Electronic Supplementary Material (ESI) for Green Chemistry

Synthesis of Substituted Amines and Isoindolinones: Catalytic Reductive Amination using Abundantly Available $AlCl_3$/PMHS

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Supporting information

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Experimental

General

$AlCl_3$ was purchased from Fisher Scientific India Pvt. Ltd. (Acros Organics). Silica gel (60-120 mesh) used for column chromatography was purchased from Sisco Research Laboratories Pvt. Ltd. India and all other chemicals were purchased from Spectrochem, India, Merck, Germany, and Sigma-Aldrich, USA and were used without further purification. NMR spectra were recorded on a Bruker Avance-300 and 600 spectrometers. Mass spectra were recorded on QTOF-Micro of Waters Micromass and Maxis-Bruker. The GC-MS analysis was carried out on a Shimadzu (QP 2010) series Gas Chromatogram-Mass Spectrometer (Tokyo, Japan), AOC-20i auto-sampler coupled, and a DB-5MS capillary column, (30 m x 0.25 mm i.d., 0.25µm). The initial temperature of column was 70 °C held for 4 min. and was programmed to 230 °C at 4°C/min., then held for 15 min. at 230 °C; the sample injection volume was 2 µl in GC grade dichloromethane. Helium was used as carrier gas at a flow rate of 1.1 ml min^{-1} on split mode (1:50). UV-Vis spectra were recorded on UV-Vis 2450 spectrophotometer from Shimadzu.

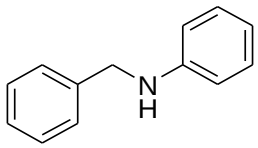
General experimental procedure for reductive amination of carbonyl compounds catalyzed by $AlCl_3$/PMHS system: To a stirred suspension of $AlCl_3$ (0.02 mmol) in ethanol (4 mL) were added carbonyl compound (1.0 mmol), amine (1.0 mmol) and PMHS (2.0 H equiv.) at room temperature and then the temperature was raised to 70 ^oC. On completion of the reaction (as monitored by TLC), reaction mixture was dried under vacuum and crude product was analyzed directly by GC-MS. For the purification of desired product column chromatography was carried out (*n*-hexane: ethyl acetate).

General experimental procedure for synthesis of N-substituted isoindolinones catalyzed by $AlCl_3$/PMHS system: To a stirred suspension of $AlCl_3$ (0.02 mmol) in ethanol (4 mL) were added 2-carboxybenzaldehyde (1.0 mmol), amine (1.0 mmol) and PMHS (2.0 H equiv.) at room temperature and then the temperature was raised to 70 ^{o}C. On completion of the reaction (as monitored by TLC), reaction mixture was dried under vacuum and product was purified by crystallization with absolute ethanol.

Experimental procedure for recyclability of the catalyst: The recyclability of the catalyst was evaluated by carrying out the reductive amination of benzaldehyde with aniline as test reaction. On completion of the reaction (as monitored by TLC), reaction mixture was dried under vacuum and the crude product was extracted with ethyl acetate (2 x 5mL). The residue left was dried under vacuum for 15 minutes. Successive reactions were carried out by sequential addition of fresh substrates, PMHS and ethanol to the crude remains after extracting the product.

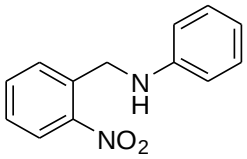
NMR data of isolated compounds

1. *N*-Benzylaniline (Table 2, entry 1)



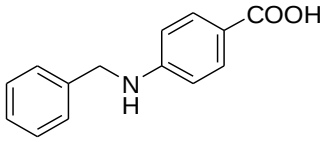
^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.06 (brs, 1H), 4.37 (s, 2H), 6.68 (d, 2H, J = 7.7 Hz), 6.76 (t, 1H, J = 7.3 Hz), 7.19-7.24 (m, 2H), 7.31-7.43 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 48.7, 113.2, 117.9, 127.6, 127.9, 129.0, 129.6, 139.8, 148.5.

2. *N*-(2'-Nitrobenzyl)aniline (Table 2, entry 2)



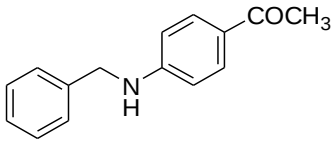
^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.38 (brs, 1H), 4.75 (s, 2H), 6.59 (d, 2H, J = 7.7 Hz), 6.75 (t, 1H, J = 7.3 Hz), 7.15-7.21 (m, 2H), 7.41-7.47 (m, 1H), 7.56-7.61 (m, 1H), 7.70 (d, 1H, J = 7.6 Hz), 8.10 (d, 1H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 46.1, 113.3, 118.4, 125.5, 128.3, 129.7, 130.1, 134.0, 136.0, 147.7, 148.6.

3. 4-(*N*-Benzylamino)benzoic acid (Table 2, entry 10)



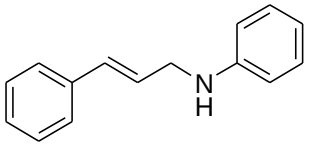
^{1}H NMR (CD_3OD, 300 MHz) δ 4.24 (s, 2H), 6.46 (d, 2H, J = 8.7 Hz), 7.07-7.21 (m, 5H), 7.63 (d, 2H, J = 8.7 Hz); ^{13}C NMR (CD_3OD, 75 MHz) δ 48.2, 112.9, 119.0, 128.4, 128.6, 129.9, 133.1, 141.1, 154.7, 171.3; HRESIMS calcd for $C_{14}H_{13}NNaO_2$ $[M+Na]^+$ 250.0844, found 250.0842.

4. 4-(*N*-Benzylamino)acetophenone (Table 2, entry 11)



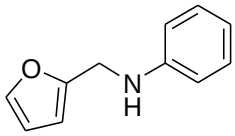
^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.49 (s, 3H), 4.40 (s, 2H), 5.22 (brs, 1H), 6.62 (d, 2H, J = 8.5 Hz), 7.28-7.31 (m, 5H), 7.84 (d, 2H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 47.8, 112.0, 127.1, 127.7, 127.9, 129.2, 131.2, 138.8, 152.6, 197.0.

5. *N*-Cinnamylaniline (Table 2, entry 13)



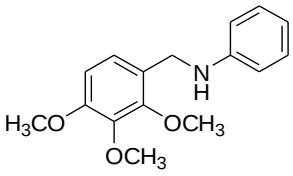
^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.90 (brs, 1H), 4.00 (d, 2H, J = 5.6 Hz), 6.36-6.45 (m, 1H), 6.67-6.76 (m, 3H), 6.82 (t, 1H, J = 7.3 Hz), 7.26-7.33 (m, 2H), 7.37-7.47 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 46.6, 113.5, 118.1, 126.8, 127.5, 128.0, 129.0, 129.7, 131.9, 137.3, 148.5; HRESIMS calcd for $C_{15}H_{16}N$ $[M+H]^+$ 210.1283, found 210.1247.

6. *N*-Furfurylaniline (Table 2, entry 15)



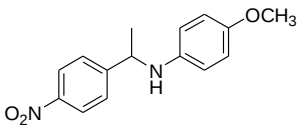
^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.07 (brs, 1H), 4.37 (s, 2H), 6.29-6.39 (m, 2H), 6.72-6.75 (m, 2H), 6.78-6.83 (m, 1H), 7.23-7.28 (m, 2H), 7.43-7.46 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 41.8, 107.4, 110.7, 113.6, 118.4, 129.6, 142.3, 148.1, 153.2.

7. *N*-(2',3',4'-trimethoxybenzyl)aniline (Table 2, entry 16)



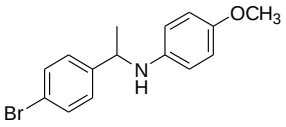
^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.89 (s, 1H), 3.97 (s, 3H), 4.00 (s, 3H), 4.34 (s, 2H), 6.66-6.80 (m, 4H), 7.06-7.08 (m, 1H), 7.22-7.27 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 43.6, 56.4, 61.2, 61.5, 107.6, 113.4, 117.8, 123.8, 125.6, 129.6, 142.7, 148.8, 152.3, 153.6.

8. 1-(4-Methoxyphenylamino)-1-(4-nitrophenyl)ethane (Table 3, entry 3)



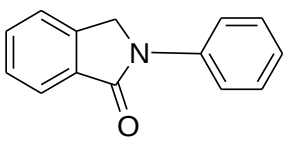
^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.53-1.55 (m, 3H), 3.71 (s, 3H), 4.48-4.54 (m, 3H), 6.42 (d, 2H, J = 8.6 Hz), 6.71 (d, 2H, J = 8.6 Hz), 7.56 (d, 2H, J = 7.3 Hz), 8.20 (d, 2H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.3, 54.4, 56.1, 114.9, 115.2, 124.4, 127.1, 141.0, 147.4, 152.7, 153.8; HRESIMS calcd for $C_{15}H_{16}N_2NaO_3$ $[M+Na]^+$ 295.1059, found 295.1053.

9. 1-(4-Bromophenylamino)-1-(4-nitrophenyl)ethane (Table 3, entry 4)



^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.49 (d, 3H, J = 6.7 Hz), 3.72 (s, 3H), 4.36-4.42 (m, 1H), 6.45-6.48 (m, 2H), 6.69-6.76 (m, 2H), 7.25-7.28 (m, 2H), 7.44-7.47 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.4, 54.2, 56.1, 115.0, 115.2, 120.8, 128.1, 132.1, 141.6, 145.0, 152.5.

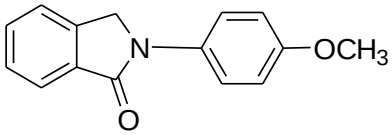
10. *N*-Phenylisoindolone (Table 4, entry 1)



^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.76-4.88 (m, 2H), 7.17-7.22 (m, 1H), 7.42-7.50 (m, 3H), 7.52-7.55 (m, 1H), 7.59-7.61 (m, 1H), 7.78 (m, 1H), 7.88-7.96 (m, 2H); ^{13}C NMR

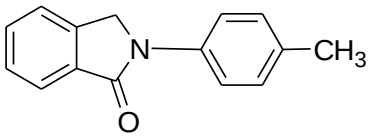
($CDCl_3$, 75 MHz) δ 51.1, 119.8, 123.0, 124.5, 124.8, 128.7, 129.5, 132.4, 133.6, 139.9, 140.5, 168.0; HRESIMS calcd for $C_{14}H_{11}NNaO$ $[M+Na]^+$ 232.0738, found 232.0739.

11. *N*-(4'-methoxyphenyl)isoindolinone (Table 4, entry 2)



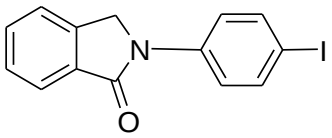
^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.82 (s, 3H), 4.79 (s, 2H), 6.97 (d, 2H, J = 8.8 Hz), 7.48-7.60 (m, 3H), 7.75 (d, 2H, J = 8.8 Hz), 7.92 (d, 1H, J = 7.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.5, 55.8, 114.7, 121.8, 122.9, 124.3, 128.0, 128.8, 132.2, 133.6, 140.5, 157.0, 167.6.

12. *N*-(4'-methylphenyl)isoindolinone (Table 4, entry 3)



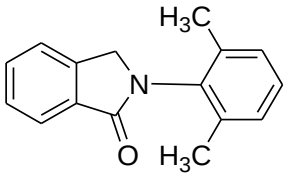
^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.36 (s, 3H), 4.82 (s, 2H), 7.24 (d, 2H, J = 8.0 Hz), 7.50-7.52 (m, 2H), 7.57-7.62 (m, 1H), 7.75 (d, 2H, J = 8.0 Hz), 7.93 (d, 1H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.2, 51.2, 119.9, 122.9, 124.4, 128.7, 130.0, 132.3, 133.7, 134.5, 137.3, 140.5, 167.7.

13. *N*-(4-Iodophenyl)isoindolinone (Table 4, entry 4)



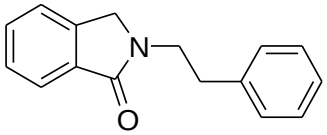
^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.80 (s, 2H), 7.50-7.52 (m, 2H), 7.59-7.61 (m, 1H), 7.64-7.72 (m, 4H), 7.90 (d, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 50.8, 88.2, 121.3, 123.0, 124.5, 128.9, 132.7, 133.2, 138.4, 139.6, 140.2, 167.9.

14. *N*-(2,6-dimethylphenyl)isoindolinone (Table 4, entry 8)



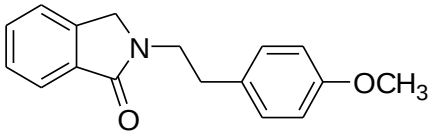
^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.20 (s, 6H), 4.62 (s, 2H), 7.16-7.21 (m, 3H), 7.52-7.56 (m, 2H), 7.61-7.63 (m, 1H), 7.99 (d, 1H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.3, 51.6, 123.3, 124.7, 128.6, 128.91, 128.98, 132.1, 132.7, 134.8, 137.2, 142.1, 168.3.

15. *N*-Phenethylisoindolinone (Table 4, entry 9)



^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.01 (t, 2H, J = 7.3 Hz), 3.89 (t, 2H, J = 7.3 Hz), 4.22 (s, 2H), 7.21-7.33 (m, 5H), 7.39 (d, 1H, J = 7.2 Hz), 7.43-7.54 (m, 2H), 7.86 (d, 1H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 35.3, 44.5, 51.0, 123.0, 124.0, 126.9, 128.3, 129.0, 129.1, 131.5, 133.2, 139.2, 141.5, 168.8; HRESIMS calcd for $C_{16}H_{15}NNaO$ $[M+Na]^+$ 260.1051, found 260.1042.

