Crystal and Molecular Structure of a Carbohydrate-derived Oxetan-3-one. Definitive Evidence for a Novel Participation of a Pyranose Ring Oxygen Atom

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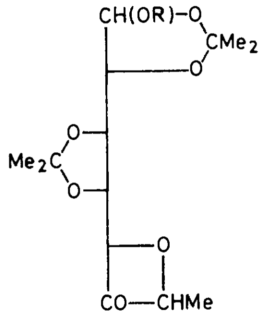
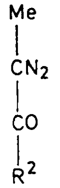
The crystal and molecular structure of (1*S*)-5,7-anhydro-8-deoxy-1,2:3,4-di-*O*-isopropylidene-1-*O*-methyl-D-*glycero*-D-*galacto*-octos-6-ulose has been determined by *X*-ray analysis. It crystallizes in the tetragonal $P4_1$ ($P4_3$) space group, with $a = b = 10.239(5)$, $c = 16.369(7)$ Å, $Z = 4$. The structure was solved by direct methods and refined to an R value of 5.3%. The octose chain is bent in such a way as to keep C-2, -3, -4, and -5 in the same plane. The formation of this compound during the methanolysis of 7,8-dideoxy-7-diazo-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-octos-6-ulopyranose(3) by participation of the pyranose ring oxygen atom is discussed in the light of current ideas on diazo-ketone substitution.

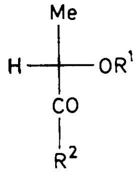
WE report the first determination of the solid state structure of an oxetan-3-one. The compound was obtained[1] by boron trifluoride-catalysed methanolysis of the sugar-derived diazo-ketone (3). The partial constitution (1) was considered highly probable from a consideration of spectral properties.[1] However the determination of structure appeared to be desirable because (*a*) the suggested constitution (1) implies the formation of a four-membered ring by the opening of a six-membered ring, and a new and remarkable mode of participation of the ring oxygen atom of a pyranose sugar, and (*b*) oxetan-3-ones are a little-known family of which only six representatives have so far been described.[2]



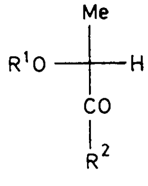
(1) R = Me
(2) R = Ac



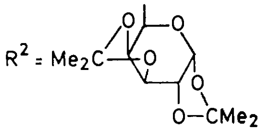
(3)



(4) R^1 = Me
(5) R^1 = Ac



(6) R^1 = Me
(7) R^1 = Ac



EXPERIMENTAL

A crystal of size 0.4 × 0.4 × 0.4 mm was used.

Crystal data. $C_{15}H_{24}O_7$, $M = 316$. Tetragonal, space group $P4_1$ or $P4_3$, $a = b = 10.239$ (5), $c = 16.369$ (7) Å, $U = 1\,716$ Å^3, $D_m = 1.21$, $Z = 4$, $D_c = 1.223$ g cm^{-3}, $F(000) = 680$, $\lambda = 1.541\,8$ Å.

For data collection automatic four-circle diffractometer (θ—2θ scan, at 3° mm^{-1}) was used, with two background measurements per reflection, up to 2θ = 136° (graphite monochromator). The number of measured reflections was 1 830, and the number of observed reflections 1 301. The structure was solved for the $P4_1$ space-group by the direct multi-solution method.[3] The best E map showed all the heavy atoms. Only 15 hydrogen atoms out of 24 were located on the difference Fourier series, and introduced into the calculation. The 9 non-localised hydrogen atoms belonged to the three methyl groups of C-8, C-9, and C-15. The positional and thermal parameters of the heavy atoms were refined by full matrix least squares. The temperature factors were anisotropic for heavy atoms, and isotropic for the 15 localised hydrogen atoms (same value for B as that of the bonded carbon atom), whose positions were not refined. The final R value for all the 1 301 reflections is 5.3%. The mean δ/σ for the last cycle is 0.2.† The atomic scattering factors used were those of Doyle and Turner[4] for

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† Amplitudes of observed and calculated structure factors are available as Supplementary Publication No. SUP 21776 (10 pp., 1 microfiche). For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin II*, 1975, Index issue.

[1] S. David and J. C. Fischer, *Carbohydrate Res.*, 1974, **38**, 147; 1976, **46**, 273.

