

Easy Synthesis of a C-Disaccharide

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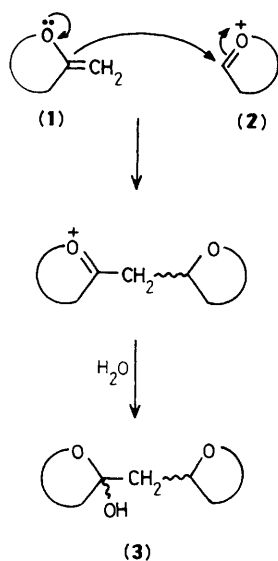
1-Deoxy-3,4,6-tri-*O*-benzyl-D-fructofuranose (4), reacts with $\text{BF}_3 \cdot \text{OEt}_2$ to afford an anomeric mixture of C-disaccharides (5a) and (5b).

Compounds in which two sugar moieties are linked through a carbon rather than an oxygen bridge ('C-disaccharides') are of current interest,¹⁻³ owing to their potential role in inhibition of glycosidases and more generally as unmetabolizable analogues of disaccharides.

The examples of synthesis of C-disaccharides reported to date^{1,3} involve multistep procedures. In particular, the syntheses of C-disaccharides in which both anomeric carbons are involved in the C-glycosidic linkage are particularly challenging.³

Looking for an easy way to synthesize this last class of C-disaccharides, we studied the possibility of condensing a glycosidic enolic system (1) with a glycosyl oxonium ion (2) (Scheme 1). We now report a method for this, in which both reactants (1) and (2) come from the same precursor (Scheme 2).

Compound (4) was prepared in quantitative yield by reaction of MeLi with the easily available 2,3,5-tri-*O*-benzyl-D-arabinono-1,4-lactone.⁴ When (4) was treated with $\text{BF}_3 \cdot \text{OEt}_2$ in MeCN at 0°C, an anomeric mixture ($R_f >$; $R_f <$ ratio 44:56)[†] of two C-disaccharides (5a) and (5b) was obtained in 93% yield. The anomers (5a) and (5b) can be separated by flash chromatography (silica gel, hexane-ethyl acetate, 8:2). On the basis of nuclear Overhauser enhancement (n.O.e.) experiments, $[\alpha]_D$ values (Hudson's rule⁵) and ¹³C chemical shifts of the carbons linked to the 'anomeric' centres,⁶ we attributed to the higher R_f product ($[\alpha]_D -32.9^\circ$,

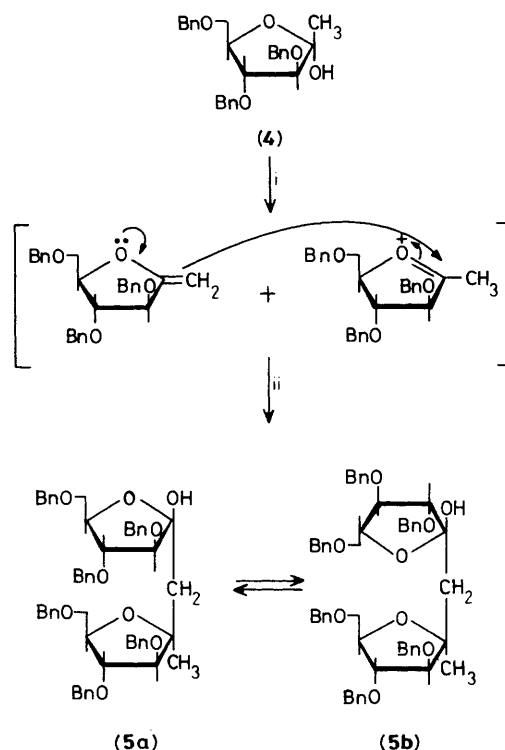


Scheme 1

[†] Deduced by h.p.l.c. (Merck Si-60 silica gel, hexane-ethyl acetate, 89:11).

c 1, CHCl_3) the structure (5a), and to the lower R_f product ($[\alpha]_D +22.8^\circ$, c 1, CHCl_3) the structure (5b).[‡]

Treatment of each separated C-disaccharide with $\text{BF}_3 \cdot \text{OEt}_2$, as reported for (4), afforded the original mixture of (5a) and (5b). It is noteworthy that only two of the four possible stereoisomers are formed, indicating that the attack



Scheme 2. Reagents and conditions: i, $\text{BF}_3 \cdot \text{OEt}_2$, MeCN, 0°C; ii, H_2O (Bn = PhCH_2).

[‡] Data for (5a): ¹³C n.m.r. (CDCl_3): δ 23.03 (q, CH_3), 49.01 (t, C-1), 90.58 (s, C-2'), 113.45 (s, C-2); ¹H n.m.r. (CDCl_3 , 300 MHz): δ 1.53 (s, CH_3), 2.11 (d, J 14 Hz, H-1a), 2.99 (d, J 14 Hz, H-1b), 3.51 (2 H, d, J 6 Hz, $\text{CH}_2\text{OCH}_2\text{Ph}$), 3.30–3.66 (2 H, m, $\text{CH}_2\text{OCH}_2\text{Ph}$), 3.92 (1 H, d, J 4 Hz), 4.00 (d, J 6 Hz, H-3, 6% n.O.e. with H-1b), 4.26 (d, J 2.5 Hz, H-3'), 10% n.O.e. with CH_3), 4.05–4.40 (3 H, m), 4.40–4.80 (12 H, OCH_2Ph), 7.4 (30 H, PhH). Satisfactory elemental analyses were obtained.

Data for (5b): ¹³C n.m.r. (CDCl_3): δ 23.66 (q, CH_3), 46.14 (t, C-1), 89.04 (s, C-2'), 116.97 (s, C-2); ¹H n.m.r. (CDCl_3 , 300 MHz): δ 1.48 (s, CH_3), 2.18 (d, J 15 Hz, H-1a), 2.40 (d, J 15 Hz, H-1b), 3.43 (dd, J 5 and 10.5 Hz, H-6a), 3.52 (dd, J 5 and 10.5 Hz, H-6b), 3.63 (dd, J 4.5 and 10 Hz, H-6'a), 3.67 (dd, J 6 and 10 Hz, H-6'b), 3.87 (dd, J 2.5 and 5 Hz, H-4), 3.96 (d, J 2.5 Hz, H-3, no n.O.e. with H-1), 3.99 (dd, J 2 and 6 Hz, H-4'), 4.10 (q, J 5 Hz, H-5), 4.19 (dt, J 4.5, 6 and 6 Hz, H-5'), 4.34 (d, J 2 Hz, H-3', 27% n.O.e. with CH_3), 4.35–4.75 (12 H, OCH_2Ph), 7.4 (30 H, PhH). Satisfactory elemental analyses were obtained.

on the oxonium ion is highly stereoselective. This is, to our knowledge, the easiest synthesis of a C-disaccharide so far reported.

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 - 5 R. J. Ferrier, in 'The Carbohydrates II,' vol. 1B, eds. W. Pigman and D. Horton, Academic Press, New York, 1980, p. 1356.
 - 6 It has been shown that in C-glycosides the ^{13}C chemical shift of the carbon atom attached to the 'anomeric' position is at higher fields when this atom has a *cis* relationship with the C(2)-OR group, than when there is a *trans* relationship: F. Nicotra, L. Panza, and G. Russo, *J. Org. Chem.*, 1987, **52**, 5627; F. G. de las Eras, P. Fernández-Resa, *J. Chem. Soc., Perkin Trans. 1*, 1982, 903, and references cited therein.
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