DMSO-$K_2S_2O_8$ Mediated Iodine free Conversion of Glycal C-3 Ether to 3-Enopyranones: Synthesis of Furo[3,2-c] Pyrans

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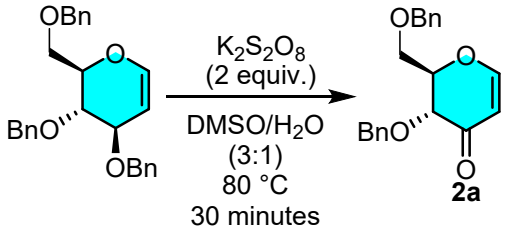
1. General Consideration:

^{1}H and ^{13}C NMR spectra were recorded using 400 MHz and 101 MHz spectrometers with TMS as internal standards. Chemical shifts are expressed in parts per million (δ ppm). Silica gel-coated aluminum plates were used for TLC. The products were purified by column chromatography on silica gel (60- 120 mesh) using Hexane–ethyl acetate as the eluent to obtain the pure products. The Exact masses of all products were derived by using HRMS having a QTOF analyzer. Reagents used were mostly purchased from Sigma Aldrich, TCI, and Avra.

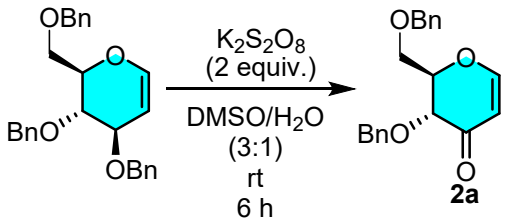
2.1 General experimental procedures for the synthesis of 3-keto glycals

2.1a Method A:



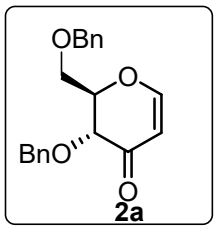
By taking Tri-*O*-benzyl-D-glucal as an example. A round bottom flask equipped with a magnetic stir bar was charged with Tri-*O*-benzyl-D-glucal (1 equiv.) and dissolved in DMSO /H_2O (3:1). To this stirred solution was added $K_2S_2O_8$ (2 equiv.) and stirred at 80 °C for 30 minutes. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was treated with ice-cold water and then extracted with ethyl acetate thrice, the organic phase was dried over sodium sulfate and evaporated under reduced pressure to get the crude product which was purified by filtration through a short pad of silica gel column (hexane: ethyl acetate;95:5) to afford **2a**.

2.1b Method B:

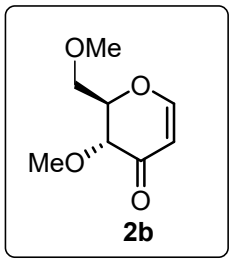


By taking Tri-*O*-benzyl-D-glucal as an example. A round bottom flask equipped with a magnetic stir bar was charged with Tri-*O*-benzyl-D-glucal (1 equiv.) and dissolved in DMSO /H_2O (3:1). To this stirred solution was added $K_2S_2O_8$ (2 equiv.) and stirred at room temperature for 6 hours. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was treated with ice-cold water and then extracted with ethyl acetate thrice, the organic phase was dried over sodium sulfate and evaporated under reduced pressure to get the crude product which was purified by filtration through a short pad of silica gel column (hexane: ethyl acetate;95:5) to afford **2a**.

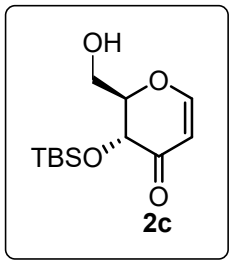
2.2 Characterization data & NMR spectra of 3-keto glycals



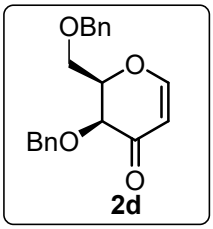
The compound **2a** was synthesized according to the general procedure **(2.1a Method A)** using Tri-*O*-benzyl-D-glucal (50 mg, 0.12 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane /ethyl acetate (95:05) as eluent to obtain **2a** as a yellow gummy liquid (77 % yield, 30 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.28 (d, J = 4.4 Hz, 3H), 7.27 (d, J = 1.2 Hz, 1H), 7.24 (d, J = 1.1 Hz, 4H), 7.22 (d, J = 1.7 Hz, 2H), 5.30 (d, J = 5.9 Hz, 1H), 4.99 (d, J = 11.1 Hz, 1H), 4.60 (s, 1H), 4.52 (d, J = 9.0 Hz, 1H), 4.50 (d, J = 9.9 Hz, 1H), 4.44 (d, J = 12.1 Hz, 1H), 4.34 (dt, J = 11.6, 3.2 Hz, 1H), 4.16 (d, J = 11.6 Hz, 1H), 3.72 (d, J = 3.2 Hz, 2H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 193.6 (Cq), 162.3, 137.5 (Cq), 137.4 (Cq), 128.5, 128.45, 128.4, 128.39, 128.3, 128.0, 127.9, 127.8, 105.2, 81.0, 74.6 (CH_2), 74.1, 73.6 (CH_2), 67.9 (CH_2). **HRMS (ESI, m/z)** for $C_{20}H_{21}O_4$ $[M+H]^+$: calcd 325.1440, found, 325.1456.



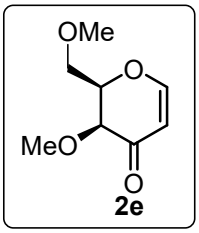
The compound **2b** was synthesized according to the general procedure **(2.1a Method A)** using Tri-*O*-methyl-D-glucal (50 mg, 0.26 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane /ethyl acetate (92:08) as eluent to obtain yellow gummy liquid (77 % yield, 35.2 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.25 (d, *J* = 5.8 Hz, 1H), 5.30 (dd, *J* = 5.8, 2.1 Hz, 1H), 4.28 (dt, *J* = 11.6, 3.2 Hz, 1H), 3.89 (dd, *J* = 11.6, 2.1 Hz, 1H), 3.69 (d, *J* = 3.4 Hz, 2H), 3.57 (s, 3H), 3.39 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 193.4 (Cq), 162.2, 105.0, 80.9, 76.9, 70.3 (CH_2), 60.7 (CH_3), 59.4 (CH_3). **HRMS (ESI, m/z)** for $C_8H_{13}O_4$ $[M+H]^+$: calcd 173.0814, found, 173.0821.



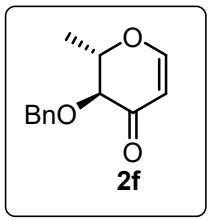
The compound **2c** was synthesized according to the general procedure **(2.1a Method A)** using Tri-*O*-tertbutyldimethylsilyl-D-glucal (50 mg, 0.10 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (98:02) as eluent to obtain yellow gummy liquid (83 % yield, 30.3 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.21 (d, *J* = 5.8 Hz, 1H), 5.26 (dd, *J* = 5.8, 1.0 Hz, 1H), 4.32 (d, *J* = 12.5 Hz, 1H), 4.15 (dt, *J* = 12.7, 3.3 Hz, 1H), 3.95 (dd, *J* = 12.3, 2.6 Hz, 1H), 3.85 (dd, *J* = 12.3, 4.0 Hz, 1H), 0.82 (d, *J* = 1.0 Hz, 10H), 0.13 (s, 3H), 0.00 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 193.9 (Cq), 161.8, 105.0, 83.2, 69.8, 61.3 (CH_2), 25.8 (CH_3),18.5 (Cq), -4.0 (CH_3), -5.6 (CH_3). **HRMS (ESI, m/z)** for $C_{12}H_{22}O_4SiNa$ $[M+Na]^+$: calcd 281.1185, found, 281.1197.



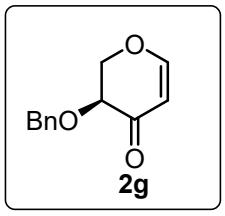
The compound **2d** was synthesized according to the general procedure **(2.1a Method A)** using Tri-*O*-benzyl-D-galactal (50 mg, 0.12 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane /ethyl acetate (95:05) as eluent to obtain yellow gummy liquid (78 % yield, 29.64 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.32 – 7.10 (m, 11H), 5.35 (dd, *J* = 6.1, 1.6 Hz, 1H), 4.63 (d, *J* = 11.9 Hz, 1H), 4.49 (d, *J* = 11.9 Hz, 1H), 4.43 (s, 1H), 4.41 – 4.36 (m, 2H), 3.83 (dd, *J* = 10.2, 7.1 Hz, 1H), 3.66 (dd, *J* = 10.2, 5.3 Hz, 1H), 3.61 (t, *J* = 2.1 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 189.5 (Cq), 162.8, 137.5 (Cq), 137.0 (Cq), 128.6, 128.5, 128.46, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 105.2, 80.6, 77.5, 77.1, 76.8, 74.2, 73.7 (CH_2), 72.0 (CH_2), 67.6 (CH_2). **HRMS (ESI, m/z)** for $C_{20}H_{21}O_4$ $[M+H]^+$: calcd 325.1440, found, 325.1451.



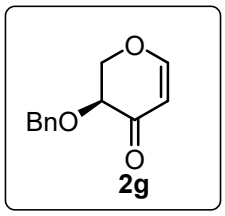
The compound **2e** was synthesized according to the general procedure **(2.1a Method A)** using Tri-*O*-methyl-D-galactal (50 mg, 0.26 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane /ethyl acetate (92:08) as eluent to obtain yellow gummy liquid (70 % yield, 31.4 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.31 (d, *J* = 6.0 Hz, 1H), 5.36 (dd, *J* = 6.1, 1.7 Hz, 1H), 4.42 (ddd, *J* = 7.4, 4.9, 2.5 Hz, 1H), 3.79 (dd, *J* = 10.5, 7.5 Hz, 1H), 3.67 (dd, *J* = 10.5, 4.8 Hz, 1H), 3.41 (t, *J* = 2.1 Hz, 1H), 3.38 (s, 3H), 3.36 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 189.3 (Cq), 162.7, 105.0, 80.4, 77.1, 70.1 (CH_2), 59.5, 58.5. **HRMS (ESI, m/z)** for $C_8H_{13}O_4$ $[M+H]^+$: calcd 173.0814, found, 173.0819.



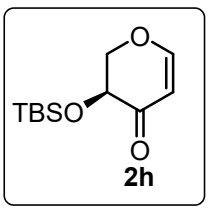
The compound **2f** was synthesized according to the general procedure **(2.1a Method A)** using 3,4-Di-*O*-benzyl-L-rhamnal (50 mg, 0.16 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane /ethyl acetate (97:04) as eluent to obtain yellow gummy liquid (80 % yield, 28.1 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.31 – 7.22 (m, 5H), 7.18 (d, *J* = 5.9 Hz, 1H), 5.30 (d, *J* = 5.9 Hz, 1H), 4.95 (d, *J* = 11.5 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 4.40 (dq, *J* = 9.7, 6.4 Hz, 1H), 3.64 (d, *J* = 9.8 Hz, 1H), 1.35 (d, *J* = 6.4 Hz, 3H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 193.1 (Cq), 162.2, 137. 4(Cq), 105.0, 78.7, 78.6, 77.4, 77.1, 76.8, 73.9, 17.2 (CH_3). **HRMS (ESI, m/z)** for $C_{13}H_{18}NO_3$ $[M+NH_4]^+$: calcd 236.1287, found, 236.1295.



The compound **2g** was synthesized according to the general procedure **(2.1a Method A)** using 3,4-Di-*O*-benzyl-D-xylal (50 mg, 0.17 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane /ethyl acetate (95:05) as eluent to obtain yellow gummy liquid (75 % yield, 26.02 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.28 – 7.23 (m, 5H), 7.21 (d, *J* = 6.0 Hz, 1H), 5.30 (dd, *J* = 5.9, 0.9 Hz, 1H), 4.73 (d, *J* = 11.9 Hz, 1H), 4.54 (d, *J* = 16.6 Hz, 1H), 4.35 (dd, *J* = 12.3, 6.3 Hz, 1H), 4.24 (dd, *J* = 12.4, 4.0 Hz, 1H), 3.74 – 3.68 (m, 1H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 190.5 (Cq), 163.2, 137.2 (Cq), 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 105.3, 73.6, 72.5 (CH_2), 71.3 (CH_2). **HRMS (ESI, m/z)** for $C_{12}H_{16}NO_3$ $[M+NH_4]^+$: calcd 222.1130, found, 222.1143.

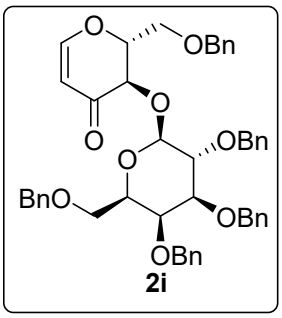


The compound **2g** was synthesized according to the general procedure **(2.1a Method A)** using 3,4-Di-*O*-benzyl-L-arabinal (50 mg, 0.17 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane /ethyl acetate (95:05) as eluent to obtain yellow gummy liquid (75 % yield, 25.7 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.27 (h, *J* = 3.5, 2.9 Hz, 5H), 7.22 (d, *J* = 6.1 Hz, 1H), 5.35 – 5.28 (m, 1H), 4.75 (dd, *J* = 12.0, 2.8 Hz, 1H), 4.51 (dd, *J* = 11.9, 2.8 Hz, 1H), 4.37 (ddt, *J* = 12.4, 6.4, 2.3 Hz, 1H), 4.29 – 4.23 (m, 1H), 3.73 (dd, *J* = 6.3, 3.7 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$) δ** 190.5 (Cq), 163.2, 137.2 (Cq), 128.54, 128.5, 128.2, 128.1, 105.3, 73.6, 72.5 (CH_2), 71.2 (CH_2). **HRMS (ESI, m/z)** for $C_{12}H_{13}O_3$ $[M+H]^+$: calcd 205.0865, found, 205.0870.



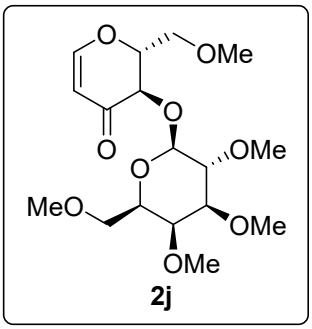
The compound **2h** was synthesized according to the general procedure **(2.1a Method A)** using 3,4-Di-*O*-tertbutyldimethylsilyl-L-Arabinal (50 mg, 0.145 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (98:02) as eluent to obtain yellow gummy liquid (75 % yield, 21.9 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.17 (d, *J* = 5.9

Hz, 1H), 5.24 (d, *J* = 5.9 Hz, 1H), 4.32 – 4.22 (m, 1H), 4.15 – 4.06 (m, 2H), 0.78 (s, 9H), 0.05 (s, 3H), 0.00 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 192.2 (Cq), 162.7, 105.1, 72.4, 69.4, 25.7 (CH_3), 18.4 (Cq), -4.6 (CH_3), -5.4 (CH_3). **HRMS (ESI, m/z)** for $C_{11}H_{21}O_3Si$ $[M+H]^+$: calcd 229.1260, found, 229.1267.



2i

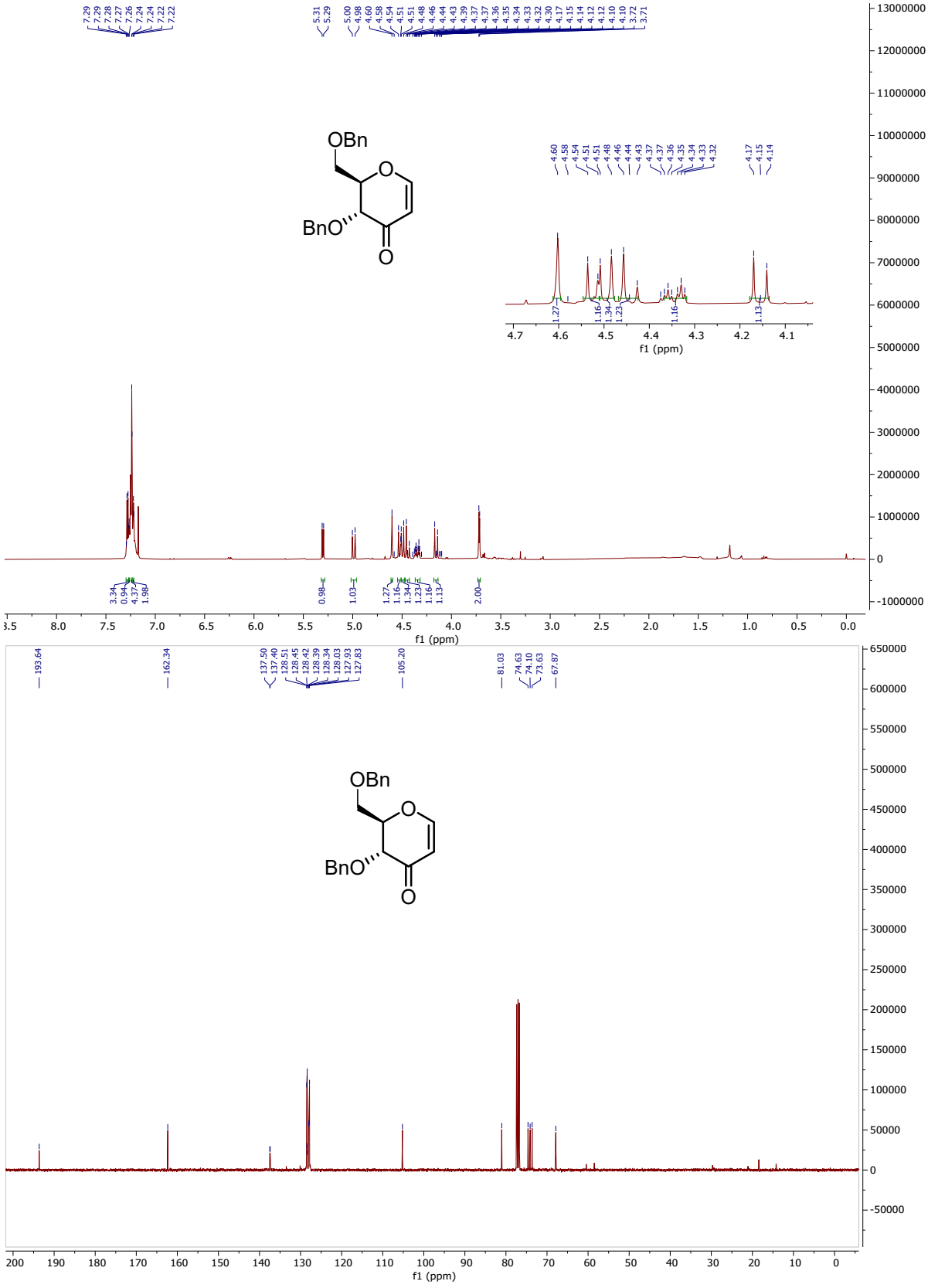
The compound **2i** was synthesized according to the general procedure **(2.1a Method A)** using 3,6-Di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-D-glucal (50 mg, 0.059 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane /ethyl acetate (95:05) as eluent to obtain yellow gummy liquid (70 % yield, 31.2 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.21 (m, 14H), 7.18 (m, *J* = 8.7 Hz, 12H), 5.28 (d, *J* = 5.9 Hz, 1H), 4.84 (dd, *J* = 11.7, 4.2 Hz, 1H), 4.73 (d, *J* = 10.3 Hz, 2H), 4.62 (s, 3H), 4.50 (dd, *J* = 11.5, 5.7 Hz, 2H), 4.40 (d, 2H), 4.32 (d, 2H), 3.85 – 3.78 (m, 2H), 3.75 – 3.70 (m, 1H), 3.60 (d, *J* = 11.0 Hz, 1H), 3.53 – 3.43 (m, 3H), 3.36 (d, 2H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 190.3 (Cq), 161.8, 138.8 (Cq), 138.7 (Cq), 138.6 (Cq), 138.4 (Cq), 138.0 (Cq), 137.9 (Cq), 137.6 (Cq), 128.5, 128.46, 128.4, 128.3, 128.24, 128.2, 128.04, 128.0, 127.96, 127.93, 127.9, 127.88, 127.85, 127.81, 127.8, 127.7, 127.6, 127.6, 127.5, 105.5, 103.3, 82.5, 81.3, 79.4, 75.3, 74.9 (CH_2), 74.7, 74.6 (CH_2), 73.7, 73.51 (CH_2), 73.5, 73.4 (CH_2), 72.8 (CH_2), 68.5 (CH_2), 67.5 (CH_2). **HRMS (ESI, m/z)** for $C_{47}H_{52}NO_9$ $[M+NH_4]^+$ calcd 774.3642, found, 774.3653.



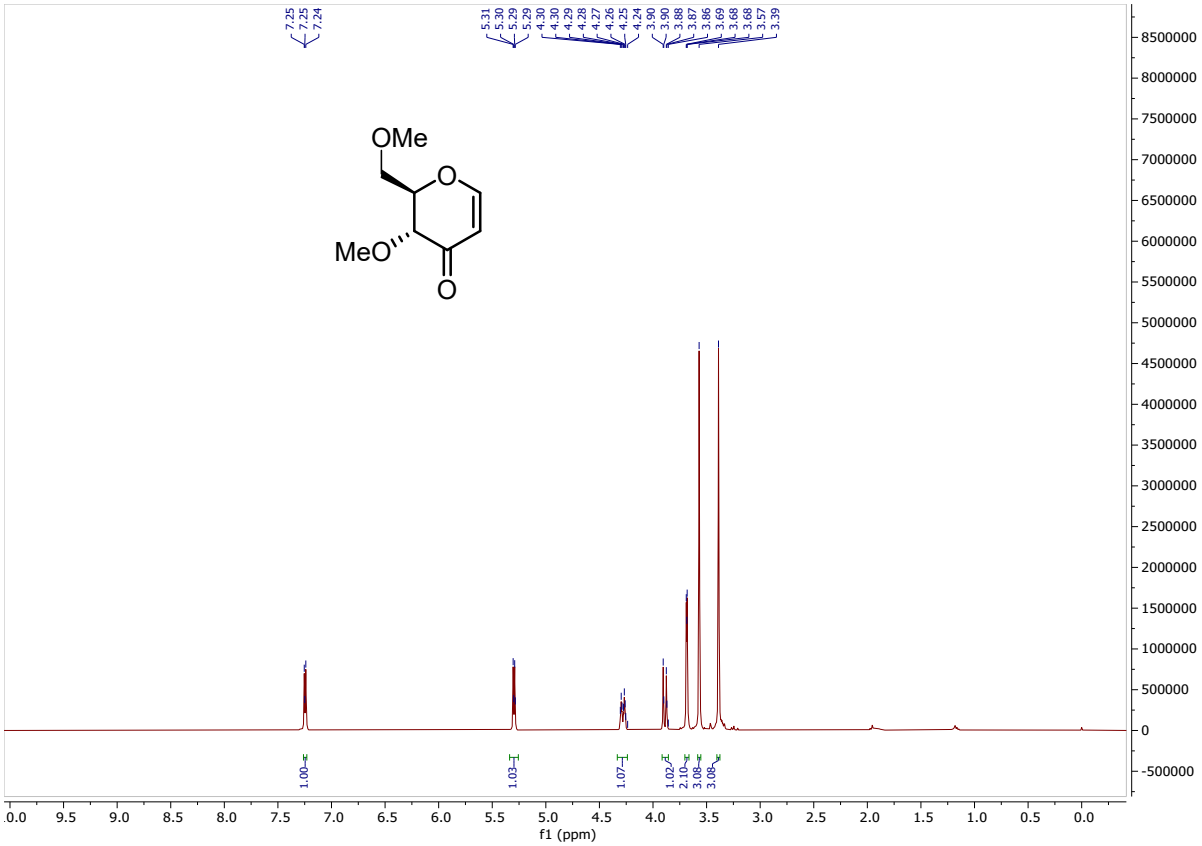
2j

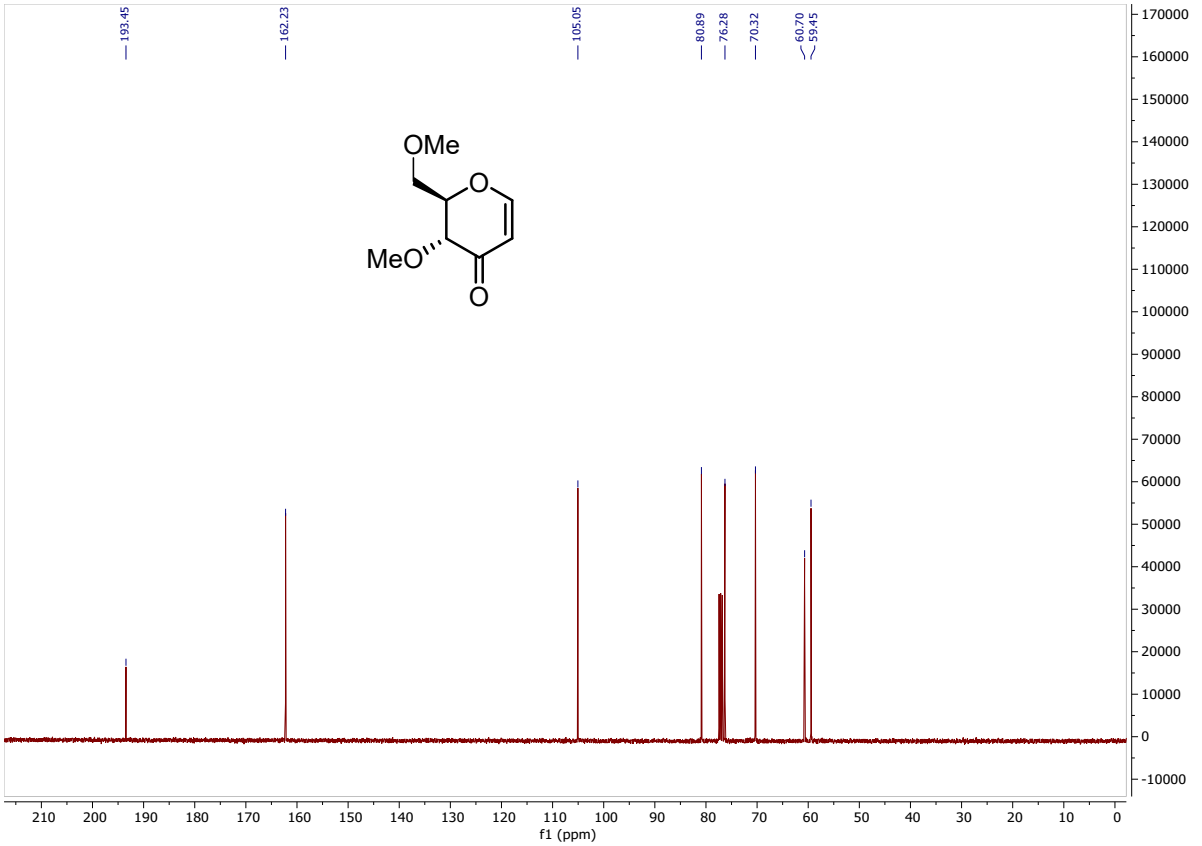
The compound **2j** was synthesized according to the general procedure **(2.1a Method A)** using 3,6-Di-*O*-methyl-4-*O*-(2,3,4,6-tetra-*O*-methyl-β-D-galactopyranosyl)-D-glucal (50 mg, 0.132 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane /ethyl acetate (90:10) as eluent to obtain yellow gummy liquid (75 % yield, 35.9 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.22 (d, *J* = 5.9 Hz, 1H), 5.31 (dd, *J* = 5.9, 0.8 Hz, 1H), 4.40 (m, *J* = 4.9 Hz, 2H), 4.31 (d, *J* = 7.6 Hz, 1H), 3.79 (dd, *J* = 11.0, 3.6 Hz, 1H), 3.72 – 3.66 (m, 1H), 3.58 (d, *J* = 3.2 Hz, 1H), 3.54 (d, *J* = 1.6 Hz, 1H), 3.51 (s, 3H), 3.48 (s, 3H), 3.45 (s, 3H), 3.41 (d, *J* = 8.4 Hz, 1H), 3.37 (s, 3H), 3.35 – 3.31 (m, 2H), 3.30 (s, 3H), 3.06 (dd, *J* = 9.6, 3.1 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 190.5 (Cq), 161.8, 105.5, 103.3, 84.3, 81.2, 80.3, 74.7, 74.4, 73.2, 70.4 (CH_2), 69.7 (CH_2), 61.1 (CH_3), 60.9 (CH_3), 59.2 (CH_3), 59.1 (CH_3), 58.1 (CH_3). **HRMS (ESI, m/z)** for $C_{17}H_{29}O_9$ $[M+H]^+$: calcd 377.1812, found, 377.1820.

^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **2a** in $CDCl_3$

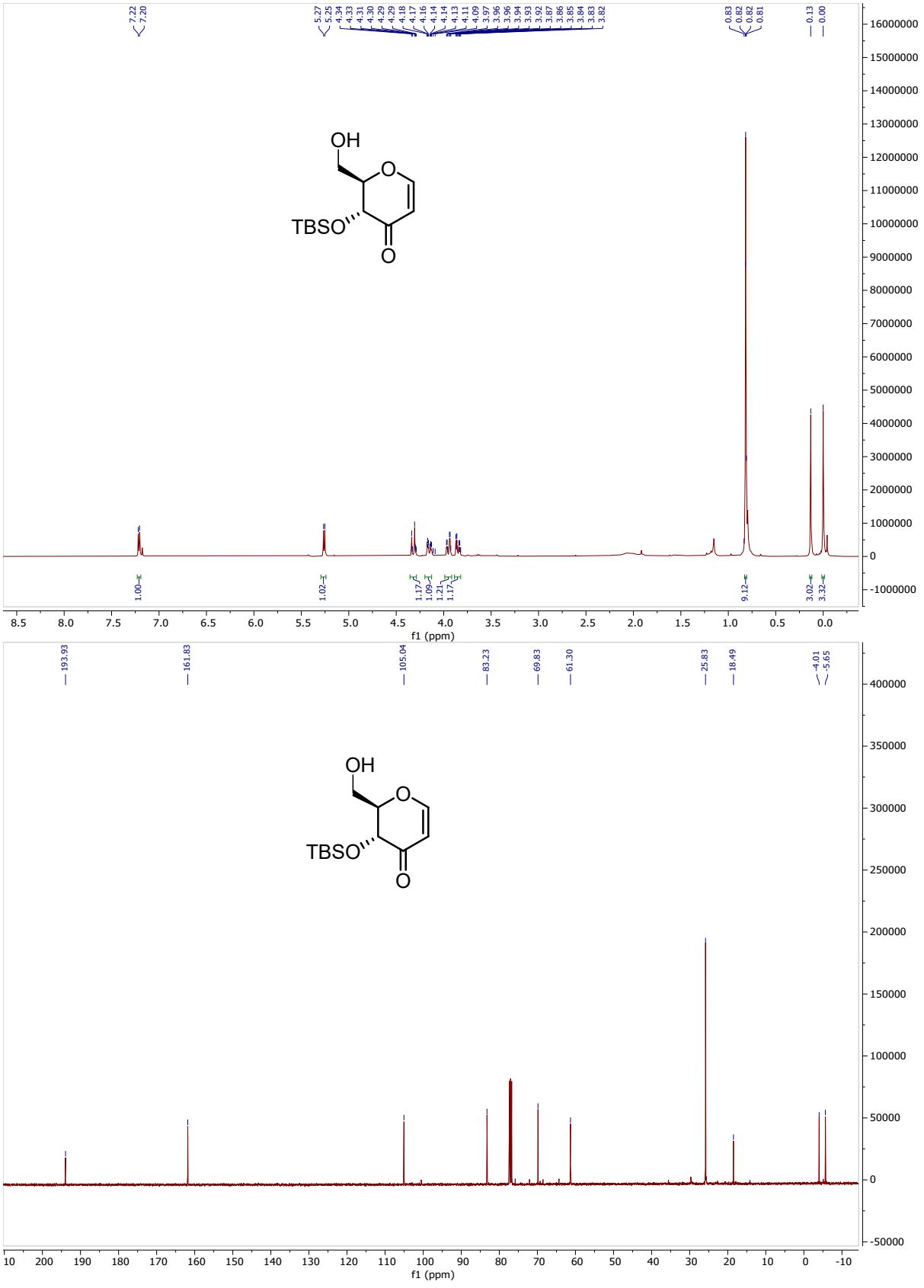


^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **2b** in $CDCl_3$

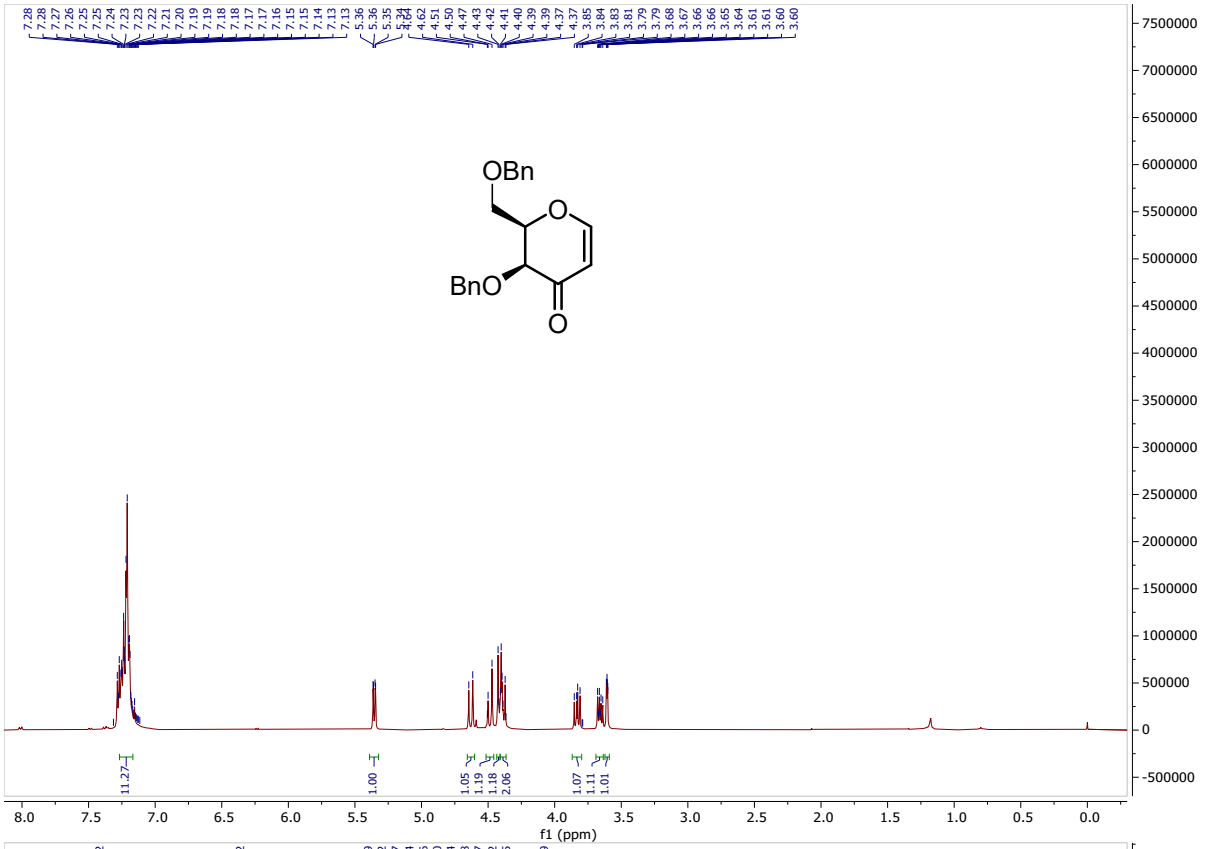


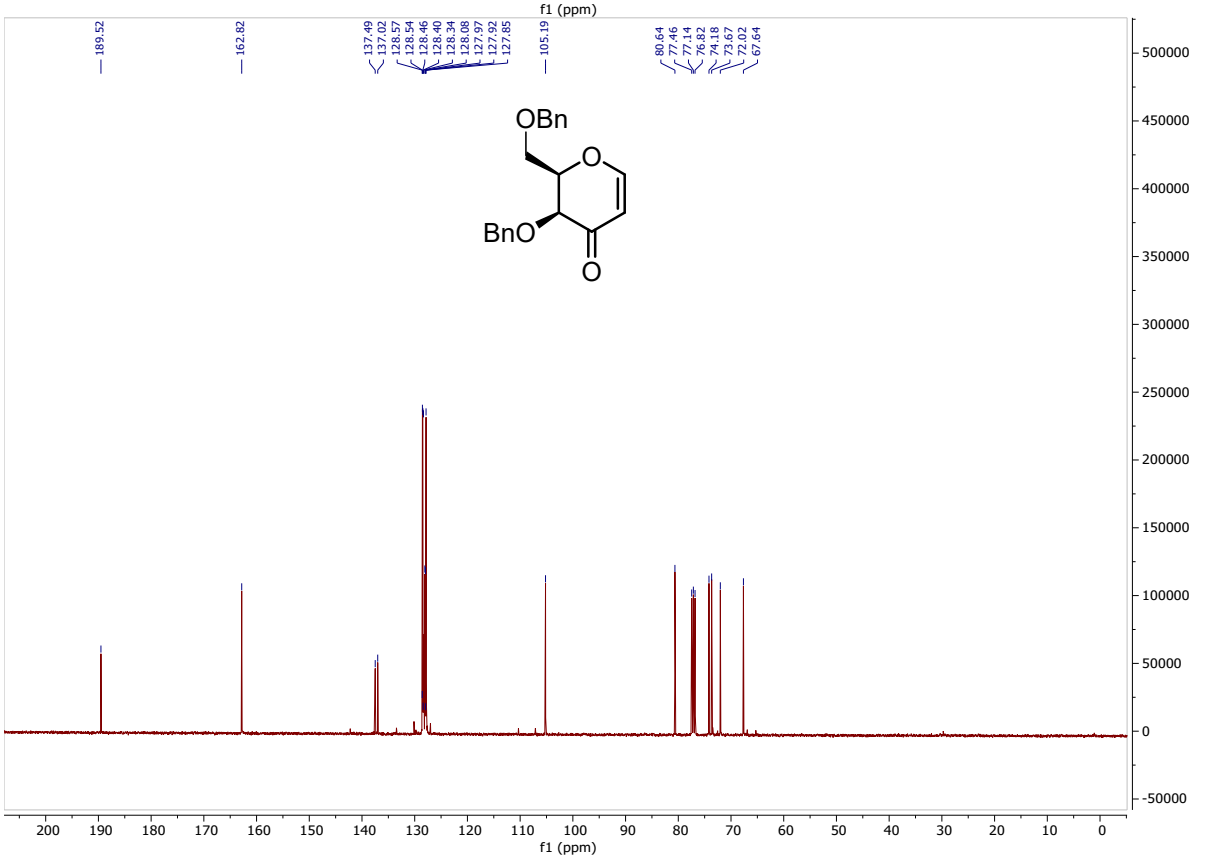


^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **2c** in $CDCl_3$

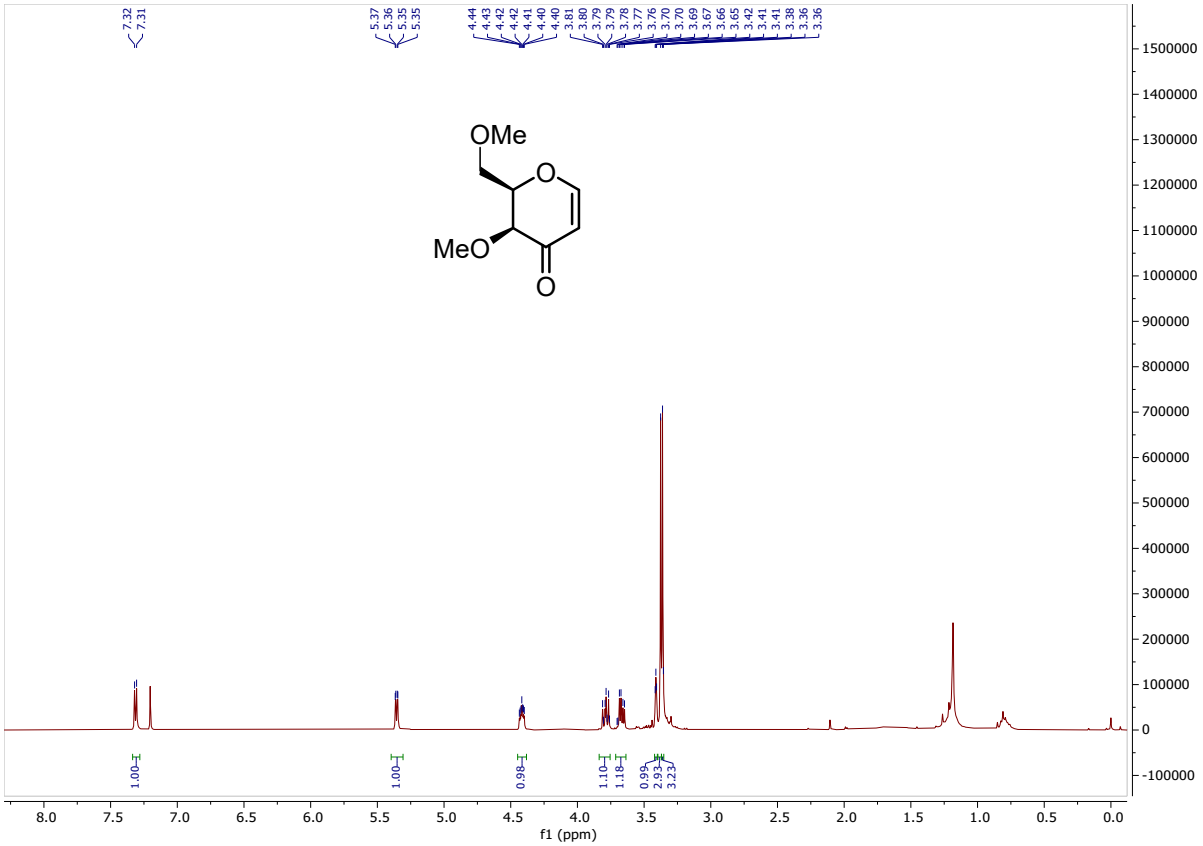


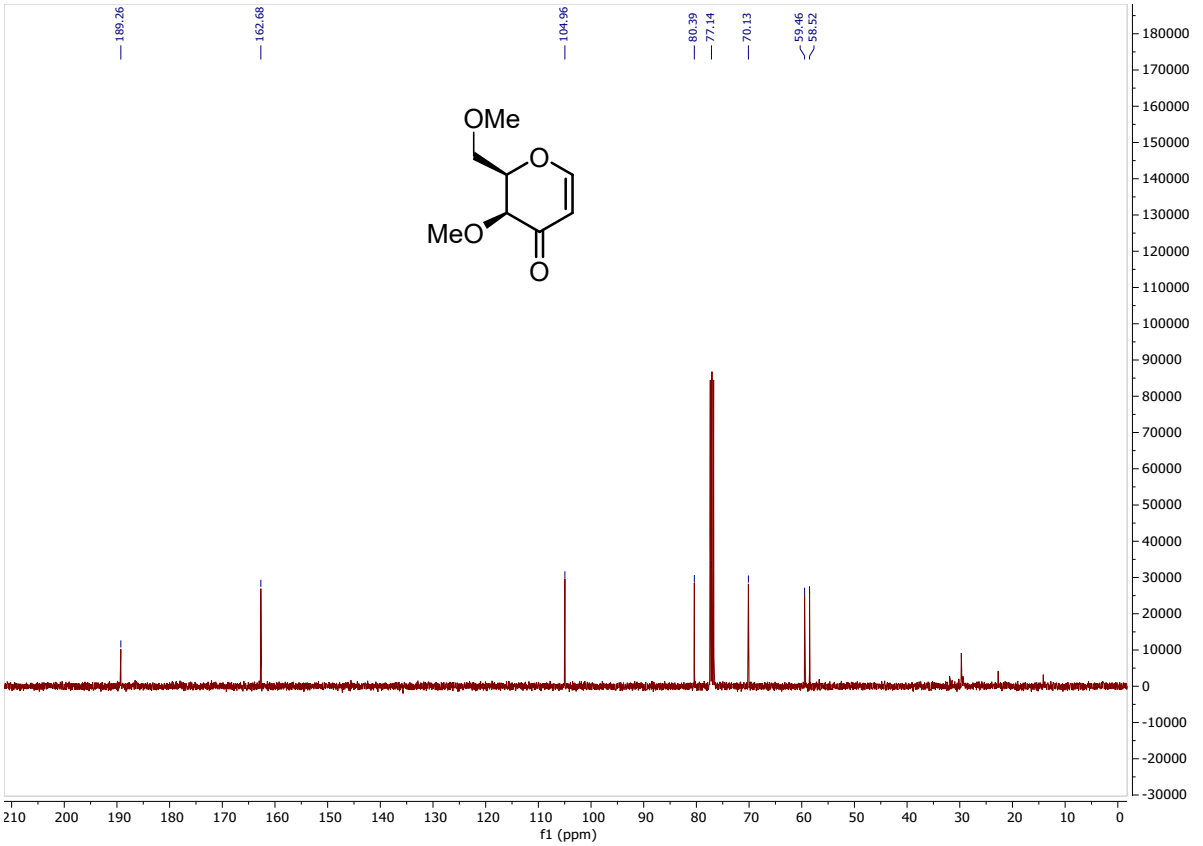
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **2d** in $CDCl_3$



