Supplementary Material (ESI) for Chemical Communications

SUPPORTING INFORMATION FOR:

Monoalkylation of Primary Amines and *N*-Sulfinylamides

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Contents

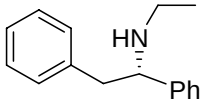
General Methods

^{1}H-NMR spectra were acquired at 200 or 300 MHz and ^{13}C-NMR were acquired at 50 or 75 MHz (unless otherwise indicated). Chemical shifts (δ) are reported in ppm relative to $CDCl_3$ (7.26 and 77.0 ppm). Flash column chromatography was performed using silica gel Merk-60 (230-400 mesh). For synthesis of *p*-tolylsulfinamides[1] were used anhydrous solvents and under argon atmosphere. THF was distilled from sodium-benzophenone under argon. *n*-BuLi (2.5 M solution in hexane) and amines were purchased from Aldrich. Products **1a-b**, **2a-b** and **4a-b** were synthesized following experimental procedure described in the literature.[2] Ra-Ni was purchased from Fluka (reference 83440-Activated Nickel Catalyst, puriss-suspension in water).

General Procedure for the Synthesis of the compounds 3a-b (Scheme 2) [2]

To a solution of the corresponding amine (**4a-b**) or sulfinamide (**1a-b**) in EtOH (1.5 mL) was added a suspension of activated Raney nickel (1.2g).[3] The reaction was stirred for 2 hours, and the residue was purified by SCX column to afford pure amine. Yield is indicated in each case.

N-Ethyl-1,2-diphenylethylamine (3a)

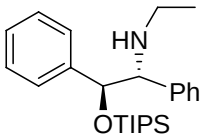


Yield from **4a**: 90%. Yield from **1a**: 65%. Colorless oil. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.35-7.10 (m, 10H), 3.85 (dd, *J* = 7.5, 6.5 Hz, 1H),

[1] (a) J. L. Garcia Ruano, A. Parra, F. Yuste, V. M. Mastranzo *Synthesis*, 2008, 311. (b) J. L. Garcia Ruano, R. Alonso, M. Zarzuelo, P. Noheda, *Tetrahedron: Asymmetry* 1995, **6**, 1133.
[2] (a) J. L. García Ruano, J. Alemán and J. F. Soriano *Org. Lett.* 2003, **5**, 677. (b) J. L. García Ruano and J. Alemán *Org. Lett.* 2003, **5**, 4513.
[3] Raney-Nickel must be recently purchased and should be activated by washing 3 times the suspension with EtOH.

2.94-2.92 (m, 2H), 2.42 (q, *J* = 7.1 Hz, 2H), 0.98 (t, *J* = 7.1 Hz, 3H).[13]C-NMR (75 MHz, $CDCl_3$): δ 129.3, 128.3, 128.2, 127.2, 126.9, 126.3, 125.9, 125.7, 64.8, 45.2, 42.0, 15.2.

(1*R*, 2*S*)-*N*-Ethyl-1,2-diphenyl-2-triisopropylsilaniloxyethylamine (3b)



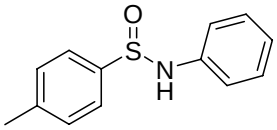
We have used as starting material the optically pure amine-alcohol derivative **4b**, obtaining the corresponding product **3b** without epimerization at the chiral centers. Yield from **4a**: 91%. Yield from **1a**: 75%. Yellow oil. [1]H-NMR (200 MHz, $CDCl_3$): δ 7.50-7.20 (m, 10H), 4.98 (d, *J* = 5.6 Hz, 1H), 3.92 (d, *J* = 5.6 Hz, 1H), 2.49-2.32 (m, 2H), 0.99 (t, *J* = 7.1 Hz, 3H), 0.98-0.71 (m, 21H). [13]C-NMR (75 MHz, $CDCl_3$): δ 141.5, 128.9, 127.8, 127.7, 127.6, 127.5, 127.2, 127.1, 79.1, 69.8, 41.7, 17.9, 17.8, 12.3. $[\alpha]^{D}_{20}$= -4.6 (*c* 0.8, $CHCl_3$). HRMS calcd for $C_{25}H_{39}NOSi$ [M +1] 398.2873, found 398.2875.

General Procedure for the Synthesis of *p*-Tolylsulfinamides (5a-e)[1]

To a stirred solution of the corresponding methyl *p*-tolylsulfinate[4] (1.0 mmol) in THF (4 mL) at room temperature under argon was added via cannula a solution of the lithium amide of the corresponding primary or secondary amine (prepared from 1.2 equiv. of the amine in THF (4 mL) and 1.2 equiv. of *n*-BuLi at -78˚C). The reaction was monitored by TLC. Upon completion (1-1.5 h), an aqueous 0.1 M solution of Na_2HPO_4 (5 mL) were added and the mixture was extracted with CH_2Cl_2 (3x20 mL). The organic phase was dried ($MgSO_4$) and concentrated under vacuum. The residue was purified by flash column chromatography (eluent is indicated each case) or precipitated in hexane affording the corresponding *N*-*p*-tolylsufinamide.

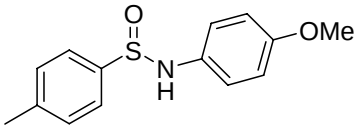
[4] P. Brownbrigde, I. C. Jowett *Synthesis* 1988, 252.

_N_-Phenyl-_p_-tolylsulfinamide (5a)[1,5]



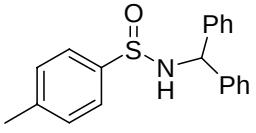
Sulfinamide was obtained by precipitation in hexane. Yield: 80%. White solid; m.p: 122-124 ºC (hexane), [Lit.[1] 127-128ºC]. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.66 (d, *J* = 4.6 Hz, 2H), 7.34-7.24 (m, 5H), 7.09 (d, *J* = 4.3 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 141.4, 141.2, 140.9, 129.6, 129.2, 125.5, 123.1, 118.6, 21.3.

_N_-Methoxyphenyl-_p_-Tolylsulfinamine (5b)[6]



Sulfinamide was obtained by precipitation in hexane. Yield: 77%. White solid; m.p: 102-106 ºC (Hexane), [Lit.[3] 98-101 ºC]. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.9 Hz, 2H), 1.12 (d, *J* = 8.9 Hz, 2H), 6.14 (bs, 1H), 3.78 (s, 3H), 2.43 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 156.6, 141.6, 141.5, 132.9, 129.6, 125.5, 122.7, 55.4, 21.4.

_N_-Diphenylmethyl-_p_-Tolylsulfinamine (5d)[7]

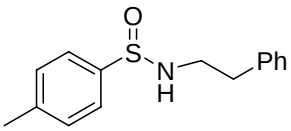


Sulfinamide was obtained by precipitation in hexane. Yield: 71%. White solid, mp: 114-116˚C (hexane). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 7.2 Hz, 2H), 7.12-7.02 (m, 10H), 5.52 (d, *J* = 4.1 Hz, 1H), 4.64 (d, *J* = 3.9 Hz, 1H); ^{13}C-NMR (75 MHz,

[5] A. Felim, Toussaint, P. Aurelie, R. L. Courtney, V. A. Dominique, L. Fensterbank, E. Lacote, M.. Malacria, *Org. Lett.* 2006, **8**, 337.
[6] M. C. Carreno; M. Ribagorda *J. Org. Chem.* 2000, **65**, 1231.
[7] R. Ding, C. H. Zhao, Y. J. Chen, L. Liu, D. Wang, C. J. Li *Tetrahedron Lett.* 2004, **45**, 2995.

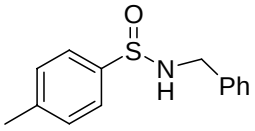
$CDCl_3$): δ 141.9, 141.5, 141.3, 140.9, 129.1, 128.4, 128.2, 127.9, 127.4, 127.2, 127.1, 125.3, 60.1, 21.1.

