Supporting Information

Synthetic and Biosynthetic Studies of FR900482 and Mitomycin C: An Efficient and Stereoselective Hydroxymethylation of an Advanced Benzazocane Intermediate

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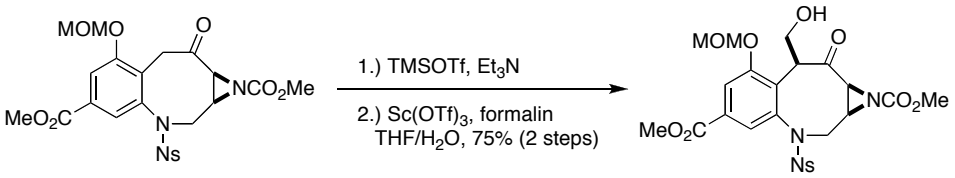
General Experimental Methods. Unless otherwise noted, all reagents were obtained from commercial suppliers and used as received. All air or moisture sensitive reactions were performed under a positive pressure of argon in glassware that had been flame-dried and cooled under a stream of argon. Tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), acetonitrile (MeCN), triethylamine (Et_3N), toluene, diethyl ether (Et_2O), and *N*,*N*-dimethylformamide (DMF) were obtained from a dry solvent system (activated alumina columns, positive pressure of argon, according to the method of Grubbs[1]). Column chromatography was performed using Merck silica gel 60 (230-400 mesh). Melting points were determined in open-ended capillary tubes and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian 300, 400, or 500 MHz spectrometers. Chemical shifts are reported in ppm relative to $CHCl_3$ at δ 7.27 (^{1}H NMR) and δ 77.23 (^{13}C NMR) or tetramethylsilane (TMS) δ 0.00 where noted. Mass spectra were obtained on Fisons VG Autospec. IR spectra were obtained from thin films on an NaCl plate using a Perkin-Elmer 1600 series FT-IR spectrometer. Optical rotations were collected at 589 nm on a Rudolph Research Automatic Polarimeter Autopol III.

6 **7**

Compound 6. The benzazocane **9**[2] (500 mg, 0.736 mmol, 1.0 equiv) was dissolved with DMF (7.0 mL) and H_2O (0.70 mL) in a 50 mL round-bottomed flask. To the solution was added tris(dimethylamino)sulfur (trimethylsilyl) difluoride (TASF) (406 mg, 1.47 mmol, 2.0 equiv) at room temperature. After stirring for 3 h at room temperature, saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc×5. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (EtOAc) to give the corresponding secondary alcohol as a pale yellow oil (370 mg, 91%). Major diastereomer: $[\alpha]^{20}_D$ –30.5 (*c* 1.90, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6, 373K) δ 7.90-7.93 (1H, m), 7.85–7.74 (3H, m), 7.65 ((1/3)H, d, *J* = 1.5 Hz), 7.63 ((2/3)H, dt, *J* = 1.5 Hz), 7.30 ((1/3)H, d, *J* = 1.5 Hz), 7.07 ((2/3)H, d, *J* = 1.5 Hz), 5.30 (1H, s), 4.25 (1H, dd, *J* = 14.5, 5.5 Hz), 4.20–4.14 (1H, m), 4.00 (1H, dd, *J* = 14.5, 2.5 Hz), 3.82 ((1/5)3H, s), 3.78 ((4/5)3H, s), 3.70 ((1/5)3H, s), 3.66 ((4/5)3H, s), 3.46 ((4/5)3H, s), 3.44

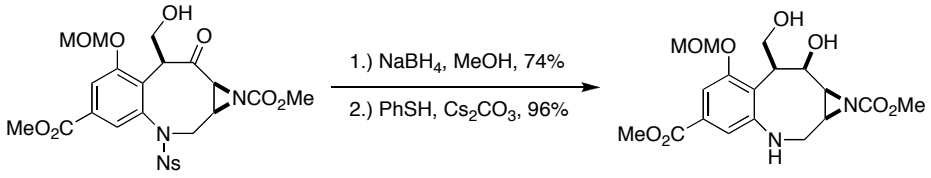
((1/5)3H, s), 3.02–2.92 (3H, m), 2.70–2.61 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) (note: at room temperature, this compound exists as an equilibrating mixture of conformational isomers on the NMR time scale) δ 165.4, 163.2, 155.8, 147.8, 138.9, 134.0, 133.6, 132.3, 131.3, 130.0, 124.2, 124.0, 115.0, 94.4, 56.4, 54.0, 52.2, 45.9, 41.5, 36.4, 29.2; IR (neat) 3420, 2955, 1724, 1671, 1545, 1437, 1298, 1243, 1168, 732 cm^{-1}; HRMS (FAB) *m* / *z* calcd for $C_{23}H_{26}N_3O_{11}S$ $(M + H)^+$ 552.1283, found 552.1288.

The secondary alcohols (370 mg, 0.672 mmol, 1.0 equiv) were dissolved in CH_2Cl_2 (7.0 mL) in a 50 mL round-bottomed flask. To the solution was added Dess-Martin periodinane (427 mg, 1.01 mmol, 1.5 equiv) at room temperature. After stirring for 45 min, Et_2O (21 mL) and a solution of 1.4 g of $Na_2S_2O_3$•$5H_2O$ in saturated aqueous $NaHCO_3$ (21 mL) were added to the reaction mixture. The resulting mixture was stirred vigorously at room temperature until both phases appeared transparent. The layers were separated, and the aqueous layer was extracted with EtOAc×3. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting oil was purified by silica gel column chromatography (1:3 hexane/EtOAc) to give the ketone **6** as a colorless oil (351 mg, 95%) (note: at room temperature, this compound exists as an equilibrating mixture of conformational isomers on the NMR time scale). Major diastereomer: $[\alpha]^{20}_D$ –37.6 (*c* 0.40, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO–d_6, 373K): δ 7.97–7.87 (3H, m), 7.83–7.74 (2H, m), 7.69 (1H, d, *J* = 1.5 Hz), 6.93 (1H, s), 5.34 (1H, d, *J* = 6.5 Hz), 5.30 (1H, d, *J* = 6.5 Hz), 4.34–4.23 (1H, m), 4.04 (1H, br s), 3.98 (1H, br s), 3.78 (3H, s), 3.84–3.73 (1H, m), 3.61 (3H, s), 3.47 (3H, s), 3.38 (1H, d, *J* = 7.0 Hz), 3.20–3.14 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) (note: at room temperature, this compound exists as an equilibrating mixture of conformational isomers on the NMR time scale) δ 200.0, 165.3, 165.0, 161.8, 161.2, 155.8, 153.9, 148.1, 147.9, 138.3, 138.2, 136.1, 134.5, 134.4, 134.2, 133.0, 132.6, 131.6, 131.2, 131.0, 130.7, 129.7, 129.2, 124.1, 123.9, 122.3, 116.4, 115.3, 94.7, 94.2, 56.5, 56.3, 54.1, 53.8, 53.4, 52.2, 51.1, 48.6, 46.7, 45.4, 42.5, 42.1, 35.2; IR (neat) 3096, 3002, 2955, 1716, 1582, 1547, 1437, 1290, 1014, 730 cm^{-1}; MS: *m* / *z* = 550 (12), 307 (28), 154 (100), 137 (73); HRMS (FAB) *m* / *z* calcd for $C_{23}H_{24}N_3O_{11}S$ $(M + H)^+$ 550.1126, found 550.1138.



7 **8**, α:β = 9:91

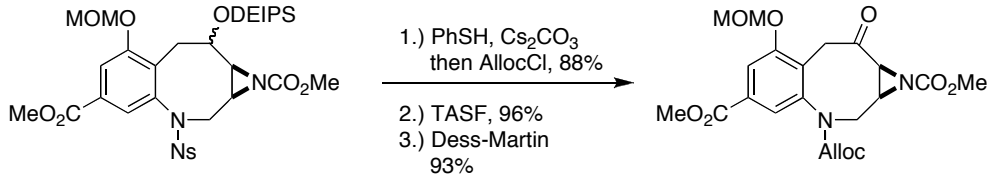
Compound 7. The ketone **6** (96.9 mg, 0.177 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (1.8 mL) in a 25 mL round-bottomed flask. To the solution were added Et_3N (61.5 μL, 0.441 mmol, 2.5 equiv) and TMSOTf (63.9 μL, 0.353 mmol, 2.0 equiv) dropwise by syringe at room temperature. After stirring for 2 h, the reaction mixture was passed through a short column of activated, neutral alumina using hexane-EtOAc (1 : 3) as the eluent, and the combined filtrates were concentrated *in vacuo*. The resulting crude silyl enol ether (105 mg) was dissolved in a mixture of THF/H_2O (9:1, v/v) (0.56 mL) in a 10 mL round-bottomed flask. To the solution was added 37% aqueous formaldehyde solution (68.5 μL, 0.845 mmol, 5.0 equiv.) containing $Sc(OTf)_3$ (8.3 mg, 0.0169 mmol, 0.1 equiv) at room temperature. After stirring for 3.5 h, brine was added to the reaction mixture. The layers were separated, and the aqueous portion was extracted with CH_2Cl_2×4. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (30:1 CH_2Cl_2/MeOH) to give the hydroxymethyl ketone (**7**) as a colorless oil (76.6 mg, 75%, 2 steps, α : β = 9 : 91): ^{1}H NMR (300 MHz, $CDCl_3$) δ TMS 7.92 (1H, br s) 7.87–7.81 (1H, m), 7.68–7.64 (3H, m), 7.12 (1H, d, *J* = 1.3 Hz), 5.45 (1H, d, *J* = 7.1 Hz), 5.41 (1H, d, *J* = 7.1 Hz), 4.67 (1H, dd, *J* = 11.2, 8.8 Hz), 4.52 (1H, dd, *J* = 8.8, 3.1 Hz), 4.32 (1H, dd, *J* = 13.7, 2.9 Hz), 3.93 (1H, dd, *J* = 13.7, 6.0 Hz), 3.89 (3H, s), 3.75 (3H, s), 3.80–3.71 (1H, m), 3.60 (3H, s), 3.31 (1H, d, *J* = 7.1 Hz), 2.98 (1H, br s), 2.80 (1H, ddd, *J* = 7.1, 6.0, 2.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.1, 165.2, 162.2, 156.6, 149.2, 137.8, 135.2, 132.8, 132.6, 132.0, 131.5, 129.9, 124.3, 123.0, 115.9, 95.0, 61.8, 57.1, 54.3, 52.8, 52.3, 51.9, 45.6, 40.6; IR (neat) 3545, 2955, 2253, 1724, 1578, 1547, 1438, 1375, 1289, 1223, 1174, 1016, 730 cm^{-1}; HRMS (FAB) *m* / *z* calcd for $C_{24}H_{26}N_3O_{12}S$ $(M + H)^+$ 580.1232, found 550.1246.



8, α:β = 9:91 **9**

Compound 8. The hydroxymethylated ketone **7** (21.8 mg, 0.0377 mmol, 1.0 equiv) was dissolved with MeOH (0.5 mL) in a 10 mL round-bottomed flask. To the solution was added $NaBH_4$ (1.4 mg, 0.0377 mmol, 1.0 equiv) at 0 °C. After stirring for 30 min at 0 °C, saturated aqueous NH_4Cl was added. The layers were separated, and the aqueous portion was extracted with CH_2Cl_2×5. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (30:1 CH_2Cl_2/MeOH) to give the corresponding diol as a colorless oil (16.2 mg, 74%) (note: at room temperature, this compound exists as an equilibrating mixture of conformational isomers on the NMR time scale). $[\alpha]^{20}_D$ +20.4 (*c* 1.00, $CHCl_3$); Major rotamer: ^{1}H NMR (300 MHz, $CDCl_3$) δ TMS: 7.56–7.80 (5H, m), 7.02 (1H, d, *J* = 1.5 Hz), 5.32 (2H, s), 4.97 (1H, dd, *J* = 2.9, 2.6 Hz), 4.55 (1H, dd, *J* = 10.7, 10.3 Hz), 4.31 (1H, dd, *J* = 13.2, 4.8 Hz), 4.15–4.22 (1H, m), 4.12 (1H, dd, *J* = 13.2, 7.0 Hz), 3.87–3.92 (1H, m), 3.83 (3H, s), 3.70 (3H, s), 3.53 (3H, s), 2.77 (1H, s), 2.45 (1H, dd, *J* = 6.6, 2.6 Hz), 2.38 (1H, ddd, *J* = 7.0, 6.6, 4.8 Hz), 2.09 (1H, s). Minor rotamer: ^{1}H NMR (300 MHz, $CDCl_3$) δ TMS: 7.80–7.56 (5H, m), 7.07 (1H, d, *J* = 1.5 Hz), 5.26 (1H, d, *J* = 6.6 Hz), 5.22 (1H, d, *J* = 6.6 Hz), 4.86 (1H, dd, *J* = 15.4, 5.5 Hz), 4.62–4.58 (1H, m), 4.39 (1H, dd, *J* = 11.7, 9.2 Hz), 4.10 (1H, dd, *J* = 11.7, 5.1 Hz), 4.02–3.97 (1H, m), 3.79 (3H, s), 3.74 (3H, s), 3.47 (3H, s), 3.40–3.32 (1H, m), 3.18 (1H, dd, *J* = 6.6, 4.4 Hz), 3.13 (1H, dd, *J* = 15.4, 9.2 Hz), 2.64 (1H, s), 2.18 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 165.5, 163.4, 163.0, 157.5, 157.1, 148.9, 148.0, 141.7, 138.2, 136.3, 134.6, 134.5, 134.3, 132.7, 132.6, 131.8, 131.6, 131.3, 130.2, 129.9, 124.3, 124.0, 123.7, 116.3, 115.6, 94.9, 94.8, 68.4, 65.2, 64.4, 62.3, 56.9, 56.8, 54.7, 54.2, 54.1, 52.6, 52.5, 51.3, 49.1, 47.1, 43.9, 42.8, 42.4, 40.9, 36.2; IR (neat) 3502, 2954, 1723, 1546, 1437, 1373, 1299, 1238, 1019 and 731 cm^{-1}; HRMS (FAB) *m* / *z* calcd for $C_{24}H_{28}N_3O_{12}S$ $(M + H)^+$ 582.1388, found 552.1373.

The diol (160 mg, 0.275 mmol, 1.0 equiv) was dissolved with MeCN (2.8 mL) in a 50 mL round-bottomed flask. To the solution were added PhSH (42.4 μL, 0.413 mmol, 1.5 equiv) and Cs_2CO_3 (135 mg, 0.413 mmol, 1.5 equiv) at room temperature. After stirring for 3 h at room temperature, saturated aqueous NH_4Cl was added. The layers were separated, and the aqueous portion was extracted with EtOAc×5. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (30:1 CH_2Cl_2/MeOH) to give the corresponding amine **8** as a colorless solid (105 mg, 96%) (recrystallized from CH_2Cl_2-hexane to give colorless prisms); $[\alpha]^{20}_D$ +156.7 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD) δ TMS: 7.90 (2H, br d, *J* = 2.5 Hz), 7.60 (1H, br s), 7.54 (1H, br s), 5.30 (2H, s), 4.76 (1H, br s), 4.04–3.96 (1H, m), 3.89 (3H, s), 3.77 (1H, dd, *J* = 10.3, 9.5 Hz), 3.68 (3H, s), 3.62 (1H, dd, *J* = 10.3, 4.4 Hz), 3.50 (3H, s), 3.54–3.46 (2H, m), 2.57 (1H, br d, *J* = 6.6 Hz), 2.40–2.34 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 164.0, 156.2, 146.3, 131.6, 130.6, 122.1, 94.8, 68.4, 64.8, 63.6, 56.7, 53.9, 52.5, 50.3, 44.0, 42.9, 37.2; IR (neat) 3303, 2952, 1720, 1580, 1440, 1299, 1235, 1048, 757 cm^{-1}; HRMS (FAB) *m* / *z* calcd for $C_{18}H_{25}N_2O_8$ $(M + H)^+$ 397.1605, found 397.1596.



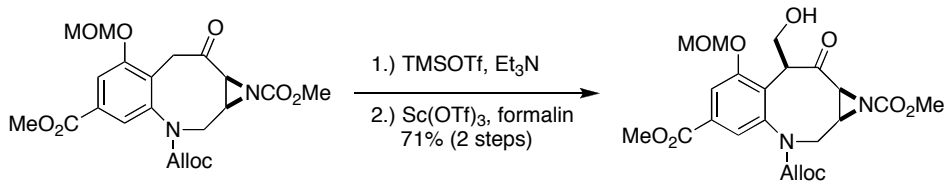
6 **10a**

Compound 10a. Benzazocane **9** (1.00 g, 1.47 mmol, 1.0 equiv) was dissolved in MeCN (15 mL) in a 50 mL round-bottomed flask. To the solution were added PhSH (227 μL, 2.21 mmol, 1.5 equiv) and Cs_2CO_3 (960 mg, 2.95 mmol, 2.0 equiv) at room temperature. After stirring for 3.5 h, allyl chloroformate (313 μL, 2.95 mmol, 2.0 equiv) was added, and the reaction mixture was stirred for 2 h. Following the addition of saturated aqueous NH_4Cl, the layers were separated, and the aqueous layer was extracted with EtOAc×3. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (1:2 hexane/EtOAc) to give the corresponding allyl carbamate as a colorless oil (820 mg, 96%) (note: at room temperature, this compound exists as an equilibrating mixture of conformational isomers on the

NMR time scale). Major diastereomer: $[\alpha]^{20}_{D}$ +30.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6 393K) δ 7.62 (1H, d, *J* = 1.5 Hz), 7.41 (1H, d, *J* = 1.5 Hz), 5.89 (1H, m), 5.31 (1H, d, *J* = 6.5 Hz), 5.27 (1H, d, *J* = 6.5 Hz), 5.23–5.13 (1H, m), 4.62 (0.25H, d, *J* = 5.0 Hz), 4.56 (0.75H, d, *J* = 5.0 Hz), 4.42–4.33 (1H, m), 4.20–4.06 (1H, br s), 3.87 (3H, s), 3.86–3.75 (1H, m), 3.66 (3H, s), 3.48 (3H, s), 3.07–2.82 (4H, m), 2.71–2.63 (2H, m), 1.04–0.95 (13H, m), 0.75–0.66 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.2, 164.5, 163.6, 156.3, 156.1, 155.8, 155.1, 154.7, 142.7, 142.6, 142.4, 132.8, 132.6, 132.0, 131.8, 131.1, 130.8, 130.6, 129.1, 123.2, 122.8, 117.9, 117.4, 117.1, 114.1, 113.7, 113.2, 95.1, 94.6, 70.4, 66.9, 66.4, 65.8, 56.5, 53.8, 53.7, 52.5, 52.4, 49.9, 48.7, 47.4, 46.2, 40.6, 39.0, 30.1, 29.7, 29.5, 17.4, 17.3, 17.2, 12.9, 7.2, 3.8, 3.6; IR (neat) 2953, 1726, 1583, 1437, 1295, 1240, 1015 cm^{-1}; HRMS (FAB) *m* / *z* calcd for $C_{28}H_{43}N_2O_9Si$ $(M + H)^+$ 579.2732, found 579.2721.

The allyl carbamate (820 mg, 1.42 mmol, 1.0 equiv) was dissolved in DMF (14 mL) and H_2O (1.4 mL) in a 100 mL round-bottomed flask. To the solution was added tris(dimethylamino)sulfur (trimethylsilyl) difluoride (TASF) (782 mg, 2.84 mmol, 2.0 equiv) at room temperature. After stirring for 3 h at room temperature, saturated aqueous NH_4Cl was added. The layers were separated, and the aqueous portion was extracted with EtOAc×5. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (EtOAc) to give the corresponding secondary alcohol (608 mg, 95%) as a colorless oil (note: at room temperature, this compound exists as an equilibrating mixture of conformational isomers on the NMR time scale). Major diastereomer: $[\alpha]^{20}_{D}$ +14.9 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ TMS: 7.68 (1H, br s), 7.53 (0.4H, br s), 7.47 (0.6H, br s), 6.03–5.92 (0.4H, m), 5.82–5.71 (0.6H, m), 5.37 (0.6H, d, *J* = 7.0 Hz), 5.25 (2H, s), 5.13–5.01 (1.4H, m), 4.65 (1H, br d, *J* = 3.6 Hz), 4.53 (2H, br s), 4.19 (1H, br s), 3.87 (1.8H, s), 3.85 (1.2H, s), 3.73 (1.8H, s), 3.70 (1.2H, s), 3.66–3.54 (1H, m), 3.48 (1.8H, s), 3.47 (1.2H, s), 3.21 (1H, br d, *J* = 10.2 Hz), 2.93–2.42 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.1, 163.7, 163.3, 156.4, 155.6, 155.1, 154.8, 143.2, 142.3, 141.9, 132.8, 132.6, 131.3, 130.9, 130.6, 129.6, 123.3, 122.9, 118.0, 117.5, 117.3, 114.3, 114.1, 113.8, 95.1, 94.6, 69.1, 66.9, 66.5, 63.5, 56.5, 54.3, 54.2, 52.5, 52.4, 51.1, 48.7, 46.3, 46.1, 41.5, 41.1, 39.9, 29.9, 29.3, 28.1; IR (neat) 3481, 2953, 1719, 1583, 1437, 1296, 1240, 1014 cm^{-1}; HRMS (FAB) *m* / *z* calcd for $C_{21}H_{27}N_2O_9$ $(M + H)^+$ 451.1711, found 451.1722.

