Electronic Supplementary Material (ESI) for RSC Advances

Synthesis of C-spiro-glyconjugates from sugar lactones via zinc mediated Barbier reaction

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General information.

^{1}H and ^{13}C NMR spectra were recorded on Bruker 400 and 500 MHz spectrometers (Model No. D 205/52-2382, Avance 500) with TMS as the internal standard. Chemical shifts are expressed in parts per million (δ ppm). MS were recorded on Waters LC Mass spectrometer (Model No. Symapt MS). Silica gel coated aluminium plates were used for TLC. Elemental analyses were performed on Vario Elementar (Model No. EL). Reagents and solvents used were mostly of LR grade.

General procedures for the synthesis of sugar 1,5 lactones (1,2,3,5)

General Procedure 1 for Acetylation/Glycosylation: The unprotected monosaccharide (1.0 mmol) was suspended in acetic anhydride (2.0 mmol/unprotected hydroxyl groups). At 0 °C several drops of perchloric acid (69%, aqueous) were added. The reaction mixture was stirred for another 60 minutes at 0 °C. Afterwards the reaction solution was diluted with dichloromethane, washed with water and saturated sodium bicarbonate solution. The combined organic phases were dried over sodium sulphate and concentrated in vacuo. The crude product was used for the subsequent glycosylation purification of these compounds by column chromatography. Under nitrogen atmosphere the crude penta acetate (1.0 mmol) was dissolved in anhydrous dichloromethane (1.5 mL) and $BF_3.Et_2O$ (1.2 mmol) was added. At 0 °C thiophenol (1.2 mmol) was added drop wise, and the reaction mixture was allowed to warm to rt. After completion of reaction monitored by TLC, saturated sodium bicarbonate solution was added until all BF_3 was hydrolysed. The organic phase was washed with water and saturated sodium bicarbonate solution several times. The combined organic phases were dried over sodium sulfate, concentrated in vacuo and purified by crystallography or column chromatography (indicated conditions).

General Procedure 2 for deacetylation: The acetylated compounds (1.0 mmol) were dissolved in anhydrous methanol (3 mL) and treated with a catalytic amount of a 0.5 M sodium methoxide solution. The reaction mixture was stirred at room temperature until completion. Then Amberlite IR-120 H+ was added for neutralization. The ion exchange resin was filtered and the solvent removed in vacuo. The crude product was used without further purification.

General procedure 3 for benzylation: The partially unprotected monosaccharide (1.0 mmol) was added in portions over a period of 30 minutes to a suspension of sodium hydride (1.5 mmol/unprotected hydroxyl groups) in anhydrous DMF (7.5 mL) at 0 °C under nitrogen atmosphere. The reaction mixture was stirred for another 2 hours at room temperature and a catalytic amount of TBAI (0.1 mmol) was added. Then benzylbromide (1.1

mmol/unprotected hydroxyl groups) was added drop wise over a period of 45 minutes and the reaction mixture was stirred over night at room temperature. After completion ethanol was added until gas evolution ceased. The reaction mixture was diluted with water and ethyl acetate, the phases separated and the aqueous phase extracted with ether several times. The combined organic phases were dried over sodium sulfate, concentrated in vacuo and purified by column chromatography.

General procedure 4 for hydrolysis of Thioglycosides: The thioglycoside (1.0 mmol) was dissolved in a mixture of acetone/water (9:1 v/v, 15 mL). Then NIS (2.0-2.5 mmol) was added at rt and the reaction mixture was stirred for the given time. After completion the reaction mixture was diluted with water, extracted with ethyl acetate several times and the combined organic phases washed with saturated sodium bicarbonate solution and dried over sodium sulfate. After removal of the solvent, the crude product was purified by column chromatography.

General procedure 5 for oxidation: The hemiacetal (1.0 mmol) was dissolved in anhydrous DMSO (10 mL) and heated to 30 °C. Then acetic anhydride (20 mmol) was added and the reaction mixture was stirred over night at 30 °C. After completion the reaction mixture was diluted with water, extracted with ether several times and the combined organic phases dried over sodium sulfate, concentrated in vacuo and purified by column chromatography.

General procedure for *gem*-diallylation of sugar lactones (6):

Allyl bromide (4.0 equiv.) was added to Zn powder (6.0 equiv.) activated with TMSCl (0.3 equiv) in dry THF under nitrogen atmosphere at rt. The reaction mixture was stirred for 15 mins. The sugar lactone (1.0 mmol dissolved in THF) was added slowly and then stirred for further 4h. The completion of reaction was monitored by TLC and quenched with the 0.1N HCl. The resulting mixture was extracted with ethyl acetate (3 x 15 ml). The combined ethyl acetate layers were washed with brine solution, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification of the crude product by silica gel chromatography (eluent: Hexane/EtOAc = 9.5/0.5, 8.0/2.0) afforded the corresponding bisallyl sugar derivatives.

3,3′-(2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosylidene)bis(1-propene) (1a). Prepared by using the general procedure **6** using 0.92 mmol (500 mg) of **1** to yield the desired product **1a** (95%, 533 mg) as oily liquid. IR ($CHCl_3$): 3076, 3032, 1642, 998 cm^{-1}. $[\alpha]^{25}_{D}$ = +38.2 (c 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.24 (m, 20H), 5.84-5.76 (m, 2H), 5.12 – 4.99 (m, 4H), 4.93 (d, *J* = 11.4 Hz, 1H), 4.75 (d, *J* = 10.9 Hz, 1H), 4.62 (t, *J* = 10.9 Hz, 1H), 4.54 (m, 5H), 4.16 (d, *J* = 6.3 Hz, 1H), 4.14 (d, *J* = 2.0 Hz, 1H), 3.71 – 3.67 (m, 2H), 3.64 – 3.61

(m, 2H), 2.46 (dd, *J* = 13.9, 7.6 Hz, 1H), 2.37-2.31 (m, 2H), 2.20 – 2.08 (m, 1H). ^{13}C NMR ($CDCl_3$, 100MHz) δ 139.0, 138.0, 137.9, 137.8, 133.9, 133.8, 128.47, 128.45, 128.43, 128.41, 128.38, 128.36, 128.34, 128.30, 128.28, 128.25, 128.21, 128.19, 128.15, 128. 12, 128.09, 128.06, 128.04, 128.01, 127.99, 127.95, 118.5, 118.4, 80.6, 78.9, 76.7, 75.8, 75.1, 74.5, 73.5, 71.5, 70.7, 69.8, 40.8, 40.5. ESI-MS; 605 $(M+H)^+$; Anal. Cal. For $C_{40}H_{44}O_5$; C, 79.44; H, 7.33; Found C, 79.36, H, 7.45.

3,3′-(2,3,4,6-Tetra-*O*-benzyl-D-galactopyranosylidene)bis(1-propene) (2a):

Prepared by using the general procedure **6** using 0.55 mmol (300 mg) of **2** to yield the desired product **2a** (89%, 298 mg) as oily liquid. IR ($CHCl_3$): 3065, 3031, 1639, 997 cm^{-1}. $[\alpha]^{25}_D$ = +46.3 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.32–7.25 (m, 20H), 5.90 -5.86 (m, 1H), 5.84–5.80 (m, 1H), 5.13–5.06 (m, 4H), 4.89 (d, *J* = 2.10 Hz, 1H), 4.78 (d, *J* = 2.08 Hz, 1H), 4.62 (d, *J* = 7.2 Hz, 1H), 4.60 (d, *J* = 7.11 Hz, 1H), 4.58 – 4.51 (m, 3H), 4.47 (d, *J* = 2.1 Hz, 1H), 4.17 (d, *J* = 2.06 Hz, 1H), 4.15 (d, *J* = 2.02 Hz, 1H), 3.85 (d, *J* = 1.92 Hz, 1H), 3.61 (d, *J* = 1.74 Hz, 1H), 3.60-3.56 (m, 2H), 2.44–2.36 (m, 3H), 2.27-2.24 (m, 1H); ^{13}C NMR ($CDCl_3$, 100MHz) δ 138.6, 138.1, 138.0, 137.7, 133.9, 133.7, 128.46, 128.44, 128.41, 128.36, 128.32, 128.28, 128.20, 128.16, 128.08, 128.02, 127.96, 127.92, 127.85, 127.81, 127.68, 127.61, 127.53, 127.49, 127.45, 127.44,118.88, 118.44, 80.89, 79.25, 78.78, 75.46, 74.51, 74.49, 73.63, 73.35, 71.17, 69.94, 41.44, 40.21. ESI-MS; 605 $(M+H)^+$; Anal. Cal. For $C_{40}H_{44}O_5$; C, 79.44; H, 7.33; Found C, 79.37, H, 7.42.

3,3′-(2,3,4,6-Tetra-*O*-benzyl-D-mannopyranosylidene)bis(1-propene) (3a):

Prepared by using the general procedure **6** using 0.46 mmol (250 mg) of **3** to yield the desired product **3a** (92%, 258 mg) as oily liquid. IR ($CHCl_3$): 3069, 3033, 1639, 998 cm^{-1}. $[\alpha]^{25}_D$ = +58 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.22 (m, 20H), 5.86-5.76 (m, 2H), 5.11 – 4.98 (m, 4H), 4.94 (d, *J* = 11.0 Hz, 1H), 4.78 (d, *J* = 11.0 Hz, 1H), 4.67 (d, *J* = 11.0 Hz, 1H), 4.59-4.47 (m, 5H), 4.16 (d, *J* = 2.4 Hz, 1H) 4.15- 4.13 (m, 1H), 3.75 – 3.70 (m, 2H), 3.68 – 3.64 (m, 2H), 2.50-2.48 (m, 1H), 2.39-2.31 (m, 2H), 2.18 – 2.11 (m, 1H). ^{13}C NMR ($CDCl_3$, 100MHz) δ 138.9, 138.2, 137.9, 137.6, 133.8, 133.4, 128.47, 128.43, 128.40, 128.35, 128.31, 128.27, 128.22, 128.14, 128.03, 128.01, 127.95, 127.91, 127.84, 127.79, 127.67, 127.60, 127.54, 127.48, 127.46, 127.43,118.7, 118.3, 80.5, 79.4, 78.9, 75.4, 74.9, 74.5, 73.6, 73.2, 71.3, 69.8, 41.2, 40.3. ESI-MS; 627 $(M+Na)^+$; Anal. Cal. For $C_{40}H_{44}O_5$; C, 79.44; H, 7.33; Found C, 79.36, H, 7.41.

3,3′-(2,3,4,-Tri-*O*-benzyl-L-rhamnopyranosylidene)bis(1-propene)) (4a):

Prepared by using the general procedure **6** using mmol (280 mg) of **4** to yield the desired product **4a** (87%, 280 mg) as oily liquid. IR ($CHCl_3$): 3044, 3029, 1638, 996cm^{-1}. $[\alpha]^{25}_D$ =

+4.7 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.34-7.25 (m, 15H), 5.90-5.86 (m, 1H), 5.84-5.80 (m, 1H), 5.19-4.98 (m, 4H), 4.78 (d, *J* = 7.43 Hz, 1H), 4.76 (d, *J* = 7.65 Hz, 1H), 4.70 (d, *J* = 11.48 Hz, 1H), 4.64 (d, *J* = 11.12 Hz, 1H), 4.61 (d, *J* = 10.05 Hz, 1H), 4.59 (d, *J* = 10.08 Hz, 1H), 4.21-4.19 (m, 1H), 4.03 (t, *J* = 3.97 Hz, 1H), 3.68 (d, *J* = 4.06 Hz, 1H), 3.65-3.60 (m, 2H), 2.57-2.54 (m, 1H), 2.41-2.35 (m, 2H), 2.25-2.22 (m, 1H), 1.21 (d, *J* = 3.95 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) δ 138.0, 137.8, 137.7, 134.3, 133.7, 128.57, 128.55, 128.52, 128.50, 128.49, 128.40, 128.30, 128.21, 128.19, 128.17, 128.09, 128.01, 127.94, 127.85, 127.82, 118.3, 118.1, 84.0, 82.5, 79.2, 76.1, 75.4, 73.7, 73.5, 68.4, 41.2, 40.8, 19.9. Anal. Cal. For $C_{33}H_{38}O_4$; C, 79.48; H, 7.68; Found C, 79.38, H, 7.61.

3,3$^{/}$-(3,4,6-Tri-*O*-benzyl,2-deoxy-D-glucopyranosylidene)bis(1-propene)) (5a):

Prepared by using the general procedure **6** using 0.34 mmol (150 mg) of **5** to yield the desired product **5a** (84%, 144 mg) as oily liquid. IR ($CHCl_3$): 3069, 3033, 1639, 998 cm^{-1}. $[\alpha]^{25}_D$ = +27 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.23 (m, 15H), 5.94 – 5.66 (m, 2H), 5.07 (m, 4H), 4.70 (d, *J* = 11.0 Hz, 1H), 4.62 (d, *J* = 11.9 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.56 (d, *J* = 13.6 Hz, 1H), 4.54 (d, *J* = 13.6 Hz, 1H), 4.47 (d, *J* = 11.0 Hz, 1H), 4.11 – 4.05 (m, 1H), 4.00 (d, *J* = 3.2 Hz, 1H), 3.81 (dt, *J* = 11.1, 5.6 Hz, 1H), 3.72 – 3.59 (m, 2H), 2.30 – 2.04 (m, 4H), 1.91 – 1.77 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.1, 137.9, 137.8, 134.2, 134.1, 128.70, 128.65, 128.53, 128.48, 128.42, 128.35, 128.34, 128.32, 128.30, 128.25, 128.19, 128.15, 128.06, 128.01, 127.99, 119.1, 118.8, 76.8, 76.6, 74.7, 74.6, 73.2, 73.0, 72.5, 71.4, 44.8, 44.1, 36.1. ESI-MS; 499 $(M+H)^+$; Anal. Cal. For $C_{33}H_{38}O_4$; C, 79.48; H, 7.68; Found C, 79.36, H, 7.73.

