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Application of the 4-Trifluoromethylbenzenepropargyl Ether Group as an Unhindered, Electron Deficient Protecting Group for Stereoselective Glycosylation

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Abstract

4-Trifluoromethylbenzenepropargyl ethers are stable and sterically minimal alcohol protecting groups that are readily cleaved in a single step by exposure to lithium naphthalenide. In conjunction with the 4,6-*O*-benzylidene protecting group, glycosylation reactions of 2-*O*-4-trifluoromethylbenzenepropargyl-protected mannosyl donors are extremely β selective.

Introduction

Protecting groups continue to play a central role in modern organicsynthesis,¹ and the ability/inability to achieve selective deprotection of one protecting group in the presence of another is often key to the success/failure of a synthetic route. In response to a problem arising from the influence of protecting group size on the stereoselectivity of a glycosylation reaction, we described the application of a propargyl ether as a sterically minimal donor protecting group for β -mannosylation with donor **1**.²

While the propargyl ethers were readily introduced and had the anticipated effect on stereoselectivity, they required a two-step deprotection protocol, namely an initial treatment with the base followed by catalytic osmylation of the resulting allenyl ether.² Subsequently, to facilitate deprotection, the propargyl ether system was modified in such a way as to be cleavable in a single step, orthogonal to the ubiquitous benzyl ethers. This was achieved through the use of the naphthyl propargyl system, which is removed in a single step with DDQ.³ Donors **2** and **3**, however, had two limitations: incompatibility with glycosylation reactions owing to cyclization onto the oxacarbenium ion and direct reaction of the electron rich triple bond with glycosylation promoters. Nevertheless, the naphthylpropargyl system was ideal for use at the 3-*O*-position of donors, as in **4**, provided that it was used in conjunction with the sulfoxide glycosylation method and a sacrificial alkene.³ Extending this series we now describe an electron poor arylpropargyl system compatible with the 2-*O*-position and removable under dissolving metal conditions.

Alkylation of 1,2:5,6-di-*O*-acetone-*D*-glucofuranose with sodium hydride and 4-trifluoromethylphenyl propargyl bromide **5**⁴ gave the model ether **6**, with which different reductive conditions were explored (Scheme 1). Exposure of **6** to samarium iodide, generated under standard conditions,⁵ resulted in no reaction. When **6** was exposed to samarium iodide generated by mixing samarium and iodine,⁶ partial loss of an isopropylidene group was observed with no formation of the desired product. Presumably unreacted iodine acted as a Lewis acid resulting in the loss of an isopropylidene group.⁷ However, sodium in liquid ammonia,⁸ and lithium naphthalenide⁹ proved effective in removing the electron-deficient propargyl ether and in affording the required deprotected sugar in good yield.

To examine the effect of the new electron poor protecting group on the stereoselectivity of glycosylation reactions when located at *O*2, donor **8** was prepared by reaction of glycoside **7**¹⁰ with propargyl bromide **5** (Scheme 2).

Treatment of **8** with triflic anhydride in the presence of BSP¹¹ and TTBP¹² (Figure 2) at -70°C in CH_2Cl_2 , to give an intermediate glycosyl triflate,¹¹ followed by addition of 1-adamantanol, resulted in the formation of the β -mannoside **9** with impeccable selectivity (Table 1, entry 1). A number of further couplings were then conducted with more standard glycosyl acceptors, leading to the yields collected in Table 1.

Exposure of mannoside **9** to Na in liquid ammonia cleanly gave fully deprotected 1-adamantanyl- β -*D*-mannopyranoside **16** (Scheme 3).

Selective deprotection was achieved using lithium naphthalenide in THF by warming a -70°C reaction mixture to 0°C over a period of 2–3 h when **17** was obtained in 85% yield. This strategy was extended to glycosides **10** to **15** (Table 2). In almost all cases minor amounts of debenzylated products were obtained as the side products.

Conclusion

To conclude, we report the development of the electron poor 4-trifluoromethylbenzenepropargyl ether system as an alcohol protecting group. In conjunction with the BSP glycosylation method, when introduced at the 2-position of 4,6-*O*-benzylidene-protected mannosyl donors, this system affords extremely β -selective coupling reactions and the possibility of orthogonal cleavage in a single step with lithium naphthalenide.

