Stereoselective Synthesis of Sugar-Fused (or 1,2-Annulated) Isochromans and Isochromanones by Using Oxa-Pictet-Spengler Reaction

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1. General Information

All the reactions were performed under nitrogen atmosphere and glassware were oven dried before use. Common reagents and solvents were dried by following standard procedures. Thin layer chromatography was done by preparing thin layers of silica gel on microscopic slides. The visualisation of spots on TLC plates was done by exposing to iodine, or by spraying 10% H_2SO_4 followed by charring. Purification of compounds was carried out by column chromatography over silica gel (100-200 mesh) by using appropriate eluents. $CDCl_3$ and D_2O solvents were used for the ^1H (500 MHz or 400 MHz) and ^{13}C (125 MHz or 100 MHz). Chemical shifts are reported in ppm downfield to tetramethylsilane. Coupling constants are mentioned in Hertz, splitting patterns are designated as br (broad), s (singlet), d (doublet), dd (double doublet), q (quartet), m (multiplet). Infrared spectra are recorded on a Bruker Vector 22 FT-IR spectrometer and the absorption bands are reported in reciprocal centimeters (cm^{-1}). The mass spectra are recorded on high-resolution ESI mass spectrometer using a Q-TOF analyzer. The purity of selected compounds was determined by HPLC (Waters 2998 PDA detector, 515 HPLC pump) using a C-18 column (detection at 254 nm) and chiral HPLC was analysed by IC-Column. Rotation values are recorded on an Autopol II automatic polarimeter cell size (6 cm) at 28 °C.

2. Experimental Details

General procedure for C-Arylation of glycal epoxide (A): Arylboronic acid (192 mg, 1.1 equiv) was dissolved in dry toluene (12 ml) to which a 1 M solution of Et_2Zn (3.78 mL, 3 equiv) was added under nitrogen atmosphere at room temperature. The reaction mixture was stirred at 60 °C for 1 h, brought it to room temperature and added 1,2-anhydrosugar (500 mg, 1 equiv). The reaction mixture was again warmed to 60 °C and stirred for 3 h. Upon completion of reaction (TLC monitoring) it was quenched by dropwise addition of a saturated aqueous solution of NH_4Cl (5 ml) and extracted with EtOAc (2 x 30 ml). The combined organic layers were washed with brine (10 ml) and dried over anhydrous Na_2SO_4. Evaporation of the solvent under vacuum, followed by silica gel column chromatography of the resulting crude residue using hexane:EtOAc as eluent afforded the pure product.

General procedure for the $BF_3.OEt_2$ catalyzed oxa-Pictet-Spengler cyclization (B): To a stirred solution of C2-hydroxy-α-*C*-aryl glycoside (200 mg, 1 equiv) and the corresponding aldehyde (1.2 equiv) in anhydrous CH_2Cl_2 (5 mL) at 0 °C was added $BF_3.OEt_2$ (1.2 equiv)

and the mixture stirred at room temperature for appropriate time. Upon consumption of the starting material (monitored by TLC), the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$. It was extracted with CH_2Cl_2 (2 x 15 ml), washed with brine (5 ml) and dried over anhydrous Na_2SO_4. Evaporation of organic layer *in vacuo*, followed by silica gel column chromatography of the resulting crude residue using hexane:EtOAc as eluent afforded the pure product.

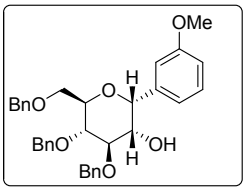
General procedure for debenzylation (C): To a stirred solution of sugar-fused 1,2-annulated isochroman (200 mg) in methanol (4 mL) was added 40 mg (20 % w/w) of $Pd(OH)_2$ (10% on C). The mixture was then degassed under vacuum and stirred under hydrogen gas (1 atm). After 30 min, complete consumption of the starting material (monitored by TLC) was observed. The reaction mixture was filtered on celite pad and concentrated *in vacuo* and the resultant solid residue was washed with CH_2Cl_2 and dried *in vacuo* to obtain the product.

General procedure for the acetylation (D): The hydroxy compound (200 mg, 1 equiv) was dissolved in acetic anhydride (5 mL) and cooled to 0 ^oC. To it was added triethylamine (6 equiv) dropwise under nitrogen atmosphere. The reaction mixture was then stirred at room temperature for 5 h (reaction monitored by TLC) and quenched by dropwise addition of saturated aqueous solution of $NaHCO_3$ (15 ml) and extracted with Et_2O (3 x 20 ml). The combined organic extracts were washed with brine (10 ml) and evaporated under reduced pressure to get the crude product, which was purified by silica gel column chromatography using hexane:EtOAc as eluent to afford the pure product.

General procedure for the oxidation of isochroman to isochromanone (E): A sugar-fused isochroman derivative (200 mg, 1 equiv) was dissolved in a mixture of solvents comprising of carbon tetrachloride (6 ml), acetonitrile (6 ml) and water (9 ml) in 2:2:3 ratio respectively. The mixture was cooled to 0 ^oC and with vigorous stirring $NaIO_4$ (430 mg, 4 equiv) was added to it, followed by addition of $RuCl_3.nH_2O$ (2.2 mg, 10 mol%). The reaction mixture was brought to room temperature and stirred additionally for 5 h (reaction monitored by TLC). It was then diluted with CH_2Cl_2 (20 ml) and extracted with CH_2Cl_2 (2 x 20 ml). The combined organic extract were washed with brine (10 ml) and dried over anhydrous Na_2SO_4. Solvent was evaporated under reduced pressure and the resulting residue purified by column chromatography to obtain the pure product.

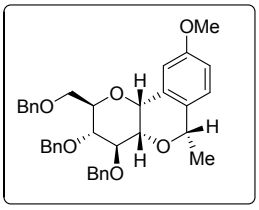
3. Characterization of products

(2R,3S,4R,5R,6R)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-2-(3-methoxyphenyl) tetrahydro-2H-pyran-3-ol (1):



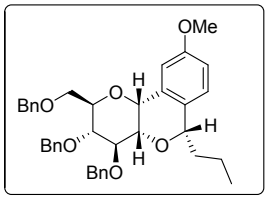
Following the general procedure **A**, compound **1** was isolated as a yellow liquid in 73% yield (455 mg); R_f = 0.5 (9/3hexane/EtOAc); $[\alpha]_D^{28}$ = +27.89° (c = 0.17, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3503.25, 3030.03, 2932.00, 1601.40, 1453.75, 1261.40, 1075.38, 737.67, 697.93; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.18 (m, 16H), 7.05–6.95 (m, 2H), 6.81–6.77 (m, 1H), 4.93 (d, J = 1.5 Hz, 1H), 4.64–4.47 (m, 6H), 4.32 (td, J = 6.3, 2.5 Hz, 1H), 3.96–3.91 (m, 1H), 3.90–3.74 (m, 6H), 3.72–3.70 (m, 1H), 3.26 (d, J = 9.9 Hz, 1H); ^{13}C NMR (100 MHz $CDCl_3$) δ 159.58, 140.70, 138.21, 137.87, 137.34, 129.11, 128.67, 128.62, 128.46, 128.08, 128.05, 127.75, 119.09, 113.09, 112.47, 76.05, 74.89, 73.55, 73.26, 72.84, 72.27, 71.31, 70.48, 67.82, 55.30; HRMS calcd for $C_{34}H_{36}NaO_6$ $[M + Na]^+$ 563.2410, found 563.2419.

(2R,3R,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3a):



Following the typical procedure **B**, compound **3a** was isolated as a yellow liquid in 89% yield (186 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +38.25° (c = 0.25, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3030.11, 2862.51, 1503.75,1453.96, 1094.97, 737.06, 697.48 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.21 (m, 15H), 7.06 (d, J = 8.6 Hz, 1H), 6.97 (d, J = 2.7 Hz, 1H), 6.83 (dd, J = 8.6, 2.7 Hz, 1H), 4.89–4.75 (m, 4H), 4.63–4.43 (m, 4H), 4.05–3.95 (m, 2H), 3.93–3.85 (m, 2H), 3.79–3.67 (m, 5H), 1.59 (d, J = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.71, 138.81, 138.57, 138.50, 133.43, 132.31, 128.48, 128.46, 128.44, 128.21, 127.95, 127.76, 127.70, 127.69, 124.92, 114.94, 113.68, 83.28, 78.54, 75.06, 74.20, 73.56, 73.28, 71.50, 70.65, 67.82, 55.38, 20.86; HRMS calcd for $C_{36}H_{42}NO_6$ $[M + NH_4]^+$ 584.3012, found 584.3018.

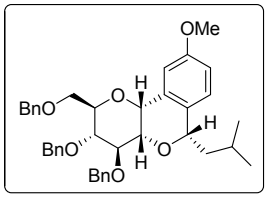
(2R,3R,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-propyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3b):



Following the typical procedure **B**, compound **3b** was isolated as a yellow liquid in 80% yield (176 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +27.71° (c = 0.20, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 2955.96, 2868.87,

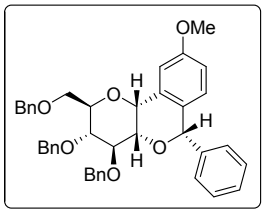
1611.43, 1498.33, 1453.02, 1087.67. 1028.64, 734.54, 697.00; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.23 (m, 15H), 7.08 (d, *J* = 8.6 Hz, 1H), 6.96 (d, *J* = 2.6 Hz, 1H), 6.83 (dd, *J* = 8.6, 2.7 Hz, 1H), 4.92–4.74 (m, 4H), 4.61–4.44 (m, 4H), 4.06–3.87 (m, 4H), 3.79–3.69 (m, 5H), 2.08–1.97 (m, 1H), 1.82–1.72 (m, 1H), 1.70–1.60 (m, 1H), 1.59–1.49 (m, 1H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.58, 138.78, 138.64, 138.54, 133.75, 131.41, 128.50, 128.45, 128.21, 127.96, 127.76, 127.72, 124.80, 114.99, 114.09, 83.44, 78.93, 75.39, 74.89, 74.83, 74.26, 73.57, 73.14, 70.79, 67.77, 55.39, 36.61, 18.64, 14.2; HRMS calcd for $C_{38}H_{46}NO_6$ $[M + NH_4]^+$ 612.3325 , found 612.3326.

(2R,3R,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6-isobutyl-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3c):



Following the typical procedure **B**, compound **3c** was isolated as a colorless liquid in 82% yield (184 mg); R_f = 0.9 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +37.53° (*c* = 0.32, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3030.26, 2953.73, 1610.65, 1498.45, 1114.25, 1092.06, 735.23, 697.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.22 (m, 13H), 7.04–7.01 (m, *J* = 6.5, 3.0 Hz, 2H), 7.04 (d, *J* = 2.3 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 1H), 6.78 (dd, *J* = 8.6, 2.6 Hz, 1H), 5.17 (d, *J* = 6.6 Hz, 1H), 4.97 (d, *J* = 10.8 Hz, 1H), 4.89–4.76 (m, 3H), 4.64 (d, *J* = 11.9 Hz, 1H), 4.54 (d, *J* = 11.9 Hz, 1H), 4.47 (d, *J* = 10.7 Hz, 1H), 4.30–4.28 (m, 1H), 3.82–3.62 (m, 7H), 3.53–3.42 (m, 1H), 2.07–1.94 (m, 1H), 1.69–1.58 (m, 2H), 0.97 (d, *J* = 6.5 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.84, 138.82, 138.17, 138.11, 133.37, 131.21, 128.51, 128.11, 128.01, 127.84, 125.90, 114.71, 109.51, 79.15, 78.31, 75.12, 74.46, 74.35, 73.77, 72.19, 69.64, 69.39, 69.17, 55.39, 47.19, 24.24, 24.13, 21.90; HRMS calcd for $C_{39}H_{44}NaO_6$ $[M + Na]^+$ 631.3036, found 631.3038.

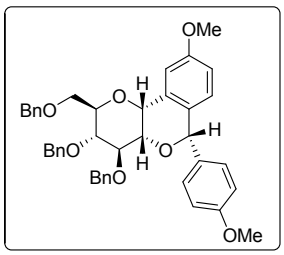
(2R,3R,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-phenyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3d):



Following the typical procedure **B**, compound **3d** was isolated as a yellow liquid in 81% yield (188 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +47.55° (*c* = 0.27, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.59, 2916.43, 16.08.49, 1496.73, 1103.42, 1068.61, 730.43, 697.44; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.10 (m, 21H), 6.71–6.68 (m, 2H), 5.80 (s, 1H), 4.99–4.91 (m, 2H), 4.77 (d, *J* = 11.4 Hz, 1H), 4.65–4.56 (m, 3H), 4.51–4.45 (d, *J* = 9.4 Hz, 1H), 3.86–3.79 (m, 2H), 3.81–3.75 (m, 5H), 3.74– 3.68 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.79, 142.31,

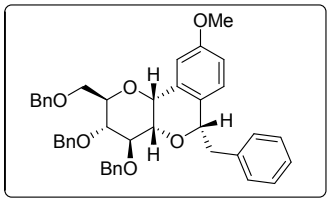
139.08, 138.49, 135.93, 129.24, 128.88, 128.57, 128.50, 128.39, 128.14, 128.13, 127.92, 127.82, 127.74, 127.64, 127.59, 114.19, 109.51, 84.34, 81.12, 80.13, 79.83, 77.94, 75.39, 75.05, 73.63, 73.55, 69.53, 55.42; HRMS calcd for $C_{41}H_{40}NaO_6$ $[M + Na]^+$ 651.2723 found 651.2728.

(2R,3R,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-(4-methoxyphenyl)-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3e):



Following the typical procedure **B**, compound **3e** was isolated as a yellow liquid in 82% yield (200 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +17.22° (c = 0.22, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.70, 2905.19, 1610.64, 1512.59, 1497.55, 1248.16, 1090.52, 736.86, 698.03; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.23 (m, 15H), 7.16– 7.06 (m, 3H), 6.87–6.82 (m, 2H), 6.67–6.63 (m, 2H), 5.63 (s, 1H), 5.31 (d, J = 6.4 Hz, 1H), 5.02 (d, J = 11.2 Hz, 1H), 4.90 (d, J = 11.2 Hz, 1H), 4.82 (d, J = 10.8 Hz, 1H), 4.65 (d, J = 11.9 Hz, 1H), 4.55–4.51 (m, 2H), 4.41 (dd, J = 9.1, 6.5 Hz, 1H), 3.96 (t, J = 8.9 Hz, 1H), 3.82–3.67 (m, 9H), 3.56–3.53 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.74, 159.16, 138.87, 138.22, 138.15, 134.38, 133.68, 130.12, 130.09, 128.56, 128.51, 128.08, 128.03, 127.86, 127.84, 127.79, 114.80, 114.06, 109.45, 78.92, 78.34, 77.41, 77.16, 76.91, 75.29, 75.10, 74.29, 74.19, 73.78, 72.47, 69.57, 69.46, 55.42, 55.39; HRMS calcd for $C_{42}H_{43}O_7$ $[M + H]^+$ 659.3009, found 659.3004.

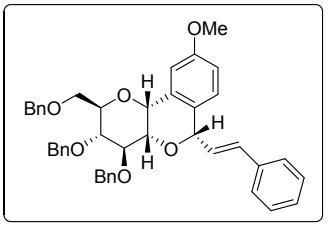
(2R,3R,4S,4aS,6S,10bR)-6-benzyl-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3f):



Following the typical procedure **B**, compound **3f** was isolated as a yellow liquid in 75% yield (178 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +49.7° (c = 0.37, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3028.99, 2860.36, 1611.03, 1453.41, 1498.01, 1090.28, 1028.02, 736.91, 697.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.10 (m, 21H), 6.99 (d, J = 2.7 Hz, 1H), 6.86 (dd, J = 8.6, 2.7 Hz, 1H), 4.85–4.80 (m, 2H), 4.69 (dd, J = 9.9, 3.0 Hz, 1H), 4.60–4.34 (m, 5H), 4.00 (t, J = 8.7 Hz, 1H), 3.92–3.83 (m, 3H), 3.79–3.65 (m, 5H), 3.43 (dd, J = 14.0, 3.0 Hz, 1H), 2.97 (dd, J = 14.0, 9.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.79, 139.06, 138.70, 138.58, 138.49, 133.85, 130.85, 129.85, 128.48, 128.43, 128.29, 128.23, 127.81, 127.76, 127.72, 127.48, 126.34, 124.72, 114.97, 114.53, 83.29, 79.45, 76.37, 75.66, 74.37,

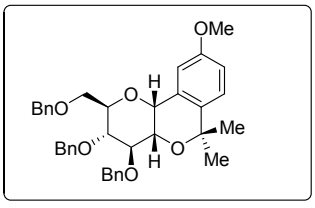
74.33, 73.52, 72.77, 70.84, 67.60, 55.39, 41.03; HRMS calcd for $C_{42}H_{46}NO_6$ $[M + NH_4]^+$ 660.3325, found 660.3323.

(2R,3R,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-((E)-styryl)-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3g):



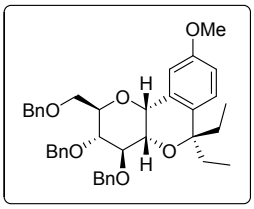
Following the typical procedure **B**, compound **3g** was isolated as a yellow liquid in 63% yield (152 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +12.28° (c = 0.35, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.12, 1608.76, 1494.05, 1460.32, 1098.57, 741.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.05 (m, 21H), 6.92 (d, J = 8.6 Hz, 1H), 6.75 (dd, J = 8.6, 2.7 Hz, 1H), 6.54 (d, J = 15.7 Hz, 1H), 6.15 (dd, J = 15.8, 7.9 Hz, 1H), 5.24 (d, J = 6.6 Hz, 1H), 5.12 (d, J = 7.8 Hz, 1H), 4.99 (d, J = 11.5 Hz, 1H), 4.91 (d, J = 11.4 Hz, 1H), 4.82 (d, J = 10.8 Hz, 1H), 4.65 (d, J = 11.9 Hz, 1H), 4.56–4.51 (m, 2H), 4.41 (dd, J = 9.2, 6.6 Hz, 1H), 3.87 (t, J = 8.9 Hz, 1H), 3.78–3.64 (m, 6H), 3.57–3.48 (m, 1H). ^{13}C NMR (100 MHz, , $CDCl_3$) δ 159.29, 138.80, 138.03, 137.98, 136.30, 133.52, 133.30, 128.96, 128.63, 128.55, 128.49, 128.46, 128.40, 128.17, 128.06, 127.99, 127.86, 127.81, 127.62, 127.33, 126.79, 114.68, 109.63, 78.64, 78.47, 75.04, 74.53, 74.25, 73.71, 73.23, 72.27, 69.44, 69.19, 55.36; ; HRMS calcd for $C_{43}H_{43}O_6$ $[M + H]^+$ 655.3060 found 655.3055.

(2R,3R,4S,4aS,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6,6-dimethyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3h):



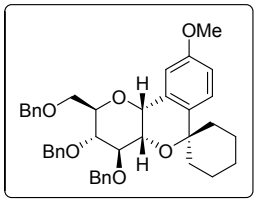
Following the typical procedure **B**, compound **3h** was isolated as a yellow liquid in 85% yield (182 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +25.87° (c = 0.16, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3030.50, 2908.18, 1613.00, 1502.75, 1454.04, 1243.49, 1114.26, 736.60, 698.02; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.19 (m, 15H), 7.05 (d, J = 8.6 Hz, 1H), 6.92 (d, J = 2.6 Hz, 1H), 6.82 (dd, J = 8.6, 2.7 Hz, 1H), 4.92–4.75 (m, 4H), 4.59–4.51 (m, 3H), 4.26–4.20 (m, 1H), 3.99–3.93 (m, 1H), 3.89–3.83 (m, 2H), 3.78–3.66 (m, 5H), 1.61 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.33, 138.82, 138.54, 138.47, 135.60, 131.85, 128.47, 128.44, 128.41, 128.13, 128.11, 127.89, 127.87, 127.79, 127.76, 127.71, 127.68, 125.79, 115.40, 112.94, 83.22, 77.41, 77.16, 76.91, 75.82, 74.60, 74.29, 74.24, 73.61, 73.34, 73.07, 70.49, 68.07, 55.35, 55.32, 30.76, 29.51; HRMS calcd for $C_{37}H_{40}NaO_6$ $[M + Na]^+$ 603.2723, found 603.2727.

(2R,3R,4S,4aS,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6,6-diethyl-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3i):



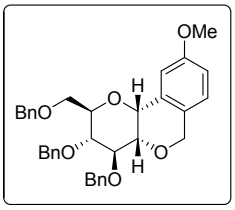
Following the typical procedure **B**, compound **3i** was isolated as a yellow liquid in 79% yield (178 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +36.29° (c = 0.28, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3030.01, 2930.66, 1611.99, 1498.01, 1453.79, 1091.66, 1028.23, 735.40, 697.50; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.12 (m, 15H), 6.97 (d, J = 8.6 Hz, 1H), 6.93 (d, J = 2.7 Hz, 1H), 6.83 (dd, J = 8.6, 2.8 Hz, 1H), 5.03–4.68 (m, 4H), 4.61–4.52 (m, 3H), 4.24–4.13 (m, 1H), 3.98 (dd, J = 8.9, 8.1 Hz, 1H), 3.94–3.83 (m, 2H), 3.80–3.64 (m, 5H), 1.99 (dd, J = 14.1, 7.2 Hz, 1H), 1.89–1.71 (m, 2H), 1.63 (dd, J = 14.5, 7.2 Hz, 1H), 0.91 (t, J = 7.4 Hz, 3H), 0.76 (t, J = 7.3 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.09, 138.63, 138.54, 138.47, 133.76, 133.32, 128.49, 128.46, 128.41, 128.02, 127.89, 127.79, 127.71, 126.09, 115.34, 113.06, 83.03, 78.78, 75.87, 74.48, 74.03, 73.51, 73.03, 72.28, 70.36, 67.85, 55.28, 32.54, 31.44, 8.42, 8.08; HRMS calcd for $C_{39}H_{45}O_6$ $[M + H]^+$ 609.3216, found 609.3219.

(2'R,3'R,4'S,4a'S,10b'R)-3',4'-bis(benzyloxy)-2'-((benzyloxy)methyl)-9'-methoxy-3',4',4a',10b'-tetrahydro-2'H-spiro[cyclohexane-1,6'-pyrano[3,2-c]isochromene] (3j):



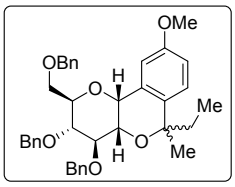
Following the typical procedure **B**, compound **3j** was isolated as a yellow liquid in 86% yield (198 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +28.24° (c = 0.25, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3030.28, 2930.22, 1611.89, 1498.21, 1453.44, 1090.61, 1118.48, 735.80, 697.78; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.20 (m, 15H), 7.08 (d, J = 8.7 Hz, 1H), 6.92 (d, J = 2.7 Hz, 1H), 6.82 (dd, J = 8.6, 2.7 Hz, 1H), 4.96–4.79 (m, 4H), 4.62–4.43 (m, 3H), 4.15 (t, J = 4.3 Hz, 1H), 4.04–3.85 (m, 3H), 3.78–3.67 (m, 5H), 2.03–1.81 (m, 4H), 1.80–1.50 (m, 4H), 1.49–1.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.16, 138.65, 138.54, 138.47, 136.05, 132.27, 128.54, 128.48, 128.45, 128.14, 128.11, 127.76, 127.70, 125.57, 115.21, 113.48, 83.56, 77.48, 77.16, 76.84, 75.64, 75.17, 74.64, 74.29, 73.82, 73.55, 72.69, 70.60, 67.88, 55.32, 38.08, 35.87, 25.66, 22.23, 21.81; HRMS calcd for $C_{40}H_{44}NaO_6$ $[M + Na]^+$ 643.3036 found 643.3033.

(2R,3R,4R,4aS,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3k):



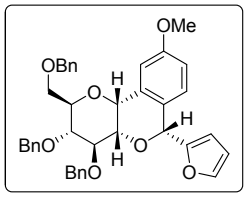
Following the typical procedure **B**, compound **3k** was isolated as a yellow liquid in 65% yield (134 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +21.42° (c = 0.21, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.22, 2904.35, 1612.38, 1500.94, 1453.46, 1092.70, 1111.99, 736.36, 697.50; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.22 (m, 13H), 7.13–7.10 (m, 2H), 7.04 (d, J = 2.4 Hz, 1H), 6.87 (d, J = 8.5 Hz, 1H), 6.77 (dd, J = 8.5, 2.6 Hz, 1H), 5.13 (d, J = 6.2 Hz, 1H), 4.92 (d, J = 11.2 Hz, 1H), 4.88–4.79 (m, 2H), 4.72–4.61 (m, 3H), 4.57–4.49 (m, 2H), 4.25 (dd, J = 8.8, 6.4 Hz, 1H), 3.81 (dd, J = 16.6, 7.9 Hz, 1H), 3.77–3.67 (m, 6H), 3.53 (ddd, J = 9.6, 4.1, 2.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.12, 138.78, 138.22, 138.18, 133.29, 128.51, 128.03, 127.98, 127.85, 127.82, 127.04, 125.15, 114.90, 110.28, 78.38, 78.09, 74.95, 74.81, 74.15, 73.74, 72.62, 69.49, 69.33, 62.63, 55.43; HRMS calcd for $C_{35}H_{36}NaO_6$ [M + Na]$^+$ 575.2410, found 575.2418.

(2R,3R,4S,4aS,10bR)-3,4-bis(benzyloxy)-2-(benzyloxymethyl)-6-ethyl-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3l):



Following the typical procedure **B**, compound **3l** was isolated as a yellow liquid in 87% yield (192 mg); R_f = 0.6 (9/1 hexane/EtOAc); IR (ν_{max}/cm^{-1}) 3062.89, 3029.91, 2924.05, 1611.03, 1497.70, 1453.94, 1092.13, 1116.21, 735.49, 697.87; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.17 (m, 17.56H), 7.03 – 6.95 (m, 2.31H), 6.83 (ddd, J = 11.3, 8.7, 2.8 Hz, 1.16H), 4.95 – 4.76 (m, 4.69H), 4.61 – 4.48 (m, 3.48H), 4.24 (dd, J = 6.6, 5.1 Hz, 1H), 3.94 – 3.74 (m, 5.70H), 3.73 (d, J = 4.8 Hz, 3.58H), 1.70 (ddt, J = 25.7, 14.2, 6.9 Hz, 2.32H), 1.58 (d, J = 9.5 Hz, 3.59H), 0.87 – 0.75 (m, 3.48H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.35, 138.86, 138.31, 134.90, 132.45, 128.50, 128.48, 128.12, 128.07, 127.92, 127.83, 127.78, 127.66, 126.18, 114.97, 111.51, 82.84, 77.48, 77.16, 77.09, 76.84, 76.27, 74.47, 73.92, 73.83, 73.66, 73.20, 70.06, 68.71, 55.34, 35.86, 28.10, 8.37; HRMS calcd for $C_{38}H_{46}NO_6$ [M + NH_4]$^+$ 612.3325, found 612.3322.

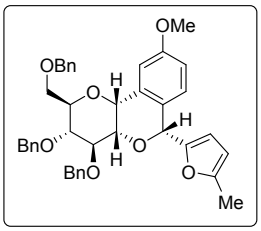
(2R,3R,4S,4aS,6R,10bR)-3,4-bis(benzyloxy)-2-(benzyloxymethyl)-6-(furan-2-yl)-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (3m):



Following the typical procedure **B**, compound **3m** was isolated as a yellow liquid in 83% yield (191 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +33.44° (c = 0.30, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.57, 2907.48, 1611, 1498.09, 1453.66, 1090.03, 1070.69, 738.52, 697.98; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 14H), 7.17 – 7.13 (m, 2H), 7.06 (d, J = 2.4 Hz, 1H), 6.82 (d, J = 8.6 Hz, 1H), 6.75 (dd, J = 8.6, 2.6 Hz, 1H), 6.32 (dd, J = 3.3, 1.9 Hz, 1H), 6.16 (d, J = 3.2 Hz, 1H), 5.72 (s, 1H), 5.22 (d, J = 6.0 Hz, 1H), 4.95 (d, J = 11.3 Hz, 1H), 4.84 (dd, J = 11.0, 8.7 Hz, 2H), 4.67 – 4.45 (m, 4H), 4.37 (dd, J = 8.2, 6.0 Hz, 1H), 3.89 (t, J = 8.5 Hz, 1H), 3.76 (dd, J = 9.6, 2.7 Hz, 2H), 3.71 (s, 3H), 3.58 (ddd, J = 9.7, 3.8, 2.5 Hz, 1H); 13C NMR (100 MHz, $CDCl_3$) δ 159.45, 153.86, 143.24, 138.66, 138.14, 138.11, 133.80, 128.54, 128.50, 128.14, 128.08, 128.03, 127.88, 127.82, 127.75, 127.20, 126.72,

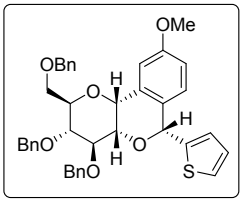
114.90, 110.40, 110.23, 109.69, 79.03, 77.62, 74.96, 74.91, 73.83, 73.72, 72.90, 69.53, 68.84, 67.99, 55.37; HRMS calcd for $C_{39}H_{42}NO_7$ $[M + NH_4]^+$ 636.2961, found 636.2962.

(2R,3R,4S,4aS,6R,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-(5-methylfuran-2-yl)-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene 3n.



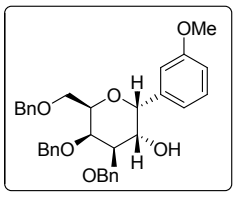
Following the typical procedure **B**, compound **3n** was isolated as a yellow liquid in 81% yield (189 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +37.27° (c = 0.37, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.92, 2921.00, 1610.75, 1498.04, 1453.65, 1112.67, 1089.77, 737.64, 697.88; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 13H), 7.15 (dd, J = 7.0, 1.9 Hz, 2H), 7.05 (d, J = 2.5 Hz, 1H), 6.85 (d, J = 8.6 Hz, 1H), 6.74 (dd, J = 8.6, 2.6 Hz, 1H), 6.02 (d, J = 3.0 Hz, 1H), 5.90 (d, J = 2.3 Hz, 1H), 5.70 (s, 1H), 5.21 (d, J = 6.0 Hz, 1H), 4.97 (d, J = 11.3 Hz, 1H), 4.84 (dd, J = 11.0, 8.2 Hz, 2H), 4.63 (d, J = 11.9 Hz, 1H), 4.55 – 4.48 (m, 2H), 4.38 (dd, J = 8.2, 6.1 Hz, 1H), 3.89 (t, J = 8.5 Hz, 1H), 3.76 (dd, J = 12.6, 5.8 Hz, 3H), 3.71 (s, 3H), 3.61 – 3.55 (m, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.40, 153.17, 151.93, 138.76, 138.20, 138.15, 133.87, 128.52, 128.38, 128.11, 128.06, 127.94, 127.89, 127.85, 127.80, 127.36, 126.98, 114.81, 110.83, 110.36, 106.23, 79.20, 77.62, 74.99, 73.88, 73.74, 72.93, 69.59, 68.94, 68.17, 55.40, 13.83; HRMS calcd for $C_{40}H_{44}NO_7$ $[M + NH_4]^+$ 650.3118, found 650.3117.

(2R,3R,4S,4aS,6R,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-(thiophen-2-yl)-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene 3o.



Following the typical procedure **B**, compound **3o** was isolated as a yellow liquid in 79% yield (186 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +22.25° (c = 0.35, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.50, 2923.19, 2855.11, 1610.25, 1497.48, 1453.52, 1090.36, 1069.82, 735.59, 696.52; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 13H), 7.17 – 7.12 (m, 2H), 7.05 (d, J = 2.5 Hz, 1H), 7.00 – 6.88 (m, 2H), 6.84 (d, J = 8.6 Hz, 1H), 6.73 (dd, J = 8.6, 2.6 Hz, 1H), 5.91 (s, 1H), 5.21 (d, J = 6.1 Hz, 1H), 5.00 – 4.94 (m, 1H), 4.84 (dd, J = 15.4, 11.1 Hz, 2H), 4.64 (d, J = 11.9 Hz, 1H), 4.52 (dd, J = 13.3, 11.5 Hz, 2H), 4.39 (dd, J = 8.5, 6.1 Hz, 1H), 3.90 (t, J = 8.4 Hz, 1H), 3.77 – 3.72 (m, 3H), 3.71 (s, 3H), 3.58 (ddd, J = 9.7, 4.0, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.41, 145.70, 138.66, 138.11, 133.32, 129.05, 128.59, 128.52, 128.42, 128.15, 128.09, 128.06, 127.96, 127.90, 127.85, 127.79, 127.00, 126.62, 126.39, 114.84, 110.10, 78.95, 77.80, 74.96, 74.91, 73.97, 73.73, 72.82, 70.10, 69.47, 68.95, 55.39; HRMS calcd for $C_{39}H_{38}NaO_6$ S $[M + Na]^+$ 657.2287, found 657.2289.

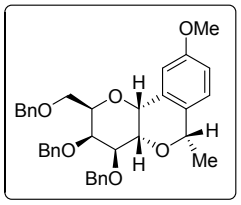
(2R,3S,4R,5S,6R)-2-(acetoxymethyl)-5-hydroxy-6-(3-methoxyphenyl)tetrahydro-2H-pyran-3,4-diyl diacetate (4):



Following the typical procedure **A**, compound **4** was isolated as a yellow liquid in 70% yield (438 mg); R_f = 0.5 (9/3 hexane/EtOAc); $[\alpha]_D^{28}$ = +25.29° (c = 0.15, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3468.79, 3029.99, 2916.01, 2865.72, 1601.29, 1454.19, 1255.34, 1108.42, 1048.25, 737.41, 698.80;

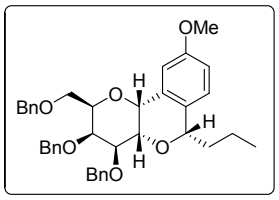
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.19 (m, 14H), 7.10–6.97 (m, 3H), 6.94–6.78 (m, 2H), 5.05 (d, *J* = 11.2 Hz, 1H), 4.67–4.26 (m, 5H), 4.08 (d, *J* = 2.8 Hz, 1H), 3.79–3.73 (m, 6H), 3.71–3.53 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.70, 142.54, 137.84, 137.69, 137.49, 129.12, 128.55, 128.49, 128.35, 128.09, 128.07, 128.03, 127.95, 127.84, 117.67, 113.03, 111.46, 79.57, 78.23, 75.76, 75.46, 74.68, 73.70, 71.88, 69.15, 55.28; HRMS calcd for $C_{27}H_{29}NaO_5$ $[M + Na]^+$ 456.1913, found 456.1911.

(2R,3S,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5a):



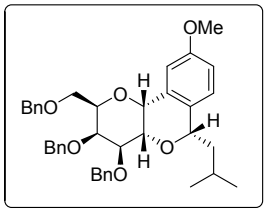
Following the typical procedure **B**, compound **5a** was isolated as a yellow liquid in 91% yield (191 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +33.94° (*c* = 0.36, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3030.01, 2870.10, 1613.51, 1503.79, 1453.70, 1240.56, 1099.81, 735.33, 697.53; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.21 (m, 15H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.91–6.88 (m, 2H), 4.79–4.59 (m, 8H), 4.40–4.35 (m, 1H), 4.25–4.12 (m, 2H), 3.96–3.85 (m, 3H), 3.74 (s, 3H), 1.55 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.43, 138.67, 138.60, 133.13, 132.24, 128.42, 128.37, 127.79, 127.61, 127.56, 127.50, 125.16, 115.33, 114.35, 77.74, 75.97, 75.35, 74.49, 73.12, 72.95, 72.83, 72.59, 66.77, 64.38, 55.34, 21.26; HRMS calcd for $C_{36}H_{38}NaO_6$ $[M + Na]^+$ 589.2566, found 589.2562.

(2R,3S,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-propyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5b):



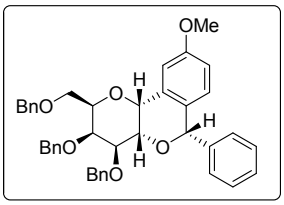
Following the typical procedure **B**, compound **5b** was isolated as a colorless liquid in 85% yield (188 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +46.59° (*c* = 0.27, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3030.53, 2957.14, 1613.97, 1503.68, 1454.17, 1258.40, 1096.03, 735.24, 697.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.22 (m, 15H), 7.06–7.01 (m, 1H), 6.87–6.85 (m, 2H), 4.80–4.56 (m, 8H), 4.40–4.32 (m, 1H), 4.26–4.09 (m, 2H), 3.93–3.88 (m, 3H), 3.76 (s, 3H), 2.71–2.07 (m, 1H), 1.84–1.70 (m, 1H), 1.58–1.42 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.31, 138.74, 138.72, 138.61, 133.56, 131.27, 128.45, 128.40, 127.83, 127.64, 127.57, 127.45, 125.11, 115.35, 114.49, 77.90, 75.79, 75.70, 75.44, 74.49, 73.20, 72.91, 66.84, 64.50, 55.39, 37.32, 18.28, 14.31; HRMS calcd for $C_{38}H_{42}NaO_6$ $[M + Na]^+$ 617.2879, found 617.2877.

(2R,3S,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6-isobutyl-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5c):



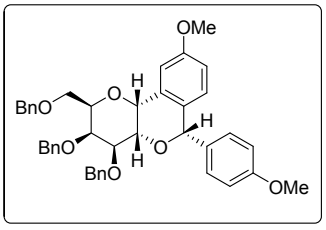
Following the typical procedure **B**, compound **5c** was isolated as a yellow liquid in 91% yield (205 mg); R_f = 0.9 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +29.24° (c = 0.20, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3030.12, 2952.90, 1613.14, 1498.28, 1453.91, 1096.51, 1028.50, 733.94, 697.22; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.25 (m, 15H), 7.03 (d, J = 8.5 Hz, 1H), 6.86–6.80 (m, 2H), 4.80–4.72 (m, 3H), 4.67–4.59 (m, 5H), 4.38–4.31 (m, 1H), 4.27–4.16 (m, 2H), 3.93– 3.85 (m, 3H), 3.75 (s, 3H), 2.21–2.05 (m, 1H), 1.86–1.70 (m, 2H), 1.02–0.93 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.34, 138.74, 138.63, 133.48, 131.84, 128.48, 128.44, 127.86, 127.73, 127.67, 127.59, 127.46, 125.04, 115.24, 114.62, 78.34, 76.32, 75.52, 74.47, 74.29, 73.27, 73.14, 72.87, 67.04, 64.79, 55.42, 44.33, 24.38, 24.22, 21.77; HRMS calcd for $C_{39}H_{48}NO_6$ $[M + NH4]^+$ 626.3482, found 626.3481.

(2R,3S,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-phenyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5d):



Following the typical procedure **B**, compound **5d** was isolated as a colorless liquid in 84% yield (196 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +34.15° (c = 0.40, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.80, 2868.41, 1610.35, 1496.94, 1454.06, 1095.47, 1028.73, 735.44, 698.46; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.12 (m, 20H), 7.05 (d, J = 2.5 Hz, 1H), 6.72–6.56 (m, 2H), 5.41 (s, 1H), 5.20 (d, J = 5.5 Hz, 1H), 4.87 (d, J = 11.6 Hz, 1H), 4.74 (d, J = 12.0 Hz, 1H), 4.69–4.49 (m, 5H), 4.04 (t, J = 2.3 Hz, 1H), 3.88–3.63 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.95, 141.89, 138.56, 138.28, 138.23, 133.71, 129.78, 128.83, 128.63, 128.50, 128.45, 128.40, 128.26, 128.10, 128.00, 127.93, 127.85, 127.78, 127.75, 114.77, 110.33, 75.41, 74.58, 74.27, 73.83, 73.61, 72.47, 71.39, 70.96, 69.04, 68.53, 55.33; HRMS calcd for $C_{41}H_{40}NaO_6$ $[M + Na]^+$ 651.2723 found 651.2725.

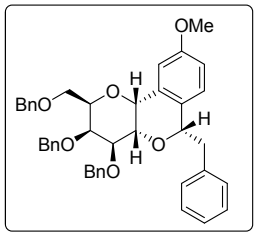
(2R,3S,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-(4-methoxyphenyl)-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5e):



Following the typical procedure **B**, compound **5e** was isolated as a yellow liquid in 85% yield (208 mg); R_f = 0.5 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +23.53° (c = 0.36, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.78,

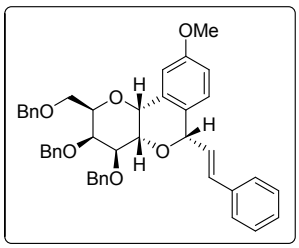
2903.03, 1611.64, 1512.98, 1498.63, 1248.10, 1094.64, 1030.11, 830.12, 734.63, 697.52; ^{1}H NMR (400 MHz, , $CDCl_3$) δ 7.4 –7.22 (m, 17H), 6.92–6.84 (m, 3H), 6.70 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.58 (d, *J* = 8.6 Hz, 1H), 5.52 (s, 1H), 4.89–4.61 (m, 7H), 4.49–4.41 (m, 1H), 4.33 (dd, *J* = 11.2, 8.5 Hz, 1H), 4.18 (dd, *J* = 5.7, 2.7 Hz, 1H), 4.10–3.98 (m, 2H), 3.90 (dd, *J* = 11.3, 3.4 Hz, 1H), 3.78 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.62, 158.58, 138.84, 138.64, 138.58, 134.25, 133.32, 131.21, 130.09, 128.49, 128.41, 127.88, 127.65, 127.60, 127.57, 127.51, 115.45, 113.99, 113.91, 79.84, 75.68, 75.49, 74.60, 73.22, 73.16, 72.50, 66.51, 63.59, 55.44, 55.39; HRMS calcd for $C_{42}H_{42}NaO_7$ $[M + Na]^+$ 681.2828, found 681.2826.

(2R,3S,4S,4aS,6S,10bR)-6-benzyl-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5f):



Following the typical procedure **B**, compound **5f** was isolated as a yellow liquid in 82% yield (196 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +32.91° (*c* = 0.24, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3062.38, 3029.58, 2867.91, 1612.60, 1497.21, 1453.80, 1256.30, 1097.72, 734.01, 698.00; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.09 (m, 21H), 6.92–6.78 (m, 2H), 4.81–4.72 (m, 2H), 4.69–4.58 (m, 4H), 4.48–4.37 (m, 2H), 4.34 (dt, *J* = 7.8, 4.8 Hz, 1H), 4.19–4.07 (m, 2H), 3.91–3.81 (m, 3H), 3.76 (s, 3H), 3.34 (dd, *J* = 14.2, 3.2 Hz, 1H), 2.97 (dd, *J* = 14.1, 9.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.59, 139.03, 138.81, 138.71, 138.63, 133.68, 130.77, 129.77, 128.47, 128.42, 128.29, 128.21, 127.82, 127.71, 127.66, 127.41, 127.32, 126.28, 125.17, 115.27, 114.84, 78.36, 76.47, 75.63, 74.55, 73.27, 73.10, 72.83, 67.08, 64.78, 55.42, 42.04; HRMS calcd for $C_{42}H_{42}NaO_6$ $[M + Na]^+$ 665.2879, found 665.2877.

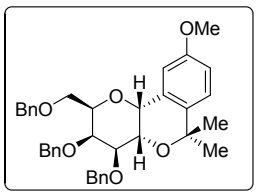
(2R,3S,4S,4aS,6S,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6-((E)-styryl)-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5g):



Following the typical procedure **B**, compound **5g** was isolated as a yellow liquid in 68% yield (165 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +18.87° (*c* = 0.37, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3028.57, 2906.47, 1606.95, 1496.50, 1453.51, 1093.78, 1028.58, 734.85, 697.12; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.23 (m, 20H), 7.02 (d, *J* = 2.5 Hz, 1H), 6.88 (d, *J* = 8.6 Hz, 1H), 6.76 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.47 (d, *J* = 15.8 Hz, 1H), 6.16 (dd, *J* = 15.8, 7.4 Hz, 1H), 5.10 (d, *J* = 5.4 Hz, 1H), 5.09–4.85 (m, 2H), 4.76 (d, *J* = 12.0 Hz, 1H), 4.65–4.48 (m, 5H), 4.03 (t, *J* = 2.4 Hz, 1H), 3.88–3.62 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.14, 138.34,

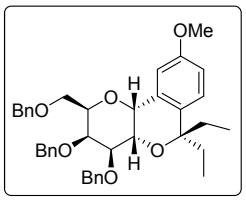
136.64, 133.46, 129.03, 128.91, 128.68, 128.52, 128.44, 128.28, 128.24, 128.01, 127.85, 127.83, 127.19, 126.84, 119.85, 114.85, 110.90, 75.51, 74.23, 73.81, 73.62, 73.28, 72.59, 71.60, 70.54, 68.93, 68.23, 55.41; HRMS calcd for $C_{43}H_{43}O_6$ $[M + H]^+$ 655.3060, found 655.3057.

(2R,3S,4S,4aS,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-6,6-dimethyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5h):



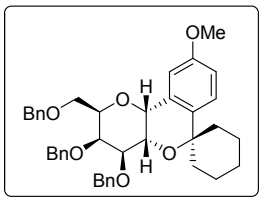
Following the typical procedure **B**, compound **5h** was isolated as a yellow liquid in 87% yield (188 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +34.78° (c = 0.28, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.87, 2931.96, 1613.20, 1498.06, 1453.77, 1242.18, 1094.21, 735.14, 697.57; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.23 (m, 15H), 7.02 (d, J = 8.6 Hz, 1H), 6.87–6.79 (m, 2H), 4.81–4.60 (m, 7H), 4.39–4.31 (m, 1H), 4.28–4.09 (m, 3H), 3.95–3.86 (m, 2H), 3.75 (s, 3H), 1.55 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.12, 138.80, 138.67, 135.72, 131.97, 128.44, 128.41, 127.84, 127.62, 127.57, 126.08, 115.70, 113.92, 75.03, 74.92, 74.56, 73.14, 73.01, 72.68, 70.00, 66.84, 64.52, 55.39, 31.13, 28.33; HRMS calcd for $C_{37}H_{40}NaO_6$ $[M + Na]^+$ 603.2723, found 603.2727.

(2R,3S,4S,4aS,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6,6-diethyl-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5i):



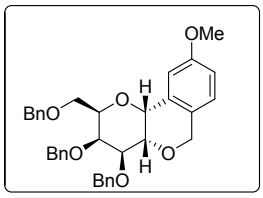
Following the typical procedure **B**, compound **5i** was isolated as a yellow liquid in 87% Yield (196 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +47.26° (c = 0.30, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 2967.85, 2932.70, 1612.55, 1497.75, 1453.72, 1241.69, 1095.12, 735.64, 697.34; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.24 (m, 15H), 6.94 (d, J= 8.6 Hz, 1H), 6.87–6.77 (m, 2H), 4.81–4.54 (m, 7H), 4.44–4.33 (m, 2H), 4.27–4.15 (dd, J = 5.3, 2.8 Hz, 1H), 3.99–3.91 (dd, J = 4.1, 1.8 Hz, 1H), 3.92–3.76 (m, 5H), 1.93 (dq, J = 14.4, 7.2 Hz, 1H), 1.81 (dq, J = 14.8, 7.4 Hz, 1H), 1.69–1.57 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H), 0.67 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.96, 138.92, 138.66, 138.60, 134.05, 133.44, 128.43, 127.93, 127.59, 126.11, 115.74, 113.94, 79.54, 74.99, 74.54, 73.21, 73.14, 72.32, 69.30, 66.38, 63.95, 55.38, 32.53, 31.92, 8.41, 8.22; HRMS calcd for $C_{39}H_{44}NaO_6$ $[M + Na]^+$ 631.3036, found 631.3036.

(2'R,3'S,4'S,4a'S,10b'R)-3',4'-bis(benzyloxy)-2'-((benzyloxy)methyl)-9'-methoxy-3',4',4a',10b'-tetrahydro-2'H-spiro[cyclohexane-1,6'-pyrano[3,2-c]isochromene] (5j):



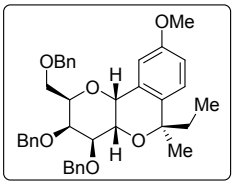
Following the typical procedure **B**, compound **5j** was isolated as a colorless liquid in 86% yield (198 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +25.47° (*c* = 0.23, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3030.00, 2931, 1612.61, 1498.12, 1453.51, 1259.75, 1095.57, 735.36, 698.03; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.24 (m, 15H), 7.04 (d, *J* = 8.6 Hz, 1H), 6.84–6.78 (m, 2H), 4.84–4.71 (m, 2H), 4.69–4.59 (m, 5H), 4.36–4.29 (m, 1H), 4.24–4.16 (m, 2H), 4.01 (dd, *J* = 4.5, 2.2 Hz, 1H), 3.90–3.83 (m, 2H), 3.75 (s, 3H), 1.95–1.70 (m, 5H), 1.64–1.49 (m, 3H), 1.40–1.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.01, 138.80, 138.65, 136.16, 132.45, 128.46, 128.42, 127.84, 127.72, 127.66, 125.93, 115.43, 114.14, 78.00, 77.48, 77.16, 76.84, 75.20, 75.14, 74.37, 73.19, 73.11, 72.87, 69.42, 66.97, 64.73, 55.38, 38.72, 34.95, 25.65, 22.17, 21.69; HRMS calcd for $C_{40}H_{44}NaO_6$ $[M + Na]^+$ 643.3036, found 643.3039.

