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THE CRYSTAL STRUCTURE OF 2,4:3,5-DI-*O*-BENZYLIDENE-D-ARABINOSE DIETHYL DITHIOACETAL, AND RELATED MOLECULAR-MECHANICS CALCULATIONS

T. BRUCE GRINDLEY, SRIHARI KUSUMA, T. STANLEY CAMERON, AND AMARITA KUMARI
Department of Chemistry, Dalhousie University, Halifax, Nova Scotia B3H 4J3 (Canada)

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ABSTRACT

A new di-*O*-benzylidene derivative of D-arabinose diethyl dithioacetal, obtained by benzylidenation with α,α-dimethoxytoluene, was shown by X-ray crystallography to have the 2,4:3,5-di-*O*-benzylidene structure. The two *O*-benzylidene rings are *trans*-fused, and the $CH(SEt)_2$ group adopts an axial orientation at C-4 of a 2-phenyl-1,3-dioxane ring. The axial group is twisted, and there is some distortion of the chair conformation of the ring. ^1H-N.m.r. coupling-constants showed that the conformation is similar in solution. Molecular-mechanics calculations using a modified MM2 program indicated that the distortions are caused by intramolecular interactions. They also suggest that rotation about the bond from the acetal carbon atom to the phenyl ring in 2-phenyl-1,3-dioxanes is not free, as previously calculated. The parallel conformation was calculated to be a minimum, and the perpendicular conformation a saddlepoint 0.95 kcal.mol^{-1} higher on the potential-energy surface. The ^1H- and ^{13}C-n.m.r. parameters of this system and other *trans*-fused 3,7-diphenyl-2,4,6,8-tetraoxa[4,4]bicyclodecanes do not fit the ranges previously proposed for structural assignment of benzylidene acetals. The ranges have been revised to include this type of compound.

INTRODUCTION

2,3:4,5-Di-*O*-benzylidene-D-arabinose diethyl dithioacetal was needed as an intermediate for the preparation of compounds to be used in the study of aldose equilibria. Available synthetic methods gave the compound in 29 (ref. 1) and 44% yields[2]. More recently, it has been shown that kinetic benzylidenation with α,α-dimethoxytoluene often gives higher yields of benzylidene acetals than does reaction under the normal, thermodynamic conditions[3]. Application of this method to D-arabinose diethyl dithioacetal resulted in a new crystalline di-*O*-benzylidene derivative, shown here to be 2,4:3,5-di-*O*-benzylidene-D-arabinose diethyl dithioacetal (1).

It has previously been shown that structural assignments for α-benzylidene and *O*-ethylidene derivatives could be made from several ^1H- and ^{13}C-n.m.r.

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parameters[4,5]. The values obtained for these parameters for **1** did not lie within the ranges previously observed for the common types of substituted benzylidene acetals[4].

The crystal structure of **1** was determined, and is reported herein. This structure is particularly interesting, because it contains a 1,3-dioxane ring having a large, axial substituent at C-4, a position where axial substitution causes more strain than it does in cyclohexane rings[6].

EXPERIMENTAL

General. — For most of the general methods, see ref. 4. 361.08-MHz, ^{1}H-n.m.r. spectra were recorded with a Nicolet NT-360 NB spectrometer.