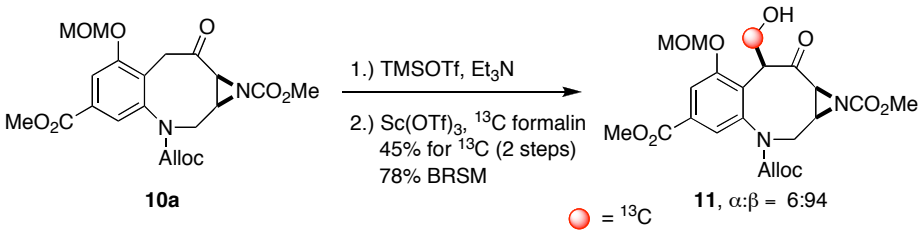
The secondary alcohol (280 mg, 0.622 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (6.2 mL) in a 50 mL round-bottomed flask. To the solution was added Dess-Martin periodinane (396 mg, 0.933 mmol, 1.5 equiv) at room temperature. After stirring for 1 h at room temperature, Et_2O and a solution of saturated aqueous $NaHCO_3$ containing $Na_2S_2O_3{\cdot}5H_2O$ were added. The mixture was vigorously stirred for 5 min (until both layers are transparent) at room temperature. The layers were separated, and the aqueous layer was extracted with EtOAc×3. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (1: 2 hexane/EtOAc) to give the ketone **10a** (258 mg, 93%) as a colorless oil (note: at room temperature, this compound exists as an equilibrating mixture of conformational isomers on the NMR time scale). $[\alpha]^{20}_{D}$ –50.6 (*c* = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ TMS: 7.66–7.74 (1H, m), 7.56–7.41 (1H, m), 6.02–5.70 (1H, m), 5.60 (0.2H, d, *J* = 34.7 Hz), 5.33–5.22 (2H, m), 5.15–4.99 (1.6H, m), 4.88–4.41 (3.4H, m), 4.16 (1H, d, *J* = 17.3 Hz), 3.91–3.85 (3H, m), 3.75 (0.6H, br s), 3.65–3.06 (8.8H, m), 2.84 (0.2H, br s), 2.76–2.46 (0.2H, m), 2.57 (0.2H, d, *J* = 17.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.7, 202.7, 202.2, 166.1, 166.0, 161.8, 156.0, 155.5, 154.6, 153.8, 141.6, 140.6, 133.8, 132.4, 132.1, 131.2, 130.3, 129.9, 124.3, 124.1, 123.0, 122.7, 121.7, 118.5, 117.9, 117.6, 117.5, 115.7, 115.3, 114.4, 114.1, 95.6, 95.4, 94.8, 94.5, 67.4, 66.8, 56.8, 56.5, 54.8, 54.4, 54.1, 53.0, 52.6, 52.5, 51.5, 50.8, 47.6, 47.4, 47.0, 46.8, 46.5, 45.6, 42.6, 41.4, 41.1, 34.5, 34.0; IR (neat) 2954, 1722, 1582, 1438, 1388, 1318, 1286, 1264, 1243 1153, 1015, 767 cm^{-1}; HRMS (FAB) *m* / *z* calcd for $C_{21}H_{25}N_2O_9$ $(M + H)^+$ 449.1555, found 449.1557.



10a **11**, α:β = 6:94

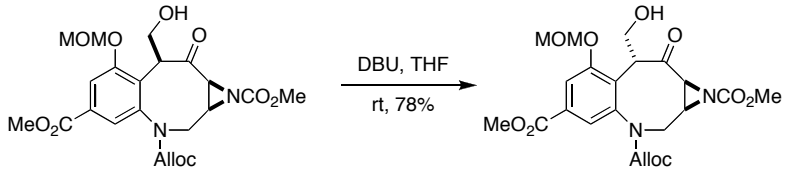
Compound 11. The ketone **10a** (215 mg, 0.480 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (2.4 mL) in a 25 mL round-bottomed flask. To the solution were added Et_3N (0.167 mL, 1.20 mmol, 2.5 equiv) and TMSOTf (0.174 mL, 0.960 mmol, 2.0 equiv) at room temperature. After stirring for 2 h, the reaction mixture was passed through a short

plug of activated, neutral alumina using EtOAc-hexane (3:1), and the combined filtrates were concentrated *in vacuo*. The resulting silyl enol ether (285 mg) was dissolved in THF/H_2O (9:1, v/v) (1.6 mL) in a 25 mL round-bottomed flask. To the solution was added 37% aqueous formaldehyde solution (0.195 mL, 2.40 mmol, 5.0 equiv) containing $Sc(OTf)_3$ (23.6 mg, 0.0480 mmol, 0.1 equiv) at room temperature. After stirring for 30 min, the reaction was quenched with H_2O and the layers were separated. The aqueous layer was extracted with CH_2Cl_2×3, and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (1:5 hexane/EtOAc) to give the hydroxymethyl ketone **11** as a colorless oil (147 mg, 62%, 2 steps, α : β = 6 : 94): ^{1}H NMR (300 MHz, $CDCl_3$) δ TMS 7.83 (1H, d, *J* = 1.5 Hz), 7.52 (1H, br s), 5.90–5.76 (1H, m), 5.37 (1H, d, *J* = 7.3 Hz), 5.34 (1H, d, *J* = 7.3 Hz), 5.21–5.12 (1H, m), 4.55–4.51 (1H, m), 4.47 (1H, dd, *J* = 8.9, 3.7 Hz), 4.43–4.36 (1H, m), 4.16–4.09 (1H, m), 3.92 (3H, s), 3.71 (3H, s), 3.54 (3H, s), 3.56–3.46 (1H, m), 3.28 (1H, d, *J* = 7.0 Hz), 2.86–2.79 (1H, m), 2.77 (1H, ddd, *J* = 7.0, 5.9, 3.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 165.7, 162.2, 156.0, 140.4, 132.6, 132.0, 131.0, 123.3, 118.7, 114.8, 94.9, 67.4, 61.4, 57.0, 54.3, 52.8, 51.9, 48.5, 45.6, 41.6, 29.9; IR (neat) 3527 (br), 2954, 1721, 1578, 1438, 1390, 1292, 1251, 1217, 1154, 1018, 732 cm^{-1}; HRMS (FAB) *m* / *z* calcd for $C_{22}H_{27}N_2O_{10}$ $(M + H)^+$ 479.1666, found 479.1655.



10a **11**, α:β = 6:94

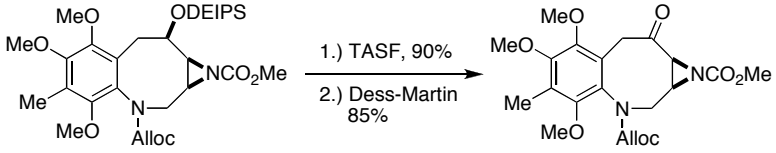
Preparation of ^{13}C-labelled compound 11. The ketone **10a** (50.0 mg, 0.112 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (1.2 mL) in a 10 mL round-bottomed flask. To the solution were added Et_3N (38.9 μL, 0.279 mmol, 2.5 equiv) and TMSOTf (40.4 μL, 0.223 mmol, 2.0 equiv) at room temperature. After stirring for 2 h, the reaction mixture was passed through a short column of activated, neutral alumina using EtOAc-hexane (3:1) as an eluent, and the combined filtrates were concentrated *in vacuo*. The resulting silyl enol ether (52.1 mg) was dissolved with THF (0.33 mL) in a 10 mL round-bottomed flask. To the solution was added 20% aqueous ^{13}C-formaldehyde solution (86.6 μL, 0.558 mmol, 5.0 equiv) containing $Sc(OTf)_3$ (5.5 mg, 0.011 mmol, 0.1 equiv) at 0 °C. After stirring for 2 h at 0 °C, the reaction was quenched with H_2O. The layers were separated, and the aqueous portion was extracted with CH_2Cl_2×4. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (40: 1 CH_2Cl_2/MeOH) to give the hydroxyl-^{13}C-methyl ketone **^{13}C-11** (30.5 mg, 73%, 2 steps, α : β = 4 : 96 inseparable mixture) as a colorless oil, and the recovered ketone **10a** (20.6 mg, 41%): ^{1}H NMR (400 MHz, $CDCl_3$) δ TMS: 7.82 (1H, d, *J* = 1.1 Hz), 7.50 (1H, br s), 5.86–5.72 (1H, m), 5.35 (1H, d, *J* = 6.8 Hz), 5.32 (1H, d, *J* = 6.8 Hz), 5.26–5.05 (2H, m), 4.50 (2H, br s), 4.49–4.23 (2H, m), 3.90 (3H, s), 3.68 (3H, s), 3.51 (3H, s), 3.40–3.27 (1H, m), 3.26 (1H, d, *J* = 7.2 Hz), 2.83–2.75 (1H, m), 2.74 (1H, ddd, *J* = 7.2, 6.3, 3.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 165.7, 162.2, 156.0, 155.2, 140.4, 132.6, 132.0, 131.6, 130.9, 123.3, 118.7, 114.8, 94.9, 67.4, 61.4 (^{13}C), 57.0, 54.3, 52.8, 52.1, 51.7, 48.5, 45.6, 41.6; IR (neat) 3532 (br), 2954, 1722, 1578, 1438, 1390, 1291, 1251, 1217, 1153, 1018, 731 cm^{-1}. Multiple attempts to obtain a high-resolution mass spectrum of pure material were unsuccessful.



11β **11α**

Epimerization Procedure for 11. The ketone **11** (28.5 mg, 0.0596 mmol, 1.0 equiv) was dissolved in THF (2.9 mL) in a 10 mL round-bottomed flask. To the solution was added DBU (4.46 μL, 0.0298 mmol, 0.5 equiv) at room temperature. After stirring for 15 h, saturated aqueous NH_4Cl was added to the reaction mixture. The layers were separated, and the aqueous portion was extracted with EtOAc×4. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (1: 5 hexane/EtOAc) to give the hydroxymethyl ketone **11α** as a colorless oil (22.2 mg, 78%, α : β = 87 : 13): ^{1}H NMR (300 MHz, $CDCl_3$) δ TMS: 7.80 (1H, d, *J* = 1.5 Hz), 7.46 (1H, br s), 5.96–5.80 (1H,

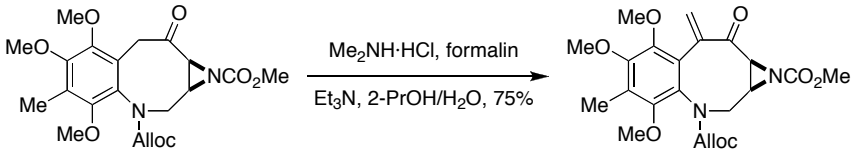
m), 5.46 (1H, d, J = 6.8 Hz), 5.36 (1H, d, J = 6.8 Hz), 5.27–5.12 (2H, m), 4.78 (1H, br d, J = 15.6 Hz), 4.58 (2H, br s), 4.45 (1H, dd, J = 9.0, 2.9 Hz), 4.16–4.06 (1H, m), 3.96 (3H, s), 3.67 (3H, s), 3.73–3.62 (1H, m), 3.55 (3H, s), 3.36 (1H, d, J = 6.8 Hz), 3.20 (1H, br dd, J = 6.8, 3.1 Hz), 2.85–2.79 (1H, m); ^{13}C NMR (300 MHz, $CDCl_3$) δ 205.9, 165.9, 161.6, 155.0, 154.0, 140.7, 133.3, 132.0, 131.2, 121.8, 118.8, 114.6, 94.3, 67.7, 61.6, 56.5, 54.1, 53.5, 52.6, 46.4, 46.2, 45.5; IR (neat) 3537 (br), 2954, 1721, 1580, 1437, 1389, 1290, 1262, 1154, 1015, 732 cm^{-1}; HRMS (FAB) m / z calcd for $C_{22}H_{27}N_2O_{10}$ $(M + H)^+$ 479.1660, found 479.1669.



12 **13**

Compound 13. To compound **12** (370 mg, 0.66 mmol) in 15 mL of a 10:1 solution of DMF/water was added tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TASF) (270 mg, 0.99 mmol). The reaction mixture was stirred at ambient temperature overnight (12 h). Addition of 20 mL saturated aqueous NH_4Cl followed by extraction with CH_2Cl_2 (4 × 10 mL) provided the crude product. The residue was purified by column chromatography (3:1 ethyl acetate/hexanes) to afford the corresponding secondary alcohol (260 mg, 90%) as a white foam: $[\alpha]^{23}_D$ –0.3 (*c* 1.00, $CHCl_3$); Spectral complexity due to rotameric mixtures (compound did not coalesce at 393 K), precluded integration of individual ^{1}H signals ^{1}H NMR (500 MHz, $CDCl_3$, mixture of carbamate rotamers) δ 6.07–5.95 (m), 5.87–5.75 (m), 5.43–5.34 (m), 5.32–5.23 (m), 5.16–5.06 (m), 4.82 (d), 4.79 (d), 4.74 (d), 4.72–4.65 (m), 4.60–4.54 (m), 4.14–4.06 (m), 3.87 (s), 3.86 (s), 3.85 (s), 3.84 (d), 3.82 (d), 3.77 (s), 3.74 (s), 3.70 (s), 3.69 (s), 3.68 (s), 3.67 (s), 3.66 (s), 3.42 (ddd), 3.12–3.02 (m), 2.93–2.85 (m), 2.78–2.57 (m), 2.51 (d), 2.44 (d), 2.35 (t), 2.19 (s), 2.18 (s), 2.17 (s), 1.40 (br s); ^{13}C NMR (100 MHz, $CDCl_3$, mixture of carbamate rotamers) δ 168.6, 164.4, 164.1, 156.0, 155.4, 155.3, 152.0, 151.2, 147.7, 133.1, 133.0, 133.9, 133.8, 129.3, 129.1, 117.7, 117.6, 117.5, 117.0, 71.3, 71.0, 66.8, 66.5, 66.4, 63.4, 61.0, 60.9, 60.8, 60.4, 60.3, 60.2, 54.3, 54.1, 47.8, 47.7, 46.7, 46.6, 42.0, 41.7, 29.2, 29.1, 9.10, 9.8, 9.7; IR (film) 3439, 2942, 1706, 1468, 1252, 1091 cm^{-1}; HRMS (FAB) calcd for $C_{21}H_{28}N_2O_8$ $(M+H)^+$ 437.1923, found 437.1926.

To the secondary alcohol (260 mg, 0.60 mmol) in dichloromethane (20 mL) was added Dess-Martin periodinane (490 mg, 1.02 mmol) and stirred until complete consumption of starting material by TLC (2 h). The reaction was diluted with ether (75 ml) and poured into 75 mL of a saturated aqueous solution of $NaHCO_3$ with a seven-fold excess of $Na_2S_2O_3$•$5H_2O$ (1.1 g), and stirred for 15 minutes. After separation of the layers, the aqueous layer was extracted with Et_2O×3. The organic extracts were combined, washed once with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude oil was purified by column chromatography (3:1 hexanes/ethyl acetate) to give ketone **13** (220 mg, 85%) as a white foam: $[\alpha]^{23}_D$ –44.9 (*c* 2.20, $CHCl_3$); Spectral complexity due to rotameric mixtures (compound did not coalesce at 393 K), precluded integration of individual ^{1}H signals ^{1}H NMR (400 MHz, $CDCl_3$, mixture of carbamate rotamers) δ 6.05–5.91 (m), 5.86–5.73 (m), 5.38–5.22 (m), 5.10–5.02 (dd), 4.77–4.43 (m), 4.07 (dd), 3.92 (d), 3.87 (s), 3.83 (s), 3.81 (s), 3.77 (s), 3.74 (s), 3.73 (s), 3.65 (s), 3.62 (s), 3.61 (s), 3.58 (s), 3.54 (s), 3.50 (s), 3.43 (s), 3.39 (s), 3.33 (d), 3.29 (d), 3.20 (d), 3.14–3.09 (m), 2.83–2.80 (m), 2.14 (s), 2.13 (s); ^{13}C NMR (100 MHz, $CDCl_3$, mixture of carbamate rotamers) δ 204.3, 204.1, 203.5, 203.0, 162.4, 162.1, 161.9, 155.6, 155.3, 152.9, 152.8, 152.0, 150.4, 147.7, 147.5, 146.0, 133.0, 132.6, 129.7, 128.6, 127.7, 127.5, 125.8, 125.7, 124.5, 118.4, 118.1, 118.0, 117.6, 67.4, 67.2, 66.7, 61.3, 61.0, 60.9, 60.5, 60.4, 60.3, 54.4, 54.2, 54.0, 47.0, 46.9, 46.8, 46.6, 45.8, 45.3, 45.0, 42.7, 41.3, 35.3, 34.6, 9.9, 9.8, 9.7, 1.2; IR (film) 3377, 2941, 2845, 1698, 1591, 1469, 1334, 1274, 1083 cm^{-1}; HRMS (FAB) calcd for $C_{21}H_{26}N_2O_8$ 435.1767, found 435.1764.



13 **14**

Compound 14. To ketone **13** (77 mg, 0.18 mmol) in 9:1 *i*-PrOH/H_2O was added Me_2NH·HCl (17 mg, 0.21 mmol), formalin (70 μL, 0.87 mmol), and triethylamine (8 μL, 0.054 mmol) in a small vial. The vial was then capped and heated at 90 °C overnight (10h). The reaction mixture was cooled to ambient temperature, diluted with chloroform,

and washed once each with 10% citric acid, saturated aqueous $NaHCO_3$, and brine. The organic layer was then dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Column chromatography (4:1) hexanes/ethyl acetate afforded enone **14** (60 mg, 75%) as a white foam: $[\alpha]^{23}_D$ –4.8 (*c* 0.65, $CHCl_3$); Spectral complexity due to rotameric mixtures (compound did not coalesce at 393 K), precluded integration of individual ^1H signals ^1H NMR (400 MHz, $CDCl_3$, mixture of carbamate rotamers) δ 6.43 (d), 6.41 (d), 6.31 (d), 6.29 (d), 6.19 (d), 6.05 (d), 6.01–5.86 (m), 5.96 (d), 5.84 (d), 5.81–5.68 (m), 5.36–5.21 (m), 5.17–5.02 (m), 4.69–4.39 (m), 4.22–4.03 (m), 3.93 (s), 3.92 (s), 3.90 (s), 3.89 (s), 3.81 (s), 3.80 (s), 3.79 (s), 3.77 (s), 3.70 (s), 3.69 (s), 3.67 (s), 3.65 (s), 3.63 (s), 3.58 (s), 3.57 (s), 3.25 (d), 3.18–3.08 (m), 2.75 (q), 2.24 (s), 2.23 (s), 2.21, (s), 2.20 (s); ^{13}C NMR (100 MHz,$CDCl_3$, mixture of carbamate rotamers) δ 196.1, 161.5, 155.1, 152.7, 149.8, 146.7, 140.1, 123.6, 130.8, 130.5, 129.8, 129.0, 128.4, 128.0, 126.1, 118.5, 118.0, 117.6, 67.4, 66.8, 60.9, 60.5, 53.9, 47.1, 46.8, 46.3, 45.5, 44.1, 43.6, 41.5, 29.9, 10.0, 9.9; IR (film) 3346, 2937, 1717, 1598, 1466, 1389, 1258, 1134, 1023 cm^{-1}; HRMS (FAB) calcd for $C_{22}H_{26}N_2O_8$ 447.1767, found 447.1751.

X-ray Crystal structure of diol 9:

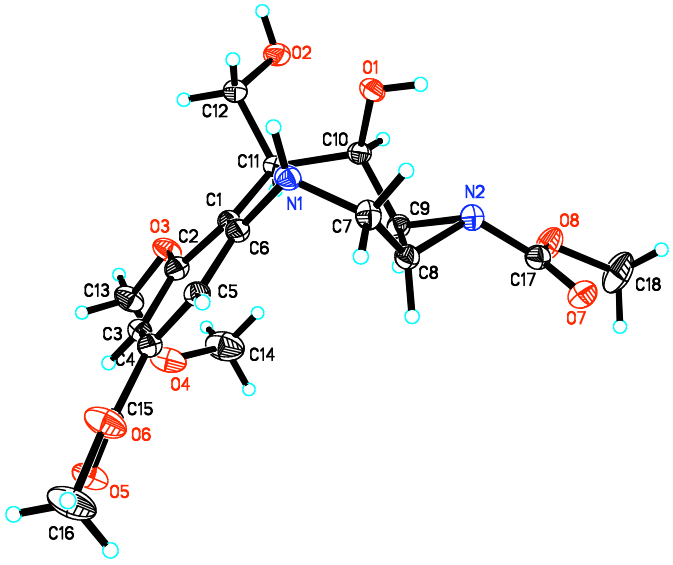


Table 1. Crystal data and structure refinement for rw105.

