Higher-Carbon Sugars. Part 13.[1] The Catalytic Osmylation of Some α,β-Unsaturated Octuronic Acid Derivatives and a Synthesis of (*meso*)-*threo*-*gluco*-Octitol

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In compliance with Kishi's empirical rule, catalytic osmylation of methyl [methyl (*E*)-2,3,4-tri-*O*-benzyl-6,7-dideoxy-α-D-*gluco*-oct-6-enopyranosid]uronate (**6**) produced a mixture of methyl (methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*gluco*-octopyranosid)uronate (**9**) and the corresponding α-D-*threo*-D-*gluco* isomer (**10**) in the ratio *ca.* 9:1, respectively. Similar osmylation of the (*E*)-D-*manno*-octenopyranosiduronate (**8**) furnished a mixture of methyl (methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*manno*-octopyranosid)uronate (**12**) and the corresponding α-D-*threo*-D-*manno* isomer (**13**) in the ratio *ca.* 6:1. In each instance, the stereoselectivity of the osmylation reaction for the (*E*)-octenopyranosiduronate is higher than that of the corresponding (*E*)-octenopyranoside. The catalytic osmylation of methyl (*E*)-3,5-*O*-benzylidene-6,7-dideoxy-1,2-*O*-isopropylidene-α-D-*gluco*-oct-6-enofuranuronate (**24**), on the other hand, breached Kishi's empirical rule to provide a mixture of methyl 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-*threo*-D-*gluco*-octofuranuronate (**25**) and the corresponding β-L-*threo*-D-*gluco* isomer (**26**) in the ratio *ca.* 2:1, respectively. Acid hydrolysis of the protected octofuranose (**27**) obtained from the octofuranuronate (**25**), and reduction of the resulting octose gave the new octitol (*meso*)-*threo*-*gluco*-octitol (**28**). The stereochemistry of the osmylation product (**26**) was established by *X*-ray crystallography.

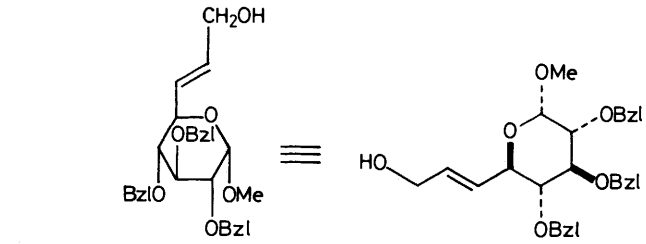
The catalytic osmylation of such unsaturated sugar derivatives as methyl 2,3,4-tri-*O*-benzyl-6,7-dideoxy-α-D-*gluco*-oct-6-enopyranoside (**1**) has provided an attractive and stereoselective approach to new higher-carbon sugars,[1-3] the stereochemistry of which can be predicted by application of Kishi's empirical rule.[4] In the example cited, methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*gluco*-octopyranoside (**2**) and the corresponding α-D-*threo*-D-*gluco* isomer (**3**) were formed in the ratio *ca.* 3:1, respectively.[1] In agreement with Kishi's formulation,[4] the newly introduced 6-OH and O-5 (the pyranose ring-oxygen atom) have an *erythro* arrangement in the major stereoisomer (**2**) formed on osmylation of the octenopyranoside (**1**). The diafacial stereoselectivity exhibited by the octenopyranoside (**1**) can be rationalised[1,4] by assuming that the allylic system adopts an eclipsed conformation,[5] and that the reagent approaches the least compressed conformation (**4**; $R^1 = CH_2OH$, $R^2 = H$; the substituents on the pyranose ring have been omitted for clarity) from the direction *anti* to the pyranose ring-oxygen atom. A similar rationalisation accounts for the stereoselectivities observed with hept-5-enofuranose systems.[2,6]

As part of a continuing programme concerned with the synthesis of higher-carbon sugars, we have examined the catalytic osmylation of such carbohydrate-based conjugate esters as methyl [methyl (*E*)-2,3,4-tri-*O*-benzyl-6,7-dideoxy-α-D-*gluco*-oct-6-enopyranosid]uronate (**6**) with two objectives in mind. First, as a direct and stereoselective route to octuronic acid derivatives of predictable stereochemistry. Second, by reduction of the octuronic acid derivatives so obtained to the parent octoses, as a possible means of overcoming the modest stereoselectivities exhibited by some oct-6-enopyranose systems such as (**1**) towards osmylation. Our own work[2] and that of others[4,7-9] had indicated that conjugate esters possessing the (*E*)-geometry are often highly and predictably stereoselective towards catalytic osmylation, whereas the corresponding (*Z*)-conjugate esters often exhibit[2,4,9] lower and unpredictable stereoselectivities, sometimes breaching Kishi's empirical rule.

Results and Discussion

The protected D-*gluco*-hexodialdopyranoside[1] (**5**) reacted with (methoxycarbonylmethylene)triphenylphosphorane[10] in boiling benzene to give, after chromatography, the (*E*)-octenopyranosiduronate (**6**) in 86% yield. A similar reaction with the D-*manno*-hexodialdopyranoside[1,11] (**7**) provided methyl [methyl (*E*)-2,3,4-tri-*O*-benzyl-6,7-dideoxy-α-D-*manno*-oct-6-enopyranosid]uronate (**8**) in 64.5% yield. The *E*-geometry assigned to each of the conjugate esters (**6**) and (**8**) was clearly indicated[12] by the magnitude of the spin-spin coupling ($J_{6,7}$ 15.8 Hz) of the olefinic protons.