Experimental Section

3-*O*-[3-(4-Trifluoromethylphenyl)-prop-2-ynyl]-1,2:5,6-di-*O*-isopropylidene- α -*D*-glucofuranose (**6**)

Sodium hydride (60% in mineral oil, 16 mg, 1.1 eq) was added to a stirred solution of diacetone *D*-glucose (99 mg, 0.4 mmol, 1 eq) in DMF (8 mL) at 0°C and allowed to stir for 30 min. This yellow mixture was cooled to 0°C and treated with propargyl bromide **5** (120 mg, 1.1 eq) in DMF (1 mL). The dark brown reaction mixture was allowed to stir for an hour at room temperature and quenched (at 5°C – 10°C) with saturated aqueous ammonium chloride (2 mL). The crude product was extracted with methylene chloride (3 $\times$ 3 mL), dried (MgSO_4) and concentrated. The residue was purified by column chromatography on silica (5% to 20% Ethyl acetate:Hexane as eluent) to afford **6** (100 mg, 60%). Viscous oil. $[\alpha]^{24}_{\text{D}} -6.3$ (c 1.7, CHCl_3). $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 1.29 (s, 3H), 1.32 (s, 3H), 1.40 (s, 3H), 1.48 (s, 3H), 4.00 (q, $J = 8.5$ Hz, 1H), 4.07–4.10 (m, 3H), 4.14 (d, $J = 9.1$ Hz, 1H), 4.30 (q, $J = 6.9$ Hz, 1H), 4.96 (s, 2H), 4.66 (d, $J = 3.5$ Hz, 1H), 5.88 (d, $J = 3.5$ Hz, 1H), 7.51–7.56 (m, 4H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): δ 25.3, 26.1, 26.7, 26.8, 58.6, 67.2, 72.5, 76.8, 81.0, 81.5, 82.8, 85.1, 87.2,

105.2, 109.0, 111.9, 125.2, 126.2, 131.9; ^{19}F -NMR (471 MHz, CDCl_3): δ -64.47. ESI-HRMS calcd for $\text{C}_{22}\text{H}_{25}\text{F}_3\text{O}_6$ $[\text{M}]^+$ 442.1603, found 442.1593.

Phenyl 4,6-O-benzylidene-2-O-[3-(4-trifluoromethylphenyl)-prop-2-ynyl]-1-thio- α -D-mannopyranoside (8)

Sodium hydride (60% in mineral oil, 0.29 g, 1.6 eq) was added in three portions to a stirred solution of alcohol **7** (2.1 g, 4.7 mmol, 1 eq) in DMF (100 mL) at 0 °C and allowed to stir for 30 min. This yellow mixture was cooled to 0 °C and treated with propargyl bromide **5** (1.33 g, 1.08 eq) in DMF (10 mL). Dark brown reaction mixture was allowed to stir for an hour at room temperature and quenched (at 5 °C–10 °C) with saturated aqueous ammonium chloride (20 mL). The crude product was extracted with methylene chloride (3×30 mL), dried (MgSO_4) and concentrated. The residue was purified by column chromatography on silica (5% to 20% Ethyl acetate: Hexane in 5% increments) to afford 2 g (68%) of mannopyranoside **8**. Viscous oil. $[\alpha]_D^{24} +69.4$ (c 1.7, CHCl_3); ^1H -NMR (500 MHz, CDCl_3): δ 3.95 (t, J = 10 Hz, 1H), 4.06 (dd, J = 3.2 Hz, 10 Hz, 1H), 4.29–4.39 (m, 4H), 4.68 (q, J = 16.2 Hz, 2H), 4.82 (d, J = 12.5 Hz, 1H), 4.97 (d, J = 12.5 Hz, 1H), 5.70 (s, 1H), 5.77 (s, 1H), 7.26–7.32 (m, 2H), 7.32–7.34 (m, 2H), 7.42–7.47 (m, 10H), 7.55–7.60 (m, 5H); ^{13}C -NMR (125 MHz, CDCl_3): δ 59.6, 65.4, 68.6, 73.5, 76.1, 78.6, 79.3, 85.6, 87.5, 87.8, 101.6, 125.31, 125.33, 126.1, 127.7, 127.8, 128.3, 128.5, 129.0, 129.2, 131.5, 132.0, 133.9, 137.6, 138.3; ESI-HRMS calcd for $\text{C}_{36}\text{H}_{31}\text{F}_3\text{O}_5\text{SNa}$ $[\text{M}+\text{Na}]^+$ 655.1742, found 655.1739.

