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Copper-Catalyzed Asymmetric Propargylic Substitution Reactions of Propargylic Acetates with Amines: A Novel Synthetic Approach to Chiral Propargylic Amines

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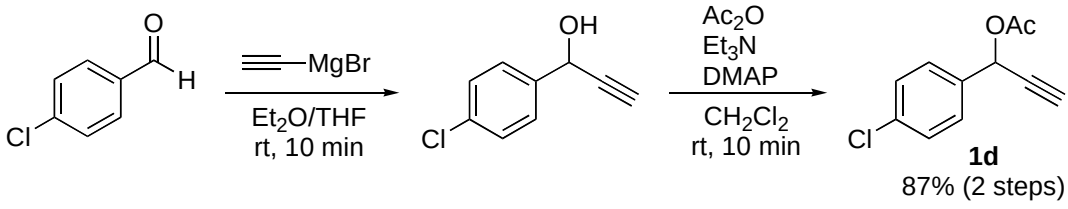
General Method. ^{1}H NMR (270 MHz) and ^{13}C NMR (67.8 MHz) spectra were measured on a JEOL Excalibur 270 spectrometer using $CDCl_3$ as solvent. GLC analyses were performed on a Shimadzu GC-14A instrument equipped with a flame ionization detector using a 25 m x 0.25 mm CBP10 fused silica capillary column. HPLC analyses were performed on Hitachi L-7100 apparatus equipped with a UV detector using 25 cm x 4.6 mm DAICEL Chiralcel OD, OJ-H, and Chiralpak AD columns. Elemental analyses were performed at Microanalytical Center of The University of Tokyo. Mass spectra were measured on a JEOL JMS-700 mass spectrometer. IR spectra were recorded on a JASCO FT/IR-4100 spectrometer.

All reactions were carried out under a dry nitrogen atmosphere. Optically pure diphosphines are commercially available reagents. Preparation of propargylic acetates (**1a, 1c, 1g,** and **1h**) was carried out according to the literature methods.[S1] Other propargylic alcohols were prepared by the reactions of the corresponding propargylic alcohols with acetic anhydride. Copper complex, CuOTf·$(benzene)_{0.5}$, is commercial available and storted under a nitrogen atmosphere. Amines are commercial available and distilled prior to use. Solvents such as methanol were distilled under N_2 and degassed.

General Procedure for the Preparation of Propargylic Acetates. A typical experimental procedure for the preparation of 1-(4-chlorophenyl)prop-2-ynyl acetate (**1d**) is described below. In a 100 mL round-bottomed flask were placed 4-chlorobenzaldehyde (1.51 g, 10.7 mmol) and anhydrous diethyl ether (10 mL). Ethynylmagnesium bromide (0.5 M in tetrahydrofuran; 22.0 mL, 11.0 mmol) was added to the solution and the mixture was stirred at room temperature for 10 min. The reaction was quenched by saturated NH_4Cl solution (20 mL), and organic materials were extracted with diethyl ether (20 mL x 2). The combined extracts were washed with brine, and dried over anhydrous $MgSO_4$. The solvent was concentrated under reduced pressure by an aspirator to give crude propargylic alcohol. The resulting crude material was used for the next step without further purification.

In a 100 mL round-bottomed flask were placed the propargylic alcohol, triethylamine (1.31 g, 12.9 mmol), and anhydrous dichloromethane (10 mL). Acetic anhydride (1.30 g, 12.7 mmol) and 4-dimethylaminopyridine (60.0 mg, 0.5 mmol) were added to the solustion and the mixture was stirred at room temperature for 10 min. The reaction was quenched by water (10 mL), and organic materials were extracted with dichloromethane (20 mL x 2). The combined extracts were washed with brine, and dried over anhydrous $MgSO_4$. The solvent was concentrated under reduced pressure by an aspirator and the residue was purified by the column chromatography (SiO_2) with hexane and ethyl acetate (9:1) as eluent to give 1-(4-chlorophenyl)prop-2-ynyl acetate (**1d**) as a pale yellow oil (1.95 g, 9.35 mmol; 87% isolated yield).

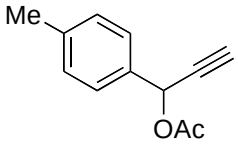
Scheme S1. Preparation of propargylic acetate 1d



1-(4-Chlorophenyl)prop-2-ynyl acetate (1d): A pale yellow oil. ^{1}H NMR δ 2.11 (s, 3H), 2.66 (d, *J* = 2.4 Hz, 1H), 6.41 (d, *J* = 2.4 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 2 H), 7.47 (d, *J* =

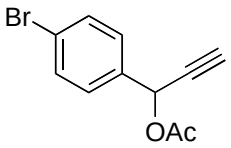
7.8 Hz, 2H). ^{13}C NMR δ 20.9, 64.5, 75.7, 79.8, 128.9, 129.1, 135.0, 135.1, 169.6. Anal. Calcd for $C_{11}H_9ClO_2$: C, 63.32; H, 4.35. Found: C, 63.54; H, 4.55.

Spectroscopic data and isolated yield of other products are as follows.



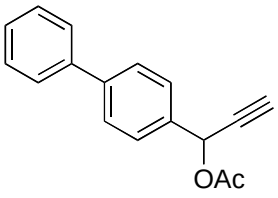
1b

1-(4-Methylphenyl)prop-2-ynyl acetate (1b): A pale yellow oil. ^{1}H NMR δ 2.10 (s, 3H), 2.36 (s, 3H), 2.64 (d, *J* = 2.4 Hz, 1H), 6.42 (d, *J* = 2.4 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR δ 21.2, 65.2, 75.1, 80.4, 88.7, 127.7, 129.4, 133.6, 139.1, 169.7. HRMS Calcd for $C_{12}H_{12}O_2$ [M]: 188.0837. Found: 188.0839.



1e

1-(4-Bromophenyl)prop-2-ynyl acetate (1e): A yellow oil. ^{1}H NMR δ 2.11 (s, 3H), 2.66 (d, *J* = 2.4 Hz, 1H), 6.40 (d, *J* = 2.4 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 2 H), 7.52 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR δ 20.9, 64.6, 75.7, 79.7, 123.3, 129.4, 131.9, 135.5, 169.5. HRMS Calcd for $C_{11}H_9BrO_2$ [M]: 251.9786. Found: 251.9782.

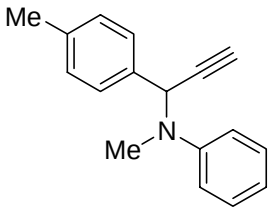


1f

1-Biphenylprop-2-ynyl acetate (1f): A white solid, 69.8-71.3 °C. ^{1}H NMR δ 2.13 (s, 3H), 2.68 (d, *J* = 2.2 Hz, 1H), 6.49 (d, *J* = 2.2 Hz, 1H), 7.36 (t, *J* = 6.5 Hz, 1 H), 7.45 (dd, *J* = 6.5, 6.5 Hz, 2H), 7.57-7.61 (m, 6H). ^{13}C NMR δ 21.0, 65.1, 75.5, 80.2, 127.2, 127.46, 127.59, 128.2, 128.8, 135.4, 140.4, 142.1, 169.7. Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.77; H, 5.80.

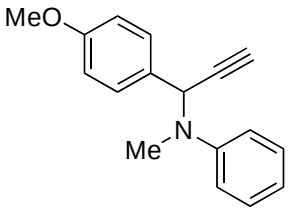
Copper-Catalyzed Asymmetric Propargylic Substitution Reactions of Propargylic Acetates with Amines. A typical experimental procedure for the reaction of 1-phenyl-2-propynyl acetate (**1a**) with *N*-methylaniline is described below. In a 20 mL round-bottomed flask were placed CuOTf ·(benzene)$_{0.5}$ (2.5 mg, 0.010 mmol) and (*R*)-Cl-MeO-BIPHEP (13.0 mg, 0.020 mmol) under N_2. Anhydrous methanol (1.0 mL) was added, and then the mixture was magnetically stirred at 60 °C for 1 h. Then, **1a** (34,8 mg, 0.20 mmol), *N*-methylaniline (42.8 mg, 0.40 mmol), and diisopropylethylamine (103.3 mg, 0.80 mmol) in anhydrous methanol (1.0 mL) were added under N_2, and the reaction flask was kept at 0 °C for 12 h. The solvent was concentrated under reduced pressure by an aspirator, and the residue was purified by the column chromatography (SiO_2) with hexane and ethyl acetate (97:3) as eluent to give *N*-methyl-*N*-(1-phenyl-2-propynyl)aniline (**2a**)[S2] as a pale yellow solid (42.5 mg, 0.19 mmol; 96% isolated yield). $[\alpha]_D^{22}$ = +10.7 (c 1.42, $CHCl_3$). The optical purity of **2a** was determined by HPLC analysis; DAICEL Chiralpak AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 5.64 min (minor) and 7.04 min (major), 85% ee.

Spectroscopic data and isolated yield of other products are as follows.



2b

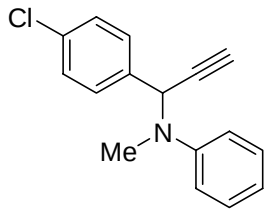
***N*-Methyl-*N*-[1-(4-methylphenyl)-2-propynyl]aniline (2b):** Yield 98%. A pale yellow oil. ^{1}H NMR δ 2.36 (s, 3H), 2.50 (d, *J* = 2.4 Hz, 1H), 2.69 (s, 3H), 5.77 (br, 1H), 6.85 (t, *J* = 7.8 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 7.8 Hz, 2H), 7.29 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR δ 21.1, 33.5, 56.1, 74.6, 80.2, 115.2, 118.8, 127.4, 129.10, 129.15, 134.8, 137.5, 150.1. HRMS Calcd for $C_{17}H_{17}N$ [M]: 235.1361. Found: 235.1366. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 5.7 min (minor) and 7.4 min (major), 81% ee.



2c

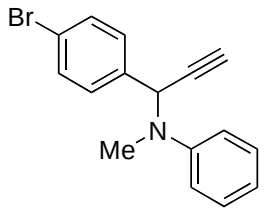
***N*-Methyl-*N*-[1-(4-methoxyphenyl)-2-propynyl]aniline (2c):** Yield 99%. A pale yellow oil. ^{1}H NMR δ 2.50 (d, *J* = 2.2 Hz, 1H), 2.68 (s, 3H), 3.81 (s, 3H), 5.75 (br, 1H), 6.82-6.92 (m, 3H), 6.99 (d, *J* = 7.8 Hz, 2H), 7.28 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.48 (d, *J* = 7.8 Hz, 2H).

^{13}C NMR δ 33.4, 55.3, 55.8, 74.6, 80.2, 113.7, 115.3, 118.9, 128.7, 129.1, 129.8, 150.1, 159.2. HRMS Calcd for $C_{17}H_{17}NO$ [M]: 251.1310. Found: 251.1302. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 9.0 min (minor) and 11.0 min (major), 82% ee.



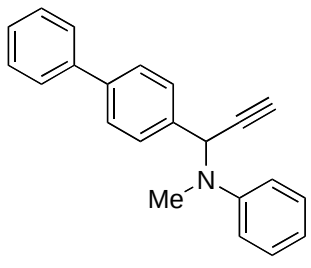
2d

***N*-Methyl-*N*-[1-(4-chlorophenyl)-2-propynyl]aniline (2d):** Yield 94%. A pale yellow oil. ^{1}H NMR δ 2.53 (d, *J* = 2.4 Hz, 1H), 2.68 (s, 3H), 5.73 (br, 1H), 6.87 (t, *J* = 7.8 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 2H), 7.25-7.36 (m, 4H), 7.52 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR δ 33.7, 56.0, 75.2, 79.5, 115.5, 119.3, 128.6, 128.9, 129.2, 133.7, 136.4, 149.9. HRMS Calcd for $C_{16}H_{14}ClN$ [M]: 255.0815. Found: 255.0815. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 6.5 min (minor) and 7.7 min (major), 85% ee.



2e

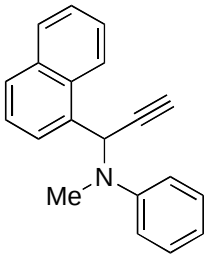
***N*-Methyl-*N*-[1-(4-bromophenyl)-2-propynyl]aniline (2e):** Yield 91%. A pale yellow oil. ^{1}H NMR δ 2.53 (d, *J* = 2.2 Hz, 1H), 2.69 (s, 3H), 5.72 (br, 1H), 6.87 (t, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 2H), 7.29 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.46 (d, *J* = 8.9 Hz, 2H), 7.50 (d, *J* = 8.9 Hz, 2H). ^{13}C NMR δ 33.7, 56.1, 75.3, 79.4, 115.5, 119.3, 121.8, 129.21, 129.25, 131.5, 137.0, 149.9. HRMS Calcd for $C_{16}H_{14}BrN$ [M]: 299.0310. Found: 299.0305. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 6.8 min (minor) and 8.0 min (major), 85% ee.



2f

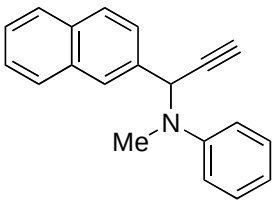
***N*-Methyl-*N*-(1-biphenyl-2-propynyl)aniline (2f):** Yield 99%. A pale yellow oil. ^{1}H NMR δ 2.53 (d, *J* = 2.4 Hz, 1H), 2.74 (s, 3H), 5.83 (br, 1H), 6.89 (t, *J* = 7.8 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 2H), 7.21-7.36 (m, 3H), 7.43 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.51-7.66 (m, 6H). ^{13}C NMR δ 33.7, 56.2, 74.9, 79.9, 115.3, 119.0, 127.08, 127.14, 127.4, 127.9, 128.8, 129.2, 136.9, 140.63, 140.74, 150.1. HRMS

Calcd for $C_{22}H_{19}N$ [M]: 297.1517. Found: 297.1524. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 8.4 min (minor) and 11.7 min (major), 84% ee.



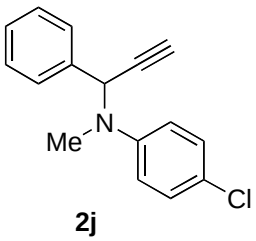
2g

***N*-Methyl-*N*-[1-(naphtalen-1-yl)-2-propynyl]aniline (2g):** Yield 99%. A white solid, 126.8-129.0 °C. ^{1}H NMR δ 2.56 (d, *J* = 2.2 Hz, 1H), 2.63 (s, 3H), 6.35 (br, 1H), 6.90 (t, *J* = 8.1 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.33-7.53 (m, 5H), 7.84-7.88 (m, 2H), 7.93 (d, *J* = 8.1 Hz, 1H), 8.04 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR δ 33.1, 53.3, 75.1, 80.1, 114.7, 118.7, 123.6, 125.0, 125.9, 126.6, 127.0, 128.7, 129.21, 129.35, 131.3, 132.7, 133.9, 149.5. HRMS Calcd for $C_{20}H_{17}N$ [M]: 271.1361. Found: 271.1350. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 6.7 min (minor) and 10.4 min (major), 85% ee.



2h

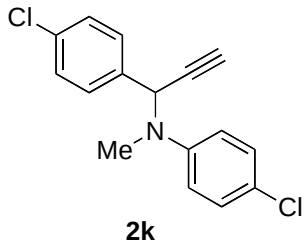
***N*-Methyl-*N*-[1-(Naphtalen-2-yl)-2-propynyl]aniline (2h):** Yield 99%. A white solid, 105.3-107.0 °C. ^{1}H NMR δ 2.60 (d, *J* = 2.4 Hz, 1H), 2.72 (s, 3H), 5.94 (br, 1H), 6.88 (t, *J* = 8.6 Hz, 1H), 7.05 (d, *J* = 8.6 Hz, 2H), 7.32 (dd, *J* = 8.6, 8.6 Hz, 2H), 7.47-7.51 (m, 2H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.81-7.84 (m, 3H), 8.11 (s, 1H). ^{13}C NMR δ 33.6, 56.5, 75.1, 79.8, 115.3, 119.0, 125.4, 126.14, 126.22, 126.48, 127.6, 128.12, 128.27, 129.2, 133.00, 133.16, 135.3, 150.1. HRMS Calcd for $C_{20}H_{17}N$ [M]: 271.1361. Found: 271.1350. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 8.1 min (minor) and 9.6 min (major), 83% ee.



2j

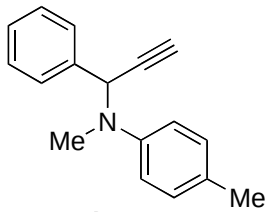
4-Chloro-*N*-methyl-*N*-(1-phenyl-2-propynyl)aniline (2j): Yield 96%. A pale yellow oil. ^{1}H NMR δ 2.53 (d, *J* = 2.4 Hz, 1H), 2.69 (s, 3H), 5.72 (br, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.32-7.38 (m, 3H), 7.55 (d, *J* = 8.6 Hz, 2H). ^{13}C NMR δ 33.9, 56.6, 75.0, 79.6, 116.6, 123.8, 127.4, 128.0, 128.5, 129.0, 137.4, 148.6. HRMS

Calcd for $C_{16}H_{14}ClN$ [M]: 255.0815. Found: 255.0821. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 7.4 min (minor) and 10.6 min (major), 89% ee.



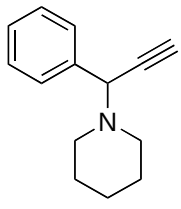
2k

4-Chloro-*N*-methyl-*N*-[1-(4-chlorophenyl)-2-propynyl]aniline (2k): Yield 92%. A pale yellow oil. ^{1}H NMR δ 2.55 (d, *J* = 2.4 Hz, 1H), 2.67 (s, 3H), 5.66 (br, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR δ 34.0, 56.3, 75.5, 79.1, 116.8, 124.2, 128.66, 128.84, 129.03, 133.9, 136.0, 148.5. HRMS Calcd for $C_{16}H_{13}Cl_2N$ [M]: 289.0425. Found: 289.0416. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 9.0 min (minor) and 11.4 min (major), 89% ee.



