Supporting Information

[3,3]-Sigmatropic Rearrangement/5-Exo-Dig Cyclization Reactions of Benzyl Alkynyl Ethers: Synthesis of Substituted 2-Indanones and Indenes

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Spectroscopic data for compounds:

^{1}HNMR and ^{13}CNMR spectra for compounds:

General Methods. Distilled water was used in all of the experiments. Organic extracts were dried over Na_2SO_4, filtered, and concentrated using a rotary evaporator at aspirator pressure (20-30mmHg). Chromatography refers to flash chromatography and was carried out on SiO_2 (silica gel 60, 230-400 mesh). ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ at 400 MHz and 100 MHz, respectively, using Me_4Si as internal standard. Chemical shifts are reported in ppm downfield (δ) from Me_4Si.

Representative procedure for the synthesis of ***3a, 3b, 3e, 14a-e***

A mixture of diazoacetophenone (136 mg, 1mmol) and benzyl alcohol (162 mg, 1.5 mmol) were dissolved in dry toluene (4 mL) under argon and stirred at room temperature for 2 minutes. Indium (III) trifluoromethanesulfonate (56.2 mg, 0.1 mmol, 10 mol%) was added and a rapid evolution of nitrogen gas was observed. The reaction was monitored by TLC, and when complete consumption of the starting material was observed, saturated $NaHCO_3$ (10 mL) was added and the reaction mixture was diluted with ether (20 mL). The phases were separated and the aqueous phase was back-extracted with ether (1 x 20mL). The combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO_2) afforded α-alkoxyketones **3**.

Representative procedure for the synthesis of ***3c, 3d, 3f-j****.*

To a cooled (0 °C) suspension of NaH (60% in mineral oil, 1.0 g, 69 mmol) in 47 ml THF was added a solution of bromoacetic acid (1.36 g, 9.8 mmol) in 6.75 ml THF. The suspension was warmed to room temperature and stirred until the evolution of hydrogen stopped. Benzyl alcohol (1.04 ml, 10.0 mmol) was then added dropwise at 0 °C and the resulting grey/milky suspension was stirred at room temperature until the evolution of hydrogen stopped again. After addition of tetrabutylammonium iodide (217 mg, 0.59 mmol) the resulting white/milky reaction mixture was heated at reflux temperature for 3½ h and then cooled to 0 °C. EtOH (3 ml) was added and the mixture was concentrated to give a light-yellow oil, which was diluted with 20 ml sat. aq. $NaHCO_3$ and 20 ml Et_2O. The phases were separated and the organic layer was extracted with sat. aq. $NaHCO_3$ (2 × 20 ml). The combined aqueous extracts were then acidified to pH 2 with conc. HCl and extracted with Et_2O (3 × 20 ml). The combined organic extracts were once washed with 20 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated under reduced pressure, which gave the crude benzyloxyacetic acid as a yellow oil (12.8 g, directly used for the next step without further purification).

To a solution of benzyloxy acetic acid (1 g, 6 mmol) in 11 mL dichloromethane at 0°C was added 1,1'-carbonyl diimidazole (1.26 g, 7.82 mmol) at 0°C. The solution bubbled and upon completion it was warmed to room temperature for 30 minutes. The solution was cooled to 0°C and triethylamine (1.1 mL, 8.4 mmol) was added, followed by the Weinreb amine hydrochloride salt (0.82 g, 8.4 mmol). The solution was allowed to warm to room temperature and was stirred overnight. The mixture was diluted with 1M HCl (10 mL) and EtOAc (20 mL). The phases were separated and the aqueous phase was back-extracted with EtOAc (1 x 20 mL). The combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Crude amide **10** was taken directly to the next step without further purification.

To a solution of Weinreb amide **10** (5 mmol) in THF (5 mL) at -78°C under argon was added a solution of aryllithium reagent (generated from the corresponding aryl bromide 1M in THF by the addition of 0.95 equiv. *n*-BuLi) dropwise. Upon completion of the addition, TLC indicated complete conversion to the aryl ketone. The mixture was allowed to warm to -20°C and was quenched with saturated NH_4Cl solution (10 mL). The mixture was diluted with ether (3m L) and was allowed to stir at room temperature for one hour. The phases were separated and the aqueous phase was back-extracted with EtOAc (1 x 20 mL). The combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO_2) afforded α-alkoxyketones **3**.

*Representative procedure for enol triflate (**11a-i**) formation*

Hexamethyldisilazane (0.29 mL, 2.5 mmol) dissolved in dry THF (1mL) under argon was cooled to 0°C in an ice bath and *n*-BuLi (0.75 mL), 2M in cyclohexane, 1.5 mmol) was added dropwise. After 10 minutes, the mixture was cooled to -78°C and a solution of α-alkoxyketone (1 mmol) in THF (1 mL) was added dropwise. The reaction mixture was stirred for one hour at -78°C and then a solution of *N*-phenyl triflimide (1.5 mmol) in 1:1 THF:DMPU (1mL) was added rapidly (1s). The mixture was allowed to warm to room temperature and then was stirred for one hour, at which time TLC indicated >90% consumption of starting material. The phases were separated and the aqueous phase was back-extracted with ether (1 x 20 mL). The combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude enol triflate was accomplished by rapid chromatography over silica gel employing 1% Et_3N in the eluant (95:5 hexanes:ether).

*Representative procedure for alkynyl ether (**12a-i**) formation and sigmatropic rearrangement/cyclization to indanones **13a-i** and **15a-d**.*

Enol triflate obtained from the above procedure (~1 mmol) was dissolved in THF (1 mL) under argon and cooled to -78°C. A solution of potassium *tert*-butoxide (1M in THF, 3.0 mL, 3.0 mmol) was added dropwise, and the reaction mixture darkened in color. After 20 minutes, a solution of saturated $NaHCO_3$ (10 mL) was added and the mixture was allowed to warm to room temperature with stirring. Ether (10 mL) was added, and the phases were separated. The aqueous later was back-extracted with ether (1 x 20 mL), and the combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude alkynyl ether was then dissolved in toluene (2 mL) and heated on an oil bath under argon for one hour, at which time TLC indicated complete conversion to the indanone product. Concentration *in vacuo* and purification of the residue by flash chromatography (SiO_2) afforded indanones **13a-i** and **15a-d**.

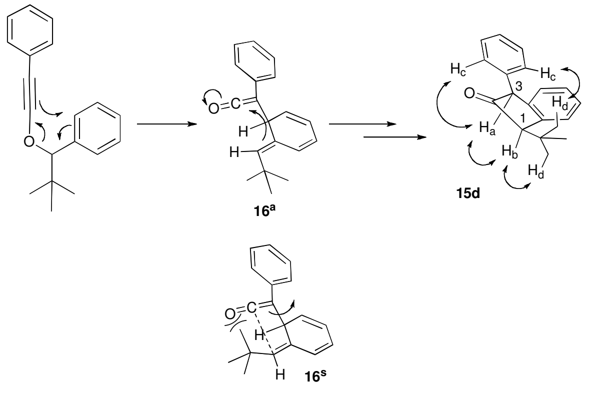
*Procedure for the synthesis of indene **18b**.*

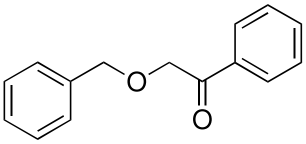
To a solution of diethyl(cyanomethyl)phosphonate (531 mg, 3.0 mmol) in THF (1 mL) was added NaH (100 mg, 2.5 mmol) at 0°C and the solution was allowed to stir for 30 minutes. Then a solution of 2-indanone **13b** (100 mg, 0.45 mmol) in THF (1 mL) was added and the mixture was allowed to stir 4 hours at room temperature. The mixture was diluted with saturated $NaHCO_3$ (10 mL). Ether (20 mL) was added, and the phases were separated. The aqueous later was back-extracted with ether (1 x 20 mL), and the combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO_2) afforded indene **18b**.

*Procedure for the synthesis of indene **19b***

To a solution of nitrile **18b** (35.0 mg, 0.142 mmol) in methanol (1.2 mL) at 0°C were added Boc_2O (69.0 mg, 0.32 mmol) and $NiCl_2•6H_2O$ (3.8 mg, 0.016 mmol). Then $NaBH_4$ (42.4 mg, 1.12 mmol) was added in small portions over 30 minutes. After warming to room temperature and stirring for 2 hours, the mixture was diluted with saturated $NaHCO_3$ (10 mL) and concentrated in vacuo to remove methanol. Ethyl acetate (10 mL) was added and the phases were separated. The aqueous later was back-extracted with ethyl acetate (1 x 10mL), and the combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO_2) afforded indene **19b**.

Ref. 15: For the transformation leading to **15d**, we believe that steric interactions between the *tert*-butyl group and the phenyl-substituted ketene in the corresponding *syn* form (**16**^{s}, see below) hinder alignment of the ketene carbonyl carbon with the benzylic carbon atom (which is necessary for 5-exo-dig cyclization to occur) by favoring rotamers in which the ketene is directed away from the benzylic carbon atom. Thus, despite the allylic strain present in **16**^{a} , it is likely that the reaction proceeds preferentially through **16**^{a} to **15d**.





3a

Purification: SiO_2(10% EtOAc in hexanes) afforded **3a** (87%).

See spectra on pages S19 and S20 **(see also reference 3, main text)**

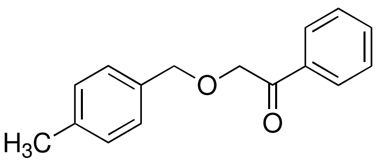
^{1}H NMR: (400 MHz, $CDCl_3$)

7.93 (d, *J*=7.6 Hz, 2H); 7.57 (t, *J*=7.6 Hz, 1H); 7.46 (t, *J*=8.0 Hz, 2H); 7.40- 7.27 (m, 5H); 4.82 (s, 2H); 4.70 (s, 2H).

^{13}C NMR: (100 MHz, $CDCl_3$)

197.2; 136.97; 134.6; 133.9; 129.4; 128.8; 128.6; 128.2; 127.9; 127.1; 123.6; 73.4; 72.4

HRMS (ESI): calculated for $C_{15}H_{14}NaO_2$ 249.0892 found 249.0854 $(M+Na)^+$



3b

Purification: SiO_2(10% EtOAc in hexanes) afforded **3b** (82%).

See spectra on pages S21 and S22

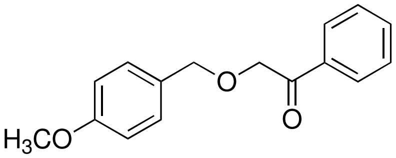
^{1}H NMR: (400 MHz, $CDCl_3$)

7.90 (d, *J*=7.6 Hz, 2H); 7.51 (t, *J*=7.6 Hz, 1H); 7.46-7.27 (m, 6H); 4.72 (s, 2H); 4.65 (s, 2H); 2.34 (s, 3H)

^{13}C NMR: (100 MHz, $CDCl_3$)

196.3; 137.6; 135.0; 134.4; 133.5; 129.2; 128.7; 128.2; 128.0; 73.2; 72.5; 21.2

HRMS (ESI): calculated for $C_{16}H_{16}NaO_2$ 263.1048 found 263.1107 $(M+Na)^+$



3c

Purification: SiO_2(10% EtOAc in hexanes) afforded **3c** (71%).

See spectra on pages S23 and S24

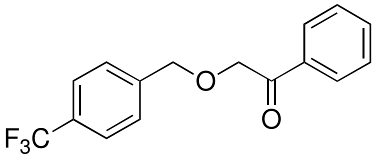
^{1}H NMR: (400 MHz, $CDCl_3$)

7.83 (dd, *J*=8.4, 1.2 Hz, 2H); 7.45-7.25 (m, 5H); 6.83 (d, *J*=8.8 Hz, 2H); 4.62 (s, 2H); 4.54 (s, 2H); 3.67 (s, 3H)

^{13}C NMR: (100 MHz, $CDCl_3$)

196.3, 159.4; 134.9; 133.4; 129.7; 129.4; 128.6; 128.3; 127.8; 113.8; 72.9; 72.2; 55.1.

HRMS (ESI): calculated for $C_{16}H_{16}NaO_3$ 279.0997, found 279.1098 $(M+Na)^+$



3d

Purification: SiO_2(5% EtOAc in hexanes) afforded **3d** (68%).

See spectra on pages S25 and S26

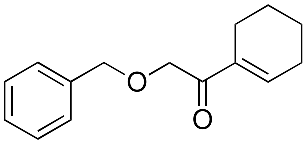
^{1}H NMR: (400 MHz, $CDCl_3$)

7.91 (dd, *J*=9.6 Hz, 2H); 7.61-7.42 (m, 7H); 4.81 (s, 2H); 4.72 (s, 2H).

^{13}C NMR: (100 MHz, $CDCl_3$)

196.0; 141.6; 134.7; 133.7; 129.5; 128.8; 127.9; 127.8; 125.4; 125.3; 115.4; 72.8; 72.5

HRMS (ESI): calculated for $C_{16}H_{13}F_3NaO_2$ 317.0765, found 317.0852 $(M+Na)^+$



3e

Purification: SiO_2 (5% EtOAc in hexanes) afforded **3e** (61%).

See spectra on pages S27 and S28

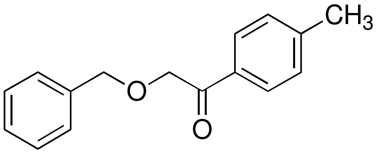
^{1}H NMR: (400 MHz, $CDCl_3$)

7.34-7.25 (m, 5H); 6.80 (t, *J*=4.0 Hz, 1H); 4.57 (s, 2H); 4.04 (s, 2H); 2.18 (m, 4H); 1.57 (m, 4H).

^{13}C NMR: (100 MHz, $CDCl_3$)

196.8; 140.7; 138.2; 128.5; 128.2; 128.1; 74.1; 72.3; 25.4; 22.1; 21.0; 20.8.

HRMS (ESI): calculated for $C_{15}H_{18}NaO_2$ 253.1205 found 253.1275 $(M+Na)^+$



3f

Purification: SiO_2 (10% EtOAc in hexanes) afforded **3f** (69%).

See spectra on pages S29 and S30

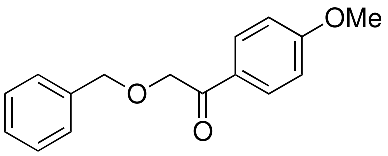
^{1}H NMR: (400 MHz, $CDCl_3$)

7.83-7.80 (d, *J*=8.4 Hz, 2H); 7.41-7.23 (m, 7H); 4.73 (s, 2H); 4.68 (s, 2H); 2.39 (s, 3H).

^{13}C NMR: (100 MHz, $CDCl_3$)

195.9; 144.4; 137.4; 132.4; 129.3; 128.5; 128.1; 128.0; 73.3; 72.5; 21.7

HRMS (ESI): calculated for $C_{16}H_{16}NaO_2$ 263.1048, found 263.1055 $(M+Na)^+$



3g

Purification: SiO_2(10% EtOAc in hexanes) afforded **3g** (82%).

See spectra on pages S31 and S32

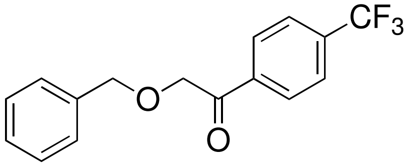
^{1}H NMR: (400 MHz, $CDCl_3$)

7.89 (d, *J*=8.8 Hz, 2H); 7.40-7.32 (m, 5H); 6.88 (d, *J*=8.8 Hz, 2H); 4.69 (s, 2H); 4.66 (s, 2H); 3.81 (s, 3H)

^{13}C NMR: (100 MHz, $CDCl_3$)

194.9; 163.8; 150.6; 137.5; 130.3; 128.5; 128.0; 127.9; 116.2; 114.7; 113.9; 73.3; 72.5; 55.4.

HRMS (ESI): calculated for $C_{16}H_{16}NaO_3$ 279.0997 found 279.0780 $(M+Na)^+$



3h

Purification: SiO_2(5% EtOAc in hexanes) afforded **3h** (73%).

See spectra on pages S33 and S34

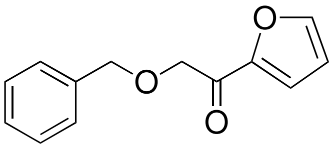
^{1}H NMR: (400 MHz, $CDCl_3$)

8.05 (d, *J*=8.0 Hz, 2H); 7.74 (d, *J*=8.4 Hz, 2H); 7.39-7.33 (m, 5H); 4.76 (s, 2H); 4.70 (s, 2H)

^{13}C NMR: (100 MHz, $CDCl_3$)

195.6; 137.5; 136.9; 134.8; 128.6; 128.4; 128.2; 128.1; 125.7; 73.5; 72.8.

HRMS (ESI): calculated for $C_{16}H_{13}F_3NaO_2$ 317.0765, found 317.0923 $(M+Na)^+$



3i

Purification: SiO_2(10% EtOAc in hexanes) afforded **3i** (85%).

See spectra on pages S35 and S36

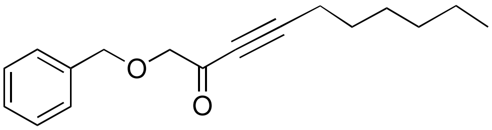
^{1}H NMR: (400 MHz, $CDCl_3$)

7.53 (s, 1H); 7.52-7.24 (m, 6H); 6.47 (m, 1H); 4.63 (s, 2H); 4.54 (s, 2H)

^{13}C NMR: (100 MHz, $CDCl_3$)

185.5; 150.9; 146.7; 137.3; 128.5; 128.3; 128.0; 127.9; 118.2; 112.3; 73.4; 72.2.

HRMS (ESI): calculated for $C_{13}H_{12}NaO_3$ 239.0684 found 239.0717 $(M+Na)^+$



3j

Purification: SiO_2(5% Et_2O in hexanes) afforded **3j** (92%).

See spectra on pages S37 and S38

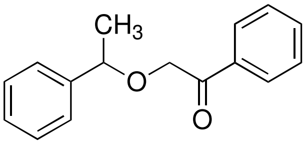
^{1}H NMR: (400 MHz, $CDCl_3$)

7.36-7.25 (m, 5H); 4.62 (s, 2H); 4.19 (s, 2H); 2.37 (t, *J*=6.8 Hz, 2H); 1.56 (m, *J*=7.2 Hz, 2H); 1.38-1.26 (m, 5H); 0.89 (t, *J*=6.8 Hz, 3H).

^{13}C NMR: (100 MHz, $CDCl_3$)

185.0; 137.1; 128.4; 127.9; 97.5; 82.7; 75.8; 73.3; 31.2; 28.5; 27.5; 22.5; 22.4; 19.0; 14.0

HRMS (ESI): calculated for $C_{17}H_{22}NaO_2$ 281.1517 found 281.1582 $(M+Na)^+$



14a

Purification: SiO_2(5% EtOAc in hexanes) afforded **14a** (75%).

See spectra on pages S39 and S40

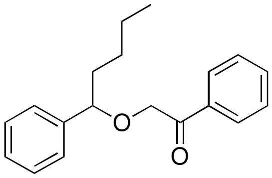
^{1}H NMR: (400 MHz, $CDCl_3$)

7.82 (d, *J*= 7.6 Hz, 2H); 7.46 (t, *J*= 7.6 Hz, 1H); 7.36-7.25 (m, 7H); 4.65 (d, *J*=16.8 Hz, 1H); 4.54 (q, *J*=6.4 Hz, 1H); 4.52 (d, *J*=16.8 Hz, 1H); 1.54 (d, *J*=6.4Hz, 3H)

^{13}C NMR: (100 MHz, $CDCl_3$)

195.9; 142.9; 135.0; 131.1; 128.6; 128.5; 128.2; 127.8; 127.7; 126.3; 78.3; 77.9; 71.2; 24.0; 23.9

HRMS (ESI): calculated for $C_{16}H_{16}NaO_2$ 263.1048 found 263.1632 (M+Na)+



14b

Purification: SiO_2(3% Et_2O in hexanes) afforded **14b** (78%).

See spectra on pages S41 and S42

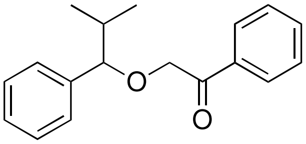
^{1}H NMR: (400 MHz, $CDCl_3$)

7.84 (d, *J*= 8.4 Hz, 2H); 7.50 (t, *J*= 7.6 Hz, 1H); 7.40-7.25 (m, 7H); 4.63 (d, *J*=16.8 Hz, 1H); 4.49 (d, *J*=16.8 Hz, 1H); 4.40 (t, *J*=6.8 Hz, 1H); 1.97 (m, 1H); 1.72 (m, 1H); 1.43 (m, 1H); 1.30 (m, 1H); 0.86 (t, *J*=7.6 Hz, 3H)

^{13}C NMR: (100 MHz, $CDCl_3$)

196.4; 141.7; 135.1; 133.3; 128.6; 128.5; 128.3; 127.9; 127.0; 83.1; 71.3; 37.9; 28.0; 22.6; 14.0.

HRMS (ESI): calculated for $C_{19}H_{22}NaO_2$ 305.1517 found 305.1343 (M+Na)+



14c

Purification: SiO_2(3% Et_2O in hexanes) afforded **14c** (73%).

See spectra on pages S43 and S44

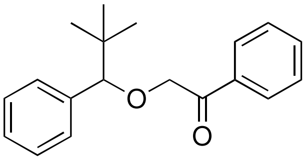
^{1}H NMR: (400 MHz, $CDCl_3$)

7.76 (d, *J*= 8.0 Hz, 2H); 7.43 (t, *J*= 7.8 Hz, 1H); 7.33-7.21 (m, 7H); 4.52 (d, *J*=16.0 Hz, 1H); 4.35 (d, *J*=16.0 Hz, 1H); 3.97 (d, *J*=8.0 Hz, 1H); 1.96 (m, *J*=8.0 Hz, 1H); 0.98 (d, *J*=8.0 Hz, 3H); 0.65 (d, *J*=8.0 Hz, 3H);

^{13}C NMR: (100 MHz, $CDCl_3$)

196.6; 140.3; 135.2; 133.3; 128.6; 128.5; 128.2; 128.0; 127.8; 127.7; 88.6; 71.6; 34.8; 19.2; 19.0.

HRMS (ESI): calculated for $C_{18}H_{20}NaO_2$ 291.1361 found 291.1440 (M+Na)+



14d

Purification: SiO_2(3% Et_2O in hexanes) afforded **14d** (66%).

See spectra on pages S45 and S46

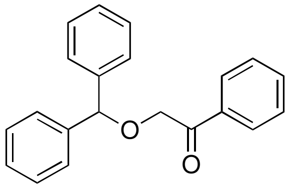
^{1}H NMR: (400 MHz, $CDCl_3$)

7.85 (d, *J*= 8.0 Hz, 2H); 7.49 (t, *J*= 7.8 Hz, 1H); 7.37 (t, *J*= 7.8 Hz, 2H); 7.32-7.25 (m, 5H); 4.62 (d, *J*=16.0 Hz, 1H); 4.41 (d, *J*=16.0 Hz, 1H); 4.15 (s, 1H); 0.96 (s, 9H)

^{13}C NMR: (100 MHz, $CDCl_3$)

196.5; 138.8; 135.3; 133.3; 128.6; 128.5; 128.0; 127.7; 127.6; 90.6; 71.9; 35.8; 26.4.

HRMS (ESI): calculated for $C_{19}H_{22}NaO_2$ 305.1517 found 305.1962 (M+Na)+



14e

Purification: SiO_2(5% Et_2O in hexanes) afforded **14e** (71%).

See spectra on pages S47 and S48

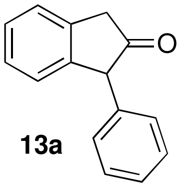
^{1}H NMR: (400 MHz, $CDCl_3$)

7.90 (d, *J*= 7.6 Hz, 2H); 7.55 (t, *J*= 7.4 Hz, 1H); 7.46-7.41 (m, 6H); 7.35 (t, *J*=7.6 Hz, 4H); 7.28 (t, *J*=7.8 Hz, 2H); 5.64 (s, 1H); 4.77 (s, 2H)

^{13}C NMR: (100 MHz, $CDCl_3$)

196.3; 141.3; 135.1; 133.5; 128.7; 128.5; 128.0; 127.8; 127.4; 83.8; 77.4; 77.1; 76.8; 71.4

HRMS (ESI): calculated for $C_{21}H_{18}NaO_2$ 325.1204 found 325.1541 (M+Na)+



13a

Purification: SiO_2(10% EtOAc in hexanes) afforded **11a** (98%).

***See spectra on pages S49 and S50* (see also reference 3, main text)**

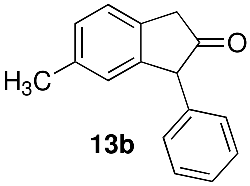
^{1}H NMR: (400 MHz, $CDCl_3$)

7.43-7.22 (m, 7H); 7.17 (d, *J*=7.6 Hz, 2H); 4.71 (s, 1H); 3.68 (s, 2H).

^{13}C NMR: (100 MHz, C_6D_6)

213.8; 141.4; 138.2; 137.3; 128.8; 128.5; 128.0; 127.9; 127.3; 126.0; 124.9; 59.8; 43.0

HRMS (ESI): calculated for $C_{15}H_{12}NaO$ 231.0786, found 231.0777 $(M+Na)^+$



13b

Purification: SiO_2(10% EtOAc in hexanes) afforded **13b** (93%).

See spectra on pages S51 and S52

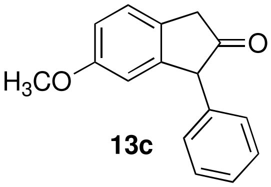
<u>^{1}H NMR</u>: (400 MHz, $CDCl_3$)

7.36-7.24 (m, 3H); 7.17-7.10 (m, 3H); 7.01 (s, 1H); 4.63 (s, 1H); 3.62 (s, 2H); 2.33 (m, 3H).

<u>^{13}C NMR</u>: (100 MHz, C_6D_6)

216.8; 143.3; 140.0; 137.7; 128.8; 128.5; 128.0; 127.9; 126.7; 124.3;123.1; 60.2; 47.1; 23.5

<u>HRMS (ESI):</u> calculated for $C_{16}H_{14}NaO$ 245.0942, found 245.1399 $(M+Na)^+$



13c

Purification: SiO_2(10% EtOAc in hexanes) afforded **13c** (65%).

See spectra on pages S53 and S54

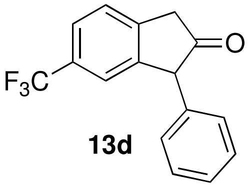
<u>^{1}H NMR</u>: (400 MHz, $CDCl_3$)

7.36-7.27 (m, 4H); 7.15 (d, *J*=7.6 Hz, 2H); 6.93 (m, 1H); 6.74 (m, 1H); 4.66 (s, 1H); 3.78 (s, 3H); 3.62 (s, 2H).

<u>^{13}C NMR</u>: (100 MHz, $CDCl_3$)

214.2; 159.5; 142.4; 138.0; 129.1; 128.8; 128.4; 127.3; 125.7; 114.7; 110.7; 60.2; 55.4; 42.3.

<u>HRMS (ESI):</u> calculated for $C_{16}H_{14}NaO_2$ 261.0891, found 261.0922 $(M+Na)^+$



13d

Purification: SiO_2(5% EtOAc in hexanes) afforded **13d** (72%).

See spectra on pages S55 and S56

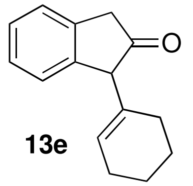
^{1}<u>H NMR</u>: (400 MHz, $CDCl_3$)

7.63-7.26 (m, 7H); 7.11 (dd, *J*=9.2 Hz, 1H); 4.75 (m, 1H); 3.72 (s, 2H)

^{13}<u>C NMR</u>: (100 MHz, $CDCl_3$)

212.3; 142.2; 137.2; 130.5; 130.2; 129.0; 128.4; 128.1; 127.2; 126.4; 125.0; 123.0; 122.9; 122.7; 59.6; 42.8.

<u>HRMS (ESI):</u> calculated for $C_{16}H_{11}F_3NaO$ 299.0660, found 299.0598 $(M+Na)^+$



13e

Purification: SiO_2(5% EtOAc in hexanes) afforded **13e** (95%).

See spectra on pages S57 and S58

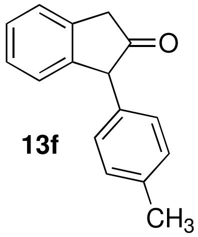
^{1}<u>H NMR</u>: (400 MHz, $CDCl_3$)

7.30-7.24 (m, 4H); 5.54 (s, 1H); 3.98 (s, 1H); 3.53 (s, 2H); 1.67-1.49 (m, 8H).

^{13}<u>C NMR</u>: (100 MHz, C_6D_6)

215.8; 141.3; 137.3; 134.7; 127.6; 127.5; 127.0; 125.3; 124.7; 62.3; 43.4; 26.1; 25.4; 22.7; 22.1.

<u>HRMS (ESI):</u> calculated for $C_{15}H_{16}NaO$ 235.1099, found 235.1174 $(M+Na)^+$



13f

Purification: SiO_2(5% EtOAc in hexanes) afforded **13f** (90%).

See spectra on pages S59 and S60

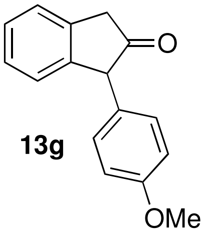
^{1}<u>H NMR</u>: (400 MHz, $CDCl_3$)

7.38-7.30 (m, 3H); 7.21 (d, *J*=7.2 Hz, 1H); 7.14 (d, *J*=7.6 Hz, 2H); 7.02 (d, *J*=8.0 Hz, 2H); 4.63 (s, 1H); 3.65 (s, 2H); 2.34 (s, 3H).

^{13}<u>C NMR</u>: (100 MHz, $CDCl_3$)

214.2; 141.5; 137.2; 137.0; 135.2; 129.5; 128.5; 128.3; 127.9; 127.8; 126.0; 124.8; 59.4; 42.9; 21.1.

<u>HRMS (ESI):</u> calculated for $C_{16}H_{14}NaO$ 245.0942, found 245.0921 (M+Na)



13g

Purification: SiO_2(10% EtOAc in hexanes) afforded **13g** (88%).

See spectra on pages S61 and S62

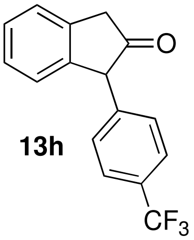
^{1}<u>H NMR</u>: (400 MHz, $CDCl_3$)

7.38-7.20 (m, 5H); 7.05 (d, *J*=6.4 Hz, 2H); 6.87 (d, *J*=6.4 Hz, 2H); 4.63 (s, 1H); 3.78 (s, 3H); 3.66 (s, 2H).

^{13}<u>C NMR</u>: (100 MHz, $CDCl_3$)

214.4; 158.9; 141.6; 137.2; 130.3; 129.5; 128.3; 127.9; 127.8; 126.0; 124.8; 114.2; 58.9; 55.2; 42.8.

<u>HRMS (ESI):</u> calculated for $C_{16}H_{14}NaO_2$ 261.0891, found 261.0664 $(M+Na)^+$



13h

Purification: SiO_2(5% EtOAc in hexanes) afforded **13h** (91%).

See spectra on pages S63 and S64

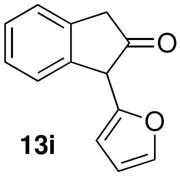
^{1}H NMR: (400 MHz, $CDCl_3$)

8.06 (d, *J*=8.0 Hz, 1H); 7.75 (d, *J*=8.4 Hz, 2H); 7.61 (d, *J*=8.0 Hz, 2H); 7.45-7.18 (m, 5H); 4.71 (s, 1H); 3.73 (m, 2H).

^{13}C NMR: (100 MHz, $CDCl_3$)

212.9, 140.2; 136.7; 129.8; 129.4; 128.9; 128.5; 128.2; 126.9; 125.9; 125.7; 125.6; 125.4; 59.4; 42.8.

HRMS (ESI): calculated for $C_{16}H_{11}F_3NaO$ 299.0659, found 299.0721 $(M+Na)^+$



13i

Purification: SiO_2(10% EtOAc in hexanes) afforded **13i** (62%).

See spectra on pages S65 and S66

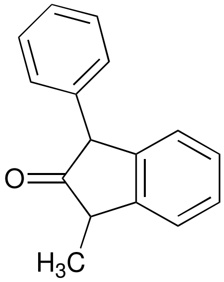
^{1}H NMR: (400 MHz, $CDCl_3$)

7.39-7.27 (m, 5H); 6.35 (m, 1H); 6.16 (m, 1H); 4.82 (s, 1H); 3.72 (d, *J*=8.0 Hz, 2H).

^{13}C NMR: (100 MHz, $CDCl_3$)

211.4; 150.5; 142.7; 136.9; 128.3; 127.8; 125.6; 124.9; 110.4; 107.8; 53.3; 42.9.

HRMS (ESI): calculated for $C_{13}H_{10}NaO_2$ 221.0578, found 221.0842 $(M+Na)^+$



15a

Purification: SiO_2 (10% Et_2O in hexanes) afforded **15a** (61%) (dr = 1:1).

See spectra on pages S67 and S68

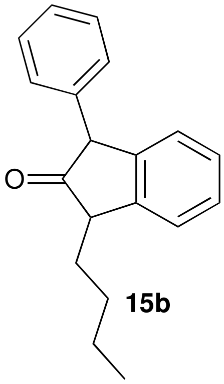
^{1}H NMR: (400 MHz, $CDCl_3$)

7.41-7.26 (m, 6H); 7.18-7.10 (m, 3H); 4.70 (s, 1H); 3.61 (q, J=4.2 Hz, 1H); 1.48 (d, J=5.6 Hz, 3H);

^{13}C NMR: (100 MHz, $CDCl_3$)

216.4; 143.2; 140.1; 138.3; 128.9; 128.6; 128.0; 127.6; 126.0; 124.2; 59.0; 46.7; 15.8.

HRMS (ESI): calculated for $C_{16}H_{14}NaO$ 245.0942, found 245.4017 $(M+Na)^+$.



15b

Purification: SiO_2 (10% Et_2O in hexanes) afforded **15b** (53%) (dr= 4:1).

See spectra on pages S69 and S70

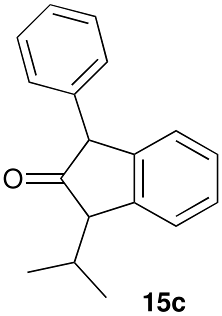
^{1}H NMR: (400 MHz, $CDCl_3$)

7.33-7.21 (m, 9H), 4.42 (s, 1H), 3.34 (t, J=5.4Hz, 1H), 1.86 (m, 2H), 1.41-1.19 (m, 4H), 0.80 (t, J=6.0, 3H);

^{13}C NMR: (100 MHz, $CDCl_3$)

214.2; 142.3; 141.0; 128.9; 128.5; 128.0; 127.7; 127.5; 58.9; 52.0; 31.2; 28.8; 22.7; 19.6.

HRMS (ESI): calculated for $C_{19}H_{20}NaO$ 287.1412, found 287.1361 $(M+Na)^+$.



15c

Purification: SiO_2 (10% Et_2O in hexanes) afforded **15c** (48%) (dr= 2:1).

See spectra on pages S71 and S72

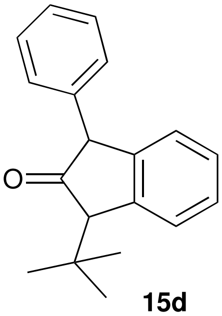
^{1}H NMR: (400 MHz, $CDCl_3$)

7.24-7.01 (m, 9H); 4.38 (s, 1H); 3.25 (d, *J*=3.6Hz, 1H); 2.29 (m, *J*=4.0Hz, 1H); 1.01 (d, *J*=6.4Hz, 3H); 0.89 (d, *J*=6.4Hz, 3H).

^{13}C NMR: (100 MHz, $CDCl_3$)

213.8; 141.3; 140.9; 138.0; 128.9; 128.4; 128.0; 127.7; 127.5; 126.9; 126.1; 124.7; 58.9; 58.0; 31.2; 19.9; 19.6.

HRMS (ESI): calculated for $C_{18}H_{18}NaO$ 273.1255, found 273.1271 $(M+Na)^+$.



15d

Purification: SiO_2 (10% Et_2O in hexanes) afforded **15d** (69%) (cis:trans = >95:5).

