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Approaches Towards the Synthesis of Pyrrolidine Derived Aza Sugars

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***Abstract*—** In this paper attempts towards the synthesis of some poly hydroxylated derivatives of aza heterocycles *viz*., pyrrolidine analogs which could act as glycosidase inhibitors have been demonstrated. Two different approaches were followed using the chemistry of glycals. However, the advanced intermediates obtained during these approaches could not be cyclized to the final products.

***Keywords*—** Aza sugars; glycosidate inhibitors; poly hydroxylated pyrrolidines

I. INTRODUCTION

Iminosugars or azasugars[1] are compounds in which the ring oxygen of a monosaccharide has been replaced by an imino group. Many polyhydroxylated pyrimidine alkaloids have attracted considerable attention due to their ability to inhibit glycosidases[2]. Because glycosidases are involved in several important biological processes, these polyhydroxylated alkaloids have stimulated interest in the development of specific glycosidase inhibitors such as diabetes[3]or as antiviral, antibacterial and anticancer agents[4]. In particulars, glycosidase inhibitors have shown potential as therapeutic agents for type II diabetes[5] and HIV-I infection[6].

In this direction various glycosidase inhibitors have been synthesized such as amidines[7], imidazoles[8], trizoles[9] and tetrazoles[10]

II. Results and discussion

Due to the emerging importance of hybrid molecules[11] we tried to synthesize pyrrolidine analog of aza heterocycles, which could act as glycosidase inhibitors from tri-*O*-bengyl-D-glucal. Two approaches were followed using the chemistry of D-glycal.

Approach-1: In this approach 3, 4, 6-tri-*O*-benzyl-D-glucal was converted to tribenzylated allylic alcohol 1 by the known literature procedure[12] *via* two steps viz., formylation followed by $NaBH_4$ reduction. Compound **1** on benzylation with benzyl bromide in presence of NaH in DMSO forms benzylated compound **2** in 89% yield, which was characterized from its ^{1}H NMR data, ^{13}C NMR data and by mass spectral data. Compound **2** on dihydroxylation with OsO_4-NMO formed a diol **3** in 94% yields, which in its ^{1}H NMR spectrum showed a singlet for anomeric proton at δ 5.36-5.39. IR spectrum of the compound **3** showed the absorption peak for -OH group at 3408 cm^{-1}. Compound **3** on oxidative cleavage with $NaIO_4$ in acetonitrile formed compound **4** in 83% yield. Compound **4** was directly obtained from compound **2** by ozonolysis process.

Compound **4** in its ^{1}H NMR spectrum showed a peak at δ 7.78 for -OCOH group. A multiplet at δ 5.15-5.17 was seen for C-5 proton. IR spectrum of compound **4** showed a peak at 1726 cm^{-1} for -OCHO group. Compound **4** on hydrolysis with K_2CO_3/ MeOH[13] formed compound **6**, which on oxidation with IBX formed compound **7**. However, compound **4** on $LiAlH_4$ reduction formed a diol **5** in 70% yield, which was confirmed from its ^{1}H NMR spectrum. IR spectrum of compound **5** showed a peak for the hydroxy group at 3437cm^{-1} (Scheme1). Diol **5** was also confirmed from its corresponding diacetate **10**, which in its ^{1}H NMR spectrum showed two singlets at δ 1.92 and 1.98 cm^{-1} for the two –$COCH_3$ groups (Pl. ref. experimental section).

Diol 5 on oxidation with IBX in ethyl acetate forms a diketo derivative **7**. Diol **5** was also oxidized by CrO_3/H_2SO_4 to form a diketo product **7**. Compound **7** on treatment with $BnNH_2$ in presence of $NaCNBH_3$/AcOH[14] didn't form a cyclized aza product **8** (Scheme 1).

