Substituent-Guided Palladium-Ene Reaction for the Synthesis of Carbazoles

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A dissertation submitted for the partial fulfilment of BS-MS dual degree in science

Indian Institute of Science Education and Research Mohali
April 2019

Certificate of Examination

This is to certify that the dissertation titled "Substituent-Guided Palladium-Ene Reaction for the Synthesis of Carbazoles" submitted by Mr. Animesh Singh (Reg. No. MS14010) for the partial fulfilment of BS-MS dual degree programme of the Institute, has been examined by the thesis committee duly appointed by the Institute. The committee finds the work done by the candidate satisfactory and recommends that the report be accepted.

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Dated: April 26, 2019

Declaration

The work presented in this dissertation has been carried out by me under the guidance of **Dr. S. S. V. Ramasastry** at the Indian Institute of Science Education and Research Mohali.

This work has not been submitted in part or in full for a degree, a diploma, or a fellowship to any university or institute. Whenever contributions of others are involved, every effort is made to indicate this clearly, with due acknowledgement of collaborative research and discussion. This thesis is a bonafide record of original work done by me and all sources listed within have been detailed in the bibliography.

Animesh
(Candidate)

Dated: April 26, 2019

In my capacity as the supervisor of the candidate's project work, I certify that the above statements by the candidate are true to the best of my knowledge.

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(Supervisor)

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My sincere thanks to Ms. Sonu, Mr. Uttam and Mr. Bara for helping me during the project work.

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I am thankful to library, IR, NMR and HRMS facilities of IISER-Mohali.

Last but not the least, I would like to acknowledge my family for always standing behind me with their love and support.

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Notations and Abbreviations

NMR	Nuclear magnetic resonance
IR	Infra-red
HRMS	High resolution mass spectroscopy
TLC	Thin layer chromatography
δ	Chemical shift in ppm
ppm	Parts per million
EtOAc	Ethyl acetate
s	Singlet
d	Doublet
t	Triplet
q	Quartet
m	Multiplet
dd	Doublet of doublet
dt	Doublet of triplet
td	Triplet of doublet
ddd	Doublet of doublet of doublet
M. P.	Melting point

Contents

Abstract

- Chapter 1 : Screening of different catalysts and conditions is presented for the hydroamination of terminal alkenes.
- Chapter 2 : Synthesis of Carbazoles through the formation of a palladium π allyl complex is presented.

Chapter 1

Hydroamination of Unactivated Terminal Alkene

1.1 Introduction

Tetrahydro-β-carboline are very fascinating heterocycles, having variety of biological and pharmacological activities. They show a broad range of pharmacological activities like antiviral[1], antitumor[1], antimalarial[1], antioxidant[2], radical scavengers[2], potential neuroactivity[3] etc.

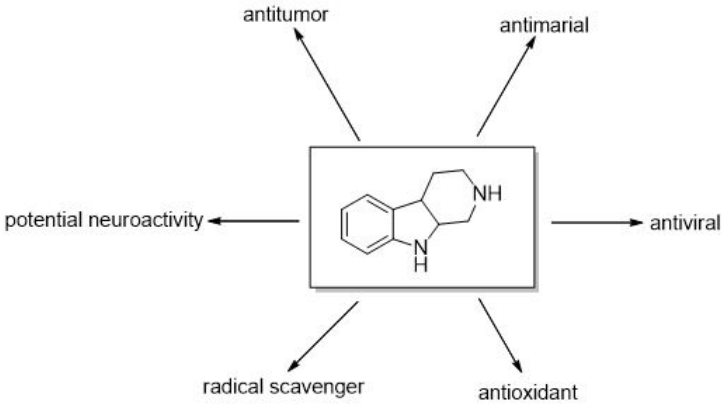
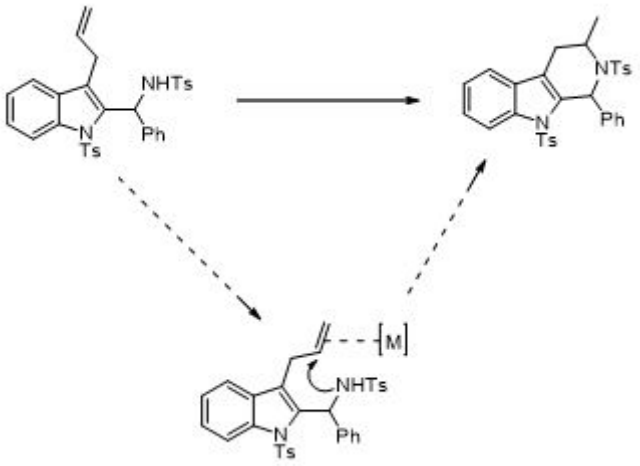
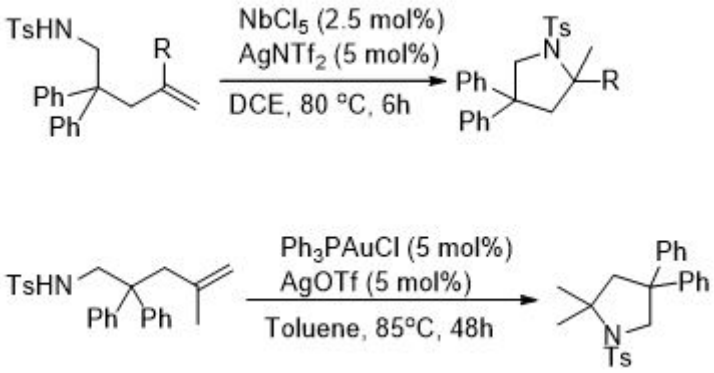


Figure 1.1: Biological and pharmaceutical activity range of tetrahydro-β-carboline

Through an unprecedented one-pot triple-orthogonal-metal relay catalysis[4] β-Carbolines were synthesized by our group in 2016. So we hypothesized of getting the precursor to β-carboline that is tetrahydro-β-carbolines by employing pi acids to bring about the hydroamination.



Scheme 1.1: Our hypothesis



Scheme 1.2: Some of the previous reports

We hypothesized from recent studies[5,6] that a suitable pi acid will activate the terminal alkene leading to the formation of the desired product.

