Organoboron-Disaccharides; II[1]. 2,6-Anhydro-β-D-fructofuranose by O-Ethylboron-Induced Cleavage of Sucrose

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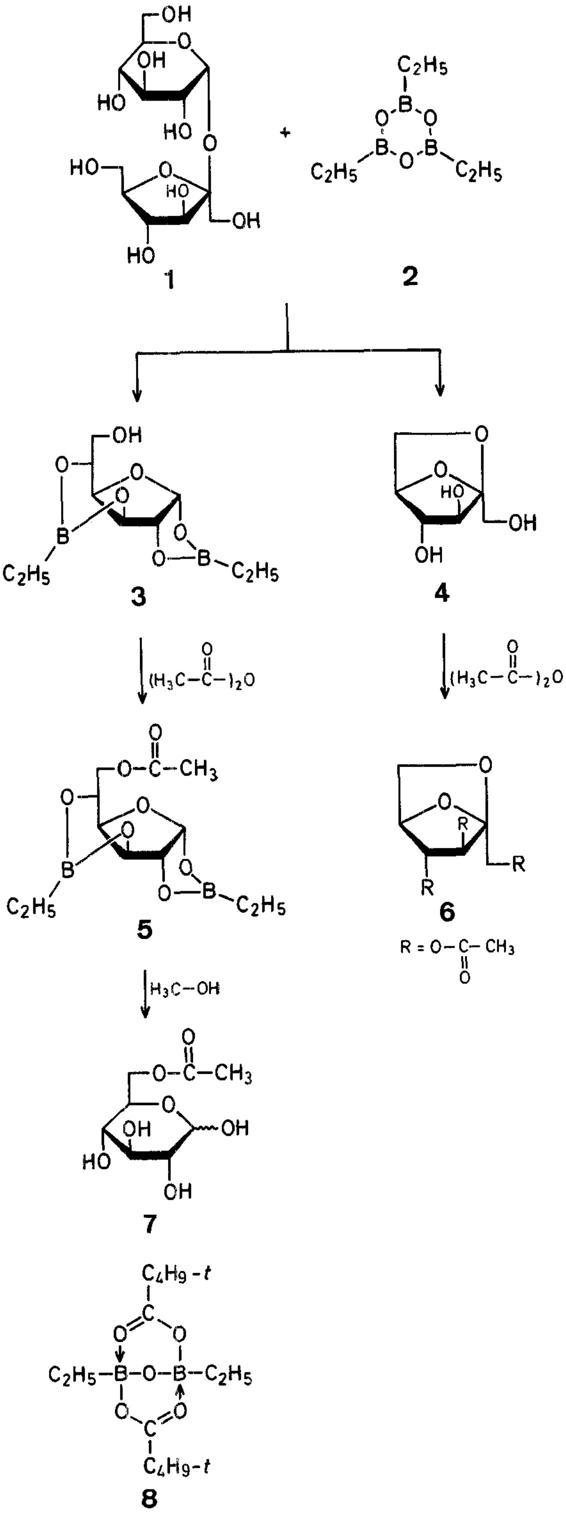
2,6-Anhydro-β-D-fructofuranose (**4**) was first obtained from sucrose (**1**) in 9% yield under rather drastic hydrogenolysis conditions[2]. The thermolysis of **1** has been investigated in detail[3,4,5], but no improvement in the yield of **4** could be achieved. Compound **4** is also obtained in 1% yield by pyrolysis of D-fructose[6].

In the course of our work dealing with the uses of organoboron reagents for achieving selective transformations of carbohydrates[7], we have now found that *O*-ethylboranediylation of **1**[1] can be used to obtain **4** in 69% yield (based on ~65% conversion) without the necessity for chromatographic separation.

Recently, we reported on the direct *O*-ethylboronation of **1** using triethylboroxine (**2**) and 1,2:1′,2′-bis[ethyl-pivaloyloxy]diboroxane (**8**) in pyridine at 80 °C to give 4,6-*O*-ethylboranediylsucrose as the sole product in both cases[1]. As the degree of conversion was 80% using **8** and only 30% using **2**, attempts to achieve quantitative conversion by raising the reaction temperature and increasing the amount of reagents were undertaken. This strategy led to the efficient cleavage of sucrose (**1**) to give **4** as described below.

On heating a suspension of **1** in pyridine/toluene with 2/3 mol-equiv. of **2** or 1 mol-equiv. of **8** to 130 °C and subsequent *O*-acetylation, a vacuum distillable product mixture consisting of 1,2:3,5-diethylboranediyl-6-*O*-acetyl-α-D-glucofuranose (**5**) and 1,3,4-tri-*O*-acetyl-2,6-anhydro-β-D-fructofuranose (**6**) is obtained (see Scheme). Thus, **1** must have been cleaved to 1,2:3,5-di-*O*-ethylboranediyl-α-D-glucofuranose (**3**) and 2,6-anhydro-β-D-fructofuranose (**4**) by these boron reagents. In the absence of **2** and **8**, no cleavage was observed under these reaction conditions. The acetylated cleavage products **5** and **6** are readily separated from unreacted **1**, which is found as a residue after the distillation, in the form of its octa-*O*-acetate. Deboronation of **5** in the mixture of **5** and **6** is easily done by adding methanol in portions and concentrating in vacuum each time. A boron-free mixture of **6** and 6-*O*-acetyl-α/β-D-glucopyranose (**7**)[8] is obtained in quantitative yield. The chloroform-soluble **6** is then separated from **7** by addition of several portions of chloroform and filtering off the insoluble **7**. Concentration of the chloroform solution gives **6** in an overall yield of 69%. Pure **7** is obtained in almost quantitative yield (based on 67% conversion).



