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Supporting Information

Pd-catalyzed Cross-coupling Reactions with Carbonyls: Application in a Very Efficient Synthesis of 4-Aryltetrahydropyridines

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Supporting information

Experimental procedures and spectroscopic data

General considerations: All reactions were carried out in a RR98030 12 place Carousel Reaction Station™ from Radleys Discovery Technologies, equipped with gas-tight threaded caps with a valve, cooling reflux head system, and digital temperature controller. Dioxane, dichloromethane, pentane and hexanes were dried using the procedures described in D. Perrin *Purification of Laboratory Chemicals,* Pergamon Press Ltd. 1980, 2nd Ed. $Pd_2(dba)_3$ is purchased from Strem Chemical co. and used without further purification. All ligands are commercially available from Strem Chemical co. or Aldrich Chemical co. and used without further purification. LiO^tBu was purchased from Fluka, stored in a flask purged with nitrogen and weighted in the air. All aryl halides and 4-piperidones are commercially available from Aldrich Chemical co. and Acros Organics Chemical co. and were used without further purification. *N*-Tosylhydrazones **3** derived from 4-piperidones **1** were prepared following the procedure described in V. K. Aggarwal, E. Alonso, I. Bae, G. Hynd, K.M. Lydon, M.J. Palmer, M. Patel, M. Porcelloni, J. Richardson, R.A. Stenson, J.R. Studley, J-L. Vasse, and C.L. Winn, *J. Am. Chem. Soc.* **2003**, *125*, 10926. NMR spectra were recorded at 400 or 300 MHz for ^{1}H and 100 or 75 MHz for ^{13}C, with tetramethylsilane as internal standard for ^{1}H and the residual solvent signals as standard for ^{13}C. Chemical shifts are given in ppm. The data is being reported as s = singlet, d = doublet, t = triplet, c = quatriplet and m = multiplet or unresolved, chemical shifts in ppm and coupling constant(s) in Hz. Mass spectra were obtained by EI (70 eV).

General procedure for the cross-coupling of *N*-Tosylhydrazones 3 with aryl halides.

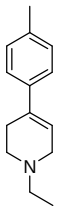
A carousel reaction tube under nitrogen atmosphere was charged with 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (Xphos) (19.1 mg, 0.04 mmol, 4 mol %), tris(dibenzylideneacetone)dipalladium(0) (9.16 mg, 0.005 mmol, 1 mol %), lithium *t*-butoxide (201.6 mg, 2.4 mmol), the tosylhydrazone **1** (1.1 mmol) and dioxane

(4 mL). After 1 minute, the aryl halide (1 mmol) was added. The system was heated at 110ºC with stirring and reflux. The reaction was monitored by GCMS. When the reaction was completed, the crude reaction mixture was allowed to cool to room temperature, taken up in dry pentane, hexanes or dichloromethane (15 mL), and filtered through celite. The solvents were evaporated under reduced pressure; if necessary, the residue was purified by flash chromatography on silica gel.

General procedure for the cross-coupling of 4-piperidone 1 with aryl halides. Synthesis of 4-aryltetrahydropyridines 2.

A carousel reaction tube under nitrogen atmosphere was charged with 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (Xphos) (19.1 mg, 0.04 mmol, 4 mol %), tris(dibenzylideneacetone)dipalladium(0) (9.16 mg, 0.005 mmol, 1 mol %), lithium *t*-butoxide (201.6 mg, 2.4 mmol for *N*-protected piperidones) (284.7 mg, 3.4 mmol for 4-piperidone hydrochlorides), the 4-piperidone **1** (1.1 mmol), the tosylhydrazine (1.16 mmol) and dioxane (4 mL). After 1 minute, the aryl halide (1 mmol) was added. The system was heated at 110 ºC with stirring and reflux. The reaction was monitored by GCMS. When the reaction was completed, the crude reaction mixture was allowed to cool to room temperature, taken up in dry pentane, hexanes or dichloromethane (15 mL), and filtered through celite. The solvents were evaporated under reduced pressure; if necessary, the residue was purified by flash chromatography on silica gel.

1-ethyl-1,2,3,6-tetrahydro-4-*p*-tolylpyridine (2b):

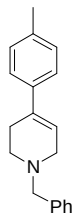


p-bromotoluene (85.5 mg, 0.5 mmol), 1-ethyl-4-piperidone **1** (70.0 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2b** (81.5 mg, 81% yield) as a colourless oil.

HRMS (EI): calcd. for $C_{14}H_{19}N$: 201.1512; found: 201.1507.

^{1}H NMR (300 MHz, $CDCl_3$): d = 1.24 (t, ^{3}J = 7.2 Hz, 3H), 2.35 (s, 3H), 2.60-2.70 (m, 4H), 2.77-2.80 (m, 2H), 3.22-3.25 (m, 2H), 6.04 (br. s, 1H), 7.14 (d, ^{3}J = 8.1 Hz, 2H), 7.30 (d, ^{3}J = 8.1 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): d = 12.0 (CH_3), 21.0 (CH_3), 27.7 (CH_2), 49.8 (CH_2), 51.9 (CH_2), 52.4 (CH_2), 120.2 (CH), 124.8 (2xCH), 128.9 (2xCH), 134.9 (C), 136.7 (C), 137.8 (C).

1-benzyl-4-*p*-tolyl-1,2,3,6-tetrahydropyridine (2c):



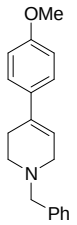
p-bromotoluene (85.5 mg, 0.5 mmol), 1-benzyl-4-piperidone **1** (104.1 mg, 0.55 mmol) and p-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2c** (117.1 mg, 89 % yield) as a yellow solid.

HRMS (EI): calcd. for $C_{19}H_{21}N$: 263.1669; found: 263.1672.

^{1}H-NMR (300 MHz, $CDCl_3$) d(ppm) = 2.36 (s, 3H), 2.59 (m, 2H), 2.72-2.77 (m, 2H), 3.20 (m, 2H), 3.67 (s, 2H), 6.06 (m, 1H), 7.13-7.17 (m, 2H), 7.30 (d, ^{3}J = 8 Hz, 2H), 7.33-7.36 (m, 3H), 7.40 (d, ^{3}J = 8 Hz, 2H); **^{13}C-NMR** (75 MHz, $CDCl_3$) d(ppm) = 21.0 (CH_3), 27.9 (CH_2), 49.9 (CH_2), 53.2 (CH_2), 62.7 (CH_2), 120.9 (CH), 124.7 (2xCH), 127.0 (CH), 128.2 (2xCH), 128.8, (2xCH), 129.1 (2xCH), 134.7 (C), 136.5 (C), 138.0 (C), 138.2 (C).

Spectroscopic data in agreement with those reported in C. Morrill and N. S. Mani, *Org. Lett*. **2007;** *9*, 1505.

1-benzyl-4-(4-methoxyphenyl)-1,2,3,6-tetrahydropyridine (2d):



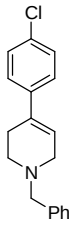
p-bromoanisole (93.5 mg, 0.5 mmol), 1-benzyl-4-piperidone **1** (104.1 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2c** (138.2 mg, 99% yield) as a yellow solid.

HRMS (EI): calcd. for $C_{19}H_{21}NO$: 279.1612; found: 279.1615.

^{1}H-NMR (400 MHz, $CDCl_3$) d(ppm) = 2.58 (m, 2H), 2.75 (t, ^{3}J = 5.8 Hz, 2H), 3.20 (m, 2H), 3.68 (s, 2H), 3.83 (s, 3H), 6.01 (m, 1H), 6.89 (d, ^{3}J = 8.9 Hz, 2H), 7.32 (m, 1H), 7.35-7.40 (m, 4H), 7.43 (d, ^{3}J = 7.88 Hz, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$) d(ppm) = 28.0 (CH_2), 49.9 (CH_2), 53.2 (CH_2), 55.1 (CH_3), 62.7 (CH_2), 113.5 (2xCH), 120.1 (CH), 125.8 (2xCH), 127.0 (CH), 128.1 (2xCH), 129.1 (2xCH), 133.4 (C), 134.2 (C), 138.2 (C), 158.6 (C).

Spectroscopic data in agreement with those reported in C. Morrill and N. S. Mani, *Org. Lett*. **2007;** *9*, 1505.

1-benzyl-4-(4-chlorophenyl)-1,2,3,6-tetrahydropyridine (2e):



p-bromochlorobenzene (95.7 mg, 0.5 mmol), 1-benzyl-4-piperidone **1** (104.1 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2e** (138.7 mg, 98 % yield) as a yellow solid.

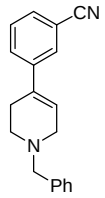
HRMS (EI): calcd. for $C_{18}H_{18}ClN$: 283.1122; found: 283.1121.

^{1}H-NMR (400 MHz, $CDCl_3$) d(ppm) = 2.52-2.58 (m, 2H), 2.74 (t, ^{3}J = 5.8 Hz, 2H), 3.20 (m, 2H), 3.66 (s, 2H), 6.08(m, 1H), 7.27-7.28 (m, 1H), 7.30-7.31 (m, 2H), 7.32-

7.33 (m, 2H), 7.34-7.35 (m, 1H), 7.35-7.36 (m, 1H), 7.38-7.39 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$) d(ppm) = 27.9 (CH_2), 49.8 (CH_2), 53.2 (CH_2), 62.6 (CH_2), 122.4 (CH), 126.1 (2xCH), 127.1 (CH), 128.2 (2xCH), 128.3 (2xCH), 129.2 (2xCH), 132.5 (C), 133.9 (C), 138.0 (C), 139.2 (C).

Spectroscopic data in agreement with those reported in S. Sakamuri, I. J., Enyedy, A. P. Kozikowski, W. A. Zaman, K. M. Johnson and S. Wang, *Biorg. Med. Chem. Lett.* **2001;** *11*, 495.

3-(1-benzyl-1,2,3,6-tetrahydropyridin-4-yl)benzonitrile (2f):

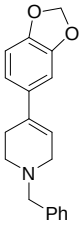


3-bromobenzonitrile (91.0 mg, 0.5 mmol), 1-benzyl-4-piperidone **1** (104.1 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2f** (134.3 mg, 98 % yield) as a pale brown solid.

HRMS (EI): calcd. for $C_{19}H_{18}N_2$: 274.1465; found: 274.1462.

^{1}H-NMR (300 MHz, $CDCl_3$) d(ppm) = 2.55 (m, 2H), 2.75 (t, ^{3}J = 5.7 Hz, 2H), 3.20 (m, 2H), 3.66 (s, 2H), 6.15 (m, 1H), 7.29 (d, ^{3}J = 6.9 Hz, 1H), 7.34-7.44 (m, 5H), 7.52 (d, ^{3}J = 7,9 Hz, 1H), 7.62 (d, ^{3}J = 7.9 Hz, 1H), 7.66 (s, 1H); **^{13}C-NMR** (75 MHz, $CDCl_3$) d(ppm) = 27.8 (CH_2), 49.4 (CH_2), 52.9 (CH_2), 62.4 (CH_2), 112.2 (C), 118.8 (CH), 124.2 (CH), 127.0 (CH), 128.0 (CH), 128.1 (CH), 128.3 (2xCH), 129.0 (2xCH), 130.1 (CH), 133.0 (C), 137.8 (C), 141.7 (C), 150.4 (C).

4-(benzo[d][1,3]dioxol-5-yl)-1-benzyl-1,2,3,6-tetrahydropyridine (2g):

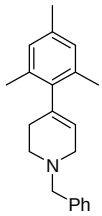


5-chlorobenzo[d][1,3]dioxole (78.3 mg, 0.5 mmol), 1-benzyl-4-piperidone **1** (104.1 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2g** (142.2 mg, 97 % yield) as a pale brown solid.

HRMS (EI): calcd. for $C_{19}H_{19}NO_2$: 293.1410; found: 293.1405.

^{1}H-NMR (300 MHz, $CDCl_3$) d(ppm) = 2.55(m, 2H), 2.73 (t, ^3J = 5.5 Hz, 2H), 3.18 (m, 2H), 3.67 (s, 2H), 5.96 (d, ^3J = 1.1 Hz, 2H), 5.99 (m, 1H), 6.80 (d, ^3J = 8.6 Hz, 1H), 6.89 (d, ^3J = 8.6 Hz, 1H), 6.94 (s, 1H), 7.31-7.44 (m, 5H); **^{13}C-NMR** (75 MHz, $CDCl_3$) d(ppm) = 28.2 (CH_2), 49.8 (CH_2), 53.2 (CH_2), 62.6 (CH_2), 100.8 (CH_2), 105.4 (CH), 107.8 (CH), 118.1 (CH), 120.8(CH), 127.0 (CH), 128.1 (2xCH), 129.1 (2xCH), 134.3 (C), 135.2 (C), 138.1 (C), 146.4 (C), 147.5 (C).

1-benzyl-4-mesityl-1,2,3,6-tetrahydropyridine (2h):

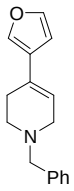


2-bromomesitylene (99.6 mg, 0.5 mmol), 1-benzyl-4-piperidone **1** (104.1 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2h** (134.0 mg, 92 % yield) as a pale brown oil.

HRMS (EI): calcd. for $C_{21}H_{25}N$: 291.1982; found: 291.1982.

^{1}H-NMR (300 MHz, $CDCl_3$) d(ppm) = 2.28 (s, 9H), 2.33 (s, 2H), 2.77 (t, ^3J = 5.6 Hz, 2H), 3.18-3.21 (m, 2H), 3.73 (s, 2H), 5.48 (m, 1H), 6.92 (s, 2H), 7.33-7.35 (m, 1H), 7.38-7.47 (m, 4H); **^{13}C-NMR** (75 MHz, $CDCl_3$) d(ppm) = 19.7 (2xCH_3), 20.9 (CH_3), 30.0 (CH_2), 49.8 (CH_2), 52.7 (CH_2), 62.5 (CH_2), 123.4 (CH), 126.9 (CH), 127.9 (2xCH), 128.1 (2xCH), 129.0 (2xCH), 135.4 (2xC), 135.7 (C), 135.8 (C), 138.4 (C), 139.4 (C).

1-benzyl-4-(furan-3-yl)-1,2,3,6-tetrahydropyridine (2i):

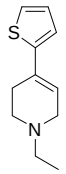


3-bromofurane (73.5 mg, 0.5 mmol), 1-benzyl-4-piperidone **1** (104.1 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2i** (110.0 mg, 92% yield) as a pale brown oil.

HRMS (EI): calcd. for $C_{16}H_{17}NO$: 239.1305; found: 239.1301.

^{1}H-NMR (400 MHz, $CDCl_3$) d(ppm) = 2.44 (m, 2H), 2.71 (t, ^{3}J = 5.8 Hz, 2H), 3.16 (m, 2H), 3.66 (s, 2H), 5.94 (m, 1H), 6.53 (s, 1H), 7.31 (d, ^{3}J = 6.9 Hz, 1H), 7.34-7.45 (m, 6H); **^{13}C-NMR** (100 MHz, $CDCl_3$) d(ppm) = 27.6 (CH_2), 49.5 (CH_2), 52.9 (CH_2), 62.7 (CH_2), 107.2 (CH), 120.0 (CH), 127.0 (C), 127.2 (CH), 128.2 (2xCH), 129.1 (2xCH), 137.8 (CH), 138.2 (C), 143.1 (CH).

1-ethyl-1,2,3,6-tetrahydro-4-(thiophen-2-yl)pyridine (2j):

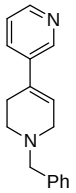


2-bromotiophene (63.3 mg, 0.5 mmol), 1-ethyl-4-piperidone **1** (70.0 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2j** (86.9 mg, 90% yield) as a pale brown oil.

HRMS (EI): calcd. for $C_{11}H_{15}NS$: 193.0925; found: 193.0922.

^{1}H NMR (300 MHz, $CDCl_3$): d = 1.15 (t, ^{3}J = 7.2 Hz, 3H), 2.49-2.61 (m, 4H), 2.67-2.71 (m, 2H), 3.12-3.14 (m, 2H), 6.09 (m, 1H), 6.94-6.95 (m, 2H), 7.10-7.12 (m, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): d = 12.3 (CH_3), 28.2 (CH_2), 49.5 (CH_2), 51.8 (CH_2), 52.2 (CH_2), 120.8 (CH), 121.5 (CH), 123.0 (CH), 127.0 (CH), 129.5 (C), 145.2 (C).

3-(1-benzyl-1,2,3,6-tetrahydropyridin-4-yl)pyridine (2k):

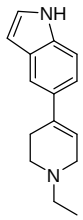


3-bromopyridine (79.0 mg, 0.5 mmol), 1-benzyl-4-piperidone **1** (104.1 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2k** (123.8 mg, 99% yield) as a pale brown oil.

HRMS (EI): calcd. for $C_{17}H_{18}N_2$: 250.1465; found: 250.1465.

^{1}H-NMR (300 MHz, $CDCl_3$) d(ppm) = 2.57 (m, 2H), 2.74 (t, ^3J = 5.9 Hz, 2H), 3.20 (m, 2H), 3.66 (s, 2H), 6.14 (m, 1H), 7.19-7.22 (m, 1H), 7.26-7.39 (m, 5H), 7.66 (d, ^3J = 7.6 Hz, 1H), 8.48 (d, ^3J = 5 Hz, 1H), 8.66 (s, 1H); **^{13}C-NMR** (75 MHz, $CDCl_3$) d(ppm) = 27.7 (CH_2), 49.6 (CH_2), 53.1 (CH_2), 62.6 (CH_2), 123.0 (CH), 123.7 (CH), 127.1 (CH), 128.2 (2xCH), 129.1 (2xCH), 132.0, (CH), 132.3 (C), 136.0 (C), 137.9 (C), 146.5 (CH), 148.0 (CH).

5-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)-1H-indole (2l):

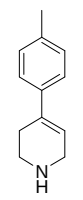


5-bromoindole (98.0 mg, 0.5 mmol), 1-ethyl-4-piperidone **1** (70.0 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2l** (97.2 mg, 86 % yield) as a yellow solid.

HRMS (EI): calcd. for $C_{15}H_{18}N_2$: 226.1470; found: 226.1472.

^{1}H NMR (300 MHz, $CDCl_3$): d = 1.21 (t, ^3J = 7.2 Hz, 3H), 2.61 (c, ^3J = 7.2 Hz, 2H), 2.71 (m, 2H), 2.81 (m, 2H), 3.23 (m, 2H), 6.05 (m, 1H), 6.52 (m, 1H), 7.18 (m, 1H), 7.25-7.34 (m, 2H), 7.65 (m, 1H), 8.51 (br. s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): d = 12.2 (CH_3), 28.6 (CH_2), 50.2 (CH_2), 52.0 (CH_2), 52.8 (CH_2), 102.6 (CH), 110.7 (CH), 116.9 (CH), 119.7 (CH), 119.8 (CH), 124.5 (CH), 127.8 (C), 133.0 (C), 135.1 (C). 135.8 (C).

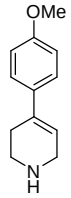
4-*p*-tolyl-1,2,3,6-tetrahydropyridine (2m):



p-bromotoluene (85.5 mg, 0.5 mmol), 1-piperidinone monohydrate hydrochloride **1** (84.5 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2m** (81.4 mg, 94 % yield) as a yellow solid. **2m** was purified by flash chromatography using methanol as eluent.

^{1}H-NMR (400 MHz, $CDCl_3$) d(ppm) = 2.36 (s, 3H), 2.56 (m, 2H), 3.21 (m, 2H), 3.63 (m, 2H), 6.05 (m, 1H), 7.14 (d, ^{3}J = 10.7 Hz, 2H), 7.27 (d, ^{3}J = 10.7 Hz, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$) d(ppm) = 20.9 (CH_3), 26.4 (CH_2), 42.4 (CH_2), 44.2 (CH_2), 120.1 (CH), 124.6 (2xCH), 129.0 (2xCH), 135.2 (C), 137.0 (C), 137.6 (C).