See spectra on pages S73 and S74 and NOESY S75 and S76

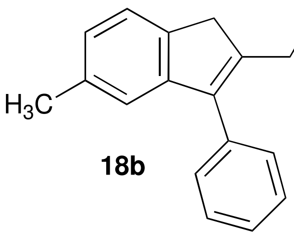
^{1}H NMR: (400 MHz, $CDCl_3$)

7.42 (d, *J*=10.0 Hz, 2H); 7.31 (m, 1H); 7.20-7.09 (m, 6H); 4.40 (s, 1H), 3.09 (s, 1H), 0.99 (s, 9H).

^{13}C NMR: (100 MHz, $CDCl_3$)

213.3; 141.3; 140.7; 138.6; 128.5; 128.0; 127.9; 127.6; 127.3; 126.6; 62.3; 58.6; 35.0; 30.5; 28.6.

HRMS (ESI): calculated for $C_{19}H_{20}NaO$ 287.1412, found 287.1438 $(M+Na)^+$.



18b

Purification: SiO_2 (5% EtOAc in hexanes) afforded **16b** (91%)

See spectra on pages S77 and S78

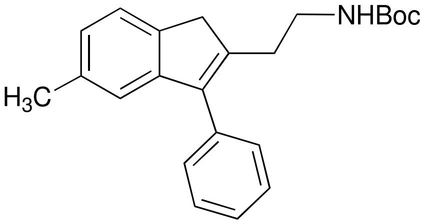
^{1}<u>H NMR</u>: (400 MHz, $CDCl_3$)

7.53-7.35 (m, 6H); 7.09-7.05 (m, 2H); 3.63 (s, 2H); 3.55 (s, 2H); 2.35 (s, 3H)

^{13}<u>C NMR</u>: (100 MHz, $CDCl_3$)

144.8; 139.1; 136.4; 133.6; 130.5; 128.9; 128.8; 128.1; 126.5; 123.6; 121.2; 40.2; 21.5; 17.9

<u>HRMS (ESI):</u> calculated for $C_{18}H_{15}NNa$ 268.1102, found 268.1099 $(M+Na)^+$.



19b

Purification: SiO_2 (10% EtOAc in hexanes) afforded **17b** (60%)

See spectra on pages S79 and S80

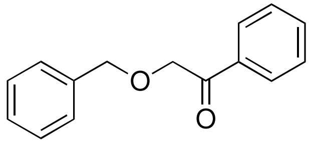
^{1}<u>H NMR</u>: (400 MHz, $CDCl_3$)

7.49-7.35 (m, 6H); 7.00 (m, 2H); 3.47 (s, 2H); 3.35 (m, 2H); 2.71 (t, *J*=6.8 Hz, 2H); 2.34 (s, 3H); 1.41 (s, 9H).

^{13}<u>C NMR</u>: (100 MHz, $CDCl_3$)

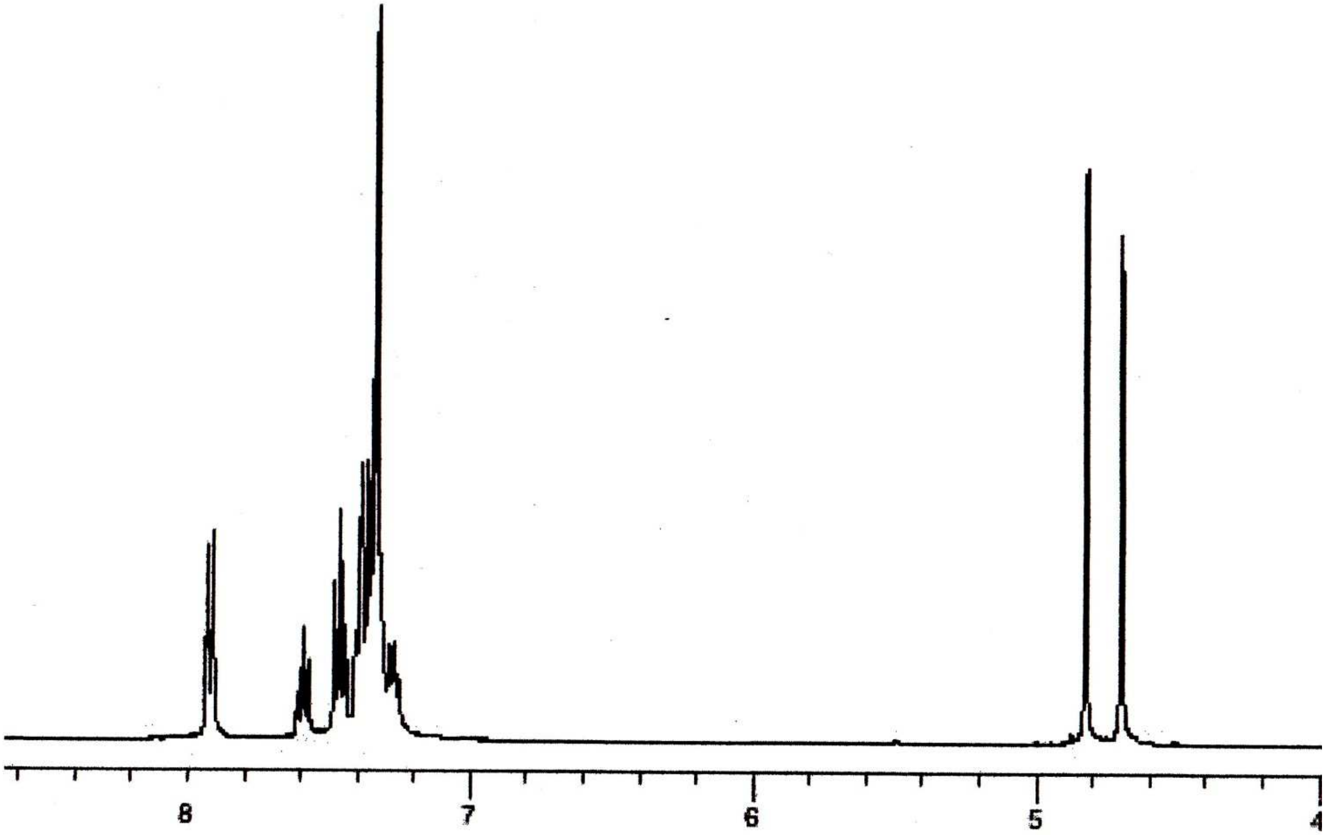
155.7; 146.3; 141.1; 138.0; 135.2; 129.1; 128.5; 128.3; 127.3; 125.3; 123.3; 120.4; 100.0; 79.2; 40.2; 40.0; 29.4; 28.3; 21.5

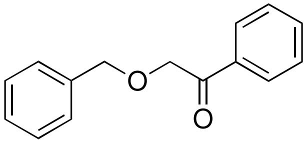
<u>HRMS (ESI):</u> calculated for $C_{23}H_{27}NNaO_2$ 372.1939, found 372.1763 $(M+Na)^+$.