_N_-Phenethyl-_p_-tolylsulfinamide (5e)[8]



Sulfinamide was purified by flash column chromatography using as eluyent 3:1 hexane/ ethyl acetate. Yield: 63%. Yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.53 (*J* = 8.2 Hz, 2H), 7.30-7.19 (m, 5H), 7.14 (d, *J* = 6.7 Hz, 2H), 4.53 (t, *J* = 6.3 Hz, 1H), 4.40-3.30 (m, 1H), 3.12-3.01 (m, 1H), 2.82 (t, *J* = 14.1 Hz, 2H), 2.39 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 140.8, 140.8, 138.3, 129.2, 128.6, 128.3, 126.2, 125.7, 41.8, 36.6, 21.1.

_N_-Benzyl-_p_-tolylsulfinamide (5e)[1]



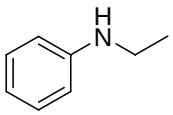
Sulfinamide was obtained by precipitation in hexane. Yield: 70%. White solid; mp: 74-76˚C (hexane) [Lit.[1] mp: 77-79˚C]. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.35-7.27 (m, 7H), 4.33 (bs, 1H), 4.25 (dd, *J* = 8.1, 5.1 Hz, 1H), 3.91 (dd, *J* = 6.7, 6.1 Hz, 1H), 2.43 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 141.3, 140.8, 137.7, 129.6, 128.6, 128.3, 127.6, 125.7, 44.5, 21.3.

[8] M. Harmata, P. Zheng, C. Huang, M. G. Gomes, W. Ying, K. O. Ranyanil, G. Balan, N. L. Calkins *J. Org. Chem.* 2007, **72**, 683.

N-Alkylation General Procedure of *N*-sulfinylimines and amines (6a-e, 8 and 9)

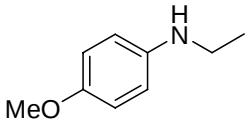
To the corresponding free-amine or *p*-tolylsulfinamide (0.20 mmol) dissolved in the corresponding alcohol (1.5 mL) was added a suspension of activated Raney nickel (1.2 g)[9] into the corresponding alcohol (5 mL) for the time indicated in table 1 and 2.[10] The reaction was vigorous stirred and monitored by TLC. When the reaction is finished, the crude mixture was filtered through celite. Excess alcohol was removed under vacuum to afford the pure amine without additional purification. Yield is indicated in each case.

N-Ethylbenzenamine (6a) [CAS: 103-69-5][11]



Yield obtained from **5a**: 81%. Yield obtained from aniline **7a**: 83%. Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.22-7.15 (m, 2H), 6.77-6.63 (m, 3H), 3.17 (q, *J* = 7.2 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 147.6, 129.6, 117.2, 113.5, 37.8, 15.1.

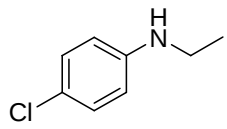
N-Ethyl-4-methoxybenzenamine (6b) [CAS: 104-48-3][12]



Yield obtained from **5b**: 83%. Yield obtained from *p*-anisidine **7b**: 86%. Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 6.80 (d, *J* = 8.9 Hz, 2H), 6.60 (d, *J* = 8.8 Hz, 2H), 3.77 (s, 3H), 3.13 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 152.0, 142.8, 114.9, 114.1, 55.8, 39.4, 14,9.

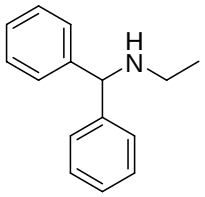
[9] Raney-Nickel must be recently purchased and should be activated by washing 3 times the suspension with the corresponding alcohol which is used also in the reaction as solvent.
[10] Longer reactions times that those indicated in table 2 determine the formation of dialkylated products.
[11] Y. Matsushita, N. Ohba, T. Suzuki, T., Ichimura *Catal. Today* 2008, **132**, 153.
[12] M. O. Sydnes, M. Isobe *Tetrahedron Lett.* 2008, **49**, 1199.

4-Chloro-*N*-ethylbenzenamine (6c) [CAS: 13519-75-0][13]



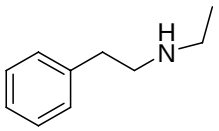
Yield obtained from **7c**: 81%. Brown oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.03 (d, *J* = 8.9 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 3.10 (q, *J* = 7.2 Hz, 2H), 1.13 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 145.7, 129.6, 122.7, 114.1, 37.8, 15,9.

***N*-Benzhydrylethanamine (6d) [CAS: 53693-47-3]**[14]



Yield obtained from **5d**: 77%. Yield obtained from d **7d**: 82%. Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.54-7.40 (m, 2H), 7.37-7.23 (m, 8H), 5.28 (bs, 1H), 5.00 (s, 1H), 2.73 (q, *J* = 7.1 Hz, 2H), 1.20 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 141.6, 130.0, 128.6, 127.5, 66.9, 42.1, 14.1.

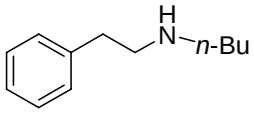
***N*-Ethyl-2-phenylethanamine (6e) [CAS: 22002-68-2]**[15]



Yield obtained from **5e**: 89%. Yield obtained from **7e**: 79%. Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.34-7.22 (m, 5H), 3.03 (bs, 1H), 2.96-2.79 (m, 6H), 1.21 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.4, 126.9, 126.6, 126.3, 47.0, 46.0, 33.1, 11.9.

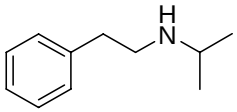
[13] A. C. Fernandes, C. C. Romao *J. Mol. Cat. A: Chemical* 2007, **272**, 60.
[14] A. E.Goeta, G.Punte B, E. Rivero, L. B.Blanch Acta Crystallographica, Section C: Crystal Structure Communications 1997, **C53**, 1913.
[15] (a) O. Phanstiel, Q. X. Wang, D. H.Powell, M. P.Ospina, B. A. Leeson *J. Org. Chem.* 1999, **64**, 803. (b) Y. Ishihara, K.Kato, G. Goto *Chem. Pharm. Bull.* 1991, **39**, 3225.

***N*-Phenethylbutan-1-amine (8e) [CAS: 71594-24-6]**.[16]



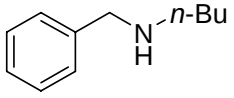
Yield obtained from 2-phenylethanamine **7e** using *n*-butanol as alcohol: 74%. Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.22-7.17 (m, 2H), 7.15-7.08 (m, 3H), 2.78-2.66 (m, 2H), 2.64-2.50 (m, 2H), 2.43 (t, *J* = 5.9 Hz, 2H), 1.82 (bs, 1H), 1.41-1.36 (m, 2H), 1.35-1.29 (m, 2H), 0.84 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 140.1, 128.5, 128.3, 125.8, 56.1, 53.8, 51.9, 36.3, 29.2, 14.2.

***N*-phenethylpropan-2-amine (9e) [CAS: 38449-56-8]**.[17]



Yield obtained from 2-phenylethanamine **7e** using 2-butanol as alcohol: 80%. Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.37-7.17 (m, 5H), 1.56-1.58 (m, 2H), 1.52-1.54 (m, 3H), 1,50 (bs, 1H), 0.99 (d, *J* = 7.0 Hz, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 139.4, 128.7, 127.7, 126.0, 48.7, 45.7, 36.4, 23.7.

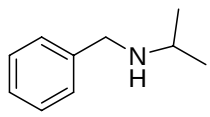
***N*-Benzylbutan-1-amine (8f) [CAS: 2403-22-7]**[18]



Yield obtained from benzylamine **7f** using *n*-propanol as alcohol: 72%. Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.29-7.12 (m, 5H), 3.45 (s, 1H), 2.31 (t, *J* = 7.0 Hz , 2H), 1.41-1.31 (m, 2H), 1.27-1.17 (m, 2H), 0.78 (t, *J* = 7.23 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 140.3, 128.8, 128.7, 126.5, 58.6, 53.5, 29.2, 20.6, 14.0.

