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2,3,3′,6-Tetra-*O*-acetyl-4,1′,6′-trichloro-4,1′,4′,6′-tetradeoxygalactosucrose

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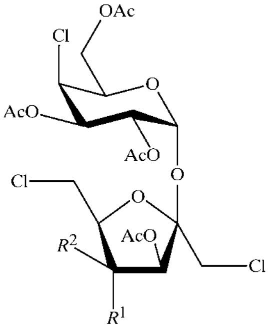
At 160 K, one of the Cl atoms in the furanoid moiety of 3-*O*-acetyl-1,6-dichloro-1,4,6-trideoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranoside, $C_{20}H_{27}Cl_3O_{11}$, is disordered over two orientations, which differ by a rotation of about 107° about the parent C—C bond. The conformation of the core of the molecule is very similar to that of 3-*O*-acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-tagatofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranoside, particularly with regard to the conformation about the glycosidic linkage.

Comment

Halogenated analogues of sucrose are unique among sugar compounds in that they are generally intensely sweet, some of these compounds being several thousand times sweeter than sucrose (Lee, 1982, 1983, 1987). There is still no clear explanation for this. Although the Shallenberger & Acree–Kier AH,B,γ hypothesis (Shallenberger & Acree, 1967; Kier, 1972) is currently the most accepted model for explaining the sweetness of a compound, the location of this tripartite glucophore for this group of compounds is still being debated intensely. It is fairly widely accepted that the intense sweetness of the halodeoxysucrose analogues is directly related to the presence of one or more of the halogen substituents. For this reason, we are interested in the syntheses and structures of these analogues and, as part of this programme, the crystal structure of the title compound, (I), has been determined.

The absolute configuration of (I) has been determined confidently by refinement of the absolute structure parameter (Flack, 1983) and is shown in Fig. 1. The Cl atom of the chloromethyl substituent at C7 in the furanoid moiety is disordered over two orientations, which differ by a rotation of approximately 107° about the parent C7—C12 bond. The major conformation is present in approximately 94% of the molecules. The bond lengths and angles exhibit normal values, and generally agree with those of sucrose (Brown & Levy, 1963, 1973; Hanson *et al.*, 1973) and the related chlorinated derivatives 3-*O*-acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranoside, (II) (Lee, 1982, 1983), and 3-*O*-acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-tagatofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranoside, (III) (Lee *et al.*, 1999). The torsion angles about the anomeric O1 atom (Table 1) are also very similar to those in sucrose and (III), but differ from those in (II).



(I) $R^1{=}R^2{=}H$
(II) $R^1{=}Cl; R^2{=}H$
(III) $R^1{=}H; R^2{=}Cl$

The C5 hydroxymethyl and C10 chloromethyl substituents have *gauche–trans* conformations, while the major conformation of the C7 chloromethyl substituent is *gauche–gauche*. These conformations are the same as in the related chlorinated derivatives, (II) and (III), and sucralose (Kanters *et al.*, 1988). In sucrose, however, both the C5 and C10 hydroxymethyl substituents are *gauche–gauche*, while that at C7 is *trans–gauche*. The *gauche–trans* conformation for O6 in (I) avoids any 1,3-*peri* interaction between atoms O6 and Cl4. For the major conformation of the C7 chloromethyl substituent, the *gauche–gauche* conformation places atom Cl2*A* under the furanose ring, thereby avoiding both possible *peri* interactions with atoms O10 and O8, and also a repulsive dipole–dipole interaction between atom Cl2*A* and the anomeric O1 atom.

The minor conformation of the C7 chloromethyl substituent has a *trans–gauche* conformation, as found in sucrose. This actually brings atom Cl2*B* within 2.589 (10) Å of atom O19 of the acetyl substituent at C8, which is unreasonably close. However, the enlarged atomic displacement ellipsoids for atoms O19 and C20 suggest that these atoms might also be disordered, thereby alleviating the short Cl2*B*···O19 contact caused by the use of averaged positions for the latter atom. However, due to the very low proportion of this disordered component in the structure, no attempt was made to define disordered positions for atoms O19 and C20.

