Supporting Information

for

Amide Synthesis from Alcohols and Amines by the Extrusion of Dihydrogen

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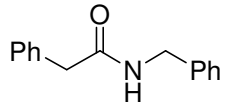
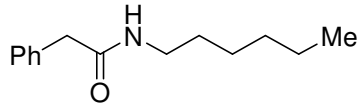
General methods:
All chemicals were obtained from Aldrich and used without further purification, except for $PCyp_3 \cdot HBF_4$ (prepared according to a known procedure[1]), PCy_2(*o*-biphenyl) (generously donated by Saltigo GmbH, Germany), and imidazolium salt **E** (obtained from Dr. Anders Riisager, Technical University of Denmark). Toluene was distilled from sodium and benzophenone under a nitrogen atmosphere. NMR spectra were recorded on a Varian Mercury 300 spectrometer with residual solvent signals as reference.[2] IR spectra were obtained on a Bruker alpha-P spectrometer. Mass spectrometry was performed by direct inlet on a Shimadzu GCMS-QP5000 instrument. GC yields were obtained on a Shimadzu GC2010 instrument equipped with an Equity™ 1 column using dodecane as the internal standard. Optical rotation was measured on a Perkin-Elmer 241 polarimeter. Column chromatography separations were carried out on silica gel (220-440 mesh).

General procedure for amide formation (5 mol% catalyst loading):
$Ru(COD)Cl_2$ (7.0 mg, 0.025 mmol), $PCyp_3 \cdot HBF_4$ (8.2 mg, 0.025 mmol), 1,3-diisopropylimidazolium chloride (4.7 mg, 0.025 mmol), and *t*BuOK (11.2 mg, 0.10 mmol) were placed in an oven dried Schlenk tube. Vacuum was applied and the tube was then filled with argon (repeated twice). Toluene (1 mL) was added and the mixture was heated to reflux under an argon atmosphere for 20 min in an oil bath. The flask was removed from the oil bath and the alcohol (0.5 mmol) and the amine (0.5 mmol) were added. The mixture was heated to reflux under an argon atmosphere in the oil bath for 24 hours. The reaction mixture was cooled to room temperature and the solvent removed *in vacuo*. The residue was purified by silica gel column chromatography (eluent: pentane/EtOAc 4:1 $\rightarrow$ 1:1) to afford the amide.

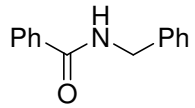
[1] Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 12527-12530.
[2] Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512-7515.



N-Benzyl-2-phenylacetamide
Catalyst loading: 2 mol%
Isolated yield: 93 %
White solid
IR (KBr): 3288, 3063, 3030, 1637, 1551, 1454, 1431, 1029, 693, 602.
Mp. 118-119 ºC. Lit[3]: 118-119 ºC
^{1}H NMR ($CDCl_3$): δ 7.38-7.15 (m, 10H, Ar), 5.88 (bs, 1H, -CON*H*-), 4.40 (d, 2H, *J* = 5.8 Hz, N-C*H*$_2$-Ph), 3.61 (s, 2H, Ph-C*H*$_2$-CO). ^{13}C NMR ($CDCl_3$): δ 171.0 (*C*=O), 138.2, 134.9, 129.5, 129.1, 128.7, 127.6, 127.5, 127.5 (Ar), 43.9, 43.6 (2 × -*C*H$_2$-).
MS: *m/z* 226 [M+H].



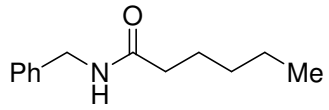
N-Hexyl-2-phenylacetamide
Catalyst loading: 2 mol%
Isolated yield: quant.
White solid
IR (KBr): 3254, 3066, 2937, 1628, 1552, 1477, 1156, 692, 544.
Mp. 55-57 ºC. Lit[4]: 53-54 ºC
^{1}H NMR ($CDCl_3$): δ 7.33-7.18 (m, 5H, Ar), 6.13 (bs, 1H, -CON*H*-), 3.48 (s, 2H, Ph-C*H*$_2$-N), 3.18-3.09 (m, 2H, N-C*H*$_2$-CH$_2$-), 1.38 (p, 2H, *J* = 7.0 Hz, N-CH$_2$-C*H*$_2$-), 1.26-1.13 (m, 6H, 3 × -C*H*$_2$-), 0.82 (t, 1H, *J* = 6.7 Hz, -C*H*$_3$). ^{13}C NMR ($CDCl_3$): δ 171.0 (*C*=O), 135.3, 129.2, 128.7, 127.0 (Ar), 43.6 (Ph-*C*H$_2$-N), 39.6 (N-*C*H$_2$-CH$_2$-), 31.3, 29.3, 26.4, 22.4 (4 × -*C*H$_2$-), 13.9 (-*C*H$_3$).
MS: *m/z* 219 [M].



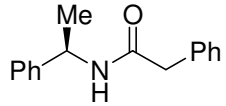
N-Benzylbenzamide
Catalyst loading: 5 mol%
Isolated yield: 78 %
White solid
IR (neat): 3322, 1642, 1543, 1418, 1313, 1260, 728, 693.
Mp. 98-100 ºC (recryst. from H_2O/EtOH). Lit[5]: 104 ºC

[3] Choi, D.; Stables, J. P.; Kohn, H. *Bioorg. Med. Chem.* **1996**, *4*, 2105-2114.
[4] Kametani, T.; Umezawa, O. *Chem. Pharm. Bull.* **1966**, *14*, 369-375.
[5] Maki, T.; Ishihara, K.; Yamamoto, H. *Org. Lett.* **2006**, *8*, 1431-1434.

^{1}H NMR ($CDCl_3$): δ 7.82-7.77 (m, 2H, Ar), 7.55-7.25 (m, 8H, Ar), 6.54 (bs, 1H, -CON*H*-), 4.64 (d, 2H, *J* = 5.7 Hz, N-C*H*$_2$-Ph). ^{13}C NMR ($CDCl_3$): δ 167.5 (*C*=O), 138.3, 134.5, 131.7, 128.9, 128.7, 128.0, 127.7, 127.1, (Ar), 44.2 (N-*C*H$_2$-Ph).
MS: *m/z* 211 [M].



N-Benzylhexanamide
Catalyst loading: 5 mol%
Isolated yield: 60 %
Colorless crystals
IR ($CHCl_3$): 3291, 3085, 2957, 2928, 1639, 1552.1454, 697.
Mp. 50-52 ºC (recryst. from pentane). Lit[6]: 52-53.5 ºC.
^{1}H NMR ($CDCl_3$): δ 7.37-7.25 (m, 5H, Ar), 5.69 (bs, 1H, CON-*H*), 4.45 (d, 2H, *J* = 5.7 Hz, N-C*H*$_2$-Ph), 2.21 (t, 2H, *J* = 7.4 Hz, -C*H*$_2$-C=O), 1.66 (p, 2H, *J* = 7.5 Hz, -C*H*$_2$-CH$_2$-C=O), 1.37-1.24 (m, 4H, CH$_3$-C*H*$_2$-C*H*$_2$-), 0.89 (t, 3H, *J* = 6.8 Hz, C*H*$_3$-). ^{13}C NMR ($CDCl_3$): δ 173.2 (*C*=O), 138.5, 128.8, 127.9, 127.6 (Ar), 43.6 (N-*C*H$_2$-Ph), 36.9 (-*C*H$_2$-C=O, 31.6 (-*C*H$_2$-), 25.6 (-*C*H$_2$-), 22.5 (-*C*H$_2$-CH$_3$), 14.1 (-*C*H$_3$).
MS: *m/z* 205 [M].



2-Phenyl-*N*-((*R*)-1-phenylethyl)acetamide
Catalyst loading: 5 mol%
Isolated yield: 70 %
$[\alpha]_D$ +3.4 (*c* = 1.0, $CHCl_3$). Ref[7]: $[\alpha]_D$ +3.3 (*c* = 1.0, $CHCl_3$).
$[\alpha]_{436}$ +11.9 (*c* = 1.0, $CHCl_3$). Ref: $[\alpha]_{436}$ +11.4 (*c* = 1.0, $CHCl_3$).
IR (KBr): 3307, 3063, 3028, 2974, 1649, 1541, 1494, 1445, 1356, 1246, 1208, 761, 697.
Mp. 115-116 ºC (recryst. from H_2O/EtOH). Lit[8]: 117-118 ºC.
^{1}H NMR ($CDCl_3$): δ 7.39-7.61 (m, 10H, Ar), 5.72 (d, 1H, *J* = 7.1 Hz, -CON*H*-), 5.12 (p, 1H, *J* = 7.0 Hz, PhC*H*(Me)N-), 3.57 (s, 2H, Ph-C*H*$_2$-), 1.40 (d, 3H, *J* = 6.9 Hz, -C*H*$_3$). ^{13}C NMR ($CDCl_3$): δ 170.1 (C=O), 143.2, 135.0, 129.5, 129.1, 128.7, 127.4, 127.4, 126.0 (Ar), 48.8 (Ph*C*H(Me)N-), 44.0 (Ph-*C*H$_2$-), 21.9 (-*C*H$_3$).
MS: *m/z* 239 [M].

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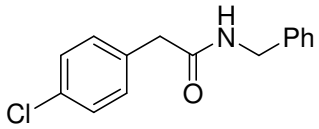
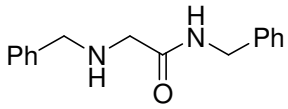
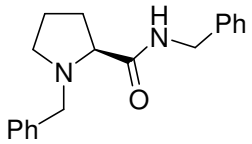
[6] Shioiri, T.; Yokoyama, Y.; Kasai, Y.; Yamada, S. *Tetrahedron* **1976**, *32*, 2211-2217.
[7] Compound prepared by acylation of optically pure amine (1.05 equiv.) with acid chloride (1 equiv.) in Et_3N/CH_2Cl_2 (1:10) at 0 °C → r.t. overnight. Water was added and the mixture was extracted with CH_2Cl_2. The organic phase was washed successively with 2 M H_2SO_4, $NaHCO_3$ and brine. Dried (Na_2SO_4), filtered and concentrated. Residue was recrystallized from H_2O/EtOH.
[8] Guranda, D. T.; van Langen, L. M.; van Rantwijk, F.; Sheldon, R. A.; Švedas, V. K. *Tetrahedron: Asymmetry* **2001**, *12*, 1645-1650.