General Procedure for Coupling of Mannosyl Donor **8 with Acceptors**

To a stirred solution of donor **8** (0.10 g, 0.16 mmol, 1 eq). BSP (1.5 eq), TTBP (2 eq), and 4Å molecular sieves in 3.2 mL (0.05 M) of dichloromethane at -70 °C under an Ar atmosphere, was added TiF_2O (1.1 eq) slowly. The resulting yellow mixture was stirred at this temperature for 30 min, and then a solution of acceptor (2.0 eq) in dichloromethane 2 mL was added. The stirring was continued for another 30 min and the reaction mixture was poured into saturated aqueous NaHCO_3 solution. The crude product was extracted with dichloromethane (3×4 mL). The organic layer was separated, dried (MgSO_4) and concentrated. The residue was purified by column chromatography (hexane/ethyl acetate) on silica gel to give the corresponding coupled products.

1-Adamantanyl 4,6-O-benzylidene-2-O-[3-(4-trifluoromethylphenyl)-prop-2-ynyl]- β -D-mannopyranoside (9)

Viscous oil. $[\alpha]_D^{25} -37.5$ (c 1, CHCl_3). ^1H -NMR (500 MHz, CDCl_3): δ 1.58–1.67 (m, 6H), 1.78–1.87 (m, 6H), 2.26 (s, 3H), 3.32–3.37 (m, 1H), 3.68 (dd, J = 10 Hz, J = 3.2 Hz, 1H), 3.93 (t, J = 8.1 Hz, 1H), 4.07 (d, J = 2.5 Hz, 1H), 4.16 (t, J = 9.7 Hz, 1H), 4.28 (dd, J = 10 Hz, J = 4.7 Hz, 1H), 4.80–4.92 (m, 5H), 5.61 (s, 1H), 7.23 (m, 4H), 7.38 (m, 5H), 7.53 (m, 5H). ^{13}C -NMR (125 MHz, CDCl_3): δ 30.6, 36.2, 42.4, 60.8, 67.2, 68.8, 72.5, 75.5, 76.9, 78.5, 84.8, 88.7, 94.7, 101.4, 125.2, 126.1, 126.8, 127.5, 128.3, 128.4, 128.9, 132.1, 137.7, 138.4. ^{19}F -NMR (471 MHz, CDCl_3): δ -64.33. ESI-HRMS calcd for $\text{C}_{40}\text{H}_{41}\text{F}_3\text{O}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ 697.2748, found 697.2749.

Methyl 2,3,6-tri-O-benzyl-4-O-[4,6-O-benzylidene-2-O-[3-(4-trifluoromethylphenyl)-prop-2-ynyl]-3-O-benzyl- β -D-mannopyranosyl]- α -D-glucopyranoside (10)

Viscous oil. $[\alpha]_D^{14} -13.4$ (c 0.5, CHCl_3). ^1H -NMR (500 MHz, CDCl_3): δ 3.02–3.07 (m, 1H), 3.35 (s, 3H), 3.38–3.40 (m, 1H), 3.50–3.56 (m, 2H), 3.60 (d, J = 9 Hz, 1H), 3.67–3.77 (m, 2H), 3.86–3.89 (m, 2H), 3.92–3.96 (m, 1H), 4.03–4.07 (m, 2H), 4.35 (d, J = 12 Hz, 1H), 4.45 (s, 1H), 4.63–4.68 (m, 3H), 4.72 (d, J = 7 Hz, 2H), 4.79–4.83 (m, 3H), 5.05 (d, J = 10.5 Hz, 1H), 5.52 (s, 1H), 7.24–7.27 (m, 6H), 7.30–7.37 (m, 8H), 7.40–7.41 (m, 4H), 7.43–7.44 (m, 5H), 7.48 (dd, J = 8 Hz, J = 1.5 Hz, 3H), 7.52 (d, J = 8 Hz, 2H). ^{13}C -NMR (125 MHz, CDCl_3): δ

55.4, 60.6, 67.2, 68.5, 68.6, 69.6, 72.7, 73.6, 75.3, 76.4, 77.7, 78.6, 79.1, 80.2, 88.4, 98.4, 101.3, 101.4, 125.2, 126.1, 127.3, 127.4, 127.6, 127.8, 127.9, 128.1, 128.2, 128.24, 128.3, 128.6, 128.9, 132.0, 137.5, 137.6, 138.3, 138.5, 139.3. ^{19}F -NMR (471 MHz, CDCl_3): δ -64.40. ESI-HRMS calcd for $\text{C}_{58}\text{H}_{57}\text{F}_3\text{O}_{11}\text{Na}$ $[\text{M}+\text{Na}]^+$ 1009.3745, found 1009.3744.