4-(4-methoxyphenyl)-1,2,3,6-tetrahydropyridine (2n):



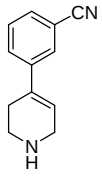
p-bromoanisole (93.5 mg, 0.5 mmol), 1-piperidinone monohydrate hydrochloride **1** (84.5 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2n** (85.1 mg, 90% yield) as a yellow solid. **2n** was purified by flash chromatography using methanol as eluent.

HRMS (EI): calcd. for $C_{12}H_{15}NO$: 189.1148; found: 189.1143.

^{1}H-NMR (400 MHz, $CDCl_3$) d(ppm) = 2.45 (m, 2H), 3.12 (m, 2H), 3.54 (m, 2H), 3.82 (s, 3H), 6.05 (m, 1H), 6.85 (d, ^{3}J = 8.7 Hz, 2H), 7.33 (d, ^{3}J = 8.7 Hz, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$) d(ppm) = 27.1 (CH_2), 42.8 (CH_2), 44.8 (CH_2), 55.0 (CH_3), 113.5 (2xCH), 120.8 (CH), 125.6 (2xCH), 133.5 (C), 134.5 (C), 158.6 (C).

Spectroscopic data in agreement with those reported in P. R. Eastwood, *Tetrahedron Lett*. **2000;** *41*, 3705.

3-(1,2,3,6-tetrahydropyridin-4-yl)benzonitrile (2o):

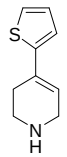


3-bromobenzonitrile (91.0 mg, 0.5 mmol), 1-piperidinone monohydrate hydrochloride **1** (84.5 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2o** (85.6 mg, 93 % yield) as a pale brown oil. **2o** was purified by flash chromatography using methanol as eluent.

HRMS (EI): calcd. for $C_{12}H_{12}N_2$: 184.0995; found: 184.0992.

^{1}H-NMR (400 MHz, $CDCl_3$) d(ppm) = 2.41 (m, 2H), 3.10 (m, 2H), 3.55 (m, 2H), 6.19 (m, 1H), 7.40 (t, ^3J = 7.7 Hz, 1H), 7.48 (d, ^3J = 7.7 Hz, 1H), 7.57 (d, ^3J = 7.7 Hz, 1H), 7.60 (s, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$) d(ppm) = 27.6 (CH_2), 43.1 (CH_2), 45.5 (CH_2), 112.5 (C), 119.0 (CH), 126.0 (CH), 128.6 (CH), 129.1 (CH), 130.2 (CH), 133.6 (C), 140.3 (C), 142.4 (C).

4-(thiophen-2-yl)-1,2,3,6-tetrahydropyridine (2p):

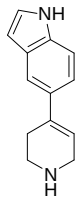


2-bromotiophene (63.3 mg, 0.5 mmol), 1-piperidinone monohydrate hydrochloride **1** (84.5 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2p** (57.8 mg, 70 % yield) as a pale brown oil. **2p** was purified by flash chromatography using methanol as eluent.

HRMS (EI): calcd. for $C_9H_{11}NS$: 165.0607; found: 165.0601.

^{1}H NMR (300 MHz, $CDCl_3$): d = 2.45 (m, 2H), 3.08 (m, 2H), 3.49 (m, 2H), 6.14 (m, 1H), 6.99 (m, 2H), 7.11 (m, 1H)**; ^{13}C NMR** (75 MHz, $CDCl_3$): d = 27.7 (CH_2), 42.9 (CH_2), 45.0 (CH_2), 121.3 (CH), 122.4 (CH), 123.0 (CH), 127.1 (CH), 129.8 (C), 145.8 (C).

5-(1,2,3,6-tetrahydropyridin-4-yl)-3H-indole (2q):



2q

5-bromoindole (98.0 mg, 0.5 mmol), 4-piperidinone monohydrate hydrochloride **1** (84.5 mg, 0.55 mmol) and p-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **2q** (75.3 mg, 76 % yield) as a white solid. **2q** was purified by flash chromatography using methanol as eluent.

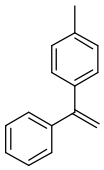
HRMS (EI): calcd. for $C_{13}H_{14}N_2$: 198.1152; found: 198.1149.

^{1}H NMR (300 MHz, $CDCl_3$): d = 2.50 (m, 2H), 3.24 (m, 2H), 3.68 (m, 2H), 6.16 (m, 1H), 6.74 (m, 1H), 7.19 (m, 1H), 7.30 (m, 2H), 7.57 (m, 1H), 8.49 (br. s, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$): d = 28.3 (CH_2), 43.5 (CH_2), 45.6 (CH_2), 102.7 (CH), 110.7 (CH), 116.7 (CH), 119.6 (CH), 121.8 (CH), 124.5 (CH), 127.9 (C), 133.6 (C), 135.1 (C). 136.1 (C).

General procedure for the cross-coupling of carbonyl compounds 5 with aryl halides. Synthesis of polysubstituted olefins 6.

A carousel reaction tube under nitrogen atmosphere was charged with 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (Xphos) (19.1 mg, 0.04 mmol, 4 mol %), tris(dibenzylideneacetone)dipalladium(0) (9.16 mg, 0.005 mmol, 1 mol %), lithium *t*-butoxide (201.6 mg, 2.4 mmol), the carbonyl compound **5** (1.1 mmol), the tosylhydrazine (1.16 mmol) and dioxane (4 mL). After 1 minute, the aryl halide (1 mmol) was added. The system was heated at 110ºC with stirring and reflux. The reaction was monitored by GCMS. When the reaction was completed, the crude reaction mixture was allowed to cool to room temperature, taken up in dry pentane, hexanes or dichloromethane (15 mL), and filtered through celite. The solvents were evaporated under reduced pressure; if necessary, the residue was purified by flash chromatography on silica gel.

1-Phenyl-1-*p*-tolyl-ethylene (6a):



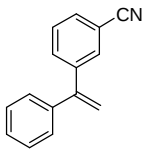
p-bromotoluene (85.5 mg, 0.5 mmol), acetophenone **5** (66.1 mg, 0.55 mmol) and p-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **6a** (68.0 mg, 70% yield) as a colourless oil.

HRMS (EI): calcd. for $C_{15}H_{14}$: 194.1090, found: 194.1089.

^{1}H NMR (300 MHz, $CDCl_3$): d = 2.41 (s, 3H), 5.45 (s, 1H), 5.47 (s, 1H), 7.18 (d, ^{3}J = 8.0 Hz, 2H), 7.28 (d, ^{3}J = 8.0 Hz, 2H), 7.36-7.38 (m, 5H); **^{13}C NMR** (75 MHz, $CDCl_3$): d = 21.1 (CH_3), 113.6 (CH_2), 127.6 (CH), 128.0 (CH), 128.1 (CH), 128.2 (CH), 128.8 (CH), 137.4 (C), 138.5 (C), 141.6 (C), 149.8 (C).

Spectroscopic data in agreement with those reported in D. Xing, B. Guan, G. Cai, Z. Fang, L. Yang, and Z. Shi, *Org. Lett*. **2006;** *8*, 693.

3-(1-phenylvinyl)benzonitrile (6b):



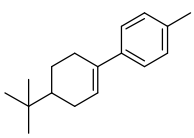
3-bromobenzonitrile (91.0 mg, 0.5 mmol), acetophenone **5** (66.1 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **6b** (98.4 mg, 96% yield) as a pale brown oil.

HRMS (EI): calcd. for $C_{15}H_{11}N$: 205.0886, found: 205.0885.

^{1}H NMR (400 MHz, $CDCl_3$): d = 5.52 (s, 1H), 5.58 (s, 1H), 7.30-7.32 (m, 2H), 7.37-7.39 (m, 3H), 7.44-7.48 (t, ^{3}J = 7.7 Hz,, 1H), 7.59-7.65 (m, 3H); **^{13}C NMR** (100MHz, $CDCl_3$): d = 112.3 (C), 115.9 (CH_2), 118.5 (C), 127.9 (CH), 128.1 (CH), 128.3 (CH), 128.9 (CH), 131.0 (CH), 131.5 (CH), 132.3(CH), 139.9 (C), 142.5 (C), 148.0 (C).

Spectroscopic data in agreement with those reported in D. R. Arnold, X. Du, and J. Chen, *Can. J. Chem*. **1995**, *73*, 307.

1-(4-*t*-Butylcyclohex-1-enyl)-4-methylbenzene (6c):



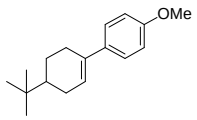
p-bromotoluene (85.5 mg, 0.5 mmol), 4-*tert*-Butylcyclohexanone **5** (84.8 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **6c** (113.0 mg, 99% yield) as a white solid.

HRMS (EI): calcd. for $C_{17}H_{24}$: 228.1872, found: 228.1874.

^{1}H NMR (300 MHz, $CDCl_3$): d = 0.95 (s, 9H), 1.26-1.44 (m, 2H), 1.94-2.03 (m, 2H), 2.23-2.32 (m, 1H), 2.38 (s, 3H), 2.42-2.58 (m, 2H), 6.12 (m, 1H), 7.15 (d, ^{3}J = 8.1 Hz, 2H), 7.32 (d, ^{3}J = 8.1 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): d = 21.0 (CH_3), 24.3 (CH_2), 27.1 (CH_3), 27.3 (CH_2), 28.8 (CH_2), 32.1 (C), 43.7 (CH), 124.0 (CH), 124.7 (CH), 128.8 (CH), 135.9 (C), 136.0 (C), 139.3 (C).

Spectroscopic data in agreement with those reported in M. E. Limmert, A. H. Roy, and J. F. Hartwig, *J. Org. Chem.* **2005**, *70*, 9364.

1-(4-*t*-butylcyclohex-1-enyl)-4-methoxybenzene (6d):

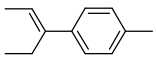


p-bromoanisole (93.5 mg, 0.5 mmol), 4-*tert*-Butylcyclohexanone **5** (84.8 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **6d** (113.5 mg, 93% yield) as a pale brown oil.

HRMS (EI): calcd. for $C_{17}H_{24}O$: 244.1822, found: 244.1820.

^{1}H NMR (300 MHz, $CDCl_3$): d = 0.93 (s, 9H), 1.28-1.42 (m, 2H), 1.93-2.02 (m, 2H), 2.22-2.28 (m, 1H), 2.34-2.56 (m, 2H), 3.81 (s, 3H), 6.05 (m, 1H), 6.86 (d, ^{3}J = 8.8 Hz, 2H), 7.34 (d, ^{3}J = 8.1 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$): d = 24.3 (CH_2), 27.2 (CH_3), 27.3 (CH_2), 28.8 (CH_2), 32.1 (C), 43.7 (CH), 55.1 (CH_3), 113.4 (CH), 123.2 (CH), 125.8 (CH), 134.8 (C), 135.5 (C), 158.3 (C).

1-methyl-4-[(E)pent-2-en-3-yl]benzene] (6e):

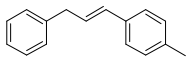


p-bromotoluene (85.5 mg, 0.5 mmol), 3-pentanone **5** (47.4 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **6e** (60.9 mg, 76% yield) as a colourless oil.

HRMS (EI): calcd. for $C_{12}H_{16}$: 160.1246, found: 160.1245.

^{1}H NMR (400 MHz, $CDCl_3$): d = 1.02 (t, ^{3}J= 7.5 Hz, 3H), 1.82 (d, ^{3}J = 6.9 Hz, 3H), 2.37 (s, 3H), 2.47 (c, ^{3}J = 7.5 Hz, 2H), 5.74 (c, ^{3}J = 6.9 Hz, 1H), 7.14 (d, ^{3}J = 8.0 Hz, 2H), 7.27 (d, ^{3}J = 8.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): d = 13.2 (CH_3), 13.8 (CH_3), 20.9 (CH_3), 22.5 (CH_2), 121.2 (CH), 125.9 (CH), 128.8 (CH), 135.9 (C), 140.1 (C), 142.0 (C).

1-methyl-4-[(*E*)-3-phenylprop-1-enyl]benzene (6f):

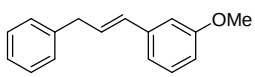


p-bromotoluene (85.5 mg, 0.5 mmol), 3-phenylpropionaldehyde **5** (72.7 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **6f** (95.7 mg, 92% yield) as a colourless liquid.

HRMS (EI): calcd. for $C_{16}H_{16}$: 208.1252, found: 208.1249.

^{1}H NMR (400 MHz, $CDCl_3$): d = 2.37 (s, 3H), 3.59 (d, ^{3}J = 8.0 Hz, 2H), 6.36 (dt, ^{3}J = 8.0 Hz, $^{3}J_{trans}$= 16.0 Hz, 1H), 6.48 (d, $^{3}J_{trans}$ = 16.0 Hz, 1H), 7.15 (d, ^{3}J = 8.0 Hz, 2H), 7.25-7.38 (m, 7H); **^{13}C NMR** (100 MHz, $CDCl_3$): d = 21.1 (CH_3), 39.3 (CH_2), 125.9 (CH), 126.0 (CH), 128.1 (CH), 128.4 (CH), 128.6 (CH), 129.1 (CH), 130.8 (CH), 134.6 (C), 136.8 (C), 140.3 (C).

1-(4-methoxycinnamyl)benzene (6g):



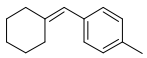
3-bromoanisole (93.5 mg, 0.5 mmol), 3-phenylpropionaldehyde **5** (72.7 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **6g** (97.5mg, 87% yield) as a yellow liquid.

HRMS (EI): calcd. for $C_{16}H_{16}O$: 224.1196, found: 224.1193.

^{1}H NMR (400 MHz, $CDCl_3$): d = 3.61 (d, ^{3}J = 6.4 Hz, 2H), 3.85 (s, 3H), 6.38-6.45 (m, 1H), 6.48 (d, $^{3}J_{trans}$ = 16.0 Hz, 1H), 6.82-6.84 (m, 1H), 6.97 (m, 1H), 7.01-7.03 (m, 1H), 7.25-7.39 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): d = 39.4 (CH_2), 55.2 (CH_3), 111.4 (CH), 112.9 (CH), 118.9 (CH), 126.3 (CH), 128.6 (CH), 128.8 (CH), 129.5 (CH), 129.6 (CH), 131.0 (CH), 139.0 (C), 140.2 (C), 159.8 (C).

Spectroscopic data in agreement with those reported in K. Manabe, K. Nakada, N. Aoyama, and S. Kobayashi, *Adv. Synth. Catal.* **2005**, *347*, 1499.

1-(cyclohexylidenemethyl)-4-methylbenzene (6h):



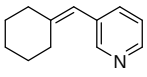
p-bromotoluene (85.5 mg, 0.5 mmol), cyclohexanecarboxaldehyde **5** (61.7 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **6h** (89.3 mg, 96 % yield) as a pale brown liquid.

HRMS (EI): calcd. for $C_{14}H_{18}$: 186.1403, found: 186.1400.

^{1}H NMR (300 MHz, $CDCl_3$): d = 1.64-1.69 (m, 6H), 2.32-2.46 (m, 7H), 6.27 (s, 1H), 7.17 (m, 4H); **^{13}C NMR** (75 MHz, $CDCl_3$): d = 21.0 (CH_3), 26.6 (CH_2), 27.8 (CH_2), 28.5 (CH_2), 29.4 (CH_2), 37.5 (CH_2), 121.7 (CH), 128.6 (CH), 128.7 (CH), 135.2 (C), 135.4 (C), 142.7 (C).

Spectroscopic data in agreement with those reported in A. R. Katritzky, D. Cheng, S. A. Henderson, and J. Li, *J. Org. Chem.* **1998**, *63*, 6704.

3-(cyclohexylidenemethyl)pyridine (6i):

