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Note

A facile synthesis of derivatives of 2,6-dideoxy-4-*O*-methyl-L-*ribo*-hexose, a component of kijanimicin

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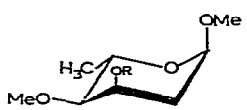
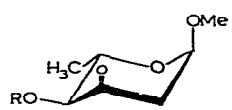
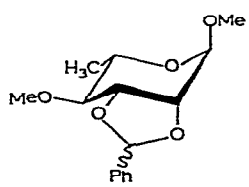
Methyl 2,6-dideoxy-4-*O*-methyl-α-L-*ribo*-hexopyranoside (**1**) is one of several glycosides released on acid-catalysed methanolysis of kijanimicin, the principal component of a complex of antibiotics produced by *Actinomadura kijaniata* nov. sp.[1,2]. This is the first reported occurrence of this novel deoxy sugar in Nature, although derivatives of its D enantiomer are known through synthesis[3,4]. Whereas the structure assigned[1] to **1** is reasonably based on spectroscopic and optical data, the assertion[5] that D-**1** is released on methanolysis of variamycin has been invalidated[3,4,6].



1 R = H
3 R = Bz



2 R = Me
5 R = $MeO(CH_2)_2OCH_2$



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The structure proposed for the kijanimicin-derived glycoside **1** is upheld by the following chemical synthesis, which emanated coincidentally from studies concerned with the reduction of keto sugars with lithium tri-*sec*-butylborohydride (L-Selectride). Thus, reduction of methyl 2,6-dideoxy-4-*O*-methyl-α-L-*erythro*-hexopyranosid-3-ulose[7] (**2**) with L-Selectride at −10° gave **1** with high stereoselectivity. The structure assigned to **1** followed from the values $J_{2ax,3}$ 3.5 and $J_{2eq,3} = J_{3,4} =$ 3 Hz extracted from its p.m.r. spectrum, and from the expected formation of the axial alcohol on reduction of **2** with L-Selectride[8]. Moreover, the p.m.r. and i.r. spectra of the benzoate **3** were identical to those of its D enantiomer[3], previously prepared by an unambiguous route. In this instance, there is no need to use a bulky

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reducing-agent to secure the desired stereochemistry, since reduction of **2** with sodium borohydride afforded **1** with equal stereoselectivity and in better yield.

Since **2** is readily obtained[7] by the expulsion of benzaldehyde from the acetal **4** through the action of butyl-lithium, **1** and its derivatives are available by an exceptionally short route from L-rhamnose. Additionally, we have shown[9] that borohydride reduction, *etc.*, of the analogously prepared 2-methoxyethoxymethyl (MEM) ether **5** provides an equally convenient route to L-digitoxose (2,6-dideoxy-L-*ribo*-hexose), which is the principal component of the branched tetrasaccharide moiety of kijanimicin[2].

EXPERIMENTAL

General methods. — P.m.r. spectra were recorded for solutions in deuteriochloroform (containing tetramethylsilane as internal standard) by use of a Bruker Spectrospin (90 MHz) spectrometer. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter.

*Methyl 2,6-dideoxy-4-O-methyl-α-*L-ribo-*hexopyranoside* (**1**). — (*a*) *Using L-Selectride.* A 100-ml, three-necked flask equipped with a dropping funnel, a stirring bar, and a gas-inlet tube was flushed with nitrogen and charged with anhydrous tetrahydrofuran (10 ml) and L-Selectride (4 ml of a ~M solution). The contents of the flask were cooled to −10° and a solution of **2**[7] (0.35 g, 2 mmol) in anhydrous tetrahydrofuran (15 ml) was added dropwise, with stirring, so that the temperature was maintained at −10°. Stirring was continued at −10° for 1 h, whereafter aqueous 3M sodium hydroxide (1 ml) and 30% hydrogen peroxide (5 ml) were added. After the solution had attained room temperature, it was saturated with potassium carbonate and diluted with chloroform, and the chloroform layer was decanted and dried ($MgSO_4$). T.l.c. (benzene–ether, 3:1) showed that substantially one product was formed. Removal of the solvent gave **1** (0.21 g, 59%), b.p. 68–71° (bath)/0.1 mmHg, $[\alpha]_D$ −204.5° (*c* 0.8, chloroform) (Found: C, 54.3; H, 9.1. $C_8H_{16}O_4$ calc.: C, 54.5; H, 9.15%). The p.m.r. spectrum of **1** was indistinguishable from that reported[1] for the kijanimicin-derived glycoside having $[\alpha]_D$ −209.2° (*c* 0.3, chloroform).

(*b*) *Using sodium borohydride.* Sodium borohydride (0.3 g) was added in portions to a stirred solution of **2**[7] (0.25 g) in methanol (10 ml) at room temperature, whereafter stirring was continued for 1 h; t.l.c. (benzene–ether, 3:1) then showed that substantially a single product had been formed. The solvent was removed and the residue was partitioned between chloroform and water. Work-up of the organic extract in the usual way, with distillation, gave **1** (0.215 g, 85%), b.p. 68–71° (bath)/0.1 mmHg, $[\alpha]_D$ −203° (*c* 0.8, chloroform), which was indistinguishable by all the usual criteria from the product obtained in (*a*).

*Methyl 3-O-benzoyl-2,6-dideoxy-4-O-methyl-α-*L-ribo-*hexopyranoside* (**3**). — Conventional treatment of **1** with benzoyl chloride in pyridine gave, after work-up and chromatography on silica gel (elution with benzene–ether, 3:1), **3** (97%), b.p.

102–103° (bath)/0.1 mmHg, $[\alpha]_D$ −164° (*c* 0.5, chloroform) (Found: C, 64.4; H, 7.0. $C_{15}H_{20}O_5$ calc.: C, 64.3; H, 7.2%). The i.r. and p.m.r. spectra of **3** were indistinguishable from those of the D enantiomer[3] (kindly provided by Dr. A. S. Mengech).

ACKNOWLEDGMENTS

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