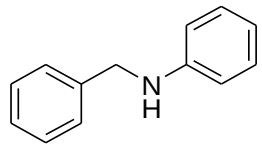
16. *N*-(4'-Methoxyphenethyl)isoindolinone (Table 4, entry 10)

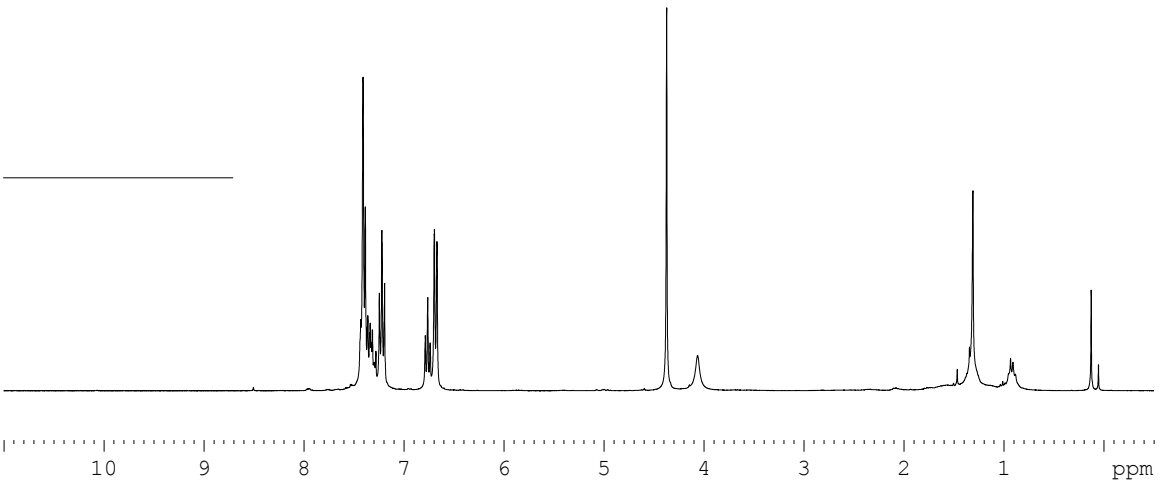


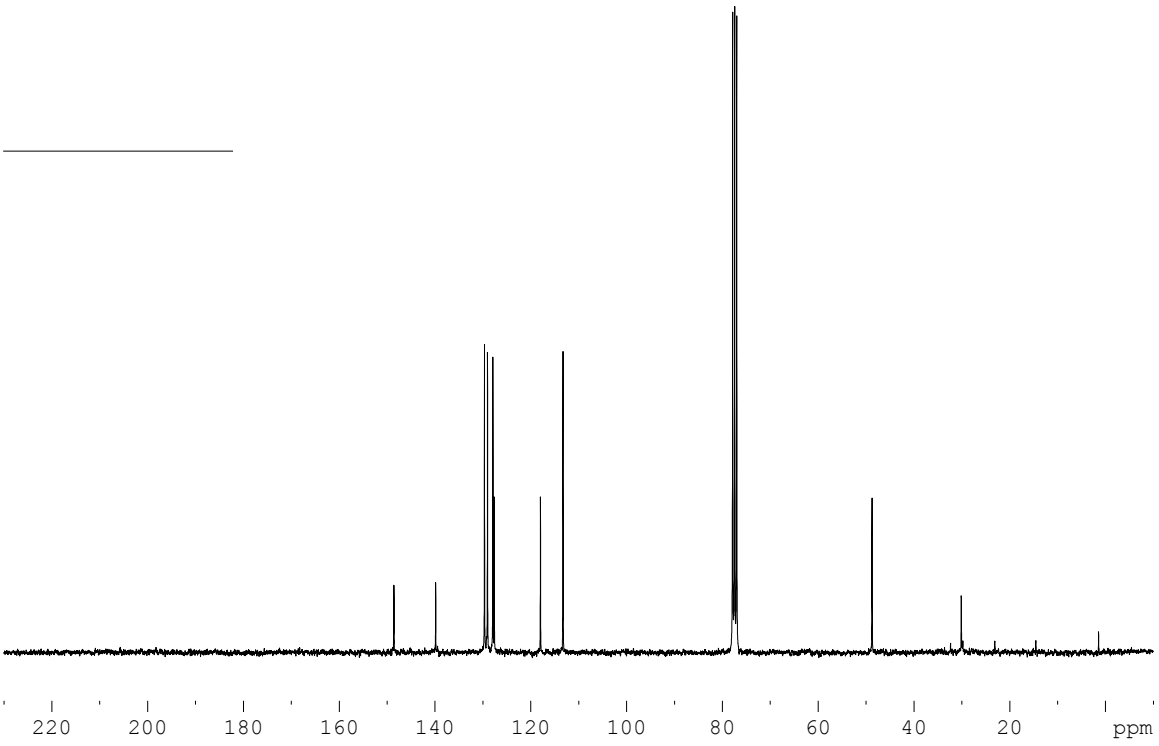
^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.92-2.97 (m, 2H), 3.78 (s, 3H), 3.81-3.86 (m, 2H), 4.20 (s, 2H), 6.83 (d, 2H, J = 8.3 Hz), 7.16 (d, 2H, J = 8.3 Hz), 7.38 (d, 1H, J = 7.3 Hz), 7.42-7.53 (m, 2H), 7.85 (d, 1H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 34.3, 44.6, 51.0, 55.6, 114.4, 123.0, 123.9, 128.3, 130.0, 131.2, 131.5, 133.2, 141.5, 158.6, 168.8; HRESIMS calcd for $C_{17}H_{17}NNaO_2$ $[M+Na]^+$ 290.1157, found 290.1162.

^{1}H and ^{13}C NMR spectra of isolated compounds

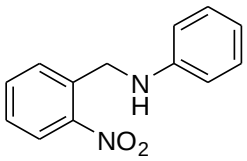
N-Benzylaniline (Table 2, entry 1)

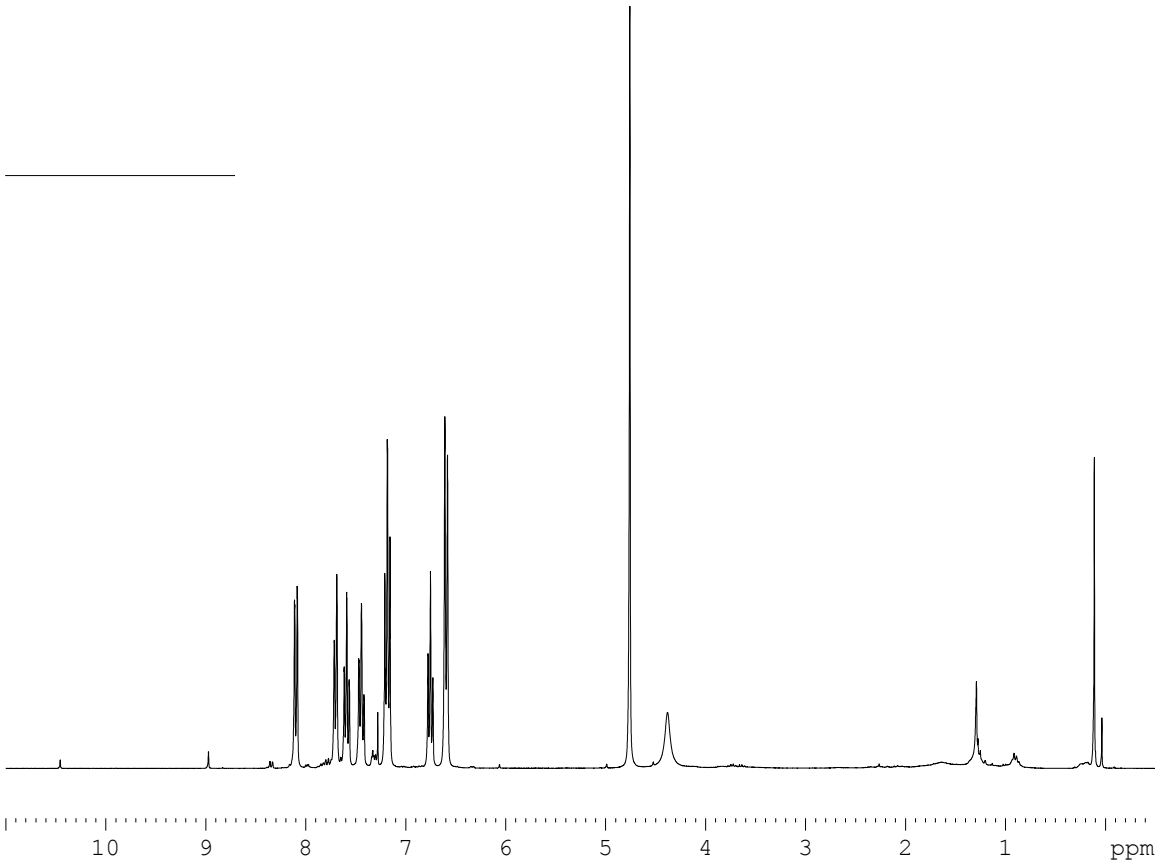


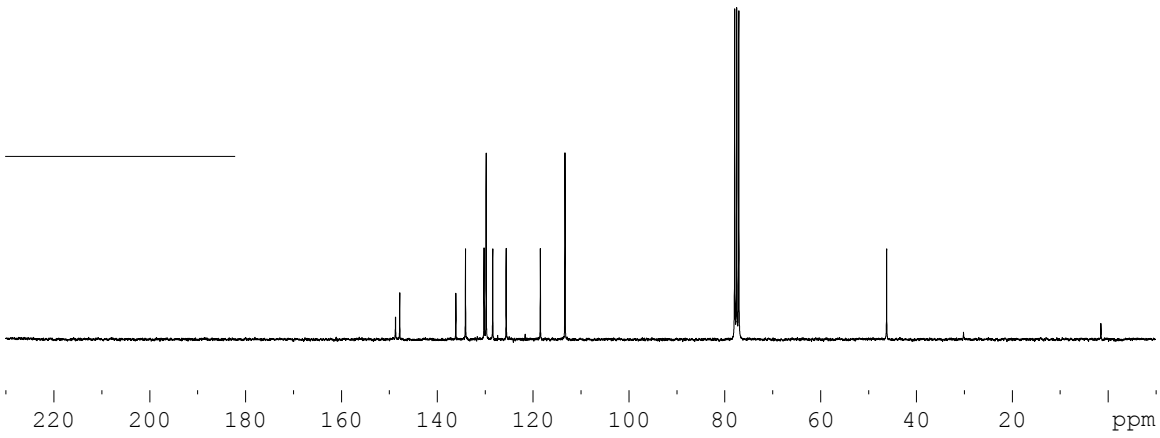




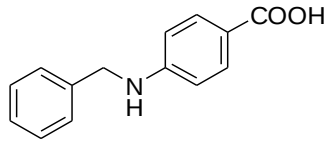
_N_-(2'-Nitrobenzyl)aniline (Table 2, entry 2)

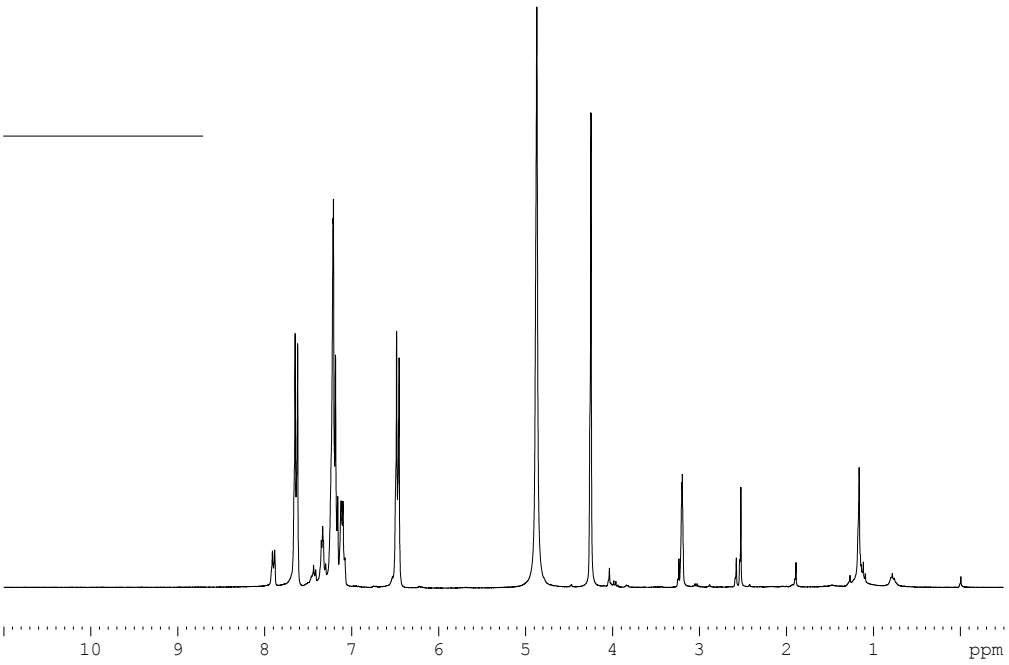


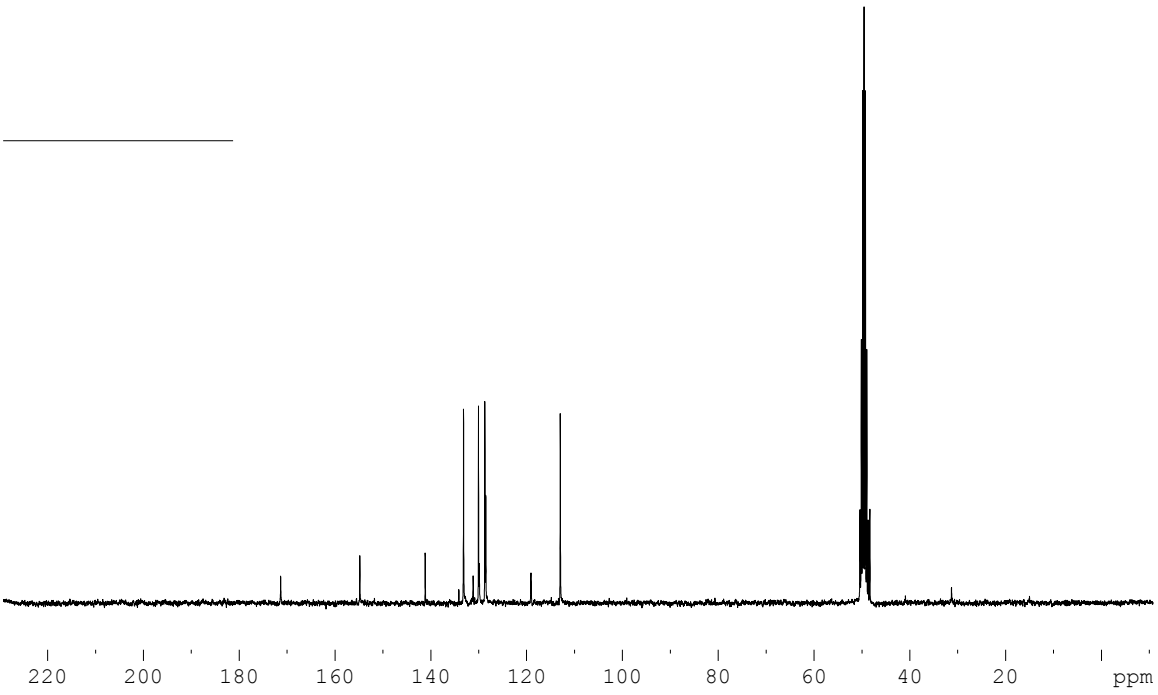




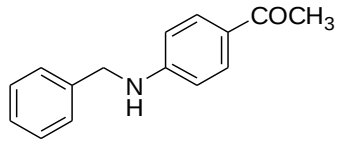
4-(*N*-Benzylamino)benzoic acid (Table 2, entry 10)