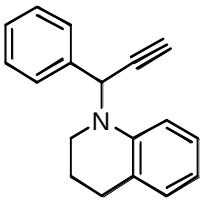
2l

4-Methyl-*N*-methyl-*N*-(1-phenyl-2-propynyl)aniline (2l): Yield 97%. A pale yellow oil. ^{1}H NMR δ 2.29 (s, 3H), 2.51 (d, *J* = 2.2 Hz, 1H), 2.66 (s, 3H), 5.73 (br, 1H), 6.93 (d, *J* = 8.6 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 7.31-7.40 (m, 3H), 7.59 (d, *J* = 8.6 Hz, 2H). ^{13}C NMR δ 20.4, 33.8, 57.1, 74.9, 79.9, 115.9, 127.6, 127.7, 128.4, 128.5, 129.7 137.9, 148.1. HRMS Calcd for $C_{17}H_{17}N$ [M]: 235.1361. Found: 235.1368. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 5.7 min (minor) and 8.0 min (major), 82% ee.



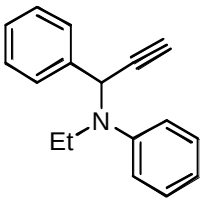
2m

1-(1-Phenyl-2-propynyl)piperidine (2m): Yield 64%. A pale yellow oil. ^{1}H NMR δ 1.40-1.64 (m, 6H), 2.47 (t, *J* = 8.6 Hz, 4H), 2.52 (d, *J* = 2.4 Hz, 1H), 4.58 (d, *J* = 2.4 Hz, 1H), 7.25-7.37 (m, 3H), 7.57 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR δ 24.4, 26.1, 50.4, 61.7, 75.3, 80.0, 127.5, 128.0, 128.3, 138.1. HRMS Calcd for $C_{14}H_{17}N$ [M]: 199.1361. Found: 199.1355. The optical purity was determined by HPLC analysis; Daicel Chiralcel OJ-H, hexane/^{i}PrOH = 95/5, flow rate = 0.5 mL/min, λ = 254 nm, retention time; 8.8 min (major) and 11.4 min (minor), 80% ee.



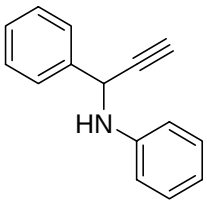
2n

1,2,3,4-Tetrahydro-1-(1-phenyl-2-propynyl)quinoline (2n): Yield 97%. A pale yellow oil. ^{1}H NMR δ 1.89 (tt, *J* = 6.2, 6.2 Hz, 2H), 2.47 (d, *J* = 2.4 Hz, 1H), 2.69-2.88 (m, 2H), 2.95 (dt, *J* = 11.1, 5.4 Hz, 1H), 3.19 (dt, *J* = 11.1, 5.4 Hz, 1H), 5.87 (br, 1H), 6.69 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.87 (d, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 7.3 Hz, 1H), 7.09 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.28-7.40 (m, 3H), 7.58 (d, *J* = 7.3 Hz, 2H). ^{13}C NMR δ 22.3, 28.0, 44.0, 53.7, 74.2, 80.4, 111.9, 117.5, 124.6, 127.0, 127.4, 127.7, 128.5, 129.3, 137.6, 145.1. HRMS Calcd for $C_{18}H_{17}N$ [M]: 247.1361. Found: 247.1369. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 0.5 mL/min, λ = 254 nm, retention time; 10.5 min (minor) and 11.7 min (major), 81% ee.



2o

***N*-Ethyl-*N*-(1-phenyl-2-propynyl)aniline (2o):** Yield 95%. A pale yellow oil. ^{1}H NMR δ 1.07 (t, *J* = 7.3 Hz, 3H), 2.50 (d, *J* = 2.4 Hz, 1H), 3.20-3.37 (m, 2H), 5.68 (br, 1H), 6.81 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 2H), 7.21-7.38 (m, 5H), 7.58 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR δ 13.4, 42.3, 56.0, 74.4, 81.2, 115.9, 118.6, 127.54, 127.67, 128.4, 129.0, 138.2, 148.1. HRMS Calcd for $C_{17}H_{17}N$ [M]: 235.1361. Found: 235.1366. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 0.5 mL/min, λ = 254 nm, retention time; 9.8 min (minor) and 11.0 min (major), 83% ee.



2p

***N*-(1-phenyl-2-propynyl)aniline (2p):**[S2] Yield 90%. A pale yellow oil. The optical purity was determined by HPLC analysis; Daicel Chiralcel AD, hexane/^{i}PrOH = 97/3, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 18.8 min (major) and 26.5 min (minor), 53% ee.

Preparation of (*S*)-*N*,*N*-Methylphenyl-(1-phenylpropyl)amine (3a). In a 20 mL round-bottomed flask was placed (*S*)-*N*-phenyl(1-phenylpropyl)amine[S3] (0.113 g, 0.53 mmol) under N_2. Anhydrous tetrahydrofuran (1.5 mL) was added, and the solution was cooled at –78 ºC. A solution of *n*-butyllithium (1.57 M, 0.34 mL, 0.53 mmol) was added dropwise and the reaction mixture was stirred at –78 ºC for 30 min. Iodomethane (33 μL, 053 mmol) was added dropwise and then the reaction mixture was allowed to slowly warm up to room temperature over 3 h. The solvent was concentrated under reduced pressure, and then the residue was filtered through a short column (SiO_2, eluent: hexane/AcOEt = 5/1). The crude mixture was purified by the preparative thin layer chromatography (eluent: hexane/AcOEt = 10/1) to give (*S*)-*N*,*N*-methylphenyl-(1-phenylpropyl)amine[S4] (**3a**) as a colorless oil (79.0 mg, 0.33 mmol, 62% isolated yield). ^{1}H NMR δ 0.98 (t, *J* = 7.3 Hz, 3H), 1.91-2.14 (m, 2H), 2.69 (s, 3H), 4.85 (q, *J* = 5.9, 9.4 Hz, 1H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 2H), 7.19-7.32 (m, 7H). ^{13}C NMR δ 11.7, 24.9, 31.5, 62.9, 112.8, 116.4, 126.8, 127.1, 128.3, 129.1, 141.7, 150.9. $[\alpha]_D^{22}$ = -246.3 (c 1.11, $CHCl_3$). The optical purity was determined by HPLC analysis; Daicel Chiralcel OD, hexane/^{i}PrOH = 49/1, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 8.0 min (major) and 10.5 min (minor), 95% ee.

Determination of the absolute configuration of 1-phenyl-2-propynyl acetate (1a). In a 20 mL round-bottomed flask was placed 10% Pd/C (34 mg). Anhydrous ethanol (2 mL) and **1a** (34.0 mg, 0.15 mmol) were added, and then the reaction mixture was magnetically stirred at room temperature for 4 h under H_2 (1 atm). The reaction mixture was filtered over celite cake. The filtrated solution was concentrated under reduced pressure by an aspirator, and then the residue was purified by column chromatography (SiO_2) with hexane and AcOEt (97:3) as eluent to give *N*,*N*-methylphenyl-(1-phenylpropyl)amine (**3a**) as a colorless oil (18.0 mg, 0.080 mmol, 53% yield. The optical purity was determined by HPLC analysis; Daicel Chiralcel OD, hexane/^{i}PrOH = 49/1, flow rate = 1.0 mL/min, λ = 254 nm, retention time; 8.0 min (major) and 10.5 min (minor), 83% ee. The hydrogenated product **3a** was revealed to have an *S* absolute configuration.

References

[S1] R. J. Detz, M. M. E. Delville, H. Hiemstra, J. H. van Maarseveen, *Angew. Chem. Int. Ed.* **2008**, in press.

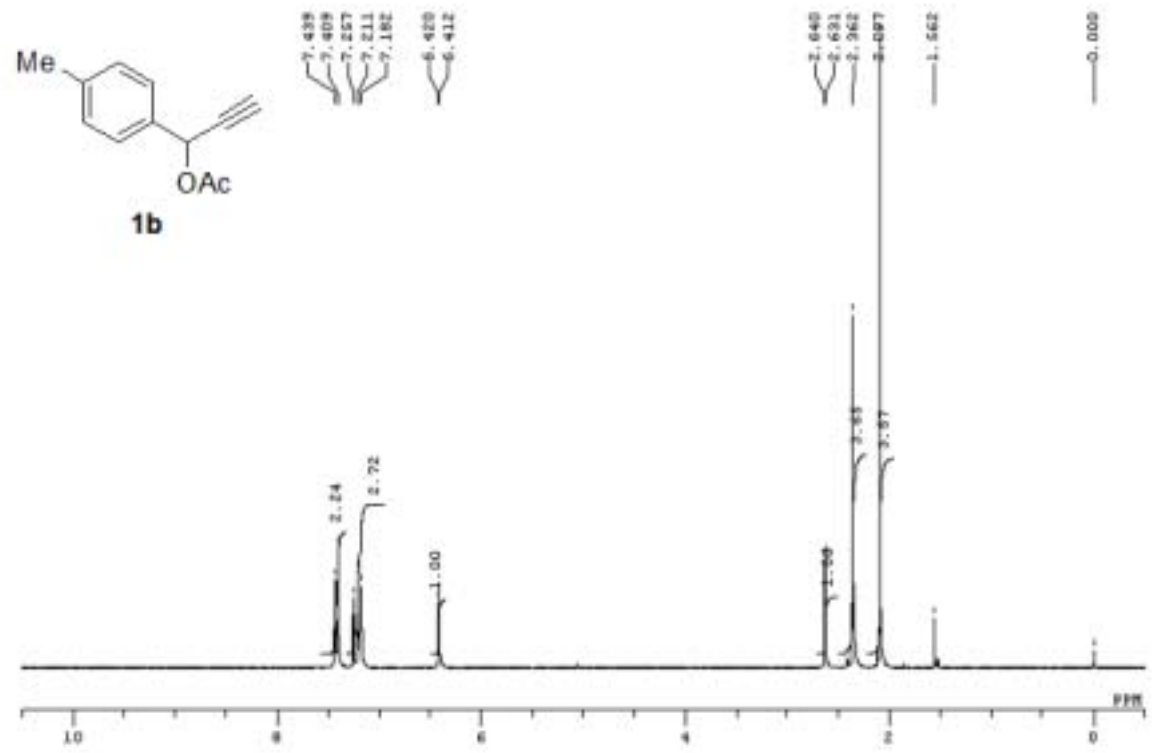
[S2] Y. Nishibayashi, M. D. Milton, Y. Inada, M. Yoshikawa, I. Wakiji, M. Hidai, S. Uemura, *Chem. Eur. J.* **2005**, *11*, 1433.

[S3] D. Pei, Z. Wang, S. Wei, Y. Zhang, J. Sun, *Org. Lett.* **2006**, *8*, 5913.

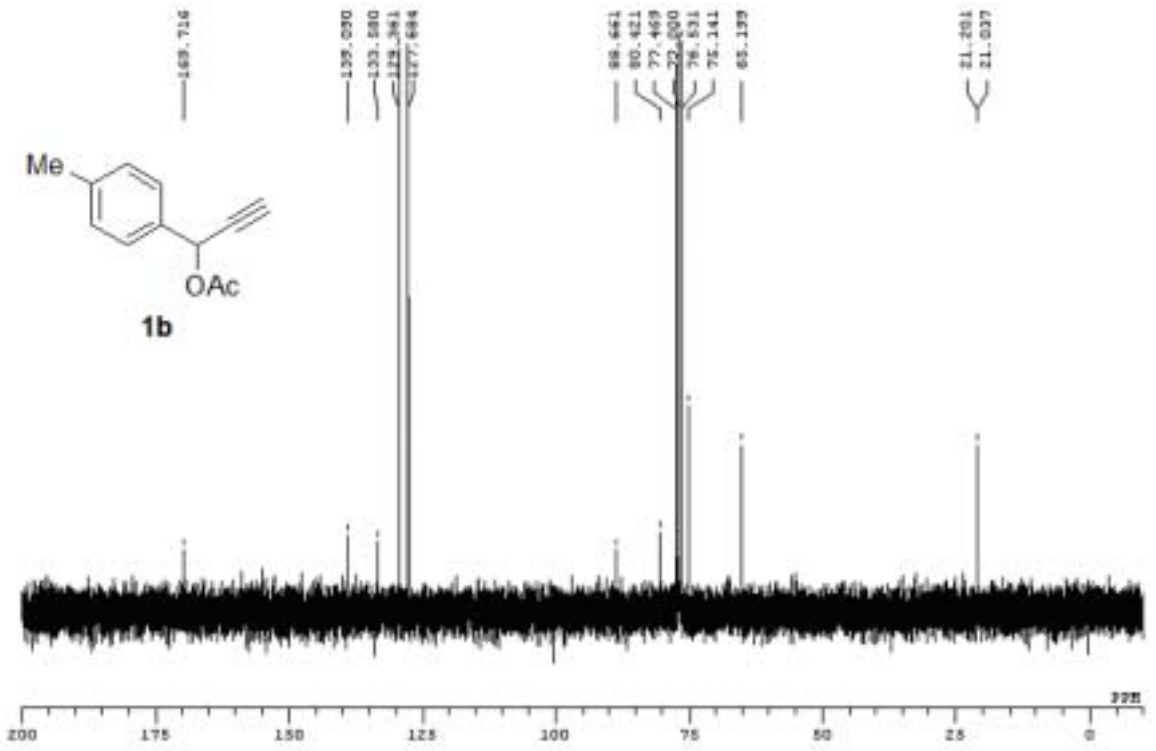
[S4] J. J. Eisch, S. K. Dua, C. A. Kovacs, *J. Org. Chem.* **1987**, *52*, 4437.

^{1}H and ^{13}C NMR spectra of propargylic acetates (**1b** and **1e**) and propargylic amines (**2b**-**2h** and **2j**-**2o**) are shown in the following pages.

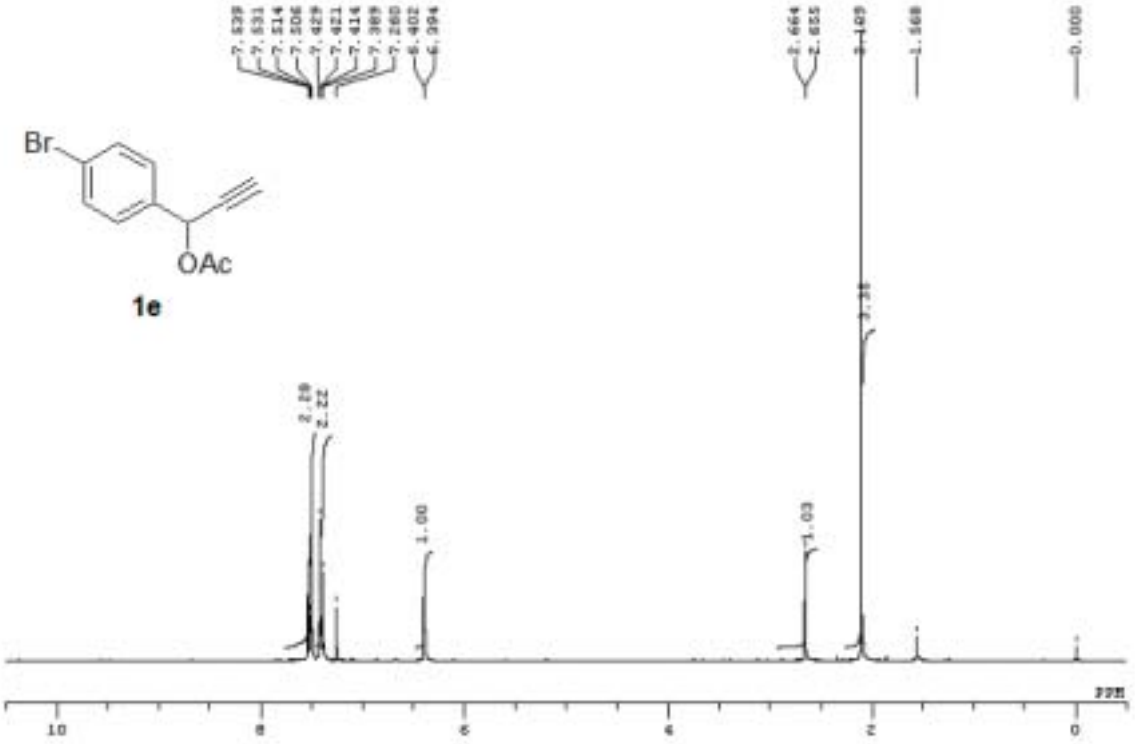
^{1}H NMR (**1b**)