N-Benzyl-2-(4-chlorophenyl)acetamide
Catalyst loading: 2 mol%
Isolated yield: 83 %
Colorless crystals
IR (neat/solid): 3277, 3026, 2917, 1642, 1539, 1491, 1246, 690.
Mp. 151-153 ºC. Lit[9]: 155-156 ºC
^{1}H NMR (DMSO-*d6*): δ 8.58 (t, 1H, *J* = 5.7 Hz, -CON*H*-), 7.39-7.20 (m, 9H, Ar), 4.27 (d, 2H, *J* = 5.9 Hz, N-C*H*$_2$-Ph), 3.49 (s, 2H, Ar-C*H*$_2$-CO). ^{13}C NMR (DMSO-*d6*): δ 169.7 (*C*=O), 139.3, 135.3, 131.0, 130.8, 128.2, 128.1, 127.2, 126.7 (Ar), 42.2, 41.4 (2 × -CH$_2$-).
MS: *m/z* 259 [M].



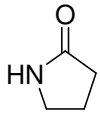
N-Benzyl-2-(benzylamino)acetamide
Catalyst loading: 5 mol%
Isolated yield: 90%
Clear oil
IR (neat): 3319, 3029, 1654, 1522, 1453, 1261, 1029, 737, 699.
^{1}H NMR (CDCl$_3$): δ 7.53 (bs, 1H, -CON*H*-), 7.40-7.20 (m, 10H, Ar), 4.47 (d, 2H, *J* = 6.0 Hz, Ph-C*H*$_2$-NC(=O)-), 3.76 (s, 2H, Ph-C*H*$_2$-NH-CH$_2$-), 3.36 (s, 2H, Ph-CH$_2$-NH-C*H*$_2$-), 1.80 (bs, 1H, -CH$_2$-N*H*-CH$_2$). ^{13}C NMR (CDCl$_3$): δ 171.5 (*C*=O), 139.4, 138.5, 128.8, 128.7, 128.2, 127.8, 127.6, 127.5 (Ar), 54.1, 52.1 (2 × -*C*H$_2$-), 43.1 (Ph-*C*H$_2$-NC(=O)-).
MS: *m/z* 255 [M+H].



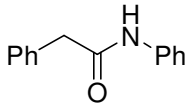
N,*N'*-Dibenzyl-L-prolinamide
Catalyst loading: 5 mol%
Isolated yield: 60 %
Clear oil
[α]$_D$ -48.2 ° (*c* = 1.0, CHCl$_3$). Ref[10]: [α]$_D$ -46.3 ° (*c* = 1.0, CHCl$_3$).
IR (neat): 3346, 3061, 2968, 2806, 1670, 1514, 1454, 1028, 748, 700.

[9] Agwada, V. C. *J. Chem. Eng. Data* **1982**, *27*, 481-483.
[10] Compound prepared by HBTU mediated coupling between *N*-benzyl-L-prolinol and BnNH$_2$ as described in Traverse, J. F.; Zhao, Y.; Hoveyda, A. H.; Snapper, M. L. *Org. Lett.* **2005**, *7*, 3151-3154.

^{1}H NMR ($CDCl_3$): δ 7.74 (bs, 1H, -CON*H*-), 7.22-7.37 (m, 8H, Ar), 7.17-7.11 (m, 2H, Ar), 4.41 (d, 2H, *J* = 5.7 Hz, Ph-CH_2-NC(=O)-), 3.85 (d, 1H, *J* = 12.8 Hz, Ph-CH_aH$_b$-N-), 3.48 (d, 1H, *J* = 12.8 Hz, Ph-CH$_a$$H_b$-N-), 3.29 (dd, 1H, *J* = 4.9 Hz, *J* = 10.2 Hz, H-2), 3.00 (ddd, 1H, *J* = 2.2 Hz, *J* = 6.6 Hz, *J* = 8.9 Hz, H-5a), 2.20-2.41 (m, 2H, H-3a, H-5b), 1.95 (ddd, 1H, *J* = 4.0 Hz, *J* = 8.2 Hz, *J* = 13.0 Hz, H-3b), 1.84-1.61 (m, 2H, H-4a, H-4b).
^{13}C NMR ($CDCl_3$): δ 174.5 (*C*=O), 138.5, 138.5, 128.7, 128.7, 128.4, 127.6, 127.4, 127.3 (Ar), 67.3 (C-2), 60.0, 53.9 (C-5, Ph-*C*H$_2$-N), 42.9 (Ph-*C*H$_2$-NC(=O)-), 30.7 (C-3), 24.2 (C-4).
MS: *m/z* 295 [M+H].

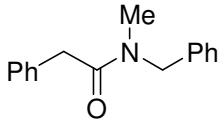


2-Pyrrolidinone
Catalyst loading: 5 mol%
Isolated yield: 65 %
Colorless crystals
IR (neat): 3247, 3198, 2921, 2867, 1679, 1462, 1283, 419.
Mp. 26-27 ºC. Lit[11]: 25 ºC.
^{1}H NMR ($CDCl_3$): δ 6.50 (bs, 1H, -CON*H*-), 3.39 (t, 2H, *J* = 7.0 Hz, NH-CH_2-CH$_2$-), 2.35-2.25 (m, 2H, CO-CH_2-CH$_2$-), 2.20-2.05 (m, 2H, NH-CH$_2$-CH_2-). ^{13}C NMR ($CDCl_3$): δ 179.3 (*C*=O), 42.4 (NH-*C*H$_2$-CH$_2$-), 30.1 (CO-*C*H$_2$-CH$_2$-), 20.9 (NH-CH$_2$-*C*H$_2$-).
MS: *m/z* 85 [M].

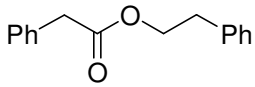


N,2-Diphenylacetamide
Catalyst loading: 5 mol%
Isolated yield: 21 %
Colorless crystals
IR ($CHCl_3$): 3286, 3257, 3060, 1655, 1599, 1547, 1495, 1442, 1166, 751, 723, 692.
Mp. 114-115 ºC (recryst. from heptane). Lit[12]: 115-116 ºC.
^{1}H NMR ($CDCl_3$): δ 7.46-7.20 (m, 10H, Ar, CON-*H*), 7.12-7.05 (m, 1H, Ar), 3.73 (s, 2H, Ph-CH_2-C=O). ^{13}C NMR ($CDCl_3$): δ 169.3 (C=O), 137.7, 134.5, 129.6, 129.3, 129.0, 127.8, 124.6, 119.9 (Ar), 44.9 (Ph-*C*H$_2$-C=O).
MS: *m/z* 211 [M].

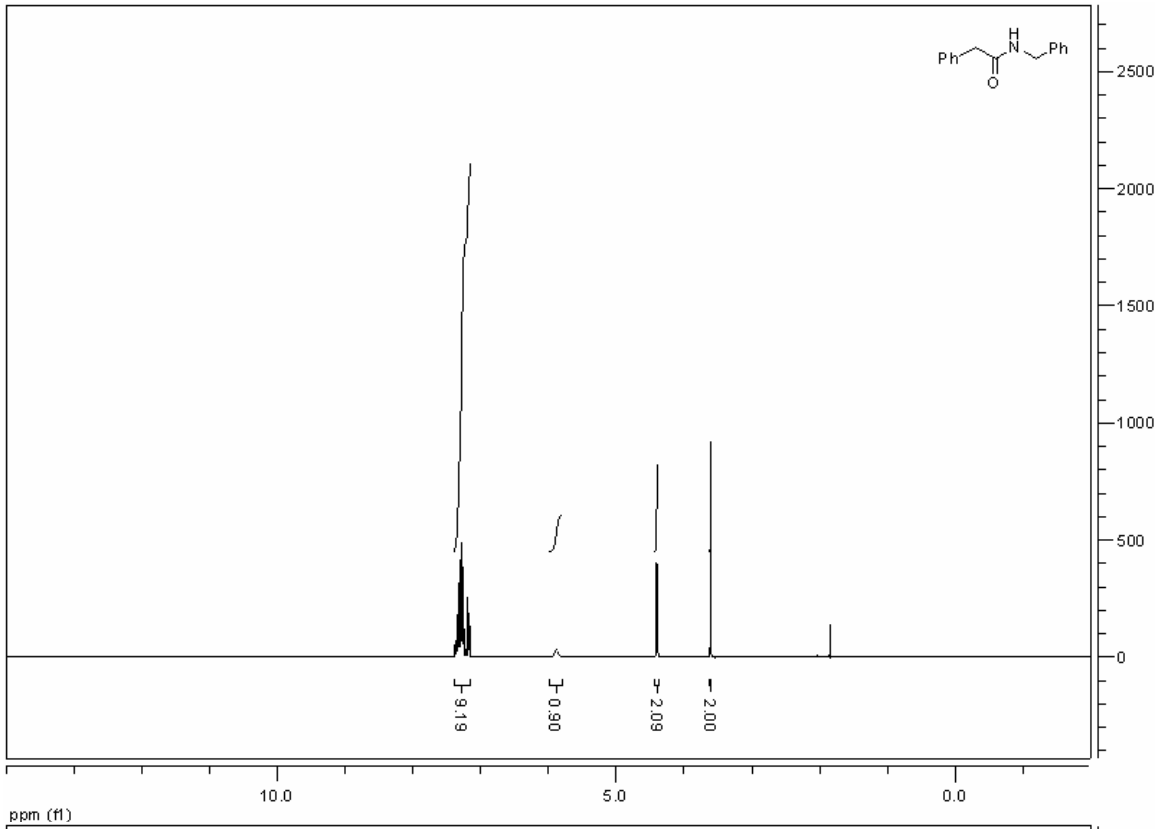
[11] Drechsel, E. K. *J. Org. Chem.* **1957**, *22*, 849-851.
[12] Underwood, H. W.; Gale, J. C. *J. Am. Chem. Soc.* **1934**, *56*, 2117-2120.



