ELECTRONIC SUPPLEMENTARY INFORMATION FOR *CHEM. COMMUN.*

Asymmetric total synthesis of securinine

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EXPERIMENTAL PROCEDURES, CHARACTERIZATION DATA and NMR SPECTRA

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General Information on the X-ray data collection, solution and refinement of compounds (16) and (1)

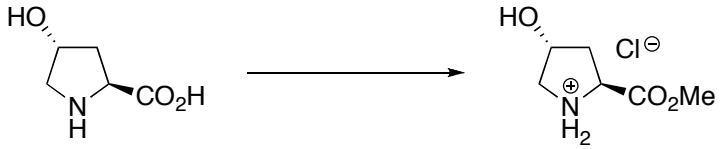
The subject crystals were covered in Nujol®, mounted on a goniometer head and rapidly placed in the the dry N_2 cold-stream of the low-temperature apparatus (Kryoflex) attached to the diffractometer. The data were collected using the SMART[1] software on a Bruker APEX CCD diffractometer using a graphite monochromator with MoKα radiation (λ = 0.71073 Å). For each crystal, a hemisphere of data was collected using a counting time of 30 seconds per frame at -100 °C. Details of crystal data, data collection and structure refinement are listed in the respective CIF files. Data reduction was performed using the SAINT-Plus[2] software and the data were corrected for absorption using SADABS.[3] The structures were solved by direct methods using SIR97[4] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-hydrogen atoms using SHELXL-97[5,6] and the WinGX[7] software package and thermal ellipsoid plots were produced using SHELXTL.[5,8] In both structures, the hydrogen atoms attached to carbon atoms were placed in geometrically-reasonable positions and were assigned isotropic displacement parameters equal to 1.2 U_{eq} of the carbon atom to which they are bonded. For the alkyne structure, the position of the hydrogen atom attached to the oxygen atom was located in the Fourier difference map, and subsequently refined using an isotropic displacement parameter. Because the structures were collected using MoKα radiation and neither contain atoms heavier than oxygen, only the relative stereochemistry of the molecules could be determined reliably thus the Friedl opposites were merged in the final refinement (therefore a Flack parameter was not calculated) and the absolute stereochemistry of the molecules is assigned on the basis of the known stereochemistry of the starting materials and the synthetic procedures employed.

1. *SMART*, (2001) Bruker AXS Inc., Madison, WI.
2. *SAINTPlus*, (2001) Bruker AXS Inc., Madison, WI.
3. *SADABS*, (2001) Bruker AXS Inc., Madison, WI.
4. A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. A. G. G., G. Polidori and R. Spagna, *SIR97*, (1997) CNR-IRMEC, Bari.
5. G. M. Sheldrick, *Acta Crystallographica Section A*, 2008, **64**, 112-122.
6. G. M. Sheldrick, *SHELXL-97*, (1997) Universitat Gottingen, Gottingen.
7. L. J. Farrugia, *J. Appl. Crystallogr.*, 1999, **32**, 837-838.
8. G. M. Sheldrick, *SHELXTL*, (2001) Bruker AXS Inc., Madison, WI.

General Information. THF was dried and distilled over sodium/benzophenone ketal. DMF was dried and distilled over calcium hydride. All other solvents were dried over alumina in a series of Grubbs'-type columns.[9] All other reagents were used as received (Aldrich, Acros). Silica gel (60 Å, 230-400 mesh) was obtained from Silicycle and used as received. Melting points are uncorrected, and were measured on a Fisher-Johns melting point apparatus. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded at 300 or 500 MHz and 75 or 125 MHz respectively on a Bruker Spectrospin 300 or 500 MHz spectrometer. Proton chemical shifts were internally referenced to the residual proton resonance in $CDCl_3$ or C_6D_6 (δ 7.26 and 7.16 respectively). Carbon chemical shifts were internally referenced to the deuterated solvent signals in $CDCl_3$ or C_6D_6 (δ 77.00 and 128.06 respectively). Infrared spectra were obtained on a Bruker VECTOR22 FT-IR spectrometer. HRMS-CI and HRMS-ESI were performed on a Waters/Micromass GCT time-of-flight mass spectrometer and a Waters/Micromass Q-TOF Global quadrupole time-of-flight mass spectrometer respectively.

I. Experimental procedures and characterization data

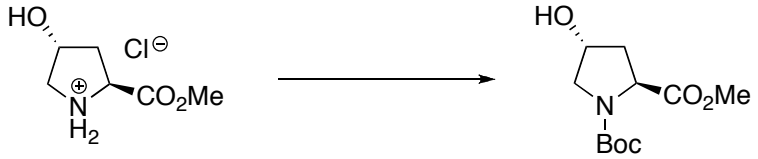
(2*S*, 4*R*)-4-Hydroxy-2-(methoxycarbonyl)pyrrolidinium chloride (7a)[10,11]



7 **7a**

To a stirred solution of *trans* 4-hydroxy-L-proline (12.00 g, 91.5 mmol) in MeOH (200 mL) at 0 °C was added $SOCl_2$ (6.68 mL, 91.5 mmol) dropwise over 20 min. The reaction mixture was then allowed to warm to rt stirred for a further 6 h at rt. All volatiles were removed *in vacuo*. **7a** was obtained as a white, microcrystalline solid (16.62 g, quantitative). The crude material was used in the next step without further purification. **7a**: m.p. = 169-171 °C (MeOH).

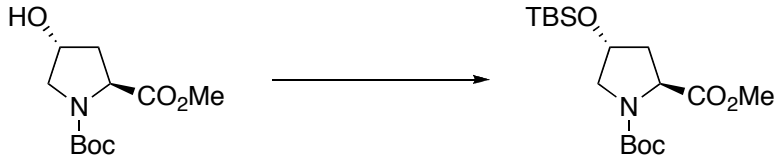
(2*S*, 4*R*)-1-*tert*-Butyl 2-Methyl 4-Hydroxypyrrolidine-1,2-dicarboxylate (7b)[11,12]



7a **7b**

To a solution of **7a** (8.213 g, 45.2 mmol) in 1,4-dioxane/H_2O (2:1, 80 mL) was added Et_3N (9.45 mL, 67.8 mmol) and Boc_2O (19.7 g, 90.4 mmol). The reaction mixture was stirred for 4 h at rt and all volatiles were evaporated *in vacuo*. The resulting solid residue was dissolved in EtOAc (250 mL), and then washed consecutively with HCl (0.5 M, 25 mL), sat. aq. $NaHCO_3$ (100 mL) and brine (100 mL). The organic extract was dried ($MgSO_4$), filtered and all volatiles were removed *in vacuo* to afford **7b** as a white solid (11.074 g, quantitative), which was used directly in the next step. The spectral data of **7b** matched the previously reported data.[12]

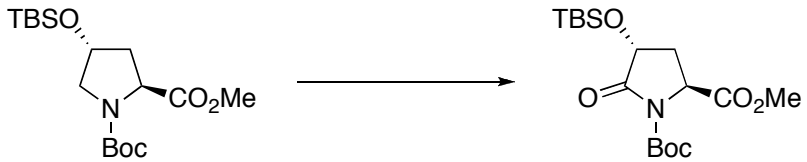
(2*S*, 4*R*)-1-*tert*-Butyl 2-Methyl 4-(*tert*-Butyldimethylsilyloxy)pyrrolidine-1,2-dicarboxylate (7c)[11,13]



7b **7c**

To a solution of **7c** (9.503 g, 38.73 mmol) in DMF (80 ml), was added *t*-butylchlorodimethyl silane (7.00 g, 46.48 mmol) and imidazole (5.27 g, 77.46 mmol). The reaction mixture was stirred at rt for 14 h. The solvent was removed *in vacuo* and Et_2O (100 mL) was added. The mixture was washed with water (3 x 100 mL), brine (2 x 100 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo* to provide **7c** as a viscous, straw-coloured oil (13.908 g, quantitative), which was used directly in the next step. The spectral data of **7c** matched the previously reported data.[5]

(2*S*, 4*R*)-1-*tert*-Butyl 2-Methyl 4-(*tert*-Butyldimethylsilyloxy)-5-oxopyrrolidine-1,2-dicarboxylate (8)[11,14]



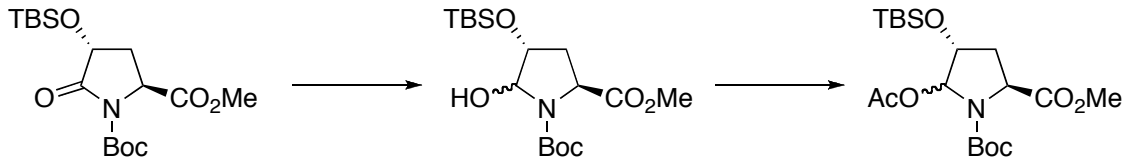
7c **8**

To a solution of $NaIO_4$ (8.900 g, 41.6 mmol) in distilled water (100 mL) was added $RuO_2 \bullet H_2O$ (186 mg, 1.4 mmol). The resulting solution was stirred for 5 min at rt followed by addition of **7c**

(5.00 g, 13.91 mmol) in EtOAc (50 mL) in one portion. The reaction mixture was stirred for 12 h at rt. Small portions of $NaIO_4$ (*ca*. 500 mg) were added every 3 h during this period to ensure that Ru black did not form. EtOAc (100 mL) was subsequently added followed by sat. aq. $NaHSO_3$, which immediately resulted in the precipitation of Ru black. The layers were separated and the organic extract was filtered through a pad of Celite®. The filtrate was then washed with brine (50 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The resulting residue was subjected to silica gel chromatography (hexanes/EtOAc, 4:1) to afford **8** as a white, crystalline solid (4.984 g, 96%).

8: m.p. = 55-56 °C (EtOAc); $[\alpha]_D^{21}$ = +28.2 (*c* 0.10, $CHCl_3$), ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.59 (1H, dd, *J* = 10.0, 1.5 Hz), 4.43 (1H, dd, *J* = 10.0, 8.5 Hz), 3.80 (3H, s), 2.37 (1H, dd, *J* = 13.0, 8.5, 1.5 Hz), 2.21 (1H, dt, *J* = 13.0, 10.0 Hz), 1.51 (9H, s), 0.90 (9H, s), 0.18 (3H, s), 0.13 (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.96, 171.76, 149.51, 83.89, 69.65, 54.96, 52.68, 31.83, 27.87, 25.66, 18.19, -4.47, -5.32; IR (KBr) υ 2956, 2931, 2887, 2858, 1801, 1753, 1723 cm^{-1}.

(2*S*, 4*R*)-1-*tert*-Butyl 2-Methyl 5-Acetoxy-4-(*tert*-butyldimethylsilyloxy)pyrrolidine-1,2-dicarboxylate (6)

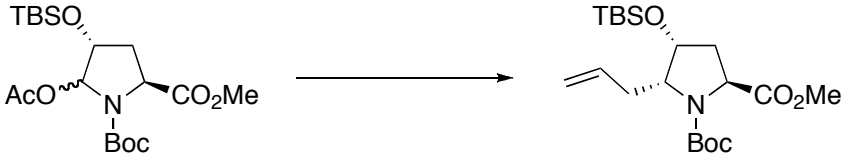


8 **9** **6**

To a solution of **8** (1.000 g, 2.68 mmol) in THF (3.0 mL) at -78 °C was added $LiBEt_3H$ (1.0 M in THF, 2.70 mL, 2.70 mmol) dropwise. The reaction mixture was stirred for 1 h at -78 °C, and then quenched with sat. aq. $NaHCO_3$ (3.0 mL) at -78 °C. H_2O_2 (two drops) was added and the reaction mixture was allowed warmed to rt. All volatiles were removed *in vacuo*. CH_2Cl_2 (20 ml) was added followed by brine (10 mL). The mixture was stirred and the layers were separated. The organic phase was dried ($MgSO_4$), filtered and concentrated *in vacuo*. The resulting pale yellow oil was dissolved in CH_2Cl_2 (10 mL). Et_3N (0.56 mL, 4.02 mmol), Ac_2O (304 μL, 3.22 mmol) and cat. DMAP (20 mg) were then added successively. The reaction mixture was stirred at rt for 8 h prior to the addition of sat. aq. $NaHCO_3$ (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was subjected to silica gel chromatography (hexanes:EtOAc = 4:1) to afford **9** as a clear, colourless oil (970 mg, 87%).