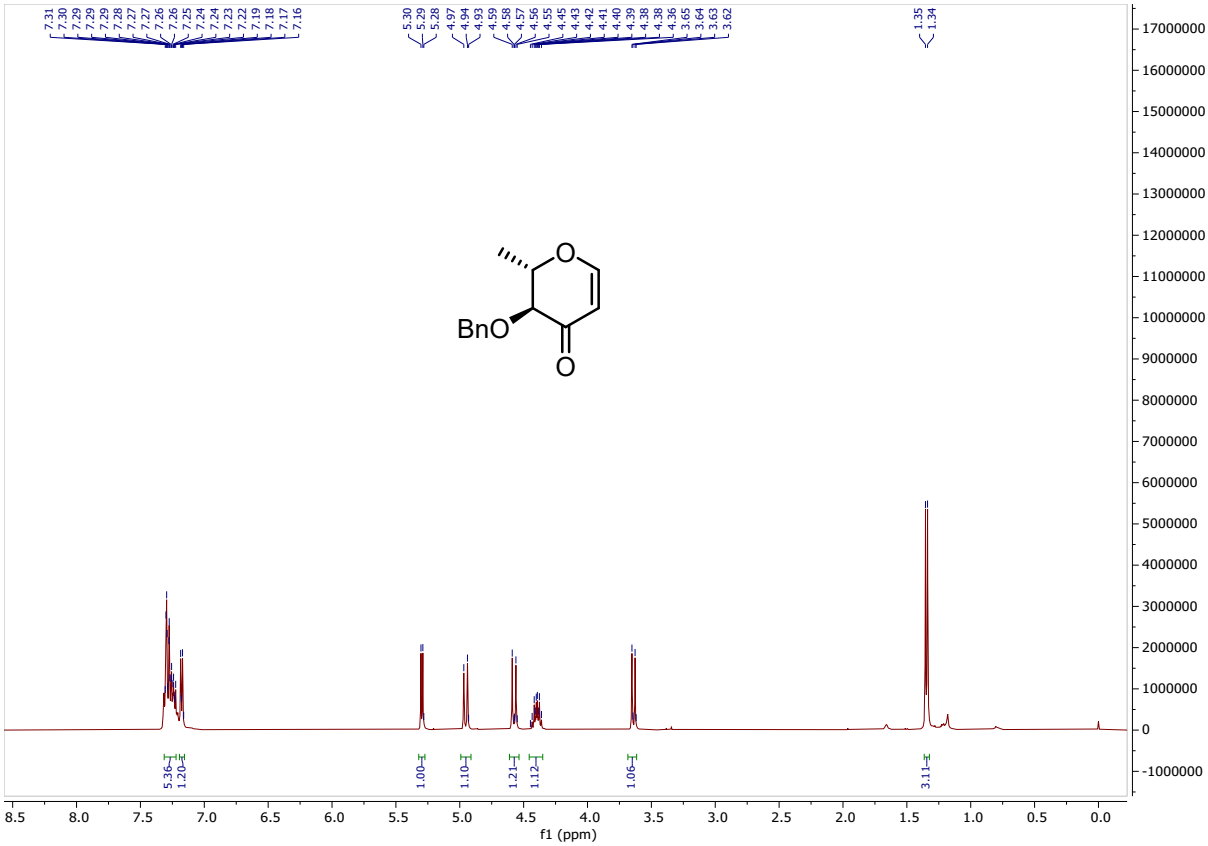


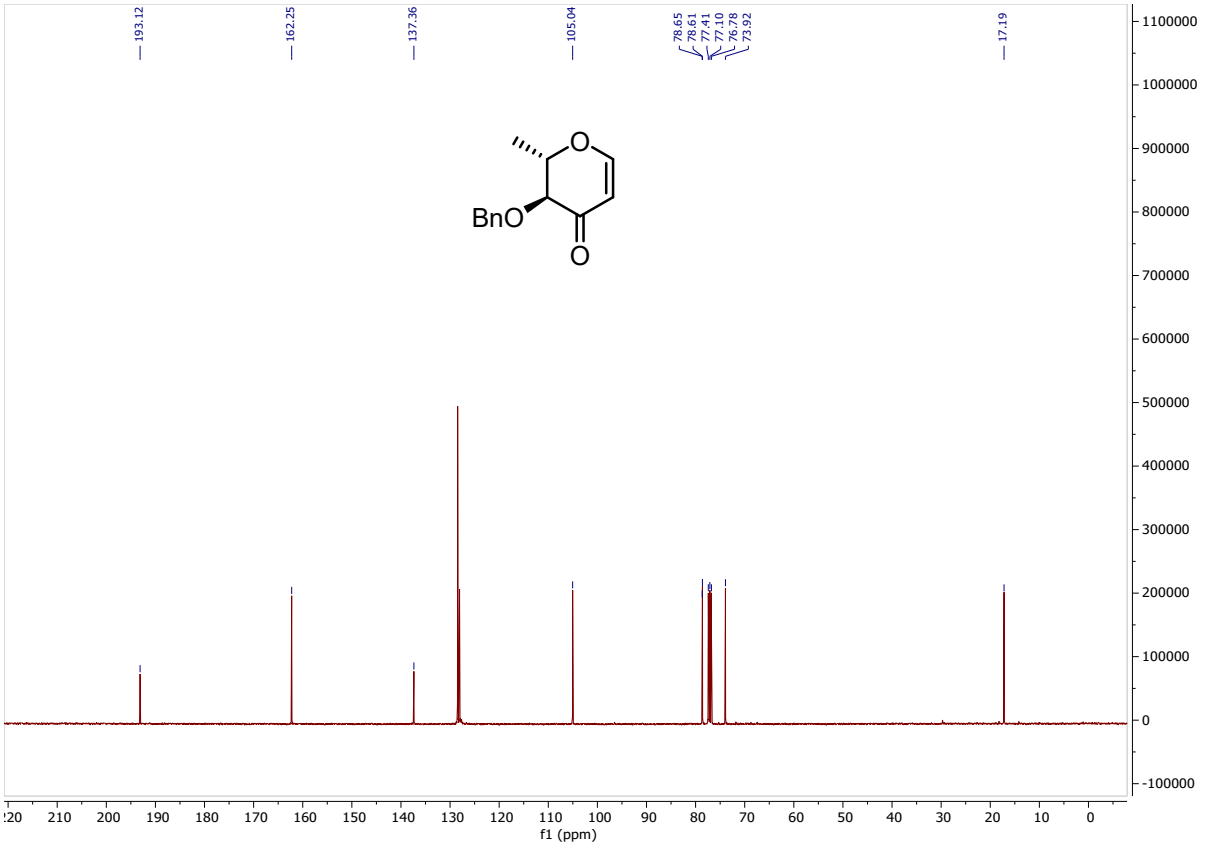
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **2e** in $CDCl_3$



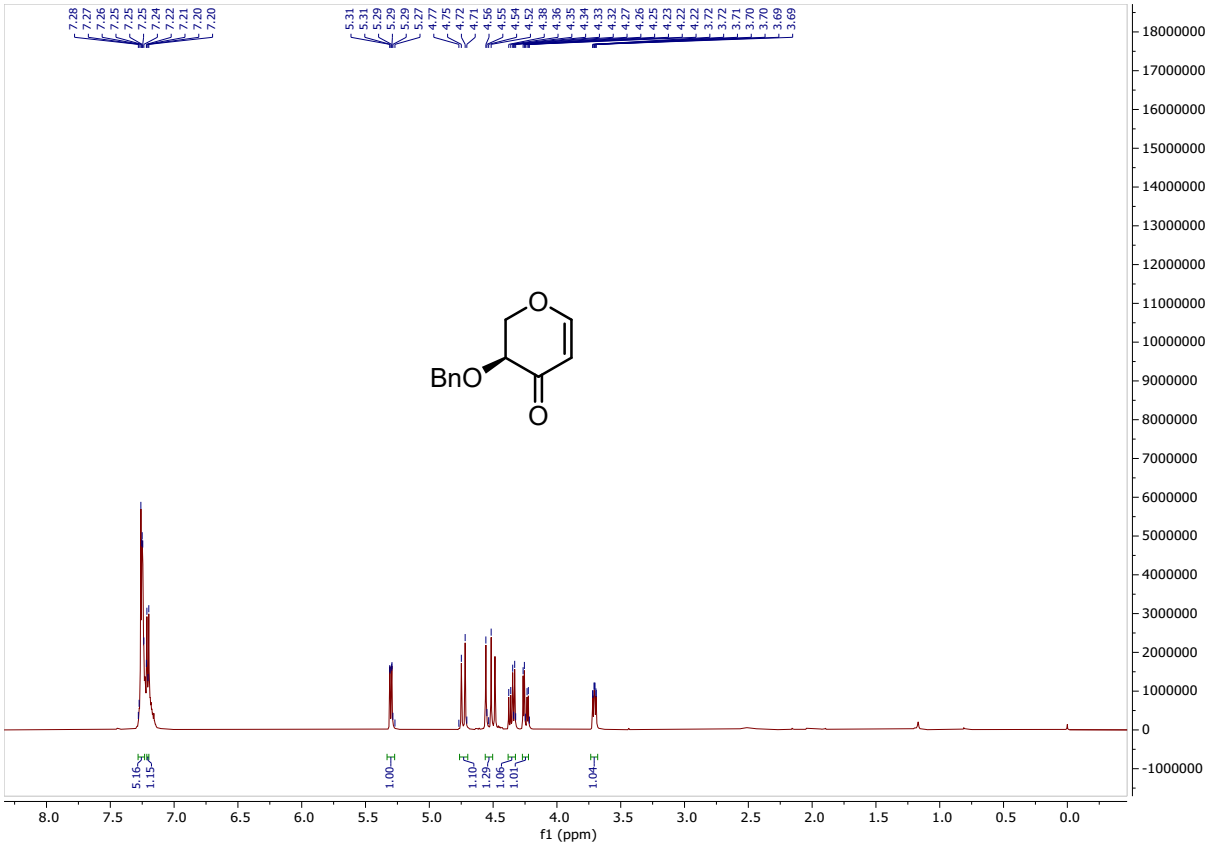


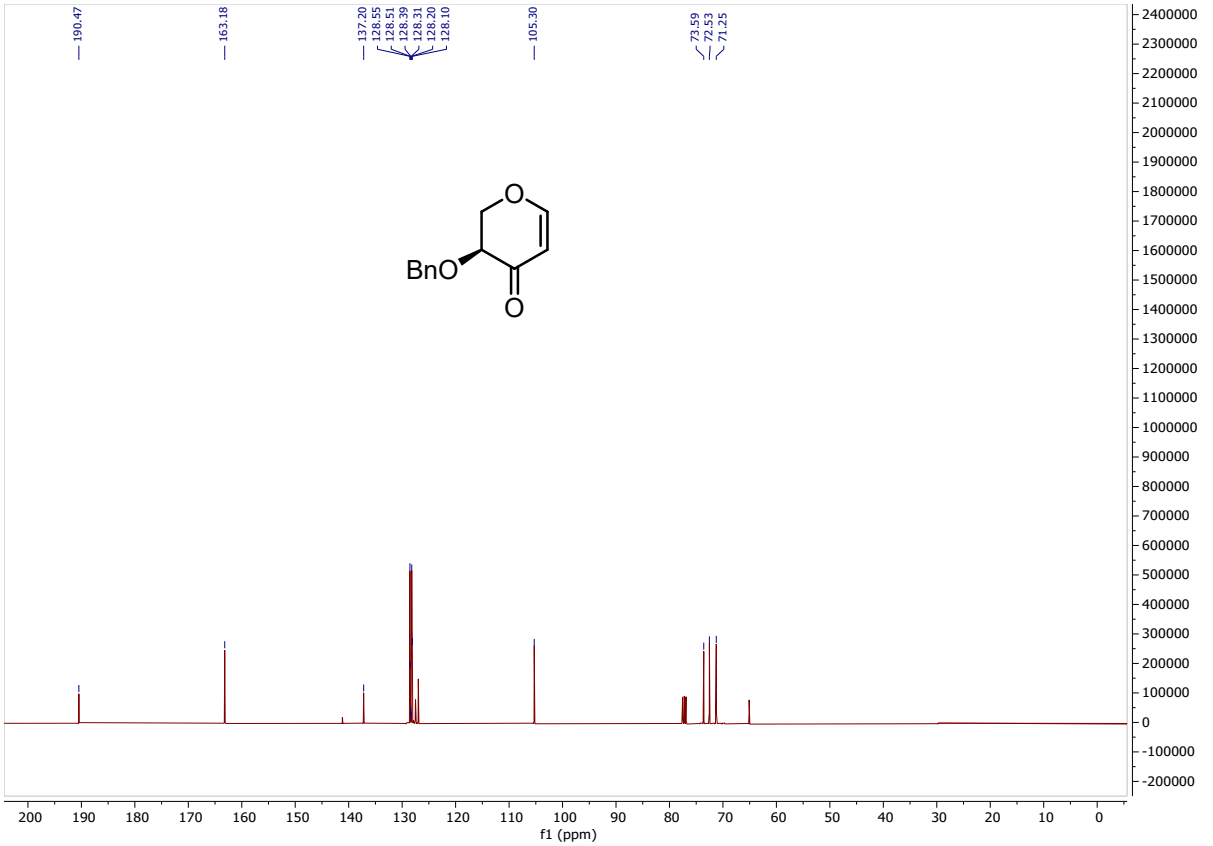
^{1}H NMR (400 MHz) & 13C NMR {1H} (101 MHz) of **2f** in $CDCl_3$



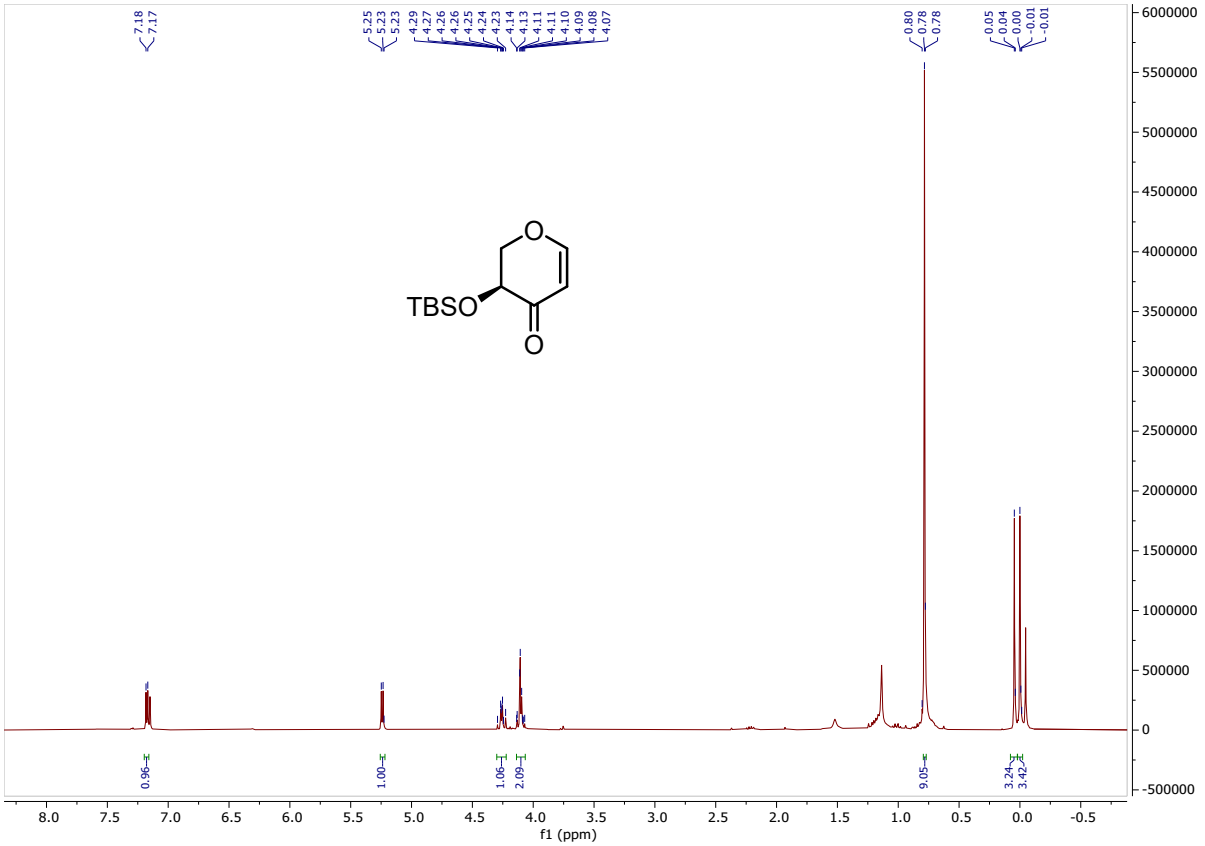


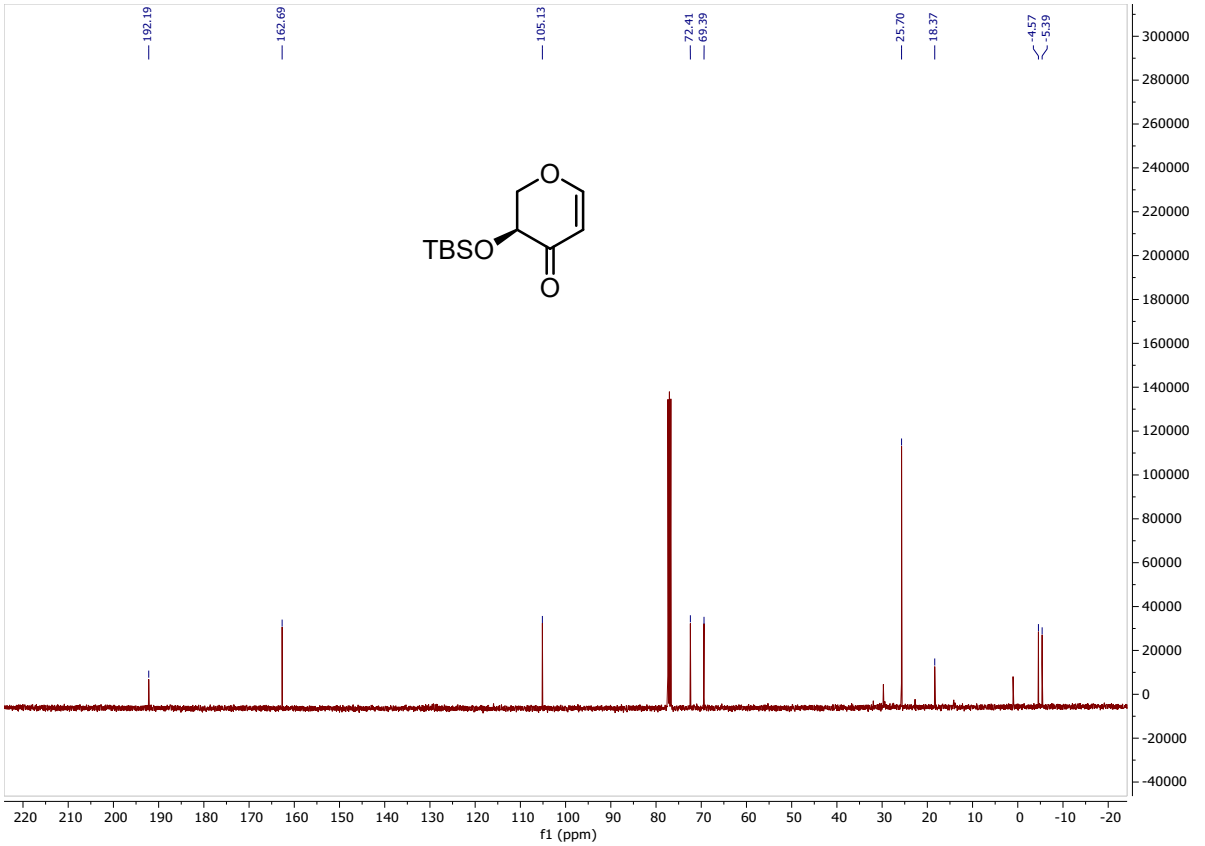
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **2g** in $CDCl_3$



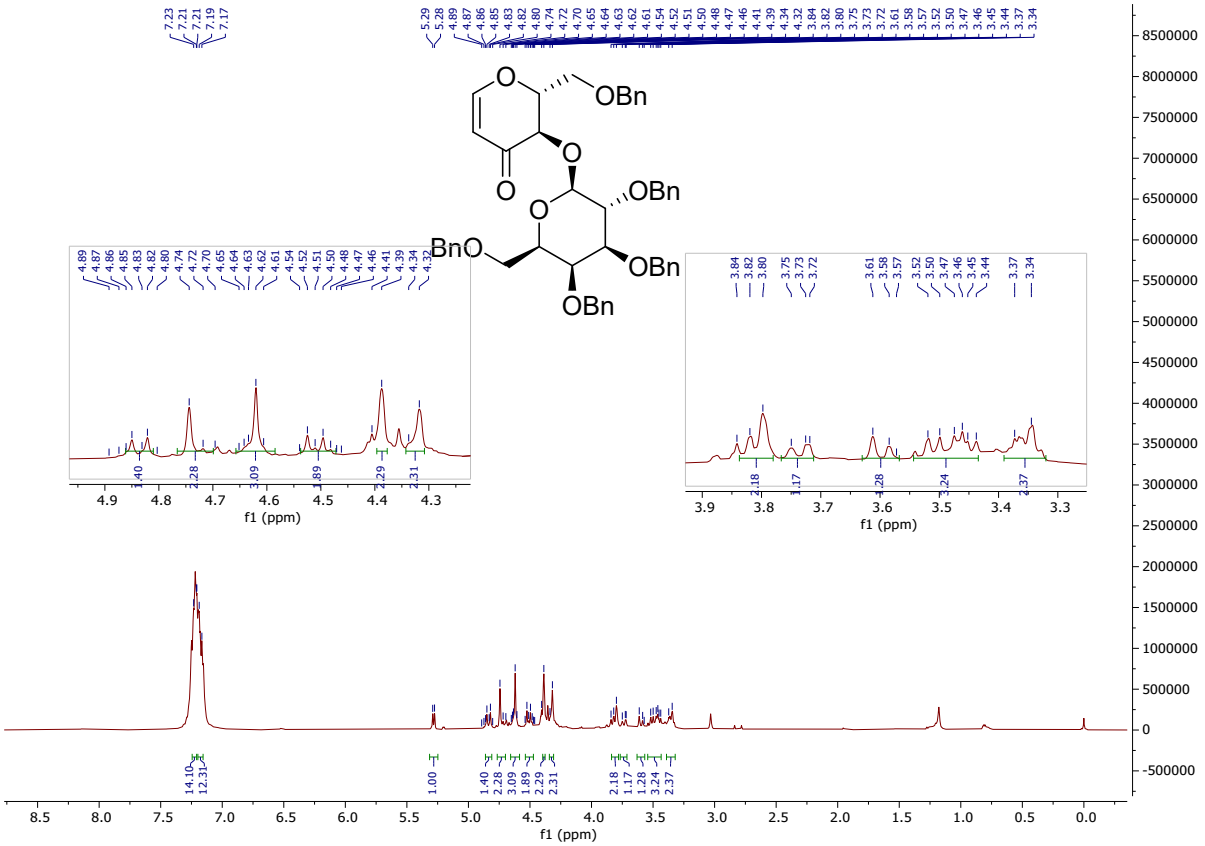


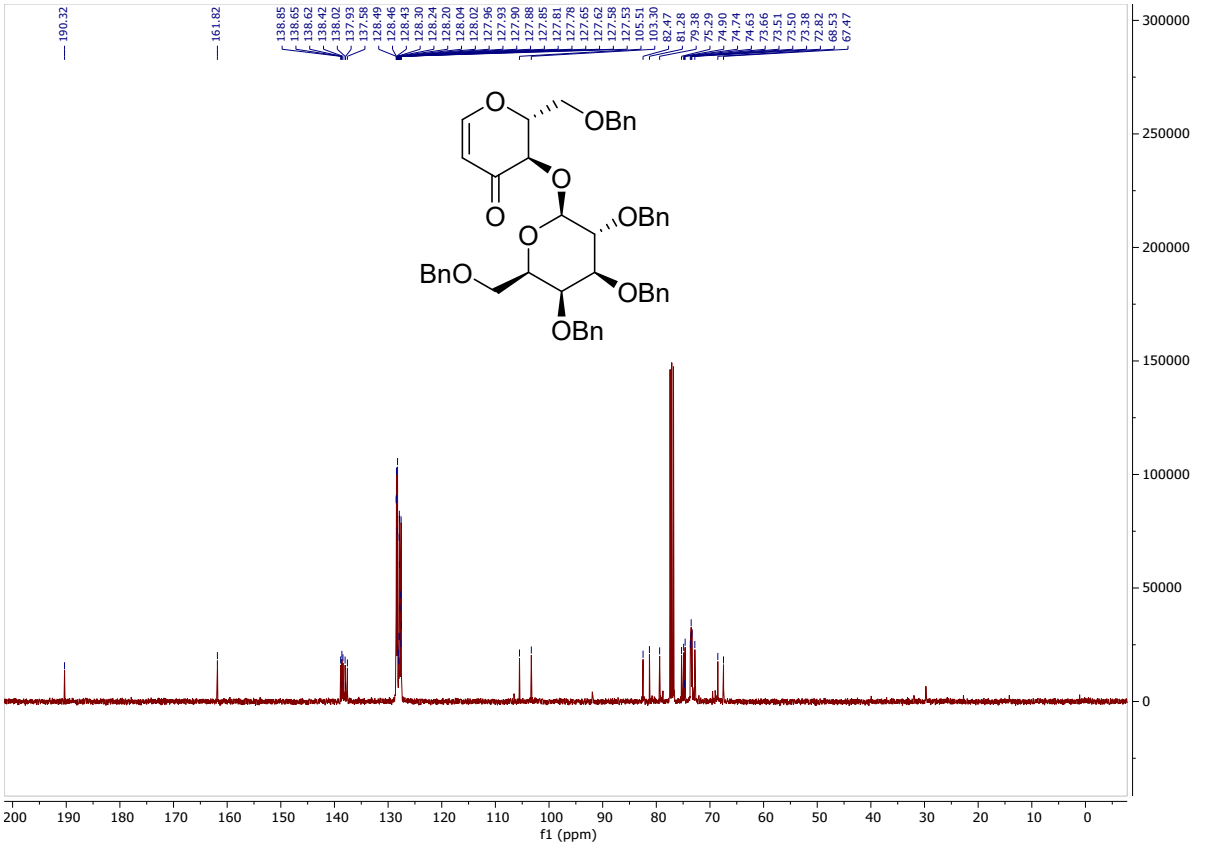
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **2h** in $CDCl_3$



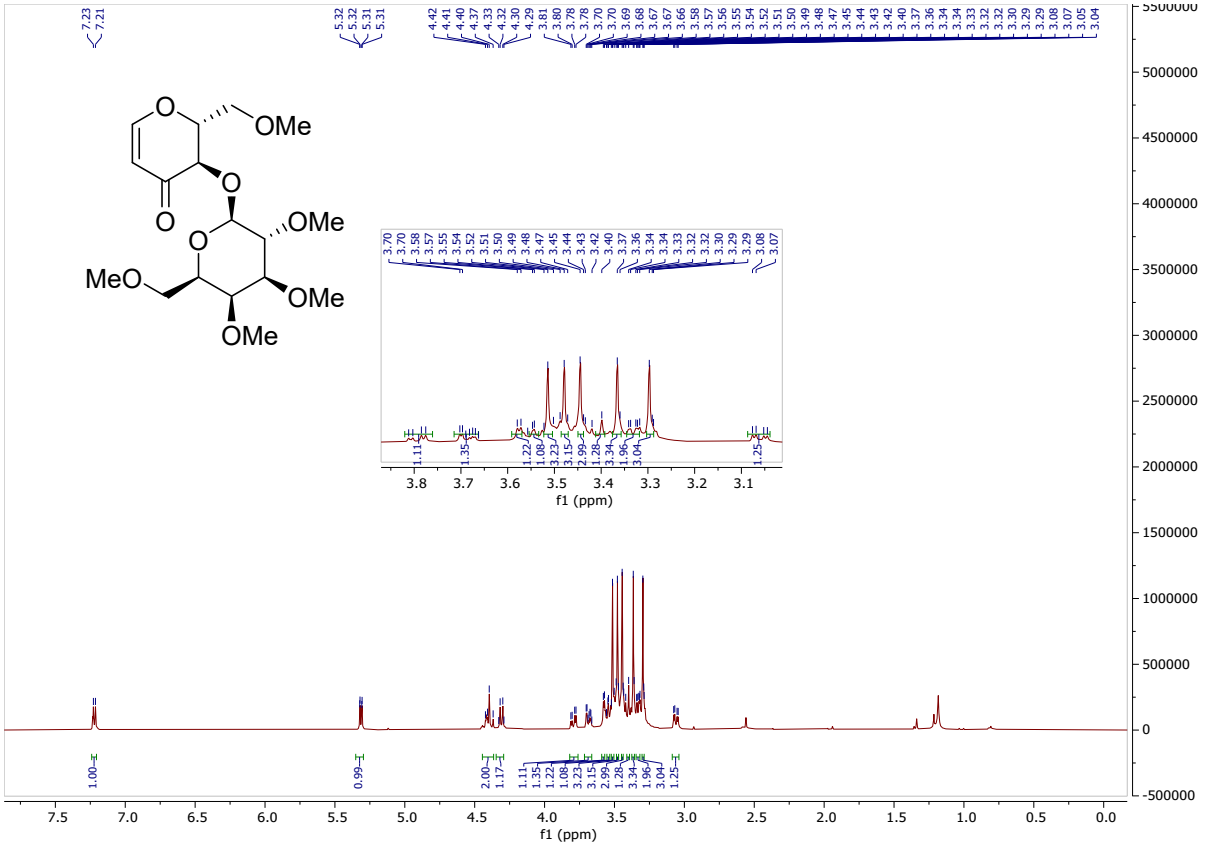


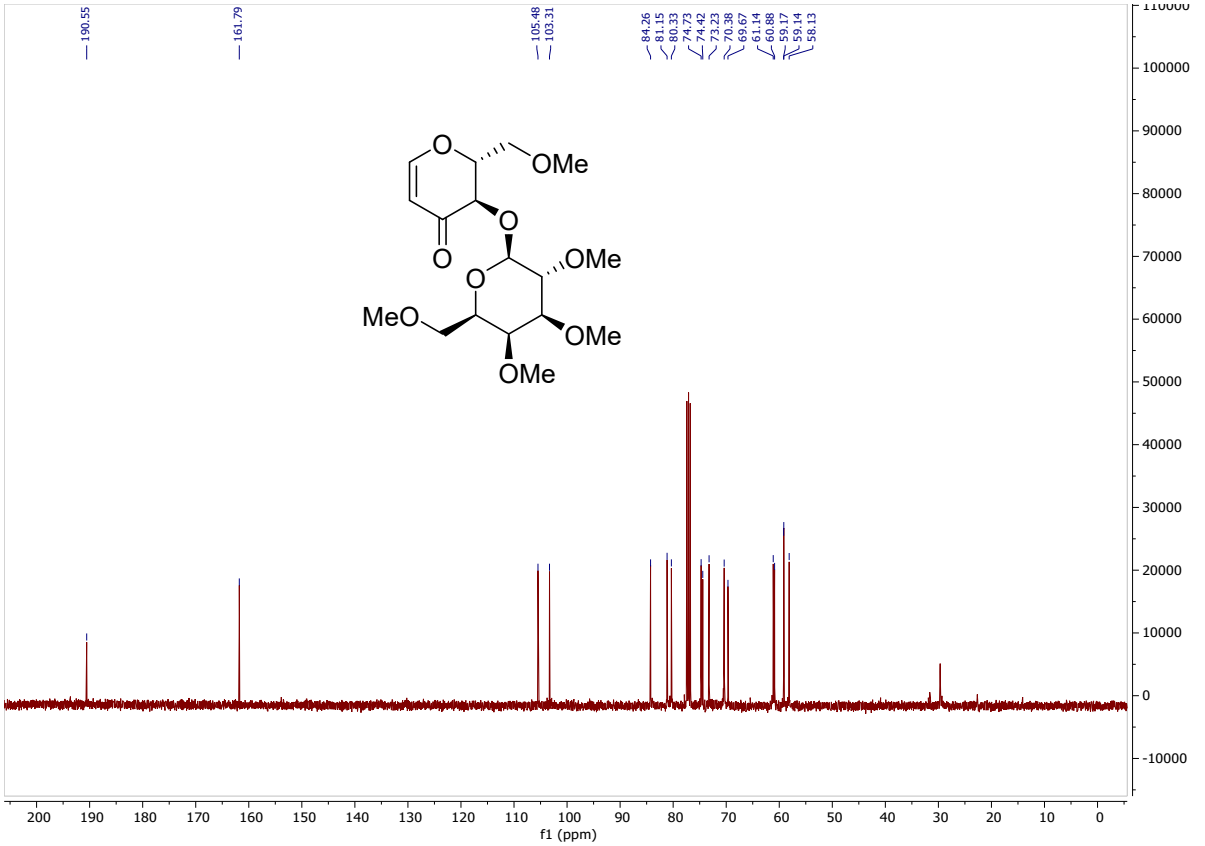
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **2i** in $CDCl_3$



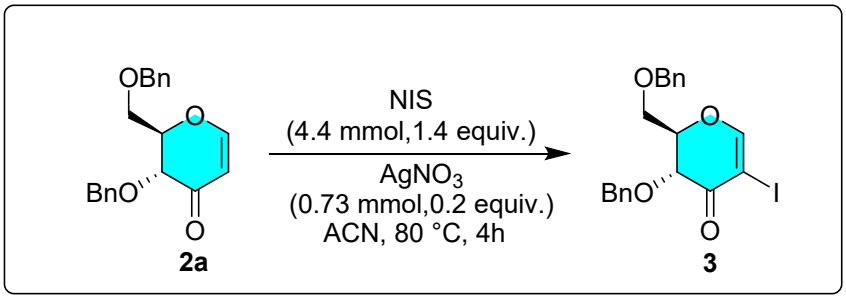


^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **2j** in $CDCl_3$



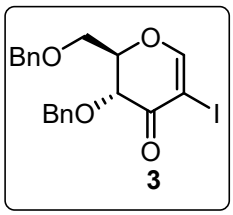


2.3 General experimental procedure for the synthesis of 2-iodo-enopyranones 3-6:

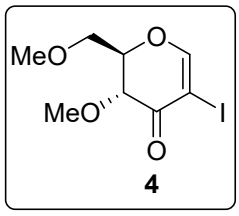


By taking **2a** as an example. To a stirred solution of Hex-1-enopyran-3-ulose (1 g) in dry CH_3CN (10 mL) at 80 ℃ under N_2 atmosphere was added successively NIS (991 mg, 4.4 mmol) and $AgNO_3$ (124 mg, 0.73 mmol) and stirred for 4 h. On consumption of starting material (TLC monitoring), the reaction mixture was filtered through a sintered funnel and then extracted with ethyl acetate, and a saturated solution of sodium thiosulfate was added. The filtrate was collected and to it was added anhydrous sodium sulfate, evaporated to give a crude product which was purified by silica gel column chromatography EtOAc/hexane (4:96) to obtain the resulting compound in 75 % yield.

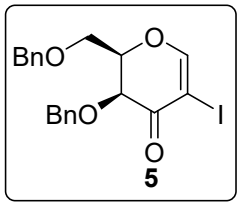
2.4 Characterization data & NMR spectra of 2-iodo-enopyranones 3-6:



The compound **3** was synthesized according to the general procedure **(2.3)** using **2a** (50 mg, 0.154 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (96:4) as eluent to obtain yellow gummy liquid (75 % yield, 51.9 mg).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.60 (s, 1H), 7.26 – 7.22 (m, 7H), 7.20 (dd, J = 6.5, 1.7 Hz, 3H), 4.96 (d, J = 10.9 Hz, 1H), 4.52 – 4.42 (m, 4H), 4.27 (d, J = 11.4 Hz, 1H), 3.70 (d, J = 3.1 Hz, 2H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 188.4 (Cq), 165.1, 137.4 (Cq), 137.1 (Cq), 128.6, 128.5, 128.4, 128.2, 128.0, 127.8, 81.8, 74.7 (CH_2), 74.1 (Cq), 74.0, 73.7 (CH_2), 67.6 (CH_2). **HRMS (ESI, m/z)** for $C_{20}H_{20}IO_4$ $[M+H]^+$: calcd 451.0406, found, 451.0417.

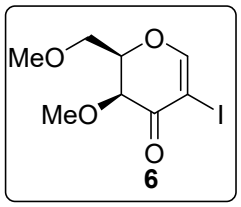


The compound **4** was synthesized according to the general procedure **(2.3)** using **2b** (50 mg, 0.29 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (92:8) as eluent to obtain yellow gummy liquid (78 % yield, 67.53 mg).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.70 (s, J = 1.4 Hz, 1H), 4.53 – 4.43 (m, 1H), 4.08 (dd, J = 11.2, 1.2 Hz, 1H), 3.75 (dd, J = 3.2, 1.2 Hz, 2H), 3.63 (s, 3H), 3.44 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 188.1 (Cq), 164.8, 81.7, 76.3, 73.8 (Cq), 70.1 (CH_2), 60.7, 59.6. **HRMS (ESI, m/z)** for $C_8H_{12}IO_4$ $[M+H]^+$: calcd 298.9780, found, 298.9791.



The compound **5** was synthesized according to the general procedure **(2.3)** using **2d** (50 mg, 0.154 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (96:4) as eluent to obtain yellow gummy liquid (77 % yield, 53.36 mg).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.67 (s, 1H), 7.27 – 7.22 (m, 5H), 7.20 – 7.17 (m, 5H), 4.58 (d, J = 1.9 Hz, 1H), 4.51 – 4.47 (m, 1H), 4.42 (dd, J = 16.0, 1.8 Hz, 2H), 4.37 (dd, J = 5.7, 1.8 Hz, 1H), 3.89 (d, J = 2.3 Hz, 1H), 3.80 (ddd, J = 8.8, 6.8, 1.9 Hz, 1H), 3.65 (ddd, J = 10.3, 5.6, 1.9 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 184.2 (Cq), 165.6, 137.3 (Cq), 136.6 (Cq), 128.6, 128.6, 128.5, 128.4, 128.2, 128.0, 127.8, 127.6, 127.0, 81.4,

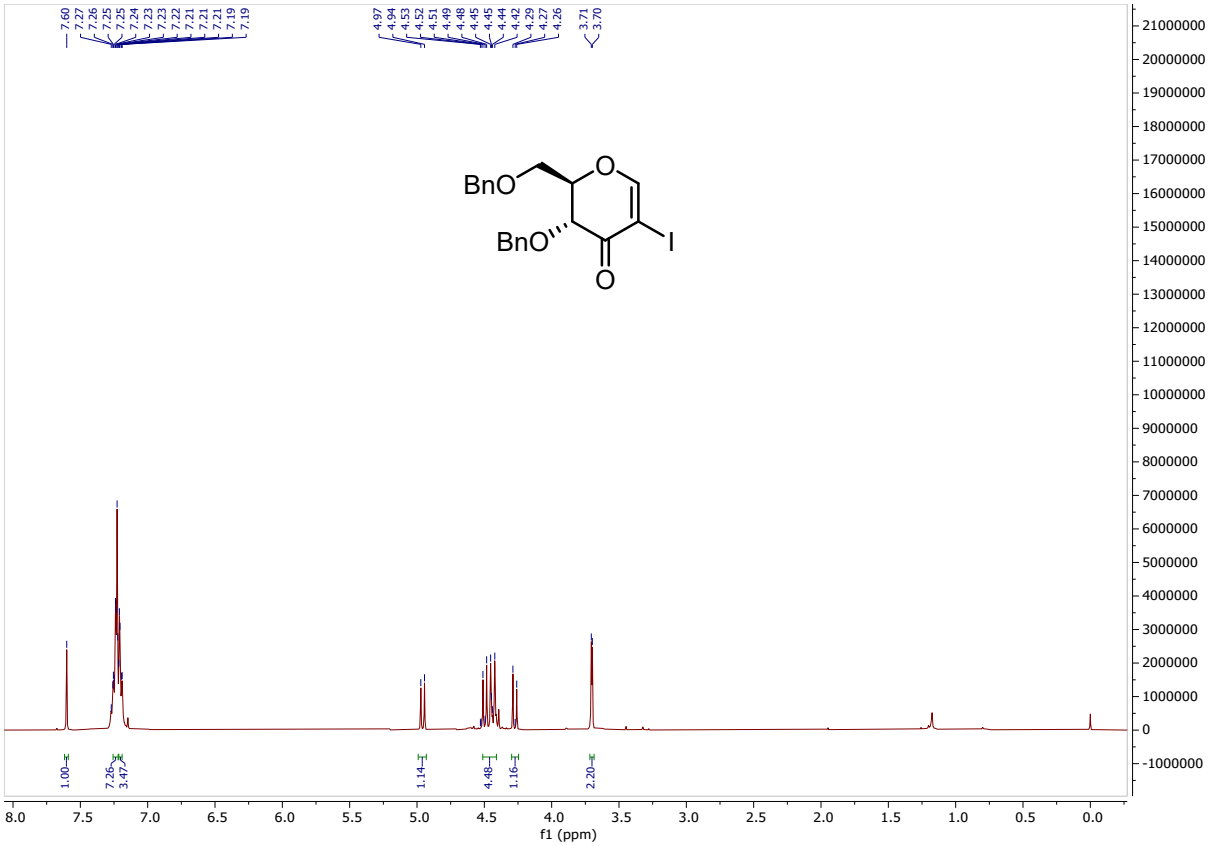
74.9, 73.7 (CH_2), 73.5, 72.3 (CH_2), 67.2 (CH_2). **HRMS (ESI, m/z)** for $C_{20}H_{20}IO_4$ $[M+H]^+$: calcd 451.0406, found, 451.0419.