(2R,3S,4R,4aS,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene (5k):



Following the typical procedure **B**, compound **5k** was isolated as a yellow liquid in 75% yield (154 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +32.66° (*c* = 0.36, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3028.72, 2904.35, 1612.24, 1501.35, 1453.34, 1097.43, 1028.35, 735.64, 697.62; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.24 (m, 15H), 6.96 (d, *J* = 2.5 Hz, 1H), 6.86–6.75 (m, 2H), 4.95 (d, *J* = 4.5 Hz, 1H), 4.83 (d, *J* = 11.6 Hz, 1H), 4.74 (d, *J* = 11.8 Hz, 1H), 4.65–4.53 (m, 6H), 4.30 (dd, *J* = 7.4, 4.6 Hz, 1H), 4.04 (t, *J* = 2.6 Hz, 1H), 3.96–3.87 (m, 2H), 3.79–3.69 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.88, 138.61, 138.44, 138.34, 133.22, 128.57, 128.52, 128.46, 128.05, 127.96, 127.91, 127.89, 127.80, 127.34, 125.11, 115.09, 112.03, 76.04, 74.05, 73.91, 73.51, 73.45, 73.11, 72.21, 68.34, 67.10, 64.41, 55.43; HRMS calcd for $C_{35}H_{36}NaO_6$ $[M + Na]^+$ 575.2410, found 575.2413.

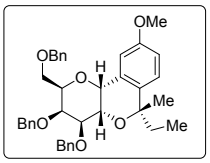
(2R,3S,4S,4aS,6R,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6-ethyl-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene 5l1:



Following the typical procedure **B**, compound **5l1**was isolated as a yellow liquid in 72% yield (158 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +33.12° (*c* = 0.35, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3028.93, 2966.90, 2928.19, 1611.28, 1497.36, 1453.06, 1094.50, 734.77, 696.95**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 15H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.84 (dt, *J* = 8.3, 2.6 Hz, 2H), 4.77 (dd, *J* = 11.6, 7.6 Hz, 2H), 4.71 (d, *J* = 2.9 Hz, 1H), 4.62 (dd, *J* = 8.1, 4.4 Hz, 4H), 4.24 (dt, *J* = 8.2, 4.3 Hz, 1H), 4.19 – 4.12 (m, 3H), 3.85 – 3.80 (m, 2H), 3.75 (s, 3H), 1.79 (dq, *J* = 14.7, 7.3 Hz, 1H), 1.65 – 1.54 (m, 1H), 1.48 (s, 3H), 0.85 (t, *J* =

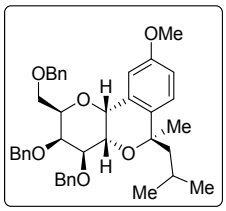
7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.14, 138.71, 138.51, 135.81, 132.33, 128.48, 128.46, 128.41, 127.88, 127.69, 126.15, 115.39, 113.16, 77.82, 77.48, 77.36, 77.16, 76.84, 76.53, 74.53, 74.31, 73.27, 73.04, 72.75, 69.80, 67.34, 65.51, 55.39, 33.82, 27.53, 8.34; HRMS calcd for $C_{38}H_{46}NO_6$ $[M + NH_4]^+$ 612.3325, found 612.3327.

(2R,3S,4S,4aS,6R,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6-ethyl-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene 5l2:



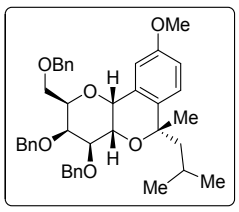
Following the typical procedure **B**, compound **5l2** was isolated as a yellow liquid in 13% yield (29 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +24.03° (c = 0.15, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.46, 2967.04, 2927.82, 1612.82, 1497.30, 1453.47, 1094.36,734.33, 696.94; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 15H), 6.96 (d, J = 8.6 Hz, 1H), 6.85 (dd, J = 8.5, 2.7 Hz, 1H), 6.77 (d, J = 2.6 Hz, 1H), 4.82 – 4.77 (m, 1H), 4.69 – 4.61 (m, 5H), 4.36 (ddd, J = 25.8, 14.1, 7.2 Hz, 2H), 4.16 – 4.13 (m, 1H), 4.02 – 3.98 (m, 1H), 3.94 – 3.90 (m, 1H), 3.85 (dd, J = 10.9, 2.4 Hz, 1H), 3.80 – 3.76 (m, 3H), 3.75 (t, J = 5.5 Hz, 1H), 1.88 – 1.77 (m, 2H), 1.38 (s, 3H), 0.71 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.01, 138.93, 138.77, 138.58, 134.09, 133.22, 128.45, 127.94, 127.90, 127.68, 127.60, 127.52, 126.06, 115.99, 114.18, 77.61, 77.48, 77.16, 76.89, 76.84, 75.20, 74.63, 73.32, 73.13, 72.25, 69.43, 66.28, 63.69, 55.42, 36.28, 27.04, 8.29; HRMS calcd for $C_{38}H_{46}NO_6$ $[M + NH_4]^+$ 612.3325, found 612.3325.

(2R,3S,4S,4aS,6R,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6-isobutyl-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene 5m1:



Following the typical procedure **B**, compound **5m1** was isolated as a colorless liquid in 71% yield (164 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +34.25° (c = 0.39, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.56, 2950.74, 2866.90, 1612.31, 1497.21, 1453.80, 1094.46, 734.05, 697.17; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (ddt, J = 12.5, 7.7, 6.3 Hz, 15H), 6.98 (d, J = 9.3 Hz, 1H), 6.85 – 6.80 (m, 2H), 4.66 (ddd, J = 15.5, 13.7, 3.6 Hz, 7H), 4.31 – 4.20 (m, 2H), 4.13 (d, J = 3.0 Hz, 2H), 3.85 – 3.79 (m, 2H), 3.76 (s, 3H), 1.89 – 1.77 (m, 1H), 1.68 (dd, J = 14.7, 7.2 Hz, 2H), 1.51 (s, 3H), 0.92 (d, J = 6.8 Hz, 3H), 0.82 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.10, 138.82, 138.65, 136.30, 132.15, 128.48, 128.45, 127.89, 127.73, 127.68, 126.47, 115.57, 113.27, 77.48, 77.35, 77.16, 76.84, 74.60, 74.27, 73.19, 72.89, 72.63, 69.19, 67.00, 64.80, 55.42, 48.91, 28.59, 25.36, 24.38, 23.90; HRMS calcd for $C_{40}H_{47}O_6$ $[M + H]^+$ 623.3373, found 623.3375.

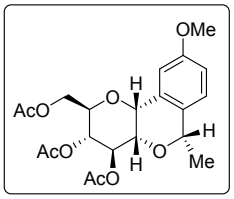
(2R,3S,4S,4aS,6R,10bR)-3,4-bis(benzyloxy)-2-((benzyloxy)methyl)-6-isobutyl-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene 5m2.



Following the typical procedure **B**, compound **5m2** was isolated as a colorless liquid in 11% yield (26 mg); R_f = 0.7 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +23.39° (c = 0.14, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 3029.57, 2950.18, 2866.18, 1613.25, 1497.38, 1453.69, 1247.05, 1095.19, 734.14, 697.13; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.25 (m, 15H), 6.94 (d, J = 8.6 Hz, 1H), 6.83 (dd, J = 8.6, 2.6 Hz, 1H), 6.76 (d, J = 2.5 Hz, 1H), 4.83 – 4.77 (m, 1H), 4.70 – 4.58 (m, 5H), 4.50 (d, J = 6.8 Hz, 1H), 4.35 (d, J = 8.1 Hz, 2H), 4.14 – 4.10 (m, 1H), 3.99 – 3.96 (m, 1H), 3.94 – 3.89 (m, 1H), 3.85 (d, J = 8.5 Hz, 1H), 3.79 (s, 3H), 1.81 (dd, J = 14.3, 4.6

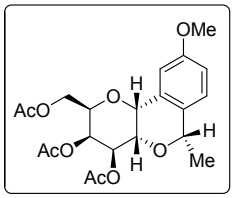
Hz, 1H), 1.68 (dd, *J* = 14.4, 6.6 Hz, 1H), 1.57 – 1.49 (m, 1H), 1.35 (s, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.63 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.98, 138.96, 138.77, 138.44, 134.42, 132.97, 128.45, 127.97, 127.91, 127.74, 127.71, 127.62, 127.54, 126.42, 115.87, 114.34, 78.25, 77.36, 76.70, 75.19, 74.15, 73.41, 73.12, 72.06, 69.37, 66.12, 63.39, 55.41, 51.75, 27.89, 24.84, 24.51, 24.32; HRMS calcd for $C_{40}H_{47}O_6$ $[M + H]^+$ 623.3373, found 623.3375.

(2R,3R,4R,4aS,6S,10bR)-2-(acetoxymethyl)-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene-3,4-diyl diacetate (7):



Following the typical procedure debezylation **C** followed acetylation **D**, compound **7** was isolated as a colorless liquid in overall 85% yield (127 mg); R_f = 0.6 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +40.46°(*c* = 0.30, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 2939.21, 2838.61, 1745.27, 1614.42, 1504.24, 1370.71, 1230.12, 1102.44, 1039.94; ^{1}H NMR (400 MHz $CDCl_3$) δ 7.08 (d, *J* = 8.6 Hz, 1H), 6.97 (d, *J* = 2.5 Hz, 1H), 6.88 (dd, *J* = 8.6, 2.6 Hz, 1H), 5.17 (t, *J* = 5.3 Hz, 1H), 4.97 (dd, *J* = 7.2, 5.6 Hz, 1H), 4.86 (d, *J* = 4.2 Hz, 1H), 4.70 (q, *J* = 6.4 Hz, 1H), 4.52 (dd, *J* = 12.7, 7.1 Hz, 1H), 4.12 – 4.01 (m 2H), 4.03 (t, *J* = 4.8 Hz, 1H), 3.82 (s, 3H), 2.12 (s, 6H), 2.05 (s, 3H), 1.56 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.91, 170.14, 169.79, 158.87, 132.30, 131.85, 125.55, 115.33, 112.80, 72.16, 71.84, 71.66, 71.16, 68.41, 66.92, 62.37, 55.45, 21.32, 21.07, 20.99, 20.95; HRMS calcd for $C_{21}H_{26}NaO_9$ $[M + Na]^+$ 445.1475, found 445.1473.

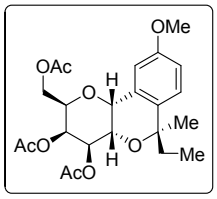
(2R,3S,4R,4aS,6S,10bR)-2-(acetoxymethyl)-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene-3,4-diyl diacetate (9):



Following the typical procedure debezylation **C** followed acetylation **D**, compound **9** was isolated as a colorless liquid in overall 86% yield (129 mg); R_f = 0.5 (9/3 hexane/EtOAc); $[\alpha]_D^{28}$ = +29.34°(*c* = 0.23, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 2933.31, 1747.58, 1371.72, 1228.43, 1041.84; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 8.6 Hz, 1H), 6.93 (d, *J* = 2.7 Hz, 1H), 6.88 (dd, *J* = 8.6, 2.6 Hz, 1H), 5.55 (dd, *J* = 5.3, 3.2 Hz, 1H), 5.26 (dd, *J* = 5.4, 3.3 Hz, 1H), 4.99 (dd, *J* = 12.1, 9.1 Hz, 1H), 4.87 (d, *J* = 2.7 Hz, 1H), 4.76 (q, *J* = 6.5 Hz, 1H), 4.29 (ddd, *J* = 9.0, 5.2, 3.9 Hz, 1H), 4.04 (dd, *J* = 12.0, 3.6 Hz, 1H), 3.98 (dd, *J* = 5.4, 2.8 Hz, 1H), 3.82 (s, 3H), 2.13 (s, 3H), 2.12 (s, 3H), 2.10 (s, 3H), 1.54 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.16, 169.94, 169.78, 158.72, 131.88, 131.85, 125.67, 115.78, 113.43, 77.48, 77.16, 76.84, 72.44,

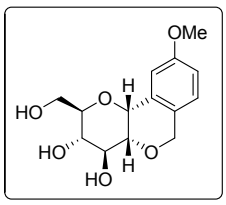
72.25, 72.19, 70.14, 66.79, 65.00, 60.30, 55.42, 21.68, 21.10, 20.89; HRMS calcd for $C_{21}H_{30}NO_9$ [M + NH4]$^+$ 440.1921, found 440.1924.

(2R,3S,4R,4aS,10bR)-2-(acetoxymethyl)-6-isobutyl-9-methoxy-6-methyl-2,3,4,4a,6,10b-hexahydropyrano[3,2-c]isochromene-3,4-diyl diacetate (10):



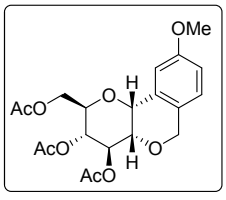
Following the typical procedure debezylation **C** followed acetylation **D**, compound **10** was isolated as a yellow liquid in 84% yield (127 mg); R_f = 0.4 (9/1 hexane/EtOAc); $[\alpha]_D^{28}$ = +28.78° (c = 0.35, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 2971.53, 2937.85, 1747.74, 1372.60, 1236.69, 1085.69; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (dd, J = 12.3, 5.6 Hz, 2H), 6.91 – 6.84 (m, 1H), 5.39 (t, J = 2.9 Hz, 1H), 5.09 – 5.00 (m, 2H), 4.51 (dd, J = 13.1, 9.3 Hz, 1H), 4.39 (dd, J = 8.9, 5.2 Hz, 1H), 4.08 – 4.02 (m, 2H), 3.84 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H), 1.69 (dd, J = 8.9, 7.4 Hz, 2H), 1.45 (s, 3H), 0.71 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.79, 170.49, 170.19, 158.56, 133.93, 131.54, 126.82, 115.39, 110.28, 77.48, 77.16, 76.84, 76.72, 69.78, 69.69, 68.42, 67.80, 67.54, 61.74, 55.37, 37.51, 28.65, 20.94, 20.82, 8.03; HRMS calcd for $C_{23}H_{34}NO_9$ [M + NH_4]$^+$ 468.2234, found 468.2232.

(2R,3S,4S,4aR,10bR)-2-(hydroxymethyl)-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano-[3,2-c]isochromene-3,4-diol (11):



Following the typical procedure debenzylation **C**, compound **11** was isolated as a white solid in 96% yield (98 mg); R_f = 0.0 (9/3 hexane/EtOAc); IR (ν_{max}/cm^{-1}) 3390.32, 2924.43, 2854.02, 1613.10, 1503.42, 1101.86, 1074.32, 1101.86; ^{1}H NMR (400 MHz, D_2O) δ 7.10–7.01 (m, 2H), 6.89 (dd, J = 8.6, 2.6 Hz, 1H), 5.08 (d, J = 6.3 Hz, 1H), 4.87 (s, 1H), 4.69 (d, J = 15.6 Hz, 1H), 4.03 (dd, J = 9.5, 6.3 Hz, 1H), 3.86–3.71 (m, 6H), 3.46 (t, J = 9.4 Hz, 1H), 3.32–3.19 (m, 1H); ^{13}C NMR (100 MHz, D_2O) δ 158.19, 132.29, 127.04, 125.70, 114.66, 110.03, 74.37, 73.53, 69.88, 68.98, 68.69, 61.43, 60.95, 55.38; HRMS calcd for $C_{14}H_{22}NO_6$ [M + NH4]$^+$ 300.1447, found 300.1445.

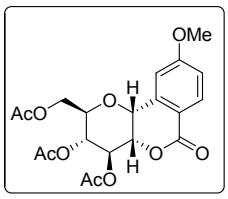
(2R,3R,4R,4aS,10bR)-2-(acetoxymethyl)-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano-[3,2-c]isochromene-3,4-diyl diacetate (12):



Following the typical procedure acetylation **D**, compound **12** was isolated as a colorless liquid in 95% yield (138 mg); R_f = 0.5 (9/3 hexane/EtOAc); $[\alpha]_D^{28}$ = +18.49° (c = 0.33, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 2925.17, 2853.70, 1746.14, 1614.34, 1503.97, 1238.56, 1042.27; ^{1}H NMR (500 MHz $CDCl_3$) δ 7.05–6.94 (m, 2H), 6.86 (dd, J = 8.5, 2.1 Hz, 1H), 5.33 (t, J = 9.4 Hz, 1H), 5.22 (d, J = 6.6 Hz, 1H), 5.07 (t, J = 9.5 Hz, 1H), 4.91 (d, J = 15.5 Hz, 1H), 4.64 (d, J = 15.6 Hz, 1H), 4.31–4.23 (m, 2H), 4.10 (dd, J = 12.0, 1.3 Hz, 1H), 3.80 (d, J = 10.6 Hz, 3H), 3.70–3.64 (m,

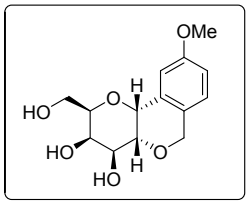
1H), 2.15–2.02 (m, 6H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.69, 170.52, 169.61, 159.13, 131.60, 127.07, 125.69, 114.93, 109.68, 71.58, 69.50, 69.42, 69.12, 68.76, 62.57, 62.16, 55.35, 20.93, 20.82, 20.64; HRMS calcd for $C_{20}H_{24}NaO_9$ $[M + Na]^+$ 431.1318, found 431.1314.

(2R,3R,4R,4aS,10bR)-2-(acetoxymethyl)-9-methoxy-6-oxo-2,3,4,4a,6,10b-hexahydro-pyrano[3,2-c]isochromene-3,4-diyl diacetate (13):



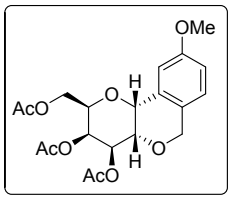
Following the typical oxidation procedure **E**, compound **13** was isolated as a white solid in 70% yield (146 mg); R_f = 0.4(9/3 hexane/EtOAc); $[\alpha]_D^{28}$ = +18.49° (*c* = 0.33, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 2947.44, 1746.85, 1732.16, 1606.54, 1376.69, 1228.47, 1096.71, 1037.16; ^{1}H NMR (500 MHz $CDCl_3$) δ 8.13 (d, *J* = 8.7 Hz, 1H), 7.05–6.94 (m, 2H), 5.54 (d, *J* = 6.6 Hz, 1H), 5.23 (t, *J* = 9.6 Hz, 1H), 5.06 (t, *J* = 9.5 Hz, 1H), 4.72 (dd, *J* = 9.8, 6.6 Hz, 1H), 4.33 (dd, *J* = 12.3, 5.5 Hz, 1H), 4.16 (dd, *J* = 12.2, 2.4 Hz, 1H), 3.92 (s, 3H), 3.89 (ddd, *J* = 9.6, 5.5, 2.4 Hz, 1H), 2.15 (s, 3H), 2.10 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz $CDCl_3$) δ 170.64, 170.18, 169.49, 165.01, 161.38, 138.10, 134.05, 116.71, 115.16, 109.85, 75.46, 71.02, 70.57, 68.64, 68.23, 62.35, 55.82, 20.85, 20.79, 20.62; HRMS calcd for $C_{20}H_{23}O_{10}$ $[M + H]^+$ 423.1291, found 423.1295.

(2R,3R,4S,4aR,10bR)-2-(hydroxymethyl)-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano-[3,2-c]isochromene-3,4-diol (14):



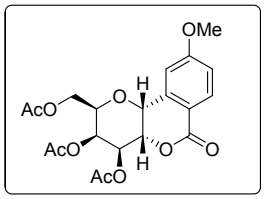
Following the typical procedure debenzylation **C**, compound **14** was isolated as a white solid in 93% yield (95 mg); R_f = 0.0 (9/3 hexane/EtOAc); IR (ν_{max}/cm^{-1}) 3373.57, 2920.83, 2850.98, 1737.47, 1607.78, 1502.35, 1464.07, 1258.13, 1083.47; ^{1}H NMR (500 MHz, D_2O) δ 7.08 (, 2H), 6.90 (dd, *J* = 8.5, 2.6 Hz, 1H), 5.12 (d, *J* = 6.2 Hz, 1H), 4.83 (d, *J* = 15.6 Hz, 1H), 4.70 (d, *J* = 15.6 Hz, 1H), 4.27 (dd, *J* = 9.8, 6.3 Hz, 1H), 3.91–3.75 (m, 6H), 3.68 (dd, *J* = 12.0, 3.8 Hz, 1H), 3.47 (dd, *J* = 8.4, 3.2 Hz, 1H). ^{13}C NMR (100 MHz, D_2O) δ 160.02, 134.22, 129.07, 127.52, 116.63, 112.10, 75.42, 75.35, 72.95, 72.92, 71.27, 71.21, 70.50, 70.46, 67.44, 63.29, 63.21, 63.18, 57.27; HRMS calcd for $C_{14}H_{18}NaO_6$ $[M + Na]^+$ 305.1001, found 305.1009.

(2R,3S,4R,4aS,10bR)-2-(acetoxymethyl)-9-methoxy-2,3,4,4a,6,10b-hexahydropyrano-[3,2-c]isochromene-3,4-diyl diacetate (15):



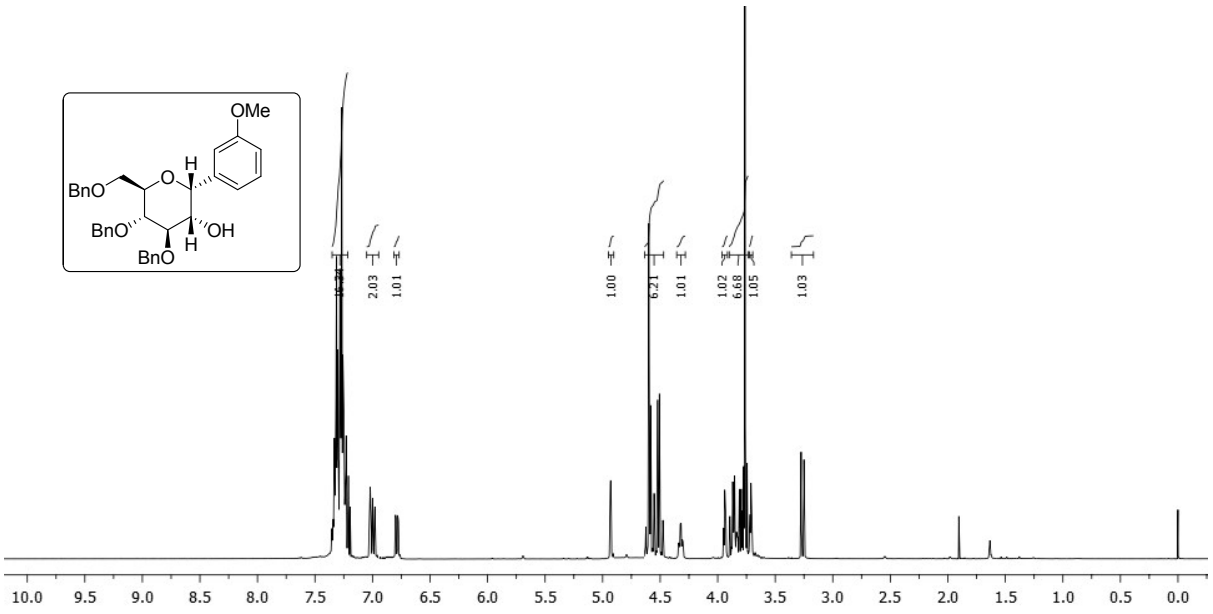
Following the typical procedure acetylation **D**, compound **15** was isolated as a colorless liquid in 95% yield (138 mg); R_f = 0.5 (9/3 hexane/EtOAc); $[\alpha]_D^{28}$ = +24.75° (c = 0.39, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 2955.46, 2840.02, 1747.39, 1613.83, 1503.52, 1373.77, 1235.41, 1104.86, 1087.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, J = 2.5 Hz, 1H), 6.95 (d, J = 8.5 Hz, 1H), 6.85 (dd, J = 8.5, 2.6 Hz, 1H), 5.35 (dd, J = 3.5, 1.7 Hz, 1H), 5.29–5.18 (m, 2H), 4.74–4.68 (m, 2H), 4.42 (dd, J = 9.9, 6.1 Hz, 1H), 4.28 (dd, J = 11.4, 7.4 Hz, 1H), 4.07 (dd, J = 11.5, 5.4 Hz, 1H), 3.93–3.81 (m, 4H), 2.17 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.62, 170.49, 170.34, 159.20, 131.81, 126.91, 125.63, 115.09, 110.30, 69.12, 69.04, 68.76, 68.26, 66.45, 62.45, 62.20, 55.42, 21.00, 20.86; HRMS calcd for $C_{20}H_{28}NO_9$ $[M + NH_4]^+$ 426.1764, found 426.1769.

(2R,3S,4R,4aS,10bR)-2-(acetoxymethyl)-9-methoxy-6-oxo-2,3,4,4a,6,10b-hexahydro-pyrano[3,2-c]isochromene-3,4-diyl diacetate (16):

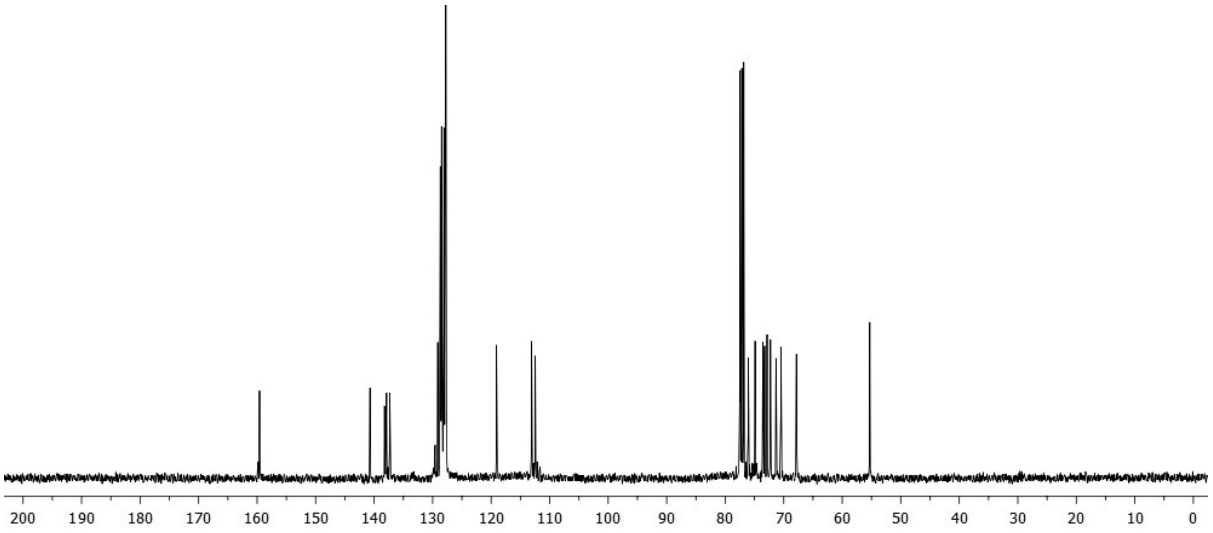


Following the typical oxidation procedure **E**, compound **16** was isolated as a yellow liquid in 74% yield (153 mg); R_f = 0.4 (9/3 hexane/EtOAc); $[\alpha]_D^{28}$ = +30.91° (c = 0.24, CH_2Cl_2); IR (ν_{max}/cm^{-1}) 2923.20, 1747.63, 1605.70, 1373.52, 1234.17, 1086.01; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15–8.01 (m, 1H), 7.71–6.67 (m, 2H), 5.56 (d, J = 6.4 Hz, 1H), 5.37 (d, J = 3.2 Hz, 1H), 5.11 (dd, J = 10.1, 3.3 Hz, 1H), 4.95 (dd, J = 10.1, 6.4 Hz, 1H), 4.34 (td, J = 9.8, 4.6 Hz, 1H), 4.11–4.03 (m, 2H), 3.93 (s, 3H), 2.19 (s, 3H), 2.10 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.52, 169.98, 164.98, 161.62, 138.18, 133.78, 116.54, 115.33, 109.91, 77.42, 77.10, 76.78, 73.02, 69.50, 68.79, 68.53, 67.89, 61.95, 55.78, 20.79; HRMS calcd for $C_{20}H_{23}O_{10}$ $[M + H]^+$ 423.1291, found 423.1298.

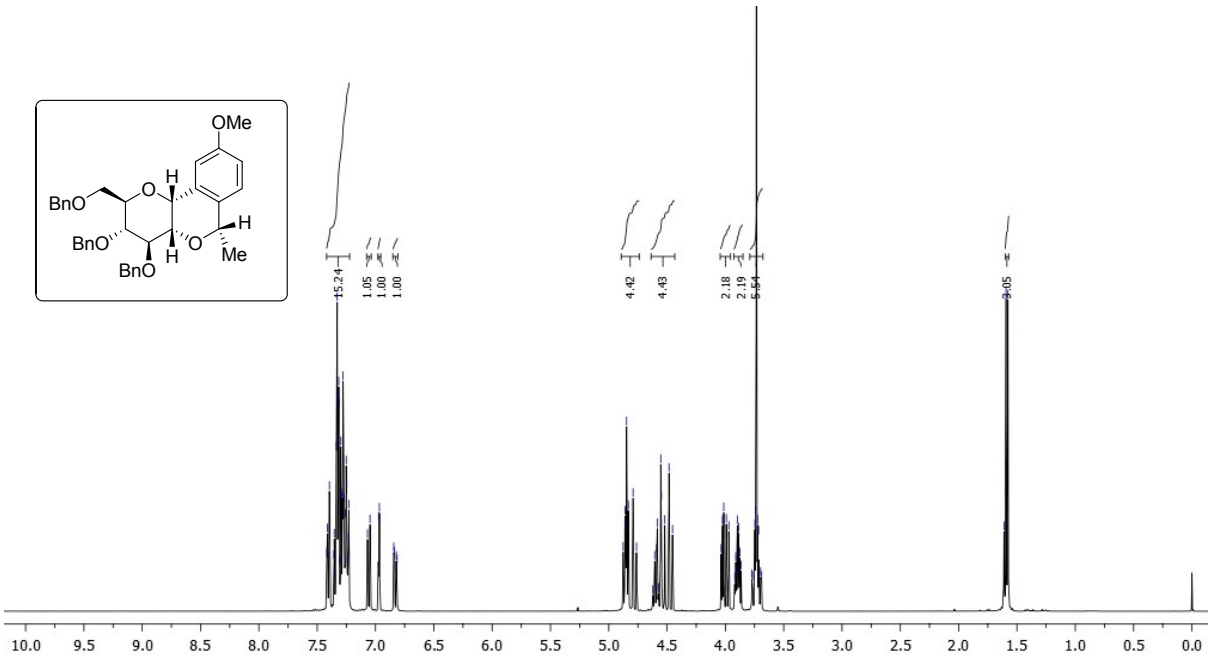
4. NMR Spectra



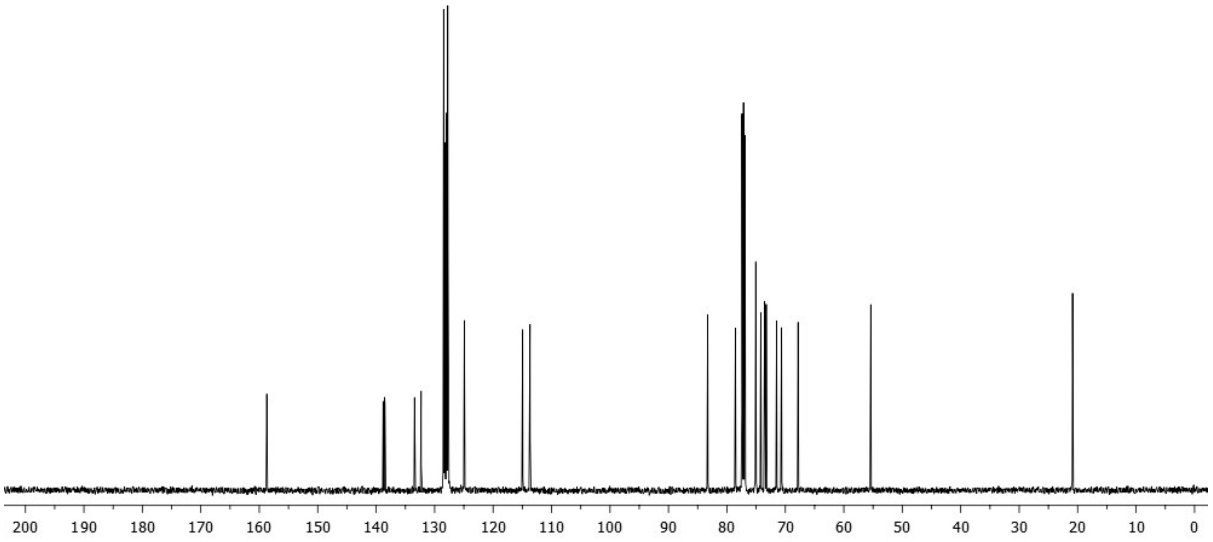
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **1**



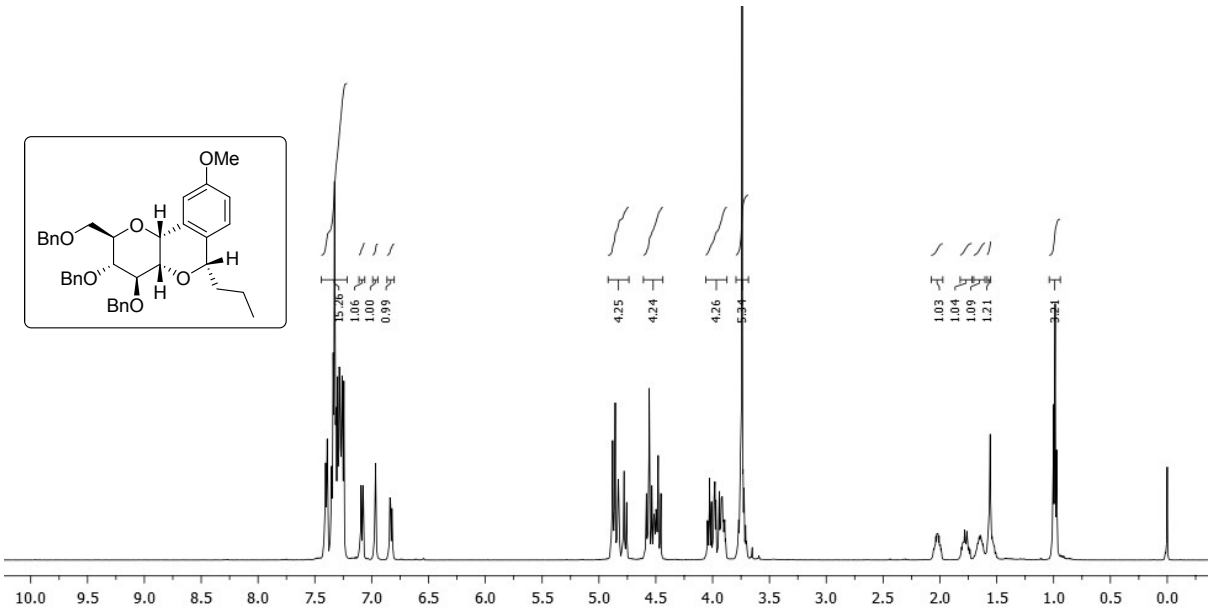
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **1**



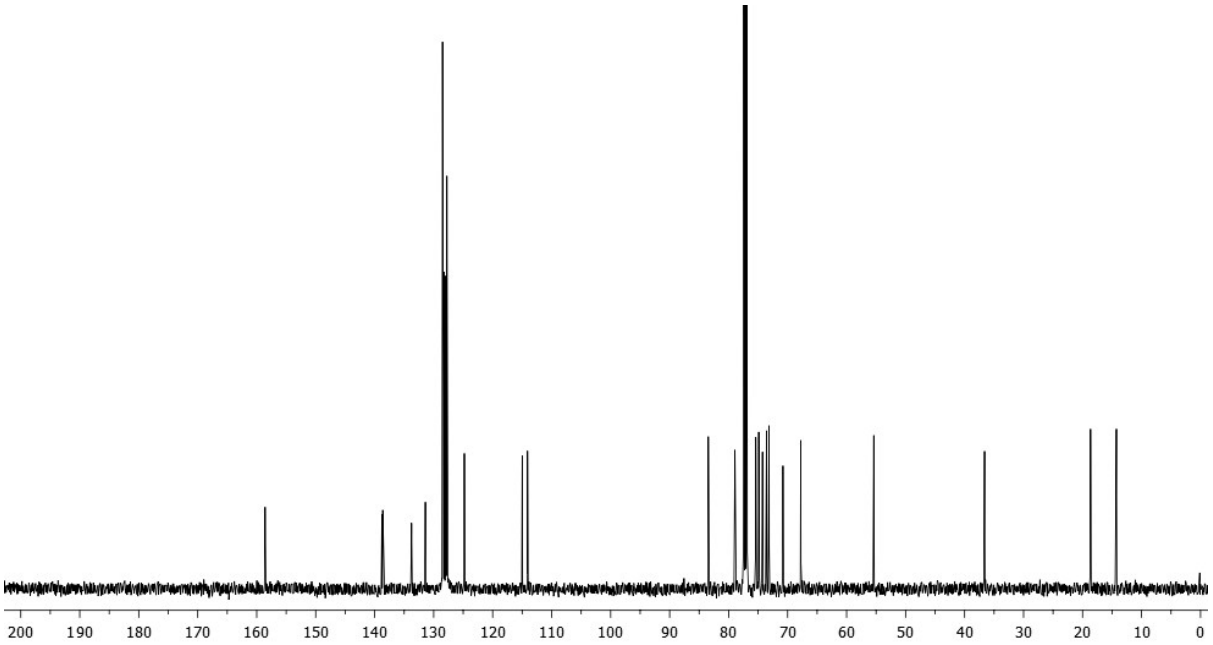
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3a**



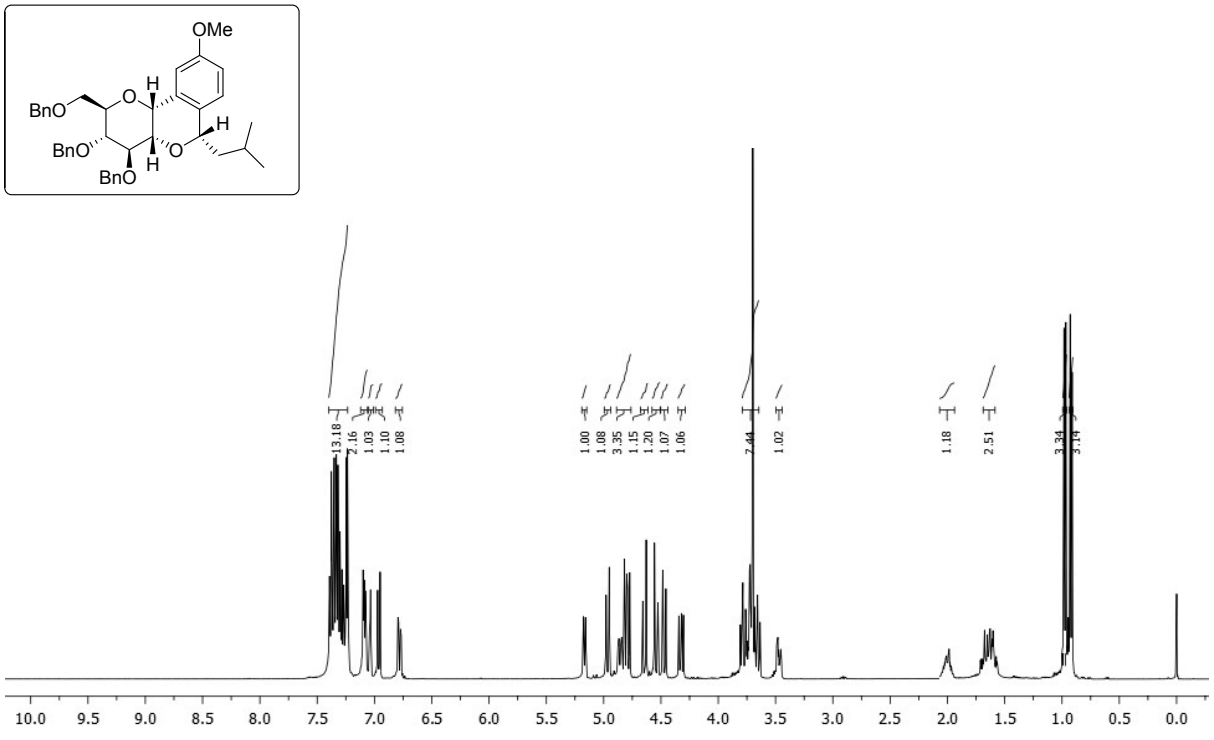
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of compound **3a**



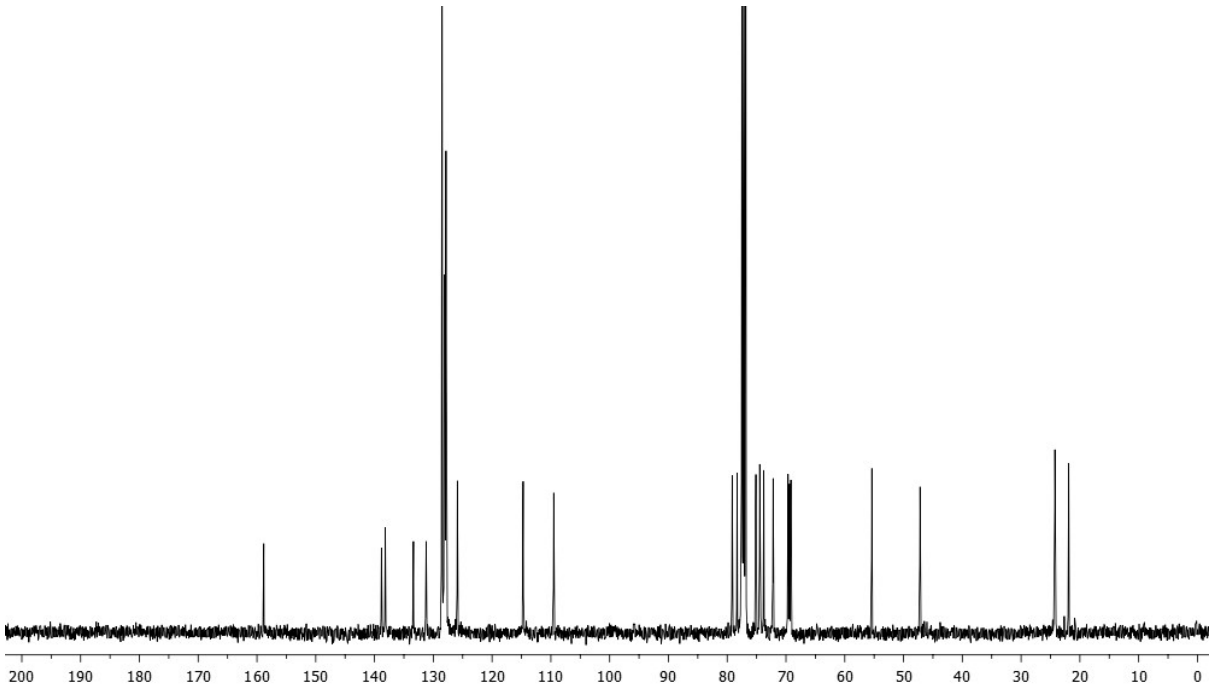
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **3b**



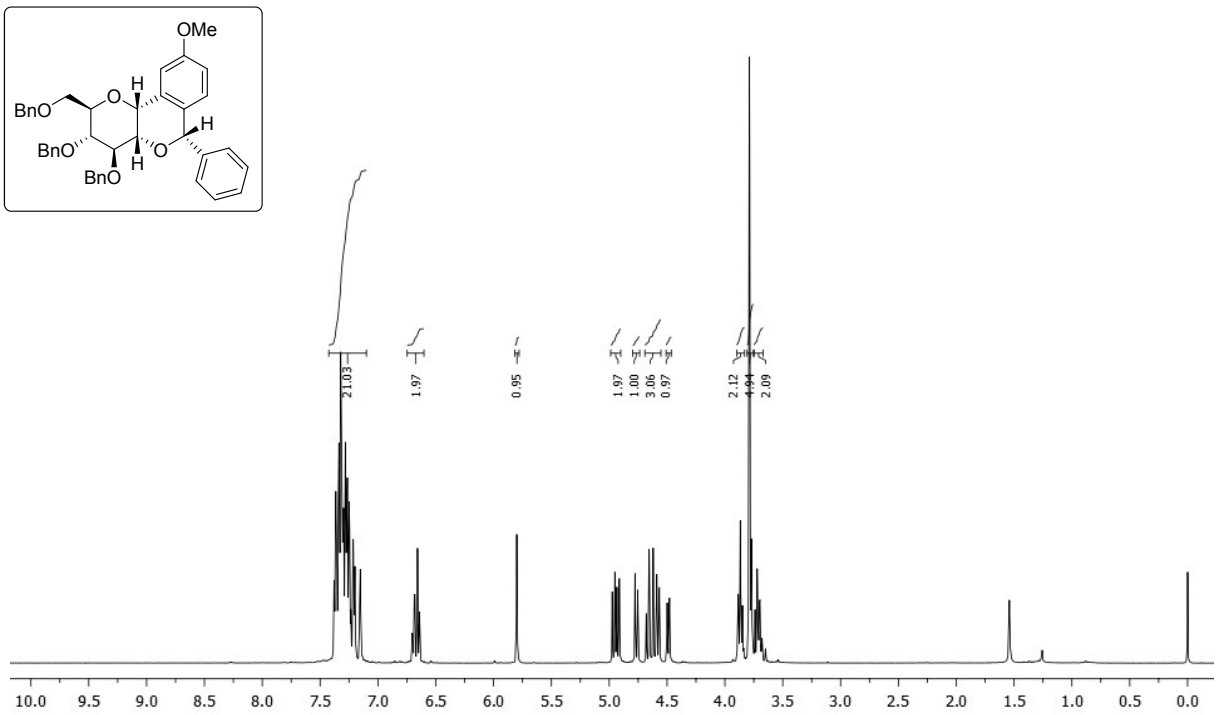
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of compound **3b**



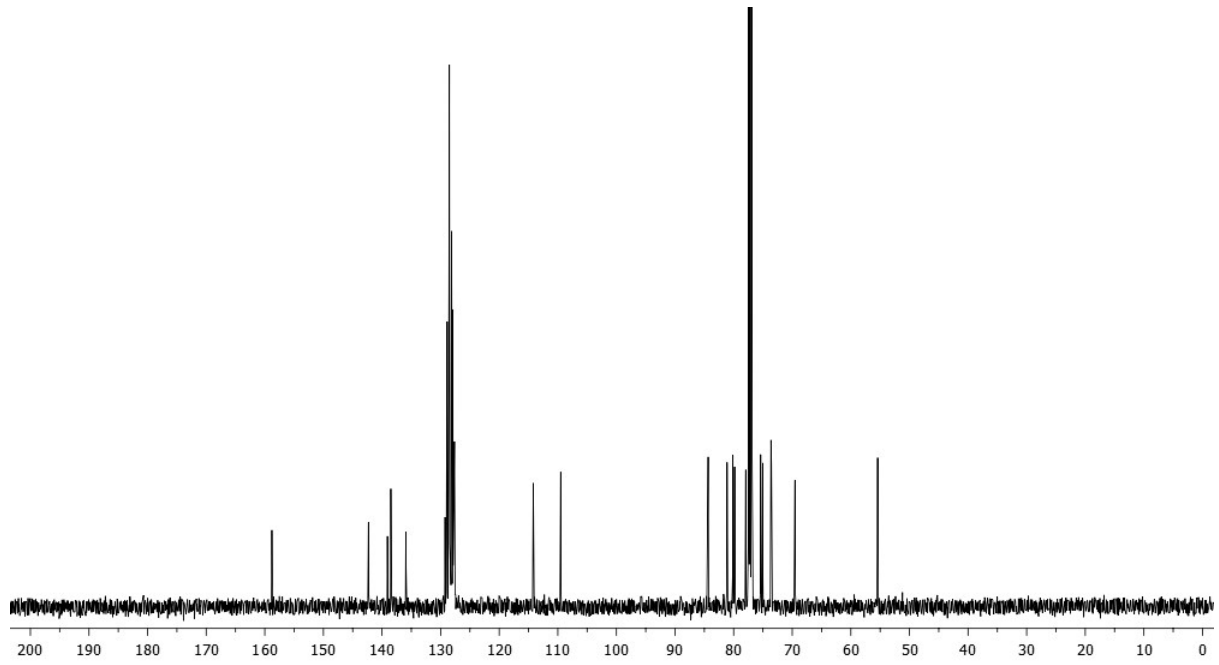
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3c**