6: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.17 (1H, s), 4.53 – 4.38 (1H, m), 4.16 (1H, br s), 3.77 (3H, s), 2.22 – 2.00 (5H, m), 1.45 (9H, s), 0.87 (9H, s), 0.14 (3H, s), 0.10 (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.90, 172.54, 170.07, 169.82, 153.62, 153.26, 88.48, 88.01, 81.46, 81.40, 74.66, 73.84, 59.03, 58.39, 52.24, 52.13, 36.76, 36.15, 28.21, 25.62, 21.20, 17.91, -4.83, -5.09 (+ 4 overlapped signals); IR (film) υ 2955, 2932, 2859, 1751, 1738, 1715 cm^{-1}.

(2*S*, 4*R*, 5*R*)-1-*tert*-Butyl 2-Methyl 5-Allyl-4-(*tert*-butyldimethylsilyloxy)pyrrolidine-1,2-dicarboxylate (10)[11,15,16]

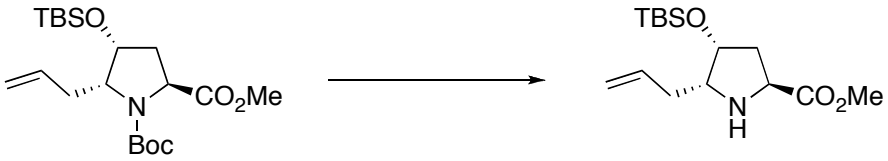


9 **10**

To a solution of **9** (6.108 g, 14.6 mmol) in diethyl ether (100 mL) at -78 °C was added $BF_3{\cdot}Et_2O$ (2.26 mL, 18.3 mmol) and allyltrimethylsilane (10.4 mL, 65.7 mmol). The reaction mixture was stirred for 15 min at -78 °C and then allowed to warm to rt (1 h) and stirred for a further 2 h at rt. Sat. aq. $NaHCO_3$ (75 mL) was added and the layers were separated. The aqueous later was extracted with Et_2O (2 x 50 mL) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was subjected to silica gel chromatography (hexanes:EtOAc = 5:1) to afford **10** as a 4:1 mixture of diastereomers (+ rotamers) (main diastereomer shown). **10** was isolated as a clear, colourless oil (5.112 g, 88%).

10 (main diastereomer, rotamers): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.93 – 5.78 (1H, m), 5.15 – 5.03 (2H, m), 4.60 – 4.40 (1H, m), 4.32 – 4.10 (1H, m), 3.88 – 3.62 (4H, m), 2.70 – 2.45 (2H, m), 2.20 – 1.99 (2H, m), 1.47 (3H, s, rotamer), 1.45 (6H, s, rotamer), 0.86 (9H, s), 0.07 (3H, s), 0.04 (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.04, 173.92 (rotamer), 153.94, 153.40 (rotamer), 134.91, 117.28, 80.04 (br), 74.33 (rotamer), 73.37, 67.31 (rotamer), 67.02, 59.78 (rotamer), 58.88, 52.18 (rotamer), 51.99, 37.83, 37.36 (rotamer), 33.85 (rotamer), 33.04, 28.42, 28.26 (rotamer), 25.78, -4.37 (br), -4.76; IR (film) υ 3077, 2954, 2934, 2859, 1754, 1704, 1641, 1439, 1391 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{20}H_{38}NO_5Si$ (MH^+) 400.2519, found 400.2538.

(2*S*, 4*R*, 5*R*)-Methyl 5-Allyl-4-(*tert*-butyldimethylsilyloxy)pyrrolidine-2-carboxylate (11)[15]



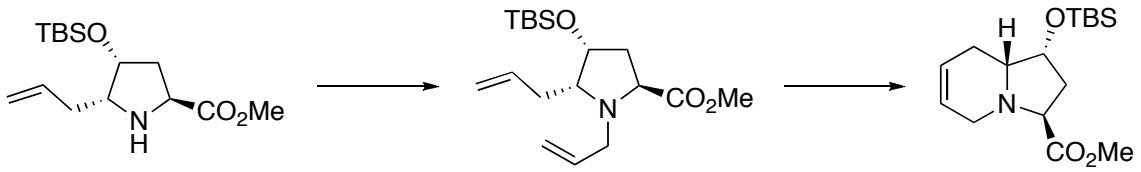
10 **11**

To a solution of **10** (6.205 g, 15.5 mmol) in CH_2Cl_2 (100 mL) at 0 °C was added TFA (11.5 mL, 155 mmol). The reaction mixture was stirred at rt for 10 h. Sat. aq. $NaHCO_3$ (100 mL) was carefully and slowly added at 0 °C. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was subjected to silica gel chromatography (gradient, hexanes:EtOAc = 15:1 to 3:1) to afford **11** as a yellow oil (3.563 g, 77%).

11: $[\alpha]_D^{20}$ = -89.4 (*c* 1.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.90 – 5.75 (1H, m), 5.10 (1H, d, *J* = 17.0 Hz), 5.04 (1H, d, *J* = 10.0 Hz), 4.25 – 4.20 (1H, m), 4.02 (1H, t, *J* = 8.0 Hz), 3.72 (3H, s), 3.14 (1H, dt, *J* = 7.0, 2.0 Hz), 2.33 – 2.20 (3H, m), 2.13 (1H, ddd, *J* = 13.0, 8.0, 1.5 Hz),

2.04 (1H, ddd, *J* = 13.0, 8.0, 4.5 Hz), 0.90 (9H, s), 0.08 (3H, s), 0.07 (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.87, 136.16, 116.51, 73.40, 63.48, 57.75, 52.14, 39.88, 34.19, 25.92, 18.17, -4.37, -4.81; IR (film) υ 3352, 3077, 2954, 2932, 2899, 2858, 1740, 1641 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{15}H_{30}NO_3Si$ (MH^+) 300.1995, found 300.1991.

(1*R*, 3*S*, 8a*R*)-Methyl 1-(*tert*-Butyldimethylsilyloxy)-1, 2, 3, 5, 8, 8a-hexahydroindolizine-3-carboxylate (13a)[15]

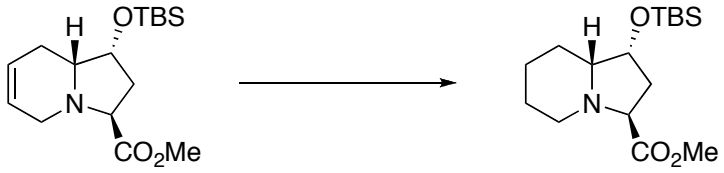


11 **12** **13a**

To a solution of **11** (3.004 g, 10.0 mmol) in DMF (65 mL) at rt was added Et_3N (3.48 mL, 25 mmol). The reaction mixture was stirred for 16 h at rt. Et_2O (75 mL) was then added and the organic layer was washed with sat. aq. $NaHCO_3$ (50 mL). The layers were separated and the aqueous later was extracted with diethyl ether (2 x 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The resulting pale, yellow oil (**12**) (3.40 g, 10.0 mmol) was dissolved in CH_2Cl_2 (100 mL) and the 2nd generation Grubbs' catalyst (425 mg, 0.5 mmol) was added. The reaction mixture was then refluxed for 8 h. All volatiles were then removed *in vacuo* and the residue was subjected to silica gel chromatography (hexanes:EtOAc = 4:1) to afford **13a** as a pale, yellow oil (2.894 g, 93% over two steps).

13a: $[\alpha]_D^{20}$ = -85.0 (*c* 1.18, $CHCl_3$) ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.85 – 5.78 (1H, m), 5.68 – 5.60 (1H, m), 4.55 – 4.45 (1H, m), 3.92 (1H, dd, *J* = 9.0, 3.0 Hz), 3.70 (3H, s), 3.33 – 3.20 (2H, m), 3.18 (1H, dt, *J* = 10.5, 5.0 Hz), 2.38 – 2.27 (2H, m), 2.06 (1H, ddd, *J* = 13.5, 9.0, 4.5 Hz), 1.91 – 1.84 (1H, m), 0.89 (9H, s), 0.06 (6H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.94, 125.10, 124.22, 72.12, 62.44, 59.17, 51.43, 47.42, 37.92, 25.84, 24.68, 18.21, -4.77, -4.91; IR (film) υ 3034, 2954, 2931, 2891, 2857, 1748, 1672 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{16}H_{30}NO_3Si$ (MH^+) 312.1995, found 312.2003.

(1*R*, 3*S*, 8a*R*)-Methyl 1-(*tert*-Butyldimethylsilyloxy)octahydroindolizine-3-carboxylate (13)[15]



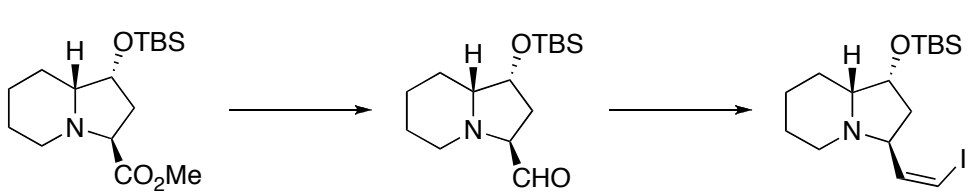
13a **13**

To a solution of **13a** (2.803 g, 8.99 mmol) in EtOAc (100 mL) was added 10% Pd/C (2.0 g). The reaction mixture was stirred under an atmosphere of H_2 for 18 h. The crude reaction mixture was

then filtered through a pad of Celite®, and the pad was washed with EtOAc (3 x 25 mL). The filtrate was concentrated *in vacuo* to afford **13** as a pale, yellow oil (2.810 g, quantitative).

13: $[\alpha]_D^{20}$ = -24.8 (*c* 0.77, $CHCl_3$) ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.42 – 4.34 (1H, m), 3.90 (1H, d, *J* = 8.5 Hz), 3.03 (1H, d, *J* = 11.0 Hz), 2.80 – 2.73 (1H, m), 2.41 – 2.33 (1H, m), 2.30 (1H, ddd, *J* = 10.0, 7.5, 2.5 Hz), 2.01 (1H, ddd, *J* = 13.0, 9.0, 3.0 Hz), 1.86 – 1.79 (1H, m), 1.57 – 1.38 (4H, m), 1.30 – 1.20 (1H, m), 0.88 (9H, s), 0.05 (6H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.72, 73.03, 63.96, 62.58, 51.20, 48.50, 37.97, 25.95, 25.48, 24.31, 23.76, 18.40, -4.78 (signal overlap); IR (film) υ 2933, 2857, 1736 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{16}H_{32}NO_3Si$ (MH^+) 314.2151, found 312.2169.

(1*R*, 3*S*, 8a*R*)-1-(tert-Butyldimethylsilyloxy)-3-((*Z*)-2-iodovinyl)octahydroindolizine (15)



13 **14** **15**

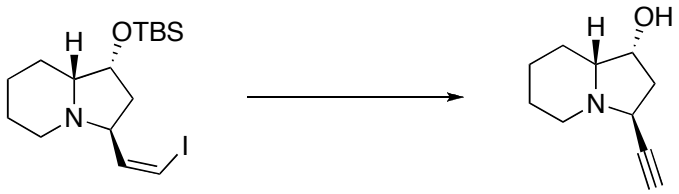
To a solution of **13** (1.701 g, 5.41 mmol) in anhydrous $PhCH_3$ (50 mL) cooled to -78 °C was added a solution of DIBAL-H (1.0 M in $PhCH_3$, 10.8 mL, 10.8 mmol) dropwise over 15 min. The reaction mixture was stirred for a further 2 h at -78 °C. Anhydrous EtOH (15 mL) was then added and the mixture was allowed to warm to -20 °C. Potassium sodium tartrate (1M in H_2O, 50 mL) was added and the biphasic mixture was vigorouly stirred for 1 h while warming to rt. The layers were separated and the aqueous later was extracted with Et_2O (3 x 25 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford **14** as a pale, yellow oil (1.50 g, 98%). **14** was prone to decomposition at rt over several hours and was hence immediately reacted as shown below

To a suspension of iodomethyltriphenylphosphonium iodide (3.60 g, 6.80 mmol) in anhydrous THF (20 mL) at -10 °C was added NaHMDS (1.0 M in THF, 6.8 mL, 6.8 mmol). The mixture was stirred for 15 min at -10 °C. The reaction mixture was then cooled to -78 °C and a solution of the aldehyde (1.50 g, 5.27 mmol) in anhydrous THF (5 mL) was added. The mixture was stirred for 30 min at -78 °C, and another 1.5 h at -10 °C. Hexanes (15 mL) was then added, and the solids were filtered off. The solid residue was rinsed with hexanes (2 x 15 mL). The combined organic filtrate was dried ($MgSO_4$), filtered and concentrated *in vacuo*. The dark yellow residue was subjected to silica gel chromatography (hexanes:acetone = 9:1) to afford **15** (1.752 g, 80% over two steps) as a yellow oil.

