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# 2,6-Dimethylylbenzoic Acid-2,6-dimethylylpyridine-18-crown-5

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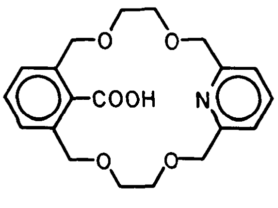
**Abstract.** $C_{20}H_{23}NO_6$, $M_r = 373{\cdot}4$, orthorhombic, $Pbca$, $Z = 8$; at room temperature: $a = 8{\cdot}843\,(2)$, $b = 20{\cdot}558\,(4)$, $c = 19{\cdot}783\,(6)$ Å, $U = 3596{\cdot}4$ Å$^3$, $D_x = 1{\cdot}379$ g cm$^{-3}$; at −160°C: $a = 8{\cdot}752\,(3)$, $b = 20{\cdot}498\,(6)$, $c = 19{\cdot}664\,(5)$ Å, $U = 3527{\cdot}7$ Å$^3$, $D_x = 1{\cdot}406$ g cm$^{-3}$. The least-squares refinement converged at $R(F) = 0{\cdot}062$ for 1822 (low-temperature) observations. The molecule has approximate $C_2$ symmetry, and its overall conformation is determined by polar intramolecular interactions. The transannularly located carboxylic acid and pyridine substituents link *via* an O—H···N hydrogen bond (2·66 Å), thus effectively filling the space within the macrocyclic ring.

**Introduction.** The title compound is one of several crown ether species which we have studied in order to examine the conformational features of various macrocyclic polyether ligands, and to assist in the interpretation of their binding properties. An earlier paper reported the structure of 2,6-dimethylylbenzoic acid-18-crown-5 (Goldberg, 1976; referred to hereafter as BACR5), and showed that the molecular conformation in the solid is uniquely stabilized by internal hydrogen bonding which involves the convergent carboxylic acid group. We report here the structural results for a similar macrocyclic moiety that also contains one 2,6-dimethylylpyridine unit as part of the 18-membered ring. Chemical information on both compounds has recently been published (Newcomb, Timko, Walba & Cram, 1977; Newcomb, Moore & Cram, 1977).



Single crystals were prepared by Newcomb and Cram (University of California at Los Angeles). The diffraction experiment was carried out at −160 ± 5°C, and there is no apparent phase transition in the range between room temperature and −160°C. Intensity data were collected from a crystal of dimensions 0·15 × 0·40 × 0·40 mm on a four-circle diffractometer (Syntex $P\bar{1}$, graphite monochromator, Mo $K\alpha$ radiation, $\lambda = 0{\cdot}7107$ Å), utilizing the $\theta$–$2\theta$ scan method with a constant scan speed of 4° min$^{-1}$. 3287 unique reflexions were recorded to $\sin\theta/\lambda = 0{\cdot}595$ Å$^{-1}$. The structure was solved by a straightforward application of the program *MULTAN* 74 (Main, Woolfson, Lessinger, Germain & Declercq, 1974), and refined by least-squares analysis with 1822 observations above threshold $[F^2 \geq 4\sigma(F^2)]$. The H positions were calculated from stereochemical considerations but were not subsequently refined. Anisotropic refinement of the non-hydrogen atom framework yielded $R = 0{\cdot}062$. The resulting value of $[\sum w(\Delta F)^2/(n - m)]^{1/2}$ was 2·51 for 244 refined parameters. A final difference

