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Two ethyl 2-deoxy-α-D-hexo-3,7-pyranoso-3-octulosonate derivatives

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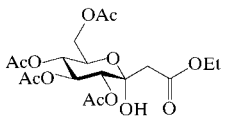
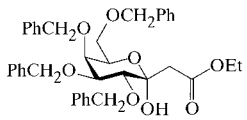
In each of the two pyranoid sugars, ethyl 2-deoxy-4,5,6,8-tetra-*O*-acetyl-α-D-*gluco*-3,7-pyranoso-3-octulosonate, $C_{18}H_{26}O_{12}$, and ethyl 2-deoxy-4,5,6,8-tetra-*O*-benzyl-α-D-*galacto*-3,7-pyranoso-3-octulosonate, $C_{38}H_{42}O_8$, the anomeric configuration is α. The acetoxymethyl substituent on the hexopyranose ring of the former compound and the ethoxycarbonylmethyl substituents in both sugars all have the *gauche–trans* conformation, while the benzyloxymethyl substituent of the galactopyranose sugar has the *trans–gauche* conformation. In each structure, the anomeric hydroxy group forms an intramolecular hydrogen bond with the carbonyl O atom of the ethoxycarbonylmethyl substituent.

Comment

C-Glycosides are now widely used as chiral templates for the synthesis of complex target molecules (Martin *et al.*, 1991; Jiang *et al.*, 1996), many of which have been found to show interesting and useful biological activities (Pougny *et al.*, 1981; Martin *et al.*, 1991; Watson *et al.*, 1994; Bichard *et al.*, 1995). One group of *C*-glycosides that have not been widely studied for their enzyme-inhibition activities is that where the compounds contain an exocyclic double bond at the anomeric centre. We are presently interested in studying the synthesis and structure of this class of derivatives and now report the low-temperature crystal structures of ethyl 2-deoxy-4,5,-6,8-tetra-*O*-acetyl-α-D-*gluco*-3,7-pyranoso-3-octulosonate, (I), and ethyl 2-deoxy-4,5,6,8-tetra-*O*-benzyl-α-D-*galacto*-3,7-pyranoso-3-octulosonate, (II), which are precursors used in the synthesis of their exocyclic alkenylic analogues.



(I)



(II)

Figs. 1 and 2 depict the correct absolute configurations of compounds (I) and (II), which were assigned to agree with the known chirality of the precursor sugars, *viz.* D-glucose and D-galactose, respectively. Both sugars are α-anomers and the pyranose ring in each compound has a slightly distorted $^4C_1$ chair conformation. The ring puckering parameters (Cremer & Pople, 1975) are Q = 0.570 (2) Å, q_2 = 0.062 (2) Å, q_3 = 0.567 (3) Å, φ_2 = 68.5 (18)° and θ = 6.4 (2)° for compound (I), and Q = 0.590 (3) Å, q_2 = 0.054 (2) Å, q_3 = 0.588 (3) Å, φ_2 = 157 (3)° and θ = 5.2 (2)° for compound (II). The bond lengths and angles exhibit normal values and generally agree with the corresponding parameters found for other α-pyranose sugars (Berman *et al.*, 1967).

The conformation of the C5 acetoxymethyl group in (I) is *gauche–trans* [O5—C5—C6—O6 72.1 (2)° and C4—C5—C6—O6 −168.41 (17)°]. In contrast, the corresponding benzyloxymethyl group in (II) has a *trans–gauche* conformation [O5—C5—C6—O6 −170.90 (19)° and C4—C5—C6—O6

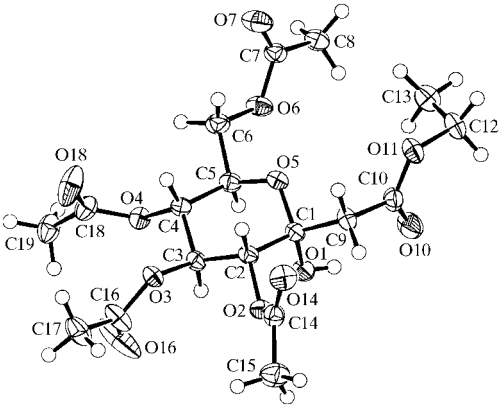


Figure 1
A view of the molecule of (I) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented by spheres of arbitrary size.