On catalytic osmylation,[13] the (*E*)-octenopyranosiduronate (**6**) furnished a mixture of methyl (methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*gluco*-octopyranosid)uronate (**9**) and the corresponding α-D-*threo*-D-*gluco* isomer (**10**) in the ratio *ca.* 9:1, respectively. This ratio, which was determined by integration over the signals for the 1-OMe group in the 360 MHz ^{1}H n.m.r. spectrum, shows a marked improvement over that (*ca.* 3:1) obtained[1] on catalytic osmylation of the corresponding hydroxymethyl compound (**1**). The major octopyranosiduronate (**9**) was freed from the contaminating isomer by crystallisation, and, on reduction of the ester group, gave the known octopyranoside derivative[1] (**2**), which was further characterised as the crystalline triacetate[1] (**11**). Catalytic osmylation[13] of the (*E*)-D-*manno*-octenopyranosiduronate (**8**) produced a mixture of methyl (methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*manno*-octopyranosid)uronate (**12**) and the corresponding α-D-*threo*-D-*manno* isomer (**13**) in the ratio *ca.* 6:1, respectively. Reduction of this mixture of octopyranosiduronates gave the octopyranoside derivatives (**14**) and (**15**) in the ratio *ca.* 6:1, respectively. This ratio represents a slight improvement on that (*ca.* 4:1) obtained[1] for these compounds on catalytic osmylation of the (*E*)-D-*manno*-octenopyranoside (**16**), although it has to be set against the modest yield (41.5%, not optimised) obtained in the reduction step. The major isomer (**14**) was isolated and characterised as



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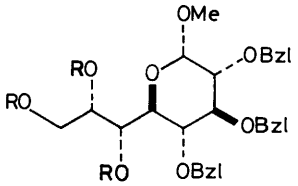
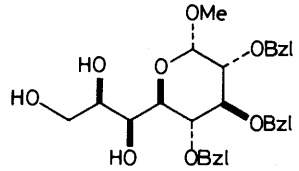


(2) R = H
(11) R = Ac



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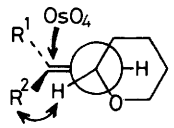

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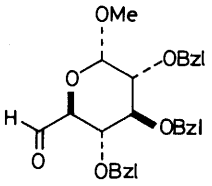

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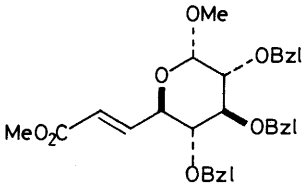

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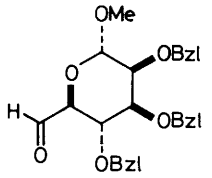

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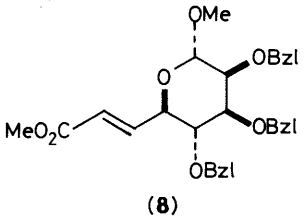

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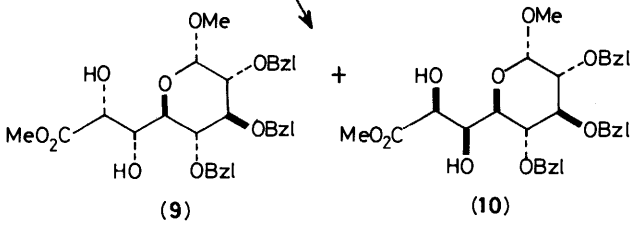
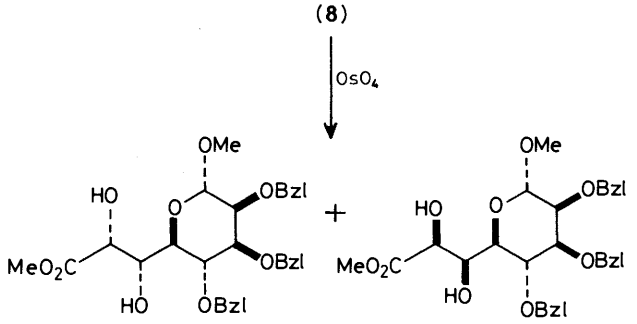


(9) (10)



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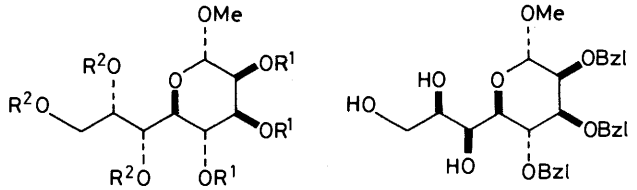
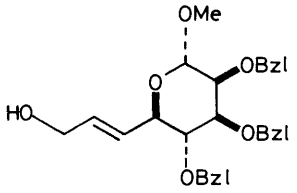


(14) R^1 = Bzl, R^2 = H
(17) R^1 = R^2 = Ac

(15)



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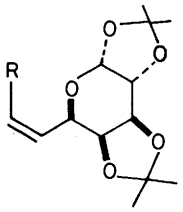
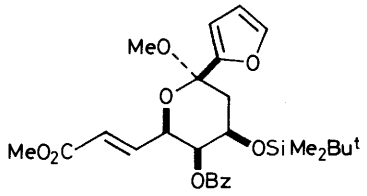


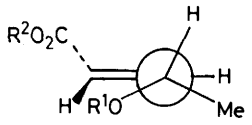
(18) R = CO_2Me
(19) R = CH_2OH



(20)

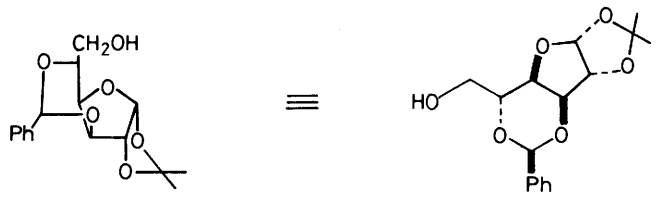
the crystalline hexa-acetate (**17**) in the manner described previously.[1]

