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Note

A synthesis of methyl 6-deoxy-3-*C*-methyl-α-D-gulopyranoside (methyl α-virenoside)*

JOHN S. BRIMACOMBE**, RODERICK HANNA, AND LESLIE C. N. TUCKER
Chemistry Department, Dundee University, Dundee DD1 4HN (Great Britain)
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Chemical and spectroscopic evidence have established[2] the structure of virenose, a branched-chain sugar found as a component of the antitumour antibiotic virenomycin[3], as 6-deoxy-3-*C*-methyl-D-gulose. A recent synthesis[4] of methyl β-virenoside (**1**) from D-galactose has confirmed this assignment of structure. An attempt to synthesise derivatives of methyl α-virenoside (**2**) from D-glucose was abandoned[4] because reduction of key intermediate **3** with sodium borohydride gave only methyl 2,3-di-*O*-benzyl-6-deoxy-3-*C*-methyl-α-D-allopyranoside (**4**), from which **3** was originally prepared. Nor was it possible to invert the configuration at C-4 of the methanesulphonate **5** by means of a benzoate-displacement reaction[4].

These results prompt us to report briefly on a synthesis of methyl α-virenoside (**2**) from **3**, which was prepared straightforwardly from methyl 4,6-*O*-benzylidene-3-*C*-methyl-α-D-allopyranoside[5] (available in five steps from D-glucose) essentially as described by Yoshimura and co-workers[4]†.

In previous papers[1,6], we showed that L-Selectride[7] (lithium tri-*sec*-butylborohydride) reduces stereoselectively such keto sugars as **6** to the axial alcohol, whereas reduction with sodium borohydride affords[8] only the equatorial alcohol. A rationale for these results is found in the knowledge[7] that bulky alkyl substituents on boron substantially enhance attack of the borohydride anion on the carbonyl group from the equatorial direction. However, reduction of **3** with L-Selectride in anhydrous tetrahydrofuran at −40° gave only **4**, which was characterised as the crystalline acetate **7**. Reasoning that the axial benzyloxy group of **3** might impede the approach of the bulky reducing-agent from the equatorial direction, **3** was de-

*Branched-chain Sugars, Part XV. For Part XIV, see ref. 1.
**To whom enquiries should be addressed.
†Except for minor variations, our route to **3** duplicates that reported[4], so that no experimental details are given. However, on route to **3**, we obtained methyl 2,3-di-*O*-benzyl-3-*C*-methyl-6-*O*-toluene-*p*-sulphonyl-α-D-allopyranoside in crystalline form (*cf.* ref. 4), m.p. 126.5–127.5° (from ether–chloroform–hexane), $[\alpha]_D$ +48° (*c* 0.5, chloroform) (Found: C, 64.2; H, 6.4; S, 6.0. $C_{29}H_{34}O_8S$ calc.: C, 64.2; H, 6.3; S, 5.9%).

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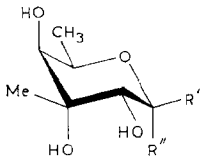
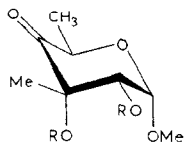
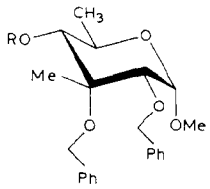


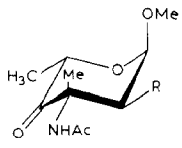
1 R′ = OMe, R″ = H
2 R′ = H, R″ = OMe



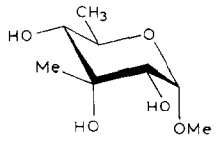
3 R = CH_2Ph
8 R = H



4 R = H
5 R = Ms
7 R = Ac



6 R = H or OMe



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benzylated catalytically to give **8**, which then afforded crystalline methyl α-virenoside (**2**) in 58% yield following reduction with L-Selectride at −40°. No attempt was made to optimise the yield of **2**, although, probably, the extraction procedure could be improved. P.m.r. spectroscopy of the crude product showed that little or none of the equatorial isomer **9** was formed on reduction of **8**. The structure of **2** was clearly indicated by p.m.r. spectroscopy, which distinguished it from **9** (obtained on debenzylation of **4**) and also showed H-4 of **2** as a singlet, in keeping with the axial disposition of the geminal hydroxyl group.

The clean conversion of **8** into **2** underlines the usefulness of L-Selectride when an oxidation–reduction sequence[1,6,9] is used to invert the configuration of an equatorial hydroxyl group. There is also a clear indication that heavily protected keto sugars, such as **3**, may not respond in the same way, presumably for steric reasons.

