Electronic Supplementary Material (ESI) for RSC Advances

Diverse Products Accessible *via* [2+2] Photocycloadditions of 3-Aminocyclopentenones

Andrew J. A. Roupany, James R. Baker*

Department of Chemistry, University College London, 20 Gordon St, London
j.r.baker@ucl.ac.uk

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General Information

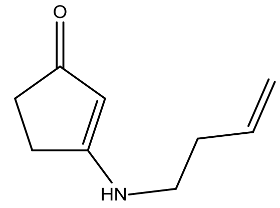
All reactions were carried out at atmospheric pressure, under argon unless otherwise stated. Solvents and reagents purchased from suppliers (Alfa Aesar and Aldrich) and used without any further purification. Normal phase silica gel (BDH), and sand (VWR) were used for flash chromatography unless otherwise stated where basic aluminium oxide Brockmann grade I (alumina) (Aldrich) was used. All reactions were monitored by thin layer chromatography (TLC) unless otherwise stated. TLC plates pre-coated with silica gel 60 F254 on aluminium (Merck KGaA) were used, detection was by UV (254 nm) or chemical stain ($KMnO_4$ or vanillin). Mass Spectrometry was performed using a VG70 SE operating in EI, CI (+ or -) or ES (+ or -) depending on the sample. ^1H NMR spectra were recorded at 300 MHz, 400 MHz, 500 MHz or 600 MHz and ^{13}C NMR at 100 MHz, 125 MHz or 150 MHz on a Bruker AMX300, AMX400, AMX500 or AMX600 at ambient temperature unless otherwise stated. All NMR spectra were recorded in $CDCl_3$ unless otherwise stated. Chemical shifts (δ) are quoted in ppm. The multiplicity of the signal is indicated as: s-singlet, d-doublet, t-triplet, q-quartet, sext-sextet, dd-doublet of doublets, dt-doublet of triplets, td-triplet of doublet, qd-quartet of doublets, ddd-doublet of doublet of doublets, dtd-doublet of triplet of doublets, ddt-doublet of doublet of triplets, dddd-doublet of doublet of doublet of doublets, br-broad, m-multiplet defined as all multipeak signals where overlap or complex coupling of signals makes definitive descriptions of peaks difficult. All peaks should be taken as sharp unless otherwise described. Coupling constants are quoted in Hz to one decimal place. Infrared spectra were obtained on a Perkin Elmer Spectrum 100 FTIR Spectrometer operating in ATR mode. Melting points were measured with a Gallenkamp apparatus and are uncorrected. The term ‘degassed’ refers to the process of removing O_2 from a solution by bubbling argon through a vessel containing the solution. Irradiations were carried out using a medium pressure 125W mercury lamp in a Pyrex immersion well, cooled *via* running water.

Abbreviations

Within this text, room temperature is defined as between 19 ºC - 22 ºC. The term *in vacuo* is used to describe solvent removal by Büchi rotary evaporation between 17 ºC and 60 ºC, at approx. 10 mmHg. For NMR experiments, $CDCl_3$ is fully deuterated (d_3) chloroform, DMSO is fully deuterated (d_6) dimethylsulfoxide, and MeOD is fully deuterated (d_4) methanol. Solvents were chosen according to the position of solvent peak in spectra and solubility of substrate. Petroleum ether is petroleum ether (40-60 ºC), EtOAc is ethyl acetate, DCM is dichloromethane, MeOH is methanol, Et_2O is diethyl ether, MeCN is acetonitrile, PhMe is toluene, NEt_3 is triethylamine and TFA is trifluoroacetic acid.

Experimental Details

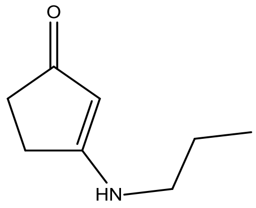
3-(but-3-en-1-ylamino)cyclopent-2-enone (1)



To a suspension of 1,3-cyclopentadione (181 mg, 1.85 mmol) in dry PhMe (6 mL) was added 3-buten-1-amine hydrochloride (199 mg, 1.85 mmol) and NEt_3 (256 µL, 187 mg, 1.85 mmol). The mixture was stirred at reflux under Dean-Stark conditions for 18 h. The solvent was removed *in vacuo* and purification by flash chromatography (10 % MeOH in EtOAc) afforded vinylogous amide **1** as a white solid (226 mg, 1.50 mmol) in 81 % yield. mp 122.7-123.4 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (ddt, 1H, *J* = 17.2, 10.3 and 6.8), 5.09-5.59 (m, 4H), 3.25 (q, *J* = 6.0, 2H), 2.58-2.61 (m, 2H), 2.37-2.45 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) 204.6 (C), 176.4 (C), 134.6 (CH), 118.2 (CH_2), 99.7 (CH), 44.0 (CH_2), 33.7 (CH_2), 33.0 (CH_2), 28.2 (CH_2); IR (solid, cm^{-1}) 3193 (w), 2977 (w), 2929 (w), 2861 (w), 1634 (m), 1568 (s), 1525 (s); MS (EI) *m*/z (relative intensity): 151 (M^+, 17), 144 (13), 110 (54), 88 (16), 86 (100); Exact mass calculated for [$C_9H_{13}NO$] requires *m/z* 151.09917, found 151.09966 (EI).

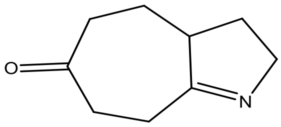
3-(propylamino)cyclopent-2-enone (2)



To a suspension of 1,3-cyclopentadione (1.30 g, 13.3 mmol) in dry PhMe (20 mL) was added propylamine (2.70 mL, 1.94 g, 33.3 mmol) and the mixture stirred at reflux under Dean-Stark conditions for 2.5 h. The solvent was removed *in vacuo* and purification by flash chromatography (10 % MeOH in EtOAc) afforded vinylogous amide **2** as a white solid (1.83 g, 13.2 mmol) in 99 % yield. mp 113.4-113.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (br, 1H), 5.06 (s, 1H), 3.14 (td, *J* = 7.3, 4.9, 2H), 2.59-2.62 (m, 2H), 2.41-2.44 (m, 2H), 1.66 (sext, *J* = 7.3, 2H), 0.99 (t, *J* = 7.4, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) 204.5 (C), 176.7 (C), 99.4 (CH), 47.0 (CH_2), 33.7 (CH_2), 28.3 (CH_2), 22.2 (CH_2), 11.5 (CH_3); IR (solid, cm^{-1}) 3192 (w), 2958 (m), 2929 (m), 2873 (m), 1643 (m), 1571 (s), 1523 (s); MS (EI) *m*/z (relative intensity): 139 (M^+, 60), 111 (17), 110 (32), 96 (13), 88 (16), 86 (100); Exact mass calculated for [$C_8H_{13}NO$] requires *m/z* 139.09917, found 139.09923 (EI).

3,3a,4,5,7,8-hexahydrocyclohepta[b]pyrrol-6(2H)-one (3)

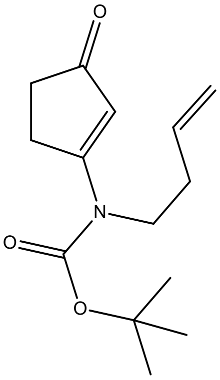


Method 1: A solution of vinylogous amide **1** (180 mg, 1.20 mmol) in MeCN (60 mL) was degassed for 20 min and irradiated for 2.5 h. The solvents were removed *in vacuo* and purification by flash chromatography on alumina (DCM) afforded keto-imine **3** as a light yellow oil (171 mg, 1.14 mmol) in 95 % yield.

Method 2: To a solution of Boc protected amino-cyclobutane **7** (20.0 mg, 0.0797 mmol) in DCM (2 mL) was added TFA (2 mL) and the mixture stirred for 1 h. The solvents were removed *in vacuo* and purification by flash chromatography on alumina (DCM) afforded **3** as a light yellow oil (10.2 mg, 0.0677 mmol) in 85 % yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.81 - 3.91 (m, 1H), 3.64 - 3.73 (m, 1H), 2.77 - 2.89 (m, 2H), 2.57 - 2.68 (m, 4H), 2.46 - 2.55 (m, 1H), 2.27 (dtd, *J* = 13.0, 8.8, 4.1, 1H), 1.99 - 2.05 (m, 1H), 1.53 - 1.69 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.6 (C), 178.4 (C), 58.8 (CH_2), 51.1 (CH), 42.5 (CH_2), 39.6 (CH_2), 31.4 (CH_2), 29.3 (CH_2), 28.2 (CH_2); IR (solid, cm^{-1}) 3008 (w), 2970 (m), 2941 (m), 2864 (w), 1740 (s), 1633 (m), 1572 (w); MS (CI) *m*/z (relative intensity): 152 (M+, 100), 123 (13), 110 (7); Exact mass calculated for [$C_9H_{14}NO$] requires *m/z* 152.10754, found 152.10802 (CI).

***tert*-butyl but-3-en-1-yl(3-oxocyclopent-1-en-1-yl)carbamate (5)**

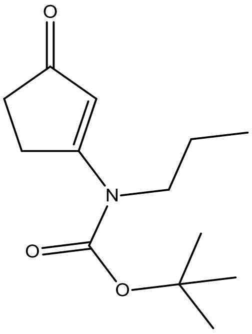


To a solution of vinylogous amide **1** (500 mg, 3.31 mmol) in DCM (12 mL) was added a solution of di-*tert*-butyl dicarbonate (865 mg, 3.97 mmol) and 4-dimethylaminopyridine (20.2 mg, 0.166 mmol) in DCM (3 mL) and the solution stirred at room temperature for 18 h. The solvents were removed *in vacuo* and purification by flash chromatography (Et_2O) afforded Boc protected vinylogous amide **5** as an orange-brown oil (739 mg, 2.95 mmol) in 89 % yield.

^{1}H NMR (600 MHz, MeOD) δ 5.79-5.87 (m, 2H), 5.05-5.12 (m, 2H), 3.78 (t, *J* = 7.4, 2H), 3.14-3.16 (m, 2H), 2.42-2.43 (m, 2H), 2.38 (qt, *J* = 7.3, 1.0, 2H), 1.55 (s, 9H); ^{13}C NMR (150 MHz, MeOD) 210.5 (C), 177.1 (C), 153.2 (C), 135.7 (CH), 117.8

(CH_2), 112.7 (CH), 84.8 (C), 48.8 (CH_2), 35.1 (CH_2), 33.4 (CH_2), 31.8 (CH_2), 28.2 (CH_3); IR (oil, cm^{-1}) 2978 (m), 2933 (m), 1728 (s), 1703 (w), 1680 (s), 1578 (s); MS (ES-) *m*/z (relative intensity): 250 (M^+ - H^+, 100), 188 (38), 171 (56), 157 (50), 146 (88); Exact mass calculated for $[C_{14}H_{21}NO_3]$-H^+ requires *m/z* 250.1443, found 250.1443 (ES-).

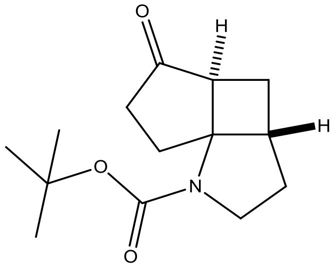
***tert*-butyl (3-oxocyclopent-1-en-1-yl)(propyl)carbamate (6)**



To a solution of vinylogous amide **2** (1.83 g, 13.2 mmol) in DCM (20 mL) was added a solution of di-*tert*-butyl dicarbonate (3.47 g, 15.9 mmol) and 4-dimethylaminopyridine (81.0 mg, 0.665 mmol) in DCM (10 mL) and the solution stirred at room temperature for 18 h. The solvents were removed *in vacuo* and purification by flash chromatography (Et_2O) afforded Boc protected vinylogous amide **6** as an orange oil (3.08 g, 12.9 mmol) in 98 % yield.

^1H NMR (600 MHz, MeOD) δ 5.80 (s, 1H), 3.68 (t, *J* = 7.7, 2H), 3.16-3.19 (m, 2H), 2.43-2.46 (m, 2H), 1.67 (sext, *J* = 7.6, 2H), 1.57 (s, 9H), 0.91 (t, *J* = 7.5, 3H); ^{13}C NMR (150 MHz, MeOD) 210.5 (C), 177.3 (C), 153.3 (C), 112.5 (CH), 84.7 (C), 51.2 (CH_2), 35.0 (CH_2), 31.8 (CH_2), 28.2 (CH_3), 22.2 (CH_2), 11.3 (CH_3); IR (oil, cm^{-1}) 2971 (m), 2878 (m), 1725 (s), 1677 (s), 1563 (s); MS (CI) *m*/z (relative intensity): 240 (M^++H^+, 100), 212 (19), 184 (86), 168 (27), 130 (42); Exact mass calculated for $[C_{13}H_{21}NO_3]$+H^+ requires *m/z* 240.1522, found 240.1903 (CI).

(3aS*,4aS*)-*tert*-butyl 5-oxooctahydro-1H-cyclopenta[1,4]cyclobuta[1,2-b]pyrrole-1-carboxylate (7)

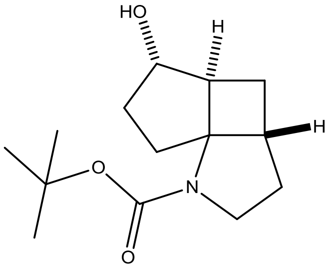


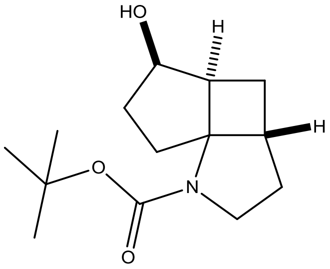
A solution of Boc protected vinylogous amide **5** (275 mg, 1.49 mmol) in MeCN (90 mL) was degassed for 30 min and irradiated for 30 min. The solvent was removed *in vacuo* and purification by flash chromatography (25 % Et_2O in petroleum ether with 2 % NEt_3) afforded Boc protected aminocyclobutane **7** as a yellow oil (307 mg, 1.22 mmol) in 82 % yield.

^{1}H NMR (400 MHz, $CDCl_3$, 330 K*) δ 3.71-3.78 (m, 1H), 3.62 (ddd, *J* = 8.2, 6.3, 4.9, 1H), 2.80 (qd, *J* = 7.6, 3.2, 1H), 2.57-2.73 (m, 4H), 2.12 (ddd, *J* = 8.1, 7.6, 5.2, 1H), 2.01-2.05 (m, 2H), 1.87-1.93 (m, 1H), 1.76 (dddd, *J* = 7.9, 7.6, 4.8, 3.3, 1H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 330 K*) 218.7 (C), 154.3 (C), 80.2 (C), 69.5 (C), 48.8 (CH_2), 46.0 (CH), 43.5 (CH), 38.5 (CH_2), 30.6 (CH_2), 29.6 (CH_2), 28.7 (CH_3), 25.6 (CH_2); IR (oil, cm^{-1}) 2973 (w), 2938 (w), 2872 (w), 1735 (s), 1693 (s); MS (ES-) *m*/z (relative intensity): 501 (100), 250 (M$^+$, 25), 212 (22), 194 (24); Exact mass calculated for $[C_{14}H_{21}NO_3]$-H$^+$ requires *m/z* 250.1443, found 250.1145 (ES-).

* NMR at ambient temperature showed the presence of rotomers which disappeared upon heating to 330 K.

(3aS*,4aS*,5S*)-tert-butyl 5-hydroxyoctahydro-1H-cyclopenta[1,4]cyclobuta[1,2-b]pyrrole-1-carboxylate (8) and (3aS*,4aS*,5R*)-tert-butyl 5-hydroxyoctahydro-1H-cyclopenta[1,4]cyclobuta[1,2-b]pyrrole-1-carboxylate (9)





To a solution of Boc protected vinylogous amide **7** (71.0 mg, 0.283 mmol) in MeOH (5 mL) was added sodium borohydride (21.5 mg, 0.566 mmol) and the mixture stirred for 20 min. The solvent was removed *in vacuo* and the white solid was dissolved in aqueous HCl (2M, 2 mL), extracted with DCM (3 x 5 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed *in vacuo* and purification by flash chromatography (50 % Et_2O in petroleum ether (2 % NEt_3)) afforded alcohol **8** as a colourless oil (43.7 mg, 0.173 mmol) in 61 % yield and alcohol **9** as a colourless oil (23.1 mg, 0.0913 mmol) in 32 % yield.

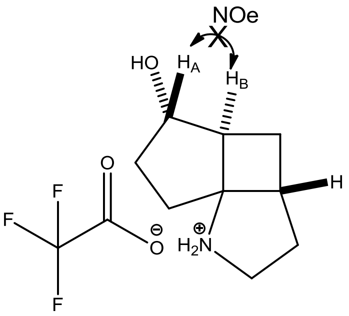
8 ^{1}H NMR (400 MHz, $CDCl_3$, 330 K*) δ 4.25 (br, 1H), 3.92 (m, 1H), 3.76 (ddd, *J* = 11.1, 8.1, 3.7, 1H), 3.37 (ddd, *J* = 11.2, 8.9, 7.0, 1H), 2.39-2.55 (m, 3H), 2.22 (dddd, *J* = 12.8, 9.0, 7.0, 3.9, 1H), 1.97-2.06 (m, 2H), 1.69-1.82 (m, 2H), 1.57 (ddd, *J* = 13.0, 8.3, 6.3, 1H), 1.46-1.50 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 330 K*) 154.0 (C), 80.0 (C), 76.2 (CH), 71.8 (C), 49.1 (CH_2), 48.7 (CH), 40.5 (CH), 33.4 (CH_2), 32.7 (CH_2), 30.1 (CH_2), 28.5 (CH_3), 24.9 (CH_2); IR (oil, cm^{-1}) 3420 (br, m), 2966 (m), 2933 (m), 2869 (w), 1664 (s); MS (ES+) *m*/z (relative intensity): 276 (M^+ +Na, 76), 261 (100), 245 (30), 220 (68), 180 (46), 136 (29); Exact mass calculated for $[C_{14}H_{23}NO_3]$+Na, requires *m/z* 276.1576 found 276.1571 (ES+).

9 ^{1}H NMR (400 MHz, $CDCl_3$, 330 K*) δ 4.52 (ddd, *J* = 10.3, 7.7, 6.3, 1H), 3.76 (ddd, *J* = 11.1, 7.8, 6.4, 1H), 3.47 (ddd, *J* = 11.2, 7.7, 6.5, 1H), 2.48-2.60 (m, 2H), 3.35 (ddd, *J* = 13.4, 11.7, 7.1, 1H), 2.08-2.20 (m, 3H), 1.69-1.84 (m, 2H), 1.54 (ddd, *J* = 13.1, 9.3, 5.5, 1H), 1.43-1.49 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$, 330 K*) 154.2 (C), 79.3 (C), 72.9 (CH), 70.8 (C), 48.7 (CH_2), 42.5 (CH), 42.4 (CH), 32.9 (CH_2), 31.3 (CH_2), 31.0 (CH_2), 28.6 (CH_3), 20.0 (CH_2); IR (oil, cm^{-1}) 3416 (br, w), 2944 (m), 2964 (m), 2869 (m), 1693 (s), 1672 (s); MS (ES+) *m*/z (relative intensity): 276 (M^+ + Na, 16), 261 (19), 239 (30), 220 (27), 198 (50), 180 (67), 136 (100); Exact mass calculated for $[C_{14}H_{23}NO_3]$+Na requires *m/z* 276.1576, found 276.1566 (ES+).

* NMR at ambient temperature showed the presence of rotomers which disappeared upon heating to 330 K.

N.B. Stereochemistry inferred from NOESY data after Boc removal (**10** and **11**).

(3aS*,4aS*,5S*)-5-hydroxyoctahydro-1H-cyclopenta[1,4]cyclobuta[1,2-b]pyrrol-1-ium 2,2,2-trifluoroacetate (10)

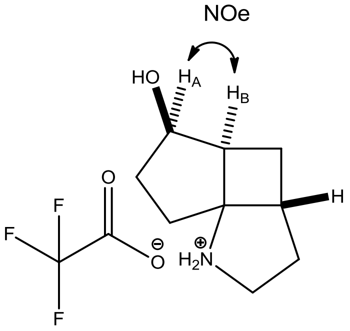


To a solution of alcohol **8** (165 mg, 0.652 mmol) in DCM (3 mL) was added TFA (3 mL) and the mixture was stirred at room temperature for 1 h. The solvent was removed *in vacuo* and the resulting oil was triturated with MeOH (2 mL). The solvent was removed *in vacuo* to afford aminocyclobutane **10** as a yellow oil (162 mg, 0.607 mmol) in 93 % yield.

^{1}H NMR (600 MHz, MeOD) δ 4.02 (m, 1H, H_A), 3.54-3.62 (m, 2H), 2.61 (ddd, *J* = 9.2, 8.0, 4.7, 1H), 2.56-2.59 (m, 1H, H_B), 2.08-2.22 (m, 3H), 2.00-2.06 (m, 1H), 1.92-1.96 (m, 2H), 1.78-1.83 (m, 1H), 1.70-1.75 (m, 1H); ^{13}C NMR (150 MHz, MeOD)

163.1 (q, ${}^{2}J_{CF}$ = 34.5, C), 118.2 (q, ${}^{1}J_{CF}$ = 291, CF_3), 76.6 (CH), 75.3 (C), 47.4 (CH), 47.1 (CH_2), 38.5 (CH), 34.0 (CH_2), 31.3 (CH_2), 30.8 (CH_2), 24.5 (CH_2); IR (oil, cm^{-1}) 3362 (br, w), 2962 (m), 2951 (m), 2873 (w), 2763 (w), 2502 (w), 1669 (s); MS (EI) *m*/z (relative intensity): 153 (M^+, 15), 136 (26), 108 (15), 95 (16), 84 (35), 83 (100), 82 (23), 80 (17), 69 (29); Exact mass calculated for [$C_9H_{15}NO$] requires *m/z* 153.11482, found 153.11541 (EI).

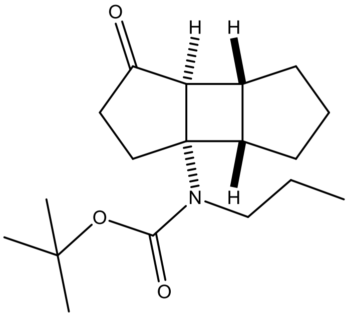
(3aS*,4aS*,5R*)-5-hydroxyoctahydro-1H-cyclopenta[1,4]cyclobuta[1,2-b]pyrrol-1-ium 2,2,2-trifluoroacetate (11)

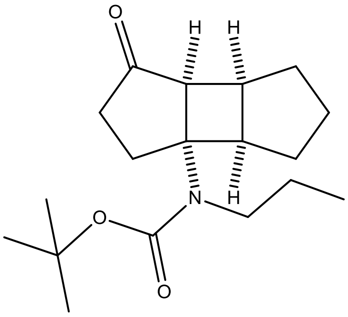


To a solution of alcohol **9** (96.9 mg, 0.383 mmol) in DCM (3 mL) was added TFA (3 mL) and the mixture was stirred at room temperature for 1 h. The solvent was removed *in vacuo* and the resulting oil was triturated with MeOH (2 mL). The solvent was removed *in vacuo* to afford aminocyclobutane **11** as a yellow oil (85.1 mg, 0.319 mmol) in 83 % yield.

^{1}H NMR (600 MHz, MeOD) δ 4.28 (ddd, *J* = 10.0, 7.7, 6.5, 1H, H_A), 3.54-3.64 (m, 2H), 2.69 (ddd, *J* = 9.7, 8.2, 5.4, 1H, H_B), 2.64 (ddd, *J* = 9.2, 7.7, 4.8, 1H), 2.27 (ddd, 13.4, 9.1, 5.3, 1H), 2.06-2.19 (m, 2H), 1.89-1.98 (m, 3H), 1.81-1.87 (m, 1H), 1.55 (ddd, *J* = 13.4, 9.8, 4.8, 1H); ^{13}C NMR (150 MHz, MeOD) 163.0 (q, ${}^{2}J_{CF}$ = 34.5, C), 118.1 (q, ${}^{1}J_{CF}$ = 290, CF_3), 73.5 (C), 72.3 (CH), 47.0 (CH_2), 41.7 (CH), 39.8 (CH), 32.7 (CH_2), 31.4 (CH_2), 30.0 (CH_2), 19.9 (CH_2); IR (oil, cm^{-1}) 3368 (br, m), 2962 (m), 2950 (m), 2874 (w), 2764 (w), 2502 (w), 1667 (s); MS (EI) *m*/z (relative intensity): 153 (M^+, 11), 136 (22), 108 (14), 95 (16), 84 (34), 83 (100), 82 (25), 80 (19), 69 (34); Exact mass calculated for [$C_9H_{15}NO$] requires *m/z* 153.11482, found 153.11523 (EI).

tert-butyl ((3aS*,3bR*,6aS*,6bS*)-1-oxodecahydrocyclobuta[1,2:3,4]di[5]annulen-3a-yl)(propyl)carbamate (12a) and **_tert_-butyl ((3aS*,3bS*,6aR*,6bS*)-1-oxodecahydrocyclobuta[1,2:3,4]di[5]annulen-3a-yl)(propyl)carbamate (12b)**





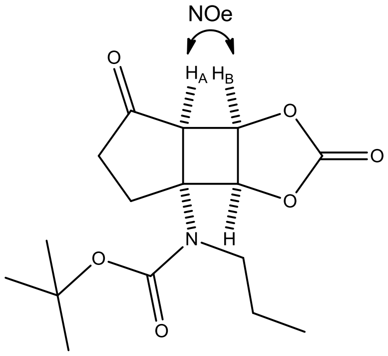
A solution of Boc protected vinylogous amide **6** (360 mg, 1.50 mmol) in a 3:1 mixture of MeCN and cyclopentene (75 mL) was degassed for 30 min and irradiated for 2.5 h. The solvents were removed *in vacuo* and the resulting oil was purified by flash chromatography (gradient elution from 10 % EtOAc in petroleum ether (1 % NEt_3) to 20 % EtOAc in petroleum ether (1 % NEt_3)). The still impure product was further purified by flash chromatography on alumina (gradient elution from 25 % Et_2O in petroleum ether to 33 % Et_2O in petroleum ether) to afford Boc protected aminocyclobutanes **12a** and **12b** as a white solid (237 mg, 0.772 mmol) in 51 % yield as 3:1 ratio of **12a** to **12b** in an inseparable mixture diastereoisomers (measured by integration of ^{1}H NMR spectrum). Dec. >150 °C

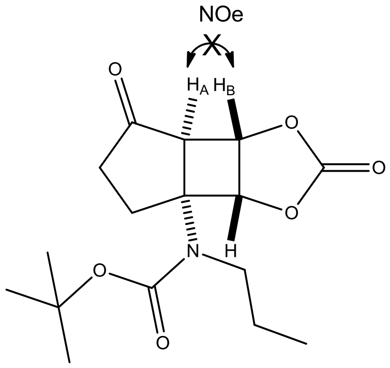
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.14-3.19 (m, $1H_a$), 2.96-3.01 (m, $1H_a$ and $2H_b$), 2.78-2.80 (m, $1H_a$) 2.58-2.64 (m, $1H_a$ and $2H_b$), 2.49-2.54 (m, $1H_a$), 2.36-2.45 (m, $3H_a$ and $2H_b$), 2.20-2.28 (m, $1H_a$ and $1H_b$), 1.67-1.80 (m, $3H_a$ and $3H_b$), 1.52-1.63 (m, $3H_a$ and $5H_b$) 1.32-1.46 (m, $11H_a$ and $11H_b$), 0.81-0.89 (m, $3H_a$ and $3H_b$); ^{13}C NMR shows two sets of peaks - ^{13}C NMR (150 MHz, $CDCl_3$) – Major diastereoisomer – 219.1 (C), 155.2 (C), 79.9 (C), 61.4 (C), 52.0 (CH), 50.8 (CH), 46.5 (CH_2), 39.1 (CH_2), 38.2 (CH), 37.1 (CH_2), 33.4 (CH_2), 28.6 (CH_3), 28.5 (CH_2), 25.3 (CH_2), 24.0 (CH_2), 11.3 (CH_3). Minor diastereoisomer – 219.5 (C), 154.6 (C), 79.5 (C), 62.1 (C), 52.9 (CH), 49.7 (CH), 46.7 (CH_2), 38.3 (CH_2), 37.9 (CH), 37.5 (CH_2), 33.4 (CH_2), 28.4 (CH_3), 27.8 (CH_2), 25.6 (CH_2), 24.5 (CH_2), 11.5 (CH_3); IR (solid, cm^{-1}) 2957 (m), 2876 (w), 1726 (s), 1679 (s); MS (CI) *m*/*z* (relative intensity): 308 (M^++H^+, 82), 240

(21), 208 (100); Exact mass calculated for $[C_{18}H_{29}NO_3]+H^+$ requires *m/z* 308.22257, found 308.22311 (CI).

N.B. Stereochemistry inferred from NOESY data after reduction and Boc removal (**17**).

***tert*-butyl ((3aS*,3bR*,6aR*,6bR*)-2,6-dioxohexahydro-3aH-cyclopenta[3,4]cyclobuta[1,2-d][1,3]dioxol-3b-yl)(propyl)carbamate (13)** and ***tert*-butyl ((3aR*,3bR*,6aR*,6bS*)-2,6-dioxohexahydro-3aH-cyclopenta[3,4]cyclobuta[1,2-d][1,3]dioxol-3b-yl)(propyl)carbamate (14)**





To a solution of Boc protected vinylogous amide **6** (200 mg, 0.840 mmol) in MeCN (40 mL) was added vinylene carbonate (266 µL, 360 mg, 4.18 mmol) and the mixture degassed for 15 min and irradiated for 1 h. The solvents were removed *in vacuo* and the resulting oil was purified by flash chromatography (33 % EtOAc in petroleum ether to 50 % EtOAc in petroleum ether) to afford Boc protected aminocyclobutane **13** as a colourless oil (10.8 mg, 0.0332 mmol) in 4 % yield and Boc protected aminocyclobutane **14** as a colourless oil (221 mg, 0.680 mmol) in 81 % yield.

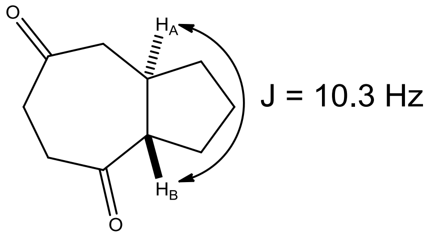
13 ^{1}H NMR (400 MHz, $CDCl_3$, 330 K*) δ 5.20 (d, *J* = 4.7, 2H, H_B), 3.38 (t, *J* = 4.7, 1H, H_A), 3.30-3.10 (m, 2H), 2.87 (ddd, *J* = 15.0, 10.9, 5.1, 1H), 2.69 (dddd, *J* = 19.7, 11.5, 5.1, 1.5, 1H), 2.47 (dddd, *J* = 19.7, 10.8, 8.3, 0.7, 1H), 2.01 (ddd, *J* = 15.0, 11.5, 8.3, 1H), 1.46-1.59 (m, 11H), 0.93 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 330 K*) 209.9 (C), 154.7 (C), 154.6 (C), 81.6 (C), 77.6 (CH), 72.0 (CH), 69.0 (C), 52.9 (CH), 46.8 (CH_2), 39.8 (CH_2), 29.0 (CH_2), 28.3 (CH_3), 23.4 (CH_2), 11.1

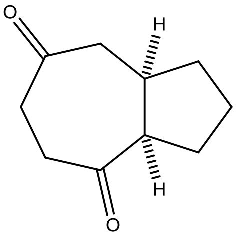
(CH_3); IR (oil, cm^{-1}) 2971 (m), 2934 (w), 2877 (w), 1828 (s), 1808 (s), 1744 (s), 1688 (s); MS (ES+) *m*/z (relative intensity): 324 ($M^+ + H^+$, 22), 280 (85), 252 (100), 206 (39), 178 (18); Exact mass calculated for $[C_{16}H_{21}NO_6]+H^+$ requires *m/z* 324.1447, found 324.1450 (ES+).

14 ^{1}H NMR (400 MHz, $CDCl_3$, 330 K*) δ 5.03 (d, *J* = 5.1, 1H), 4.77 (dd, *J* = 5.1, 2.2, 1H, H_B), 3.18-3.26 (m, 2H, H_A), 3.01 (ddd, *J* = 14.9, 9.7, 5.9, 1H), 2.55 (dddd, *J* = 18.4, 11.0, 9.0, 1.4, 1H), 2.28-2.45 (m, 3H), 1.38-1.57 (m, 11H), 0.85 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 330 K*) 210.4 (C), 154.4 (C), 154.3 (C), 81.0 (C), 80.3 (CH), 72.7 (CH), 66.0 (C), 56.8 (CH), 47.2 (CH_2), 38.1 (CH_2), 33.4 (CH_2), 28.2 (CH_3), 23.5 (CH_2), 10.9 (CH_3); IR (oil, cm^{-1}) 2974 (m), 2935 (w), 2875 (w), 1717 (s), 1620 (m), 1594 (m); MS (ES+) *m*/z (relative intensity): 324 ($M^+ + H^+$, 25), 280 (82), 252 (100), 206 (33), 178 (19); Exact mass calculated for $[C_{16}H_{21}NO_6]+H^+$ requires *m/z* 324.1447, found 324.1458 (ES+).