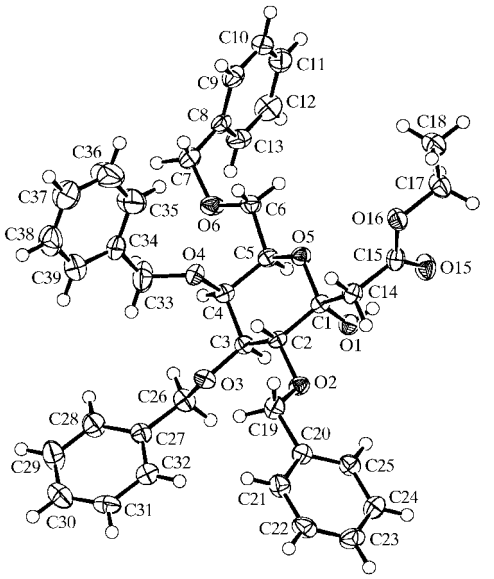


Figure 2
A view of the molecule of (II) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented by spheres of arbitrary size.

−50.0 (3)°]. In D-glucopyranose, a *trans–gauche* conformation would be forbidden because of the resultant unfavourable steric interaction between O4 and O6, but most galactopyranoses have either the *gauche–trans* or the *trans–gauche* conformation (Longchambon *et al.*, 1975; Kanters *et al.*, 1988), with a slight preference for the *gauche–trans* form (Kanters *et al.*, 1978). The *gauche–gauche* conformation is not usually observed for galactopyranoses, because this results in an unfavourable 1,3-*peri* interaction between the synaxial atoms O4 and O6.

The conformation of the C1 ethoxycarbonylmethyl substituent in each sugar is also *gauche–trans* [O5—C1—C9—C10 −66.7 (2)° and C2—C1—C9—C10 177.68 (18)° for (I), and O5—C1—C14—C15 −62.5 (3)° and C2—C1—C14—C15 178.6 (2)° for (II)]. In each sugar, the anomeric C1 hydroxy group forms an intramolecular hydrogen bond with the ethoxycarbonyl O atom (Tables 1 and 2), thereby closing a six-membered loop with a graph-set motif of *S*(6) (Bernstein *et al.*, 1995).

