Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Selective *N*-Alkylation of Primary Amines with R-NH_2.HBr and Alkylbromides using Competitive Deprotonation/Protonation Strategy

Shubhankar Bhattacharyya, Uma Pathak*, Sweta Mathur, Subodh Vishnoi

Synthetic Chemistry Division, Defence R & D Establishment, Jhansi Road, Gwalior-474002 (M. P.) India.

Contents

1. General details

Reagents were obtained from commercial suppliers, and used without further purification. Solvents were purified by the usual method and stored over molecular sieves. Column chromatographic purification of products was performed on neutral alumina. ^{1}H NMR and ^{13}C spectra were recorded on a Bruker AVANCE II 400 and 600 MHz. Chemical shifts were expressed in parts per millions (δ) downfield from the internal standard tetramethylsilane and were reported as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet) and m (multiplet). Mass spectra was obtained from Agilent 5975C GC-MS with HP5-MS column and Elemental analysis was performed on Elementar vario MICRO cube CHNS analyser.

2. Experimental procedure

2.1 Experimental procedure for preparation o*f* *N*-benzylbutan-1-amine -

1 mmol of amine hydrobromide salt (188 mg), 1.1 mmol of butyl bromide (118 µl) and 0.25gm of 4Å molecular sieves were taken in 1 ml dry DMF at 20-25°C . Triethylamine (1 mol, 144 µl) was mixed with 1 ml of DMF and added to the reaction mixture portionwise ($1/40^{th}$) over a period of 8 hrs with continuous stirring. Progress of the reaction was monitored by TLC and GC-MS. After the addition is

over, reaction was further continued for one hr at the same temperature. pH of the solution was adjusted to 4-5 with 10% Aq. HCl and DMF was removed under vacuum. Contents were neutralized with 5% Na_2CO_3 and extracted with ethylacetate. The organic layer was dried over anhydrous sodium sulfate and solvent was distilled off to yield a light yellow oil. Further purification was achieved through column chromatography neutral alumina, hexane-ethylacetate (98:2).

3. Spectroscopic characterization data

1) ***N*-benzylbutan-1-amine:[1]** Oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37-7.35 (m, 4H), 7.31-7.26 (m, 1H), 3.82 (s, 2H), 2.67 (t, 2H, *J*=7.2 Hz), 1.56-1.51 (m, 2H), 1.42-1.36 (m, 2H), 0.95 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 140.60, 128.39, 128.13, 126.87, 54.14, 49.23, 32.28, 20.52, 14.05; EIMS: m/z 65(8%), 91(100%), 106 (5%), 120 (47%).

2) ***N*-benzyloctan-1-amine:[2]** Oil; ^{1}H NMR (400 MHz, CD_3OD): δ 7.31-7.30 (d, 4H, *J*=4.4 Hz), 7.24 (t, 1H, *J*=4.0 Hz), 3.72 (s, 2H), 2.53 (t, 2H, *J*= 7.2 Hz), 1.51 (t, 2H, *J*=6.8 Hz),1.28 (s, 10H), 0.87 (t, 3H, *J*=6.8 Hz); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 138.24, 128.64, 128.56, 127.44, 53.31, 48.76, 31.82, 29.43, 29.25, 29.19, 27.26, 22.66, 14.12; EIMS: m/z 65(6%), 91(100%), 106(9%), 120(80%), 132(7%), 160(10%).

3) ***N*-benzyl-2-phenylethanamine:[3]** Oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38-7.16 (m, 10H), 3.85 (s, 2H), 2.95 (t, 2H, *J*=6.0 Hz), 2.88 (m, 2H, *J*=6.0 Hz); ^{13}C NMR (150.9 MHz, CDCl3) δ 140.04, 139.65, 128.42, 128.31, 128.20, 128.12, 127.10, 126.95, 53.89, 50.56, 36.36; EIMS: m/z 65 (11%), 91(100%), 118(11%), 120(52%)

4) ***N*-(1-phenylethyl)butan-1-amine:[4]** Oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37-7.33 (m, 4H), 7.29-7.25 (m, 1H), 3.78 (q, 1H, *J*=6.0 Hz), 2.55-2.51 (m, 1H), 2.47-2.43 (m, 1H), 1.53-1.42 (m, 2H), 1.38 (d, 3H, *J*=6.0 Hz), 1.37-1.29 (m, 2H), 0.91 (t, 3H, *J*=6.0 Hz); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 145.89, 128.40, 126.82, 126.55, 58.42, 47.59, 32.43, 24.32, 20.51, 14.01; EIMS: m/z 77(17%), 79(14%), 91(8%), 103(9%), 105(100%), 106(21%), 134(12%), 162(65%)

5) **Methyl 3-(benzylamino)propanoate:[5]** Oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.26 (m, 5H), 3.82 (s, 2H), 3.69 (s, 3H), 2.92 (t, 2H, *J*=6.4 Hz), 2.56 (t, 2H, *J*=6.4 Hz), 1.89 (s, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 173.24, 140.03,

128.43, 128.10, 127.01, 53.75, 51.62, 44.43, 34.51; EIMS: m/z 55(14%), 65(11%), 91(100%), 106(50%), 118(10%), 120(21%).

6) ***N*-(2,4-dichlorobenzyl)butan-2-amine:** Oil ; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39-7.38 (m, 2H), 7.24-7.23 (m, 1H), 3.84 (ABq, 2H, *J*=18.0 Hz), 2.62-2.57 (m, 1H), 1.57-1.50 (m, 1H), 1.45-1.35 (m, 1H), 1.09 (d, 3H, *J*=6.0 Hz), 0.91 (t, 3H, *J*=6.0 Hz); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 136.92, 134.29, 133.09, 130.96, 129.23, 127.04, 53.89, 48.24, 29.55, 19.86, 10.24; EIMS: m/z 89(7%), 123(7%), 159(100%), 160(8%), 161(63%), 163(10%), 202(49%), 204(31%); Anal. Calcd for $C_{11}H_{15}Cl_2N$. C, 56.91; H, 6.51; N, 6.03; Found: C, 57.01; H, 6.55; N, 5.98.

7) ***N*-phenethylpentan-2-amine:[6]** Oil, ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34-7.31 (m, 2H), 7.25-7.22 (m, 3H), 2.97-2.93 (m, 1H), 2.88-2.81 (m, 3H), 2.68-2.63 (m, 1H), 1.47-1.40 (m, 1H), 1.34-1.24 (m, 3H), 1.05 (d, 3H, *J*=6.0 Hz), 0.91 (t, 3H, *J*=6.0 Hz); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 140.18, 128.70, 128.45, 126.13, 52.84, 48.61, 39.38, 36.61, 20.27, 19.19, 14.25; EIMS: m/z 58(9%), 77(9%), 91(13%), 100(100%), 105(54%), 148(31%); Anal. Calcd for $C_{13}H_{21}N$. C, 81.61; H, 11.06; N, 7.32; Found: C, 81.69; H, 11.01; N, 7.29

8) ***N*-phenethylpropan-2-amine:[7]** Oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33-7.31 (m, 2H), 7.25-7.22 (m, 3H), 2.91-2.88 (m, 2H), 2.85-2.81 (m, 3H), 1.07 (d, 6H, *J*=6.0 Hz); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 140.16, 128.70, 128.47, 126.13, 48.81, 48.55, 36.60, 22.93; EIMS: m/z 65(6%), 72(100%), 77(8%), 91(12%), 105(24%).

9) **Ethyl 2-(benzylamino) propanoate:[8]** Oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.29 (m, 4H), 7.25-7.22 (m, 1H), 4.18 (q, 2H, *J*=7.2 Hz), 3.81 (d, 1H, *J*=12.8 Hz), 3.69 (d, 1H, *J*=12.8 Hz), 3.38 (q, 1H, *J*=7.2 Hz), 1.32 (d, 3H, *J*=6.8 Hz), 1.27 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 175.42, 139.36, 128.42, 128.36, 127.16, 60.70, 55.85, 51.81, 18.91, 14.27; EIMS: m/z 65(10%), 91(100%), 106(9%), 134(73%).

10) **Ethyl 2-(phenethylamino) propanoate:[9]** Oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.28 (t, 2H, *J*=7.2), 7.23-7.20 (m, 3H), 4.17 (q, 2H, *J*=7.2 Hz), 3.40 (q, 1H, *J*=6.8 Hz), 2.91-2.87 (m, 2H), 2.85-2.80 (m, 2H), 1.32 (d, 3H, *J*=7.2 Hz), 1.26 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 175.16, 139.50, 128.77, 128.68, 128.47, 126.26, 60.77, 56.61, 49.10, 36.28, 18.74, 14.22; EIMS: m/z 56(49%), 77(14%), 79(10%), 91(16%), 102(30%), 103(12%), 105(76%), 130(100%), 148(81%); Anal. Calcd for $C_{13}H_{19}NO_2$. C, 70.56; H, 8.65; N, 6.33; Found C, 70.71; H, 8.61; N, 6.31.

11) **Ethyl 2-(cyclohexylamino) propanoate:** Oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.14 (q, 2H, *J*=6.8 Hz), 3.45 (q, 1H, *J*=6.8 Hz), 2.46 (br, s, 1H), 2.38-2.33 (br m, 1H), 1.85 (d, 1H, *J*=12.0 Hz), 1.74-1.66 (m, 3H), 1.55 (d, 1H, *J*=9.6), 1.26-1.00 (m, 10H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 175.92, 60.61, 55.13, 53.43, 33.80, 32.58, 25.88, 24.98, 24.72, 19.46, 14.18; EIMS: m/z 55(8%), 126(%), 127(9%), 156(7%); Anal. Calcd for $C_{11}H_{21}NO_2$. C, 66.29; H, 10.62; N, 7.03; Found C, 66.51; H, 10.58; N, 6.99

12) ***N*-phenethylcyclohexanamine:**[10] Oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33-7.31 (m, 2H), 7.25-7.23 (m, 3H), 2.93 (t, 2H, *J*=6.0 Hz), 2.83 (t, 2H, *J*=6.0 Hz) 2.48-2.44 (m, 1H), 1.90-1.87 (m, 2H), 1.75-1.72 (m, 2H), 1.32-1.23 (m, 3H), 1.21-1.14 (m, 1H), 1.11-1.05 (m, 2H); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 140.18, 128.70, 128.45, 126.12, 56.75, 48.23, 36.64, 33.54, 26.17, 25.08; EIMS: m/z 55(12%), 77(6%), 83(8%), 91(8%), 105(11%), 112(100%).

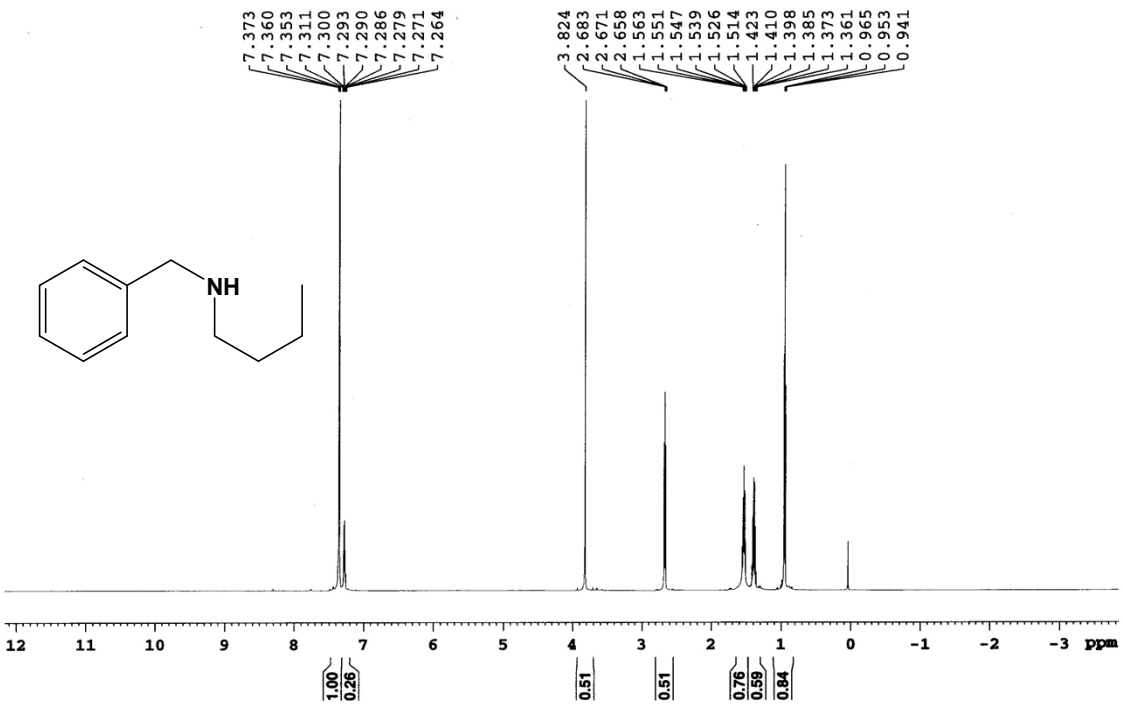
13) ***N*-butylcyclohexanamine:**[11] Oil; ^{1}H NMR (400 MHz, CD_3OD): δ 2.55 (t, 2H, *J*=7.6 Hz), 2.38-2.37 (m, 1H), 1.90-1.87 (m, 2H), 1.74-1.71(m, 2H), 1.63-1.60 (m, 1H), 1.47-1.04 (complex m, 10H), 0.91 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 56.93, 46.57, 33.37, 32.34, 26.09, 25.08, 20.55, 13.98; EIMS: m/z 55(10%), 56(15%), 84(6%), 112(100%), 155(7%).

