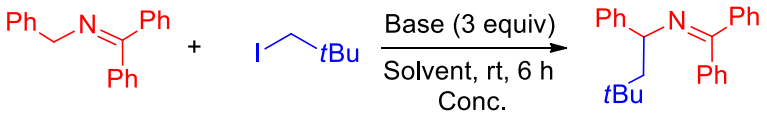
***Set up*:**

Experiments were set up inside a glovebox under a nitrogen atmosphere. A 24-well aluminum block containing 1 mL glass vials were firstly dosed with $NaN(SiMe_3)_2$ (30 µmol) or $LiN(SiMe_3)_2$ (30 µmol) in THF. The solvent was removed to dryness using a GeneVac. and a parylene stir bar was then added to each reaction vial. Ketimine **1a** (20 µmol/reaction) and neopentyl iodide **6a** (10

μmol) were then dosed together into each reaction vial as a solution in different solvents (50 μL, 0.2 M). For 0.1 M reactions, extra 50 μL solvent was added. The 24-well plate was then sealed with screws and stirred for 6 h at 23 °C.

***Work up*:**

Upon opening the plate to air, 500 μL of a solution of biphenyl (used as internal standard to measure UPLC yields) in acetonitrile (0.002 mol/L) was added into each vial. The plate was covered again and the vials stirred for 10 min. to ensure good homogenization. Into a separate 96-well LC block was added 700 μL of acetonitrile, followed by 25 μL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated UPLC instrument for analysis.



1a **6a** **8aa**

- Solvent: THF, CPME, DME, MTBE, toluene, cyclohexane
- Base: $LiN(SiMe_3)_2$ and $NaN(SiMe_3)_2$
- Concentration: 0.1 M and 0.2 M

Solvent	Base	Conc.	PDT/IS
THF	$LiN(SiMe_3)_2$	0.2	13.29
CPME	$LiN(SiMe_3)_2$	0.2	6.57
DME	$LiN(SiMe_3)_2$	0.2	13.02
MTBE	$LiN(SiMe_3)_2$	0.2	7.88
Tol	$LiN(SiMe_3)_2$	0.2	5.14
Cyclohexane	$LiN(SiMe_3)_2$	0.2	6.93
THF	$LiN(SiMe_3)_2$	0.1	13.05
CPME	$LiN(SiMe_3)_2$	0.1	5.95
DME	$LiN(SiMe_3)_2$	0.1	12.47

MTBE	$LiN(SiMe_3)_2$	0.1	6.77
Tol	$LiN(SiMe_3)_2$	0.1	5.43
Cyclohexane	$LiN(SiMe_3)_2$	0.1	5.94
THF	$NaN(SiMe_3)_2$	0.2	13.62
CPME	$NaN(SiMe_3)_2$	0.2	11.95
DME	$NaN(SiMe_3)_2$	0.2	13.99
MTBE	$NaN(SiMe_3)_2$	0.2	15.28
Tol	$NaN(SiMe_3)_2$	0.2	13.17
Cyclohexane	$NaN(SiMe_3)_2$	0.2	12.70
THF	$NaN(SiMe_3)_2$	0.1	12.22
CPME	$NaN(SiMe_3)_2$	0.1	11.70
DME	$NaN(SiMe_3)_2$	0.1	13.29
MTBE	**$NaN(SiMe_3)_2$**	**0.1**	**15.71**
Tol	$NaN(SiMe_3)_2$	0.1	12.73
Cyclohexane	$NaN(SiMe_3)_2$	0.1	11.79

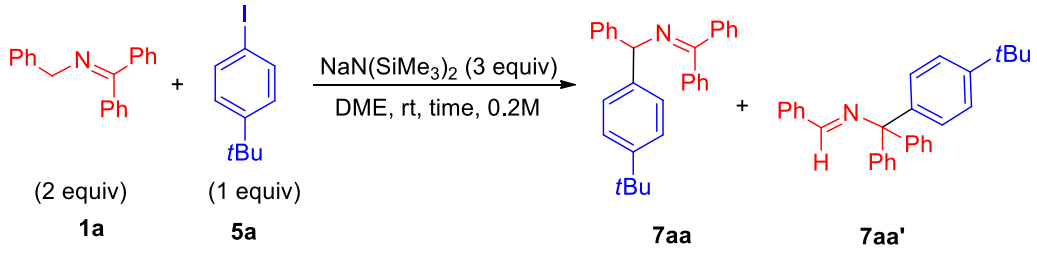
Reaction Profile of Coupling between 1a and 5a.

***Set up*:**

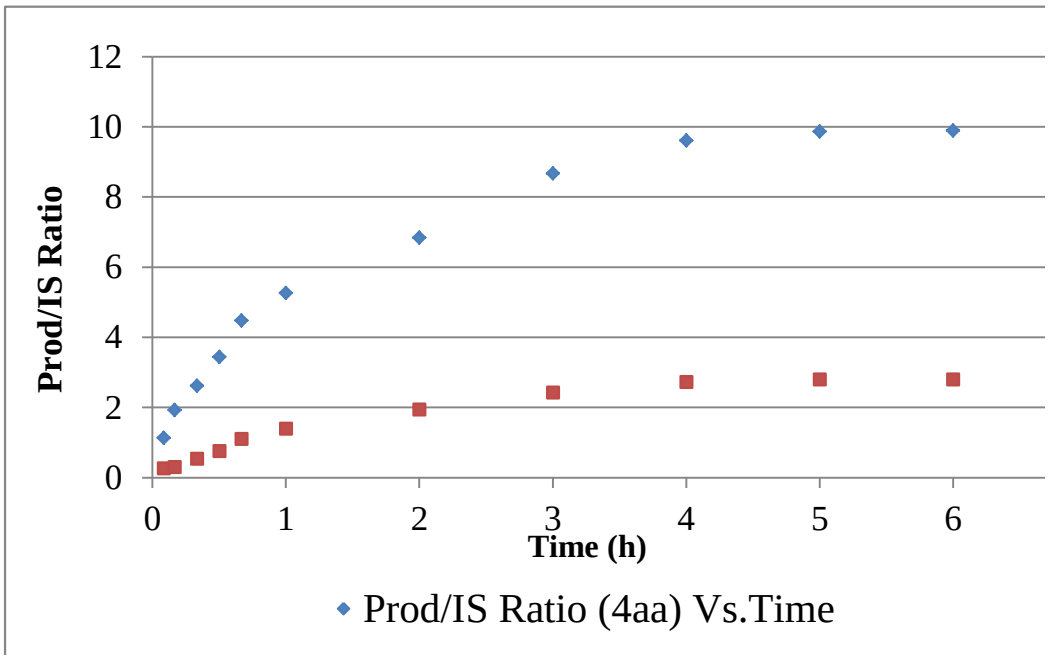
Experiments were set up inside a glovebox under a nitrogen atmosphere. 2 mL crimp top glass vials placed in a auto-sampler vial rack were firstly dosed with $NaN(SiMe_3)_2$ (60 µmol) in THF. The solvent was removed to dryness using a GeneVac. and a parylene stir bar was then added to each reaction vial. Ketimine **1a** (40 µmol/reaction) and 1-(*tert*-butyl)-4-iodobenzene **2a** (20 µmol) were dosed together into as a solution in DME (100 µL). Total volume of the reactions is 100 µL, 0.2 M. The vials were sealed with crimp caps, removed from the glovebox and stirred at 23 ^{o}C. Vials were sequentially quenched with 1 drop of water via syringe through the rubber septum at reaction time listed in the Supplementary Figure 1.

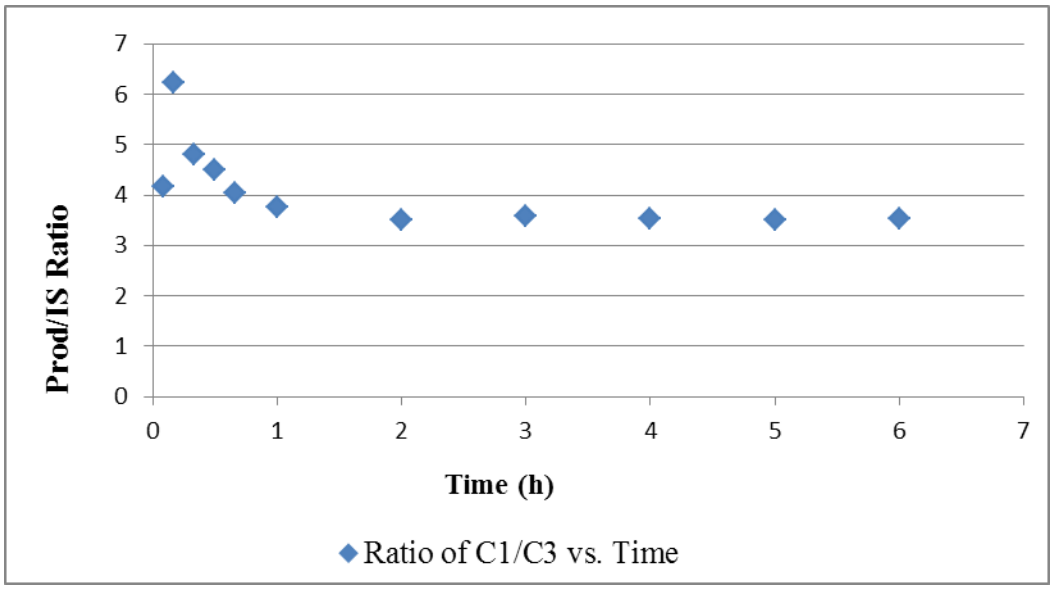
***Work up*:**

Upon opening the crimp cap with tweezers, 500 µL of a solution of biphenyl (used as internal standard to measure UPLC yields) in acetonitrile (0.002 mol/L) was added into each vial. The vials were stirred for 10 min. to ensure good homogenization. Into a separate 96-well LC block was added 700 µL of acetonitrile, followed by 25 µL of the diluted reaction mixtures. The LC block was then sealed with a silicon-rubber storage mat and mounted on an automated UPLC instrument for analysis.



(2 equiv) **1a** + (1 equiv) **5a** → **7aa** + **7aa'**





Supplementary Figure 1. Reaction Profile of Coupling between **1a** and **5a**.

Reaction Profile of Coupling between 1a and 6a.

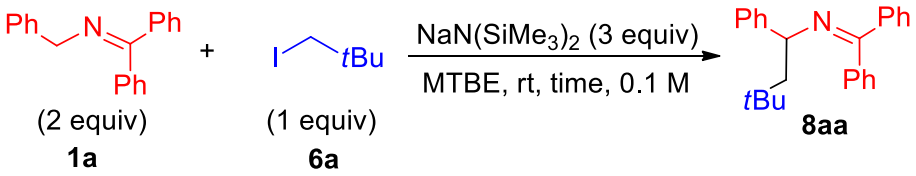
***Set up*:**

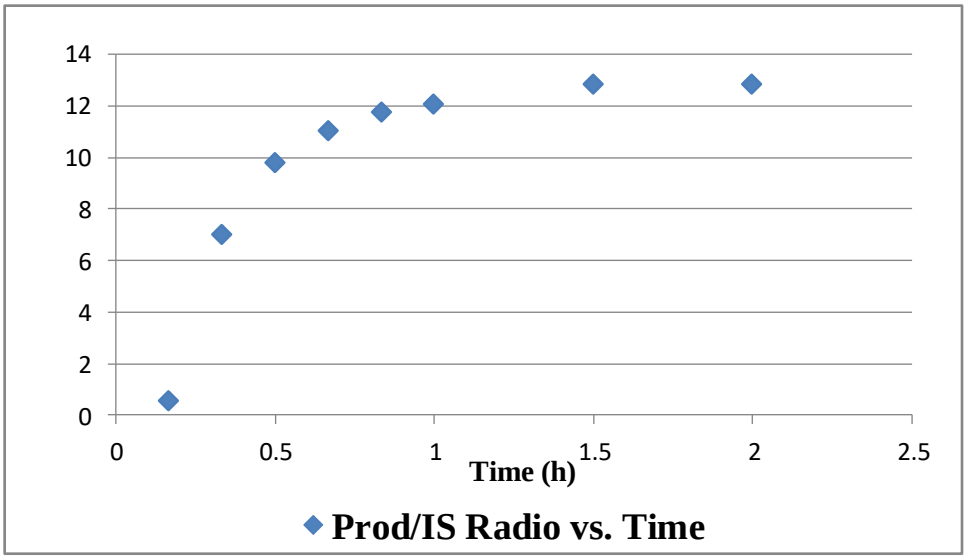
Experiments were set up inside a glovebox under a nitrogen atmosphere. 2 mL crimp top glass vials were placed in a auto-sampler vial rack. A parylene stir bar was then added to each reaction vial. Ketimine **1a** (20 µmol/reaction) and neopentyl iodide **6a** (10 µmol) were dosed together into as a solution in MTBE (50 µL). $NaN(SiMe_3)_2$ (30 µmol/reaction) was then dosed into the vials as a solution in MTBE (50 µL). Total volume of the reactions is 100 µL, 0.1 M. The vials were sealed with crimp caps, removed from the glovebox and stirred at 23 ^{o}C. Vials were sequentially quenched with 1 drop of water via syringe through the rubber septum at reaction time listed in the Supplementary Figure 2.

***Work up*:**

Upon opening the crimp cap with tweezers, 500 µL of a solution of biphenyl (used as internal standard to measure UPLC yields) in acetonitrile (0.002 mol/L) was added into each vial. The vials stirred for 10 min. to ensure good homogenization. Into a separate 96-well LC block was added 700 µL of acetonitrile, followed by 25 µL of the diluted reaction mixtures. The LC block was

then sealed with a silicon-rubber storage mat and mounted on an automated UPLC instrument for analysis.

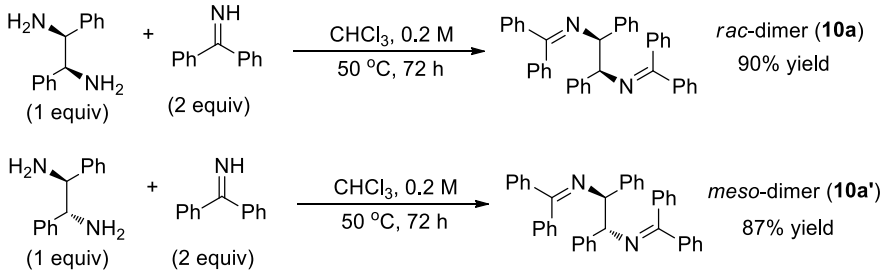




Supplementary Figure 2. Reaction Profile of Coupling between **1a** and **6a**.

Study of Azaallyl Dimer 10a and 10a'

Rac- and *meso*-dimer product standards were prepared by condensation of the (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine and *meso*-1,2-diphenylethylenediamine with benzophenone imine following the procedure:



An oven-dried 8 mL microwave vial equipped with a stir bar was charged with diphenylethylenediamine (212.3 mg, 1 mmol) and benzophenone imine (362.4 mg, 2 mmol). $CHCl_3$ (5 mL) was added via syringe. The vial was then sealed with cap.The reaction mixture was stirred at 50 ^oC for 72 h. The reaction mixture was concentrated *in vacuo* till all solvent was removed. The entire crude material was loaded onto a deactivated silica gel (eluted with hexanes to diethyl ether:hexanes = 1:100) to give the *rac*-dimer **10a** (486.6 mg, 90% yield) and *meso*-dimer **10a'** (470.4 mg, 87% yield) as white solids. The ^1H NMR data for this compound match the literature data.[34]

3.6. Acknowledgement

I would like to thank Professor Osvaldo Gutierrez, Dr. Ana Pascual-Escudero, Ahmet Yeşilçimen, Guogang Deng and Lucas Matuszewski for their collaboration and contribution. Prof. Osvaldo conducted the entire DFT calculation in the mechanistic study of vinylation. Ana and Ahmet synthesized radical clock **2k** and **2i** of Scheme 3.8. Guogang synthesized radical clock **5l** and completed chromatographic purification of **7al** in Scheme 3.11. Lucas synthesized the starting meterials alkyl halides **6c** and **6d** of Table 3.5, **5k** of Scheme 3.11 and **6g** of Scheme 3.12.

3.7. References.

1. (a) Diederich, F.; Stang, P. J., *Metal-Catalyzed Cross-Coupling Reactions, Wiley-VCH* **1998**; (b) Magano, J.; Dunetz, J. R., *Chem. Rev.* **2011,** *111*, 2177; (c) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F., *Chem. Soc. Rev.* **2011,** *40*, 4740; (d) Newhouse, T.; Baran, P. S., *Angew. Chem. Int. Ed.* **2011,** *50*, 3362; (e) McMurray, L.; O'Hara, F.; Gaunt, M. J., *Chem. Soc. Rev.* **2011,** *40*, 1885; (f) Li, B. J.; Shi, Z. J., *Chem. Soc. Rev.* **2012,** *41*, 5588; (g) Sun, C. L.; Shi, Z. J., *Chem. Rev.* **2014,** *114*, 9219; (h) Giri, B. P.; Prasad, G.; Mehrotra, K. N., *Can. J. Chem.* **1979,** *57*, 1157.

2. Yan, M.; Lo, J. C.; Edwards, J. T.; Baran, P. S., *J. Am. Chem. Soc.* **2016,** *138*, 12692.

3. (a) Shaw, M. H.; Twilton, J.; MacMillan, D. W., *J. Org. Chem.* **2016,** *81*, 6898; (b) Heitz, D. R.; Rizwan, K.; Molander, G. A., *J. Org. Chem.* **2016,** *81*, 7308; (c) Tellis, J. C.; Kelly, C. B.; Primer,

D. N.; Jouffroy, M.; Patel, N. R.; Molander, G. A., *Acc. Chem. Res.* **2016,** *49*, 1429; (d) Candish, L.; Freitag, M.; Gensch, T.; Glorius, F., *Chem. Sci.* **2017**; (e) Koike, T.; Akita, M., *Acc. Chem. Res.* **2016,** *49*, 1937; (f) Nakajima, K.; Miyake, Y.; Nishibayashi, Y., *Acc. Chem. Res.* **2016,** *49*, 1946; (g) Kelly, C. B.; Patel, N. R.; Primer, D. N.; Jouffroy, M.; Tellis, J. C.; Molander, G. A., *Nat. Protoc.* **2017,** *12*, 472; (h) Romero, N. A.; Nicewicz, D. A., *Chem. Rev.* **2016,** *116*, 10075; (i) Skubi, K. L.; Blum, T. R.; Yoon, T. P., *Chem. Rev.* **2016,** *116*, 10035.

4. (a) Qin, T.; Cornella, J.; Li, C.; Malins, L. R.; Edwards, J. T.; Kawamura, S.; Maxwell, B. D.; Eastgate, M. D.; Baran, P. S., *Science* **2016,** *352*, 801; (b) Cornella, J.; Edwards, J. T.; Qin, T.; Kawamura, S.; Wang, J.; Pan, C. M.; Gianatassio, R.; Schmidt, M.; Eastgate, M. D.; Baran, P. S., *J. Am. Chem. Soc.* **2016,** *138*, 2174; (c) Toriyama, F.; Cornella, J.; Wimmer, L.; Chen, T. G.; Dixon, D. D.; Creech, G.; Baran, P. S., *J. Am. Chem. Soc.* **2016,** *138*, 11132.

5. (a) Doni, E.; Murphy, J. A., *Chem. Commun.* **2014,** *50*, 6073; (b) Murphy, J. A., *J. Org. Chem.* **2014,** *79*, 3731.

6. Farwaha, H. S.; Bucher, G.; Murphy, J. A., *Org. Biomol. Chem.* **2013,** *11*, 8073.

7. Hanson, S. S.; Doni, E.; Traboulsee, K. T.; Coulthard, G.; Murphy, J. A.; Dyker, C. A., *Angew. Chem. Int. Ed.* **2015,** *54*, 11236.

8. Zard, S. Z., *Chem. Soc. Rev.* **2008,** *37*, 1603.

9. (a) Li, J. J.; *in Contemporary Drug Synthesis; Wiley–Interscience*, **2004**, pp. 221. (b) Grant, J. A.; Riethuisen, J.-M.; Moulaert, B.; DeVos,C., *Ann. Allergy. Asthma. Immunol.* **2002**, *88*, 190. (c) Doggrell, S. A.; Liang, L. C.; *N-S Arch. Pharmacol.* **1998**, *357*, 126. (d) Plobeck, N.; Delorme, D.; Wei, Z.-Y.; Yang, H.; Zhou, F.; Schwarz, P.; Gawell, L.; Gagnon, H.; Pelcman, B.; Schmidt, R.; Yue, S. Y.; Walpole, C.; Brown, W.; Zhou, E.; Labarre, M.; Payza, K.; St-Onge, S.; Kamassah, A.; Morin, P.-E.; Projean, D.; Ducharme, J.; Roberts, E., *J. Med. Chem.* **2000**, *43*, 3878.

10. Wendlandt, A. E.; Stahl, S. S., *Org. Lett.* **2012,** *14*, 2850.

11. Fu, G. C., *ACS Cent Sci.* **2017**, *3*, 692.

12. (a) Li, M.; Berritt, S.; Walsh, P. J., *Org. Lett.* **2014,** *16*, 4312; (b) Li, M.; González-Esguevillas, M.; Berritt, S.; Yang, X.; Bellomo, A.; Walsh, P. J., *Angew. Chem. Int. Ed.* **2016,** *128*, 2875; (c) Li, M.; Yucel, B.; Adrio, J.; Bellomo, A.; Walsh, P. J., *Chem. Sci.* **2014,** *5*, 2383; (d) Li, M.; Yucel, B.; Jiménez, J.; Rotella, M.; Fu, Y.; Walsh, P. J., *Adv. Syn. Catal.* **2016,** *358*, 1910.

13. (a) Tang, S.; Park, J. Y.; Yeagley, A. A.; Sabat, M.; Chruma, J. J., *Org. Lett.* **2015,** *17*, 2042; (b) Yeagley, A. A.; Lowder, M. A.; Chruma, J. J., *Org. Lett.* **2009,** *11*, 4022.

14. (a) Kauffmann, T.; Berger, D.; Scheerer, B.; Woltermann, A., *Angew. Chem. Int. Ed.* **1970,** *9*, 961; (b) Pandiancherri, S.; Lupton, D. W., *Tetrahedron Lett.* **2011,** *52*, 671.

15. (a) Taber, D. F.; Sahli, A.; Yu, H.; Meagley, R. P., *J. Org. Chem.* **1995,** *60*, 6571; (b) Taber, D. F.; Sikkander, M. I.; Storck, P. H., *J. Org. Chem.* **2007,** *72*, 4098.

16. (a) Bernasconi, C. F.; Rappoport, Z., *Acc. Chem. Res.* **2009,** *42*, 993; (b) Rappoport, Z., *Acc. Chem. Res.* **1981,** *14*, 7; (c) Rappoport, Z., *Acc. Chem. Res.* **1992,** *25*, 474.

17. (a) Bach, R. D.; Baboul, A. G.; Schlegel, H. B., *J. Am. Chem. Soc.* **2001,** *123*, 5787; (b) Castro, E. A.; Gazitua, M.; Santos, J. G., *J. Org. Chem.* **2005,** *70*, 8088; (c) Castro, E. A.; Ramos, M.; Santos, J. G., *J. Org. Chem.* **2009,** *74*, 6374; (d) Williams, A., *Accounts of Chemical Research* **1989,** *22*, 387.

18. (a) Fernandez, I.; Bickelhaupt, F. M.; Uggerud, E., *J. Org. Chem.* **2013,** *78*, 8574; (b) Guthrie, J. P., *J. Am. Chem. Soc.* **1996,** *118*, 12878.

19. The anionic adduct in the stepwise process (prior to bromide elimination) can be accessed by tuning the electronic properties of the substrate. For instance, the introduction of an electron-

withdrawing group (para-NO_2) at the aryl ring or substitution of Br with weaker leaving group (F) on the styryl substrate led to a discrete anionic tetrahedral intermediate at all levels of theory (See Supporting Information for details). Thus, it appears that the combination of good leaving group (Br^-) and weakly stabilizing β-phenyl group is not sufficient to favor such an intermediate.

20. 3 equiv of $LiN(SiMe_3)_2$ in 0.2 M DME at rt for 1 h yielded 10% E-product, 4% Z-product, and elimination product (alkyne).

21. (a) Baum, A. A.; Karnischky, L. A., *J. Am. Chem. Soc.* **1973,** *95*, 3072; (b) Dannenberg, J. J.; Tanaka, K., *J. Am. Chem. Soc.* **1985,** *107*, 671; (c) Malassa, A.; Agthe, C.; Görls, H.; Friedrich, M.; Westerhausen, M., *J. Organomet. Chem.* **2010,** *695*, 1641.

22. Pallagi, I.; Toró, A.; Horváth, G., *J. Org. Chem.* **1999,** *64*, 6530.

23. Giese, B., *Angew. Chem. Int. Ed.* **1989,** *28*, 969.

24. Studer, A.; Curran, D. P., *Angew. Chem. Int. Ed.* **2011,** *50*, 5018.

25. Danielczyk, W., *J. Neural. Transm. Suppl.* **1995,** *46*, 399.

26. Leophonte, P., *Bull. Acad. Natl. Med.* **2005**, 341.

27. Hughes, P.; Olejnik, O.; Schiffman, R., *Patent Application US 2005031652* **2005**.

28. O'Donnell, M. J.; Polt, R. L., *J. Org. Chem.* **1982,** *47*, 2663.

29. Rossi, R. A.; Pierini, A. B.; Penenory, A. B., *Chem. Rev.* **2003,** *103*, 71.

30. Newcomb, M., Radical Kinetics and Clocks. *In Encyclopedia of Radicals in Chemistry, Biology and Materials*, John Wiley & Sons, Ltd: **2012**.

31. (a) Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.; Kwong, F. Y.; Lei, A., *J. Am. Chem. Soc.* **2010,** *132*, 16737; (b) Liu, C.; Liu, D.; Lei, A., *Acc. Chem. Res.* **2014,** *47*, 3459.

32. (a) Cherney, A. H.; Reisman, S. E. *J. Am. Chem. Soc.* **2014**, *136*, 14365; (b) Naskar, D.; Roy, S. *Tetrahedron* **2000**, *56*, 1369; (c) Naskar, D.; Chowdhury, S.; Roy, S. *Tetrahedron Lett.* **1998**, *39*, 699; (d) Lloyd-Jones, G. C.; Butts, C. P. *Tetrahedron* **1998**, *54*, 901.

33. Ciaccio, J. A.; Aman, C. E. *Synth. Commun.* **2006**, *36*, 1333.

34. Giri, B. P.; Prasad, G.; Mehrotra, K. N., *Can. J. Chem.* **1979**, *57*, 1157.

Chapter 4. Benzylic Chloromethyl-Coupling Polymerization (BCCP) with Sulfenate Anions as Organocatalysts.

4.1. Introduction.

Innovations in polymer chemistry and materials science often have their genesis in the introduction of novel small molecule catalysts.[1] This is particularly true in the developing field of organocatalytic polymerization chemistry.[2] Organocatalytic polymerization reactions have a number of advantages over their metal-catalyzed counterparts, including environmental friendliness, reduced toxicity and cost, ease of catalyst synthesis and storage, and access to alternative reaction pathways. Furthermore, organocatalysts circumvent problems caused by metal residue contamination of polymers, which can severely limit biomedical and electronic applications and complicate polymer purification and processing.[2]

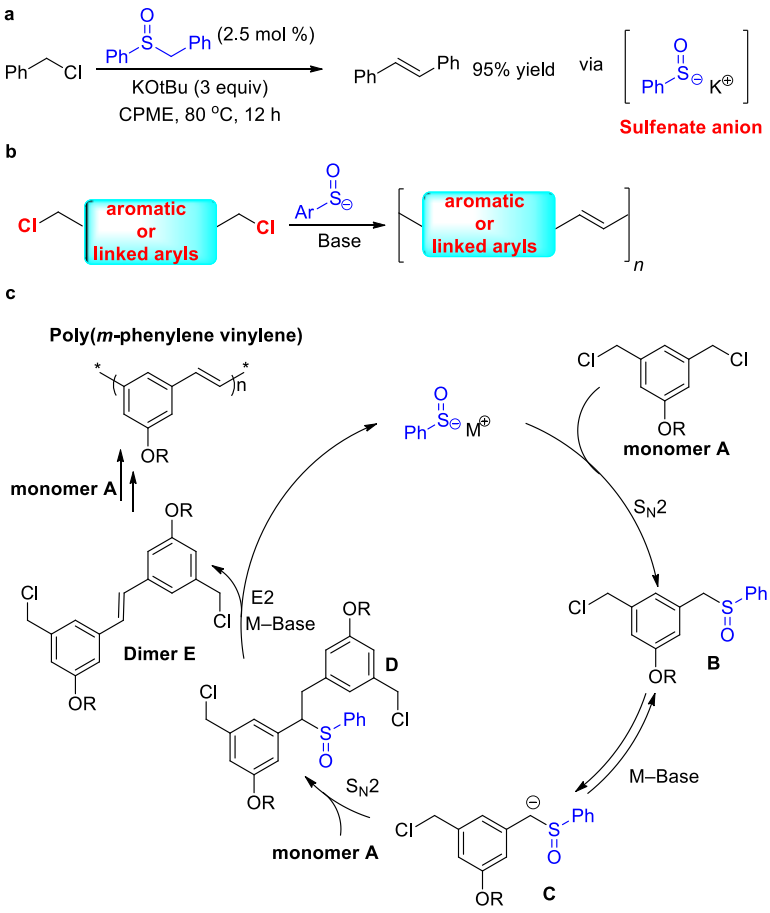
The majority of organocatalytic polymerizations involve ring-opening polymerizations (ROP) using cyclic esters, carbonates, ethers, siloxanes, anhydrides, and phosphoesters.[2b] Herein, we introduce a new class of organo-polymerization processes termed benzylic-chloromethyl-coupling polymerization (BCCP). BCCP represents the first application of sulfenate anion organocatalysts to polymerization processes. The sulfenate anion catalyzed process proceeds via an umpolung mechanism and represents a rare example of an organocatalysts that enchains monomers by C=C bond formation.[3] BCCP has been developed in the context of poly(*m*-phenylene vinylene) synthesis. In this study, P^{m}PV's with degrees of polymerization up to 47, M_n as high as 17,400, and with very high *trans*-selectivity were obtained. BCCP is applicable to non-conjugated polymers, as demonstrated by its application to produce a novel polymer bearing quaternary -$C(CF_3)_2$ spacers between stilbene units in the polymer backbone. Both of these polymers cannot be easily prepared by classical routes.

4.2. Result and Disscussion.

4.2.1. C=C Enchainment Enabled by Sulfenate Anions.

Sulfenate anions ($ArSO^-$) are highly reactive intermediates in biological chemistry and in organic reactions.[4] Our group recently discovered that sulfenate anions can act as organocatalysts, and reported their ability to catalytically couple benzyl halides under basic conditions to yield *trans*-stilbenes (Scheme 4.1, a)[5] and their application to catalytic cross-coupling of benzyl chlorides with benzaldehyde derivatives to produce diarylacetylenes.[6] The efficiency of sulfenate anion catalysts in these reactions, and their high selectivity for formation of *trans*-stilbenes, inspired us to explore their potential in polymerization reactions. We hypothesized that substrates bearing two benzylic chloromethyl groups would be suitable monomers for polymerization. The benzylic chloromethyl substituents could be located on the same aromatic system or on different aromatic rings separated by linking groups, as represented in Scheme 4.1, b.

Based on this hypothesis, we designed the 1,3-bis(chloromethyl)benzene monomer **A** (Scheme 4.1, c). We envisioned that the sulfenate anion would react with monomer **A** via an S_N2 reaction to generate sulfoxide **B**. In the presence of base, sulfoxide **B** is reversibly deprotonated to generate carbanion **C**. Anion **C** is a reactive unpolung nucleophile and undergoes S_N2 with monomer **A** to form the first C–C bond. Base promoted E2 elimination of intermediate **D** provides dimer **E** and liberates the sulfenate anion to further catalyze the polycondensation of **E**. Notably, the product is a poly(phenylene vinylene) (PPV), which is an important class of organic semiconductors with applications in optoelectronics, such as organic light emitting diodes (OLEDs), solar cells, organic lasers, sensors and displays.[7] Although the synthesis of PPV's has been developed, including precursor routes,[8] olefin metathesis polymerizations,[8e] nucleophilic condensations,[9] and cross-coupling polymerizations,[10] to the best of our knowledge, this is the first organocatalytic method for the synthesis of this important class of polymers. Moreover, poly(*m*-phenylene vinylene) (P^mPV)[10d,11] is a challenging target, because *meta*-linkages preclude formation of quinodimethane intermediates, prohibiting classic PPV precursor routes.[12]



Scheme 4.1. Sulfenate Anions Catalyzed Reactions.

4.2.2. Development of a High-Throughput Screening Protocol for Rapid Survey of BCCP.

Current polymerization reaction discovery, optimization and analysis in academic settings have not changed significantly in recent years. Research is largely performed by conducting one to a few lab scale reactions per day (with large amount consumption of monomers and solvents in cumbersome workups). At Upenn and our group, we have successfully applied microscale High-Throughput Screening (HTS) techniques into reaction optimization of many different organic methodology developments. Hence, we firstly developed an easily accessible HTS[13] process to investigate our polycondensation reactions (Figure 4.1). Reactions in this protocol are conducted on very small scales (10 µmol), plates are dosed with organocatalysts in THF, which is removed under vacuum using a GeneVac. Appropriate monomers and reagents to be tested are added,

and the plates are securely sealed with a rubber sheet. To workup the reaction, water is added to quench the reactions and then volatile materials are removed in the GeneVac. Next, $CHCl_3$ is added into each vial to dissolve the polymer followed by cold methanol to precipitate the polymer. The slurry is then transferred onto a filter plate positioned on the vacuum slot of a Freeslate CM2 reaction deck. After the MeOH/$CHCl_3$ solution is filtered, the polymer mainly remains on the filter plate. In the last step, a collection plate is put beneath the filter plate and THF is added into the filter plate well to dissolve the polymer in the well and finally collected in the collection plate under vacuum. The polymer solution is transferred into a LC-block and analyzed by an GPC automatically.

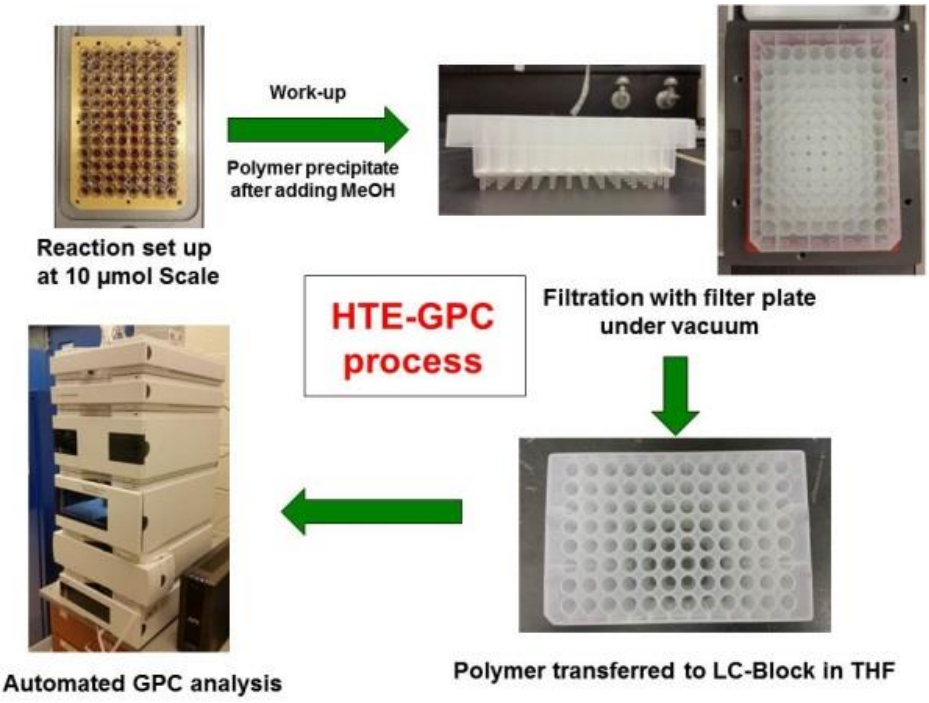


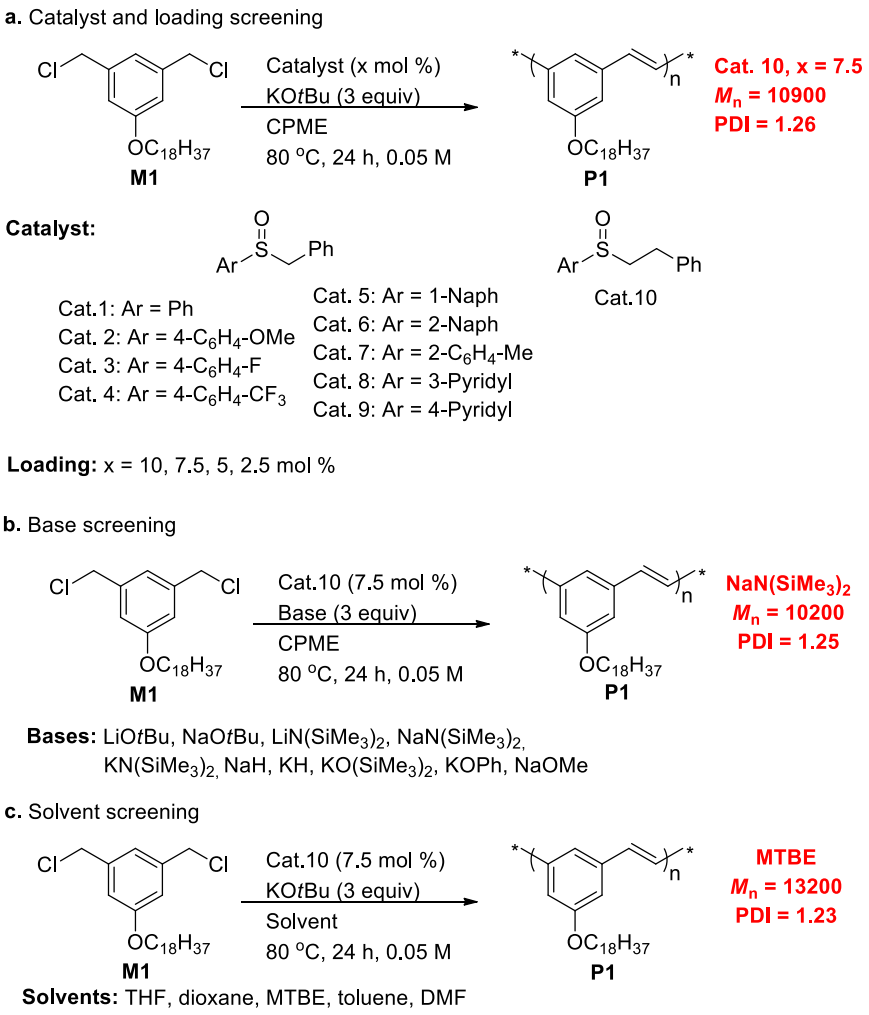
Figure 4.1. A HTE-GPC Process.

4.2.3. Result of BCCP.

Starting from the optimized coupling of benzyl chlorides used in our stilbene synthesis (Scheme 4.1, a),[5] we selected CPME (cyclopentyl methyl ether) as solvent, KO*t*Bu as base at 80 ^{o}C to optimize the polymerization of monomer **M1** (Scheme 4.2). Initial reactions were conducted in 24

well plates on 10 µmol scales by adapting small molecule High-Throughput-Experimentation (HTE)[13b, 13d] techniques to polymerizations. As shown in Scheme 4.2, a, we initially focused on air-stable benzylic sulfoxide catalysts (**1**–**9**) $ArSOCH_2Ph$ with various Ar–S groups and one precatalyst (**10**) with 4 catalyst loadings (10, 7.5, 5.0, and 2.5 mol %). In this screen we observed complete polymerization at 10, 7.5, and 5.0 mol % catalyst loading. There was little impact of the substituents on the aryl ring of the sulfenate anion ($ArSO^-$), with similar M_n and PDI (M_n's ~10,000 were observed at 10 and 7.5 mol % loading and M_n's ~9,000 at 5.0 mol % loading). Lower catalyst loadings of 2.5 mol % led to oligomerization.

The advantage of using catalysts like benzyl phenyl sulfoxides **1**–**9** is that they install a phenyl end group on the polymer. Thus, different benzylic substituents on the sulfoxide precatalyst should enable introduction of a variety of functionalized aryl end groups. At this stage of our investigations, however, we chose to employ precatalyst **10**. Under the basic conditions of the polymerization, **10** rapidly undergoes E2 elimination to form styrene and generate the sulfenate anion.[6] The most promising results with precatalyst **10** were with 7.5 mol % (M_n 10,900, PDI 1.26). At this loading, we conducted a second screen focused on 10 bases [LiO*t*Bu, NaO*t*Bu, $LiN(SiMe_3)_2$, $NaN(SiMe_3)_2$, $KN(SiMe_3)_2$, NaH, KH, $KOSiMe_3$, KOPh, NaOMe] under otherwise identical conditions (Scheme 4.2, b). Analysis of the resulting reactions indicated that polymer was obtained only with $LiN(SiMe_3)_2$, $NaN(SiMe_3)_2$, $KN(SiMe_3)_2$ with M_n's all *lower* than with KO*t*Bu from the first screen. The next step in the optimization was a solvent screen. We examined 5 solvents [THF, dioxane, MTBE (methyl *tert*-butyl ether), toluene, and DMF]. As shown in Scheme 4.2, c, the most promising result was obtained in MTBE (M_n 13,200, PDI 1.23).

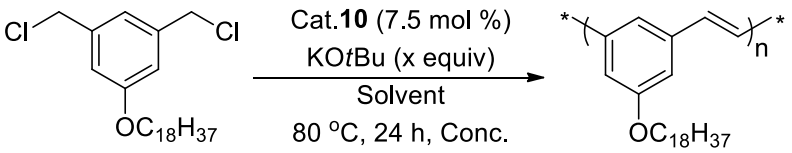


Scheme 4.2. Optimization by HTE Screening.

After narrowing our optimization parameters to precatalyst **10** (7.5 mol %), KO*t*Bu, and CPME and MTBE as two top solvents, we conducted lab-scale (0.1 mmol) polymerizations to validate the microscale results and further optimize the BCCP (Table 4.1). Lab-scale polycondensation of monomer **M1** with both CPME and MTBE at 0.05 M concentration yielded polymer **P1** with M_n 10,400, PDI 1.28 in 91% isolated yield for CPME and polymer with M_n 13,600, PDI 1.21 in 69% isolated yield with MTBE. The results confirmed that M_n and PDI of polymers obtained at 10 µmol scale could be reproduced at 0.1 mmol scale. With CPME as solvent, increasing concentration to

0.1 M and 0.2 M (entries 3–4) led to higher M_n (11,200 at 0.1 M and 12,200 at 0.2 M) with similar PDIs. The yields, however, dropped from 91% (0.05 M) to 86% (0.1 M) and 73% (0.2 M). With MTBE as solvent, increasing concentration led to higher M_n of 15,300 (0.1 M, entry 5) in 72% yield and 17,400 (0.2 M, entry 6) in 71% yield, with PDI of the corresponding polymers of 1.41. Employing 4 and 5 equivalents of KO*t*Bu afforded polymer product with similar M_n, PDI and yield (entries 7–8). The M_n dropped to 10,200 when 6 equiv of base were employed (entry 9). Also We observed complete consumption of monomer after 10 min. A rapid loss of monomer at the beginning of the polymerization indicates that the polycondensation process proceeds by a step-growth mechanism.

Table 4.1. BCCP Optimization.

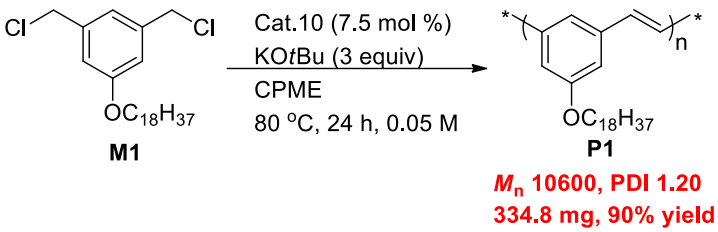


entry	solvent	x=	conc. (M)	yield (%)	M_n	PDI
1	CPME	3	0.05	91	10400	1.28
2	MTBE	3	0.05	69	13600	1.21
3	CPME	3	0.1	86	11200	1.26
4	CPME	3	0.2	73	12200	1.29
5	MTBE	3	0.1	72	15300	1.41
6	MTBE	3	0.2	71	17400	1.42
7	CPME	4	0.05	92	10600	1.23
8	CPME	5	0.05	92	10300	1.22
9	CPME	6	0.05	91	10200	1.22

Reactions were conducted using monomer **1** (0.1 mmol). The products were obtained by reprecipitation from $CHCl_3$-CH_3OH. Polymer data (M_n, PDI) were estimated by GPC calibrated on polystyrene standards with THF as eluent.

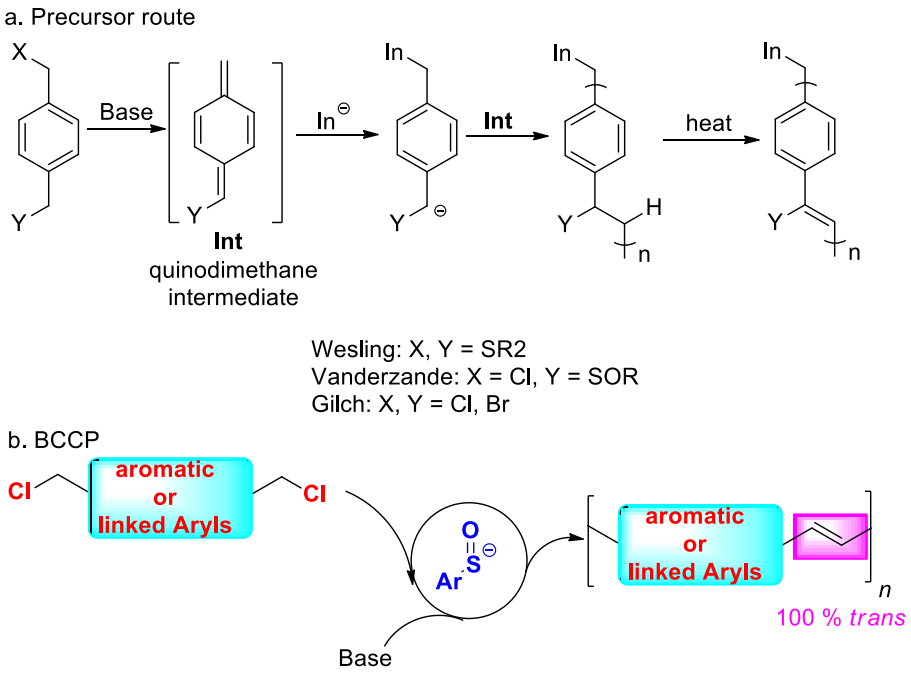
Scalability is an important attribute of polymerization catalysts. We next scaled the polycondensation to 1 mmol using the conditions outlined in Table 1, entry 1. Under the reaction

conditions shown in Scheme 4.3, the polymer product was obtained with Mn 10,600 and PDI 1.20 in 90% yield (334.8 mg).



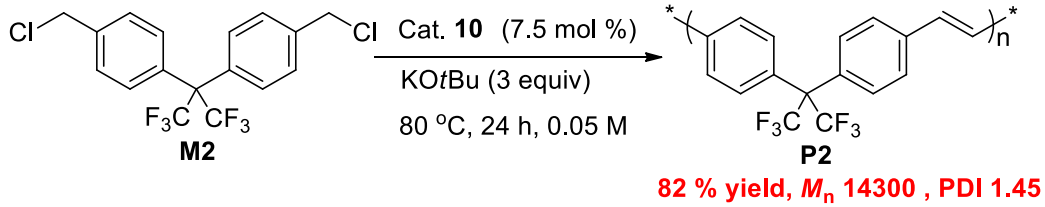
Scheme 4.3. Scale-up of BCCP Reaction.

Traditionally, PPVs were synthesized mostly by a sequential substitution/ elimination protocol (precursor route). In which, the substitution step replies on a quinodimethane intermediate and the elimination step sometimes used sulfoxides as leaving group (Scheme 4.4, a). In a sharp contrast, sulfenate anion catalyzed BCCP possesses totally different mechanism which is the chemoselective construction of *trans* C=C bonds out of each catalytic cycles involving sulfoxide intermediates. This unique C=C enchainment ensure that the polymer has 100% *trans* vinylene motives (No defect). Moreoever, as the vinylene groups are derived from monomers bearing benzylic chloromethyl groups, there is significant potential for monomer variability (Scheme 4.4, b).



Scheme 4.4. Comparison of BCCP with Traditional Precursor Route.

To highlight the mechanistic difference, we designed a monomer with two benzyl chloromethyl substituents linked by a -C(CF_3)$_2$ bridge (Scheme 4.5). It is noteworthy that such polymer could not be prepared by precursor route. Polycondensation using the conditions in Table 4.1 (entry 1) afforded the polymer in 82% yield with *M*n 14,100 and PDI 1.45.



Scheme 4.5 New polymer synthesis.

4.3. Summary and Outlook.

In summary, we introduced a new class of catalytic polymerization processes termed BCCP (benzylic chloromethyl-coupling polymerizations). The organocatalysts for this process, sulfenate

anions, are operationally trivial to generate from bench stable sulfoxide precursors in the presence of base. Sulfenate anion organocatalysts are unique in that they enable generation of C=C double bonds of the type found in PPV's and other stilbene-based polymers. We demonstrated the application of sulfenate anion catalyzed transfer polycondensation methods to novel polymers bearing isolated stilbene motifs. The important conceptual advance of this work is that it suggests that small organic molecules that can activate substrates via nucleophilic attack, acidify neighboring hydrogens leading to umpolung reactivity, and then behave as leaving groups can be considered in polymerization processes to forge C=C enchainments.

Further studies are now underway to broaden the classes of polymers accessible, prepare novel functionalized polymers and study their electrochemical behaviors.

4.4. Experimental Section.

Materials and methods:

All reactions were conducted under a nitrogen atmosphere with oven-dried glassware and standard Schlenk or vacuum line techniques. All solutions were handled under nitrogen and transferred via syringe. Anhydrous solvents were purchased from Sigma-Aldrich and directly used. Unless otherwise stated, reagents were commercially available and used as purchased. Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar or Matrix Scientific, and solvents were purchased from Fisher Scientific and used as purchased.

In monomer synthesis, progress of reactions was monitored by thin-layer chromatography using Whatman Partisil K6F 250 μm precoated 60 Å silica gel plates and visualized by short-wave ultraviolet light as well as by treatment with iodine or ceric ammonium molybdate (CAM) stain. Flash chromatography was performed with silica gel (230–400 mesh, Silicycle).

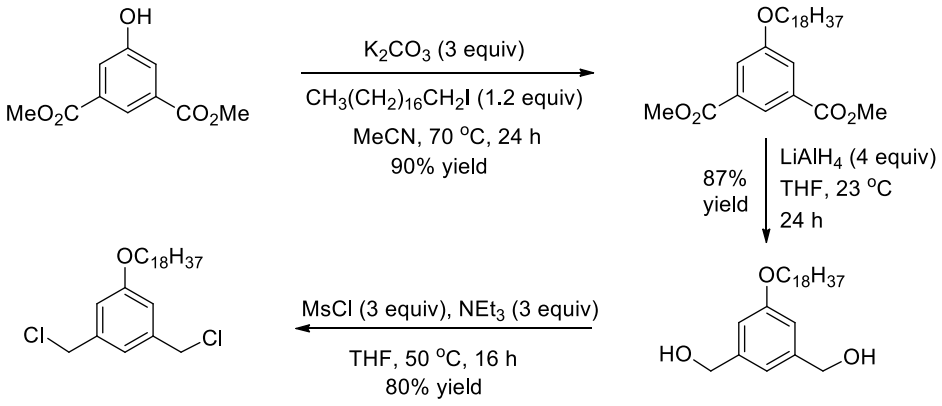
^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were obtained using a Brüker AM-500 Fourier-transform NMR spectrometer at 500 and 125 MHz, respectively. Chemical shifts were reported in units of parts

per million (ppm) downfield from tetramethylsilane (TMS), and all coupling constants were reported in hertz.

The infrared spectra were taken with KBr plates with a Perkin-Elmer Spectrum 100 Series spectrometer.

Gel permeation chromatography (GPC) was performed on an Agilent 1200 system equipped with a infinity micro vacuum degasser, (model G1379B), a Binary Pump SL (model G1312B), a High Performance Autosampler SL (model G1367D), a thermostatted column compartment SL (model G1316B), and a Diode Array Detector SL (model G1315C) using THF as eluent at a flow rate of 1 mL min^{-1} on a Agilent PL1113-6300 resipore (300 × 75 mm) column at 40 ^{o}C. The system was calibrated with Agilent polystyrene medium Easivials (162–500000 g/mol) calibration kit.

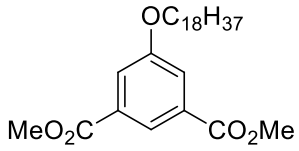
Preparation of monomer M1:



An oven-dried 250 mL Schlenk tube equipped with a stir bar was charged with a mixture of dimethyl 5-hydroxybenzene-1,3-dioate (6.3 g, 30.0 mmol), 1-iodooctadecane (13.7 g, 36.0 mmol) and K_2CO_3 (12.4 g, 90.0 mmol). MeCN (50 mL) was added via syringe through the rubber septum. The reaction mixture was then heated to 70 ^{o}C for 24 h. After cooling to room temperature, the mixture was diluted with water (100 mL) and was extracted with EtOAc (50 mL × 3). The

combined organic layers were washed with saturated brine (200 mL), then dried over anhydrous Na_2SO_4 and concentrated, dried under vacuum to afford dimethyl 5-(octadecyloxy)benzene-1,3-dioate in 12.47 g, 90% yield as a white solid.

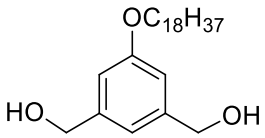
Dimethyl 5-(octadecyloxy)benzene-1,3-dioate:



m.p. 63–65 ^{o}C. R_f = 0.59 (hexanes : ethyl acetate = 9 : 1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (t, *J* = 1.5, 1H), 7.74 (d, *J* = 1.5, 2H), 4.03 (t, *J* = 6.5, 2H), 3.94 (s, 6H), 1.83–1.77 (m, 2H), 1.48–1.44 (m, 2H), 1.26 (m, 28H), 0.89 (t, J = 6.5, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.4, 159.5, 131.9, 122.9, 120.0, 68.8, 52.5, 32.1, 29.91, 29.89, 29.87, 29.80, 29.77, 29.57, 29.56, 29.3, 26.2, 22.9, 14.3 ppm. IR (thin film): 3436, 2914, 2840, 1730, 1471, 1346, 1253, 754 cm^{-1}; HRMS calc'd for $C_{28}H_{46}O_5^+$ 462.3345, observed 462.3322 $[M\text{-}C_2H_4]^+$.

An oven-dried 100 mL Schlenk tube equipped with a stir bar was charged with dimethyl 5-(octadecyloxy)benzene-1,3-dioate (2.4 g, 5.2 mmol). The Schlenk tube was sealed with a rubber septum, connected to a Schlenk line, and evacuated and refilled with nitrogen (repeated three times). Anhydrous THF (15 mL) was added under nitrogen via syringe through the rubber septum and the solution was stirred at 0 ^{o}C for 30 min. Next, 10.4 mL of $LiAlH_4$ (20.8 mmol, 2.0 M solution in THF) was added dropwise into the Schlenk tube via syringe. The mixture was warmed to room temperature and stirred for 24 h under nitrogen. After cooling to 0 ^{o}C for 30 mins, an aqueous solution of HCl (22 mL, 1 M) was added slowly. The mixture was diluted with ethyl acetate (20 mL), the layers were separated, the organic layer was washed with saturated brine (20 mL) and the mixture was concentrated, dried under vacuum to afford 1,3-bis(hydroxymethyl)-5-(octadecyloxy)benzene in 1.84 g, 87% yield as a white solid.

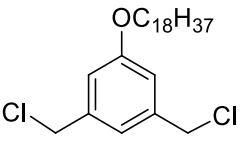
1,3-Bis(hydroxymethyl)-5-(octadecyloxy)benzene:



m.p. 81–83 °C. R_f = 0.27 (hexanes : ethyl acetate = 1 : 1). ^{1}H NMR (500 MHz, THF-d_8): δ 6.84–6.83 (m, 1H), 6.76–6.75 (m, 2H), 4.50 (d, *J* = 4.5, 4H), 4.06–4.04 (m, 2H), 3.94 (t, *J* = 6.5, 2H), 1.77–1.73 (m, 2H), 1.50–1.44 (m, 2H), 1.29 (m, 28H), 0.89 (t, J = 6.5, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, THF-d_8): δ 160.6, 145.2, 117.3, 111.7, 68.5, 65.1, 33.0, 30.8, 30.80, 30.79, 30.77, 30.6, 30.54, 30.48, 27.6, 25.9, 23.7, 14.6 ppm. IR (thin film): 2915, 2850, 913, 747 cm^{-1}; HRMS calc'd for $C_{26}H_{46}O_3Na^+$ 429.3345, observed 429.3346 $[M+Na]^+$.

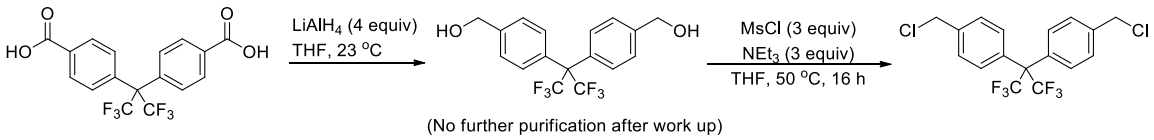
An oven-dried 250 mL round bottom flask equipped with a stir bar was charged with 1,3-bis(hydroxymethyl)-5-(octadecyloxy)benzene (1.4 g, 3.45 mmol). Chloroform (50 mL) was added via syringe and the solution was cooled to 0 °C. Methane sulfonyl chloride (0.8 mL, 10.35 mmol) and triethylamine (1.5 mL, 10.35 mmol) was added dropwise into the round bottom flask via syringe at 0 °C. The, reaction vessel was sealed with a septum, put in an oil bath, stirred at 50 °C for 16 h and cooled to room temperature. After quenching the reaction mixture with water (20 mL) the layers were separated. The reaction mixture was then extracted with chloroform (10 mL × 3). The combined organic phases was, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel, hexanes to hexanes : ethyl acetate = 20 : 1) to afford 1.22 g of the momomer **1** (80% yield) as a white solid.

1,3-bis(chloromethyl)-5-(octadecyloxy)benzene:



m.p. 59–60 °C. R_f = 0.75 (hexanes : ethyl acetate = 9 : 1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.97 (s, 1H), 6.87 (s, 2H) , 4.53 (s, 4H), 3.96 (t, *J* = 6.0, 2H), 1.77 (m, 2H), 1.46 (m, 2H), 1.27 (m, 28H), 0.88 (m, 3H) ppm; ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 159.9, 139.5, 120.8, 114.9, 68.4, 46.1, 32.2, 29.9, 29.89, 29.82, 29.79, 29.6, 29.4, 26.2, 22.9, 14.3 ppm. IR (thin film): 2926, 2854, 2359, 2340, 969, 738 cm^{-1}; HRMS calc'd for $C_{26}H_{44}OCl_2^+$ 442.2769, observed 442.2782 $[M+H]^+$.

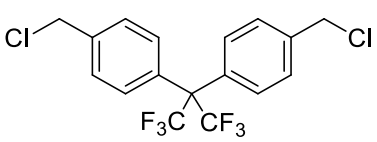
Preparation of monomer M2:



An oven-dried 100 mL Schlenk tube equipped with a stir bar was charged with dimethyl 4,4'-(perfluoropropane-2,2-diyl) dibenzoic acid (2.0 g, 5.0 mmol). The Schlenk tube was sealed with a rubber septum, connected to a Schlenk line, and evacuated and refilled with nitrogen (repeated three times). Anhydrous THF (15 mL) was added under nitrogen via syringe through the rubber septum and the solution was stirred at 0 ^{o}C for 30 min. Next, 10.0 mL of $LiAlH_4$ (20.0 mmol, 2.0 M solution in THF) was added dropwise into the Schlenk tube via syringe. The mixture was warmed to room temperature and stirred for 24 h under nitrogen. After cooling to 0 ^{o}C, an aqueous solution of HCl (22 mL, 1 M) was added slowly. The mixture was diluted with ethyl acetate (20 mL), the layers were separated, the organic layer was washed with saturated brine (20 mL), dried over anhydrous Na_2SO_4 and mixture was concentrated in a 250 mL round bottom flask. The mixture was next dried under vacuum for 12 h and used as obtained in the next step.

A stir bar was added to the round bottom flask. chloroform (50 mL) was added via syringe and the solution was cooled to 0 ^{o}C. Methane sulfonyl chloride (1.2 mL, 15.1 mmol) and triethylamine (2.2 mL, 15.1 mmol) was added dropwise into the round bottom flask via syringe at 0 ^{o}C. The resulting mixture was sealed, then put in an oil bath and stirred at 50 ^{o}C for 16 h and then cooled to room temperature. After quenching the reaction with water (20 mL), the layers were separated. The reaction mixture was extracted with chloroform (10 mL × 3). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel, hexanes) to afford 1.30 g of the momomer **2** (65% yield over 2 steps).

4,4'-(perfluoropropane-2,2-diyl)bis((chloromethyl)benzene):



m.p. 83-85 °C. R_f = 0.18 (hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42–7.37 (m, 8H), 4.59 (s, 4H) ppm; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 138.7, 133.6, 130.8, 128.6, 124.2 (d, $J_{C\text{-}F}$ = 284), 64.5, 45.4 ppm. IR (thin film): 2354, 1770, 1517, 1447, 1250, 1174, 869, 772 cm^{-1}; HRMS calc'd for $C_{17}H_{12}F_6Cl_2^+$ 400.0220, observed 400.0211 $[M+H]^+$.

High-Throughput Experimentation screenings for polymerization:

Parallel High-throughput Experimentation Screening was accomplished in an MBraun glovebox operating with a constant N_2-purge (oxygen typically <5 ppm). The experimental design was accomplished using Accelrys Library Studio. Screening reactions were carried out in 1 mL vials (30 mm height×8 mm diameter) in 24-well plate aluminum reactor block. Liquid chemicals were dosed using multi-channel or single-channel pipettors. Solid chemicals were dosed manually as solutions or slurries in appropriate solvents. Undesired additional solvent was removed using a GeneVac system located inside the glovebox. The reactions were heated and stirred on a heating block with a tumble-stirrer (V&P Scientific) using 1.98 mm diameter×4.80 mm length parylene stir bars. The tumble stirring mechanism helped to insure uniform stirring throughout the 96-well plate. The reactions were sealed in the 96-well plate during reaction. Below each reactor vial in the aluminum 96-well plate was a 0.062 mm thick silicon-rubber gasket. Directly above the glass vial reactor tops was a Teflon perfluoroalkoxy copolymer resin sealing gasket and above that, two more 0.062 mm thick silicon-rubber gaskets. The entire assembly was compressed between an aluminum top and the reactor base with 9 evenly-placed screws.

General procedure

Set up:

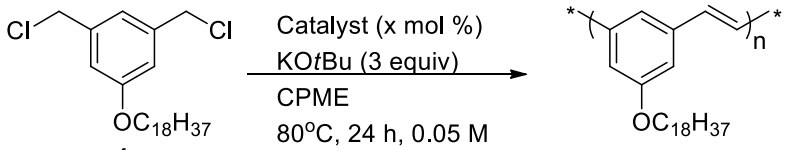
Experiments were set up inside a glovebox under a nitrogen atmosphere. A 96-well aluminum block containing 1 mL glass vials was dosed with sulfoxide catalyst in THF. The solvent was

removed to dryness using a GeneVac. Monomer **M1** (10 µmol) and the corresponding base (30 µmol) were seperately dosed into each reaction vial with the corresponding solvent (100 µL each, total volumn 200 µL , 0.05 M). The plate was then sealed with screwdriver and stirred for 24 h at 80 ^{o}C.

work up:

Upon cooling to room temperature, the plate was opened in the glovebox, water (10 µL) was added into each vial with a pipetman to quench the reactions and then solvent was removed to dryness using a GeneVac. Next, $CHCl_3$ (200 µL) was added into each vial and the slurry solution was allowed to stir for 10 min. Cold methanol (600 µL) was added into each vial to precipitate the polymer and the slurry solution was allowed to stir for 10 min. The slurry is then transferred with a multichannel pipetman onto a filter plate positioned on the vacuum slot of a Freeslate CM2 reaction deck. After the MeOH/$CHCl_3$ solution was filtered, the polymer remains on the filter plate. Finally, a 96-well collection plate was put beneath the filter plate and 800 µL THF was added into the filter plate well to dissolve the polymer. The polymer solution was transferred into a 96-well LC-block and analyzed by GPC.

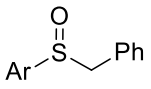
Screening of sulfoxide catalysts and solvents.

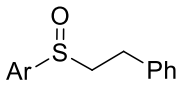


1

Variants:

Catalyst:





Cat.10

Cat.1: Ar = Ph
Cat.2: Ar = 4-C_6H_4-OMe
Cat.3: Ar = 4-C_6H_4-F
Cat.4: Ar = 4-C_6H_4-CF_3
Cat.5: Ar = 1-Naph
Cat.6: Ar = 2-Naph
Cat.7: Ar = 2-C_6H_4-Me
Cat.8: Ar = 3-Pyridyl
Cat.9: Ar = 4-Pyridyl

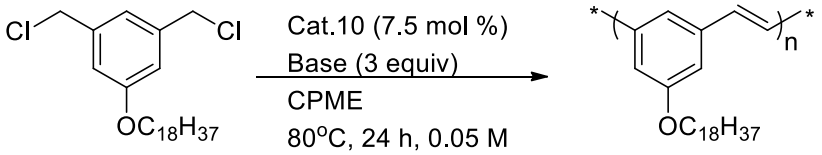
Loading: x = 10, 7.5, 5, 2.5

Entry	Loading (mol %)	M_n	PDI
Cat.1	10	11685	1.22
Cat.2	10	10755	1.25
Cat.3	10	10928	1.24
Cat.4	10	10555	1.25
Cat.5	10	10470	1.24
Cat.6	10	11260	1.26
Cat.7	10	10844	1.25
Cat.8	10	11447	1.28
Cat.9	10	10061	1.26
Cat.10	10	11761	1.23
Cat.1	7.5	11502	1.27
Cat.2	7.5	11253	1.24
Cat.3	7.5	11420	1.28
Cat.4	7.5	10582	1.25
Cat.5	7.5	10970	1.23
Cat.6	7.5	11169	1.28
Cat.7	7.5	11262	1.25
Cat.8	7.5	11272	1.26
Cat.9	7.5	8401	1.33
Cat.10	7.5	10854	1.26
Cat.1	5	10160	1.24
Cat.2	5	9960	1.25
Cat.3	5	9834	1.25
Cat.4	5	9504	1.26
Cat.5	5	7739	1.38

Cat.6	5	10253	1.25
Cat.7	5	9325	1.25
Cat.8	5	8293	1.36
Cat.9	5	5749	1.37
Cat.10	5	9638	1.27

Note: Catalyst loading to 2.5 mol % led to incomplete polymerization and data were not further processed.

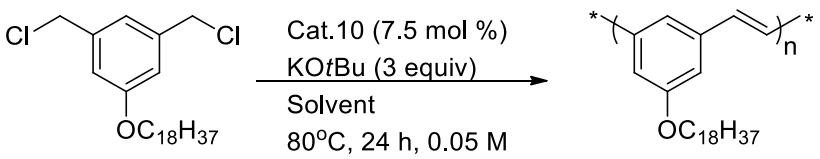
Screening of Base.



Variants: 10 bases

Base	Mn	PDI
LiO*t*Bu	No Polymerization	
NaOtBu	No Polymerization	
$LiN(SiMe_3)_2$	5500	1.35
$NaN(SiMe_3)_2$	10173	1.25
$KN(SiMe_3)_2$	8278	1.37
NaH	No Polymerization	
KH	No Polymerization	
$KOSiMe_3$	No Polymerization	
KOPh	No Polymerization	
NaOMe	No Polymerization	

Screening of solvent.



Variants: 5 solvent

Solvent	Mn	PDI
THF	10216	1.20
Dioxane	10730	1.23
MTBE	13164	1.23
Tol	9829	1.24
DMF	6271	1.55

General Procedure for the lab-scale polymerization

An oven-dried 8 mL microwave vial equipped with a stir bar was charged with monomer **1** (44.4 mg, 0.10 mmol) under a nitrogen atmosphere in a glove box. A solution of precatalyst **10** (1.73 mg, 0.075 mmol) in 1.0 mL anhydrous CPME was added by syringe. Next, a solution of KO*t*Bu (33.6 mg, 0.30 mmol) in 1.0 mL anhydrous CPME was added by syringe. The reaction was stirred for 24 h at 80 ºC, quenched with 2 drops of H_2O via syringe, cooled to room temperature and opened to air. After the volatile materials were removed with rotary evaporator, $CHCl_3$ (2 mL) was added into each vial and the slurry solution was allowed to stir for 10 min. Cold methanol (6 mL) was then added into each vial to precipitate the polymer and the slurry solution with polymer suspension was allowed to stir for 10 min. The mixture was then transferred with a pipette onto a Whatman autovial syringeless filter (5 mL, 0.45 µm PTFE membrane). After the MeOH/$CHCl_3$ solution was filtered, polymer that remained in the filter was washed sequentially with 5 mL MeOH and 5 mL pentane. Finally, the polymer remaining in the filter was transferred into a 20 mL vial with spatula and dried in under vacuum to yield a pale yellow solid in 33.8 mg, 91% yield.