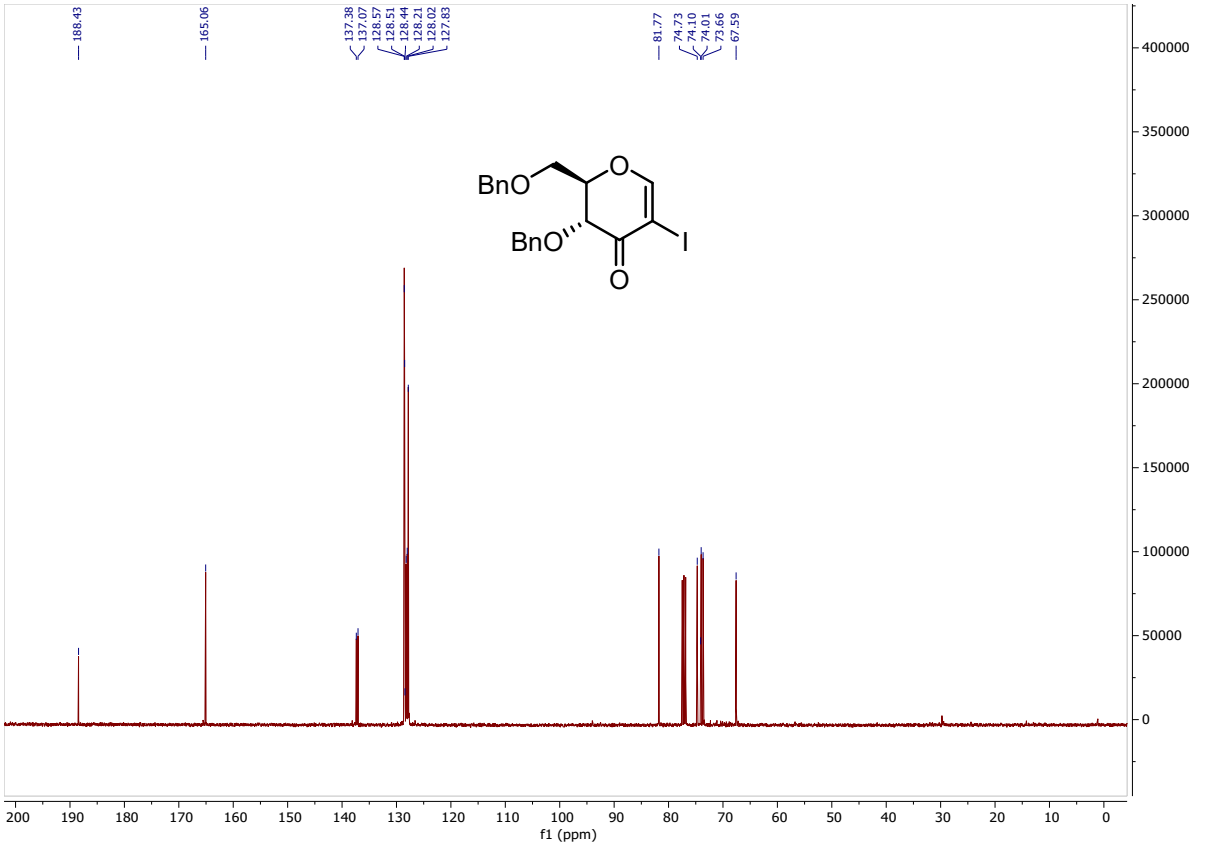


6

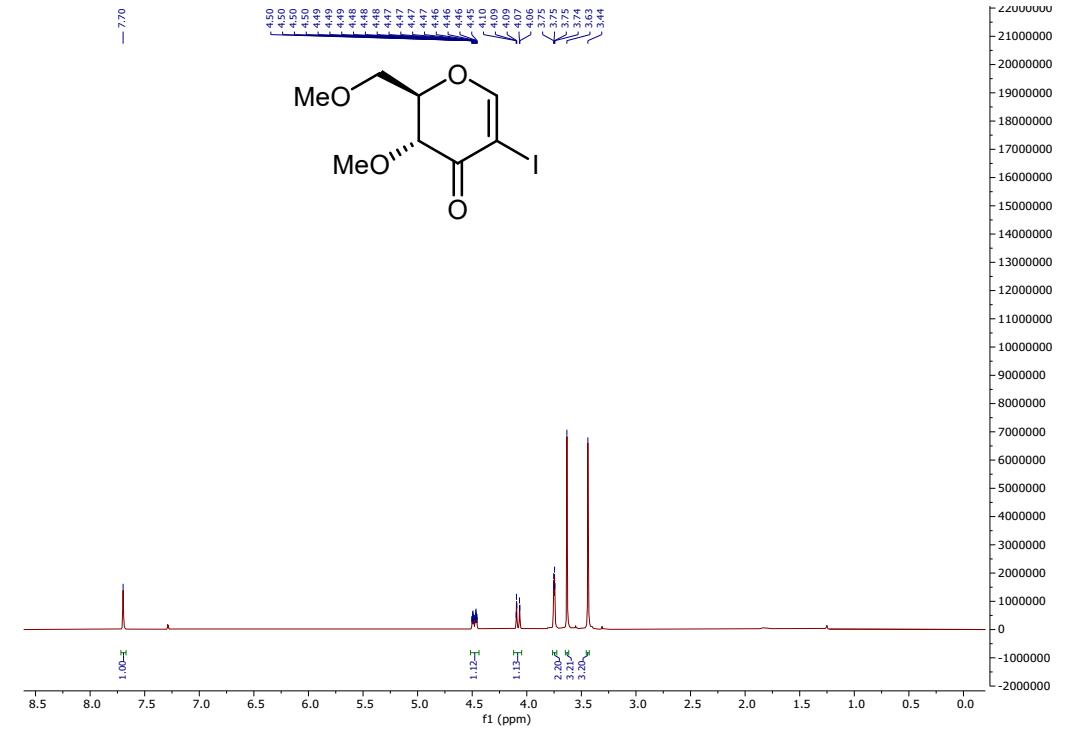
The compound **6** was synthesized according to the general procedure **(2.3)** using **2e** (50 mg, 0.290 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (96:4) as eluent to obtain yellow gummy liquid (77 % yield, 66.6 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.79 (d, *J* = 0.9 Hz, 1H), 4.60 (dddd, *J* = 7.1, 5.3, 2.4, 0.9 Hz, 1H), 3.83 (dd, *J* = 10.5, 7.2 Hz, 1H), 3.78 (d, *J* = 2.4 Hz, 1H), 3.74 (dd, *J* = 10.4, 5.3 Hz, 1H), 3.44 (s, 3H), 3.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.80, 165.42, 81.12, 76.54, 74.60, 69.63, 59.47, 58.80. **HRMS (ESI, m/z)** for $C_8H_{12}IO_4$ $[M+H]^+$: calcd 298.9780, found, 298.9785.

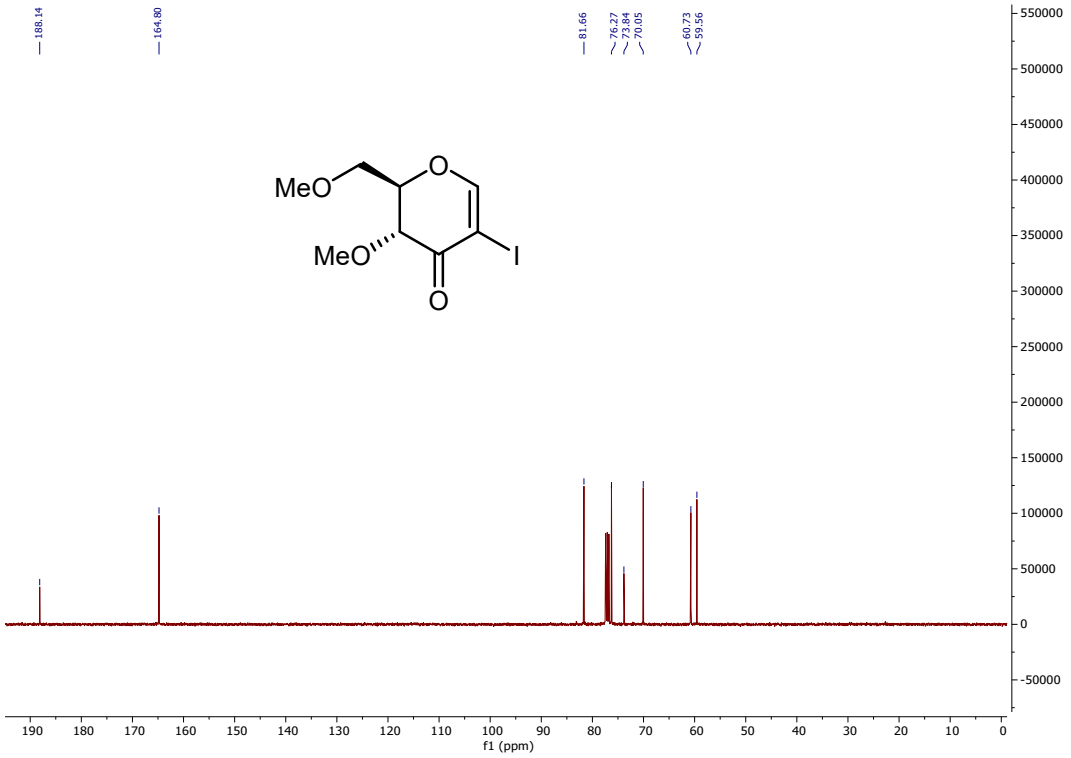
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **3** in $CDCl_3$



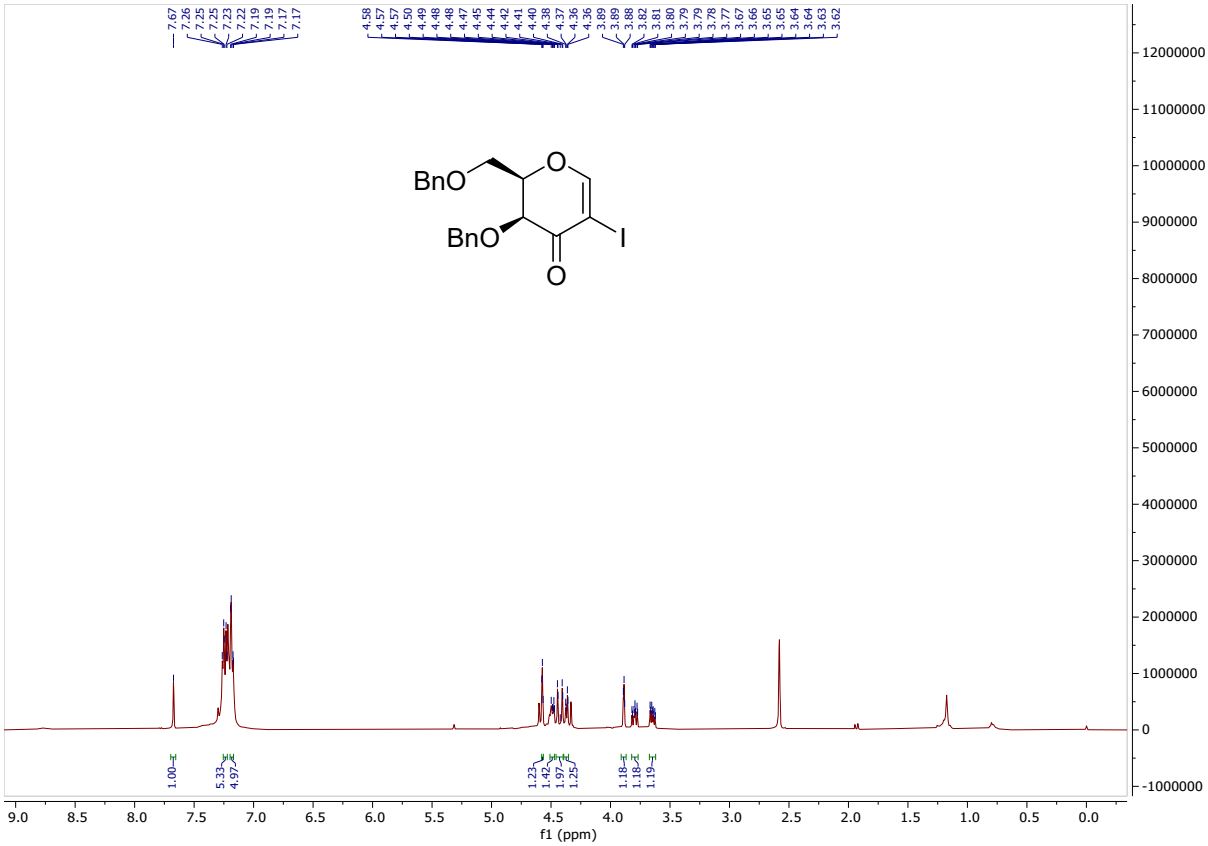


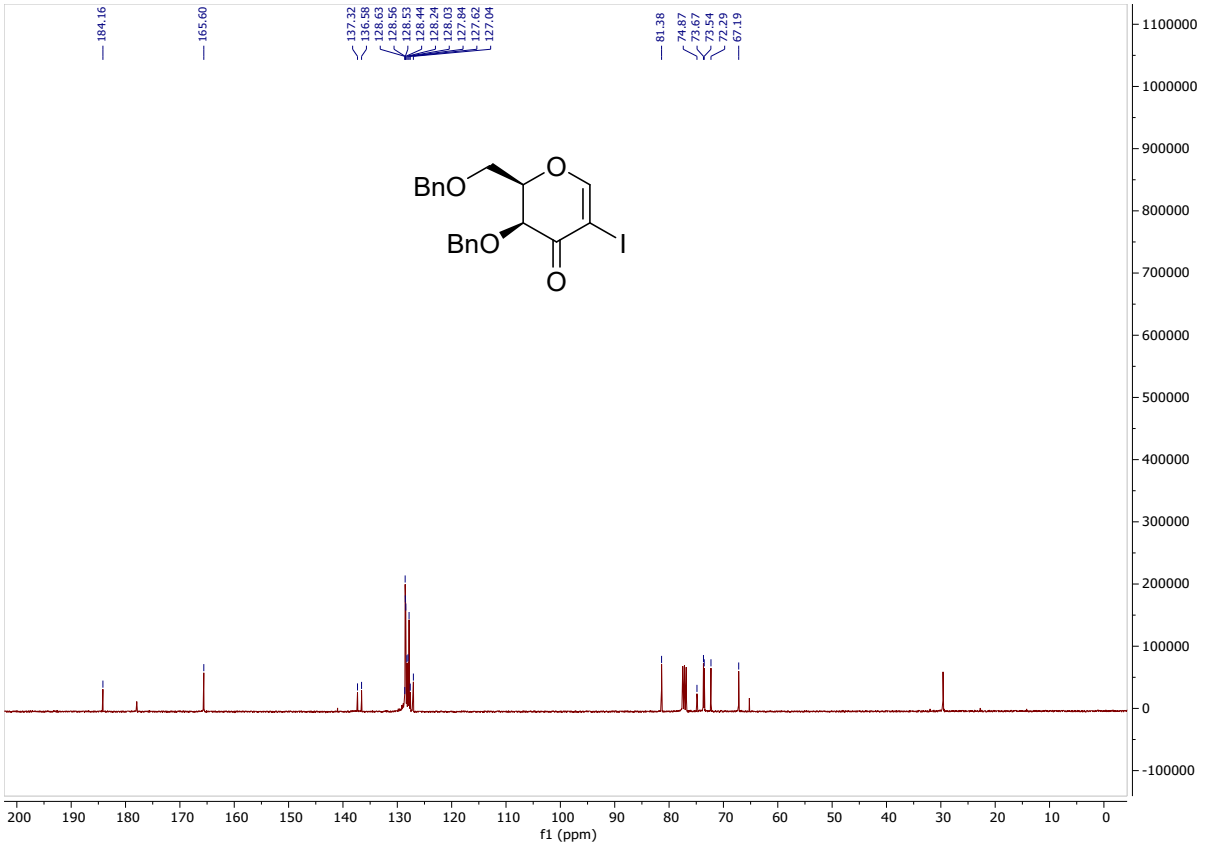
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **4** in $CDCl_3$



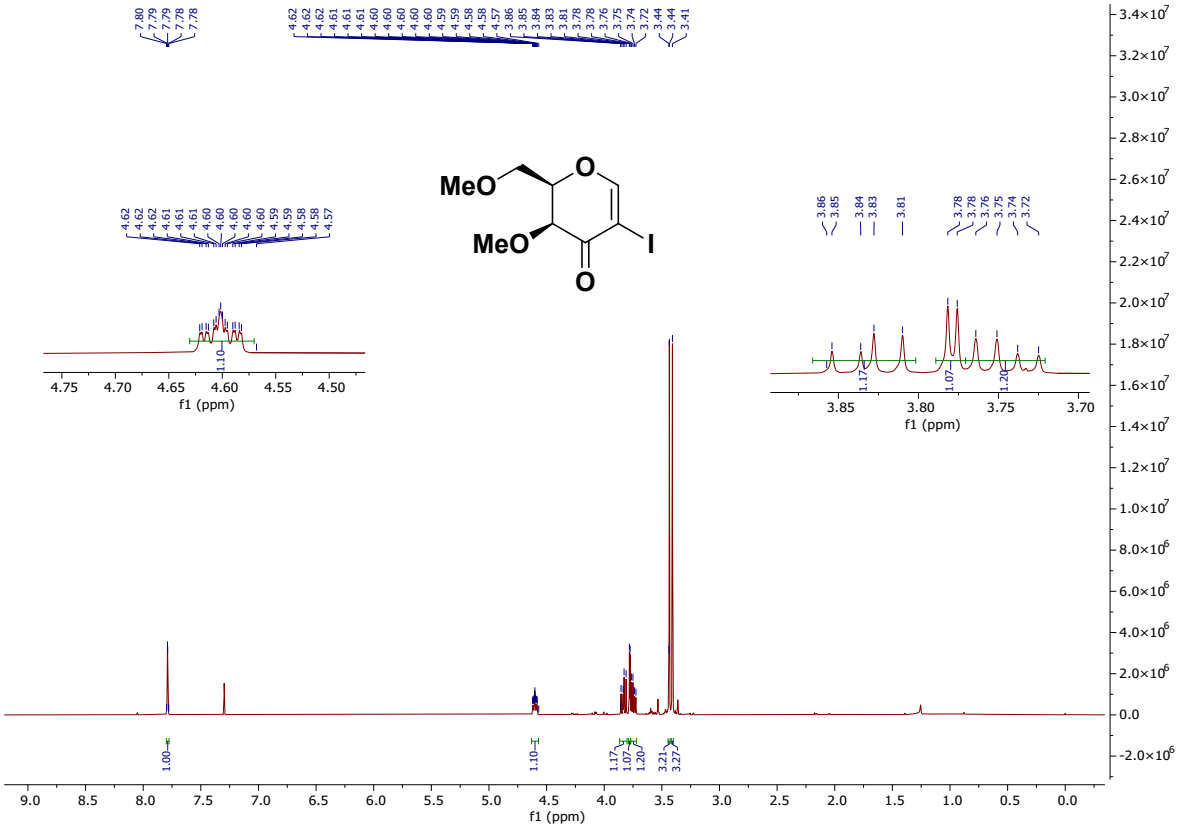


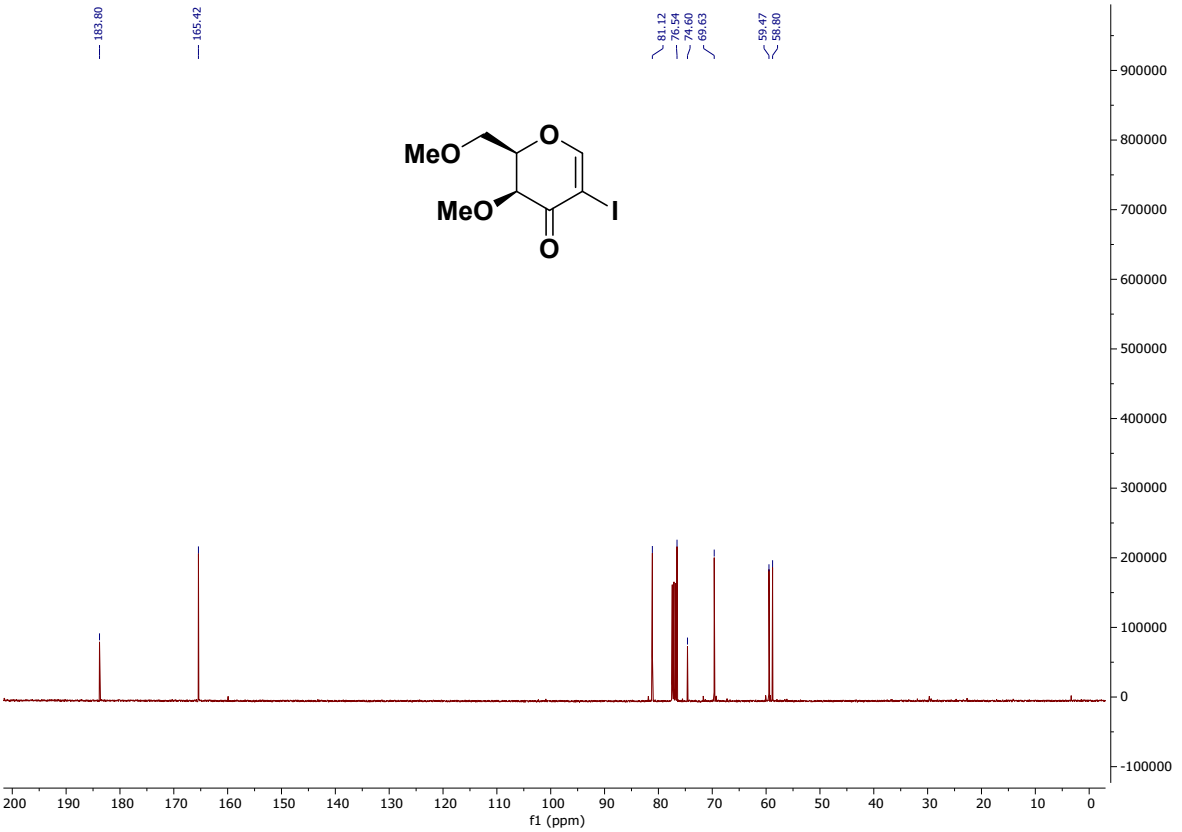
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **5** in $CDCl_3$



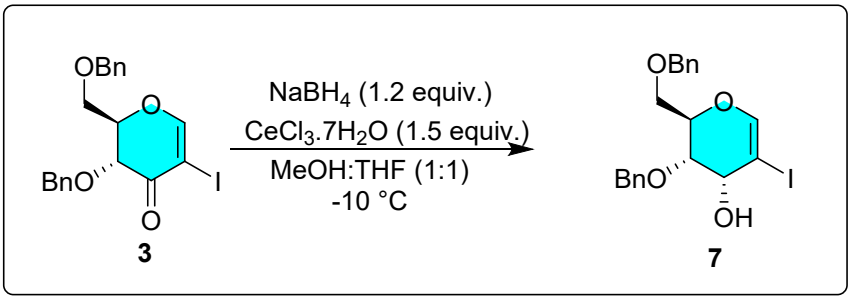


^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **6** in $CDCl_3$



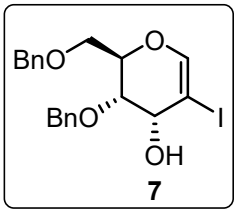


2.5 General procedure for Luche reduction of 2-iodo-enopyranone:

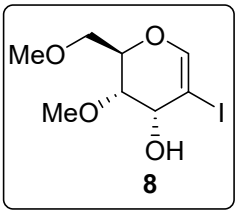


By taking **3** as an example. Compound **7** was synthesized using **3** (50 mg, 0.11 mmol, 1.0 equiv.) in MeOH: THF (1:1), sodium borohydride (1.2 equiv.), and $CeCl_3.7H_2O$ (1.5 equiv.) were added slowly at -10 °C. Stir the reaction mixture until complete consumption of starting material was observed by TLC analysis. Then the reaction mixture was diluted with ethyl acetate and quenched by the addition of saturated aqueous NH_4Cl solution. The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated in vacuo. The residue left was purified by column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (90:10) as eluent to obtain compound **7** as a white solid (45.2 mg, 90%).

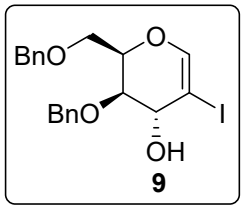
2.6 Characterization data & NMR spectra of compounds 7-10:



The compound **7** was synthesized according to the general procedure **(2.5)** using **3** (50 mg, 0.11 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (85:15) as eluent to obtain it as white solid (90 % yield, 45.2 mg).**^{1}H NMR (400 MHz, $CDCl_3$)** ***δ*** 7.28 – 7.22 (m, 8H), 7.20 – 7.16 (m, 2H), 6.63 (s, 1H), 4.58 – 4.51 (m, 3H), 4.49 (d, *J* = 2.8 Hz, 1H), 4.18 (d, *J* = 3.9 Hz, 1H), 4.04 (dt, *J* = 10.2, 3.0 Hz, 1H), 3.87 (dd, *J* = 10.2, 3.9 Hz, 1H), 3.73 – 3.70 (m, 2H).**^{13}C NMR (101 MHz, $CDCl_3$)** ***δ*** 149.2, 137.8 (Cq), 137.1 (Cq), 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 128.0, 127.8, 74.1, 73.7 (CH_2), 72.5 (CH_2), 72.0, 68.5, 68.1 (CH_2), 67.3 (Cq). **HRMS (ESI, m/z)** for $C_{20}H_{21}INaO_4$ $[M+Na]^+$: calcd 475.0382, found, 475.0393.

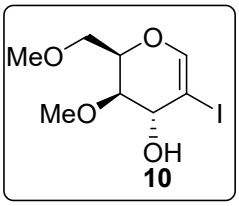


The compound **8** was synthesized according to the general procedure **(2.5)** using **4** (50 mg, 0.167 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (85:15) as eluent to obtain it as white solid (92 % yield, 46.30 mg); (R/S: 3.3:1).**^{1}H NMR (400 MHz, $CDCl_3$)** ***δ*** 6.63 (s, 1H), 4.30 (d, J = 3.8 Hz, 1H), 4.06 (td, J = 7.4, 6.8, 2.8 Hz, 1H), 3.99 (ddd, J = 10.2, 4.0, 2.4 Hz, 1H), 3.61 (d, J = 2.7 Hz, 1H), 3.48 (s, 1H), 3.41 (s, 3H), 3.35 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)** ***δ*** 149.1, 78.8, 76.1, 71.7, 70.6 (CH_2), 67.8 (Cq), 59.4, 57.9. **HRMS (ESI, m/z)** for $C_8H_{17}INO_4$ $[M+NH_4]^+$: calcd 318.0202, found, 318.0211.



The compound **9** was synthesized according to the general procedure **(2.5)** using **5** (50 mg, 0.11 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (85:15) as eluent to obtain it as white solid (90 % yield, 45.20 mg).**^{1}H NMR (400 MHz, $CDCl_3$)** ***δ*** 7.25 (m, 3H), 7.21 (m, 7H), 6.56 (s, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.55 – 4.49 (m, 1H), 4.44 (d, *J* = 11.9 Hz, 1H), 4.37 (d, *J* = 11.9 Hz, 1H), 4.20 – 4.09 (m, 2H), 3.94 (dd, *J* = 4.9, 2.8 Hz, 1H), 3.68 (dd, *J* = 10.1, 6.1 Hz, 1H), 3.52 (dd, *J* = 10.2, 5.5 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$)** ***δ*** 147.9, 137.5 (Cq), 137.4 (Cq),

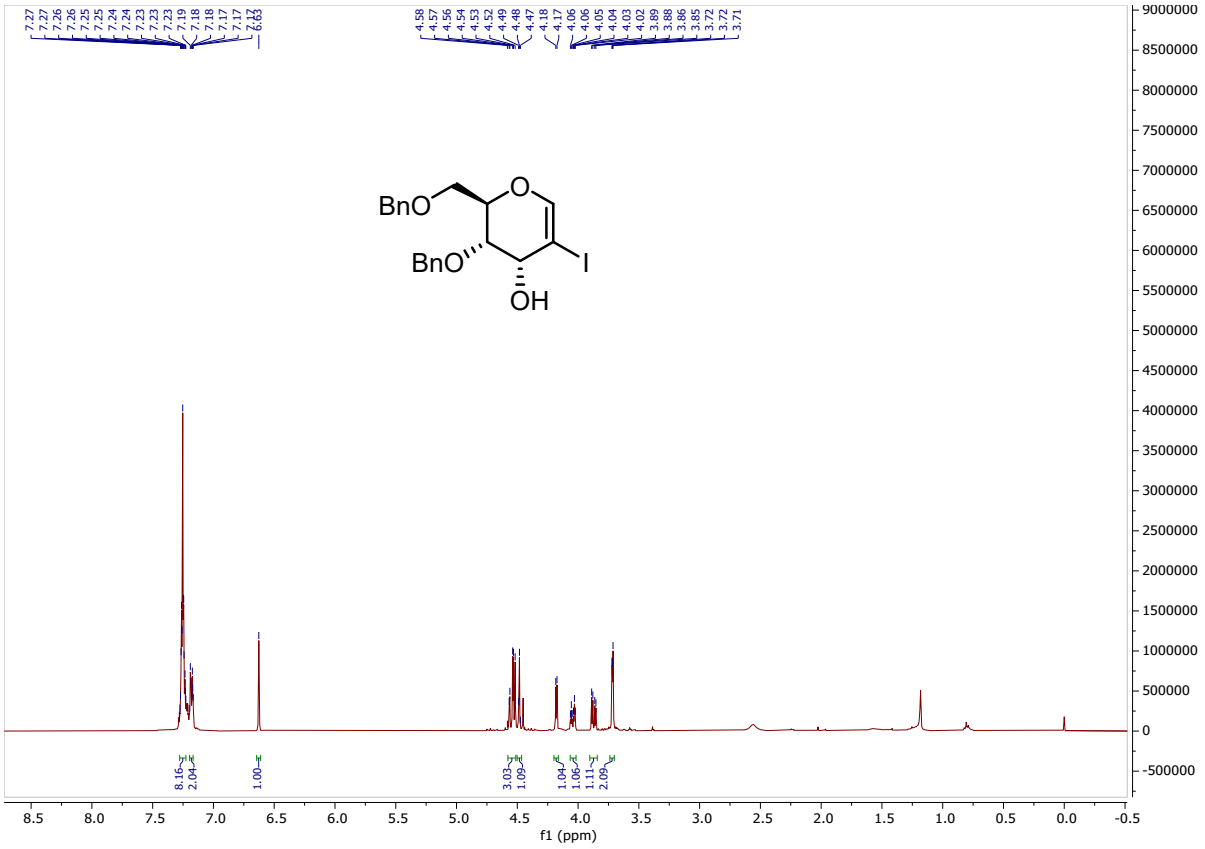
128.7, 128.6, 128.3, 128.2, 128.0, 127.9, 127.6, 74.6 (Cq), 74.2 (CH_2), 73.6 (CH_2), 73.56, 67.8 (CH_2), 67.7. **HRMS (ESI, m/z)** for $C_{20}H_{21}INaO_4$ $[M+Na]^+$: calcd 475.0382, found, 475.0389.

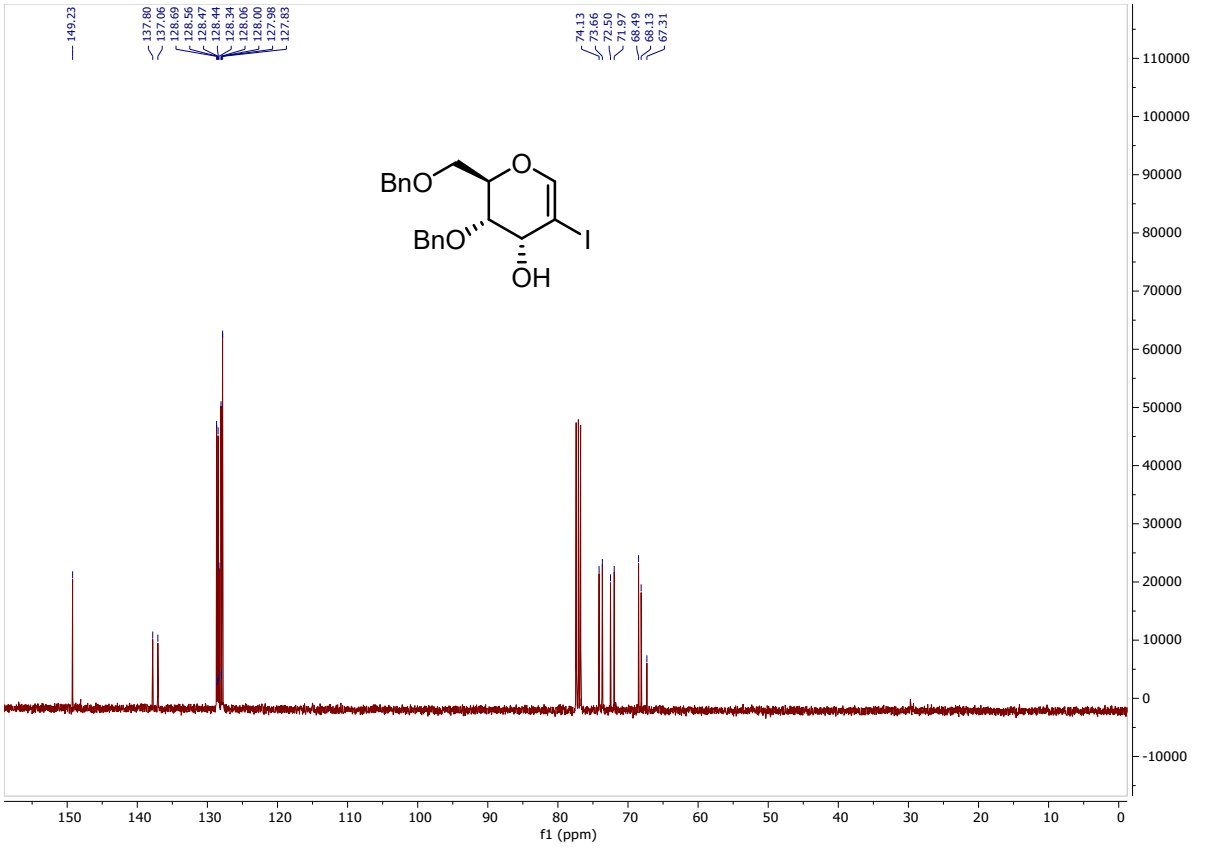


10

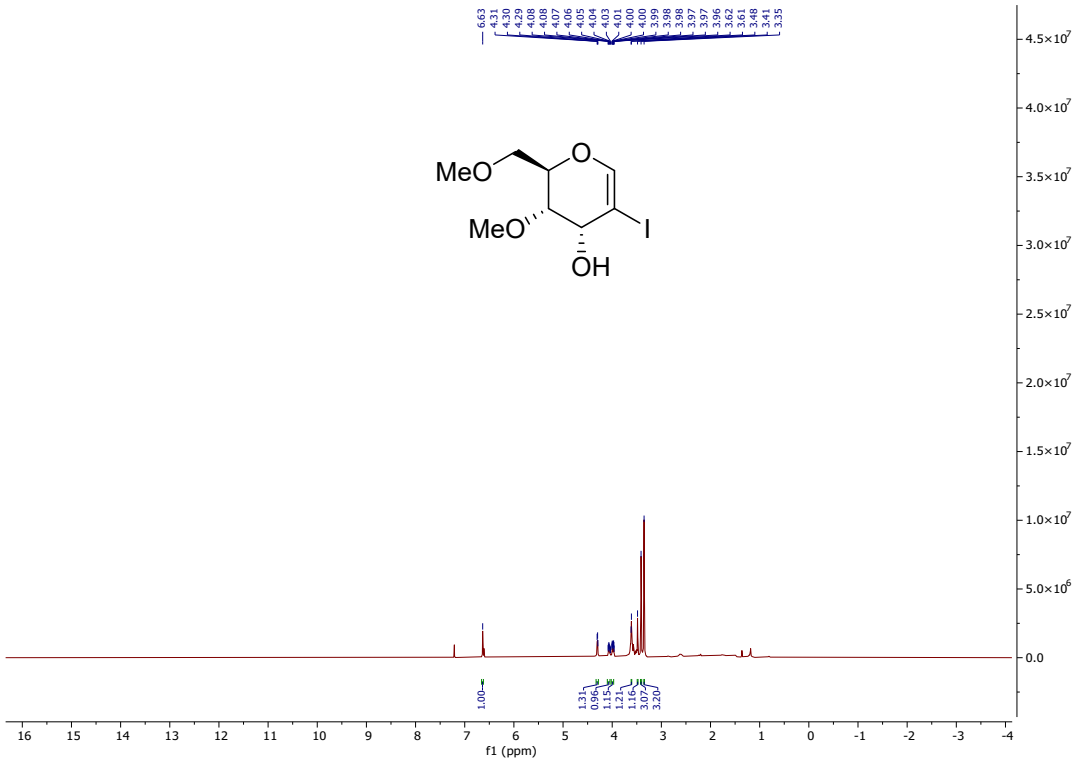
The compound **10** was synthesized according to the general procedure **(2.5)** using **6** (50 mg, 0.167 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (85:15) as eluent to obtain it as white solid (90 % yield, 45.30 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 6.69 (d, *J* = 1.2 Hz, 1H), 4.31 – 4.22 (m, 2H), 3.82 (dd, *J* = 4.8, 2.8 Hz, 1H), 3.75 (dd, *J* = 10.2, 6.2 Hz, 1H), 3.61 (d, *J* = 5.5 Hz, 1H), 3.59 (s, 3H), 3.43 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$) δ** 146.79, 74.73, 74.07, 73.35, 69.20, 66.42, 59.42, 58.29. **HRMS (ESI, m/z)** for $C_8H_{13}INaO_4$ $[M+Na]^+$: calcd 322.9756, found, 322.9763.