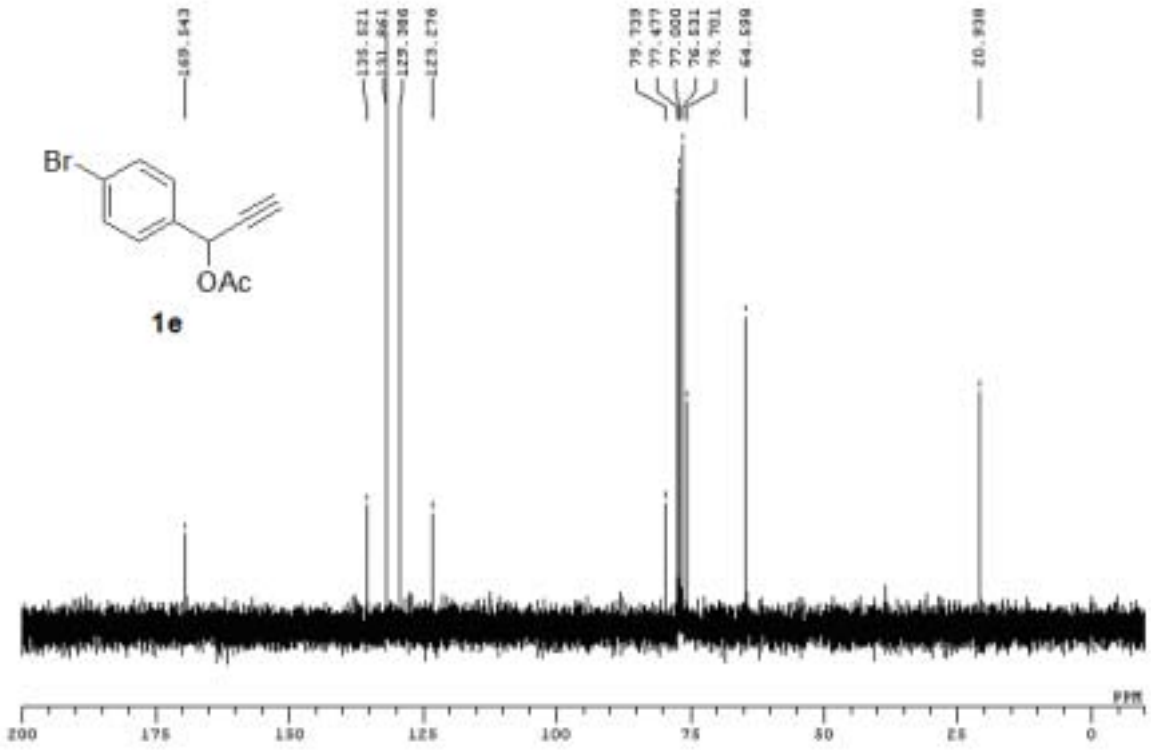
^{13}C NMR (**1b**)



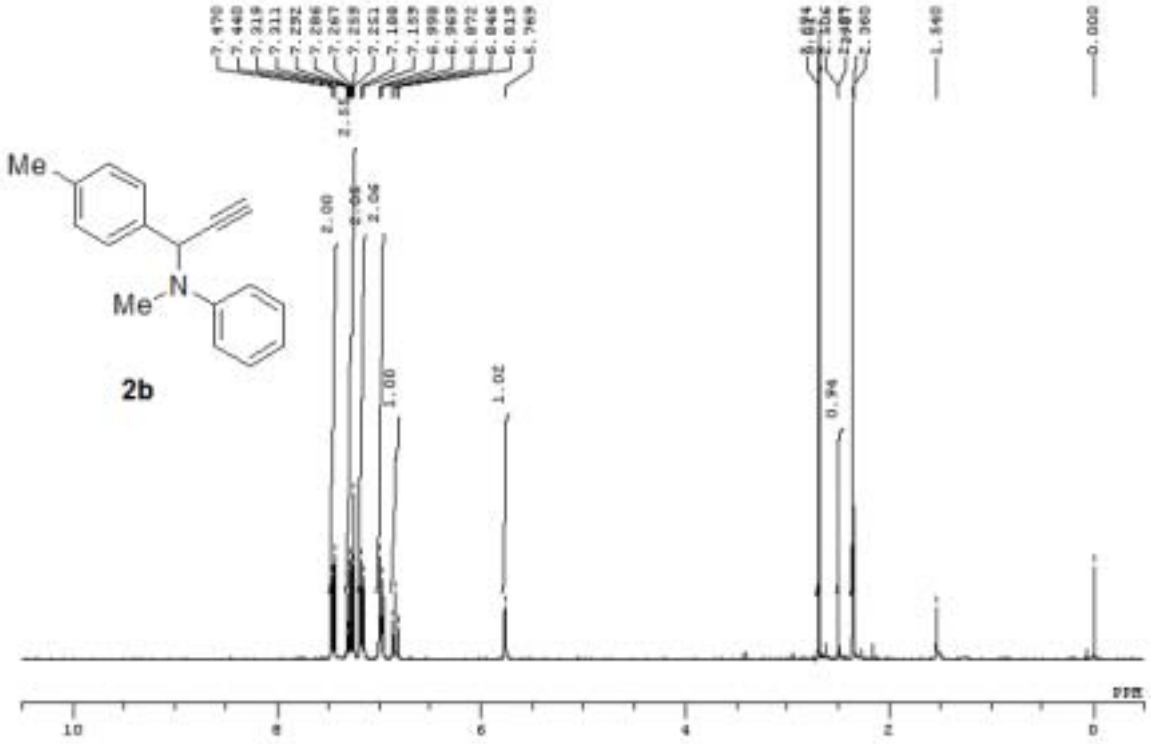
^{1}H NMR (**1e**)



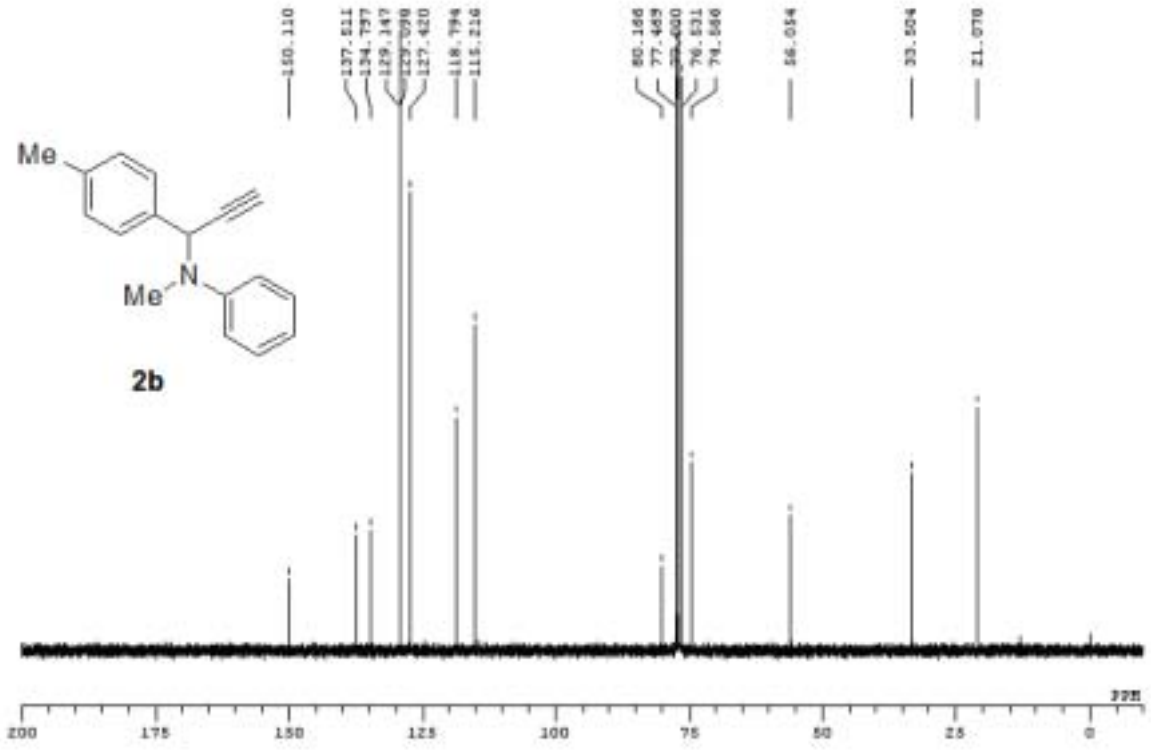
^{13}C NMR (**1e**)



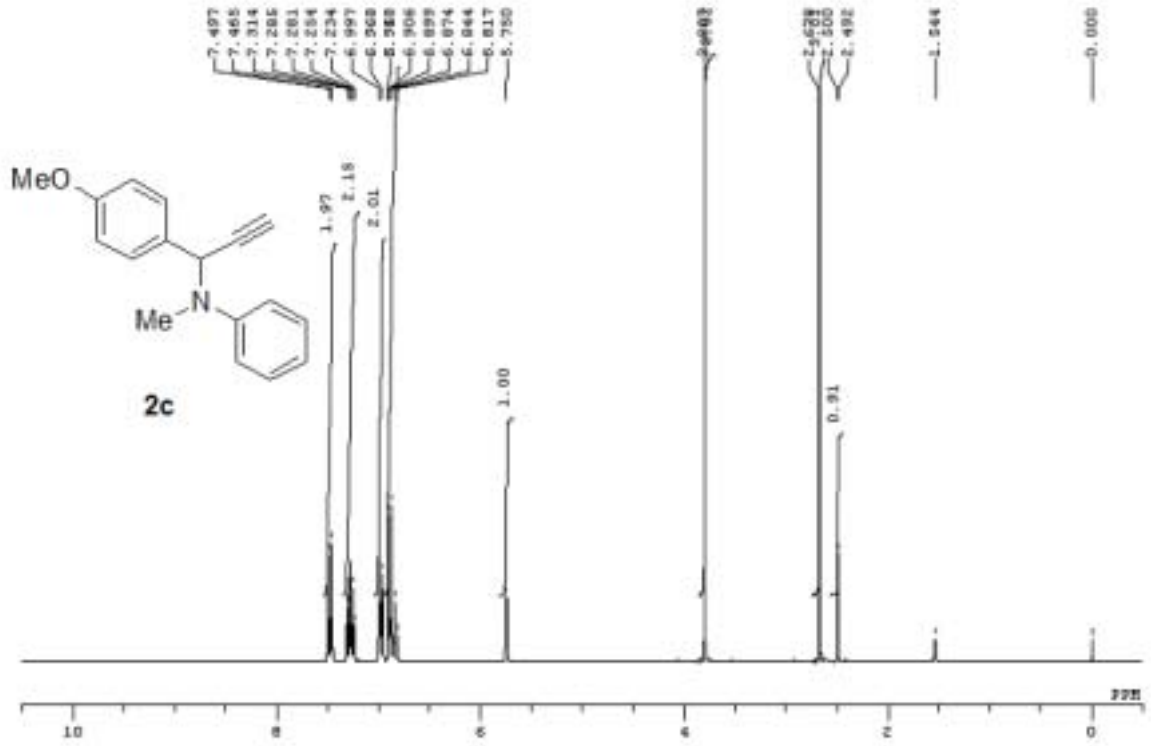
^{1}H NMR (**2b**)



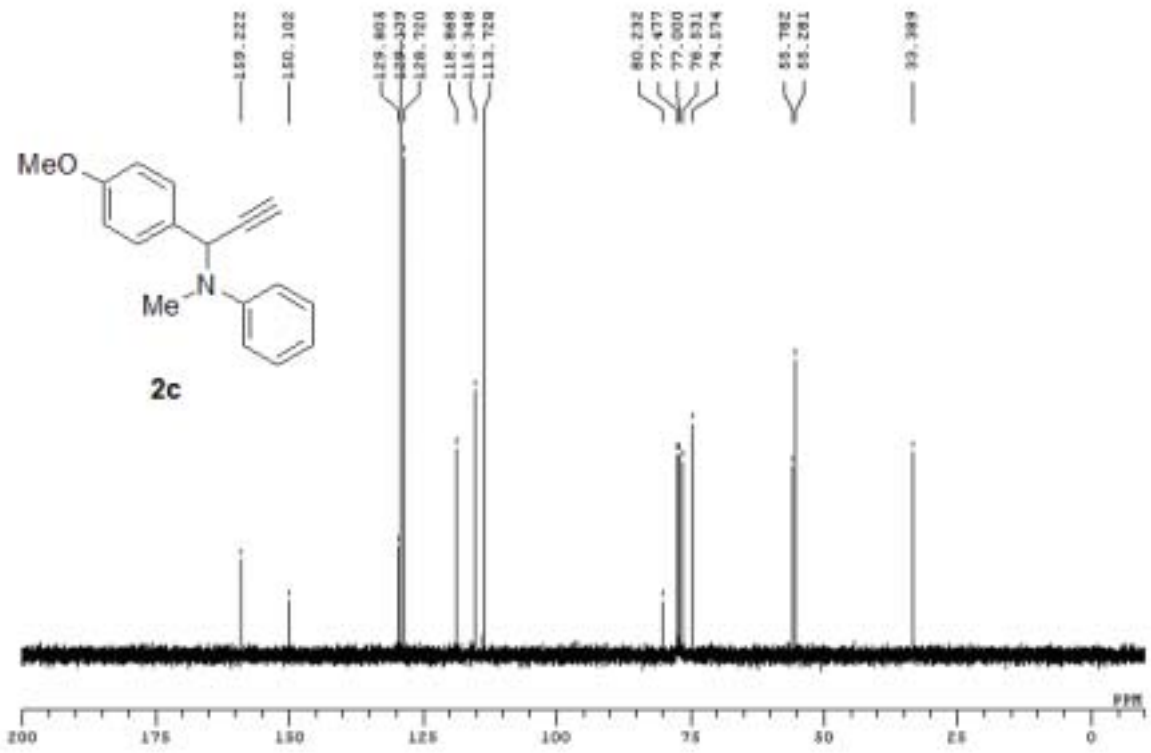
^{13}C NMR (**2b**)



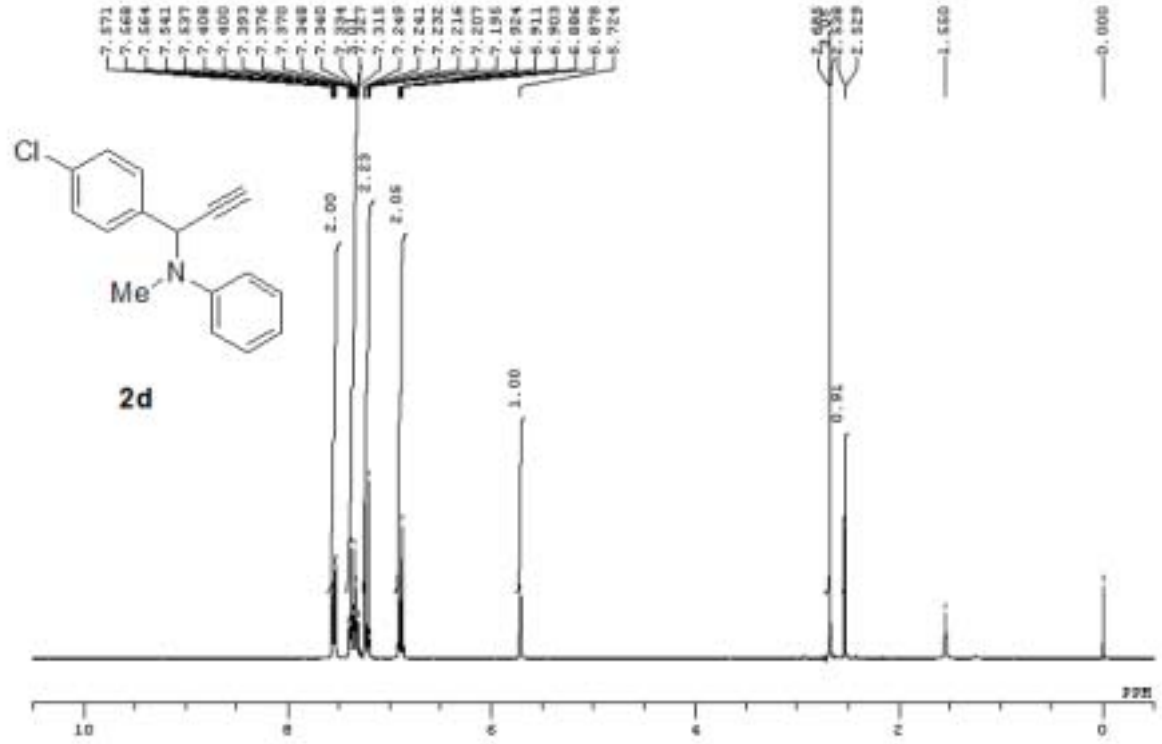
^{1}H NMR (**2c**)



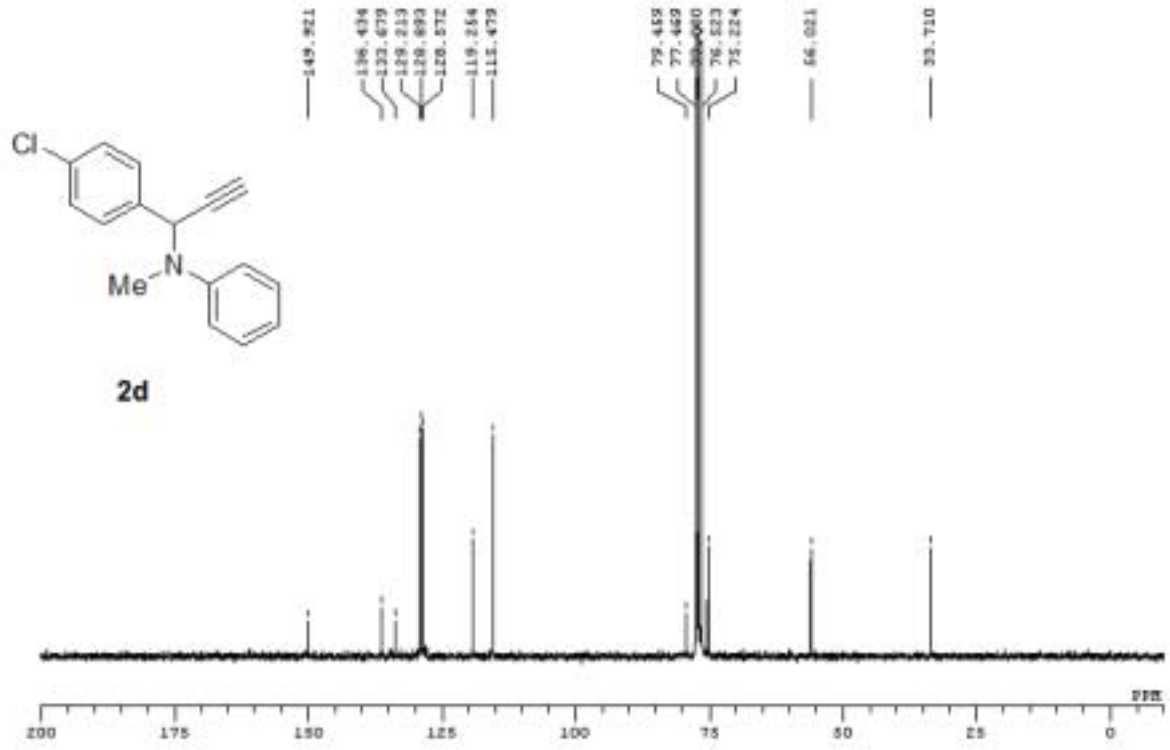
^{13}C NMR (**2c**)



