Carbohydrate Research, 168 (1987) c5–c7
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Preliminary communication

Higher-carbon sugars: the synthesis of new octitols from D-glucose and D-mannose derivatives *via* osmylation

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(Recieved July 24th, 1987; accepted for publication, August 3rd, 1987)

Catalytic osmylation of (*E*)-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-oct-6-enopyranose (**1**) proceeds[1] in accordance with Kishi's empirical rule[2,]** to produce a mixture of 1,2:3,4-di-*O*-isopropylidene-β-L-*threo*-D-*galacto*-octopyranose (**2**) and the corresponding α-D-*threo*-D-*galacto* isomer **3** in the ratio ~7:1. Whilst this reaction and others like it provided ready access to eight-carbon sugars possessing the D-*galacto* configuration at C-2 to C-5, it is not known whether similar stereocontrol would be exerted in other series, particularly where the approach of a large electrophile like OsO_4 to heavily and bulkily substituted substrates might be impeded. In seeking to provide this information, we have examined the catalytic osmylation of methyl (*E*)-2,3,4-tri-*O*-benzyl-6,7-dideoxy-α-D-*gluco*-oct-6-enopyranoside (**6**) and the corresponding α-D-*manno* isomer **14**.

The reaction of methyl 2,3,4-tri-*O*-benzyl-α-D-*gluco*-hexodialdo-1,5-pyranoside (**4**) (prepared by Swern oxidation[3] of methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside) with formylmethylenetriphenylphosphorane[4] in boiling benzene provided the (*E*)-enal **5** (75%), m.p. 60–60.5°, $[\alpha]_D$ +90.5° (*c* 0.9, chloroform), which, on reduction with di-isobutylaluminium hydride in dichloromethane at 0°, afforded **6** (84%), m.p. 63.5–64.5°, $[\alpha]_D$ +25° (*c* 1.1, chloroform). On catalytic osmylation[5], **6** furnished a mixture (76%) of methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*gluco*-octopyranoside (**7**) and the corresponding α-D-*threo*-D-*gluco* isomer **8** in the ratio ~3:1[†]. Acetylation of this mixture provided methyl 6,7,8-tri-*O*-acetyl-2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*gluco*-octopyranoside (**9**, 54%), m.p. 107.5–108.5°, $[\alpha]_D$ +16° (*c* 1.1, chloroform), whose stereochemistry was established by X-ray crystallography[6]. Zemplén deacetylation of **9** gave **7** (90%), m.p. 113.5–114.5°, $[\alpha]_D$ +36°

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According to Kishi's empirical rule[2] for the osmylation of chiral allylic alcohols, the relative stereochemistry between the pre-existing hydroxyl (or alkoxyl) group and the newly introduced hydroxyl group of the major product is *erythro*. For such pyranoid compounds as **1, the ring-oxygen atom is considered to influence the stereochemical outcome of the reaction in the same way as does an alkoxyl group[1].

[†] This and the other ratio reported were determined by integration over the signals for the methoxyl groups in the 360-MHz ^{1}H-n.m.r. spectra.

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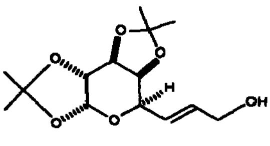

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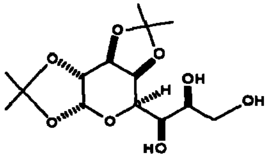

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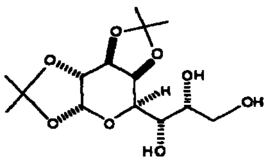

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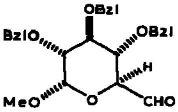

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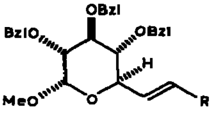

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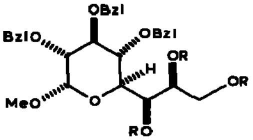

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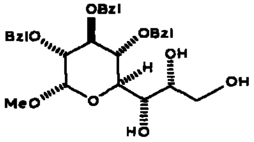
9 R = Ac



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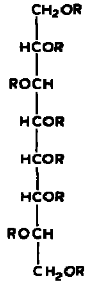

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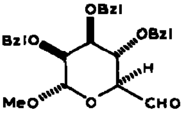
11 R = H