A series of trial experiments shows that 55% cleavage has already occurred after 5 h. A decrease in yield to 37% is observed if the toluene/water azeotrope is not removed in the course of the reaction. Similarly, less cleavage results when slightly less reagent is added to **1** (see Table).

The reactions of other di- and oligosaccharides with **2** and **8** are currently being investigated.

Table. Reaction of **1** with **2**

Amount of **1** used (mmol)	Amount of **2** used (mmol)	Ratio of **1**: $>B-C_2H_5$	Reaction time[a]	Cleavage [%][b]
14.6	10.7	1 : 2.2	5 h	55
14.6	10.7	1 : 2.2	22 h	60
14.6	10.7	1 : 2.2	5 h[c]	37
14.6	9.6	1 : 1.98	22 h	35

[a] All reactions run in 1 : 1 toluene/pyridine at 130°C (bath temperature) with removal of toluene/water azeotrope.

[b] Determined from amounts of distilled products after conversion to **5** and **6**.

[c] Toluene/water azeotrope was not removed.

1,3,4-Tri-*O*-acetyl-2,6-anhydro-*β*-D-fructofuranose (6) and 1-*O*-Acetyl-*α*/*β*-D-glucopyranose (7):

To a stirred slurry of **1** (23.25 g, 67.9 mmol) in a 1 : 1 mixture of pyridine/toluene (200 ml) is added triethylboroxine (**2**; 9.3 ml, 8.37 g, 50 mmol). The three-necked flask is then fitted with a Dean-Stark trap and a condenser. The mixture is heated at 130°C (bath temperature) for 22 h during which time the toluene/water azeotrope distils off. After cooling to room temperature, acetic anhydride (70 ml) is added and the solution is stirred for 8 h at 30°C, before removing all the volatile components at 100°C (bath)/10^{-3} torr. The brown syrupy product mixture is distilled to give pale yellow mixture of **5** and **6**; yield: 25.7 g (65%); b.p. 110-115°C/10^{-3} torr.

The residue after distillation (15 g, 33%) is washed several times with methanol to give pure octa-*O*-acetylsucrose.

The distillate of **5** and **6** is deboronated by adding methanol (20 ml) several times and concentrating to dryness at 30°C/12 torr. The boron-free mixture of **6** and **7** is then triturated with chloroform (4 × 50 ml), the chloroform extracts are combined and then concentrated at room temperature/12 torr to give **6** which is further purified by vacuum distillation; yield: 9 g (46%); b.p. 110°C/10^{-3} torr; $[\alpha]_D^{20}$: $-85.2°$ (*c* 0.8, $CHCl_3$) [Lit.[2], $[\alpha]_D^{20}$: $-108°$ (*c* 1.3, $CHCl_3$) and Lit.[6], $[\alpha]_D^{25}$: $-70°$ (*c* 1.3, $CHCl_3$)].

$C_{12}H_{16}O_8$	calc.	C 50.00	H 5.59
(288.3)	found	50.36	5.21

M.S. (70 eV): No M^+; $m/e = 245$ (relative intensity 1.4); 229 (4); 211 (6); 170 (1.4); 115 (4); 43 (100).

^{1}H-N.M.R. (400 MHz, CD_3OD/TMS_{int}): $\delta = 5.00$ ($J_{3\text{-H},4\text{-H}} = 1.5$ Hz, $J_{4\text{-H},5\text{-H}} = 1.6$ Hz, 4-H); 4.85 (m, $J_{4\text{-H},5\text{-H}} = 1.6$ Hz, $J_{5\text{-H},6\text{-H}} \approx 0$ Hz, $J_{5\text{-H},6'\text{-H}} = 4.1$ Hz, 5-H); 4.84 (d, $J_{3\text{-H},4\text{-H}} = 1.5$ Hz, 3-H); 4.42 (d, $J_{1\text{-H},1'\text{-H}} = -12.6$ Hz, 1-H); 4.40 (d, $J_{1\text{-H},1'\text{-H}} = -12.6$ Hz, 1'-H); 3.87 (d, $J_{6\text{-H},6'\text{-H}} = -7.5$ Hz, 6-H); 3.77 (dd, $J_{5\text{-H},6'\text{-H}} = 4.1$ Hz, $J_{6\text{-H},6'\text{-H}} = -7.5$ Hz, 6'-H); 2.14 (s), 2.13 (s), 2.11 ppm (s, OAc).