14) ***N*-butylaniline:**[12] Oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25-7.22 (m, 2H), 6.75 (t, 1H, *J*=7.2 Hz), 6.66 (d, 2H, *J*=7.8 Hz), 3.17 (t, 2H, *J*=7.2 Hz), 1.69-1.64 (quin, 2H, *J*=7.2 Hz), 1.53-1.46 (m, 2H), 1.02 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 148.61, 129.26, 117.11, 112.74, 43.72, 31.74, 20.36, 13.97; EIMS: m/z 77(12%), 106(100%), 107(8%), 149(22%)

15) **4-methoxy-*N*-pentylbenzenamine:**[13] Oil; ^{1}H NMR (400 MHz, CD_3OD): δ 6.73 (d, 2H, *J*=8.8 Hz), 6.62 (d, 2H, *J*=8.8 Hz), 3.70 (s, 3H), 2.99 (t, 2H, *J*=7.2 Hz), 1.60-1.56 (br, m, 2H), 1.38-1.35 (m, 4H), 0.91 (t, 3H, *J*=6.8Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.03, 142.74, 114.89, 114.17, 55.82, 45.12, 29.41, 29.36, 22.56, 14.11; EIMS: m/z 108(7%), 121(5%), 136(100%), 137(9%), 193(24%)

4. Copies of ^{1}H NMR, ^{13}C NMR:

1. **^{1}H NMR spectra of *N*-benzylbutan-1-amine**
2. **^{13}C NMR spectra of *N*-benzylbutan-1-amine**
3. **^{1}H NMR spectra of *N*-benzyloctan-1-amine**
4. **^{13}C NMR spectra of *N*-benzyloctan-1-amine**
5. **^{1}H NMR spectra of *N*-benzyl-2-phenylethanamine**
6. **^{13}C NMR spectra of *N*-benzyl-2-phenylethanamine**
7. **^{1}H NMR spectra of *N*-((*S*)-1-phenylethyl)butan-1-amine**
8. **^{13}C NMR spectra of *N*-((*S*)-1-phenylethyl)butan-1-amine**
9. **^{1}H NMR spectra of methyl 3-(benzylamino)propanoate**
10. **^{13}C NMR spectra of methyl 3-(benzylamino)propanoate**