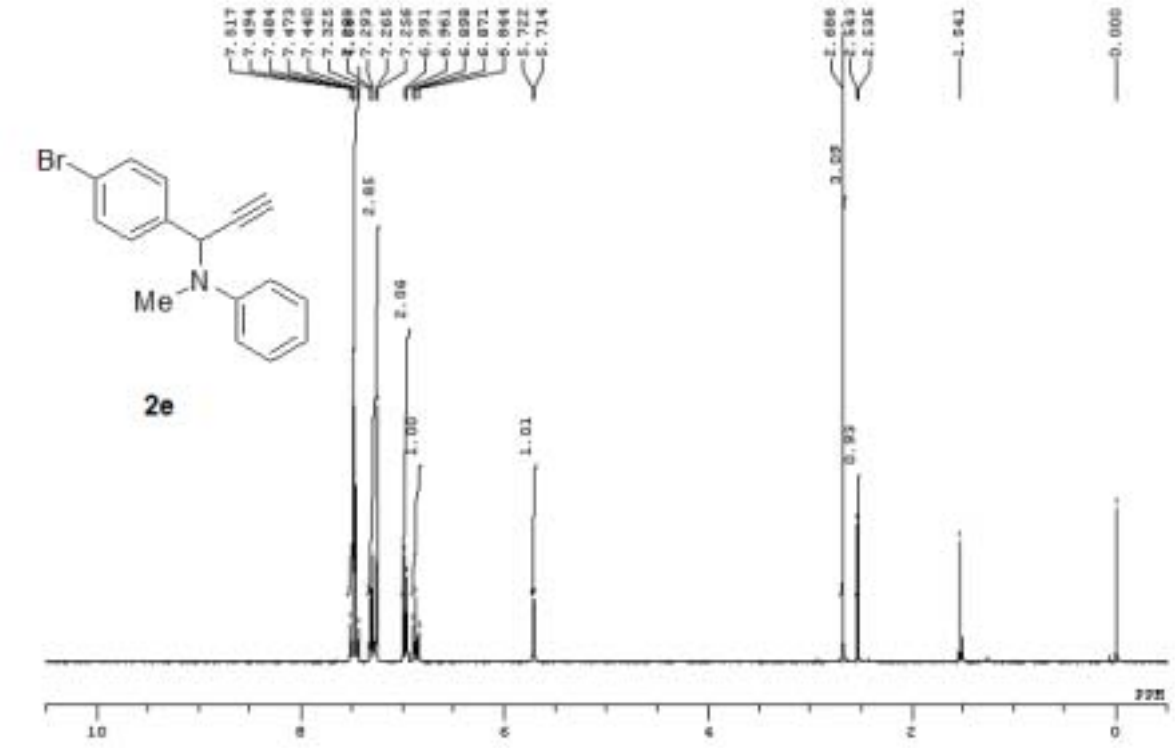
^{1}H NMR (**2d**)



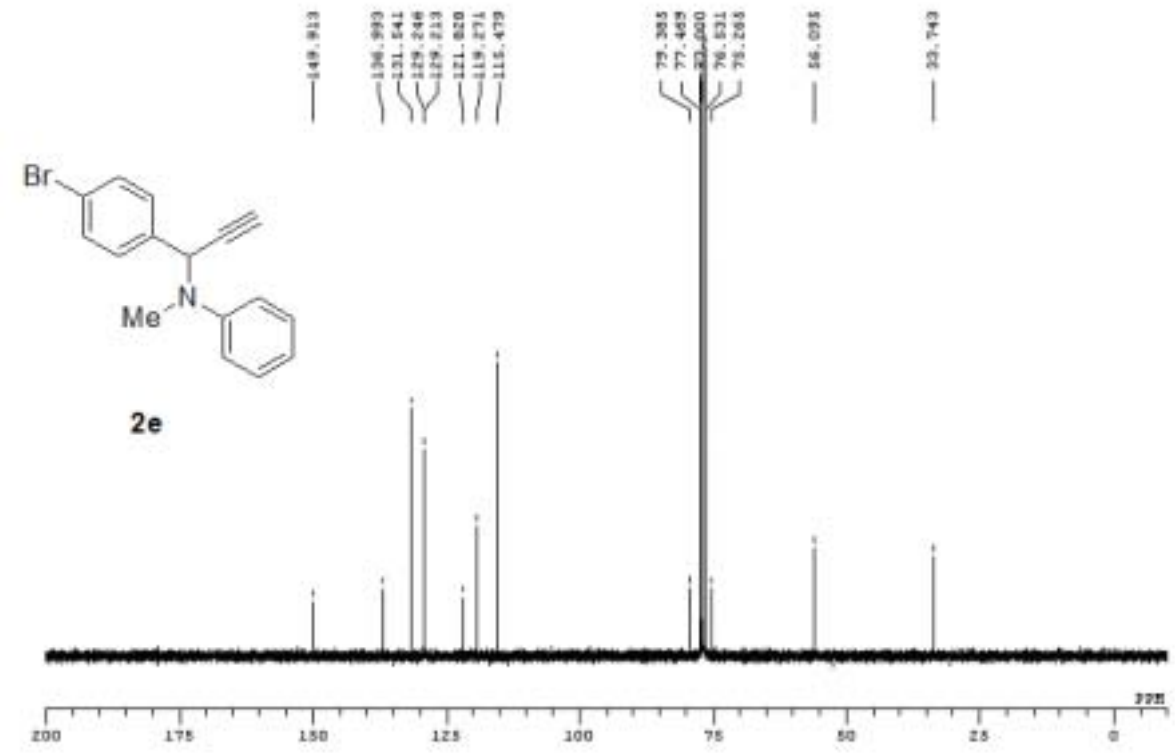
^{13}C NMR (**2d**)



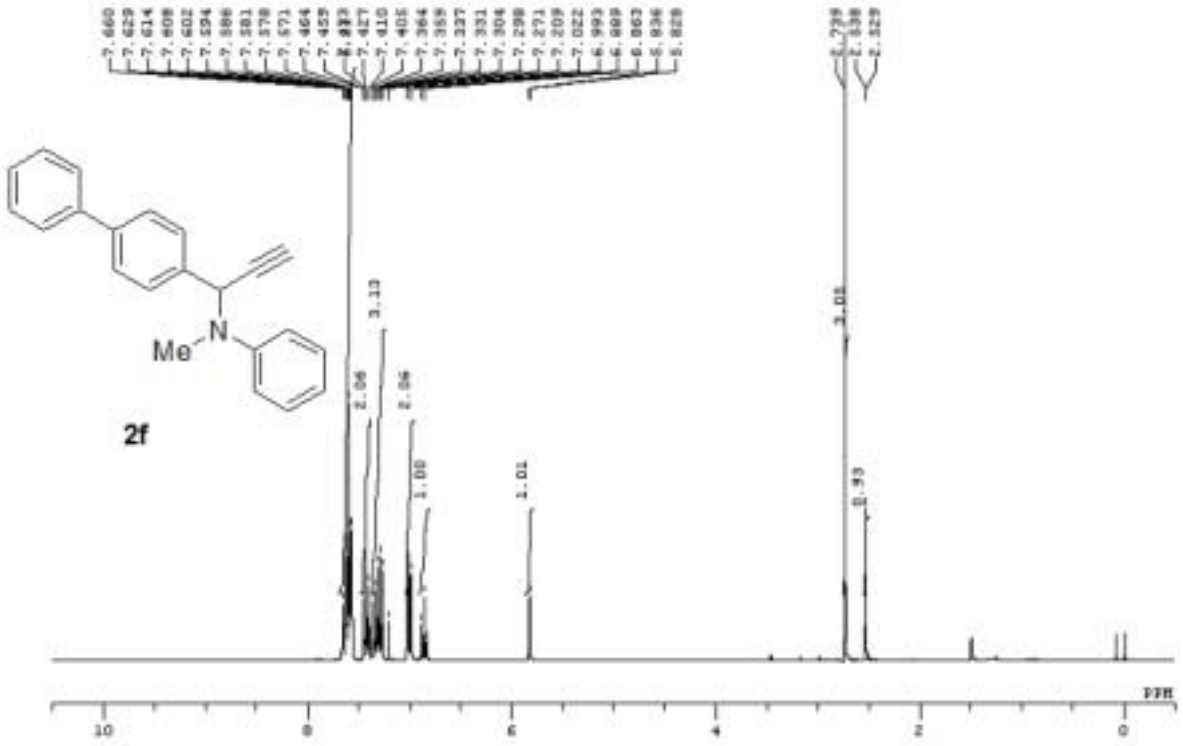
^{1}H NMR (**2e**)



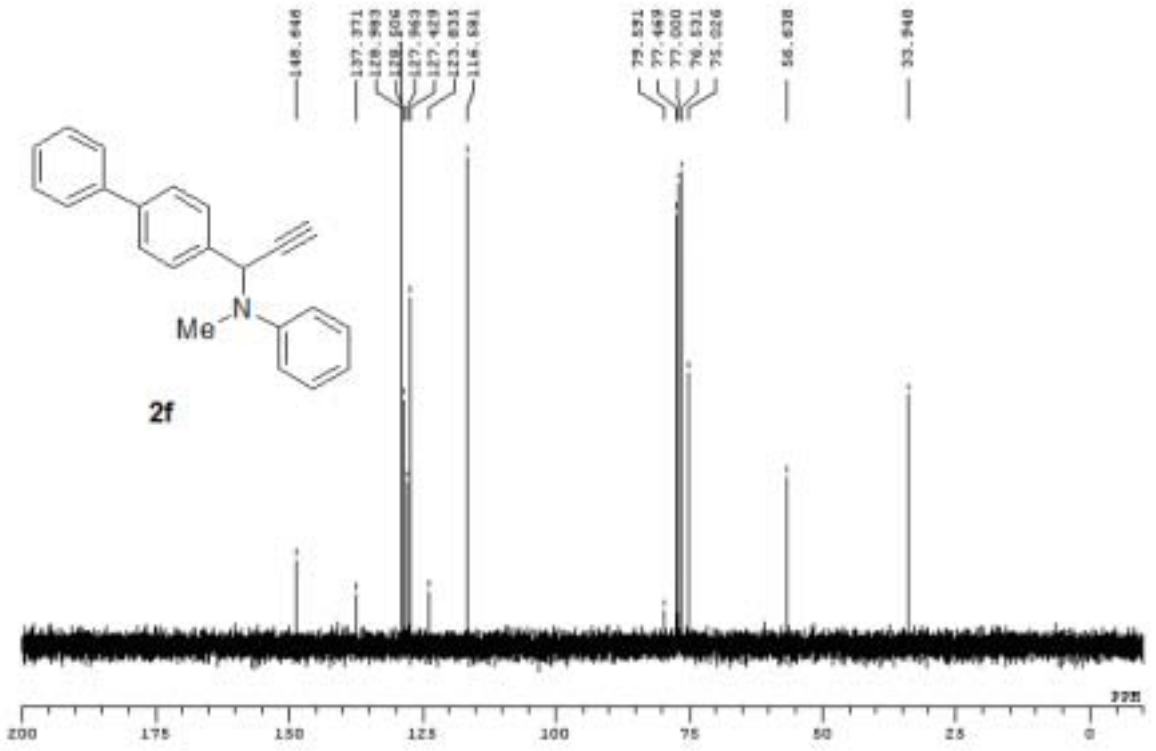
^{13}C NMR (**2e**)



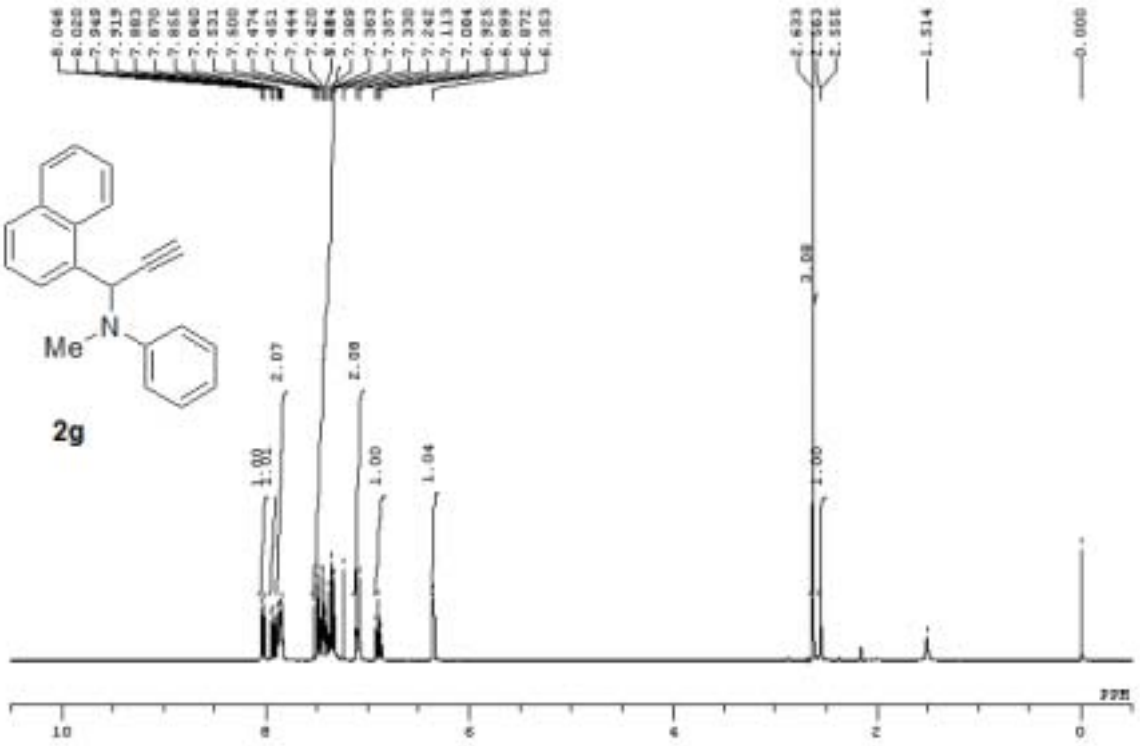
^{1}H NMR (**2f**)



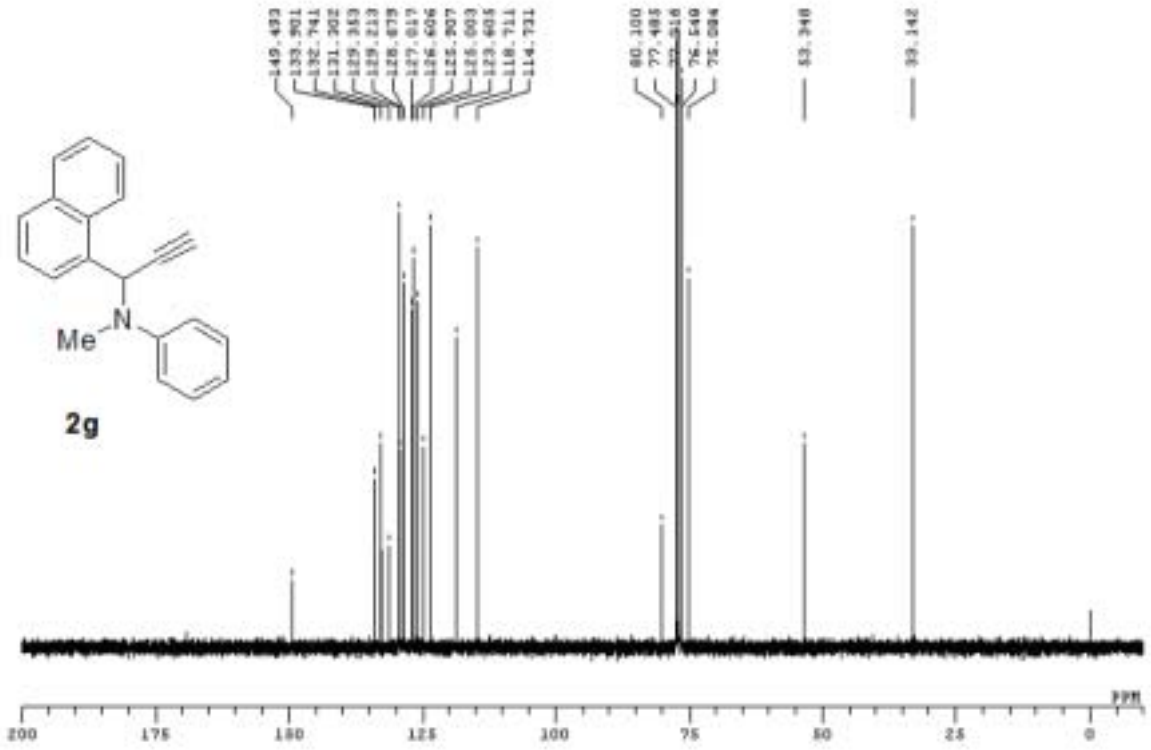
^{13}C NMR (**2f**)



