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Note

# The crystal structure of methyl 5-*O*-acetyl-2-*O*-benzo l-3,4-*O*-isopropylidene-β-L-idoseptanoside

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Vicinal proton–proton spin-coupling constants for methyl 5-*O*-acetyl-2-*O*-benzoyl-3,4-*O*-isopropylidene-β-L-idoseptanoside (**1**) have led to the assignment [1] of the twist-chair conformation, $^{O,1}TC_{2,3}$ [2], for the seven-membered ring in **1** in which the pseudo-axis of symmetry passes through C-5. Since this is in contrast to a structure isomeric at C-5, methyl 2,5-di-*O*-acetyl-3,4-*O*-isopropylidene-α-D-glucoseptanoside (**2**), in which the seven-membered ring adopts the twist-chair conformation $^{4,5}TC_{6,O}$ with the pseudo-axis of symmetry passing through C-2 [3], we have carried out a single-crystal X-ray diffraction study of **1** in order to determine its solid state conformation.

Bond angles within the seven-membered ring are all greater than the tetrahedral angle. This is in keeping with the values found for a large number of septanose carbohydrates [4–19] and for the parent heterocycle, oxepane, as determined by Bocian and Strauss [20,21].

An examination of the ring torsional angles shows that the ring conformation is a twist-chair with the pseudo-axis of symmetry passing through C-5, conformation $^{O,1}TC_{2,3}$ [2]. In their study of oxepane, Bocian and Strauss [20] concluded that there are two pairs of low-energy twist-chair conformations, with the pseudo-axis of symmetry passing through a carbon atom attached to oxygen (twist-chair C and C′) and passing through a carbon atom once removed from oxygen (twist-chair B and B′). For

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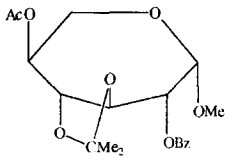
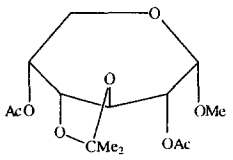
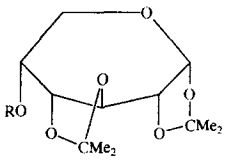
aldohexoseptanose derivatives, which do not possess the symmetry elements of oxepane itself, these conformations (with the atom through which the pseudo-axis of symmetry passes in brackets) are as follows: $^{5,6}TC_{3,4}$ and $^{3,4}TC_{5,6}$ (C-1), $^{3,4}TC_{1,2}$ and $^{1,2}TC_{3,4}$ (C-6) (corresponding to twist-chairs C and C′ of oxepane); and $^{4,5}TC_{6,O}$ and $^{6,O}TC_{4,5}$ (C-2), $^{2,3}TC_{O,1}$ and $^{O,1}TC_{2,3}$ (C-5) (corresponding to twist-chair B and B′ of oxepane); which account for eight of the fourteen possible twist-chair conformations. For examples of compounds for which the pseudo-axis of symmetry passes through C-1, see refs. [5–7,13–15,18].




1

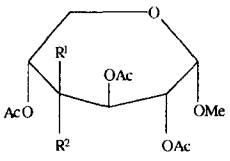



2




**3a** R = $COCH_2Cl$

**3b** R = Ac




**4** $R^1$ = H; $R^2$ = OAc

**5** $R^1$ = OAc; $R^2$ = H

We have found examples of the twist-chair B,B′ conformations in which the pseudo-axis of symmetry passes through C-2 of the aldohexoseptanose ring in 5-*O*-chloroacetyl-1,2:3,4-di-*O*-isopropylidene-α-D-glucoseptanose (**3a**) [4] and the corresponding 5-acetate, **3b** [17], methyl α-D-glucoseptanoside tetraacetate (**4**) [9], and methyl α-D-galactoseptanoside tetraacetate (**5**) [11]. The close relationship between the conformation

Table 1
Ring torsional angles (°) [a]

| Compound | $\tau_1$ | $\tau_2$ | $\tau_3$ | $\tau_4$ | $\tau_5$ | $\tau_6$ | $\tau_7$ |
|---|---|---|---|---|---|---|---|
| **1** | −32 | −49 | 95 | −68 | 49 | −79 | 98 |
| **3a** | −32 | −48 | 92 | −65 | 50 | −84 | 97 |
| **3b** | −29 | −49 | 90 | −66 | 52 | −84 | 94 |
| **3b** | −26 | −53 | 92 | −64 | 51 | −84 | 93 |
| **4** | −31 | −46 | 84 | −63 | 53 | −85 | 95 |
| **5** | −34 | −45 | 85 | −61 | 50 | −84 | 98 |
| Oxepane | −47 | −34 | 84 | −70 | 54 | −80 | 102 |

