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$AuBr_3$ mediated glycosidations: synthesis of tetrasaccharide motif of the *Leishmania donovani* lipophosphoglycan

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Abstract Tetrasaccharide cap present in lipophosphoglycan of the *Leishmania donovani* responsible for *visceral Leishmaniaisis* is synthesized as a fully protected propargyl glycoside. $AuBr_3$ mediated selective glycosylation of propargyl 1,2-orthoester in the presence of propargyl glycoside is employed as a key step to obtain propargyl containing oligomers. Further, propargyl tetrasaccharide is connected with a long chain hydrocarbon containing azidothiol functionality situated at two terminal ends *via* 'click' reaction.

Keywords Glycosidation · Leishmania · Gold catalysis · Orthoester · Lipophosphoglycan · Tetrasaccharide

The human disease *visceral Leishmaniasis* is currently found in nearly 88 countries where a few million people are affected and surprisingly, 60000 people lose their lives annually [1]. Unfortunately, no effective vaccine successfully emerged yet to prevent the spreading of disease [2]. However, many drugs such as antimony compounds, diamidine were approved for the treatment of *Leishmaniases*. These drugs are still having a series of disadvantages, as they are capable of producing more side effects, high cost and ineffective to patients who are residing in many parts of the world. Thus, an effective therapy is still a question mark to the *Leishmaniasis* affected patients and is a significant prerequisite in order to control and annihilate the spreading of disease in human population.

The risky disease is caused by *Leishmania donovani* which is a protozoan parasite and lives in the alimentary tract of the sand fly [2]. The parasite penetrates in the macrophages while sand fly feeding blood on the surface of skin of the human body. After ingestion of parasite by mammalian macrophages, the promastigote parasite enters in phagolysosome compartment where they are supposed to kill by oxidative toxic products and hydrolytic enzymes. Instead, the parasite cleverly adapts the conditions and transforms to amastigote form. Infected parasites after multiplication of amastigote start the infection to other macrophages and organs [3–6]. So far, it has been understood that *Leishmania* parasites exist in the form of promastigote fabricates lipophosphoglycan (LPG) on its entire cell surface. These LPGs are further implicated in many biological functions to adhesion, survival and infectivity of the parasites in both the sand fly and human macrophages. On contrary, amastigote form of the parasite can't synthesize LPG but can participate in the human macrophages to be infected [6].

Earlier reports on the structural analyses of *Leishmania donovani* LPG [7–15] described that LPG is a heterogenous glycolipid containing four domains: (i) a neutral oligosaccharide cap at the terminal non-reducing end, (ii) a repeating phosphoglycan unit, (iii) a phosphosaccharide core in which an unusual galactofuranosyl unit is present, and (iv) glycosylphosphatidylinositol (GPI) anchor as shown in Fig. 1. Each fragment has been identified tentatively to play a significant role in the sand fly as well as in human macrophages [7–20]. The foregoing discussion on the significance of membrane-bound lipophosphoglycan prompted to develop a route for immunogenic LPG fragments that could in turn facilitate carbohydrate based vaccine development for Leishmaniasis. Thus several research groups have synthesized

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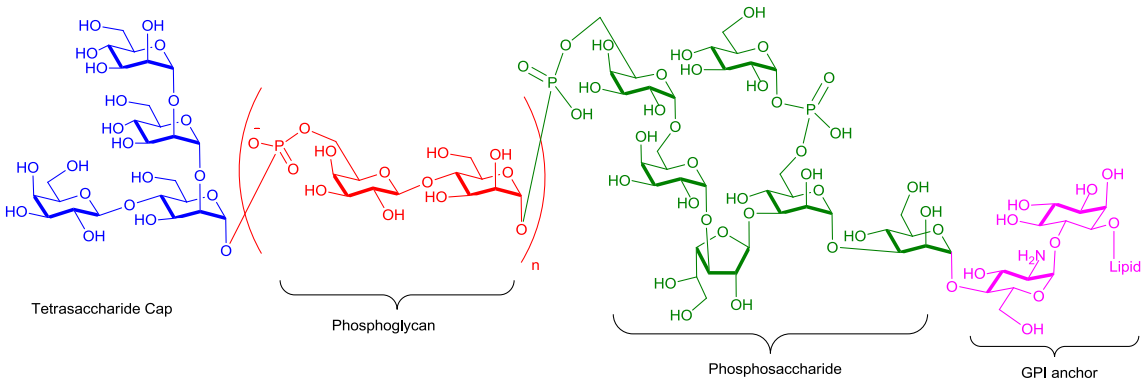
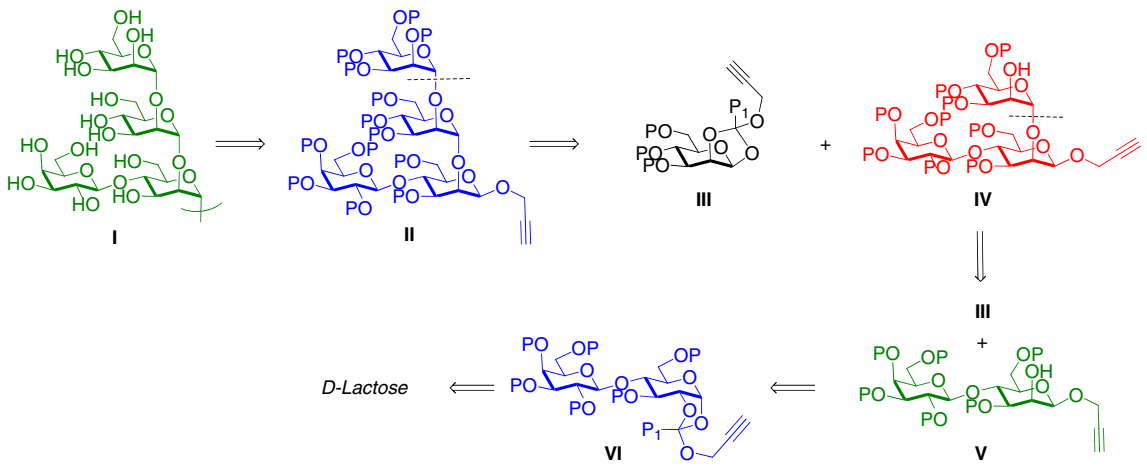


Fig. 1 General structure of Lipophosphoglycan of Leishmania Donovani

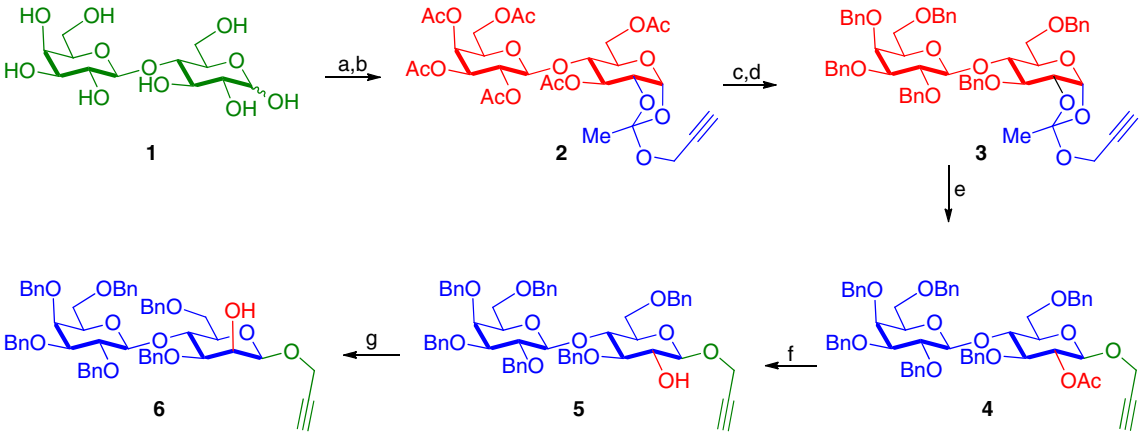
different portions of LPG [21–35]. Of which, Seeberger's spacer-equipped with amine and thiol functionality of the tetrasaccharide cap for attaching carrier molecules is noteworthy for the future development of carbohydrate-based synthetic vaccines against *Leishmaniasis* [28, 35]. However, the introduction of a new spacer with a different functionality at the reducing end needs refinement of the synthesis protocol for the entire tetrasaccharide. In order to avoid multiple glycosylations for the attachment of linkers, we thought to install a stable and functionable protecting group early at the anomeric center of saccharide that enables synthesis of tetrasaccharide library with different spacers. In this context, we envisioned that the installation of the propargyl group as a stable linker at the reducing end of tetrasaccharide would be advantageous since (i) propargyl group can be 'clicked' efficiently with azide bearing organic molecules and (ii) propargyl group can be introduced at the anomeric position of sugar directly by modified Fischer glycosidation.