* NMR at ambient temperature showed the presence of rotomers which disappeared upon heating to 330 K.

(3aS*, 8aR*)-Octahydroazulene-4,7-dione (15a) and (3aR*, 8aR*)-Octahydroazulene-4,7-dione (15b)[1]





To a solution of Boc protected aminocyclobutane **12** (as a 3:1 ratio of diastereomers) (42.0 mg, 0.137 mmol) in DCM (3 mL) was added TFA (3 mL) and the mixture was stirred at room temperature for 1 h. The solution was neutralised with aqueous saturated $NaHCO_3$ (20 mL) and the aqueous layer was extracted with DCM (3 x 20 mL). The combined organics were dried ($MgSO_4$), filtered and the solvent was removed *in vacuo*. Purification by flash chromatography (Et_2O) afforded diketones

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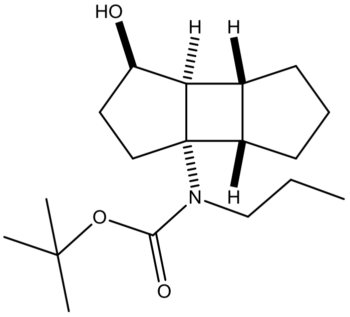
[1] House, H. O.; Gaa, P. C.; Lee, J. H. C.; VanDerveer, D. *J. Org. Chem.* **1983**, 48,1670-1678.

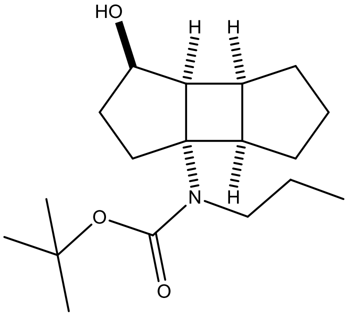
15a and **15b** as a white solid (22.7 mg, 0.137 mmol) in quantitative yield as a 10:1 ratio of **15a** to **15b** in an inseparable mixture of diastereomers (measured by integration of ^{1}H NMR spectrum). mp 68.8-69.3 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.32 (ddd, *J* = 10.3, 8.1, 6.4, 1H_{Ba}), 2.82 - 2.91 (m, 1H_a and 1H_b), 2.73 - 2.77 (m, 1H_b), 2.62 - 2.70 (m, 1H_a and 2H_b), 2.48 - 2.60 (m, 4H_a and 2H_b, H_{Aa}), 2.24 - 2.34 (m, 2H_a and 1H_b), 1.99 - 2.09 (m, 2H_b), 1.88 (dtd, *J* = 12.3, 6.4, 2.8, 1H_a), 1.73 - 1.83 (m, 1H_a and 2H_b), 1.66 - 1.71 (m, 1H_a and 1H_b), 1.45 - 1.53 (m, 1H_a and 1H_b), 1.35 - 1.40 (m, 1H_b), 1.13 - 1.20 (m, 1H_a); ^{13}C NMR shows two sets of peaks - ^{13}C NMR (150 MHz, $CDCl_3$) – Major diastereoisomer – 210.5 (C), 209.9 (C), 52.8 (CH), 46.4 (CH_2), 38.6 (CH), 38.5 (CH_2), 38.2 (CH_2), 34.3 (CH_2), 25.6 (CH_2), 25.1 (CH_2). Minor diastereoisomer – 210.9 (C), 209.3 (C), 58.0 (CH), 50.1 (CH_2), 40.7 (CH), 39.8 (CH_2), 38.0 (CH_2), 35.5 (CH_2), 25.8 (CH_2), 24.3 (CH_2); IR (solid, cm^{-1}) 2947 (m), 2879 (m), 1699 (s); MS (CI) *m*/z (relative intensity): 168 ($M^+ + H^+$, 73), 149 (37), 149 (38) Exact mass calculated for $[C_{10}H_{14}NO_2]+H^+$ requires *m/z* 167.10720, found 167.10674 (CI). Spectroscopic data is consistent with the literature[1]

N.B. A homonuclear decoupling experiment and computational J value prediction were employed (using PcModel by Serena Software) to determine that the major diastereomer present was the trans product. Upon decoupling of H_{Aa}, the J value of 10.3 Hz experienced by H_{Ba} disappears (see spectrum on p50). This proves that this J value is caused by the coupling of H_{Aa} to H_{Ba}. The *cis*-fused and *trans*-fused ring systems were modelled to predict the J-values; J_{cis} was predicted to be 6.8 Hz and J_{trans} predicted to be 10.8 Hz. Thus the 10.3 Hz coupling of H_{Aa} to H_{Ba} observed for the major diasteomer is consistent with the prediction for the trans product.

***tert*-butyl ((1R*,3aS*,3bR*,6aS*,6bS*)-1-hydroxydecahydrocyclobuta[1,2:3,4]di[5]annulen-3a-yl)(propyl)carbamate (16a)** and ***tert*-butyl ((1R*,3aS*,3bS*,6aR*,6bS*)-1-hydroxydecahydrocyclobuta[1,2:3,4]di[5]annulen-3a-yl)(propyl)carbamate (16b)**



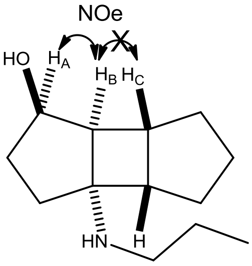


To a solution of Boc protected aminocyclobutane **12** (as a 6:1 ratio of diastereomers) (104 mg, 0.339 mmol) in MeOH (5 mL) was added sodium borohydride (25.7 mg, 0.676 mmol) and the mixture stirred for 1.5 h. Aqueous HCl (2M, 5 mL) was added and the aqueous layer was extracted with DCM (3 x 10 mL), the combined organics were dried ($MgSO_4$) and filtered. The solvent was removed *in vacuo* and purification by flash chromatography on basic alumina (gradient elution from 50 % Et_2O in petroleum ether to 70 % Et_2O in petroleum ether) afforded alcohols **16a** and **16b** as a colourless oil (105 mg, 0.339 mmol) in quantitative yield as a 3:1 ratio of **16a** to **16b** in an inseparable mixture diastereoisomers (measured by integration of ^1H NMR spectrum).

^1H NMR (600 MHz, $CDCl_3$) δ 4.29-4.36 (m, 1H_a and 1H_b), 3.00-3.09 (m, 2H_a and 1H_b, 2.92-2.97 (m, 1H_b), 2.59-2.62 (m, 1H_b), 2.45-2.52 (m, 1H_a and 1H_b), 2.37-2.40 (m, 1H_a and 1H_b), 2.26-2.31 (m, 1H_a), 2.16-2.22 (m, 1Ha and 1H_b), 1.97-2.01 (m, 1H_a and 1H_b), 1.78-1.85 (m, 1H_a and 1H_b), 1.66-1.69 (m, 2H_a and 2H_b), 1.49-1.58 (m, 7H_a and 7H_b), 1.42-1.44 (m, 9H_a and 9H_b), 0.84-0.88 (m, 3H_a and 3H_b); ^{13}C NMR shows two sets of peaks - ^{13}C NMR (150 MHz, $CDCl_3$) Major diastereoisomer – 155.9 (C), 79.4 (C), 74.8 (CH), 64.3 (C), 49.3 (CH), 48.4 (CH), 46.9 (CH_2), 38.7 (CH_2), 33.7 (CH_2), 31.3 (CH_2), 30.2 (CH), 29.5 (CH_2), 28.6 (CH_3), 25.8 (CH_2), 23.6 (CH_2), 11.5 (CH_3). Minor diastereoisomer – 150.0 (C), 78.9 (C), 75.0 (CH), 65.1 (C), 48.9 (CH), 47.3 (CH), 46.9 (CH_2), 37.6 (CH_2), 34.3 (CH_2), 31.4 (CH_2), 30.4 (CH), 29.5 (CH_2), 28.8 (CH_3), 26.1 (CH_2), 24.1 (CH_2), 11.6 (CH); IR (oil, cm^{-1}) 3305 (br), 2928 (s), 2861 (m), 1730 (m), 1692 (s); MS (CI) *m*/z (relative intensity): 310 (M^++H^+, 76), 252 (100), 208 (90);); Exact mass calculated for [$C_{18}H_{31}NO_3$]+H^+ requires *m/z* 310.2377, found 310.2354 (CI).

N.B. Stereochemistry inferred from NOESY data after reduction and Boc removal (**17**).

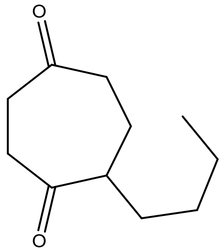
(1R*,3aS*,3bS*,6aR*,6bS*)-3a-(propylamino)decahydrocyclobuta[1,2:3,4]di[5]annulen-1-ol (17)

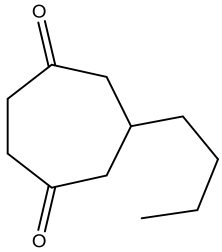


To a solution of alcohols **16** (as a 6:1 mixture of diastereomers) (72.6 mg, 0.235 mmol) in DCM (5 mL) was added TFA (5 mL) and the mixture was stirred at room temperature for 1.5 h. The solution was neutralised with aqueous NaOH (5 mL) and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organics were dried ($MgSO_4$), filtered and the solvent was removed *in vacuo*. Purification by flash chromatography (10 % MeOH in EtOAc to 100% MeOH) afforded a white powder which was triturated with DCM (2 mL). The solvent was removed in vacuo to afford aminocyclobutane **17** as a colourless oil (14.1 mg, 0.067 mmol) in 29 % yield.

NMR ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm 4.30 (dt, *J* = 10.9, 6.4, 1H, H_A), 2.38 - 2.44 (m, 2H), 2.36 (t, *J* = 7.2, 2H), 1.96 - 2.06 (m, 1H), 1.79 - 1.92 (m, 4H, H_B), 1.67 - 1.79 (m, 2H), 1.58 (dd, *J* = 12.8, 7.2, 1H), 1.43 - 1.55 (m, 5H, H_C), 0.92 (t, *J* = 7.5, 3H); ^{13}C (150 MHz, $CDCl_3$) 74.5 (CH), 61.8 (C), 52.5 (CH), 46.3 (CH), 45.1 (CH_2), 35.0 (CH_2), 32.9 (CH_2), 32.1 (CH_2), 30.2 (CH), 27.5 (CH_2), 27.0 (CH_2), 23.8 (CH_2), 12.1 (CH_3); IR (oil, cm^{-1}) 3308 (br), 2940 (s), 2858 (m); MS (CI) *m*/z (relative intensity): 210 (M^{+}+H^{+}, 100), 151 (70), 133 (64); Exact mass calculated for $[C_{13}H_{23}NO]+H^{+}$ requires *m/z* 210.1850, found 210.1858 (CI).

5-butylcycloheptane-1,4-dione (18) and **6-butylcycloheptane-1,4-dione (19)**



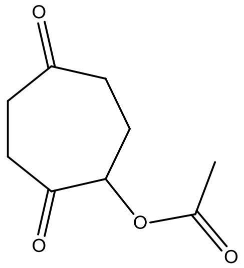


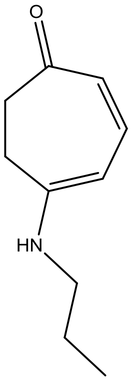
A solution of Boc protected vinylogous amide **6** (360 mg, 1.50 mmol) in a 3:1 mixture of MeCN and 1-hexene (50 mL) was degassed for 30 min and irradiated for 1 h. The solvents were removed *in vacuo* and the resulting oil was dissolved in DCM (10 mL) and TFA (10 mL) was added slowly. The mixture was stirred for 1 h before the solvents were removed *in vacuo*. The resulting oil was purified by flash chromatography (50 % Et_2O in hexane) to afford diketone **18** as a colourless oil (129 mg, 0.71 mmol) in 47 % yield and diketone **19** as a colourless oil (71.0 mg, 0.39 mmol) in 26 % yield.

18 ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.53-2.69 (m, 7H), 2.01-2.06 (m, 1H), 1.73-1.79 (m, 1H), 1.58-1.65 (m, 1H), 1.21-1.38 (m, 5H), 0.88 (t, *J* = 7.2, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) 212.6 (C), 210.9 (C), 52.4(CH), 41.9 (CH_2), 38.2 (CH_2), 37.4 (CH_2), 30.6 (CH_2), 29.6 (CH_2), 27.0 (CH_2), 22.8 (CH_2), 14.0 (CH_3); IR (oil, cm^{-1}) 2955 (m), 2930 (m), 2860 (m), 1703 (s); MS (ES-) *m*/z (relative intensity): 181 (M^{+} - H^{+}, 16), 174 (47), 171 (37), 169 (100), 161 (18), 143 (15); Exact mass calculated for $[C_{11}H_{18}O_2]$-H^{+} requires *m/z* 181.1229, found 181.1511 (ES-).

19 ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.71 (dd, *J* = 13.5, 4.0, 2H), 2.58-2.68 (m, 4H), 2.53 (dd, *J* = 13.5, 9.3, 2H), 2.02-2.08 (m, 1H), 1.27-1.36 (m, 6H), 0.88 (t, *J* = 7.1, 3H); ^{13}C NMR (150 MHz, CDCl$_3$) 210.3 (C), 49.4 (CH$_2$), 38.3 (CH$_2$), 36.1 (CH$_2$), 32.5 (CH), 29.0 (CH$_2$), 22.6 (CH$_2$), 14.1 (CH$_3$); IR (oil, cm^{-1}) 2956 (m), 2929 (m), 2860 (m), 1700 (s); MS (ES-) *m*/z (relative intensity): 181 (M$^+$ - H$^+$, 22), 174 (50), 171 (35), 169 (100), 161 (15); Exact mass calculated for [C$_{11}$H$_{18}$O$_2$]-H$^+$ requires *m/z* 181.1229, found 181.1522 (ES-).

2,5-dioxocycloheptyl acetate (20) and **5-(propylamino)cyclohepta-2,4-dienone (21)**



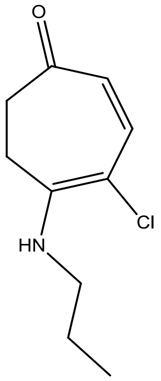


A solution of Boc protected vinylogous amide **6** (239 mg, 1.00 mmol) in MeCN (29 mL) and vinyl acetate (1 mL) was degassed for 15 min and irradiated for 45 min. The solvents were removed *in vacuo* and the resulting oil was dissolved in DCM (10 mL) and TFA (10 mL) was added slowly. The mixture was stirred for 1 h before the solvents were removed *in vacuo*. The resulting oil was dissolved in DCM (10 mL), washed with aqueous NaHCO$_3$ (1 M, 2 x 20 mL) and water (20 mL), dried (Na$_2$SO$_4$), filtered and the solvents were removed *in vacuo*. The resulting oil was purified by flash chromatography (Et$_2$O to 5 % MeOH in Et$_2$O) to afford diketone **20** as a clear oil (85.7 mg, 0.466 mmol) in 47 % yield and conjugated enamine **21** as a yellow solid (42.4 mg, 0.257 mmol) in 26 % yield. mp 102.1-103.2 °C.

20 ^{1}H NMR (600 MHz, CDCl$_3$) δ 5.27 (dd, *J* = 10.1, 4.8, 1H), 2.63-2.79 (m, 5H), 2.53-2.57 (m, 1H), 2.20 (dddd, *J* = 14.7, 7.5, 4.5, 4.2, 1H), 2.15 (s, 3H), 1.97-2.04 (m, 1H); ^{13}C NMR (150 MHz, CDCl$_3$) 209.1 (C), 204.2 (C), 170.1 (C), 78.0 (CH), 39.0 (CH$_2$), 37.4 (CH$_2$), 35.2 (CH$_2$), 26.0 (CH$_2$), 20.7 (CH$_3$); IR (oil, cm^{-1}) 2941 (w), 1741 (s), 1712 (s), 1703 (s); MS (CI+) *m*/z (relative intensity): 185 (M^+ +H^+, 32), 143 (25), 141 (10), 125 (100), 98 (12), 97 (13); Exact mass calculated for $[C_9H_{11}O_4]+H^+$ requires *m/z* 185.08138, found 185.08099 (CI+).

21 ^{1}H NMR (600 , $CDCl_3$) δ 6.70 (dd, *J* = 11.9, 8.9, 1H), 5.60 (d, *J* = 11.9, 1H), 4.86 (d, *J* = 9.0, 1H), 4.50 (br, 1H), 3.02 (td, *J* = 7.2, 5.5, 2H), 2.58-2.60 (m, 2H), 2.43-2.45 (m, 2H), 1.63 (sext, *J* = 7.3, 2H), 0.98 (t, *J* = 7.4, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) 200.0 (C), 160.0 (C), 144.2 (CH), 117.9 (CH), 92.0 (CH), 45.3 (CH_2), 39.0 (CH_2), 30.1 (CH_2), 21.9 (CH_2), 11.7 (CH_3); IR (solid, cm^{-1}) 3287 (br, w), 3078 (w), 2961 (w), 2933 (w), 2875 (w), 1736 (w), 1617 (m), 1586 (w), 1504 (s); MS (EI) *m*/z (relative intensity): 165 (M^+, 100), 137 (42), 136 (40), 122 (42), 108 (71), 94 (31); Exact mass calculated for $[C_{10}H_{15}NO]$ requires *m/z* 165.11481, found 165.11488 (EI).

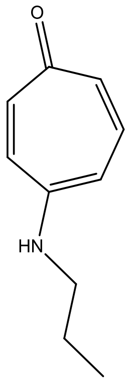
4-chloro-5-(propylamino)cyclohepta-2,4-dienone (22)



To a solution of Boc protected vinylogous amide **6** (239 mg, 1.00 mmol) in MeCN (50 mL) was added *trans* 1,2-dichloroethylene (385 µL, 485 mg, 5.00 mmol) and the mixture degassed for 15 min and irradiated for 2 h. The solvents were removed *in vacuo* and the resulting oil was dissolved in DCM (10 mL) and TFA (10 mL) was added slowly. The mixture was stirred for 1 h before the solvents were removed *in vacuo*. NEt_3 (5 mL) was added and the mixture stirred for a further 5 min before the solvent was removed in vacuo. The resulting oil was purified by flash chromatography (25 % Et_2O in hexane) to afford conjugated enamine **22** as a yellow solid (153 mg, 0.769 mmol) in 77 % yield. mp 97.0-97.4 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (d, *J* = 12.6, 1H), 5.62 (d, *J* = 12.6, 1H), 5.30 (br, 1H), 3.25 (td, *J* = 7.2, 6.1, 2H), 2.66-2.69 (m, 2H), 2.59-2.62 (m, 2H), 1.63 (sext, *J* = 7.3, 2H), 1.01 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 198.7 (C), 154.3 (C), 143.1 (CH), 117.2 (CH), 100.2 (C), 45.6 (CH_2), 38.5 (CH_2), 24.0 (CH_2), 21.9 (CH_2), 11.2 (CH_3); IR (solid, cm^{-1}) 3316 (br, w), 2964 (w), 2932 (w), 2872 (w), 1724 (m), 1638 (m), 1591 (s), 1530 (s); MS (ES+) *m*/z (relative intensity): 202 (^{37}Cl M$^+$ +H$^+$, 21), 200 (^{35}Cl M$^+$ +H$^+$, 62) 174 (33), 164 (32), 129 (21), 105 (64); Exact mass calculated for $[C_{10}H_{14}NO^{35}Cl]+H^+$ requires *m/z* 200.0842, found 200.0841 (ES+).

4-(propylamino)cyclohepta-2,4,6-trienone (23)

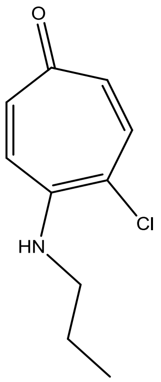


A solution of conjugated enamine **22** (50.0 mg, 0.250 mmol) in PhMe (3 mL) was heated to reflux for 3 h. The solvent was removed *in vacuo* and purification by flash chromatography (EtOAc) afforded aminotropone **23** as a yellow solid (39.2 mg, 0.240 mmol) in 96 % yield. dec. >150 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.04 (t, *J* = 10.3, 1H), 6.93 (dd, *J* = 12.9, 2.6, 1H), 6.87 (dd, *J* = 13.0, 2.3, 1H), 6.40 (dd, *J* = 11.7, 2.6, 1H), 6.13 (br, 1H), 5.84 (dd, *J* = 10.3, 2.1, 1H), 3.04-3.07 (m, 2H), 1.67 (sext, *J* = 7.3, 2H), 0.98 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 185.9 (C), 155.0 (C), 142.2 (CH), 140.3 (CH), 133.2 (CH), 126.2 (CH), 105.1 (CH), 45.4 (CH_2), 21.6 (CH_2), 11.8 (CH_3); IR (solid, cm^{-1}) 3247 (br, m), 3058 (m), 2961 (m), 2932 (m), 2874 (m), 1636 (m), 1587 (s), 1492 (s);

MS (ES+) *m*/z (relative intensity): 164 (M^+ +H^+, 100), 135 (12); Exact mass calculated for $[C_{10}H_{13}NO]+H^+$ requires *m/z* 164.0997, found 164.0936 (ES+).

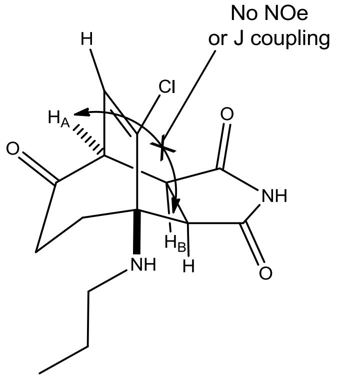
4-chloro-5-(propylamino)cyclohepta-2,4,6-trienone (25)



A solution of conjugated enamine **22** (30.0 mg, 0.150 mmol) and NEt_3 (105 µL, 76.0 mg, 0.750 mmol) in PhMe (2 mL) was heated to reflux for 48 h open to air. The solvents were removed in vacuo and purification by flash chromatography (EtOAc) afforded aminochlorotropone **25** as a yellow solid (14.9 mg, 0.0756 mmol) in 50 % yield. dec. >165 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 12.8, 1H), 7.14 (dd, *J* = 13.3, 2.8, 1H), 7.04 (d, *J* = 13.3, 1H), 6.48 (dd, *J* = 12.8, 2.8. 1H), 5.37 (br, 1H), 3.35 (td, *J* = 7.1, 5.6, 2H), 1.74 (sext, *J* = 7.3, 2H), 1.06 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 184.4 (C), 148.5 (C), 141.8 (CH), 139.7 (CH), 126.3 (CH), 124.7 (CH), 116.1 (C), 45.8 (CH_2), 22.9 (CH_2), 11.3 (CH_3); IR (solid, cm^{-1}) 3405 (w), 3290 (br, w), 2963 (w), 2932 (w), 2875 (w), 1632 (m), 1577 (m), 1544 (s), 1509 (s); MS (EI) *m*/z (relative intensity): 199 (^{37}Cl M^+, 6), 197 (^{35}Cl M^+, 16), 162 (17), 142 (29), 140 (100), 105 (18); Exact mass calculated for $[C_{10}H_{12}NO^{35}Cl]-H^+$ requires *m/z* 196.0529, found 196.0522 (ES-).

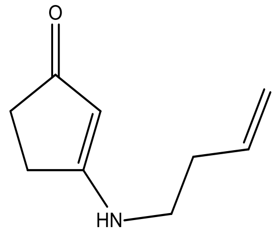
(3aR*,4R*,8R*,8aR*)-9-chloro-8-(propylamino)-3a,4,6,7,8,8a-hexahydro-4,8-ethenocyclohepta[c]pyrrole-1,3,5(2H)-trione (26)



To a solution of conjugated enamine **22** (70.0 mg, 0.352 mmol) in PhMe (4 mL) was added maleimide (68.3 mg, 0.704 mmol) and the mixture was stirred at reflux for 1 h. The solvent was removed *in vacuo* and purification by flash chromatography (50 % Et_2O in petroleum ether to 100 % Et_2O) afforded Diels-Alder adduct **26** as a white powder (82.5 mg, 0.279 mmol) in 79 % yield. dec. >210 °C.

^{1}H NMR (600 MHz, DMSO) δ 11.57 (s, 1H), 6.25 (d, *J* = 8.1, 1H), 3.76 (d, *J* = 8.5, 1H), 3.38 (d, *J* = 8.5, 1H, H_B), 3.22 (d, *J* = 8.1, 1H, H_A), 2.73-2.78 (m, 1H), 2.50-2.58 (m, 3H), 2.34 (dd, *J* = 9.9, 3.9, 1H), 2.13 (dt, *J* = 14.1, 7.0, 1H), 1.93 (dt, *J* = 14.1, 7.0, 1H), 1.47 (sext, *J* = 7.3, 2H), 0.93 (t, *J* = 7.3, 3H); ^{13}C NMR (150 MHz, DMSO) 204.3 (C), 178.4 (C), 178.1 (C), 140.9 (C), 122.4 (CH), 60.6 (C), 51.1 (CH), 47.4 (CH), 43.7 (CH), 43.6 (CH_2), 37.7 (CH_2), 33.7 (CH_2), 23.5 (CH_2), 11.9 (CH_3); IR (solid, cm^{-1}) 3204 (m), 3096 (w), 2964 (w), 2932 (w), 2871 (w), 1777 (m), 1717 (s), 1686 (s), 1625 (m); MS (ES+) *m*/*z* (relative intensity): 330 (100), 297 (M^+ +H^+, 43), 202 (29), 200 (83); Exact mass calculated for $[C_{14}H_{17}N_2O_3Cl]+H^+$ requires *m/z* 297.1006, found 297.1003 (ES+).

^{1}H and ^{13}C NMR spectra



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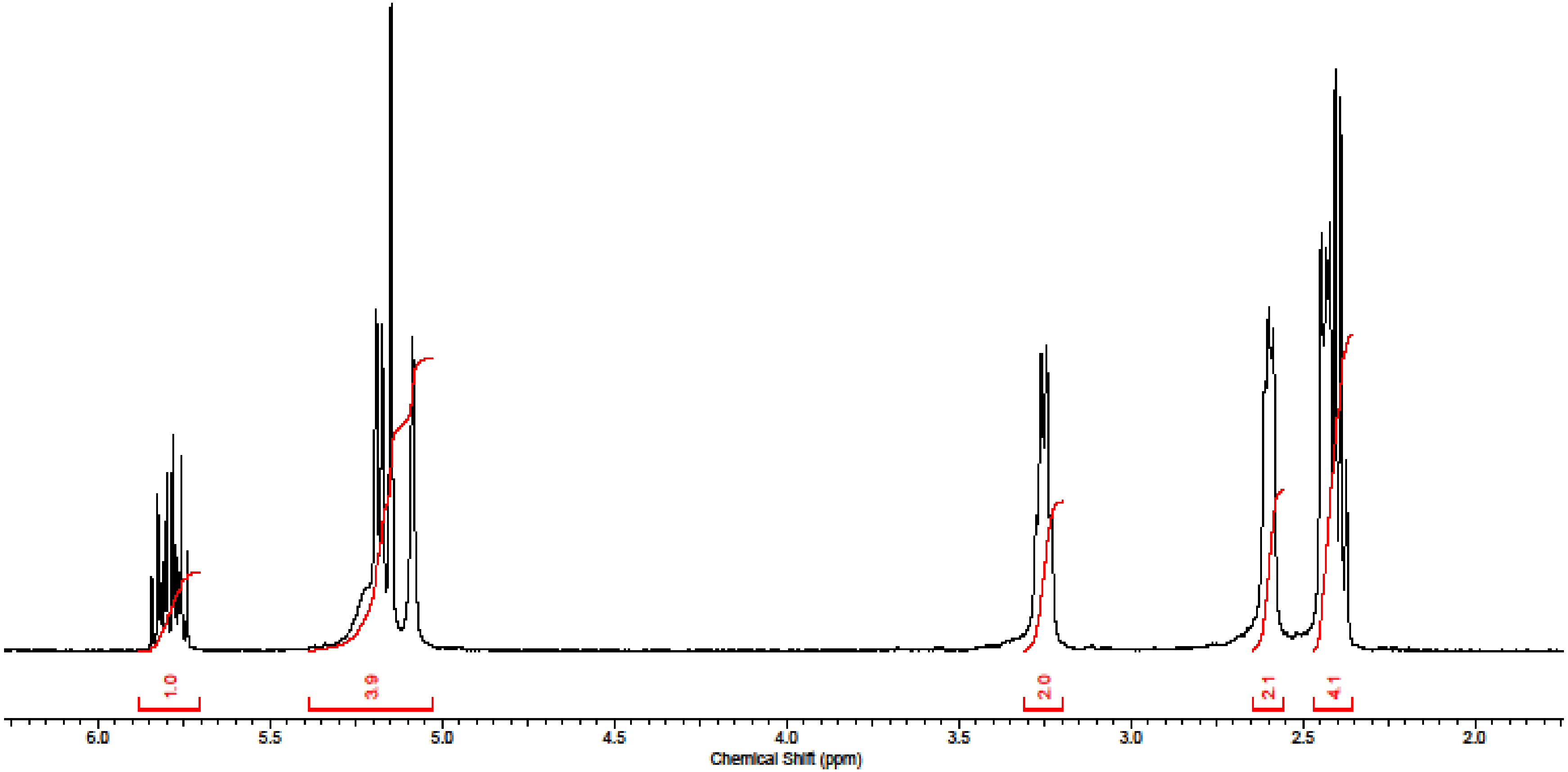