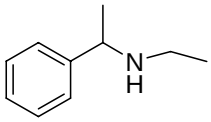
[16] R. N. Salvatore, A. S. Nagle, K. W. Jung *J. Org. Chem.* 2002, **67**, 674.
[17] Z. Zhang, D. Leith, C. David, L. Man, B. O. Patrick, L. L. Schafer *Chem. Eur. J* 2007, **13**, 2012.
[18] M. R. Saidi, R. S. Brown, A. Ziyaei-Halimjani *J. Ira. Chem. Soc.* 2007, **4**, 194.

_N_-Benzylpropan-2-amine (9f) [CAS: 102-97-6][19]



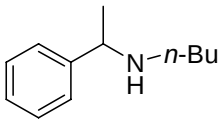
Yield obtained from benzylamine **7f**: 70%. Yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.26-7.15 (m, 5H), 3.73 (s, 1H), 2.77 (septuplet, J = 6.2 Hz, 1H), 0.97 (d, J = 6.2 Hz, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 140.3, 128.3, 128.1, 126.9, 53.1, 51.5, 48.0, 22.8.

_N_-Ethyl-1-phenylethanamine (6g) [CAS: 10137-87-8][20]



Yield obtained from α-ethylphenylamine **7g** using ethanol as alcohol: 78%. Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23-7.15 (m, 5H), 3.82 (q, J= 6.6 Hz, 1H), 2.55 (q, J= 6.3 Hz, 2H), 1.64 (bs, 1H), 1.27 (d, J= 6.6 Hz, 3H), 0.94 (t, J= 6.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.8, 136.9, 128.4, 126.4, 55.0, 45.5, 24.7, 23.9.

_N_-(1-Phenylethyl)butan-1-amine (8g) [CAS: 5412-64-6][21]



Yield obtained from α-ethylphenylamine **7g** using *n*-propanol as alcohol: 75%. Yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.29-7.13 (m, 5H), 3.90 (q, J= 6.7 Hz, 1H), 2.42-2.27 (m, 2H), 1.37-1.16 (m, 7H), 0.78 (t, J = 7.0 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.3, 128.4, 127.9, 126.9, 55.0, 49.6, 29.8, 20.5, 16.5, 14.1.

[19] D. Gnanamgari, A., Moores, E. Rajaseelan, R.H., Crabtree *Organometalic* 2007, **26**, 1236.
[20] X. Huang, N. Fujioka, G. Pescitelli, F. E. Koehn, R. T. Williamson, K. Nakanishi, N. Berova *J. Am. Chem. Soc.* 2002, **124**, 10320.
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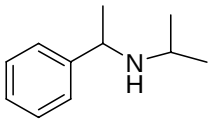
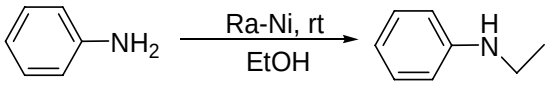
***N*-Isopropyl-(1-phenylethyl)-amine (9g) [CAS: 19302-16-0]**[22]



Yield obtained from α-ethylphenylamine **7g** using *i*-propanol as alcohol: 80%. Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.29-7.36 (m, 5H), 3.87-3.94 (m, 1H), 2.59-2.71 (m, 1H), 1.62 (s, 1H), 1.35-1.37 (m, 3H), 1.00-1.05 (m, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 146.38, 128.80, 127.12, 126.85, 55.49, 45.93, 25.27, 24.41, 22.55.

Experiments for recovered Ra-Ni in consecutive cycles

Table ESI-1. Recovered Ra-Ni in consecutive cycles [a]



5a

Entry	Cycle	t (min)	Yield
1	1	20	82
2	2	20	83
3	3	25	78
4	4	30	80

[a] All the reactions were performed in 0.20 mmol scale.

One of the advantages of our method derives from the fact that Raney-nickel is a non-expensive reagent and heterogeneous (and therefore easily separable) catalyst. Nevertheless, the need of using a large amount of Raney-nickel is a clear disadvantage. This inconvenient could be diminished if the recovering and reusing of the catalyst were possible, which would be also desirable for environment point of view. Consequently, we investigate the mono-alkylation of the aniline with ethanol under standard conditions and we used the catalyst, recovered by filtration, in three consecutives reactions with the results indicated in Table ESI-1. Raney-nickel mantains the efficiency after four cycles with almost identical isolated yields and only slighly longer reactions times. The procedure for

[22] C. Salmi, Y. Letourneux, J. M. Brunel *Lett. Org. Chem.* 2006, **3,** 396.

recovering the catalyst is based on the filtration of Ra-Ni over celite which is reused and placed in the flask with the same amount of EtOH (5 mL) and aniline (0.20 mmol).[23] This procedure was repeated four times with the results indicated in Table ESI-1.

[23] In this case, it is not necessary to re-activate the Ra-Ni by washing it with EtOH because it is enough activated for the next alkylation. When Ra-Ni is activated, this catalyst could burned spontaneously in the presence of air, and precautions should be taken (avoiding the excessively dryness of Ra-Ni during the vacuum filtration).

NMR spectra of compounds 4b, 6a-e, 8e-g, and 9e-g.

