Acta Chemica Scandinavica B 33 (1979) 197—202

Reactions between Aldehydes and Polyhydric Alcohols V.* X-Ray Structure and Conformational Analysis of (5Z,12Z)-1,3,8,10-Tetraoxacyclotetradeca-5,12-diene

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The crystal structure of (5*Z*,12*Z*)-1,3,8,10-tetraoxacyclotetradeca-5,12-diene has been determined by X-ray diffraction methods using 822 observed reflections measured on an automatic diffractometer. The unit cell dimensions are $a = 7.985(2)$ Å; $b = 4.6031(2)$ Å; $c = 16.097(7)$ Å; $\beta = 116.64(2)°$. The final least-squares refinement has a unit weighted residual of 0.047. The molecule has the conformation in the crystal state that could be predicted by empirical rules assuming analogy between the *cis*-CH=CH-unit and a CH_2 group. The acetal C—O bonds are significantly shorter (1.399 Å) than the other C—O ether bonds (1.429 Å).

The conformation of the molecule in solution has been studied by NMR techniques and found to be the same.

In a previous paper [2] the isolation of (5*Z*,12*Z*)-1,3,8,10-tetraoxacyclotetradeca-5,12-diene (*1*) from the reaction between (*Z*)-2-butene-1,4-diol and paraformaldehyde was reported.

The conformation of cycloalkanes and of saturated cyclic ethers and polyethers has been studied extensively,[3,4] and the structure of 1,3,8,10-tetraoxacyclotetradecane (*2*, the saturated analogue of *1*) has been established by X-ray crystallography.[5] To our knowledge, no conformational analysis has been carried out on unsaturated compounds containing the 1,3-dioxa grouping in a larger ring, and we have therefore undertaken this investigation, in order to examine whether the generalizations valid for the comparison of the conformations of saturated and unsaturated cyclic hydrocarbons hold for these compounds.

It is known from conformational studies of alicyclic hydrocarbons [4] that the rigid angular CH=CH-unit of a *cis*-double bond is roughly equivalent to a CH_2-group, with proper adjustment of valency and torsional angles of adjacent atoms and bonds. If this relationship holds in the present case, the conformation of *1* can be derived from that 1,3,7,9-tetraoxacyclododecane (*3*). The conformation of *3* (as well as that of cyclododecane) is the square [3 3 3 3] conformation *a* (Fig. 1). Replacement of the two methylene groups (C5 and C11) by *cis*-CH=CH-units, and changes of the torsional angles of the bonds adjacent to C8 (in *a*) from g^+g^+ to g^-g^- lead to the conformation *b*. This predicted conformation of *1* is closely related to the known conformation of *2* (*c*, Fig. 1), the only major difference being the size of the torsional angles of the bonds adjacent to the double bonds.

EXPERIMENTAL

Spectroscopic measurements. ^1H and ^{13}C NMR spectra were obtained as previously described.[1]

Crystallographic examination. By recrystallizing *1* from absolute ethanol large transparent needles were obtained, which had to be shortened for X-ray diffraction work.

* Part IV, see Ref. 1.

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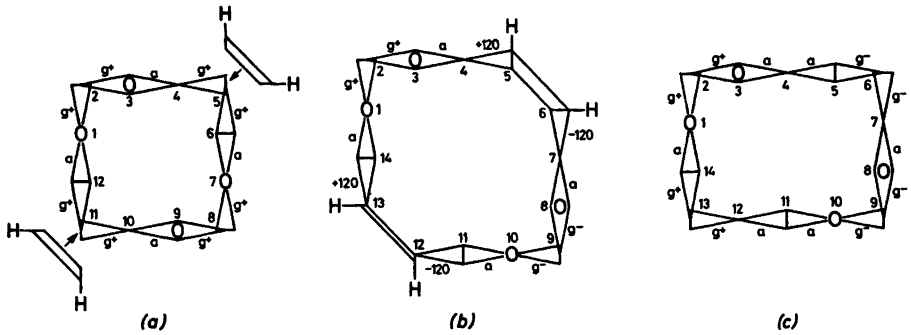

Fig. 1. Known conformations of 1,3,7,9-tetraoxacyclododecane (*a*) and 1,3,8,10-tetraoxacyclotetradecane (*c*) and predicted conformation of (5*Z*, 12*Z*)-1,3,8,10-tetraoxacyclotetradeca-5,12-diene (*b*).