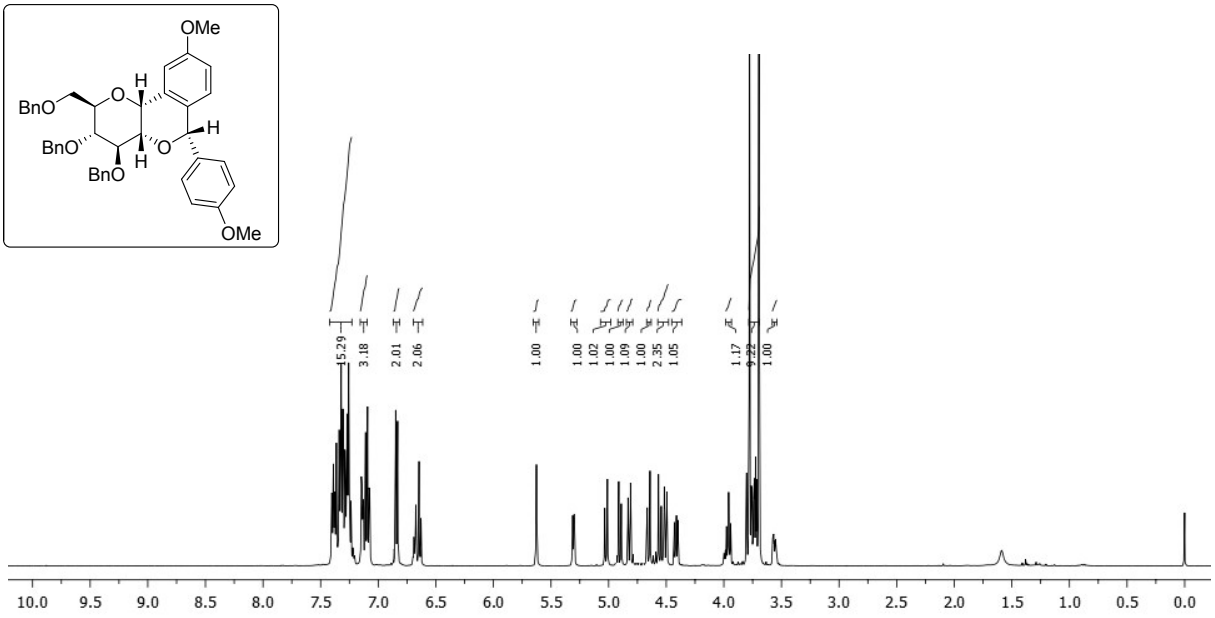
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3c**



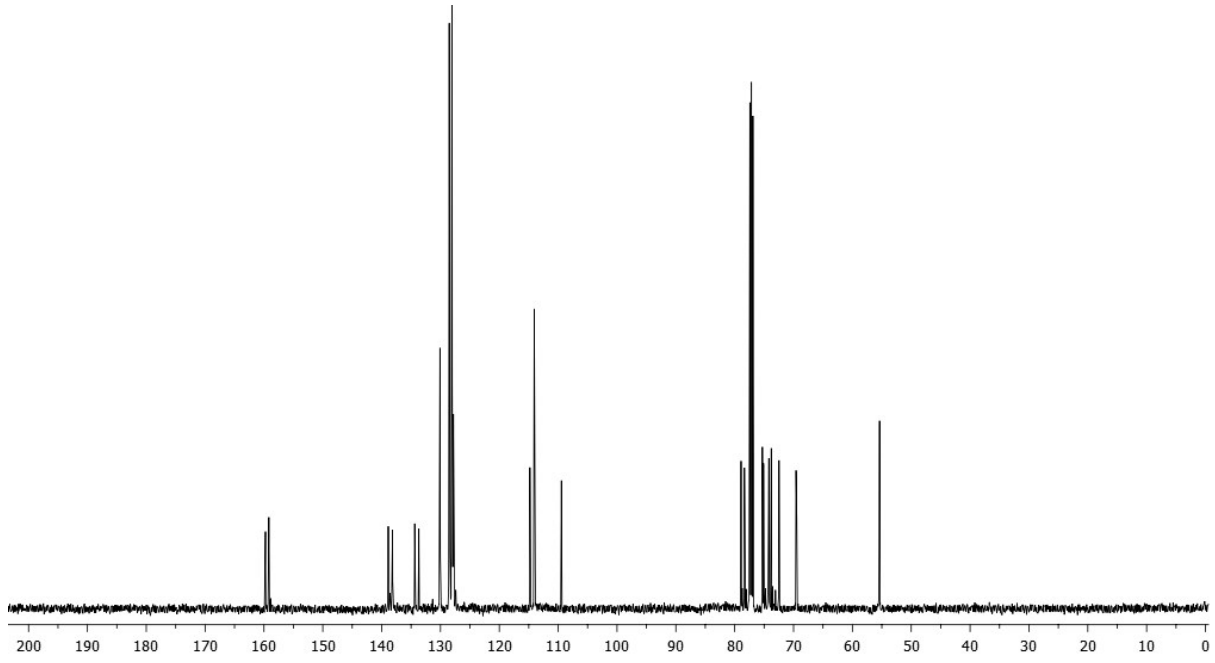
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **3d**



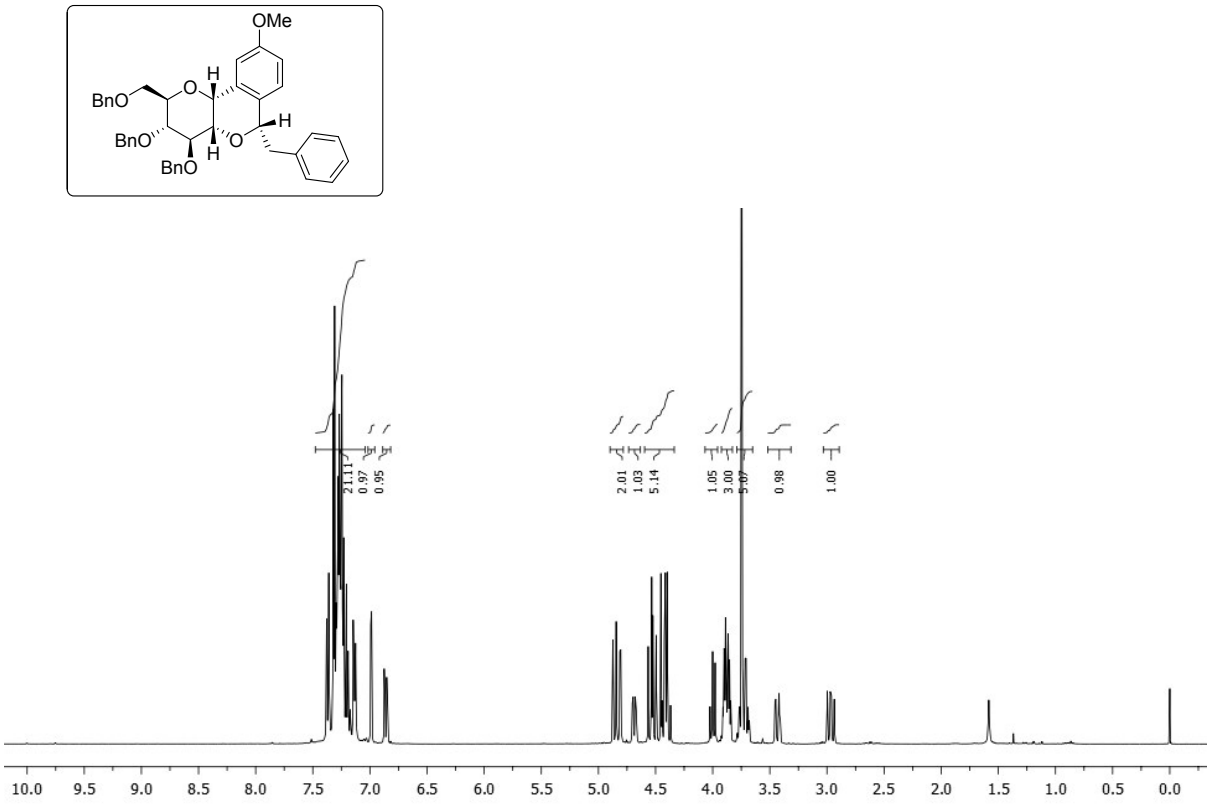
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of compound **3d**



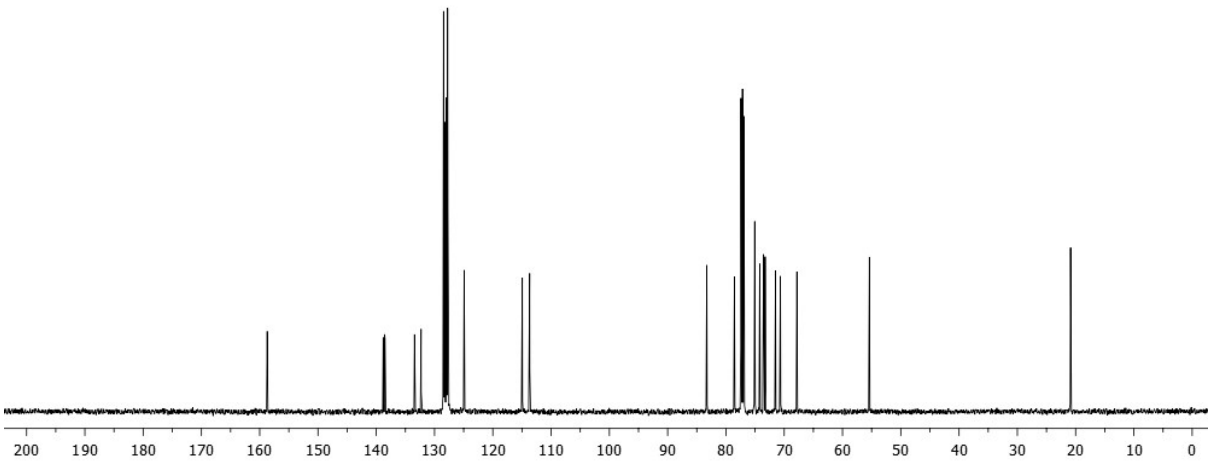
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **3e**



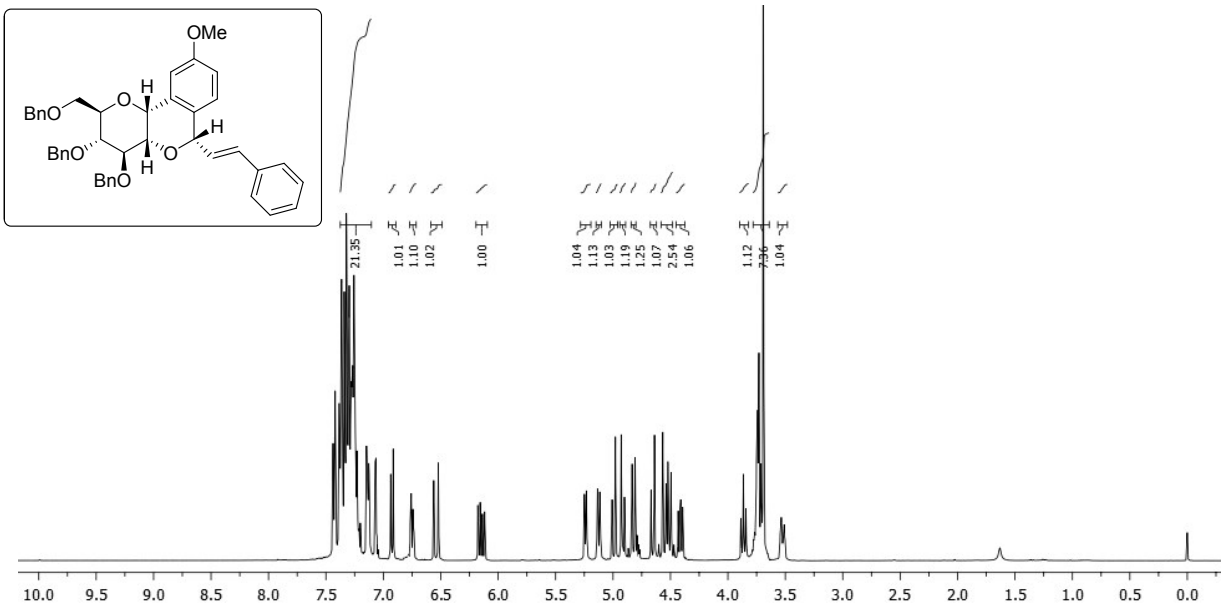
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of compound **3e**



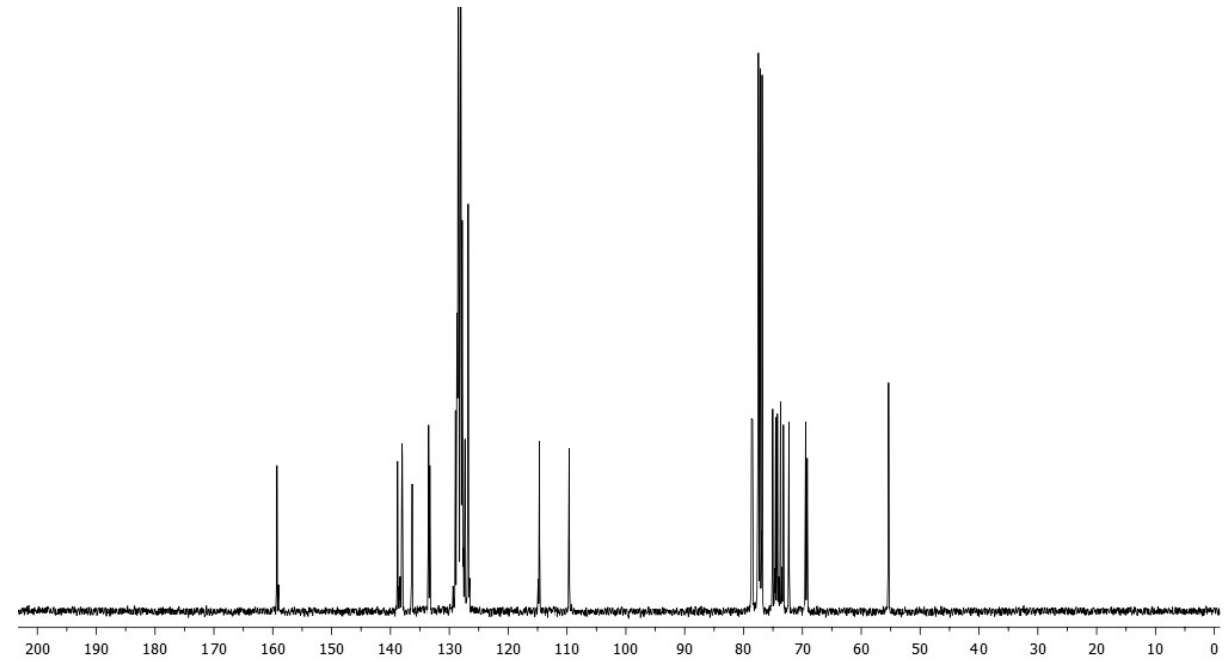
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3f**



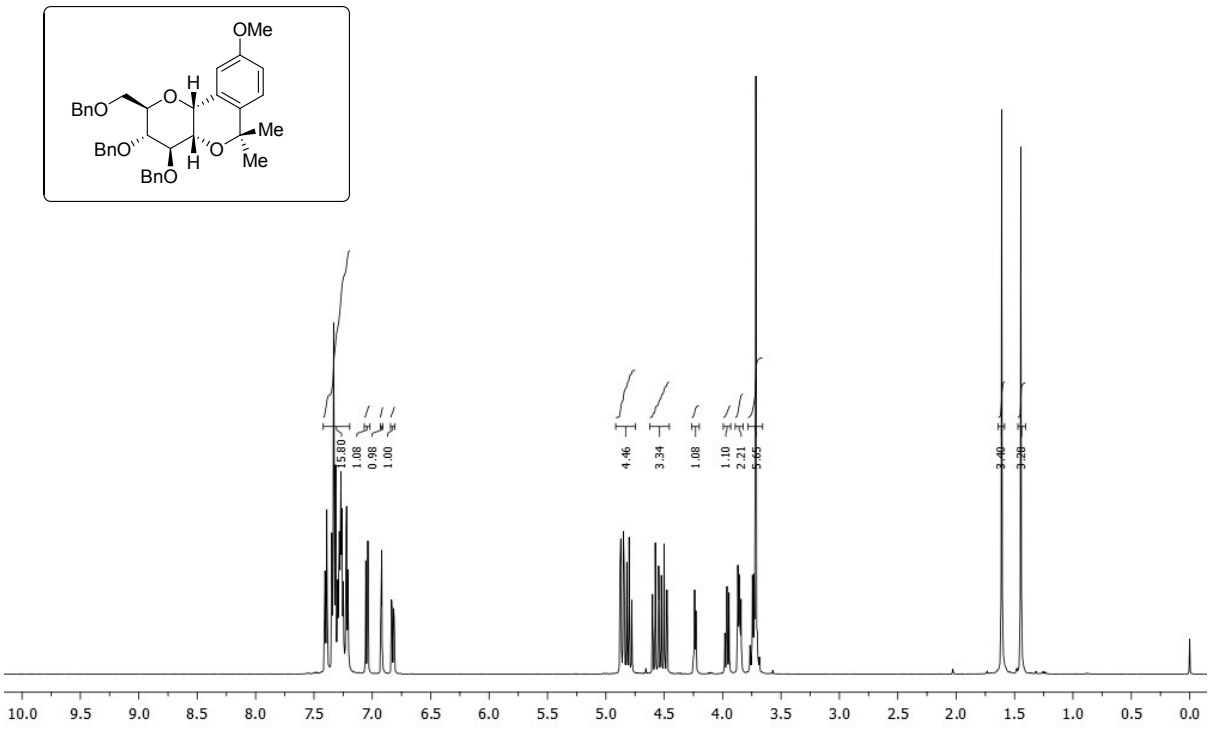
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3f**



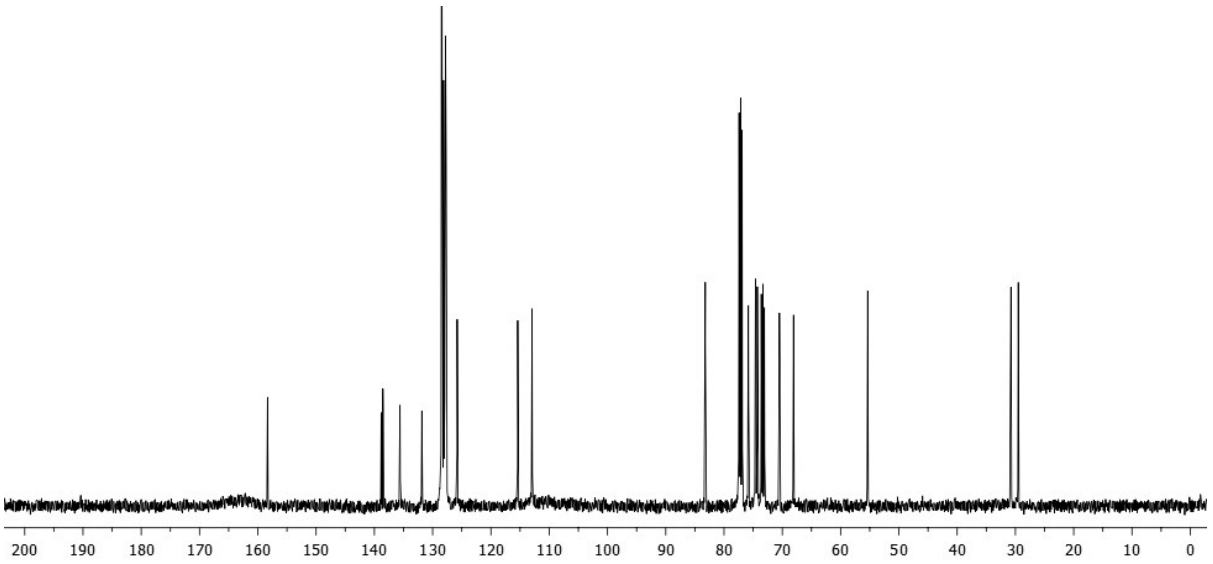
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3g**



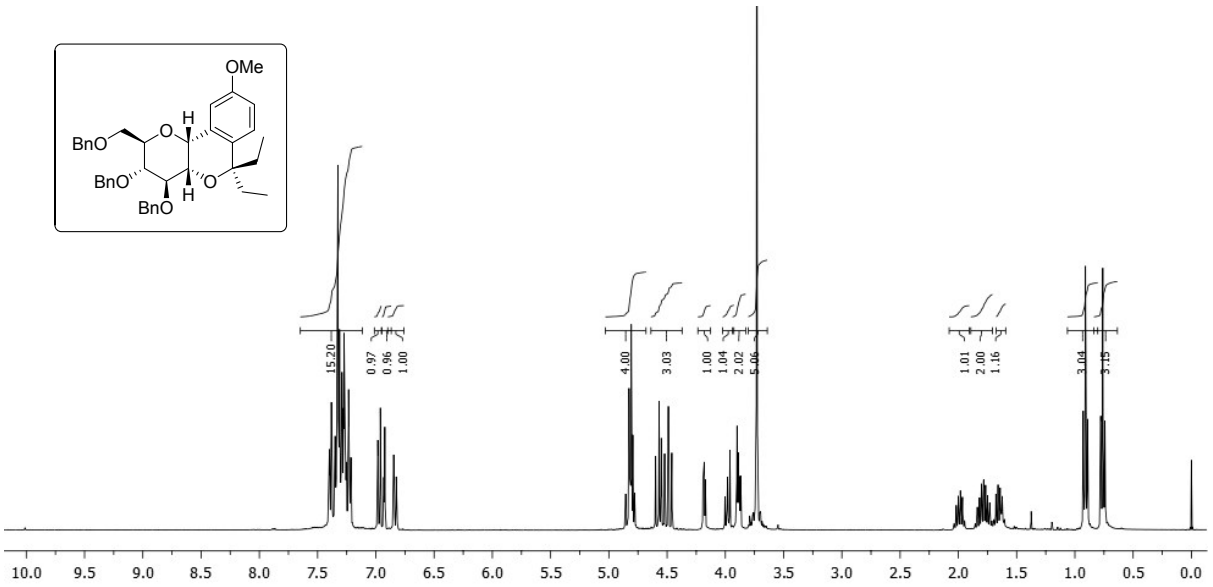
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3g**



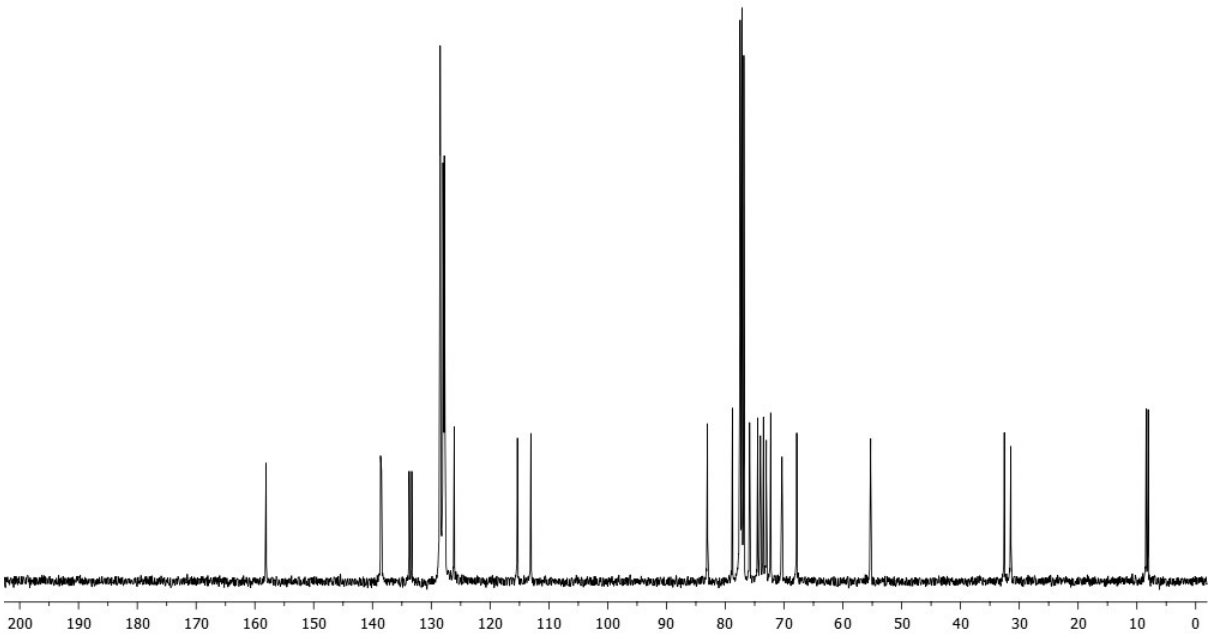
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **3h**



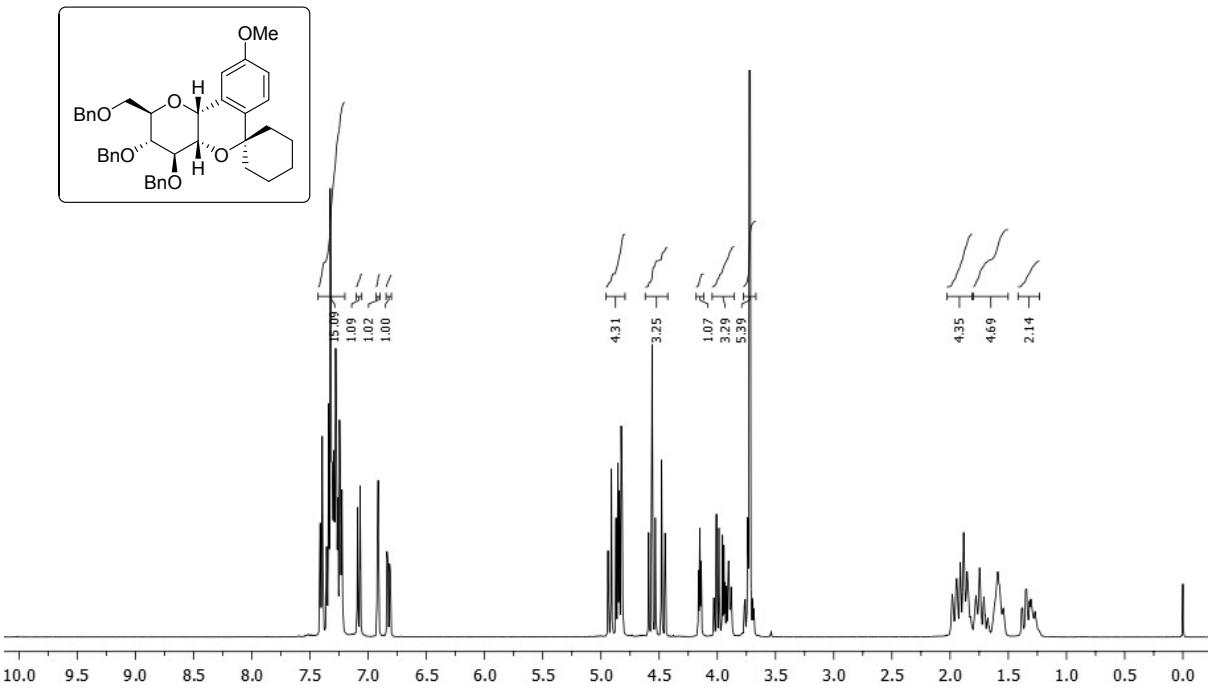
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of compound **3h**



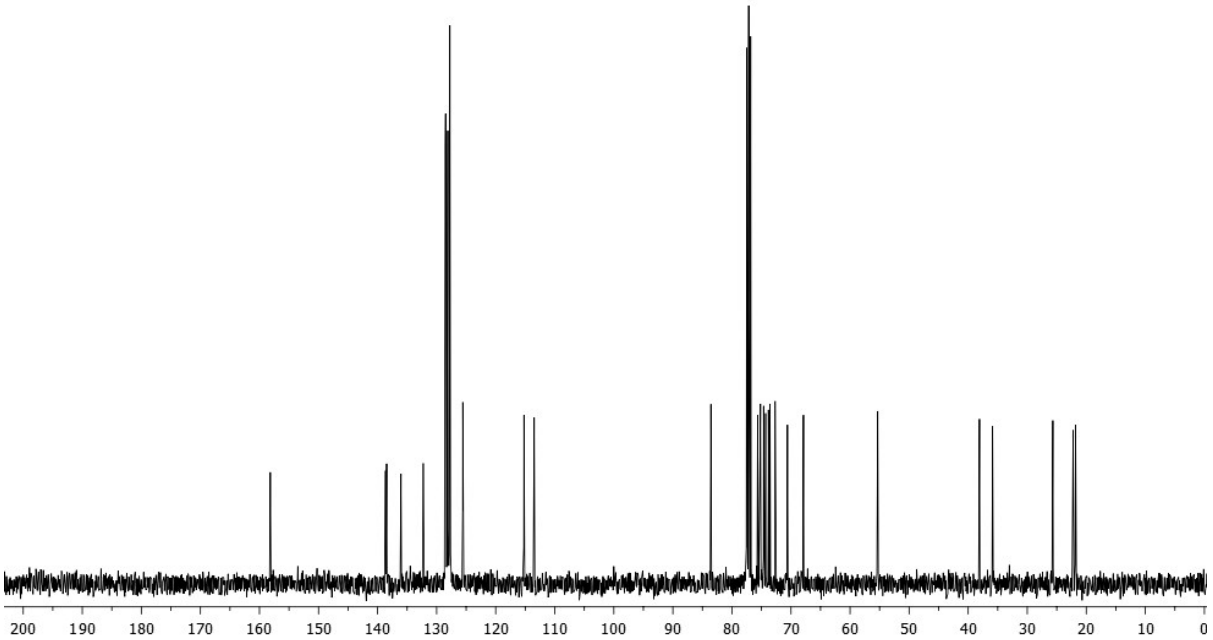
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3i**



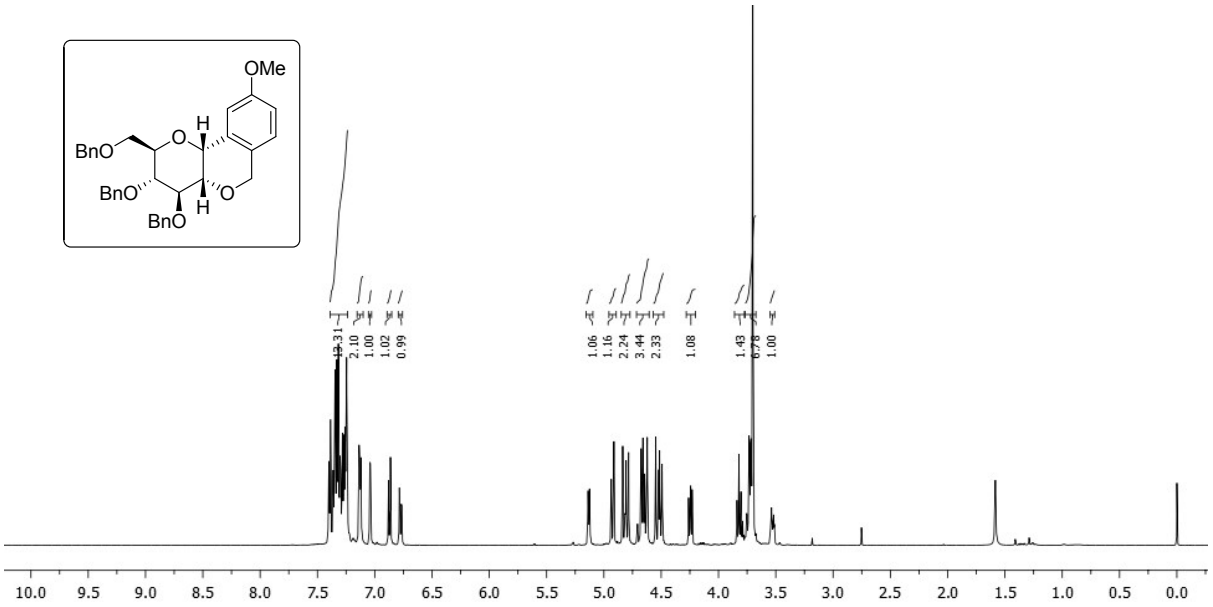
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3i**



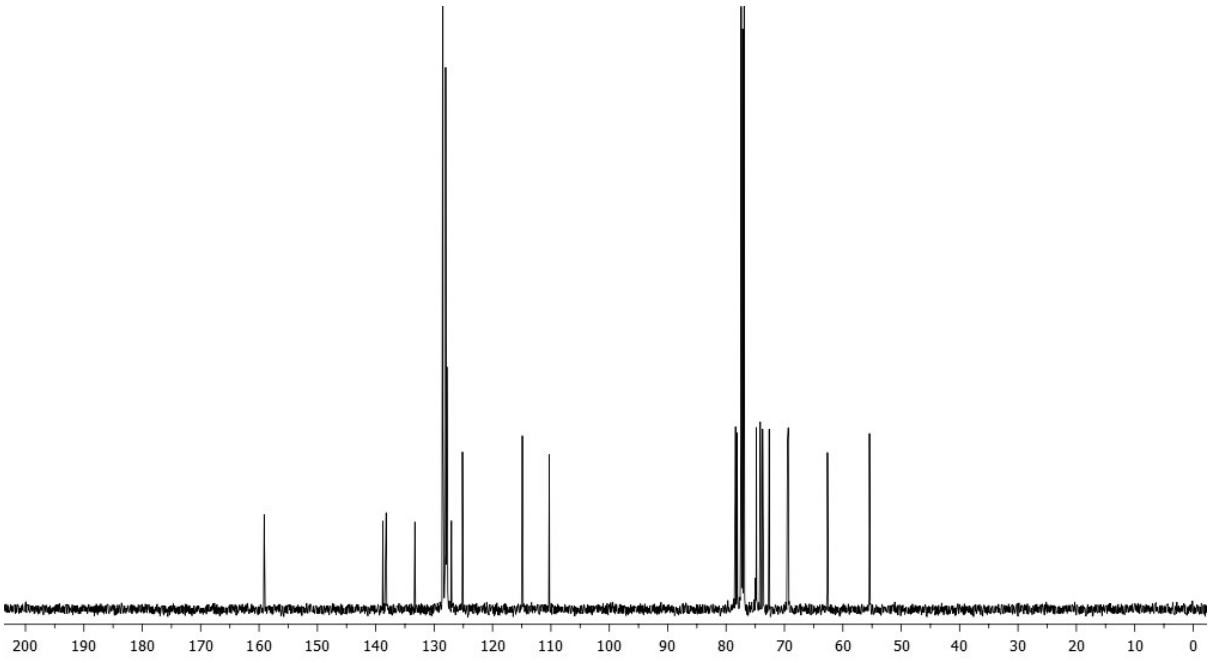
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3j**



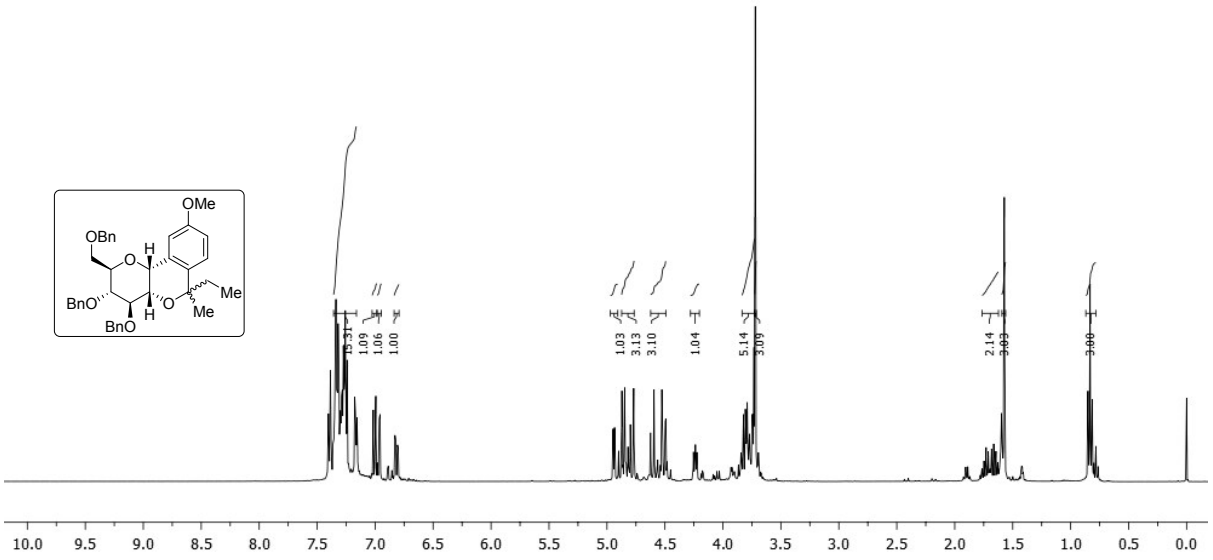
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3j**



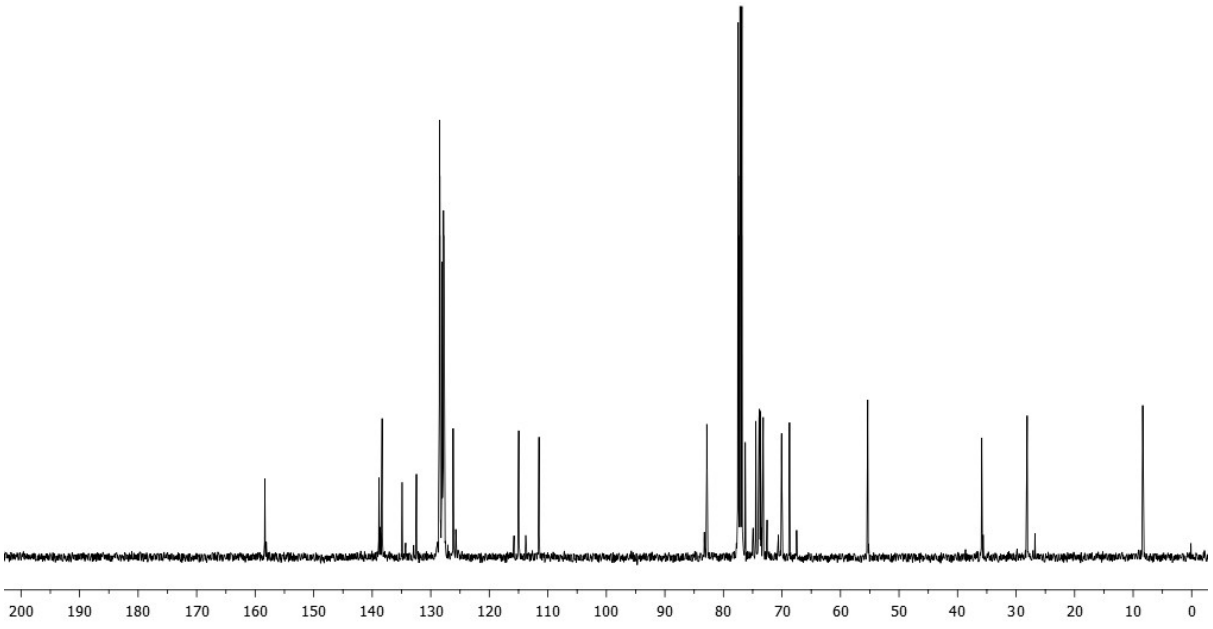
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **3k**



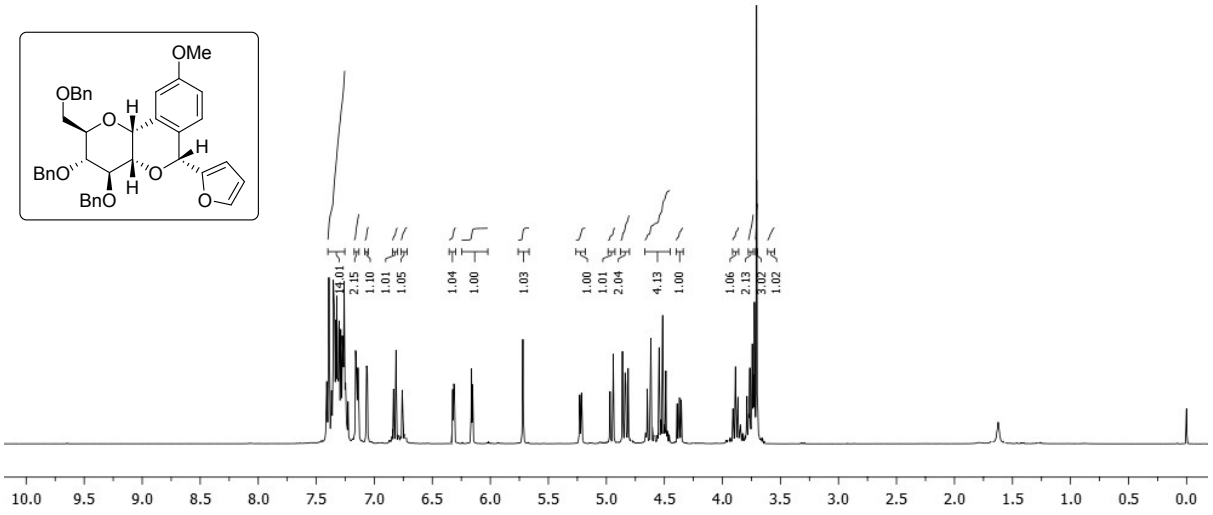
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of compound **3k**



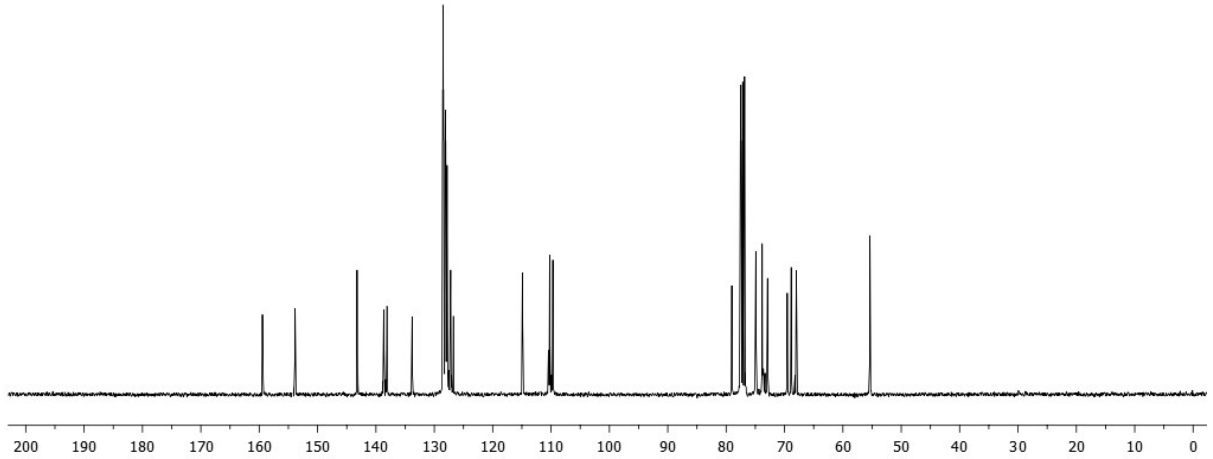
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3L**



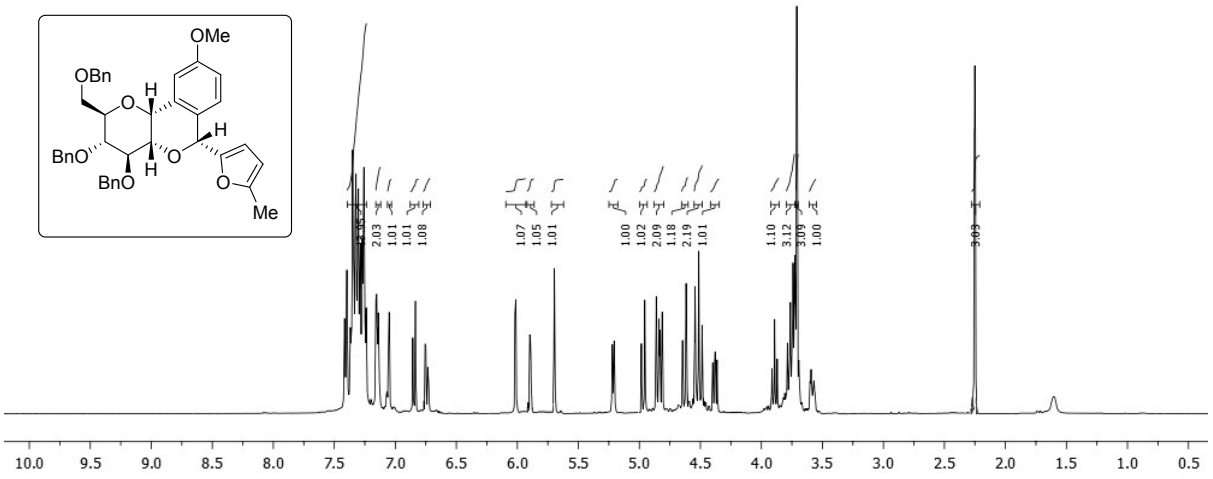
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3L**



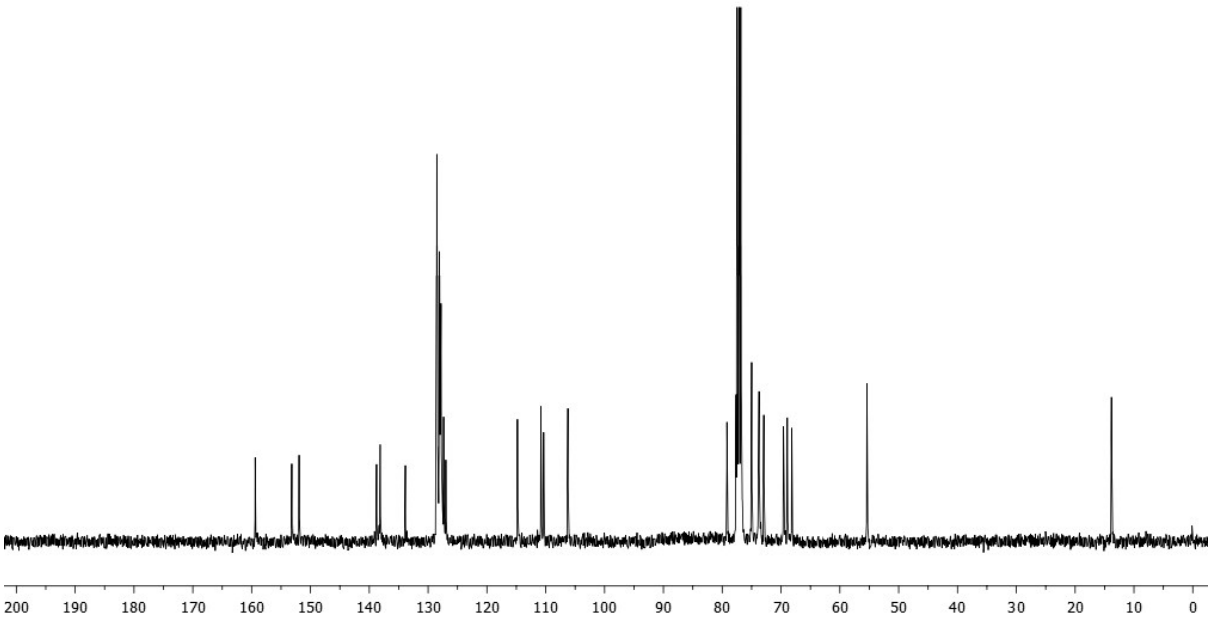
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3M**