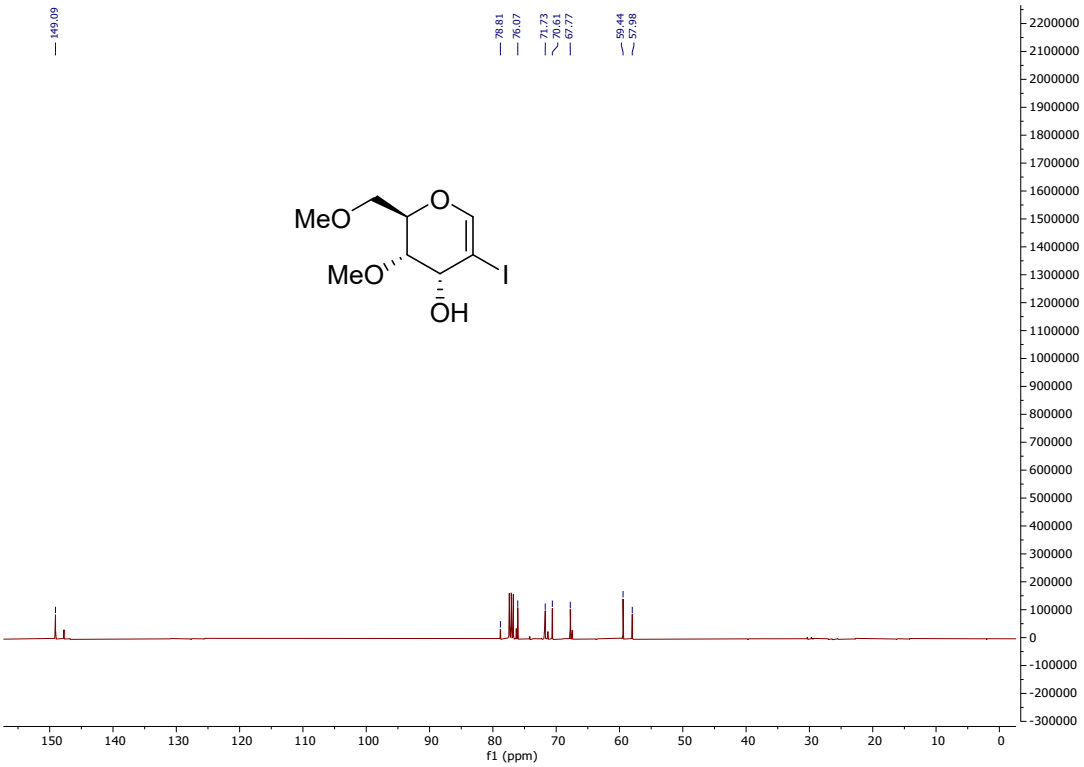
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **7** in $CDCl_3$[2]



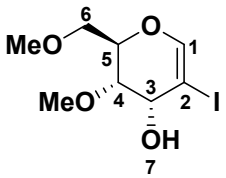


^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **8** in $CDCl_3$[2]





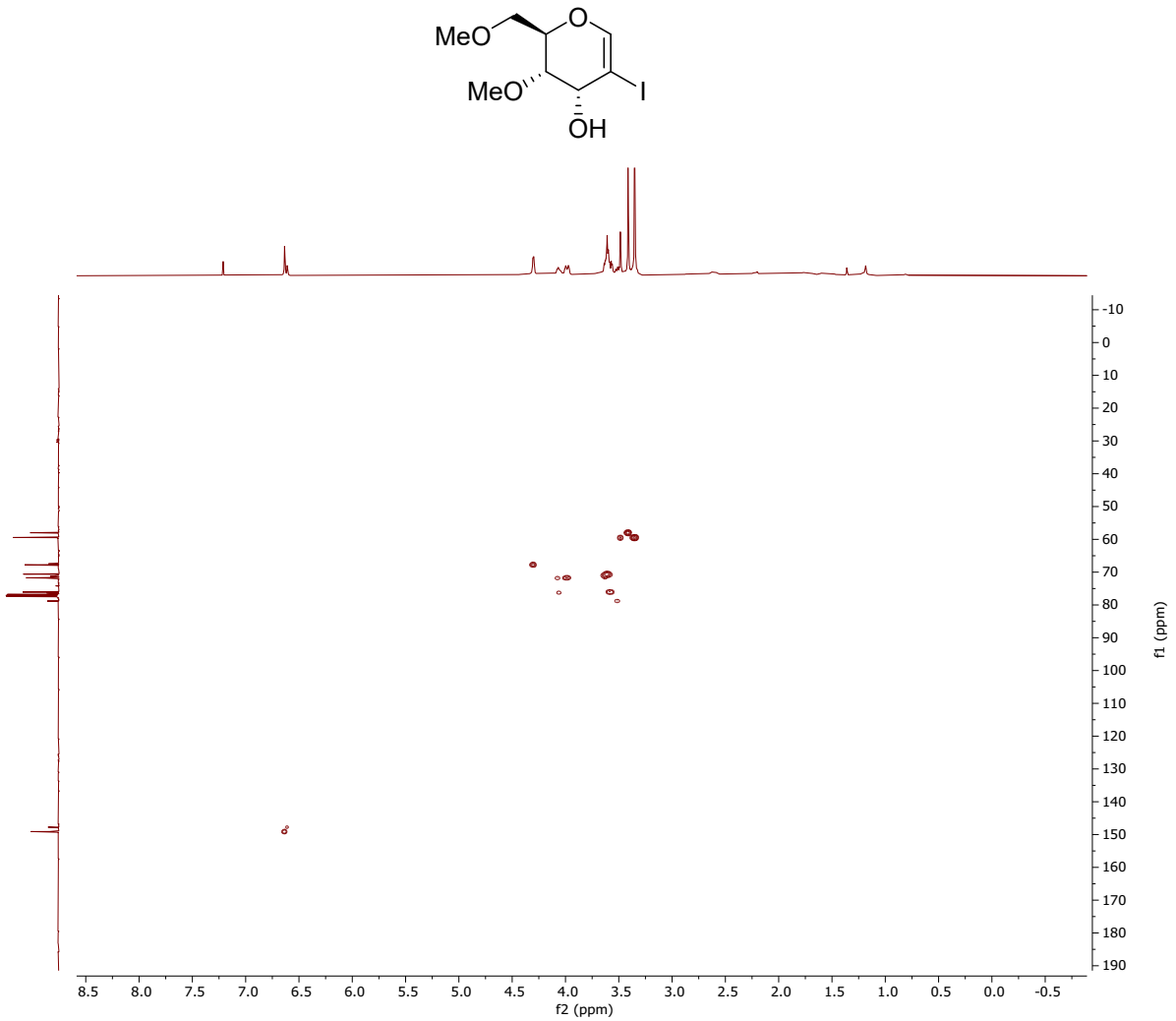
HSQC of compound **8**



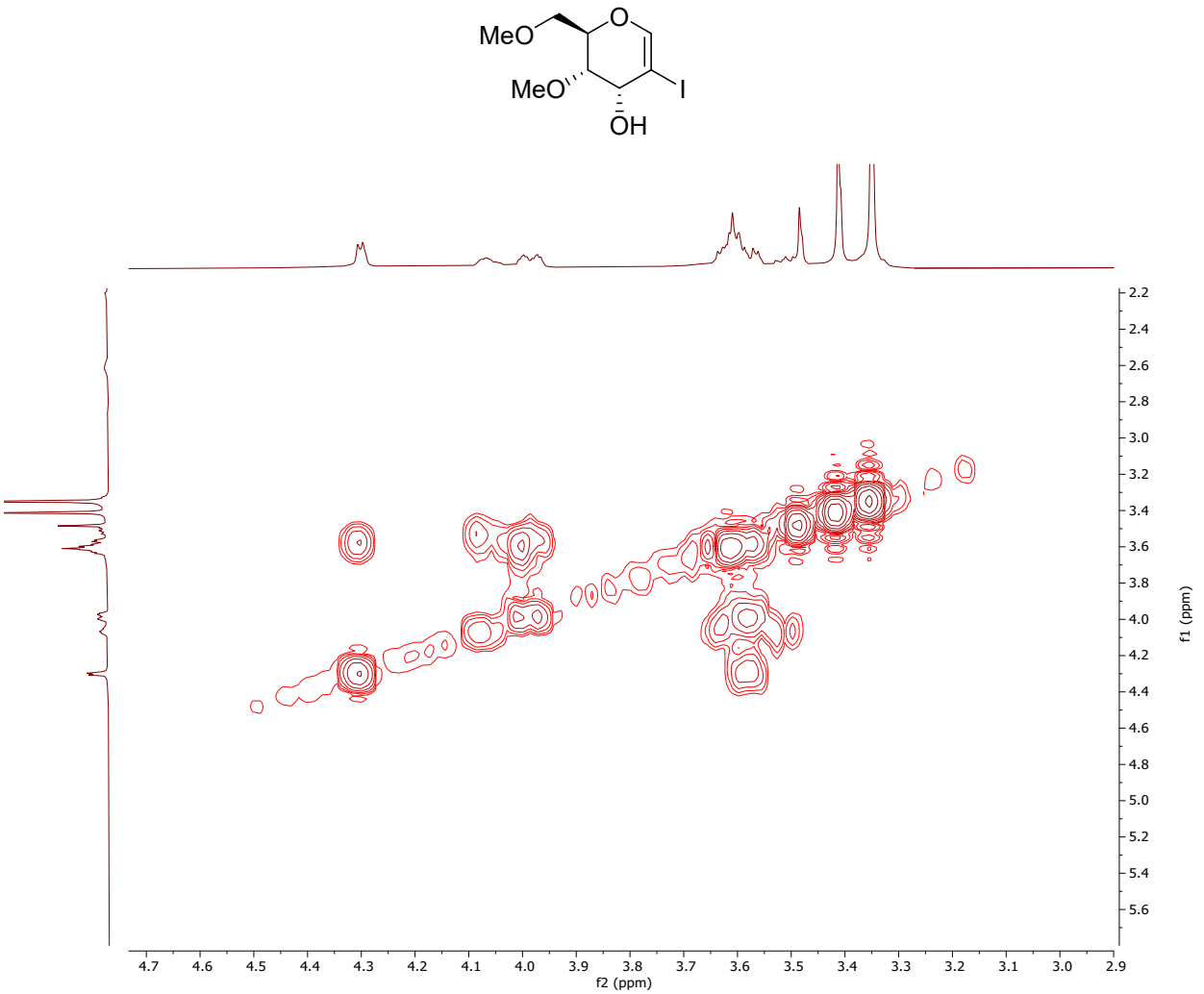
HSQC Table of compound **8**

Position	δ_H	δ_C
1	6.63 (s, 1H)	149.09
2	-	78.81
3	4.3 (d, *J* = 4.0 Hz, 1H)	67.77
4	3.99 (ddd, *J* = 10.2, 4.0, 2.4 Hz, 1H)	71.73
5	4.07 (td, *J* = 7.4, 6.8, 2.8 Hz, 1H)	76.07
6	3.61,3.39	70.60

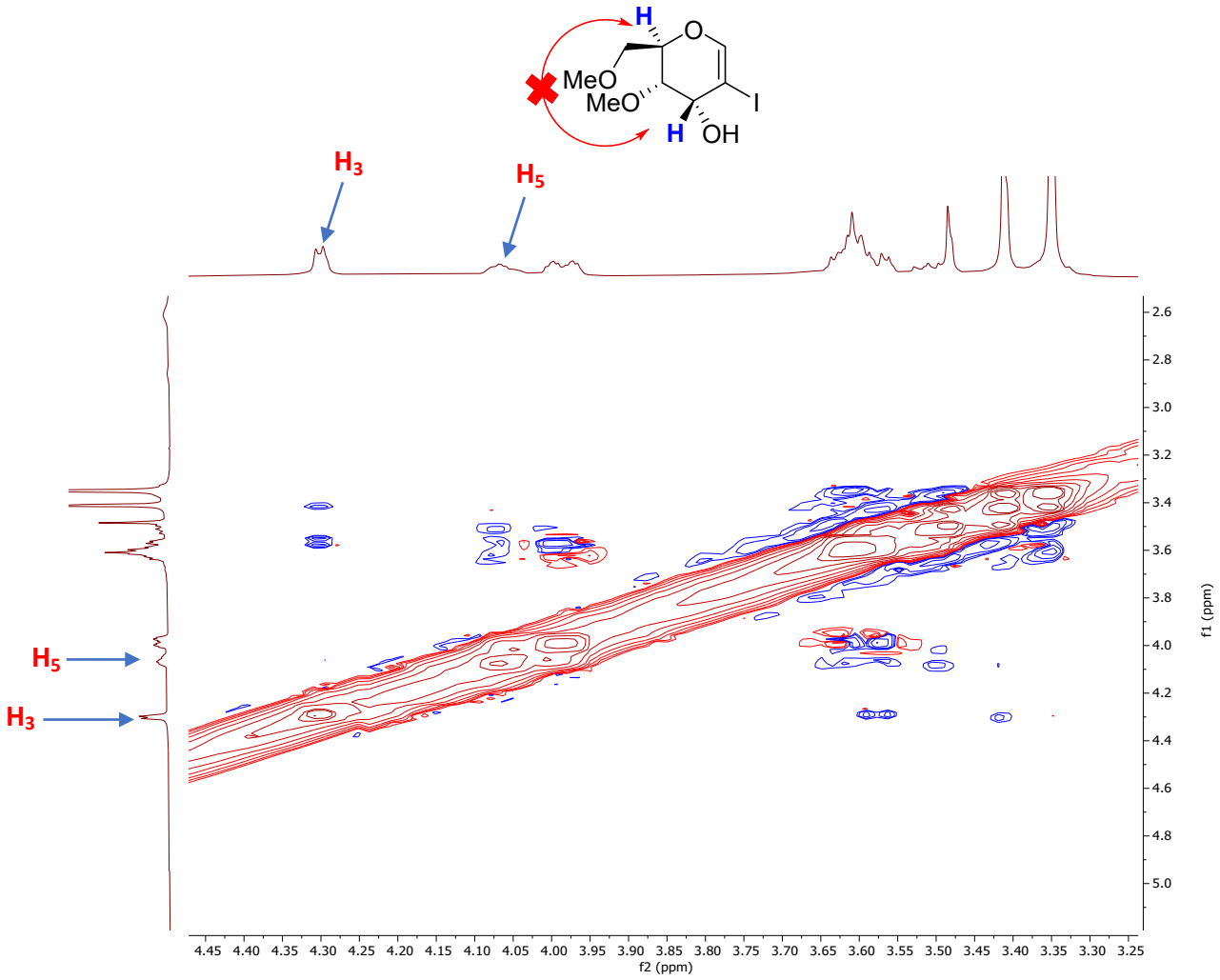
HSQC spectra of compound **8**



COSY spectra of compound **8**

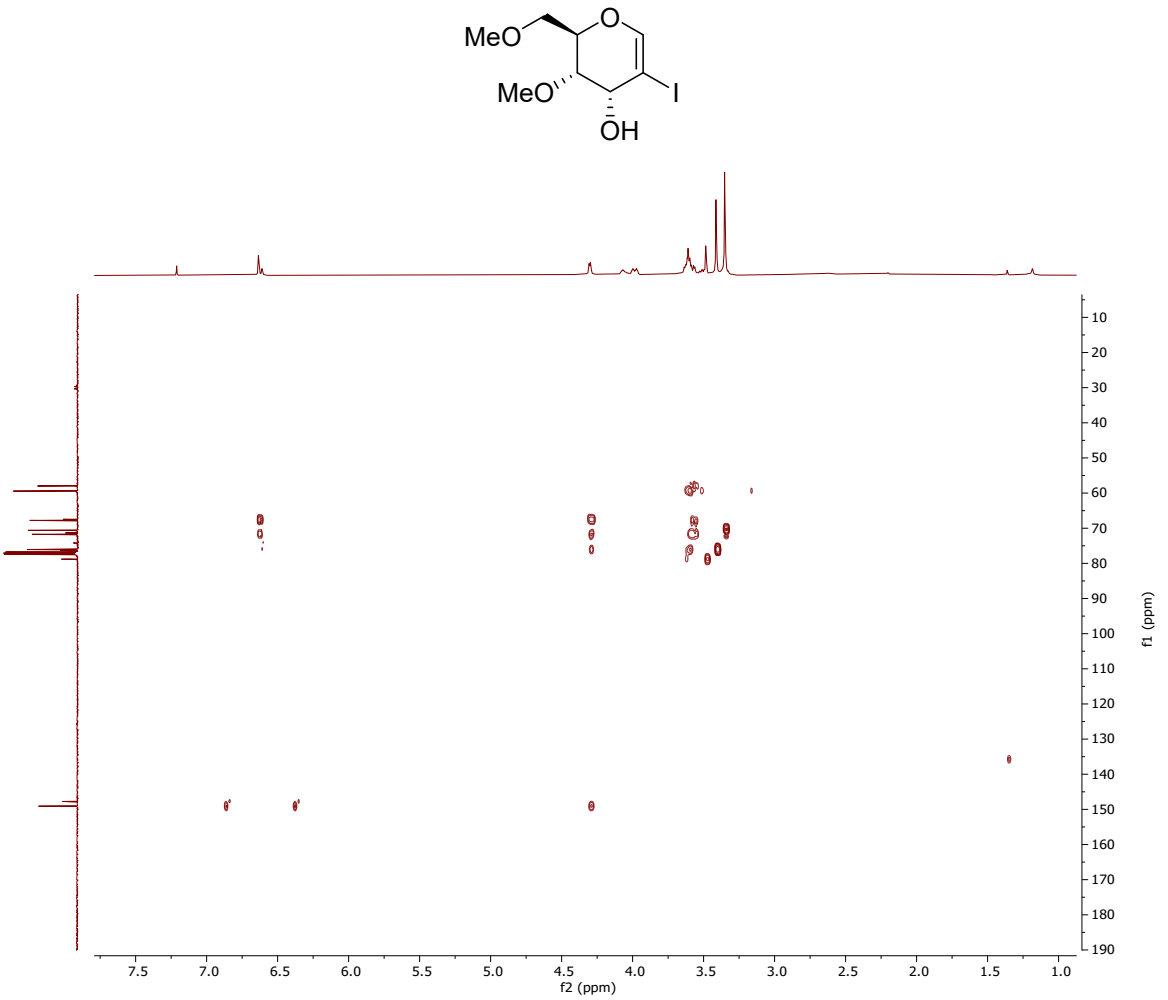


NOESY spectra of compound **8**

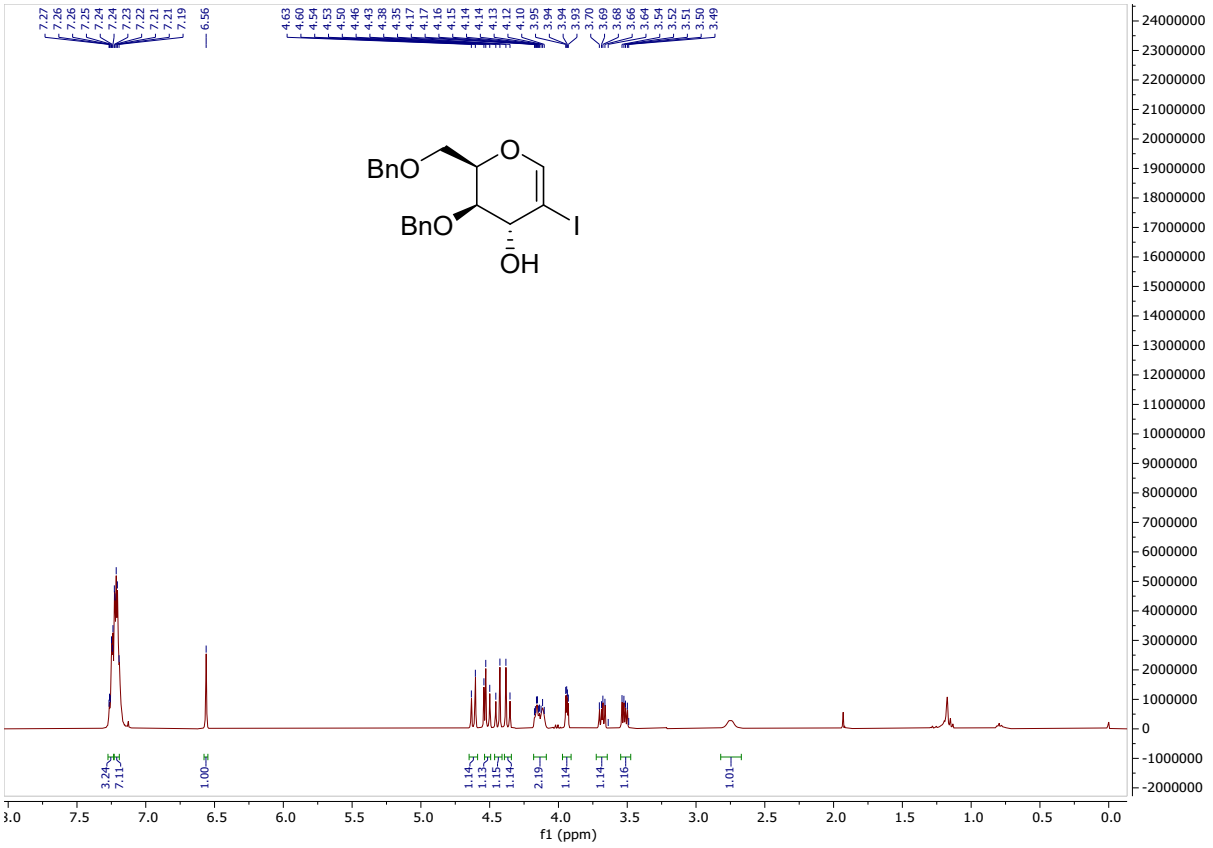


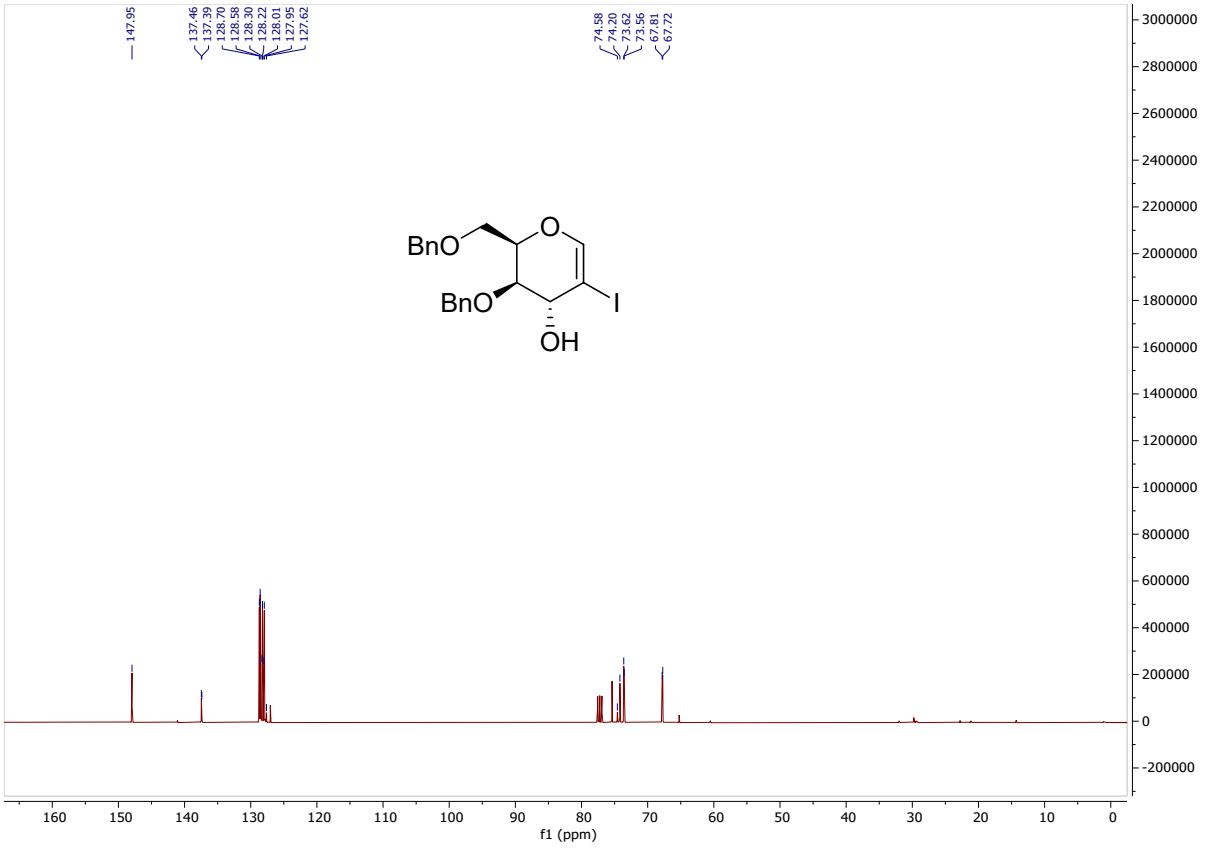
No correlation is observed in NOESY between H3 (4.3 ppm (d, *J* = 4.0 Hz, 1H)) & H5 (4.07 (td, *J* = 7.4, 6.8, 2.8 Hz, 1H)) confirming α-stereochemistry at C-3.

HMBC spectra of compound **8**

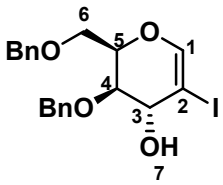


^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **9** in $CDCl_3$[2]



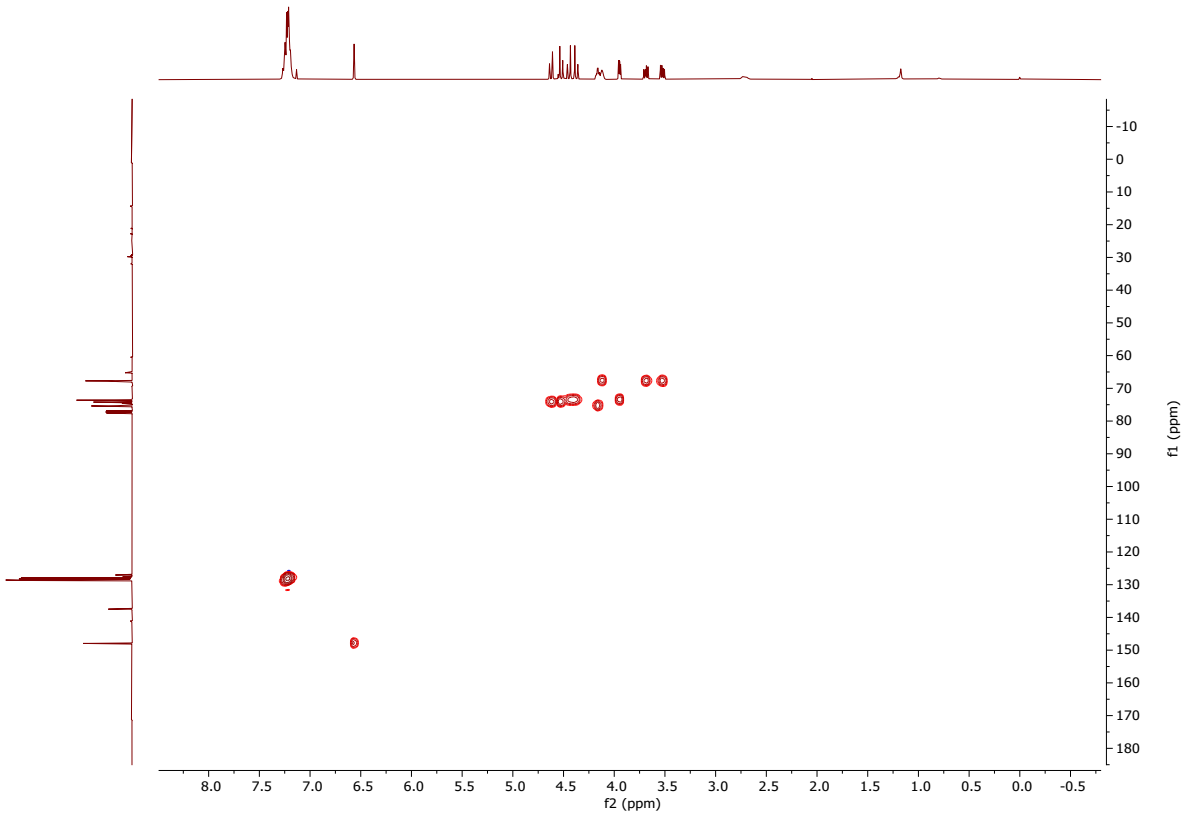


HSQC table of compound **9**

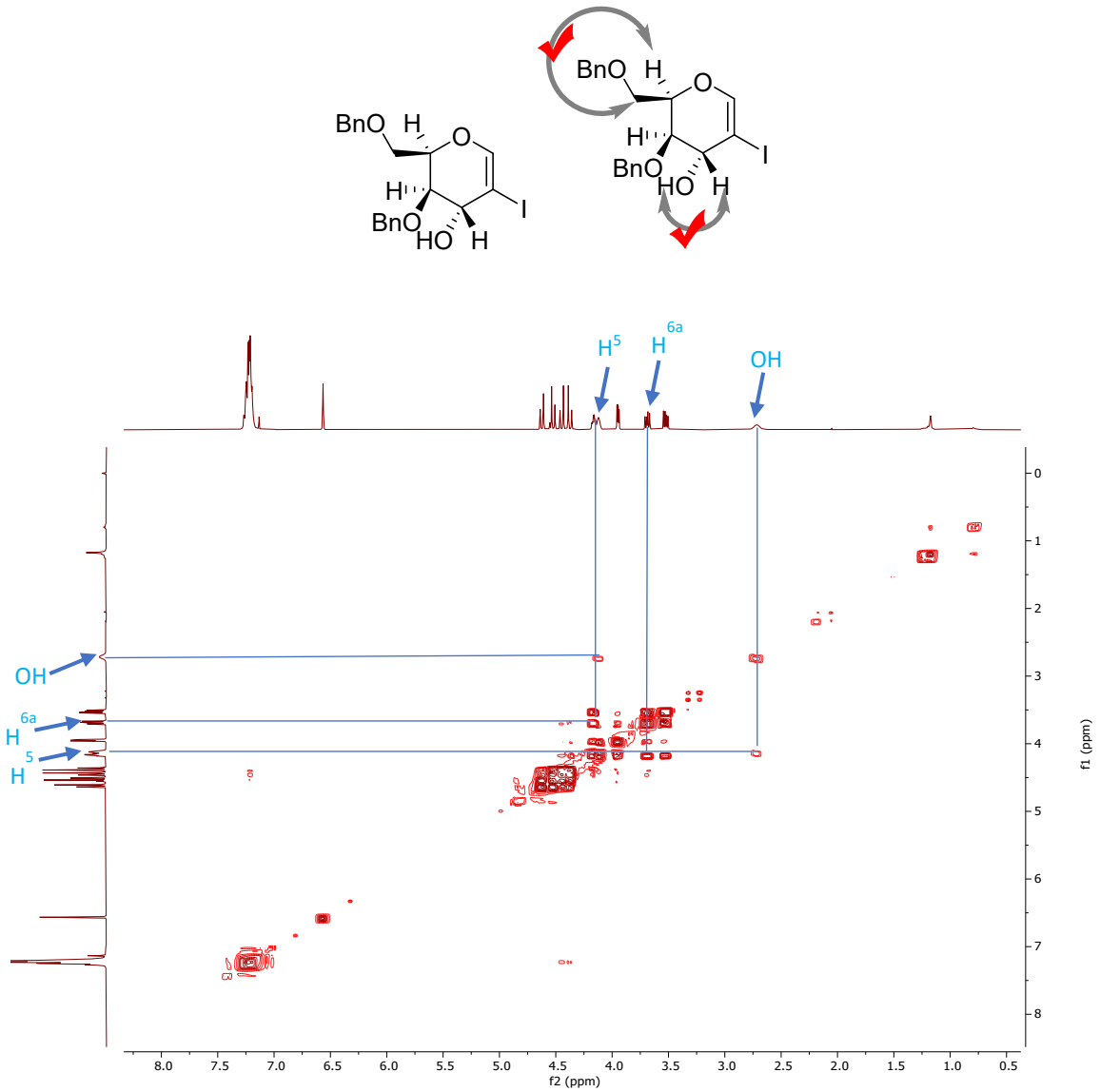


Position	δ_H	δ_C
1	H_1= 6.57 (s, 1H)	147.95
2	-	74.58
3	H_3= 4.12	67.72
4	H_4= 3.95 (dd, *J* = 4.9, 2.8 Hz, 1H)	73.56
5	H_5= 4.16 (td, *J* = 5.8, 2.7 Hz, 1H)	75.39
6	H_{6a}=3.52 (dd, *J* = 10.2, 5.5 Hz, 1H)	67.81
6	H_{6a}=3.68 (dd, *J* = 10.2, 6.1 Hz, 1H)	67.81
7	H_7 =2.72 (brs,1H)	-

HSQC spectra of compound **9**



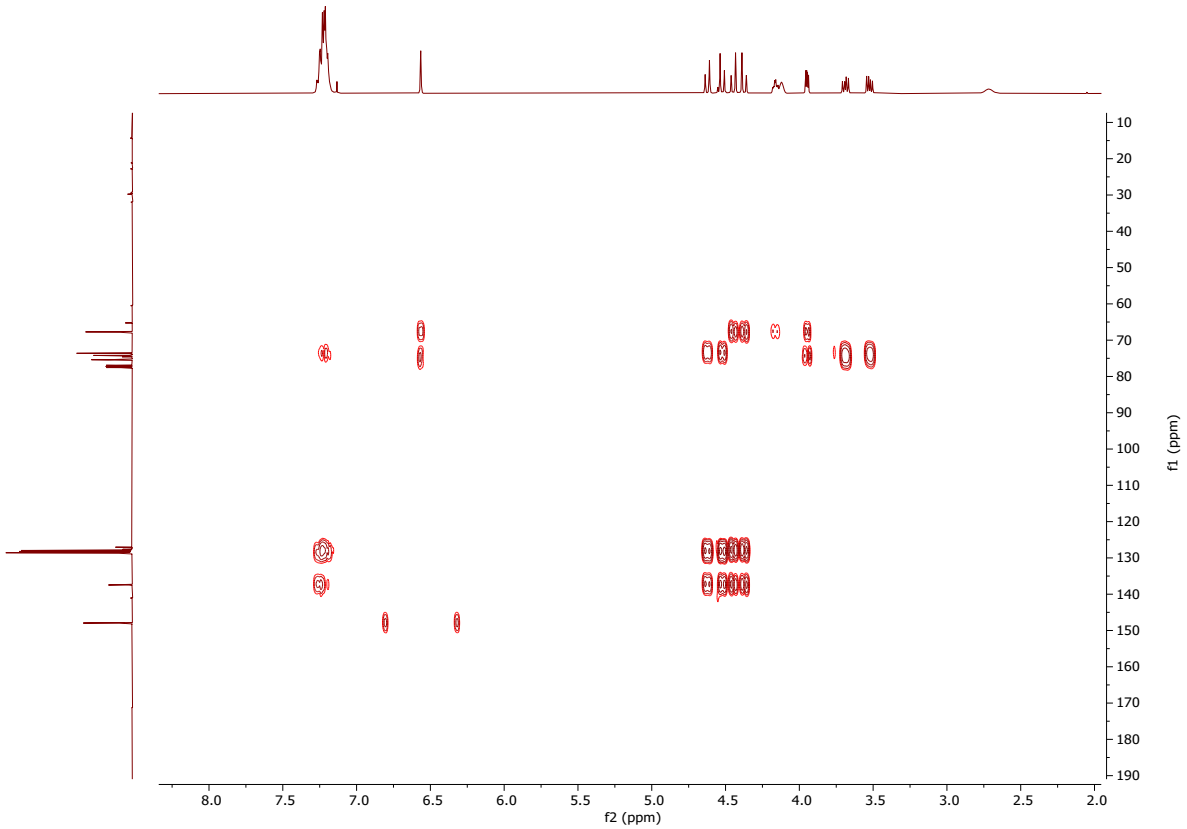
COSY spectra of compound **9**



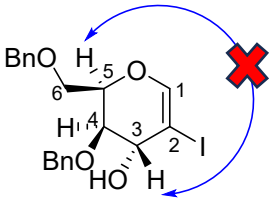
In the COSY experiment, a correlation was observed between the O-H proton at 2.7 ppm and a proton at 4.12 ppm, confirming this as H-3. Additionally, the proton at 4.16 ppm (td) shows correlation with one of the benzylic CH_2 protons at 3.68 ppm, identifying it as H-5, with the proton at 3.95 ppm (dd) subsequently assigned as H-4.

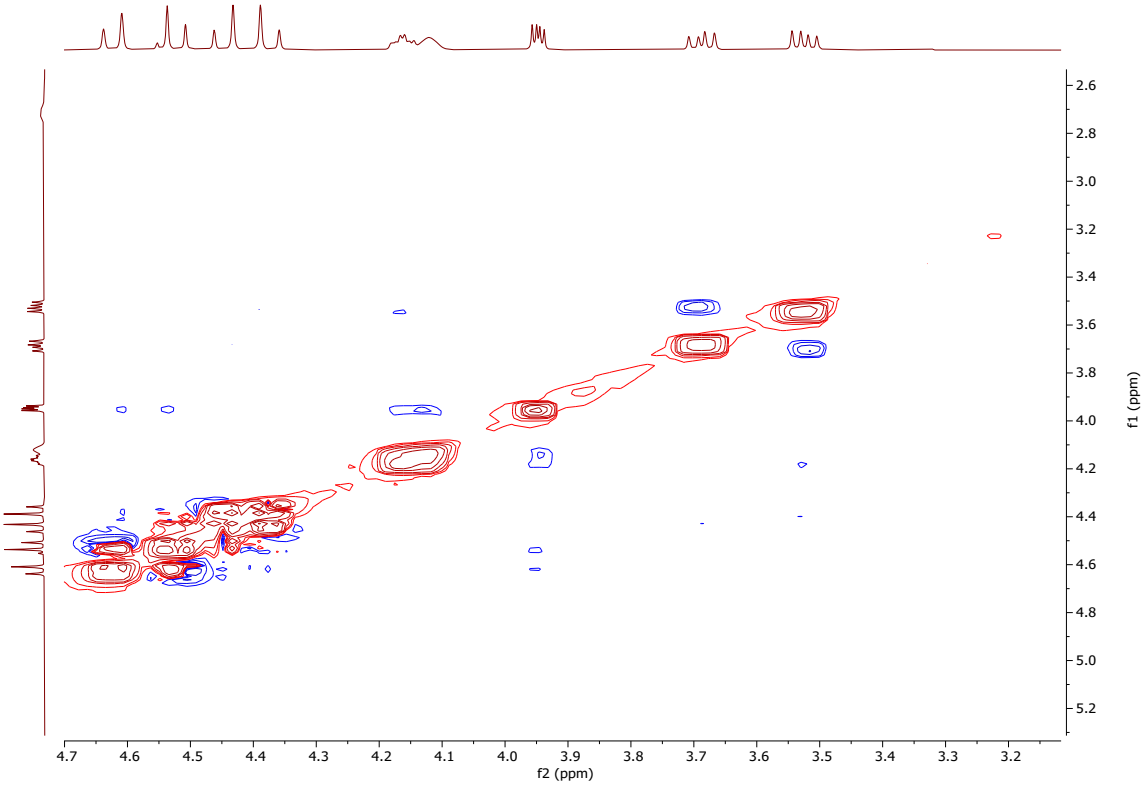
To further confirm the exact assignments of protons and carbons at positions 3, 4, and 5, acetylation of the C-3 hydroxyl group was performed. This modification caused a more pronounced downfield shift for the proton at C-3 compared to those at the other two positions, supporting the assignment.

HMBC spectra of compound **9**



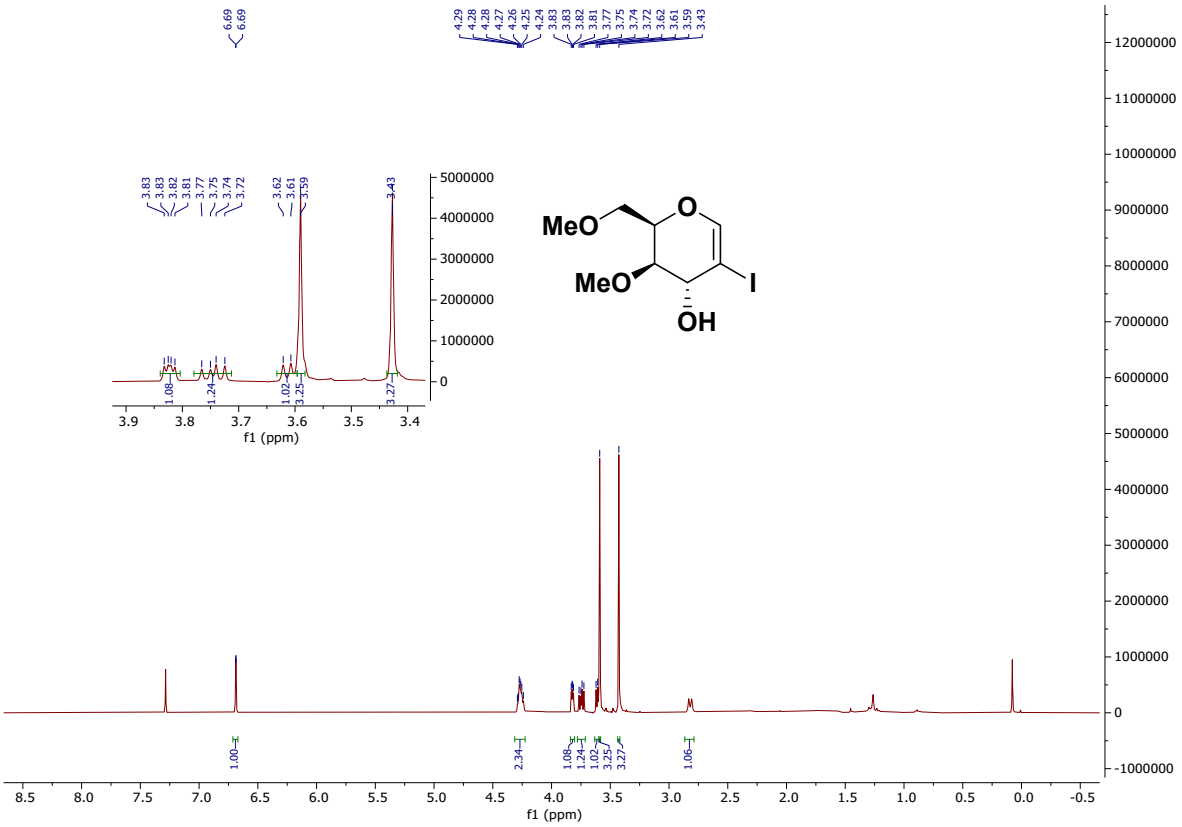
NOESY spectra of compound **9**

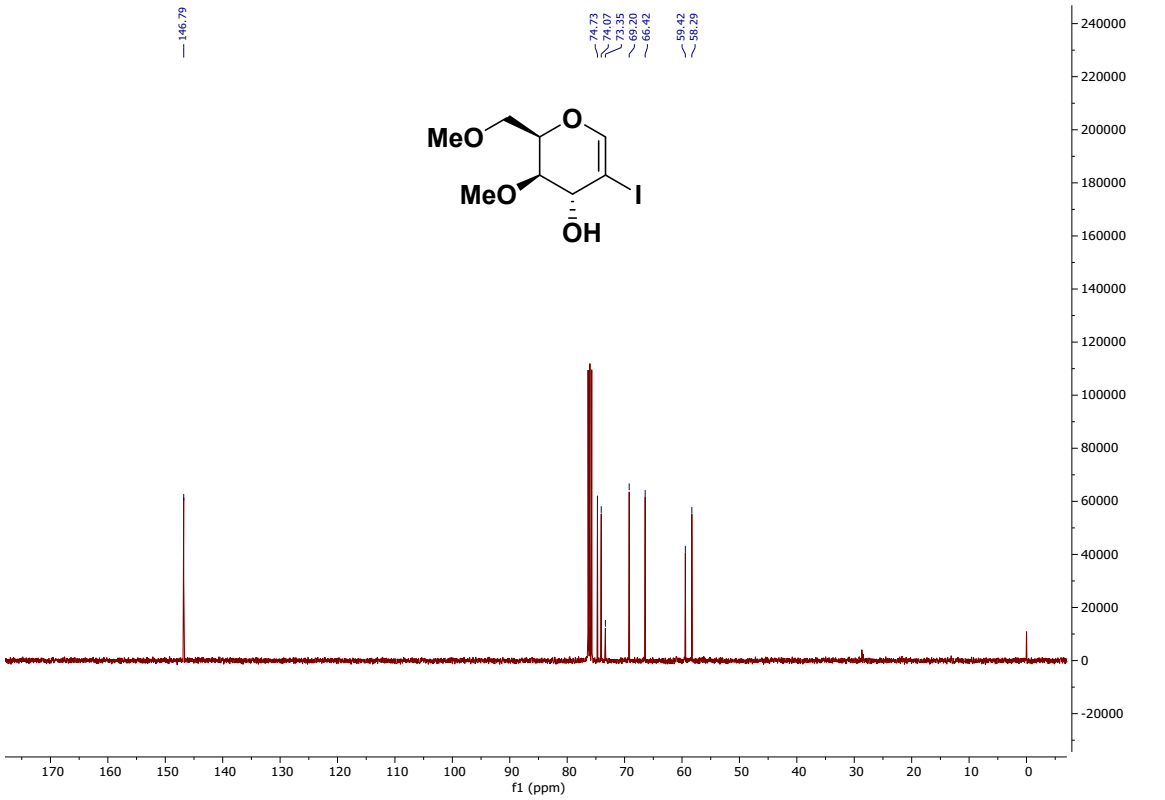




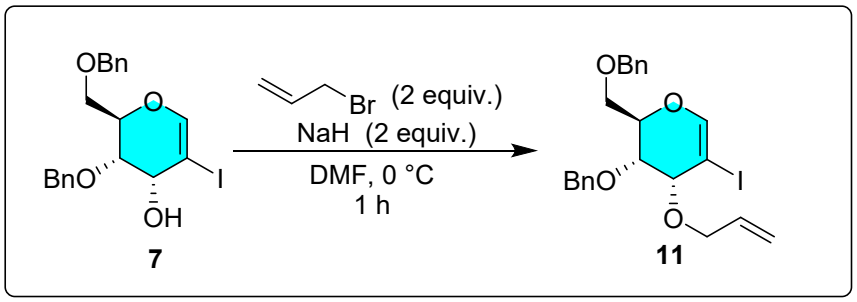
In the NOESY experiment, we observed no correlation between the H_3 and H_5 proton, confirming the α stereochemistry of OH at C-3.

^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **10** in $CDCl_3$



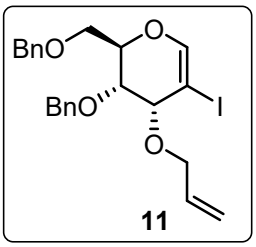


2.7 General procedure for allylation:

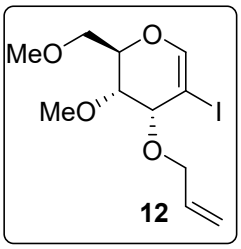


By taking **7** as an example. Compound **11** was synthesized using **7** (30 mg, 0.066 mmol,1 equiv.) in solvent DMF (2 ml) and to this was added NaH (2 equiv.) and allyl bromide (2 equiv.) at 0 ℃ sequentially and portion-wise. The reaction mixture was allowed to stir until complete consumption of the starting material was observed by TLC analysis. Then the reaction mixture was extracted with ethyl acetate and ice-cold water thrice and the organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuo. The residue left was purified by column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (94:6) as eluent to obtain compound **11** as a pale gummy liquid (31.02 mg, 95%).

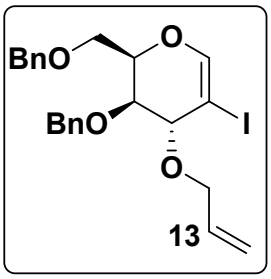
2.8 Characterization data & NMR spectra of compounds 11-14:



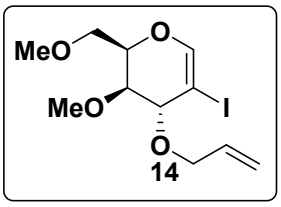
The compound **11** was synthesized according to the general procedure **(2.7)** using **7** (30 mg, 0.066 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (94:6) as eluent to obtain it as a pale gummy liquid (95 % yield, 31.02 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.28 – 7.23 (m, 7H), 7.22 – 7.15 (m, 3H), 6.60 (s, 1H), 5.93 (ddt, *J* = 17.3, 10.3, 6.0 Hz, 1H), 5.22 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.12 (dq, *J* = 10.3, 1.3 Hz, 1H), 4.60 (d, *J* = 11.4 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 3.9 Hz, 1H), 4.45 (d, *J* = 4.5 Hz, 1H), 4.28 (ddt, *J* = 12.4, 5.8, 1.4 Hz, 1H), 4.22 – 4.13 (m, 2H), 3.99 (d, *J* = 3.5 Hz, 1H), 3.89 (dd, *J* = 10.7, 3.5 Hz, 1H), 3.73 (dd, *J* = 5.2, 2.9 Hz, 2H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 149.2, 137.9 (Cq), 137.5 (Cq), 135.2, 128.5, 128.4, 128.0, 128.0, 127.8, 127.8, 127.7, 117.6 (CH_2), 75.5, 75.2, 73.6 (CH_2), 73.2 (CH_2), 72.7, 72.4 (CH_2), 68.4 (CH_2), 64.9 (Cq). **HRMS (ESI, m/z)** for $C_{23}H_{26}IO_4$ $[M+H]^+$: calcd 493.0876, found, 493.0880.