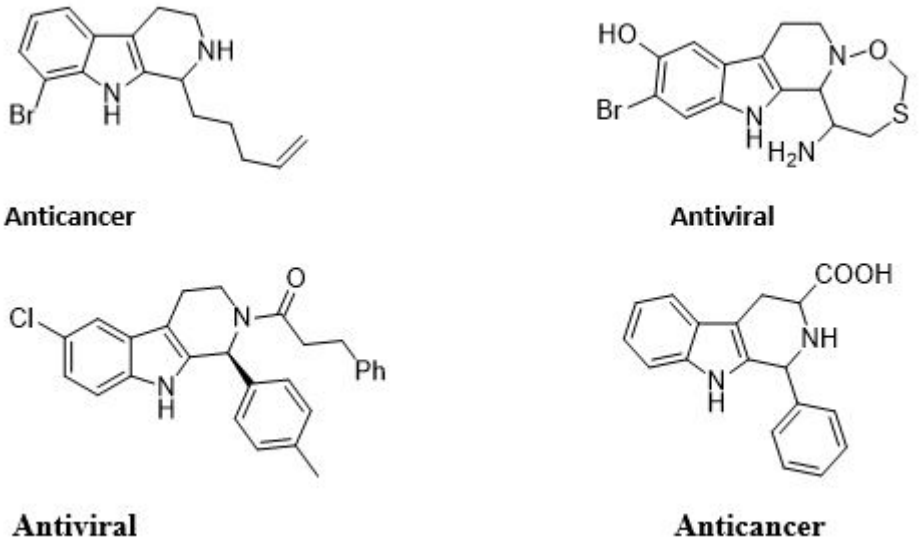
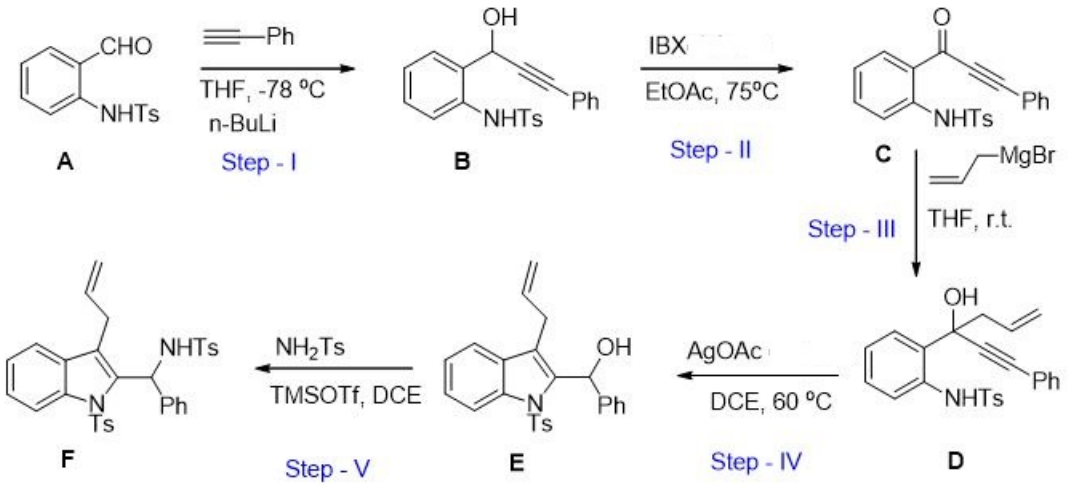


Figure 1.2: Pharmaceutical importance of the backbone

1.2 Results and Discussion

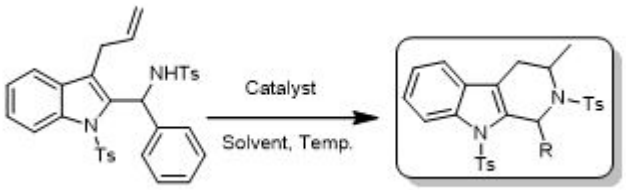
Starting from 2-aminobenzaldehydes **A**, n-Butyllithium mediated addition of alkynes to amino benzaldehydes **A** afforded ynols **B** which upon IBX oxidation generated the ynones **C**. Further addition of allylmagnesium chlorides to ynones **C** furnished enynols **D** which on further treatment with silver acetate gave indolyl alcohol **E**. Treatment of this with acid and NH_2Ts furnished the starting material.



Scheme 1.3: Synthesis of starting material

The screening was done with different pi acids to achieve successful conversion to tetrahydro-β-carboline as discussed in Table 1.

Table 1: Screening of different catalysts and conditions.

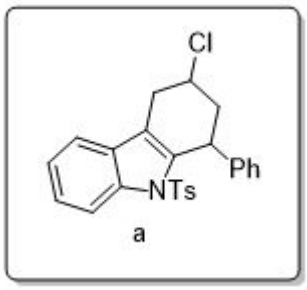


Entry	Catalyst(10 mol%)	Solvent	Temperature(^oC)	Time (hrs)	Yield
1	$NbCl_5$	ACN	60	24	a(31)
2	$NbCl_5$	Toluene	100	24	a(29)
3	$NbCl_5$	DMF	100	24	a(25)
4	$NbCl_5$	DCE	60	24	a(34)
5	AgOAc	ACN	60	24	-
6	AgOAc	Toluene	100	24	-
7	AgOAc	DMF	100	24	-
8	AgOAc	DCE	60	24	-
9	$AgBF_4$	ACN	60	24	-
10	$AgBF_4$	Toluene	100	24	-
11	$AgBF_4$	DMF	100	24	-
12	$AgBF_4$	DCE	60	24	-

Entry	Catalyst(10mol%)	Solvent	Temperature(^oC)	Time(hrs)	Yield
13	AuCl	ACN	60	24	-
14	AuCl	Toluene	100	24	-
15	AuCl	DMF	100	24	-
16	AuCl	DCE	60	24	-
17	AgOTf	ACN	60	24	-
18	AgOTf	Toluene	100	24	-
19	AgOTf	DMF	100	24	-
20	AgOTf	DCE	60	24	-
21	$CuCl_2$	ACN	60	24	-
22	$CuCl_2$	Toluene	100	24	-
23	$CuCl_2$	DMF	100	24	-
24	$CuCl_2$	DCE	60	24	-
25	CuOTf	ACN	60	24	-
26	CuOTf	Toluene	100	24	-
27	CuOTf	DMF	100	24	-
28	CuOTf	DCE	60	24	-
29	HgOTf	ACN	60	24	-
30	HgOTf	Toluene	100	24	-
31	HgOTf	DMF	100	24	-
32	HgOTf	DCE	60	24	-
33	$HgCl_2$	ACN	60	24	-
34	$HgCl_2$	Toluene	100	24	-
35	$HgCl_2$	DMF	100	24	-
36	$HgCl_2$	DCE	60	24	-
37	$[Ir(OCH_3)(C_8H_{12})]_2$	ACN	60	24	-
38	$[Ir(OCH_3)(C_8H_{12})]_2$	Toluene	100	24	-
39	$[Ir(OCH_3)(C_8H_{12})]_2$	DMF	100	24	-
40	$[Ir(OCH_3)(C_8H_{12})]_2$	DCE	60	24	-

Entry	Catalyst(10mol%)	Solvent	Temperature(^oC)	Time(hrs)	Yield
41	$Rh_2(OOCCH_3)_4$	ACN	60	24	-
42	$Rh_2(OOCCH_3)_4$	Toluene	100	24	-
43	$Rh_2(OOCCH_3)_4$	DMF	100	24	-
44	$Rh_2(OOCCH_3)_4$	DCE	60	24	-
45	$AuCl_3$	ACN	60	24	a(27)
46	$AuCl_3$	Toluene	100	24	a(30)
47	$AuCl_3$	DMF	100	24	a(29)
48	$AuCl_3$	DCE	60	24	a(32)
49	$Ni(COD)_2$	ACN	60	24	-
50	$Ni(COD)_2$	Toluene	100	24	-
51	$Ni(COD)_2$	DMF	100	24	-
52	$Ni(COD)_2$	DCE	60	24	-
53	$AuCl_3/K_2CO_3$	DCE	60	24	a(40)
54	$AuCl/K_2CO_3$	DCE	60	24	-
55	$AuCl/AgBF_4$	Methanol	r.t.	24	-
56	AgOTf	1,4-Dioxane	100	24	-
57	$CuBr_2$	ACN	60	24	-
58	$CuBr_2$	Toluene	100	24	-
59	$CuBr_2$	DMF	100	24	-
60	$CuBr_2$	DCE	60	24	-

