

Short Note

6,7,8,10-Tetra-*O*-benzyl-1,2,3,4-tetradeoxy- α -D-glucodec-5-ulopyranosyl 2,3,4,6-Tetra-*O*-benzyl- α -D-glucopyranoside

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Abstract: The title compound **1** was synthesized by the coupling reaction of 6,7,8,10-tetra-*O*-benzyl-1,2,3,4-tetradeoxy- α -D-glucodec-5-ulopyranose (**2**) with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**3**) in the presence of 5 mol% bismuth(III) triflate in dichloromethane at 0 °C.

Keywords: trehalose mimic; ketose; glucose; bismuth triflate

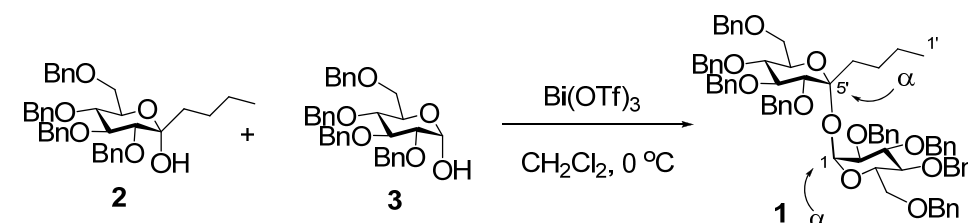
The addition reaction of RLi (or RMgX) to a sugarlactone derivative is an established technique for synthesizing some artificial ketoses whose anomeric carbons are bound to functional groups, such as alkyl, alkynyl, alkenyl, and aryl groups *via* a carbon–carbon linkage [1]. As the ketoses prepared by this method from naturally occurring aldoses retain the ring structures of the starting aldoses, they are regarded as the analogues of aldose. Currently, these ketoses form a new class of carbohydrate reagents useful for synthesizing some valuable and complicated compounds such as enzyme inhibitors [2–5], oligosaccharide mimics [6,7], spiroketals [8–13], *exo*-glycals [14,15], and *C*- or *O*-glycosides [16–18].

Our former research revealed the synthesis of non-reducing disaccharides by the coupling reaction of benzylated 1-deoxy- α -D-glucodec-5-ulopyranoses with 1-hydroxy-aldopyranose derivatives using 5 mol% of bismuth(III) triflate (Bi(OTf)₃) or bis(trifluoromethane)sulfonamide as an activator [19,20]. The synthesized non-reducing disaccharides are the mimics of trehalose which is composed of two glucose molecules linked to each other by an α -glucopyranosidic group. As trehalose is well-known for its various biological functions such as the suppressive effect on osteoporosis

progress [21], it is important to synthesize various kinds of trehalose mimics which are expected to show novel useful functions. This paper describes the synthesis of the title compound **1** by the coupling reaction of 6,7,8,10-tetra-*O*-benzyl-1,2,3,4-tetra-deoxy- α -D-glucopyranose (**2**) [22] with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**3**).

Compound **1** was obtained in a good yield of 70% by the coupling reaction of **2** with **3** in the presence of 5 mol% Bi(OTf)₃ in dichloromethane at 0 °C for 3 h. Various NOE and ¹H NMR experiments were performed with **1**. The NOE interaction between H-6' and H-4' was observed. This observation inevitably indicates the equatorial orientation of the butyl group and determines the α -ketopyranosidic linkage. The α -aldopyranosidic linkage is confirmed by the coupling constant ($J = 3.5$ Hz) of H-1 [23]. Thus, both of the glycosidic linkages of **1** are α [24]. Based on TLC monitoring of the reaction, the self-condensation product from **2** or **3** was not observed at all.

Scheme 1. Coupling reaction of **2** with **3** in the presence of Bi(OTf)₃ to produce **1**.