Di-O-benzylidenation of D-*arabinose diethyl dithioacetal.* — A solution of D-arabinose diethyl dithioacetal (12.8 g, 50 mmol), α,α-dimethoxytoluene (18.24 g, 120 mmol), and *p*-toluenesulfonic acid (0.5 g) in anhydrous *N,N*-dimethylformamide was stirred for 3 h at 75–80° at 2.66 kPa, cooled, poured into ice-cold sodium hydrogencarbonate solution (3%, 300 mL), and the mixture extracted with ether (3 × 200 mL). The extracts were combined, washed with water (100 mL), dried ($\mathrm{MgSO_4}$) and evaporated to a pale-yellow syrup (22.53 g). When the syrup was taken up in hot ethanol (15 mL), and the mixture cooled, a precipitate (6.25 g) was obtained. Recrystallization from dichloromethane–petroleum ether (b.p. 30–60°) gave 2,4:3,5-di-*O*-benzylidene-D-arabinose diethyl dithioacetal (**1**); yield 2.652 g, 12%. A second recrystallization from the same solvent gave colorless needles, m.p. 173–174°; $[\alpha]_D^{23}$ +78° (*c* 1.44, chloroform); ^{1}H-n.m.r. (361.08 MHz, benzene-d_6 (spectral parameters for the six skeletal protons from iterative simulation using the program LAME[7], r.m.s. deviation 0.32 on 147 of 231 transitions having appreciable intensity): δ 1.052, 1.089 (2 t, 6 H, J 7.30, 7.39 Hz, $\mathrm{SCH_2}\mathit{CH}_3$), 2.51–2.75 (complex m, 4 H, s $\mathit{CH}_3\mathrm{CH_3}$), 3.585 (m, 1 H, $J_{4,5a}$ 9.6, $J_{5a,5e}$ − 10.1 Hz, H-5*a*), 4.017 (m, 1 H, $J_{2,3}$ 5.4, $J_{3,4}$ 9.3 Hz, H-3), 4.044 (m, 1 H, $J_{4,5e}$ 4.7 Hz, H-4), 4.217 (m, 1 H, H-5*e*), 4.483 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 4.609 (dd, 1 H, H-2), 5.322, 6.232 (2 s, 2 H, benzylidene H), 7.0–7.3 (complex m, 6 H, Ph), 7.674 (d, 2 H, J 7.29 Hz, 2 ortho Ph H), and 7.784 (d, 2 H, J 7.25 Hz, 2 ortho Ph H): ^{1}H-n.m.r. (361.08 MHz, chloroform-*d*; chemical shifts and those J values listed for skeletal protons were obtained by simulation as above): δ 1.208, 1.294 (2 t, 6 H, J 7.41, 7.43 Hz, 2 $\mathrm{SCH_2}\mathit{CH}_3$), 2.60–2.90 (complex m, 4 H, 2 $\mathrm{S}\mathit{CH}_2\mathrm{CH_3}$), 3.891 (m, 1 H, H-5*a*), 4.322, 4.342, 4.405 (complex m, 3 H, H-3,4,5*e*, respectively), 4.564 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.591 (m, 1 H, $J_{2,3}$ 5.7 Hz, H-2), 5.672, 6.225 (2 s, benzylidene H), 7.30–7.43 (m, 6 H, Ph), and 7.50–7.60 (m, 4 H, Ph); ^{13}C-n.m.r. (20 MHz, chloroform-*d*): δ 14.1, 14.2 (2 Me), 24.1, 24.8 (2 $\mathrm{SCH_2}$), 50.6 (C-1), 67.6 (C-4), 69.1 (C-5), 75.9, 76.8 (C-2, C-3), 97.0 (acetal C, $^1J_{\mathrm{C,H}}$ 168 Hz), 102.2 (acetal C, $^1J_{\mathrm{C,H}}$ 157 Hz), 126.2, 126.3, 128.2, 128.3, 129.0 (Ph C), 137.4, and 137.5 (quaternary Ph C); *m/z* 432 (18, M^+), 370 (1, M − SEt), 369 (1), 297 (7), 265 (15), 221 (13), 205 (4), 203 (3), 193 (5), 191 (17), 177 (4), 159 (9), 149 (10), 145 (12), 137 (17), 136 (13), 135 (100,

TABLE I

ATOMIC PARAMETERS[a]

Atom	x/a	y/b	z/c	*Temperature factor*[b]	*Atom*	x/a	y/b	z/c	*Temperature factor*[b]
S-1	−547(4)	569(1)	2209(1)	611(12)	H-1	−3110(16)	613(4)	1478(3)	1110(300)
S-2	−3042(4)	−756(1)	1569(1)	669(13)	H-11	69(22)	1502(5)	−63(3)	700(260)
O-1	2335(9)	1101(3)	1388(2)	449(28)	H-12	2670(22)	2149(5)	68(3)	750(250)
O-2	656(11)	2027(3)	819(2)	528(31)	H-13	−3947(20)	−101(5)	−851(3)	1430(320)
O-3	−2047(10)	−14(3)	561(2)	456(28)	H-14	−7551(22)	−1019(6)	−1156(4)	1010(320)
O-4	−3563(11)	917(3)	−20(2)	612(35)	H-15	−9666(21)	−2031(6)	−613(4)	760(240)
C-1	−1666(16)	290(4)	1608(3)	530(45)	H-16	−8531(20)	−2033(5)	242(3)	630(210)
C-11	−1783(22)	1550(5)	132(3)	655(55)	H-17	−5189(18)	−1068(5)	559(3)	680(210)
C-12	−4472(16)	−502(5)	−114(3)	577(48)	H-19	3568(21)	3148(5)	821(3)	510(200)
C-13	−5029(20)	−501(5)	−609(3)	768(62)	H-2	1625(14)	−188(4)	1285(3)	270(160)
C-14	−6961(22)	−1040(6)	−783(4)	864(71)	H-20	7059(24)	4094(6)	1105(5)	1770(450)
C-15	−8220(21)	−1594(6)	−477(4)	835(71)	H-21	8352(22)	4089(6)	1950(5)	1170(340)
C-16	−7574(20)	−1601(5)	1(3)	743(62)	H-22	6635(20)	3037(6)	2477(4)	1190(340)
C-17	−5694(18)	−1056(5)	183(3)	658(52)	H-23	3270(18)	2027(5)	2193(3)	1320(360)
C-18	3233(14)	2521(4)	1478(3)	472(41)	H-241	−3815(19)	−301(8)	2616(4)	1610(450)
C-19	4268(21)	3111(5)	1187(3)	807(62)	H-242	−5488(19)	637(8)	2494(4)	3560(1100)
C-2	653(14)	407(4)	1256(3)	476(41)	H-251	−1224(33)	359(10)	3135(4)	1482(530)
C-20	6174(24)	3656(6)	1351(5)	1039(85)	H-252	−4604(33)	407(10)	3307(4)	1570(440)
C-21	6958(22)	3634(6)	1817(5)	896(76)	H-253	−2954(33)	1309(10)	3109(4)	2370(720)
C-22	5948(20)	3063(6)	2110(4)	848(69)	H-261	−1080(21)	−1412(5)	2199(4)	4470(1380)
C-23	4080(18)	2486(5)	1952(3)	671(56)	H-262	1726(21)	−1357(5)	1819(4)	1980(600)
C-24	−3564(19)	355(8)	2553(4)	916(78)	H-271	−272(6)	−246(1)	167(1)	138(43)
C-25	−3124(33)	647(10)	3062(4)	1258(111)	H-272	56(6)	−267(1)	186(1)	162(49)
C-26	−423(21)	−1390(5)	1830(4)	932(76)	H-273	1(6)	−213(1)	132(1)	280(78)
C-27	−705(56)	−2229(9)	1681(13)	2598(249)	H-4	−629(15)	1968(4)	1509(3)	470(180)
C-4	1210(15)	1901(4)	1311(3)	481(47)	H-6	−3035(15)	1509(4)	871(3)	440(190)
C-6	−1241(15)	1432(4)	662(3)	450(49)	H-7	1674(15)	538(4)	512(2)	760(240)
C-7	−119(15)	581(4)	725(2)	448(44)	H-9	−599(16)	40(4)	−114(3)	490(180)
C-9	−2488(16)	116(4)	66(3)	520(50)					