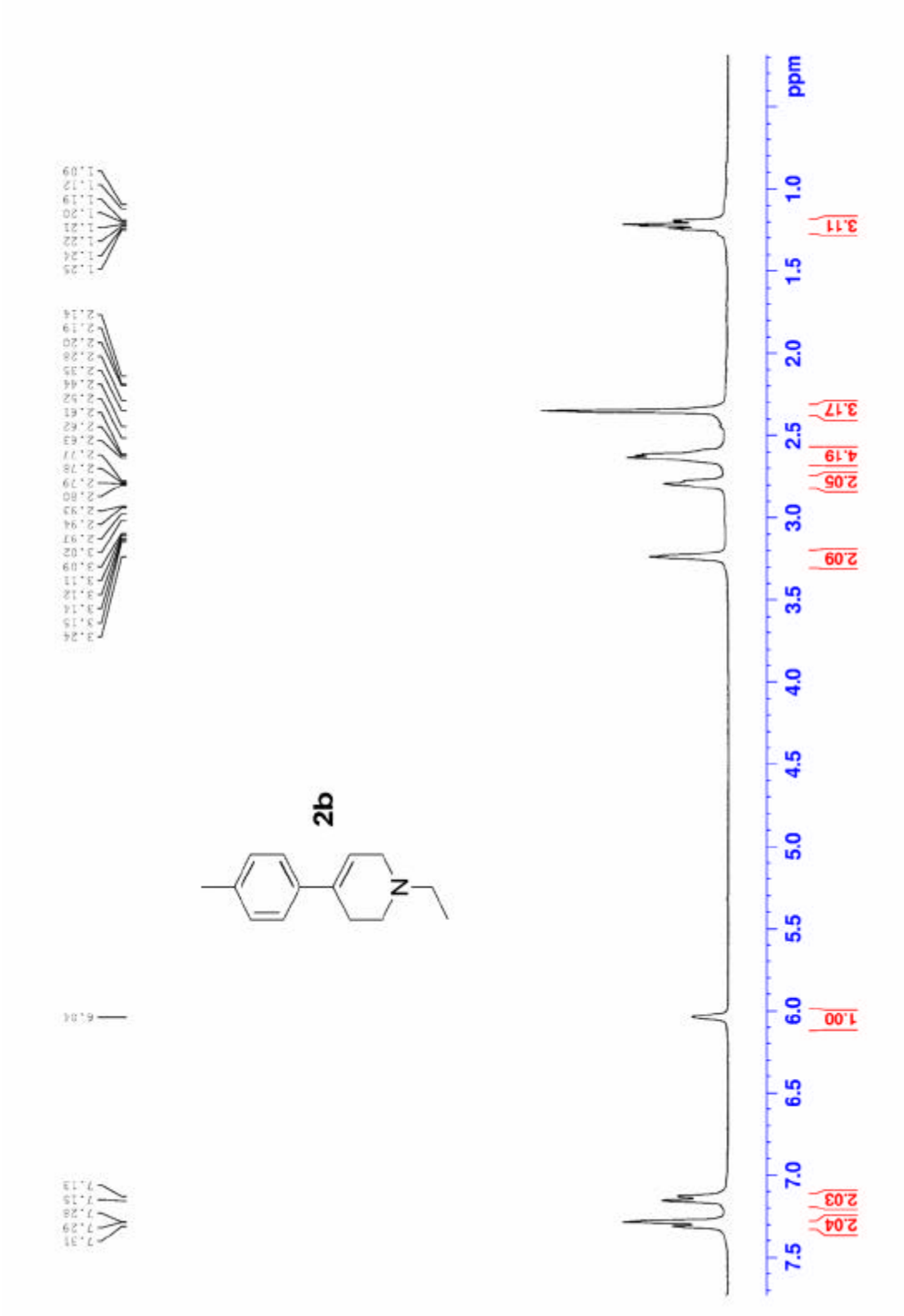


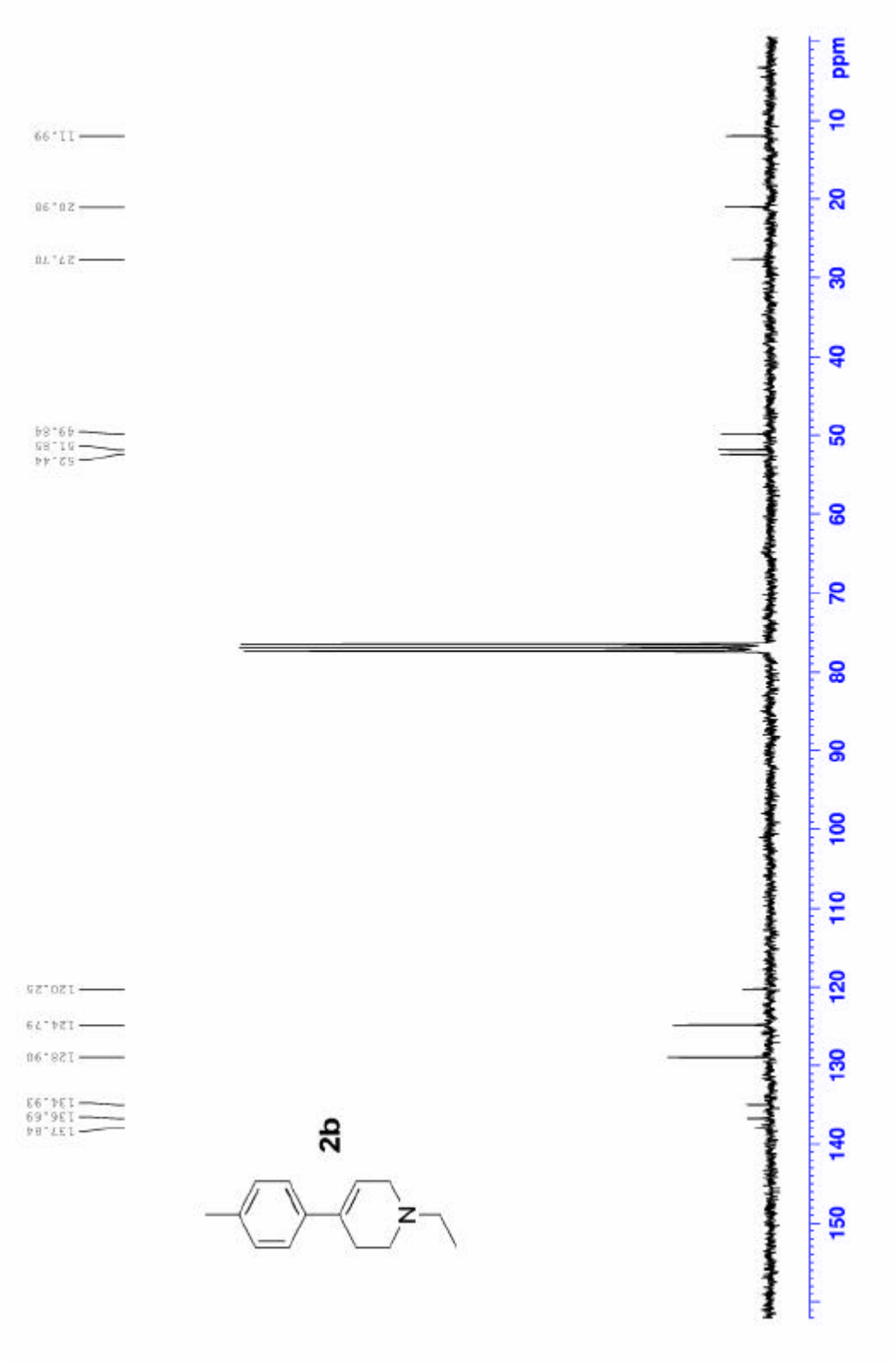
3-bromopyridine (85.5 mg, 0.5 mmol), cyclohexanecarboxaldehyde **5** (61.7 mg, 0.55 mmol) and *p*-toluenesulfonylhydrazide (118.8 mg, 1.16 mmol) afforded **6i** (57.1 mg, 66 % yield) as a yellow oil. **6i** was purified by flash chromatography using a mixture of hexanes/ethyl acetate 3:1 as eluent. R_f(hexanes/ethyl acetate 1:1) = 0.40.

HRMS (EI): calcd. for $C_{12}H_{15}N$: 173.1199; found: 173.1203.

^{1}H NMR (400 MHz, $CDCl_3$,): d = 1.54-1.68 (m, 6H), 2.27-2.35 (m, 4H), 6.16 (s, 1H), 7.23-7.28 (m, 1H), 7.50-7.52 (m, 1H), 8.42-8.46 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): d = 26.4 (CH_2), 27.7 (CH_2), 28.4 (CH_2), 29.4 (CH_2), 37.5 (CH_2), 118.0 (CH), 123.0 (CH), 134.0 (C), 136.2 (CH), 146.2 (C), 146.4 (CH), 149.6 (CH).

[1]H, 13C NMR spectra for compounds 2:

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20.90
27.70
49.84
51.85
52.44
120.25
124.79
128.90
134.93
136.69
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60
70
80
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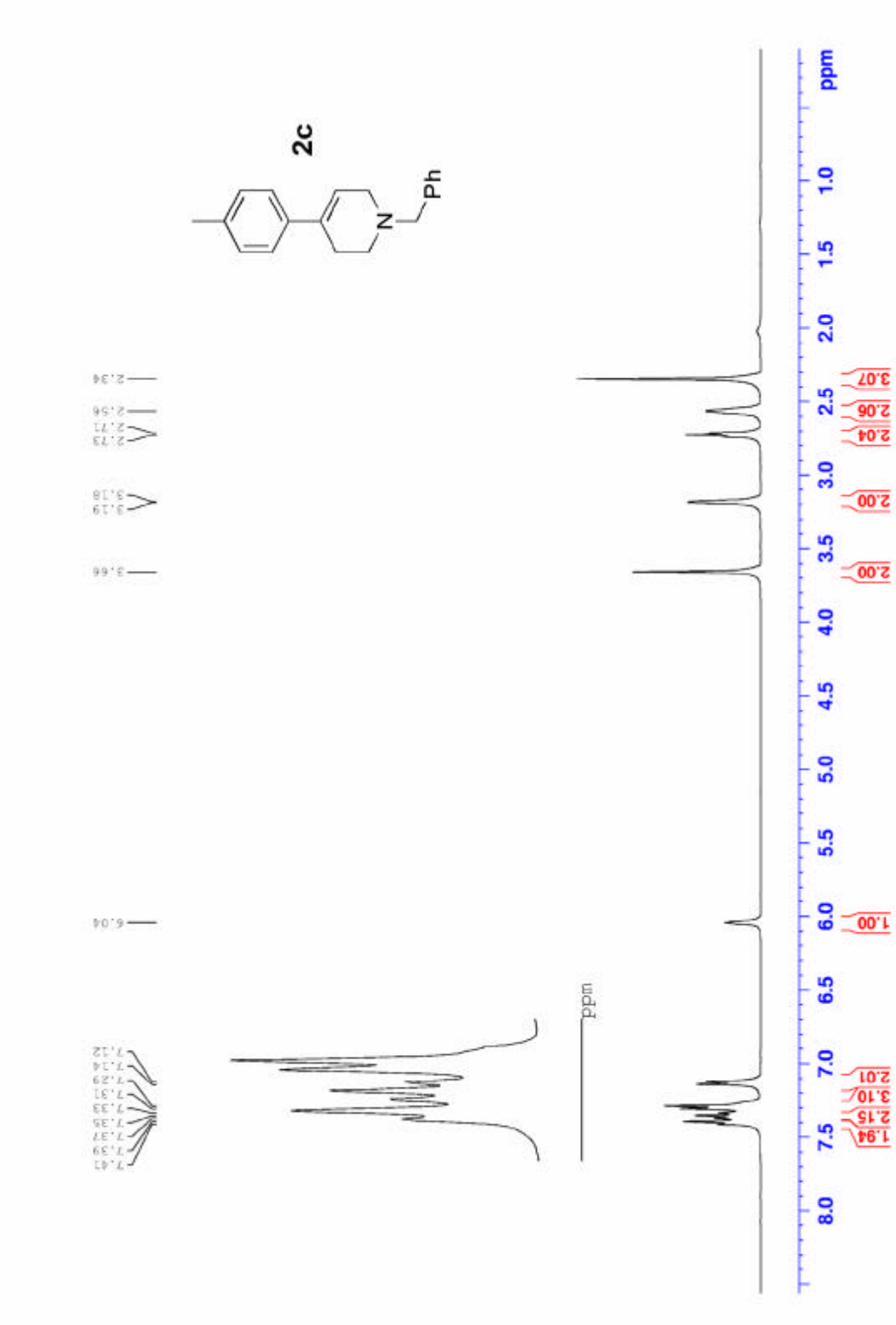
150


