106. Synthesis and X-Ray Structural Studies of '4,7,13-Trioxa-1,10-diaza-5,6-benzocyclopentadecane-2,9-dione' (= 5,6,9,10-Tetrahydro-2*H*,8*H*-benzo[*b*][1,4,10]trioxa[7,13]diazacyclopentadecene-3,11(4*H*,12*H*)-dione) and '4,7,13,16-Tetraoxa-1,10-diaza-5,6-benzocyclooctadecane-2,9-dione' (= 5,6,8,9,12,13-Hexahydro-2*H*,11*H*-benzo[*b*][1,4,10,13]tetraoxa-[7,16]diazacyclooctadecene-3,14(4*H*,15*H*)-dione)

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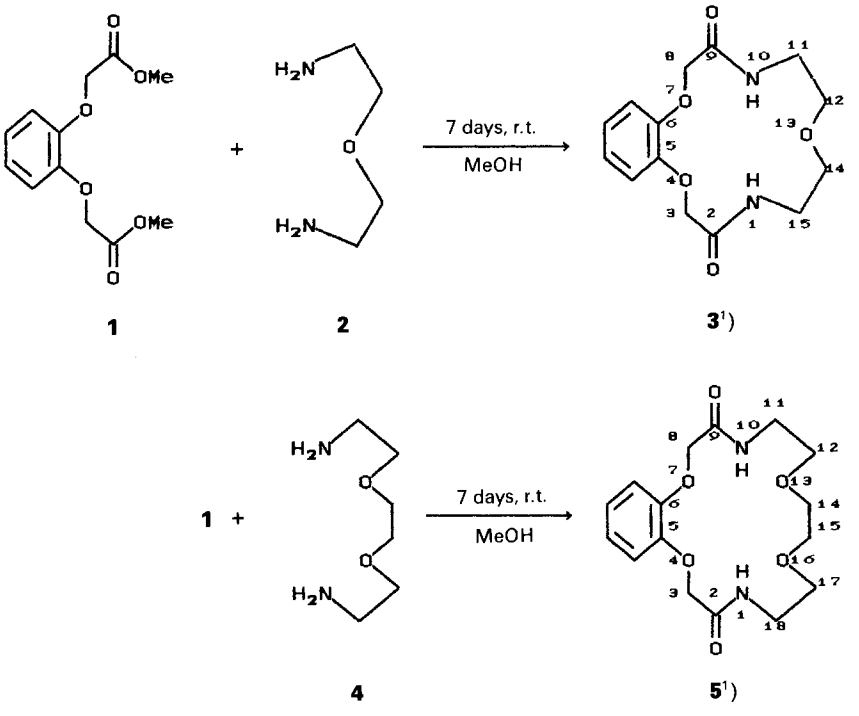
The molecular structures of the title compounds **3** and **5** were investigated by NMR and X-ray structural methods. The NMR results suggest two equivalent halves for both molecules. The X-ray study shows an approximate mirror plane for **3** and an approximate twofold axis for a significant portion of the macrocycle of **5**.

Introduction. – Since *Pedersen*'s studies [1] on the crown ethers, interest in synthetic macrocyclic receptors has grown continuously. The coordination abilities of these compounds depend on the number of heteroatoms occurring in the macrocycles. Introduction of N-atoms into macrocyclic structures leads to a class of host molecules known as azacoronands. Studies aimed at rational design and synthesis of more elaborate macrocyclic structures with specific complexing properties are now well advanced [2]. However, synthesis of polyfunctional, tailor-made azacoronands requires more efficient and selective methods [3].

Recently, we developed a new general method of synthesis of diazacoronands, based on the intermolecular macrocyclization of α,ω-diamines with dimethyl esters of α,ω-diacids, carried out in MeOH as solvent, under normal or high pressure [4]. Some of the products obtained by these procedures were examined by X-ray diffraction methods [5–8].

In the present paper, we report further applications of our method to the synthesis of benzo-diazacoronands **3** and **5**. Moreover, we use both diazacoronands as models for investigating favoured conformations of other 15- and 18-membered macrocycles annulated to a benzene ring.

Scheme



Experimental. – *'4,7,13-Trioxa-1,10-diaza-5,6-benzocyclopentadecane-2,9-dione'* (= *5,6,9,10-Tetrahydro-2*H,*8*H-*benzo[*b*][1,4,10]trioxa[7,13]diazacyclopentadecene-3,11(4*H,*12*H*)-dione;* **3**). A soln. of 0.254 g (1 mmol) of dimethyl 2,2'-(1,2-phenylenedioxy)bis(acetate) (**1**) and 0.104 g (1 mmol) of 2,2'-oxybis(ethylamine) (**2**) in 10 ml of MeOH was left for 7 days at r.t. The solvent was evaporated and the residue dissolved in $CHCl_3$ and chromatographed twice (alumina, then silica gel, 1–10% MeOH/$CHCl_3$). The solid obtained was crystallized from acetone/heptane: 0.191 g (65%) of **3**. Colourless needles. M.p. 221–222°. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.38 (br. *s*, 2 NH); 6.8–7.1 (*m*, 4 arom. H); 4.49 (*s*, 4 H, OCH_2CO); 3.68 (*t*, *J* = 5.3 Hz, 4 H, OCH_2CH_2N): 3.64 ppm (*t*, 4 H, OCH_2CH_2N). ^{13}C-NMR (125 MHz, $CDCl_3$): 167, 146, 122, 112, 69, 67, 38 ppm. Anal. calc. for $C_{14}H_{18}N_2O_5$: C 57.14, H 6.12, N 9.52; found: C 57.28, H 6.39, N 9.32.