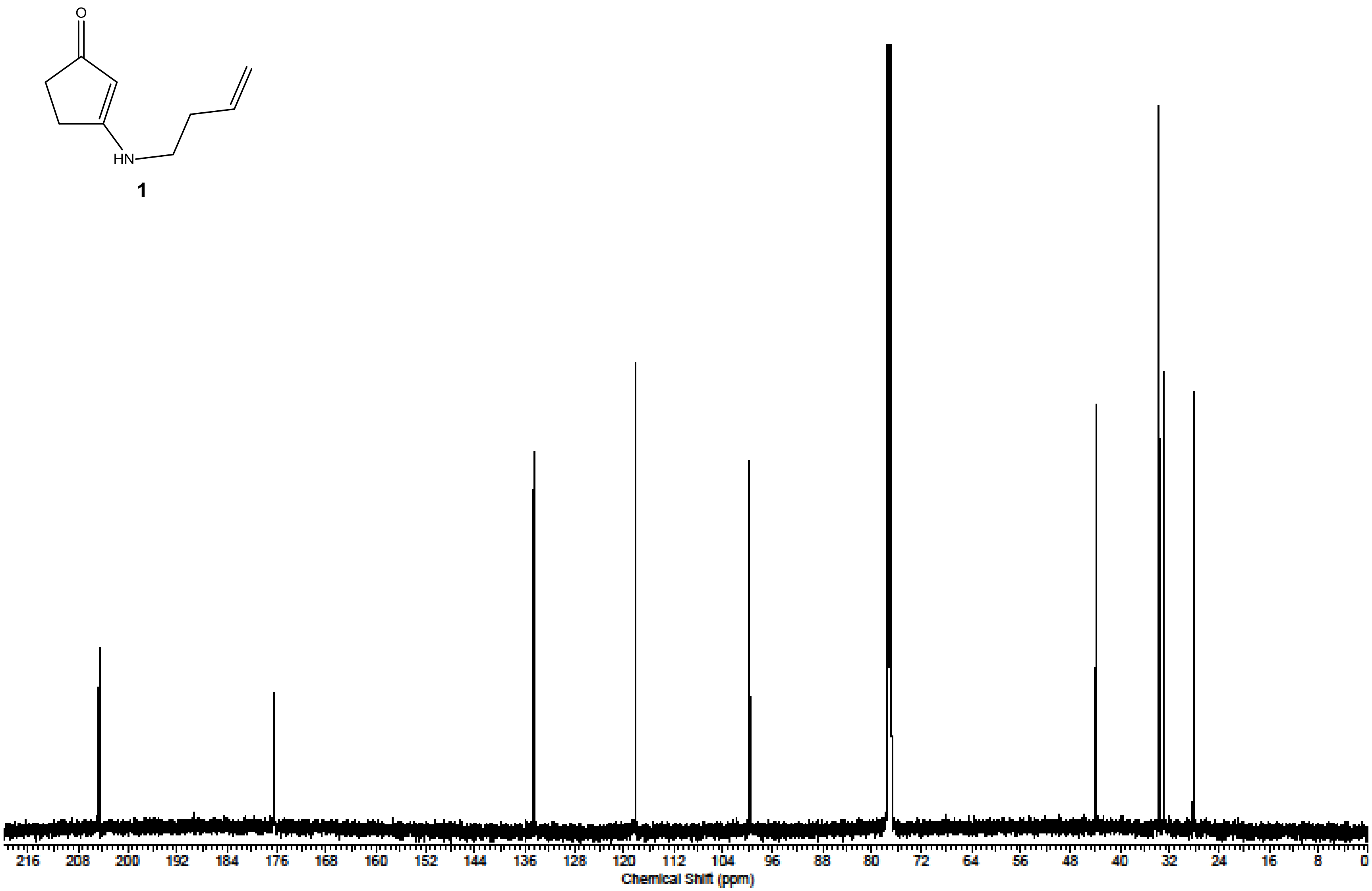
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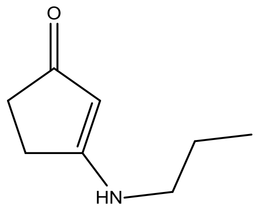
1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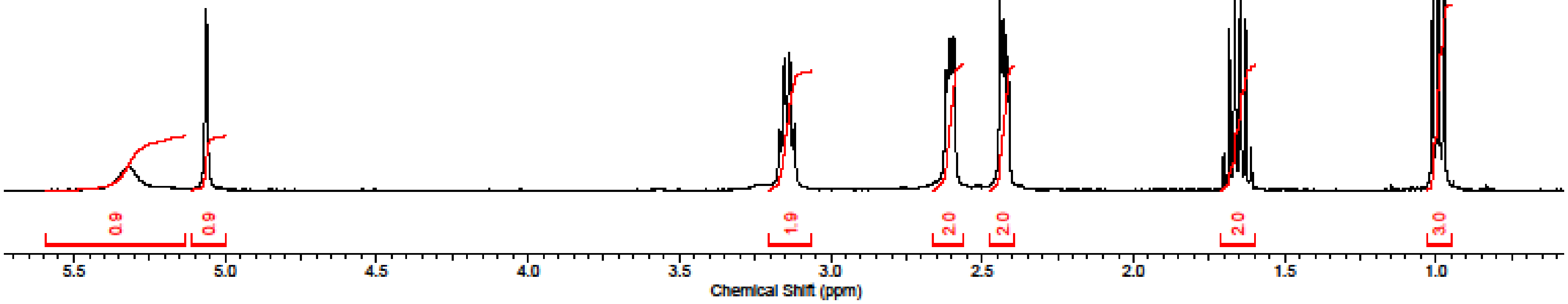
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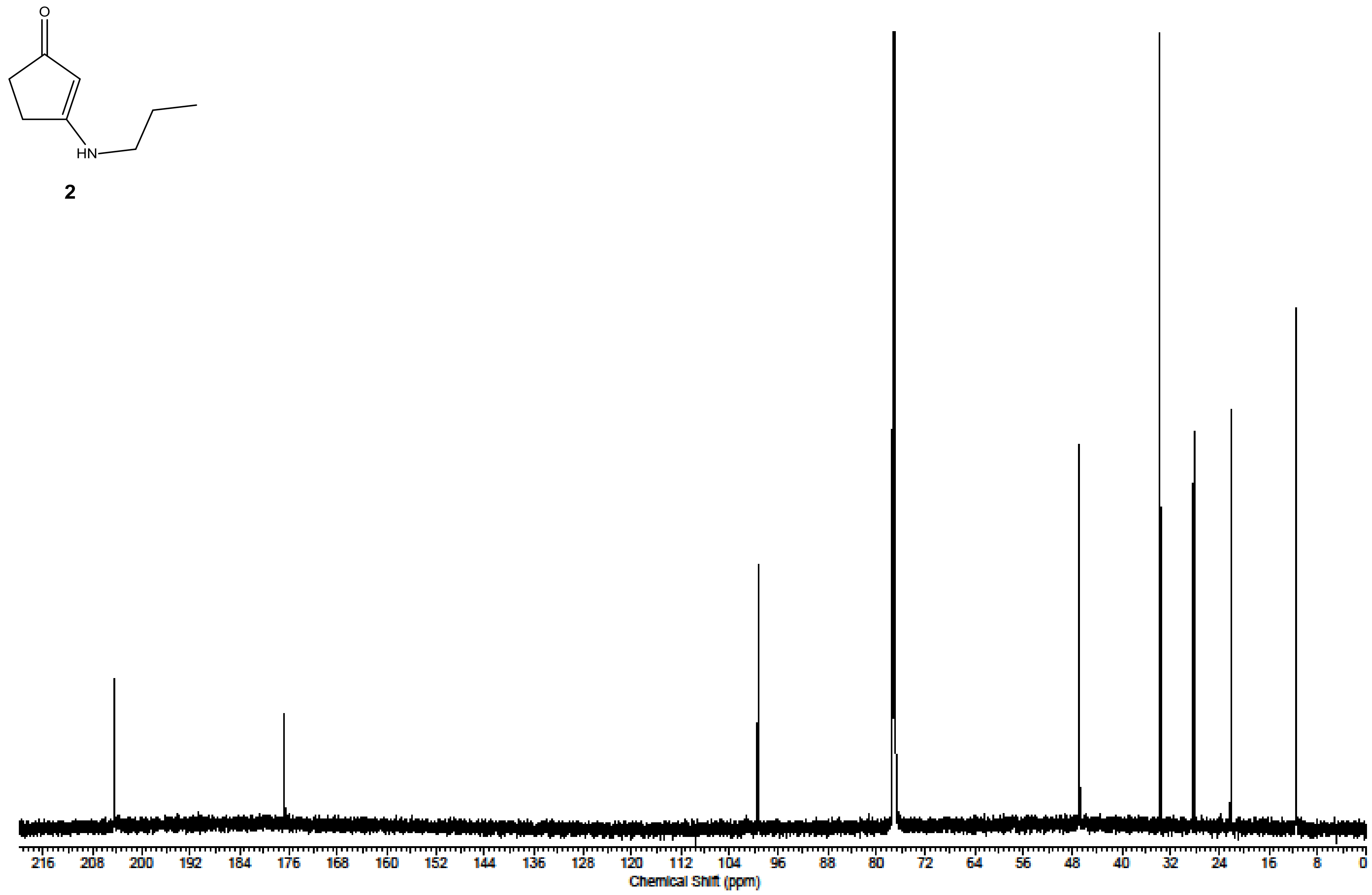

2

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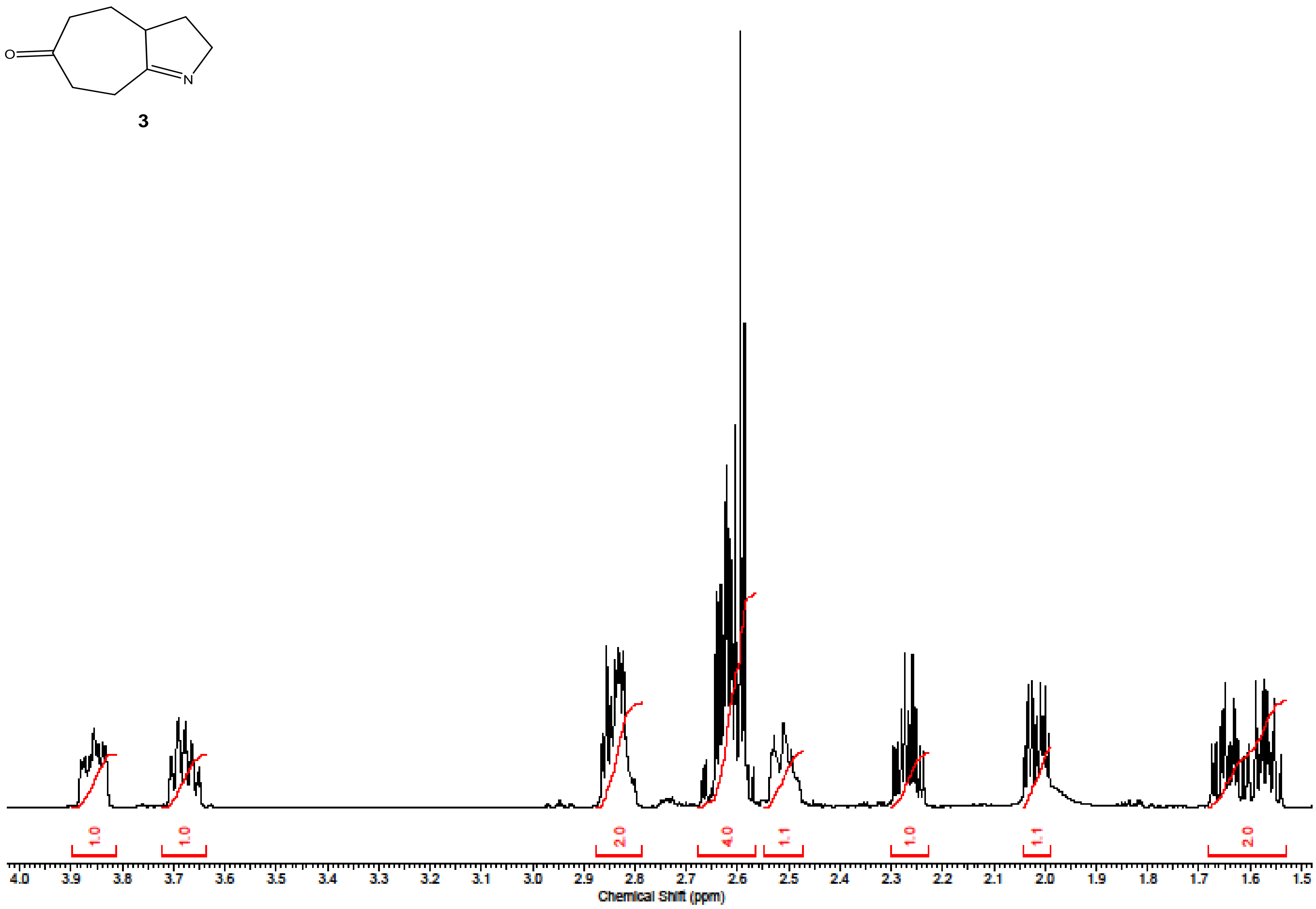

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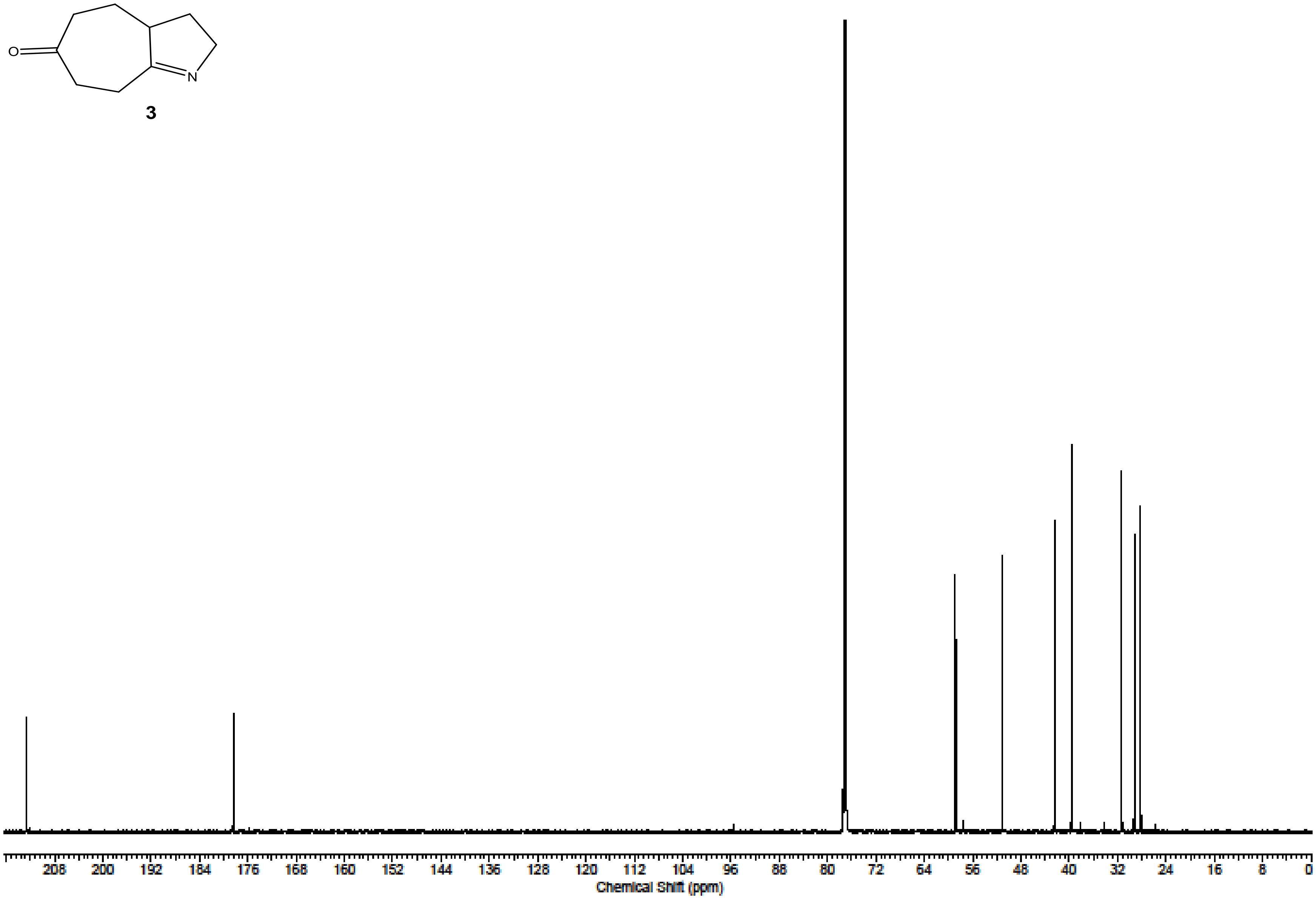
Chemical Shift (ppm)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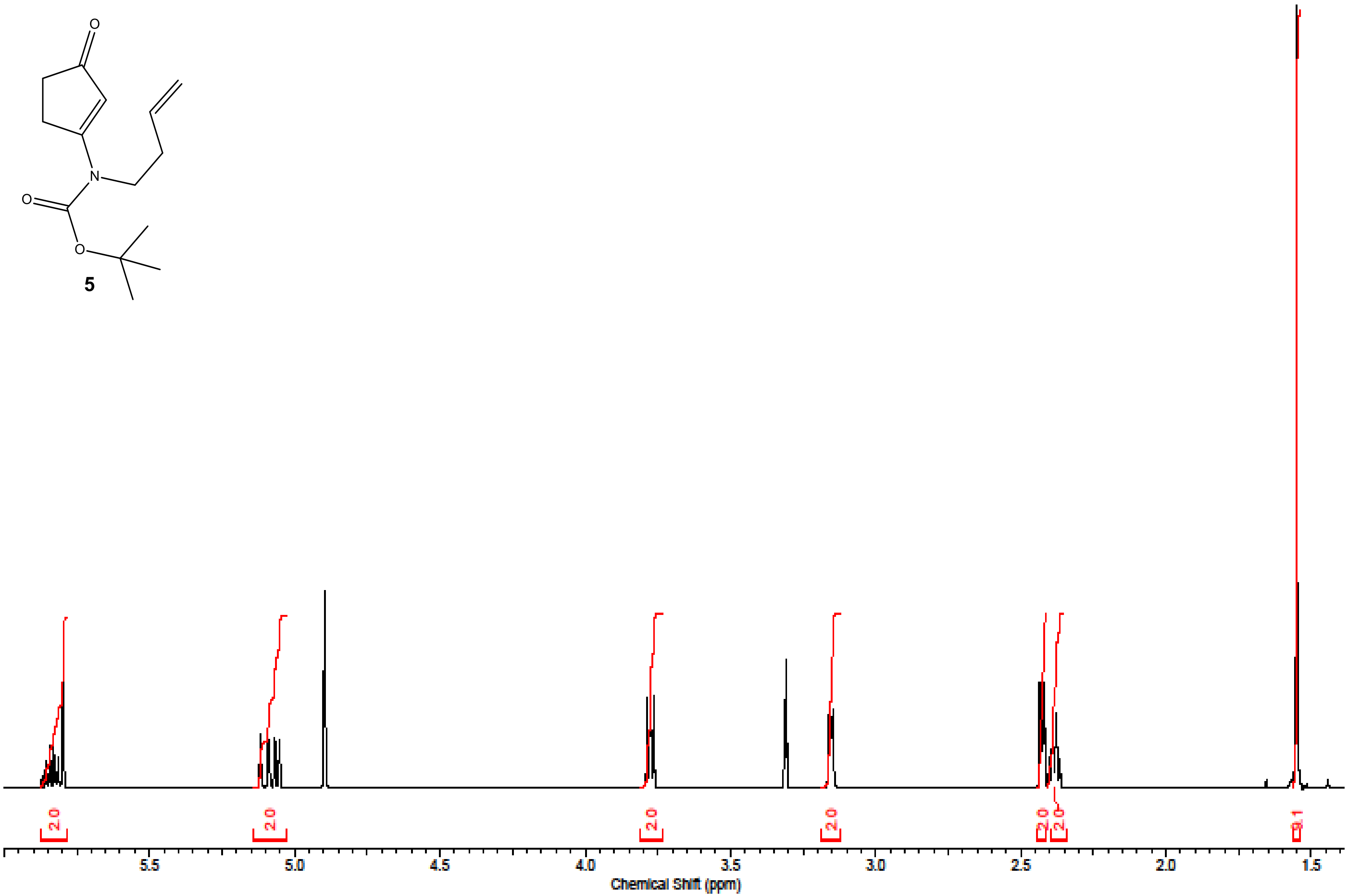
Chemical Shift (ppm)

3



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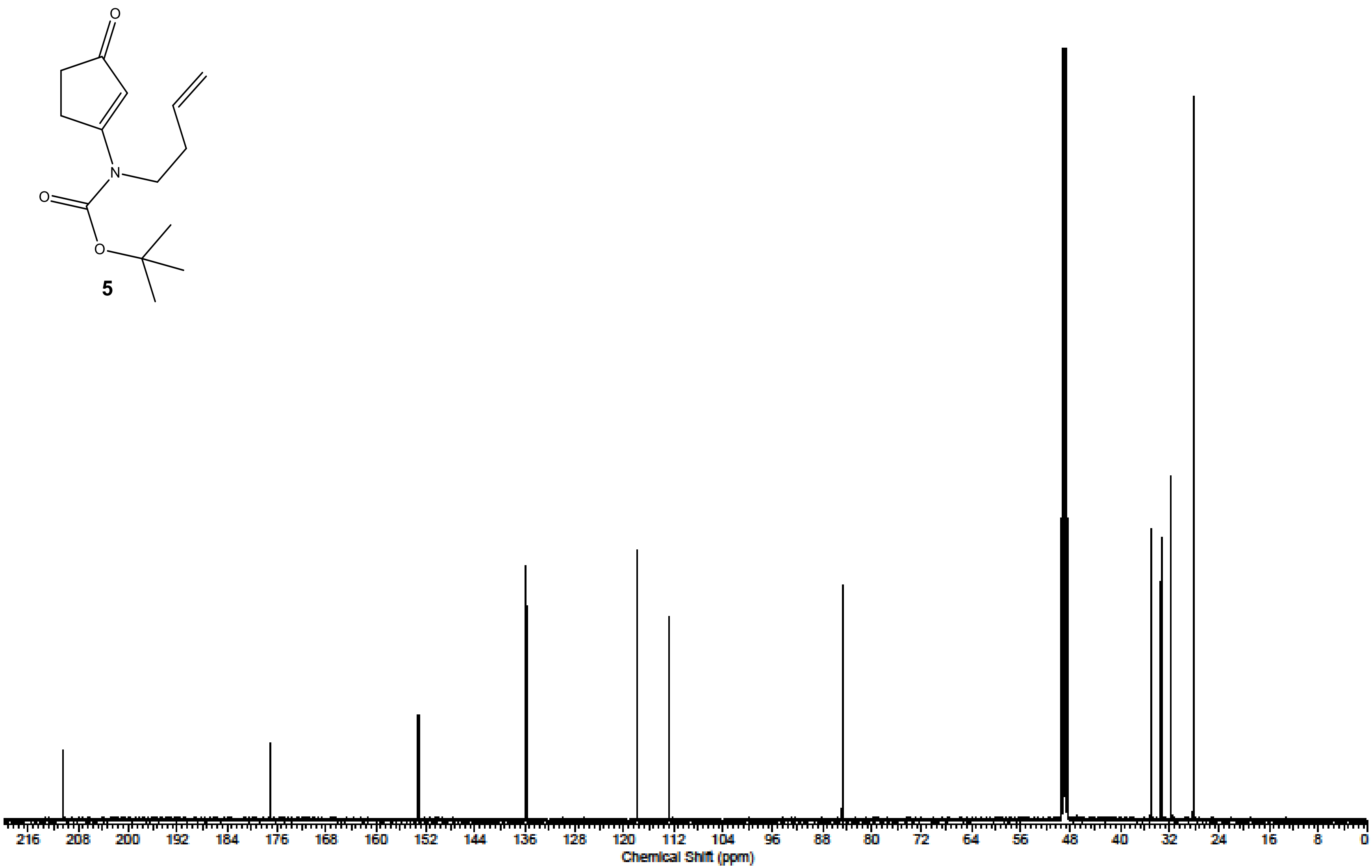

5

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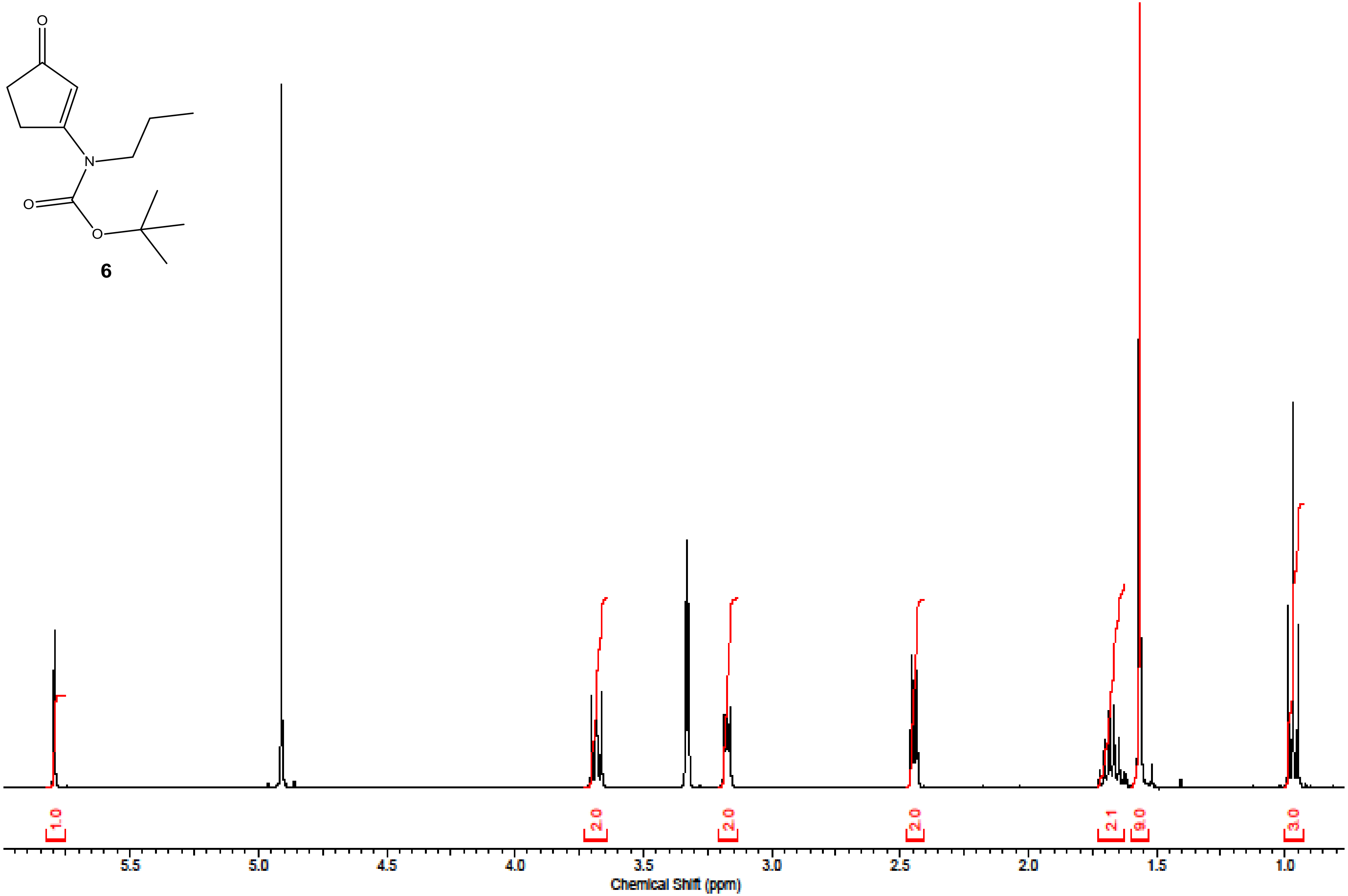
Chemical Shift (ppm)



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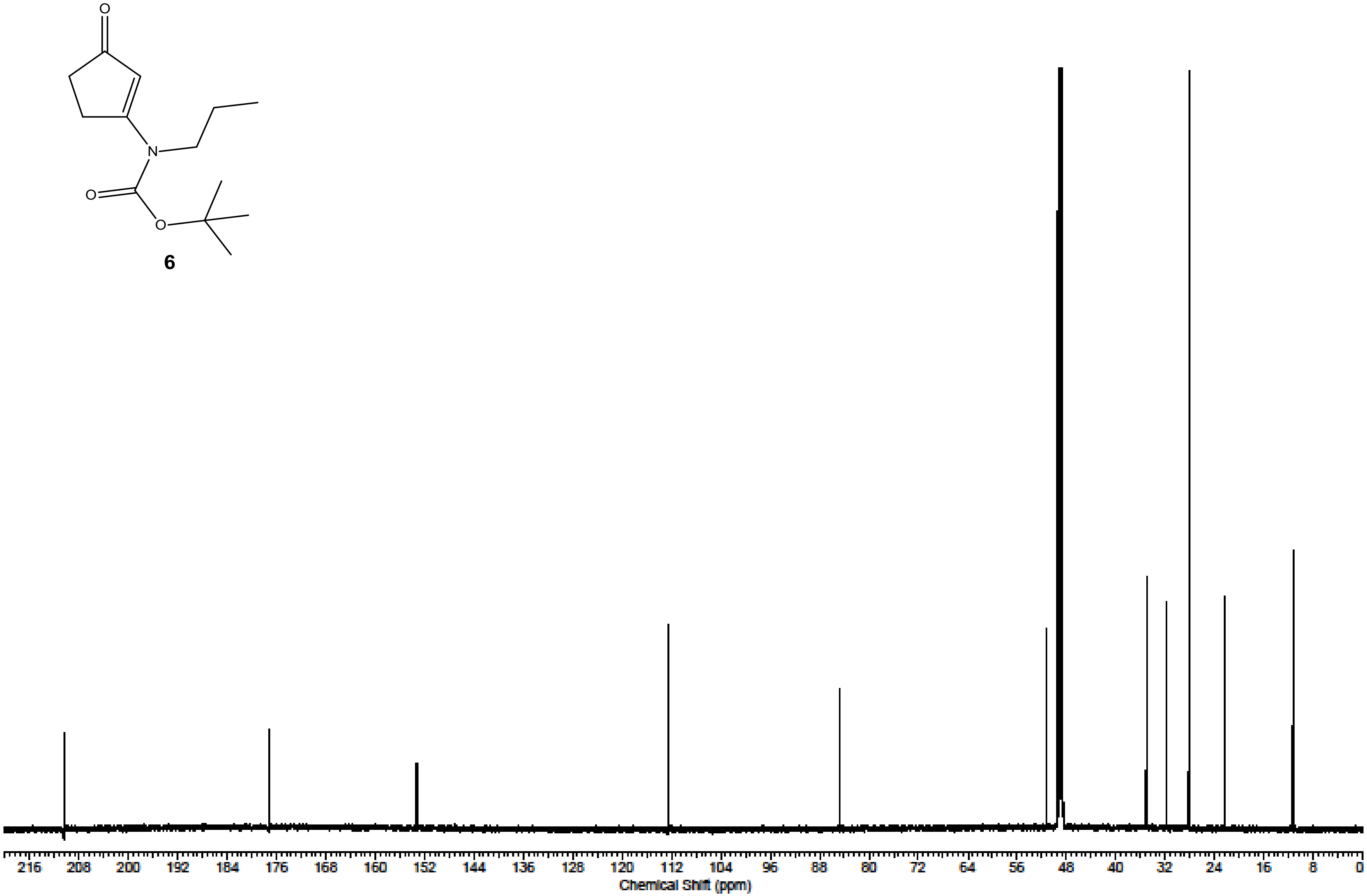
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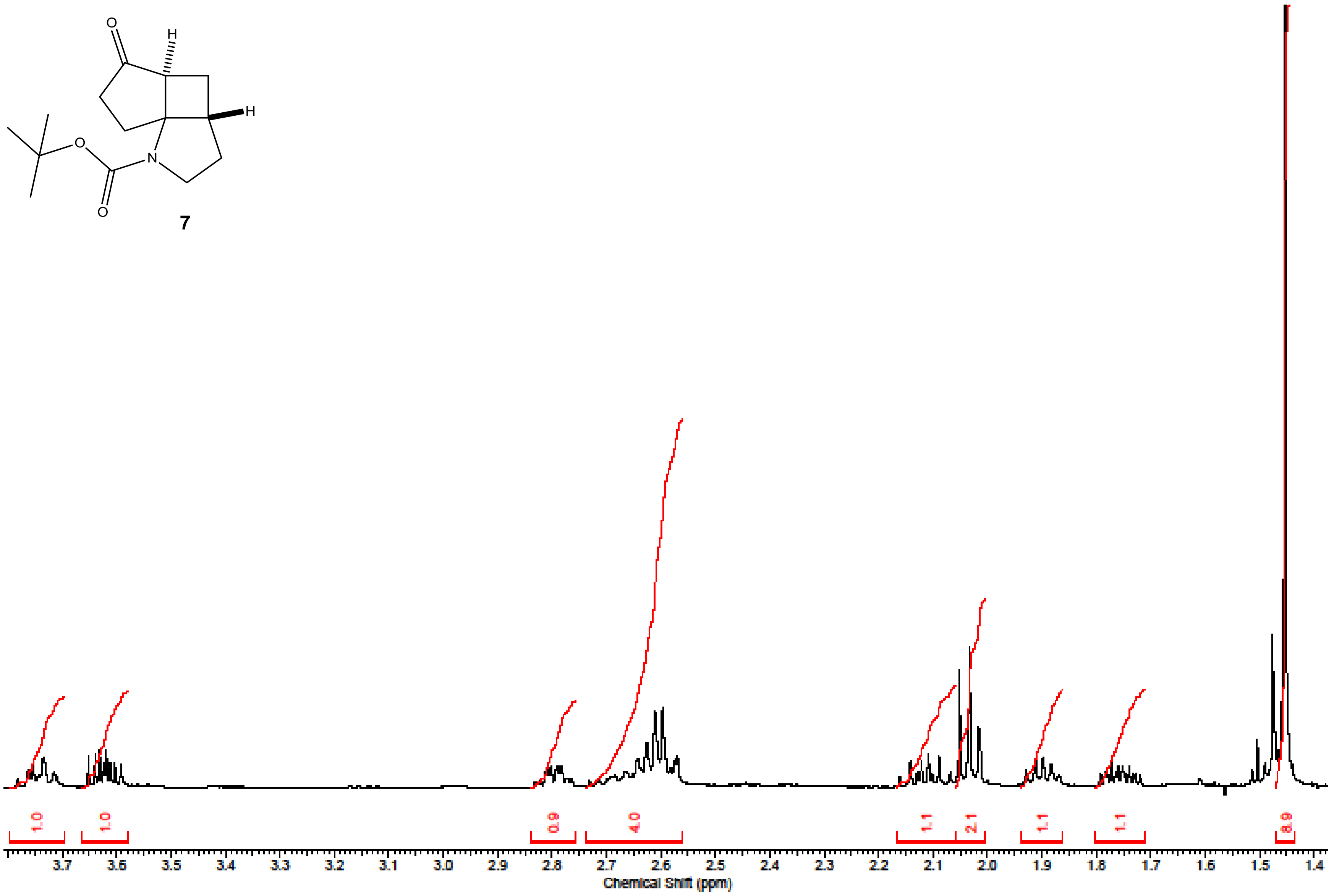
Chemical Shift (ppm)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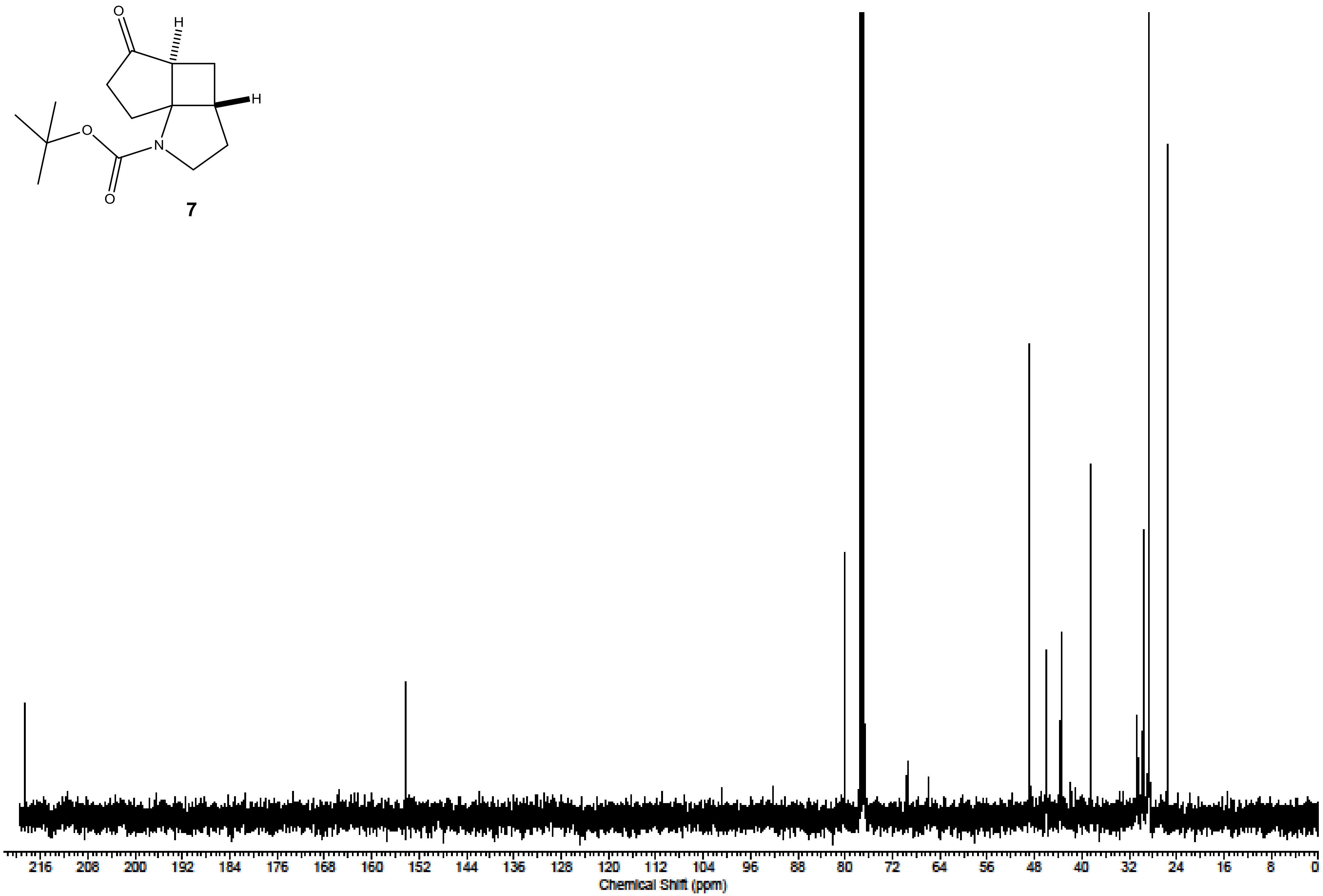
Chemical Shift (ppm)