Identification code	rw105	
Empirical formula	C18 H24 N2 O8	
Formula weight	396.39	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 9.7860(10) Å	α= 90°.
	b = 10.0112(11) Å	β= 107.503(2)°.
	c = 10.4204(11) Å	γ = 90°.
Volume	973.62(18) $Å^3$	

Z	2
Density (calculated)	1.352 Mg/m^3
Absorption coefficient	0.107 mm^{-1}
F(000)	420
Crystal size	0.45 x 0.34 x 0.30 mm^3
Theta range for data collection	2.05 to 28.28°.
Index ranges	-12<=h<=13, -13<=k<=13, -13<=l<=13
Reflections collected	9293
Independent reflections	4516 [R(int) = 0.0183]
Completeness to theta = 28.28°	98.2 %
Absorption correction	multi-scan
Max. and min. transmission	0.9686 and 0.9534
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4516 / 1 / 253
Goodness-of-fit on F^2	1.041
Final R indices [I>2sigma(I)]	R1 = 0.0368, wR2 = 0.1030
R indices (all data)	R1 = 0.0374, wR2 = 0.1040)
Largest diff. peak and hole	0.544 and -0.440 $e.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for rw105. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	9826(1)	6226(1)	189(1)	19(1)
O(2)	7835(1)	5411(1)	1813(1)	23(1)
O(3)	10345(1)	7353(1)	5164(1)	22(1)
O(4)	12100(1)	6943(1)	7215(1)	32(1)
O(5)	14082(1)	11173(1)	6251(1)	29(1)
O(6)	13626(1)	12121(1)	4215(1)	32(1)
O(7)	14895(1)	5058(1)	447(1)	25(1)
O(8)	13556(1)	3602(1)	1213(1)	28(1)
N(1)	10989(1)	8702(1)	934(1)	18(1)
N(2)	12734(1)	5677(1)	713(1)	19(1)
C(1)	10768(1)	7917(1)	3125(1)	16(1)
C(2)	11012(1)	8200(2)	4506(1)	18(1)
C(3)	11883(1)	9256(2)	5137(1)	19(1)
C(4)	12441(1)	10105(1)	4355(1)	18(1)
C(5)	12110(1)	9928(1)	2971(1)	18(1)
C(6)	11278(1)	8831(1)	2357(1)	17(1)
C(7)	12226(2)	8208(1)	525(1)	20(1)
C(8)	12971(2)	7005(2)	1342(1)	18(1)
C(9)	12173(1)	5929(1)	1835(1)	17(1)
C(10)	10555(1)	5838(1)	1528(1)	17(1)
C(11)	10028(1)	6600(1)	2587(1)	16(1)
C(12)	8391(2)	6733(1)	2099(2)	20(1)
C(13)	10729(2)	7427(2)	6598(1)	25(1)
C(14)	12188(2)	5526(2)	7139(2)	43(1)
C(15)	13456(2)	11170(2)	5061(2)	20(1)
C(16)	14676(2)	13134(2)	4813(2)	39(1)
C(17)	13852(2)	4803(2)	801(1)	20(1)
C(18)	14565(2)	2565(2)	1163(2)	41(1)

Table 3. Bond lengths [Å] and angles [°] for rw105.

O(1)-C(10)	1.4170(15)
O(2)-C(12)	1.4278(17)
O(3)-C(2)	1.3734(17)
O(3)-C(13)	1.4284(16)
O(4)-C(13)	1.389(2)
O(4)-C(14)	1.425(2)
O(5)-C(15)	1.2068(18)
O(6)-C(15)	1.3406(19)
O(6)-C(16)	1.4453(19)
O(7)-C(17)	1.2124(18)
O(8)-C(17)	1.3370(18)
O(8)-C(18)	1.4440(19)
N(1)-C(6)	1.4297(16)
N(1)-C(7)	1.4841(18)
N(2)-C(17)	1.3821(18)
N(2)-C(9)	1.4552(17)
N(2)-C(8)	1.4695(18)
C(1)-C(6)	1.4026(19)
C(1)-C(2)	1.4140(18)
C(1)-C(11)	1.5271(18)
C(2)-C(3)	1.3924(19)
C(3)-C(4)	1.398(2)
C(4)-C(5)	1.3908(18)
C(4)-C(15)	1.4916(19)
C(5)-C(6)	1.4021(19)
C(7)-C(8)	1.5280(19)
C(8)-C(9)	1.5081(19)
C(9)-C(10)	1.5212(18)
C(10)-C(11)	1.5523(18)
C(11)-C(12)	1.5332(19)
C(2)-O(3)-C(13)	118.36(11)
C(13)-O(4)-C(14)	112.82(14)
C(15)-O(6)-C(16)	115.28(13)

C(17)-O(8)-C(18)	114.76(13)
C(6)-N(1)-C(7)	113.82(11)
C(17)-N(2)-C(9)	122.60(12)
C(17)-N(2)-C(8)	121.83(12)
C(9)-N(2)-C(8)	62.08(9)
C(6)-C(1)-C(2)	118.00(12)
C(6)-C(1)-C(11)	124.35(12)
C(2)-C(1)-C(11)	117.58(11)
O(3)-C(2)-C(3)	123.24(12)
O(3)-C(2)-C(1)	115.11(12)
C(3)-C(2)-C(1)	121.64(12)
C(2)-C(3)-C(4)	118.54(12)
C(5)-C(4)-C(3)	121.11(13)
C(5)-C(4)-C(15)	121.00(12)
C(3)-C(4)-C(15)	117.83(12)
C(4)-C(5)-C(6)	119.68(12)
C(1)-C(6)-C(5)	120.55(12)
C(1)-C(6)-N(1)	122.67(12)
C(5)-C(6)-N(1)	116.78(12)
N(1)-C(7)-C(8)	113.40(11)
N(2)-C(8)-C(9)	58.50(9)
N(2)-C(8)-C(7)	118.70(11)
C(9)-C(8)-C(7)	122.92(12)
N(2)-C(9)-C(8)	59.42(9)
N(2)-C(9)-C(10)	116.18(11)
C(8)-C(9)-C(10)	125.75(11)
O(1)-C(10)-C(9)	112.02(11)
O(1)-C(10)-C(11)	112.82(11)
C(9)-C(10)-C(11)	111.64(11)
C(1)-C(11)-C(12)	112.34(11)
C(1)-C(11)-C(10)	117.60(11)
C(12)-C(11)-C(10)	110.13(11)
O(2)-C(12)-C(11)	106.49(11)
O(4)-C(13)-O(3)	112.34(12)
O(5)-C(15)-O(6)	123.32(14)
O(5)-C(15)-C(4)	124.40(14)

O(6)-C(15)-C(4)	112.26(12)
O(7)-C(17)-O(8)	124.78(14)
O(7)-C(17)-N(2)	124.64(14)
O(8)-C(17)-N(2)	110.30(12)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for rw105. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

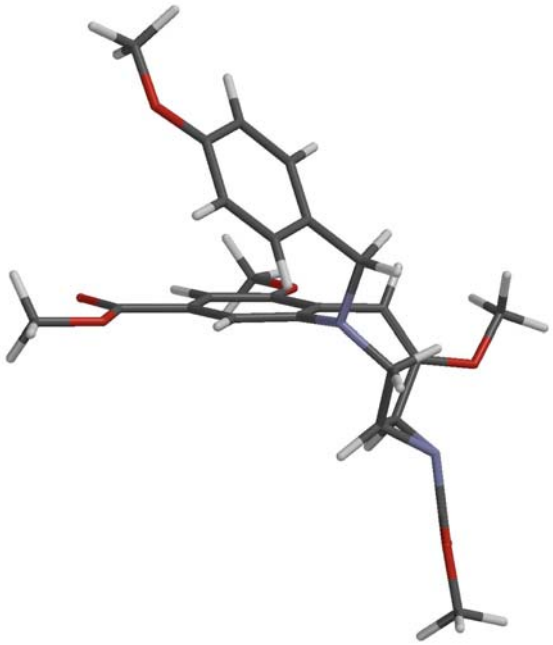
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	21(1)	19(1)	15(1)	-2(1)	2(1)	-1(1)
O(2)	18(1)	22(1)	26(1)	-3(1)	3(1)	-3(1)
O(3)	24(1)	27(1)	16(1)	-2(1)	7(1)	-9(1)
O(4)	33(1)	31(1)	26(1)	4(1)	-1(1)	-10(1)
O(5)	29(1)	33(1)	21(1)	-5(1)	3(1)	-11(1)
O(6)	38(1)	24(1)	28(1)	0(1)	1(1)	-14(1)
O(7)	19(1)	29(1)	28(1)	0(1)	8(1)	0(1)
O(8)	26(1)	20(1)	41(1)	5(1)	16(1)	6(1)
N(1)	19(1)	18(1)	15(1)	1(1)	2(1)	2(1)
N(2)	20(1)	18(1)	19(1)	-1(1)	7(1)	1(1)
C(1)	15(1)	15(1)	17(1)	-1(1)	3(1)	1(1)
C(2)	17(1)	20(1)	18(1)	1(1)	5(1)	1(1)
C(3)	18(1)	21(1)	17(1)	-3(1)	4(1)	-1(1)
C(4)	16(1)	18(1)	21(1)	-2(1)	3(1)	1(1)
C(5)	17(1)	16(1)	20(1)	1(1)	4(1)	-1(1)
C(6)	17(1)	17(1)	16(1)	0(1)	2(1)	2(1)
C(7)	25(1)	18(1)	16(1)	3(1)	8(1)	3(1)
C(8)	19(1)	18(1)	17(1)	0(1)	5(1)	1(1)
C(9)	17(1)	17(1)	17(1)	1(1)	5(1)	2(1)
C(10)	16(1)	17(1)	17(1)	-1(1)	3(1)	0(1)
C(11)	16(1)	17(1)	16(1)	-1(1)	3(1)	-2(1)
C(12)	17(1)	21(1)	21(1)	-3(1)	5(1)	-1(1)
C(13)	30(1)	32(1)	16(1)	-2(1)	9(1)	-9(1)
C(14)	45(1)	33(1)	42(1)	4(1)	-2(1)	-7(1)
C(15)	20(1)	19(1)	22(1)	-4(1)	5(1)	-1(1)
C(16)	45(1)	29(1)	35(1)	1(1)	1(1)	-21(1)
C(17)	19(1)	21(1)	19(1)	-1(1)	4(1)	1(1)
C(18)	37(1)	24(1)	66(1)	8(1)	25(1)	13(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for rw105.

	x	y	z	U(eq)
H(1A)	10140	5785	-347	28
H(2A)	6954	5449	1403	34
H(1B)	10154	8898	353	21
H(3A)	12092	9396	6078	22
H(5A)	12447	10547	2445	21
H(7A)	12930	8941	628	23
H(7B)	11889	7959	-438	23
H(8A)	13970	7175	1932	22
H(9A)	12731	5501	2701	21
H(10A)	10326	4873	1606	21
H(11A)	10239	5993	3385	20
H(12A)	8043	7148	2804	24
H(12B)	8086	7294	1280	24
H(13A)	10675	8369	6868	30
H(13B)	10033	6905	6912	30
H(14A)	13172	5238	7595	65
H(14B)	11918	5251	6193	65
H(14C)	11535	5115	7576	65
H(16A)	14723	13783	4123	58
H(16B)	15616	12715	5192	58
H(16C)	14400	13591	5529	58
H(18A)	14274	1724	1485	61
H(18B)	15522	2814	1736	61
H(18C)	14583	2453	234	61

Computational Studies of Various Hydroxymethylation Reaction Enol Ether Intermediates

Method: After several initial conformational searches (Monte Carlo conformer distribution, Spartan '04), the lowest energy orientations of certain functional groups like the aromatic ester, *N*-carbomethoxy group, the aromatic methyl ether, and the methyl group of the enol ether were consistently lower in energy in the spatial representations shown. It was assumed that a methyl ether could be substituted for a methoxymethyl ether or a benzyl ether on the aromatic ring and that a methyl enol ether could replace the enol or silyl enol ether intermediate without affecting the conformational profile. To further simplify computational assessment of equilibrium geometries, the orientations of these functional groups were frozen in their lowest energy positions. To establish the lowest energy conformation for the eight-membered ring, conformers were drawn that contained the two possible relationships of the nucleophilic *cis*-olefin. Another conformational search was performed to find variations in ring topology. Geometries of the resulting structures were optimized first by semi-emperical methods (AM1), and then by using Hartree-Fock (HF/6-31G*) theory. Because software limitations led to insurmountable problems when attempts were made to characterize stationary points, we could not calculate frequencies to determine the nature of the stationary point represented by each of the low-energy molecular geometries. Consequently, because the identification of the low-energy geometries was repeatable, we must reasonably conclude that they are minima, and that the global minimum structure is the lowest energy minimum found. Lastly, the HF/6-31G* geometries were analyzed at the HF/6-31G** level of theory to produce the energies shown. For each low-energy conformation of the intermediates in question, pertinent details from the Spartan output file, Cartesian coordinates, and energies are provided.

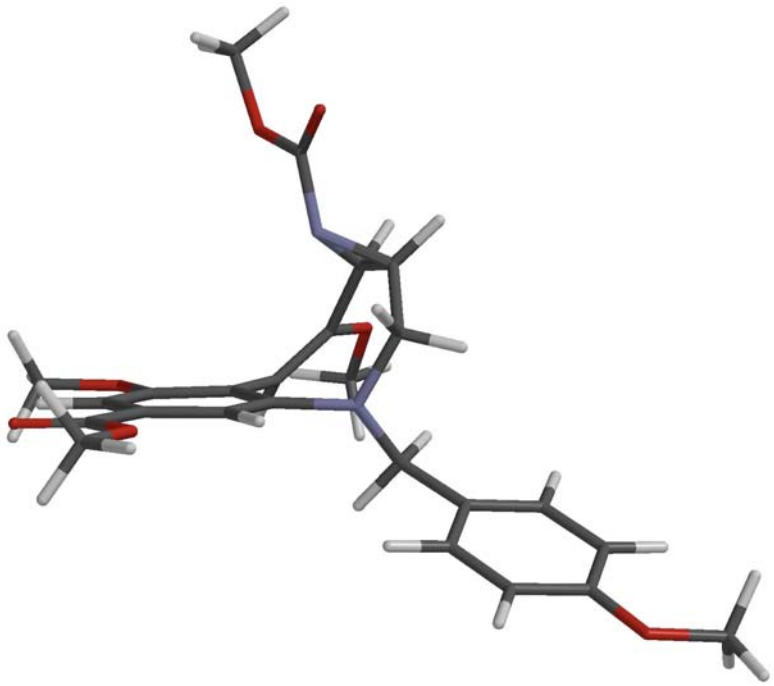


```
Spartan 'O4 Quantum Mechanics Module 124

Macintosh (OS-X ppc)
---------------------------------------------------------------
User input:
---------------------------------------------------------------
$molecule
READ
$end
$rem
EXCHANGE          HF
BASIS             6-31G**
VARTHRESH         0
SMALL_PROD_XCMAT  10
SYMMETRY          FALSE
SYM_IGNORE        TRUE
GUI                GUI_SPARTAN
TERSE_OUTPUT       TRUE
SCF_GUESS          READ
$end
---------------------------------------------------------------
Processing $rem in /Applications/Spartan 04/Spartan
04.app/Contents/MacOS/../SharedSupport//qchem/aux/../config/preferences.
   (Site specific preferences.)
  ... THRESH             9
  ... SCF_CONVERGENCE    7
  ... SMALL_PROD_XCMAT   9
  ... BASIS_LIN_DEP_THRESH     5
  ... ONEEXE_SPAR TRUE
  ... GUI              GUI_SPARTAN
  ... TERSE_OUTPUT     TRUE
Processing $rem in system registry
  ... MEM_TOTAL 768 # MB
Processing $rem in the input.
  ... EXCHANGE          HF
  ... BASIS             6-31G**
  ... VARTHRESH         0
  ... SMALL_PROD_XCMAT  10
  ... SYMMETRY          FALSE
  ... SYM_IGNORE        TRUE
  ... GUI                GUI_SPARTAN
  ... TERSE_OUTPUT       TRUE
  ... SCF_GUESS          READ

Total Memory Limit in MB = 768
Mega-Array Size in MB = 31
 -----------------------------------------------------
       Standard Nuclear Orientation (Angstroms)
    I     Atom         X            Y            Z
 -----------------------------------------------------
    1      C       1.519570      .443392     1.950407
    2      C       1.859990    -1.933279     -.131811
    3      C        .997101     -.758363     2.693328
    4      H       2.560611      .252965     1.711548
    5      H       1.503436     1.299400     2.619703
    6      C        .483445    -1.423120     -.390448
    7      C       1.422880    -2.119523     2.284686
```

8	H	.021278	-.665169	3.140130
9	N	1.996678	-1.487892	3.432088
10	H	.744528	-2.933084	2.480117
11	C	-2.159828	-.702023	-.922151
12	C	-.359937	-2.253011	-1.156907
13	C	-.020211	-.209243	.074209
14	C	-1.351646	.126547	-.177879
15	C	-1.662073	-1.898820	-1.427369
16	O	.205472	-3.399270	-1.596092
17	H	-1.725333	1.051564	.206755
18	H	-2.311977	-2.521249	-2.006661
19	C	-3.578122	-.361554	-1.227320
20	N	.740263	.787960	.766323
21	O	-4.290615	-1.035558	-1.905333
22	O	-3.974169	.769225	-.668184
23	C	-5.304184	1.180630	-.925736
24	H	-5.426250	2.117809	-.405169
25	H	-6.007048	.448718	-.553375
26	H	-5.459560	1.318488	-1.986225
27	C	-.550719	-4.301048	-2.354444
28	H	-.888065	-3.855065	-3.284044
29	H	-1.408609	-4.664482	-1.799037
30	H	.105697	-5.129387	-2.575600
31	C	1.783748	-1.986274	4.701337
32	O	1.786164	-3.139559	4.991508
33	O	1.616120	-1.000076	5.566366
34	C	1.465426	-1.370961	6.925263
35	H	1.339008	-.446622	7.466873
36	H	2.343983	-1.893520	7.275167
37	H	.598677	-2.003183	7.053706
38	C	2.284434	-2.289623	1.072699
39	O	3.466164	-2.844538	1.372069
40	H	2.457681	-2.134269	-1.000250
41	C	4.375141	-3.117191	.342295
42	H	4.668561	-2.208089	-.171958
43	H	3.957339	-3.816119	-.374054
44	H	5.240478	-3.557721	.813597
45	C	1.485881	1.691913	-.111103
46	H	2.065042	2.340716	.537263
47	C	.622037	2.553408	-1.004497
48	H	2.202533	1.140883	-.719682
49	C	-.958484	4.189105	-2.641059
50	C	-.186440	3.553529	-.459182
51	C	.618966	2.403909	-2.374470
52	C	-.161466	3.209855	-3.201402
53	C	-.965014	4.357593	-1.255618
54	H	-.205239	3.693408	.607566
55	H	1.229187	1.642312	-2.827936
56	H	-.132096	3.052629	-4.262296
57	H	-1.586632	5.126327	-.835672
58	O	-1.756614	5.026269	-3.336639
59	C	-1.813080	4.927314	-4.730292
60	H	-.843472	5.113517	-5.181109
61	H	-2.507423	5.686068	-5.058642
62	H	-2.174208	3.953427	-5.045354

Nuclear Repulsion Energy = 3650.5184544506 hartrees

```
There are      124 alpha and      124 beta electrons
Requested basis set is 6-31G(d,p)
There are 220 shells and 650 basis functions

A restricted Hartree-Fock SCF calculation will be
performed using Pulay DIIS extrapolation
SCF converges when DIIS error is below 1.0E-07
---------------------------------------
 Cycle       Energy         DIIS Error
---------------------------------------
   1   -1595.9125350766      1.22E-04
   2   -1595.9133938857      7.51E-05
   3   -1595.9136871467      2.44E-05
   4   -1595.9137563597      6.08E-06
   5   -1595.9137600114      2.44E-06
   6   -1595.9137608288      1.14E-06
   7   -1595.9137608989      4.77E-07
   8   -1595.9137610630      2.33E-07
   9   -1595.9137611661      6.93E-08 Convergence criterion met
---------------------------------------
```