2c
Ph
N
ppm
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3.10
2.15
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2.00
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6.04
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3.19
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7.33
7.31
7.29
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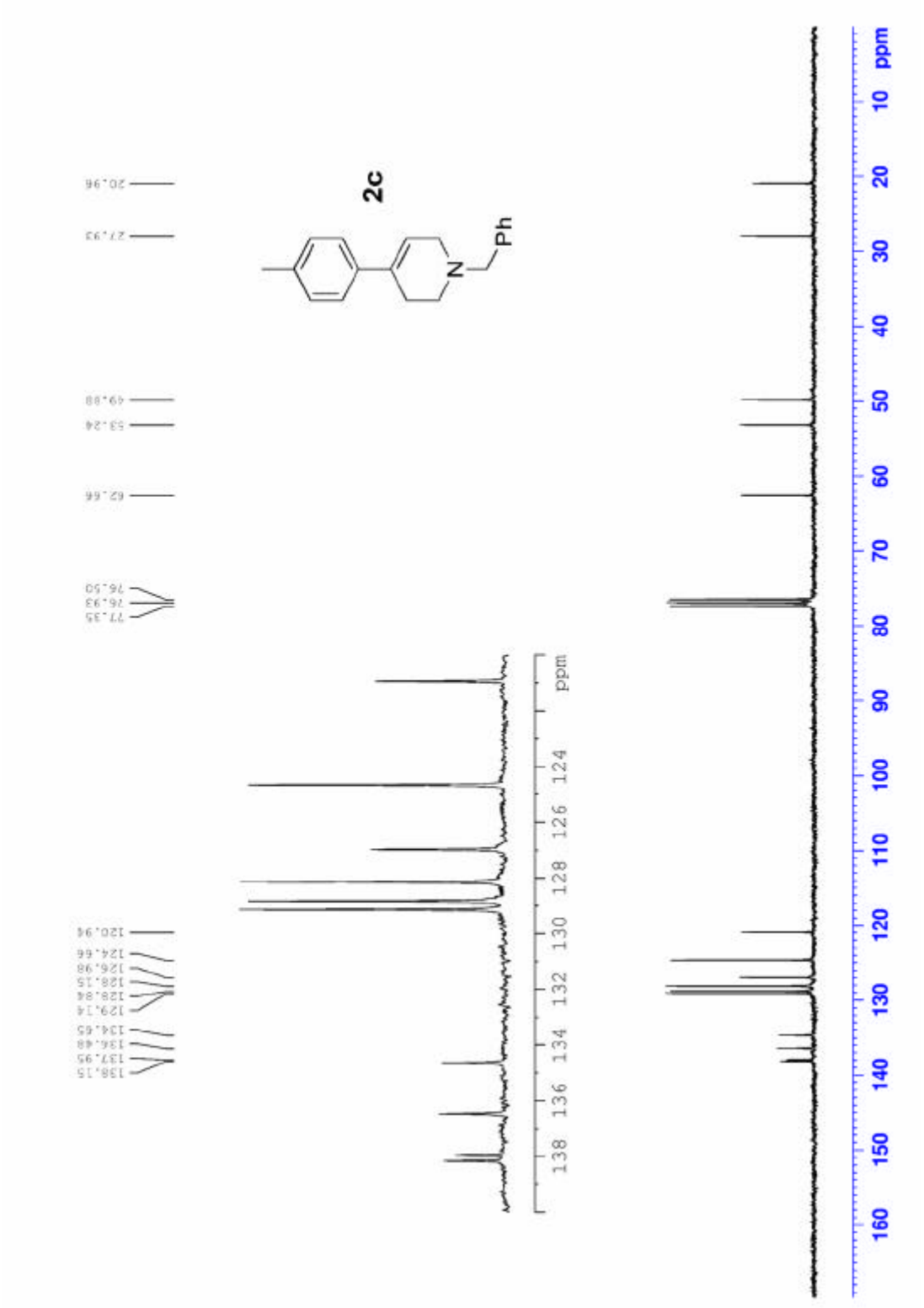
7.12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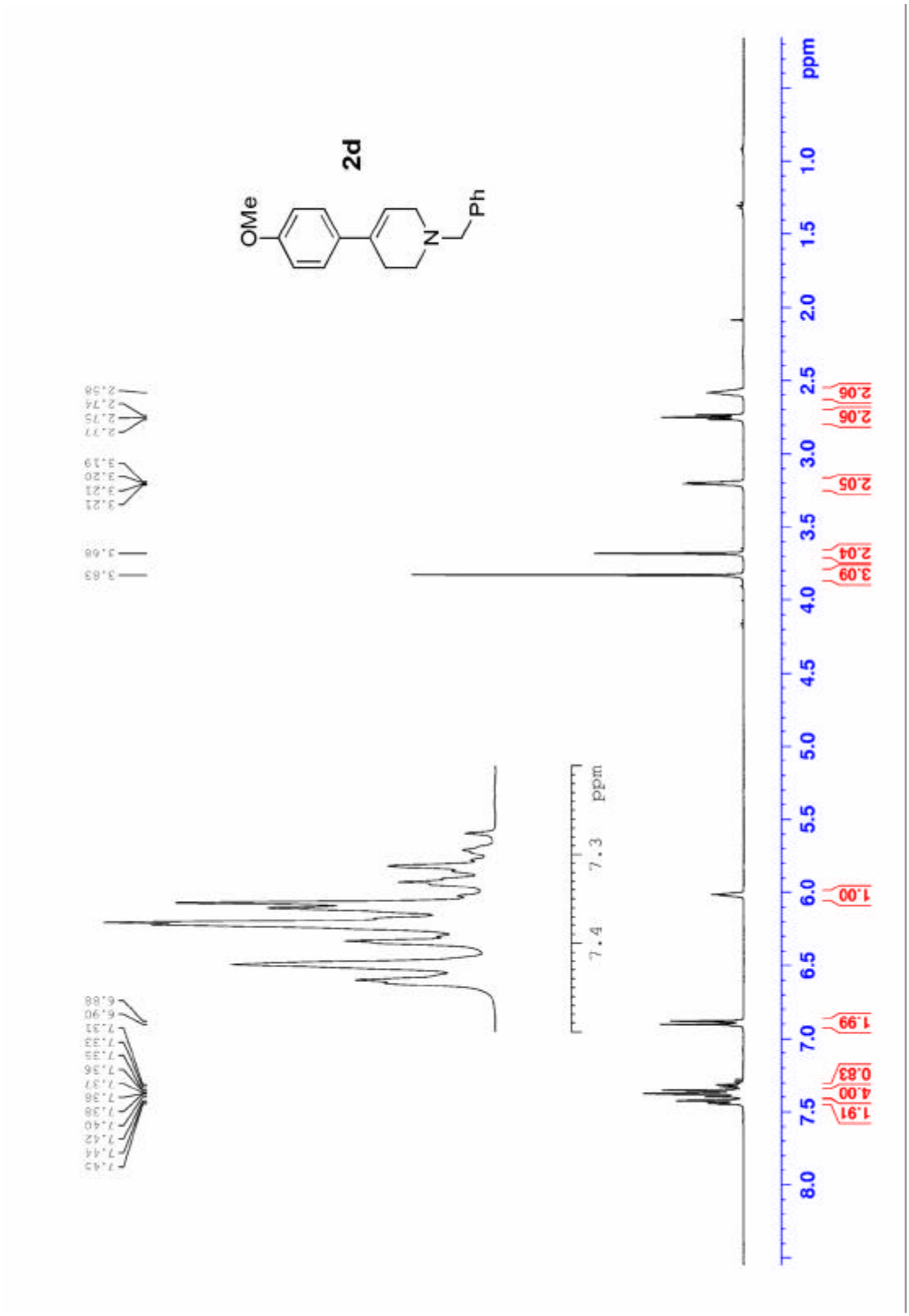
49.88
53.24
63.66
76.50
76.93
77.35
120.94
124.66
126.98
128.15
128.84
129.14
134.65
136.48
137.95
138.15
138 136 134 132 130 128 126 124 ppm
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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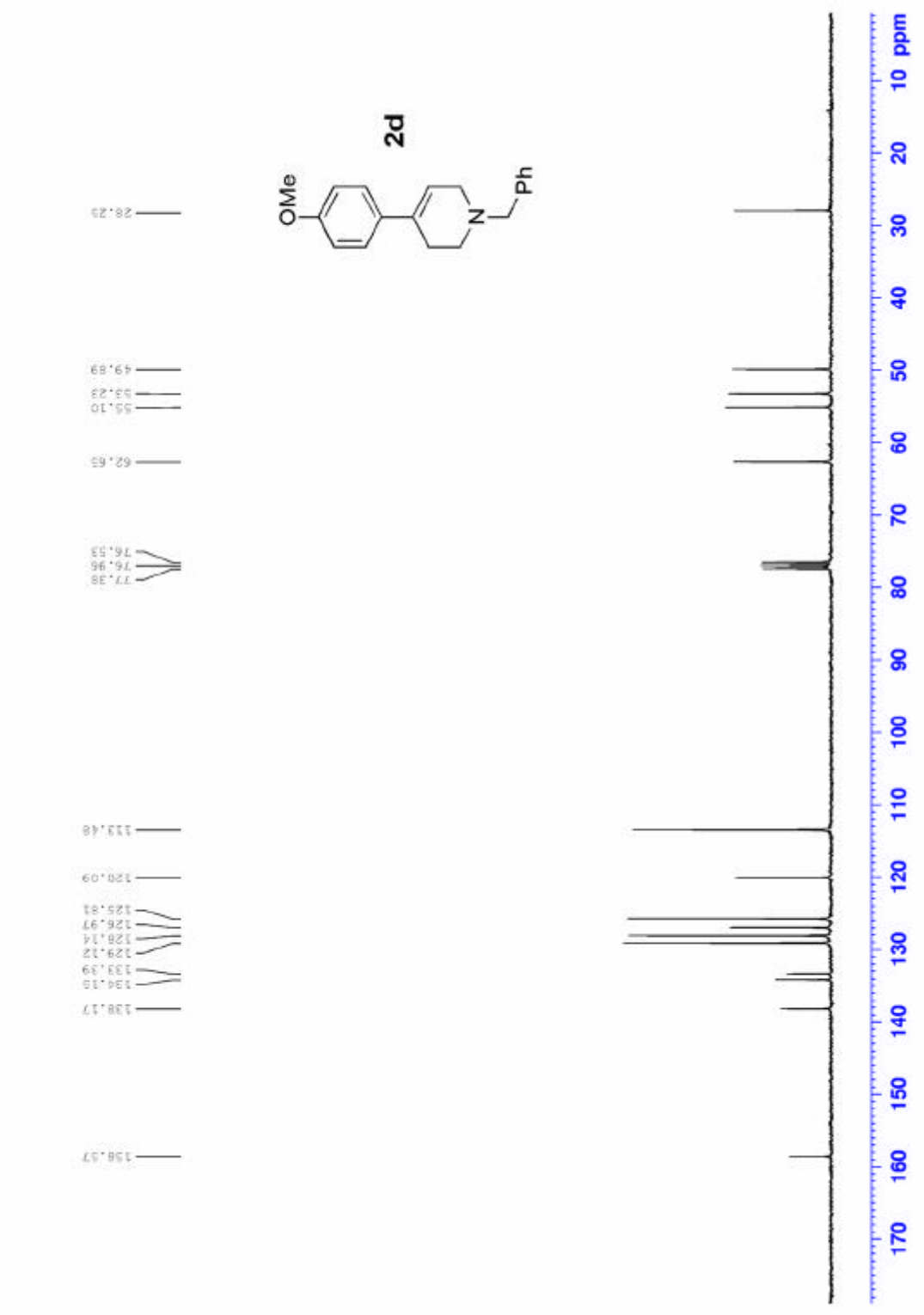
2.04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55.10
62.65
76.53
76.96
77.38
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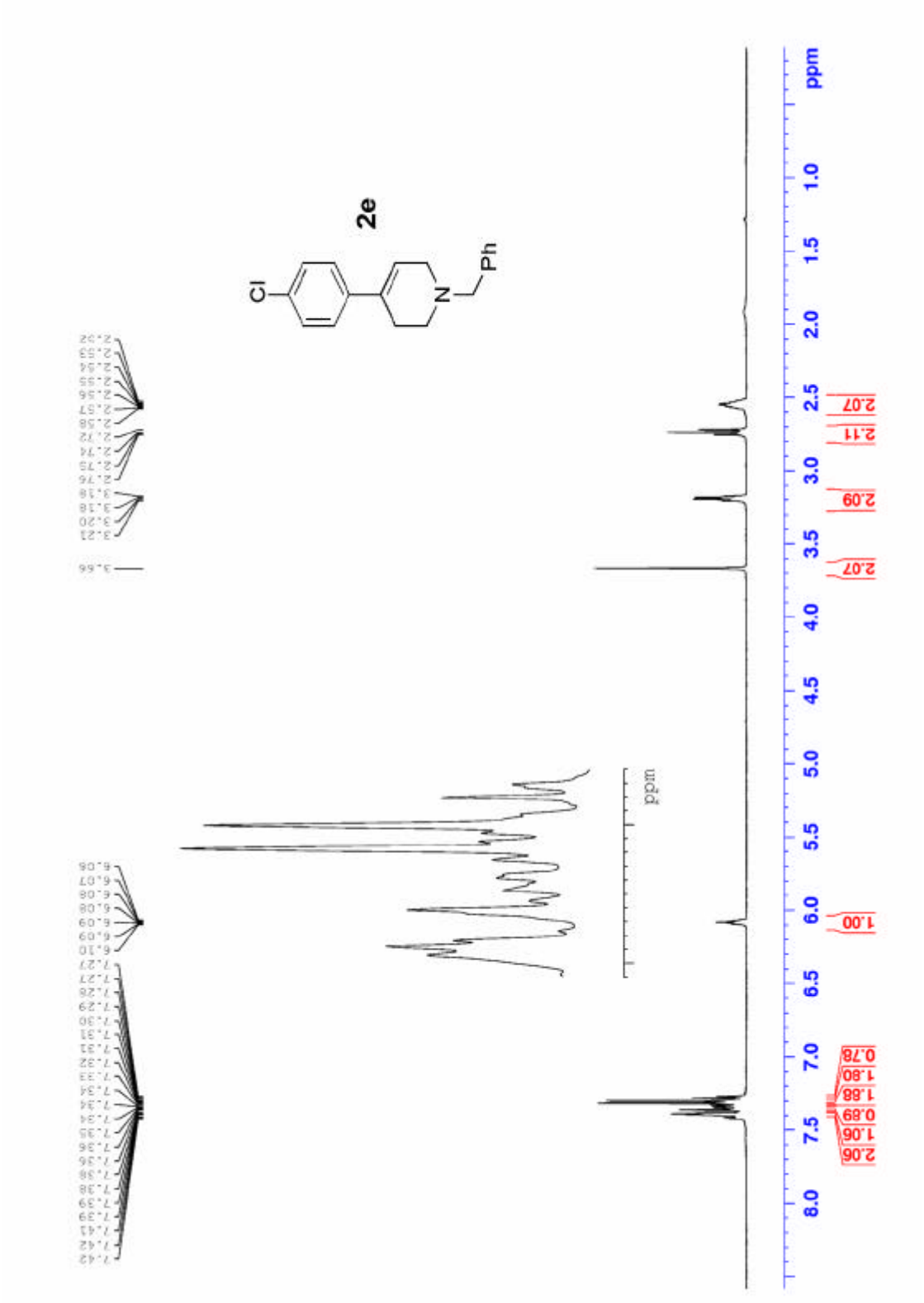
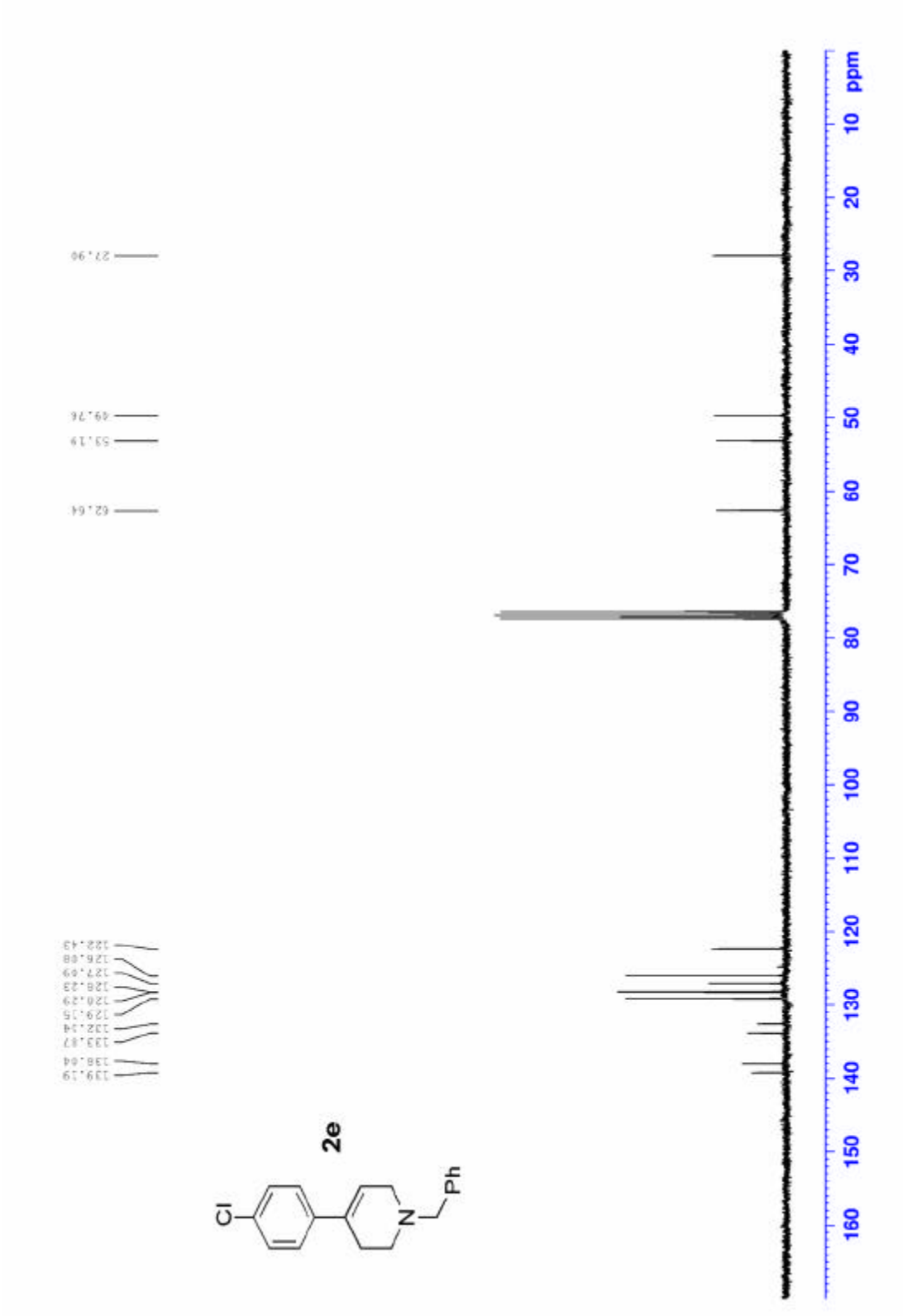
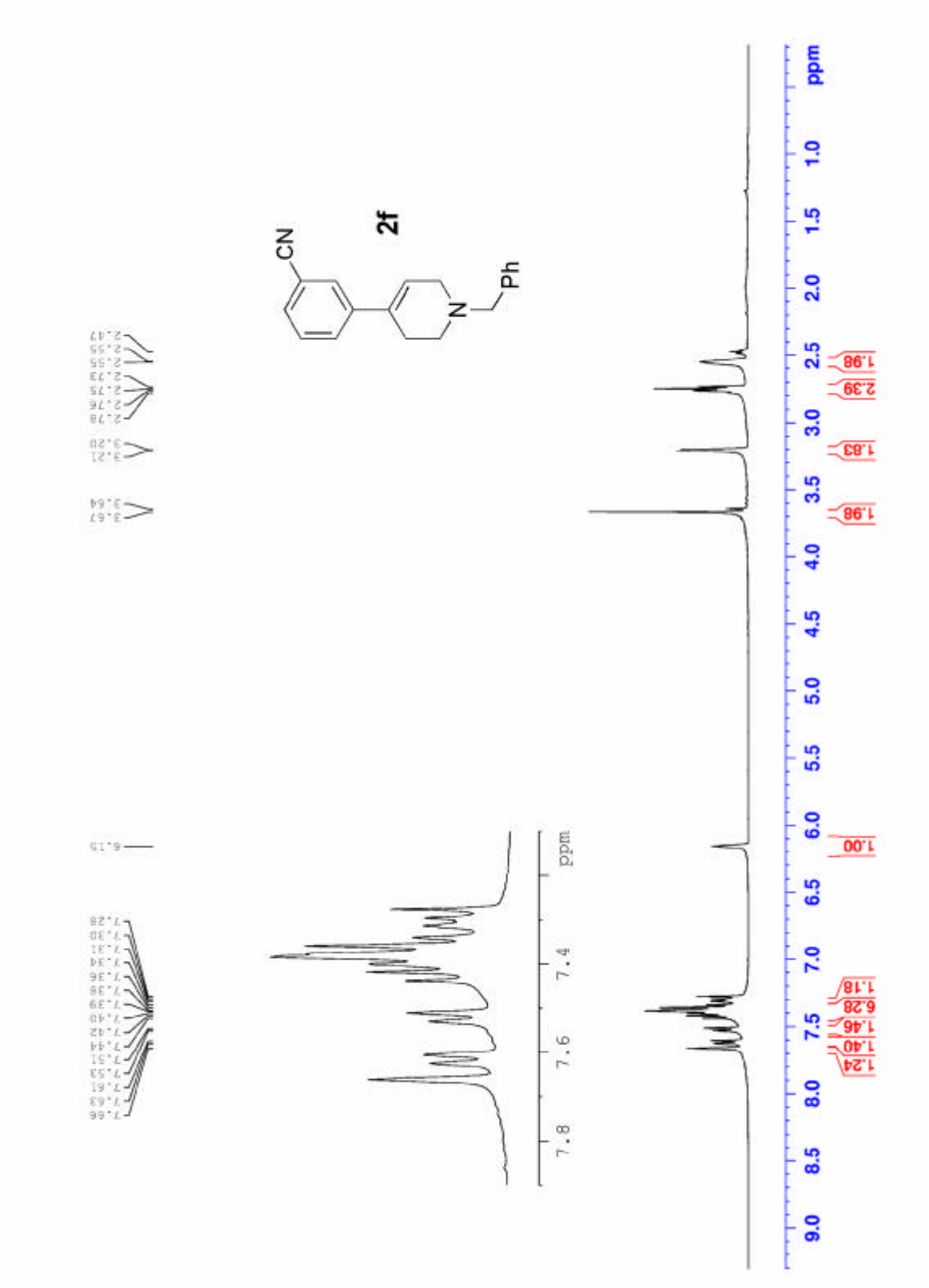
125.83
126.97
128.14
129.12
133.39
136.15
138.17
158.57
10 ppm


