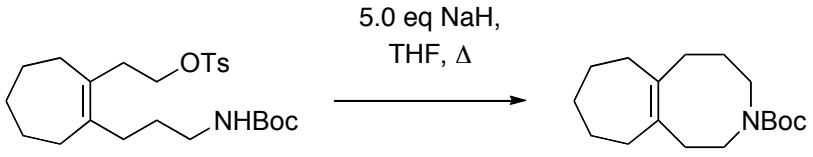
Experimental

General techniques: All reactions requiring anhydrous conditions were conducted in flame-dried glass apparatus under an atmosphere of N_2. THF was freshly distilled from sodium benzophenone ketyl prior to use. Preparative chromatographic separations were performed on Fluka silica gel 60 (35-70 μm, 220-440 mesh) and reactions followed by thin layer chromatography (TLC) analysis using Merck aluminum-backed kieselgel 60 plates (2-25 μm) with fluorescent indicator (254 nm) and visualised with UV, iodine, phosphomolybdic acid, basic $KMnO_4$ or ninhydrin. All commercially available reagents were purchased from Aldrich and were used as received unless otherwise noted. Commercial NaH (as a 55-60% dispersion in oil) was washed with pentane (2 portions that cover the amount of NaH dispersion used) and the last traces of pentane are removed under high vacuum. "Aqueous half saturated brine" refers to a water:brine, 1:1 (v:v) solution.

Melting points were recorded using open capillary tubes on a Heidolph melting point apparatus and are uncorrected. Infra-red spectra were recorded on a Bruker Alpha-P FT-IR spectrometer using an Opus Wizard Interface. ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in Fourier transform mode at the field strength specified on Varian Mercury 300 spectrometer at ambient temperature. Spectra were obtained from the specified deuterated solvents in 5 mm diameter tubes. Chemical shift in ppm is quoted relative to residual solvent signals calibrated as follows: **$CDCl_3$** δ_H ($CHCl_3$) = 7.26 ppm, δ_C = 77.2 ppm; **C_6D_6** δ_H (C_6HD_5) = 7.16 ppm, δ_C = 128.0 ppm. Multiplicities in the ^{1}H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, ´quint´ (pseudo-quintet) m = multiplet, br = broad; coupling constants are reported in Hz. Electrospray (ES) mass spectra (MS and HRMS) were obtained with a Micromass LCT spectrometer. Ion mass/charge (*m*/*z*) ratios are reported as values in atomic mass units.

(Z)-*tert*-Butyl 1,2,5,6,8,9,10,11-octahydro-4*H*-cyclohepta[*d*]azocine-3(7*H*)-carboxylate 11

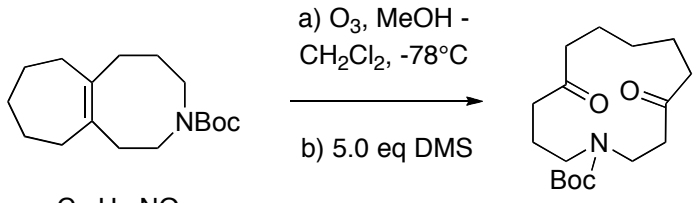


$C_{24}H_{37}NO_5S$ (451.62) $C_{17}H_{29}NO_2$ (279.42)

To an ice cold solution of the tosylate of alcohol **10** (2.26 g, 5.0 mmol, 1.0 eq.) in THF (70 mL) was added dropwise an ice cold suspension of NaH (0.59 g of a 55% NaH dispersion in oil, corresponding to 0.32 g of NaH, 25 mmol, 5.0 eq.) in THF (210 mL). The resulting mixture was refluxed for 6 h, recooled to 0 °C, carefully quenched with a saturated NH_4Cl aqueous solution (50 mL) and extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4) and the solvents were removed under vacuum. The residue obtained was purified by flash chromatography (Et_2O:pentane, 1:9) to afford the bicyclic amine **11** as a clear viscous oil (1.23 g, 88%).