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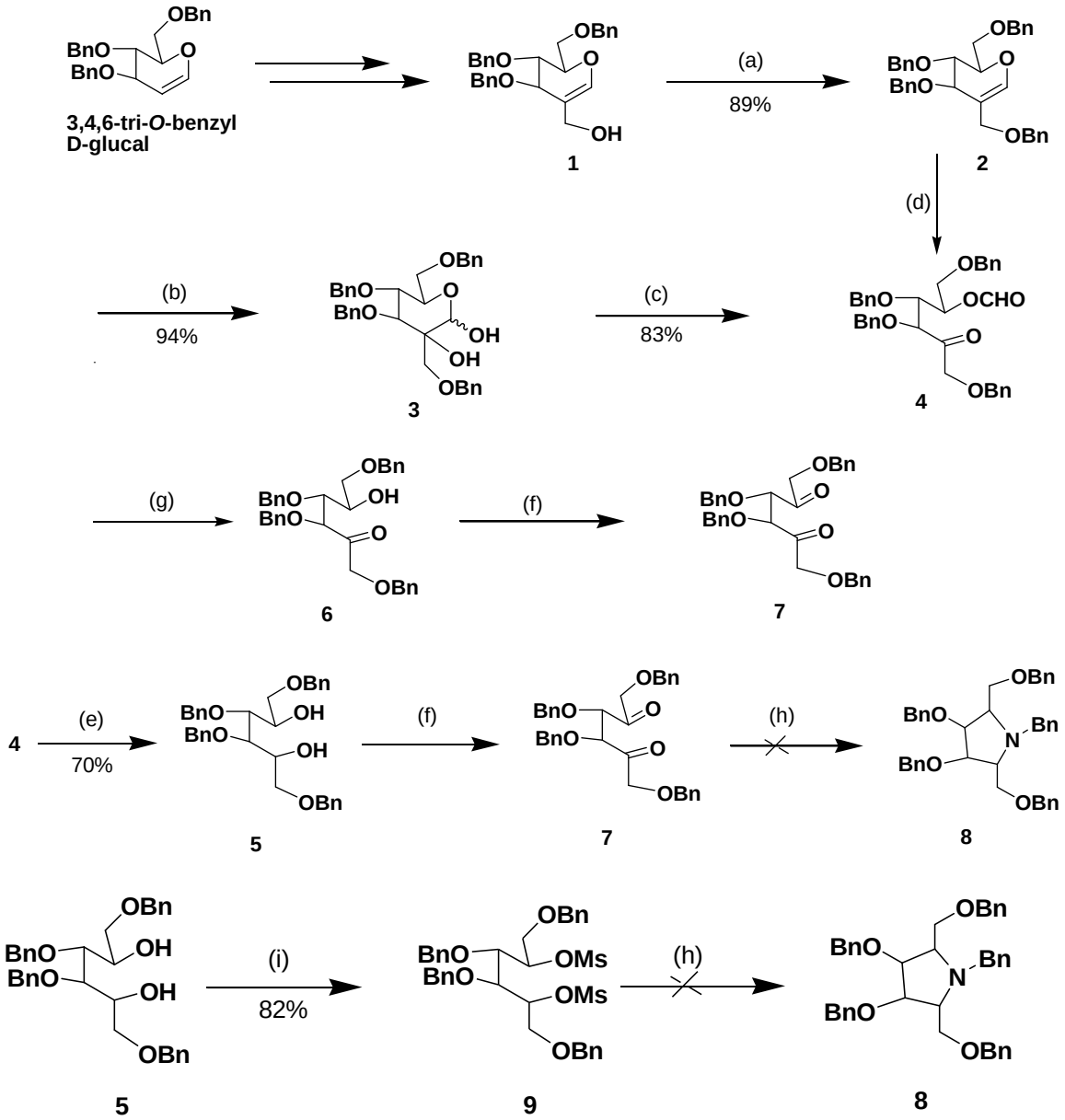

Reagents and conditions: (a) BnBr, NaH, DMSO, rt, 5 h; (b) OsO_4-NMO, Acetone:H_2O :^{t}BuOH (1:1:0.5), $Na_2S_2O_5$, rt, 2.5 h; (c) $NaIO_4$, CH_3CN/H_2O, 0°C to 10 °C, 2 h; (d) O_3, DCM, 15 min; (e) $LiAlH_4$, THF, rt, 1 h; (f) IBX, EtOAc, 80°C, reflux, 4 h; (g) K_2CO_3, MeOH, rt, 1 h; (h) $BnNH_2$, $NaCNBH_3$/AcOH, 0ºC to rt; (i) MsCl, Et_3N, DCM, 2 h. (j) $BnNH_2$, NaH, CH_2Cl_2, 0ºC to rt.

Scheme 1

However, the diol **5** was mesylated with MsCl to form a dimesylated product **9** in 82 % yield, which in its ^{1}H NMR spectrum showed a singlet at δ 2.96 for the mesyl group. Compound **9** on treatment with $BnNH_2$/NaH didn't form a cyclized product **8**.