(5S,6R)-2,2-diallyl-5-(benzyloxy)-6-((benzyloxy)methyl)-5,6-dihydro-2H-pyran (6a):

Prepared by using the general procedure **6** using 0.46 mmol (150 mg) of **6** to yield the desired product **6a** (81%, 146 mg) as oily liquid. IR ($CHCl_3$): 3078, 3033, 1638, 998cm^{-1}. $[\alpha]^{25}_D$ = +49.0 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40 – 7.20 (m, 10H), 5.97 – 5.78 (m, 2H), 5.71 (d, *J* = 12.3 Hz, 1H), 5.44 (dd, *J* = 12.3, 8.6 Hz, 1H), 5.16 – 5.05 (m, 4H), 4.85 (t, *J* = 8.1 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.38 (d, *J* = 11.6 Hz, 1H), 3.80 (d, J = 3.6 Hz, 1H), 3.78 (d, J = 3.6 Hz, 1H), 3.51 (dd, *J* = 10.6, 8.4 Hz, 1H), 2.41 – 2.19 (m, 4H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 139.9, 139.8, 138.0, 137.8, 133.9, 133.8, 128.38, 128.32, 128.28, 128.21, 128.15, 128.10, 128.04, 127.91, 127.41, 127.11, 118.5, 118.4, 76.7, 76.6, 73.0, 71.6, 71.4, 71.3, 46.2, 45.1. ESI-MS; 413$(M+Na)^+$; Anal. Cal. For $C_{26}H_{30}O_3$; C, 79.97; H, 7.74; Found C, 79.89, H, 7.81.

3,3$^{/}$-(2,3,5-tri-*O*-benzyl-D-ribofuranosylidene)bis(1-propene)) (7a):

Prepared by using the general procedure **6** using 0.23 mmol (100 mg) of **7** to yield the desired

product **7a** (67%, 77mg) as oily liquid. IR ($CHCl_3$): 3044, 3029, 1638, 998cm^{-1}. $[\alpha]^{25}_D$ = +52.1 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.36-7.25 (m, 15H), 5.89 - 5.82 (m, 2H), 5.14-5.01 (m, 4H), 4.83 (d, *J* = 10.8 Hz, 1H), 4.77 (d, *J* = 10.8 Hz, 1H), 4.66 (d, *J* = 3.6 Hz, 1H), 4.63 (d, *J* = 3.6 Hz, 1H), 4.59-4.55 (m, 2H), 4.11 (t, *J* = 4.0 Hz, 1H), 3.93 (dd, J = 4.8, 8.4 Hz, 1H), 3.88 – 3.70 (m, 2H), 3.64 (d, J = 4.4 Hz, 1H), 2.41 – 2.24 (m, 4H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 137.7, 137,6, 137.4, 134.1, 133.7, 128.49, 128.45, 128.35, 128.29, 128.19, 128.14, 128.09, 127.96, 127.94, 127.83, 127.80, 127.54, 127.68, 127.61, 127.56. ESI-MS; 485 $(M+H)^+$; Anal. Cal. For $C_{32}H_{36}O_4$; C, 79.31; H, 7.49; Found C, 79.39, H, 7.36.

3,3$^{/}$-(l,2;5,6-di--*O*-(l-methyIethyIidene)-D-mannofuranosylidene bis(1-propene)) (9a):

Prepared by using the general procedure **6** using 0.77 mmol (200 mg) of **9** to yield the desired product **9a** (86%, 216mg) as oily liquid. IR ($CHCl_3$): 1638, 998cm^{-1}. $[\alpha]^{25}_D$ = +89.6 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz) δ 5.90-5.80 (m, 2H), 5.22-5.15 (m, 4H), 4.32 (d, *J* = 6.0 Hz, 1H), 4.16 (dd, *J* = 5.2, 7.6 Hz, 1H), 4.11 (dd, *J* = 2.4, 6.0 Hz, 1H), 4.07 (dd, *J* = 2.0, 6.0 Hz, 1H), 4.05-4.04 (m, 1H), 3.80 (d, *J* = 8.0 Hz, 1H), 2.52-2.50 (m, 2H), 2.38-2.32 (m, 2H), 1.55 (s, 3H), 1.41 (s, 3H), 1.35 (s, 6H). ^{13}C NMR ($CDCl_3$, 100MHz) δ 132.6, 131.9, 119.9, 119.8, 108.9, 107.7, 79.9, 75.8, 75.5, 73.3, 71.5, 67.2, 42.4, 39.7, 27.0, 26.1, 25.4, 25.2. ESI-MS; 325$(M+H)^+$; Anal. Cal. For $C_{18}H_{28}O_5$; C, 66.64; H, 8.70; Found C, 66.56, H, 8.78.

General procedure for the synthesis of hemiacetal compounds (7)

Propargyl/Crotyl bromide (2.0 equiv.) was added to Zn powder (4.0 equiv.) activated with TMSCl (0.1 equiv) in dry THF under nitrogen atmosphere at rt. The reaction mixture was stirred for 15 mins. The sugar lactone (1.0 mmol dissolved in THF) was added slowly and then stirred for further 4h. The completion of reaction was monitored by TLC and quenched with the 0.1N HCl. The resulting mixture was extracted with ethyl acetate (3 x 15 ml). The combined ethyl acetate layers were washed with brine solution, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification of the crude product by silica gel chromatography (eluent: Hexane/EtOAc = 9.0/1.0, 8.0/2.0) afforded the corresponding hemiacetal sugar derivatives.

Synthesis of compound 11

Prepared by using the general procedure **7** using 0.24 mmol (130 mg) of **1** to yield the desired product **11** (85%, 118.3 mg, (β;α ; 9:1) as oily liquid. IR ($CHCl_3$): 3078, 3033, 2178, 998cm^{-1}. $[\alpha]^{25}_D$ = +18.0 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.25 (m, 20H), 4.96 – 4.82 (m, 4H), 4.73 – 4.54 (m, 4H), 4.01 – 3.99 (m, 2H), 3.71.3.62 (m, 4H), 3.04 (s, 1H), 2.69

– 2.65, 2.52 – 2.50 (m, 1H), 2.04 (t, J = 2.50 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.4, 138.1, 137.6, 137.1, 128.55, 128.53, 128.48, 128.39, 128.35, 128.30, 128.25, 128.18, 128.13, 128.08, 128.02, 127.97, 127.94, 127.90, 127.88, 127.84, 127.80, 127.76, 127.72, 127.59, 96.9, 83.5, 80.5, 78.7, 78.2, 75.6, 75.5, 74.9, 73.3, 72.3, 71.9, 68.4, 29.5. ESI-MS; 601$(M+Na)^+$; Anal. Cal. For $C_{37}H_{38}O_6$; C, 76.79; H, 6.62; Found C, 76.75; H, 6.58.

General procedure for ring closing metathesis (8):

Gem diallyl compound (**1a**, **2a, 4a)** was placed in a 100-mL flask. After the flask had been flushed with nitrogen, oxygen-free CH_2Cl_2 (3 mM) was added by syringe followed by addition of Grubbs' II catalyst (5 mol %). After the reaction mixture had been stirred at rt for 6 h, TLC monitoring showed the complete transformation of the starting material. The resulting black solution was concentrated under reduced pressure. The residual dark oil was taken up in diethyl ether, stirred overnight under air to decompose the catalyst, and filtered. After removal of the solvent in vacuum followed by silica gel chromatography. (eluent: Hexane/EtOAc: 90/10; 75/25) the corresponding C-spiroglycosides were obtained.

2,3,4,6-Tetra-*O*-benzylspiro[1,5-anhydro-D-glucitol-1,4$^{/}$-cyclopent- 1$^{/}$-ene] (12):

Prepared by using the general procedure **8** using 0.49 mmol (300 mg) of **1a** to yield the desired product **12** (85%, 286 mg) as oily liquid. $[\alpha]^{25}_D$ = +18.0 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42 – 7.19 (m, 20H), 5.66 (m, 1H), 5.62 (m, 1H), 4.95 (d, *J* = 11.6 Hz, 1H), 4.89 (d, *J* = 11.6 Hz, 1H), 4.75 (d, *J* = 11.0 Hz, 1H), 4.65 (d, *J* = 11.6 Hz, 1H), 4.60 (d, *J* = 3.1 Hz, 1H), 4.57 (d, *J* = 2.6 Hz, 1H), 4.55 (d, *J* = 5.8 Hz, 1H), 4.53 (d, *J* = 2.9 Hz, 1H), 4.12 (d, *J* = 4.7 Hz, 1H), 3.98 (dd, *J* = 6.0, 3.5 Hz, 1H), 3.72 (dd, *J* = 6.6, 3.4 Hz, 1H), 3.66 – 3.63 (m, 1H), 3.62 (s, 1H), 3.61 – 3.58 (m, 1H), 2.58 (d, *J* = 17.3 Hz, 1H), 2.35 (t, *J* = 15.3 Hz, 2H), 2.14 (t, *J* = 12.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ, 138.7, 137.9, 137.8, 137.6, 128.7, 128.69, 128.65, 128.5, 128.42, 128.38, 128.34, 128.25, 128.15, 128.05, 128.03, 128.00, 127.95, 127.90, 127.86, 127.81, 127.76, 127.72, 127.66, 127.61, 127.55, 127.48, 82.8, 81.8, 79.1, 78.2, 74.5, 74.3, 73.5, 73.2, 71.3, 70.7, 45.5, 44.2 .ESI-MS; 577 $(M+H)^+$; Anal. Cal. For $C_{38}H_{40}O_5$; C, 79.14; H, 6.99; Found C, 79.06, H, 7.08.

2,3,4,6-Tetra-*O*-benzylspiro[1,5-anhydro-D-galactitol-1,4$^{/}$-cyclopent- 1$^{/}$-ene] (13):

Prepared by using the general procedure **8** using 0.24 mmol (150 mg) of **2a** to yield the desired product **13** (81%, 115 mg) as oily liquid. $[\alpha]^{25}_D$ = +32.0 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.32–7.25 (m, 20H), 5.69-5.66 (m, 1H), 5.64–5.62 (m, 1H), 4.89 (d, *J* = 2.10 Hz, 1H), 4.78 (d, *J* = 2.08 Hz, 1H), 4.62 (d, *J* = 7.2 Hz, 1H), 4.60 (d, *J* = 7.11 Hz, 1H), 4.58 – 4.51 (m, 3H), 4.47 (d, *J* = 2.1 Hz, 1H), 4.17 (d, *J* = 2.06 Hz, 1H), 4.15 (d, *J* = 2.02 Hz, 1H), 3.85 (d, *J* = 1.92 Hz, 1H), 3.61 (d, *J* = 1.74 Hz, 1H), 3.60-3.56 (m, 2H), 2.48–2.35 (m,

3H), 2.27-2.24 (m, 1H). ESI-MS; 577$(M+H)^+$; Anal. Cal. For $C_{38}H_{40}O_5$; C, 79.14; H, 6.99; Found C, 79.20, H, 7.07.

2,3,4-Tri-*O*-benzylspiro[1,5-anhydro-L-rhamnocitol-1,4′-cyclopent- 1′-ene (14):

Prepared by using the general procedure **8** using 0.20 mmol (100 mg) of **4a** to yield the desired product **14** (86%, 81 mg) as oily liquid. $[\alpha]^{25}_D$ = +15.0 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400MHz) δ 7.33-7.24 (m, 15H), 5.69-5.65 (m, 2H), 4.81-4.75 (m, 2H), 4.74-4.67 (m, 2H), 4.11 (dd, *J* = 7.2, 14.4 Hz, 1H), 4.00 (t, *J* = 4.0 Hz, 1H), 3.76 (d, *J* = 3.6 Hz, 1H), 3.67 (dd, *J* = 4.0, 6.4 Hz, 1H), 2.74-2.70 (m, 1H), 2.55-2.51(m, 1H), 2.44-2.39 (m, 1H), 2.30-2.25 (m, 1H), 1.24 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) 138.1, 138.0, 137.9, 128.6, 128.59, 128.54, 128.48, 128.43, 128.39, 128.35, 128.29, 128.25, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 84.6, 83.1, 82.3, 80.3, 74.6, 73.6, 73.5, 68.3, 45.6, 45.1, 19.9. ESI-MS; 493$(M+Na)^+$; Anal. Cal. For $C_{31}H_{34}O_4$; C, 79.12; H, 7.28; Found C, 79.02, H, 7.36.