[a] Fractional coordinates: ×10⁴ for non-hydrogen atoms; ×10³ for hydrogen atoms. [b] Mod (U) $[(U_{11} \times U_{22} \times U_{33})^{1/3}]$ for non-hydrogen atoms and the isotropic temperature factor U for the hydrogen atoms, Å^2.

TABLE II

BOND DISTANCES AND ANGLES

Bond distances (Å)			
S-1–C-1	1.824(8)	C-12–C-9	1.50(1)
S-1–C-24	1.83(1)	C-13–C-14	1.39(1)
S-2–C-1	1.828(8)	C-14–C-15	1.39(1)
S-2–C-26	1.82(1)	C-15–C-16	1.37(1)
O-1–C-2	1.451(8)	C-16–C-17	1.39(1)
O-1–C-4	1.426(8)	C-18–C-19	1.35(1)
O-2–C-4	1.414(9)	C-18–C-23	1.39(1)
O-2–C-6	1.422(9)	C-18–C-4	1.50(1)
O-3–C-7	1.437(8)	C-19–C-20	1.38(2)
O-3–C-9	1.414(9)	C-2–C-7	1.557(10)
O-4–C-11	1.42(1)	C-20–C-21	1.36(2)
O-4–C-9	1.422(9)	C-21–C-22	1.33(2)
C-1–C-2	1.53(1)	C-22–C-23	1.39(1)
C-11–C-6	1.51(1)	C-24–C-25	1.51(2)
C-12–C-13	1.41(1)	C-26–C-27	1.42(3)
C-12–C-17	1.36(1)	C-6–C-7	1.494(10)
Bond angles (°)			
C-1–S-1–C-24	100.5(4)	O-1–C-2–C-1	111.9(6)
C-1–S-2–C-26	102.9(4)	O-1–C-2–C-7	104.2(5)
C-2–O-1–C-4	115.6(5)	C-1–C-2–C-7	116.3(6)
C-4–O-2–C-6	109.6(5)	C-19–C-20–C-21	120(1)
C-7–O-3–C-9	108.4(5)	C-20–C-21–C-22	120(1)
C-11–O-4–C-9	111.4(6)	C-21–C-22–C-23	121.7(10)
S-1–C-1–S-2	113.5(4)	C-18–C-23–C-22	118.7(8)
S-1–C-1–C-2	108.9(5)	S-1–C-24–C-25	108.3(8)
S-2–C-1–C-2	111.2(5)	S-2–C-26–C-27	110(1)
O-4–C-11–C-6	108.3(6)	O-1–C-4–O-2	110.7(5)
C-13–C-12–C-17	120.4(8)	O-1–C-4–C-18	106.8(6)
C-13–C-12–C-9	117.5(7)	O-2–C-4–C-18	109.7(6)
C-17–C-12–C-9	122.1(7)	O-2–C-6–C-11	109.7(6)
C-12–C-13–C-14	118.7(9)	O-2–C-6–C-7	109.4(6)
C-13–C-14–C-15	120.4(9)	C-11–C-6–C-7	107.3(6)
C-14–C-15–C-16	119.7(9)	O-3–C-7–C-2	110.4(5)
C-15–C-16–C-17	120.6(9)	O-3–C-7–C-6	108.8(5)
C-12–C-17–C-16	120.1(8)	C-2–C-7–C-6	111.9(6)
C-19–C-18–C-23	118.7(7)	O-3–C-9–O-4	111.1(6)
C-19–C-18–C-4	122.9(7)	O-3–C-9–C-12	109.6(6)
C-23–C-18–C-4	118.3(7)	O-4–C-9–C-12	107.2(6)
C-18–C-19–C-20	121.1(9)		

$^+CH(SEt)_2$), 107 (11), 106 (7), 105 (46), 91 (21), 87 (14), 79 (7), 77 (13), and 75 (15).