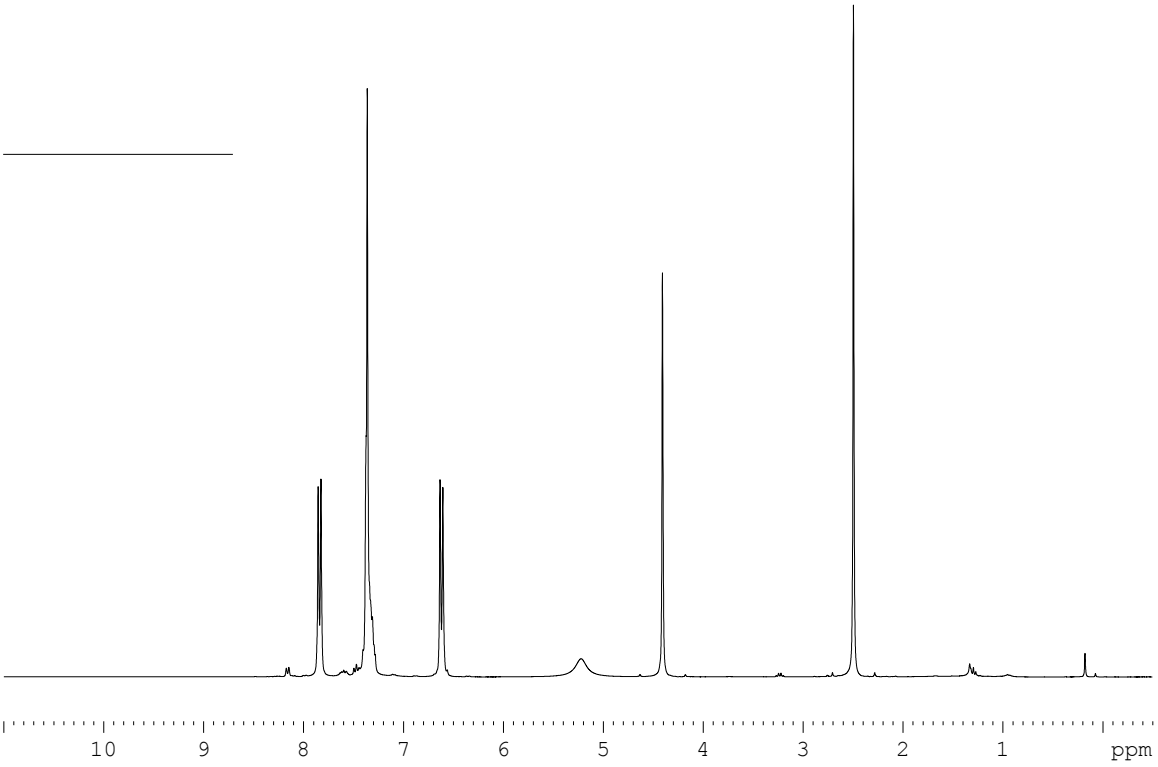


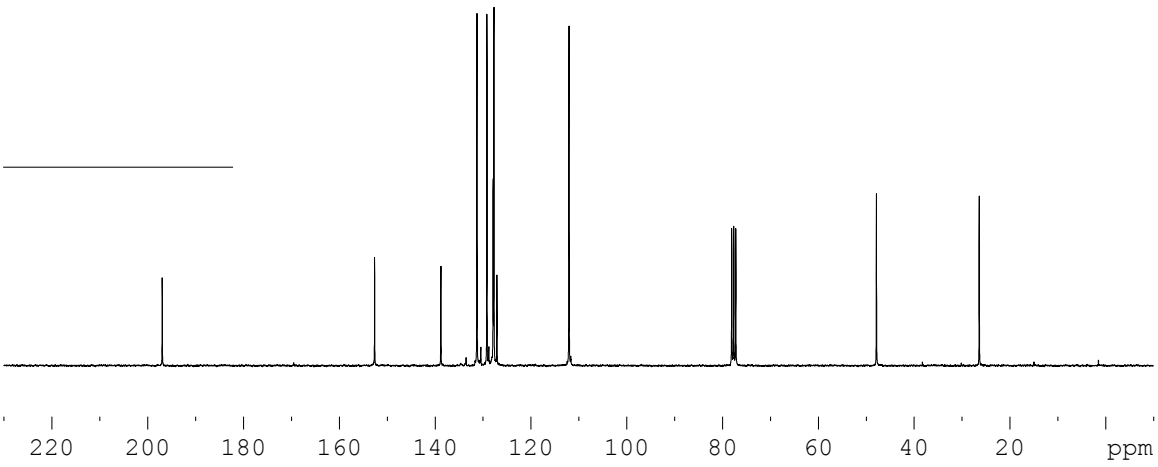




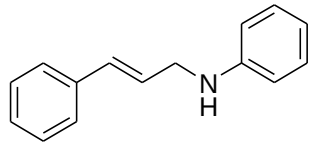
4-(*N*-Benzylamino)acetophenone (Table 2, entry 11)

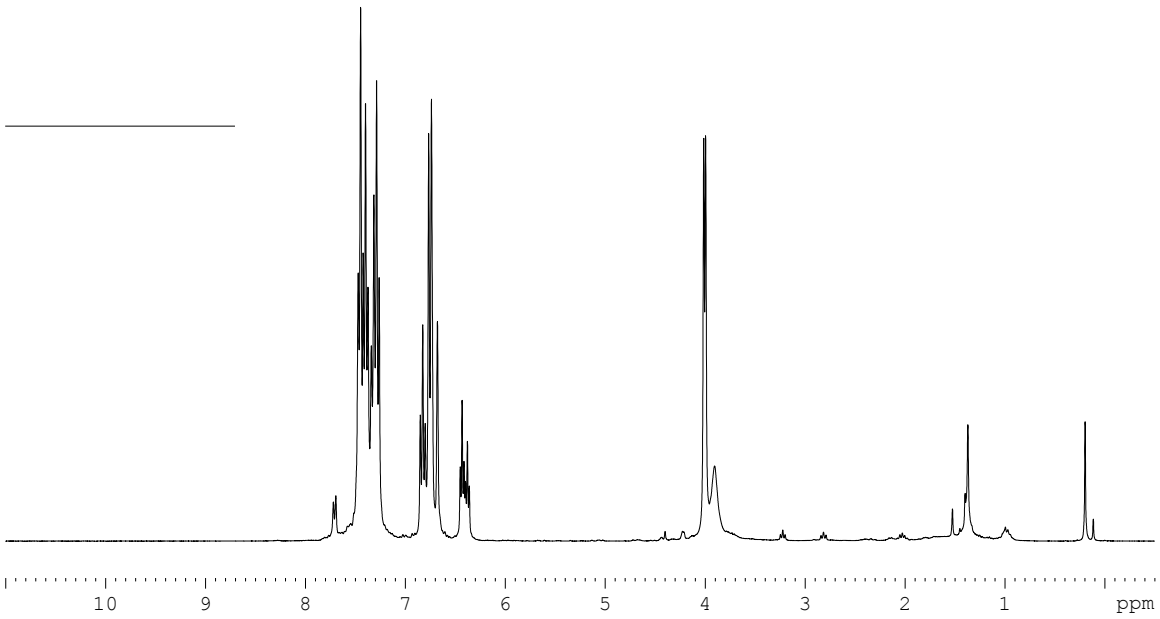


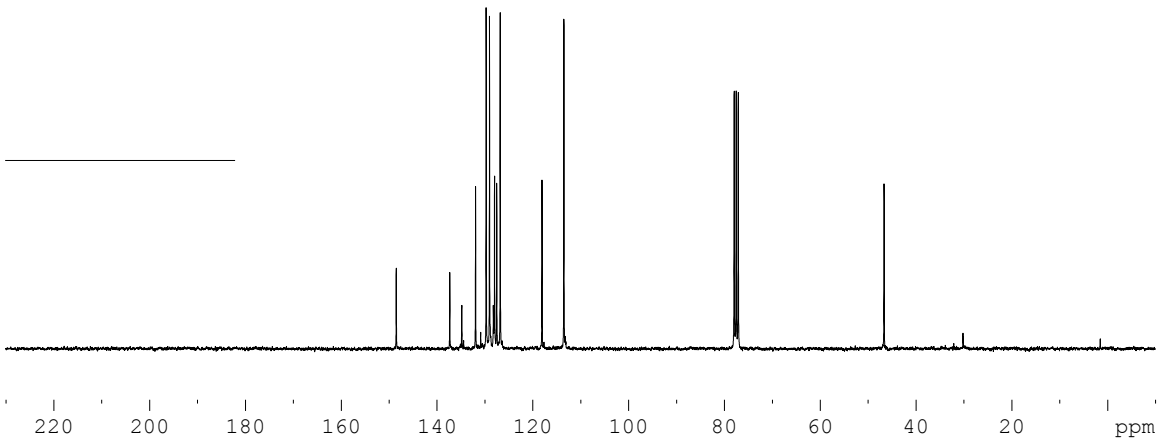




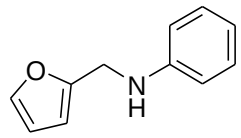
_N_-Cinnamylaniline (Table 2, entry 13)

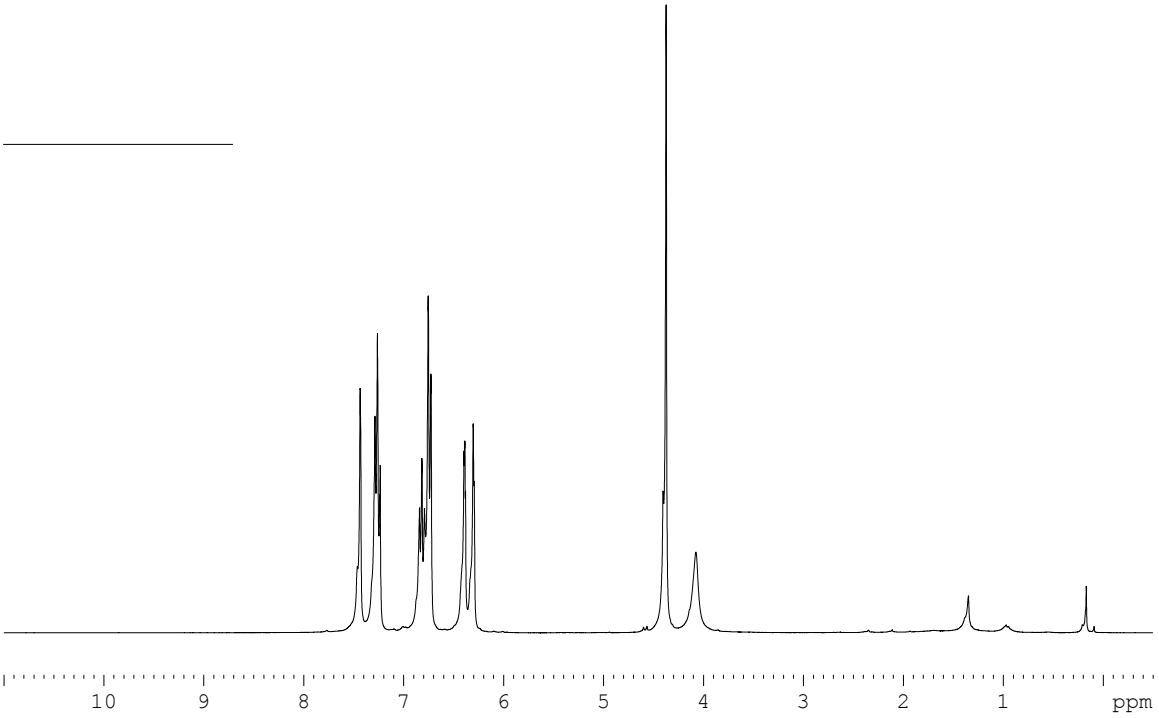


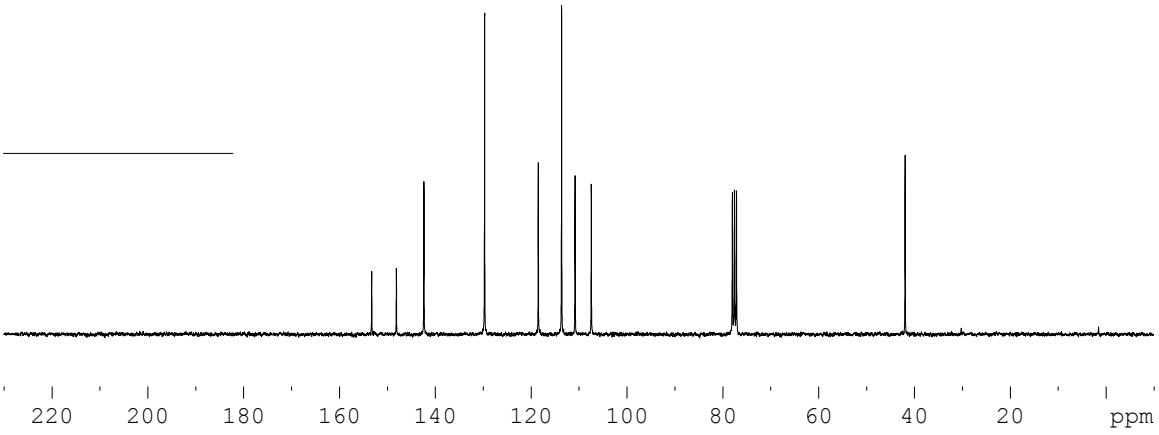




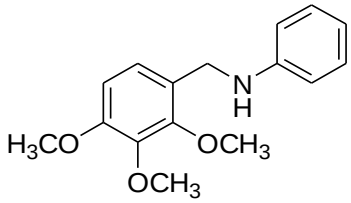
_N_-Furfurylaniline (Table 2, entry 15)