Preparation of compound 15: The compound **12** (150 mg, 0.26 mmol) was dissolved in anhydrous $CHCl_3$. *mCPBA* (2.0 equiv., 89 mg) was added slowly over 30 mins and stirred at rt for overnight. Completion of the reaction was monitored through TLC. The reaction mixture was extracted with ethyl acetate (3 x 15 ml). The combined organic layers were washed with $NaHCO_3$ solution until benzoic acid completely neutralized, washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The obtained crude product subjected to silica gel chromatography to obtained pure product **15** in 68% (104 mg) as colourless oily liquid. $[\alpha]^{25}_D$ = +46.0 (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 – 7.21 (m, 20H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.80 (d, *J* = 11.6 Hz, 1H), 4.68 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 9.2 Hz, 1H), 4.54 (s, 1H), 4.52 (s, 1H), 4.43-4.41 (m, 2H), 4.10 (d, *J* = 6.4 Hz, 1H), 4.06 (dd, *J* = 6.7, 2.9 Hz, 1H), 3.77 (dd, *J* = 6.7, 2.8 Hz, 1H), 3.62-3.60 (m, 2H), 3.57 – 3.55 (m, 2H), 3.54 (d, *J* = 3.58 Hz, 1H), 2.14 (d, *J* = 14.5 Hz, 1H), 2.08 – 2.01 (m, 1H), 1.93 (d, *J* = 14.5 Hz, 1H), 1.77 (d, *J* = 14.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.7, 138.3, 138.2, 138.0, 128.62, 128.61, 128.57, 128.55, 128.52, 128.43, 128.41, 128.38, 128.35, 128.33, 128.30, 128.28, 128.26, 128.24, 127.94, 127.88, 127.77, 127.73, 127.68, 127.44, 80.0, 79.2, 78.8, 78.5, 74.7, 74.4, 73.4, 73.4, 71.6, 70.5, 57.6, 57.4, 39.4, 37.0. ESI-MS; 593 $(M+H)^+$; Anal. Cal. For $C_{38}H_{40}O_6$; C, 77.00; H, 6.80; Found C, 77.05, H, 6.89.

Preparation of of compound 16.

The compound **15** (0.13mmol, 80mg) was dissolved in 8:1 MeOH: H_2O (5ml). NH_4Cl (1.0 equiv., 8mg) and NaN_3 (1.5 equiv., 14mg) were added and the reaction mixture was heated at 80 ^oC for 12h. Completion of the reaction was monitored through TLC. The reaction mixture was concentrated under reduced pressure, extracted with ethyl acetate (3x10ml) and the

combine organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The obtained crude product subjected to silica gel chromatography to obtained title product (**16**) in 64% (54 mg) as yellow oily liquid. IR ($CHCl_3$): 3073, 3034, 2109 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.21 (m, 20H), 4.94 – 4.82 (m, 1H), 4.72 (d, *J* = 5.6 Hz, 1H), 4.69 (d, *J* = 5.6 Hz, 1H), 4.64 (d, *J* = 7.2 Hz, 1H), 4.62 (s, 1H), 4.61 (d, *J* = 2.9 Hz, 1H), 4.58 (d, *J* = 2.7 Hz, 1H), 4.54 (d, *J* = 1.8 Hz, 1H), 4.15 – 4.07 (m, 1H), 4.07 – 3.90 (m, 3H), 3.78 – 3.69 (m, 1H), 3.66-3.64 (m, 2H), 3.53 (ddd, *J* = 9.7, 6.7, 4.0 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.88 – 1.78 (m, 1H), 1.72 (dd, *J* = 14.1, 6.7 Hz, 1H), 1.58 (dd, *J* = 13.9, 6.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.23, 138.15 , 137.89 , 137.88 – 137.84 , 137.56 , 137.32, 128.86, 128.83, 128.78, 128.66, 128.63, 128.60, 128.56, 128.47, 128.36, 128.25, 128.15, 128.08, 128.04, 128.00, 127.97, 127.86, 127.83, 82.9, 82.8, 81.3, 81.1, 78.9, 78.8, 77.8, 77.7,77.5, 77.4, 74.86, 74.7, 74.6, 73.5, 73.4, 73.3, 71.26 , 71.21 , 70.8, 70.7, 68.3, 68.1, 43.5, 42.7, 42.0, 41.5. ESI-MS; 658 $(M+Na)^+$.

Preparation of compound 17:

The compound **16** (0.08 mmol, 50mg) was dissolved in DCM: aqu. NaOH(1:1, 4 ml). TBAB (0.1 equiv., 3mg), propargyl bromide (1.2 equiv., 11.5 µL) were added and the reaction mixture was stirred at rt for 6h. Completion of the reaction was monitored through TLC. The reaction mixture was extracted with DCM (3 x 10 ml) and the combine organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The obtained crude product was subjected to silica gel column chromatography for purification. The isolated product (0.07 mmol, 48mg) was dissolved in acetonitrile (4 ml). CuI (5 mol%, 5.5 mg) was added and stirred at rt for 18h. Completion of the reaction was monitored through TLC and reaction mixture was concentrated under reduced pressure followed by ethyl acetate extraction (3x8 ml). The combined organic layers washed with brine, dried over anhydrous Na_2SO_4. The crude product was subjected to silica gel chromatography to obtained title compound **17** (87%, 46 mg) as colourless oily liquid.

^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.34-7.25 (m, 20H), 5.13-5.09 (m, 1H), 4.8 (m, 4H), 4.63 – 4.50 (m, 4H), 4.30 (m, 3H), 4.13 (dd, *J* = 8.5, 5.6 Hz, 1H), 3.91 (dt, *J* = 15.8, 6.6 Hz, 2H), 3.77 (2H), 3.49 – 3.29 (m, 2H), 2.65 – 2.55 (m, 1H), 2.45 – 2.32 (m, 1H), 2.17 – 2.00 (m, 1H), 1.83 – 1.73 (m, 1H).

General procedure for the synthesis of β-C-glycosides from hemiacetal (9):

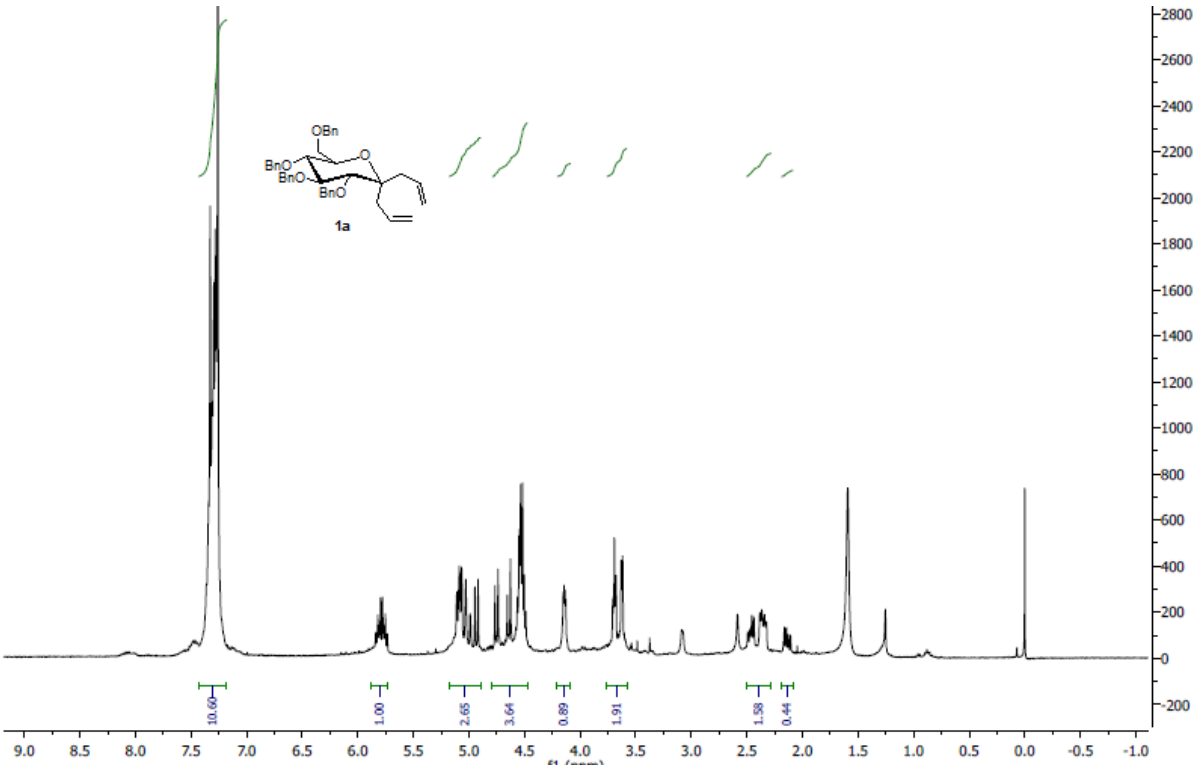
Hemiacetals was dissolved in dry DCM followed by an injection of Et_3SiH (1.0 equiv.) and $BF_3.Et_2O$ (1.2 equiv.) at -10 ^oC. The reaction mixture was stirred for 4h. After completion of

reaction as monitored by TLC, the reaction mixture was poured in water and extracted with DCM (3 x 15 ml). The combined organic layers were washed with brine solution, dried with anhydrous Na_2CO_3 and concentrated under reduced pressure. The obtained crude products were subjected to silica gel column chromatography to yield the corresponding glycosides.

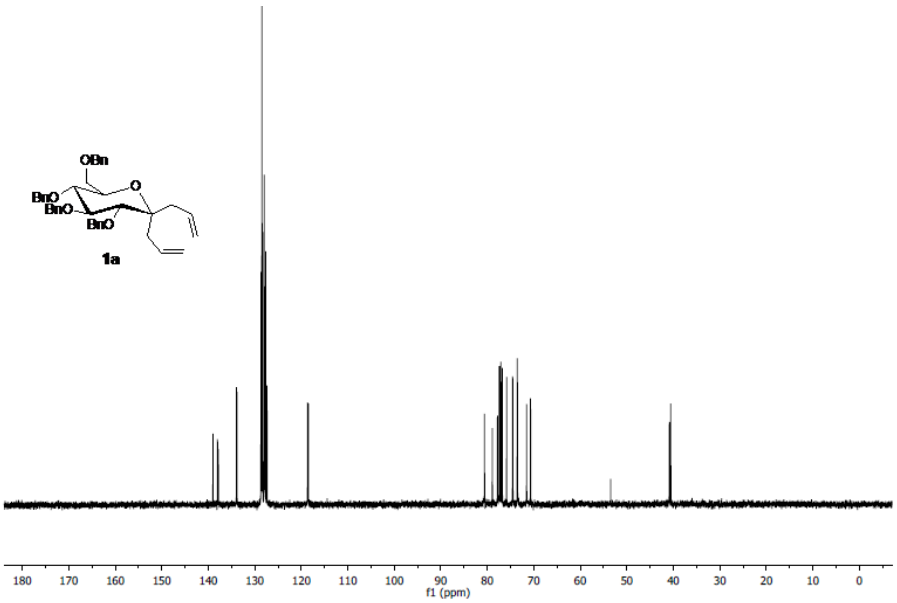
Preparation of compound 19:

Prepared by the general procedure **8** using 0.26 mmol (150 mg) of **11** to yield the desired product **19** (72%, 104 mg) as oily liquid. IR ($CHCl_3$); 3290, 2122. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.09 (m, 20H), 4.95 – 4.87 (m, 3H), 4.82 (d, *J* = 10.7 Hz, 1H), 4.74 (d, *J* = 10.8 Hz, 1H), 4.66 (d, *J* = 12.3 Hz, 1H), 4.60 (s, 1H), 4.57 (d, *J* = 3.3 Hz, 1H), 3.75-3.72 (m, 2H), 3.71 (d, *J* = 8.8 Hz, 1H),, 3.66 – 3.62 (m, 1H), 3.60 (dd, *J* = 11.8, 6.5 Hz, 1H), 3.48 (dd, *J* = 9.3, 3.5 Hz, 1H), 3.40 (dt, *J* = 9.1, 4.4 Hz, 1H, H-1), 2.69 (dt, *J* = 17.0, 2.9 Hz, 1H), 2.59 (ddd, *J* = 17.2, 5.2, 2.6 Hz, 1H), 2.02 (t, *J* = 2.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.5, 138.3, 138.12, 138.09, 128.55, 128.53, 128.48, 128.39, 128.35, 128.30, 128.25, 128.18, 128.13, 128.08, 128.02, 127.97, 127.94, 127.90, 127.88, 127.84, 127.80, 127.76, 127.72, 127.59, 87.0, 80.7, 80.5, 79.3, 78.5, 75.6, 75.4, 75.1, 73.5, 70.5, 68.8, 21.9. ESI-MS; 580 $(M+NH_4)^+$; Anal. Cal. For $C_{37}H_{38}O_5$; C, 78.98; H, 6.81. Found C, 77.92, H, 6.86.