[2] (*a*) L. R. Marshall and J. Walker, *J. Chem. Soc.*, 1952, 467; (*b*) G. B. Hoey, D. O. Dean, and C. T. Lester, *J. Amer. Chem. Soc.*, 1955, **77**, 391; (*c*) B. L. Murr, G. B. Hoey, and C. T. Lester, *ibid.*, p. 4430; (*d*) J. L. Harper and C. T. Lester, *J. Org. Chem.*, 1961, **26**, 1294; (*e*) J. K. Crandall, W. H. Machleder, and M. J. Thomas, *J. Amer. Chem. Soc.*, 1968, **90**, 7346; (*f*) S. H. Schroeter and C. M. Orlando, jun., *J. Org. Chem.*, 1969, **34**, 1181; (*g*) J. A. Wojtowicz and R. J. Polak, *ibid.*, 1973, **38**, 2061.

[3] G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.

[4] P. A. Doyle and P. S. Turner, *Acta Cryst.*, 1968, **A24**, 390.

the heavy atoms, and those of Stewart, Davidson, and Simpson [5] for hydrogen atoms.

RESULTS

The molecular structure of (1*S*)-5,7-anhydro-8-deoxy-1,2:3,4-di-*O*-isopropylidene-1-*O*-methyl-D-*glycero*-D-*galacto*-octos-6-ulose is represented in Figure 1. The final atomic parameters and their standard deviations are given in Tables 1 and 2. Bond distances and angles are listed in Tables 3 and 4.

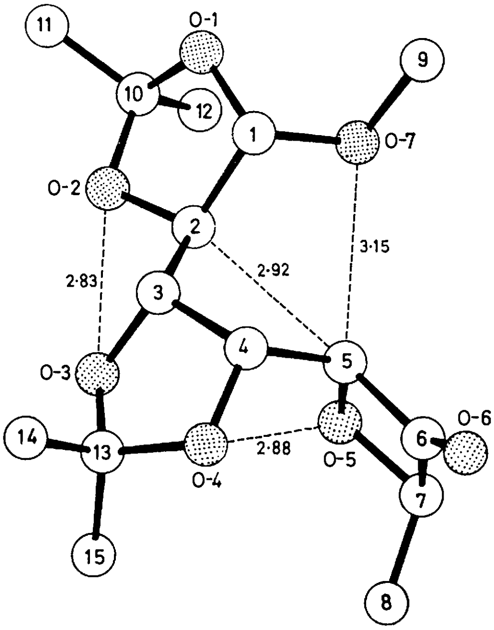

FIGURE 1 ORTEP [9] drawing of the molecule, including the shortest non-bonded interatomic distances

The four carbon atoms C-2, -3, -4, and -5 are nearly coplanar (see Table 5 for mean planes). The torsion angles of the octose carbon chain, can be represented as:

$$\text{C-1}\overset{-68^\circ}{\text{———}}\text{C-2}\overset{-22^\circ}{\text{———}}\text{C-3}\overset{-164^\circ}{\text{———}}\text{C-4}\overset{+124^\circ}{\text{———}}\text{C-5}\overset{-119^\circ}{\text{———}}\text{C-6———}$$
$$\text{C-7———C-8}$$

The oxygen atoms O-2 and -3 are in a *gauche* disposition (see Newman projections, Figure 2), with a dihedral angle of 60°. The configuration at C-1 is *S*. The 1,3-dioxolan system at C-1 and C-2 is an approximate envelope, with C-10 out of the best plane of the other four atoms, and slightly twisted ($^{\text{O-2}}T_{\text{C-10}}$); the pseudorotation angle Δ is 49°, and the puckering angle,[6] ϕ_m, is 43°. The second 1,3-dioxolan (at C-3 and -4) is a true envelope with O-3 out of the mean plane of the other atoms (Δ 29°, ϕ_m 36°).

The oxetanone ring is nearly planar (puckering angle 5.6°), O-5 being out of the C-5, C-6, C-7 plane by 0.10 Å, on the same side as O-6, C-8, and C-4. The methyl group at C-8 is *trans* with respect to H-5, and the configuration at C-7 is R.