2e
Cl
N
Ph
ppm
1.00
2.07
2.11
2.09
2.07
2.06
1.06
0.89
1.88
1.80
0.78


2e
Cl
N
Ph
ppm


2f
CN
Ph
N
ppm
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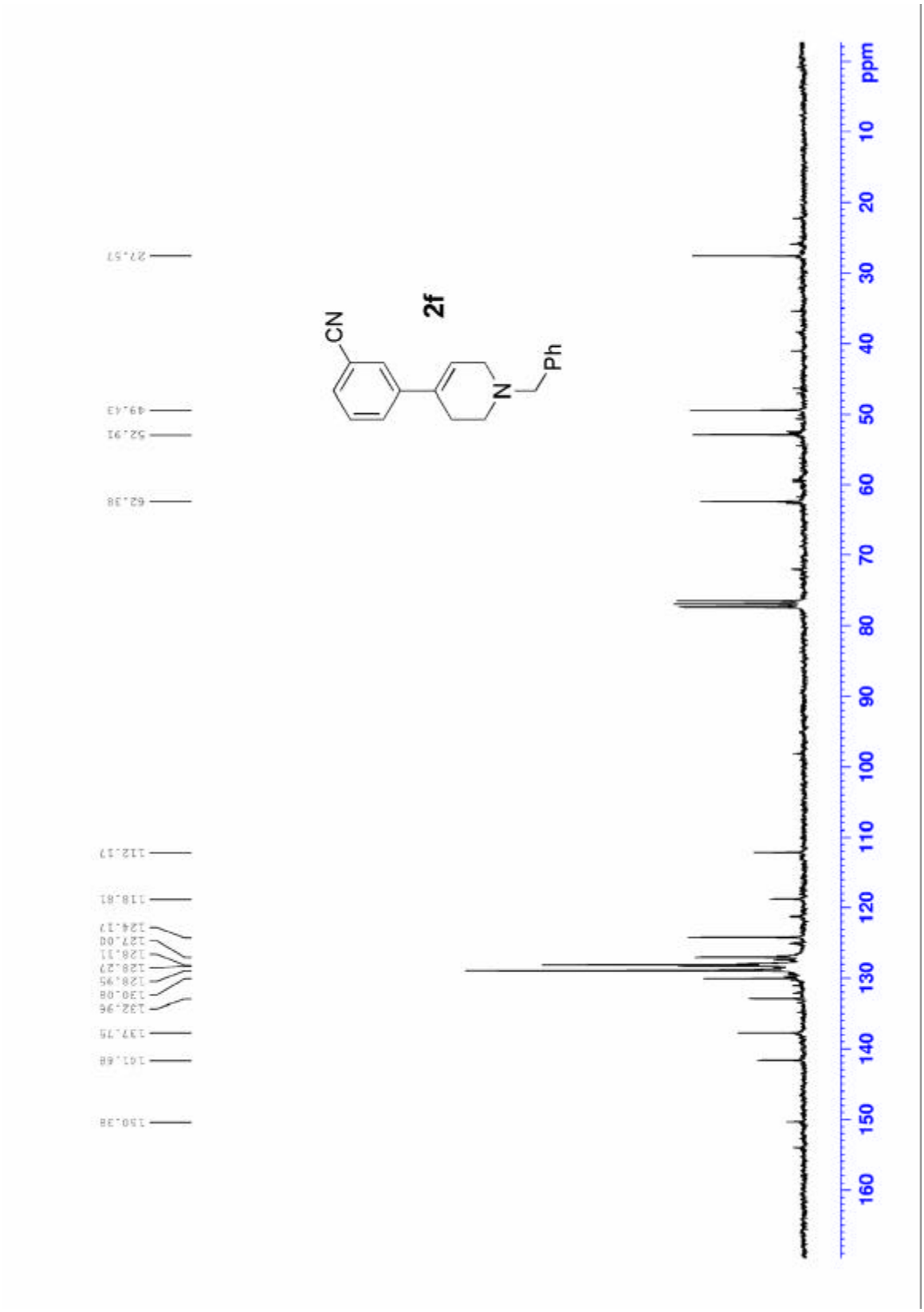
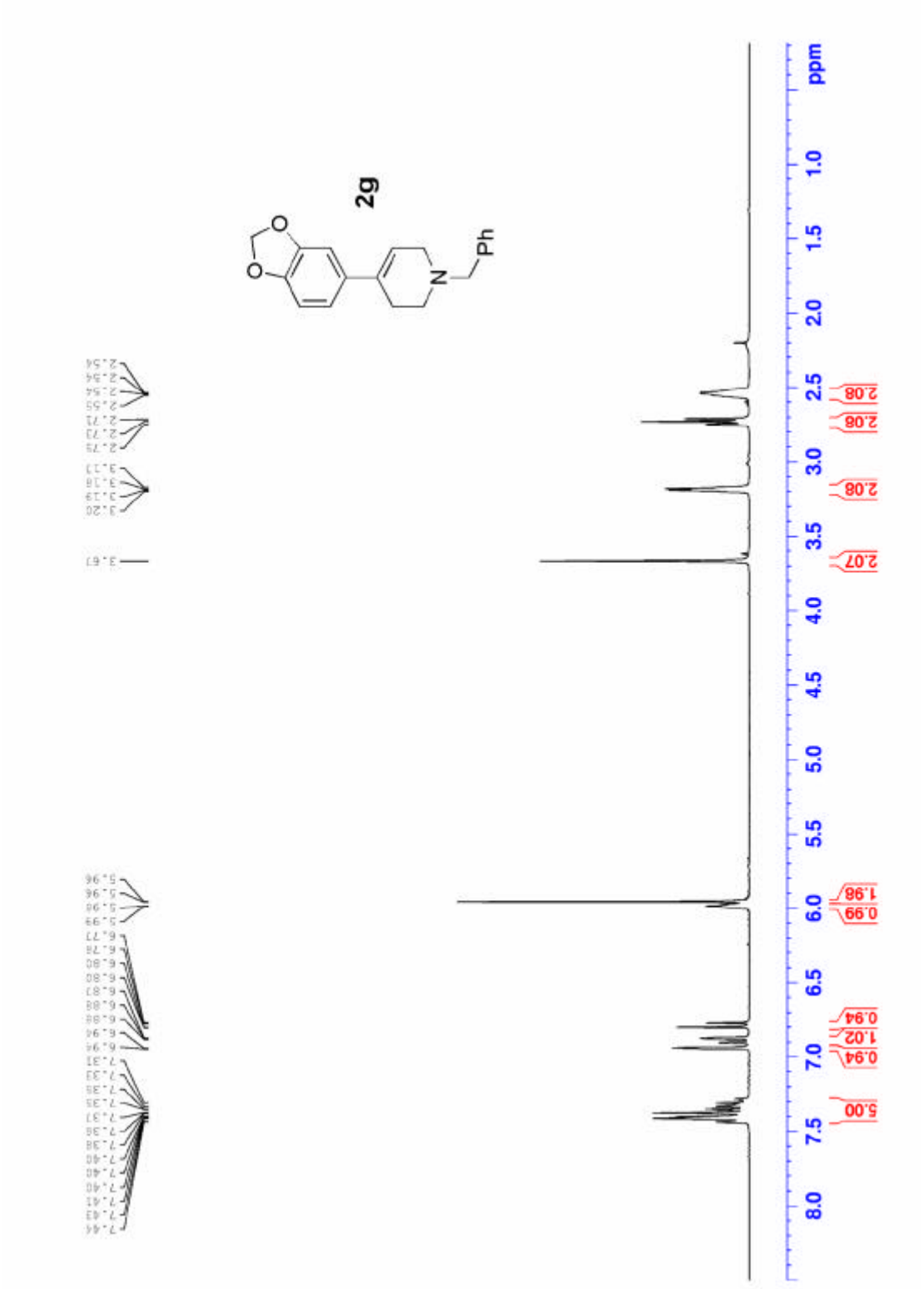
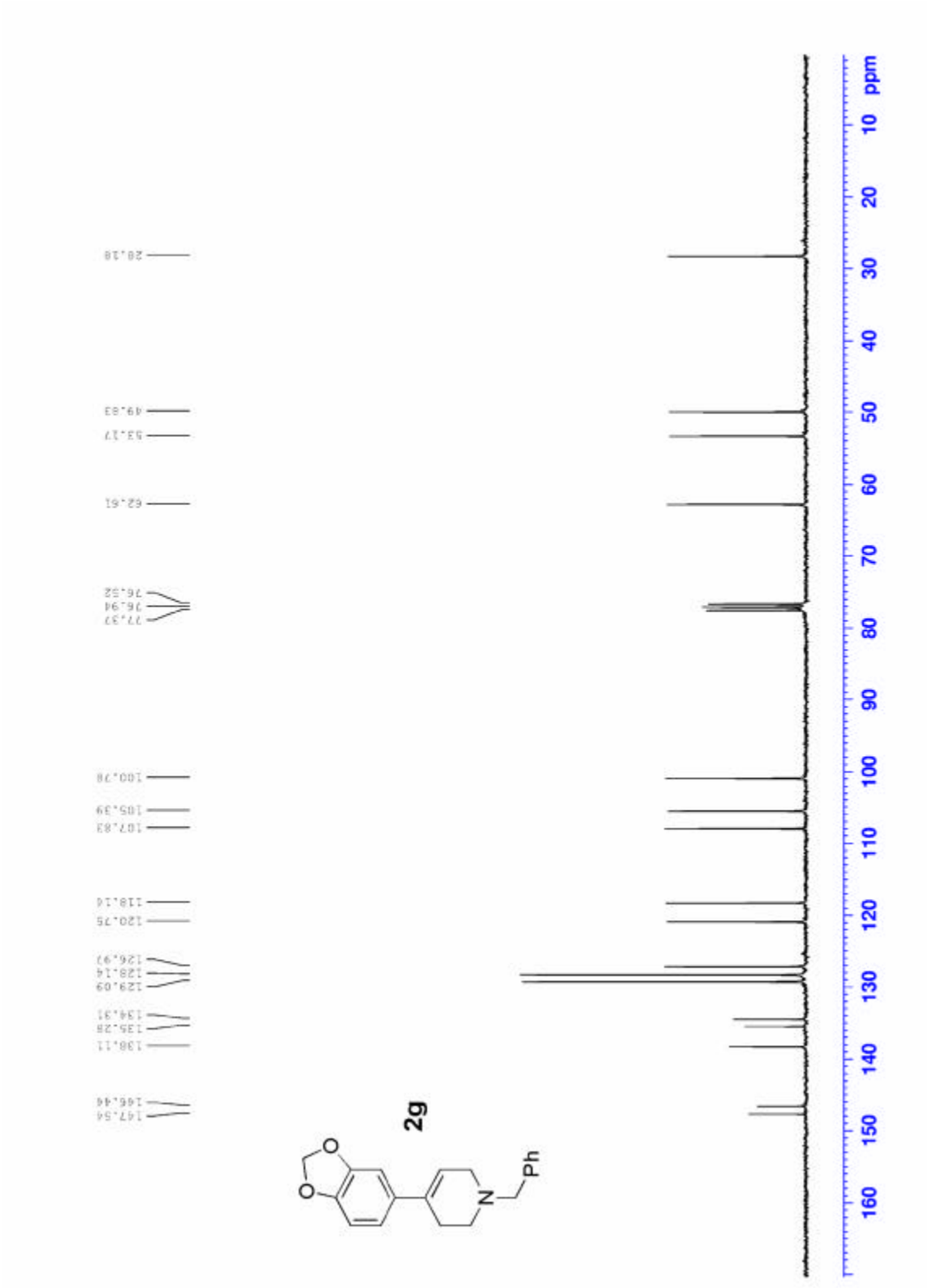
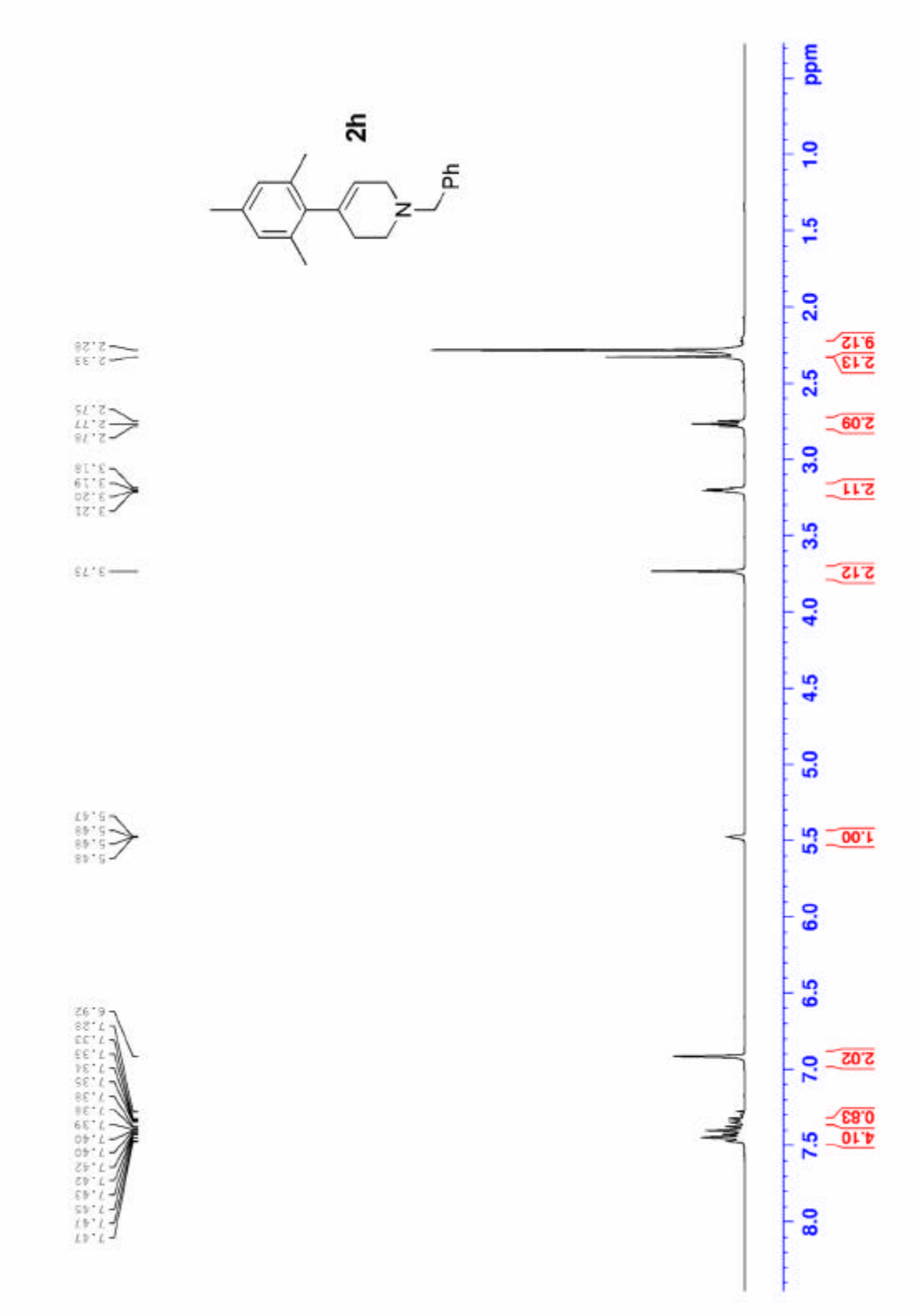
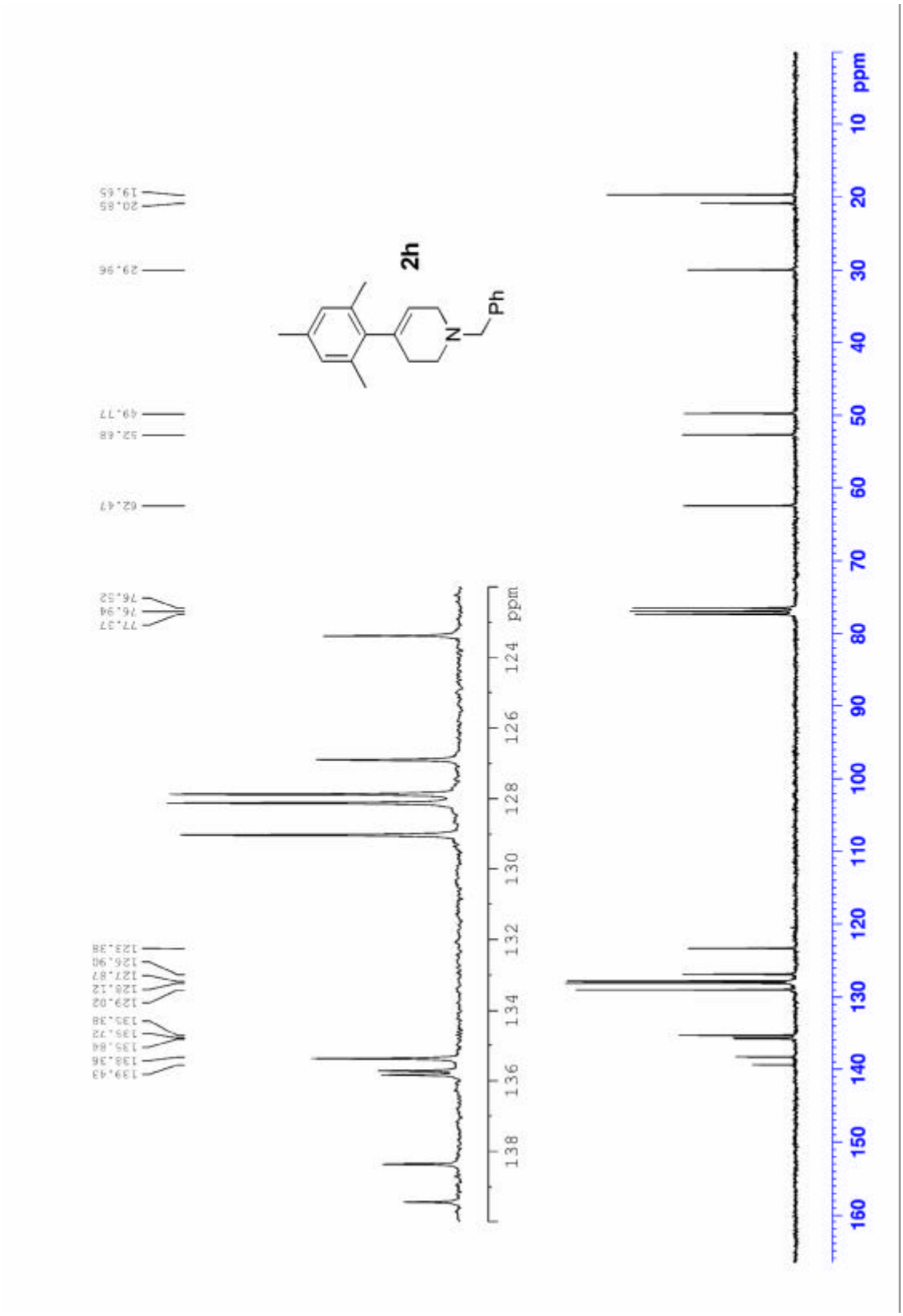
1.24
1.40
1.46
6.28
1.18
1.98
2.39
1.83
1.98

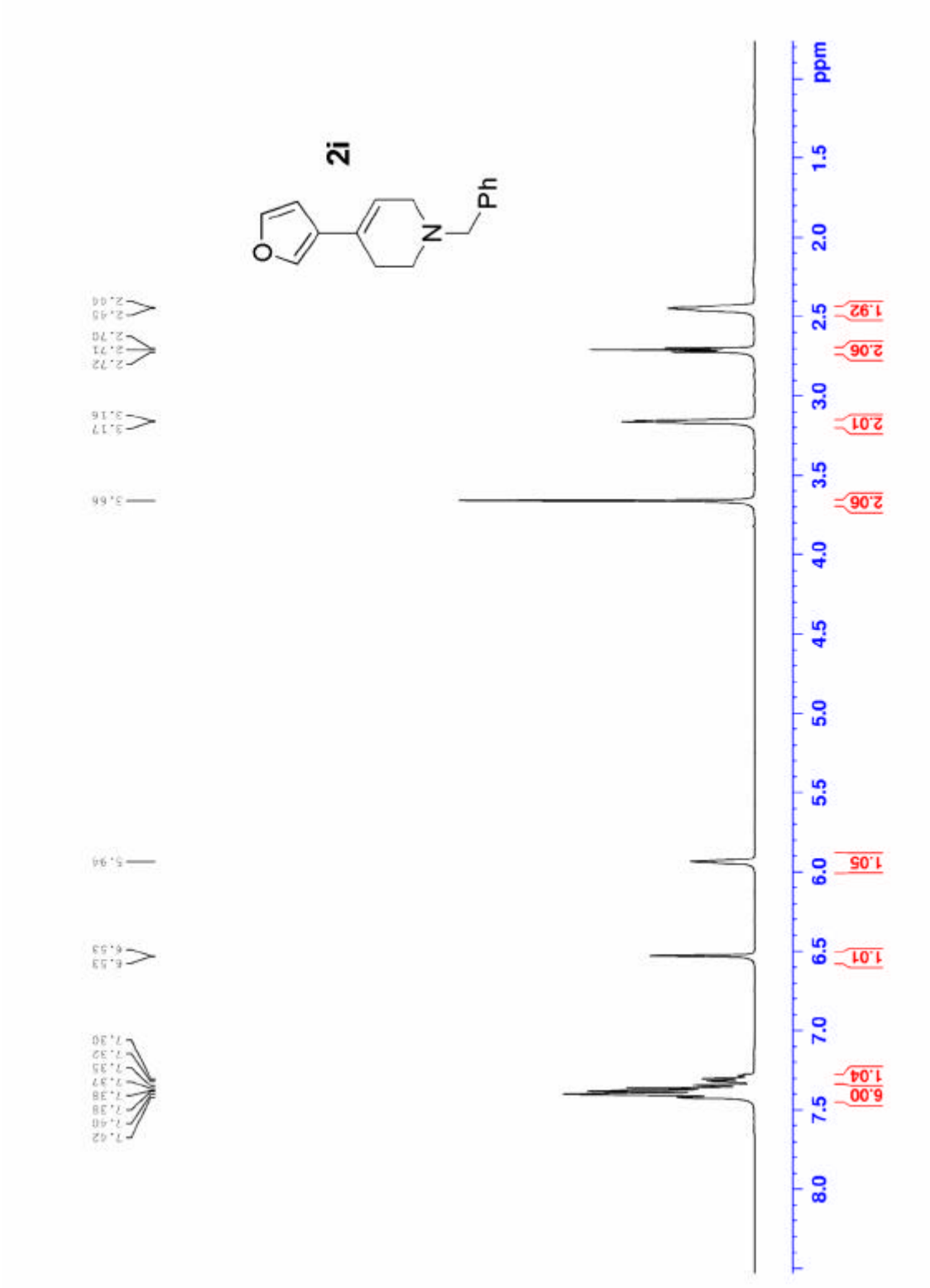

2f
CN
N
Ph
27.57
49.43
52.91
62.38
112.17
118.81
124.17
127.08
128.31
128.27
128.95
130.08
132.96
137.75
141.68
150.38
ppm

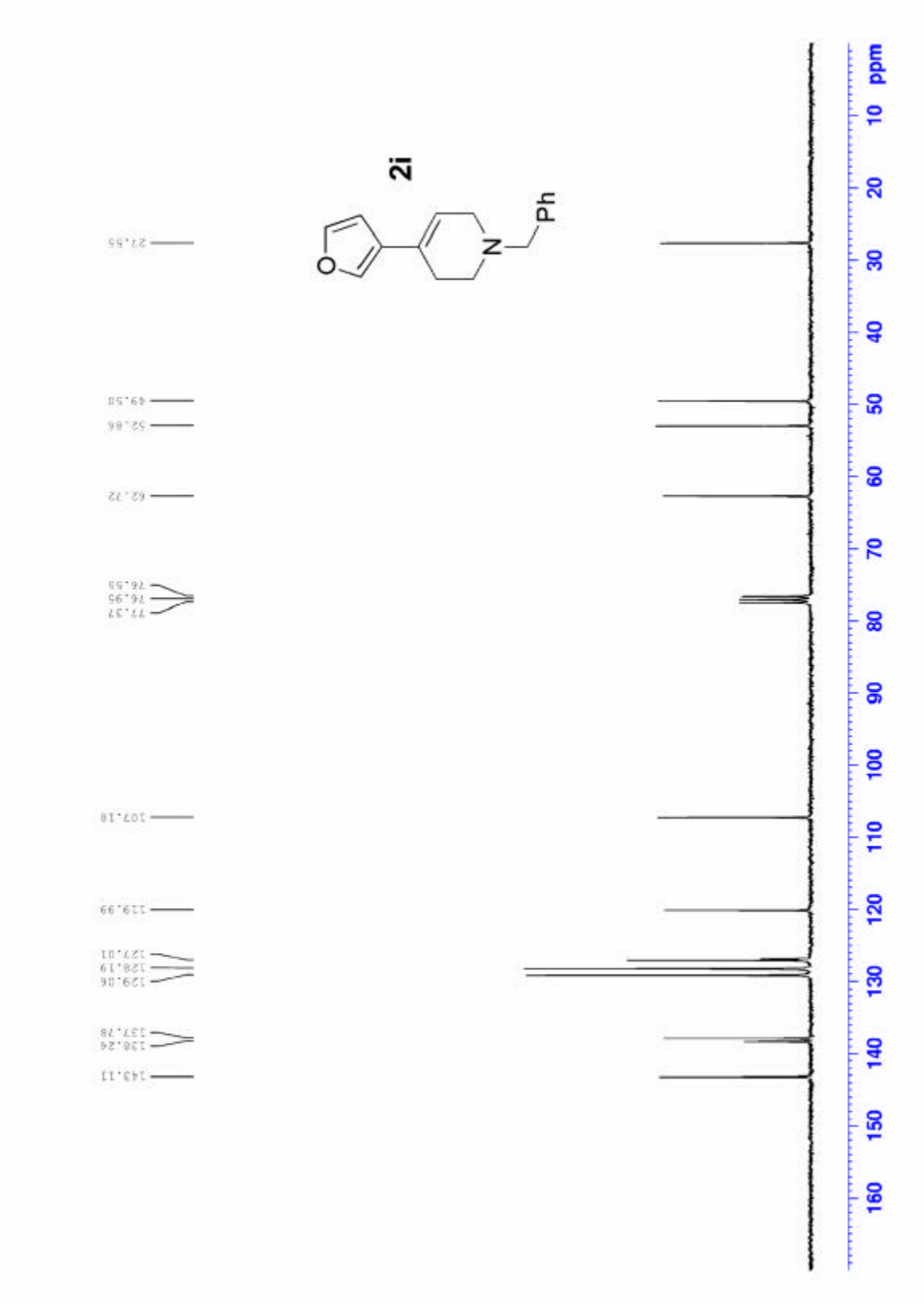

2g
O
O
N
Ph
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
5.00
0.94
1.02
0.94
0.94
1.98
0.99
2.08
2.08
2.08
2.07