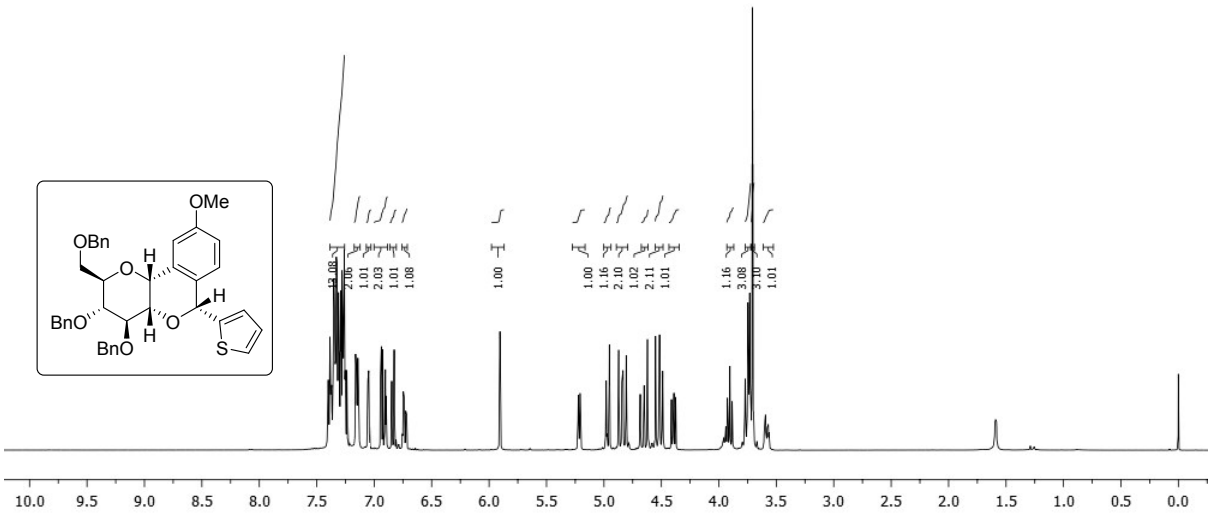
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3M**



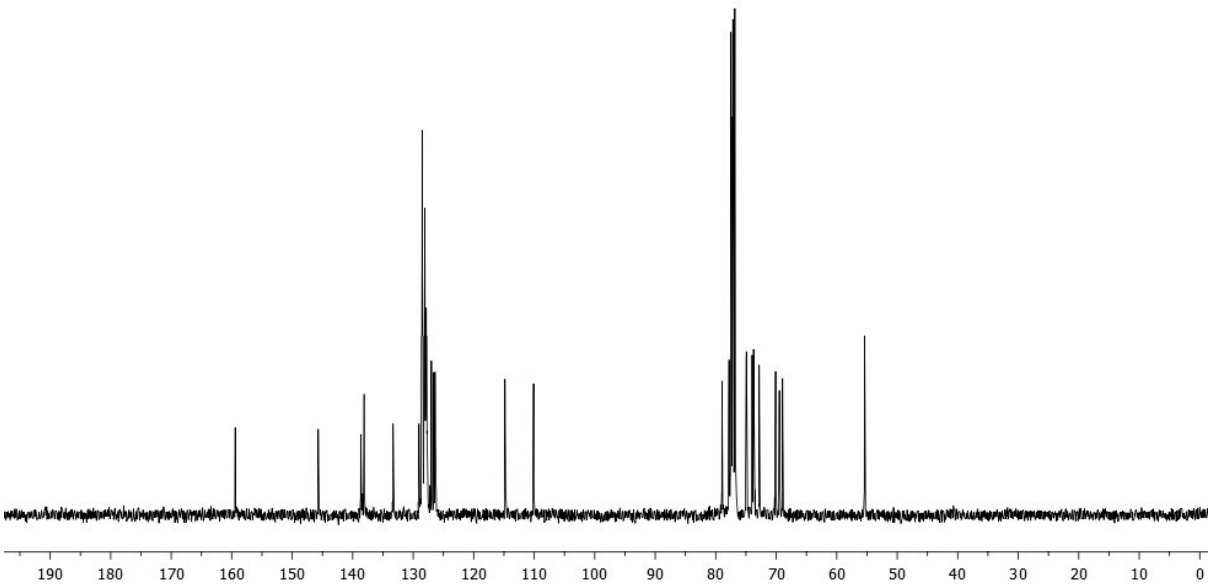
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3N**



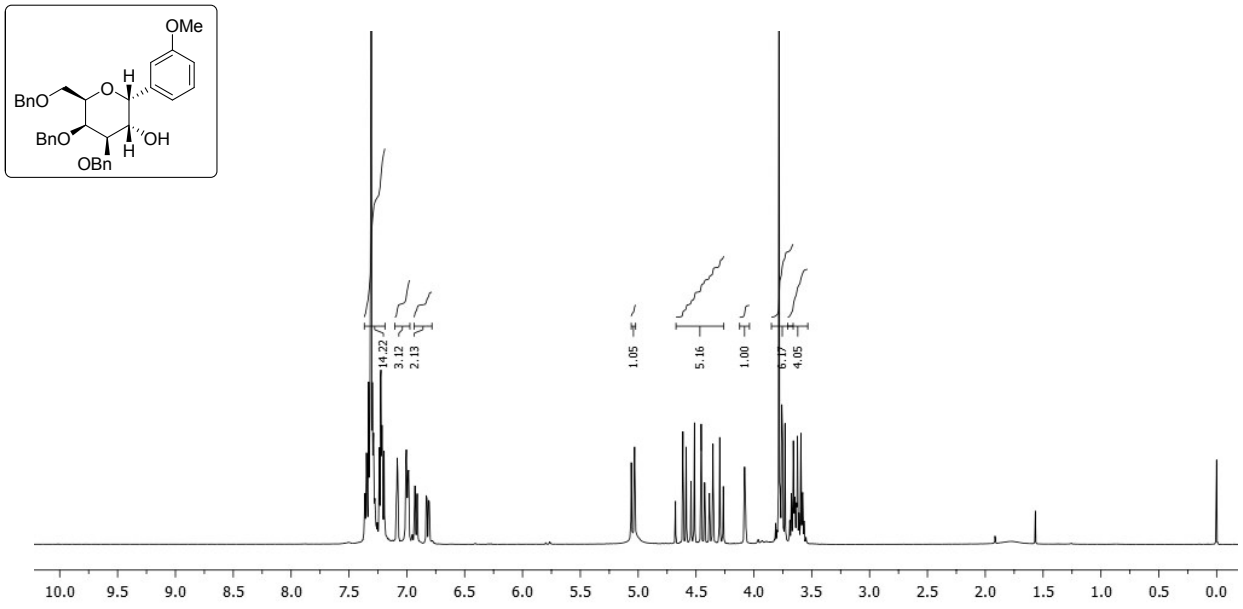
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3N**



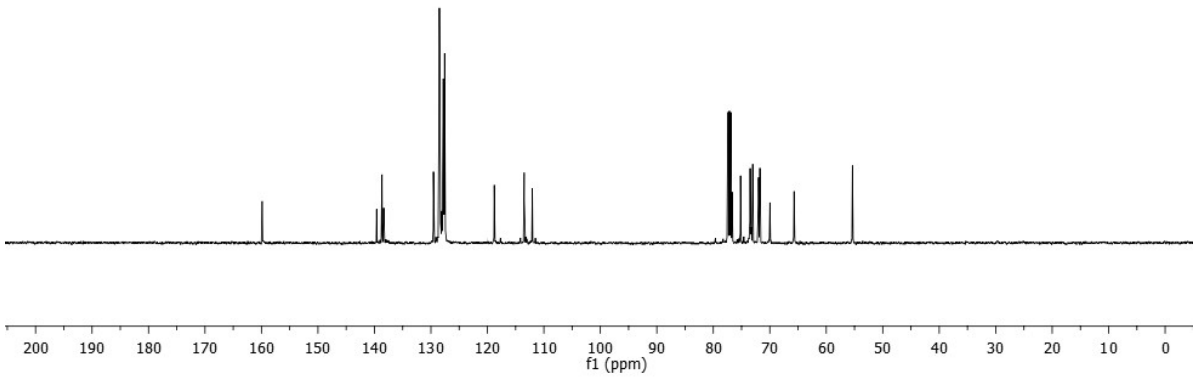
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **3O**



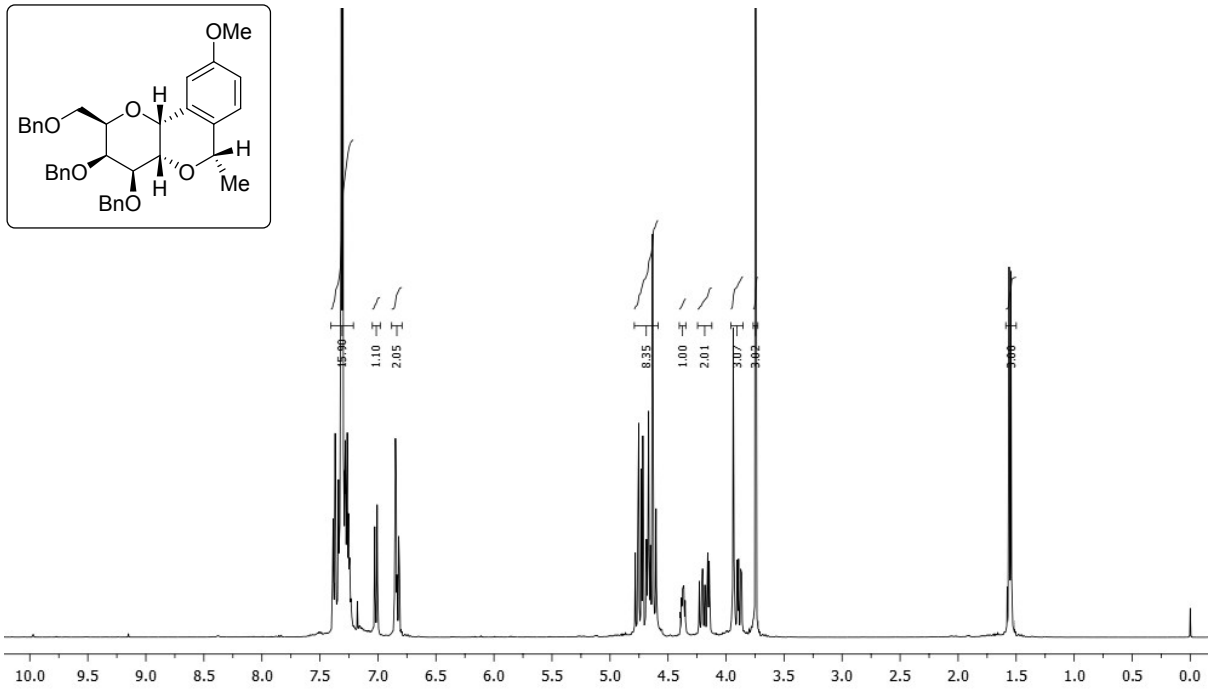
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **3O**



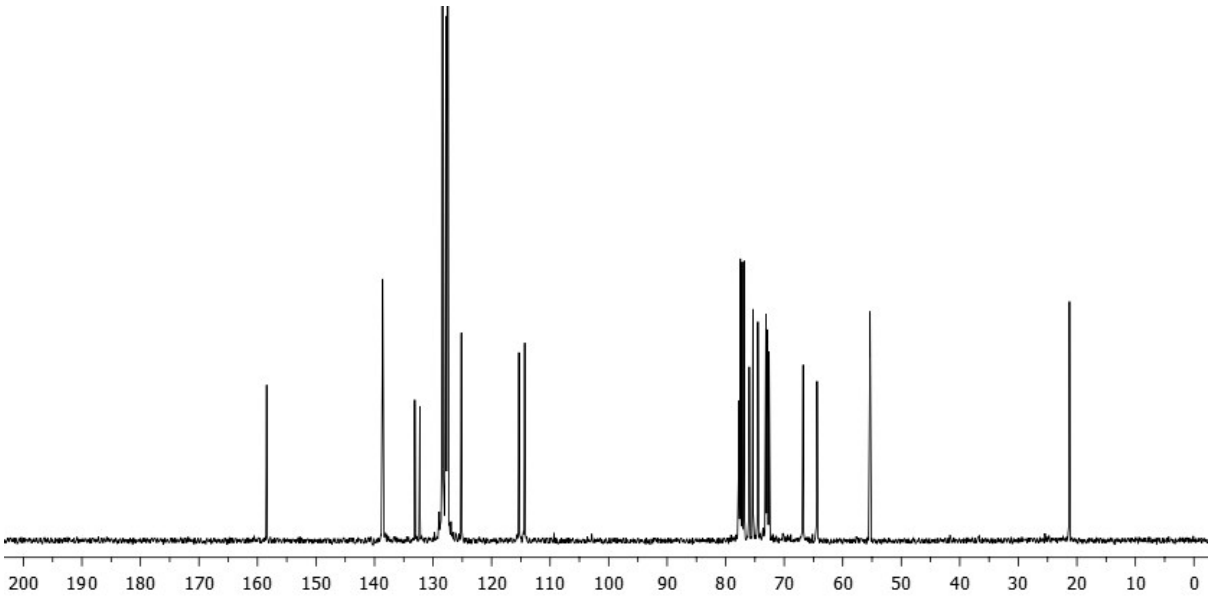
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **1**



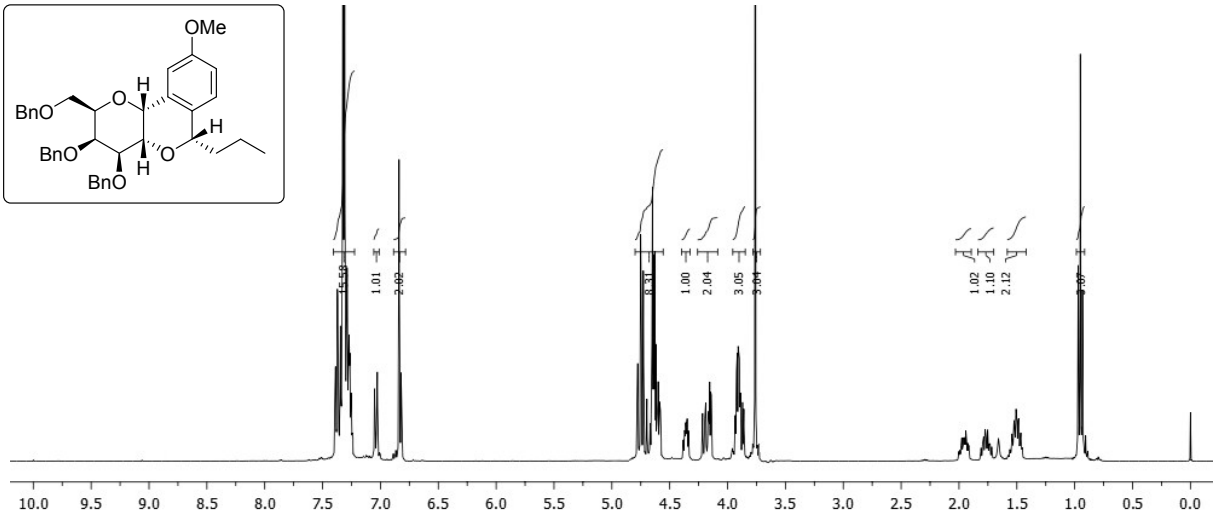
^{13}C NMR spectrum (500 MHz, $CDCl_3$) of compound **1**



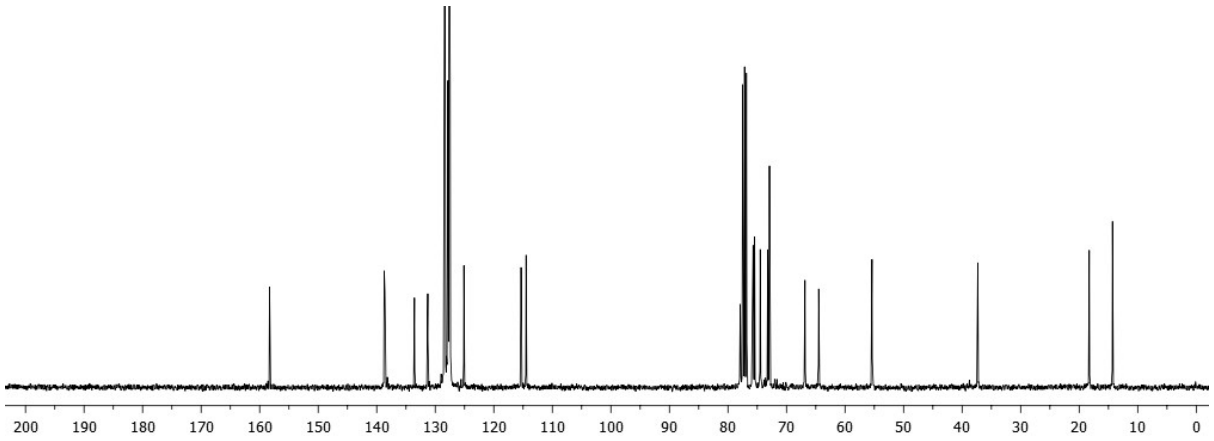
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5a**



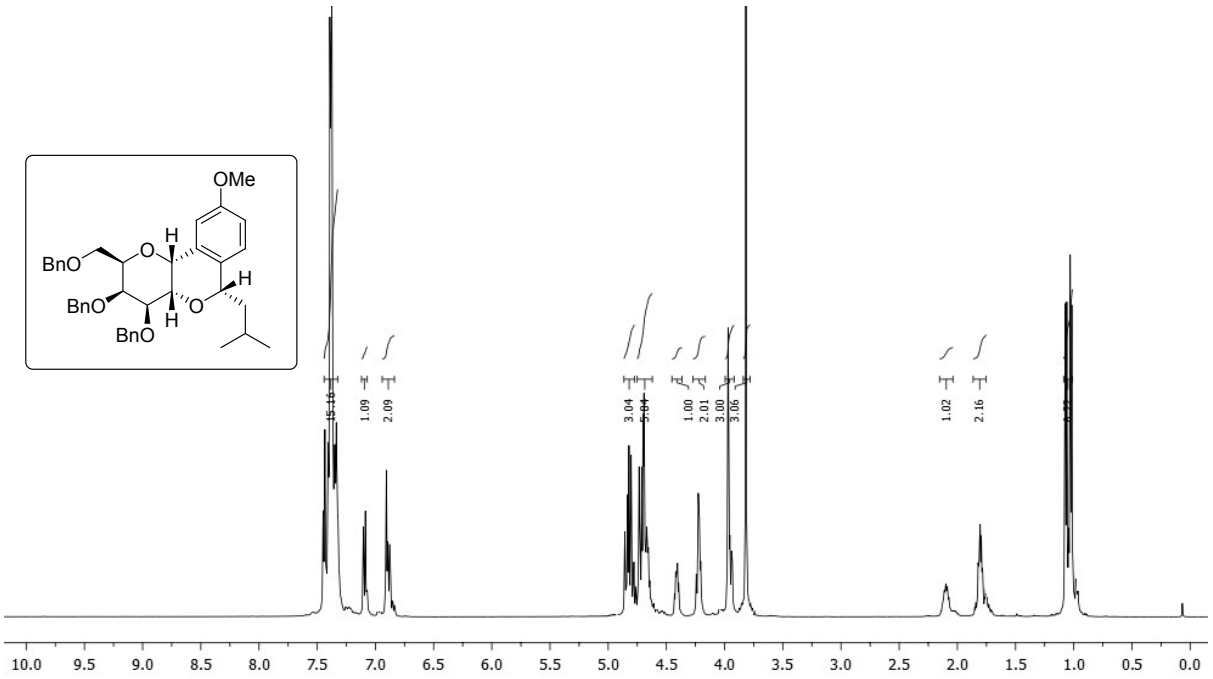
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5a**



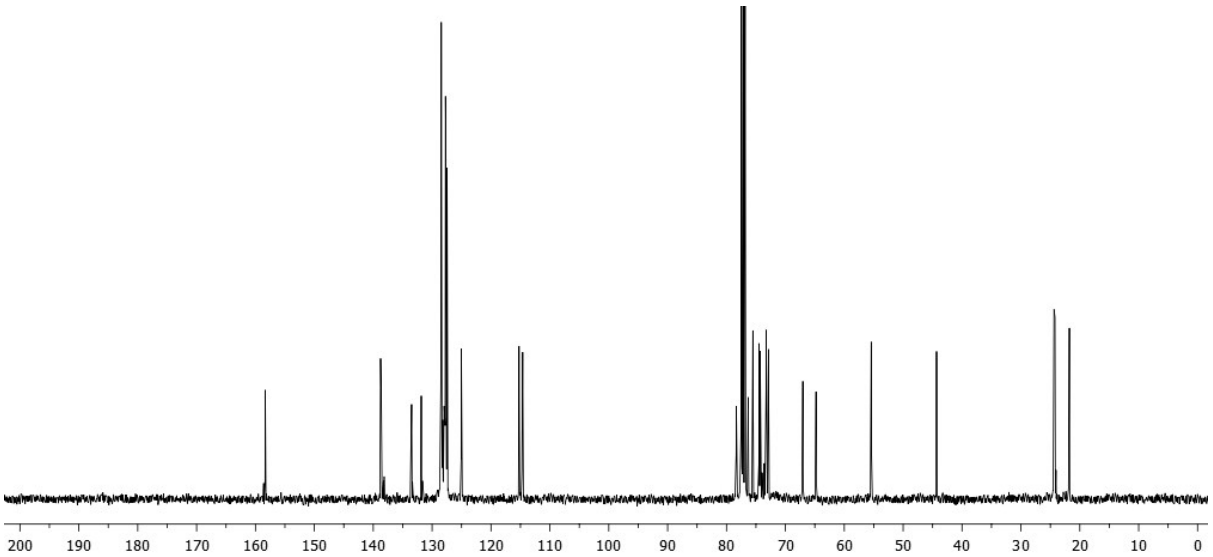
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5b**



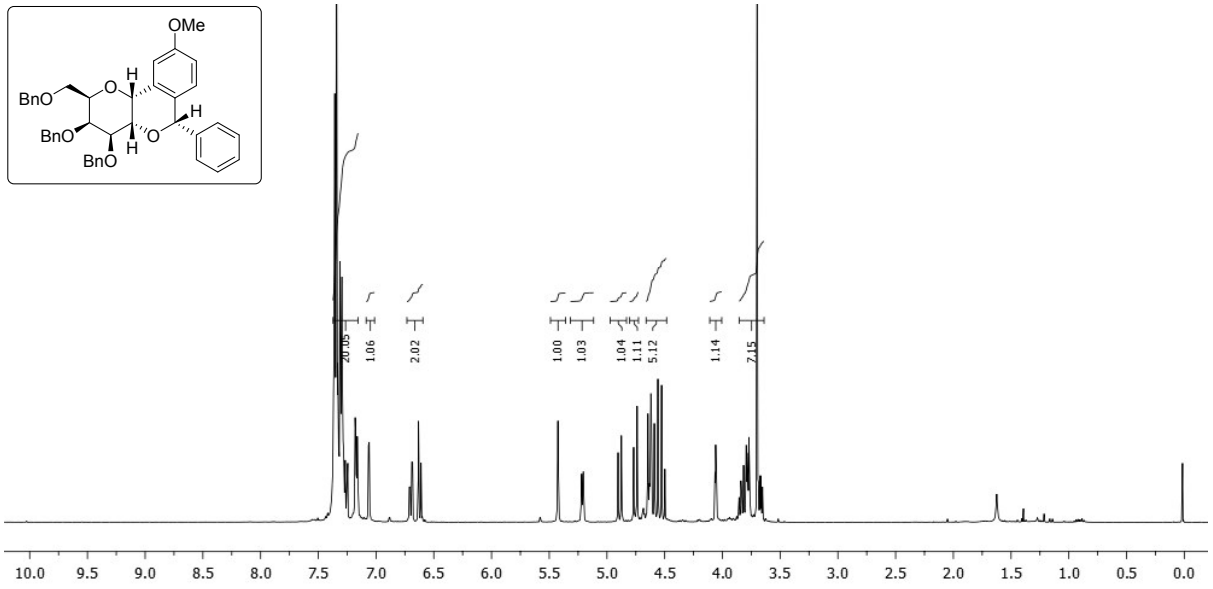
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5b**



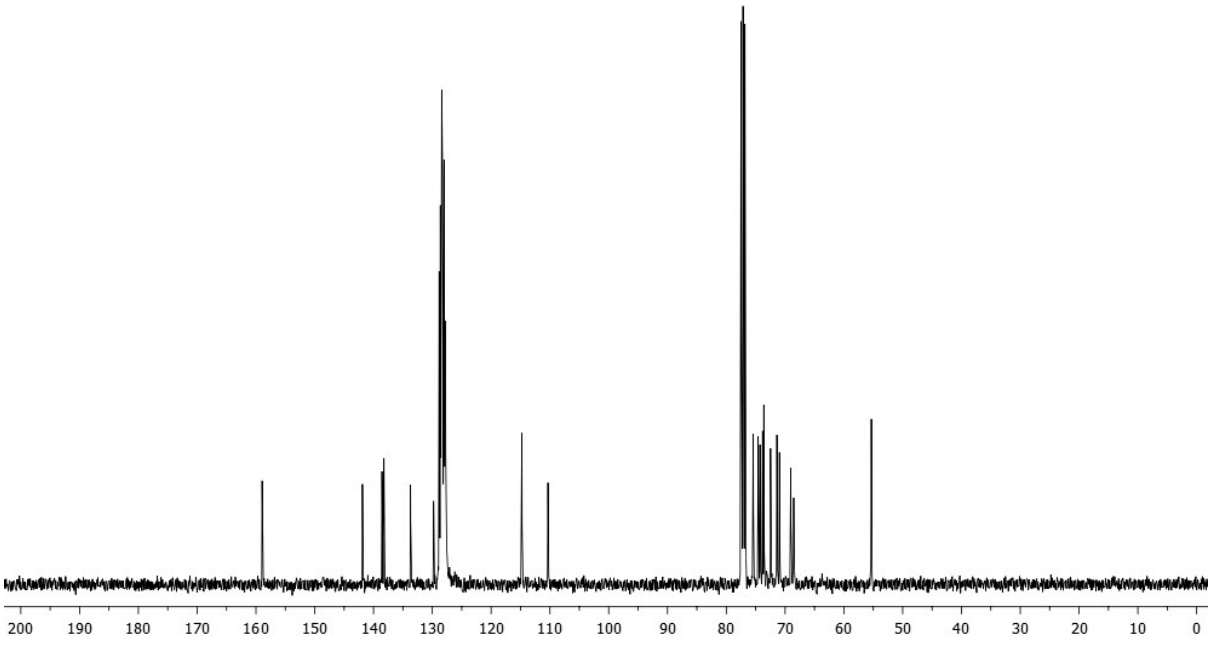
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **5c**



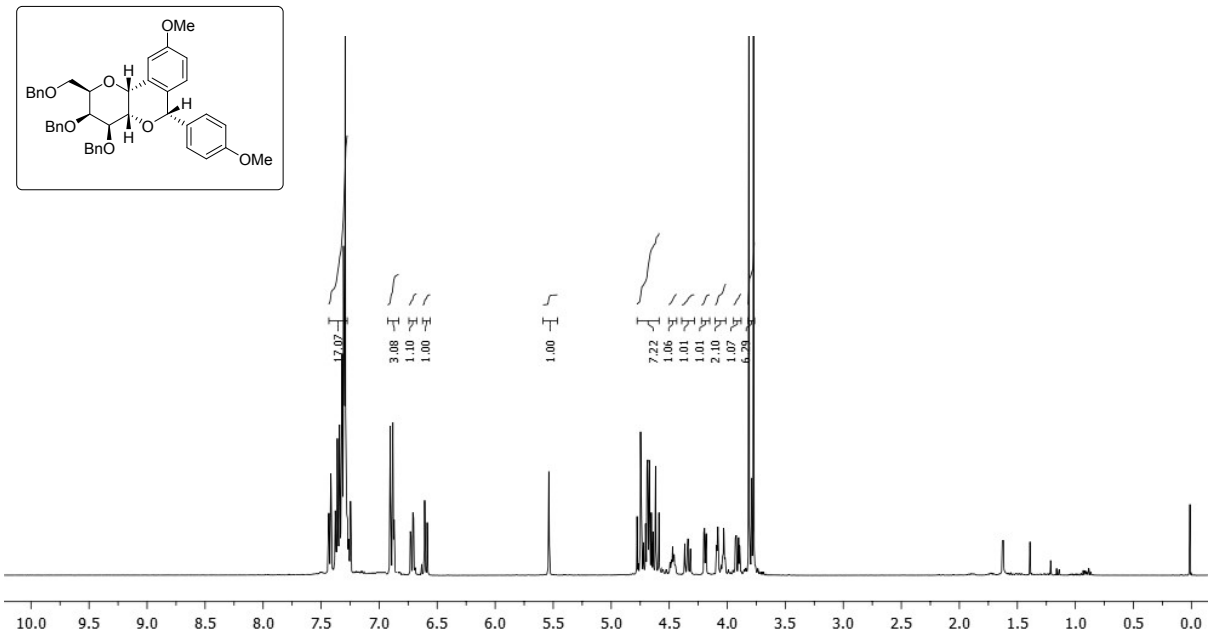
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5c**



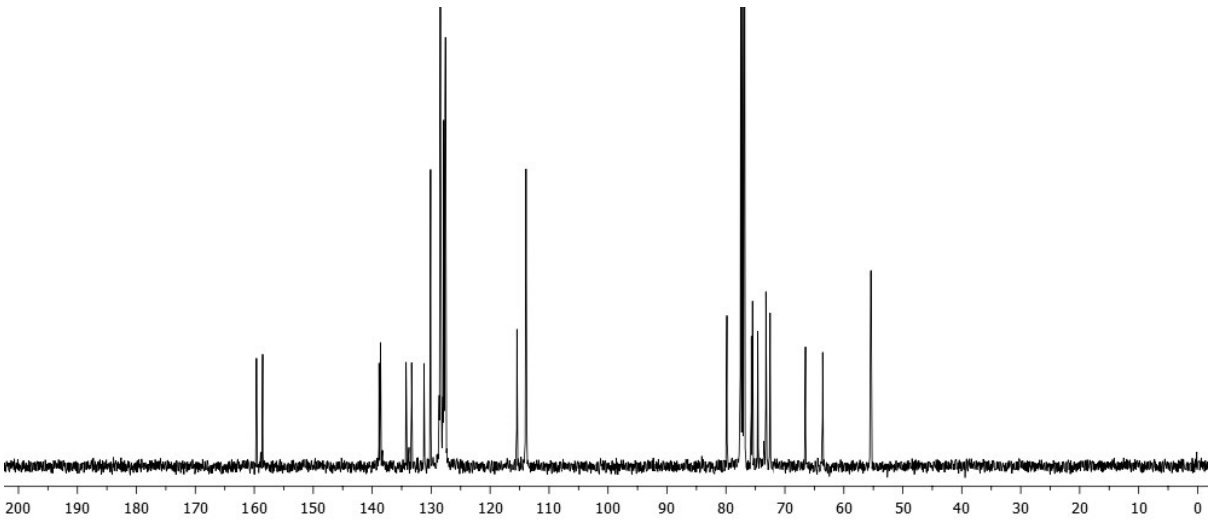
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5d**



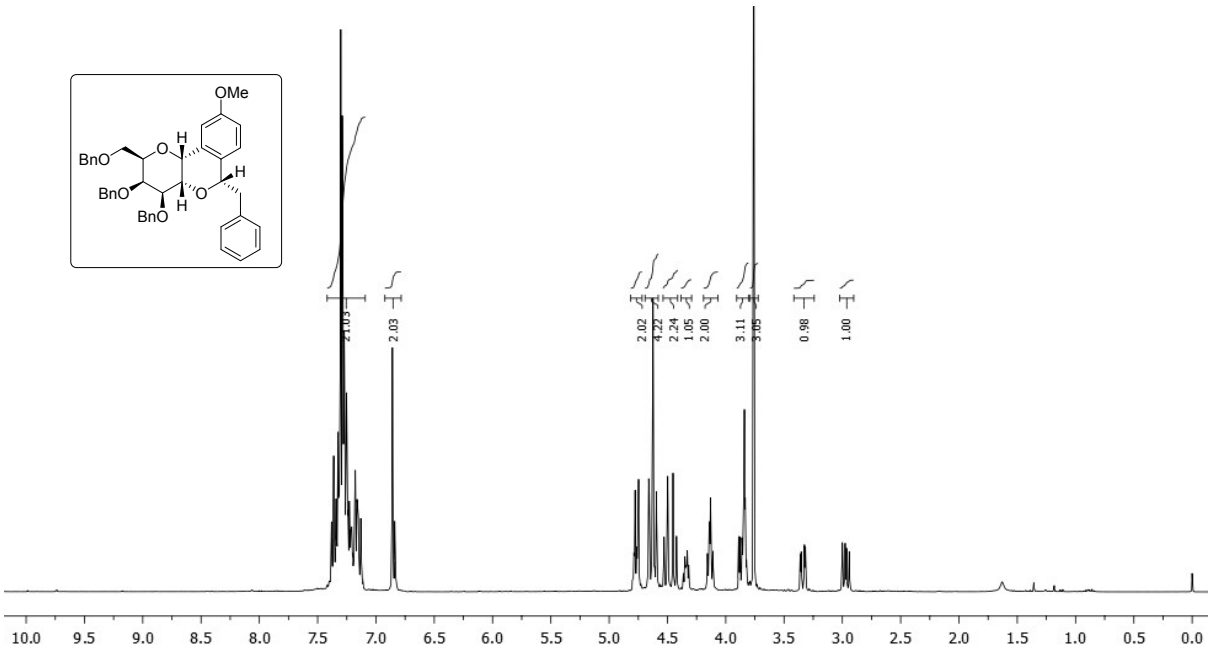
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5d**



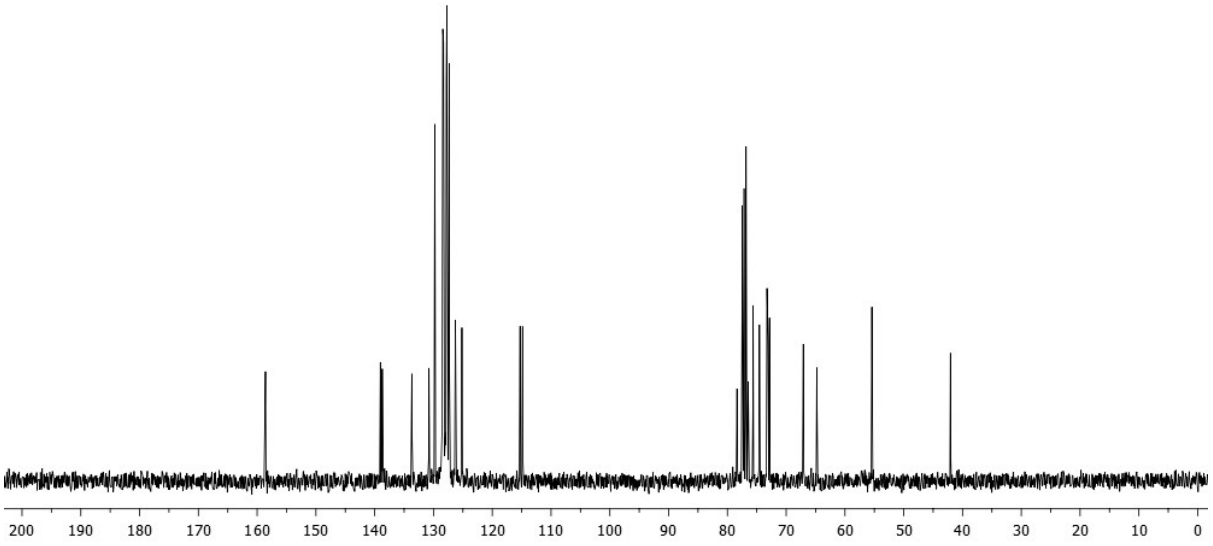
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5e**



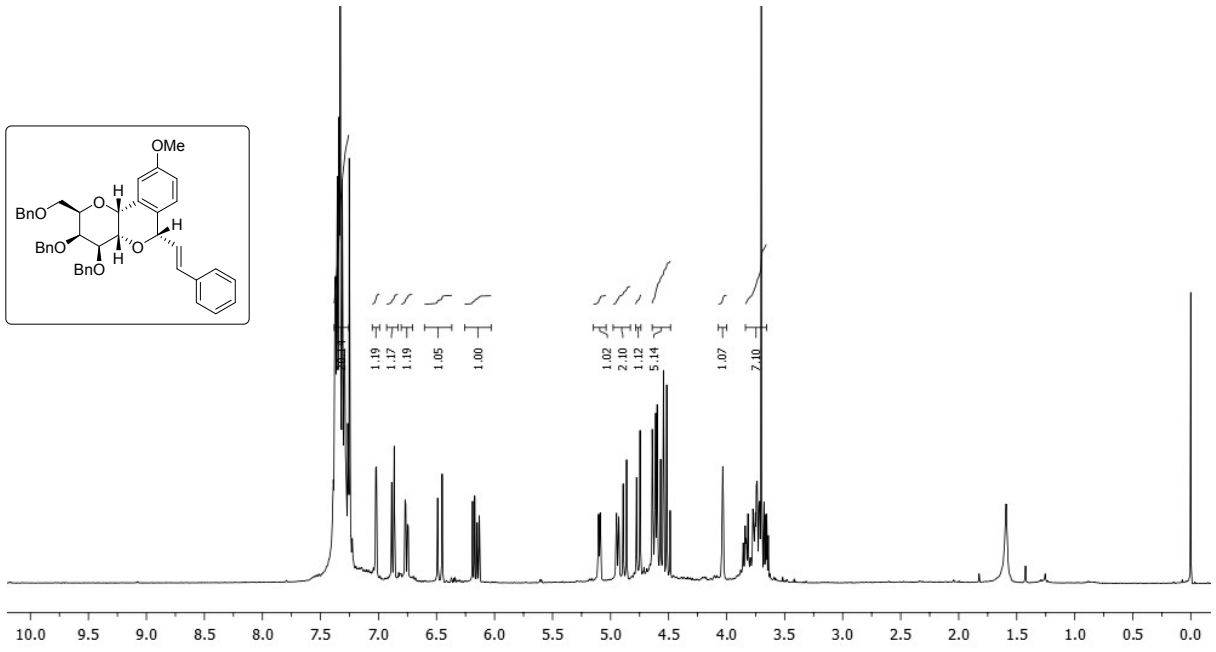
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5e**



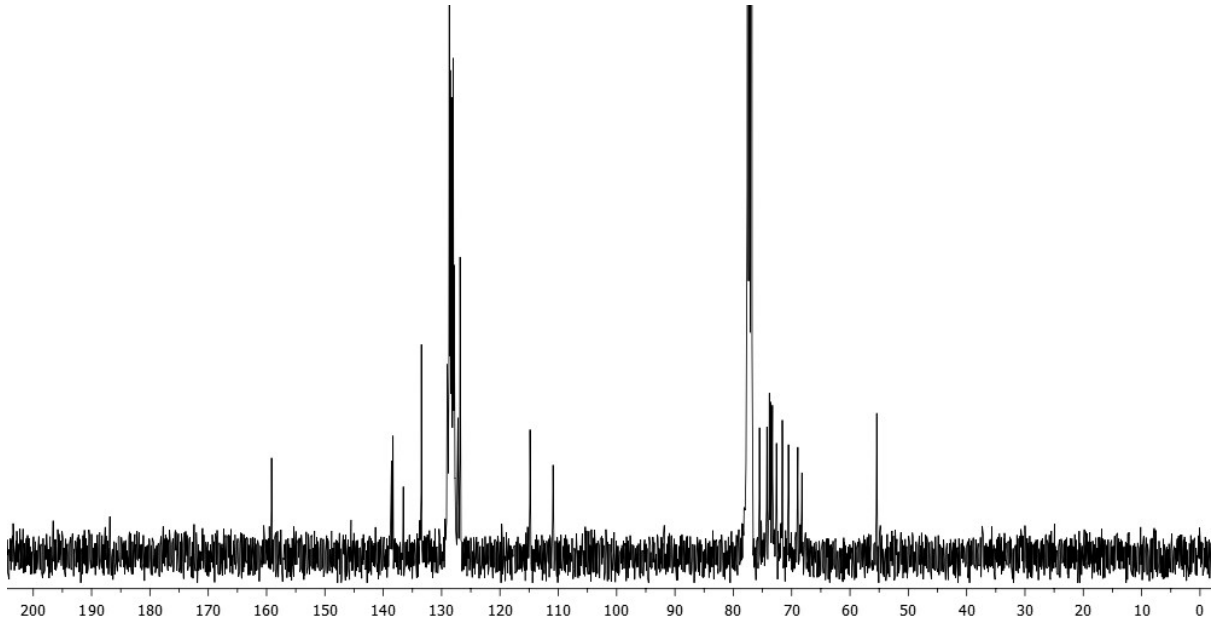
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5f**



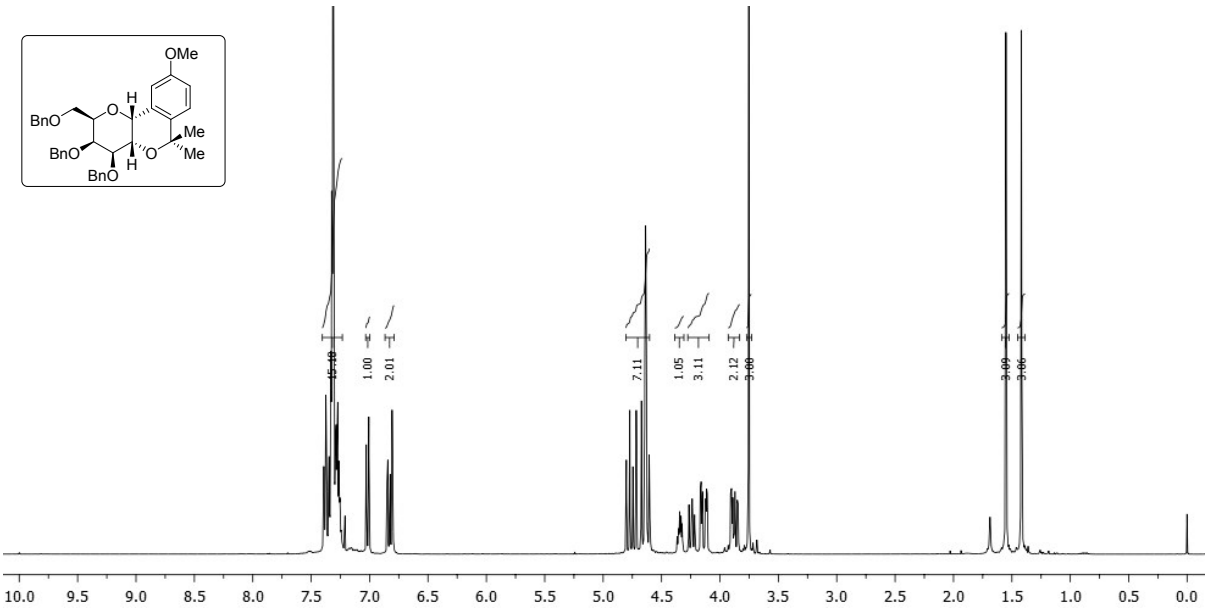
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5f**



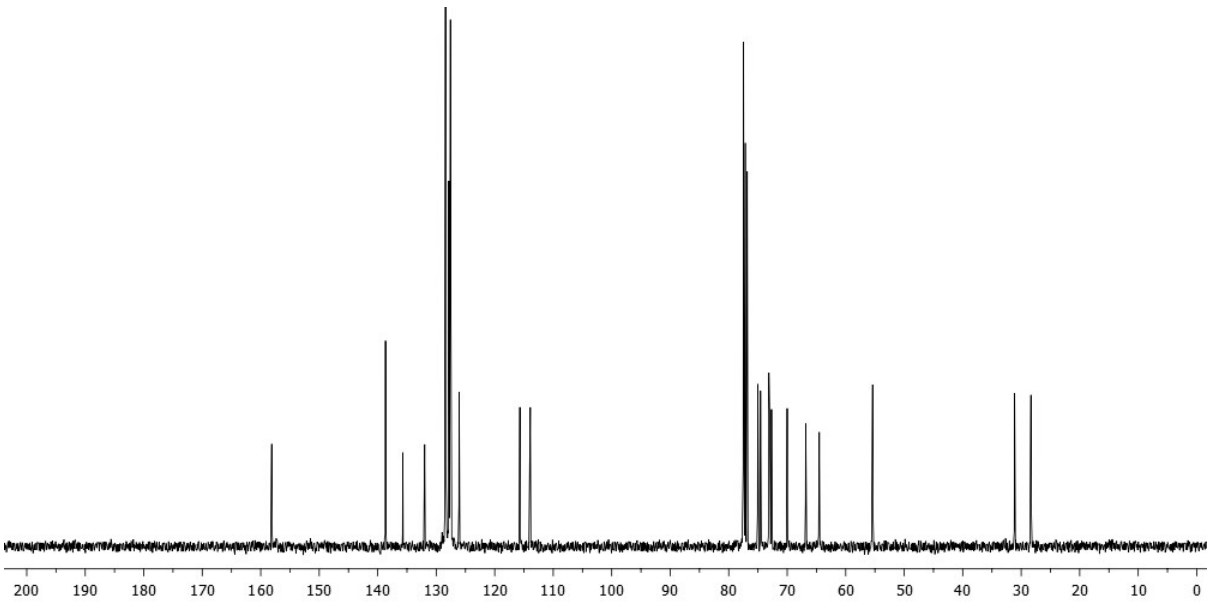
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5g**



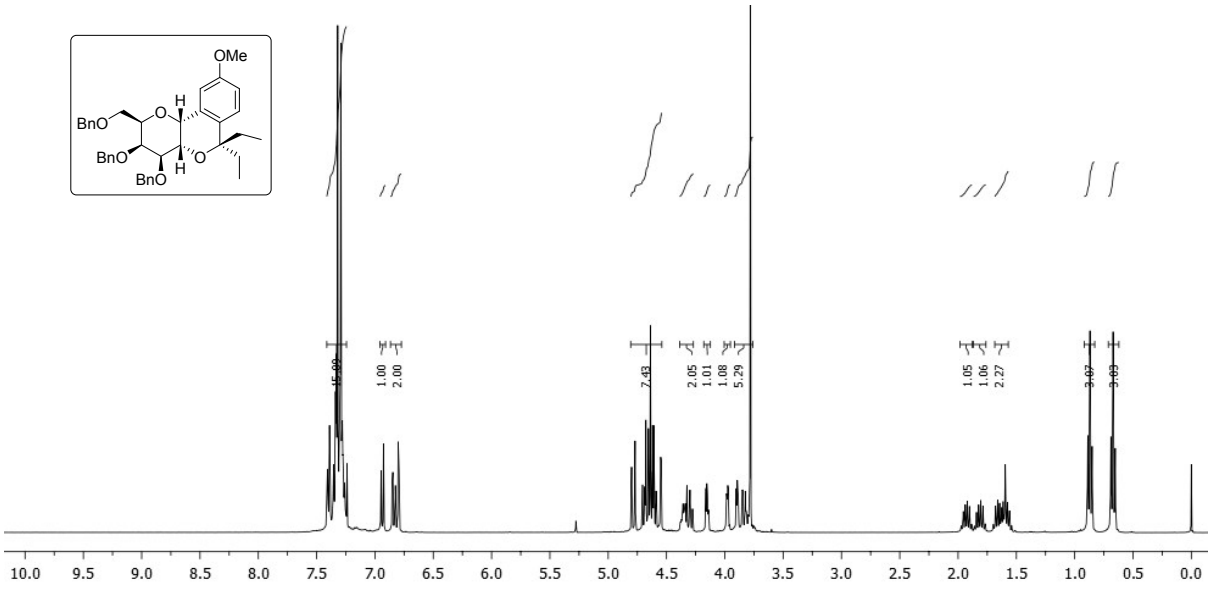
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5g**



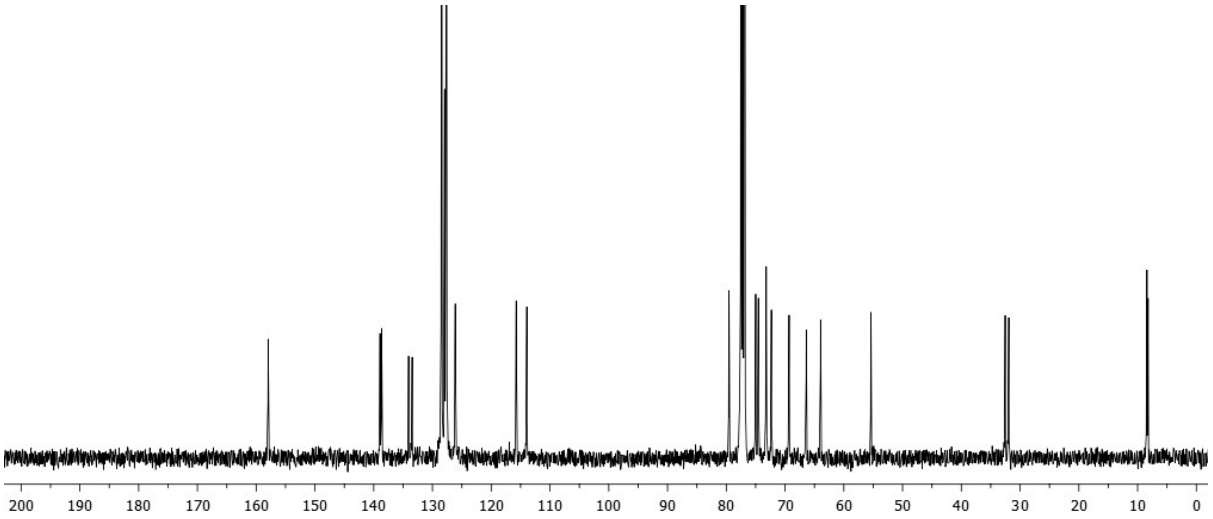
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5h**