The molecule is very compact. Short non-bonded interatomic distances are shown in Figure 1. The most interesting is HC(5) $\cdots$ O-7: 3.15 Å, with an H $\cdots$ O distance of 2.31 Å. We may consider the formation of the molecule to proceed as shown in Scheme 1. The pyranose ring, having either a boat or a chair conformation, undergoes cleavage of the O-5–C-1 bond, followed by rotation around C-2–C-3. This brings the oxygen atoms O-3 and O-2, which have been found in nearly antiparallel positions in the structure of a di-*O*-isopropylidenepyranose,[7] into a *gauche* position in order to relieve the steric hindrance created by the addition of methanol.

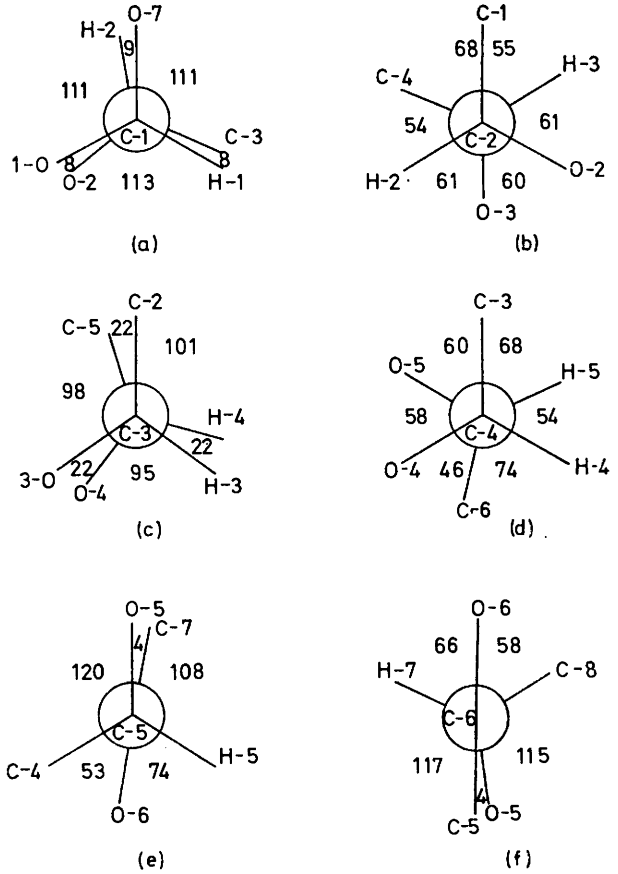

FIGURE 2 Newman projections along the octose chain (angles in degrees)

The observed and calculated values of $^3J_{\text{H,H}}$ are in excellent agreement with the assigned structure (Table 6). This suggests that conformation of the molecule in the solid state is similar to that in deuteriochloroform solution.

The packing of the molecules is determined by van der Waals forces. The only short intermolecular distances are between O-6, and the carbon atoms of two methyl

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[5] R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.

[6] C. Altona and M. Sundaralingam, *J. Amer. Chem. Soc.*, 1972, **94**, 8205.

[7] C. Riche and C. Pascard-Billy, *Acta Cryst.*, 1975, **B31**, 2565.

TABLE 1

Final atomic parameters ($\times 10^4$) for carbon and oxygen atoms and thermal parameters are in the form exp $[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$ (estimated standard deviations in parentheses)

