

Conformation of Uncomplexed Polyether Macrocycles. Structure of a Substituted 20-Crown-6 Derivative at -95°C , with Partial Conformational Disorder

BY ISRAEL GOLDBERG

Institute of Chemistry, Tel-Aviv University, Tel-Aviv, Israel

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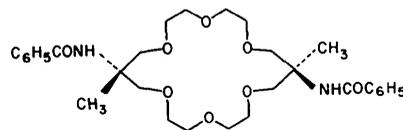
The crystal structure of an uncomplexed 20-crown-6 macrocyclic derivative containing two methyl and two benzamido substituents ($\text{C}_{30}\text{H}_{42}\text{N}_2\text{O}_6$) is discussed in detail. The structure has been determined from three-dimensional X-ray diffraction data collected at -95°C . Crystals are monoclinic, space group $P2_1/c$, with $a = 8.734(3)$, $b = 11.139(3)$, $c = 15.072(4)$ Å, $\beta = 100.00(3)^{\circ}$ and $Z = 2$. The structure was solved with *MULTAN* and refined to $R = 0.042$, using 2060 reflections with $F^2 \geq 3\sigma(F^2)$. Even at low temperature the ligand molecules are conformationally disordered, one of the $-\text{CH}_2-\text{CH}_2-$ groups within the asymmetric part of the macro-ring partially occupying two different sites; the corresponding refined occupancy factors are 0.66 and 0.34. The technique of constrained least-squares calculations has been utilized in the construction of the model of the disorder as well as in its refinement. Intramolecular $\text{N}-\text{H}\cdots\text{O}$ bonds and intermolecular $\text{C}=\text{O}\cdots\text{H}-\text{C}$ weak interactions seem to play a role in determining, respectively, the ligand overall structure and its packing arrangement in the crystal. The 20-membered ring has a chair-like conformation. The benzamido substituents approach the centre of the polyether cavity from opposite sides, thus providing steric inhibition for potential association of this ligand with various guest species.

Introduction

Previous studies of structural host-guest relationships among organic compounds have shown that many of the complexed macrocyclic polyether ligands have specific stereochemical features in common. For example, the most frequently observed conformations about the C-C and C-O aliphatic bonds in ordered crystal structures of poly-(ethylene oxide) moieties correspond, respectively, to synclinal and antiplanar arrangements. Moreover, only a very small number of C-O torsion angles are usually affected to a major extent when the macrocycle geometry is deformed in order to optimize specific ligand-substrate or intraligand interactions (Goldberg, 1977).

In order to examine further the properties of the conformations of polyether macrocyclic systems, we have extended our investigation to molecular structure determination of free ligands. In the first publication of this series (Goldberg, 1976) certain conformational aspects of uncomplexed 18-membered hexaheterocycles have been discussed, referring to previously reported studies by other workers. It has been observed that the overall shape of an uncomplexed macrocyclic ligand is often determined by intramolecular van der Waals and C-H \cdots O dipolar attractions. In the absence of stabilizing interactions of specific nature, the 'empty' molecules tend to be (partially) disordered in the crystal. The present investigation is concerned with the structure of a 20-crown-6 derivative containing two benzamido substituents (see below). In particular, it

seemed interesting to correlate the geometrical features of this compound with the fact that it reveals a rather poor binding capability toward ammonium and metal cations, in spite of the presence of eight potential oxygen-ligating sites (Cram, 1976).



We discuss here in detail the crystal structure analysis and molecular conformation of the title compound.

Experimental

Single crystals of the compound were kindly supplied by Professor D. J. Cram and Dr T. Tarnowski of the University of California at Los Angeles. The space group was determined photographically. The intensities were measured at $-95 \pm 3^{\circ}\text{C}$ on a Syntex $P\bar{1}$ diffractometer equipped with a cooling device (Strouse, 1976). A crystal of approximate dimensions $0.10 \times 0.15 \times 0.25$ mm was sealed in a Lindemann-glass capillary. Unit-cell dimensions and their estimated standard deviations were obtained from a least-squares fit of the optimized diffractometer setting angles of 15 selected reflections.

Crystal data

$C_{30}H_{42}N_2O_8$, $M_r = 558.7$, monoclinic, $a = 8.734$ (3), $b = 11.139$ (3), $c = 15.072$ (4) Å, $\beta = 100.00$ (3)°, $V = 1444.1$ Å³, $Z = 2$, $d_x = 1.285$ g cm⁻³, $F(000) = 600$. Cu $K\alpha$ radiation, $\lambda = 1.5418$ Å, $\mu(\text{Cu } K\alpha) = 7.7$ cm⁻¹. Space group $P2_1/c$ (systematic extinctions: $h0l$ with l odd and $0k0$ with k odd).