Rf (Et_2O:pentane, 1:9) 0.75; IR (neat) 2916, 1689, 1463, 1409, 1364, 1163 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.48-3.26 (m, 2H), 3.26-3.09 (m, 2H), 2.29-2.02 (m, 8H), 1.81-1.61 (m, 4H); 1.56-1.38 (m, 13H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.2, 131.7, 130.4, 79.4, 49.2, 48.3, 33.7, 32.5, 32.2, 31.8, 28.6, 28.5, 29.0, 27.3, 26.6; MS (ES) *m/z* 280 $(M+H)^+$, 265 (100), 224, 180; HRMS (ES) *m/z* 280.2242 (calcd. for $C_{17}H_{30}NO_2$: 280.2277).

***tert*-Butyl 4, 10-dioxoazacyclotridecane-1-carboxylate 12**



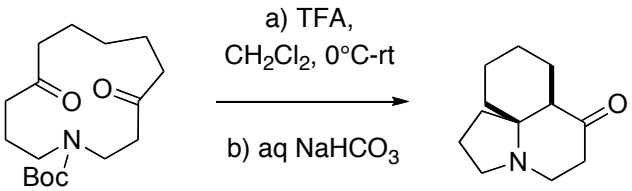
$C_{17}H_{29}NO_2$ (279.42) $C_{17}H_{29}NO_4$ (311.42)

A solution of [7,8]-bicyclic amine **11** (0.70 g, 2.5 mmol, 1.0 eq.) in CH_2Cl_2 (45 mL) and MeOH (16.5 mL) was cooled to -78°C. O_3 was then bubbled until a persistent blue color

was seen after which argon was bubbled until the blue coloration disappeared. DMS (0.90 mL, 12.5 mmol, 5.0 eq.) was added and stirring continued at -78°C for further 10 min. The reaction was allowed to warm to room temperature over 2 h, stirred overnight and then partitioned between CH_2Cl_2 (125 mL) and aqueous half saturated brine (125 mL). The layer were separated and the organic layer was dried (Na_2SO_4), the solvent removed under vacuum to afford a colorless oil which upon standing solidified (0.78 g, quantitative). A small sample was purified by flash column chromatography (Et_2O:pentane, 1:1) and recrystallized from EtOAc:Heptane.

Rf (Et_2O:hexane, 1:1) 0.17; mp 80-81°C (EtOAc:Heptane); IR (neat) 2926, 1689, 1475, 1407, 1364, 1232 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.40 (t, *J* = 5.8 Hz, 2H), 3.17 (t, *J* = 6.3 Hz, 2H), 2.68 (t, *J* = 5.8 Hz, 2H), 2.41-2.32 (m, 4H), 2.28 (t, *J* = 7.4 Hz, 2H), 1.73-1.52 (m, 6H), 1.4 (s, 9H), 1.24 (´quint´, *J* = 6.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 212.5, 210.6, 156.3, 80.0, 49.1, 44.2, 42.6, 42.1, 41.8, 38.5, 28.6, 26.8, 23.9, 23.3, 22.3; MS (ES) *m/z* 312 $(M+H)^+$ (100), 256, 212, 194, 176; HRMS (ES) *m/z* 312.4402 (calcd. for $C_{17}H_{30}NO_4$: 312.2175).

