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CONFORMATIONS OF SEPTANOSIDES. THE CRYSTAL AND MOLECULAR STRUCTURE OF 5-*O*-(CHLOROACETYL)-1,2:3,4-DI-*O*-ISOPROPYLIDENE-α-D-GLUCOSEPTANOSE

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ABSTRACT

The crystal structure of 5-*O*-(chloroacetyl)-1,2:3,4-di-*O*-isopropylidene-α-D-glucoseptanose, a seven-membered ring sugar, has been determined by using 1234 reflections measured on a diffractometer. The crystals belong to the orthorhombic space group $P2_12_12_1$, having cell dimensions $a = 27.750$, $b = 10.714$, and $c = 5.702$ Å. The measured and calculated densities are 1.25 $g.cm^{-3}$ and 1.32 $g.cm^{-3}$, respectively; the latter value assumed four molecules in the unit cell. The structure was determined by a combination of the heavy-atom technique and the tangent method. Full-matrix least-squares refinement with anisotropic temperature factors for the nonhydrogen atoms and isotropic temperature factors for the hydrogen atoms lowered the conventional *R* value to 0.066. The seven-membered ring adopts a $^{5,6}C_2$(D) twist-chair conformation. Both of the dioxolane rings have the envelope shape, the puckered atoms being C-2 and C-4 of the seven-membered ring. The molecular packing is dominated by Van der Waals forces. The conformations of three known 7-membered ring sugars are compared. It is found that the pseudorotation of the septanose ring and the dioxolane rings are correlated to the position of attachment of the latter rings to the central septanose ring.

INTRODUCTION

X-Ray diffraction studies on five- and six-membered sugar derivatives have provided a wealth of information pertaining to their molecular dimensions and conformations[1–5]. The twist form in the furanoses and the chair form in the pyranoses are by far the most prevalent. In our continuing studies on carbohydrates we have determined the crystal structure of the seven-membered ring sugar 5-*O*-(chloroacetyl)-1,2:3,4-di-*O*-isopropylidene-α-D-glucoseptanose (**1**). A preliminary communication on

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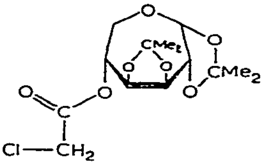
this work has already been published[7]. Since then, crystallographic structures of two other related seven-membered ring sugars, ethyl 2,3:4,5-di-*O*-isopropylidene-1-thio-β-D-glucoseptanoside (**2**) and methyl 2,3:4,5-tetra-*O*-acetyl-β-D-glucoseptanoside (**3**) have been reported[8]. The primary motivation for the present study was to obtain information on the shape of the 7-membered septanoid ring in the solid state for comparison with the coupling constants obtained from proton magnetic resonance studies in solution[9]. From theoretical calculations, Hendrickson has shown that the parent hydrocarbon cycloheptane can adopt several conformations[10]. He predicted that the twist-chair conformation is energetically the most favored. It was of interest, therefore, to study the effect of the ring-oxygen atom and the substituents on the favored conformation of the septanoid ring.



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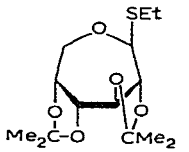

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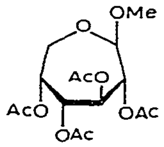

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EXPERIMENTAL

Crystals of compound **1** grown in aqueous ethanol were kindly supplied by Dr. John D. Stevens of the University of New South Wales, Australia. A crystal measuring $0.14 \times 0.21 \times 0.27$ mm^3 was used for the X-ray work. The unit-cell dimensions are given in Table I. The X-ray intensity data were collected on an automated diffractometer up to a 2θ value of 126° by using the $\theta-2\theta$ scan mode, a scan speed of 2° per min, and a take-off angle of 4°. Backgrounds were measured for 20 seconds on either side of each reflection. A standard reflection was checked every two hours and it showed a linear rate of decay. At the conclusion of the data collection,

TABLE I

CRYSTAL DATA FOR 5-*O*-(CHLOROACETYL)-1,2:3,4-DI-*O*-ISOPROPYLIDENE-α-D-GLUCOSEPTANOSE[a] (**1**)

Cell constants[b]	*Systematic absences*	*Space group*	D_{calc}	D_{obs}[c]	*Z*
a 27.750 (2) *b* 10.714 (1) *c* 5.702 (1)	$h00$, $h = 2n+1$ $0k0$, $k = 2n+1$ $00l$, $l = 2n+1$	$P2_12_12_1$	1.25 g·cm^{-3}	1.32 g·cm^{-3}	4