11. **^{1}H NMR spectra of *N*-(2,4-dichlorobenzyl)butan-2-amine**
12. **^{13}C NMR spectra of *N*-(2,4-dichlorobenzyl)butan-2-amine**
13. **^{1}H NMR spectra of N-phenethylpentan-2-amine**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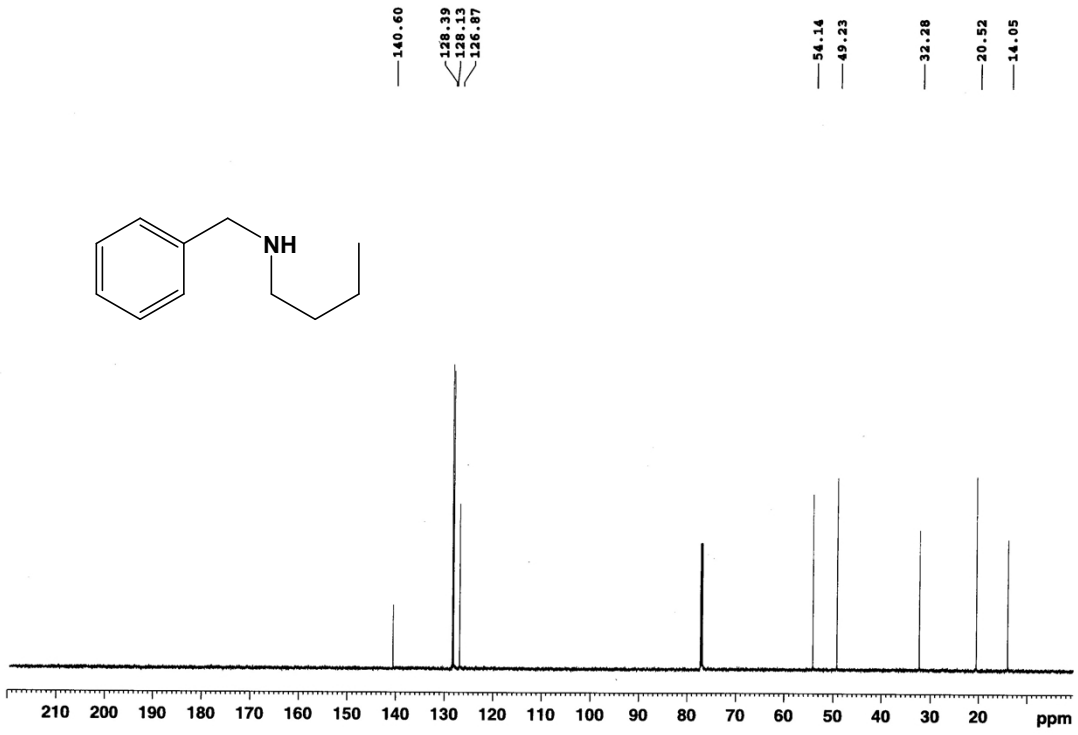
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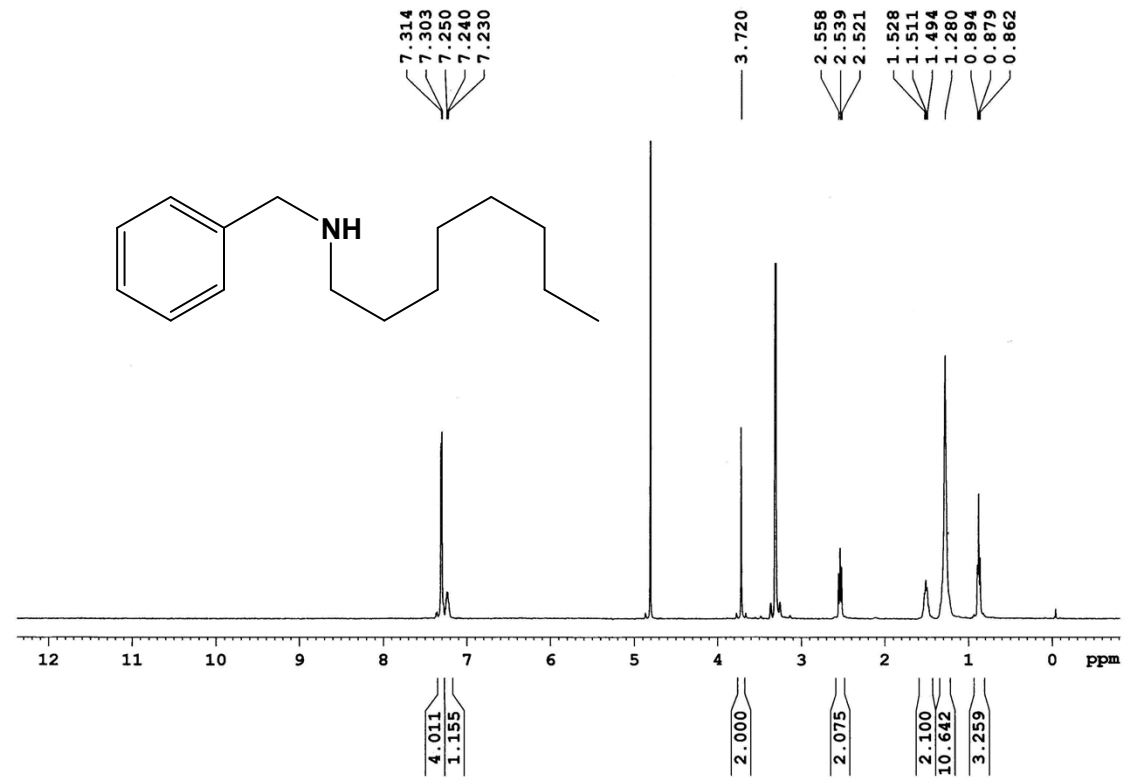
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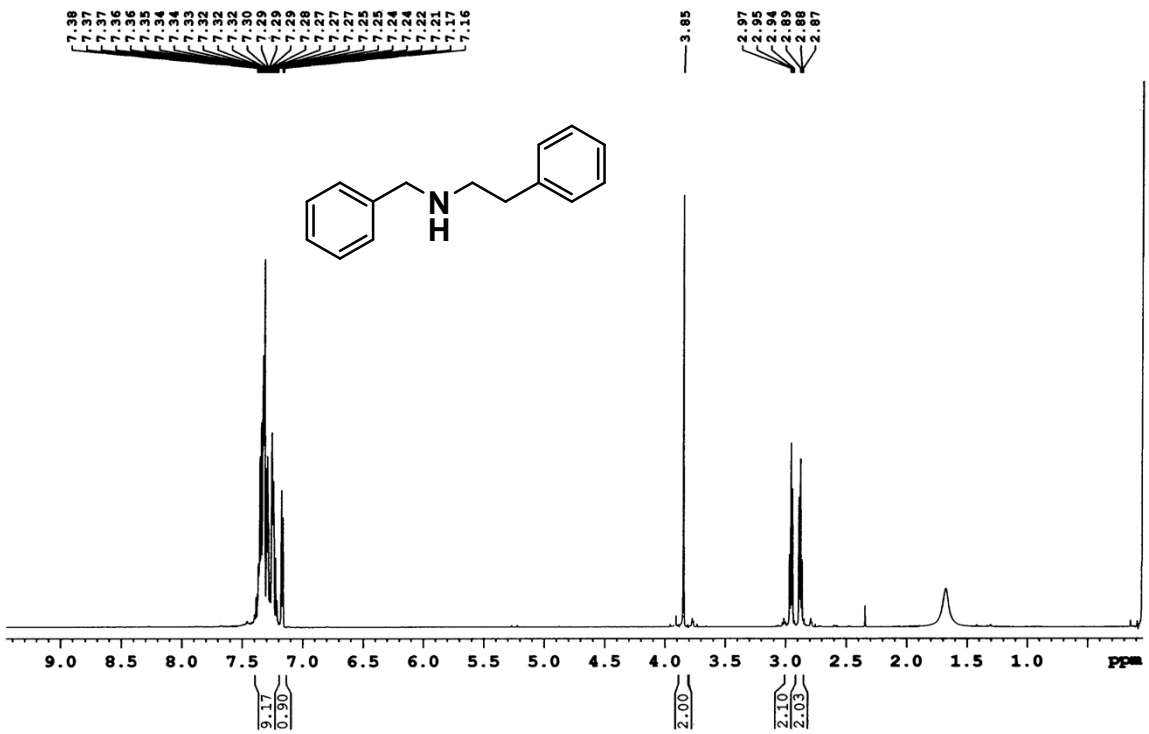
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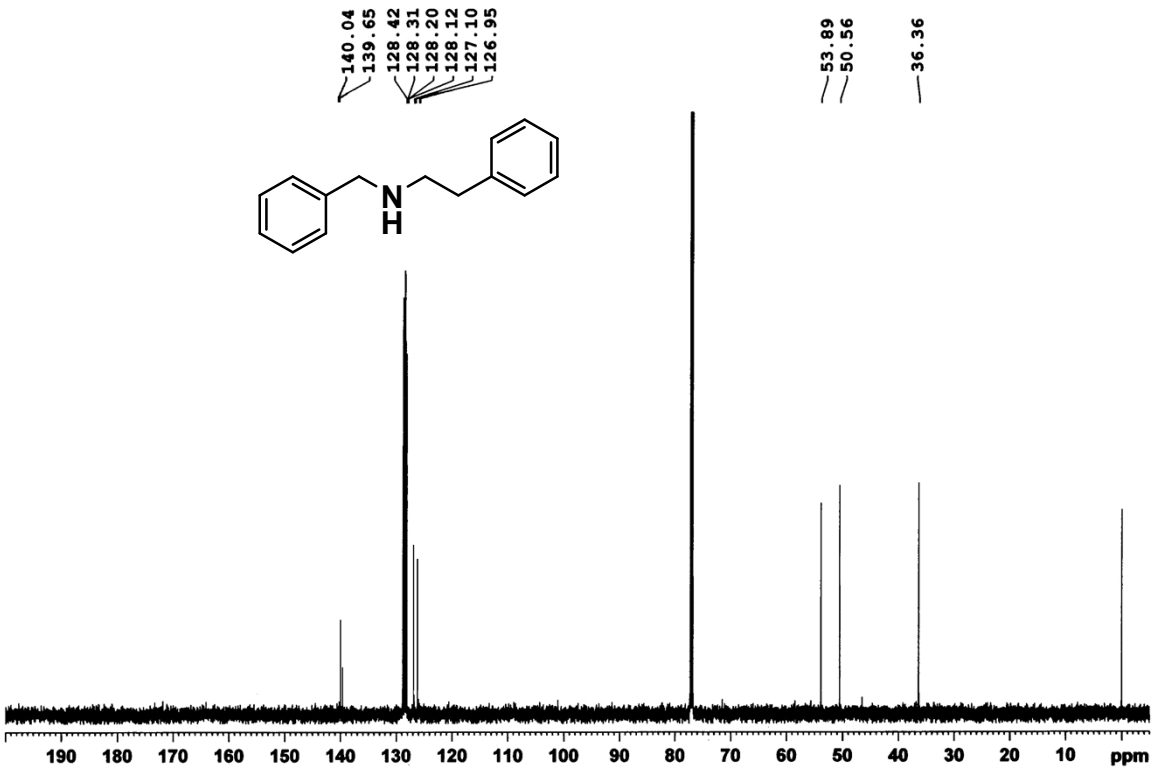
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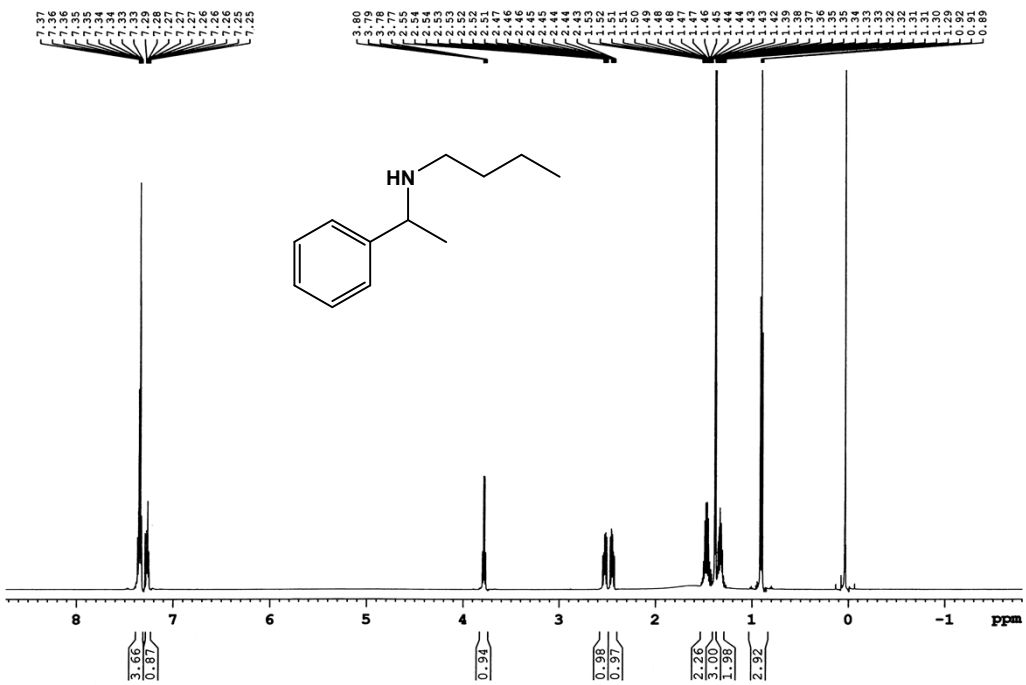
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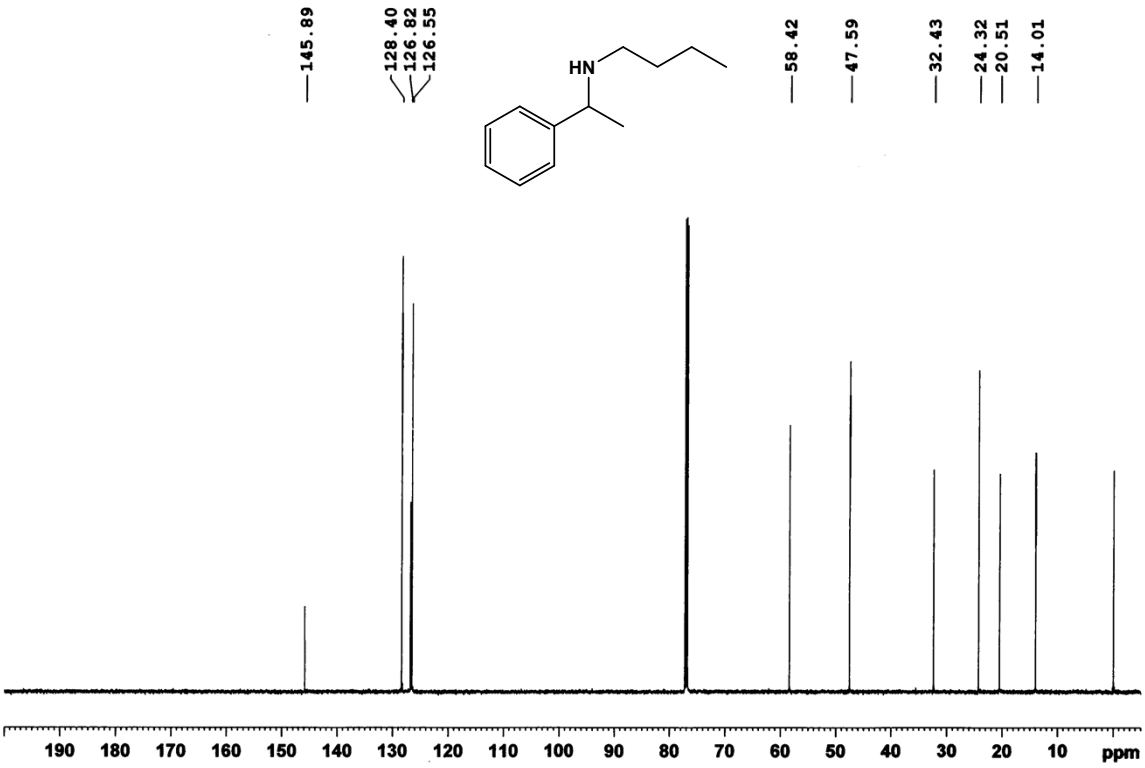