15: $[\alpha]_D^{20}$ = -100.7 (*c* 1.00, $CHCl_3$) ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.31 (1H, d, *J* = 7.5 Hz), 6.15 (1H, t, *J* = 7.5 Hz), 4.34 (1H, dt, *J* = 9.0, 3.5 Hz), 2.9 – 2.90 (1H, m), 2.65 – 2.57 (1H, m), 2.46 (1H, dt, *J* = 13.5, 1.5 Hz), 2.11 (1H, ddd, *J* = 13.5, 9.0, 3.5 Hz), 1.94 – 1.80 (2H, m), 1.61 (1H, tq, *J* = 13.0, 4.0 Hz), 1.53 – 1.43 (3H, m), 1.31 – 1.20 (1H, m), 0.89 (9H, s), 0.05 (6H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 141.12, 83.01, 72.86, 64.67, 62.88, 47.42, 39.80, 26.04, 24.23, 23.02,

23.22, 18.43, -4.63, -4.75; IR (film) υ 3070, 2932, 2856, 2794, 1602 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{16}H_{31}INOSi$ (MH^+) 408.1220, found 408.1220.

(1*R*, 3*S*, 8a*R*)-3-Ethynyloctahydroindolizin-1-ol (16)

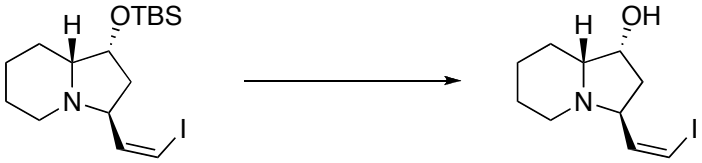


15 **16**

To a solution of **15** (204 mg, 0.5 mmol) in THF (1 mL) at rt was added TBAF (1.0 M in THF, 1.1 mL, 1.1 mmol). The reaction mixture was stirred for 18 h at rt. All volatiles were then removed *in vacuo*. The residue was subjected to silica gel chromatography (hexanes:acetone = 3:1) to afford **16** as a clear, colourless crystalline solid (62 mg, 75%). X-ray quality crystals of **16** were grown via slow evaporation of a solution of **16** in EtOAc.

16: m.p. = 62-63 °C (EtOAc); $[\alpha]_D^{20}$ = -18.9 (*c* 0.64, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 4.20 – 4.10 (1H, m), 4.03 (1H, d, *J* = 8.5 Hz), 2.95 – 2.88 (1H, m), 2.51 (1H, dt, *J* = 11.5, 3.0 Hz), 2.42 – 2.30 (2H, m), 2.27 (1H, d, *J* = 2.0 Hz), 2.10 (1H, dd, *J* = 14.0, 8.5 Hz), 1.92 – 1.63 (4H, m), 1.61 – 1.40 (2H, m), 1.34 – 1.20 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 82.51, 73.12, 72.44, 63.64, 52.29, 48.93, 42.02, 25.43, 25.33, 23.66; IR (KBr) 3359, 3305, 2932, 2856, 2190 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{10}H_{16}NO$ (MH^+) 166.1232, found 166.1246.

(1*R*, 3*S*, 8a*R*)-3-((*Z*)-2-Iodovinyl)octahydroindolizin-1-ol (17)

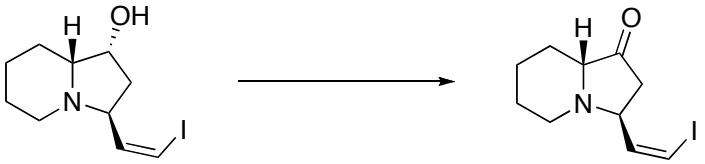


15 **17**

To a solution of **15** (204 mg, 0.5 mmol) in THF/H_2O (5:1, 2 mL) at 0 °C was added TBAF hydrate (144 mg, 0.55 mmol). The reaction mixture was stirred for 10 h at 0 °C. All volatiles were then removed *in vacuo*. The residue was subjected to silica gel chromatography (hexanes:acetone = 4:1) to afford **17** as a white solid (116 mg, 79%).

17: m.p. = 49-51 °C (EtOAc); $[\alpha]_D^{20}$ = -100.2 (*c* 0.33, $CHCl_3$) ^1H NMR ($CDCl_3$, 500 MHz) δ 5.93 (1H, d, *J* = 7.5 Hz), 5.62 (1H, dd, *J* = 8.5, 7.5 Hz), 4.09 (1H, dt, *J* = 9.0, 3.5 Hz), 3.85 – 3.78 (1H, m), 2.85 – 2.79 (1H, m), 2.16 (1H, dt, *J* = 9.0, 3.5 Hz), 2.09 – 2.00 (1H, m), 1.96 (1H, ddd, *J* = 13.5, 9.0, 3.5 Hz), 1.73 (1H, br s), 1.70 – 1.61 (1H, m), 1.55 – 1.30 (5H, m), 1.05 – 0.93 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 140.76, 83.30, 72.97, 64.80, 63.69, 48.03, 40.33, 25.78, 25.50, 24.38; IR (KBr) 3350, 3060, 2933, 2856, 1578 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{10}H_{17}INO$ (MH^+) 294.0355, found 294.0364.

(3*S*,8a*R*)-3-((*Z*)-2-iodovinyl)hexahydroindolizin-1(5*H*)-one (5)

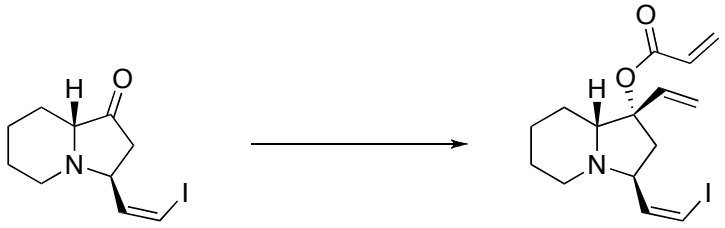


17 **5**

To a solution of DMSO (87 μL, 1.2 mmol) in CH_2Cl_2 (5 mL) at -78 °C was added a solution of oxalyl chloride (62 μL, 0.71 mmol) in CH_2Cl_2 (2mL). The reaction mixture was stirred for 15 min at -78 °C prior to the addition of a solution of **17** (181 mg, 0.61 mmol) in CH_2Cl_2 (2 mL) was added. The mixture was stirred for an additional 35 min at -78 °C. Et_3N (43 μL, 3.0 mmol) was then added dropwise and the mixture was stirred for 10 min at -78 °C and another 1 h while warming to rt. Sat. aq. $NaHCO_3$ (10 mL) was added and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The resulting residue was subjected to silica gel chromatography (hexanes:EtOAc = 85:15) to afford **5** as a pale yellow oil (169 mg, 94%).

5: $[\alpha]_D^{20}$ = -45.0 (*c* 0.32, $CHCl_3$) ^{1}H NMR (C_6D_6, 500 MHz) δ 5.93 (1H, d, *J* = 7.5 Hz), 5.55 (1H, dd, *J* = 8.5, 7.5 Hz), 4.06 (1H, dt, *J* = 8.5, 3.5 Hz), 2.80 – 2.72 (1H, m), 2.48 (1H, dd, *J* = 11.5, 3.5 Hz), 2.30 (1H, dd, *J* = 11.5, 3.5 Hz), 2.23 (1H, dt, *J* = 12.0, 3.0 Hz), 1.77 (1H, dd, *J* = 18.5, 3.5 Hz), 1.75 – 1.70 (1H, m), 1.55 – 1.48 (1H, m), 1.37 (1H, tq, *J* = 13.0, 4.0 Hz), 1.18 – 1.09 (2H, m), 0.91 (1H, tq, *J* = 13.0, 4.0 Hz); ^{13}C NMR (C_6D_6, 75 MHz) δ 211.75, 138.85, 84.49, 64.36, 61.10, 47.62, 41.65, 25.33, 24.00, 23.76; IR (film) 3062, 2936, 3855, 1754, 1638, 1613 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{10}H_{15}INO$ (MH^+) 292.0198, found 292.0208.

(1*S*, 3*S*, 8a*R*)-3-((*Z*)-2-Iodovinyl)-1-vinyloctahydroindolizin-1-yl acrylate (18)



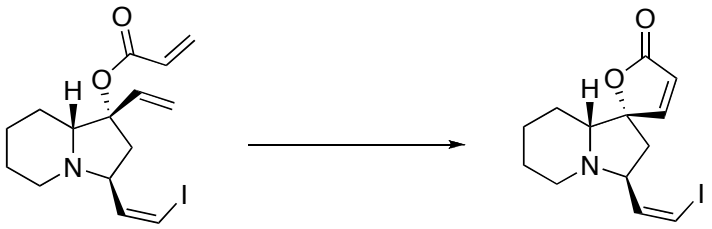
5 **18**

To a solution of **5** (146 mg, 0.50 mmol) in THF (2.0 mL) at -78 °C was added freshly prepared vinyl magnesium bromide (0.7 M in THF, 786 μL, 0.55 mmol). The reaction mixture was stirred for 30 min at -78 °C and another 30 min at -20 °C. The reaction mixture was then cooled to -78 °C prior to the addition of freshly distilled acryloyl chloride (163 μL, 2.00 mmol). The mixture was stirred for 2 h while warming to rt. Sat. aq. NH_4Cl (5 mL) and EtOAc (10 mL) were added and the layers were separated. The aqueous layer was extracted with EtOAc (5 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The

resulting residue was subjected to silica gel chromatography (gradient, hexanes:EtOAc = 90:10 to 80:20) to afford **18** as a pale yellow oil (150 mg, 80%).

18: $[\alpha]_D^{20}$ = -27.8 (*c* 1.00, $CHCl_3$) ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.42 – 6.35 (2H, m), 6.20 – 6.11 (2H, m), 5.98 (1H, dd, *J* = 17.5, 11.0 Hz), 5.79 (1H, dd, *J* = 11.0, 1.5 Hz), 5.18 (1H, d, *J* = 11.0 Hz), 5.11 (1H, d, *J* = 17.5 Hz), 3.15 – 3.07 (2H, m), 2.73 (1H, dd, *J* = 15.0, 7.5 Hz), 2.15 (1H, dd, *J* = 15.0, 9.5 Hz), 1.99 (1H, dd, *J* = 11.0, 1.5 Hz), 1.95 (1H, dd, *J* = 11.0, 2.5 Hz), 1.92 – 1.85 (1H, m), 1.80 – 1.65 (3H, m), 1.55 – 1.48 (1H, m), 1.28 – 1.20 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.18, 141.14, 138.58, 130.47, 129.39, 113.77, 86.53, 84.19, 74.23, 68.52, 52.33, 42.31, 24.93, 24.05, 23.78; IR (film) 3120, 2936, 2857, 2786, 1724, 1636, 1617, 1441 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{15}H_{21}INO_2$ (MH^+) 374.0617, found 374.0625.