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[a] M.p. 117–118°; colorless transparent crystals that became yellow on irradiation by X-rays. [b] Nickel-filtered copper radiation ($\lambda = 1.5418$ Å) was used for both cell-constant measurements and data collection. The cell constants were obtained by a least-squares refinement of the 2θ values of about 12 carefully measured reflections. [c] By flotation in KI solution; apparently the crystals showed some reactivity to the solution, hence the poor agreement with the calculated value.

the standard had decreased by 12%. The data were corrected for crystal decay, the anisotropy in absorption (~5%) caused by the inequality in crystal crosssection, and the usual Lorentz and polarization factors. Altogether, 1234 reflections were considered observed, with $F_0 \geq 1.8\ \sigma(F)$ where $\sigma(F) = (19.6 + |F_0| + 0.015\ F_0|^2)^{1/2}$.

STRUCTURE DETERMINATION AND REFINEMENT

The coordinates of the chlorine atom were obtained from the Harker sections of an E^2-1 Patterson map, where E is the normalized structure-factor. Based on the position of chlorine, the phases of 395 reflections having $E \geq 1.10$ were determined and refined by application of the tangent formula[11]. The resulting E-map revealed the complete structure unambiguously. Several cycles of full-matrix least-squares[12] refinement by using isotropic atoms gave an agreement index $R\ (=\Sigma\big||F_0|-|F_c|\big|/\Sigma|F_0|)$ of 0.13. A difference density-map revealed the positions of all of the hydrogen atoms. Further refinement was continued, with anisotropic temperature-factors for nonhydrogen atoms and isotropic temperature-factors for hydrogen atoms, until the ratios of the shifts to estimated standard errors in all of the parameters were considerably less than unity. The final R value for the 1234 observed reflections was 0.066. The difference density-map obtained by subtracting all of the atoms did not reveal any electron density above the expected background.

Cruickshank's[13] weighting scheme was used in the least-squares refinement, where

$$1/w = \sigma^2(F) = 19.6 + |F_0| + 0.015|F_0|^2.$$

The scattering factors for carbon, oxygen, and chlorine were those of Cromer and Waber[14], and that of the hydrogen atom was that of Stewart, Davidson, and Simpson[15].

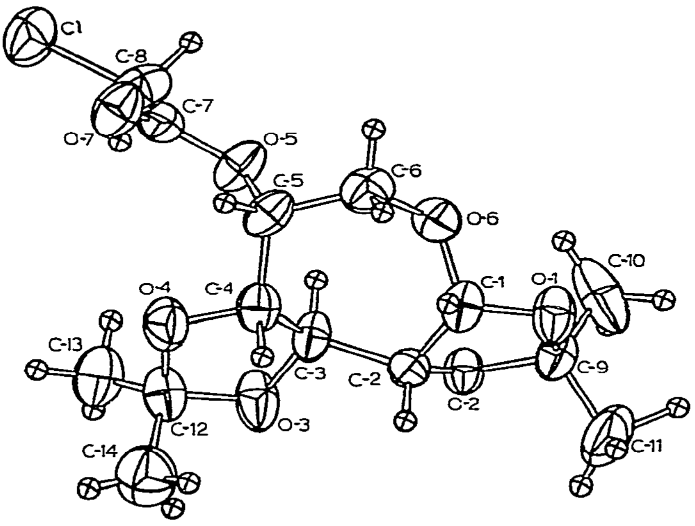

Fig. 1. The thermal ellipsoids for the nonhydrogen atoms and numbering of the atoms in **1**.

A graphic display of the thermal motion of the molecule and the numbering system adopted are shown in Fig. 1. The atomic coordinates for the nonhydrogen atoms and hydrogen atoms are given in Tables II and III, respectively. The final observed and calculated structure-factors have been deposited with NAPS-ASIS*.