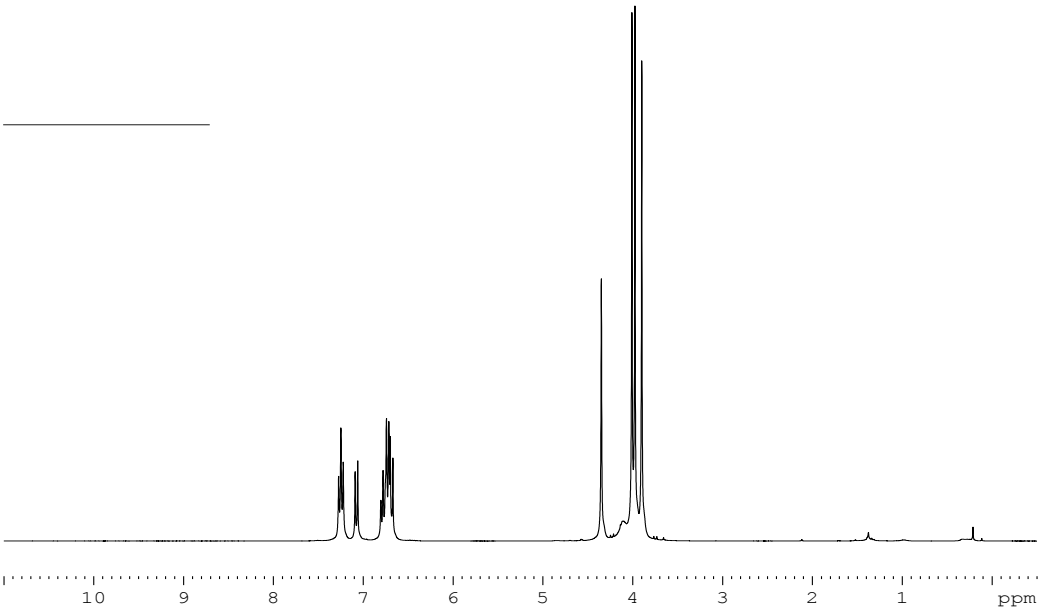


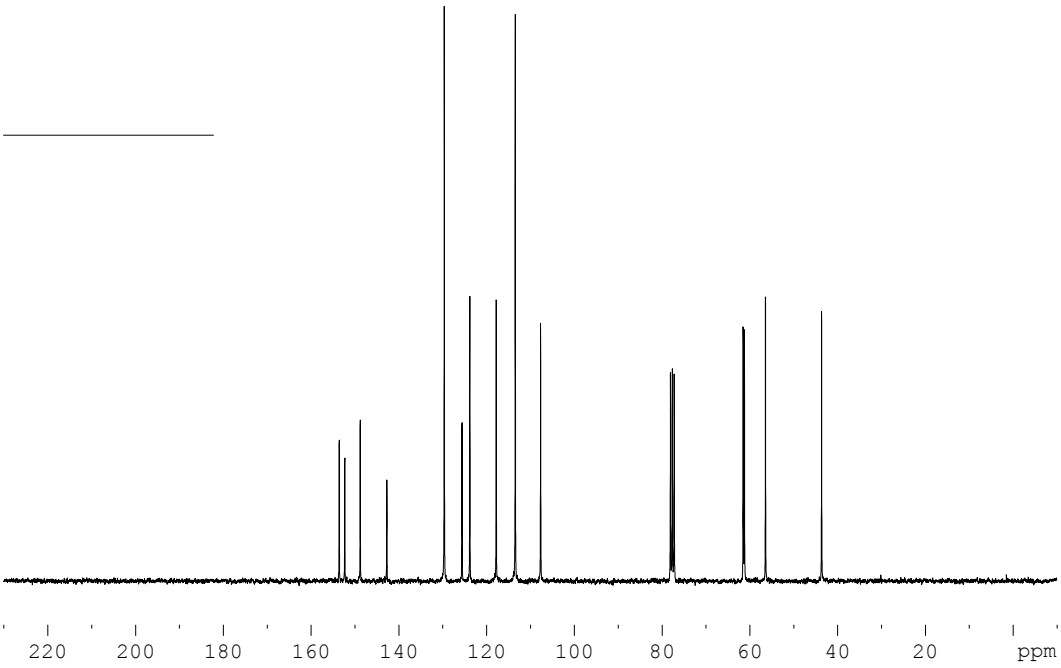




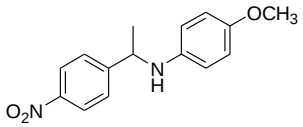
_N_-(2',3',4'-trimethoxybenzyl)aniline (Table 2, entry 16)

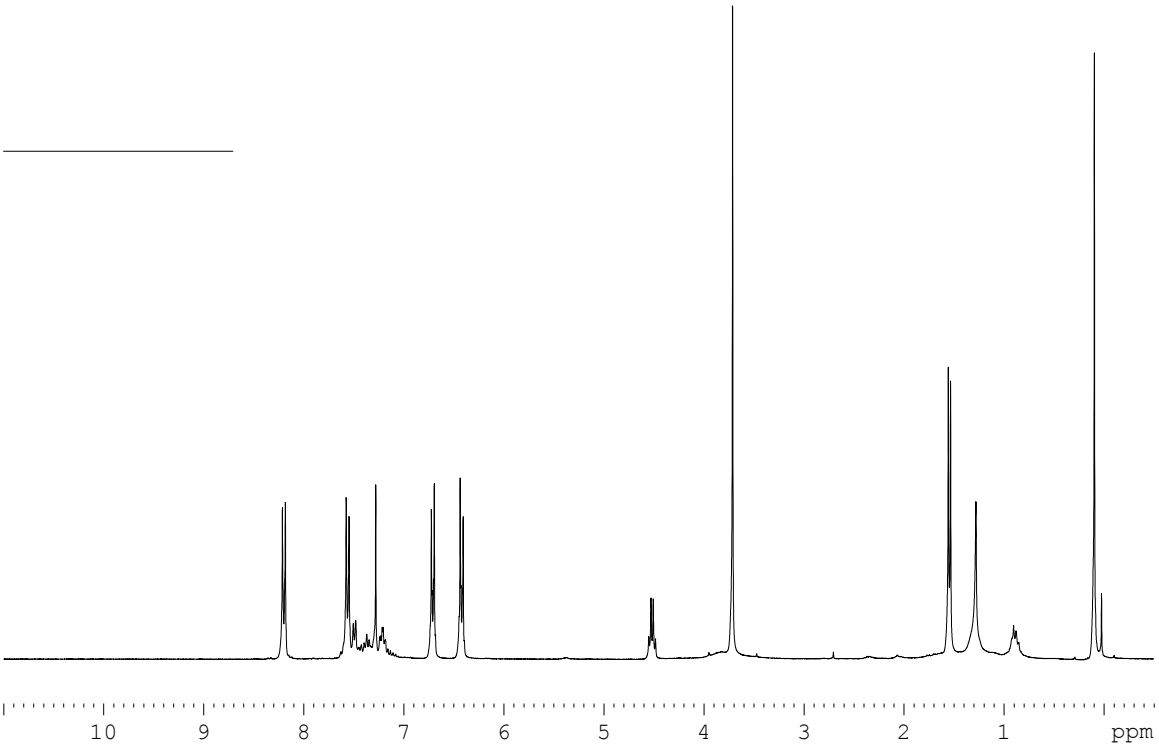


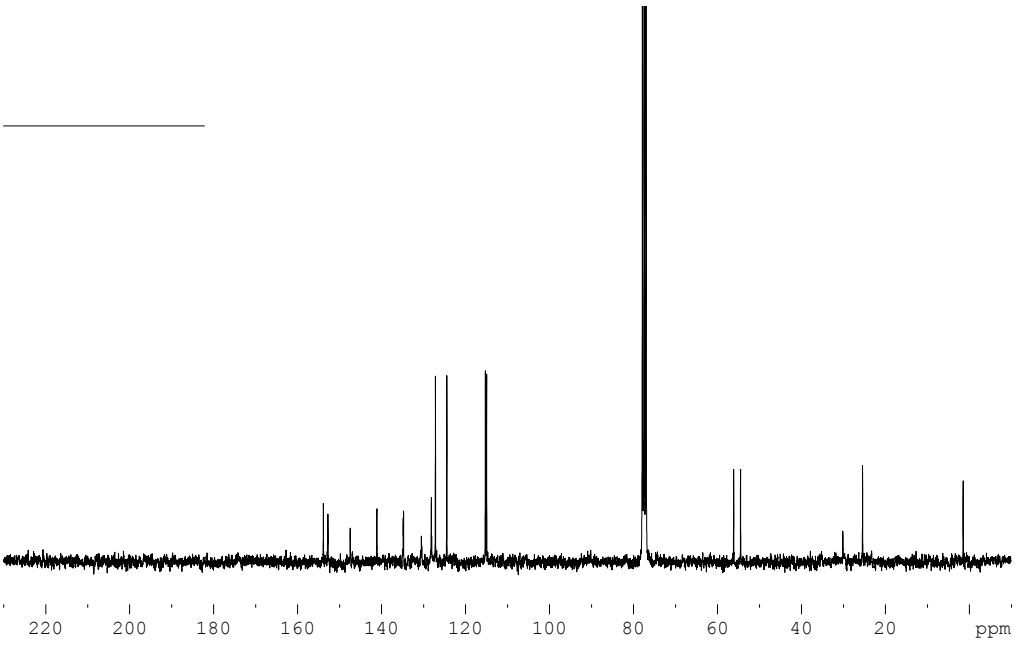




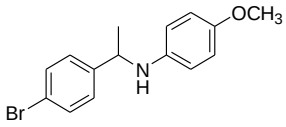
1-(4-Methoxyphenylamino)-1-(4-nitrophenyl)ethane (Table 3, entry 3)