7



7

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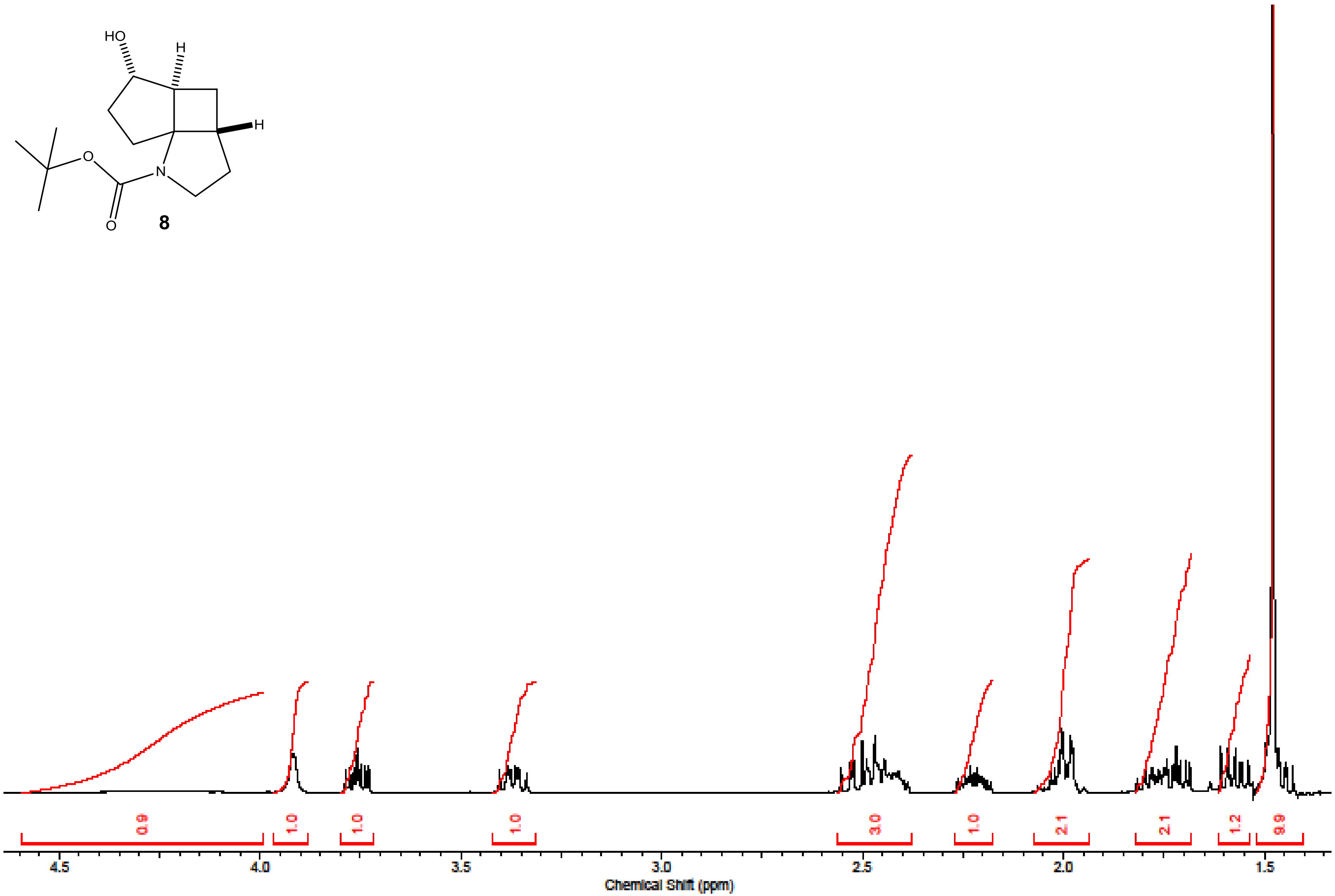
Chemical Shift (ppm)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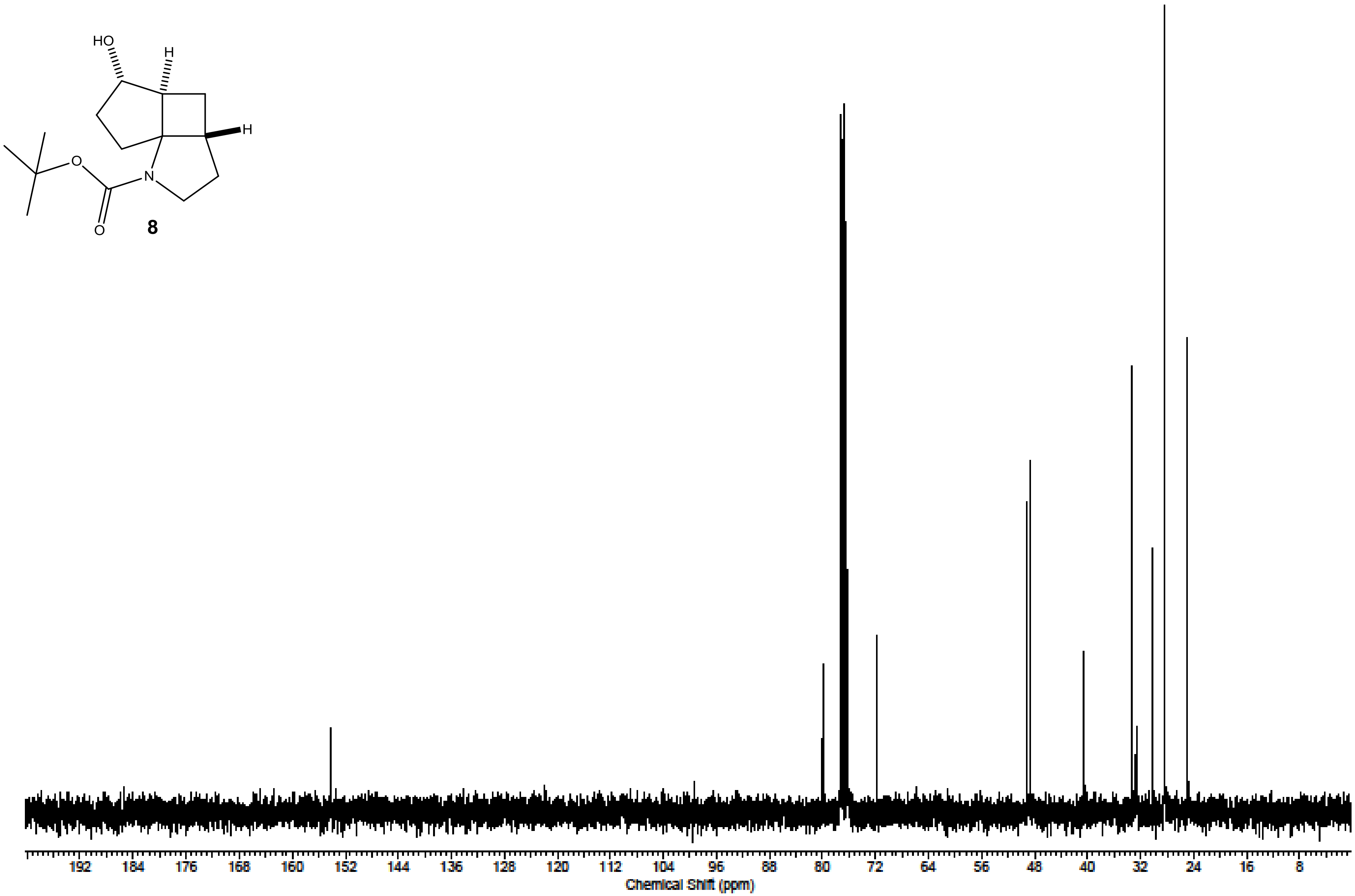
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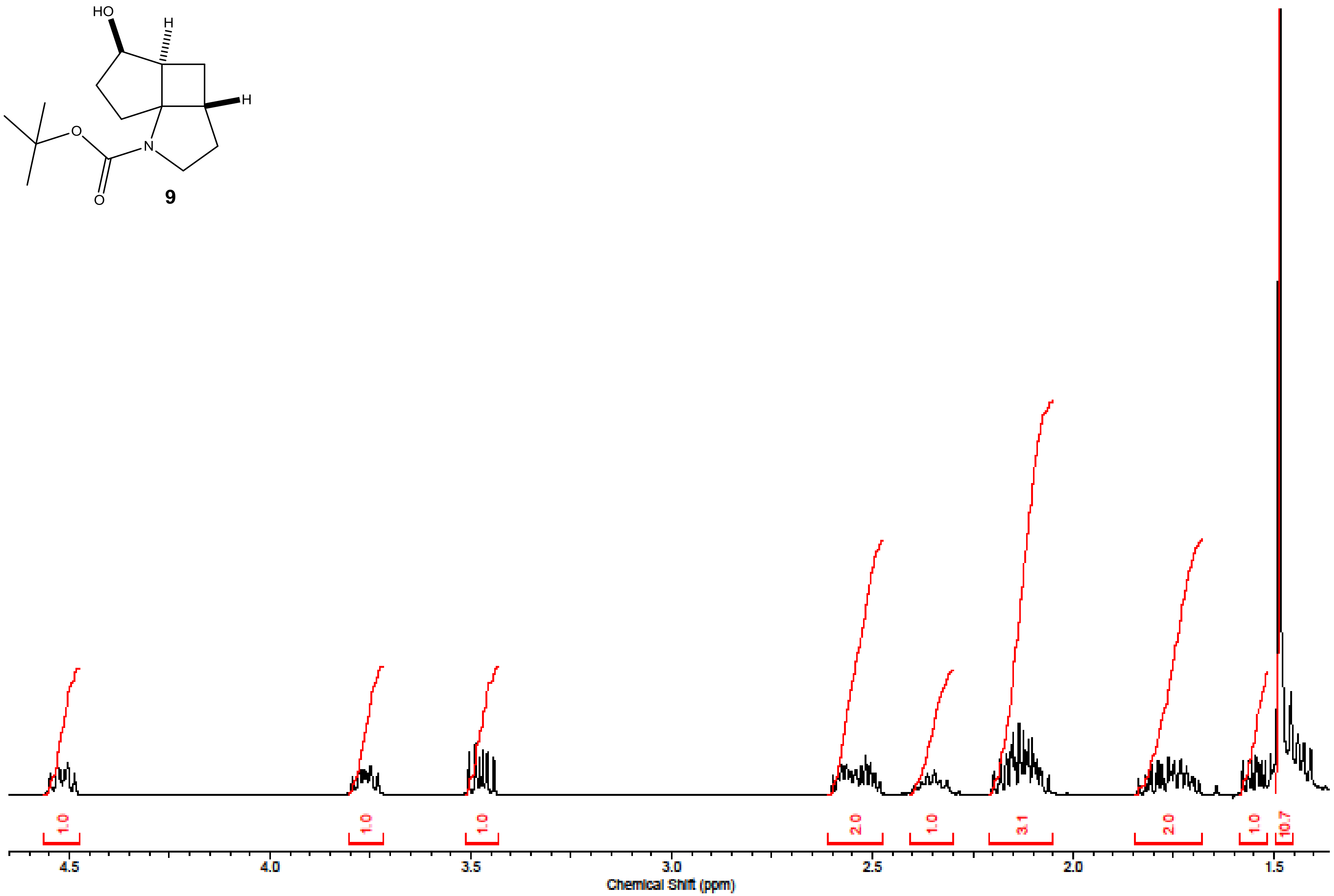
Chemical Shift (ppm)



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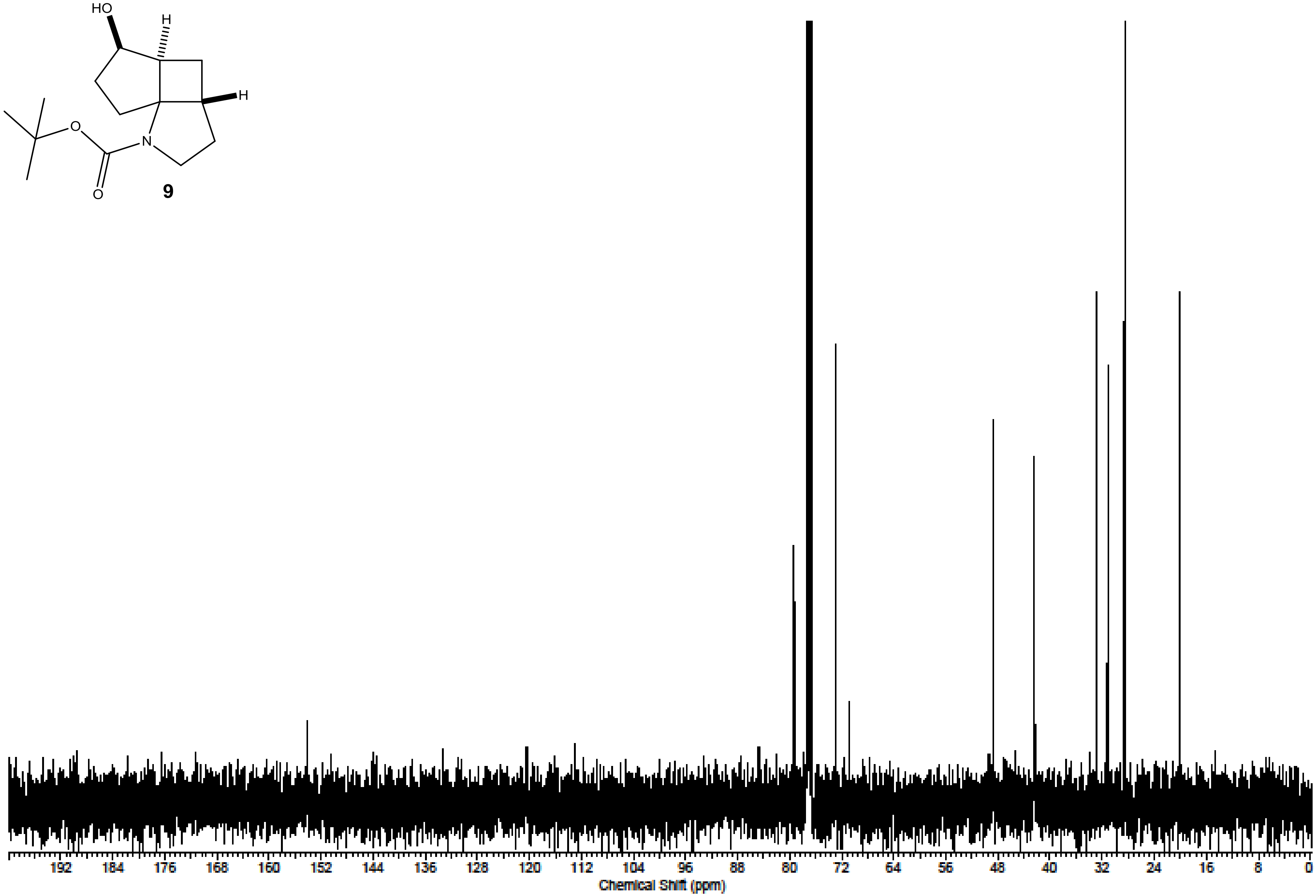
Chemical Shift (ppm)



9

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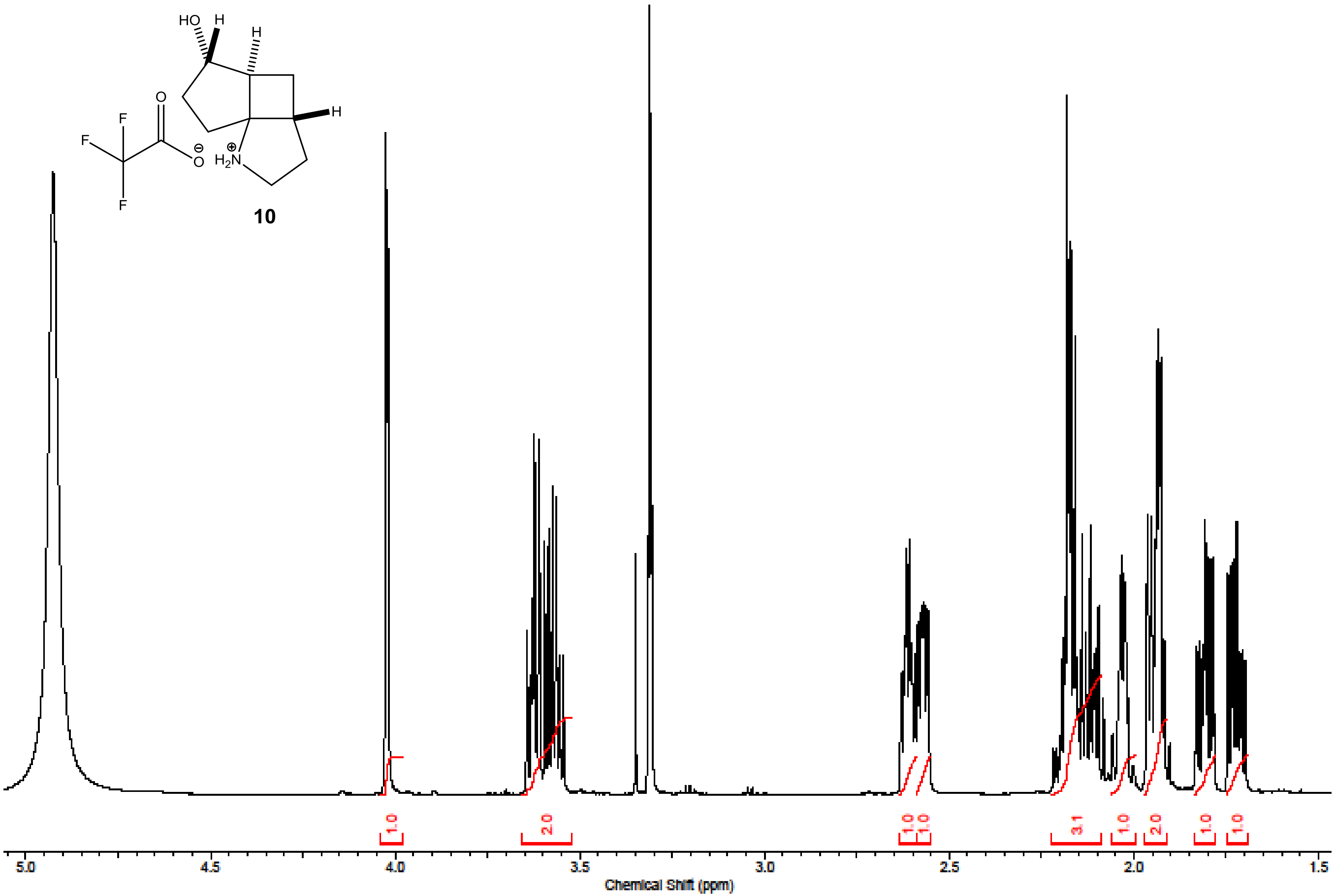
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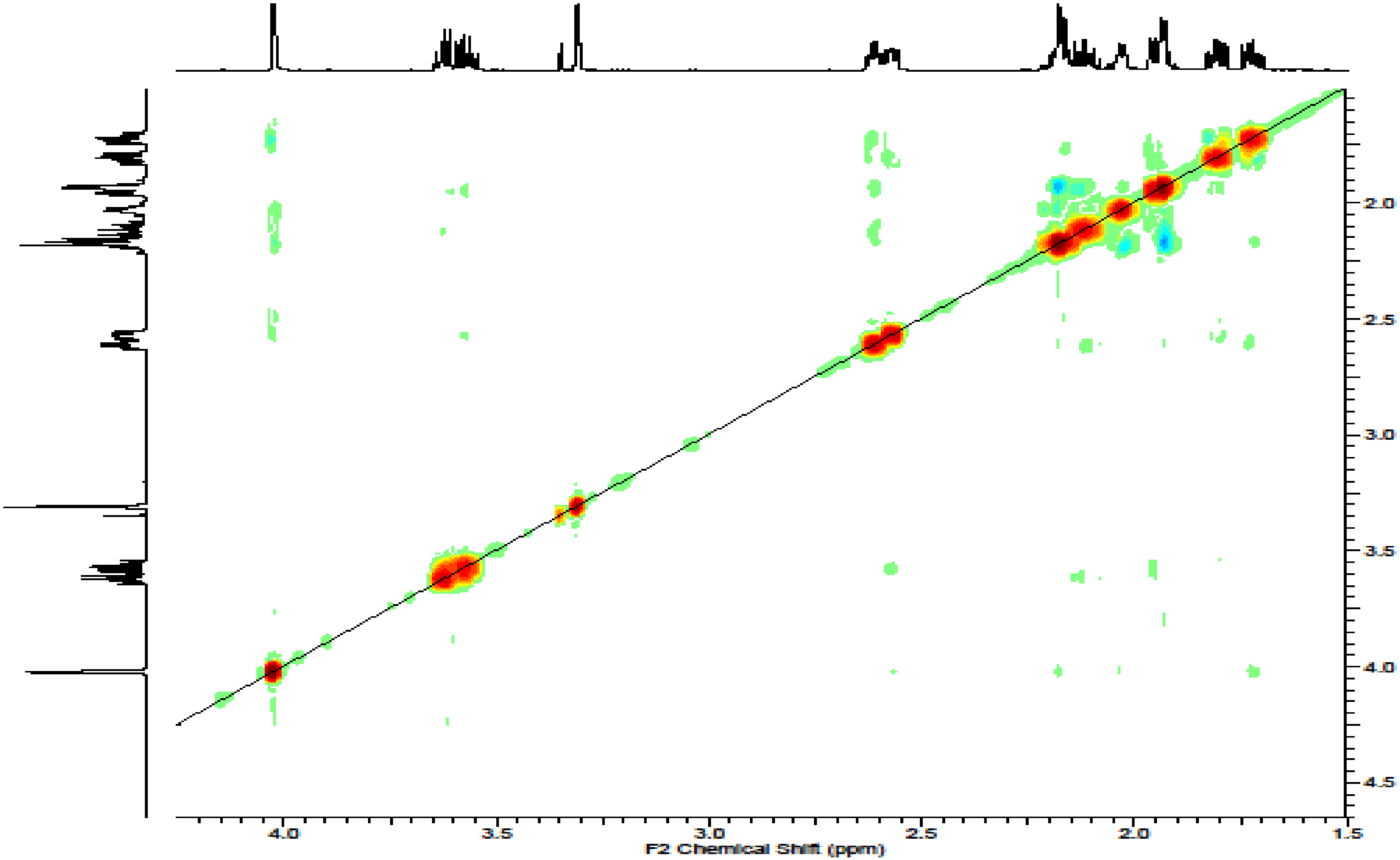
Chemical Shift (ppm)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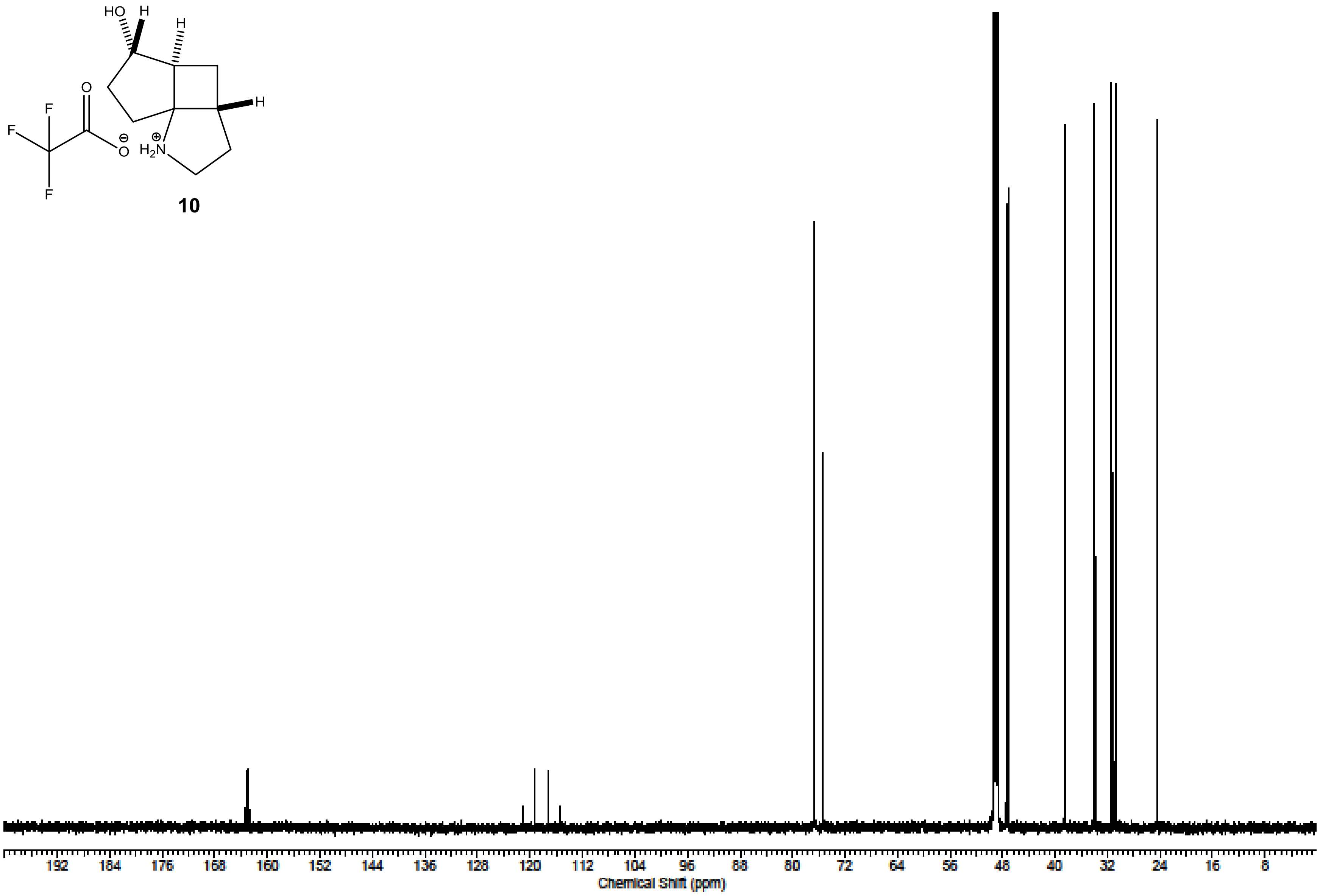
F2 Chemical Shift (ppm)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$H_2N^{\oplus}$
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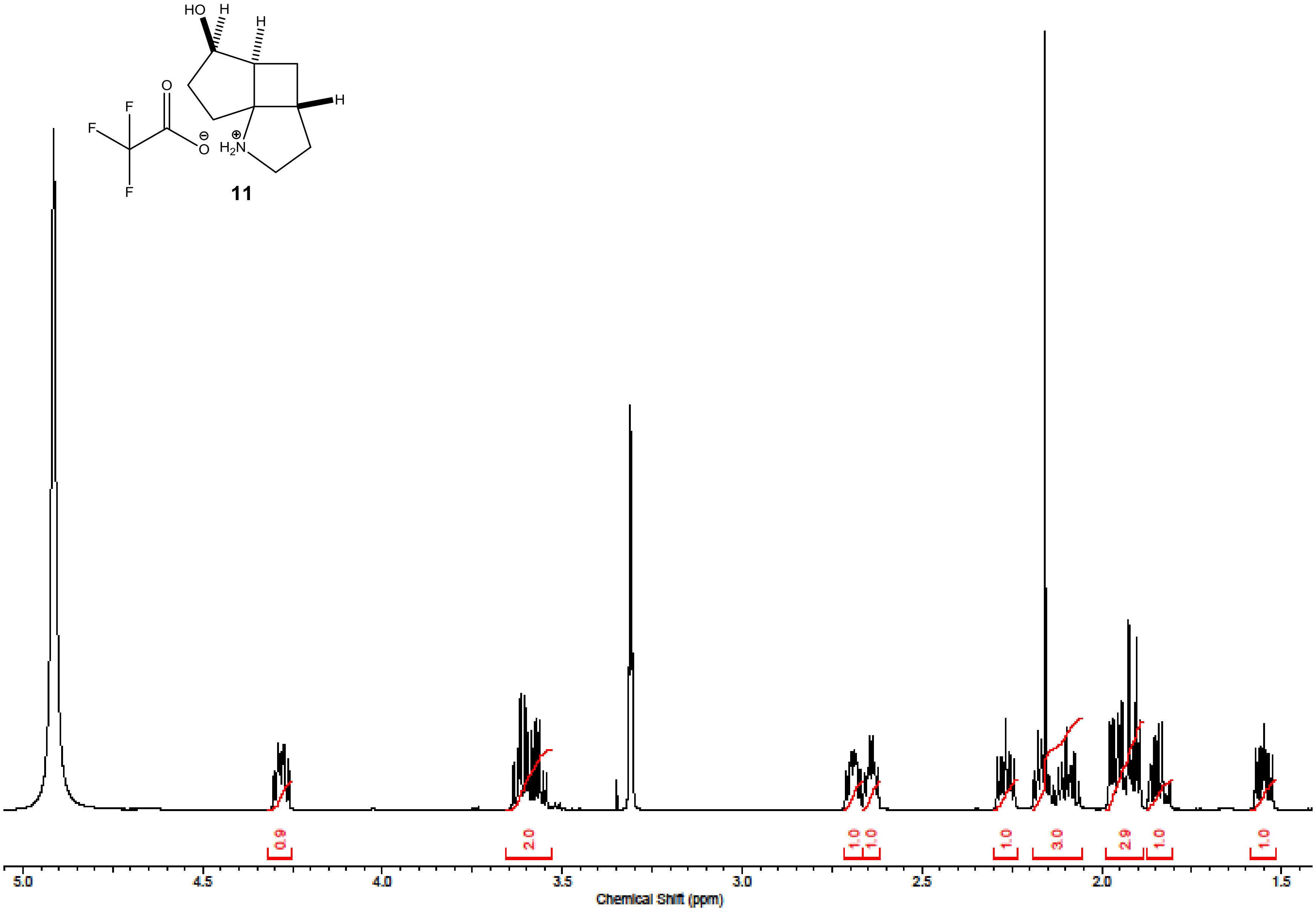
8
Chemical Shift (ppm)