Crystal data for **1**. $C_{23}H_{28}O_4S_2$; m.w. = 432.59. Orthorhombic, space group $P2_12_12_1$, with a = 5.017(3), b = 16.142(4), c = 27.869(6) Å, V = 2257.0 Å^3, Z = 4. D_c = 1.273 g.cm^{-3} (20 ±2°). Radiation: MoKα (λ = 0.70926 Å) graphite monochrometer, $\mu_{MoK\alpha}$ = 2.17 cm^{-1}, F(000) = 920 e.

Structure determination. — An Enraf–Nonius CAD-4 diffractometer was

TABLE III

TORSIONAL ANGLES[a]

C-24–S-1–C-1–S-2	−54(1)	S-1–C-1–C-2–O-1	−34(1)
C-24–S-1–C-1–C-2	−179(1)	S-1–C-1–C-2–C-7	−154.1(5)
C-1–S-1–C-24–C-25	−173(1)	S-2–C-1–C-2–O-1	−160.2(4)
C-26–S-2–C-1–S-1	−53(1)	S-2–C-1–C-2–C-7	80(1)
C-26–S-2–C-1–C-2	70(1)	O-4–C-11–C-6–O-2	177(1)
C-1–S-2–C-26–C-27	−160(1)	O-4–C-11–C-6–C-7	58(1)
C-4–O-1–C-2–C-1	−72(1)	C-17–C-12–C-13–C-14	4(1)
C-4–O-1–C-2–C-7	54(1)	C-13–C-12–C-17–C-16	−2(1)
C-2–O-1–C-4–O-2	−62(1)	C-9–C-12–C-13–C-14	−177(1)
C-2–O-1–C-4–C-18	179(1)	C-13–C-12–C-9–O-3	−176(1)
C-6–O-2–C-4–O-1	62(1)	C-13–C-12–C-9–O-4	63(1)
C-6–O-2–C-4–C-18	179(1)	C-9–C-12–C-17–C-16	178(1)
C-4–O-2–C-6–C-11	−178(1)	C-17–C-12–C-9–O-3	3(1)
C-4–O-2–C-6–C-7	−61(1)	C-17–C-12–C-9–O-4	−117(1)
C-9–O-3–C-7–C-2	−174(1)	C-12–C-13–C-14–C-15	−3(1)
C-9–O-3–C-7–C-6	63(1)	C-13–C-14–C-15–C-16	1(2)
C-7–O-3–C-9–O-4	−62(1)	C-14–C-15–C-16–C-17	1(2)
C-7–O-3–C-9–C-12	179(1)	C-15–C-16–C-17–C-12	0(1)
C-9–O-4–C-11–C-6	−58(1)	C-23–C-18–C-19–C-20	2(1)
C-11–O-4–C-9–O-3	61(1)	C-19–C-18–C-23–C-22	0(1)
C-11–O-4–C-9–C-12	−179(1)	C-4–C-18–C-19–C-20	−178(1)
C-19–C-18–C-4–O-1	121(1)	C-1–C-2–C-7–C-6	72(1)
C-19–C-18–C-4–O-2	1(1)	C-19–C-20–C-21–C-22	2(2)
C-4–C-18–C-23–C-22	−180(1)	C-20–C-21–C-22–C-23	0(2)
C-23–C-18–C-4–O-1	−59(1)	C-21–C-22–C-23–C-18	−1(2)
C-23–C-18–C-4–O-2	−179(1)	O-2–C-6–C-7–O-3	−180(1)
C-18–C-19–C-20–C-21	−3(1)	O-2–C-6–C-7–C-2	58(1)
O-1–C-2–C-7–O-3	−173.4(5)	C-11–C-6–C-7–O-3	−61(1)
O-1–C-2–C-7–C-6	−52(1)	C-11–C-6–C-7–C-2	177(1)
C-1–C-2–C-7–O-3	−50(1)		

[a] In degrees.

used to determine the unit-cell dimensions from 25 general reflections with $10 \leqslant$ 14°. The largest crystal available was rather small, measuring 0.8 × 0.2 × 0.05 mm. The data collection was taken to the limit of actual reflections; 1703 reflections were collected, of which 982 had $I > \sigma(I)$. These were used in the structure solution and refinement. The intensities were reduced by routine procedures described previously[8]. Lorentz and polarization corrections were applied, but no absorption or extinction corrections were made. Scattering factors were taken from ref. 9. The structure was solved by using the SHELX system[10].

The non-hydrogen atoms were located from the E-map. Full-matrix, least-squares refinement was performed, using first isotropic and then anisotropic temperature-factors. The hydrogen atoms were located from a difference-Fourier map. Refinement was continued with anisotropic temperature-factors on the non-hydrogen atoms, and isotropic temperature-factors on the hydrogen atoms, until R =

0.040 ($R = 0.051$ on full data set). The least-squares weights* were calculated from $w^{-1} = \sigma^2|F_o| + 0.015936\ |F_o|^2$. In the final cycle, the maximum parameter-shift (Δ/σ) was 0.38. Atomic and thermal parameters† are given in Table I, interatomic distances and bond angles in Table II, and torsional angles in Table III.