Experimental

Compounds (I) and (II) were synthesized from the corresponding 2,3,4,6-tetra-*O*-benzyl-D-glucono- or -D-galactono-1,5-lactone using the Reformatsky reaction (Shriner, 1942). The activated zinc used in the reaction was prepared by washing zinc dust successively with 5% HCl, distilled water, acetone, absolute ethanol and anhydrous ether, and then drying at 373 K under vacuum. The Reformatsky reaction produced the benzylated analogue of compound (I) and pure compound (II), respectively. Compound (I) was then obtained by converting its benzylated analogue to the acetylated derivative as follows. A solution of ethyl 2-deoxy-4,5,6,8-tetra-*O*-benzyl-α-D-*gluco*-3,7-pyranoso-3-octulosonate (0.5 g, 0.8 mmol) in ethanol (5 ml) was hydrogenated [10% palladium-on-charcoal (80 mg) under hydrogen (350 kPa)] for *ca* 12 h, after which thin-layer chromatography (hexane/ethyl acetate, 3:1) showed that all the starting material had been consumed. The solution was filtered, concentrated and acetylated with acetic anhydride (0.8 ml) in pyridine (1 ml). The reaction mixture was worked up in the usual manner and purified by flash column chromatography to give compound (I) (0.22 g, 64.2%; m.p. 383–385 K). Spectroscopic analysis: $[\alpha]_D$ 40.5° (*c* 4.38, $CHCl_3$); ^{1}H NMR ($CDCl_3$, δ, p.p.m.): 5.52 (*t*, 1H, $J_{3,4}$ = 9.5 Hz, H3), 5.09 (*t*, 1H, $J_{4,5}$ = 9.7 Hz, H4), 4.90 (*d*, 1H, $J_{2,3}$ = 9.7 Hz, H2), 4.22–4.31 (*m*, 1H, H5), 4.21 (*q*, 2H, $J_{12,13}$ = 7.1 Hz, H12*a*,*b*), 2.58, 2.64 (2 × *s*, 2H, H9*a*,*b*), 1.98, 2.01, 2.05, 2.09 (4 × *s*, 12H, 4 × CH_3CO), 1.27 (*t*, 3H, H13*a*,*b*,*c*); ^{13}C NMR ($CDCl_3$, δ, p.p.m.): 171.98, 170.01, 169.92, 169.52, 169.55 (C═O), 96.12 (C1), 72.54 (C2), 70.92 (C3), 68.52, 68.01 (C4 and C5), 61.82, 61.50 (C1 and C6), 61.50 (C9), 39.62 (C12), 20.53, 20.59 (CH_3CO), 13.88 (C13). Analysis calculated for $C_{18}H_{26}O_{12}$: C 49.79, H 9.66%; found: C 49.52, H 9.61%. Compound (II) was obtained in 85.5% yield (m.p. 389–392 K). Spectroscopic analysis: $[\alpha]_D$ −5.81 (*c* 10.69, $CHCl_3$); ^{1}H NMR ($CDCl_3$, δ, p.p.m.): 7.20–7.40 (*m*, 20H, Ar-*H*), 5.00, 4.95, 4.65, 4.61, 4.48, 4.42 (6 × *d*, 6H, *J* = 11.4–11.8 Hz, 3 × PhCH_2), 4.77 (*s*, 2H, H7*a*,*b*), 4.04–21 (*m*, 5H, H3–H5, H17*a*,*b*), 3.81 (*d*, 1H, $J_{2,3}$ = 9.8 Hz, H2), 3.74 (*dd*, 1H, $J_{5,6a}$ = 7.8 Hz, $J_{6a,6b}$ = 9.3 Hz, H6*a*), H6*a*), 3.48 (*dd*, 1H, H6*b*), 2.37, 2.83 (2 × *s*, 2H, H14*a*,*b*), 1.27 (*t*, 3H, H18*a*,*b*,*c*); ^{13}C NMR ($CDCl_3$, δ, p.p.m.): 172.44 (C═O), 127.46, 127.58, 127.72, 128.02, 128.12, 128.28, 128.32, 128.47, 138.04, 138.38, 138.77 (Ar-*C*), 97.60 (C1), 80.34 (C3), 78.34 (C2), 74.77 (C4), 72.52, 73.29, 74.60, 75.15 (PhCH_2), 70.08 (C5), 68.59 (C6 and C17), 40.56 (C14), 13.91 (C18). Analysis calculated for $C_{38}H_{42}O_8$: C 72.86, H 6.71%; found: C 72.03, H 6.80%. Suitable crystals of each compound were obtained by slow evaporation of their solutions in ethanol.

