Organoboron-Monosaccharides; X[1]. High-Yield Synthesis of a Bifunctionally Protected α-D-Lyxofuranosyl Bromide

Wilhelm Volker DAHLHOFF, Roland KÖSTER

Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm Platz 1, D-4330 Mülheim an der Ruhr

The poorly characterised tri-*O*-acyl-D-lyxofuranosyl chloride[2] and bromide[3,4,5], which have been prepared via either the methyl lyxofuranosides or mercaptal derivatives, can only be isolated in <30% yields and are not well suited for further reactions. Bifunctional protection of D-lyxose (**1**) with carbonate[6,7] or *O*-isopropylidene[8] groups gives ≤20% yields of 2,3-protected furanoses and hence 2,3-carbonyl-lyxofuranosyl bromide can only be prepared in ~10% yield[6].

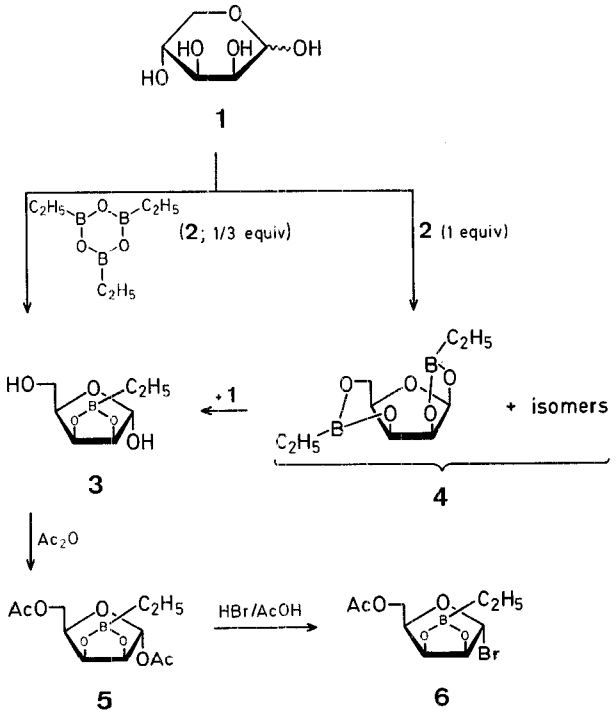
Using *O*-ethylboranediyl protection, we have realised a high-yield, simple synthesis of pure 5-*O*-acetyl-2,3-*O*-ethylboranediyl-α-D-lyxofuranosyl bromide (**6**) from **1**.

The reaction of D-lyxose (**1**) with triethylboroxine (**2**)[9] is strongly dependant on the stoichiometry used. Treatment of **1** with ≥0.67 equivalents of triethylboroxine (**2**) results in the quantitative formation of various fully *O*-ethylboranediyl-protected derivatives (**4**). 1,2:3,5-Di-*O*-ethylboranediyl-β-D-lyxofuranose (**4a**) constitutes ~67% of this equilibrium mixture, which will be described in detail elsewhere. In contrast, the reaction of **1** with exactly one third equivalent of triethylboroxine (**2**) in benzene gives the vacuum distillable 2,3-*O*-ethylboranediyl-D-lyxofuranose (**3**) in quantitative yield. Compounds **4** can be easily and totally converted to **3** by treatment with 1 equivalent of **1** in pyridine (Scheme). Compound **3** is then readily *O*-acetylated with acetic anhydride to give 1,5-di-*O*-acetyl-2,3-*O*-ethylboranediyl-α-D-lyxofuranose (**5**) in ≥95% yield after vacuum distillation.

The *O*-ethylboranediyl group in **5** is stable to a solution of hydrogen bromide in acetic acid at room temperature and hence treatment of **5** with the above reagent gives ~99% pure (G.L.C.) 2,3-*O*-ethylboranediyl-5-*O*-acetyl-α-D-lyxofuranosyl bromide (**6**) in quantitative yield.

The simple, three step procedure allows **6** to be prepared from **1** in an overall yield of ≥90%. In principle **6** can be prepared in a one-vessel manner from **1** because of the high yields in the individual steps. In order to obtain pure **6**, it is however advisable to purify **5** by distillation prior to its conversion to **6**, which then needs not be distilled. Product **6** is thermally less stable than the derivatives **3** and **5**, it can, however, be stored for many months at −30 °C without noticable decomposition.

The new furanosyl bromide is a valuable intermediate for highly stereoselective conversions into both α- and β-lyxo-



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furanose derivatives[10]. Deboronation is unproblematic as neutral conditions are used[11].

1,2:3,5-Di-*O*-ethylboranediyl-β-D-lyxofuranose (4a) and Isomers (4b, 4c):

Triethylboroxine (**2**; 10.8 g, 64.3 mmol) is added to a stirred suspension of **1** (10 g, 66.6 mmol) in benzene (50 ml) and the benzene/water azeotrope is distilled off. The remaining solvent is removed in vacuo (12 torr) and the residue distilled to give the colourless isomer mixture **4**; yield: 15 g (99%) containing ~67% of **4a** (by ^{13}C-N.M.R.); b.p. 88 °C/10^{-3} torr; $[\alpha]_D^{22}$: −5.2° (*c* 1.7, $CHCl_3$).