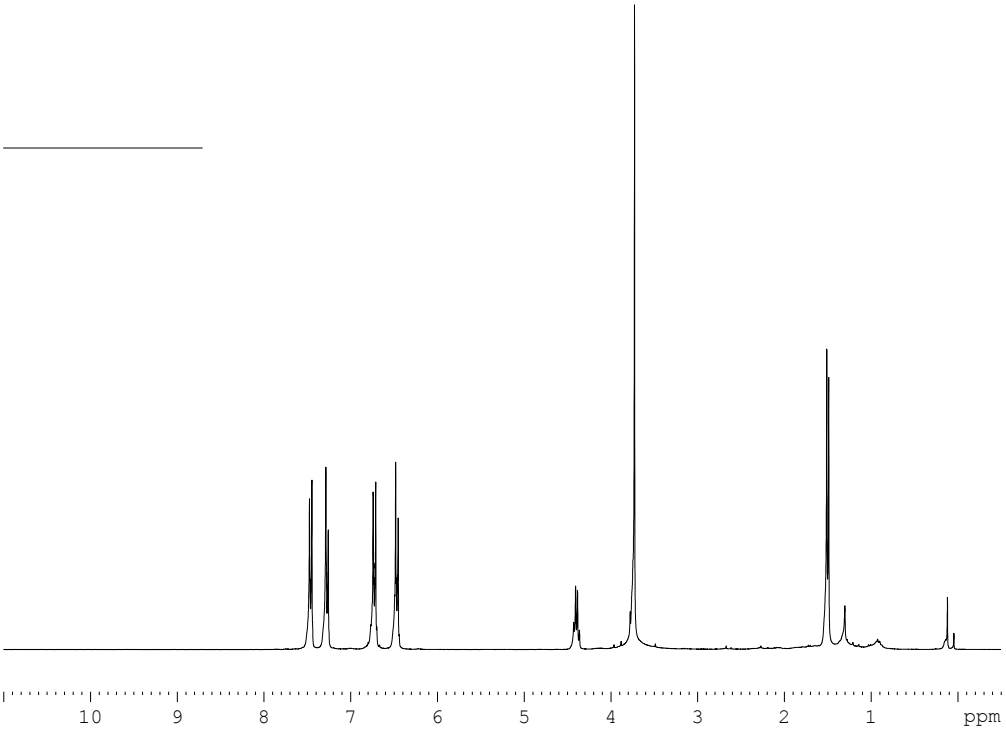


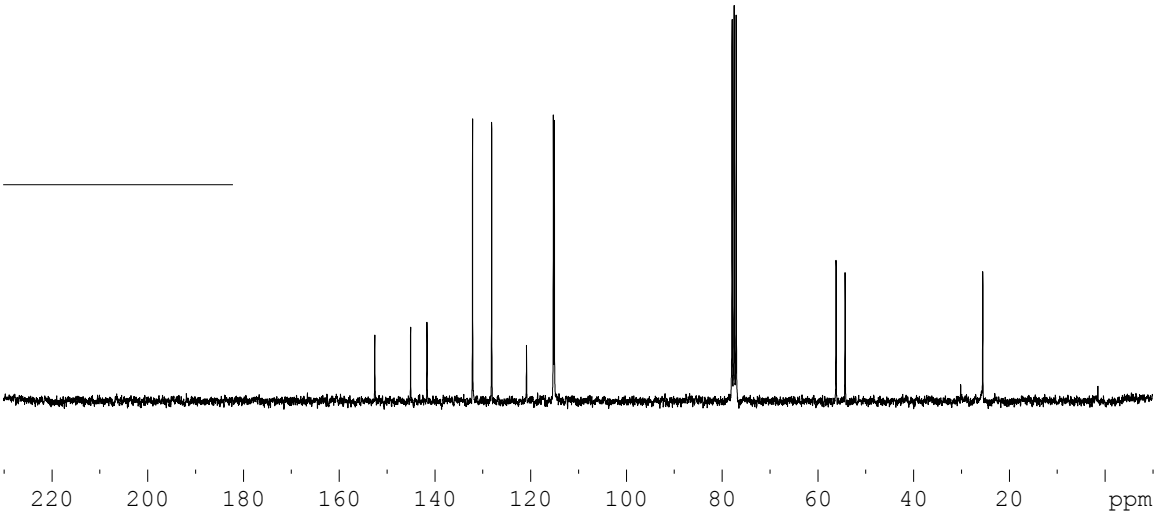




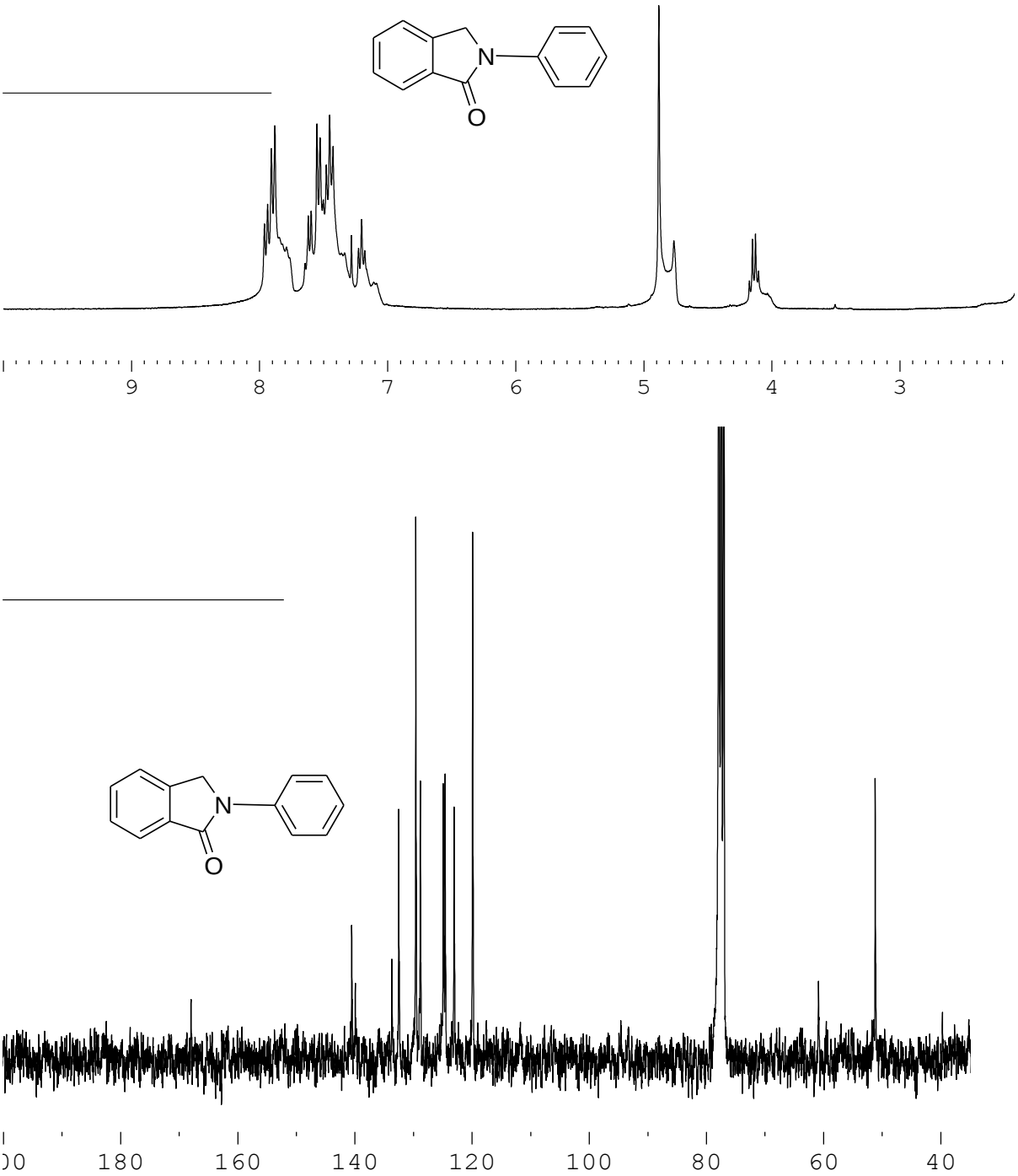
1-(4-Bromophenylamino)-1-(4-nitrophenyl)ethane (Table 3, entry 4)



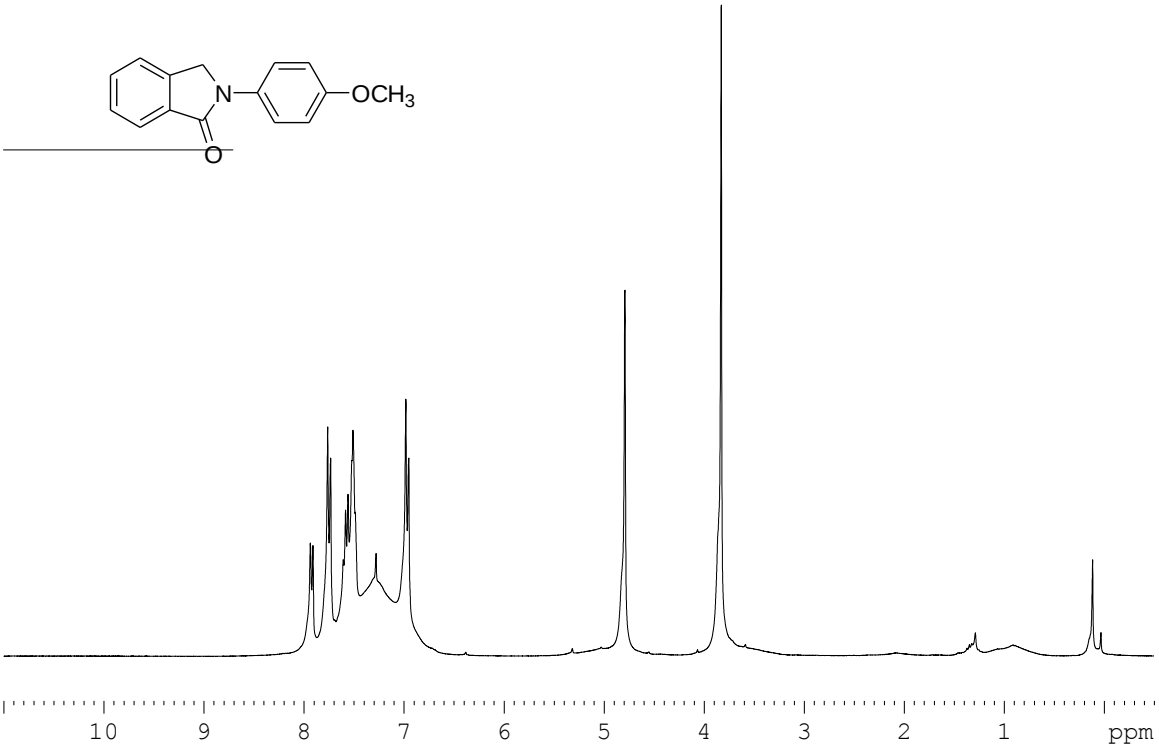


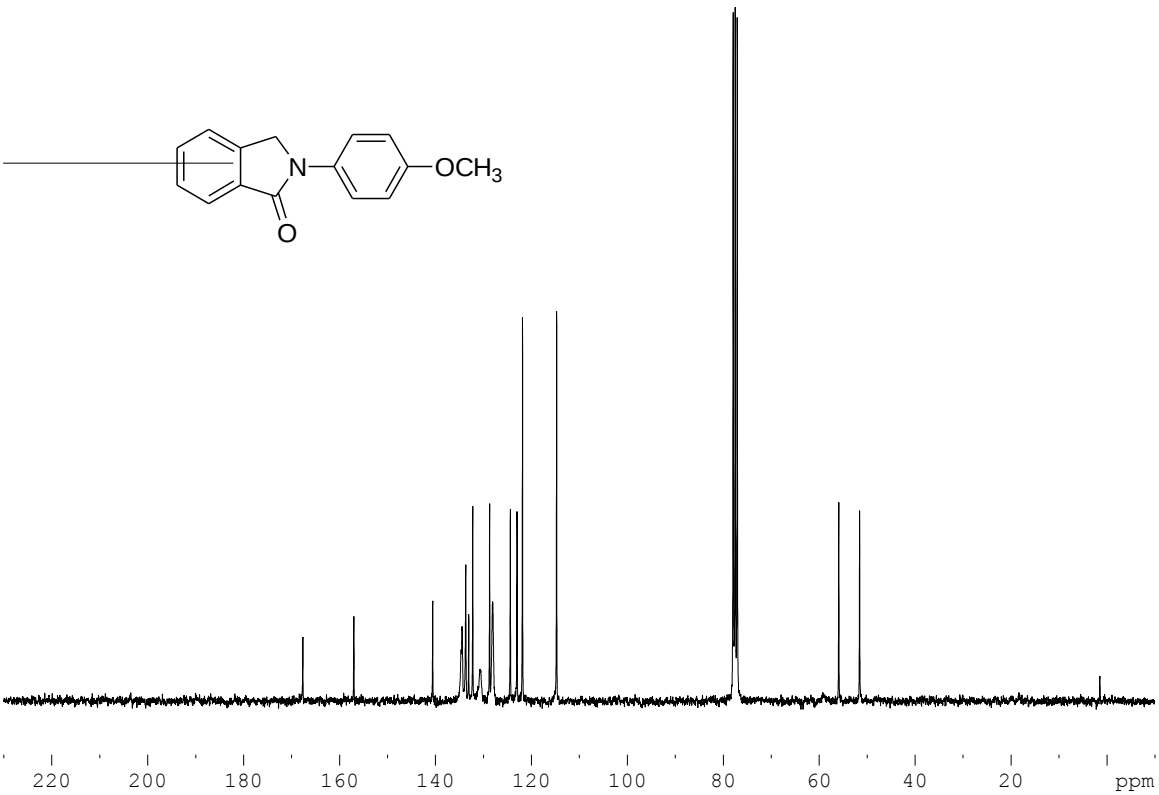


_N_-Phenylisoindolone (Table 2, entry 1)