10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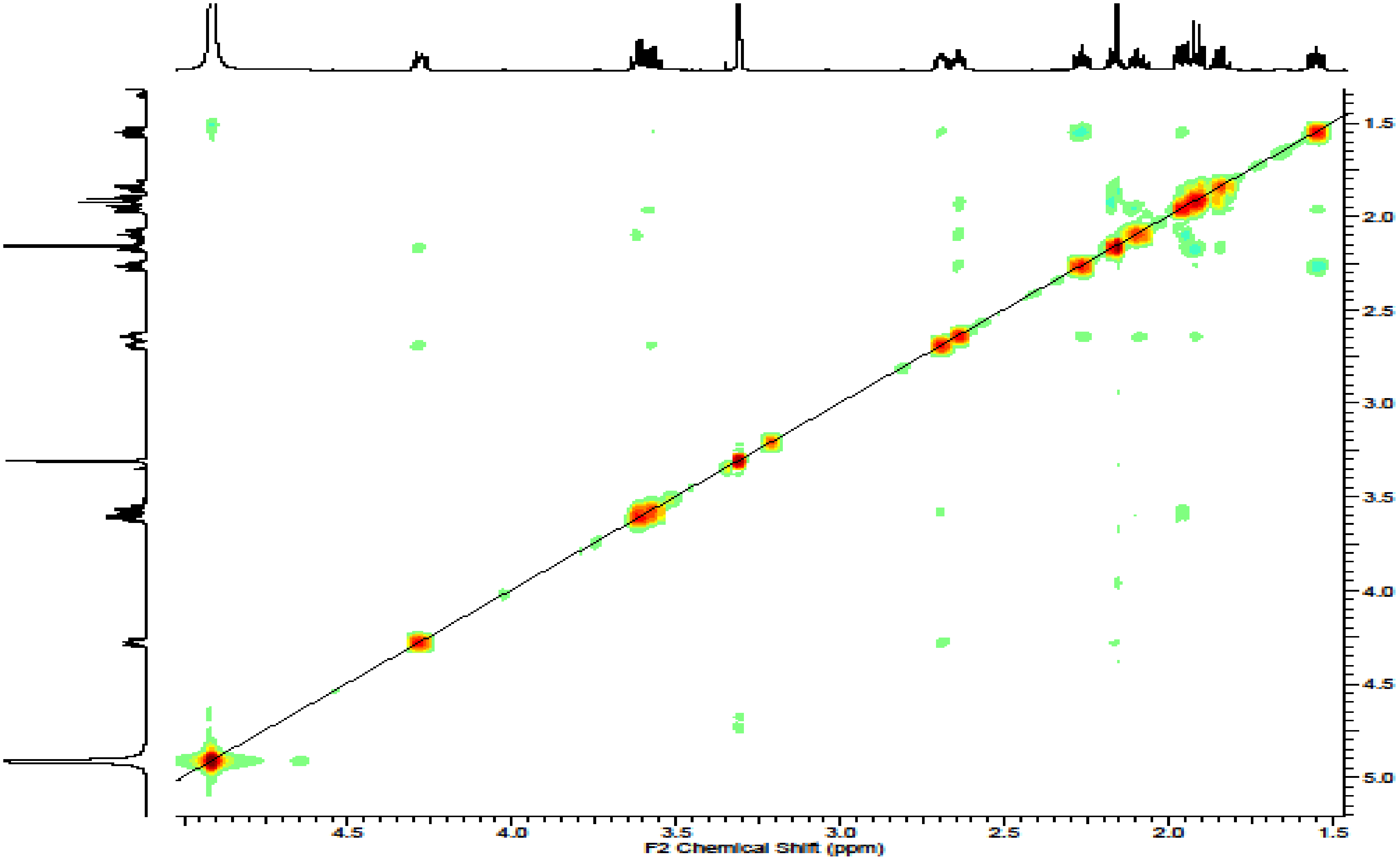
Chemical Shift (ppm)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F2 Chemical Shift (ppm)
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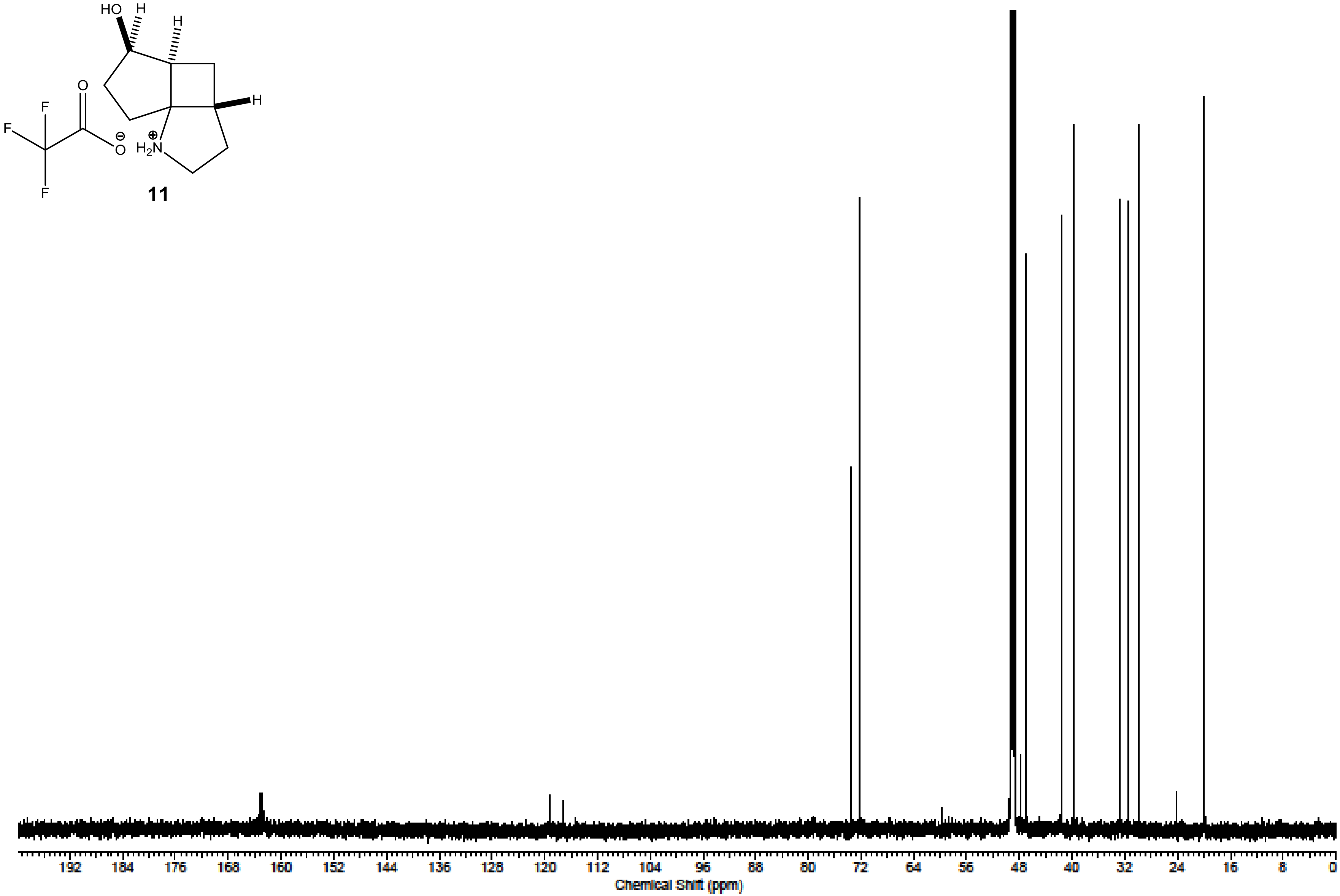
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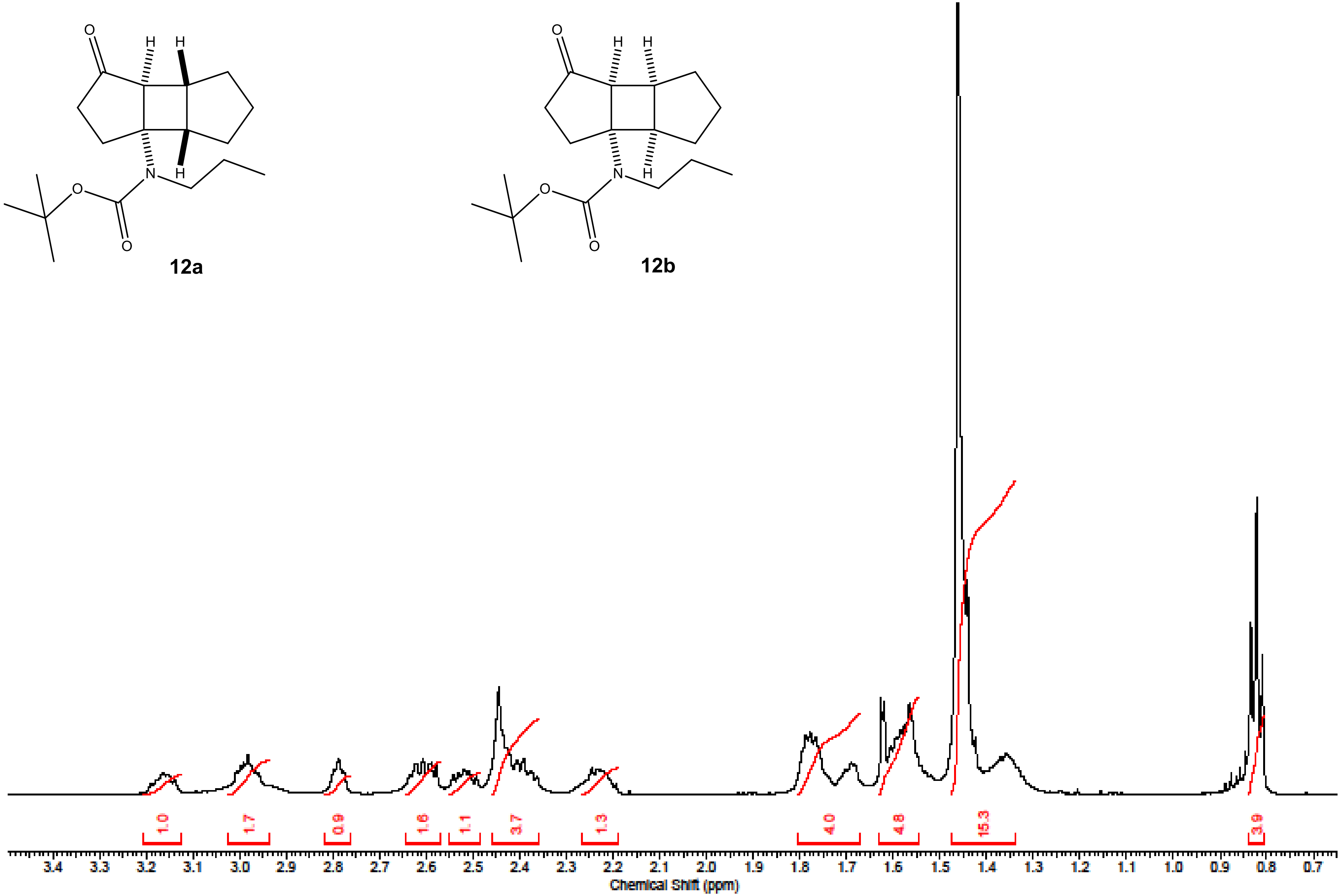
Chemical Shift (ppm)

11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H
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H
O
O

12b

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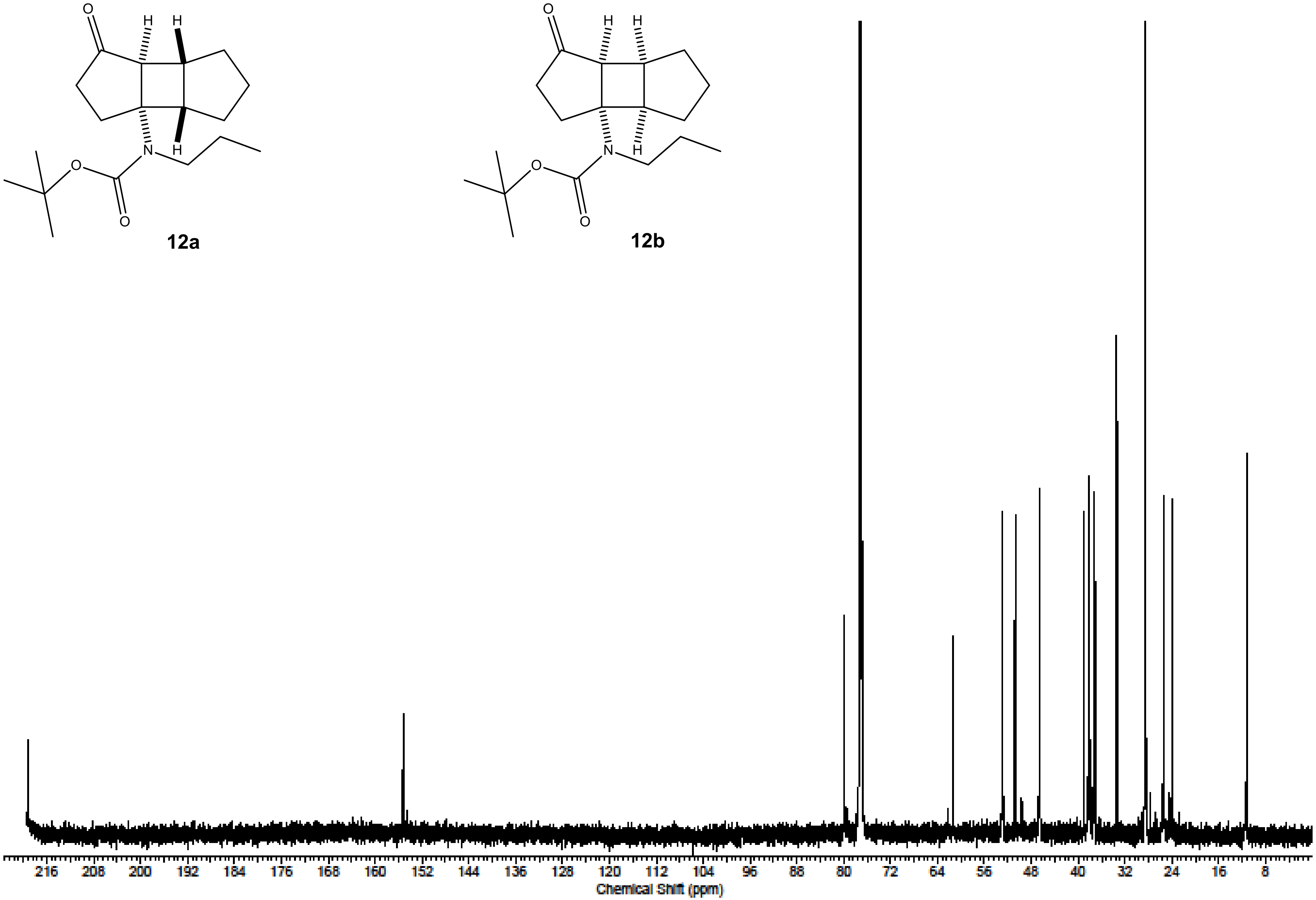
Chemical Shift (ppm)



12a

12b

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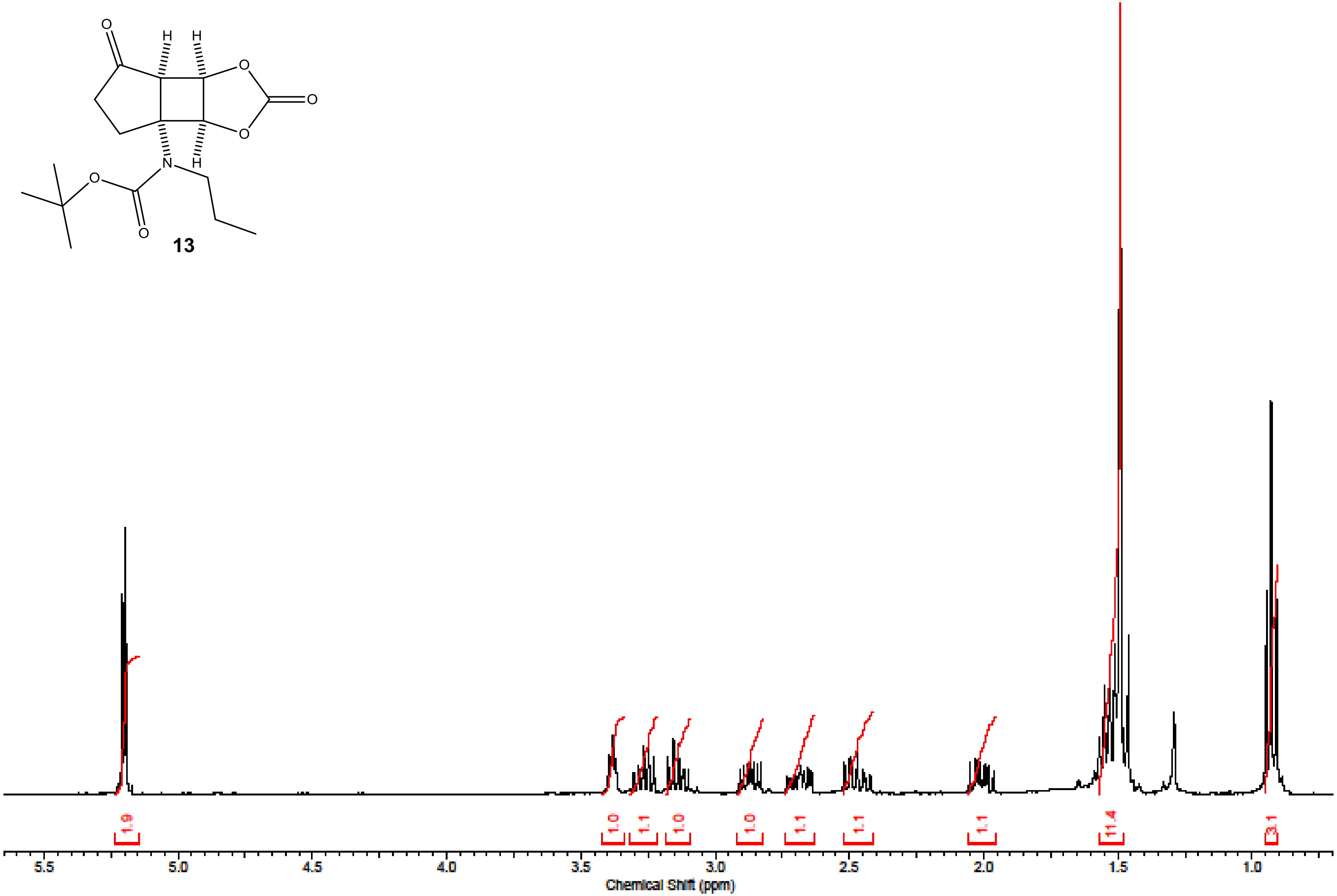
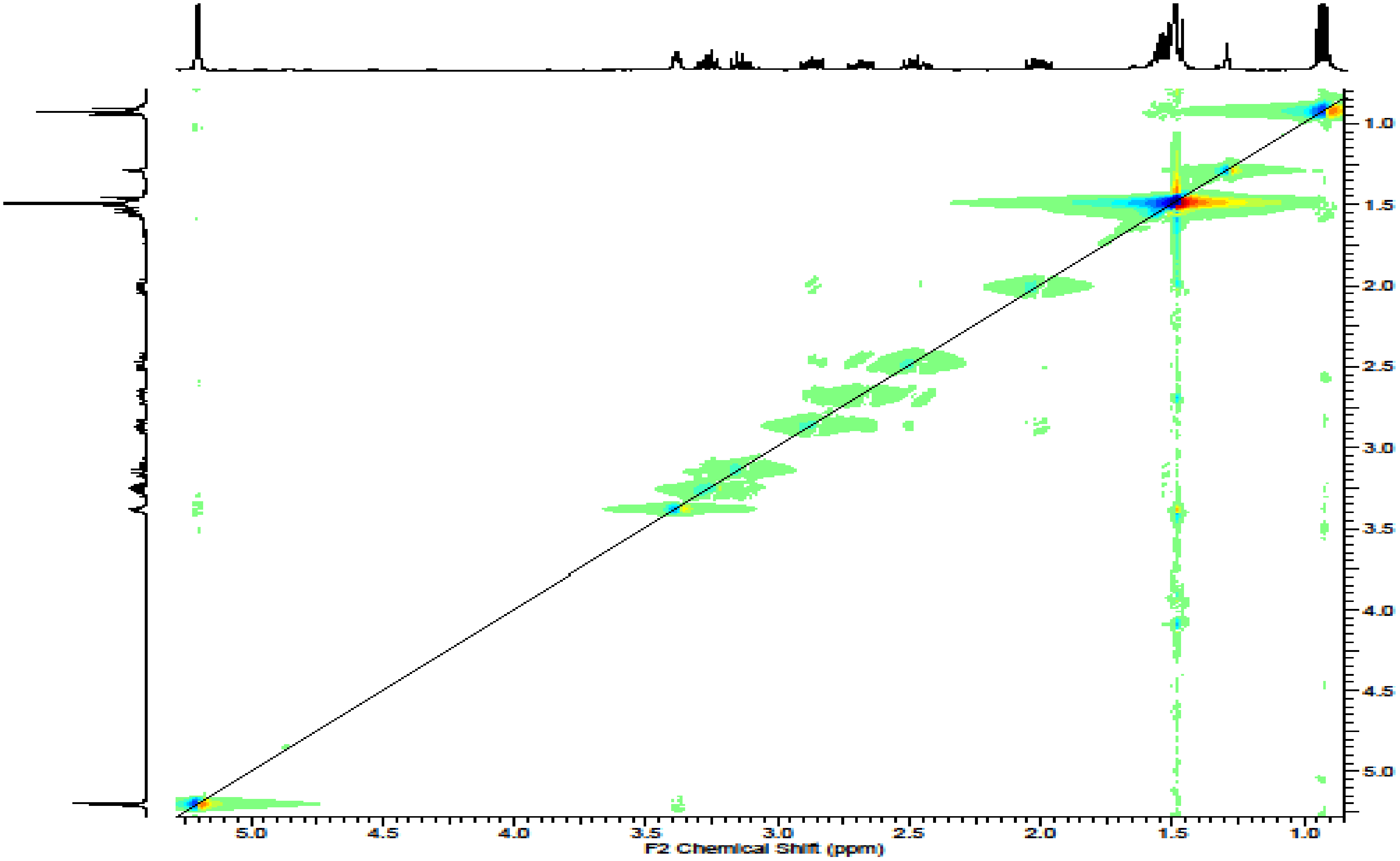
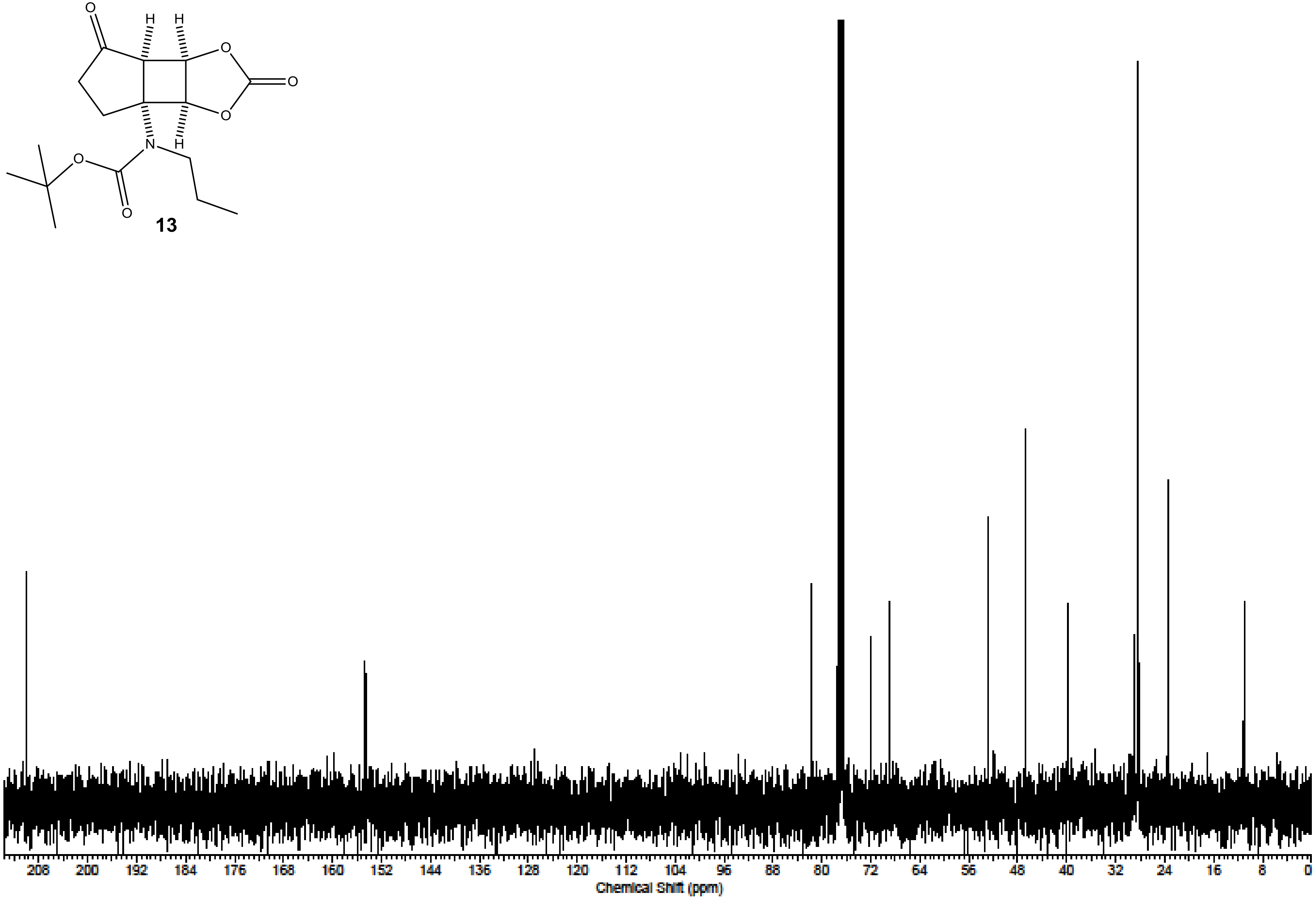
56
48
40
32
24
16
8
Chemical Shift (ppm)

O
H
H
O
O
O
N
H
O
O

13

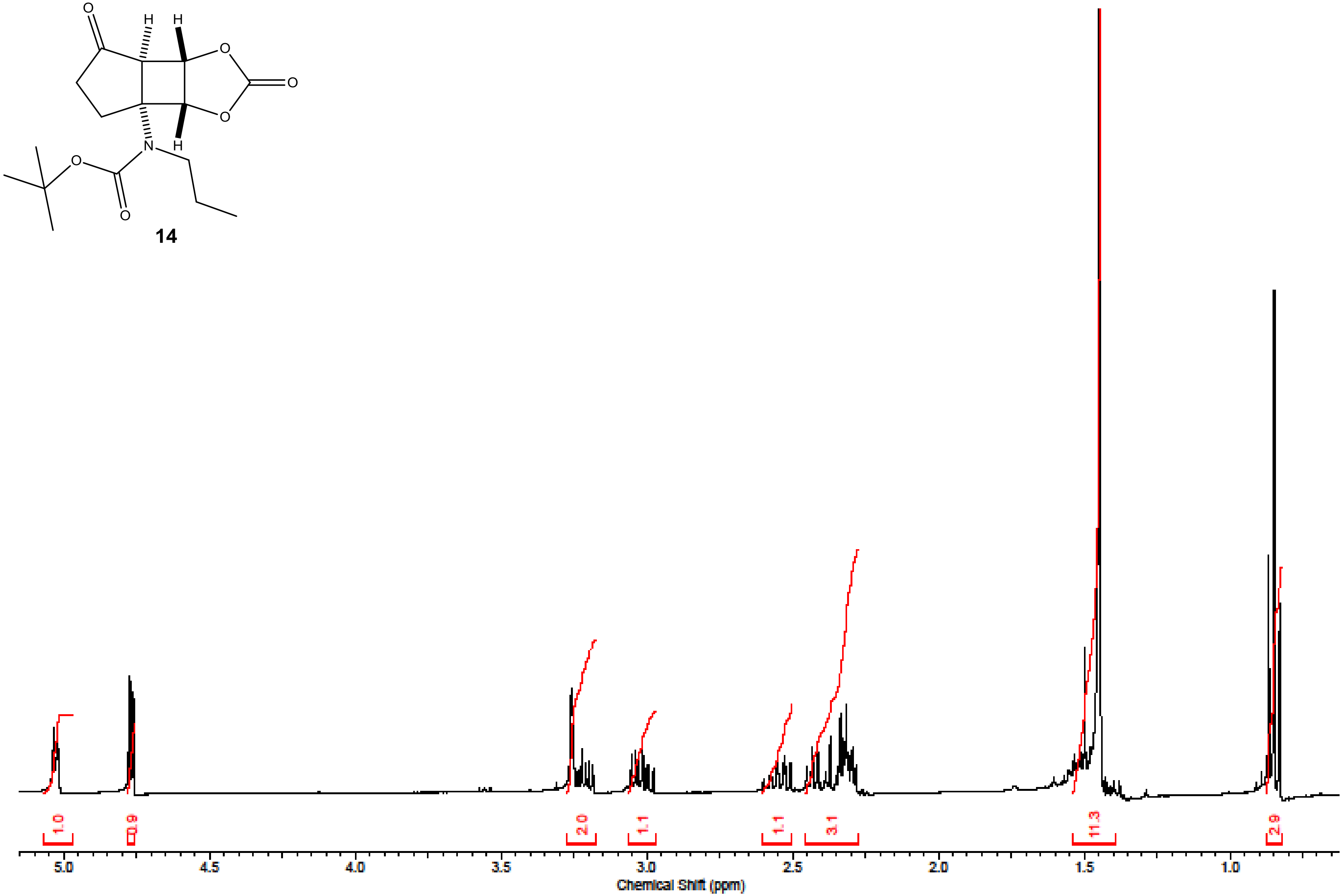

1.9
1.0
1.1
1.0
1.0
1.1
1.1
1.1
11.4
3.1
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
F2 Chemical Shift (ppm)
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0