Table 1. *Atomic fractional coordinates of the non-hydrogen atoms*

| | *x* | *y* | *z* |
|---|---|---|---|
| C(1) | 0·7932 (6) | 0·9599 (2) | 0·6395 (3) |
| O(2) | 0·6623 (4) | 0·9510 (2) | 0·6812 (2) |
| C(3) | 0·7017 (6) | 0·9407 (2) | 0·7515 (3) |
| C(4) | 0·7741 (6) | 0·8759 (3) | 0·7678 (2) |
| O(5) | 0·6663 (4) | 0·8248 (1) | 0·7553 (2) |
| C(6) | 0·7401 (6) | 0·7632 (2) | 0·7610 (2) |
| C(7) | 0·6408 (5) | 0·7111 (2) | 0·7295 (2) |
| C(8) | 0·5943 (6) | 0·6577 (2) | 0·7675 (2) |
| C(9) | 0·5040 (6) | 0·6104 (2) | 0·7366 (2) |
| C(10) | 0·4652 (5) | 0·6175 (2) | 0·6686 (2) |
| C(11) | 0·5148 (5) | 0·6712 (2) | 0·6325 (2) |
| C(12) | 0·4718 (5) | 0·6818 (2) | 0·5592 (2) |
| O(13) | 0·6055 (3) | 0·6935 (1) | 0·5205 (1) |
| C(14) | 0·5756 (5) | 0·6985 (2) | 0·4493 (2) |
| C(15) | 0·4888 (5) | 0·7592 (2) | 0·4283 (2) |
| O(16) | 0·5842 (4) | 0·8153 (1) | 0·4386 (2) |
| C(17) | 0·4970 (6) | 0·8750 (2) | 0·4399 (2) |
| C(18) | 0·5989 (5) | 0·9264 (2) | 0·4698 (2) |
| C(19) | 0·6489 (5) | 0·9792 (2) | 0·4312 (2) |
| C(20) | 0·7469 (6) | 1·0250 (2) | 0·4591 (2) |
| C(21) | 0·7937 (6) | 1·0193 (2) | 0·5261 (3) |
| C(22) | 0·7436 (6) | 0·9662 (2) | 0·5658 (2) |
| C(23) | 0·6476 (5) | 0·9202 (2) | 0·5370 (2) |
| C(24) | 0·5922 (6) | 0·8604 (3) | 0·5765 (3) |
| O(25) | 0·4594 (4) | 0·8457 (2) | 0·5854 (2) |
| O(26) | 0·7099 (4) | 0·8236 (2) | 0·6018 (2) |
| N | 0·6028 (5) | 0·7174 (2) | 0·6630 (2) |
| H(26) | 0·6650 | 0·7907 | 0·6254 |

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Fourier map (otherwise almost featureless) had, however, four peaks of approximately 0·7 e Å$^{-3}$ located in the vicinity of the carboxyl group. Although this suggested an occurrence of minor molecular disorder, attempts at defining a disordered structural model which would be more consistent with the experimental data were unsuccessful. A careful inspection of the diffractometer data set at this stage revealed to our surprise that a number of 0*kl* reflections required to be absent by the space-group symmetry showed measured intensities significantly above background. Similar deviations were apparent in a previously measured (preliminary) room-temperature set of intensity data. Subsequently, additional refinement cycles were carried out in space group $P2_1ca$ (space group *Pmca* was ruled out from packing and molecular-symmetry considerations) with a properly transformed structural model. These calculations did not converge well, and we tend, therefore, to believe that the above-mentioned inconsistencies indeed originate in minor structural disorder or crystal defects. The atomic scattering factors employed were those of Hanson, Herman, Lea & Skillman (1964) for C, N and O and of Stewart, Davidson & Simpson (1965) for H. Final positional parameters of the non-hydrogen atoms are given in Table 1.*

Table 2. *Bond distances* (Å)

| | | | |
|---|---|---|---|
| C(1)–O(2) | 1·421 (6) | O(16)–C(17) | 1·443 (6) |
| O(2)–C(3) | 1·440 (6) | C(17)–C(18) | 1·500 (7) |
| C(3)–C(4) | 1·506 (7) | C(18)–C(19) | 1·392 (6) |
| C(4)–O(5) | 1·431 (6) | C(18)–C(23) | 1·394 (6) |
| O(5)–C(6) | 1·422 (6) | C(19)–C(20) | 1·386 (7) |
| C(6)–C(7) | 1·509 (7) | C(20)–C(21) | 1·384 (7) |
| C(7)–C(8) | 1·388 (6) | C(21)–C(22) | 1·411 (7) |
| C(8)–C(9) | 1·390 (7) | C(22)–C(23) | 1·384 (6) |
| C(9)–C(10) | 1·388 (7) | C(22)–C(1) | 1·517 (7) |
| C(10)–C(11) | 1·378 (6) | C(23)–C(24) | 1·530 (7) |
| C(11)–C(12) | 1·505 (6) | C(24)–O(25) | 1·213 (6) |
| C(12)–O(13) | 1·416 (6) | C(24)–O(26) | 1·369 (6) |
| O(13)–C(14) | 1·428 (5) | C(7)–N | 1·354 (6) |
| C(14)–C(15) | 1·516 (6) | C(11)–N | 1·361 (6) |
| C(15)–O(16) | 1·435 (5) | | |