Octahydro-1*H*-pyrrolo[1,2]quinolin-7(7a*H*)-one 13

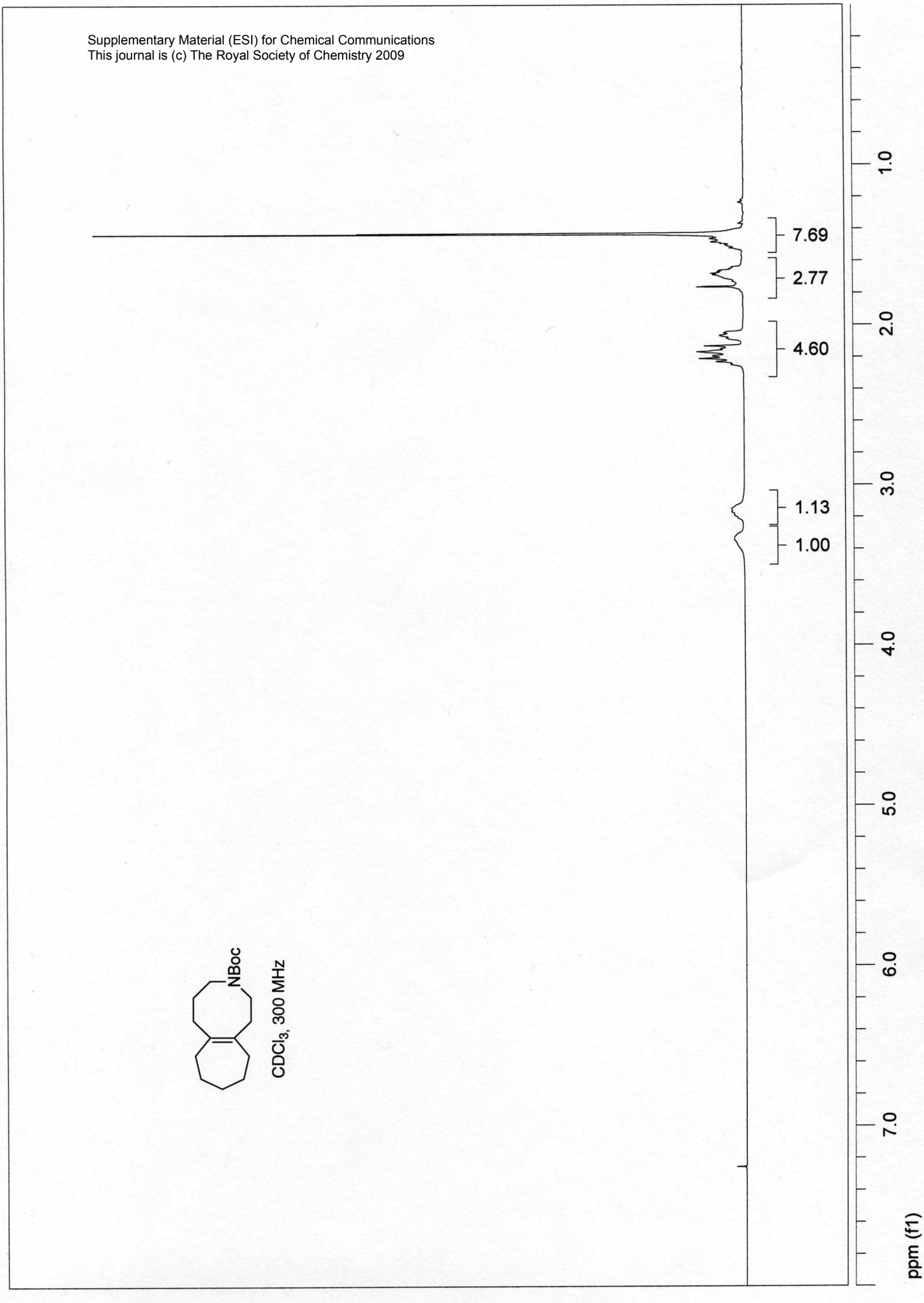


$C_{17}H_{29}NO_4$ (311.42) → $C_{12}H_{19}NO$ (193.28)

To an ice cold solution of the macrocyclic diketoamine **12** (170 mg) in CH_2Cl_2 (20 mL) was added TFA (5 mL). After stirring at 0°C for 5 mins, the cooling bath was removed and stirring continued at room temperature for further ½ h. The excess of TFA was then removed by repeated co-evaporation with toluene (3 portions of 20 mL). To the residue thus obtained was added CH_2Cl_2 (30 mL) and saturated $NaHCO_3$ (30 mL) and the resulting biphasic system was vigorously stirred for approx. 5 min.. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (5 portions of 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the obtained residue by flash column chromatography (MeOH: CH_2Cl_2, 1:9) yielded pure **13** (59 mg, 0.3 mmol, 55% from [7,8]-bicyclic amine **11**).