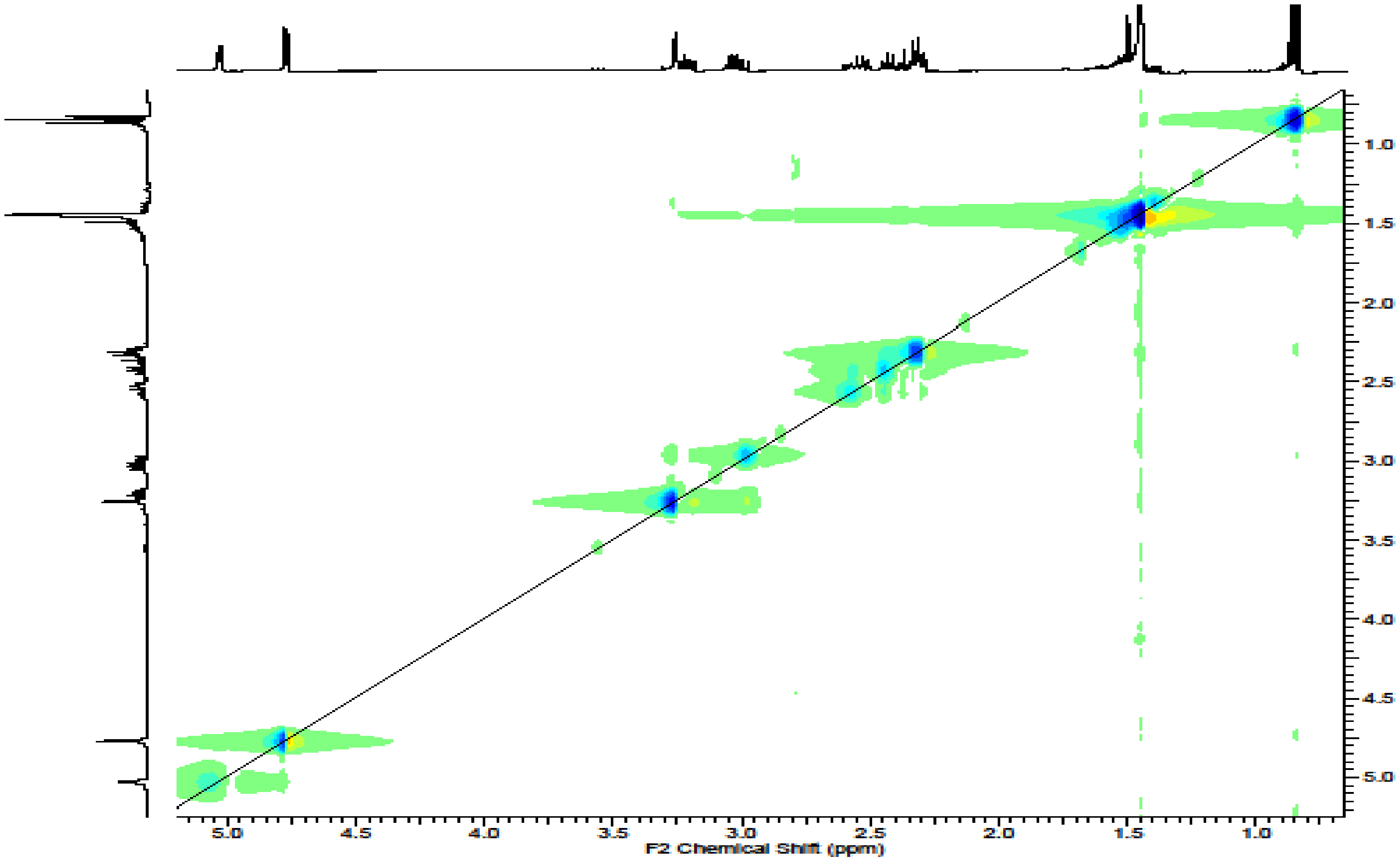

O
H
H
O
O
O
N
H
O
O

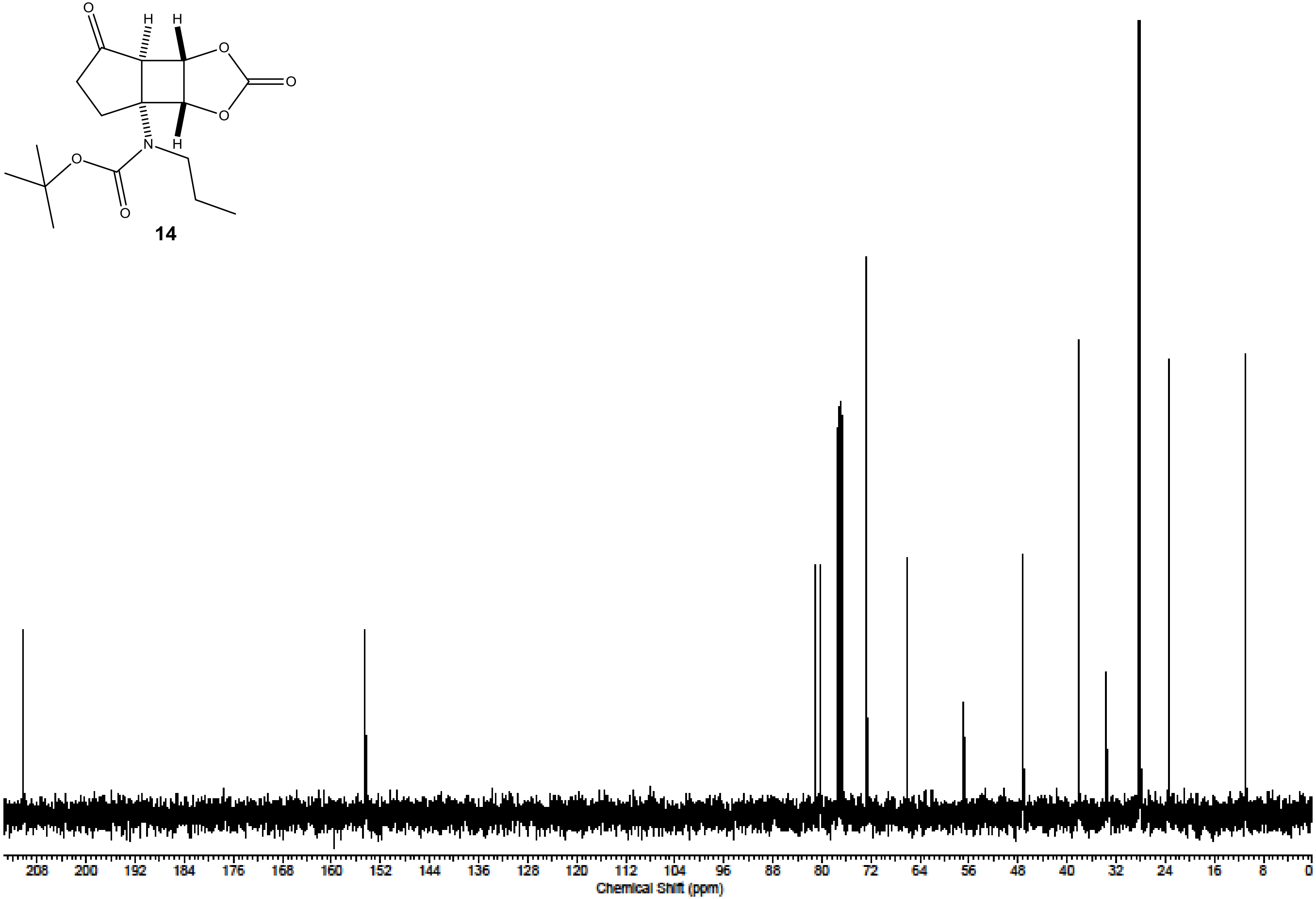
13

208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


O
H
H
O
O
O
N
H
O
O
1.0
0.9
2.0
1.1
1.1
3.1
11.3
2.9
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

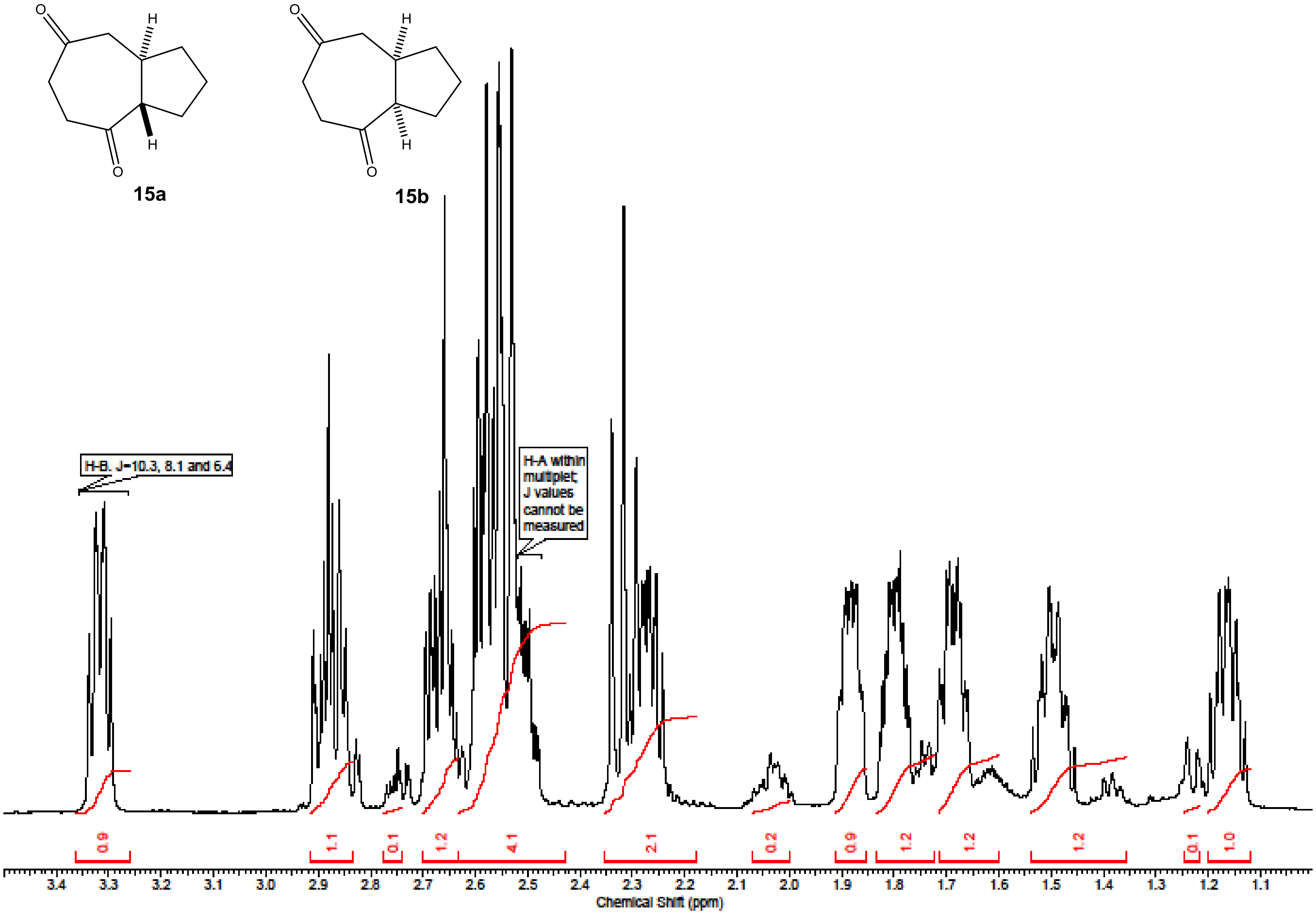
14

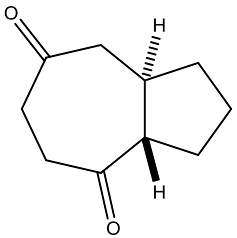

1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
F2 Chemical Shift (ppm)



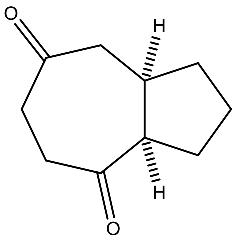
14

208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

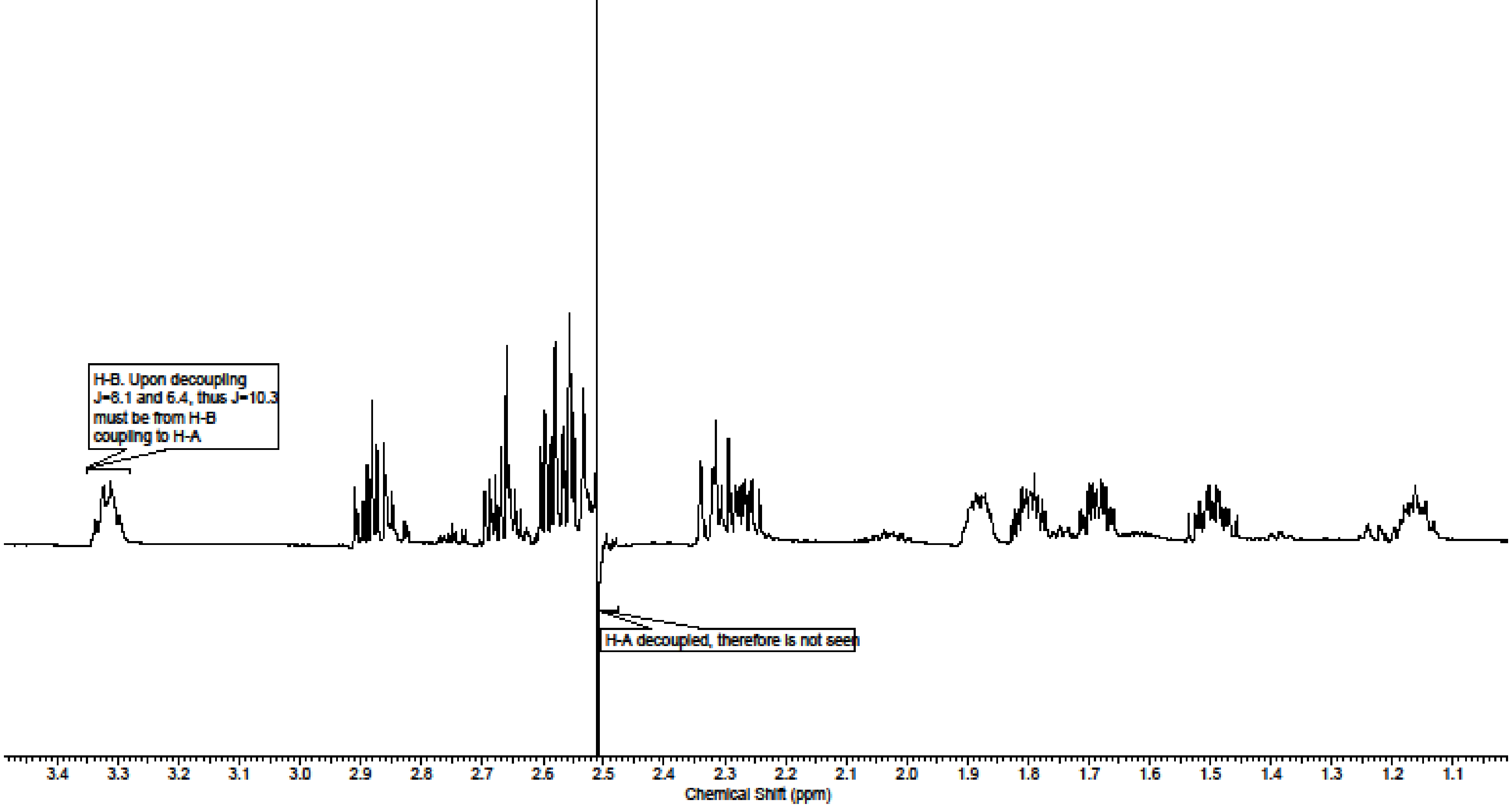

15a
15b
H-B. J=10.3, 8.1 and 6.4
H-A within multiplet; J values cannot be measured
0.9
1.1
0.1
1.2
4.1
2.1
0.2
0.9
1.2
1.2
1.2
0.1
1.0
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
Chemical Shift (ppm)

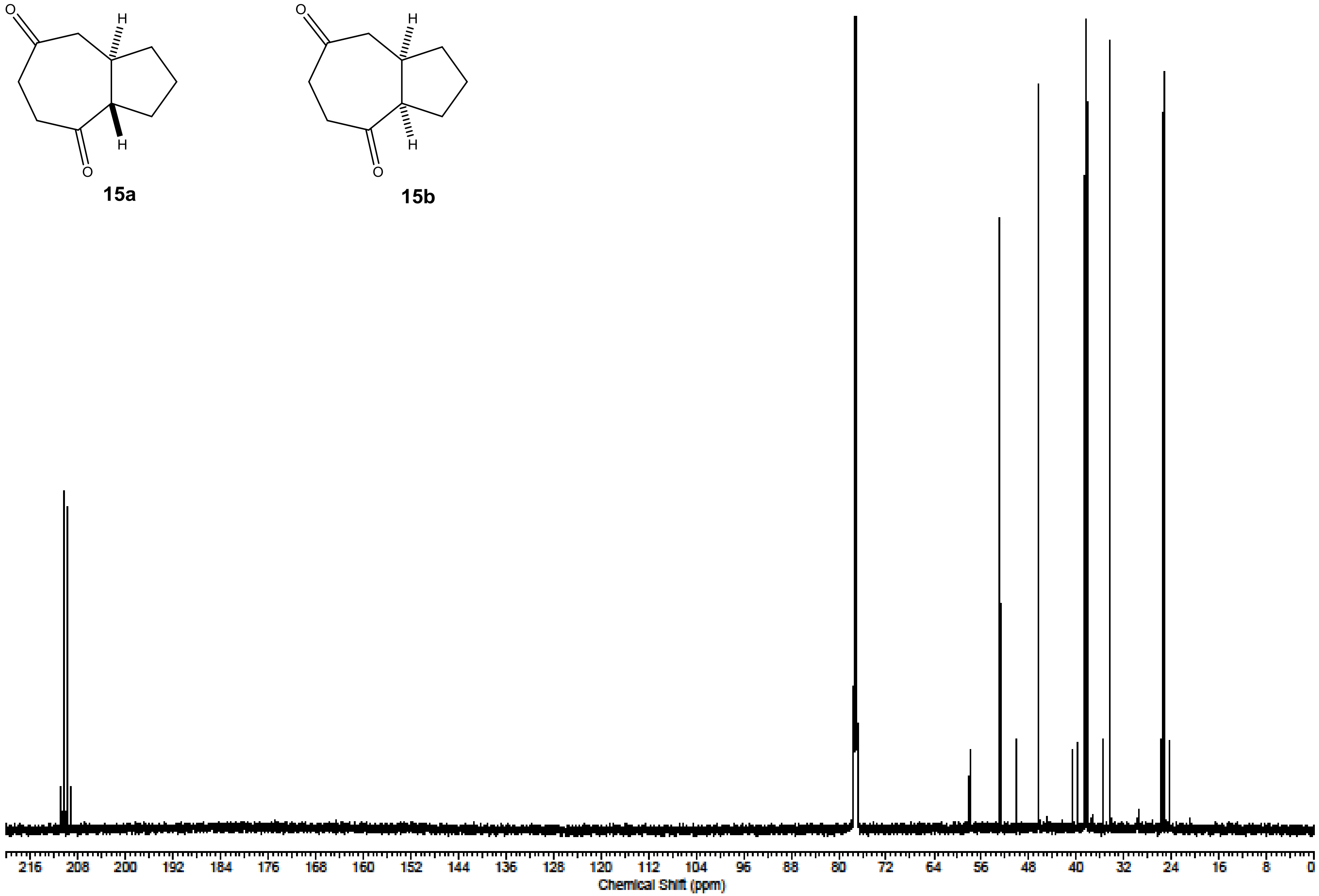

O
H
H
O

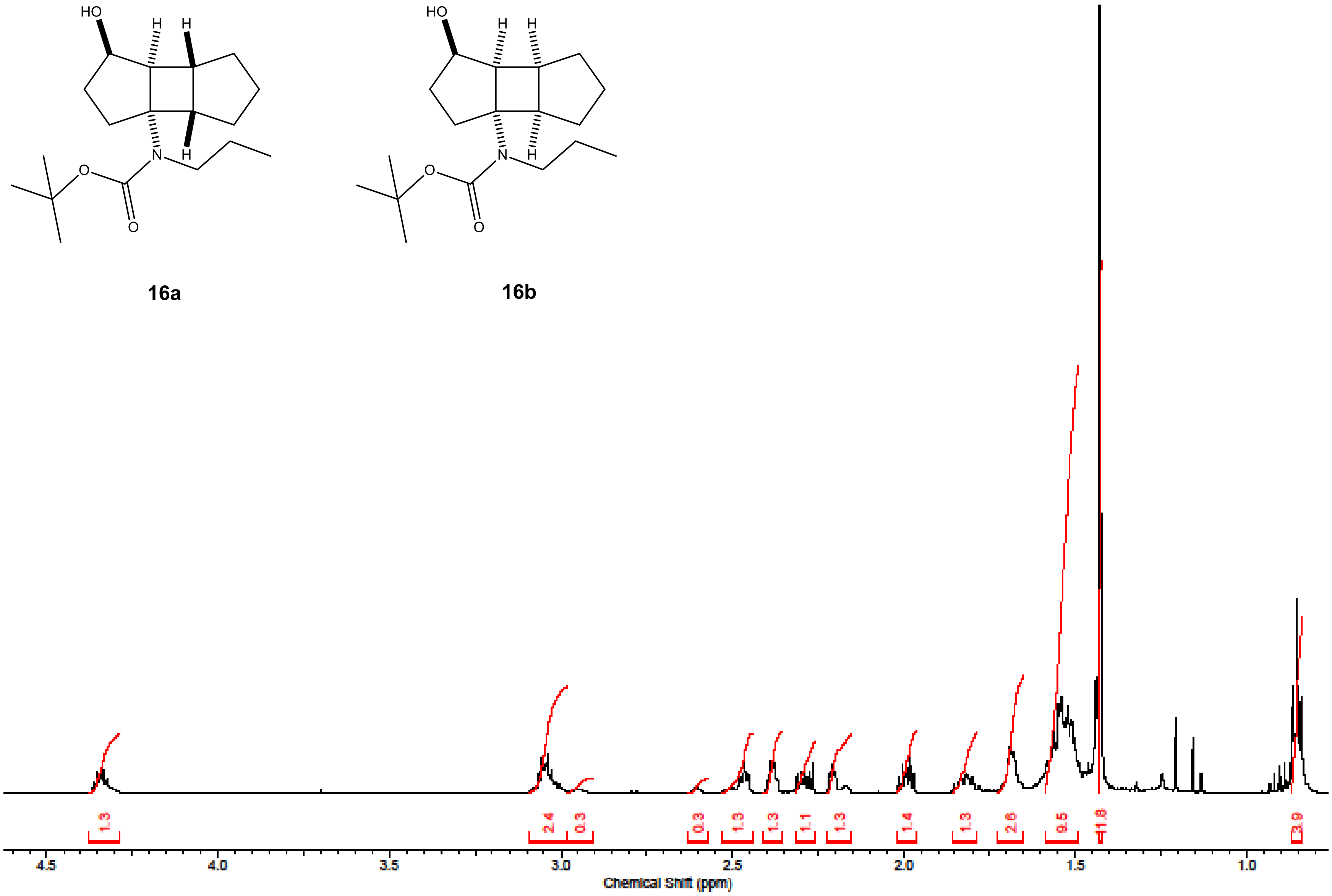
15a

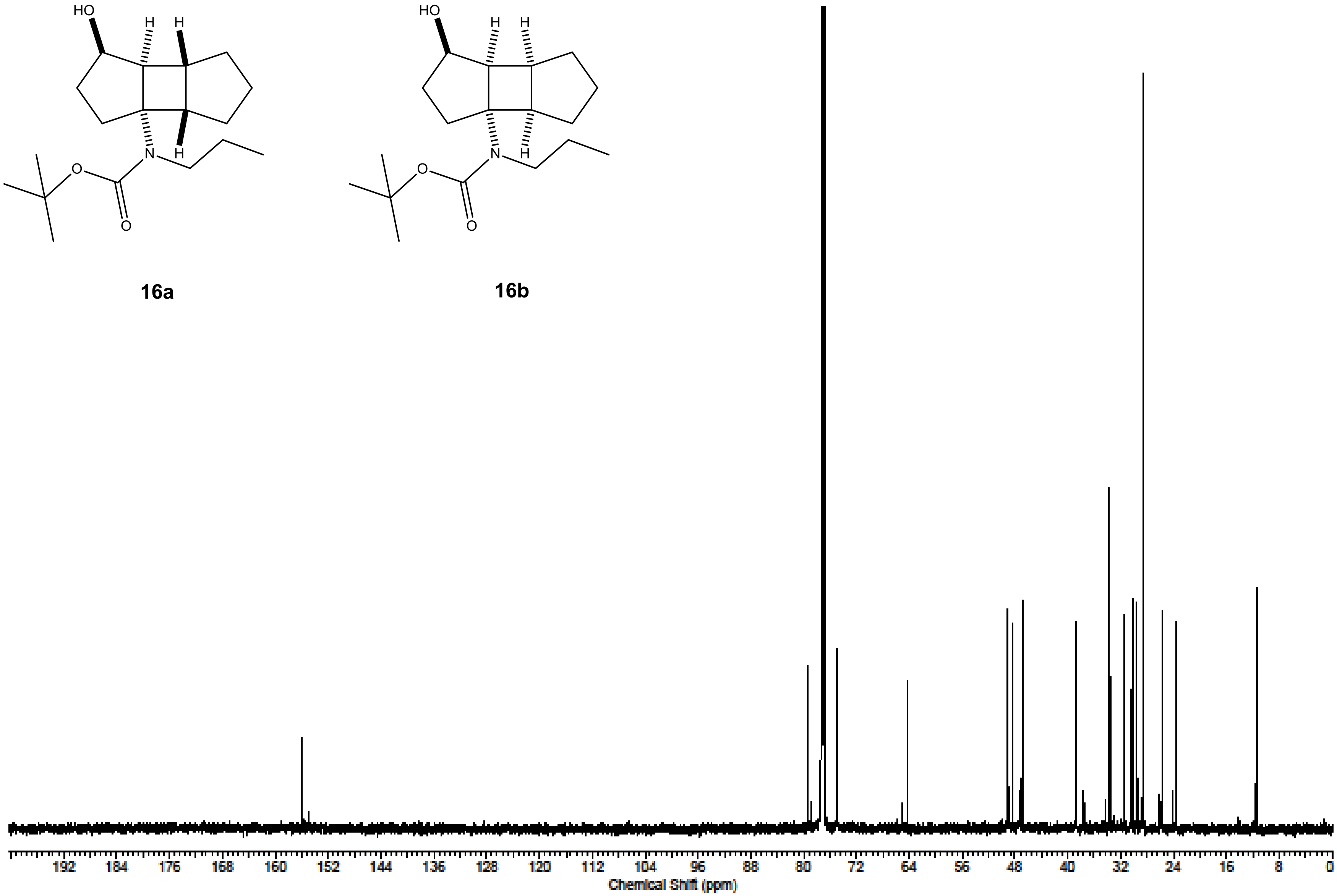

O
H
H
O

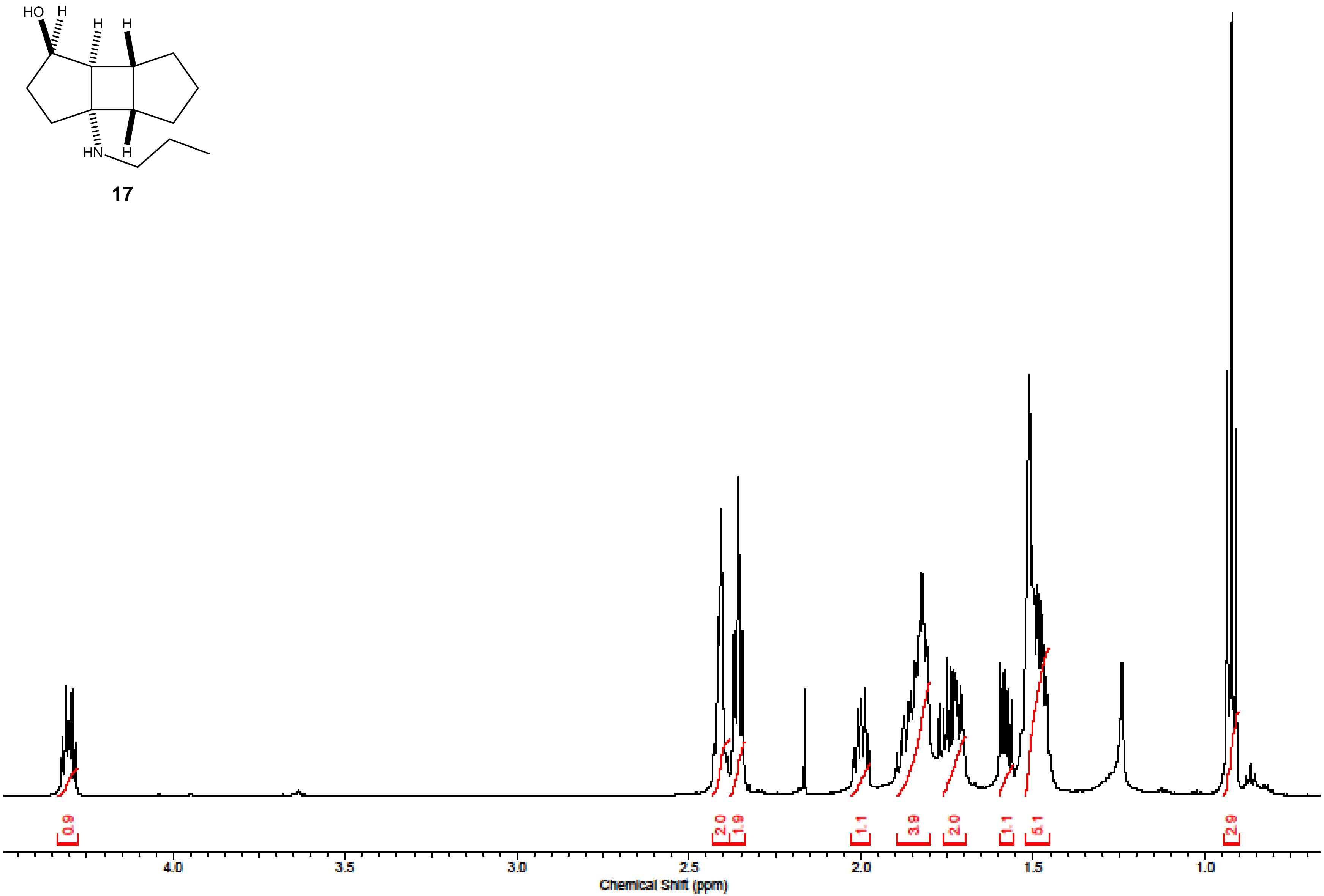
15b


H-B. Upon decoupling J=8.1 and 6.4, thus J=10.3 must be from H-B coupling to H-A
H-A decoupled, therefore is not seen
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
Chemical Shift (ppm)

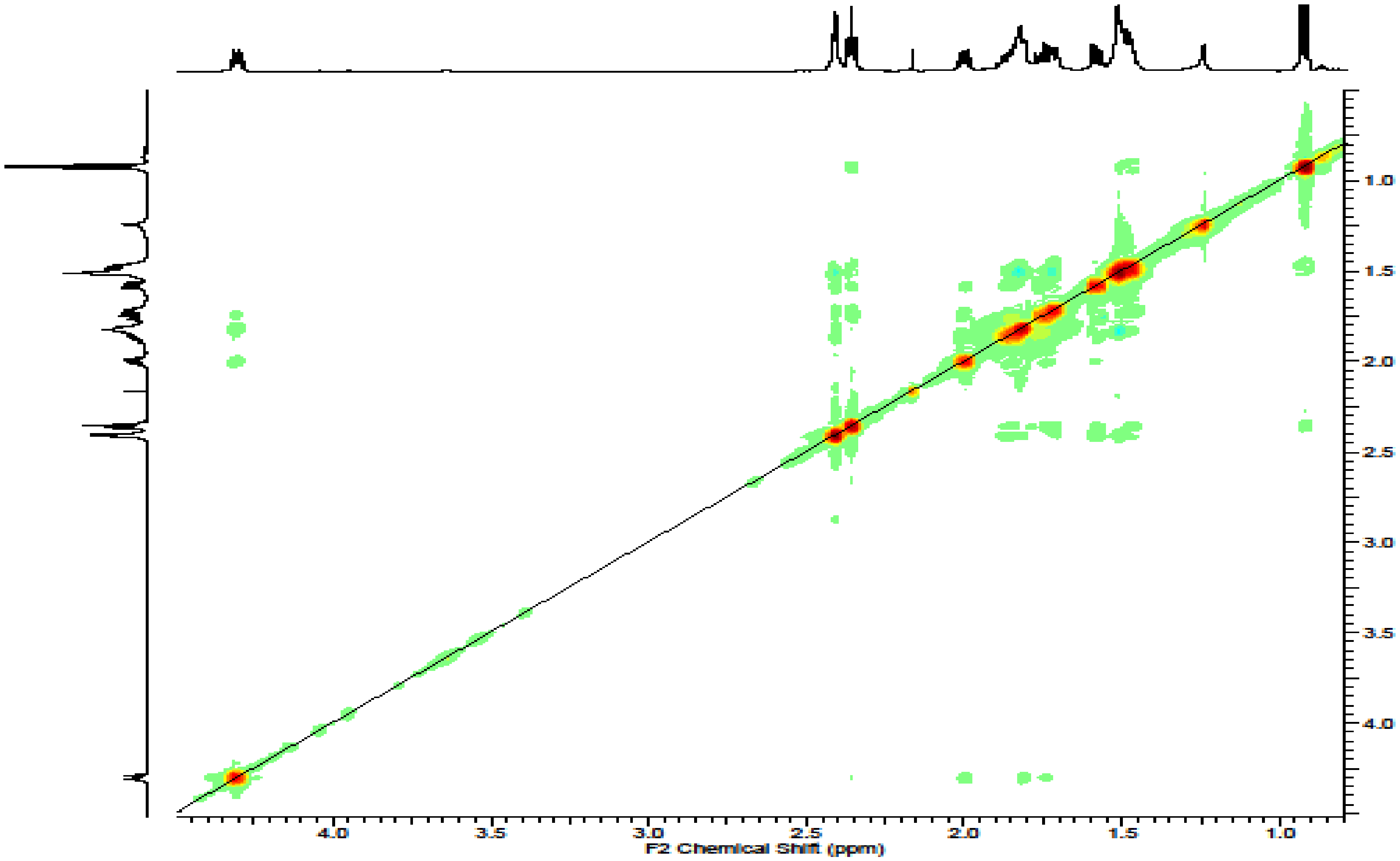

O
H
H
O
15a
O
H
H
O
15b
216
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