The crystals sublime easily and react with araldite. These difficulties were eventually overcome by mounting a long crystal with the glue PR 9247/1000 and later dissolving the excess of the crystal by means of a monomer of this glue. When the proper size of the crystal was achieved the crystal was removed from the bath and simultaneously covered with the glue.

Weissenberg and precession photographs showed that the crystals were monoclinic (space group $P2_1/c$) and provided preliminary cell dimensions. A single crystal with dimensions $0.13 \times 0.2 \times 0.4$ mm^3 was used for the data collection and for the accurate determination of unit cell parameters. The diffraction data was measured at 23 °C on a Picker FACS-1 diffractometer using graphite monochromated Cu$K\alpha$-radiation. The setting angles for 16 relatively high angle reflections were optimized automatically on the diffractometer and used in least-squares refinement of the orientation matrix and the unit cell dimensions. The diffraction data were collected in a $\theta-2\theta$ scan mode at a scan rate of 2°/min in 2θ. The scan range was symmetrical and increased with 2θ following the expression $\Delta 2\theta = 3.8° + 0.286°$ tan θ.

Reflections with $2.4° \leq 2\theta \leq 125°$ were measured in the hemisphere $h \geq 0$. Background counts were measured for 10 s each end of the scan interval. The intensities of 3 standard reflections were measured for every 40 reflections and showed that the crystal deteriorated during the data collection. Correction for this degradation of the crystal was made by using a rescale function linear in exposure time. The data were corrected for Lorentz and polarization effects but not for absorption. Symmetry equivalent reflections were averaged. A reflection was classified as observed using the criterion $I/\sigma(I) > 2.0$ where $\sigma(I)$ is the standard deviation calculated from counting statistics. The data reduction resulted in 868 reflections of which the 822 observed reflections were used in the structure solution and refinement.

During the crystallographic calculations use was made of the following computer programs: The Vanderbilt System [6] for the diffractometer operations, a local modification of the program NRC-2A [7] for data reduction, MULTAN [8] for the structure solution, the X-RAY System [9] for the refinement and crystal structure analysis, Simplex [10] for the weight analysis, ORTEP II [11] for the illustrations and the program THMB [12] for the analysis of thermal parameters.

The atomic scattering factors employed were those reported by Cromer and Mann [13] for carbon and oxygen and by Stewart, Davidson and Simpson [14] for hydrogen.

CRYSTAL DATA

(5*Z*,12*Z*)-1,3,8,10-Tetraoxacyclotetradeca-5,12-diene $C_{10}H_{16}O_4$; M = 200.24. Monoclinic, $a = 7.985(2)$ Å, $b = 4.6031(2)$ Å, $c = 16.097(7)$ Å, $\beta = 116.64(2)°$. $V = 528.84$ Å^3; $D_x = 1.04$ g cm^{-3}. μ(Cu$K\alpha$) = 6.33 cm^{-1}, $F(000) = 216$. Systematically absent reflections: $h0l$ when l odd, $0k0$ when k odd. Space group $P2_1/c$. The needle axis is parallel to the b axis.

STRUCTURE SOLUTION AND REFINEMENT

Positions for the heavier atoms were obtained by direct methods using the program system MULTAN.[8] The structure was refined by the method of least squares minimizing $\sum w(|F_o| - k|F_c|)^2$. The hydrogen atoms were found from a difference Fourier calculated after a unit weighted refinement of the scale

Table 1. Final fractional coordinates [a] and thermal parameters with estimated standard deviations. The expressions for temperature factors are $\exp\{-2\pi^2(h^2a^{*2}U_{11}+k^2b^{*2}U_{22}+l^2c^{*2}U_{33}+2hka^*b^*U_{12}+2hla^*c^*U_{13}+2klb^*c^*U_{23})\}$ for the anisotropic and $\exp(-8\pi^2U\sin^2\theta/\lambda^2)$ for the isotropic. The thermal parameters u_{ij} are in units of Å$^2\times10^{-2}$. Atom Hmn is bonded to Cm.