Approach-2: In this approach, 3,4,6-tri-*O*-benzyl glucal on treatment with oxone and $NaHCO_3$[15] formed a diol **11** which exist in the anomeric mixture (α:β =1:1) in 80% yield. Diol **12** on reduction with $LiAlH_4$ in presence of THF at room temperature formed a triol **12** in 84% yield. The formation of

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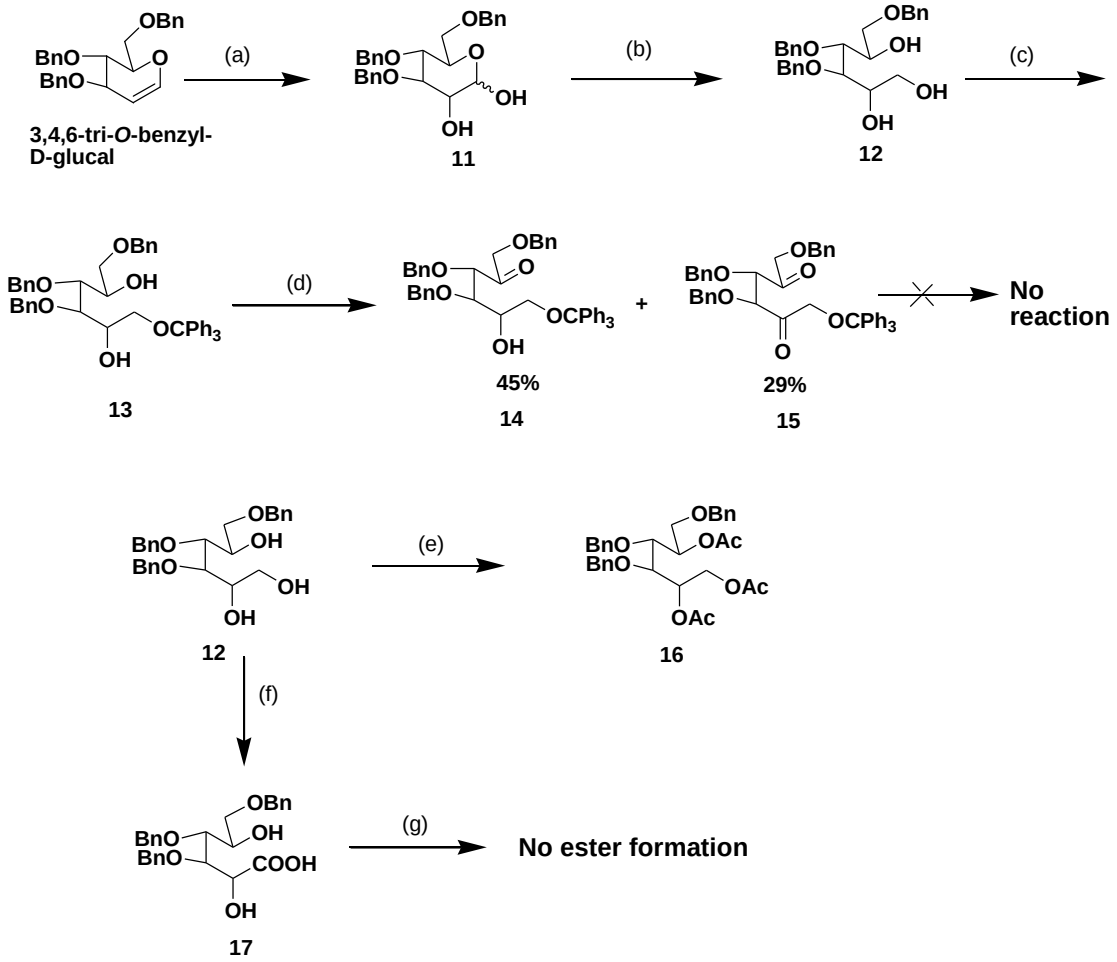
compound **12** was confirmed from its ^{1}H NMR, IR spectrum and mass data. The ^{1}H NMR of the compound **12** showed two broad singlets at δ: 3.92 and 4.04 for C-1 protons. Also, the presence of three -OH groups were confirmed by the acetylation of the triol **12** with acetic anhydride/Et_3N, which showed three singlets at δ: 1.94-2.07 for the three acetyl groups. Selective oxidation of the primary alcohol of compound **12** with TEMPO didn't give a clean NMR spectrum and thus the carboxylic acid **17** formed was as such esterified with diazomethane in THF, but no ester was formed. It may be assumed that during tempo oxidation, the aldehyde formed got cyclized to form the lactol.