The compound **12** was synthesized according to the general procedure **(2.7)** using **8** (30 mg, 0.10 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (93:7) as eluent to obtain it as a pale gummy liquid (95 % yield, 32.30 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 6.60 (s, 1H), 6.05 – 5.85 (m, 1H), 5.28 (dp, *J* = 17.2, 1.4 Hz, 1H), 5.16 (ddq, *J* = 10.3, 2.0, 1.1 Hz, 1H), 4.32 (ddq, *J* = 12.4, 5.9, 1.3 Hz, 1H), 4.22 (ddq, *J* = 12.4, 6.0, 1.3 Hz, 1H), 4.17 – 4.11 (m, 1H), 4.06 (t, *J* = 1.6 Hz, 1H), 3.63 – 3.61 (m, 1H), 3.60 – 3.55 (m, 1H), 3.42 (dd, *J* = 21.5, 1.1 Hz, 3H), 3.33 (dd, *J* = 6.2, 1.1 Hz, 3H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 149.2, 135.2, 117.7, 78.2, 77.1, 74.6, 73.1, 72.4, 70.8, 64.7, 59.4, 58.0. **HRMS (ESI, m/z)** for $C_{11}H_{21}INO_4$ $[M+NH_4]^+$: calcd 358.0515, found, 358.0520.

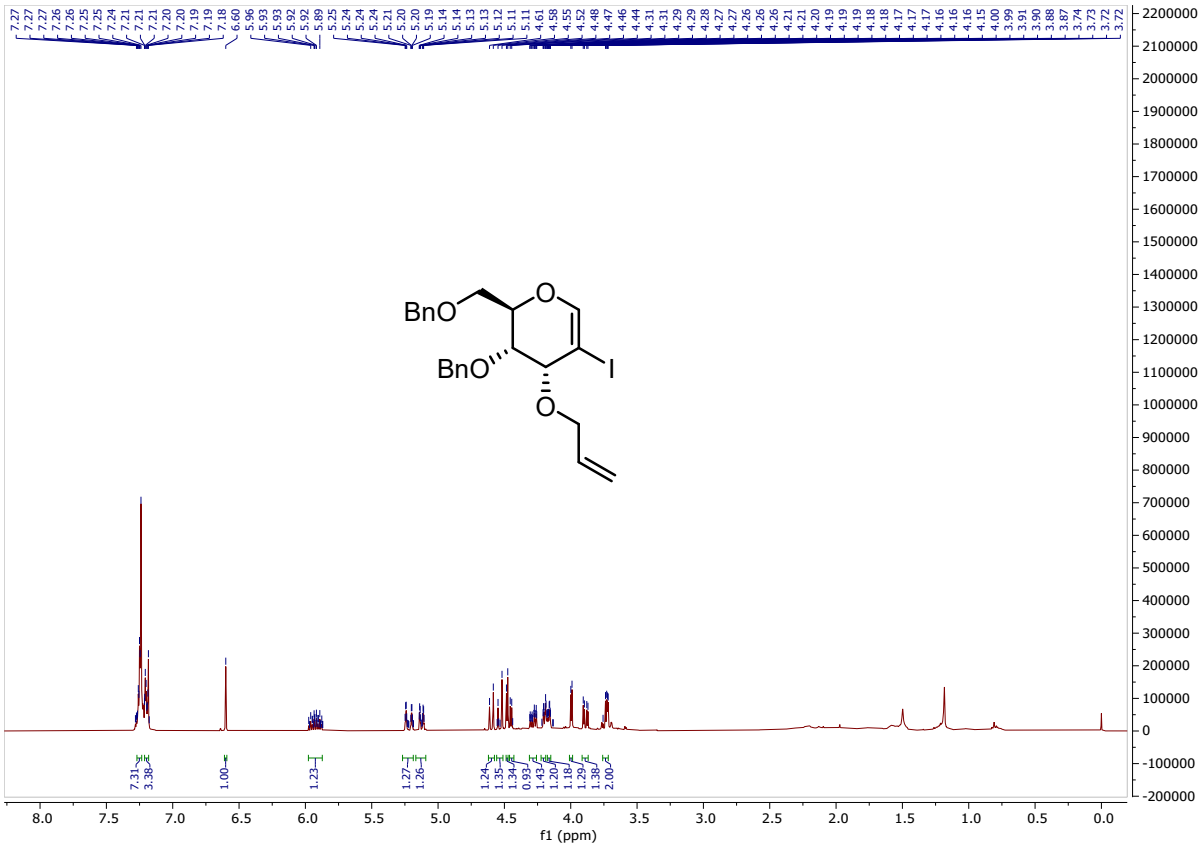


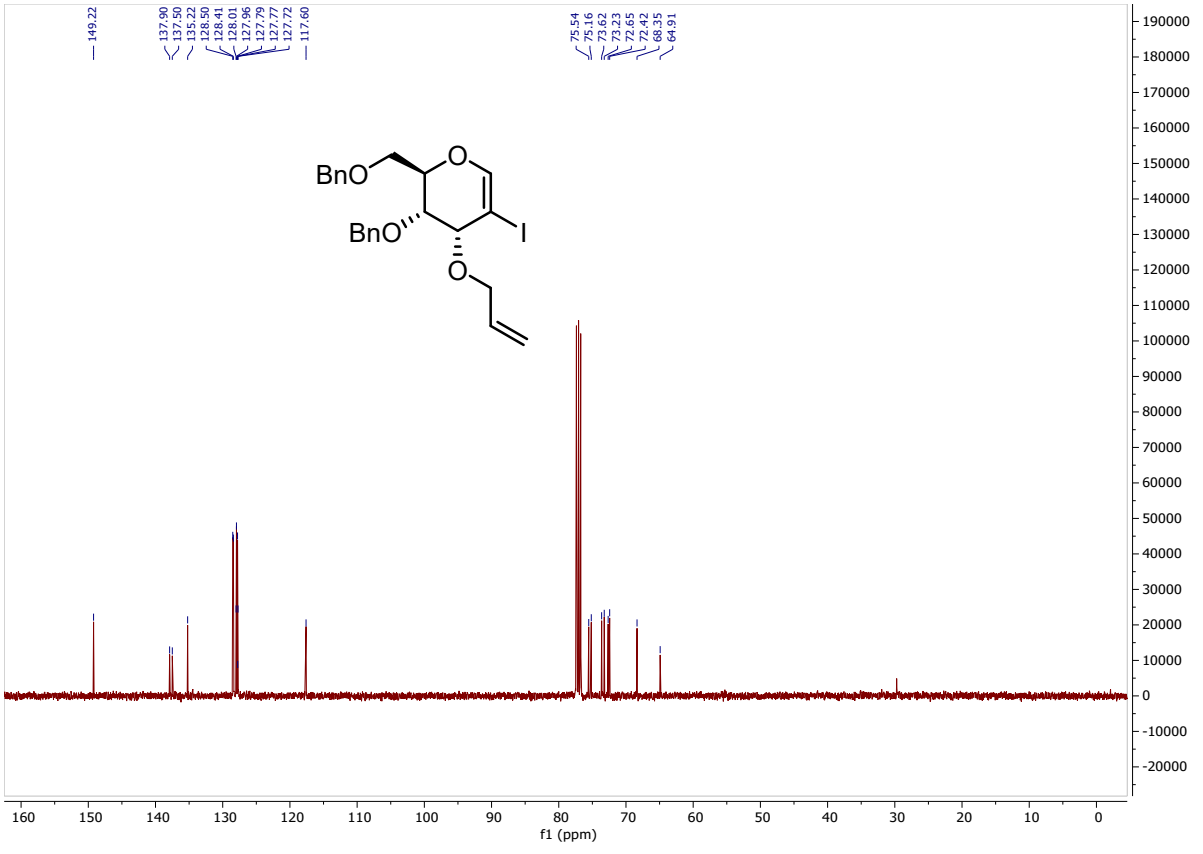
The compound **13** was synthesized according to the general procedure **(2.7)** using **9** (30 mg, 0.066 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (94:6) as eluent to obtain it as a pale gummy liquid (95 % yield, 31.02 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.31 – 7.12 (m, 10H), 6.54 (s, 1H), 5.90 (ddt, *J* = 17.3, 10.4, 5.6 Hz, 1H), 5.24 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.12 (dq, *J* = 10.4, 1.4 Hz, 1H), 4.72 (d, *J* = 11.9 Hz, 1H), 4.51 (d, *J* = 11.9 Hz, 1H), 4.42 (d, *J* = 11.8 Hz, 1H), 4.34 (d, *J* = 11.9 Hz, 1H), 4.24 (ddt, *J* = 7.0, 4.4, 2.2 Hz, 1H), 4.14 (qdt, *J* = 12.6, 5.8, 1.5 Hz, 2H), 3.93 (d, *J* = 2.2 Hz, 2H), 3.71 (dd, *J* = 10.5, 7.5 Hz, 1H), 3.60 (dd, *J* = 10.6, 4.5 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 147.6, 138.0 (Cq), 137.9 (Cq), 134.8, 134.7, 128.5, 128.5, 128.0, 128.0, 127.9, 127.8, 117.5 (CH_2), 77.5, 77.2, 76.8, 75.9, 75.5, 73.5 (CH_2), 73.3 (CH_2), 72.8 (CH_2), 72.7, 70.8 (Cq), 68.0 (CH_2). **HRMS (ESI, m/z)** for $C_{23}H_{26}IO_4$ $[M+H]^+$: calcd 493.0876, found, 493.088



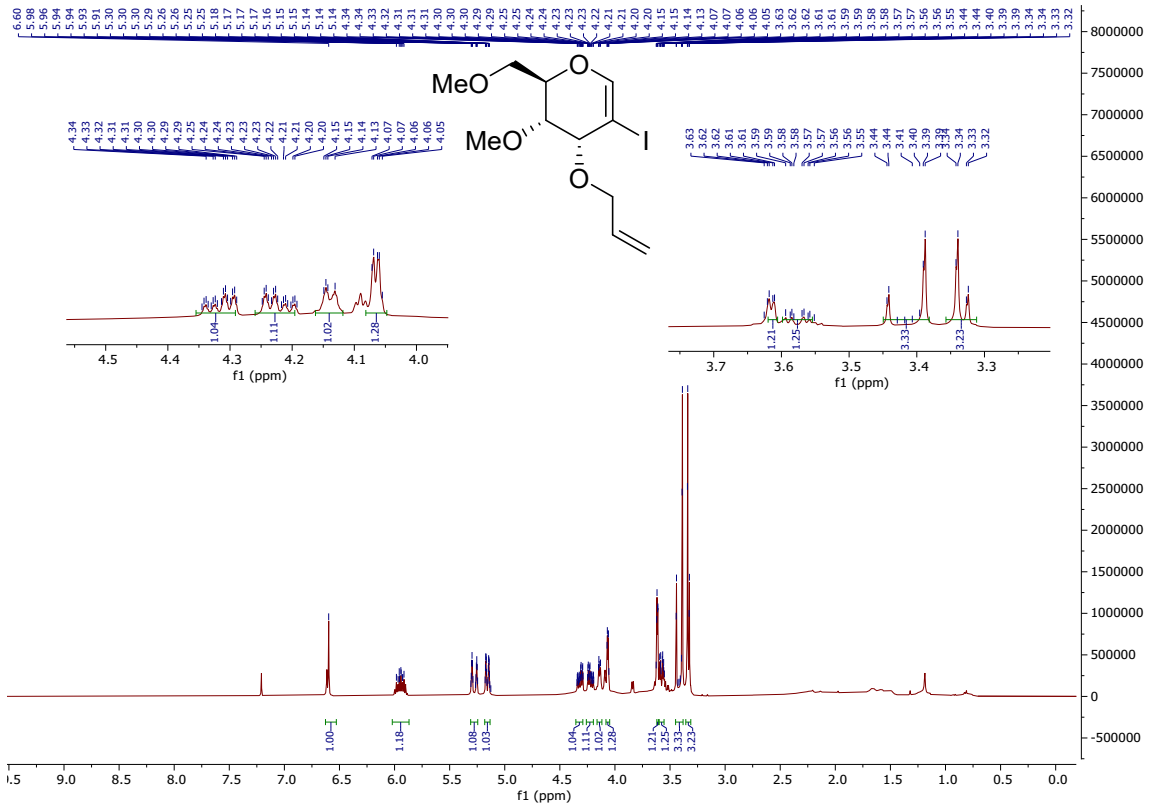
The compound **14** was synthesized according to the general procedure **(2.7)** using **10** (30 mg, 0.10 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (93:7) as eluent to obtain it as a pale gummy liquid (95 % yield, 32.30 mg).**^{1}H NMR (400 MHz, CDCl3) δ** 6.56 (d, J = 1.3 Hz, 1H), 5.93 (ddt, J = 17.4, 10.3, 5.7 Hz, 1H), 5.28 (dq, J = 17.1, 1.6 Hz, 1H), 5.15 (dq, J = 10.4, 1.5 Hz, 1H), 4.26 – 4.20 (m, 1H), 4.16 (tdt, J = 12.7, 5.8, 1.4 Hz, 2H), 3.96 (dt, J = 4.1, 1.2 Hz, 1H), 3.75 – 3.71 (m, 1H), 3.65 (dd, J = 10.5, 7.5 Hz, 1H), 3.55 (dd, J = 10.5, 4.7 Hz, 1H), 3.49 (s, 3H), 3.33 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$) δ** 147.60, 134.63, 117.55, 75.46, 75.24, 74.93, 72.57, 70.70, 70.05, 59.93, 59.20. **HRMS (ESI, m/z)** for $C_{11}H_{18}IO_4$ $[M+Na]^+$: calcd 341.0250, found, 341.0257.

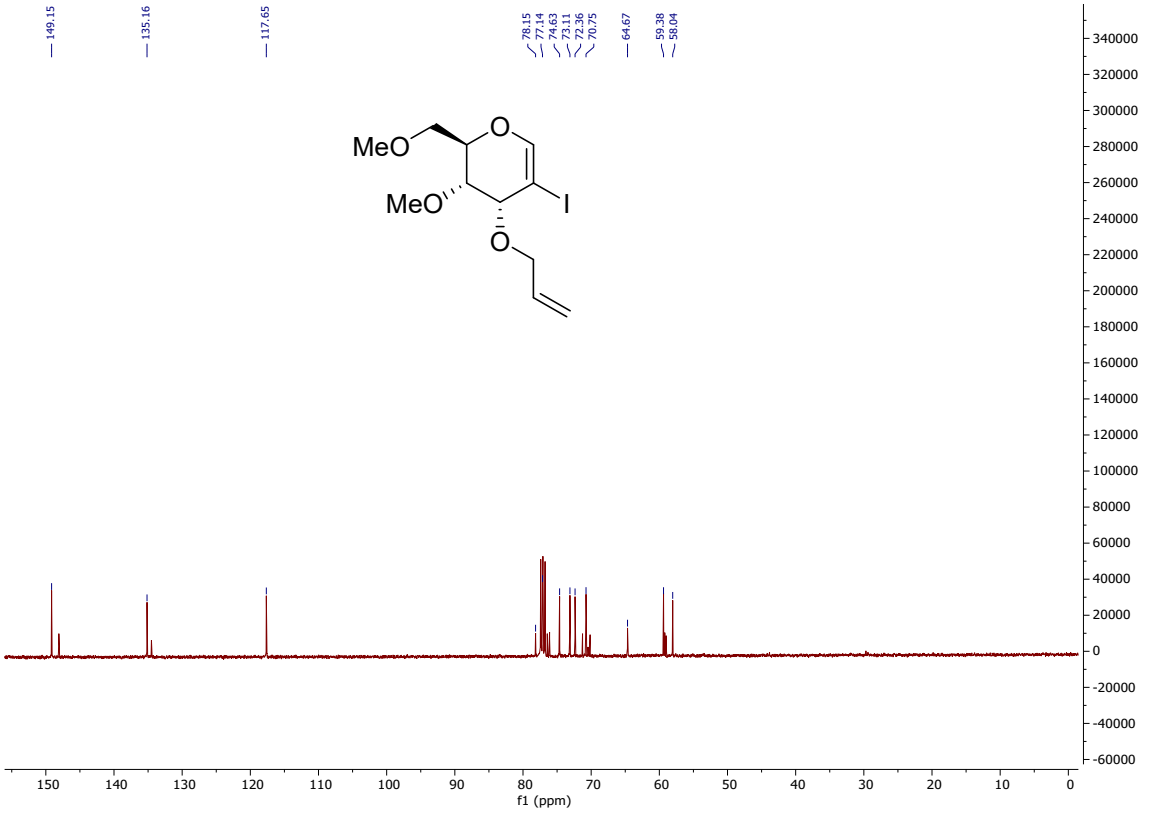
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **11** in $CDCl_3$



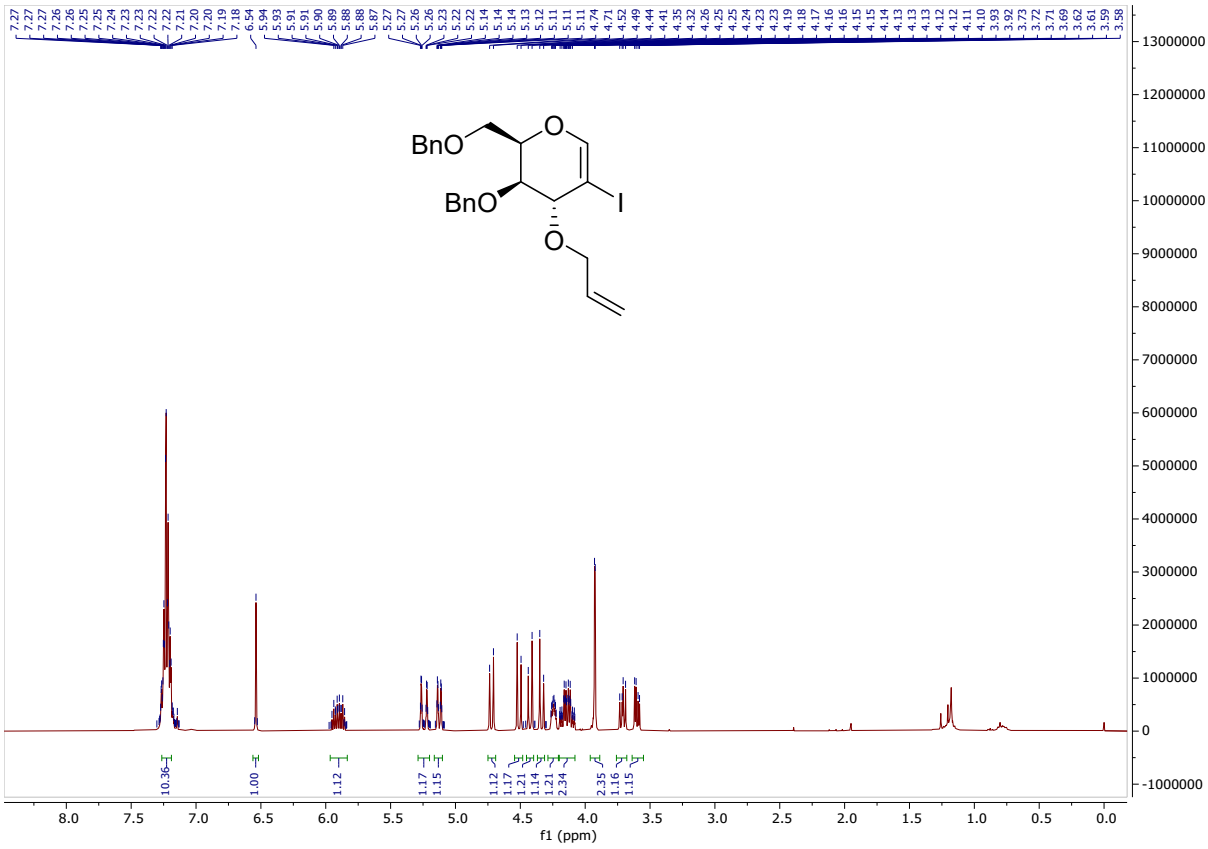


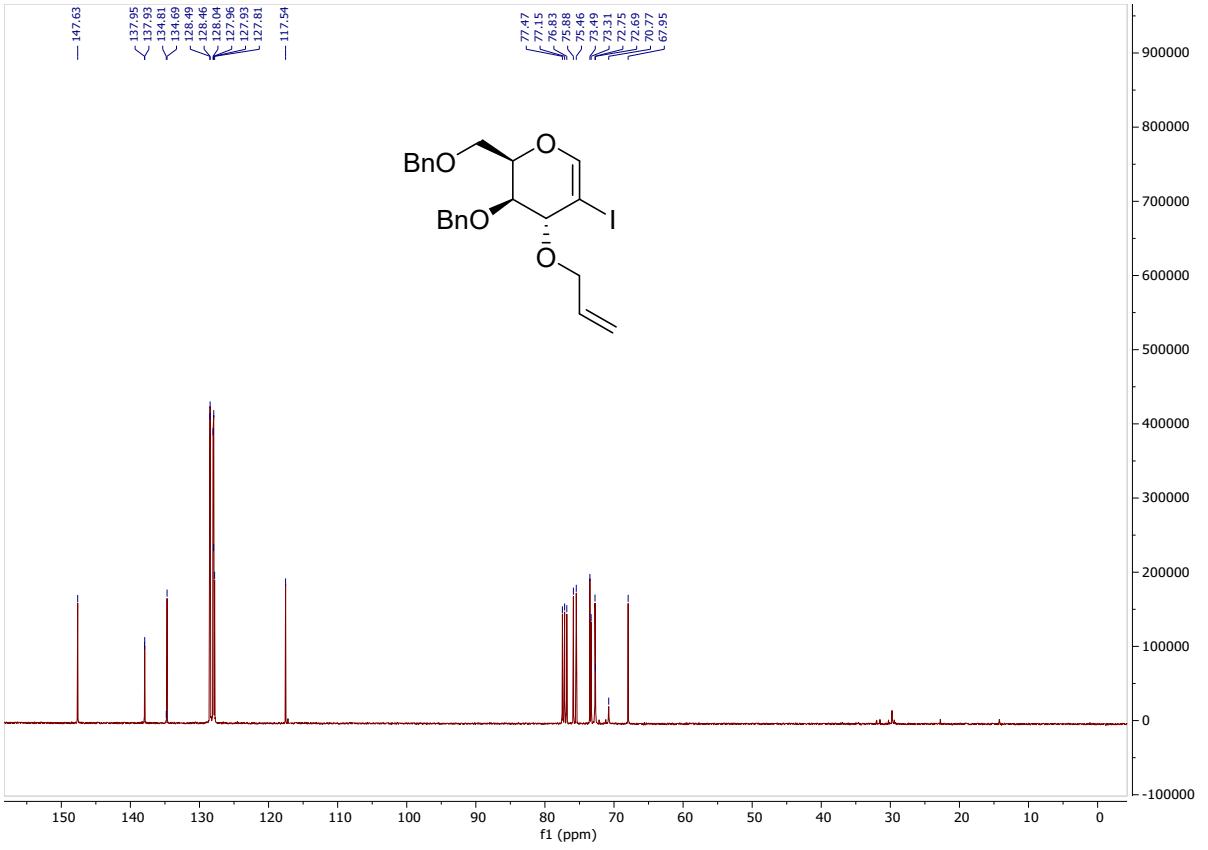
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **12** in $CDCl_3$



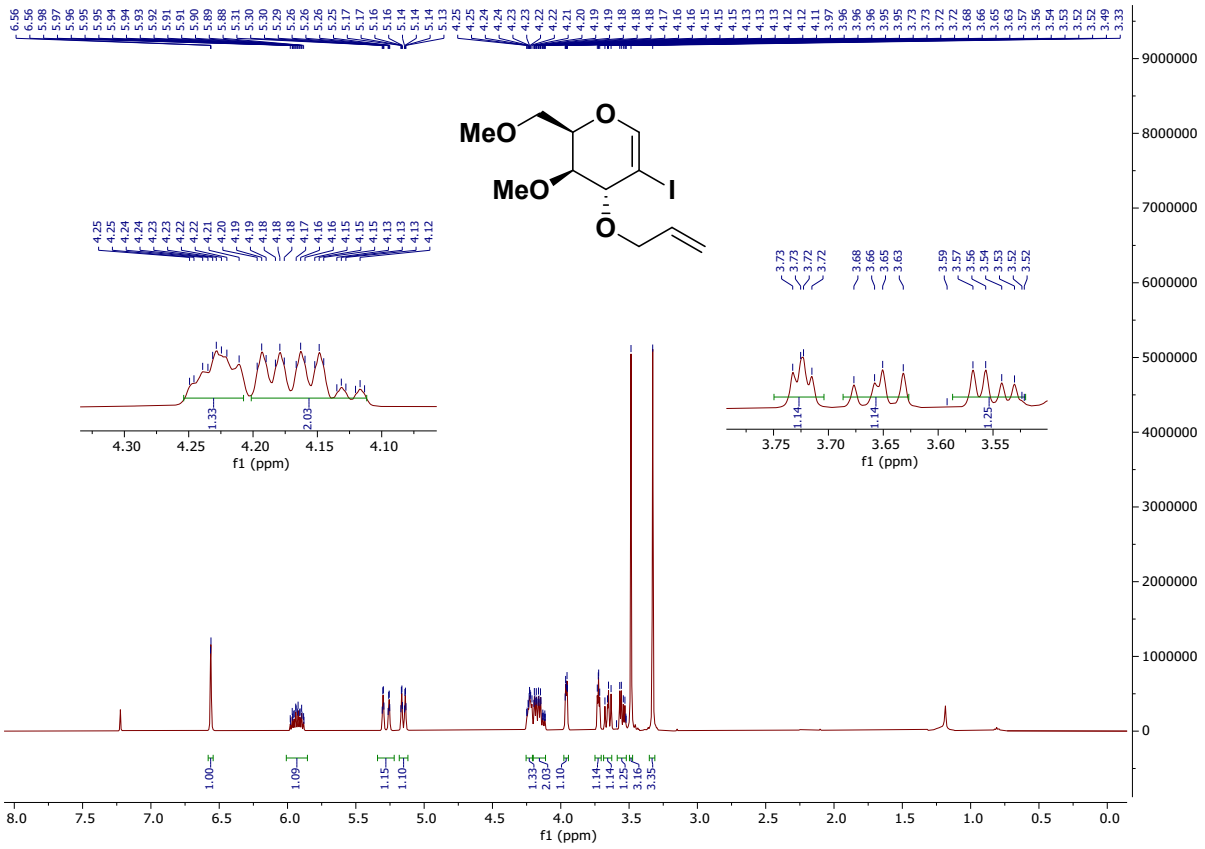


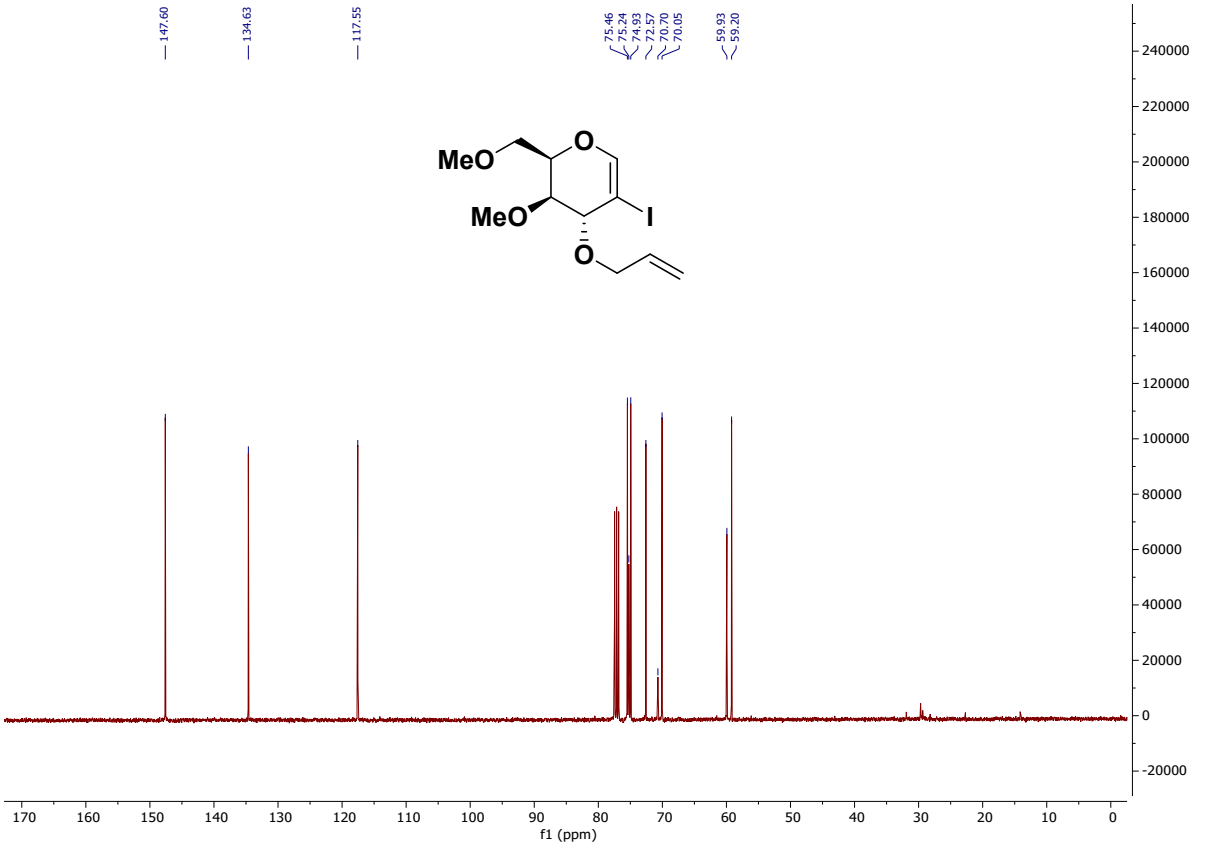
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **13** in $CDCl_3$



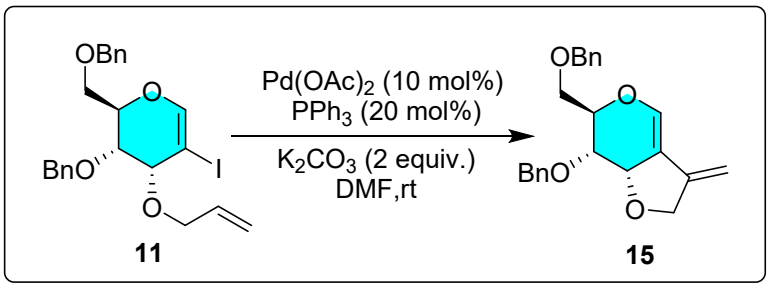


^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **14** in $CDCl_3$



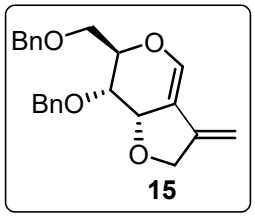


2.9 General procedure for intramolecular Heck reaction:

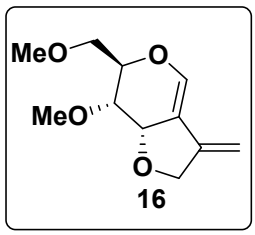


By taking **11** as an example. Compound **15** was synthesized using **11** (30 mg, 0.060 mmol,1 equiv.) in solvent DMF (2 ml) and to this was added $Pd(OAc)_2$ (10 mol%), PPh_3 (20 mol%), K_2CO_3 (2 equiv.). The reaction mixture was allowed to stir at room temperature until complete consumption of the starting material was observed by TLC analysis. Then the reaction mixture was passed through celite and the filtrate was extracted with ethyl acetate and ice-cold water thrice, then the organic layer was dried over anhydrous Na_2SO_4, and evaporated in vacuo. The residue left was purified by column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (92:8) as eluent to obtain compound **15** as pale gummy liquid (15.54 mg, 70%).

2.10 Characterization data & NMR spectra of compounds 15-18:

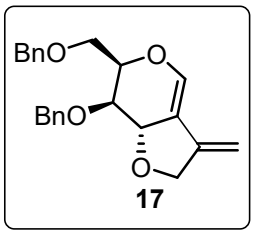


The compound **15** was synthesized according to the general procedure **(2.9)** using **11** (50 mg, 0.11 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (90:10) as eluent to obtain **15** as a pale gummy liquid (70 % yield, 15.54 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.30 – 7.24 (m, 6H), 7.20 – 7.17 (m, 4H), 6.77 (d, J = 2.2 Hz, 1H), 5.02 (t, J = 2.5 Hz, 1H), 4.82 (d, J = 12.6 Hz, 1H), 4.68 (t, J = 2.1 Hz, 1H), 4.63 (d, J = 12.6 Hz, 1H), 4.47 (d, J = 2.2 Hz, 1H), 4.45 – 4.38 (m, 3H), 4.34 (t, J = 2.5 Hz, 1H), 4.31 – 4.28 (m, 1H), 4.03 (dd, J = 4.0, 2.0 Hz, 1H), 3.43 (dd, J = 10.2, 6.7 Hz, 1H), 3.26 (dd, J = 10.2, 6.3 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 142.4 (Cq), 138.6 (Cq), 137.5 (Cq), 136.7, 128.5, 128.4, 127.9, 127.7, 127.6, 127.5, 111.4 (Cq), 97.4 (CH_2), 76.6, 74.6, 73.5 (CH_2), 73.0 (CH_2), 72.5 (CH_2), 69.3 (CH_2), 69.1. **HRMS (ESI, m/z)** for $C_{23}H_{28}NO_4$ $[M+NH_4]^+$: calcd 382.2018, found, 382.2125.

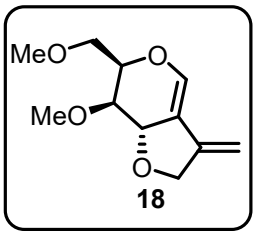


The compound **16** was synthesized according to the general procedure **(2.9)** using **12** (30 mg, 0.088 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (90:10) as eluent to obtain **16** as a pale gummy liquid (73 % yield, 13.6 mg).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 6.74 (s, 1H), 5.02 (t, J = 2.4 Hz, 1H), 4.68 (t, J = 2.0 Hz, 1H), 4.53 – 4.41 (m, 2H), 4.37 – 4.26 (m, 2H), 3.80 (dd, J = 4.1, 2.0 Hz, 1H), 3.47 (s, 3H), 3.40 (dd, J = 10.2, 7.2 Hz, 1H), 3.31 (s, 3H), 3.24 (dd, J = 10.1, 5.7 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$) δ** 142.2 (Cq), 136.5, 111.3 (Cq), 97.7 (CH_2), 75.0, 74.3, 72.52 (CH_2), 71.9, 71.9 (CH_2), 59.4, 58.9. **HRMS (ESI, m/z)** for $C_{11}H_{17}O_4$ $[M+H]^+$: calcd 213.1127, found, 213.1135.

.

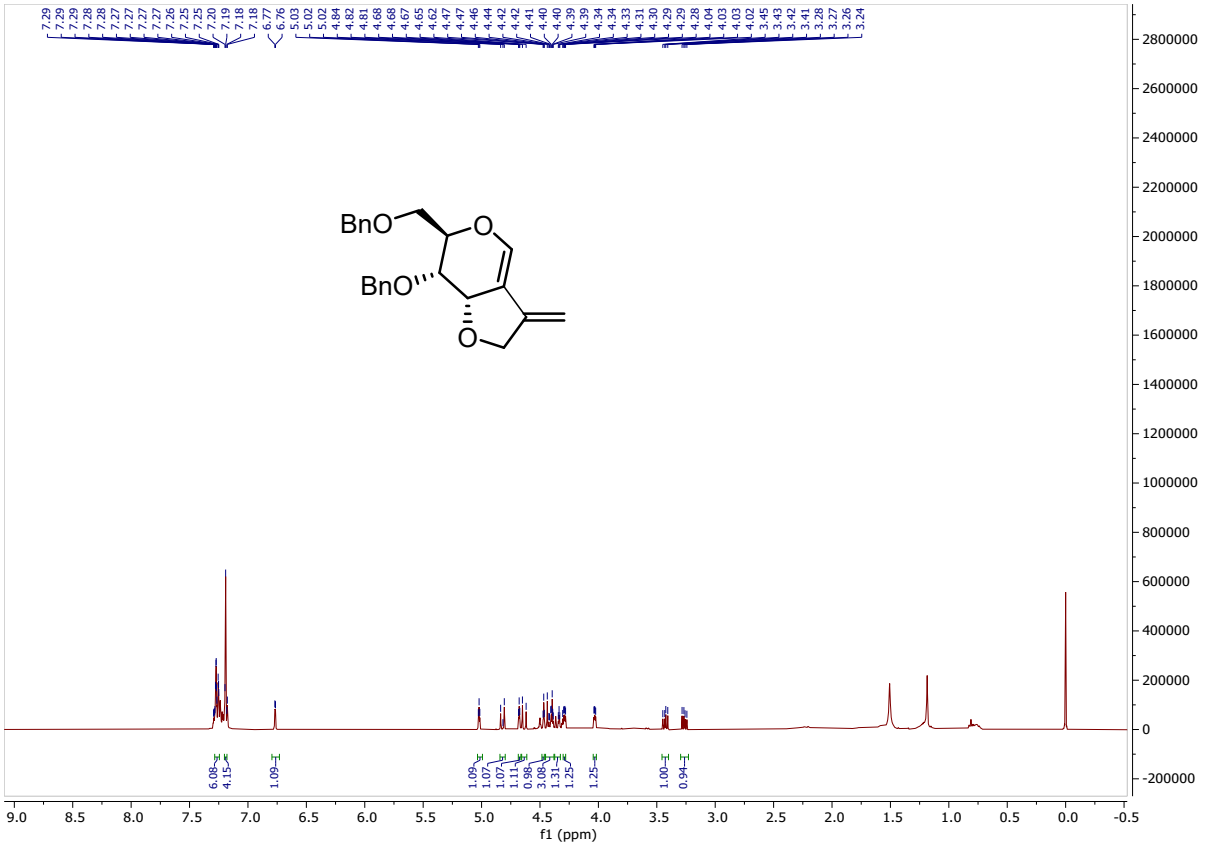


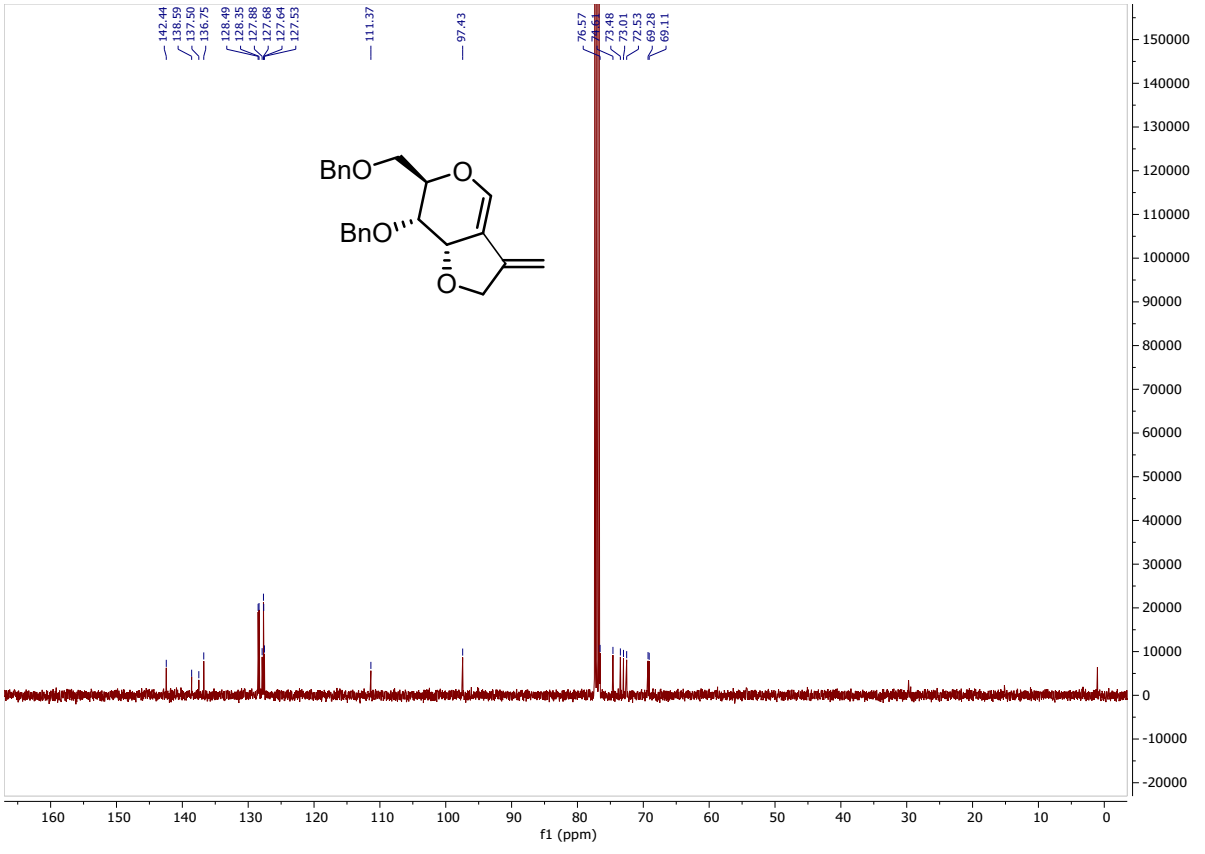
The compound **17** was synthesized according to the general procedure **(2.9)** using **13** (30 mg, 0.06 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (90:10) as eluent to obtain yellow gummy liquid (70 % yield, 15.54 mg).**^{1}H NMR (400 MHz, $CDCl_3$)** ***δ*** 7.28 – 7.20 (m, 7H), 7.21 – 7.15 (m, 3H), 6.77 (d, *J* = 2.1 Hz, 1H), 5.02 (t, *J* = 2.5 Hz, 1H), 4.86 (d, *J* = 12.0 Hz, 1H), 4.66 (t, *J* = 2.1 Hz, 1H), 4.56 – 4.48 (m, 2H), 4.46 (t, *J* = 2.1 Hz, 1H), 4.41 – 4.35 (m, 2H), 4.32 (s, 1H), 3.95 (dd, *J* = 3.7, 1.2 Hz, 1H), 3.91 (dd, *J* = 7.1, 5.8 Hz, 1H), 3.61 (dd, *J* = 9.5, 6.3 Hz, 1H), 3.48 (dd, *J* = 9.5, 6.5 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$)** ***δ*** 142.3, 138.6, 137.9, 137.7, 128.4, 128.3, 128.3, 127.9, 127.8, 127.6, 112.3, 97.5 (CH_2), 78.0, 74.8, 74.0 (CH_2), 73.5 (CH_2), 72.8 (CH_2), 69.0 (CH_2), 68.0. **HRMS (ESI, m/z)** for $C_{23}H_{28}NO_4$ $[M+NH_4]^+$: calcd 382.2018, found, 382.2120.



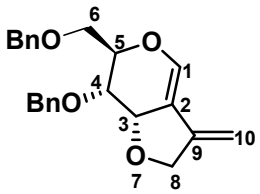
The compound **18** was synthesized according to the general procedure **(2.9)** using **14** (30 mg, 0.088 mmol) and purified using column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (90:10) as eluent to obtain yellow gummy liquid (73 % yield, 13.6 mg) **^{1}H NMR (400 MHz, $CDCl_3$)** ***δ*** 6.75 (s, 1H), 5.02 (d, *J* = 2.7 Hz, 1H), 4.66 (d, *J* = 2.2 Hz, 1H), 4.47 (dt, *J* = 12.6, 2.2 Hz, 2H), 4.32 (dt, *J* = 12.5, 2.5 Hz, 1H), 3.92 (t, *J* = 6.5 Hz, 1H), 3.71 (d, *J* = 3.8 Hz, 1H), 3.60 (dd, *J* = 6.5, 2.8 Hz, 2H), 3.50 (s, 3H), 3.36 (s, 3H), 3.32 (s, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** ***δ*** 142.00 (Cq), 137.66, 112.20 (Cq), 97.70 (CH_2), 77.74, 77.41, 77.29, 77.09, 76.77, 74.51, 72.77 (CH_2), 71.41 (CH_2), 71.11, 61.03, 59.31. **HRMS (ESI, m/z)** for $C_{11}H_{17}O_4$ $[M+H]^+$: calcd 213.1127, found, 213.1130.