TABLE II

ATOMIC COORDINATES AND ANISOTROPIC THERMAL PARAMETERS FOR THE NONHYDROGEN ATOMS[a]

Atom	x/a	y/b	z/c	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cl	1962(1)	3956 (3)	5950 (7)	12(0)	149 (4)	693(15)	4(1)	−23(2)	30 (7)
C-1	4679(3)	2278 (9)	7925(13)	9(1)	115(10)	176(22)	−4(3)	0(4)	9(14)
C-2	4523(3)	1378 (7)	5994(15)	10(1)	62 (8)	294(27)	0(2)	3(5)	14(14)
C-3	3978(3)	1339 (9)	5638(15)	8(1)	111(10)	277(26)	−5(2)	0(5)	−18(16)
C-4	3707(3)	1192 (9)	7969(15)	11(1)	97 (9)	258(26)	−3(3)	−4(5)	19(14)
C-5	3565(3)	2420 (9)	9093(16)	11(1)	119(10)	260(27)	6(3)	14(5)	9(17)
C-6	3999(3)	3168(10)	9833(15)	15(1)	112(10)	266(28)	4(3)	3(6)	−42(16)
C-7	2812(3)	3249 (9)	7864(17)	14(1)	62 (8)	385(34)	−1(3)	11(6)	0(16)
C-8	2597(4)	3833(12)	5726(21)	16(2)	142(13)	459(41)	17(4)	−13(7)	−5(23)
C-9	5174(3)	2462(10)	4669(14)	9(1)	123(10)	205(25)	−2(3)	−1(4)	−43(14)
C-10	5219(5)	3670(13)	3429(20)	31(2)	169(16)	363(38)	−46(6)	−5(9)	−25(22)
C-11	5597(4)	1646(14)	4391(28)	10(1)	228(19)	844(74)	4(4)	−17(9)	−189(38)
C-12	3399(3)	−177(10)	5258(18)	13(1)	122(11)	321(34)	−13(3)	1(6)	10(18)
C-13	3005(4)	−79(12)	3504(19)	14(1)	169(15)	359(36)	−7(4)	1(6)	30(21)
C-14	3514(4)	−1499(12)	5974(24)	21(2)	142(14)	518(47)	−3(4)	−1(9)	54(25)
O-1	5122(2)	2720 (7)	7138(11)	11(1)	149 (8)	275(20)	−11(2)	−5(4)	−34(12)
O-2	4749(2)	1842 (6)	3977 (9)	10(1)	99 (6)	213(16)	−6(2)	0(3)	−10(10)
O-3	3835(2)	324 (8)	4287(12)	14(1)	185(10)	350(24)	−23(3)	21(4)	−138(14)
O-4	3287(2)	562 (7)	7232(13)	13(1)	120 (8)	404(26)	−10(2)	18(4)	−42(13)
O-5	3284(2)	3117 (6)	7415(11)	11(1)	127 (7)	304(22)	10(2)	12(4)	55(12)
O-6	4358(2)	3323 (6)	8055(10)	14(1)	81 (6)	269(18)	−2(2)	4(4)	0(10)
O-7	2620(2)	2995 (7)	9646(12)	13(1)	147 (9)	362(24)	2(2)	18(4)	31(13)

[a]Estimated standard deviation × 10^4 in parentheses. The thermal parameters are expressed as $\exp(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+2\beta_{12}hk+2\beta_{13}hl+2\beta_{23}kl)$.

RESULTS AND DISCUSSION

Bond distances and bond angles. — The bond distances and bond angles involving the nonhydrogen atoms are shown in Fig. 2. The estimated standard errors in the distances are C–Cl = 0.010, C–O = 0.011, C–C = 0.014, and C–H = 0.10 Å. The generally high values for the errors are attributable in part to the large thermal vibration of the molecule.

In general, the bond distances are in good agreement with the values found in the five-membered[1,2] and six-membered[4–6] ring sugars. The average C–C and C–O bond-distances in the ring are 1.522 and 1.433 Å, respectively. An interesting feature of the dioxolane rings is that the C–O bonds involving O-1 and O-3 are significantly

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*Microfilm copies of this table can be obtained from the NAPS-ASIS Agency, New York, U. S. A.