The stereoselectivity observed on catalytic osmylation of each of the (*E*)-octenopyranosiduronates (**6**) and (**8**) conforms to Kishi's empirical rule[4] and can be regarded formally as being *anti* with respect to the pyranose ring-oxygen atom. Using Kishi's reactant-like model,[4] the molecule is assumed to undergo attack by OsO_4 from the direction *anti* to the pyranose ring-oxygen atom in the least compressed conformation (**4**; R^1 = CO_2Me, R^2 = H). The preference for (*E*)-conjugate esters to react in this conformation must be viewed in the light of other evidence, particularly the poor stereoselectivities and the number of exceptions to Kishi's empirical rule found[2,4,8,9] among (*Z*)-conjugate esters [for example, (**18**)[12]], which, for steric reasons, should exhibit a stronger preference for the conformation (**4**; R^1 = H, R^2 = CO_2Me) having the smallest group eclipsing the olefinic linkage. If, however, the steric interactions become too severe, (*Z*)-conjugate esters could forgo the advantages of an eclipsed conformation[5] and adopt a staggered form.[9] Such anomalies are not encountered in the osmylation of related chiral allylic alcohols [for example, (**19**)[12]], which conform to Kishi's formulation and for which the (*Z*)-allylic alcohol generally exhibits a higher degree of stereoselection than the corresponding (*E*)-allylic alcohol.[2,4]



(21)

(21) has been questioned.[15] The approach of OsO_4 to the conformation (21) would be less hindered between the hydrogen and alkoxy functions, leading to the product predicted by Kishi's empirical rule.[4] Advocates of this model suggest[7,8] that the anomalous behaviour of (*Z*)-conjugate esters towards osmylation could be explained by attack of OsO_4 on the eclipsed conformation akin to (**4**; R^1 = H, R^2 = CO_2alkyl)



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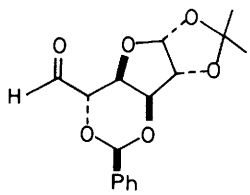

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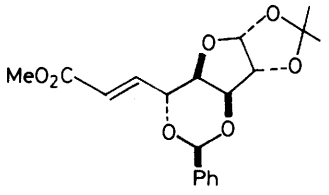

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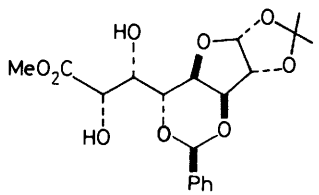

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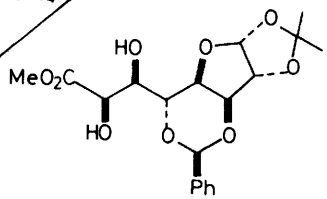

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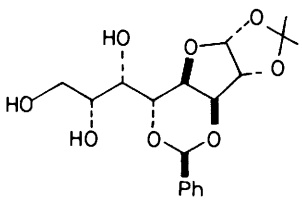

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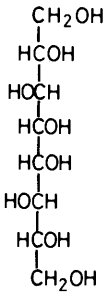

(28)

A recent *X*-ray crystallographic study[9] has shown that the O(5)-C(5) bond nearly eclipses the olefinic linkage in the *ground-state* conformation of the (*E*)-conjugate ester (**20**) (shown in the D-series for ease of comparison). The addition of OsO_4 to the less hindered α-face of this synplanar (or 'alkoxy-inside'[14]) conformation correctly predicts[9] the stereochemical outcome of the reaction, which conforms to Kishi's empirical rule.[4] The 'alkoxy-inside' conformation (**21**) was also invoked by Stork[7] and others[8] in rationalising the stereoselectivities observed in the osmylation of (*E*)-conjugate esters bearing a γ-alkoxy (or hydroxy) group, although the crucial electronic role[7,9] of the allylic substituent in favouring the conformation from the direction *syn* to the allylic oxygen function. This explanation has to be measured against the propensity for (*Z*)-allylic alcohols in the conformation (**4**) to add OsO_4 on the opposite face of the olefinic linkage *anti* to the allylic oxygen function (Kishi model[4]). Transition-state models somewhat different and more product-like than Kishi's model, which lead to the same qualitative predictions, have also been advocated.[15]

A choice between the various models is circumscribed by the fact that little is known of the precise mechanism of osmylation,[16] so that those factors ultimately responsible for the observed stereoselectivities are equally little known. It must also be borne in mind that, with complex substrates, steric

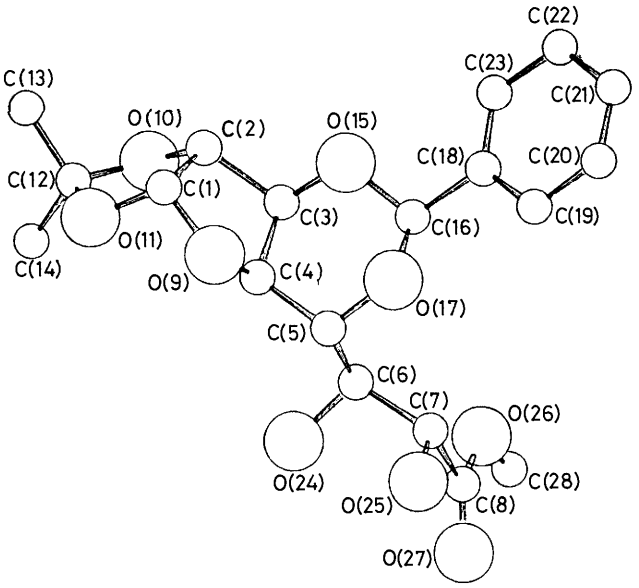

Figure. *X*-Ray molecular structure of methyl 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-β-L-*threo*-D-*gluco*-octofuranuronate (**26**)

factors other than those emanating from the allylic substituent at the adjacent stereocentre can also influence the stereochemical outcome of osmylation reactions[2,17] (also see below). Despite the deficiencies noted above, we feel that a reasonable case can be made for retaining the Kishi model[4] at this stage in the development of our understanding, since it is conveniently simple to apply and provides a rationale that needs less qualification than others for the stereoselectivities observed in most osmylations.

