Short Communication

The Conformation of *cis*-3,7-Bis(hydroxymethyl)-3,7-dimethyl-1,5,9-trioxacyclododecane

Johannes Dale, Siw B. Fredriksen and Christian Rømming
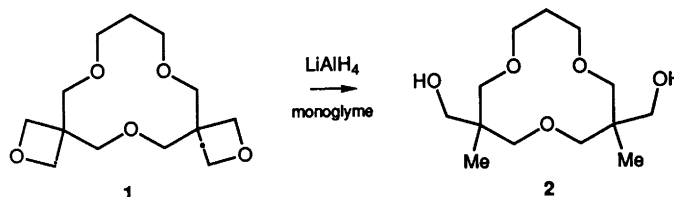
Kjemisk Institutt, Universitetet i Oslo, N-0315, Norway

The lithium-complexing property of 1,5,9-trioxacyclododecane (12-crown-3)[1,2] can be enhanced by attaching a ligating side-arm in the 3-position.[3] If additional ligating side-arms are present in the 7- and 11-positions, it is of course essential that they be *cis* to each other, since the cation is held by the ring oxygens on one side of the ring.[1,2]

In the crucial step of the synthesis of 3,7-bis(hydroxymethyl)-3,7-dimethyl-1,5,9-trioxacyclododecane (**2**), by reductive ring-opening of spiro-linked oxetane units in the precursor (**1**), two isomers were formed (Scheme 1).[3] The resolution in the ^{1}H NMR spectrum at 300 MHz was not sufficient to permit identification based on the only difference expected for the two isomers by symmetry arguments: two 11-CH$_2$ proton chemical shifts for the *cis*-isomer, but only one for the *trans*-isomer. The ^{13}C NMR spectrum would not be of any help, as the total number of lines should be the same for both isomers.

A single crystal of the main isomer, m.p. 102–103 °C, was therefore subjected to X-ray diffraction analysis.

X-Ray experiments. Crystals of the title compound were grown from chloroform–methanol. Details of the collection of X-ray data are given in Table 1. Unit cell data were calculated from the accurate setting angles of 25 reflections with $15° < 2\theta < 32°$.

Standard deviations for the intensities were taken as $\sigma(I) = [C_T + (0.03C_N)^2]^{1/2}$, where C_T is the total number of counts and C_N is the net count. The intensities were corrected for Lorentz and polarization effects but not for absorption.

Table 1. Crystal and experimental data.

Compound	$C_{13}H_{26}O_5$
M.p./°C	102–103
Diffractometer	NICOLET P3/F
Crystal dimensions/mm	0.2×0.25×0.4
Radiation	MoK$_\alpha$ (λ = 0.71069 Å)
Crystal system	Orthorhombic
a/Å	17.674(6)
b/Å	9.765(3)
c/Å	8.117(2)
V/Å^3	1400.8(8)
T/K	143
Space group	$Pmc2_1$ (No. 26)
M	262.35
$F(000)$	576
Z	4
D_x/g cm^{-3}	1.244
Scan mode	$\theta/2\theta$
Scan speed (2θ)/°min^{-1}	3.0
Scan range (2θ)/°	2.0
Maximum $(\sin\theta/\lambda)$/Å	0.76
Stability monitoring	3 Test refl./135 observ.
No. of indep. meas.	2784
No. with $I>3.0\sigma(I)$	1112
Weighting scheme	$w = [\sigma^2(F)]^{-1}$
No. of parameters refined	248
$R = \Sigma\|\|F_o\|-\|F_c\|\|/\Sigma\|F_o\|$	0.055
$R_w = [\Sigma w(F_o-F_c)^2/\Sigma wF_o^2]^{1/2}$	0.041
$S = [\Sigma w(F_o-F_c)^2/(n-m)]^{1/2}$	1.54

Structure determination and description. Systematically absent reflections were compatible with those of the three orthorhombic space groups; $Pmc2_1$ (No. 26), $Pma2$ (No.

Scheme 1.

Table 2. Atomic fractional coordinates and $U_{eq} = (1/3 \, \Sigma U_{ii})$.