(1'*S*, 3'*S*, 8a'*R*)-3'-((*Z*)-2-Iodovinyl)-3', 5', 6', 7', 8', 8a'-hexahydro-2'*H*, 5*H*-spiro[furan-2, 1'-indolizin]-5-one (4)

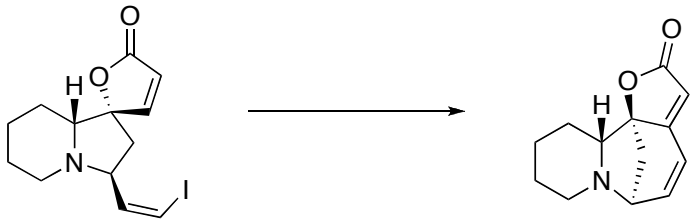


18 **4**

To a solution of **18** (51 mg, 0.137 mmol) in CH_2Cl_2 (2 mL) in a pressure tube was added 2nd generation Hoveyda-Grubbs' catalyst (9 mg, 10 mol%). The tube was sealed and the heated at 60 °C for 16 h. The tube was then unsealed, the solvent was blown off under a stream of nitrogen, and the residue was directly subjected to silica gel chromatography (hexanes:EtOAc = 80:20) to afford a yellow oil (37 mg, 78%)

4: $[\alpha]_D^{20}$ = -98.7 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.54 (1H, d, *J* = 5.5 Hz), 6.44 (1H, d, *J* = 7.5 Hz), 6.22 (1H, dd, *J* = 8.5, 7.5 Hz), 6.03 (1H, d, *J* = 5.5 Hz), 3.29 (1H, dd, *J* = 9.0, 8.5 Hz), 3.24 (1H, d, *J* = 10.5 Hz), 2.59 (1H, dd, *J* = 11.5, 2.5 Hz), 2.46 (1H, dd, *J* = 14.0, 9.0 Hz), 2.24 (1H, dd, *J* = 14.0, 7.5 Hz), 2.10 (1H, dt, *J* = 11.5, 3.0 Hz), 1.83 – 1.75 (1H, m), 1.72 – 1.62 (2H, m), 1.58 – 1.45 (2H, m), 1.20 – 1.03 (2H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.38, 158.30, 141.39, 119.90, 92.36, 83.79, 69.10, 64.52, 52.33, 36.06, 26.09, 24.65, 23.38; IR (film) 3103, 2983, 2920, 2857, 1751, 1680 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{13}H_{17}INO_2$ (MH^+) 346.0304, found 346.0295.

Securinine (1)



4 **1**: Securinine

A degassed solution of **4** (62 mg, 0.180 mmol), anhydrous NaOAc (17 mg, 0.200 mmol), $^{n}Bu_4NBr$ (12 mg, 20 mol%) and *trans*-di(μ-acetato)-bis[*o*-(di-*o*-tolylphosphino)benzyl]-dipalladium (II) (Herrmann-Beller catalyst)[17] (17 mg, 10 mol%) in DMA (1 mL) was heated at 100 °C for 12 h. The reaction mixture was then directly subjected to silica gel chromatography (hexanes:EtOAc = 80:20) to afford **1** as a yellow solid (32 mg, 82%). X-ray quality crystals were grown by slow evaporation of a solution of **1** in MeOH.

1: m.p. = 142-144 °C (MeOH); $[\alpha]_D^{20}$ = -1085 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.55 (1H, d, *J* = 9.0 Hz), 6.36 (1H, dd, *J* = 9.0, 5.5 Hz), 5.48 (1H, s), 3.76 (1H, t, *J* = 4.5 Hz), 2.91 (1H, dt, *J* = 10.5, 3.5 Hz), 2.43 (1H, dd, *J* = 9.0, 4.0 Hz), 2.36 (1H, ddd, *J* = 10.5, 7.0, 6.5 Hz), 2.04 (1H, dd, *J* = 11.0, 2.5 Hz), 1.81 (1H, d of pentet, *J* = 13.5, 3.5 Hz), 1.71 (1H, d, *J* = 9.0 Hz), 1.62 – 1.40 (4H, m), 1.25 – 1.08 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.49, 170.02, 140.13, 121.26, 104.87, 89.35. 62.84, 58.63, 48.59, 42.16, 27.13, 25.75, 24.37; IR (KBr) 2946, 2819, 1739, 1627 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}NO_2$ (MH^+) 218.1181, found 218.1189.

II. References

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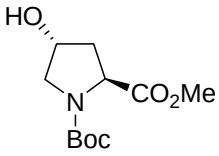
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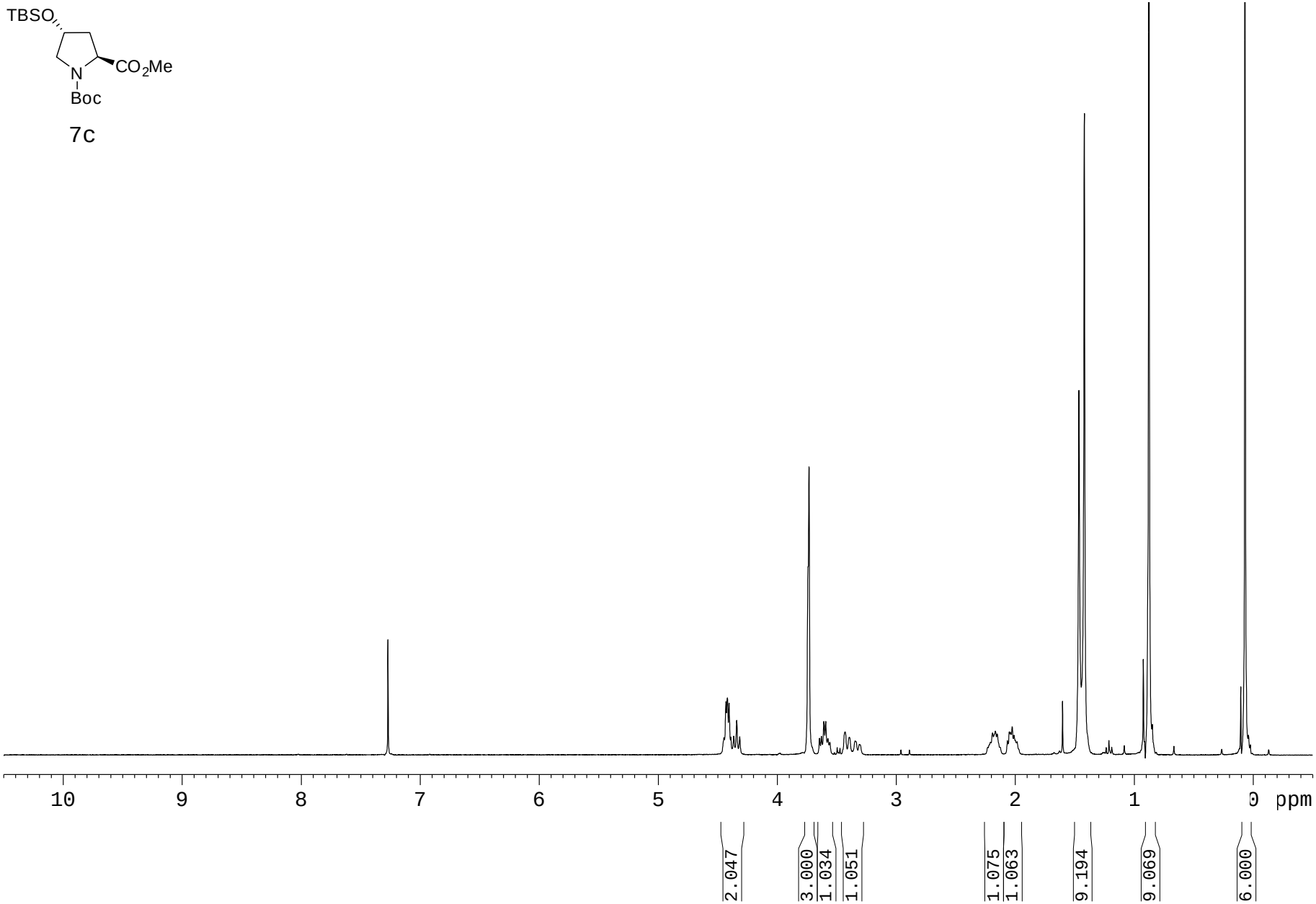

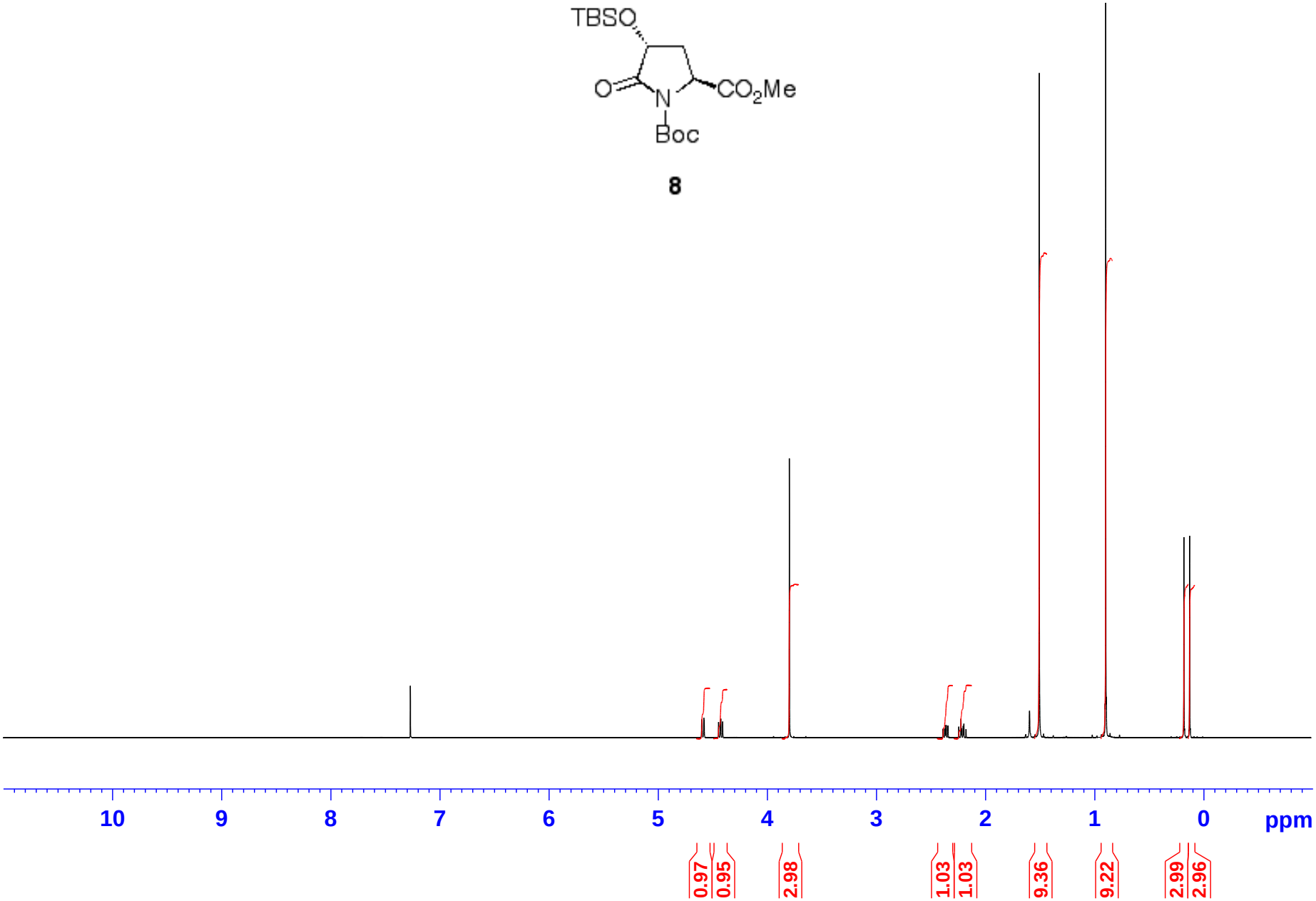
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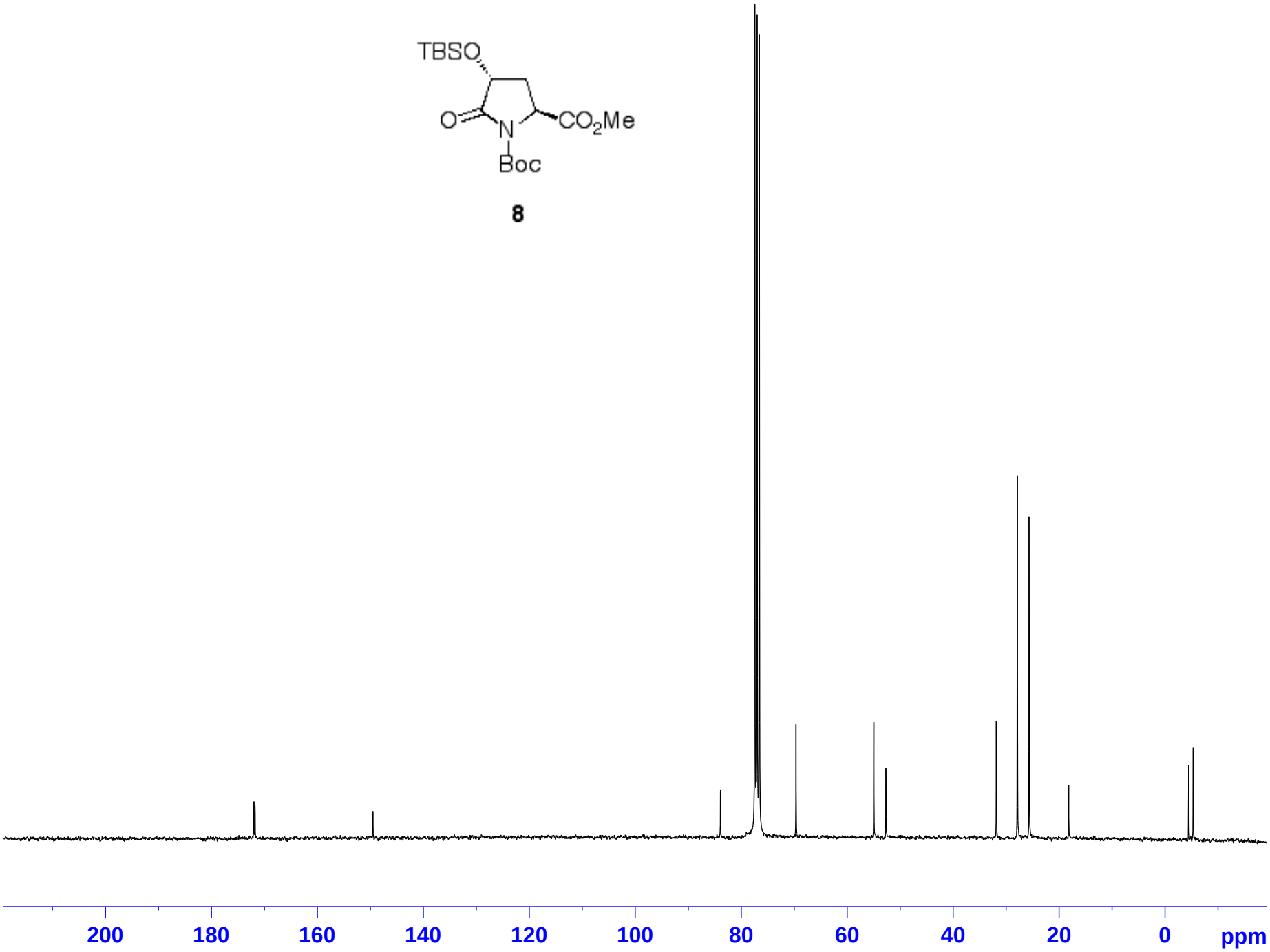