Thus, we changed our strategy and performed the selective protection of the primary alcohol of triol **12** with trityl chloride in presence of Et_3N. The tritylated compound **13** was formed in 72% yield. Compound **13** in its ^{1}H NMR spectrum showed peak for the phenyl group of tritylated functionality at δ: 7.42. Also its ^{13}C NMR as well as mass spectrum confirmed the formation of the compound. Compound **13** on oxidation with IBX in acetone formed compounds **14** and **15**. Compound **14** showed the formation of a hydroxy keto derivative. However, the compound **15** showed the formation of diketo derivative in its ^{1}H NMR spectrum. Compound **14** was further oxidized with PDC/DMF to form a diketo derivative but the reaction didn't occur. The yield of compound **15** was found to be low. Thus the oxidation of compound **13** was done with PDC/DMF and oxalyl chloride/DMSO, but the reaction did not give better results as the reaction was not clean and was forming same two spots as obtained by IBX oxidation (Scheme 2). Compound **15**, however, didn't undergo cyclization.



Reagents and conditions: (a) Oxone, $NaHCO_3$, Acetone/H_2O, rt, 45 min, 80%; (b) $LiAlH_4$, THF, 60°C, 3h, 84%; (c) TrCl, Et_3N, DCM, rt, 0.5h, 72%; (d) IBX, Acetone, 56°C, 4h, 45% for **14** and 29% for **15**; (e) Ac_2O, Et_3N, DCM, rt, 1h, 80%; (f) TEMPO, $NaHCO_3$, KBr, NaOCl, Acetone, rt, 2h; (g) CH_2N_2, THF, rt.

Scheme 2

In conclusion, we have tried two different methods for the development of Pyrrolidine based aza sugars. Though, our

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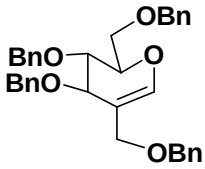
attempts remain unsuccessful, have paved way for new method development. This work is still under consideration in our lab.

III. Experimental Section

Compound 2

To a suspension of NaH (93.60 mg, 3.90 mmol) in DMSO (3 mL) was added compound **1** (1.45 g, 3.25 mmol) slowly at 10 ºC. The reaction mixture was stirred at room temperature for 15 min and then benzyl bromide (0.46 mL, 3.90 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 24 h. The reaction was monitored by TLC. The organic layer was extracted with ethyl acetate (2 x 40 mL), washed with ice cold water and dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography to obtain 1.55 g of allylic benzoate **2** as viscous liquid.

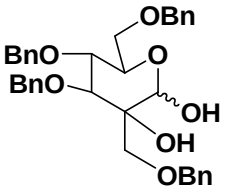


R_f = 0.70 (7:3 hexane:EtOAc); Yield = 89%; $[\alpha]_D^{25}$ = + 56.3 (*c* 0.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.69-3.80 (m, 3H), 3.89-3.92 (q, *J* = 6.54 Hz, 1H), 4.21-4.30 (m, 3H), 4.35-4.73 (m, 8H), 6.47 (s, 1H), 7.23-7.37 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 67.6, 68.1, 70.9, 72.7, 73.0, 73.3, 73.8, 74.1, 109.5, 127.4, 128.4,

137.9, 138.3, 143.7; MS (ESI): m/z = 559 $(M + Na)^+$; Anal. Calcd. for $C_{35}H_{36}O_5$ (536.26): C, 73.66; H, 6.71 % Found: C, 73.65; H, 6.70 %

Compound 3

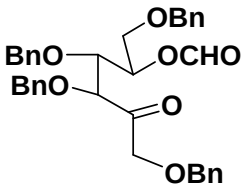
To the stirred solution of compound **2** (200 mg, 0.37 mmol) in acetone:water:^{t}BuOH (1:1:0.5) at room temperature was added NMO (60.40 mg, 0.44 mmol) and the reaction mixture was stirred for 5 min. One drop of OsO_4 was added to it and the reaction mixture was stirred for 2 h. Then $Na_2S_2O_5$ (106 mg, 0.55 mmol) was added to it and the reaction mixture was further stirred for 1h. The reaction mixture was filtered through a celite pad and the filtrate was extracted with ethyl acetate (3 x 20 mL), brine, water and dried over anhydrous Na_2SO_4. The crude sample obtained was purified by column chromatography to form 206 mg of an inseparable mixture of diol **3** as white solid.