To our dismay the desired product could not be synthesized and halo-prins annulated compound formed as the undesired product(a).



a

1.3 Experimental Procedures

General experimental methods: All the starting compounds and catalysts employed in this study were procured from Sigma-Aldrich and were used without further purification. For thin layer chromatography (TLC), silica aluminium foils with fluorescent indicator 254 nm (from Aldrich) were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of p-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), and acetic acid (10 mL) in ethanol (900 mL) followed by heating. Column chromatography was performed using SD Fine silica gel 100-200 mesh (approximately 15–20 g per 1 g of the crude product). Dry THF was obtained by distillation over sodium and stored over sodium wire. IR spectra were recorded on a Perkin–Elmer FT IR spectrometer as thin films or KBr pellet, as indicated, with max in inverse centimetres. Melting points were recorded on a digital melting point apparatus Stuart SMP30 and were uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded on a 400 MHz BrukerBiospinAvance III FT-NMR spectrometer. NMR shifts are reported as delta (δ) units in parts per million (ppm) and coupling constants (J) are reported in Hertz (Hz). The following abbreviations are utilized to describe peak patterns when appropriate: br=broad, s=singlet, d=doublet, t=triplet, q=quartet and m=multiplet. Proton chemical shifts are given in δ relative to tetramethylsilane (δ 0.00 ppm) in $CDCl_3$. Carbon chemical shifts are internally referenced to the deuterated solvent signals in $CDCl_3$ (δ 77.1 ppm). High-resolution mass spectra were recorded on a Waters QTOF mass spectrometer. Enantiomeric excess was determined by using Waters Chiral HPLC.

Representative procedure for step-I: To a stirred solution of the alkyne (2.2 equiv.) in anhydrous THF at -78^oC, was added n-butyllithium (2.0 M in cyclohexane solution, 2.2 equiv.) drop wise, and the resulting solution was allowed to stir at the same temperature for 10 min. The reaction was warmed to -40^oC. The resulting mixture was stirred at the same temperature for 1 h. After 1 h, reaction mixture was cooled to -78^oC. The N-(2-formylphenyl)- 4-methylbenzenesulfonamide **A** (1 mmol) was dissolved in THF (2 mL) and added to the reaction mixture drop wise at -78^oC and allowed to stir for 1 h at the same temperature. The reaction mixture was slowly warmed up to room temperature and stirred for a further 1 h. Upon completion, the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20-30% EtOAc/hexane) to afford **B** (80-90%

yields).

Representative procedure for step-II: Ynol **B** (1 mmol) was dissolved in EtOAc (5 mL), and IBX (1.5 mmol) was added. The resulting suspension was stirred at 75^oC until alcohol A disappeared as monitored by TLC. Cooled the reaction mixture to room temperature and filtered through celite. The residue was washed with ethyl acetate (32 mL). Organic extracts were combined and washed with saturated aq. $NaHCO_3$ solution to remove excess iodobenzoic acid. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20-30% EtOAc/hexane) to afford **C** (in 75-85% yields).

Representative procedure for step-III: An oven dried round bottom flask was charged with ynone **C** (1.0 mmol), 5 mL dry THF and placed at 0^oC. Allylmagnesium chloride (2.2 mmol) were added drop wise at the same temperature and stirred for 1h. Upon completion, the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10-20% EtOAc/hexane) to afford **D** (in 90-95% yields).

Representative procedure for step-IV: A 5 mL glass vial was charged with **D** (0.1 mmol) in 1,2-DCE and AgOAc (2 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 60^oC until the starting material D disappears, as monitored by TLC. The reaction mixture was quenched with water and extracted with EtOAc. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude mixture was purified by silica gel column chromatography using ethyl acetate/hexane (15:85) as an eluent to afford **E** (in 80-90% yield).

Representative procedure for step-V: To an oven dried round bottom flask was added **E** and stirred at 0^oC in 1,2-DCE. To it p-Toluenesulfonamide (2.0 mmol) was added followed by the addition of Trimethylsilyl trifluoromethanesulfonate (0.1 mmol) after 15 minutes. The reaction was monitored by TLC until all starting material disappeared. The reaction mixture was quenched with water and extracted with EtOAc. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude mixture was purified by silica gel column chromatography using ethyl acetate/hexane (20:80) as an eluent to afford **F** (in 75-85 % yield).

1.4 Summary

Even after extensive screening of different conditions we were unable to achieve the desired product and an undesired halo-prins annulated product was obtained.

Chapter 2

Substituent-Guided Palladium-Ene Reaction for the Synthesis of Carbazoles

2.1 Introduction

Carbazoles are very interesting heterocycles having profound application in industries and medicine. Some of the interesting properties are antifungal, antibacterial, anti-inflammatory, optoelectronic properties, use in polymers and dyes.

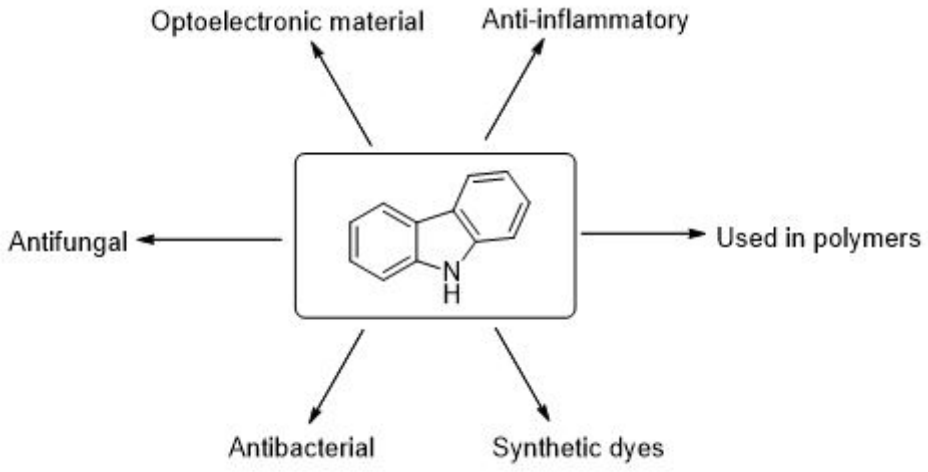
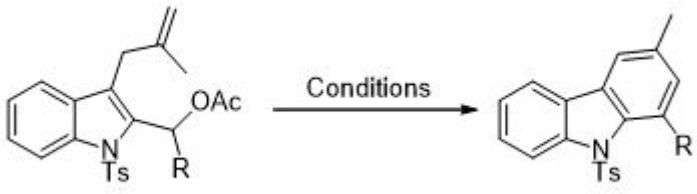