3a

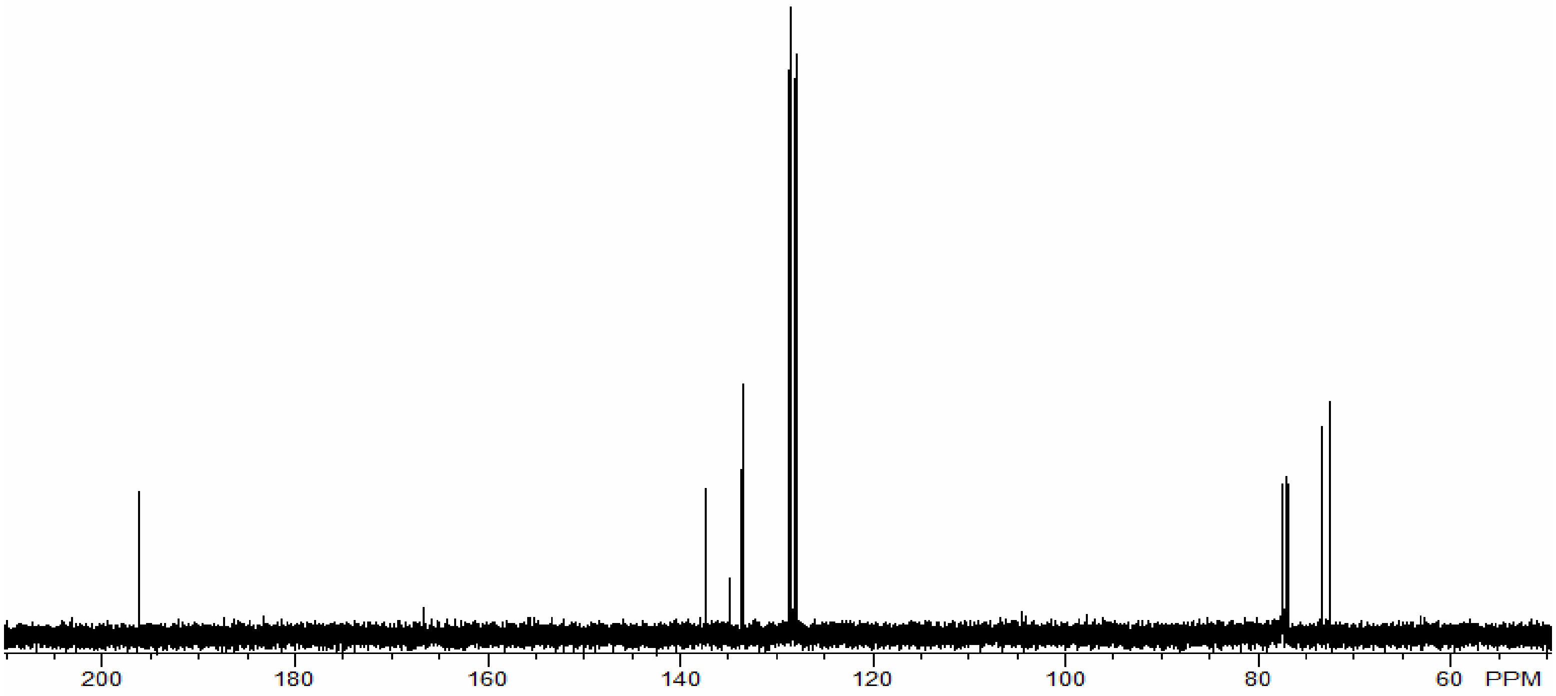
^{1}H NMR, CDCl$_3$, 400MHz

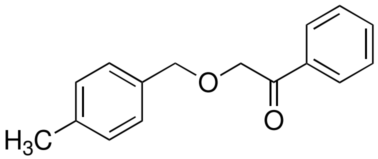




3a

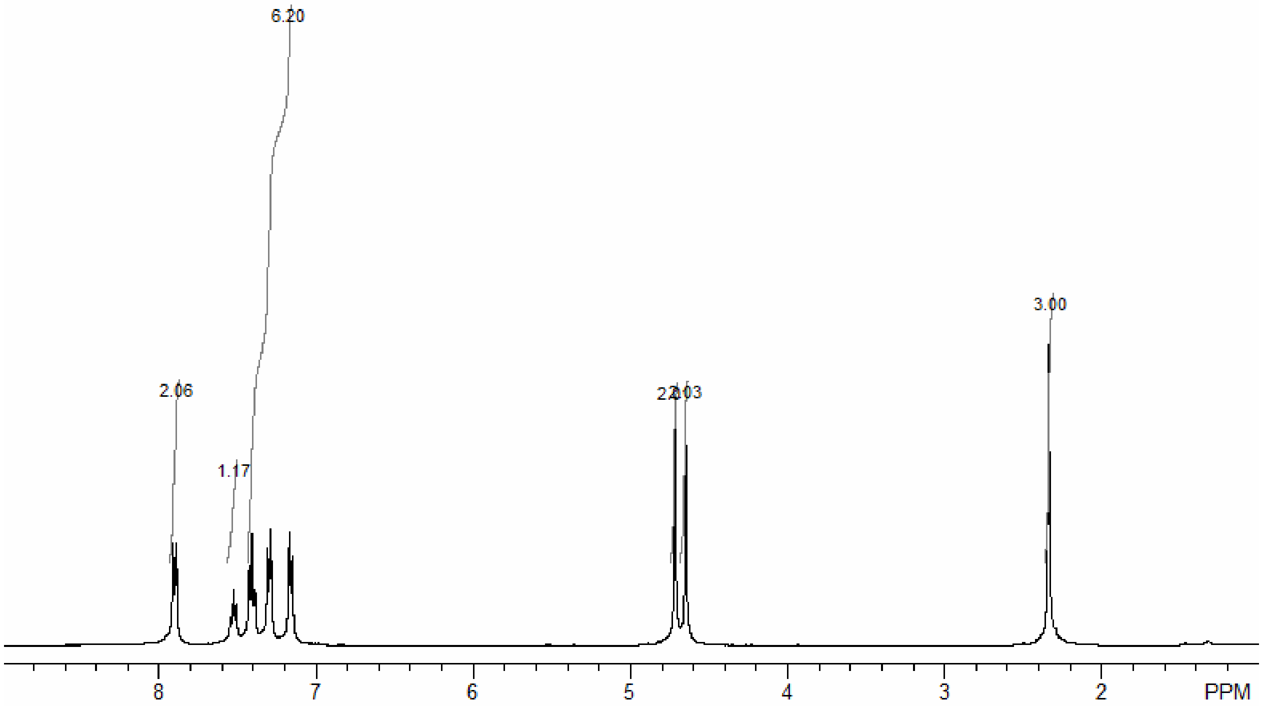
^{13}C NMR, $CDCl_3$, 100MHz

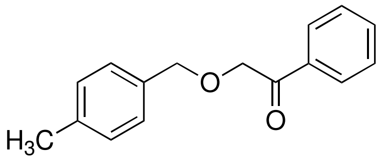




3b

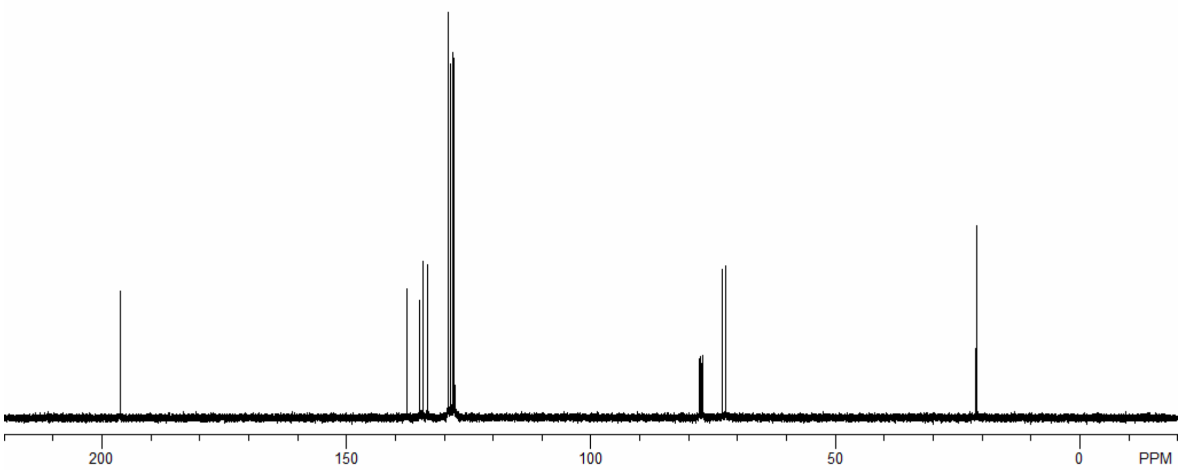
^{1}H NMR, $CDCl_3$, 400MHz

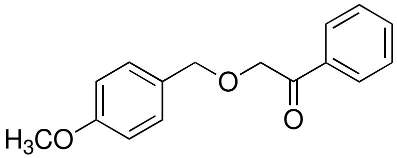




3b

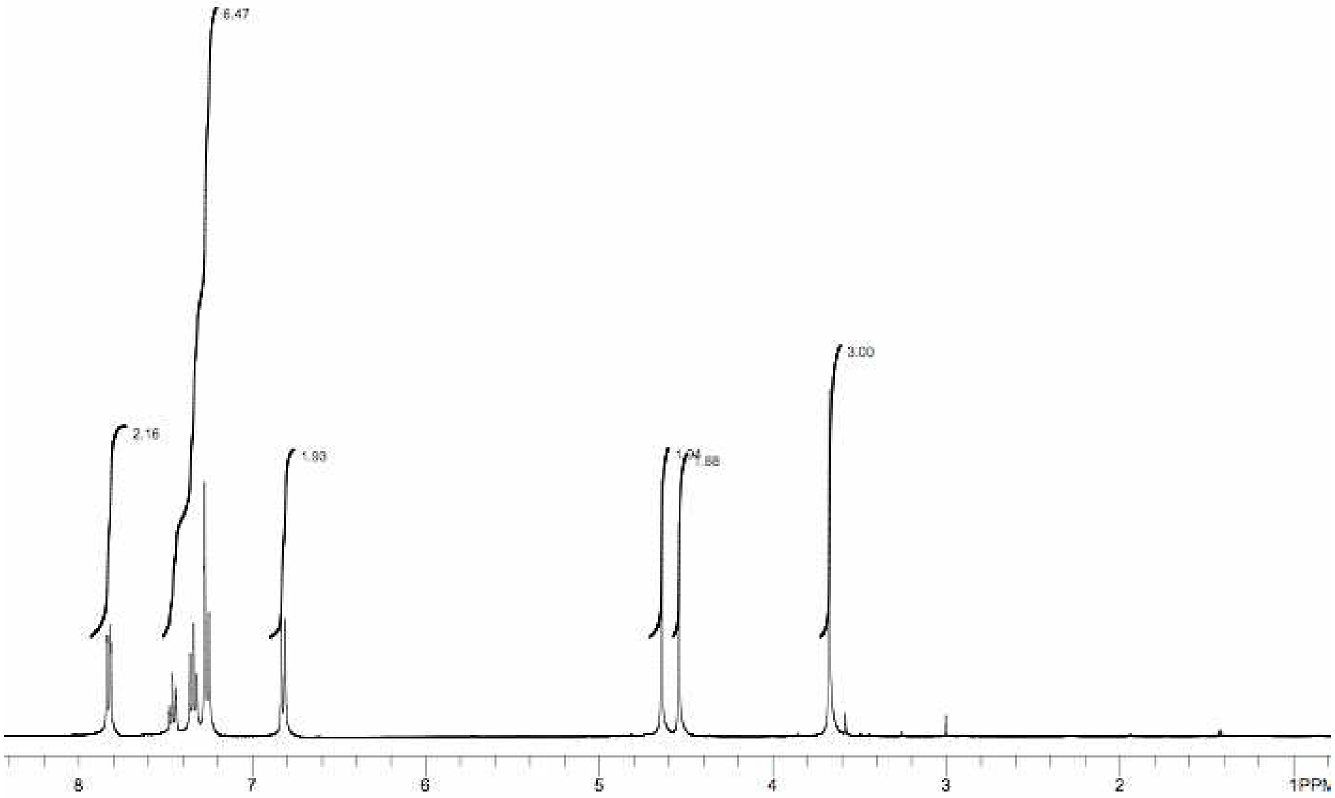
^{13}C NMR, CDCl$_3$, 100MHz

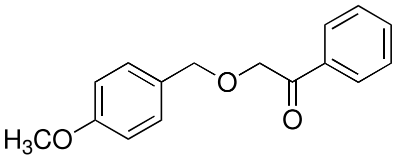




3c

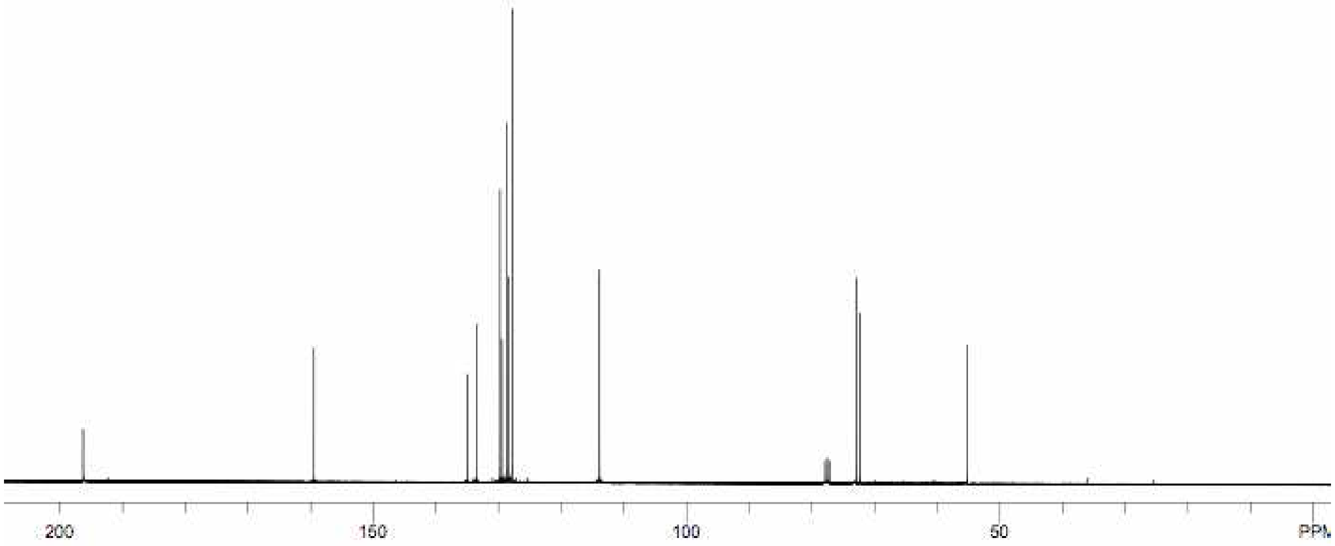
^{1}H NMR, $CDCl_3$, 400MHz

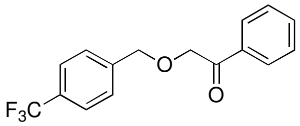




3c

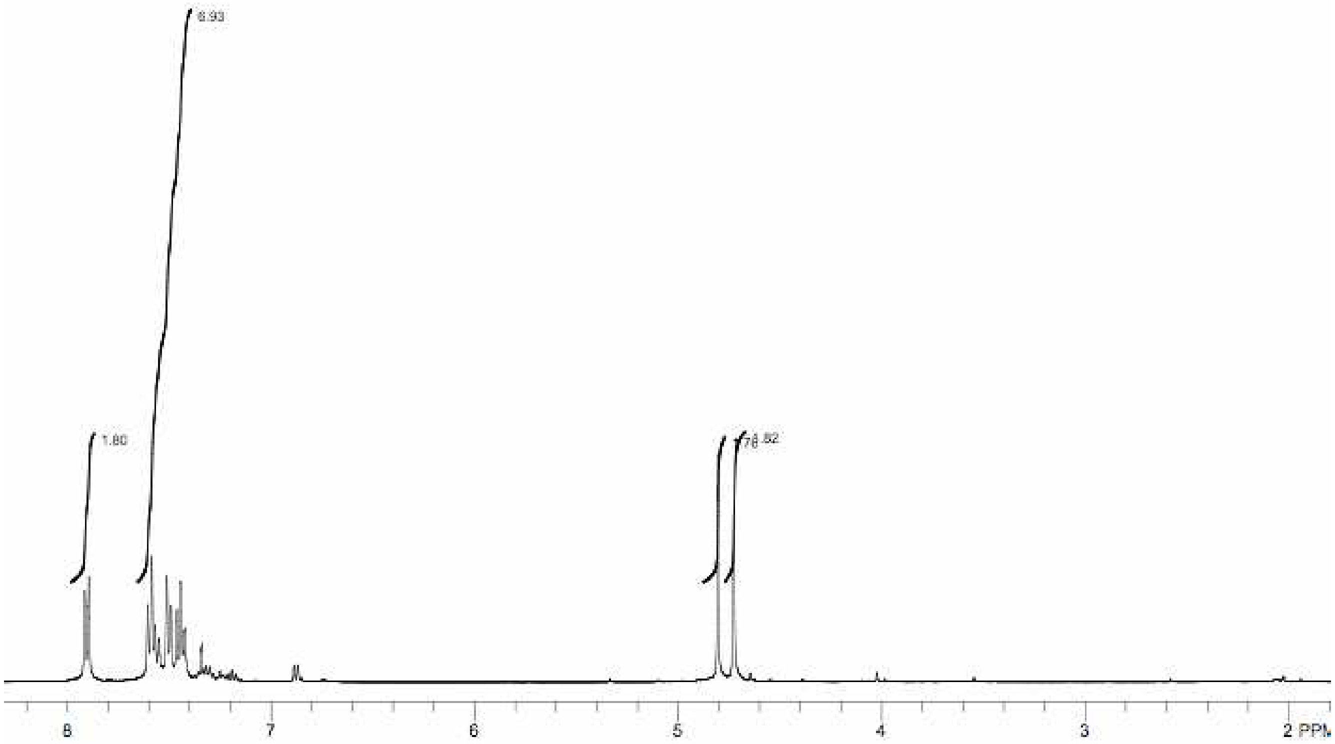
^{13}C NMR, $CDCl_3$, 100MHz

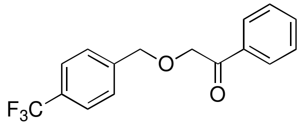




3d

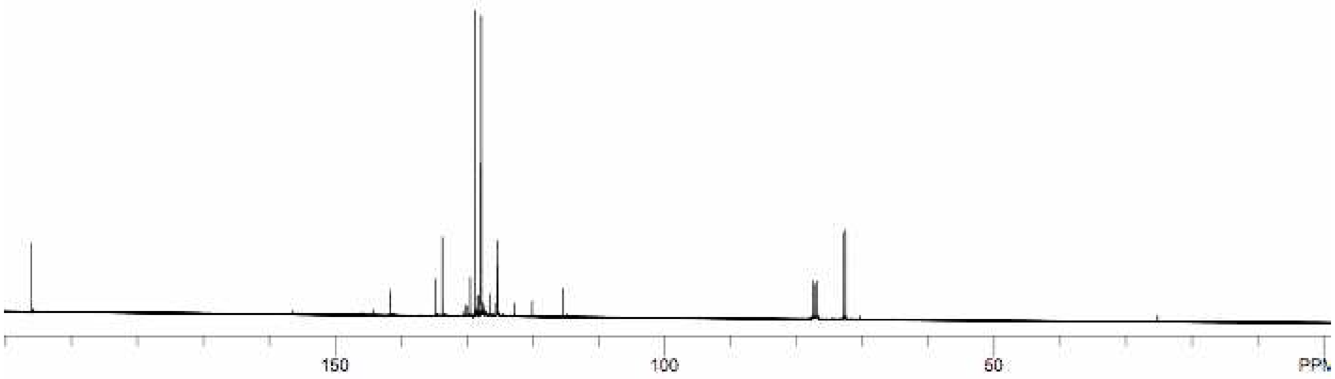
^{1}H NMR, CDCl$_3$, 400MHz

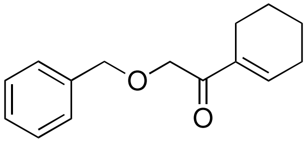




3d

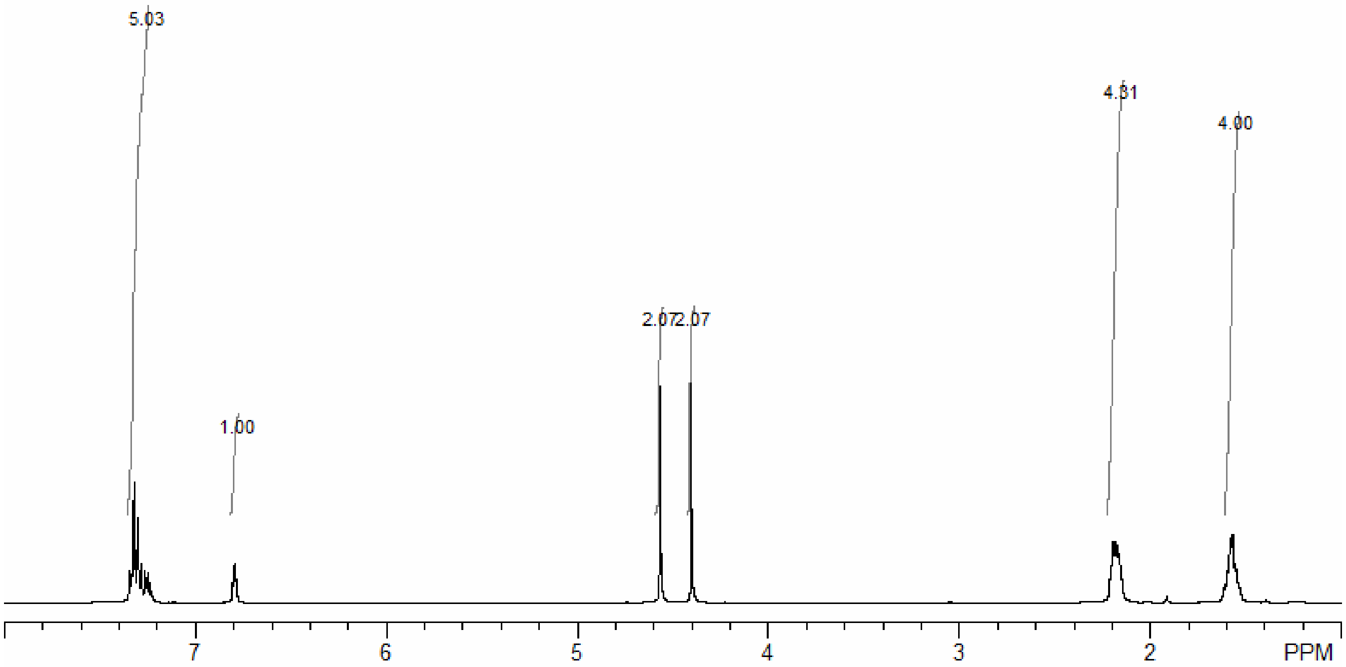
^{13}C NMR, $CDCl_3$, 100MHz

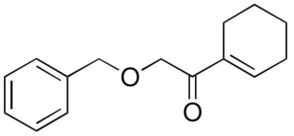




3e

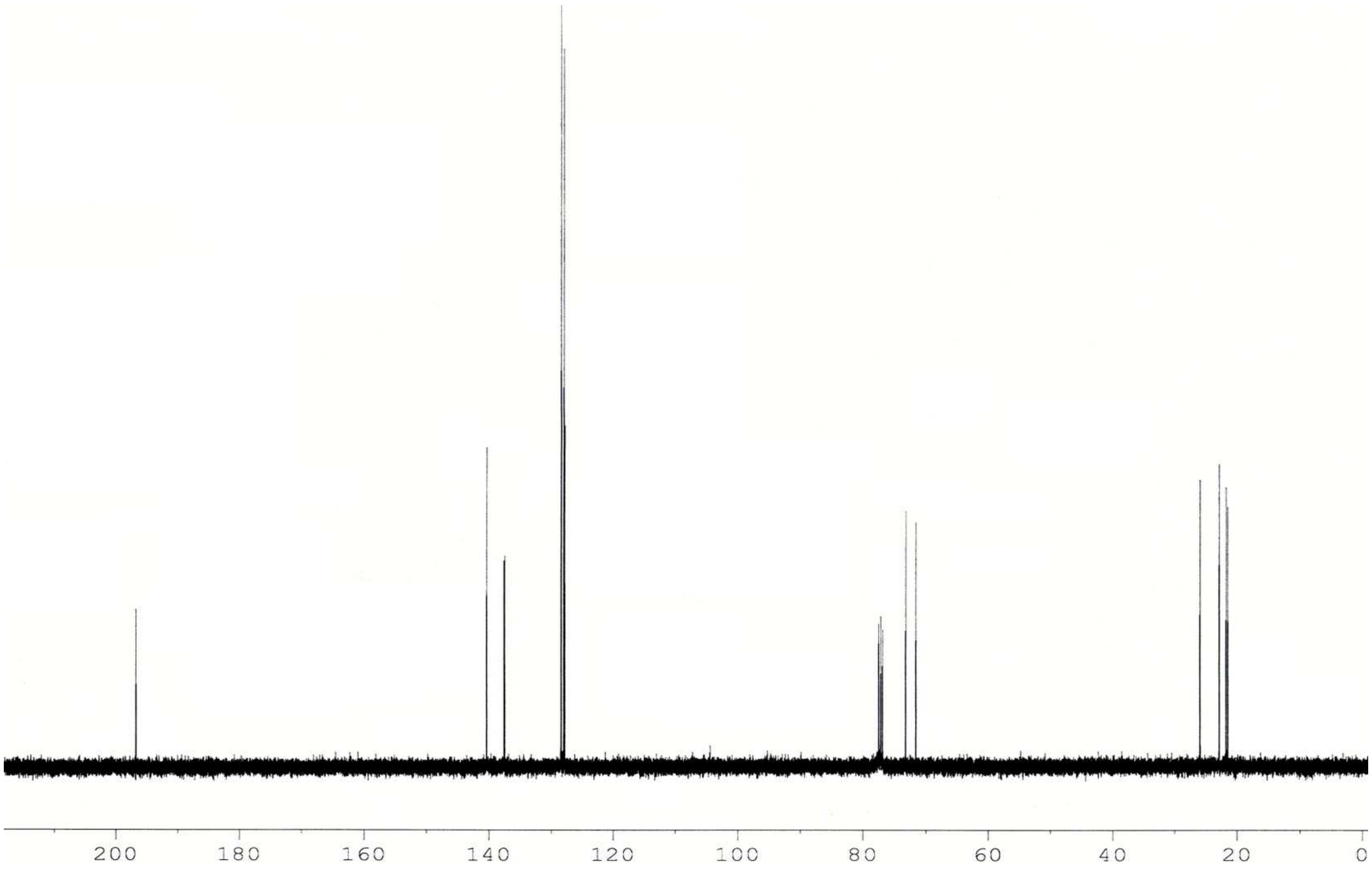
^{1}H NMR, CDCl$_3$, 400MHz

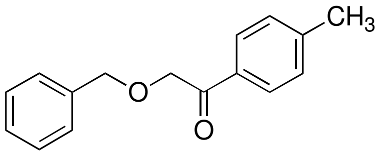




3e

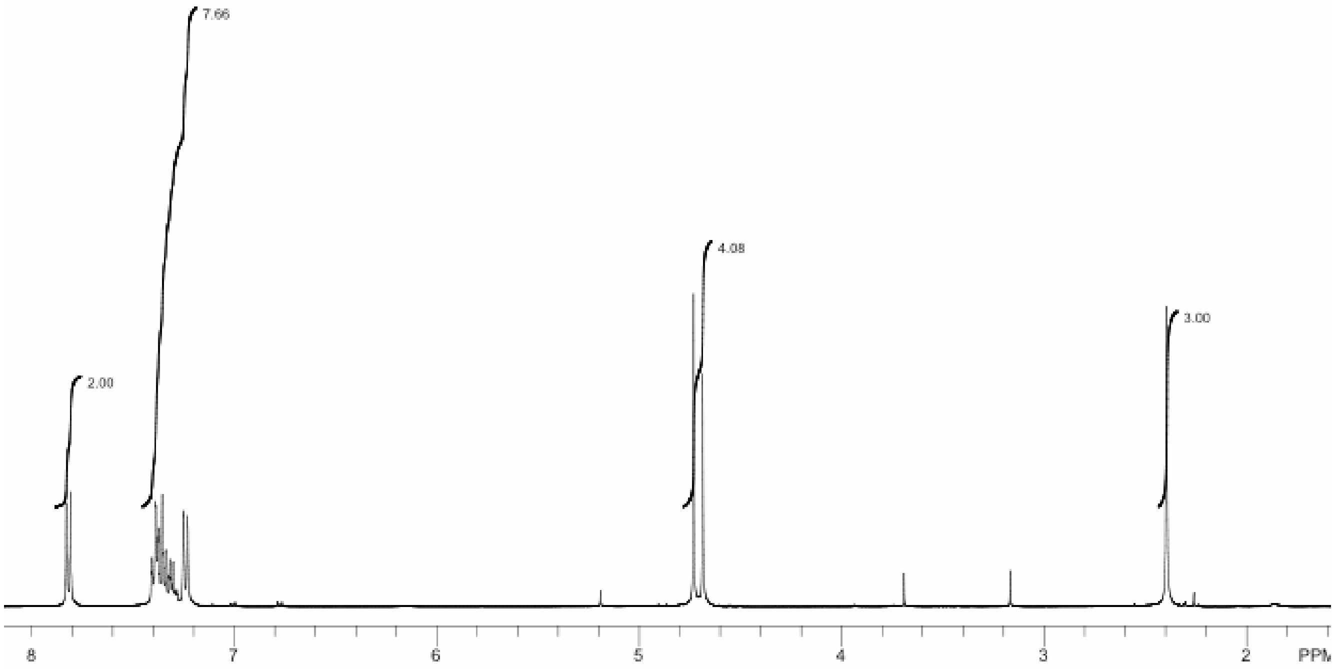
^{13}C NMR, CDCl$_3$, 100MHz

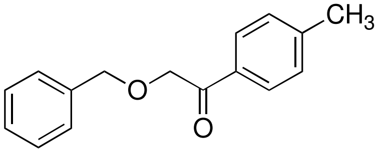




3f

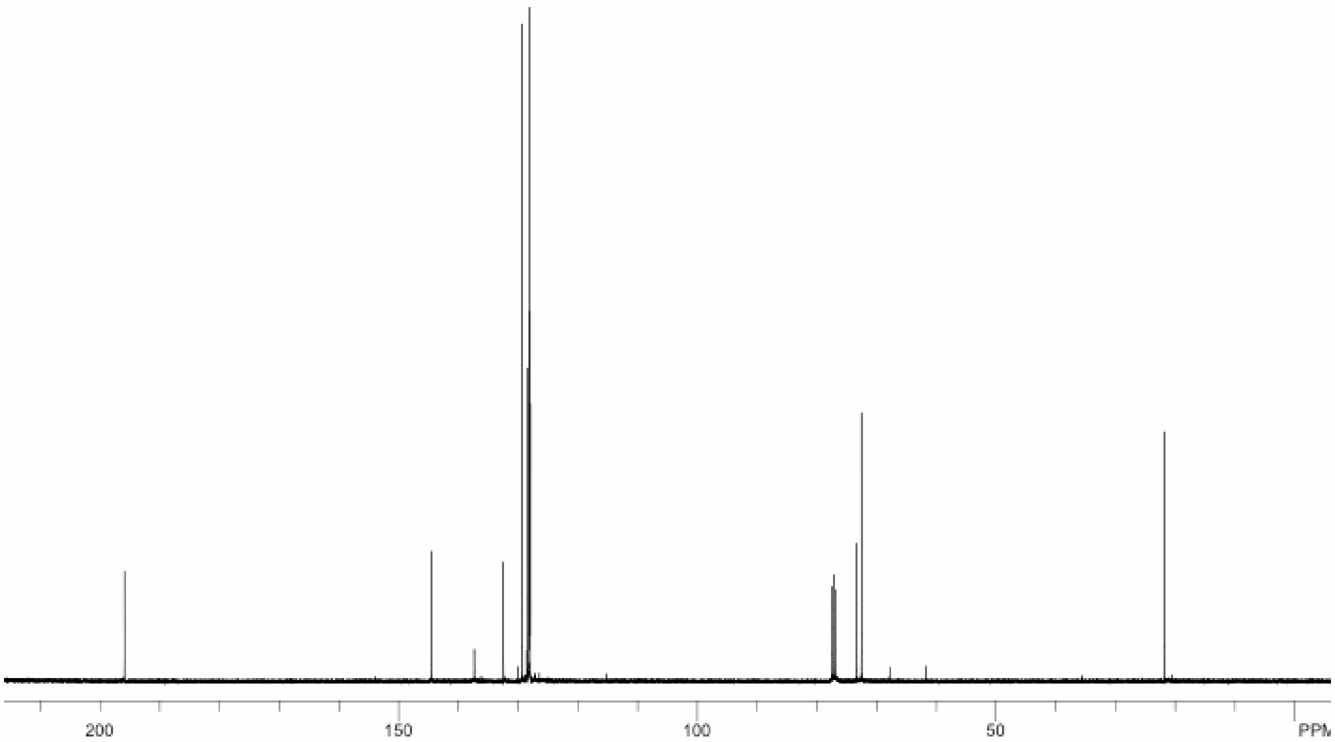
^{1}H NMR, $CDCl_3$, 400MHz

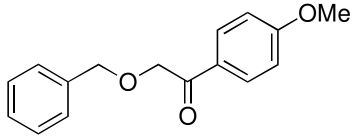




3f

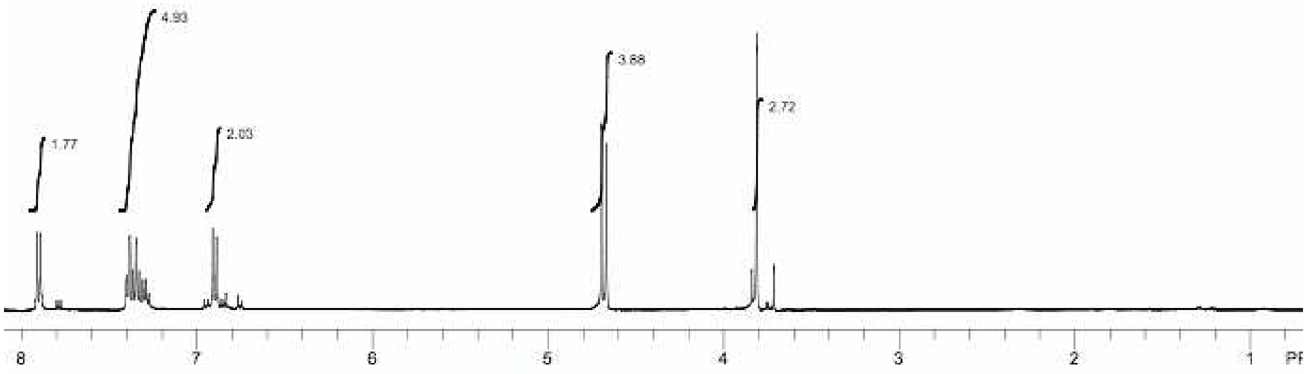
^{13}C NMR, $CDCl_3$, 100MHz

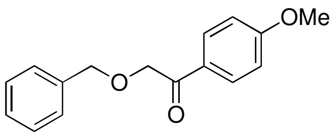




3g

^{1}H NMR, $CDCl_3$, 400MHz





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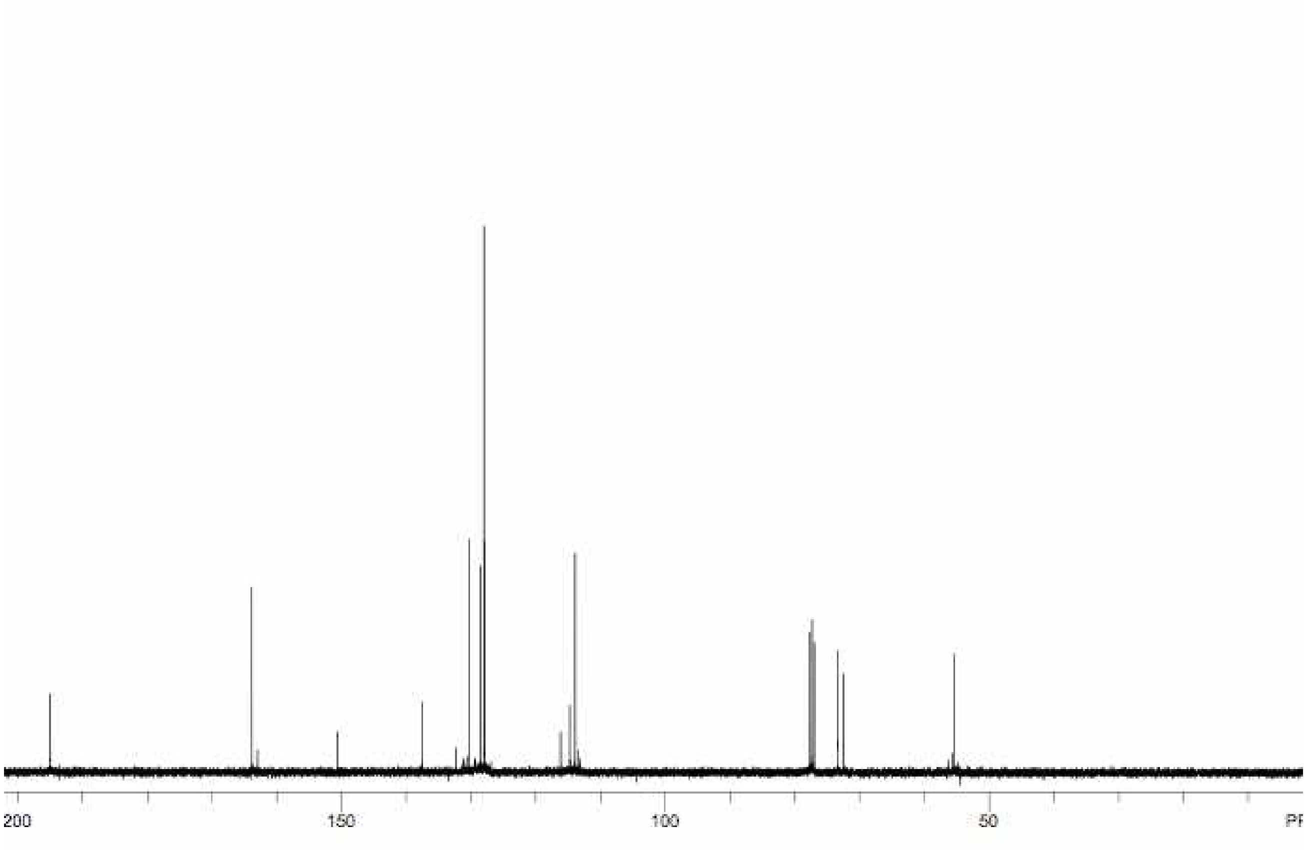
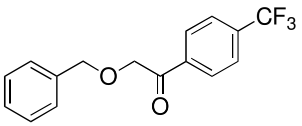
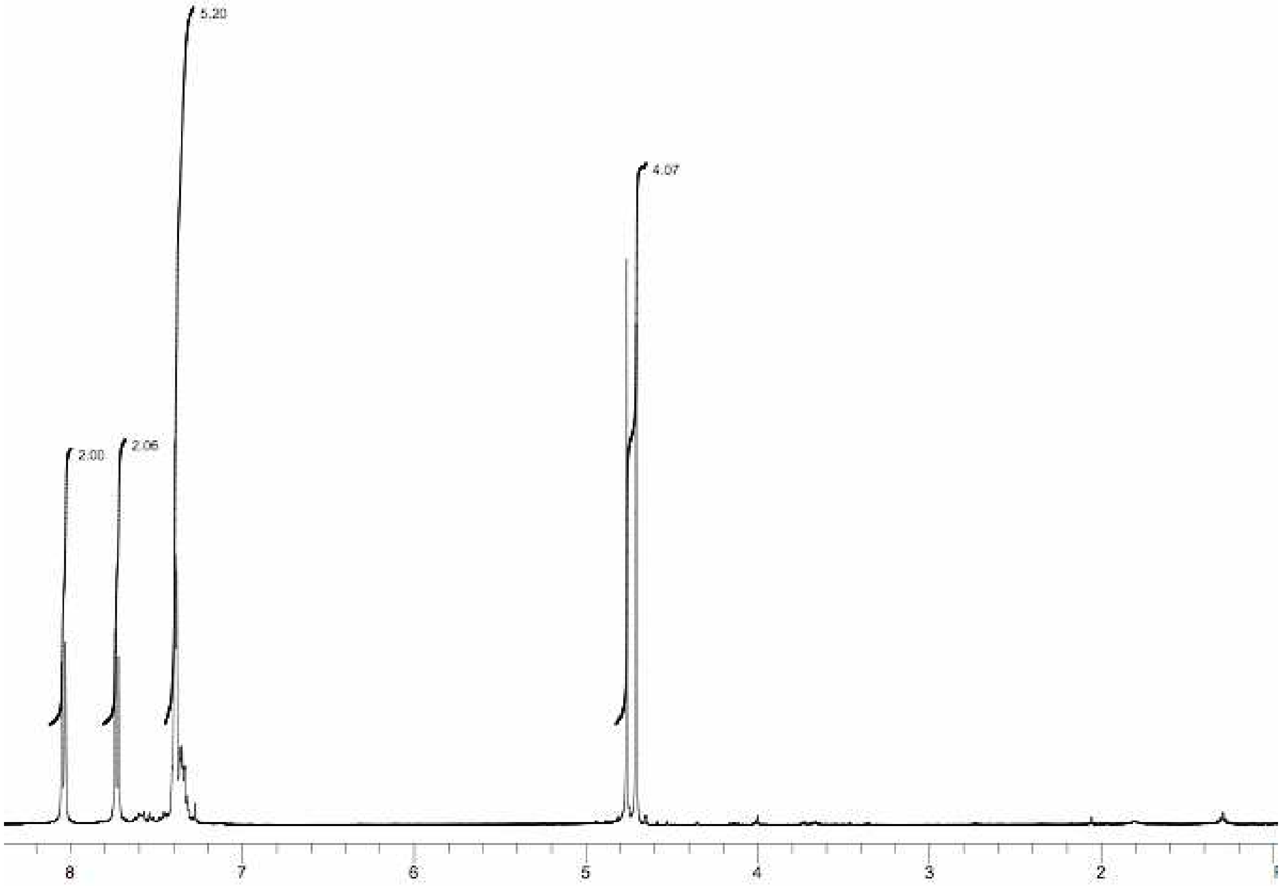
^{13}C NMR, CDCl$_3$, 100MHz

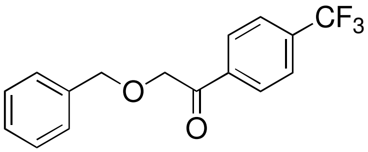




3h

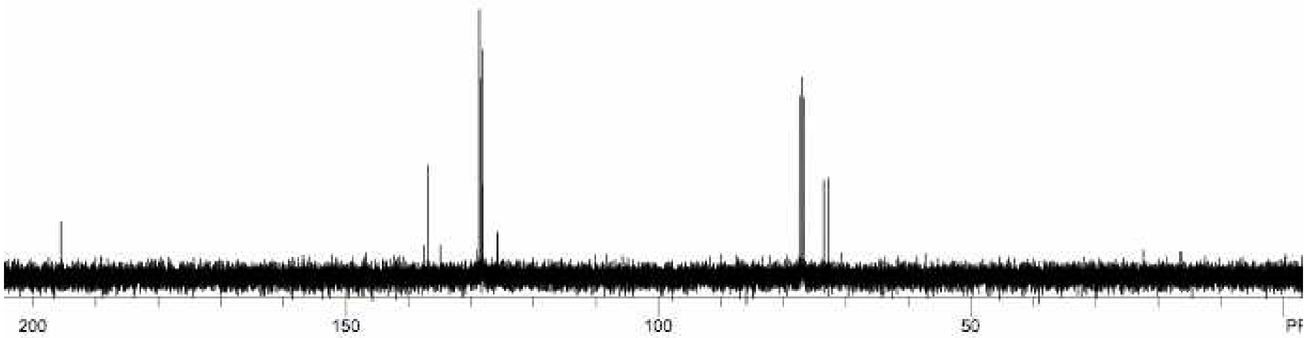
^{1}H NMR, CDCl$_3$, 400MHz

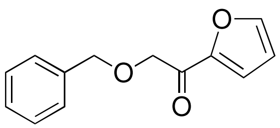




3h

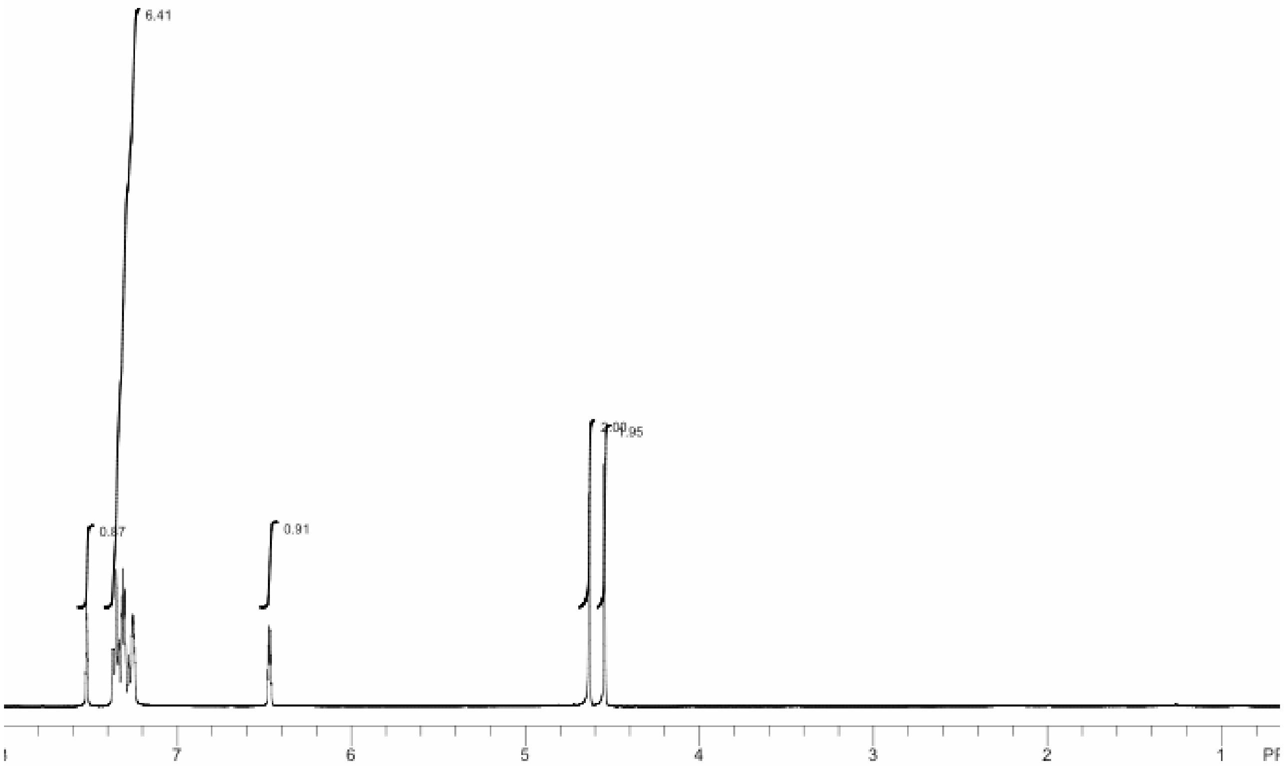
^{13}C NMR, $CDCl_3$, 100MHz

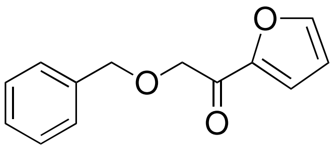




3i

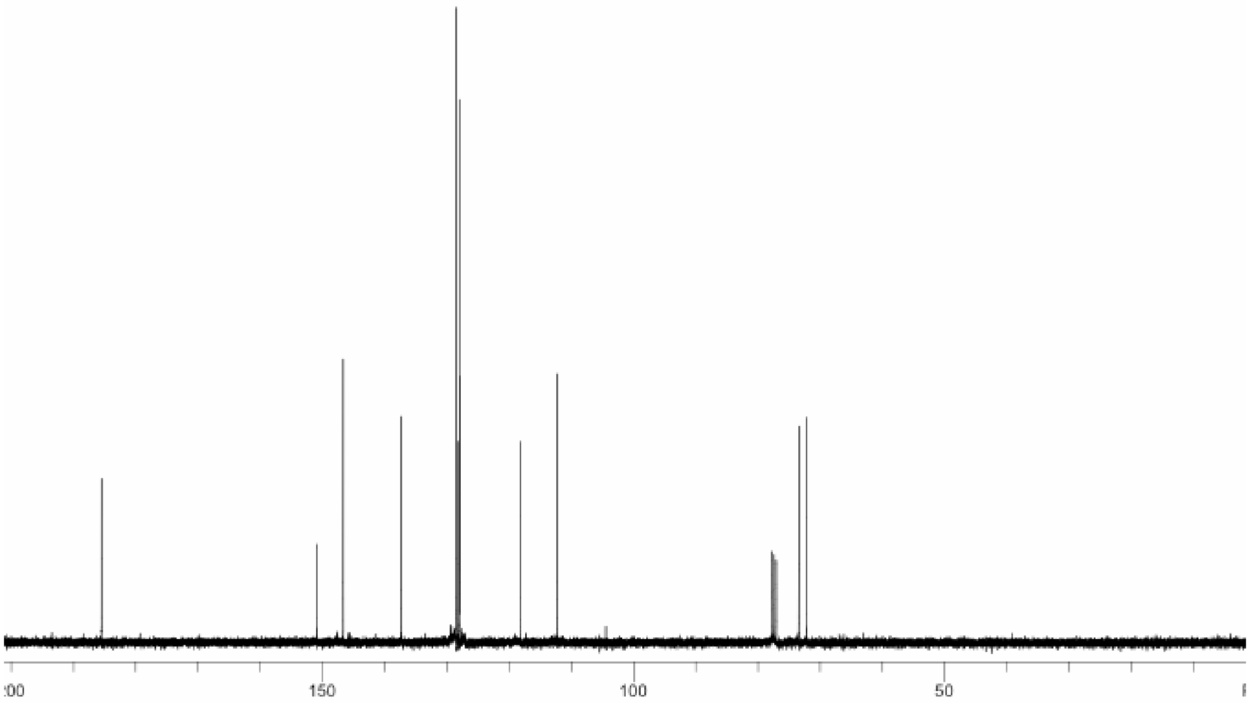
^{1}H NMR, $CDCl_3$, 400MHz

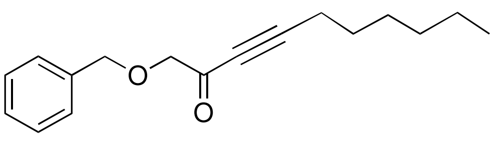




3i

^{13}C NMR, CDCl$_3$, 100MHz





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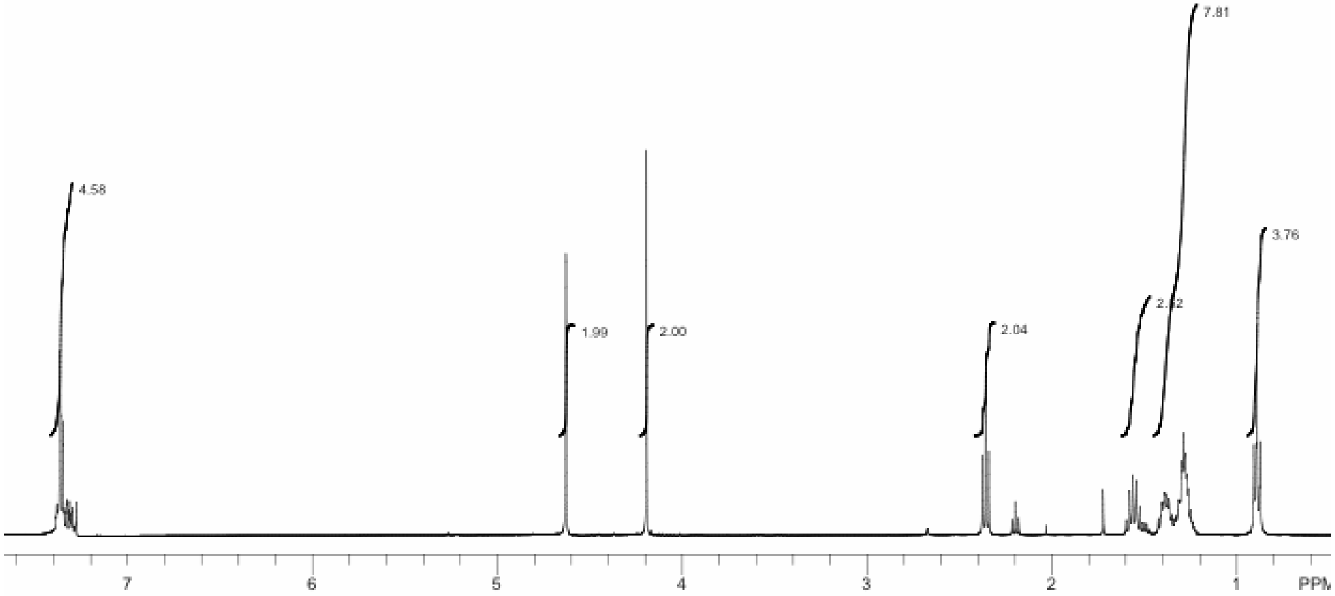

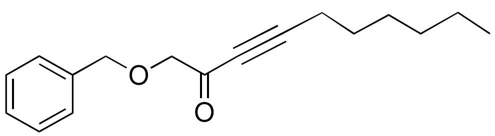

3j

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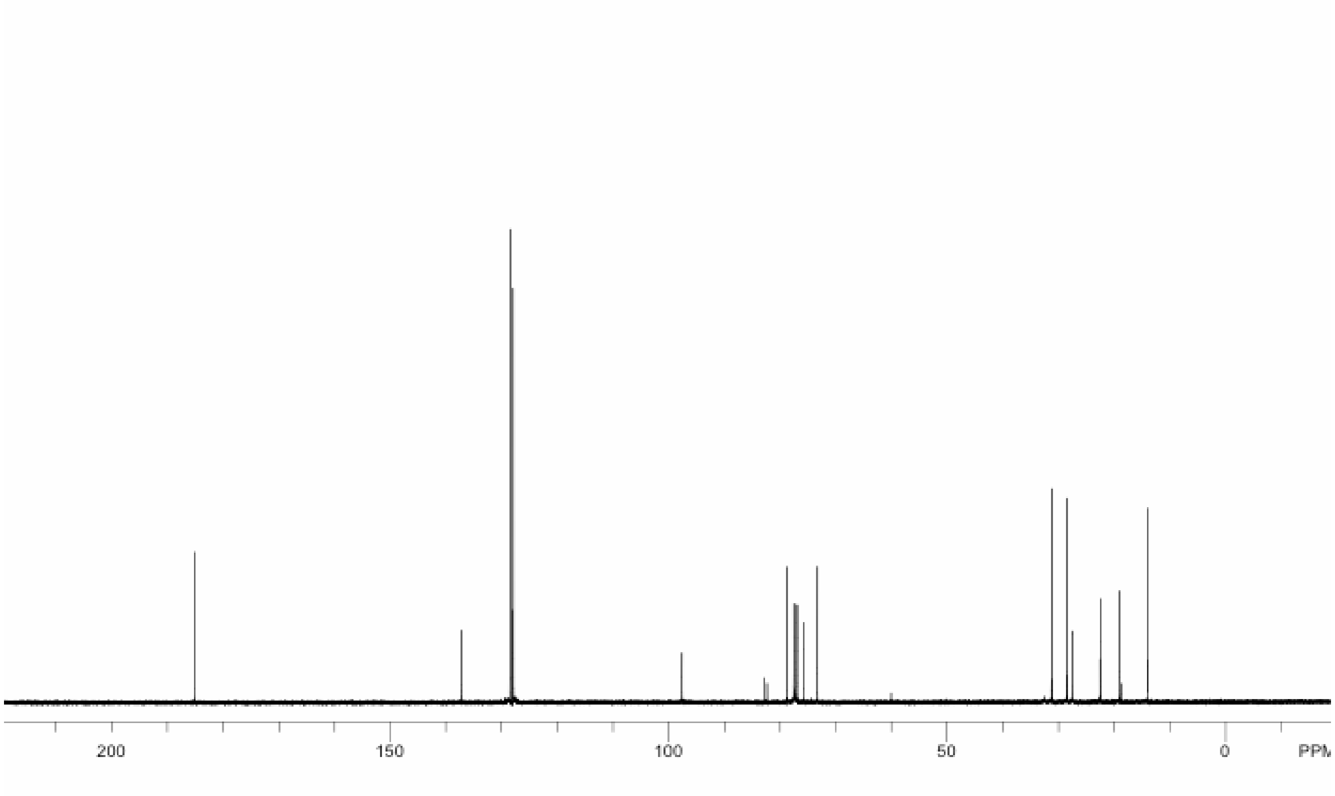
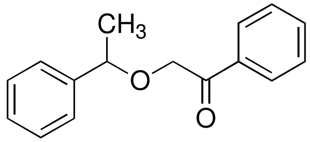
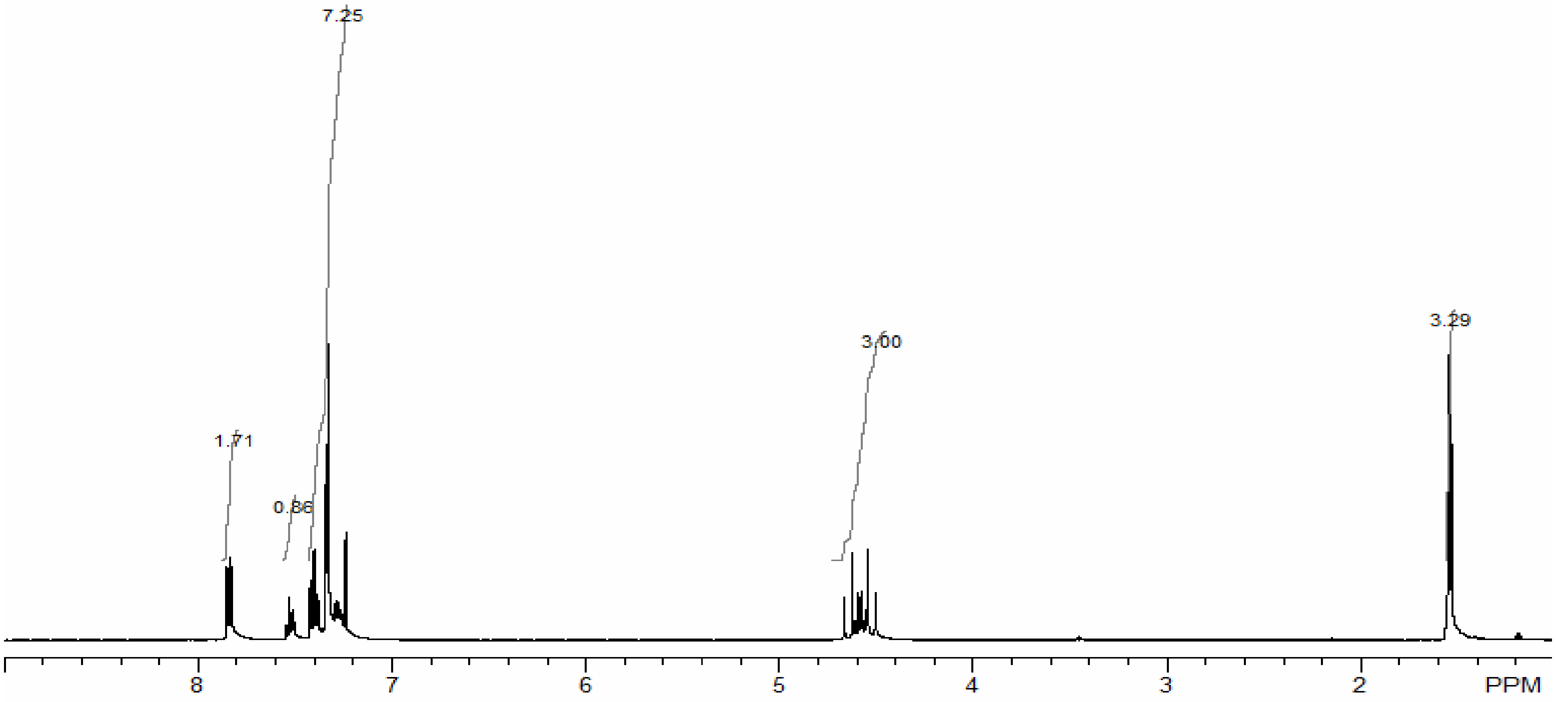
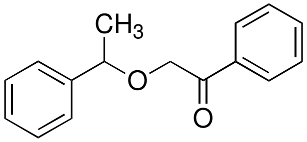