In this and other work concerned with the synthesis of eight-carbon sugars,[2,3] it has been customary to extend the carbon chain of suitably protected hexodialdopyranose derivatives [for example, (**5**)] at C-6 *via* Wittig olefination. A related strategy was adopted in examining another route to eight-carbon sugars that involved two-carbon extension of the chain of such hexodialdofuranose derivatives as (**23**), which was readily obtained on oxidation of 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-glucofuranose[18] (**22**). The latter compound was best prepared by the method of Van Cleeve *et al.*,[19] which involved protection of 1,2-*O*-isopropylidene-α-D-glucofuranose as the 6-(*p*-nitrobenzoate), followed by benzylidenation and de-esterification. The D-glucofuranose derivative (**22**) underwent oxidation rapidly with pyridinium chlorochromate[20] in methylene dichloride in the presence of molecular sieves,[21] but no attempt was made to isolate the resulting hexodialdofuranose derivative (**23**), which was allowed to react *in situ* with (methoxycarbonylmethylene)triphenylphosphorane to provide the (*E*)-octenofuranuronate (**24**) ($J_{6,7}$ 16 Hz). An analogous procedure was used[22] in preparing the ethyl ester corresponding to (**24**). One cause for concern was that, if the phenyl group attached to the chair form of the six-membered dioxane ring of (**23**) is assigned an equatorial orientation,[23] the aldehyde group attached to C-5 must then assume an axial orientation and, consequently, be prone to epimerisation to the more stable equatorial orientation. That no epimerisation occurred in the steps leading to the (*E*)-octenofuranuronate (**24**), which would also be susceptible to epimerisation at C-5, was established by crystallographic analysis of one of the products obtained in the ensuing osmylation, which afforded a mixture of methyl 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-*threo*-D-*gluco*-octofuranuronate (**25**) and the crystalline β-L-*threo*-D-*gluco* isomer (**26**) in the ratio *ca.* 2:1, respectively, based on the yields of the individual products isolated after chromatography. A single-crystal *X*-ray analysis on the minor product (**26**) established not only the L-*threo* configuration for the hydroxy groups introduced at C-6 and C-7, but also the stereochemistry of the substituents attached to the dioxane ring. It can be seen (see Figure) that the dioxane ring adopts a chair conformation having the phenyl group and the aliphatic side-chain in equatorial and axial orientations, respectively. The crystallographic evidence also established the α-D-*threo*-D-*gluco* compound (**25**) as the major osmylation product. Since O-5 and the newly introduced 6-OH of this compound have a *threo* relationship, the stereochemical outcome of the osmylation is in breach of Kishi's empirical rule,[4] which requires an *erythro* relationship between these functions. The reason for the observed stereoselectivity was not discernible from an examination of molecular models, but is presumably steric in origin.

A beneficial outcome of the foregoing approach is that it provides reasonable access to the D-*threo*-D-*gluco* configuration, which is practically inaccessible from other substrates [for example, (**1**)[1] and (**6**)] *via* osmylation and other routes. Reduction of the octofuranuronate (**25**) gave the crystalline octofuranose (**27**), a selectively protected derivative of D-*threo*-D-*gluco*-octose of potential value in the synthesis of other eight-carbon sugars. Acid hydrolysis of the octofuranose derivative (**27**) and reduction of the free sugar gave (*meso*)-*threo*-*gluco*-octitol (**28**), which, in agreement with its C_s-symmetry, exhibited only four resonances of roughly equal intensity in its ^{13}C n.m.r. spectrum.

Experimental

T.l.c. was performed on Kieselgel G, and spots are detected with 1% aqueous sulphuric acid. ^1H N.m.r. spectra were recorded for solutions in deuteriochloroform (internal tetramethylsilane) at 360 MHz by Edinburgh University n.m.r. service. The ^{13}C n.m.r. spectrum was recorded for a solution in [$^2H_6$]dimethyl sulphoxide at 90 MHz by Edinburgh University n.m.r. service; the spectrum was referenced to tetramethylsilane by means of the solvent resonance at δ_C 39.6. A Perkin-Elmer Model 141 automatic polarimeter and 1 dm tubes were used for the measurement of specific optical rotations. M.p.s were measured on a Reichert hot-plate apparatus and are uncorrected.