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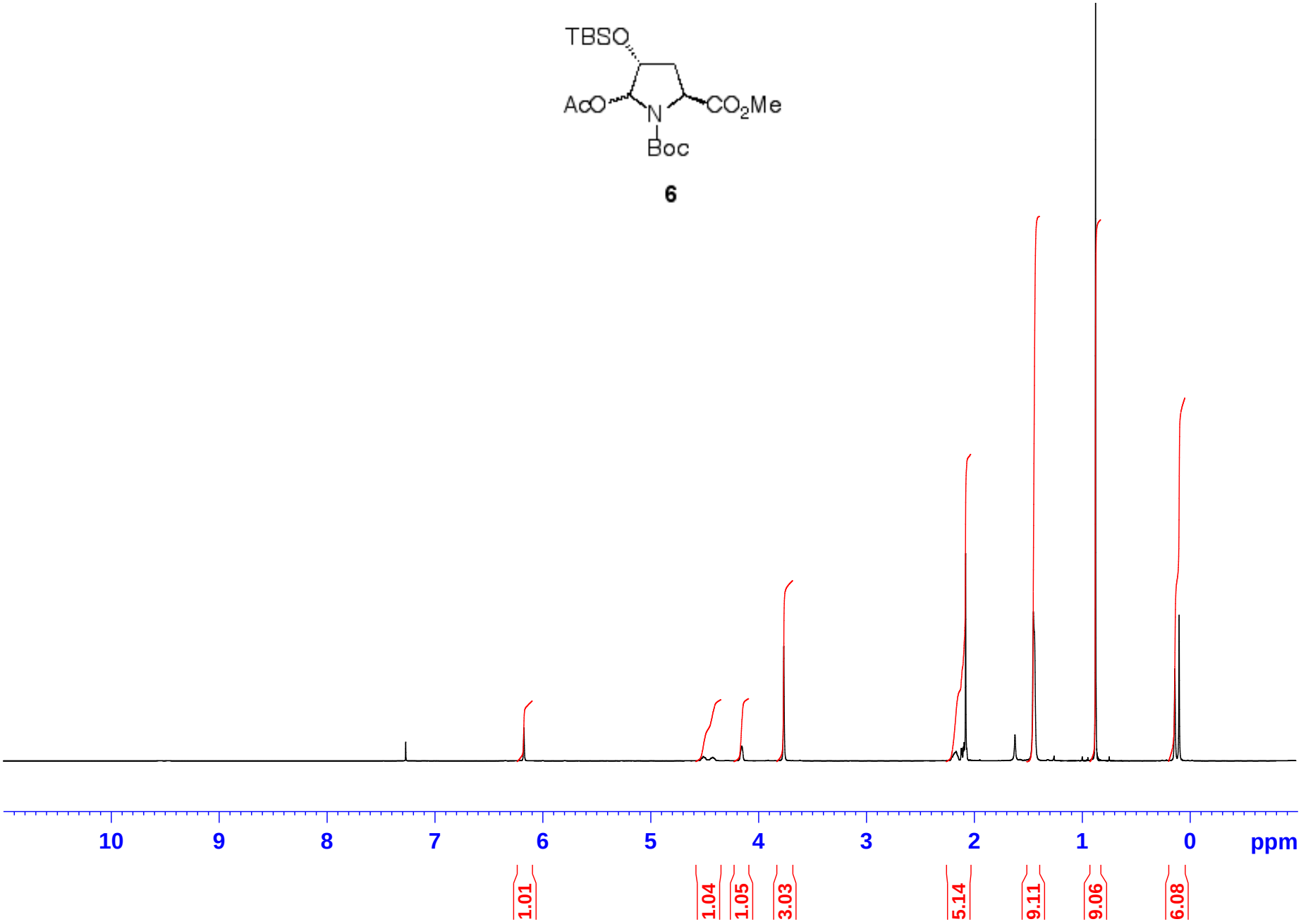
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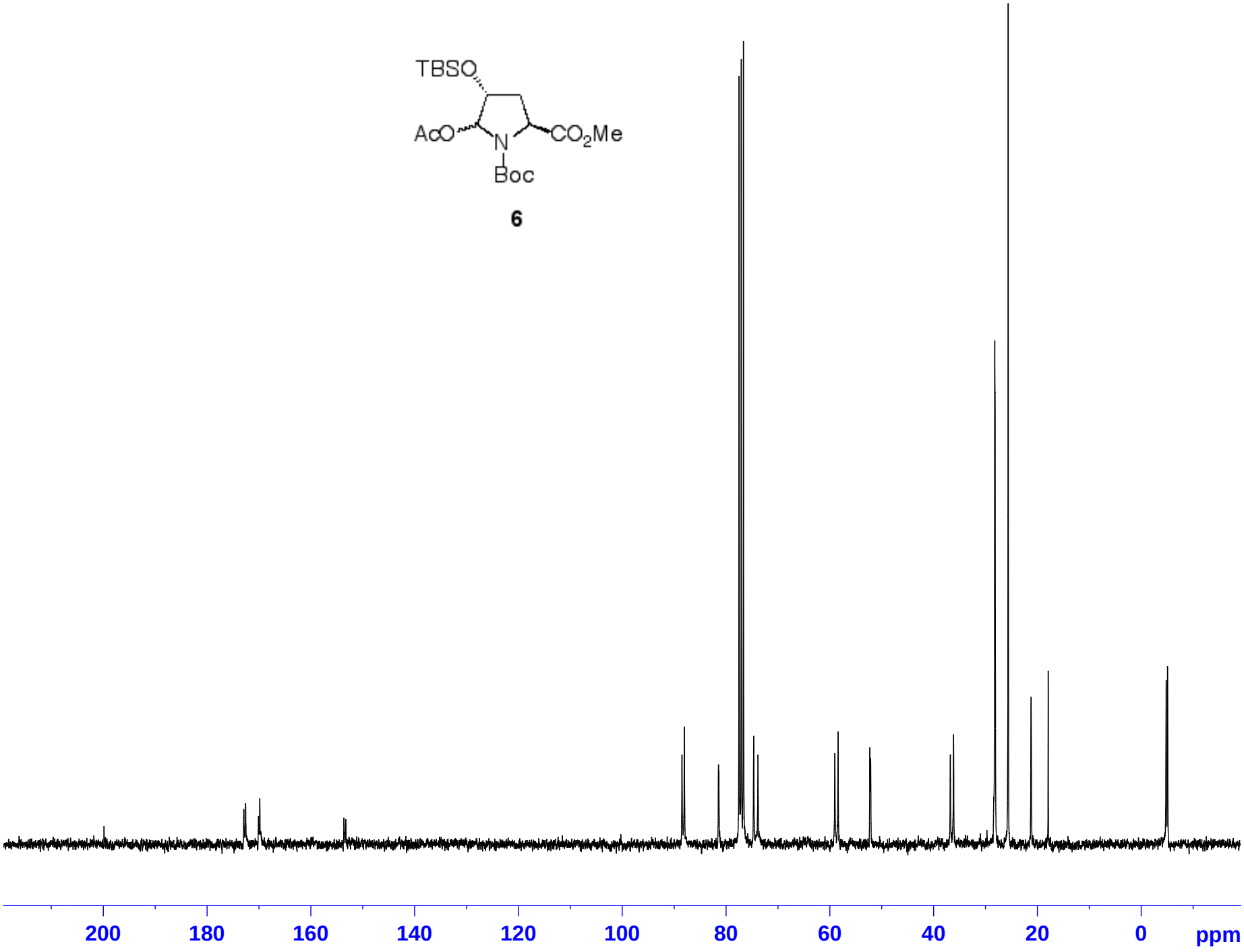
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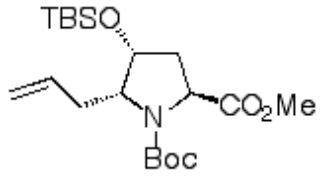
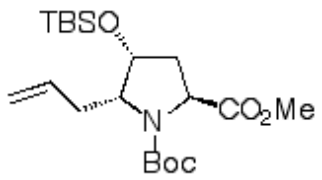