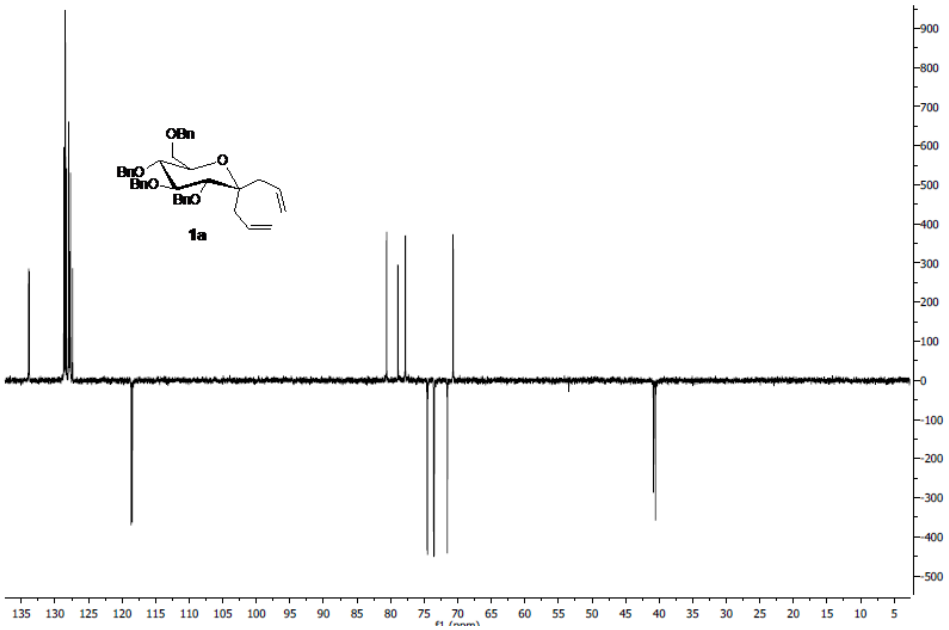
^{1}H NMR of compound 1a



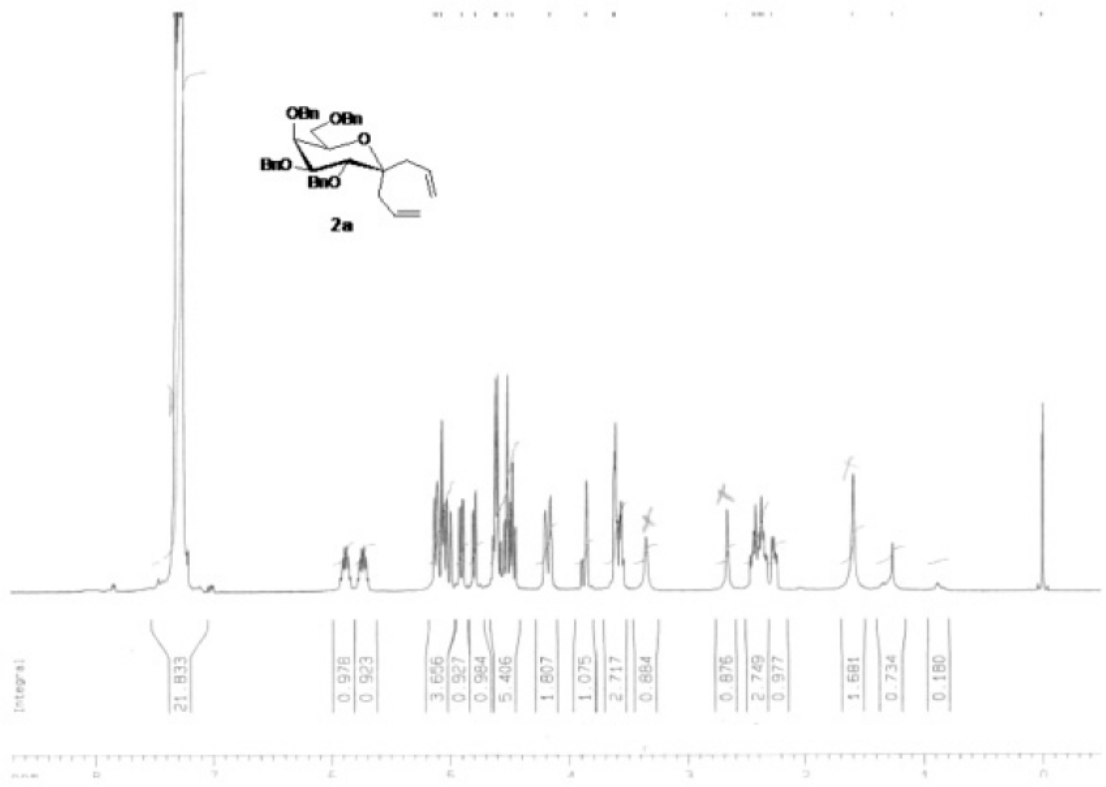
^{13}C NMR of compound 1a



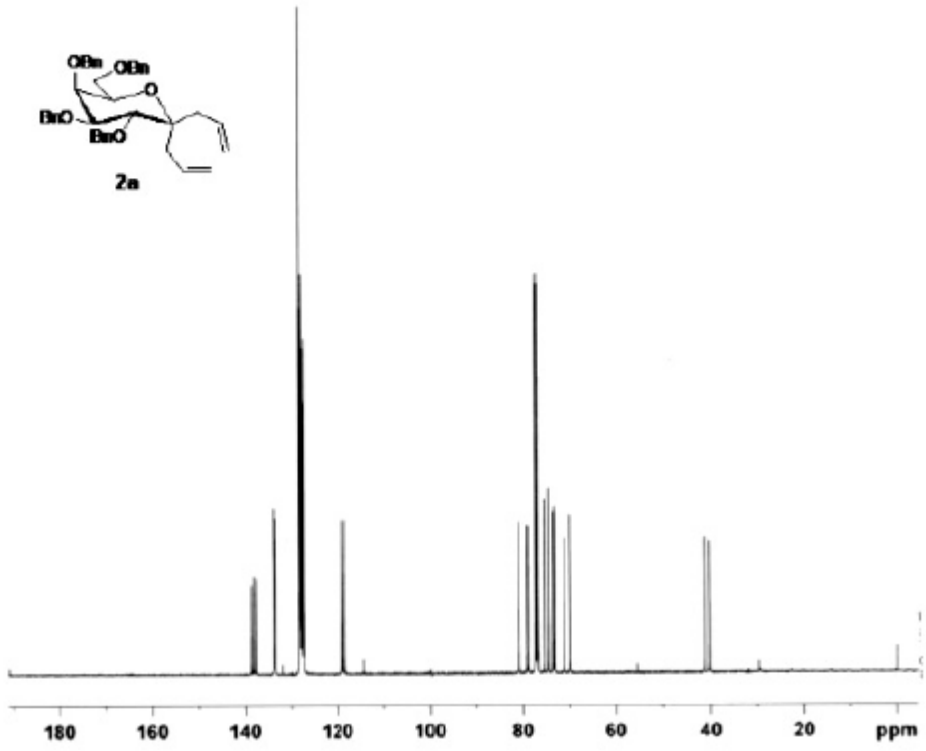
DEPT of compound 1a



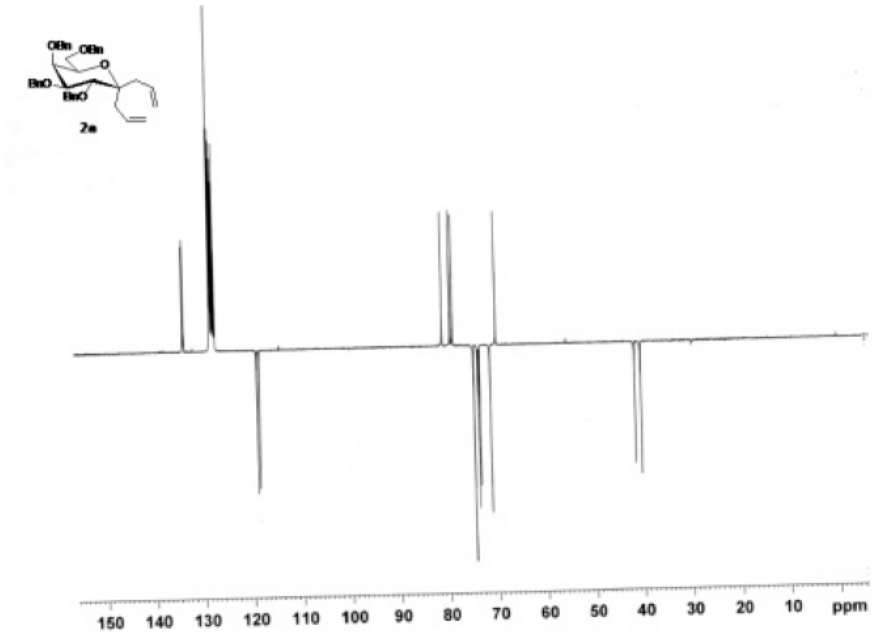
^{1}H NMR of compound 2a



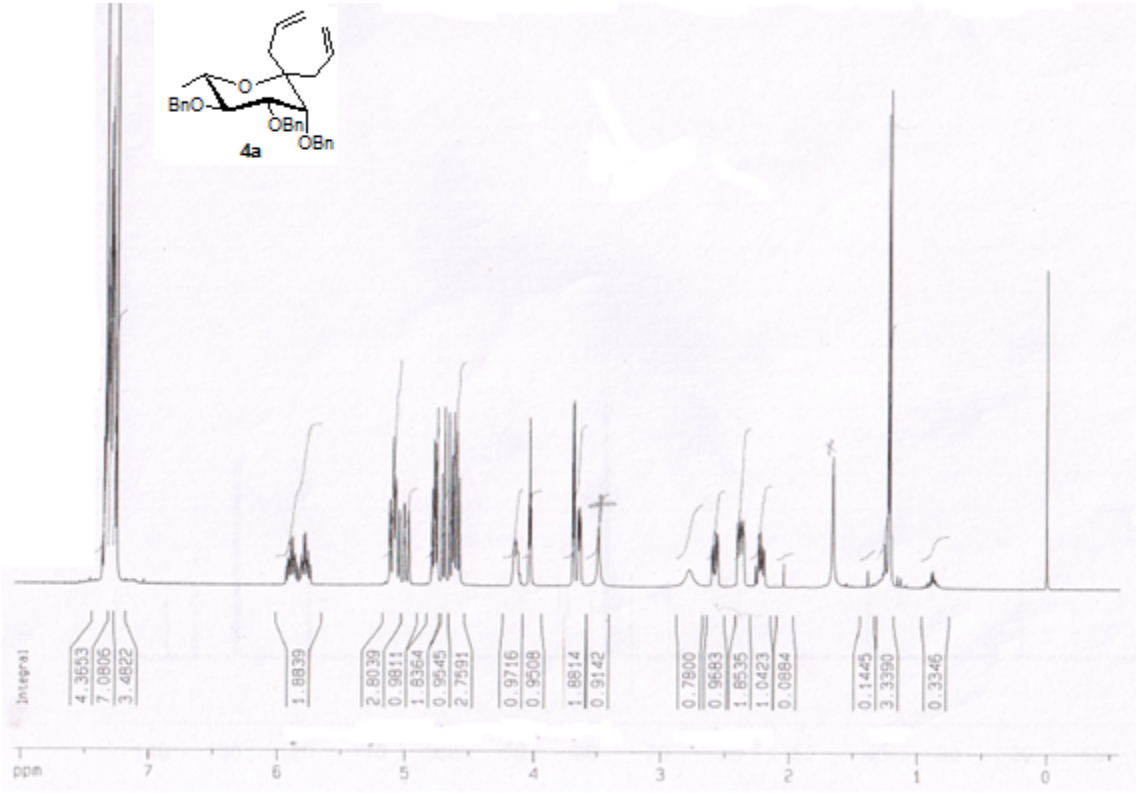
^{13}C NMR of compound 2a



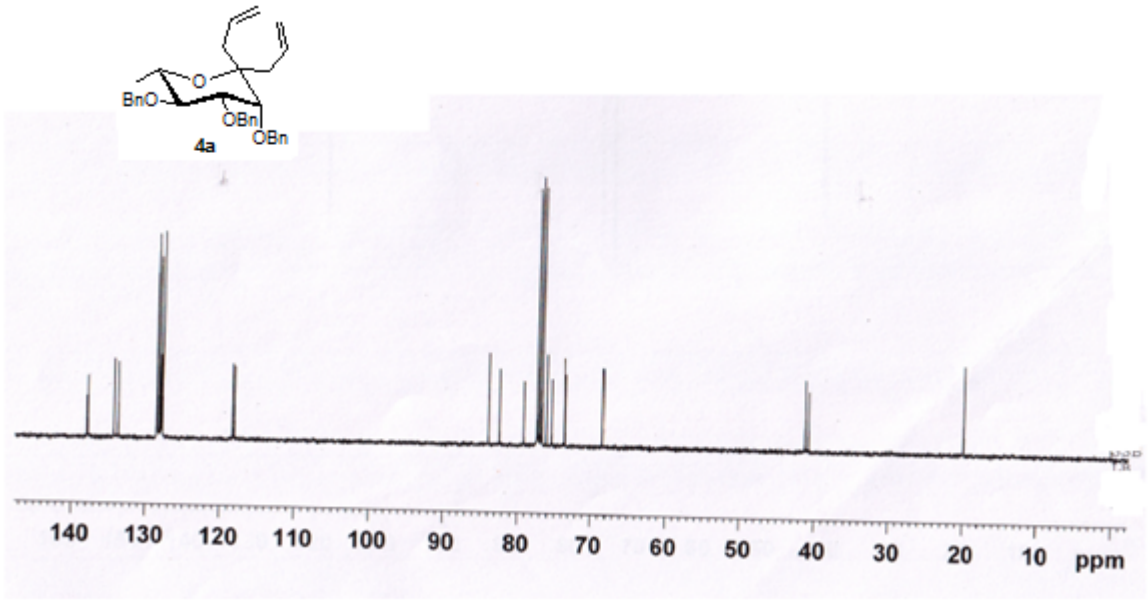
DEPT of compound 2a