N-Benzyl-*N*-methyl-2-phenylacetamide
Catalyst loading: 5 mol%
Isolated yield: 40 %
Yellow oil
IR ($CHCl_3$): 3061, 3029, 1644, 1495, 1453, 1399, 1111, 731, 697.
1:1.4 mixture of rotamers. Major rotamer:
^{1}H NMR ($CDCl_3$): δ 7.39-7.20 (m, 9H, Ar), 7.12-7.09 (m, 1H, Ar), 4.61 (s, 2H, N-C*H*$_2$-Ph), 3.78 (s, 2H, Ph-C*H*$_2$-C=O), 2.89 (s, 3H, N-C*H*$_3$). ^{13}C NMR ($CDCl_3$): δ 171.2 (*C*=O), 137.4, 135.0, 128.9, 128.8, 128.6, 128.1, 126.9, 126.4 (Ar), 51.0 (N-*C*H$_2$-Ph), 41.3 (Ph-*C*H$_2$-C=O), 35.3 (N-*C*H$_3$).
Minor rotamer:
^{1}H NMR ($CDCl_3$): δ 7.39-7.20 (m, 9H, Ar), 7.09-7.07 (m, 1H, Ar), 4.52 (s, 2H, N-C*H*$_2$-Ph), 3.75 (s, 2H, Ph-C*H*$_2$-C=O), 2.95 (s, 3H, N-C*H*$_3$).
^{13}C NMR ($CDCl_3$): δ 171.6 (*C*=O), 136.5, 135.2, 129.0, 128.9, 128.8, 127.7, 127.4, 126.9 (Ar), 53.7 (N-*C*H$_2$-Ph), 41.0 (Ph-*C*H$_2$-C=O), 34.1 (N-*C*H$_3$).
MS: *m/z* 239 [M].