14a

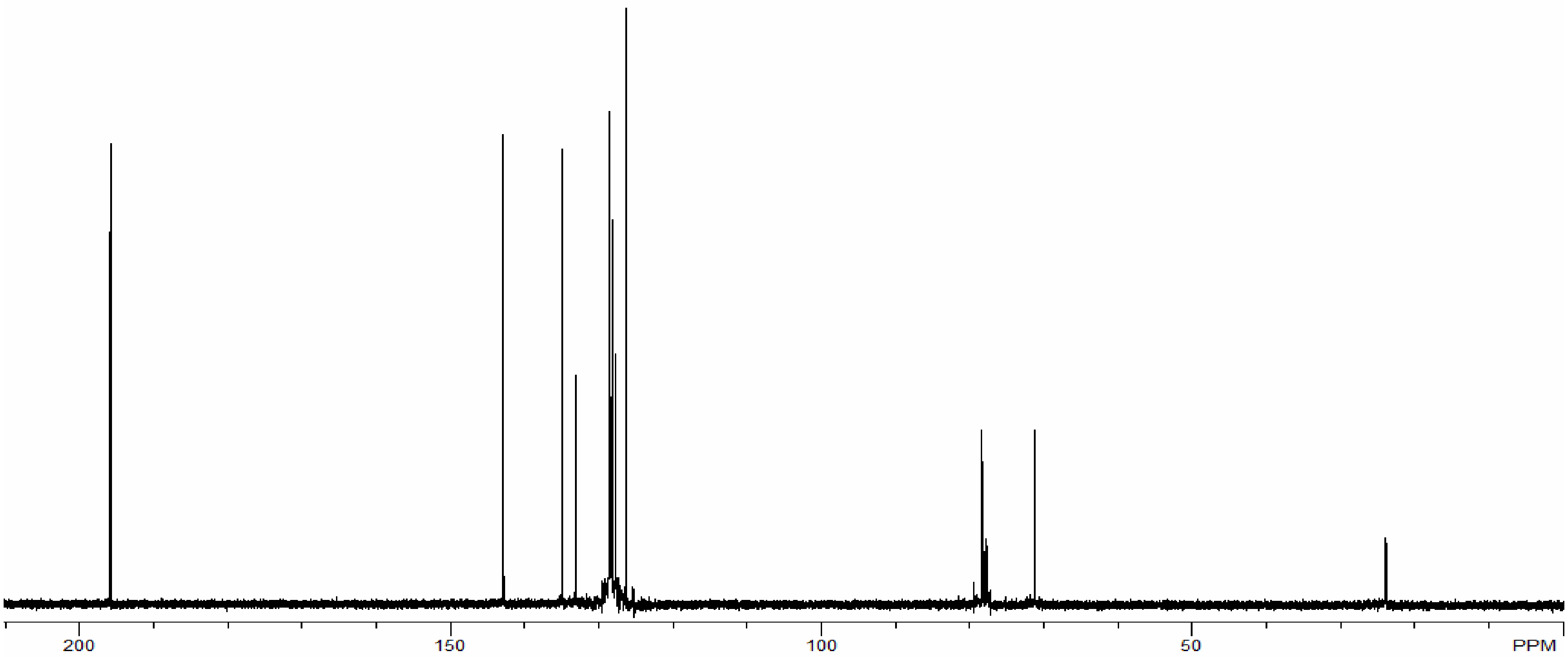
^{1}H NMR, CDCl$_3$, 400MHz

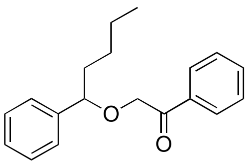




14a

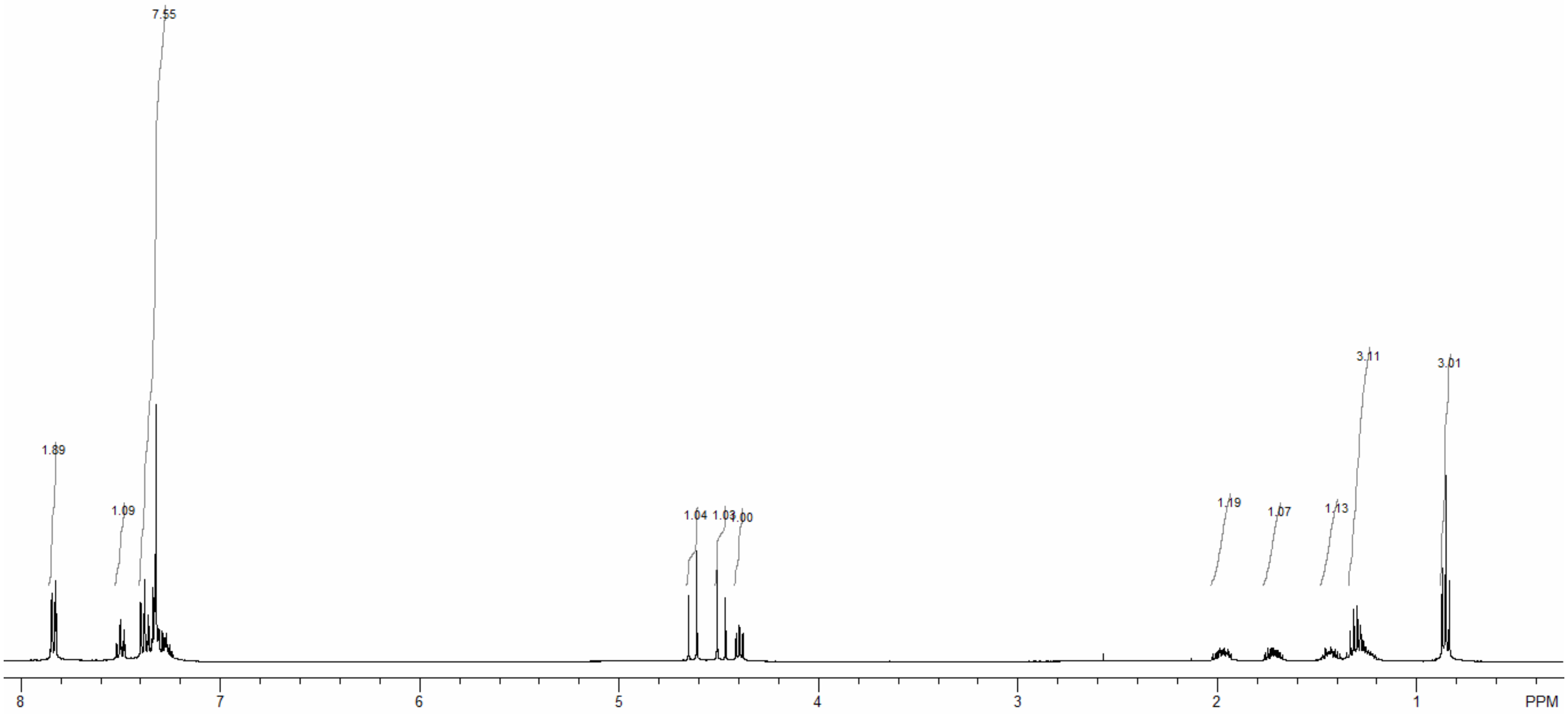
^{13}C NMR, CDCl$_3$, 100MHz

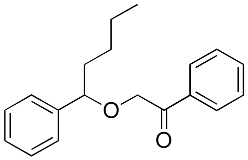




14b

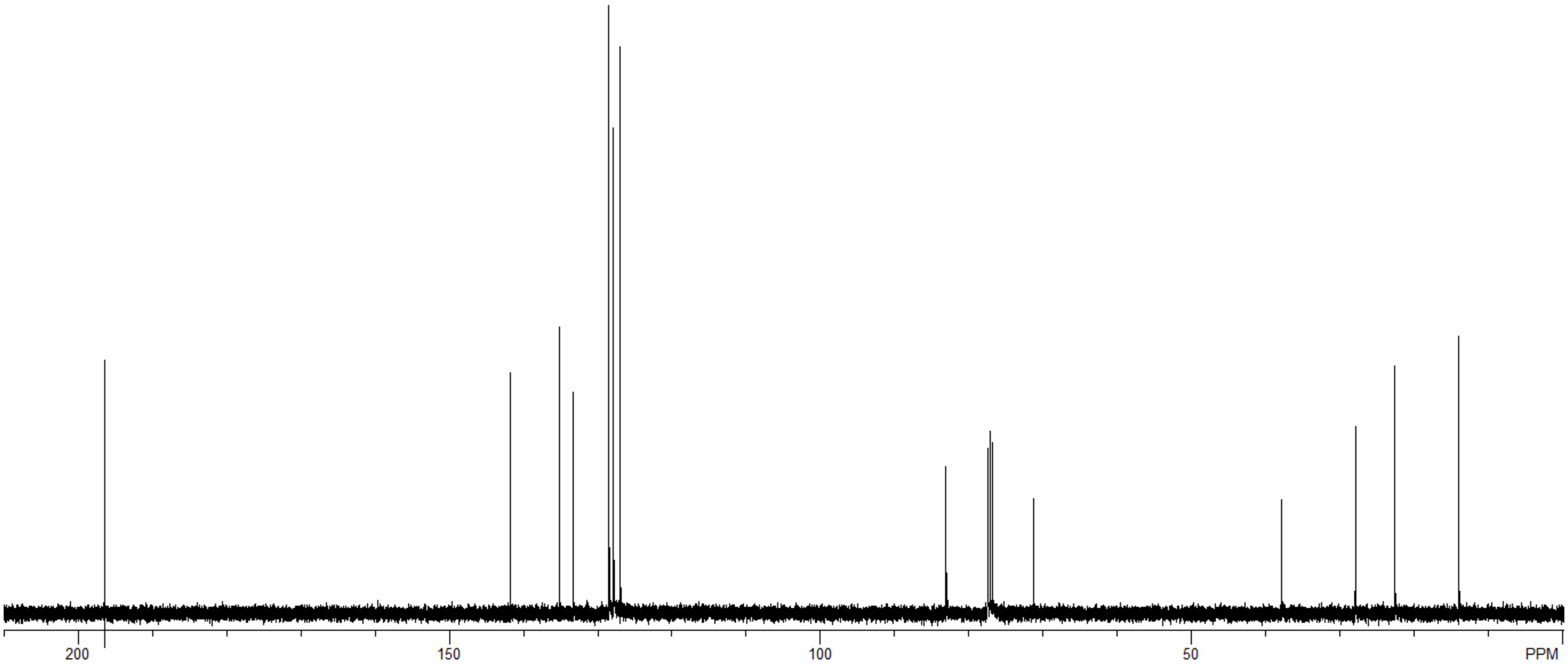
^{1}H NMR, CDCl$_3$, 400MHz

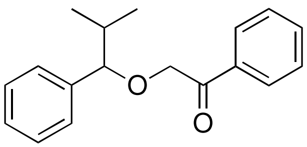




14b

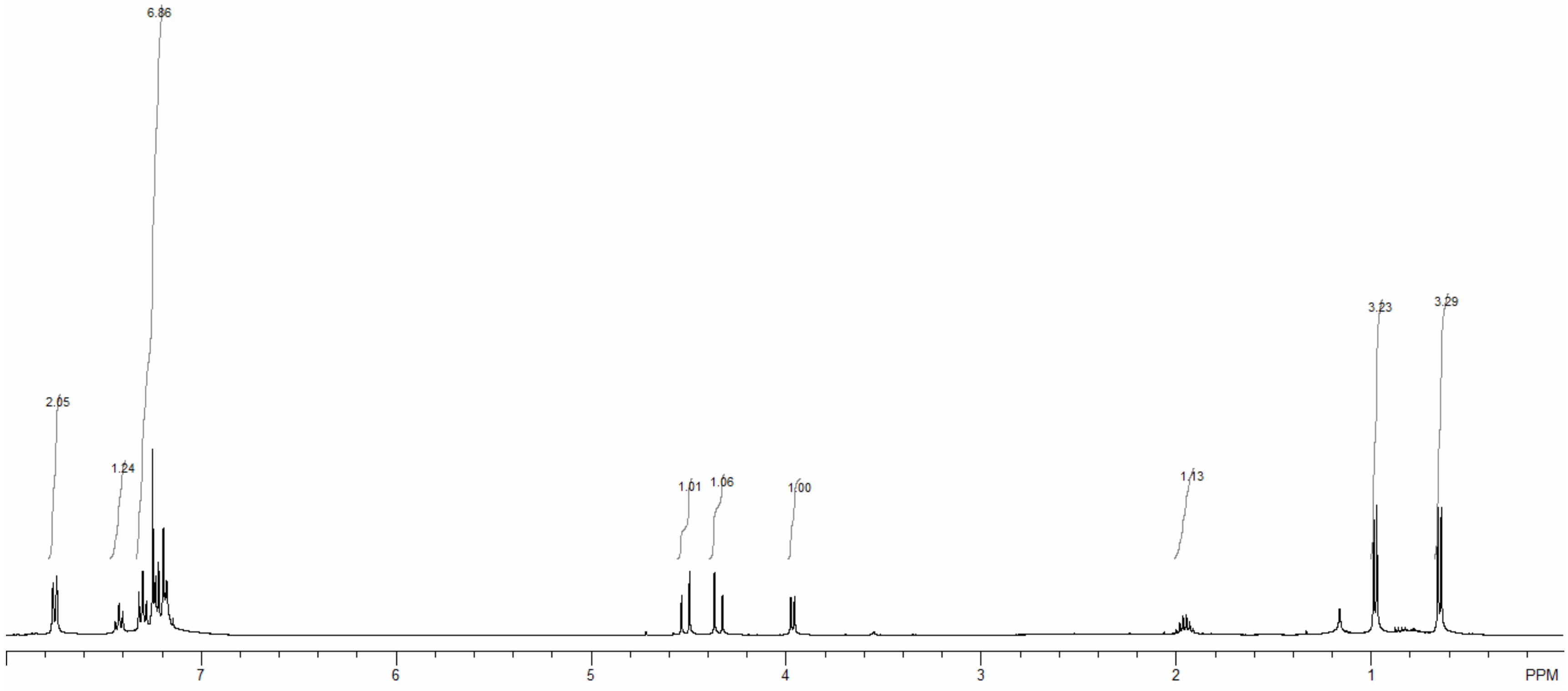
^{13}C NMR, CDCl$_3$, 100MHz

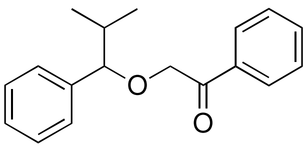




14c

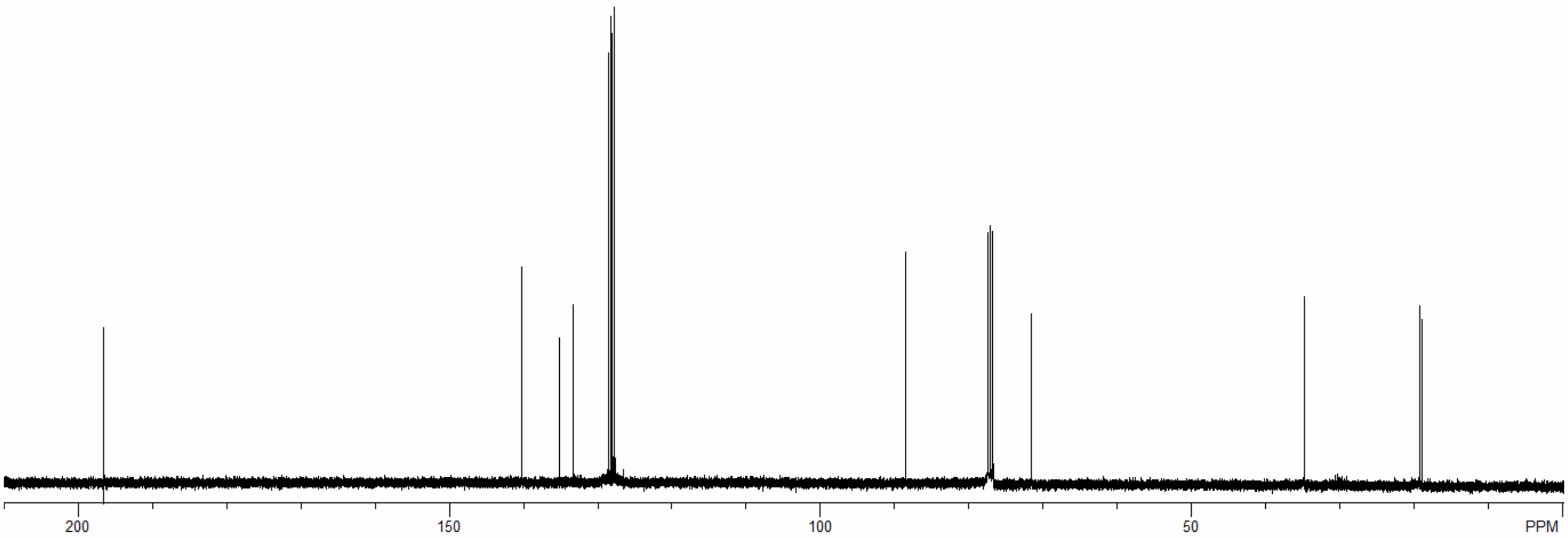
^{1}H NMR, $CDCl_3$, 400MHz

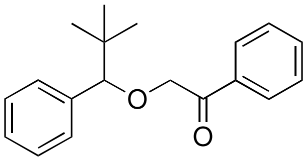




14c

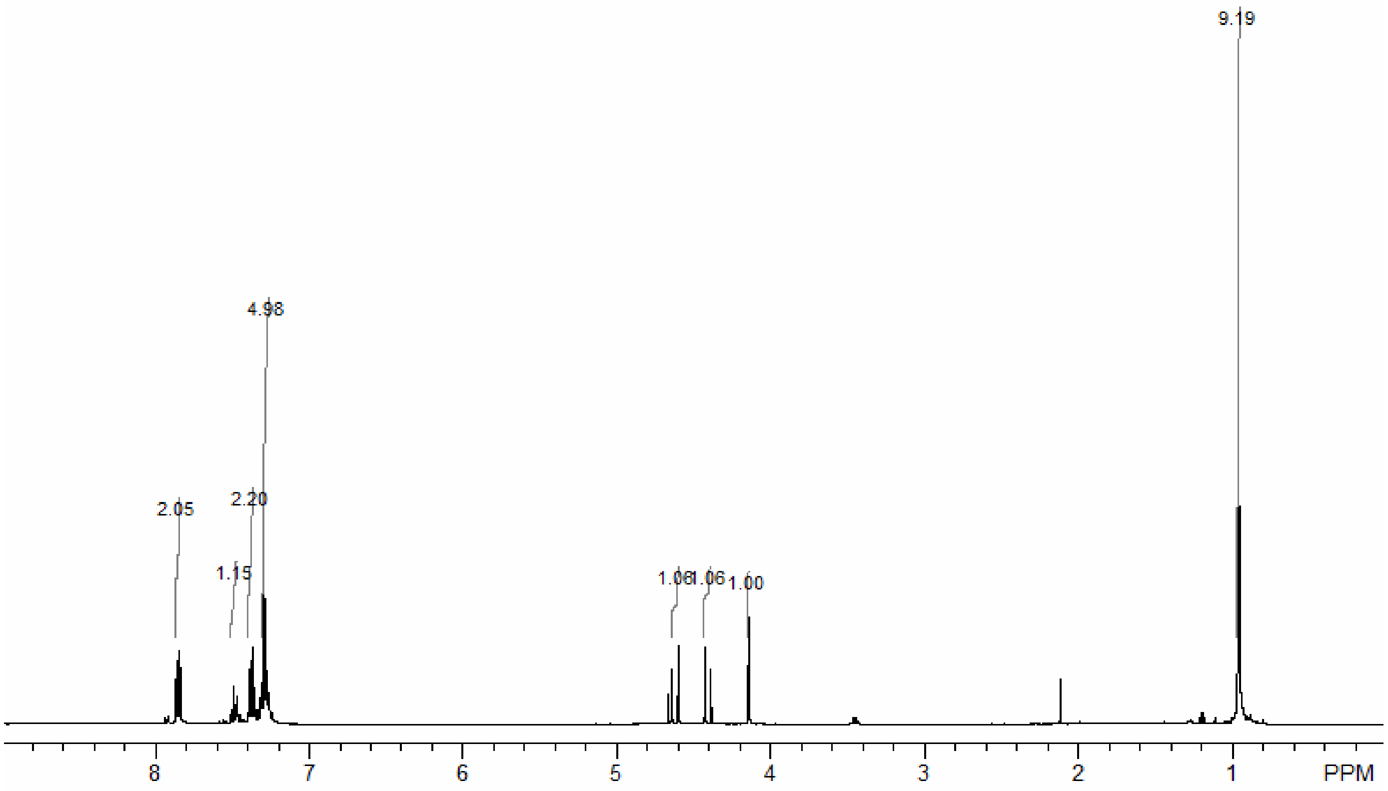
^{13}C NMR, $CDCl_3$, 100MHz

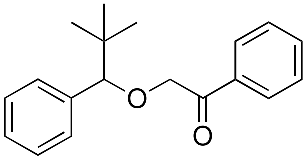




14d

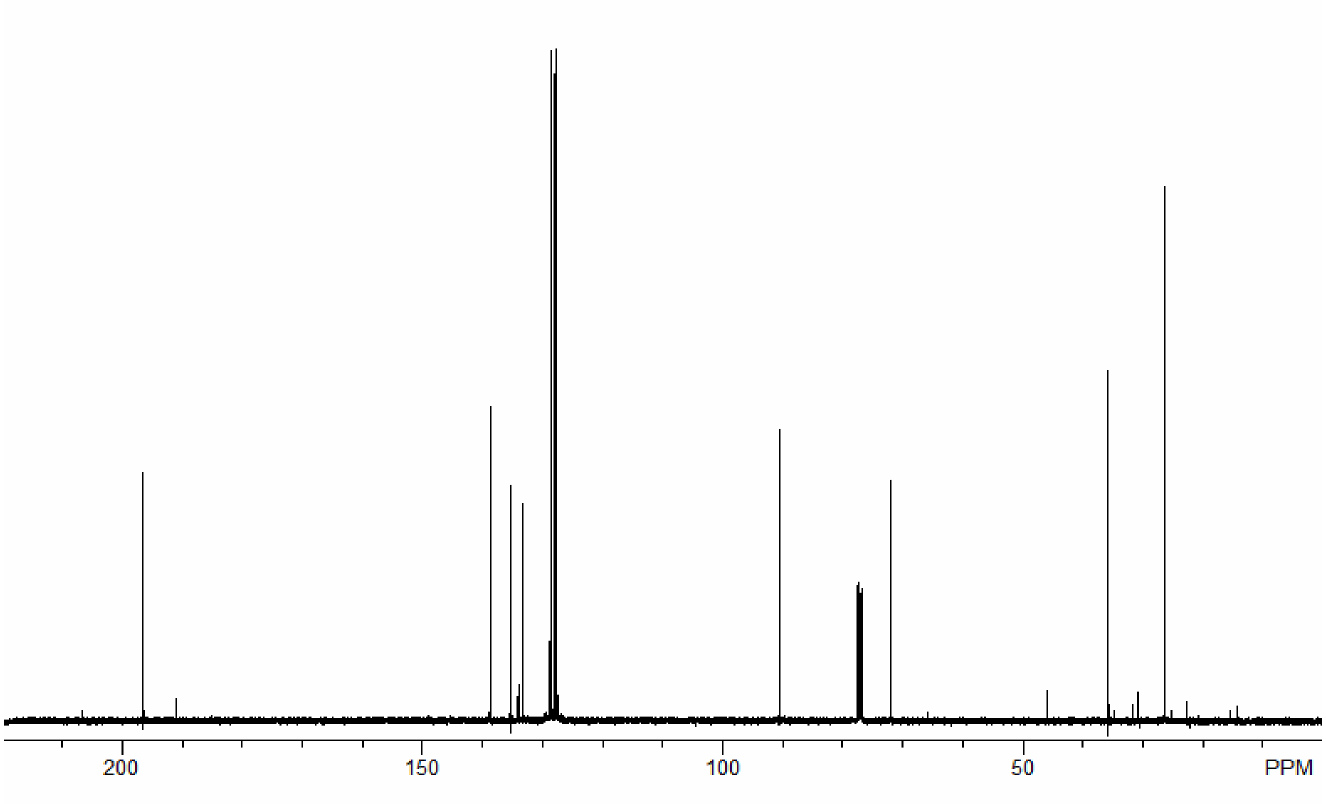
^{1}H NMR, CDCl$_3$, 400MHz

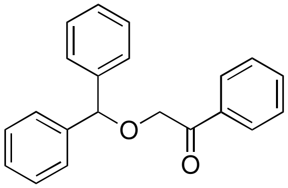




14d

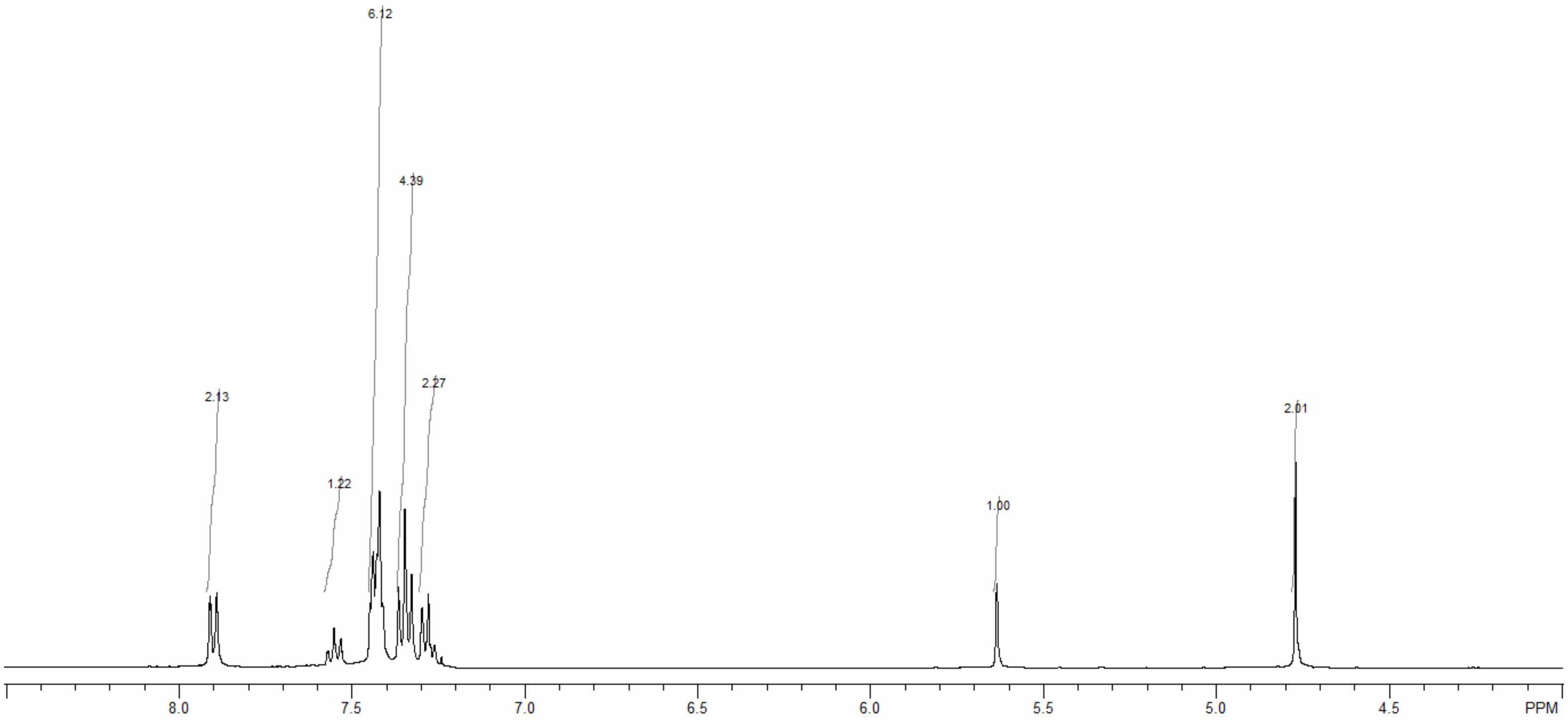
^{13}C NMR, CDCl$_3$, 100MHz

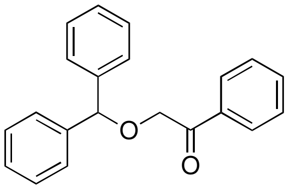




14e

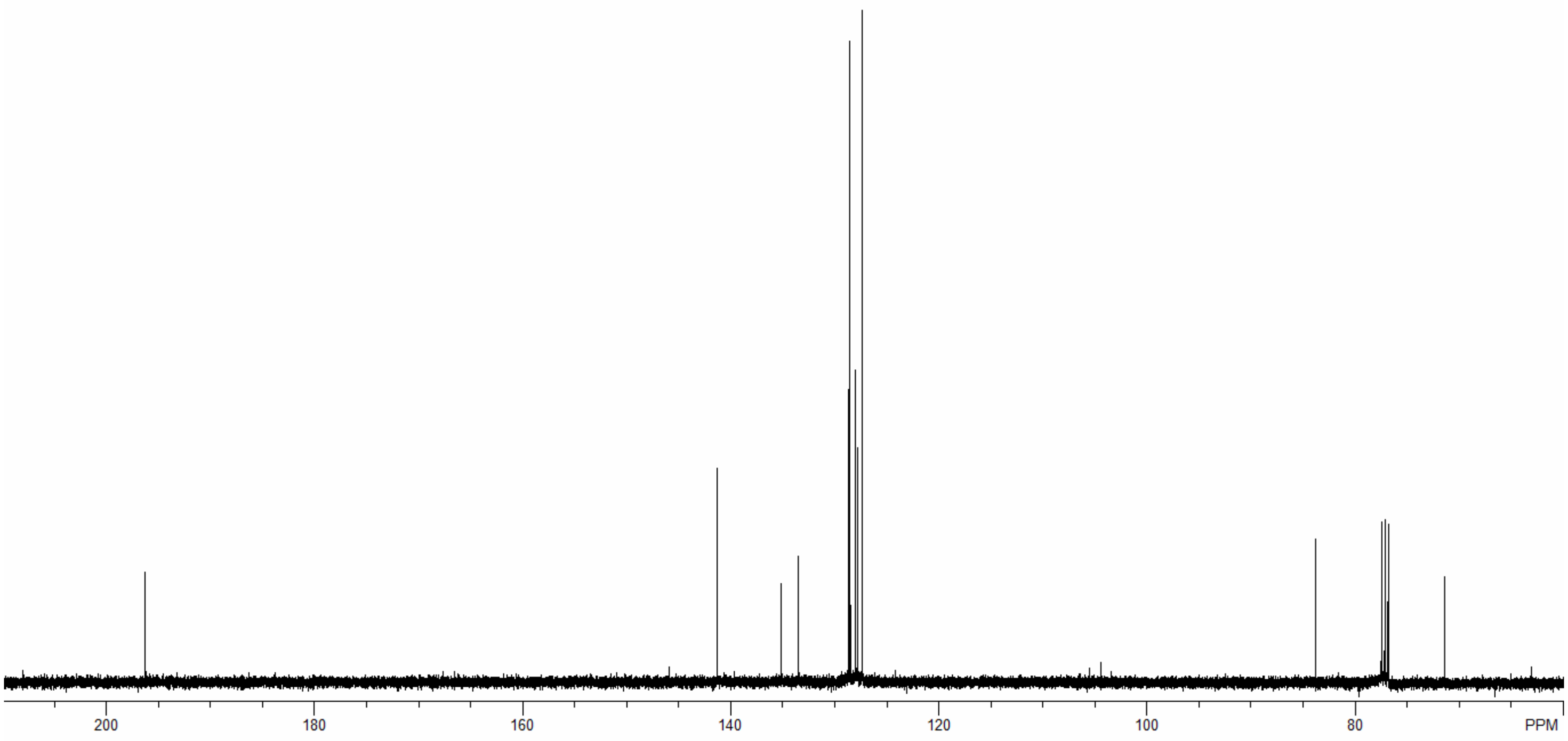
^{1}H NMR, CDCl$_3$, 400MHz

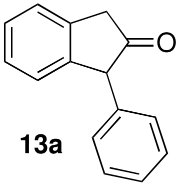




14e

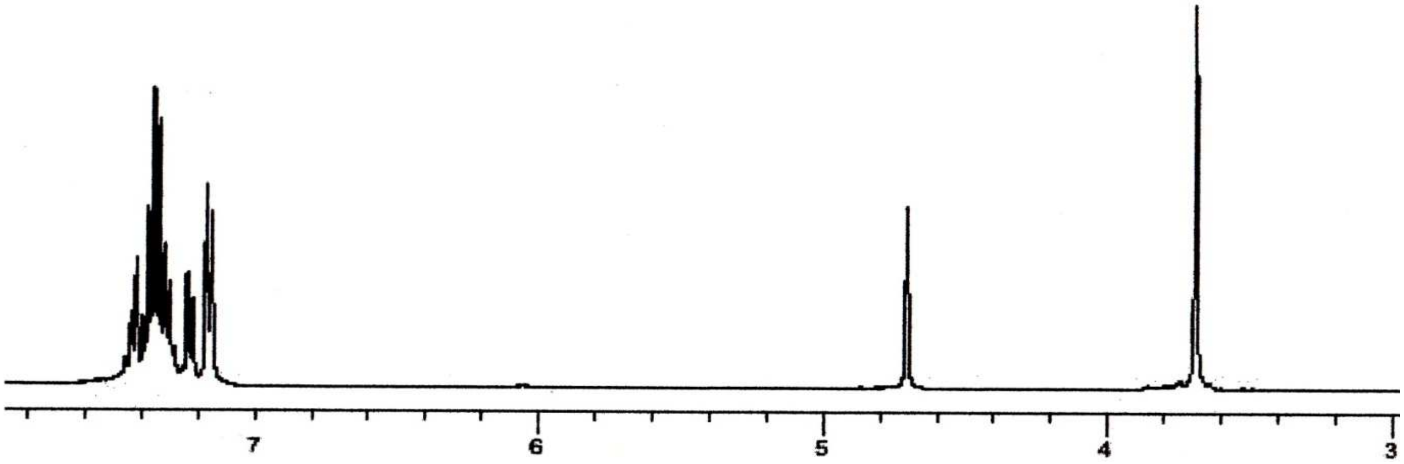
^{13}C NMR, CDCl$_3$, 100MHz

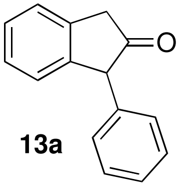




13a

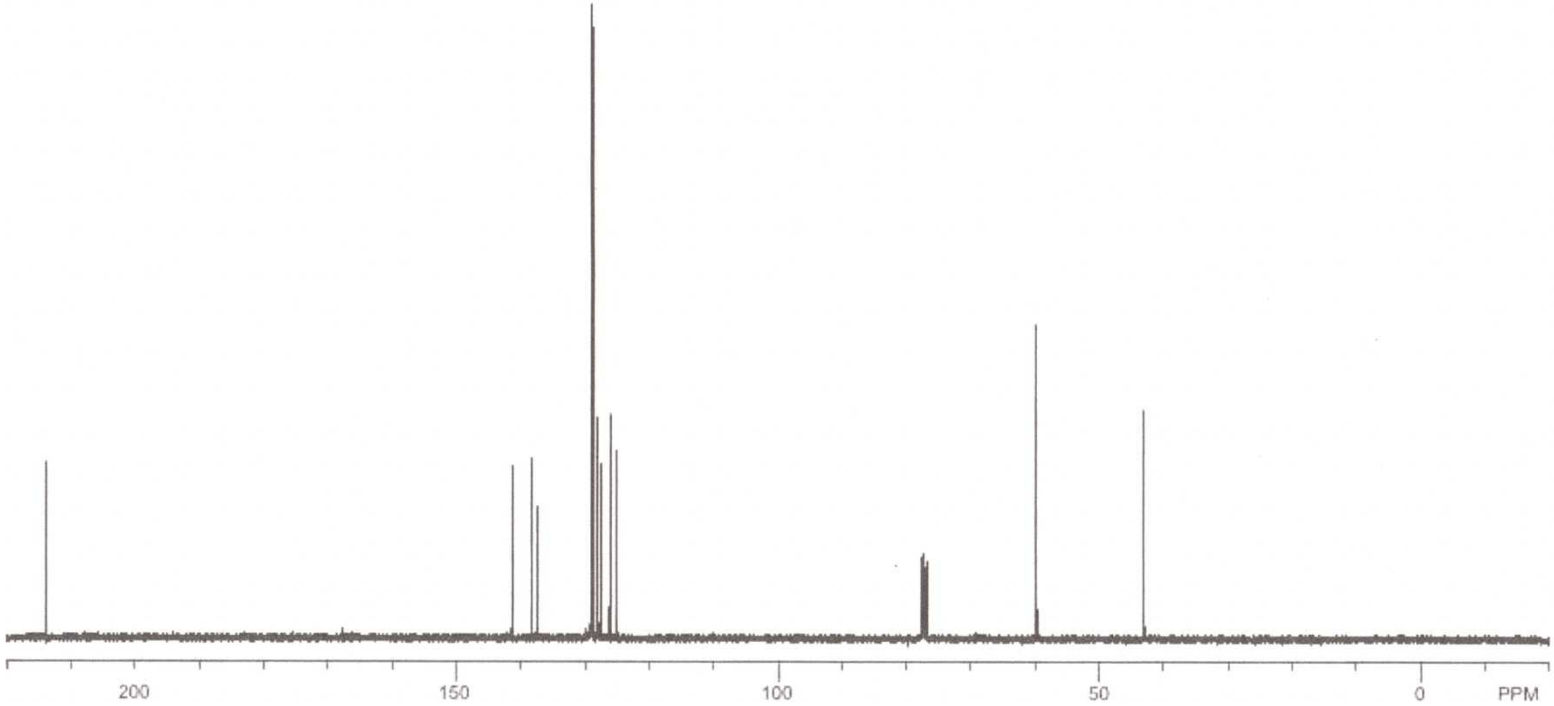
^{1}H NMR, $CDCl_3$, 400MHz

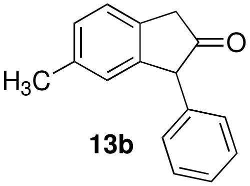




13a

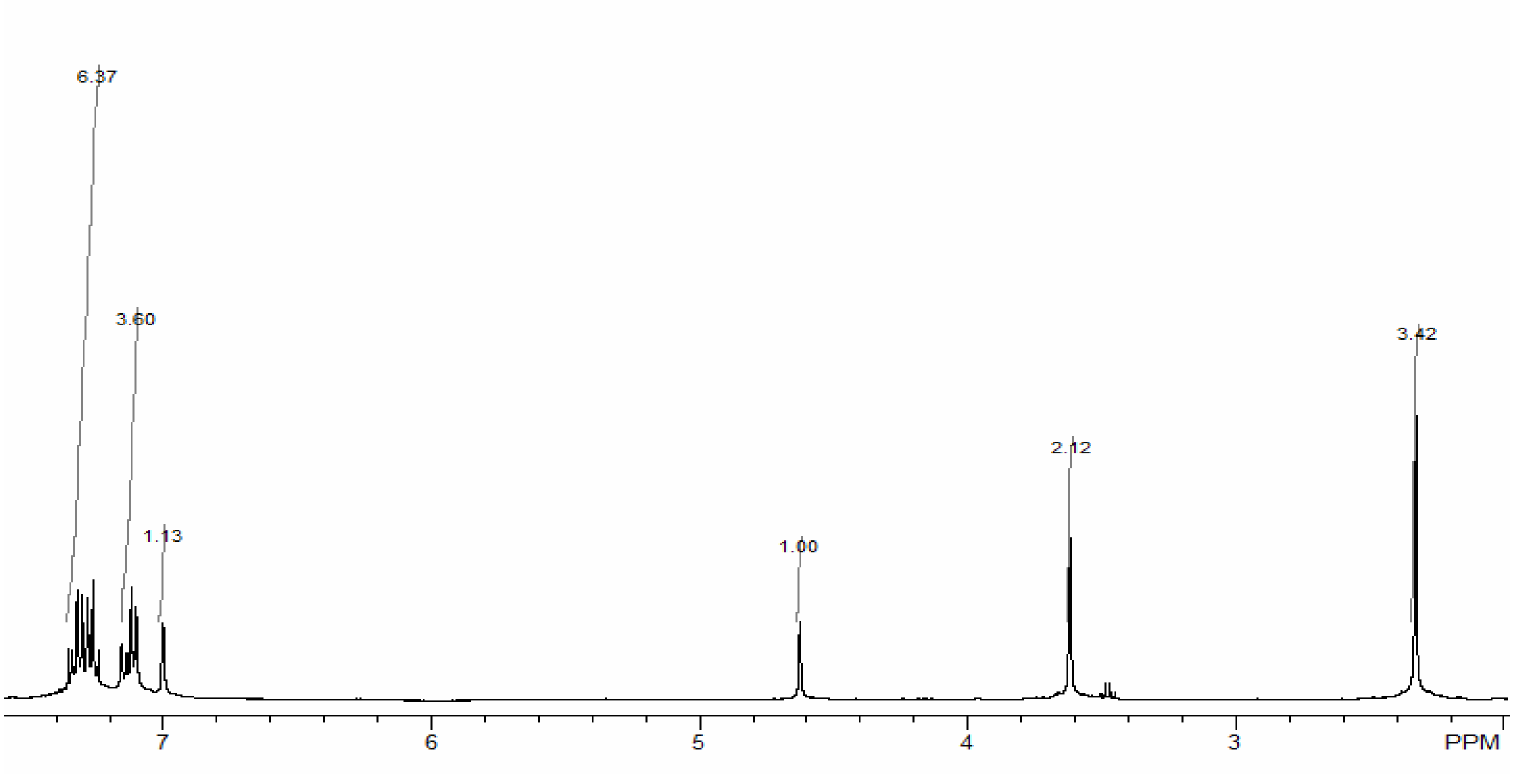
^{13}C NMR, $CDCl_3$, 100MHz

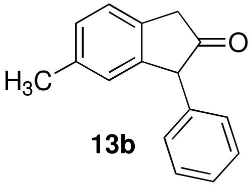




13b

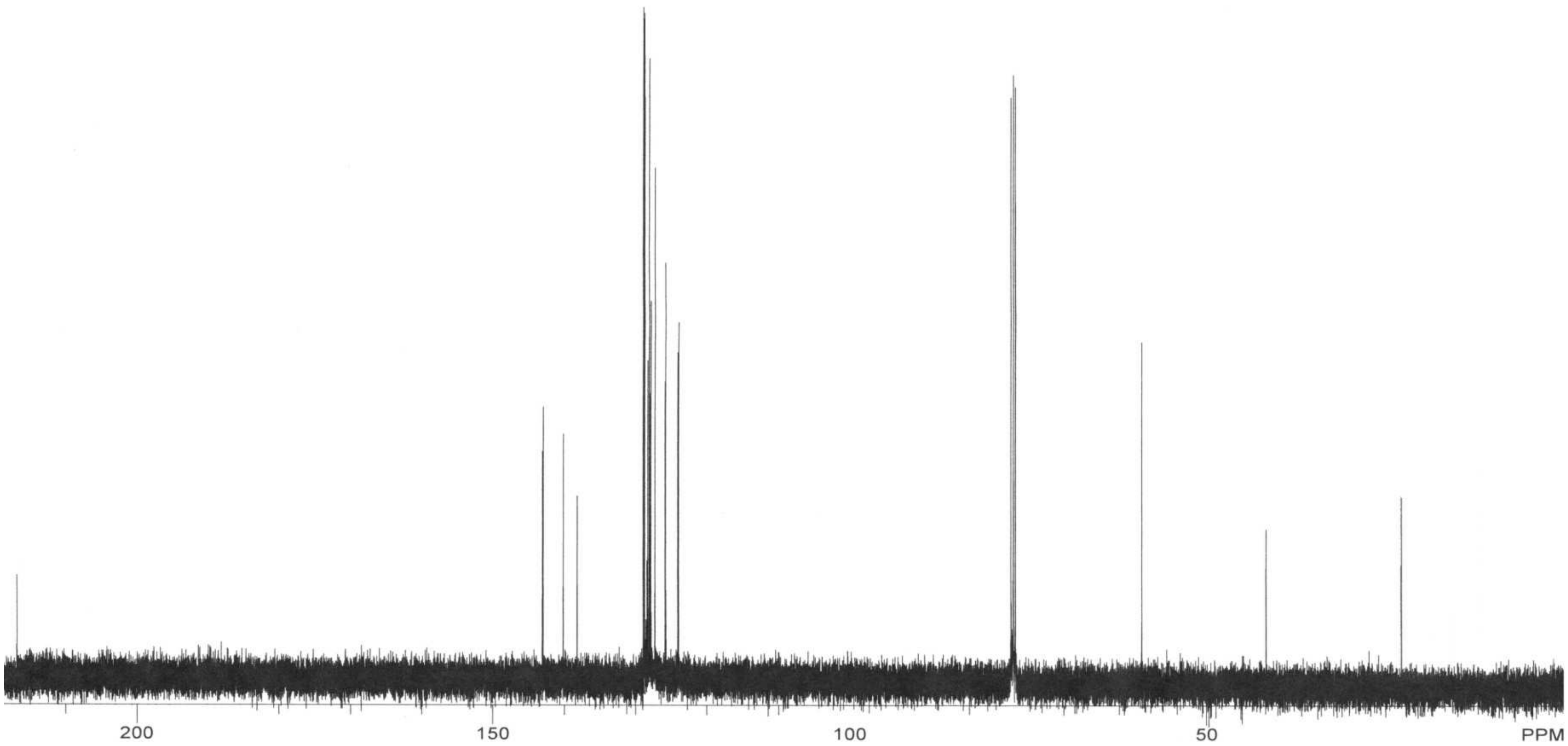
^{1}H NMR, $CDCl_3$, 400MHz

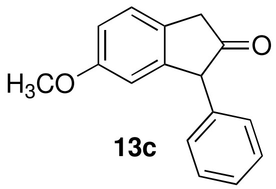




13b

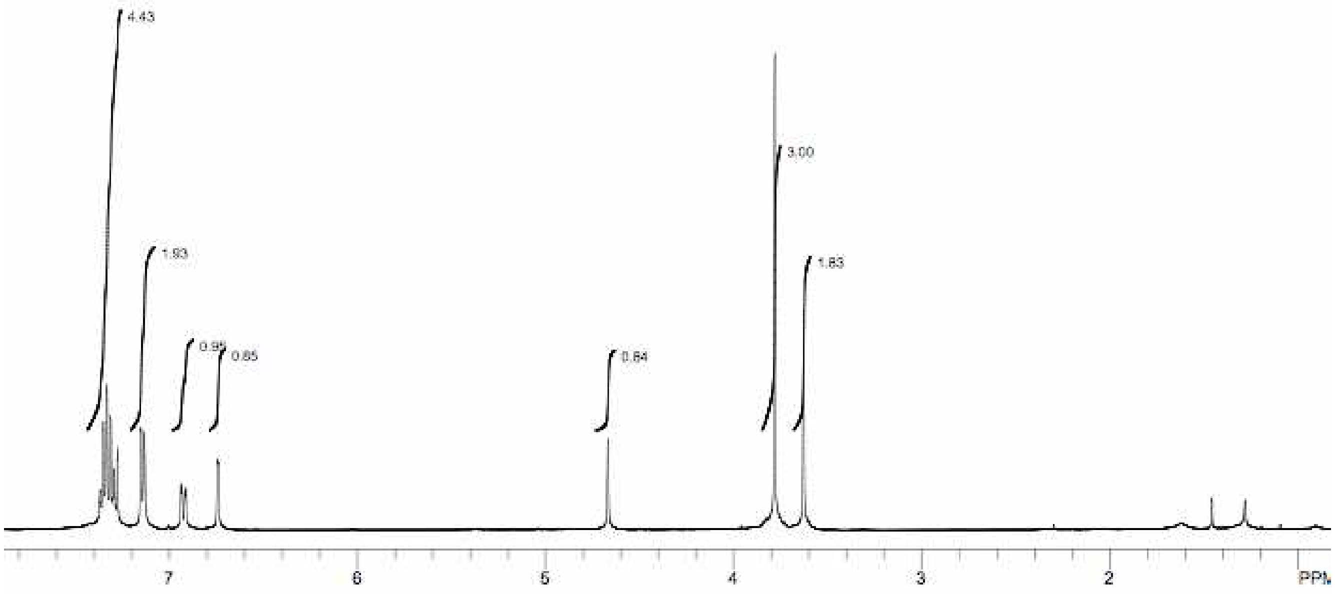
^{13}C NMR, $CDCl_3$, 100MHz

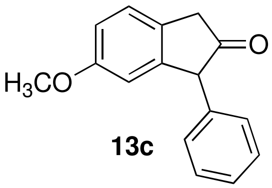




13c

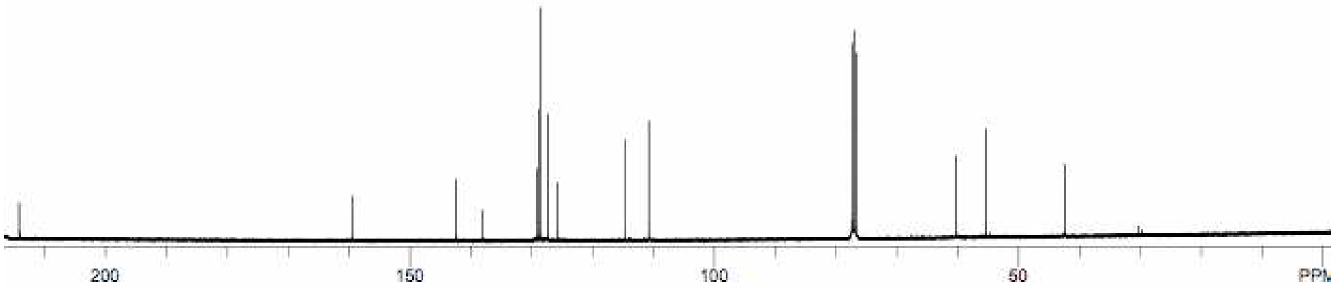