Figure 2.1: Activity[7] range of carbazoles

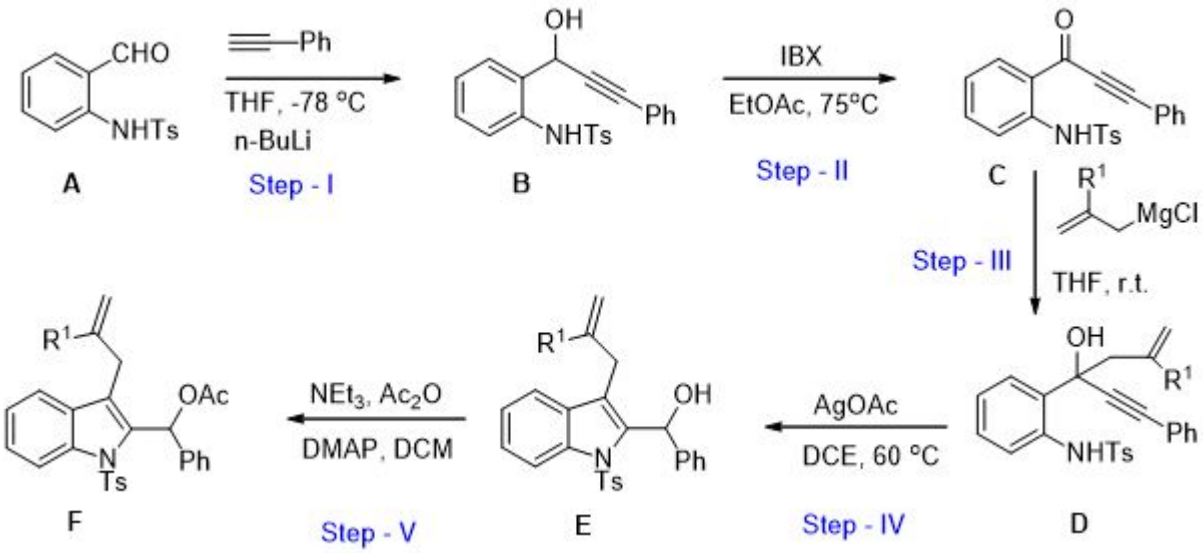
We hypothesized of getting carbazoles from allyl acetates through the formation of a π allyl complex.



Scheme 2.1: Synthesis of carbazoles

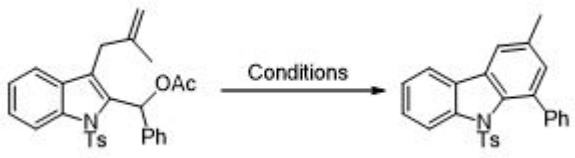
2.2 Results and Discussion

All the (3-allyl-1H-indol-2-yl)methyl acetates employed in this study were prepared following a four-step protocol starting from 2-aminobenzaldehydes **A**. n-Butyllithium mediated addition of alkynes to amino benzaldehydes **A** afforded ynols **B** which upon IBX oxidation generated the ynones **C**. Further addition of allylmagnesium chlorides to ynones C gave 3-(2-aminophenyl)hex-5-en-1-yn-3-ols **D**. Subsequent acetyl protection using triethylamine, acetic anhydride and DMAP , furnished allyl acetates.



Scheme 2.2: Synthesis of starting material (General Procedure 1)

Table 2: Optimization of reaction parameters

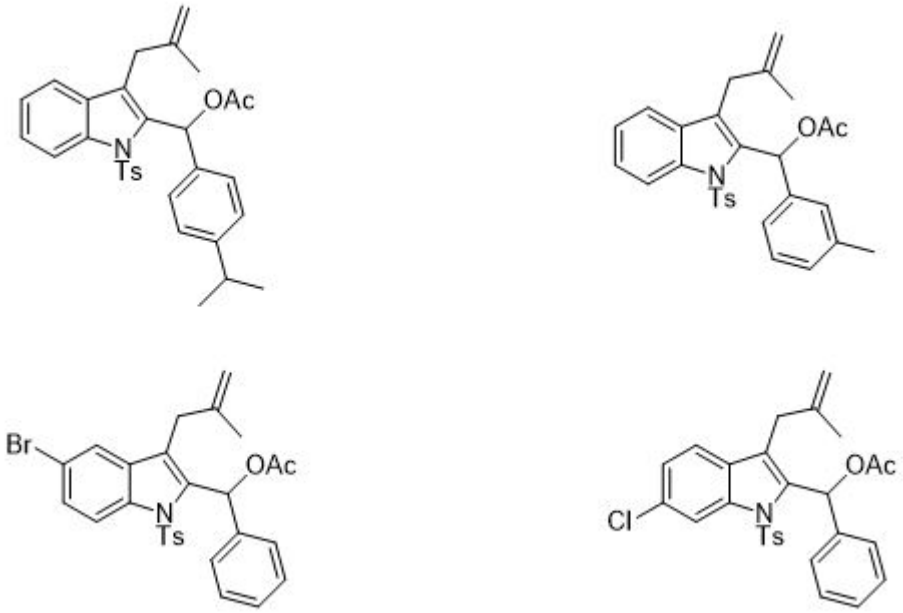


Entry	Catalyst(10 mol%)	Solvent	Temperature(^oC)	Time(hrs)	Yield
1	$Pd(PPh_3)_4$	Toluene	100	72	-
2	$Pd_2(dba)_3$	Toluene	100	72	-
3	$Pd(OAc)_2$	Toluene	80	72	20
4	$[Ir(cod)Cl_2]_2$	Toluene	100	72	33
5	$Ni(cod)_2$	Toluene	100	72	-
6	$Pd(PPh_3)Cl_2$	Toluene	80	72	-
7	$[PdCl(allyl)]_2$	Toluene	80	72	15
8	$PdCl_2$	Toluene	80	26	74
9	$PdCl_2$	1,2-DCE	80	72	52
10	$PdCl_2$	DMF	80	72	-
11	$PdCl_2$	CH_3CN	80	72	69
12	$PdCl_2$	1,4-dioxane	80	24	83
13	$PdCl_2$	1,4-dioxane	80	36	45
14[a]	$PdCl_2$	1,4-dioxane	80	18	85
15	$PdCl_2$	1,4-dioxane	80	29	66

[a]20 mol % of $PdCl_2$ was employed. While Pd(0) catalyst were unsuccessful, $Pd(OAc)_2$ successfully provided the product but with poor yields. $PdCl_2$ promoted reaction gave good yields with 1,4-Dioxane being the most optimal solvent. Reaction with higher catalyst loading completed faster.

Entry 12 was taken as the optimized condition and we proceeded to substrate scope.

Some of the Starting materials were prepared.



Scheme 2.3: Starting materials prepared

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Representative procedure for step-II: Ynol **B** (1 mmol) was dissolved in EtOAc (5 mL), and IBX (1.5 mmol) was added. The resulting suspension was stirred at 75^oC until alcohol A disappeared as monitored by TLC. Cooled the reaction mixture to room temperature and filtered through celite. The residue was washed with ethyl acetate (32 mL). Organic extracts were combined and washed with saturated aq. $NaHCO_3$ solution to remove excess iodobenzoic acid. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20-30% EtOAc/hexane) to afford **C** (in 75-85% yields).