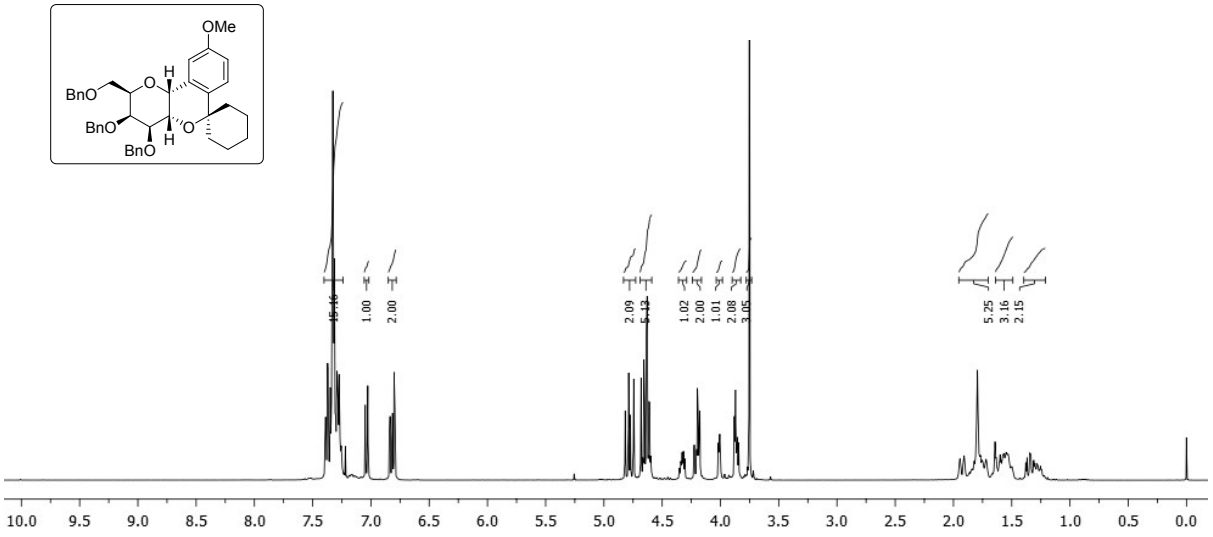
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5h**



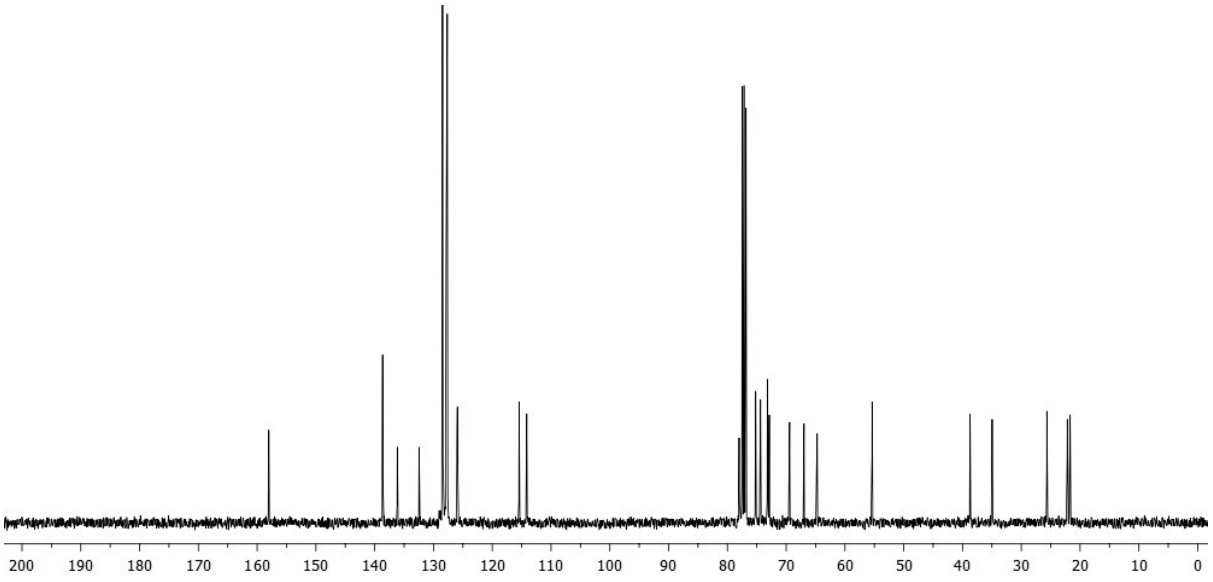
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5i**



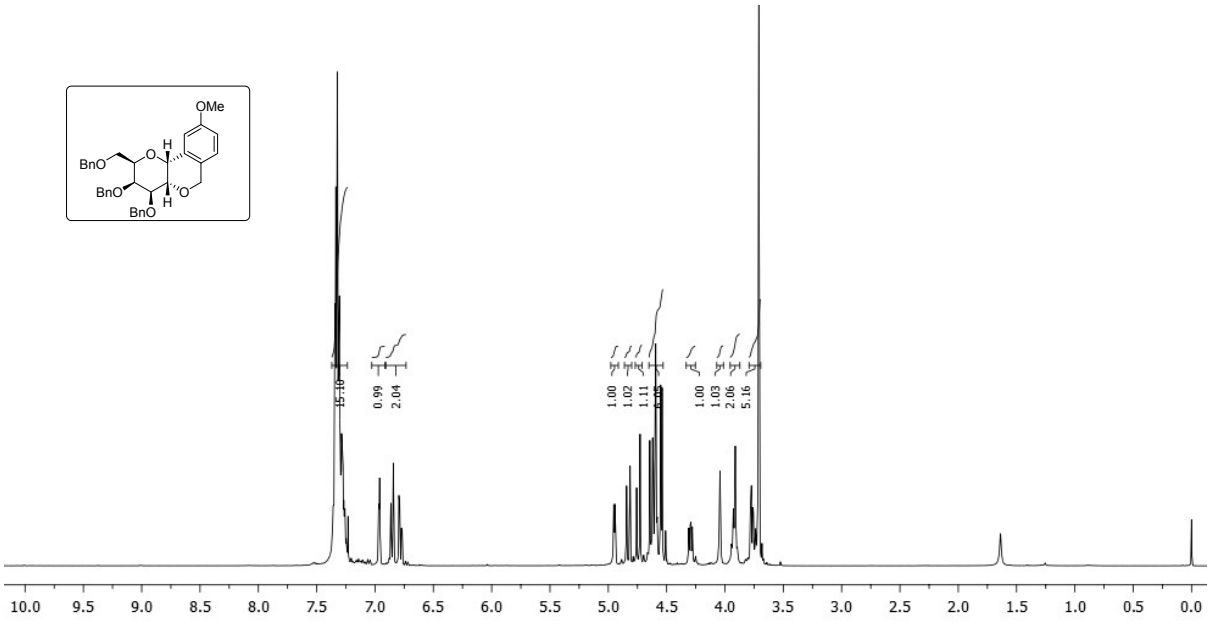
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5i**



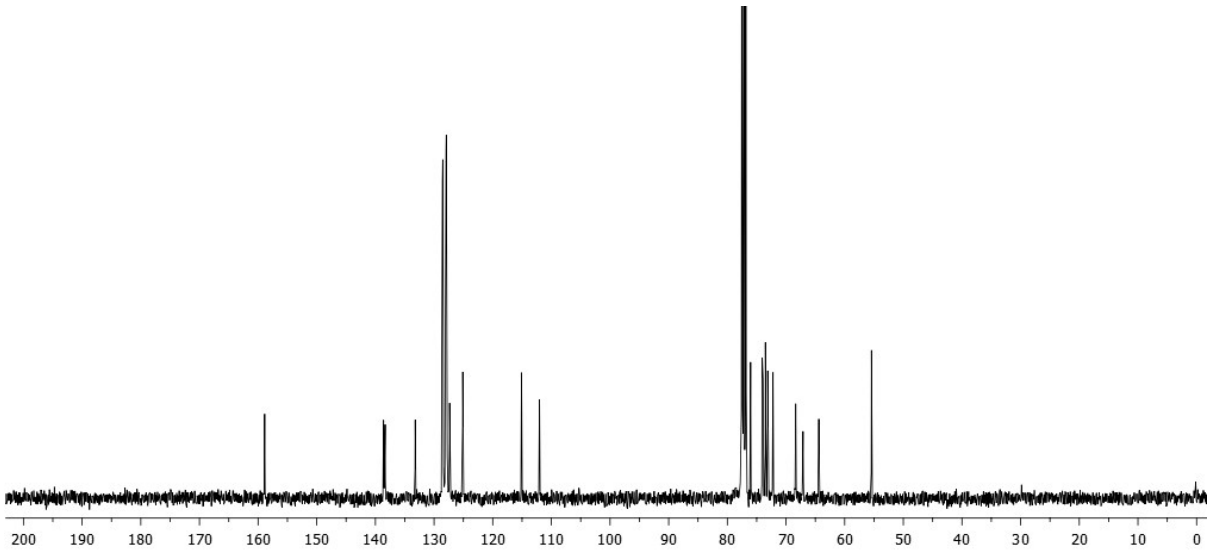
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5j**



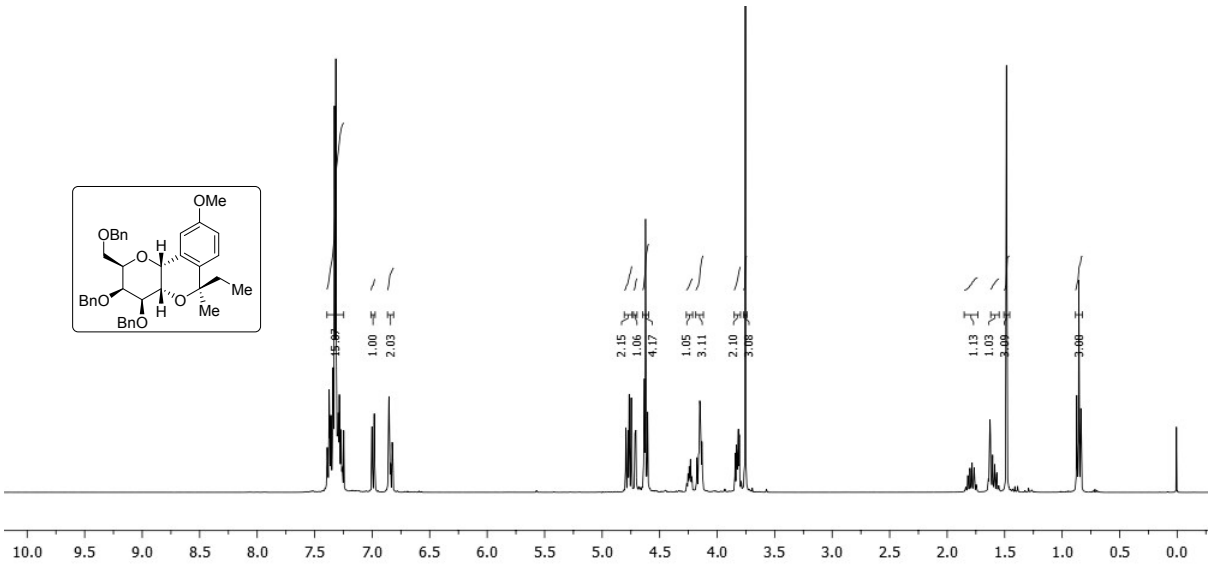
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5j**



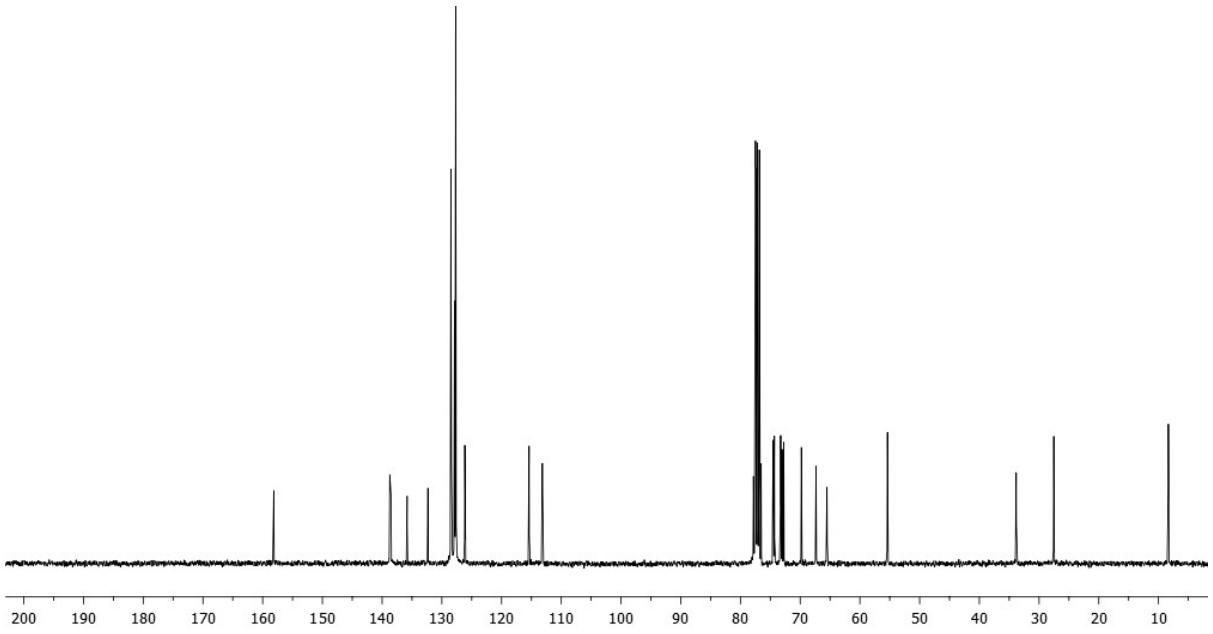
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5k**



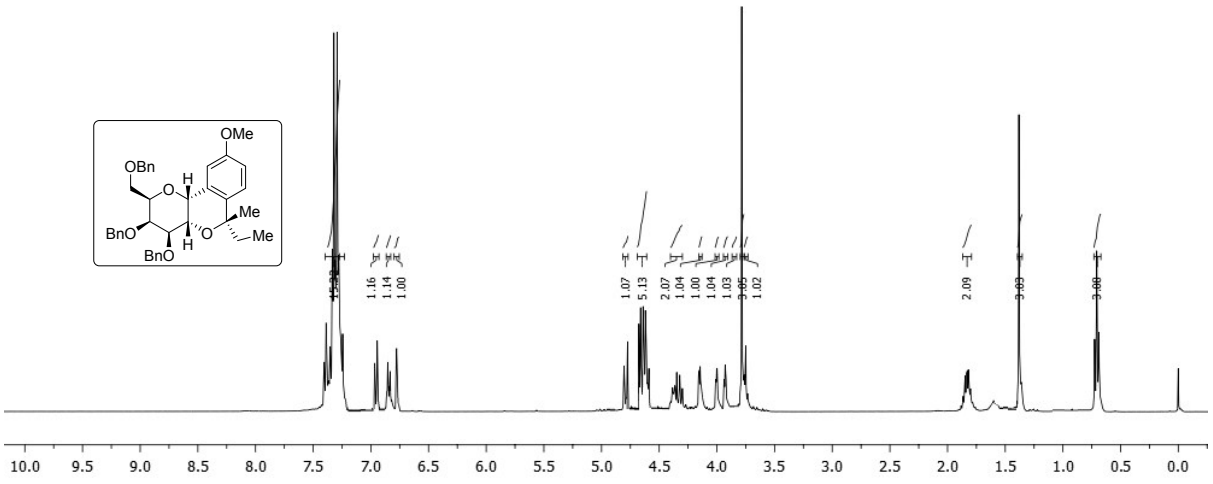
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5k**



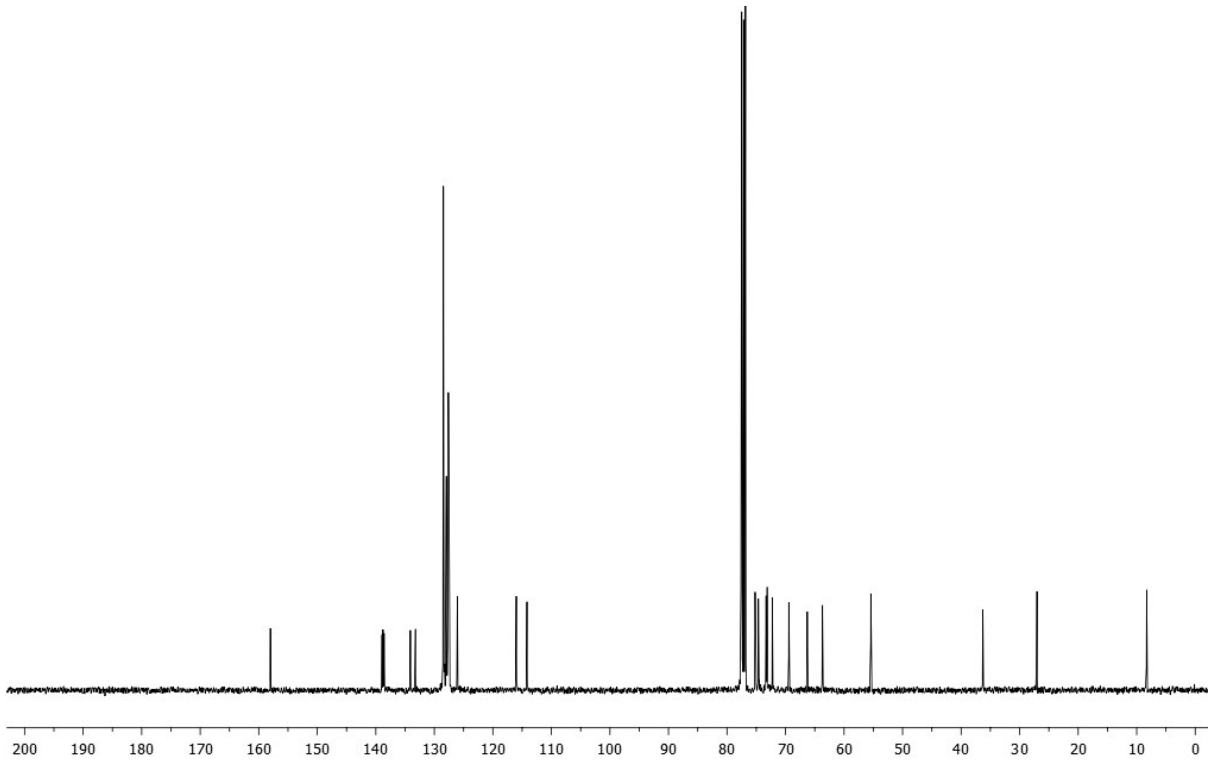
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5l1**



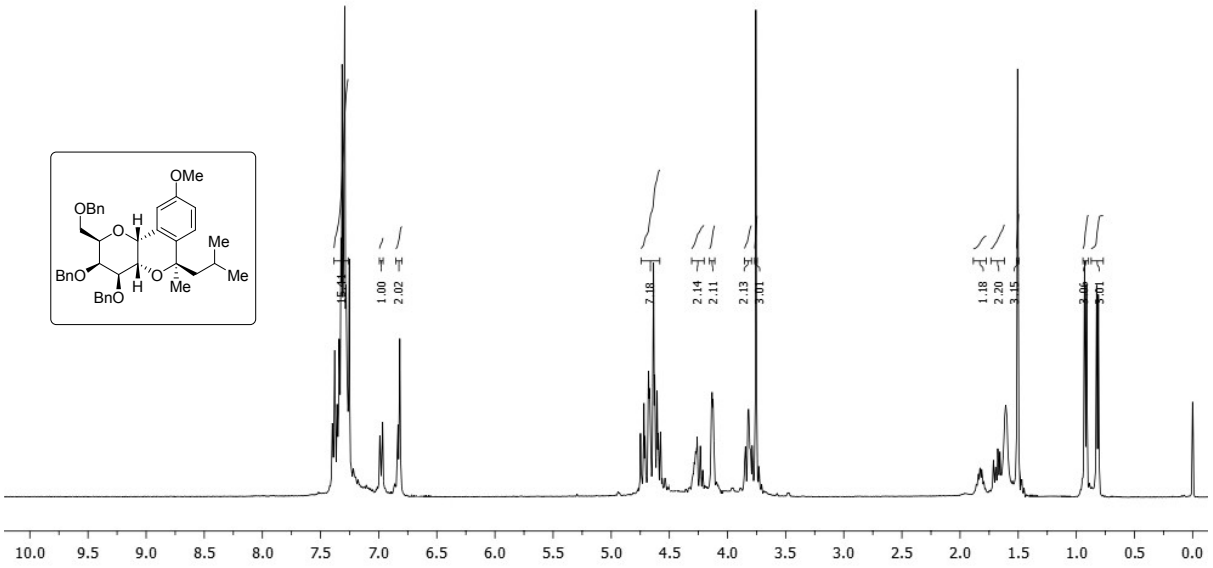
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5l1**



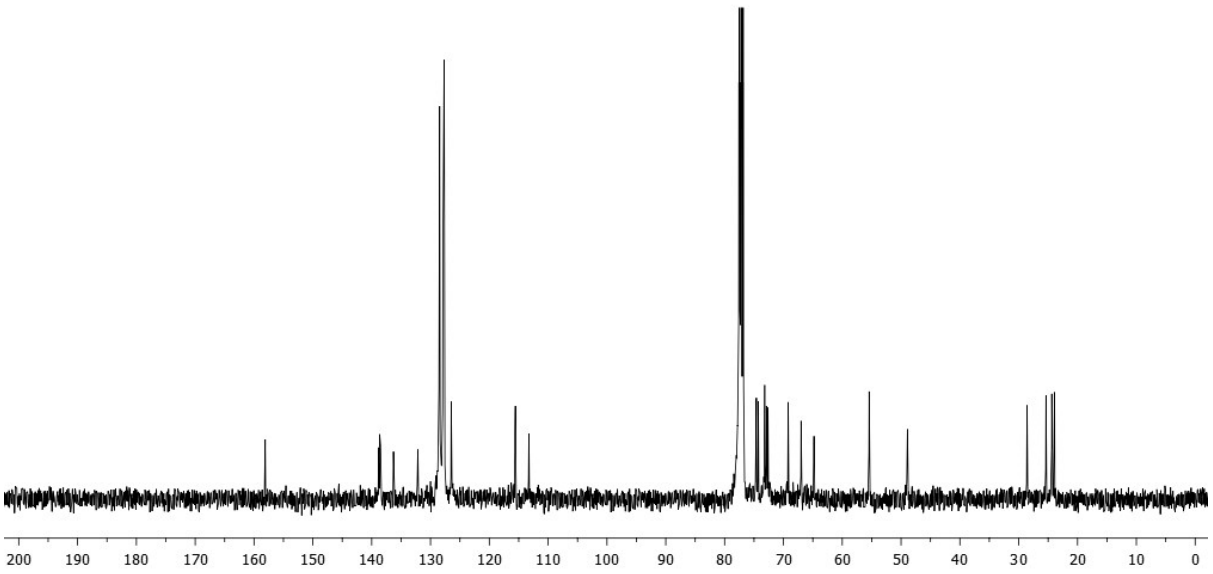
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5l2**



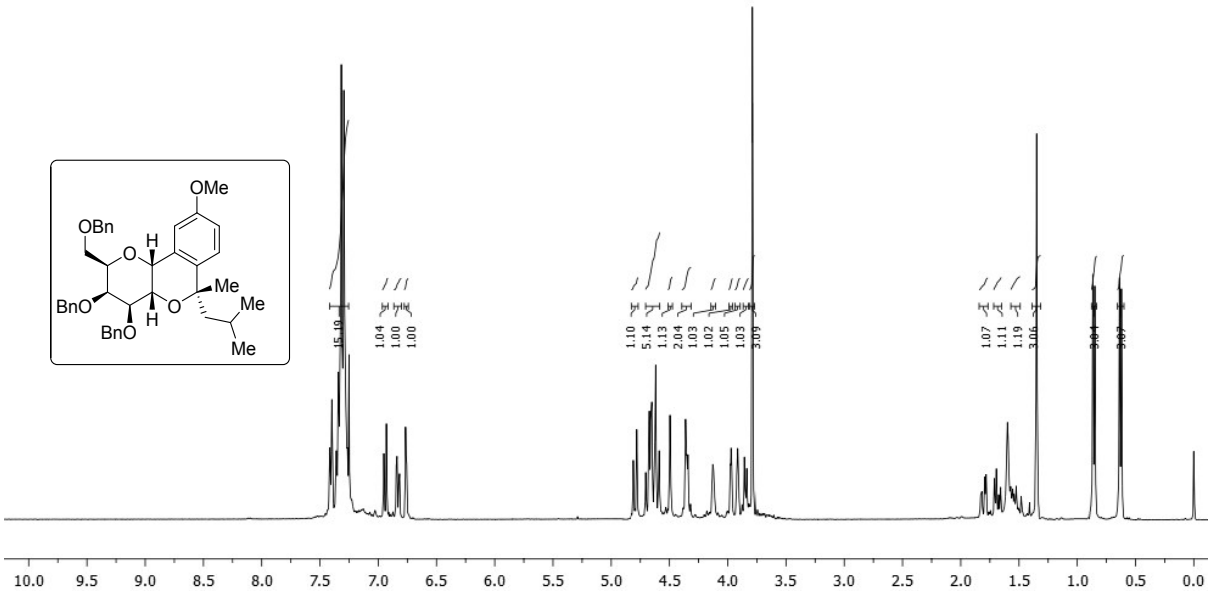
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5l2**



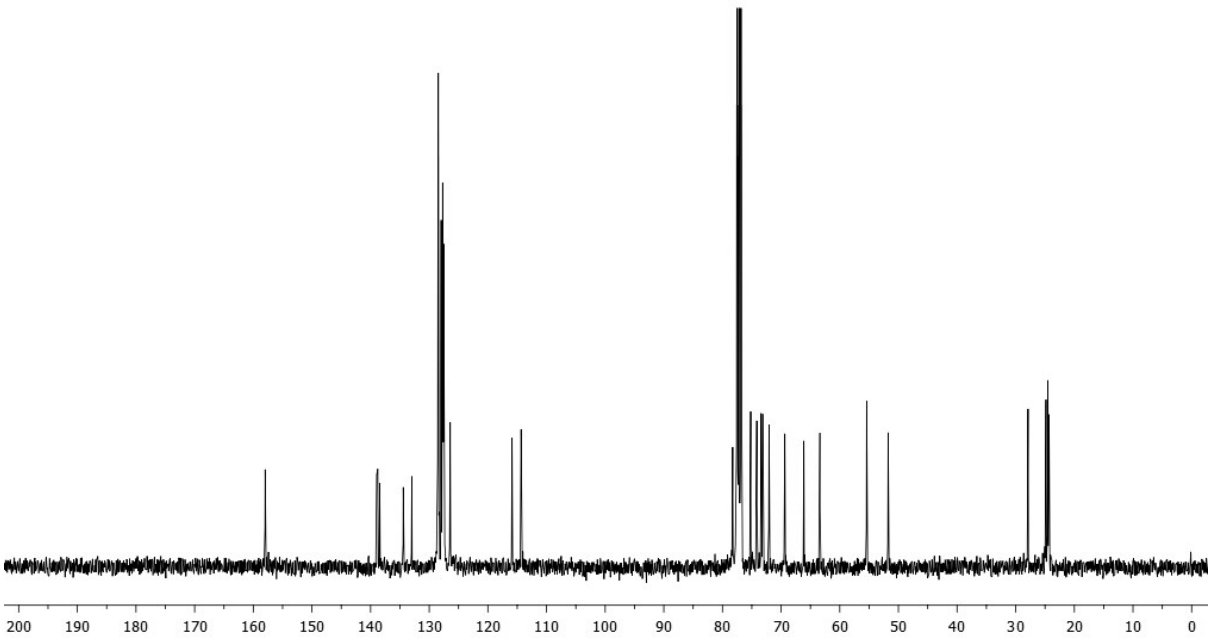
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5m1**



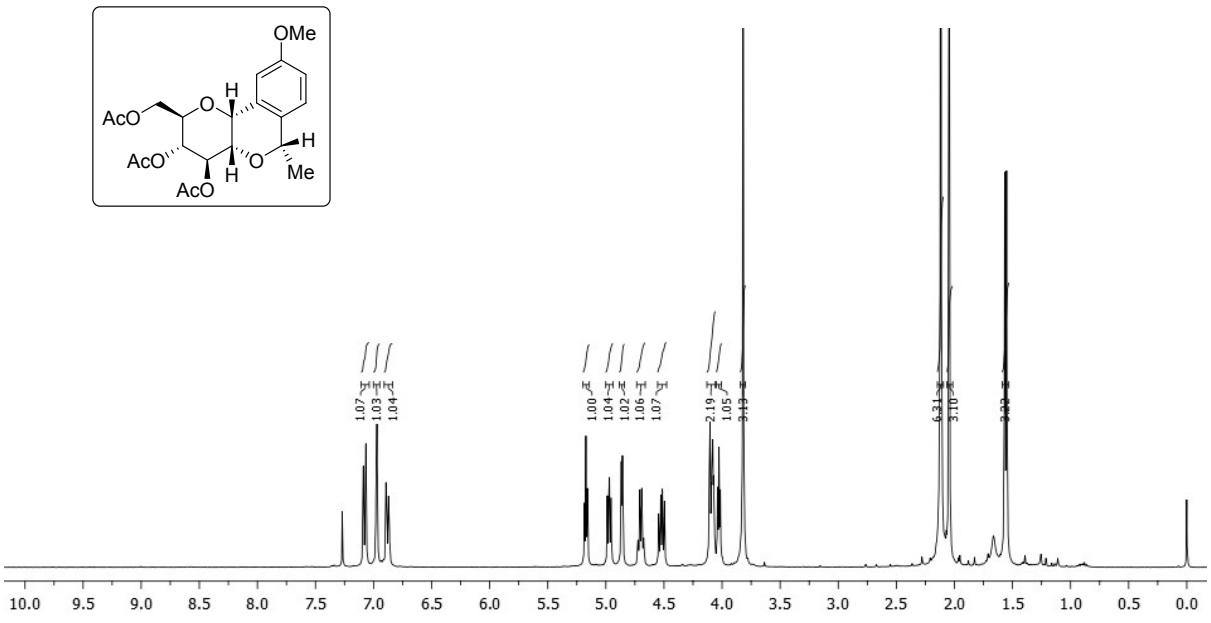
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5m1**



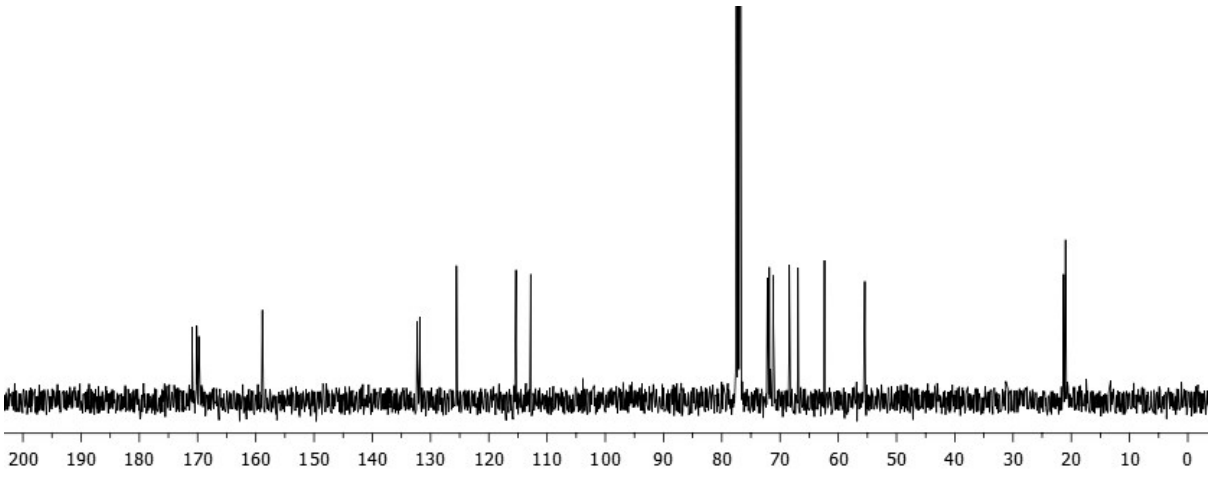
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **5m2**



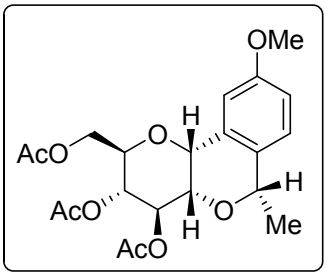
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **5m2**

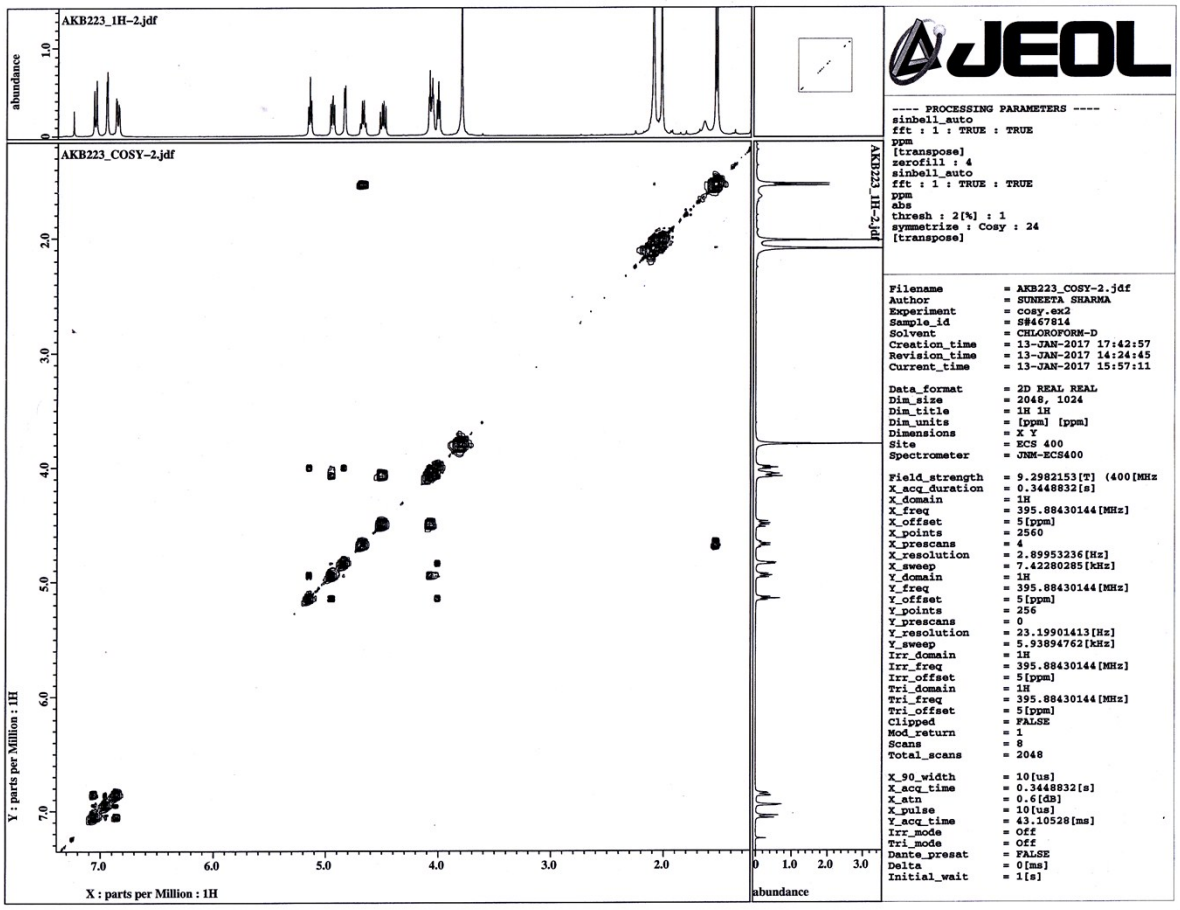


^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **7**

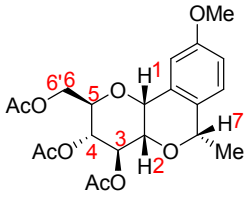


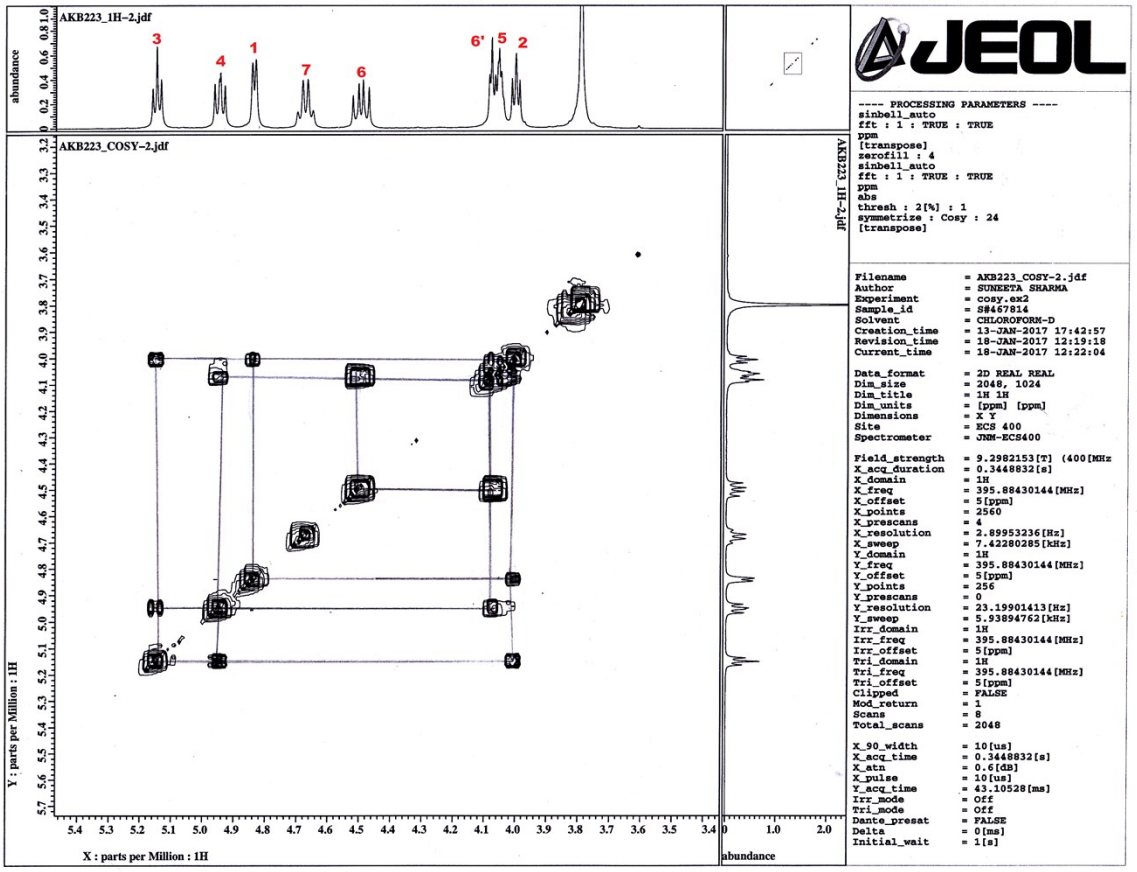
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **7**



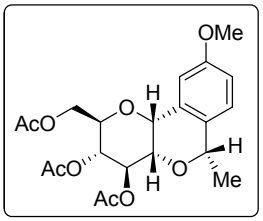


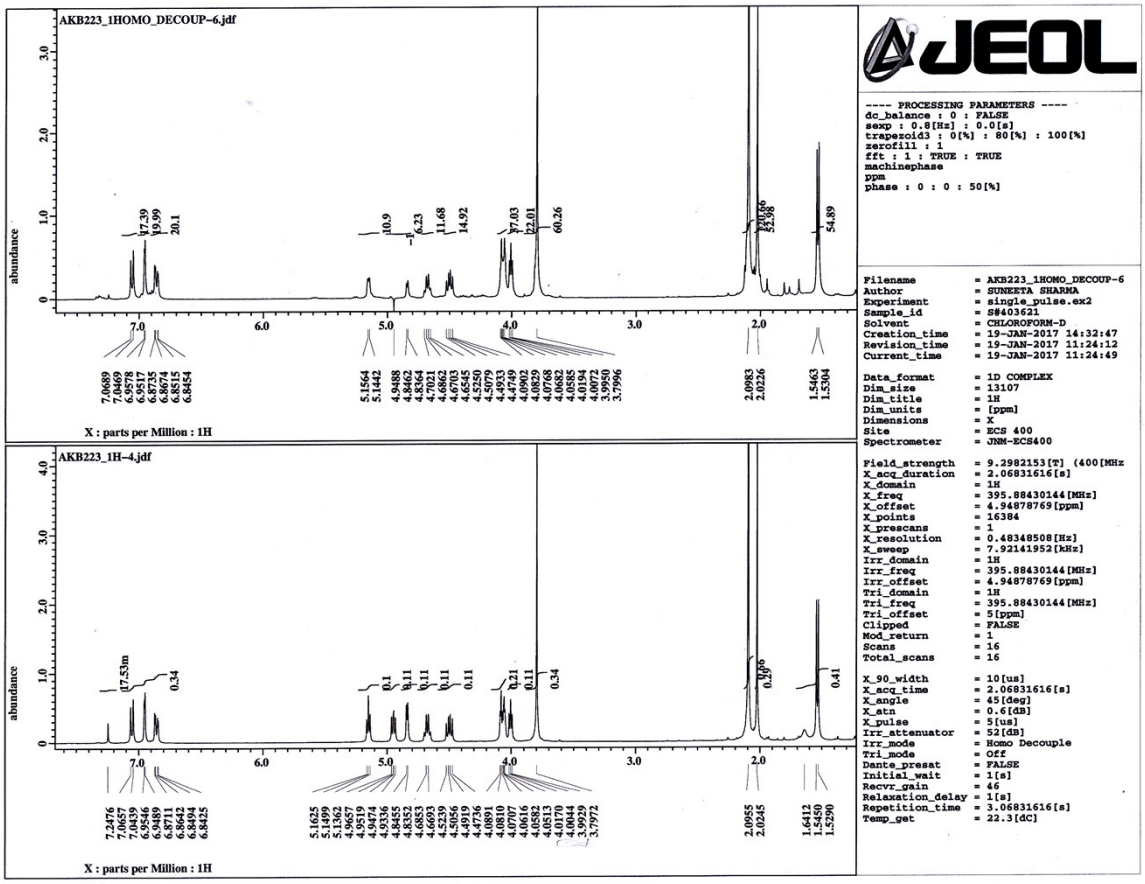
^{1}H-^{1}H COSY NMR spectrum of compound **7**



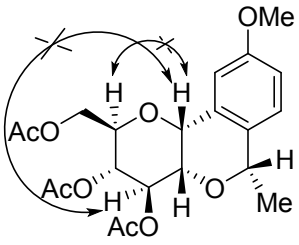


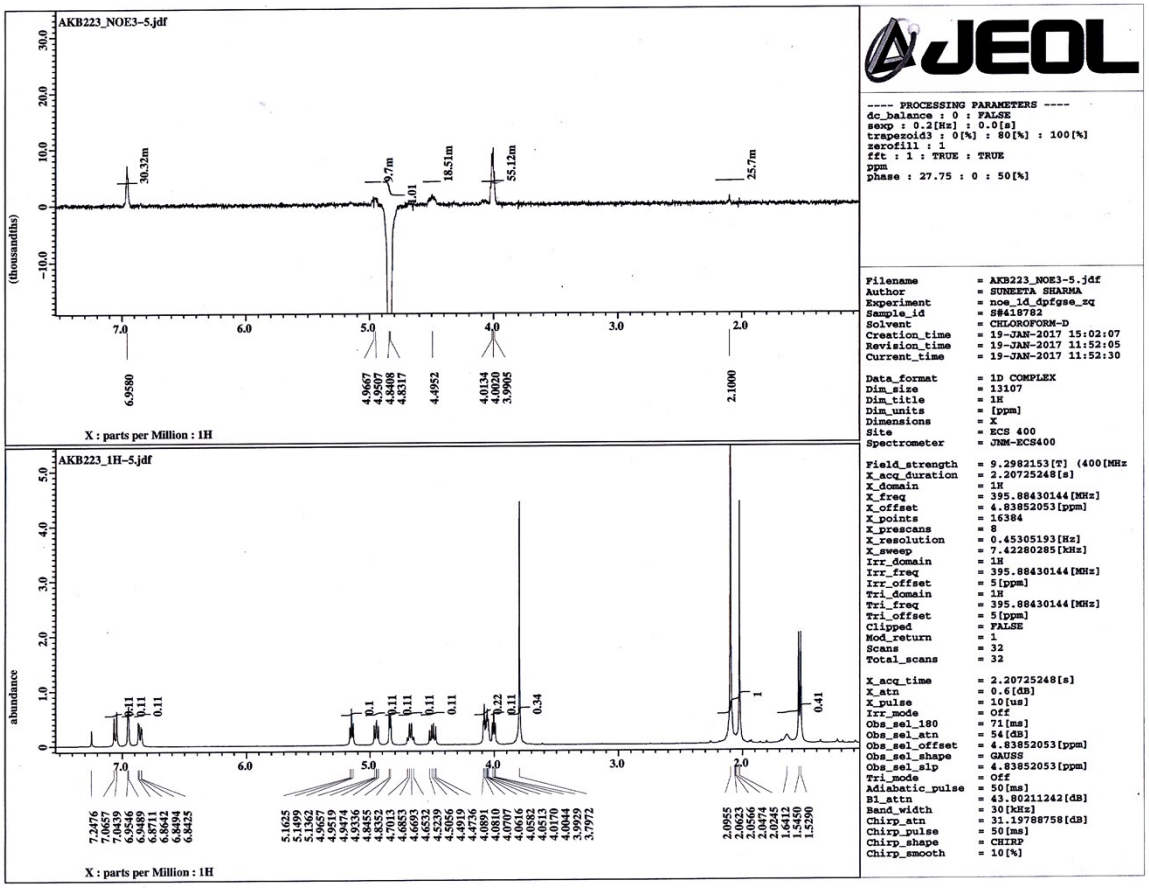
^{1}H-^{1}H COSY NMR spectrum of compound **7**