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O1	0.08468(17)	0.7196(3)	−0.11636(9)	4.60(8)	4.81(8)	5.58(8)	−0.50(6)	1.77(6)	−0.53(6)
C2	0.2788(3)	0.7195(6)	−0.06059(16)	4.73(12)	6.82(15)	6.26(13)	−0.73(11)	2.51(10)	−1.31(11)
O3	0.33215(19)	0.8582(3)	0.02471(9)	5.29(9)	6.05(9)	5.48(8)	−1.81(7)	2.28(7)	−0.98(7)
C4	0.2648(4)	0.7139(5)	0.08205(17)	7.26(16)	5.35(13)	6.31(13)	−1.16(12)	3.16(12)	−0.15(11)
C5	0.3136(3)	0.8954(5)	0.16600(14)	5.27(12)	5.85(13)	4.59(11)	−0.01(11)	1.04(9)	0.36(9)
C6	0.1971(13)	1.0159(5)	0.19302(14)	5.85(13)	5.83(13)	4.53(11)	−0.02(10)	1.45(10)	0.55(10)
C7	−0.0104(3)	0.9948(5)	0.14567(18)	5.94(14)	5.48(13)	7.26(15)	−0.57(11)	2.87(12)	0.90(12)
Atom	x	y	z	U	Atom	x	y	z	U
H21	0.335(3)	0.825(5)	−0.0941(18)	7.1(7)	H5	0.446(4)	0.932(5)	0.2019(17)	6.8(7)
H22	0.316(3)	0.510(6)	−0.0542(19)	7.8(7)	H6	0.250(3)	1.127(6)	0.250(2)	7.6(7)
H41	0.134(4)	0.689(4)	0.0486(17)	6.0(6)	H71	−0.062(4)	0.920(7)	0.187(2)	9.8(9)
H42	0.327(4)	0.511(8)	0.099(2)	10.8(10)	H72	−0.056(4)	0.863(6)	0.088(2)	8.7(8)

[a] Coordinates for the other half of the molecule can be obtained by application of the symmetry operation: $-x, 2.0-y, -z$.

factor and the anisotropic thermal and positional parameters for the heavier atoms. The positional and isotropic thermal parameters for the hydrogen atoms were included in the succeeding refinements. The weights used in the final refinements followed the expression $w = 1/(2\times10^{-3}F^2+3.8\times10^{-5}F^3)$.

After the final cycle of least-squares refinement the maximum shift was 0.04 σ and the unit weighted and weighted residuals were 0.047 and 0.061, respectively.

DESCRIPTION OF THE CRYSTAL STRUCTURE

The final atomic parameters are given in Table 1. Bond lengths, bond angles and dihedral angles are listed in Table 2. From the drawing of the molecule shown in Fig. 2 and by inspection of the dihedral angles shown in Table 2, it can be concluded that the compound *1* in the crystalline state has the expected conformation *b* of Fig. 1.

Introducing double bonds in a cyclic ether has not caused any unpredictable changes in the molecular dimensions for *1*. However, the C−C bonds, C5−C6 (1.314 Å), C4−C5 (1.485 Å) and C6−C7 (1.484 Å) are all slightly shorter than the expected values (C−C double bond

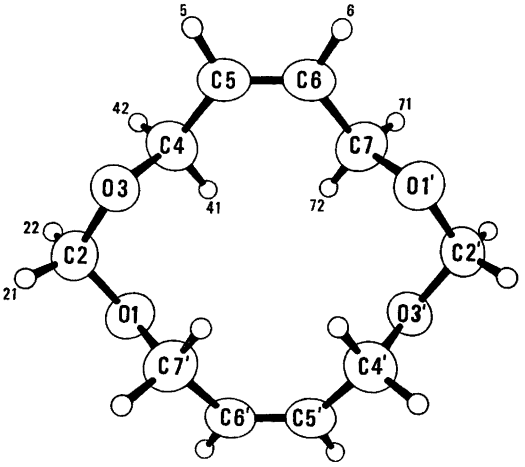

Fig. 2. ORTEP drawing showing the atomic labelling in (5*Z*,12*Z*-1,3,8,10-tetraoxacyclotetradeca-5,12-diene. The thermal ellipsoids for the heavier atoms are scaled to include 50 % probability.