[a] For **3–5**, $\tau_1$ = O-6–C-1–C-2–C-3, $\tau_2$ = C-1–C-2–C-3–C-4, etc.; and for **1**, $\tau_1$ = O-6–C-6–C-5–C-4, $\tau_2$ = C-6–C-5–C-4–C-3, etc.

of **1** and the conformations of **3**, **4**, and **5** is evident from the ring torsional angles (rounded to whole degrees) in Table 1. Oxepane values [20,21] are included in that table. Torsional angles $\tau_3$ for **1** and **3** are significantly greater than those observed for **4** and **5** This may be explained by the conformational restraints imposed by the trans-fused 1,3-dioxolane ring in **1** and **3** for which the reduction of the torsional angle O-3–C-3–C-4–O-4, compared with that of **4** and **5**, towards the optimum value for an *O*-isopropylidene ring (thought to be 18–25° [22]), results in an increase in $\tau_3$.

The orientation of the methoxy group in **1** is such that the methyl group is *gauche* to the ring oxygen O-6. This arrangement is similar to that found for a variety of glycosides [23,24] and corresponds to the low-energy conformation of dimethoxymethane as deduced by molecular orbital calculations [25].

## 1. Experimental

*Crystal data.*—Needle crystals were obtained from an ethanol–ethyl acetate solution: $C_{19}H_{24}O_8$, $M = 380.4$; orthorhombic, space group $P2_12_12_1$; $a = 9.4804(4)$, $b = 10.3935(5)$, $c = 20.2776(6)$ Å; $V = 1998.0(1)$ Å$^3$; $D_c = 1.26$ g cm$^{-3}$; $Z = 4$; $\mu_{Cu} = 7.92$ cm$^{-1}$; crystal size $0.11 \times 0.16 \times 0.47$ mm; $2\theta_{max} = 140°$; min. and max. transmission factors 0.80 and 0.90. The number of reflexions was 1796 considered observed out of 2174 unique data. Final residuals $R$ and $R_w$ were 0.048 and 0.073.

*Structure determination.*—Reflexion data were measured with an Enraf–Nonius CAD-4 diffractometer in $\theta/2\theta$ scan mode using nickel-filtered copper radiation ($\lambda$ 1.5418 Å). Data were corrected for absorption using the method of de Meulenaer and Tompa [26]. Reflexions with $I > 3\sigma(I)$ were considered observed. The structure was determined by direct phasing and Fourier methods. Hydrogen atoms were included in

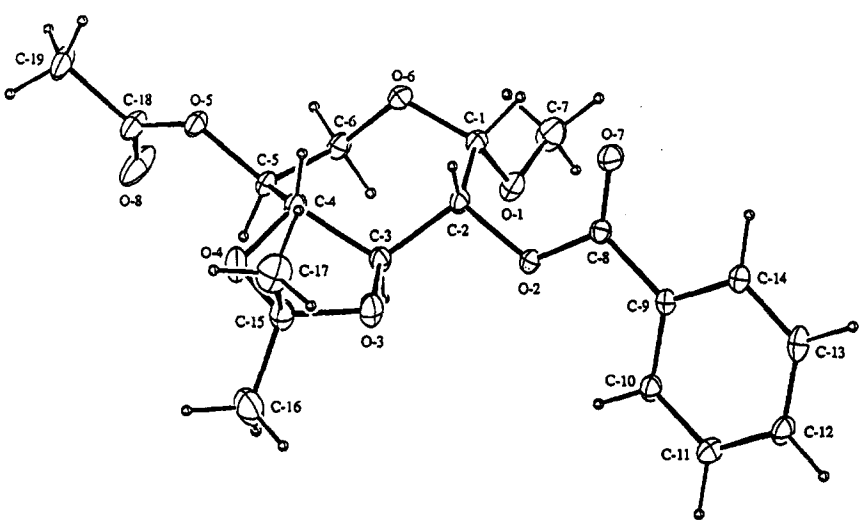



Fig. 1. ORTEP plot of **1**, showing atomic notation and thermal ellipsoids.