Methyl 2,3,6-tri-O-benzyl-6-O-[4,6-O-benzylidene-2-O-[3-(4-trifluoromethylphenyl)-prop-2-ynyl]-3-O-benzyl- β -D-mannopyranosyl]- α -D-glucopyranoside (11)

Viscous oil. $[\alpha]^{14}_{\text{D}} -6.0$ (c 0.7, CHCl_3). ^1H -NMR (500 MHz, CDCl_3): δ 3.20–3.25 (m, 1H), 3.34 (s, 3H), 3.47–3.50 (m, 3H), 3.54 (dd, $J = 9.7$ Hz, $J = 3.5$ Hz, 1H), 3.78 (m, 1H), 3.90 (t, $J = 10.5$ Hz, 1H), 4.01 (t, $J = 9$ Hz, 1H), 4.05–4.14 (m, 4H), 4.27 (dd, $J = 9.7$ Hz, $J = 4.5$ Hz, 1H), 4.55 (d, $J = 3.5$ Hz, 1H), 4.59 (d, $J = 11.7$ Hz, 1H), 4.65 (d, $J = 11.7$ Hz, 1H), 4.77–4.78 (m, 2H), 4.79–4.83 (m, 4H), 4.84 (d, $J = 8.5$ Hz, 1H), 4.88 (d, $J = 11.5$ Hz, 1H), 5.00 (d, $J = 11$ Hz, 1H), 5.58 (s, 1H), 7.21–7.23 (m, 8H), 7.39–7.33 (m, 15H), 7.43–7.45 (m, 2H), 7.49–7.52 (m, 4H). ^{13}C -NMR (125 MHz, CDCl_3): δ 55.1, 60.4, 67.4, 68.3, 68.5, 69.6, 72.5, 73.4, 74.8, 75.0, 76.1, 76.6, 77.4, 78.5, 79.9, 82.2, 85.4, 88.1, 97.9, 101.4, 102.0, 125.3, 126.0, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5, 128.9, 132.1, 137.5, 138.0, 138.3, 138.4, 138.6. ^{19}F -NMR (471 MHz, CDCl_3): δ -64.34. ESI-HRMS calcd for $\text{C}_{58}\text{H}_{57}\text{F}_3\text{O}_{11}\text{Na}$ $[\text{M}+\text{Na}]^+$ 1009.3745, found 1009.3744.

Methyl 4-O-[4,6-O-benzylidene-2-O-[3-(4-trifluoromethylphenyl)-prop-2-ynyl]-3-O-benzyl- β -D-mannopyranosyl]-2,3-O-isopropylidene- α -L-rhamnopyranoside (12)

Viscous oil. $[\alpha]^{16}_{\text{D}} -49.3$ (c 1, CHCl_3). ^1H -NMR (500 MHz, CDCl_3): δ 1.32 (s, 3H), 1.36 (s, 3H), 1.54 (s, 3H), 3.34 (s, 3H), 3.31–3.40 (m, 4H), 3.60–3.62 (m, 1H), 3.66–3.71 (m, 2H), 3.96 (t, $J = 10.2$ Hz, 1H), 4.08 (d, $J = 5.5$ Hz, 1H), 4.15–4.18 (m, 2H), 4.22 (d, $J = 3.5$ Hz, 1H), 4.28 (dd, $J = 10.5$ Hz, $J = 5$ Hz, 1H), 4.76–4.79 (m, 2H), 4.81 (s, 1H), 4.85–4.87 (m, 2H), 5.05 (s, 1H), 5.61 (s, 1H), 7.22–7.26 (m, 3H), 7.34–7.41 (m, 5H), 7.49–7.52 (m, 4H), 7.56 (d, $J = 8.5$ Hz, 2H). ^{13}C -NMR (125 MHz, CDCl_3): δ 17.7, 26.4, 27.8, 54.9, 60.6, 64.0, 67.6, 68.6, 72.5, 76.0, 76.1, 77.4, 77.9, 78.3, 78.7, 84.9, 88.4, 97.8, 99.9, 101.4, 109.5, 125.2, 125.3, 126.0, 126.7, 127.5, 128.2, 128.3, 128.9, 132.1, 137.5, 138.3. ^{19}F -NMR (471 MHz, CDCl_3): δ -64.38. ESI-HRMS calcd for $\text{C}_{40}\text{H}_{43}\text{F}_3\text{O}_{10}\text{Na}$ $[\text{M}+\text{Na}]^+$ 763.2701, found 763.2672