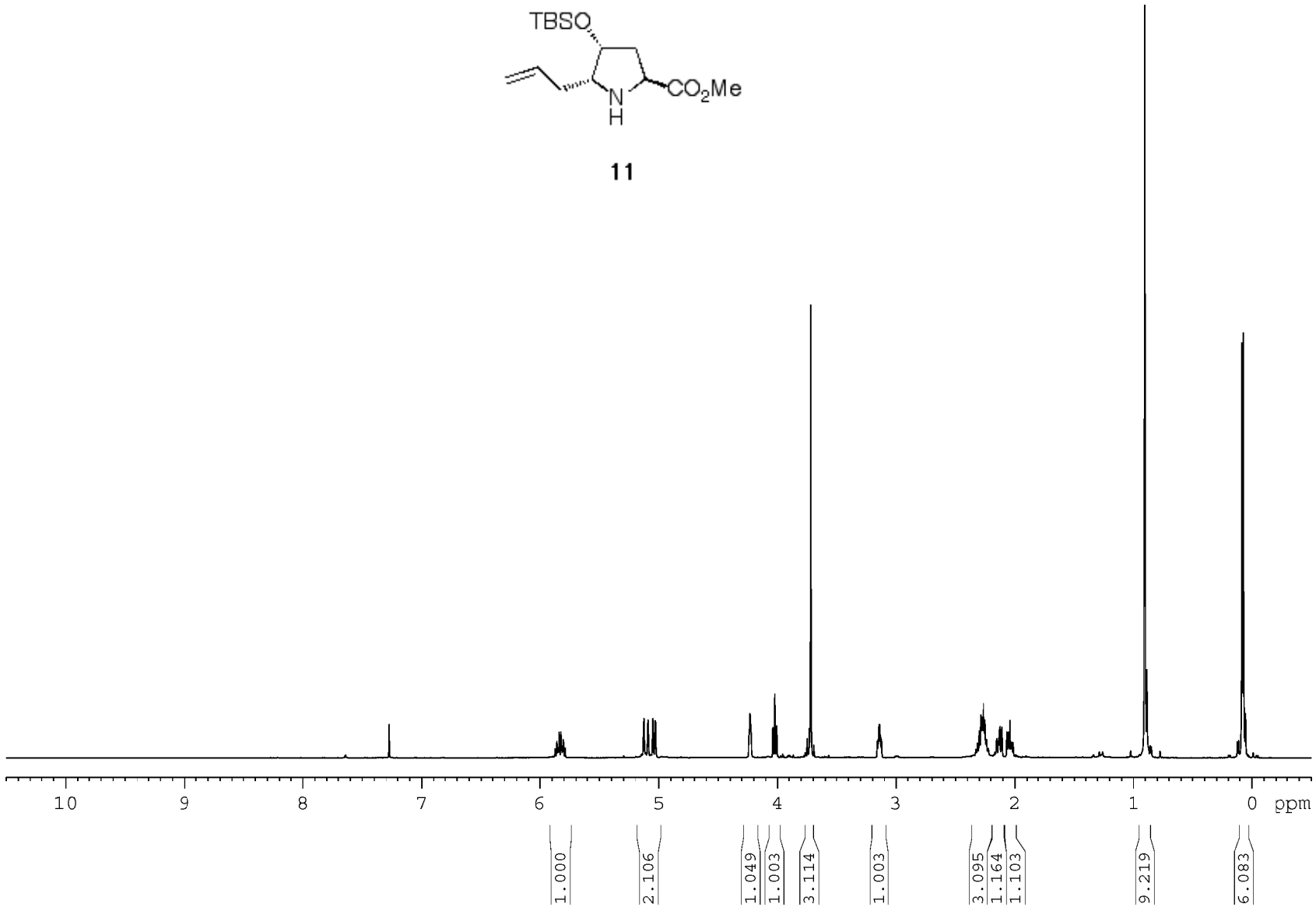
10

(4:1 mixture of diastereomers)
+ rotamers



10

(4:1 mixture of diastereomers)
+ rotamers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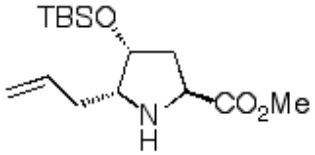

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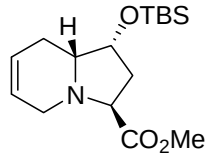
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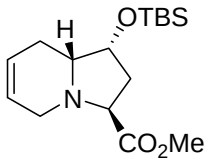
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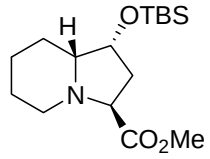
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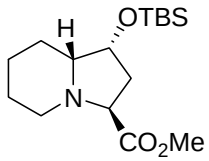
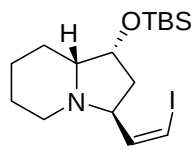


13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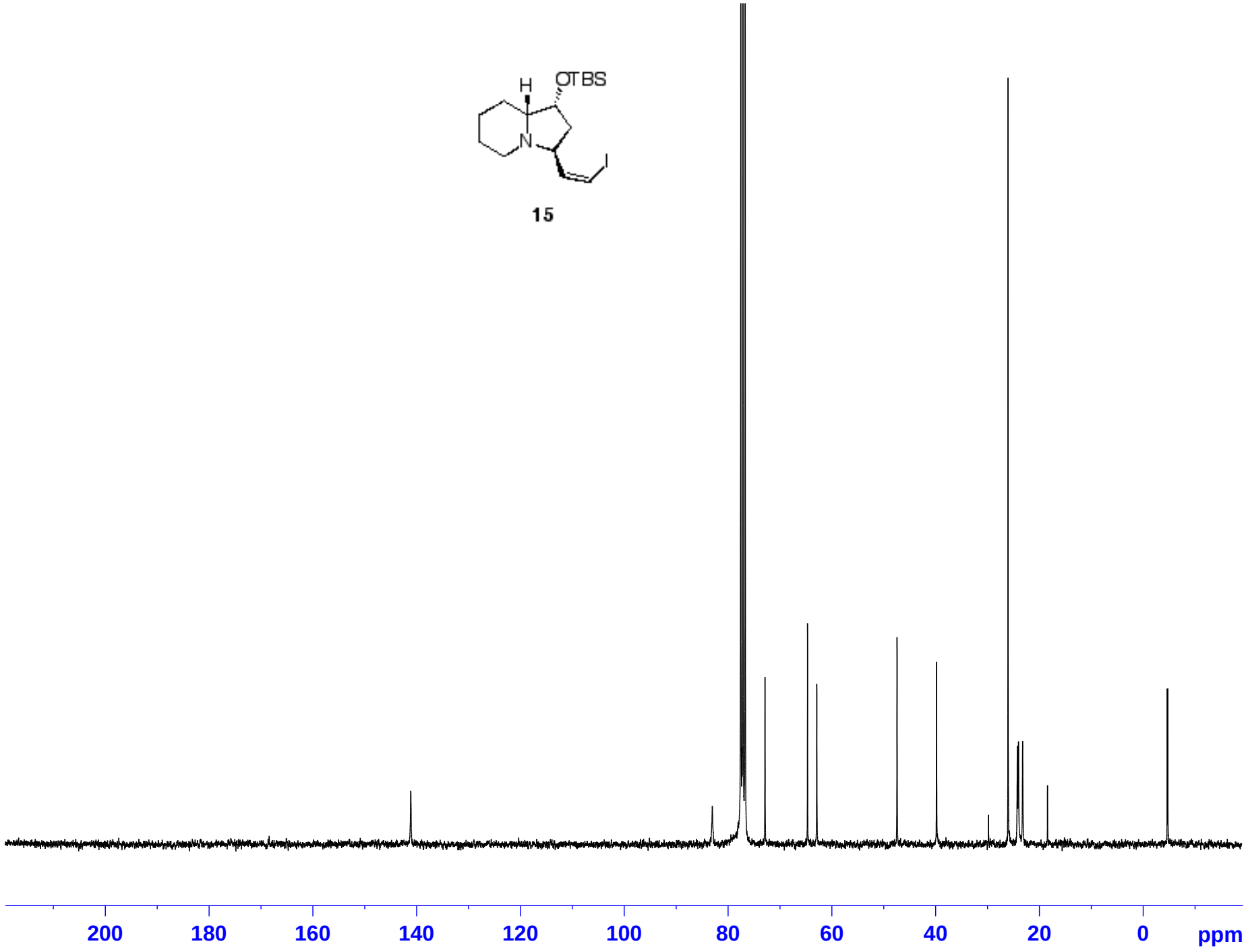
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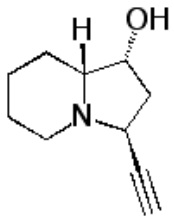

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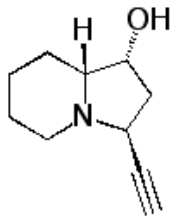