^{1}H NMR, CDCl$_3$, 400MHz

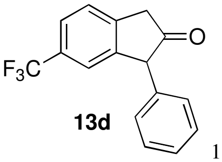




13c

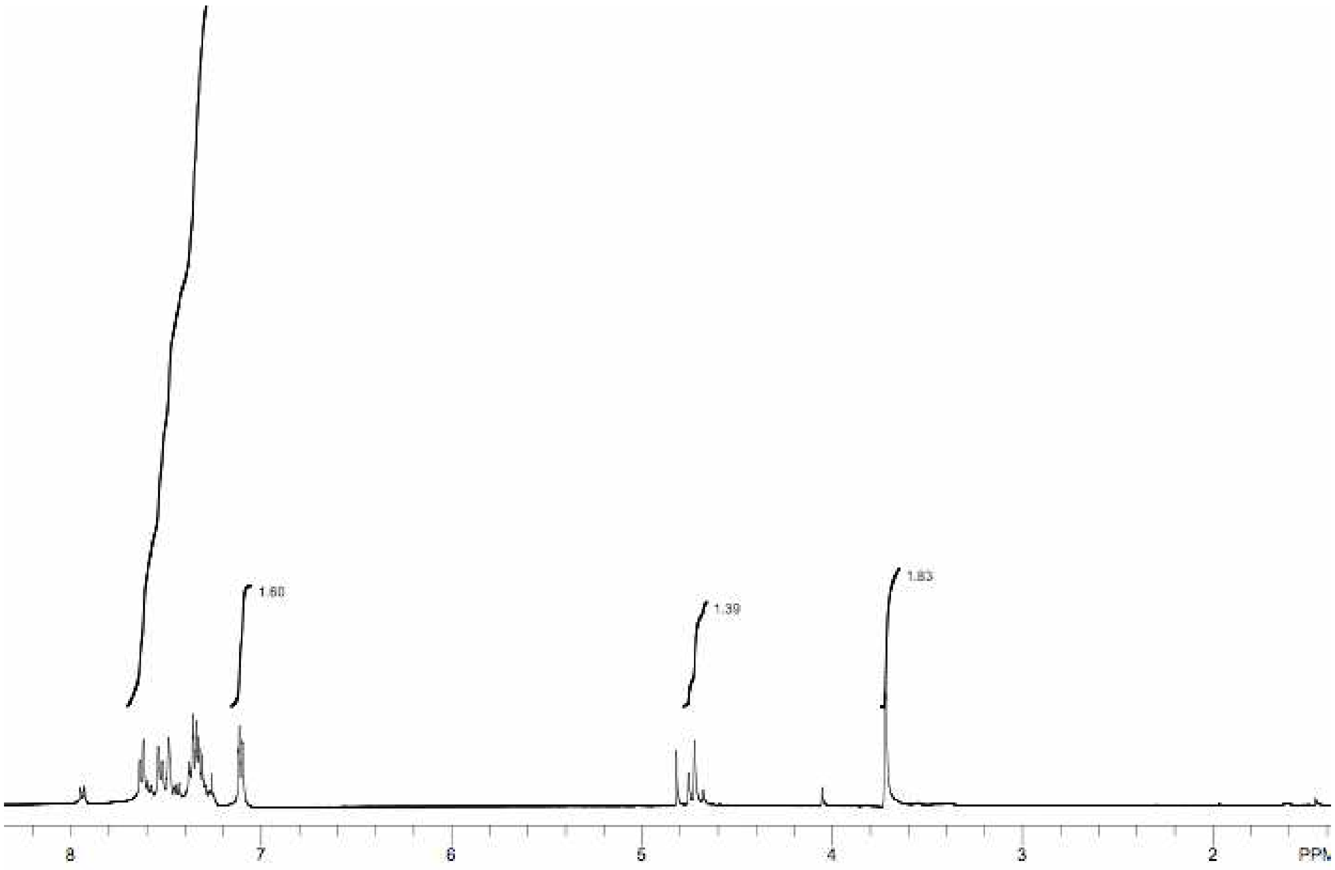
^{13}C NMR, $CDCl_3$, 100MHz

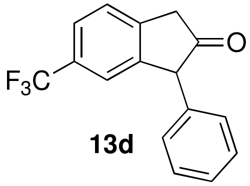




13d

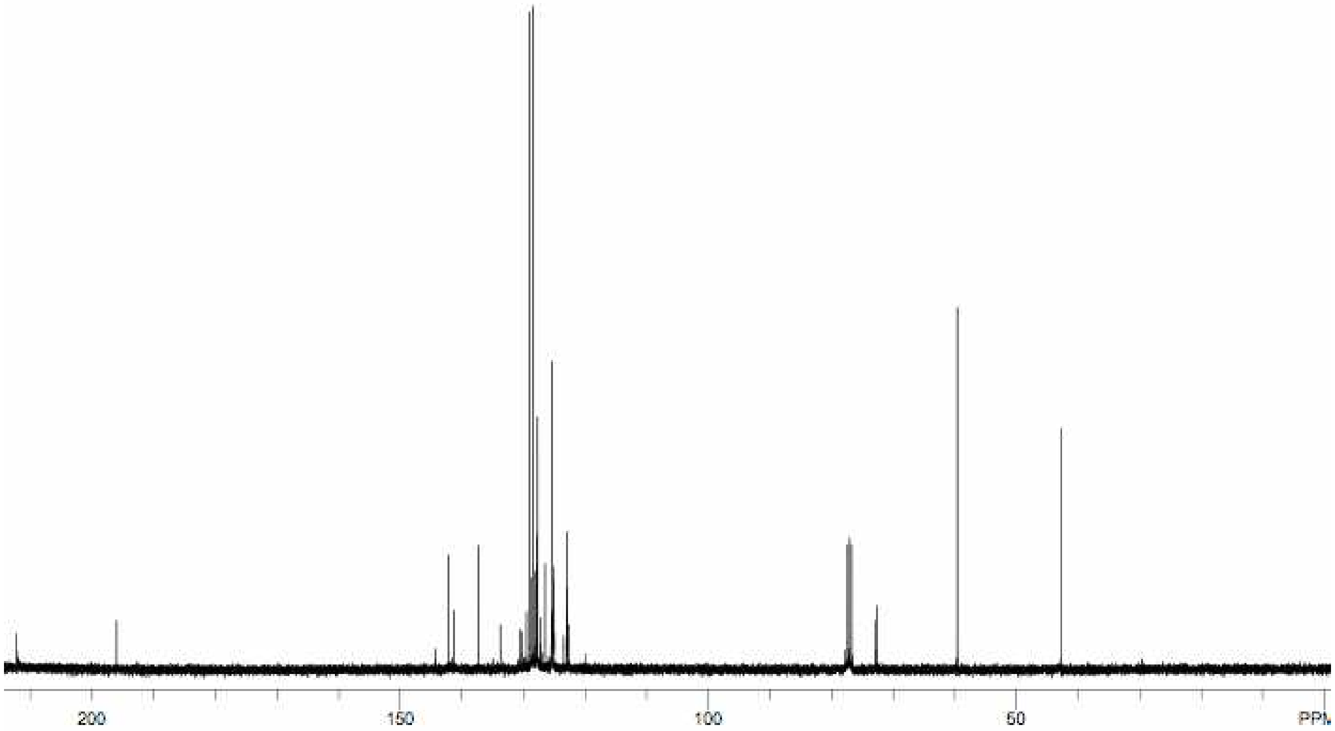
^{1}H NMR, CDCl$_3$, 400MHz

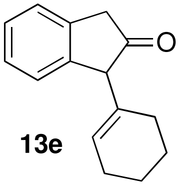




13d

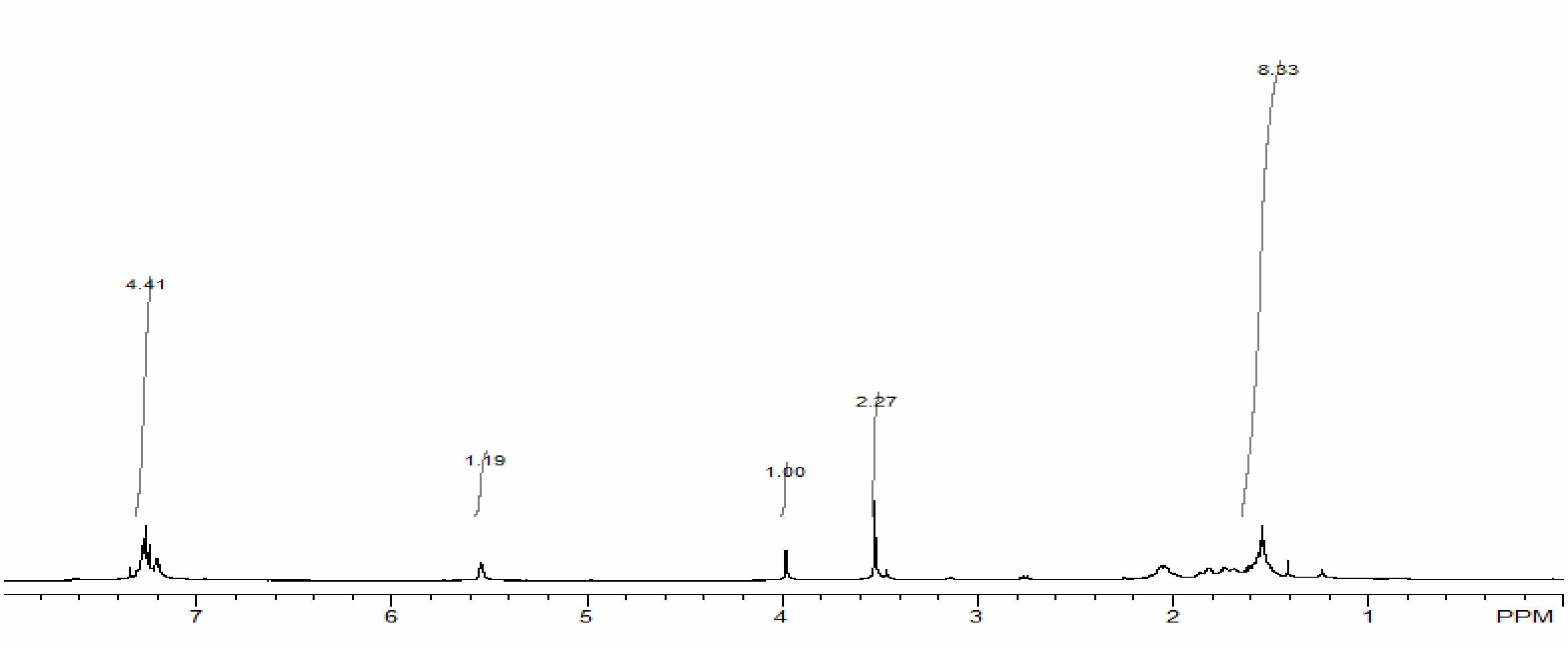
^{13}C NMR, CDCl$_3$, 100MHz

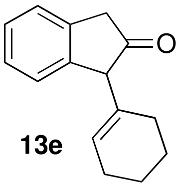




13e

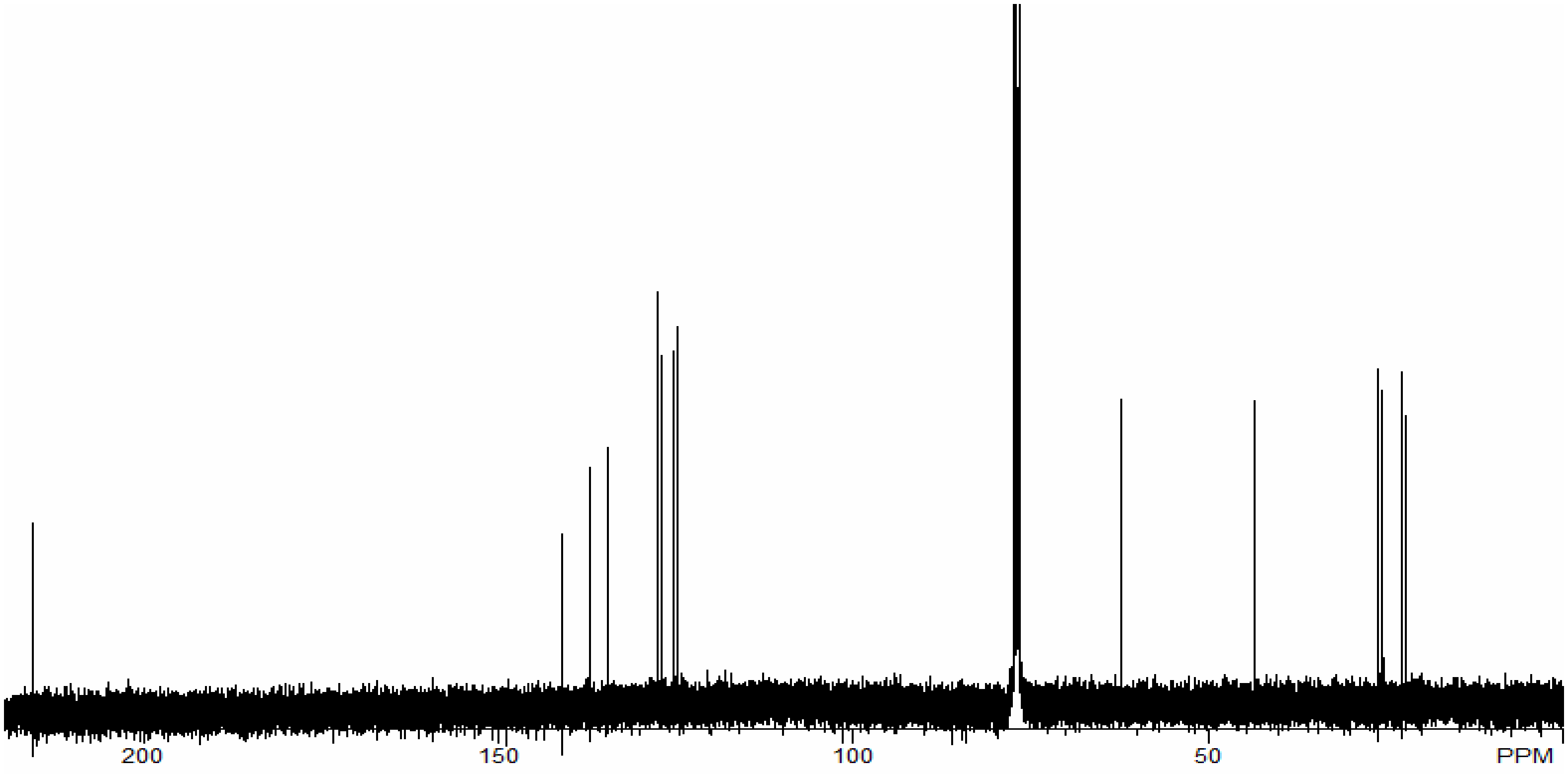
^{1}H NMR, CDCl$_3$, 400MHz

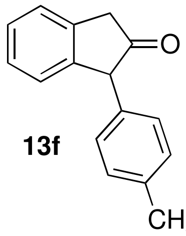




13e

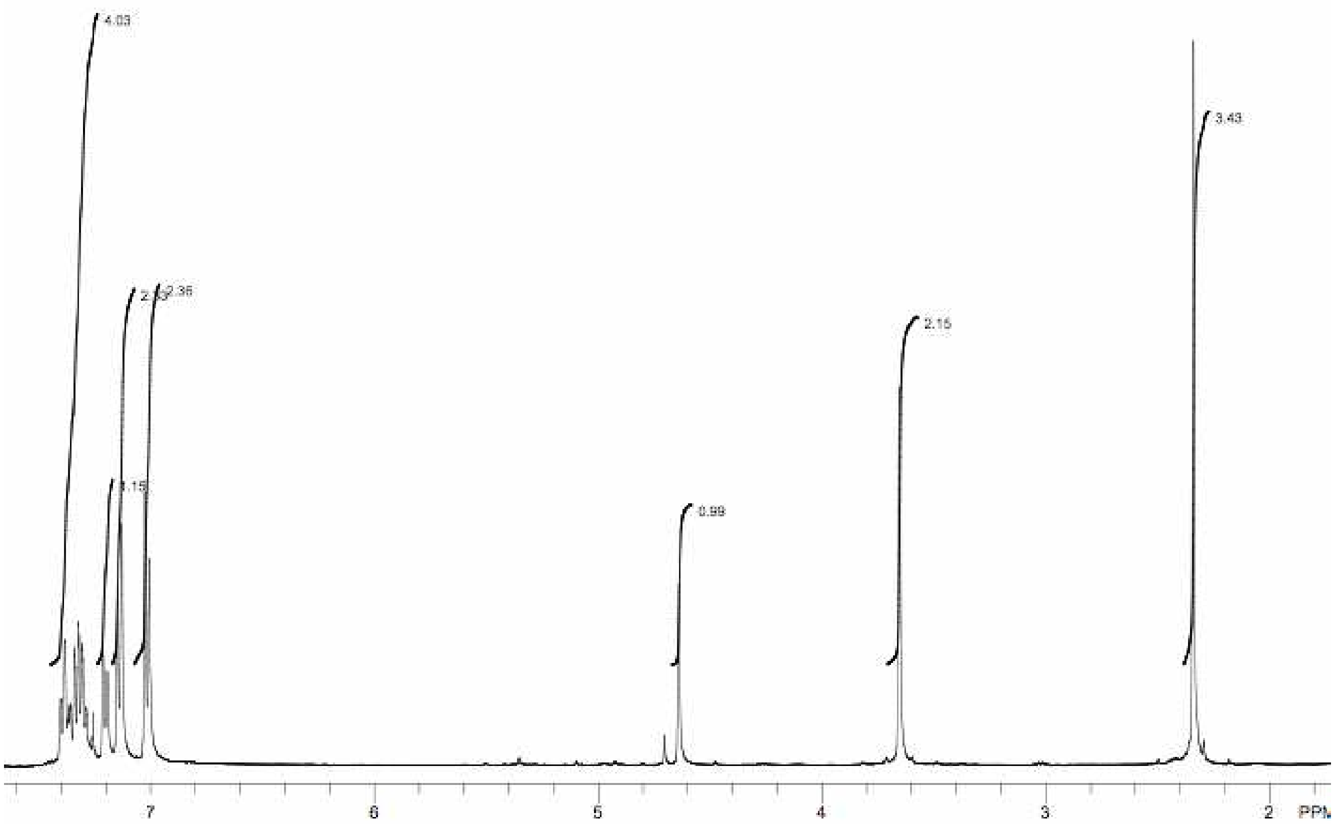
^{13}C NMR, CDCl$_3$, 100MHz

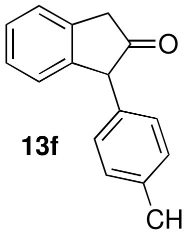




13f

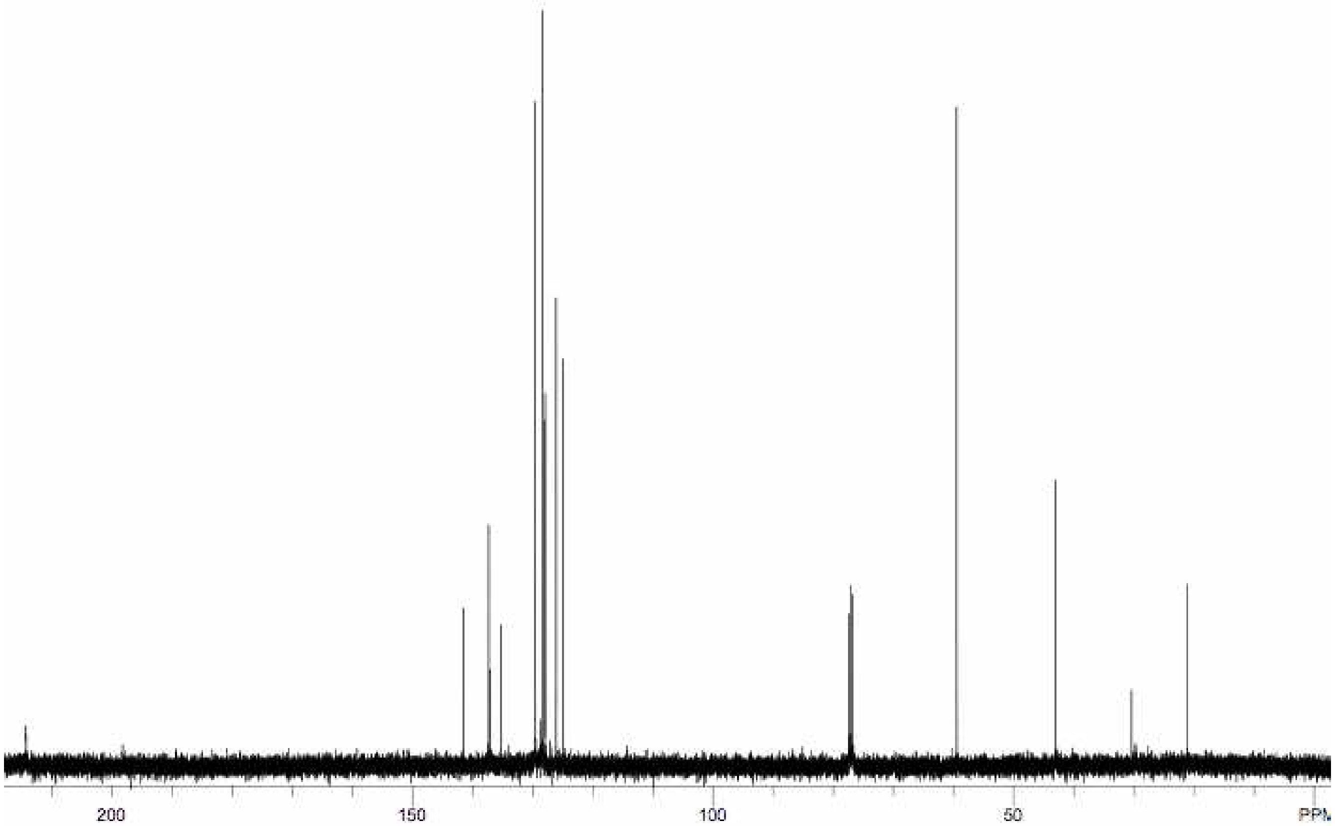
^{1}H NMR, $CDCl_3$, 400MHz

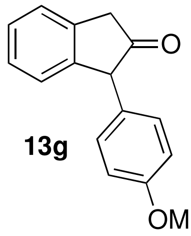




13f

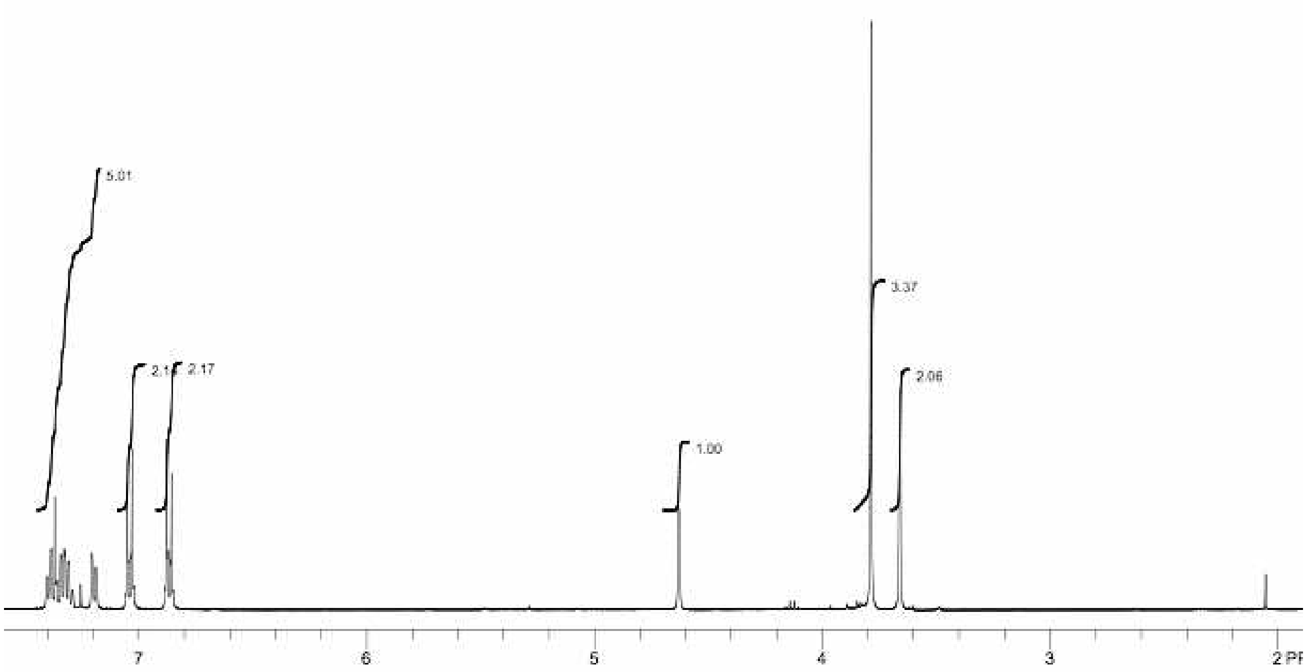
^{13}C NMR, CDCl$_3$, 100MHz

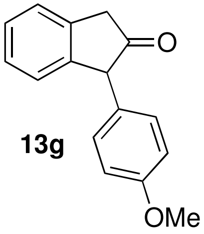




13g

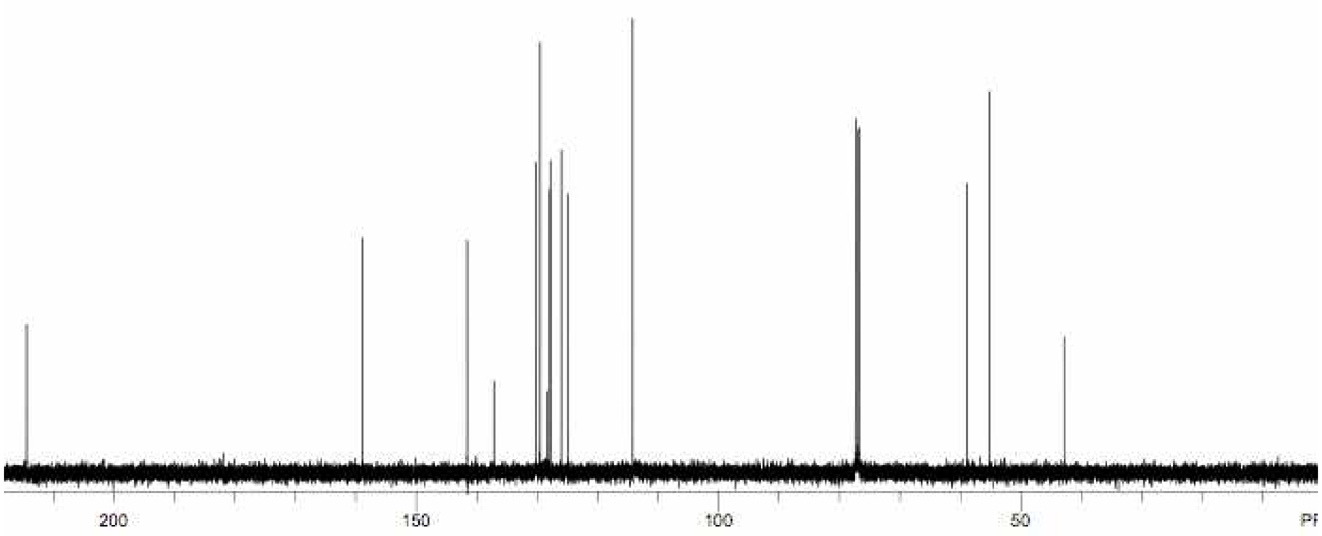
^{1}H NMR, CDCl$_3$, 400MHz

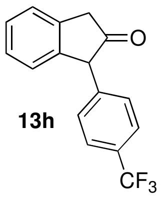




13g

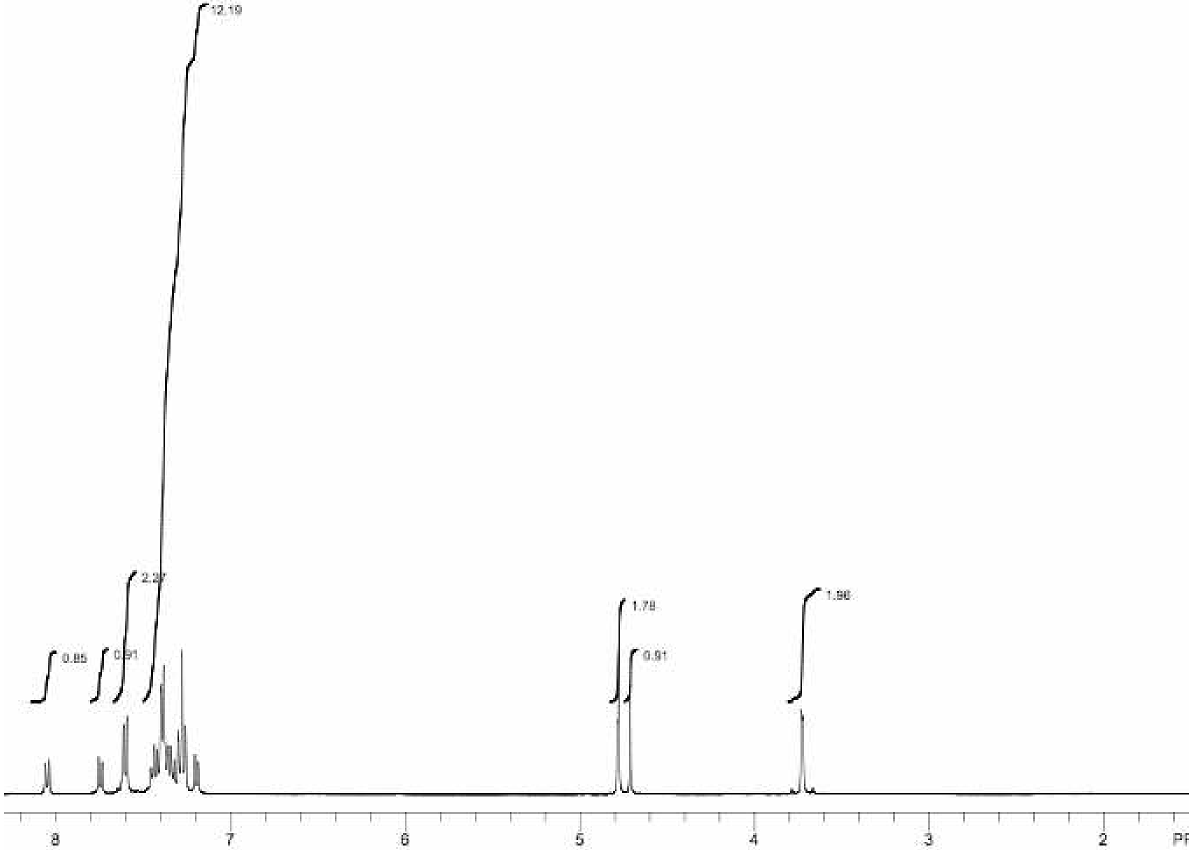
^{13}C NMR, CDCl$_3$, 100MHz

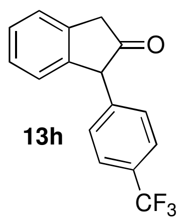




13h

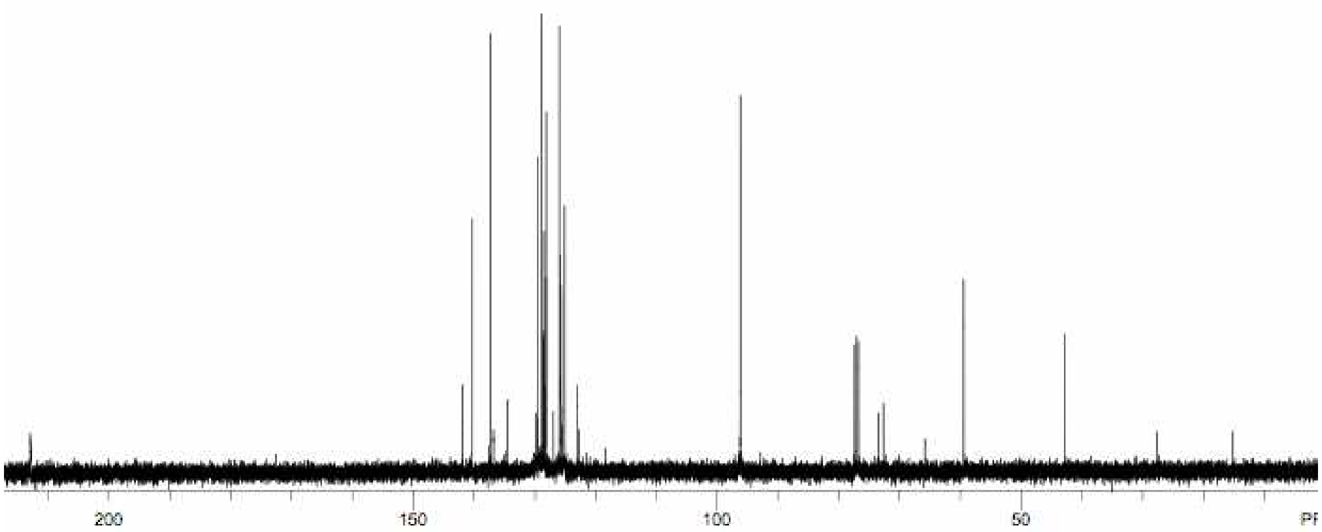
^{1}H NMR, $CDCl_3$, 400MHz

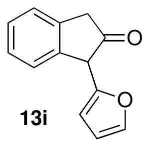




13h

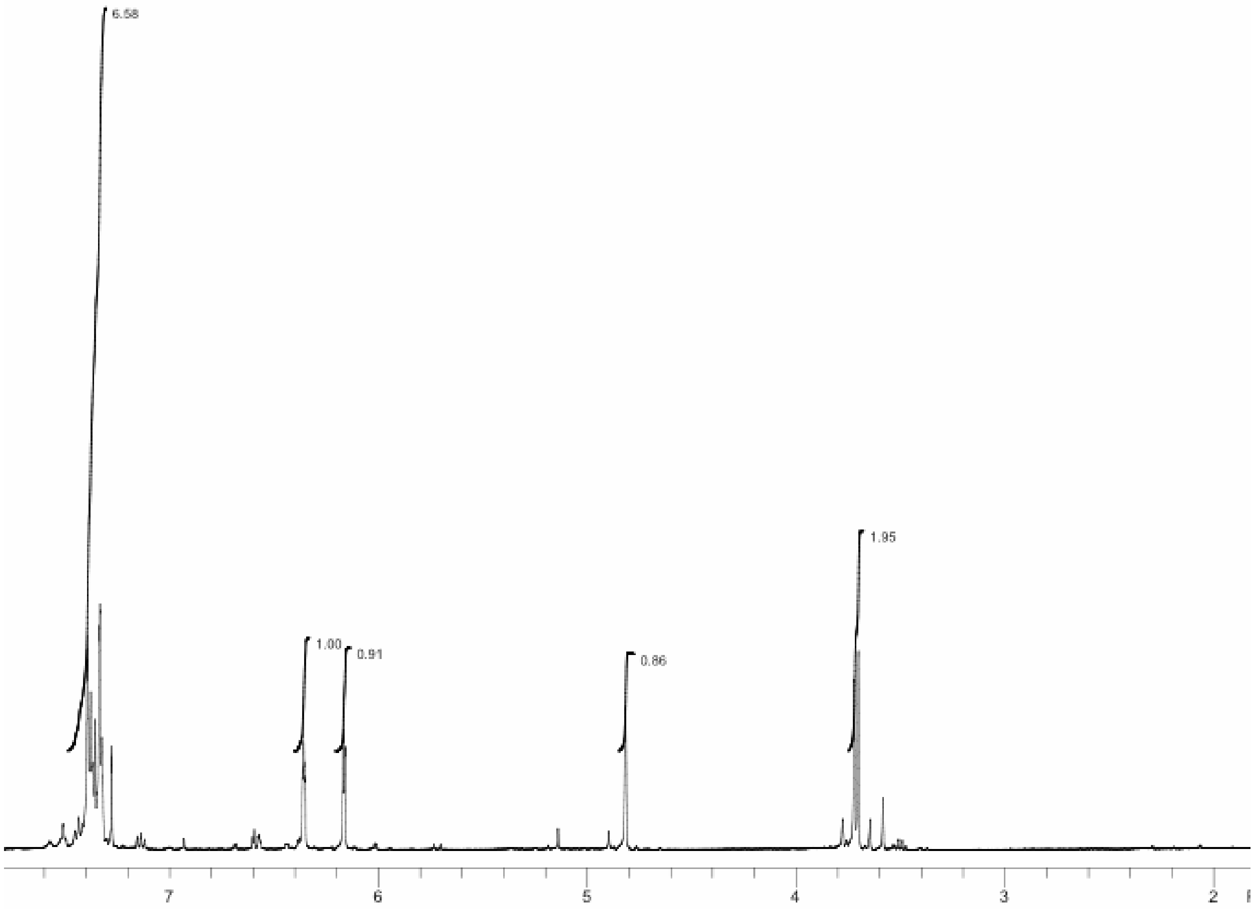
^{13}C NMR,1:3 $CDCl_3/CCl_4$, 100MHz

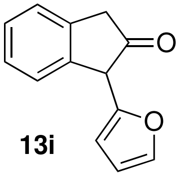




13i

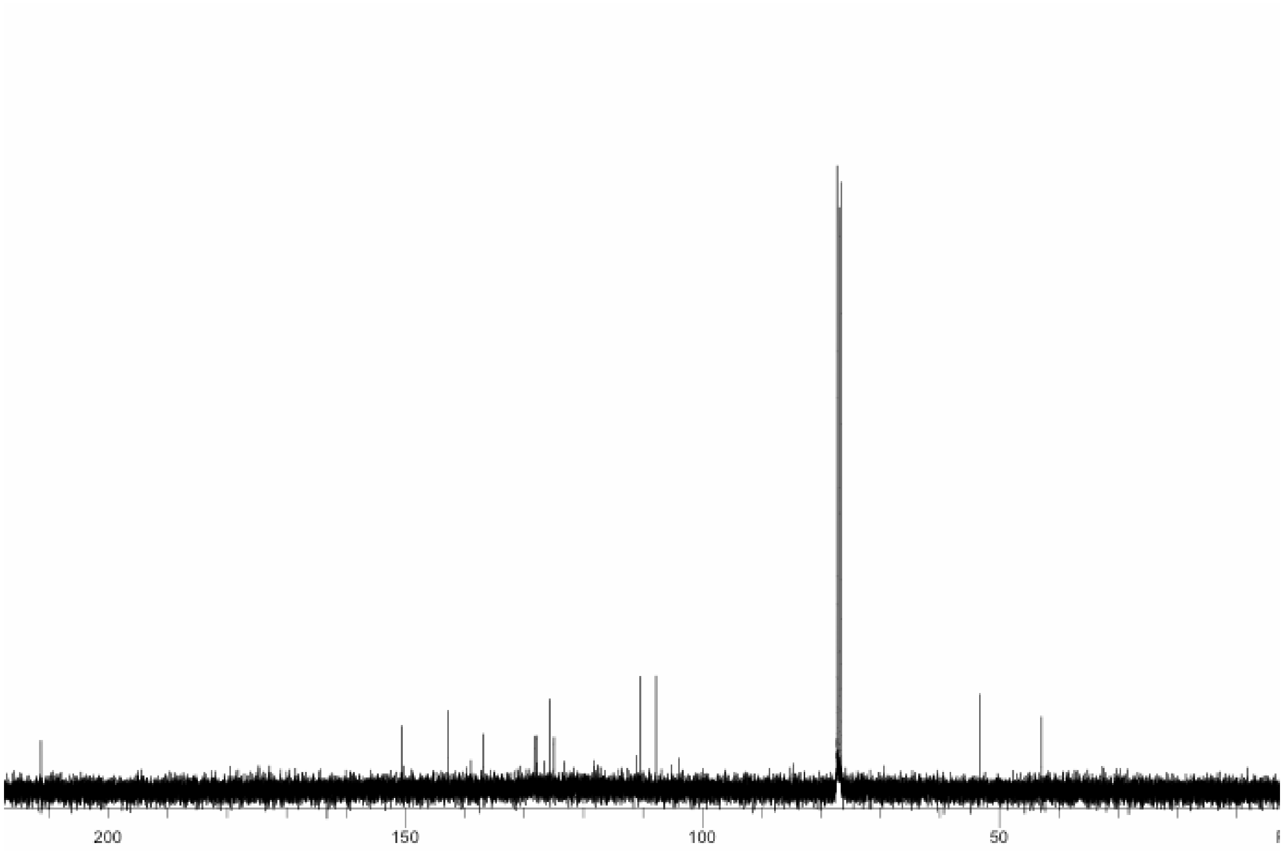
^{1}H NMR, CDCl$_3$, 400MHz

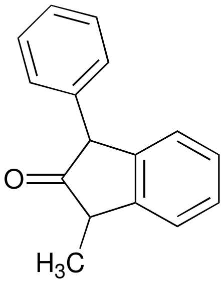




13i

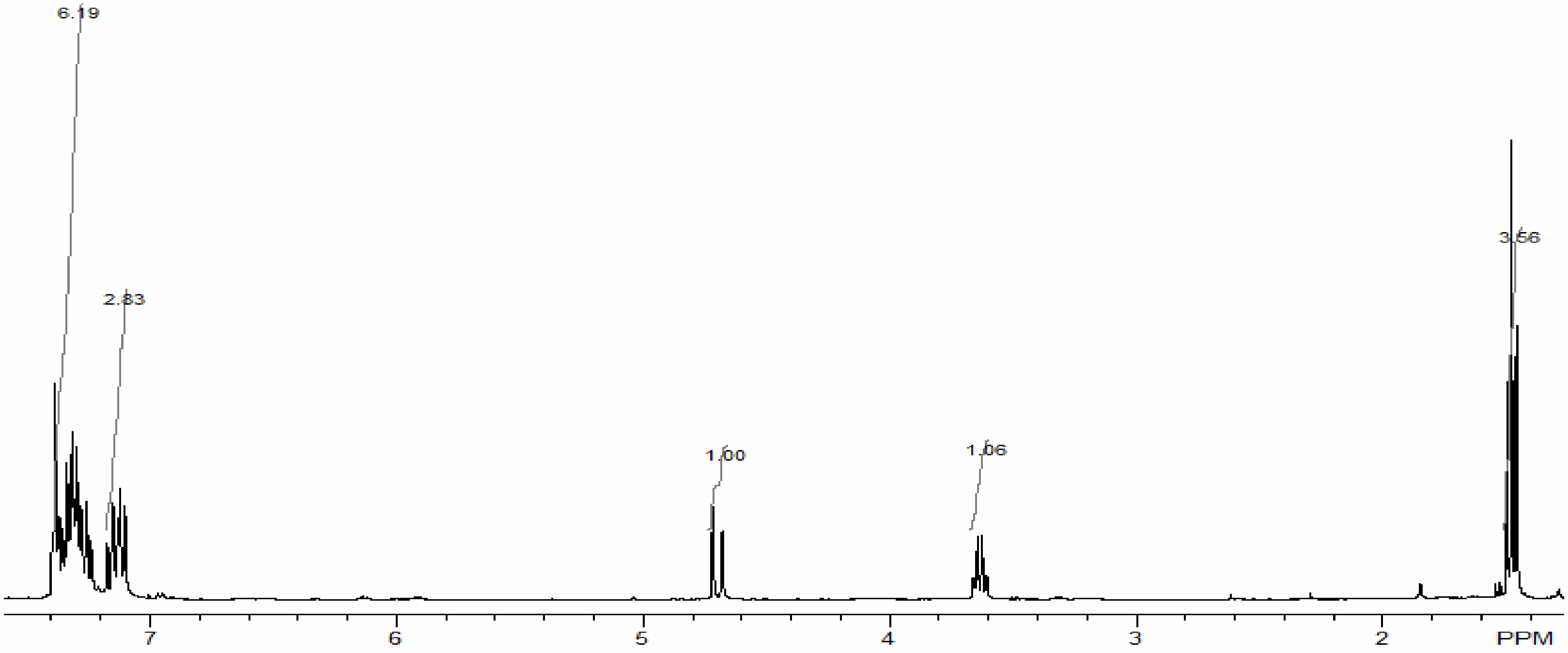
^{13}C NMR, $CDCl_3$, 100MHz

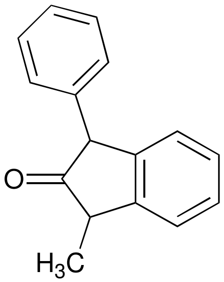




15a

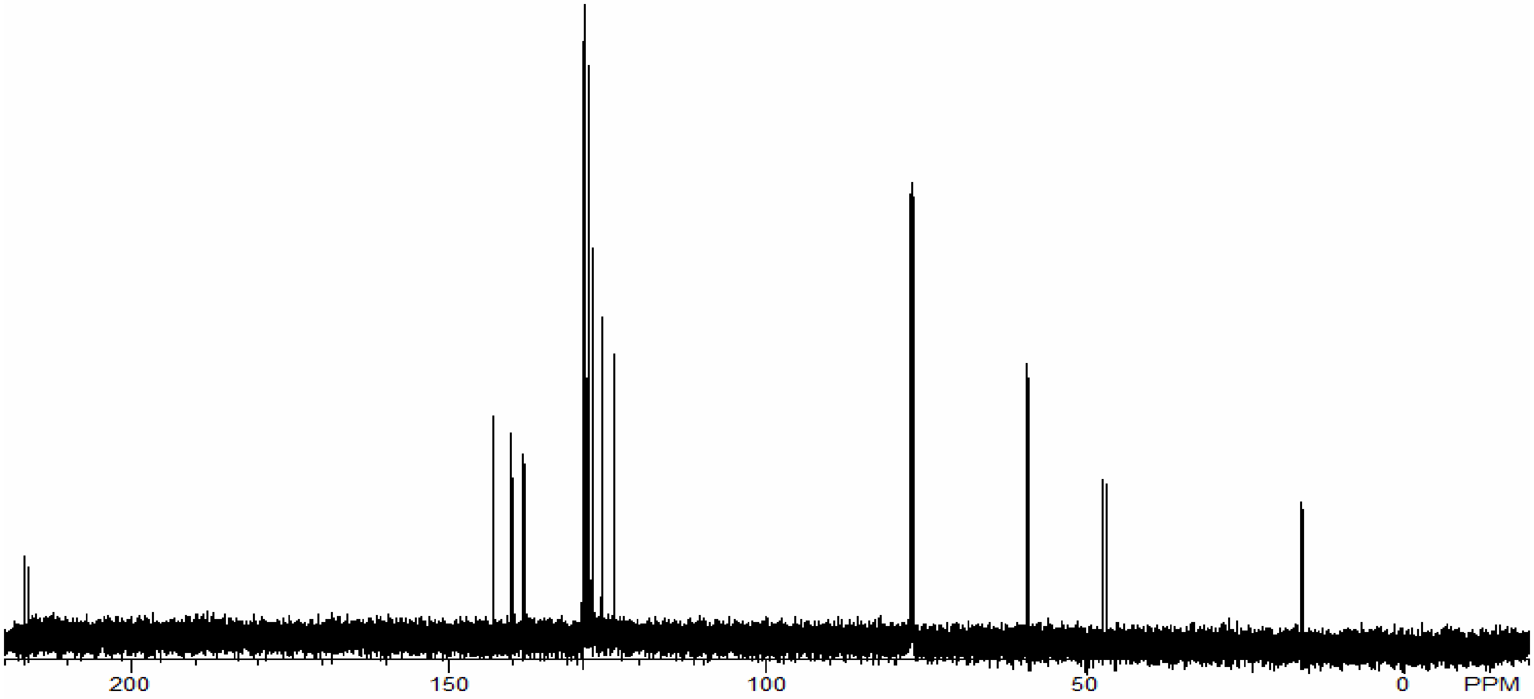
^{1}H NMR, CDCl$_3$, 400MHz

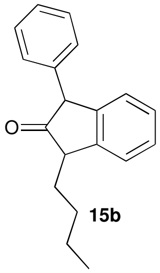