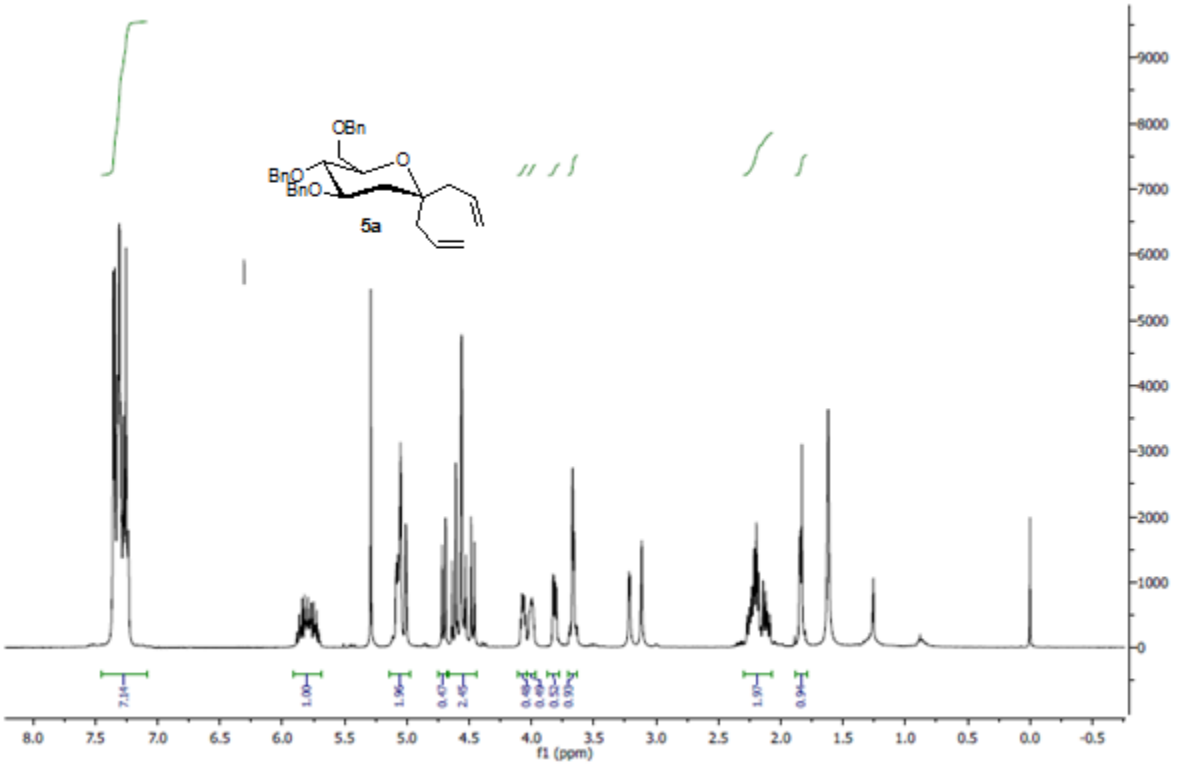
^{1}H NMR of compound 4a



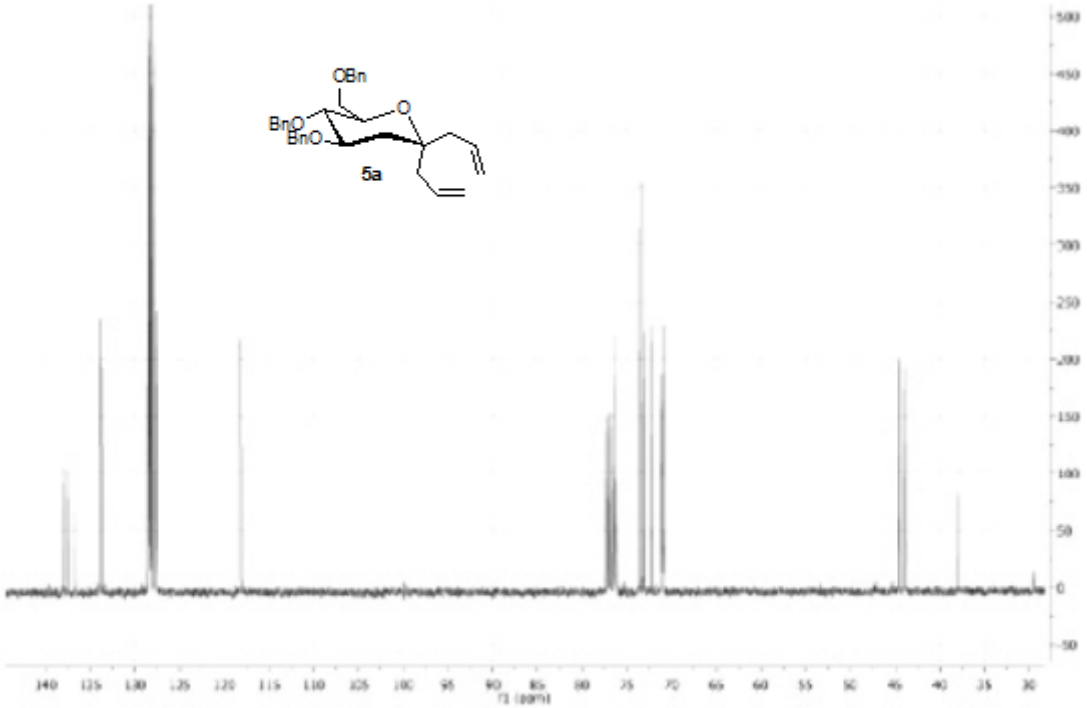
^{13}C NMR of compound 4a



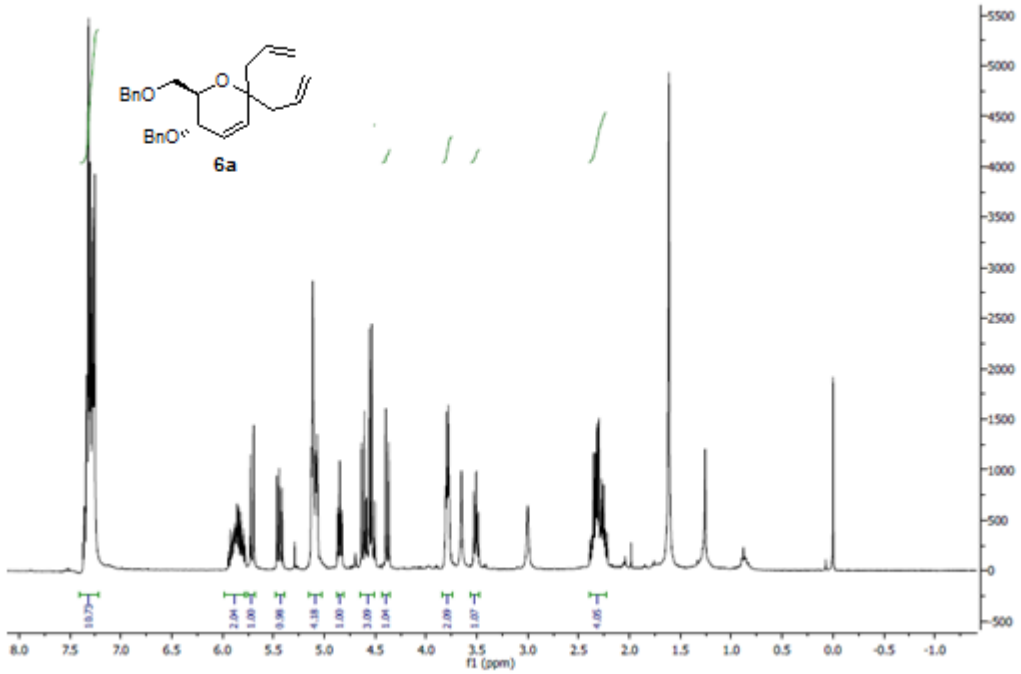
^{1}H NMR of compound 5a



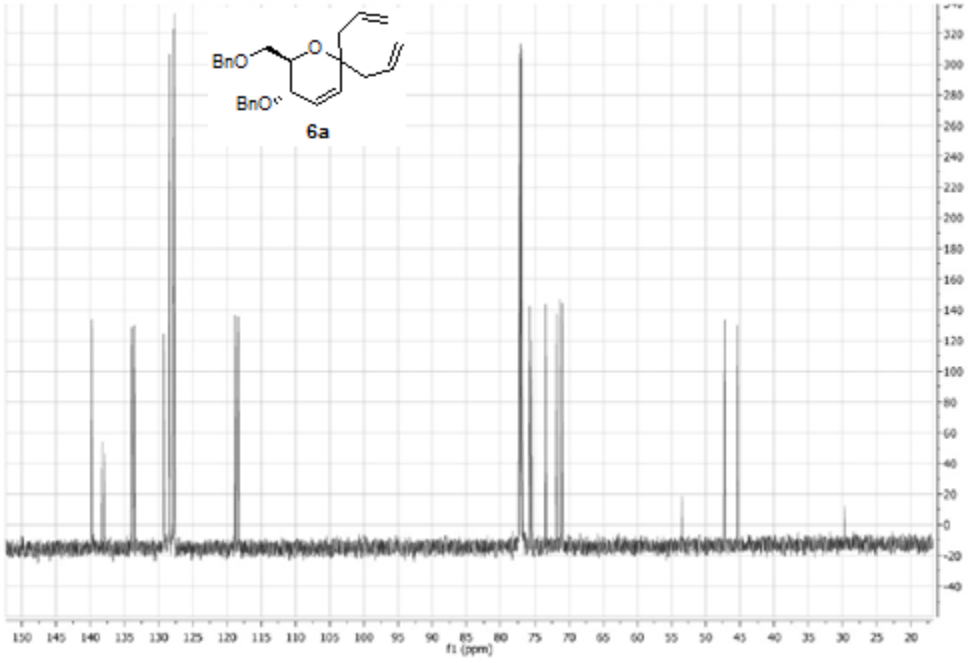
^{13}C NMR of compound 5a



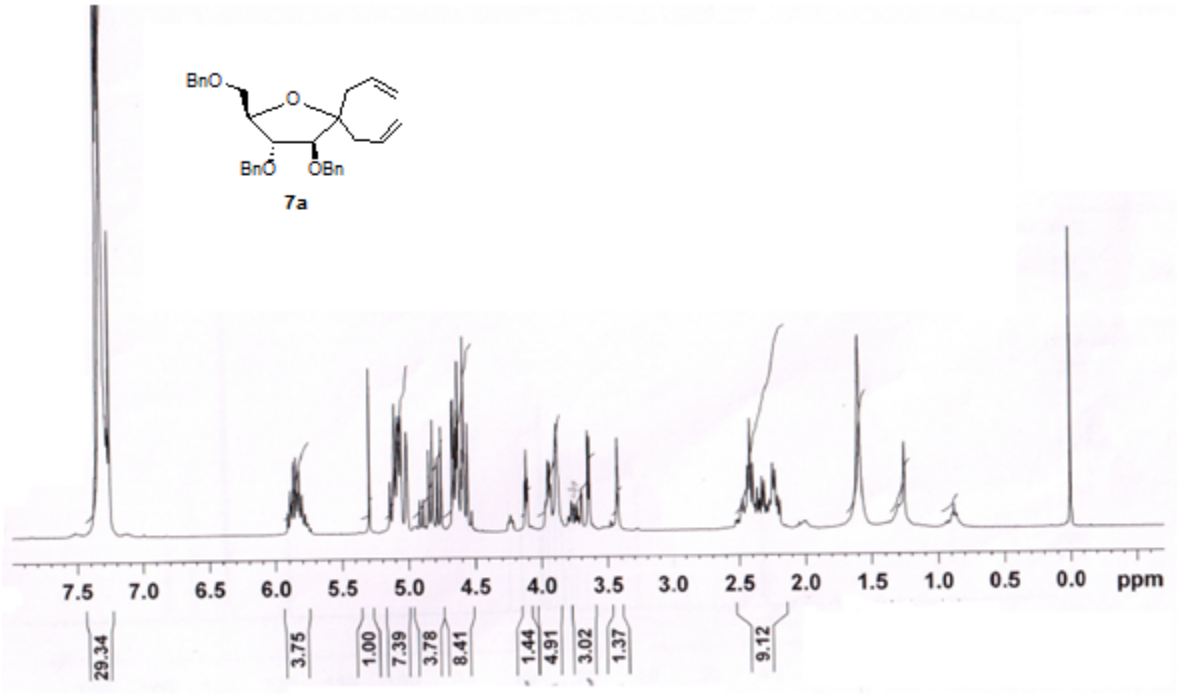
^{1}H NMR of compound 6a



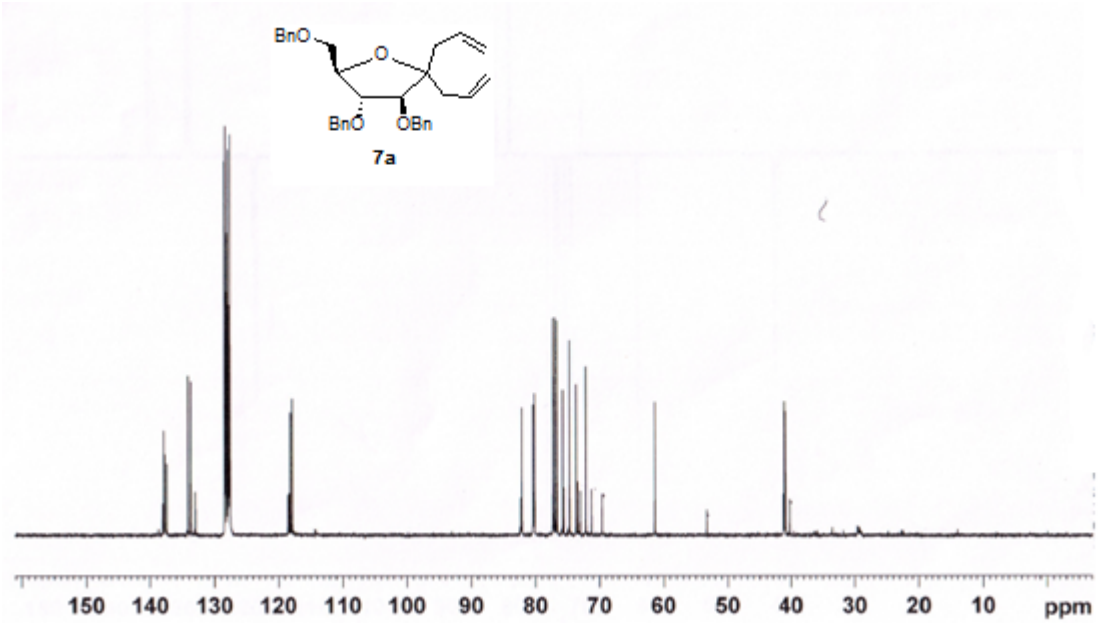