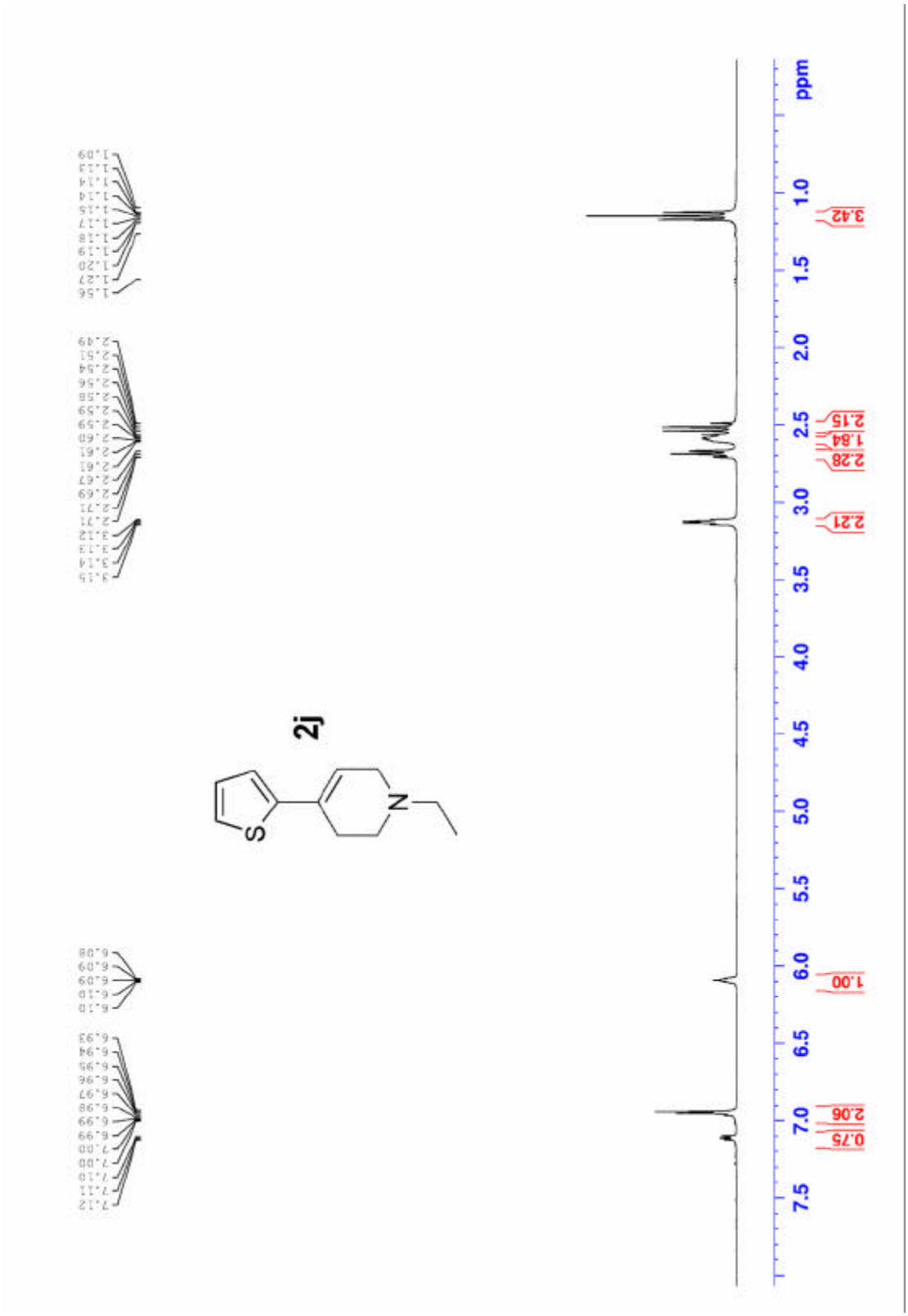

20.18
49.83
53.17
62.61
76.32
76.94
77.37
100.78
105.39
107.83
118.14
120.75
126.97
128.14
129.09
134.31
135.28
138.11
166.46
167.54
2g
O
O
N
Ph
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
ppm

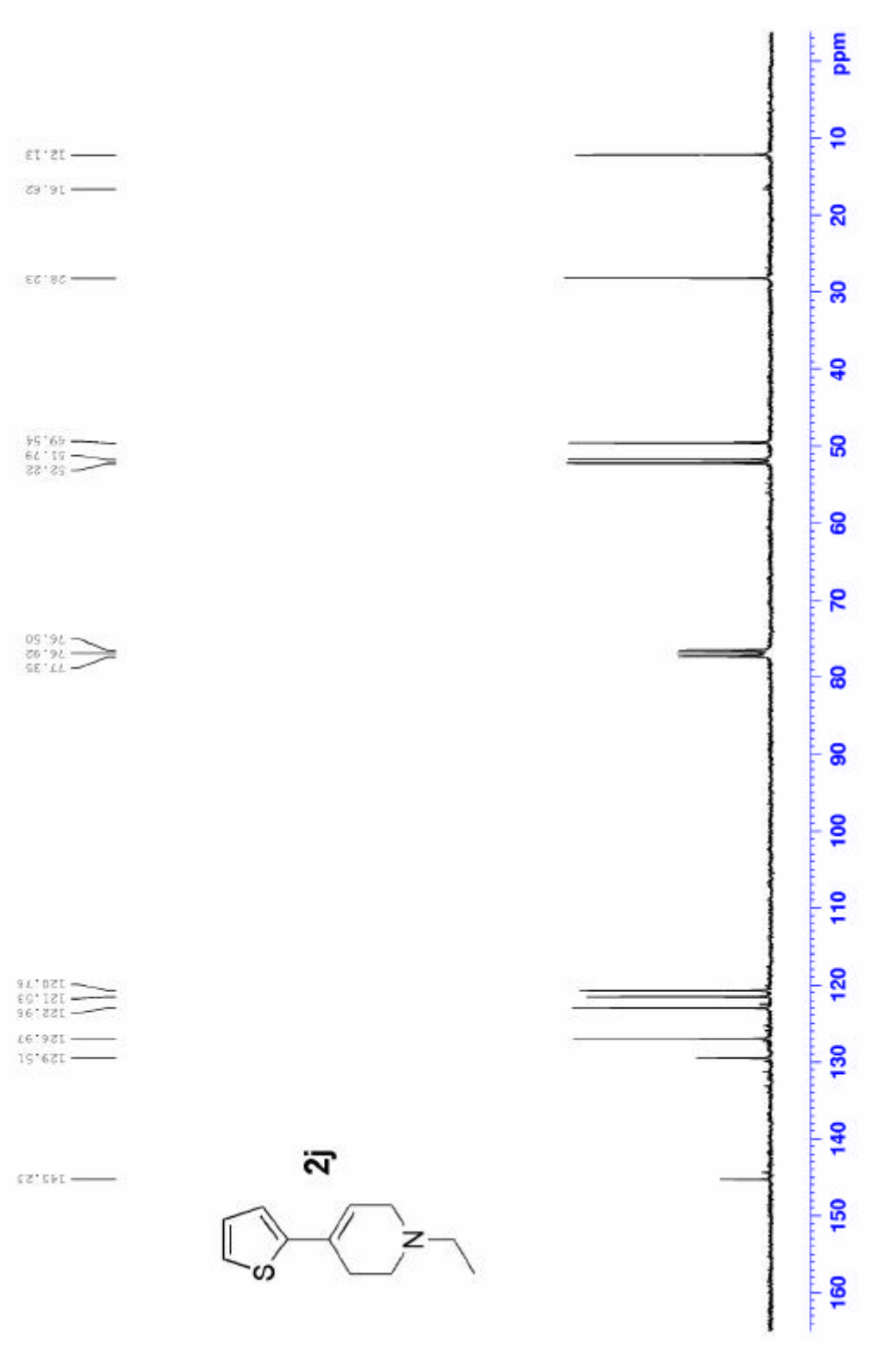

2h
Ph
N
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
9.12
2.13
2.09
2.11
2.12
1.00
2.02
0.83
4.10

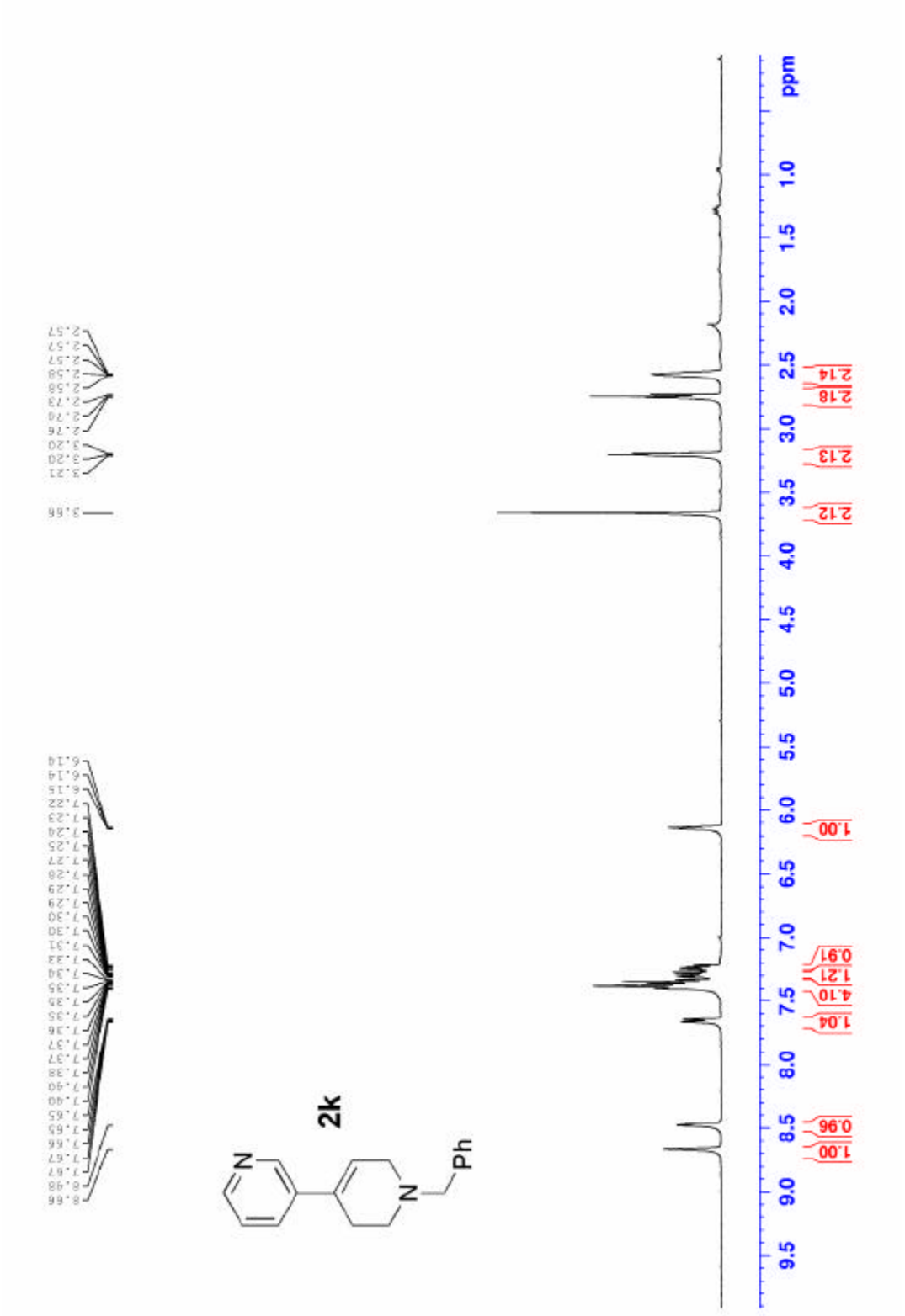

2h
Ph
N
ppm

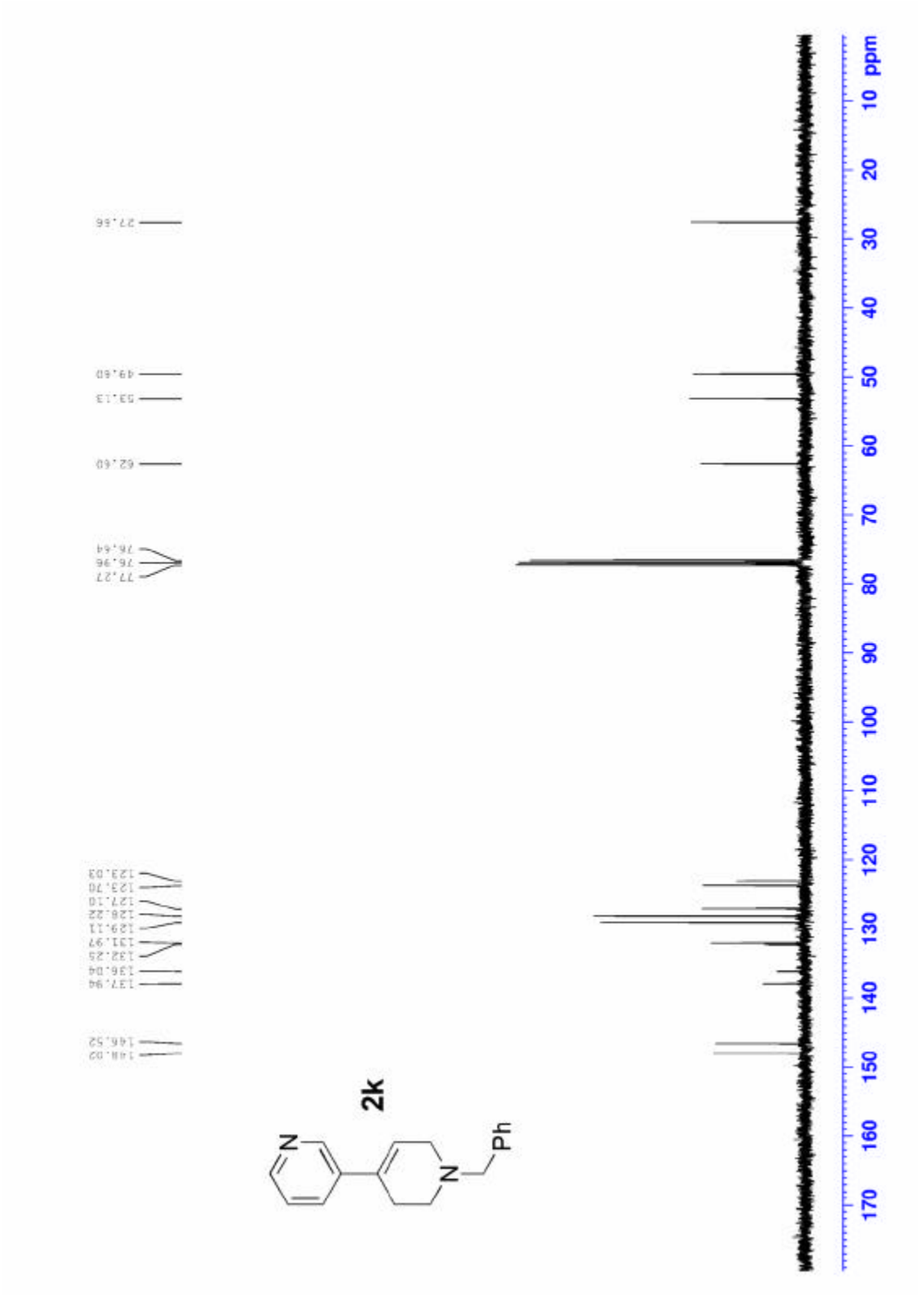

2i
Ph
N
O
ppm
1.92
2.06
2.01
2.06
1.05
1.01
1.04
6.00
2.64
2.45
2.72
2.71
2.70
3.17
3.16
3.66
5.94
6.53
6.53
7.42
7.40
7.38
7.38
7.37
7.35
7.32
7.30

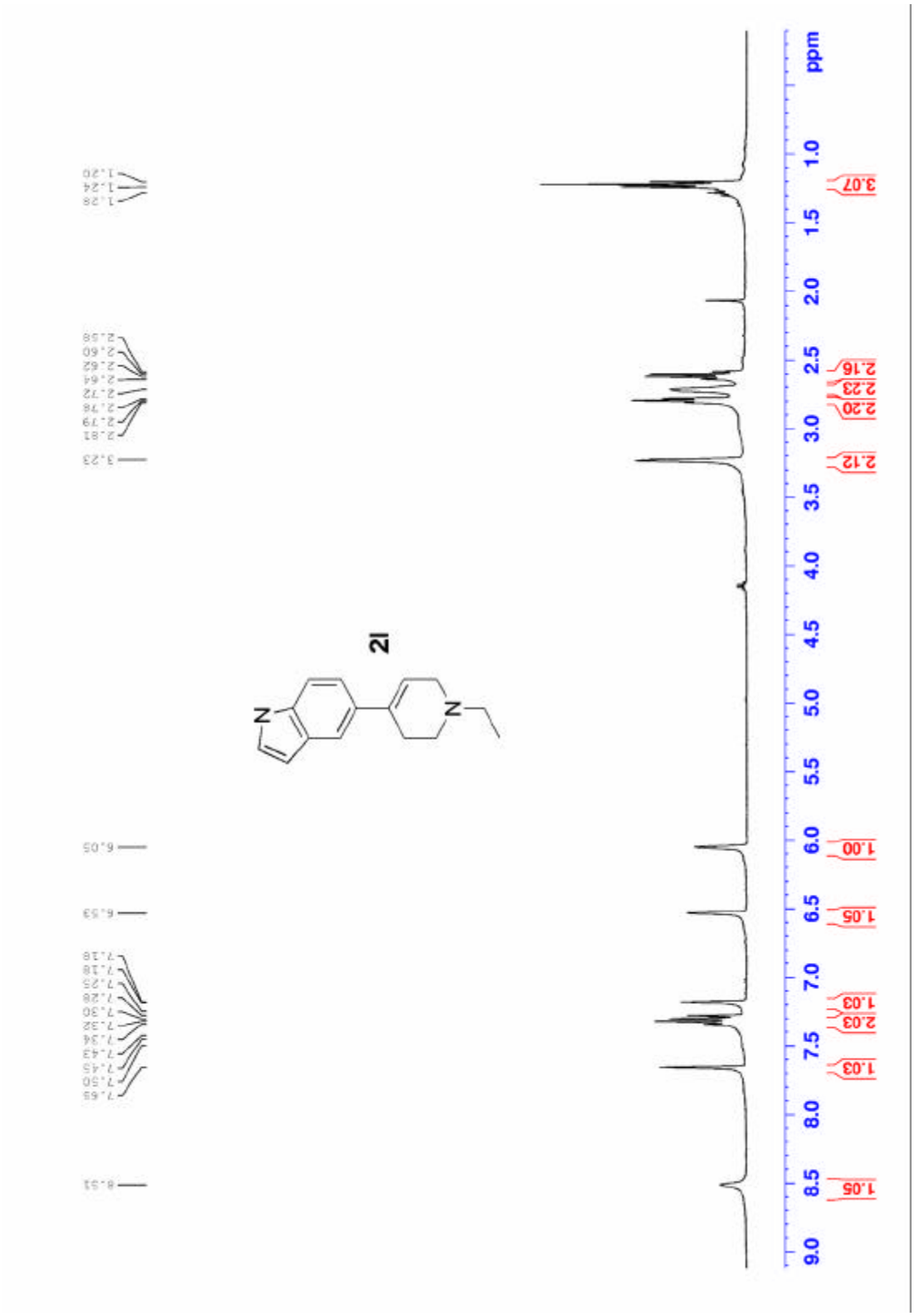

2i
O
N
Ph
143.11
138.24
137.78
129.06
128.19
127.01
119.99
107.18
77.37
76.95
76.55
62.72
52.86
49.58
27.55
ppm