Table 3. *Bond angles* (°)

| | | | |
|---|---|---|---|
| C(22)–C(1)–O(2) | 109·3 (4) | C(14)–C(15)–O(16) | 109·1 (4) |
| C(1)–O(2)–C(3) | 112·3 (4) | C(15)–O(16)–C(17) | 112·0 (3) |
| O(2)–C(3)–C(4) | 115·8 (4) | O(16)–C(17)–C(18) | 106·7 (4) |
| C(3)–C(4)–O(5) | 109·4 (4) | C(17)–C(18)–C(23) | 119·3 (4) |
| C(4)–O(5)–C(6) | 109·7 (4) | C(17)–C(18)–C(19) | 121·2 (4) |
| O(5)–C(6)–C(7) | 109·5 (4) | C(19)–C(18)–C(23) | 119·5 (4) |
| C(6)–C(7)–C(8) | 120·4 (4) | C(18)–C(19)–C(20) | 120·4 (4) |
| C(6)–C(7)–N | 118·1 (4) | C(19)–C(20)–C(21) | 120·2 (4) |
| C(8)–C(7)–N | 121·5 (4) | C(20)–C(21)–C(22) | 120·0 (4) |
| C(7)–C(8)–C(9) | 118·7 (4) | C(21)–C(22)–C(23) | 119·2 (4) |
| C(8)–C(9)–C(10) | 119·2 (4) | C(21)–C(22)–C(1) | 120·3 (4) |
| C(9)–C(10)–C(11) | 120·2 (4) | C(23)–C(22)–C(1) | 120·5 (4) |
| C(10)–C(11)–C(12) | 122·0 (4) | C(18)–C(23)–C(22) | 120·8 (4) |
| C(10)–C(11)–N | 120·5 (4) | C(22)–C(23)–C(24) | 122·0 (4) |
| C(12)–C(11)–N | 117·6 (4) | C(18)–C(23)–C(24) | 117·2 (4) |
| C(7)–N–C(11) | 119·9 (4) | C(23)–C(24)–O(25) | 125·2 (5) |
| C(11)–C(12)–O(13) | 109·5 (4) | C(23)–C(24)–O(26) | 112·8 (4) |
| C(12)–O(13)–C(14) | 112·9 (3) | O(25)–C(24)–O(26) | 122·1 (5) |
| O(13)–C(14)–C(15) | 114·7 (4) | | |

**Discussion.** The bond distances and angles in the present structure are listed in Tables 2 and 3. Fig. 1 shows two views of the molecule together with the numbering scheme used. Fig. 2 illustrates the crystal packing arrangement.

The overall molecular conformation of this ligand closely resembles that observed in the crystal structure of BACR5 (Goldberg, 1976). The molecular framework shows approximate $C_2$ symmetry with the ether O atoms of the macrocycle turning inward. The two peripheral ethyleneoxy units describe *gauche* conformations. The carboxyl group is located in the center of the molecule, forming an intramolecular hydrogen bond with the N atom [O(26)···N 2·66 Å; C(24)–O(26)···N 111°; O(26)–H(26)···N 169°]. Further-