Table 2
Non-hydrogen atomic parameters [with estimated standard deviations (esds) in parentheses]

| | $x$ | $y$ | $z$ | $B_{eq}$ [a] |
|---|---|---|---|---|
| O-1 | 0.3538(3) | 0.1902(3) | 0.1945(1) | 5.93(8) |
| O-2 | 0.4520(3) | 0.1484(3) | 0.3159(1) | 4.60(7) |
| O-3 | 0.7370(3) | 0.1728(5) | 0.3115(1) | 7.07(11) |
| O-4 | 0.8934(3) | 0.1630(4) | 0.2263(1) | 6.73(10) |
| O-5 | 0.8282(3) | 0.0928(3) | 0.0905(1) | 5.23(7) |
| O-6 | 0.5131(3) | 0.0546(3) | 0.1423(1) | 4.80(7) |
| O-7 | 0.3344(4) | −0.0324(3) | 0.3312(2) | 6.56(9) |
| O-8 | 0.8509(7) | 0.2527(4) | 0.0217(2) | 11.57(20) |
| C-1 | 0.4324(4) | 0.0811(4) | 0.2000(2) | 4.51(9) |
| C-2 | 0.5280(4) | 0.0908(4) | 0.2615(2) | 4.53(10) |
| C-3 | 0.6569(4) | 0.1779(4) | 0.2516(2) | 4.64(9) |
| C-4 | 0.7626(4) | 0.1195(4) | 0.2016(2) | 4.75(10) |
| C-5 | 0.7397(4) | 0.1701(4) | 0.1335(2) | 4.52(9) |
| C-6 | 0.5861(5) | 0.1631(4) | 0.1134(2) | 4.97(10) |
| C-7 | 0.2364(6) | 0.1776(7) | 0.1503(3) | 8.32(18) |
| C-8 | 0.3625(4) | 0.0752(4) | 0.3479(2) | 3.91(8) |
| C-9 | 0.3050(4) | 0.1374(4) | 0.4085(2) | 3.91(8) |
| C-10 | 0.3403(4) | 0.2618(4) | 0.4249(2) | 4.91(10) |
| C-11 | 0.2929(5) | 0.3110(5) | 0.4844(2) | 6.19(13) |
| C-12 | 0.2075(5) | 0.2417(5) | 0.5253(2) | 5.80(12) |
| C-13 | 0.1693(5) | 0.1177(5) | 0.5079(2) | 5.96(13) |
| C-14 | 0.2182(4) | 0.0655(4) | 0.4493(2) | 4.55(9) |
| C-15 | 0.8844(4) | 0.1640(6) | 0.2969(2) | 6.03(13) |
| C-16 | 0.9616(7) | 0.2794(9) | 0.3214(4) | 10.31(25) |
| C-17 | 0.9370(8) | 0.0422(8) | 0.3249(3) | 9.71(23) |
| C-18 | 0.8845(6) | 0.1477(5) | 0.0393(2) | 6.55(14) |
| C-19 | 0.9805(6) | 0.0583(5) | 0.0021(3) | 7.91(16) |

[a] $B_{eq}$ (Å$^2$) is the isotropic equivalent of the anisotropic temperature factor.

Table 3
Bond lengths (Å) [a]

| | | | |
|---|---|---|---|
| C-1–C-2 | 1.544(5) | C-11–C-12 | 1.365(6) |
| C-2–C-3 | 1.535(5) | C-12–C-13 | 1.384(7) |
| C-3–C-4 | 1.550(5) | C-13–C-14 | 1.387(6) |
| C-4–C-5 | 1.494(5) | C-14–C-9 | 1.386(5) |
| C-5–C-6 | 1.514(6) | C-3–O-3 | 1.433(4) |
| C-6–O-6 | 1.447(5) | C-4–O-4 | 1.411(5) |
| O-6–C-1 | 1.426(4) | O-3–C-15 | 1.431(5) |
| C-1–O-1 | 1.361(5) | C-15–O-4 | 1.435(5) |
| O-1–C-7 | 1.435(6) | C-15–C-16 | 1.491(9) |
| C-2–O-2 | 1.447(4) | C-15–C-17 | 1.474(9) |
| O-2–C-8 | 1.312(4) | C-5–O-5 | 1.452(4) |
| C-8–O-7 | 1.199(4) | O-5–C-18 | 1.300(5) |
| C-8–C-9 | 1.492(5) | C-18–O-8 | 1.192(6) |
| C-9–C-10 | 1.376(5) | C-18–C-19 | 1.503(6) |
| C-10–C-11 | 1.386(6) | | |

[a] Esds in parentheses.