^{1}H-^{1}H homonuclear decoupling (H-1) NMR spectrum of compound **7**

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3.01
18.51m
55.12m
25.7m
6.9580
4.9667
4.9607
4.8488
4.8317
4.4952
4.0134
4.0020
3.9905
2.1000
X : parts per Million : 1H
AKB223_1H-5.jdf
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0.11
0.11
0.1
0.11
0.11
0.11
0.11
0.22
0.11
0.34
1
0.41
7.2476
7.0657
7.0439
6.9546
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6.8641
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4.0044
3.9929
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1.6412
1.5460
1.5290
X : parts per Million : 1H
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zerofill : 1
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ppm
phase : 27.75 : 0 : 50[%]
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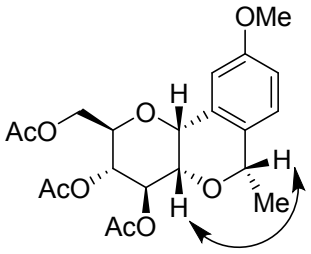
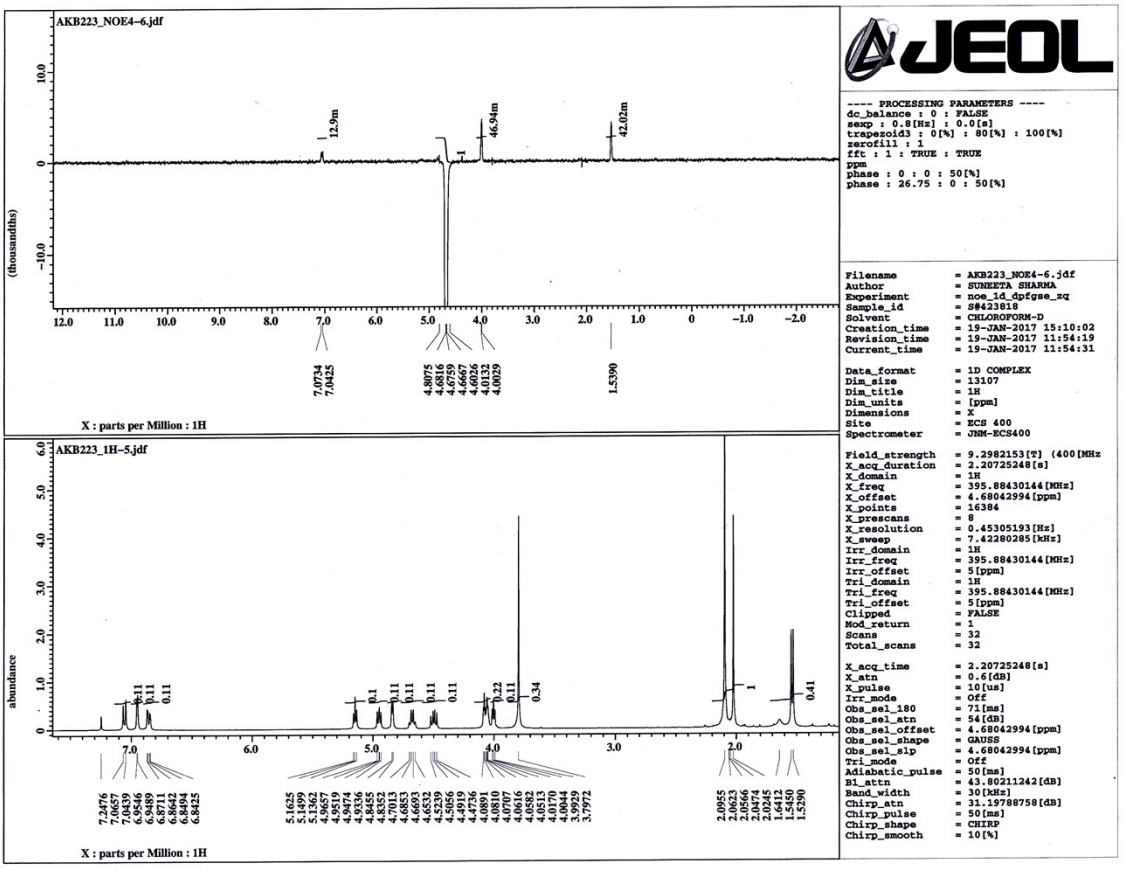
Chirp_smooth = 10[%]

nOe spectrum (irradiation of H1) of compound **7**

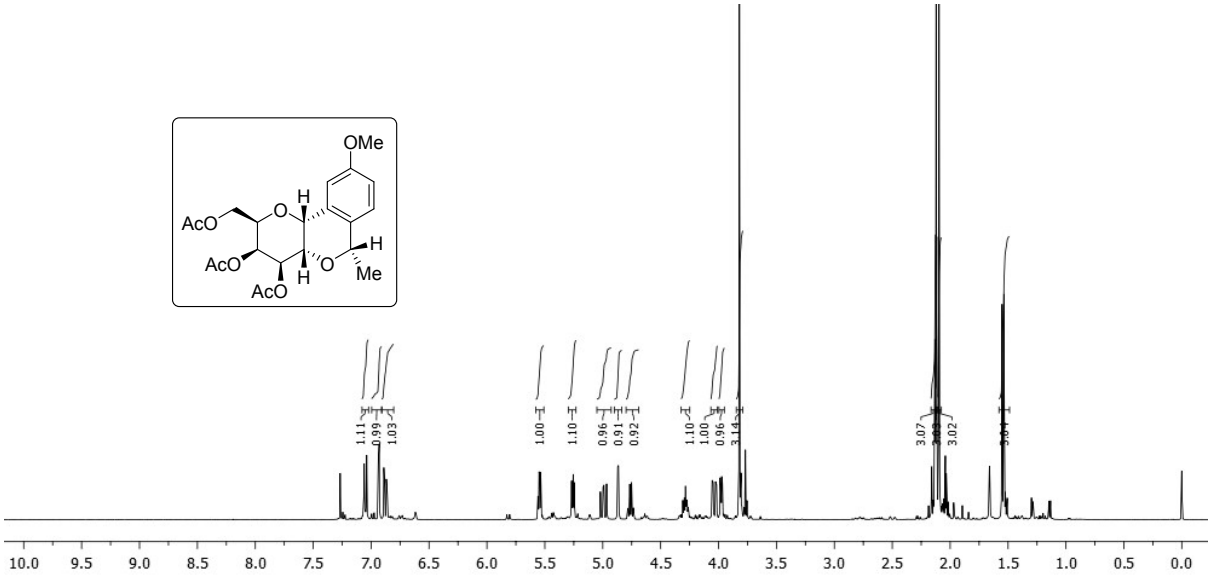
(Irradiation of the H-1 proton at δ 4.84 no enhancement of the H-3 proton at δ 5.14 and H-5 proton at δ 4.05 indicating that H-1 and H-3, H-1 and H-5 are *trans* oriented)



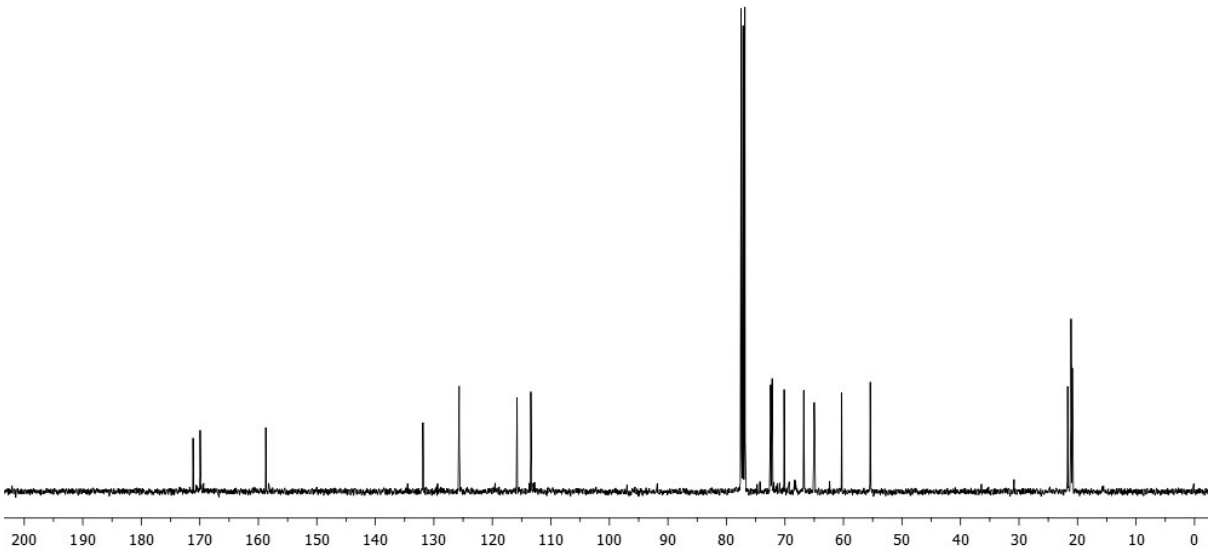


nOe spectrum (irradiation of H7) of compound **7**

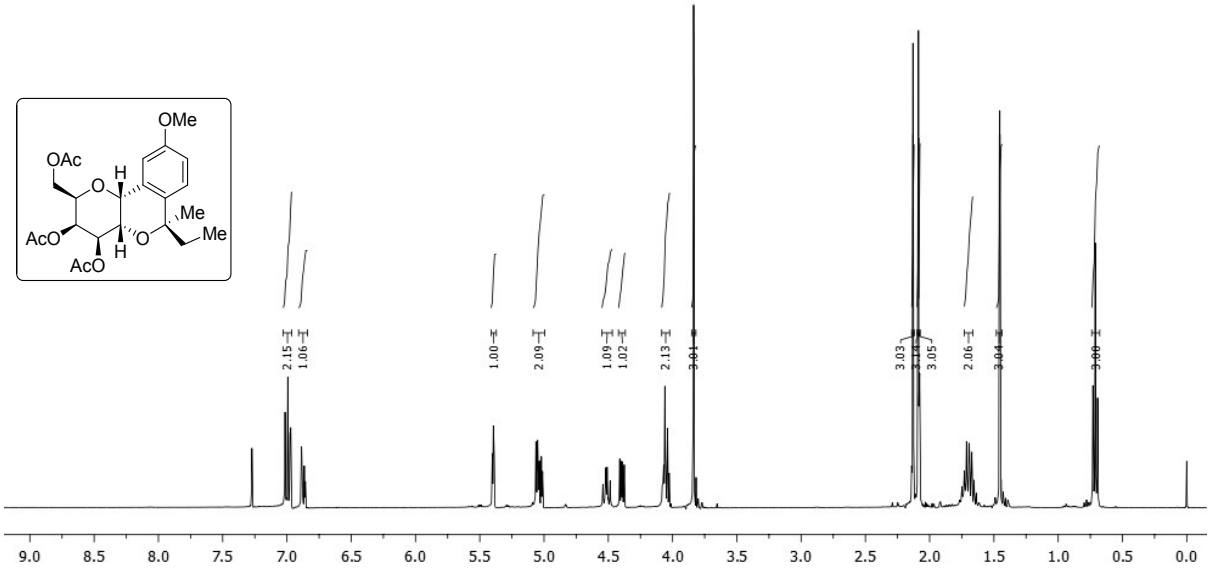
(Irradiation of the H-7 proton at δ 4.67 resulted in an enhancement of the H-2 proton at δ 4.01 indicating that H-7 and H-2 are cis oriented)



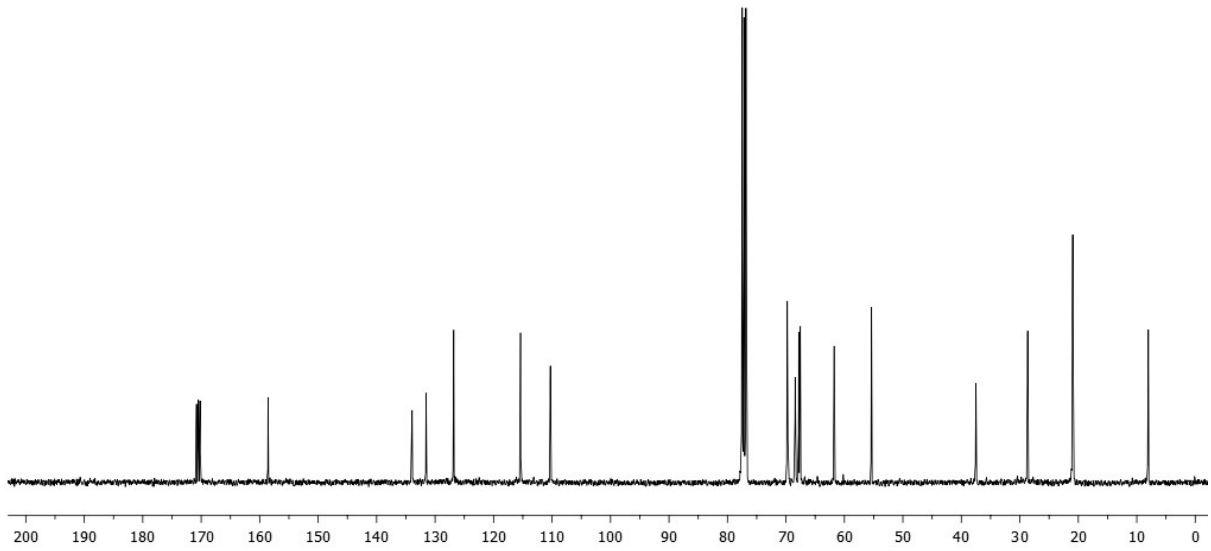
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **9**



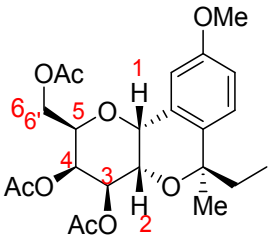
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **9**

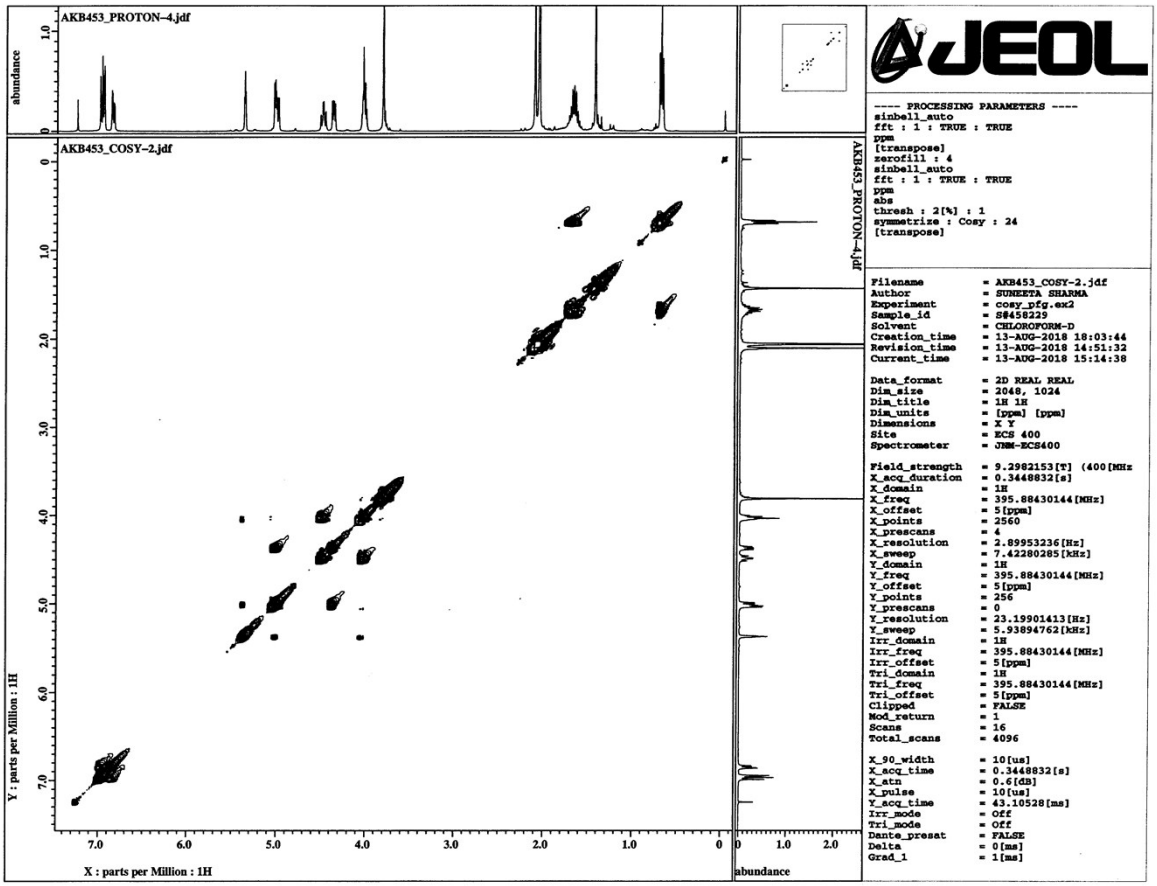


^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **10**

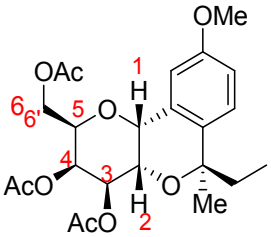


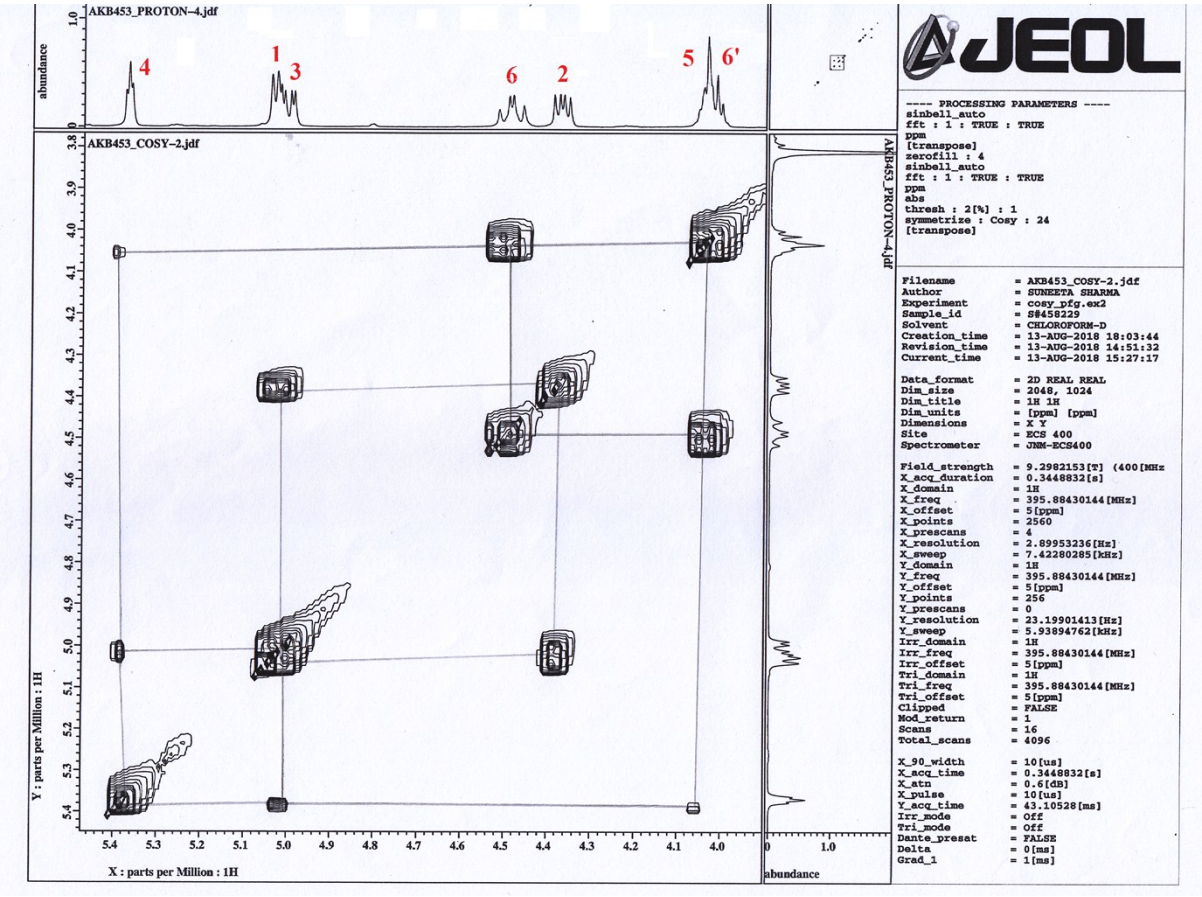
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **10**



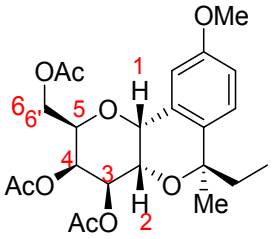


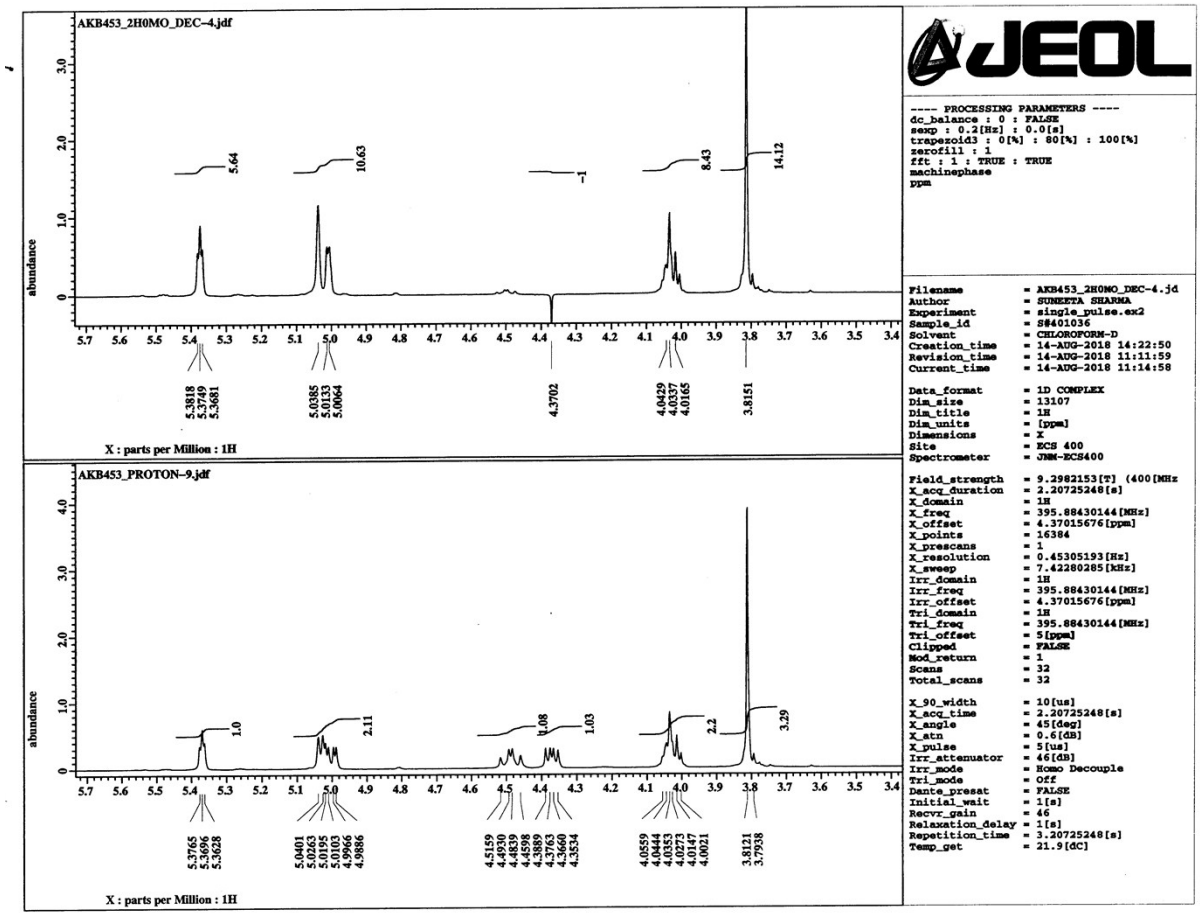
^{1}H-^{1}H COSY NMR spectrum of compound **10**



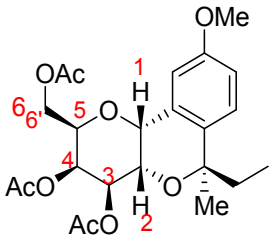


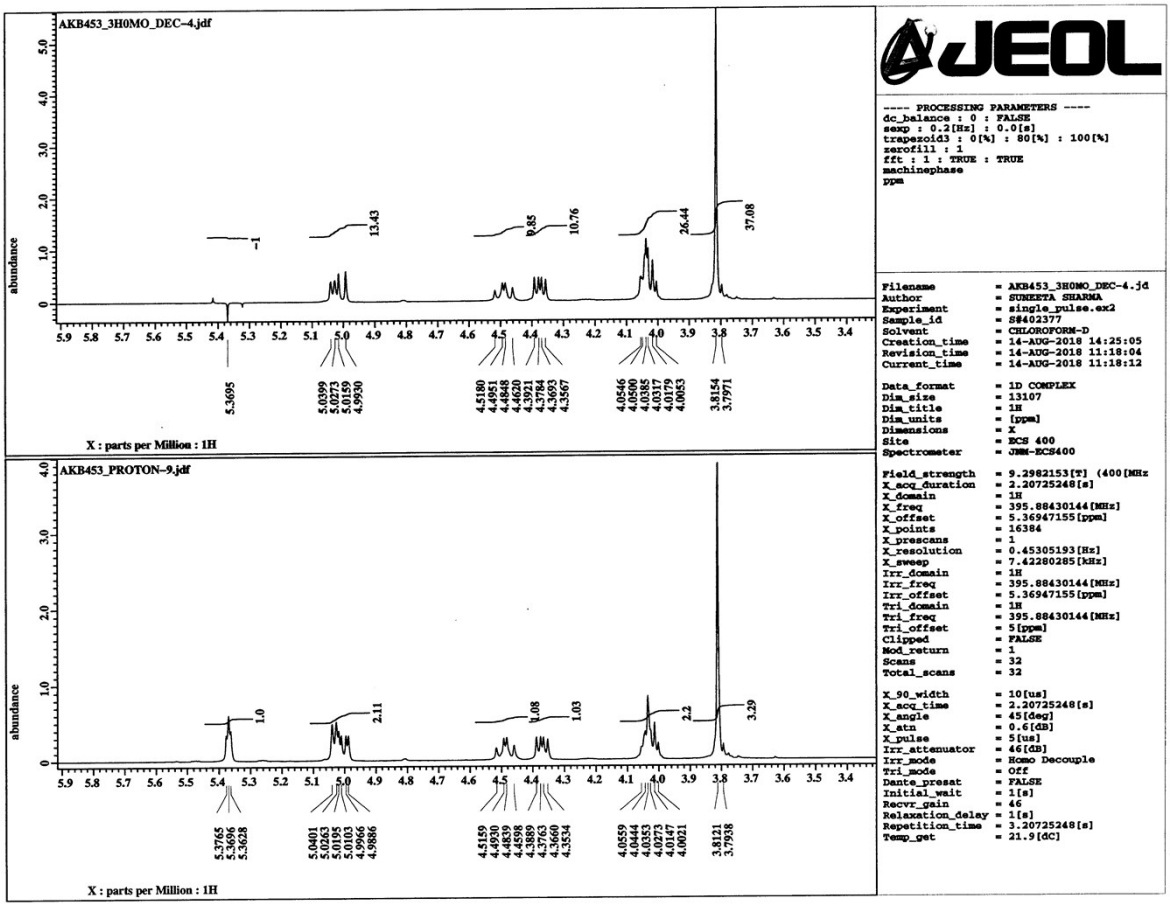
^{1}H-^{1}H COSY NMR spectrum of compound **10**



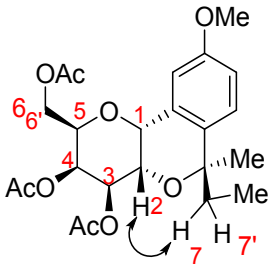


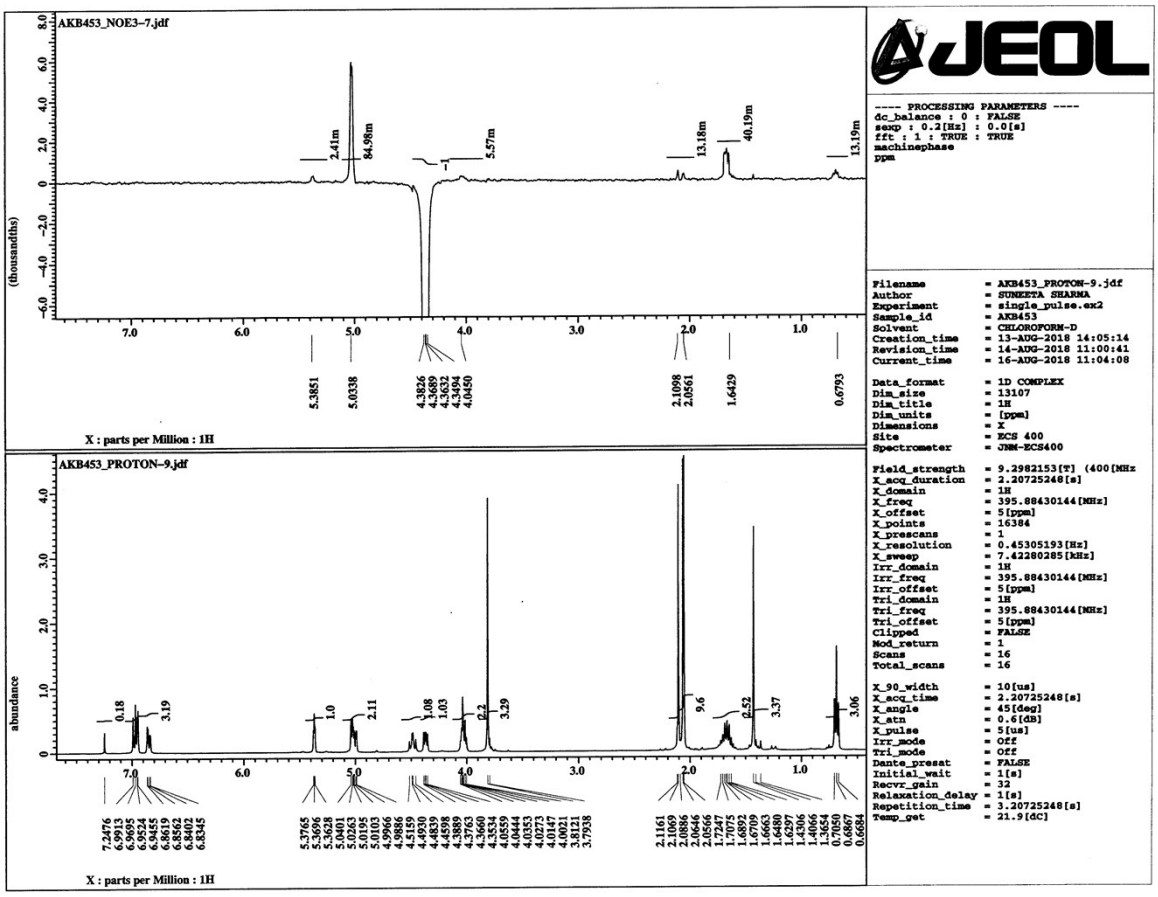
^{1}H-^{1}H homonuclear decoupling (H-2) NMR spectrum of compound **10**





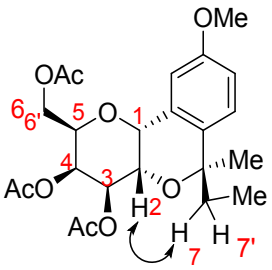
^{1}H-^{1}H homonuclear decoupling (H-4) NMR spectrum of compound **10**

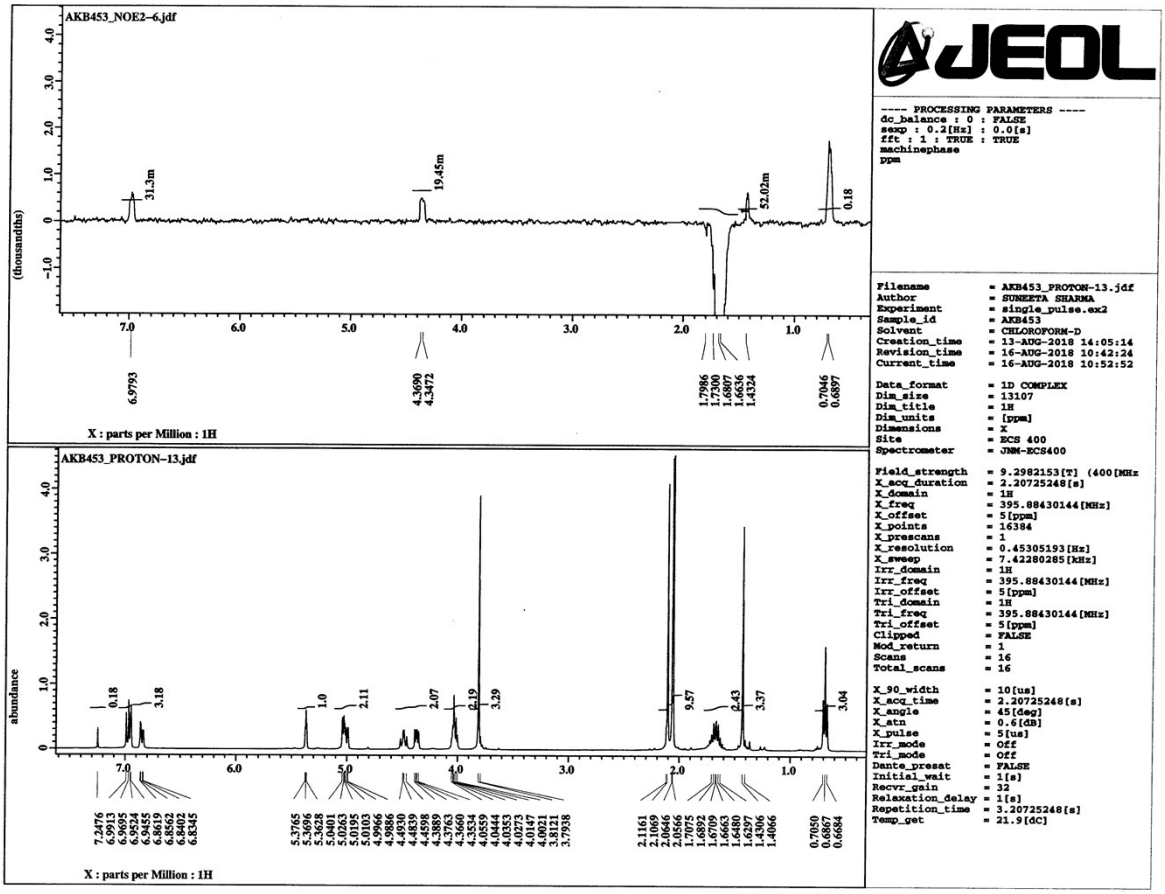




nOe spectrum (irradiation of H2) of compound **10**

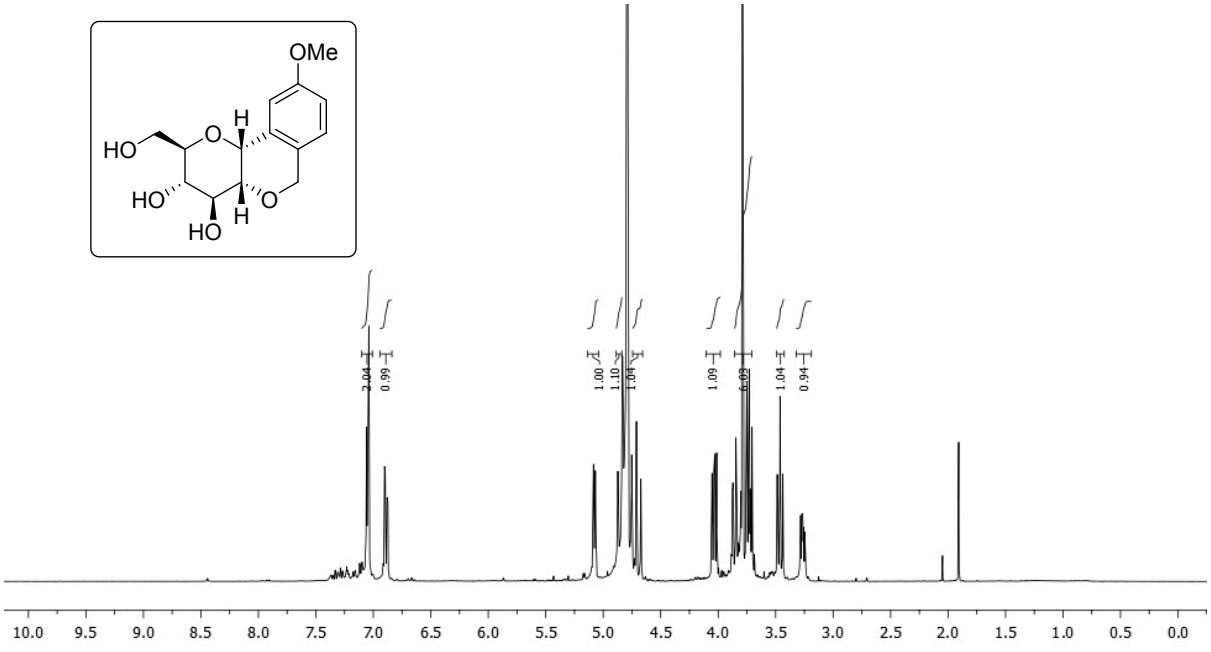
(Irradiation of the H-2 proton at δ 4.34 signal enhancement of H-7 proton at δ 1.64 indicating that H-2 and H-7, are *cis* oriented)



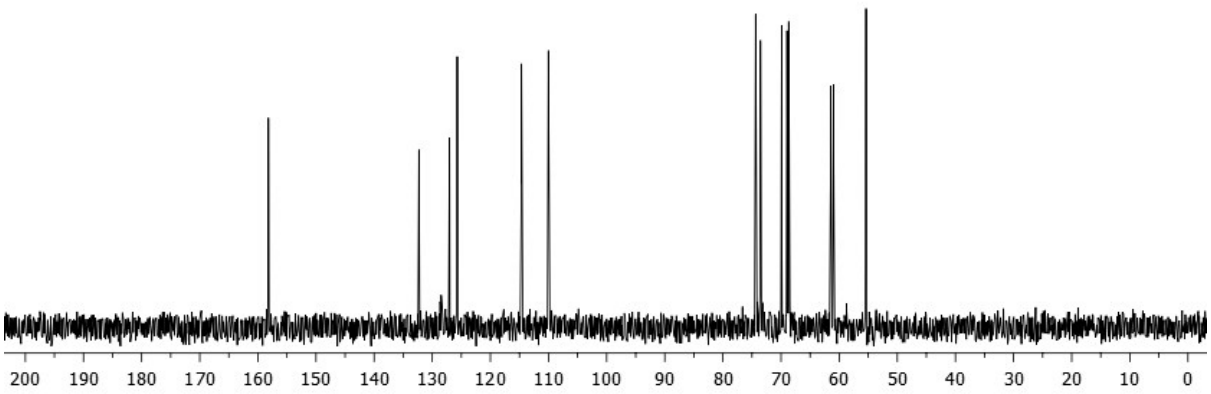


nOe spectrum (irradiation of H7) of compound **10**

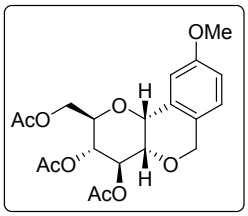
(Irradiation of the H-7 proton at δ 1.68 signal enhancement of H-2 proton at δ 4.35 indicating that H-7 and H-2, are *cis* oriented)

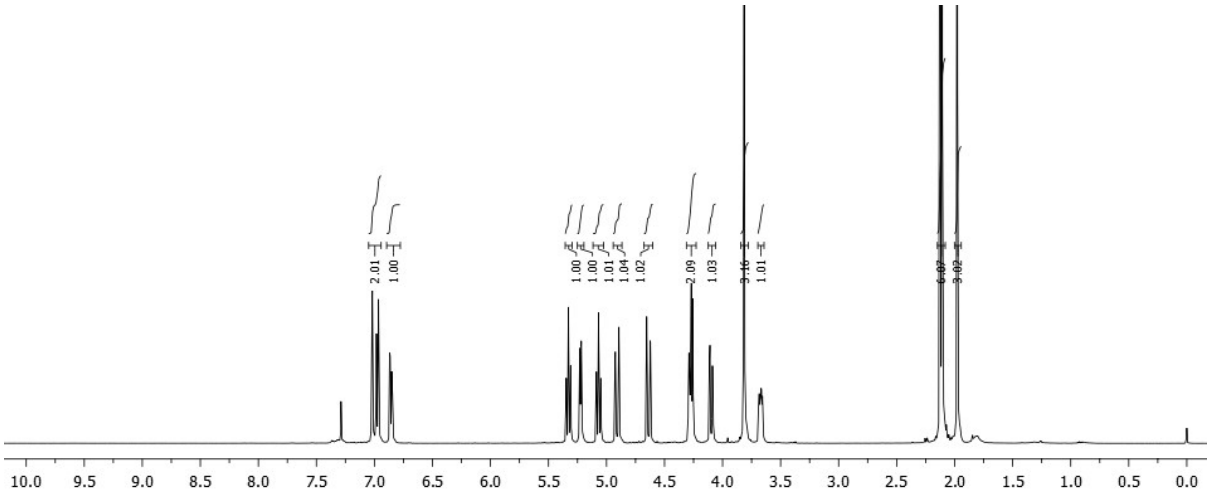


^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **11**

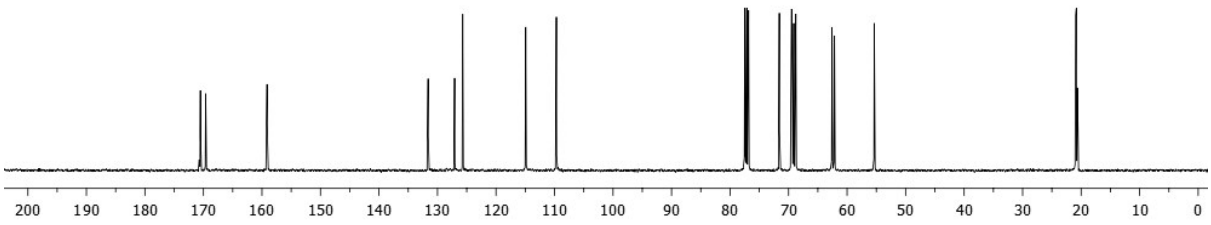


^{13}C NMR spectrum (100 MHz, D_2O) of compound **11**

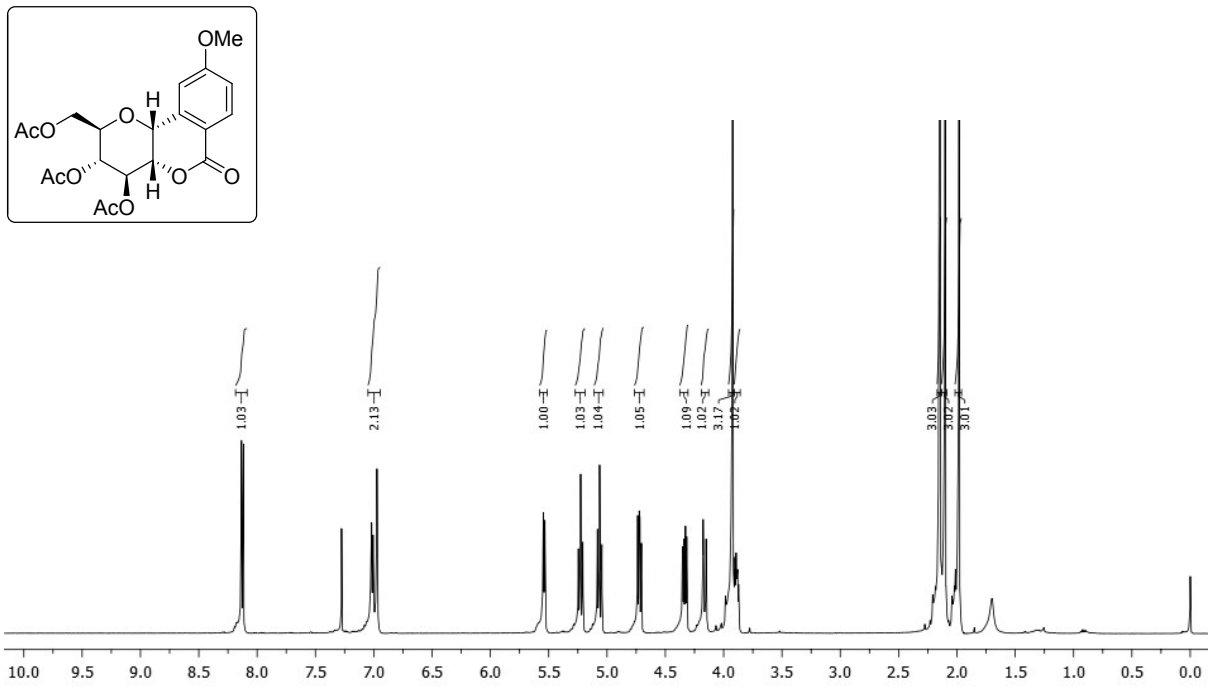




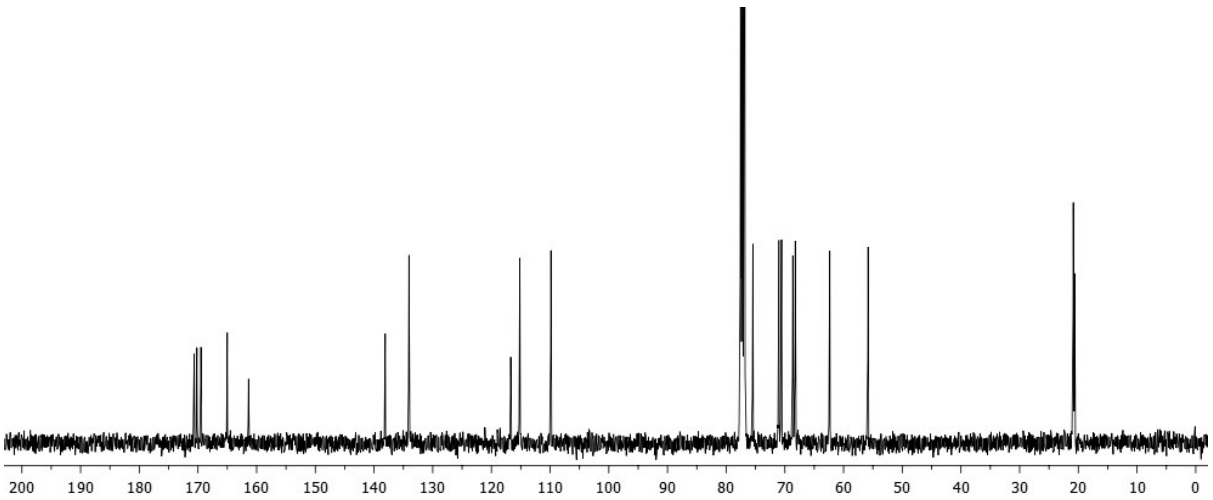
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **12**



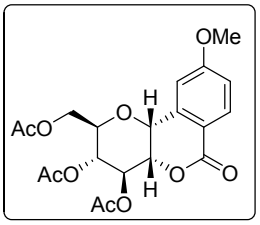
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **12**

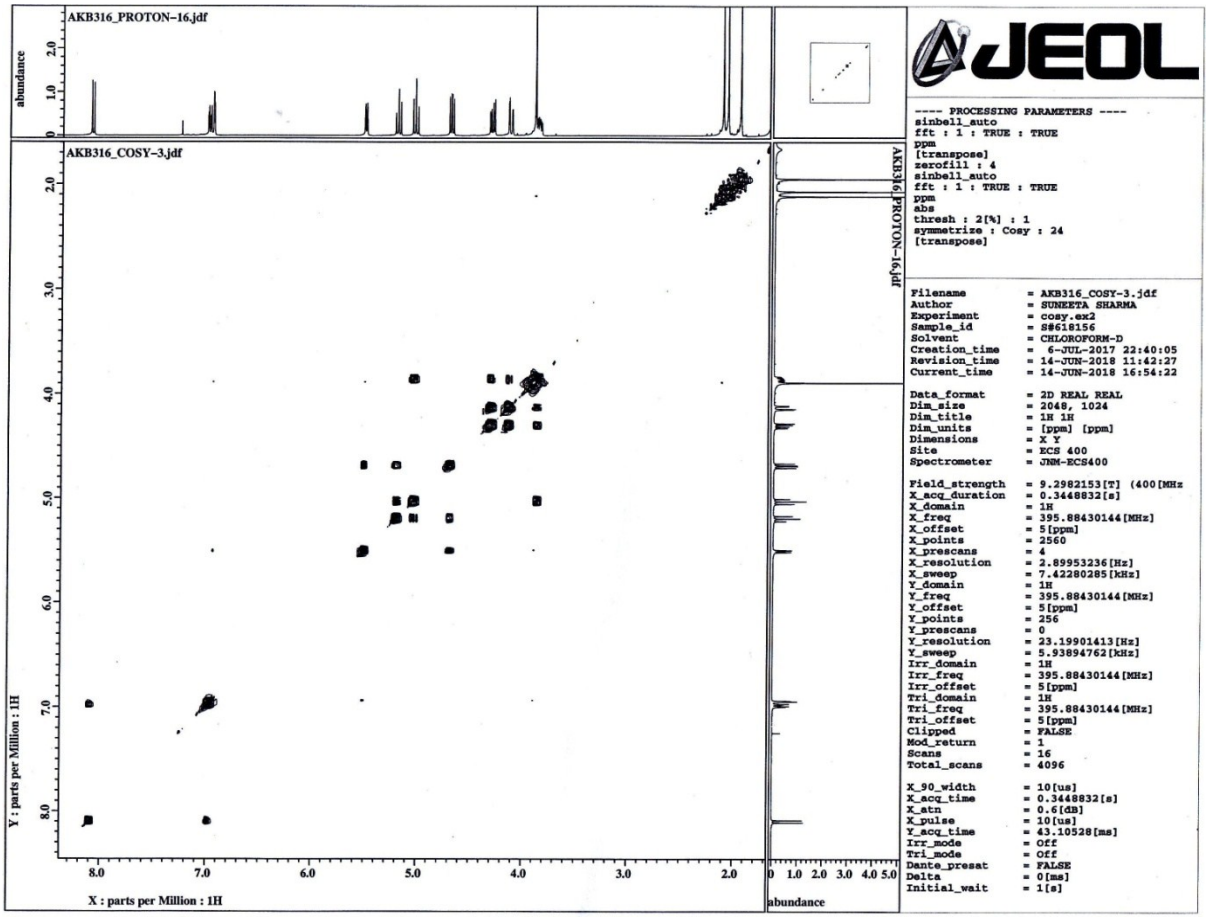


^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **13**

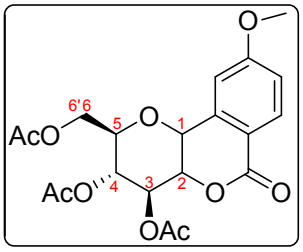


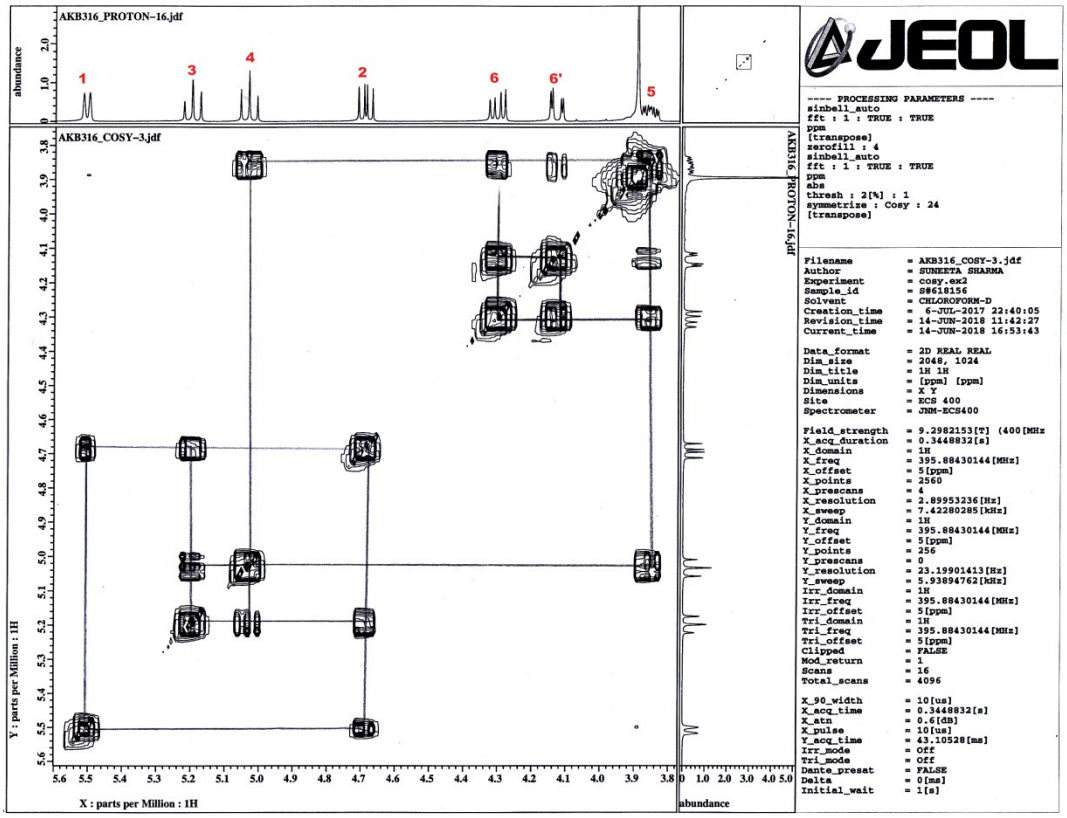
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **13**