The glucopyranosyl ring in compound (I) adopts the $^4C_1$ chair conformation. The puckering parameters (Cremer & Pople, 1975) are Q = 0.5832 (18) Å, q_2 = 0.0288 (18) Å, q_3 = 0.5825 (18) Å, θ = 2.84 (18)° and φ_2 = 113 (3)°. The puckering amplitudes ($q_3 >> q_2$) of the pyranose ring describe a slightly distorted chair. Indeed, the total puckering amplitude (Q) is only slightly lower than that of the ideal cyclohexane chair

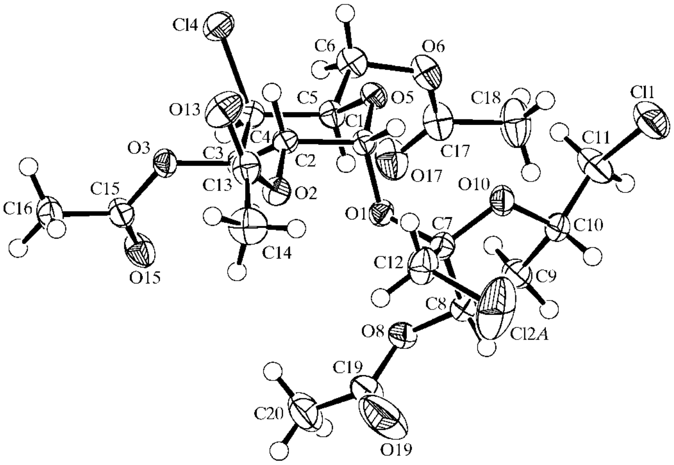


Figure 1
A view of the major conformation (94% contribution) of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented by spheres of arbitrary size.

[0.63 Å for δ(C—C) = 1.54 Å]. The magnitude of the distortion is significantly less than in the related fructofuranosyl and tagatofuranosyl derivatives, (II) and (III) [θ = 4.7 (4) and 5.0 (3)°, respectively; Lee *et al.*, 1999], but comparable with that of sucralose (θ = 1.9°; Kanters *et al.*, 1988). With φ_2 being close to 120°, the distortion is towards the boat $^{2,5}B$ conformation. The furanoid ring in (I) has the envelope ^9E conformation (*i.e.* ^4E with conventional furanosyl-ring numbering), with puckering parameters θ_2 = 0.410 (2) Å and φ_2 = 283.4 (3)°. Atom C9 lies 0.632 (3) Å from the plane defined by atoms C7, C8, C10 and O10. The same conformation is found in (III) [φ_2 = 291.3 (4)°], whereas a twisted conformation is present in (II) [φ_2 = 268.1 (6)°] (Lee *et al.*, 1999).

Experimental

Carbon tetrachloride (1 ml, 6.49 mmol) was added dropwise to a stirred solution of 3-*O*-acetyl-4-deoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (0.39 g, 0.79 mmol) and triphenylphosphine (1.65 g, 6.29 mmol) in pyridine (25 ml) under an argon atmosphere at room temperature. The reaction mixture was stirred for 30 min at room temperature, before being heated at ~358 K for 1 h. After all the starting material had reacted, as indicated by thin-layer chromatography (ethyl acetate–hexane, 1:2), the reaction mixture was diluted with dichloromethane, washed with dilute HCl (10%), saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated. The crude product was flash chromatographed (ethyl acetate–hexane, 1:2) to give the title compound, (I) (0.41 g, 87%); m.p. 381–382 K (CH_2Cl_2). Spectroscopic analysis: $[\alpha]_D$ +70.2° (*c* 0.83, $CHCl_3$); ^{1}H NMR (300.13 MHz, $CDCl_3$, δ, p.p.m.; the assignments employ the crystallographic atom numbering used in Fig. 1): 1.93–2.01 (*m*, 1H, H9*a*), 2.00–2.07 (4 × *s*, 12H, 4 × CH_3), 2.50–2.59 (*m*, 1H, H9*b*), 3.39–3.72 (*m*, 4H, H11*a*,*b*, H12*a*,*b*), 4.10–4.32 (*m*, 3H, H6*a*,*b*, H10), 4.47–4.52 (*m*, 2H, H4, H5), 5.19 (*dd*, 1H, $J_{2,3}$ = 10.8, $J_{3,4}$ = 3.0 Hz, H3), 5.25 (*dd*, 1H, $J_{1,2}$ = 3.1, $J_{2,3}$ = 10.8 Hz, H2), 5.45 (*dd*, 1H, $J_{8,9a}$ = 7.3, $J_{8,9b}$ = 9.7 Hz, H8), 5.56 (*d*, 1H, $J_{1,2}$ = 3.1 Hz, H1); ^{13}C NMR (75.47 MHz, $CDCl_3$, δ, p.p.m.): 170.3, 170.1, 169.9, 169.7 (CO*C*H_3), 104.5, (C7), 89.7 (C1), 78.4 (C10), 72.7 (C8), 68.2 (C3), 67.6 (C5), 66.8 (C2), 64.0 (C6), 59.0 (C4), 45.4, 45.1 (C11, C12), 33.0 (C9), 20.7, 20.6 (CO*C*H_3); HRMS–ESI (positive mode), calculated for $[M + Na]^+$: 571.0517:573.0487:575.0457; found: 571.0496:573.0481:575.0469. Suitable crystals were obtained by slow evaporation of a dilute solution of (I) in dichloromethane.