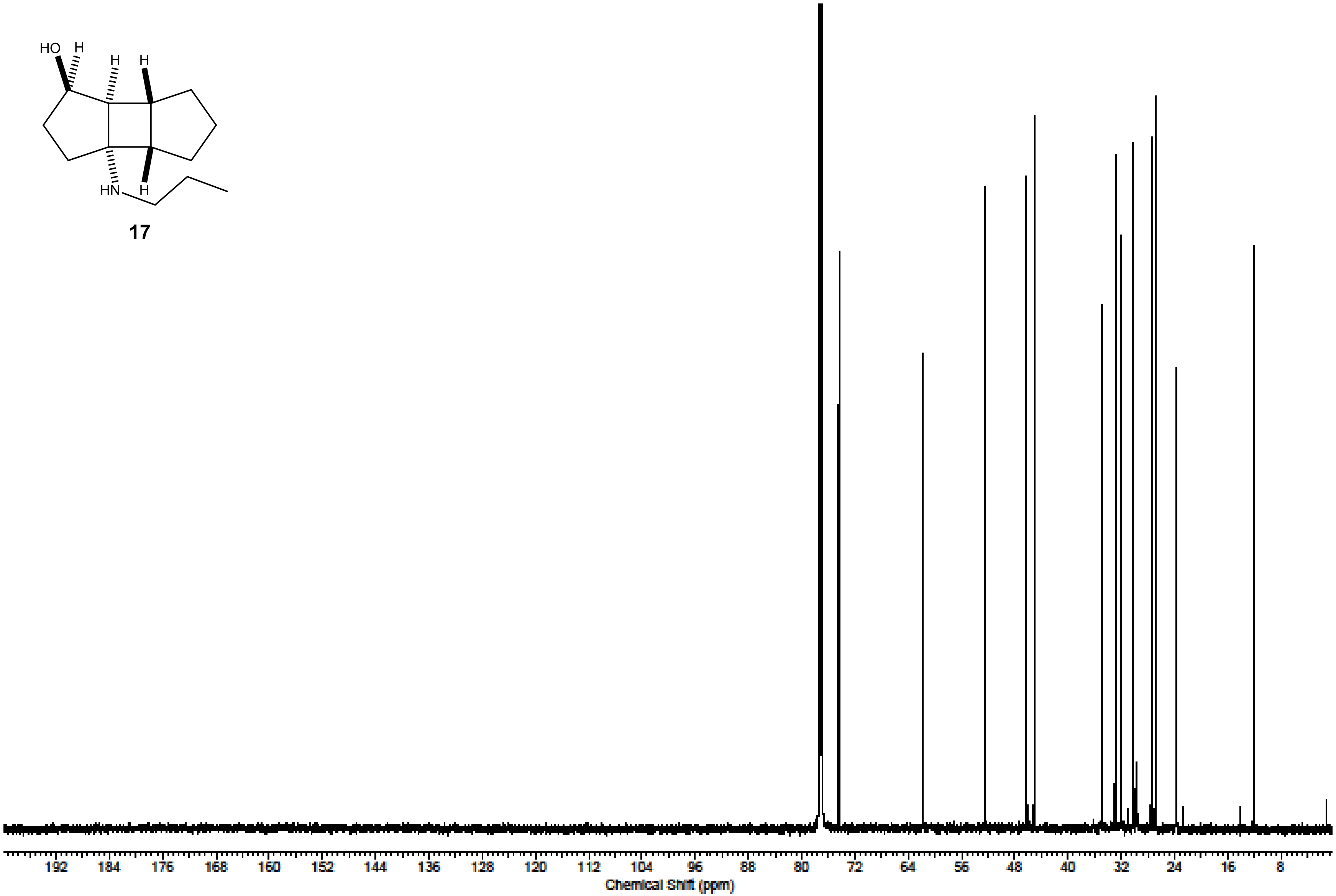

HO
H
H
N
H
O
O
16a
HO
H
H
N
H
O
O
16b
1.3
2.4
0.3
0.3
1.3
1.3
1.1
1.3
1.4
1.3
2.6
9.5
11.8
3.9
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


HO
H
H
N
O
O
16a
HO
H
H
N
O
O
16b
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

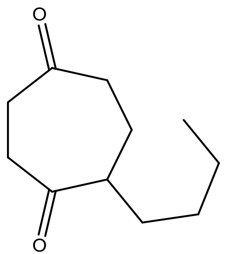

HO
H
H
H
HN
H
0.9
2.0
1.9
1.1
3.9
2.0
1.1
5.1
2.9
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

17

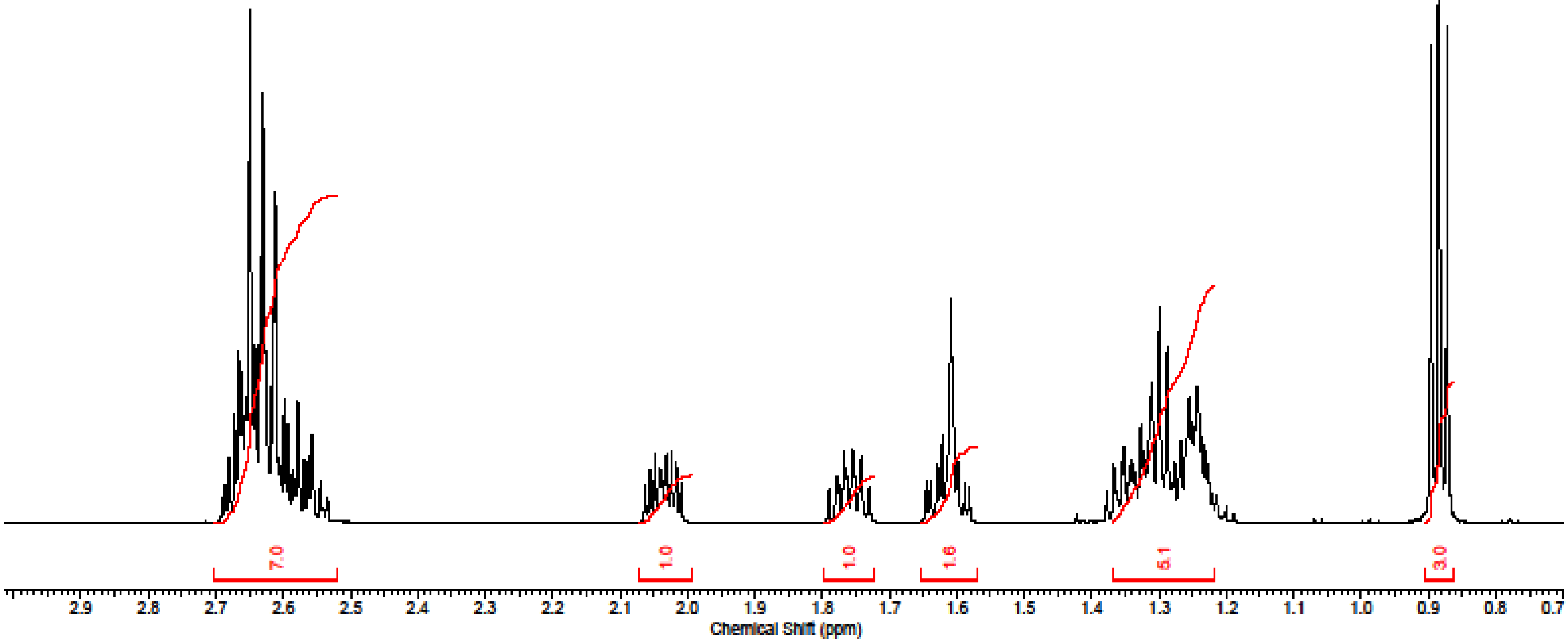

4.0
3.5
3.0
2.5
2.0
1.5
1.0
F2 Chemical Shift (ppm)
1.0
1.5
2.0
2.5
3.0
3.5
4.0

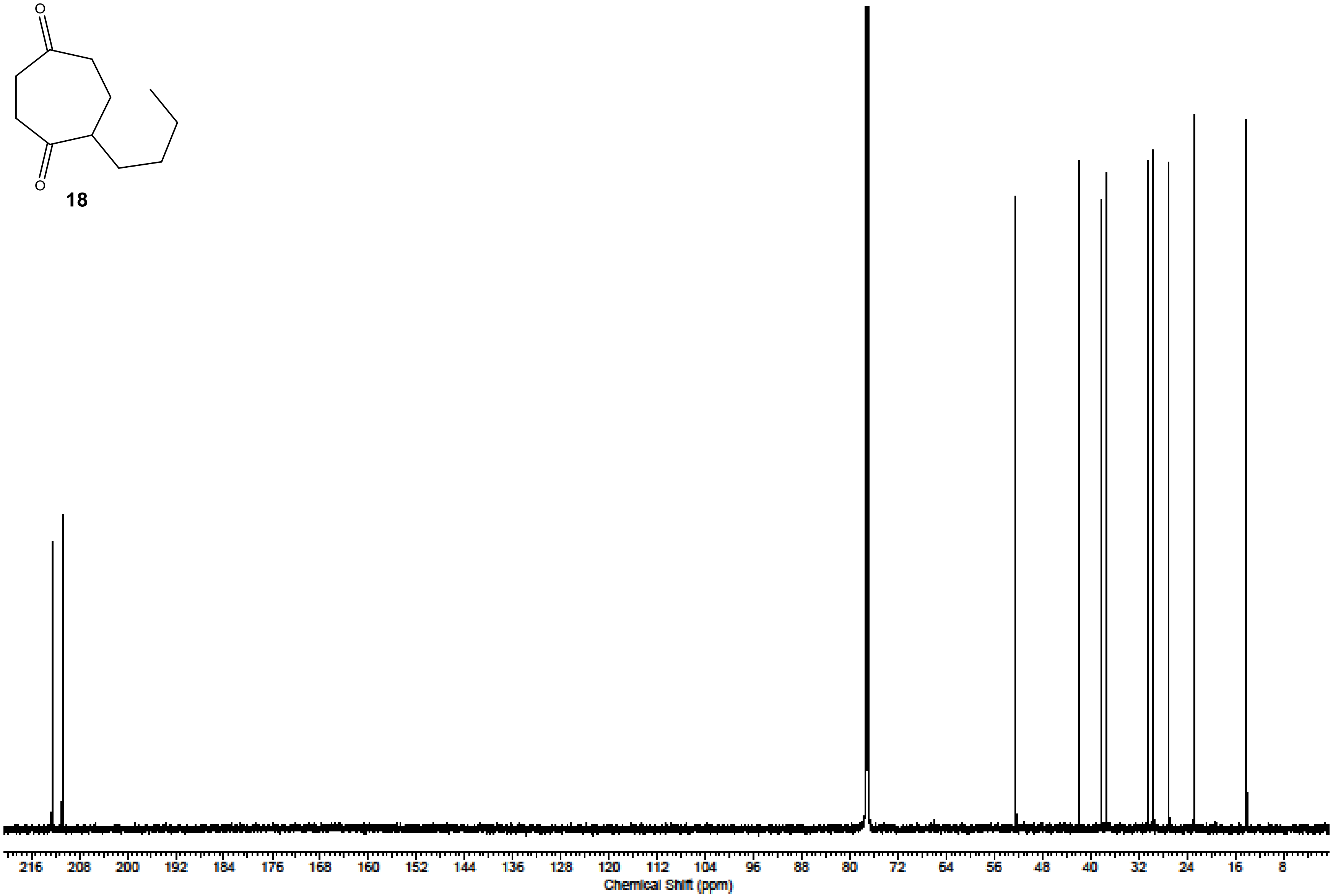

HO
H
H
H
HN
H
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

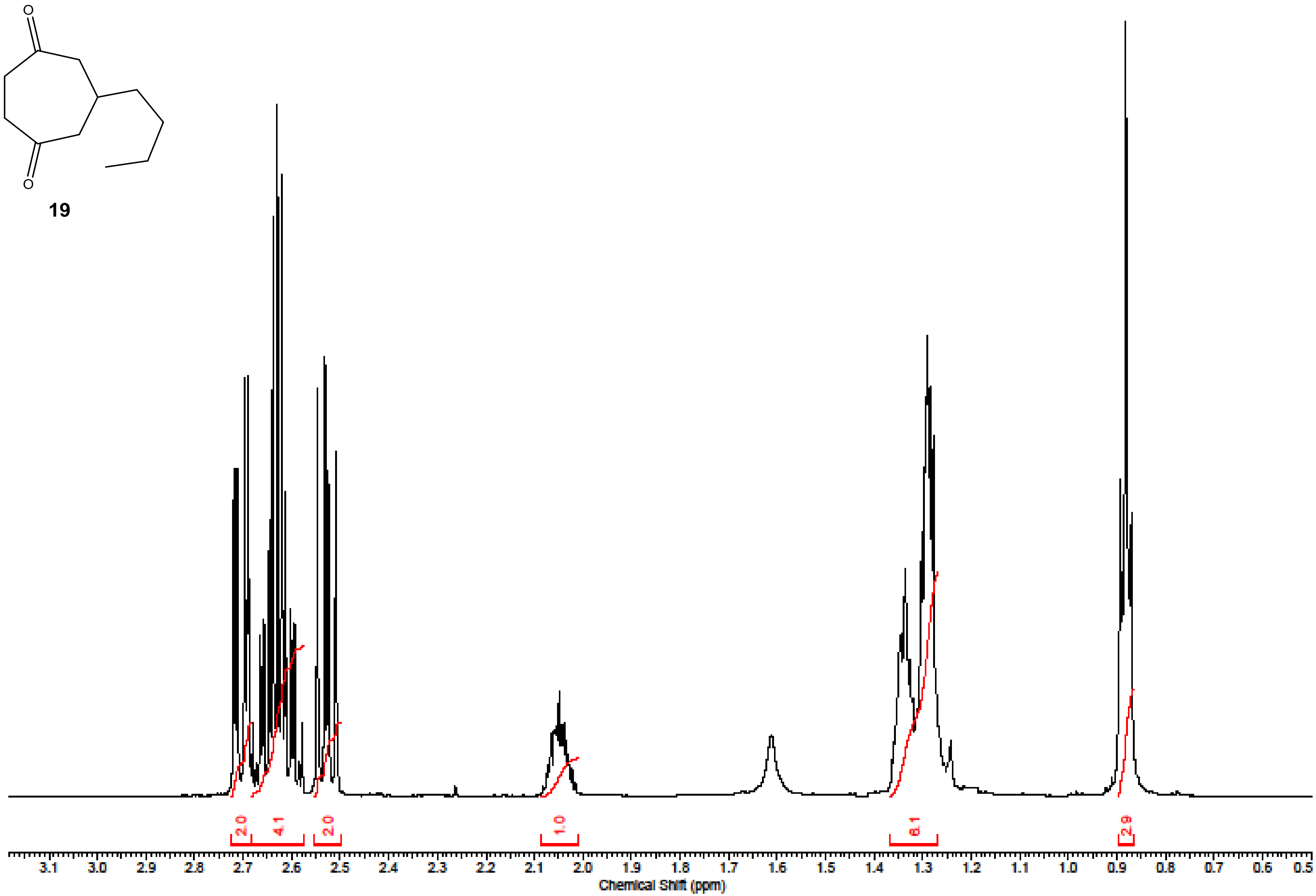
17


O
O

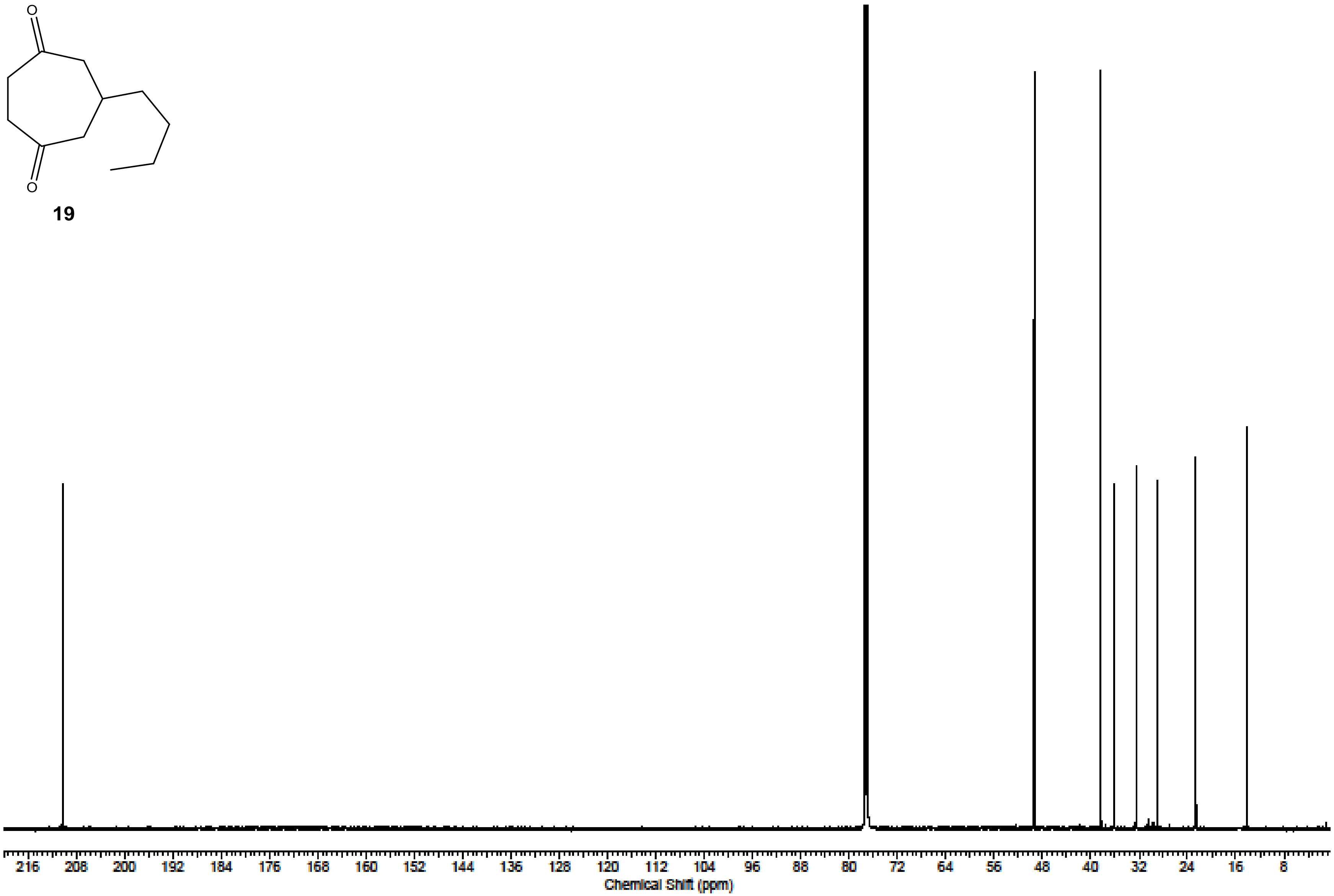
18


7.0
1.0
1.0
1.6
5.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
Chemical Shift (ppm)

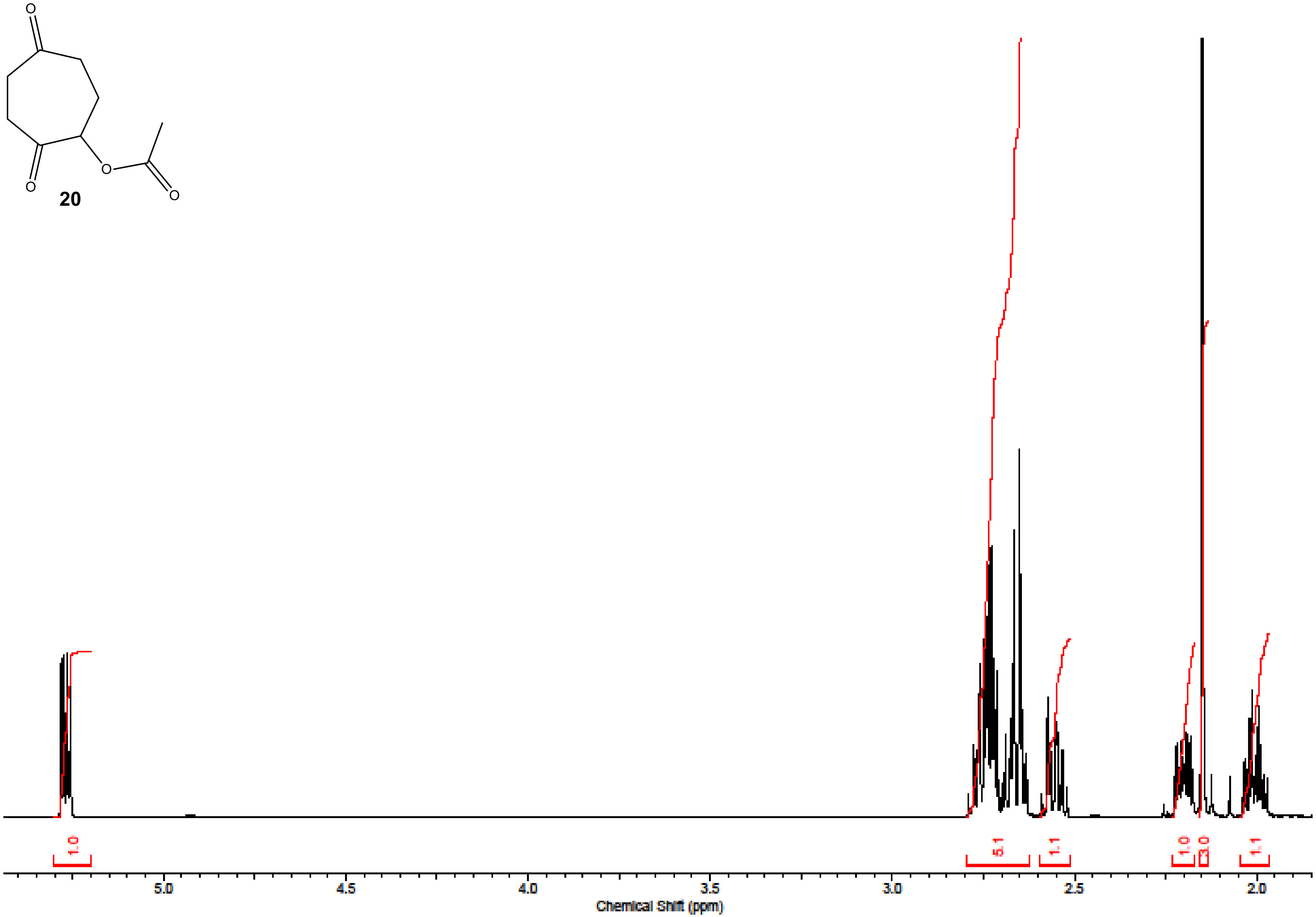

O
O
18
216
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)


O
O
2.0
4.1
2.0
1.0
6.1
2.9
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
Chemical Shift (ppm)

19

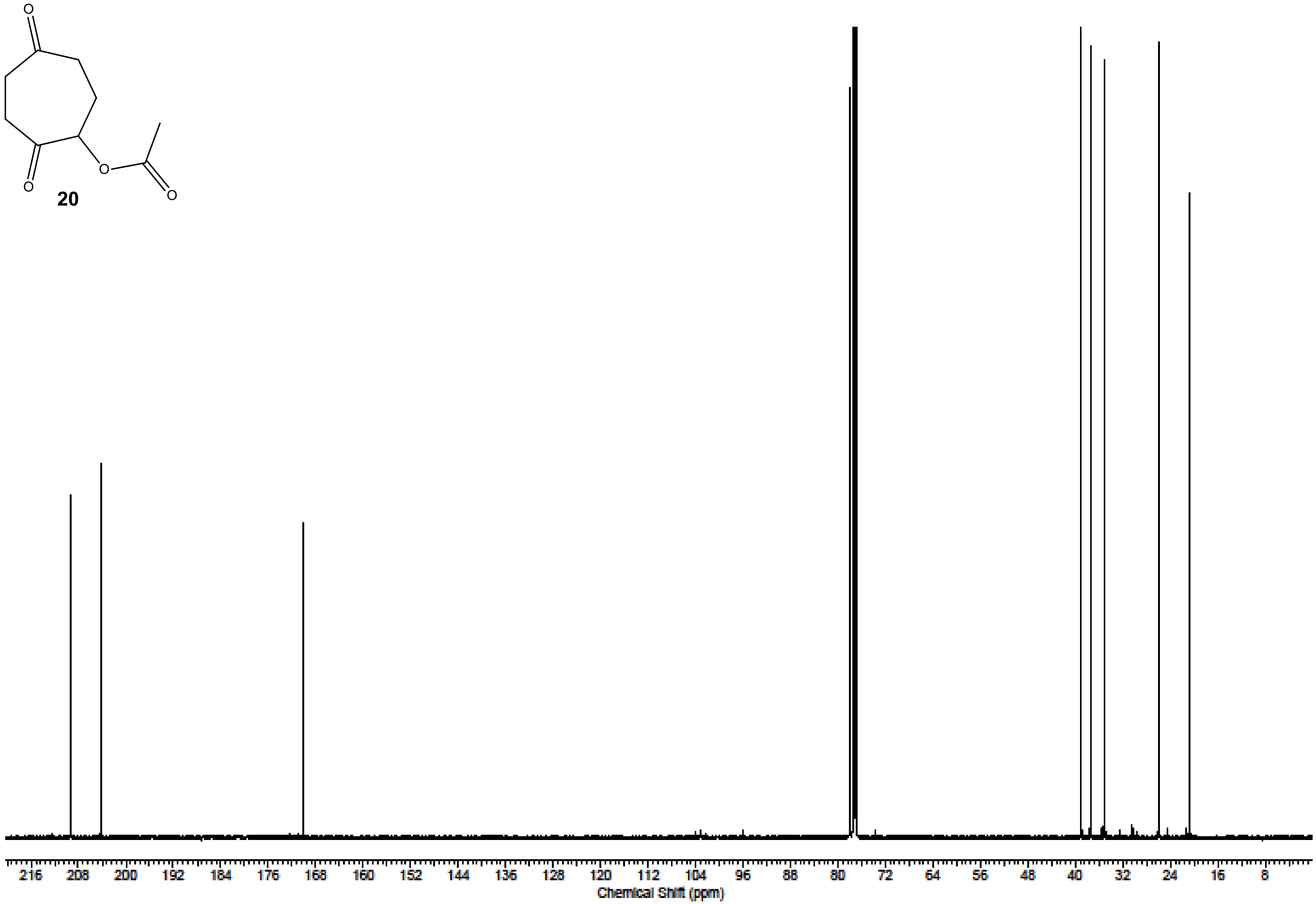

O
O
216
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

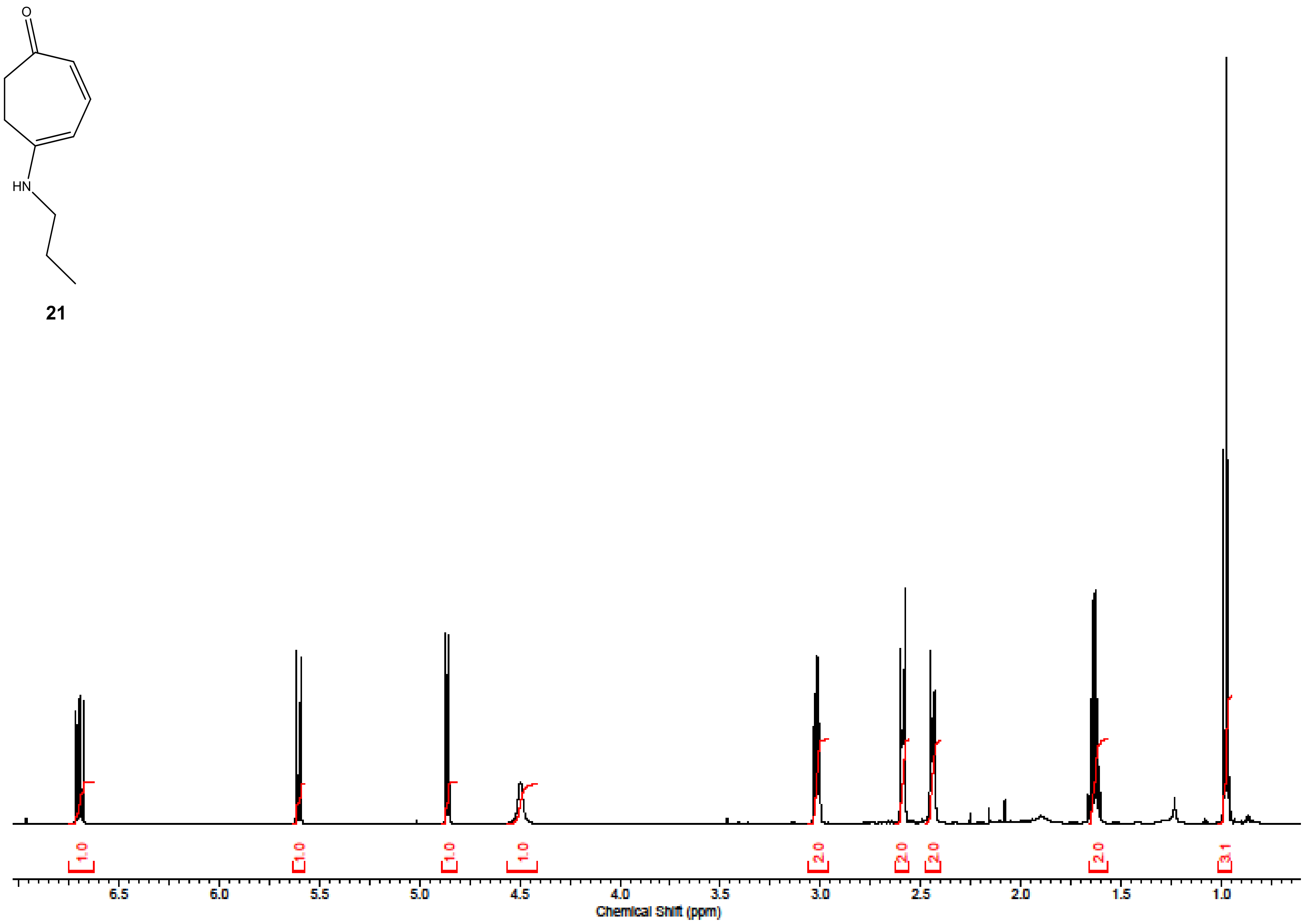
19



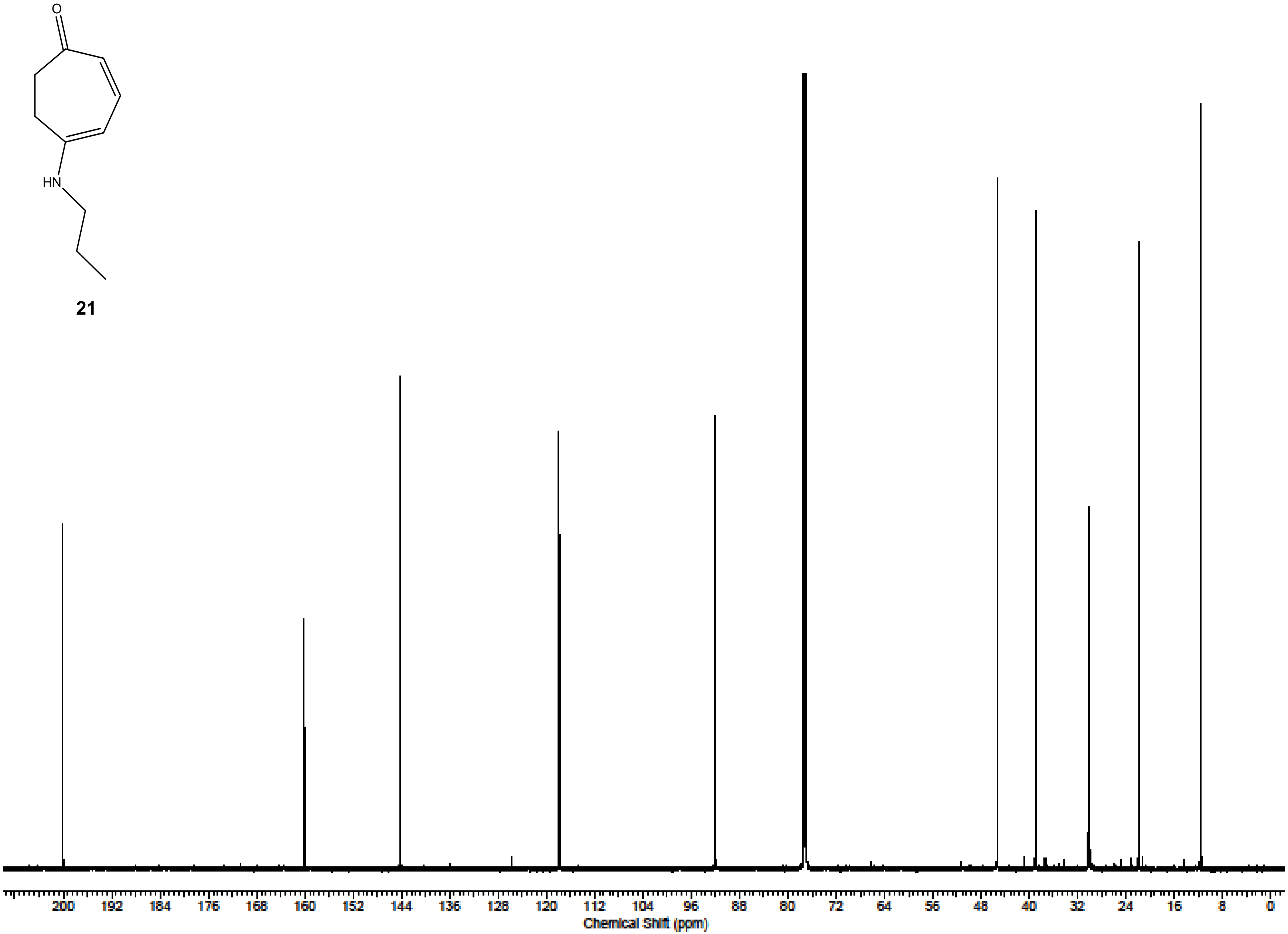
20

20


216
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)


O
HN
1.0
1.0
1.0
1.0
2.0
2.0
2.0
2.0
3.1
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