R_f = 0.50 (5:5 hexane:EtOAc); Yield = 94%; $[\alpha]_D^{25}$ = +13.2 (*c* 4.00, $CHCl_3$); IR (CH_2Cl_2) ν_{max} = 3408 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.12 (s, 1H), 3.51-3.56 (t, *J* = 9.52 Hz, 1H), 3.60-3.77 (m, 4H), 3.91-4.03 (2d, *J* = 9.76 Hz, 2H), 4.12-4.19 (m, 2H), 4.37-4.50 (m, 1H), 4.52-4.68 (m, 3H), 4.37-4.79 (m, 2H), 4.99-5.04 (m, 1H), 5.36-5.39 (s, 1H), 7.15-7.36 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:14.0, 22.6, 24.8, 28.7, 29.0, 29.2, 29.3, 29.6, 31.8, 34.0, 63.5, 173.3; MS (ESI): m/z = 588 $(M + NH_4)^+$; Anal. Calcd. for $C_{35}H_{38}O_7$ (570.26): C, 78.33; H, 6.76 % Found: C, 78.30; H, 6.77 %

Compound 4

To a stirred solution of compound **3** (560 mg, 0.98 mmol) in acetonitrile/H_2O (2.5:1.8) was added $NaIO_4$ (419 mg) in small portions at 10 ºC. The reaction mixture was stirred for 1 h and the completion of the reaction was checked by TLC. The reaction mixture was filtered through a celite pad and the filtrate was extracted with ethyl acetate (2 x 25 mL). The organic layer was washed with brine and dried over anhydrous Na_2SO_4. The crude product obtained was purified by column chromatography to form 463 mg of compound **4** as viscous liquid.



R_f = 0.60 (8:2 hexane:EtOAc); Yield = 83%; $[\alpha]_D^{25}$ = -18.0 (*c* 2.20, $CHCl_3$); IR (CH_2Cl_2) ν_{max} = 1726 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.62-3.66 (dd, *J* = 4.3 Hz, 1H), 3.70-3.74 (dd, *J* = 2.4 Hz, 1H), 4.08-4.09 (d, *J* = 3.2 Hz, 1H), 4.15-4.24 (m, 3H), 4.27-4.45 (m, 8H), 5.15-5.17 (m, 1H), 7.04-7.25 (m, 20H), 7.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 67.6, 71.4, 73.2, 74.2, 74.3, 74.6, 77.8, 82.9, 127.7-128.6, 136.1, 136.9, 137.0, 137.4, 159.8, 208.2; MS (ESI): m/z = 591(M + Na)$^+$; Anal. Calcd. for $C_{35}H_{36}O_7$ (568.25): C, 73.92; H, 6.38 % Found: C, 73.90; H, 6.37 %

Compound 5

To a suspension of $LiAlH_4$ (40 mg, 1.05 mmol) in THF (3 mL) was added compound 4 (200 mg, 0.35 mmol) in small instalments at 0 ºC. The reaction mixture was stirred at 50 ºC for 2-3 h. The completion of the reaction was monitored by TLC. The reaction mixture was cooled to 0 ºC and then ethyl acetate and water was added to it. The mixture

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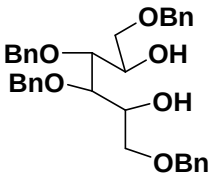
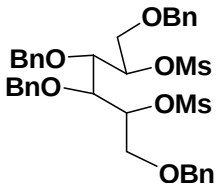
was neutralized by 1N NaOH and stirred for 15-20 min. The resulting white precipitate was removed by filtration through a celite pad and the filtrate was extracted with ethyl acetate (2 x 30 mL). The organic layer was washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent gave a crude product, which was purified by column chromatography to get 134 mg of diol **5** as white solid.