Atom	X	Y	Z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}	'B'
O(1)	7 190(3)	−3 225(3)	3 748(0)	110(3)	170(4)	59(2)	22(3)	5(2)	−3(2)	6.0
O(2)	5 230(3)	−3 898(3)	4 148(3)	133(4)	157(4)	49(1)	−21(3)	−13(2)	9(2)	5.8
O(3)	2 849(3)	−3 841(3)	3 272(3)	121(3)	147(4)	47(1)	−18(3)	−2(2)	15(2)	5.4
O(4)	2 281(3)	−2 774(3)	2 105(3)	133(4)	196(5)	58(2)	−29(3)	−13(2)	36(2)	6.7
O(5)	2 939(4)	−650(4)	3 187(3)	205(5)	176(5)	80(2)	13(4)	1(3)	8(3)	8.2
O(6)	2 880(4)	211(5)	1 274(4)	216(7)	288(8)	111(3)	−9(5)	11(4)	106(4)	11.0
O(7)	6 469(3)	−1 177(4)	3 303(4)	136(4)	154(5)	131(3)	−19(3)	−15(3)	22(3)	8.7
C(1)	6 310(5)	−2 559(5)	3 243(3)	114(5)	166(7)	59(2)	4(5)	10(3)	2(3)	6.0
C(2)	4 974(4)	−2 925(4)	3 561(4)	113(5)	136(5)	49(2)	−5(4)	2(3)	6(3)	5.2
C(3)	4 044(4)	−3 460(4)	2 909(3)	107(5)	134(5)	43(2)	−12(4)	5(3)	2(3)	4.9
C(4)	3 594(4)	−2 458(5)	2 256(3)	112(5)	164(7)	46(2)	−9(4)	10(3)	22(3)	5.5
C(5)	3 681(5)	−1 053(5)	2 485(4)	126(6)	175(8)	73(3)	−14(5)	5(3)	33(4)	6.8
C(6)	2 943(5)	−54(6)	1 979(6)	130(6)	168(7)	108(4)	−31(5)	−4(5)	56(5)	8.0
C(7)	2 237(6)	419(5)	2 762(5)	189(8)	113(6)	110(4)	4(5)	−15(5)	20(4)	8.1
C(8)	777(5)	285(6)	2 780(6)	162(7)	215(8)	132(5)	25(6)	31(5)	−6(6)	10.0
C(9)	7 674(5)	−751(6)	2 952(7)	111(6)	227(9)	213(8)	−65(6)	1(6)	73(8)	12.3
C(10)	6 486(5)	−3 623(5)	4 458(4)	122(6)	176(7)	49(2)	4(5)	−4(3)	−8(3)	5.9
C(11)	7 097(6)	−4 834(6)	4 793(4)	168(7)	219(8)	65(3)	−20(6)	−30(4)	8(4)	7.7
C(12)	6 442(6)	−2 525(6)	5 078(4)	179(8)	271(10)	68(3)	13(7)	−5(4)	−68(5)	8.7
C(13)	1 892(4)	−3 842(5)	2 636(4)	131(6)	150(6)	52(2)	−16(5)	−16(3)	19(3)	5.8
C(14)	1 846(5)	−5 065(6)	2 164(5)	189(7)	182(7)	79(3)	−5(6)	−35(4)	−10(4)	8.0
C(15)	577(4)	−3 498(6)	3 016(4)	109(5)	242(8)	77(3)	−19(5)	18(3)	15(4)	7.6

TABLE 2

Fractional co-ordinates ($\times 10^3$) for hydrogen atoms

Atom	X	Y	Z	Atom	X	Y	Z	Atom	X	Y	Z
H(1)	640	−285	266	H(7)	238	124	291	H(12)	590	−309	561
H(2)	456	−214	382	H(11)	644	−542	530	H(12)	601	−169	500
H(3)	447	−422	263	H(11)	794	−467	496	H(14)	601	−568	257
H(4)	413	−260	175	H(11)	715	−547	439	H(14)	95	−494	182
H(5)	462	−78	254	H(12)	739	−253	543	H(14)	260	−537	207

TABLE 3

Bond distances (Å)

O(1)–C(1)	1.400(6)	O(7)–C(9)	1.429(8)
O(1)–C(10)	1.426(6)	C(1)–C(2)	1.511(6)
O(2)–C(2)	1.409(6)	C(2)–C(3)	1.531(7)
O(2)–C(10)	1.411(6)	C(3)–C(4)	1.551(7)
O(3)–C(3)	1.415(5)	C(4)–C(5)	1.489(7)
O(3)–C(13)	1.430(7)	C(5)–C(6)	1.518(9)
O(4)–C(4)	1.405(5)	C(6)–C(7)	1.548(12)
O(4)–C(13)	1.452(7)	C(10)–C(11)	1.493(8)
O(5)–C(5)	1.437(8)	C(10)–C(12)	1.516(8)
O(5)–C(7)	1.483(7)	C(13)–C(14)	1.472(8)
O(6)–C(6)	1.188(12)	C(13)–C(15)	1.524(7)
O(7)–C(1)	1.428(6)	C(7)–C(8)	1.501(8)

TABLE 4

Bond angles (Å)