1,6-Anhydro-4-O-[4,6-O-benzylidene-2-O-[3-(4-trifluoromethylphenyl)-prop-2-ynyl]-3-O-benzyl- β -D-mannopyranosyl]-2,3-O-isopropylidene- β -D-mannopyranose (13)

Viscous oil. $[\alpha]^{15}_{\text{D}} -68.5$ (c 0.9, CHCl_3). ^1H -NMR (500 MHz, CDCl_3): δ 1.30 (s, 3H), 1.53 (s, 3H), 3.34–3.39 (m, 1H), 3.68 (dd, $J = 10$ Hz, $J = 3$ Hz, 1H), 3.77 (t, $J = 7$ Hz, 1H), 3.94 (t, $J = 10$ Hz, 1H), 3.98 (d, $J = 7$ Hz, 1H), 4.02 (dd, $J = 6$ Hz, $J = 3$ Hz, 1H), 4.09 (s, 1H), 4.20 (t, $J = 9.5$ Hz, 1H), 4.25 (d, $J = 3$ Hz, 1H), 4.32 (d, $J = 10.5$ Hz, $J = 5$ Hz, 1H), 4.37 (d, $J = 6$ Hz, 1H), 4.59 (d, $J = 6$ Hz, 1H), 4.77–4.89 (m, 5H), 5.33 (d, $J = 2.5$ Hz, 1H), 5.62 (s, 1H), 7.23–7.26 (m, 4H), 7.33–7.41 (m, 5H), 7.49–7.57 (m, 5H); ^{13}C -NMR (125 MHz, CDCl_3): δ 25.9, 26.0, 61.0, 64.3, 67.7, 68.4, 72.1, 72.4, 72.8, 74.9, 75.3, 76.1, 78.4, 85.1, 88.0, 99.5, 99.9, 110.0, 125.2, 125.3, 126.0, 126.6, 127.6, 128.3, 128.4, 129.0, 132.1, 137.3, 138.0; ^{19}F -NMR (471 MHz, CDCl_3): δ -64.39; ESI-HRMS calcd for $\text{C}_{39}\text{H}_{39}\text{F}_3\text{O}_{10}\text{Na}$ $[\text{M}+\text{Na}]^+$ 747.2389, found 747.2373

3-O-[4,6-O-Benzylidene-2-O-[3-(4-trifluoromethylphenyl)-prop-2-ynyl]-3-O-benzyl- β -D-mannopyranosyl]-1,2:5,6-di-O-isopropylidene- α -D-glucofuranose (14)

Viscous oil. $[\alpha]^{23}_{\text{D}} -18.8$ (c 1.2, CHCl_3). ^1H -NMR (500 MHz, CDCl_3): δ 1.25 (s, 3H), 1.37 (s, 3H), 1.44 (s, 3H), 1.49 (s, 3H), 3.33 (m, 1H), 3.68 (d, $J = 8$ Hz, 1H), 3.92 (t, $J = 10.2$ Hz, 1H), 4.09 (d, $J = 8.5$ Hz, 1H), 4.16–4.18 (m, 2H), 4.21–4.22 (m, 2H), 4.31–4.32 (m, 2H), 4.37–4.40 (m, 2H), 4.50 (s, 1H), 4.62 (s, 1H), 4.71–4.79 (m, 3H), 4.90 (d, $J = 12.5$ Hz, 1H), 5.62 (s, 1H), 5.85 (s, 1H), 7.25–7.27 (m, 3H), 7.35–7.38 (m, 5H), 7.48–7.49 (m, 2H), 7.55–7.56 (m,