EXPERIMENTAL

General methods. — T.l.c. was performed on Kieselgel G, and detection was effected with 1% sulphuric acid. I.r. spectra were routinely recorded for Nujol mulls or liquid films with a Perkin–Elmer Infracord spectrometer, and p.m.r. spectra were recorded for solutions in deuteriochloroform or deuteriomethanol (internal tetramethylsilane) by use of a Bruker Spectrospin (90 MHz) spectrometer. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter. Melting points are uncorrected.

*Methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-6-deoxy-3-*C*-methyl-α-*D*-allopyranoside* (**7**).

— Conventional treatment of **4**[4] with acetic anhydride in pyridine gave, after work-up, **7** (93%), m.p. 77–79° (from aqueous methanol), $[\alpha]_D$ +115.5° (*c* 0.8, chloroform) (Found: C, 69.7; H, 7.1. $C_{24}H_{30}O_6$ calc.: C, 69.5; H, 7.3%). P.m.r. data ($CDCl_3$): δ 7.36 (m, 10 H, 2 *Ph*CH_2), 5.06–4.54 (6 H, 2 PhCH_2, H-1,4), 4.04 (m, 1 H, H-5), 3.38 (s, 3 H, OMe), 3.36 (d, 1 H, $J_{1,2}$ 4 Hz, H-2), 2.08 (s, 3 H, OAc), 1.27 (s, 3 H, Me-3), and 1.07 (d, 3 H, $J_{5,6}$ 6 Hz, Me-5).

*Methyl 6-deoxy-3-C-methyl-α-*D*-ribo-hexopyranosid-4-ulose* (**8**). — A solution of **3**[4] (0.86 g) in methanol (20 mL) and acetic acid (5 mL) containing 10% palladium-on-charcoal (0.3 g) was shaken under a slight overpressure of hydrogen at room temperature for 22 h. The catalyst and solvents were then removed, toluene was distilled several times from the residue, which was then dissolved in chloroform, and the solution was dried (Na_2CO_3). Removal of the solvent gave **8** (0.4 g, 91%), m.p. 97–99° (from chloroform–hexane), $[\alpha]_D$ +239° (*c* 1, chloroform), ν_{max} 1730 cm^{-1} (C=O) (Found: C, 50.7; H, 7.3. $C_8H_{14}O_5$ calc.: C, 50.5; H, 7.4%). P.m.r. data ($CDCl_3$): δ 4.92 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.49 (q, 1 H, $J_{5,6}$ 7 Hz, H-5), 3.69 (d, 1 H, H-2), 3.54 (s, 3 H, OMe), 1.42 (s, 3 H, Me-3), and 1.33 (d, 3 H, Me-5).

*Methyl 6-deoxy-3-C-methyl-α-*D*-gulopyranoside* (*methyl α-virenoside*) (**2**). — Reduction of **8** (0.335 g, 1.76 mmol) in anhydrous tetrahydrofuran (25 mL) with L-Selectride (3.5 mL of a ~M solution) at −40° was conducted as previously described[6]. Work-up after 3 h and chromatography on silica gel (elution with chloroform–methanol, 4:1) gave **2** (0.196 g, 58%), m.p. 138–139.5° (from chloroform–hexane), $[\alpha]_D$ +143° (*c* 0.5, chloroform) (Found: C, 49.9; H, 8.1. $C_8H_{16}O_5$ calc.: C, 50.0; H, 8.4%). P.m.r. data (CD_3OD): δ 4.61 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.27 (q, 1 H, $J_{5,6}$ 6 Hz, H-5), 3.61 (d, 1 H, H-2), 3.40 (s, 3 H, OMe), 3.16 (s, 1 H, H-4), 1.26 (s, 3 H, Me-3), and 1.18 (d, 3 H, Me-5).

Similar reduction of **3**[4] gave, after acetylation, a single product (76%) identified (m.p. and mixture m.p., i.r. and p.m.r. spectroscopy) as **7**.

*Methyl 6-deoxy-3-C-methyl-α-*D*-allopyranoside* (**9**). — Catalytic debenzylation of **4**[4], essentially as described for **3**, gave **9** (~97%), $[\alpha]_D$ +110° (*c* 1, chloroform). P.m.r. data (CD_3OD): δ 4.61 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 3.74 (m, 1 H, H-5), 3.40 (s overlapping a d, 4 H, OMe and H-2), 2.90 (d, 1 H, $J_{4,5}$ 10 Hz, H-4), 1.28 (s, 3 H, Me-3), and 1.25 (d, 3 H, $J_{5,6}$ 6 Hz, Me-5). The p.m.r. spectrum of **9** in deuteriochloroform was indistinguishable from that reported for an authentic sample[10].

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