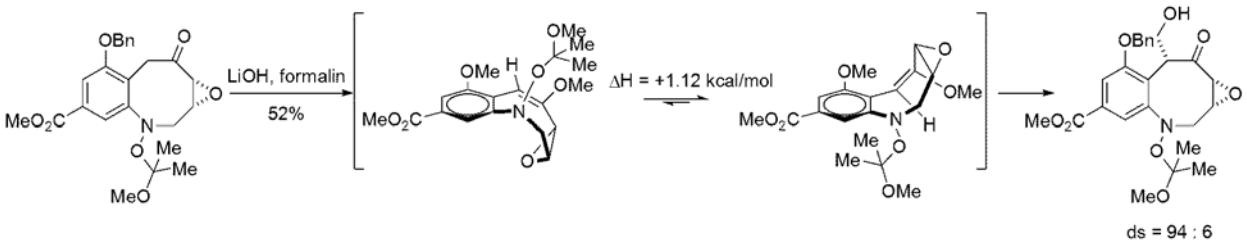


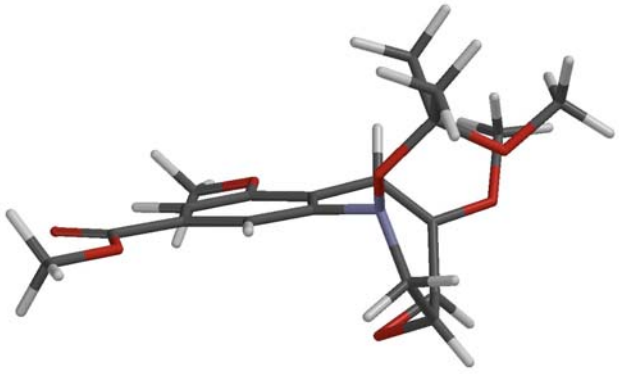
```
Spartan 'O4 Quantum Mechanics Module    124

Macintosh (OS-X ppc)
------------------------------------------------------------
User input:
------------------------------------------------------------
$molecule
READ
$end
$rem
EXCHANGE          HF
```

```
BASIS             6-31G**
VARTHRESH         0
SMALL_PROD_XCMAT  10
SYMMETRY          FALSE
SYM_IGNORE        TRUE
GUI                GUI_SPARTAN
TERSE_OUTPUT       TRUE
SCF_GUESS          READ
$end
---------------------------------------------------------------
Processing        $rem        in        /Applications/Spartan        04/Spartan
04.app/Contents/MacOS/../SharedSupport//qchem/aux/../config/preferences.
   (Site specific preferences.)
  ... THRESH             9
  ... SCF_CONVERGENCE    7
  ... SMALL_PROD_XCMAT   9
  ... BASIS_LIN_DEP_THRESH     5
  ... ONEEXE_SPAR TRUE
  ... GUI              GUI_SPARTAN
  ... TERSE_OUTPUT     TRUE
Processing $rem in system registry
  ... MEM_TOTAL 768 # MB
Processing $rem in the input.
  ... EXCHANGE          HF
  ... BASIS             6-31G**
  ... VARTHRESH         0
  ... SMALL_PROD_XCMAT  10
  ... SYMMETRY          FALSE
  ... SYM_IGNORE        TRUE
  ... GUI                GUI_SPARTAN
  ... TERSE_OUTPUT       TRUE
  ... SCF_GUESS          READ

Total Memory Limit in MB = 768
Mega-Array Size in MB = 31
 ----------------------------------------------------
       Standard Nuclear Orientation (Angstroms)
    I     Atom         X            Y            Z
 ----------------------------------------------------
    1      C       -.247123      .608781     1.566271
    2      C       -.551454     2.060146     1.235448
    3      H      -1.174648      .173801     1.924967
    4      H        .444344      .593420     2.399783
    5      C       -.403940      .263116    -1.790903
    6      C       -.155040     2.846752      .020302
    7      H       -.658984     2.666413     2.122580
    8      N      -1.487273     2.351729      .195888
    9      H       -.016749     3.897661      .209288
   10      C      -2.215515    -1.844099    -1.604048
   11      C      -1.192164     -.110266    -2.893961
   12      C       -.501102     -.477536     -.618106
   13      C      -1.417461    -1.523332     -.527850
   14      C      -2.096775    -1.144527    -2.801853
   15      O      -1.000571      .618670    -4.014935
   16      H      -1.482116    -2.077623      .386756
   17      H      -2.719497    -1.429207    -3.624512
   18      C      -3.210399    -2.952294    -1.551970
```

```
  19      N        .305761     -.222212      .524074
  20      O      -3.903264    -3.266846    -2.469493
  21      O      -3.252955    -3.560205     -.377152
  22      C      -4.179910    -4.621930     -.239813
  23      H      -3.961007    -5.410275     -.945416
  24      H      -5.187942    -4.268131     -.400992
  25      H      -4.066360    -4.981314      .771029
  26      C      -1.780541      .365553    -5.149610
  27      H      -2.835590      .510332    -4.944312
  28      H      -1.622625     -.639728    -5.525895
  29      H      -1.462783     1.077900    -5.896366
  30      C      -2.579496     3.169584      .392626
  31      O      -3.282096     3.133378     1.352989
  32      O      -2.768354     3.968649     -.641340
  33      C      -3.914043     4.800369     -.597801
  34      H      -3.896258     5.367794    -1.514956
  35      H      -3.872034     5.462851      .254679
  36      H      -4.812991     4.203712     -.543241
  37      C        .539265     1.389926    -1.956590
  38      C        .674164     2.439317    -1.159195
  39      H       1.160579     1.328841    -2.828671
  40      O       1.612968     3.402152    -1.321877
  41      C       2.537505     3.313906    -2.368849
  42      H       3.188418     4.169491    -2.267095
  43      H       2.043716     3.351173    -3.333527
  44      H       3.124164     2.404022    -2.300764
  45      C       1.754463     -.257932      .412121
  46      H       2.190513      .736510      .365812
  47      H       1.994845     -.742314     -.526480
  48      C       2.410456    -1.018594     1.550622
  49      C       3.671028    -2.450991     3.605237
  50      C       2.034904    -2.331059     1.850573
  51      C       3.419502     -.455063     2.302350
  52      C       4.056123    -1.154383     3.327596
  53      C       2.650300    -3.037912     2.854509
  54      H       1.246873    -2.795519     1.285684
  55      H       3.732964      .555146     2.100538
  56      H       4.833564     -.670291     3.886419
  57      H       2.363244    -4.047626     3.083232
  58      O       4.209693    -3.227202     4.569307
  59      C       5.227266    -2.714787     5.379807
  60      H       6.101506    -2.443607     4.796866
  61      H       5.491683    -3.503758     6.067905
  62      H       4.889253    -1.850530     5.942318
-----------------------------------------------------
Nuclear Repulsion Energy =  3632.5208644261 hartrees
There are      124 alpha and      124 beta electrons
Requested basis set is 6-31G(d,p)
There are 220 shells and 650 basis functions

A restricted Hartree-Fock SCF calculation will be
performed using Pulay DIIS extrapolation
SCF converges when DIIS error is below 1.0E-07
---------------------------------------
 Cycle       Energy         DIIS Error
---------------------------------------
   1   -1595.9136785930      1.23E-04
```

```
    2   -1595.9145616149      7.53E-05
    3   -1595.9148511866      2.43E-05
    4   -1595.9149212034      5.71E-06
    5   -1595.9149242595      2.28E-06
    6   -1595.9149248226      1.00E-06
    7   -1595.9149246506      4.13E-07
    8   -1595.9149245694      2.12E-07
    9   -1595.9149245540      7.20E-08 Convergence criterion met
 ---------------------------------------
```

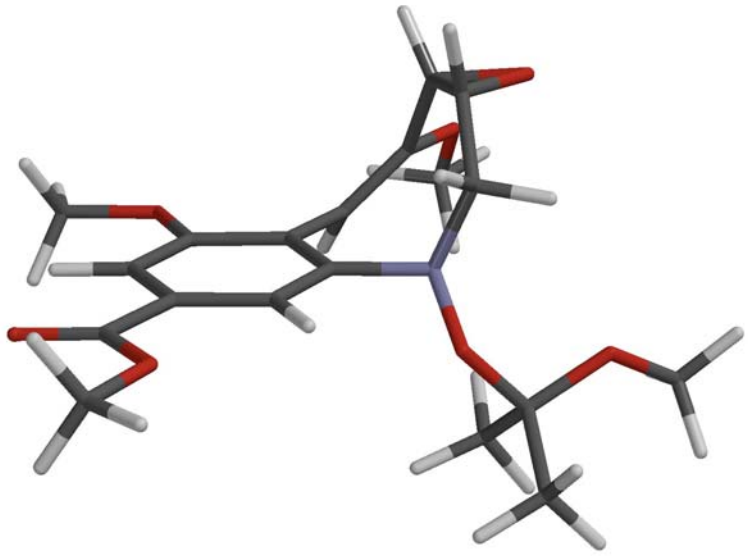




```
Spartan '04 Quantum Mechanics Module    124

Macintosh (OS-X ppc)
------------------------------------------------------------------
User input:
------------------------------------------------------------------
$molecule
READ
$end
$rem
EXCHANGE          HF
BASIS             6-31G**
SYMMETRY          FALSE
SYM_IGNORE        TRUE
MEM_STATIC        57
GUI                GUI_SPARTAN
TERSE_OUTPUT       TRUE
SCF_GUESS          READ
$end
```

```
---------------------------------------------------------------
Processing $rem in /Applications/Spartan 04/Spartan
04.app/Contents/MacOS/../SharedSupport//qchem/aux/../config/preferences.
   (Site specific preferences.)
  ... THRESH             9
  ... SCF_CONVERGENCE    7
  ... SMALL_PROD_XCMAT   9
  ... BASIS_LIN_DEP_THRESH     5
  ... ONEEXE_SPAR TRUE
  ... GUI              GUI_SPARTAN
  ... TERSE_OUTPUT     TRUE
Processing $rem in system registry
  ... MEM_TOTAL 1999 # MB
Processing $rem in the input.
  ... JOBTYPE    FREQ
  ... EXCHANGE          HF
  ... BASIS             6-31G**
  ... SYMMETRY          FALSE
  ... SYM_IGNORE        TRUE
  ... MEM_STATIC        57
  ... GUI                GUI_SPARTAN
  ... TERSE_OUTPUT       TRUE
  ... SCF_GUESS          READ

Total Memory Limit in MB = 1999
Mega-Array Size in MB = 57
 -----------------------------------------------------
       Standard Nuclear Orientation (Angstroms)
    I     Atom         X            Y            Z
 -----------------------------------------------------
    1      C        .203962     1.765994     1.693453
    2      C       1.174190    -1.666087      .974915
    3      C        .520401      .999696     2.951037
    4      H        .892498     2.594907     1.637083
    5      H       -.802134     2.173089     1.790582
    6      C       -.186435    -1.328731      .509699
    7      C       1.222598     -.272440     3.093825
    8      O       -.168397     -.185962     3.239599
    9      C      -2.740329     -.802137     -.468613
   10      C      -1.091222    -2.376829      .255540
   11      C       -.588373     -.030530      .239659
   12      C      -1.868772      .237933     -.241107
   13      C      -2.353763    -2.119734     -.224731
   14      O       -.619393    -3.617490      .503035
   15      H      -2.156699     1.246563     -.451511
   16      H      -3.057664    -2.902280     -.418639
   17      C      -4.120096     -.578457     -.984862
   18      N        .348916     1.032847      .444183
   19      O      -4.897434    -1.454864    -1.205477
   20      O      -4.404918      .699822    -1.177830
   21      C      -5.700206      .999614    -1.664159
   22      H      -5.738763     2.074143    -1.752977
   23      H      -6.454537      .652955     -.972759
   24      H      -5.860237      .537431    -2.627581
   25      C      -1.453976    -4.725863      .317208
   26      H      -1.763564    -4.822075     -.718232
   27      H      -2.332376    -4.669465      .950723
```

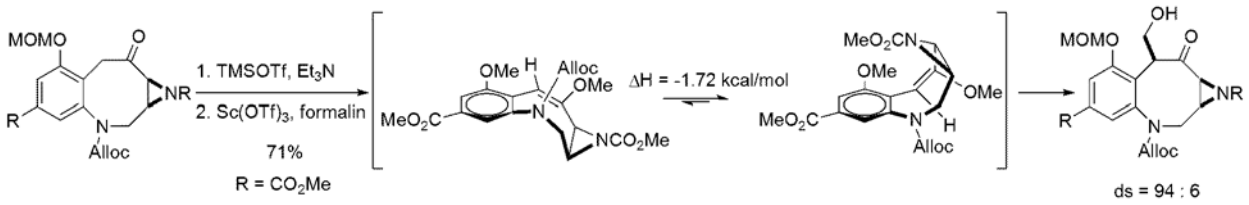
```
  28      H       -.870084    -5.590641      .595236
  29      C       1.794494    -1.147679     2.023987
  30      O       3.069800    -1.421191     2.379384
  31      H       1.678384    -2.408735      .387286
  32      C       3.861451    -2.237511     1.564800
  33      H       3.938995    -1.833270      .561226
  34      H       3.465717    -3.246018     1.515358
  35      H       4.840021    -2.260294     2.020950
  36      O        .164582     1.980313     -.568995
  37      H        .586626     1.664718     3.799670
  38      H       1.747517     -.427567     4.021441
  39      C       1.315231     2.221216    -1.328897
  40      O       2.233486     2.816206     -.452578
  41      C        .854324     3.226928    -2.377488
  42      C       1.844433      .936213    -1.957163
  43      C       3.566260     2.956521     -.842884
  44      H       4.047133     3.555523     -.082004
  45      H       3.667299     3.468909    -1.795417
  46      H       4.076710     2.001211     -.903128
  47      H       1.678449     3.528566    -3.013675
  48      H        .456866     4.103681    -1.881807
  49      H        .081863     2.794714    -3.002068
  50      H       2.633399     1.147322    -2.670114
  51      H       1.039620      .441751    -2.487243
  52      H       2.224146      .267062    -1.197939
----------------------------------------------------
Nuclear Repulsion Energy =  2733.4455745264 hartrees
There are      101 alpha and      101 beta electrons
Requested basis set is 6-31G(d,p)
There are 183 shells and 530 basis functions

A restricted Hartree-Fock SCF calculation will be
performed using Pulay DIIS extrapolation
SCF converges when DIIS error is below 1.0E-07
---------------------------------------
 Cycle       Energy         DIIS Error
---------------------------------------
   1   -1312.4288651131      5.05E-09
   2   -1312.4288652094      2.33E-08 Convergence criterion met
---------------------------------------
```

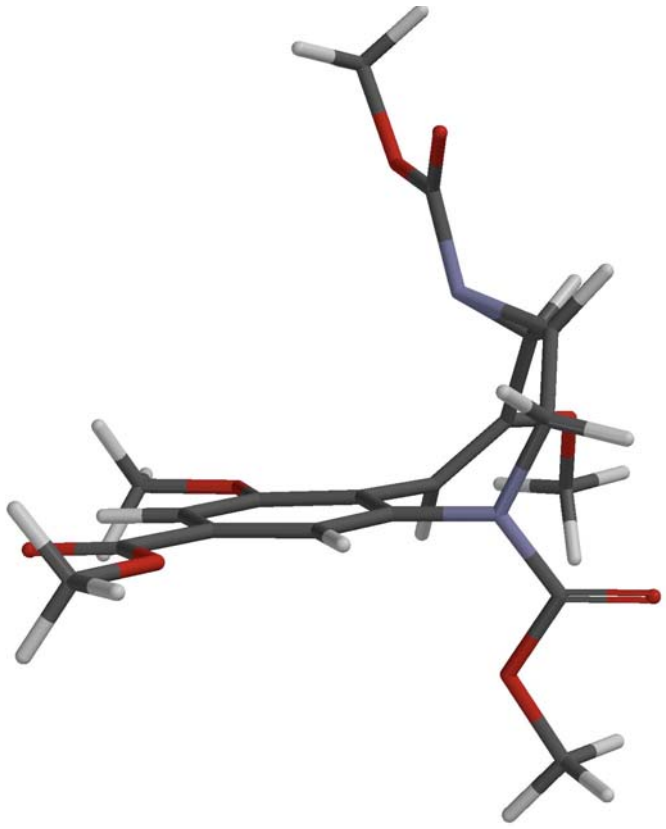


```
Spartan 'O4 Quantum Mechanics Module    124

Macintosh (OS-X ppc)
---------------------------------------------------------------
User input:
---------------------------------------------------------------
$molecule
READ
$end
$rem
EXCHANGE          HF
BASIS             6-31G**
VARTHRESH         0
SMALL_PROD_XCMAT  10
SYMMETRY          FALSE
SYM_IGNORE        TRUE
GUI                GUI_SPARTAN
TERSE_OUTPUT       TRUE
SCF_GUESS          READ
$end
---------------------------------------------------------------
Processing $rem in /Applications/Spartan 04/Spartan
04.app/Contents/MacOS/../SharedSupport//qchem/aux/../config/preferences.
   (Site specific preferences.)
  ... THRESH             9
  ... SCF_CONVERGENCE    7
  ... SMALL_PROD_XCMAT   9
  ... BASIS_LIN_DEP_THRESH     5
  ... ONEEXE_SPAR TRUE
  ... GUI              GUI_SPARTAN
  ... TERSE_OUTPUT     TRUE
Processing $rem in system registry
  ... MEM_TOTAL 768 # MB
Processing $rem in the input.
  ... EXCHANGE          HF
  ... BASIS             6-31G**
  ... VARTHRESH         0
```

```
  ... SMALL_PROD_XCMAT  10
  ... SYMMETRY          FALSE
  ... SYM_IGNORE        TRUE
  ... GUI                GUI_SPARTAN
  ... TERSE_OUTPUT       TRUE
  ... SCF_GUESS          READ

Total Memory Limit in MB = 768
Mega-Array Size in MB = 31
 ------------------------------------------------------
       Standard Nuclear Orientation (Angstroms)
    I     Atom         X            Y            Z
 ------------------------------------------------------
    1      C        .380969    -2.172458     -.949486
    2      C       1.209885    -1.837348    -2.169713
    3      H       1.029481    -2.640133     -.210933
    4      H       -.366159    -2.891086    -1.244786
    5      C        .897972     1.047391     -.405931
    6      C       1.218236     -.621859    -2.977087
    7      O        .546664    -1.771324    -3.406083
    8      C       1.866202      .566693     2.163069
    9      C       1.743234     1.977309      .234795
   10      C        .548989     -.105274      .278580
   11      C       1.037228     -.351530     1.563368
   12      C       2.225513     1.740766     1.499813
   13      O       2.018116     3.089855     -.478143
   14      H        .742574    -1.240289     2.080752
   15      H       2.870476     2.432674     2.000454
   16      C       2.414622      .360401     3.534108
   17      N       -.324782    -1.044603     -.356251
   18      O       3.136105     1.134476     4.082539
   19      O       2.021192     -.774668     4.088015
   20      C       2.495709    -1.048284     5.394237
   21      H       2.172649     -.281194     6.083083
   22      H       3.574850    -1.103690     5.401569
   23      H       2.070013    -2.001212     5.666975
   24      C       2.838091     4.082416      .073416
   25      H       3.831660     3.702147      .284815
   26      H       2.409582     4.492075      .981826
   27      H       2.906821     4.861552     -.670944
   28      C        .355258     1.392043    -1.736491
   29      C        .417201      .629156    -2.816429
   30      H       -.097573     2.362735    -1.800368
   31      O       -.092224      .946506    -4.021317
   32      C       -.838400     2.119801    -4.175015
   33      H      -1.181188     2.126488    -5.198754
   34      H       -.231014     3.000332    -3.993825
   35      H      -1.693609     2.130895    -3.507928
   36      O      -1.167238    -1.582771      .621857
   37      H       2.117660    -2.418835    -2.219315
   38      H       2.122207     -.426630    -3.535095
   39      C      -2.529077    -1.462429      .312767
   40      C      -3.233506    -2.052176     1.528854
   41      O      -2.736585    -2.274952     -.807029
   42      C      -2.913937     -.005727      .075893
   43      H      -4.307926    -2.059106     1.383868
   44      H      -3.011859    -1.471792     2.416695
```

```
  45      H      -2.895920    -3.069994     1.678928
  46      H      -3.989351      .104495     -.004442
  47      H      -2.451381      .372025     -.824729
  48      H      -2.579895      .590567      .916458
  49      C      -3.912526    -2.148167    -1.549033
  50      H      -4.802280    -2.247845     -.932988
  51      H      -3.904869    -2.951875    -2.271438
  52      H      -3.957897    -1.205547    -2.083180
-----------------------------------------------------
Nuclear Repulsion Energy =  2720.6612089095 hartrees
There are      101 alpha and      101 beta electrons
Requested basis set is 6-31G(d,p)
There are 183 shells and 530 basis functions

A restricted Hartree-Fock SCF calculation will be
performed using Pulay DIIS extrapolation
SCF converges when DIIS error is below 1.0E-07
---------------------------------------
 Cycle       Energy         DIIS Error
---------------------------------------
   1   -1312.4261554157      1.27E-04
   2   -1312.4268304166      7.43E-05
   3   -1312.4270275329      2.59E-05
   4   -1312.4270796194      6.04E-06
   5   -1312.4270822622      2.51E-06
   6   -1312.4270827999      1.06E-06
   7   -1312.4270828245      4.83E-07
   8   -1312.4270829969      2.17E-07
   9   -1312.4270831471      7.04E-08 Convergence criterion met
---------------------------------------
```