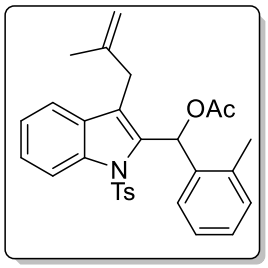
Representative procedure for step-III: An oven dried round bottom flask was charged with ynone **C** (1.0 mmol), 5 mL dry THF and placed at 0^oC. Allylmagnesium chloride (2.2 mmol) were added drop wise at the same temperature and stirred for 1h. Upon completion, the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10-20% EtOAc/hexane) to afford **D** (in 90-95% yields).

Representative procedure for step-IV: A 5 mL glass vial was charged with **D** (0.1 mmol) in 1,2-DCE and AgOAc (2 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 60^oC until the starting material **D** disappears, as monitored by TLC. The reaction mixture was quenched with water and extracted with EtOAc. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude mixture was purified by silica gel column chromatography using ethyl acetate/hexane (15:85) as an eluent to afford **E** (in 80-90 %).

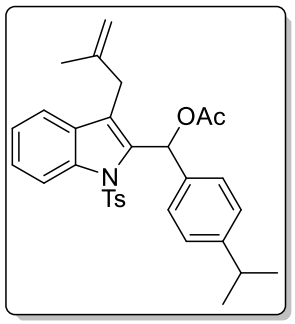
Representative procedure for step-V: (0.1 mmol) was taken in an oven dried RB flask, DCM was added followed by triethylamine (0.15 mmol) at 0^oC. The reaction mixture was then allowed to stir for 5 mins at the same temperature and acetic anhydride (0.15 mmol) was introduced to the reaction mixture, followed by DMAP (5 mol%). The resultant solution was then allowed to stir at 0^oC for the next 1 hour. The reaction mixture was quenched with aq. NH_4Cl and extracted with DCM. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude compound was purified by silica gel column chromatography using ethyl acetate/hexane (10:90) as an eluent to afford the starting material (in 70-90% yield).

(3-(2-Methylallyl)-1-tosyl-1*H*-indol-2-yl)(*o*-tolyl)methyl acetate :

This compound was isolated as transparent viscous liquid by following the general procedure **1**. R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3065, 1741, 1220, 719**. ^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.17-8.15 (m, 2H), 7.7 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 7.1 Hz, 1H), 7.36-7.33 (m, 1H), 7.30-7.25 (m, 3H), 7.14 (d, *J* = 8.3 Hz, 2H), 7.10-7.06 (m, 1H), 7.04-7.02 (m, 1H), 4.74 (s, 1H), 4.22 (s, 1H), 3.64 (d, *J* = 17.4 Hz, 1H), 3.35 (d, *J* = 17.4 Hz, 1H), 2.43 (s, 3H), 2.33 (s, 3H), 2.07 (s, 3H), 1.83 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 170, 144.6, 142.6, 137.6, 136.3, 135.5, 135.4, 133.7, 131, 130.7, 129.5 (2CH), 128.8, 127.8, 127.06 (2CH), 125.9, 125, 123.4, 121.7, 119.6, 115.08, 111.4, 69.2, 32.8, 23.4, 21.5, 20.8, 19.1. **HRMS (ESI)**: m/z calcd for $C_{29}H_{31}NO_4S$ $(M+H)^+$: 488.1896, Found: 488.1889.



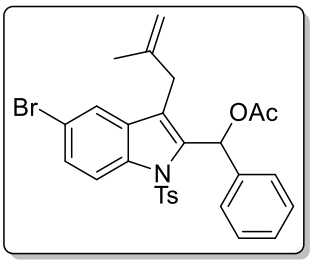
(4-Isopropylphenyl)(3-(2-methylallyl)-1-tosyl-1*H*-indol-2-yl)methyl acetate :



This compound was isolated as transparent viscous liquid by following the general procedure **1**. R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2962, 1742, 1229, 577**. ^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.22 (d, *J* = 8.4 Hz, 1H), 8.12 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.47 (d , *J* = 7.8 Hz, 1H), 7.38-7.32 (m, 3H), 7.29-7.23 (m, 3H), 7.14 (d, *J* = 8.2 Hz, 2H), 4.76 (s, 1H), 4.27 (s, 1H), 3.76 (d, *J* = 17.2 Hz, 1H), 3.42 (d, *J* = 17.2 Hz, 1H), 2.96 (dt, *J* = 13.8 and 6.9 Hz, 1H), 2.3 (s, 3H), 2.11 (s, 3H), 1.82 (s, 3H), 1.31 (d, *J* = 7 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 169.9, 149, 144.6, 142.8, 136.5, 135.56, 135.52, 134.6, 131.01, 129.5 (2CH), 127.9 (2CH), 127.0 (3CH), 126.2 (2CH), 125.09, 123.5, 121.5, 119.7, 115.3, 111.4, 70.9, 33.8, 33.01, 24, 23.2, 21.5, 20.9. **HRMS (ESI)**: *m/z* calcd for $C_{31}H_{34}NO_4S$ $(M+H)^+$: 516.2209, Found: 516.2195.

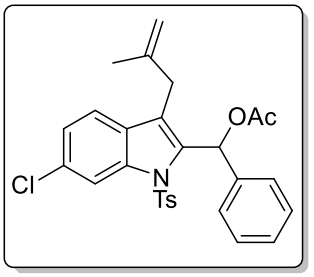
(5-Bromo-3-(2-methylallyl)-1-tosyl-1*H*-indol-2-yl)(phenyl)methyl acetate :