^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **15** in $CDCl_3$





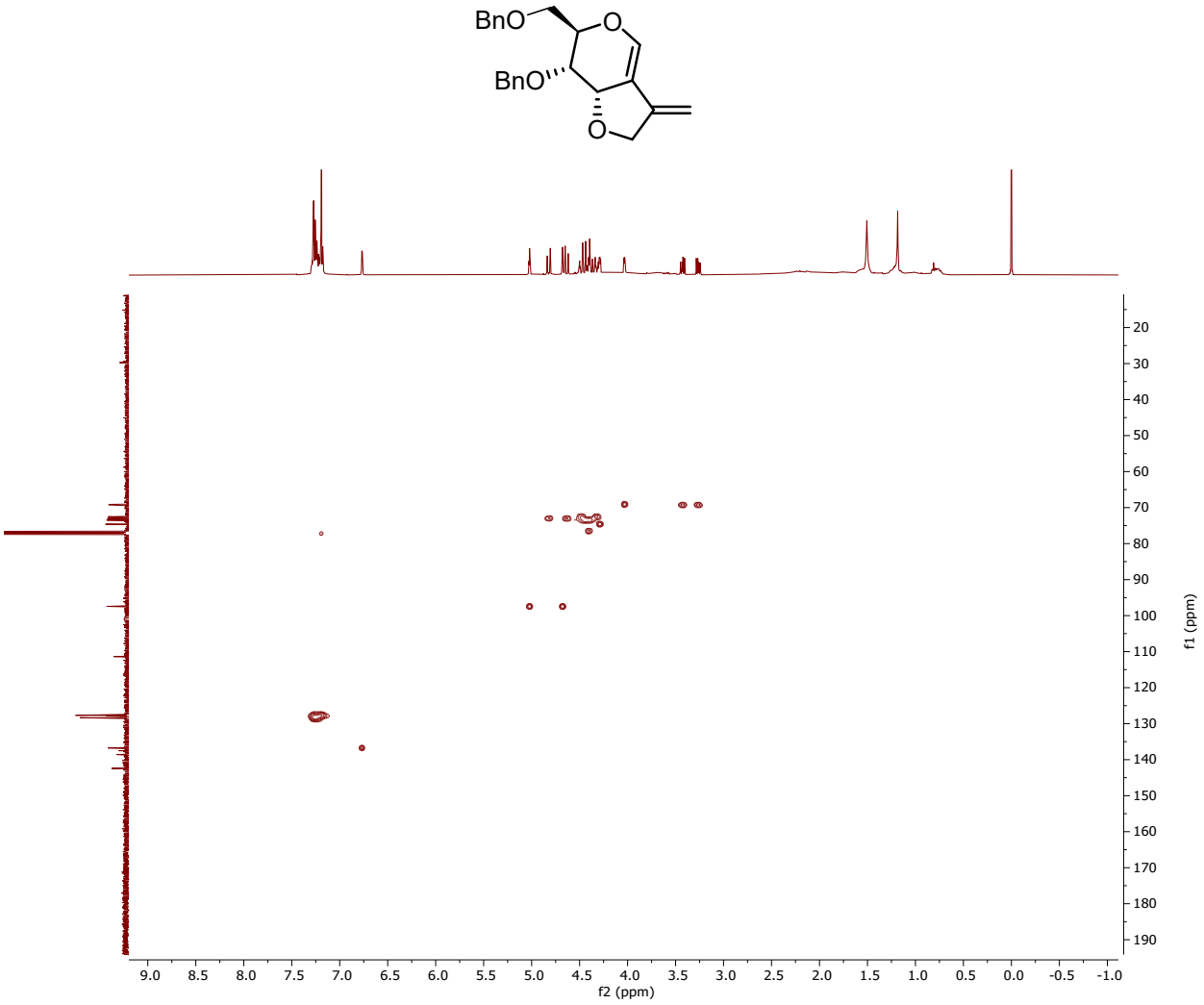
HSQC of compound **15**



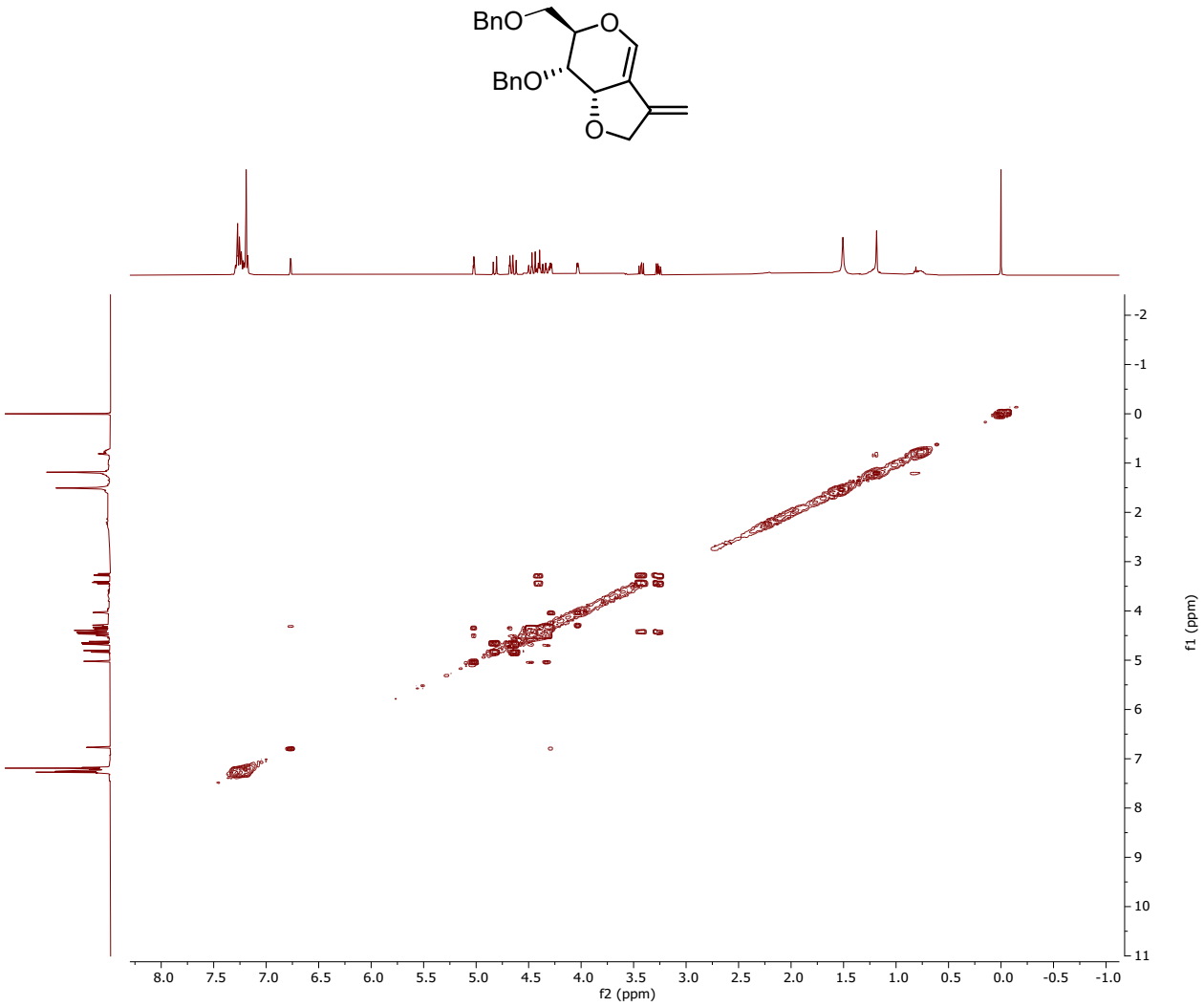
HSQC Table of compound **15**

Position	δ_H	δ_C
1	6.76	136.75
2	-	142.44
3	4.41	76.57
4	4.03	69.11
5	4.29	74.61
6	3.43,3.26	69.28
9	-	111.37
10	4.67,5.01	97.43

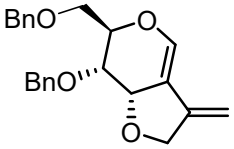
HSQC spectra of compound **15**

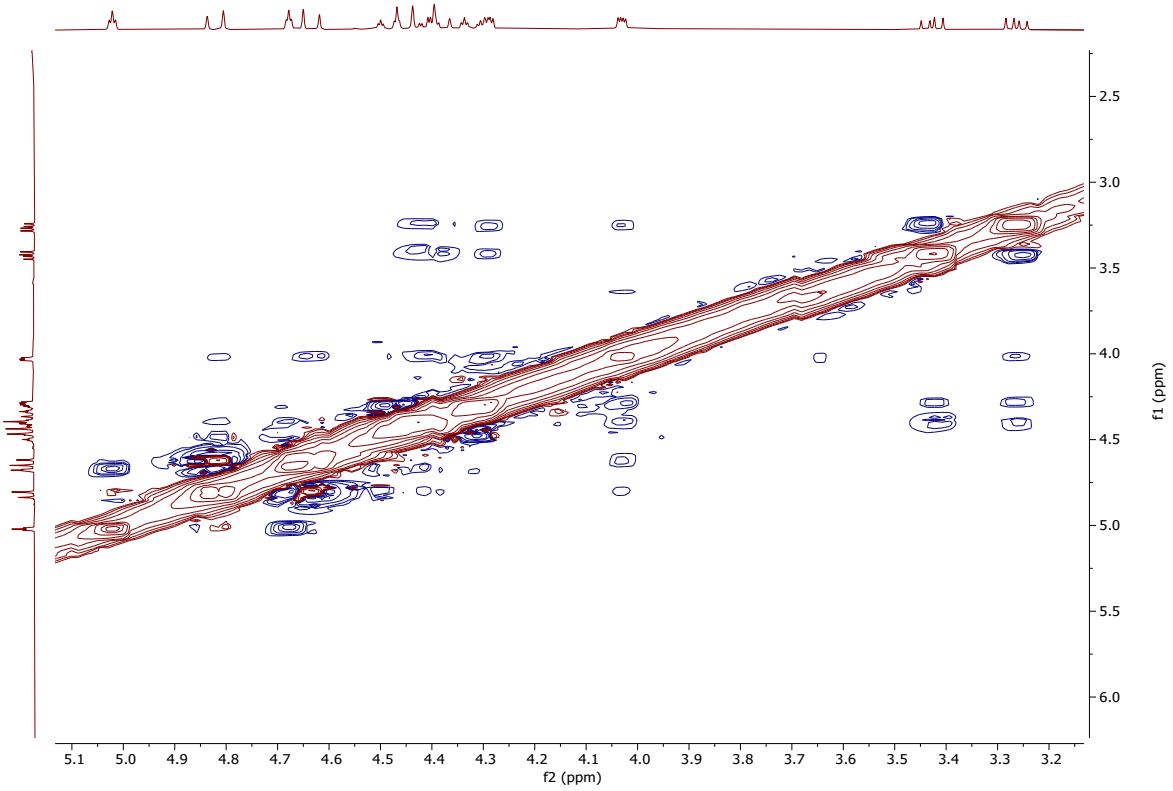


COSY spectra of compound **15**



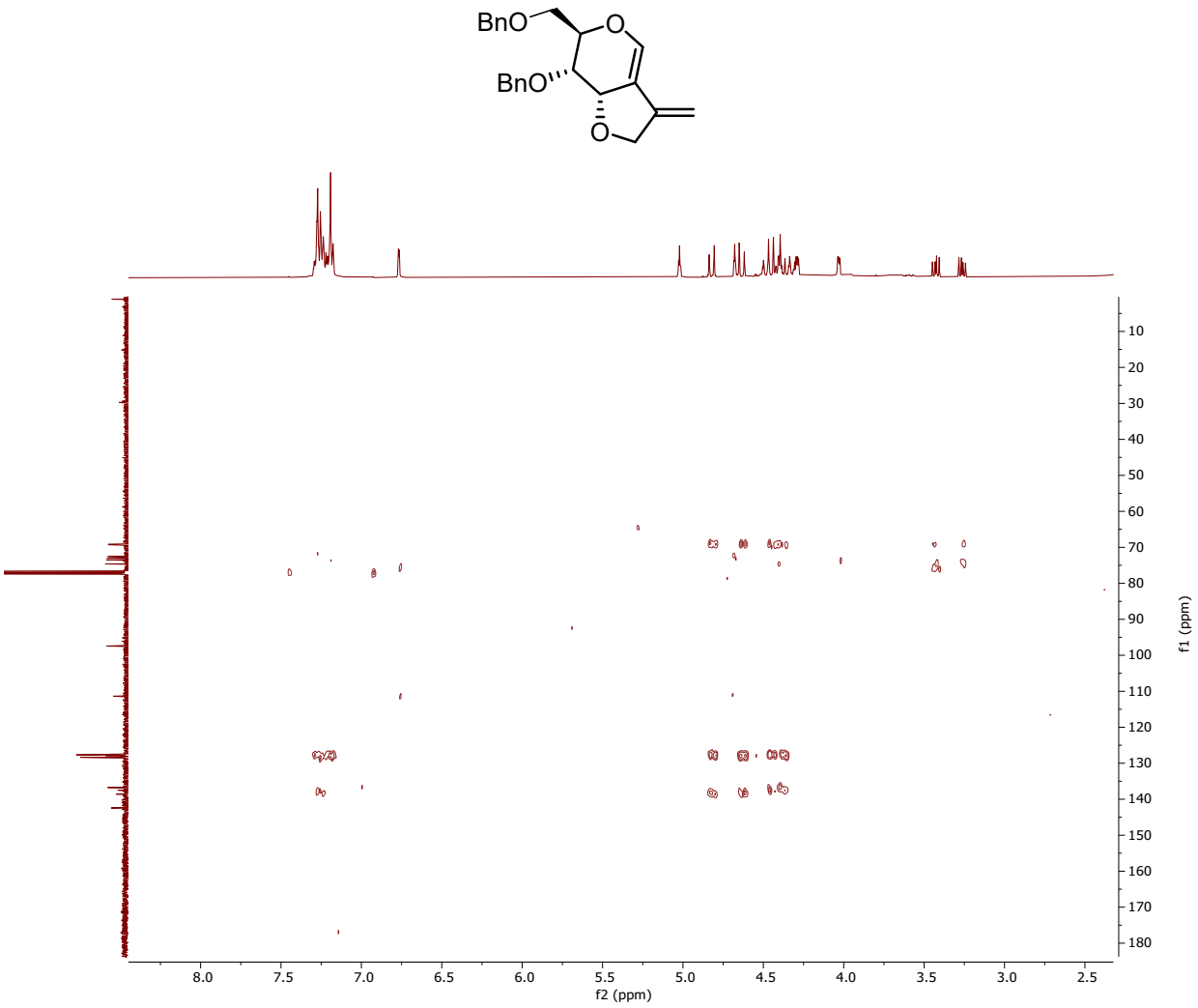
NOESY spectra of compound **15**



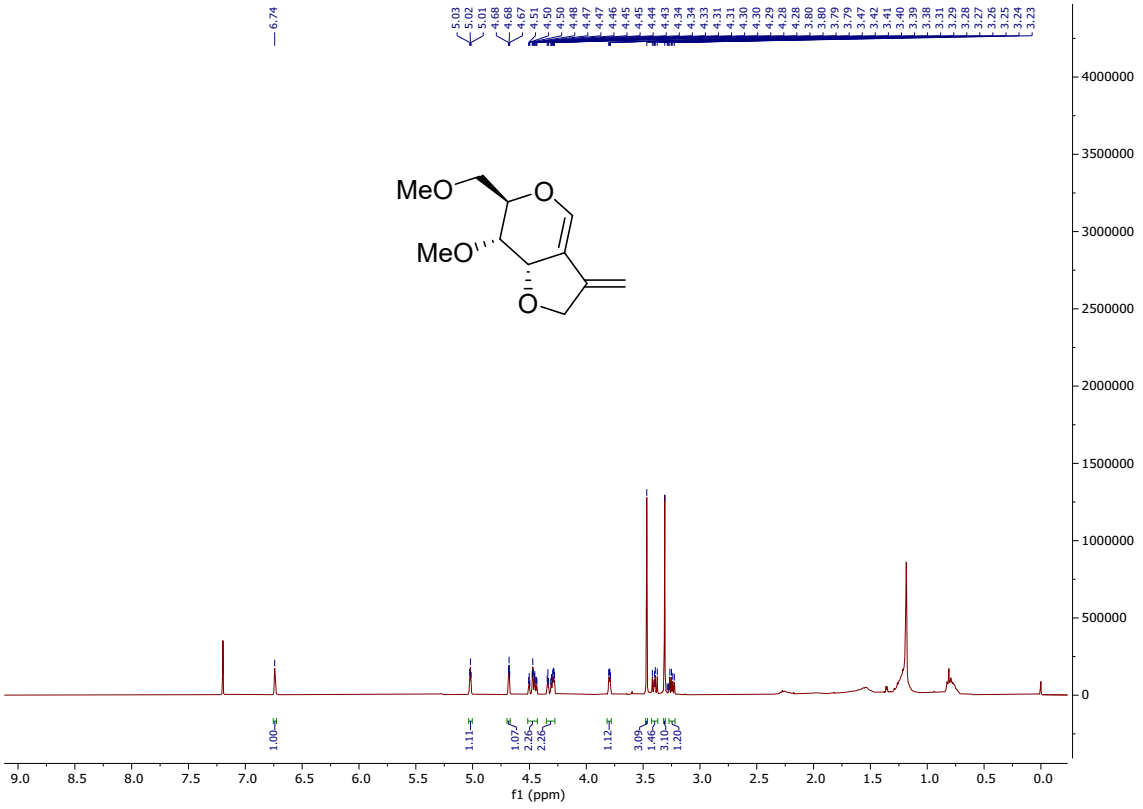


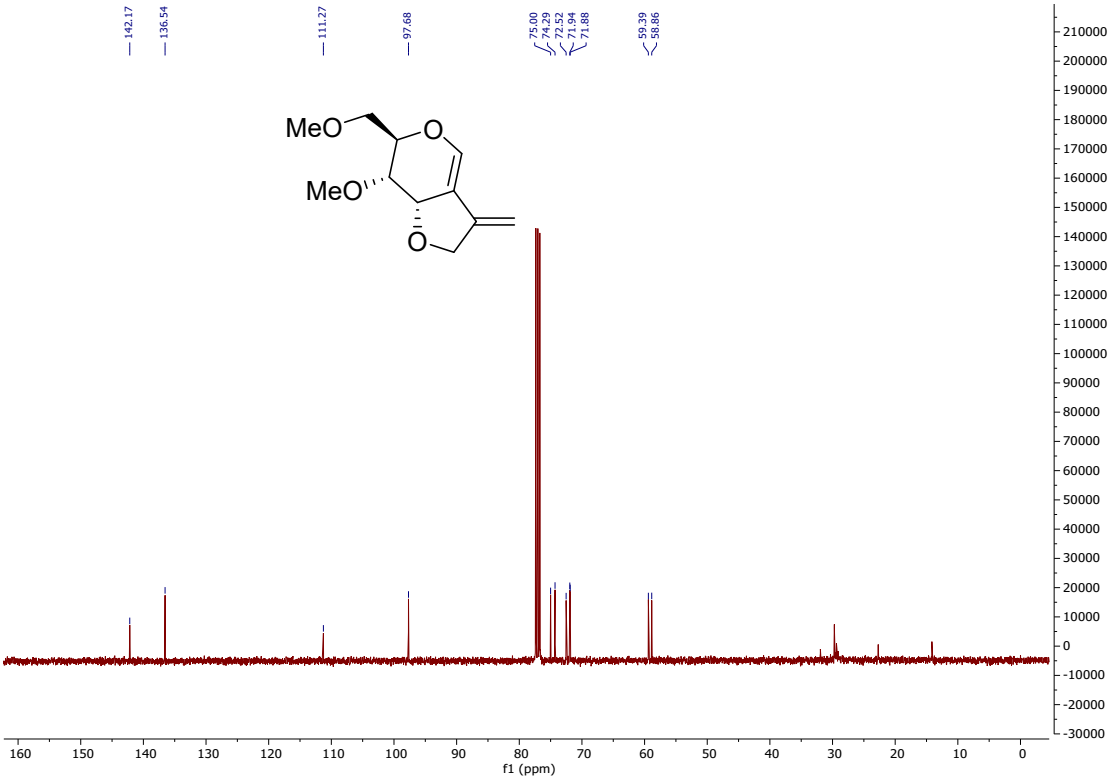
No correlation is observed in NOESY between H3 (4.41 ppm) & H5 (4.29 ppm) confirming α-stereochemistry at C-3.

HMBC spectra of compound **15**

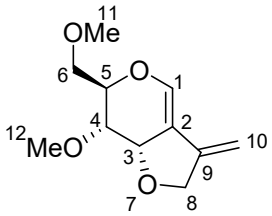


^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **16** in $CDCl_3$





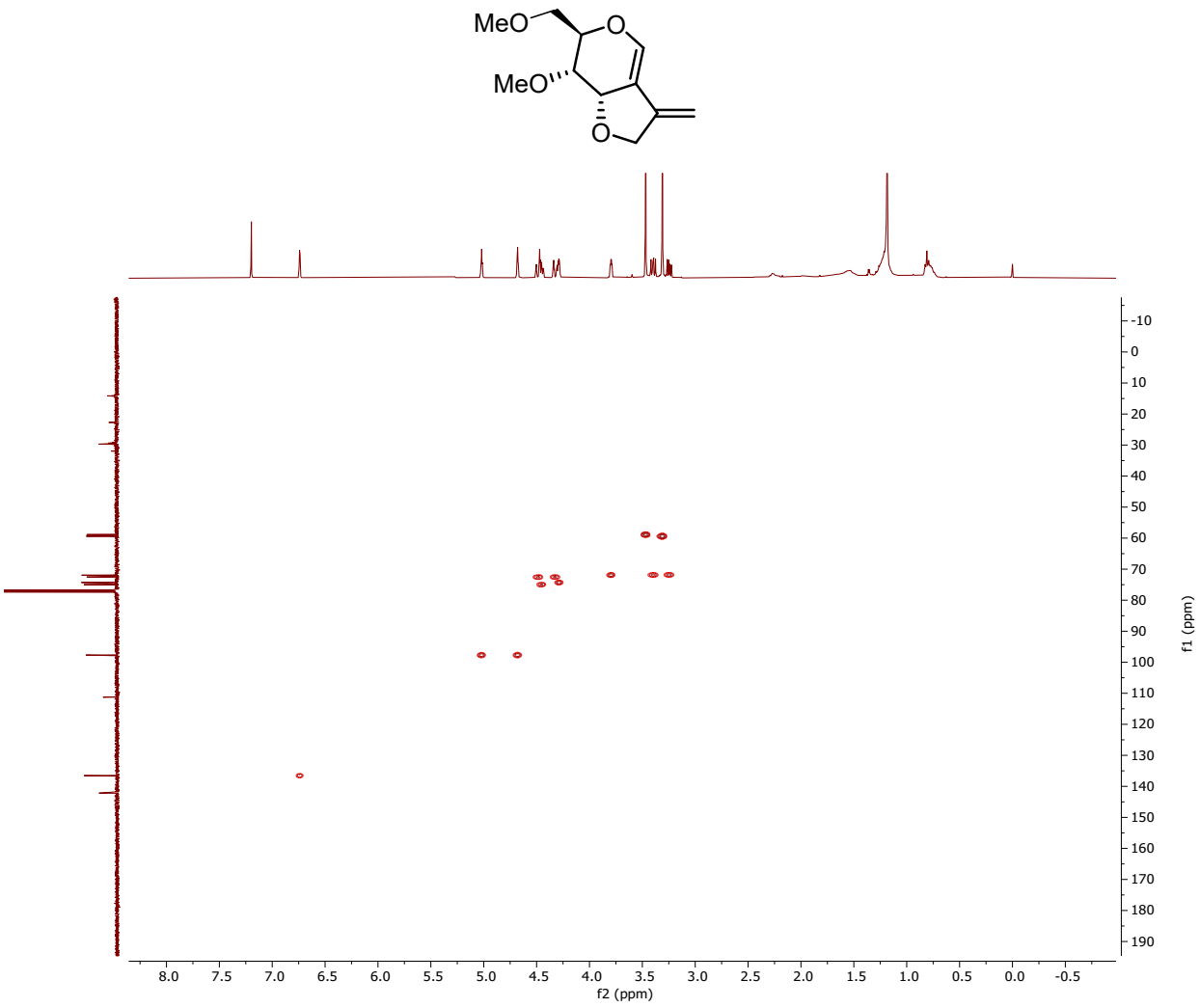
HSQC spectra of compound **16**



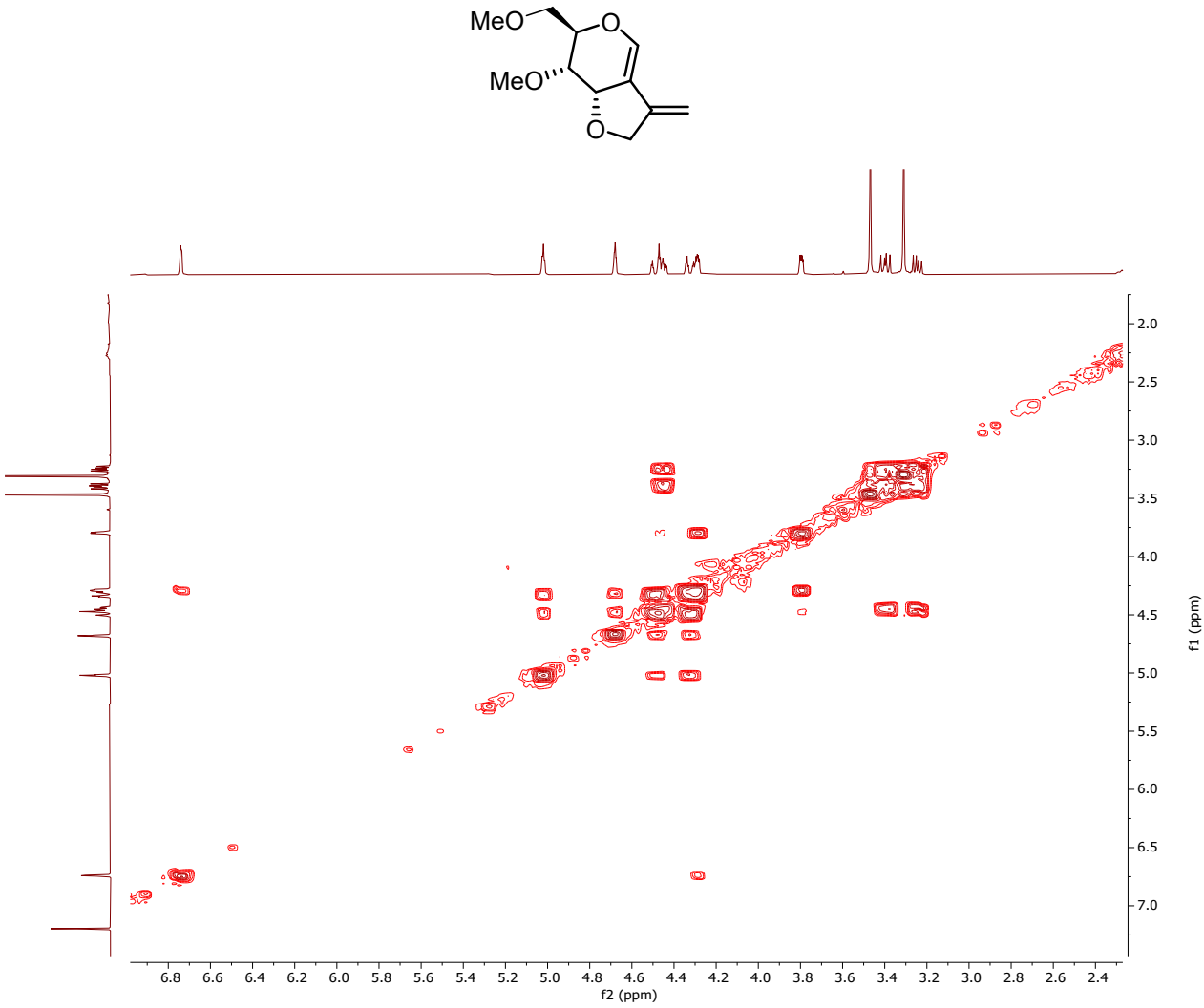
HSQC Table of compound **16**

Position	δ_H	δ_C
1	6.74 (d, *J* = 2.3 Hz, 1H)	136.54
2	-	111.27
3	4.45 (ddd, *J* = 7.7, 5.1, 1.4 Hz, 1H)	75.00
4	3.79 (ddd, *J* = 4.1, 2.1, 0.6 Hz, 1H)	71.93
5	4.28 (td, *J* = 3.8, 2.3 Hz, 1H)	74.29
6	4.33,4.49	72.52
8	3.24 (dd, *J* = 10.1, 5.7 Hz, 1H),3.39 (dd, *J* = 10.2, 7.0 Hz, 1H)	71.87
9	-	142.17
10	4.68 (t, *J* = 2.1 Hz, 1H),5.02 (t, *J* = 2.5 Hz, 1H)	97.68

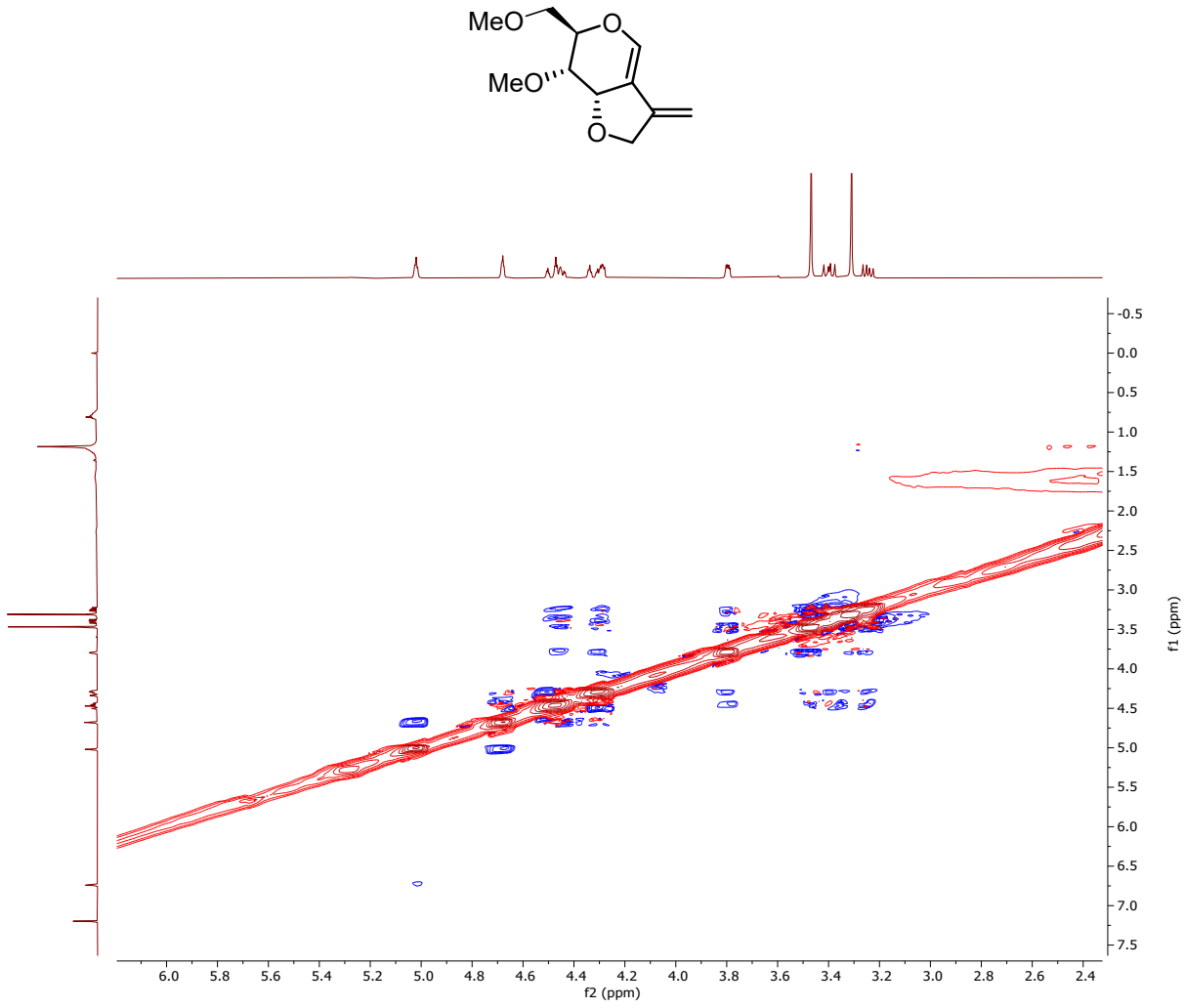
HSQC spectra of compound **16**



COSY spectra of compound **16**

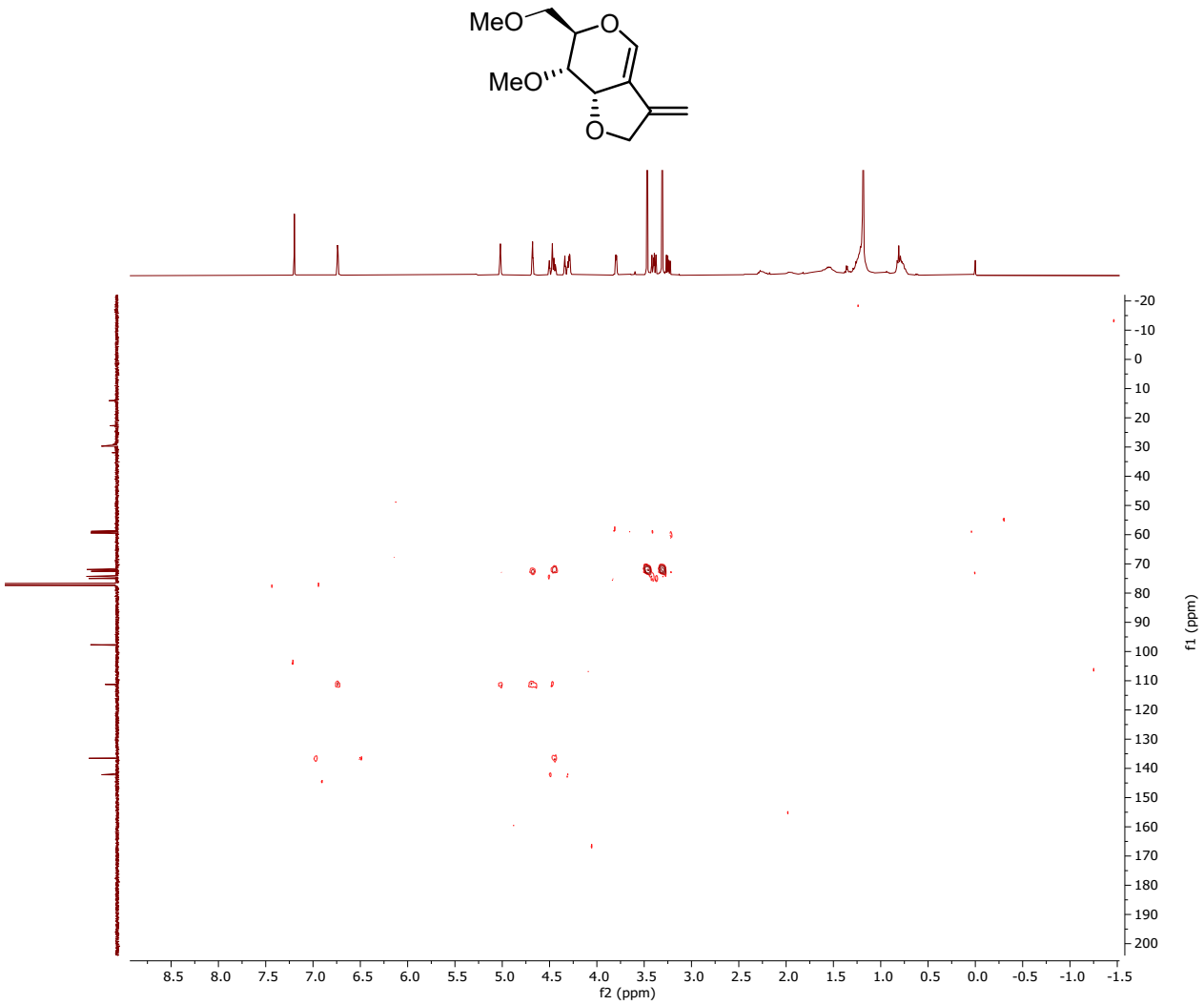


NOESY spectra of compound **16**

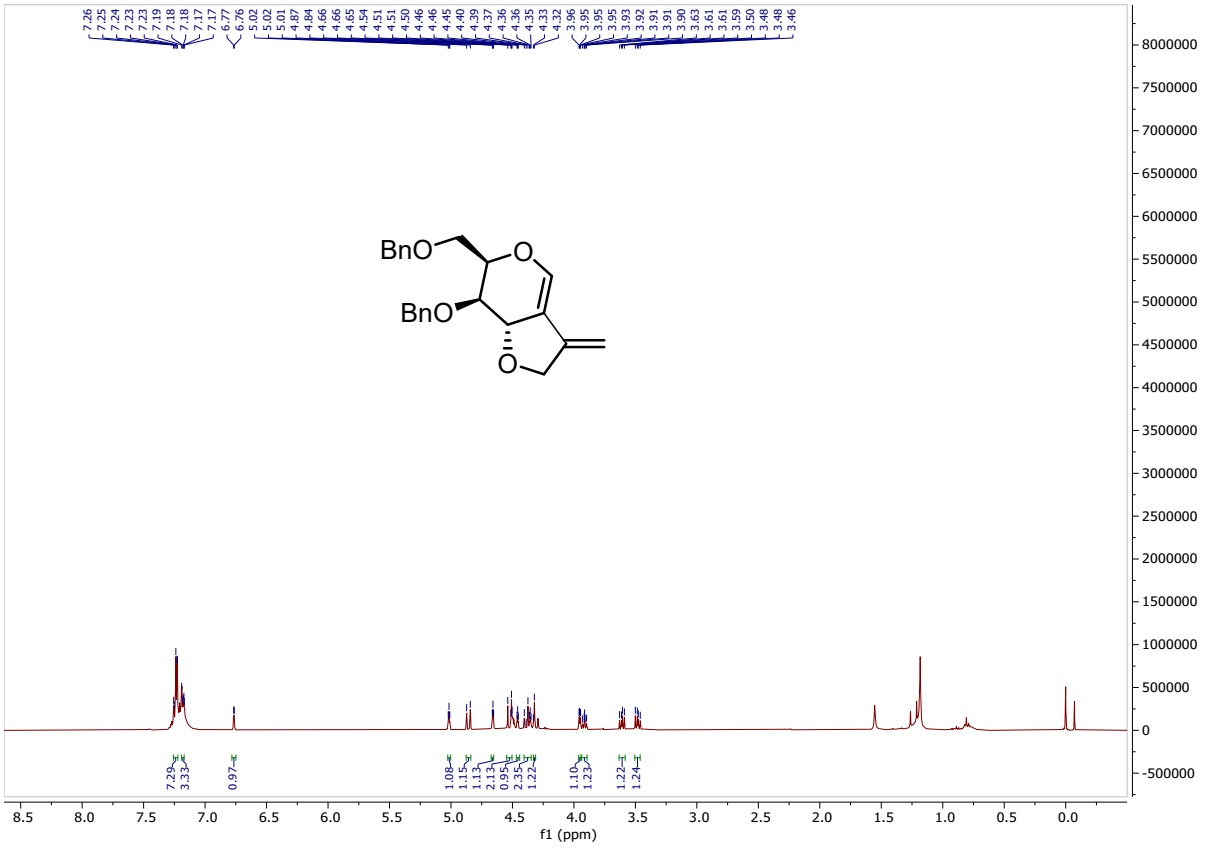


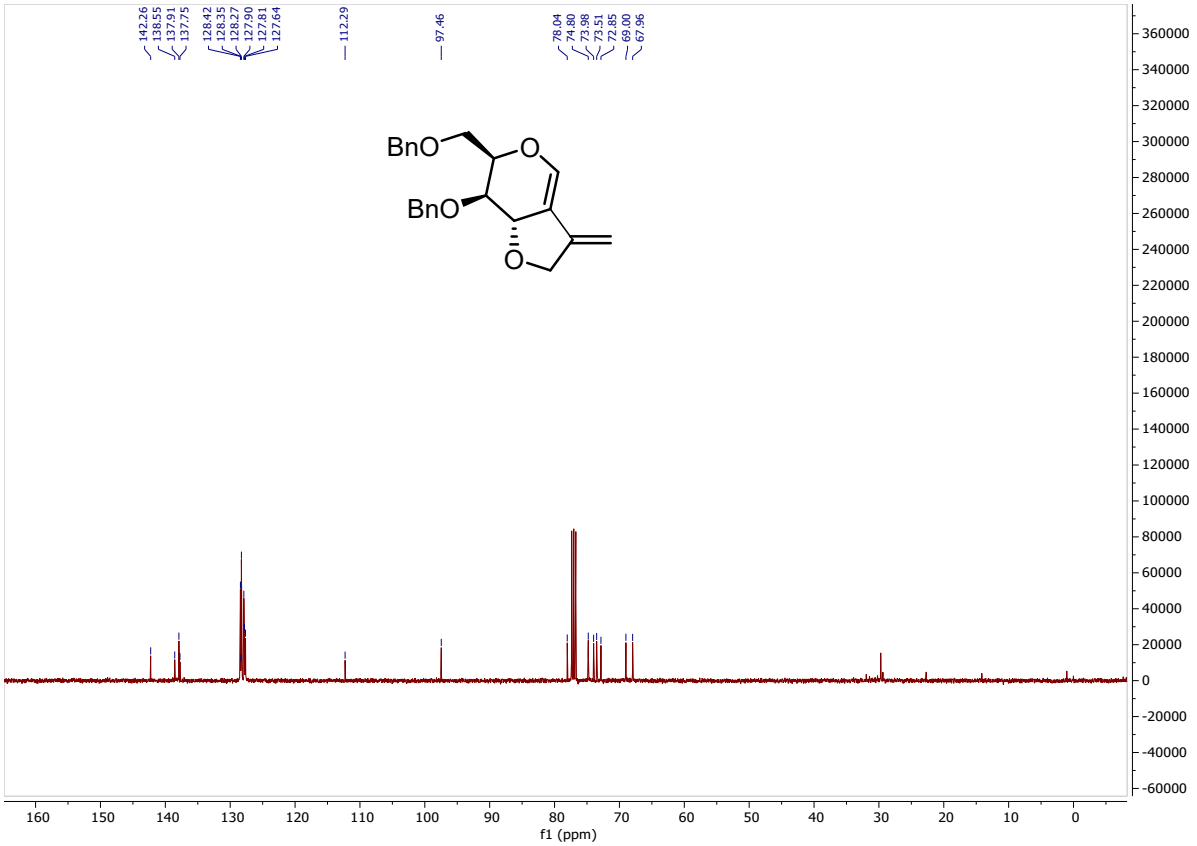
In the NOESY experiment, we observed no correlation between the H_3 (4.45 (ddd, J = 7.7, 5.1, 1.4 Hz, 1H) and H_5 (td, J = 3.8, 2.3 Hz, 1H), confirming the α stereochemistry of OH at C-3.