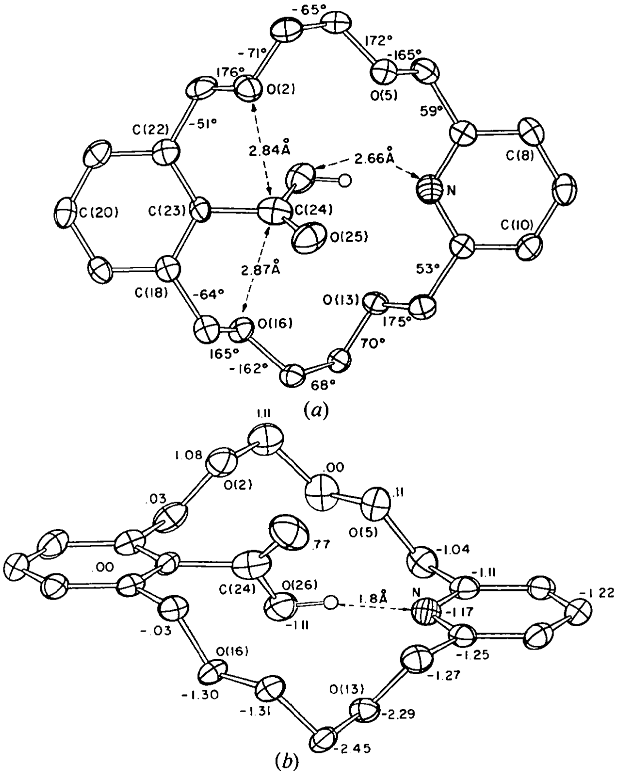

Fig. 1. Two views of the molecular unit showing 50% probability thermal ellipsoids. (*a*) Dihedral angles (°) about the peripheral bonds; the structure is projected on the plane of the benzene moiety. (*b*) Deviations (Å) of all atoms from this plane.

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* Lists of structure factors, anisotropic thermal parameters and hydrogen atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33587 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

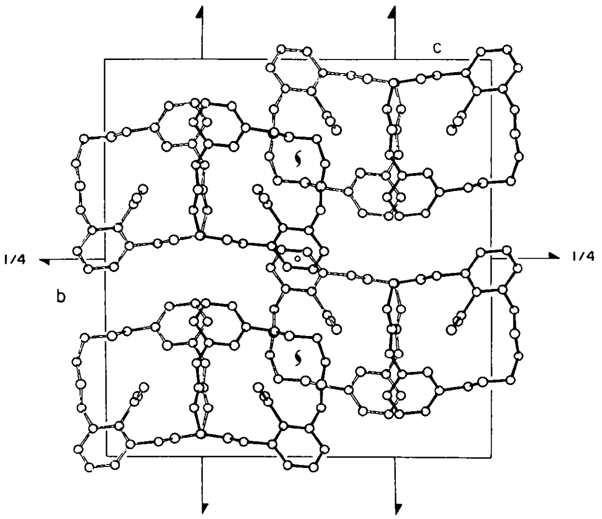

Fig. 2. Projection of the crystal structure down the *a* axis. Molecules with filled bonds are centered at $x = 0{\cdot}63$ and $0{\cdot}87$, while those with open bonds are at $x = 0{\cdot}13$ and $0{\cdot}37$.

more, O(ring)···C=O dipole–dipole attractive interactions involving the carboxyl substituent and two of the ether O atoms result in relatively short intramolecular contacts: O(2)···C(24) 2·84 Å and O(16)···C(24) 2·87 Å. In the observed conformation, the planar phenyl and pyridine rings are nearly parallel to each other; they form dihedral angles of 57 and 60° with the plane of the C—COOH fragment. All polar groups of the molecule are hidden within the macrocycle and covered by a lipophilic skin of C—H bonds.

In good correspondence with the above observations, this crystal structure, as well as that of BACR5, seems to be stabilized mainly by ordinary van der Waals forces. The remarkable similarity of the molecular conformations in both structures, differing significantly in their intermolecular arrangements, leads us to assume that crystal forces have little influence on the molecular geometry. Frequently, the conformations adopted by polyether macrocycles are determined primarily by intramolecular interactions (*e.g.* Goldberg, 1978; Dunitz & Seiler, 1974).

The bond distances and angles exhibit no extraordinary features, and are in good agreement with the average values of the corresponding parameters in previously reported crown ether structures. The geometry of the carboxyl group has been determined with a relatively low precision because of the disorder. The packing diagram (Fig. 2) shows that the mean planes of the molecular units are roughly perpendicular to the *a* axis; on cooling to −160°C the unit cell is contracted mainly along this direction.

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# Benzyloxycarbonylglycyl-D,L-proline

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**Abstract.** $C_{15}H_{18}N_2O_5$, $M_r = 306{\cdot}3$, orthorhombic, $Pbc2_1$; $a = 10{\cdot}227\ (3)$, $b = 10{\cdot}490\ (1)$, $c = 28{\cdot}590\ (1)$ Å; $Z = 8$, $D_x = 1{\cdot}327$, $D_m = 1{\cdot}324$ g cm$^{-3}$. $R = 0{\cdot}060$ for 3014 reflections. Two independent molecules exist in the crystal, and are related to each other by a spurious center of symmetry.