GPC distribution plots of polymer product P1 in Table 4.1

Table 4.1, entry 1:

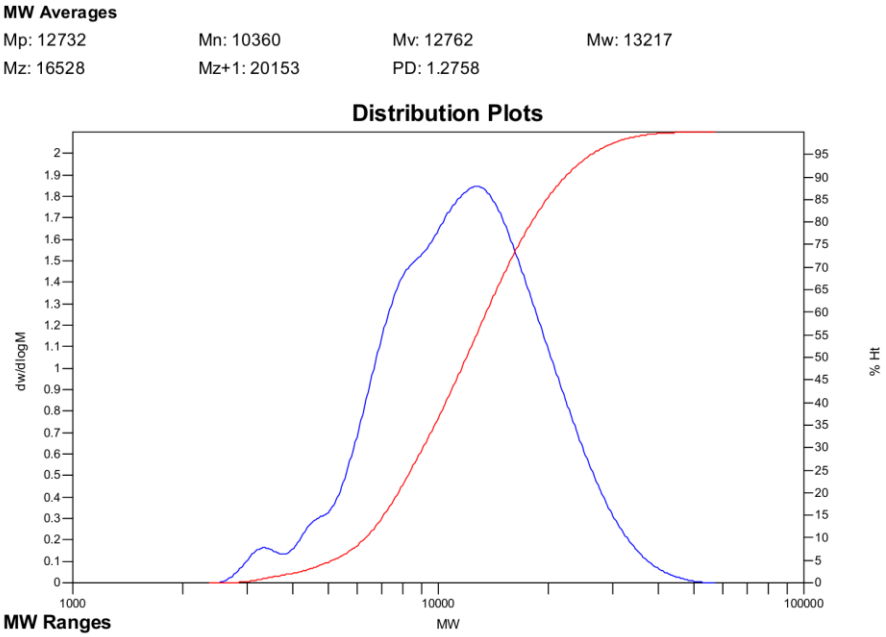


Table 4.1, entry 2:

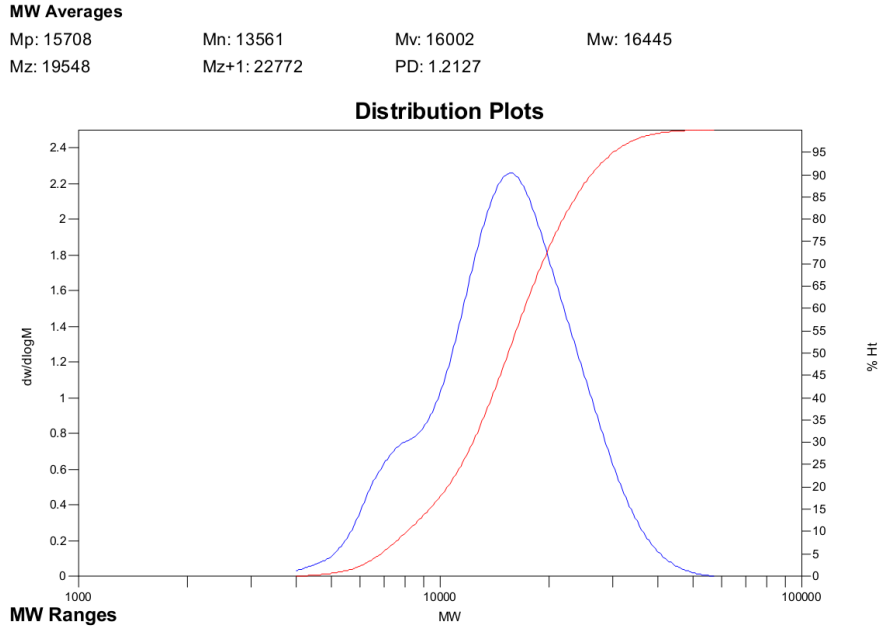


Table 4.1, entry 3:

MW Averages

Mp: 13167	Mn: 11152	Mv: 13628	Mw: 14081
Mz: 17317	Mz+1: 20774	PD: 1.2626	

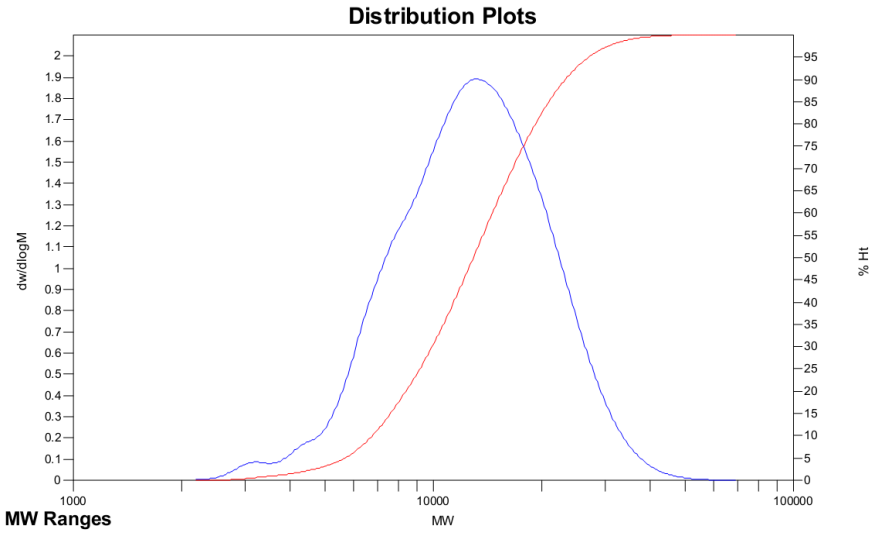


Table 4.1, entry 4:

MW Averages

Mp: 14693	Mn: 12173	Mv: 15145	Mw: 15691
Mz: 19615	Mz+1: 23887	PD: 1.2890	

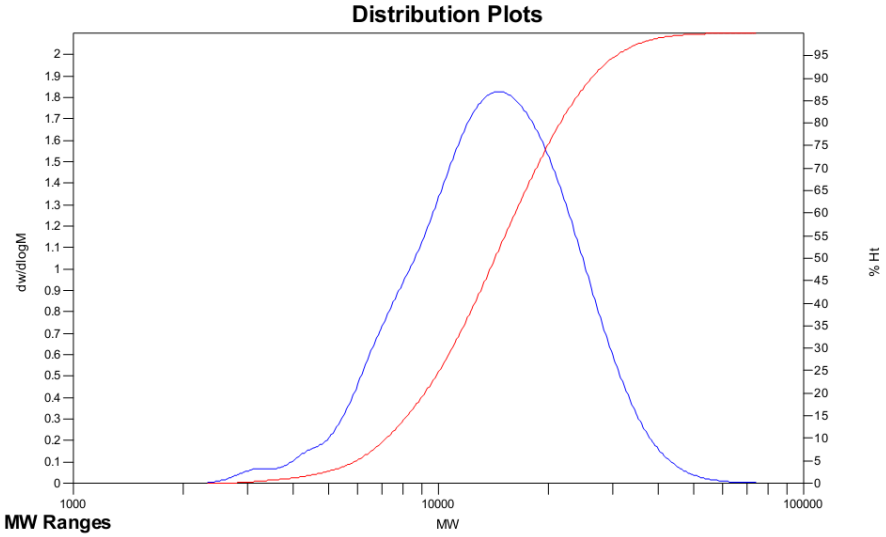


Table 4.1, entry 5:

MW Averages

Mp: 18638	Mn: 15227	Mv: 20484	Mw: 21500
Mz: 29255	Mz+1: 38526	PD: 1.4120	

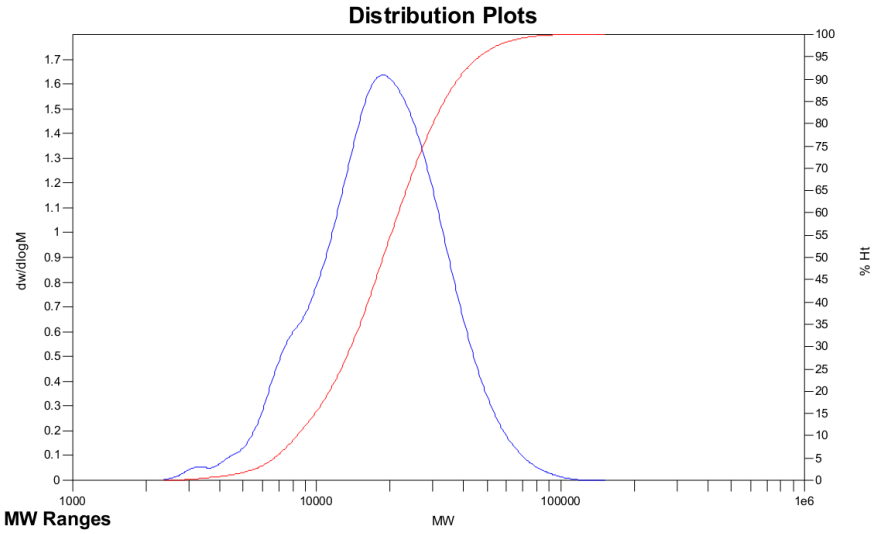


Table 4.1, entry 6:

MW Averages

Mp: 20342	Mn: 17382	Mv: 23520	Mw: 24780
Mz: 35047	Mz+1: 49323	PD: 1.4256	

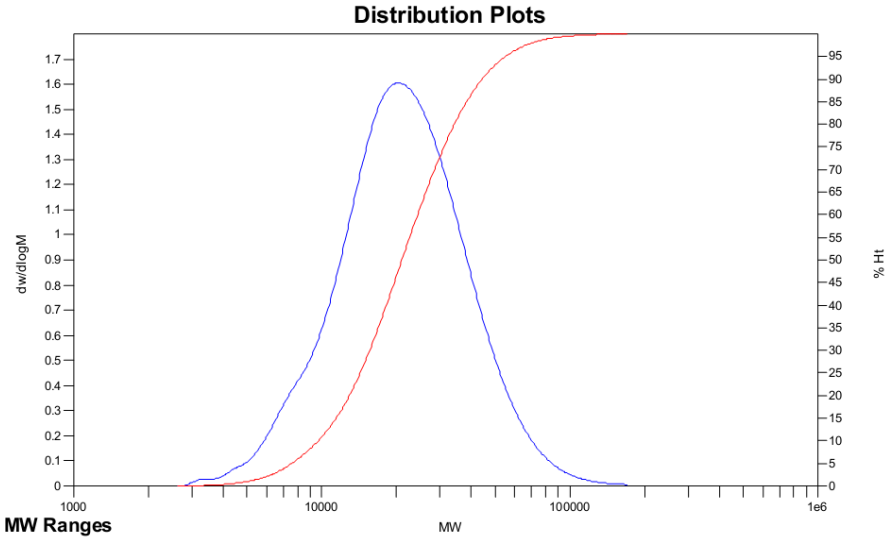


Table 4.1, entry 7:

MW Averages

Mp: 12256	Mn: 10564	Mv: 12501	Mw: 12876
Mz: 15694	Mz+1: 19234	PD: 1.2189	

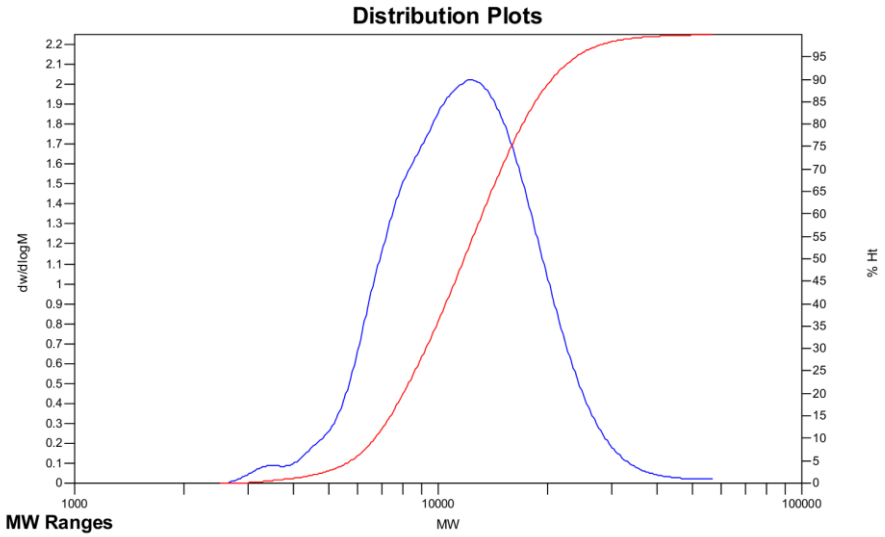


Table 4.1, entry 8:

MW Averages

Mp: 12593	Mn: 10344	Mv: 12240	Mw: 12585
Mz: 15008	Mz+1: 17524	PD: 1.2166	

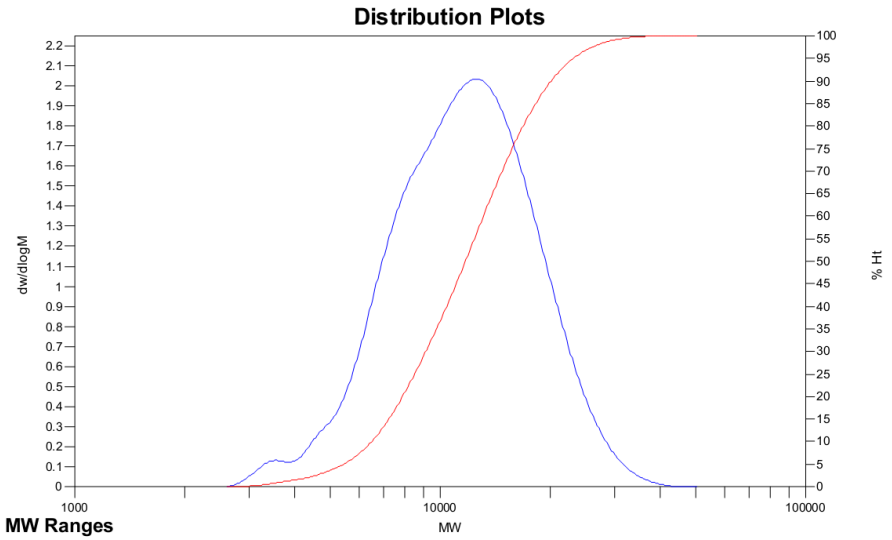
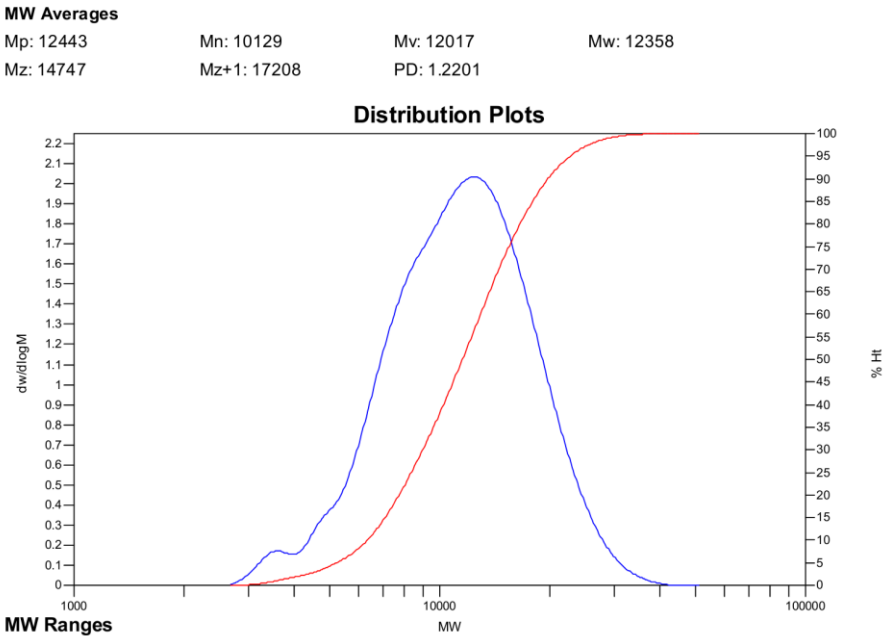
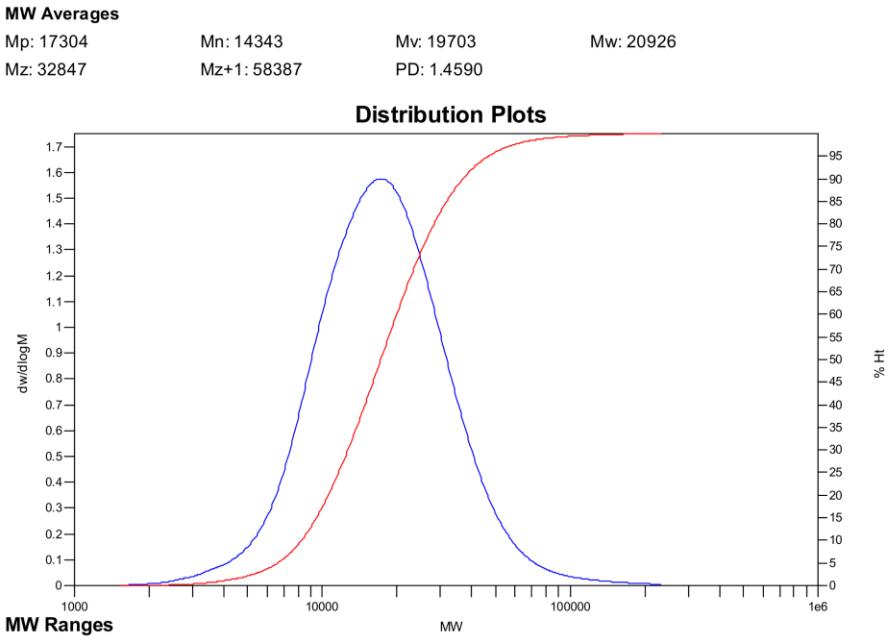


Table 1, entry 9:

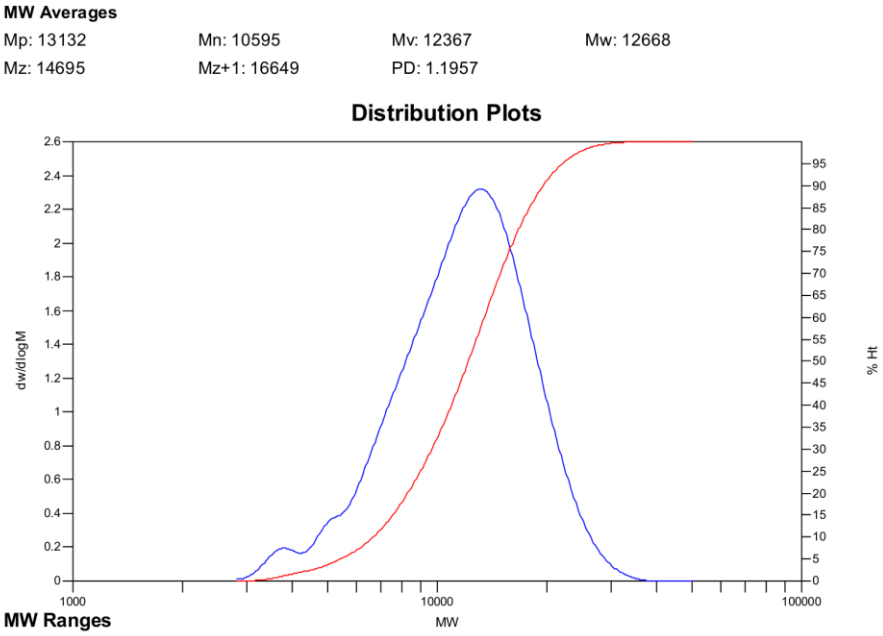


GPC distribution plots of polymer P2



Procedure for the scale-up (1 mmol) polymerization

An oven-dried 100 mL Schlenk tube equipped with a stir bar was charged with monomer **M1** (444.0 mg, 1.0 mmol) and precatalyst **10** (17.3 mg, 0.75 mmol). The Schlenk tube was sealed with a rubber septum and was connected to a Schlenk line, evacuated, and refilled with nitrogen (repeated three times). Next, a solution of KO*t*Bu (33.6 mg, 0.30 mmol) in 20 mL anhydrous CPME was added by syringe. The reaction was stirred for 24 h at 80 ºC, cooled to room temperature, opened to air and quenched with 1 mL of H_2O. The reaction mixture was firstly transferred to a 250 mL round bottom flask and the volatile materials were removed with rotary evaporator. Next, $CHCl_3$ (20 mL) was added into flask and the slurry solution was allowed to stir for 10 min. Cold methanol (60 mL) was added into the flask to precipitate the polymer and the slurry solution with polymer suspension was allowed to stir for 10 min. The mixture was then filtered on a glass fritted filter funnel (75 mL), After the MeOH/$CHCl_3$ solution was filtered, solid was washed by pentane (20 mL *3), collected and dried in a vacuum as pale yellow solid to provide 334.8 mg, 90% yield of the polymer **P1**.



4.5. Acknowledgement

I would like to thank Carol Wang and Bing Zheng for their collaboration and contribution. Bing zheng synthesized catalyst 1-9 and Carol Wang synthesized catalyst 10 of Scheme 4.2.

4.6. References.

1. (a) Ober, C. K.; Cheng, S. Z. D.; Hammond, P. T.; Muthukumar, M.; Reichmanis, E.; Wooley, K. L.; Lodge, T. P., *Macromolecules* **2009,** *42*, 465; (b) Hawker, C. J.; Wooley, K. L., *Science* **2005,** *309*, 1200.

2. (a) Kiesewetter, M. K.; Shin, E. J.; Hedrick, J. L.; Waymouth, R. M., *Macromolecules* **2010,** *43*, 2093; (b) Ottou, W. N.; Sardon, H.; Mecerreyes, D.; Vignolle, J.; Taton, D., *Prog. Polym. Sci.* **2016,** *56*, 64.

3. (a) Hong, M.; Chen, E. Y., *Angew. Chem. Int. Ed.* **2014,** *53*, 11900; (b) Hong, M.; Tang, X.; Falivene, L.; Caporaso, L.; Cavallo, L.; Chen, E. Y., *J. Am. Chem. Soc.* **2016,** *138*, 2021.

4. (a) Maitro, G.; Vogel, S.; Sadaoui, M.; Prestat, G.; Madec, D.; Poli, G., *Org. Lett.* **2007,** *9*, 5493; (b) O'Donnell, J. S.; Schwan, A. L., *J. Sulfur Chem.* **2004,** *25*, 183; (c) Schwan, A. L.; Söderman, S. C., *Phosphorus, Sulfur Silicon Relat. Elem.* **2013,** *188*, 275; (d) Soderman, S. C.; Schwan, A. L., *J. Org. Chem.* **2013,** *78*, 1638.

5. Zhang, M.; Jia, T.; Yin, H.; Carroll, P. J.; Schelter, E. J.; Walsh, P. J., *Angew. Chem. Int. Ed.* **2014,** *53*, 10755.

6. Zhang, M.; Jia, T.; Wang, C. Y.; Walsh, P. J., *J. Am. Chem. Soc.* **2015,** *137*, 10346.

7. (a) Weder, C.; Montali, A.; Sarwa, C.; Bastiaansen, C.; Smith, P., *ACS Symp. Ser.* **1999,** *735*, 258; (b) Cheng, Y. J.; Yang, S. H.; Hsu, C. S., *Chem. Rev.* **2009,** *109*, 5868; (c) Gunes, S.; Neugebauer, H.; Sariciftci, N. S., *Chem. Rev.* **2007,** *107*, 1324; (d) Thompson, B. C.; Frechet, J. M., *Angew. Chem. Int. Ed.* **2008,** *47*, 58; (e) Spanggaard, H.; Krebs, F. C., *Sol. Energ. Mat. Sol.*

Cells **2004,** *83*, 125; (f) Grimsdale, A. C.; Chan, K. L.; Martin, R. E.; Jokisz, P. G.; Holmes, A. B., *Chem. Rev.* **2009,** *109*, 897.

8. (a) Junkers, T.; Vandenbergh, J.; Adriaensens, P.; Lutsen, L.; Vanderzande, D., *Polym. Chem.* **2012,** *3*, 275; (b) Becker, H.; Spreitzer, H.; Ibrom, K.; Kreuder, W., *Macromolecules* **1999,** *32*, 4925; (c) Gilch, H. G.; Wheelwright, W. L., *Journal of Polymer Science Part A-1: Polymer Chemistry* **1966,** *4*, 1337; (d) Ravnsbæk, J. B.; Swager, T. M., *ACS. Macro. Lett.* **2014,** *3*, 305; (e) Zaquen, N.; Lutsen, L.; Vanderzande, D.; Junkers, T., *Polym. Chem.* **2016,** *7*, 1355.

9. (a) McCullough, R. D.; Lowe, R. D., *Journal of the Chemical Society, Chemical Communications* **1992**, 70; (b) Lenz, R. W.; Handlovits, C. E., *J. Org. Chem.* **1960,** *25*, 813; (c) Suzuki, Y.; Hashimoto, K.; Tajima, K., *Macromolecules* **2007,** *40*, 6521; (d) Schenk, R.; Gregorius, H.; Meerholz, K.; Heinze, J.; Muellen, K., *J. Am. Chem. Soc.* **1991,** *113*, 2634; (e) Yang, Z.; Geise, H. J., *Synt. Met.* **1992,** *47*, 105; (f) Conticello, V. P.; Gin, D. L.; Grubbs, R. H., *J. Am. Chem. Soc.* **1992,** *114*, 9708.

10. (a) Zou, Y.; Hou, J.; Yang, C.; Li, Y., *Macromolecules* **2006,** *39*, 8889; (b) Schneider, J. A.; Dadvand, A.; Wen, W.; Perepichka, D. F., *Macromolecules* **2013,** *46*, 9231; (c) Bao, Z.; Chan, W. K.; Yu, L., *J. Am. Chem. Soc.* **1995,** *117*, 12426; (d) Wakioka, M.; Ikegami, M.; Ozawa, F., *Macromolecules* **2010,** *43*, 6980; (e) Katayama, H.; Nagao, M.; Nishimura, T.; Matsui, Y.; Fukuse, Y.; Wakioka, M.; Ozawa, F., *Macromolecules* **2006,** *39*, 2039; (f) Katayama, H.; Nagao, M.; Nishimura, T.; Matsui, Y.; Umeda, K.; Akamatsu, K.; Tsuruoka, T.; Nawafune, H.; Ozawa, F., *J. Am. Chem. Soc.* **2005,** *127*, 4350; (g) Yu, L.; Lee, Y.; Liang, Y., *Synlett* **2006,** *2006*, 2879.

11. (a) Cyriac, A.; Amrutha, S. R.; Jayakannan, M., *J. Polym. Sci. A Polym. Chem.* **2008,** *46*, 3241; (b) Drury, A.; Maier, S.; Davey, A. P.; Dalton, A. B.; Coleman, J. N.; Byrne, H. J.; Blau, W. J., *Synthetic Metals* **2001,** *119*, 151; (c) Liao, L.; Pang, Y.; Ding, L.; Karasz, F. E.,

Macromolecules **2001,** *34*, 7300; (d) Liao, L.; Pang, Y.; Ding, L.; Karasz, F. E., *Macromolecules* **2001,** *34*, 6756.

12. Yan, M.; Rothberg, L. J.; Kwock, E. W.; Miller, T. M., *Phys. Rev. Lett.* **1995,** *75*, 1992.

13. (a) Brocchini, S.; James, K.; Tangpasuthadol, V.; Kohn, J., *J. Am. Chem. Soc.* **1997,** *119*, 4553; (b) Zhang, H.; Marin, V.; Fijten, M. W. M.; Schubert, U. S., *J. Polym. Sci. A Polym. Chem.* **2004,** *42*, 1876; (c) Majoros, L. I.; Dekeyser, B.; Hoogenboom, R.; Fijten, M. W. M.; Geeraert, J.; Haucourt, N.; Schubert, U. S., *J. Polym. Sci. A Polym. Chem.* **2010,** *48*, 570; (d) Potyrailo, R.; Rajan, K.; Stoewe, K.; Takeuchi, I.; Chisholm, B.; Lam, H., *ACS. Comb. Sci.* **2011,** *13*, 579.

Appendix A1. NMR Spectra Relevant to Chapter 1.

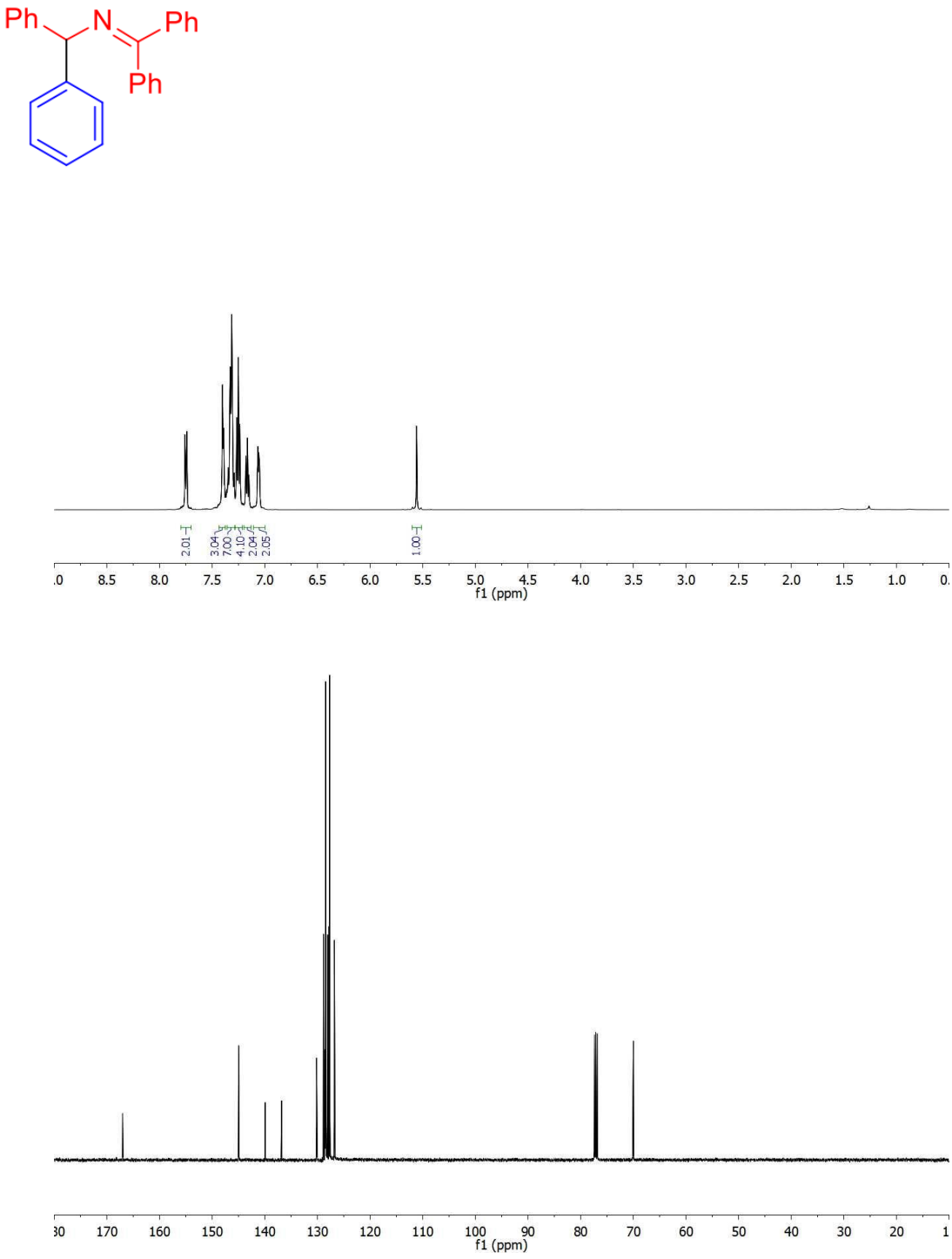


Figure A1.1 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3ab in $CDCl_3$

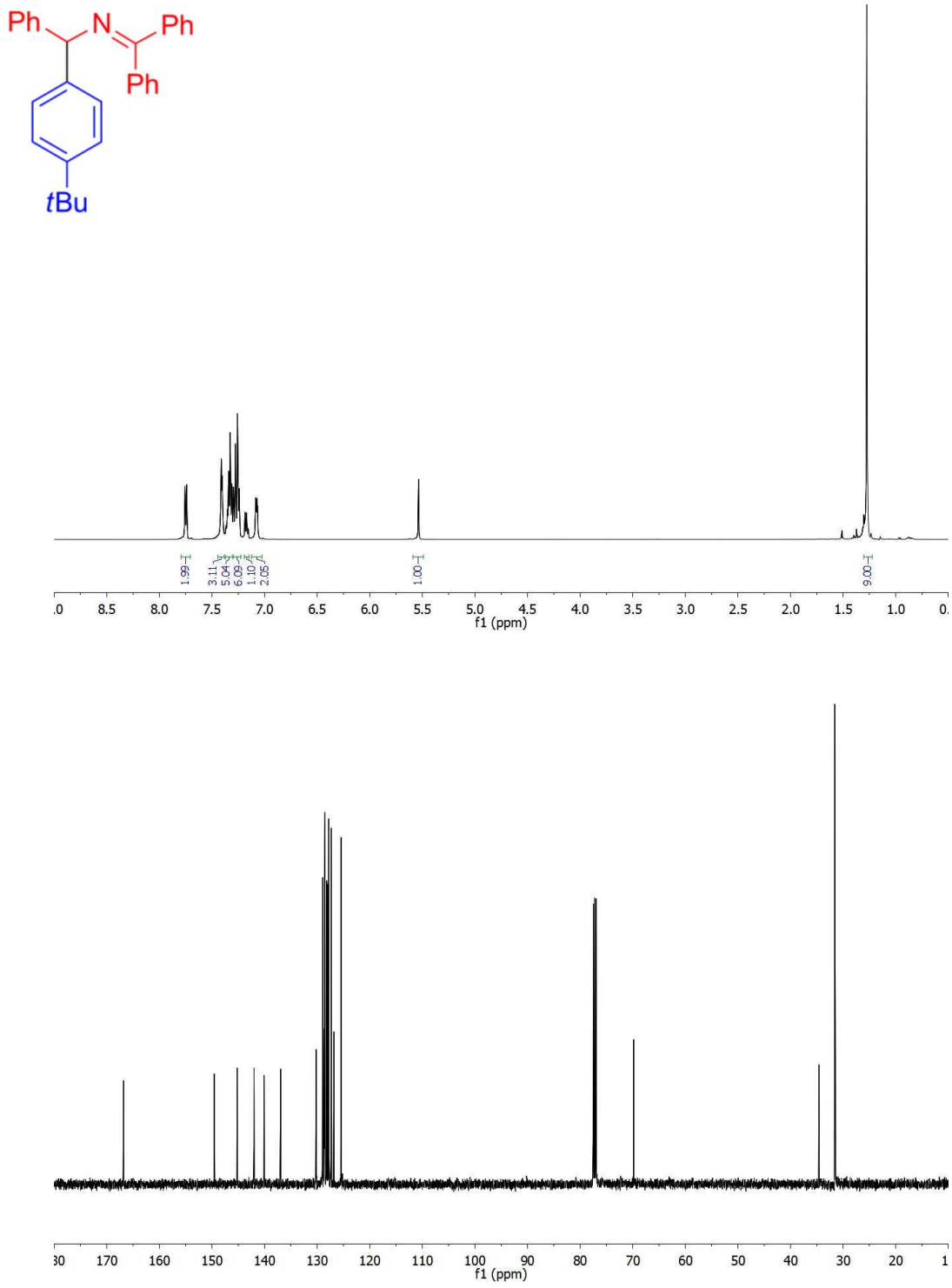


Figure A1.2 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3ac in $CDCl_3$

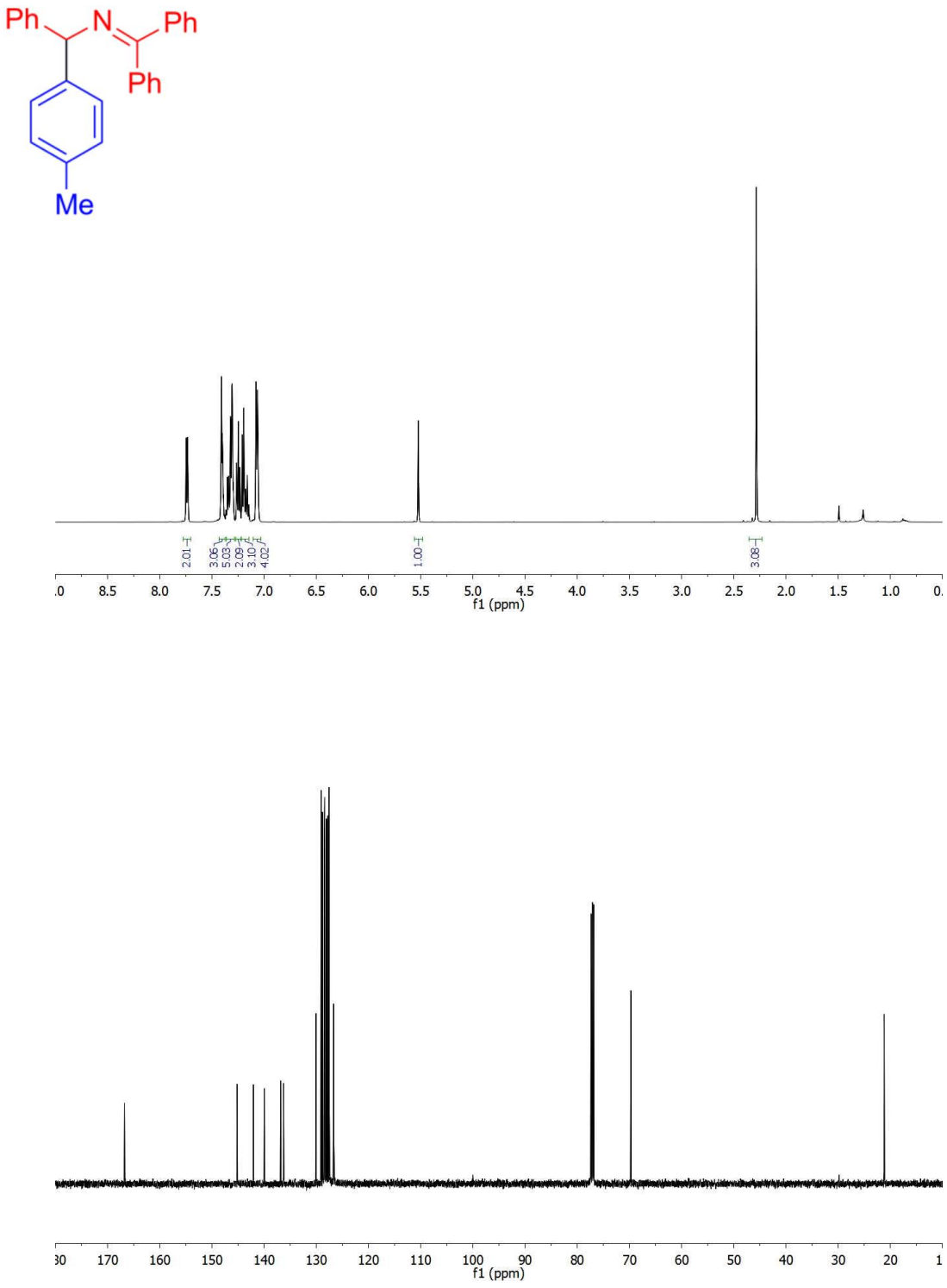


Figure A1.3 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.3bb in $CDCl_3$

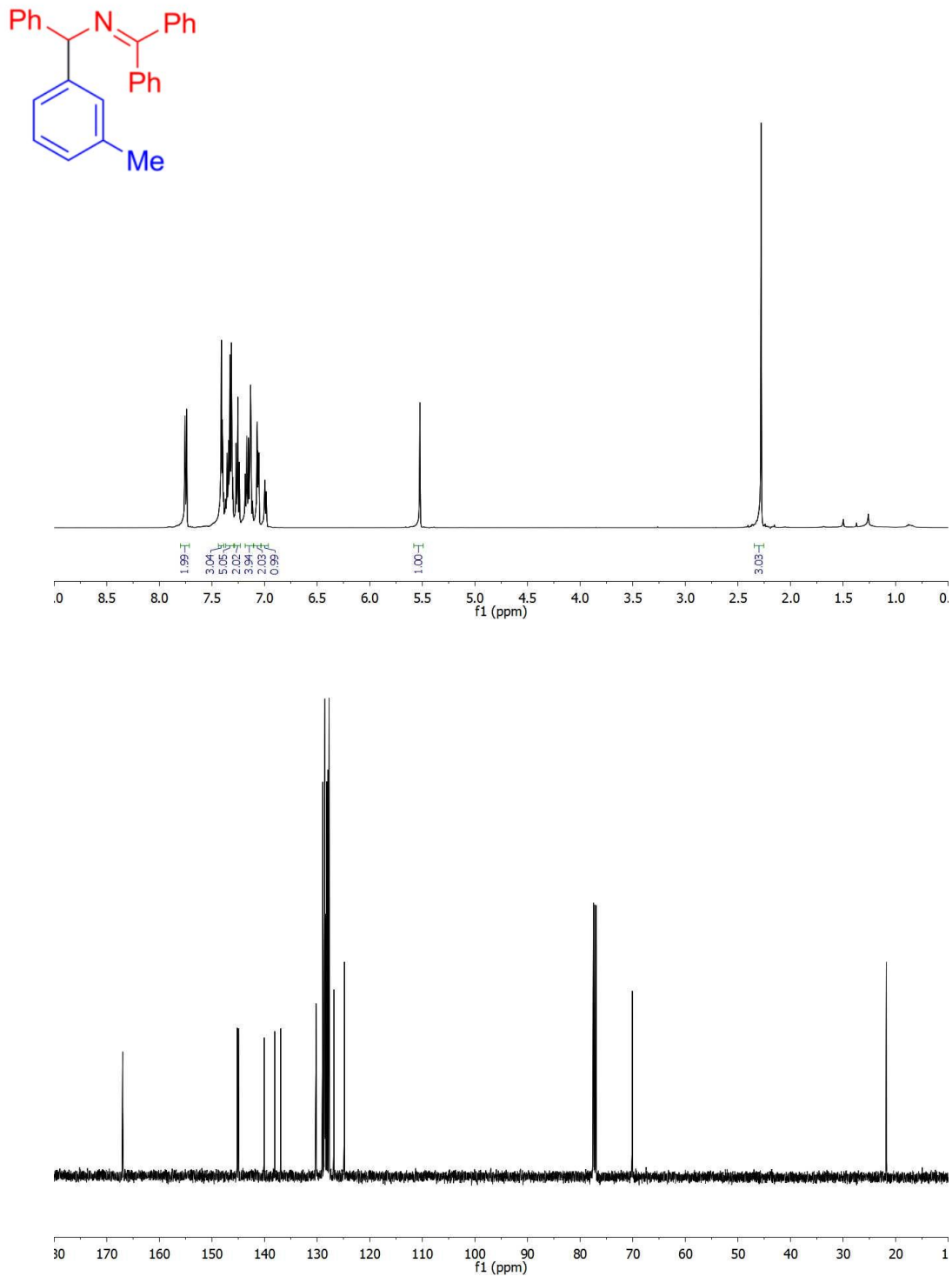


Figure A1.3 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3ae in $CDCl_3$

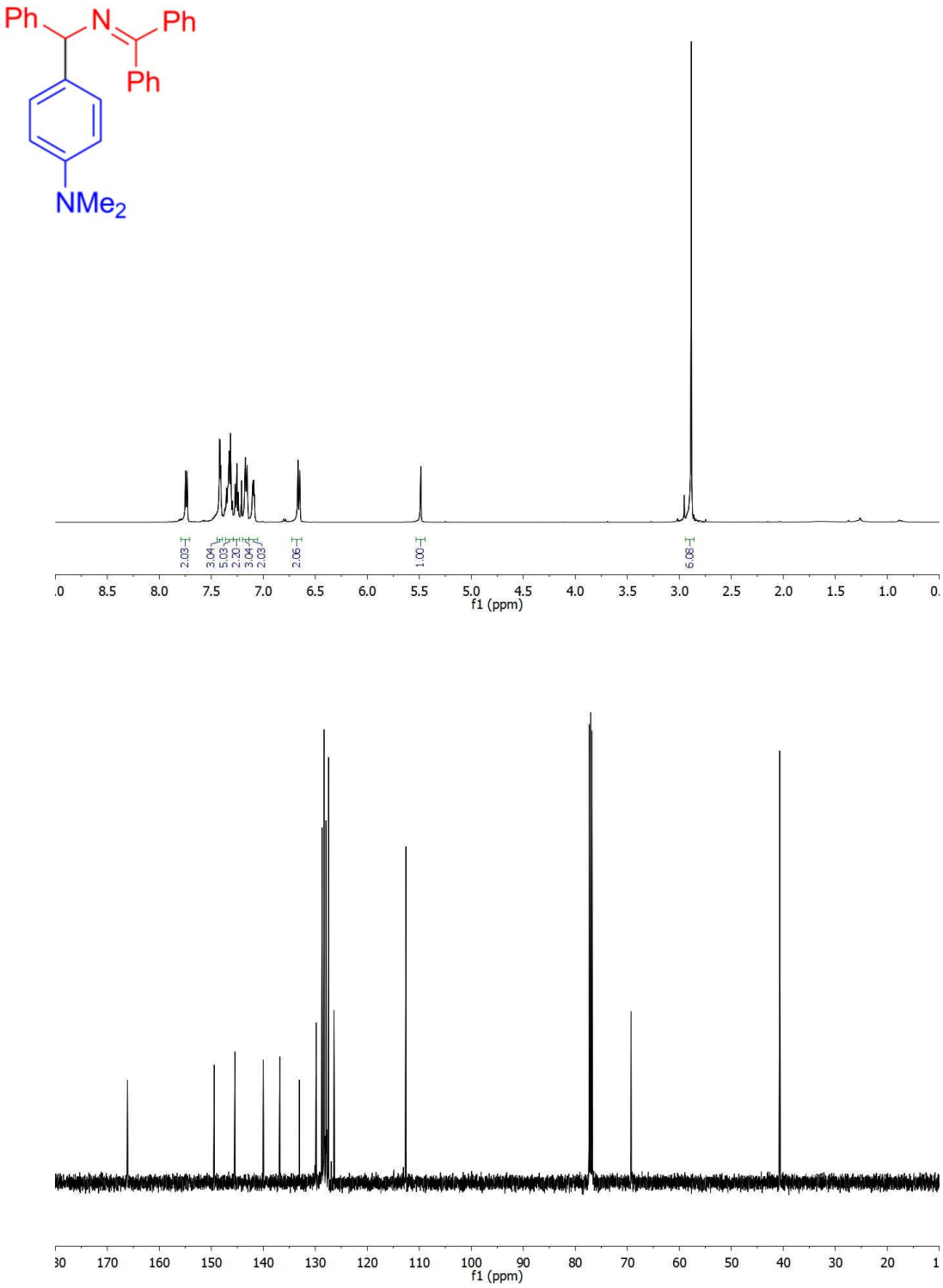


Figure A1.4 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3af in $CDCl_3$

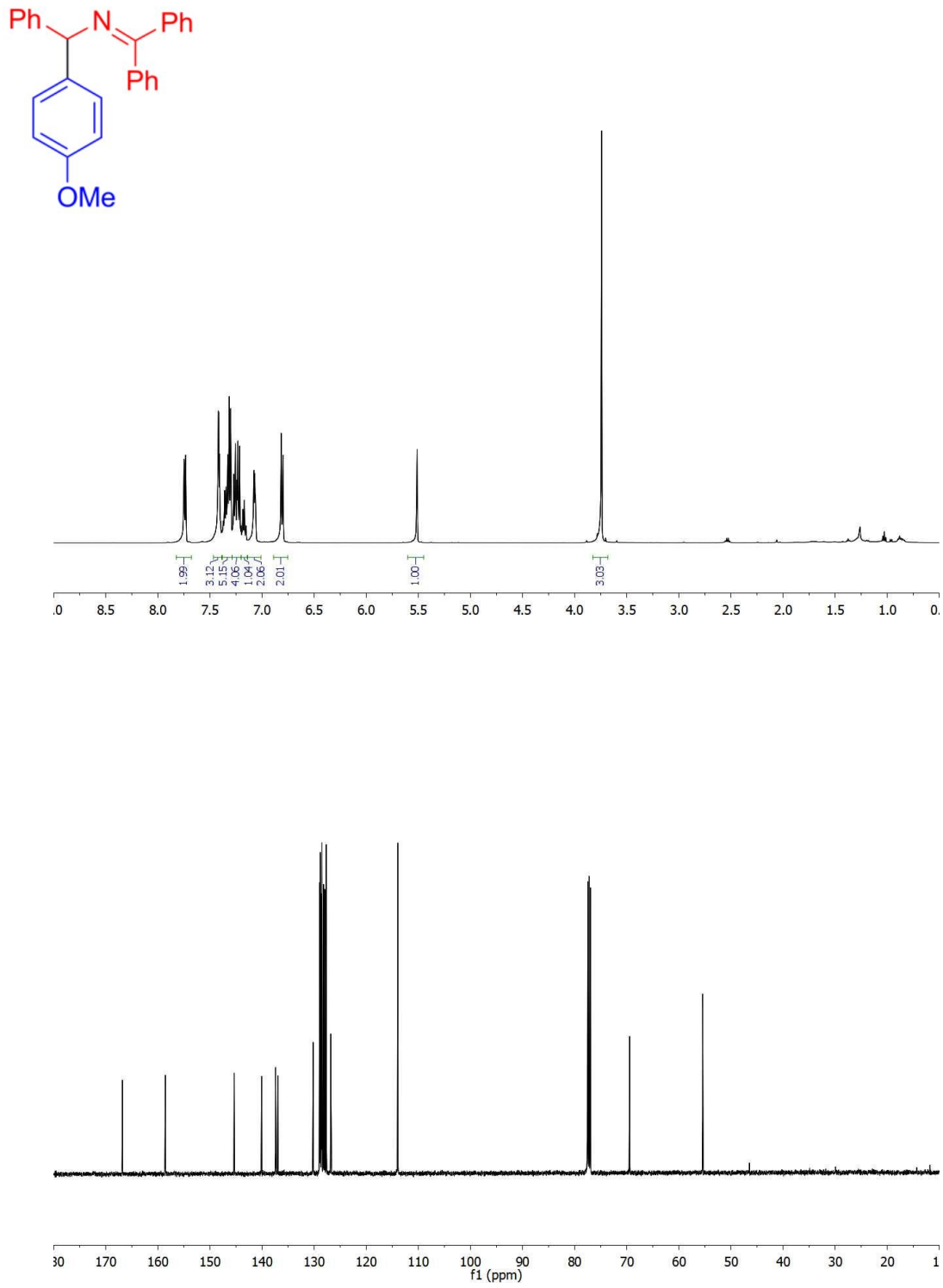


Figure A1.4 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3cb in $CDCl_3$

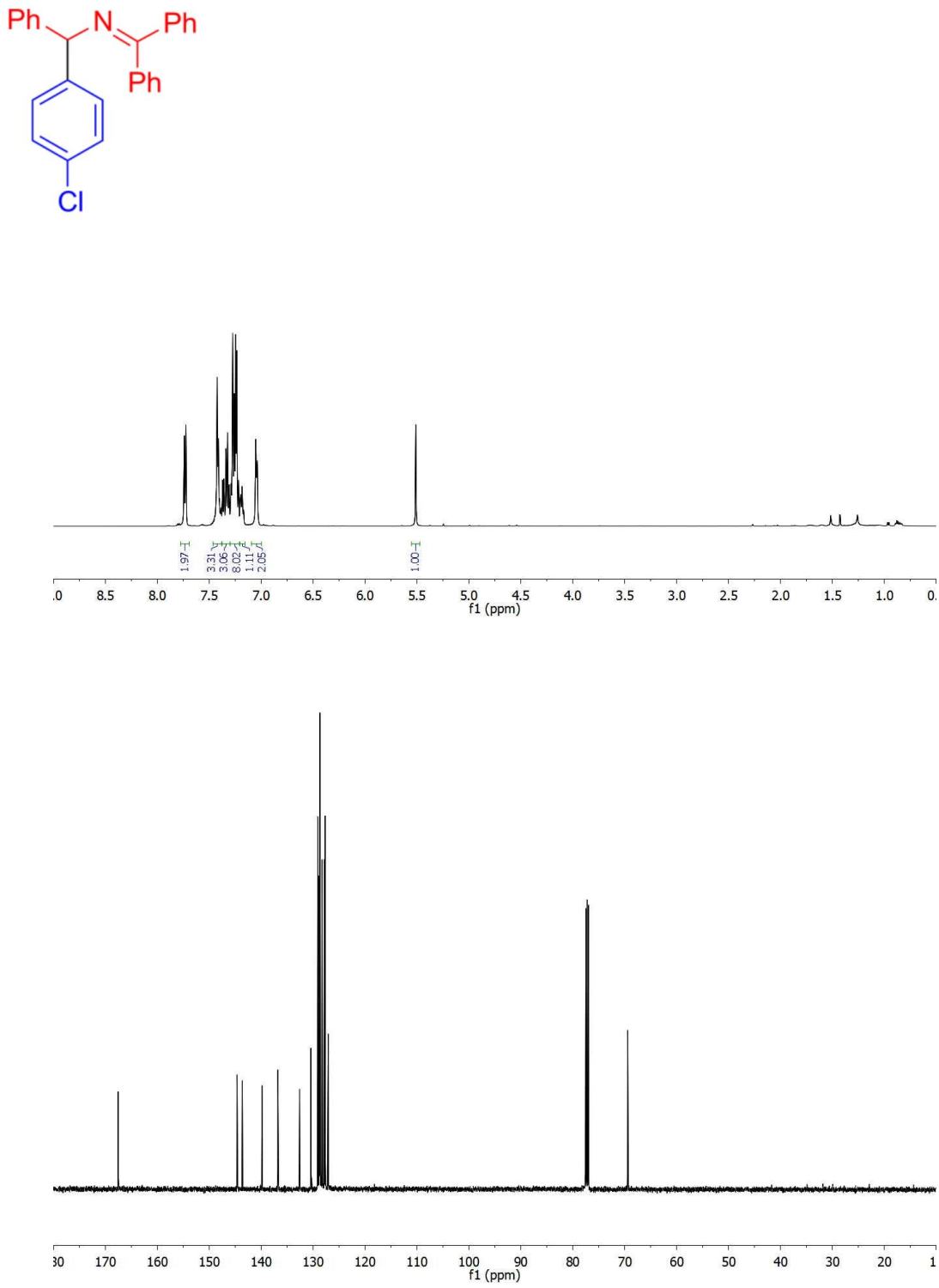


Figure A1.5 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3eb in $CDCl_3$

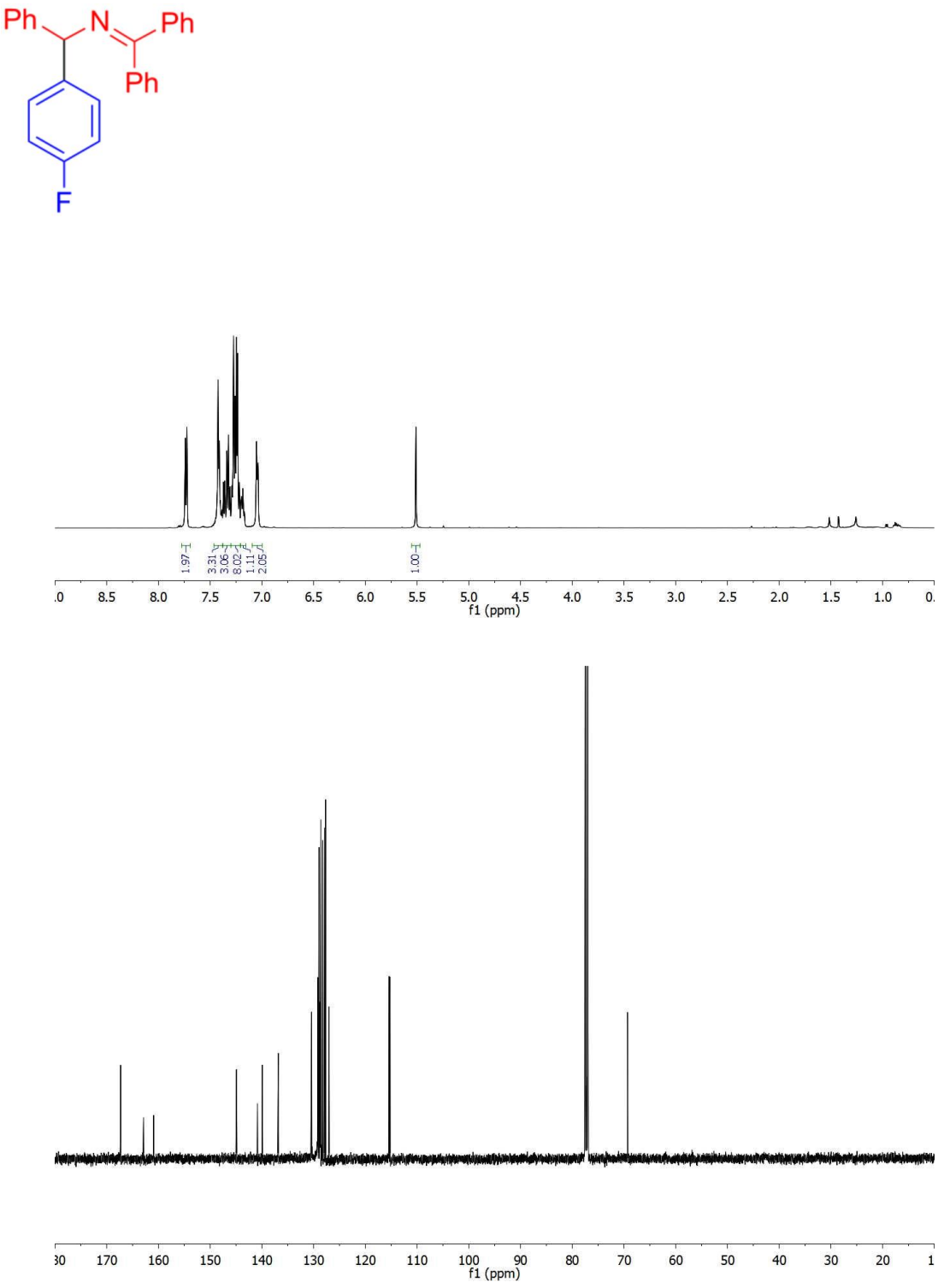


Figure A1.6 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3db in $CDCl_3$

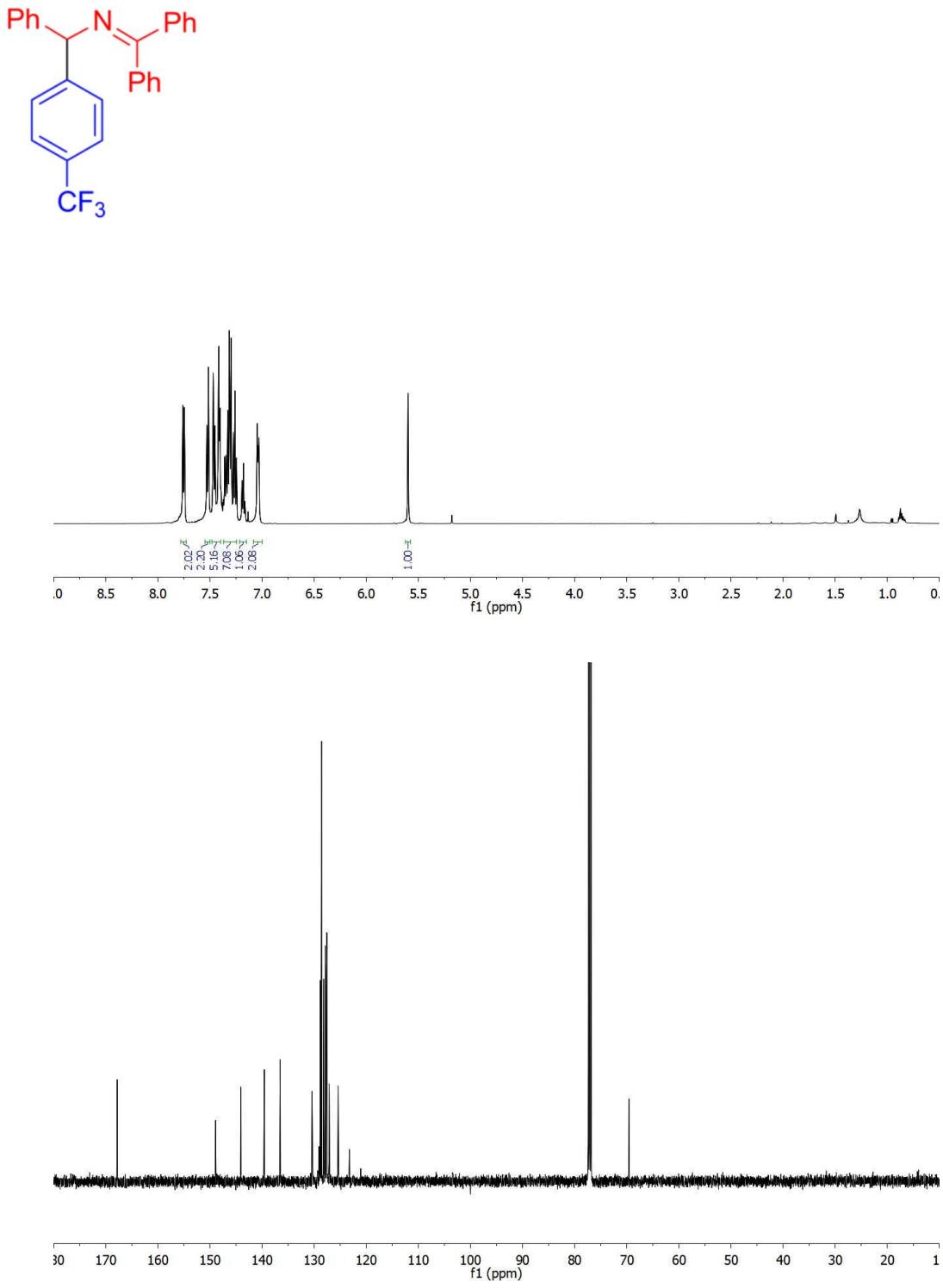


Figure A1.7 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3aj in $CDCl_3$

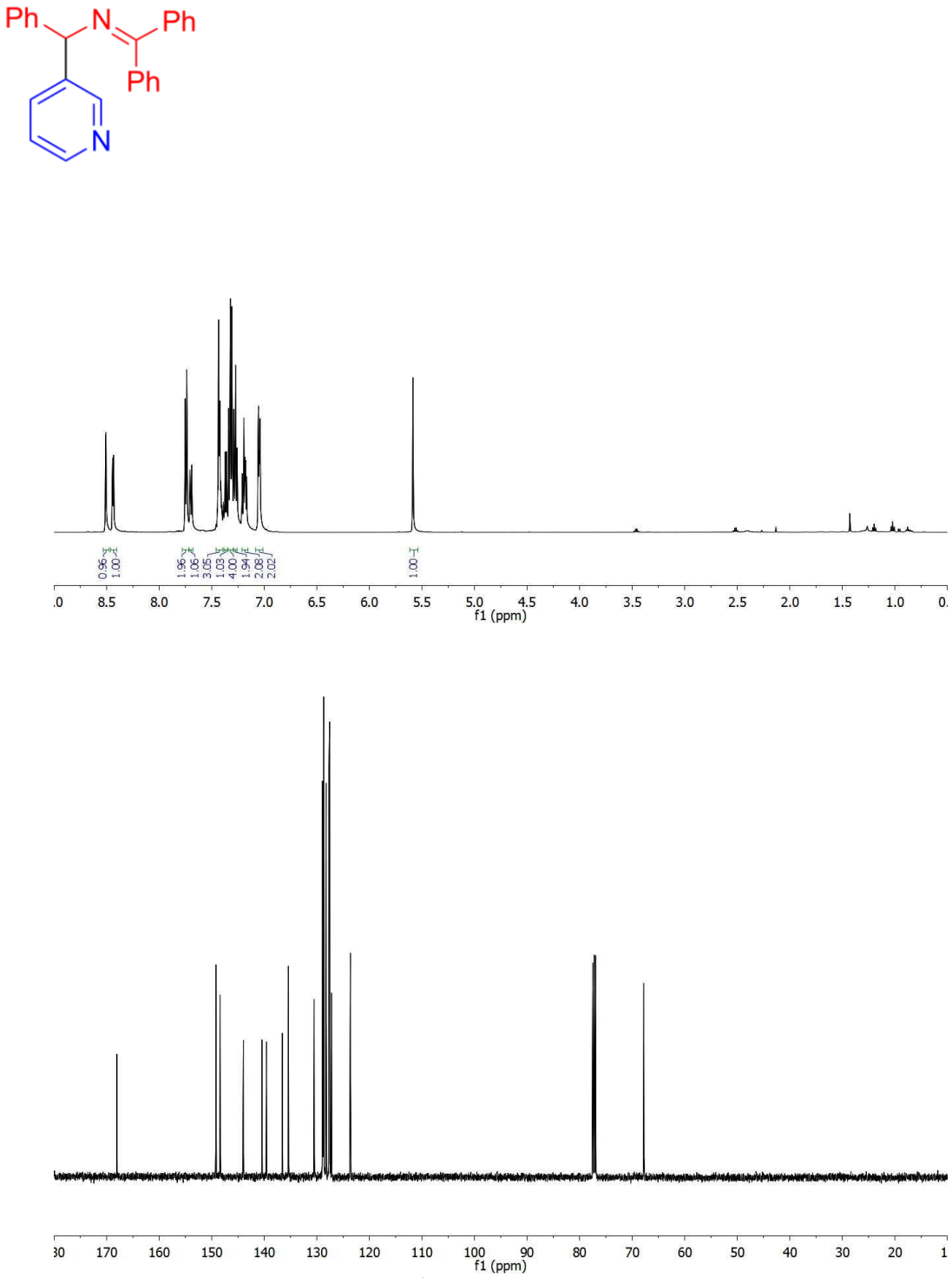


Figure A1.8 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.3hb in $CDCl_3$

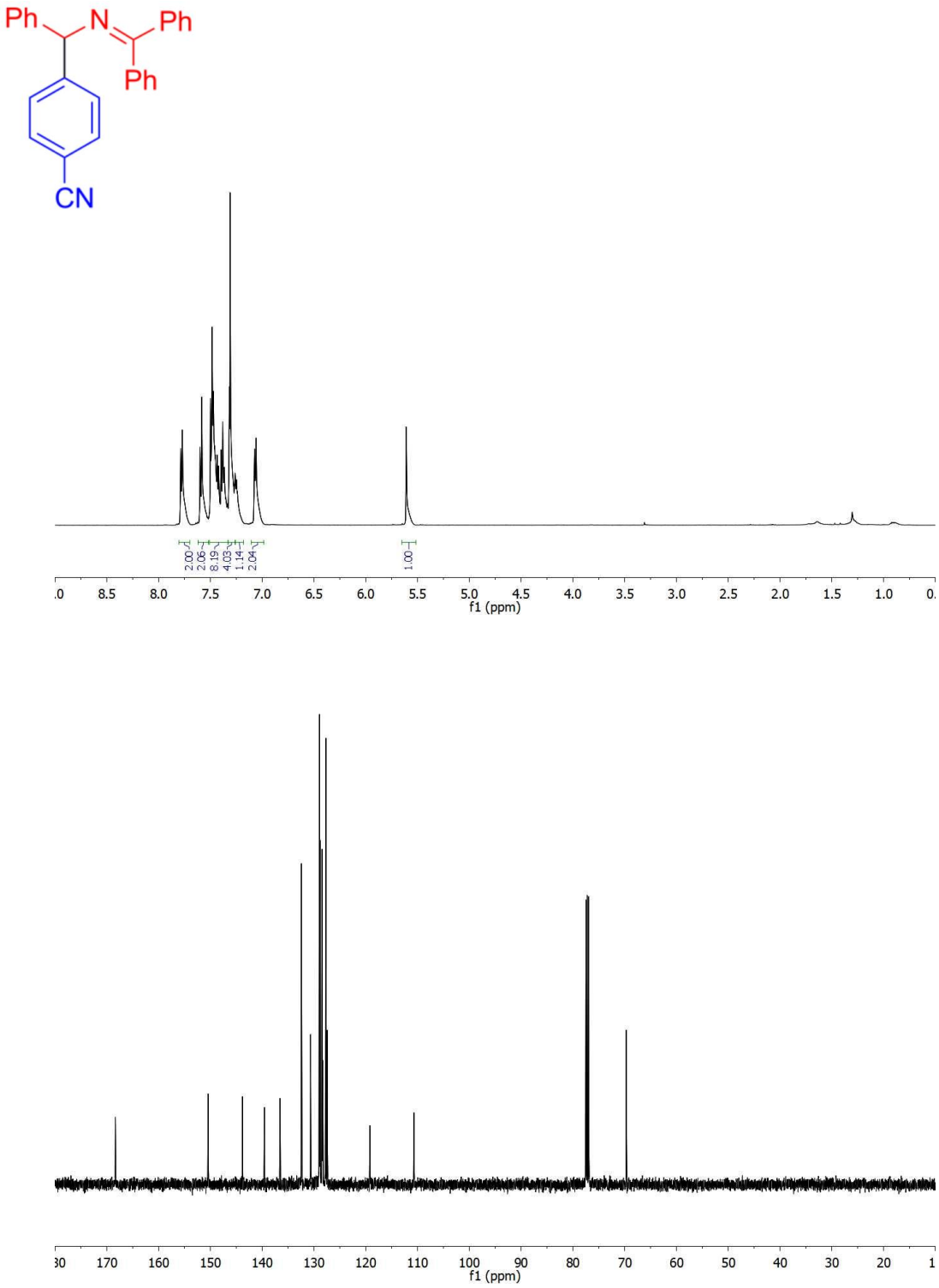


Figure A1.9 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3al in $CDCl_3$

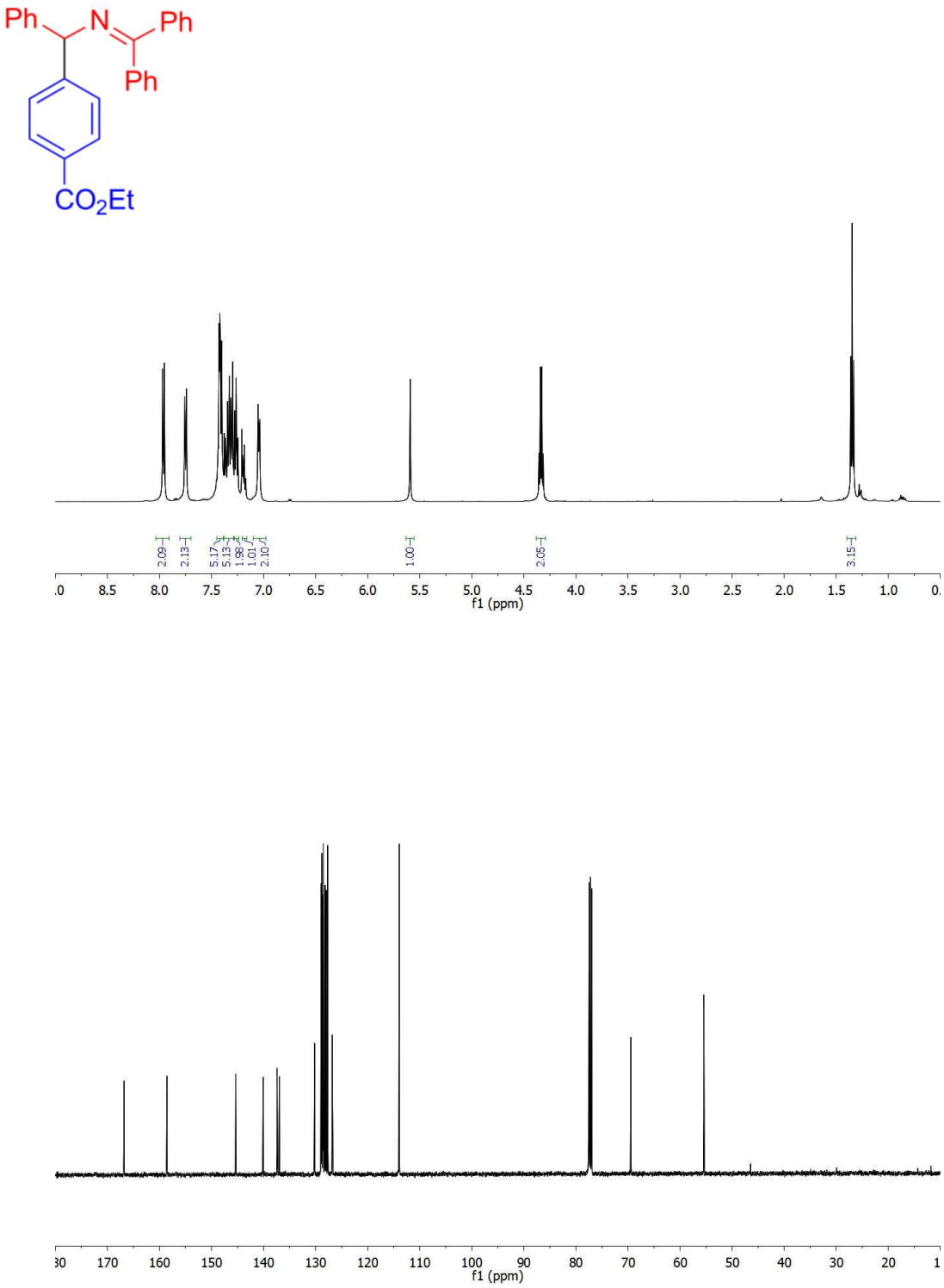


Figure A1.10 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3am in $CDCl_3$

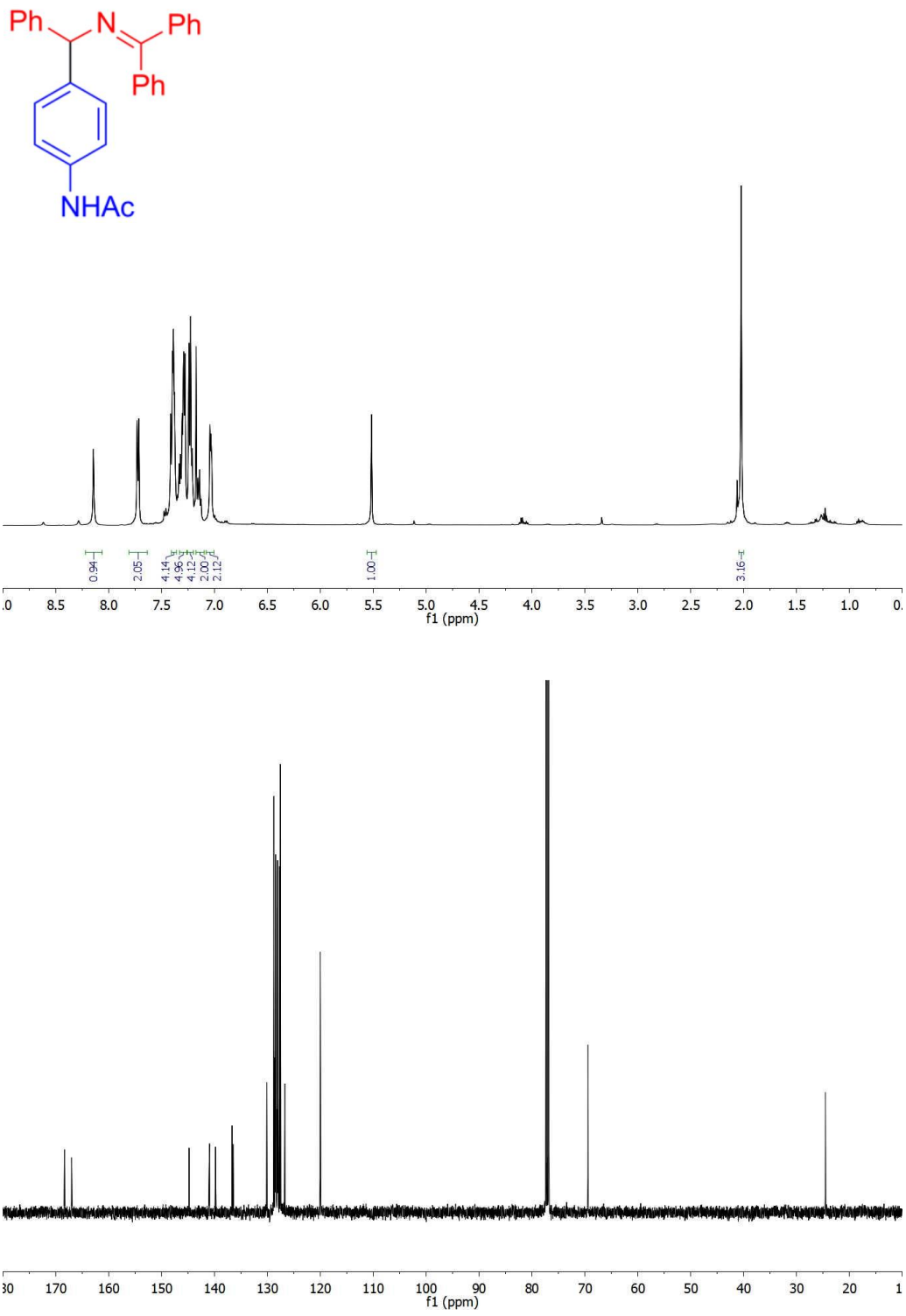


Figure A1.11 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3an in $CDCl_3$

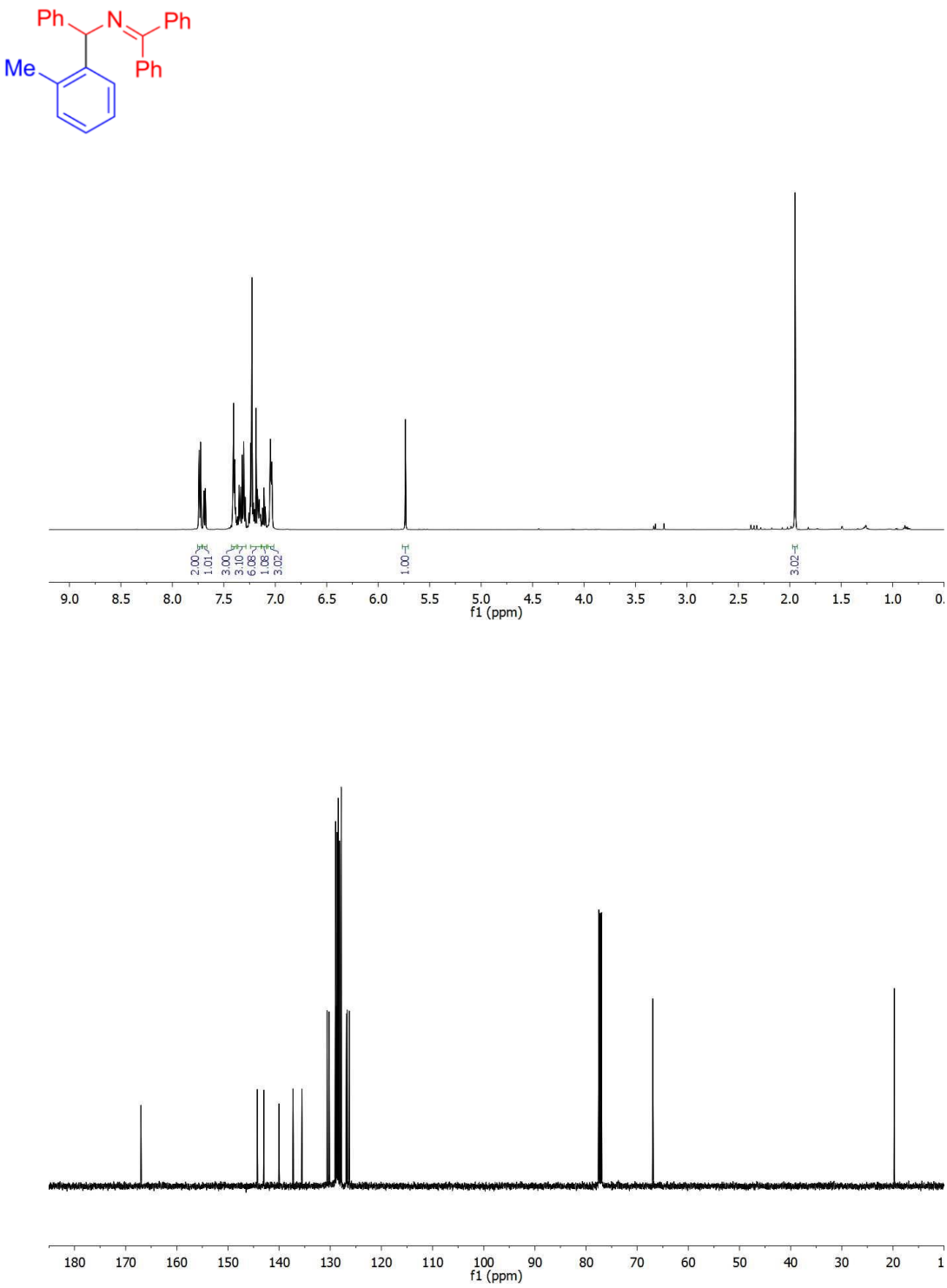


Figure A1.12 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3ao in $CDCl_3$

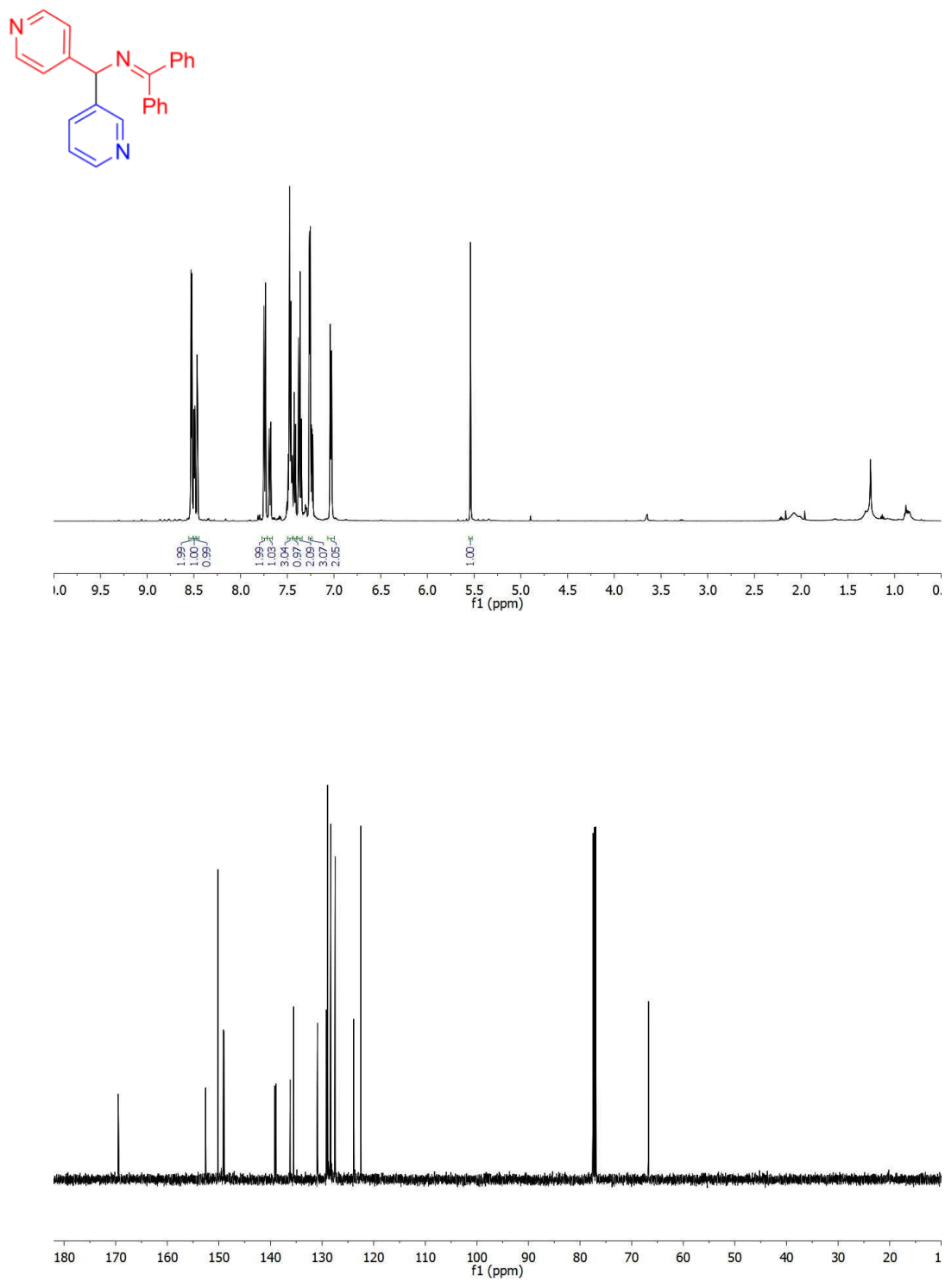


Figure A1.13 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3ik in $CDCl_3$