Molecular-mechanics calculations. — Molecular-mechanics calculations were performed by using the MM2 program (1980 version)[11], modified for use on a Perkin–Elmer computer[12]. The program was modified locally, in order to incorporate improvements in the force-field for alkylbenzenes[13] and for the anomeric effect[14]. Calculations were performed on a Perkin–Elmer 3230 computer.

DISCUSSION

Structural features. — The structure was found to be (*R*),(*R*)-2,4:3,5-di-*O*-benzylidene-D-arabinose diethyl dithioacetal, a structure having two *trans*-fused 1,3-dioxane rings and the (large) $CH(SEt)_2$ group axial. Fig. 1 shows a stereoview of the molecular structure, and Fig. 2 shows the crystal packing. Table I lists the atomic parameters. Bond distances and angles are given in Table II, and Table III shows the torsional angles.

The crystal structures of some simple 2-phenyl-1,3-dioxanes have been determined[15,16]. The 1,3-dioxane rings are puckered at the acetal center (dihedral angles 61–63°), but flattened at the aliphatic end (dihedral angles, 53–55°), with angles similar to those of cyclohexanes. The crystal structures of a number of carbohydrate examples have been published, although many papers do not include tables of torsional angles. The torsional angles in most of those having all-equatorial substituents[17–19] were similar in pattern to those just mentioned[15,16]. The additional substituents present in the carbohydrates cause the aliphatic end to be more puckered, the dihedral angles normally being in the 55–59° range.

Only one example of a 2-phenyl-1,3-dioxane ring having an axial substituent at C-4 has previously been examined[20]. Equilibration studies have shown that the axial–equatorial energy-difference is larger at this position than in cyclohexane, but less than at C-2 of a 1,3-dioxane ring[6]. The previous example, where the axial substituent was part of a *cis*-fused ring, was greatly distorted[20]. Table IV compares torsional angles in this compound (angles calculated from data in ref. 20) with those in **1**.

The 2,4-*O*-benzylidene ring of **1** will be called ring A and the other ring, ring B, in subsequent discussion. Ring A is less distorted than the *cis*-fused 1,3-dioxane ring, mainly because it is *trans*-fused to another 1,3-dioxane ring. A decrease in the dihedral angle about the bond common to the two rings in ring A causes the corresponding angle in ring B to increase. However, an increase in X–C–C–Y dihedral

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*A table of σ will be provided by the authors on request.

†Lists of structure factors and anisotropic thermal parameters have been deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/350 *Carbohydr. Res.*, 159 (1987) 171–183.

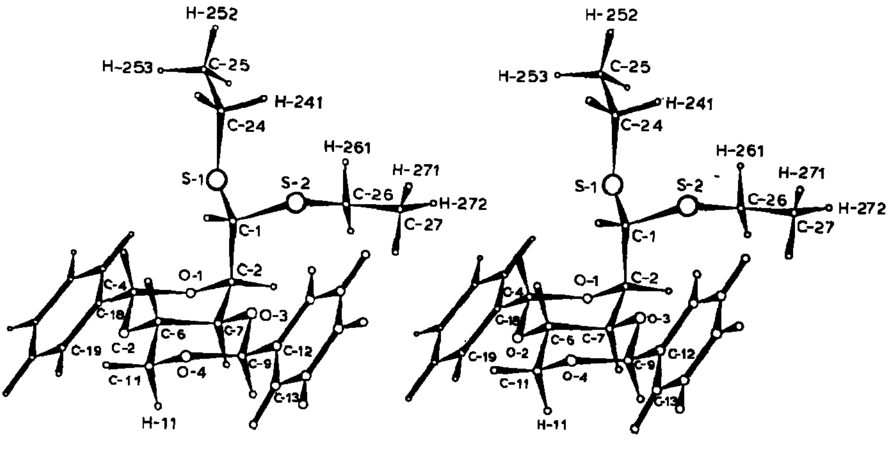

Fig. 1. Stereoview of the crystal structure of 1.

angles beyond 60° in six-membered rings is energetically unfavorable. The torsional angles observed were close to 60°: 59° in ring A, and −61° in ring B.

Ring A is flattened about the axial $CH(SEt)_2$ group, with adjacent torsional angles of 54 and −52°. This type of flattening increases the dihedral angles that the carbon atom of the axial group has with the ring atoms, and hence moves the group farther from the ring. The flattening brings the equatorial substituent O-3, which is