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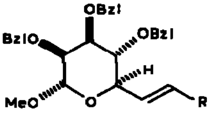

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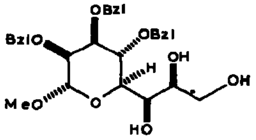
14 R = CH_2OH



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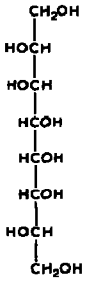

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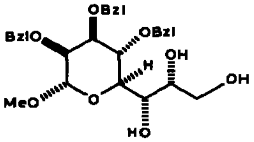

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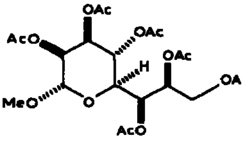

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(*c* 1, chloroform), which, on deprotection [(i) 10% Pd/C in methanol, and (ii) M H_2SO_4 at 100°], reduction ($NaBH_4$) of the resulting octose, and conventional acetylation of the crude octitol, gave L-*threo*-L-*altro*-octitol (L-*threo*-D-*gluco*-octitol) octa-acetate (**10**), $[\alpha]_D \sim -30°$ (*c* 1.5, chloroform). Finally, Zemplén deacetylation of **10** furnished L-*threo*-L-*altro*-octitol (**11**, 81%), m.p. 121.5–122.5°, $[\alpha]_D$ −2.3° (*c* 1, water). ^{13}C-N.m.r. data [$(CD_3)_2SO$]: δ 73.89, 73.15, 71.82, 71.27, 70.78, 69.39, 62.96, and 62.59.

A similar route was used to obtain methyl (*E*)-2,3,4-tri-*O*-benzyl-6,7-dideoxy-α-D-*manno*-oct-6-enopyranoside (**14**), $[\alpha]_D$ +45.5° (*c* 0.95, chloroform), in good yield from the dialdose derivative **12** (prepared by Swern oxidation[3] of methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside) *via* the enal **13** (not extensively purified). Catalytic osmylation[5] of **14** afforded a mixture (64%) of two products in the ratio

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*The compounds **6** and **14** differ only in the orientation of the C-2 benzyloxy group on the pyranose ring. Examination of molecular models indicated that, irrespective of its orientation, this group is most unlikely to threaten the stereochemical outcome of the osmylation reactions.

~4:1, which, by reasonable analogy with the osmylation of **6***, were assigned as methyl 2,3,4-tri-*O*-benzyl-*β*-L-*threo*-D-*manno*-octopyranoside (**15**) and the corresponding *α*-D-*threo*-D-*manno* isomer **16**, respectively. Catalytic debenzylation of this mixture and conventional acetylation of the products gave methyl 2,3,4,6,7,8-hexa-*O*-acetyl-*β*-L-*threo*-D-*manno*-octopyranoside (**17**, 46%), m.p. 132–133.5°, $[\alpha]_D$ +33° (*c* 1.1, chloroform). Zemplén deacetylation of **17**, hydrolysis (M H_2SO_4 at 100°), and reduction ($NaBH_4$) of the resulting octose then furnished D-*erythro*-L-*altro*-octitol (L-*threo*-D-*manno*-octitol) (**18**, 75%), m.p. 144–145°, $[\alpha]_D$ ~+1° (*c* 1, water). ^{13}C-N.m.r. data [$(CD_3)_2SO$]: δ 71.94, 71.57, 71.51, 71.03, 70.76, 70.49, 64.06, and 63.19.

As with **1**, the catalytic osmylation of both **6** and **14** is *anti* (Kishi) stereoselective[2] with respect to the pyranose ring-oxygen atom, and provides satisfactory routes to the new octitols **11** and **18**. Debenzylation of appropriate derivatives of the triols **7** and **15** would be expected to yield compounds for which the well-established chemistry of the pyranose ring might be exploited in effecting configurational changes, thereby opening up routes to other eight-carbon sugars.

New compounds had elemental analyses and/or spectroscopic properties in agreement with the structures assigned.

ACKNOWLEDGMENTS

We thank Dr. I. H. Sadler and his colleagues at Edinburgh University for the 90-MHz ^{13}C-n.m.r. spectra, and the Commonwealth Scholarship Commission in the United Kingdom for financial support (to A.K.M.S.K.).

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