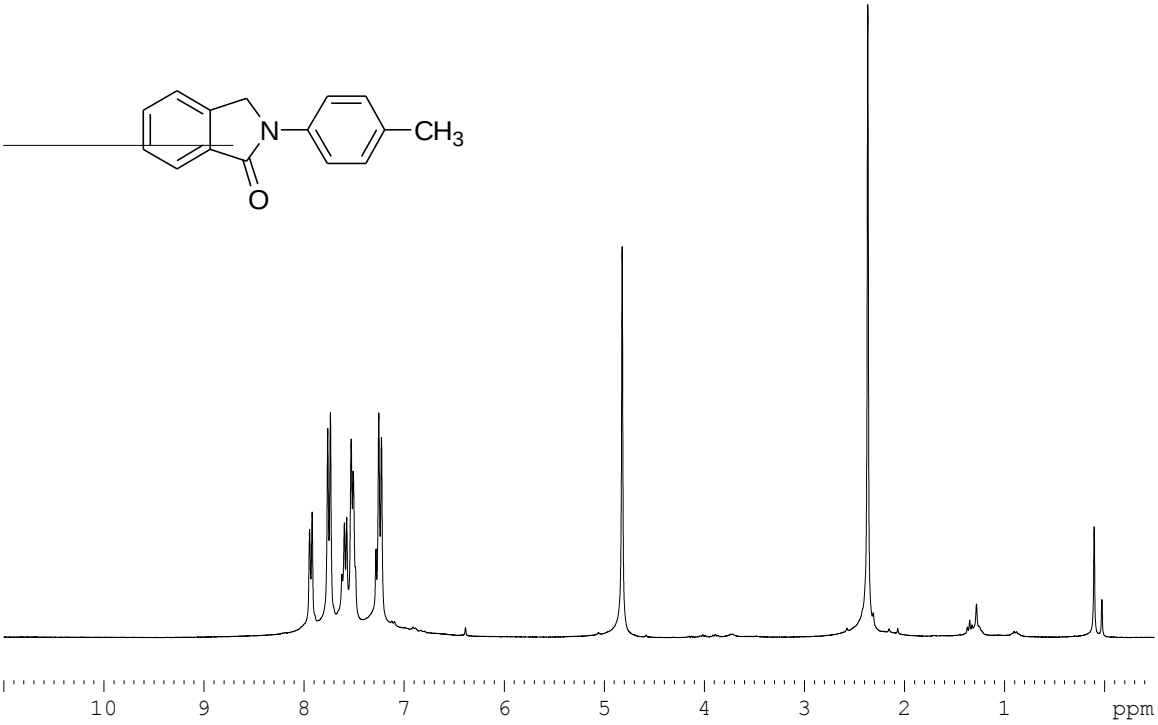


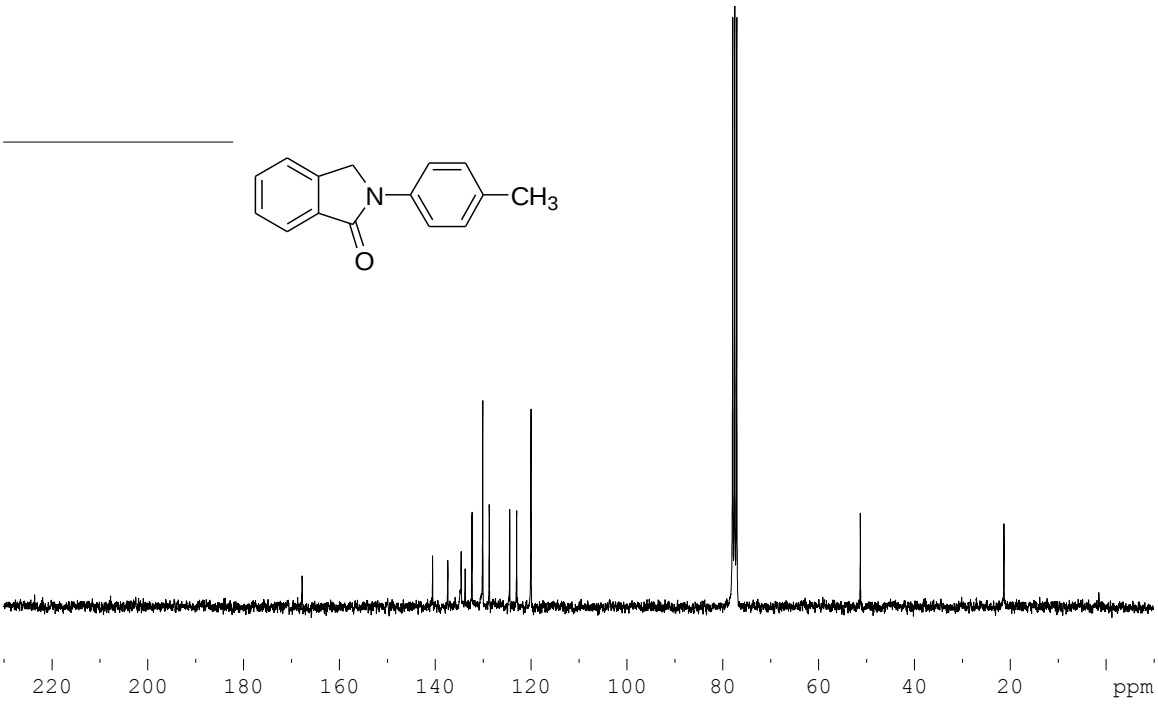
_N_-(4-methoxyphenyl)isoindolinone (Table 2, entry 2)



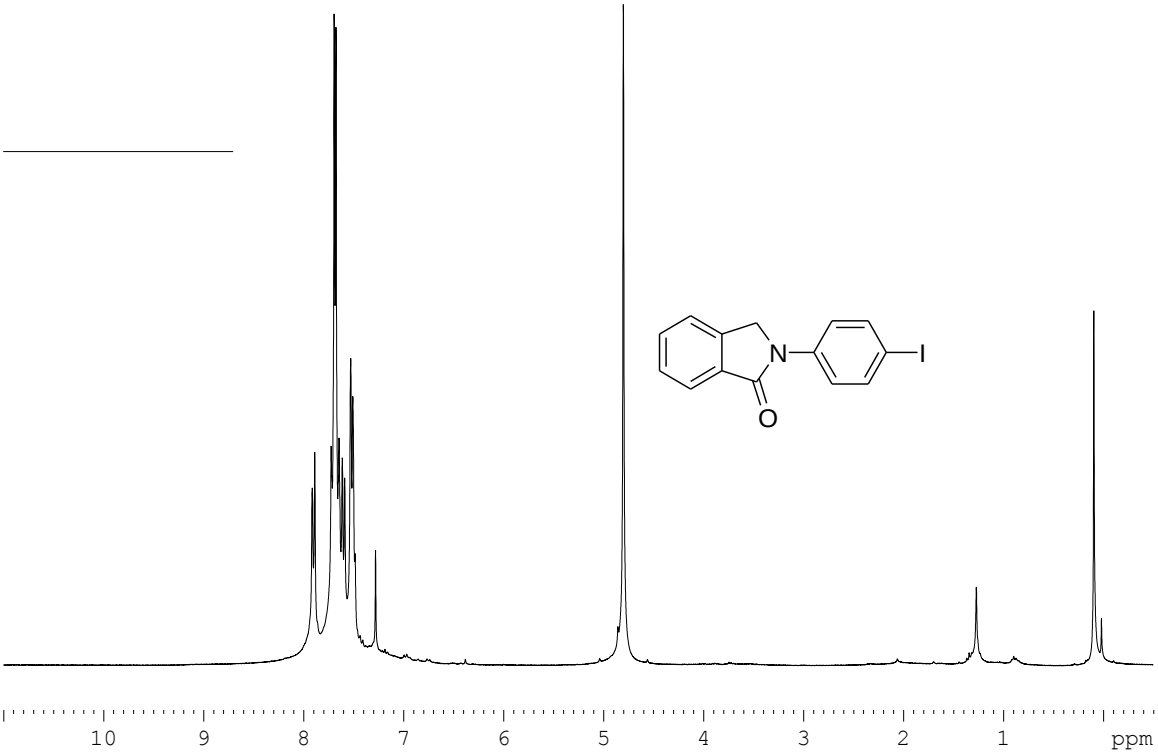


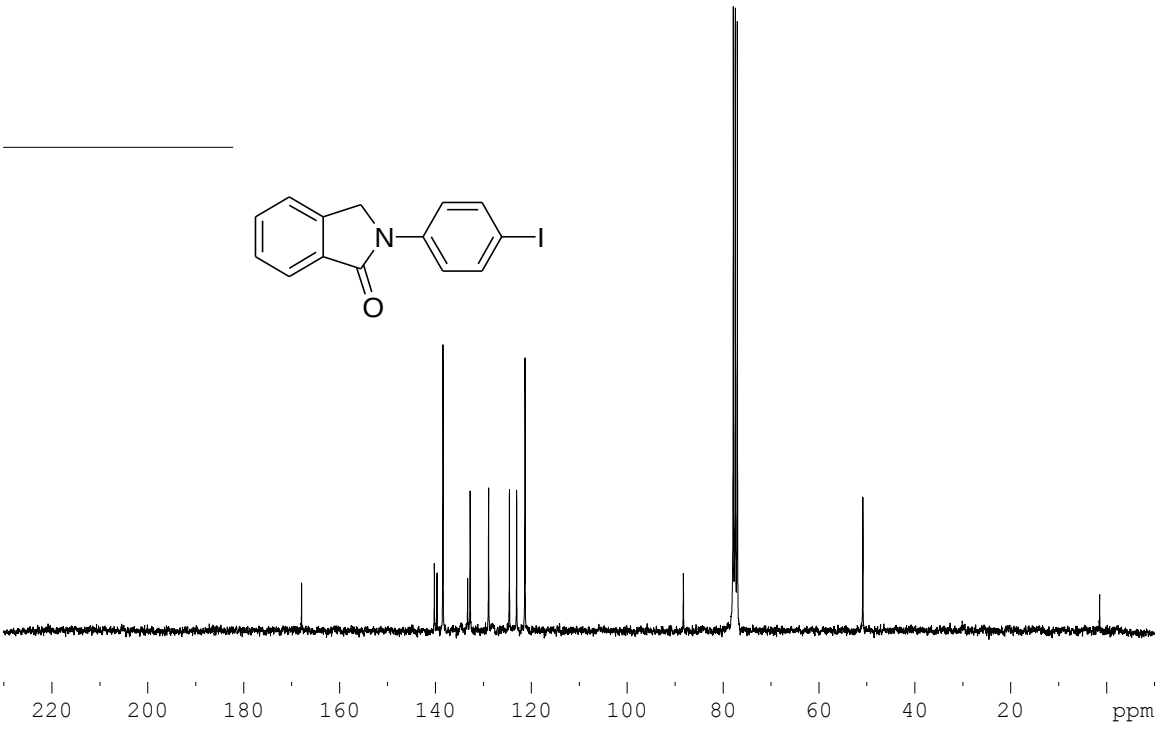
_N_-(4-methylphenyl)isoindolinone (Table 2, entry 3)



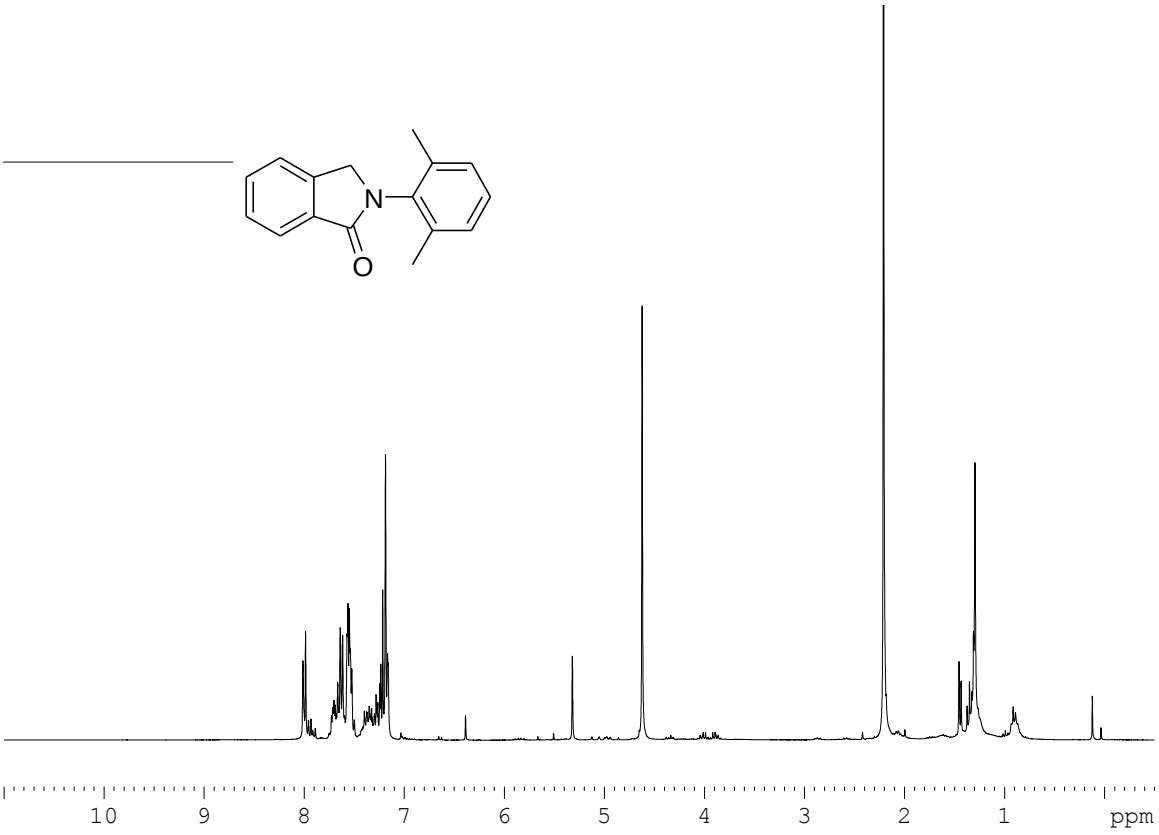


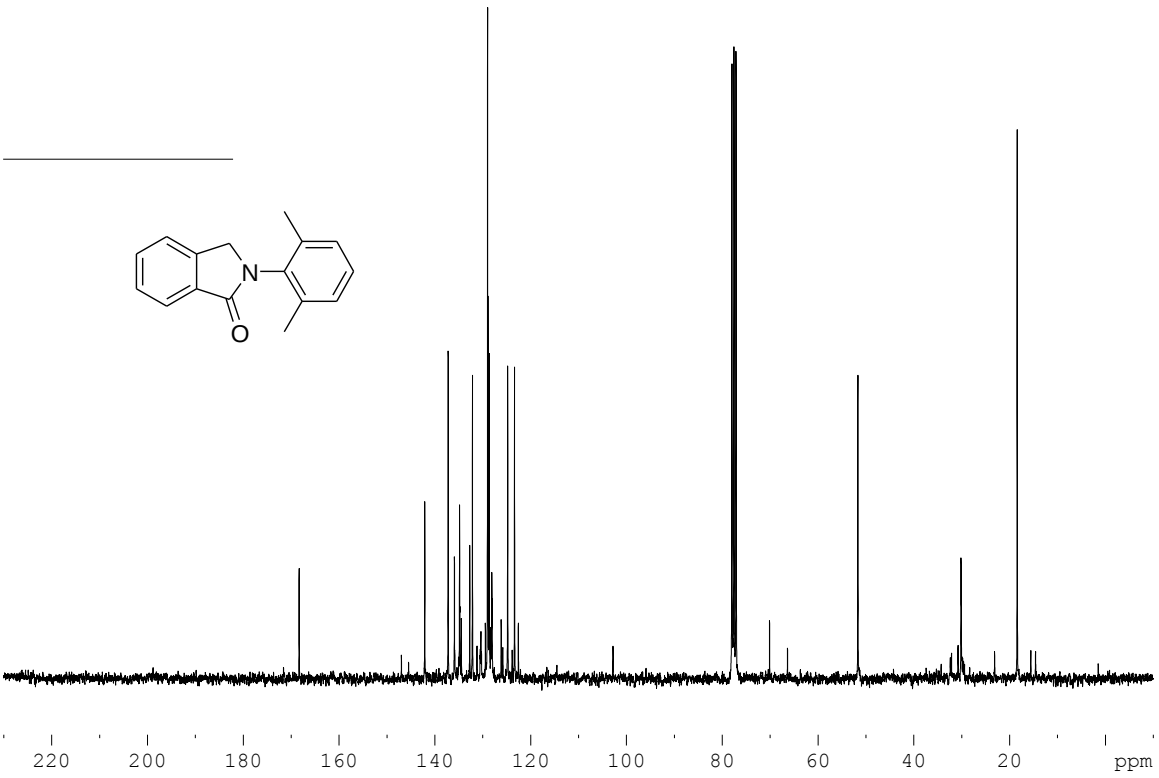
_N_-(4-Iodophenyl)isoindolinone (Table 2, entry 4)



