

## Easy Synthesis of a C-Disaccharide

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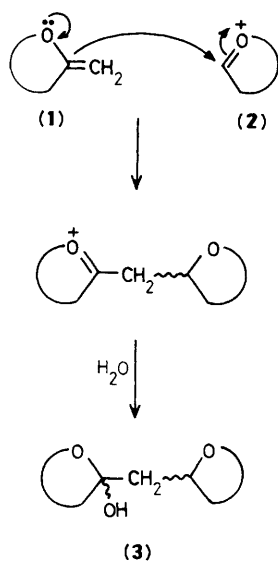
1-Deoxy-3,4,6-tri-*O*-benzyl- $\beta$ -D-fructofuranose (**4**), reacts with  $\text{BF}_3 \cdot \text{OEt}_2$  to afford an anomeric mixture of C-disaccharides (**5a**) and (**5b**).

Compounds in which two sugar moieties are linked through a carbon rather than an oxygen bridge ('C-disaccharides') are of current interest,<sup>1–3</sup> 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<sup>1,3</sup> 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.<sup>3</sup>

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).

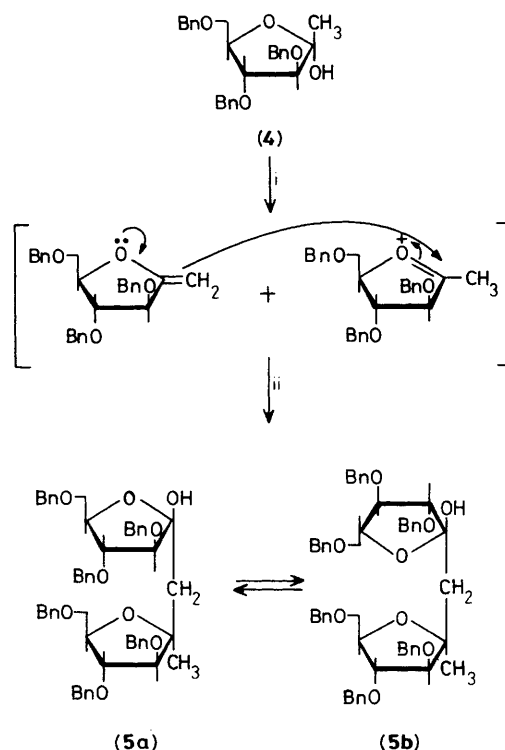
Compound (**4**) was prepared in quantitative yield by reaction of MeLi with the easily available 2,3,5-tri-*O*-benzyl-D-arabinono-1,4-lactone.<sup>4</sup> When (**4**) was treated with  $\text{BF}_3 \cdot \text{OEt}_2$  in MeCN at 0 °C, an anomeric mixture ( $R_f >: R_f <$  ratio 44:56)<sup>†</sup> 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 rule<sup>5</sup>) and <sup>13</sup>C chemical shifts of the carbons linked to the 'anomeric' centres,<sup>6</sup> we attributed to the higher  $R_f$  product ( $[\alpha]_D -32.9^\circ$ ,



Scheme 1

$c$  1,  $\text{CHCl}_3$ ) the structure (**5a**), and to the lower  $R_f$  product ( $[\alpha]_D +22.8^\circ$ ,  $c$  1,  $\text{CHCl}_3$ ) the structure (**5b**).<sup>‡</sup>

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,  $\text{H}_2\text{O}$  (Bn =  $\text{PhCH}_2$ ).

<sup>‡</sup> Data for (**5a**): <sup>13</sup>C n.m.r. ( $\text{CDCl}_3$ ):  $\delta$  23.03 (q,  $\text{CH}_3$ ), 49.01 (t, C-1), 90.58 (s, C-2'), 113.45 (s, C-2); <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  1.53 (s,  $\text{CH}_3$ ), 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  $\text{CH}_3$ ), 4.05–4.40 (3 H, m), 4.40–4.80 (12 H,  $\text{OCH}_2\text{Ph}$ ), 7.4 (30 H, PhH). Satisfactory elemental analyses were obtained.

Data for (**5b**): <sup>13</sup>C n.m.r. ( $\text{CDCl}_3$ ):  $\delta$  23.66 (q,  $\text{CH}_3$ ), 46.14 (t, C-1), 89.04 (s, C-2'), 116.97 (s, C-2); <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  1.48 (s,  $\text{CH}_3$ ), 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  $\text{CH}_3$ ), 4.35–4.75 (12 H,  $\text{OCH}_2\text{Ph}$ ), 7.4 (30 H, PhH). Satisfactory elemental analyses were obtained.

<sup>†</sup> Deduced by h.p.l.c. (Merck Si-60 silica gel, hexane–ethyl acetate, 89:11).

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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- 6 It has been shown that in C-glycosides the  $^{13}\text{C}$  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.