^{13}C NMR of compound 6a



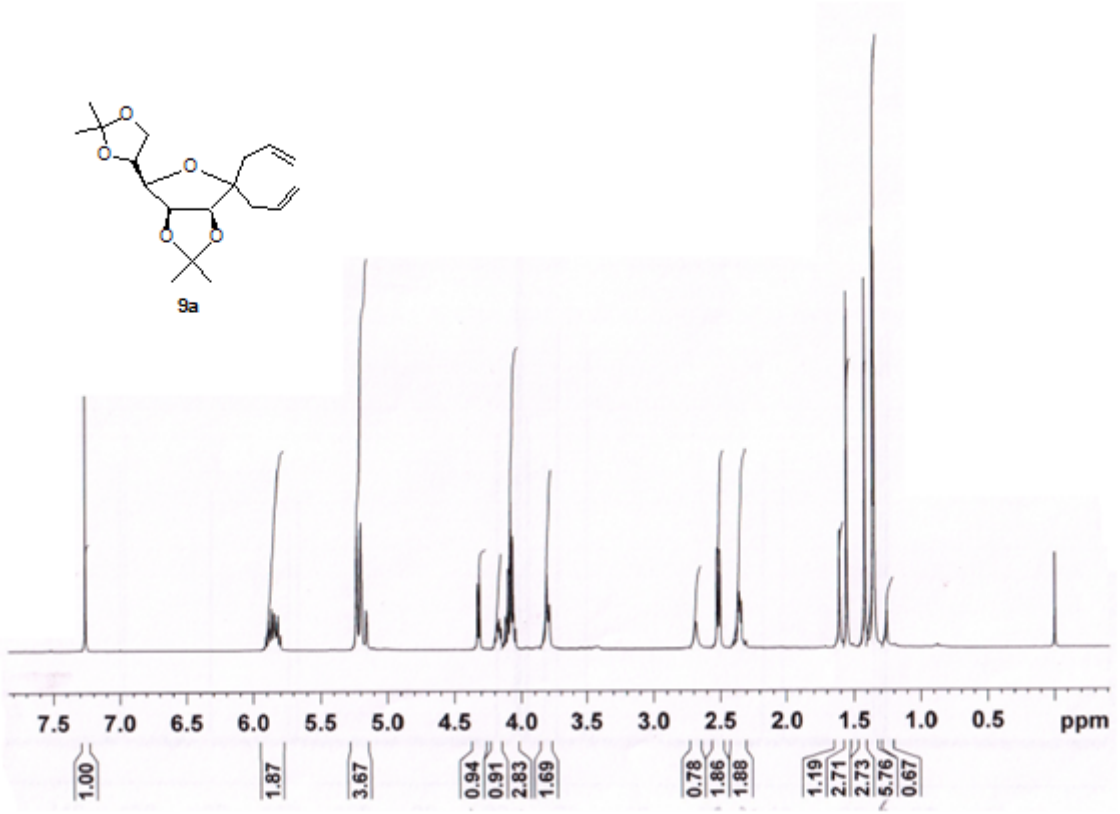
^{1}H NMR of compound 7a



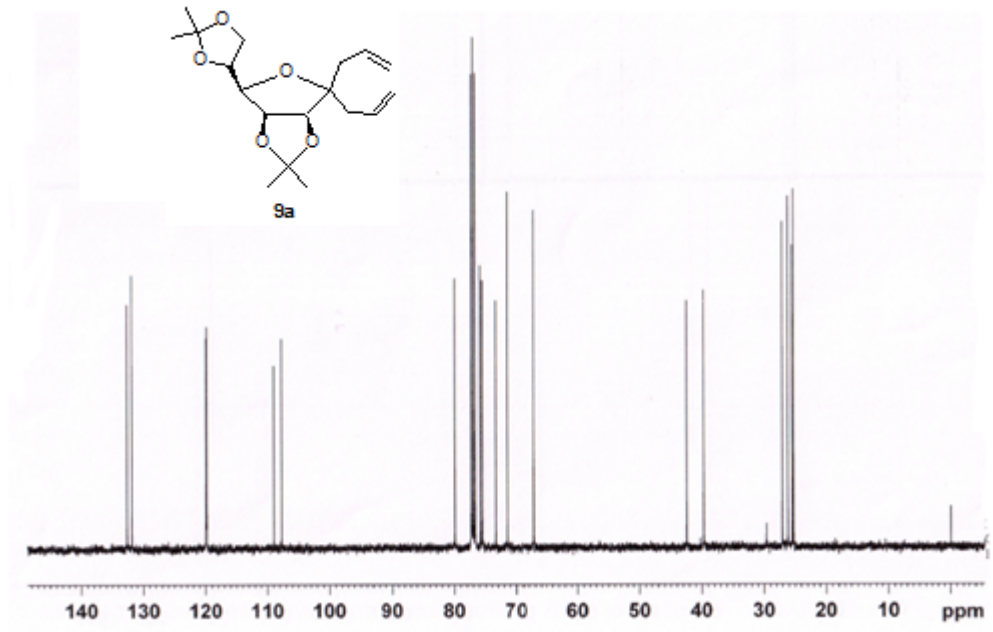
^{13}C NMR of compound 7a



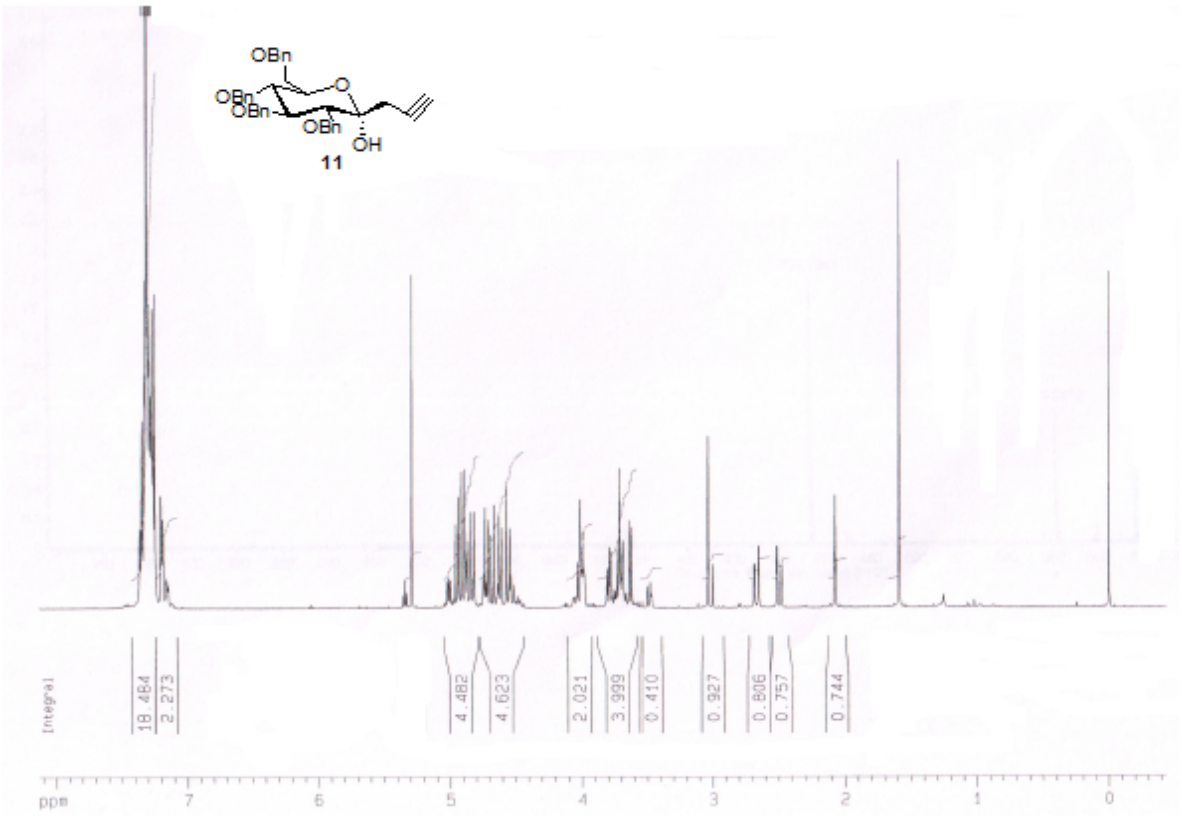
^{1}H NMR of compound 9a



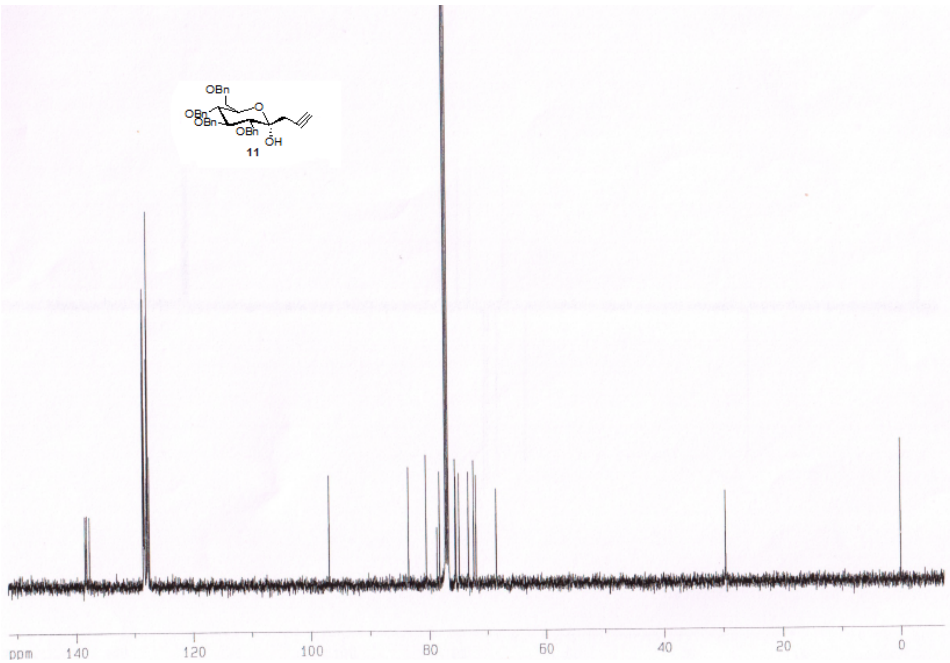
^{13}C NMR of compound 9a



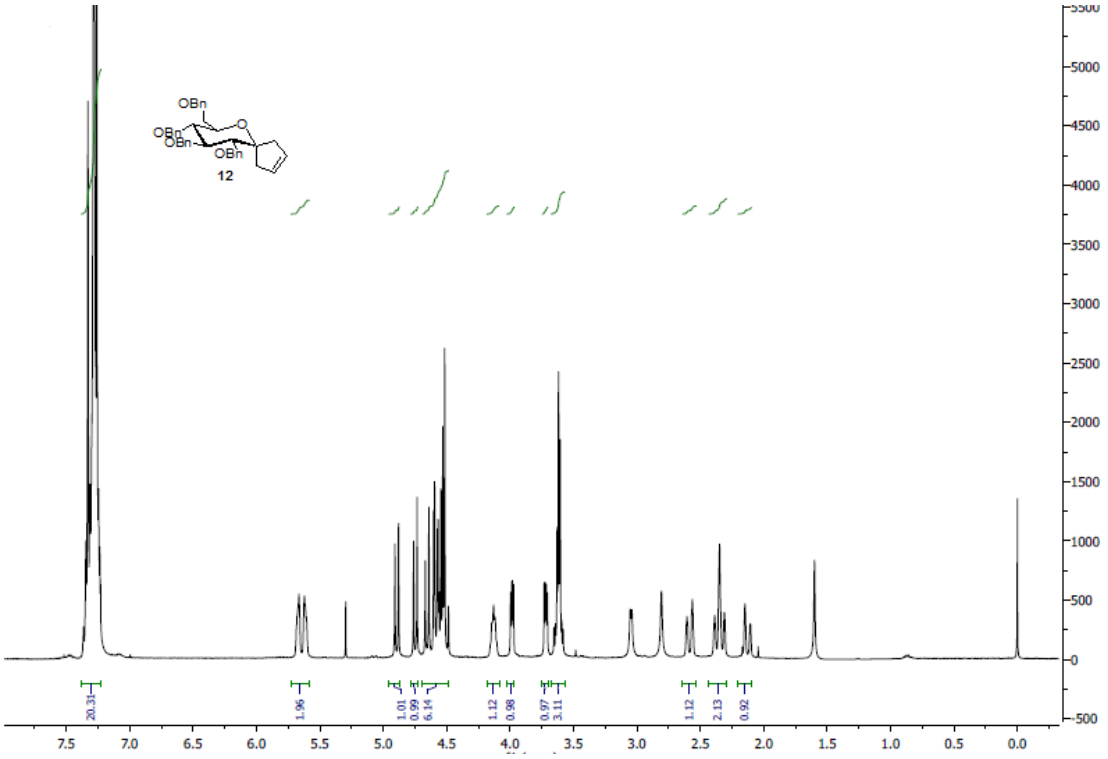
^{1}H NMR of compound 11



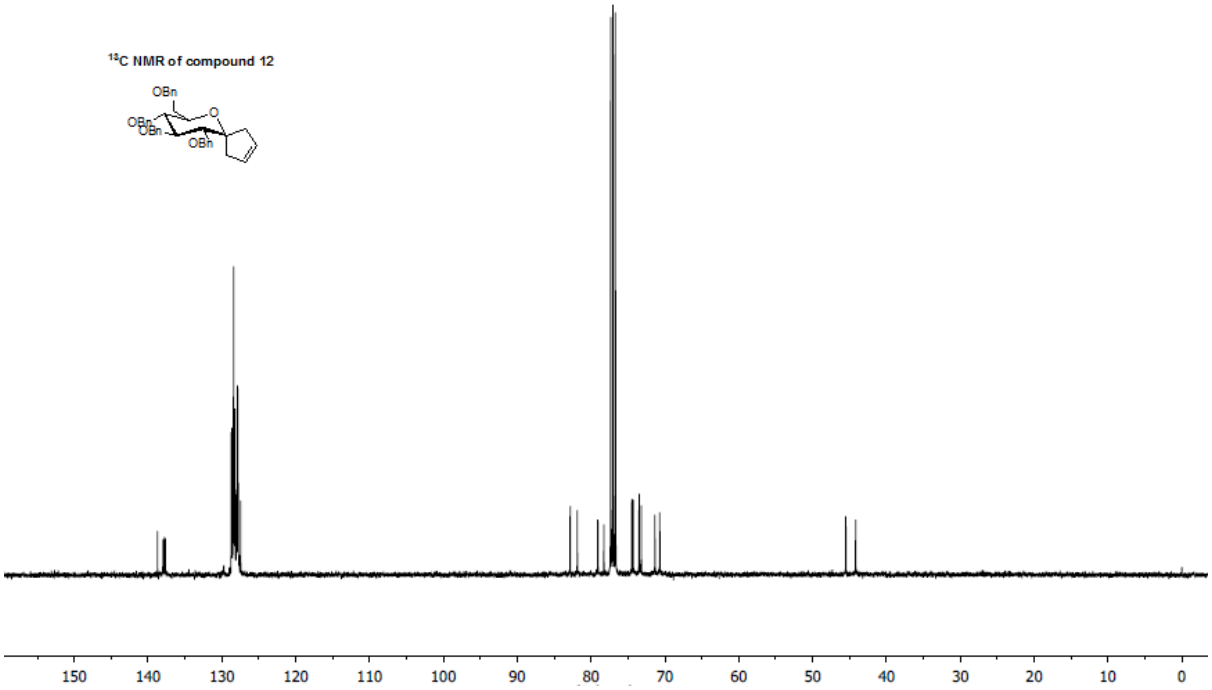