15a

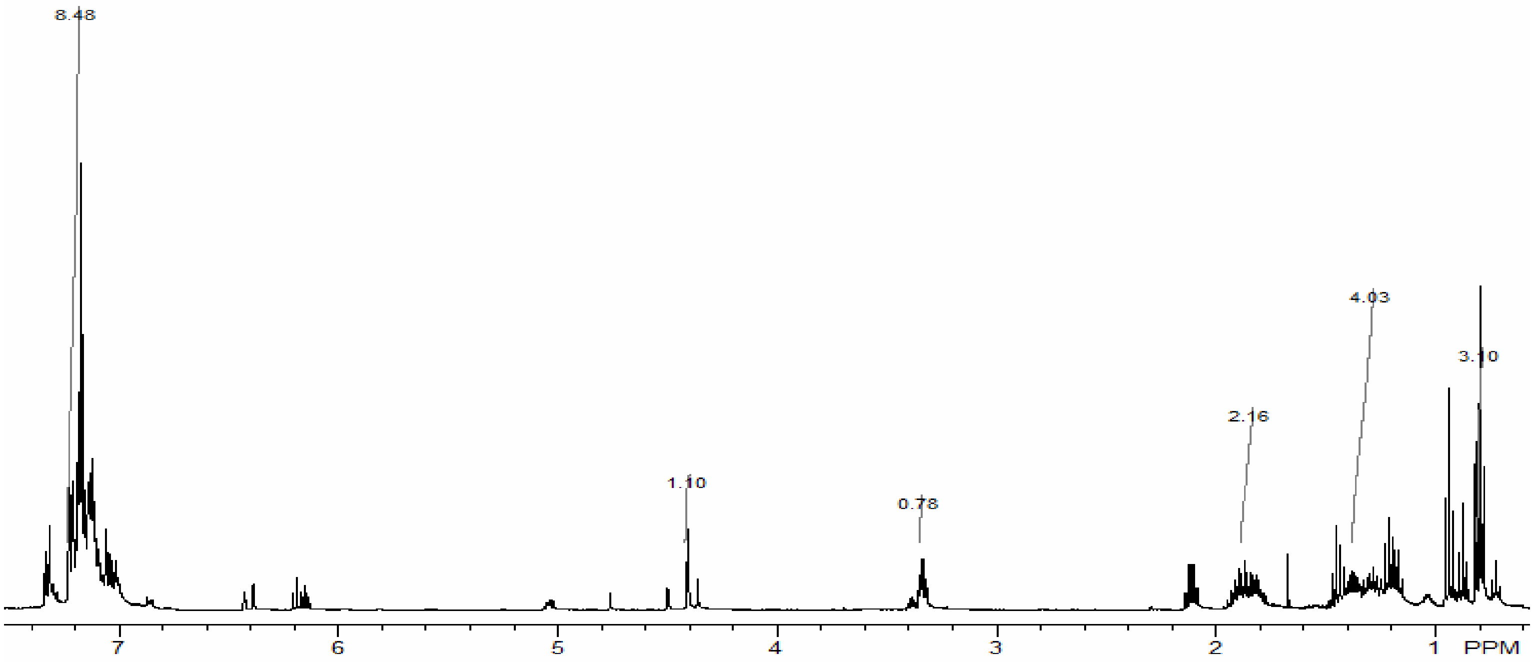
^{13}C NMR, $CDCl_3$, 100MHz

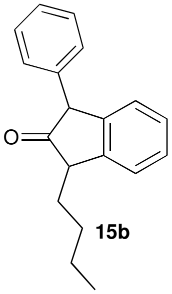




15b

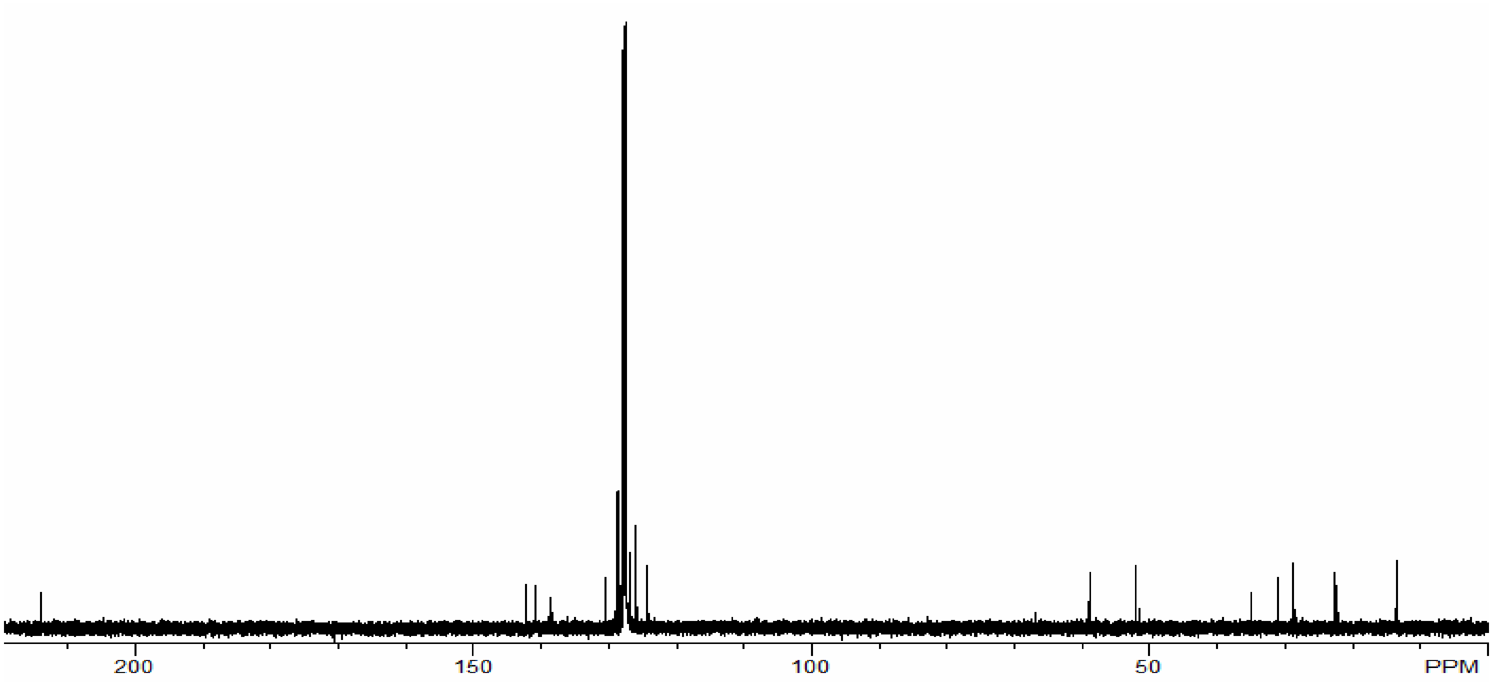
^{1}H NMR, CDCl$_3$, 400MHz

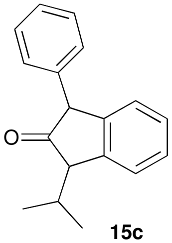




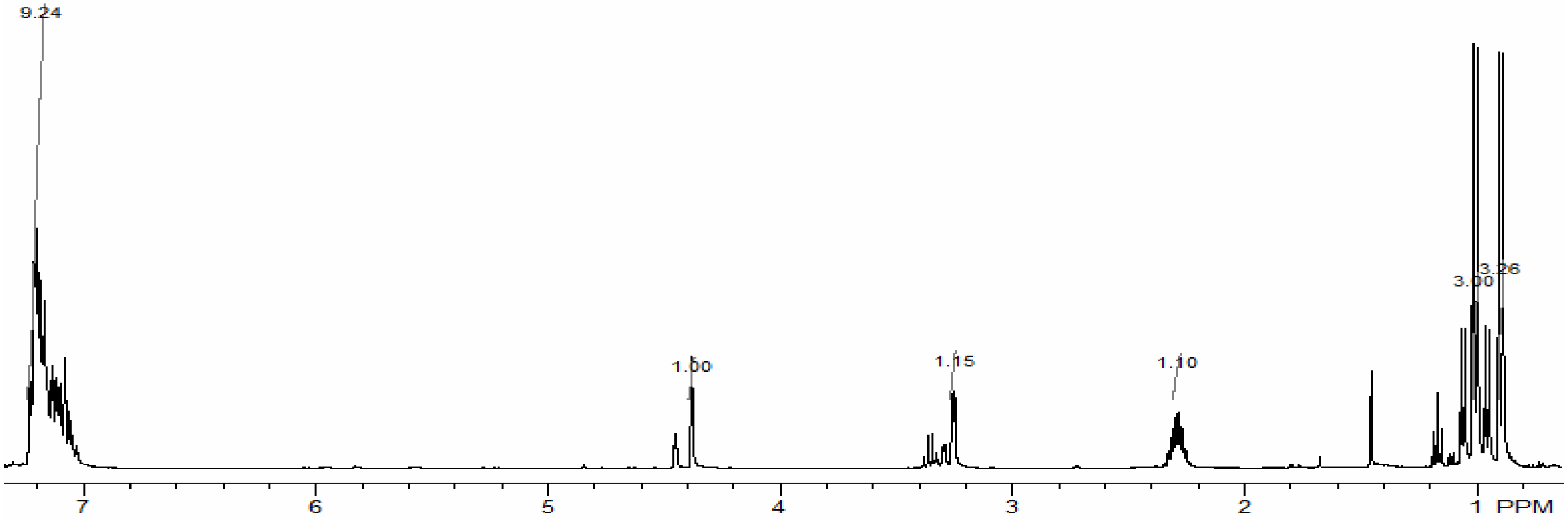
15b

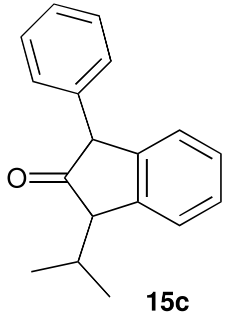
^{13}C NMR, $CDCl_3$, 100MHz



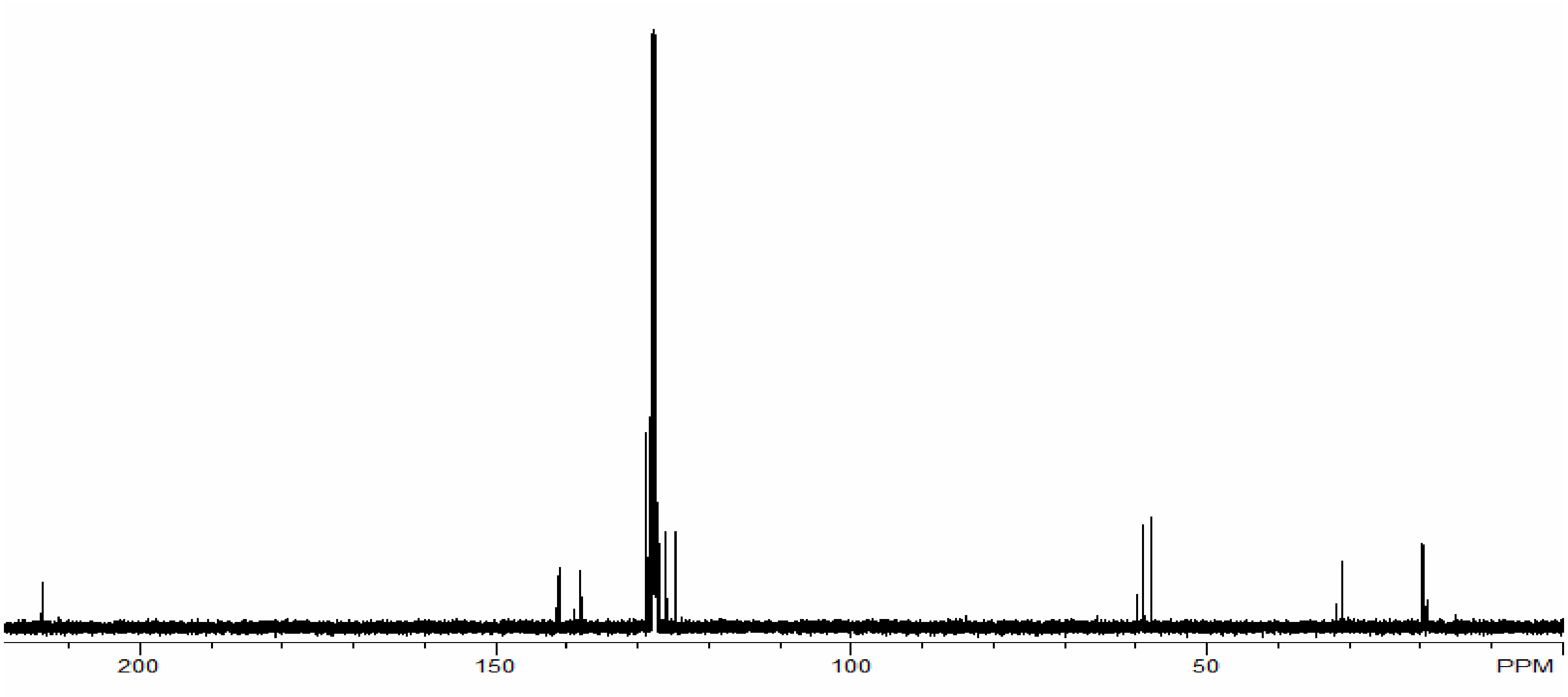


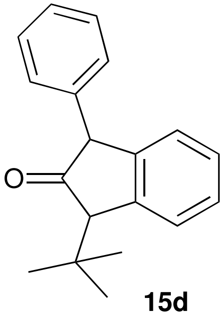
15c ^{1}H NMR, CDCl$_3$, 400MHz



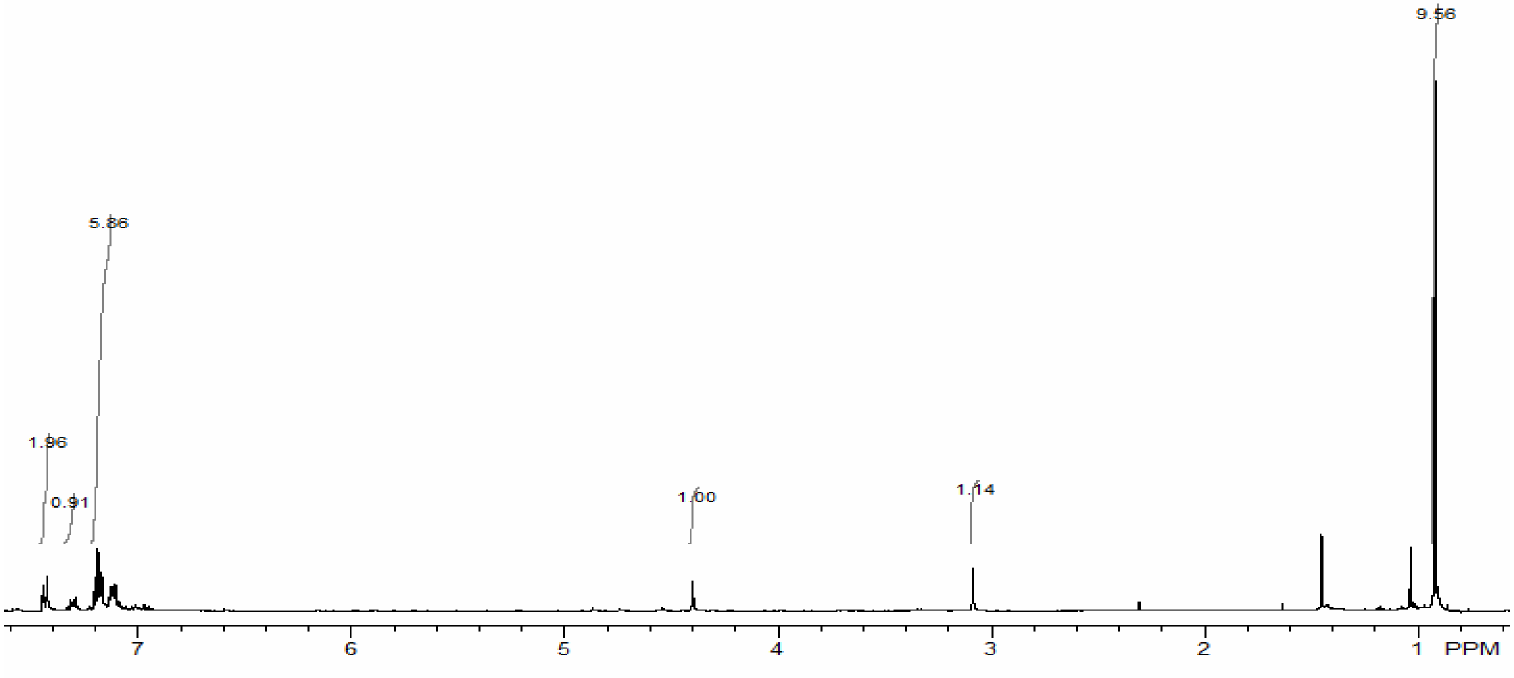


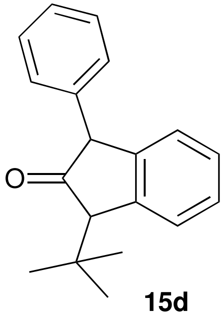
15c ^{13}C NMR, $CDCl_3$, 100MHz



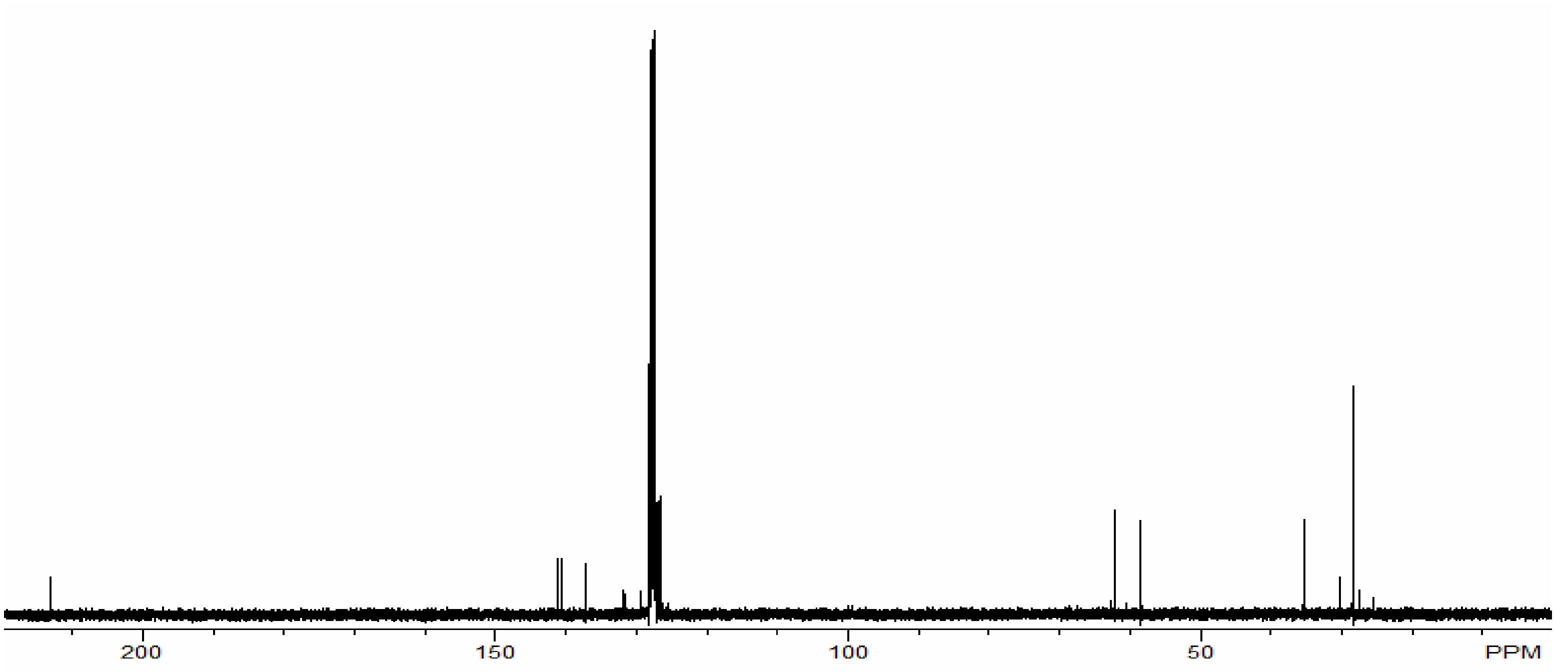


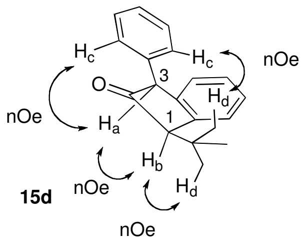
15d ^{1}H NMR, CDCl$_3$, 400MHz





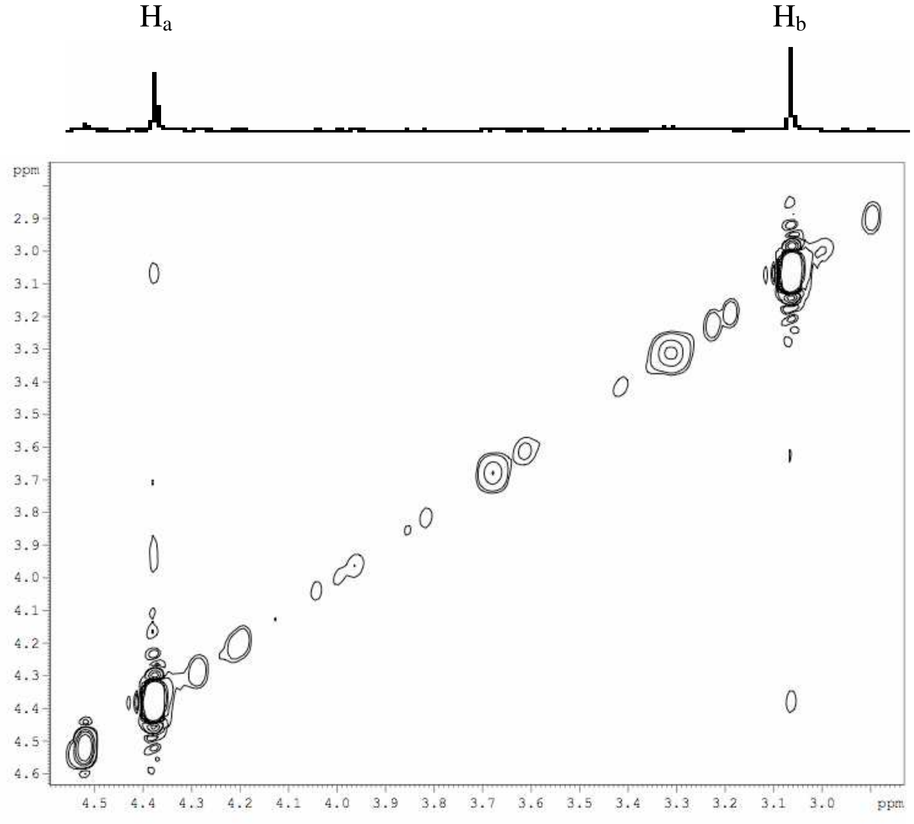
15d ^{13}C NMR, $CDCl_3$, 100MHz



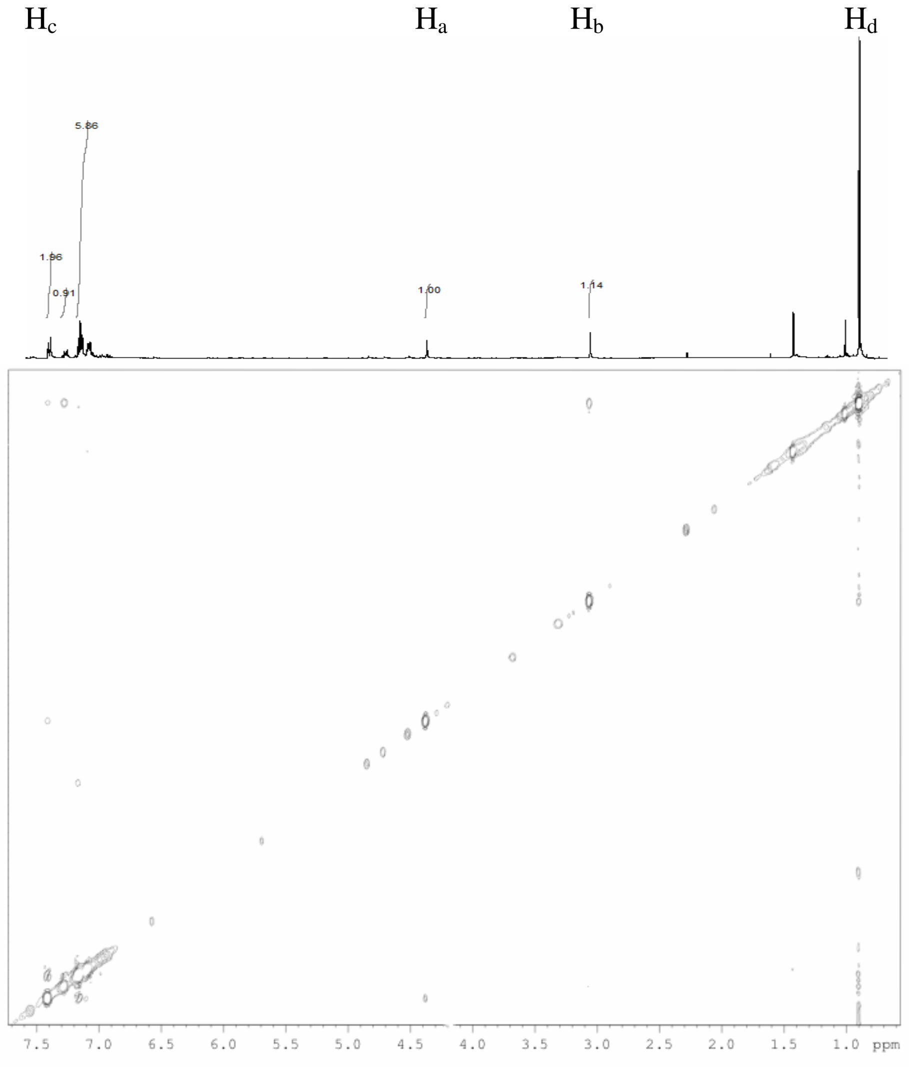


15d

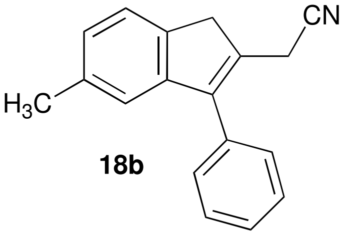
NOESY



NOESY of **15d** showing the $H_a \Leftrightarrow H_d$ nOe

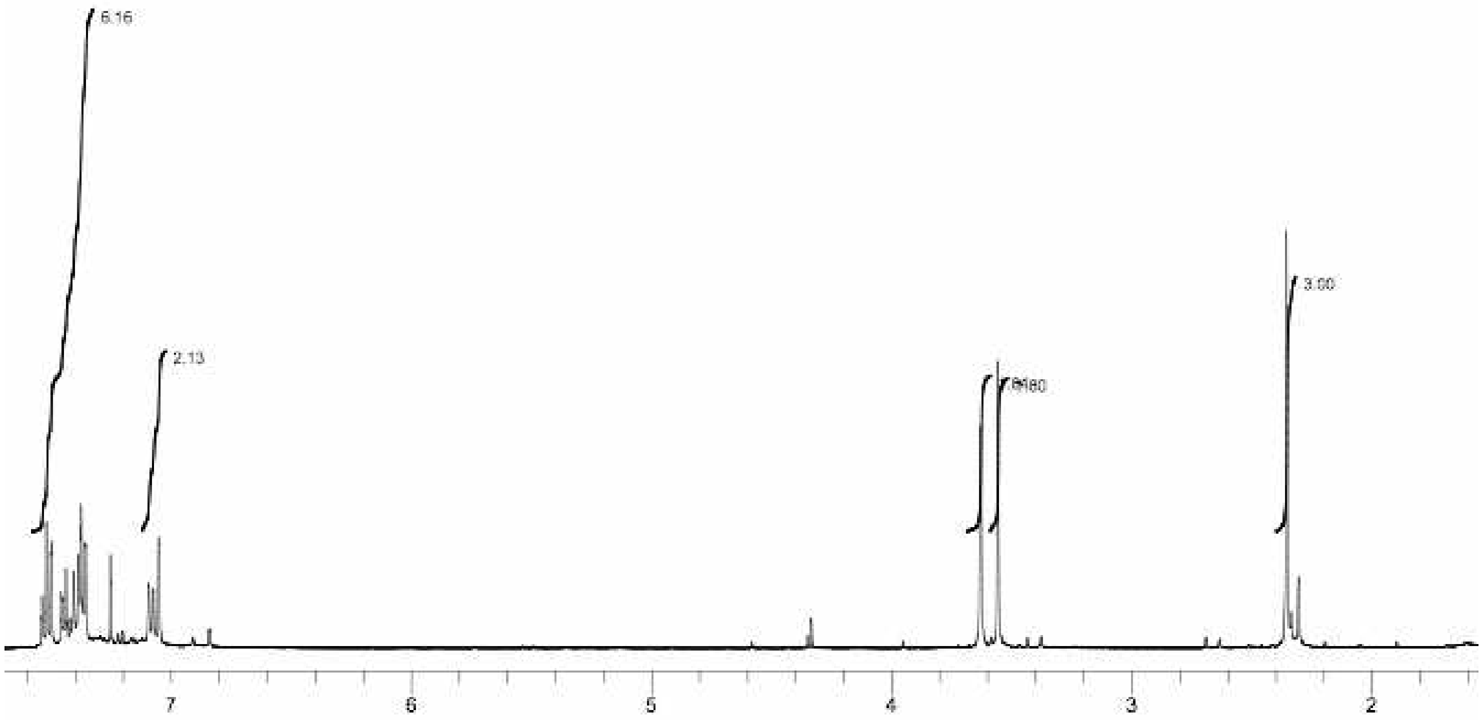


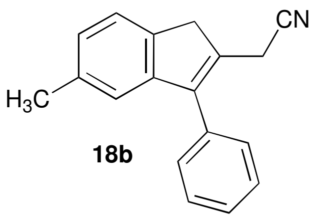
NOESY of **15d** showing the $H_c \Leftrightarrow H_d$, $H_c \Leftrightarrow H_a$, and $H_b \Leftrightarrow H_d$ nOes



18b

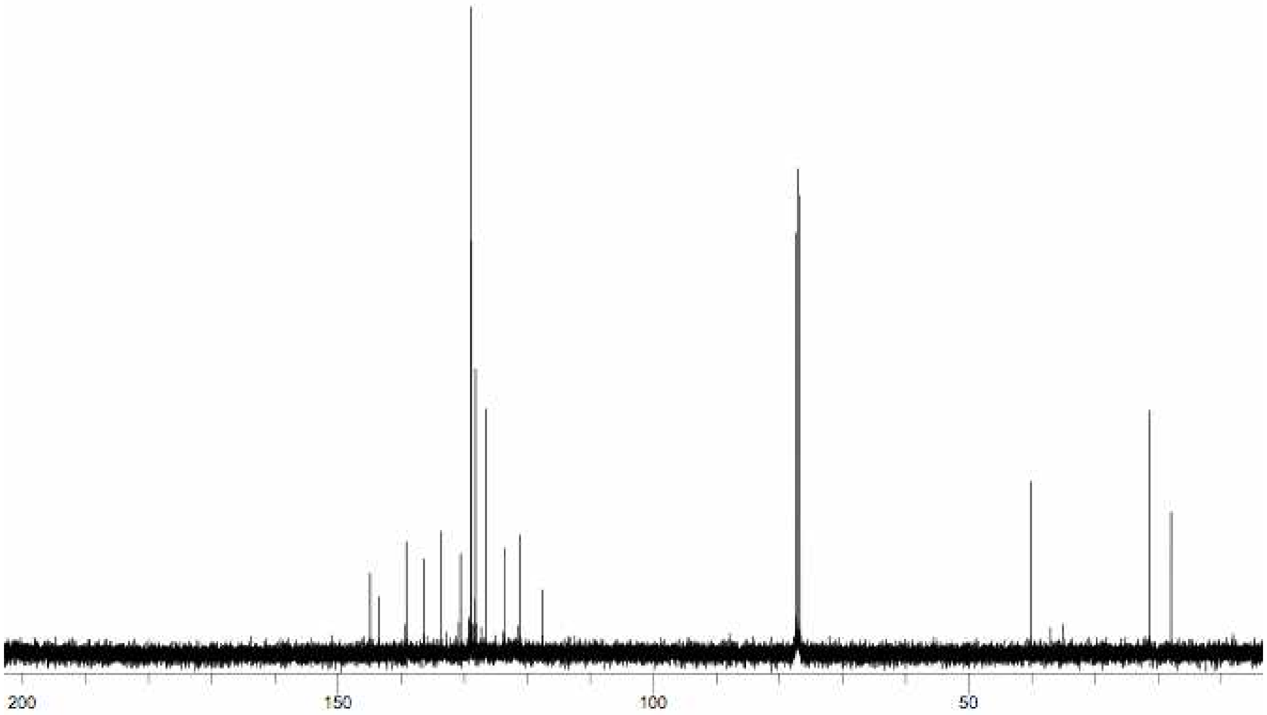
^{1}H NMR, CDCl$_3$, 400MHz

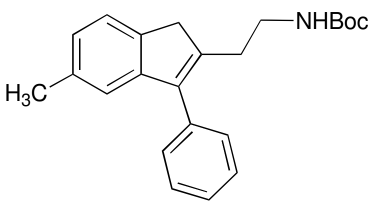




18b

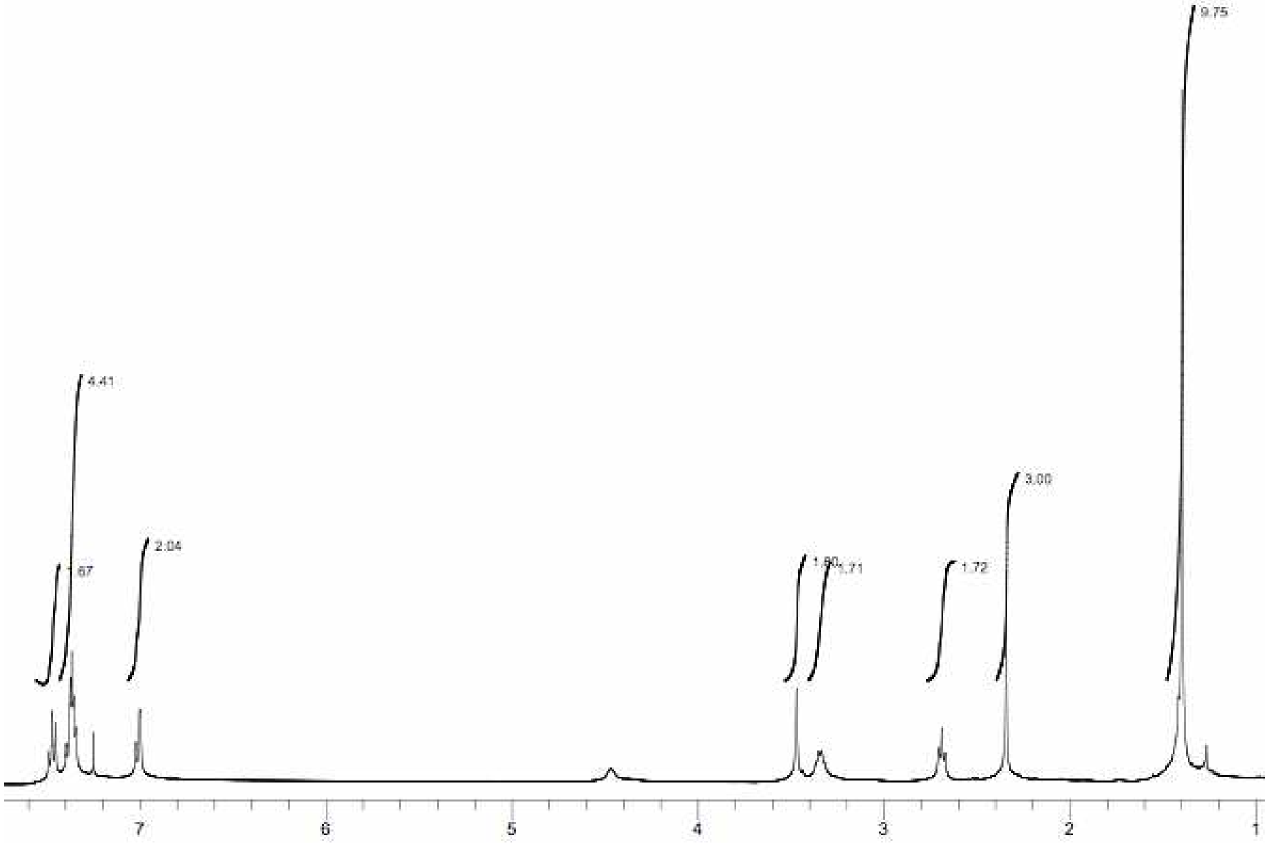
^{13}C NMR, CDCl$_3$, 100MHz

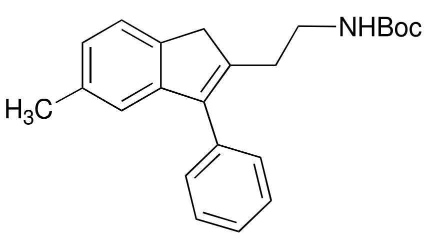




19b

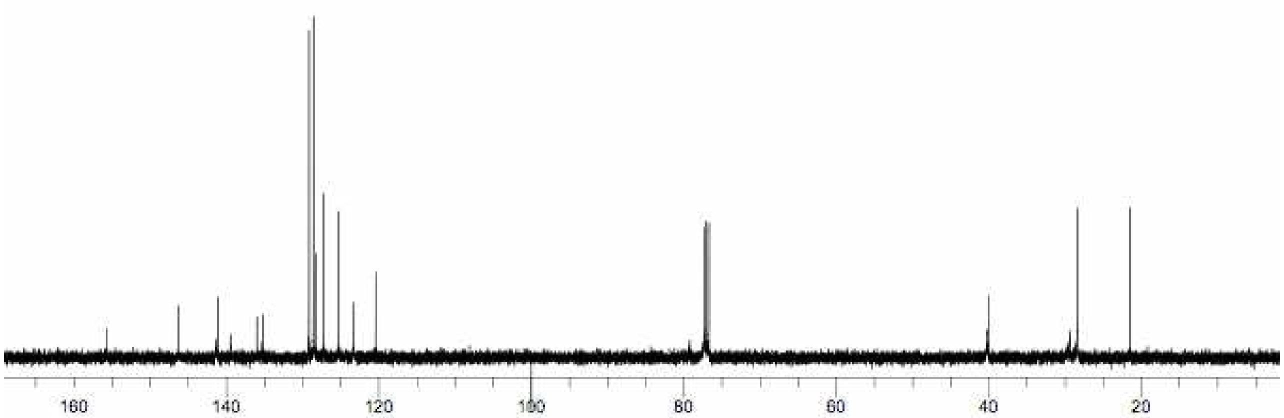
^{1}H NMR, CDCl$_3$, 400MHz





19b

^{13}C NMR, CDCl$_3$, 100MHz



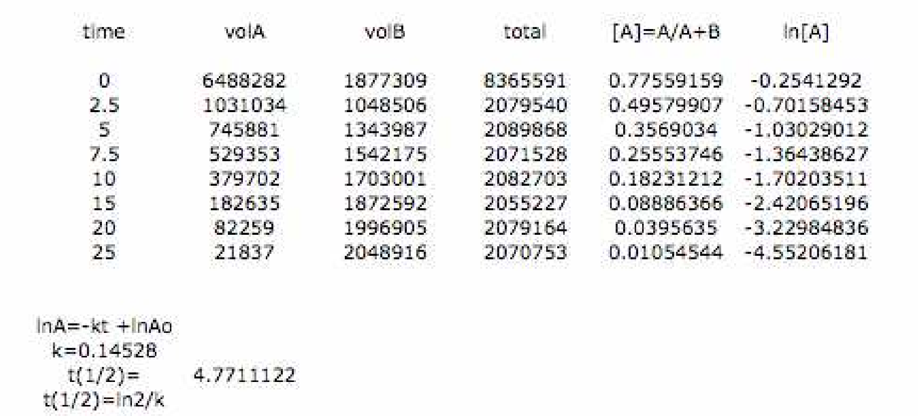
NMR studies:

A 0.5 M solution of alkynyl ether **12** in $CDCl_3$ (0.5 mL) was heated to 330K in the NMR spectrometer and spectra were recorded at 2.5 minute intervals (for t=0 to t=15 minutes), five-minute intervals (for t=15 minutes to t=30 minutes), and 10 minute intervals (for t=30 minutes to t=50 minutes). Integrals of the benzylic protons of **12** and the methylene protons of **13** were measured for each spectrum. The relative concentration or mole fraction of **12** at time t, [**12**]$_t$, was calculated as follows: [**12**]$_t$=(area CH2 **12**)$_t$**/[**(area CH_2 **12**)$_t$+ (area CH_2 **13**)$_t$]. The half-life for each reaction was calculated assuming a first-order process for the rearrangement/cyclization reaction, such that ln[**12**]$_t$=-kt + ln[**12**]$_o$

A plot of ln[**12**]$_t$ vs. t gives a straight line with slope=-k.

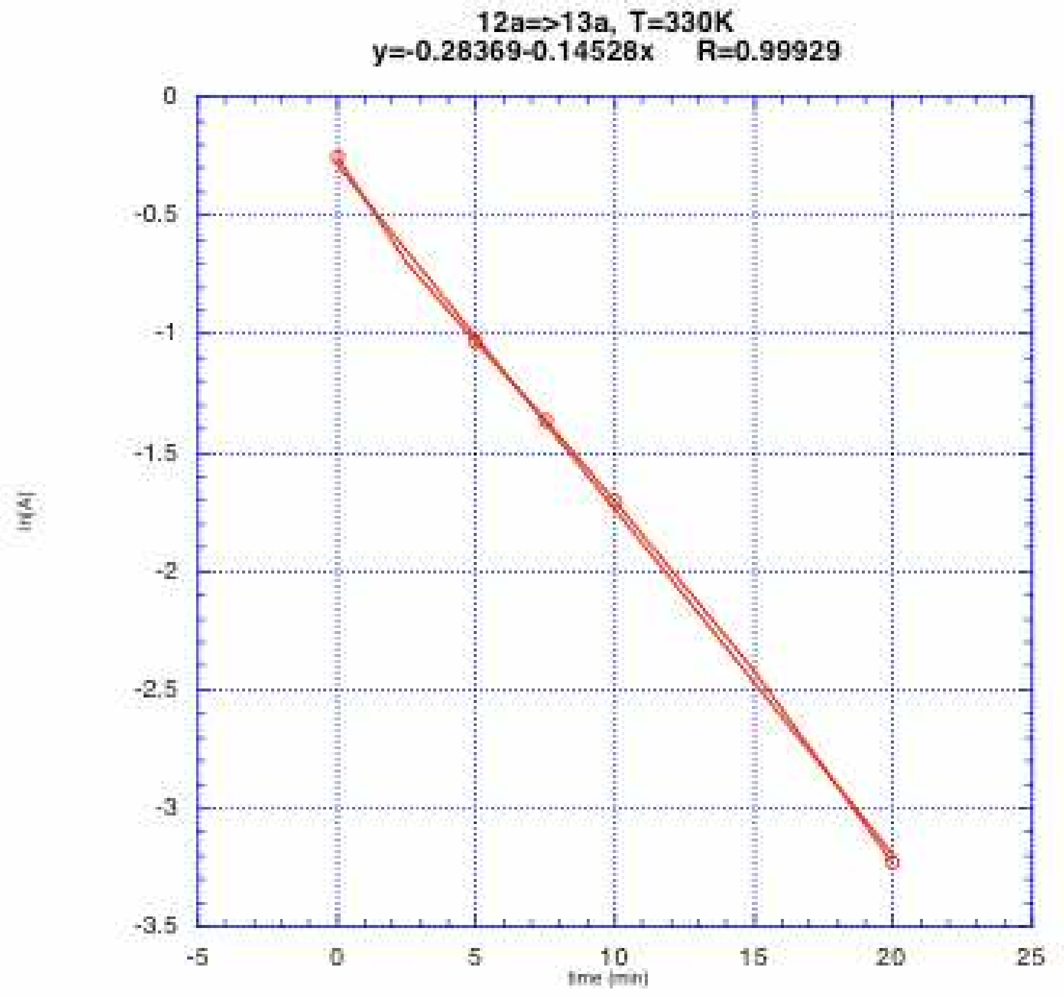
and ln2/k=$t_{1/2}$

T=330K, **12a→13a (t$_{1/2}$=4.8 minutes)**

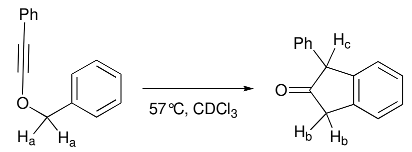


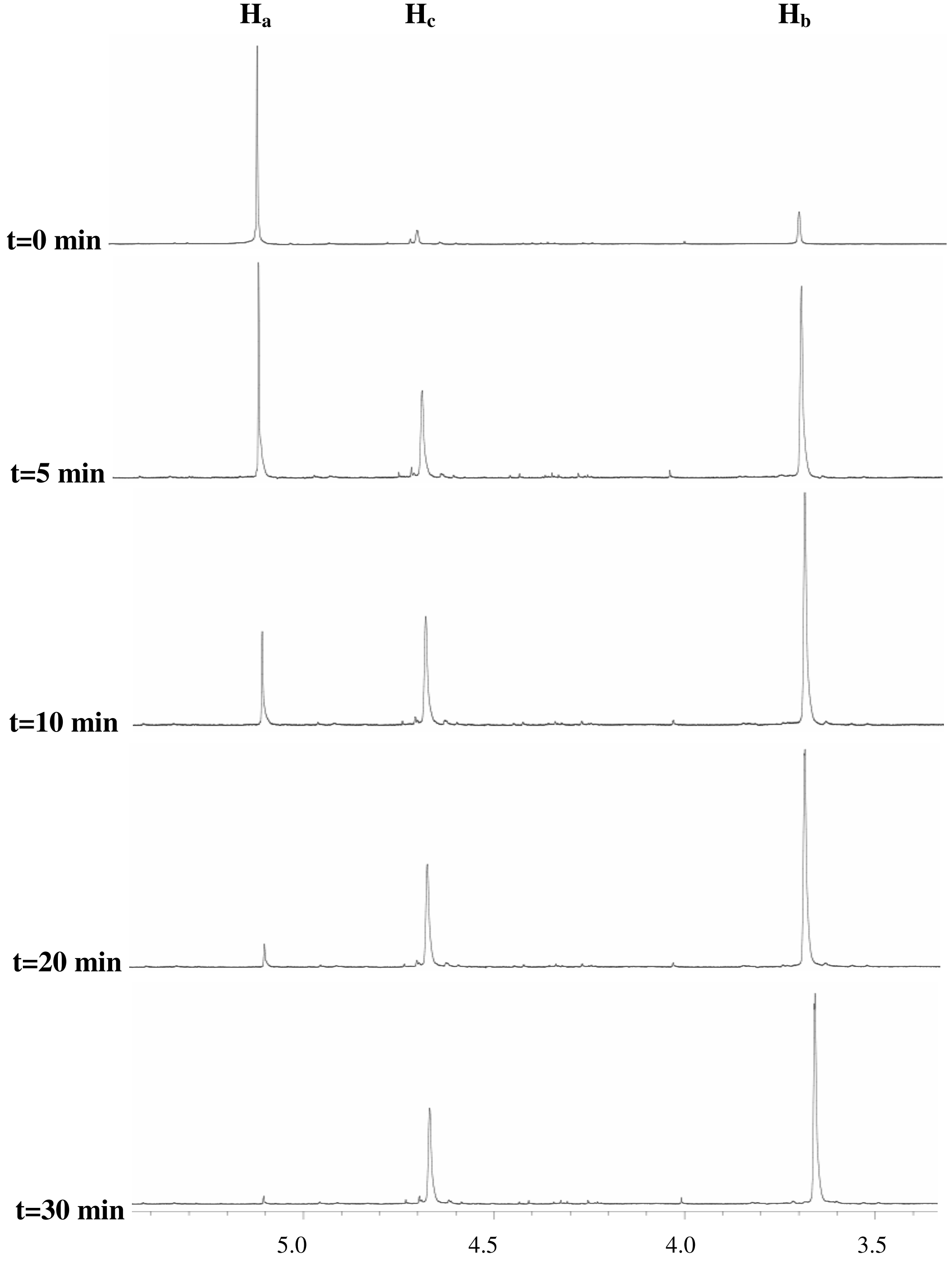
time	volA	volB	total	[A]=A/A+B	ln[A]
0	6488282	1877309	8365591	0.77559159	-0.2541292
2.5	1031034	1048506	2079540	0.49579907	-0.70158453
5	745881	1343987	2089868	0.3569034	-1.03029012
7.5	529353	1542175	2071528	0.25553746	-1.36438627
10	379702	1703001	2082703	0.18231212	-1.70203511
15	182635	1872592	2055227	0.08886366	-2.42065196
20	82259	1996905	2079164	0.0395635	-3.22984836
25	21837	2048916	2070753	0.01054544	-4.55206181

lnA=-kt +lnAo
k=0.14528
t(1/2)= 4.7711122
t(1/2)=ln2/k

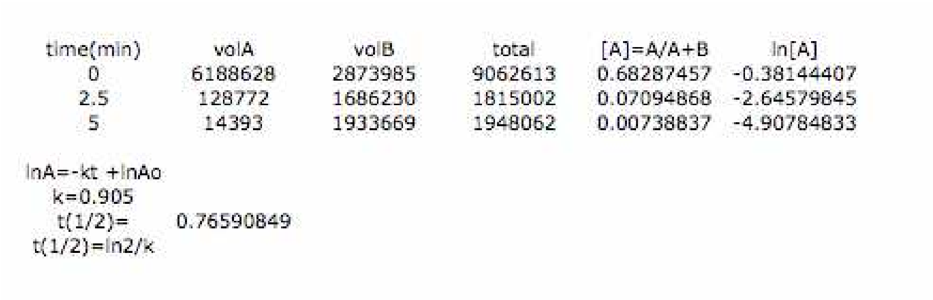


T=330K, **12a→13a ($t_{1/2}$=4.8 minutes)**





T=330K, **12b➔13d ($t_{1/2}$=0.8 minutes)**



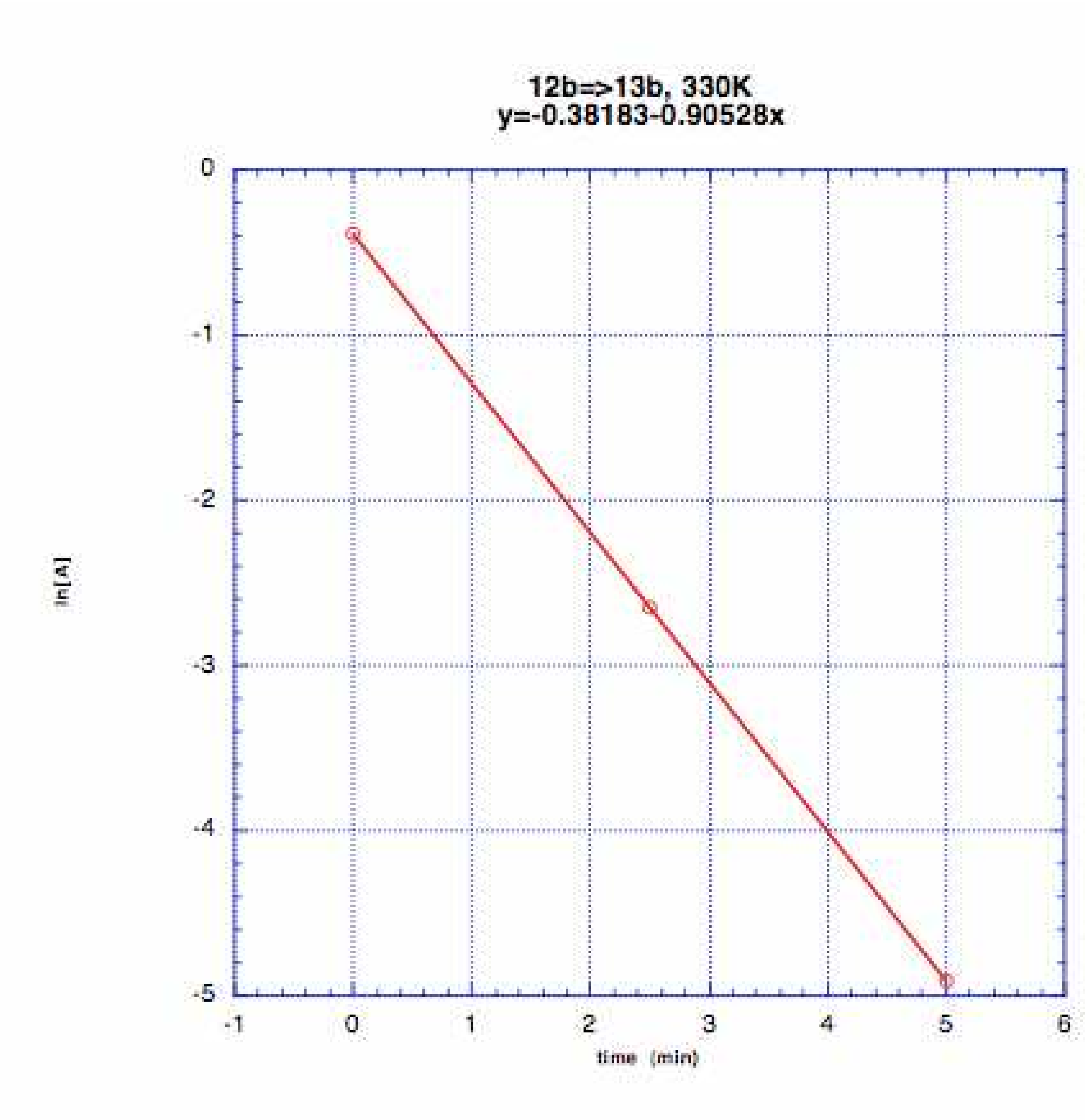
time(min)	volA	volB	total	[A]=A/A+B	ln[A]
0	6188628	2873985	9062613	0.68287457	-0.38144407
2.5	128772	1686230	1815002	0.07094868	-2.64579845
5	14393	1933669	1948062	0.00738837	-4.90784833