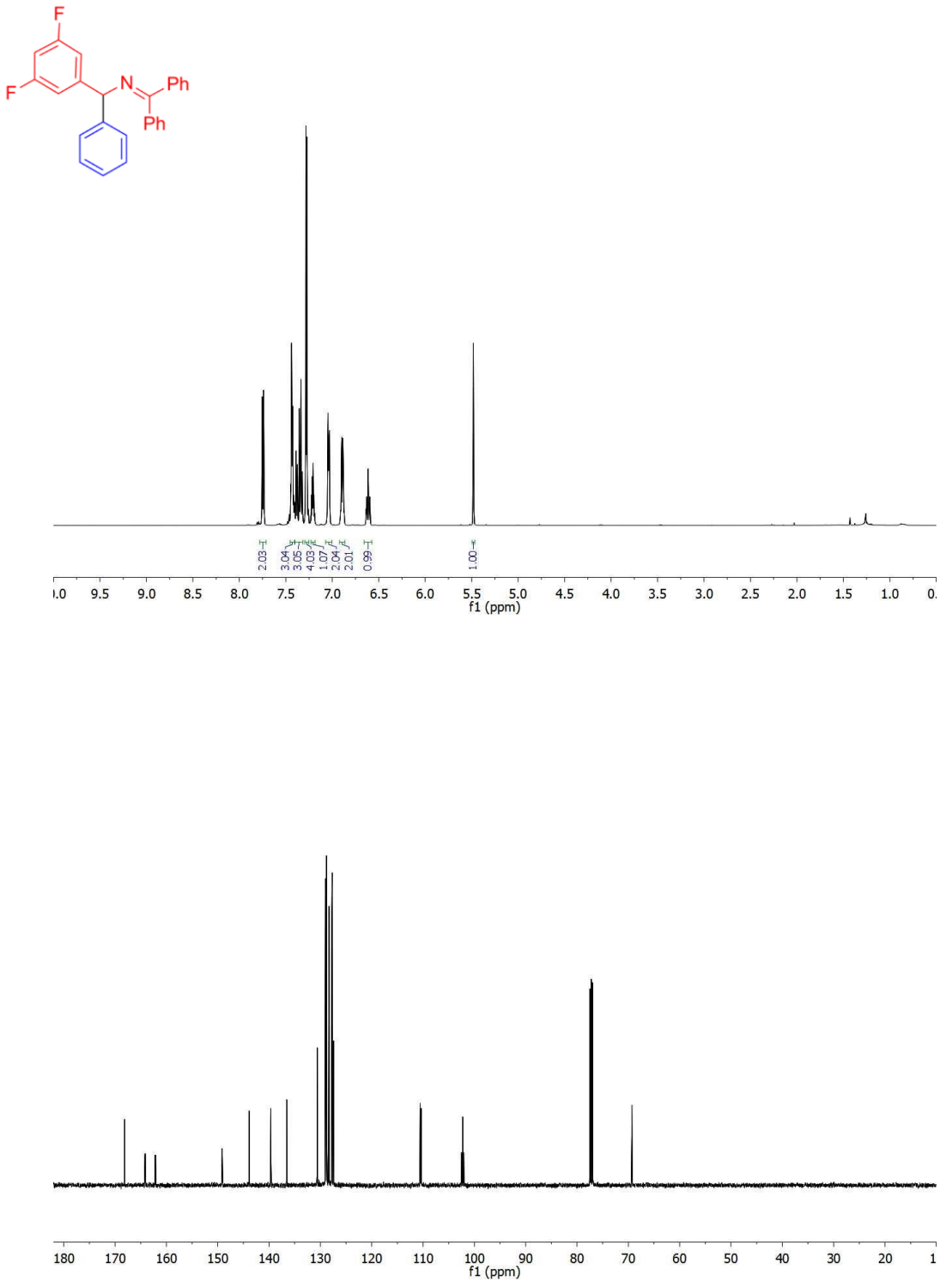


Figure A1.14 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.3fb in $CDCl_3$

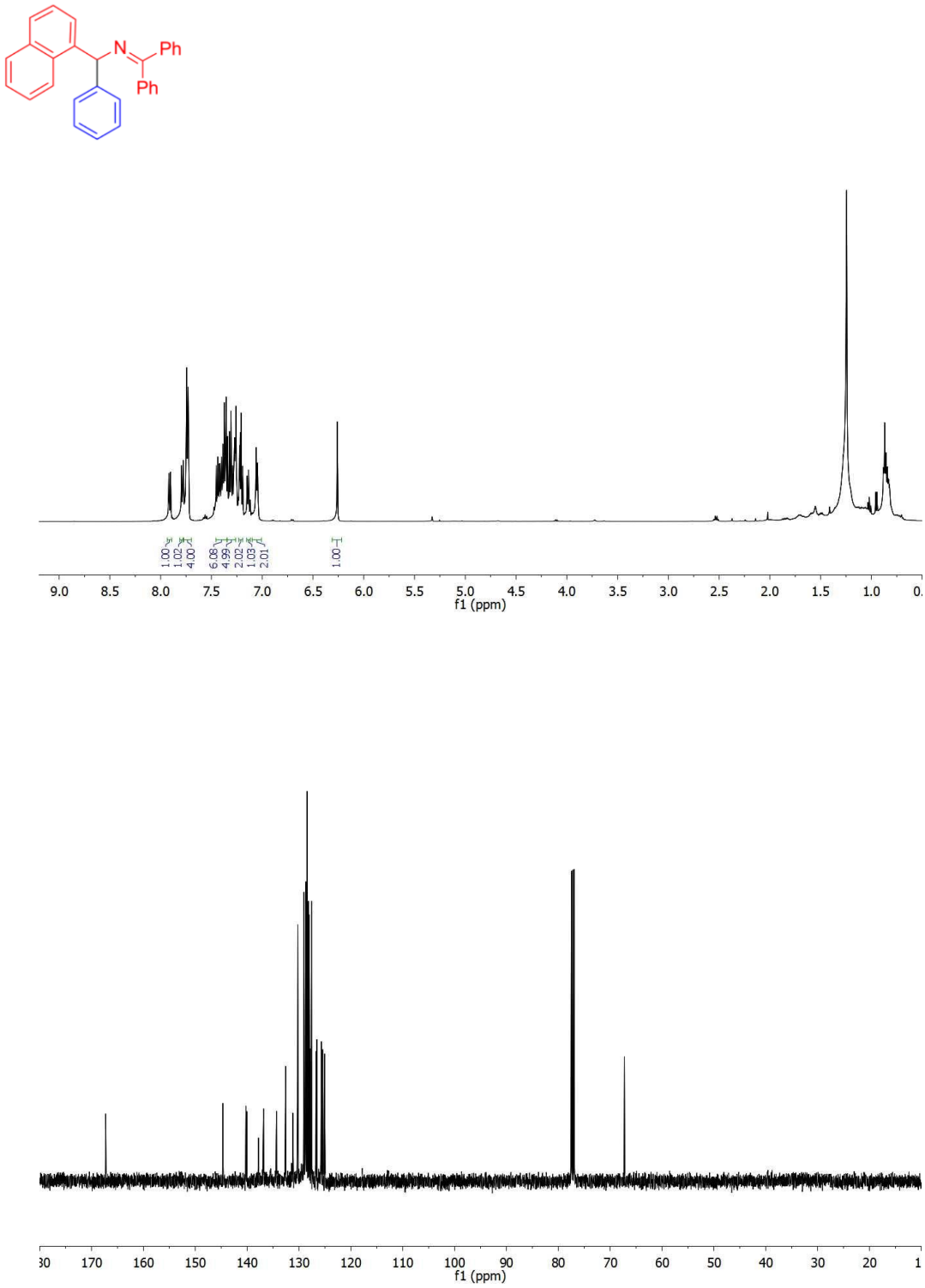


Figure A1.15 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3gb in $CDCl_3$

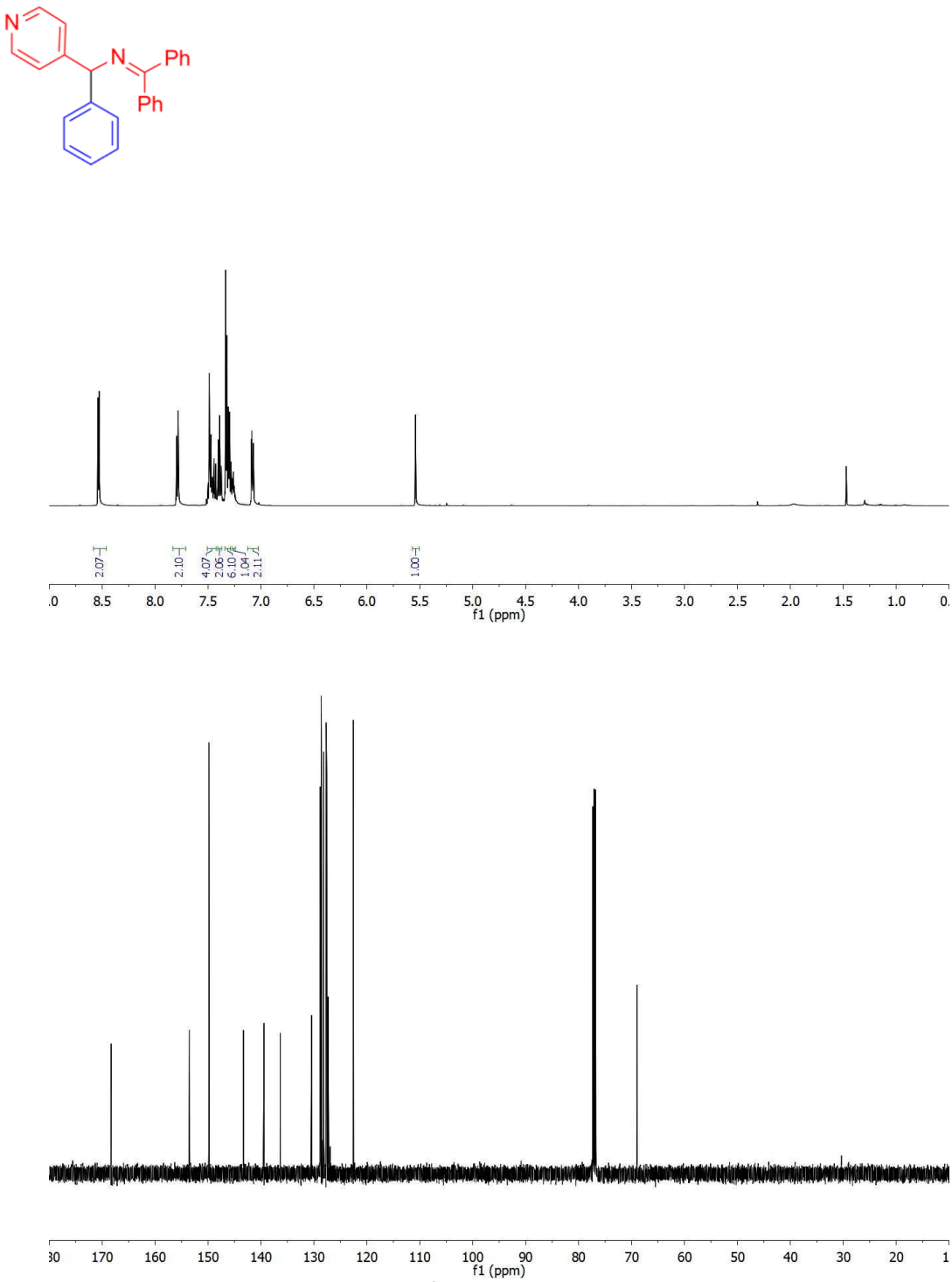


Figure A1.16 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3ib in $CDCl_3$

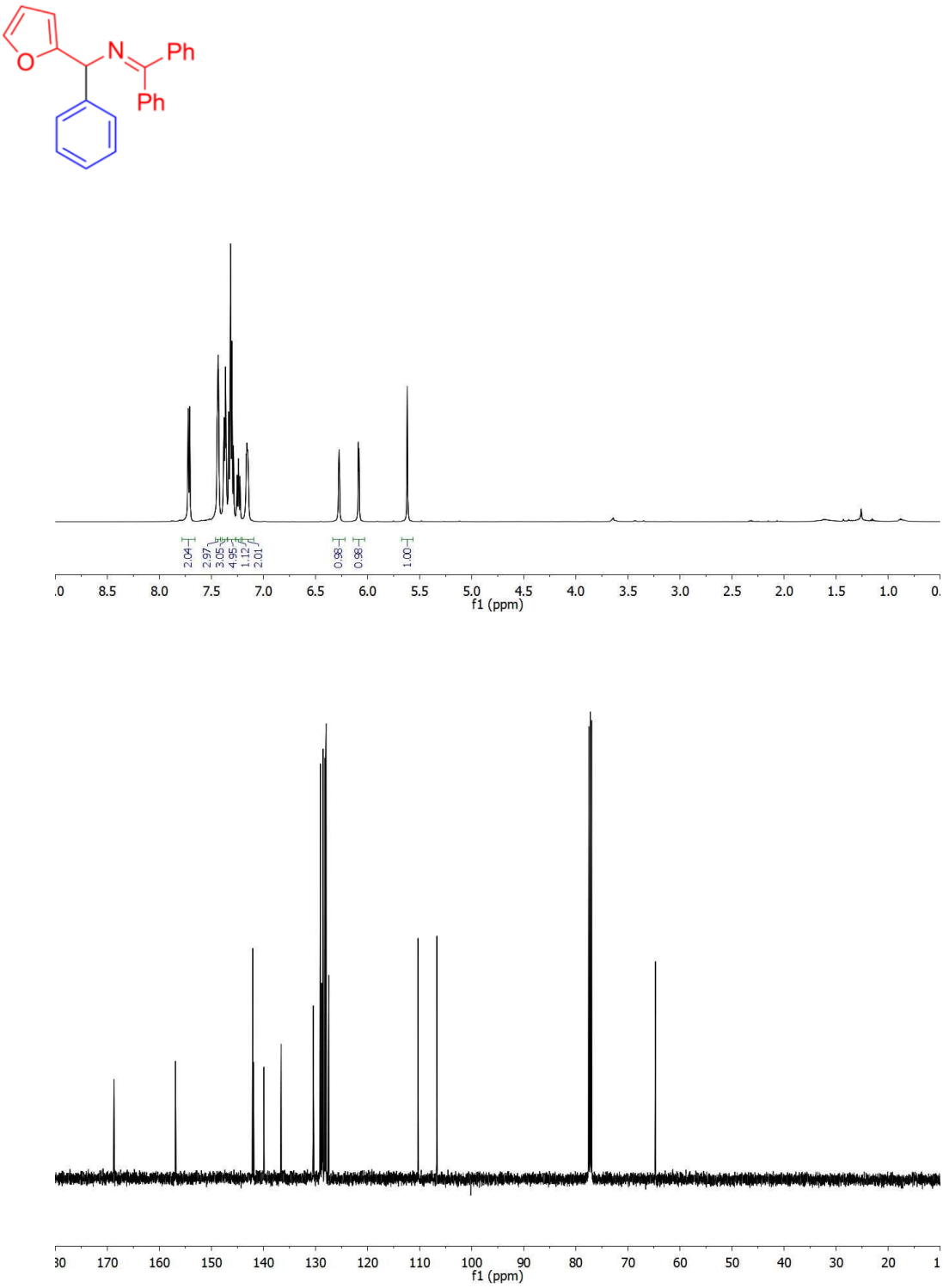


Figure A1.17 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3jb in $CDCl_3$

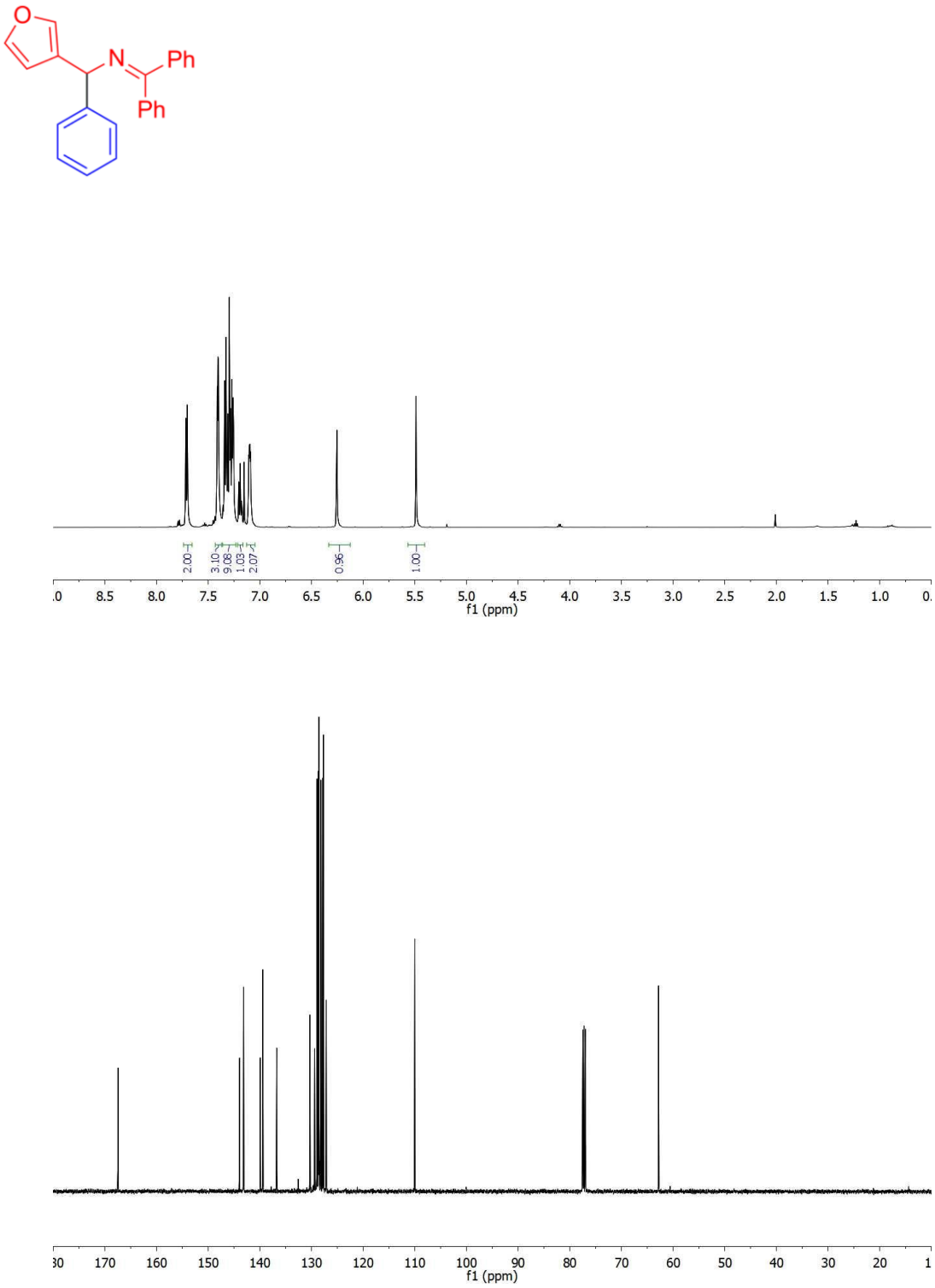


Figure A1.18 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3lb in $CDCl_3$

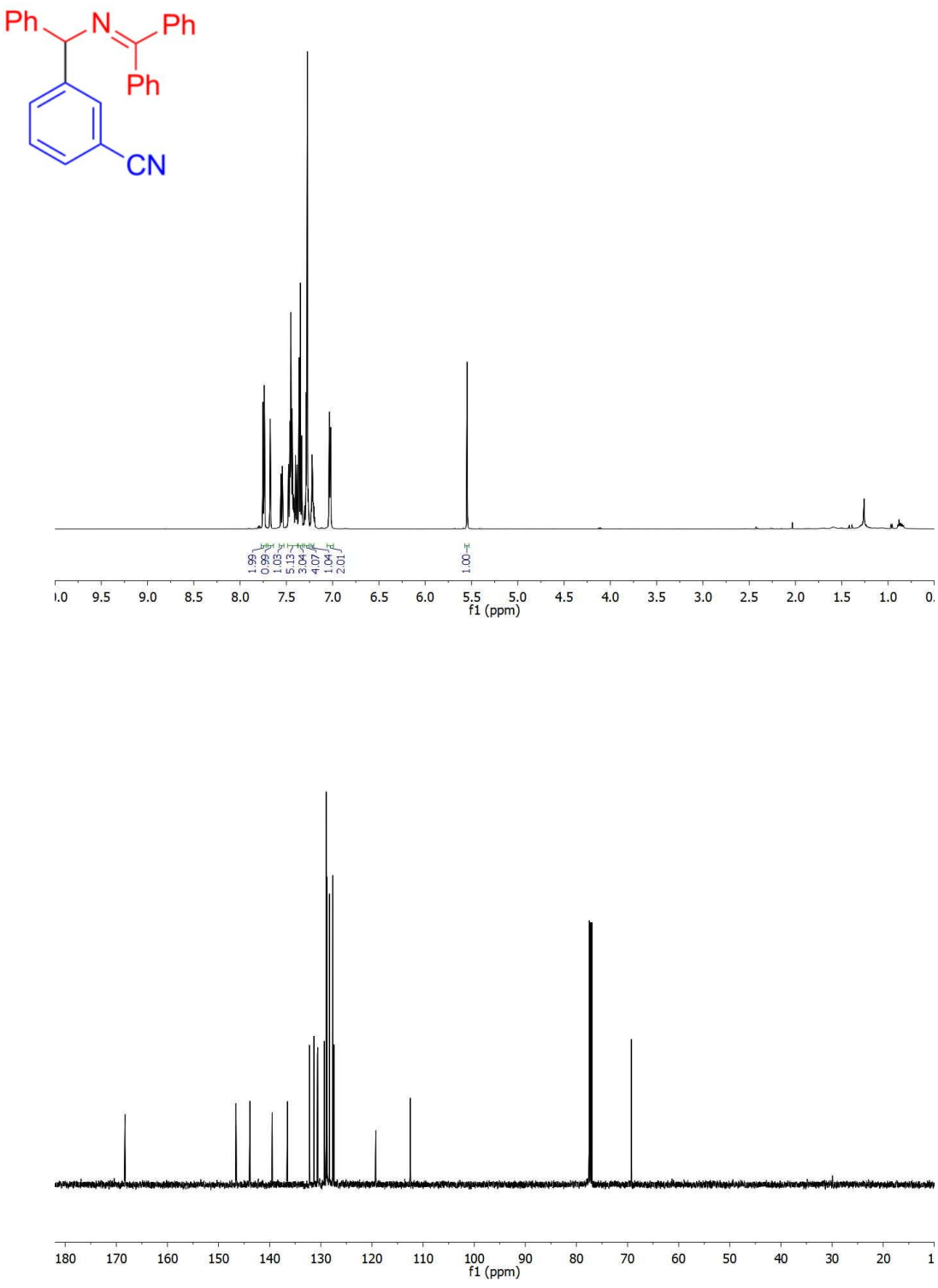


Figure A1.19 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3ap in $CDCl_3$

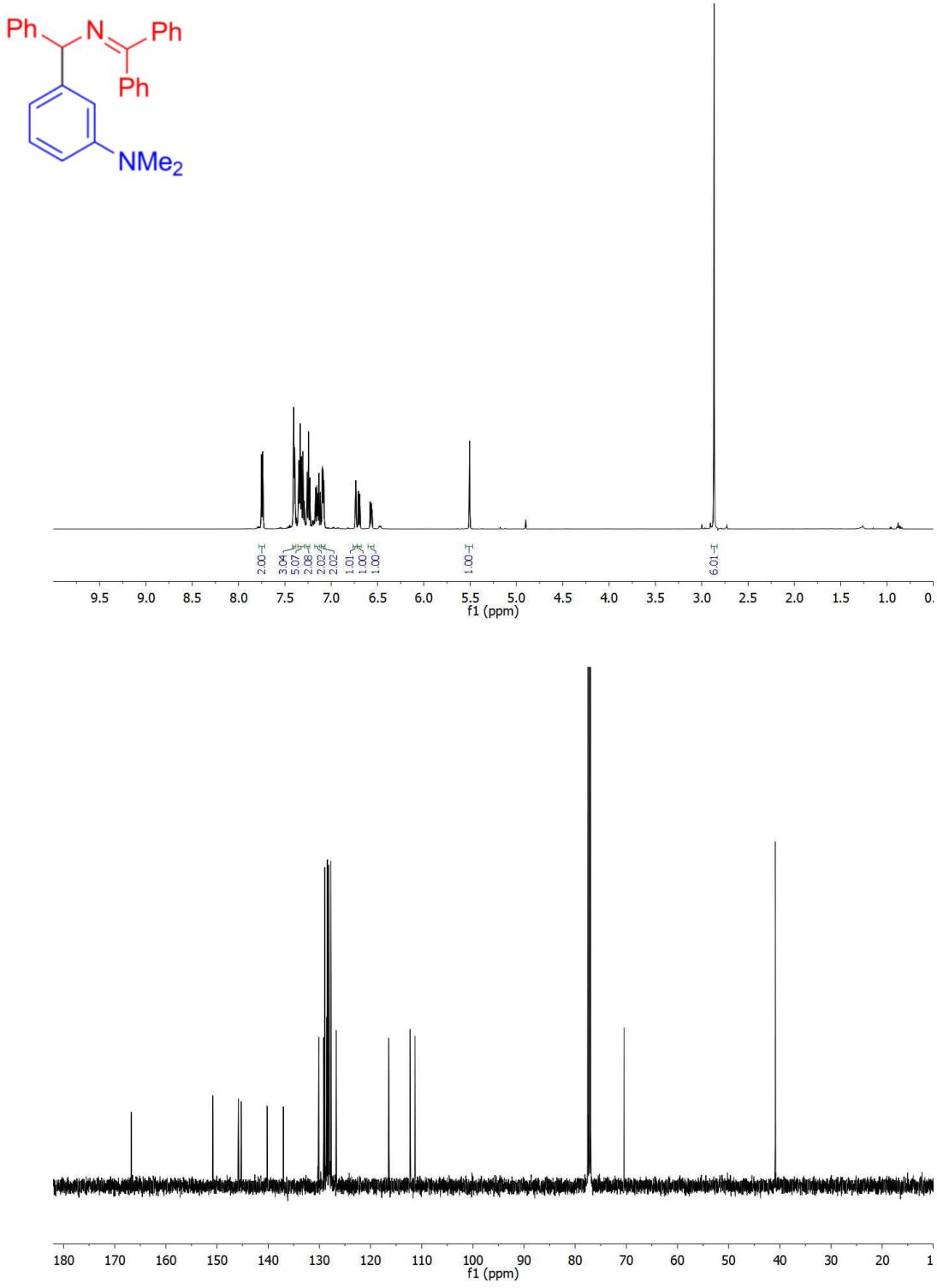


Figure A1.20 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.3aq in $CDCl_3$

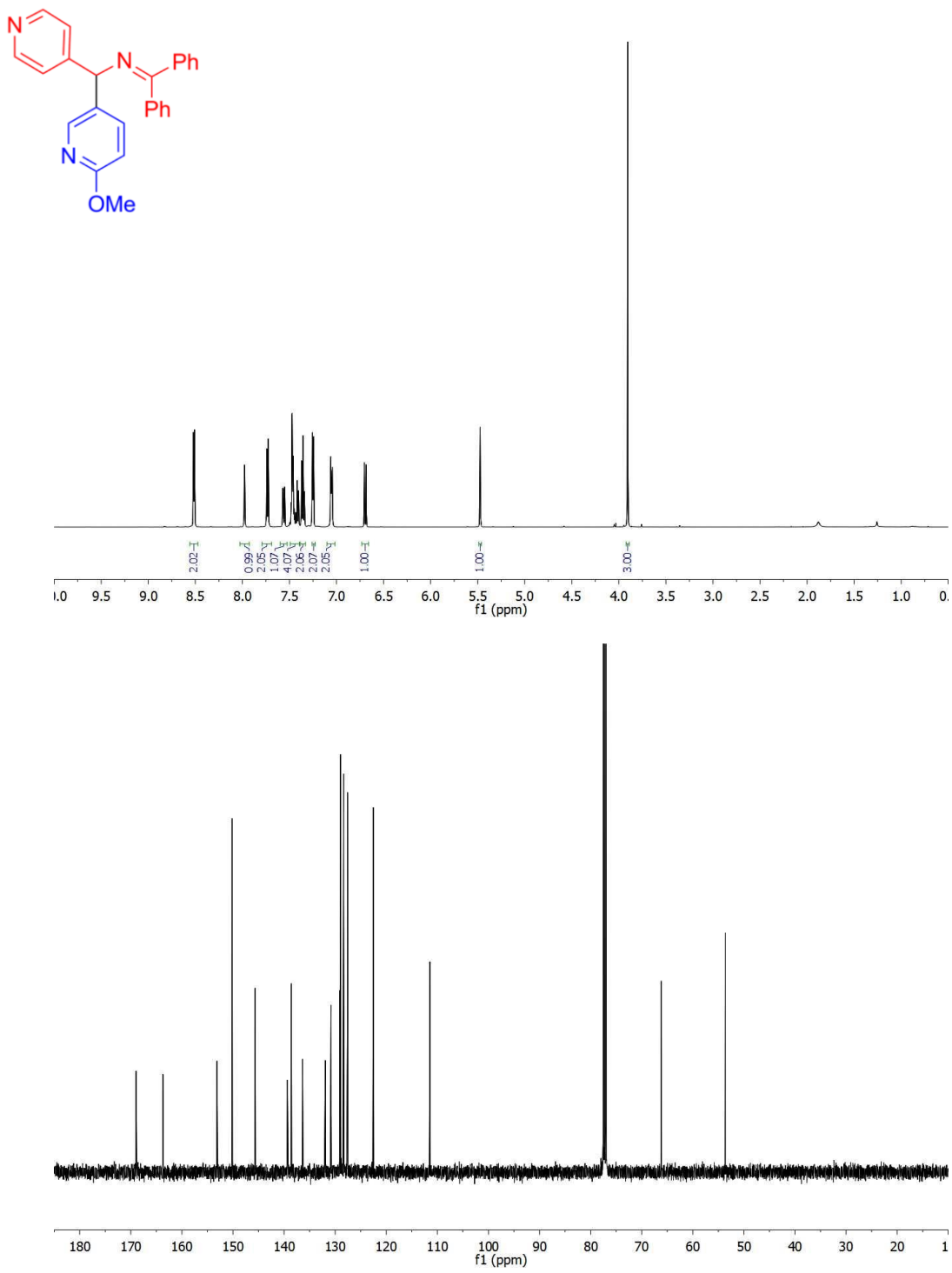


Figure A1.21 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.3js in $CDCl_3$

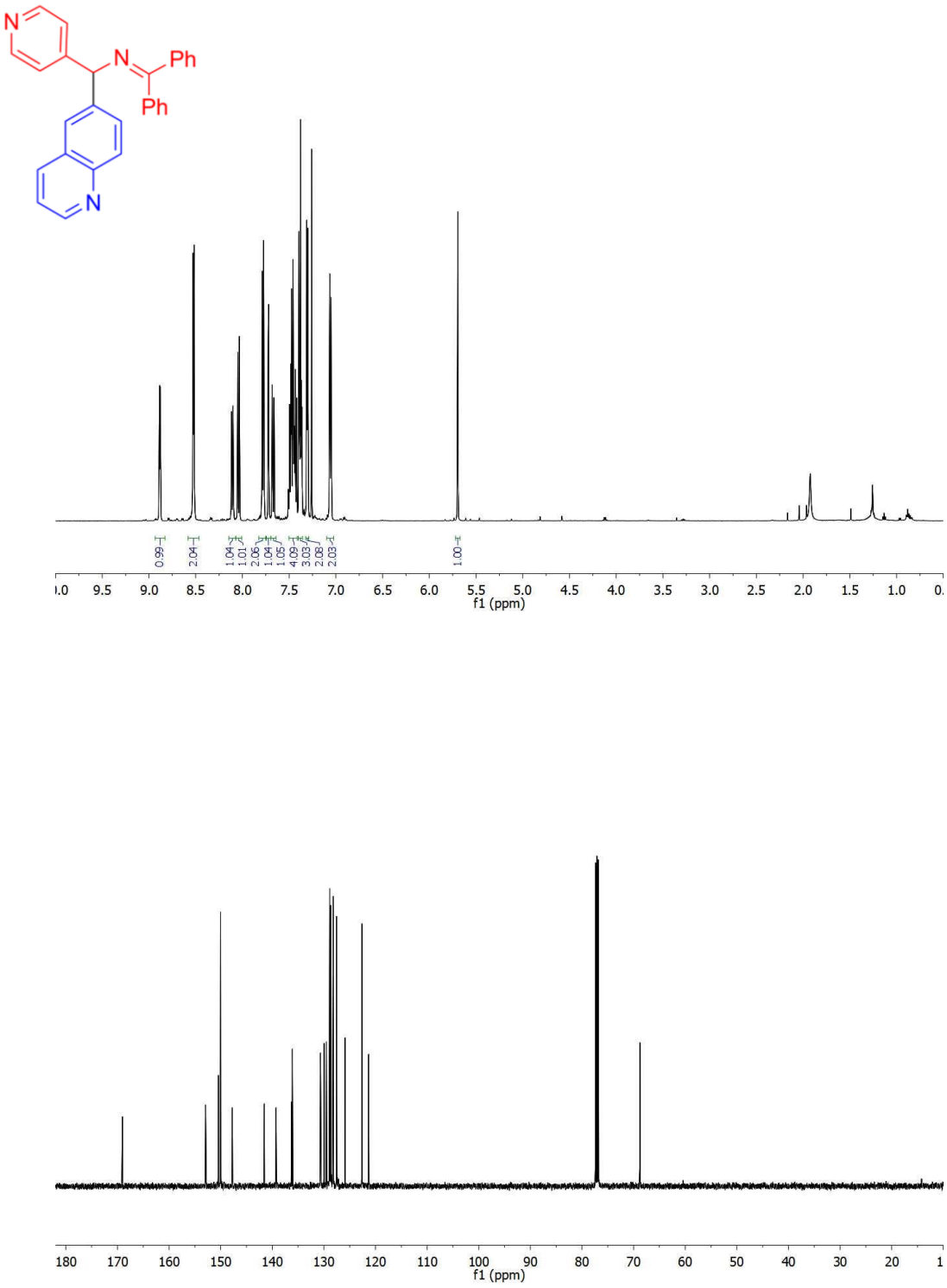


Figure A1.22 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.3it in $CDCl_3$

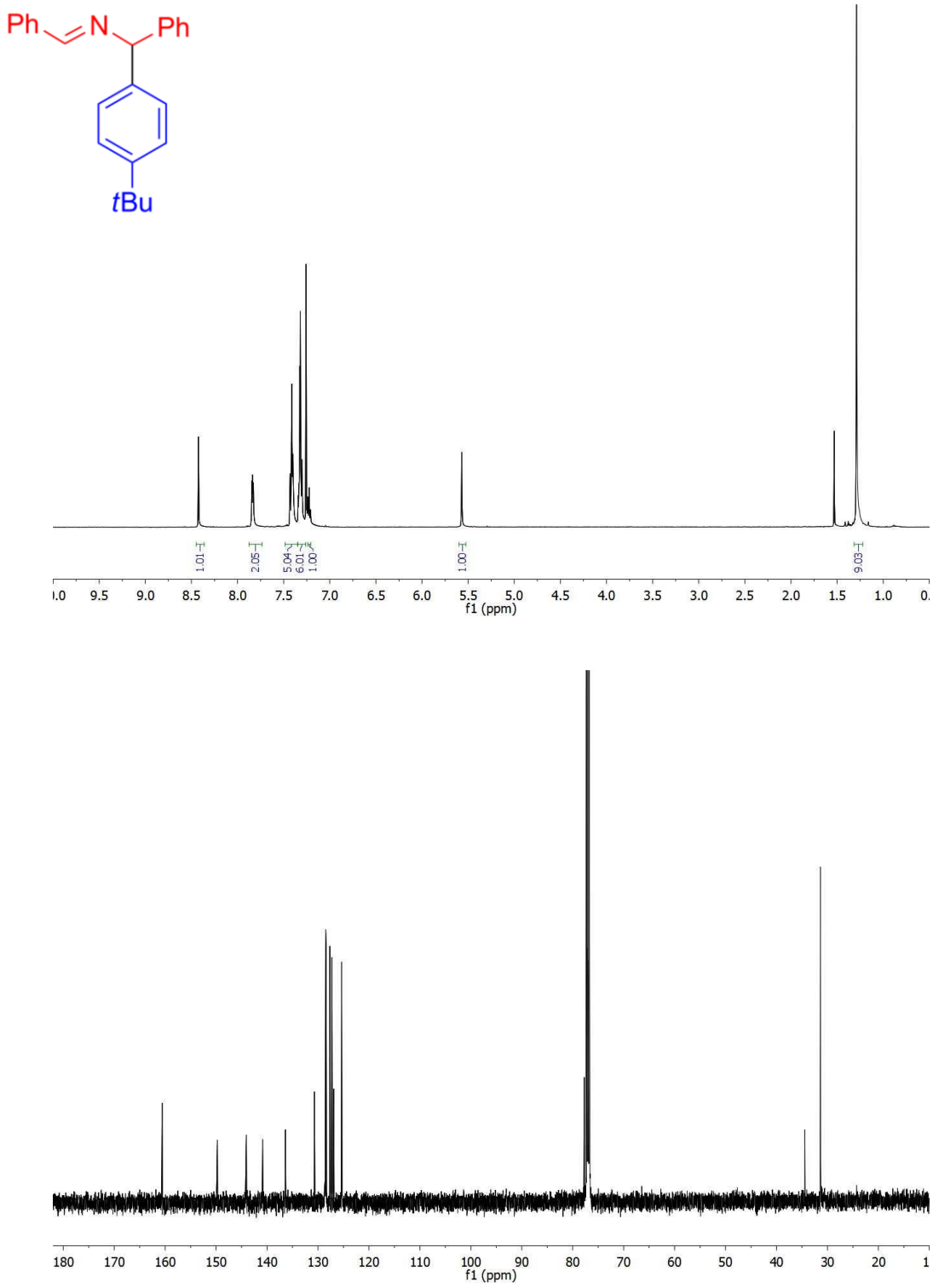


Figure A1.23 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.10ac in $CDCl_3$

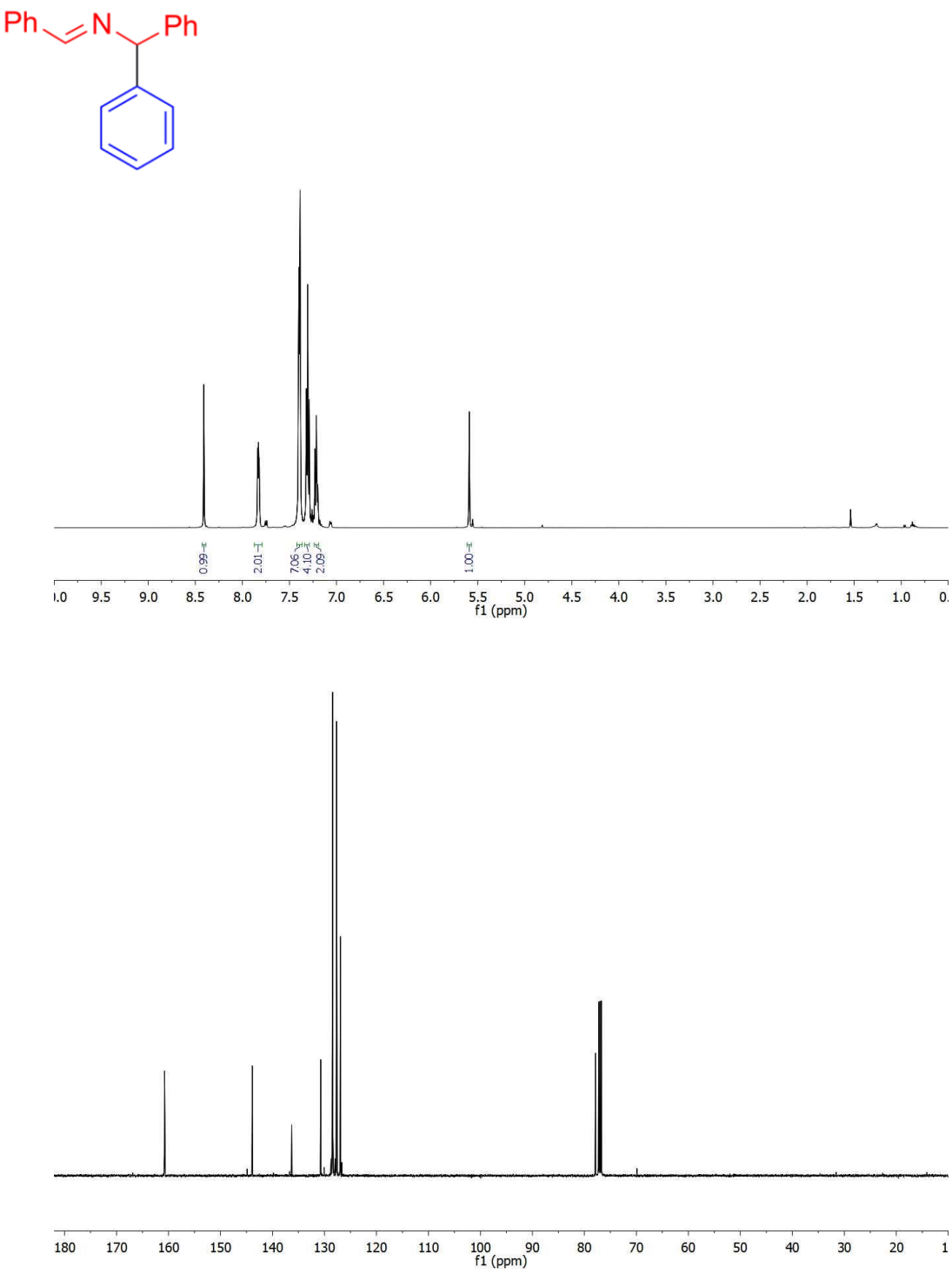


Figure A1.24 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.10ab in $CDCl_3$

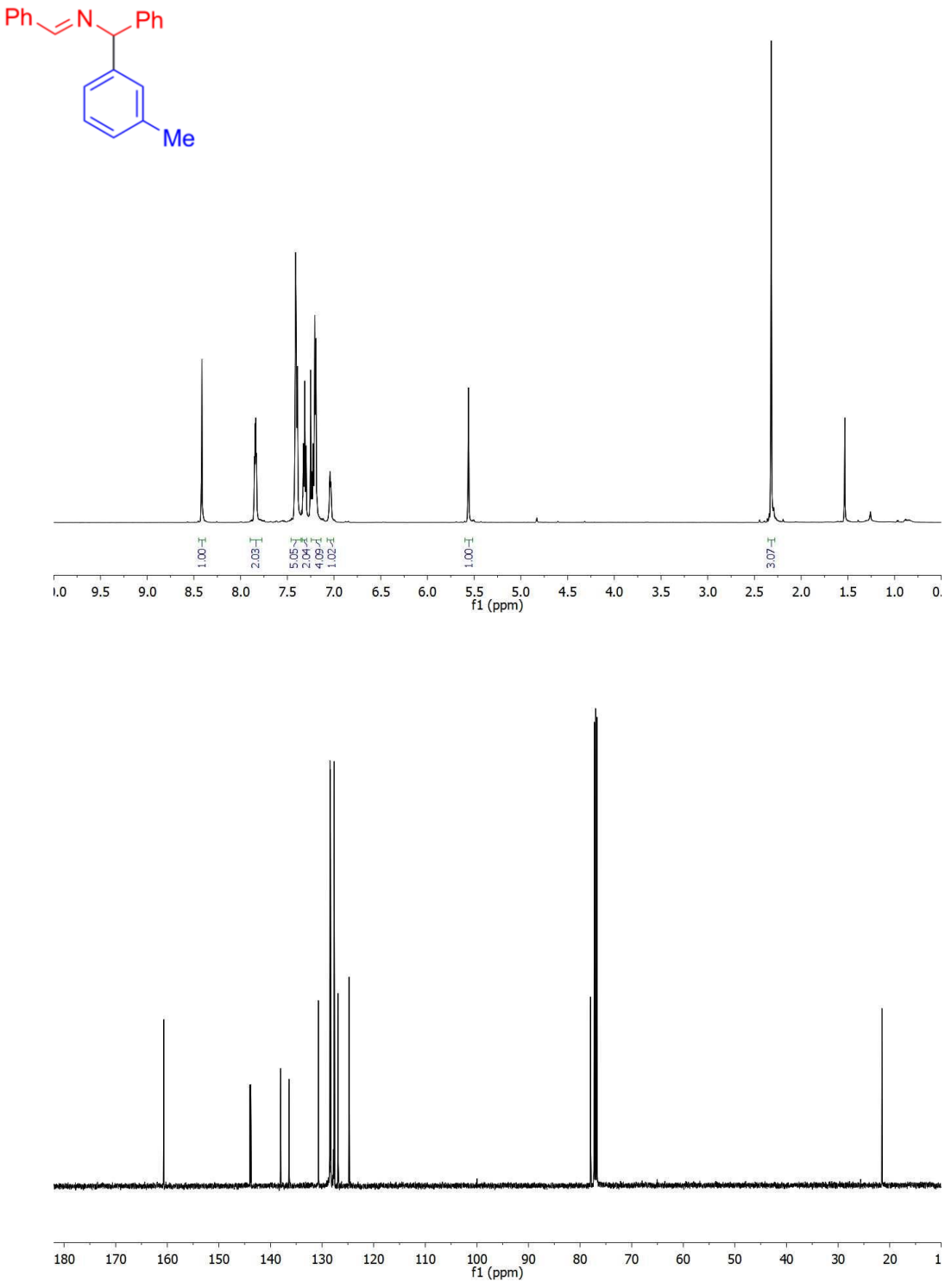


Figure A1.25 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.10ae in $CDCl_3$

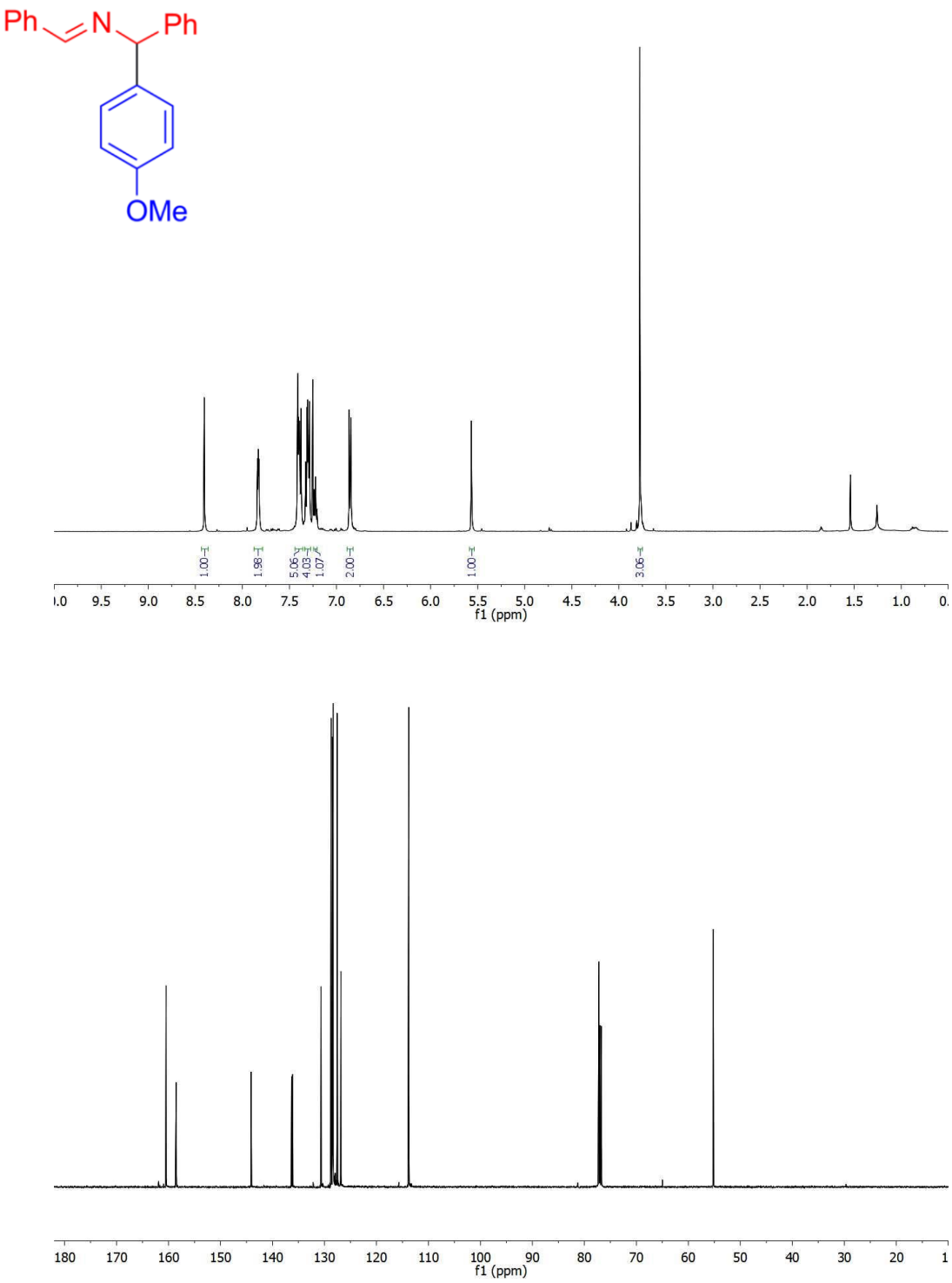


Figure A1.26 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10ag in $CDCl_3$

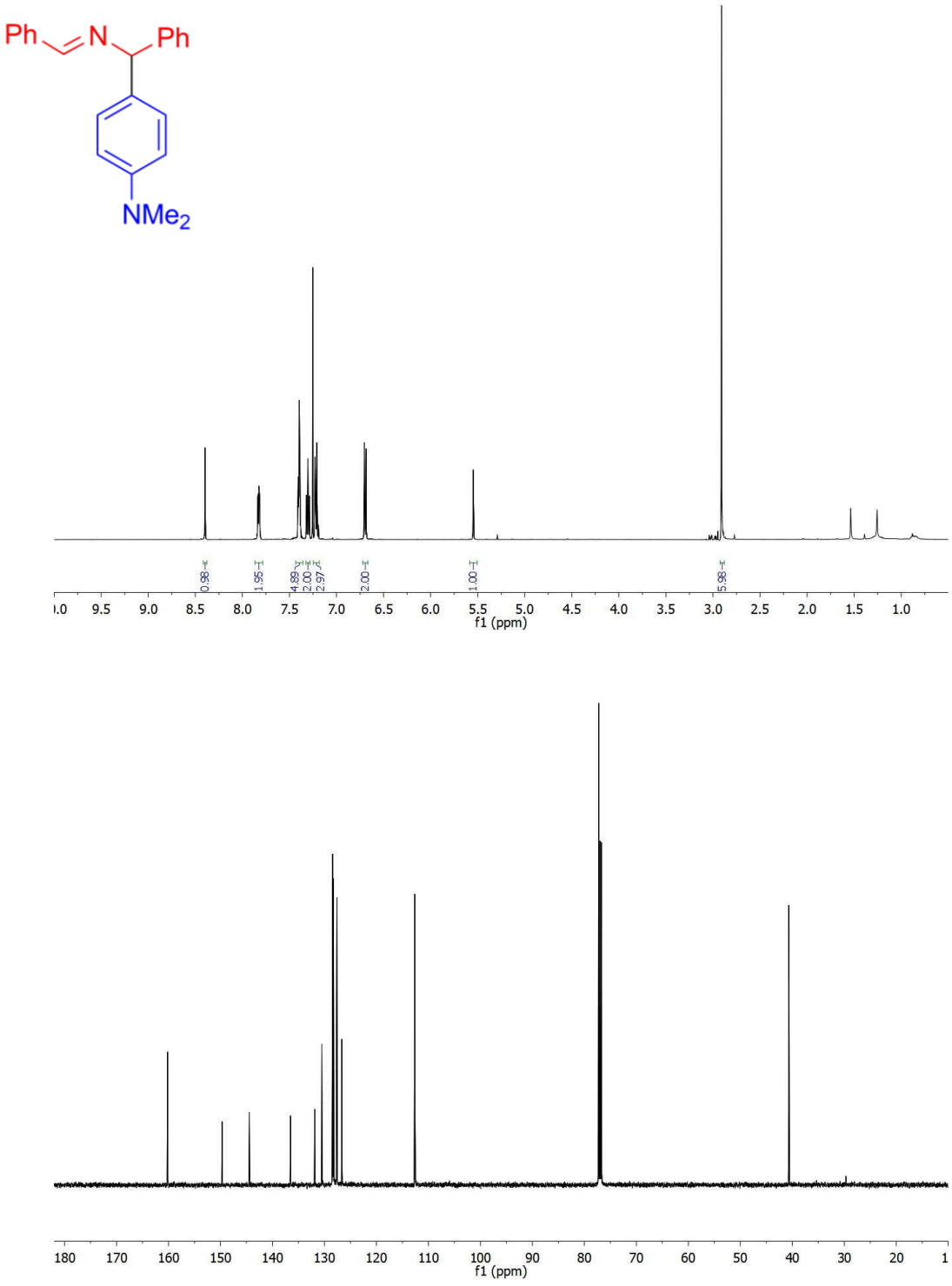


Figure A1.27 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.10af in $CDCl_3$

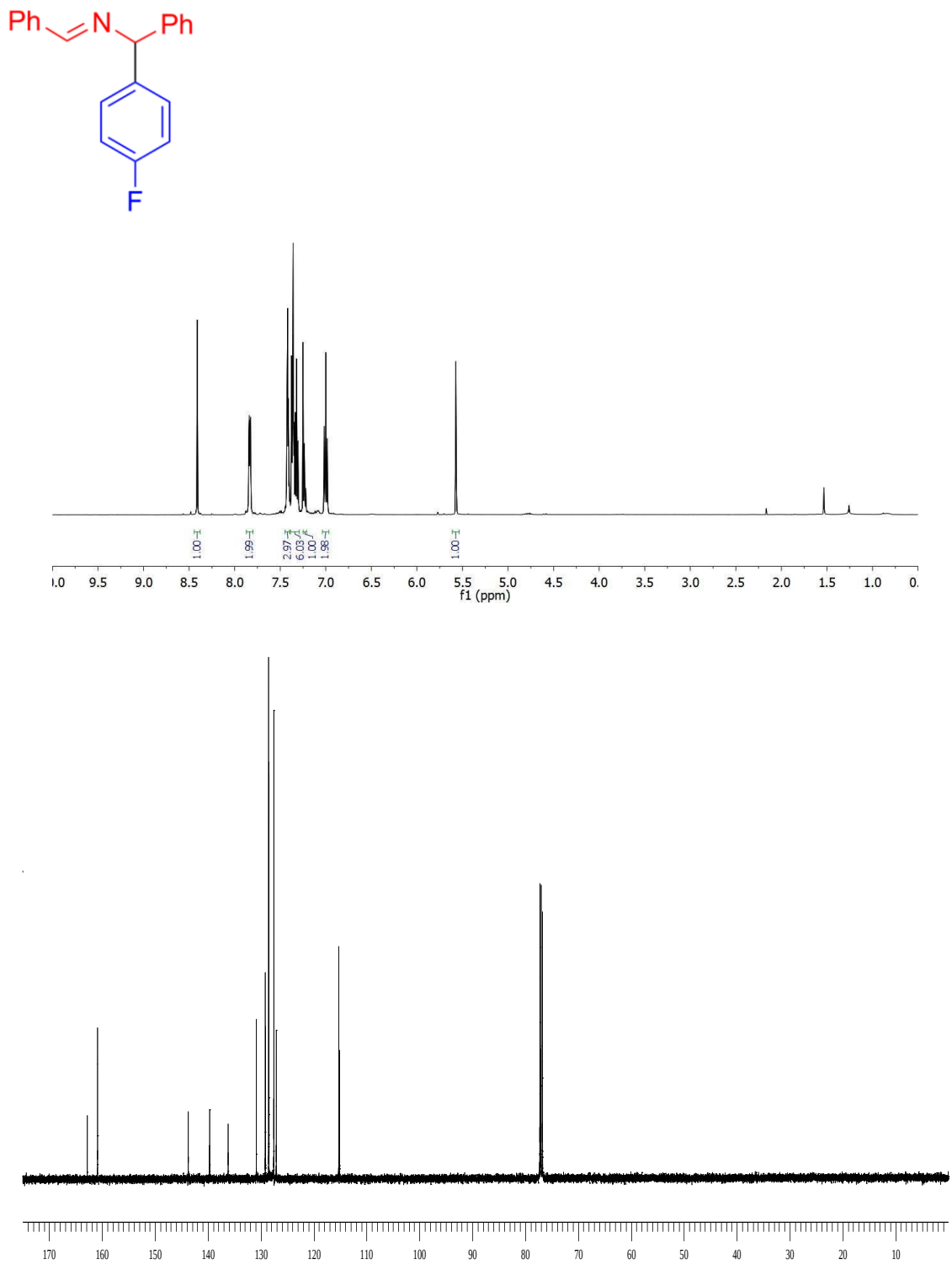


Figure A1.28 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10ai in $CDCl_3$

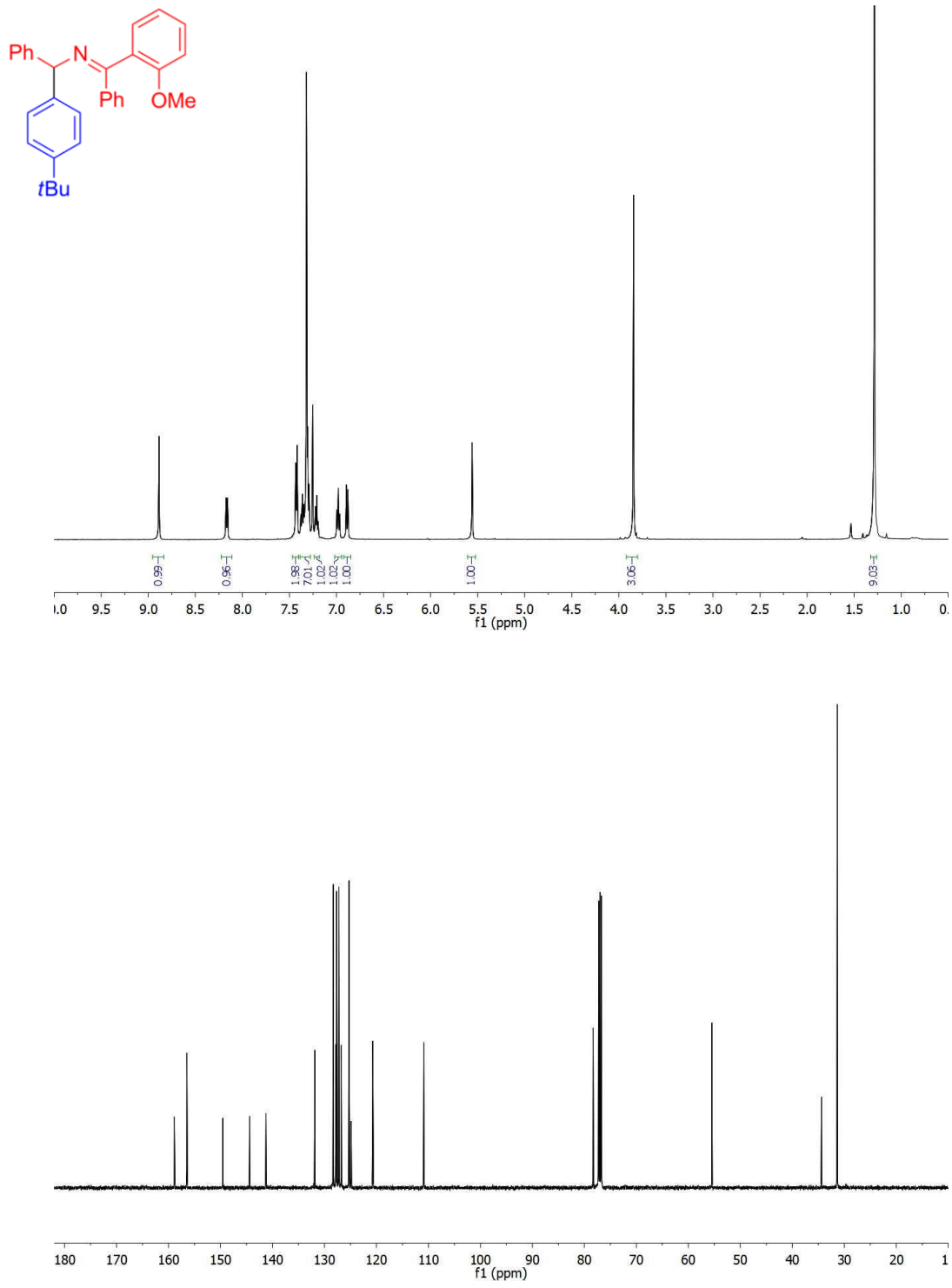


Figure A1.29 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10ba in $CDCl_3$

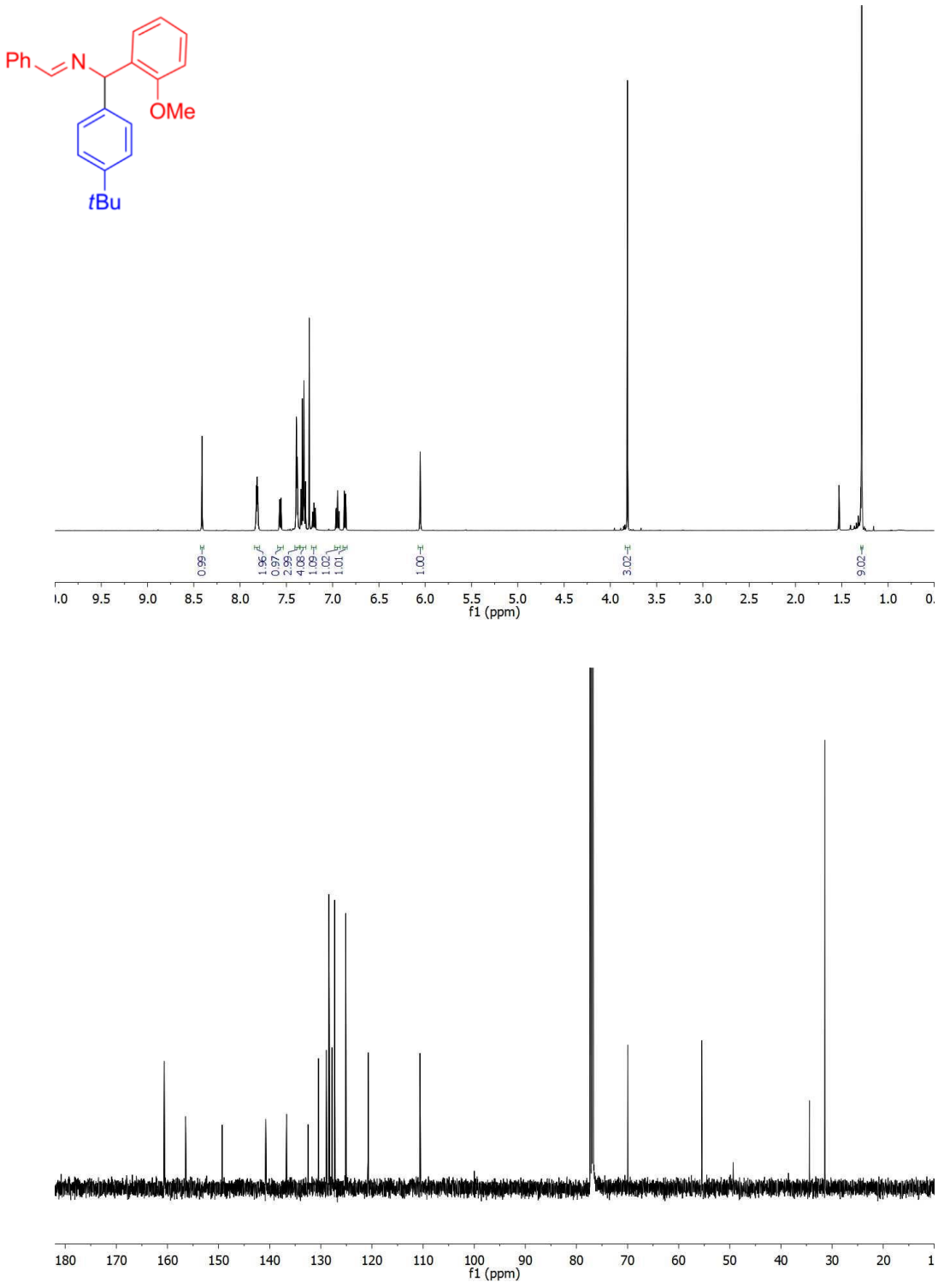


Figure A1.30 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10ba' in $CDCl_3$

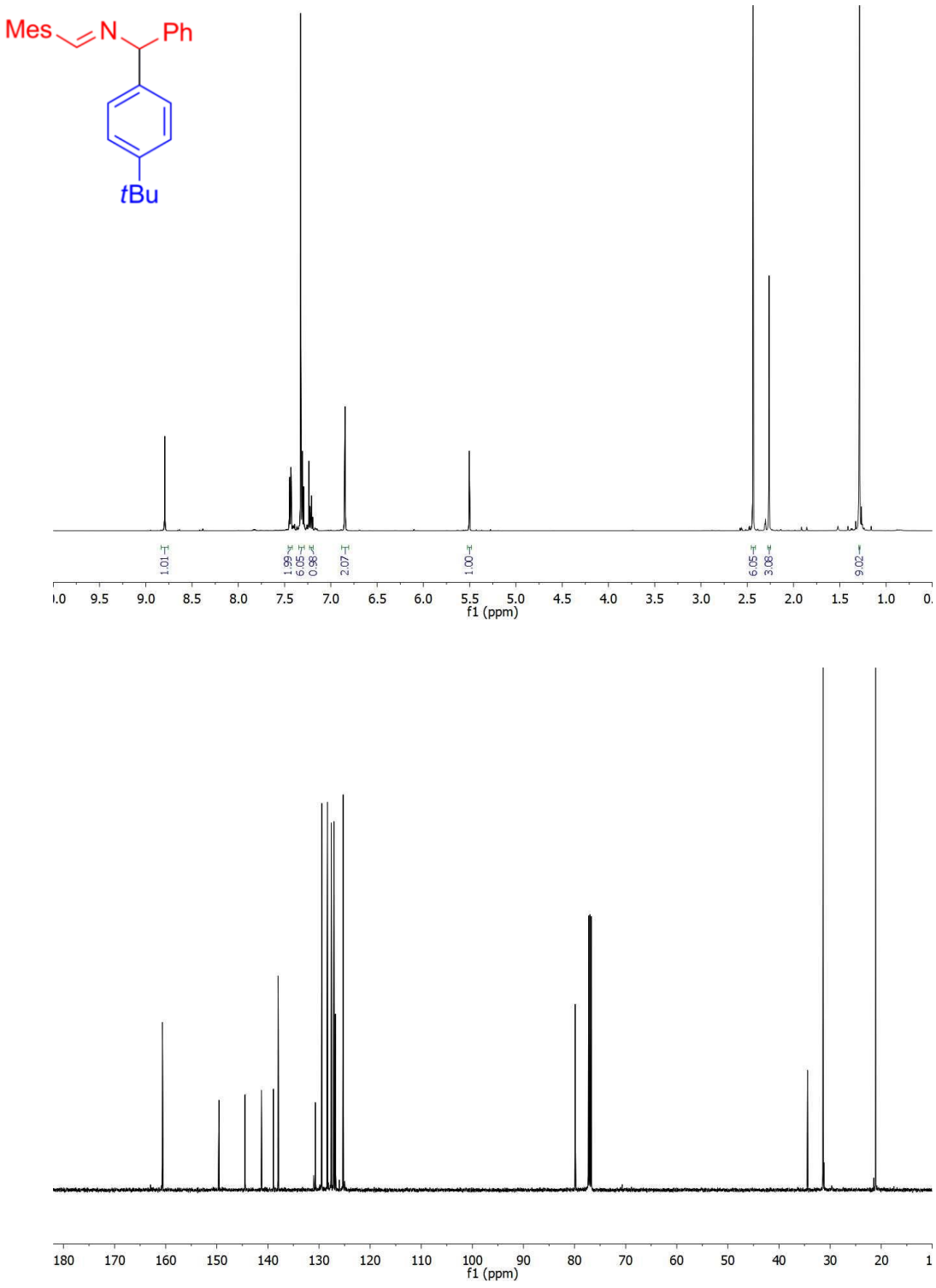


Figure A1.31 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10cc in $CDCl_3$

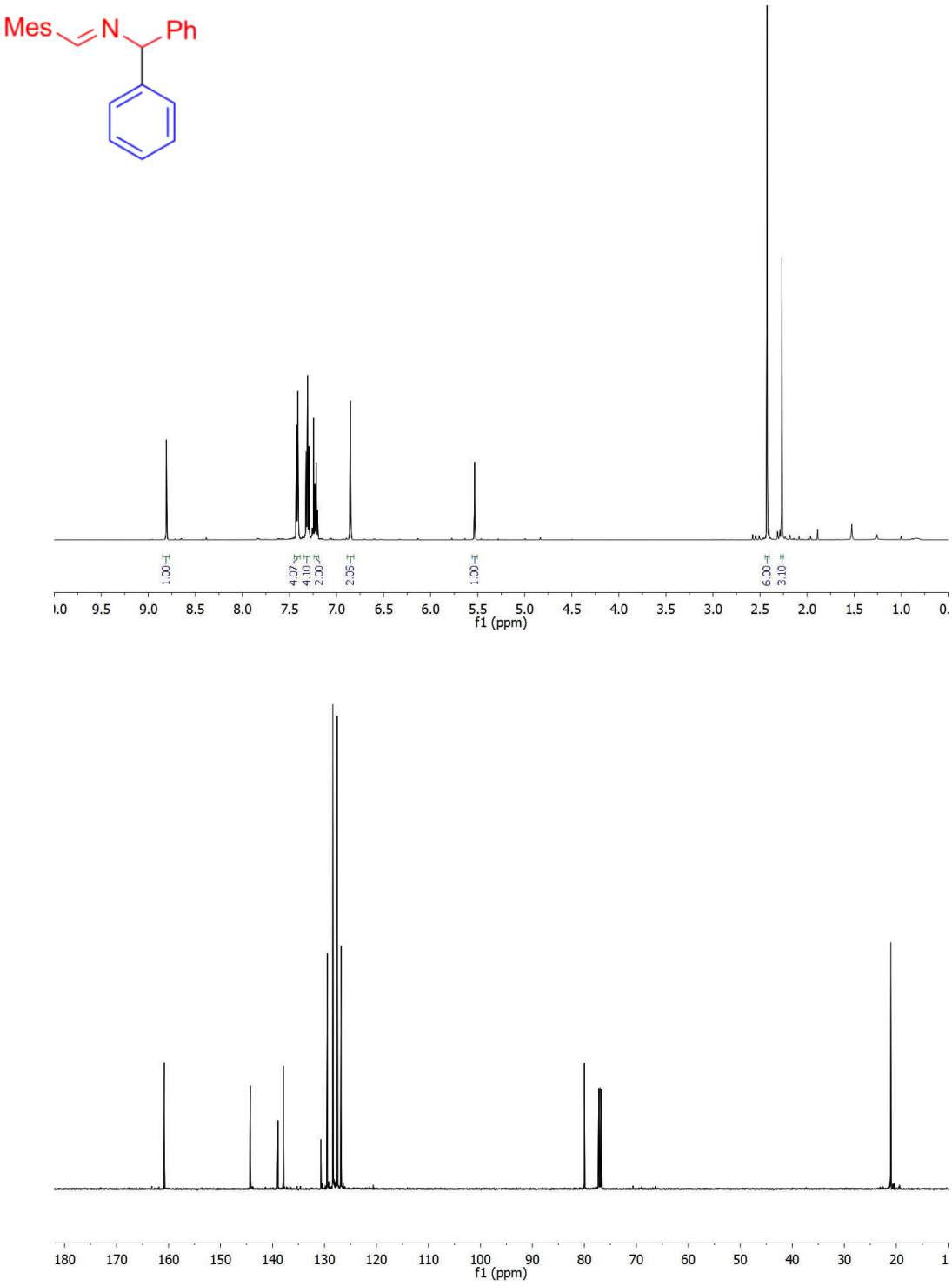


Figure A1.32 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10cb in $CDCl_3$

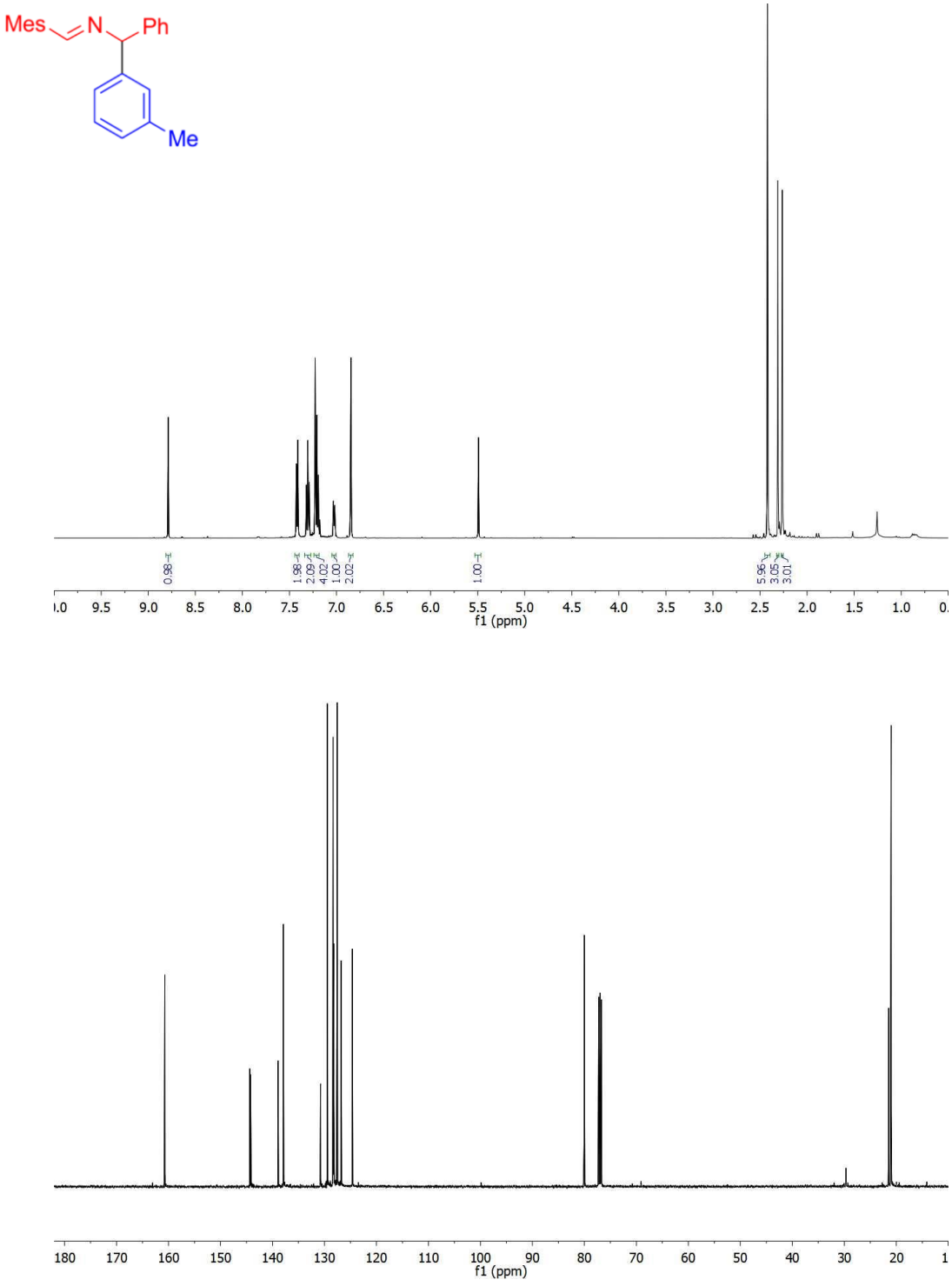


Figure A1.33 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10ce in $CDCl_3$