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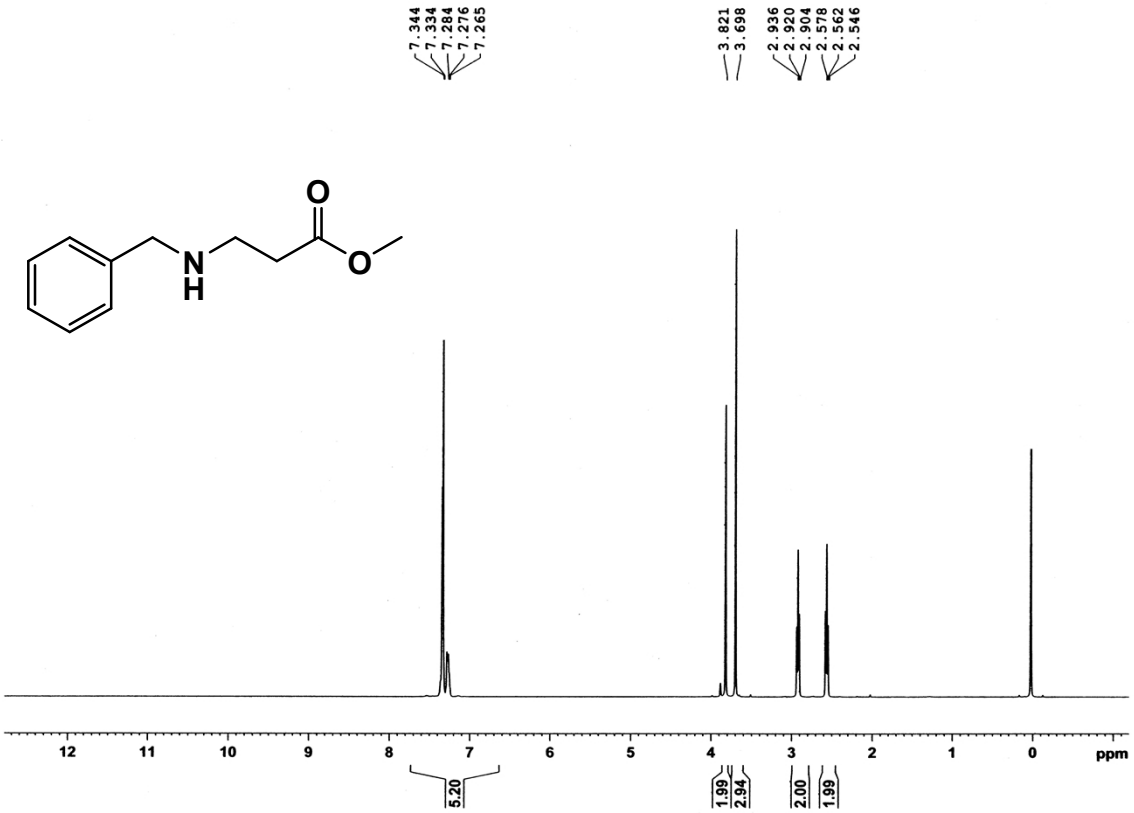
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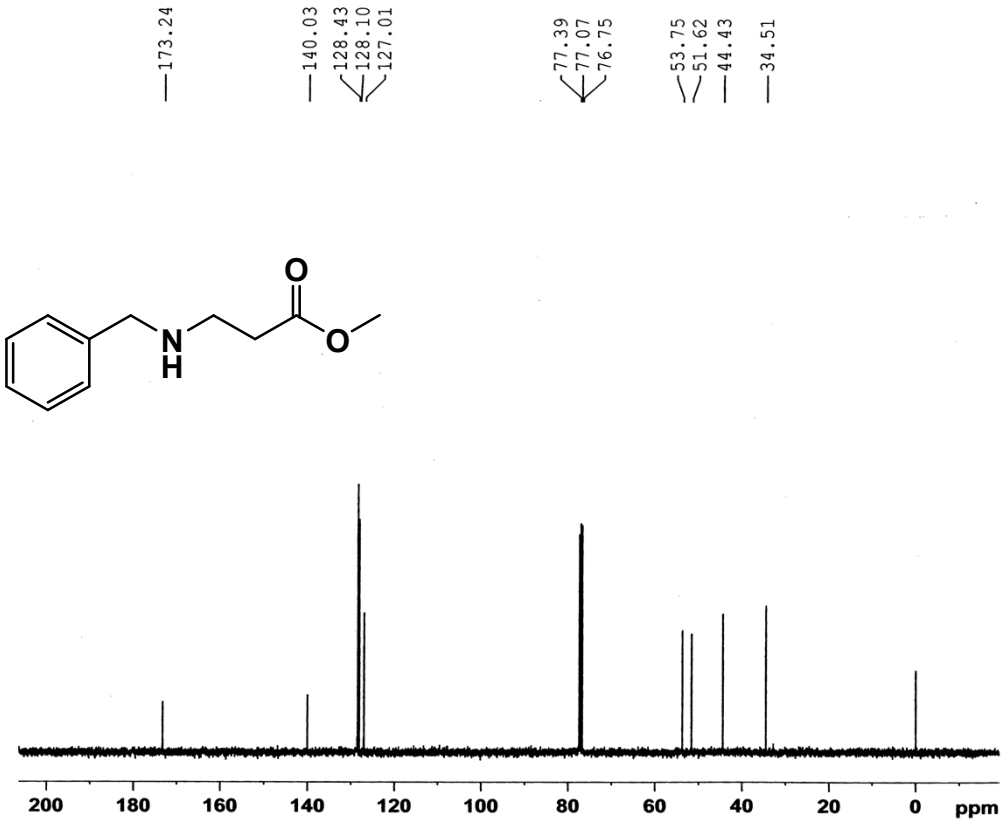
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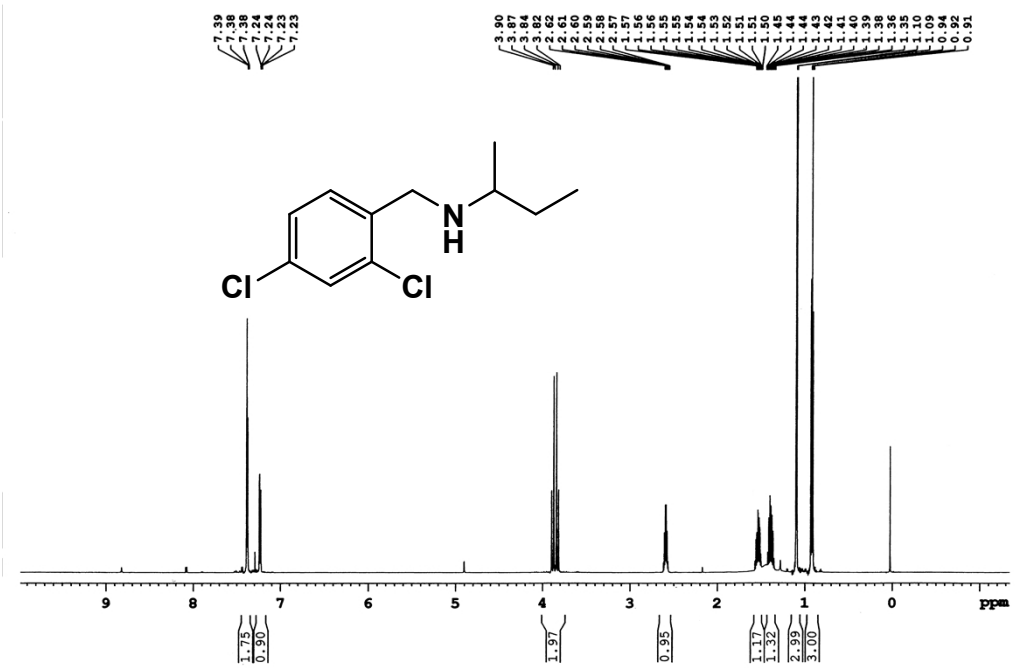
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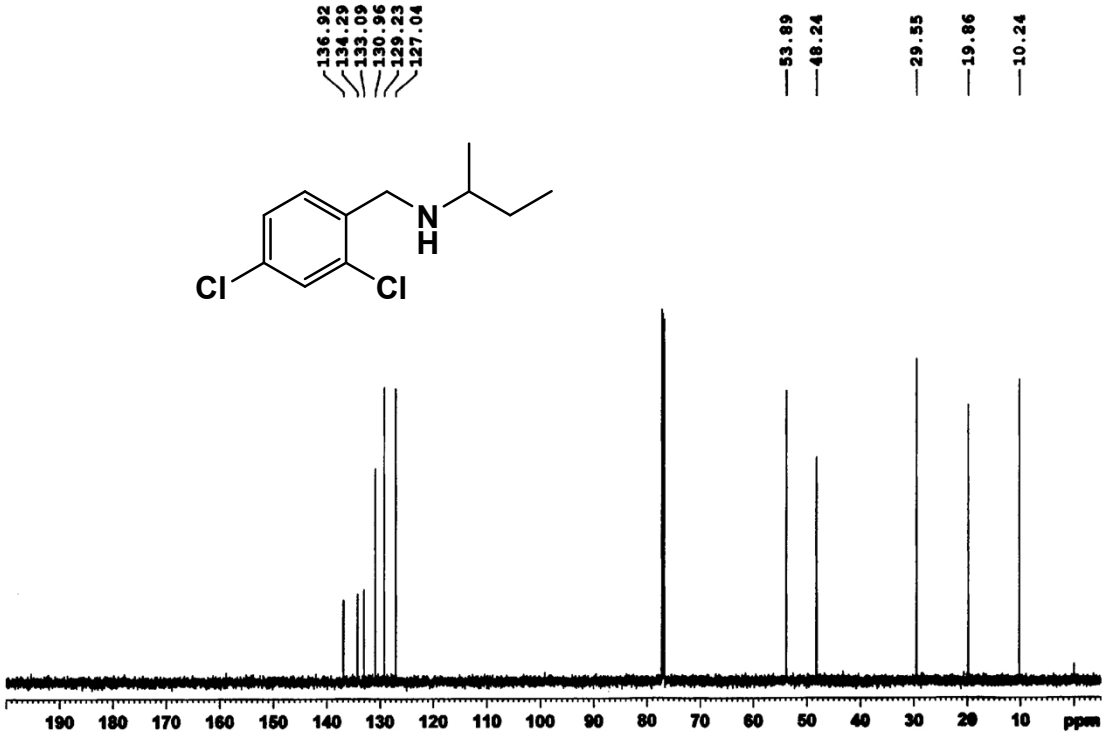
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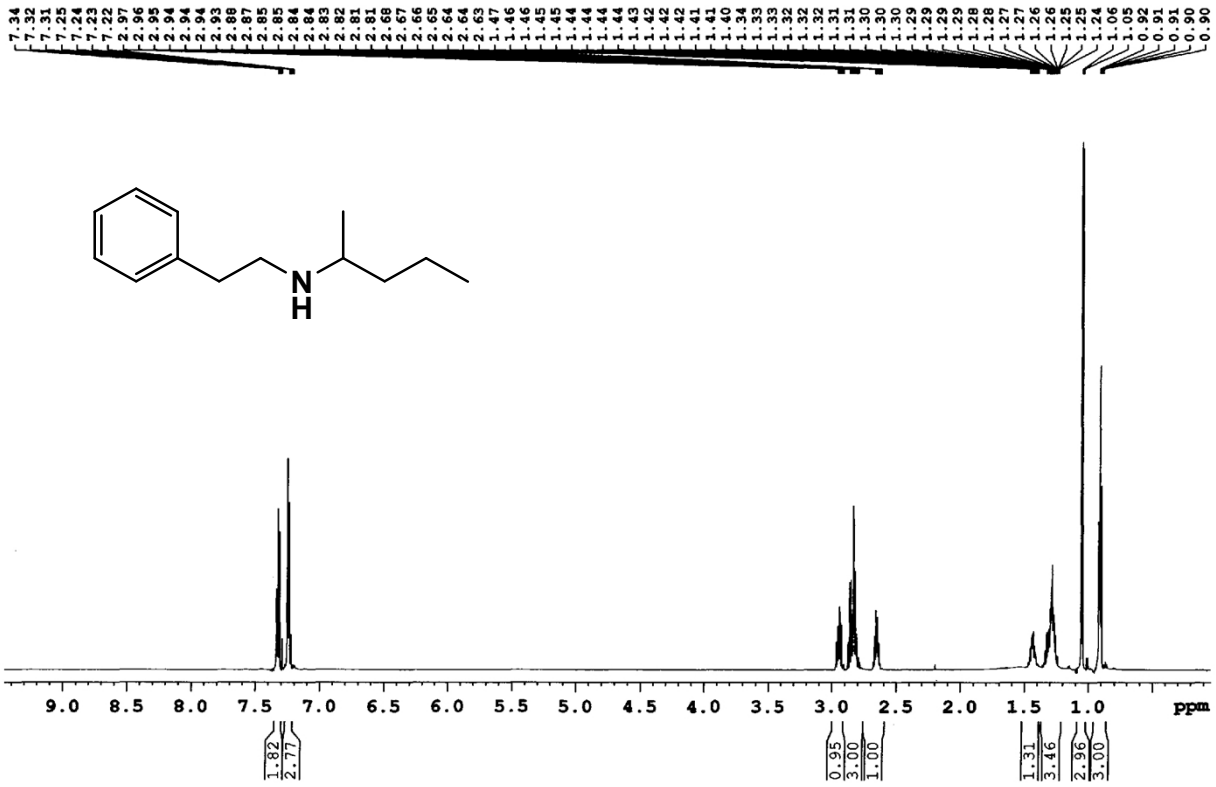
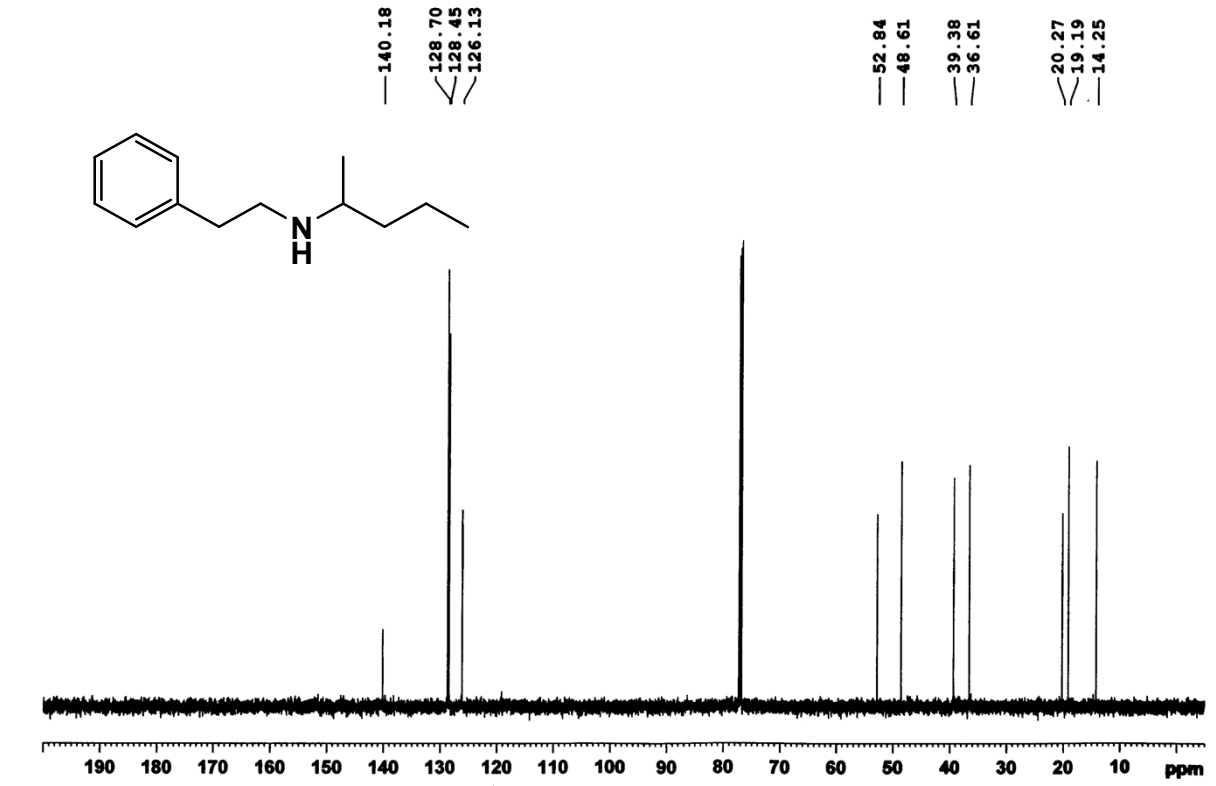
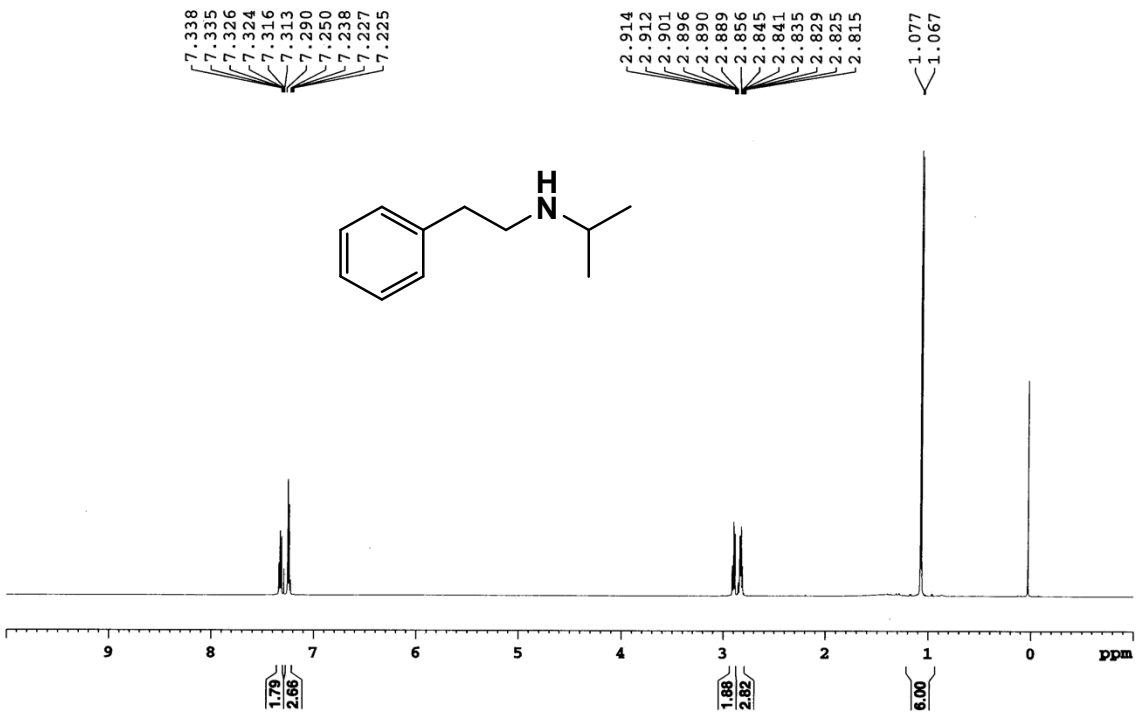
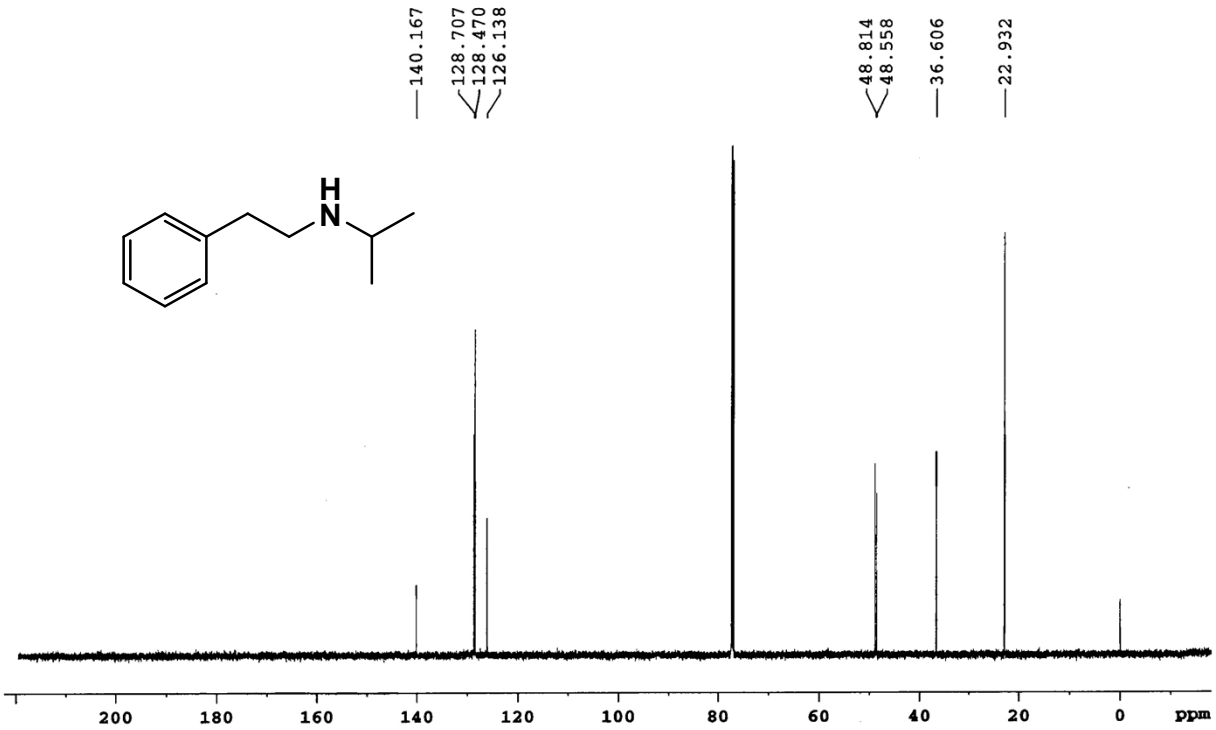
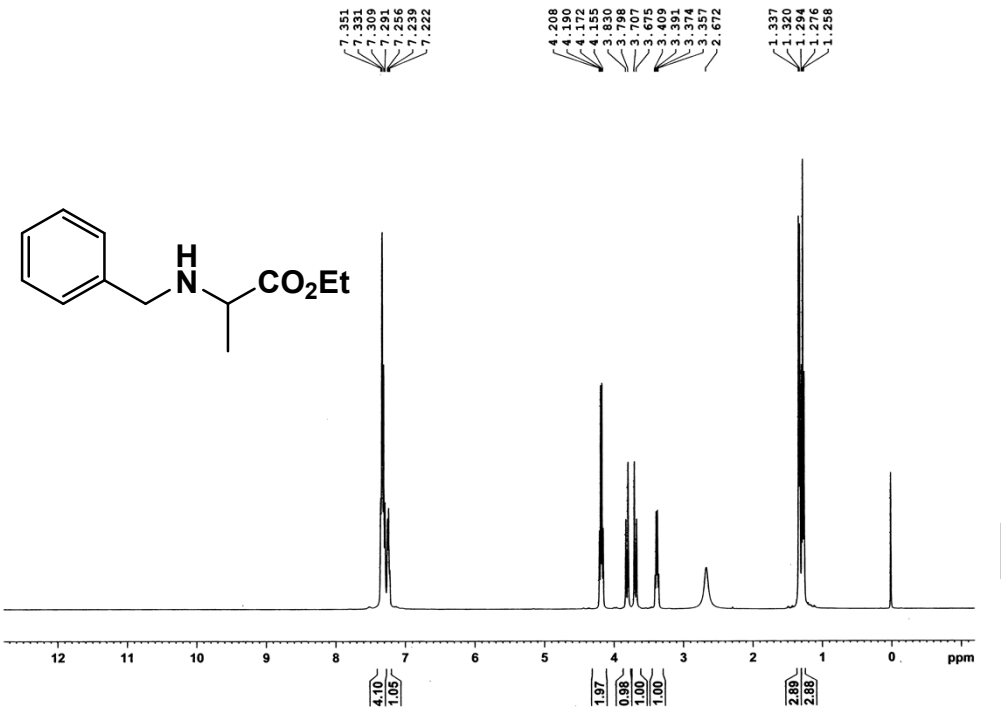
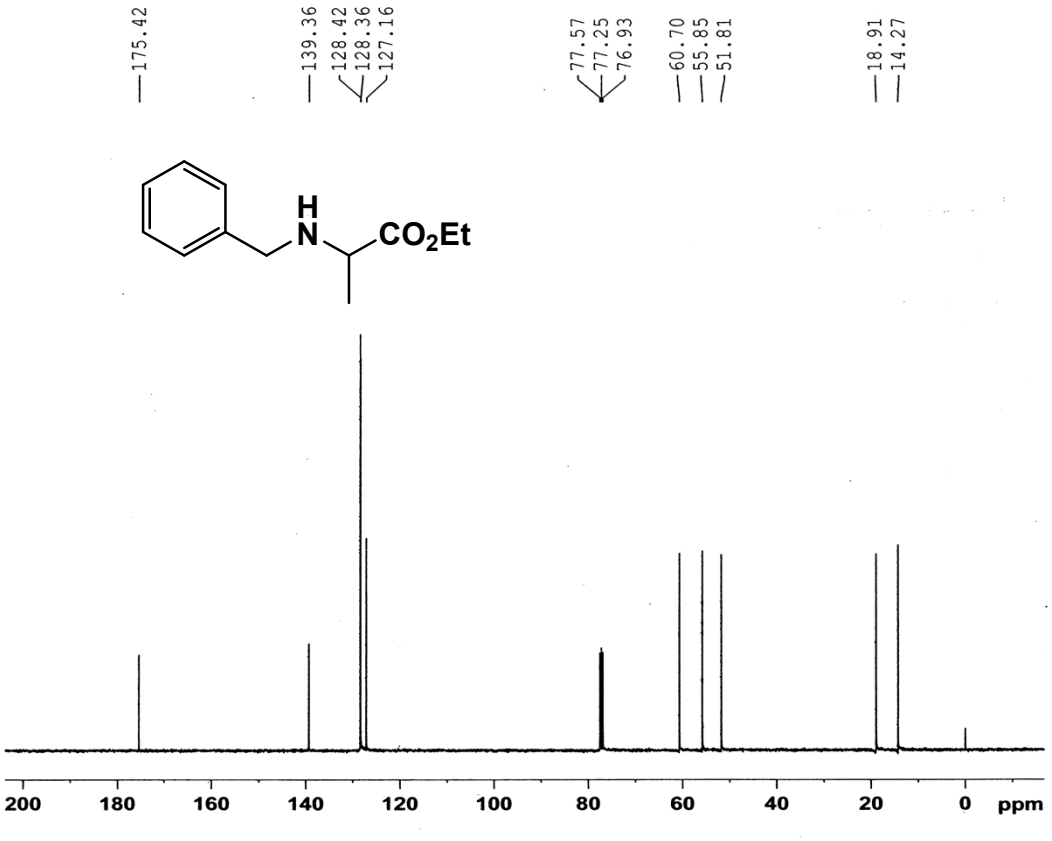