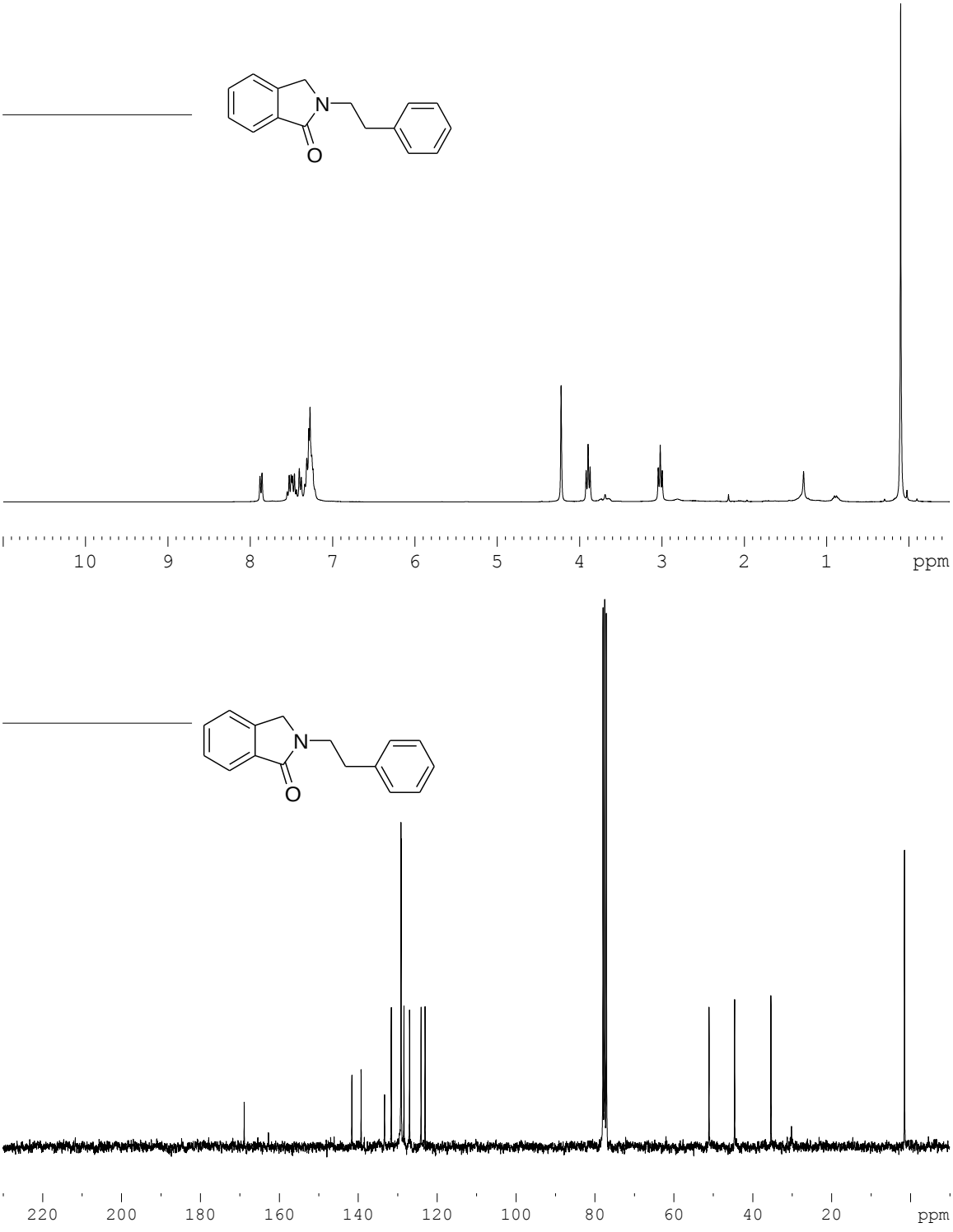


_N_-(2,6-dimethylphenyl)isoindolinone (Table 2, entry 8)

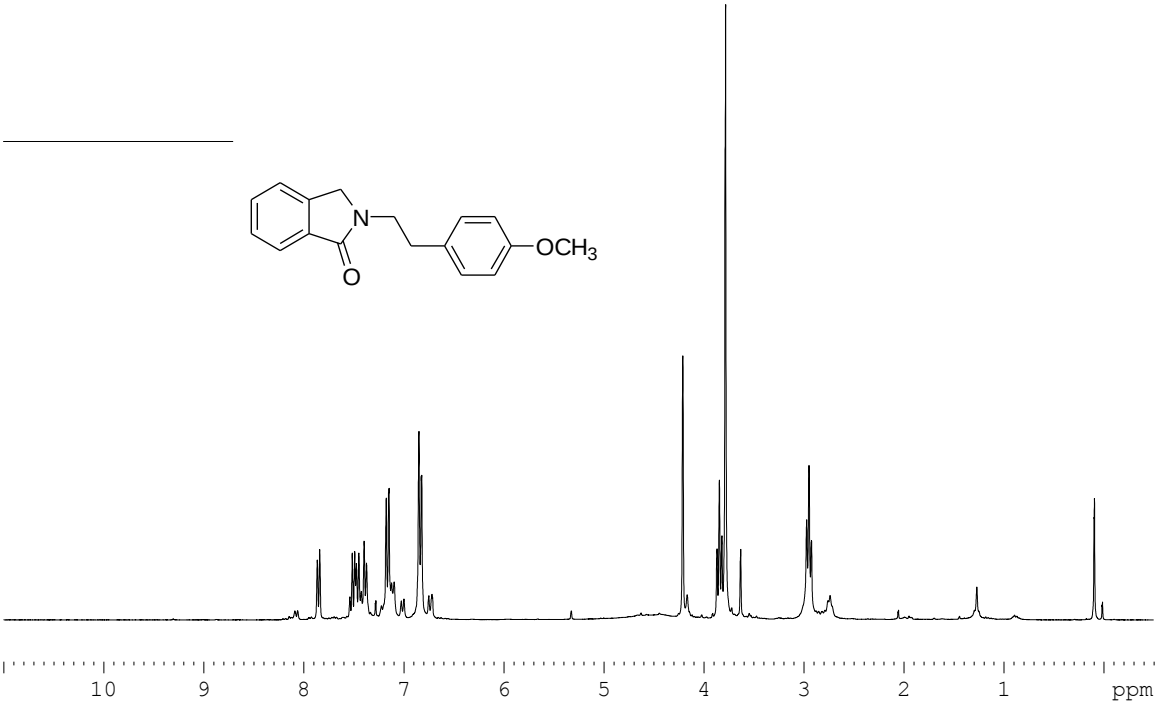


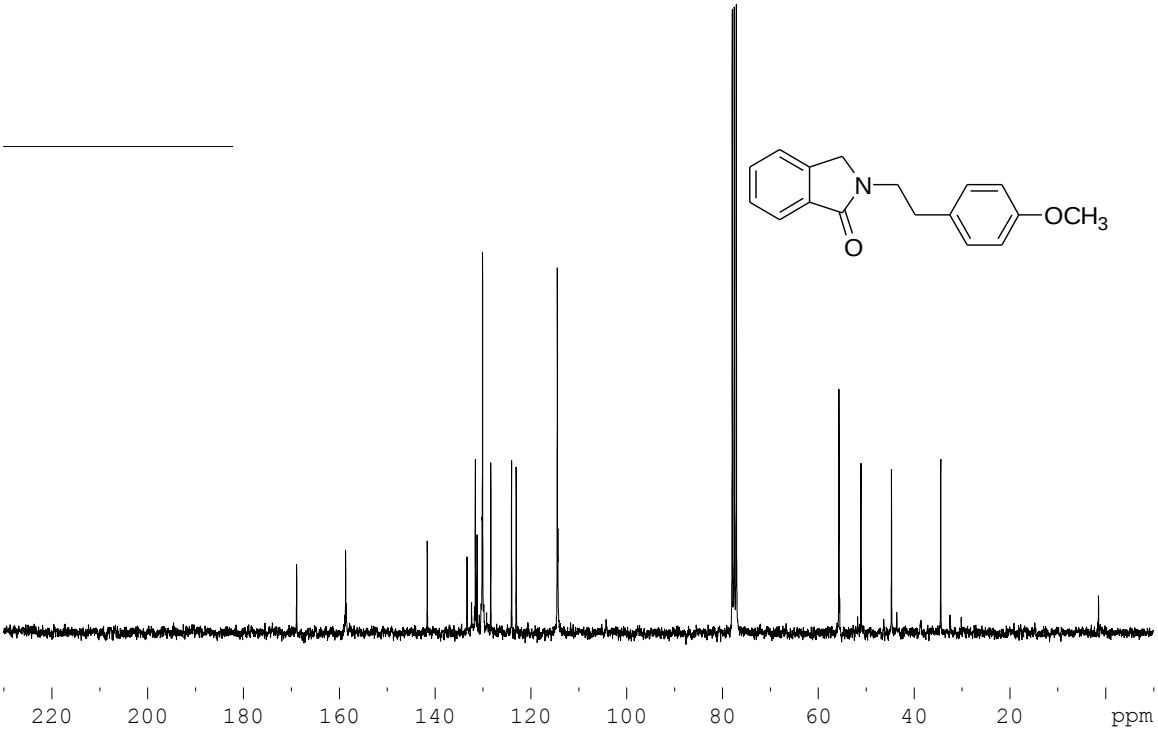


_N_-Phenethylisoindolinone (Table 3, entry 2)



_N_-(4'-Methoxyphenethyl)isoindolinone (Table 3, entry 4)

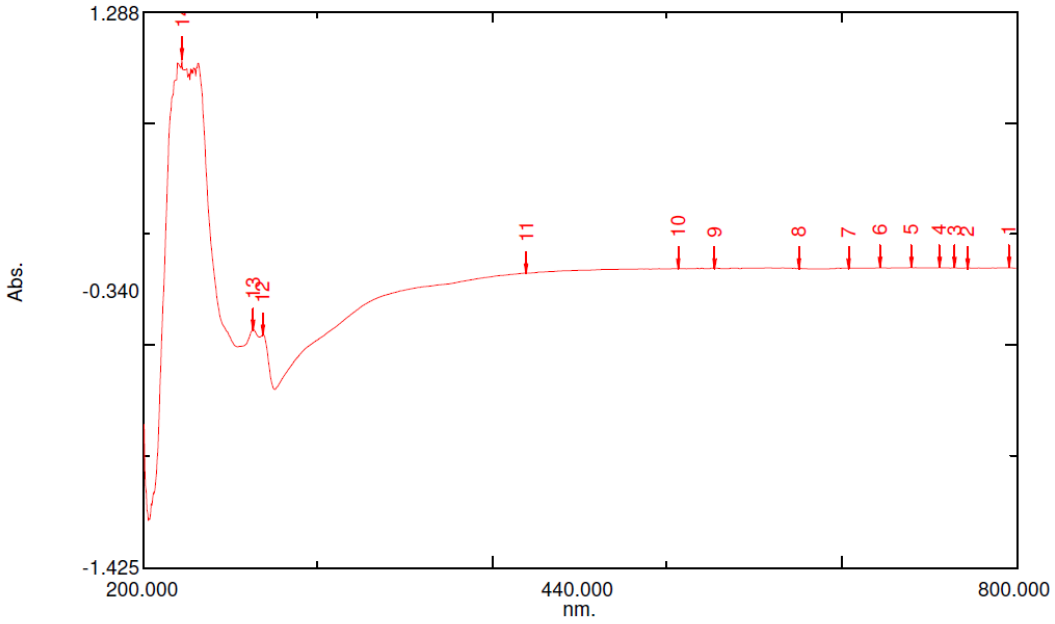




Mechanistic investigation

Study of imine activation by $AlCl_3$ using UV-Vis spectroscopy

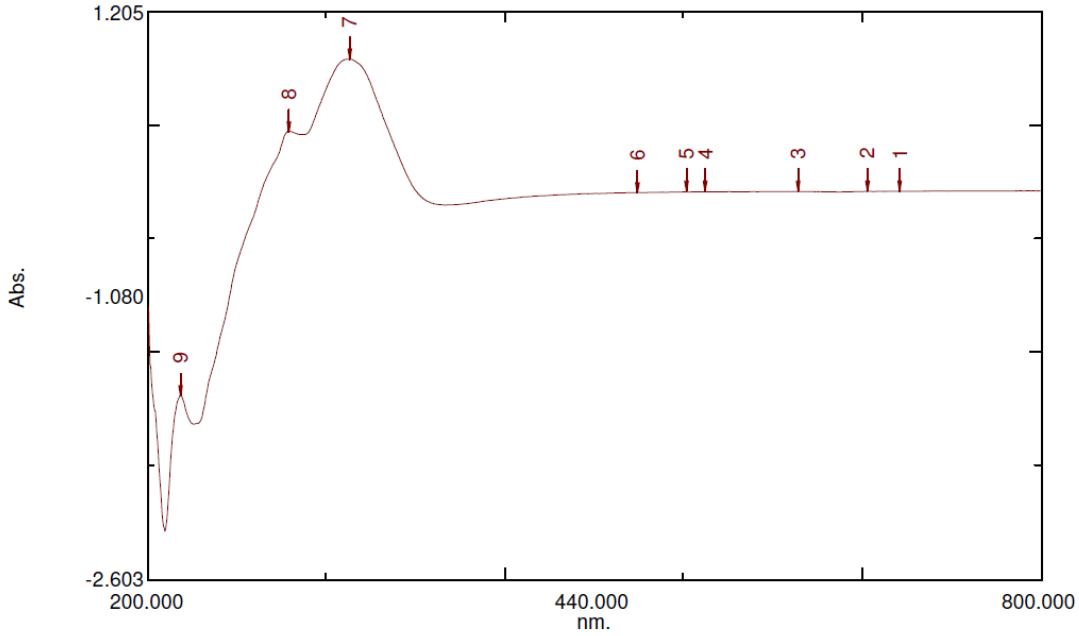
UV-Vis spectrum of $AlCl_3$ in Ethanol



Measurement Properties	
Wavelength Range (nm.):	200.000 to 800.000
Scan Speed:	Slow
Sampling Interval:	0.5
Auto Sampling Interval:	Enabled
Scan Mode:	Auto
Instrument Properties	
Instrument Type:	UV-2400PC Series
Measuring Mode:	Absorbance
Slit Width:	1.0 nm
Light Source Change Wavelength:	360.0 nm
S/R Exchange:	Normal
Attachment Properties	
Attachment:	None