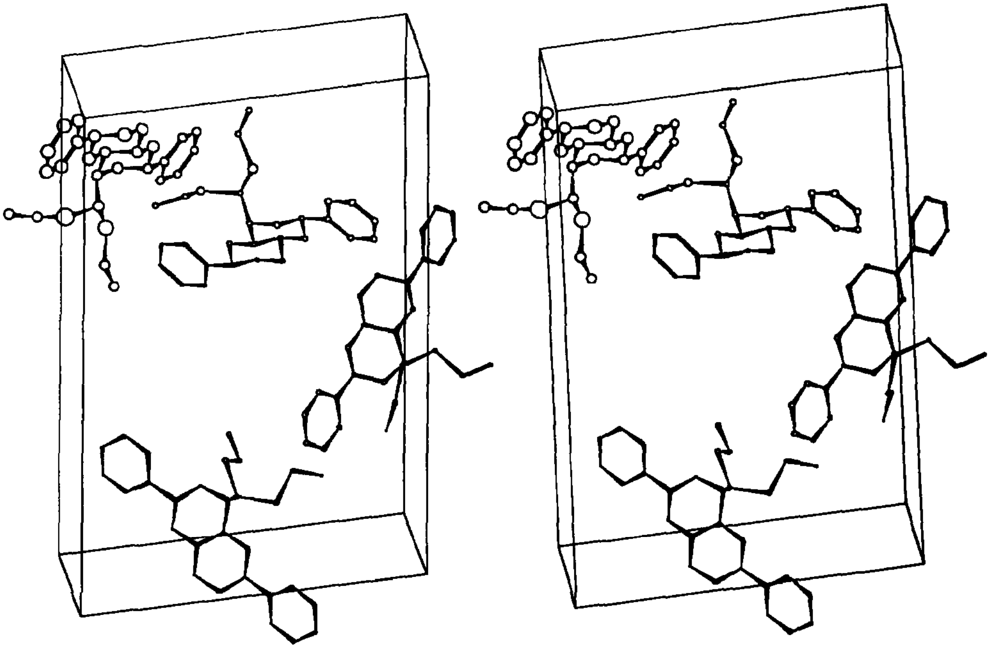

Fig. 2. The crystal packing of 1.

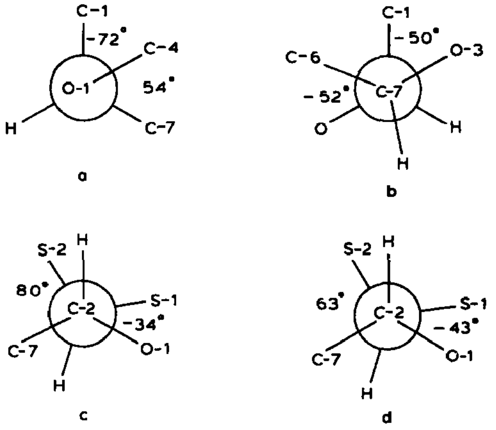

Fig. 3. "Newman" projections in the region of **1** that is in the vicinity of the $CH(SEt)_2$ group. [Parts (a) and (b) show projections along ring bonds towards the carbon atom bearing this group. Part (c) shows the relationships that the sulfur atoms have to adjacent atoms in **1**, and (d) shows the same relationships calculated by using the MM2 program on *trans*-4-(dimethyldithio)methyl-2-phenyl-1,3-dioxane with the 4-substituent axial.]

gauche to the $CH(SEt)_2$ group, closer to it. As a result, the two sulfur atoms are far from being staggered with the substituents on C-2, but are twisted away from O-3. Fig. 3 shows the torsional angles about this group. The distances between H-1 and H-4 and H-6 also reflect this twisting, being 2.518 (10) and 2.225 (10) Å, respectively.

Molecular-mechanics calculations were performed in order to determine whether the distortions just noted for 4-substituted 1,3-dioxane derivatives can be attributed to intramolecular interactions. An MM2 program[11,12], modified to incorporate recent improvements in force fields for alkylbenzenes[13] and compounds

TABLE IV

TORSIONAL ANGLES (DEGREES) IN 2-PHENYL-1,3-DIOXANE DERIVATIVES

Bond[a]	*X-Ray results*				*MM2 results*		
	Parent[b]	*Ring A*	*Cis-analog*[c]	*Ring B*	*Parent*	*4-Me*	*4-(MeS)₂CH*
O-1–C-2	63	62	68	−62	67	67	66
C-2–O-3	−63	−62	−61	61	−67	64	−65
O-3–C-4	59	54	48	−58	60	55	57
C-4–C-5	−55	−52	−43	58	−51	47	−49
C-5–C-6	55	58	52	−61	51	50	52
C-6–O-1	−59	−61	−63	63	−60	−61	−60

[a] Numbered so that axial substituents are at C-4, ring fusion for rings A and B are across the C-5–C-6 bond, and across C-4–C-5 for the *cis* analog. [b] Values from ref. 15. [c] From ref. 20.

having anomeric effects[14], was used. The difference in strain energy between axial and equatorial 4-methyl-1,3-dioxane was calculated to be 2.66 kcal.mol^{-1}, in good agreement with the experimental value[6] of 2.9 kcal.mol^{-1}. An earlier calculation, using the MM1 force field gave[21] much poorer agreement (1.7 kcal.mol^{-1}). Torsional angles calculated for 2-phenyl-1,3-dioxane and its derivatives having axial methyl and (dimethyldithio)methyl substitutents at C-4 are shown in Table IV. The present force-field reproduced the experimentally observed puckering at the acetal end of 2-phenyl-1,3-dioxane and the flattening at the aliphatic end, but exaggerated the effects (see Table IV). The calculations confirmed that an axial substituent at C-4 in a 1,3-dioxane ring causes flattening. The axial (dimethyldithio)methyl group in *trans*-4-(dimethyldithio)methyl-2-phenyl-1,3-dioxane was found to deviate from being staggered with the ring in the same direction as the (diethyldithio)methyl group in **1** (see Fig. 3). Changing the O-1–C-2–C-1–S-1 torsional angle to −34°, as in **1**, increases the energy by only 0.15 kcal.mol^{-1}. The major cause of this twisting is the smaller repulsive van der Waals interactions of the sulfur atoms with O-3 and its lone pairs than with C-5 and its equatorial hydrogen atom. Comparison of geometries of compounds with and without a *trans*-fused ring confirmed the effect of the *trans*-fused ring on torsional angles about the common bond.