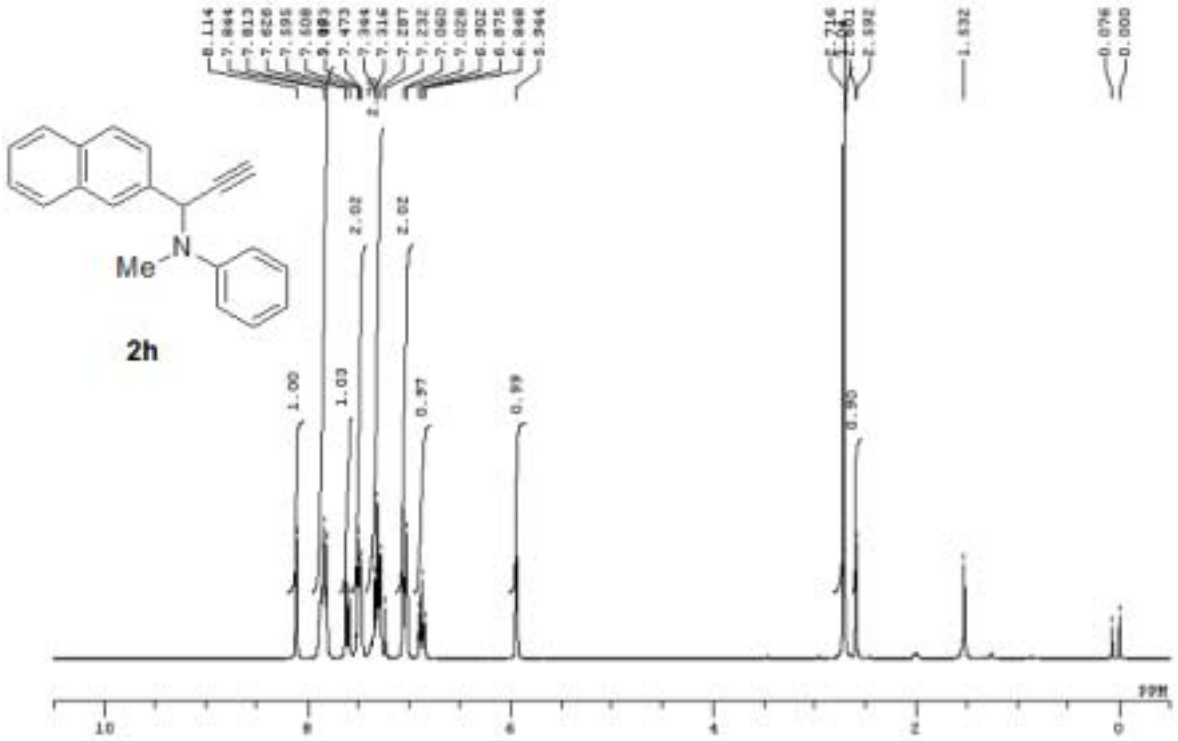
^{1}H NMR (**2g**)



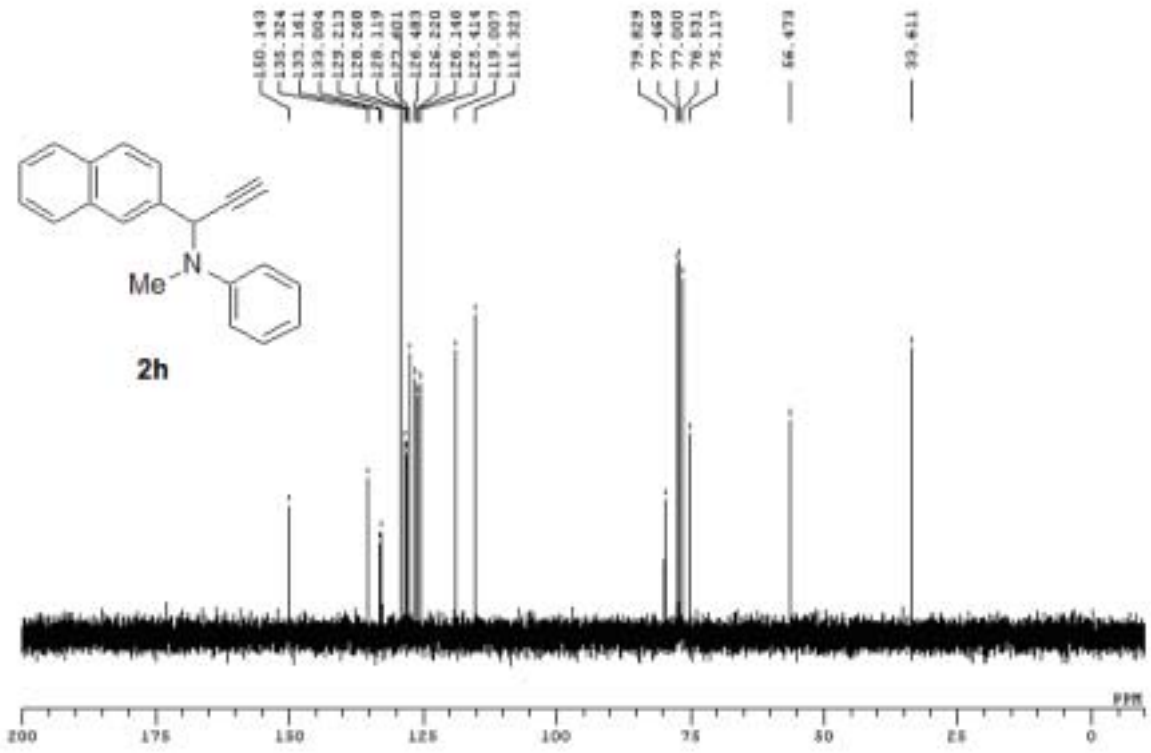
^{13}C NMR (**2g**)



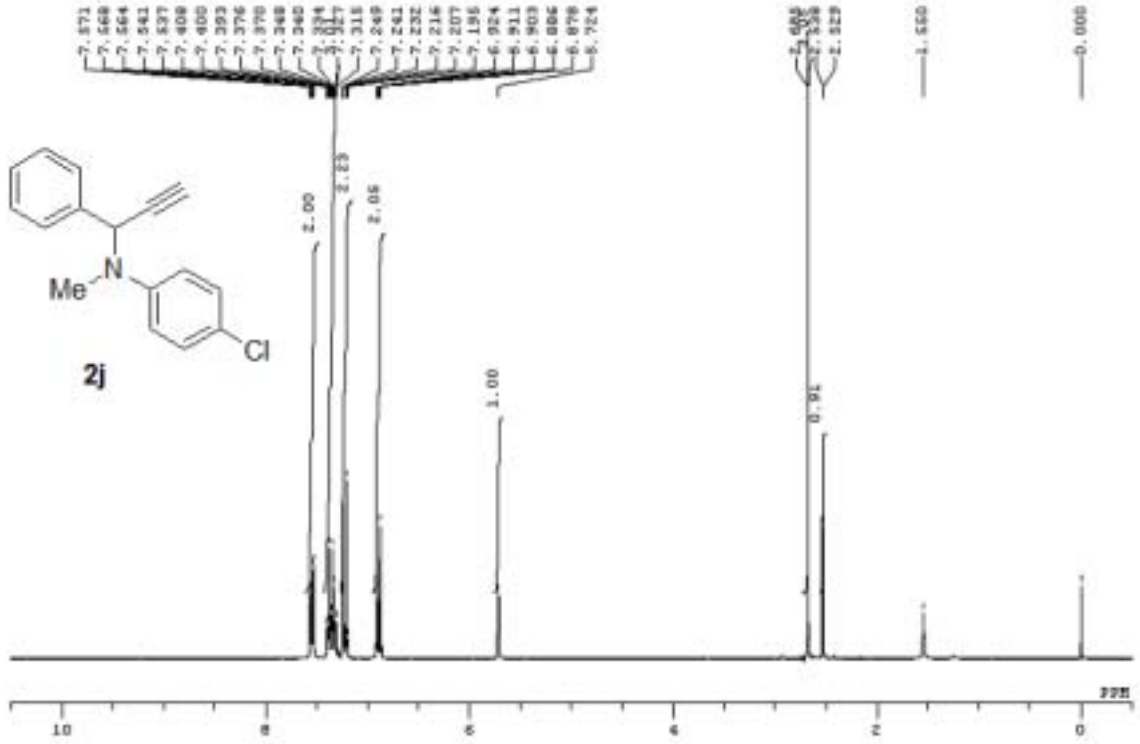
^{1}H NMR (**2h**)



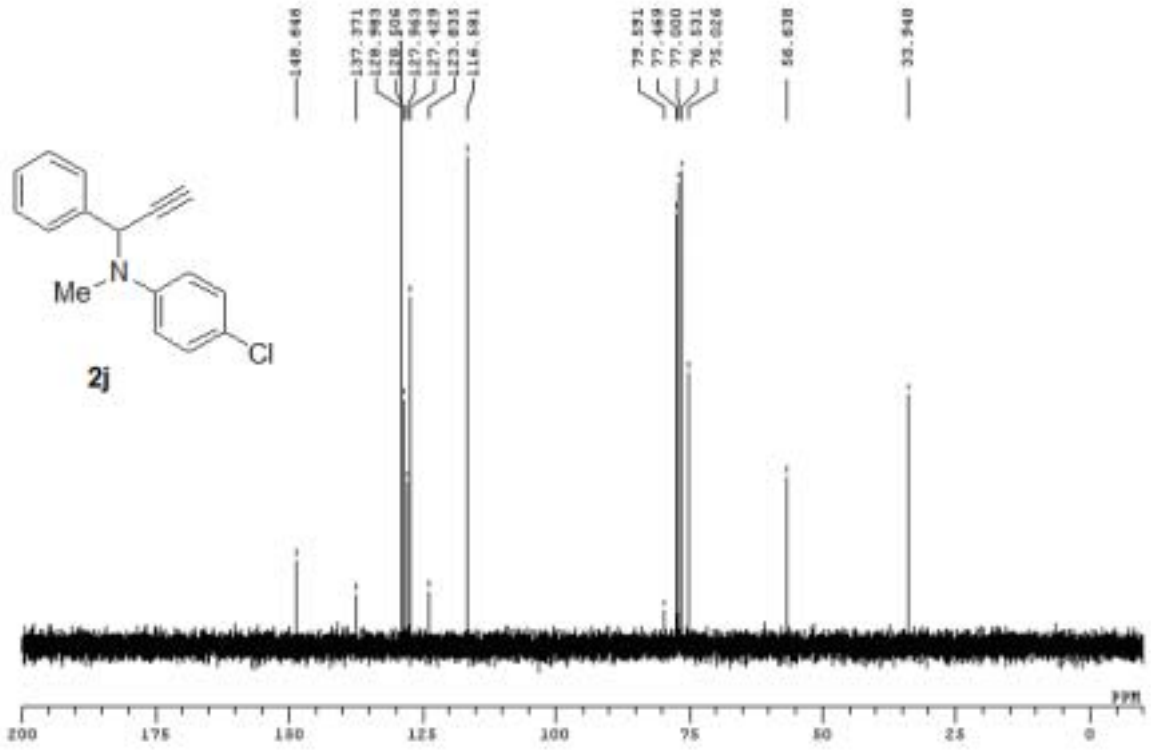
^{13}C NMR (**2h**)



^{1}H NMR (**2j**)



^{13}C NMR (**2j**)



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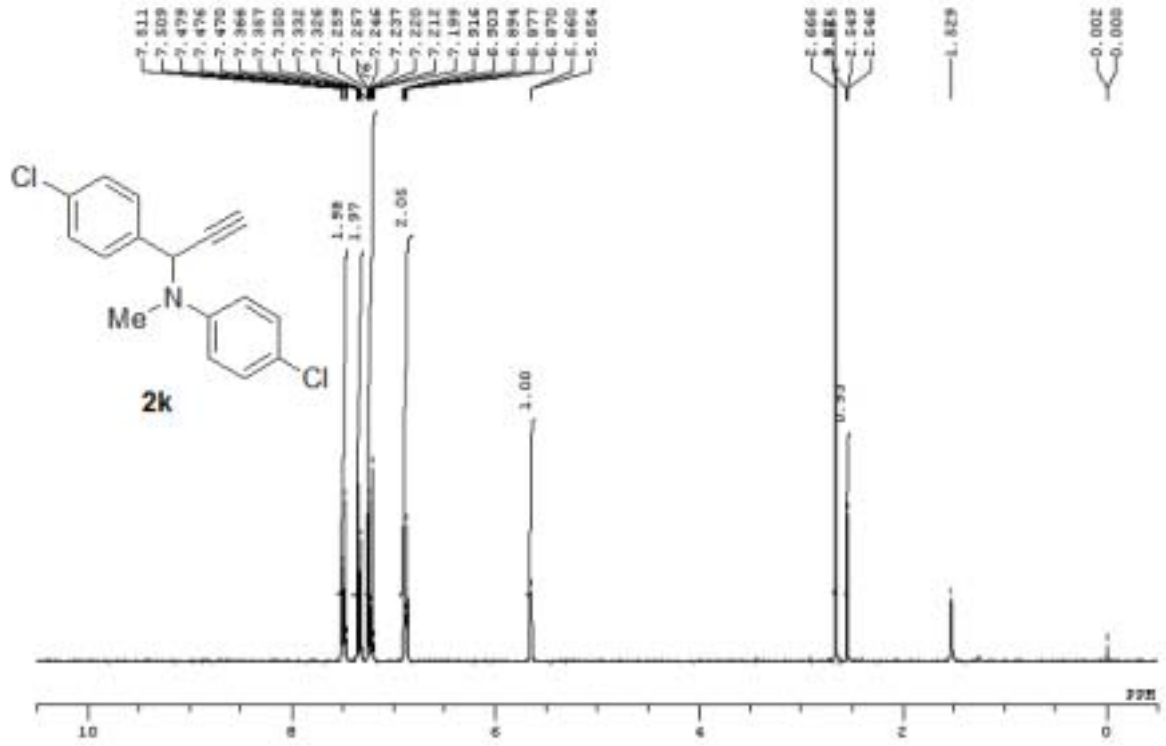
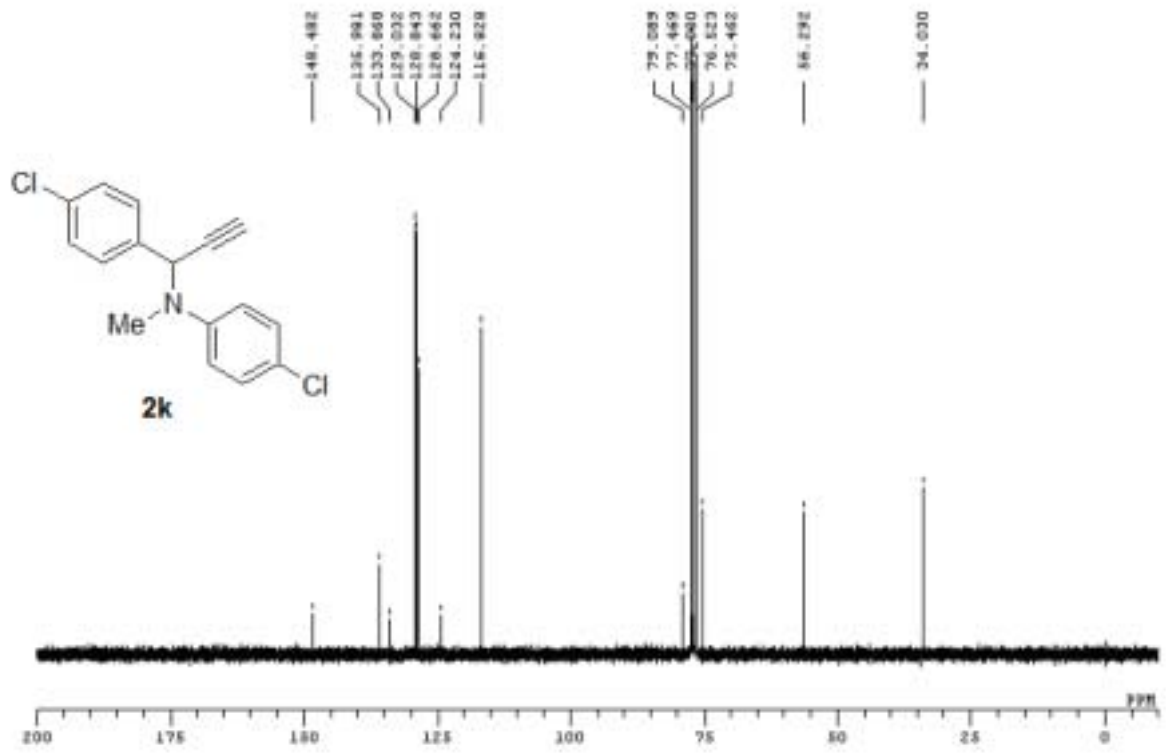


^{13}C NMR (**2k**)