7.34 7.32 7.31 7.25 7.24 7.23 7.22 2.97 2.96 2.95 2.94 2.94 2.94 2.93 2.88 2.87 2.85 2.85 2.84 2.84 2.83 2.82 2.81 2.81 2.68 2.67 2.66 2.65 2.64 2.64 2.63 1.47 1.46 1.46 1.45 1.45 1.44 1.44 1.44 1.44 1.43 1.42 1.42 1.42 1.41 1.41 1.40 1.34 1.33 1.33 1.32 1.32 1.32 1.31 1.31 1.30 1.30 1.29 1.29 1.29 1.29 1.28 1.28 1.27 1.27 1.26 1.26 1.25 1.25 1.24 1.06 1.05 0.92 0.91 0.91 0.90 0.90
N H
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.82 2.77 0.95 3.00 1.00 1.31 3.46 2.96 3.00

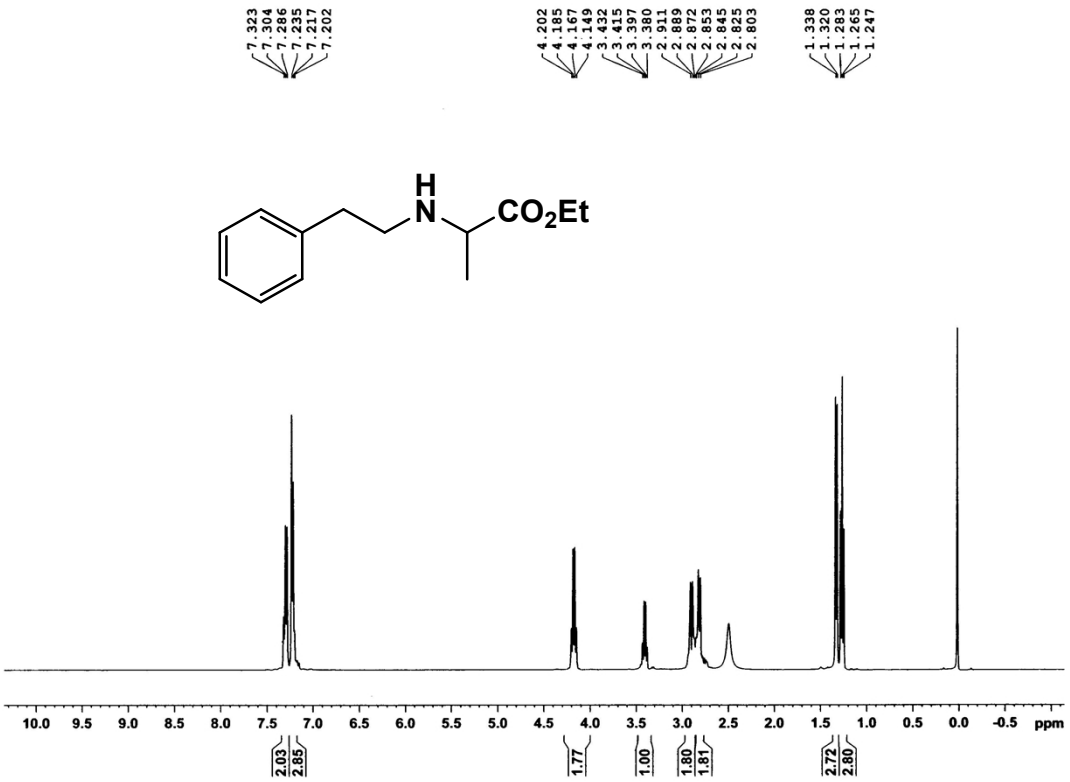

140.18 128.70 128.45 126.13 52.84 48.61 39.38 36.61 20.27 19.19 14.25
N H
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

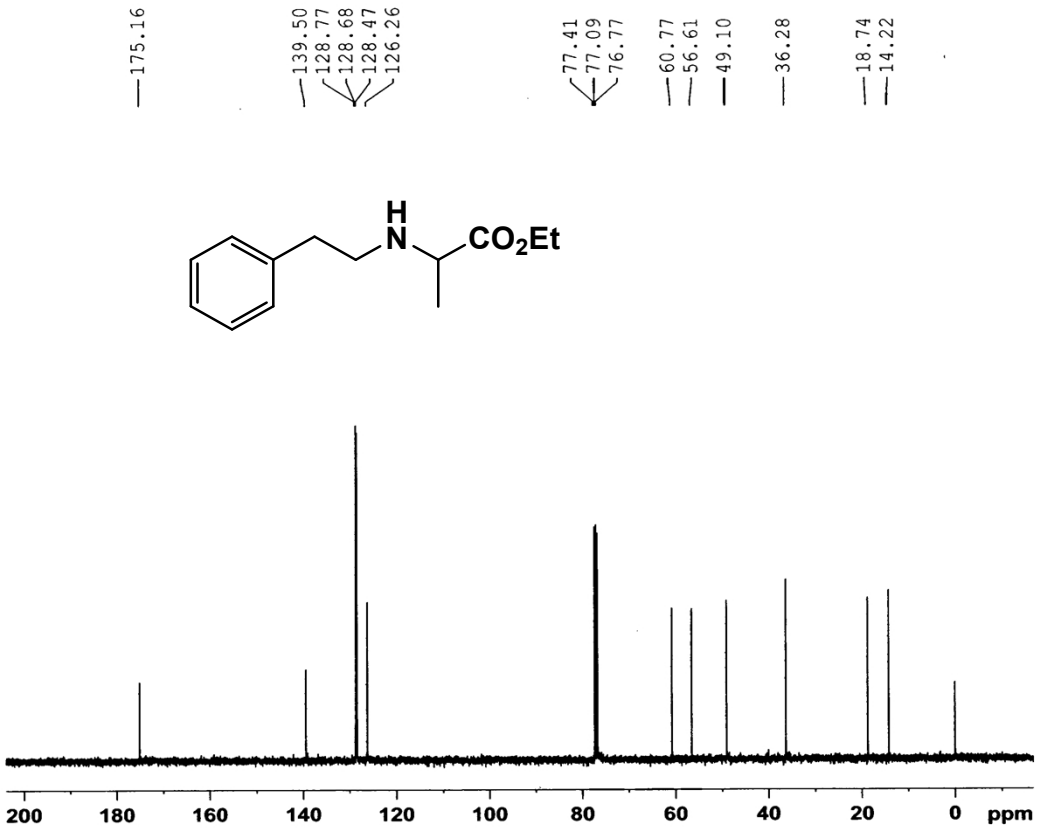

7.338
7.335
7.326
7.324
7.316
7.313
7.290
7.250
7.238
7.227
7.225
2.914
2.912
2.901
2.896
2.890
2.889
2.856
2.845
2.841
2.835
2.829
2.825
2.815
1.077
1.067
H
N
9
8
7
6
5
4
3
2
1
0
ppm
1.79
2.66
1.88
2.82
6.00

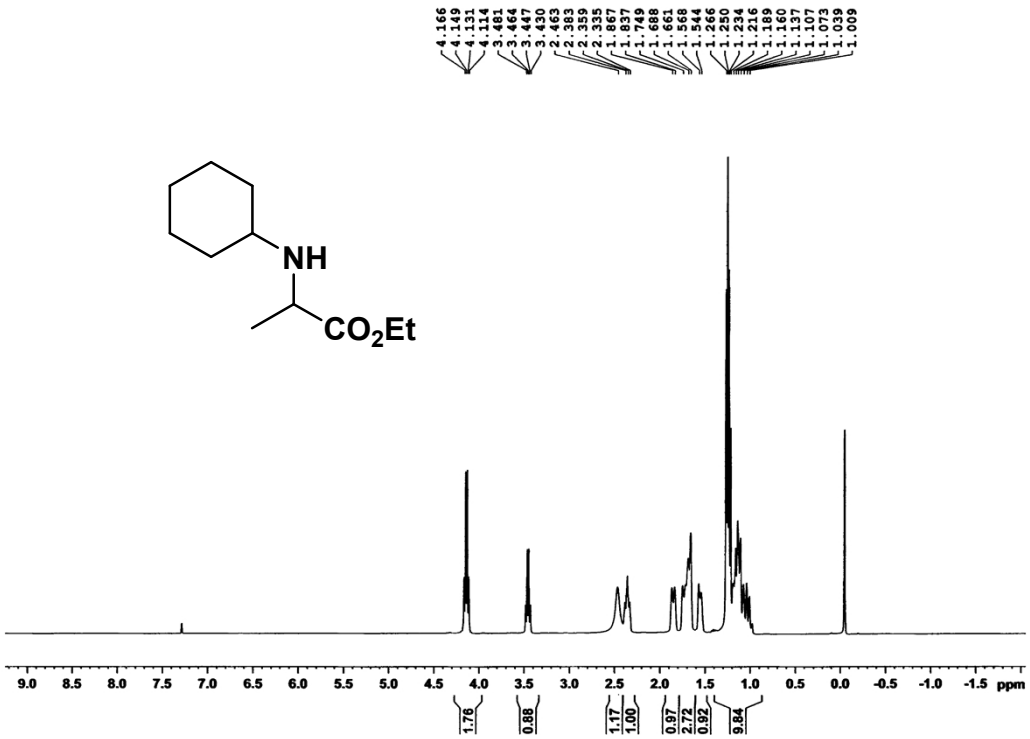

140.167
128.707
128.470
126.138
48.814
48.558
36.606
22.932
H
N
200
180
160
140
120
100
80
60
40
20
0
ppm

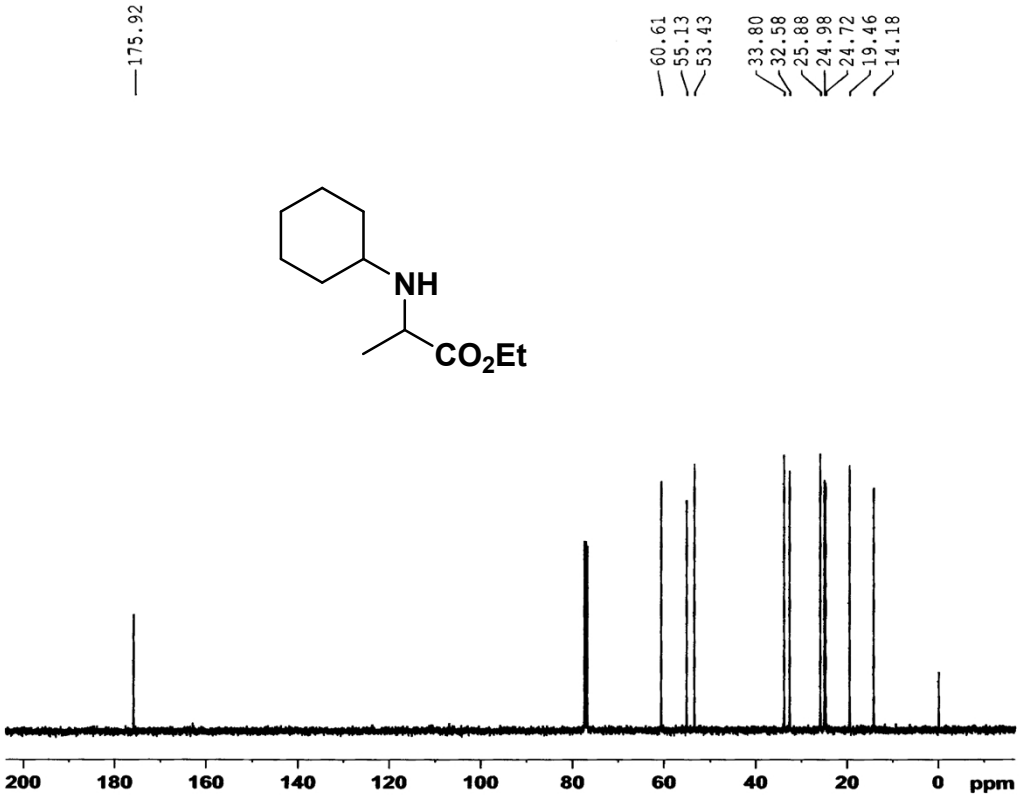

7.351
7.331
7.309
7.291
7.256
7.239
7.222
4.208
4.190
4.172
4.155
3.830
3.798
3.707
3.675
3.409
3.391
3.374
3.357
2.672
1.337
1.320
1.294
1.276
1.258
H
N
CO2Et
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
4.10
1.05
1.97
0.98
1.00
1.00
2.89
2.88