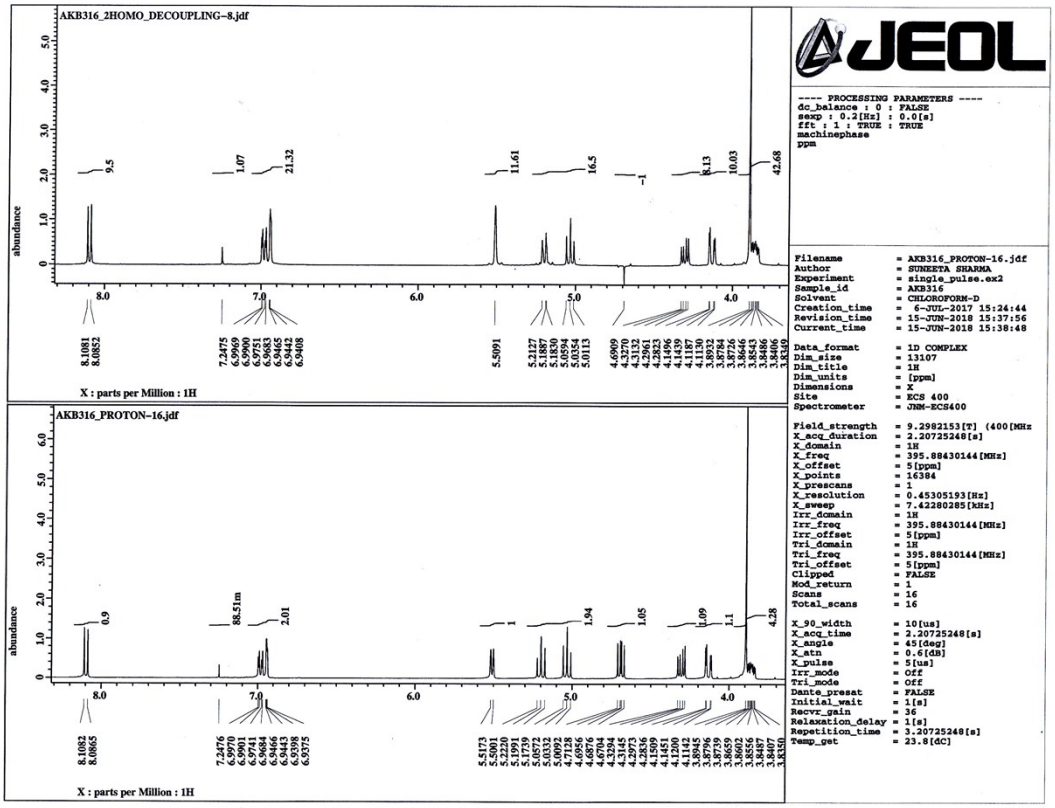


^{1}H-^{1}H COSY NMR spectrum of compound **13**

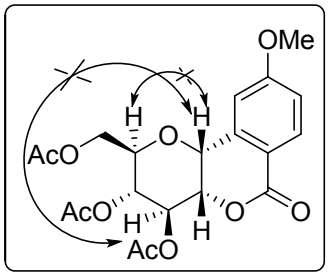


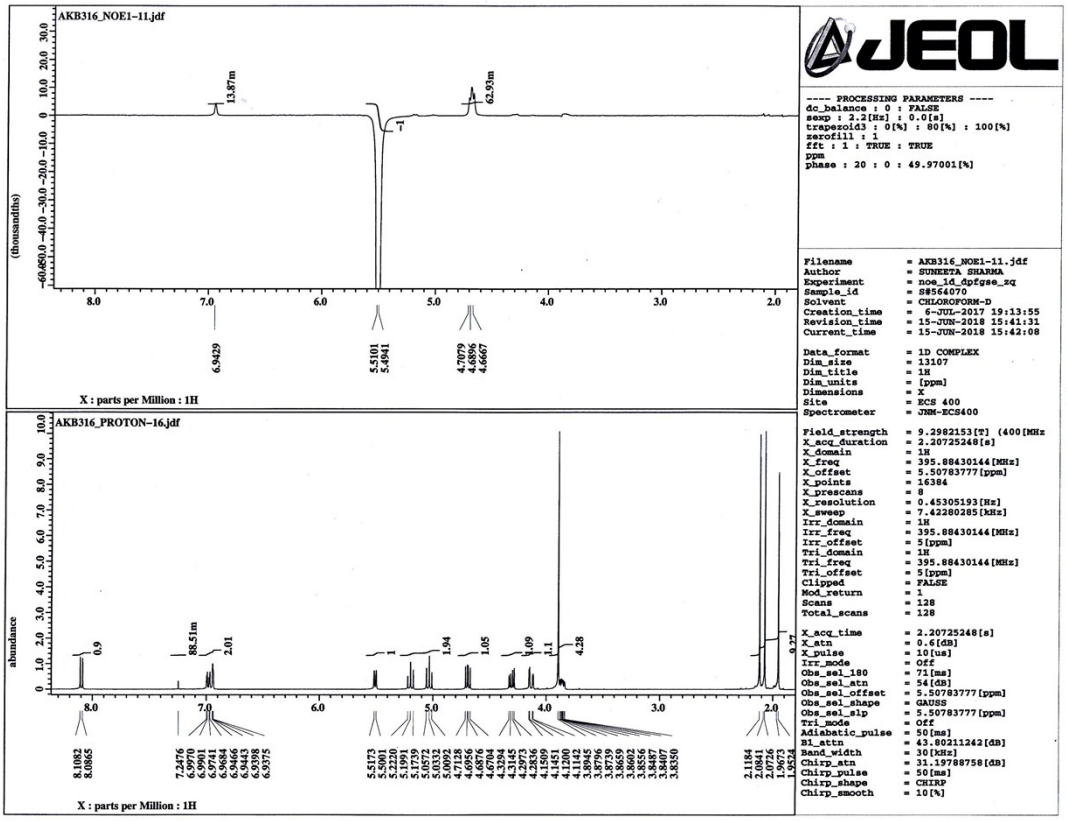


^{1}H-^{1}H COSY NMR spectrum of compound **13**



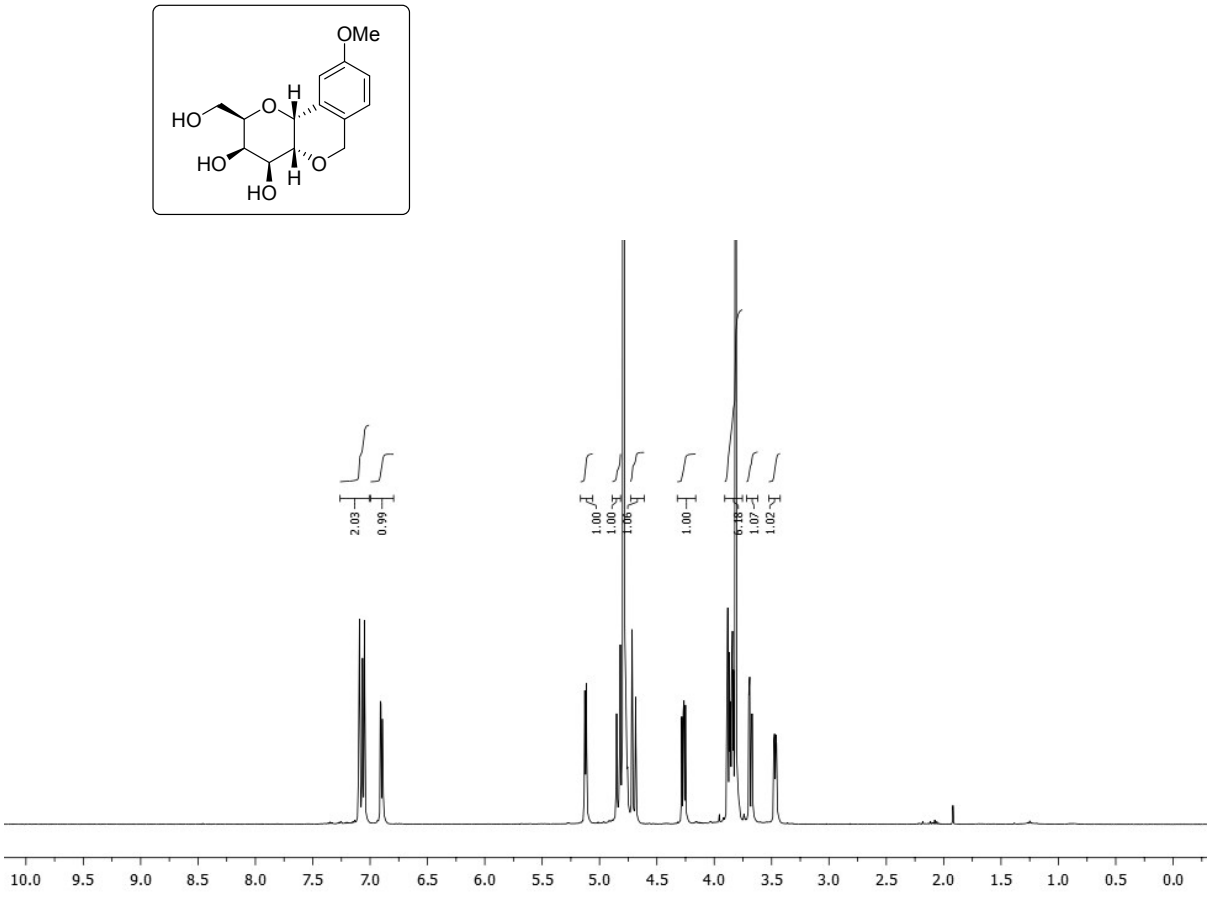
^{1}H-^{1}H homonuclear decoupling (H-1) NMR spectrum of compound **13**



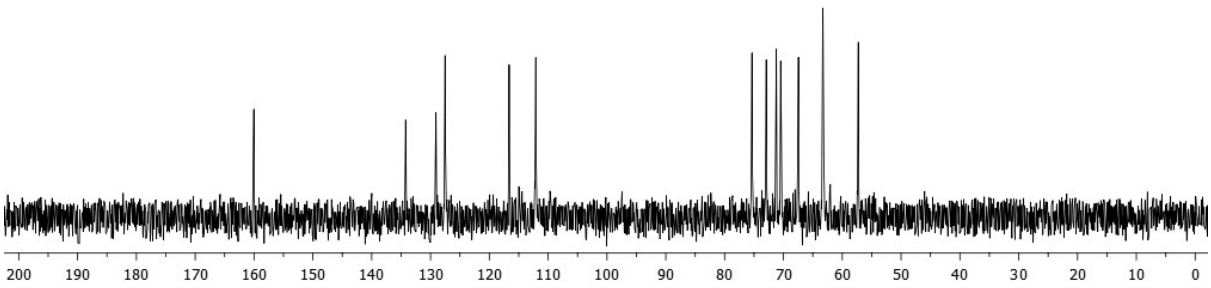


nOe spectrum (irradiation of H1) of compound **13**

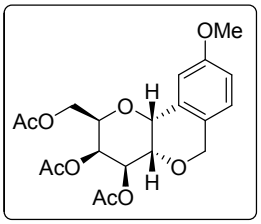
(Irradiation of the H-1 proton at δ 5.51 no signal enhancement of H-3 proton at δ 5.19 and H-5 proton at δ 3.85 indicating that H-1 and H-3, H-1 and H-5 are trans oriented)

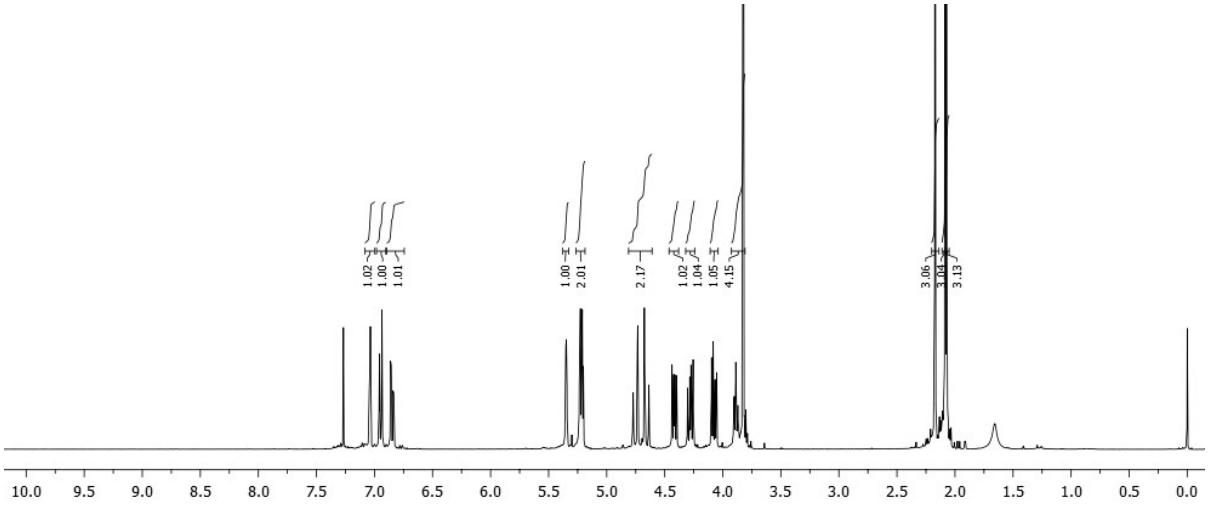


^{1}H NMR spectrum (500 MHz, $CDCl_3$) of compound **14**

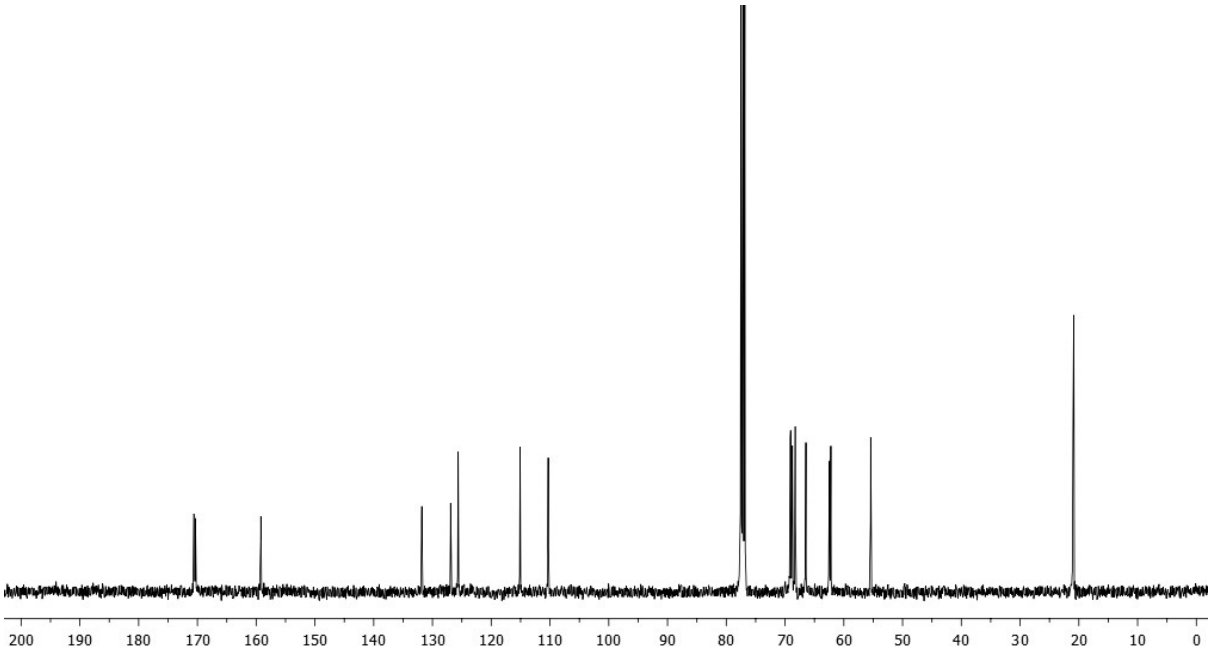


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **14**

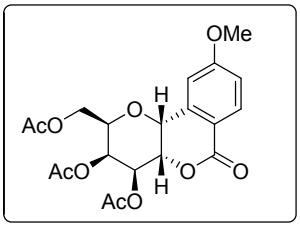


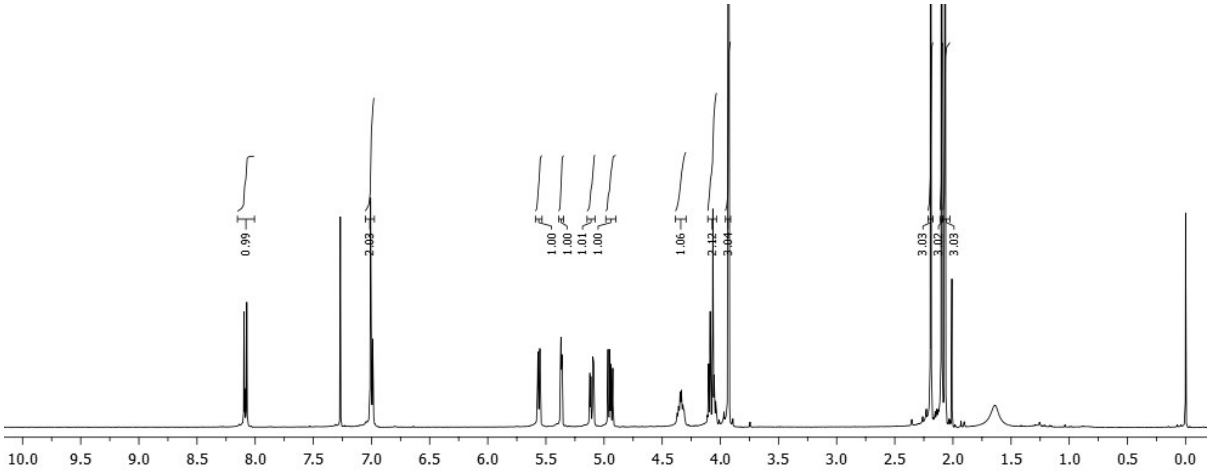


^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **15**

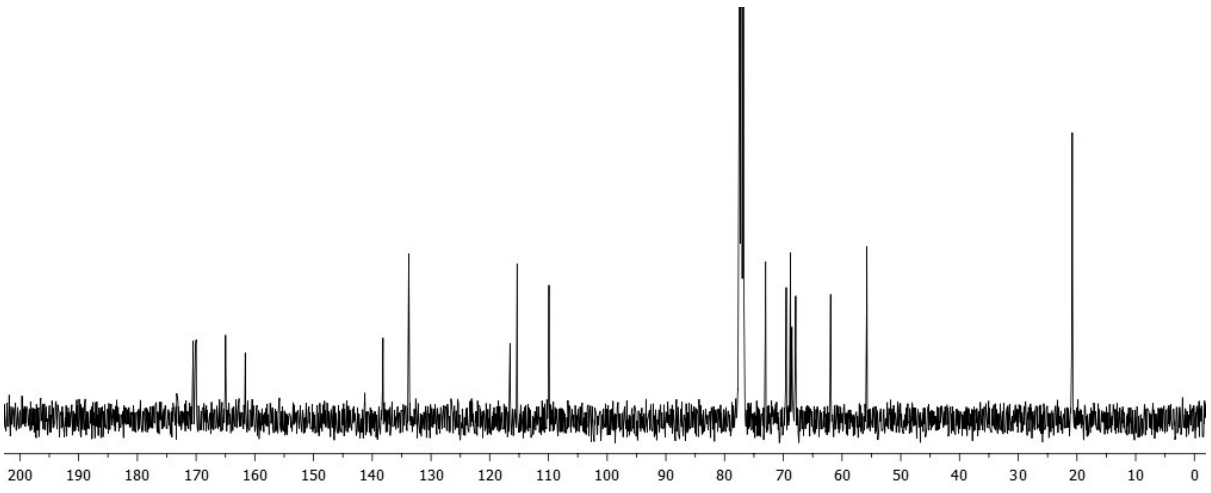


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **15**

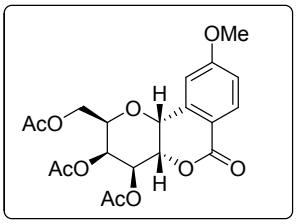


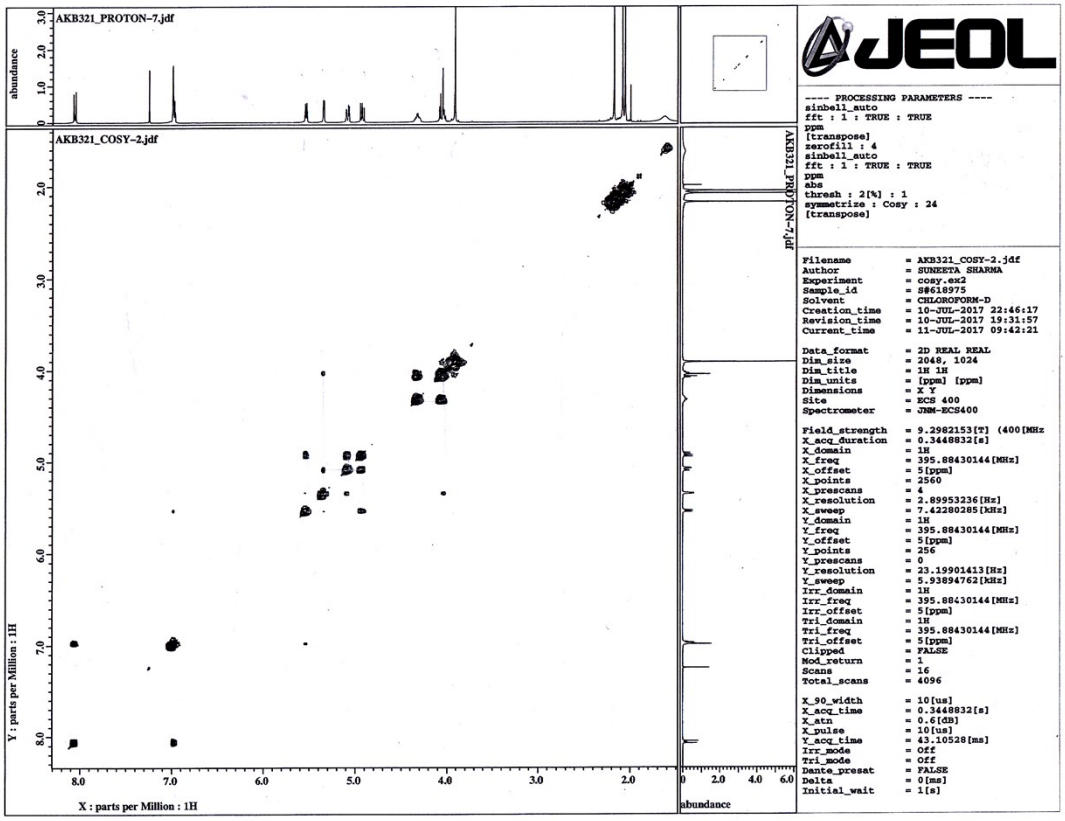


^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **16**

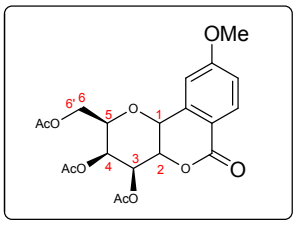


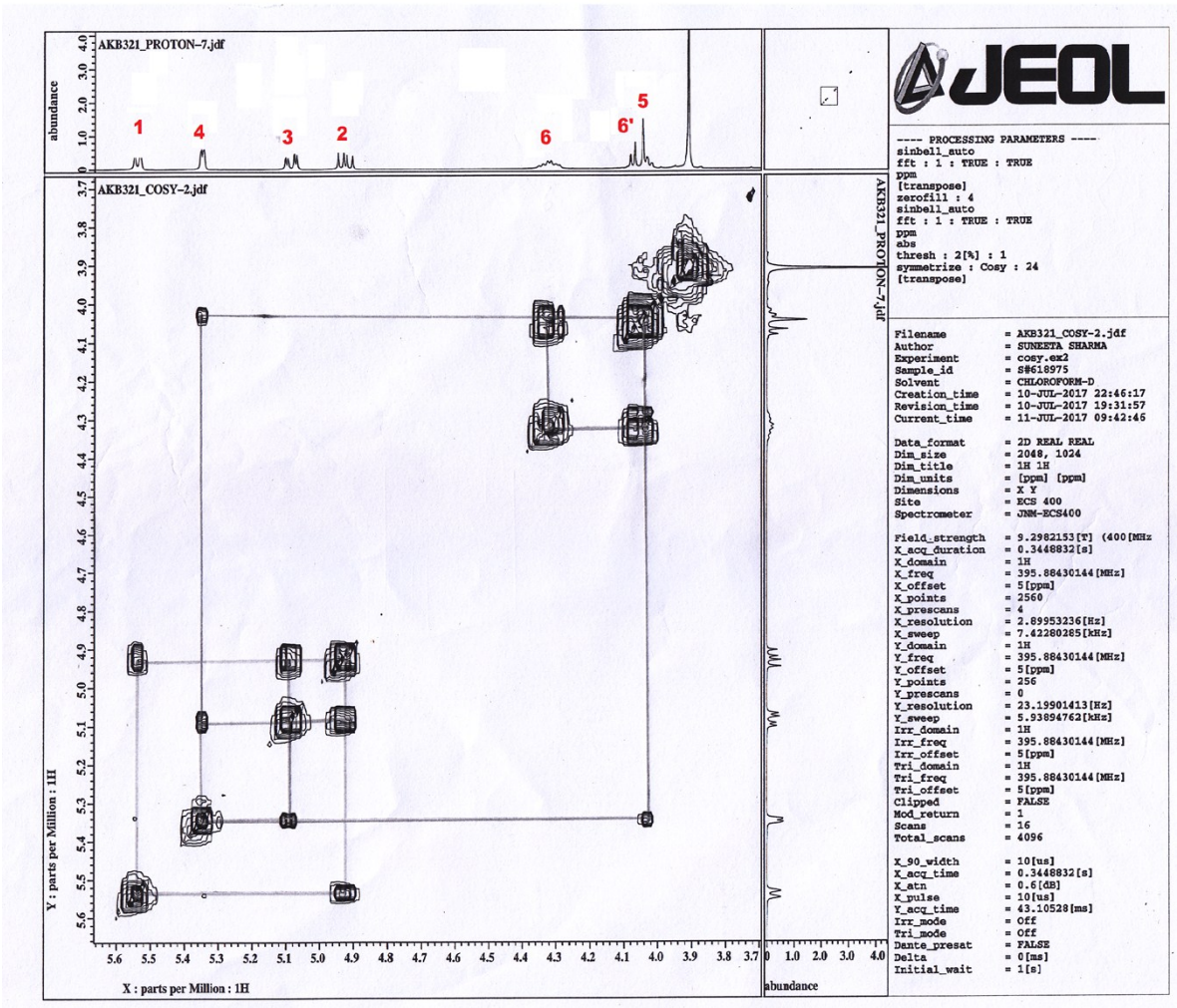
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **16**



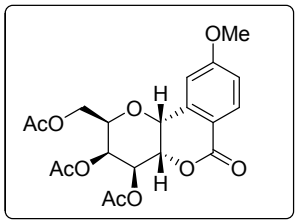


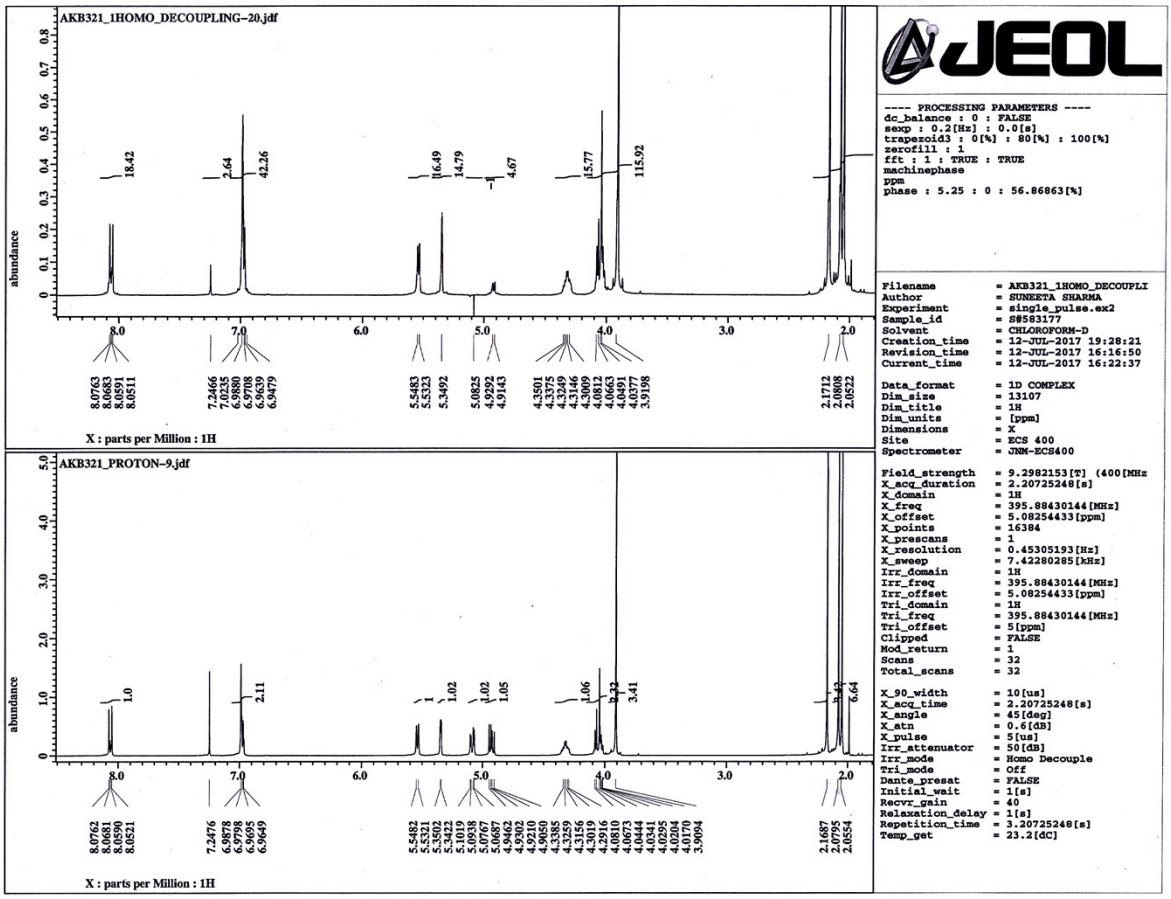
^{1}H-^{1}H COSY NMR spectrum of compound **16**



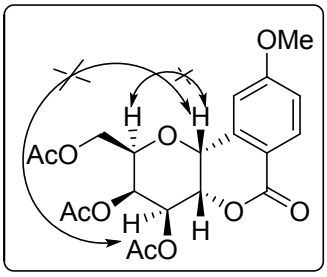


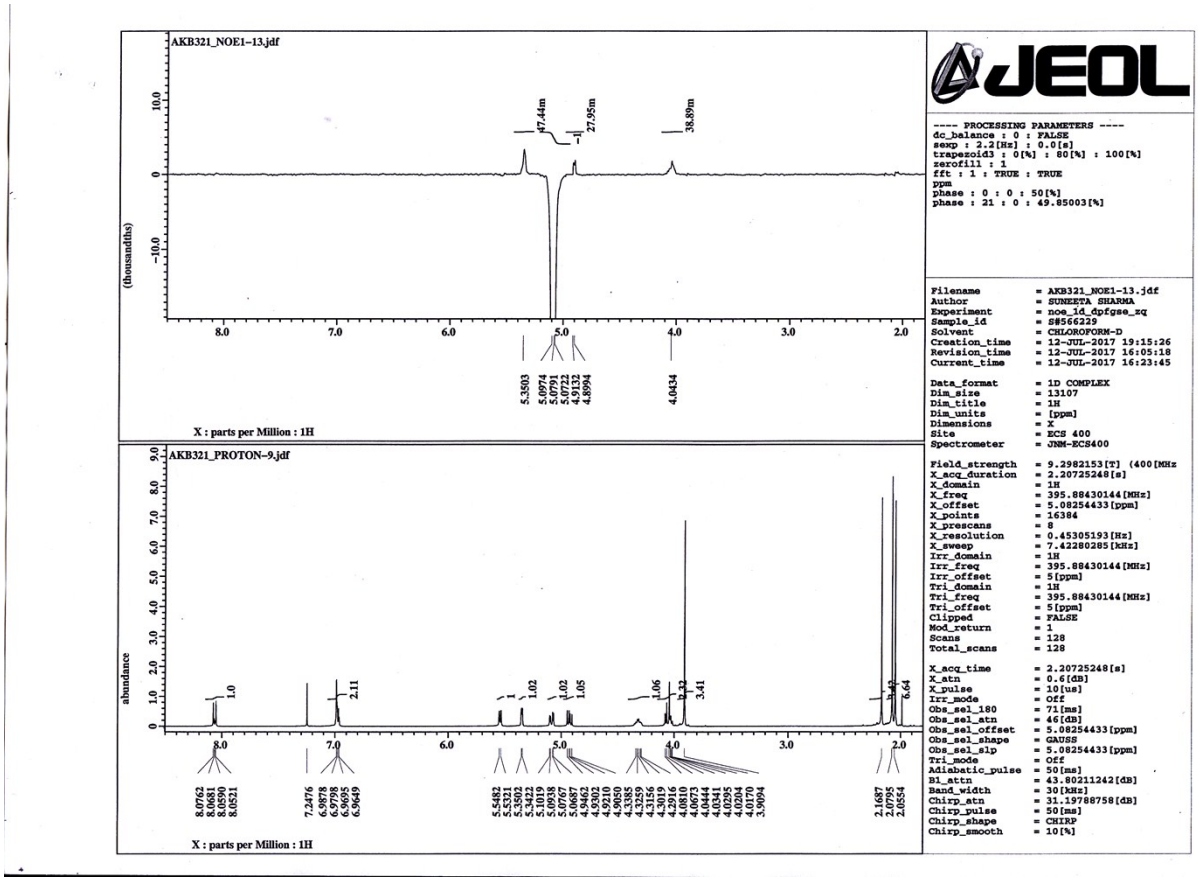
^{1}H-^{1}H COSY NMR spectrum of compound **16**





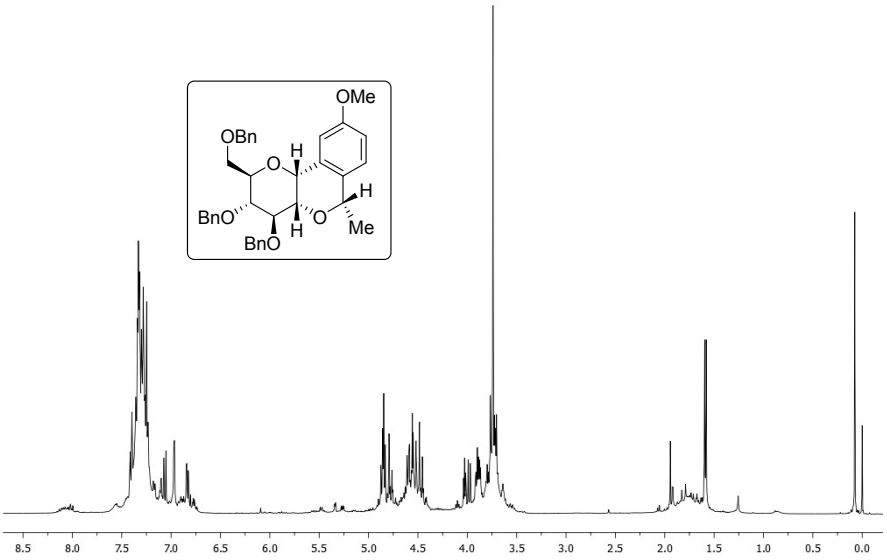
^{1}H-^{1}H homonuclear decoupling (H-1) NMR spectrum of compound **16**





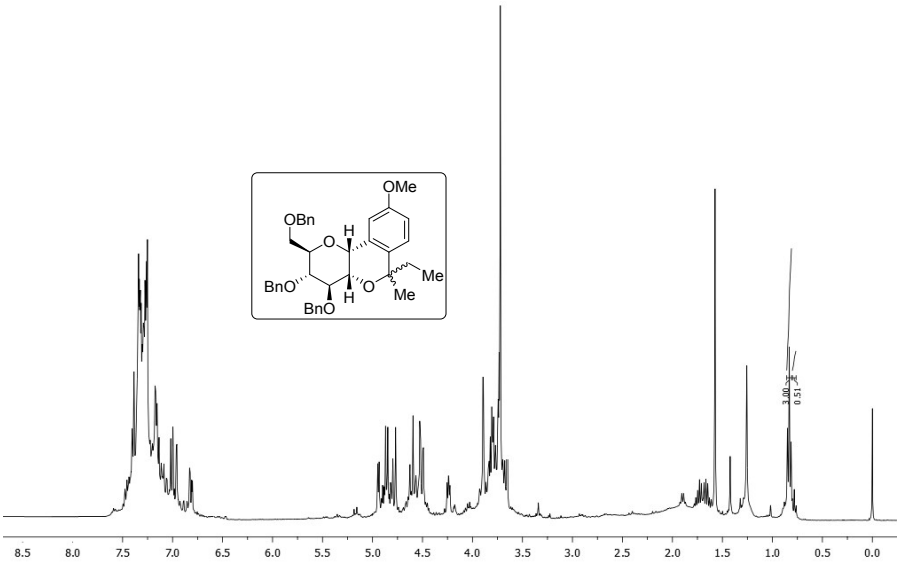
nOe spectrum (irradiation of H3) of compound **16**

(Irradiation of the H-3 proton at δ 5.07 no enhancement of H-1 proton at δ 5.54 and H-5 proton at δ 4.01 indicating that H-1 and H-3, H-1 and H-1 and H-5 are trans oriented)



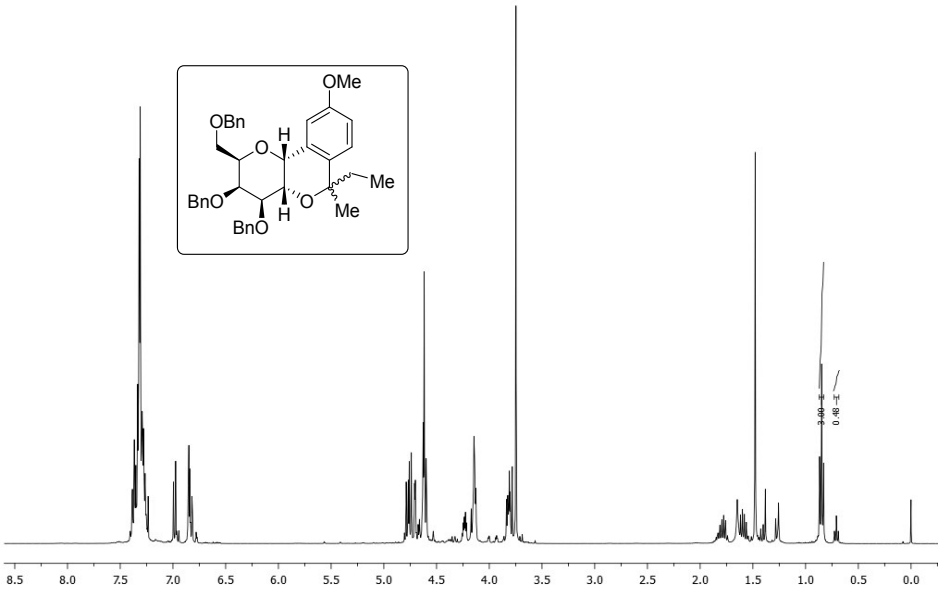
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of crude compound **3a**

(Filtered through short silica gel column)



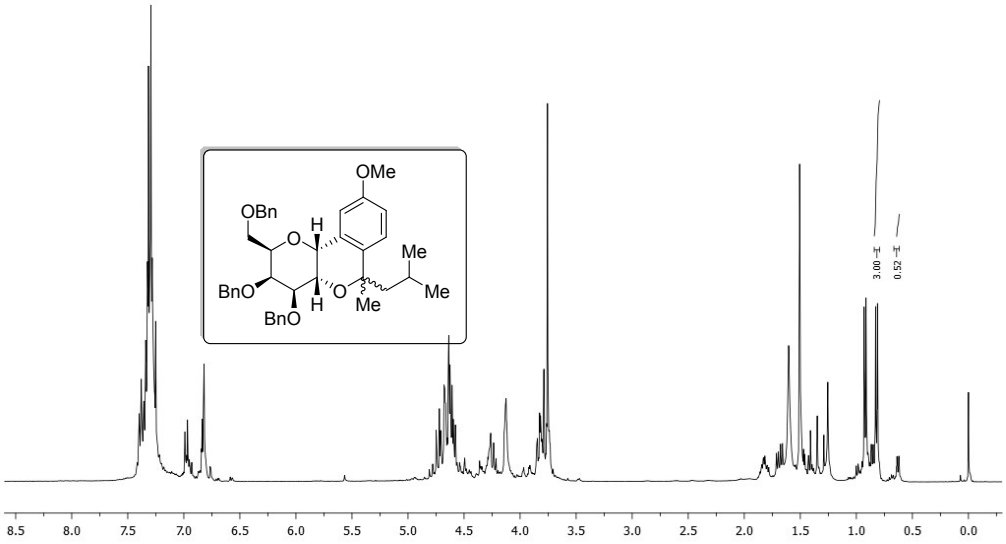
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of crude compound **3l**

(Filtered through short silica gel column)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of crude compound **5l** (**5l1** and **5l2**)

(Filtered through short silica gel column)



^{1}H NMR spectrum (400 MHz, $CDCl_3$) of crude compound **5m**

(Filtered through short silica gel column)

5. Copies of selected HPLC chromatograms

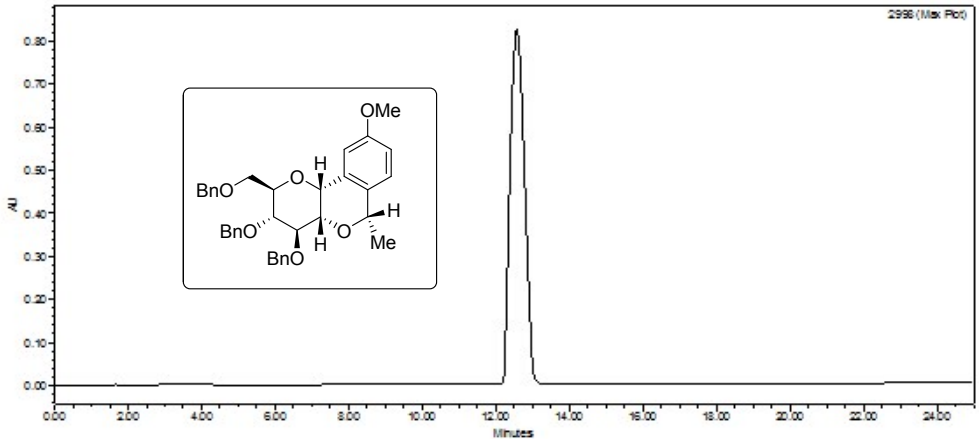


Figure 1. HPLC chromatogram of compound **3a**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 12.159 min

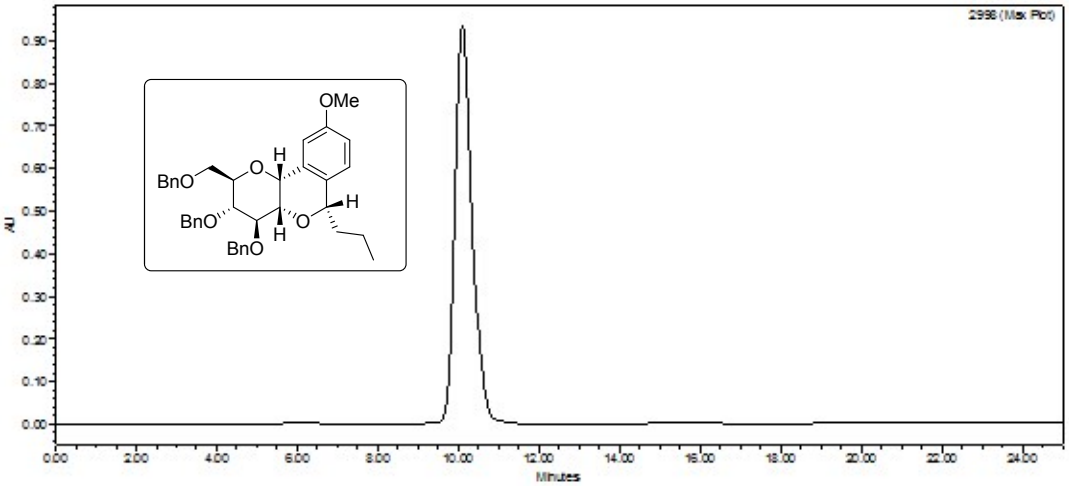


Figure 2. HPLC chromatogram of compound **3b**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 10.069 min

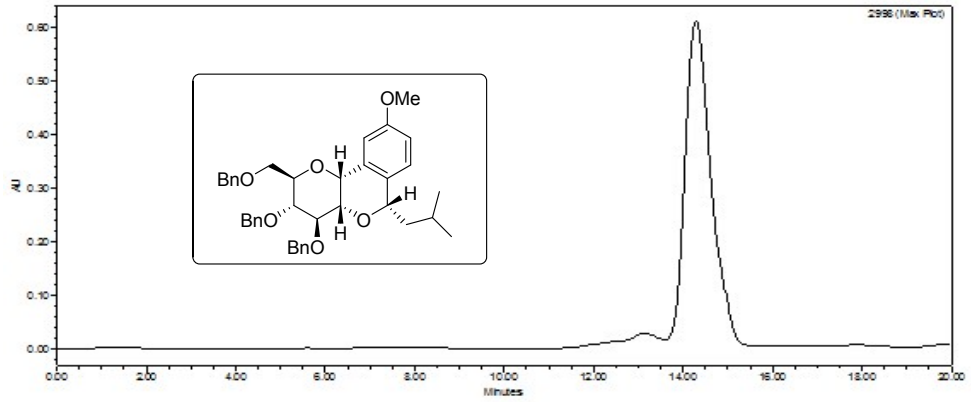


Figure 3. HPLC chromatogram of compound **3c**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 20 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 14.527 min