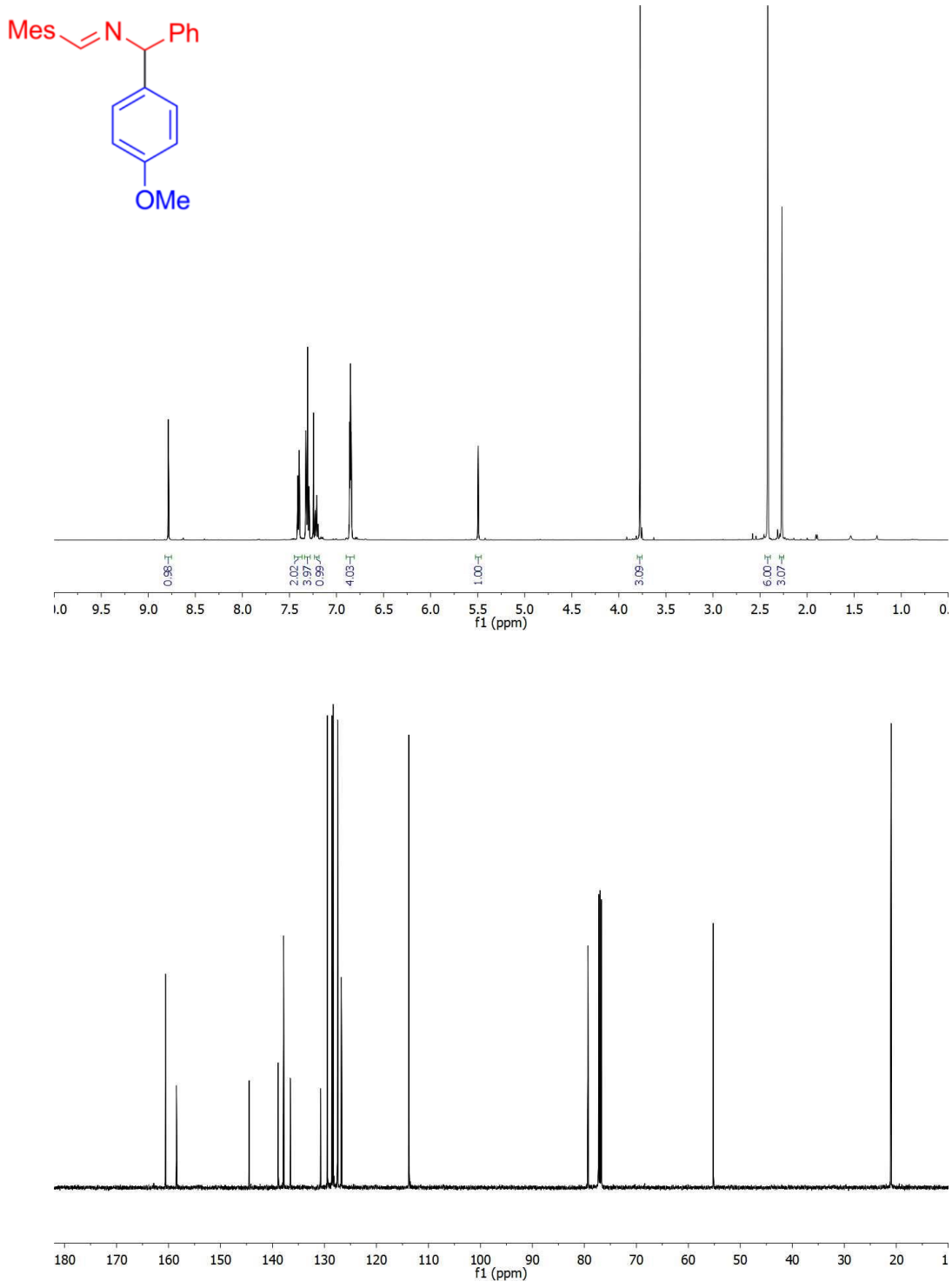


Figure A1.34 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10cg in $CDCl_3$

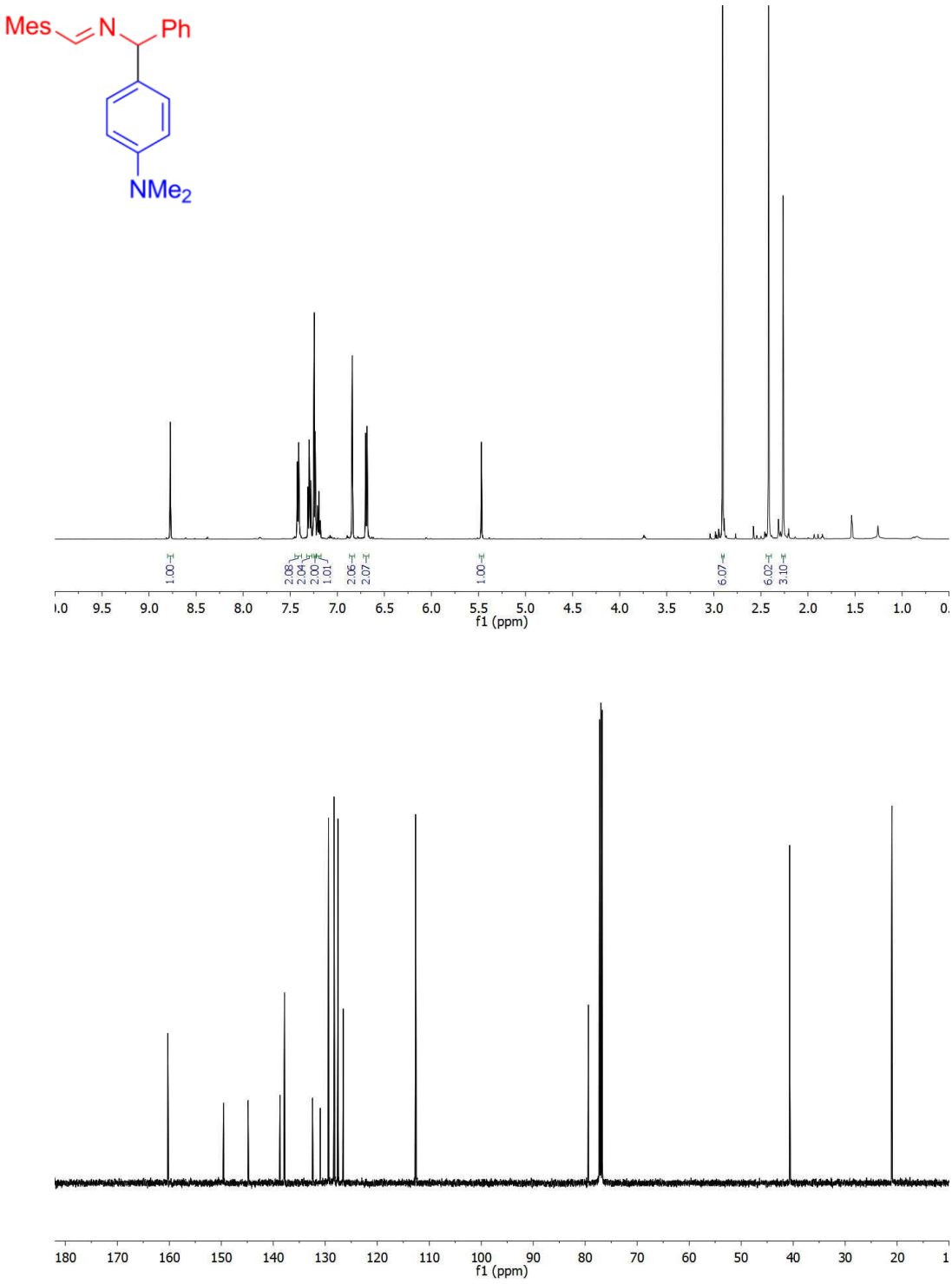


Figure A1.35 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10cf in $CDCl_3$

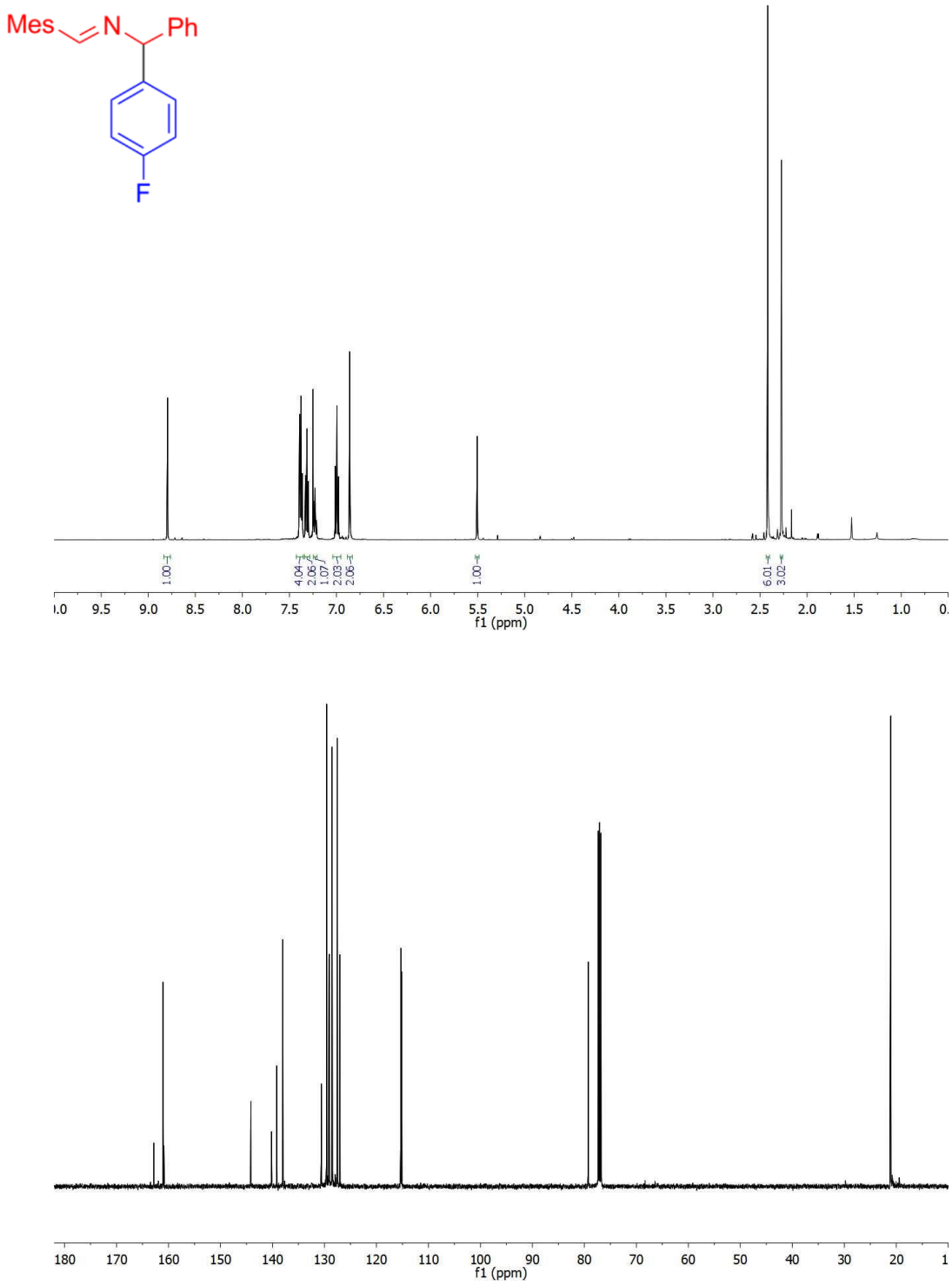


Figure A1.36 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10ci in $CDCl_3$

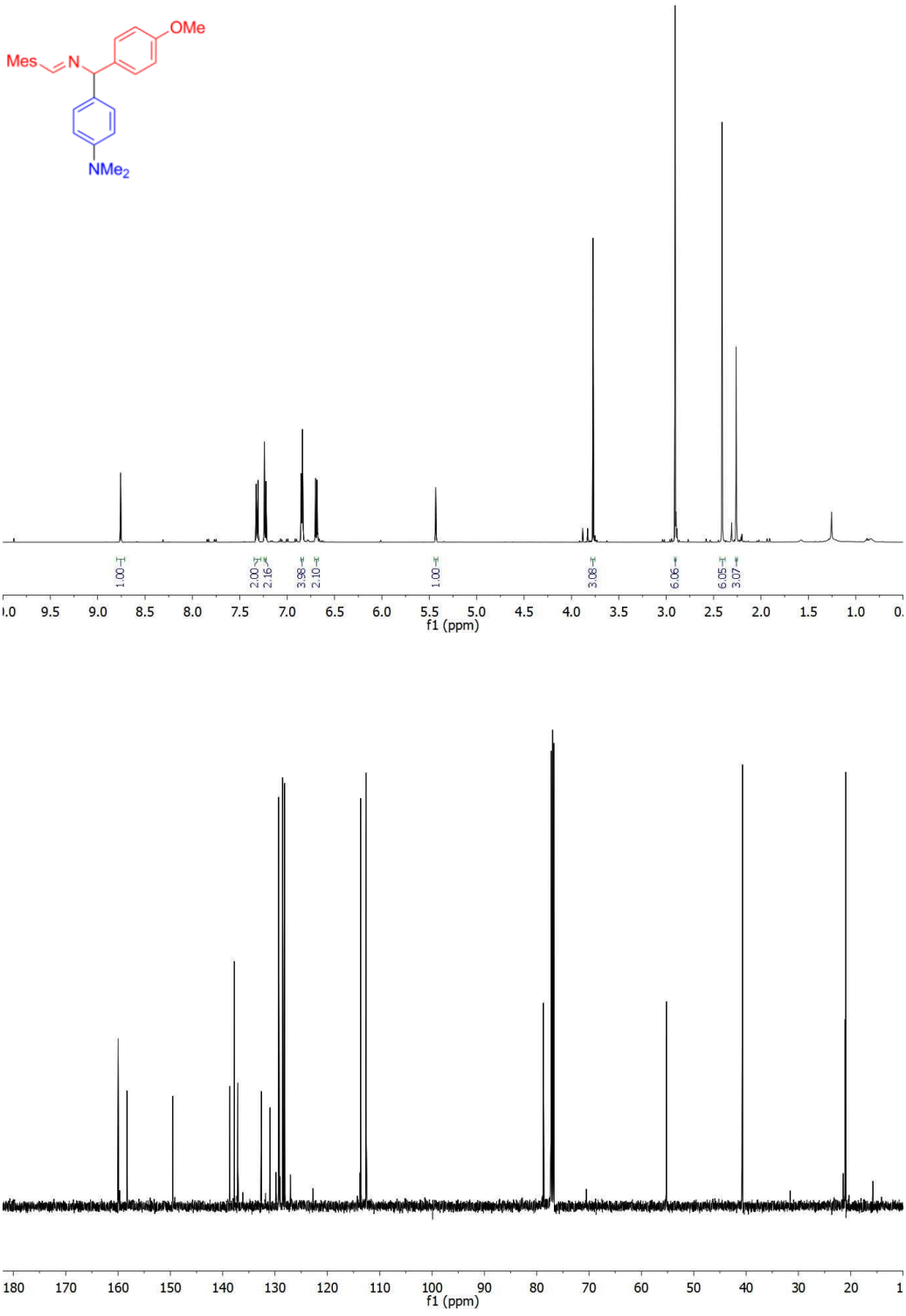


Figure A1.37 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10df in $CDCl_3$

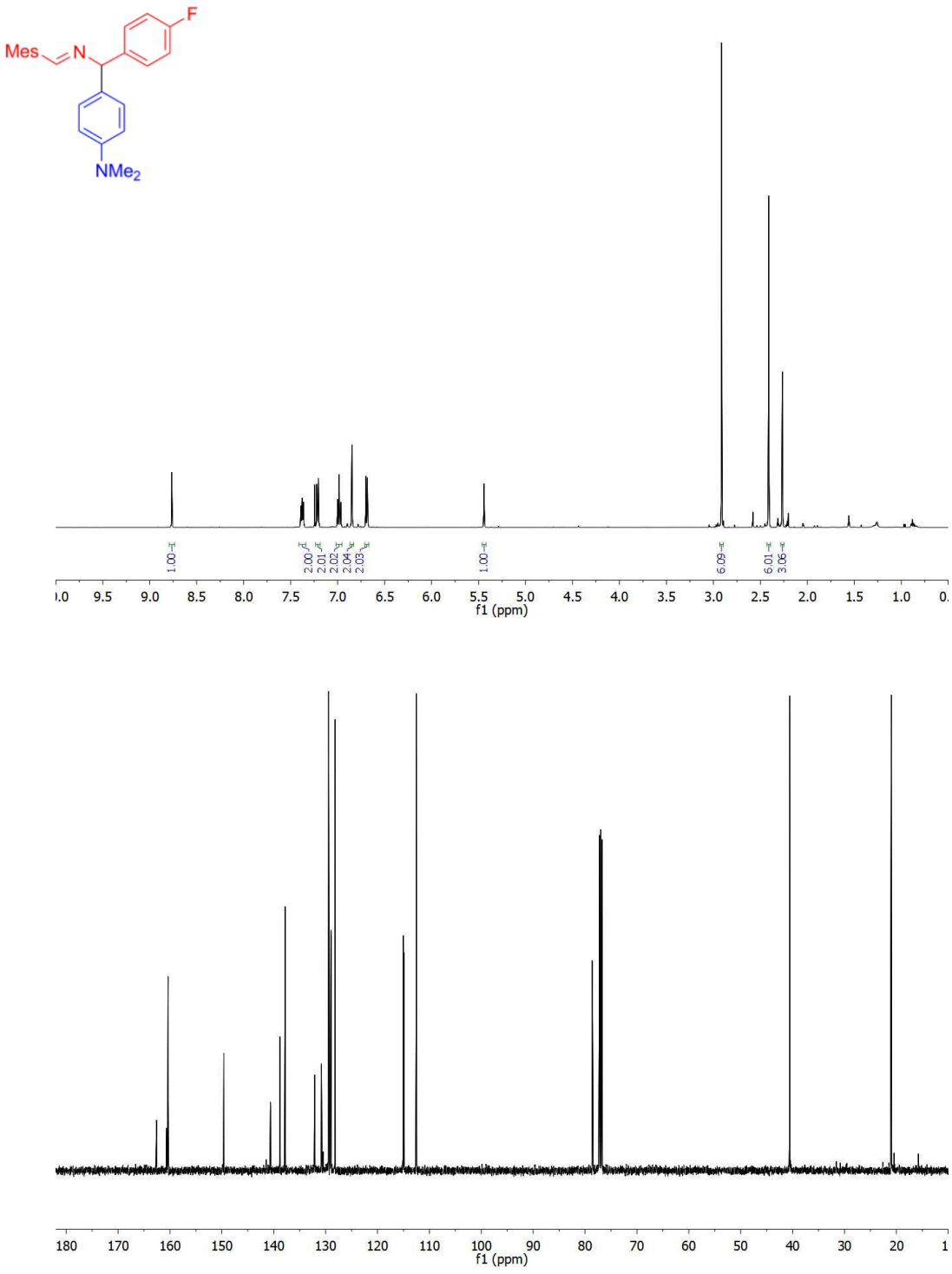


Figure A1.38 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10ef in $CDCl_3$

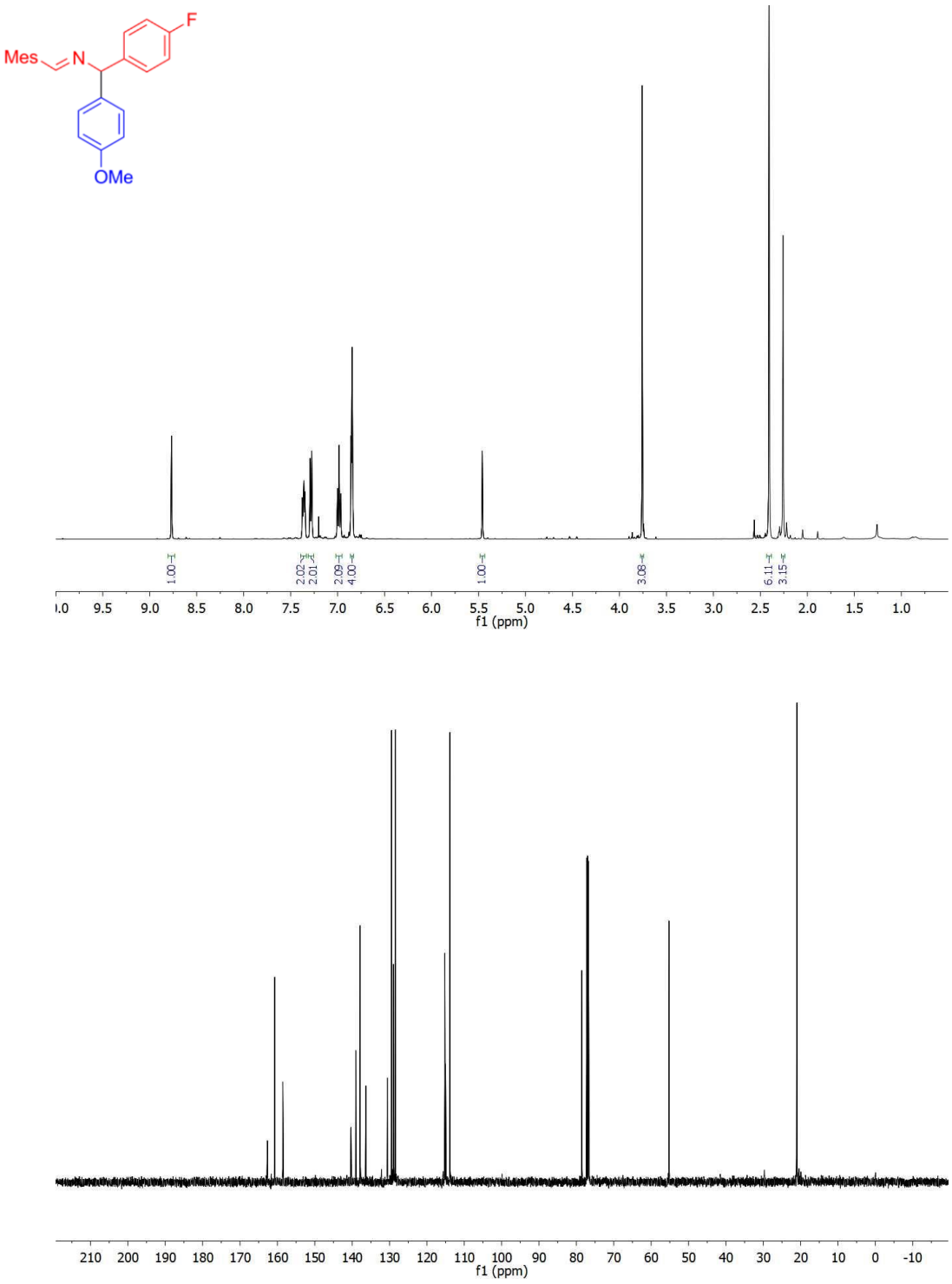


Figure A1.39 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10eg in $CDCl_3$

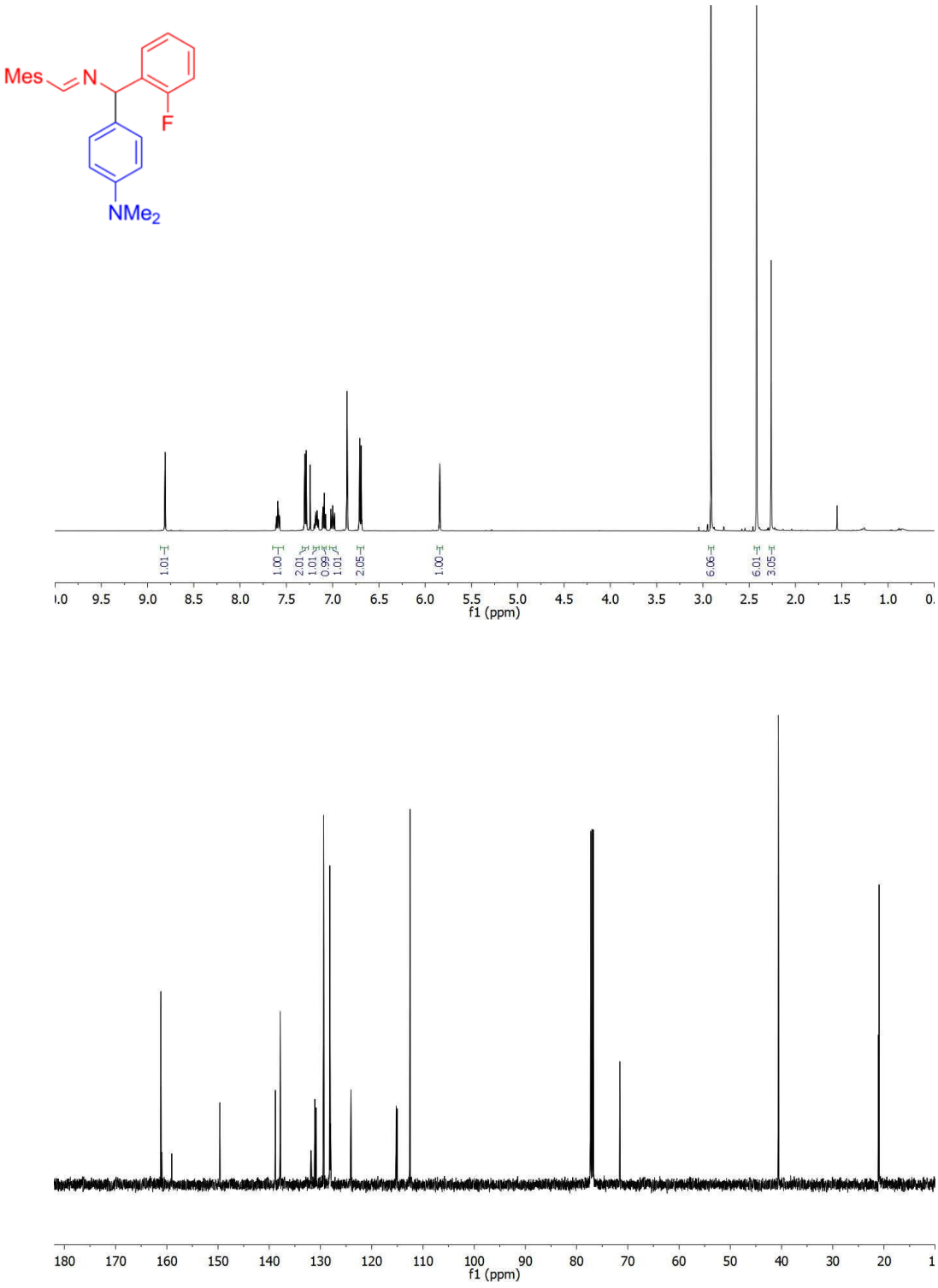


Figure A1.40 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.10ff in $CDCl_3$

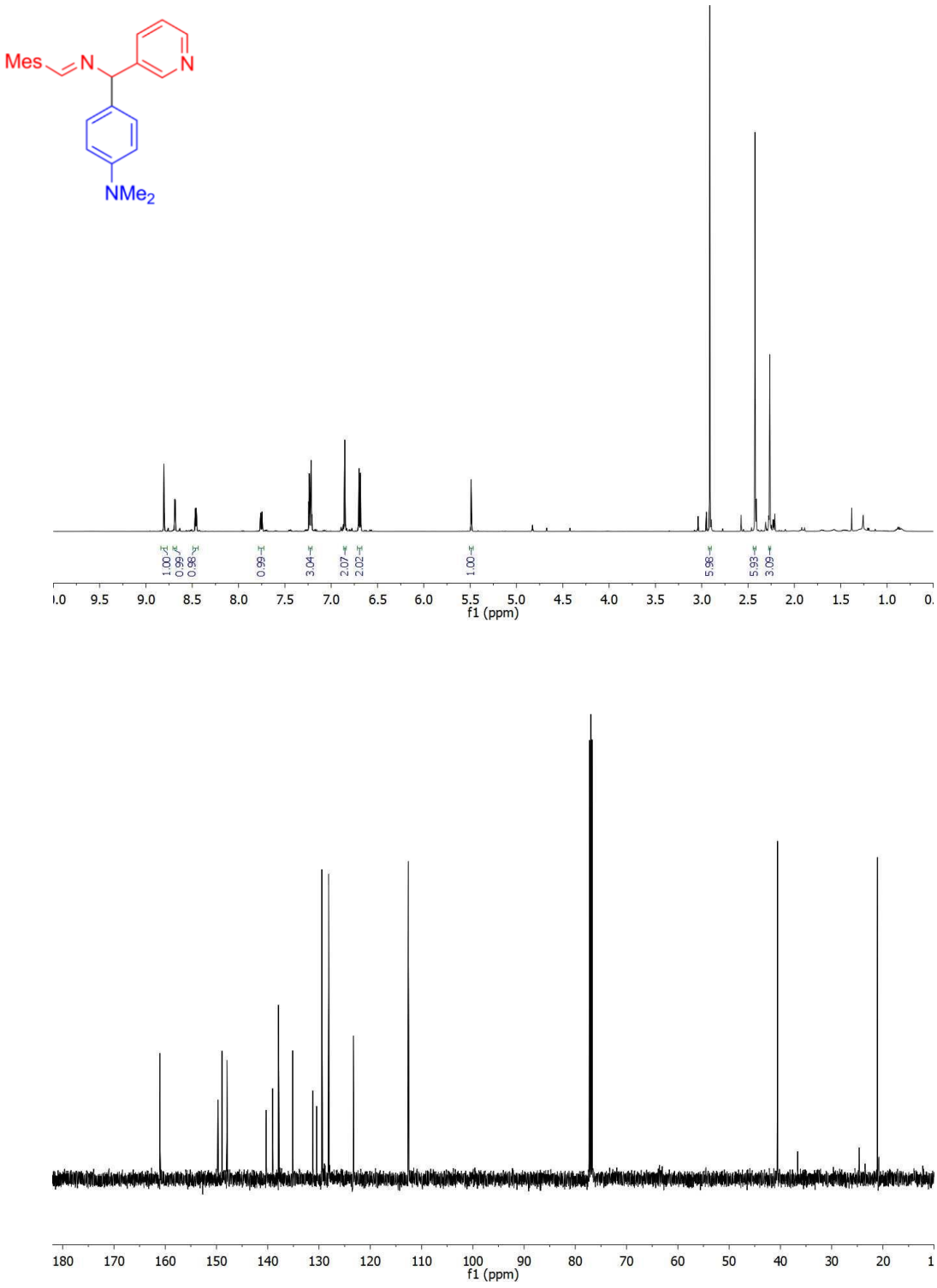


Figure A1.41 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.10gf in $CDCl_3$

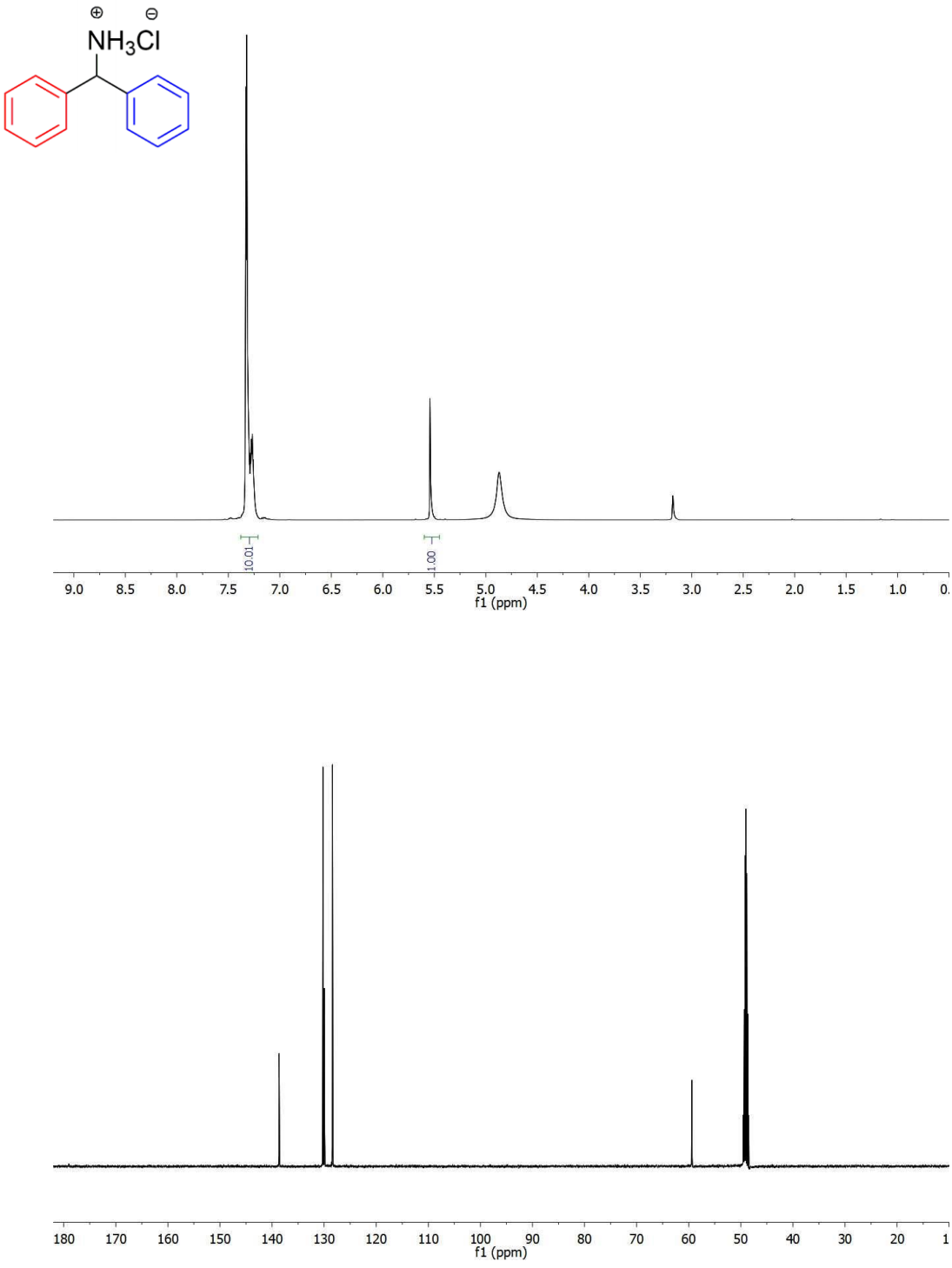


Figure A1.42 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.7a in $CDCl_3$

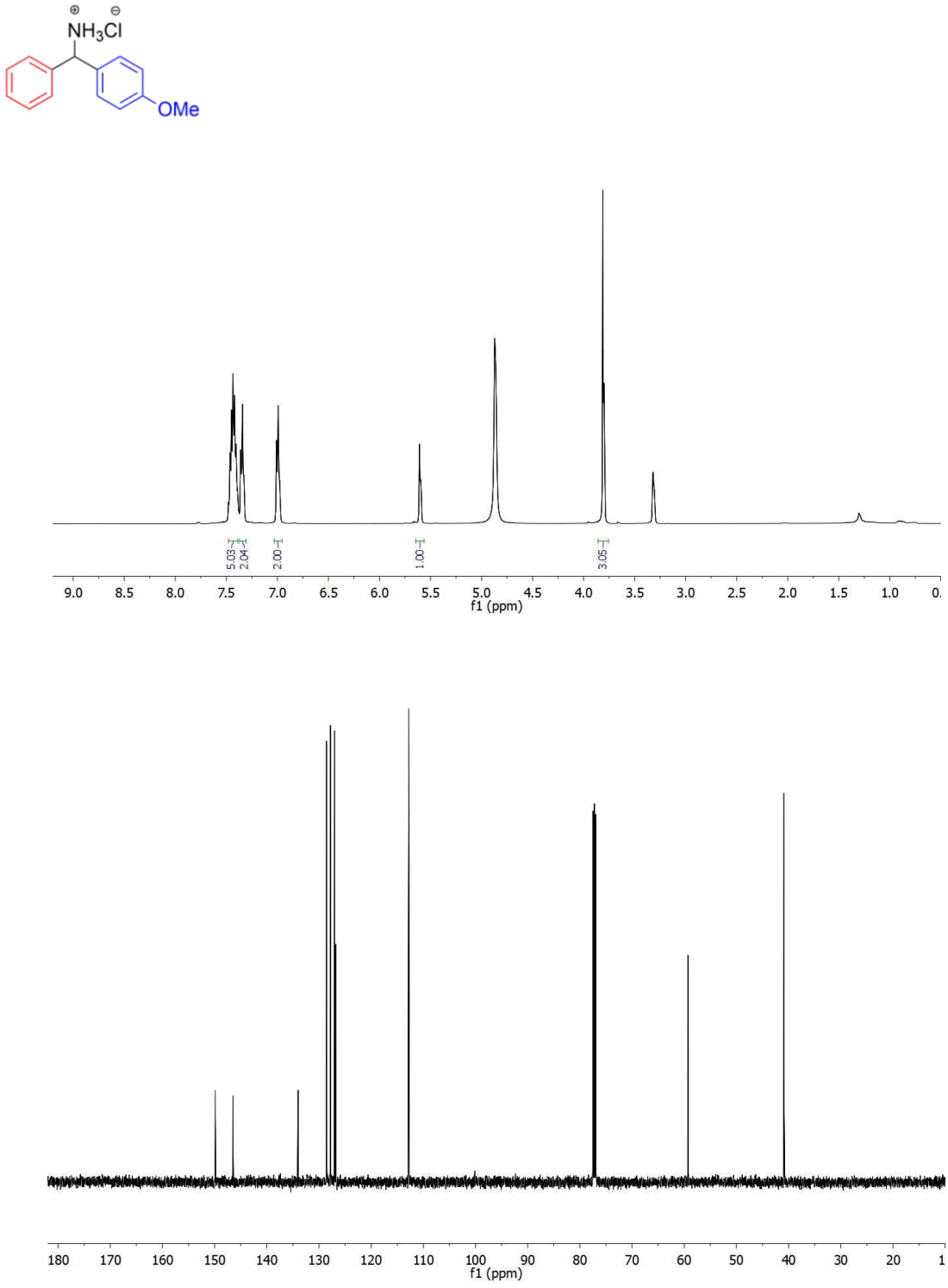


Figure A1.43 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.7b in $CDCl_3$

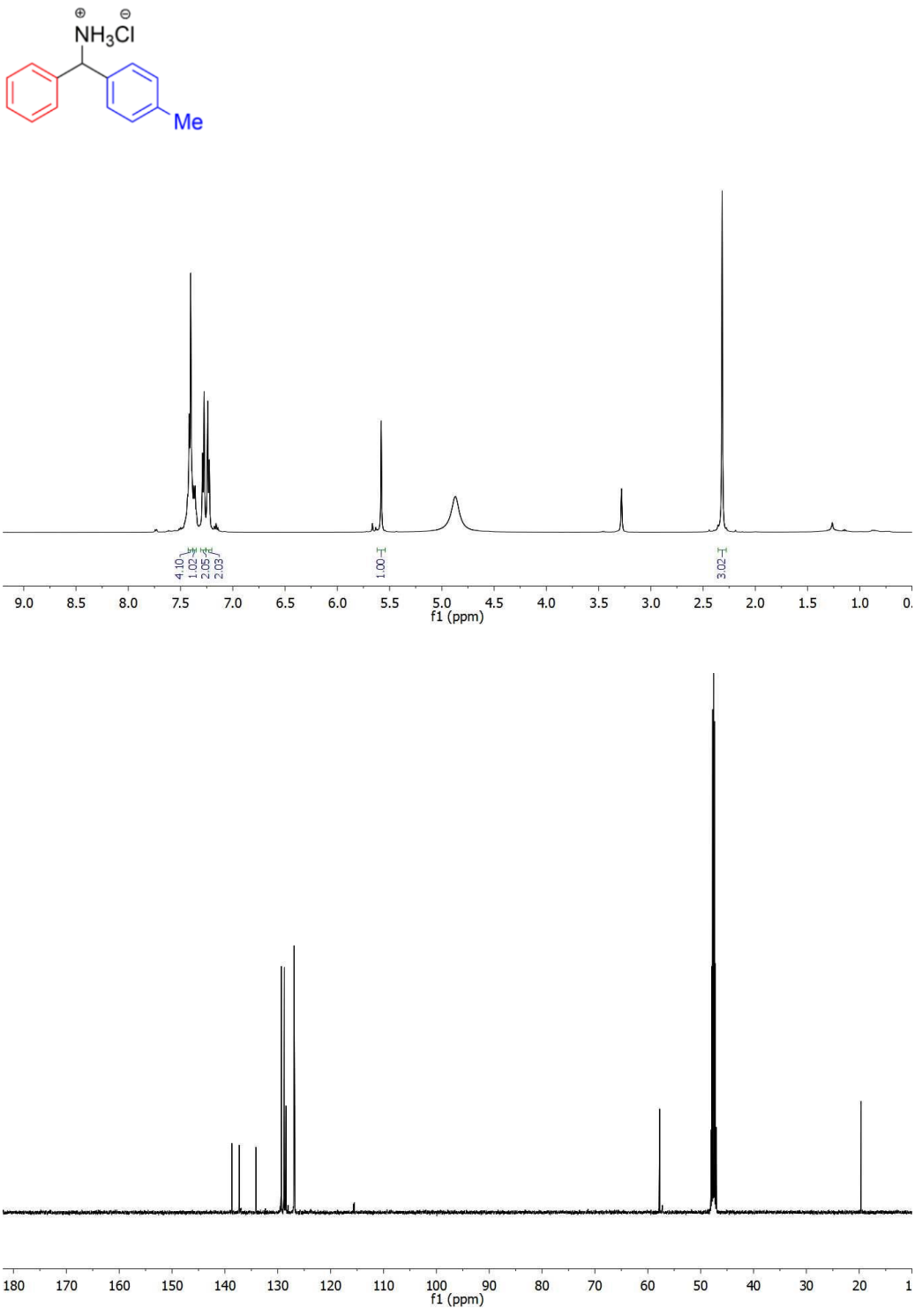


Figure A1.44 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.7c in $CDCl_3$

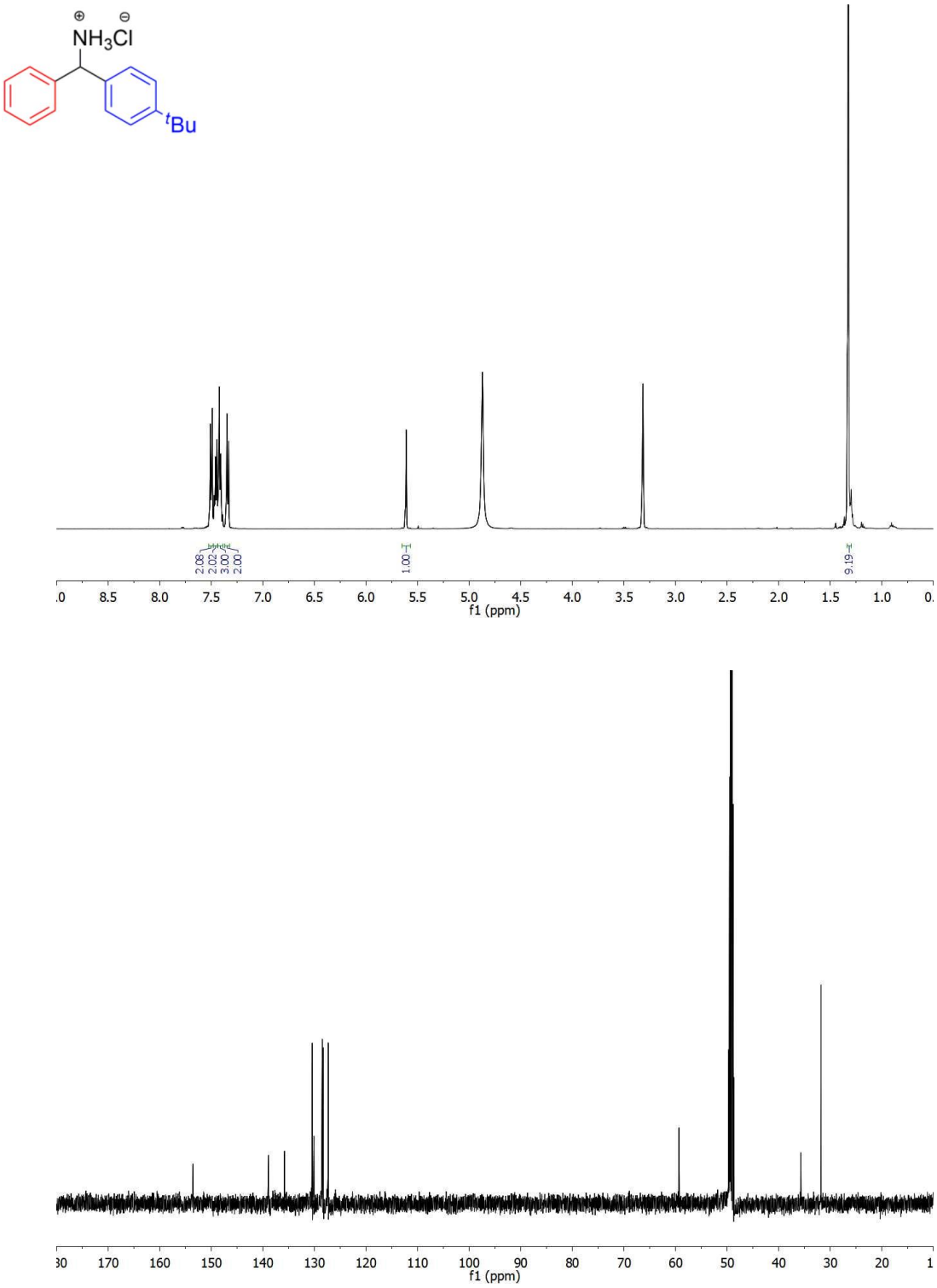


Figure A1.45 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.7d in $CDCl_3$

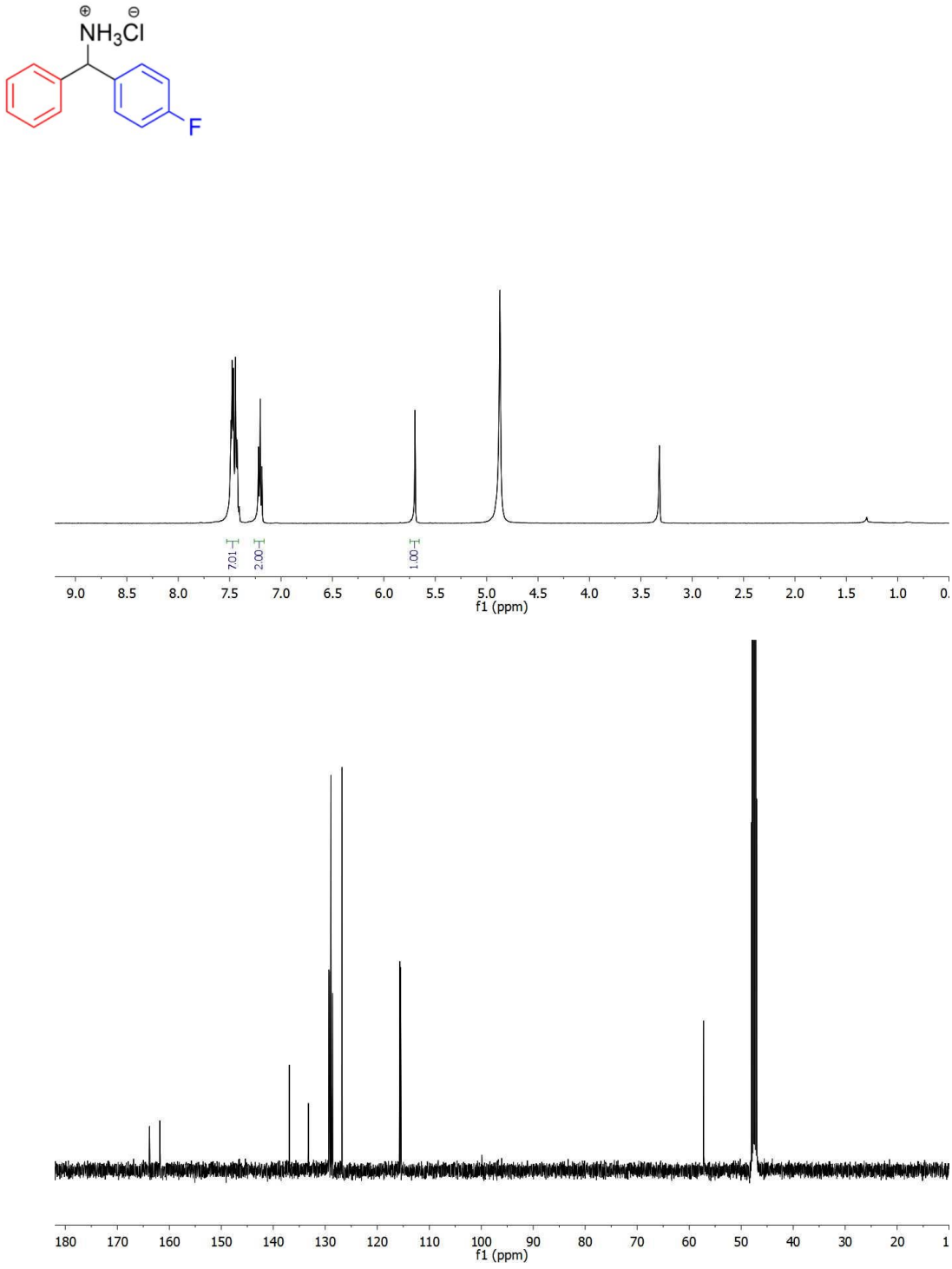


Figure A1.46 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.7e in $CDCl_3$

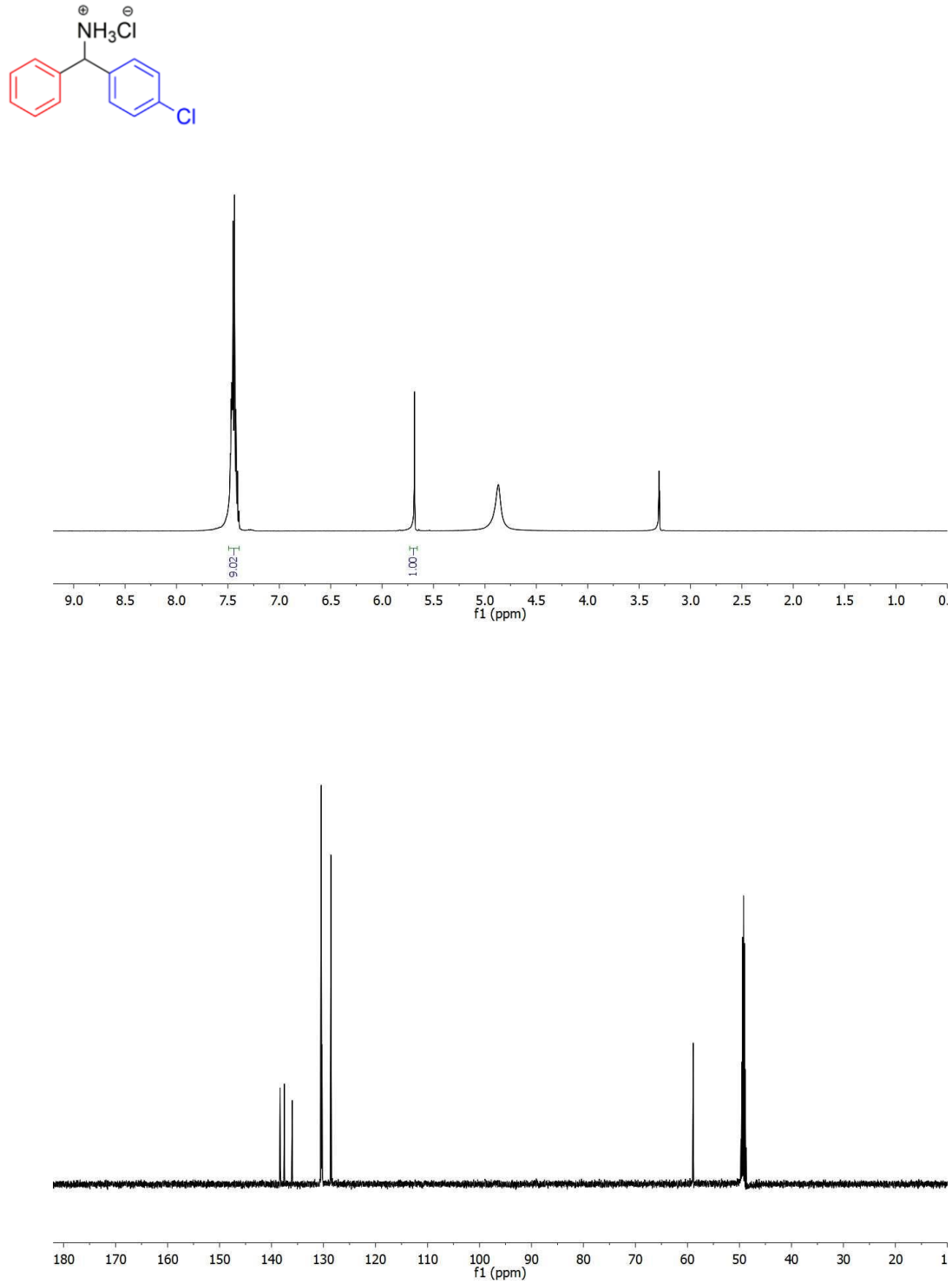


Figure A1.47 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.7f in $CDCl_3$

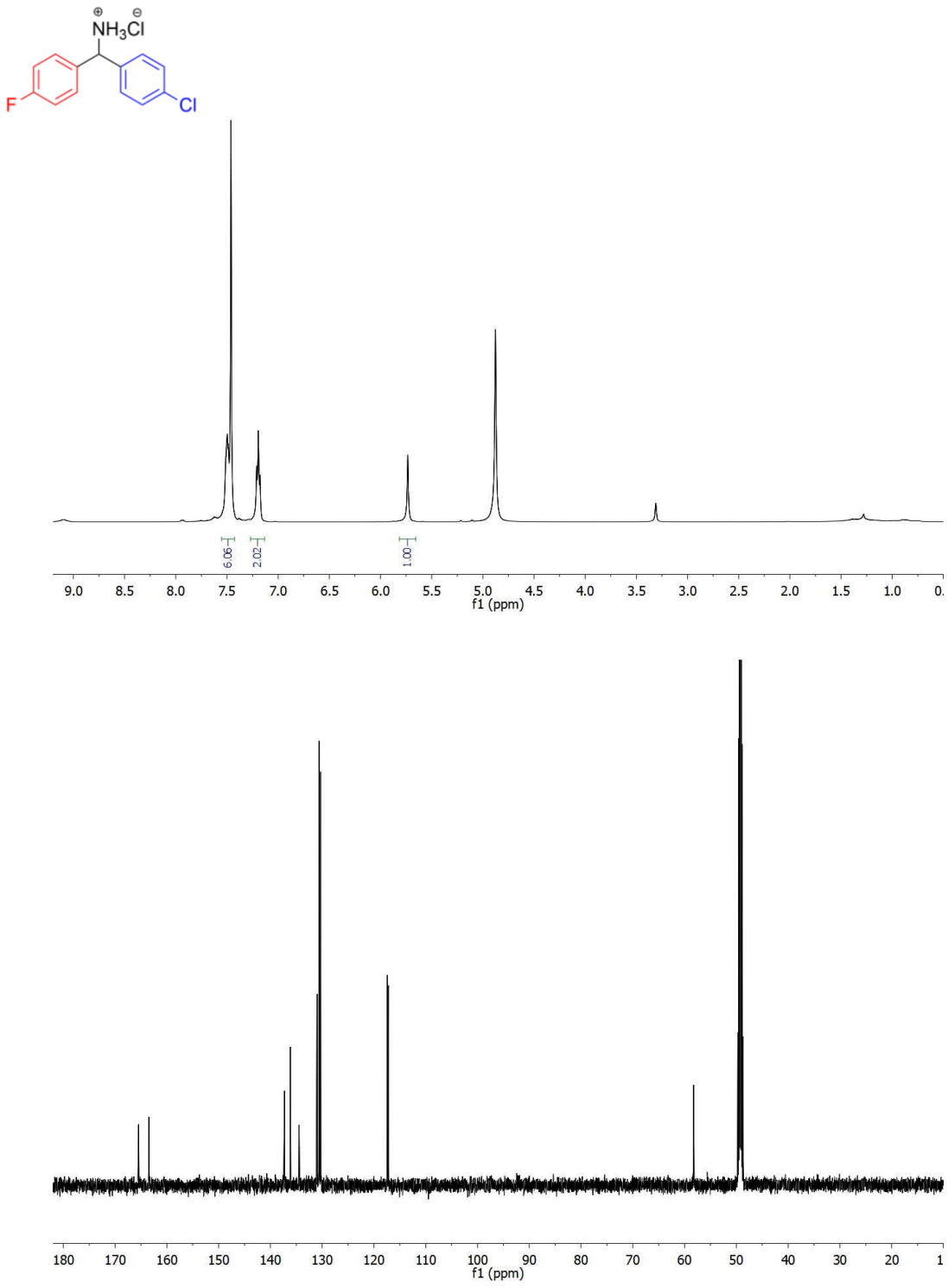


Figure A1.48 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.7g in $CDCl_3$

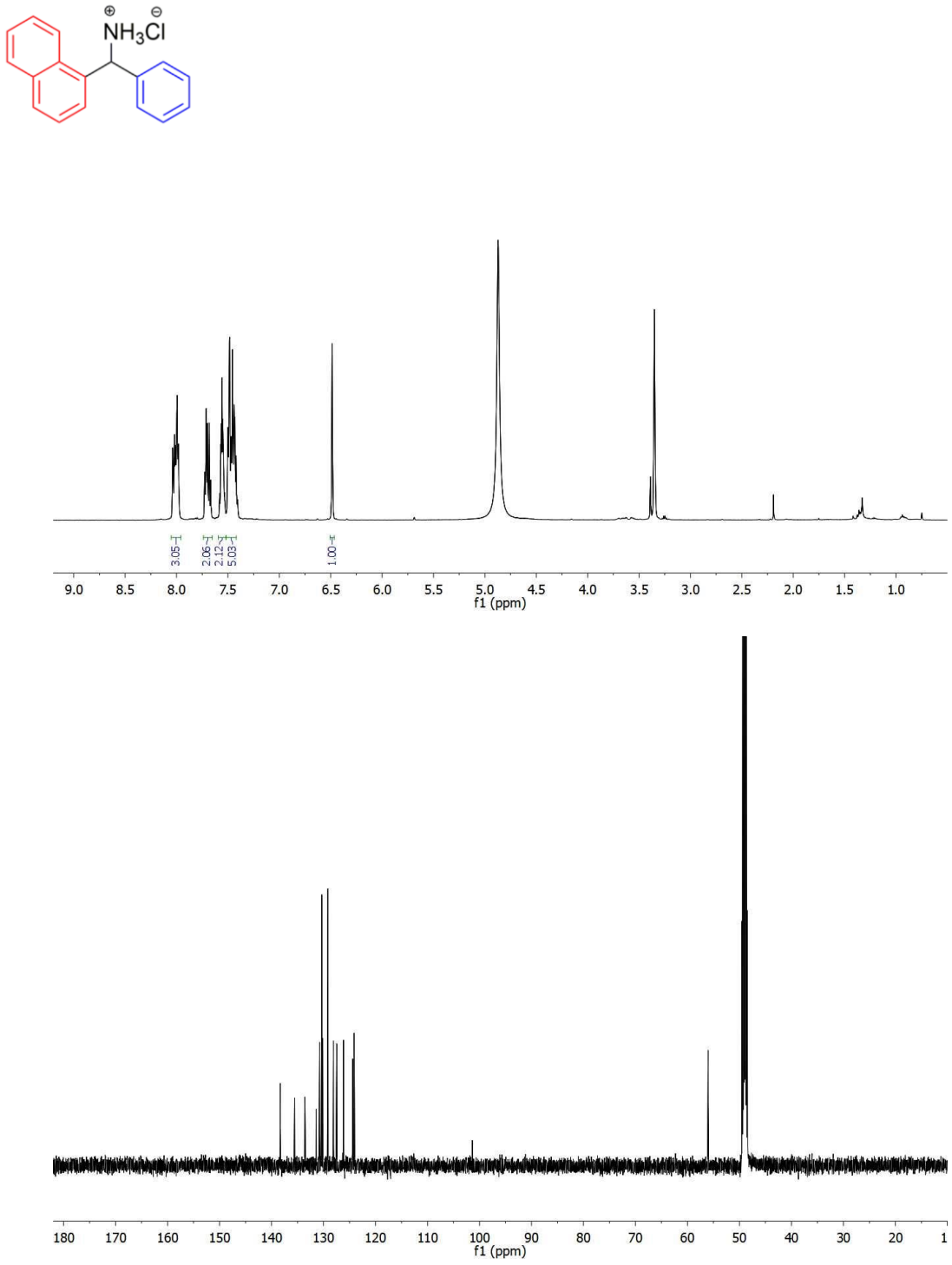


Figure A1.49 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 1.7h in $CDCl_3$

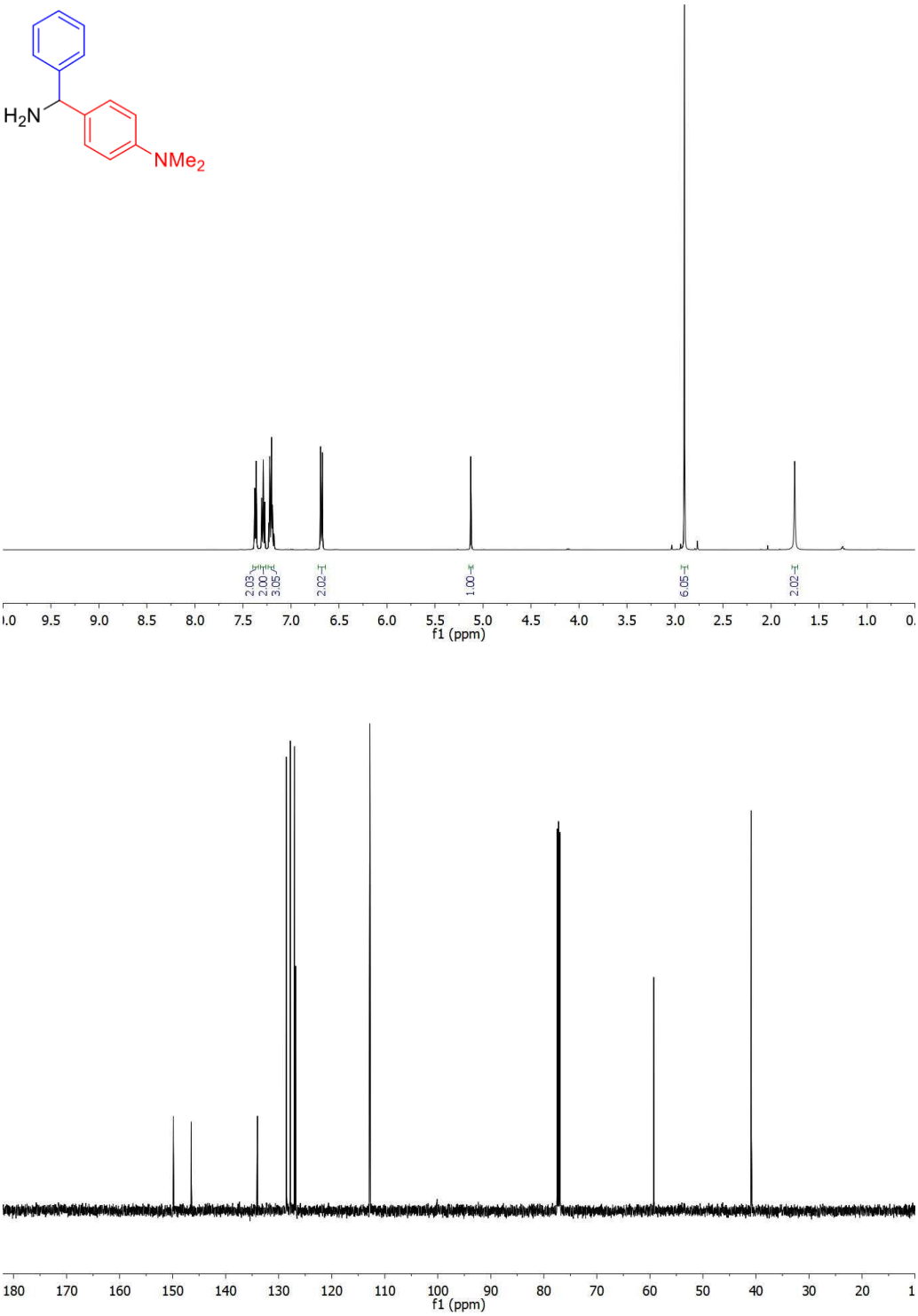
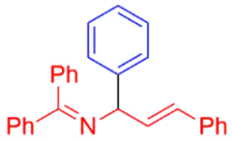


Figure A1.50 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 1.12af in $CDCl_3$

Appendix A2. NMR Spectra Relevant to Chapter 2.



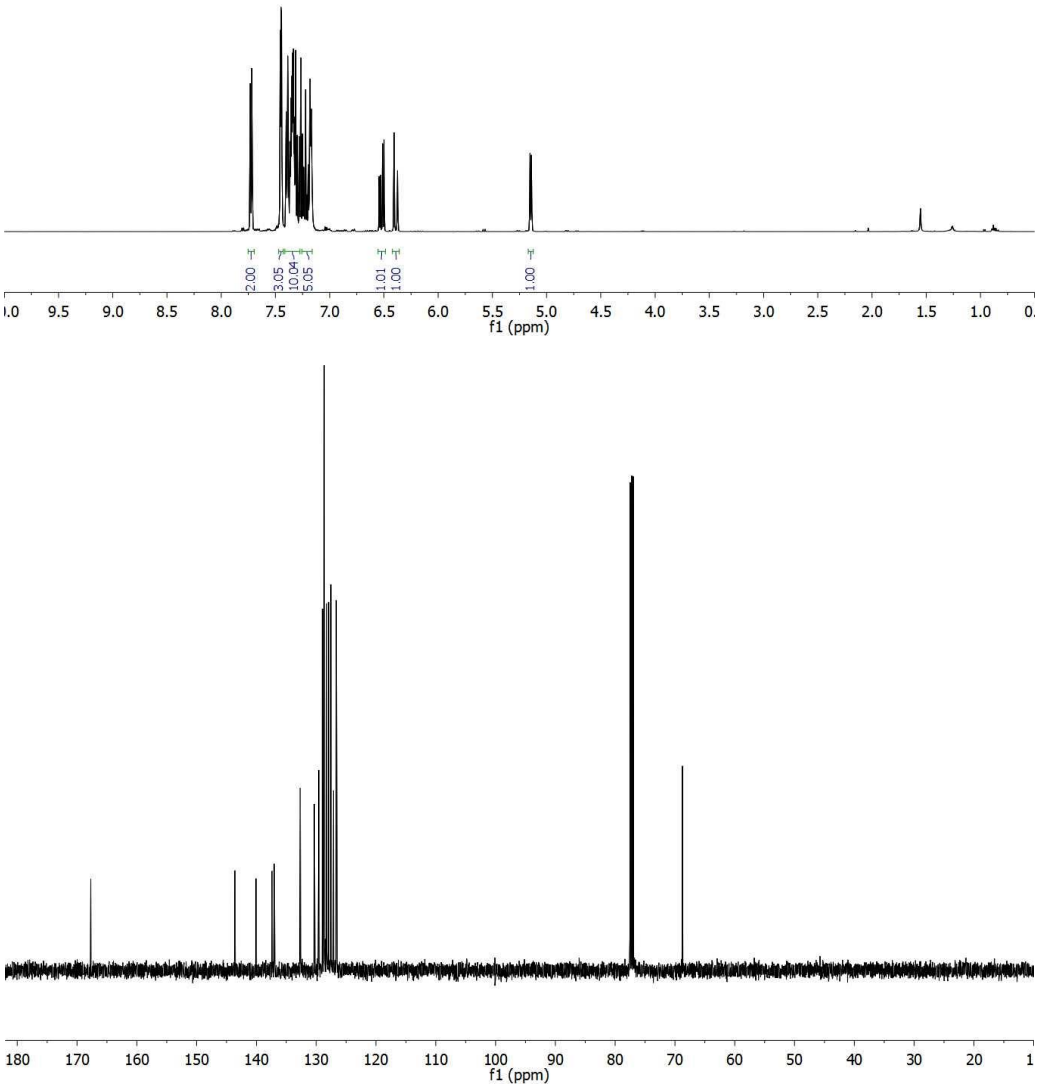


Figure A2.1 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.3aa in $CDCl_3$

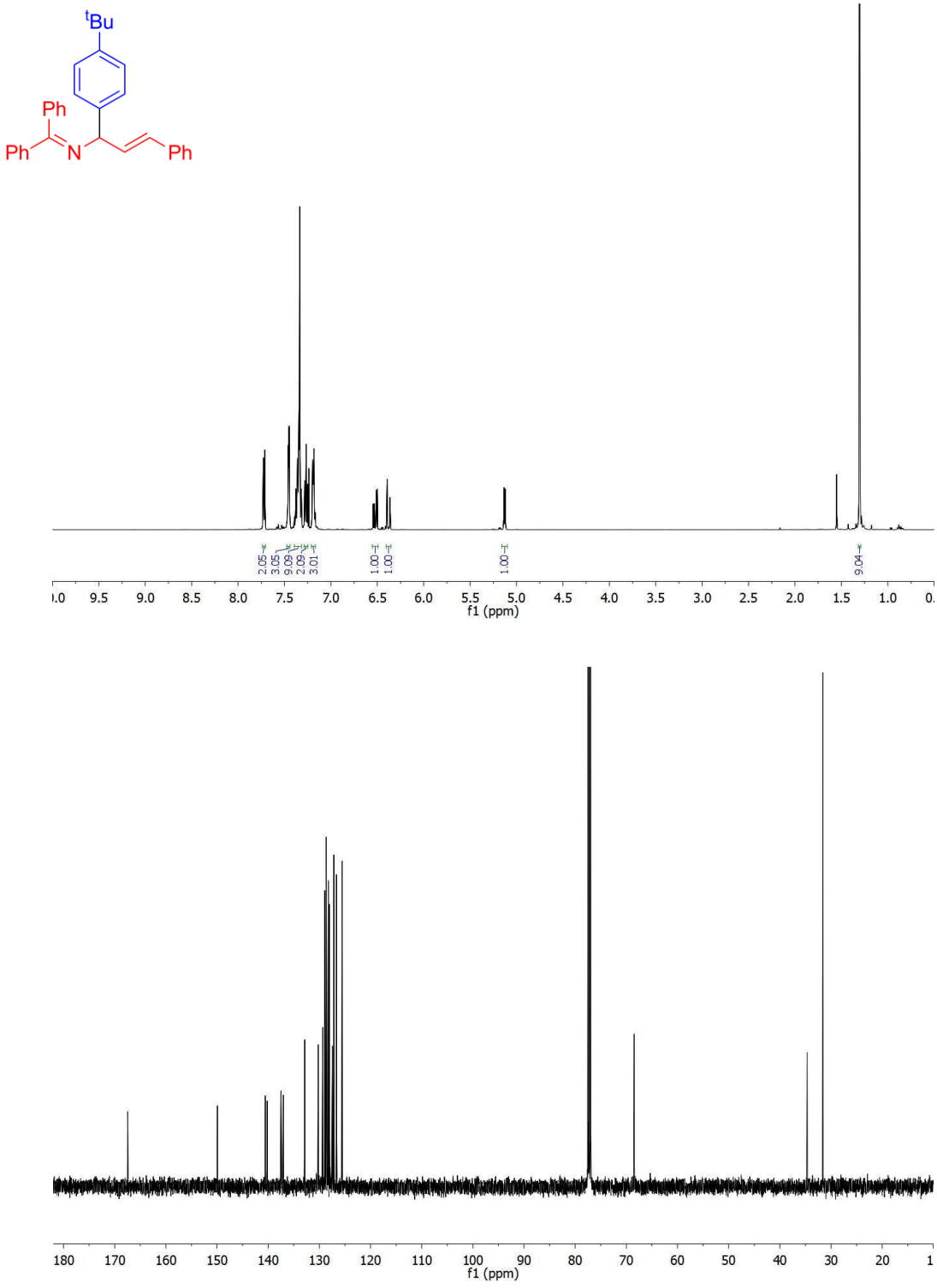


Figure A2.2 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.3ab in $CDCl_3$

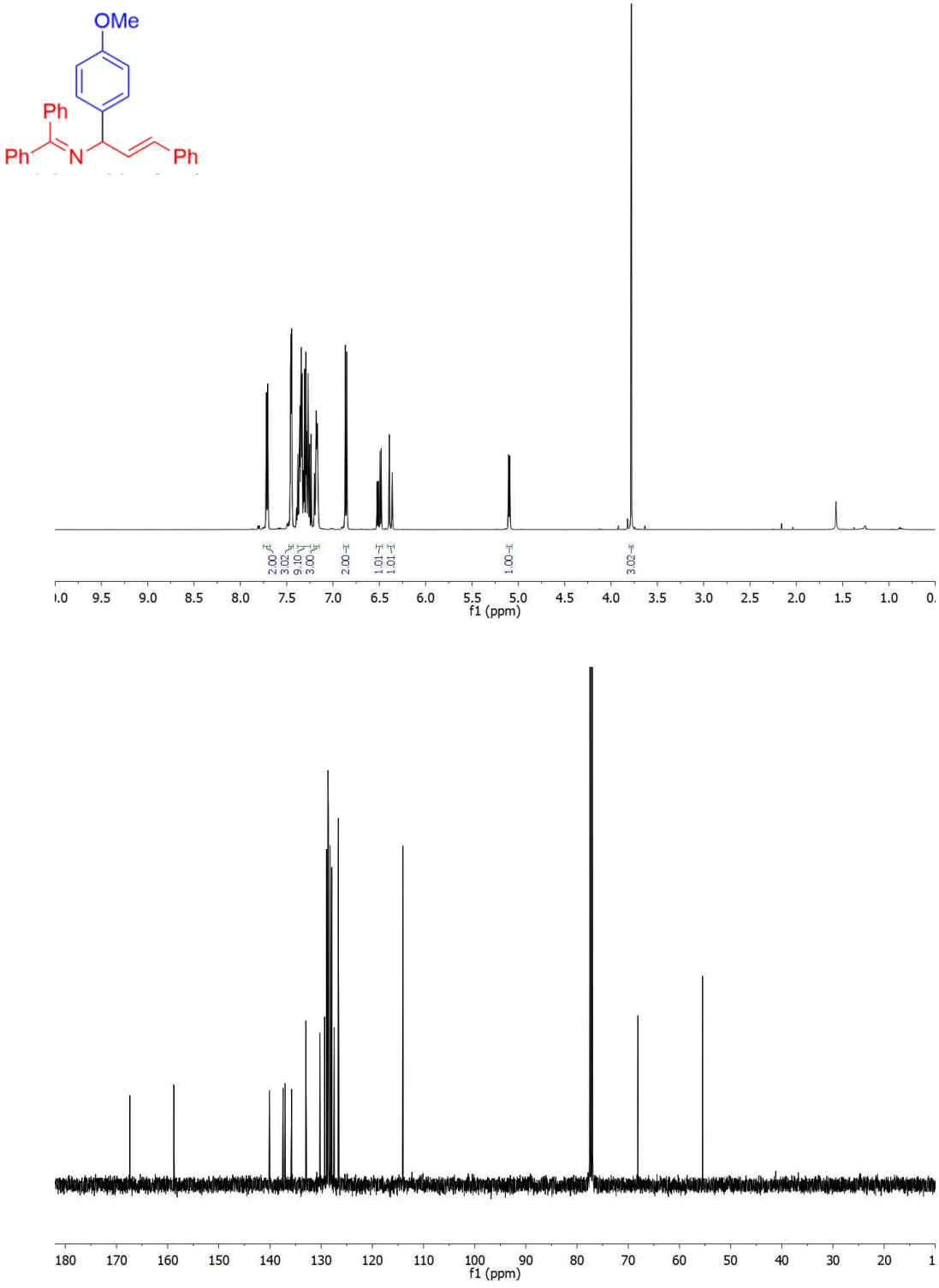


Figure A2.3 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.3ac in $CDCl_3$

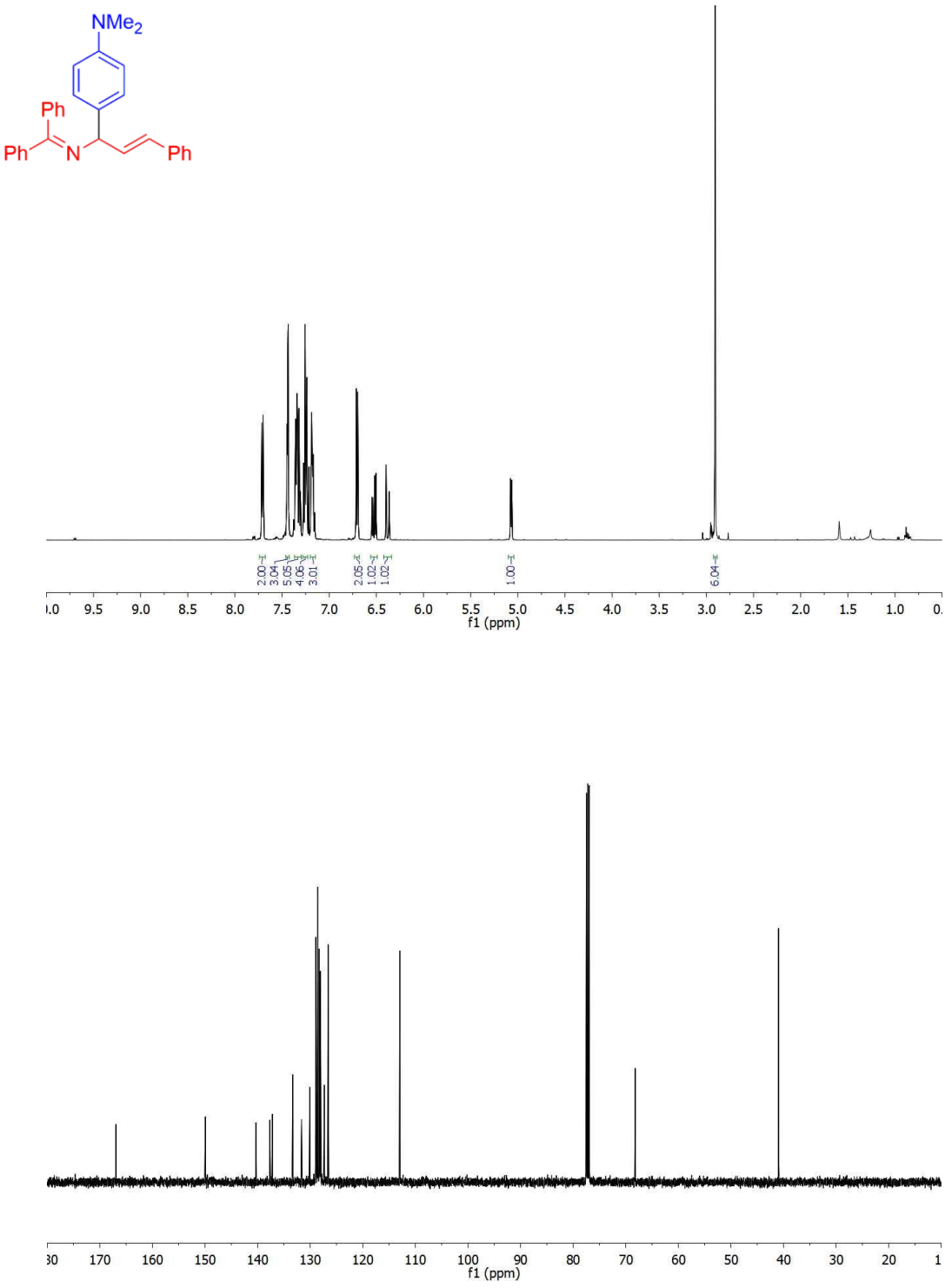


Figure A2.4 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.3ad in $CDCl_3$