Gold catalysed glycosidations are explored recently for the synthesis of oligosaccharides and glycoconjugates [36–48]. From our laboratory [36–44], we identified propargyl 1,2-orthoesters as glycosyl donors in the presence of catalytic amount of $AuBr_3$ [38]. Subsequently, propargyl 1,2-orthoesters were successfully activated in the presence of propargyl glycosides facilitating the synthesis of 1,2-*trans* propargyl saccharides [40]. Herein, we report the synthesis of a tetrasaccharide cap of lipophosphoglycan present on the surface of *Leishmania donovani* as a propargyl glycoside using gold catalyzed propargyl 1,2-orthoester-based glycosyl donors.

To begin our investigation, we needed better strategy and thought for the tetrasaccharide **I**, which can be prepared by the deprotection of fully protected propargyl tetrasaccharide **II**, which in turn can be disconnected into two building blocks, namely, mannose propargyl 1,2-*O*-orthoester **III** and propargyl trisaccharide **IV** in a linear sequence (Scheme 1). These two fragments can be coupled by using catalytic amount of $AuBr_3$ in dichloromethane at room temperature. The trisaccharide acceptor **IV** can be synthesized by gold catalyzed selective glycosylation of mannose propargyl 1,2-orthoester **III** in the presence of propargyl disaccharide **V,** which in turn can be derived efficiently from propargyl 1,2-orthoester of lactose **VI**. The synthetic endeavour for disaccharide acceptor **6** commenced from lactose (Scheme 2). One pot conversion of lactose **1** to lactopyranosyl bromide was accomplished under acetylation conditions $Ac_2O/AcOH/Conc.H_2SO_4$ followed by the



Scheme 1 Retrosynthetic analysis of tetrasaccharide



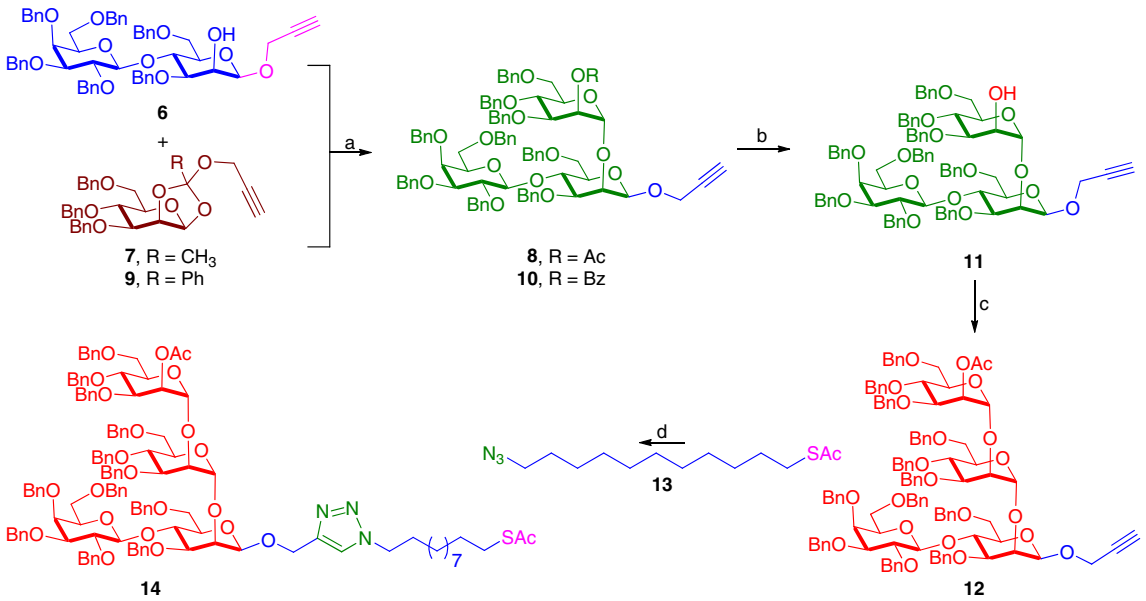
Scheme 2 Synthesis of disaccharide aglycone. *Reagents and conditions*: (**a**) i) Ac_2O, AcOH, Conc. H_2SO_4, 30 min; ii) HBr-AcOH, 5 h; (**b**) 2,6-lutidine, TBAI, propargyl alcohol, CH_2Cl_2, 70 °C, 36 h, 55 % (over two steps); (**c**) NaOMe, MeOH, 2 h, 100 %; (**d**) NaH, DMF, BnBr, TBAI, 4 h, 0–25 °C, 83 %; (**e**) TMSOTf, CH_2Cl_2, propargyl alcohol, 25 °C, 15 min, 85 %; (**f**) NaOMe, MeOH, 25 °C, 8 h, 90 %; (**g**) i) DMSO, Ac_2O, 24 h, 25 °C; ii) $NaBH_4$, CH_2Cl_2 : CH_3OH (1:1), 4 h, 0–25 °C, 82 % (over two steps)

addition of 33 % hydrobromic acid in glacial acetic acid [49–51]. Subsequently, lactopyranosyl bromide is treated with propargyl alcohol, 2,6-lutidine and catalytic amount of tetra-*n*-butylammonium iodide (TBAI) in anhydrous CH_2Cl_2 at 70 °C for 36 h to give the corresponding propargyl 1,2-orthoacetate **2** in 55 % yield ([38] Supporting Information). Further, *O*-acetyl groups of 1,2-orthoester **2** were deprotected under Zemplén conditions and the resulting hydroxyl groups were allowed to react with sodium hydride, benzyl bromide and catalytic amount of TBAI in anhydrous DMF at 0-25 °C for 4 h to obtain per-*O*-benzylated lactose 1,2-orthoacetate **3** as a viscous oil in 83 % yield (Supporting Information).

Thereafter, isomerization of lactosyl propargyl 1,2-orthoacetate **3** to propargyl lactoside (**4**) with a *O*-acetyl group at *C*-2 position was achieved efficiently in 85 % yield by the use of a catalytic amount of TMSOTf and propargyl alcohol in anhydrous CH_2Cl_2 at room temperature for 15 min (Supporting Information [52]). Propargyl lactoside **4** was then treated with a solution of sodium methoxide in anhydrous methanol to deprotect acetate group and thus obtained equatorial alcohol **5** was oxidized under conditions DMSO/Ac_2O/25 °C/24 h followed by reduction with sodium borohydride in a mixture of anhydrous CH_2Cl_2 and CH_3OH (1:1) to obtain the required disaccharide acceptor (**6**) in 82 % yield (Scheme 2) ([28, 53, 54] Supporting Information). In parallel, mannose 1,2-orthoacetate **7** was conveniently prepared from D-(+)-mannose as per the sequences involved in the formation of per-*O*-benzylated lactose 1,2-orthoester **3** (Supporting Information).