Compound (I)

Crystal data

$C_{18}H_{26}O_{12}$
M_r = 434.39
Monoclinic, $P2_1$
a = 9.3164 (15) Å
b = 13.038 (2) Å
c = 9.3130 (15) Å
β = 106.224 (12)°
V = 1086.2 (3) Å^3
Z = 2
D_x = 1.328 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 25 reflections
θ = 19.0–20.0°
μ = 0.11 mm^{-1}
T = 173 (1) K
Prism, colourless
0.46 × 0.33 × 0.24 mm

Data collection

Rigaku AFC-5*R* diffractometer
ω/2θ scans
6676 measured reflections
3285 independent reflections
2717 reflections with $I > 2\sigma(I)$
R_{int} = 0.024
θ_{max} = 30°
h = 0 → 13
k = −18 → 18
l = −13 → 12
3 standard reflections
every 150 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.106
S = 1.03
3285 reflections
280 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0554P)^2 + 0.1486P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.49 e Å^{-3}
$\Delta\rho_{min}$ = −0.36 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °) for (I).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O10	0.79 (4)	2.11 (4)	2.794 (3)	146 (4)

Compound (II)

Crystal data

$C_{38}H_{42}O_8$
M_r = 626.72
Orthorhombic, $P2_12_12_1$
a = 14.977 (2) Å
b = 19.832 (7) Å
c = 11.326 (2) Å
V = 3364.0 (14) Å^3
Z = 4
D_x = 1.237 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 25 reflections
θ = 11.0–17.5°
μ = 0.09 mm^{-1}
T = 173 (1) K
Prism, colourless
0.50 × 0.33 × 0.30 mm

Data collection

Rigaku AFC-5*R* diffractometer
ω/2θ scans
4998 measured reflections
4302 independent reflections
3230 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 27.5°
h = 0 → 19
k = −1 → 25
l = −1 → 14
3 standard reflections
every 150 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.042$
$wR(F^2) = 0.103$
$S = 1.03$
4302 reflections
421 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0379P)^2 + 0.5383P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.22$ e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.0024 (5)

Table 2
Hydrogen-bonding geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O15	0.77 (3)	2.10 (3)	2.765 (3)	145 (3)

Examination of the structure of (I) with *PLATON* (Spek, 2001) revealed that the unit-cell parameters can be transformed metrically to an orthorhombic *C* lattice, but that the overall structure itself is not consistent with the higher symmetry. For (I), the anisotropic displacement ellipsoids for O16 and, to a lesser extent, O18 are significantly elongated. In addition, the maximum peak of residual electron density of 0.49 e Å^{-3} is 1.0 Å from O16 and the next highest peak is only 0.25 e Å^{-3}. This suggests that these two atoms may be disordered, particularly O16. Indeed, the position of O16 could be divided into two almost equally occupied sites that are approximately 0.5 Å apart, and the refinement of this model reduced $R(F)$ to 0.035 and the maximum peak of residual electron density to 0.25 e Å^{-3}. Nevertheless, the anisotropic displacement ellipsoid for one of the disordered positions became even more elongated than that of O16 in the ordered model, even when light restraints were applied, and more severe restraints upset the realism of the geometric parameters. Therefore, it was considered to be more appropriate to use the ordered model in the final refinement. For each compound, the methyl H atoms were constrained to an ideal geometry (C—H = 0.98 Å) with $U_{iso}(H) = 1.5U_{eq}(C)$, but were allowed to rotate freely about the C—C bonds. The positions of the hydroxy H atoms were refined freely, along with individual isotropic displacement parameters. All other H atoms were placed in geometrically idealized positions (C—H = 0.95–1.00 Å) and constrained to ride on their parent atoms, with $U_{iso}(H) = 1.2U_{eq}(C)$. The absolute configuration could not be determined because of the absence of significant anomalous scatterers in the compound, and attempts to confirm the absolute structure by refinement of the Flack parameter (Flack, 1983) led to inconclusive values (Flack & Bernardinelli, 2000) for this parameter [−0.7 (7) for (I) and −0.3 (11) for (II)]. Therefore, Friedel equivalents [3030 for (I) and 560 for (II)] were merged before the final refinements. The enantiomer used in each model was based on the known chirality of the precursor sugars, *viz.* D-glucose and D-galactose, from which (I) and (II), respectively, were synthesized.

For both compounds, data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1991); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1999); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97 and *PLATON* (Spek, 2001).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1083). Services for accessing these data are described at the back of the journal.

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