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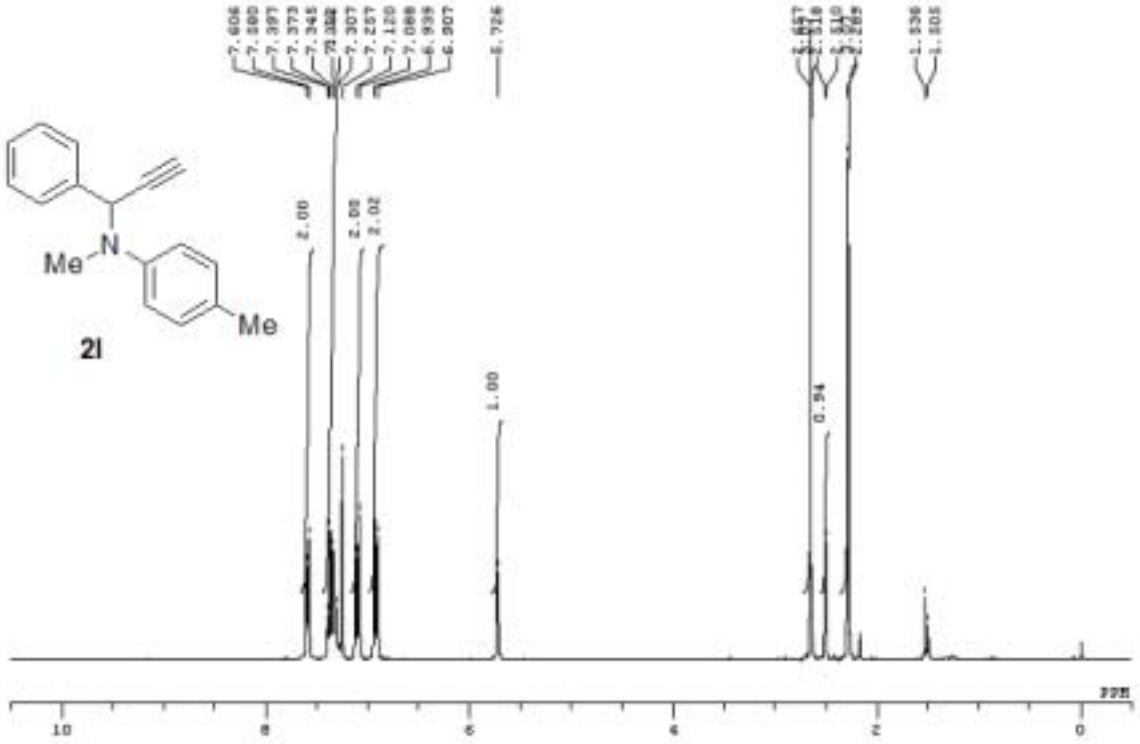
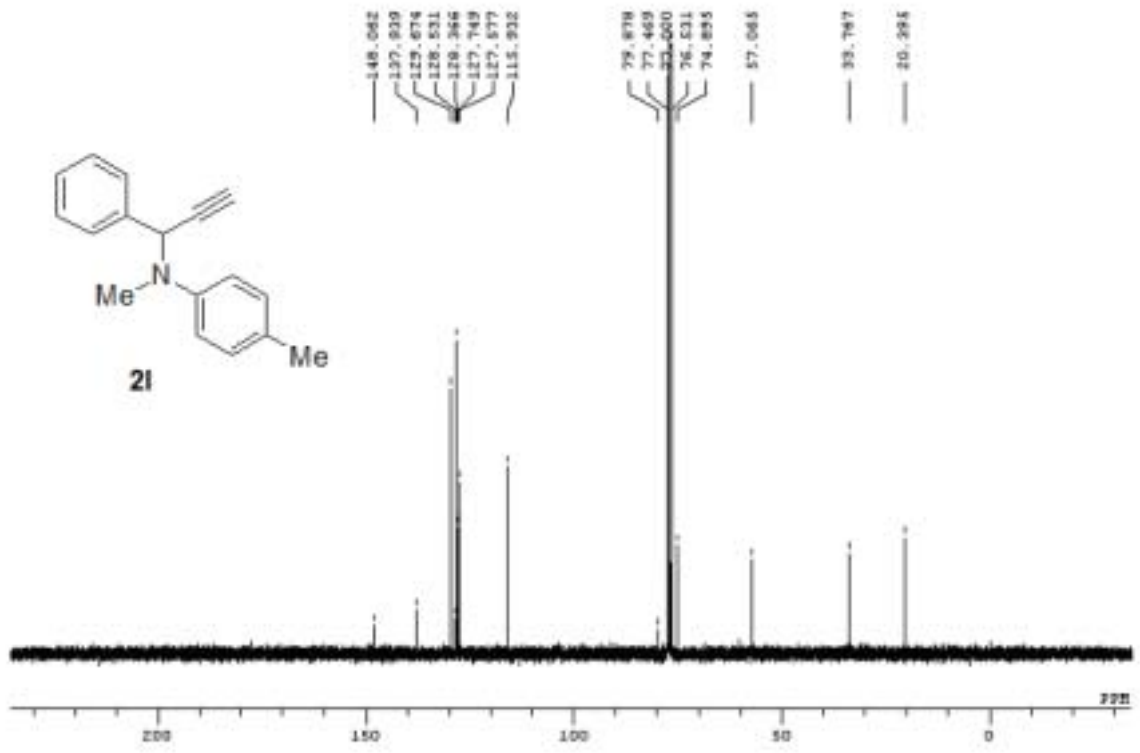


^{13}C NMR (**2l**)



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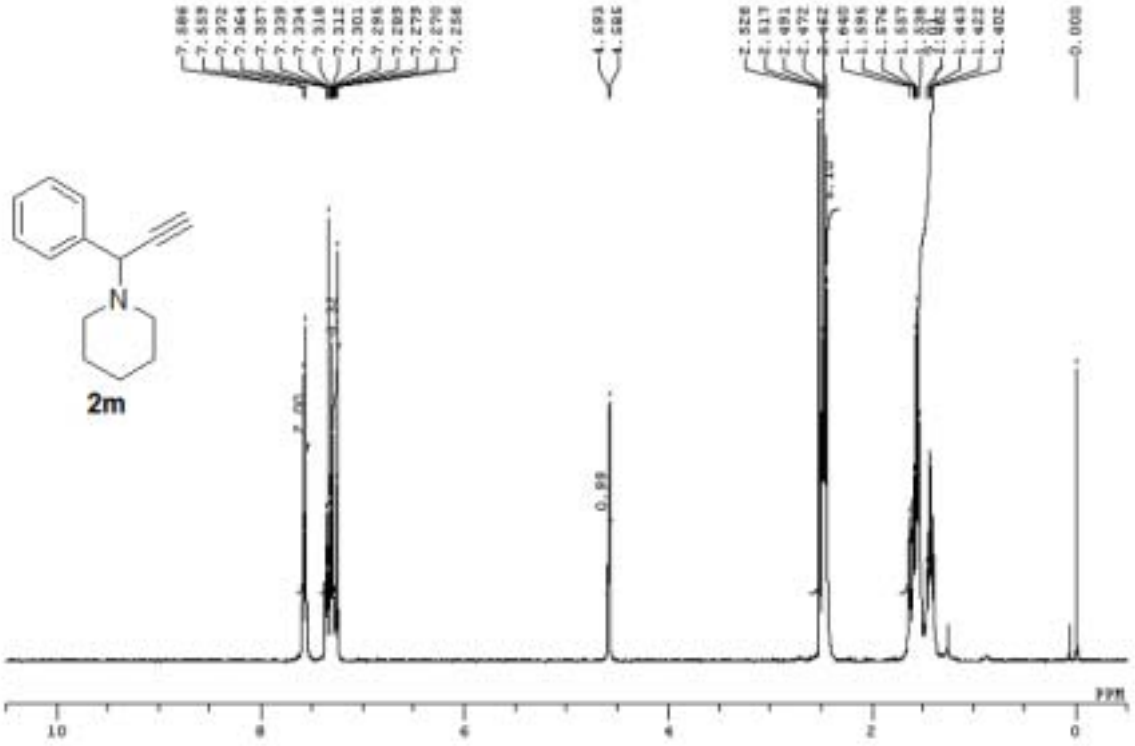
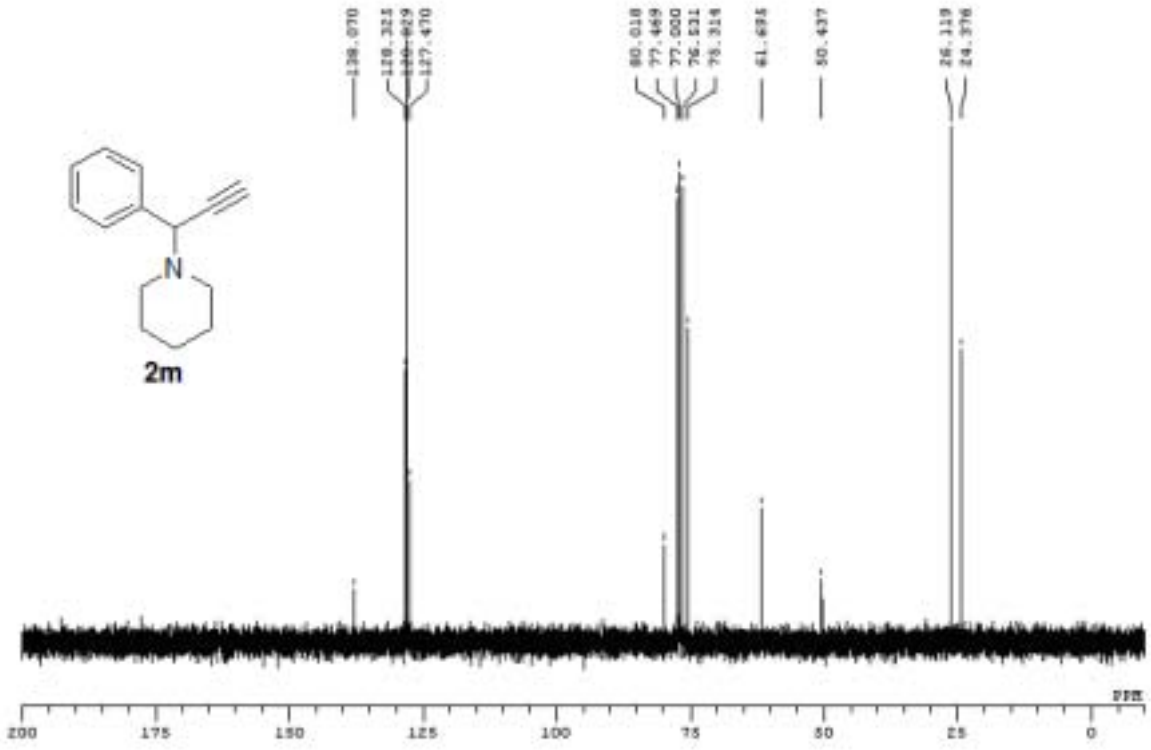


^{13}C NMR (**2m**)



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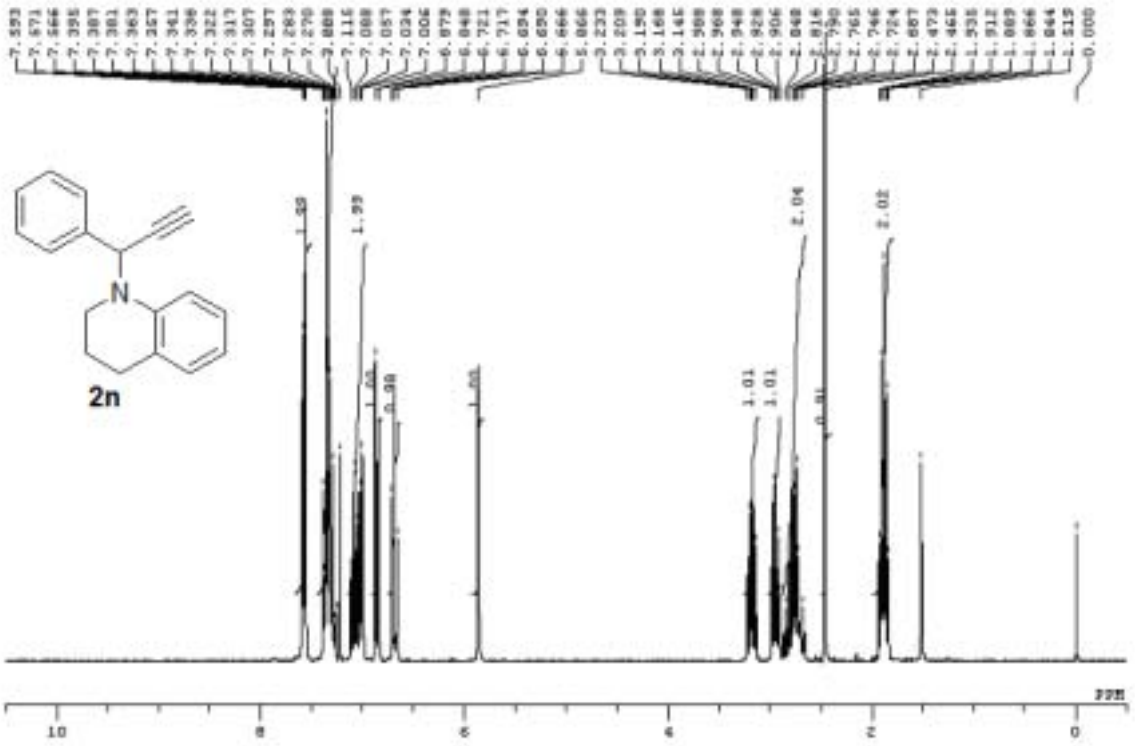
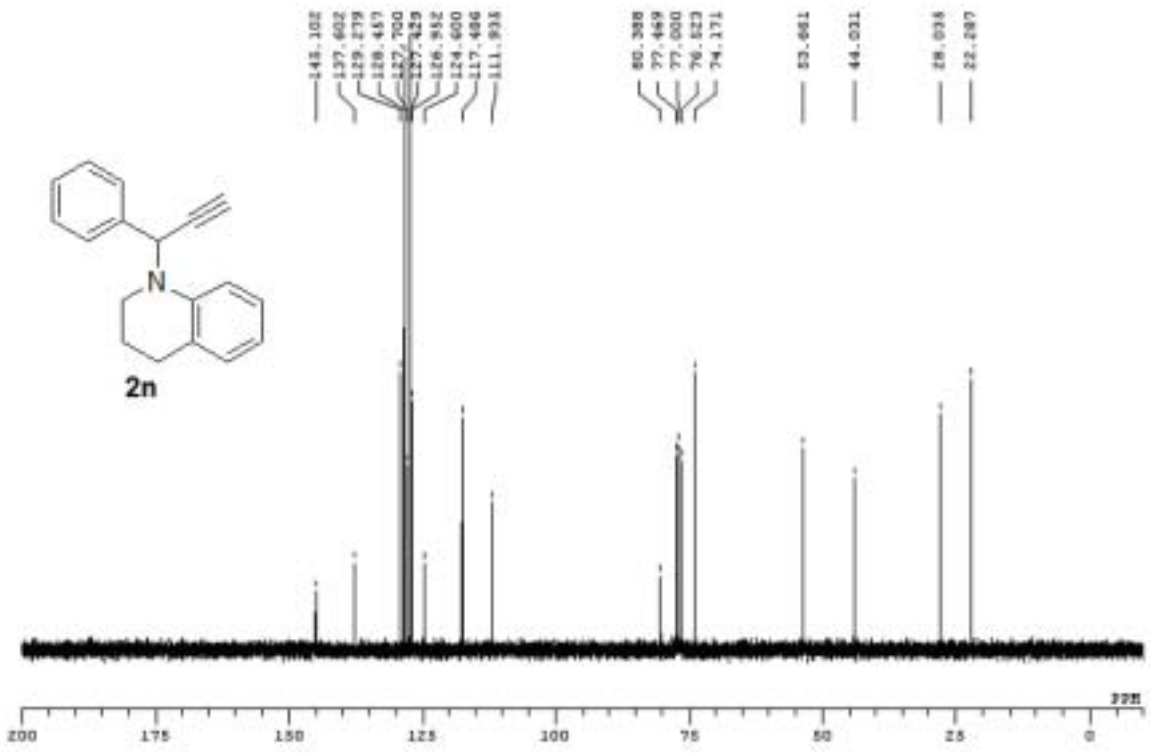


^{13}C NMR (**2n**)