Having the glycosyl donor **7** and acceptor **6** in hand, the glycosylation reaction was carried out in the presence of 10 mol% $AuBr_3$/CH_2Cl_2/25 °C/4 Å MS powder in order to get tri-saccharide **8** in good yield (Scheme 3). But, the reaction proceeded very slowly and did not complete even after 24 h. However, the reaction is completed when 20 mol% of $AuBr_3$ is used and afforded propargyl trisaccharide **8** in 48 % yield (Supporting Information). Further, $AuBr_3$ mediated glycosylation performed with more equivalents of glycosyl donor **7** and glycosyl acceptor **6** did not improve the overall performance of the reaction. Furthermore, glycosylation between the disaccharide acceptor **6** and per-*O*-benzylated mannose 1,2-orthobenzoate (**9**) under 20 mol% $AuBr_3$/CH_2Cl_2/4 Å MS powder/25 °C/12 h resulting in the trisaccharide (**10**) as a propargyl glycoside in 46 % yield (Supporting Information). Saponification of compounds **8** and **10** under Zemplén conditions afforded propargyl trisaccharide **11** (90 %) (Supporting Information). Acceptor **11** was subsequently coupled with mannose 1,2-orthoacetate **7** under aforementioned conditions to obtain the desired propargyl tetrasaccharide **12** in 35 % yield (Supporting Information). Furthermore, propargyl tetrasaccharide **12** was allowed to react with *S*-acetyl-11-azidothioundecane **13** under CuI/DIPEA/CH_3CN/25 °C for the synthesis of a 1,2,3-triazole 'clicked' glycolipid (**14**) with thioacetyl group at terminal end in excellent yield (Scheme 3) (Supporting Information).

In conclusion, we have synthesized the tetrasaccharide cap of *Leishmania donovani* lipophosphoglycan with a propargyl group at the reducing end using gold mediated selective activation of propargyl 1,2-orthoester in the presence of propargyl glycoside. Propargyl moiety was further exploited for introducing a thiol containing long chain hydrocarbon *via* 'click' reaction. The immunological studies with carrier proteins and the effect of triazole ring for further development of vaccine are currently in progress. Besides, propargyl tetrasaccharide is a valuable intermediate for synthesizing various other orthogonal functional groups such as alkene, aldehyde and carboxylic acid that are highly useful for bioconjugation.



Scheme 3 Synthesis of propargyl tri- and tetrasaccharides. *Reagents and conditions*: (**a**) $AuBr_3$ (20 mol%), CH_2Cl_2, 25 °C, 4 Å MS powder (1 h, 48 % for **8**), (12 h, 46 % for **10**); (**b**) NaOMe, MeOH, 25 °C, 8 h, 90 %; (**c**) **7**, $AuBr_3$ (20 mol%), CH_2Cl_2, 25 °C, 4 Å MS powder, 2 h, 35 %; (**d**) CuI, DIPEA, CH_3CN, 25 °C, 1 h, 85 %

Experimental section

Synthesis of 3,6-di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranose-1,2-(prop-2-ynyl orthoacetate) (**2**)

To a suspension of D-lactose (10 g, 27.8 mmol) in glacial acetic acid (50 mL) was added acetic anhydride (24 mL, 249.8 mmol) followed by catalytic amount of conc. H_2SO_4 and the reaction mixture was stirred at room temperature for 30 min. Then a solution of 33 % hydrobromic acid in glacial acetic acid (75 mL) was added at 0 °C and the resulting solution was stirred for an additional 5 h at room temperature. After completion of the reaction as judged by TLC, the reaction mixture was poured into ice and extracted with dichloromethane (2×100 mL). Combined organic layers were washed with water (3×200 mL), saturated $NaHCO_3$ solution, water, dried over anhydrous sodium sulfate and concentrated *in vacuo* to give hepta-*O*-acetyl-α-D-lactopyranosyl bromide (18.3 g) that was redissolved in anhydrous dichloromethane (50 mL). To that, 2,6-lutidine (10 mL), propargyl alcohol (7.6 mL, 130.82 mmol) followed by a catalytic amount of tetra-*n*-butylammonium iodide (0.2 g) were added at room temperature under argon atmosphere. The reaction mixture was stirred at 70 °C for 36 h under argon atmosphere, quenched with a saturated solution of oxalic acid and extracted with dichloromethane (2×100 mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* to obtain a brownish black residue, which was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to give the corresponding lactose propargyl 1,2-orthoacetate **2** (10.35 g, 55 % (over 2 steps). Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.1)=+74.89; IR (ν, cm^{-1}): 1218, 1749, 2879, 2972, 3302; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 1.76 (3 H, s), 1.98 (3 H, s), 2.04 (3 H, s), 2.06 (3 H, s), 2.12 (6 H, s), 2.18 (3 H, s), 2.43 (1 H, t, *J*=2.41 Hz), 3.65 (1 H, d, *J*=9.61 Hz), 3.76–3.88 (1 H, m), 3.94 (1 H, t, *J*=6.64 Hz), 4.05–4.17 (3 H, m), 4.19 (2 H, d, *J*=2.38 Hz), 4.25 (1 H, dd, *J*=2.24, 12.05 Hz), 4.37 (1 H, dd, *J*=2.54, 4.86 Hz), 4.61 (1 H, d, *J*=7.81 Hz), 5.0 (1 H, dd, *J*=3.4, 10.41 Hz), 5.19 (1 H, dd, *J*=7.89, 10.29 Hz), 5.38 (1 H, d, *J*=3.07 Hz), 5.55 (1 H, d, *J*=2.73 Hz), 5.7 (1 H, d, *J*=5.15 Hz); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 20.1, 20.4, 20.5, 20.5, 20.6, 20.7, 20.8, 51.7, 60.8, 63.2, 66.7, 66.9, 68.7, 69.6, 70.7, 70.8, 72.4, 73.8, 77.4, 79.5, 96.9, 102.3, 121.4, 168.9, 169.3, 169.9, 170.2, 170.3, 170.6; Mol. Wt. calculated for $C_{29}H_{38}O_{18}$: 674.20, Found: 697.52 $(M+Na)^+$.

Synthesis of 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-α-D-glucopyranose-1,2-(prop-2-ynyl orthoacetate) (**3**)

To a solution of 3,6-di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranose-1,2-(prop-2-ynyl orthoacetate) **2** (6 g, 12.94 mmol) in anhydrous methanol (75 mL) was added sodium metal (~50 mg) at room temperature under argon atmosphere. The reaction mixture was stirred for 2 h at the same temperature. After completion of the reaction, the reaction mixture was concentrated under reduced pressure to give deacetylated lactose 1,2-orthoester

(3.75 g, 100 %). To a solution of deacetylated product (3.75 g, 8.88 mmol) in anhydrous DMF (25 mL) was added NaH (2.48 g, 62.15 mmol) at 0 °C and the reaction mixture was stirred for 1 h at room temperature. Benzyl bromide (8 mL, 66.59 mmol) followed by a catalytic amount of TBAI (0.1 g) were added at 0 °C under argon atmosphere and the stirring was continued for an additional 4 h at room temperature. After completion of the reaction as judged by TLC, excess NaH was quenched by slow addition of methanol followed by cold water and subsequently extracted with diethyl ether (2x70mL). Combined organic layers were washed with water, brine and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the resulting crude was purified by conventional silica gel column chromatography using petroleum ether and ethyl acetate as the mobile phase to give 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-α-D-gluco pyranose-1,2-(prop-2-ynyl orthoacetate) **3** as a white amorphous solid (7.1 g, 83 %). Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 0.9)=+71.44; IR (ν, cm^{-1}): 1099, 1605, 1585, 2867, 2921, 3289; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 1.67 (3 H, s), 2.36 (1 H, t, *J*=2.39 Hz), 3.35–3.57 (4 H, m), 3.60–3.65 (2 H, m), 3.76 (2 H, dd, *J*=7.82, 9.33 Hz), 3.87 (1 H, d, *J*=2.91 Hz), 3.98 (1 H, d, *J*=9.18 Hz), 4.13–4.19 (1 H, m), 4.14 (2 H, d, *J*=2.40 Hz), 4.23–4.45 (6 H, m), 4.5–4.78 (7 H, m), 4.93 (1 H, d, *J*=11.52 Hz), 5.73 (1 H, d, *J*=5.24 Hz), 7.15–7.4 (30 H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 20.5, 51.5, 68.5, 68.9, 69.8, 71.7, 72.8, 73.1, 73.2, 73.3, 73.5, 73.5, 73.6, 74.6, 74.9, 75.5, 76.7, 79.1, 79.9, 81.9, 97.5, 105.3, 120.9, 127.4–128.3, 137.6, 138.0, 138.1, 138.3, 138.5, 138.5; Mol. Wt. calculated for $C_{59}H_{62}O_{12}$: 962.42, Found: 985.81 $(M+Na)^+$.