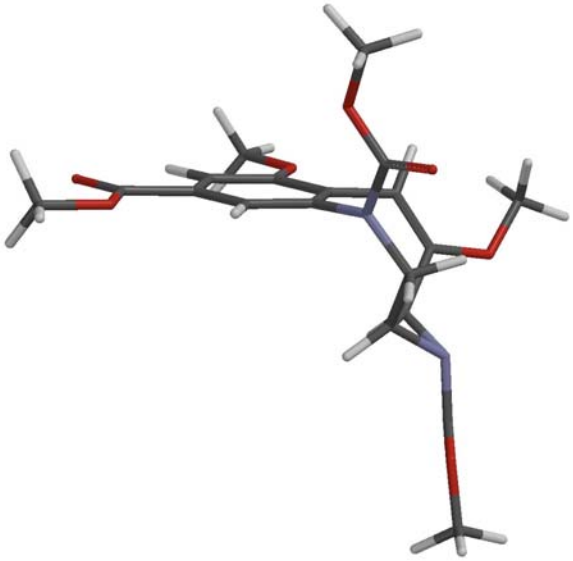




```
Spartan '04 Quantum Mechanics Module    124

Macintosh (OS-X ppc)
------------------------------------------------------------
User input:
------------------------------------------------------------
$molecule
READ
$end
$rem
EXCHANGE          HF
BASIS             6-31G**
VARTHRESH         0
SMALL_PROD_XCMAT  10
SYMMETRY          FALSE
SYM_IGNORE        TRUE
GUI                GUI_SPARTAN
TERSE_OUTPUT       TRUE
SCF_GUESS          READ
$end
------------------------------------------------------------
```

```
Processing $rem in /Applications/Spartan 04/Spartan
04.app/Contents/MacOS/../SharedSupport//qchem/aux/../config/preferences.
   (Site specific preferences.)
  ... THRESH             9
  ... SCF_CONVERGENCE    7
  ... SMALL_PROD_XCMAT   9
  ... BASIS_LIN_DEP_THRESH     5
  ... ONEEXE_SPAR TRUE
  ... GUI              GUI_SPARTAN
  ... TERSE_OUTPUT     TRUE
Processing $rem in system registry
  ... MEM_TOTAL 768 # MB
Processing $rem in the input.
  ... EXCHANGE          HF
  ... BASIS             6-31G**
  ... VARTHRESH         0
  ... SMALL_PROD_XCMAT  10
  ... SYMMETRY          FALSE
  ... SYM_IGNORE        TRUE
  ... GUI                GUI_SPARTAN
  ... TERSE_OUTPUT       TRUE
  ... SCF_GUESS          READ

Total Memory Limit in MB = 768
Mega-Array Size in MB = 31
 ----------------------------------------------------
       Standard Nuclear Orientation (Angstroms)
    I     Atom         X            Y            Z
 ----------------------------------------------------
    1      C        .735446      .289582     2.565496
    2      C        .328410     1.705294     2.221225
    3      H       -.130985     -.205687     2.990919
    4      H       1.504090      .325467     3.319545
    5      C        .335904     -.154720     -.764485
    6      C        .627348     2.470960      .969929
    7      H        .241717     2.322659     3.101887
    8      N       -.673268     1.926799     1.227880
    9      H        .733578     3.531589     1.119846
   10      C      -1.327743    -2.363938     -.409298
   11      C       -.525317     -.575489    -1.789678
   12      C        .364849     -.891168      .410047
   13      C       -.463294    -1.987044      .597408
   14      C      -1.355714    -1.661776    -1.610330
   15      O       -.474390      .150891    -2.925686
   16      H       -.416892    -2.535840     1.516784
   17      H      -2.031573    -1.987801    -2.373679
   18      C      -2.245974    -3.529290     -.271800
   19      N       1.245573     -.511255     1.467354
   20      C       2.577238     -.787594     1.431039
   21      O      -2.989073    -3.893344    -1.129162
   22      O      -2.155335    -4.125886      .905380
   23      C      -2.998087    -5.243667     1.122983
   24      H      -2.790771    -6.020520      .401478
   25      H      -4.036336    -4.954412     1.048619
   26      H      -2.775534    -5.588751     2.120496
   27      C      -1.326847     -.164128    -3.991108
   28      H      -2.368761     -.078662    -3.702058
```

```
  29      H      -1.139336    -1.163759    -4.368742
  30      H      -1.113316      .554980    -4.767654
  31      C      -1.791006     2.698730     1.466895
  32      O      -2.444213     2.641618     2.460236
  33      O      -2.063498     3.475029      .435464
  34      C      -3.242687     4.255665      .524013
  35      H      -3.286404     4.821310     -.393193
  36      H      -3.196056     4.920419     1.374142
  37      H      -4.110811     3.619190      .614423
  38      O       3.371320     -.408345     2.242452
  39      O       2.900967    -1.546898      .396965
  40      C       4.267179    -1.895074      .275447
  41      H       4.331852    -2.506273     -.611367
  42      H       4.597070    -2.452236     1.140001
  43      H       4.877509    -1.010152      .167379
  44      C       1.244748      .985405    -1.008214
  45      C       1.410972     2.051226     -.237205
  46      H       1.816103      .910593    -1.912734
  47      O       2.315310     3.026951     -.471152
  48      C       3.228307     2.901557    -1.524662
  49      H       3.877985     3.761603    -1.462395
  50      H       2.723551     2.901673    -2.484467
  51      H       3.816195     1.995522    -1.426661
----------------------------------------------------
Nuclear Repulsion Energy =  3005.3913879132 hartrees
There are      107 alpha and      107 beta electrons
Requested basis set is 6-31G(d,p)
There are 182 shells and 545 basis functions

A restricted Hartree-Fock SCF calculation will be
performed using Pulay DIIS extrapolation
SCF converges when DIIS error is below 1.0E-07
---------------------------------------
 Cycle       Energy         DIIS Error
---------------------------------------
   1   -1440.1139369126      1.69E-04
   2   -1440.1148716936      1.16E-04
   3   -1440.1153210753      2.97E-05
   4   -1440.1153986580      8.16E-06
   5   -1440.1154025122      2.88E-06
   6   -1440.1154031677      1.39E-06
   7   -1440.1154030811      6.09E-07
   8   -1440.1154030718      3.15E-07
   9   -1440.1154031169      9.70E-08 Convergence criterion met
---------------------------------------
```



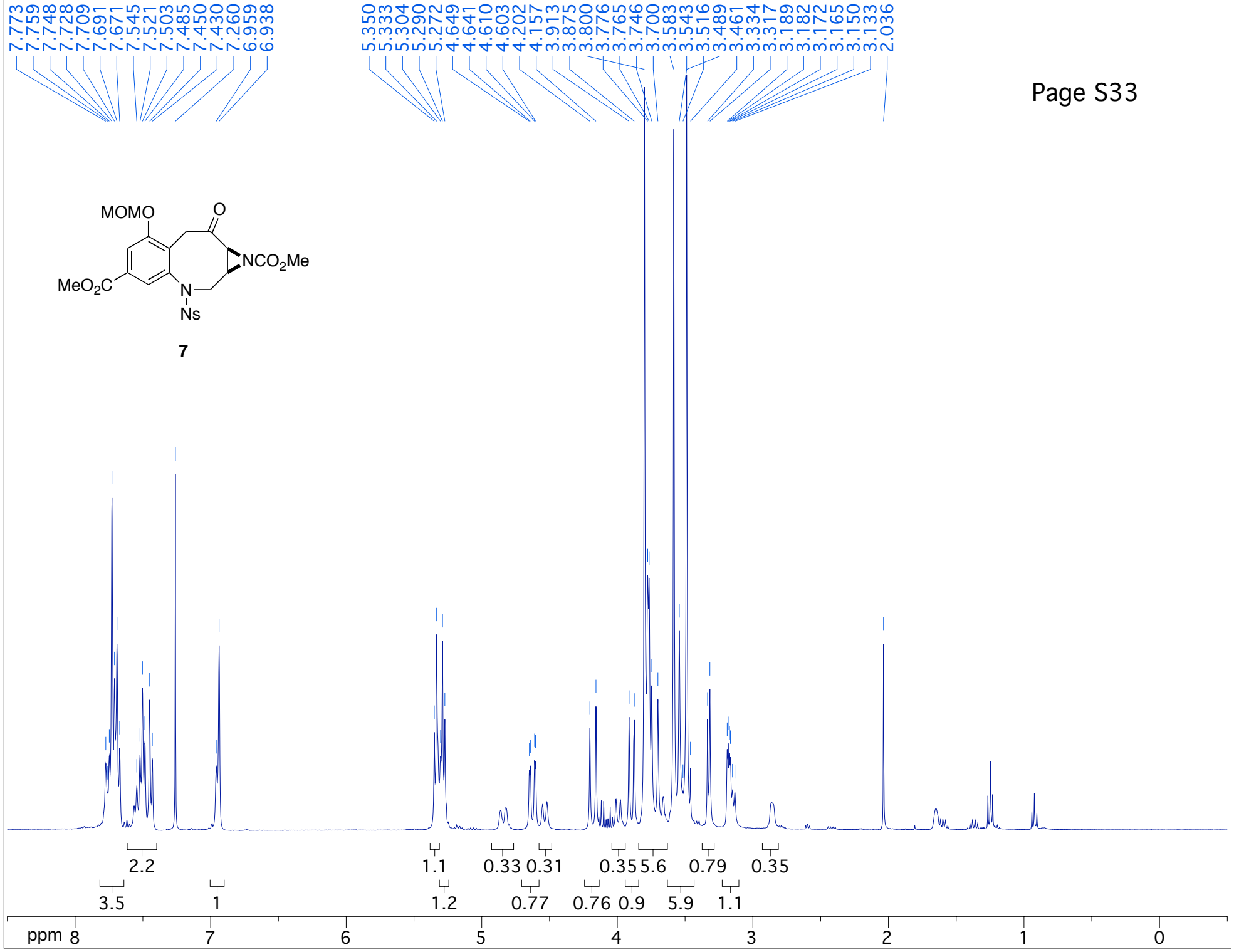
```
Spartan '04 Quantum Mechanics Module    124

Macintosh (OS-X ppc)
---------------------------------------------------------------
User input:
---------------------------------------------------------------
$molecule
READ
$end
$rem
EXCHANGE          HF
BASIS             6-31G**
SYMMETRY          FALSE
SYM_IGNORE        TRUE
GUI                GUI_SPARTAN
TERSE_OUTPUT       TRUE
SCF_GUESS          READ
$end
---------------------------------------------------------------
Processing $rem in /Applications/Spartan 04/Spartan
04.app/Contents/MacOS/../SharedSupport//qchem/aux/../config/preferences.
   (Site specific preferences.)
  ... THRESH             9
  ... SCF_CONVERGENCE    7
  ... SMALL_PROD_XCMAT   9
  ... BASIS_LIN_DEP_THRESH     5
  ... ONEEXE_SPAR TRUE
  ... GUI              GUI_SPARTAN
  ... TERSE_OUTPUT     TRUE
Processing $rem in system registry
  ... MEM_TOTAL 768 # MB
Processing $rem in the input.
  ... EXCHANGE          HF
  ... BASIS             6-31G**
  ... SYMMETRY          FALSE
  ... SYM_IGNORE        TRUE
  ... GUI                GUI_SPARTAN
  ... TERSE_OUTPUT       TRUE
```

```
  ... SCF_GUESS          READ

Total Memory Limit in MB = 768
Mega-Array Size in MB = 31
 -----------------------------------------------------
       Standard Nuclear Orientation (Angstroms)
    I     Atom         X            Y            Z
 -----------------------------------------------------
    1      C       1.011897     1.936923      .501896
    2      C       1.702635    -1.166221     -.400079
    3      C        .707009     1.061170     1.693187
    4      H       2.082999     1.987791      .378551
    5      H        .663441     2.943125      .696052
    6      C        .257928     -.994027     -.711900
    7      C       1.353681     -.265062     1.858768
    8      H       -.268861     1.173691     2.134432
    9      N       1.814912      .868141     2.592155
   10      H        .807789    -1.001594     2.424721
   11      C      -2.474475     -.791092    -1.239312
   12      C       -.531365    -2.145773     -.888336
   13      C       -.352907      .246085     -.838548
   14      C      -1.718902      .349007    -1.081052
   15      C      -1.880438    -2.047115    -1.150636
   16      O        .126669    -3.317681     -.781430
   17      H      -2.166110     1.318849    -1.162805
   18      H      -2.496375    -2.912605    -1.281841
   19      C      -3.939185     -.740297    -1.513786
   20      N        .403347     1.454028     -.743852
   21      C        .717640     2.180988    -1.849239
   22      O      -4.616307    -1.707351    -1.673616
   23      O      -4.416653      .492089    -1.561312
   24      C      -5.802411      .632406    -1.822807
   25      H      -5.995711     1.693613    -1.816250
   26      H      -6.383920      .139289    -1.057660
   27      H      -6.049559      .211542    -2.786584
   28      C       -.566766    -4.523835     -.948352
   29      H      -1.004197    -4.596346    -1.938417
   30      H      -1.344975    -4.639568     -.201631
   31      H        .164593    -5.307936     -.823673
   32      C       1.694741      .929953     3.966572
   33      O       1.908971      .026706     4.709311
   34      O       1.347857     2.146460     4.348008
   35      C       1.271080     2.373868     5.744639
   36      H       1.021173     3.417198     5.856082
   37      H       2.219391     2.161220     6.215544
   38      H        .504323     1.754790     6.187957
   39      O       1.367721     3.185158    -1.814307
   40      O        .230258     1.664596    -2.966691
   41      C        .512932     2.371386    -4.160895
   42      H        .103476     3.370056    -4.118571
   43      H        .041846     1.805657    -4.949670
   44      H       1.579101     2.429481    -4.324958
   45      C       2.217175     -.834934      .776539
   46      O       3.482872    -1.000953     1.174281
   47      H       2.294280    -1.666409    -1.142735
   48      C       4.410425    -1.560346      .285111
   49      H       4.502107     -.957934     -.612202
```

```
  50      H       4.129673    -2.572239      .013705
  51      H       5.355174    -1.575948      .806640
---------------------------------------------------
Nuclear Repulsion Energy =  2939.5878152767 hartrees
There are      107 alpha and      107 beta electrons
Requested basis set is 6-31G(d,p)
There are 182 shells and 545 basis functions

A restricted Hartree-Fock SCF calculation will be
performed using Pulay DIIS extrapolation
SCF converges when DIIS error is below 1.0E-07
---------------------------------------
 Cycle       Energy         DIIS Error
---------------------------------------
   1   -1440.1112223065      1.65E-04
   2   -1440.1121394800      1.13E-04
   3   -1440.1125680347      2.98E-05
   4   -1440.1126448367      8.08E-06
   5   -1440.1126486964      2.84E-06
   6   -1440.1126495991      1.38E-06
   7   -1440.1126497183      6.20E-07
   8   -1440.1126498120      3.15E-07
   9   -1440.1126497710      9.16E-08 Convergence criterion met
---------------------------------------
```

References:

1. Pangborn, A. B.; Giardello, M. H.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996,** 15, 1518-1520.
2. Ducept, P.; Gubler, D. A.; Williams, R. M. *Heterocycles* **2006,** 67, 597-619.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7.503
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7.430
7.260
6.959
6.938
5.350
5.333
5.304
5.290
5.272
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4.641
4.610
4.603
4.202
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3.800
3.776
3.765
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3.150
3.133
2.036
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NCO2Me
MeO2C
N
Ns
7
2.2
1.1
0.33
0.31
0.35
5.6
0.79
0.35
3.5
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1.2
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0.76
0.9
5.9
1.1
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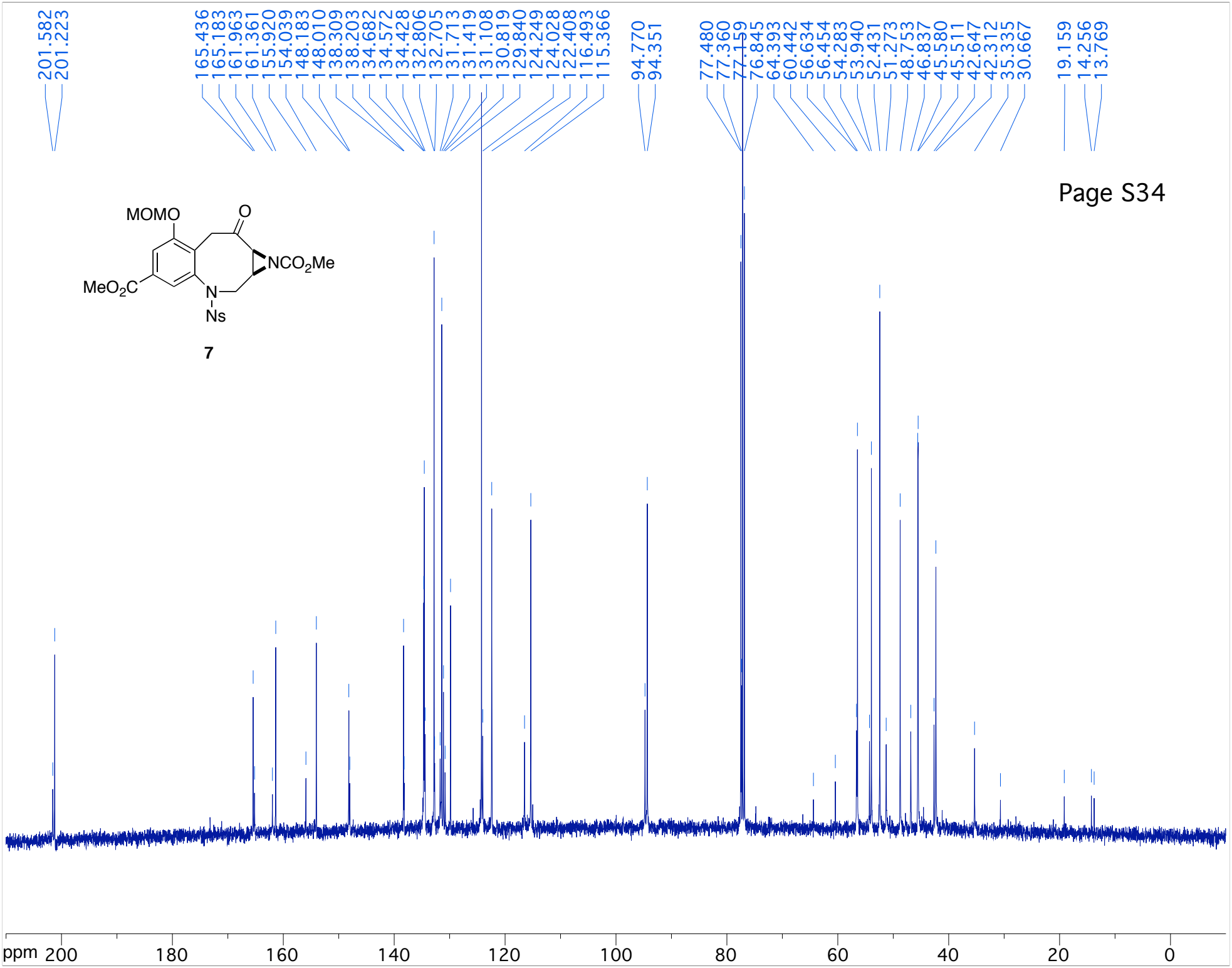
8
7
6
5
4
3
2
1
0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124.249
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42.647
42.312
35.335
30.667
19.159
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13.769
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MeO2C
N
Ns
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Page S34
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120
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60
40
20
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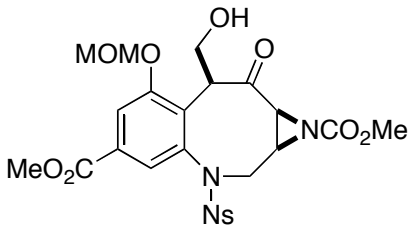
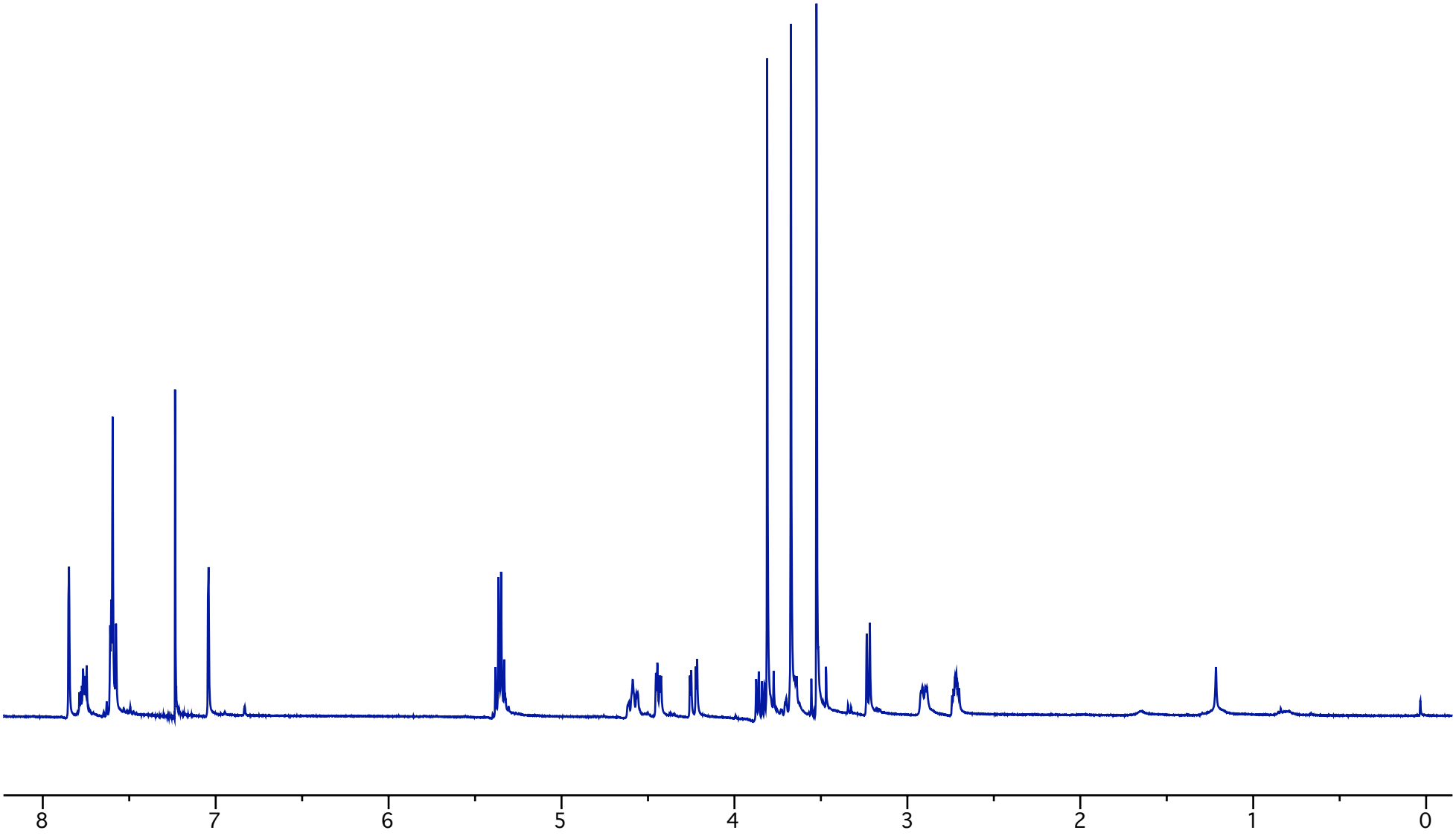