2-Phenylethyl 2-phenylacetate
Clear oil
IR (neat): 3029, 2957, 1730, 1496, 1454, 1245, 1138, 1000, 748, 723, 696.
^{1}H NMR ($CDCl_3$): δ 7.40-7.17 (m, 10H, Ar), 4.36 (t, 2H, *J* = 7.0 Hz, O-C*H*$_2$-CH$_2$-Ph), 3.65, (s, 2H, Ph-C*H*$_2$-C=O), 2.96 (t, 2H, *J* = 6.9 Hz, O-CH$_2$-C*H*$_2$-Ph). ^{13}C NMR ($CDCl_3$): δ 171.8 (*C*=O), 138.0, 134.3, 129.6, 129.2, 128.8, 128.8, 127.3, 126.8 (Ar), 65.6 (O-*C*H$_2$-CH$_2$-Ph), 41.7 (Ph-*C*H$_2$-C=O), 35.3 (O-CH$_2$-*C*H$_2$-Ph).
MS: *m/z* 240 [M].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H
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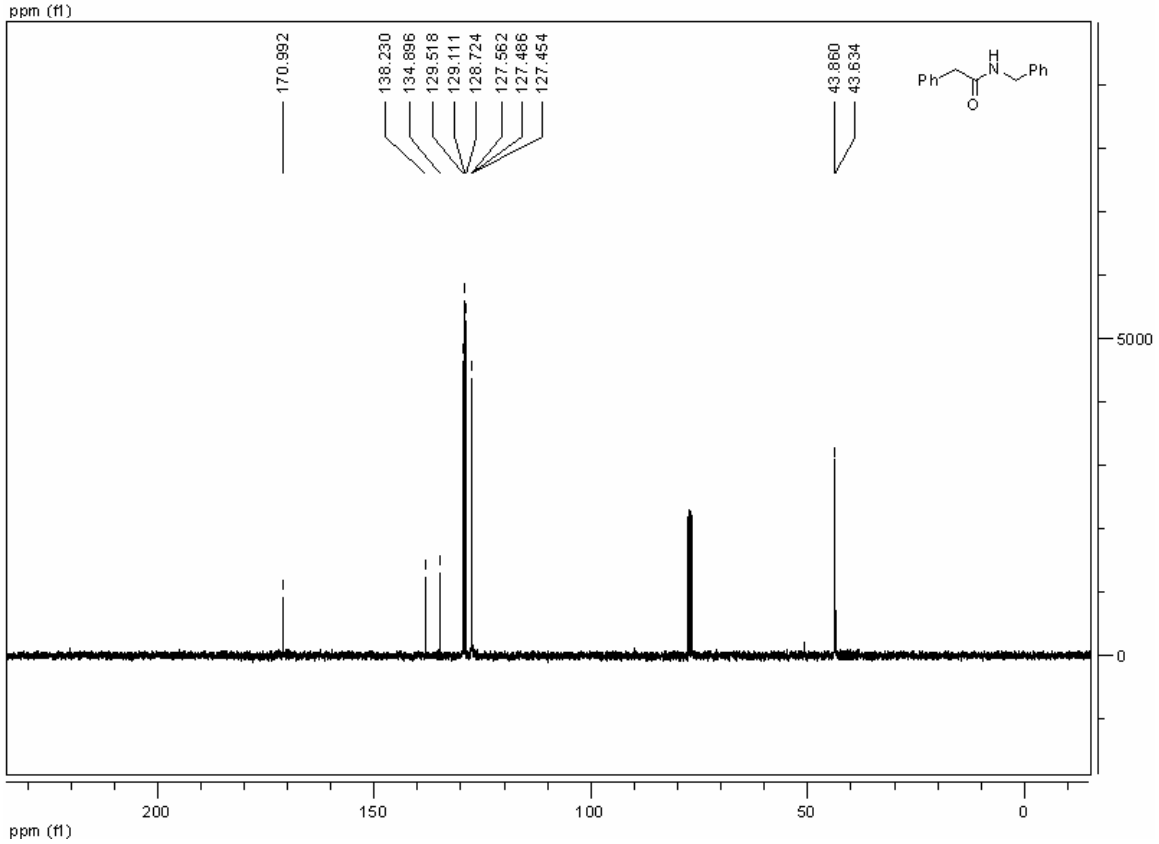
ppm (f1)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H
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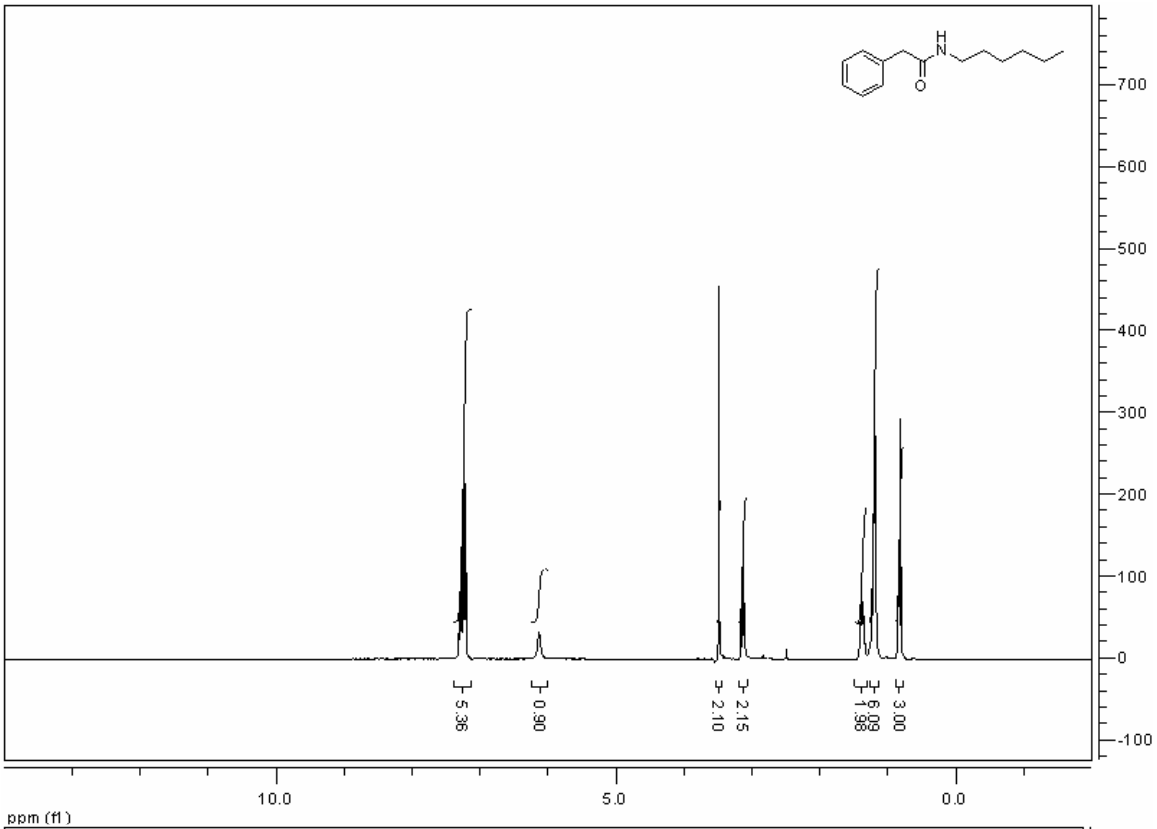
0
ppm (f1)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2.15
6.09