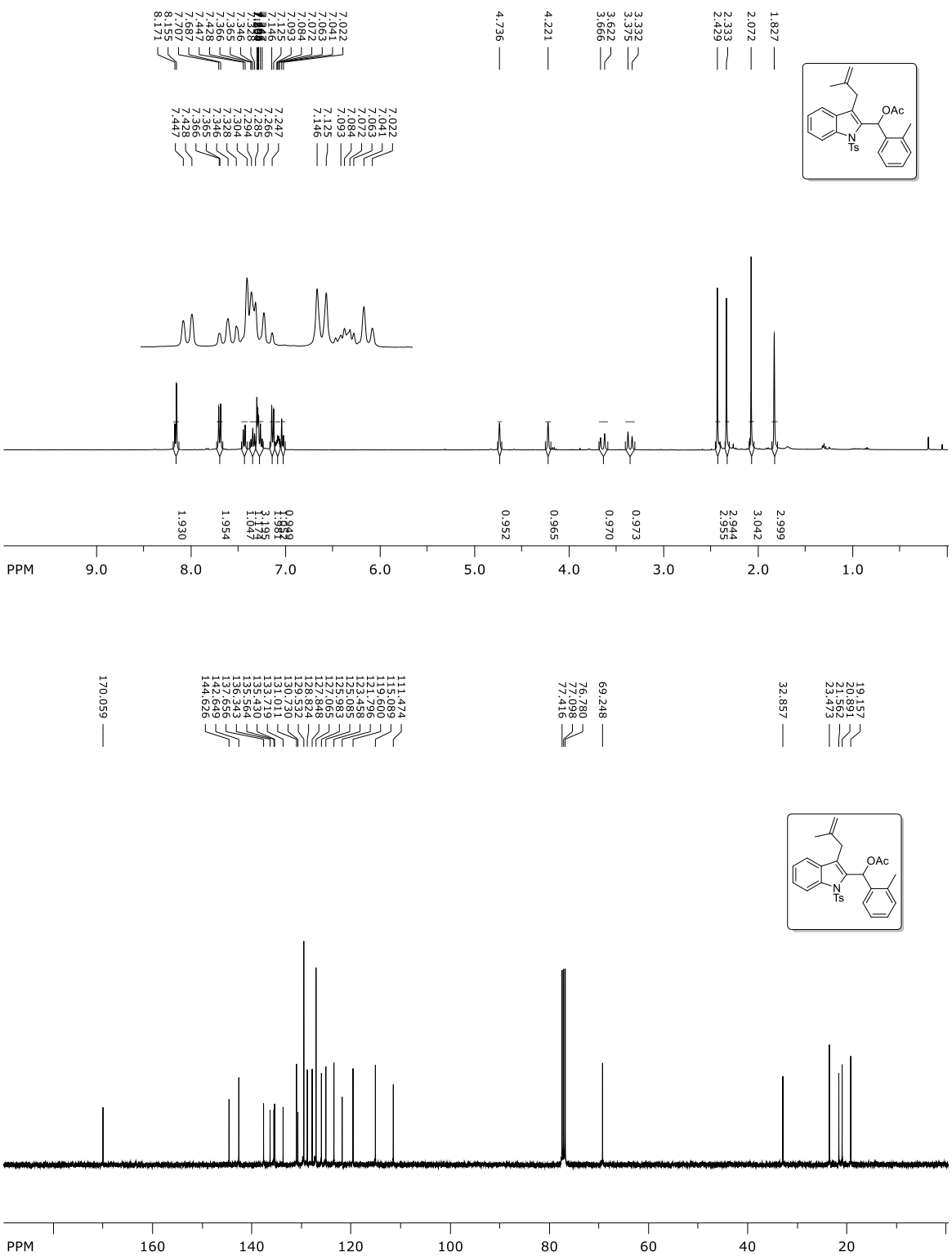
This compound was isolated as colourless viscous liquid by following the general procedure **1.** R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2961, 1750, 1225, 570**. ^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.09-8.07 (m, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.57-7.55 (m, 1H), 7.45-7.43 (m, 1H), 7.39-7.33 (m, 5H), 7.20-7.16 (m, 2H), 4.75 (s, 1H), 4.22 (s, 1H), 3.66 (d, *J* = 17.3 Hz, 1H), 3.32 (d, *J* = 17.2 Hz, 1H), 2.35 (s, 3H), 2.11 (s, 3H), 1.8 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 169.8, 145.09, 142.3, 137.9, 135.8, 135.2, 135.1, 132.7, 129.7 (2CH), 128.6 (2CH), 128.3, 128, 127.6 (2CH), 127 (2CH), 122.4, 120.8, 117.1, 116.8, 111.7, 70.6, 32.8, 23.2, 21.6, 21. **HRMS (ESI)**: m/z calcd for $C_{28}H_{27}BrNO_4S$ $(M+H)^+$: 552.0844, Found: 552.0851.



(6-Chloro-3-(2-methylallyl)-1-tosyl-1*H*-indol-2-yl)(phenyl)methyl acetate :

This compound was isolated as colorless viscous liquid by following the general procedure **1**. R_f = 0.5 (Hexane/EtOAc = 9/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 2950, 1742, 1228, 575**. ^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.21 (d, *J* = 1.7 Hz, 1H), 8.01 (s, 1H), 7.7 (d, *J* = 8.4 Hz, 2H), 7.35-7.29 (m, 6H), 7.2 (dd, *J* = 8.2 and 1.8 Hz, 1H), 7.18 (d, *J* = 8.3 Hz, 2H), 4.71 (s, 1H), 4.21 (s, 1H), 3.61 (d, *J* = 17.2 Hz, 1H), 3.31 (d, *J* = 17.1 Hz, 1H), 2.36 (s, 3H), 2.09 (s, 3H), 1.73 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 169.8, 145, 142.5, 137.9, 136.7, 135.2, 135.03, 131.1, 129.7 (2CH), 129.2, 128.5 (2CH), 128.2, 127.5 (2CH), 127 (2CH), 124.1, 121.2, 120.5, 115.4, 111.5, 70.5, 32.8, 23.1, 21.5, 20.9. **HRMS (ESI)**: *m/z* calcd for $C_{28}H_{26}ClNNaO_4S$ $(M+Na)^+$: 530.1169, Found: 530.1151.