Synthesis of prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galacto- pyranosyl)-β-D-glucopyranoside (**5**)

To a solution of propargyl 1,2-orthoester of lactose **3** (1.8 g, 1.869 mmol), propargyl alcohol (0.11 mL, 1.869 mmol) and freshly activated 4 Å molecular sieves powder (0.5 g) in dichloromethane (15 mL) was added a catalytic amount of TMSOTf (2 drops) at room temperature under argon atmosphere. The reaction mixture was stirred for 15 min., filtered through a celite pad and the filtrate was concentrated *in vacuo.* The resulting crude residue was purified by silica gel column chromatography using petroleum ether-ethyl acetate as eluent to give prop-2-ynyl 2-*O*-acetyl-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside **4** as a colourless liquid (1.54 g, 85 %). Prop-2-ynyl lactoside (2.08 g, 2.16 mmol) was dissolved in anhydrous methanol (25 mL). Sodium metal (~50 mg) was added at room temperature under argon atmosphere and the reaction mixture was stirred till the consumption of starting material. The solvent was concentrated *in vacuo* and the resulting crude residue was purified by silica gel column chromatography using petroleum ether-ethylacetate as the mobile phase to afford prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-glucopyranoside **5** (1.79 g, 90 %) as a colourless oil. Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.00)=-30.15; IR (ν, cm^{-1}): 1091, 1585, 1605, 2120, 2869, 2912, 3289, 3444.13; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 2.45 (1 H, bs), 2.46 (1 H, t, *J*=2.35 Hz), 3.3–3.6 (7 H, m), 3.65–4.05 (5 H, m), 4.23–4.57 (9 H, m), 4.65–4.74 (3 H, m), 4.79 (2 H, d, *J*=3.44 Hz), 4.96 (1 H, d, *J*=11.51 Hz), 5.08 (1 H, d, *J*=11.08 Hz), 7.1–7.4 (30 H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 55.6, 67.9, 68.0, 72.4, 72.9, 73.0, 73.1, 73.3, 73.4, 74.5, 74.7, 75.1, 75.1, 75.4, 75.9, 78.7, 79.8, 82.3, 82.5, 100.1, 102.6, 127.2–128.3, 137.9, 138.1, 138.4, 138.7, 138.8, 138.9; Mol. Wt. calculated for $C_{57}H_{60}O_{11}$: 920.41, Found: 943.74 $(M+Na)^+$.

Synthesis of prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galacto- pyranosyl)-β-D-mannopyranoside (**6**)

Propargyl lactoside **5** (1.7 g, 1.84 mmol) was dissolved in 30 mL of DMSO and Ac_2O mixture (2:1). The resulting solution was stirred at room temperature for 24 h under argon atmosphere, concentrated directly under reduced pressure and the resulting crude residue was directly taken for the next step without further purification. The disaccharide ketone (1.69 g, 1.83 mmol) was dissolved in 75 mL of CH_2Cl_2: MeOH (1:1). To that, sodium borohydride (0.25 g, 6.43 mmol) was added at 0 °C under argon atmosphere. The reaction mixture was stirred at room temperature for 4 h, quenched with water and extracted with dichloromethane (2x100mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* to obtain a yellowish crude oil, which was purified by flash silica gel (230-400 mesh) column chromatography using petroleum ether-ethyl acetate as eluent to afford prop-2-ynyl 3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside **6** (1.39 g, 82 % over two steps) as a white solid. Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.00)=-30.91; IR (ν, cm^{-1}): 1099, 1585, 1605, 2868, 2920, 3285, 3510; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ, 2.43 (1 H, t, *J*=2.33 Hz), 2.5 (1 H, bs) 3.37–3.6 (6 H, m), 3.72 (1 H, d, *J*=7.83 Hz), 3.79 (2 H, d, *J*=3.31 Hz), 3.91 (1 H, d, *J*=2.56 Hz), 4.11 (2 H, d, *J*=7.74 Hz), 4.25–4.85 (15 H, m), 4.96 (1 H, d, *J*=11.52 Hz), 7.11–7.4 (30 H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 55.4, 68.3, 68.5, 68.6, 72.4, 72.5, 72.9, 73.1, 73.4, 73.4, 74.1, 74.5, 75.0, 75.1, 75.3, 78.7, 79.1, 79.8, 82.4, 96.9, 103.1, 127.4–128.4, 137.9, 138.3, 138.4, 138.4, 138.6, 138.9; Mol. Wt. calculated for $C_{57}H_{60}O_{11}$: 920.41,Found: 943.81 $(M+Na)^+$.

Synthesis of 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthoacetate) (**7**)

Preparative protocol is same as delineated above for compounds **2** and **3**. Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.00)=+28.54; IR (ν, cm^{-1}): 1588, 1605, 2126, 2869, 2923, 3284; ^1H NMR ($CDCl_3$, 200.13 MHz): δ 1.77 (3 H, s), 2.41 (1 H, t, *J*=2.42 Hz), 3.43 (1 H, ddd, *J*=2.61, 4.1, 9.25 Hz), 3.71 (1 H, d, *J*=2.72 Hz), 3.73 (2 H, dd, *J*=4.0, 6.8 Hz), 3.91 (1 H, t, *J*=9.23 Hz), 4.18 (2 H, d, *J*=2.39 Hz), 4.44 (1 H, dd, *J*=2.66, 3.91 Hz), 4.57 (2 H, d, *J*=3.26 Hz), 4.59 (1 H,d, *J*=11.47 Hz), 4.79 (2 H, s), 4.88 (1 H, d, *J*=10.74 Hz), 5.37 (1 H, d, *J*=2.61 Hz), 7.19–7.45 (15 H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 24.6, 50.6, 68.9, 72.3, 73.3, 73.4, 74.0, 74.2, 75.2, 76.9, 78.8, 79.8, 97.6, 123.7, 127.5–128.5, 137.7, 138.1, 138.1; Mol. Wt. calculated for $C_{32}H_{34}O_7$: 530.23, Found: 553.47 $(M+Na)^+$.

Synthesis of prop-2-ynyl 2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside (**8**)