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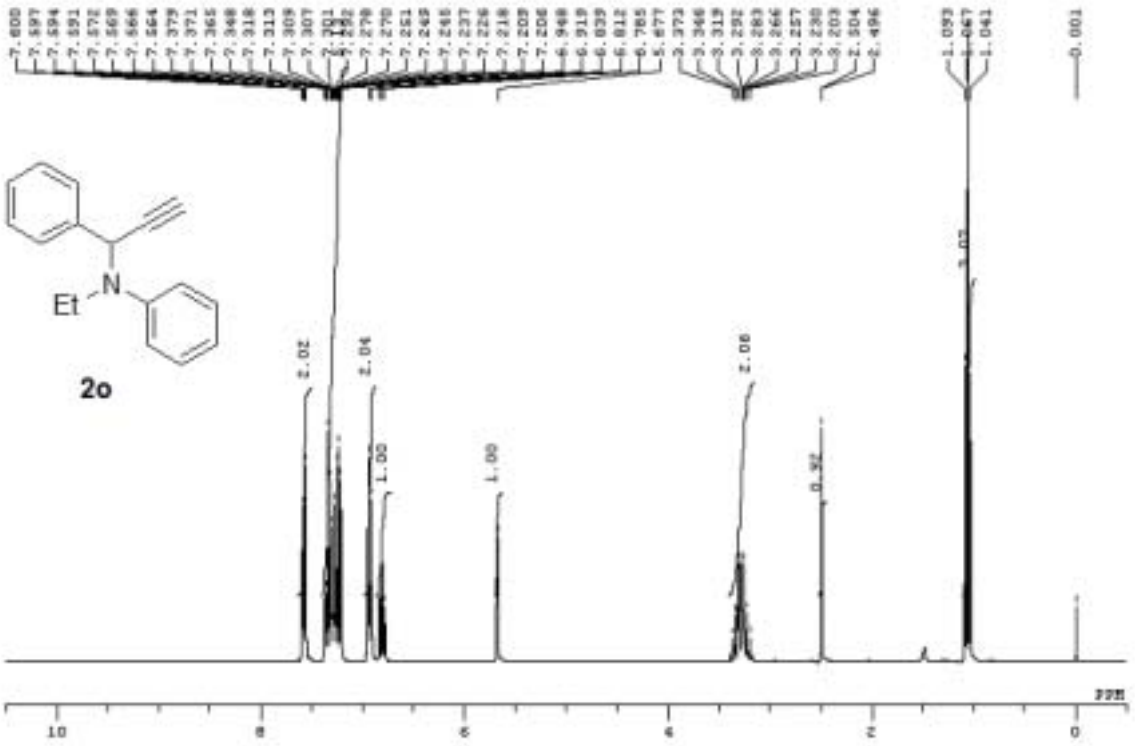
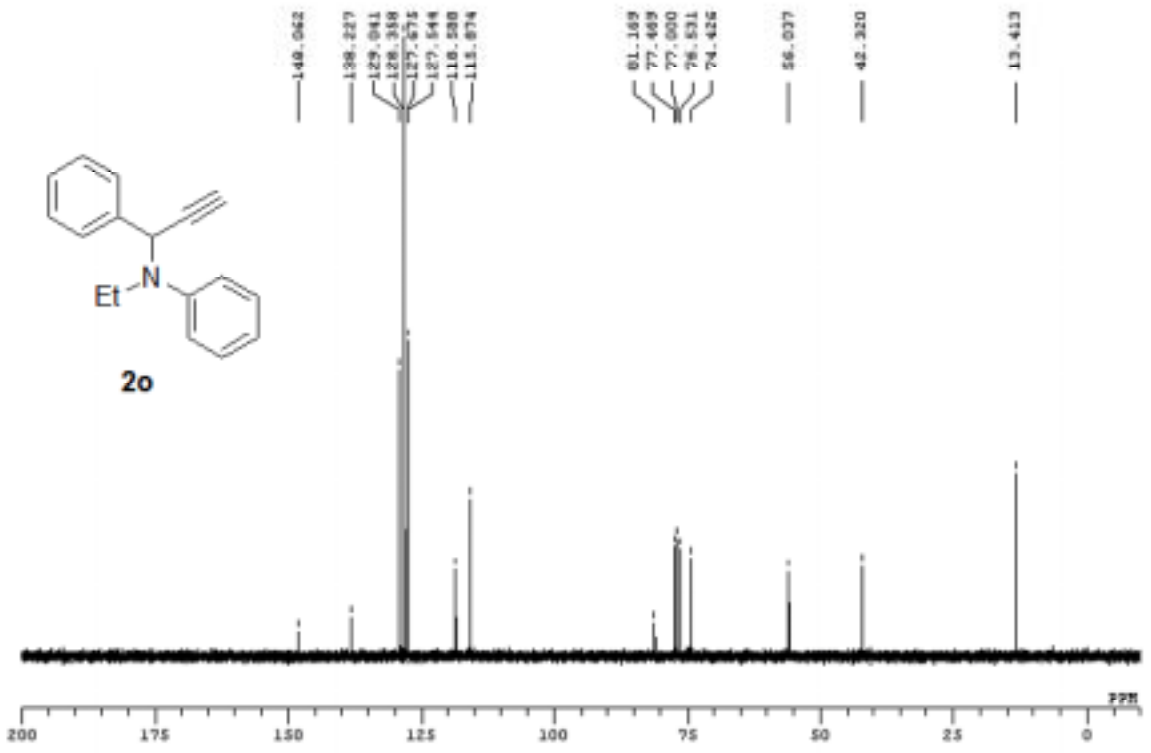


^{13}C NMR (**2o**)



Charts of propargylic amines (**2a**-**2h** and **2j**-**2p**) and amine (**3a**) by HPLC analysis are shown in the following pages.

2a

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3.86

8.92 5.57

D-7000 INTEGRATOR REPORT

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METHOD : OPERATOR:
CHANNEL : 1 <DIGITAL> SSD : 3

FILE : 0 MODULE I-PROG : DETECTOR= 1
CALC-METHOD: AB/MIN <AREA> COMPONENT TBL : 0

NO.	RT	AREA	CONC	EC
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2	5.57	2884288	48.555	88
3	8.92	2807764	48.638	88
TOTAL		5378614	100.000	
PEAK REJ :		0		

29

FILE 0 SYS 1 SSD 1 OFFS 0 07/08/07 09:22
CH.1<0> C.S 2.50 ATT 10

8.31
3.84
5.04

7.04

D-7000 INTEGRATOR REPORT

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CHANNEL : 1 <DIGITAL> SSD : 1

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CALC-METHOD: AB/MIN <AREA> COMPONENT TBL : 0

NO.	RT	AREA	CONC	EC
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4	7.04	8214148	92.720	88
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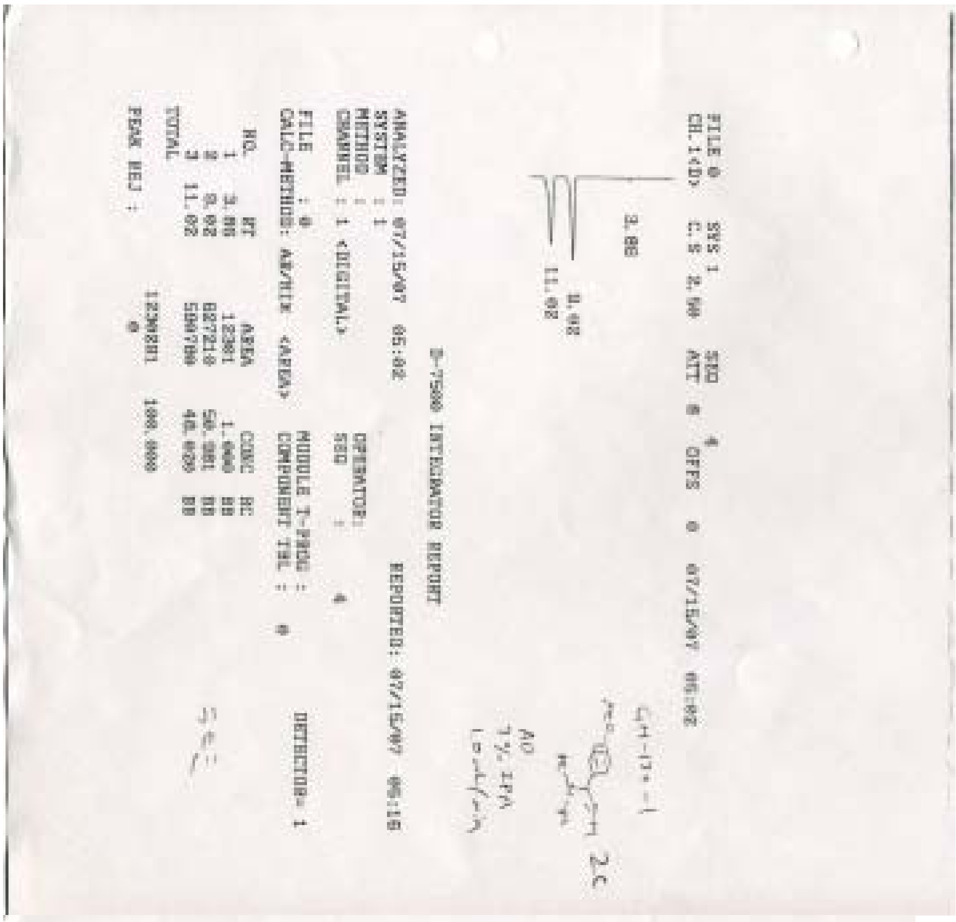
29

2b

2c



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D-7500 INTEGRATOR REPORT

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CALC-METHOD: AR/RIX <AREA>   COMPONENT TBL : 0

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2	9.02	627210	50.981	BB
3	11.02	590700	48.020	BB
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PEAK REJ :   0

FILE 0   SYS 1   SEQ   1
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D-7500 INTEGRATOR REPORT

ANALYZED: 07/16/07 09:58   REPORTED: 07/16/07 10:13
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METHOD :   OPERATOR:
CHANNEL : 1 <DIGITAL>   SEQ   :   1

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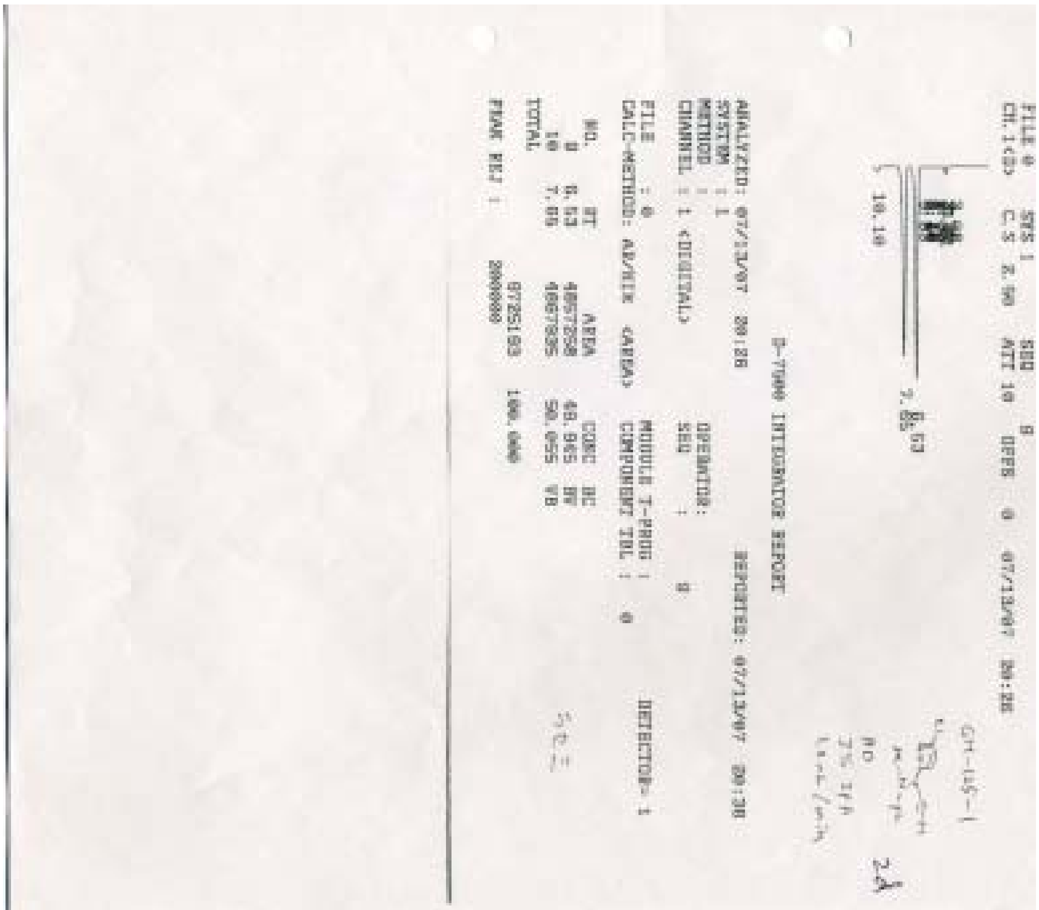
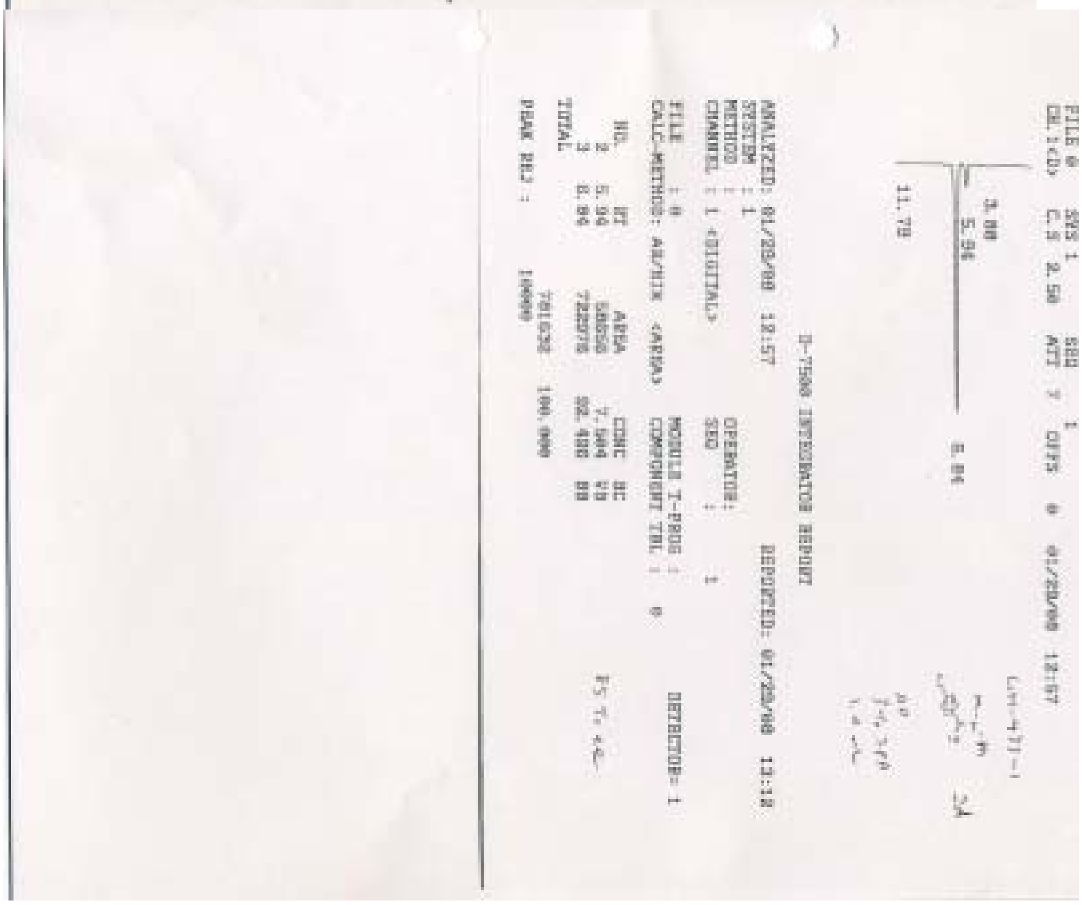
PEAK REJ :   250000

2d





2e

FILE 0 SYS 1 SEQ 10
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8.89 8.83 8.85

D-7500 INTEGRATOR REPORT

ANALYZED: 07/13/07 20:44 REPORTED: 07/13/07 20:54
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METHOD :
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SEQ : 10
FILE : 0 MODULE I-PRO : DETECTOR= 1
CALC-METHOD: AB/HIK <AREA> COMPONENT TBL : 0

NO.	RT	AREA	CONC	BC
7	8.83	5102251	49.955	BV
8	8.85	5111467	50.045	VB
TOTAL		10213718	100.000	

PEAK REJ : 2000000

FILE 0 SYS 1 SEQ 1
CH.1<D> C.S 2.90 ATT 10 OFFS 0 07/15/07 15:05

8.84

D-7500 INTEGRATOR REPORT

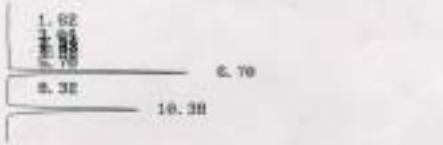
ANALYZED: 07/15/07 15:05 REPORTED: 07/15/07 15:17
SYSTEM : 1
METHOD :
CHANNEL : 1 <DIGITAL> OPERATOR:
SEQ : 1
FILE : 0 MODULE I-PRO : DETECTOR= 1
CALC-METHOD: AB/HIK <AREA> COMPONENT TBL : 0