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600
500
400
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200
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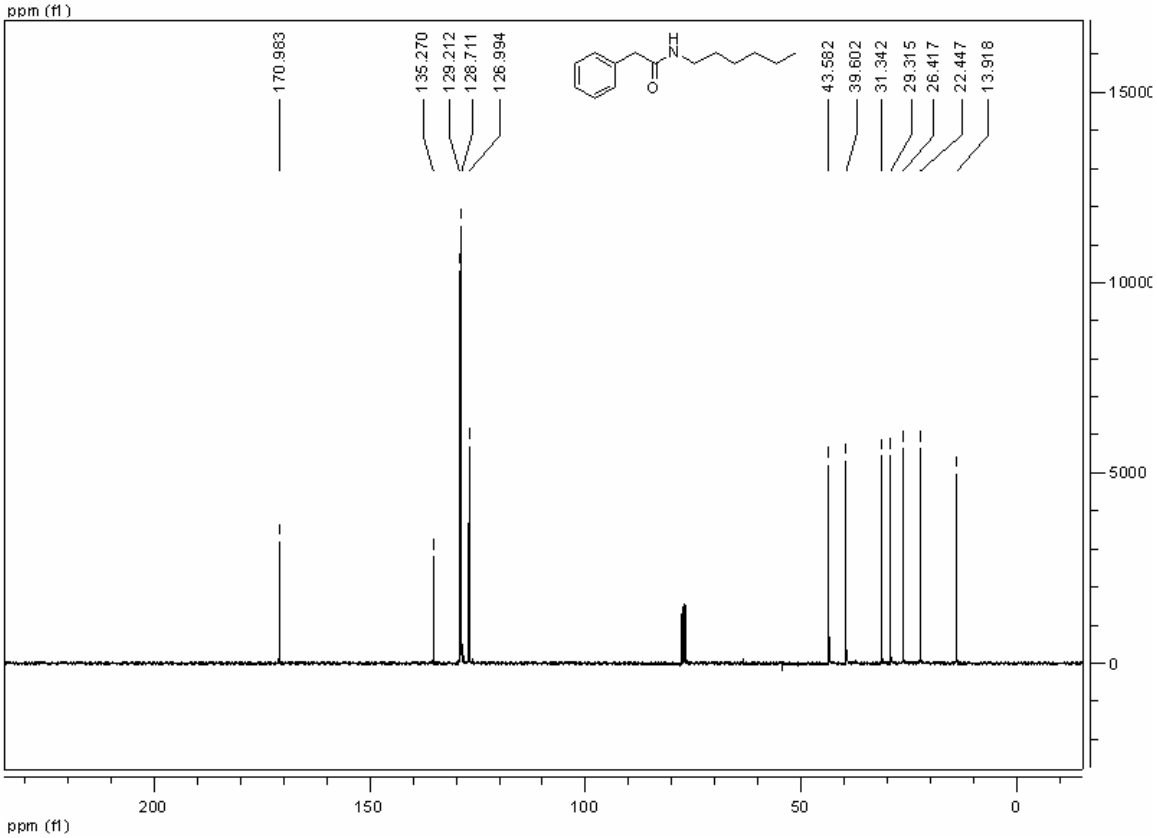
ppm (f1)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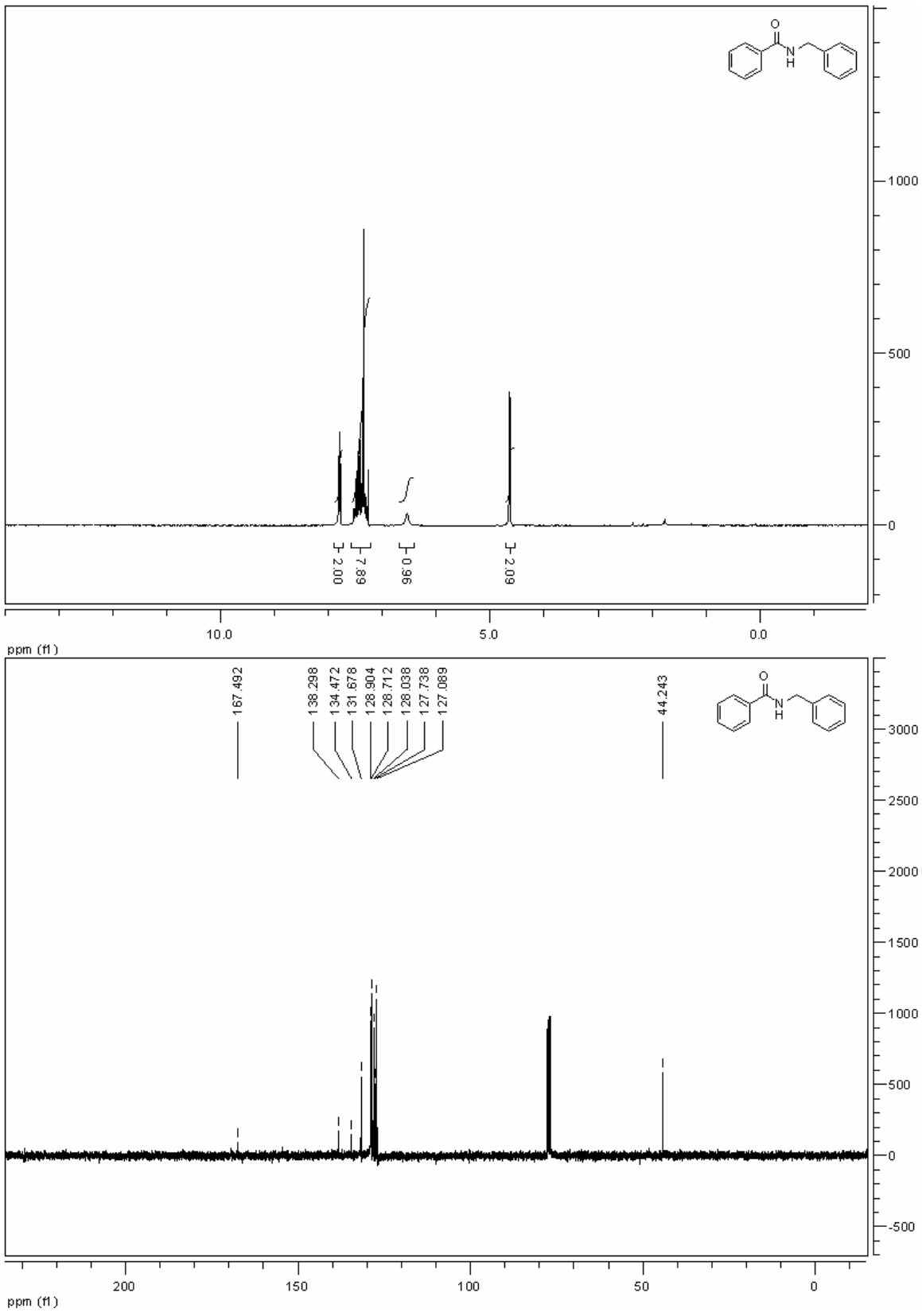
100
50
0
ppm (f1)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0.96
2.09
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0
10.0
5.0
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ppm (f1)
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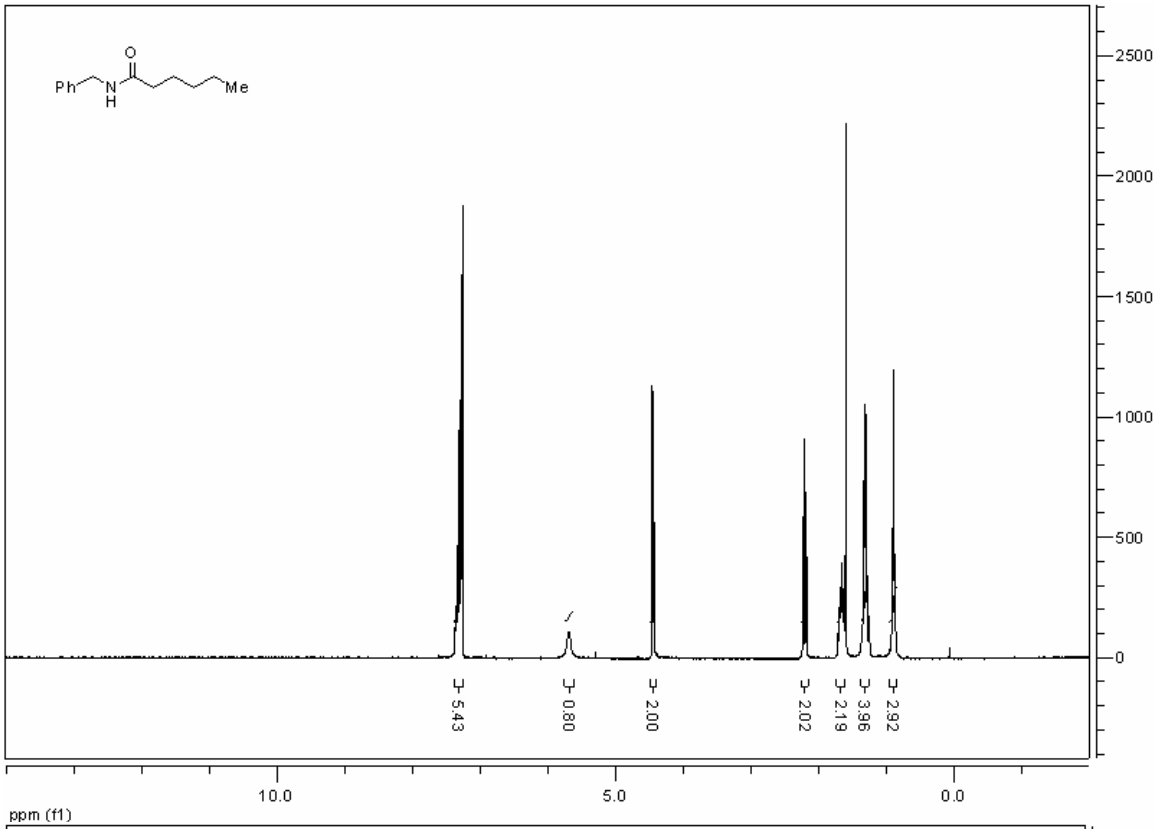
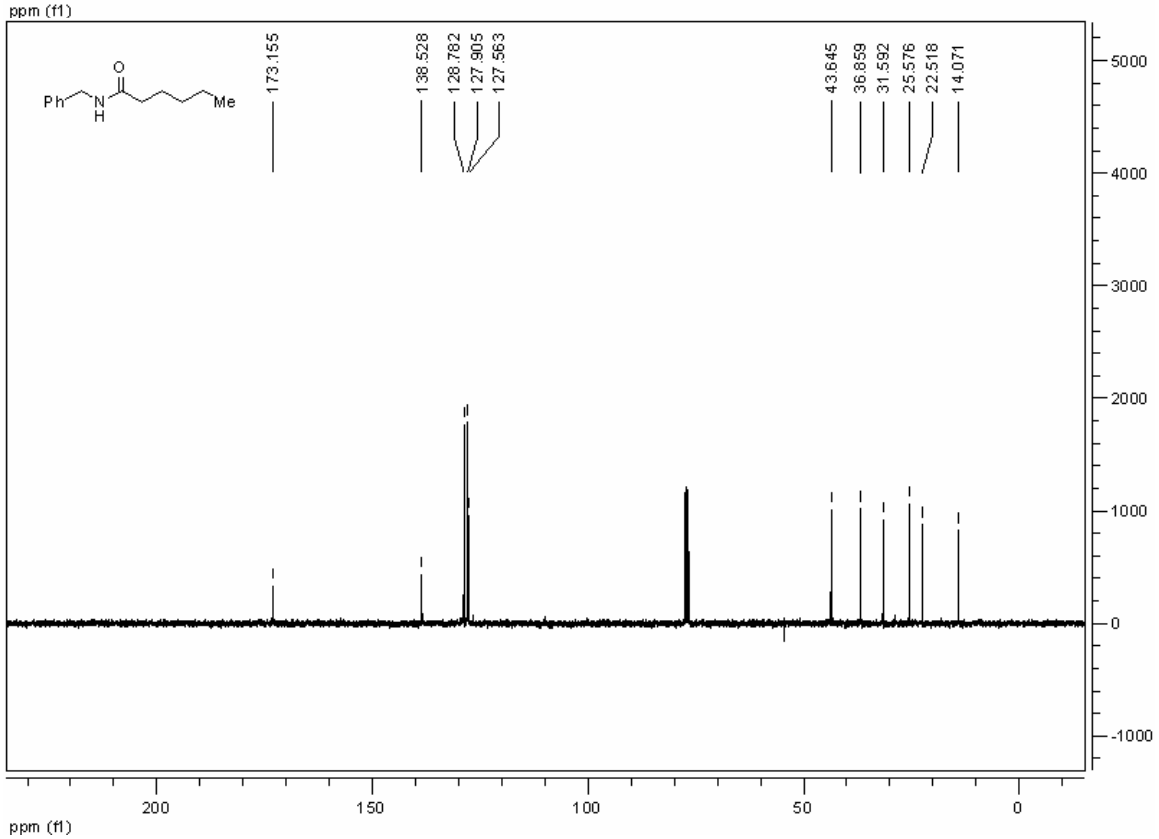
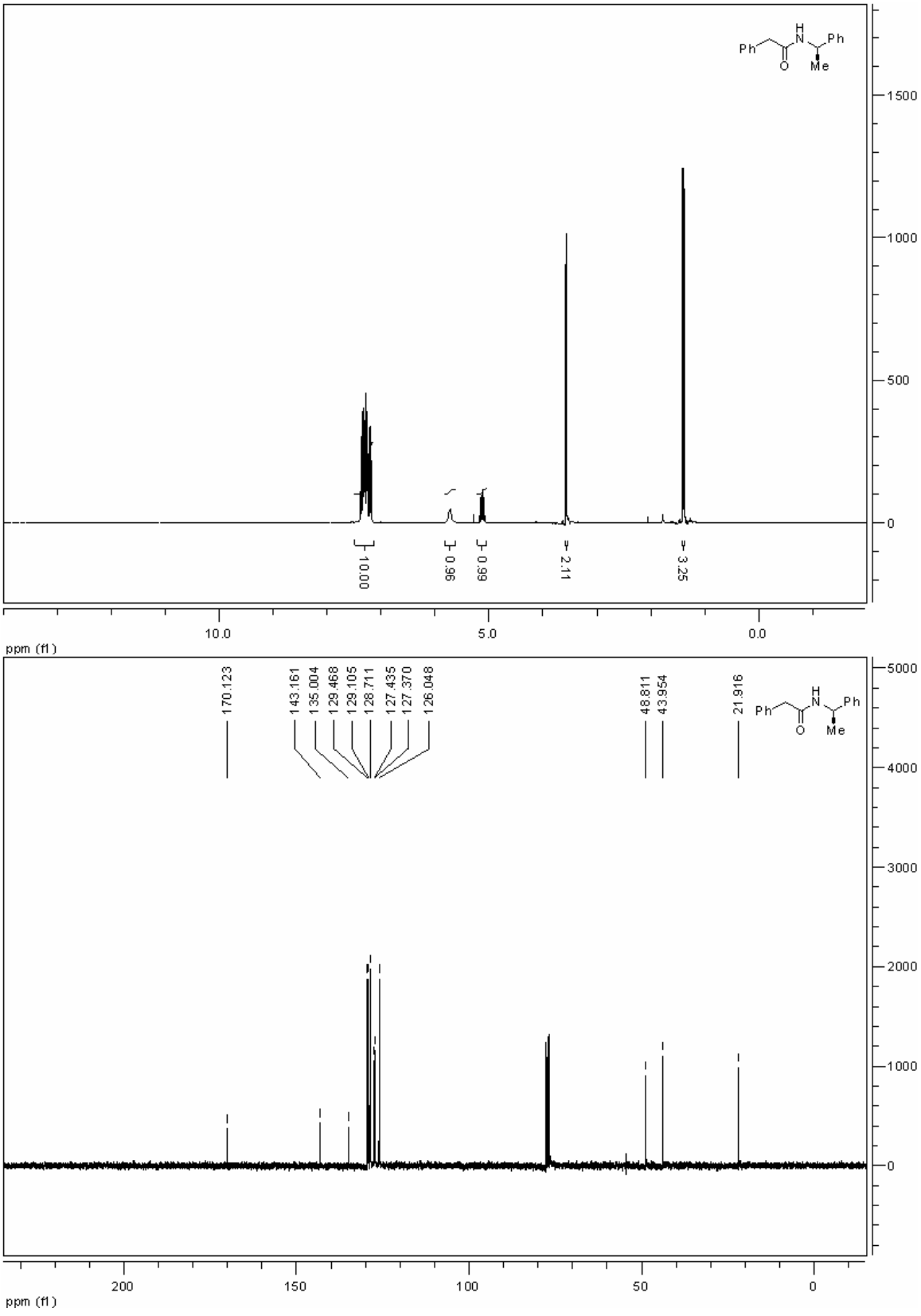
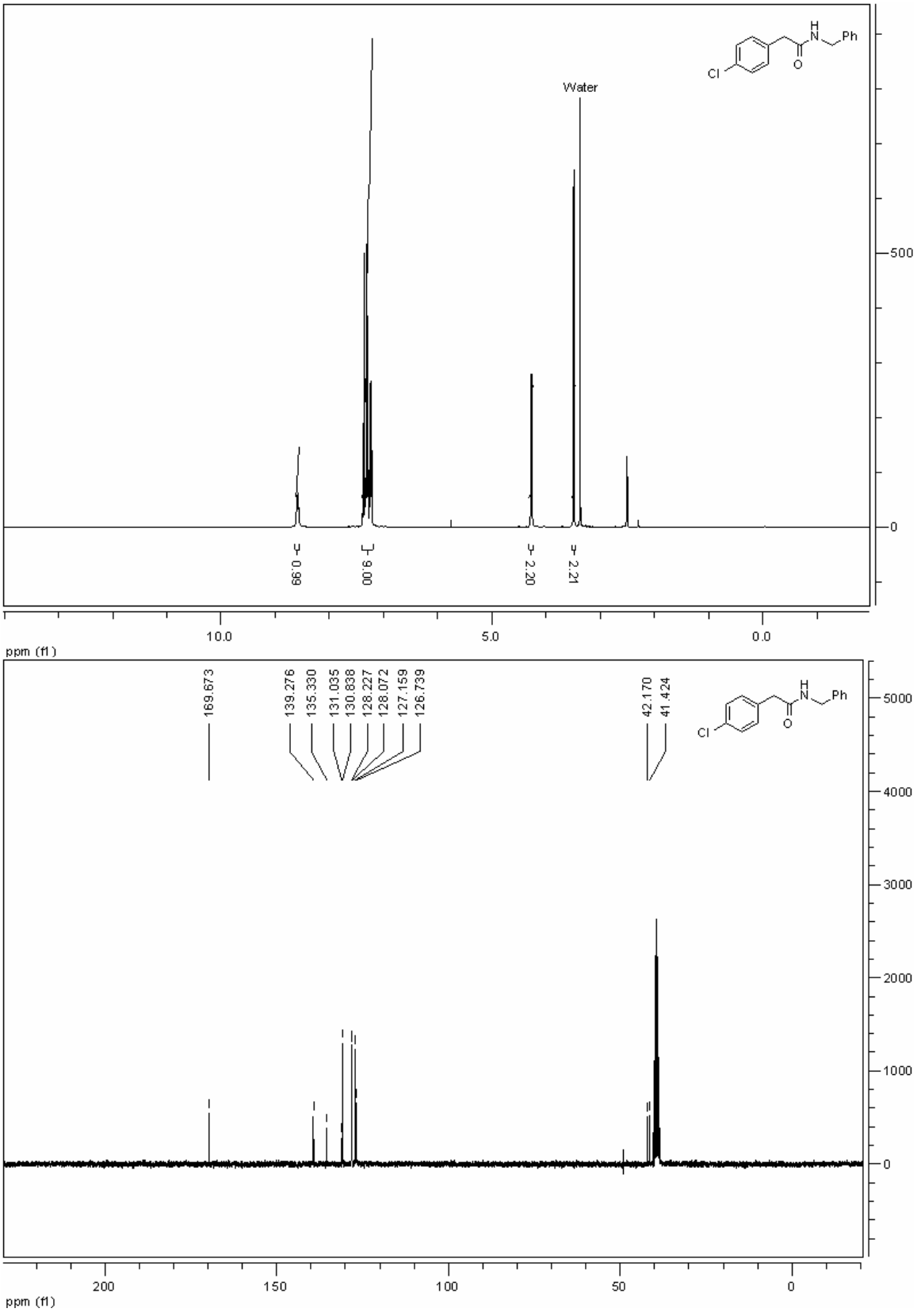
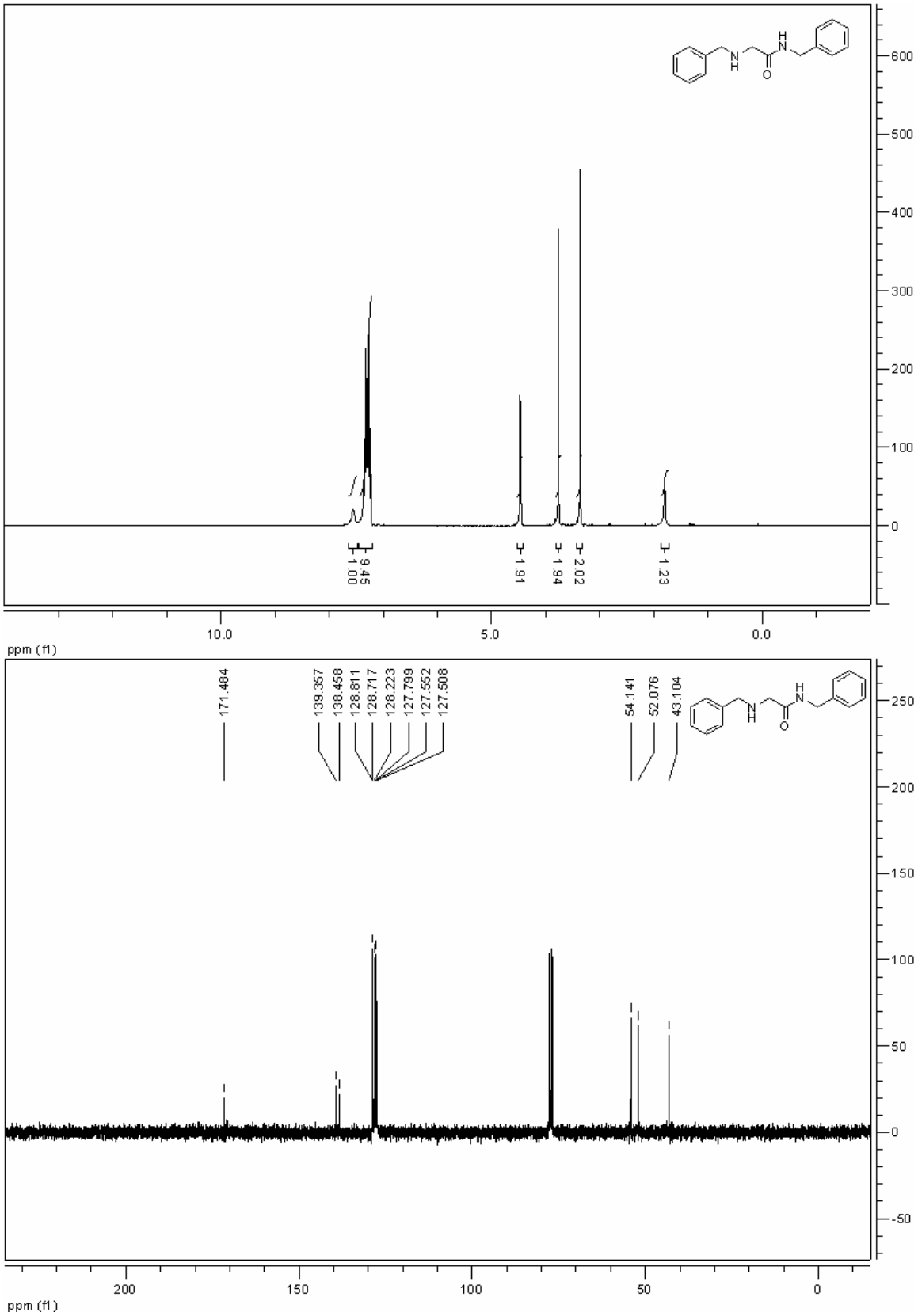
134.472
131.678
128.904
128.712
128.038
127.738
127.089
44.243
3000
2500
2000
1500
1000
500
0
-500
200
150
100
50
0
ppm (f1)