To a solution of mannose 1,2-orthoester **7** (0.1 g, 0.188 mmol) and disaccharide acceptor **6** (0.173 g, 0.188 mmol) in anhydrous dichloromethane (5 mL) was added freshly activated 4 Å molecular sieves powder (50 mg) followed by solid $AuBr_3$ (16 mg, 0.038 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred for 1 h at room temperature. After completion of the reaction as judged by TLC, the reaction mixture was filtered through a celite pad and the filtrate was concentrated *in vacuo*. The resulting crude residue was purified by flash silica gel column chromatography using petroleum ether-ethyl acetate as eluent to obtain propargyl trisaccharide **8** (125 mg, 48 %) as a thick syrup. Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 0.9)=-15.57; IR (ν, cm^{-1}): 1100, 1588, 1605, 1746, 2867, 2928, 3297; ^1H NMR ($CDCl_3$, 500.13 MHz): δ 2.03 (3 H, s), 2.35(1 H, t, *J*=2.33 Hz), 3.38 (2 H, ddd, *J*=4.9, 8.49, 19.73 Hz), 3.44 (1 H, dd, *J*=2.82, 9.78 Hz), 3.46–3.51 (1 H, m), 3.51 (1 H, t, *J*=8.49 Hz), 3.57 (1 H, dd, *J*=2.83, 8.78 Hz), 3.66 (1 H, dd, *J*=1.67, 10.76 Hz), 3.70 (1 H, dd, *J*=7.77, 9.57 Hz), 3.77 (1 H, dd, *J*=5.44, 10.99 Hz), 3.79–3.90 (4 H, m), 4.02 (1 H, dd, *J*=3.33, 9.58 Hz), 4.14 (1 H, t, *J*=8.94 Hz), 4.2 (1 H, d, *J*=2.65 Hz), 4.21 (1 H, d, *J*=11.74 Hz), 4.29–4.35 (5 H, m), 4.38 (1 H, d, *J*=12.02 Hz), 4.41 (1 H, d, *J*= 5.59 Hz), 4.44 (1 H, d, *J*=7.10 Hz), 4.5 (1 H, t, *J*=11.54 Hz), 4.52 (1 H, d, *J*=6.81 Hz), 4.54 (1 H, d, *J*=2.35 Hz), 4.59–4.68 (5 H, m), 4.71 (2 H, d, *J*=11.57 Hz), 4.79 (2 H, dd, *J*=4.15, 10.97 Hz), 4.86 (1 H, d, *J*=11.56 Hz), 4.93 (1 H, d, *J*=12.13 Hz), 5.16 (1 H, d, *J*=1.14 Hz), 5.61 (1 H, dd, *J*=1.71, 3.28 Hz), 7.10–7.35 (45 H, m); ^{13}C NMR ($CDCl_3$, 125.76 MHz): δ 21.1, 55.4, 67.9, 68.5, 68.7, 68.9, 70.9, 71.9, 72.1, 72.4, 72.6, 73.0, 73.0, 73.1, 73.2, 73.3, 74.3, 74.4, 74.8, 74.8, 74.9, 75.1, 75.7, 78.6, 78.9, 79.8, 80.0, 82.6, 97.0, 98.9, 103.1, 126.5–128.3, 138.0, 138.3, 138.4, 138.4, 138.5, 138,7, 138.7, 138.8, 138.9, 169.8; Mol. Wt. calculated for $C_{86}H_{90}O_{17}$: 1394.62, Found: 1418.26 $(M+Na)^+$.

Synthesis of 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthobenzoate) (**9**)

To a solution of 3,4,6-tri-*O*-benzoyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthobenzoate) (2.5 g, 3.94 mmol) in anhydrous THF (20 mL) was added a solution of sodium methoxide in methanol at room temperature under argon atmosphere. The resulting solution was stirred for 1 h at room temperature and concentrated *in vacuo* to obtain a yellowish crude oil which was purified by flash silica gel (230-400 mesh) column chromatography using dichloromethane followed by a mixture of ethyl acetate and acetone solvent to get the triol of mannose 1,2-orthobenzoate (1.17 g, 92 %) as a viscous liquid. The triol prepared *vide supra* was dissolved in anhydrous DMSO (10 mL). Powdered KOH (1.83 g, 32.59 mmol) followed by benzyl chloride (2.5 mL, 21.72 mmol) were added at room temperature under argon atmosphere. The reaction mixture was stirred for 4 h, quenched with water and extracted with diethyl ether (2×50 mL). Combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* to obtain a dark yellow oil, which was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to give 3,4,6-tri-*O*-benzyl-β-D-mannopyranose-1,2-(prop-2-ynyl orthobenzoate) **9** (1.89 g, 88 %) as a colourless viscous liquid. Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.2)=-36.43; IR (ν, cm^{-1}): 1100, 1588, 1605, 2869, 2925, 3287; ^1H ($CDCl_3$, 200.13 MHz): δ 2.4 (1 H, t, *J*=2.42 Hz), 3.46–3.6 (2 H, m), 3.67 (1 H, dd, *J*=4.91, 10.74 Hz), 3.9 (1 H, d, *J*=3.83 Hz), 3.91 (1 H, ABq, *J*=9.17 Hz), 4.09 (2 H, d, *J*=2.44 Hz), 4.42 (2 H, s), 4.62 (1 H, d, *J*=10.81 Hz), 4.75–4.94 (4 H, m), 5.53 (1 H, d, *J*=3.04 Hz), 7.2–7.45 (18 H, m), 7.65–7.75 (2 H, m); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 52.3, 69.1, 71.9, 73.2, 73.7, 74.2, 75.0, 75.2, 76.0, 78.1, 79.7, 98.0, 122.2, 126.8–129.4, 135.6, 137.7, 138.2, 138.3; Mol. Wt. calculated for $C_{37}H_{36}O_7$: 592.25, Found: 615.60 $(M+Na)^+$.

Synthesis of prop-2-ynyl 2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside (**10**)

To a solution of propargyl 1,2-orthoester of mannose **9** (100 mg, 0.169 mmol) and disaccharide acceptor **6** (0.156 g, 0.169 mmol) in anhydrous dichloromethane (7 mL) was

added freshly activated 4 Å molecular sieves powder (100 mg) followed by solid $AuBr_3$ (15 mg, 0.034 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred for 12 h at same temperature, filtered through a celite pad and the filtrate was concentrated *in vacuo* to obtain a gummy residue, which was purified by flash silica gel column chromatography (230-400 mesh) using petroleum ether-ethyl acetate as eluent to afford propargyl trisaccharide **10** (0.113 g, 46 %) as a colourless viscous liquid. Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.00)=-53.83; IR (ν, cm^{-1}): 1070, 1269, 1585, 1602, 1724, 2867, 2923, 3301; ^1H NMR ($CDCl_3$, 500.13 MHz): δ 2.36 (1 H, t, *J*=2.46 Hz), 3.4 (1 H, dd, *J*=3.44, 8.56 Hz), 3.43–3.55 (4 H, m), 3.58 (1 H, m), 3.69–3.95 (6 H, m), 4.07 (1 H, td, *J*=3.5, 9.59 Hz), 4.14–4.22 (3 H, m), 4.24 (1 H, dd, *J*=3.59, 11.68 Hz), 4.31–4.37 (3 H, m), 4.38 (2 H, t, *J*=3.98 Hz), 4.41 (1 H, d, *J*=3.24 Hz), 4.46–4.82 (14 H, m), 4.85 (1 H, dd, *J*=3.39, 11.56 Hz), 4.94 (1 H, dd, *J*=3.4, 12.17 Hz), 5.32 (1 H, s), 5.82–5.85 (1 H, m), 6.98–7.54 (48 H, m), 8.0–8.07 (2 H, m); ^{13}C NMR ($CDCl_3$, 125.76 MHz): δ 55.4, 67.9, 68.9, 69.0, 69.1, 71.4, 71.6, 72.4, 72.5, 72.6, 73.1, 73.2, 73.2, 73.3, 73.7, 74.4, 74.5, 74.8, 74.9, 75.0, 75.2, 75.8, 78.6, 78.9, 79.7, 79.9, 82.5, 97.0, 98.8, 103.1, 126.7–129.9, 132.7, 138.1, 138.3, 138.4, 138.5, 138.6, 138.7, 138.7, 138.8, 138.9, 165.1; Mol. Wt. calculated for $C_{91}H_{92}O_{17}$: 1456.63, Found: 1480.37 $(M+Na)^+$.