No.	P/V	Wavelength	Abs.	Description
1	↑	795.000	0.037	
2	↑	766.500	0.037	
3	↑	758.000	0.037	
4	↑	747.500	0.037	
5	↑	728.000	0.038	
6	↑	707.000	0.037	
7	↑	685.500	0.036	
8	↑	651.000	0.035	
9	↑	592.500	0.035	
10	↑	567.500	0.034	
11	↑	462.500	0.012	
12	↑	282.000	-0.291	
13	↑	275.000	-0.266	
14	↑	226.000	1.062	

UV-Vis spectra of imine, 4-(methoxybenzylidene)-4-methoxyaniline in Ethanol



Measurement Properties	
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Scan Speed:	Slow
Sampling Interval:	0.5
Auto Sampling Interval:	Enabled
Scan Mode:	Auto
Instrument Properties	
Instrument Type:	UV-2400PC Series
Measuring Mode:	Absorbance
Slit Width:	1.0 nm
Light Source Change Wavelength:	360.0 nm

No.	P/V	Wavelength	Abs.	Description
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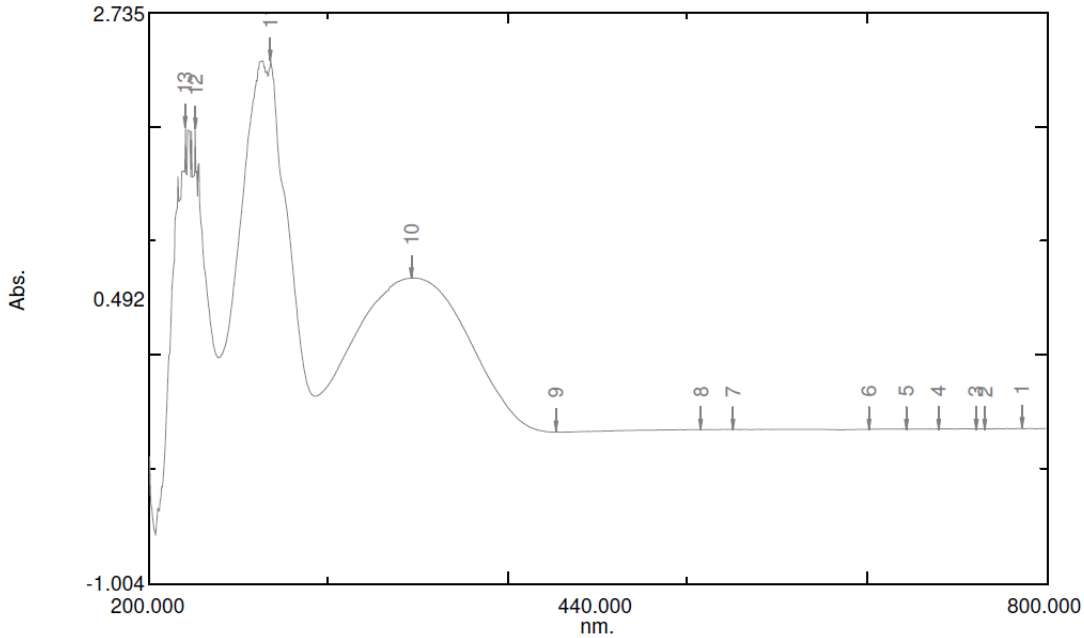
2	↑	683.500	-0.001	
3	↑	637.000	-0.002	
4	↑	575.000	-0.004	
5	↑	561.500	-0.005	
6	↑	529.500	-0.009	
7	↑	335.500	0.888	
8	↑	294.500	0.403	
9	↑	221.500	-1.373	

UV-Vis spectra of imine, 4-(methoxybenzylidene)-4-methoxyaniline + $AlCl_3$ in Ethanol



Measurement Properties	
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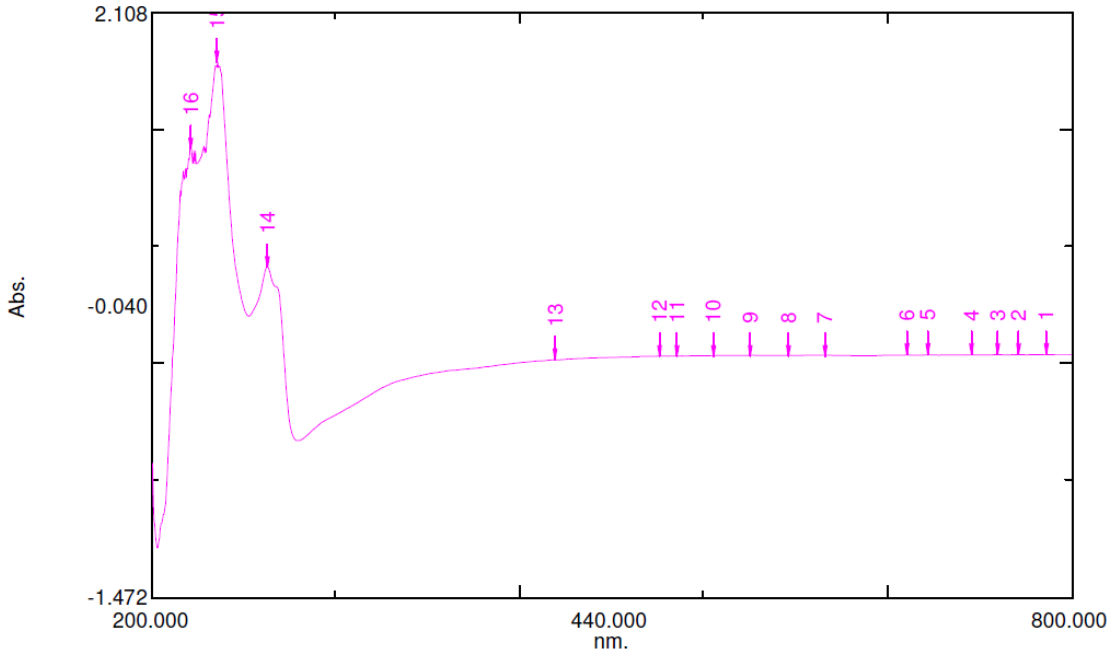
Auto Sampling Interval:	Enabled
Scan Mode:	Auto
Instrument Properties	
Instrument Type:	UV-2400PC Series
Measuring Mode:	Absorbance
Slit Width:	1.0 nm
Light Source Change Wavelength:	360.0 nm
S/R Exchange:	Normal
Attachment Properties	
Attachment:	None

No.	P/V	Wavelength	Abs.	Description
1	↑	783.500	0.007	
2	↑	758.500	0.006	
3	↑	753.000	0.006	
4	↑	728.000	0.005	
5	↑	706.500	0.004	
6	↑	682.000	0.003	
7	↑	590.500	0.002	
8	↑	569.000	0.000	
9	↑	472.000	-0.016	
10	↑	375.000	0.994	
11	↑	281.000	2.423	
12	↑	230.500	1.974	
13	↑	224.000	1.983	

UV-Vis spectra of Et_3N + $AlCl_3$ in Ethanol



Measurement Properties	
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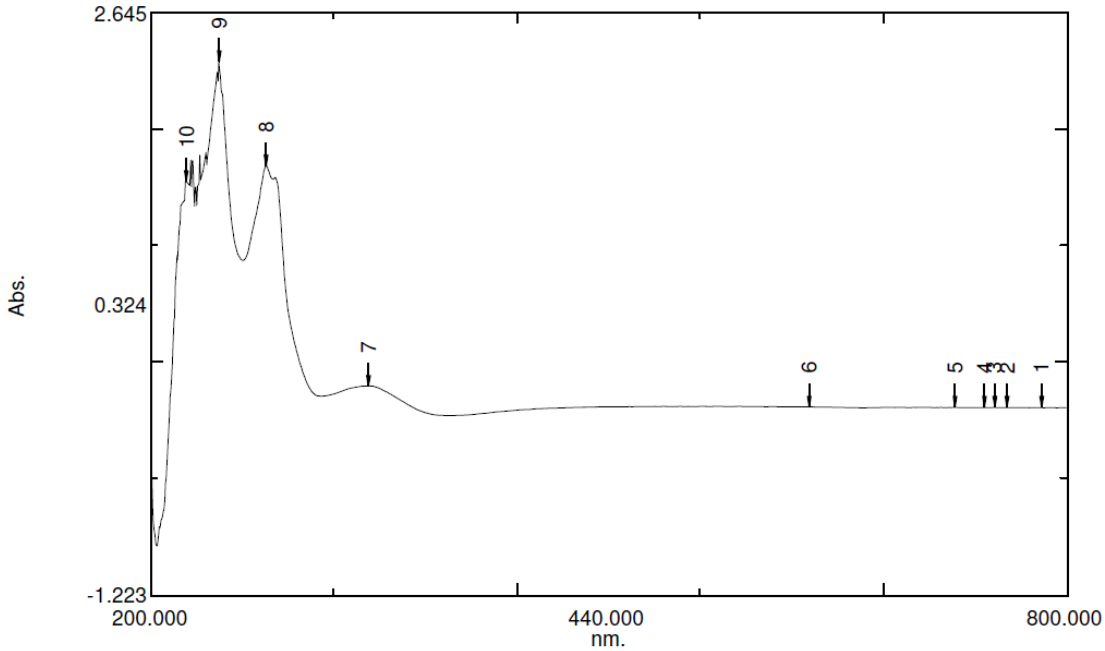
Auto Sampling Interval:	Enabled
Scan Mode:	Auto
Instrument Properties	
Instrument Type:	UV-2400PC Series
Measuring Mode:	Absorbance
Slit Width:	1.0 nm
Light Source Change Wavelength:	360.0 nm
S/R Exchange:	Normal
Attachment Properties	
Attachment:	None
Sample Preparation Properties	
Weight:	
Volume:	

No.	P/V	Wavelength	Abs.	Description
1	↑	784.000	0.012	
2	↑	766.000	0.011	
3	↑	752.000	0.010	
4	↑	735.500	0.010	
5	↑	707.000	0.009	
6	↑	692.500	0.008	
7	↑	639.500	0.008	
8	↑	615.000	0.007	
9	↑	590.500	0.007	
10	↑	567.000	0.006	
11	↑	542.500	0.003	
12	↑	531.000	0.002	
13	↑	462.500	-0.020	
14	↑	275.000	0.550	
15	↑	242.500	1.810	
16	↑	224.500	1.280	

UV-Vis spectra of Et_3N + $AlCl_3$ + imine in Ethanol



Measurement Properties	
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Scan Speed:	Slow
Sampling Interval:	0.5
Auto Sampling Interval:	Enabled
Scan Mode:	Auto
Instrument Properties	
Instrument Type:	UV-2400PC Series
Measuring Mode:	Absorbance
Slit Width:	1.0 nm
Light Source Change Wavelength:	360.0 nm
S/R Exchange:	Normal

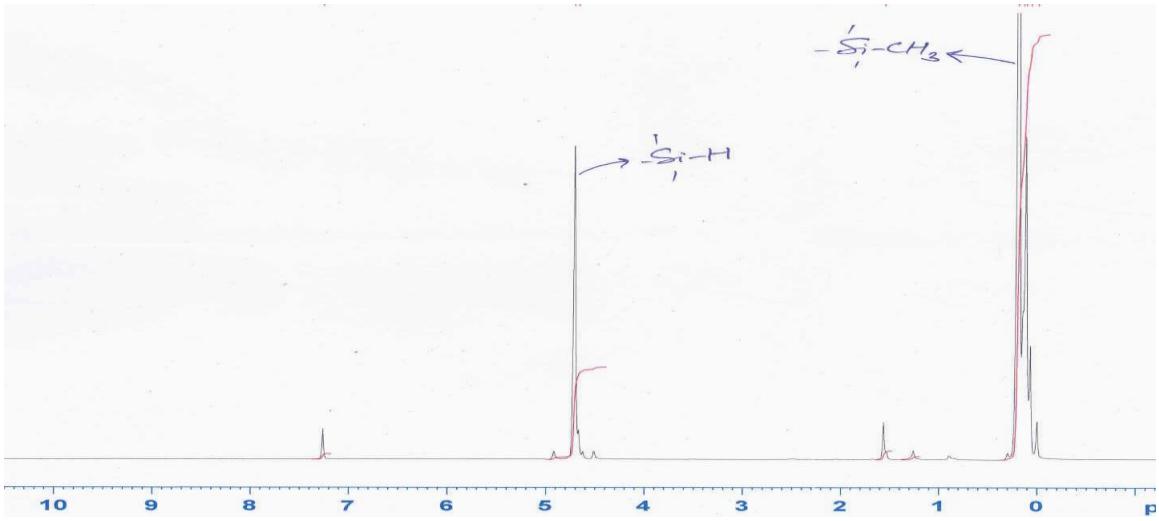
No.	P/V	Wavelength	Abs.	Description
1	↑	784.000	0.018	
2	↑	761.500	0.019	
3	↑	753.000	0.019	
4	↑	747.000	0.019	
5	↑	727.000	0.020	
6	↑	631.500	0.024	
7	↑	342.500	0.163	
8	↑	275.500	1.626	
9	↑	244.000	2.322	
10	↑	222.500	1.521	

Study of PMHS activation by $AlCl_3$ using ^{1}HNMR

Experimental procedure

To a stirred suspension of $AlCl_3$ (0.02 mmol) in ethanol (4 mL) was added PMHS (1.0 mmol) at room temperature and then the temperature was raised to 70 ^oC. The reaction was kept at 70 ^oC for 12 h. The solvent was evaporated under reduced pressure and resultant product was dissolved in $CDCl_3$ for NMR analysis.

^{1}HNMR spectrum of PMHS in $CDCl_3$



^{1}HNMR of PMHS + $AlCl_3$ in $CDCl_3$