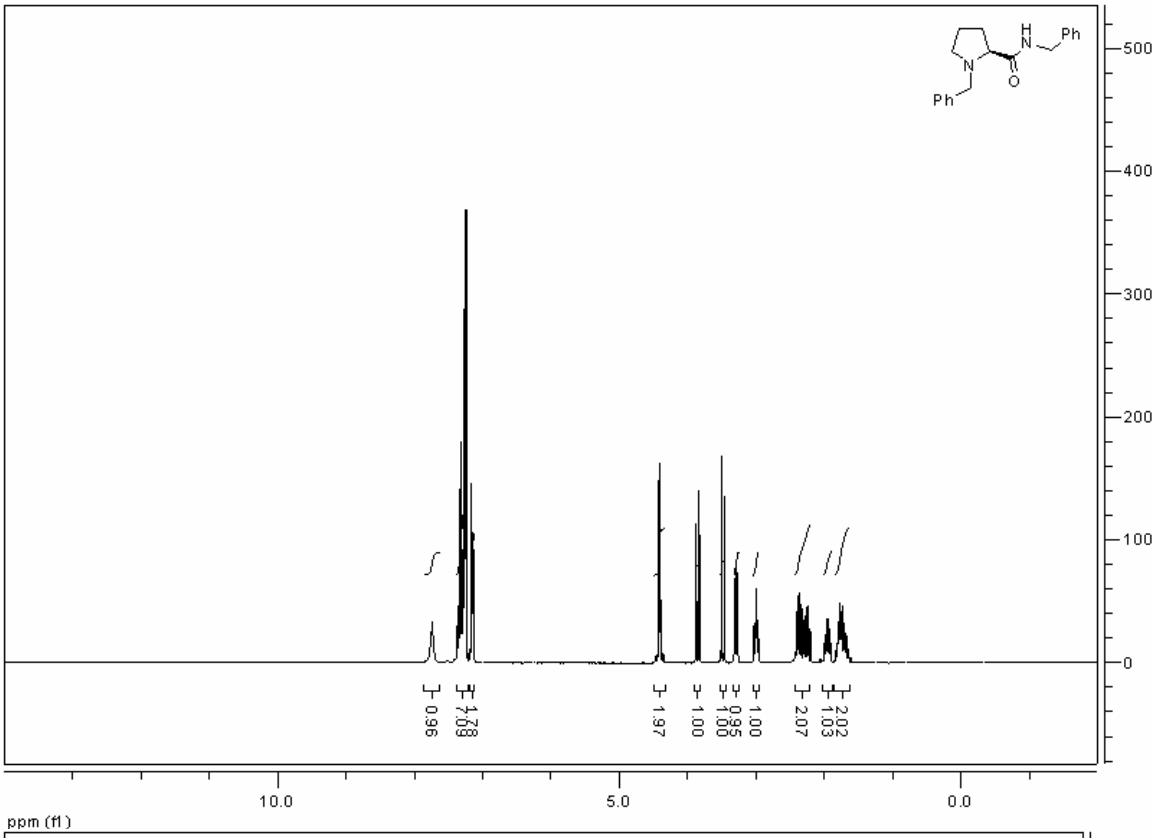

Ph
N
H
O
Me
5.43
0.80
2.00
2.02
2.19
3.96
2.92
10.0
5.0
0.0
ppm (f1)

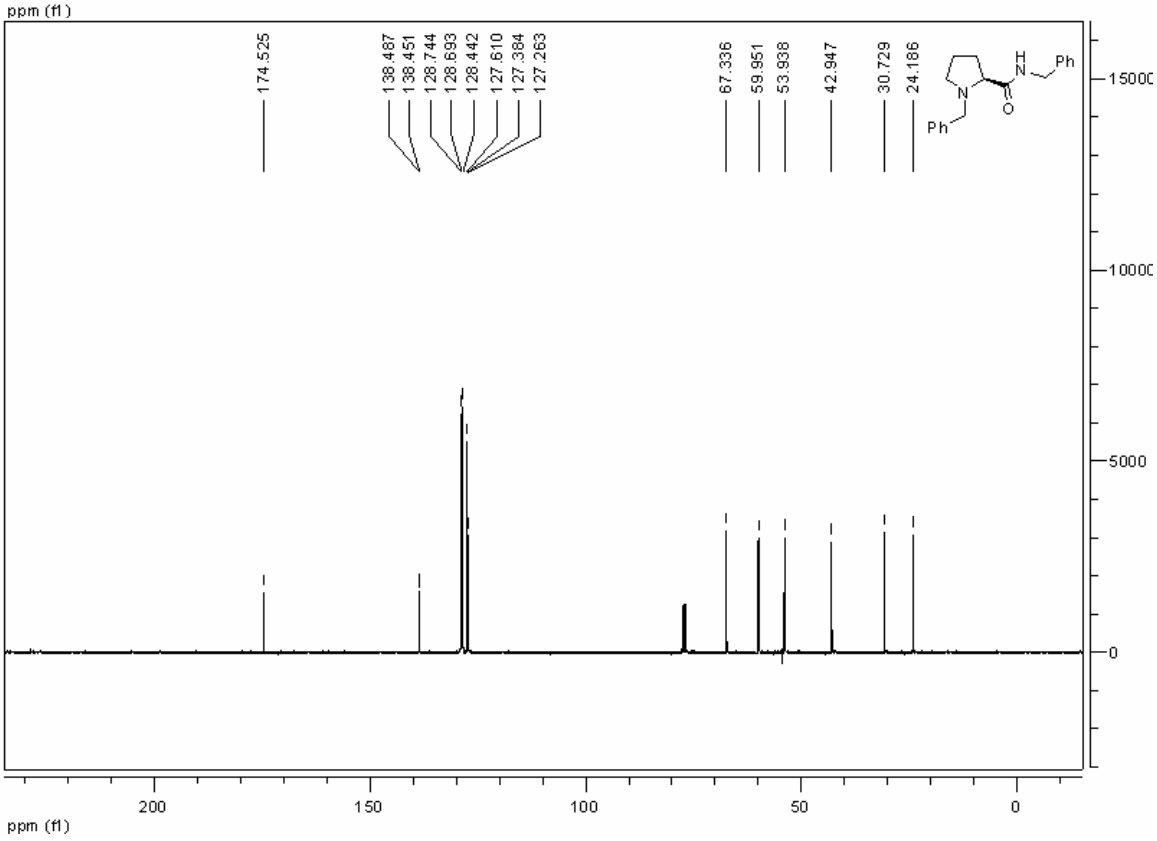

Ph
N
H
O
Me
173.155
138.528
128.782
127.905
127.563
43.645
36.859
31.592
25.576
22.518
14.071
200
150
100
50
0
ppm (f1)