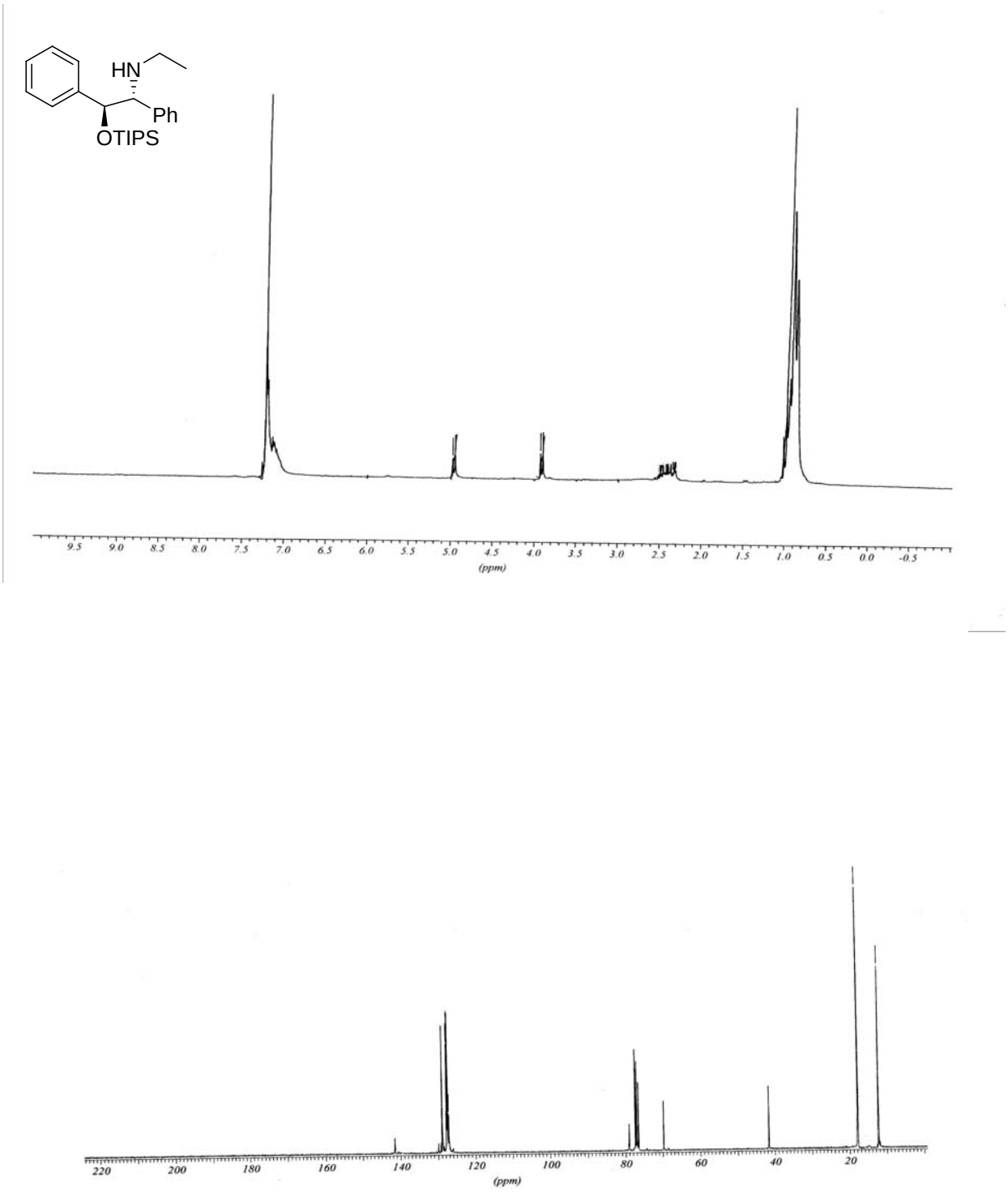


Figure S1 (300 MHz) and ^{13}C-NMR (75 MHz) of **4b**

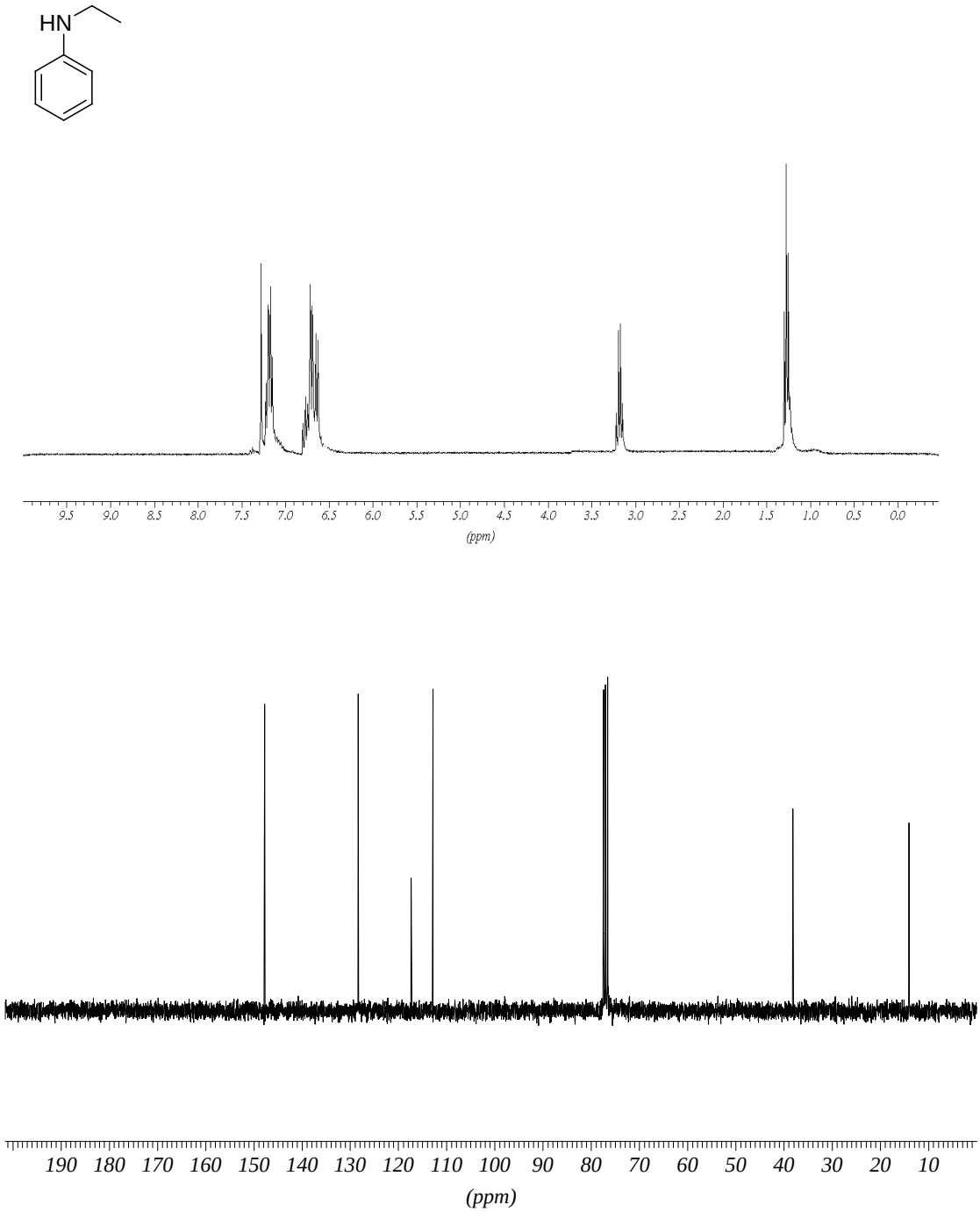


Figure S2 (300 MHz) and ^{13}C-NMR (75 MHz) of **6a**