Table 4
Selected bond angles (°) [a]

| | | | |
|---|---|---|---|
| O-6–C-1–C-2 | 111.1(3) | C-3–C-4–O-4 | 102.2(3) |
| C-1–C-2–C-3 | 113.6(3) | C-4–O-4–C-15 | 107.7(3) |
| C-2–C-3–C-4 | 111.7(3) | O-4–C-15–O-3 | 105.3(3) |
| C-3–C-4–C-5 | 111.9(3) | C-15–O-3–C-3 | 110.2(3) |
| C-4–C-5–C-6 | 111.8(3) | C-2–C-3–O-3 | 106.8(3) |
| C-5–C-6–O-6 | 112.8(3) | C-5–C-4–O-4 | 110.1(3) |
| C-6–O-6–C-1 | 116.1(3) | O-3–C-15–C-16 | 111.0(5) |
| O-6–C-1–O-1 | 112.7(3) | O-3–C-15–C-17 | 107.8(5) |
| C-2–C-1–O-1 | 109.5(3) | O-4–C-15–C-16 | 108.0(5) |
| C-1–O-1–C-7 | 113.6(4) | O-4–C-15–C-17 | 110.9(5) |
| C-1–C-2–O-2 | 110.5(3) | C-16–C-15–C-17 | 113.4(5) |
| C-3–C-2–O-2 | 104.6(3) | C-4–C-5–O-5 | 106.0(3) |
| C-2–O-2–C-8 | 117.3(3) | C-6–C-5–O-5 | 111.6(3) |
| O-3–C-3–C-4 | 101.4(3) | C-5–O-5–C-18 | 118.3(3) |

[a] Esds in parentheses.

calculated positions and were assigned thermal parameters equal to those of the atom to which they were bonded. Positional and anisotropic thermal parameters for the non-hydrogen atoms were refined using full-matrix least squares. Reflexion weights used were $1/\sigma^2(F_o)$, with $\sigma(F_o)$ being derived from $\sigma(I_o) = [\sigma^2(I_o) + (0.04I_o)^2]^{1/2}$. The weighted residual is defined as $R_w = (\Sigma w\Delta^2/\Sigma wF_o^2)^{1/2}$. Atomic scattering factors and anomalous dispersion parameters were from International Tables for X-ray Crystallography [27]. Structure solution was by MULTAN-80 [28] and refinement used BLOCKLS, a local version of ORFLS [29]. ORTEP-II [30] running on a Macintosh IIcx was used for the structural diagram, and an IBM 3090 computer was used for calculations.

Table 5
Selected torsional angles (°) [a]

| | | | |
|---|---|---|---|
| O-6–C-1–C-2–C-3 | 48.6(4) | O-6–C-1–O-1–C-7 | 71.4(4) |
| C-1–C-2–C-3–C-4 | −67.8(4) | C-2–C-1–O-1–C-7 | −164.3(4) |
| C-2–C-3–C-4–C-5 | 95.0(4) | O-6–C-1–C-2–O-2 | 165.7(3) |
| C-3–C-4–C-5–C-6 | −48.9(5) | C-4–C-3–C-2–O-2 | 171.7(3) |
| C-4–C-5–C-6–O-6 | −32.2(5) | C-1–C-2–O-2–C-8 | 77.6(4) |
| C-5–C-6–O-6–C-1 | 98.0(4) | C-3–C-2–O-2–C-8 | −159.8(3) |
| C-6–O-6–C-1–C-2 | −78.8(4) | C-2–O-2–C-8–C-9 | 171.9(3) |
| O-3–C-3–C-4–O-4 | −33.9(4) | O-2–C-8–C-9–C-10 | 3.2(5) |
| C-3–C-4–O-4–C-15 | 35.5(5) | C-1–C-2–C-3–O-3 | −177.8(3) |
| C-4–O-4–C-15–O-3 | −23.2(6) | C-5–C-4–C-3–O-3 | −151.6(4) |
| O-4–C-15–O-3–C-3 | −0.3(7) | C-2–C-3–C-4–O-4 | −147.3(3) |
| C-15–O-3–C-3–C-4 | 20.9(5) | C-6–C-5–C-4–O-4 | −161.8(4) |
| O-1–C-1–C-2–O-2 | 40.5(4) | C-3–C-4–C-5–O-5 | −170.8(3) |
| O-2–C-2–C-3–O-3 | 61.7(4) | O-6–C-6–C-5–O-5 | 86.4(3) |
| O-4–C-4–C-5–O-5 | 76.4(4) | C-4–C-5–O-5–C-18 | −146.2(4) |
| C-6–O-6–C-1–O-1 | 44.6(4) | C-6–C-5–O-5–C-18 | 91.8(5) |
| C-3–C-2–C-1–O-1 | −76.6(4) | C-5–O-5–C-18–C-19 | 176.3(4) |

[a] Esds in parentheses.

The structure and atom numbering scheme is shown in Fig. 1. Atomic parameters, bond lengths, and selected bond angles and torsional angles are given in Tables 2–5, respectively. Tables of all atom and thermal parameters, interatomic distances, angles and torsional angles, and observed and calculated structure factors have been deposited with the Cambridge Crystallographic Data Centre [1].

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[1] Data may be obtained from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.