Atom	x	y	z	$U_{eq}/\text{Å}^2$
O(11)	0.0000	0.3013(5)	0.3571(10)	0.023
O(21)	0.0870(3)	0.2806(4)	0.0053	0.031
O(31)	0.2286(2)	0.4404(4)	0.3664(7)	0.025
C(11)	0.0678(4)	0.3777(6)	0.3285(10)	0.021
C(21)	0.1314(4)	0.2763(6)	0.2838(10)	0.018
C(31)	0.1079(4)	0.1907(6)	0.1354(9)	0.022
C(41)	0.0727(4)	0.2137(7)	−0.1477(10)	0.030
C(51)	0.0000	0.1339(11)	−0.1559(15)	0.031
C(61)	0.2024(4)	0.3541(6)	0.2358(9)	0.025
C(71)	0.1463(4)	0.1796(7)	0.4297(11)	0.026
O(12)	0.5000	0.1752(6)	0.7321(9)	0.020
O(22)	0.4105(2)	0.2197(4)	1.0714(5)	0.023
O(32)	0.2905(3)	0.3693(4)	0.6600(7)	0.030
C(12)	0.4331(4)	0.0993(6)	0.7646(11)	0.021
C(22)	0.3667(4)	0.1948(6)	0.7934(10)	0.020
C(32)	0.3867(4)	0.2956(6)	0.9320(9)	0.017
C(42)	0.4270(4)	0.3032(7)	1.2118(9)	0.025
C(52)	0.5000	0.3809(10)	1.2039(13)	0.026
C(62)	0.3514(4)	0.2757(6)	0.6373(11)	0.020
C(72)	0.2973(4)	0.1098(7)	0.8404(11)	0.026

Table 3. Torsion angles. For comparison the torsion angles of molecule 2 are those of the mirror image relative to the coordinates given in Table 2.

Torsion angle				Molecule 1	Molecule 2
C1'	O1	C1	C2	−154.1(8)	−157.9(8)
C4	O2	C3	C2	172.5(8)	176.9(7)
C3	O2	C4	C5	73.1(7)	75.0(7)
O1	C1	C2	C3	56.5(6)	55.1(6)
O1	C1	C2	C6	174.4(8)	−63.5(7)
O1	C1	C2	C7	−62.8(7)	175.9(8)
C1	C2	C3	O2	54.4(6)	53.5(6)
C1	C2	C6	O3	59.5(6)	178.6(8)
C6	C2	C3	O2	−65.1(6)	172.5(8)
C3	C2	C6	O3	178.9(8)	59.6(6)
C7	C2	C3	O2	174.3(8)	−66.3(6)
C7	C2	C3	O3	−62.4(7)	−61.6(7)
C4'	C5	C4	O2	66.4(8)	68.7(8)

28) and *Pbmm* (No. 51). As it turned out, the structure was determined using the symmetry of the former, *Pmc2₁*, whereas no structure solution was achieved in the other two space groups. The structure was solved by application of the program MITHRIL[4] and refined by full-matrix least-squares calculations.[5] Hydrogen positions were found from
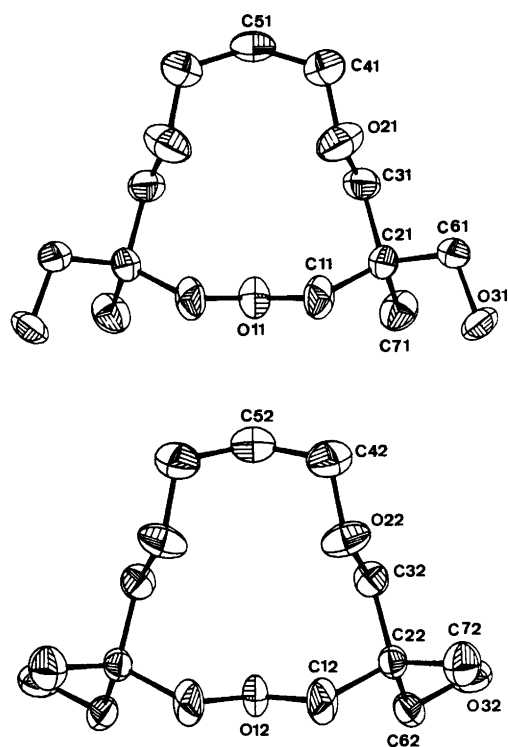