HMBC spectra of compound **16**



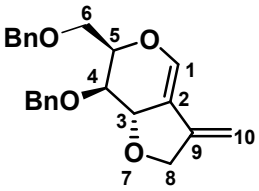
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **17** in $CDCl_3$





HSQC of compound **17**

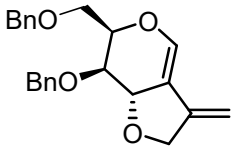
HSQC Table of compound **17**

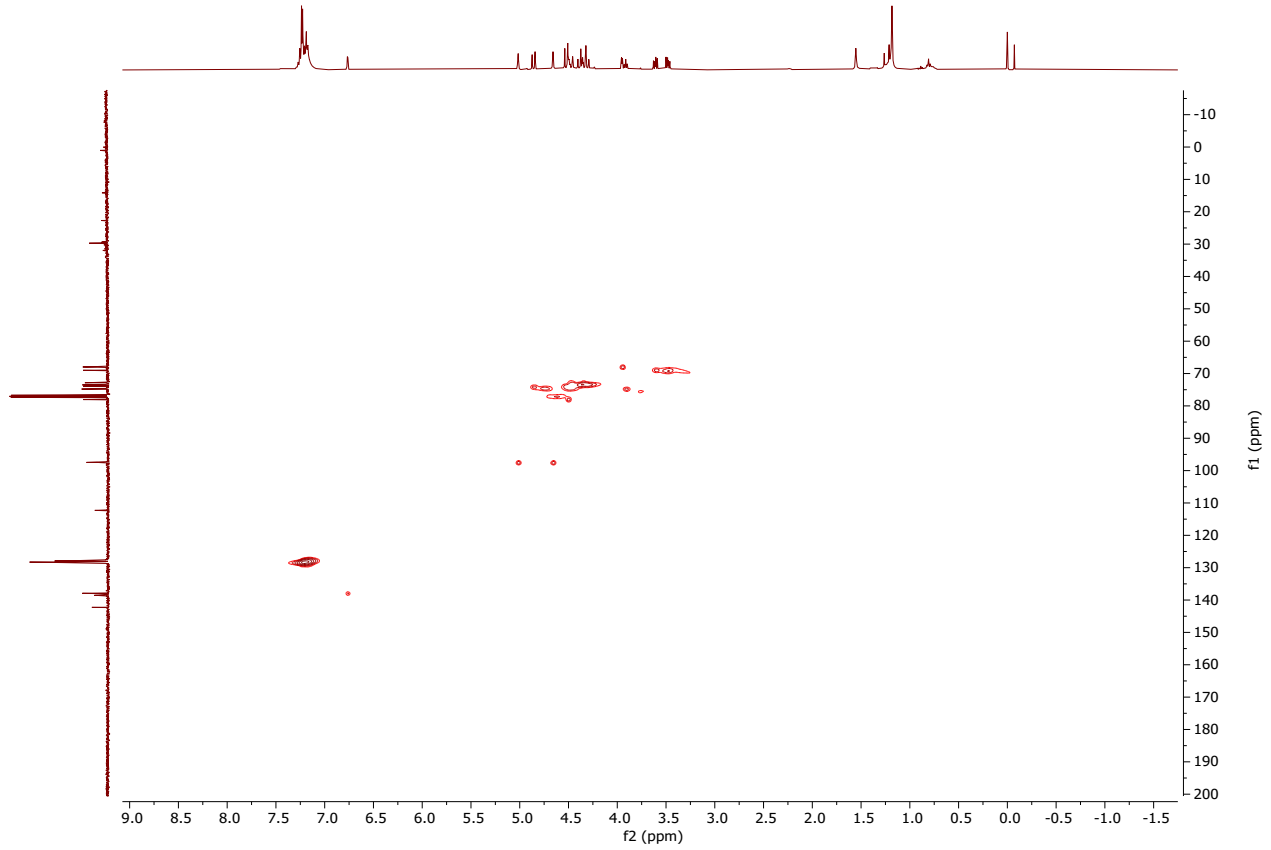


Position	δ_H	δ_C
1	H_1= 6.77	137.91
2	-	138.55
3	H_3= 4.52	78.04
4	H_4= 3.95	67.96
5	H_5= 3.91	74.80
6	H_{6a}=3.61	69.00
6	H_{6a}=3.48	69.00

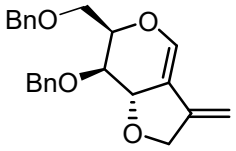
9	-	142.26
10	4.66,5.02	97.46

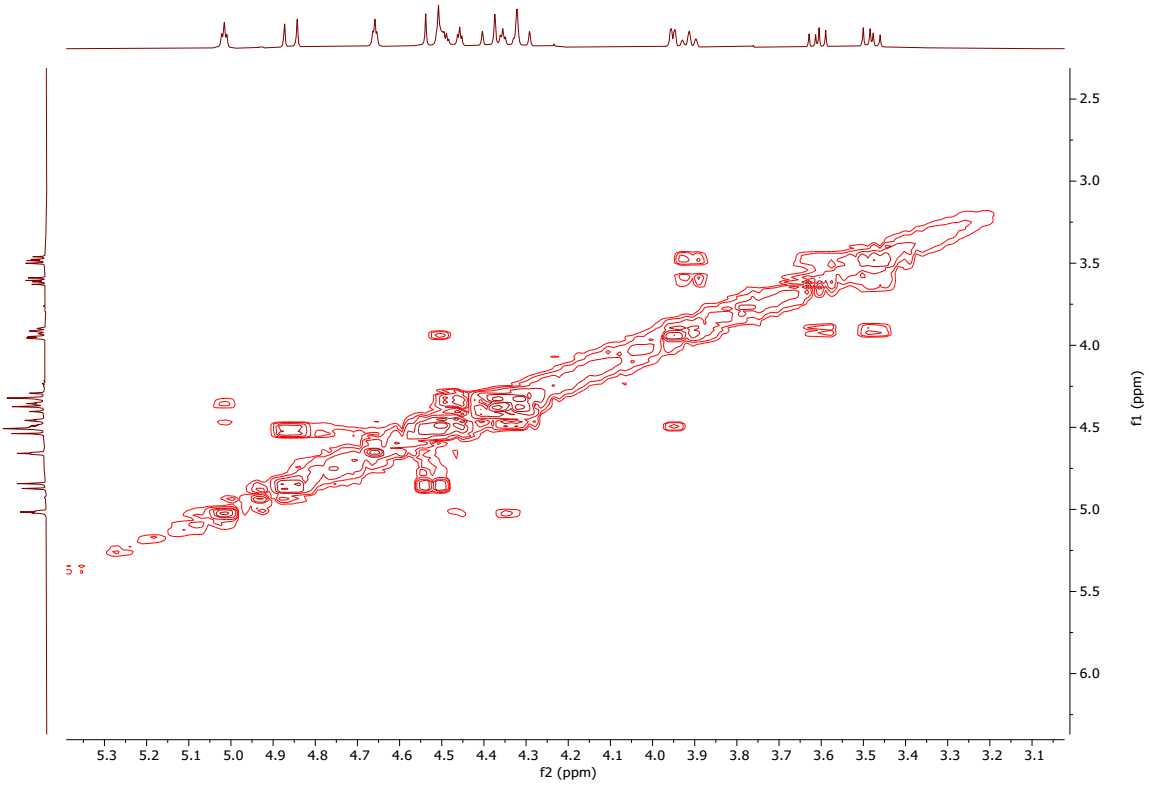
HSQC spectra of compound **17**



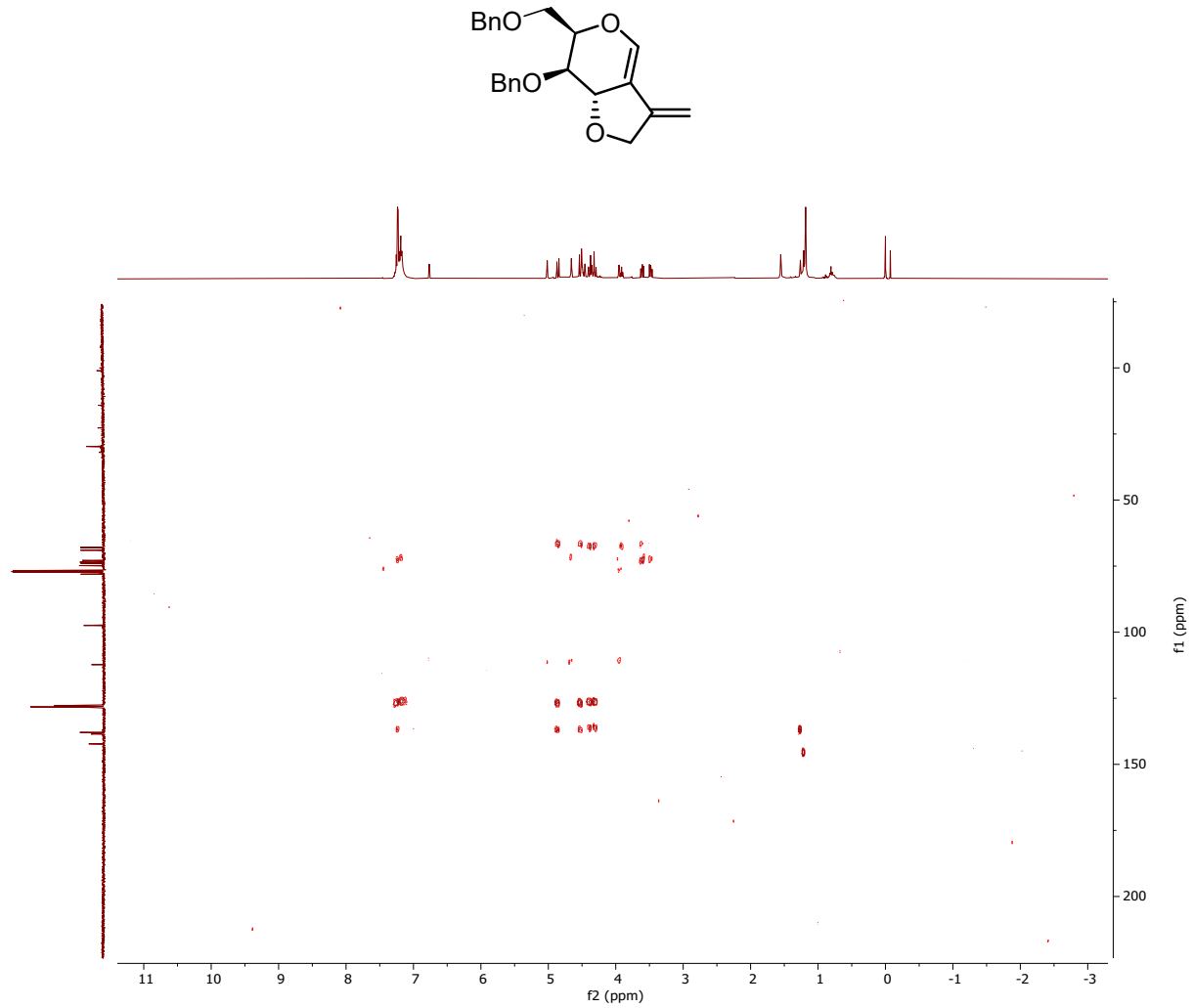


COSY spectra of compound **17**

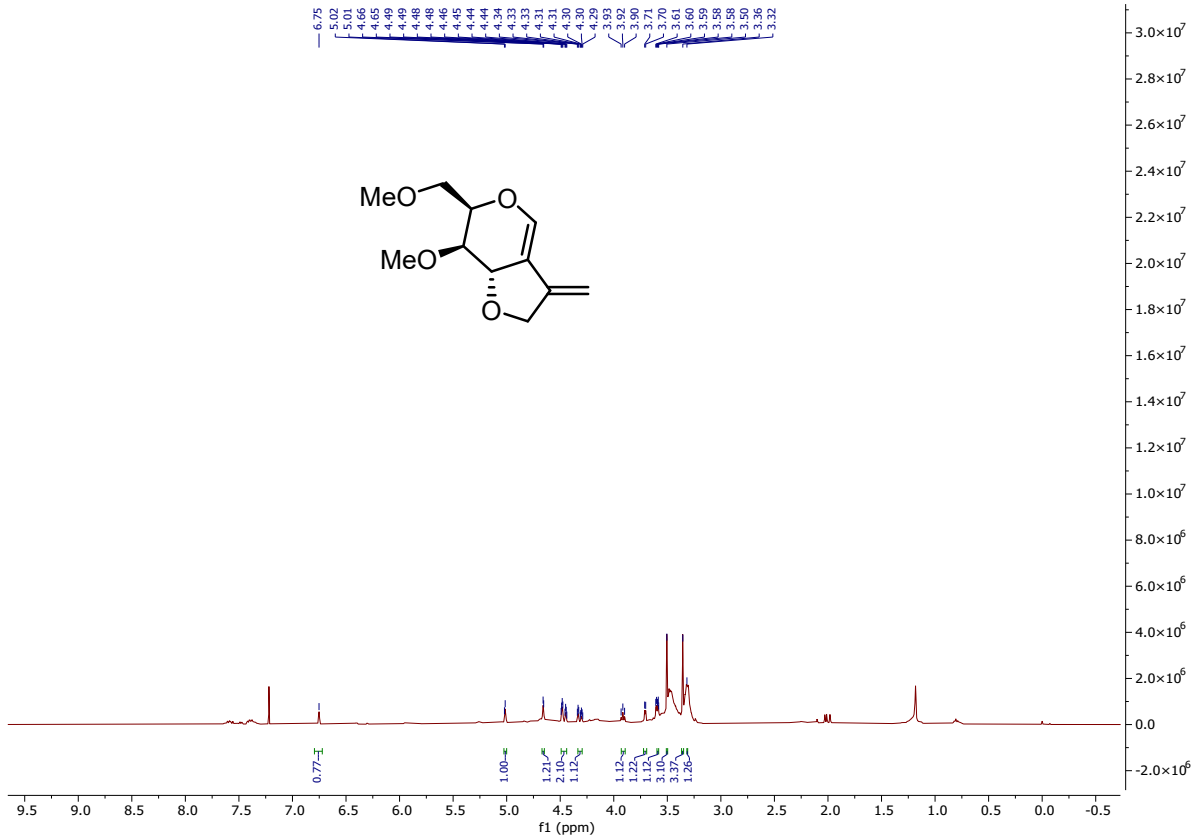

BnO
BnO
O
O

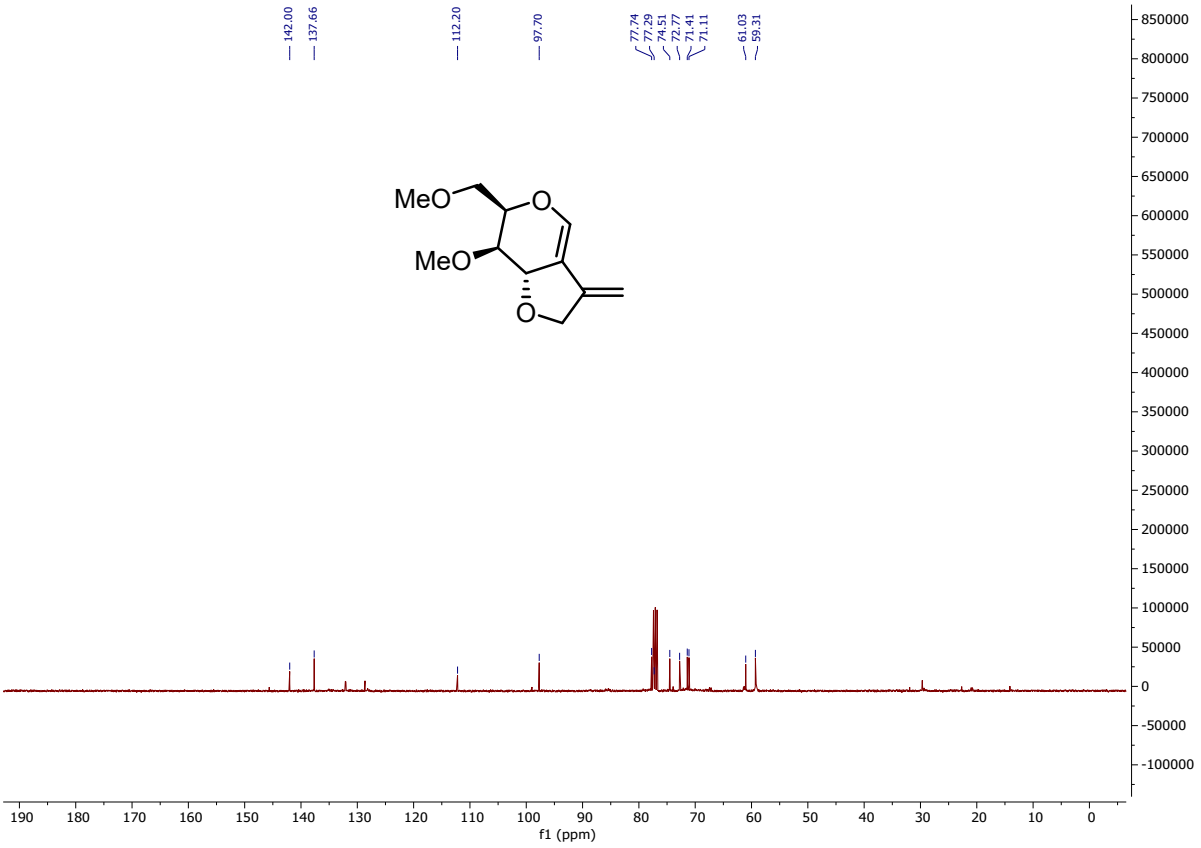

2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
f1 (ppm)
5.3
5.2
5.1
5.0
4.9
4.8
4.7
4.6
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
f2 (ppm)

HMBC spectra of compound **17**

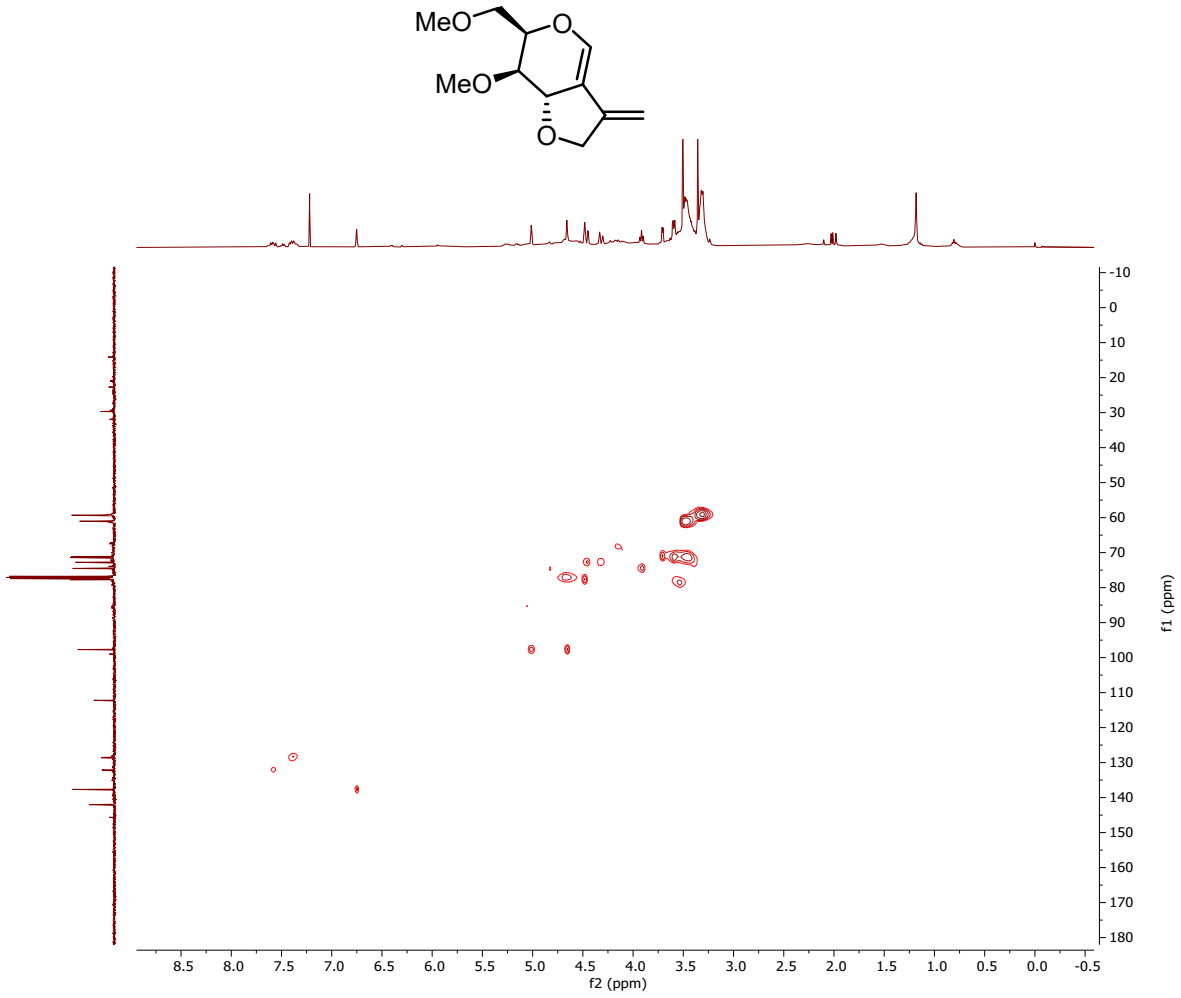


^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **18** in $CDCl_3$[2]

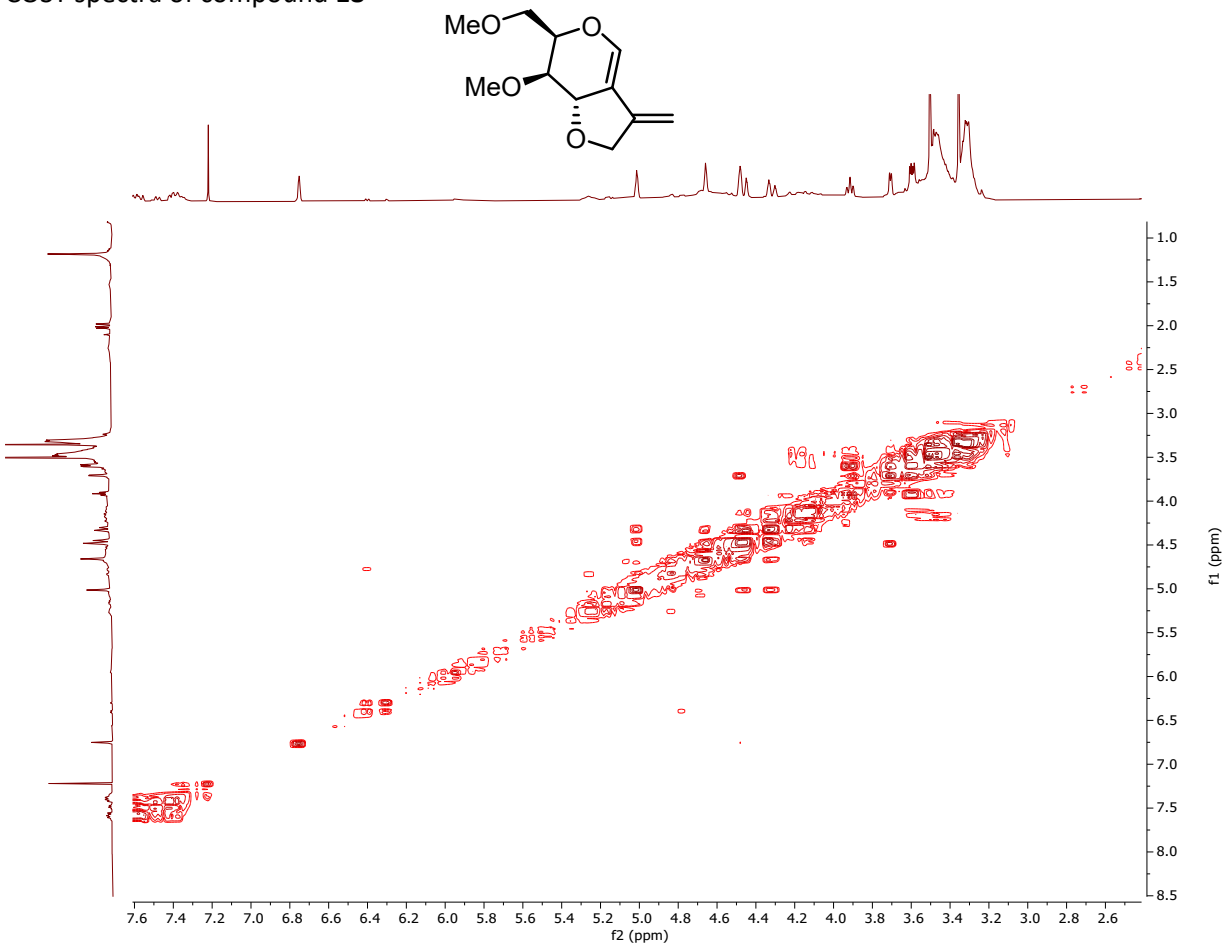




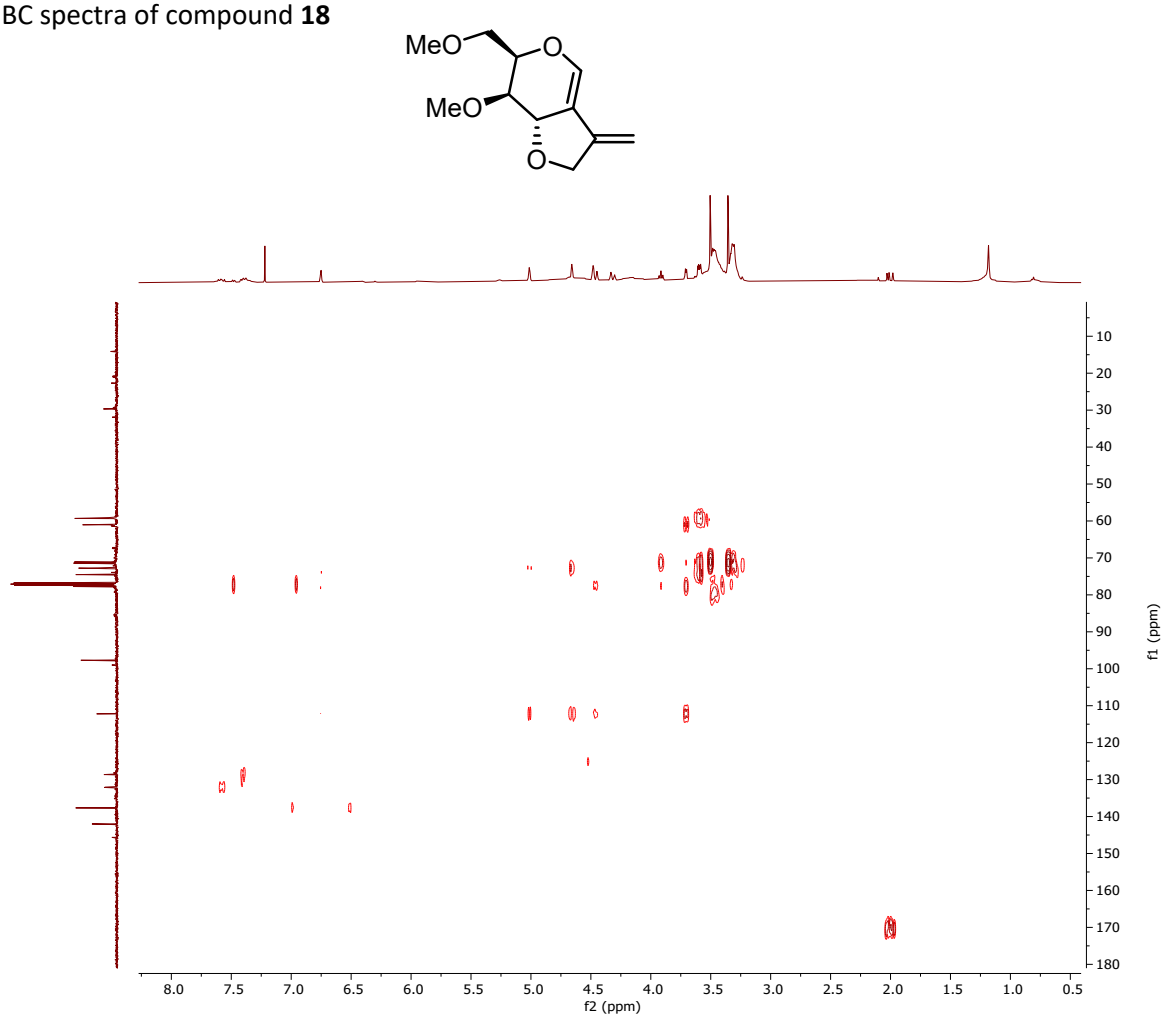
HSQC spectra of compound **18**



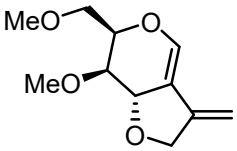
COSY spectra of compound **18**

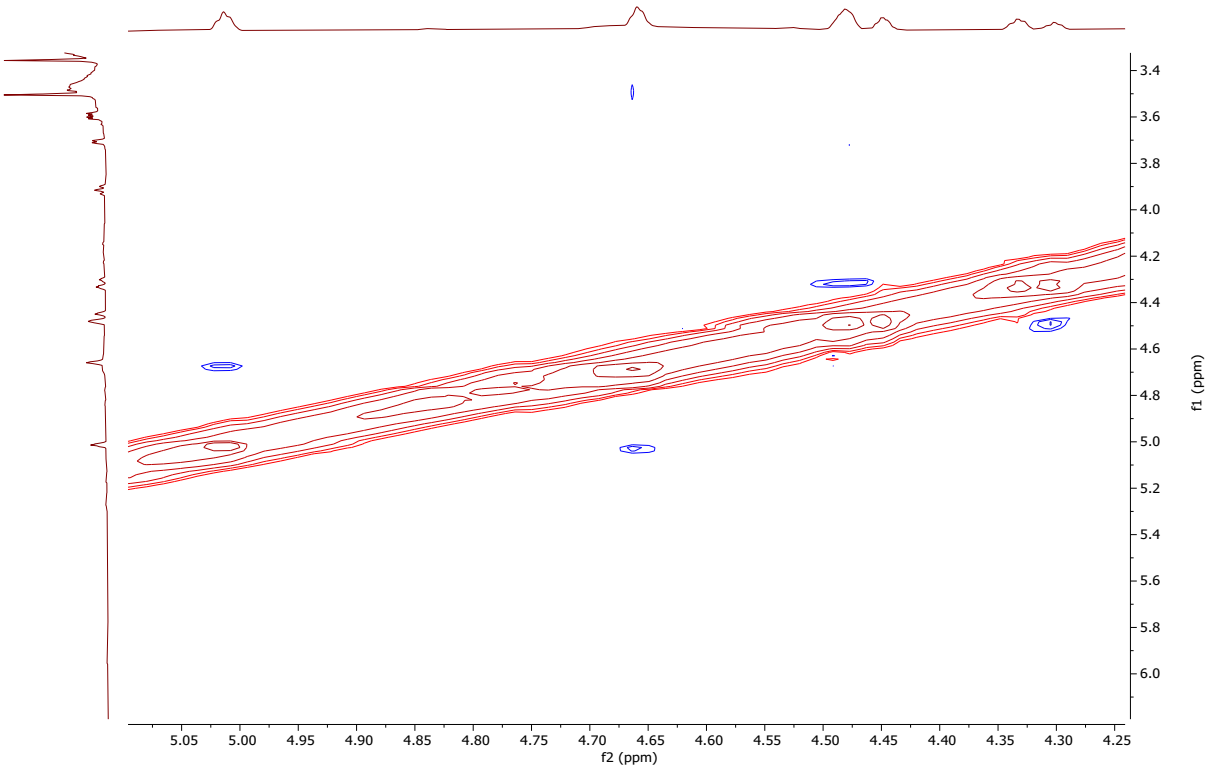


HMBC spectra of compound **18**

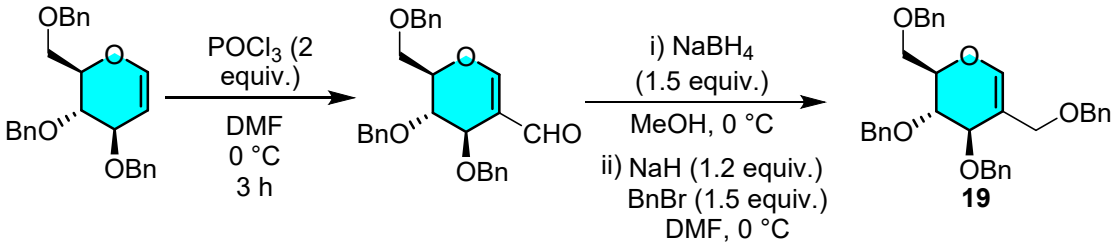


NOESY spectra of compound **18**





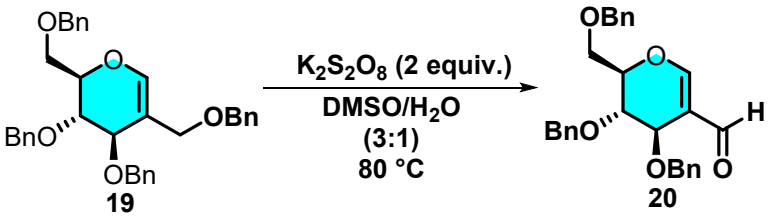
2.11 Procedure for the synthesis of compound 19:



To a solution of Tri-*O*-benzyl-D-glucal (500 mg, 1.2 mmol, 1.0 equiv.) in DMF, $POCl_3$ (2 equiv.) was added dropwise at 0 °C. The reaction mixture was then stirred at room temperature until TLC analysis confirmed the complete consumption of the starting material. Upon completion, the reaction was neutralized with a cold-saturated solution of ammonium chloride and then extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated on a rotary evaporator. The residue was purified by column chromatography on silica gel (60–120 mesh) using hexane: acetate (88:12) as the eluent, affording 2-formyl glycal as the desired product (373.1 mg, 70%).[1]

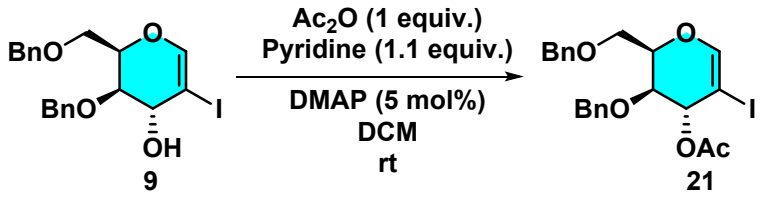
In a separate reaction, C-2-formyl glycal (300 mg, 0.67 mmol, 1 equiv.) was dissolved in anhydrous methanol at 0 °C, and sodium borohydride (1.5 equiv.) was added portion-wise over 15 minutes. The reaction mixture was allowed to reach room temperature and stirred for an additional 30 minutes, then quenched with a saturated solution of NH_4Cl. The mixture was extracted with dichloromethane (DCM), washed with brine, and the organic phase was dried over anhydrous Na_2SO_4, then concentrated on a rotary evaporator to yield the product as a pure compound (256.16 mg, 85%) which was used as such for the next step. This product was dissolved in DMF, and sodium hydride (1.2 equiv.) and benzyl bromide (1.5 equiv.) were added sequentially at 0 °C. Upon completion, the reaction mixture was treated with ice-cold water, extracted with ethyl acetate three times, dried over anhydrous Na_2SO_4, concentrated, and purified by column chromatography (hexane: acetate (96:4)) to yield the final product **19** as a gummy liquid (276.8 mg, 90%).

2.12 Procedure for the synthesis of compound 20:



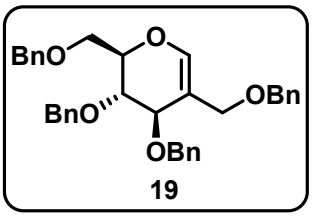
A round bottom flask equipped with a magnetic stir bar was charged with compound **19** (100 mg, 0.186 mmol 1 equiv.) and dissolved in DMSO/H_2O (3:1). To this stirred solution was added $K_2S_2O_8$ (2 equiv.) and stirred at room temperature for 6 hours. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was treated with ice-cold water and then extracted with ethyl acetate thrice, the organic phase was dried over sodium sulfate and evaporated under reduced pressure to get the crude product which was purified by filtration through a short pad of silica gel column (hexane: ethyl acetate;88:12) to afford **20** as a pale gummy liquid (62.0 mg, 75%).

2.13 Procedure for the synthesis of compound 21:

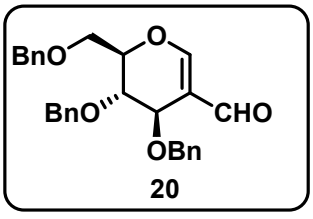


Compound **21** was synthesized using **9** (50 mg, 0.11 mmol,1 equiv.) in solvent DCM and to this was added pyridine (1.1 equiv.), DMAP (5 mol%), Ac_2O (1 equiv.). The reaction mixture was allowed to stir at room temperature until complete consumption of the starting material was observed by TLC analysis. Then the reaction mixture was quenched with saturated cupric sulfate solution and extracted with ethyl acetate and water, the organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuo. The residue left was purified by column chromatography over silica gel (60-120 mesh) using Hexane/ethyl acetate (90:10) as eluent to obtain compound **21** as a white solid (51.62 mg, 95%).

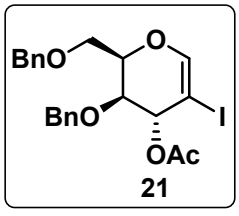
2.14 Characterization data & NMR spectra of compounds 19-21:



The compound **19** was synthesized according to the procedure (2.1.6).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.25 – 7.15 (m, 20H), 6.39 (s, 1H), 4.63 (d, J = 11.6 Hz, 1H), 4.55 (d, J = 6.9 Hz, 3H), 4.45 (s, 2H), 4.43 (d, J = 11.8 Hz, 1H), 4.29 (d, J = 11.8 Hz, 1H), 4.21 (d, J = 11.4 Hz, 1H), 4.19 – 4.15 (m, 1H), 4.15 – 4.13 (m, 1H), 3.83 (dd, J = 6.6, 5.0 Hz, 1H), 3.73 – 3.65 (m, 2H), 3.62 (dd, J = 10.6, 3.6 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$) δ** 143.9, 138.5 (Cq), 138.4 (Cq), 138.03 (Cq), 138.0 (Cq), 128.5, 128.4, 128.4, 127.9, 127.89, 127.86, 127.8, 127.7, 127.6, 109.7 (Cq), 76.6, 74.2, 73.9, 73.5 (CH_2), 73.1 (CH_2), 72.8 (CH_2), 71.1 (CH_2), 68.3 (CH_2), 67.7 (CH_2). **HRMS (ESI, m/z)** for $C_{35}H_{37}O_5$ $[M+H]^+$: calcd 537.3641, found, 537.3649.



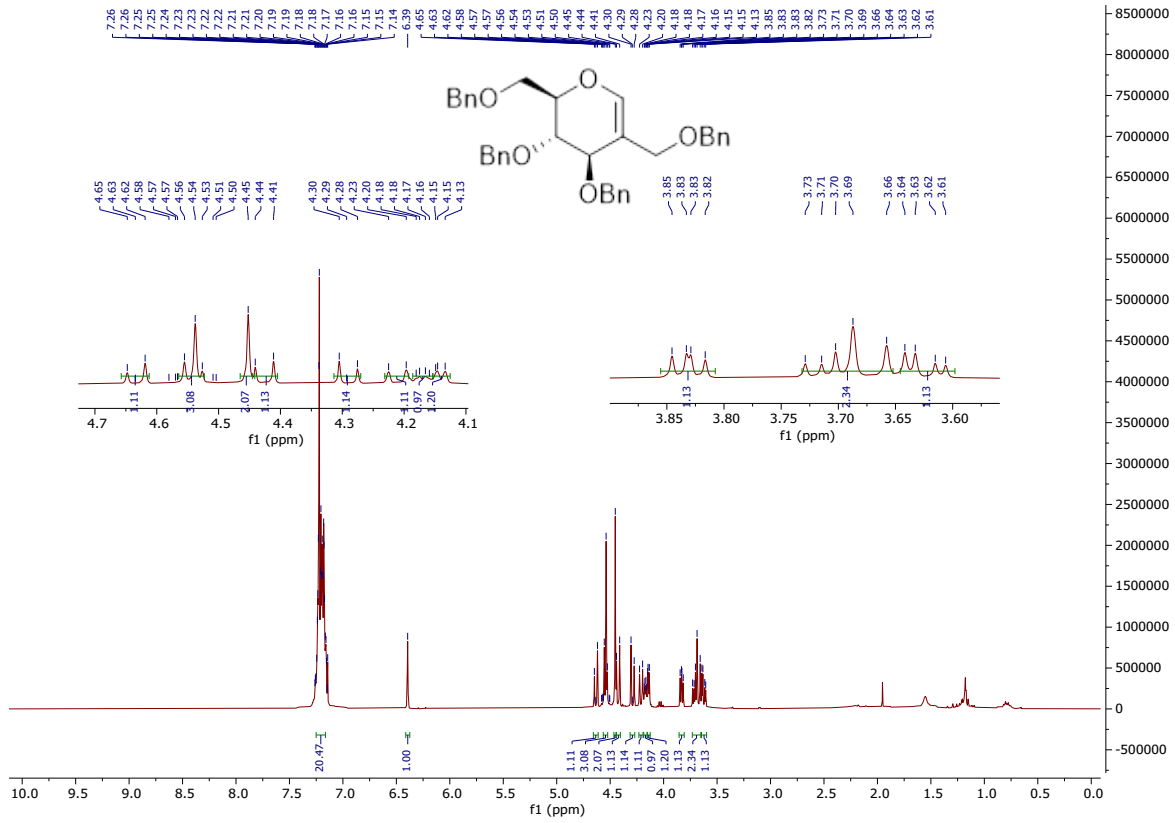
The compound **20** was synthesized according to the procedure (2.1.7).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 9.33 (s, 1H), 7.32 (s, 1H), 7.26 – 7.23 (m, 6H), 7.21 (t, J = 3.7 Hz, 6H), 7.17 (dd, J = 4.6, 1.6 Hz, 3H), 4.65 (ddt, J = 8.1, 4.3, 2.0 Hz, 1H), 4.58 (d, J = 11.5 Hz, 1H), 4.52 – 4.47 (m, 2H), 4.45 (d, J = 2.0 Hz, 1H), 4.42 (s, 1H), 4.39 (d, J = 4.2 Hz, 1H), 4.34 (t, J = 2.4 Hz, 1H), 3.76 (d, J = 2.3 Hz, 1H), 3.72 (d, J = 3.0 Hz, 1H), 3.55 (dd, J = 10.8, 4.6 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$) δ** 190.4, 164.4, 138.2 (Cq), 137.6 (Cq), 137.2 (Cq), 128.6, 128.5, 128.48, 128.4, 128.4, 128.4, 128.1, 127.9, 127.9, 127.86, 127.8, 127.7, 117.7 (Cq) 79.4, 73.4 (CH_2), 72.48 (CH_2), 71.7 (CH_2), 71.3, 68.4 (CH_2), 65.3. **HRMS (ESI, m/z)** for $C_{28}H_{29}O_5$ $[M+H]^+$: calcd 445.2015, found, 445.2021.