C(1)–O(1)–C(10)	107.2(3)	C(4)–C(5)–C(6)	119.0(5)
C(2)–O(2)–C(10)	105.9(4)	O(6)–C(6)–C(5)	135.3(7)
C(3)–O(3)–C(13)	106.6(4)	O(6)–C(6)–C(7)	135.0(7)
C(4)–O(4)–C(13)	109.3(4)	C(5)–C(6)–C(7)	89.6(5)
C(5)–O(5)–C(7)	95.4(4)	O(1)–C(10)–O(2)	103.0(4)
C(1)–O(7)–C(9)	111.9(5)	O(1)–C(10)–C(11)	109.0(4)
O(1)–C(1)–O(7)	111.6(4)	O(1)–C(10)–C(12)	110.4(4)
O(1)–C(1)–C(2)	105.0(4)	O(2)–C(10)–C(11)	110.4(4)
O(7)–C(1)–C(2)	109.0(4)	O(2)–C(10)–C(12)	111.2(4)
O(2)–C(2)–C(1)	103.9(4)	C(11)–C(10)–C(12)	112.4(5)
O(2)–C(2)–C(3)	109.8(4)	O(3)–C(13)–O(4)	104.3(4)
C(1)–C(2)–C(3)	114.3(4)	O(3)–C(13)–C(14)	113.9(4)
O(3)–C(3)–C(2)	110.1(4)	O(3)–C(13)–C(15)	107.9(4)
O(3)–C(3)–C(4)	102.4(4)	O(4)–C(13)–C(14)	109.6(4)
C(2)–C(3)–C(4)	115.4(4)	O(4)–C(13)–C(15)	108.2(4)
O(4)–C(4)–C(3)	104.7(4)	C(14)–C(13)–C(15)	112.5(5)
O(4)–C(4)–C(5)	108.9(4)	O(5)–C(7)–C(6)	86.0(5)
C(3)–C(4)–C(5)	116.6(4)	O(5)–C(7)–C(8)	113.9(5)
O(5)–C(5)–C(4)	116.5(5)	C(6)–C(7)–C(8)	116.9(6)
O(5)–C(5)–C(6)	88.8(4)		

groups: C-12, situated at $1 - x, -y, \frac{1}{2} + z$ (3.12 Å), and C-8, at $y, -x, \frac{3}{4} + z$ (3.28 Å).

Computer programs used for this analysis were a modified version of ORFLS,[8] and ORTEP.[9]

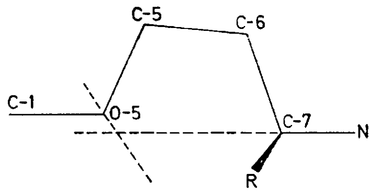


FIGURE 3 Scale model of a possible reactive conformation of the diazo-ketone (3) after protonation. Bond lengths and angles are from ref. 7 for C(1)–O(5) (1.41 Å), O(5)–C(5) (1.448 Å), C(1)–O(5)–C(5) (115.3°), and O(5)–C(5)–C(6) (108.9°). The geometry of the C(5)–C(6)–C(7) unit is considered to be the same as in acetone: C(5)–C(6) and C(6)–C(7) 1.515 Å, and C(5)–C(6)–C(7) as 116.7° (J. D. Swalen and C. C. Costain, *J. Chem. Phys.*, 1959, **31**, 1562). The dotted lines are the axes respectively, of the *s*-type lone-pair orbital of O-5, and of the CN_2^+ anti-bonding orbital. R is either Me (*S* cation) or H (*R* cation).

DISCUSSION

The boron trifluoride-catalysed methanolysis of the diazo-ketone (3) gave the keto-ethers (4) (*S*-configuration at C-7, L-*glycero*; 29%) and (6) (*R* at C-7, D-*glycero*; 11%), and a third compound (13%) to which we

[8] W. R. Busing, K. O. Martin, and H. A. Levy, ORFLS, Oak Ridge National Laboratory Report ORNL TM 305, 1962.

[9] C. K. Johnson, ORTEP, Oak Ridge National Laboratory Report ORNL 3794, 1963.