Table 2. Bond lengths (Å), bond and dihedral angles (deg) with their estimated standard deviations in parentheses.

Bond lengths		Corr [a]		
O1–C2	1.401(2)	1.404	C2–H21	0.97(3)
C2–O3	1.396(3)	1.399	C2–H22	1.00(3)
O3–C4	1.424(4)	1.431	C4–H41	0.94(3)
C4–C5	1.485(4)	1.487	C4–H42	1.04(4)
C5–C6	1.314(4)	1.318	C5–H5	0.96(2)
C6–C7	1.484(4)	1.487	C6–H6	0.97(3)
C7–O1′	1.433(3)	1.438	C7–H71	0.99(4)
			C7–H72	1.03(3)

Angles		Dihedral angles	
C7′–O1–C2	112.8(2)	C7′–O1–C2–O3	67.7(3)
O1–C2–O3	113.1(2)	O1–C2–O3–C4	64.4(3)
C2–O3–C4	112.8(2)	C2–O3–C4–C5	−174.5(2)
O3–C4–C5	107.8(2)	O3–C4–C5–C6	118.5(2)
C4–C5–C6	127.1(2)	C4–C5–C6–C7	−0.6(4)
C5–C6–C7	126.6(2)	C5–C6–C7–O1′	−116.8(3)
C6–C7–O1′	108.1(2)	C6′–C7′–O1–C2	−172.5(2)

[a] Corrected bond lengths assuming a rigid body motion.

1.334 Å, and C(sp^2)–C(sp^3) single bond 1.511 Å).[15]

The C–O distances from an acetal carbon atom are significantly shorter than the other C–O distances. The C2–O1 (1.404 Å) and C2–O3 (1.399 Å) bonds agree well with the similar bond distances in 1,3,5,7-tetroxocane [16] and 1,3,8,10-tetraoxacyclotetradecane,[5] whereas the longer C4–O3 (1.424 Å) and C7–O1′ (1.438 Å) bonds are comparable to the C–O bond lengths found in the cyclic ether 1,4,8,11-tetraoxacyclotetradecane.[17]

The crystallographic symmetry implies that the molecule has a center of inversion, further, an inspection of Table 2 shows that the overall symmetry of the molecule can be described as $2/m$ (C_{2h}) with the twofold axis connecting C2 and C2′ and the mirror plane intersecting the double bonds.

Table 3 shows some intramolecular contact distances which are shorter than the sum of the van der Waals radii [18] of the atoms by more than 0.2 Å. The stable conformation of the molecules *1* has one very short hydrogen contact H41–H72 (2.04 Å). The other interactions seem to give smaller contributions to the steric energy of the molecule. The packing of this structure is illustrated by the stereo pair in Fig. 3. The molecules are arranged so that

Table 3. Intramolecular contact distances in Å.

H41–H72	2.04
C7–H21	2.48
C2–H41	2.51
C2–H72′	2.52
C2–H42	2.61
C2–H71′	2.60
C4–H22	2.58
C5–H41	2.64
O1–C4	2.85

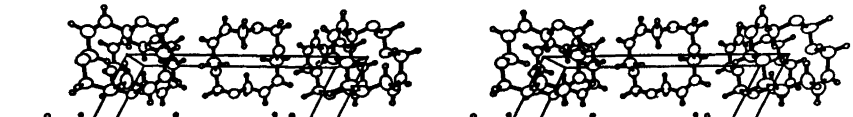

Fig. 3. Stereo pair illustrating the molecular packing viewed along the *b* axis.

the flat parts of the rings are almost perpendicular to the twofold axis. All the intermolecular distances are greater than the sum of the van der Waals radii.