Methyl [*Methyl* (E)-2,3,4-*Tri*-O-*benzyl*-6,7-*dideoxy*-α-D-gluco-*oct*-6-*enopyranosid*]*uronate* (**6**).—A solution of the D-*gluco*-hexodialdopyranoside[1] (**5**) (0.25 g, 0.54 mmol) and (methoxycarbonylmethylene)triphenylphosphorane[10] (0.2 g, 0.6 mmol) in anhydrous benzene (5 ml) was boiled under reflux for 1 h, cooled, and evaporated under diminished pressure. Chromatography of the residue on silica gel [methylene dichloride–acetone (50:1) as eluant] gave the (E)-*octenopyranosiduronate* (**6**) (0.241 g, 86%), m.p. 56—57 °C (from hexane); $[\alpha]_D$ +52° (*c* 1 in $CHCl_3$) (Found: C, 71.5; H, 6.5. $C_{31}H_{34}O_7$ requires C, 71.8; H, 6.6%); δ_H (*inter alia*) 7.39—7.26 (15 H, 3 × m, 3 × Ph), 7.04 (1 H, dd, $J_{5,6}$ 4.7, $J_{6,7}$ 15.8 Hz, 6-H), 6.13 (1 H, dd, $J_{5,7}$ 1.75 Hz, 7-H), 4.91 (2 H, ABq, J_{AB} *ca.* 10.8 Hz, PhCH_2), 4.74 (2 H, ABq, J_{AB} 11.9 Hz, PhCH_2), 4.70 (2 H, ABq, J_{AB} 10.8 Hz, PhCH_2), 4.63 (1 H, d, $J_{1,2}$ 3.6 Hz, 1-H), 3.75 (3 H, s, CO_2Me), and 3.36 (3 H, s, OMe).

Methyl [*Methyl* (E)-2,3,4-*Tri*-O-*benzyl*-6,7-*dideoxy*-α-D-manno-*oct*-6-*enopyranosid*]*uronate* (**8**).—A solution of the D-*manno*-hexodialdopyranoside[11] (**7**) (0.274 g, 0.59 mmol) and (methoxycarbonylmethylene)triphenylphosphorane[10] (0.218 g, 0.65 mmol) in anhydrous benzene (6 ml) was boiled under reflux for 1.5 h, and the reaction mixture was then processed as described in the previous experiment to give the (E)-*octenopyranosiduronate* (**8**) (0.198 g, 64.5%), $[\alpha]_D$ +69° (*c* 1.8 in

Table 1. Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses for the octofuranose derivative (**26**)

	x	*y*	*z*
C(1)	−2 394(9)	−6 160(0)	−1 955(10)
C(2)	−2 434(9)	−5 369(13)	−3 187(10)
C(3)	−3 549(8)	−4 138(14)	−3 371(9)
C(4)	−3 612(9)	−4 068(16)	−2 021(9)
C(5)	−4 998(9)	−3 468(16)	−1 939(10)
C(6)	−4 999(9)	−1 856(14)	−1 876(10)
C(7)	−6 415(9)	−1 291(14)	−1 920(10)
C(8)	−6 415(8)	398(16)	−1 974(9)
C(12)	−153(10)	−5 375(21)	−1 735(11)
C(13)	577(14)	−6 481(20)	−2 127(16)
C(14)	810(15)	−4 160(19)	−944(14)
C(16)	−6 003(8)	−3 878(15)	−4 196(8)
C(18)	−7 327(9)	−4 474(13)	−5 219(9)
C(19)	−8 572(9)	−4 555(16)	−4 985(9)
C(20)	−9 752(11)	−5 078(18)	−5 928(12)
C(21)	−9 713(12)	−5 522(18)	−7 093(12)
C(22)	−8 456(11)	−5 462(19)	−7 342(11)
C(23)	−7 278(10)	−4 932(16)	−6 412(9)
C(28)	−6 210(18)	2 278(29)	−3 280(15)
O(9)	−3 404(6)	−5 494(11)	−1 514(6)
O(10)	−1 106(6)	−4 647(11)	−2 893(7)
O(11)	−1 027(6)	−5 857(11)	−1 082(6)
O(15)	−4 852(6)	−4 738(10)	−4 244(6)
O(17)	−6 163(5)	−4 019(10)	−2 979(6)
O(24)	−3 915(6)	−1 332(10)	−753(7)
O(25)	−6 749(8)	−1 703(10)	−852(8)
O(26)	−6 277(8)	754(11)	−3 059(7)
O(27)	−6 547(7)	1 090(9)	−1 164(6)

$U_{eq} = \frac{1}{3}\Sigma_i\Sigma_j U_{ij}\, a_i^* a_j^* a_i a_j$

Table 2. Intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses for the octofuranose derivative (**26**)

(a) Bonds

C(1)–C(2)	1.515(15)	C(8)–O(27)	1.131(14)
C(1)–O(9)	1.408(13)	C(12)–O(10)	1.464(14)
C(1)–O(11)	1.416(10)	C(12)–O(11)	1.383(16)
C(2)–C(3)	1.558(15)	C(12)–C(13)	1.402(24)
C(2)–O(10)	1.433(12)	C(12)–C(14)	1.536(21)
C(3)–C(4)	1.497(14)	C(16)–O(15)	1.421(13)
C(3)–O(15)	1.448(10)	C(16)–O(17)	1.397(12)
C(4)–C(5)	1.537(15)	C(16)–C(18)	1.525(12)
C(4)–O(9)	1.404(16)	C(18)–C(19)	1.370(14)
C(5)–C(6)	1.476(20)	C(18)–C(23)	1.384(15)
C(5)–O(17)	1.423(11)	C(19)–C(20)	1.372(14)
C(6)–C(7)	1.508(14)	C(20)–C(21)	1.347(20)
C(6)–O(24)	1.423(11)	C(21)–C(22)	1.389(18)
C(7)–C(8)	1.546(19)	C(22)–C(23)	1.366(14)
C(7)–O(25)	1.372(15)	C(28)–O(26)	1.420(28)
C(8)–O(26)	1.280(14)		