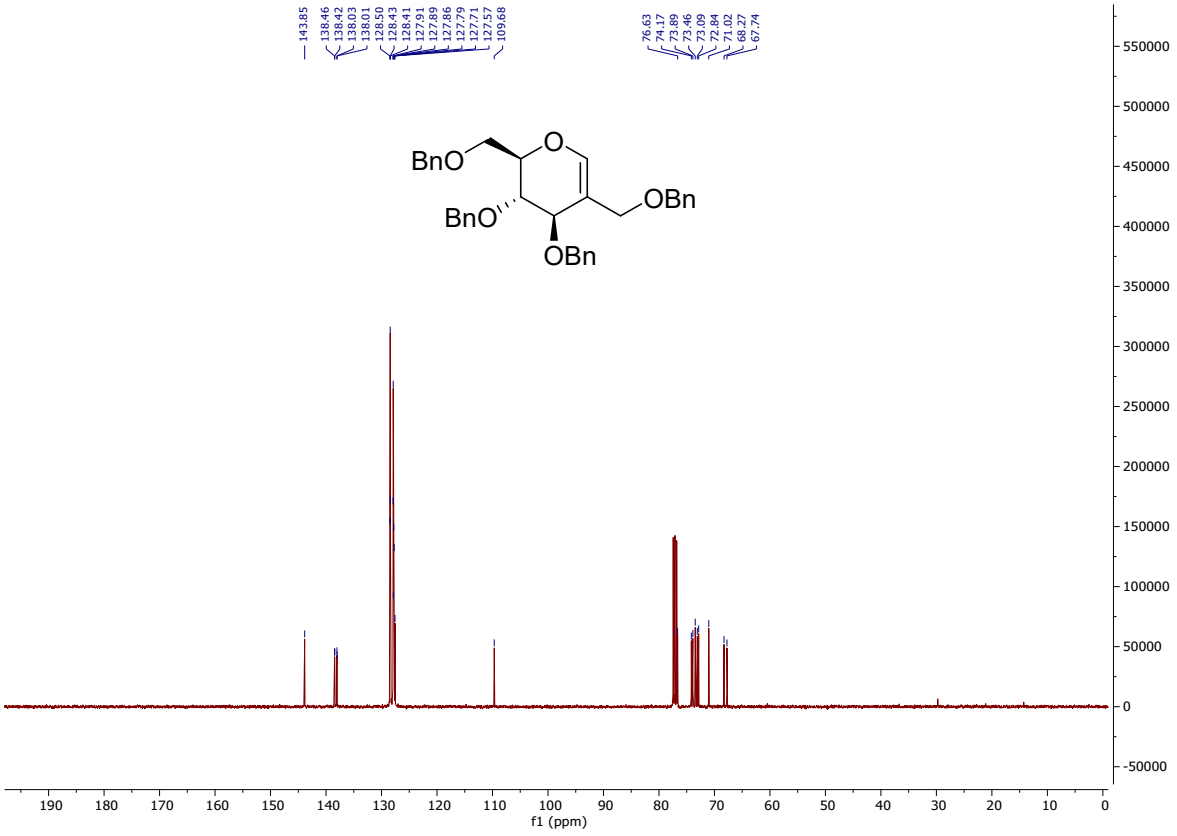


The compound **21** was synthesized according to the procedure (2.1.8).**^{1}H NMR (400 MHz, $CDCl_3$) δ** 7.28 – 7.18 (m, 10H), 6.63 (d, J = 1.2 Hz, 1H), 5.53 (dt, J = 4.4, 1.2 Hz, 1H), 4.61 (d, J = 11.8 Hz, 1H), 4.45 (d, J = 11.9 Hz, 1H), 4.39 (d, J = 7.6 Hz, 1H), 4.36 (d, J = 7.6 Hz, 1H), 4.28 (dddd, J = 7.7, 4.3, 3.3, 1.1 Hz, 1H), 4.00 (dd, J = 4.4, 3.3 Hz, 1H), 3.69 (dd, J = 10.6, 7.7 Hz, 1H), 3.55 (dd, J = 10.6, 4.3 Hz, 1H), 2.01 (s, 3H). **^{13}C NMR (101 MHz, CDCl3) δ** 170.32 (Cq), 149.34, 137.79 (Cq), 137.44 (Cq), 128.63,

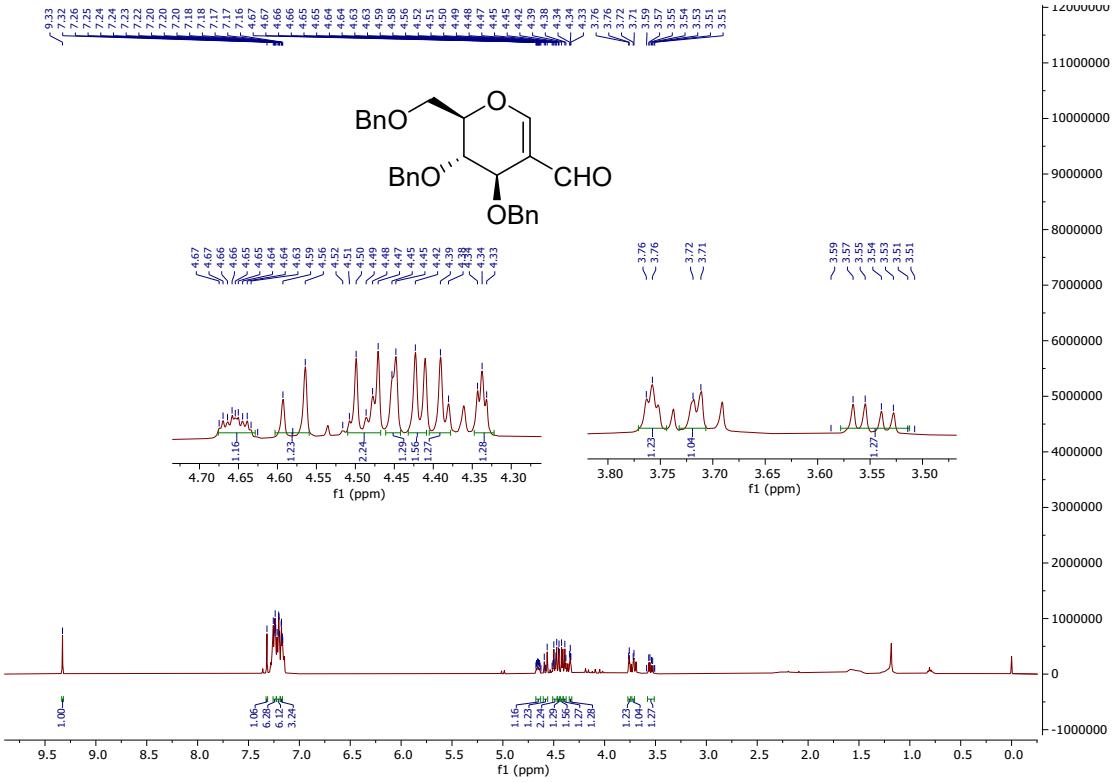
128.54, 128.49, 128.31, 128.08, 128.05, 128.00, 127.88, 127.87, 75.69, 73.48, 71.77, 68.90, 67.28, 20.96 (CH_3). **HRMS (ESI, m/z)** for $C_{22}H_{24}IO_5$ $[M+H]^+$: calcd 495.0668, found, 495.0675.

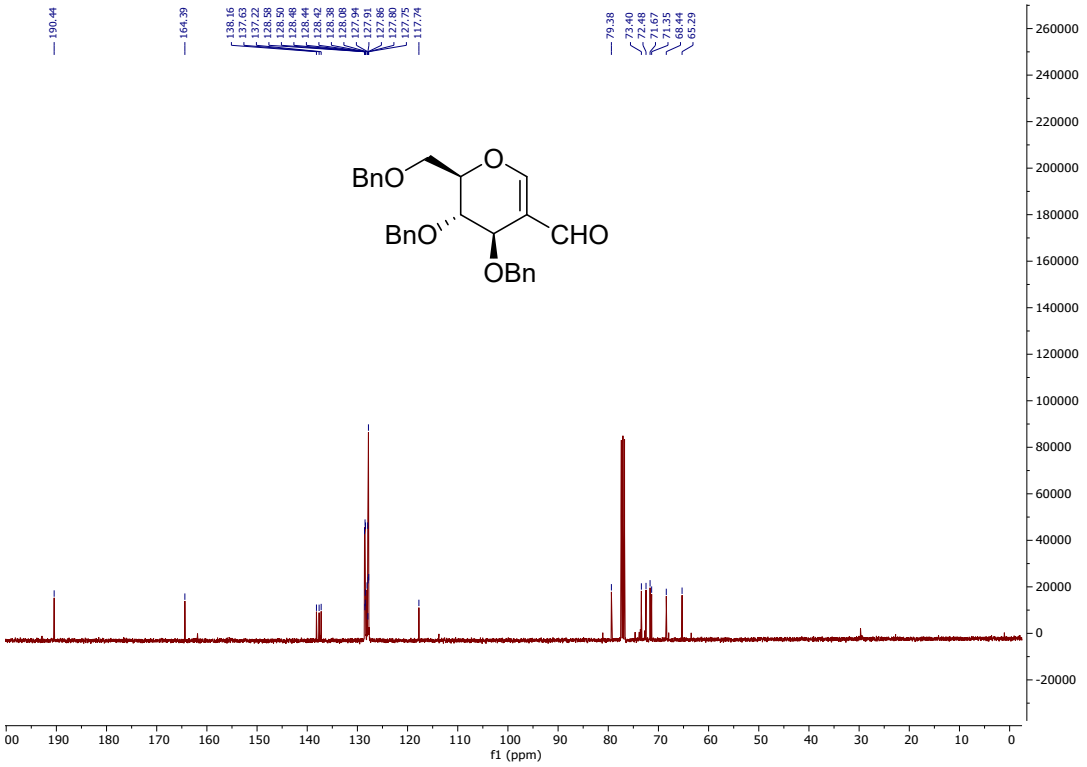
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **19** in $CDCl_3$



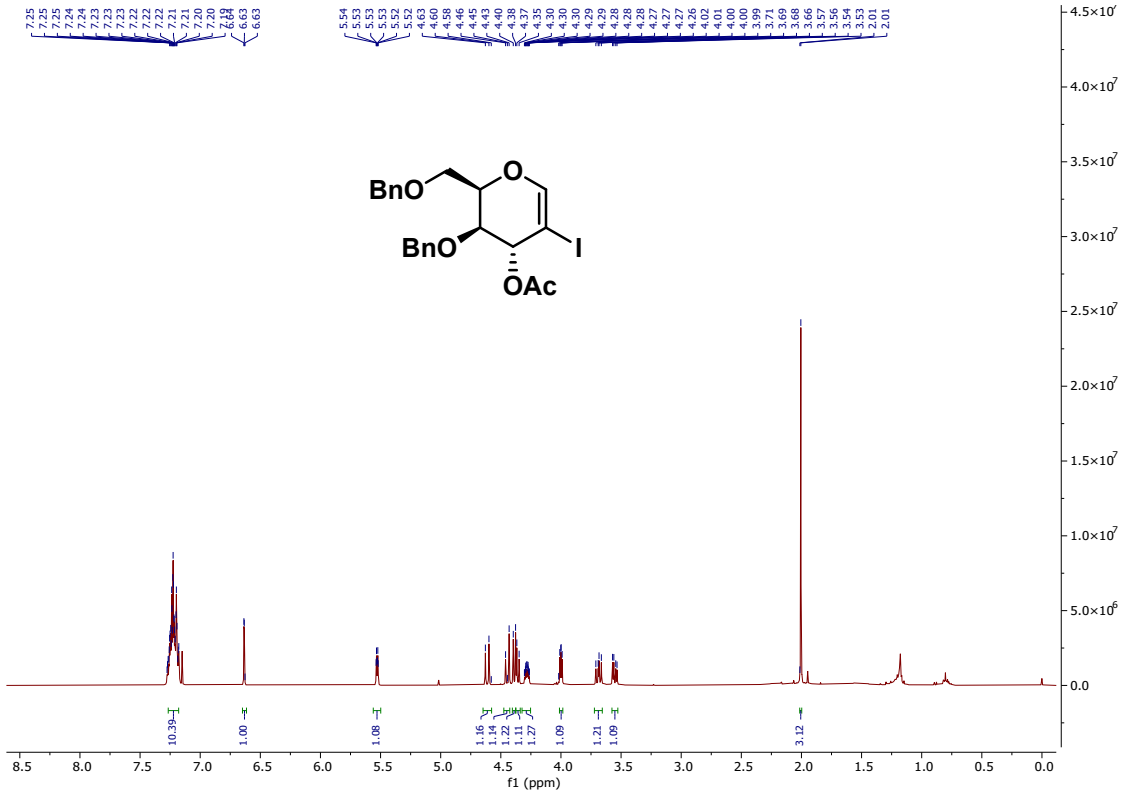


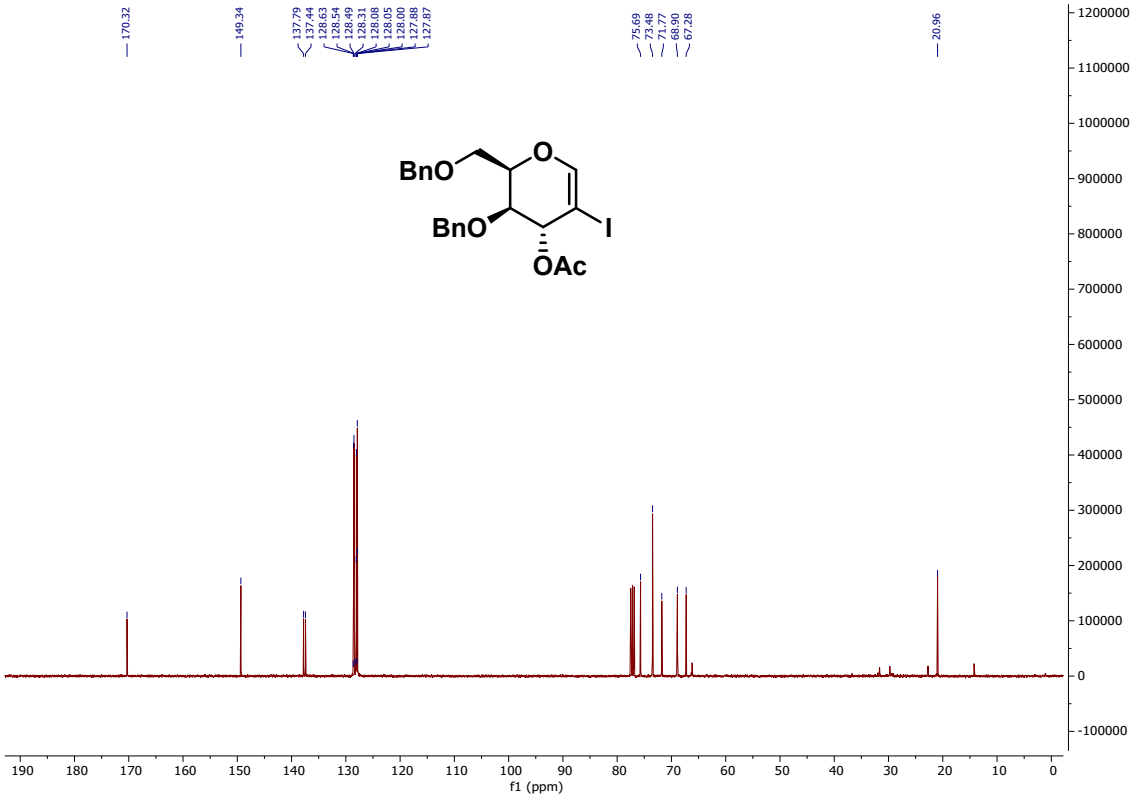
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **20** in $CDCl_3$





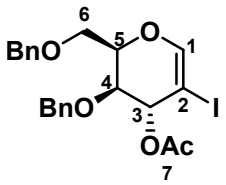
^{1}H NMR (400 MHz) & ^{13}C NMR {^{1}H} (101 MHz) of **21** in $CDCl_3$





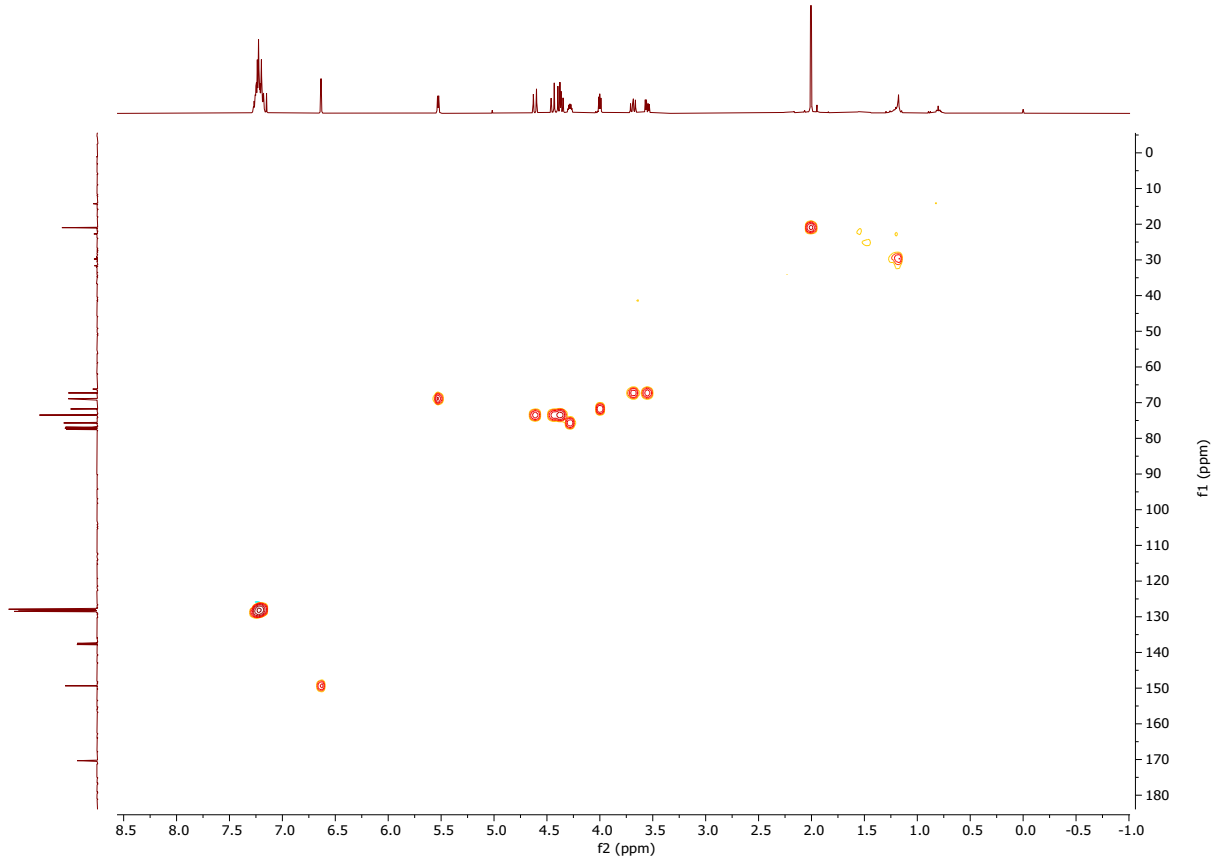
HSQC of compound **21**

HSQC table of compound **21**

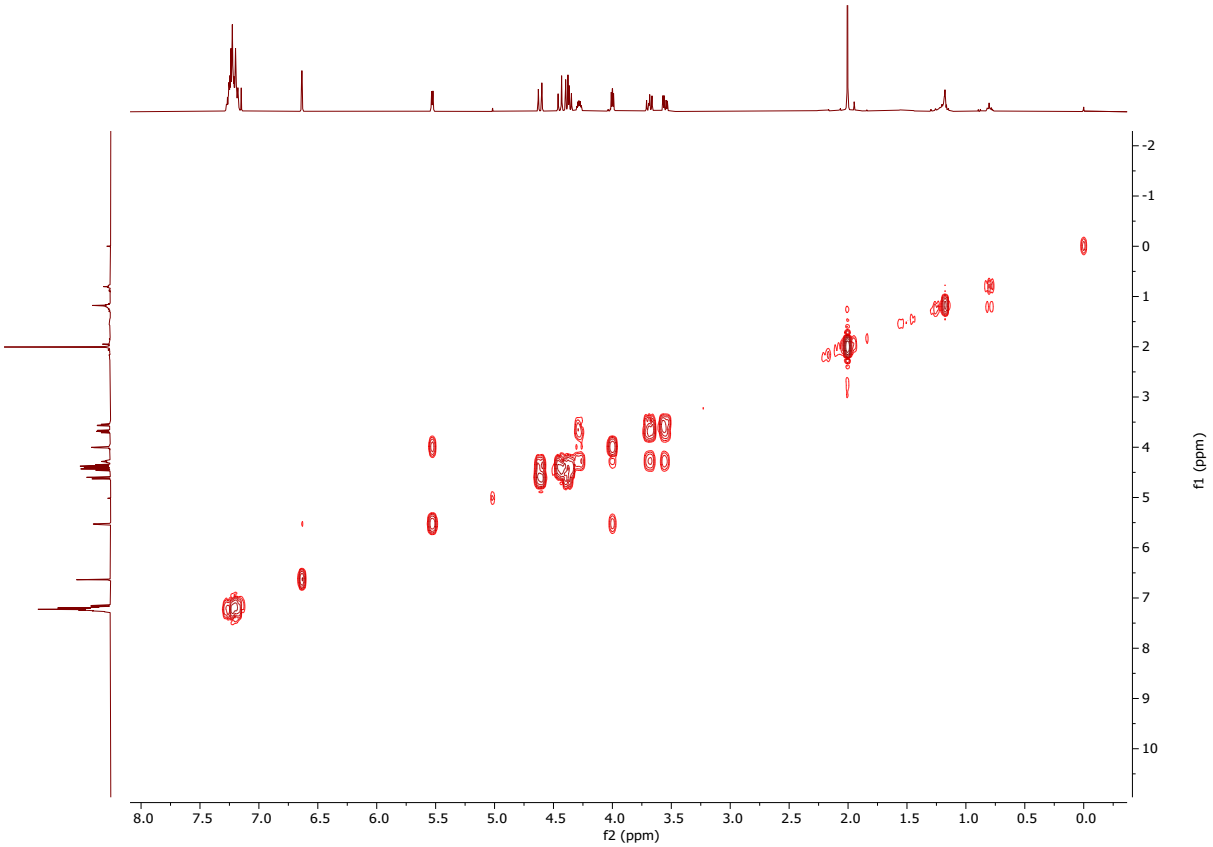


Position	δ_H	δ_C
1	H_1= 6.63 (d, *J* = 1.2 Hz, 1H)	149.34
3	H_3= 5.53 (dt, J = 4.4, 1.2 Hz, 1H)	68.90
4	H_4= 4.00 (dd, *J* = 4.4, 3.3 Hz, 1H)	71.77
5	H_5= 4.28 (dddd, J = 7.7, 4.3, 3.3, 1.1 Hz, 1H)	75.69
6	H_{6a}=3.69 (dd, *J* = 10.6, 7.7 Hz, 1H)	67.28
6	H_{6b}=3.55 (dd, J = 10.6, 4.3 Hz, 1H)	67.28
7	2.01 (s, 3H)	20.96

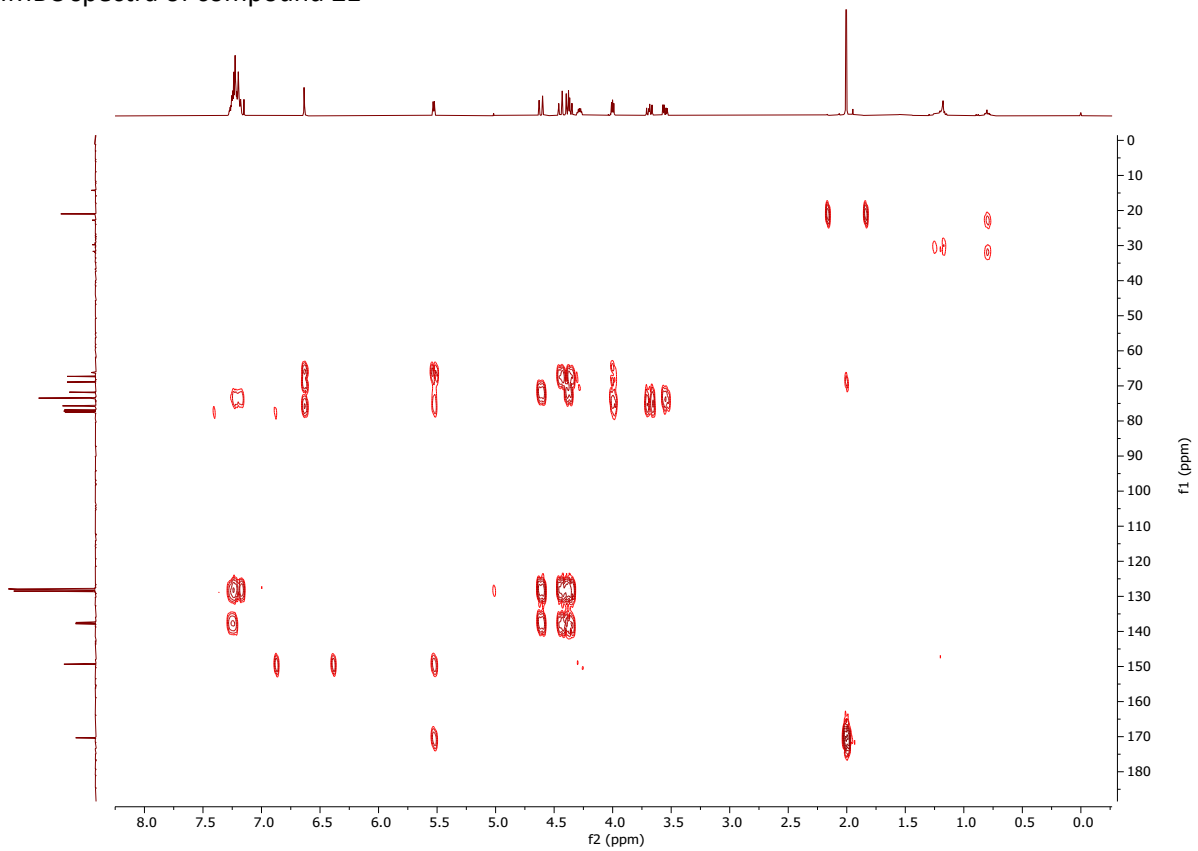
HSQC spectra of compound **21**



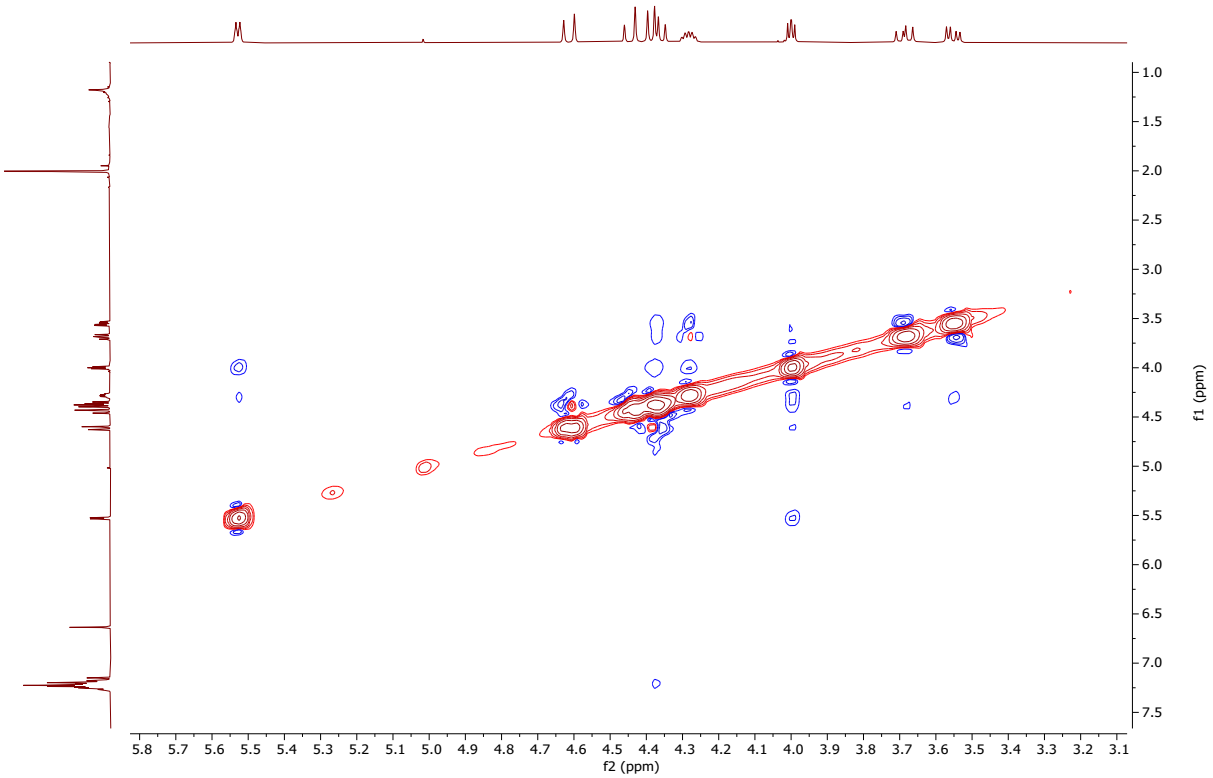
COSY spectra of compound **21**



HMBC spectra of compound **21**



NOESY spectra of compound **21**

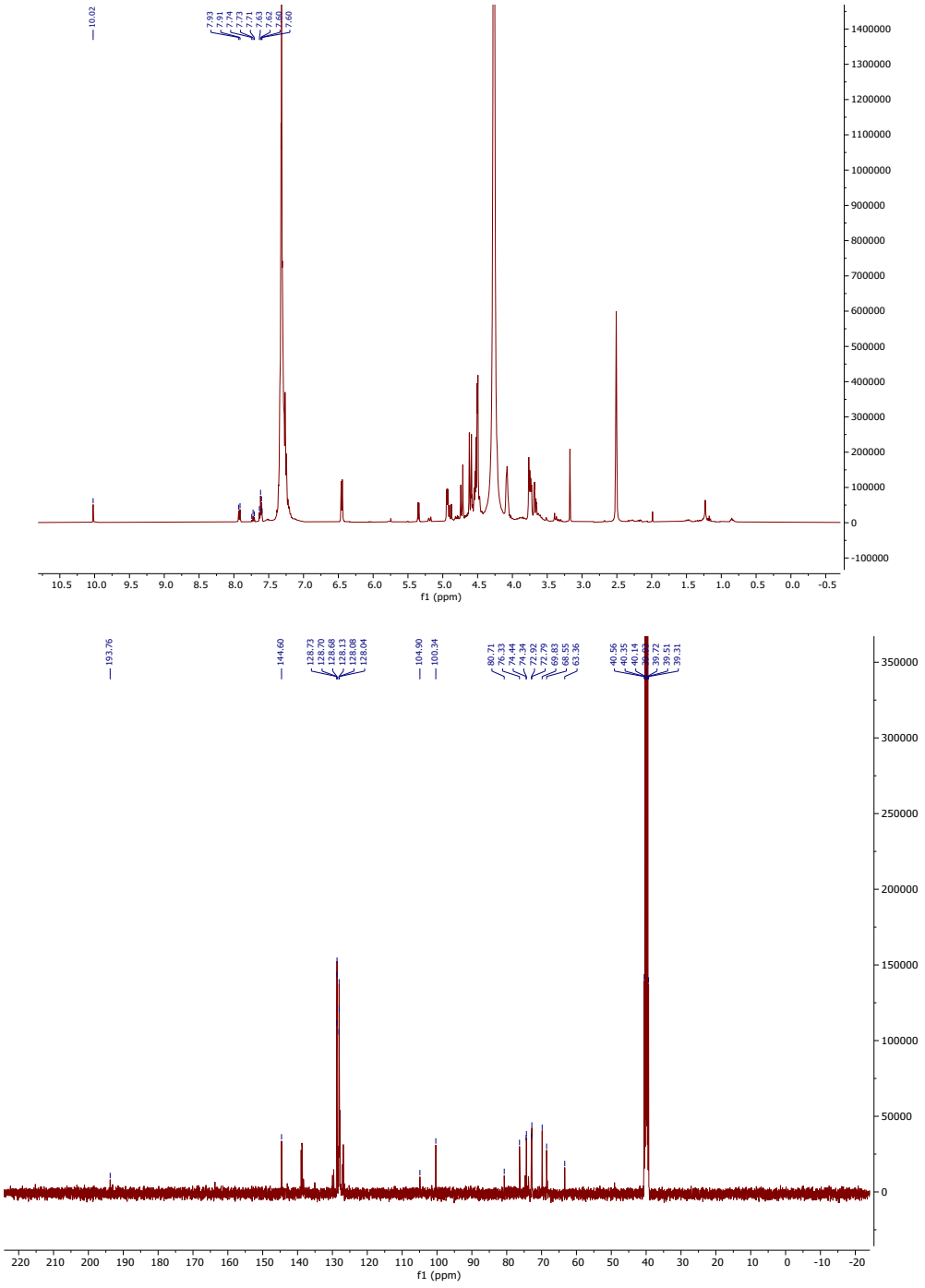


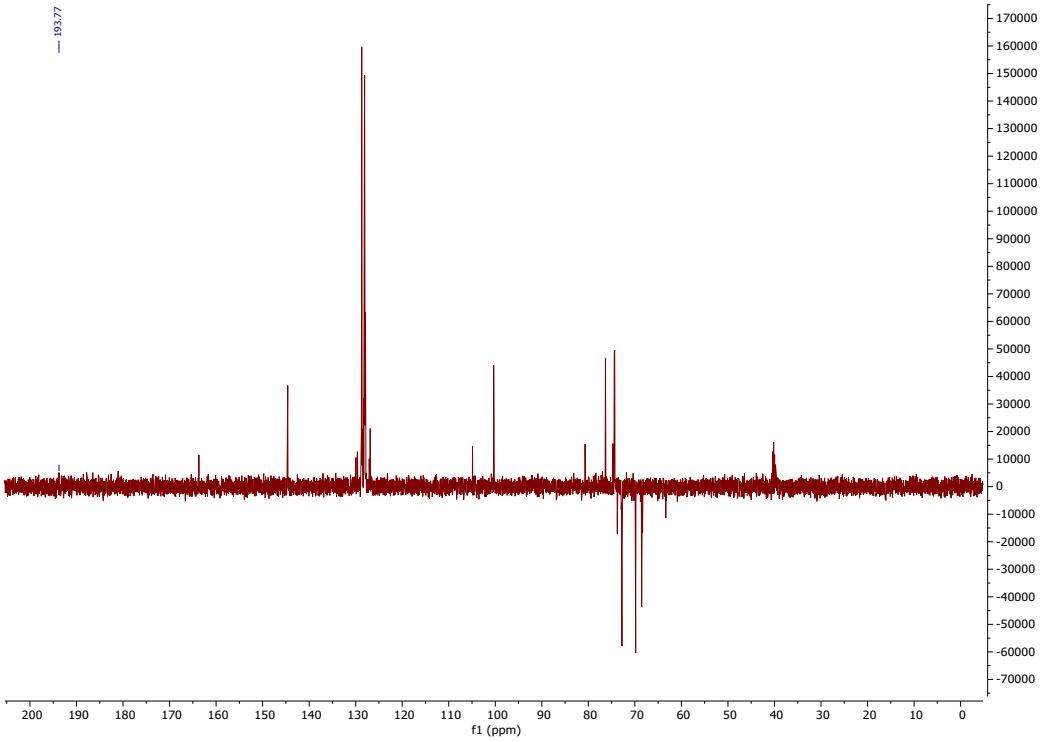
In the NOESY experiment, we observed no correlation between the H3 and the H5 protons, confirming α stereochemistry at the C-3 position.

2.15 NMR monitoring experiment in DMSO-D_6 at room temperature:

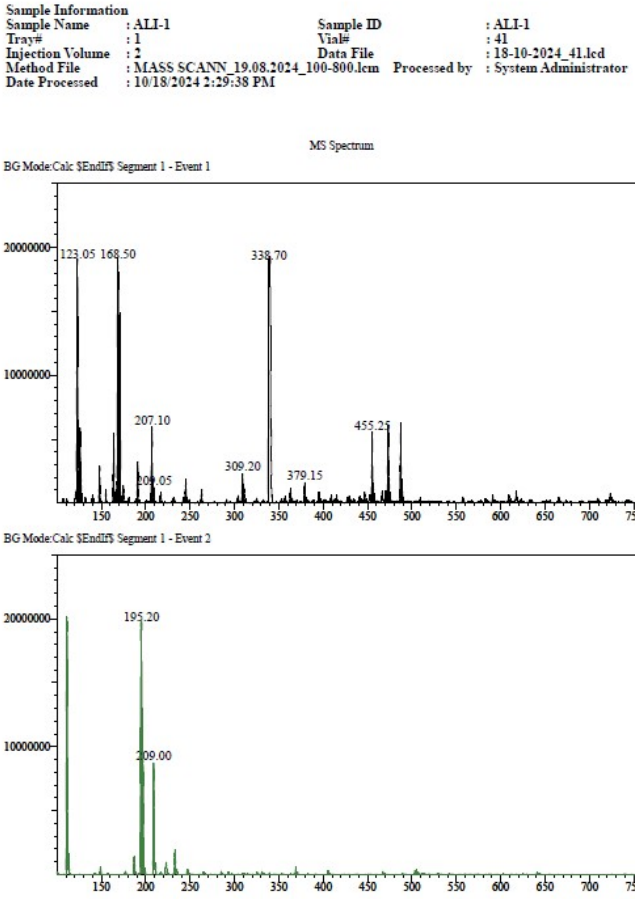
A reaction was set up by dissolving compound 1 (1 equiv.) in DMSO-D_6, followed by the addition of $K_2S_2O_8$ (2 equiv.) to the stirred solution. NMR analysis was performed at regular intervals by taking aliquots, revealing the appearance of a peak corresponding to benzaldehyde, indicating the oxidation of benzyl alcohol eliminated from the reaction. LCMS showed a peak corresponding to the benzoic acid formed probably by the overoxidation of the benzyl alcohol. Upon subsequent addition of TEMPO to the reaction mixture, LCMS detected a peak corresponding to the adduct formed by quenching the allylic radical with TEMPO.

NMR of the reaction mixture in DMSO-D_6 (Aliquot-1)

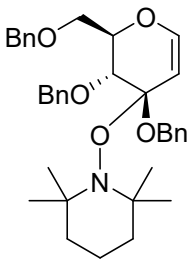




LCMS of reaction mixture (Aliquot 1)



LCMS of TEMPO adduct

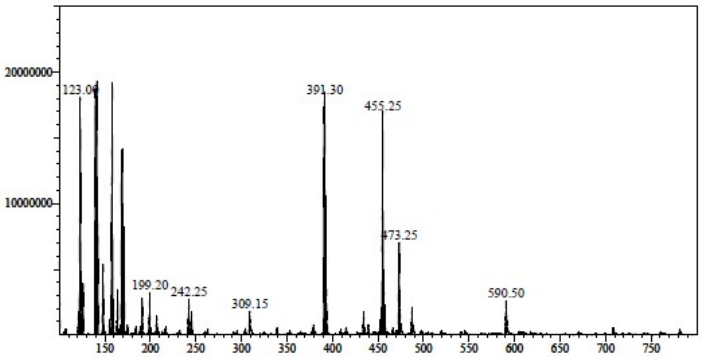


Sample Information

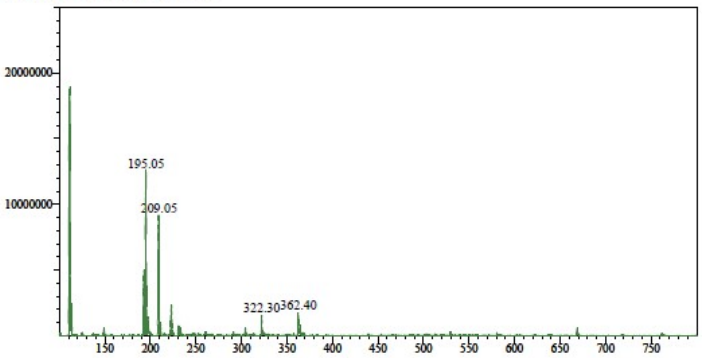
Sample Name	: ALI-2-TEMPO	Sample ID	: ALI-2-TEMPO
Tray#	: 1	Vial#	: 40
Injection Volume	: 2	Data File	: 18-10-2024_40.lcd
Method File	: MASS SCANN_19.08.2024_100-800.lcm	Processed by	: System Administrator
Date Processed	: 10/18/2024 2:29:28 PM		

MS Spectrum

BG Mode:Calc $Endlf$ Segment 1 - Event 1



BG Mode:Calc $Endlf$ Segment 1 - Event 2



GCMS of reaction mixture

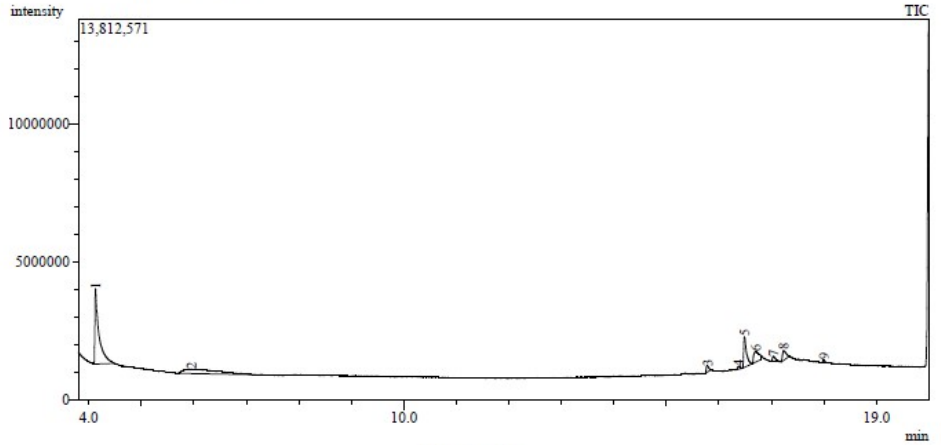
01-10-2024

Qualitative Analysis Report

CSIR-INDIAN INSTITUTE OF INTEGRATIVE MEDICINE
Quality Management and Instrumentation Division
GCMS ANALYSIS REPORT

Sample Information

Analyzed by	: Dr. Nagaraju Nekkala
Analyzed	: 01-10-2024 01:03:29
Sample Name	: SCN-DEU-RT
Sample ID	: SCN-DEU-RT
Vial #	: 10
Injection Volume	: 2.00
Data File	: D:\GCMS-2024\DATA\SEP-2024\30.09.2024-33.qgd
Method File	: D:\GCMS-2024\METHODS\GCMS_LIQ_1_5ms_01.qgm
Tuning File	: D:\GCMS-2024\TUNNING\AT_F1_Normal_CID OFF_27.09.2024_New Cylinder.qgt
Modified	: 01-10-2024 09:37:09



Peak Report TIC

Peak#	R.Time	Area	Area%	Similarity	Name
1	4.127	14614355	44.56	98	Benzaldehyde
2	5.952	7716842	23.53	91	Benzyl alcohol
3	15.779	743053	2.27	83	Methyl 2,3-di-O-benzyl-beta-d-glucofuranoside
4	16.365	316697	0.97	80	3-Benzoyl-8-oxo-6-azabicyclo[3.2.1]octan-6,7-dicarboxylic acid, dibenzyl ester
5	16.485	4141227	12.63	83	2-Thiopheneacetic acid, benzyl ester
6	16.701	2616789	7.98	89	l-Alanine, 3-chloro-N-[(phenylmethoxy)carbonyl]-, phenylmethyl ester
7	17.036	746646	2.28	73	2-Thiopheneacetic acid, benzyl ester
8	17.231	1666698	5.08	82	1,1-Dibenzyloxy-4,4-dimethyl-2-penryne
9	17.992	237884	0.73	82	2,3,4-Tri-O-benzyl- beta.D-ribopyranose
		32800191	100.00		

References:

1) N. G. Ramesh, K. K. Balasubramanian, Tetrahedron Lett. **1991**, 32, 3875.
2) A. Chennaiah, A. K. Verma and Y. D. Vankar, *J. Org. Chem.*, **2018**, *83*, 10535.
3) Zhao, J.; Wei, S.; Ma, X.; Shao, H. *Carbohydr. Res.*, **2010**, *345*, 168-171.