FORCE FIELD CALCULATIONS

A force field calculation on the molecule has been carried out with Allinger's MMI program (1973 version).[19] The original parameters have been used with a dielectricity constant of 2.2.[20]

The conformation of lowest energy is in fairly good agreement with the X-ray structure. The C–H bonds are appreciably longer (1.1 Å) which is not surprising as the centre of electron density does not coincide with the hydrogen nucleus.[21] The calculated internuclear distance of H41–H72 was 2.177 Å, *i.e.* 0.14 Å longer than found from X-ray. This discrepancy is probably due to a systematic fault in the large and hard van der Waals' parameters for hydrogen used in the calculation.[22] Another difference is found in the acetal C2–O bonds being calculated to have the same length as ordinary C–O bonds. Nevertheless we feel that the X-ray structure on the whole is satisfactorily reproduced by the force field calculation.

The prediction of *b* as the conformation of *1* was based upon the assumption, that the torsional potentials were of major importance. This assumption is supported by the force field calculation of the steric energy (48.6 kcal mol^{-1}). The major contributions to the steric energy come from bending (17.3 kcal mol^{-1}) and van der Waals' interactions (25.6 kcal mol^{-1}), whereas the amount from torsion is about zero.

THE CONFORMATION IN SOLUTION

Infrared spectra were recorded of *1* in KBr, nujol, $CHCl_3$ and CCl_4. The four spectra were very similar, the only difference being a slight broadening of the absorption bands when *1* was dissolved. These findings indicate no change of conformation when compound *1* is dissolved in $CHCl_3$ or CCl_4.

The ^{13}C NMR spectrum (30 °C, $CDCl_3$) showed three sharp lines at δ 129.2 (–C=), 93.2 (O–C–O) and 60.9 (O–*C*–C=), in agreement with a conformation as *b*.

The ^1H NMR spectrum of *1* (30 °C, $CDCl_3$) showed an $M_2AA'M_2'$ system for the CH_2–CH=CH–CH_2 system as described earlier.[2] As this is not consistent with a fixed conformation *b* (where H41 and H42 should be non-equivalent) we have obtained ^1H NMR spectra of *1* under different conditions. The spectra at *ca.* 30 °C were very similar in $CDCl_3$, CD_2Cl_2 and C_6D_6 solutions, the only variations being solvent shift changes. Addition of shift-reagents [$Eu(dpm)_3$, $Pr(fod)_3$] did shift all signals significantly, but the number of lines and the coupling constants were unchanged. At higher shift-reagent concentrations the fine structure disappeared due to dipolar broadening. These results make the possibility of accidental equivalence of H41 and H42 very improbable. Low temperature measurements (90 and 270 MHz, CD_2Cl_2 solution) down to –90 °C revealed progressive broadening of all signals below *ca.* –50 °C without other changes in the spectra. It therefore seems most likely that *1* exists in solution as a single conformer *b* which on the NMR time scale undergoes rapid site exchange for the geminal protons down to at least –90 °C. Inspection of models does indeed suggest mechanisms for such exchanges that should have low barriers.

This assumption is supported by the magnitude of the coupling constants $^3J_{AM}$ and $^4J_{AM'}$, found at 30 °C in $CDCl_3$.[2] Conformational flexibility making H41 and H42 equivalent should exhibit coupling constants to these protons which are the mean values of the coupling constants in a rigid conformation. Taking the X-ray structure of *1* as such a rigid conformation, and using the Karplus equation parametrised for the –CH=CH–CH_2-system,[23] the following coupling constants can be calculated (θ *ca.* 60 and 180°): $^3J = 3.6$ and 11.6 Hz, and $^4J = 0$ and –1.6 Hz. The calculated mean values are thus $\langle ^3J \rangle = 7.6$ Hz and $\langle ^4J \rangle = -0.8$ Hz, in excellent agreement with the experimental values $^3J_{AM} = (\pm)7.5$ Hz and $^4J_{AM'} = (\pm)1.1$ Hz.

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Received November 6, 1978.