Synthesis of prop-2-ynyl 2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside (**11**)

Preparative procedure is same as described in the preparation of compound **5**, which provided trisaccharide acceptor **11** as a colourless viscous liquid. Characterization data: $[\alpha]_D^{25}$ (CH_3OH, *c* 1.00)=+1.72; IR (ν, cm^{-1}): 1099, 1585, 1603, 2867, 2917, 3296, 3447; ^1H NMR ($CDCl_3$, 500.13 MHz): δ 2.25 (1 H, bs), 2.34 (1 H, t, *J*=2.37 Hz), 3.37–3.44 (3 H, m), 3.44 (1 H, dd, *J*=2.9, 9.92 Hz), 3.50–3.57 (2 H, m), 3.67 (1 H, dd, *J*=1.8, 10.78 Hz), 3.71–3.79 (2 H, m), 3.78 (1 H, dd, *J*=3.85, 10.74 Hz), 3.84 (1 H, dd, *J*=4.95, 11.37 Hz), 3.86-3. 91 (3 H, m), 4.05 (1 H, s), 4.15 (1 H, t, *J*=8.91 Hz), 4.21 (1 H, d, *J*=2.76 Hz), 4.25 (1 H, d, *J*=11.8 Hz), 4.30 (2 H, t, *J*=2.74 Hz), 4.38 (2 H, d, *J*=11.92 Hz), 4.43 (2 H, d, *J*=2.54 Hz), 4.46 (1 H, d, *J*=5.18 Hz), 4.48 (1 H, d, *J*=6.67 Hz), 4.51 (1 H, d, *J*=7.62 Hz), 4.54 (1 H, d, *J*=11.54 Hz), 4.59 (1 H, d, *J*=12.05 Hz), 4.61–4.72 (5 H, m), 4.7 (1 H, d, *J*=3.90 Hz), 4.76 (1 H, d, *J*=10.6 Hz), 4.76 (2 H, ABq, *J*=11.03 Hz), 4.85 (1 H, d, *J*=12.05 Hz), 4.93 (1 H, d, *J*=11.37 Hz), 5.27 (1 H, d, *J*=1.22 Hz), 7.10–7.38 (45 H, m); ^{13}C NMR ($CDCl_3$, 125.76 MHz): δ 55.3, 68.5, 68.6, 68.7, 68.8, 70.7, 71.8, 72.6, 72.8, 73.1, 73.2, 73.3, 73.3, 73.4, 73.6, 74.3, 74.4, 74.5, 74.8, 74.9, 75.2, 75.9, 78.9, 79.9, 79.9, 80.1, 82.5, 97.2, 100.1, 102.9, 127.2–128.5, 138.0, 138.2, 138.4, 138.5, 138.5, 138.7, 138.7, 138.7, 138.8; Mol. Wt. calculated for $C_{84}H_{88}O_{16}$: 1352.61, Found: 1376.39 $(M+Na)^+$.

Synthesis of prop-2-ynyl 2-*O*-(2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,6-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-β-D-mannopyranoside (**12**)

To a solution of mannose 1,2-orthoester **7** (78 mg, 0.148 mmol), trisaccharide acceptor **11** (0.2 g, 0.148 mmol) and freshly activated 4 Å molecular sieves powder (100 mg) in anhydrous dichloromethane (5 mL) was added solid $AuBr_3$ (13 mg, 0.03 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred at room temperature for 2 h. After completion of the reaction as judged by TLC, the reaction mixture was filtered through a celite pad and the filtrate was concentrated *in vacuo*. The resulting crude was purified by flash silica gel column chromatography using petroleum ether-ethyl acetate as eluent to obtain propargyl tetrasaccharide **12** (94 mg, 35 %) as a colourless viscous liquid. Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 0.9)=-15.20; IR (ν, cm^{-1}): 1096, 1585, 1605, 1742, 2866, 2917, 3285; ^1H NMR ($CDCl_3$, 400.13 MHz): δ 2.06 (3 H, s), 2.34 (1 H, t, *J*=2.27 Hz), 3.32–3.45 (5 H, m), 3.48 (1 H, d, *J*=10.4 Hz), 3.53–3.63 (2 H, m), 3.68 (1 H, dd, *J*=1.29, 11.34 Hz), 3.73 (2 H, dd, *J*=7.65, 9.63 Hz), 3.76–3.83 (3 H, m), 3.85 (1 H, d, = *J* 9.54 Hz), 3.87–3.92 (2 H, m), 3.94 (1 H, d, *J*=2.5 Hz), 3.98 (1 H, dd, *J*=3.18, 9.03 Hz), 4.01 (1 H, d, *J*=2.07 Hz), 4.04 (1 H, t, *J*=2.14 Hz), 4.08 (1 H, t, *J*=8.71 Hz), 4.21 (2 H, ABq, *J*=11.56 Hz), 4.25 (1 H, d, *J*=1.23 Hz), 4.26 (1 H, d, *J*=11.1 Hz), 4.30 (2 H, t, *J*=2.90 Hz), 4.36 (1 H, d, *J*=10.75 Hz), 4.4 (2 H, dd, *J*=2.28, 11.81 Hz), 4.41 (1 H, d, *J*=10.88 Hz), 4.45–4.72 (14 H, m), 4.74 (2 H, d, *J*=5.23 Hz), 4.8 (2 H, dd, *J*=2.81, 10.85 Hz), 4.91 (1 H, d, *J*=1.46 Hz), 4.93 (1 H, d, *J*=11.55 Hz), 5.19 (1 H, s), 5.5 (1 H, dd, *J*=0.99, 1.78 Hz), 7.07–7.38 (60 H, m); ^{13}C NMR ($CDCl_3$, 100.61 MHz): δ 21.1, 55.2, 68.1, 68.8, 68.8, 69.0, 69.2, 71.6, 71.7, 71.8, 71.9, 72.4, 72.6, 72.6, 73.1, 73.1, 73.2, 73.3, 74.1, 74.3, 73.3, 74.5, 74.6, 74.7, 74.8, 74.9, 74.9, 75.2, 75.5, 75.7, 78.2, 79.1, 79.5, 79.5, 79.9, 82.5, 97.1, 99.3, 100.0, 102.6, 127.0–128.4, 137.9, 138.1, 138.4, 138.4, 138.5, 138.6, 138.7, 138.7, 138.7, 138.8, 138.9, 139.0, 170.0; Mol. Wt. calculated for $C_{113}H_{118}O_{22}$: 1826.81, Found: 1849.79 $(M+Na)^+$ [MALDI-TOF].

Synthesis of *S*-acetyl-11-azido-thioundecane (**13**)

A solution of 10-undecen-1-ol (1 g, 5.87 mmol) in anhydrous dioxane (5 mL) was purged with argon balloon. To that was added excess of thioacetic acid (6.1 mL,

117.4 mmol) followed by AIBN (50 mg) at room temperature. The reaction mixture was purged once again with argon balloon, stirred at 75 °C for 24 h under argon atmosphere, concentrated *in vacuo* and the resulting crude was purified by silica gel column chromatography using petroleum ether-ethylacetate as eluent to afford 11-thioacetyl-undecan-1-ol (0.37 g, 26 %) as a dark liquid that was redissolved in anhydrous dichloromethane (15 mL). To that was added carbon tetrabromide (1.0 g, 3.00 mmol) followed by a dropwise solution of triphenylphosphine (0.79 g, 3.00 mmol) in dichloromethane (5 mL) at 0 °C under argon atmosphere. The reaction mixture was stirred for 1 h at room temperature, quenched with water and extracted with dichloromethane (2x20mL). Combined organic layers were washed with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting crude residue was purified by silica gel column chromatography using petroleum ether-ethyl acetate as the mobile phase to obtain 11-thioacetyl-undecylbromide (0.38 g, 83 %) as dark oil. To a solution of 11-thioacetyl-undecylbromide (0.36 g, 1.16 mmol) in anhydrous DMF (5 mL) was added carefully NaN_3 (0.38 g, 5.82 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred for 20 h at same temperature, quenched with water and extracted with diethyl ether (2x20mL). Combined organic layers were washed with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting crude was purified by silica gel column chromatography using petroleum ether and ethyl acetate as the mobile phase to give *S*-acetyl-11-azido-thioundecane **13** (0.28 g, 90 %) as a brown coloured liquid. Characterization data: IR (ν, cm^{-1}): 1693, 2096, 2855, 2928; ^{1}H NMR ($CDCl_3$, 200.13 MHz): δ 1.20–1.43 (14 H, m), 1.56 (4 H, quintet, *J*=7.1 Hz), 2.32 (3 H, s), 2.86 (2 H, t, *J*=7.37 Hz), 3.26 (2 H, t, *J*=6.89 Hz); ^{13}C NMR ($CDCl_3$, 50.32 MHz): δ 26.6, 28.7, 28.8, 29.0, 29.1, 29.1, 29.3, 29.3, 29.3, 29.4, 30.6, 51.4, 196.0; Mol. Wt. calculated for $C_{13}H_{25}N_3OS$: 271.17, Found: 294.28 $(M+Na)^+$.