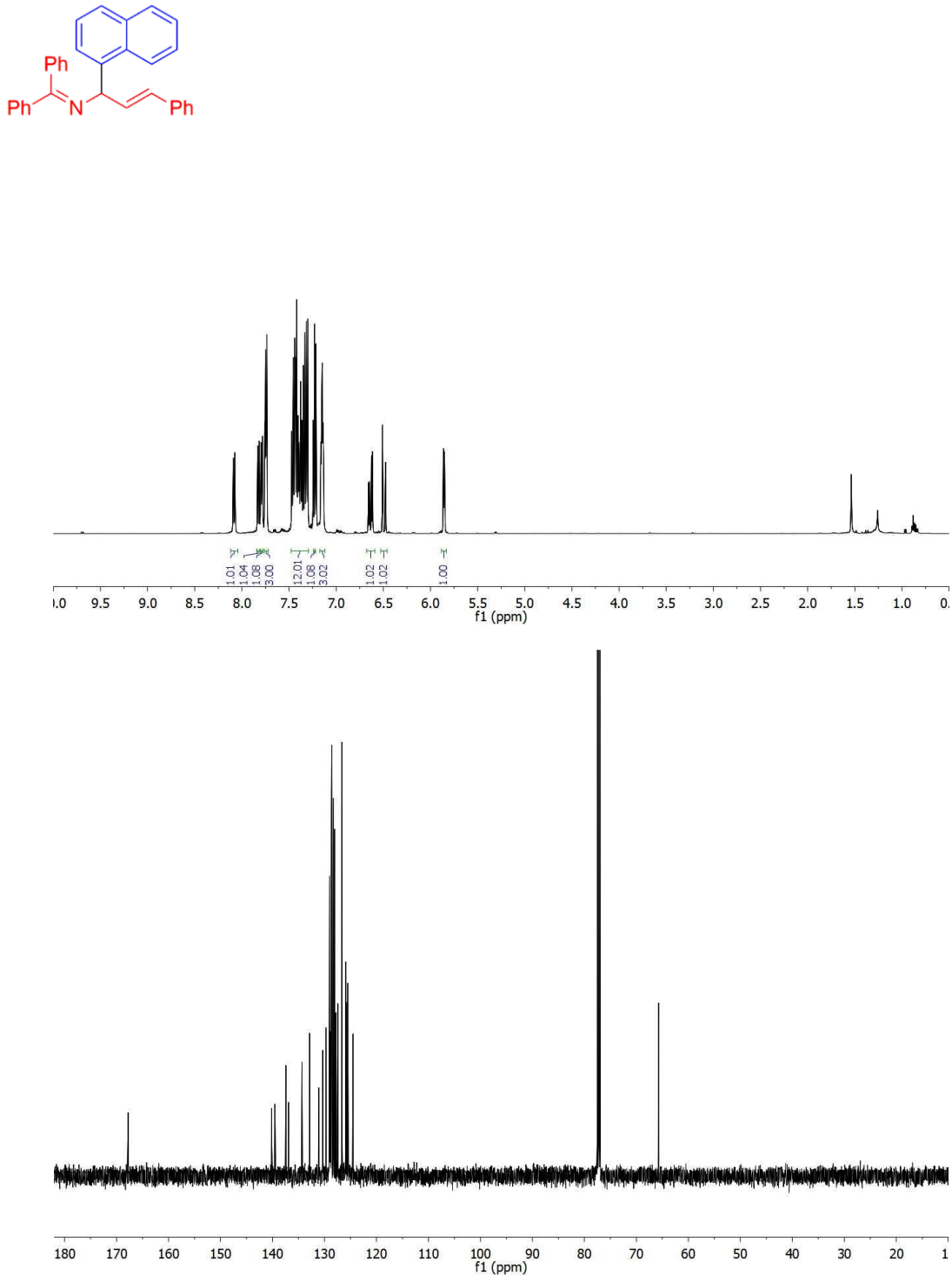


Figure A2.5 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.3ae in $CDCl_3$

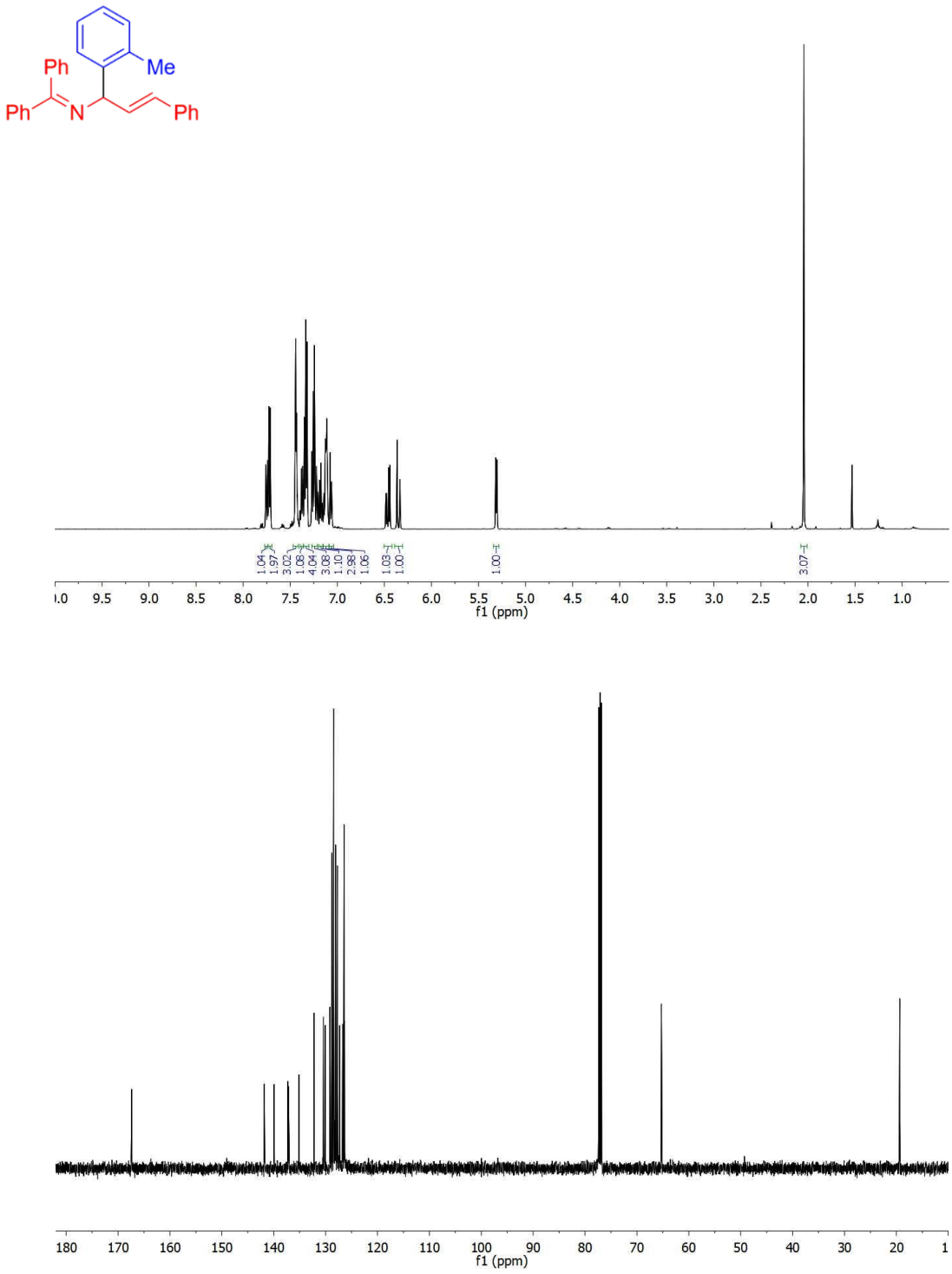


Figure A2.6 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.3af in $CDCl_3$

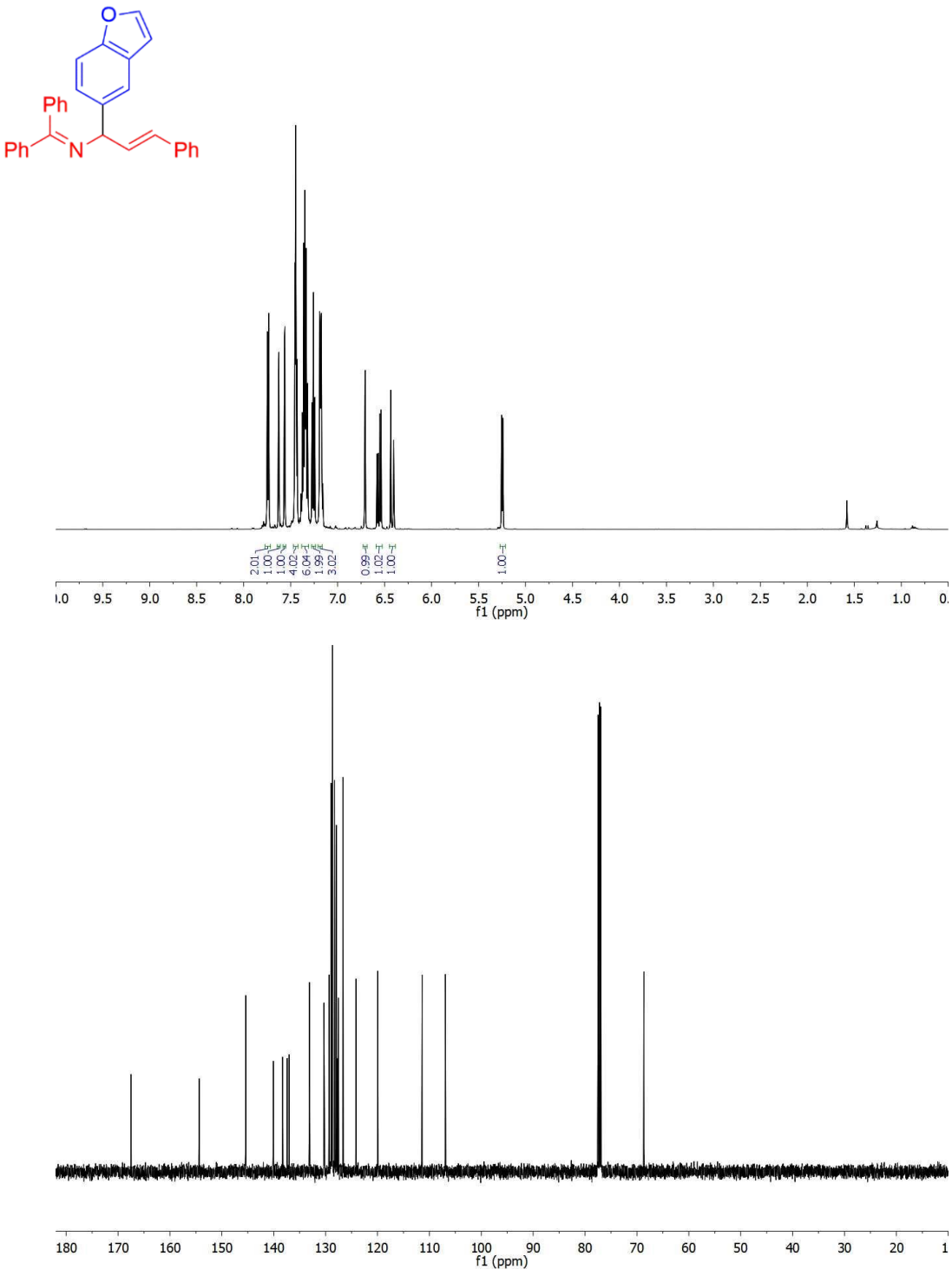


Figure A2.7 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.3ag in $CDCl_3$

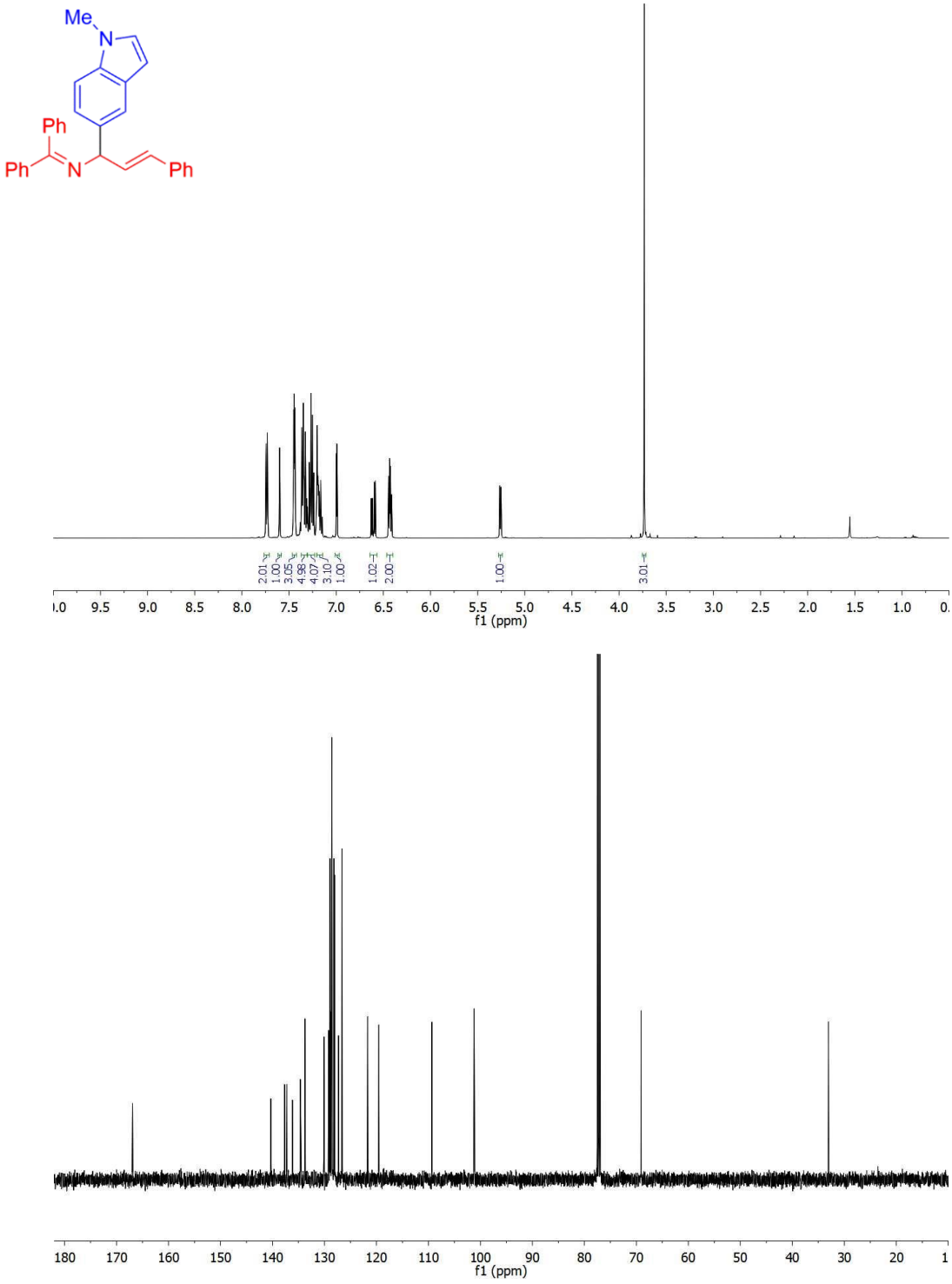


Figure A2.8 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.3ah in $CDCl_3$

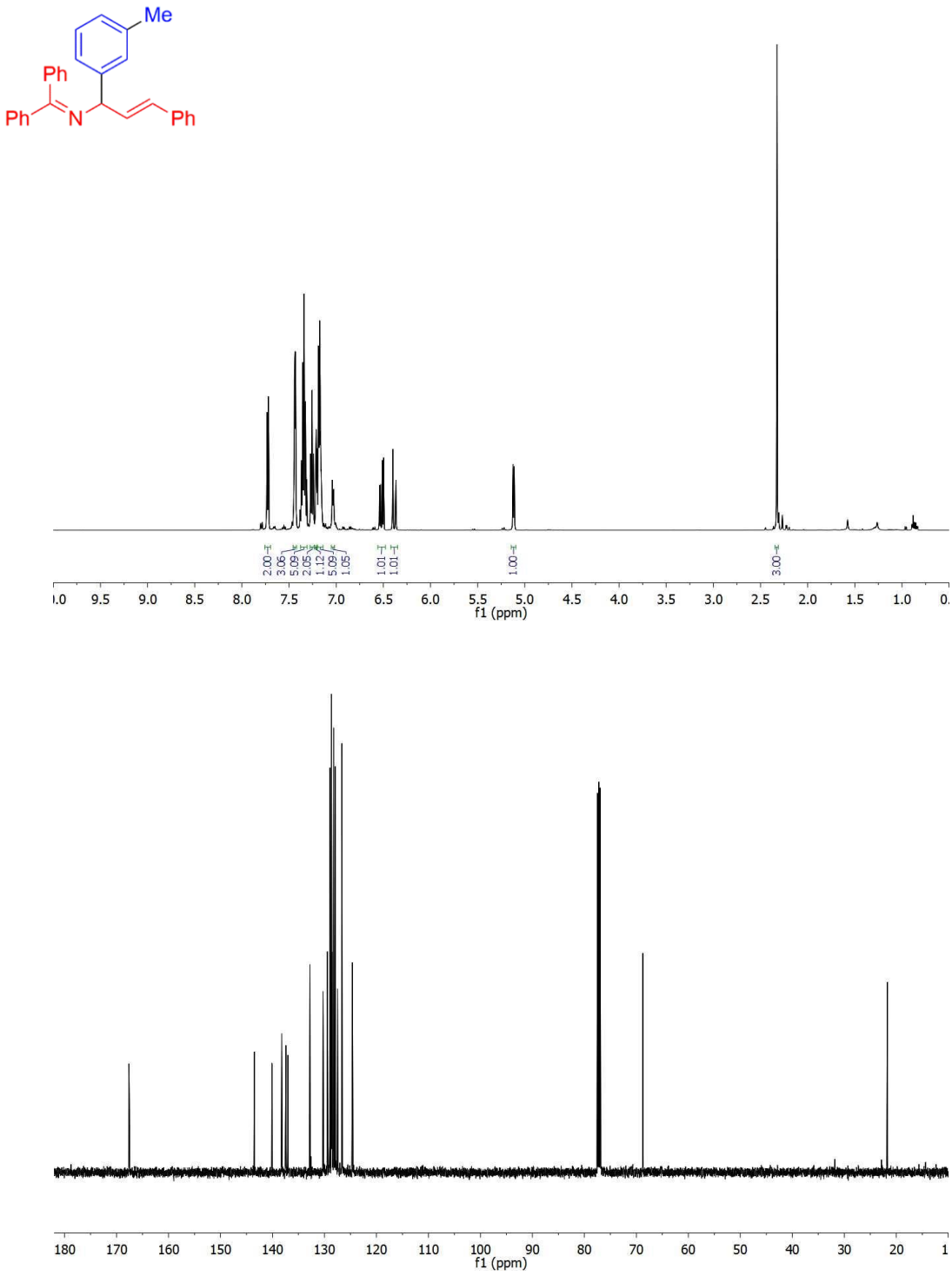


Figure A2.9 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.3ai in $CDCl_3$

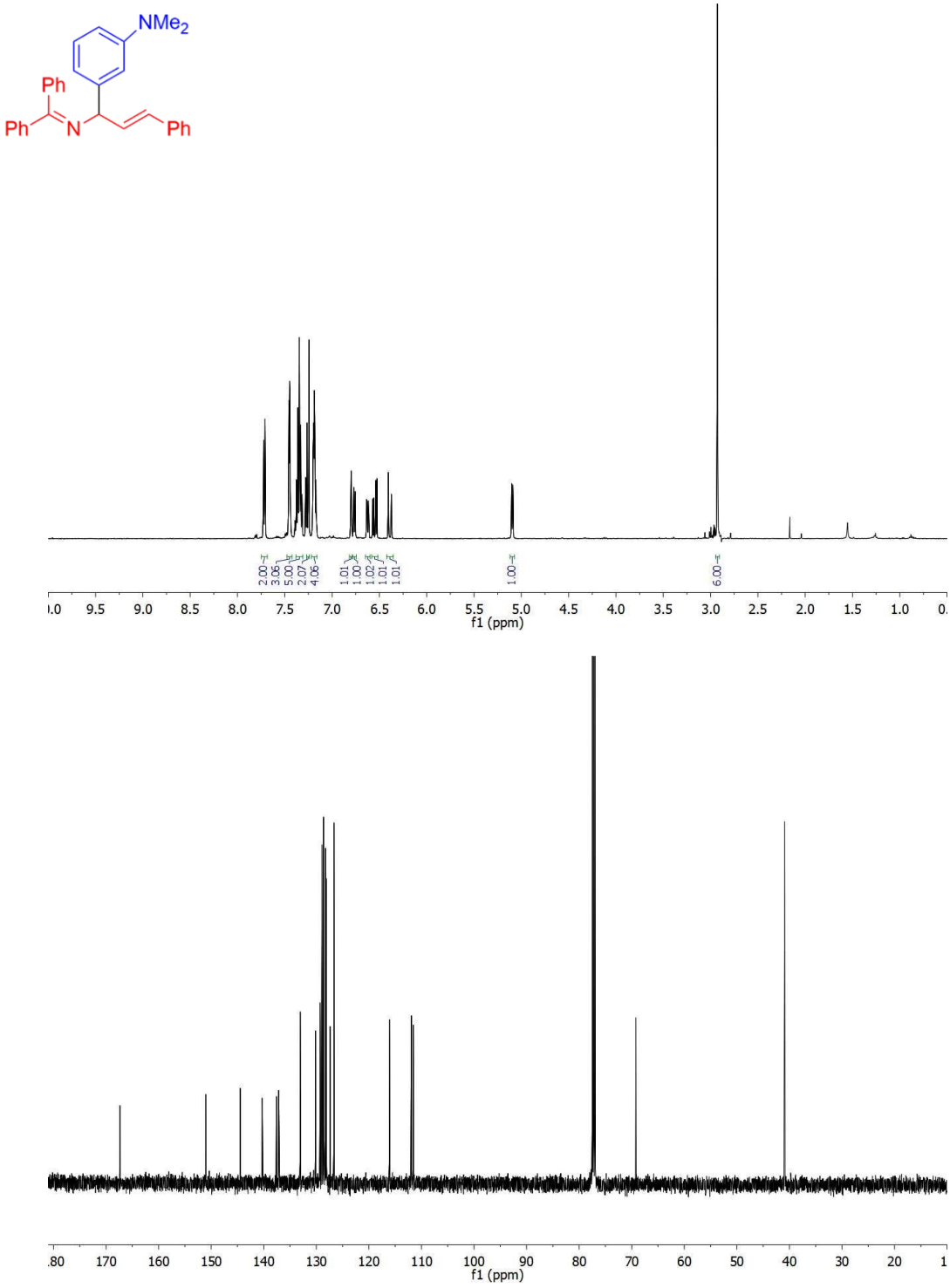


Figure A2.10 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.3aj in $CDCl_3$

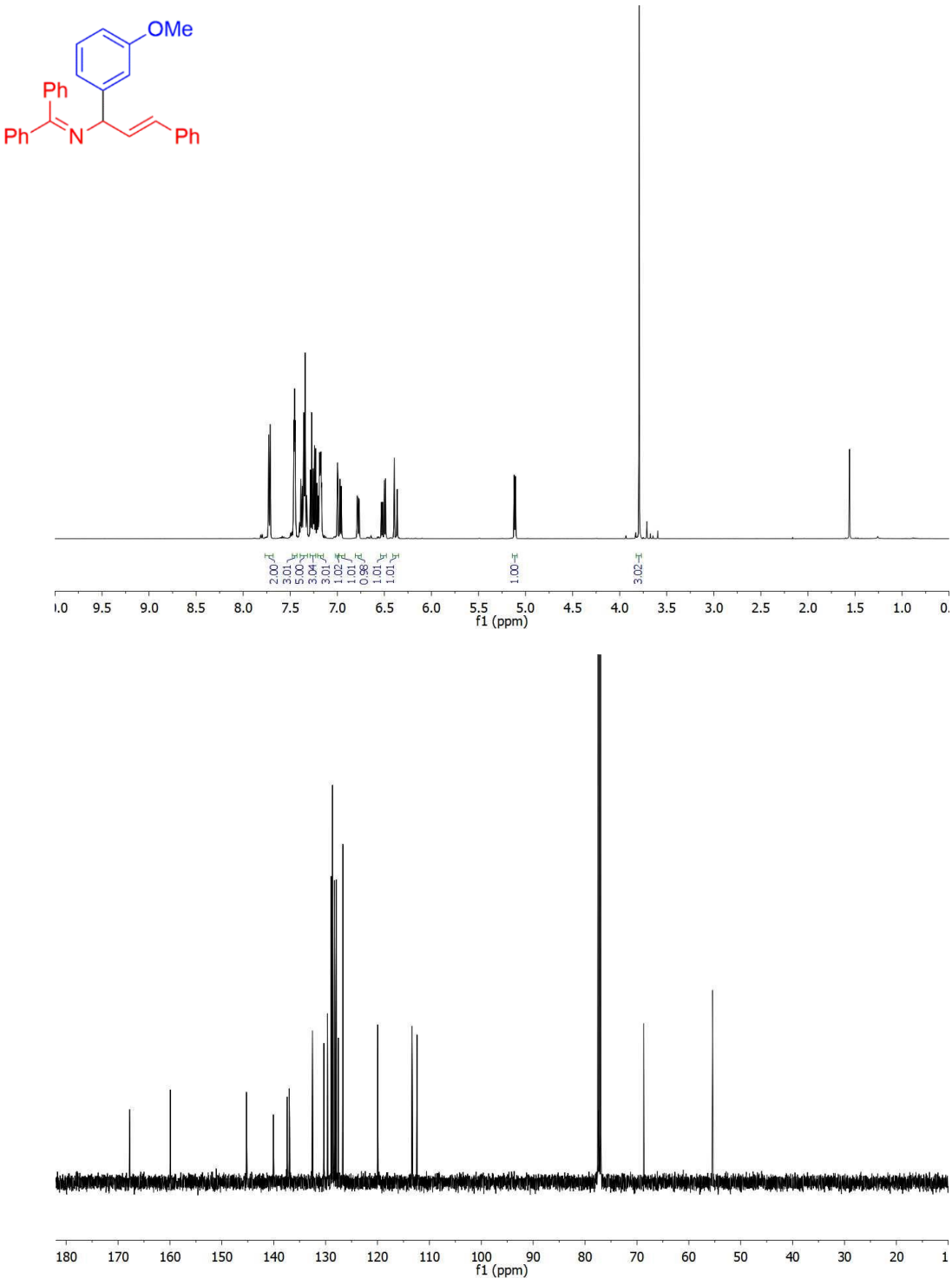


Figure A2.11 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.3ak in $CDCl_3$

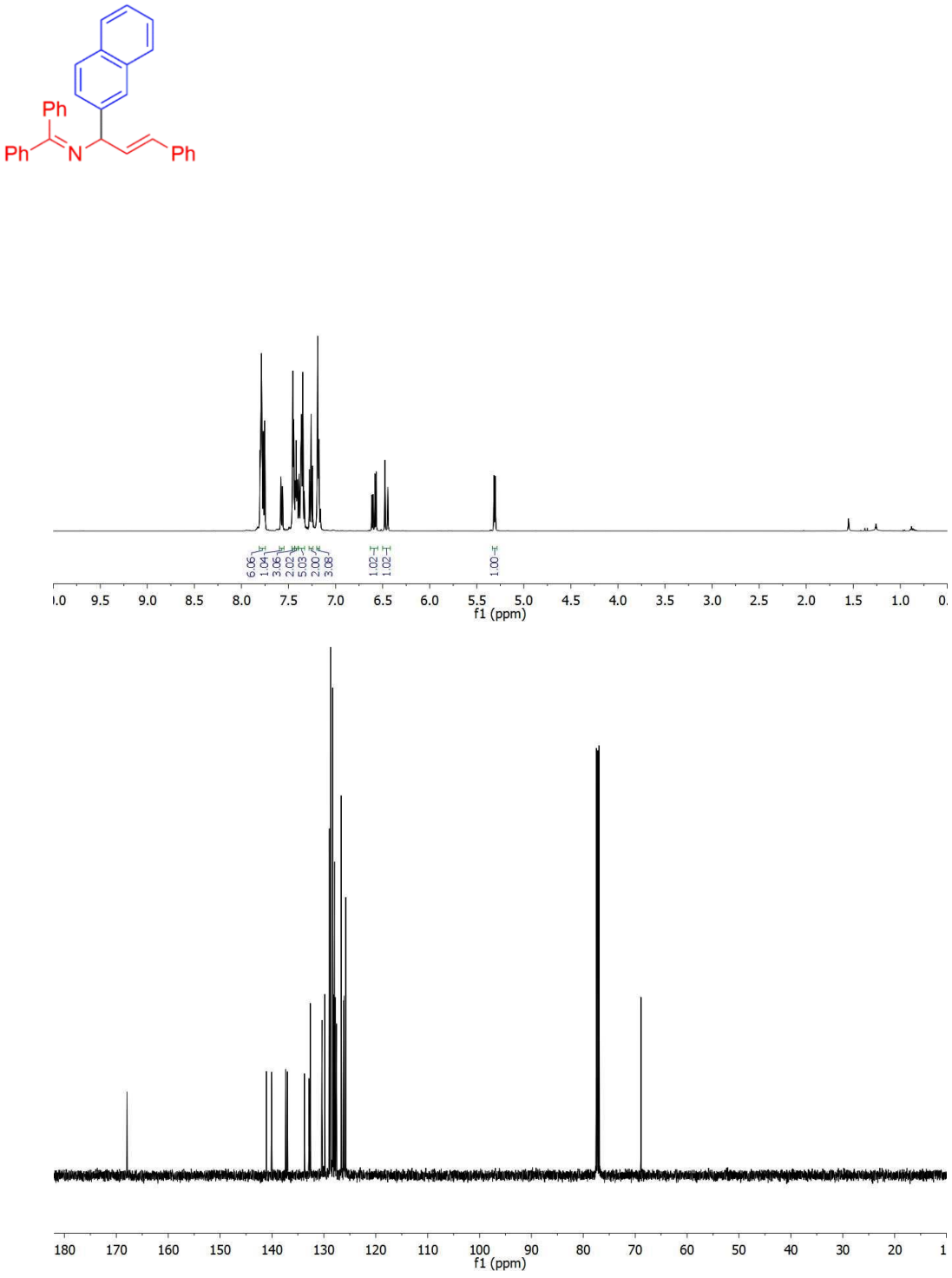


Figure A2.12 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.3al in $CDCl_3$

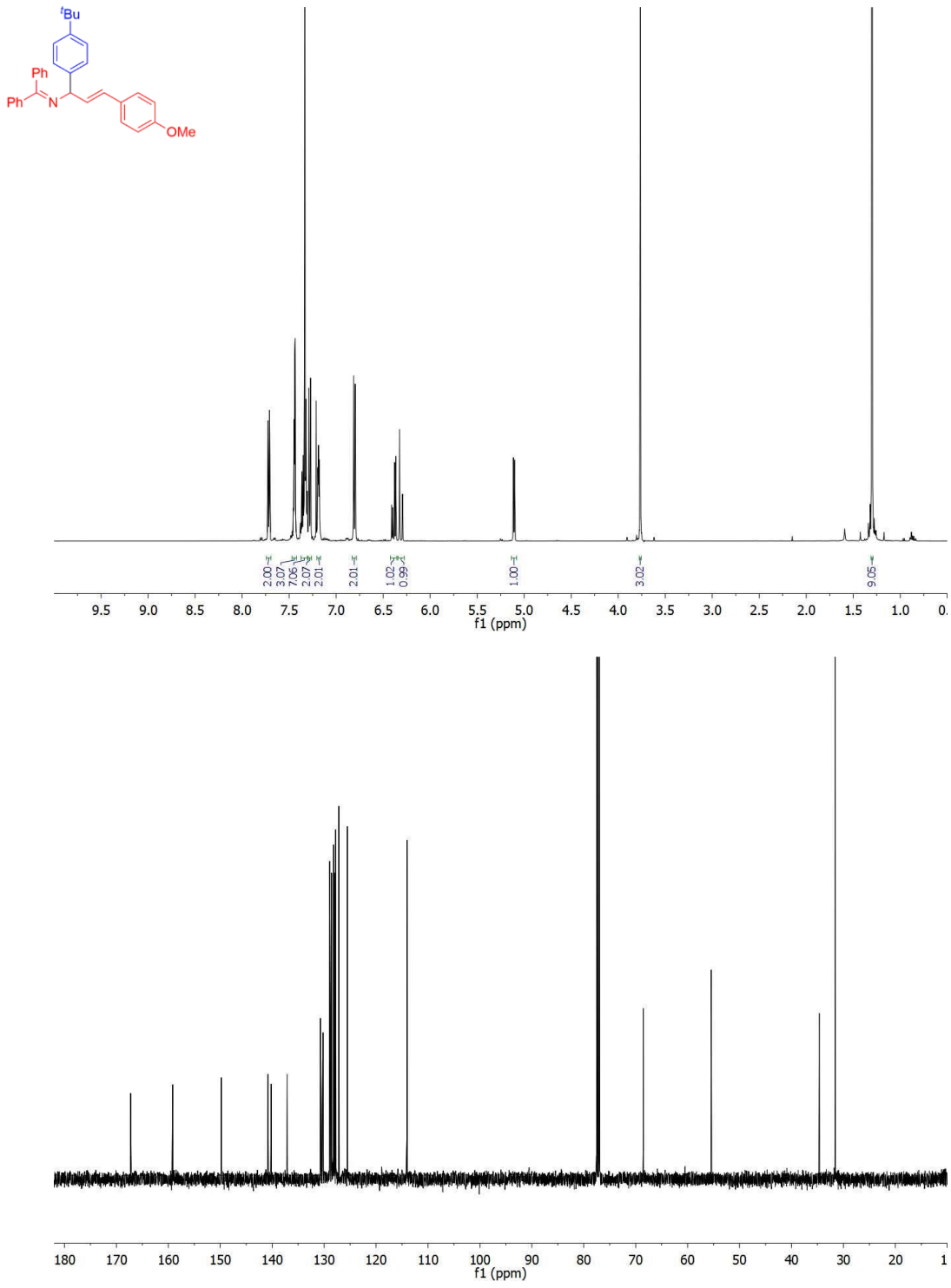


Figure A2.13 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.3bb in $CDCl_3$

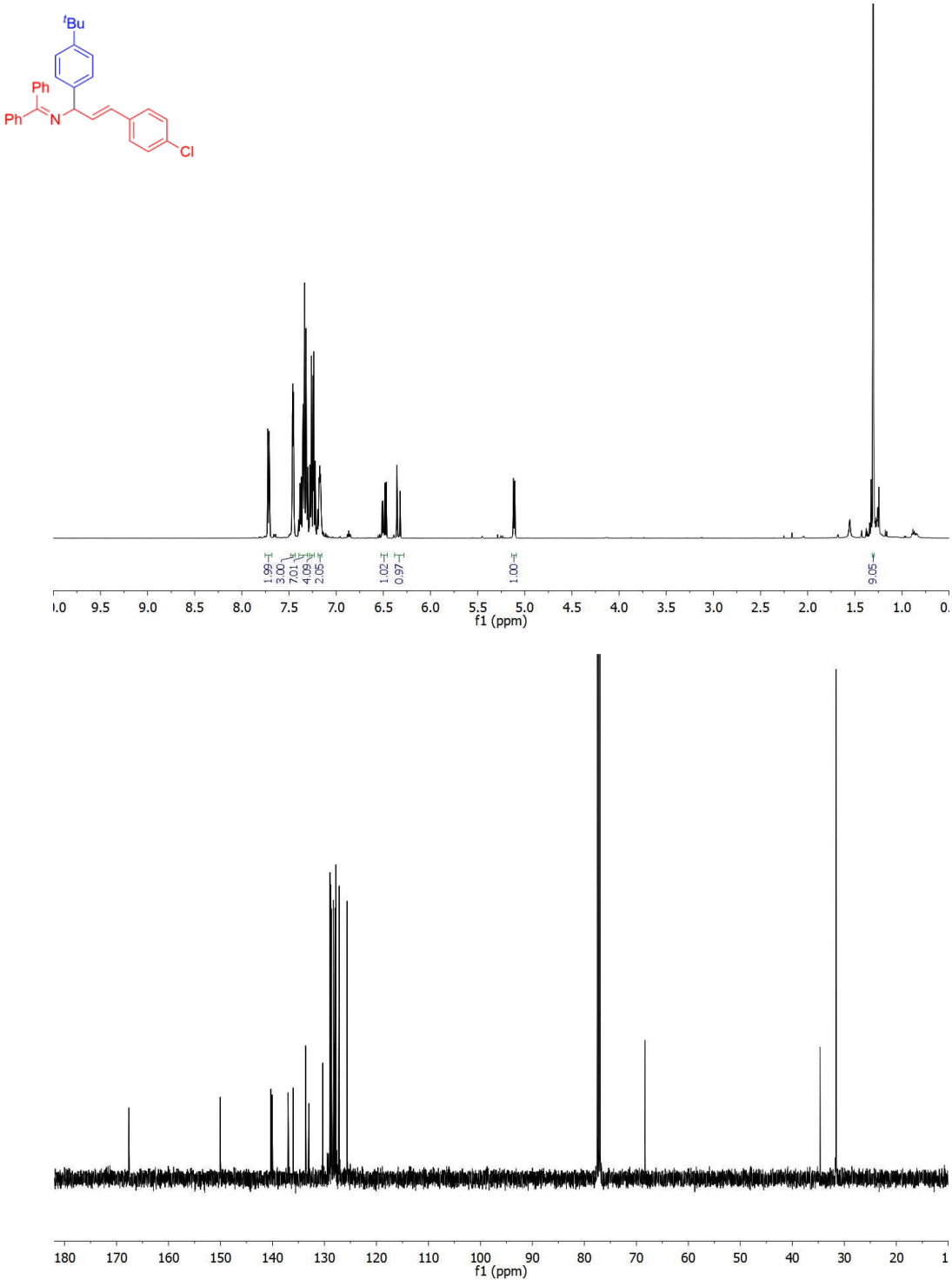


Figure A2.14 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.3cb in $CDCl_3$

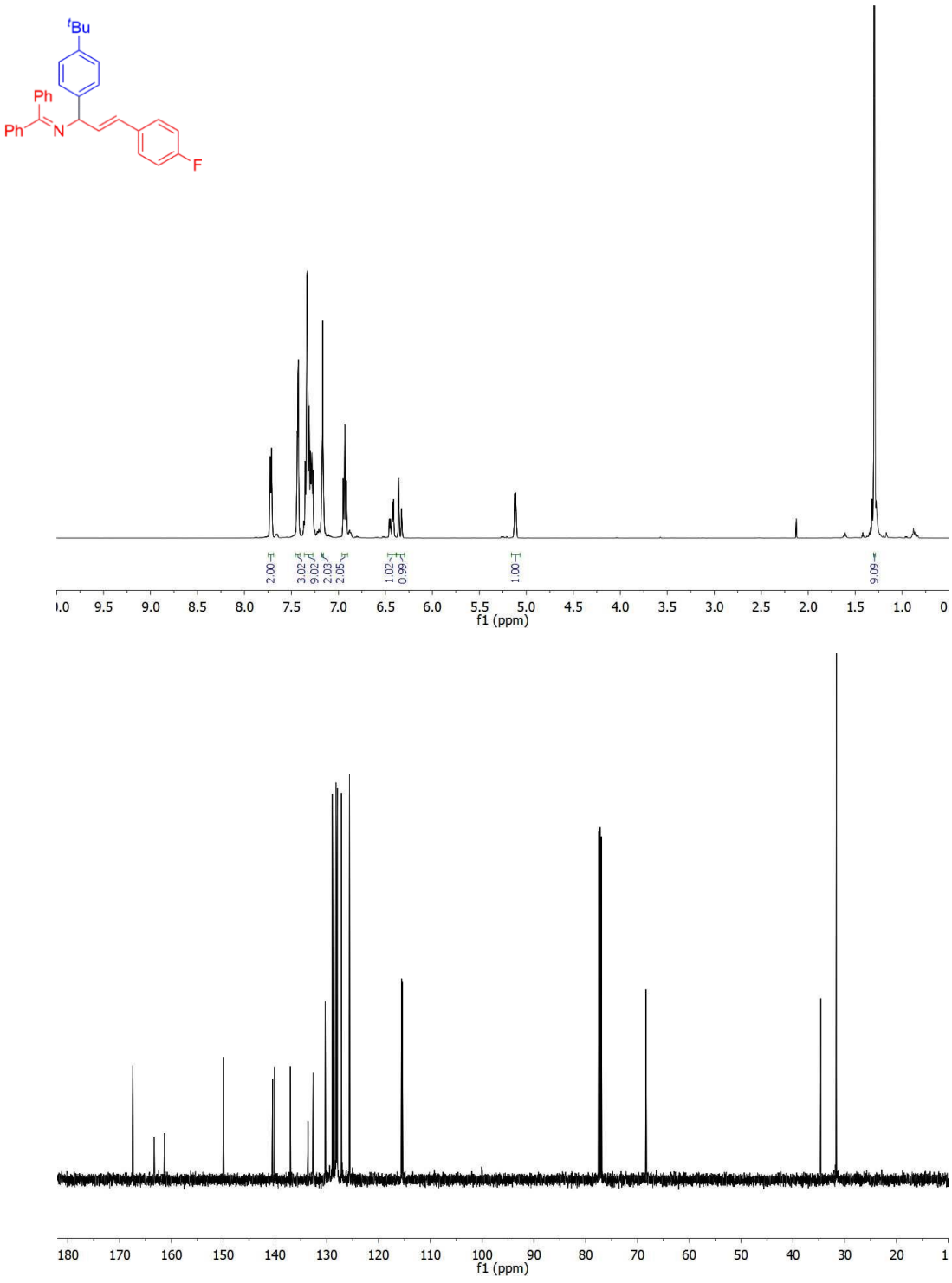


Figure A2.15 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.3db in $CDCl_3$

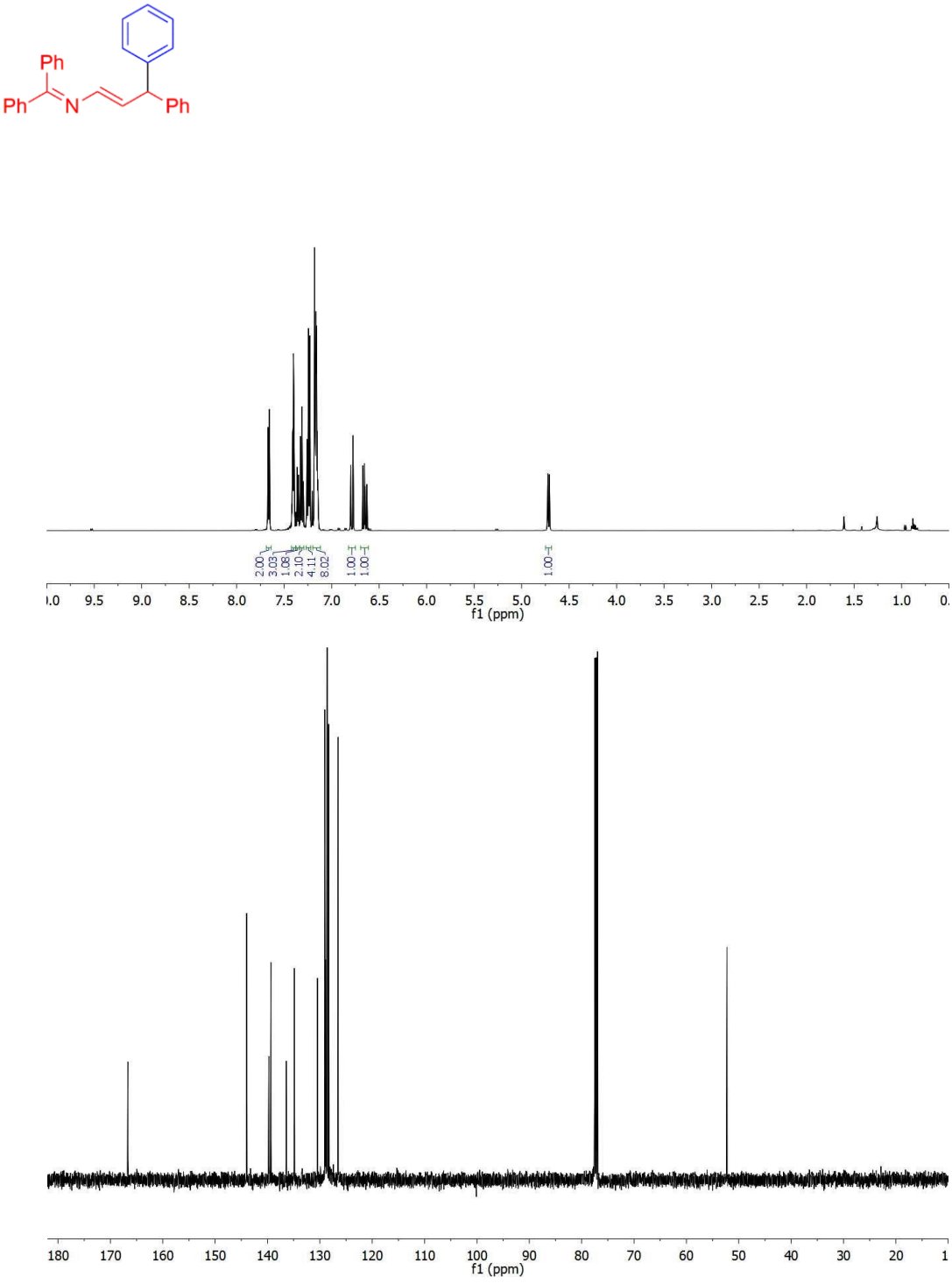


Figure A2.16 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.4aa in $CDCl_3$

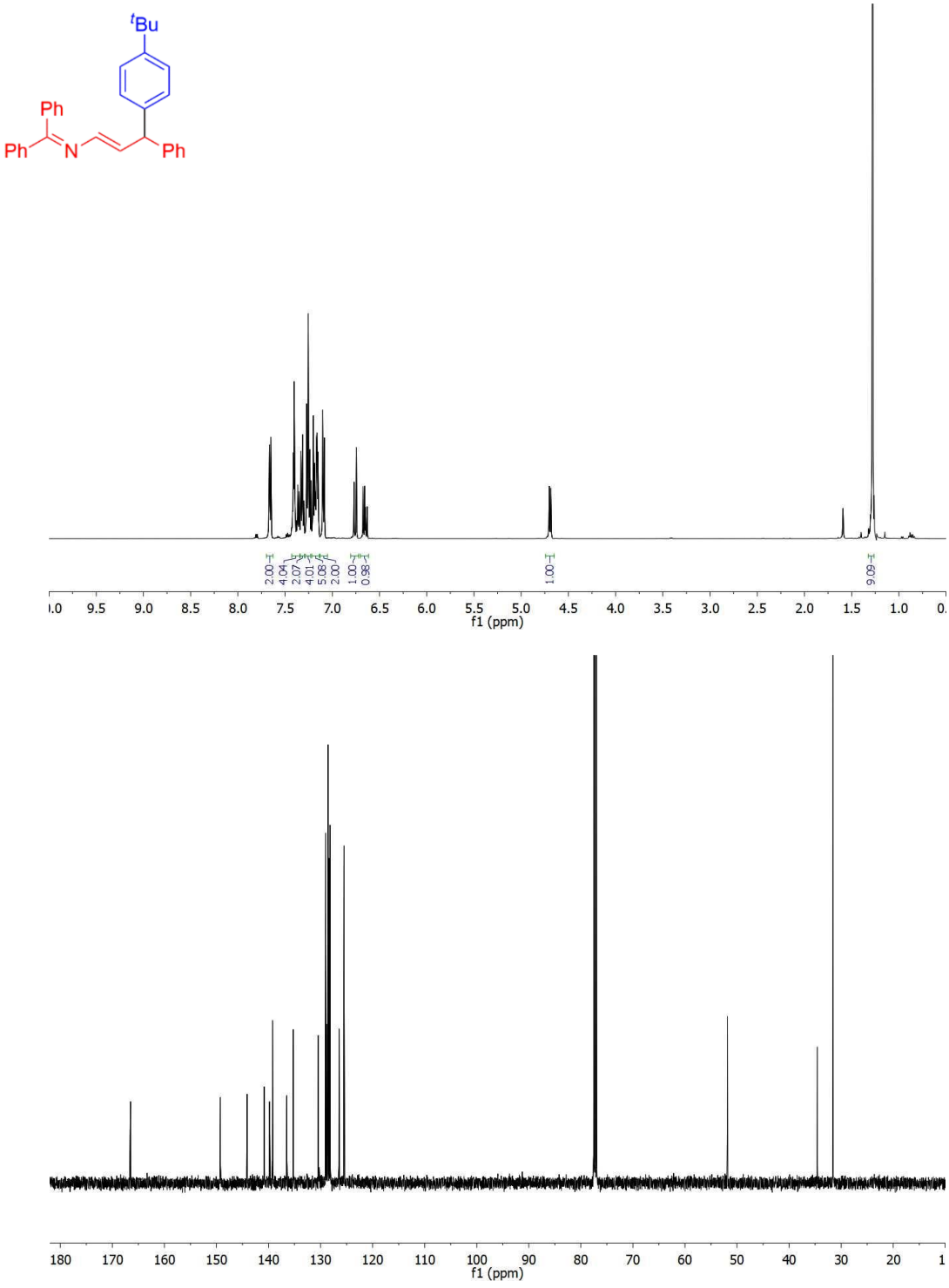


Figure A2.17 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.4ab in $CDCl_3$

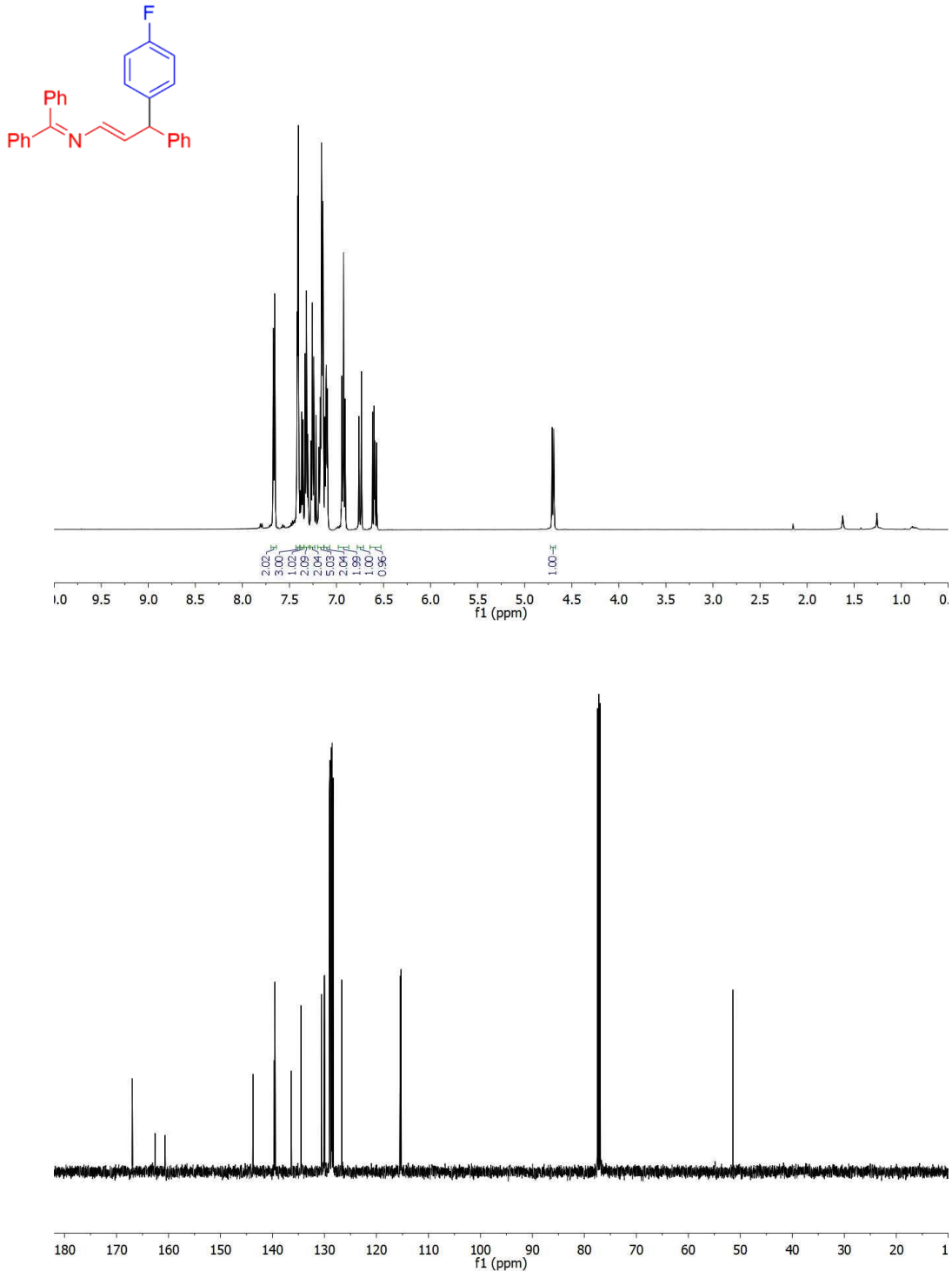


Figure A2.18 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.4am in $CDCl_3$

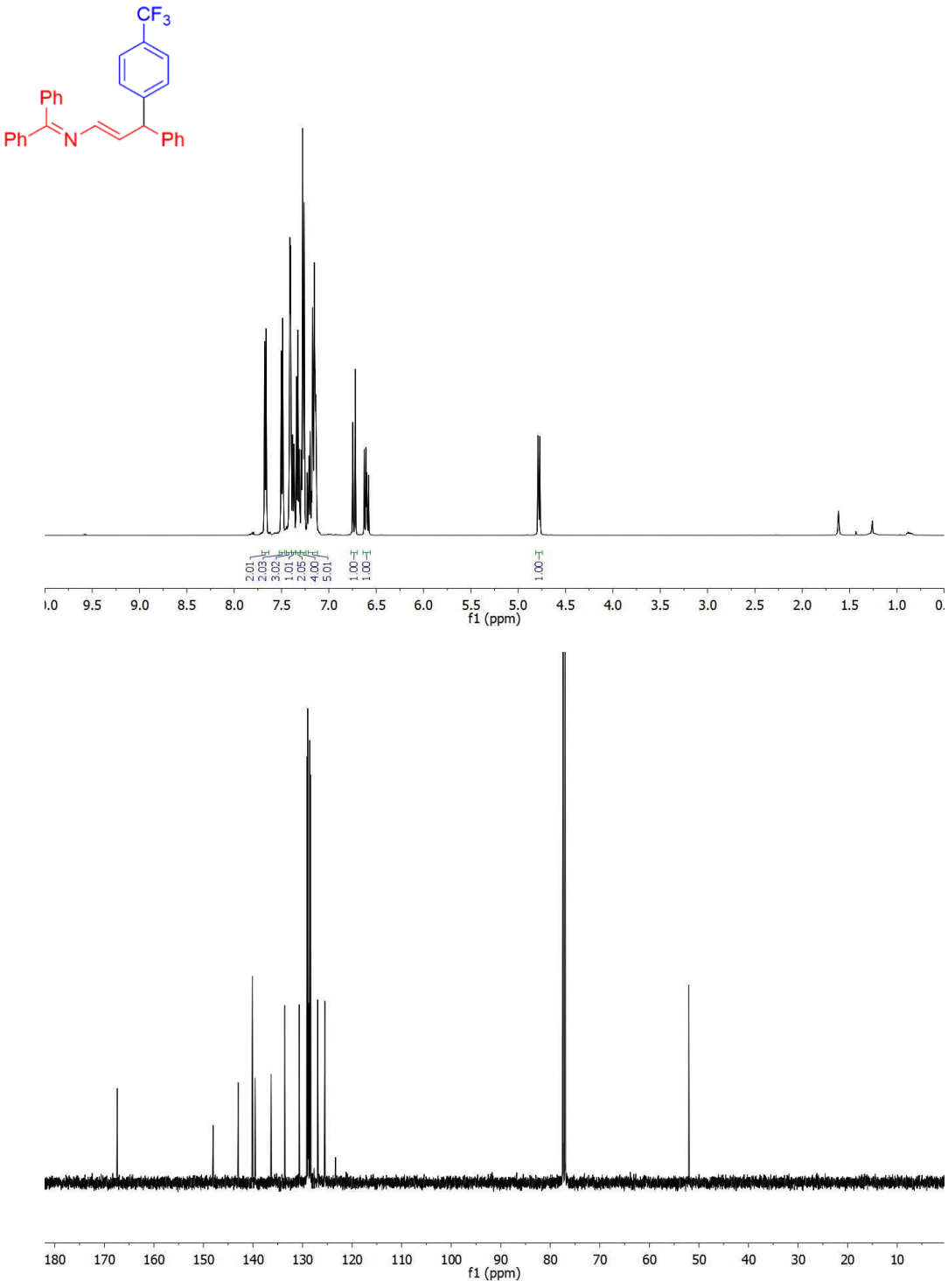


Figure A2.19 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.4an in $CDCl_3$

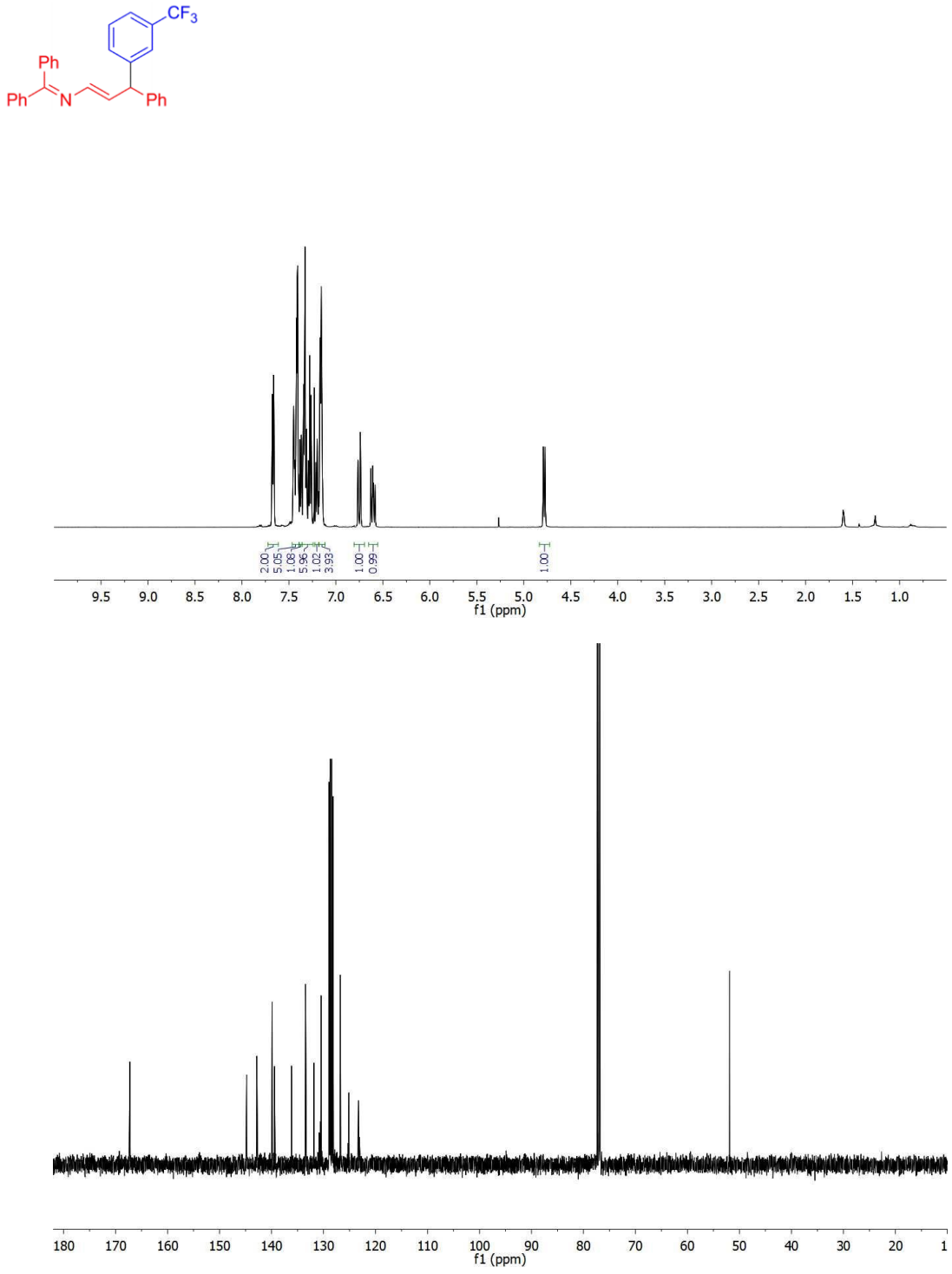


Figure A2.20 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.4ao in $CDCl_3$

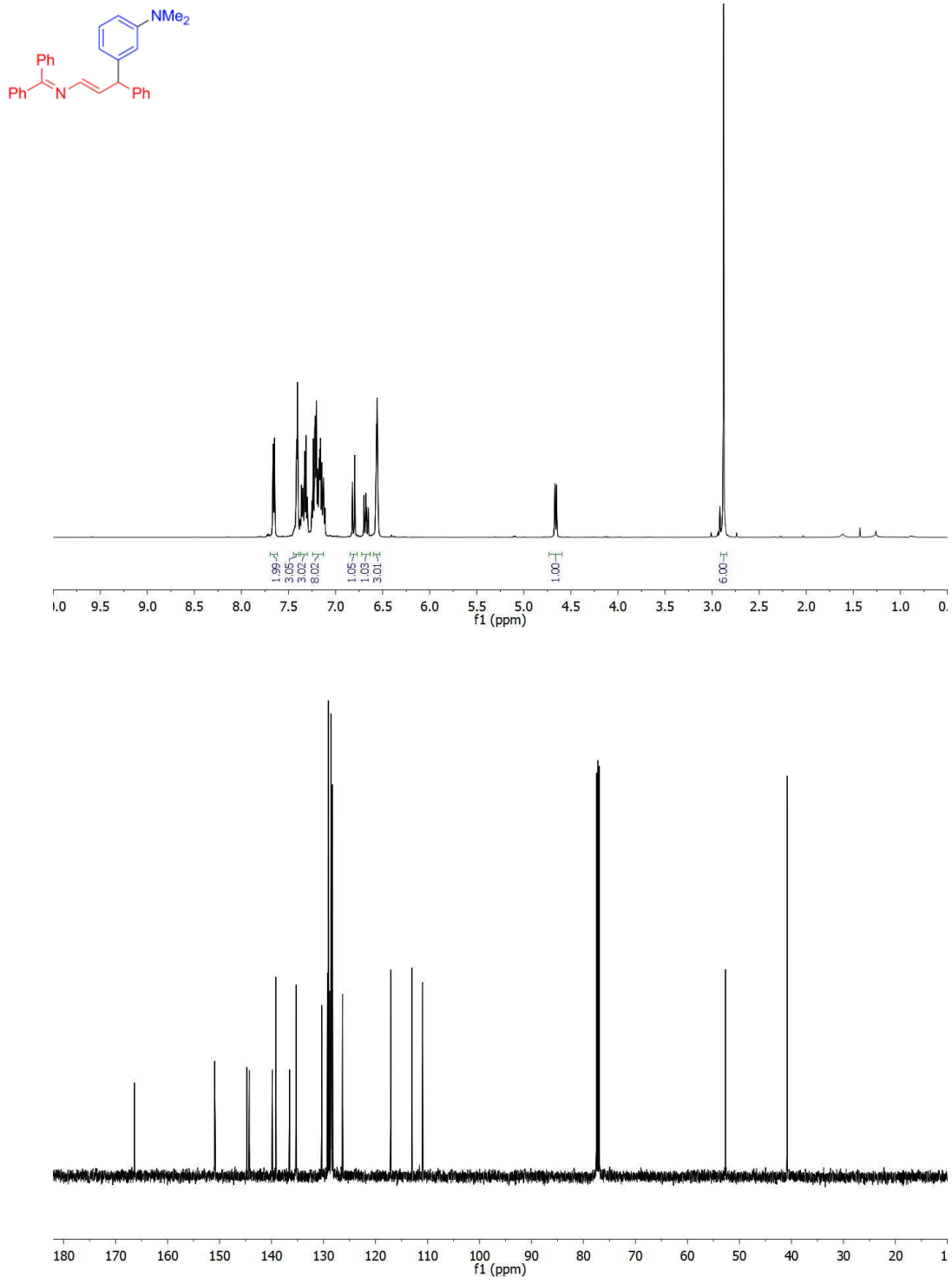


Figure A2.21 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.4aj in $CDCl_3$

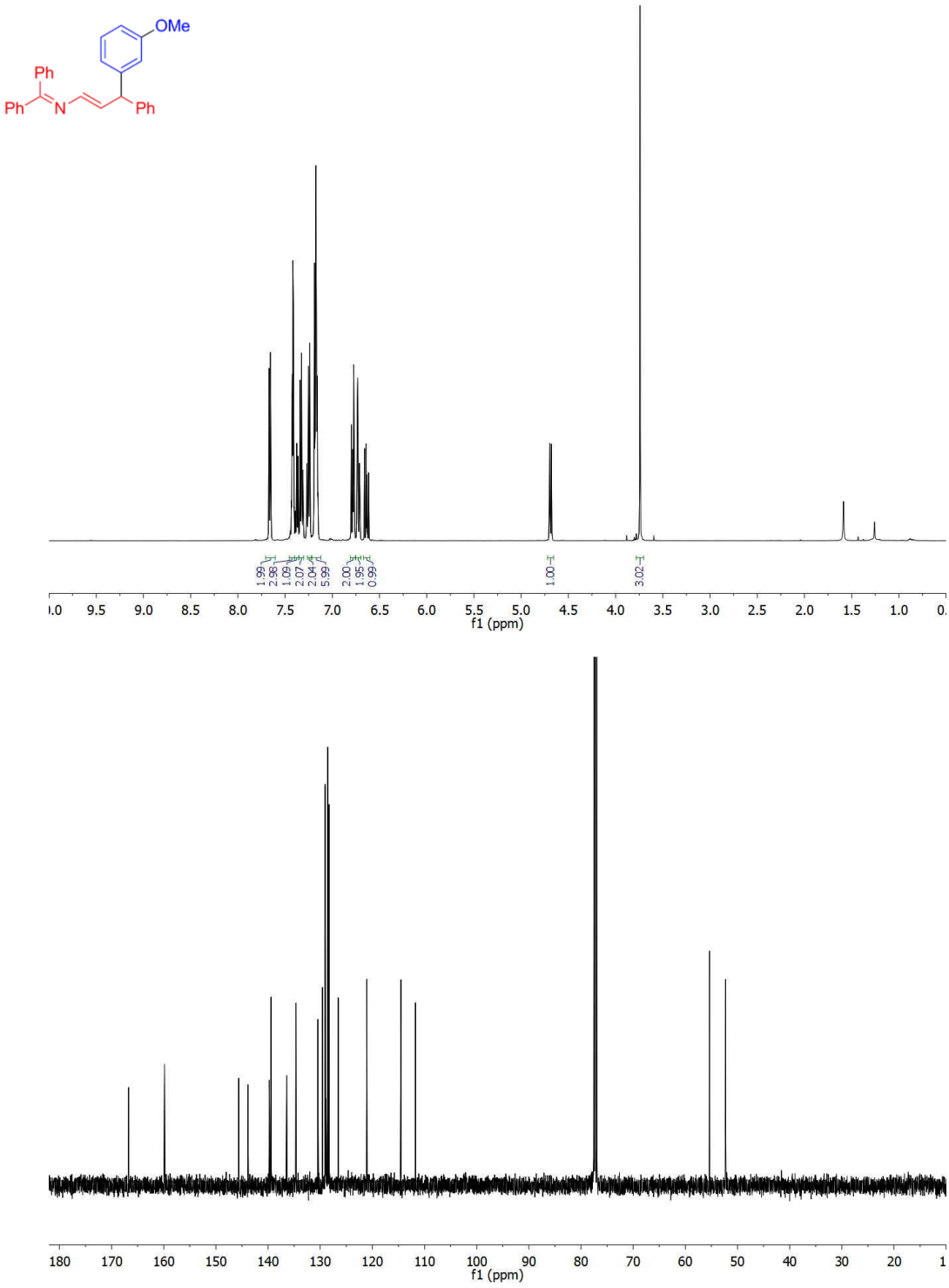


Figure A2.21 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.4ak in $CDCl_3$

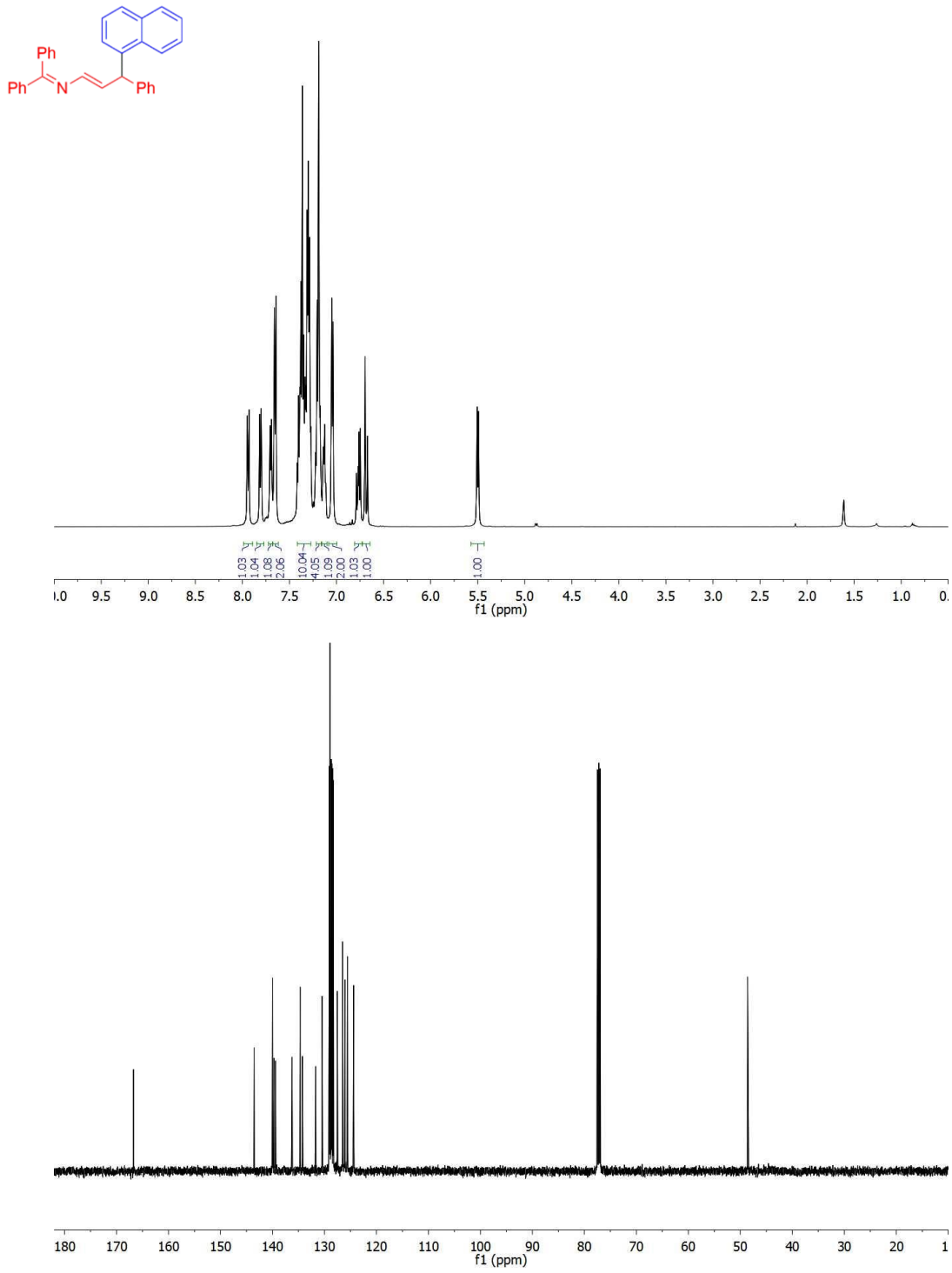


Figure A2.22 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.4ae in $CDCl_3$

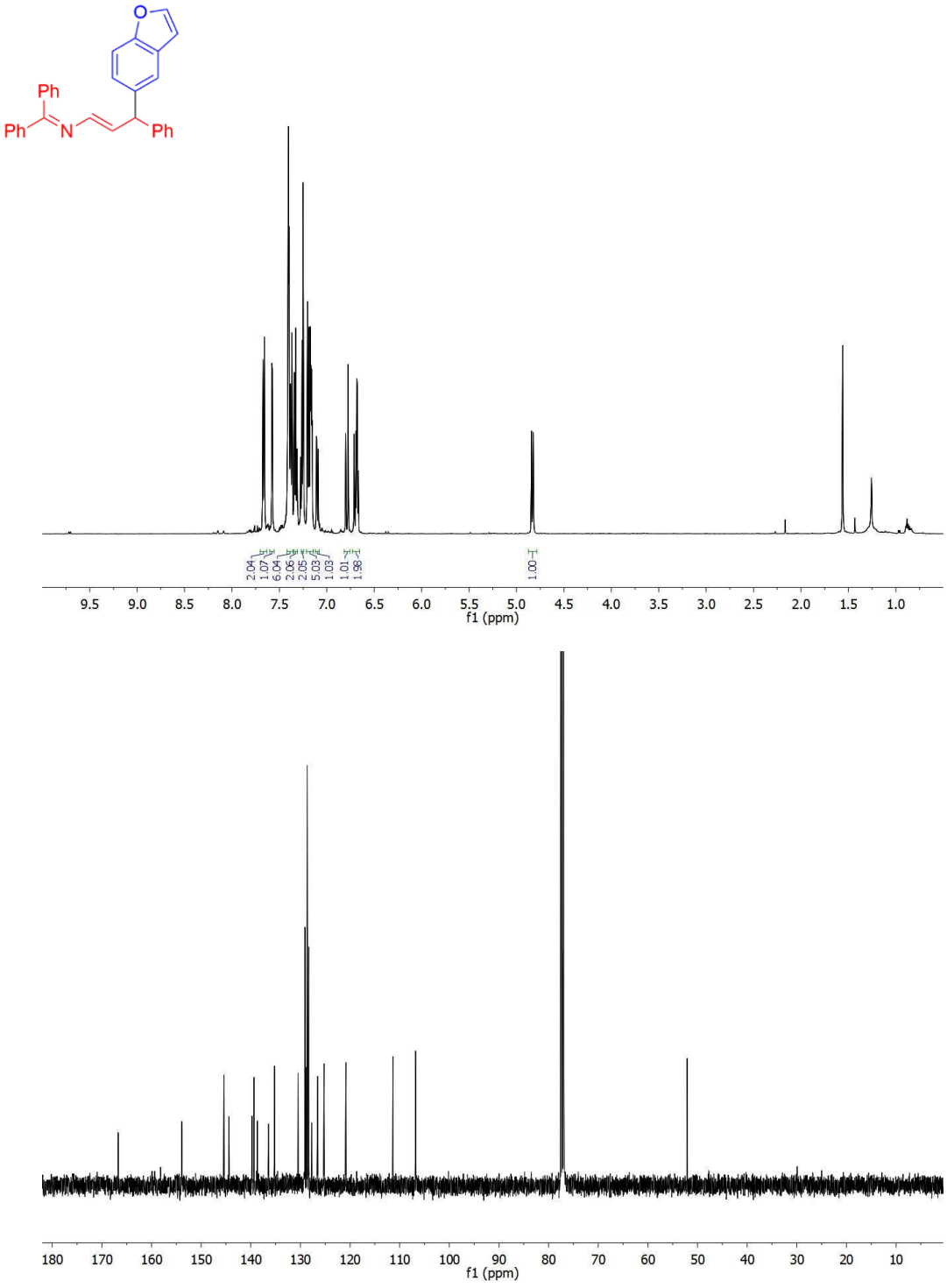


Figure A2.23 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.4ag in $CDCl_3$