'4,7,13,16-Tetraoxa-1,10-diaza-5,6-benzocyclooctadecane-2,9-dione' (= *5,6,8,9,12,13-Hexahydro-2*H,*11*H-*benzo[*b*][1,4,10,13]tetraoxa[7,16]diazacyclooctadecene-3,14(4*H,*15*H*)-dione;* **5**). A soln. of 0.254 g (1 mmol) of **1** and 0.148 (1 mmol) of 2,2'-(ethylenedioxy)bis(ethylamine) (**4**) in 10 ml of MeOH was left for 7 days. The same treatment as described for **3** gave 0.220 g (65%) of **5**. Colourless needles. M.p. 174°. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.62 (br. *s*, 2 NH); 6.85–7.05 (*m*, 4 arom. H); 4.59 (*s*, 4 H, OCH_2CO); 3.58 ppm (*m*, 12 H, $NCH_2CH_2OCH_2$). ^{13}C-NMR (125 MHz, $CDCl_3$): 168, 147, 122, 113, 70, 69, 68, 39 ppm. Anal. calc. for $C_{16}H_{22}N_2O_6$: C 56.80, H 6.51, N 8.28; found: C 57.05, H 6.68, N 8.32.

X-Ray Structural Investigations. Table 1 shows experimental conditions for X-ray diffractometric measurements of **3** and **5**. The cell constants were refined on 25 reflections in each case using the least-squares procedure implemented in the SDP system. In the case of **3**, a comparison of $I(hkl)$ with $I(-hkl)$ showed that in spite of a β angle very close to 90°, the crystal system of **3** is monoclinic. *Lorentz* and polarization but no absorption corrections were applied in both cases.

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[1]) Arbitrary numbering; for systematic names, see *Exper. Part.*

Table 1. *X-Ray Experimental Parameters for Compounds* **3** *and* **5**

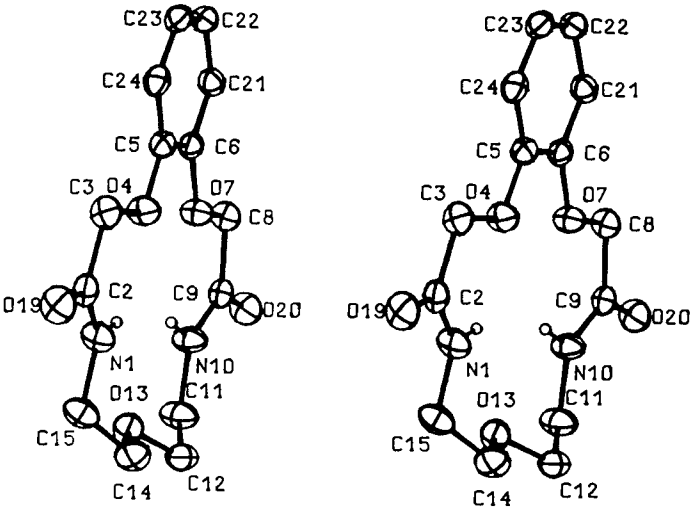
		3	**5**
Formula		$C_{14}H_{18}N_2O_5$	$C_{16}H_{22}N_2O_6$
Molecular weight		294.30	338.35
Crystal system		monoclinic	triclinic
a[Å]		15.152(2)	8.213(4)
b[Å]		4.866(2)	9.956(1)
c[Å]		18.776(2)	11.340(3)
α[deg]		–	95.93(1)
β[deg]		89.75(1)	64.20(3)
γ[deg]		–	82.72(3)
V[Å^3]		1384.3(5)	815.0(5)
Z		4	2
D_{calc} [gcm^{-1}]		1.41	1.38
Space group		$P2_1/a$	$P\bar{1}$
Radiation		MoK_α (graphite monochromated)	
Wavelength [Å]		0.71069	
μ[cm^{-1}]		0.67	0.66
F(000)		624	360
Crystal size [mm]		0.18 × 0.18 × 0.30	0.15 × 0.22 × 0.58
Temperature		−168 ± 5°	23 ± 1°
Diffractometer		*CAD-4*	
Scan mode		$\omega/2\Theta$	
Scan range (2Θ) [deg]		0–54	0–50
Octants		$\pm h + k + l$	$\pm h \pm k + l$
Number of collected data:	total	3375	3018
	unique observed ($I > 2\sigma_I$)	2431	2022
$R(F)$		0.0372	0.0433

The program SHELXS-86 [9] was used for solving the phase problem in both cases. Space group $P2_1/a$ was found for **3** from systematic absences. Positions of all 21 non-H-atoms were found from an E-map. For **5**, space group $P1$ was assumed initially. The E-map revealed the positions of 48 atoms belonging to two molecules related to each other by inversion symmetry. Thus, the averaged positions of 24 non-H-atoms of **5** (after appropriate shift) were used for refinement in space group $P\bar{1}$.