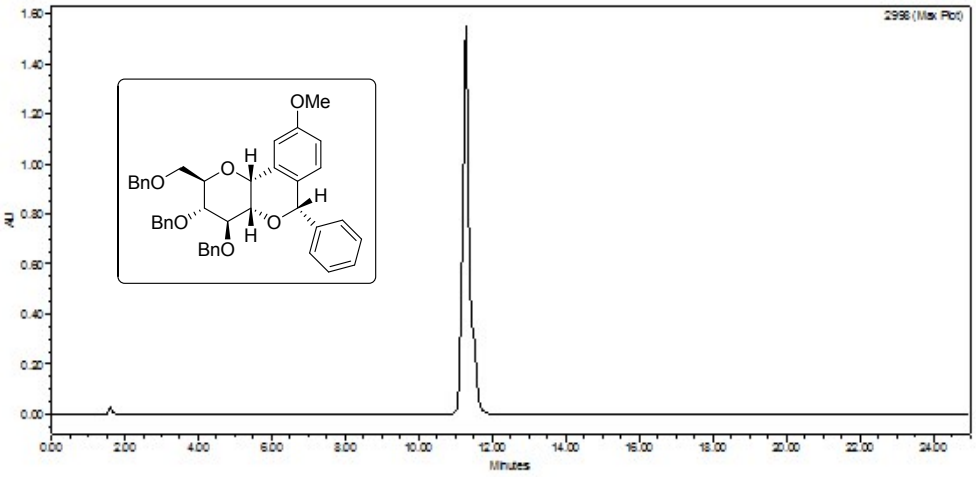


Figure 4. HPLC chromatogram of compound **3d**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 2.451

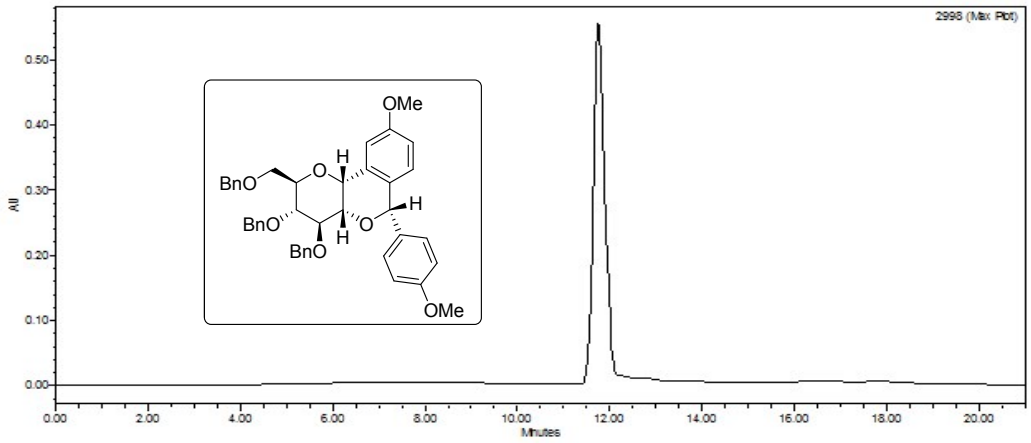


Figure 5. HPLC chromatogram of compound **3e**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 11.947 min

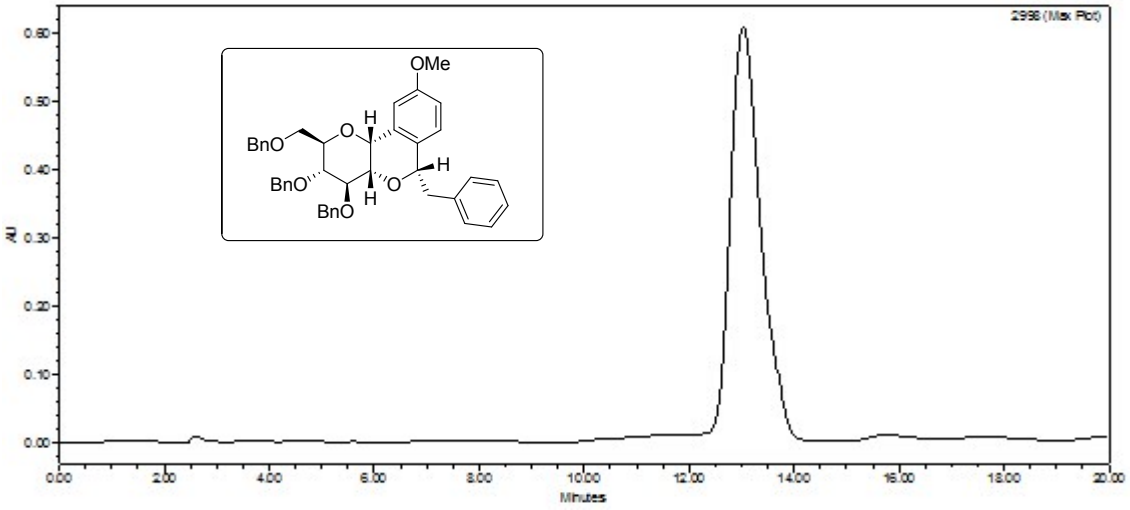


Figure 6. HPLC chromatogram of compound **3f**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 20 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 13.147 min

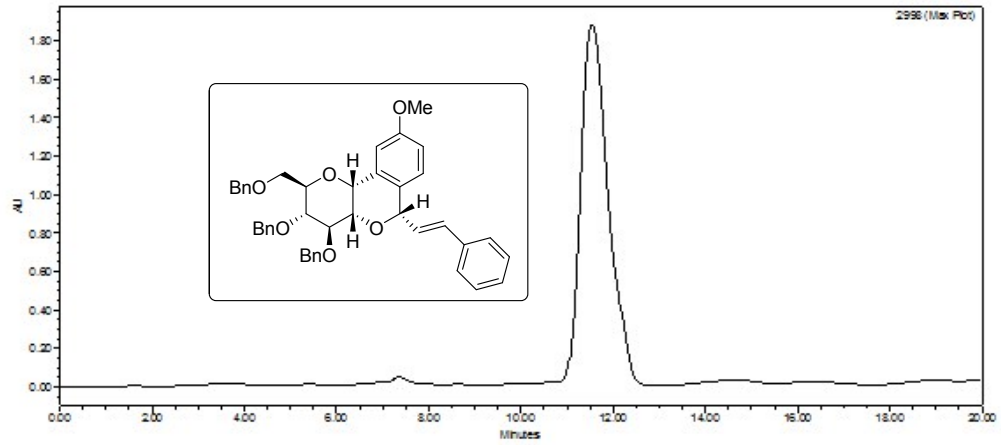


Figure 7. HPLC chromatogram of compound **3g**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 20 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 11.347 min

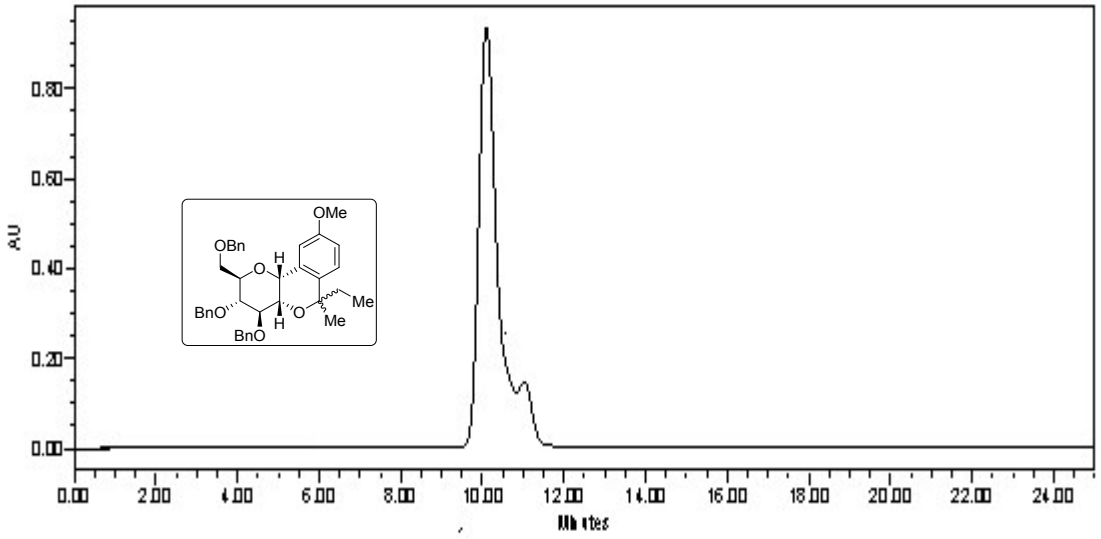


Figure 8. HPLC chromatogram of compound **3l**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time for the mazor isomer: 10.047 min

Retention Time for the minor isomer: 11.017 min

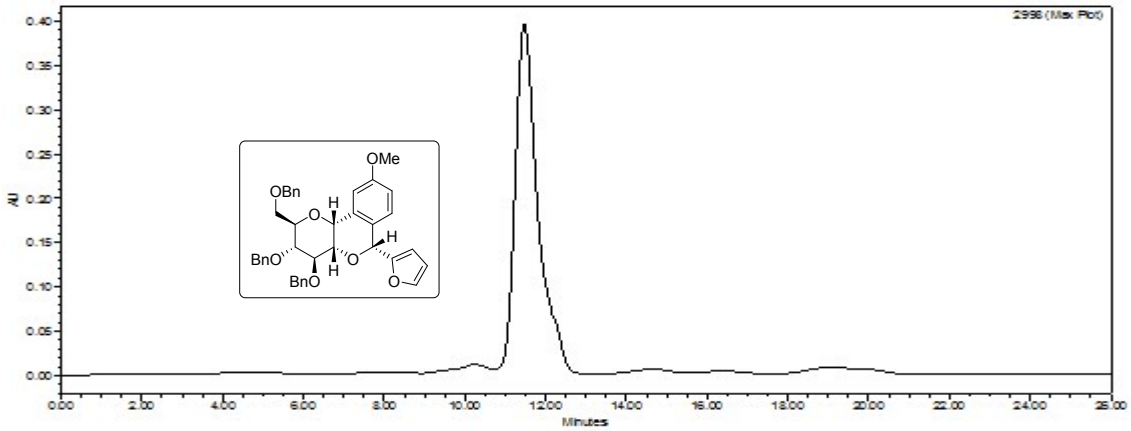


Figure 9. HPLC chromatogram of compound **3m**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 11.857 min

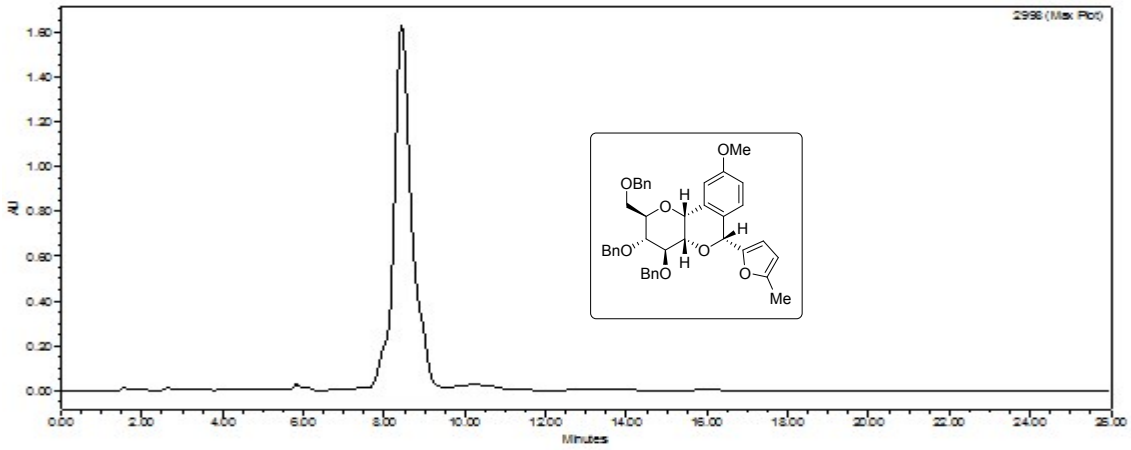


Figure 10. HPLC chromatogram of compound **3n**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 8.017 min

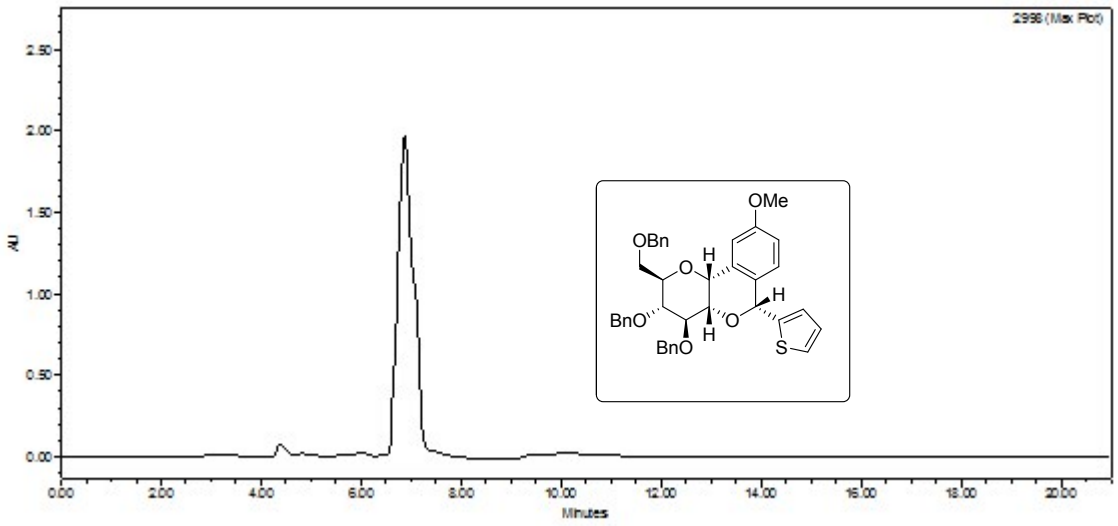


Figure 11. HPLC chromatogram of compound **3o**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 6.501 min

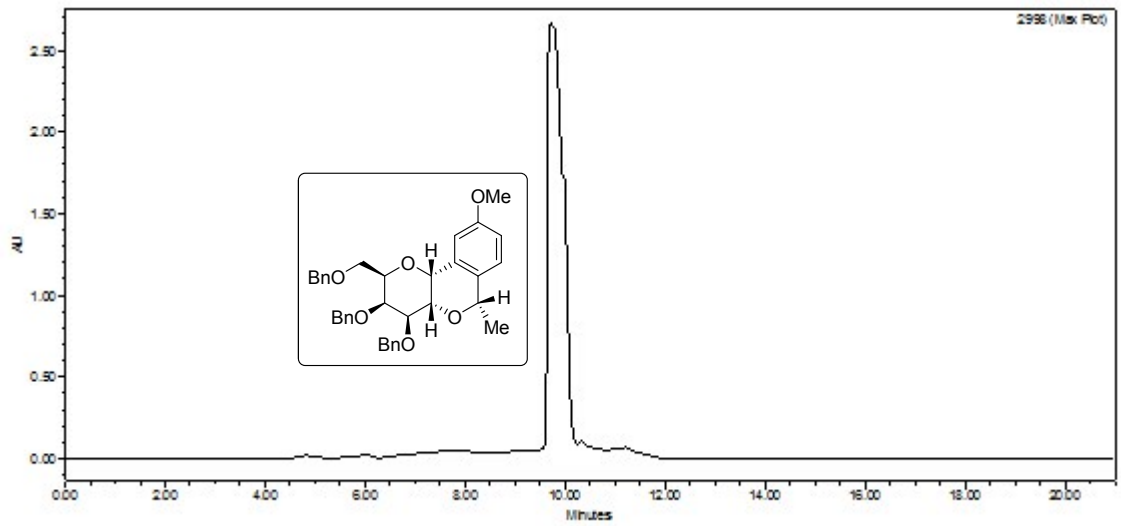


Figure 12. HPLC chromatogram of compound **5a**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 12.817 min

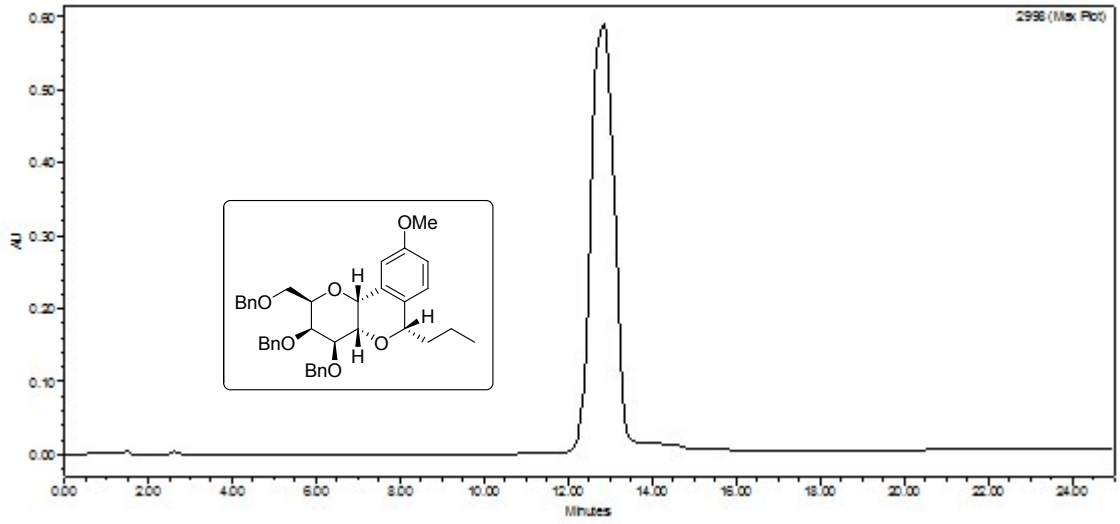


Figure 13. HPLC chromatogram of compound **5b**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 12.717 min

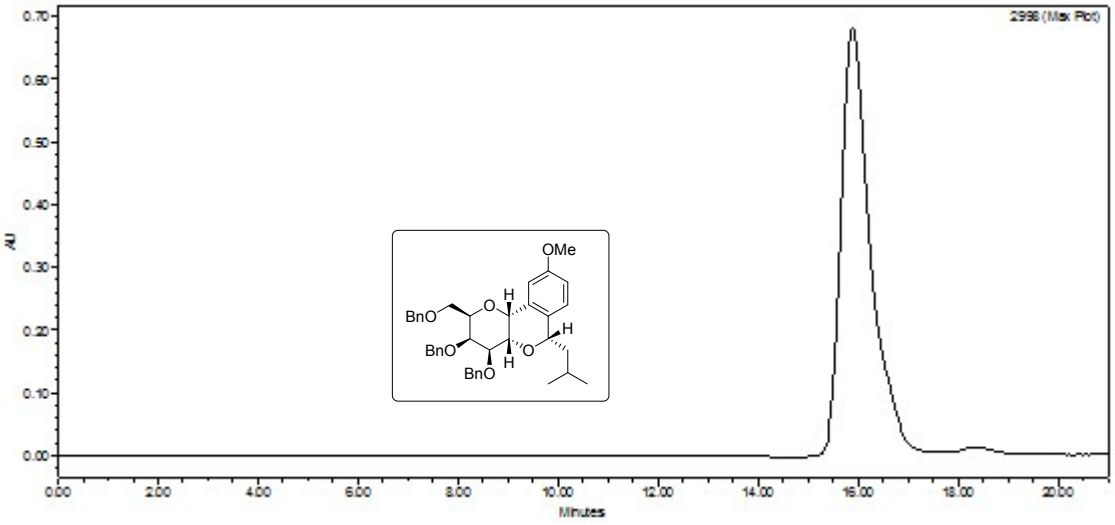


Figure 14. HPLC chromatogram of compound **5c**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 16.017 min

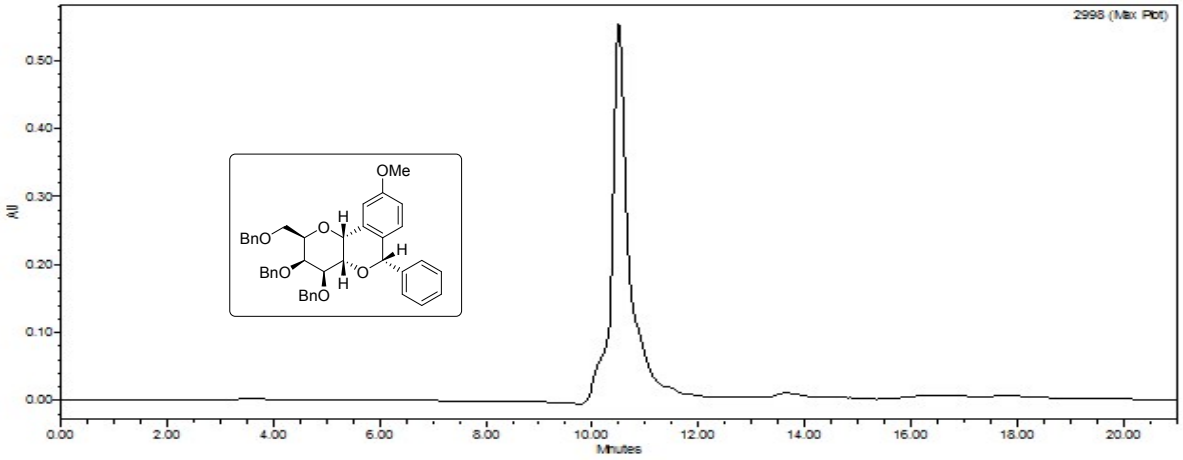


Figure 15. HPLC chromatogram of compound **5d**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 10.717 min

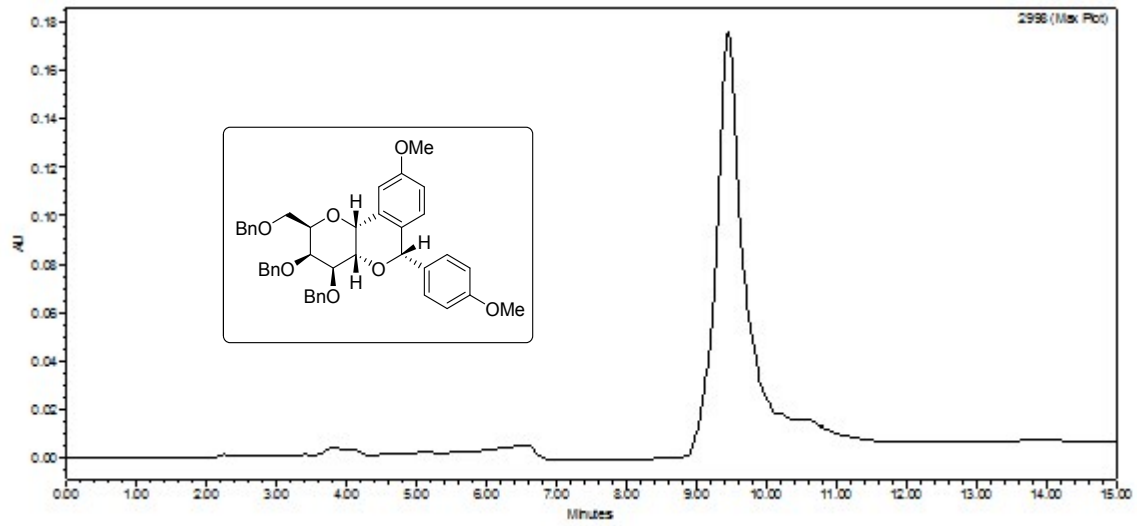


Figure 16. HPLC chromatogram of compound **5e**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 25 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 9.918 min

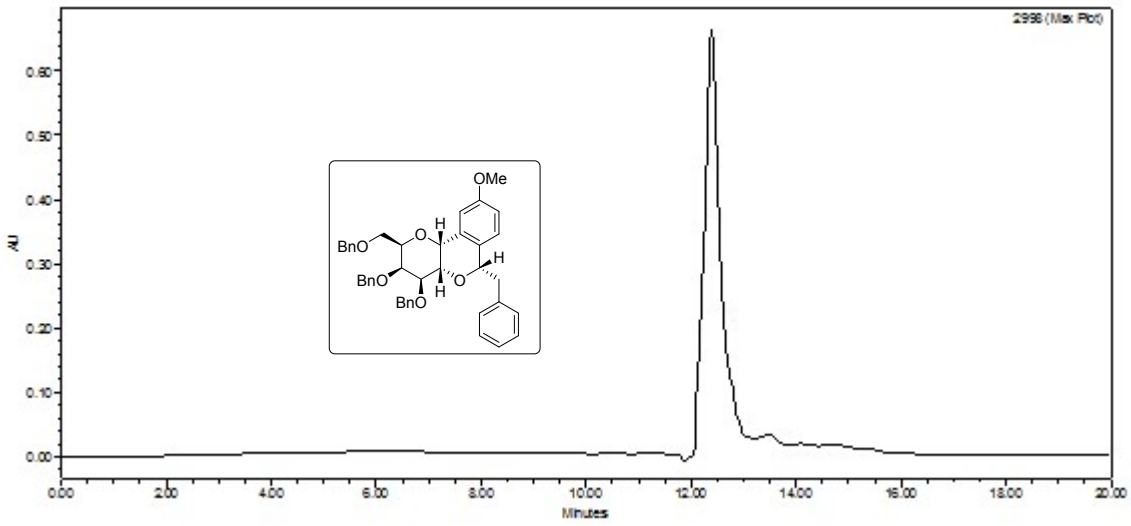


Figure 17. HPLC chromatogram of compound **5f**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O

Column: C18 (5µm) L- 250mm, Time: 20 min

Injection Volume: 10µL, Flow Rate: 1mL/min

Retention Time: 12.687 min

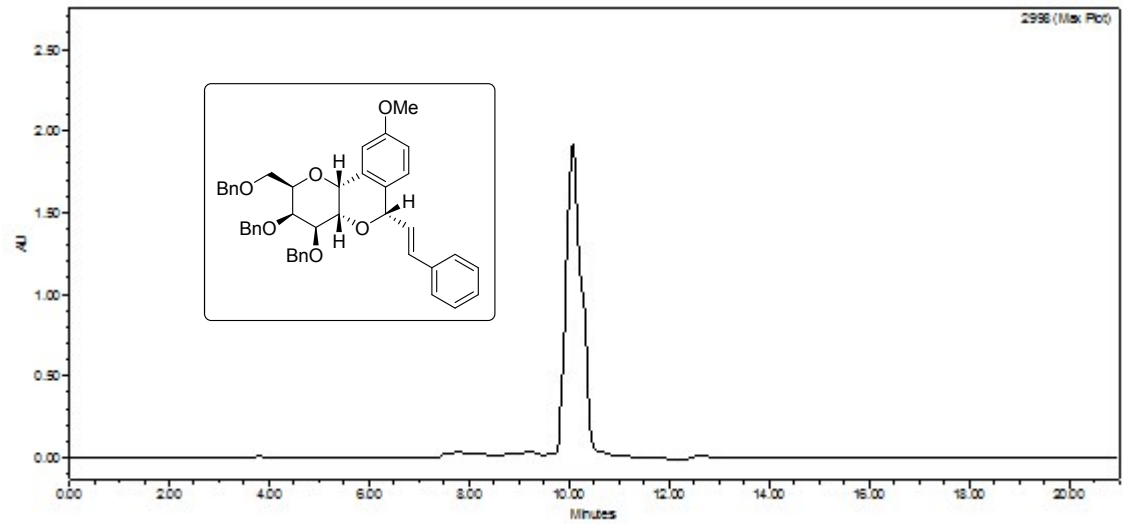


Figure 18. HPLC chromatogram of compound **5g**

Sample prepared in MeOH, Solvent System: 95:5 MeOH:H_2O
Column: C18 (5µm) L- 250mm, Time: 20 min
Injection Volume: 10µL, Flow Rate: 1mL/min
Retention Time: 10.381 min

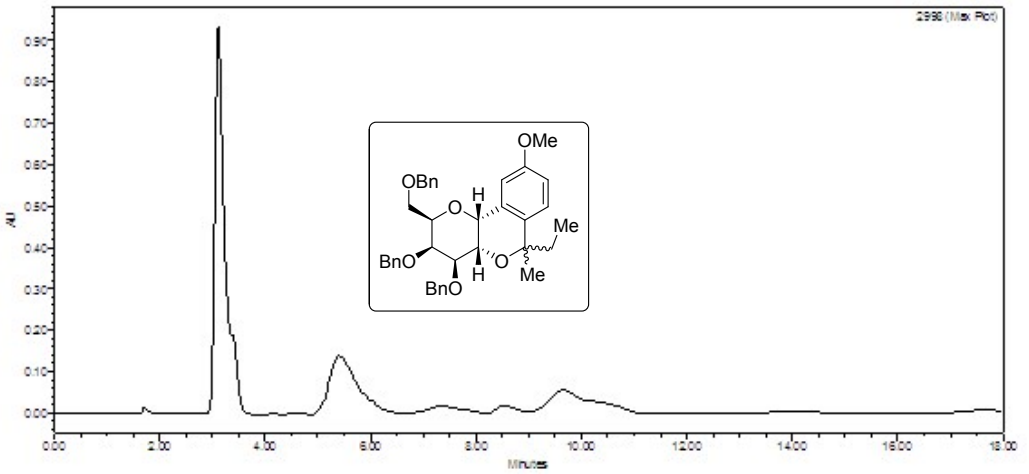


Figure 19. HPLC chromatogram of compound **5l (5l1, 5l2)**

(Crude compound **5l** after short filtration through silica gel column)

Sample prepared in MeOH, Solvent System: 99:1 MeOH:H_2O
Column: C18 (5µm) L- 250mm, Time: 20 min
Injection Volume: 10µL, Flow Rate: 1mL/min
Retention Time of major isomer: 2.979 min
Retention Time of minor isomer: 4.539 min

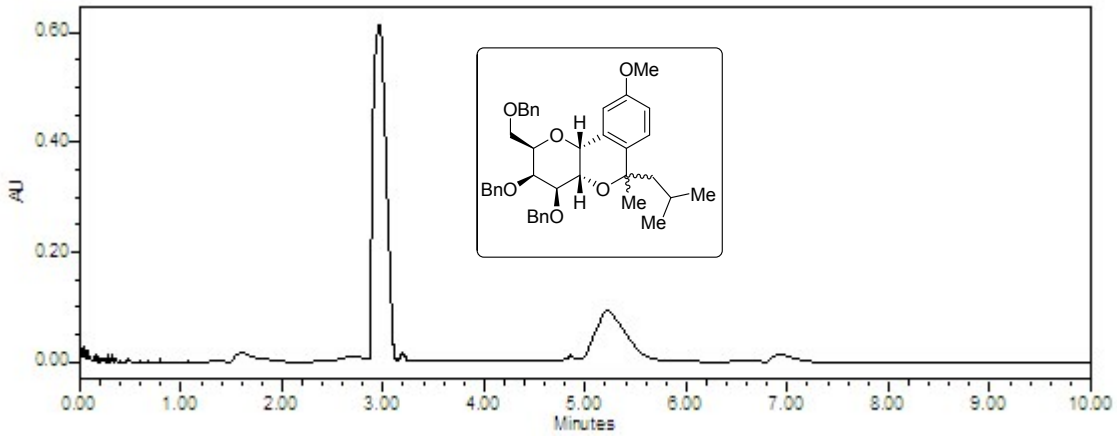


Figure 20. HPLC chromatogram of compound **5m (5m1, 5m2)**

(Crude compound **5m** after short filtration through silica gel column)

Sample prepared in MeOH, Solvent System: 99:1 MeOH:H_2O
Column: C18 (5µm) L- 250mm, Time: 20 min
Injection Volume: 10µL, Flow Rate: 1mL/min
Retention Time of major isomer: 3.135 min
Retention Time of minor isomer: 5.231

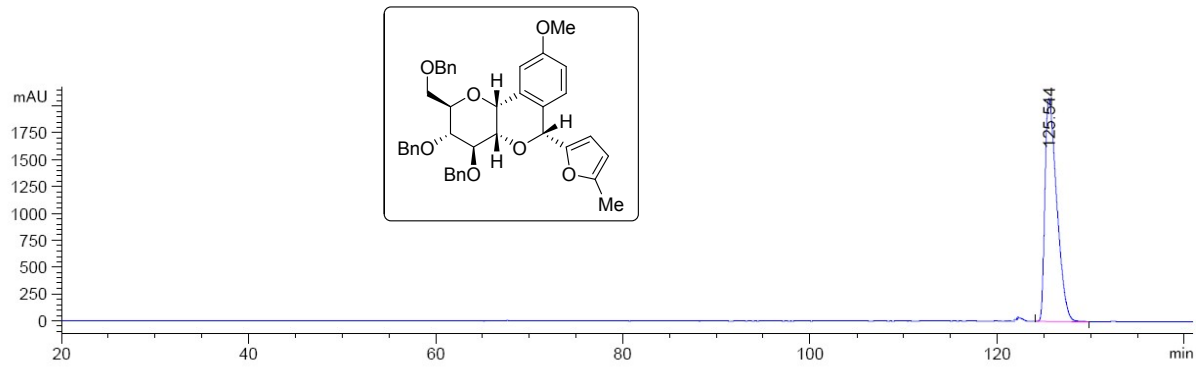


Figure 21. Chiral HPLC chromatogram of compound **3n** using IC-Column

Sample prepared in isopropanol

Solvent System: 85:15 hexane:isopropanol

```
Detector Lamp Burn Times: Current On-Time  Accumulated On-Time
DAD 1, UV Lamp          :       5.48           1762.5   h
DAD 1, Visible Lamp     :       0.00            132.0   h

   Instrument Conditions :   At Start     At Stop
   Pressure              :     35.2        41.3   bar
   Flow                  :      1.000       1.000 ml/min

Signal 2: DAD1 B, Sig=254,4 Ref=off
   Peak RetTime Type  Width     Area      Height     Area
     #   [min]        [min]   [mAU*s]     [mAU]       %
   ----|-------|----|-------|----------|----------|--------|
      1 125.544 BB    1.2043 1.81997e5  2076.96899 100.0000

Totals :                  1.81997e5  2076.96899
```

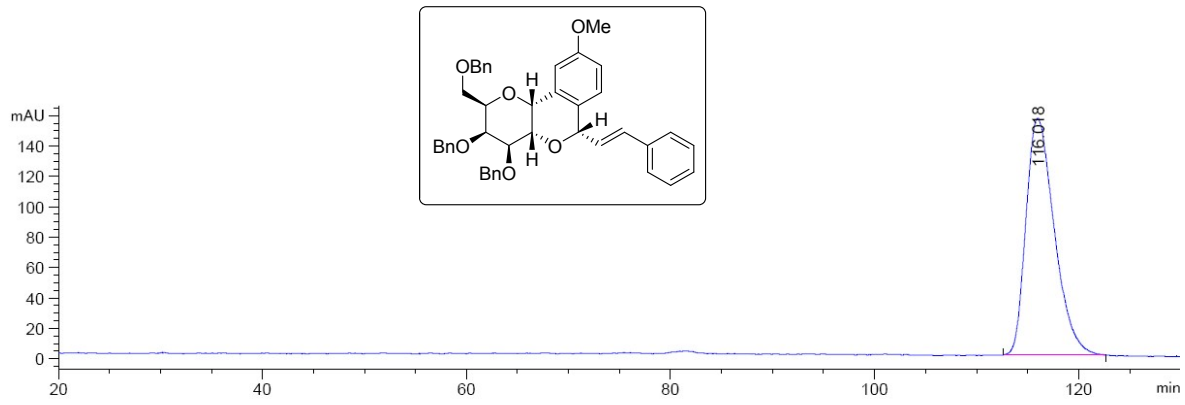


Figure 22. Chiral HPLC chromatogram of compound **5g** using IC-Column

Sample prepared in isopropanol

Solvent System: 85:15 hexane:isopropanol

Instrument Conditions	:	At Start	At Stop	
Pressure	:	35.9	35.3	bar
Flow	:	1.000	1.000	ml/min

Detector Lamp Burn Times:	Current On-Time	Accumulated On-Time	
DAD 1, UV Lamp :	3.23	1760.2	h
DAD 1, Visible Lamp :	0.00	132.0	h

Signal 4: DAD1 H, Sig=290,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	116.018	BB	2.3101	3.00188e4	155.78485	100.0000
Totals :				3.00188e4	155.78485	

6. ORTEP diagrams and Crystal data of the compounds 6, 8, 13 and 14

Compounds **6**, **8, 13** and **14** were crystallized by slow evaporation of their solution in $CHCl_3$ and EtOH over a period of 72 h. The crystals of suitable quality were mounted in glass capillaries, cooled to 273 K and the intensity data were collected on a Bruker APEX-II CCD detector system with Mo-sealed Siemens ceramic diffraction tube ($\lambda = 0.71073$) and a highly oriented graphite monochromator operating at 50 kV and 30 mA. The data were collected on a hemisphere mode and processed with SAINT-Plus.[1] Empirical absorption corrections were made using SADABS.[1] The structures were solved by direct methods using Olex2 package and refined by full matrix least-squares method based on F2 using ShelXL (Sheldrick, 2015) program.[2] All the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included in the ideal positions with fixed isotropic U values and were riding with their respective non-hydrogen atoms.

Compound	**8**	**14**	**6**	**13**
Formula	$C_{15}H_{20}O_6$	$C_{14}H_{18}O_6$	$C_{15}H_{20}O_6$	$C_{20}H_{22}O_{10}$
Formula weight	296.1260	282.1103	296.1260	422.1213
CCDC No.	1847781	1847782	1847786	1847783
Crystal colour, habit	White, Prism	White, Prism	PRISM, WHITE	PRISM, WHITE
T / K	100(2)	100(2)	100(2)	100(2)
Crystal system	Monoclinic	Orthorhombic	Monoclinic	Orthorhombic
Space group	*P*-2$_1$(no. 4)	$P2_12_12_1$(no. 19)	*P*-2$_1$(no. 4)	C222$_1$(no. 20)
a/Å	5.8896(9)	5.0069(4)	5.072(5)	10.047(5)
b/Å	10.8408(14)	9.5409(7)	10.504(5)	15.961(5)
c/Å	11.3786(15)	26.840(2)	14.874(5)	24.731(5)
α/°	90	90.00	90.000(5)	90.000(5)
β/°	102.397(5)	90.00	92.305(5)	90.000(5)
γ/°	90	90.00	90.000(5)	90.000(5)
V/Å^3	709.56(17)	1282.17(17)	791.8(9)	3966(2)
Z	2	4	2	4
D_c/g cm^{-3}	1.373	1.462	1.243	1.415
μ/mm^{-1}	0.107	0.115	0.096	0.115
Reflections measured	6708	19776	11837	20164
Unique reflections	2303	2271	2994	4110
Reflections used $I > 2\sigma(I)$]	3139	3232	3937	4949
R_1[a], wR_2[b] [$I > 2\sigma(I)$]	$R_1 = 0.059$[a] $wR_2 = 0.121$[b]	$R_1 = 0.056$[a] $wR_2 = 0.121$[b]	$R_1 = 0.054$[a] $wR_2 = 0.118$[b]	$R_1 = 0.044$[a] $wR_2 = 0.093$[b]
R_1[a], wR_2[b](all data)	R_1=0.094[a] wR_2=0.134[b]	R_1=0.099[a] wR_2= 0.146[b]	R_1=0.080[a] wR_2= 0.127[b]	R_1=0.062[a] wR_2= 0.997[b]
GOF on F^2	1.034	1.080	1.021	1.053

ORTEP diagrams:

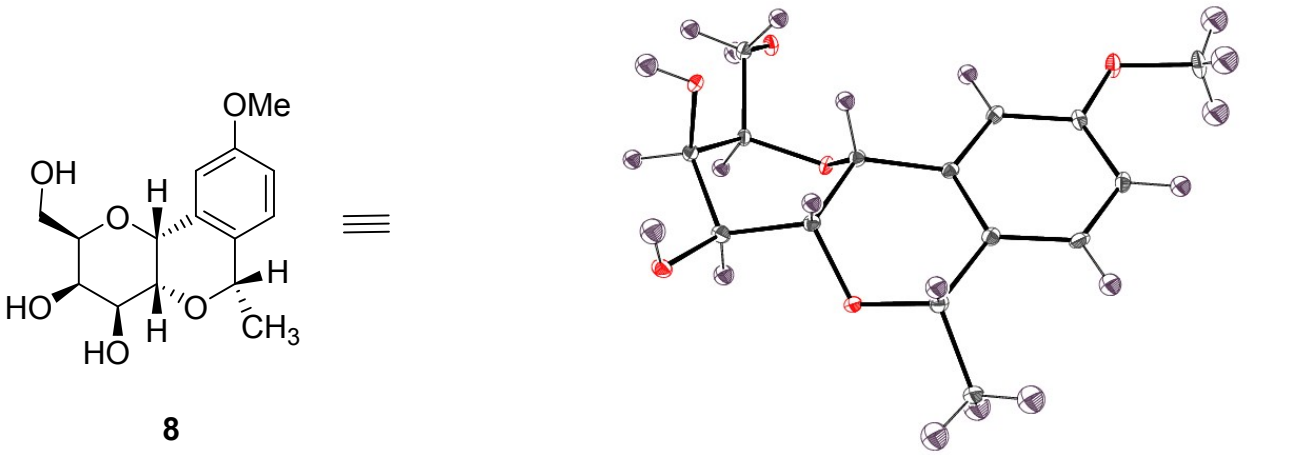


Figure 19: X-ray[3] ORTEP diagram showing 30% probability thermal ellipsoids of compound **8**

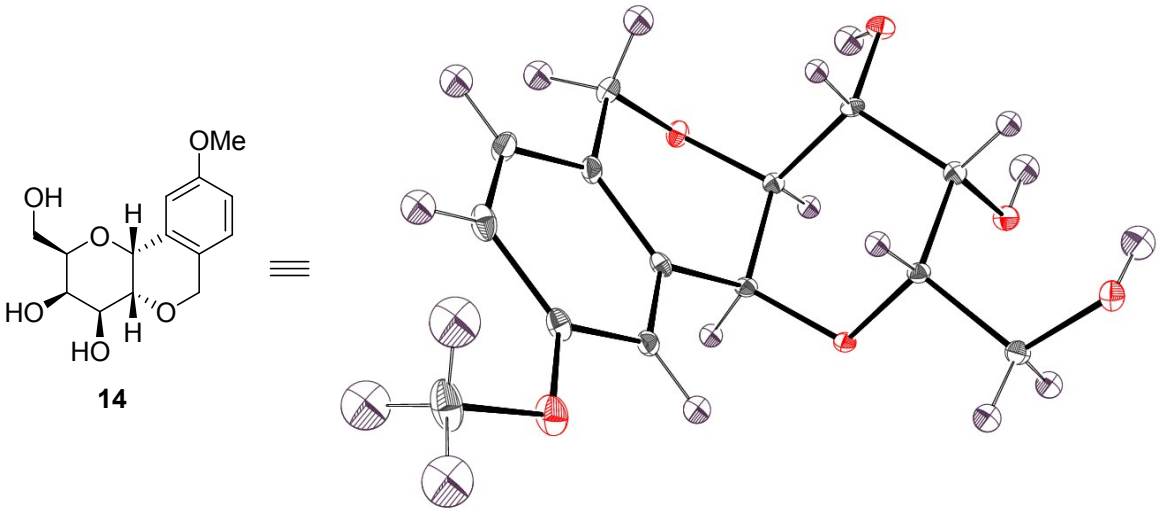


Figure 20: X-ray[3] ORTEP diagram showing 30% probability thermal ellipsoids of compound **14**

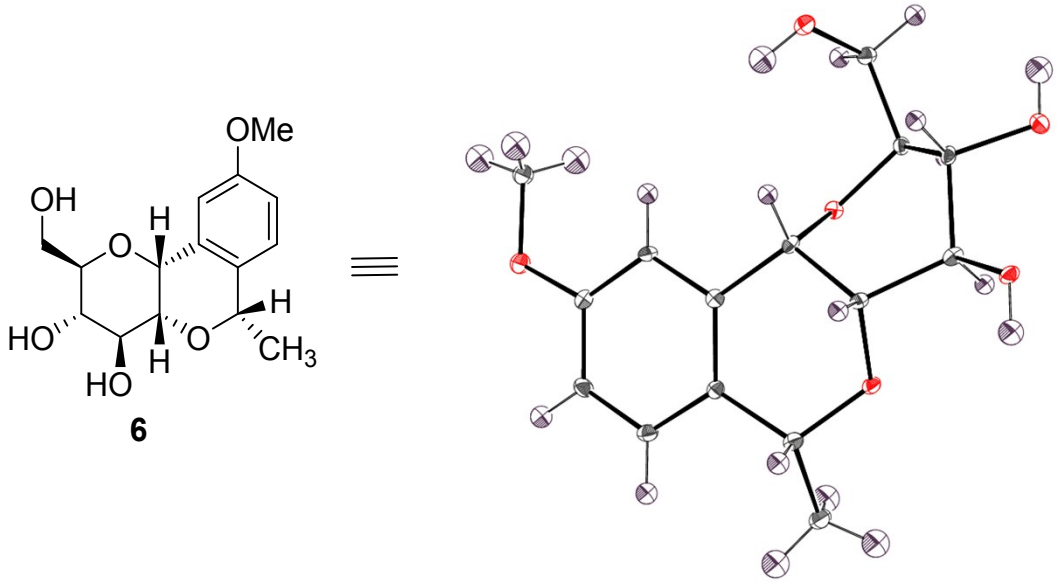


Figure 21: X-ray[3] ORTEP diagram showing 30% probability thermal ellipsoids of compound **6**

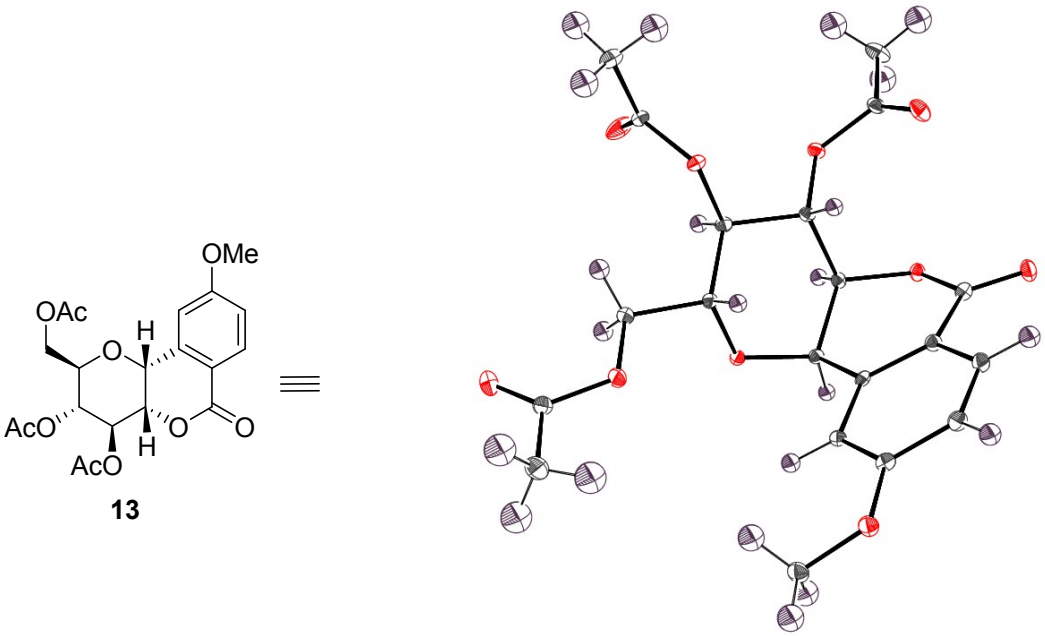


Figure 22: X-ray[3] ORTEP diagram showing 30% probability thermal ellipsoids of compound **13**

7. References

1. Bruker, SMART, SAINT-Plus, SADABS. Bruker Axs Inc. 1998 Madison, Wisconcin, USA
2. G. M. Sheldrick, *Acta Cryst.,* **2015**, C 71, 3.
3. **6**: CCDC NO. 1847786, **8**: CCDC NO. 1847781, **13**: CCDC NO. 1847783 and **14**: CCDC NO. 1847782 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www. ccdc.cam.ac.uk/data_request/cif.