Data for **4a** (in the mixture **4**):

$C_9H_{16}B_2O_5$	calc.	B 9.57	B_C 3.19
(225.8)	found	9.73	3.10

^{1}H-N.M.R. (60 MHz, CCl_4): δ = 5.78 (d, $J_{H\text{-}1,H\text{-}2}$ = 5 Hz, H-1); 4.73 (t, $J_{H\text{-}2,H\text{-}3}$ = 4 Hz, $J_{H\text{-}3,H\text{-}4}$ = 5 Hz, H-3); 4.34 (dd, $J_{H\text{-}1,H\text{-}2}$ = 5 Hz, $J_{H\text{-}2,H\text{-}3}$ = 4 Hz, H-2); 3.8–4.2 (m, H-4, 5); 0.9 ppm (m, BC_2H_5).

^{13}C-N.M.R. ($CDCl_3$): δ = 105.47 (C-1); 81.54 (C-2); 75.15 (C-4); 69.68 (C-3); 60.80 (C-5); 7.48 and 7.35 ($BCH_2\underline{C}H_3$); 2.8 ppm (br, $B\underline{C}H_2CH_3$).

2,3-*O*-Ethylboranediyl-α-D-lyxofuranose (3):

Triethylboroxine (**2**; 1.4 g, 8.3 mmol) is added to a stirred suspension of **1** (3.7 g, 24.7 mmol) in benzene (20 ml) and the benzene/water azeotrope is distilled off. The remaining solvent is removed in the vacuum range 12–10^{-3} torr, to give **3** as a colourless residue; yield: 4.1 g (99%); b.p. 144 °C/10^{-3} torr; $[\alpha]_D^{22}$: 4.7° (*c*, 1.7, DMSO).

$C_7H_{13}BO_5$	calc.	B 5.75	B_C 1.92	$H^{\oplus}$ 1.07
(188.0)	found	5.81	1.90	1.12

^{1}H-N.M.R. (100 MHz, DMSO-d_6): δ = 6.42 (d, $J_{H\text{-}1,OH}$ = 4.2 Hz, HO—C-1); 5.14 (d, $J_{H\text{-}1,OH}$ = 4.2 Hz, $J_{H\text{-}1,H\text{-}2}$ < 1 Hz, H-1); 4.85 (dd, $J_{H\text{-}2,H\text{-}3}$ = 6 Hz, $J_{H\text{-}3,H\text{-}4}$ = 4 Hz, H-3); 4.60 (br, HO—C-5); 4.58 (d, $J_{H\text{-}1,H\text{-}2}$ < 1 Hz, $J_{H\text{-}2,H\text{-}3}$ = 6 Hz, H-2); 4.1 (m, $J_{H\text{-}3,H\text{-}4}$ = 4 Hz, $J_{H\text{-}4,H\text{-}5}$ = 5.5 Hz, $J_{H\text{-}4,H\text{-}5'}$ = 6.5 Hz, H-4); 3.66 (dd, $J_{H\text{-}4,H\text{-}5}$ = 5.5 Hz, $J_{H\text{-}5,H\text{-}5'}$ = −11 Hz, H-5); 3.47 (dd, $J_{H\text{-}4,H\text{-}5'}$ = 6.5 Hz, $J_{H\text{-}5,H\text{-}5'}$ = −11 Hz, H-5'); 0.86 ppm (m, BC_2H_5).

^{13}C-N.M.R. (DMSO-d_6): δ = 100.7 (C-1); 85.7 (C-2); 80.1 (C-3, C-4); 59.1 (C-5); 7.60 ($BCH_2\underline{C}H_3$); 1.9 ppm (br, $B\underline{C}H_2CH_3$).

1,5-Di-*O*-acetyl-2,3-*O*-ethylboranediyl-α-D-lyxofuranose (5):

Method A: From **1** and **4**: Compounds **1** (8.215 g, 54.72 mmol) and **4** (12.36 g, 54.73 mmol) are dissolved in pyridine (40 ml) at room temperature. After stirring for ~10 min, acetic anhydride (20 ml) is added dropwise in 2 h at ≤35 °C. About 2 h later the volatile components are removed in vacuo (10^{-3} torr) leaving yellow viscous **5** (30 g, 100%), which is distilled to give **5** of 97.4% purity (by G.L.C.), containing about 2% (by G.L.C.) of lyxopyranose tetra-*O*-acetates; yield of **5**: 28.5 g (96%); b.p. ~112 °C/10^{-3} torr; $[\alpha]_D^{22}$: 65.5° (*c* 1.6, $CHCl_3$); 0.7 g dark brown residue.

