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A ROUTE TO BRANCHED-CHAIN SUGARS USING METHOXYVINYL-LITHIUM

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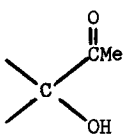
A number of antibiotics isolated in recent years contain branched-chain sugar components possessing such functionalities as 1, 2, 3 or 4 at tertiary centres. For example, eurekanic acid[1] contains the functionality 1, while 2 or 3 or 4 are found in aldgarose,[2] pillarose,[3] and a



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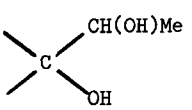

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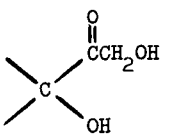

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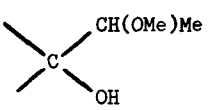

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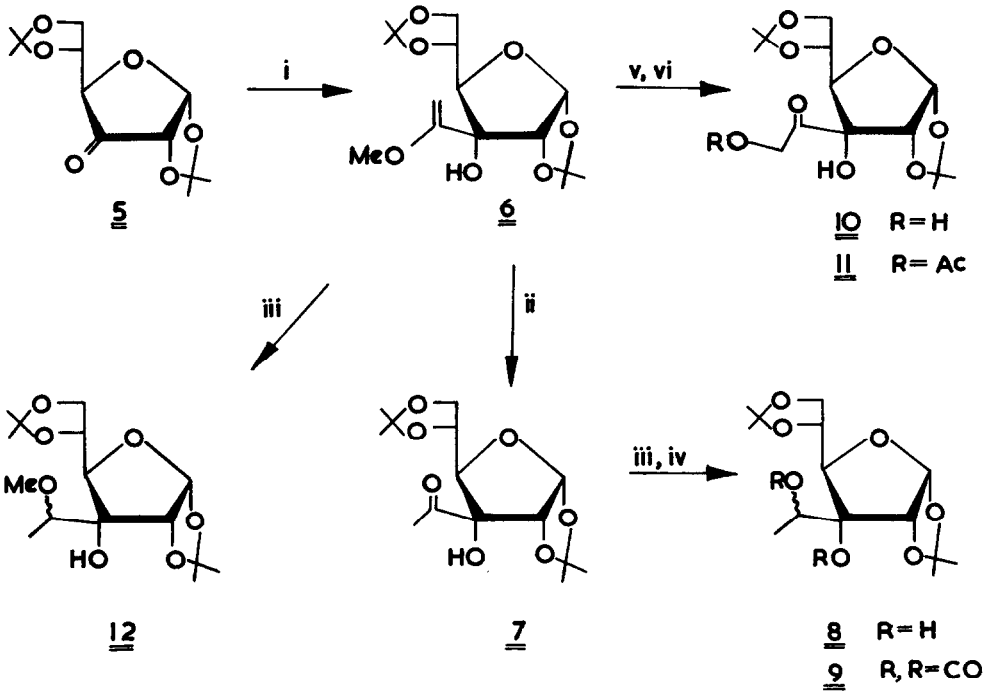
sugar component of everninomicins B[4] and D[5], respectively. Hitherto, the introduction of these branched-chain functionalities has relied upon the addition of either appropriate Grignard reagents[6,7] or dithianyl anions[8] (acyl anion equivalents) to protected keto-sugars. Recently Baldwin *et al.*[9] have shown that such structures as 3 in the corticoid hormones can be introduced *via* addition of the readily prepared methoxyvinyl-lithium[10] to steroidal ketones, followed by oxidation of the adducts with a peracid. We have examined the reaction of methoxyvinyl-lithium with 1,2:5,6-di-O-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (5), and have transformed the resulting adduct 6 to branched-chain sugars containing the functionalities 1-4.

The keto-sugar 5 reacted with methoxyvinyl-lithium[10] in THF under nitrogen at -65° to give a crystalline adduct 6 (40%), m.p. 157-158° [from chloroform-light petroleum (b.p. 60-80°)], $[\alpha]_D$ + 62° (c 1, chloroform), which was smoothly hydrolysed (0.02M hydrochloric acid in aqueous p-dioxan) to the corresponding 3-C-acetyl derivative 7, m.p. 86-87.5° (from ether-hexane), $[\alpha]_D$ + 32° (c 1, chloroform), in virtually quantitative yield. Catalytic reduction of 7 in methanol over Adams' catalyst gave one of the diastereoisomeric 3-C-(1-hydroxyethyl)-1,2:5,6-di-O-isopropylidene-α-D-allofuranoses (8) (70%), m.p. 118-119° (from ether-hexane), $[\alpha]_D$ + 25.5° (c 1, chloroform) (lit.[6] m.p. 119-119.5°, $[\alpha]_D$ + 26.8° (c 1.7, chloroform), which



Reagents; i, CH_2=CHOMe-Bu^{t}Li; ii, H_3O^+; iii, Pt-H_2; iv, $COCl_2$-C_5H_5N;
v, m-$ClC_6H_4CO_3H$-Et_2O-H_2O or OsO_4-C_5H_5N; vi, Ac_2O-C_5H_5N

was further characterised as the 3,3[1]-cyclic carbonate derivative 9, m.p. 207-208° (from ether-hexane), $[\alpha]_D$ + 26° (c 1, chloroform) (lit.[6] m.p. 205-205.5°, $[\alpha]_D$ + 25.4° (c 1.3, chloroform). The stereochemistry at C-3 of an acetylenic precursor of 8 has already been established by Horton et al.,[6] so that the adduct 6 can also be assigned the D-allo configuration. The stereochemistry at C-3 in the other reactions reported is controlled

by the stereochemistry of the initial adduct 6.

On treatment with a molar equivalent of m-chloroperbenzoic acid in wet ether, the adduct 6 afforded the C-glycolyl derivative 10 (34%), m.p. 97-98° (from chloroform-hexane), $[\alpha]_D$ + 29° (c 1, chloroform), a small proportion of 7, and an unidentified sugar derivative whose ^{1}H n.m.r. spectrum contained resonances due to aromatic protons. However, 10 was obtained in ca. 70% yield when 6 was treated overnight with osmium tetroxide in pyridine. Acetylation of 10 gave the corresponding acetate 11, m.p. 120-121° (from ether-hexane), $[\alpha]_D$ + 7° (c 0.9, chloroform).

Catalytic hydrogenation of the adduct 6 in methanol over Adams' catalyst gave a mixture of diastereoisomeric 3-C-(1-methoxyethyl) derivatives 12, which was readily separated by chromatography on silica gel (elution with dichloromethane-acetone 20:1). The derivative (37%) first eluted had m.p. 83-85° (after sublimation at ca. 80° and 15 mmHg), $[\alpha]_D$ + 3° (c 1, chloroform), while the other (31%) had m.p. 66-68° (after sublimation at ca. 60° and 0.5 mmHg), $[\alpha]_D$ + 29° (c 1, chloroform).

The foregoing procedures are clearly of potential use in routes to other branched-chain sugars containing the functionalities 1-4. The use of one such procedure in a synthesis of pillarose[3] is described in the following communication.

All new compounds gave elemental analyses and spectroscopic data compatible with the structures assigned.

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