TABLE III

ATOMIC COORDINATES AND THERMAL PARAMETERS FOR THE HYDROGEN ATOMS[a]

Atom	x/a	y/b	z/c	B (Å^2)
H-1	464(3)	202(14)	968(19)	3.0
H-2	464(2)	53 (4)	659 (6)	4.1
H-3	386(2)	216 (8)	537(20)	3.3
H-4	385(2)	44 (5)	880(16)	3.7
H-5	336(2)	220 (6)	1025(27)	3.1
H-6	415(2)	277 (8)	1132(24)	2.8
H-6′	390(2)	400 (4)	1015(12)	3.2
H-8	260(2)	312(13)	486(27)	3.2
H-8′	272(3)	482 (9)	509(24)	3.7
H-10	492(4)	418 (5)	387(15)	4.9
H-10′	528(4)	351(13)	156(11)	5.9
H-10″	554(4)	387 (8)	390(20)	4.5
H-11	570(4)	136 (6)	577(50)	12.1
H-11′	585(4)	248(13)	381(32)	5.8
H-11″	556(4)	94 (6)	343(23)	4.8
H-13	293(3)	82 (7)	304(16)	6.5
H-13′	270(5)	−35(12)	403(25)	7.1
H-13″	303(3)	−42(11)	224(18)	4.3
H-14	369(8)	−165(11)	475(36)	7.1
H-14′	328(4)	−200(11)	636(23)	5.2
H-14″	375(7)	−149(10)	714(48)	10.9

[a] Estimated standard deviation × 10^3.

different, whereas the C–O bonds involving O-2 and O-4 are equal. In both dioxolane rings the longest C–O bond is opposite the puckered atom (see later). The C–O bonds involving the anomeric carbon atom (C-1) are unequal, and the extracyclic anomeric C-1–O-1 bond (1.391 Å) is about 0.042 Å shorter than the intracyclic anomeric C-1–O-6 bond (1.433 Å). However, the intra-ring C–O bonds (C-1–O-6 and C-6–O-6) are equal. Analogous trends have been observed in equatorially substituted pyranosides[16]. It will be of interest to compare the present results with those of other septanoid systems as data become available.

The bond angles within the septanoid ring are greater than the ideal tetrahedral value and are generally larger than those found in the pyranosides. Interestingly, in the septanoid ring the average value (111.5°) of the internal angle involving the odd-numbered carbon atoms is significantly smaller than the average value (114.0°) involving the even-numbered carbon atoms. This alternation in value may be a characteristic feature of septanoid rings. The angle at the ring oxygen-atom is close to the values found in the pyranosides[17]. All of the angles in the dioxolane rings are less than the tetrahedral value; the angles at the oxygen atoms are the largest, whereas those at the fusion of the 5- and 7-membered rings are the smallest. Intermediate values are found at the isopropylidene carbon atom. The largest angles involving the isopropylidene groups are the extracyclic angles C-10–C-9–C-11 (113.5°) and C-13–C-12–C-14 (113.9°).

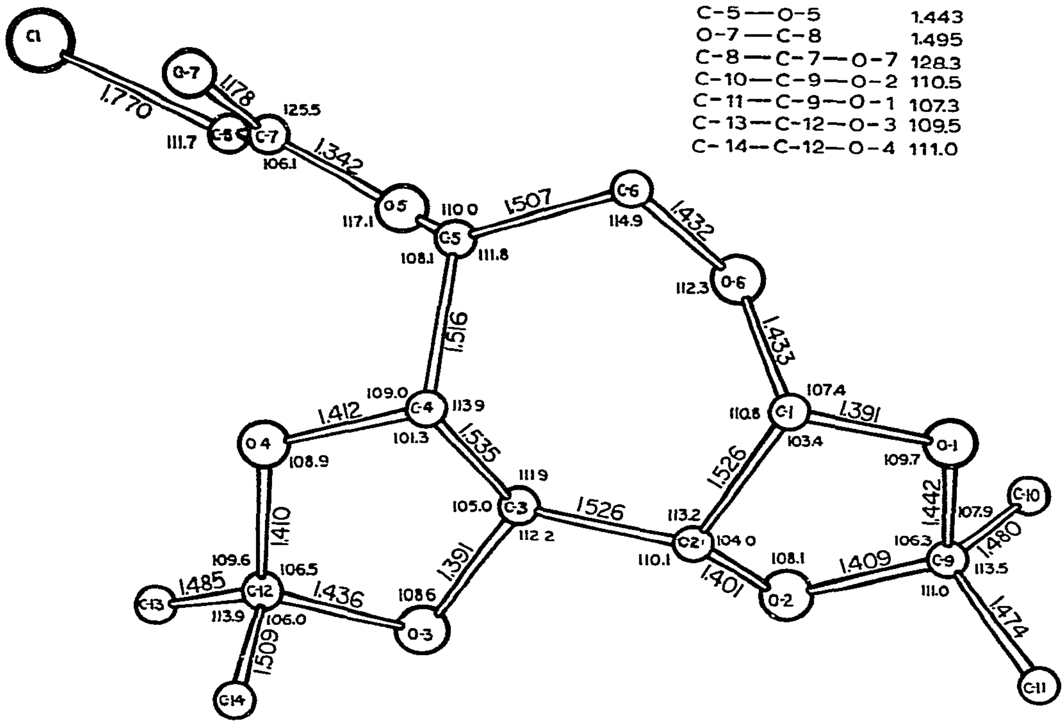


Fig. 2. Bond distances (Å) and bond angles (degrees) for the nonhydrogen atoms in **1**.