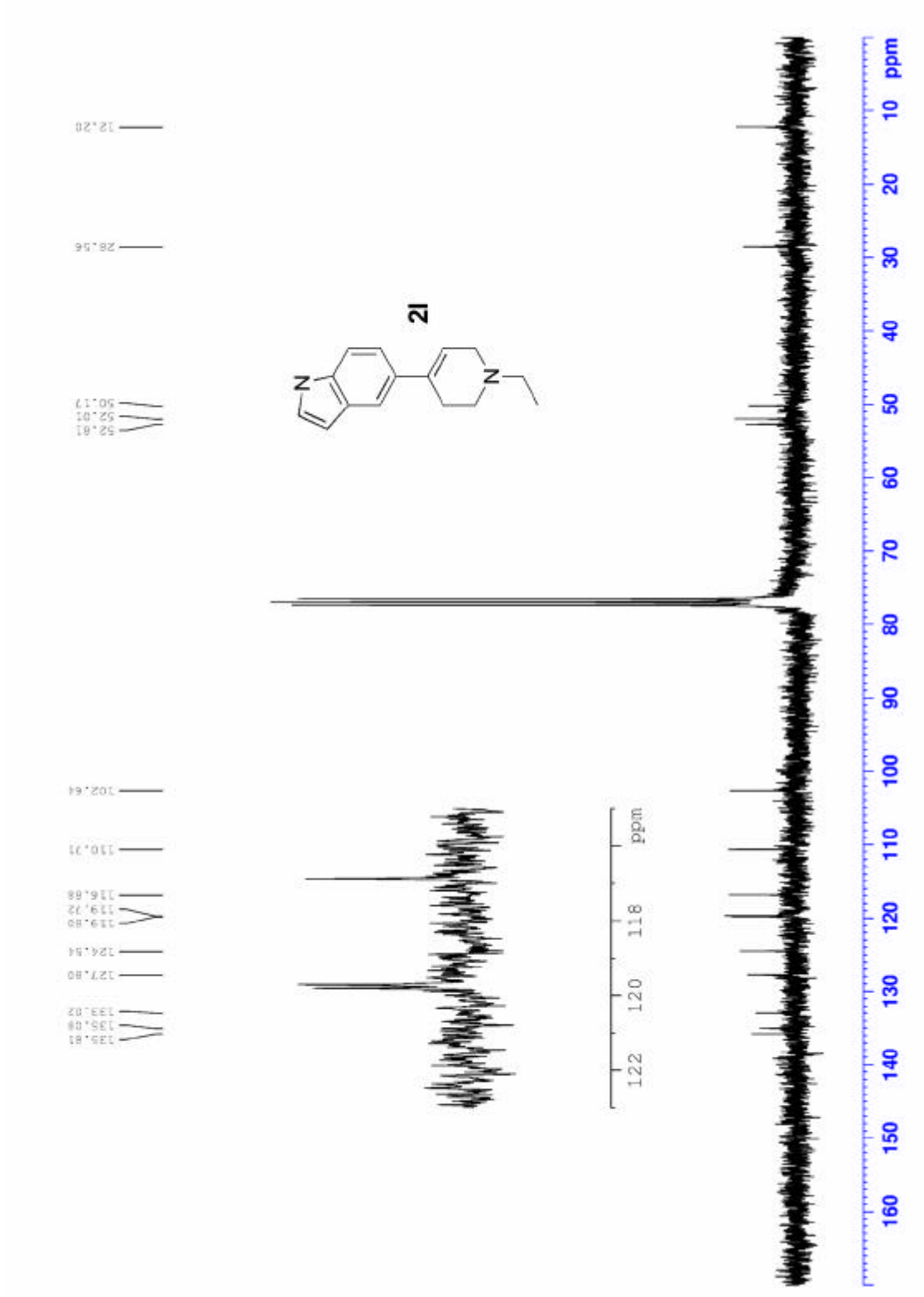

2j
S
N
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
3.42
2.15
1.84
2.28
2.21
1.00
0.75
2.06

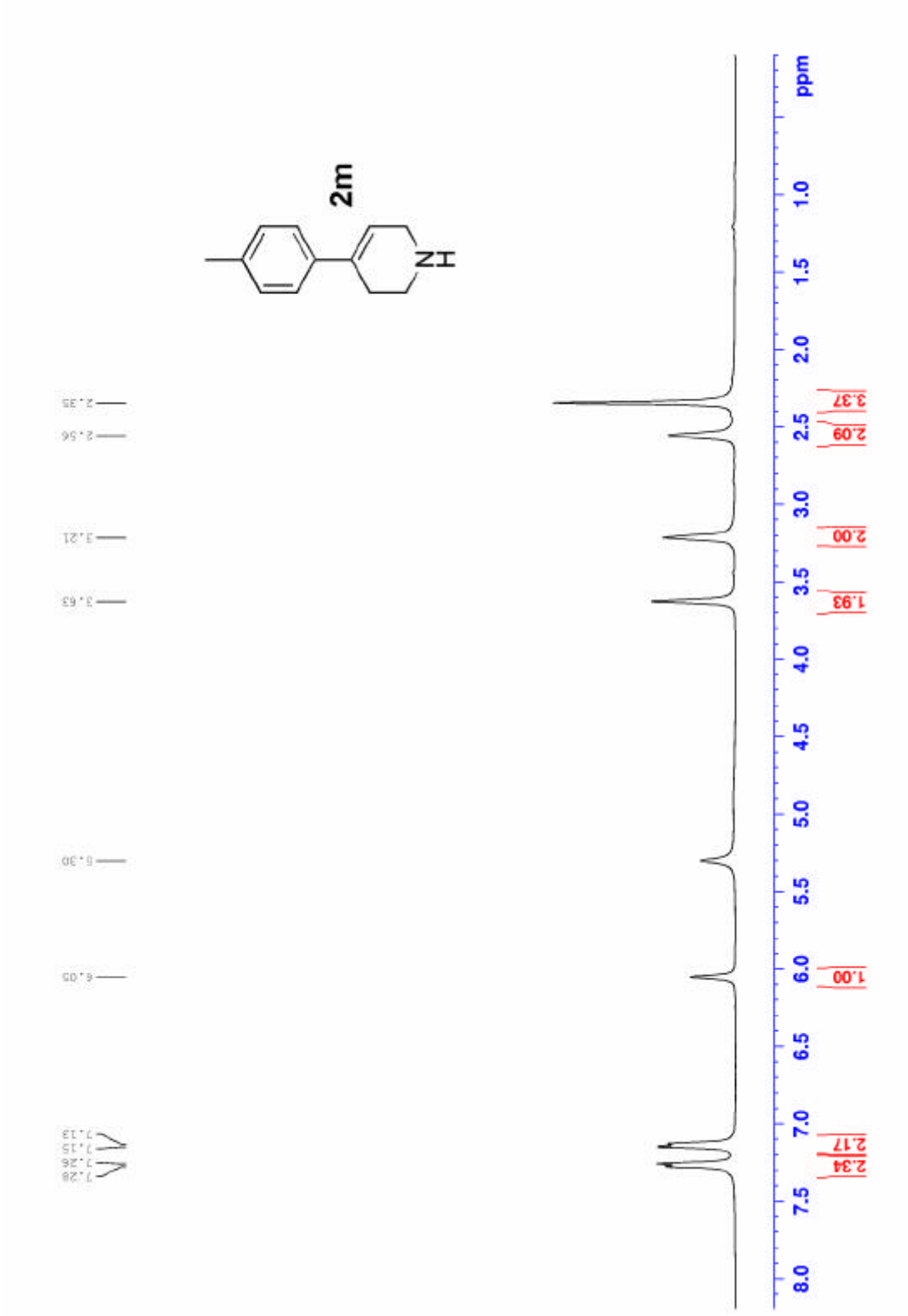

12.13
16.62
28.23
49.54
51.79
52.22
76.50
76.92
77.35
120.76
121.03
122.96
126.97
129.51
143.23
2j
S
N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160


2k
N
N
Ph
ppm
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
1.00
0.96
1.00
1.04
4.10
1.21
0.91
1.00
2.12
2.13
2.18
2.14


2k
N
N
Ph
148.05
146.52
137.94
136.04
132.25
131.97
129.11
128.22
127.10
123.70
123.03
77.27
76.96
76.64
62.60
53.13
49.60
27.66
10 ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170


2l
N
N
ppm
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
1.05
1.03
2.03
1.03
1.05
1.00
2.12
2.20
2.23
2.16
3.07
8.51
7.65
7.50
7.45
7.43
7.34
7.32
7.30
7.28
7.25
7.18
7.18
6.53
6.05
3.23
2.81
2.79
2.78
2.72
2.64
2.62
2.60
2.58
1.28
1.24
1.20


2l
12.20
28.56
50.17
52.01
52.61
102.64
110.31
116.88
119.22
119.80
124.54
127.80
133.02
135.09
135.81
ppm
122
120
118
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160


2m
NH
ppm
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2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
3.37
2.09
2.00
1.93
1.00
2.17
2.34
2.35
2.56
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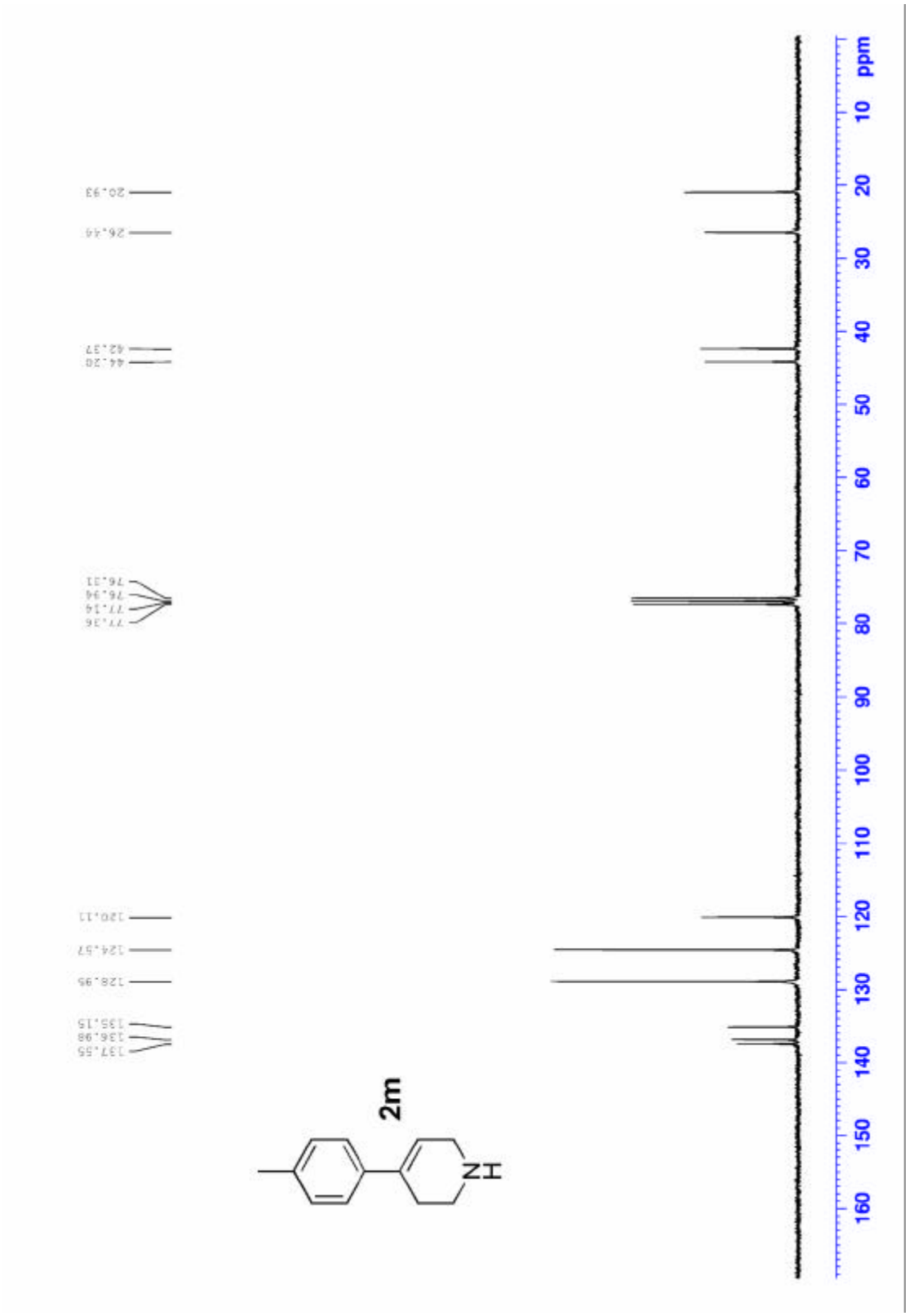
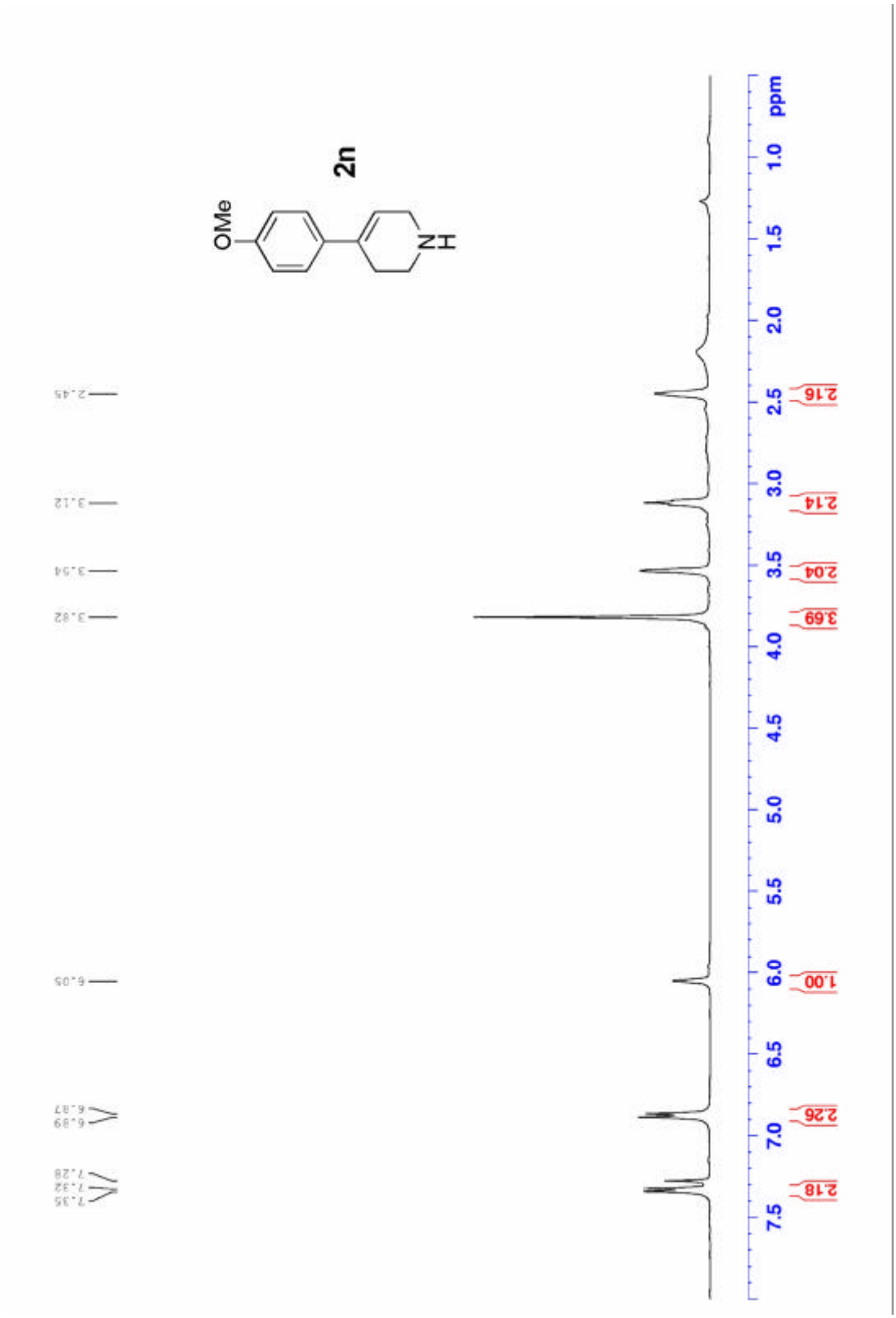
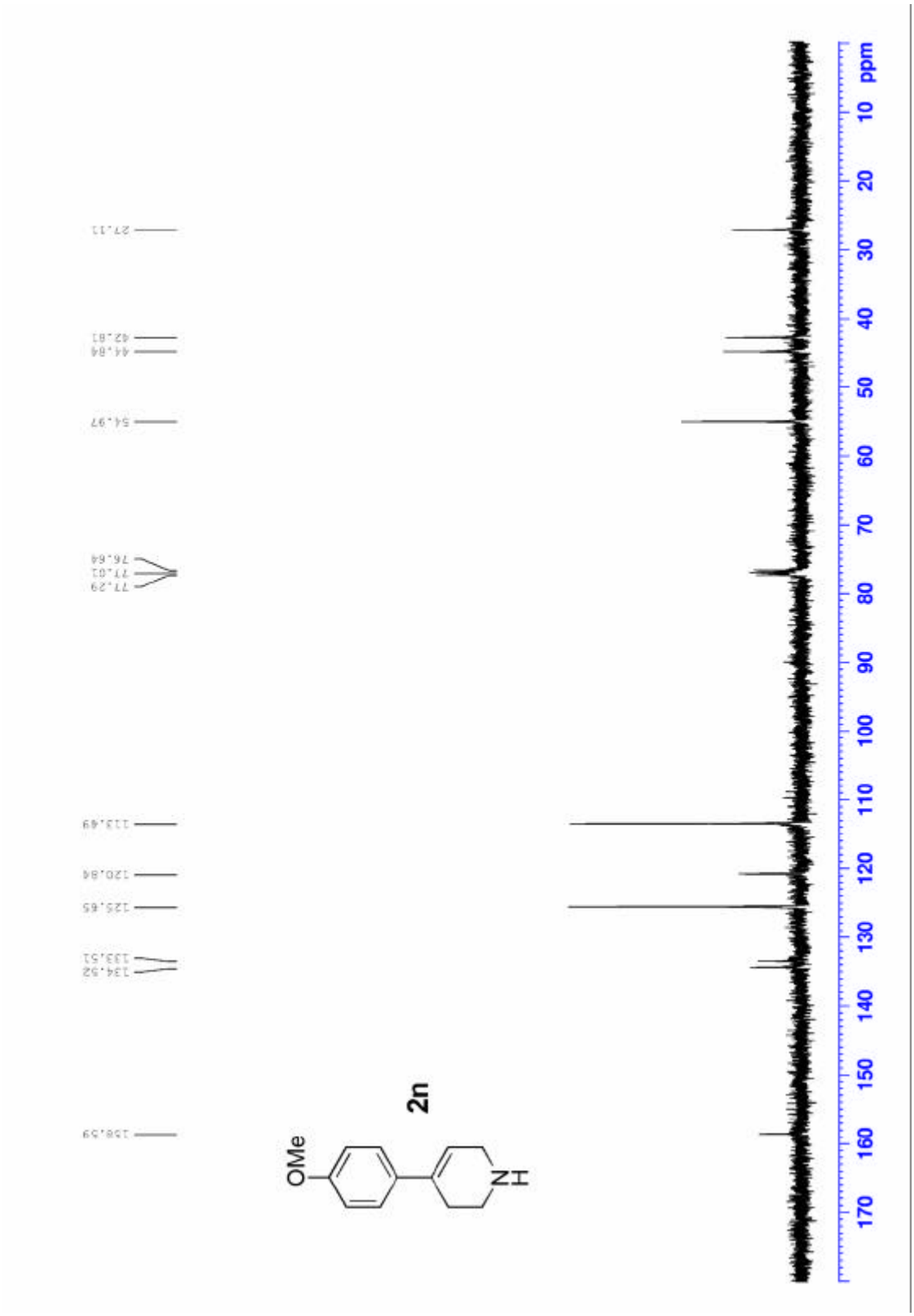
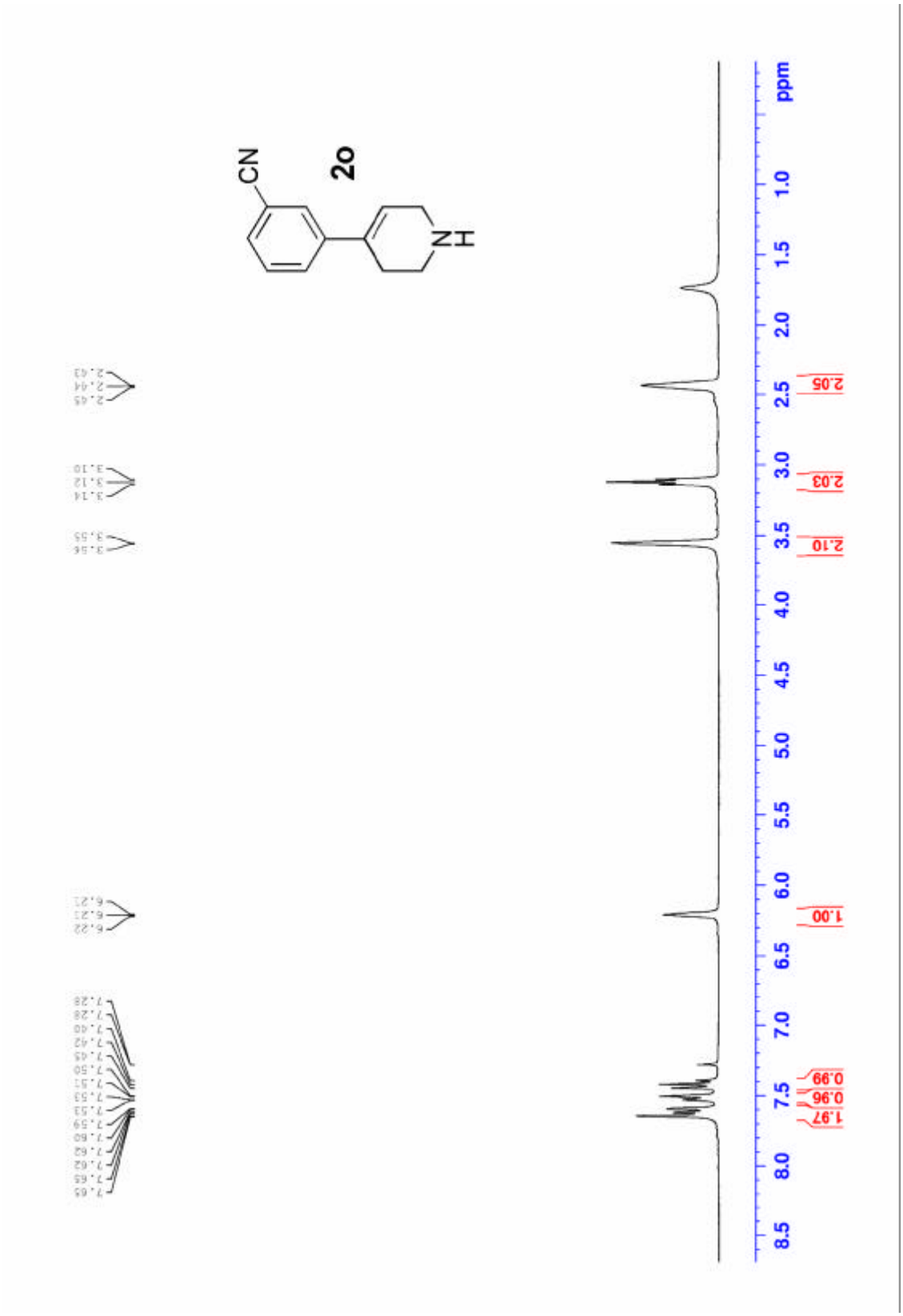
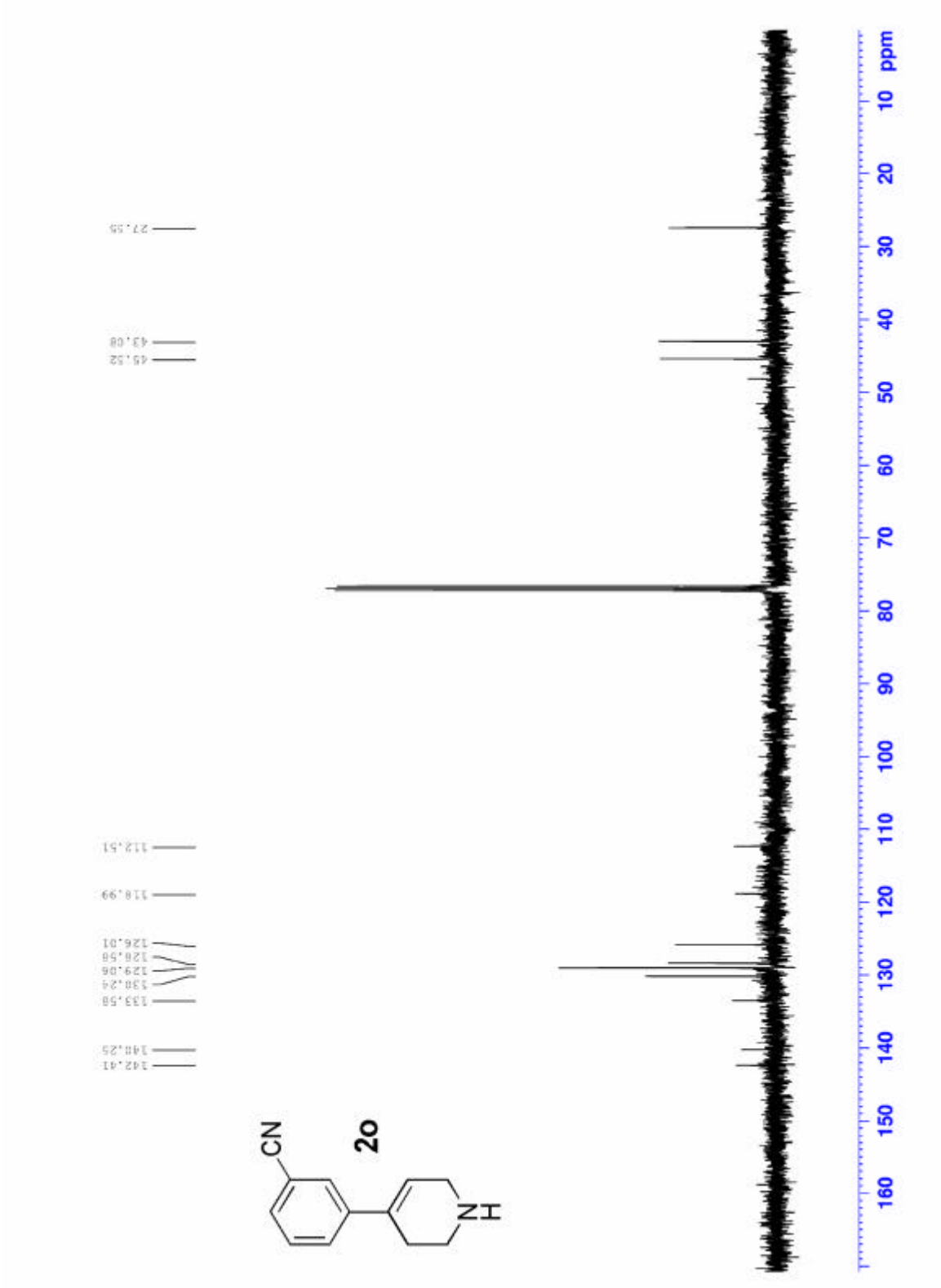
6.30
6.65
7.13
7.15
7.26
7.28