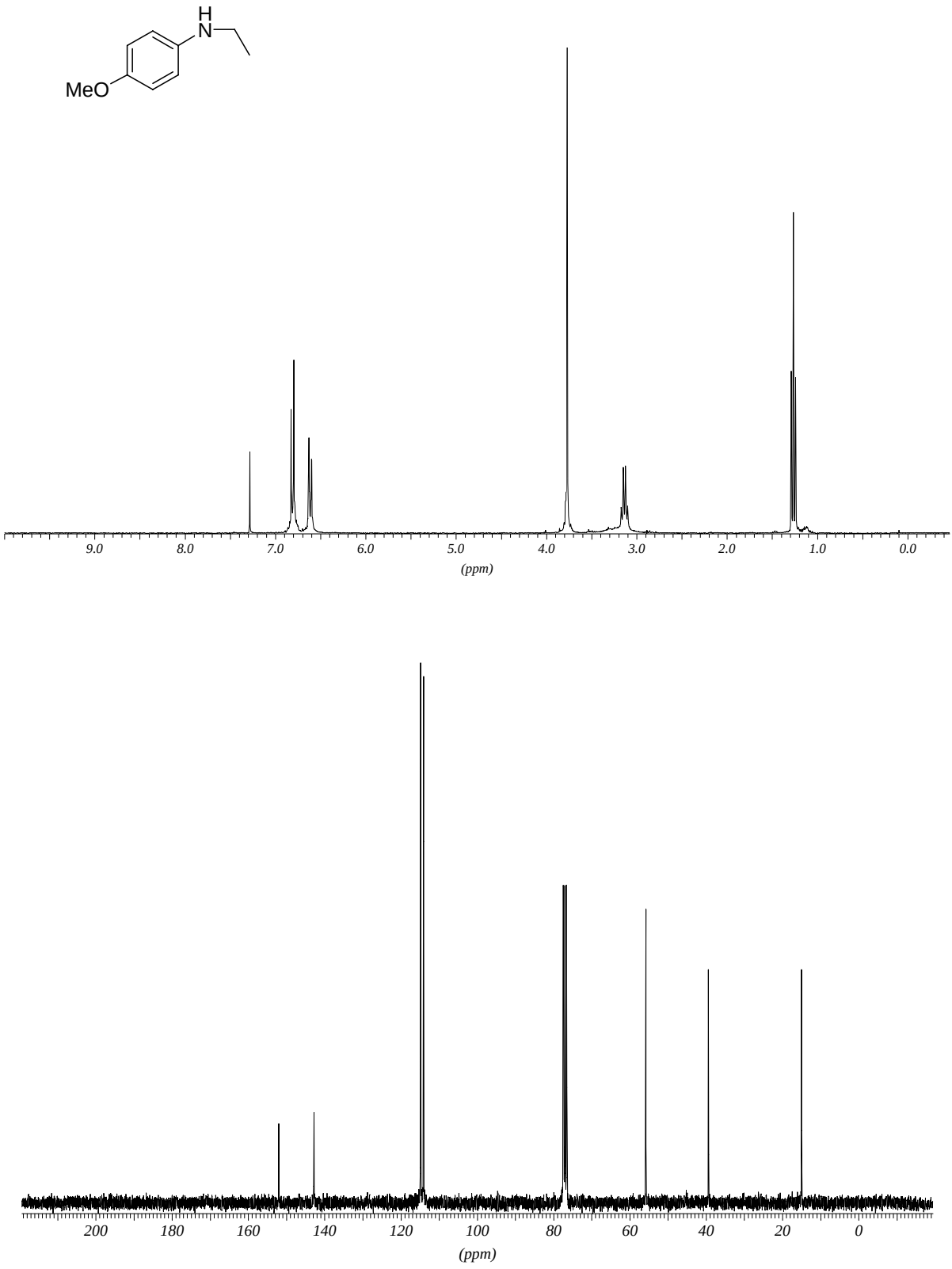


Figure S3 (300 MHz) and ^{13}C-NMR (75 MHz) of **6b**

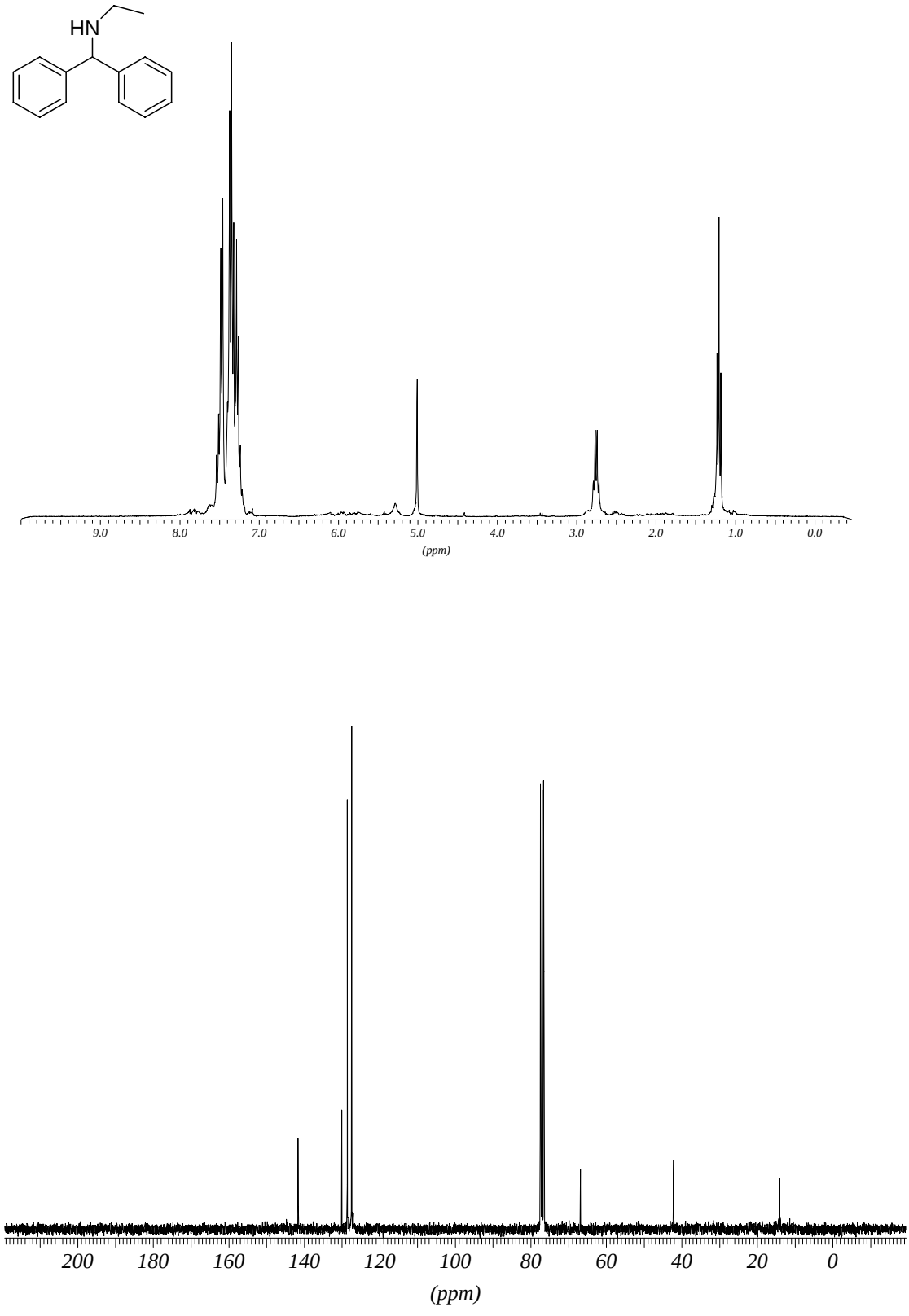


Figure S4 (300 MHz) and ^{13}C-NMR (75 MHz) of **6d**

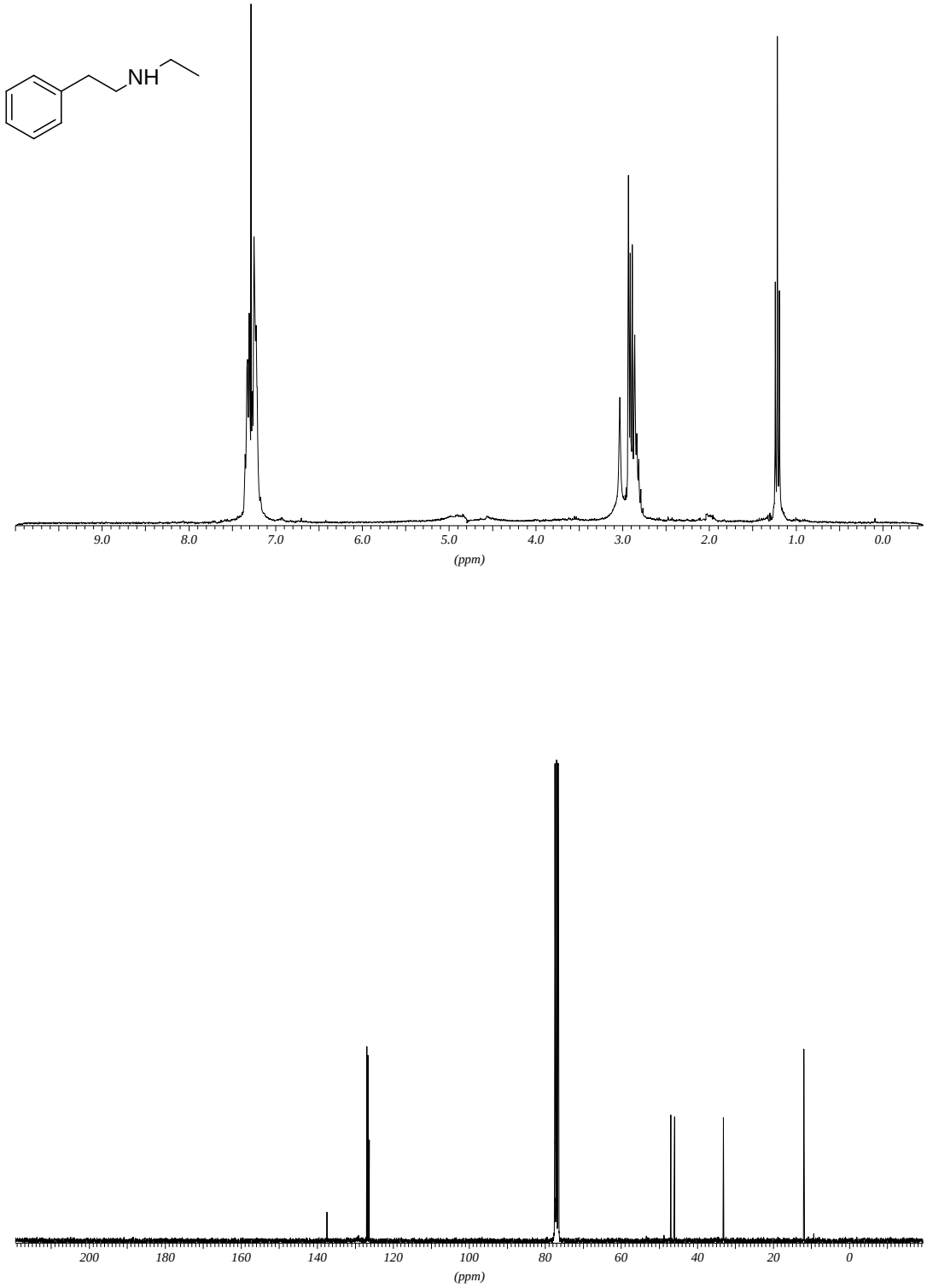