The bond distances and bond angles in the chloroacetate group are comparable to the average values found for the acetate group[18,19].

MOLECULAR CONFORMATION

The septanoid ring. — The torsional angles in the septanoid ring of **1** are given in Table IV and Fig. 3. The corresponding theoretical values[10] for the "ideal" chair and twist-chair conformations of cycloheptane are also given for comparison. It is seen that **1** is closer in conformation to the twist-chair form having the axis of symmetry passing through C-2 and the mid-point of the C-5–C-6 bond [hereinafter referred to as the $^{5,6}C_2$(D) twist-chair].

The torsional angles in the septanoid sugars **2** and **3** are also given in Table IV. It is seen that **2** is also in the cycloheptane twist-chair form[10] but the axis of symmetry here passes through C-1 and the mid-point of the C-4–C-5 bond [a conformation hereinafter referred to as the $^{4,5}C_1$(D) twist-chair]. In contrast to **1** and **2**, compound **3** is remarkably close to the chair conformation of cycloheptane. It is noteworthy that **3** falls between **1** and **2** in the pseudorotational itinerary of the septanoid ring. The differences in the pseudorotation[10] of **1** and **2** are probably influenced by the differences in the position of attachment of the two dioxolane rings to the central

TABLE IV

CONFORMATIONS OF SEPTANOSES

Angle	*Compound*[a]			*Chair*[b]	*Twist chair*[b]	
	1	2	3			
C-1–C-2	−32	36	14	0	−39	39
C-2–C-3	−48	−91	−72	−66	−39	−88
C-3–C-4	92	60	76	84	88	72
C-4–C-5	−65	−34	−56	−64	−72	−54
C-5–C-6	50	58	65	64	54	72
C-6–O-6	−84	−98	−96	−84	−72	−88
O-6–C-1	97	54	65	66	88	39

[a] **1**, 5-*O*-(chloroacetyl)-1,2:3,4-di-*O*-isopropylidene-α-D-glucoseptanose; **2**, ethyl 2,3:4,5-di-*O*-isopropylidene-1-thio-β-D-glucoseptanoside; **3**, methyl 2,3,4,5-tetra-*O*-acetyl-β-D-glucoseptanoside. [b] Values (in degrees) from Hendrickson[10].

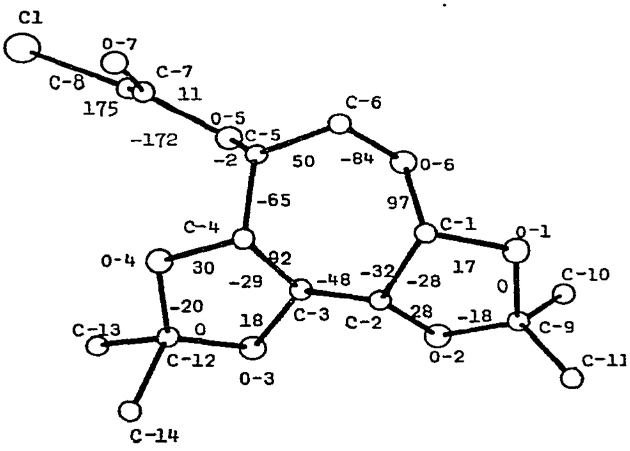


Fig. 3. Torsional angles in the molecule of **1**.

septanoid ring. The favored chair-conformation found in **3** is most probably determined by the absence of dioxolane rings. In fact, Hendrickson[10] predicted the chair conformation to be the energetically most stable conformation for cycloheptane. The ring oxygen-atom and the substituent acetate groups are the main factors responsible for the departure of the septanoid ring from the ideal-chair conformation.