Method B: From **3**: Acetic anhydride (15 ml) is added dropwise to a stirred solution of **3** (3.3 g, 17.6 mmol) in pyridine (10 ml) at room temperature. After 2 h, the volatile components are removed in vacuo (10^{-3} torr). From the residue one obtains **5** of 96% purity (by G.L.C.) containing about 4% (by G.L.C.) of tetra-*O*-acetates; yield of **5**: 4.5 g (94%); b.p. ~112 °C/10^{-3} torr; $[\alpha]_D^{21}$: 65.2° (*c* 2.3, CCl_4).

$C_{11}H_{17}BO_7$	calc.	B 3.97	B_C 1.32
(272.1)	found	3.90	1.22

M.S. (70 eV): No $M^{\oplus}$; found *m/e* = 213 (B_1, relative intensity 3%), 170 (B_1, 2), 124 (B_1, 4), 103 (B_0, 4), 43 (100).

^{1}H-N.M.R. (80 MHz, $CDCl_3$): δ = 6.19 (s, $J_{H\text{-}1,H\text{-}2}$ < 1 Hz, H-1); 4.96 (dd, $J_{H\text{-}2,H\text{-}3}$ = 6 Hz, $J_{H\text{-}3,H\text{-}4}$ = 3 Hz, H-3); 4.79 (d, $J_{H\text{-}2,H\text{-}3}$ = 6 Hz, H-2); 4–4.5 (m, H-4, 5); 2.06 (s, OAc); 2.05 (s, OAc); 0.9 ppm (m, BC_2H_5).

^{13}C-N.M.R. ($CDCl_3$): δ = 170.8 and 170 (CO—CH_3); 101.04 (C-1); 85.29 (C-2); 80.56 (C-3 or C-4); 80.26 (C-3 or C-4); 62.17 (C-5); 20.88 and 20.69 (CO—$\underline{C}H_3$); 7.49 ($BCH_2\underline{C}H_3$); ~2 ppm (br, $B\underline{C}H_2CH_3$).

^{11}B-N.M.R. (neohexane): δ = 35 ppm (half-width 250 Hz).

2,3-*O*-Ethylboranediyl-5-*O*-acetyl-α-D-lyxofuranosyl bromide (6):

A solution of hydrogen bromide in acetic acid (15 ml with 30 wt-% HBr) is added to a stirred solution of **5** (5 g, 18.5 mmol) in dichloromethane (20 ml) at room temperature and after 40 min, all the volatile components are removed in the vacuum range 12–10^{-3} torr. Two portions of dichloromethane (10 ml each) are added to the residue and removed again leaving **6** (5.3 g, 99%) as a pale yellow sirup of 99% purity (by G.L.C.) suitable for further reactions; yield: 5.3 g (99%); b.p. 97 °C/10^{-3} torr; $[\alpha]_D^{22}$: 144.4° (*c* 1.4, $CHCl_3$).

$C_9H_{14}BBrO_5$	calc.	C 36.91	H 4.82	B 3.69	Br 27.3
(292.9)	found	36.70	4.92	3.74	27.0

M.S. (70 eV): No $M^{\oplus}$; found *m/e* = 232 (B_1, relative intensity 1%), 213 (B_1, 19), 153 (B_1, 13), 111 (B_1, 11), 55 (B_0, 15), 43 (B_0, 100).

^{1}H-N.M.R. (80 MHz, $CDCl_3$): δ = 6.43 (s, $J_{H\text{-}1,H\text{-}2}$ < 1 Hz, H-1); 5.27 (d, $J_{H\text{-}2,H\text{-}3}$ = 6 Hz, H-2); 4.98 (dd, $J_{H\text{-}2,H\text{-}3}$ = 6 Hz, $J_{H\text{-}3,H\text{-}4}$ = 3.5 Hz, H-3); 4.53 (d, $J_{H\text{-}5,H\text{-}5'}$ = −12.5 Hz, H-5); 4.49 (dd, $J_{H\text{-}3,H\text{-}4}$ = 3.5 Hz, $J_{H\text{-}4,H\text{-}5'}$ = 8.5 Hz, H-4); 4.20 (dd, $J_{H\text{-}4,H\text{-}5'}$ = 8.5 Hz, $J_{H\text{-}5,H\text{-}5'}$ = −12.5 Hz, H-5); 2.07 (s, OAc); 0.9 ppm (m, BC_2H_5).

^{13}C-N.M.R. ($CDCl_3$): δ = 170.86 (CO—CH_3); 91.76 (C-1); 90.24 (C-2); 81.71 (C-3 or C-4); 79.06 (C-3 or C-4); 61.05 (C-5'); 20.79 (CO—$\underline{C}H_3$); 7.34 ($BCH_2\underline{C}H_3$); 3 ppm (br, $B\underline{C}H_2CH_3$).

^{11}B-N.M.R. (neohexane): δ = 35 ppm (half-width 250 Hz).

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