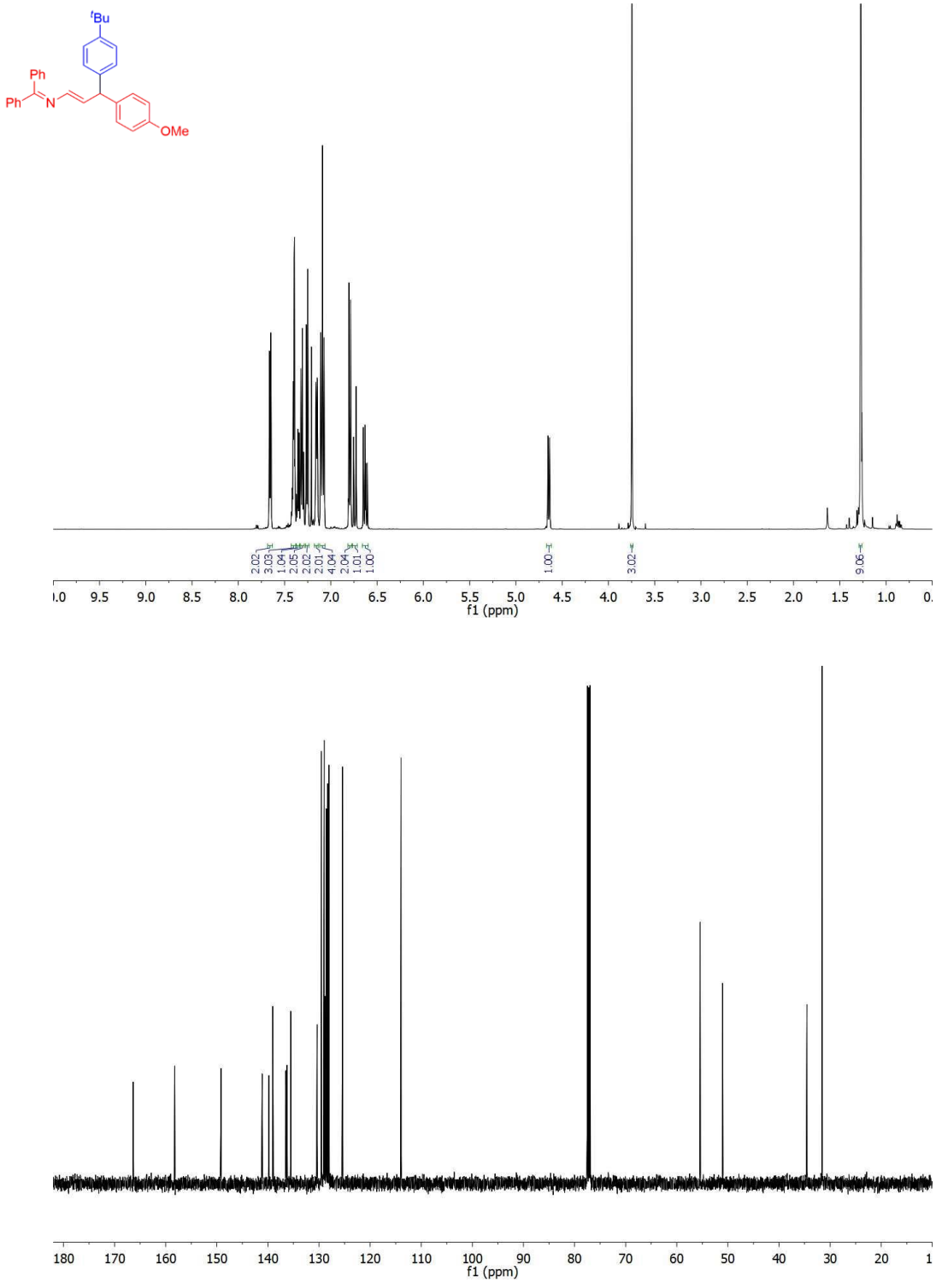


Figure A2.24 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.4bb in $CDCl_3$

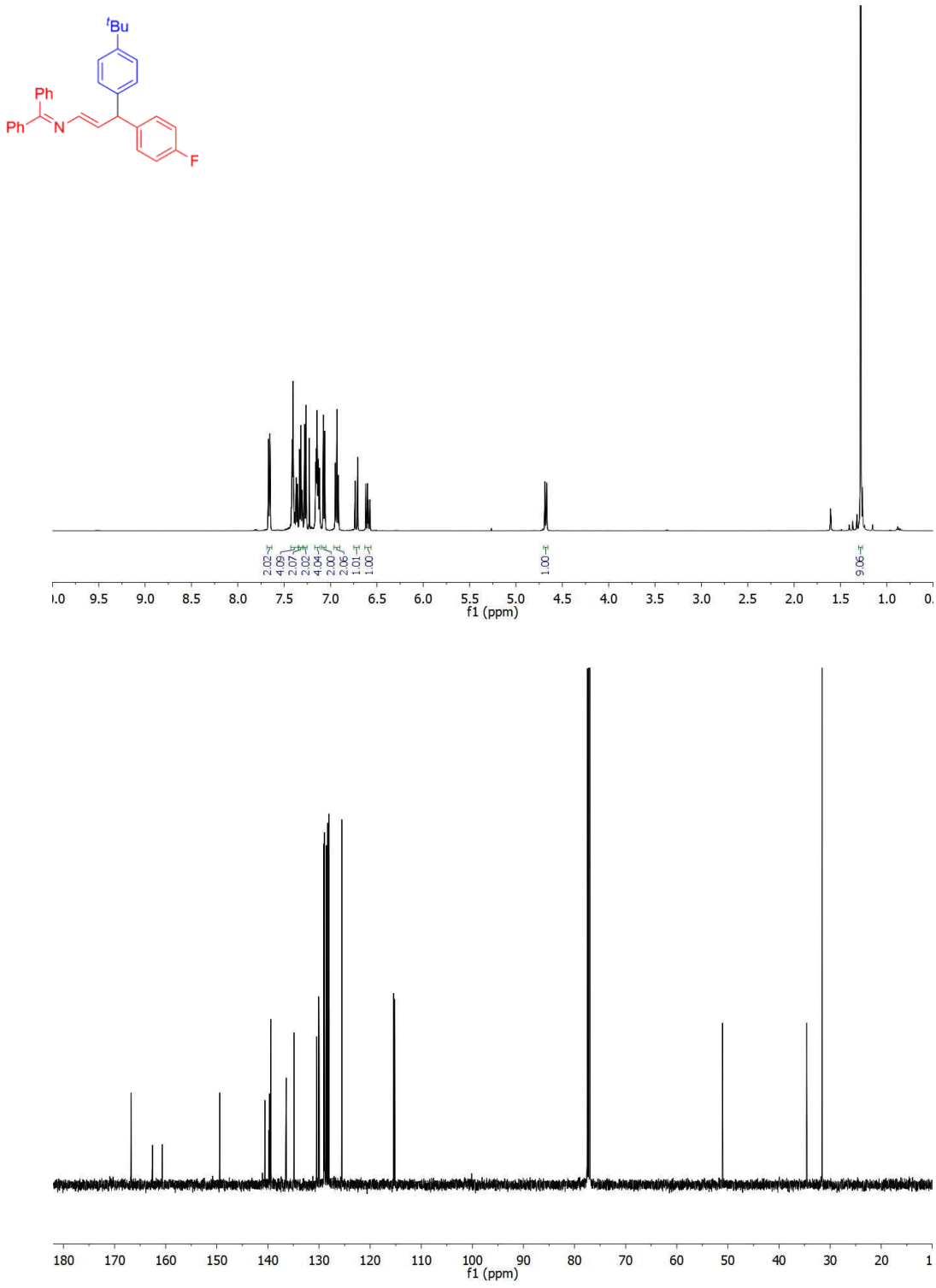


Figure A2.25 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.4db in $CDCl_3$

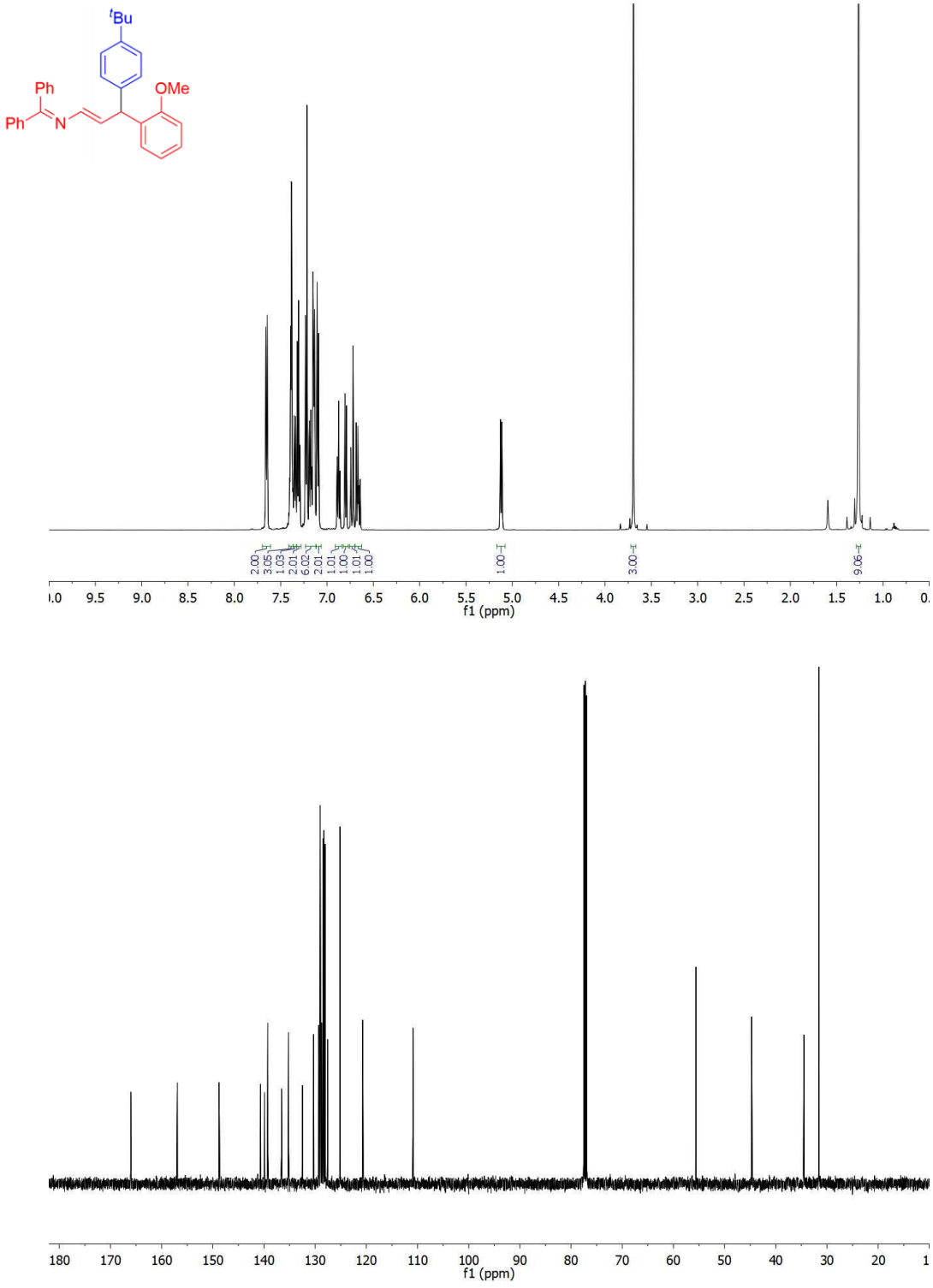


Figure A2.26 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.4eb in $CDCl_3$

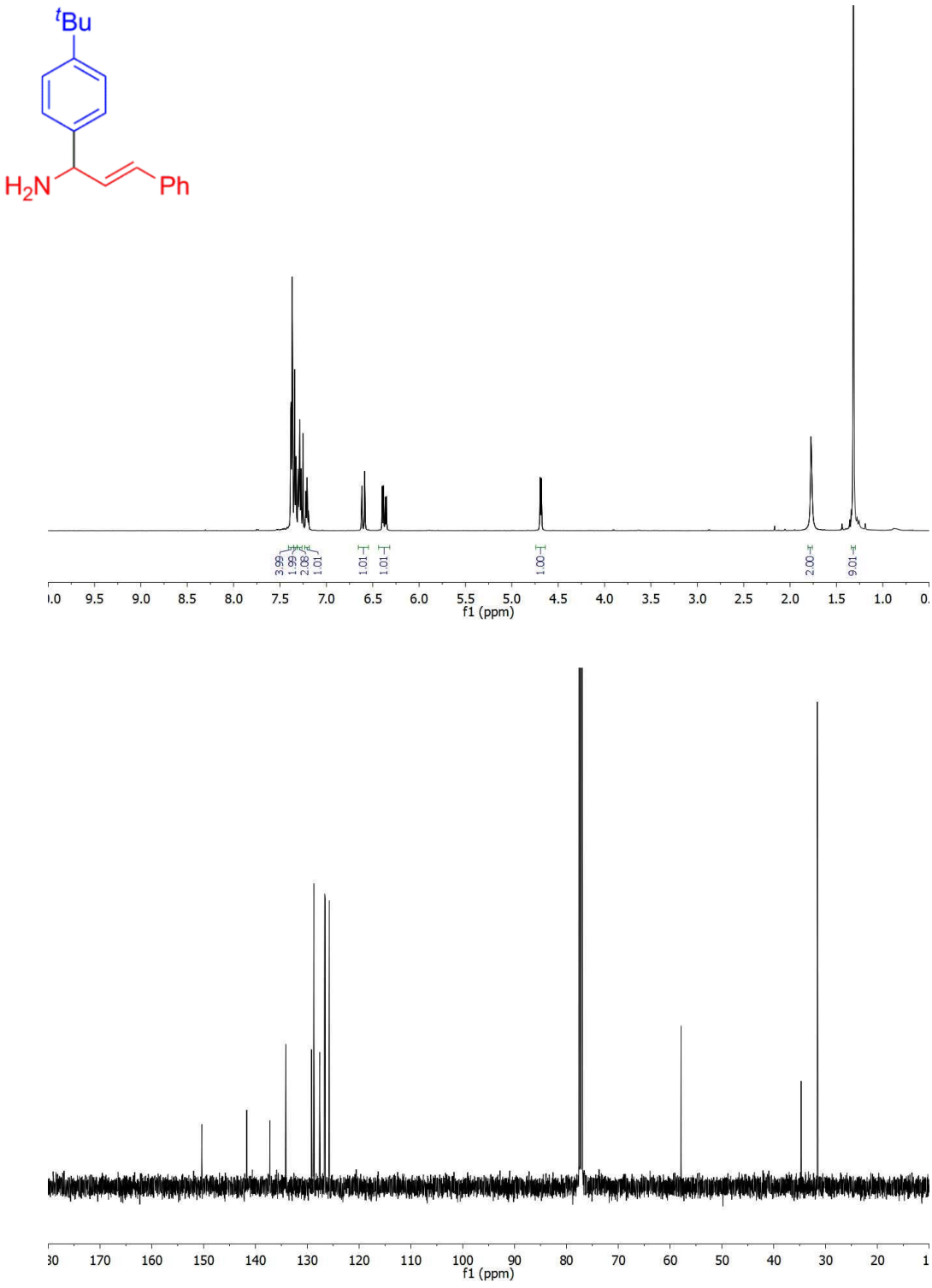


Figure A2.26 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 2.8ab in $CDCl_3$

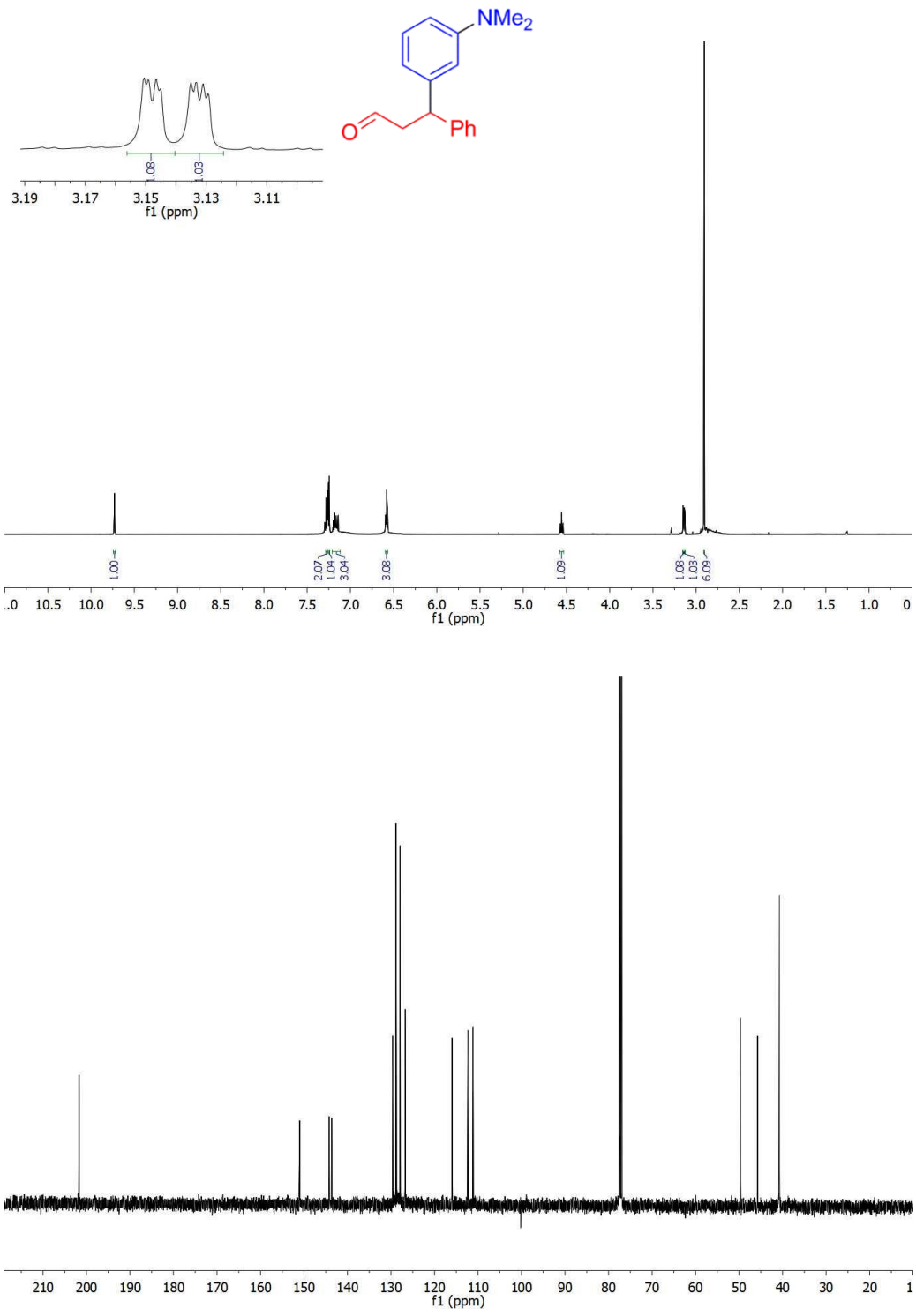


Figure A2.27 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 2.9aj in $CDCl_3$

Appendix A3. NMR Spectra Relevant to Chapter 3.

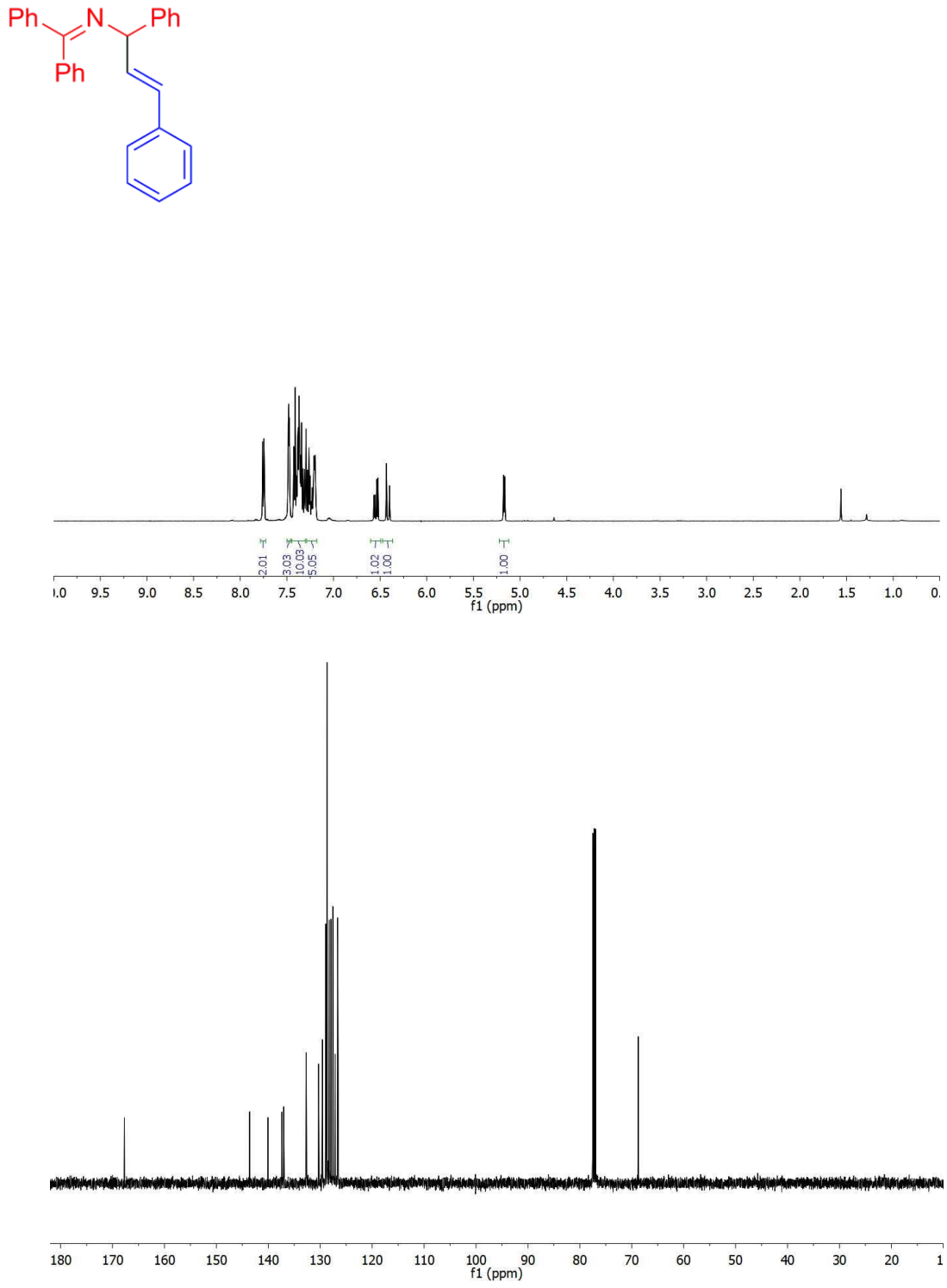


Figure A3.1 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3aa in $CDCl_3$

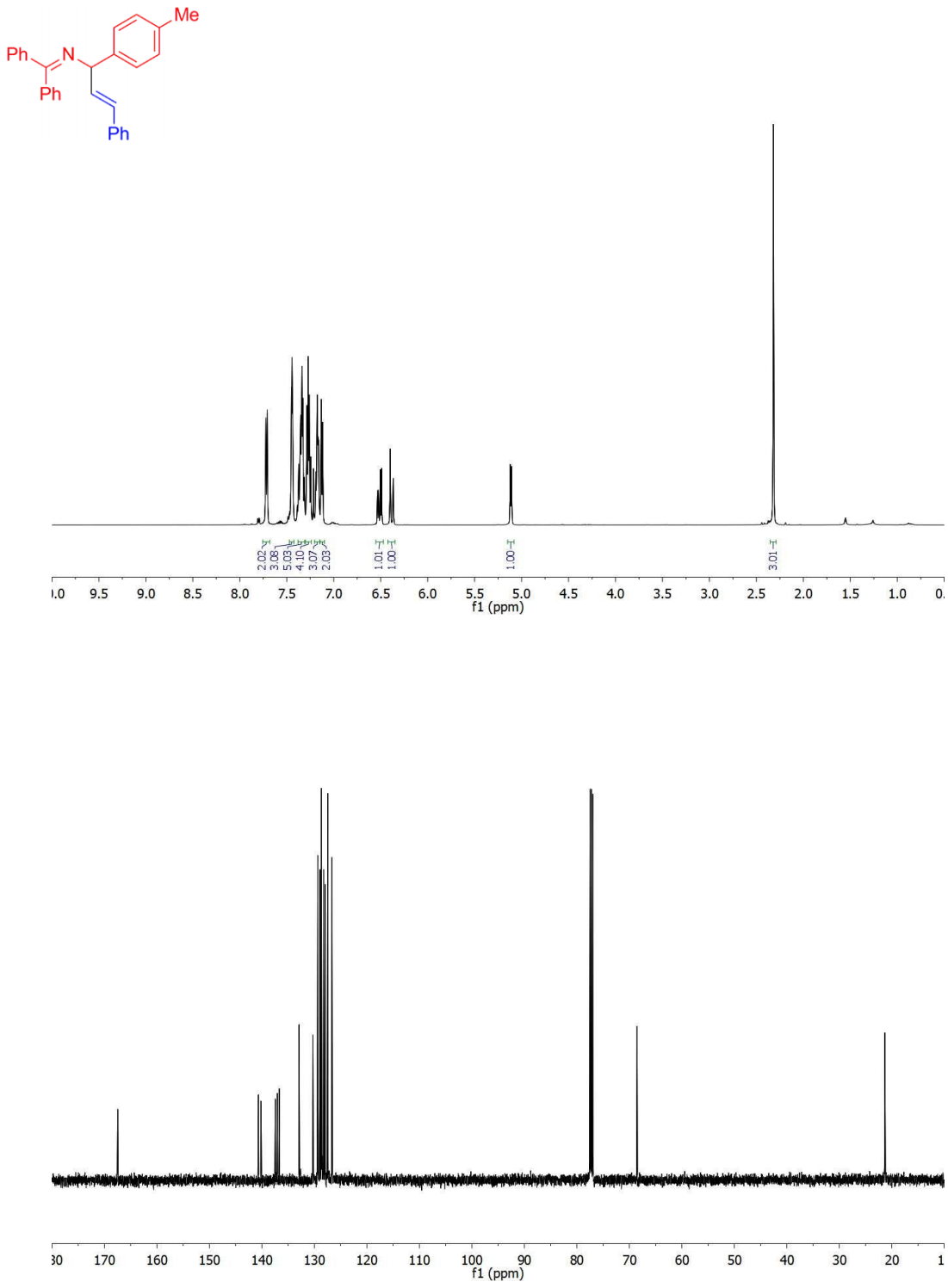


Figure A3.2 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ba in $CDCl_3$

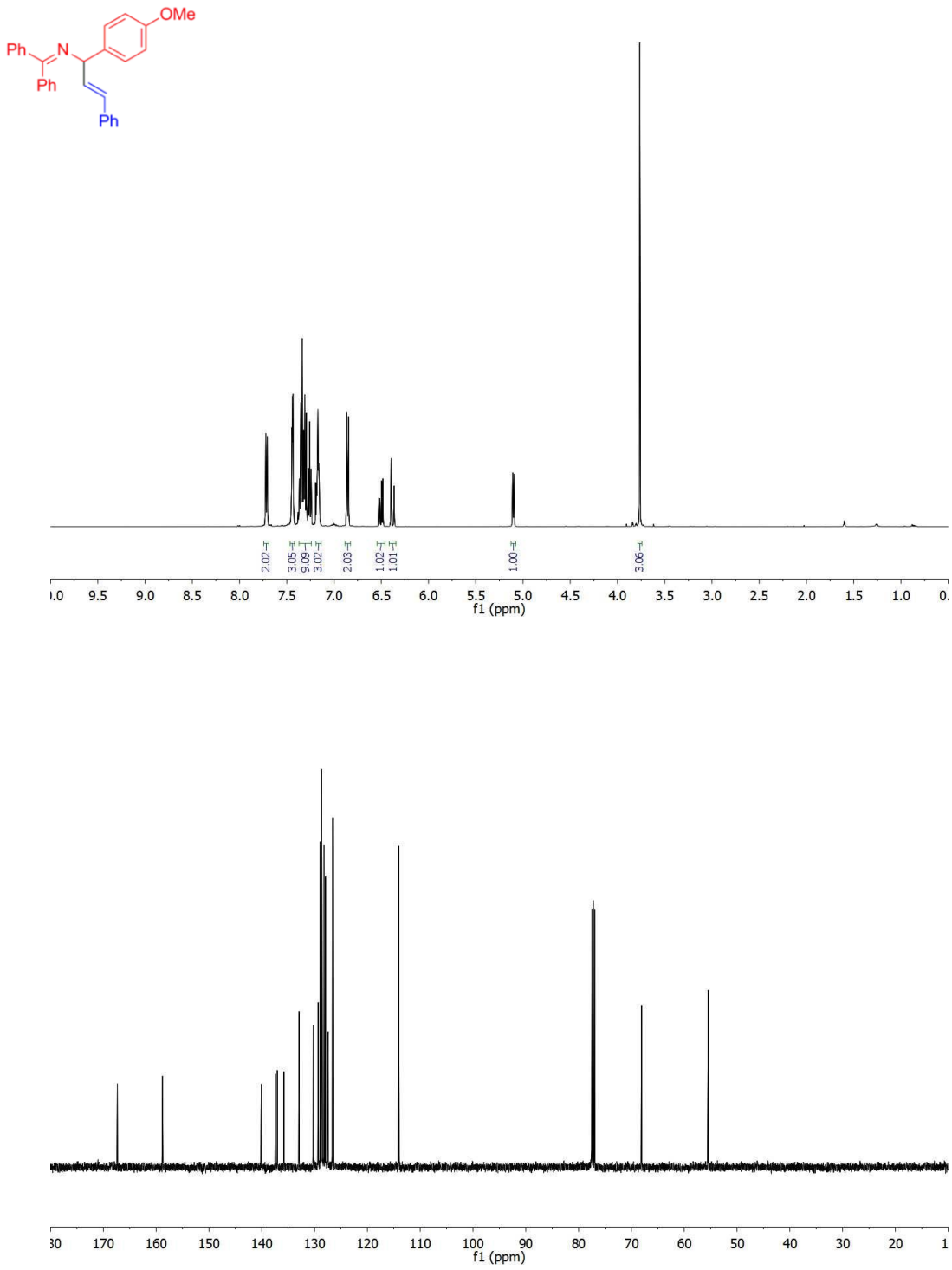


Figure A3.3 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ca in $CDCl_3$

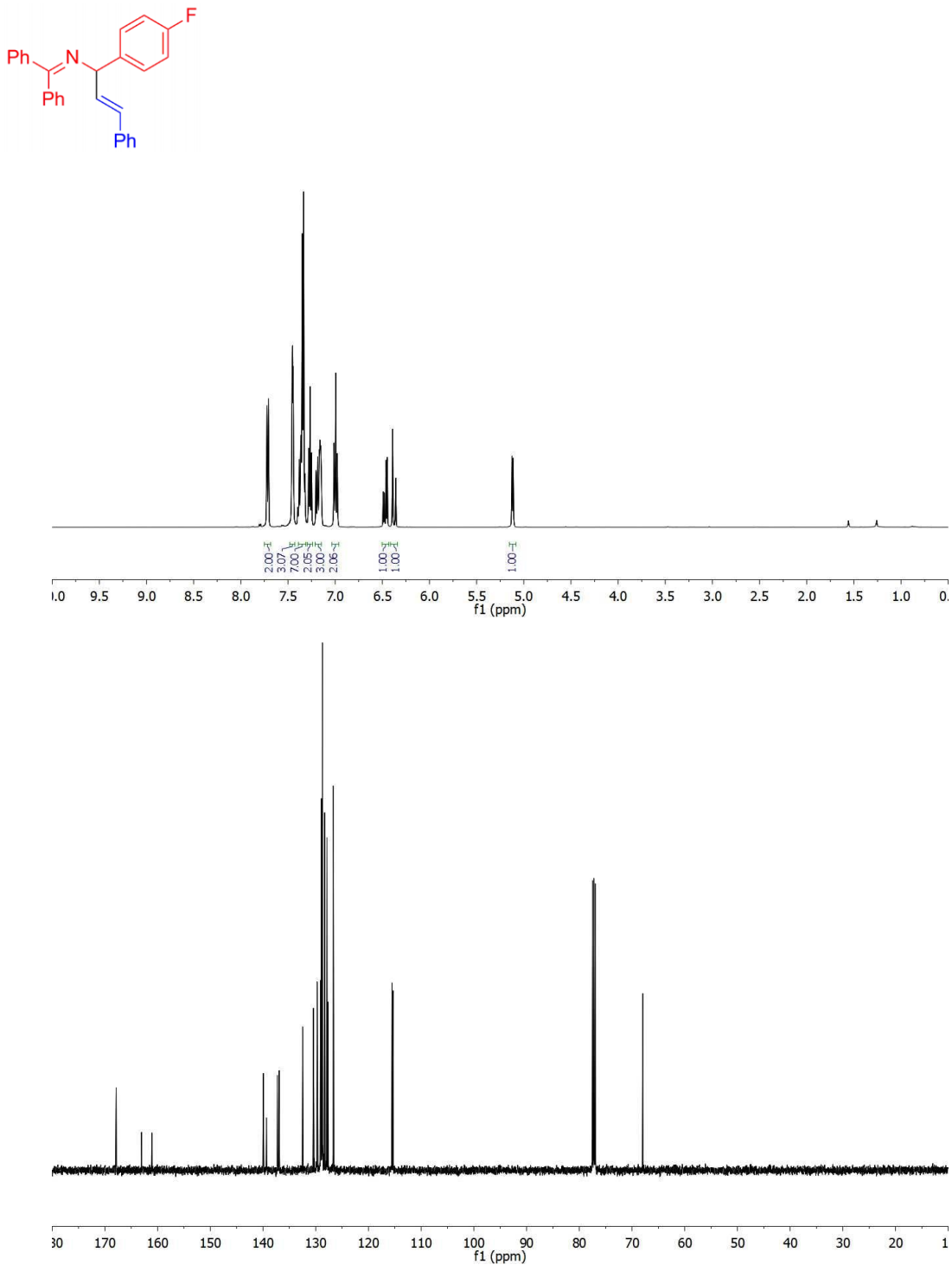


Figure A3.4 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3da in $CDCl_3$

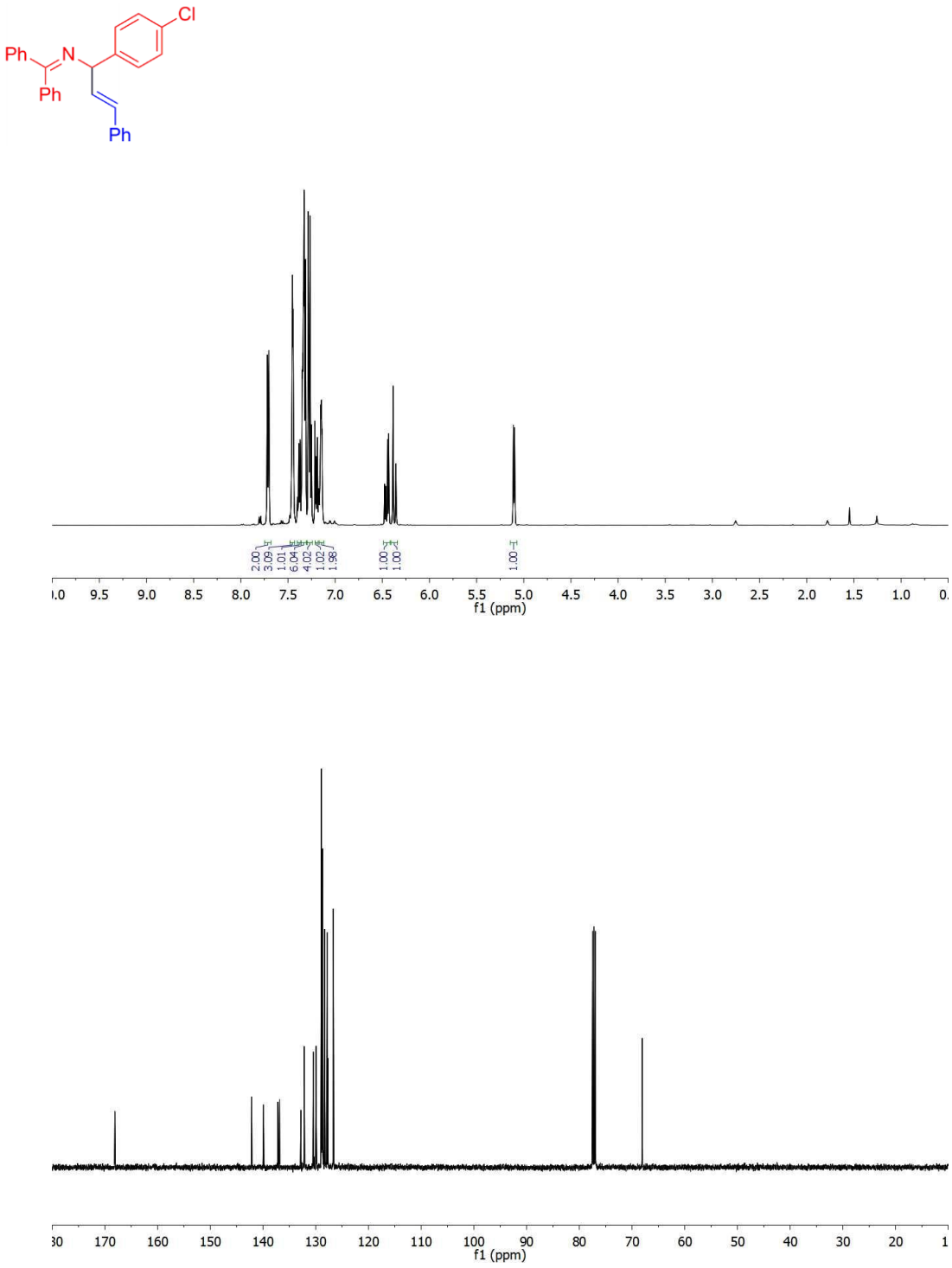


Figure A3.5 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ea in $CDCl_3$

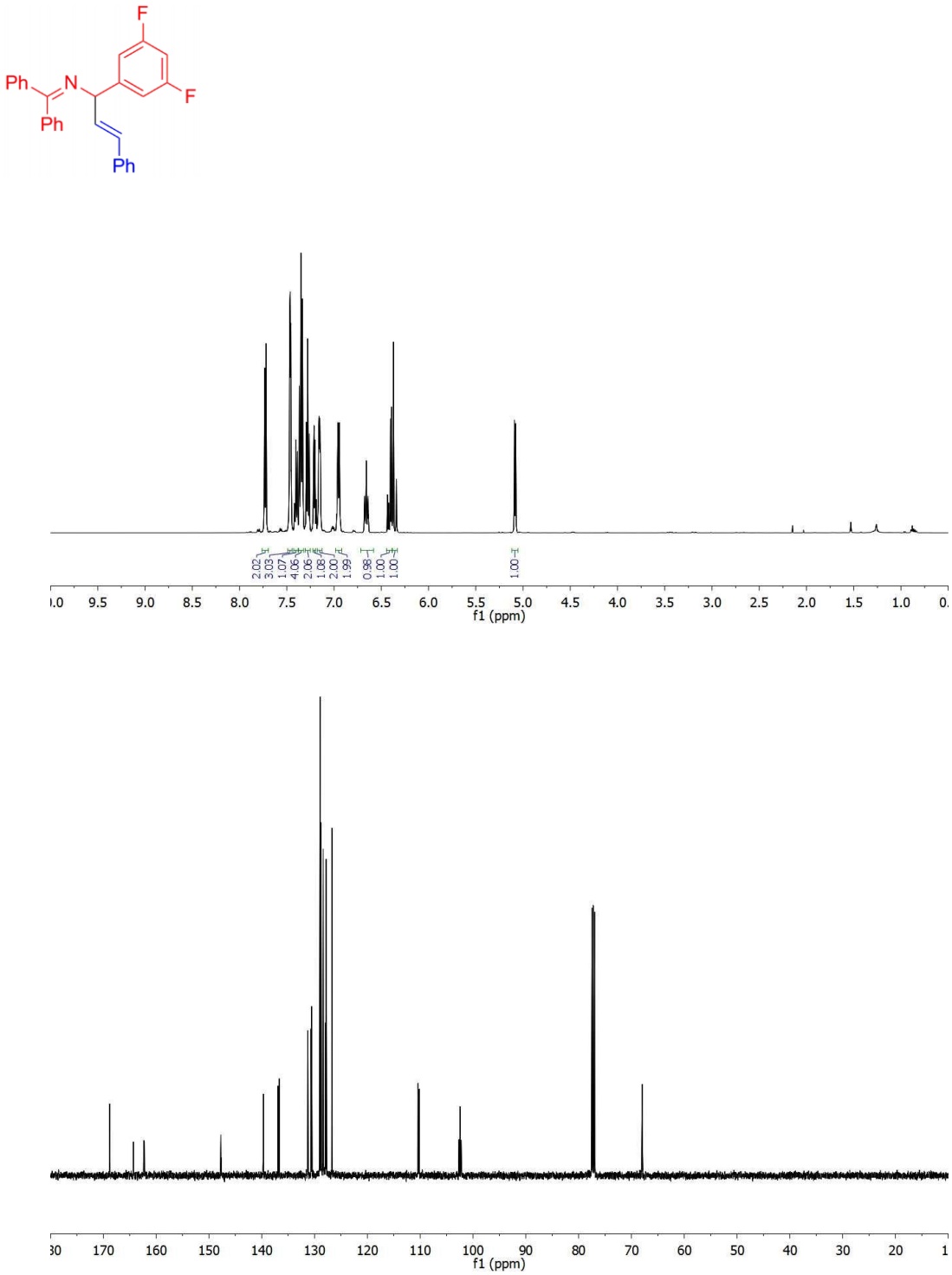


Figure A3.6 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3fa in $CDCl_3$

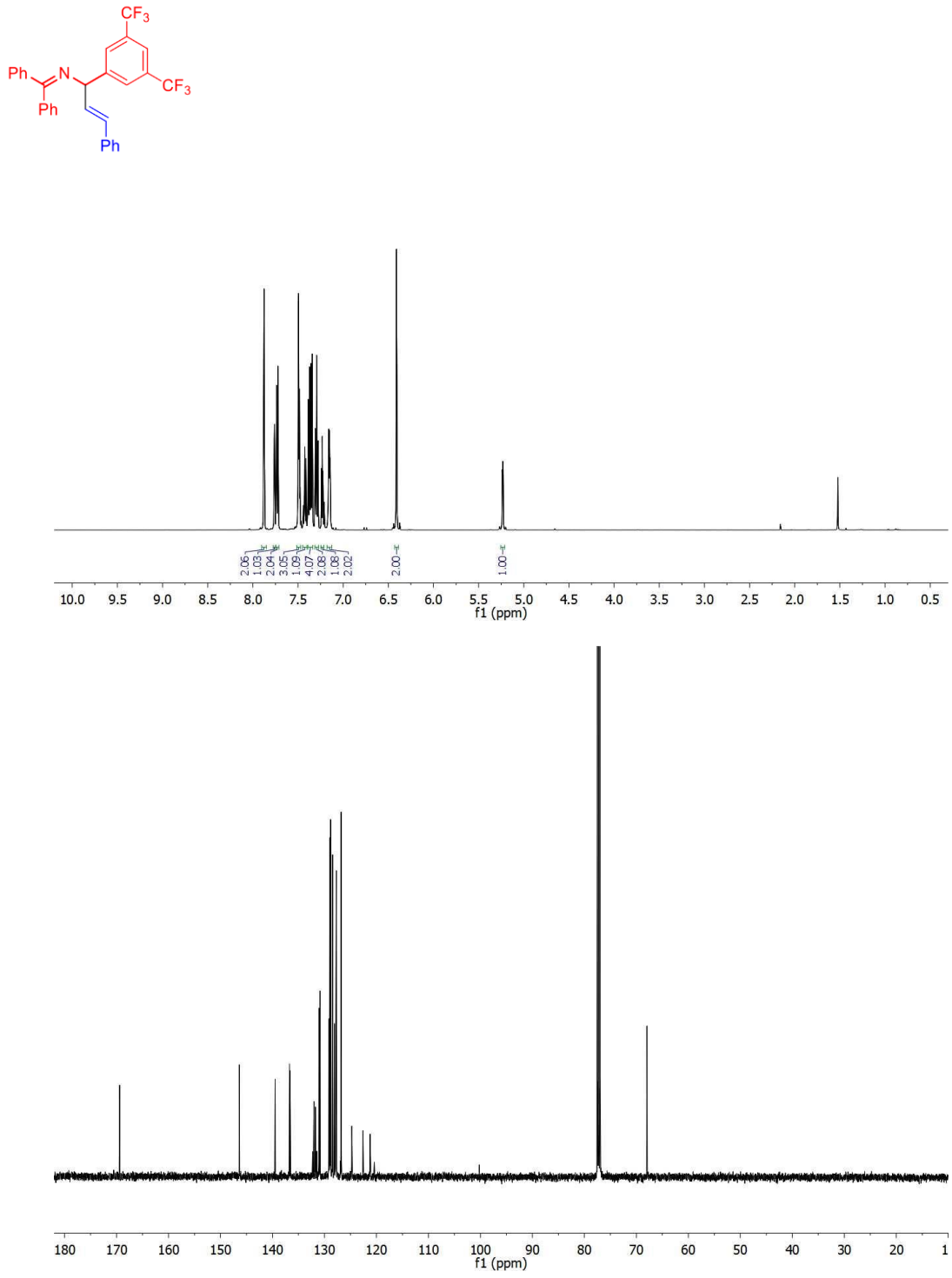


Figure A3.7 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.3ga in $CDCl_3$

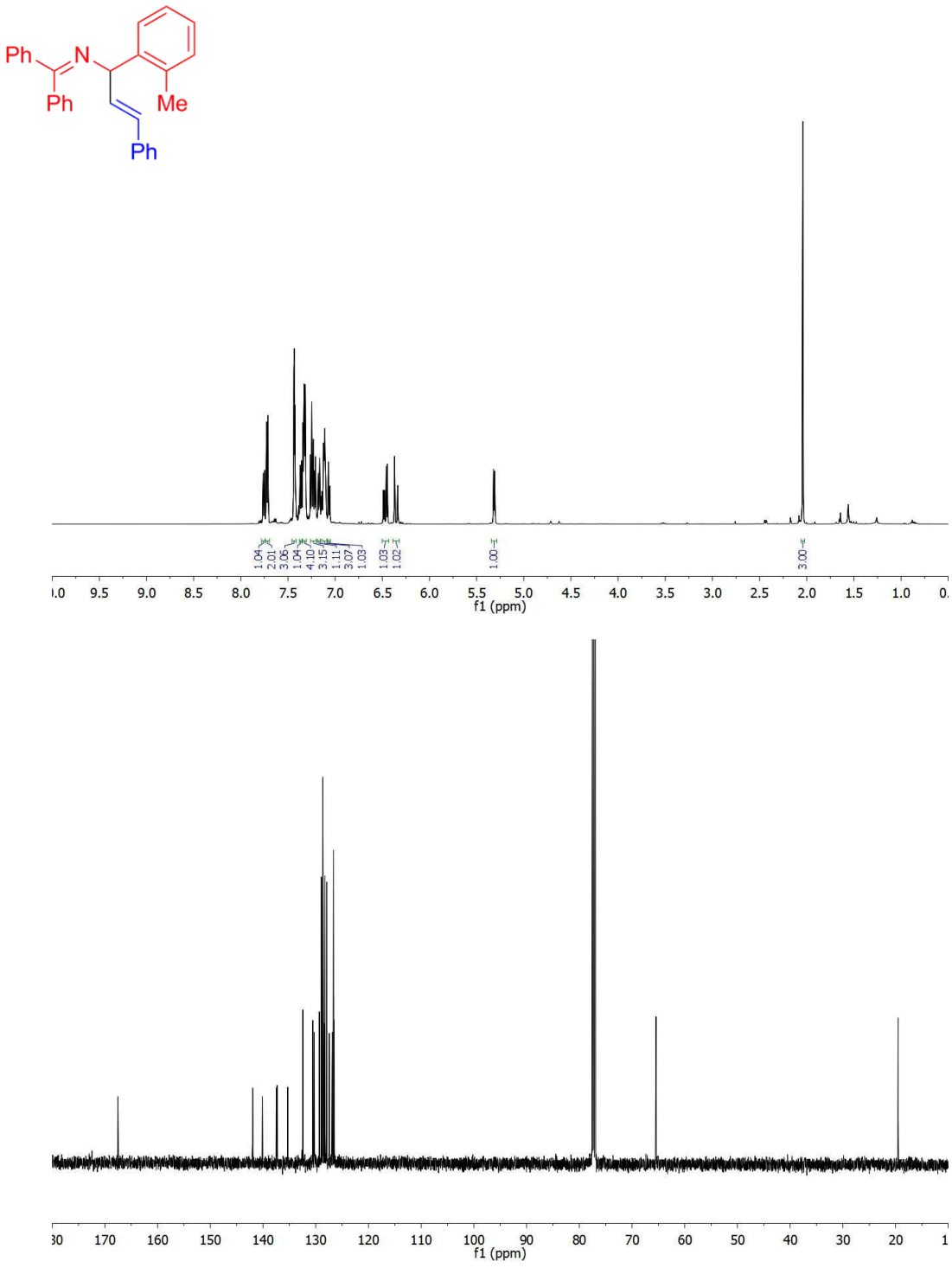


Figure A3.8 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ha in $CDCl_3$

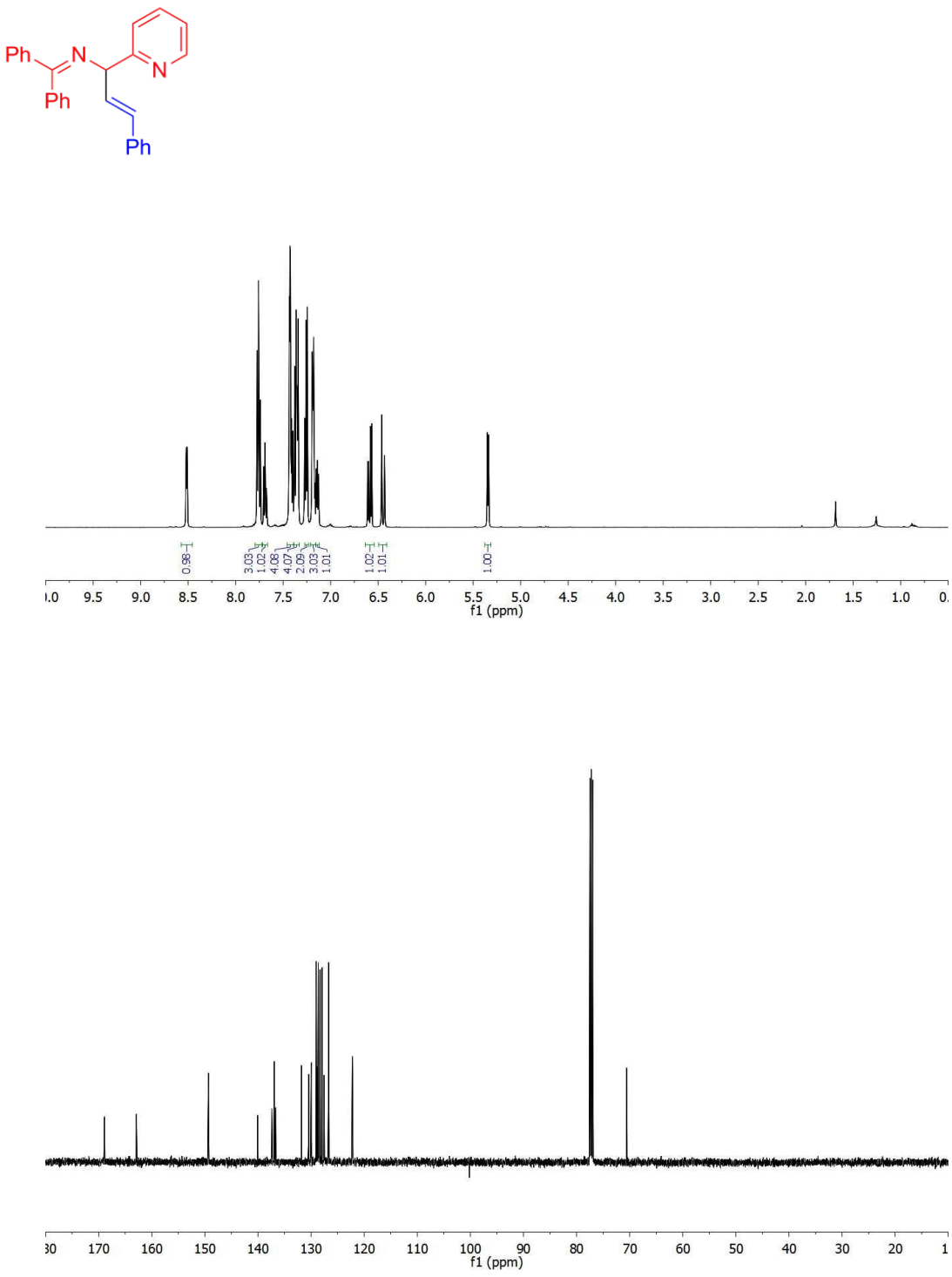


Figure A3.9 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ia in $CDCl_3$

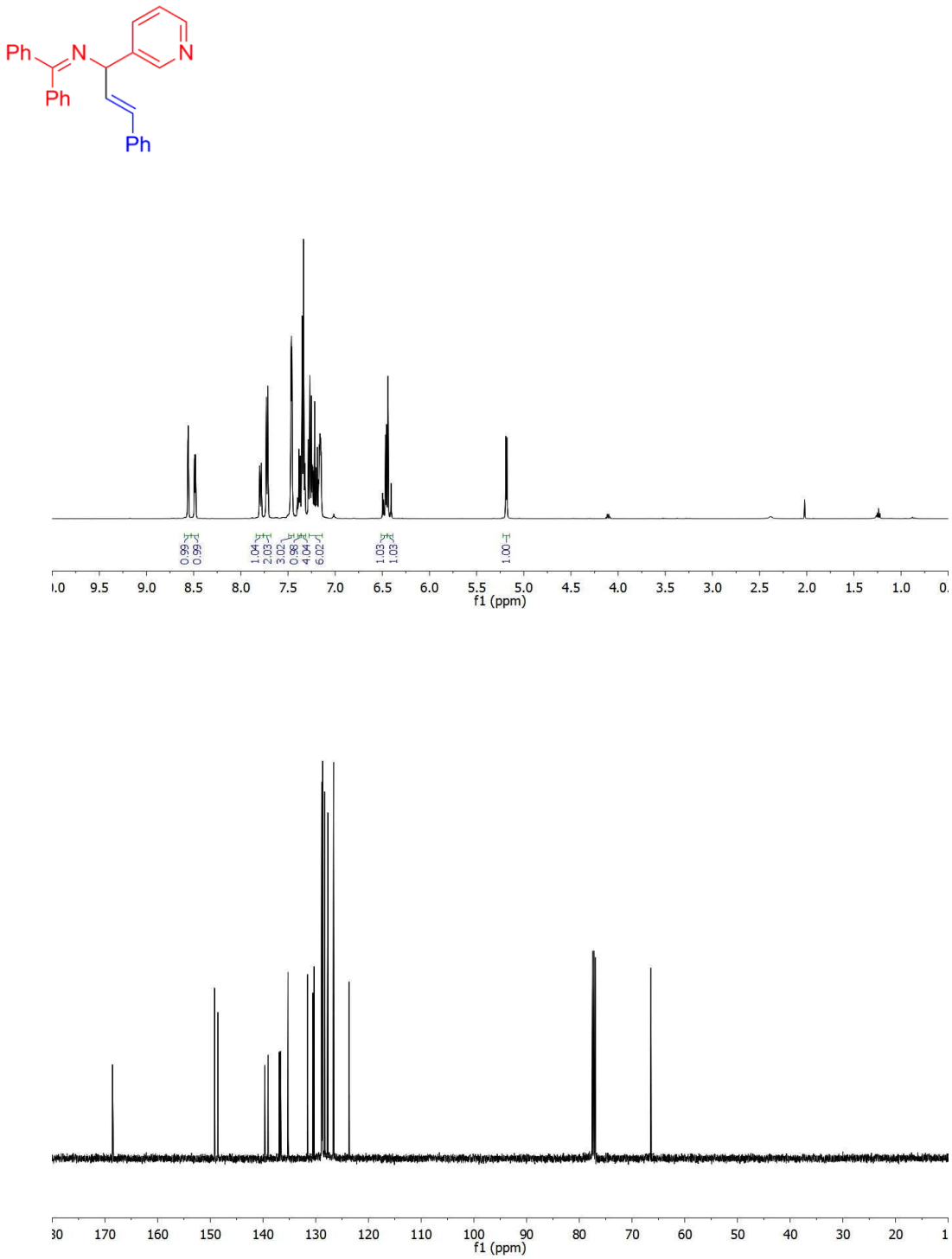


Figure A3.10 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ja in $CDCl_3$

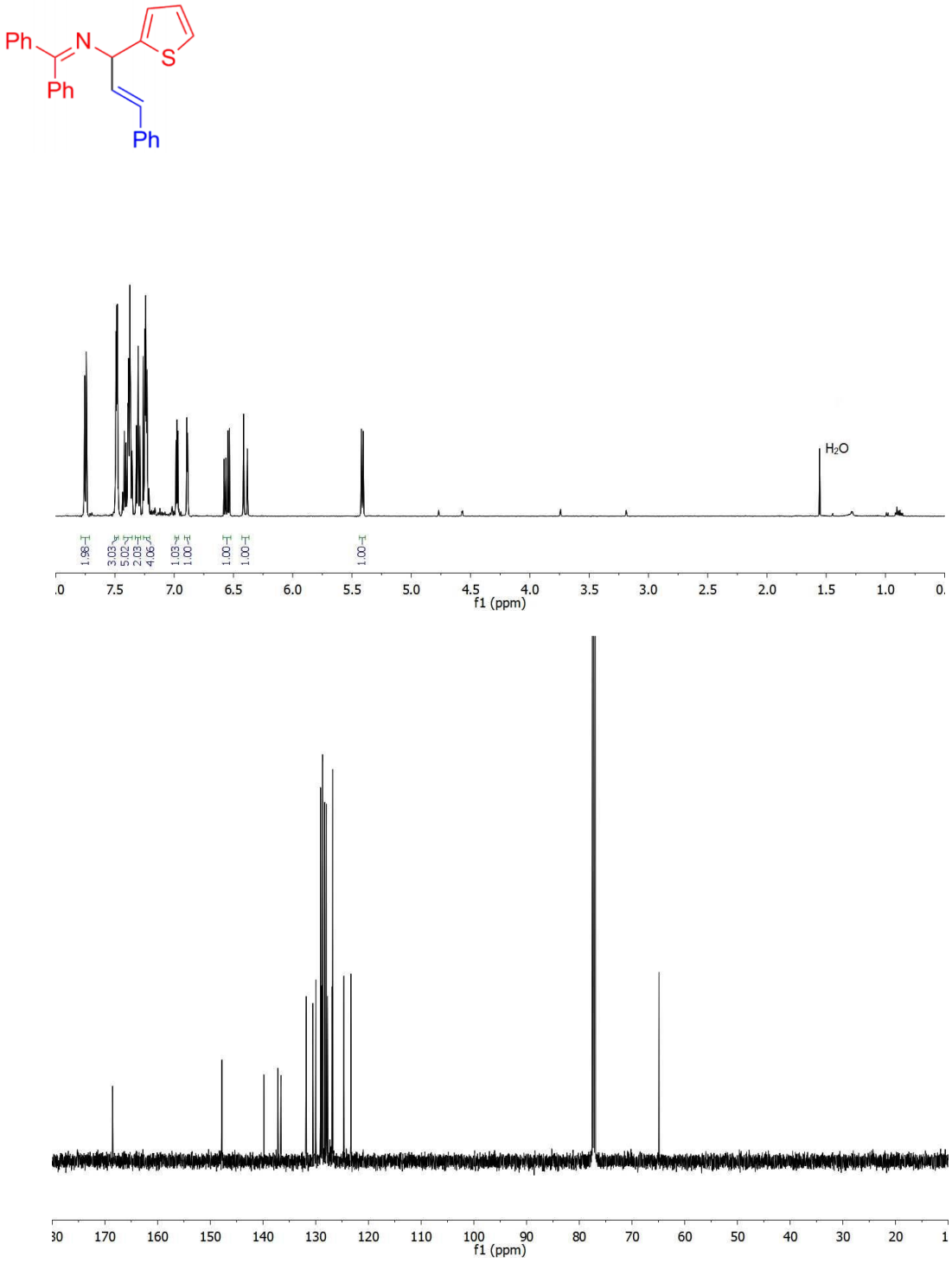


Figure A3.10 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.3ka in $CDCl_3$

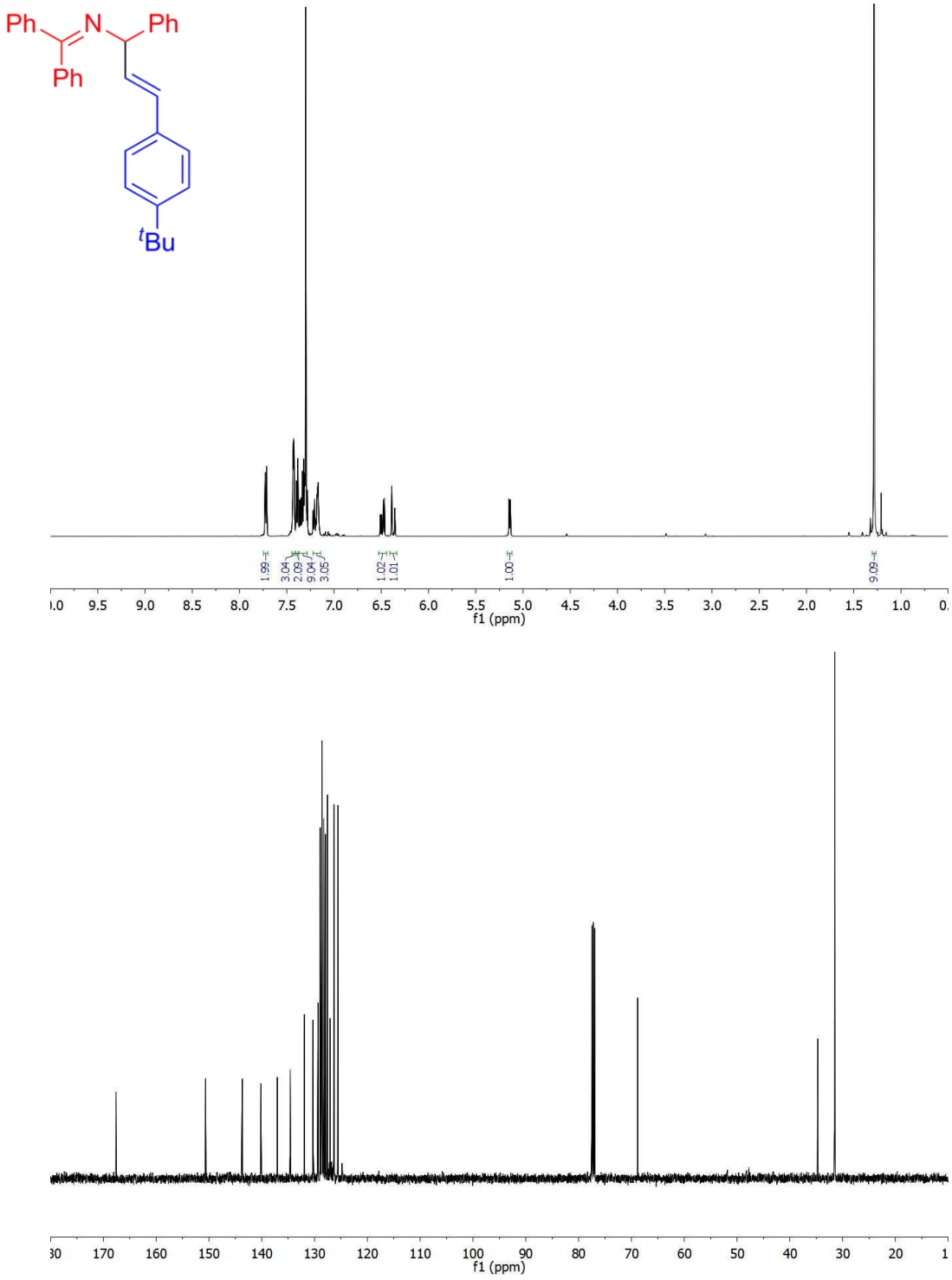


Figure A3.11 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ab in $CDCl_3$

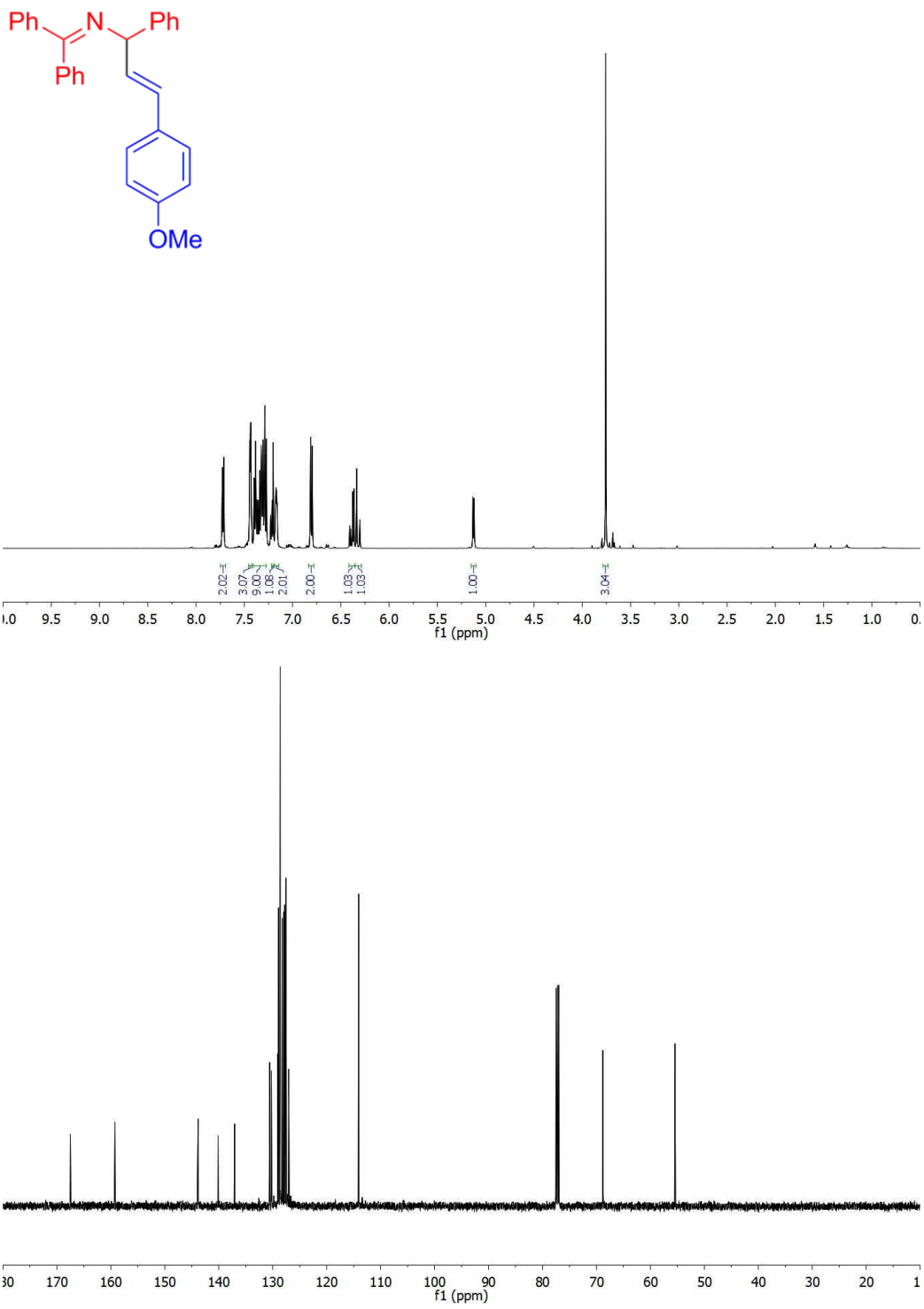


Figure A3.12 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ac in $CDCl_3$

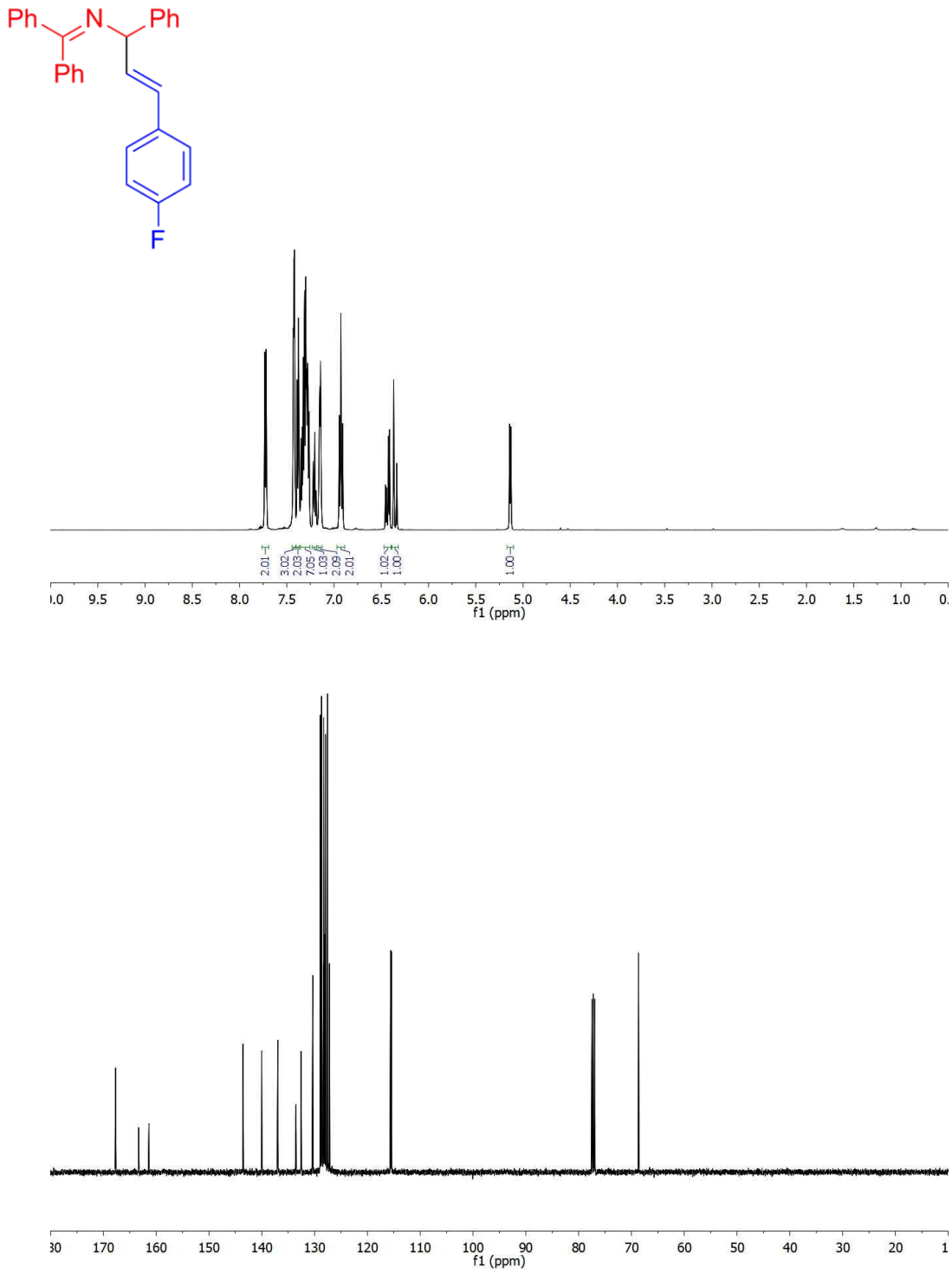


Figure A3.13 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.3ad in $CDCl_3$

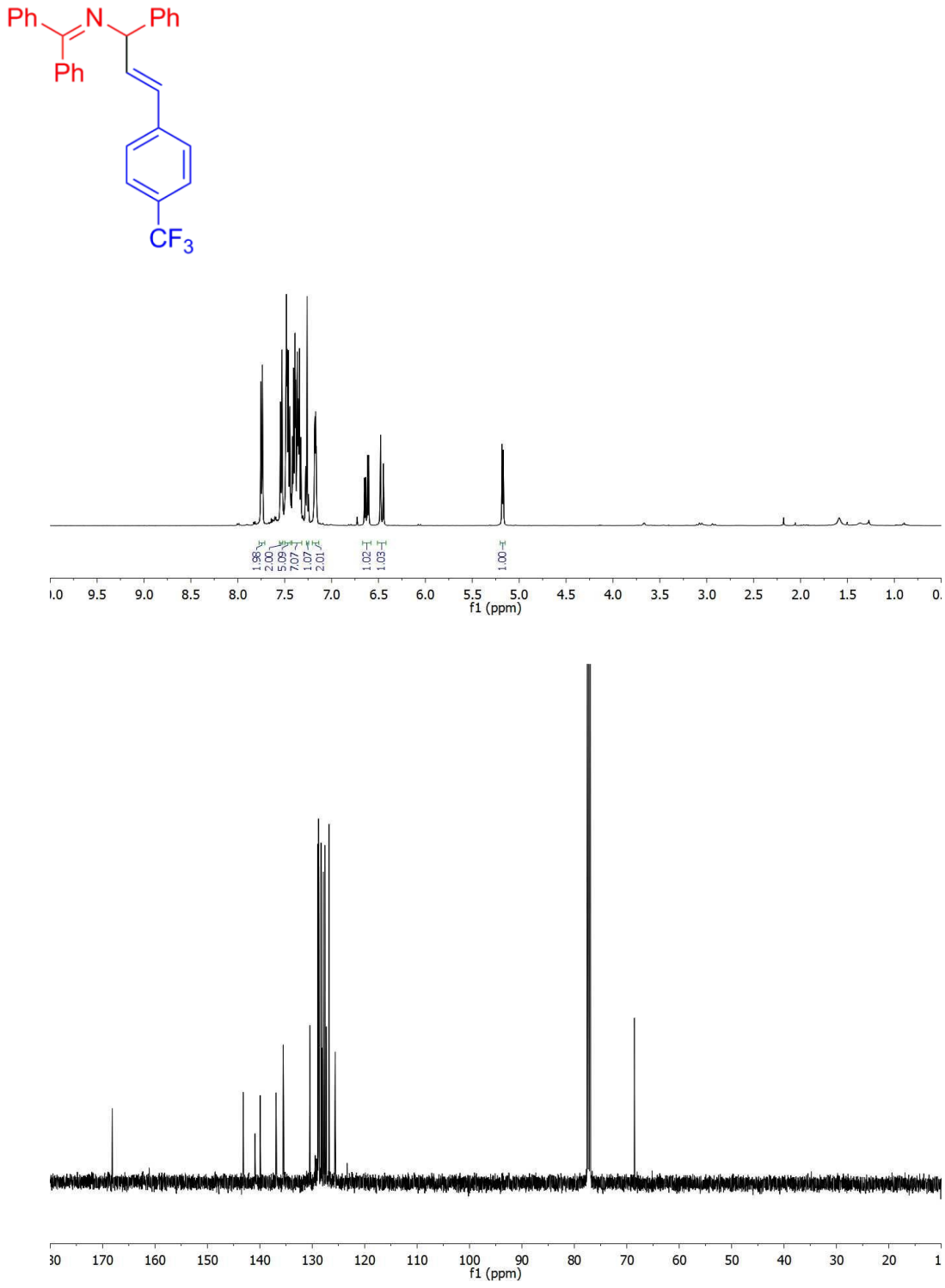


Figure A3.14 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ae in $CDCl_3$

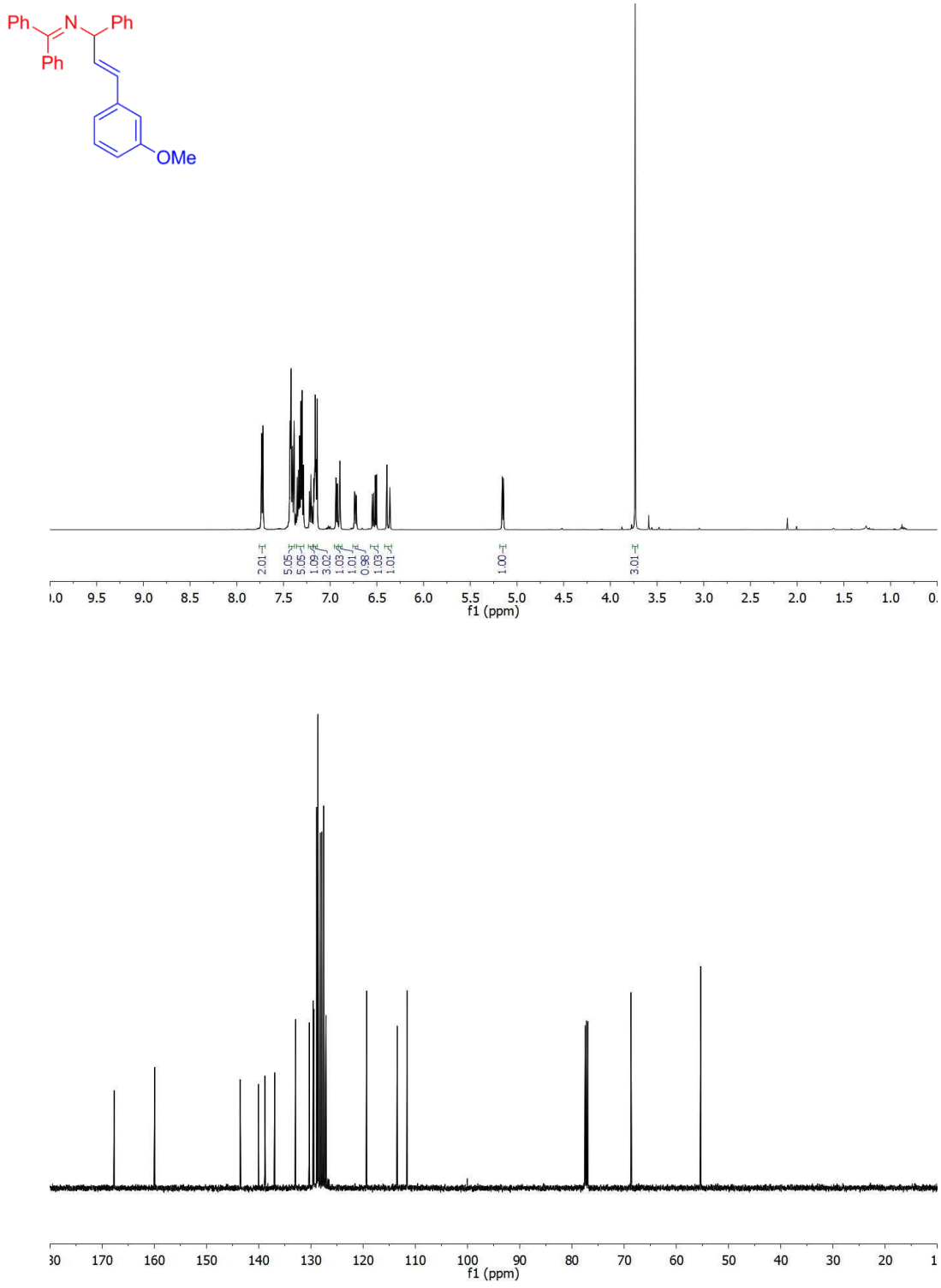


Figure A3.15 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3af in $CDCl_3$