Fig. 1. ORTEP plot of the two crystallographically non-equivalent molecules with the numbering scheme.

difference Fourier syntheses and refined with isotropic thermal parameters. Final figures of merit are given in Table 1. Atomic coordinates and U_{eq} for the heavy atoms are listed in Table 2. Tables of observed and calculated structure factors, hydrogen parameters and anisotropic thermal parameters for the heavy atoms are available from C. R. upon request.

The unit cell contains two molecules each of two slightly different conformations as shown in Fig. 1. Both display mirror symmetry, as demanded by the space group. Bond lengths and angles are normal with average C–O and C–C bonds of 1.43 Å and 1.52 Å, respectively. Torsion angles are given in Table 3. The crystals are built up by layers normal to the *b* axis. Within the layers the molecules are hydrogen bonded in such a way that every hydroxy oxygen atom acts as hydrogen donor and acceptor in hydrogen bonds [average length 2.72(1) Å] to a molecule of the other kind. Between the layers the contacts are of van der Waals type between hydrogen atoms.

Discussion

The observed structure reveals that the configuration is that of the desired *cis*-isomer. Two types of molecule are present in the unit cell, both having the same ring conformation and differing only in the disposition of the substituents. The two conformations have practically identical ring torsion angles (a deviation of only 0–4°), suggesting that they represent a single well defined energy minimum. This energy is not expected to depend on the disposition of the substituents, since these are on 'corner' positions having local C_2-symmetry and are not sterically very different (–CH₃ versus –CH₂OH).

The observed ring conformation can be defined as quadrangular [2343], where the digits indicate the number of bonds in each of the four 'sides' joined by four 'corners'.[6] A 'corner' is further defined as a sequence of two *gauche* bonds of the same sign. The much preferred conformation

for cyclododecane is [3333],[7] and this is also the conformation observed for 1,4,7,10-tetraoxacyclododecane (12-crown-4) in most of its complexes.[8] The [2343] conformation has been calculated to be of next-lowest energy for the hydrocarbon,[6] but has not so far been observed. The reason for its occurrence here is obviously that the 1,5-relationship of the geminally substituted ring atoms requires a 1,5-relationship between corner positions in order to accommodate all substituents.[9] A related conformation [1344], calculated to be still higher in energy for the hydrocarbon,[6] was observed earlier for the uncomplexed ligand 3,3,7,7,11,11-hexamethyl-1,5,9-trioxacyclododecane.[1] Clearly, the choice of conformation is again dictated by the necessity of having all three *gem*-dimethyl groups on corner positions.

It remains to be pointed out that neither the [2343] nor the [1344] conformation has the ether oxygens suitably oriented for cation complexation. A non-angular diamond-lattice conformation, forbidden for cyclododecane, has all oxygen atoms converging towards a coordination center and is the conformation invariably adopted in Li⁺ complexes.[1,2]

References

1. Dale, J., Eggestad, J., Fredriksen, S. B. and Groth, P. *J. Chem. Soc., Chem. Commun.* (1987) 1391.
2. Dale, J. and Fredriksen, S. B. *Pure Appl. Chem. 61* (1989) 1587.
3. Fredriksen, S. B. and Dale, J. *Acta Chem. Scand. 46* (1992). *In press.*
4. Gilmore, C. J. *J. Appl. Crystallogr. 17* (1984) 42.
5. Mallinson, P. R. and Muir, K. W. *J. Appl. Crystallogr. 18* (1985) 51.
6. Dale, J. *Acta Chem. Scand. 27* (1973) 1115.
7. For a review, see: Dunitz, J. D. *Perspectives in Structural Chemistry 2* (1968) 1.
8. For a review, see: Dale, J. *Isr. J. Chem. 20* (1980) 3.
9. Dale, J. *Acta Chem. Scand. 27* (1973) 1149.