R_f = 0.40 (7:3 hexane:EtOAc); Yield = 70%; $[\alpha]_D^{25}$ = + 8.00 (*c* 1.00 , $CHCl_3$); IR (CH_2Cl_2) ν_{max} = 3437 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 3.04 (br s, 2H), 3.40-3.51 (m, 2H), 3.61-3.68 (m, 2H), 3.73-3.80 (m, 2H), 4.03-4.10 (m, 2H), 4.41-4.57 (m, 7H), 4.67-4.70 (d, *J* = 11.2 Hz, 1H), 7.18-7.33 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.2, 13.0, 14.1, 18.0, 18.1, 60.1, 70.4, 71.5, 77.4, 79.9, 81.8, 122.3, 127.3-129.2, 138.1, 138.7, 145.8, 166.0; MS (ESI): m/z = 565 $(M + Na)^+$; Anal. Calcd. for $C_{34}H_{38}O_6$ (542.27): C, 75.25; H, 7.06 % Found: C, 75.22; H, 7.04 %

Compound 9

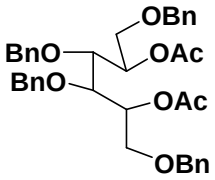
To a stirred solution of compound **5** (50 mg, 0.09 mmol) in DCM (2 mL) was added pyridine (0.02 mL, 0.34 mmol). The reaction mixture was stirred for 10 min at 0 ºC. Mesyl chloride (0.28 mL, 0.36 mmol) was added slowly to it and the mixture was stirred at room temperature for 2 h. Completion of the reaction was monitored by TLC and the organic layer was extracted with DCM and washed with water, brine and dried over anhydrous Na_2SO_4. The crude product obtained was purified by column chromatography to form 52 mg of dimesylated product **9** as viscous liquid.



R_f = 0.60 (7:3 hexane:EtOAc); Yield = 82%; $[\alpha]_D^{25}$ = + 6.00 (*c* 0.50, $CHCl_3$); IR (CH_2Cl_2) ν_{max} = 1495, 2102 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.96 (s, 6H), 3.54-3.62 (m, 2H), 3.77-3.82 (m, 1H), 3.89-3.98 (m, 3H), 4.32-4.54 (m, 5H), 4.63-4.75 (m, 3H), 4.88-4.91 (m, 1H), 4.97-4.99 (m, 1H), 7.22-7.34 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 38.3, 68.6, 73.4, 74.5, 75.1, 77.7, 78.8, 80.7, 82.1, 127.8-128.4, 137.2, 137.3; MS (ESI): m/z = 721 $(M + Na)^+$; Anal. Cacld. for $C_{36}H_{42}S_2O_{10}$ (698.22): C, 61.87; H, 6.06; S, 9.18 % Found: C, 61.86; H, 6.04; S, 9.16 %

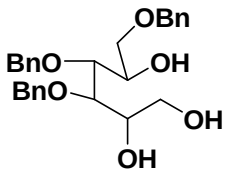
Compound 10

To a stirred solution of compound **5** (40 mg, 0.07 mmol) in dry DCM (1 mL) was added acetic anhydride (0.10 mL, 0.17 mmol) and triethyl amine (0.12 mL, 0.17 mmol) and the reaction mixture was stirred at room temperature for 1 h. After the completion of the reaction (TLC monitoring), the organic layer was extracted with DCM (3 x 20 mL), washed with water, brine solution and dried over anhydrous Na_2SO_4, to obtain a crude product which was purified by column chromatography when 36 mg of compound **10** was obtained as viscous liquid.



R_f = 0.70 (8:2 hexane:EtOAc); Yield = 78%; $[\alpha]_D^{25}$ = +1.40 (*c* 1.00, $CHCl_3$); IR (CH_2Cl_2) ν_{max} = 1740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 1.92 (s, 3H), 1.98 (s, 3H), 3.39-3.43 (dd, *J* = 5.8 Hz, 1H), 3.47-3.51 (dd, *J* = 5.4 Hz, 1H), 3.60-3.64 (m, 1H), 3.74-3.78 (m, 1H), 3.81-3.88 (m, 2H), 4.25-4.61 (m, 8H), 5.10-5.14 (m, 1H), 5.20-5.27 (m, 1H), 7.15-7.23 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.1, 67.8 (two peaks), 71.8, 72.6, 72.9, 73.1, 74.4, 75.1, 77.8, 78.7, 127.6-128.3, 137.8-138.1, 170.0, 170.6; MS (ESI): m/z = 649 (M + Na)+ ; Anal. Calcd. for $C_{38}H_{42}O_8$ (626.29): C, 72.82; H 6.75 % Found: C, 72.80; H, 6.73 %