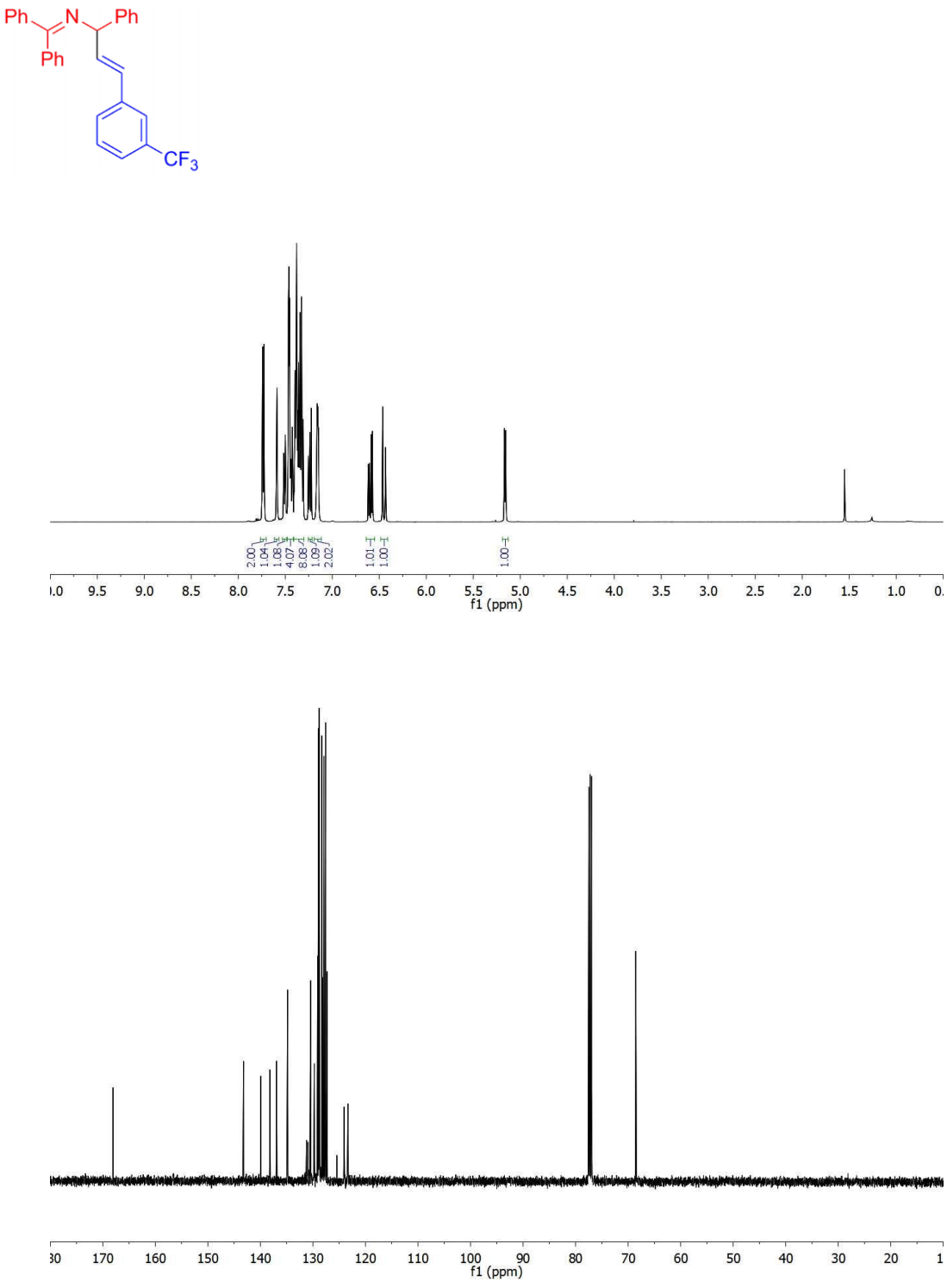


Figure A3.16 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ag in $CDCl_3$

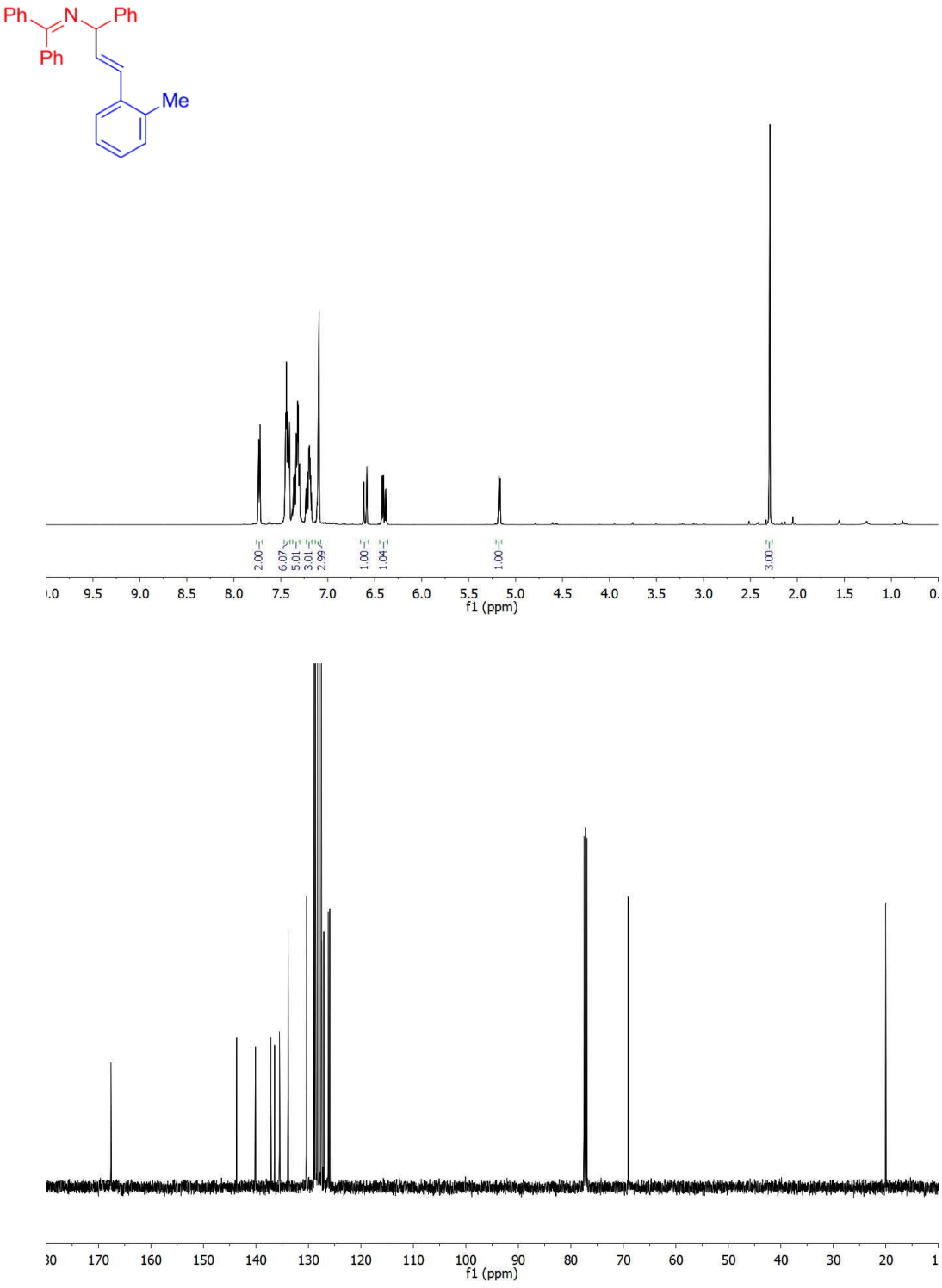


Figure A3.17 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ah in $CDCl_3$

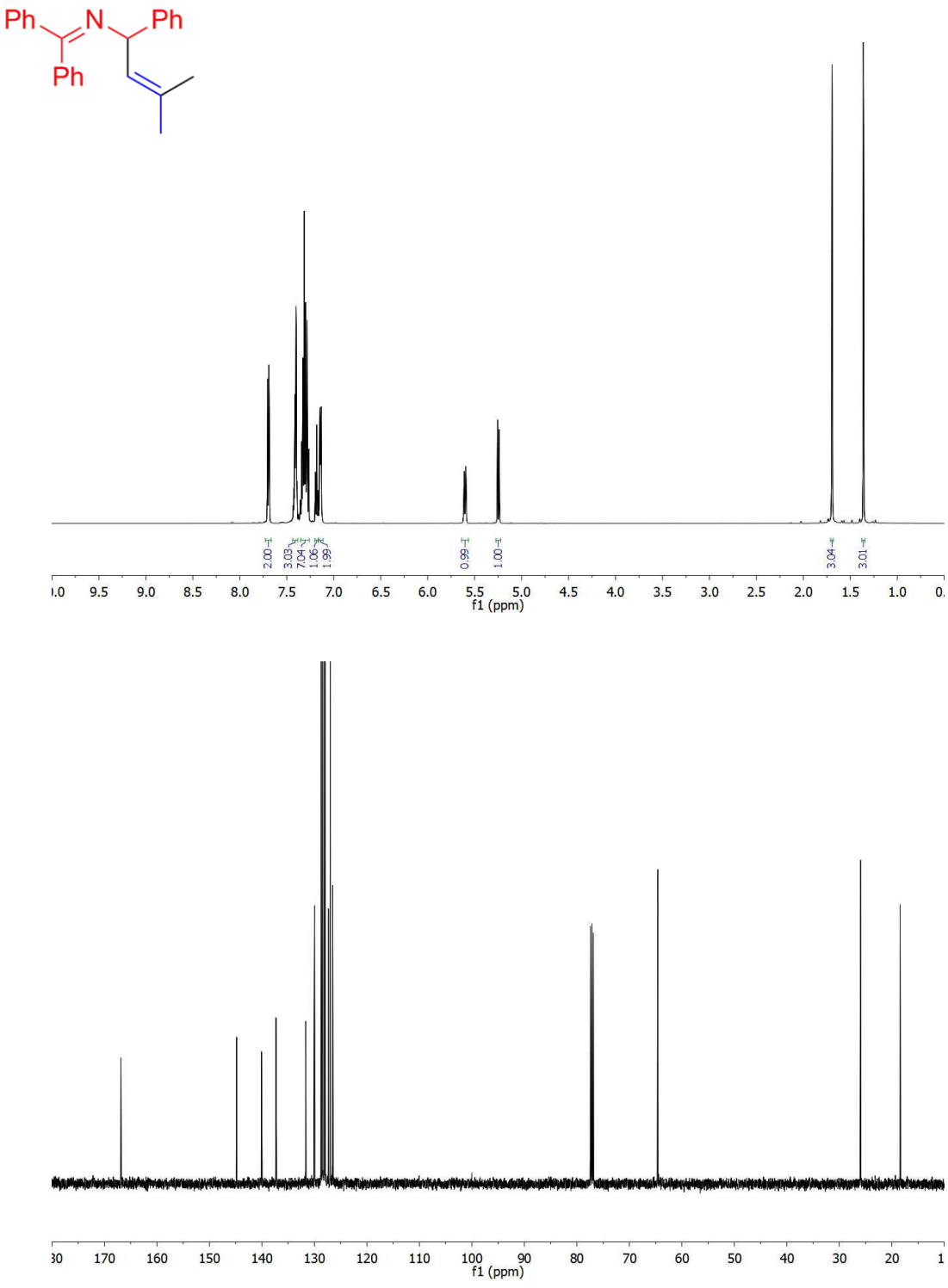


Figure A3.18 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3ai in $CDCl_3$

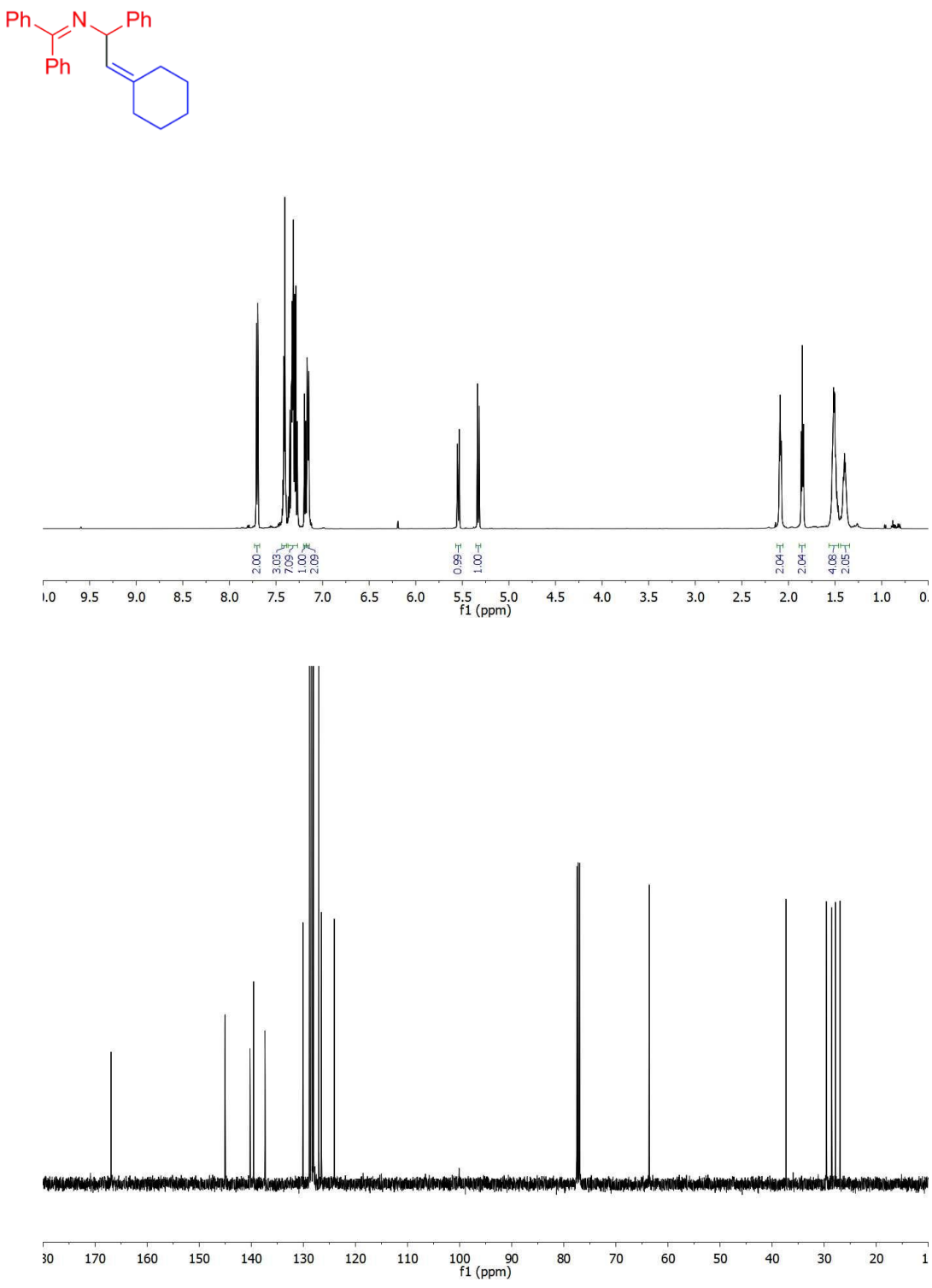


Figure A3.19 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.3aj in $CDCl_3$

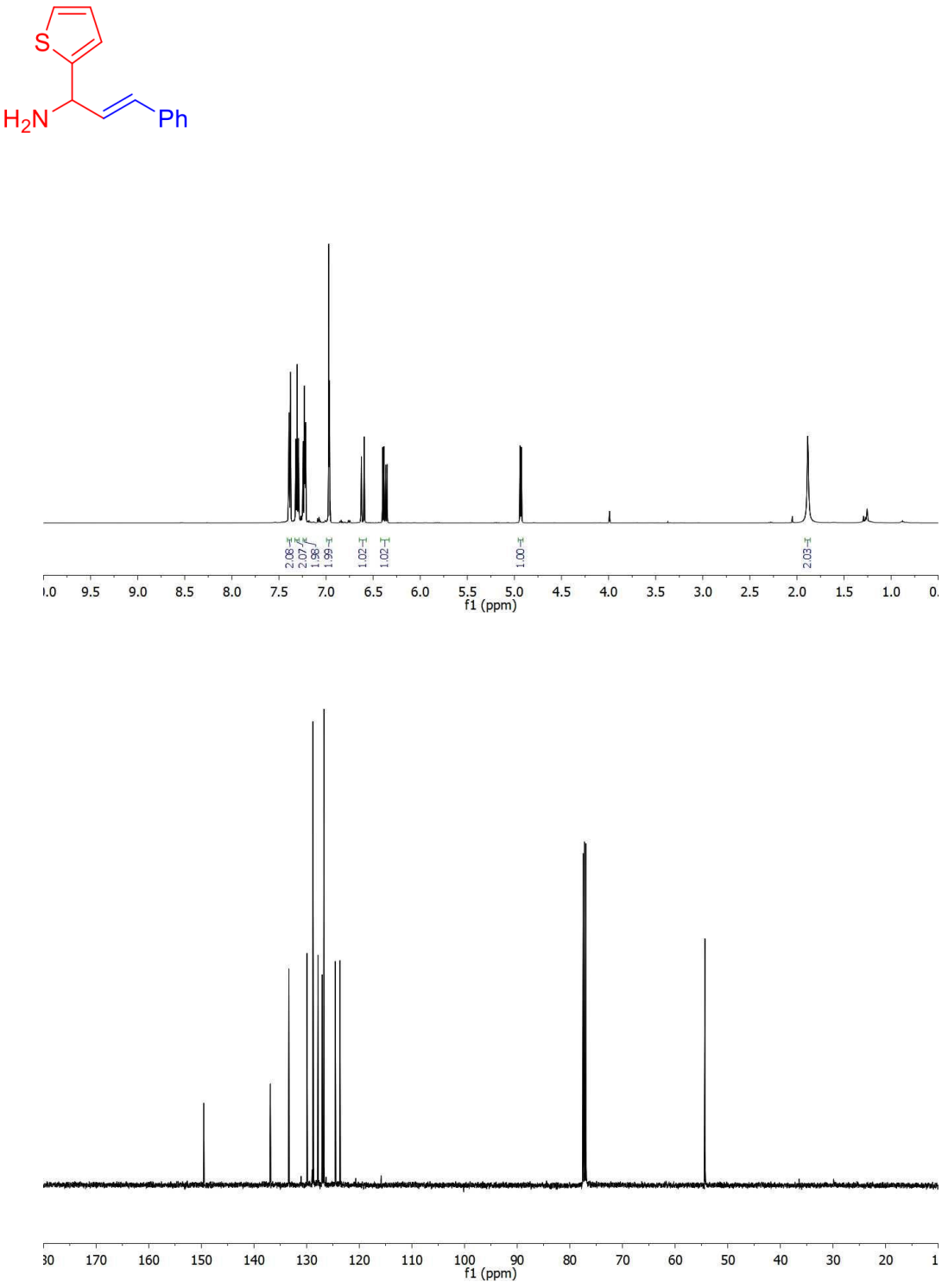


Figure A3.20 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.4ka in $CDCl_3$

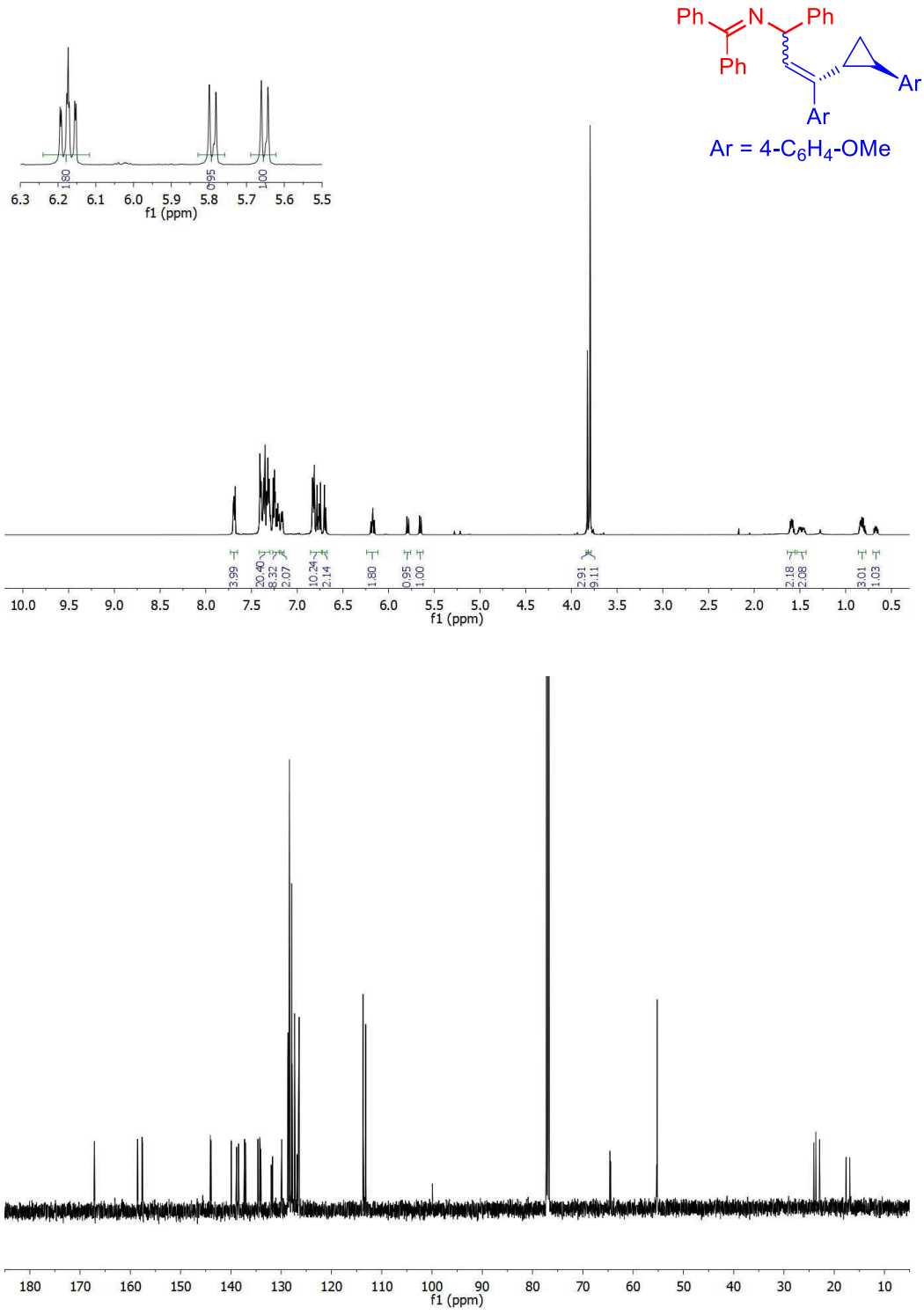


Figure A3.21 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.4ak in $CDCl_3$

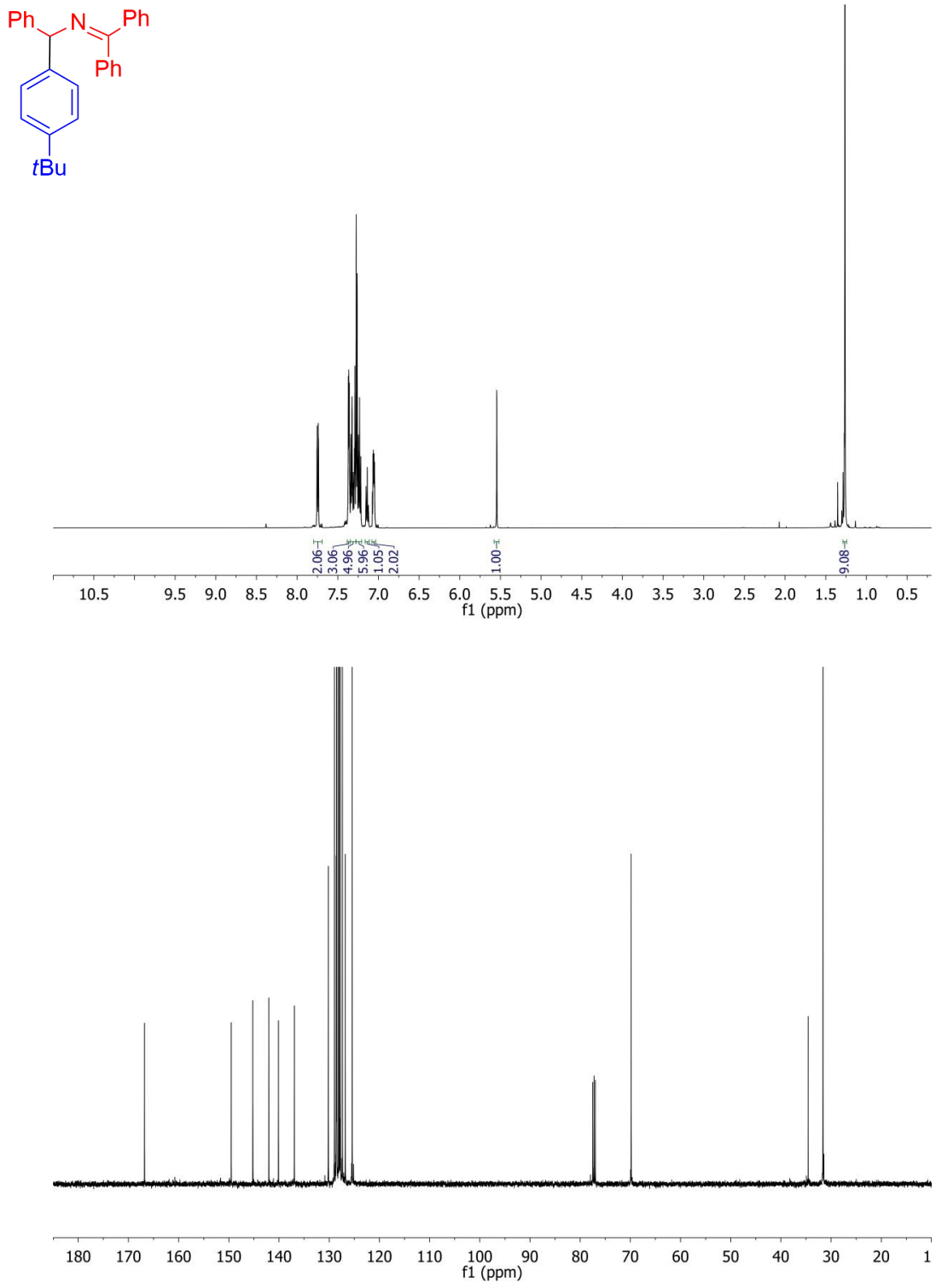


Figure A3.22 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7aa in $CDCl_3$

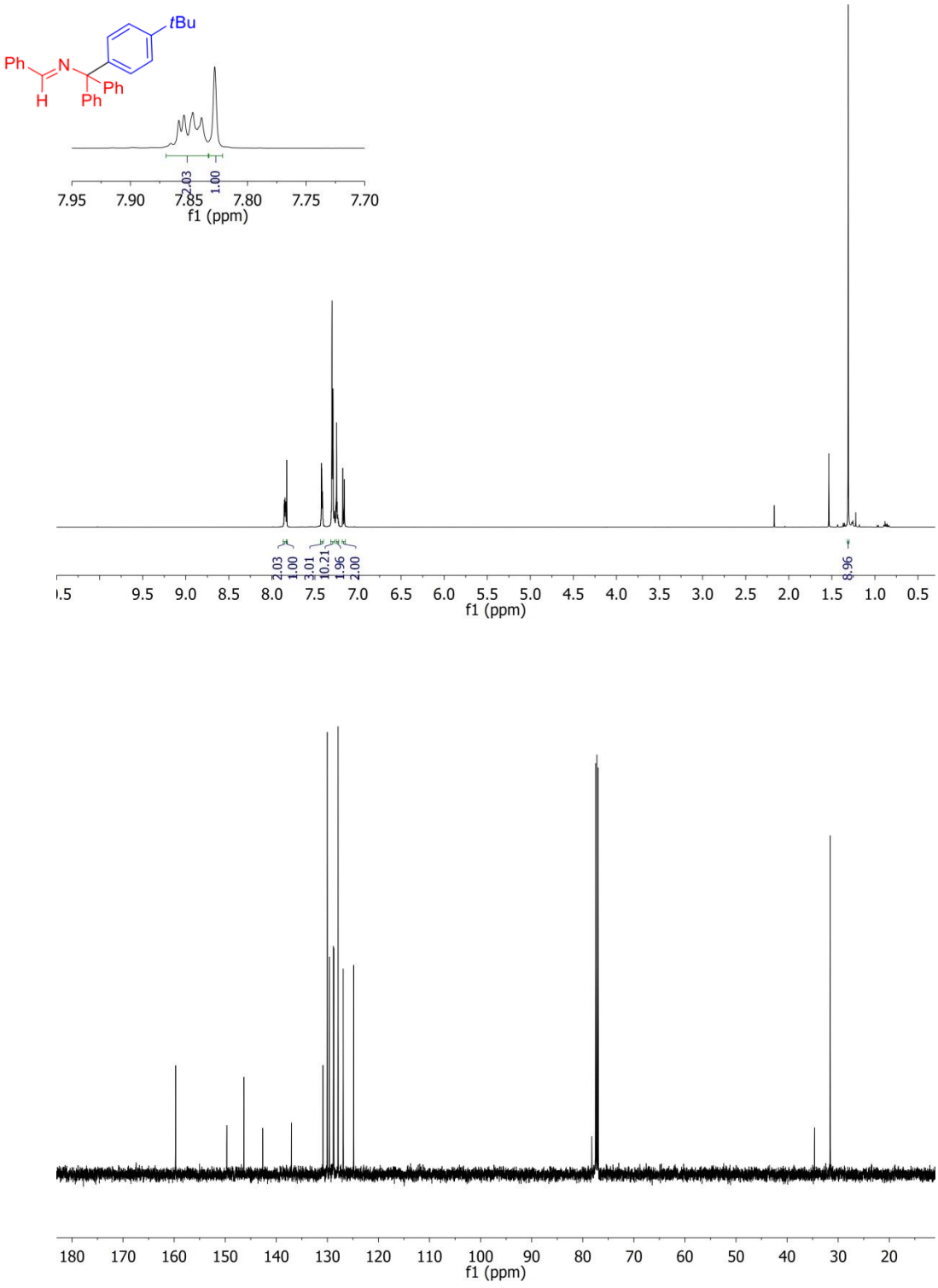


Figure A3.23 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7aa' in $CDCl_3$

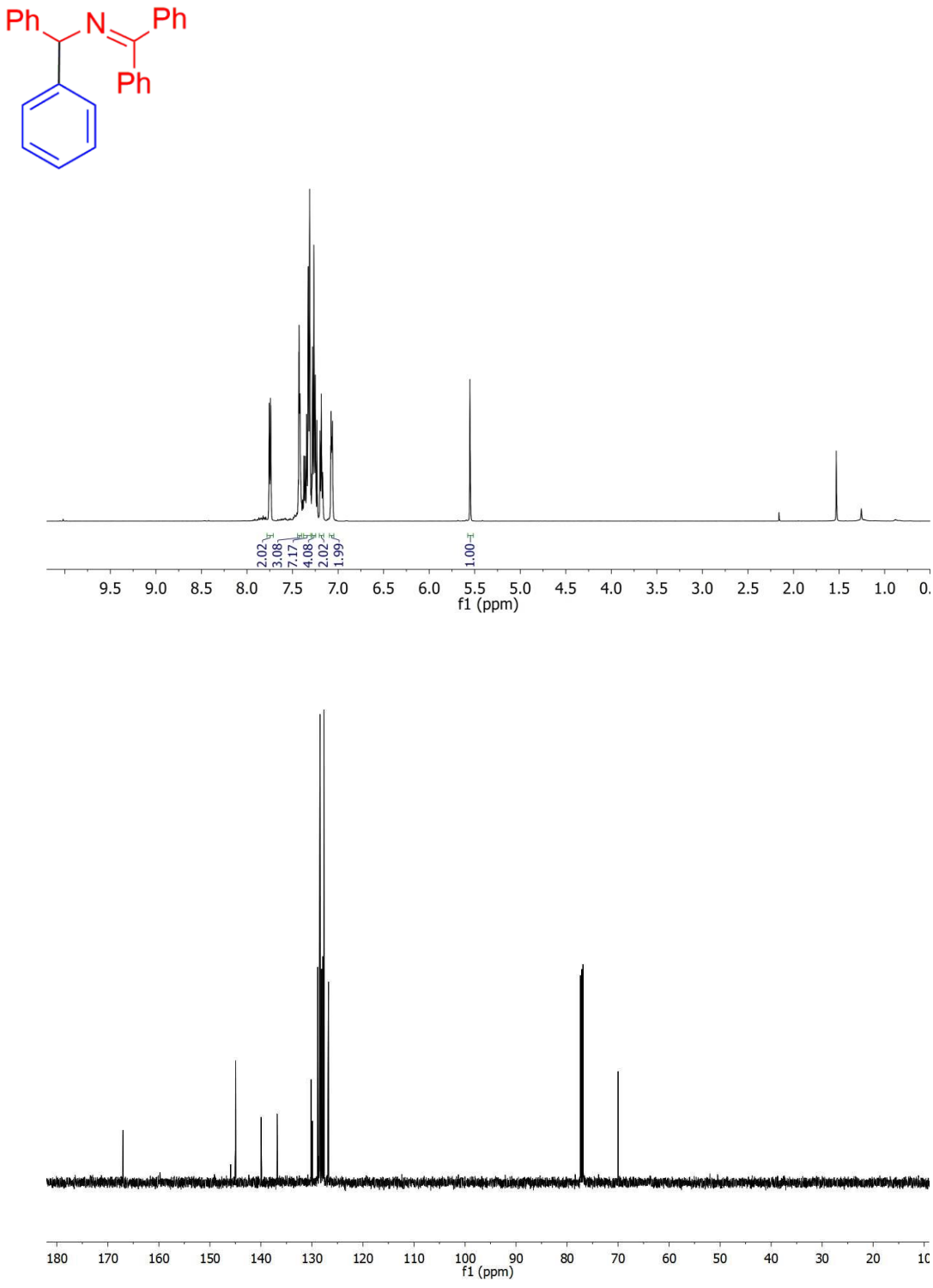


Figure A3.24 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ab in $CDCl_3$

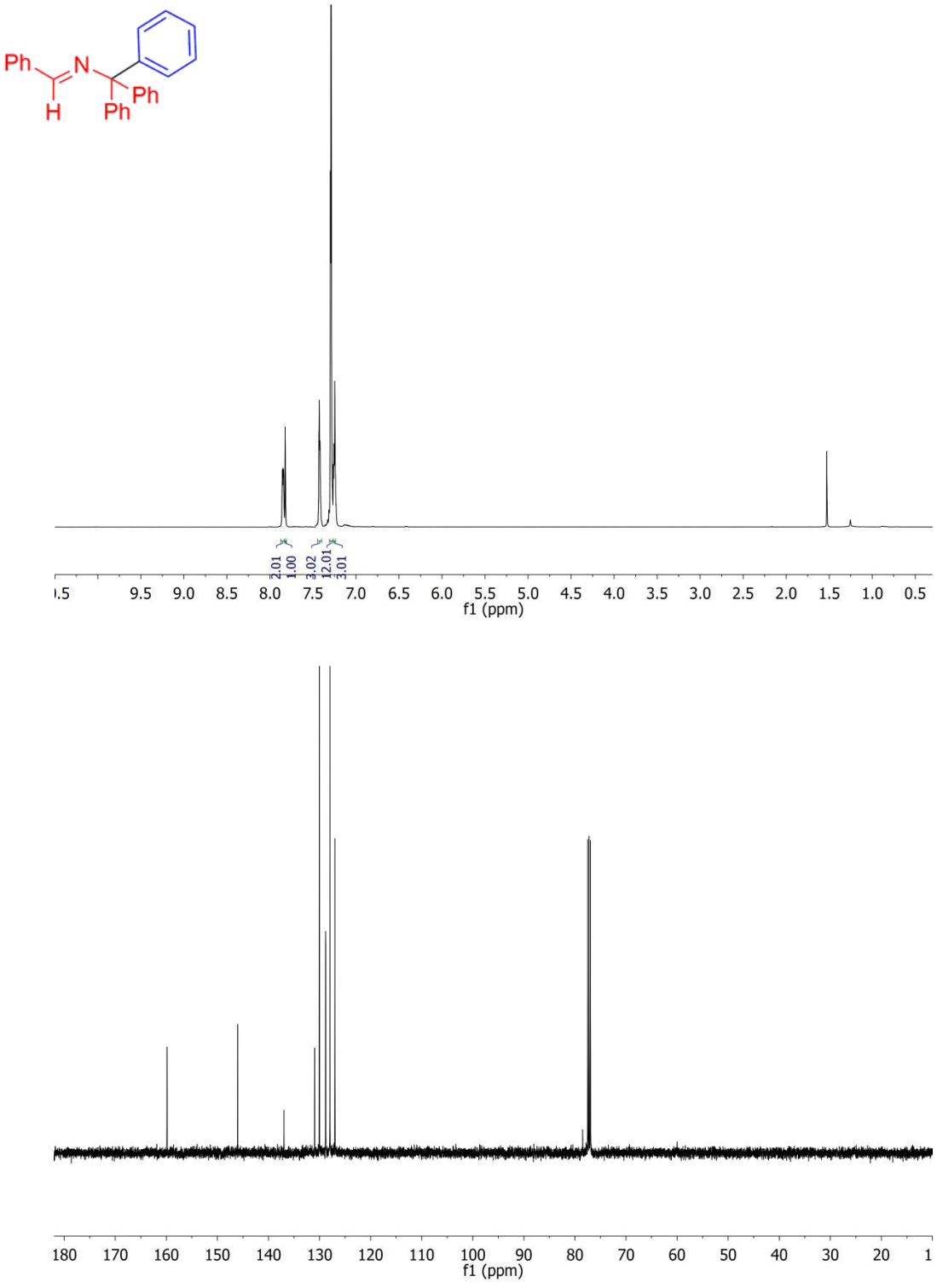


Figure A3.25 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.7ab' in $CDCl_3$

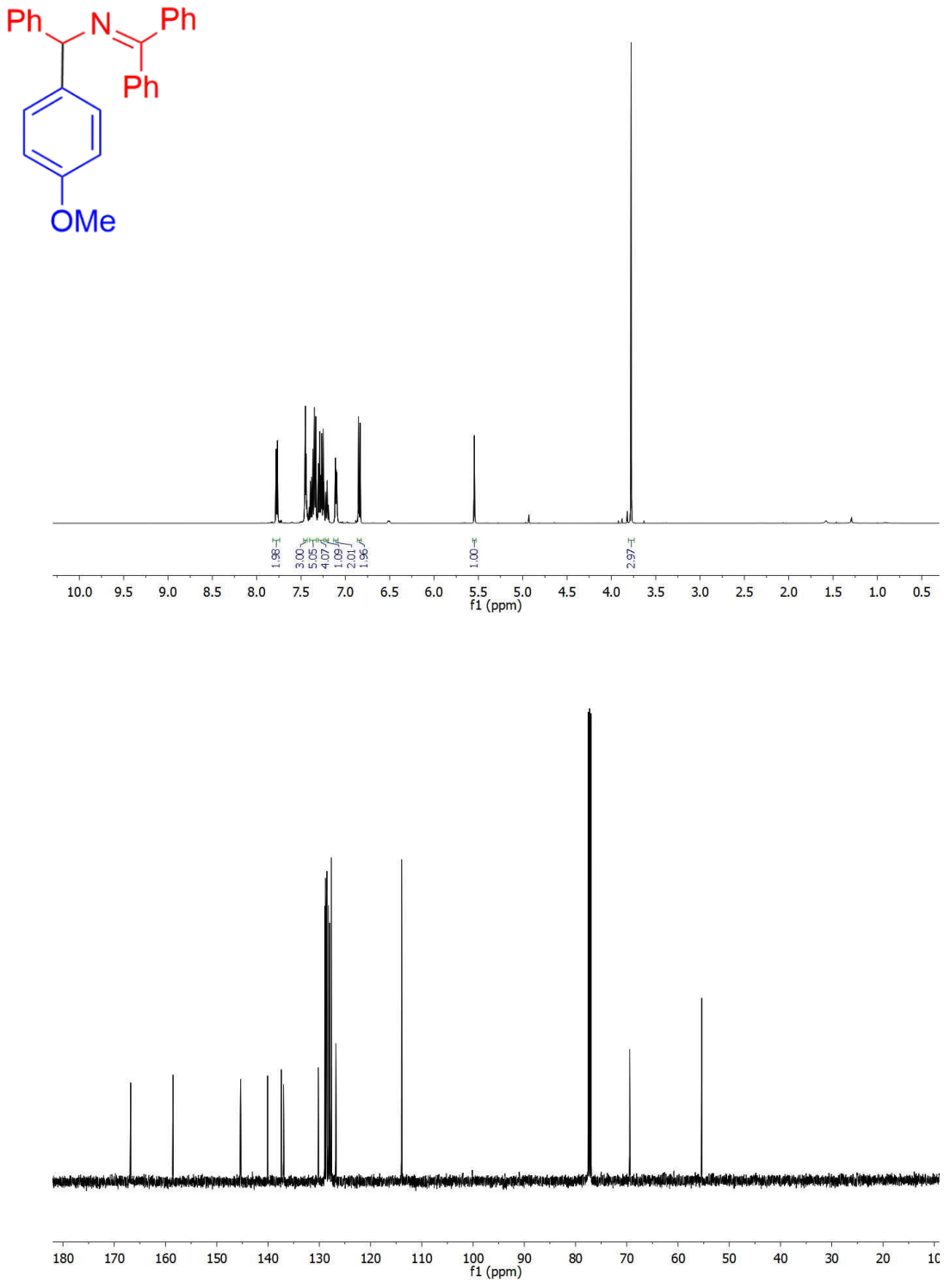


Figure A3.26 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ac in $CDCl_3$

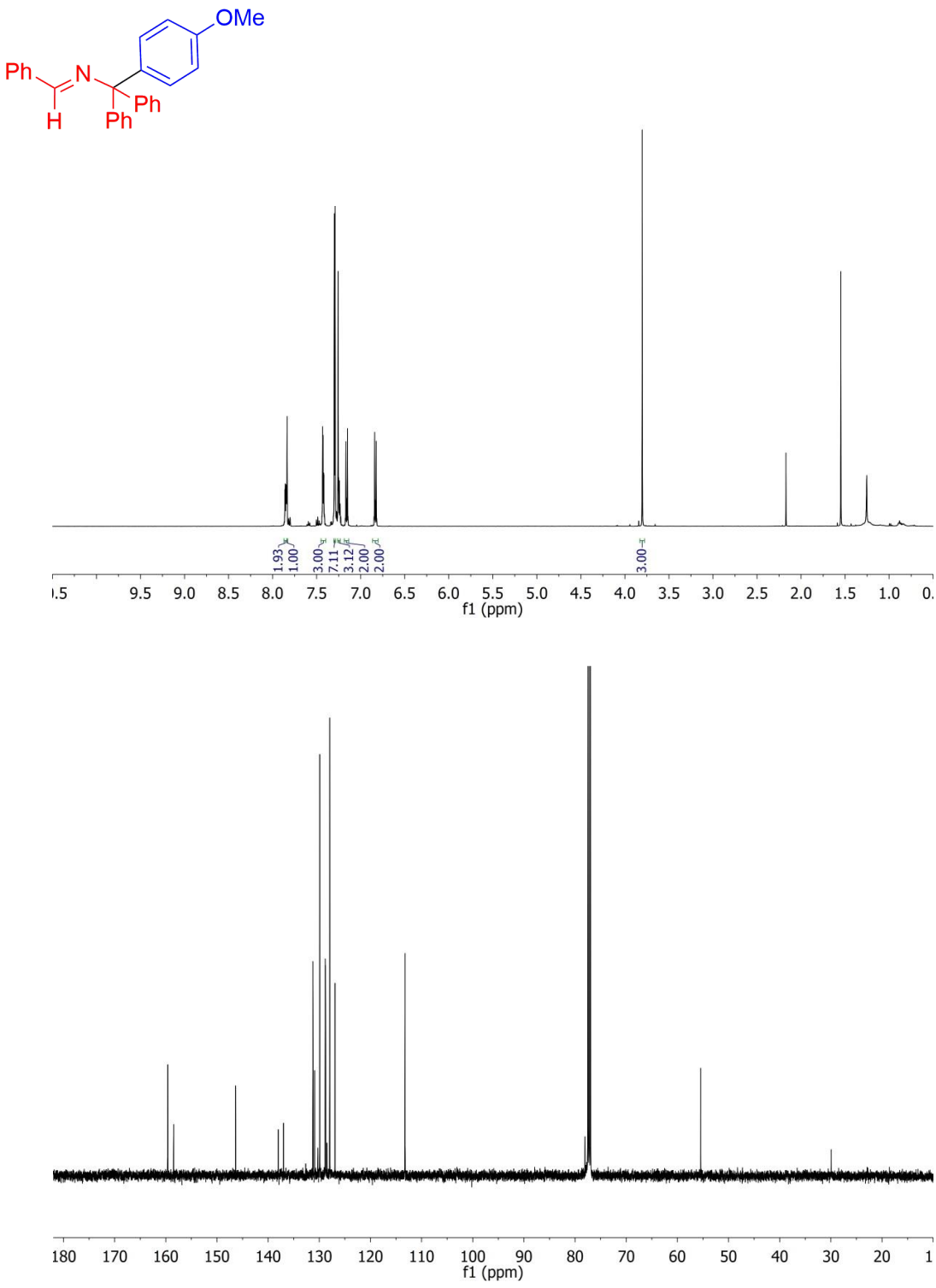


Figure A3.27 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.7ac' in $CDCl_3$

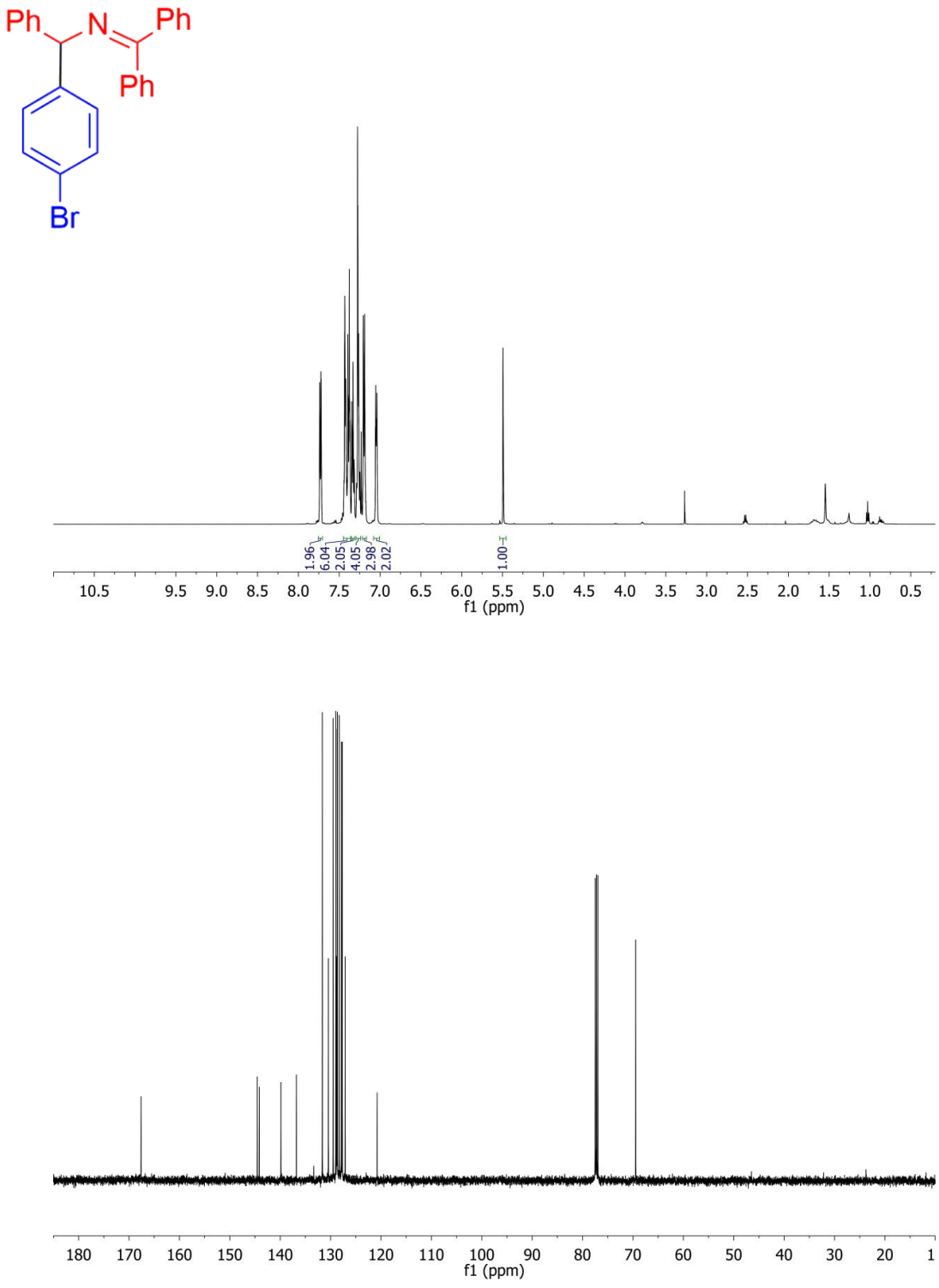


Figure A3.28 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ad in $CDCl_3$

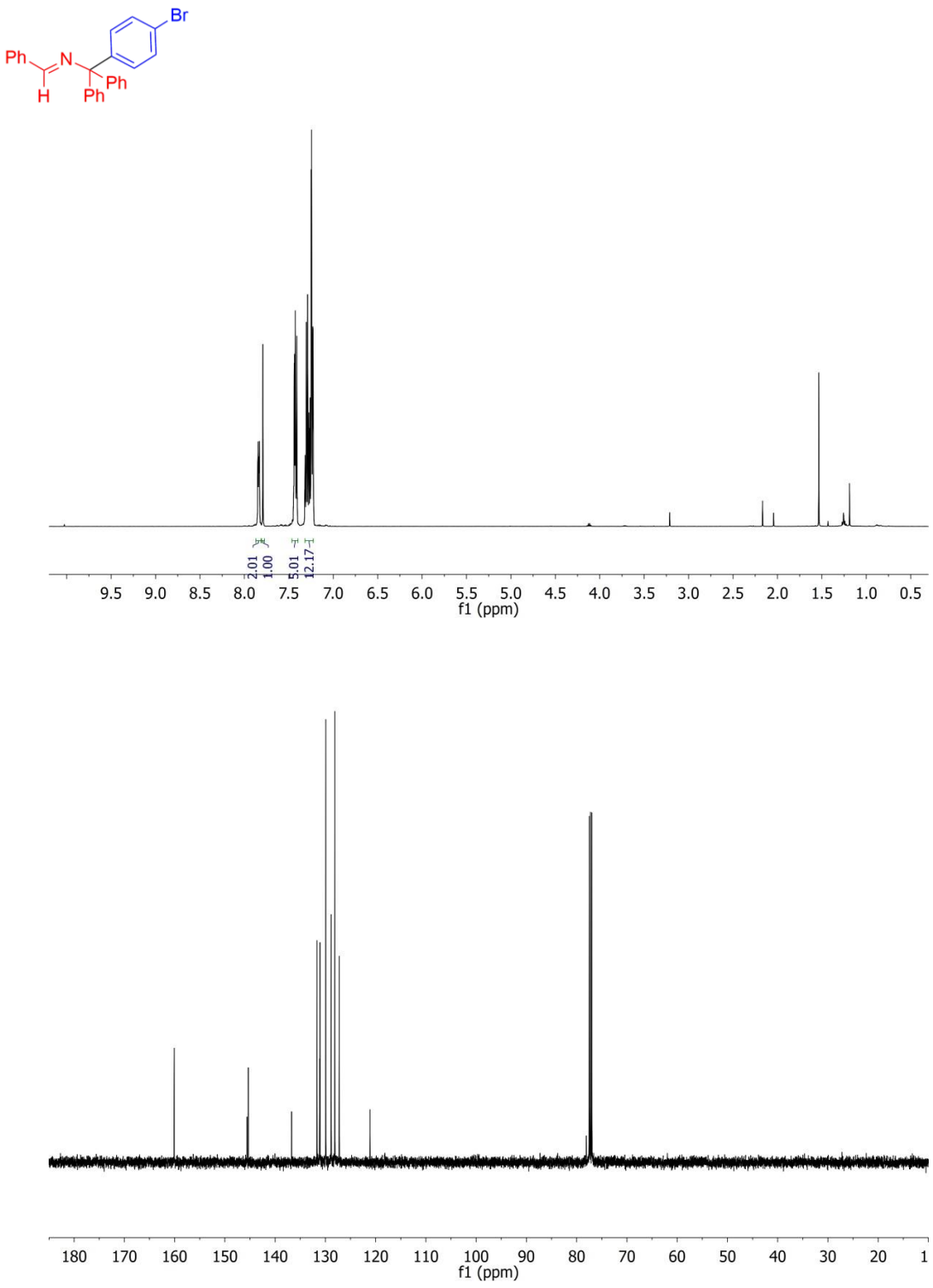


Figure A3.29 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ad' in $CDCl_3$

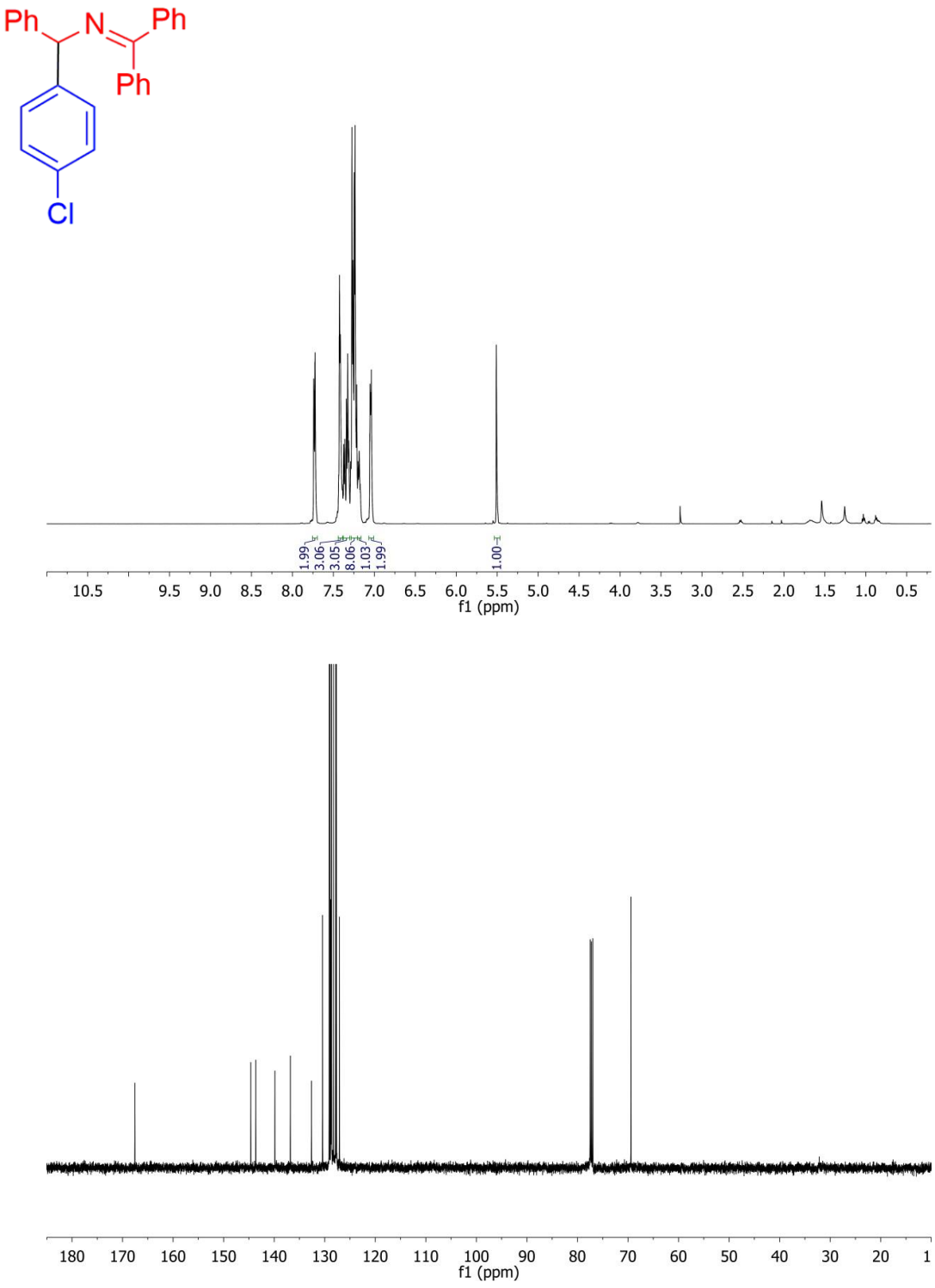


Figure A3.30 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ae in $CDCl_3$

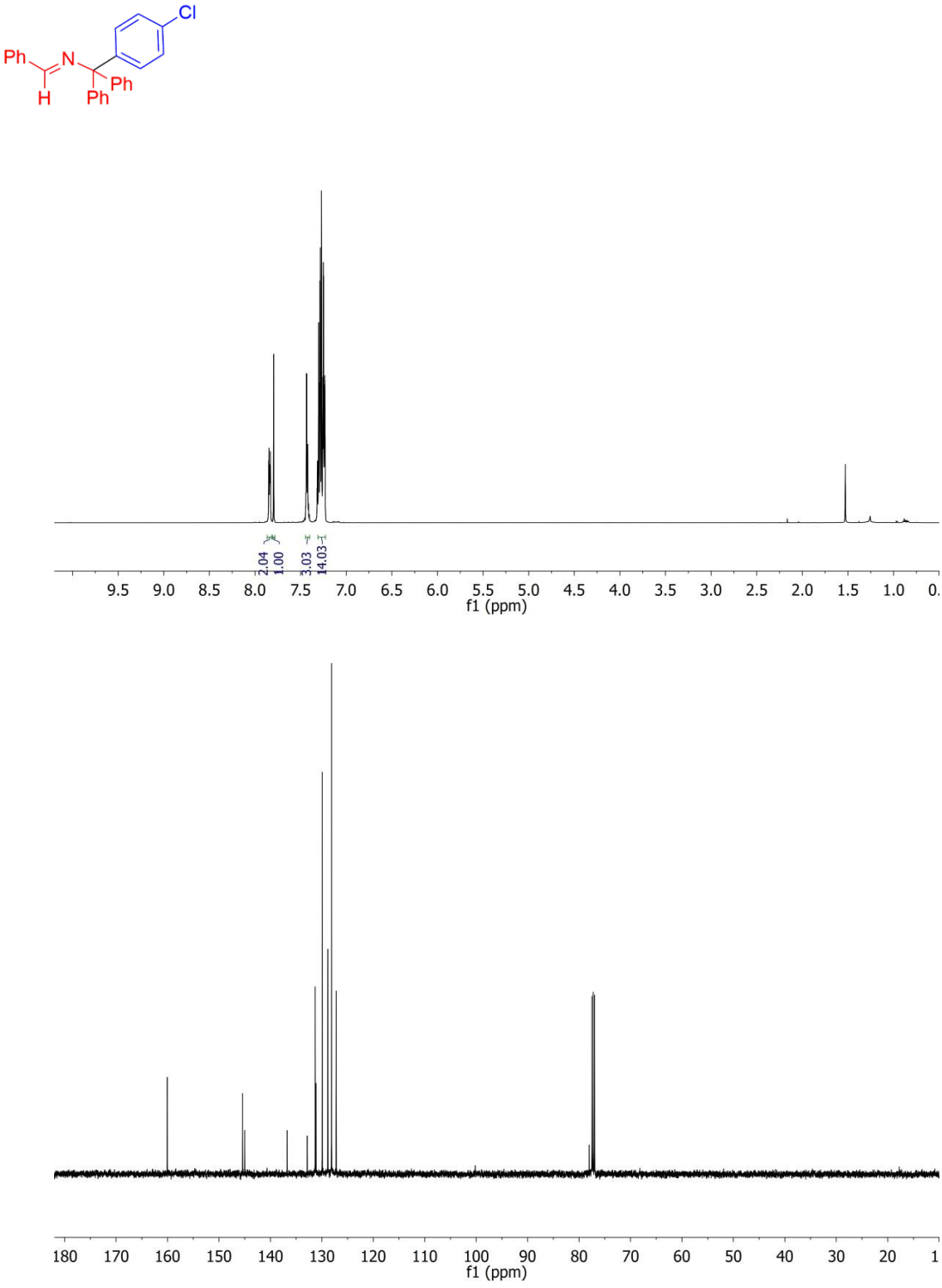


Figure A3.31 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ae' in $CDCl_3$

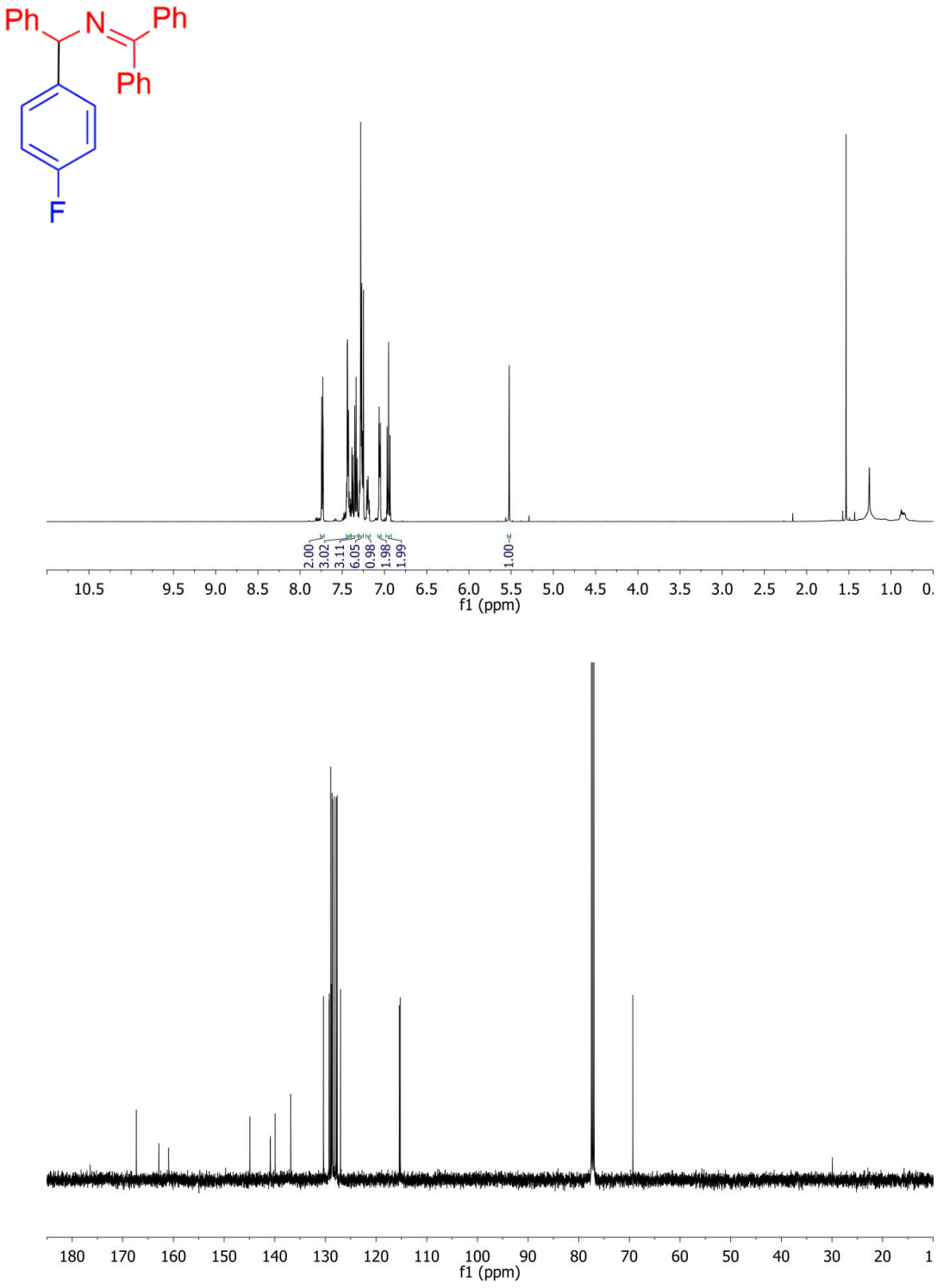


Figure A3.32 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7af in $CDCl_3$

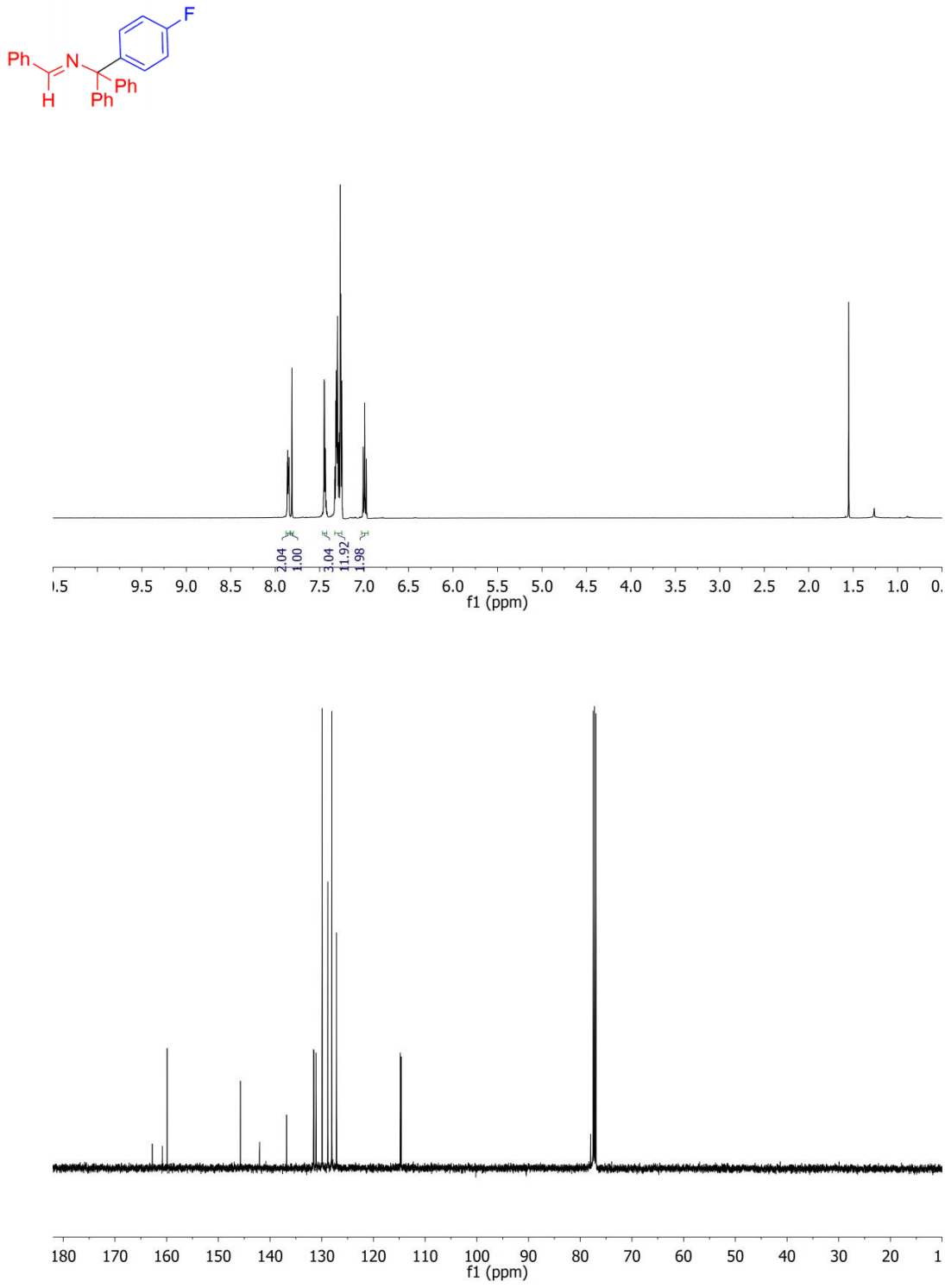


Figure A3.33 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7af' in $CDCl_3$

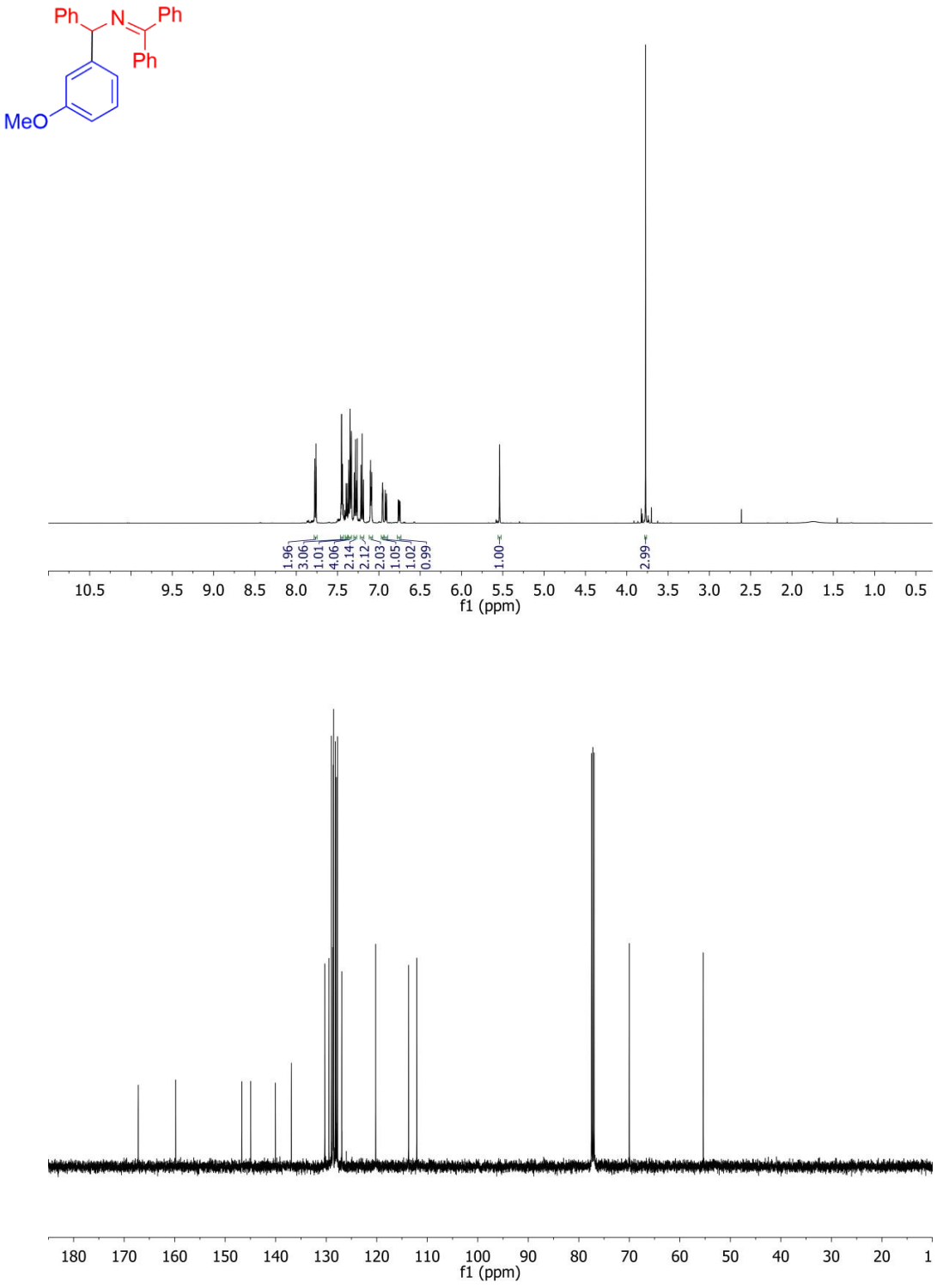


Figure A3.34 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ag in $CDCl_3$

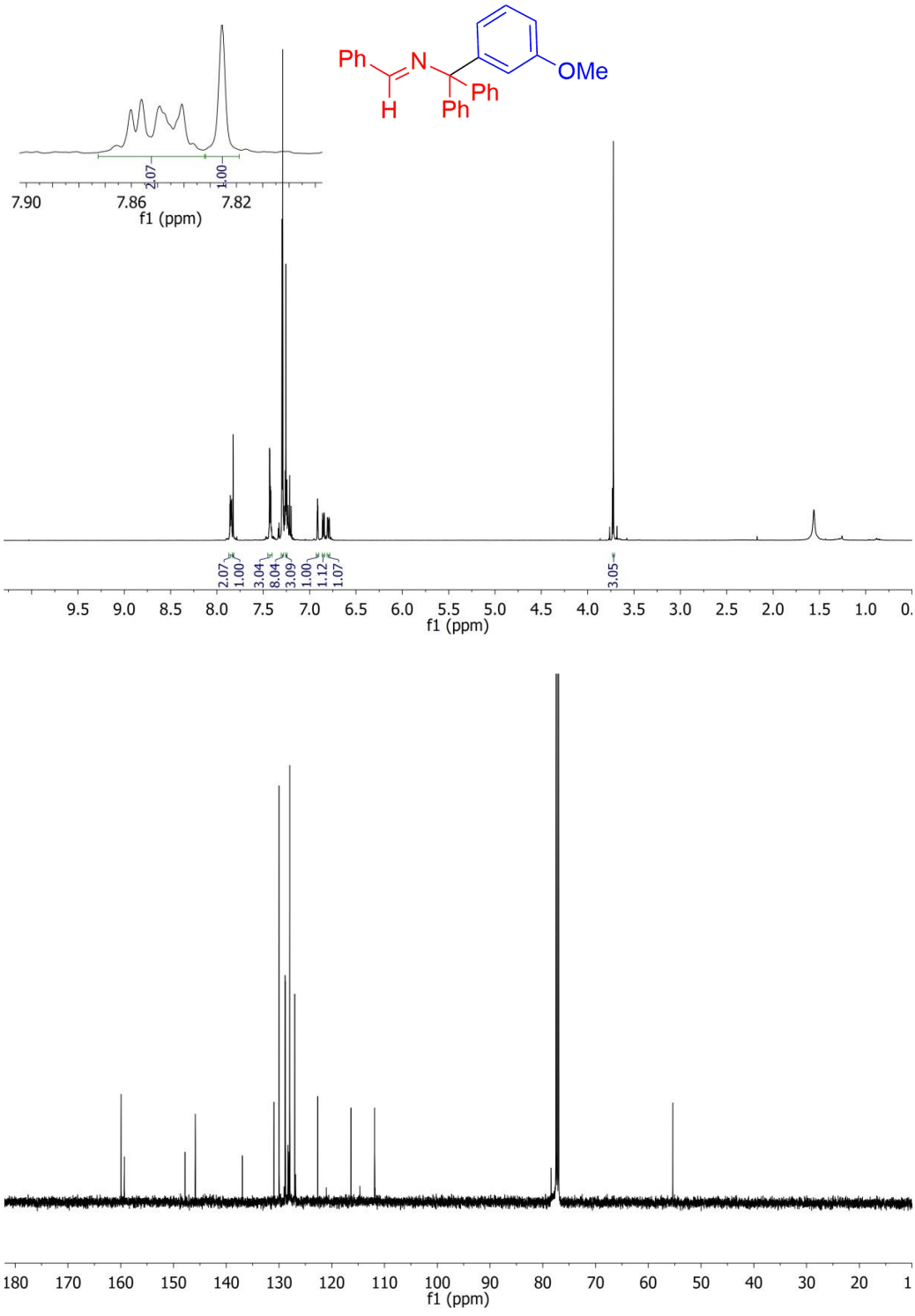


Figure A3.35 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ag' in $CDCl_3$