(b) Angles

C(2)–C(1)–O(9)	107.0(6)	O(10)–C(12)–O(11)	103.9(8)
C(2)–C(1)–O(11)	103.3(7)	C(13)–C(12)–O(10)	109.0(11)
O(9)–C(1)–O(11)	110.0(7)	C(13)–C(12)–O(11)	115.0(15)
C(1)–C(2)–C(3)	105.1(8)	C(14)–C(12)–O(10)	105.3(13)
C(1)–C(2)–O(10)	106.3(7)	C(14)–C(12)–O(11)	109.7(11)
C(3)–C(2)–O(10)	106.2(9)	C(13)–C(12)–C(14)	113.2(11)
C(2)–C(3)–C(4)	100.1(8)	O(15)–C(16)–O(17)	110.1(8)
C(2)–C(3)–O(15)	105.6(9)	C(18)–C(16)–O(15)	107.7(9)
C(4)–C(3)–O(15)	109.4(8)	C(18)–C(16)–O(17)	107.8(8)
C(3)–C(4)–C(5)	114.6(7)	C(16)–C(18)–C(19)	121.2(9)
C(3)–C(4)–O(9)	107.3(10)	C(16)–C(18)–C(23)	119.6(9)
C(5)–C(4)–O(9)	109.1(10)	C(19)–C(18)–C(23)	119.2(8)
C(4)–C(5)–C(6)	112.0(10)	C(18)–C(19)–C(20)	120.0(11)
C(4)–C(5)–O(17)	110.7(9)	C(19)–C(20)–C(21)	121.1(12)
C(6)–C(5)–O(17)	112.2(9)	C(20)–C(21)–C(22)	119.6(10)
C(5)–C(6)–C(7)	110.9(9)	C(21)–C(22)–C(23)	119.7(12)
C(5)–C(6)–O(24)	111.4(8)	C(18)–C(23)–C(22)	120.4(11)
C(7)–C(6)–O(24)	111.0(9)	C(1)–O(9)–C(4)	107.2(7)
C(6)–C(7)–C(8)	109.3(9)	C(2)–O(10)–C(12)	106.1(9)
C(6)–C(7)–O(25)	112.6(9)	C(1)–O(11)–C(12)	111.4(8)
C(8)–C(7)–O(25)	108.1(10)	C(3)–O(15)–C(16)	109.9(8)
C(7)–C(8)–O(26)	106.9(10)	C(5)–O(17)–C(16)	113.1(8)
C(7)–C(8)–O(27)	121.8(11)	C(8)–O(26)–C(28)	115.7(12)
O(26)–C(8)–O(27)	131.2(14)		

$CHCl_3$), isolated as a syrup (Found: C, 71.95; H, 6.4. $C_{31}H_{34}O_7$ requires C, 71.8; H, 6.6%); δ_H (*inter alia*) 7.39—7.26 (15 H, 3 × m, 3 × Ph), 7.13 (1 H, dd, $J_{5,6}$ 4.7, $J_{6,7}$ 15.8 Hz, 6-H), 6.23 (1 H, dd, $J_{5,7}$ 1.7 Hz, 7-H), 4.74 (4 H, 2 × ABq, J_{AB} 12.4 and 10.8 Hz, 2 × PhCH_2), 4.73 (1 H, d, $J_{1,2}$ 1.75 Hz, 1-H), 3.76 (3 H, s, CO_2Me), and 3.29 (3 H, s, OMe).

Methyl (*Methyl* 2,3,4-*Tri*-O-*benzyl*-β-L-threo-D-gluco-*octopyranosid*)*uronate* (**9**) *and Its Characterisation.*—A solution of the (*E*)-octenopyranosiduronate (**6**) (0.2 g, 0.39 mmol), *N*-methylmorpholine *N*-oxide monohydrate (0.104 g, 0.77 mmol), and osmium tetraoxide (*ca.* 0.01 g, *ca.* 0.039 mmol) in acetone–water (8:1; 2 ml) was stirred at room temperature for 2 h and then processed in the usual way.[3] Percolation of the residue in methylene dichloride–acetone (15:1) through a column of silica gel provided a mixture (0.193 g, 90.5%) of methyl (methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*gluco*-octopyranosid)uronate (**9**) [δ_H 3.42 (s, OMe)] and the corresponding α-D-*threo*-D-*gluco* isomer (**10**) [δ_H 3.39 (s, OMe)] in the ratio *ca.* 9:1, respectively, which crystallised with time. Recrystallisation from diethyl ether–hexane gave the pure *octopyranosiduronate* (**9**), m.p. 89.5—90 °C; $[\alpha]_D$ +18.5° (*c* 0.75 in $CHCl_3$) (Found: C, 67.7; H, 6.7. $C_{31}H_{36}O_9$ requires C, 67.4; H, 6.6%); δ_H (*inter alia*) 7.38—7.21 (15 H, 3 × m, 3 × Ph), 4.92 (2 H, ABq, J_{AB} 10.85 Hz, PhCH_2), 4.87 (2 H, ABq, J_{AB} 10.7 Hz, PhCH_2), 4.72 (2 H, ABq, J_{AB} 12.1 Hz, PhCH_2), 4.56 (1 H, d, $J_{1,2}$ 3.6 Hz, 1-H), 3.79 (3 H, s, CO_2Me), and 3.42 (3 H, s, OMe).

Reduction of the octopyranosiduronate (**9**) with lithium aluminium hydride in tetrahydrofuran in the usual way[12] furnished methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*gluco*-octopyranoside (**2**) in 57% yield. The 360 ^{1}H n.m.r. spectrum of this material was indistinguishable from that of an authentic sample.[1] Further characterisation was achieved by acetylation of the octopyranoside (**2**), as previously described,[1] to give the triacetate (**11**), m.p. and mixture m.p. 107—108.5 °C (from diethyl ether–hexane) (lit.,[1] m.p. 107.5—108.5 °C).