8, α:β = 9:91



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162.167
156.613
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137.805
135.143
132.741
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129.845
124.251
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94.955
61.777
57.115
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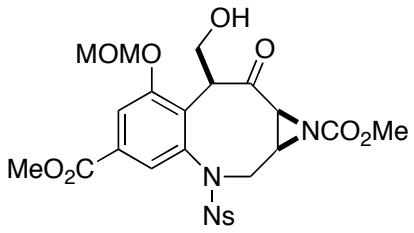
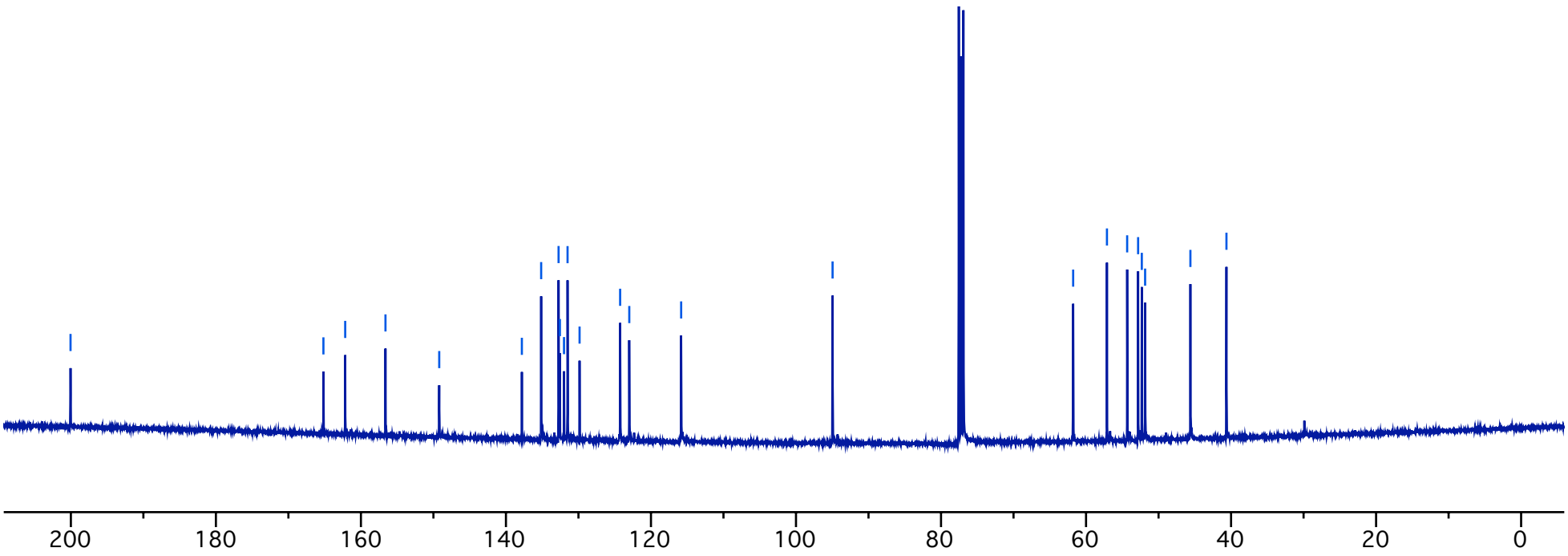
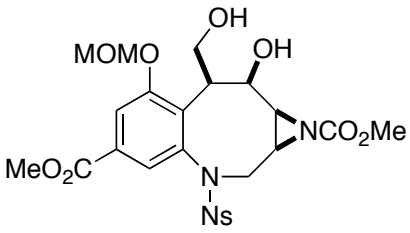
52.818
52.309
51.852
45.608
40.636



8, α:β = 9:91





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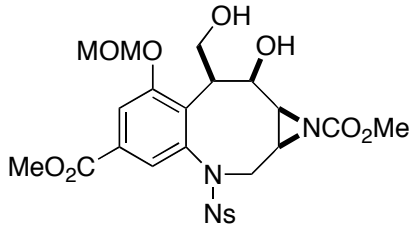
1 1.6 0.71 0.40 0.49 2 1.1 3.4 0.32 0.39 0.48 0.74 0.64

5.8 1.1 0.91 0.46 0.85 0.9 0.55 3.4 3.4 0.29 0.77 0.21 0.74 0.36

ppm 8 7 6 5 4 3 2 1 0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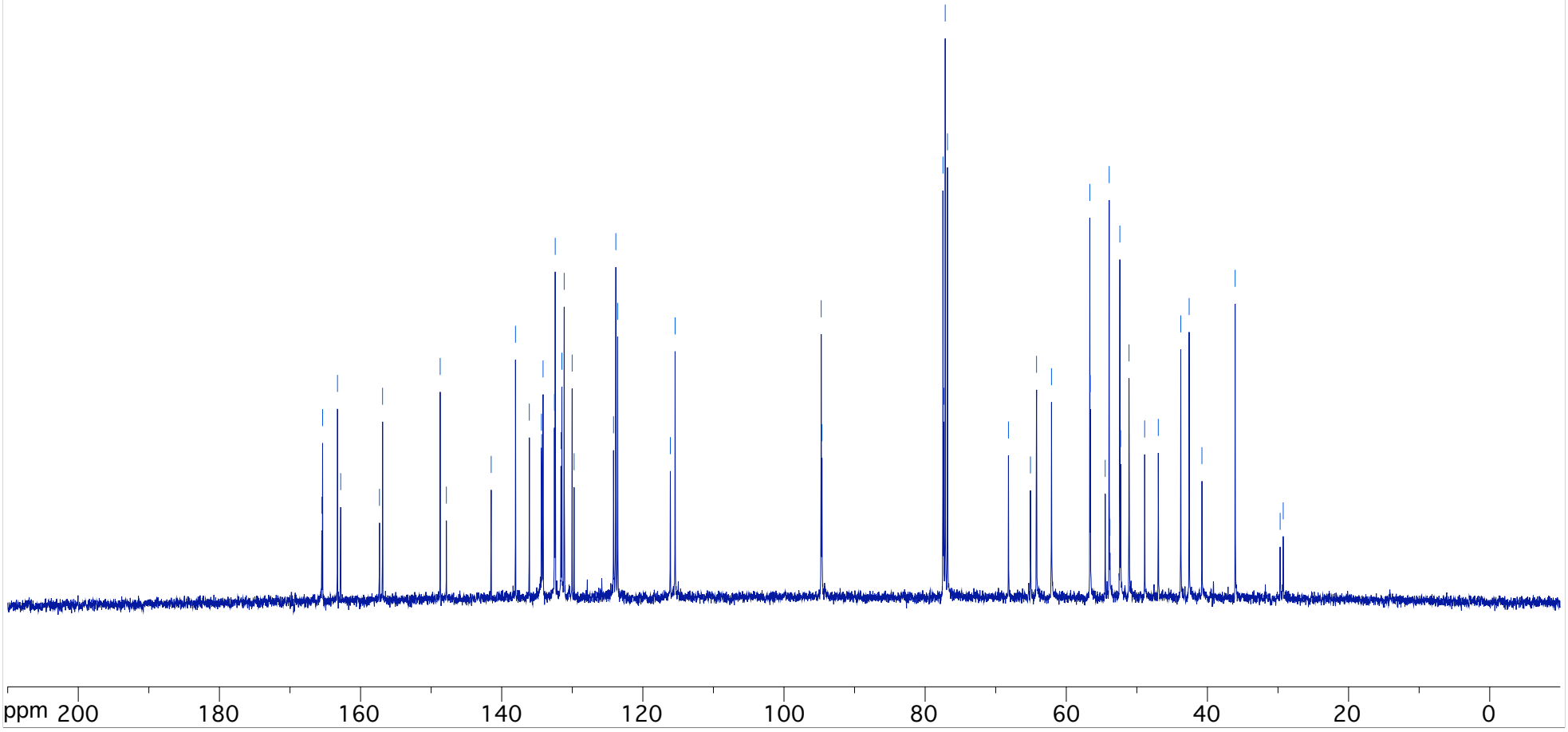
MOMO
OH
NCO2Me
MeO2C
N
Ns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147.841
141.490
138.048
136.087
134.369
134.334
134.142
132.530
132.418
131.595
131.472
131.147
130.019
129.745
124.156
123.827
123.570
116.106
115.429
94.728
94.615
77.474
77.355
77.154
76.838
68.194
65.078
64.214
62.096
56.669
56.597
54.486
53.919
53.812
52.407
52.291
51.110
48.894
46.963
43.780
42.589
40.779
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29.694
29.259
ppm
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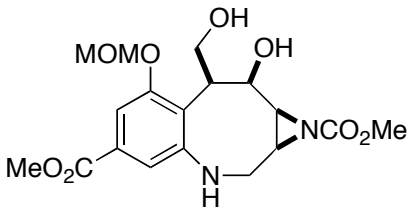
140
120
100
80
60
40
20
0


OH
MOMO
OH
NCO2Me
MeO2C
N
H

9

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7.542
7.258
5.272
4.833
4.039
3.904
3.812
3.800
3.776
3.686
3.622
3.605
3.589
3.572
3.515
3.494
2.551
2.540
2.368
1
1
2.2
1
1.3
3.4
2.5
3.6
1.4
4.7
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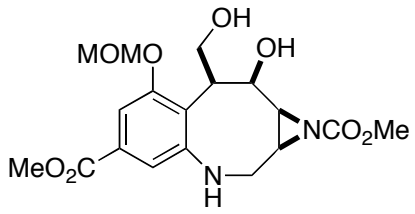
1.1
ppm
8
7
6
5
4
3
2
1
0


OH
MOMO
OH
NCO2Me
MeO2C
N
H

9

166.260
163.821
156.024
146.073
131.426
130.444
121.923
111.543
94.624
77.468
77.155
76.832
64.651
64.606
63.450
56.525
53.680
52.329
52.205
52.106
50.080
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37.057
29.671
ppm
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140
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100
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60
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20
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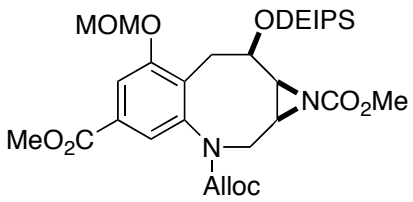
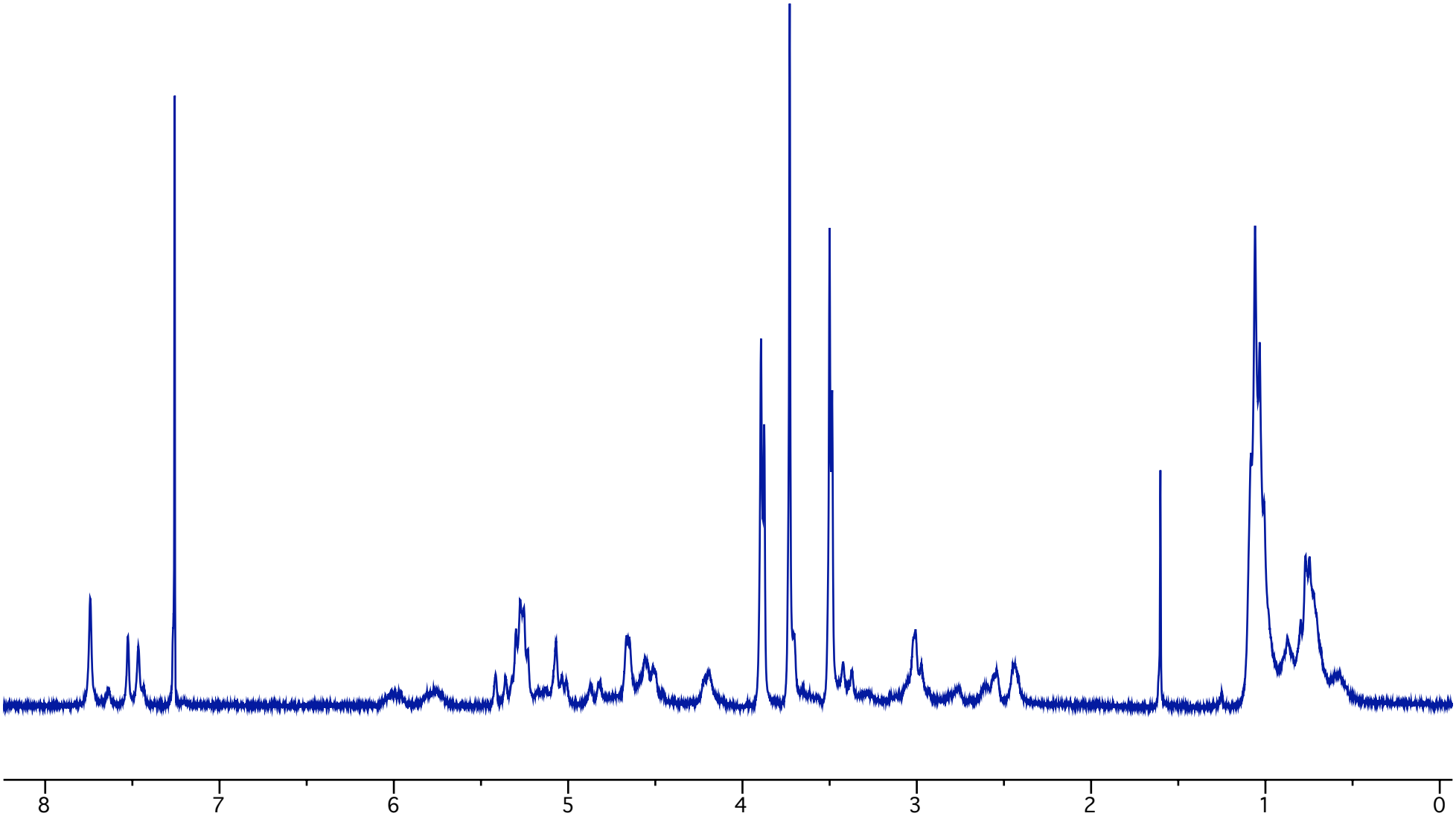
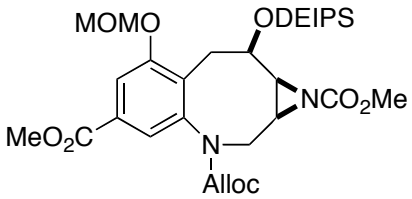

MOMO
ODEIPS
NCO2Me
MeO2C
N
Alloc


8
7
6
5
4
3
2
1
0


MOMO
ODEIPS
NCO2Me
MeO2C
N
Alloc

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132.796
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130.624
123.403
123.182
122.783
122.506
117.096
113.712
94.612
70.394
66.875
66.402
56.467
53.681
52.368
48.643
47.430
40.621
29.666
29.554
29.446
17.413
12.903
7.224
3.791
3.655
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140
120
100
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60
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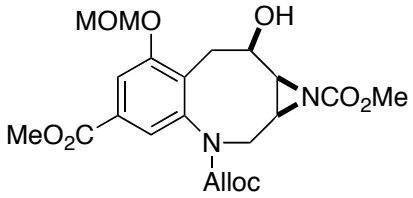
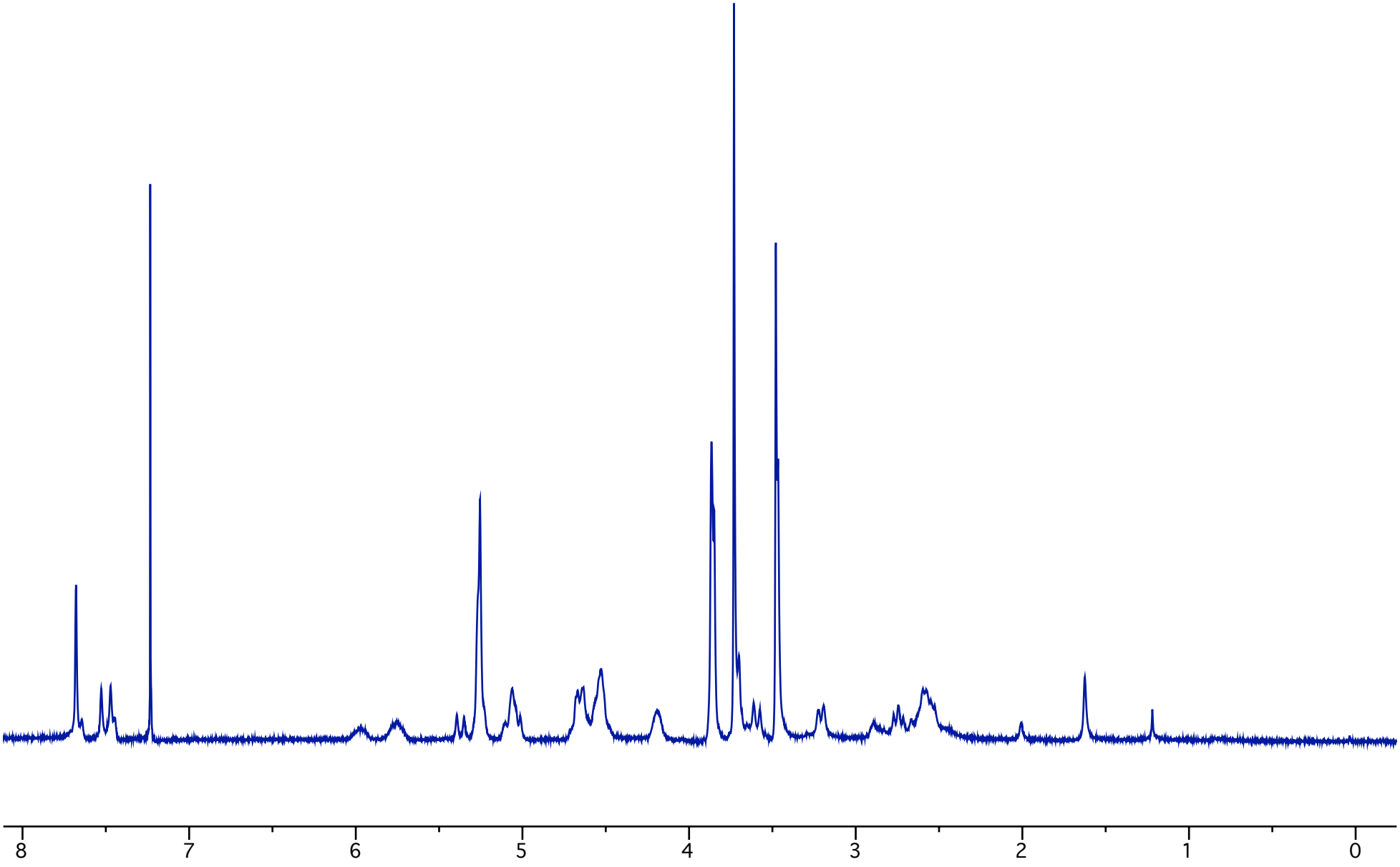
20
0