20.93
26.49
42.37
44.20
76.31
76.94
77.19
77.36
120.11
124.57
128.95
135.15
136.98
137.55
2m
NH
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160

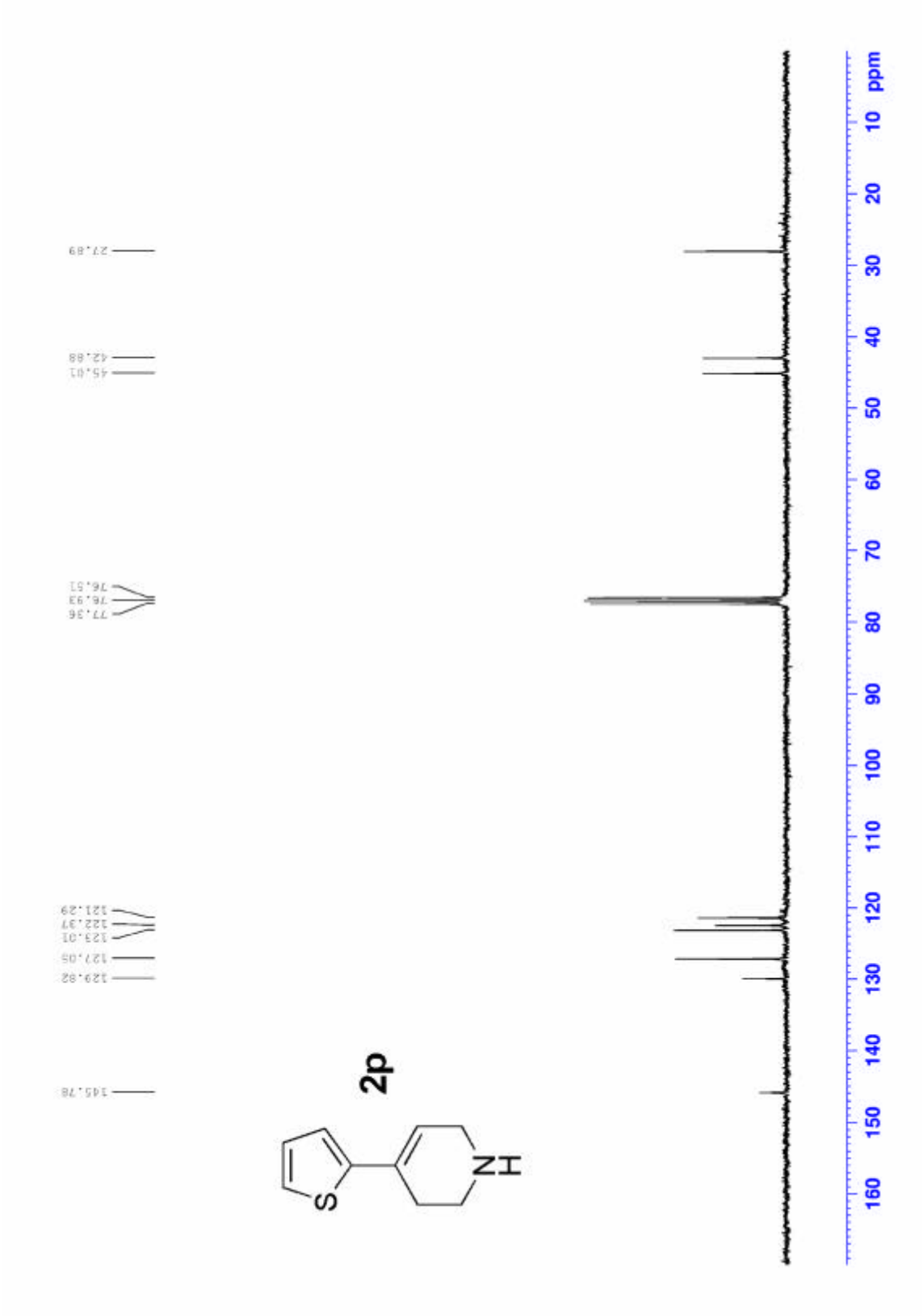

2n
OMe
NH
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
2.16
2.14
2.04
3.69
1.00
2.26
2.18
2.45
3.12
3.54
3.82
6.05
6.87
6.89
7.28
7.32
7.35

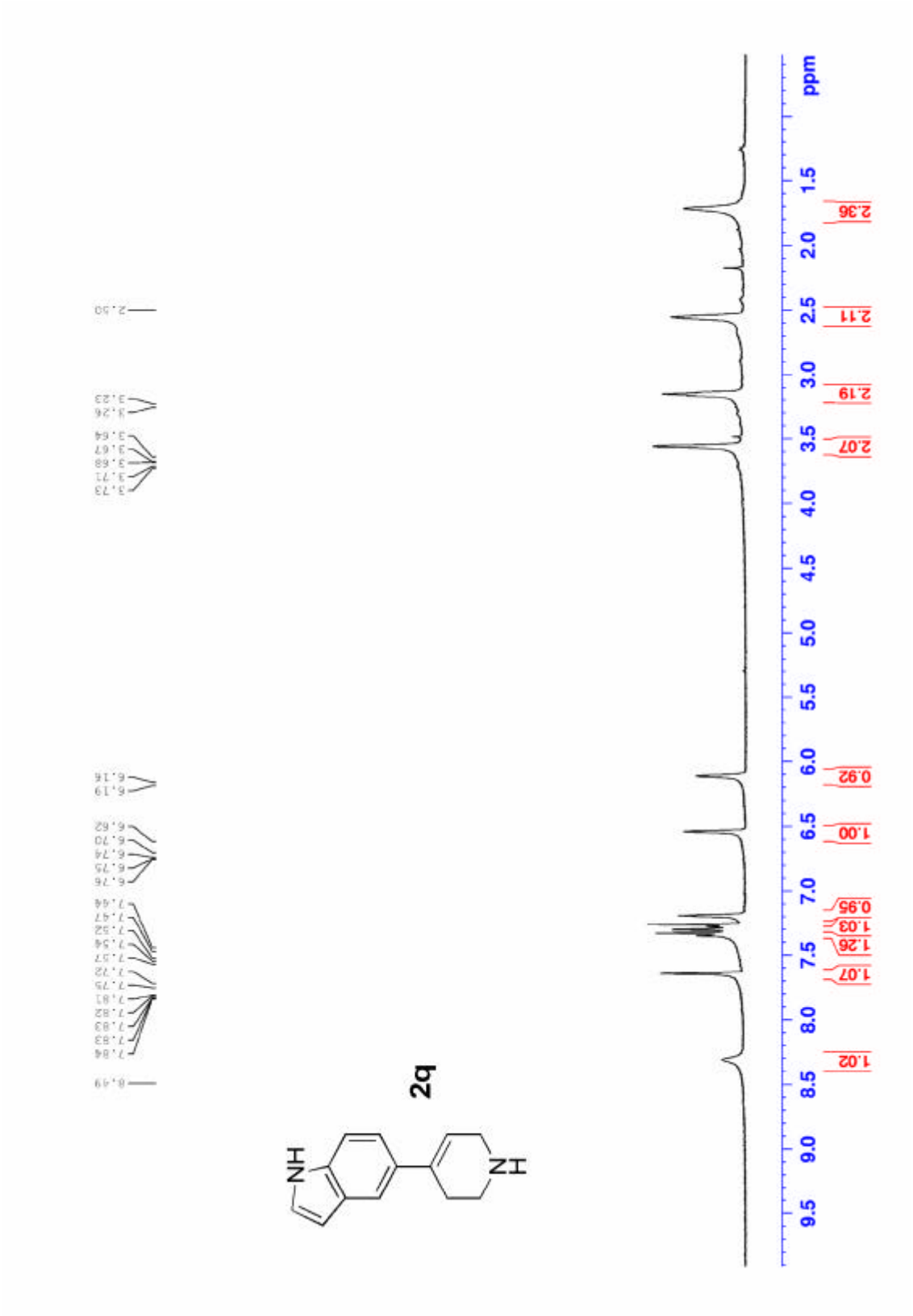

27.11
42.81
44.84
54.97
76.64
77.01
77.29
113.49
120.84
125.65
133.51
134.52
136.59
2n
OMe
NH
ppm


CN
2o
NH
ppm
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
2.05
2.03
2.10
1.00
0.99
0.96
1.97


27.55
43.08
45.52
112.51
118.99
126.01
128.58
129.06
130.25
133.58
140.25
142.41
CN
2o
NH
ppm


2p
S
NH
2.65
3.08
3.49
6.14
6.99
7.11
7.26
1.96
2.05
1.96
0.98
1.55
1.09
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5


2p
NH
S
145.78
129.82
127.05
123.01
122.37
121.29
77.36
76.93
76.51
45.01
42.88
27.89
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160


2q
NH
NH
ppm
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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
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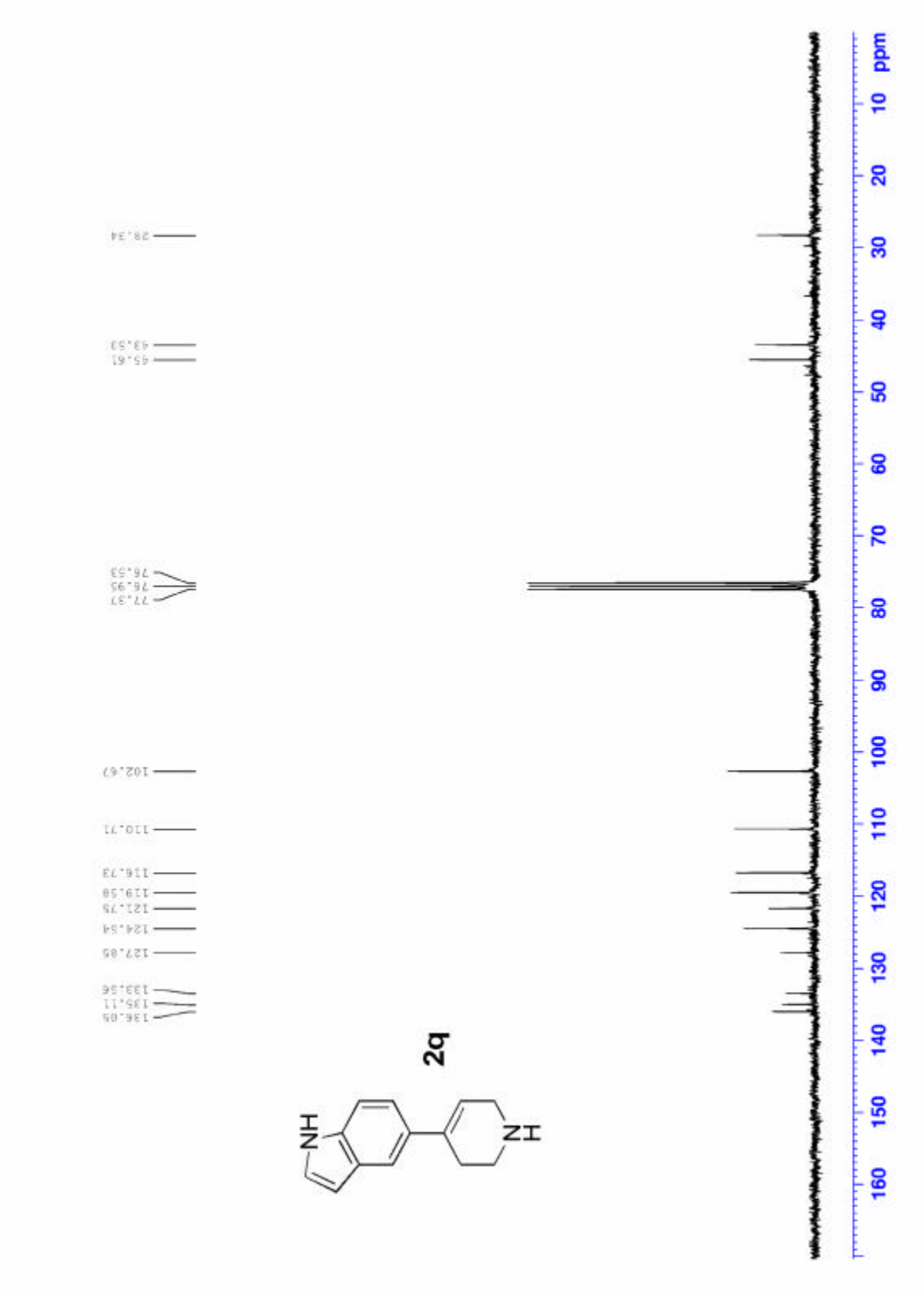
2.11
2.19
2.07
0.92
1.00
0.95
1.03
1.26
1.07
1.02


28.34
45.61
53.53
76.53
76.95
77.37
102.67
110.71
116.73
119.50
121.79
124.54
127.05
133.56
135.11
136.05
2q
NH
N
H
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160