Figure S5 (300 MHz) and ^{13}C-NMR (75 MHz) of **6e**

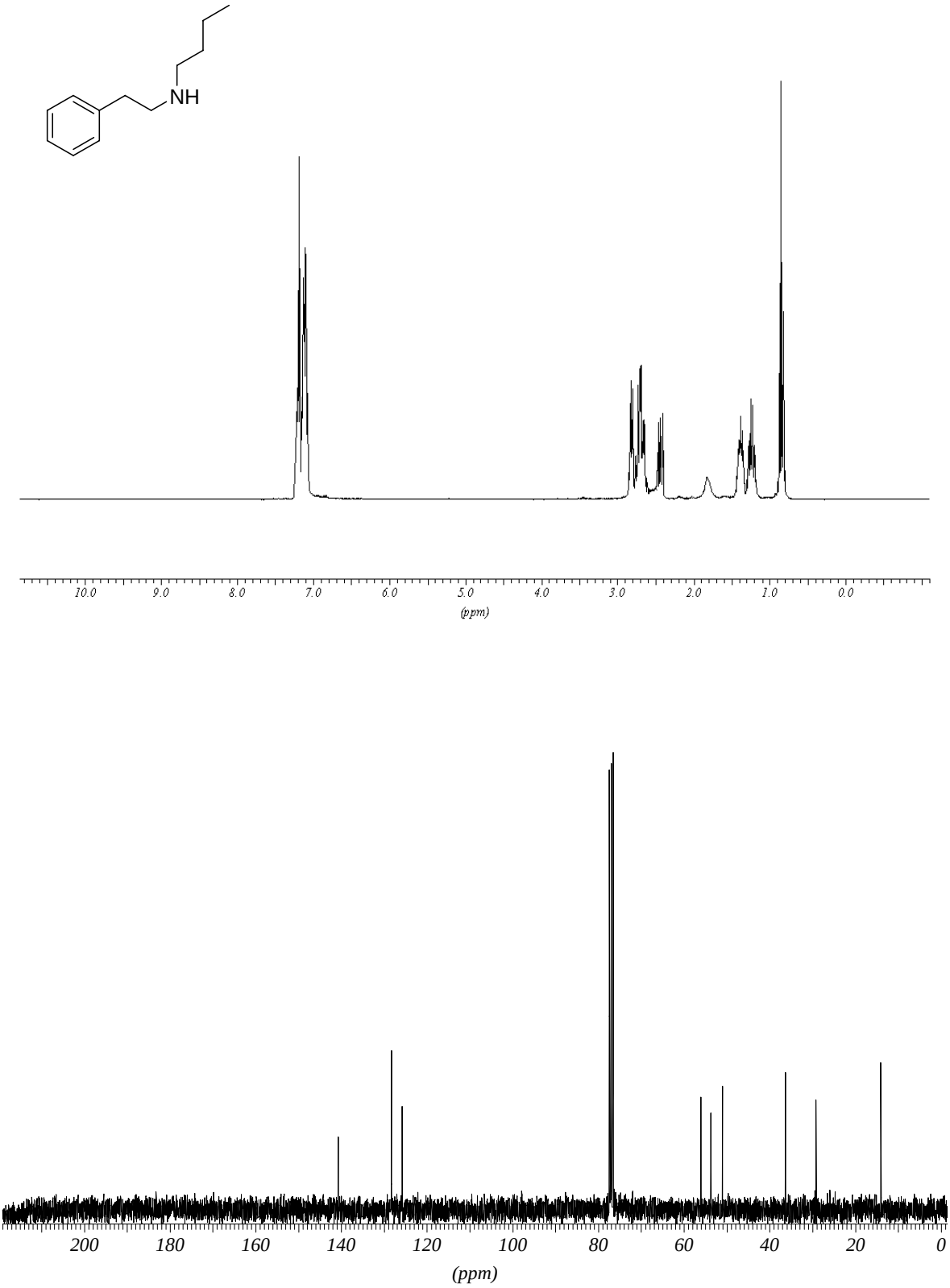


Figure S6 (300 MHz) and ^{13}C-NMR (75 MHz) of **8e**

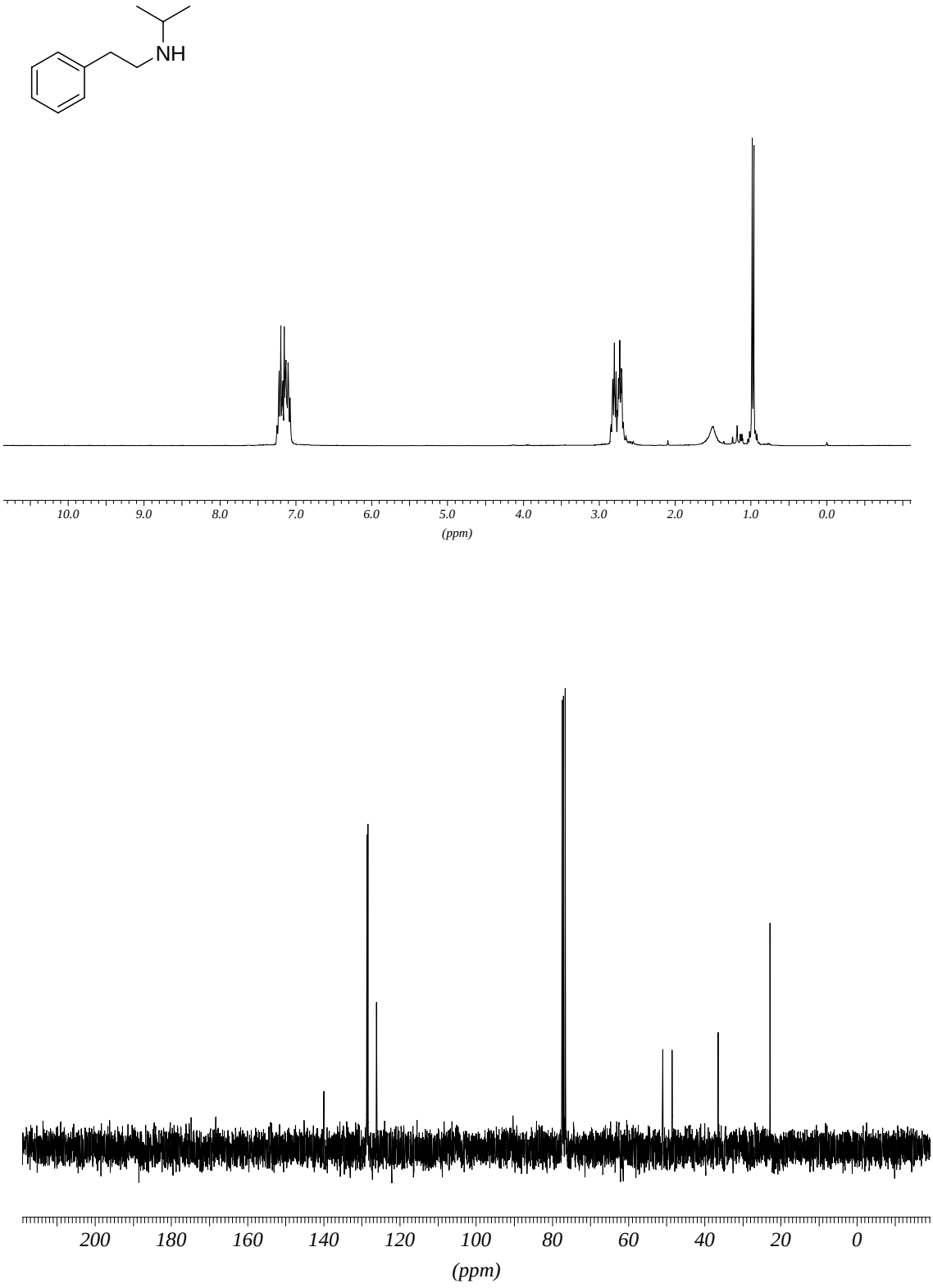