The intensities for all unique reflections with $2\theta \leq 155^\circ$ were measured with the θ - 2θ scan technique (at a constant scan rate of 2.0° min⁻¹), using graphite-monochromatized Cu $K\alpha$ radiation. The intensities of three standard reflections (220, 102, 022) monitored at frequent intervals showed no significant fluctuations during the data collection. The data were not corrected for absorption. 2060 observations with $|F_o|^2 \geq 3\sigma(|F_o|^2)$, excluding the very intense 200 and 122 reflections which appeared to suffer from secondary extinction, were used in the final refinement of the structure. The values of $\sigma^2(|F_o|^2)$ were estimated from counting statistics.

Refinement of the structural model

The structure was solved by a straightforward application of *MULTAN* (Germain, Main & Woolfson, 1971). All the nonhydrogen atoms were located in the E map based on the most self-consistent set of phases (259 E values ≥ 1.7).

The structural model was refined anisotropically by a full-matrix least-squares method. All H atoms could be located by three-dimensional Fourier difference syntheses very near to their expected positions; their coordinates and isotropic thermal parameters were included in subsequent calculations. The conventional refinement converged to $R = 0.072$. The corresponding estimated standard deviation of an observation of unit weight was 2.64.

However, the results obtained at this point were unsatisfactory in several respects. For example, an electron density difference synthesis, otherwise almost featureless, revealed a very high peak ($1.6 \text{ e } \text{Å}^{-3}$) located in the vicinity of atom C(4), the distance between the atomic positions of C(3) and C(4) appeared to be unreasonably short (1.42 Å), and the thermal parameters of these two atoms were nearly twice as large as those of the neighbouring nonhydrogen atoms. This suggested that the structure is partially disordered, and that its description is still incomplete.

A disordered model of the structure was constructed with the aid of the technique of constrained least-squares calculations, assuming that the ethylenic group $\text{CH}_2(3)\text{--CH}_2(4)$ is disordered between two different sites. Initially, the geometry of this group was kept fixed with a C—C bond length of 1.506 Å. Its orientation in one site was determined by the previously refined

positions of C(3) and C(4). The orientation of the C—C bond in the other site was defined by the relative positions of C(3) and the $1.6 \text{ e } \text{Å}^{-3}$ difference density peak. The initial occupancy factors were chosen as 0.7 and 0.3. Three cycles of constrained calculations were carried out in order to refine the various parameters of the disordered model, including a relative occupancy factor, orientational and positional parameters of the assumedly rigid $\text{CH}_2\text{--CH}_2$ groups and individual thermal parameters of the atoms. In the concluding stages of the refinement, when it seemed that the structural model was well defined, most of the geometrical constraints were released and the atomic parameters were adjusted independently. Positional and thermal parameters describing the disordered C—C fragment at the different sites were adjusted in alternating cycles of the least-squares calculation in order to avoid large correlation effects. Altogether, 266 parameters were refined excluding the isotropic temperature factors (set to $U = 0.05 \text{ Å}^2$) of atoms H(3) and H(4), and the calculated atomic positions of the H atoms located at the minor site.

At convergence, the occupancy factors associated with the $\text{CH}_2(3)\text{--CH}_2(4)$ group at the two sites were 0.66 and 0.34, in good agreement with what could be anticipated from the previous electron density difference synthesis (see above). The final R index is 0.042 for all the data, and the value of $[\sum w(\Delta F)^2 / (n - m)]^{1/2}$ is 1.47. A final difference map showed no peaks whose absolute heights exceeded $0.2 \text{ e } \text{Å}^{-3}$. A careful inspection of the structural results indicates that the geometrical and thermal parameters of the problematic ethylenic moiety are now consistent with those observed for other parts of the molecule to a significantly larger extent than prior to the assumption of disorder (see below). The above features confirm the apparent correctness of the disordered model.

The function minimized in all least-squares refinements was $\sum w(\Delta F)^2$, where $w = 1/\sigma^2(F_o)$. Scattering factors of Stewart, Davidson & Simpson (1965) were used for H, and those of Hanson, Herman, Lea & Skillman (1964) for all nonhydrogen atoms. The final positional parameters, along with their standard deviations estimated from the inverse of the least-squares matrix, are presented in Tables 1 and 2.*

Discussion of results

Fig. 1 illustrates the general conformational features of the substituted 20-crown-6 molecule, which is located in the crystal on a crystallographic centre of inversion.

* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33447 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

The macro-ring is stabilized in a chair-like conformation by intramolecular interactions of probable hydrogen-bonding nature between atoms N(12) and O(5') (in our notation, primed atoms belong to the same molecule as unprimed atoms listed in Table 1, the two sets being interrelated by inversion at $\frac{1}{2}, \frac{1}{2}, 0$). The geometry of this contact is characterized by distances N(12)···O(5') 3.28 and H(12)···O(5') 2.4 Å, by an angle N(12)—H(12)···O(5') 167°, and by an indication that the N—H bond is directed toward one of the lone pairs of atom O(5'). The existence of the intra-

ligand hydrogen bonding is clearly consistent with the observed elliptical shape of the polyether ring. Thus, the various distances across the ligand cavity O(2)···O(2') 7.81, O(5)···O(5') 5.69, and O(8)···O(8') 5.54 Å show that the ring is contracted along a direction roughly parallel to that of the N—H···O bonds (Fig. 1).

The two bulky benzamido substituents are *trans* with respect to the macro-ring, and approach its centre from

Table 1. Atomic fractional coordinates of the heavy atoms ($\times 10^4$)

	x	y	z
C(1)	6261 (3)	5584 (2)	-1838 (1)
O(2)	7261 (2)	4641 (1)	-2003 (1)
C(3)*	8593 (4)	4596 (3)	-1310 (3)
C(4)*	8543 (4)	3432 (3)	-811 (2)
O(5)	7129 (2)	3278 (1)	-469 (1)
C(6)	7212 (3)	2292 (2)	134 (1)
C(7)	7554 (3)	2649 (2)	1112 (1)
O(8)	6307 (2)	3363 (1)	1295 (1)
C(9)	6427 (3)	3628 (2)	2227 (1)
C(10)	5363 (2)	4686 (2)	2338 (1)
C(11)	5350 (3)	4881 (2)	3344 (1)
N(12)	5872 (2)	5762 (1)	1907 (1)
C(13)	7294 (2)	6266 (2)	2102 (1)
O(14)	8271 (2)	5995 (1)	2758 (1)
C(15)	7638 (2)	7203 (1)	1446 (1)
C(16)	7006 (2)	7137 (2)	531 (1)
C(17)	7413 (3)	7992 (2)	-61 (1)
C(18)	8405 (3)	8924 (2)	260 (1)
C(19)	9024 (2)	9002 (2)	1173 (1)
C(20)	8652 (2)	8134 (2)	1759 (1)
C(3)†	8619 (7)	4314 (6)	-1384 (5)
C(4)†	8360 (7)	3975 (5)	-457 (4)

* Atom at major site (occupancy 0.66).

† Atom at minor site (occupancy 0.34).

Table 2. Atomic fractional coordinates of the hydrogen atoms ($\times 10^3$)

	x	y	z
H(1a)	659 (3)	636 (2)	-204 (1)
H(1b)	627 (3)	562 (2)	-117 (1)
H(3a)*	863 (4)	529 (3)	-86 (3)
H(3b)*	961 (5)	463 (4)	-162 (3)
H(4a)*	941 (4)	333 (3)	-36 (2)
H(4b)*	856 (4)	271 (3)	-127 (2)
H(6a)	802 (3)	171 (2)	0 (2)
H(6b)	613 (3)	183 (2)	0 (2)
H(7a)	859 (3)	312 (2)	125 (2)
H(7b)	766 (3)	190 (2)	147 (2)
H(9a)	754 (3)	379 (2)	251 (2)
H(9b)	611 (3)	287 (2)	255 (2)
H(11a)	477 (3)	562 (2)	344 (2)
H(11b)	640 (3)	498 (2)	368 (2)
H(11c)	487 (3)	421 (2)	361 (2)
H(12)	518 (3)	609 (2)	149 (2)
H(16)	625 (3)	647 (2)	29 (1)
H(17)	696 (3)	793 (2)	-71 (2)
H(18)	867 (3)	955 (2)	-14 (2)
H(19)	969 (3)	968 (2)	138 (2)
H(20)	907 (3)	816 (2)	240 (1)
H(3a)†	939	503	-133
H(3b)†	912	357	-165
H(4a)†	818	477	-11
H(4b)†	933	355	-12

* Atom at major site (occupancy 0.66).

† Atom at minor site (occupancy 0.34).