The strain imposed by the axial $CH(SEt)_2$ group on the structure of **1** was also reflected in the bond distances and bond angles about the group. The bonds in ring A to C-2, the atom bearing the axial group, are unusually long, 1.451 Å to O-1, and 1.555 Å to C-7. Standard C–O and C–C bond-lengths are 1.43 ±0.01 and 1.541 ±0.003 Å, respectively[21]. Surprisingly, one bond is short, C-6–C-7 (1.494 Å). The C-4–O-1–C-2 bond angle is unusually large, 115.6°, compared with angles of 108–112° for the same position in other 2-phenyl-1,3-dioxane rings[15–19]. The C-1–C-2–C-7 bond angle is also large (116.3°). MM2 calculations on simpler molecules reproduced all of the trends noted in this paragraph, except one. A calculation on *trans*-fused-5-(dimethyldithio)methyl-2,4,6,8-tetraoxa[4,4]bicyclodecane, having the substituent axial, yielded a normal bond-length, 1.533 Å, for the bond common to both rings, in contrast to the value already observed for our compound. No explanation is currently available for this difference.

The torsional angle that the phenyl ring makes with the 1,3-dioxane ring in 2-phenyl-1,3-dioxanes has attracted considerable interest[19,22–26]. The two extreme

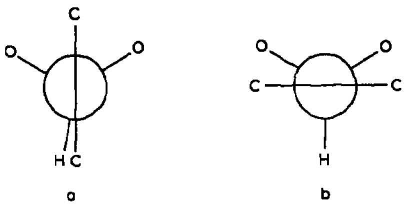

Fig. 4. "Newman" projections illustrating the names given to the two conformations arising from rotation about the bond from the acetal carbon atom to the phenyl carbon atom in acetals derived from diols and benzaldehyde: (a) parallel conformation, and (b) perpendicular conformation.

conformations, termed parallel and perpendicular, are defined by the angle that the plane of the phenyl ring makes with the α-C–H bond (see Fig. 4). In the crystal structure of **1**, the planes of both phenyl rings are virtually eclipsed with one C–O bond; the O-3–C-9–C-12–C-17 torsional angle is 4°, and the O-2–C-4–C-18–C-19 torsional angle is 1°. Other compounds containing 2-phenyl-1,3-dioxane rings have been observed to have a wide range of analogous torsional angles[15–20], although eclipsing of the phenyl rings with α-C–O bonds is uncommon. Interestingly, both of the other structures wherein this feature was observed also have axial substituents in the 1,3-dioxane ring, at C-4 (ref. 20) and C-5 (ref. 23). An earlier MM1 calculation, by Allinger and Chung[22], indicated that there is essentially no barrier to rotation in equatorial 2-phenyl-1,3-dioxane. Calorimetric investigations showed that 2-phenyl-1,3-dioxane has a high entropy-content, consistent with the foregoing conclusion[24]. A n.m.r. technique, the *J* method, suggested that the barrier is small (0.4 ±0.2 kcal.mol^{-1}), but not zero, and that the parallel conformation is favored[25]. The barrier was recalculated by driving the ortho-C–C–C–H torsional angle from 0° to 90° in 10° steps, using the modified MM2 program. The parallel conformation was calculated to be a minimum, 0.95 kcal.mol^{-1} more stable than the maximum, the perpendicular conformation. Allinger and Chung[22] interpreted the zero rotational-barrier in terms of a balance between ortho-hydrogen–ring-oxygen repulsion in the perpendicular conformation, and ortho-hydrogen–αH-repulsion in the parallel conformation[22]. Incorporation of the anomeric effect shortens the C–O distances, destabilizing the perpendicular conformation. A barrier of 0.95 kcal.mol^{-1} is compatible with the calorimetric results[24]. It can be shown that the amount by which the entropy content is reduced from the free-rotation value is only 0.29 e.u. for this barrier size[24,26] at 300 K. Thus, the evidence[15–25] appears to be consistent with a low barrier (<1 kcal.mol^{-1}), with the parallel conformation favored.

The conformations adopted by the two phenyl rings of **1** are probably a result of intermolecular interactions (see Fig. 2).