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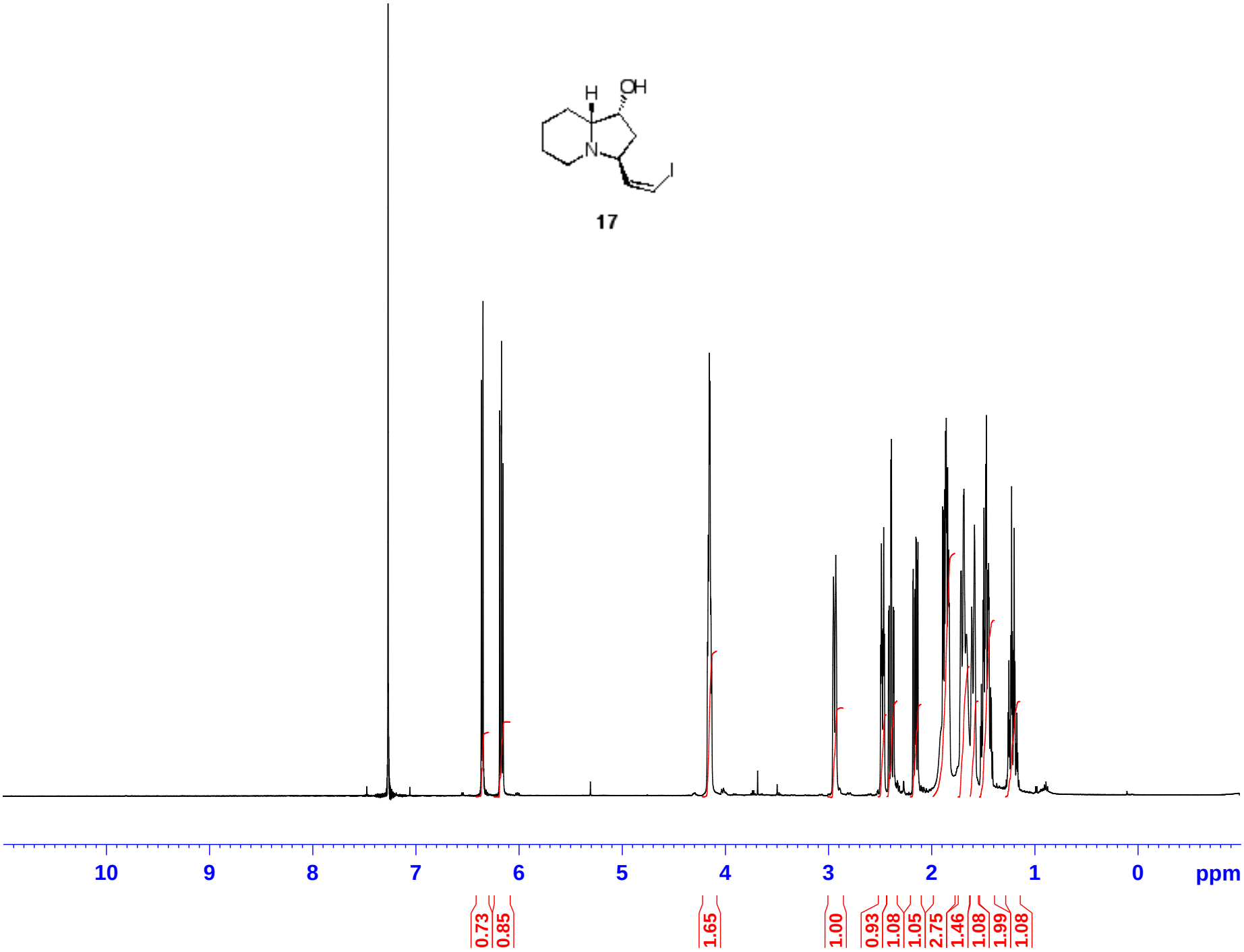
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OH
N
I
17
10
9
8
7
6
5
4
3
2
1
0
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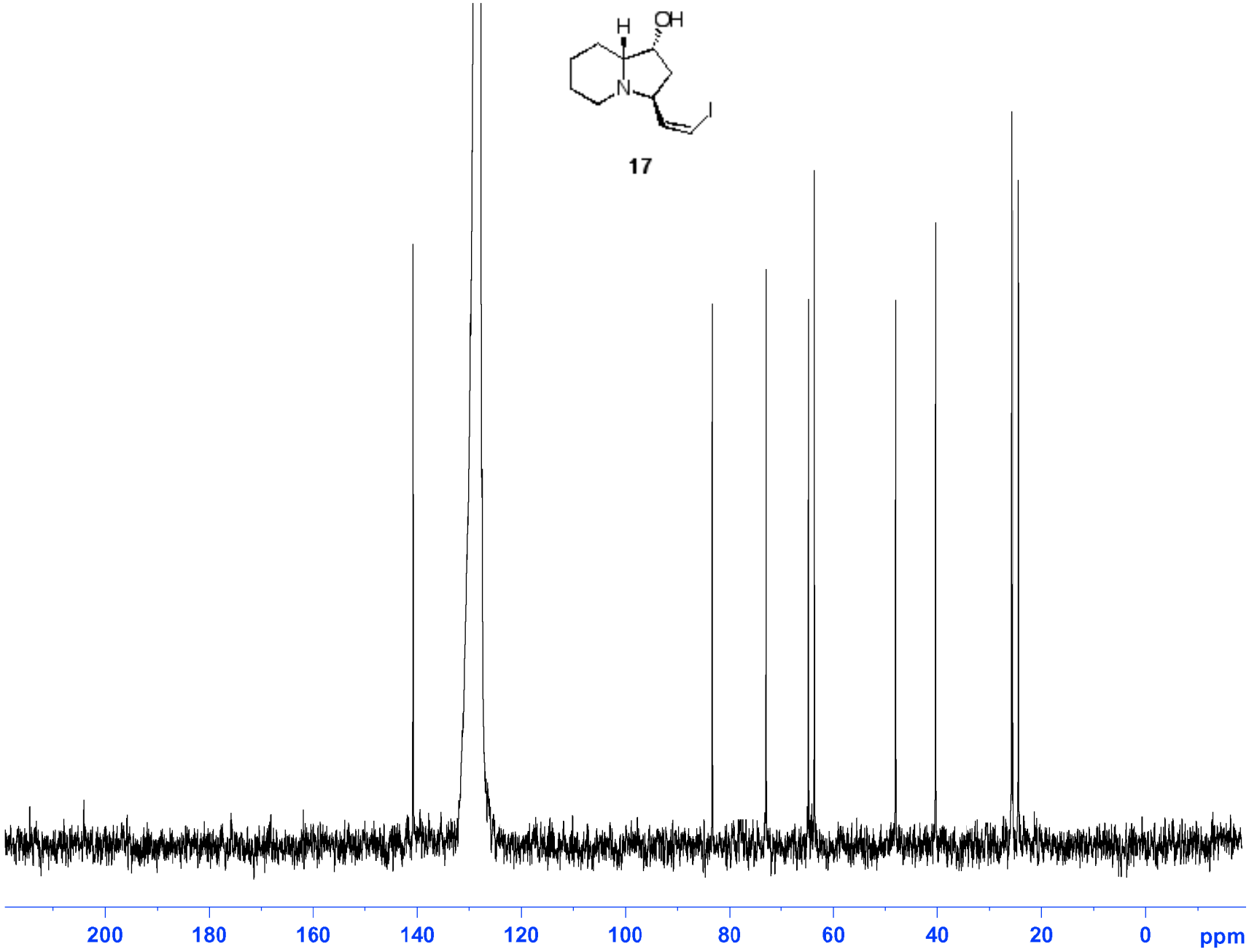
1.00
0.93
1.08
1.05
2.75
1.46
1.08
1.99
1.08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OH
N
I
17
200
180
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140
120
100
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60
40
20
0
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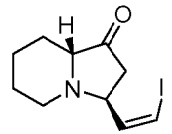
H
O
N
I

5

10
9
8
7
6
5
4
3
2
1
0 ppm
1.001
1.000
1.000
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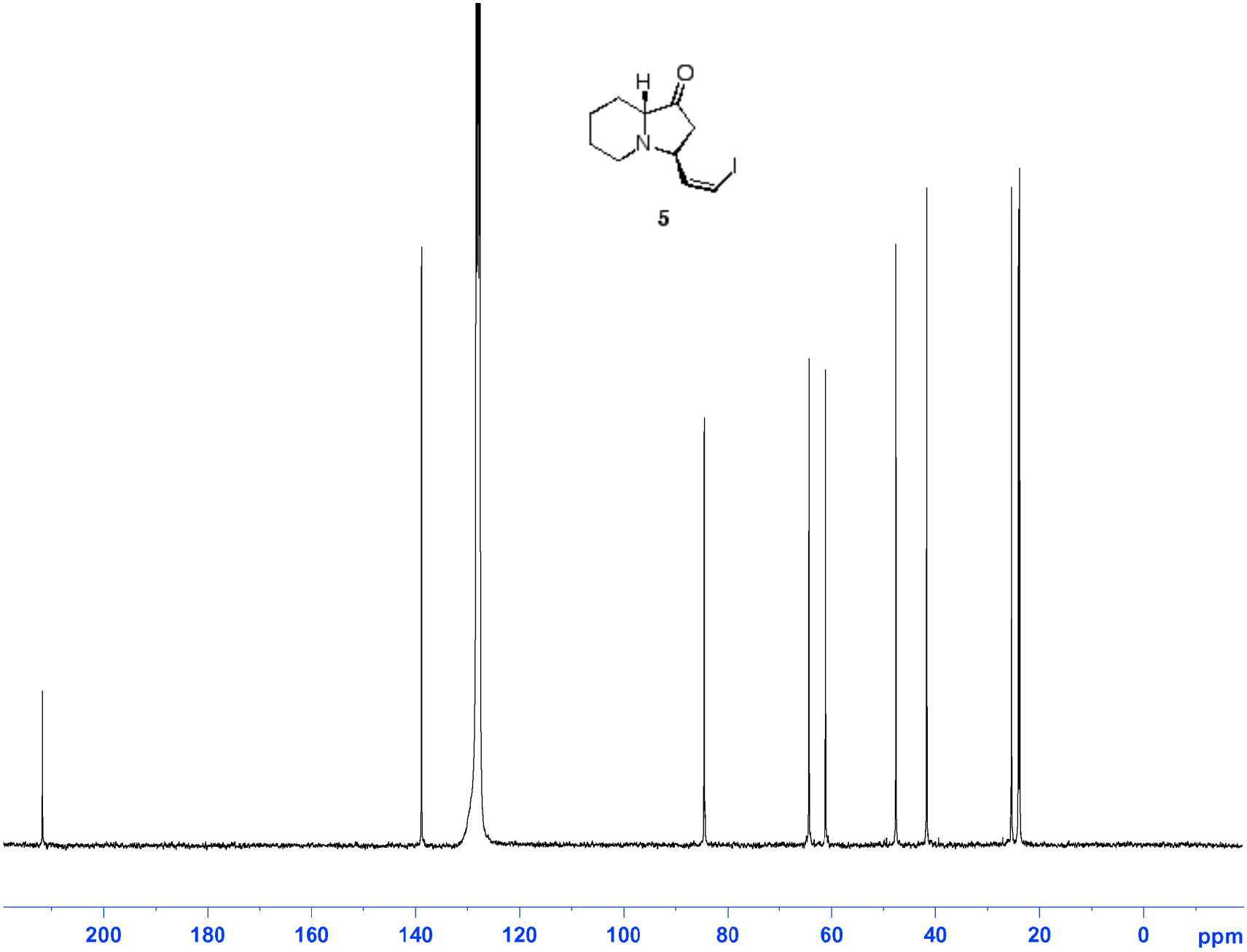
1.023
1.062
1.089
0.634
1.531
1.090
1.135
2.035
1.043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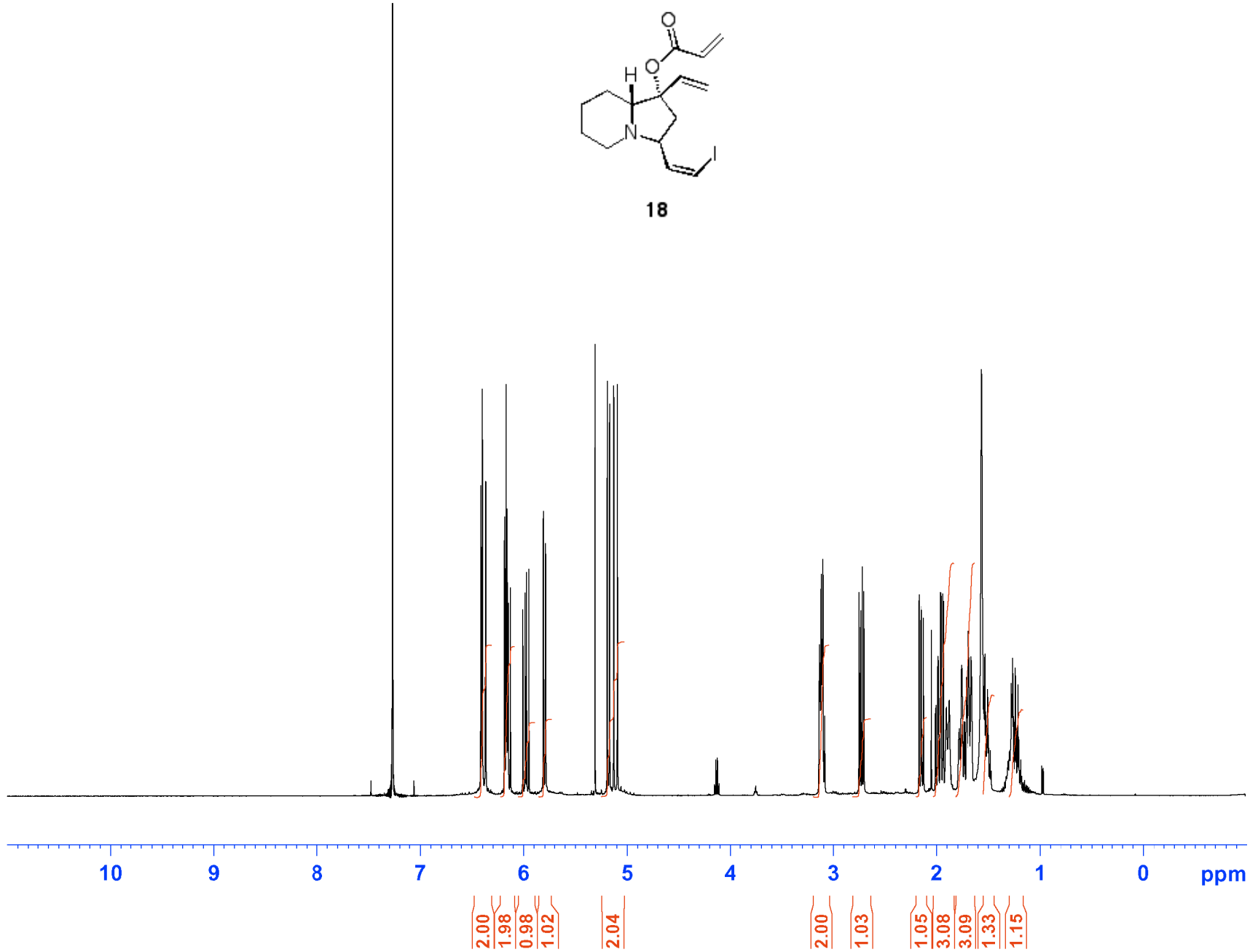
N
I
5
200
180
160
140
120
100
80
60
40
20
0
ppm