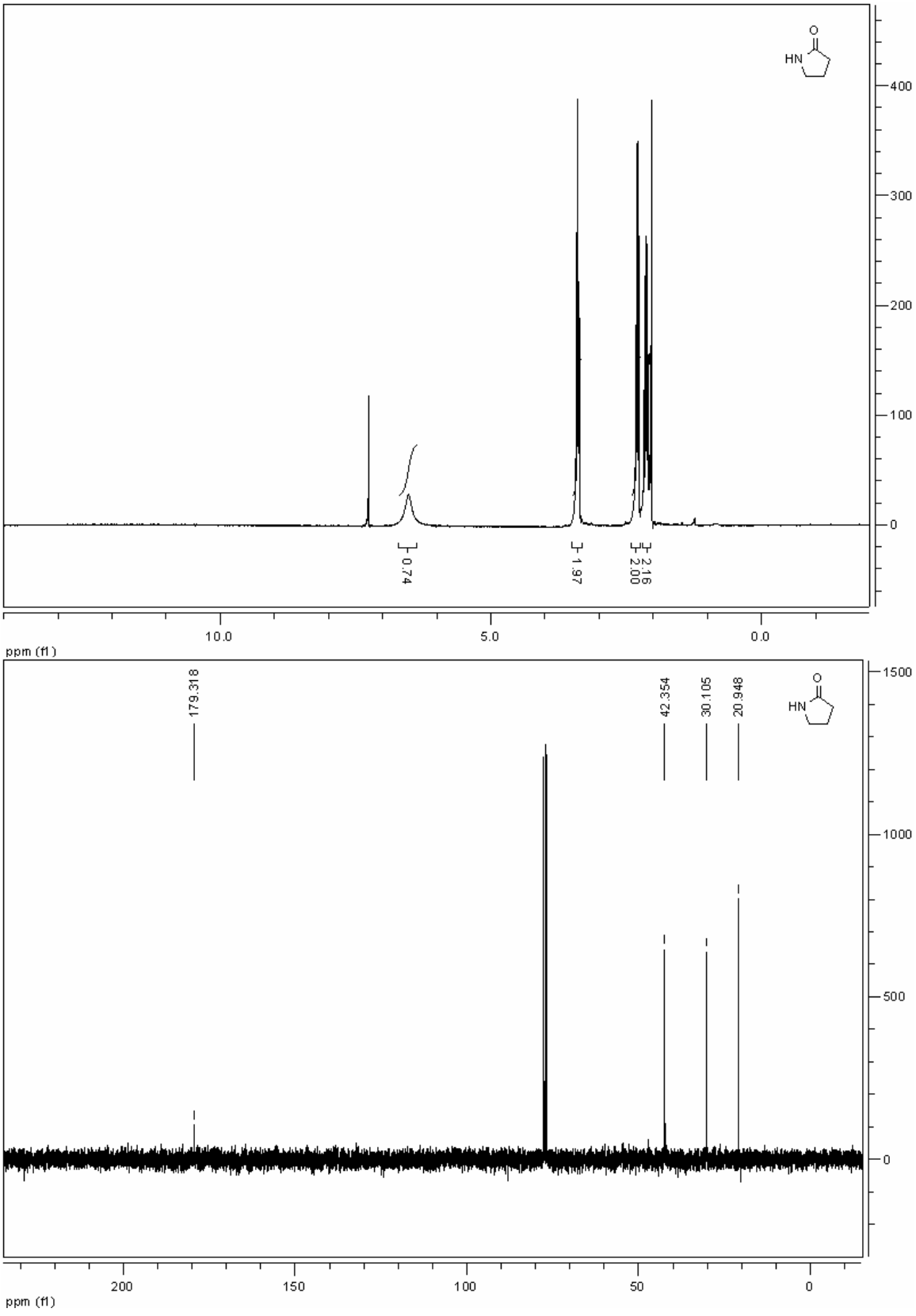

Ph
H
N
Ph
O
Me
1500
1000
500
0
1.00
0.96
0.99
2.11
3.25
10.0
5.0
0.0
ppm (f1)
170.123
143.161
135.004
129.468
129.105
128.711
127.435
127.370
126.048
48.811
43.954
21.916
5000
4000
3000
2000
1000
0
200
150
100
50
0
ppm (f1)

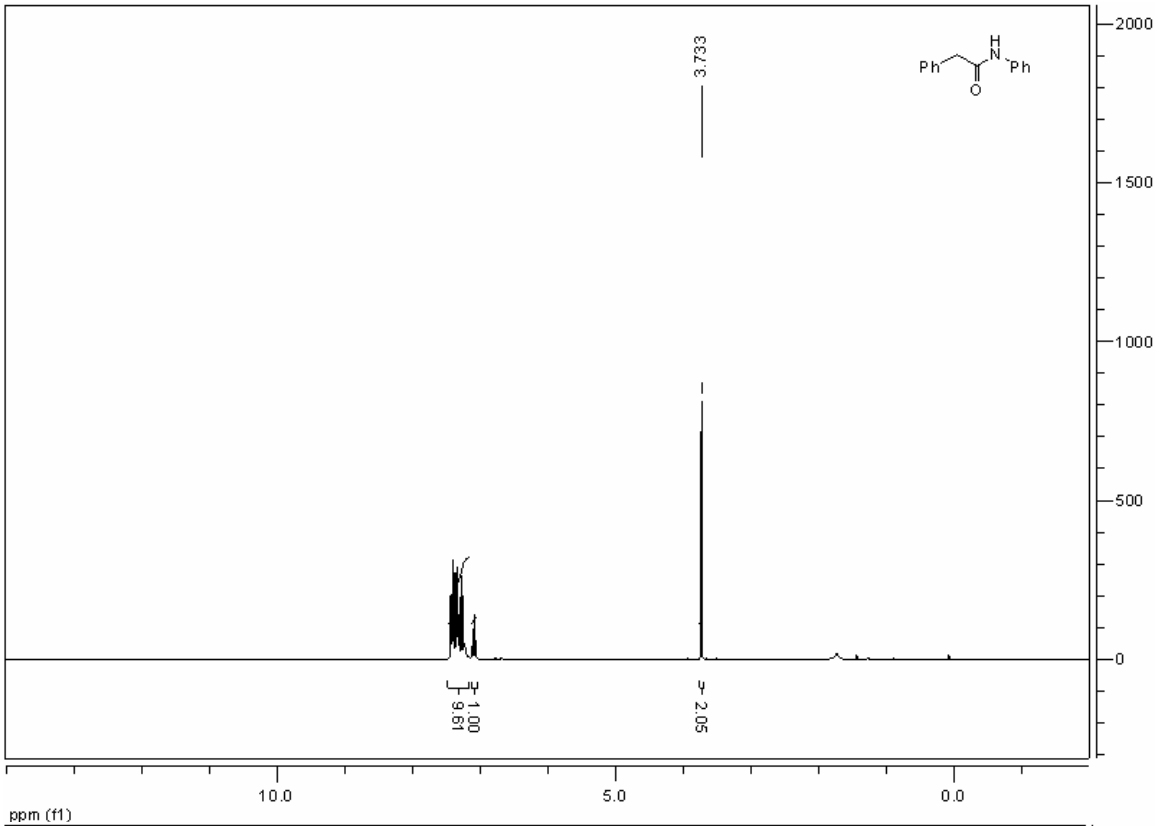

Water
0.99
9.00
2.20
2.21
10.0
5.0
0.0
ppm (f1)
169.673
139.276
135.330
131.035
130.838
128.227
128.072
127.159
126.739
42.170
41.424
200
150
100
50
0
ppm (f1)

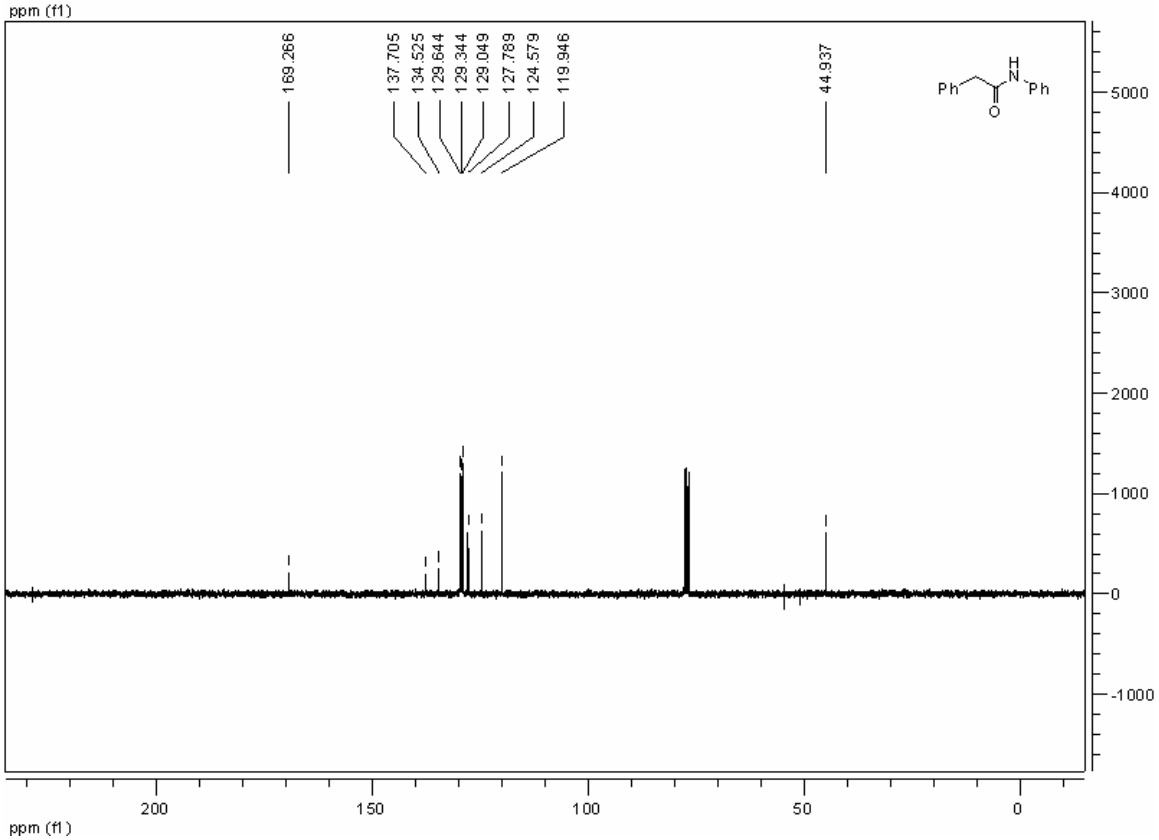

600
500
400
300
200
100
0
1.00
9.45
1.91
1.94
2.02
1.23
10.0
5.0
0.0
ppm (f1)
171.484
139.357
138.458
128.811
128.717
128.223
127.799
127.552
127.508
54.141
52.076
43.104
250
200
150
100
50
0
-50
200
150
100
50
0
ppm (f1)