Compound 12



To a suspension of $LiAlH_4$ in THF (50.6 mg, 1.32 mmol) was added compound **11** (100 mg, 0.33 mmol) slowly at 0 ºC. The reaction mixture was slowly brought to room temperature and then refluxed at 50-60 ºC for 3h. The completion of the reaction was monitored by TLC. The reaction mixture was cooled to 0 ºC and treated with EtOAc, water and neutralized with 1N NaOH and stirred for 15-20 min. The resulting white precipitate was removed by filtration through a celite pad and the filtrate was extracted with ethyl acetate (2 x 30 mL). The organic layer was washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent gave a crude product, which was purified by column chromatography to form a triol **12**.

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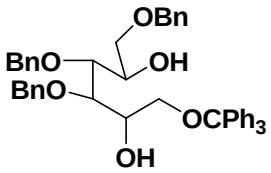
R_f = 0.30 (6:4 hexane:EtoAc); Yield = 84%; $[\alpha]_D^{25}$ = + 4.57 (*c* 1.75, $CHCl_3$); IR (CH_2Cl_2) ν_{max}= 3392 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ: 2.36 (brs, 1H), 3.20 (brs, 2H), 3.49-3.60 (m, 1H), 3.62-3.70 (m, 3H), 3.73-3.76 (m, 1H), 3.91-3.92 (brd, 1H), 4.04 (brs, 1H), 4.49-4.58 (m, 6H), 4.70-4.73 (d, *J* = 11.4 Hz, 1H), 7.21-7.36 (m, 15 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 27.0, 41.9, 68.7, 70.3, 72.7, 73.4, 74.8, 77.6, 82.5, 84.3, 92.3, 96.7, 127.7-128.4, 137.5, 138.5; MS (ESI): m/z = 470 $(M+NH_4)^+$; Anal. Calcd. for $C_{27}H_{32}O_6$ (452.22): C, 71.66, H, 7.13; Found: C, 71.65, H, 7.12.

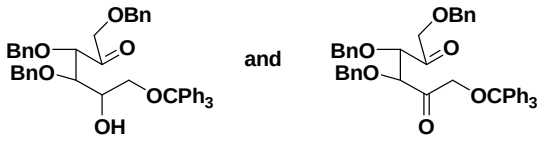
Compound 13



To a stirred solution of compound **12** (224 mg, 0.49 mmol) in DCM (3 mL) was added triethyl amine (0.07 mL, 0.53 mmol) at 0 ºC. The reaction mixture was stirred at 0 ºC for 10 min and then trityl chloride (152 mg, 0.53 mmol) was added to it. The reaction mixture was stirred for half an hour at room temperature. The completion of the reaction was monitored by TLC. The organic layer was extracted with DCM (2 x 30 mL) washed with water, brine and dried over anhydrous Na_2SO_4. The crude sample was purified by column chromatography to get the tritylated compound **13**.

R_f = 0.40 (8:2 hexane:EtoAc); Yield = 72%; $[\alpha]_D^{25}$ = + 7.00 (*c* 1.00, $CHCl_3$); IR (CH_2Cl_2) ν_{max} = 3435cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ: 2.89 (brs, 1H), 3.01 (brs, 1H), 3.10-3.14 (q, *J* = 7.3 Hz, 1H), 3.30-3.34 (q, *J* = 5.8 Hz, 1H), 3.60-3.71 (m, 3H), 3.92-3.94 (q, *J* = 2.2 Hz, 1H), 4.05-4.06 (brd, 1H), 4.12 (brs, 1H), 4.36 (d, *J* =11.2 Hz, 1H), 4.45-4.56 (m, 5H), 7.07-7.42 (m, 30H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 64.1, 69.5, 70.9, 71.0, 73.5, 74.3, 78.2, 86.6, 127.0-128.5, 137.8, 143.7; MS (ESI): m/z = 717 $(M + Na)^+$; Anal. Calcd. for $C_{46}H_{46}O_6$ (694.33): C, 79.51, H, 6.67; Found: C, 79.51, H, 6.66.