MOMO
OH
NCO2Me
MeO2C
N
Alloc


8
7
6
5
4
3
2
1
0

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155.570
155.067
154.831
141.874
132.630
131.277
130.551
123.307
122.908
117.299
113.772
94.613
69.087
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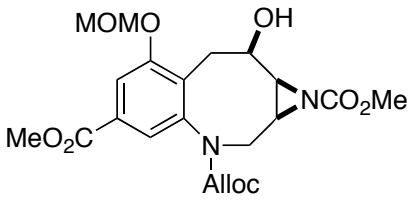
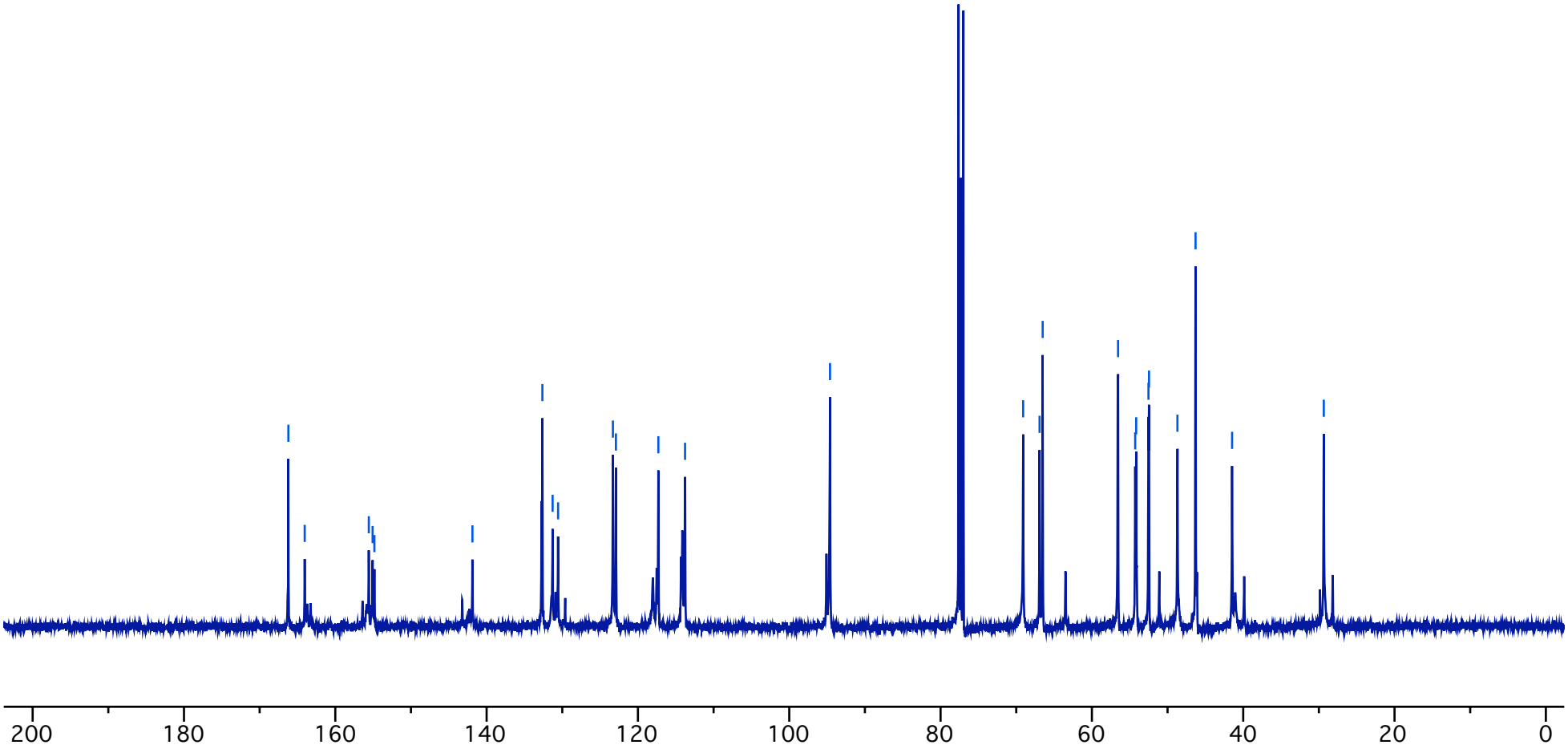
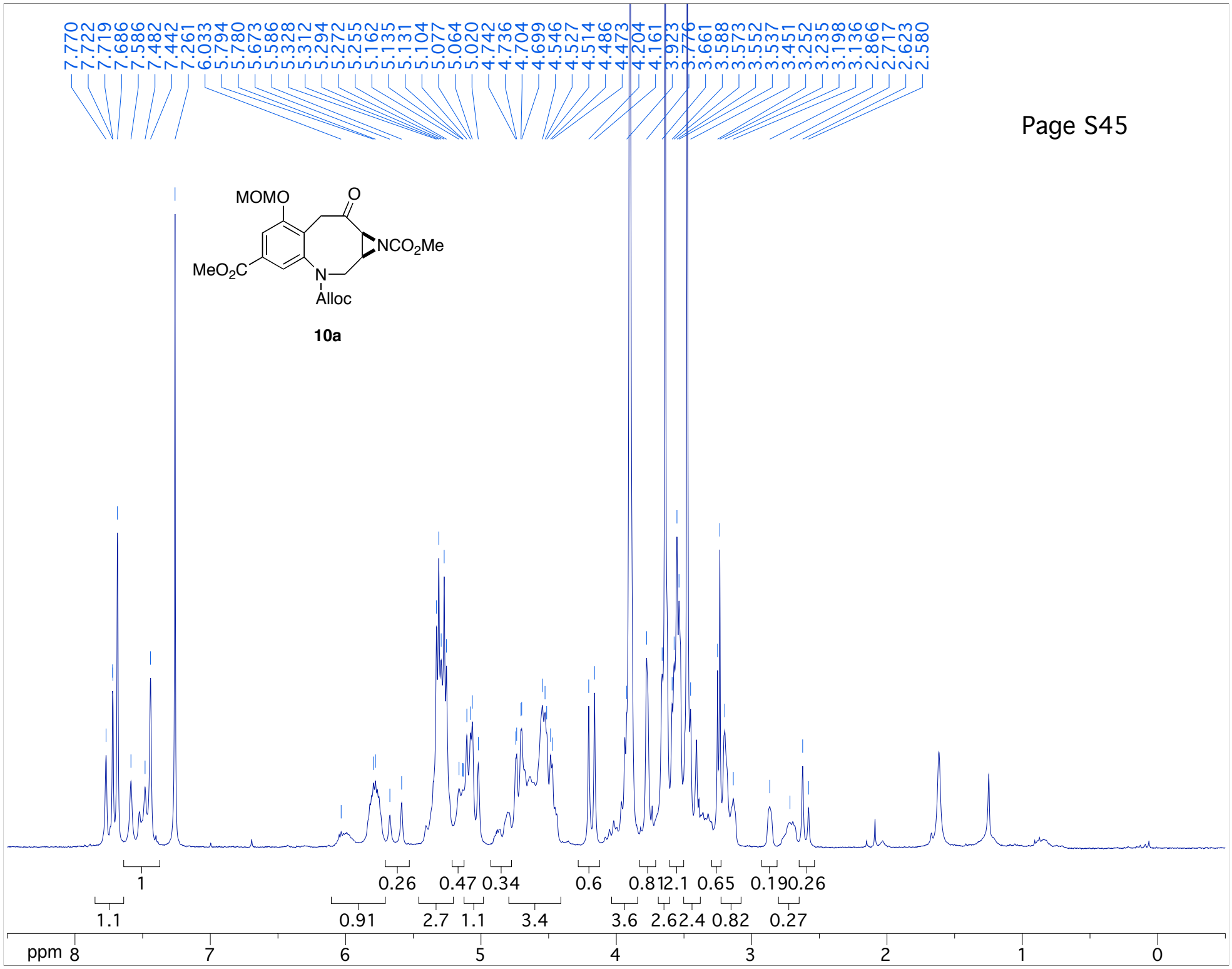
66.504
56.540
54.276
54.146
52.522
52.451
48.694
46.298
41.469
29.349



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5.780
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5.586
5.328
5.312
5.294
5.272
5.255
5.162
5.135
5.131
5.104
5.077
5.064
5.020
4.742
4.736
4.704
4.699
4.546
4.527
4.514
4.486
4.473
4.204
4.161
3.923
3.776
3.661
3.588
3.573
3.552
3.537
3.451
3.252
3.235
3.198
3.136
2.866
2.717
2.623
2.580
MOMO
O
NCO2Me
MeO2C
N
Alloc
10a
1
0.26
0.47
0.34
0.6
0.8
12.1
0.65
0.19
0.26
1.1
0.91
2.7
1.1
3.4
3.6
2.6
2.4
0.82
0.27
ppm
8
7
6
5
4
3
2
1
0

200.046
165.171
162.167
156.613
149.200
137.805
135.143
132.741
132.558
131.992
131.502
129.845
124.251
122.990
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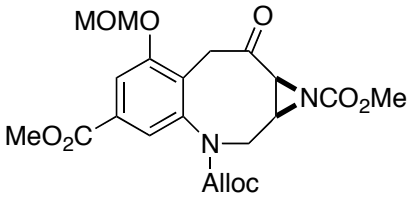
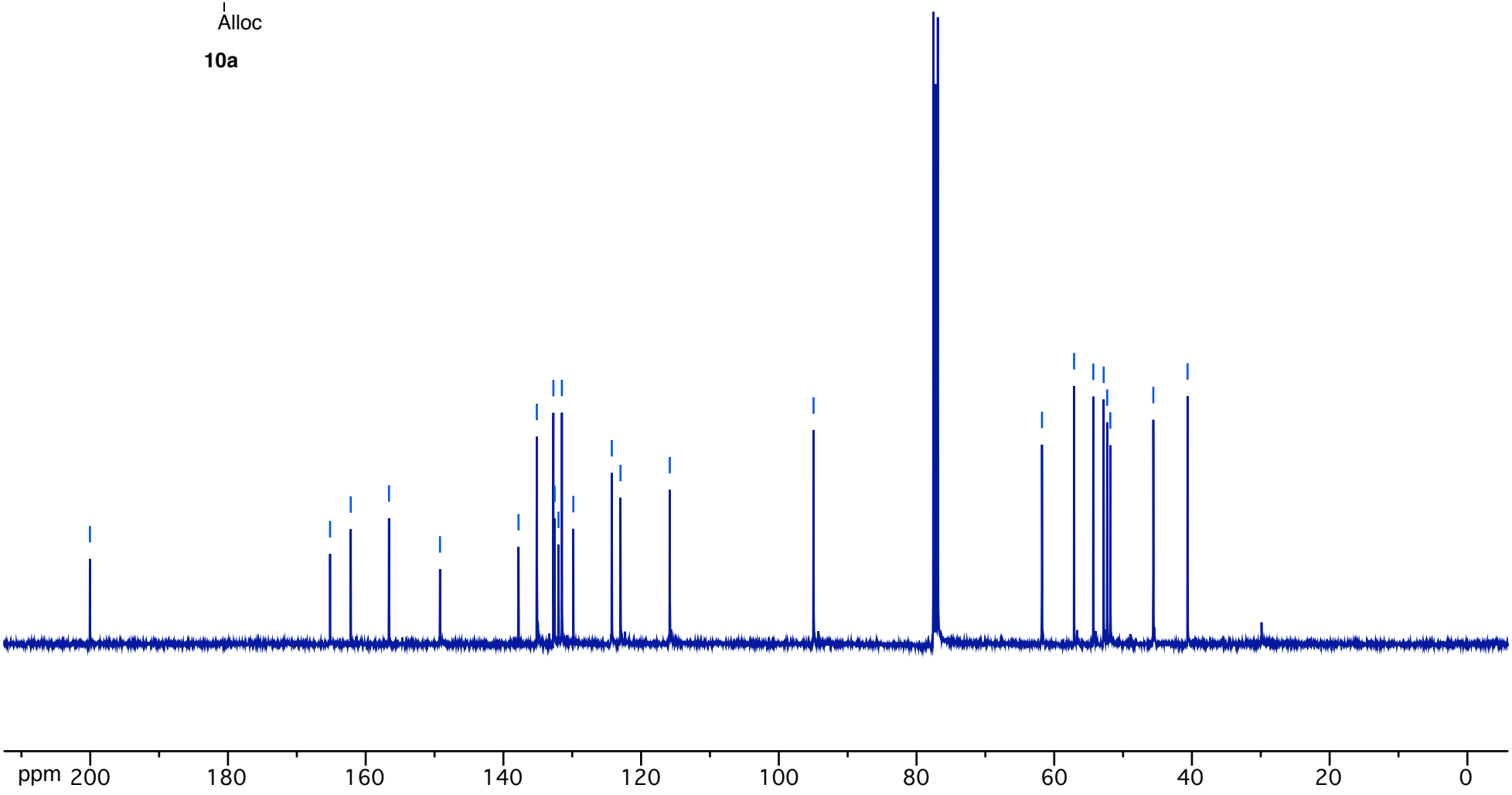
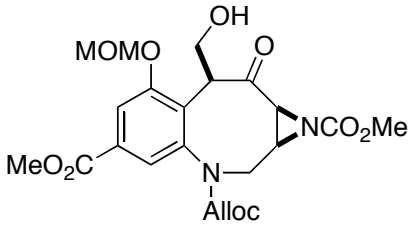
94.955
61.777
57.115
54.329
52.818
52.309
51.852
45.608
40.636

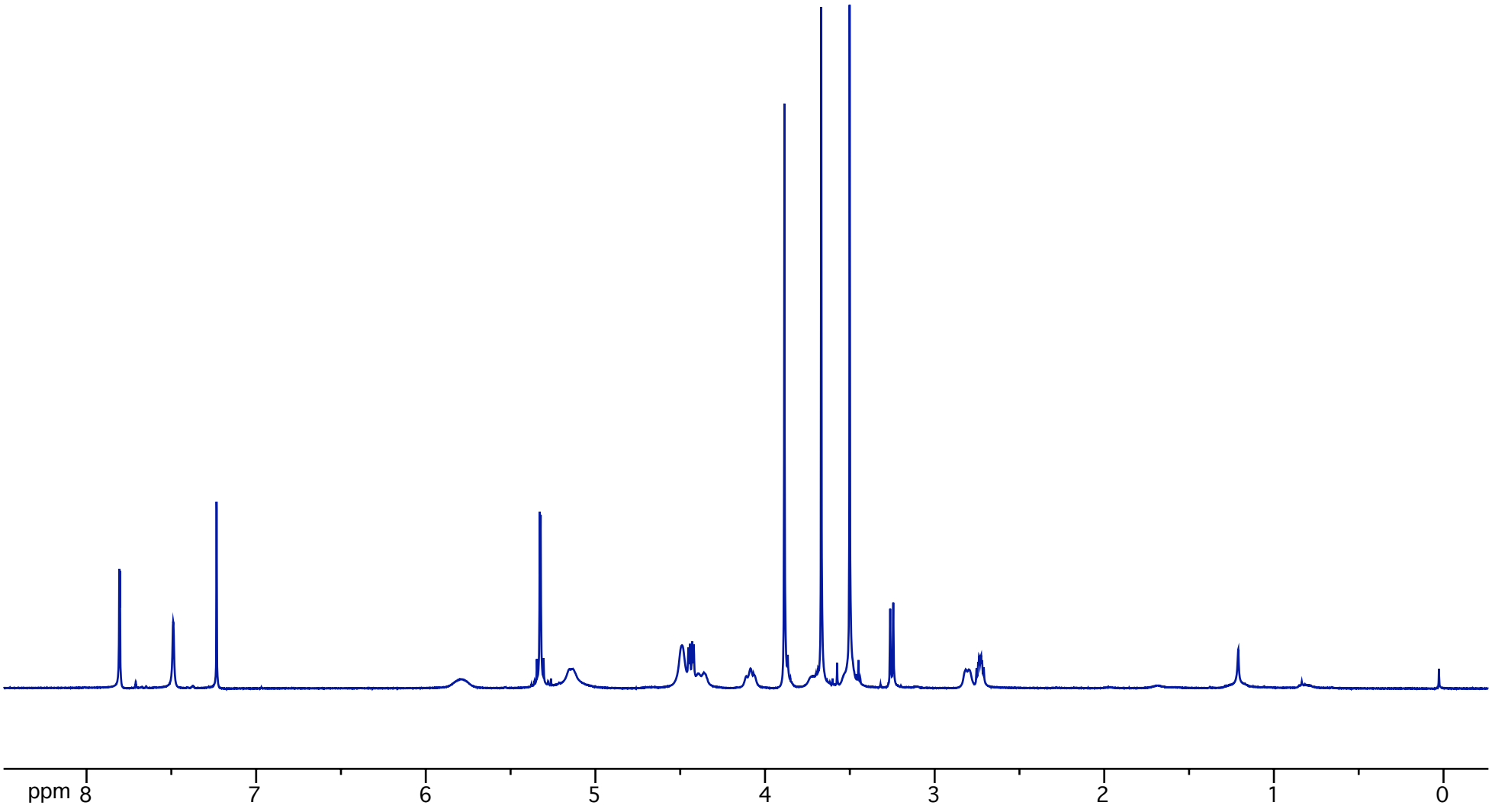


10a





11



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140.352
132.530
132.014
123.293
118.717
114.807
94.936
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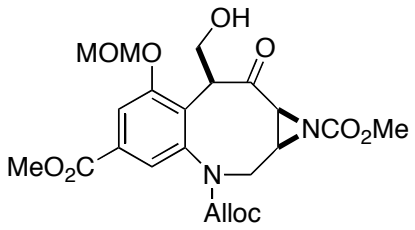
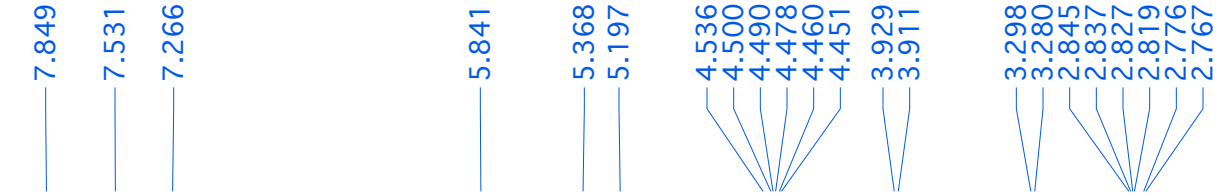
54.274
52.782
51.889
48.505
45.586
41.564