^{13}C NMR of compound 11



^{1}H NMR of compound 12

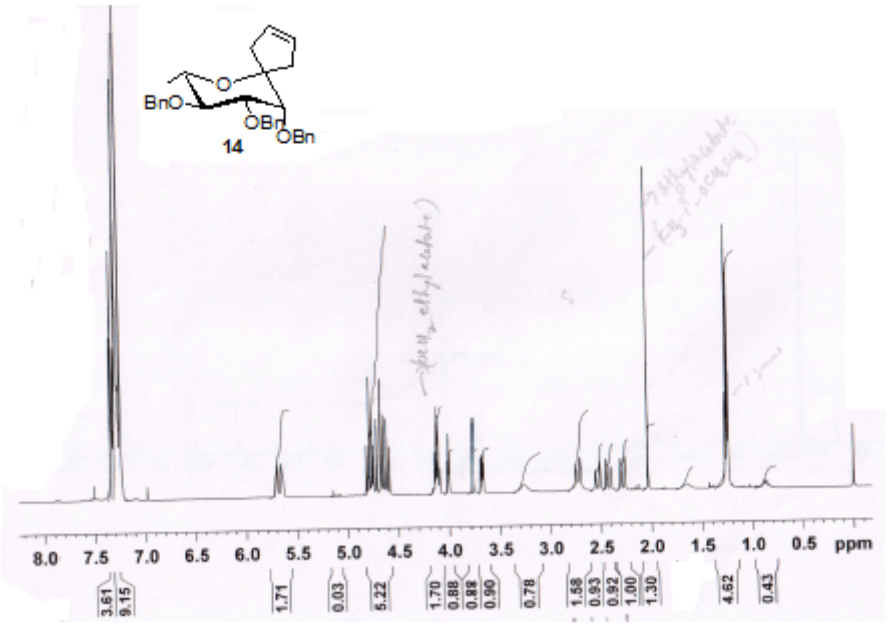


^{13}C NMR of compound 12

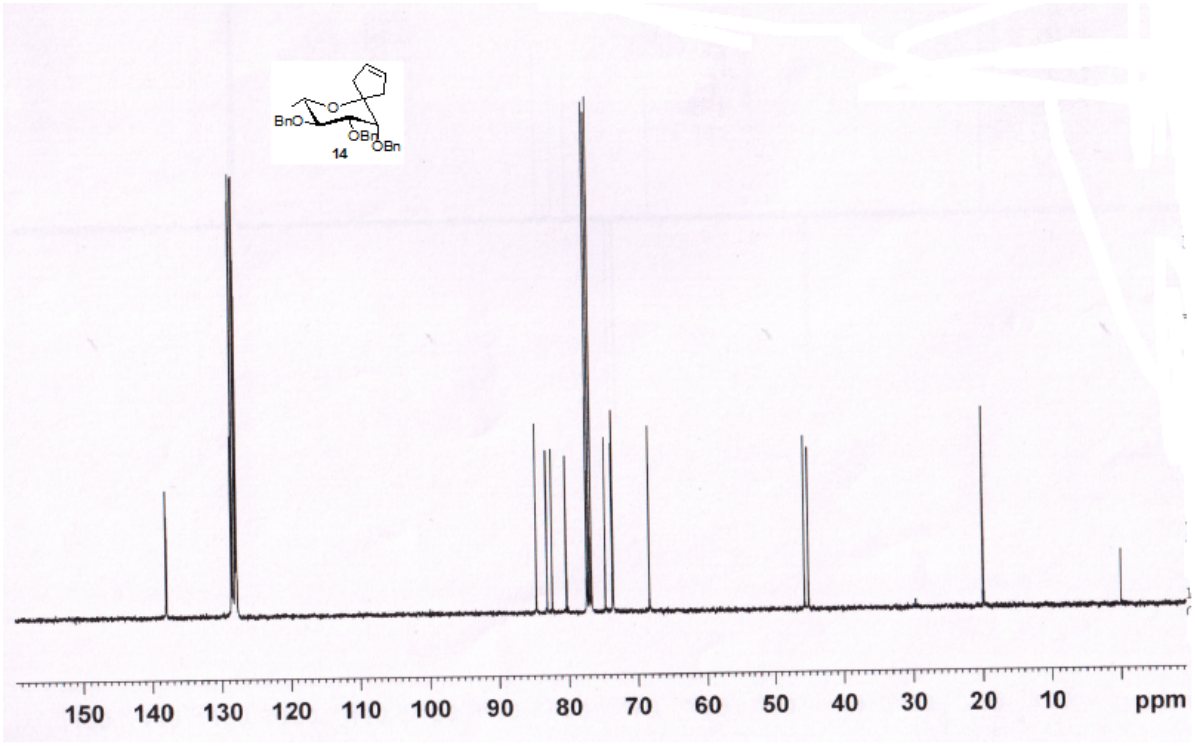


^{1}H NMR of compound 13

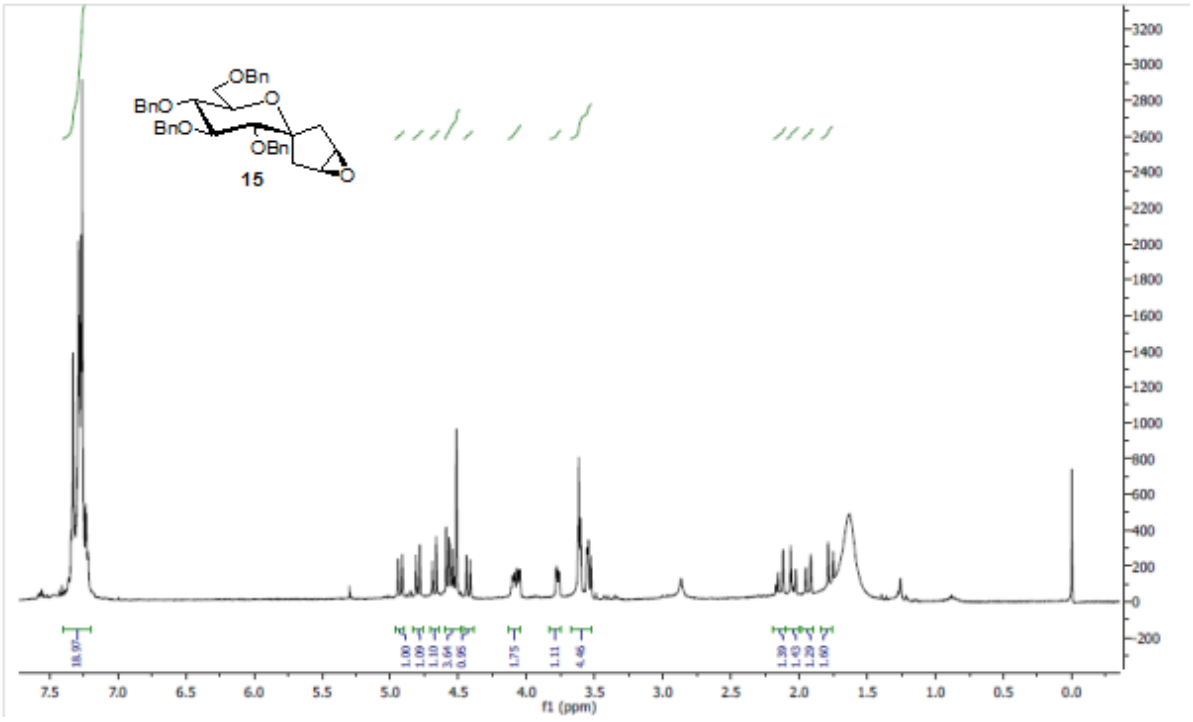
^{1}H NMR of compound 14



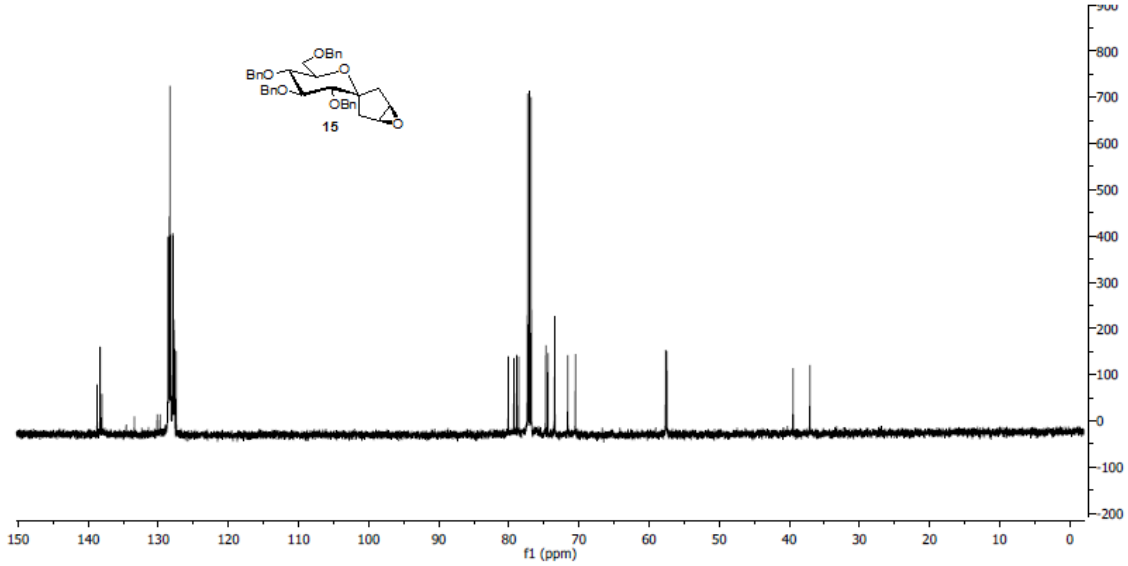
^{13}C NMR of compound 14



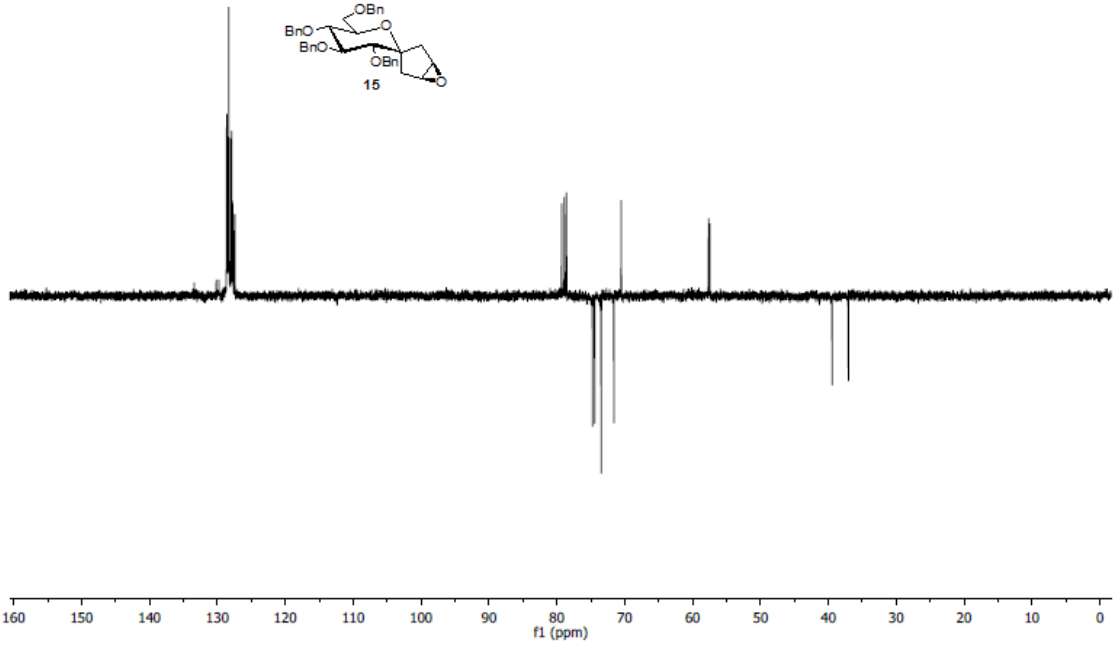