Compound 14 and 15



14 **15**

To a stirred solution of compound **13** (50 mg, 0.07 mmol) in acetone (1.50 mL) was added IBX (42 mg, 0.14 mmol) and the reaction mixture was refluxed for 24h. The completion of the reaction was monitored by TLC when two compounds **14** and **15** were obtained. The reaction mixture was filtered through a celite pad and the filtrate was evaporated. The crude product thus obtained was purified by column chromatography to get compounds **14** and **15**.

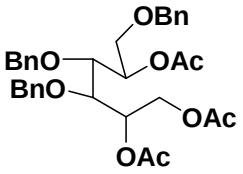
Compound 14

Rf = 0.70 (7:3 hexane:EtoAc); Yield = 45%; $[\alpha]_D^{25}$ = + 3.75 (*c* 0.80, $CHCl_3$); IR (CH_2Cl_2) ν_{max} = 3344 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ: 3.15-3.18 (d, *J* = 9.7 Hz, 1H), 3.31-3.34 (d, *J* = 9.8 Hz, 1H), 3.45-3.5 (m, 1H), 3.63-3.66 (m, 1H), 4.06 (s, 1H), 4.15-4.19 (m, 2H), 4.29-4.42 (m, 2H), 4.46-4.60 (m, 5H), 7.18-7.48 (m, 30H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 65.7, 70.5, 71.8, 72.0, 73.4, 79.8, 83.4, 84.0, 86.6, 102.4, 105.6, 126.9-128.7, 137.4, 137.9, 143.6; MS (ESI): m/z = 715 $(M + Na)^+$; Anal. Calcd .for $C_{46}H_{44}O_6$ (692.31): C, 79.74, H, 6.40; Found: C, 79.72, H, 6.39.

Compound 15

R_f = 0.65 (7:3 hexane:EtOAc); Yield = 29%; $[\alpha]_D^{25}$ = + 3.15 (*c* 1.0, $CHCl_3$); IR (CH_2Cl_2) ν_{max} = 3344 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ: 3.17-3.27 (m, 1H), 3.38-3.47 (m, 1H), 3.54-3.62 (m, 1H), 3.99-4.05, (m, 2H), 4.18-4.32 (q, *J* = 12.2 Hz, 2H), 4.41-4.52 (m, 2H), 4.55-4.71 (m, 3H), 6.99-7.43 (m, 30H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 61.6, 71.6, 72.5, 73.1, 73.5, 78.0, 82.0, 102.9, 126.9-128.7, 143.9; MS (ESI): m/z = 713 $(M + Na)^+$; Anal. Calcd. for $C_{46}H_{42}O_6$ (690.33): C, 79.98, H, 6.13; Found: C, 79.96, H, 6.10.

Compound 16



Compound **12** (45 mg, 0.09 mmol) was dissolved in DCM (2 mL). To this stirred solution was added acetic anhydride (0.04 mL, 0.40 mmol) and triethyl amine (0.06 mL, 0.04 mmol) and the solution was stirred for half an hour at room temperature. The completion of the reaction was monitored by TLC. The organic layer was extracted with DCM (2 x 30 mL) washed with water, brine and dried over anhydrous Na_2SO_4. The crude product obtained was purified by column chromatography to form triacetate **16**.

R_f = 0.73 (6:4 hexane:EtoAc); Yield = 80%; $[\alpha]_D^{25}$ = + 4.35 (*c* 1.0, $CHCl_3$); IR (CH_2Cl_2) ν_{max} =1743cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ: 1.94 (s, 3H), 1.99 (s, 3H), 2.07 (s, 3H), 3.67-3.71 (q, *J* = 5.6 Hz, 1H), 3.75-3.84 (m, 2H), 3.91-3.94 (m, 1H), 4.08-4.13 (dd, *J* = 7.08 Hz, 1H), 4.21-4.25 (dd, *J* = 4.4 Hz, 1H), 4.46-4.70 (m, 6H), 5.14-5.17 (q, *J* = 5.36 Hz, 1H), 5.35-5.39 (m, 1H), 7.24-7.34 (m, 15 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 20.6, 21.0, 62.5, 67.7, 70.5, 72.5, 73.1, 74.5,

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74.7, 76.6, 78.4, 127-128.3, 137.5, 137.8, 170.0, 170.4; MS (ESI): m/z = 601 $(M + Na)^+$; Anal. Calcd. for $C_{33}H_{38}O_9$ (578.25): C, 68.50, H, 6.62; Found: C, 68.49, H, 6.60.

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