11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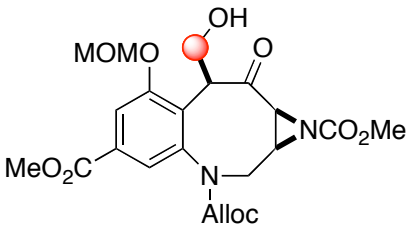
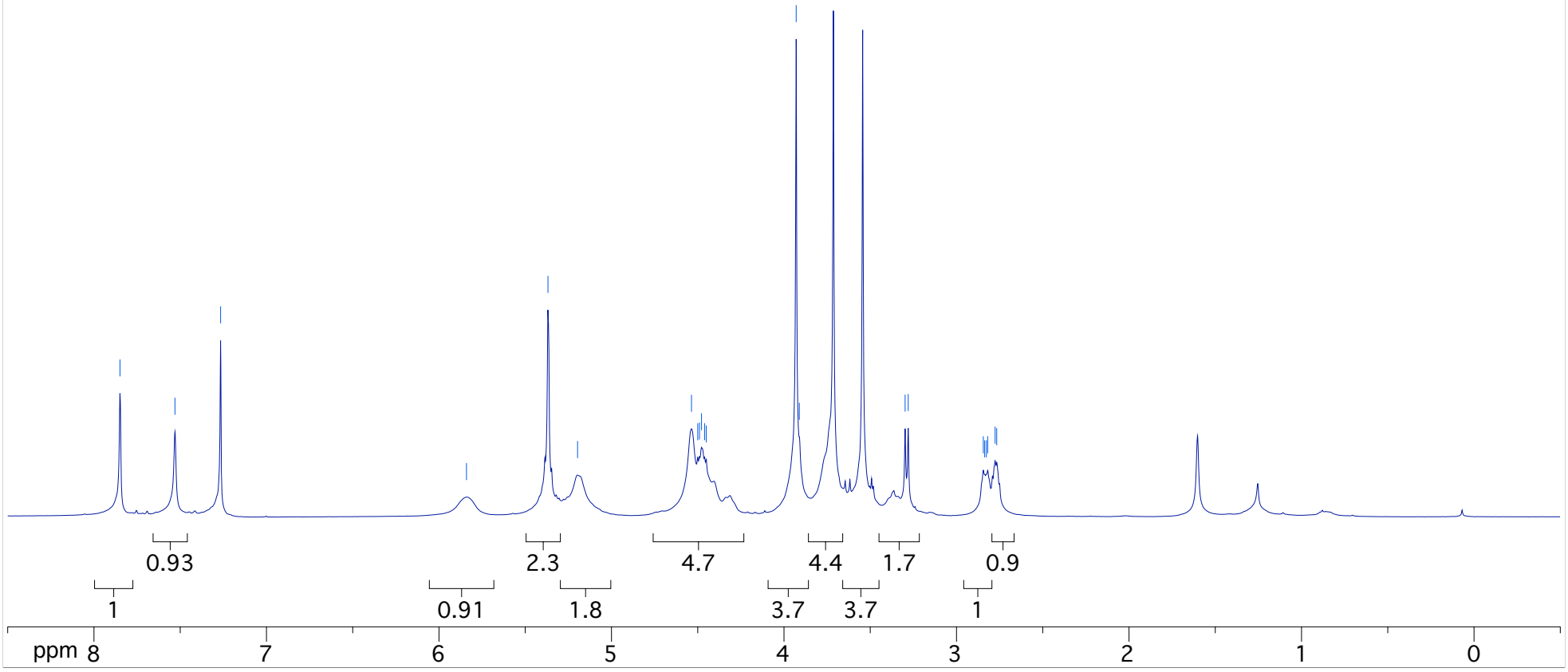
7.266
5.841
5.368
5.197
4.536
4.500
4.490
4.478
4.460
4.451
3.929
3.911
3.298
3.280
2.845
2.837
2.827
2.819
2.776
2.767


OH
MOMO
O
NCO2Me
MeO2C
N
Alloc

11

● = ^{13}C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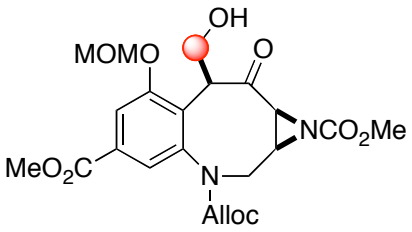
4.4
1.7
0.9
1
0.91
1.8
3.7
3.7
1
ppm
8
7
6
5
4
3
2
1
0

202.113
162.139
155.901
140.274
132.458
131.941
123.218
118.638
114.731
94.858
77.480
77.158
76.845
67.326
61.342
56.890
54.195
52.703
51.990
51.625
48.433
45.508
41.485

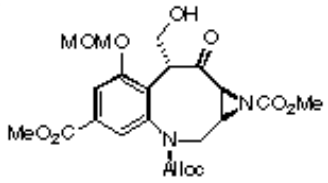


11

= ^{13}C

hn-1-408

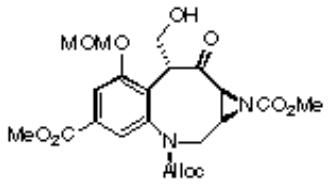
Pulse Sequence: s2pul



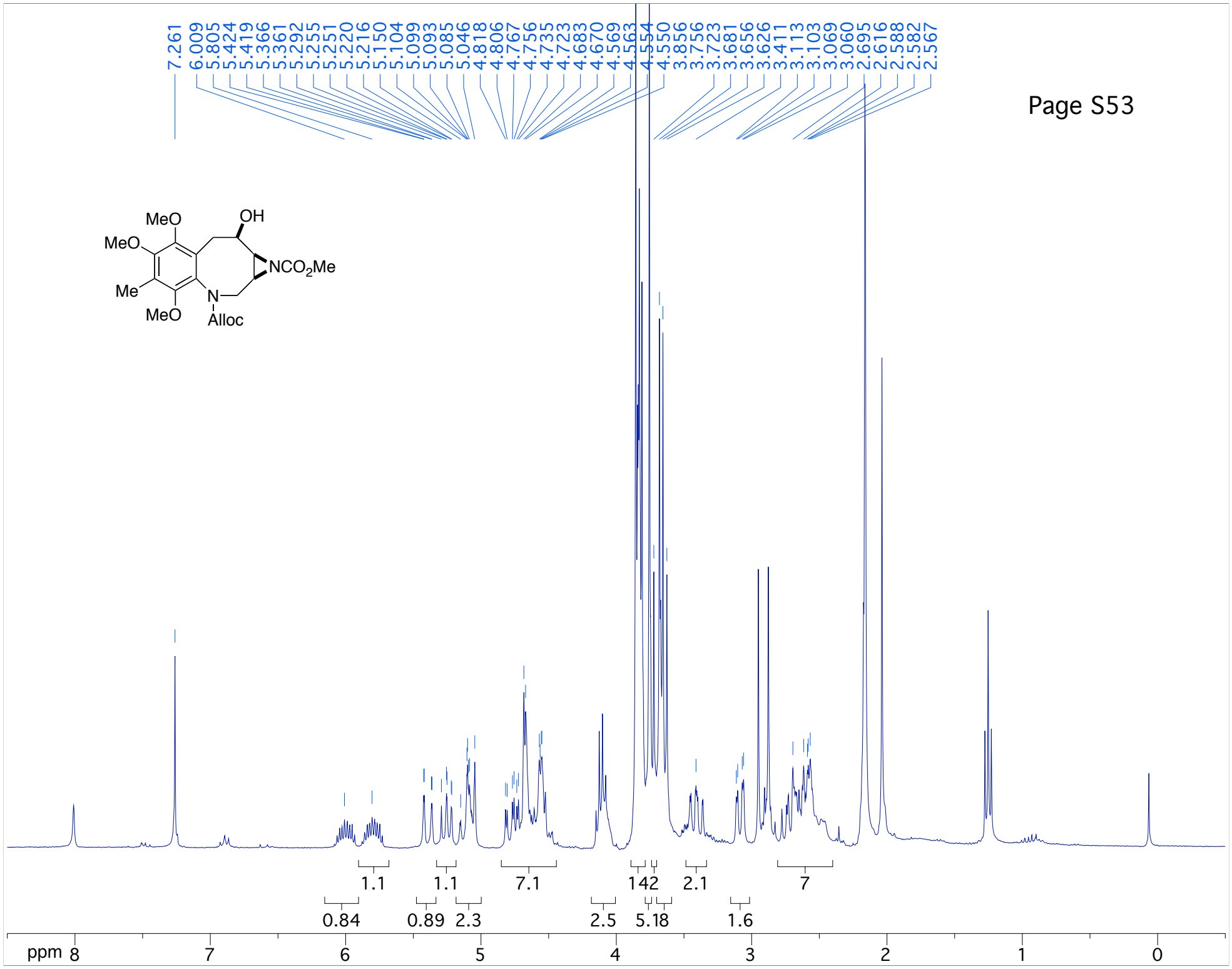
11ea

hn-1-408

Pulse Sequence: s2pul



11a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5.361
5.292
5.255
5.251
5.220
5.216
5.150
5.104
5.099
5.093
5.085
5.046
4.818
4.806
4.767
4.756
4.735
4.723
4.683
4.670
4.569
4.563
4.554
4.550
3.856
3.756
3.723
3.681
3.656
3.626
3.411
3.113
3.103
3.069
3.060
2.695
2.616
2.588
2.582
2.567
MeO
OH
MeO
NCO2Me
Me
N
MeO
Alloc
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1.1
7.1
142
2.1
7
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1.6
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7
6
5
4
3
2
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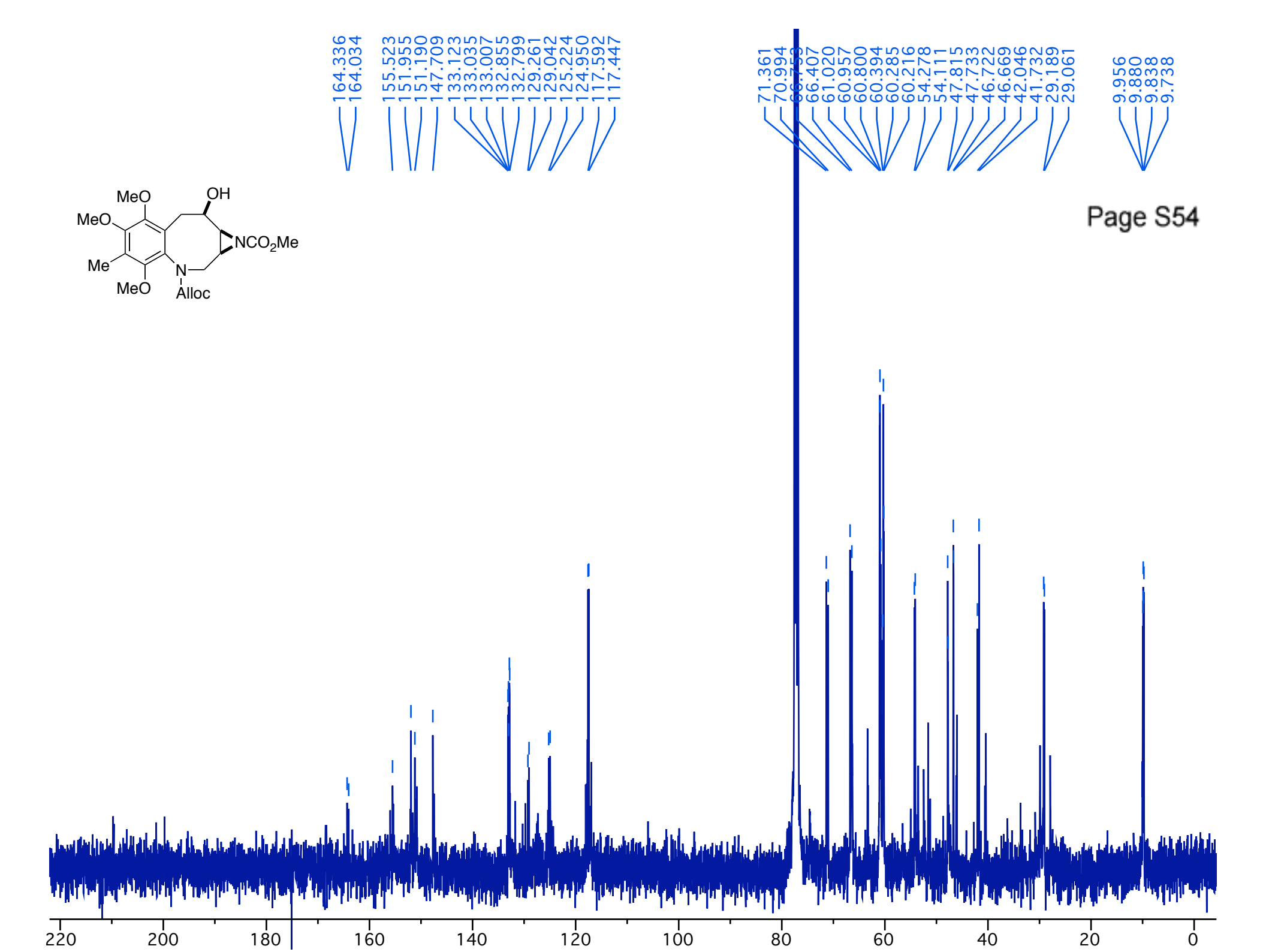
0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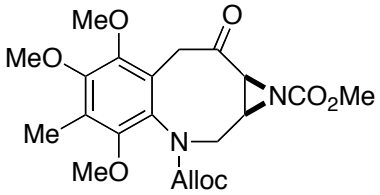
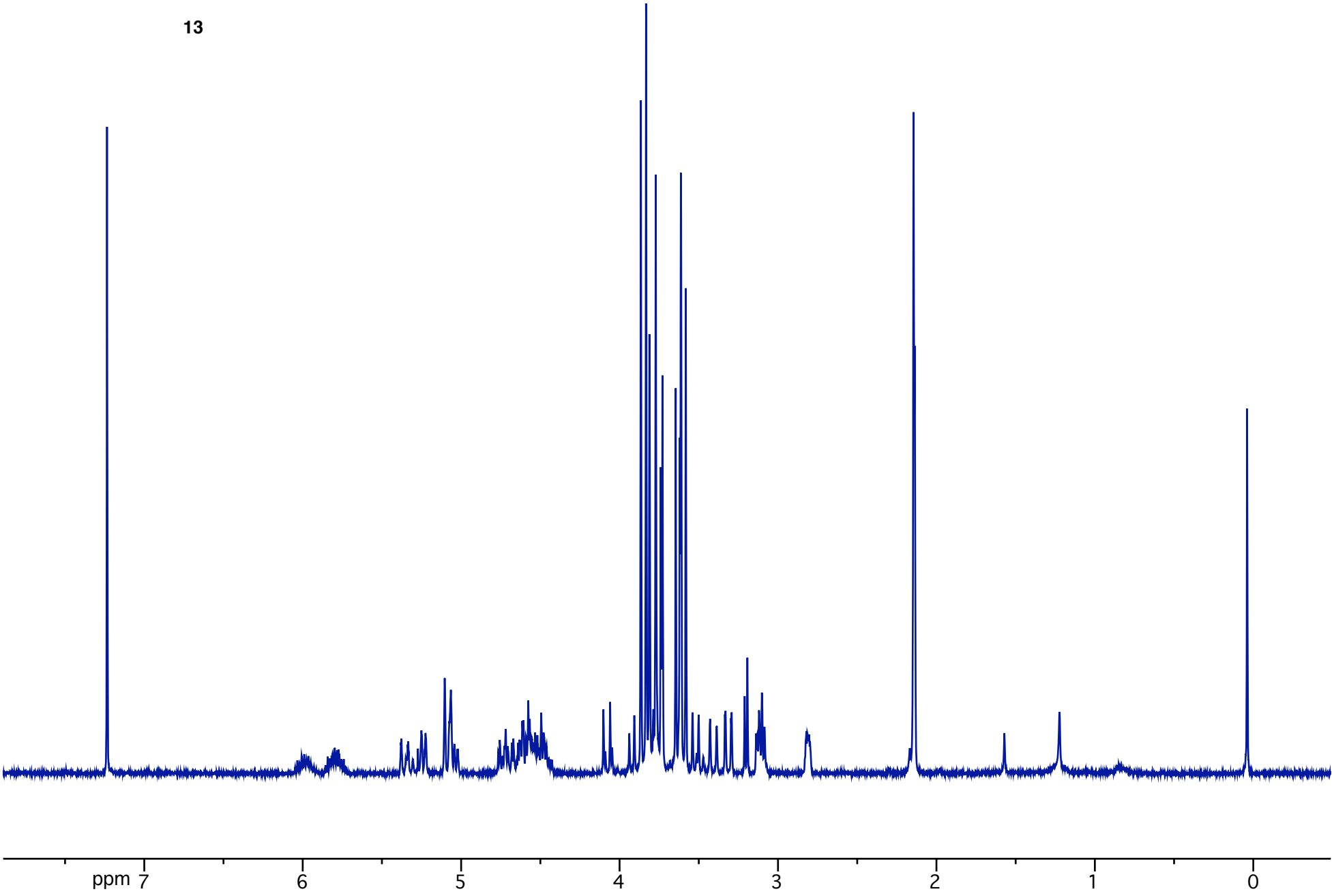
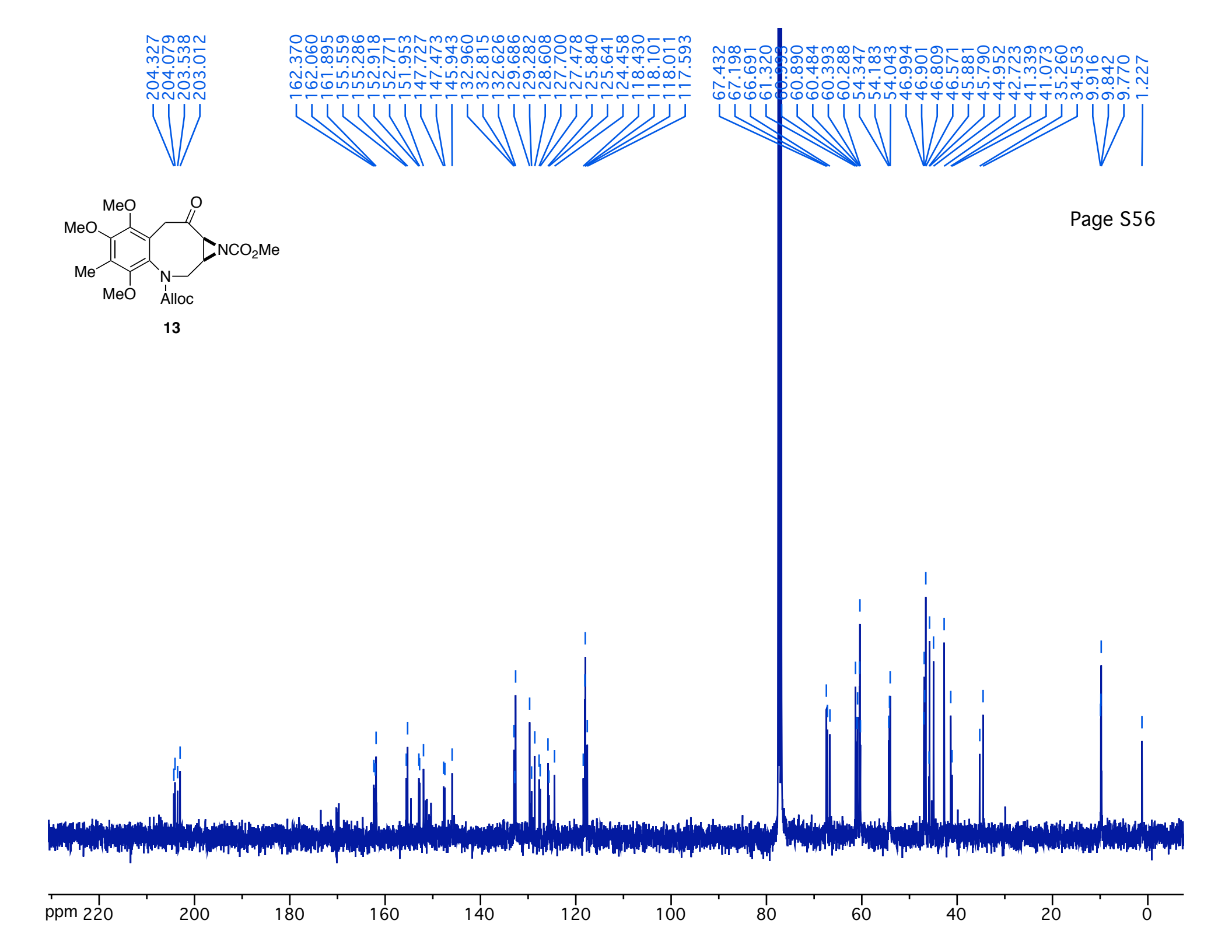
125.224
124.950
117.592
117.447
71.361
70.994
66.753
66.407
61.020
60.957
60.800
60.394
60.285
60.216
54.278
54.111
47.815
47.733
46.722
46.669
42.046
41.732
29.189
29.061
9.956
9.880
9.838
9.738
MeO
MeO
OH
NCO2Me
Me
N
MeO
Alloc
220
200
180
160
140
120
100
80
60
40
20
0



13

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203.012
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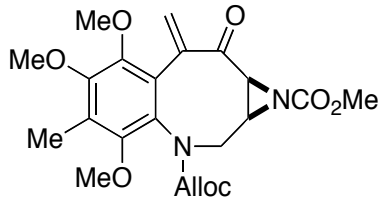
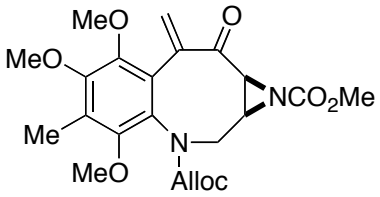
162.060
161.895
155.559
155.286
152.918
152.771
151.953
147.727
147.473
145.943
132.960
132.815
132.626
129.686
129.282
128.608
127.700
127.478
125.840
125.641
124.458
118.430
118.101
118.011
117.593
67.432
67.198
66.691
61.320
60.890
60.484
60.393
60.288
54.347
54.183
54.043
46.994
46.901
46.809
46.571
45.881
45.790
44.952
42.723
41.339
41.073
35.260
34.553
9.916
9.842
9.770
1.227
MeO
MeO
Me
MeO
O
NCO2Me
N
Alloc
13
Page S56
ppm
220
200
180
160
140
120
100
80
60
40
20
0



14



14

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60.876
60.485
53.894
47.118
45.535
43.620
29.908
9.971
1.230

220 200 180 160 140 120 100 80 60 40 20 0