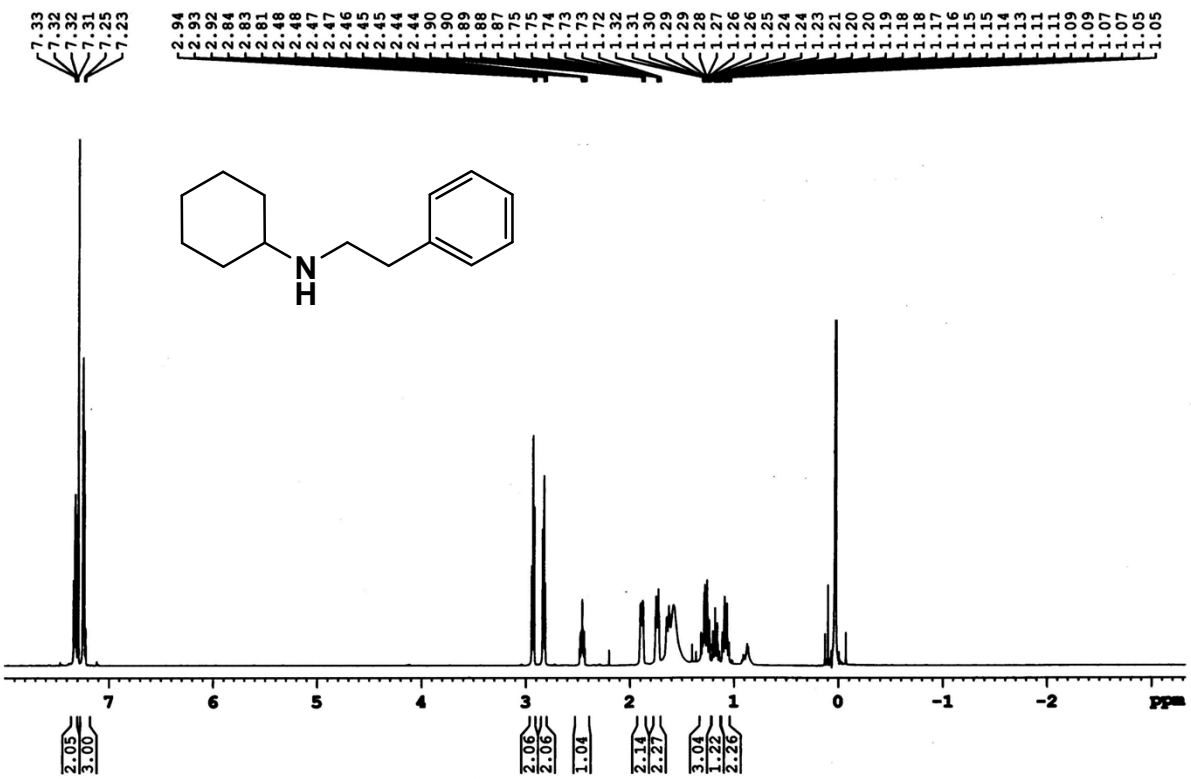

175.42
139.36
128.42
128.36
127.16
77.57
77.25
76.93
60.70
55.85
51.81
18.91
14.27
H
N
CO2Et
200
180
160
140
120
100
80
60
40
20
0
ppm

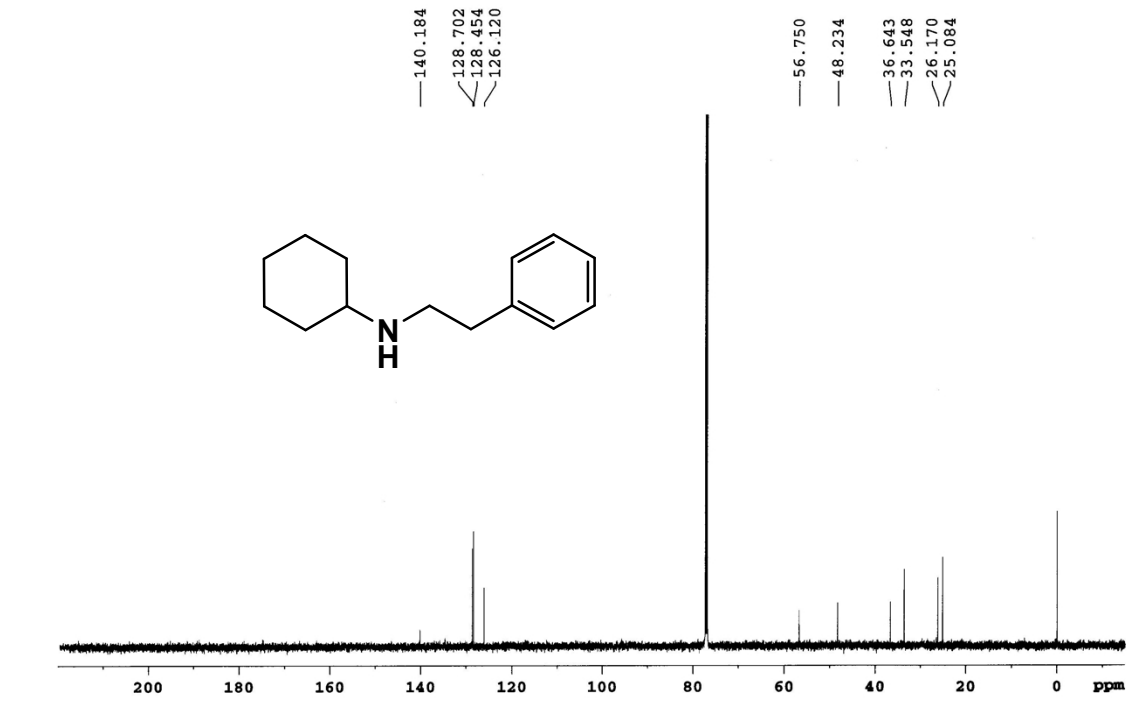

7.323
7.304
7.286
7.235
7.217
7.202
4.202
4.185
4.167
4.149
3.432
3.415
3.397
3.380
2.911
2.889
2.872
2.853
2.845
2.825
2.803
1.338
1.320
1.283
1.265
1.247
H
N
CO2Et
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm
2.03
2.85
1.77
1.00
1.80
1.81
2.72
2.80

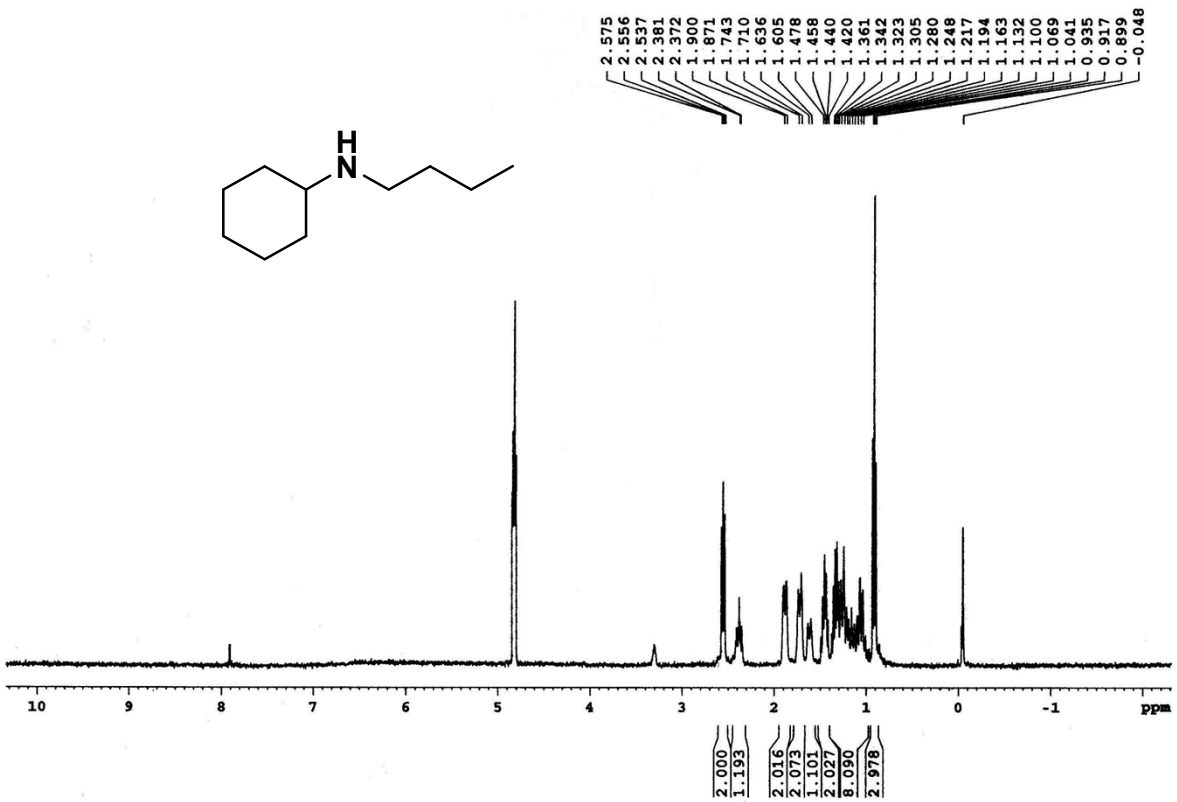

175.16
139.50
128.77
128.68
128.47
126.26
77.41
77.09
76.77
60.77
56.61
49.10
36.28
18.74
14.22
H
N
CO2Et
200 180 160 140 120 100 80 60 40 20 0 ppm

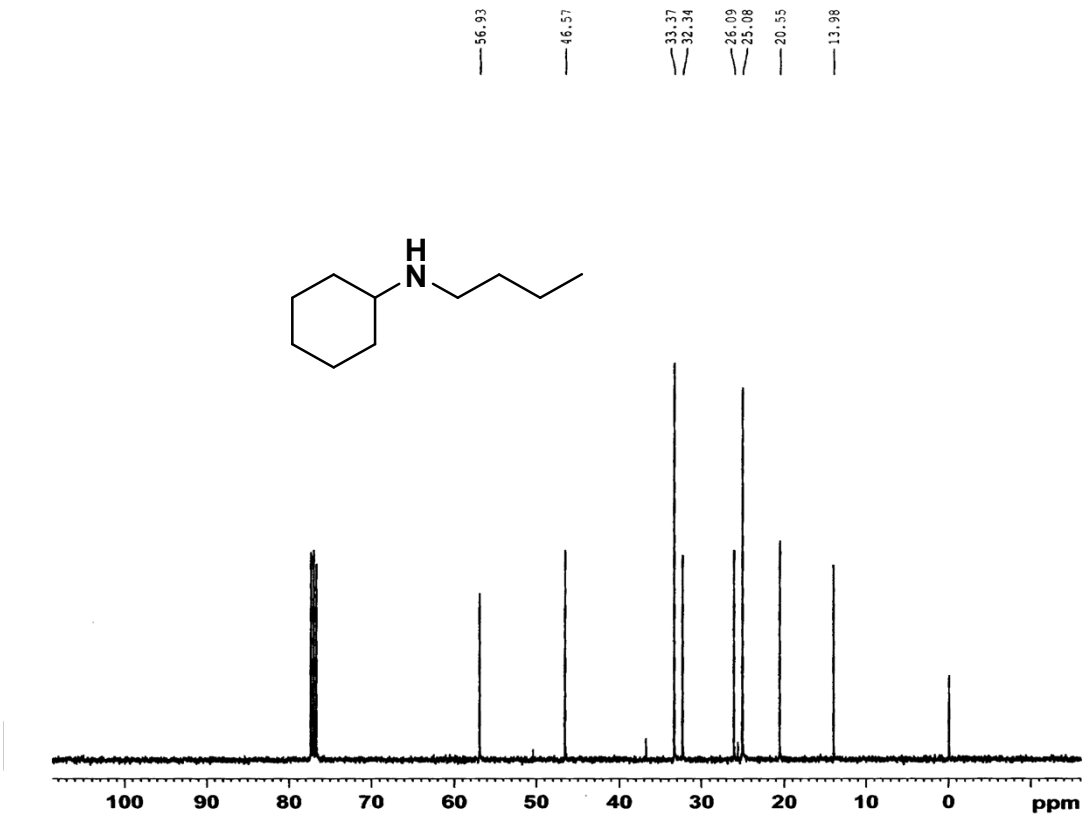

4.166
4.149
4.131
4.114
3.481
3.464
3.447
3.430
2.463
2.383
2.359
2.335
1.867
1.837
1.749
1.688
1.661
1.568
1.544
1.266
1.250
1.234
1.216
1.189
1.160
1.137
1.107
1.073
1.039
1.009
NH
CO2Et
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 ppm
1.76
0.88
1.17
1.00
0.97
2.72
0.92
9.84