O
O
H
N
I
18
10
9
8
7
6
5
4
3
2
1
0
ppm
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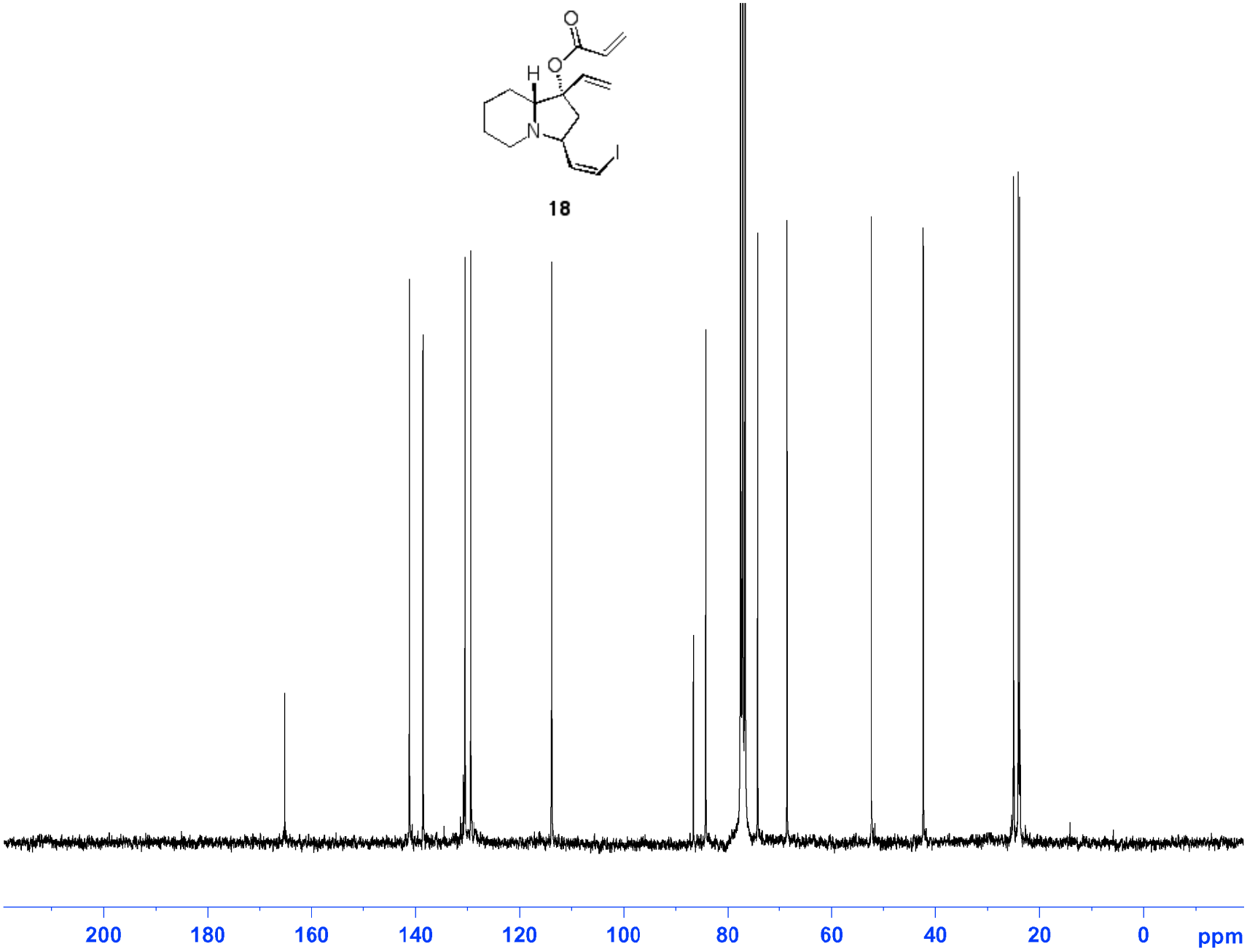
0.98
1.02
2.04
2.00
1.03
1.05
3.08
3.09
1.33
1.15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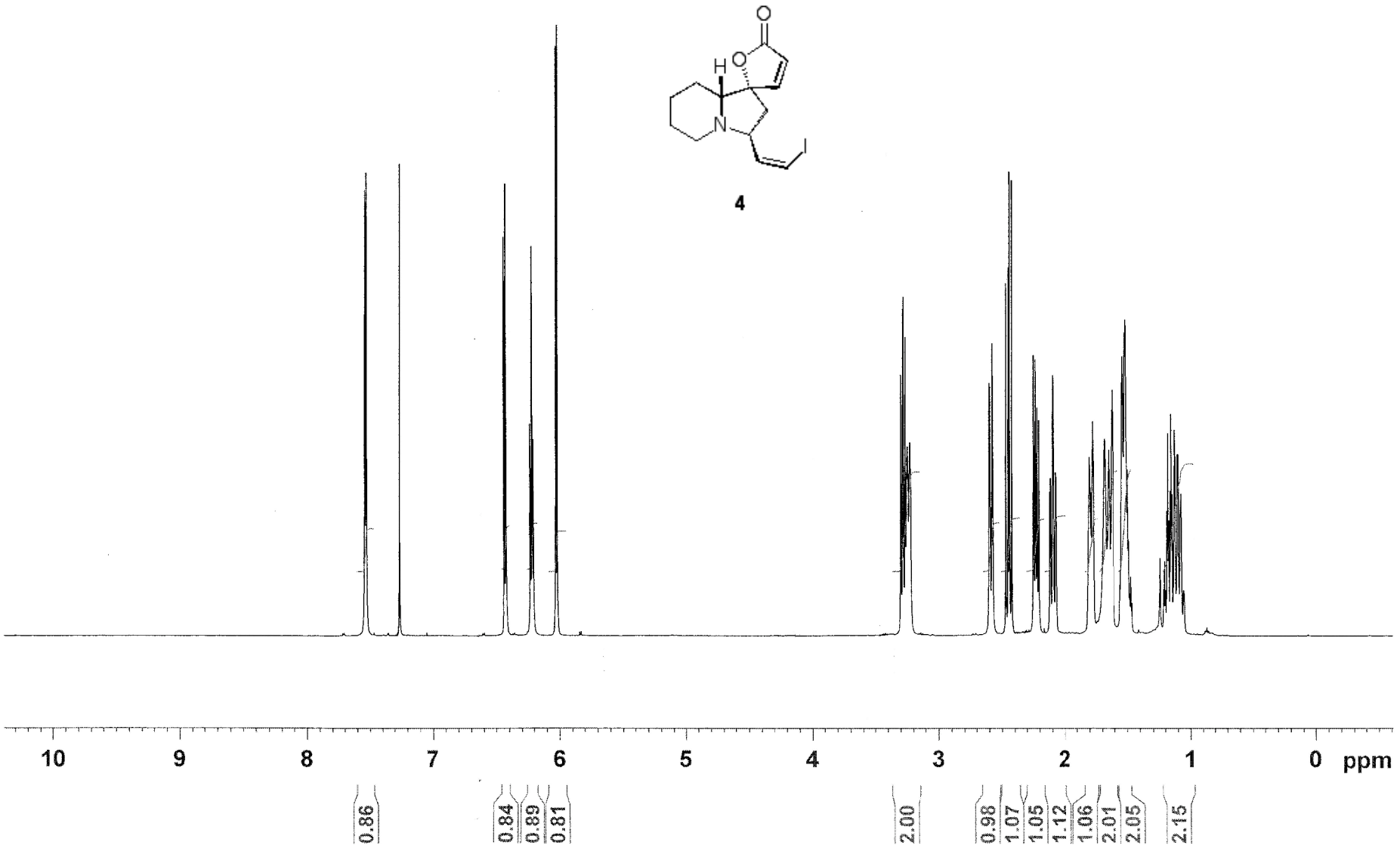
H
N
I
18
200
180
160
140
120
100
80
60
40
20
0
ppm


O
H
O
N
I
4
10
9
8
7
6
5
4
3
2
1
0
ppm
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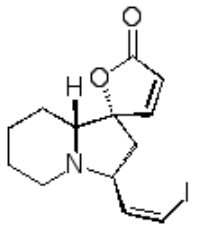
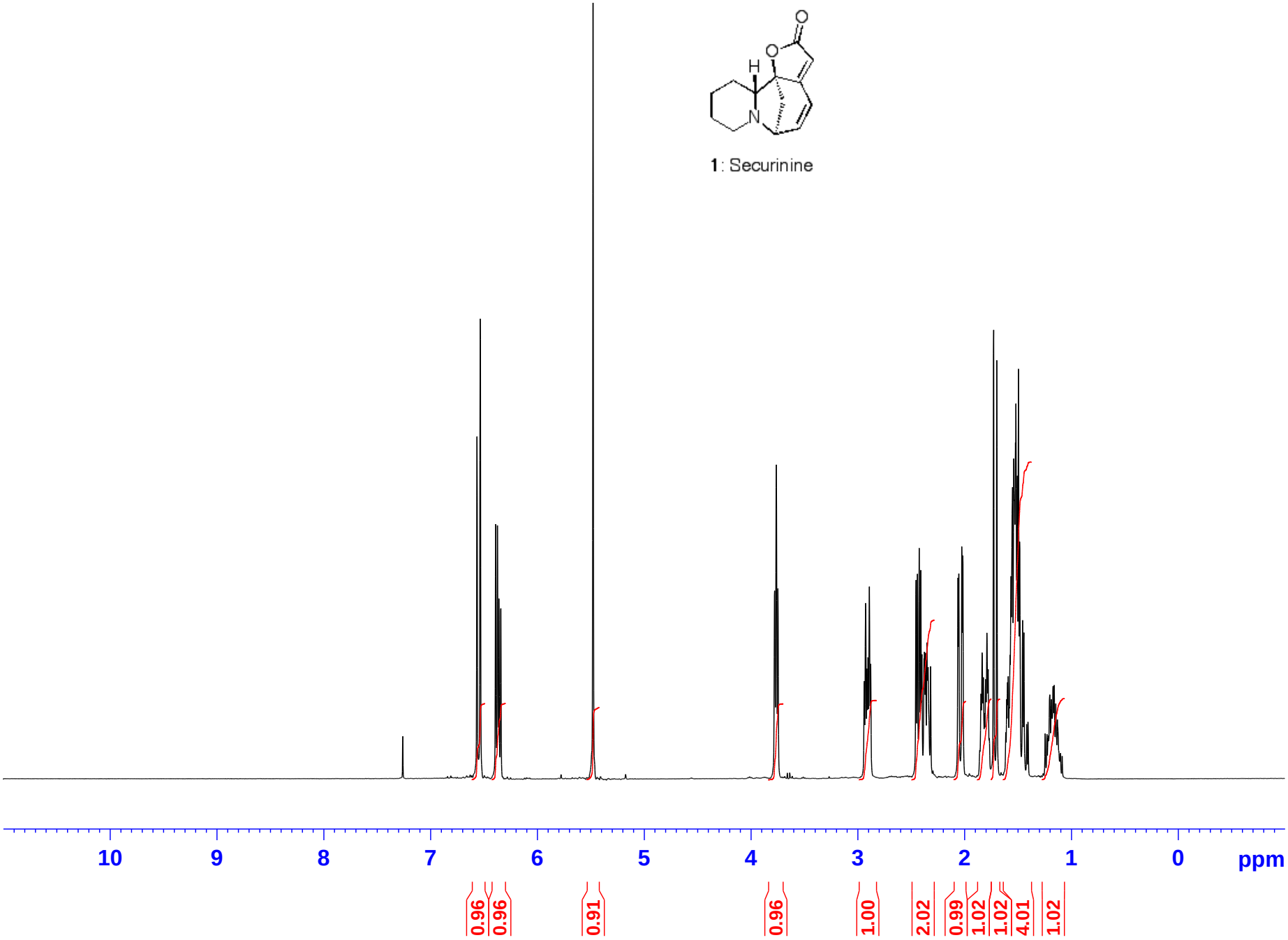
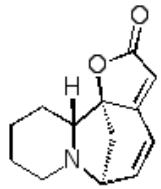
2.00
0.98
1.07
1.05
1.12
1.06
2.01
2.05
2.15



4


O
O
H
N
1: Securinine
10
9
8
7
6
5
4
3
2
1
0
ppm
0.96
0.96
0.91
0.96
1.00
2.02
0.99
1.02
1.02
4.01
1.02



1: Securinine