TABLE 5

Mean planes

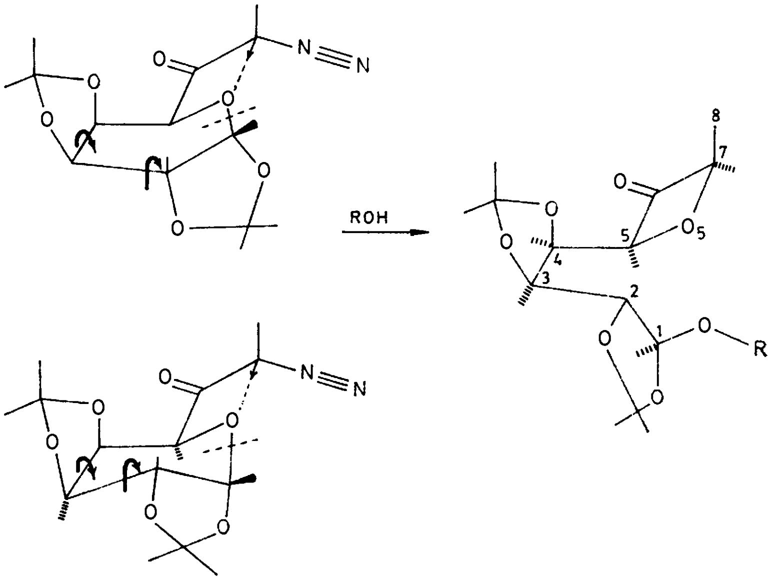
Carbon chain		Me_2CH					Oxetanone		
		A			B				
C(1)	1.461	C(1) *	0.054	* 0.000	C(3) *	0.008	C(5) *	−0.041	0.000
C(2) *	0.055	C(2) *	−0.049	* 0.000	C(4) *	−0.015	C(6) *	−0.031	0.000
C(3) *	−0.093	O(1) *	−0.009	* 0.000	O(3)	−0.494	C(7) *	−0.051	0.000
C(4) *	0.109	O(2) *	0.017	0.177	O(4) *	0.009	O(5) *	0.037	0.096
C(5) *	−0.080	C(10)	−0.520	−0.386	C(13) *	−0.011	O(6) *	0.035	0.049
C(6)	0.257	C(11)	0.011	0.230	C(14)	1.336	C(4)	1.047	1.083
C(7)	−1.599	C(12)	−2.035	−1.897	C(15)	−1.046	C(8)	1.120	1.176
C(8)	−2.834	O(7)	−1.039	−1.172	C(2)	−0.851			
Planes:	I		II	III		IV		V	VI

$\sigma = \pm 0.005$ Å

Equations of the mean planes:

$$\begin{array}{ll}
\text{I} & 0.818\,2X - 0.032\,9Y - 0.574\,0Z - 0.863\,9 = 0 \\
\text{II} & 0.012\,4X - 0.726\,3Y - 0.687\,3Z + 1.718\,2 = 0 \\
\text{III} & -0.021\,8X - 0.783\,3Y - 0.621\,3Z + 1.386\,2 = 0 \\
\text{IV} & 0.268\,8X - 0.646\,1Y - 0.714\,3Z + 0.007\,2 = 0 \\
\text{V} & -0.725\,4X - 0.666\,2Y - 0.173\,0Z + 2.678\,6 = 0 \\
\text{VI} & -0.728\,3X - 0.666\,6Y - 0.158\,8Z + 2.672\,2 = 0
\end{array}$$

* Atoms defining the planes.



SCHEME 1 Proposed scheme of the motion of the carbon atoms of the octose chain

ascribed the constitution (1).[1] This last assignment is now confirmed, and the configurations of the two carbon atoms modified in the preparation now known to be *R* at C-7 and *S* at C-1. The constitution (1) had been suggested because of some remarkable spectral properties: an exceptionally high i.r. carbonyl frequency (1 818 cm^{-1}) (although the u.v. spectrum was that of a normal ketone), and a marked deshielding of protons α to the carbonyl (δ 5.60 p.p.m.). Similar properties were observed for the six oxetan-3-ones [2] described previously.

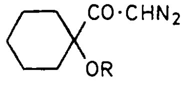
TABLE 6

First-order vicinal proton coupling constants (Hz) of compound (1)

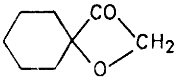
	Calc. [a]	Obs.[b]
$^3J_{1.2}$	3.3	2.5
$^3J_{2.3}$	9.2	*ca.* 10
$^3J_{3.4}$	7.0	6.9
$^3J_{4.5}$	2.7	2.5

[a] Calculated from the dihedral angles in the solid, with the help of the Karplus relation. [b] From the 100 MHz n.m.r. spectrum of a solution in $CDCl_3$.