Crystal data

$C_{20}H_{27}Cl_3O_{11}$
M_r = 549.78
Triclinic, *P*1
a = 8.2962 (1) Å
b = 9.4622 (1) Å
c = 9.9471 (3) Å
α = 61.6508 (6)°
β = 69.9690 (6)°
γ = 71.4651 (11)°
V = 634.15 (2) Å^3

Z = 1
D_x = 1.439 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 38 452 reflections
θ = 2.0–30.0°
μ = 0.42 mm^{-1}
T = 160 (1) K
Prism, colourless
0.20 × 0.15 × 0.12 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans with κ offsets
Absorption correction: multi-scan (Blessing, 1995)
T_{min} = 0.922, T_{max} = 0.953
33 175 measured reflections

7135 independent reflections
6346 reflections with $I > 2\sigma(I)$
R_{int} = 0.039
θ_{max} = 30.1°
$h = -11 \rightarrow 11$
$k = -13 \rightarrow 13$
$l = -13 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.089
S = 1.03
7125 reflections
322 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0470P)^2 + 0.0721P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max}$ = 0.004
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.32 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.050 (6)
Absolute structure: Flack (1983), with 3437 Friedel pairs
Flack parameter = 0.00 (3)

Table 1
Selected geometric parameters (Å, °).

O1—C1	1.4144 (17)	O5—C5	1.4330 (18)
O1—C7	1.4230 (18)	O10—C7	1.4062 (19)
O5—C1	1.4168 (18)	O10—C10	1.444 (2)
C1—O1—C7	118.44 (11)		
C7—O1—C1—O5	113.88 (13)	O10—C10—C11—Cl1	71.71 (19)
C7—O1—C1—C2	−126.82 (13)	C9—C10—C11—Cl1	−172.02 (13)
O5—C5—C6—O6	65.61 (16)	O1—C7—C12—Cl2*A*	179.51 (12)
C4—C5—C6—O6	−171.30 (12)	O10—C7—C12—Cl2*A*	−59.30 (17)
C17—O6—C6—C5	87.23 (18)	C8—C7—C12—Cl2*A*	60.03 (18)
C1—O1—C7—O10	−46.08 (17)	O1—C7—C12—Cl2*B*	72.2 (4)
C1—O1—C7—C8	−160.75 (12)	O10—C7—C12—Cl2*B*	−166.6 (4)
C1—O1—C7—C12	73.76 (17)	C8—C7—C12—Cl2*B*	−47.3 (4)

One Cl atom in the furanoid moiety, Cl2, is disordered over two positions, *A* and *B*. The site-occupancy factors of the disordered atoms were refined, while constraining their sum for the two conformations to 1.0. The major conformation was found to be present in 93.9 (2)% of the molecules. A bond-length restraint was applied to the C—Cl bond involving the minor conformation so as to maintain reasonable geometry. 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. All other H

Acta Cryst. (2002). C**58**, o718–o720 Linden *et al.* • $C_{20}H_{27}Cl_3O_{11}$ **o719**

atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C—H distances in the range 0.99–1.00 Å and $U_{\rm iso}$(H) = 1.2$U_{\rm eq}$(C). The determined absolute configuration agreed with that expected for a natural sucrose derivative. Ten low-angle reflections were omitted from the final cycles of refinement because their observed intensities were much lower than the calculated values, as a result of being partially obscured by the beam stop.

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *DENZO–SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO–SMN* and *SCALEPACK* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); 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, 2002).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1597). Services for accessing these data are described at the back of the journal.

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o720 Linden *et al.* • $C_{20}H_{27}Cl_3O_{11}$ *Acta Cryst.* (2002). C**58**, o718–o720