^{13}C-N.M.R. (CD_3OD, TMS_{int}): $\delta = 171.9$, 171.7, 171.6 ($\underset{\smile}{C}O-CH_3$); 106.7 (C-2); 82.2 (C-5); 80.9 (C-3); 79.6 (C-4); 67.7 (C-6); 60.6 (C-1); 20.7, 20.6, 20.5 ppm ($CO-\underset{\smile}{C}H_3$).

The chloroform-insoluble product is recrystallised from a small amount of ethanol to give colourless needles of **7**; yield: 10 g (66%); m.p. 135-137°C; $[\alpha]_D^{20}$: 67.4° (*c* 1.3, H_2O) [Lit.[8], m.p. 135°C, $[\alpha]_D^{20}$: 48° (*c* 4, H_2O)].

$C_8H_{14}O_7$	calc.	C 43.24	H 6.31	H^+ 1.81
(222.2)	found	43.36	6.37	1.72

M.S. (70 eV): No M^+; $m/e = 205$ (relative intensity 0.7); 175 (0.7); 162 (1.3); 133 (1.3); 115 (4.7); 73 (60); 43 (100).

^{1}H-N.M.R. (400 MHz, CD_3OD/TMS_{int}): $\delta = 6.34$ (d, $J_{1\text{-H},1\text{-OH}} = 4.7$ Hz, OH-1); 5.02 (d, $J_{4\text{-H},4\text{-OH}} = 5.6$ Hz, OH-4); 4.90 (t, $J_{1\text{-H},2\text{-H}} = 3.5$ Hz, $J_{1\text{-H},1\text{-OH}} = 4.7$ Hz, H-1); 4.72 (d, $J_{3\text{-H},3\text{-OH}} = 4.8$ Hz, OH-3); 4.50 (d, $J_{2\text{-H},2\text{-OH}} = 6.7$ Hz, OH-2); 4.24 (dd, $J_{6\text{-H},6'\text{-H}} = -11.6$ Hz, $J_{5\text{-H},6\text{-H}} = 2.0$ Hz, H-6); 3.98 (dd, $J_{6\text{-H},6'\text{-H}} = -11.6$ Hz, $J_{6'\text{-H},5\text{-H}} = 6.4$ Hz, H-6'); 3.77 (ddd, $J_{5\text{-H},6\text{-H}} = 2.0$ Hz, $J_{5\text{-H},6'\text{-H}} = 6.4$ Hz, $J_{4\text{-H},5\text{-H}} = 9.9$ Hz, H-5); 3.42 (ddd, $J_{2\text{-H},3\text{-H}} = 9.5$ Hz, $J_{3\text{-H},4\text{-H}} = 8.7$ Hz, $J_{3\text{-H},3\text{-OH}} = 4.8$ Hz, H-3); 3.13 (ddd, $J_{1\text{-H},2\text{-H}} = 3.5$ Hz, $J_{2\text{-H},3\text{-H}} = 9.5$ Hz, $J_{2\text{-H},2\text{-OH}} = 6.7$ Hz, H-2); 3.02 (ddd, $J_{3\text{-H},4\text{-H}} = 8.7$ Hz, $J_{4\text{-H},5\text{-H}} = 9.9$ Hz, $J_{4\text{-H},4\text{-OH}} = 5.6$ Hz, H-4); 2.00 ppm (s, 3 H, $CO-CH_3$).

^{13}C-N.M.R. (CD_3OD/TMS_{int}): $\delta = 172.9$, 172.8 ($\underset{\smile}{C}O-CH_3$); 98.1, 93.9 (C-1); 77.8, 76.1 (C-3); 75.2, 74.7 (C-2); 73.7, 71.9 (C-5); 71.6, 70.5 (C-4); 65.1, 65.0 (C-6); 20.7 ppm ($CO-\underset{\smile}{C}H_3$).

2,6-Anhydro-*β*-D-fructofuranose (4):

Sodium methoxide (0.05 g) is added to a solution of **6** (3.08 g, 10.68 mmol) in methanol (30 ml) and the mixture is stirred at room temperature for 0.5 h. Ion exchange resin (IR-120, $H^{\oplus}$-form) is added to neutralise and then removed by filtration. Charcoal (1 g) is added to the filtrate and the mixture is filtered through Celite. Concentration of the filtrate gives a syrup which is crystallised from 2-propanol to give **4**; yield: 1.5 g (88%); m.p. 116-117°C; $[\alpha]_D^{20}$: $-101°$ (*c* 0.6, H_2O) [Ref.[6], m.p. 117°C; $[\alpha]_D^{25}$: $-103°$ (*c* 1, H_2O)].

$C_6H_{10}O_5$	calc.	C 44.45	H 6.22	$H^{\oplus}$ 1.86
(162.1)	found	44.46	6.21	1.87

M.S. (70 eV): No M^+; $m/e = 115$ (1.5%); 101 (1.2); 86 (15); 73 (34); 57 (100); 44 (27); 31 (72).

^{13}C-N.M.R. (D_2O/dioxan$_{int}$): $\delta = 108.9$ (C-2); 83.9 (C-5); 82.2 (C-3); 79.0 (C-4); 67.4 (C-6); 58.5 ppm (C-1).

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