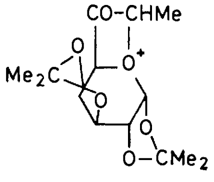
Our reaction bears a similarity to the first oxetan-3-one preparation, by Marshall and Walker.[2a] They treated compound (8) in succession with a base and with an acid, and it seems probable that the oxetan-3-one (9) was the result of the acidolysis of compound (10) (not isolated), for they observed gas evolution only at the second step. However, in our case, the internal nucleophile is not a hydroxy-function, but the oxygen atom of an acetal, so that a carbon–oxygen bond has to be broken to allow the ring closure. Participation reactions of the ring oxygen atom of a sugar have been observed when there is a good leaving-group β to this oxygen atom, at C-2 of a pyranose (leading to a 2,5-anhydride [10a]), at C-4 of a pyranose (with ring contraction [10b,c]), and at C-5 of a furanose.[10b,d] The mechanism depicted in Scheme 2 has been suggested [10b,d] for a reaction of this last type, which is the most akin to ours.



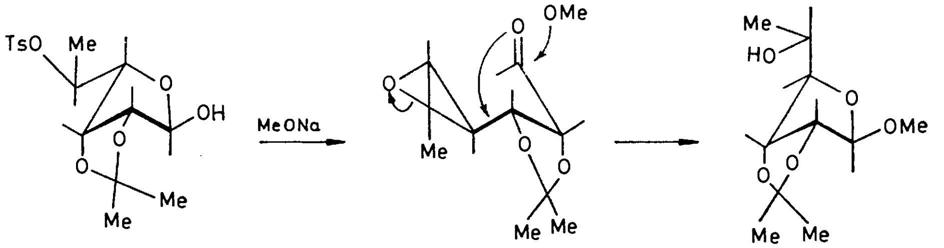
(8) R = Ac
(10) R = H



(9)



(11)



SCHEME 2 Displacement of the 5-*O*-*p*-tolylsulphonyl group by a furanose ring oxygen atom, according to ref. 10*b*

The main differences are obvious: in our new reaction the leaving group is γ to the ring oxygen atom, the glycosidic hydroxy-group is not free, the medium is acidic, and finally, we obtain the oxetan-3-one as a stable end-product, whereas the epoxide in Scheme 2 is a hypothetical intermediate.

We shall assume that the intermediates in the substitution reaction of the diazo-ketone (3) in acidic media are the protonated species $R^1CO{\cdot}CHR^2{\cdot}N_2^+$ (*cf.* ref. 11). These may be either *R* or *S* at C-7; with configurational inversion, they will respectively lead to the keto-ether (4) (*S*) or (6) (*R*). The only oxetan-3-one isolated in this reaction had the *R*-configuration at C-7; moreover substitution at C-1 by MeO had occurred with configurational inversion.

The conformations of ' diacetone-galactose ' derivatives have been found to be $B_{2,5}$ boats distorted towards twist boats, either in the solid state [7] or in solution.[12] We may therefore consider a reactive conformation such as that of Figure 3, where atoms C-1, O-5, C-6, and C-7, and the diazo-group all lie nearly in the same plane, so as to allow the best possible overlap of the antibonding CN_2^+ orbital with the orbital of the ring oxygen *s*-type lone pair. In a concerted reaction, all events, including the attack at C-1 by the solvent nucleophile, would be symmetrical with respect to this plane; moreover, broken bonds and newly formed bonds would lie almost on a straight line. However, the stereochemical course of the reaction at C-1 could also be explained either (i) through formation of the oxetanonium ion (11), a highly strained intermediate in which the cationic oxygen should be a very good leaving-group, or (ii) an attack on the ring oxygen atom by C-7 concerted with appearance of a carbocation centre at C-1. The latter would react with the solvent while still protected on one of its faces.

The acetolysis of the diazo-ketone (3), which follows a similar course, leading to the keto-acetates (5) and (7) and the oxetan-3-one (2), will be the subject of a further paper.[13]

[6/142 *Received*, 22*nd January*, 1976]

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