4H). ^{13}C -NMR (125 MHz, CDCl_3): δ 25.6, 26.2, 26.5, 26.7, 60.6, 66.0, 67.7, 68.4, 73.0, 73.5, 75.8, 77.8, 78.6, 80.3, 80.6, 82.6, 85.3, 87.9, 99.5, 101.5, 104.9, 108.5, 111.9, 125.3, 126.0, 126.5, 127.6, 127.8, 128.3, 128.4, 129.0, 132.1, 137.4, 138.1. ^{19}F -NMR (471 MHz, CDCl_3): δ -64.47. ESI-HRMS calcd for $\text{C}_{42}\text{H}_{45}\text{F}_3\text{O}_{11}\text{Na}$ $[\text{M}+\text{Na}]^+$ 805.2795, found 805.2806.

6-O-[4,6-O-Benzylidene-2-O-[3-(4-trifluoromethylphenyl)-prop-2-ynyl]-3-O-benzyl- β -D-mannopyranosyl]-1,2:3,4-di-O-isopropylidene- α -D-galactopyranose (15)

Viscous oil. $[\alpha]_{\text{D}}^{15}$ -76.2 (*c* 1.1, CHCl_3). ^1H -NMR (500 MHz, CDCl_3): δ 1.32 (s, 6H), 1.4 (s, 3H), 1.50 (s, 3H), 3.33–3.35 (m, 1H), 3.63–3.69 (m, 2H), 3.92 (t, *J* = 10.2 Hz, 1H), 4.05 (dd, *J* = 8 Hz, *J* = 2 Hz, 1H), 4.13–4.17 (m, 2H), 4.2 (dd, *J* = 8 Hz, *J* = 1.5 Hz, 1H), 4.28 (d, *J* = 3 Hz, 1H), 4.30–4.34 (m, 2H), 4.60 (dd, *J* = 8 Hz, *J* = 2.5 Hz, 1H), 4.63 (s, 1H), 4.77 (d, *J* = 6 Hz, 1H), 4.8 (d, *J* = 2H, 1H), 4.83 (s, 1H), 4.86 (d, *J* = 3.5 Hz, 1H), 7.55 (d, *J* = 5 Hz, 1H), 5.6 (s, 1H), 7.18–7.22 (m, 4H), 7.30–7.33 (m, 2H), 7.36–7.40 (m, 3H), 7.48–7.51 (m, 2H), 7.53–7.56 (m, 3H). ^{13}C -NMR (125 MHz, CDCl_3): δ 24.4, 25.1, 26.0, 60.8, 67.4, 68.1, 68.5, 70.1, 70.7, 71.5, 72.6, 75.8, 78.5, 84.8, 88.5, 96.3, 101.5, 102.5, 108.8, 109.6, 125.2, 126.0, 126.8, 127.5, 127.6, 128.2, 128.3, 128.9, 132.1, 132.2, 137.5, 138.2. ^{19}F -NMR (471 MHz, CDCl_3): δ -64.38. ESI-HRMS calcd for $\text{C}_{42}\text{H}_{45}\text{F}_3\text{O}_{11}\text{Na}$ $[\text{M}+\text{Na}]^+$ 805.2806, found 805.2787.

Global deprotection with Sodium in liquid ammonia: 1-Adamantyl- β -D-mannopyranoside (16)

Mannopyranoside **9** (0.1 g, 0.12 mmol, 1 eq) was dissolved in a mixture of liquid ammonia (2 mL), THF (4 mL) and tertiary butanol (2 mL). To this solution at -70°C was added sodium (0.03 g, 10 eq) in 4 pieces and the reaction mixture was warmed to -40°C and the intense blue solution was stirred for 1 h. After the reaction completion (TLC 10% $\text{CH}_3\text{OH}:\text{CHCl}_3$), the reaction mixture at -20°C was slowly quenched with saturated aqueous ammonium chloride solution (4 mL). The product was extracted with dichloromethane (3 $\times$ 4 mL). The organic layer was dried (MgSO_4) and concentrated to afford a crude product which was purified on a silica chromatography (2%, 4%, 5%, 8%, 10% $\text{CHCl}_3:\text{CH}_3\text{OH}$) to afford 27 mg (72%) of **16**. White solid: M.pt.: $218\text{--}220^\circ\text{C}$: $[\alpha]_{\text{D}}^{11}$ -27.4 (*c* 0.7, CH_3OH); ^1H -NMR (400 MHz, CD_3OD): δ 1.63–1.70 (m, 6H), 1.79–1.92 (m, 6H), 2.13 (m, 3H), 3.16–3.20 (m, 1H), 3.45 (dd, *J* = 8.8 Hz, *J* = 3.2 Hz, 1H), 3.65–3.69 (m, 2H), 3.82 (dd, *J* = 11.6 Hz, *J* = 2 Hz, 1H), 4.82 (d, 1H). ^{13}C -NMR (125 MHz, CD_3OD): δ 31.0, 36.2, 42.3, 61.8, 67.3, 72.9, 74.3, 74.8, 76.6, 93.4. ESI-HRMS calcd for $\text{C}_{16}\text{H}_{26}\text{NaO}_6$ $[\text{M}+\text{Na}]^+$ 337.1627, found 337.1613.