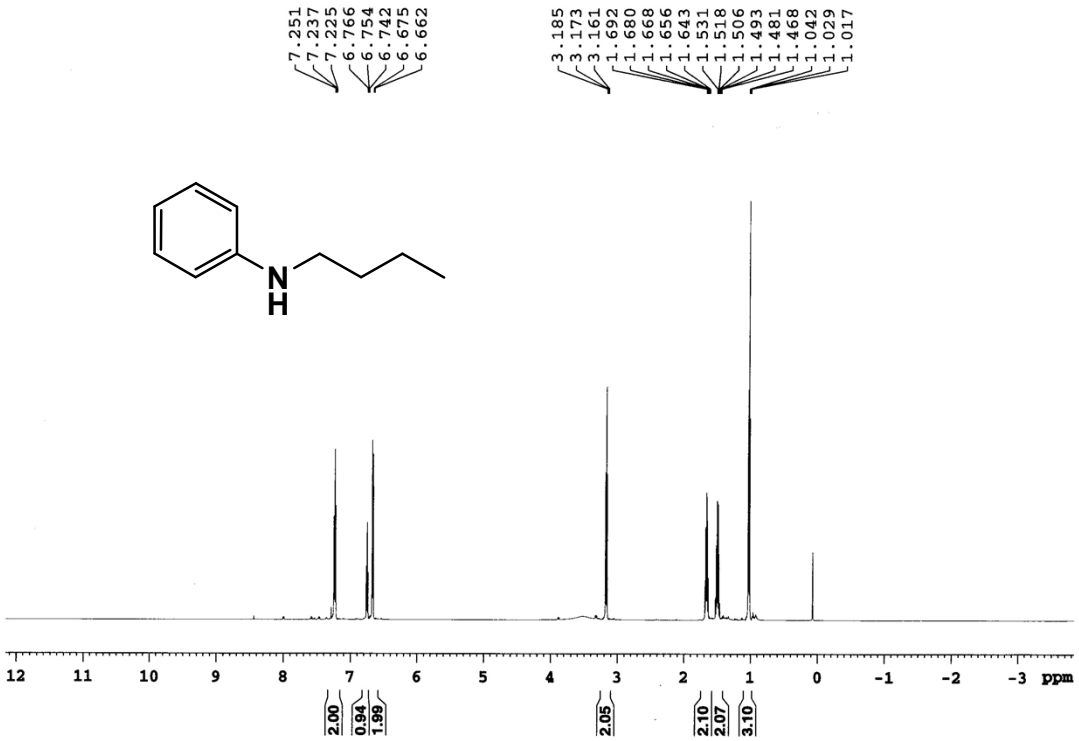

175.92
60.61
55.13
53.43
33.80
32.58
25.88
24.98
24.72
19.46
14.18
NH
CO2Et
200 180 160 140 120 100 80 60 40 20 0 ppm

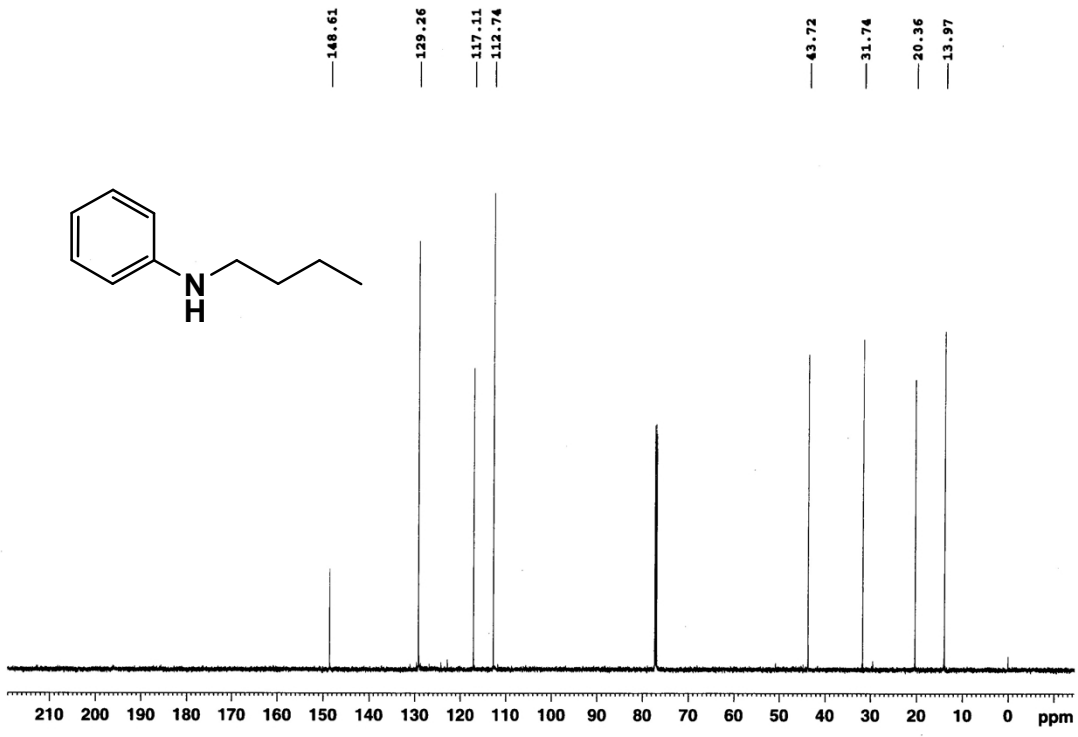

7.33
7.32
7.32
7.31
7.25
7.23
2.94
2.93
2.92
2.84
2.83
2.81
2.48
2.48
2.47
2.47
2.46
2.45
2.45
2.44
2.44
1.90
1.90
1.89
1.88
1.87
1.75
1.75
1.74
1.73
1.73
1.72
1.32
1.31
1.30
1.29
1.29
1.28
1.27
1.26
1.26
1.25
1.24
1.24
1.23
1.21
1.20
1.20
1.19
1.18
1.18
1.17
1.16
1.15
1.15
1.14
1.13
1.11
1.11
1.09
1.09
1.07
1.07
1.05
1.05
N
H
7
6
5
4
3
2
1
0
-1
-2
ppm
2.05
3.00
2.06
2.06
1.04
2.14
2.27
3.04
1.22
2.26

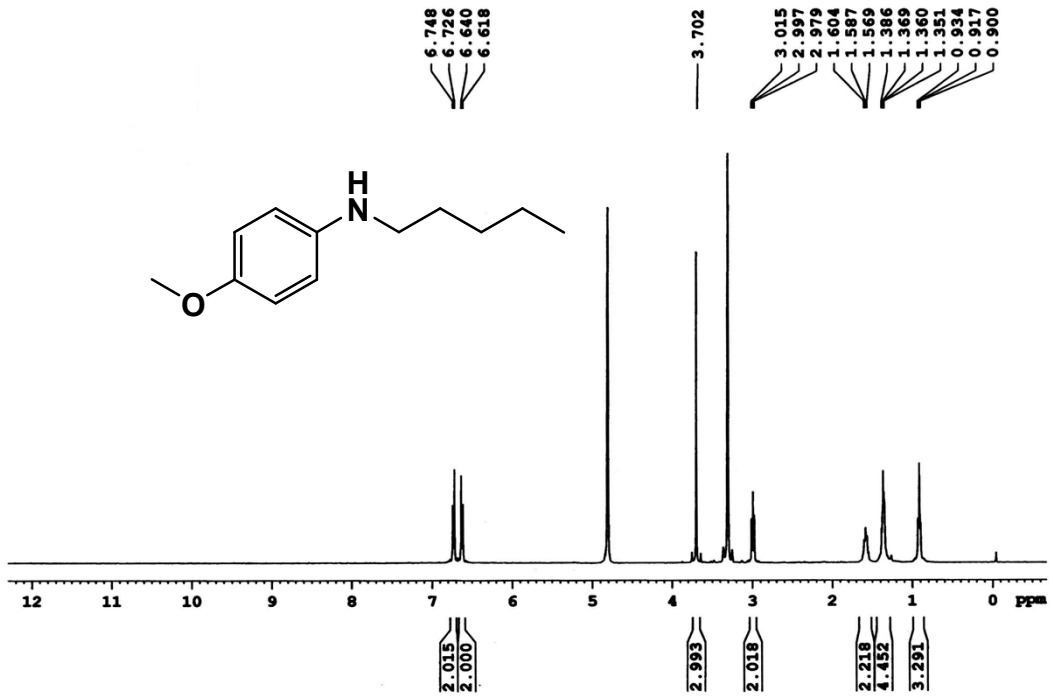

140.184
128.702
128.454
126.120
56.750
48.234
36.643
33.548
26.170
25.084
N
H
200
180
160
140
120
100
80
60
40
20
0
ppm

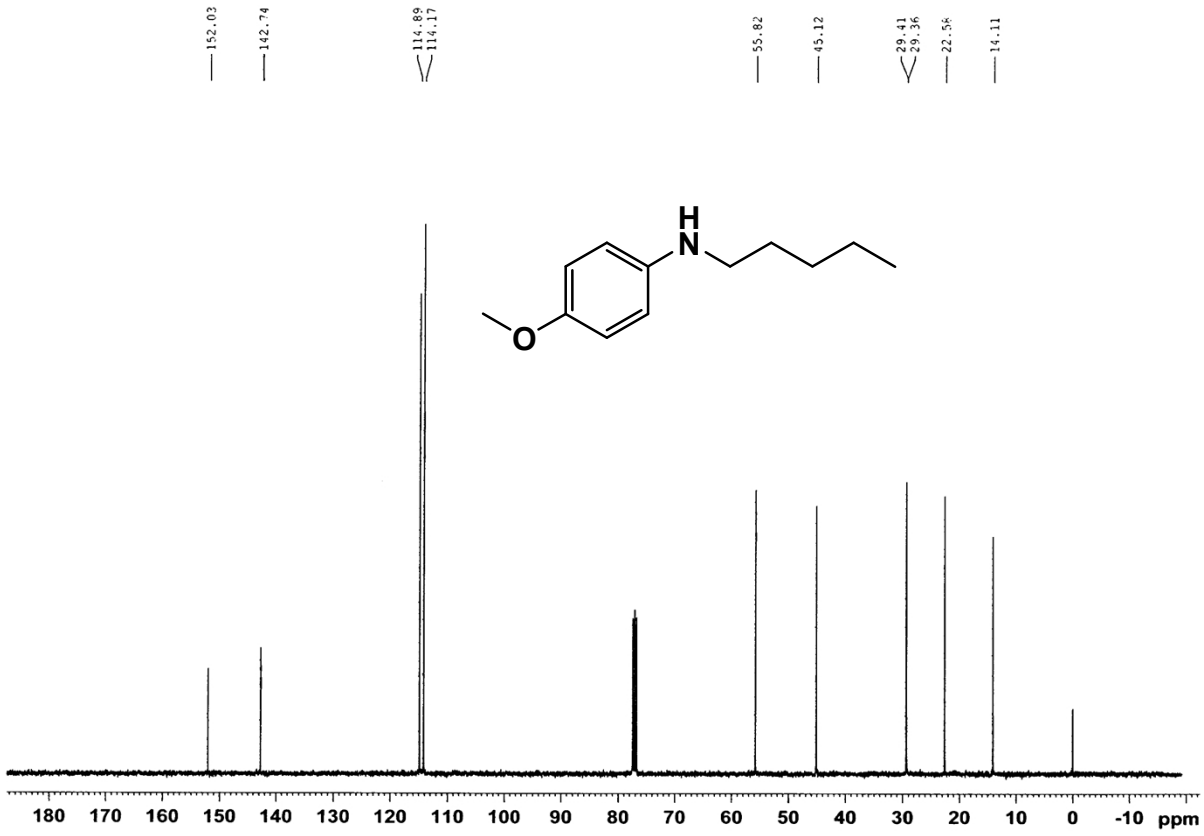

2.575
2.556
2.537
2.381
2.372
2.900
1.871
1.743
1.710
1.636
1.605
1.478
1.458
1.440
1.420
1.361
1.342
1.323
1.305
1.280
1.248
1.217
1.194
1.163
1.132
1.100
1.069
1.041
0.935
0.917
0.899
-0.048
H
N
10
9
8
7
6
5
4
3
2
1
0
-1
ppm
2.000
1.193
2.016
2.073
1.101
2.027
8.090
2.978


56.93
46.57
33.37
32.34
26.09
25.08
20.55
13.98
H
N
100
90
80
70
60
50
40
30
20
10
0
ppm


7.251
7.237
7.225
6.766
6.754
6.742
6.675
6.662
3.185
3.173
3.161
1.692
1.680
1.668
1.656
1.643
1.531
1.518
1.506
1.493
1.481
1.468
1.042
1.029
1.017
N
H
12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 ppm
2.00
0.94
1.99
2.05
2.10
2.07
3.10


148.61
129.26
117.11
112.74
43.72
31.74
20.36
13.97
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


6.748
6.726
6.640
6.618
3.702
3.015
2.997
2.979
1.604
1.587
1.569
1.386
1.369
1.360
1.351
0.934
0.917
0.900
H
N
O
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
2.015
2.000
2.993
2.018
2.218
4.452
3.291


152.03
142.74
114.89
114.17
55.82
45.12
29.41
29.36
22.58
14.11
H
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm

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