Methyl (*Methyl* 2,3,4-*Tri*-O-*benzyl*-β-L-threo-D-manno-*octopyranosid*)*uronate* (**12**) *and Its Characterisation.*—A solution of the (*E*)-octenopyranosiduronate (**8**) (*ca.* 0.14 g, *ca.* 0.27 mmol), *N*-methylmorpholine *N*-oxide monohydrate (0.073 g, 0.54 mmol), and osmium tetraoxide (*ca.* 7 mg, 0.0275 mmol) in acetone–water (8:1; 1.25 ml) was stirred at room temperature overnight and then processed in the usual way.[12] Percolation of the residue in methylene dichloride–acetone (15:1) through a column of silica gel produced a mixture (0.148 g, 99%) of methyl (methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*manno*-octopyranosid)uronate (**12**) [δ_H 3.36 (s, OMe)] and the corresponding α-D-*threo*-D-*manno* isomer (**13**) [δ_H 3.31 (s, OMe)] in the ratio *ca.* 6:1, respectively.

Reduction of the foregoing mixture of the octopyranosiduronates (**12**) and (**13**) with lithium aluminium hydride in tetrahydrofuran gave a mixture (41.5%) of methyl 2,3,4-tri-*O*-benzyl-β-L-*threo*-D-*manno*-octopyranoside (**14**) and the corresponding α-D-*threo*-D-*manno* isomer (**15**) in the ratio *ca.* 6:1, respectively. The 360 ^{1}H n.m.r. spectrum of the principal

component of this mixture was indistinguishable from that of the triol (**14**) obtained previously.[1] Further characterisation of the triol (**14**) was effected by its conversion, as described previously,[1] into the hexa-acetate (**17**), m.p. and mixture m.p. 132—134 °C (from ethanol) (lit.,[1] m.p. 132—133.5 °C).

Methyl (E)-3,5-O-*Benzylidene*-6,7-*dideoxy*-1,2-O-*isopropylidene*-α-D-gluco-*oct*-6-*enofuranuronate* (**24**).—To a solution of the D-glucofuranose derivative[18,19] (**22**) (0.95 g, 3.08 mmol) in anhydrous methylene dichloride (67 ml) containing powdered 3 Å molecular sieves[21] (3.37 g) was added pyridinium chlorochromate[20] (1.38 g, 6.4 mmol), and the mixture was stirred at room temperature for 10 min. (Methoxycarbonylmethylene)triphenylphosphorane[10] (2.15 g, 6.43 mmol) was then added and stirring was continued for 2 h, whereupon the reaction mixture was poured into diethyl ether. The ethereal solution was filtered and evaporated under reduced pressure. Chromatography of the residue on silica gel [methylene dichloride–acetone (25:1) as eluant] gave the (E)-*octenofuranuronate* (**24**) (0.738 g, 66%), m.p. 135.5—137.5 °C (from ethyl acetate–hexane); $[\alpha]_D$ +23° (*c* 0.5 in $CHCl_3$) (Found: C, 62.9; H, 6.1. $C_{19}H_{22}O_7$ requires C, 63.0; H, 6.1%); δ_H 7.49—7.34 (5 H, m, Ph), 7.07 (1 H, dd, $J_{5,6}$ 4, $J_{6,7}$ 16 Hz, 6-H), 6.20 (1 H, dd, $J_{5,7}$ 2.4 Hz, 7-H), 6.05 (1 H, d, $J_{1,2}$ 3.7 Hz, 1-H), 5.67 (1 H, s, PhC*H*), 5.05 (1 H, m, 5-H), 4.65 (1 H, d, 2-H), 4.38 and 4.18 (2 H, 2 × dd, 3- and 4-H), 3.78 (3 H, s, CO_2Me), and 1.52 and 1.33 (6 H, 2 × s, CMe_2). In subsequent scaled-up experiments, the yield of the (*E*)-octenofuranuronate (**24**) ranged from 44—66%.

Methyl 3,5-O-*Benzylidene*-1,2-O-*isopropylidene*-α-D-threo-D-gluco-*octofuranuronate* (**25**) *and the Corresponding* β-L-threo-D-gluco *Isomer* (**26**).—A solution of the (*E*)-octenofuranuronate (**24**) (0.705 g, 1.945 mmol), *N*-methylmorpholine *N*-oxide monohydrate (0.531 g, 3.93 mmol), and osmium tetraoxide (*ca.* 20 mg, *ca.* 0.08 mmol) in acetone–water (8:1; 14 ml) was stirred at room temperature overnight and then processed in the usual way.[12] Careful chromatography of the residue on silica gel [methylene dichloride–acetone (10:1) as eluant] gave first the α-D-threo-D-gluco *compound* (**25**) (0.483 g, 63%), $[\alpha]_D$ *ca.* +36° (*c* 2 in $CHCl_3$), isolated as a syrup (Found: C, 57.65; H, 6.1. $C_{19}H_{24}O_9$ requires C, 57.6; H, 6.1%); δ_H (*inter alia*) 7.47—7.32 (5 H, m, Ph), 6.03 (1 H, d, $J_{1,2}$ 3.7 Hz, 1-H), 5.95 (1 H, s, PhC*H*), 4.66 (1 H, d, 2-H), 3.75 (3 H, s, CO_2Me), and 1.52 and 1.33 (6 H, 2 × s, CMe_2). Continued elution gave the β-L-threo-D-gluco *compound* (**26**) (0.237 g, 31%), m.p. 169—171 °C (from ethyl acetate–hexane); $[\alpha]_D$ −10° (*c* 1.1 in $CHCl_3$) (Found: C, 57.8; H, 6.25%); δ_H (*inter alia*) 7.47—7.34 (5 H, m, Ph), 6.04 (1 H, d, $J_{1,2}$ 3.75 Hz, 1-H), 5.68 (1 H, s, PhC*H*), 4.66 (1 H, d, 2-H), 3.82 (3 H, s, CO_2Me), and 1.51 and 1.32 (6 H, 2 × s, CMe_2).