lnA=-kt +lnAo

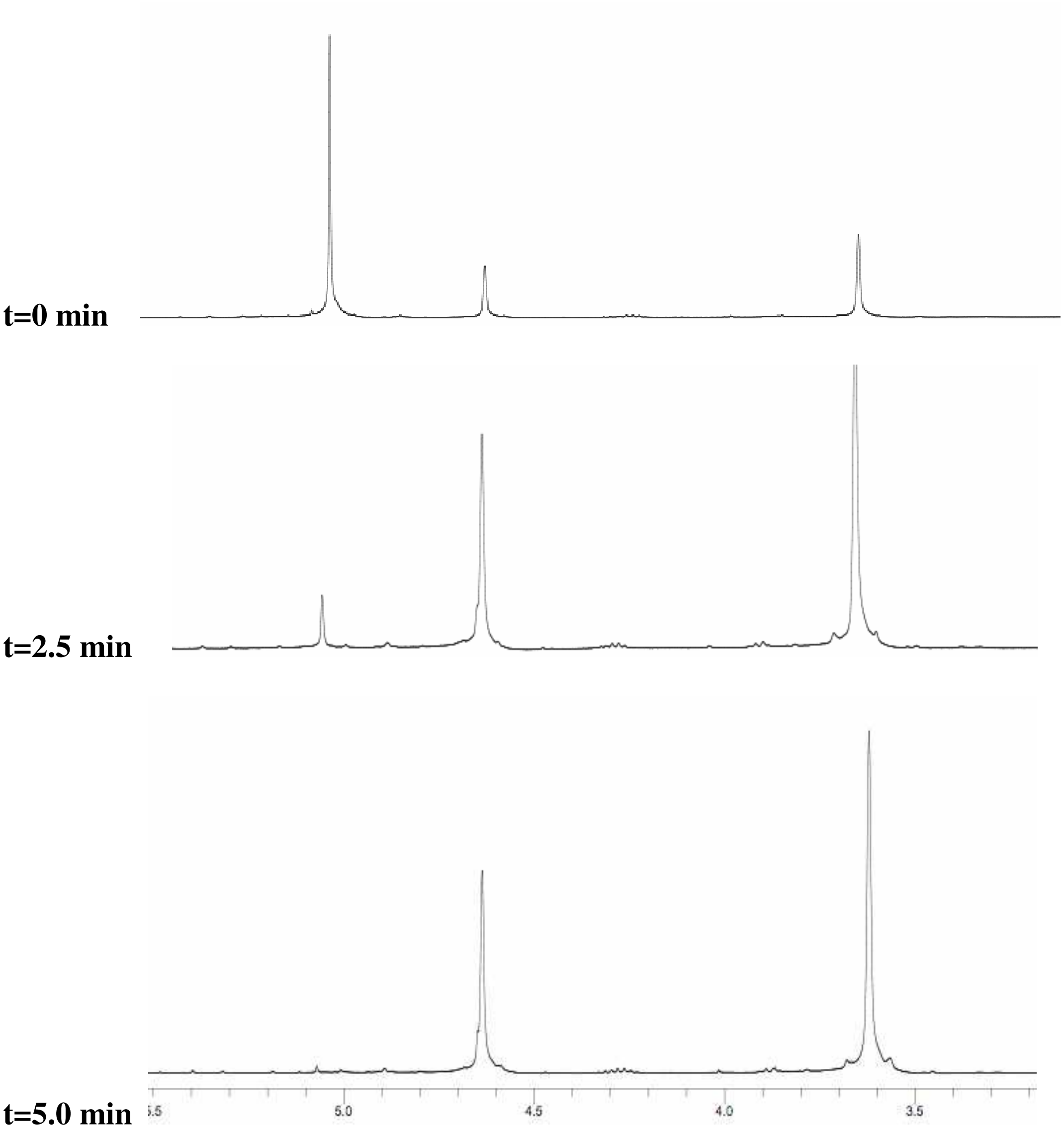
k=0.905

t(1/2)= 0.76590849

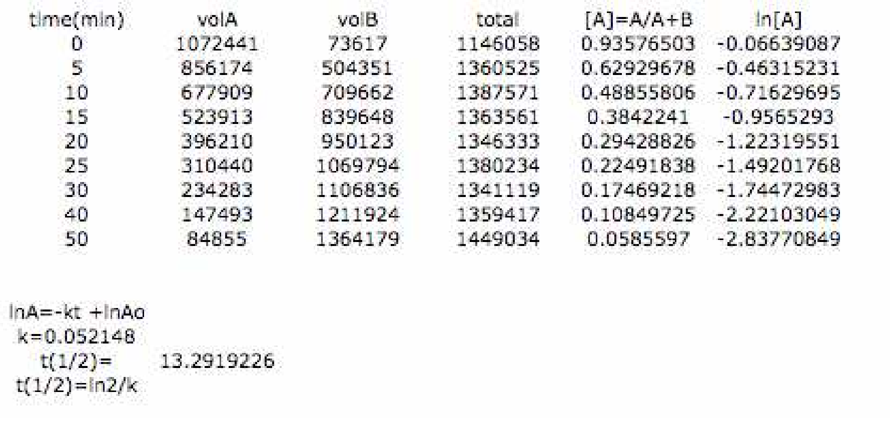
t(1/2)=ln2/k



T=330K, **12b➔13d ($t_{1/2}$=0.8 minutes)**

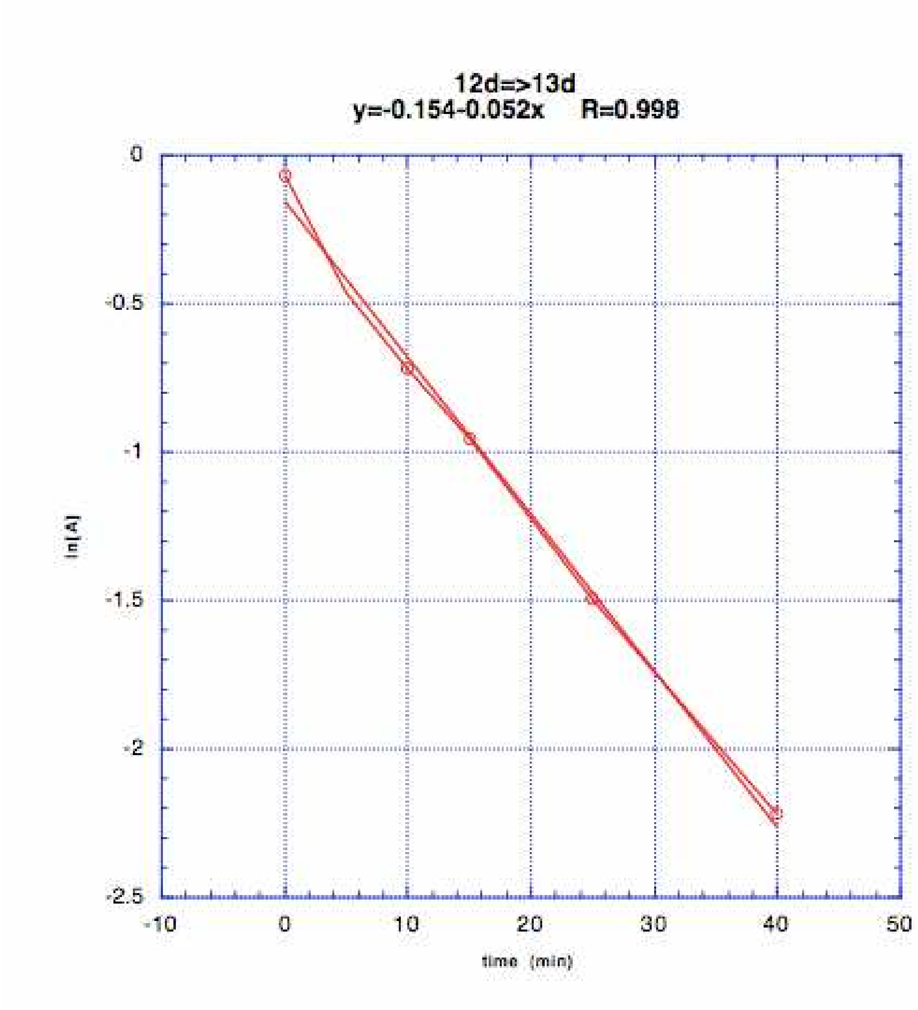


T=330K, **12d→13d ($t_{1/2}$=13.3 minutes)**

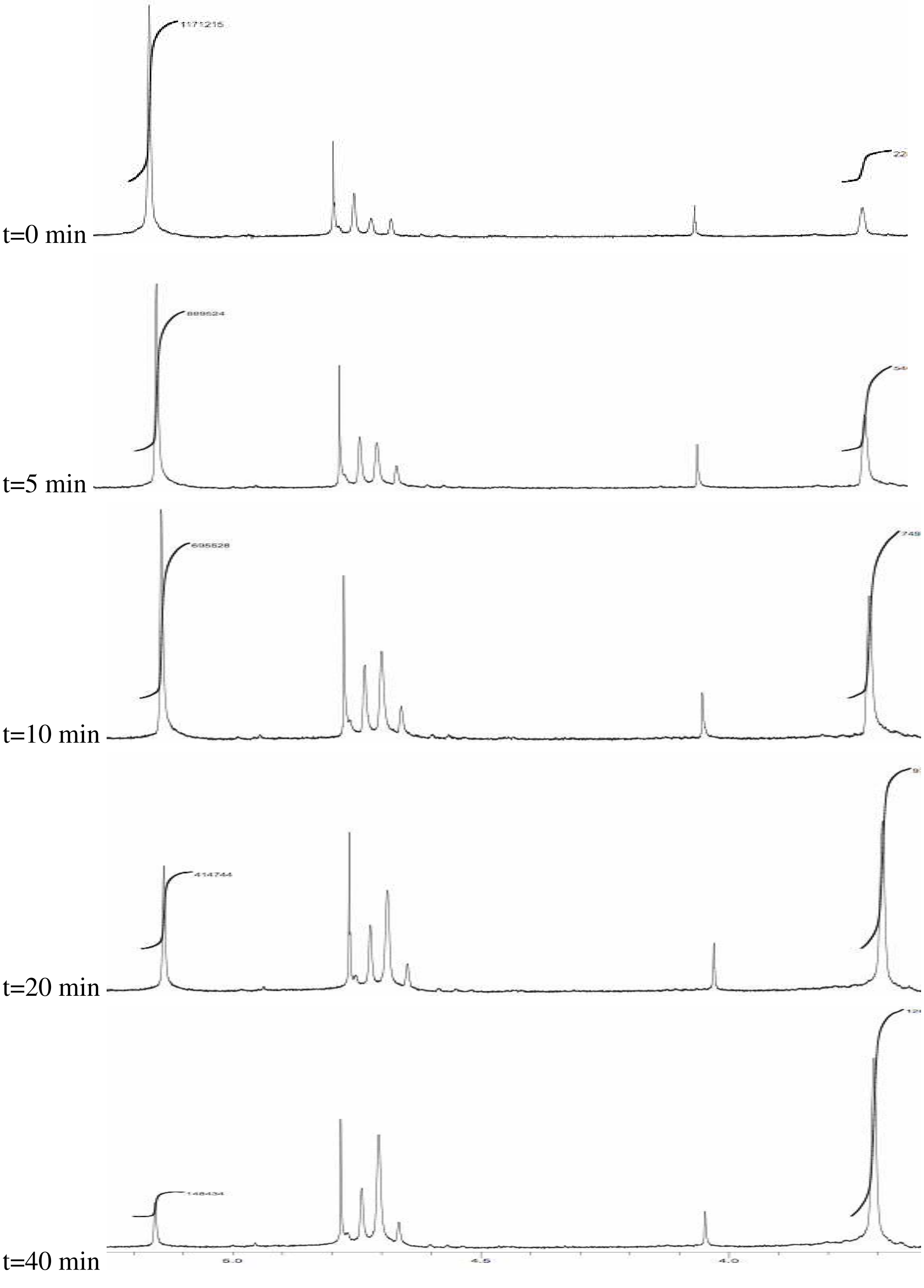


time(min)	volA	volB	total	[A]=A/A+B	ln[A]
0	1072441	73617	1146058	0.93576503	-0.06639087
5	856174	504351	1360525	0.62929678	-0.46315231
10	677909	709662	1387571	0.48855806	-0.71629695
15	523913	839648	1363561	0.3842241	-0.9565293
20	396210	950123	1346333	0.29428826	-1.22319551
25	310440	1069794	1380234	0.22491838	-1.49201768
30	234283	1106836	1341119	0.17469218	-1.74472983
40	147493	1211924	1359417	0.10849725	-2.22103049
50	84855	1364179	1449034	0.0585597	-2.83770849

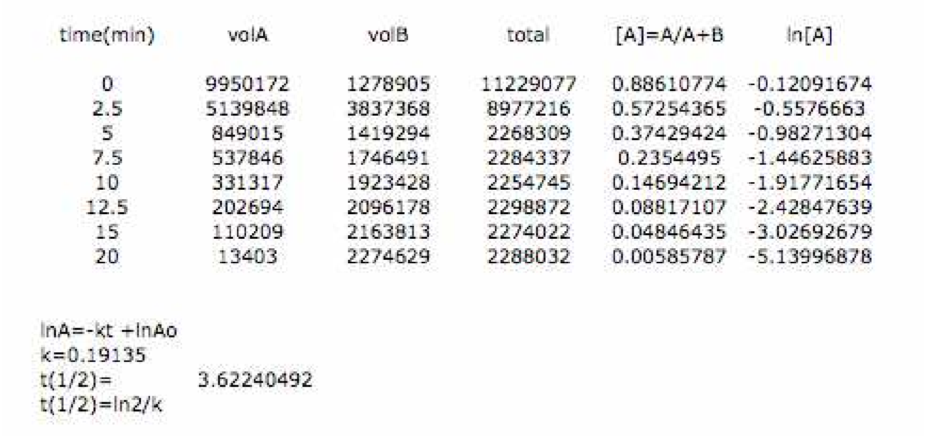
lnA=-kt +lnAo
k=0.052148
t(1/2)= 13.2919226
t(1/2)=ln2/k



T=330K, **12d→13d ($t_{1/2}$=13.3 minutes)**

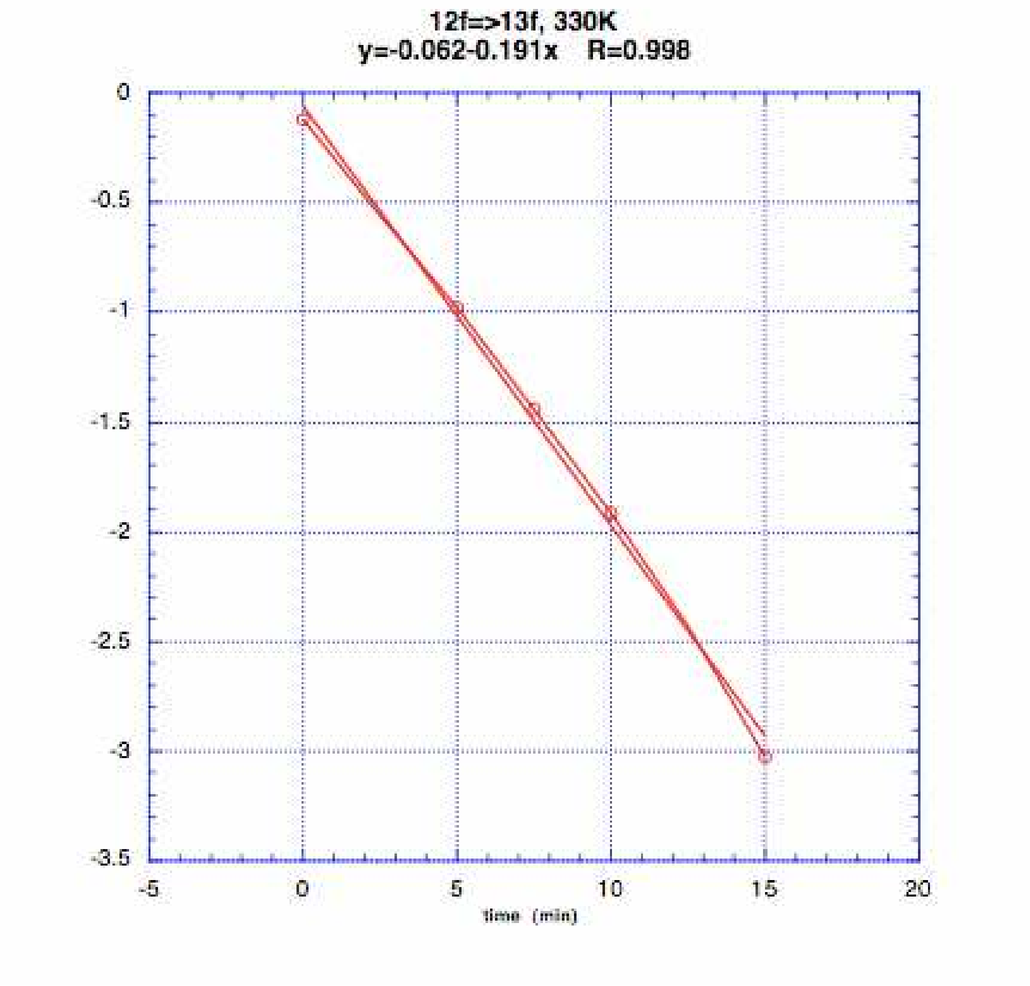


T=330K, **12f→13f (t$_{1/2}$=3.6 minutes)**

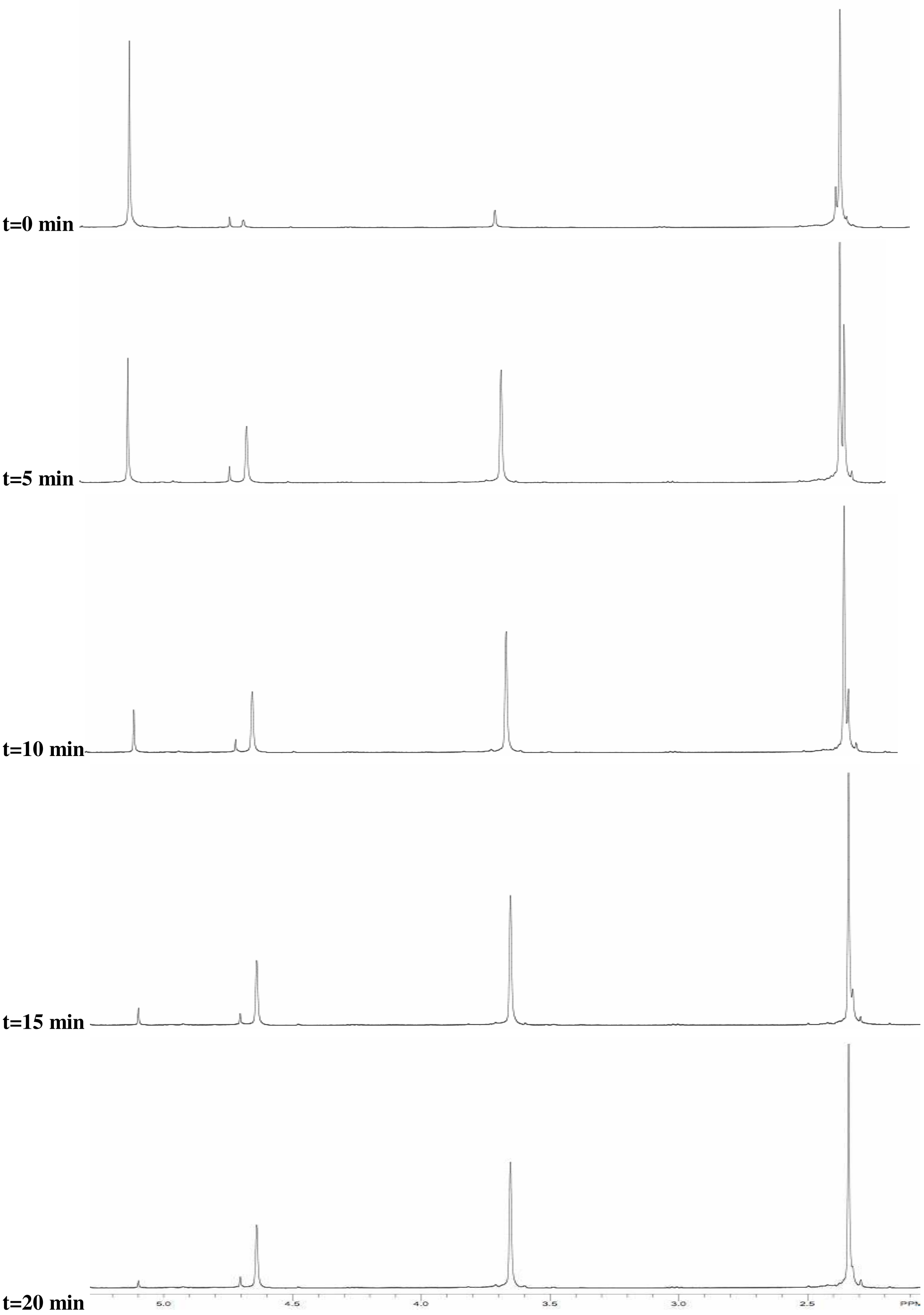


time(min)	volA	volB	total	[A]=A/A+B	ln[A]
0	9950172	1278905	11229077	0.88610774	-0.12091674
2.5	5139848	3837368	8977216	0.57254365	-0.5576663
5	849015	1419294	2268309	0.37429424	-0.98271304
7.5	537846	1746491	2284337	0.2354495	-1.44625883
10	331317	1923428	2254745	0.14694212	-1.91771654
12.5	202694	2096178	2298872	0.08817107	-2.42847639
15	110209	2163813	2274022	0.04846435	-3.02692679
20	13403	2274629	2288032	0.00585787	-5.13996878

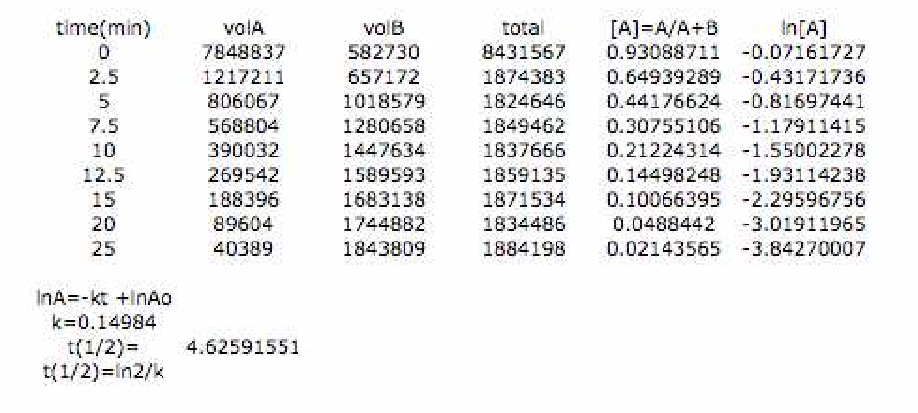
lnA=-kt +lnAo
k=0.19135
t(1/2)= 3.62240492
t(1/2)=ln2/k



T=330K, **12f→13f ($t_{1/2}$=3.6 minutes)**

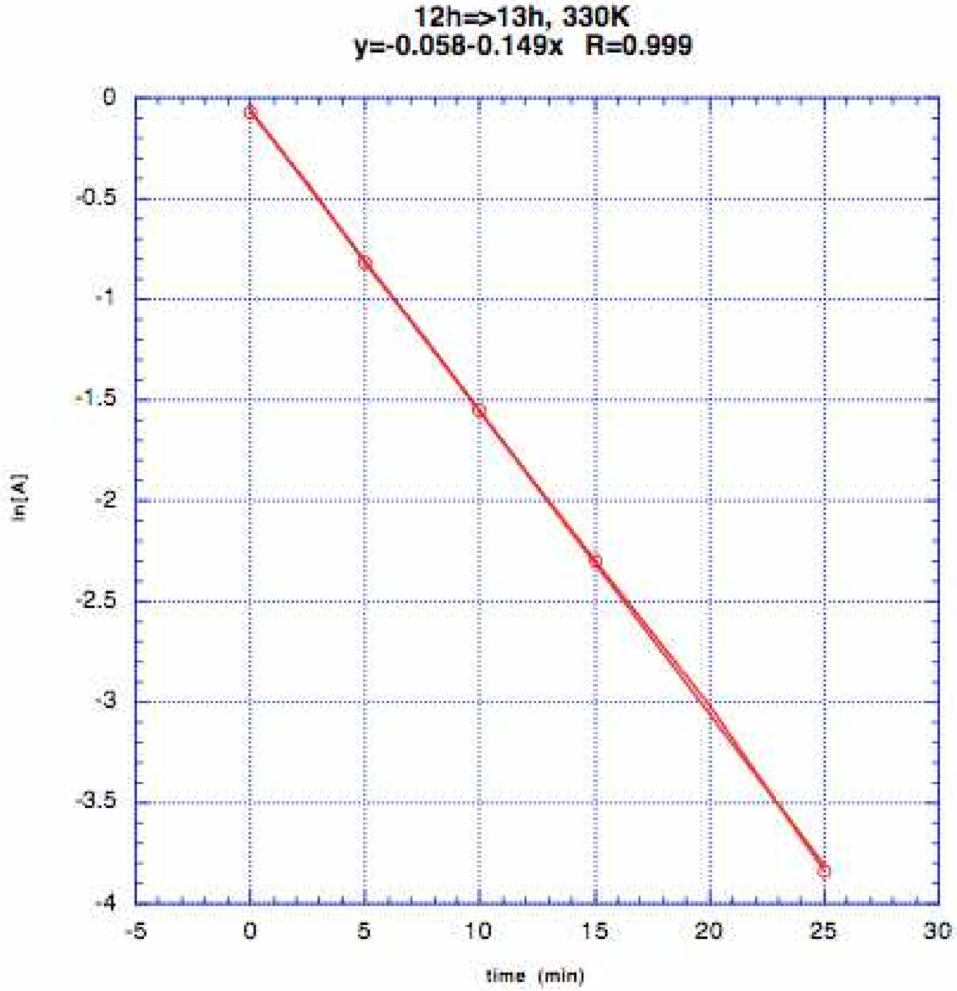


T=330K, **12h➔13h (t$_{1/2}$=4.6 minutes)**

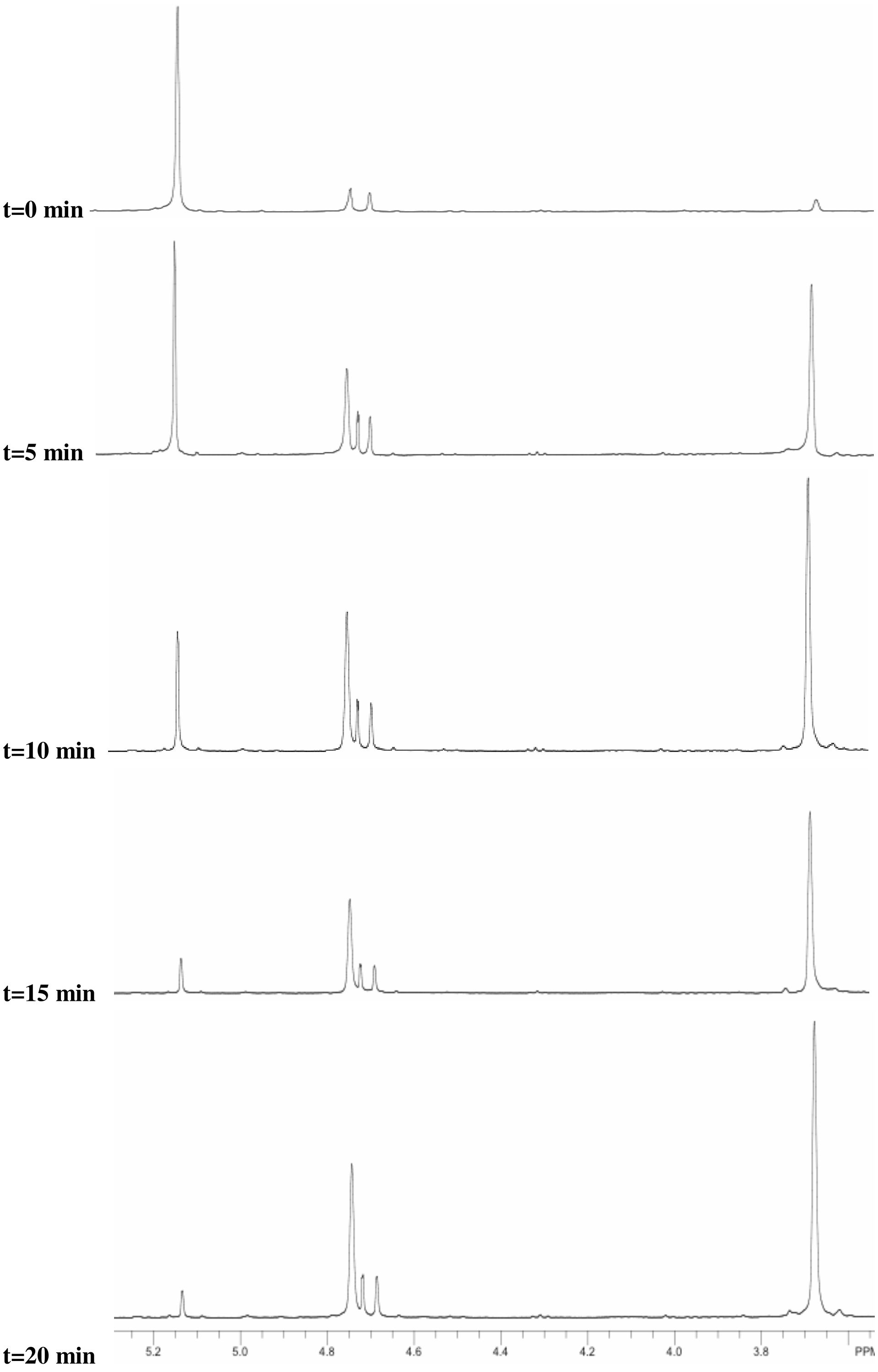


time(min)	volA	volB	total	[A]=A/A+B	ln[A]
0	7848837	582730	8431567	0.93088711	-0.07161727
2.5	1217211	657172	1874383	0.64939289	-0.43171736
5	806067	1018579	1824646	0.44176624	-0.81697441
7.5	568804	1280658	1849462	0.30755106	-1.17911415
10	390032	1447634	1837666	0.21224314	-1.55002278
12.5	269542	1589593	1859135	0.14498248	-1.93114238
15	188396	1683138	1871534	0.10066395	-2.29596756
20	89604	1744882	1834486	0.0488442	-3.01911965
25	40389	1843809	1884198	0.02143565	-3.84270007

lnA=-kt +lnAo
k=0.14984
t(1/2)= 4.62591551
t(1/2)=ln2/k



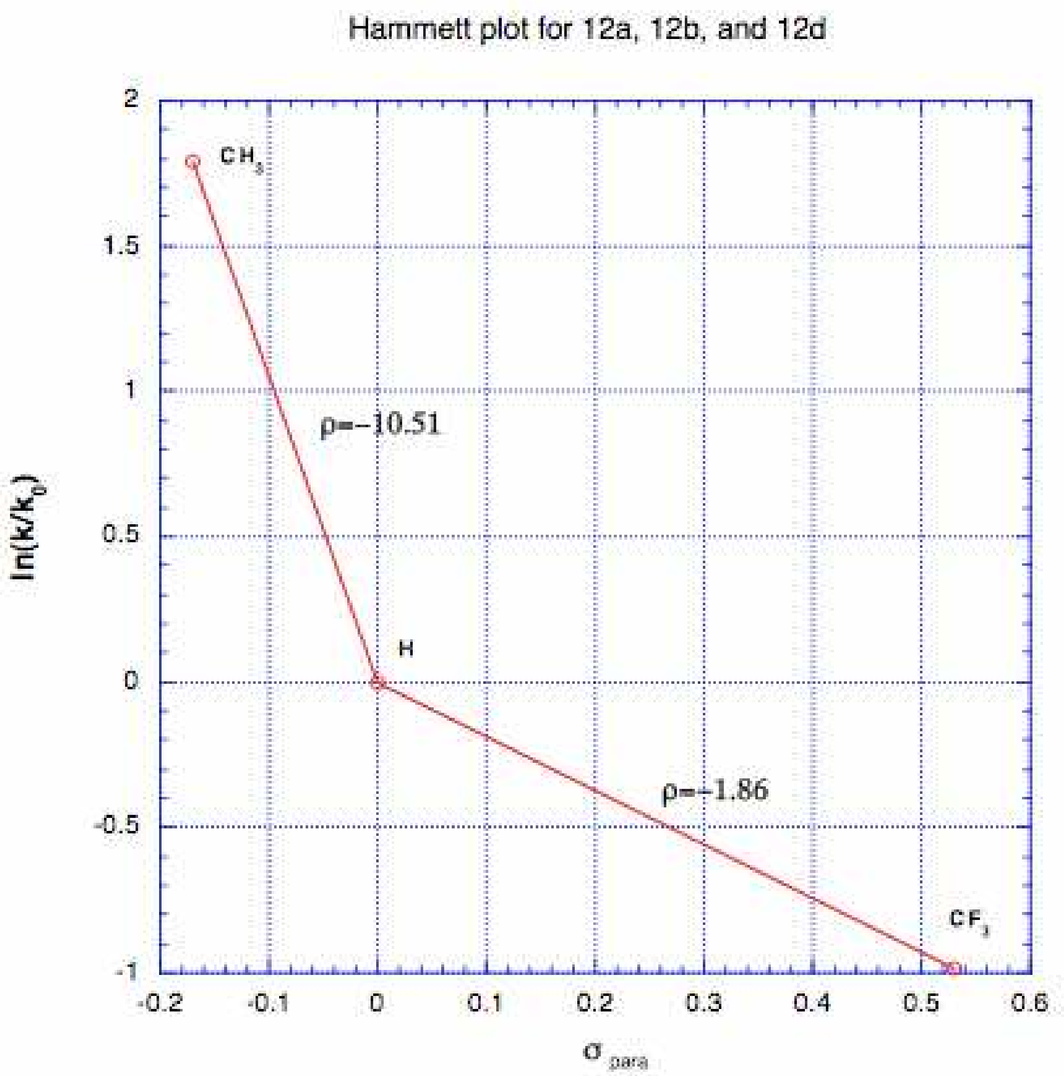
T=330K, **12h➔13h ($t_{1/2}$=4.6 minutes)**



Data for Hammett plot, 12a, 12b, 12d

Y	$\ln(k/k_0)$	σ
CF_3	-0.9877	0.53
H	0	0
CH_3	1.7871	-0.17

(σ values obtained from reference 13, main text)



Data for Hammett plot, 12a, 12f, 12h

X	ln(k/k_0)	σ
Ph-CF_3	0.0272	0.53
Ph-H	0	0
Ph-CH_3	0.2755	-0.17