R_f (MeOH: CH_2Cl_2, 1:9) 0.68; IR (neat) 2933, 1702, 1446, 1352, 1172 cm^{-1}; ^1H NMR (C_6D_6, 300 MHz) δ 2.86 (ddd, *J* = 13.1, 11.5, 3.8 Hz, 1H), 2.74-2.52 (m, 3H), 2.34 (dddd,

J = 13.5, 4.3, 4.2, 2.2 Hz, 1H), 2.22 (dddd, *J* = 14.3, 11.5, 6.9, 1.0 Hz, 1H), 1.97 (ddd, *J* = 14.3, 3.7, 2.4 Hz, 1H), 1.93 (br m, 1H), 1.68-1.15 (m, 7H), 1.10-0.90 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) δ 208.9, 66.6, 52.4, 50.1, 44.6, 38.3, 36.6, 31.4, 24.7, 23.4, 22.5, 21.6; MS (ES) *m/z* 194 $(M+H)^+$ (100), 143, 128; HRMS (ES) *m/z* 194.1483 (calcd. for $C_{12}H_{20}NO$: 194.1545)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4.60
1.13
1.00
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)

NBoc
CDCl3, 75 MHz
ppm (f1)
50
100
150
155.9
155.3
138.7
137.7
136.0
135.9
135.0
79.1
79.1
77.8
77.7
77.6
77.5
77.3
77.2
76.8
54.7
50.7
48.7
48.1
48.1
48.1
47.8
47.3
46.6
36.9
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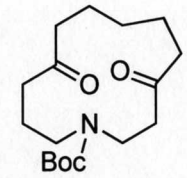
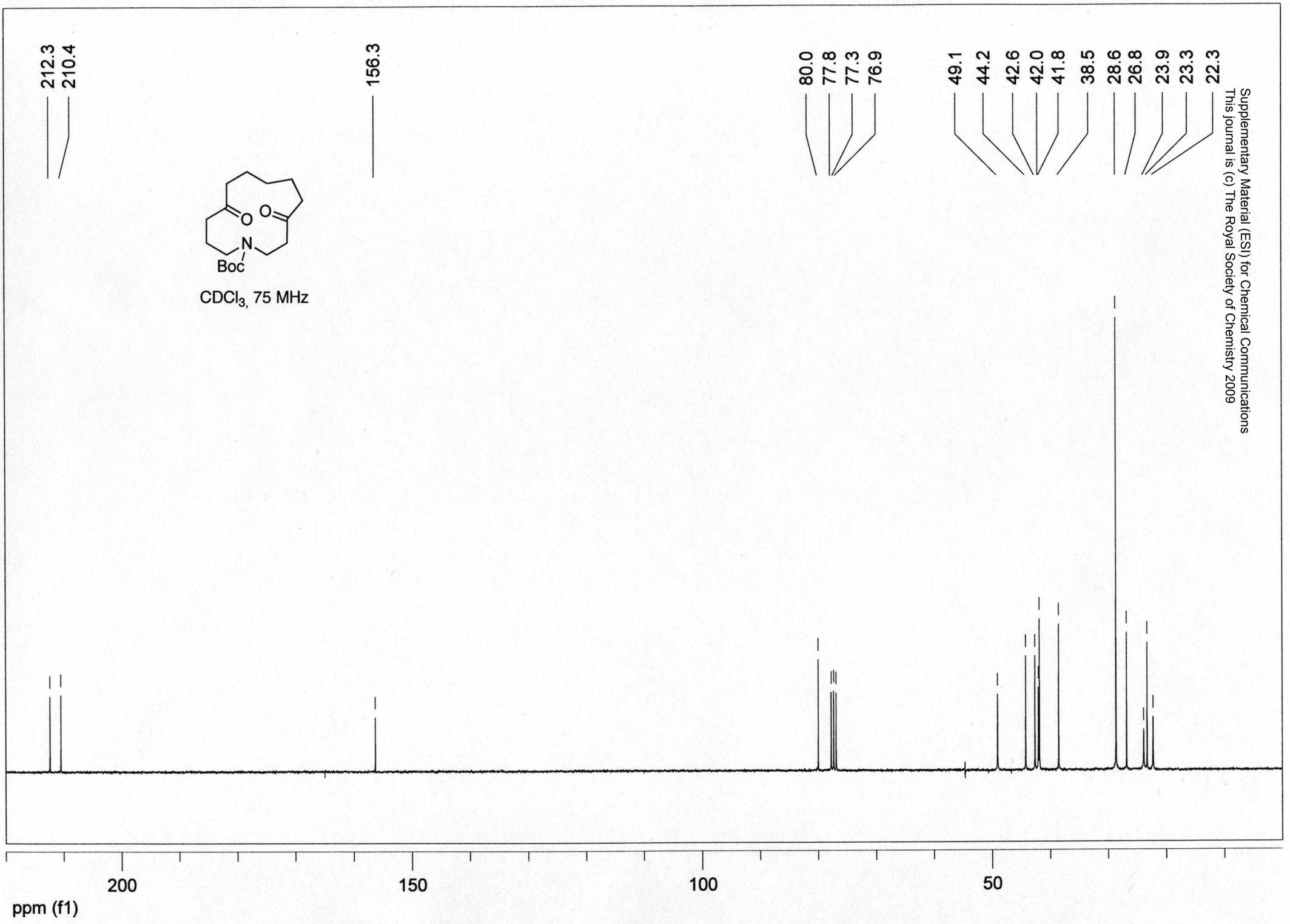
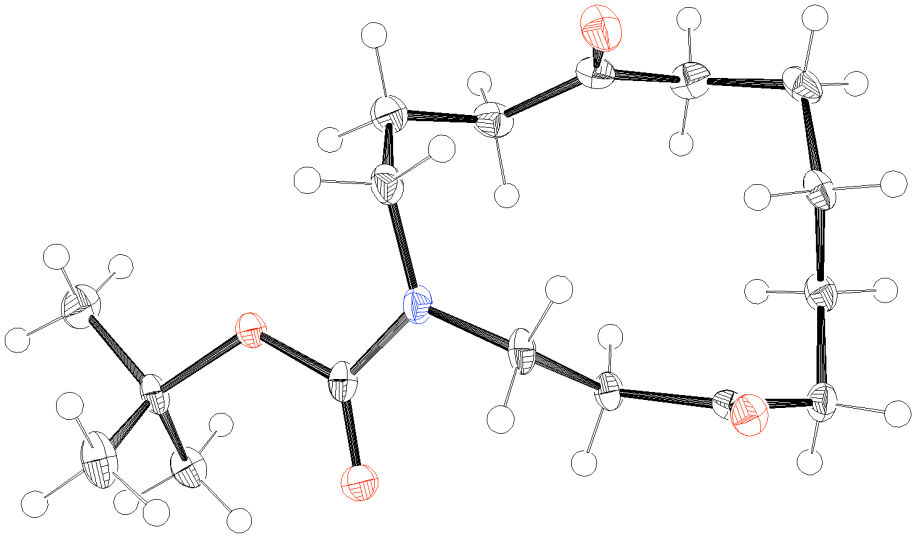
34.1
33.6
32.6
32.6
28.9
28.8