NO.	RT	AREA	CONC	BC
8	8.78	820443	7.682	BV
9	8.84	9858558	92.318	VB
TOTAL		10679002	100.000	

PEAK REJ : 1000000

2f

FILE 0 SYS 1 SEQ 3
CH. 1<D> C.S 2.50 ATT 8 OFFS 0 07/12/07 20:58



D-7500 INTEGRATOR REPORT

ANALYZED: 07/12/07 20:58 REPORTED: 07/12/07 21:11
SYSTEM : 1
METHOD :
CHANNEL : 1 <DIGITAL>
OPERATOR:
SEQ : 3

FILE : 0
CALC-METHOD: AR/HI% <AREA>
MODULE T-PROG :
COMPONENT TBL : 0
DETECTOR= 1

NO.	RT	AREA	CONC	BC
7	6.70	1210168	50.125	VV
9	10.38	1204102	49.875	BB
TOTAL		2414351	100.000	

PEAK REJ : 100000

FILE 0 SYS 1 SEQ 5
CH. 1<D> C.S 2.50 ATT 8 OFFS 0 07/13/07 14:30

D-7500 INTEGRATOR REPORT

ANALYZED: 07/13/07 14:30 REPORTED: 07/13/07 14:48
SYSTEM : 1
METHOD :
CHANNEL : 1 <DIGITAL>
OPERATOR:
SEQ : 5

FILE : 0
CALC-METHOD: AR/HI% <AREA>
MODULE T-PROG :
COMPONENT TBL : 0
DETECTOR= 1

NO.	RT	AREA	CONC	BC
3	6.85	116341	7.658	BB
4	10.88	1402916	92.342	BB
TOTAL		1519257	100.000	

PEAK REJ : 100000

2g

FILE 0 SYS 1 SEQ 4
CH. 1<D> C.S 2.50 ATT 8 OFFS 0 07/12/07 21:18

8.14
8.00

D-7500 INTEGRATOR REPORT

ANALYZED: 07/12/07 21:18 REPORTED: 07/12/07 21:30
SYSTEM : 1
METHOD :
CHANNEL : 1 <DIGITAL>
OPERATOR:
SEQ : 4

FILE : 0
CALC-METHOD: AR/HI% <AREA>
MODULE T-PROG :
COMPONENT TBL : 0
DETECTOR= 1

NO.	RT	AREA	CONC	BC
5	8.14	2402580	49.437	BV
6	9.00	2457331	50.563	VB
TOTAL		4859911	100.000	

PEAK REJ : 100000

FILE 0 SYS 1 SEQ 8
CH. 1<D> C.S 2.50 ATT 0 OFFS 0 07/13/07 14:54

8.42
10.02

D-7500 INTEGRATOR REPORT

ANALYZED: 07/13/07 14:54 REPORTED: 07/13/07 15:07
SYSTEM : 1
METHOD :
CHANNEL : 1 <DIGITAL>
OPERATOR:
SEQ : 8

FILE : 0
CALC-METHOD: AR/HI% <AREA>
MODULE T-PROG :
COMPONENT TBL : 0
DETECTOR= 1

NO.	RT	AREA	CONC	BC
4	8.42	682464	8.293	BB
5	10.02	7546636	91.707	BB
TOTAL		8229100	100.000	

PEAK REJ : 500000

2h

2j

2k

FILE 0 SYS 1 SEQ 13
CH. 1<D> C.S 2.50 ATT 10 OFFS 0 07/27/07 14:48

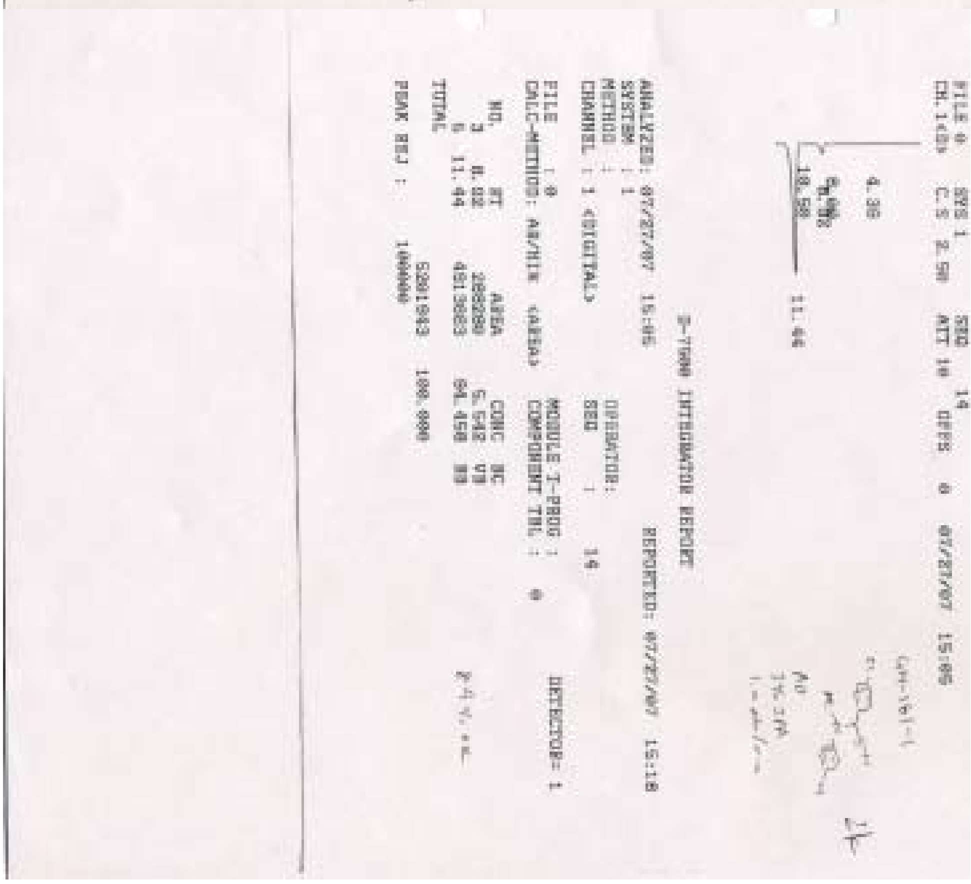
D-7500 INTEGRATOR REPORT

ANALYZED: 07/27/07 14:49 REPORTED: 07/27/07 15:03
SYSTEM : 1
METHOD : OPERATOR:
CHANNEL : 1 <DIGITAL> SEQ : 13

FILE : 0 MODULE T-PROG : DETECTOR= 1
CALC-METHOD: AR/MIX <AREA> COMPONENT TBL : 0

NO.	RT	AREA	CONC	BC
3	8.88	3919250	50.005	BB
5	11.38	3918438	49.995	VB
TOTAL		7837688	100.000	

PEAK REJ : 100000



FILE 0 SYS 1 SEQ 14
CH. 1<D> C.S 2.50 ATT 10 OFFS 0 07/27/07 15:05

D-7500 INTEGRATOR REPORT

ANALYZED: 07/27/07 15:05 REPORTED: 07/27/07 15:18
SYSTEM : 1
METHOD : OPERATOR:
CHANNEL : 1 <DIGITAL> SEQ : 14

FILE : 0 MODULE T-PROG : DETECTOR= 1
CALC-METHOD: AR/MIX <AREA> COMPONENT TBL : 0

NO.	RT	AREA	CONC	BC
3	8.82	288280	5.542	VB
5	11.44	4913663	94.458	BB
TOTAL		5201943	100.000	

PEAK REJ : 100000

2l

FILE 0 SYS 1 SEQ 3
CH.1<0> C.S 2.50 ATT 10 OFFS 0 07/19/07 16:29

5.72
7.98
8.04

D-7600 INTEGRATOR REPORT

ANALYZED: 07/19/07 16:29 REPORTED: 07/19/07 16:40
SYSTEM : 1
METHOD :
CHANNEL : 1 <DIGITAL>
OPERATOR:
SEQ : 3
FILE : 0
CALC-METHOD: AB/HIR <AREA> MODULE T-PROG :
COMPONENT IDL : 0
DETECTOR= 1

NO.	RT	AREA	CONC	BC
7	5.72	70281455	49.083	BB
10	7.98	7032888	50.917	VB
TOTAL		140811131	100.000	
PEAK REJ :		1000000		

2m

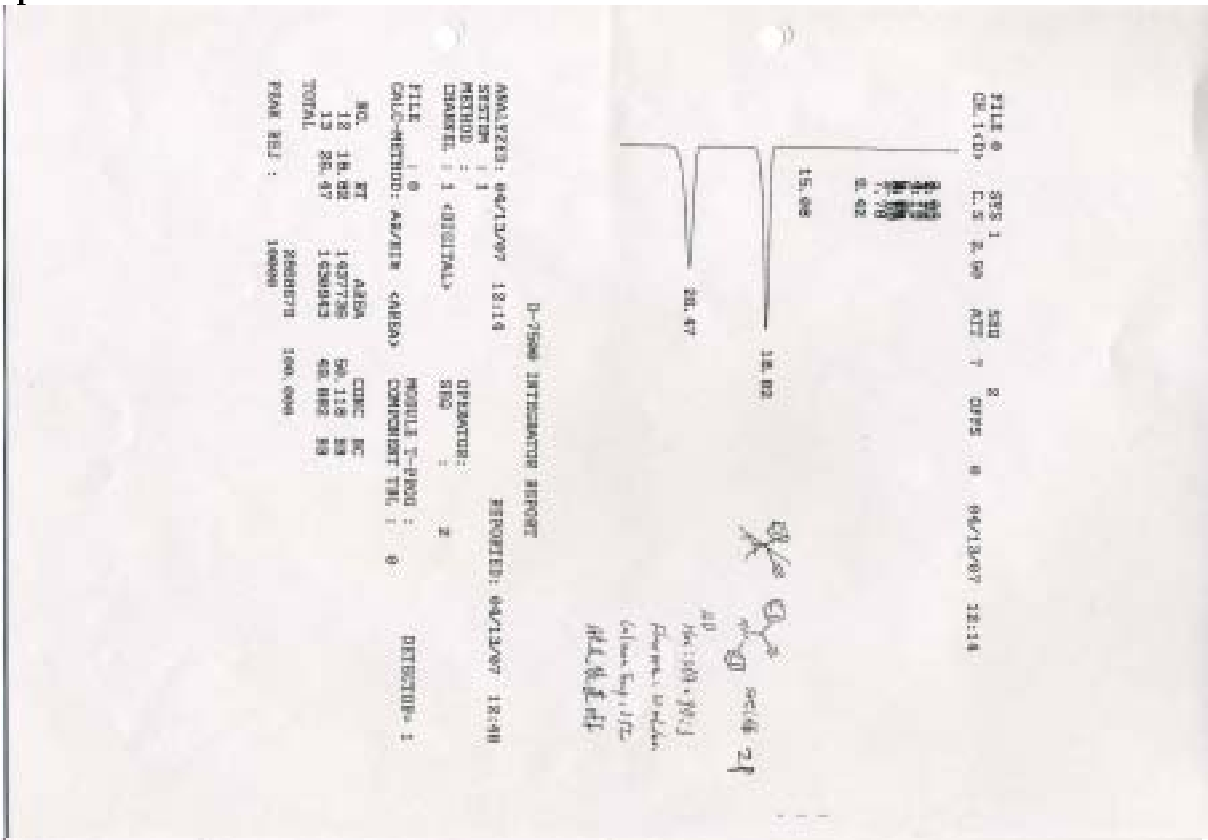
2n

FILE 0 SYS 1 SEQ 4
CH.1<D> C.S 2.50 ATT 10 OFFS 0 07/20/07 16:23
10.52
11.72
D-7500 INTEGRATOR REPORT
ANALYZED: 07/20/07 16:23 REPORTED: 07/20/07 16:37
SYSTEM : 1
METHOD :
CHANNEL : 1 <DIGITAL> OPERATOR: SEQ : 4
FILE : 0 MODULE T-PROG : DETECTOR= 1
CALC-METHOD: AR/HI% <AREA> COMPONENT TBL : 0
NO. RT AREA CONC BC
3 10.52 8547536 49.999 BV
4 11.72 8547950 50.001 VB
TOTAL 17095483 100.000
PEAK REJ : 1000000

FILE 0 SYS 1 SEQ 5
CH.1<D> C.S 2.50 ATT 10 OFFS 0 02/02/08 14:45
8.26
D-7500 INTEGRATOR REPORT
ANALYZED: 02/02/08 14:45 REPORTED: 02/02/08 14:55
SYSTEM : 1
METHOD :
CHANNEL : 1 <DIGITAL> OPERATOR: SEQ : 5
FILE : 0 MODULE T-PROG : DETECTOR= 1
CALC-METHOD: AR/HI% <AREA> COMPONENT TBL : 0
NO. RT AREA CONC BC
TOTAL 100.000

2o

2p



2g (after recrystallization)

FILE 0 SYS 1 SEQ 3
CH1.1<D> C.S 2.50 ATT 10 OFFS 0 02/20/08 19:53

8.88

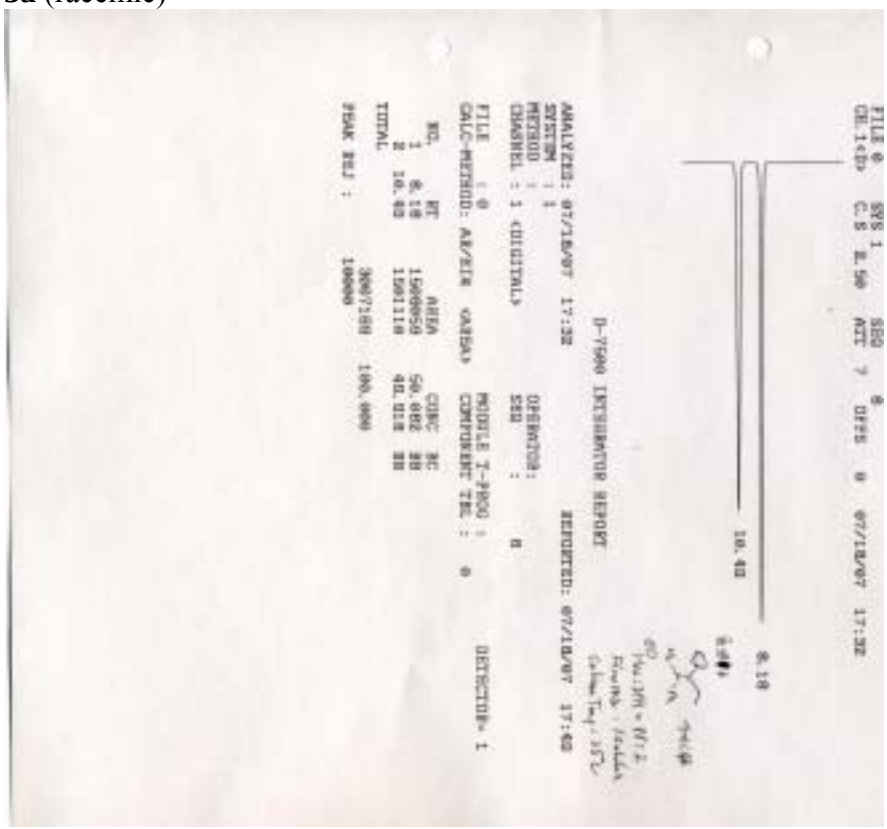
D-7500 INTEGRATOR REPORT

ANALYZED: 02/20/08 19:53 REPORTED: 02/20/08 20:05
SYSTEM : 1
METHOD : OPERATOR:
CHANNEL : 1 <DIGITAL> SEQ : 3

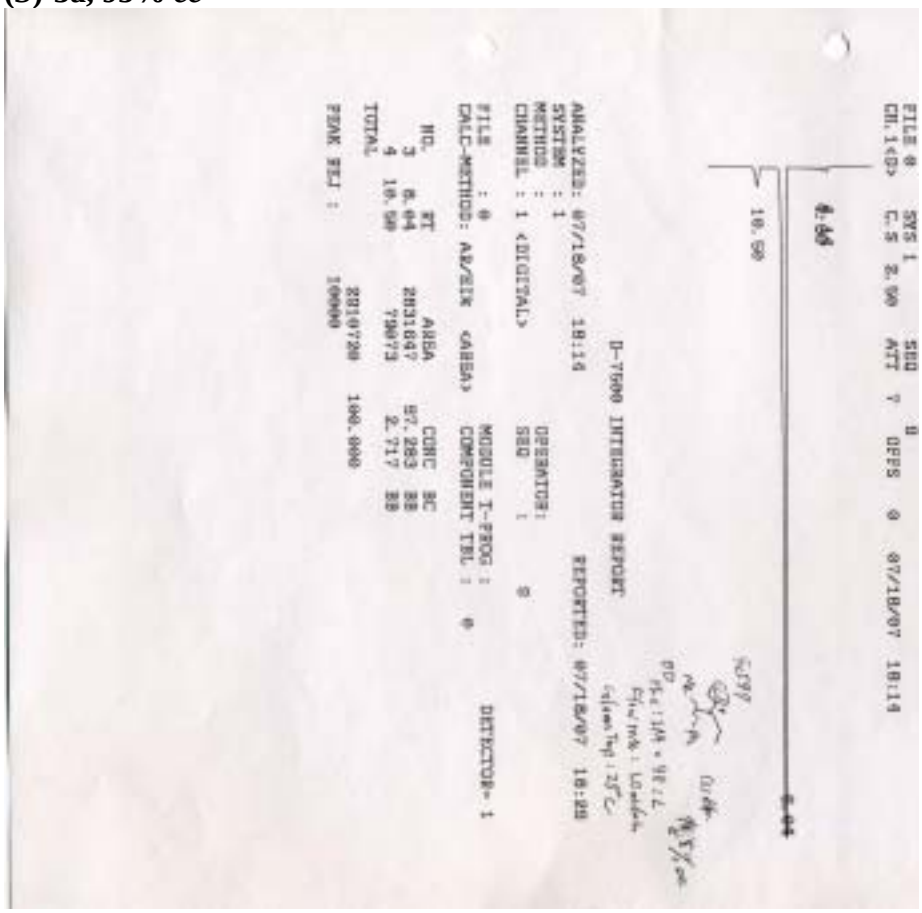
FILE : 0 MODULE T-P200 : DETECTOR= 1
CALC-METHOD: AB/Hik <AREA> COMPONENT TBL : 0

NO.	RT	AREA	CONC	BC
8	8.88	6153374	100.000	BB
TOTAL		6153374	100.000	
PEAK REJ :		30000		

3a (racemic)



(*S*)-3a, 95% *ee*



3a (after hydrogenation of **2a**)

FILE # SYS 1 SEQ 10
CHL 1 <0> T: 0 2.50 ATT 10 OFFS 0 07/18/07 18:44

6.65
8.78
7.50

D-7500 INTEGRATOR REPORT

ANALYZED: 07/18/07 18:44 REPORTED: 07/18/07 18:57
SYSTEM : 1
METHOD : OPERATOR:
CHANNEL : 1 <DIGITAL> SEQ 1 10
FILE : 0 MODULE T-PROG :
CALC-METHOD: AB/HIK <AREA> COMPONENT TBL : 0 RETENTION= 1

NO.	RT	AREA	CONC	EC
2	7.50	7102682	91.413	BB
3	8.78	687201	8.587	BB
TOTAL		7789883	100.000	

PEAK REJ : 150000