Synthesis of a triazole 'clicked' glycolipid (**14**)

To a solution of propargyl tetrasaccharide **12** (0.3 g, 0.16 mmol), *S*-acetyl-11-azido-thioundecane **13** (45 mg, 0.16 mmol) and DIPEA (57μL, 0.33 mmol) in CH_3CN (5 mL) was added CuI (33 mg, 0.17 mmol) at room temperature. The reaction mixture was stirred for 1 h at room temperature, quenched with a saturated solution of ammonium chloride and extracted with ethyl acetate (2×20 mL). Combined organic layers were washed with water, dried over anhydrous Na_2SO_4 and the solvent was concentrated *in vacuo.* The resulting crude residue was purified by silica gel column chromatography using petroleum ether and ethyl acetate as the mobile phase to afford a 1,2,3-triazole 'clicked' glycolipid **14** (0.29 g, 85 %) as a colourless viscous oil. Characterization data: $[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.10)=-(2-6); IR (ν, cm^{-1}): 1098, 1688, 1740, 2856, 2926; ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.05–1.35 (14 H, m), 1.51–1.63 (4 H, m), 2.05 (3 H, s), 2.31 (3 H, s), 2.85 (2 H, t, *J*=7.34 Hz), 3.33–3.43 (4 H, m), 3.45 (3 H, d, *J*=10.74 Hz), 3.54 (2 H, dd, *J*=3.26, 11.12 Hz), 3.60 (1 H, t, *J*=7.8 Hz), 3.7–3.8 (1 H, m), 3.74 (1 H, ABq, *J*=7.66 Hz), 3.81–3.92 (7 H, m), 3.94 (1 H, t, *J*=3.02 Hz), 3.99 (1 H, dd, *J*=2.53, 9.53 Hz), 4.03 (1 H, d, *J*=2.09 Hz), 4.05 (1 H, t, *J*=1.88 Hz), 4.1 (1 H, t, *J*=8.84 Hz), 4.22 (2 H, d, *J*=11.86 Hz), 4.23 (2 H, ABq, *J*=11.63 Hz), 4.30–4.57 (12 H, m), 4.60–4.82 (11 H, m), 4.91 (2 H, dd, *J*=1.89, 3.72 Hz), 4.94 (1 H, d, *J*=5.25 Hz), 5.23 (1 H, s), 5.49 (1 H, dd, *J*=0.93, 1.88 Hz), 7.02–7.32 (60 H, m), 7.45 (1 H, s); ^{13}C NMR ($CDCl_3$, 100.61 MHz): δ 21.1, 26.4, 28.8, 29.0, 29.1, 29.1, 29.4, 29.4, 29.4, 29.5, 30.2, 30.6, 49.9, 62.5, 68.2, 68.8, 68.9, 69.0, 69.1, 71.5, 71.7, 71.8, 71.8, 72.5, 72.5, 72.6, 73.1, 73.1, 73.2, 73.3, 73.3, 73.8, 74.2, 74.4, 74.6, 74.8, 74.9, 75.1, 75.2, 75.2, 75.6, 78.2, 79.8, 79.9, 80.0, 82.6, 98.8, 99.3, 99.6, 102.7, 122.9, 127.0–128.3, 137.9, 138.1, 138.4, 138.4, 138.5, 138.5, 138.6, 138.7, 138.7, 138.8, 138.8, 138.9, 144.4, 170.0, 196.1; Mol. Wt. calculated for $C_{126}H_{143}N_3O_{23}S$: 2097.98, Found: 2120.96 $(M+Na)^+$ [MALDI-TOF].

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References

1. Herwaldt, B.L.: Leishmaniasis. Lancet **354**, 1191–1199 (1999)
2. http://www.who.int/topics/leishmaniasis/en/
3. Sacks, D.L.: Metacyclogenesis in *Leishmania* promastigotes. Exp. Parasitol. **69**, 100–103 (1989)
4. McNeely, T.B., Tolson, D.L., Pearson, T.W., Turco, S.J.: Characterization of Leishmania donovani variant clones using anti-lipophosphoglycan monoclonal antibodies. Glycobiology **1**, 63–69 (1990)
5. Beverley, S.M., Turco, S.J.: Lipophosphoglycan (LPG) and the identification of virulence genes in the protozoan parasite *Leishmania*. Trends Microbiol. **6**, 35–40 (1998)
6. Turco, S.J., Descoteaux, A.: The Lipophosphoglycan of *Leishmania* Parasites. Annu. Rev. Microbiol. **46**, 65–92 (1992)
7. Ferguson, M.A.J., Homans, S.W., Dwek, R.A., Rademacher, T.W.: Glycosyl-phosphatidylinositol moiety that anchors Trypanosoma brucei variant surface glycoprotein to the membrane. Science **239**, 753–759 (1988)
8. Homans, S.W., Ferguson, M.A.J., Dwek, R.A., Rademacher, T.W., Anand, R., Williams, A.F.: Complete structure of the glycosyl phosphatidylinositol membrane anchor of rat brain Thy-1 glycoprotein. Nature **333**, 269–272 (1988)
9. Ferguson, M.A.J., Williams, A.F.: Cell-surface anchoring of proteins via glycosyl-phosphatidylinositol structures. Annu. Rev. Biochem. **57**, 285–320 (1988)
10. Low, M.G.: Biochim. Biophys. Acta **988**, 427–454 (1989)