^{1}H NMR of compound 15



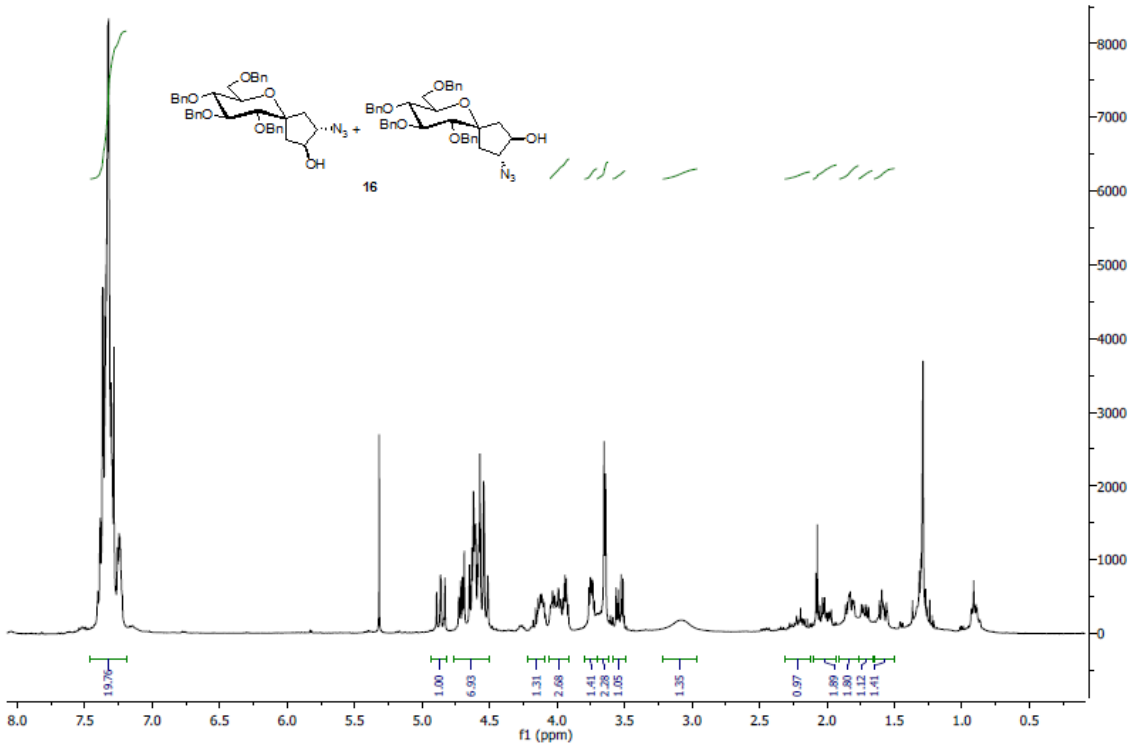
^{13}C NMR of compound 15



DEPT of compound 15



^{1}H NMR of compound 16



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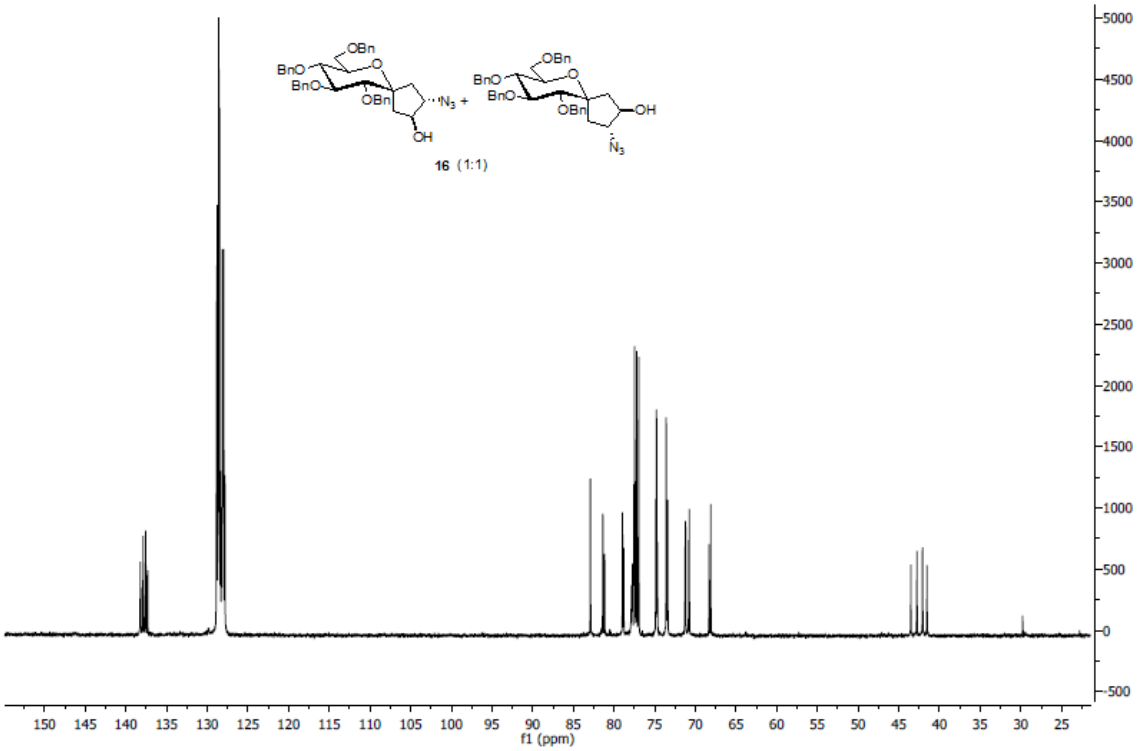
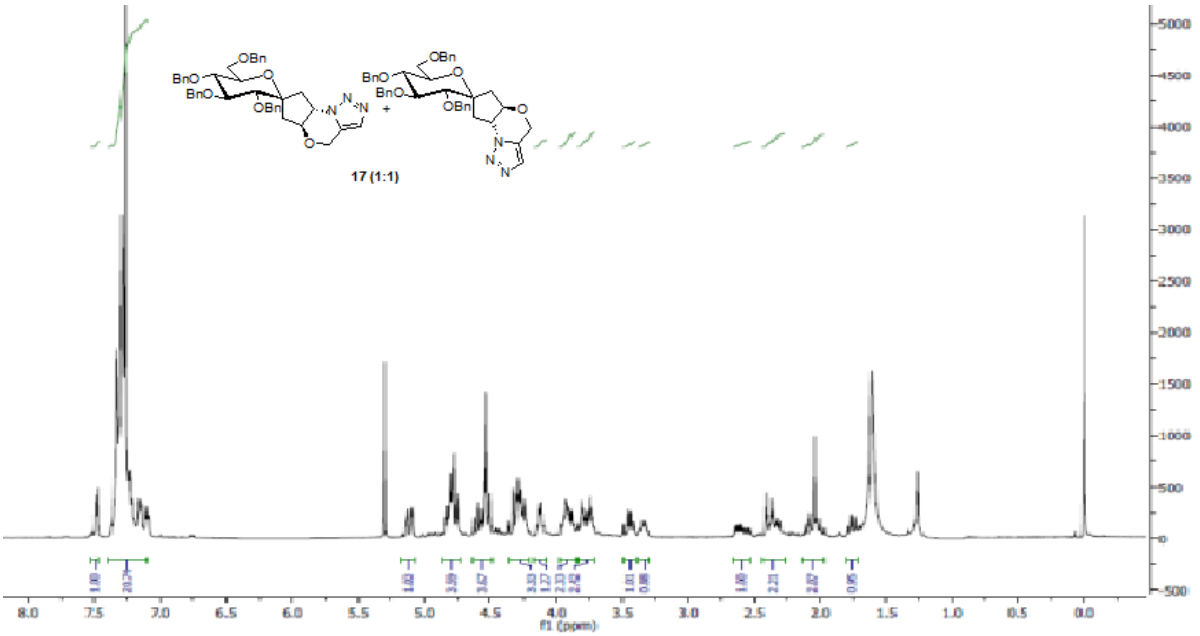
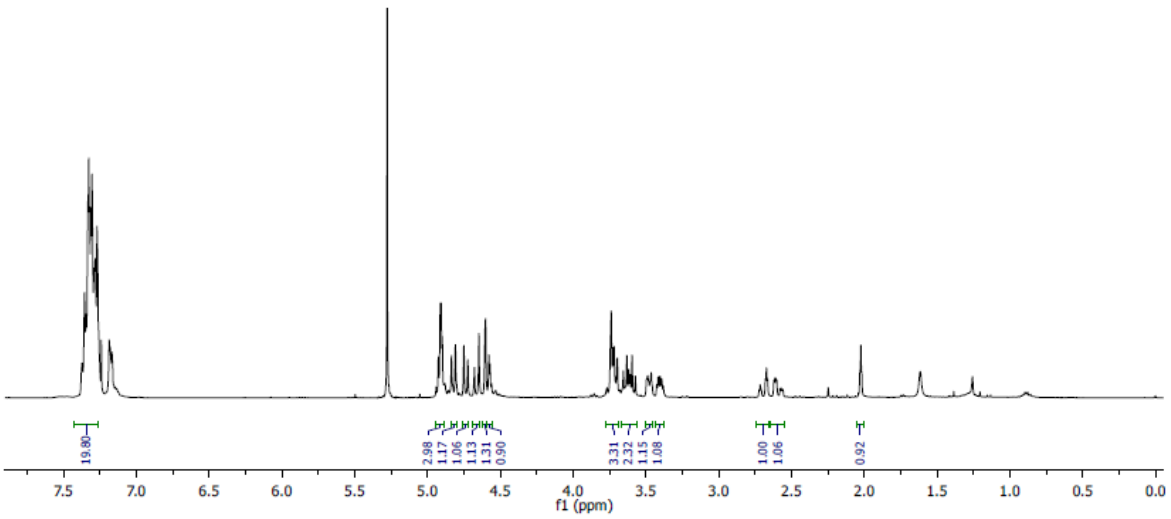


^{1}H NMR of compound 17



^{1}H NMR of compound 19



^{13}C NMR of compound 19