3,5-O-*Benzylidene*-1,2-O-*isopropylidene*-α-D-threo-D-gluco-*octofuranose* (**27**).—A solution of the octofuranuronate (**25**) (0.483 g, 1.22 mmol) in anhydrous tetrahydrofuran (2 ml) containing lithium aluminium hydride (0.5 g, *ca.* 13 mmol) was stirred at room temperature overnight before the excess of the reagent was decomposed with wet ethyl acetate. Inorganic material was filtered off and washed thoroughly with ethyl acetate, and the filtrate and the washings were combined, dried ($MgSO_4$), and evaporated under diminished pressure to give the crude product (0.291 g, 65%), which crystallised with time. Recrystallisation from ethyl acetate–hexane gave the pure *octofuranose derivative* (**27**), m.p. 189—190.5 °C; $[\alpha]_D$ +24° (*c* 1.1 in $CHCl_3$) (Found: C, 58.9; H, 6.6. $C_{18}H_{24}O_8$ requires C, 58.7; H, 6.6%); δ_H (*inter alia*) 7.46—7.33 (5 H, m, Ph), 6.14 (1 H, s, PhC*H*), 6.03 (1 H, d, $J_{1,2}$ 3.7 Hz, 1-H), 4.66 (1 H, d, 2-H), and 1.53 and 1.33 (6 H, 2 × s, CMe_2).

(meso)-threo-gluco-*Octitol* (**28**).—A solution of the octofuranose derivative (**27**) (0.153 g, 0.415 mmol) in trifluoroacetic acid–water (9:1; 3 ml) was kept at room temperature for *ca.* 20 min and then evaporated under diminished pressure with occasional additions of water. To a cooled (0 °C) and stirred solution of the resulting octose in water (6 ml) was gradually added sodium borohydride (0.1 g, *ca.* 2.6 mmol), and the reaction mixture was stirred for 3 h at 0 °C and then overnight at room temperature. Sodium ions were removed from the reaction mixture with Amberlite IR-120 (H^+) resin, and the resin was filtered off and washed thoroughly with water. The filtrate and the washings were combined and evaporated under reduced pressure, and methanol was added to, and evaporated from, the residue until no boric acid remained. The final residue crystallised on trituration with methanol to give the (meso)-*octitol* (**28**) (47 mg, 47%), m.p. 166—169.5 °C (with prior softening) (Found: C, 39.6; H, 7.35. $C_8H_{18}O_8$ requires C, 39.7; H, 7.5%); δ_C([$^2H_6$]DMSO) 73.998, 71.279, 68.712, and 62.670.

Crystal Structure Determination for the Octofuranose Derivative (**26**).—$C_{19}H_{24}O_9$, M = 396.37, monoclinic, space group $P2_1$, a = 10.12(1), b = 9.147(6), c = 10.91(2) Å, β = 109.8(1)°, V = 950.2 Å^3, Z = 2, D_c = 1.39 g cm^{-3}, monochromatic Mo-K_α radiation, λ = 0.71 069 Å, μ = 0.69 cm^{-1}.

After preliminary photographs, a crystal of *ca.* 0.12 × 0.55 × 0.28 mm was mounted on a Stoe Stadi II diffractometer. Intensities were recorded for 2 135 reflections ($-12 < h < 12$, $-2 < l < 13$) on layers k = O-8 with a 2θ limit of 50°; these reduced to 1 441 unique reflections (R_{int} = 0.085) of which 1 104 with $|F| > 4.0\sigma$ (F) were used in the refinement.

The structure was solved by direct methods using the SHELX S program system[24] and refined by full-matrix least-squares with anisotropic temperature factors for C and O. Hydrogen atoms were included at calculated positions in the last cycles of refinement using a riding model (C–H = 1.05 Å) with isotropic temperature factors refined in groups; the hydrogen atoms of the hydroxy groups were located on a difference map and refined with U = 0.070 throughout. The final R-factors were R = 0.085 and R' = 0.107. The weighting scheme used was $w = 3.4082/[\sigma^2(F) + 0.001\,320\,F^2]$. The largest features in the final difference map were 0.25, −0.58 e Å^{-3}. The molecules are arranged in hydrogen-bonded stacks parallel to the *a* axis; each molecule forms four hydrogen-bonds O(25)–H···O(9′) = 2.753 Å and O(24)–H···O(27″) = 3.082 Å to the molecules at −100 and 100. The relatively high final R-factor reflects the low diffracting power of the crystals. Despite good quality spots, there were few measurable reflections at high angles (layer k = 8 gave 24 negative intensities out of the 58 reflections measured). There are only 4.1 data per parameter in the refinement. Many of the thermal ellipsoids are large, but all are 'positive definite', and attempts at disordered models produced no significant improvements in the R-factor.

Refinement was carried out on a Prime 6350 computer using the SHELX 76 program system[25] with atomic scattering factors taken from the program library. Geometric calculations were performed using XANADU.[26]

Fractional atomic co-ordinates (corresponding to the absolute configuration) and intramolecular distances and angles are given in Tables 1 and 2.* In the numbering system used (Figure), the carbon atoms of the parent octose are numbered according to normal carbohydrate nomenclature, while the remaining atoms are numbered arbitrarily.

* *Supplementary data* (see section 5.6.3 of Instructions for Authors, 1989 in the January issue). Tables of hydrogen atom co-ordinates, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

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