Figure S7 (300 MHz) and ^{13}C-NMR (75 MHz) of **9e**

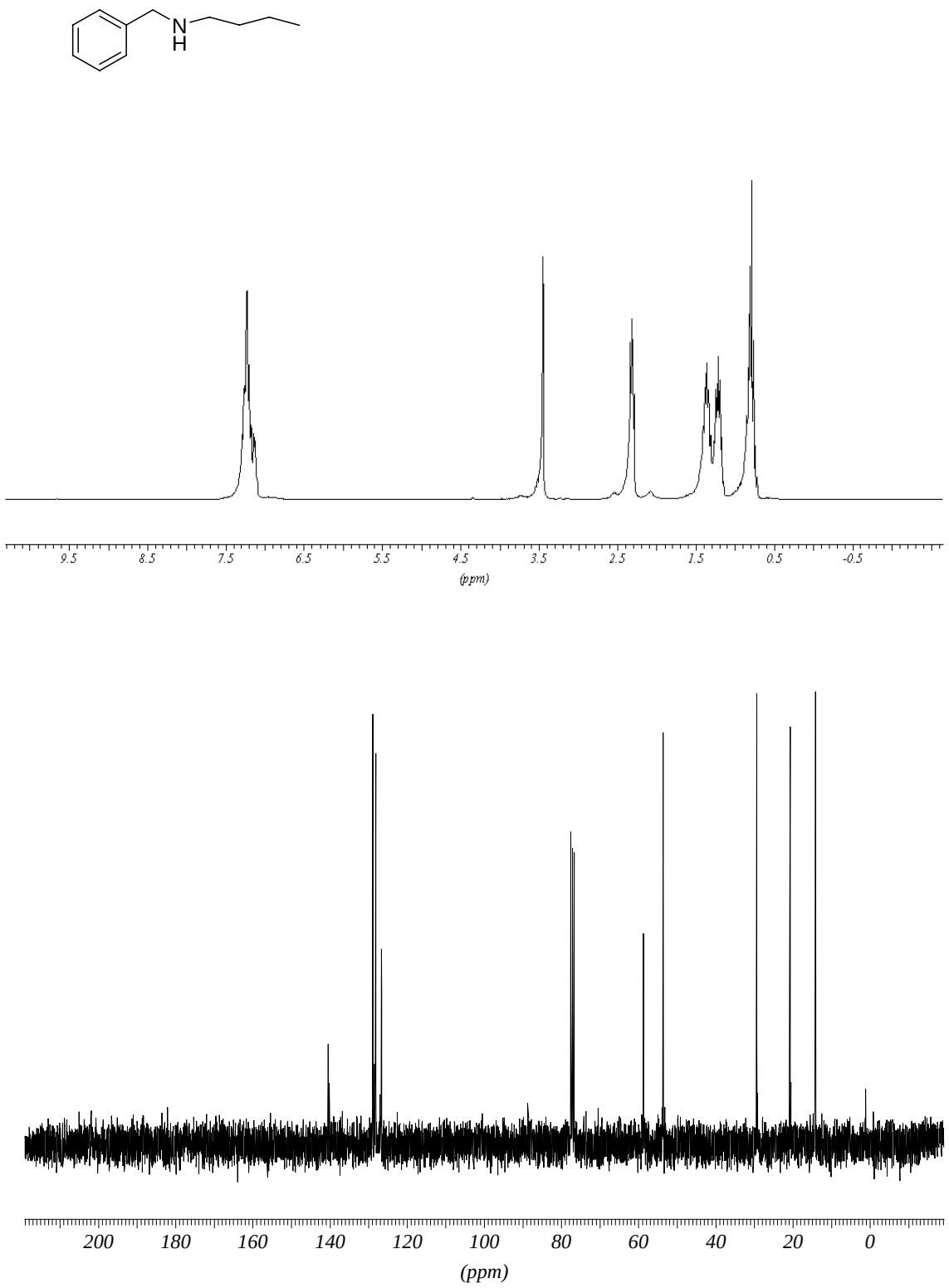


Figure S8 (300 MHz) and ^{13}C-NMR (75 MHz) of **8f**

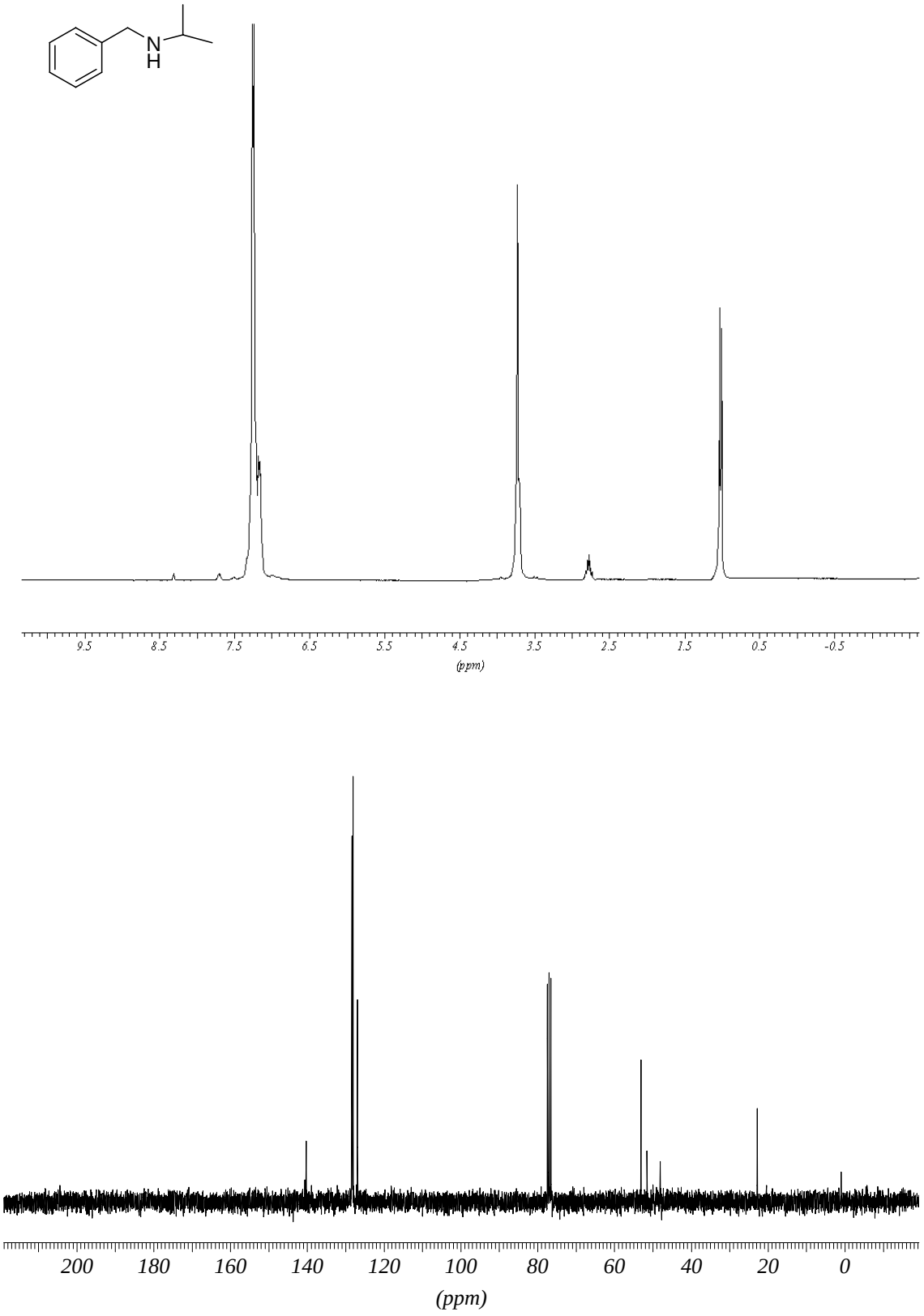


Figure S9 (300 MHz) and ^{13}C-NMR (75 MHz) of **9f**