The dihedral angles H–C–C–H involving the ring hydrogen-atoms are of interest because they are related to the coupling constants determined by proton magnetic resonance spectroscopy. These angles for **1** are:

H-1–H-2	−41°	H-4–H-5	−56°
H-2–H-3	169°	H-5–H-6	46°
H-3–H-4	−164°	H-5–H-6′	−74°.

The estimated errors in the angles are about 3–4°.

The dioxolane rings. — The torsional angles in the two dioxolane rings are given in Table V and Fig. 3. Both dioxolane-rings exhibit the ideal envelope-shape, and the torsional angles about the C-9–O-1 and C-12–O-3 bonds are 0°. These bonds, as mentioned earlier, are the largest C–O distances in the dioxolane rings, and are probably so because of the eclipsing interactions. The atoms C-2 and C-4 are displaced by 0.42 and 0.46 Å from the remaining four-atom planes of the respective dioxolane rings. In contrast, in **2** both of the dioxolane rings adopt the twist form, the displacements of O-3 and C-3 being 0.33 and 0.19 Å, respectively, on opposite sides of the three-atom plane C-2–O-2–C-7; in the second dioxolane ring the C-5 and O-5 atoms exhibit the major (0.41 Å) and minor (0.20 Å) puckering, respectively. The conformational differences of the dioxolane rings in **1** and **2** most probably arise from the different positions of their 7-membered rings. In **1** the dioxolane rings at C-1–C-2 and C-3–C-4 adopt the envelope shape, whereas in **2** the rings are in the alternative positions C-2–C-3 and C-4–C-5 and adopt the twist forms.

TABLE V

TORSIONAL ANGLES IN THE DIOXALANE RINGS

Compound **1**	*Angle (degrees)*	*Compound* **2**	*Angle (degrees)*
C-2–C-1–O-1–C-9	17	C-3–C-2–O-2–C-7	−8
C-1–O-1–C-9–O-2	0	C-2–O-2–C-7–O-3	−14
O-1–C-9–O-2–C-2	−18	O-2–C-7–O-3–C-3	31
C-9–O-2–C-2–C-1	28	C-7–O-3–C-3–C-2	−35
O-2–C-2–C-1–O-1	−28	O-3–C-3–C-2–O-2	26
C-4–C-3–O-3–C-12	18	C-5–C-4–O-4–C-10	16
C-3–O-3–C-12–O-4	0	C-4–O-4–C-10–O-5	8
O-3–C-12–O-4–C-4	−20	O-4–C-10–O-5–C-5	−31
C-12–O-4–C-4–C-3	30	C-10–O-5–C-5–C-4	40
O-4–C-4–C-3–O-3	−29	O-5–C-5–C-4–O-4	−33

In addition to the shape of the dioxolane rings being influenced by their positions on the septanoid ring, the conformation of the septanoid rings themselves [${}^{5,6}C_2$(D) twist-chair in **1** and ${}^{4,5}C_1$(D) twist-chair in **2**] is also influenced by the positions of the dioxolane ring. Thus, the pseudorotational itineraries of the septanoid and dioxolane rings are closely correlated and are dependent upon the position of the latter. It should be mentioned that the dioxolane rings not only severely limit the ranges of pseudorotation of the septanoid rings but that their own ranges of pseudorotation are also restricted.

In general, the methyl groups of the isopropylidene groups are in the staggered arrangement (Fig. 4). In only one example (Fig. 4b) is the semi-eclipsed orientation observed.