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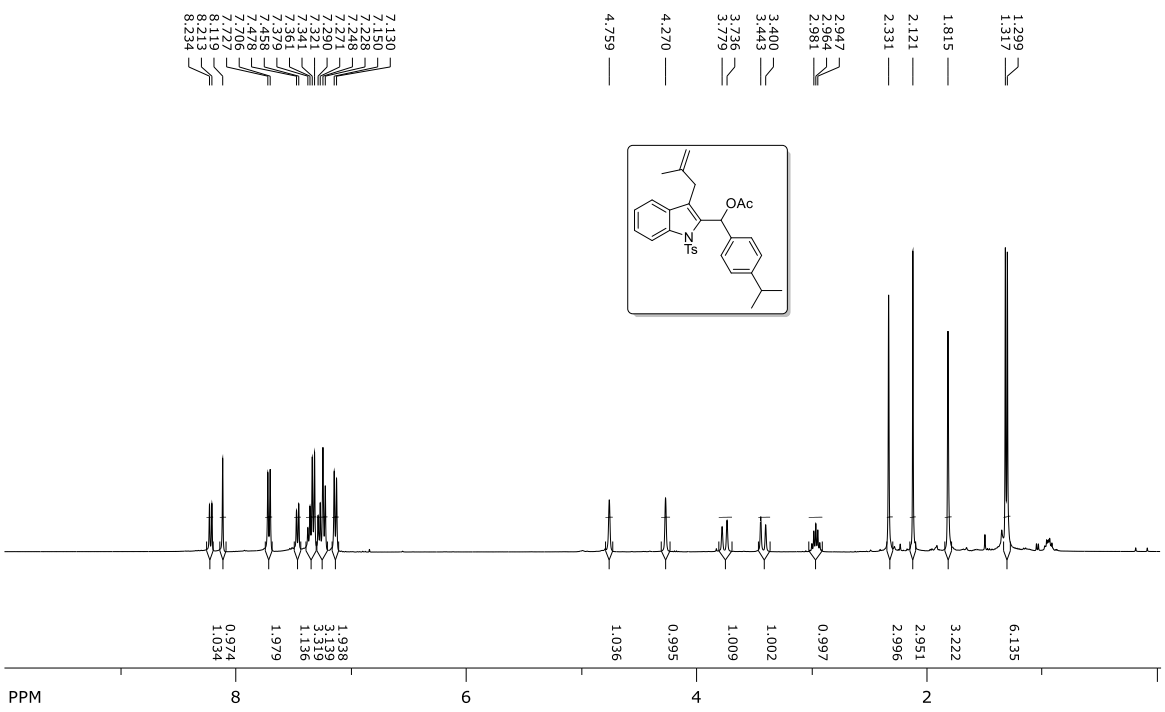
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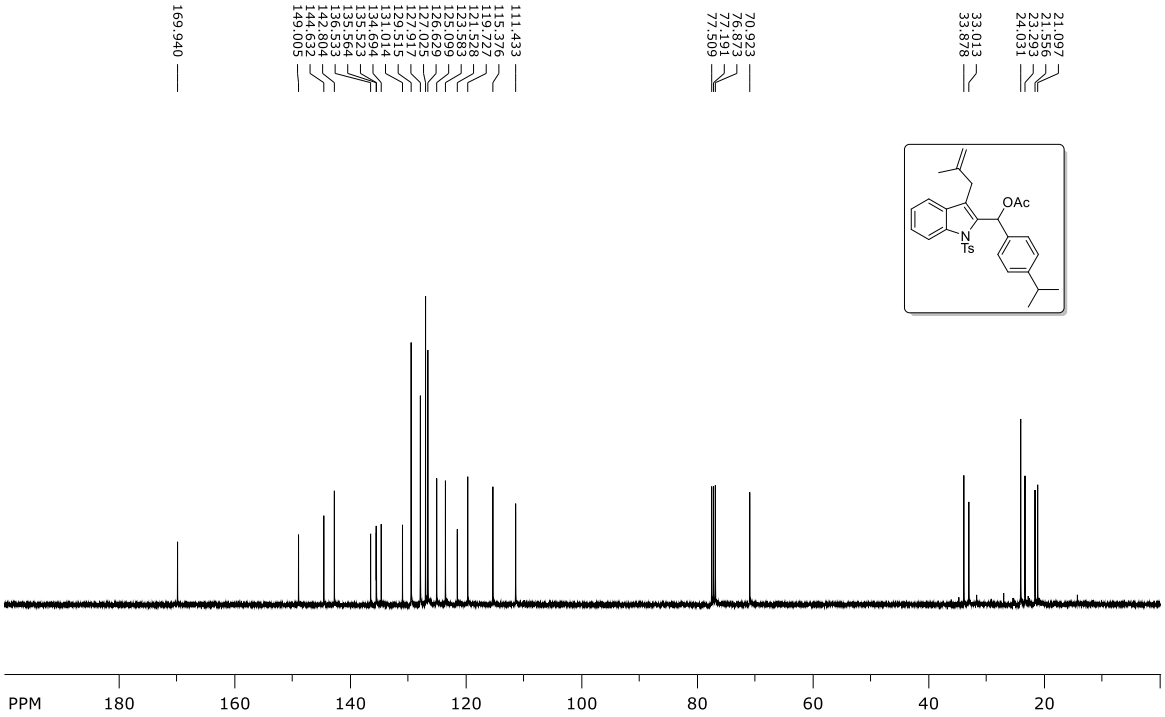
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33.013
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Ts
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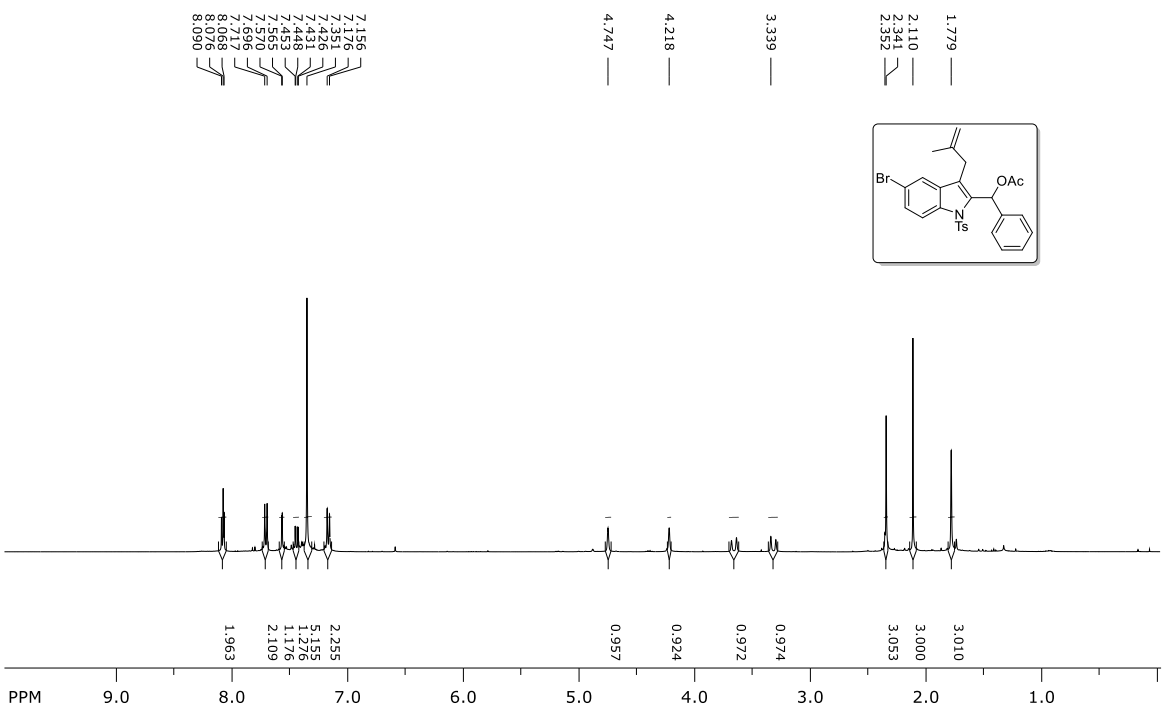
60
40
20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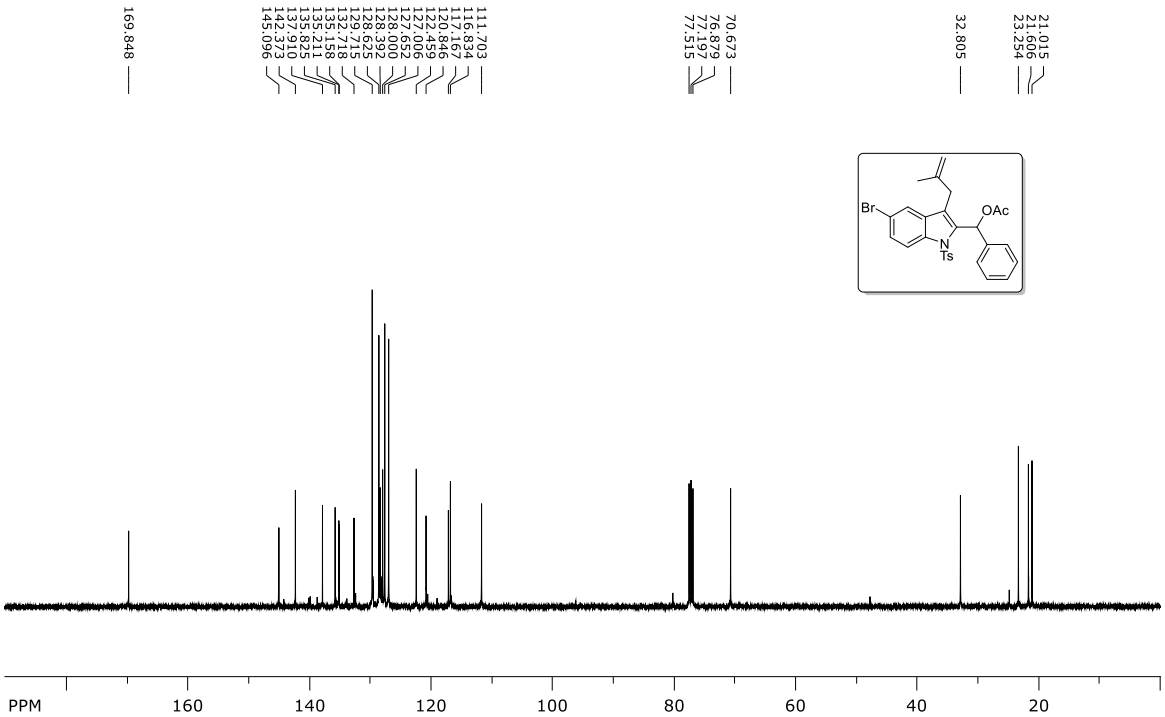