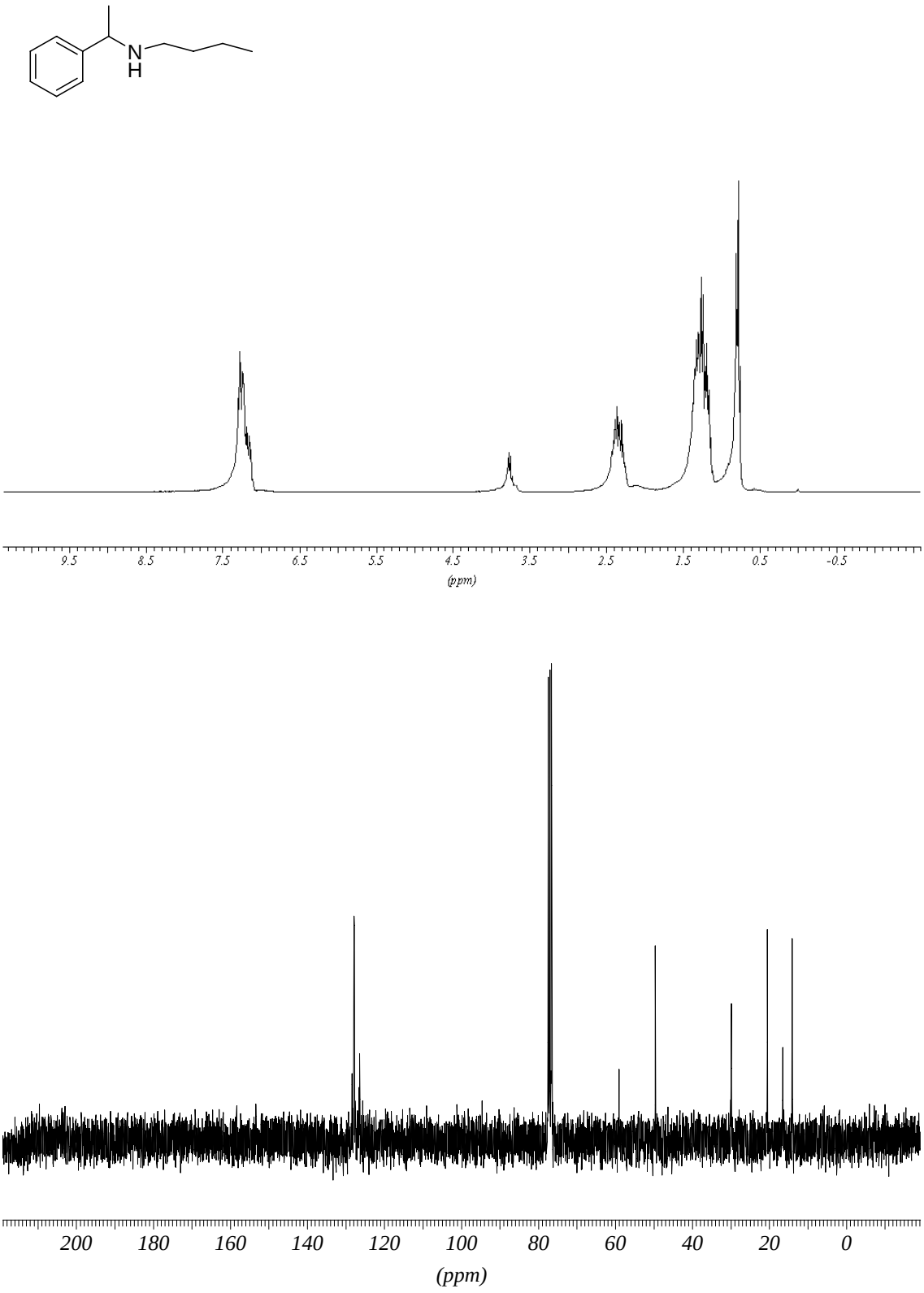


Figure S10 (300 MHz) and ^{13}C-NMR (75 MHz) of **8g**

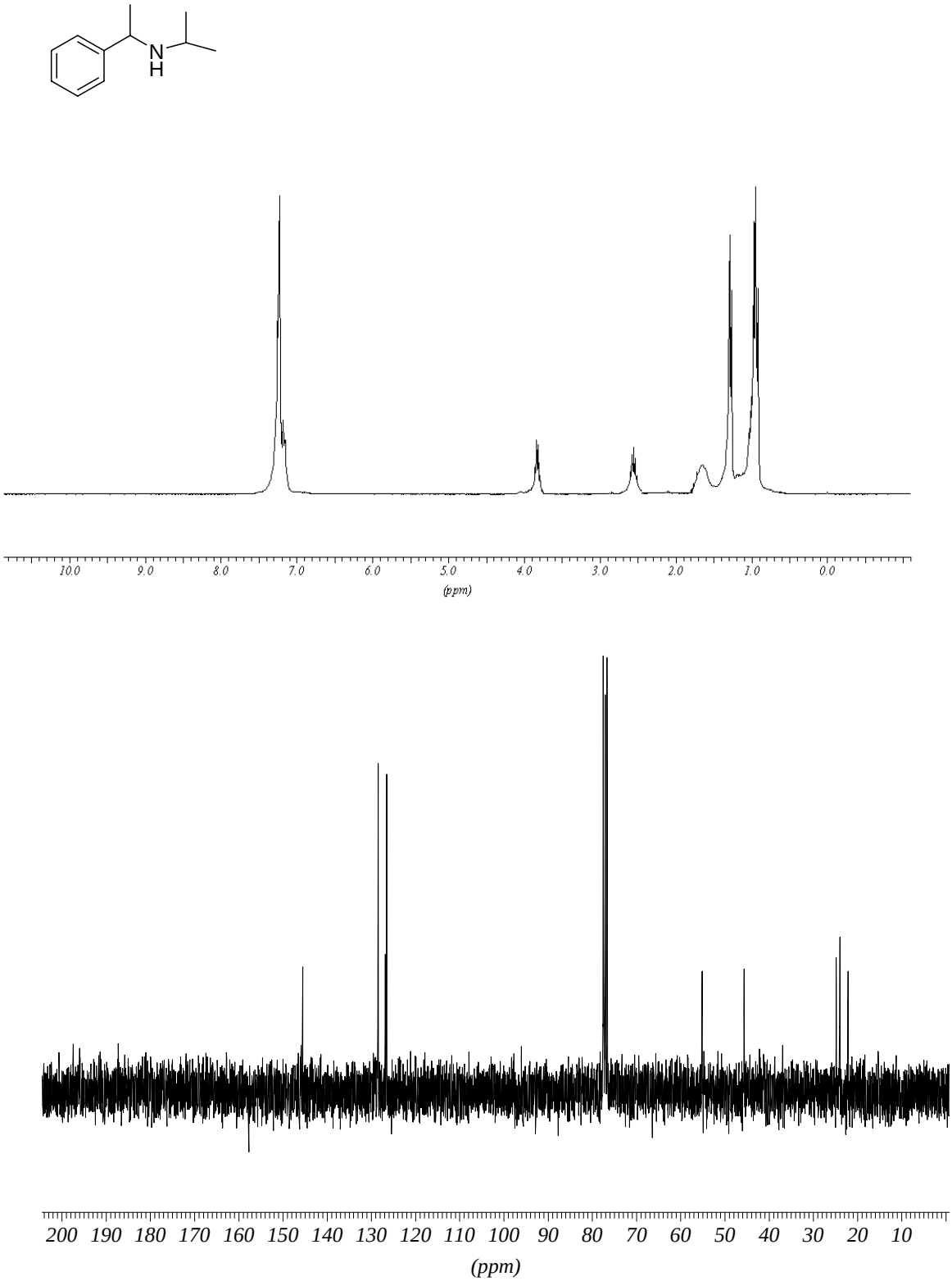


Figure S11 (300 MHz) and ^{13}C-NMR (75 MHz) of **9g**