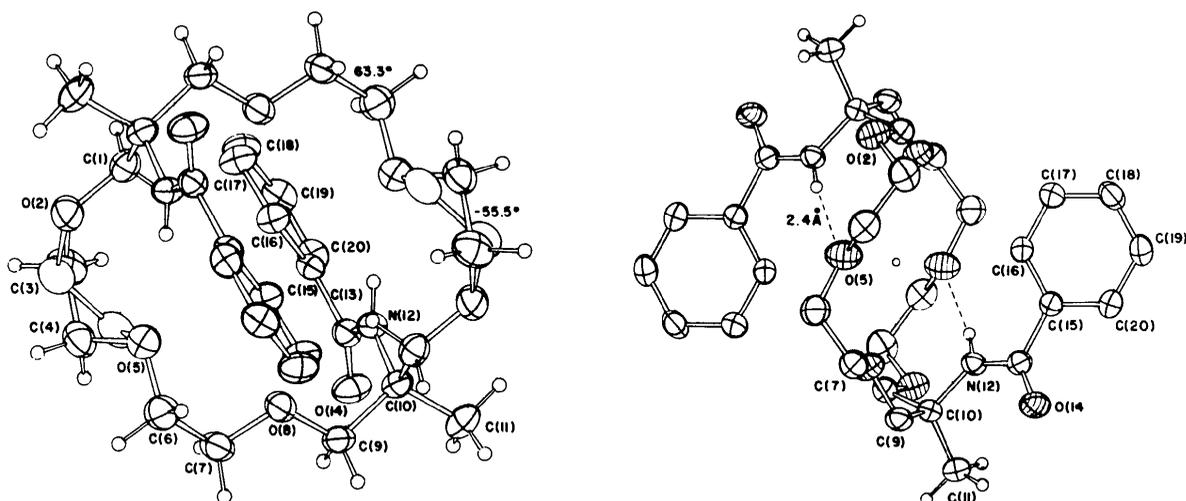


Fig. 1. Two perspective views of the molecule showing its conformation, atom numbering, and the intramolecular hydrogen-bonding interaction.

interesting to note that the C(3)–C(4) (1.503 Å) and C(6)–C(7) (1.506 Å) bonds are consistently shorter than the C(9)–C(10) (1.527 Å) and C(10)–C(1') (1.516 Å) bonds, which in turn appear to be still short with respect to the usually quoted normal value for a C(sp^3)–C(sp^3) bond distance (1.540 Å).^{*} This correlates well with a previous observation that the C–C bonds are usually shortened by about 0.03 Å in structures containing the (–O–C–C–O–) moieties, due to a specific interaction (of yet unclarified nature) between the adjacent C and O atoms (Goldberg, 1975; Hanson, Hughes & Truter, 1976).

The spatial packing arrangement of the molecules as viewed down b is shown in Fig. 3. All intermolecular distances are longer than or approximately equal to the sums of the corresponding van der Waals radii. The carbonyl O atom, which is peripheral to the ligand main structure, forms the shortest contact with non-hydrogen atoms of the surrounding molecules. Thus, the distance from O(14) at x, y, z to C(19) at $2 - x, -\frac{1}{2} + y, \frac{1}{2} - z$ is 3.43 Å, the related O(14)···H(19) distance being 2.5 Å. The crystal packing is composed of a three-dimensional network of such lateral C–H···O interactions.

Two final remarks refer to the ligand structure and reactivity. In the absence of any interacting guest species, the conformation of the macrocyclic cavity is

^{*} One should keep in mind that the quantitative aspect of this remark may not be entirely valid, since corrections for thermal motion were not applied.

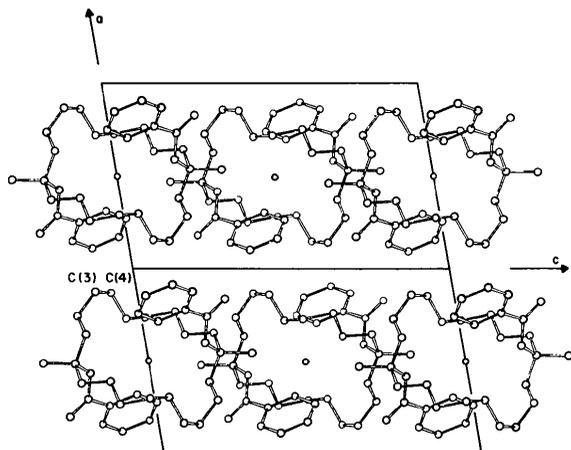


Fig. 3. Projection of crystal structure down b .

stabilized mainly by intramolecular hydrogen bonding and by van der Waals interactions with the benzamido substituents. The conformational disorder is confined to those parts of the ring which are not involved in the above interactions. In this sense the observed disorder can be classified as an intramolecular feature, particularly since the crystal forces seem to have little influence on the molecular geometry. As mentioned in the *Introduction*, the 20-crown-6 ligand turned out to be a rather poor binder of metal and ammonium cations in solution (Cram, 1976). A possible explanation of such behaviour may lie in the observed molecular conformation (Fig. 1), if we assume the molecular structure in solution to be roughly similar to that described in the present communication; in this structure the phenyl groups cover both faces of the macrocyclic cavity, thus potentially inhibiting the process of the complex formation.

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