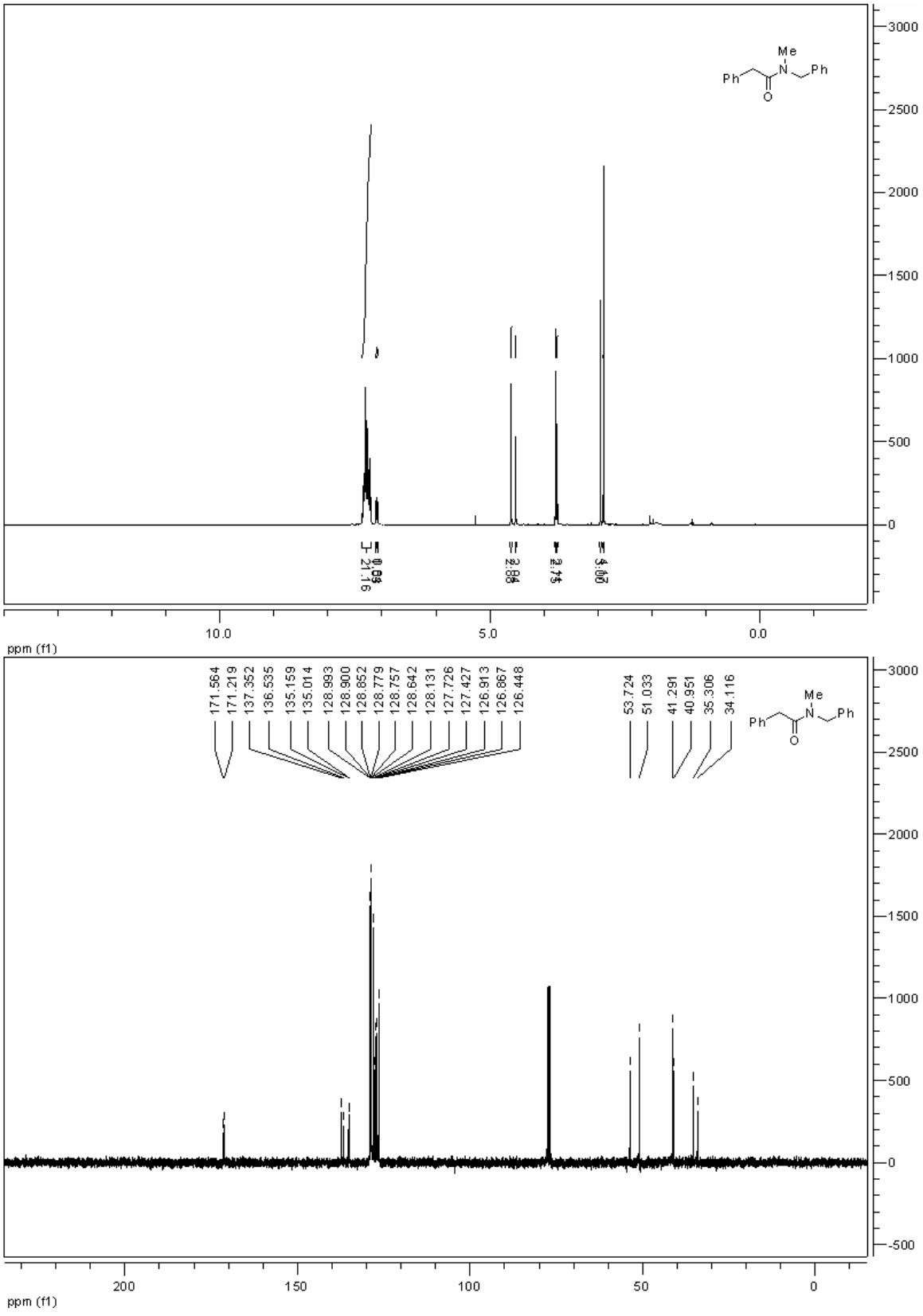

Ph
N
O
H
N
Ph
500
400
300
200
100
0
0.96
4.28
7.09
1.97
1.00
1.00
0.95
1.00
2.07
1.03
2.02
10.0
5.0
0.0
ppm (f1)

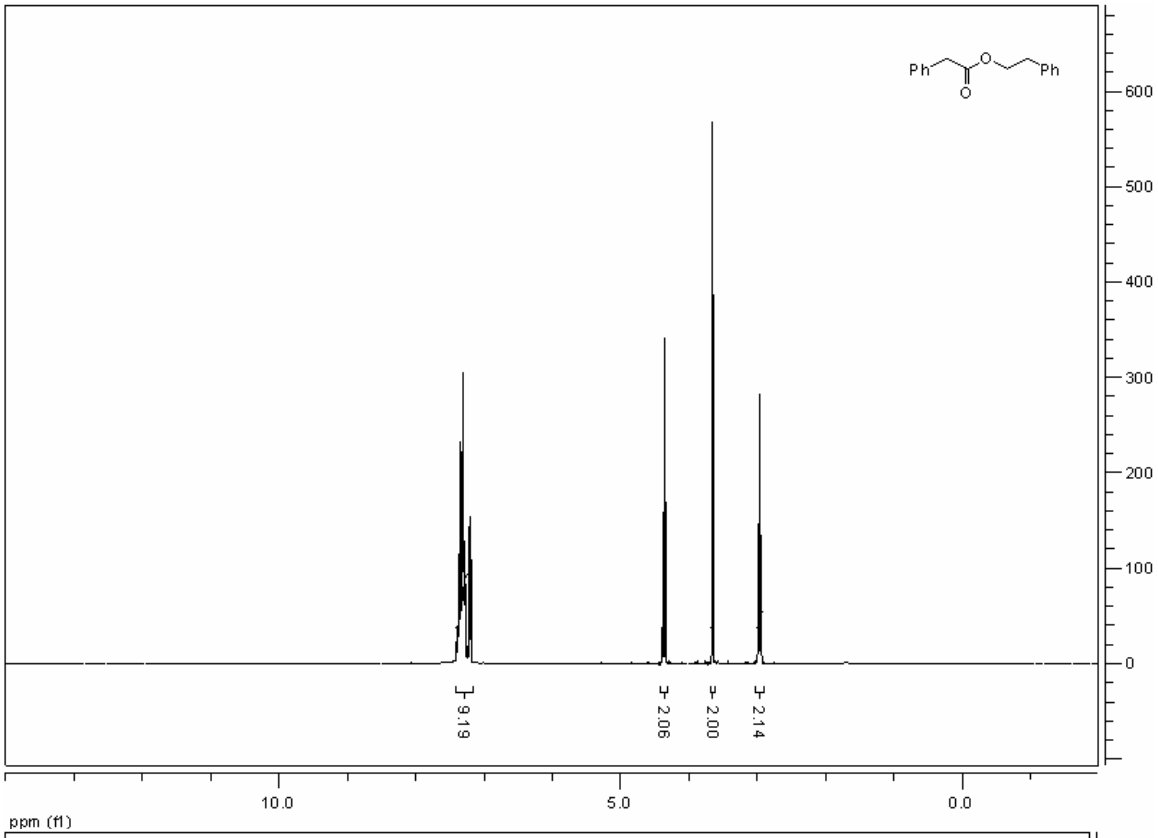

174.525
138.487
138.451
128.744
128.693
128.442
127.610
127.384
127.263
67.336
59.951
53.938
42.947
30.729
24.186
Ph
N
O
H
N
Ph
15000
10000
5000
0
200
150
100
50
0
ppm (f1)

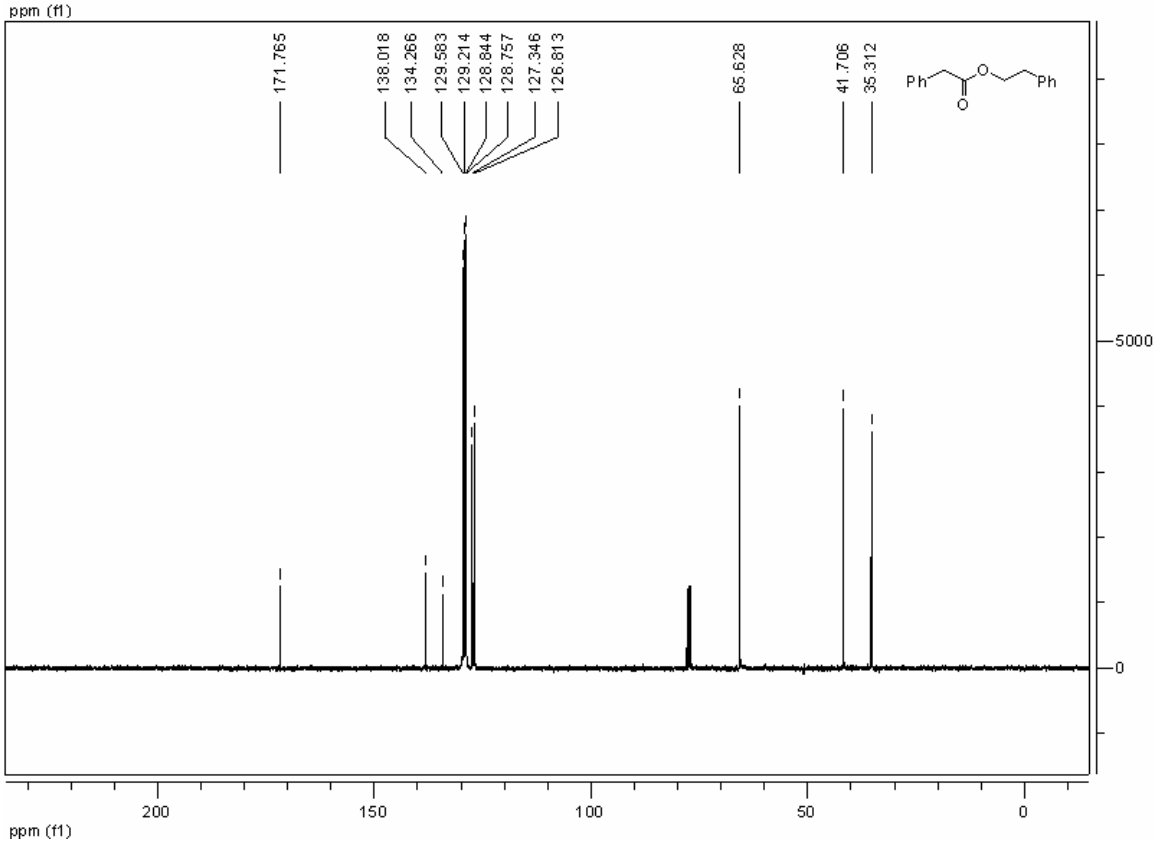

HN
O
400
300
200
100
0
0.74
1.97
2.19
2.00
10.0
5.0
0.0
ppm (f1)
179.318
42.354
30.105
20.948
1500
1000
500
0
200
150
100
50
0
ppm (f1)


3.733
Ph
N
H
Ph
O
2000
1500
1000
500
0
9.61
1.00
2.05
10.0
5.0
0.0
ppm (f1)


169.266
137.705
134.525
129.644
129.344
129.049
127.789
124.579
119.946
44.937
Ph
N
H
Ph
O
5000
4000
3000
2000
1000
0
-1000
200
150
100
50
0
ppm (f1)


Me
N
Ph
Ph
O
3000
2500
2000
1500
1000
500
0
10.0
5.0
0.0
ppm (f1)
171.564
171.219
137.352
136.535
135.159
135.014
128.993
128.900
128.852
128.779
128.757
128.642
128.131
127.726
127.427
126.913
126.867
126.448
53.724
51.033
41.291
40.951
35.306
34.116
-500
200
150
100
50
0
ppm (f1)


Ph
O
Ph
600
500
400
300
200
100
0
9.19
2.06
2.00
2.14
10.0
5.0
0.0
ppm (f1)


171.765
138.018
134.266
129.583
129.214
128.844
128.757
127.346
126.813
65.628
41.706
35.312
Ph
O
Ph
5000
0
200
150
100
50
0
ppm (f1)