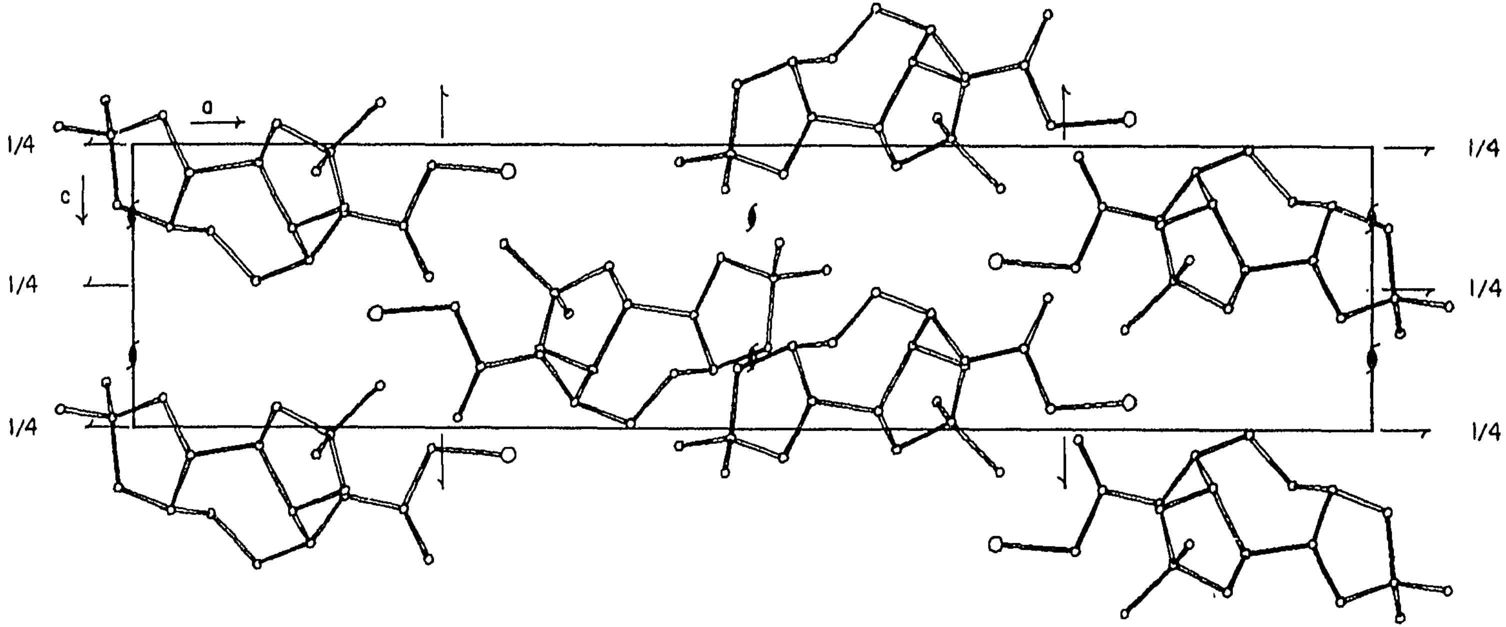
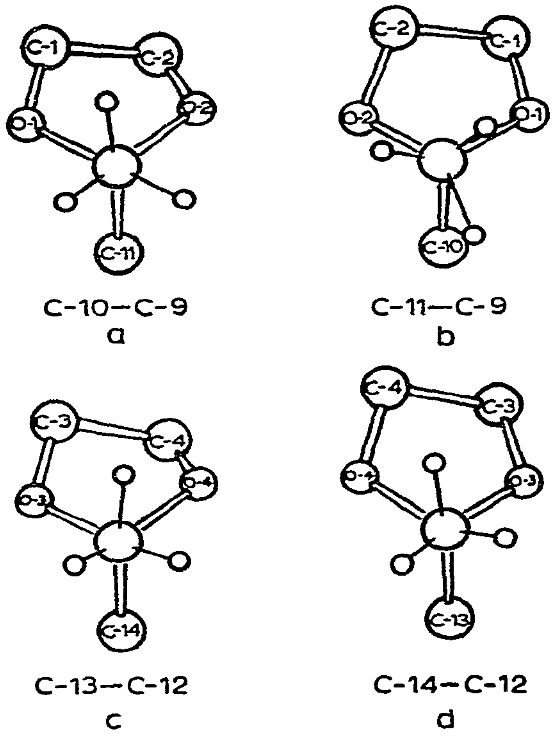


Fig. 5. Molecular packing as viewed along the *b* axis.



C-10—C-9
a

C-11—C-9
b

C-13—C-12
c

C-14—C-12
d

Fig. 4. Orientation of the methyl groups in 1.

The Chloroacetate group. — This group adopts the favored planar disposition[18,19]. The torsional angles are:

C-7–O-5–C-5–H-5 = −2° (4°)
O-7–C-7–O-5–C-5 = 11.0° (2°)
C-8–C-7–O-5–C-5 = −172.0° (2°)
Cl–C-8–C-7–O-5 = 175.3° (2°).

The values in parentheses are the estimated standard deviations in the torsional angles.

Molecular packing. — Fig. 5 shows the molecular packing in the unit cell, as viewed down the *b* axis. There are no hydrogen bonds in this structure. The closest intermolecular contact (3.46 Å) involving nonhydrogen atoms is between O-2 and C-6.

ACKNOWLEDGMENTS

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