The solid-state structure can be of use in the discussion of the n.m.r.-spectral results obtained for it in solution, but only if the conformation of **1** is the same in both. The vicinal, ^{1}H-n.m.r. coupling-constants for the skeletal protons were obtained by iterative simulation of the six-spin system from a spectrum measured in benzene-d_6. Precise correlation of the magnitude of vicinal coupling-constants with H–C–C–H torsional angles is unreliable, because substituent effects are of significant size and are dependent on geometry. Nevertheless, the values obtained were consistent with the solid-state conformation. Coupling constants are labelled by using the crystallographic numbering (see Fig. 1). The value of $J_{1,2}$ was 8.4 Hz, a smaller value than would be expected for an *anti* arrangement of coupled hydrogen atoms[27]. Thus, the axial CH(SEt)$_2$ group is not perfectly staggered in solution, or in the solid state. The $J_{2,6}$ value was 5.4 Hz, larger than the 4.6–5.0 Hz observed for axial–equatorial coupling at similar positions in all-equatorial 2,4,5-trialkyl-1,3-dioxanes[28]. Additional flattening, such as observed in the framework of the solid-state structure, should cause the H–C–C–H torsional angle to decrease, and thus result in a larger value of $J_{2,6}$. The observed solid-state H–C–C–H angle was −56.3°. The $J_{6,7}$ value, 9.3 Hz, is similar to that predicted for an exact *anti*-relationship between hydrogen atoms having the same substituents in the same geometric relationship, namely[27], 9.6 Hz. The near-60° torsional angles about this bond result in a 179.5° H–C–C–H torsional angle in **1**. The $J_{7,12}$ value, 4.7 Hz, is similar to that observed for the same hydrogen atoms in simple 1,3-dioxanes[28], as expected from the normal 1,3-dioxane torsional angles about this bond in **1**. The $J_{7,11}$ and $J_{11,12}$ values are small in absolute magnitude, 9.6 and −10.1 Hz, compared to 10.7 and −11.3 Hz in alkyl-substituted 1,3-dioxanes[28]. Both values are affected by the additional electronegative substituents present in **1**, and the effects observed are in the direction expected on the basis of the locations of the additional substituents[29,30]. The ^{1}H-n.m.r. spectrum of **1** in chloroform-*d*, the solvent in which the standard n.m.r. parameters were recorded[4], could be only partially solved. However, the similarity of the chemical-shift distribution, and of those values of the coupling constants which could be obtained from the spectrum in chloroform-*d*, to those of the benzene-d_6 spectrum, strongly indicate that the conformation in chloroform-*d* is similar to that present in benzene-d_6 and in the solid state.

N.m.r. parameters. — The values of the three n.m.r. parameters suggested for the six-membered-ring, benzylidene acetals[4] and the values obtained for **1** are shown in Table V. The ^{1}H-n.m.r. chemical-shift of 5.67 p.p.m. for the benzylidene proton in the 3,5-*O*-benzylidene ring appears to be typical of *trans*-fused 3,7-diphenyl-2,4,6,8-tetraoxa[4,4]bicyclodecanes; we have recently observed[31] chemical shifts of 5.67 and 5.72 p.p.m. for the acetal protons in 2,4:3,5-di-*O*-benzylidene-D-ribose diethyl dithioacetal (**2**). The ^{13}C-n.m.r. shifts of the acetal carbon atoms

TABLE V

N.M.R. PARAMETERS FOR 2-PHENYL-1,3-DIOXANE RINGS

Parameter	*Ring having no axial substituents at C-2 or C-4*	*Ring having axial substituent at C-4*
Chemical shifts of actal H (p.p.m.)		
Previous ranges[a]	5.44–5.58	5.79–5.90
Observed for **1**	5.67	6.23
Revised ranges	5.40–5.72[b]	5.79–6.23
Chemical shift of acetal C (p.p.m.)		
Previous ranges[a]	100.6–101.4	93.7–94.9
Observed for **1**	102.2	97.0
Revised ranges	100.6–102.2[b]	93.7–97.0
$^1J_{C,H}$ *for acetal C (Hz)*		
Previous ranges[a]	159.7–161.8	159.7
Observed for **1**	157	168
Revised ranges	157–162	157–162[c]

[a] From ref. 4. [b] Values >5.58 p.p.m. or >101.4 p.p.m. will be obtained only for *trans*-fused 3,7-diphenyl-2,4,6,8-dioxabicyclo[4,4]decane rings. [c] A larger value may be observed in fused-ring systems.

were also found to be large, 102.2 p.p.m. for ring B of **1** and 101.6 and 101.8 p.p.m. for **2**. These differences must result from the changes in geometry in ring B in comparison to normal 1,3-dioxane rings which arise from the *trans* ring-fusion. No examples of this type of ring system were considered when the original ranges were established[4]. The ranges have been slightly revised in order to include these values, and also the slightly different $^1J_{C,H}$ values (see Table V). The values of these parameters in ring A were also somewhat different from those observed for the limited number of examples of 2-phenyl-1,3-dioxane rings having 4-axial substituents previously studied[4], and the ranges for this type of structure have also been extended (see Table V). The extension of the ^{1}H-n.m.r. chemical-shift range to 5.72 p.p.m. for the signal of the acetal proton of 2-phenyl-1,3-dioxane rings produced a slight overlap with the range for 2-phenyl-1,3-dioxolane rings, 5.71–6.41 p.p.m. Similarly, the ^{13}C-n.m.r. chemical-shift ranges for the signals of acetal carbon atoms have now become slightly overlapping, 100.6–102.2 p.p.m. for the former compounds, and 101.9–105.8 p.p.m. for the latter. It is apparent that caution must be used in interpretation of n.m.r. parameters educed from fused-ring systems.

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