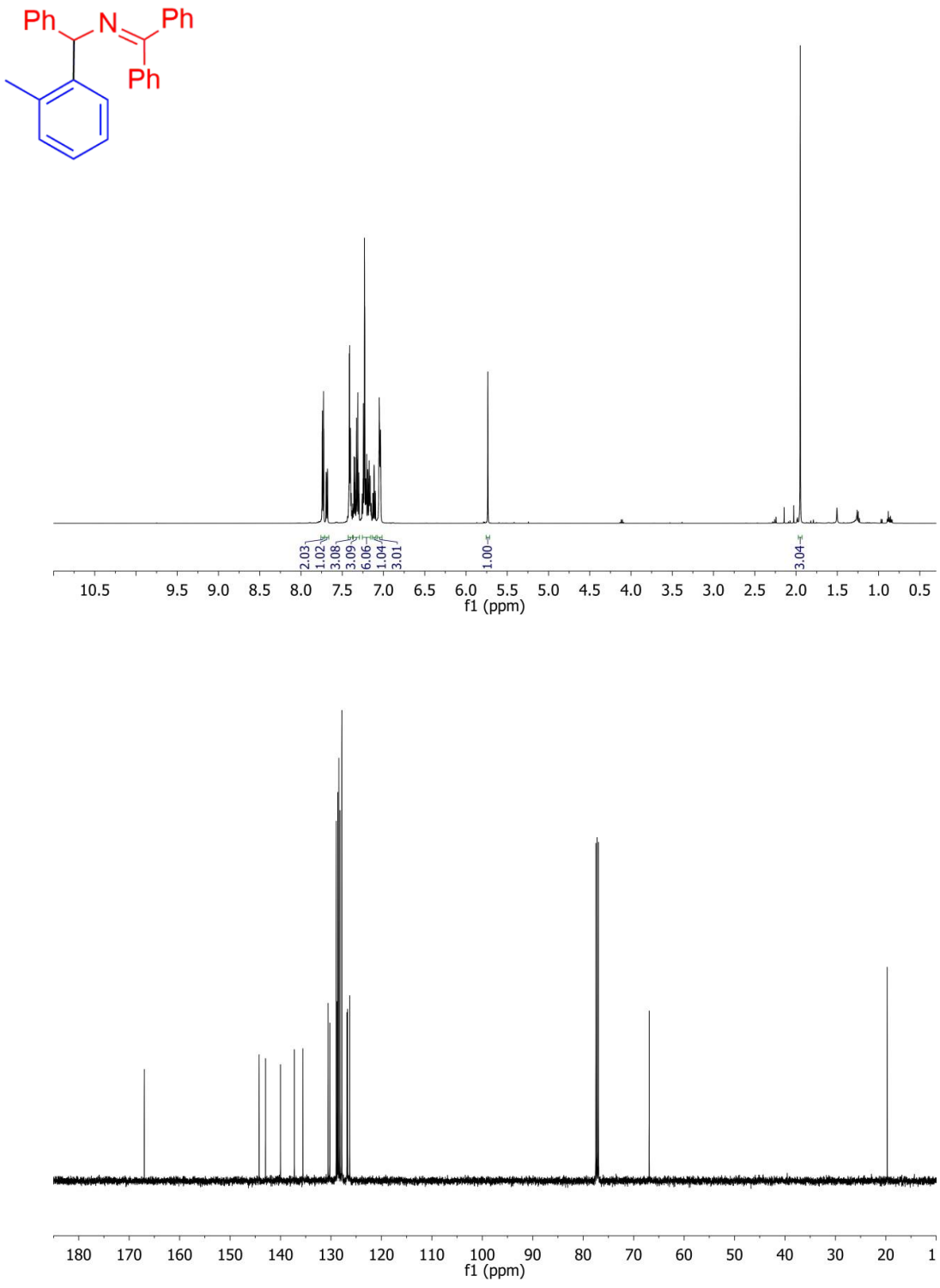


Figure A3.36 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ah in $CDCl_3$

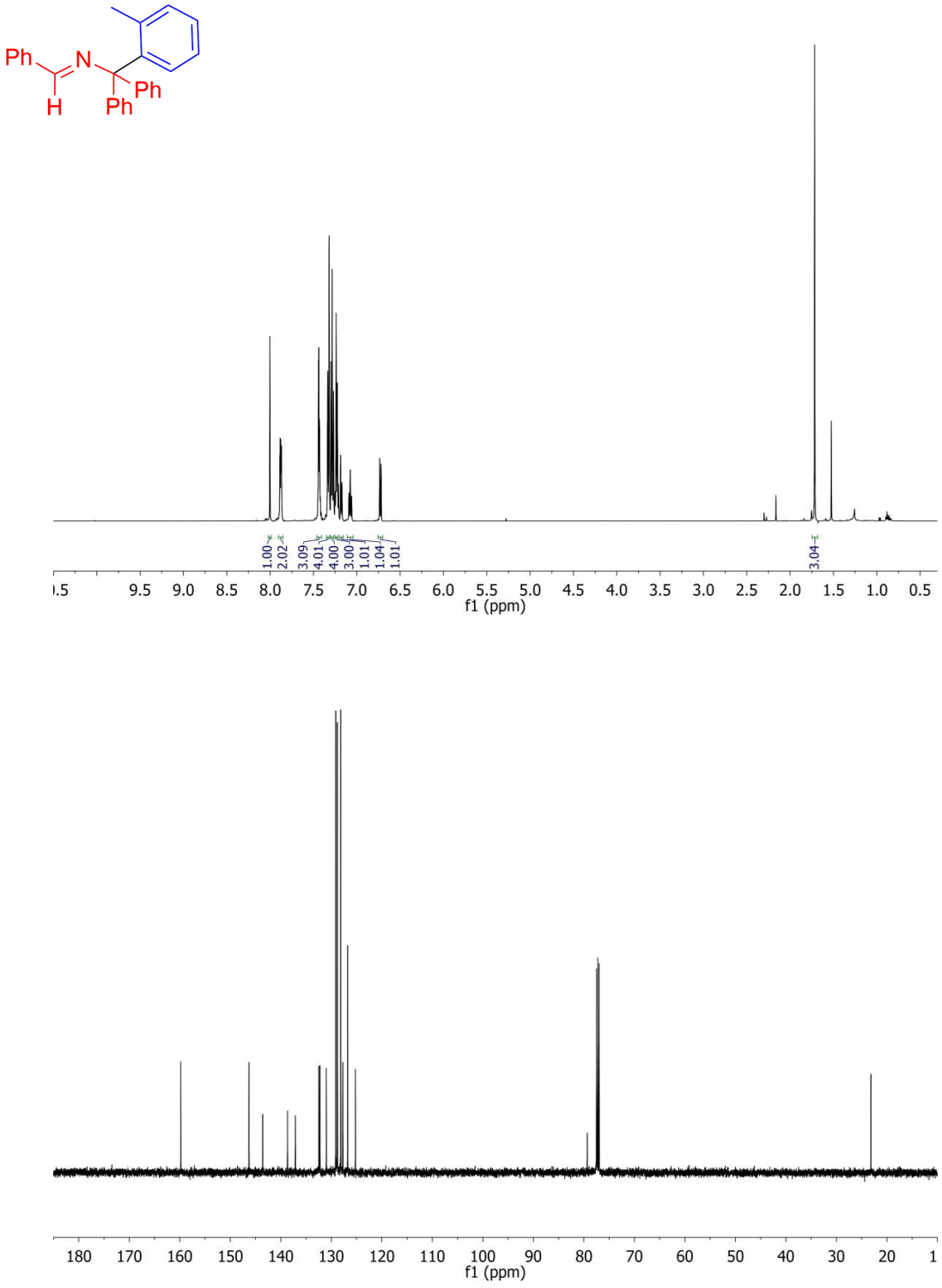


Figure A3.37 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.7ah' in $CDCl_3$

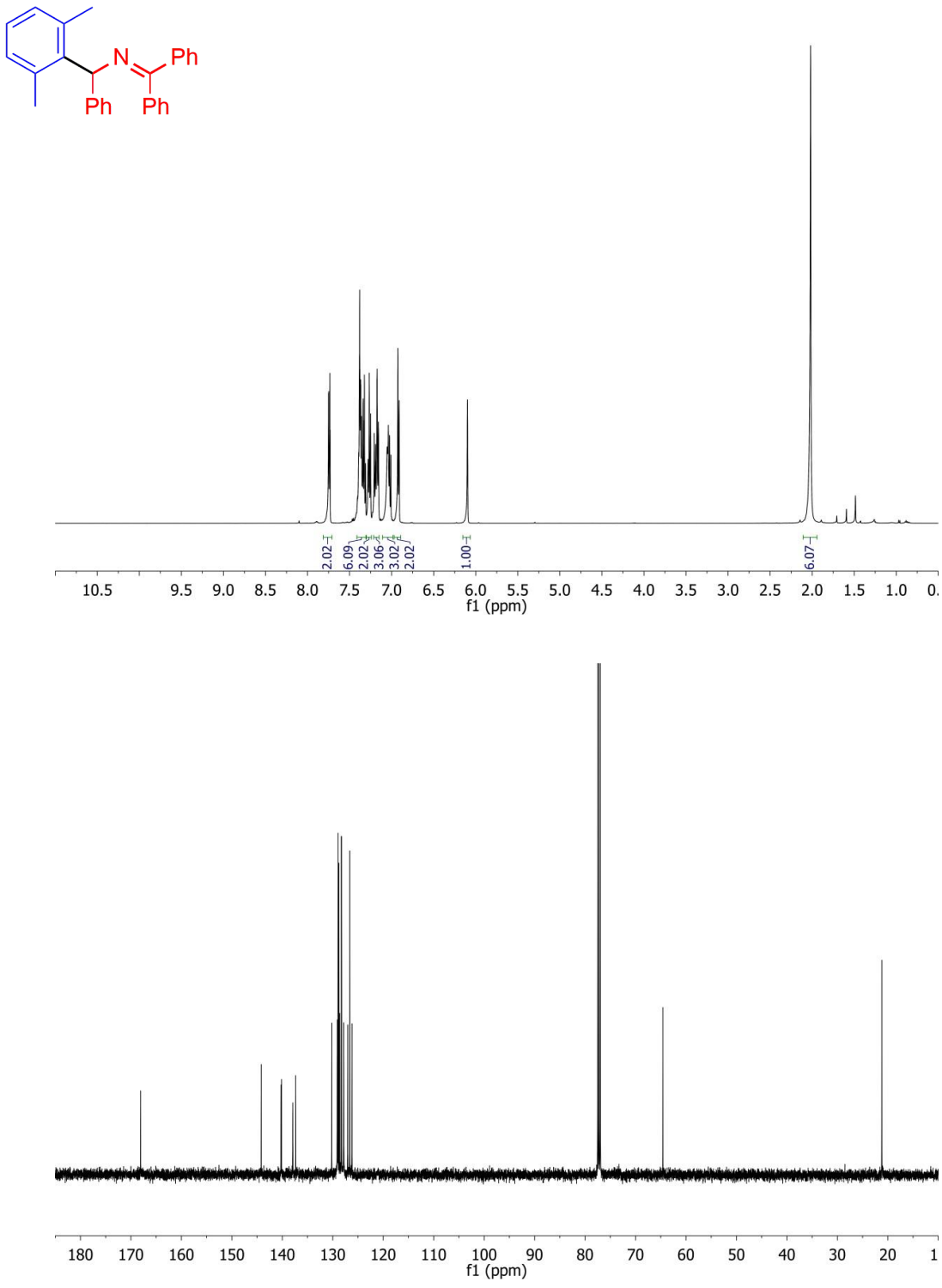


Figure A3.38 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.7ai in $CDCl_3$

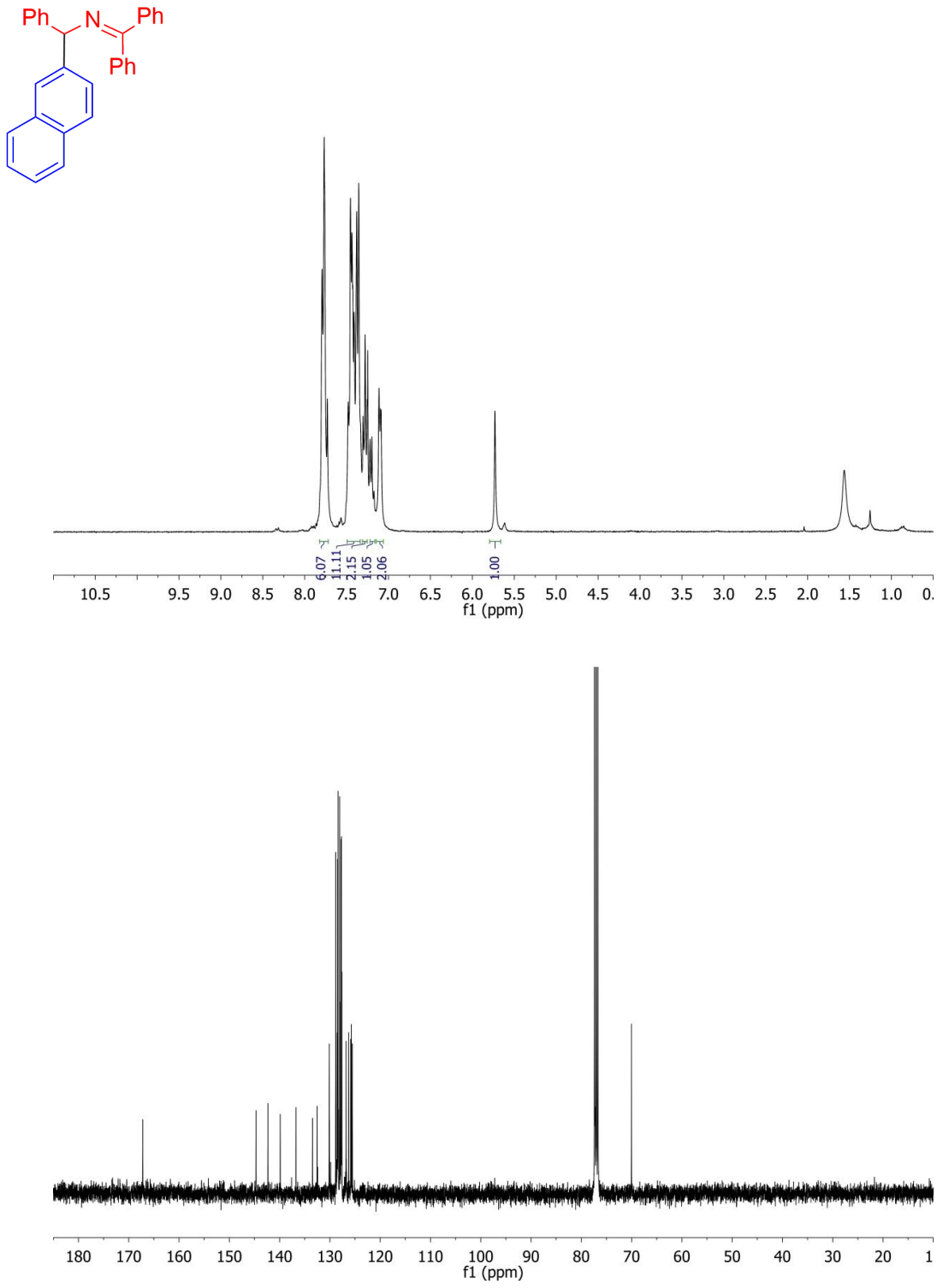


Figure A3.39 400 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7aj in $CDCl_3$

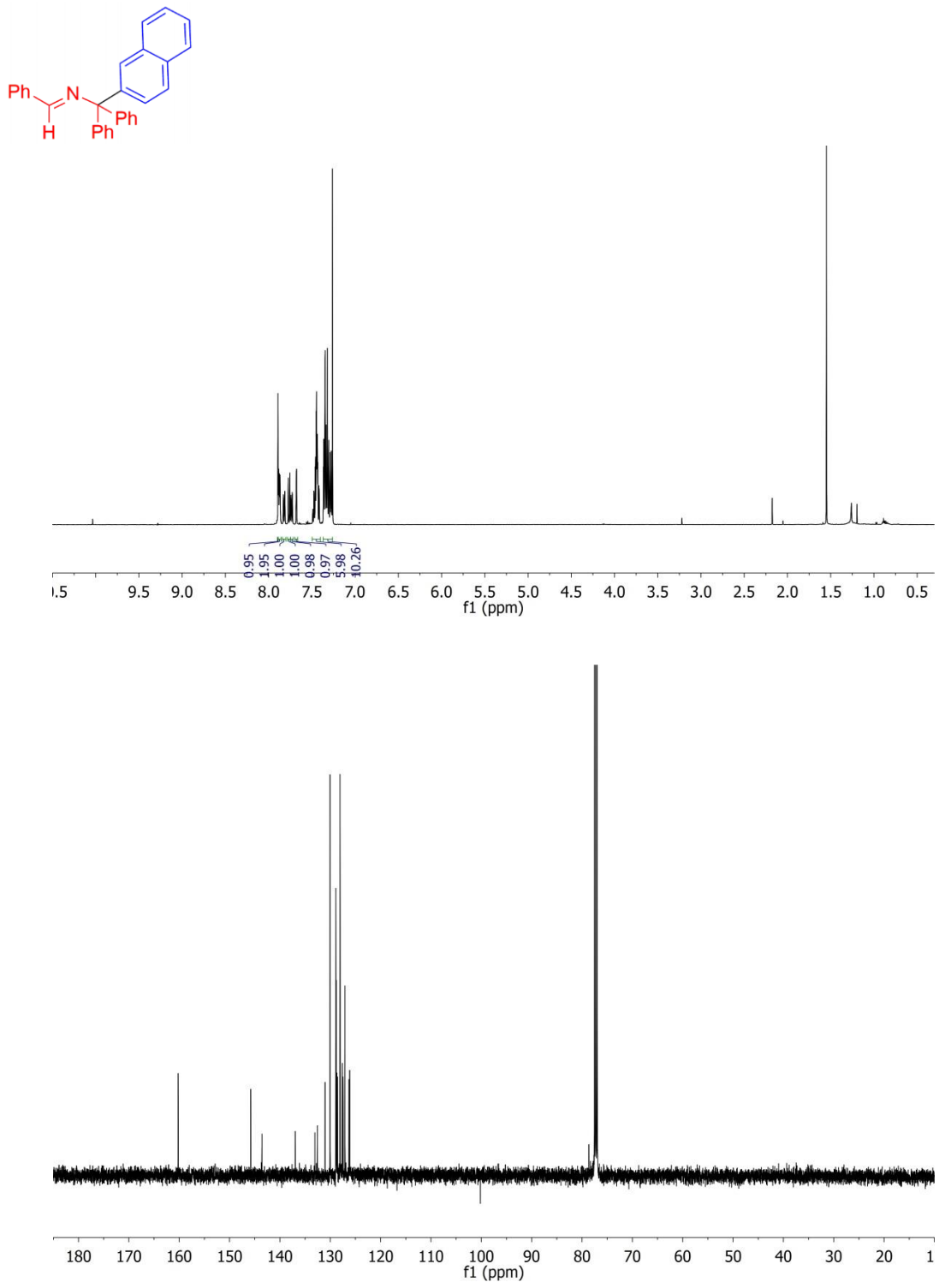


Figure A3.40 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.7aj' in $CDCl_3$

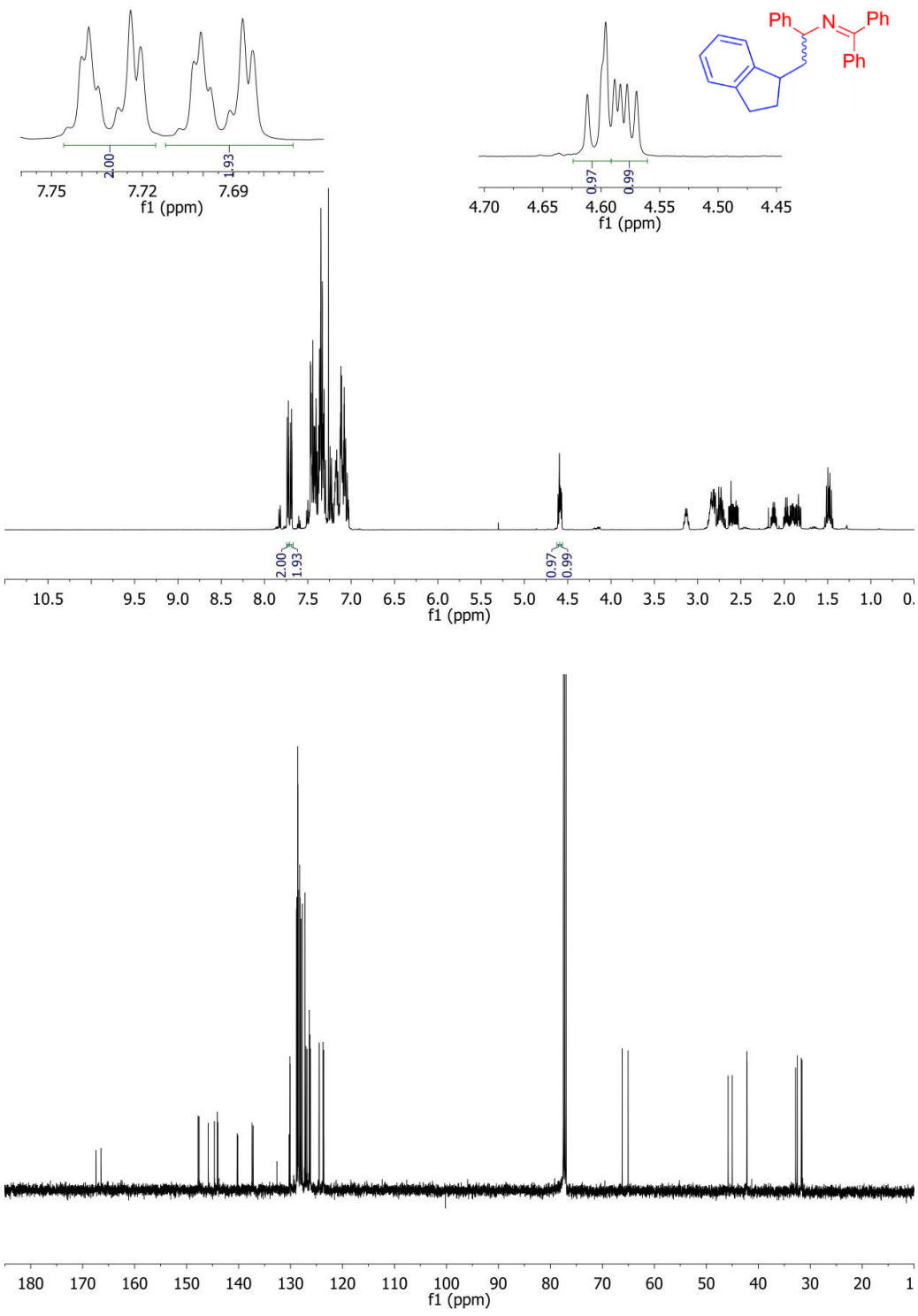


Figure A3.41 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7ak in $CDCl_3$

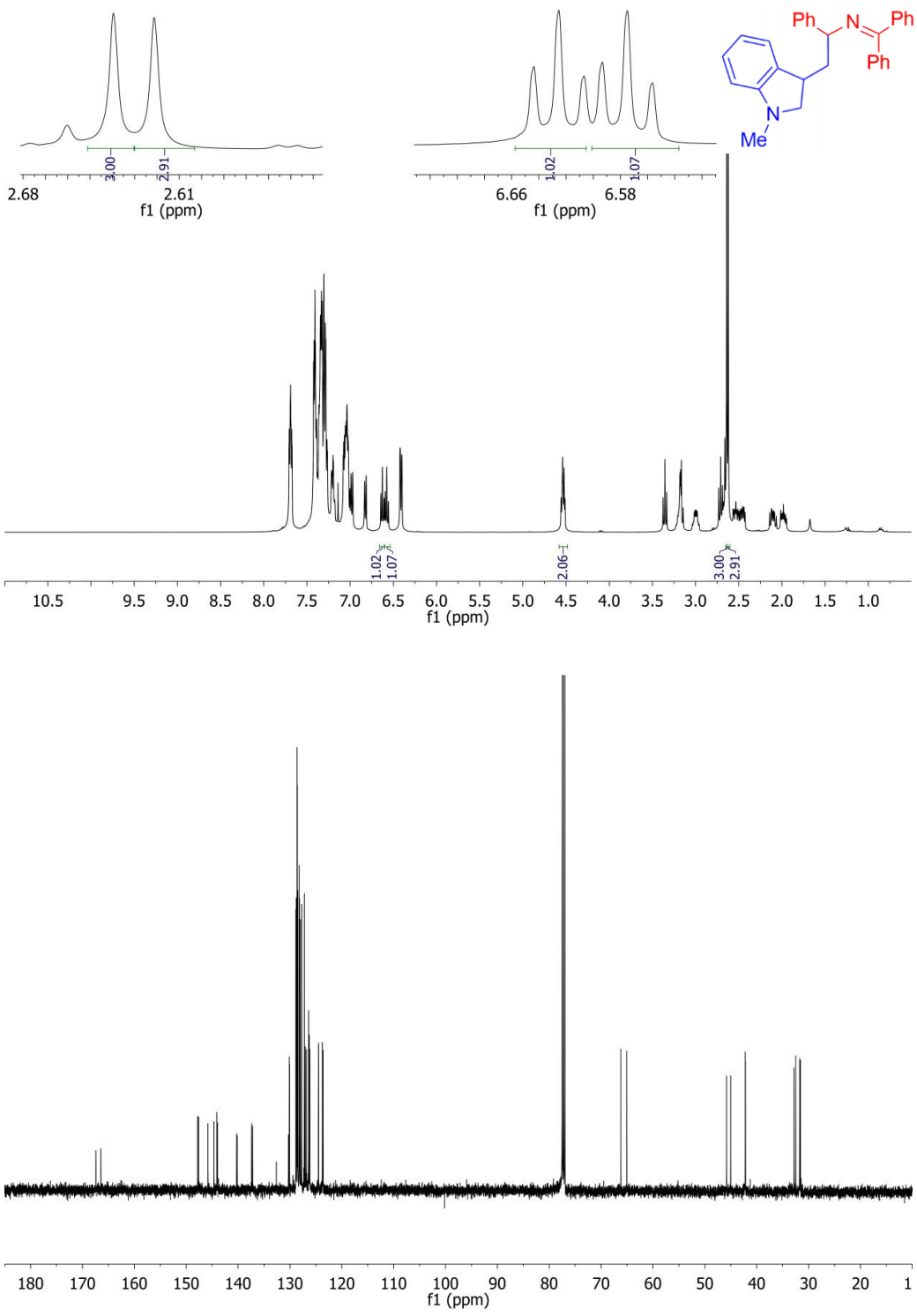


Figure A3.42 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.7al in $CDCl_3$

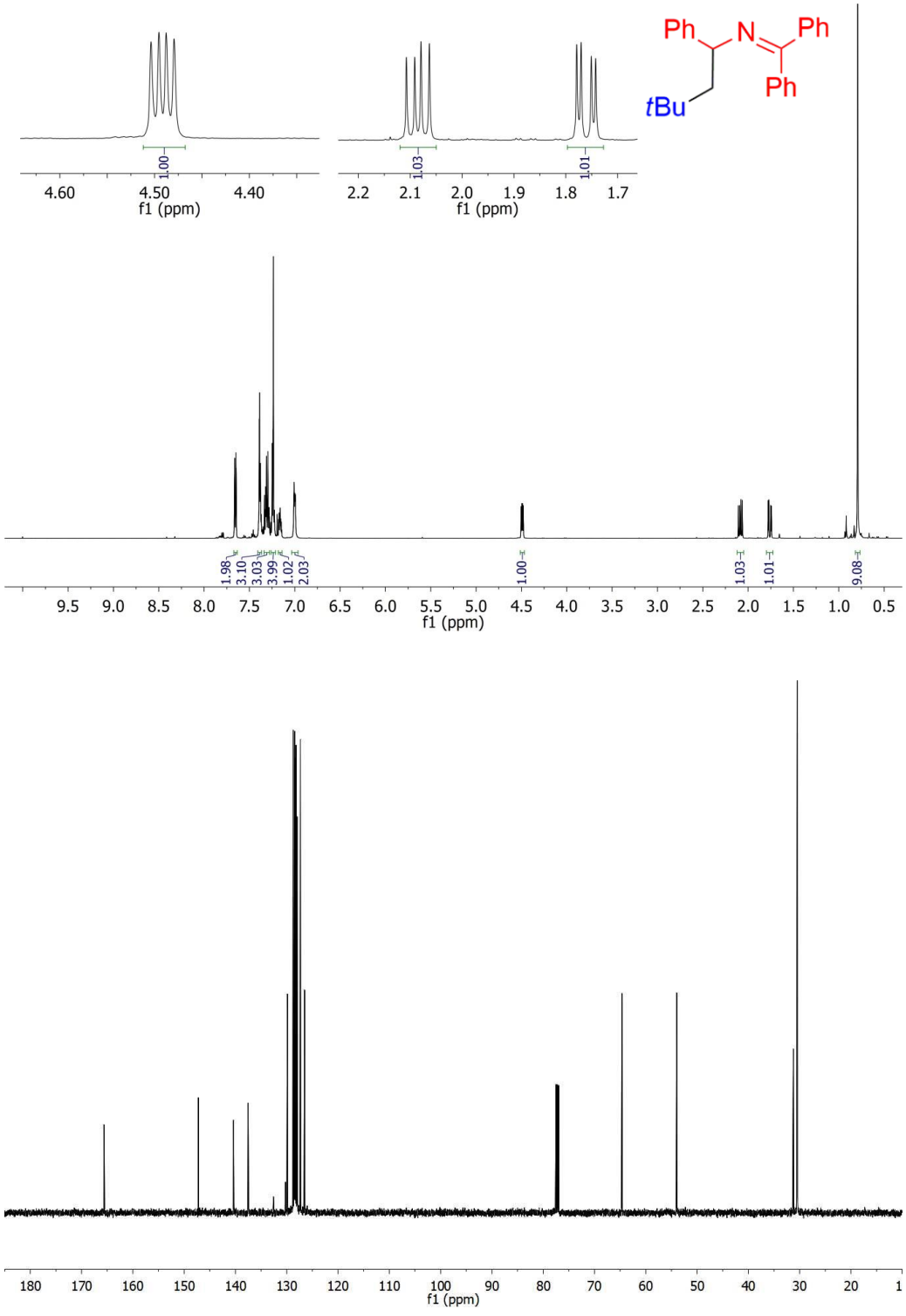


Figure A3.43 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.8aa in $CDCl_3$

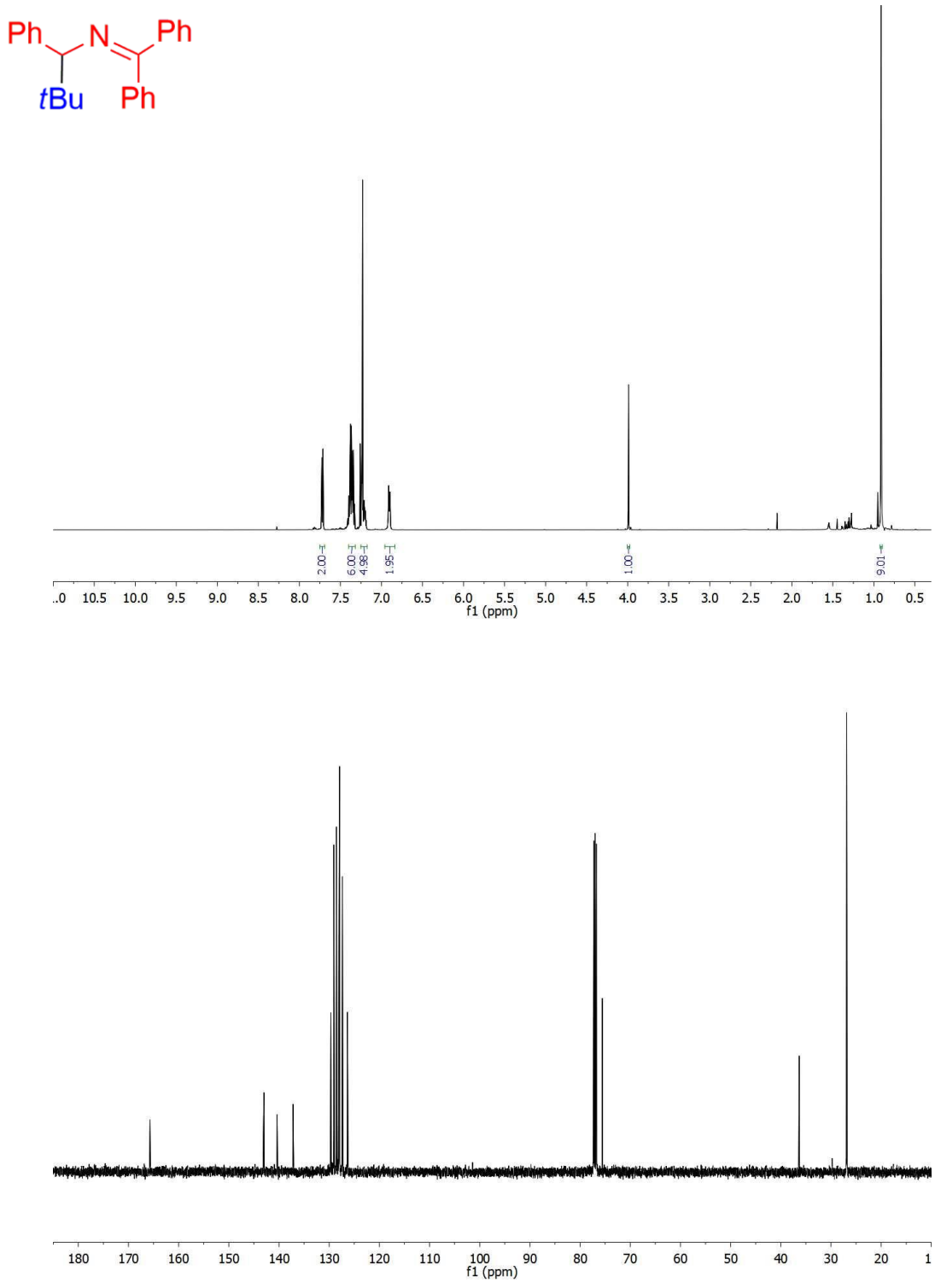


Figure A3.44 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.8ab in $CDCl_3$

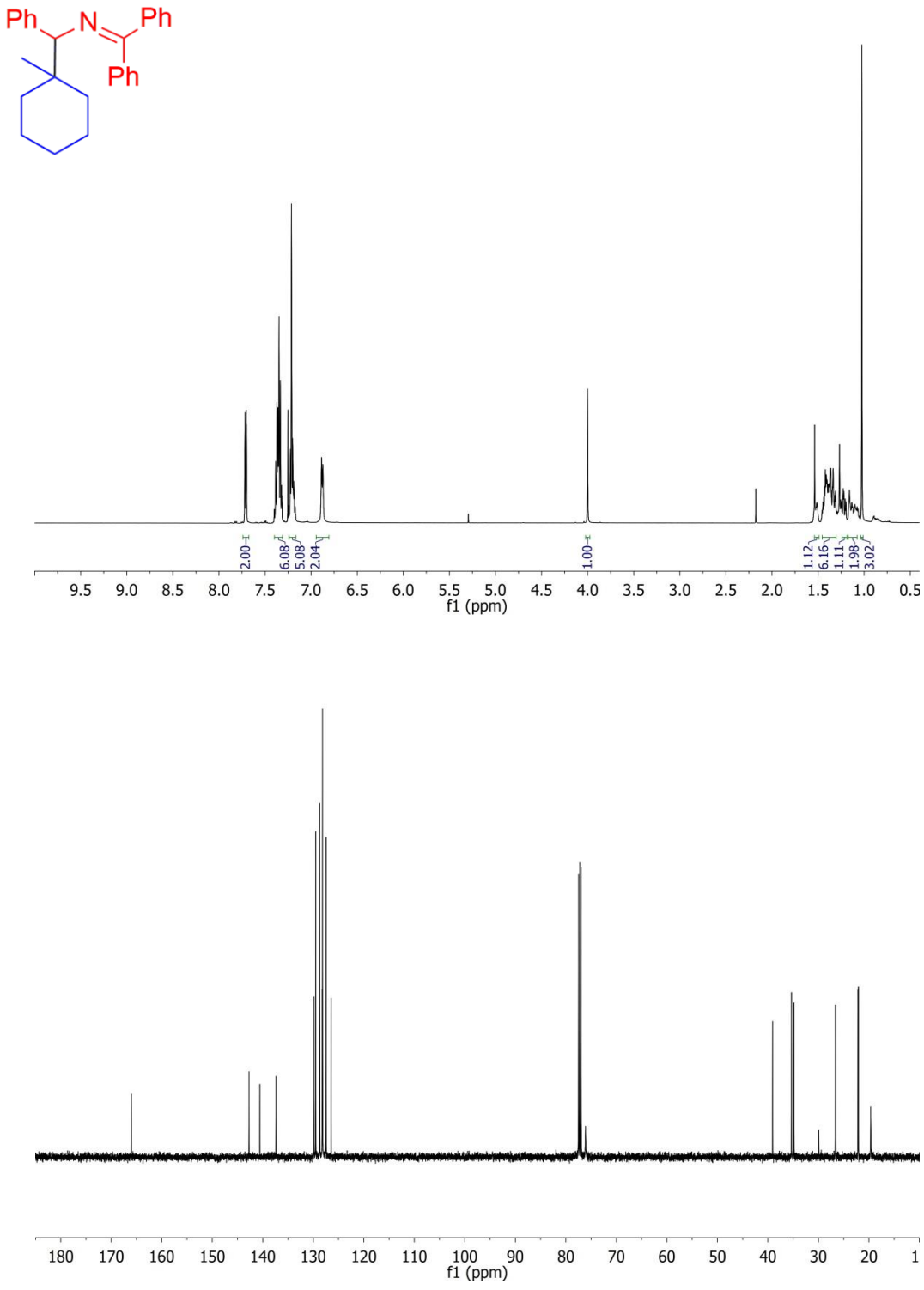


Figure A3.45 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.8ac in $CDCl_3$

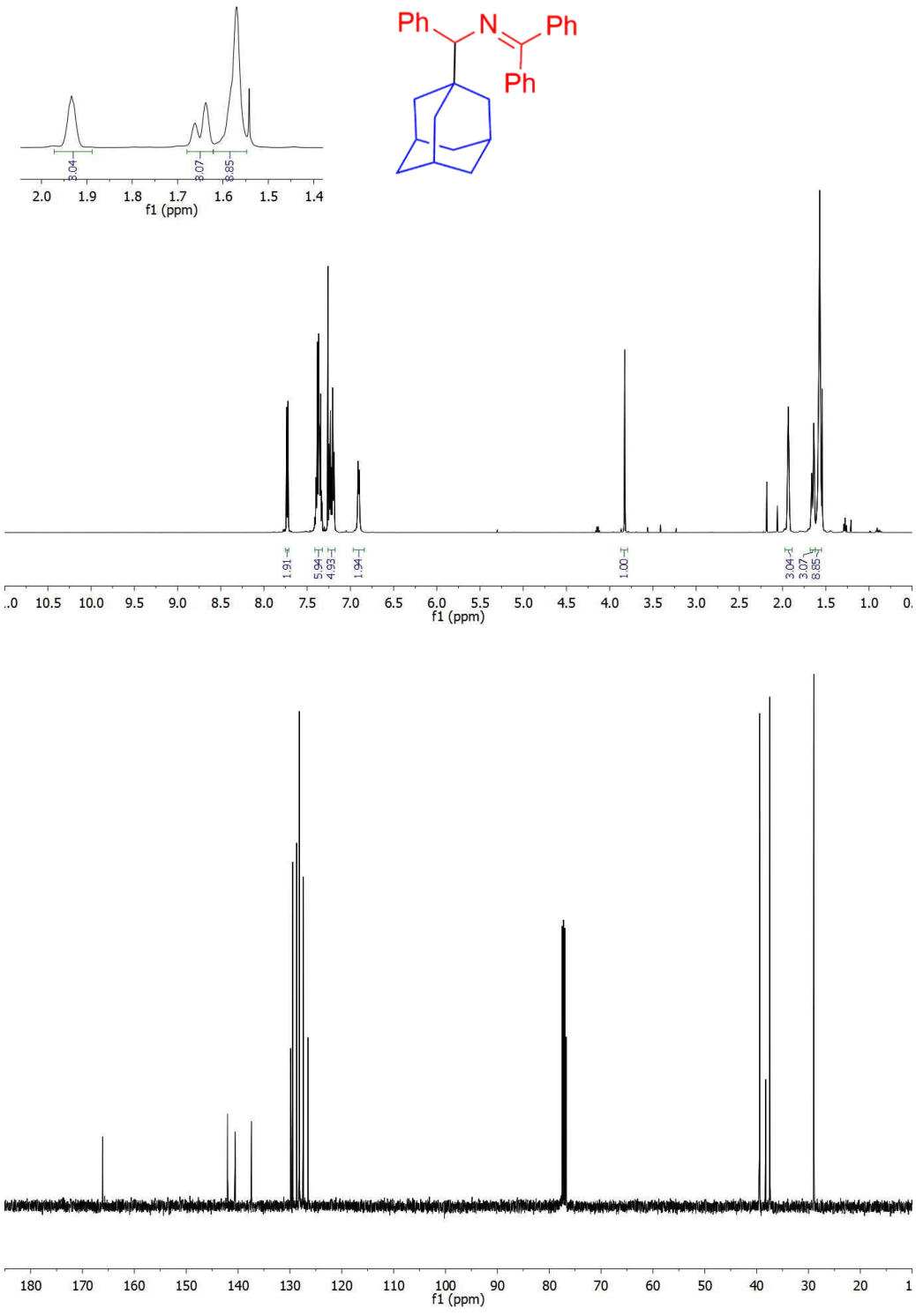


Figure A3.46 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.8ae in $CDCl_3$

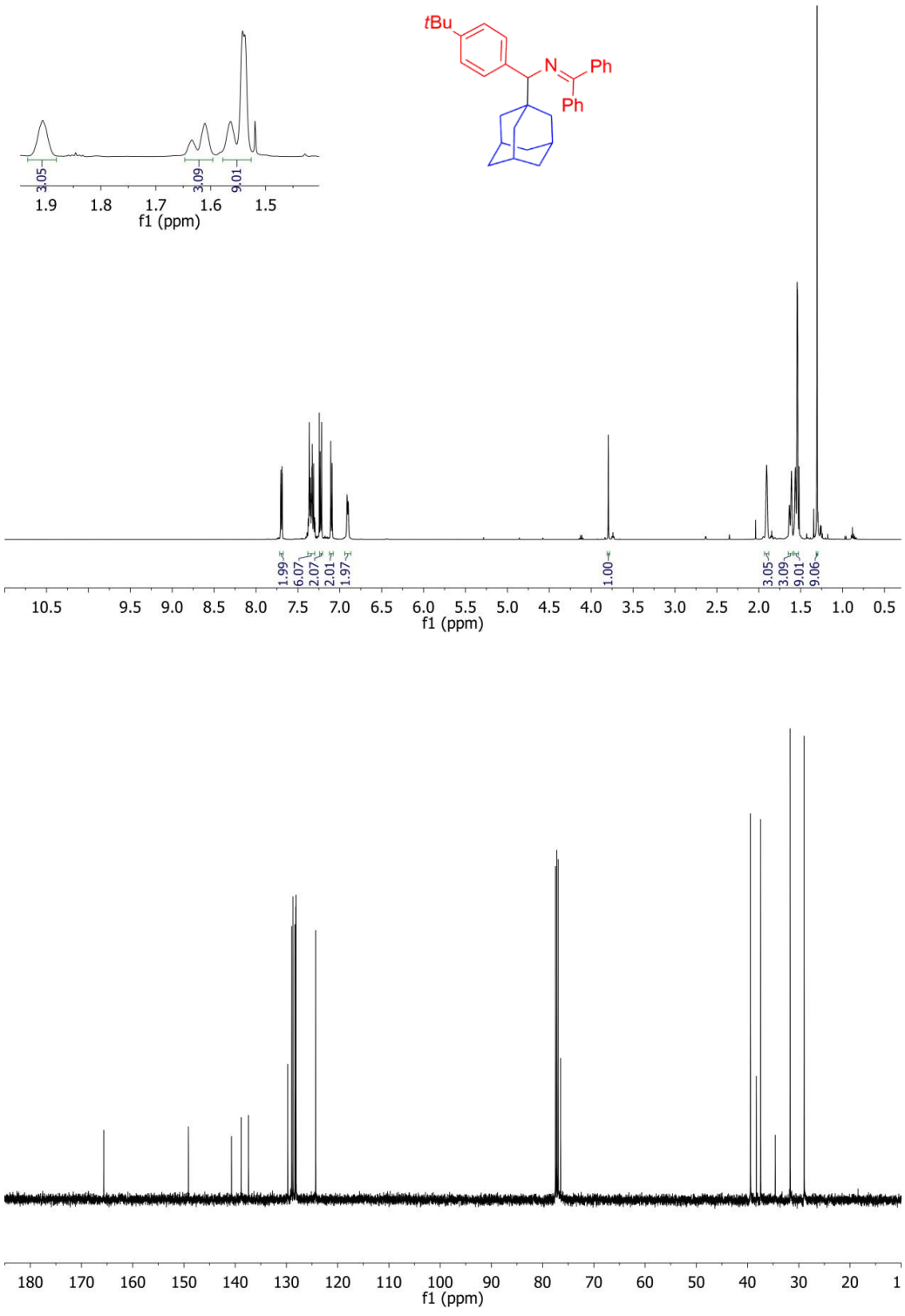


Figure A3.47 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.8be in $CDCl_3$

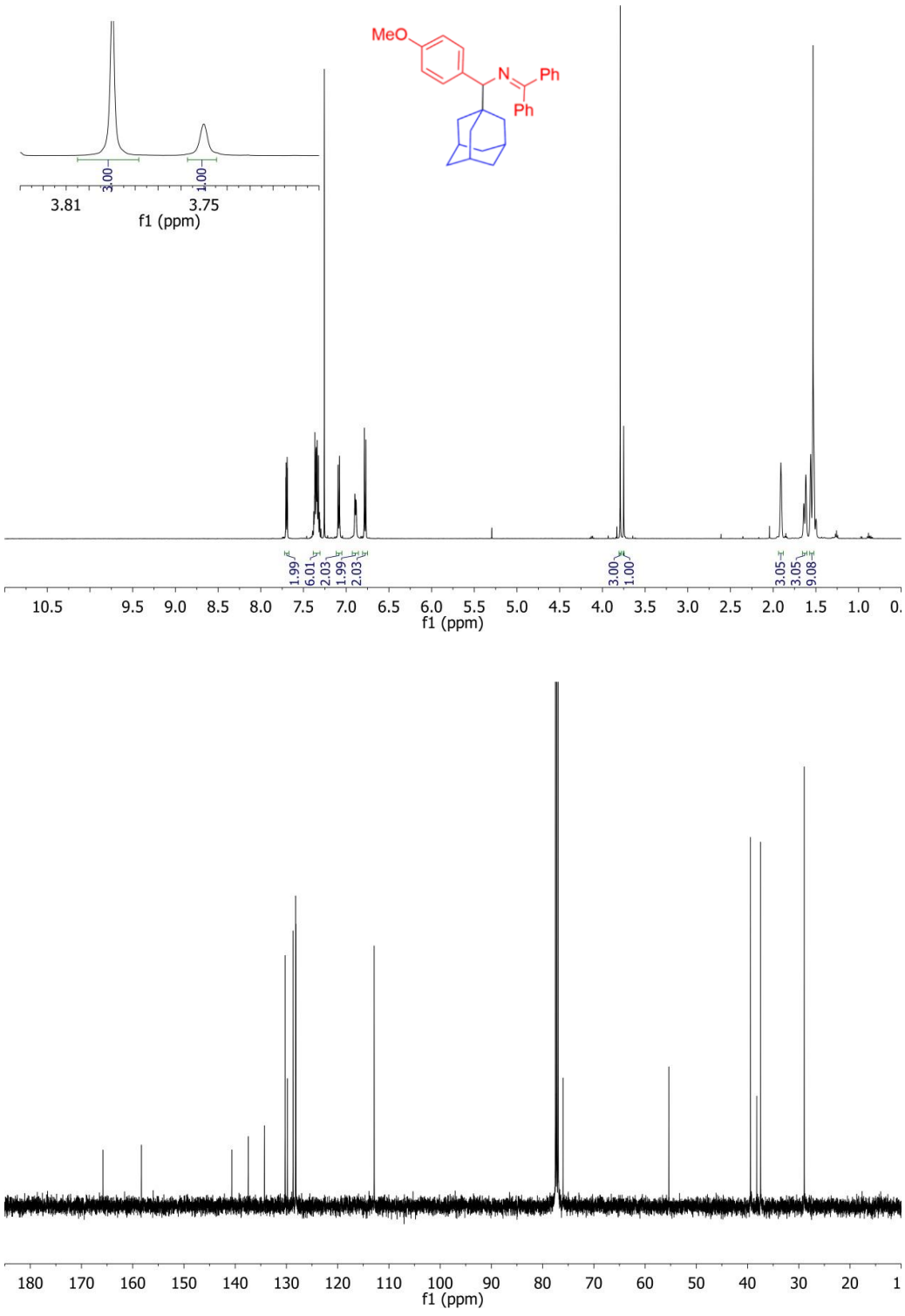


Figure A3.48 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.8ce in $CDCl_3$

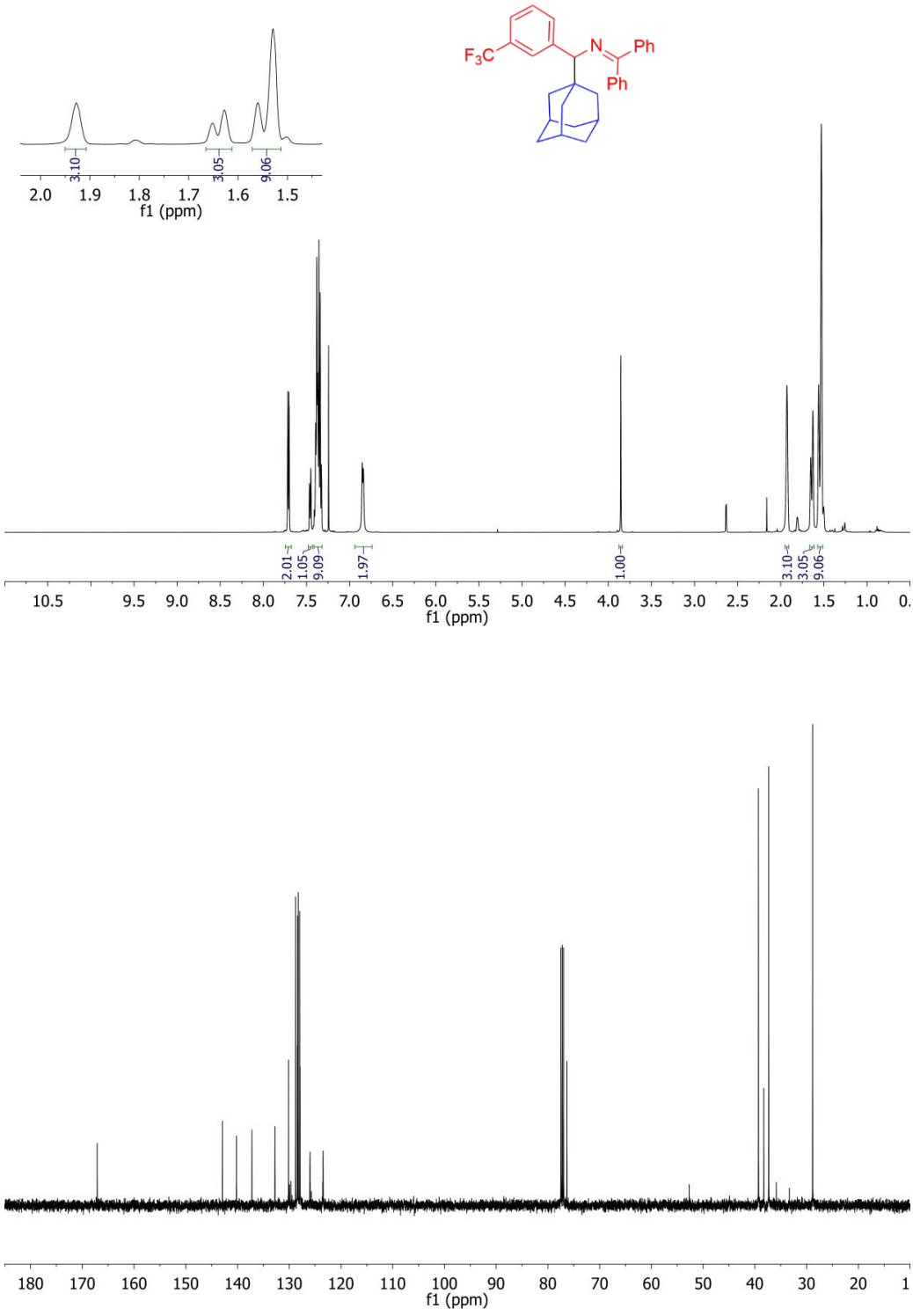


Figure A3.49 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.8de in $CDCl_3$

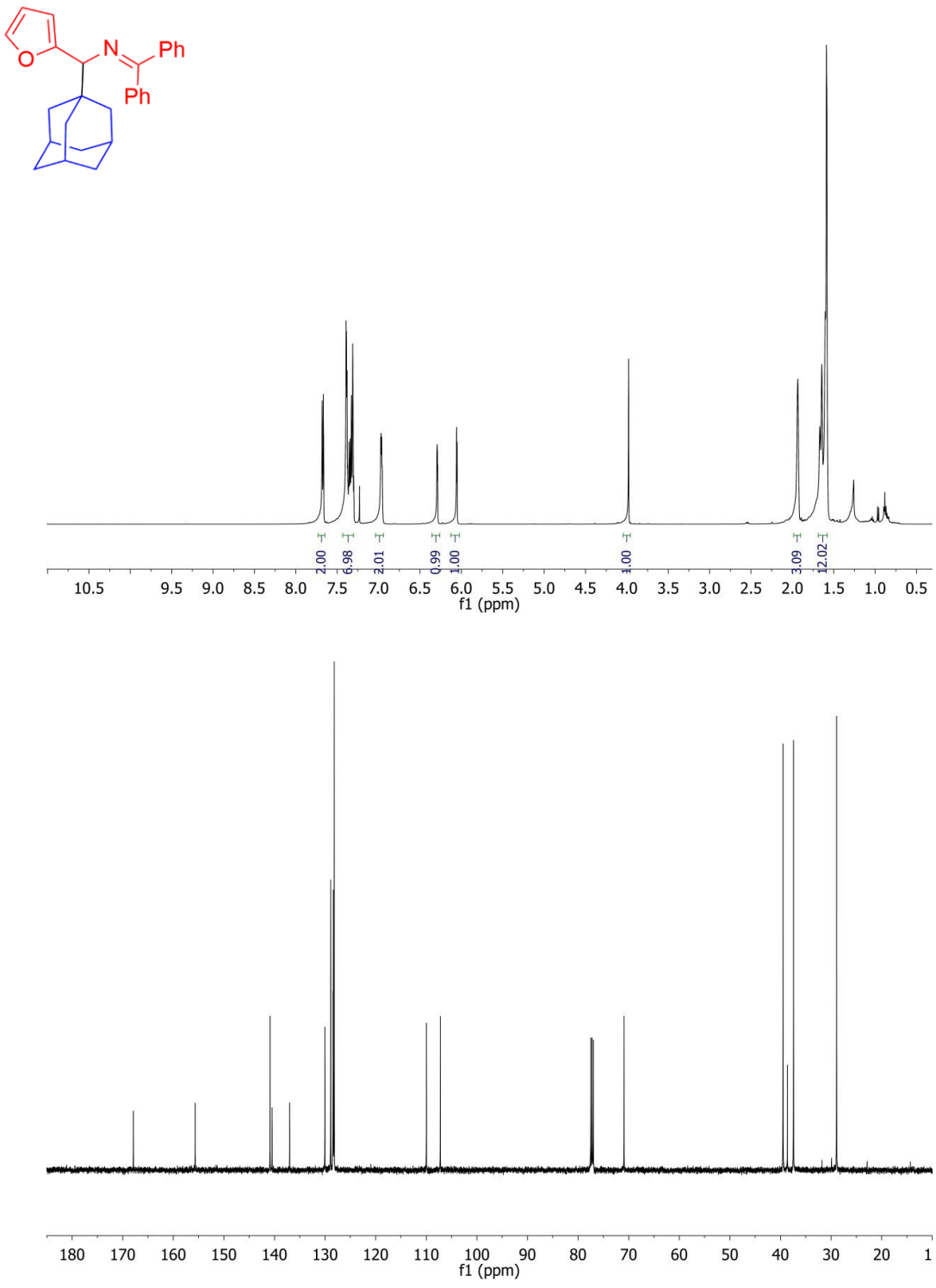


Figure A3.50 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.8ee in $CDCl_3$

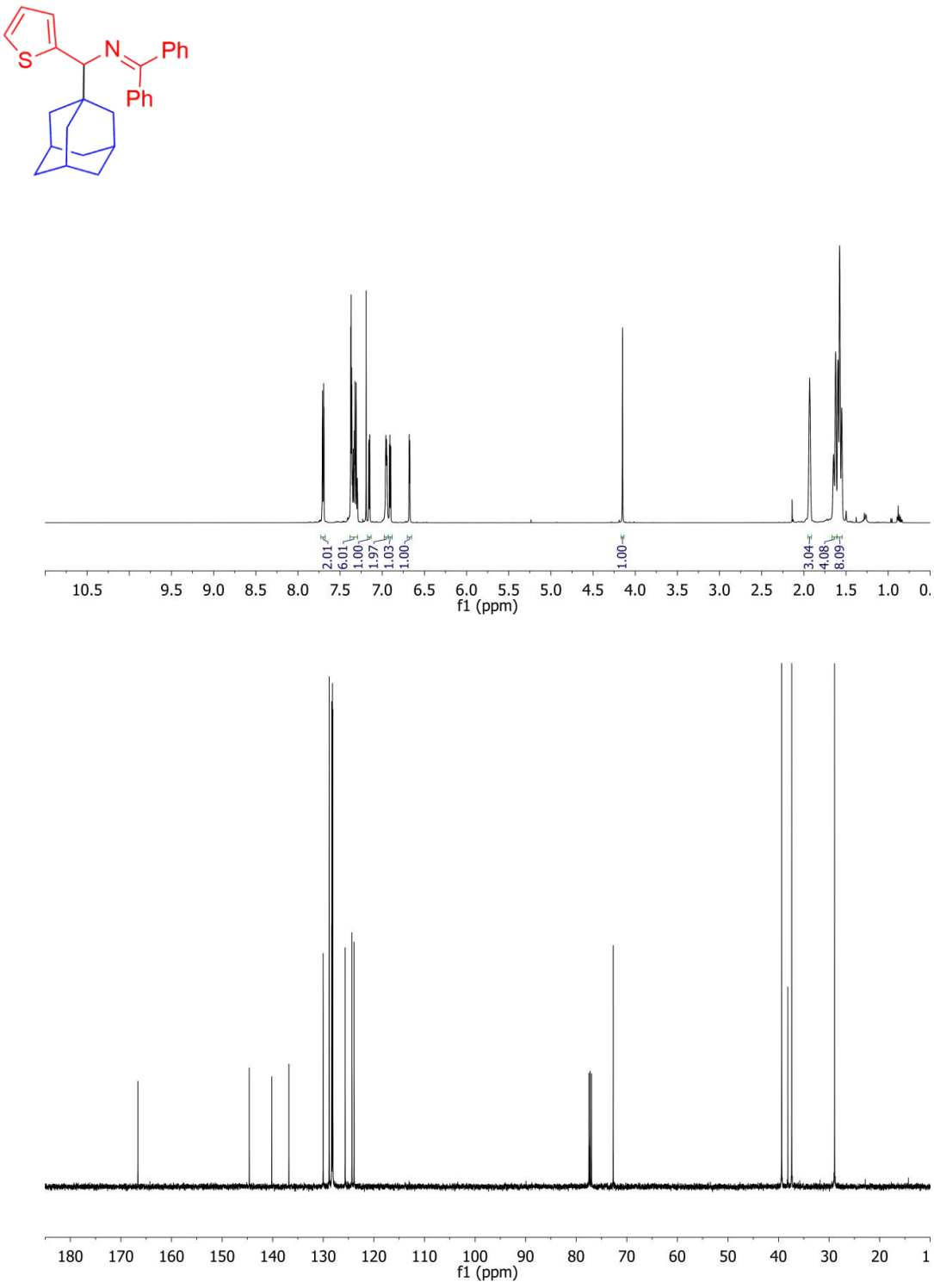


Figure A3.51 500 MHz ^{1}H and 125 MHz ^{13}C{^{1}H} NMR of 3.8fe in $CDCl_3$

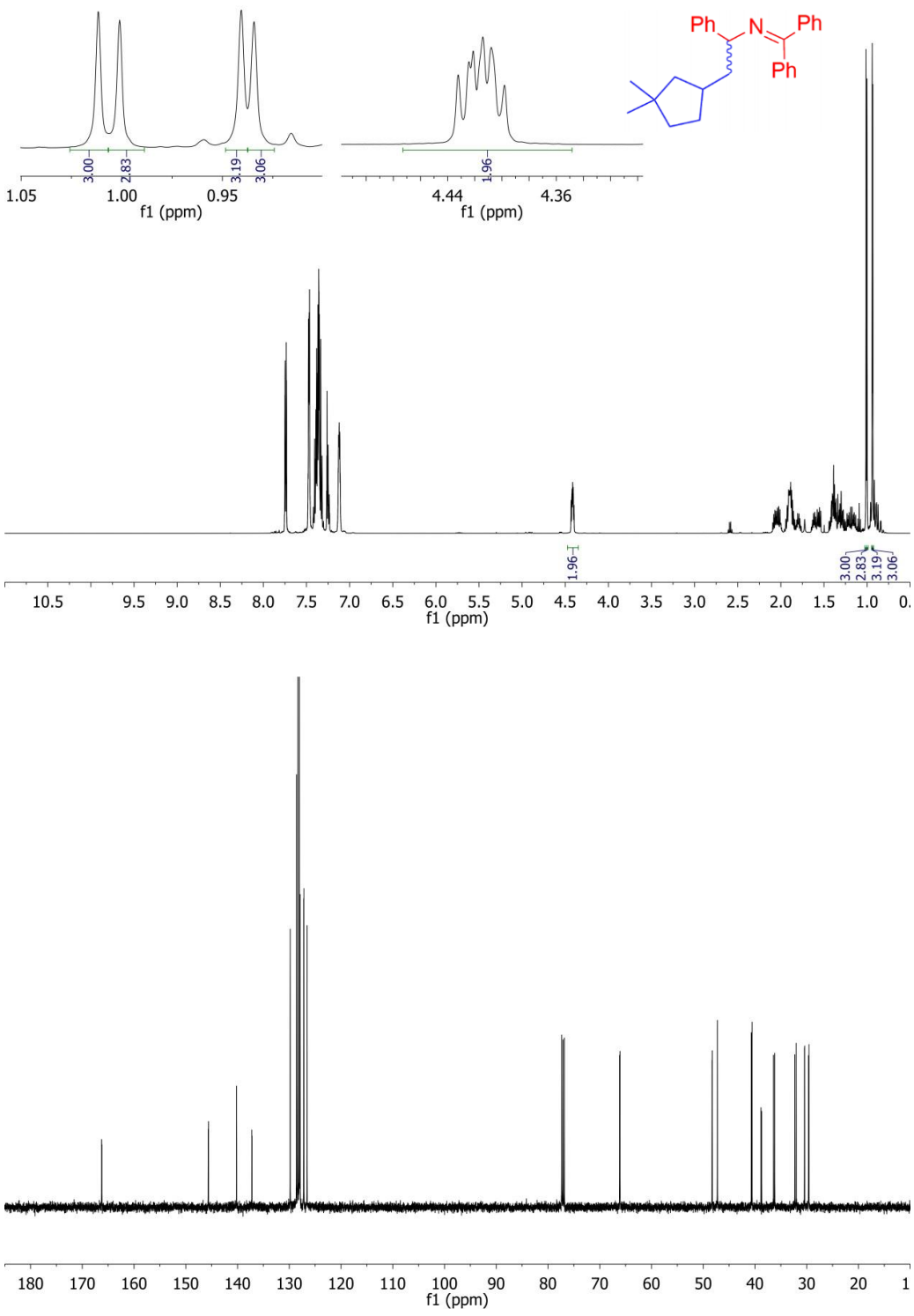


Figure A3.52 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.8ag in $CDCl_3$

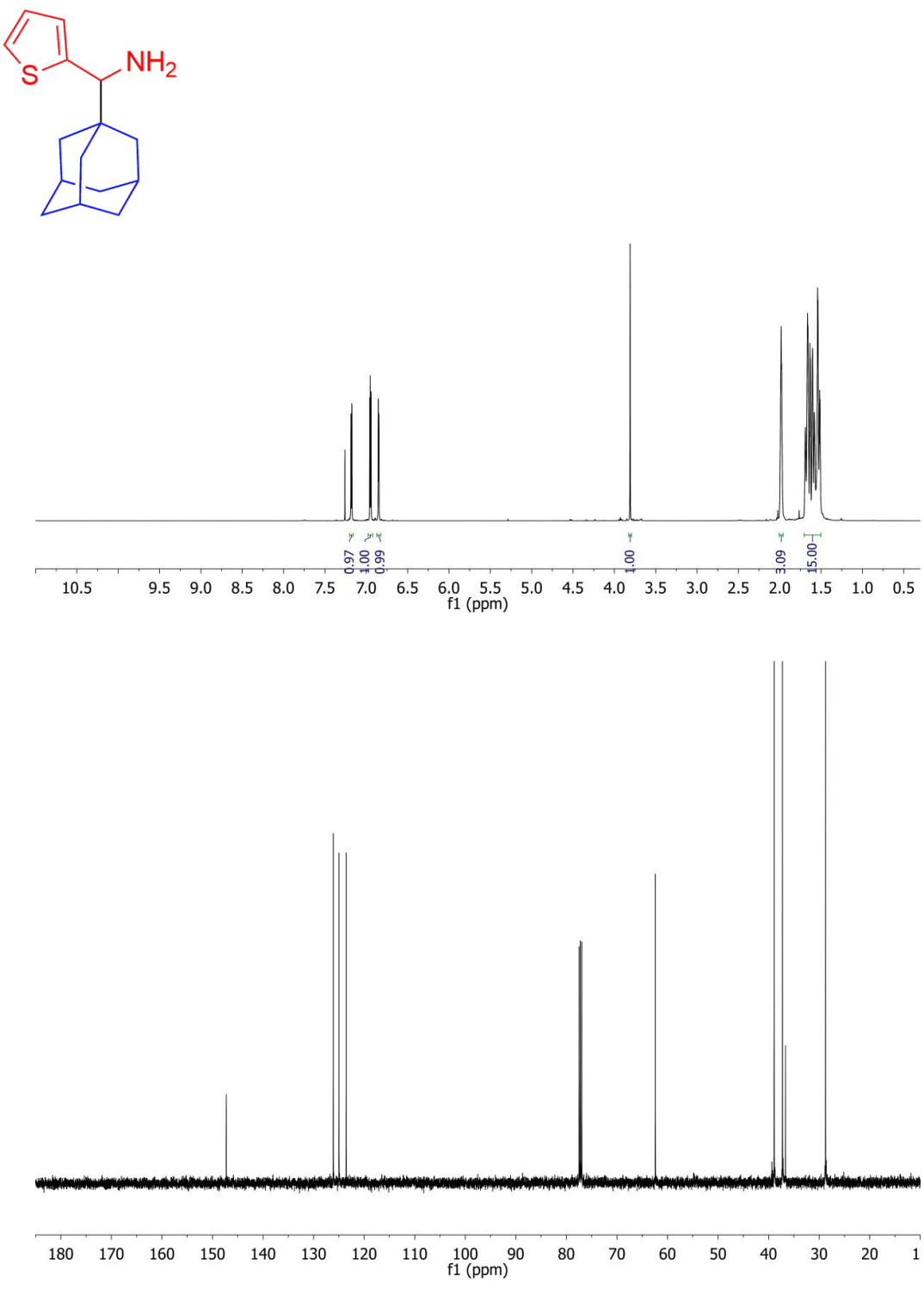


Figure A3.53 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 3.9fe in $CDCl_3$

Appendix A4. NMR Spectra Relevant to Chapter 4.

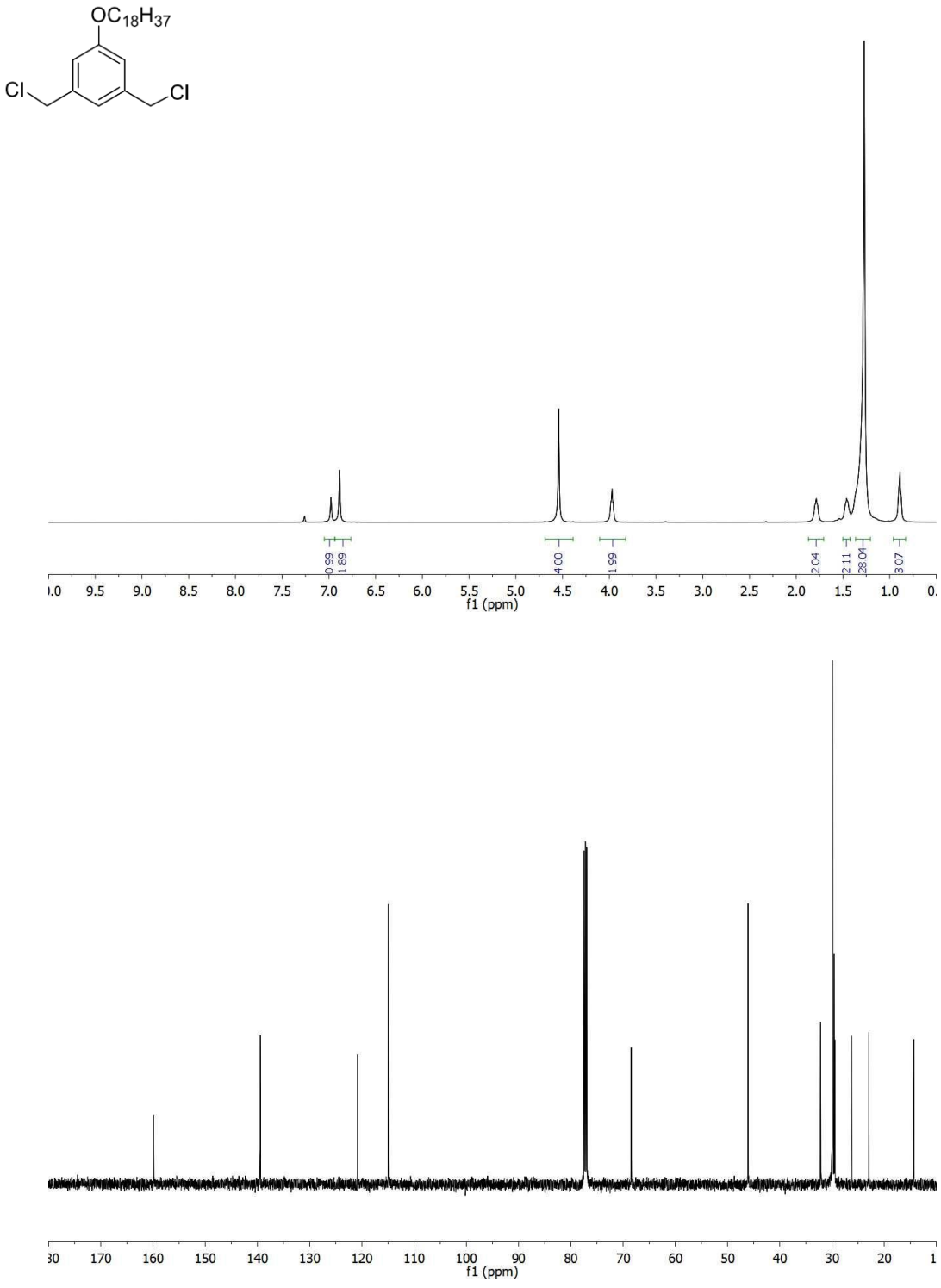


Figure A4.1 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 4.M1 in $CDCl_3$

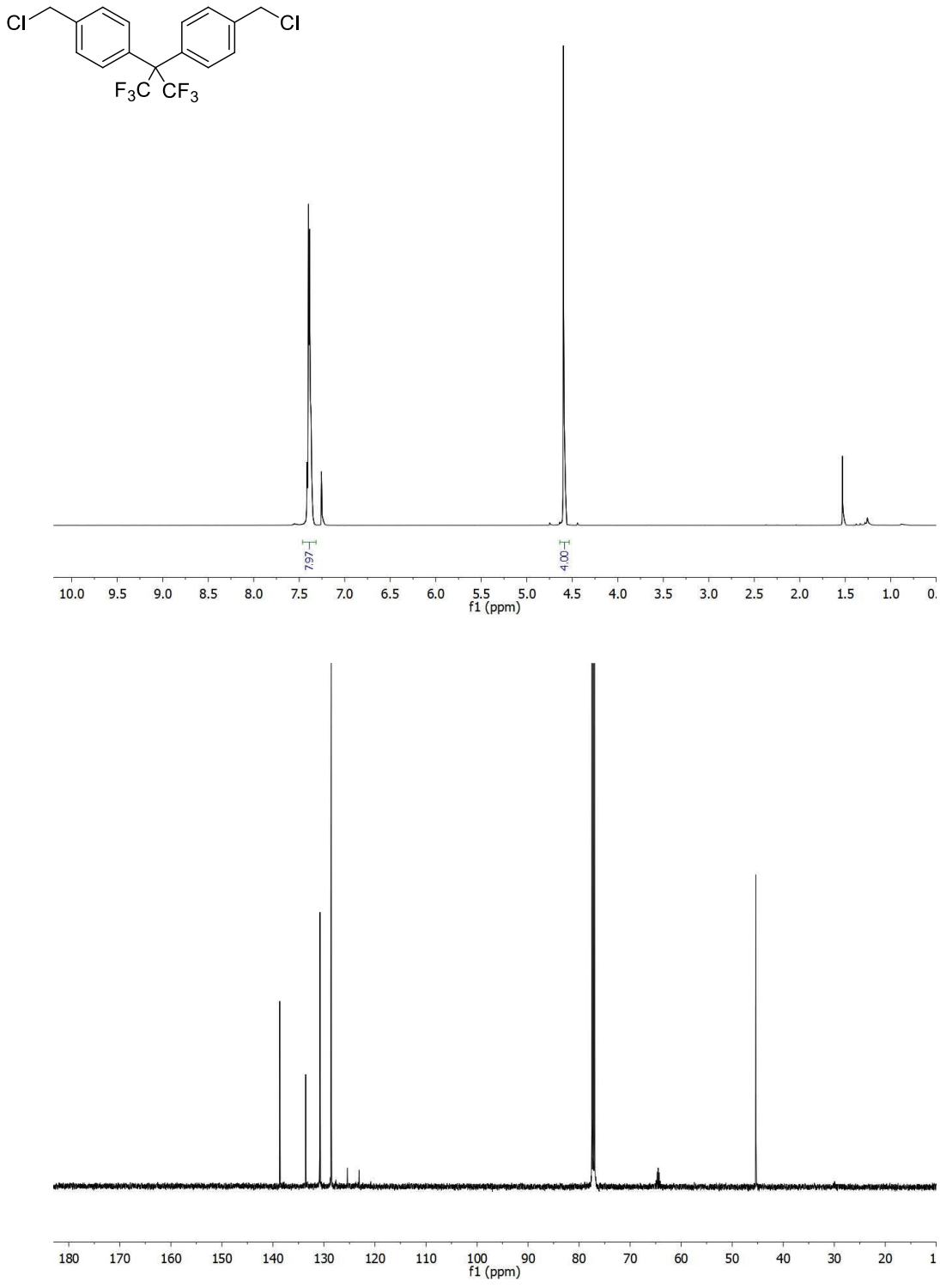


Figure A4.2 500 MHz ^{1}H and 125 MHz $^{13}C\{^{1}H\}$ NMR of 4.M2 in $CDCl_3$