Experimental

6,7,8,10-Tetra-*O*-benzyl-1,2,3,4-tetra-deoxy- α -D-glucopyranosyl 2,3,4,6-tetra-*O*-benzyl- α -D-glucopyranoside (**1**)

To a solution of Bi(OTf)₃ (4.8 mg, 0.007 mmol), **2** (52.9 mg, 0.10 mmol) and CaSO₄ (ca. 100 mg) in CH₂Cl₂ (3.5 mL) was added **3** (87.2 mg, 0.15 mmol) at 0 °C under an Ar atmosphere. The resulting mixture was stirred for 3 h. The reaction was then quenched by addition of a sat. NaHCO₃ solution (5 mL). The reaction mixture was extracted with CH₂Cl₂, and the organic layer was washed with water and a sat. NaCl solution. After the organic layer was dried over Na₂SO₄, the solvent was evaporated under reduced pressure. The crude product was purified by preparative silica gel TLC (ethyl acetate/hexane = 1/3, $R_f = 0.48$) to give **1** (77.1 mg, 70%) as a colorless oil. $[\alpha]_D^{26} + 25^\circ$ (c 3.9, CHCl₃). ¹H NMR (600 MHz, CDCl₃): δ 0.83 (3H, t, $J = 6.9$ Hz, H-1'), 1.08–1.17 (2H, m, H_a-2', H_a-3'), 1.24–1.31 (1H, m, H_b-2'), 1.40–1.45 (1H, m, H_b-3'), 1.88–1.90 (2H, m, H-4'), 3.37 (1H, d, $J = 11.0$ Hz, H_a-10'), 3.42–3.45 (2H, m, H_b-10', H_a-6), 3.54 (1H, d, $J = 9.0$ Hz, H-6'), 3.56 (1H, dd, $J = 3.4$ Hz, $J = 9.6$ Hz, H-2), 3.57–3.59 (1H, m, H_b-6), 3.59 (1H, t, $J = 10.3$ Hz, H-8'), 3.67 (1H, t, $J = 9.6$ Hz, H-4), 4.08 (1H, t, $J = 9.6$ Hz, H-3), 4.10 (1H, t, $J = 9.7$ Hz, H-7'), 4.22–4.23 (1H, m, H-5), 4.30–4.32 (1H, m, H-9'), 4.38 (1H, d, $J = 13.1$ Hz, CH₂Ph), 4.40 (1H, d, $J = 13.7$ Hz, CH₂Ph), 4.52 (1H, d, $J = 12.4$ Hz, CH₂Ph), 4.54 (1H, d, $J = 12.4$ Hz, CH₂Ph), 4.56–4.61 (3H, m, CH₂Ph), 4.66 (1H, d, $J = 11.7$ Hz, CH₂Ph), 4.69 (1H, d, $J = 12.4$ Hz, CH₂Ph), 4.80–4.95 (7H, m, CH₂Ph), 5.38 (1H, d, $J = 3.5$ Hz, H-1), 7.12–7.31 (40H, m, Ph). ¹³C NMR (150 MHz, CDCl₃): δ 14.1 (C-1'), 23.0 (C-2'), 26.6 (C-3'), 33.8 (C-4'), 68.4 (C-6), 68.7 (C-10'), 70.5 (C-5), 71.3 (C-9'), 73.0 (CH₂Ph), 73.1 (CH₂Ph), 73.3 (CH₂Ph), 74.56 (CH₂Ph), 74.65 (CH₂Ph), 74.66 (CH₂Ph), 75.3 (CH₂Ph), 75.4 (CH₂Ph), 78.2 (C-4), 78.6 (C-8'), 80.2 (C-2),

80.4 (C-6'), 81.3 (C-3), 83.0 (C-7'), 89.5 (C-1), 103.0 (C-5'), 127.2–128.3 (Ph), 138.0–138.9 (Ph). HRMS (ESI): m/z calcd for $C_{72}H_{78}O_{11}Na^+$: 1141.5436; found: 1141.5456. Anal. Calcd for $C_{72}H_{78}O_{11} \cdot 1.5 H_2O$: C, 75.43; H, 7.12. Found: C, 75.31; H, 7.13.

References and Notes

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24. The formation of the α,α -glycosyl linkages corresponded to our former reaction using 3,4,5,7-tetra-O-benzyl-1-deoxy- α -D-glucopyranose and **3**. See ref.19. **2** was more promptly activated by a catalytic amount of $\text{Bi}(\text{OTf})_3$ than **3**. Therefore, we supposed **2** worked as the glycosyl donor and **3** served as the glycosyl acceptor.