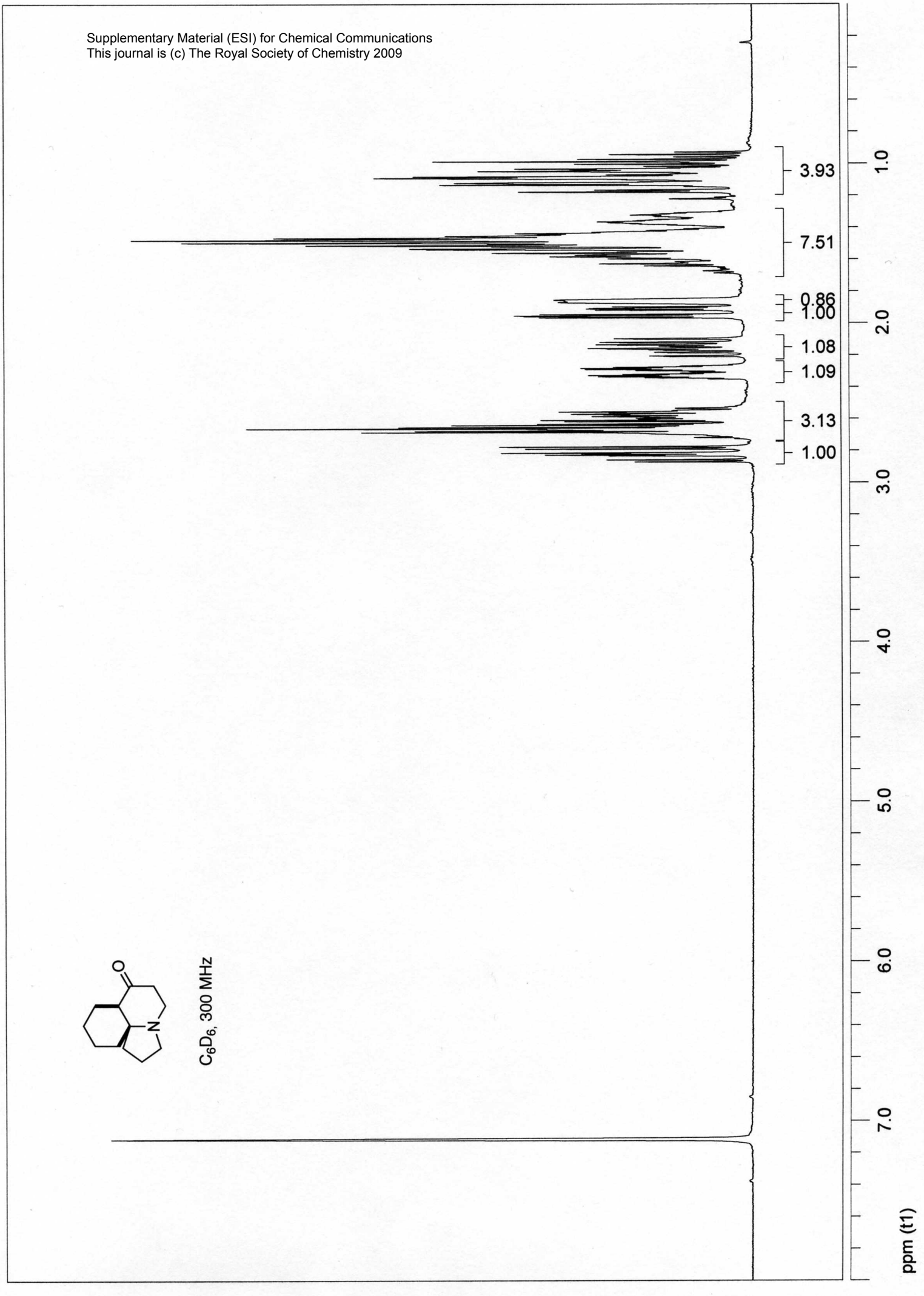


$CDCl_3$, 300 MHz





X-Ray structure in Scheme 2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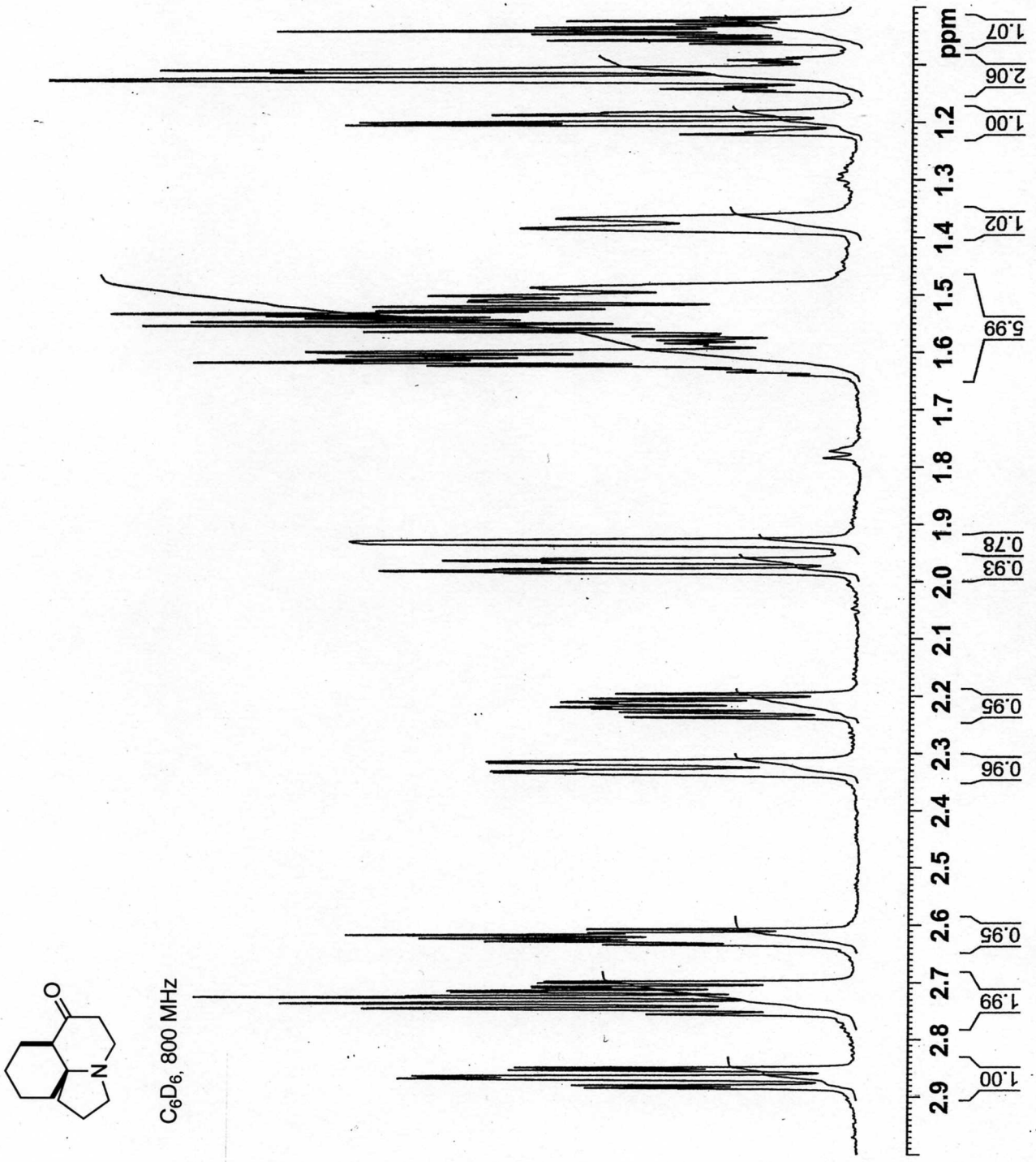
1.08
1.09
3.13
1.00
1.0
2.0
3.0
4.0
5.0
6.0
7.0
ppm (t1)
O
N
C_6D_6, 300 MHz


C6D6, 800 MHz
ppm
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2.7
2.6
2.5
2.4
2.3
2.2
2.1
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1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.00
1.99
0.95
0.96
0.95
0.93
0.78
5.99
1.02
1.00
2.06
1.07