General procedure for selective reduction. 1-Adamantyl 3-O-benzyl-4,6-O-benzylidene- β -D-mannopyranoside (17)

Lithium naphthalenide in THF (0.25 M) was generated by dissolving Li (3–5 mg) in a solution of naphthalene (64 mg, 0.5 mmol) in THF (2 mL) at room temperature and allowing the reaction mixture to stir under Ar for 2 h. This dark green solution of lithium naphthalide (10 eq) was dropwise added to a solution of sugar **9** (34 mg, 0.05 mmol, 1 eq) in THF (1 mL) kept at -78°C . The resultant reaction mixture was allowed to warm up to 0°C over a period of 3 h and then quenched with a saturated solution of aqueous ammonium chloride (2.5 mL). The crude product was extracted with methylene chloride (3 $\times$ 4 mL). The organic layer was separated, dried (MgSO_4) and concentrated. The residue was purified by column chromatography on silica (3%, 5%, 10%, 15%, 20%, 25% Ethyl acetate:Hexane) to afford **17** (21 mg, 85%). Viscous oil. $[\alpha]_{\text{D}}^{11}$ -8.7 (*c* 0.6, CHCl_3). ^1H -NMR (400 MHz, CDCl_3): δ 1.59–1.66 (m, 6H), 1.77–1.86 (m, 6H), 2.16 (m, 3H), 2.64 (s, 1H), 3.31–3.35 (m, 1H), 3.66 (dd, *J* = 9.8 Hz, *J* = 3 Hz, 1H), 3.88 (t, *J* = 9.8 Hz, 1H), 3.98 (d, *J* = 3 Hz, 1H), 4.15 (t, *J* = 9.8 Hz, 1H), 4.27 (dd, *J* = 9.8 Hz, *J* = 5 Hz, 1H), 4.78–4.86 (m, 3H), 7.26–7.32 (m, 4H), 7.33–7.40 (m, 4H), 7.49–7.50 (m, 2H). ^{13}C -NMR (125 MHz, CDCl_3): δ 30.7, 36.2, 42.4, 66.7, 68.8, 71.6, 72.3, 75.8, 78.3, 93.3, 126.1, 127.7, 127.9, 128.2, 128.9, 137.6, 138.2; ESI-HRMS calcd for $\text{C}_{30}\text{H}_{36}\text{O}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ 515.2410, found 515.2413.

Compounds 18 to 23

The spectral data for these compounds are consistent with the literature data.¹³

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Various propargyl ether protecting groups

BSP **TTBP**

Figure 2.
Coupling Reagents

Scheme 1.
Model Protection & Deprotection of *D*-Glucofuranose

Scheme 2.
Preparation of Donor **8**

Scheme 3.
Complete deprotection with sodium in liquid ammonia

Table 1

Coupling Reactions of Donor **8**

Entry	Acceptor
1
2

Acceptor

3

Entry

Acceptor

4

5

Entry

Acceptor

6

Entry

Acceptor

7

^a Isolated yields after column chromatography

^b ¹H NMR spectroscopy of crude reaction mixtures revealed only β isomer formation in all cases.

Table 2
Cleavage of 4-Trifluoromethylbenzenepropargyl Ethers

Entry	Deprotected Product
1	<p style="text-align: center;">17</p>
2	<p style="text-align: center;">18</p>
3	<p style="text-align: center;">19</p>
4	<p style="text-align: center;">20</p>

Entry

Deprotected Product

5

6

Entry

Deprotected Product

7

^a Isolated yields after column chromatography