11. Thomas, J.R., Dwek, R.A., Rademacher, T.W.: Structure, biosynthesis, and function of glycosylphosphatidylinositols. Biochemistry **29**, 5413–5422 (1990)
12. Cross, G.A.M.: Glycolipid anchoring of plasma membrane proteins. Annu. Rev. Cell. Bio. **6**, 1–39 (1990)
13. McConville, M.J.: Glycosylated-phosphatidylinositols as virulence factors in Leishmania. Cell Bio. Intl. Rep. **15**, 779–798 (1991)
14. McConville, M.J., Ferguson, M.A.J.: The structure, biosynthesis and function of glycosylated phosphatidylinositols in the parasitic protozoa and higher eukaryotes. Biochem. J. **294**, 305–324 (1993)
15. Englund, P.T.: The structure and biosynthesis of glycosyl phosphatidylinositol protein anchors. Annu. Rev. Biochem. **62**, 121–138 (1993)
16. Saltiel, A.R., Fox, J.A., Sherline, P., Cuatrecasas, P.: Insulin-stimulated hydrolysis of a novel glycolipid generates modulators of cAMP phosphodiesterase. Science **233**, 967–972 (1986)
17. Tolsen, D.J., Turco, S.J., Beecroft, R.P., Pearson, T.W.: The immunochemical structure and surface arrangement of Leishmania donovani lipophosphoglycan determined using monoclonal antibodies. Mol. Biochem. Parasitol. **35**, 109–118 (1989)
18. Chan, B.L., Chao, M.V., Saltiel, A.R.: Nerve growth factor stimulates the hydrolysis of glycosylphosphatidylinositol in PC-12 cells: a mechanism of protein kinase C regulation. Proc. Natl. Acad. Sci. U.S.A. **86**, 1756–1760 (1989)
19. Eardley, D.D., Koshland, M.E.: Glycosylphosphatidylinositol: a candidate system for interleukin-2 signal transduction. Science **251**, 78–81 (1991)
20. Pimento, P.F.P., Saraiva, E.M.B., Sacks, D.L.: The comparative fine structure and surface glycoconjugate expression of three life stages of Leishmania major. Exp. Parasitol. **72**, 191–204 (1991)
21. Nikolaev, A.V., Rutherford, T.J., Ferguson, M.A.J., Brimacombe, J.S.: The chemical synthesis of Leishmania donovani phosphoglycan fragments. Bioorg. Med. Chem. Lett. **4**, 785–788 (1994)
22. Nikolaev, A.V., Chudek, J.A., Ferguson, M.A.: The chemical synthesis of Leishmania donovani phosphoglycan via polycondensation of a glycobiosyl hydrogenphosphonate monomer. Carbohydr. Res. **272**, 179–189 (1995)
23. Arasappan, A., FraserReid, B.: *n*-Pentenyl glycoside methodology in the stereoselective construction of the tetrasaccharyl cap portion of Leishmania lipophosphoglycan. J. Org. Chem. **61**, 2401–2406 (1996)
24. Nikolaev, A.V., Watt, G.M., Ferguson, M.A.J., Brimacombe, J.S.: Parasite glycoconjugates. Part 6.[1] Chemical synthesis of phosphorylated penta- and hepta-saccharide fragments of Leishmania major antigenic lipophosphoglycan. J. Chem. Soc., Perkin Trans **1**, 969–980 (1997)
25. Higson, A.P., Tsvetkov, Y.E., Ferguson, M.A.J., Nikolaev, A.V.: The synthesis of Leishmania major phosphoglycan fragments. Tetrahedron Lett. **40**, 9281–9284 (1999)
26. Ruda, K., Lindberg, J., Garegg, P.J., Oscarson, S., Konradsson, P.: Synthesis of the Leishmania LPG Core Heptasaccharyl myo-Inositol. J. Am. Chem. Soc **122**, 11067–11072 (2000)
27. Upreti, M., Ruhela, D., Vishwakarma, R.A.: Synthesis of the tetrasaccharide cap domain of the antigenic lipophosphoglycan of Leishmania donovani parasite. Tetrahedron **56**, 6577–6584 (2000)
28. Hewitt, M.C., Seeberger, P.H.: Solution and solid-support synthesis of a potential Leishmaniasis carbohydrate vaccine. J. Org. Chem. **66**, 4233–4243 (2001)
29. Hewitt, M.C., Seeberger, P.H.: Automated solid-phase synthesiso f a branched Leishmania cap tetrasaccharide. Org Lett. **3**, 3699–3702 (2001)
30. Yashunsky, D.V., Higson, A.P., Ross, A.J., Nikolaev, A.V.: An efficient and stereoselective synthesis of β-D-Arap-(1→2)-β-D-Galp-(1→3)-β-D-Galp-(1→4)-α-D-Manp, a tetrasaccharide fragment of Leishmania majorlipophosphoglycan. Carbohydr. Res. **336**, 243–248 (2001)
31. Ruhela, D., Vishwakarma, R.A.: Efficient synthesis of the antigenic phosphoglycans of the Leishmaniaparasite. Chem. Commun. 2024–2025 (2001)
32. Gandolfi-Donadio, L., Gallo-Rodriguez, C., de Lederkremer, R.M.: Synthesis of α-D-Galp-(1→3)-β-D-Galf-(1→3)-D-man, a terminal trisaccharide of Leishmania type-2 glycoinositolphospholipids. J. Org. Chem. **67**, 4430–4435 (2002)
33. Ruhela, D., Vishwakarma, R.A.: A facile and novel route to the antigenic branched phosphoglycan of the protozoan Leishmania major parasite. Tetrahedron Lett. **45**, 2589–2592 (2004)
34. Higson, A.P., Ross, A.J., Tsvetkov, Y.E., Routier, F.H., Sizova, O.V., Ferguson, M.A.V., Nikolaev, M.A.V.: Synthetic fragments of antigenic lipophosphoglycans from Leishmania major and Leishmania mexicana and their use for characterisation of the Leishmania elongating α-D-mannopyranosylphosphate transferase. Chem. Eur. J. **11**, 2019–2030 (2005)
35. Liu, X.Y., Siegrist, S., Amacker, M., Zurbriggen, R., Pluschke, G., Seeberger, P.H.: Enhancement of the immunogenicity of synthetic carbohydrates by conjugation to virosomes: a Leishmaniasis vaccine candidate. ACS Chem. Bio. **1**, 161–164 (2006)
36. Hotha, S., Kashyap, S.: Propargyl glycosides as stable glycosyl donors: anomeric activation and glycoside syntheses. J. Am. Chem. Soc. **128**, 9620–9621 (2006)
37. Hotha, S., Kashyap, S.: Stereoselective synthesis of α-glucosides from 3-*O*-propargyl protected glucal exploiting the alkynophilicity of $AuCl_3$. Tetrahedron Lett. **47**, 2021–2023 (2006)
38. Sureshkumar, G., Hotha, S.: Propargyl 1,2-orthoesters as glycosyl donors: stereoselective synthesis of 1,2-*trans* glycosides and disaccharides. Tetrahedron Lett. **48**, 6564–6568 (2007)
39. Kashyap, S., Vidadala, S.R., Hotha, S.: Synthesis of C-2 methylene glycosides from C-2 propargyloxymethyl glycals exploiting the alkynophilicity of $AuCl_3$. Tetrahedron Lett. **48**, 8960–8962 (2007)
40. Sureshkumar, G., Hotha, S.: Gold mediated glycosylations: selective activation of propargyl 1,2-orthoesters in the presence of aglycones containing a propargyl moiety Chem. Commun. 4282–4284 (2008)
41. Vidadala, S.R., Hotha, S.: Methyl glycosides are identified as glycosyl donors for the synthesis of glycosides, disaccharides and oligosaccharides Chem. Commun. 2505–2507 (2009)
42. Vidadala, S.R., Thadke, S.A., Hotha, S.: Orthogonal activation of propargyl and n-pentenyl glycosides and 1,2-orthoesters. J. Org. Chem. **74**, 9233–9236 (2009)
43. Kayastha, A.K., Hotha, S.: Gold-catalyzed glycosidations: unusual cleavage of the interglycosidic bond while studying the armed/disarmed effect of propargyl glycosides. Tetrahedron Lett. **51**, 5269–5272 (2010)
44. Thadke, S.A., Hotha, S.: Gold-catalyzed glycosidations: synthesis of 1,6-anhydro saccharides. Tetrahedron Lett **51**, 5912–5914 (2010). Other papers on gold catalyzed glycosidations
45. Li, Y., Yang, Y., Yu, B.: An efficient glycosylation protocol with glycosyl ortho-alkynylbenzoates as donors under the catalysis of $Ph_3PAuOTf$. Tetrahedron Lett. **49**, 3604–3608 (2008)
46. Li, Y., Tank, P., Chen, Y., Yu, B.: Gold(I)-catalyzed glycosidation of 1,2-anhydrosugars. J. Org. Chem. **73**, 4323–4325 (2008)
47. Götze, S., Fitzner, R., Kunz, H.: Gold catalysis in glycosylation reactions. Synlett 3346–3348 (2009)
48. Mamidyala, S.K., Finn, M.G.: Glycosylation using unprotected alkynyl donors. J. Org. Chem. **74**, 8417–8420 (2009)
49. Kartha, K.P.R., Jennings, H.J.: A simplified, one-pot preparation of acetobromosugars from reducing sugars. J. Carbohydr. Chem. **9**, 777–781 (1990)
50. Larsen, K., Olsen, C.E., Motawia, M.S.: A facile protocol for direct conversion of unprotected sugars into phenyl 4,6-*O*-benzylidene-per-*O*-acetylated-1,2-*trans*-thioglycosides. Carbohydr. Res. **338**, 199–202 (2003)

51. Hunsen, M., Long, D.A., D'Ardenne, C.R., Smith, A.L.: Mild one-pot preparation of glycosyl bromides. Carbohydr. Res. **340**, 2670–2674 (2005)
52. Mach, M., Schlueter, U., Mathew, F., Fraser-Reid, B., Hazan, K.C.: Comparing n-pentenyl orthoesters and *n*-pentenyl glycosides as alternative glycosyl donors. Tetrahedron **58**, 7345–7354 (2002)
53. Warren, C.D., Augé, C., Laver, M.L., Suzuki, S., Power, D., Jeanloz, R.W.: The synthesis of O-β-D-mannopyranosyl-(1→4)-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-2-acetamido-2-deoxy-D-glucopyranose. Carbohydrate Res. **82**, 71–83 (1980)
54. Liu, K.K.-C., Danishefsky, S.J.: Route from glycals to mannose β-glycosides. J. Org. Chem **59**, 1892–1894 (1994)