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Ts
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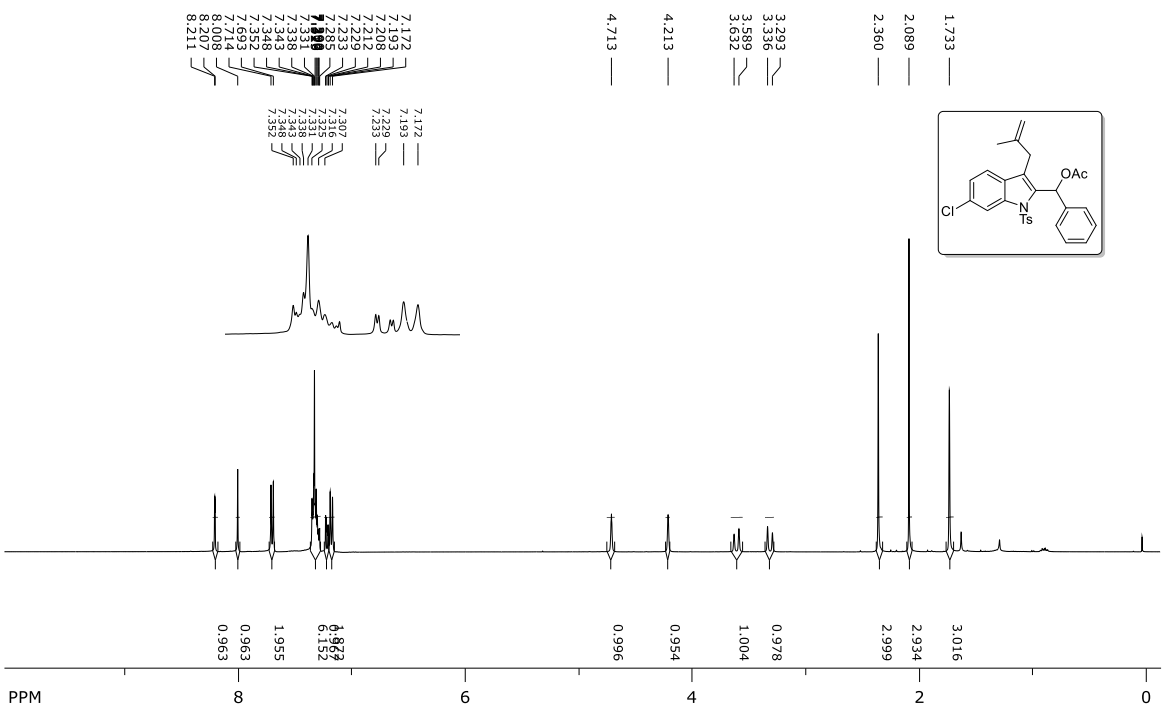
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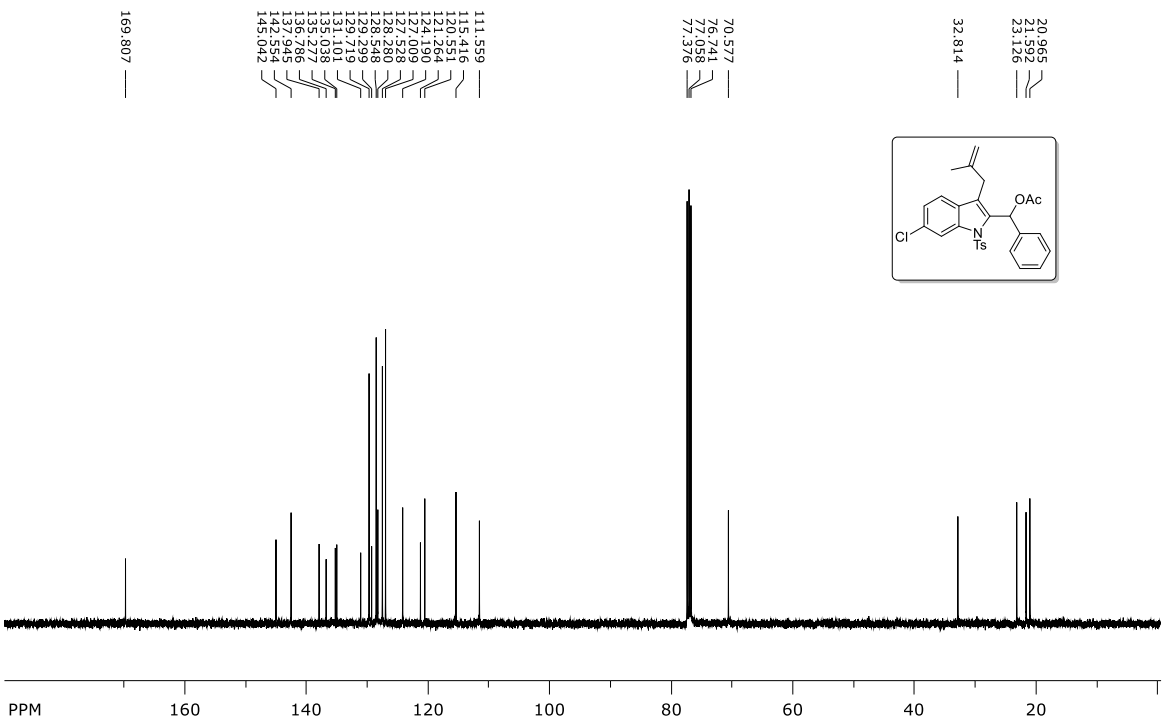
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Ts
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40
20

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