21

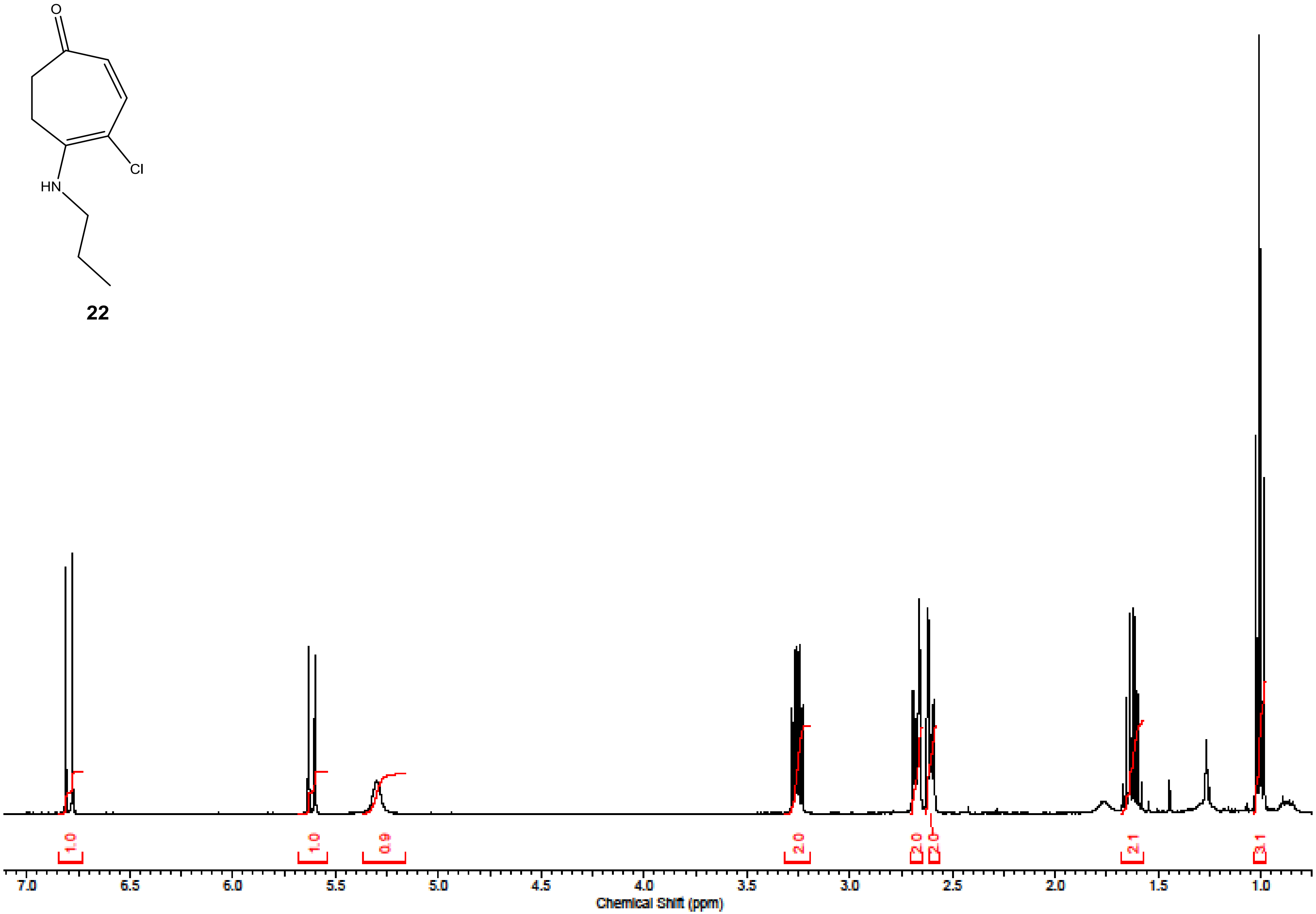

O
HN

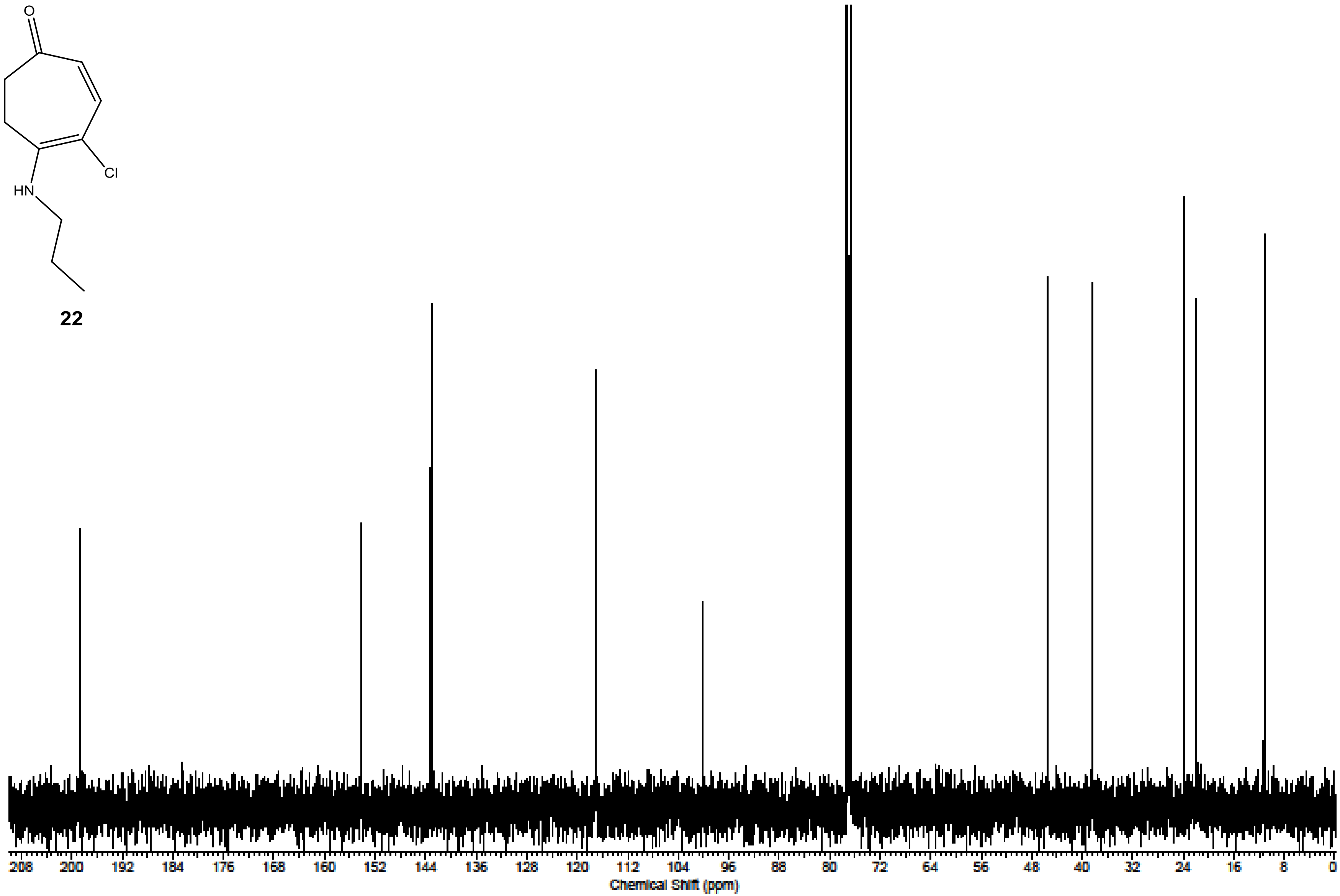
21

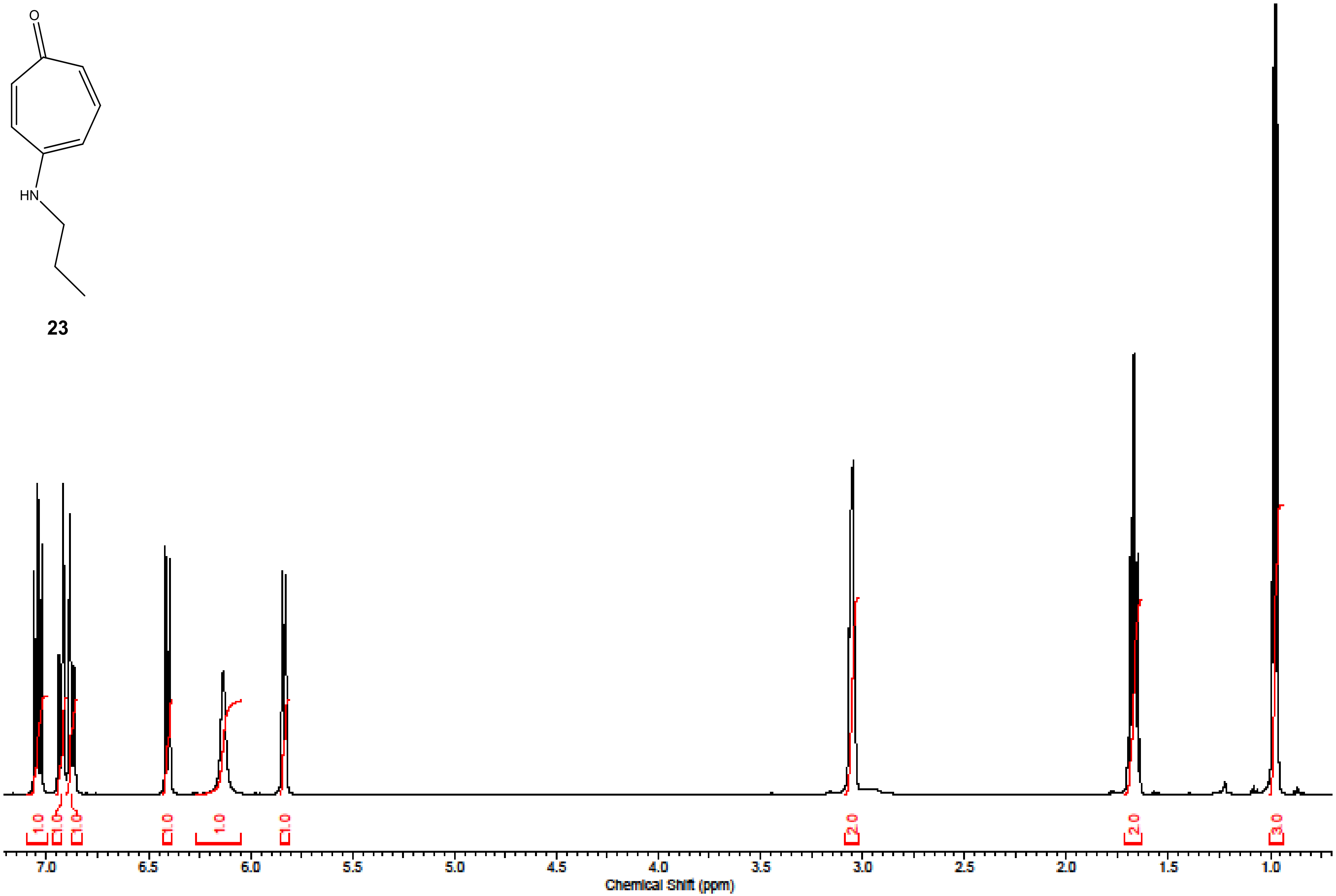
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

O
Cl
HN

22

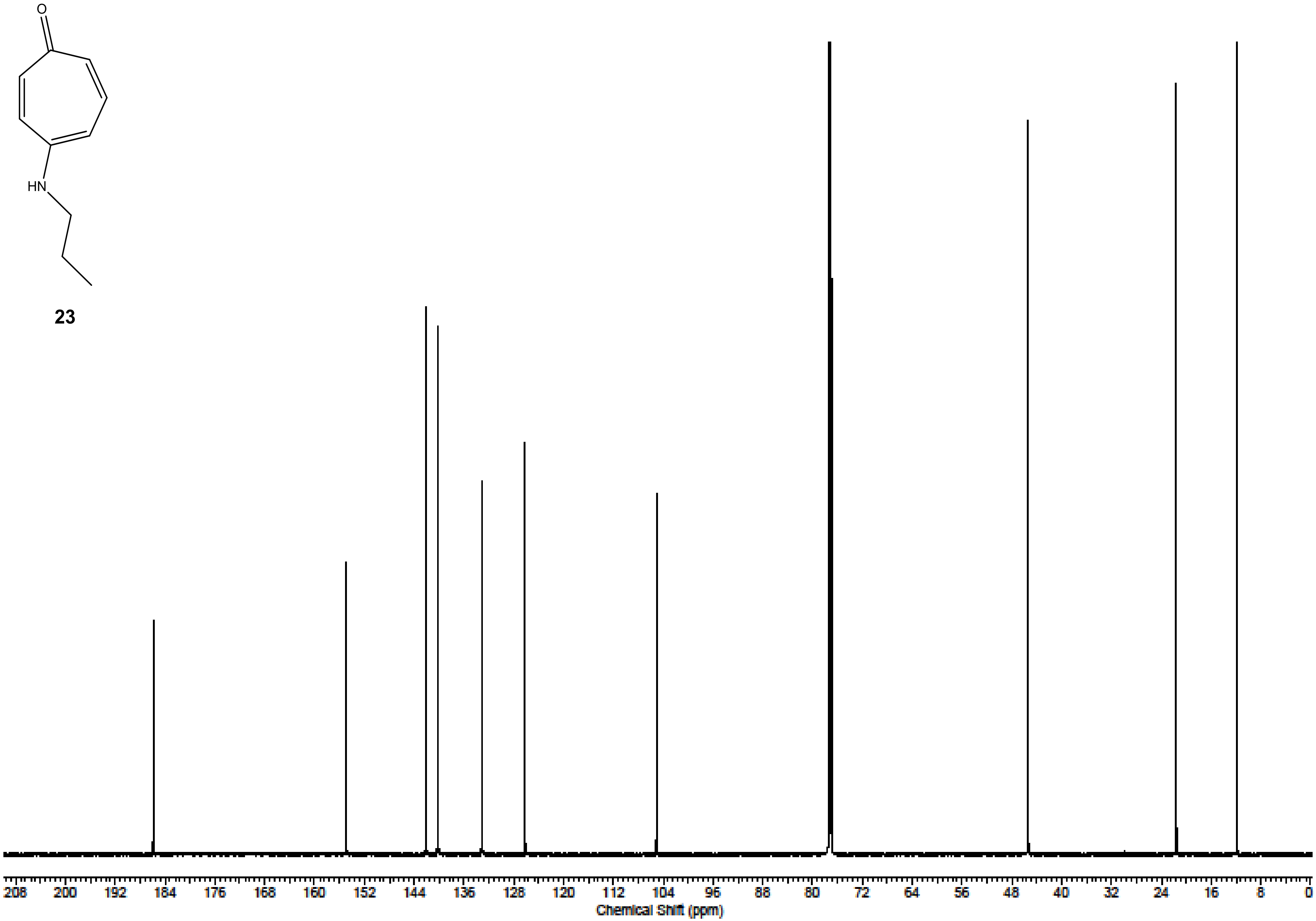

1.0
1.0
0.9
2.0
2.0
2.0
2.1
3.1
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

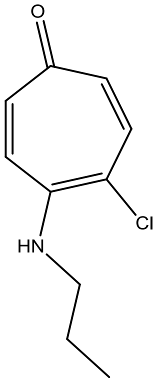

O
Cl
HN
22
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


23
O
HN
1.0
1.0
1.0
1.0
1.0
1.0
2.0
2.0
3.0
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
Chemical Shift (ppm)

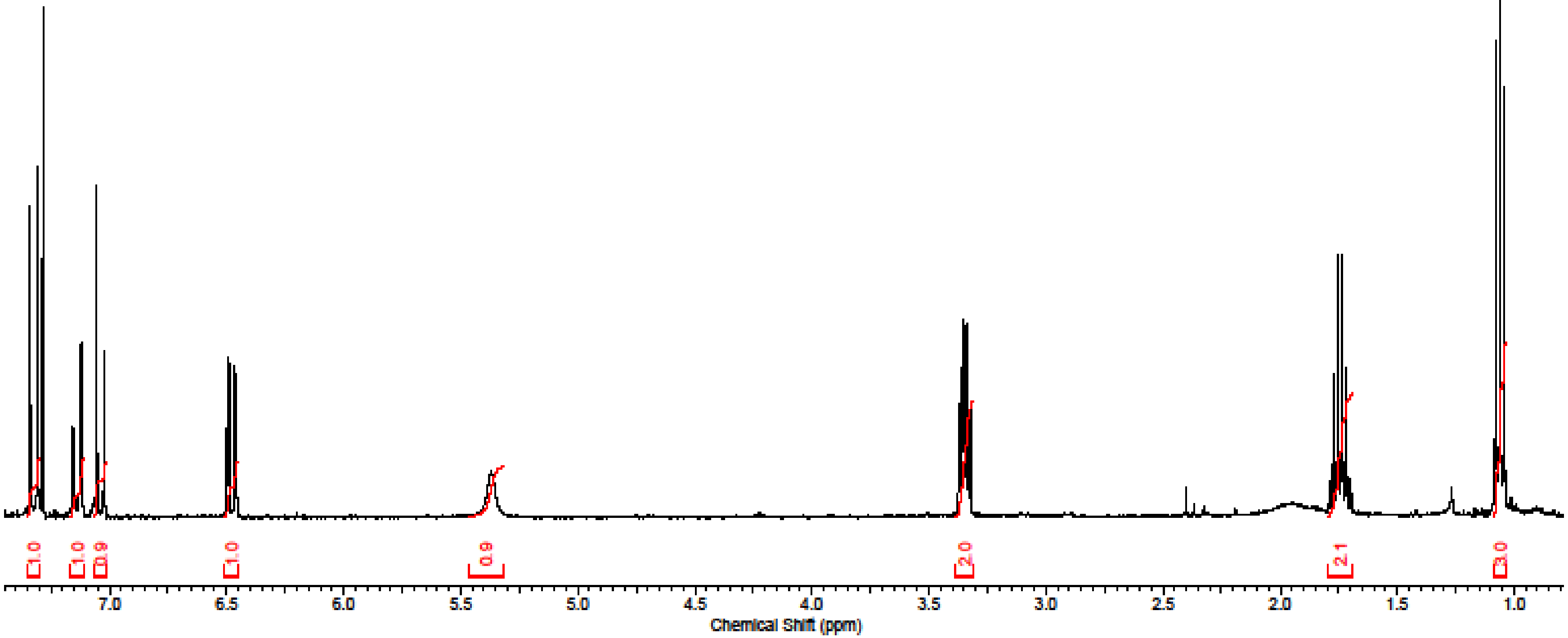
O
HN

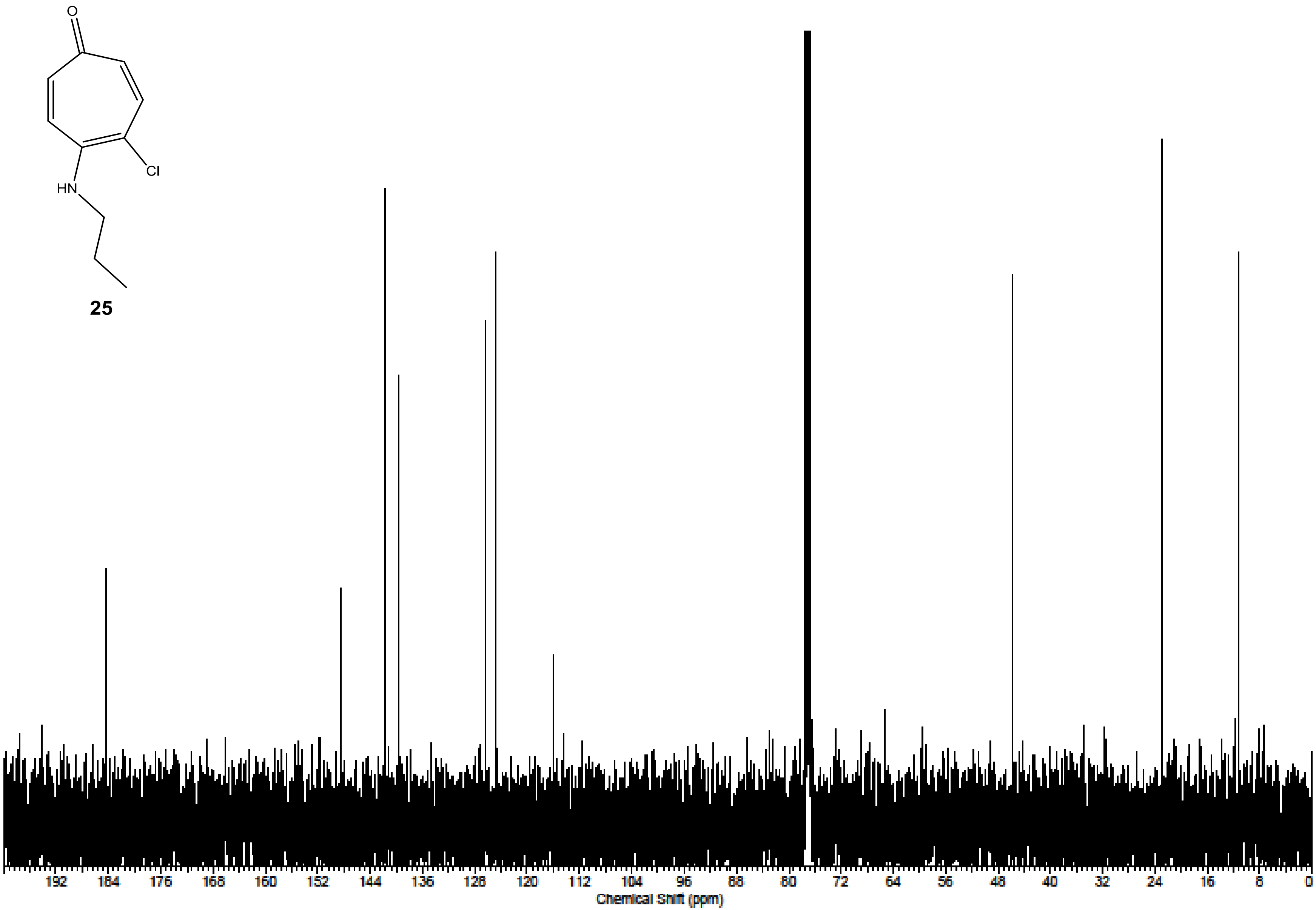
23

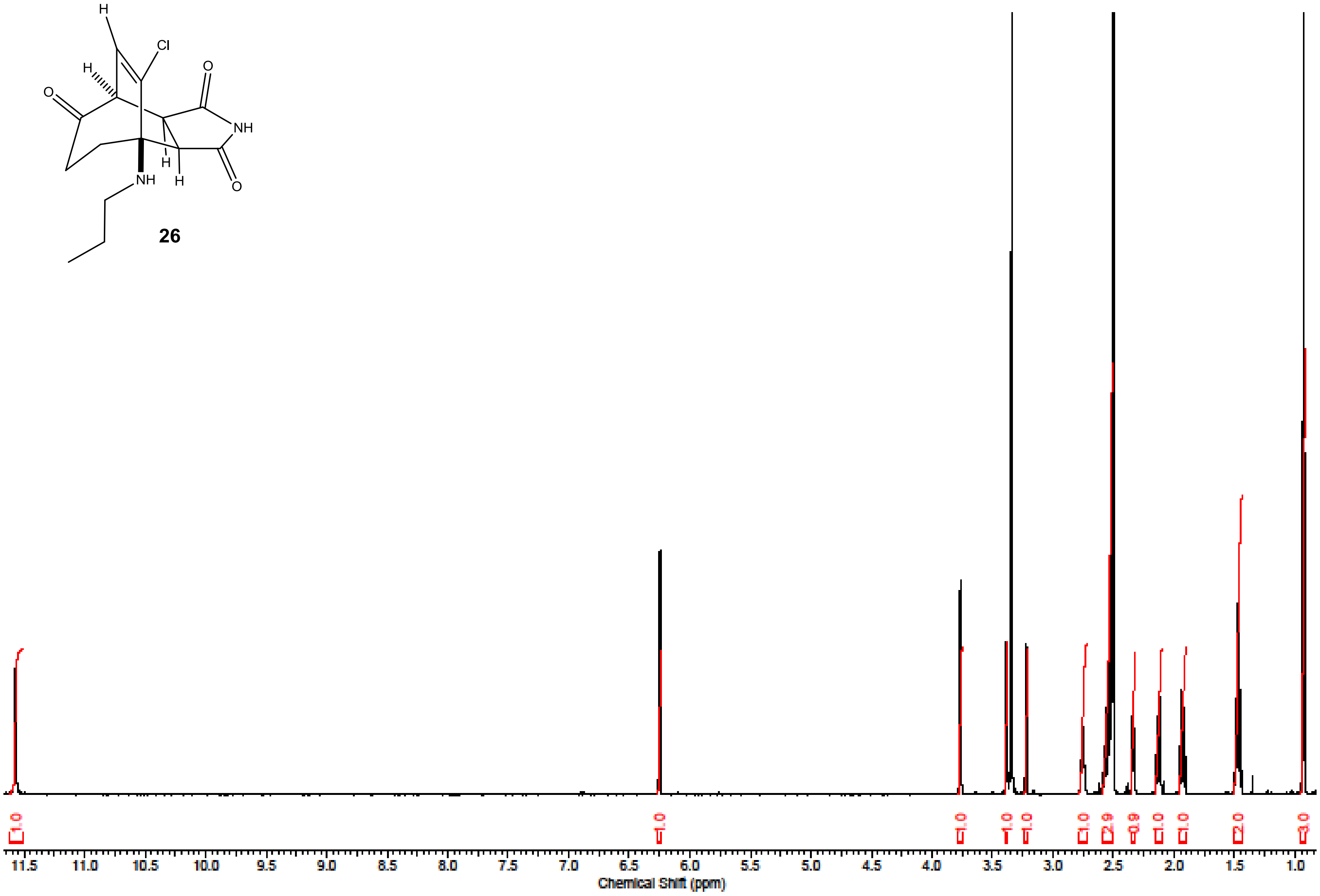

208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


O
HN
Cl

25

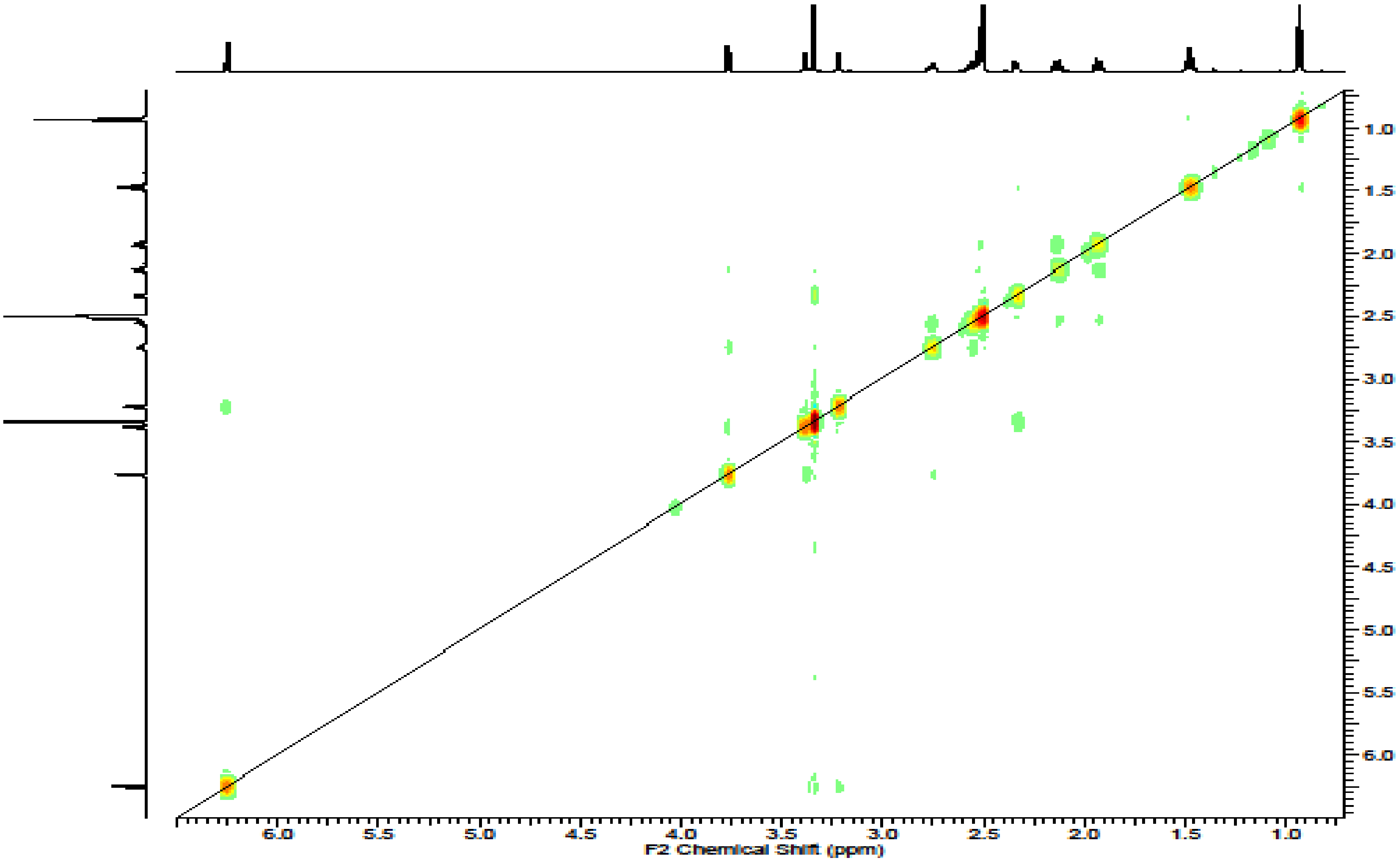

1.0
1.0
0.9
1.0
0.9
2.0
2.1
3.0
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


O
Cl
HN
25
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


H
Cl
H
O
O
NH
H
NH
H
O

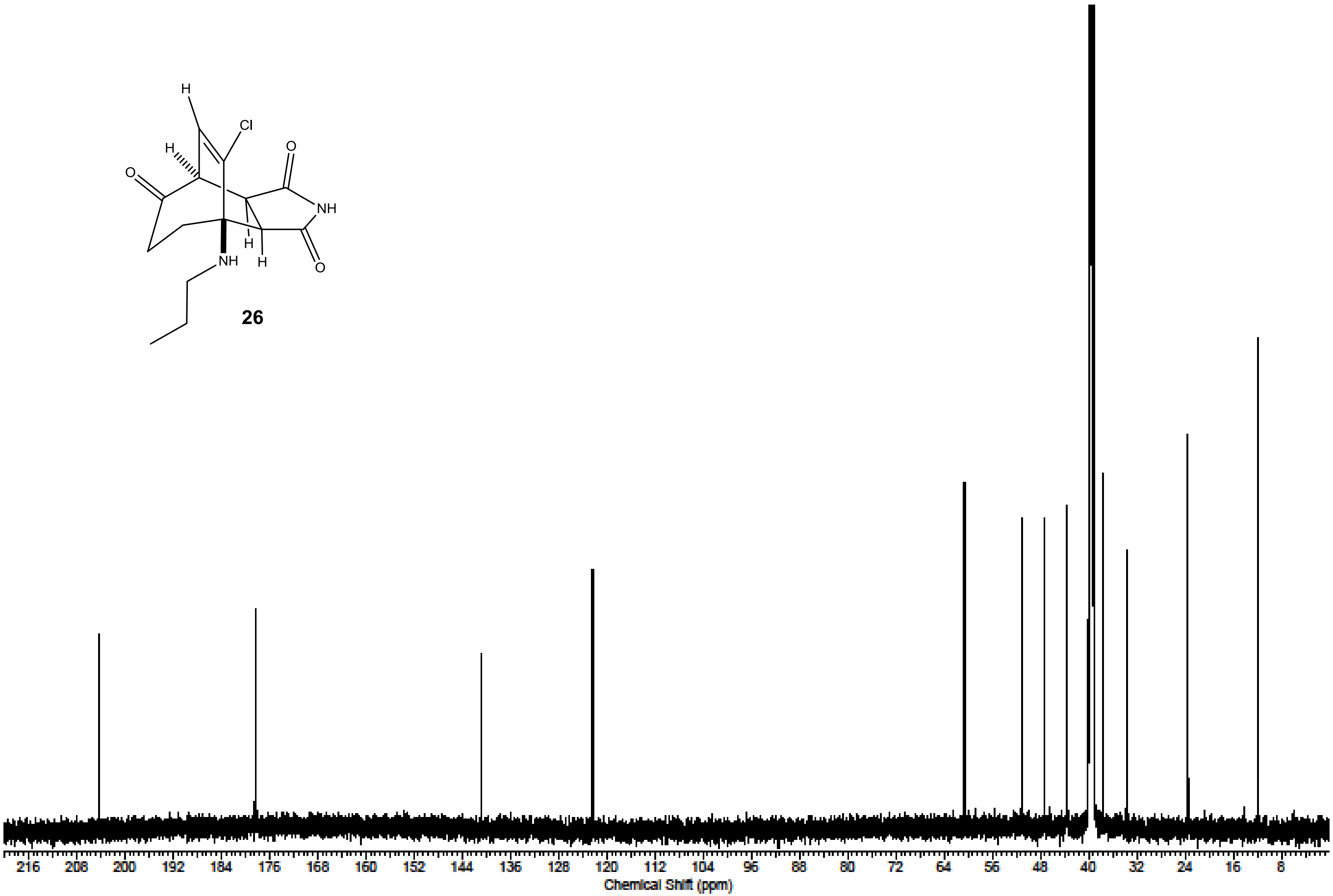
26

1.0
1.0
1.0
1.0
1.0
1.0
2.9
0.9
1.0
1.0
2.0
3.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
F2 Chemical Shift (ppm)

H
Cl
H
O
O
NH
H
H
NH
O

26


216
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)