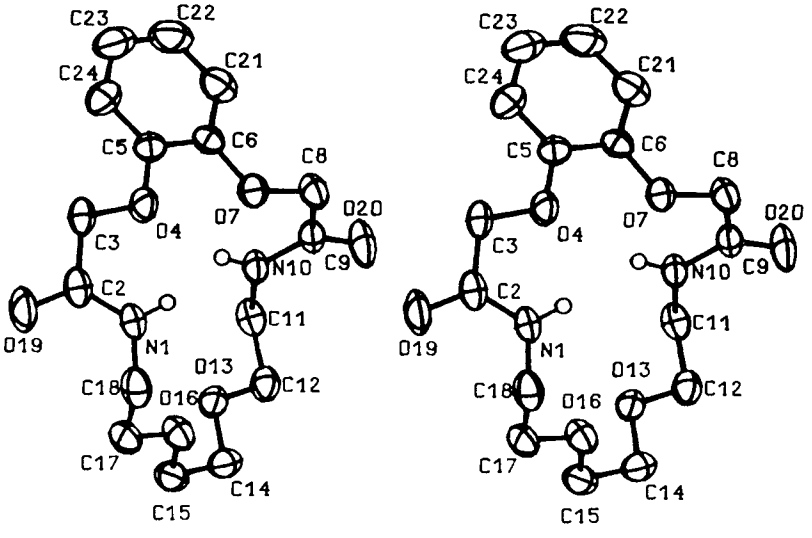
A similar refinement procedure was used for both structures (least-squares, full-matrix procedure of program SHELX-76 [10]). Initially, the refinement was done with isotropic individual temperature factors. Then, the positions of H-atoms attached to C-atoms were calculated and added to the sets of atomic parameters with isotropic individual temperature factors. After a few cycles of anisotropic full-matrix refinement of all non-H-atom parameters, the positions of amido H-atoms were found from difference *Fourier* maps and added to the refined sets. The final refinement steps involved all atomic positional and anisotropic thermal parameters (isotropic for H) with unit weights. The highest residual electron-density peaks on final difference maps were 0.27 and 0.22 e/Å^3 for **3** and **5**, respectively. Supplementary material was deposited with the *Cambridge Crystallographic Data Center*.

Results and Discussion. – Our general method to synthesize diazacoronands is also effective in the case of benzo derivatives **3** and **5** (see *Scheme*). In both cases, one can expect more rigid conformations than for non-annulated diazacoronands. Therefore, ^{1}H-NMR as well as ^{13}C-NMR spectra should reflect the preferred conformations for both the 15- and 18-membered rings (**3** and **5**, resp.) However, it was necessary to check if the apparent molecular twofold symmetry found from NMR spectra (in solution) is also present in the crystalline state. These problems were adressed by solid-state X-ray structure analysis.

The non-H-bond lengths and angles for both **3** and **5** show no unusual features and are available as supplementary materials. *Fig. 1* shows ORTEP stereoviews of single molecules of **3** and **5**.



3



5

Fig. 1. *ORTEP stereoviews of single molecules of* **3** *and* **5** *oriented at optimal viewing, with crystallographic atom labeling*[1]). For clarity reasons, the only H-atoms shown are those of amino groups.

The ^{1}H- and ^{13}C-NMR investigations indicate twofold symmetry for both molecules **3** and **5**. In the diazacoronand **3**, a well approximated noncrystallographic mirror plane is found (program INERT [11]). The plane passes through the O(13) atom and the center of the benzene ring. The r.m.s. deviation from the ideal C_s symmetry (calculated for 10 pairs of atoms) is estimated to be as small as 0.016 Å. In the diazacoronand **5**, a noncrystallographic approximate twofold axis runs from the midpoint of C(14)–C(15) to the midpoint of O(4)···O(7) and relates the chain from O(4) to C(15) to the chain from O(7) to C(14). The r.m.s. deviation from ideal C_2 symmetry (calculated for 8 pairs of atoms) is 0.066 Å. The benzene ring does not conform to this symmetry. However, rotation of this ring by *ca.* 75° around an axis defined by O(4) and O(7) produces a conformation which is practically indistinguishable from the one shown in *Fig. 2*. This rotation, if it occurs in solution, leads to an average C_2 symmetry of **5**, in agreement with solution NMR data.

Fig. 2 presents a comparison of ring conformations of **3** and **5** (in projections) exhibiting the endocyclic torsion angles and shows how closely the noncrystallographic

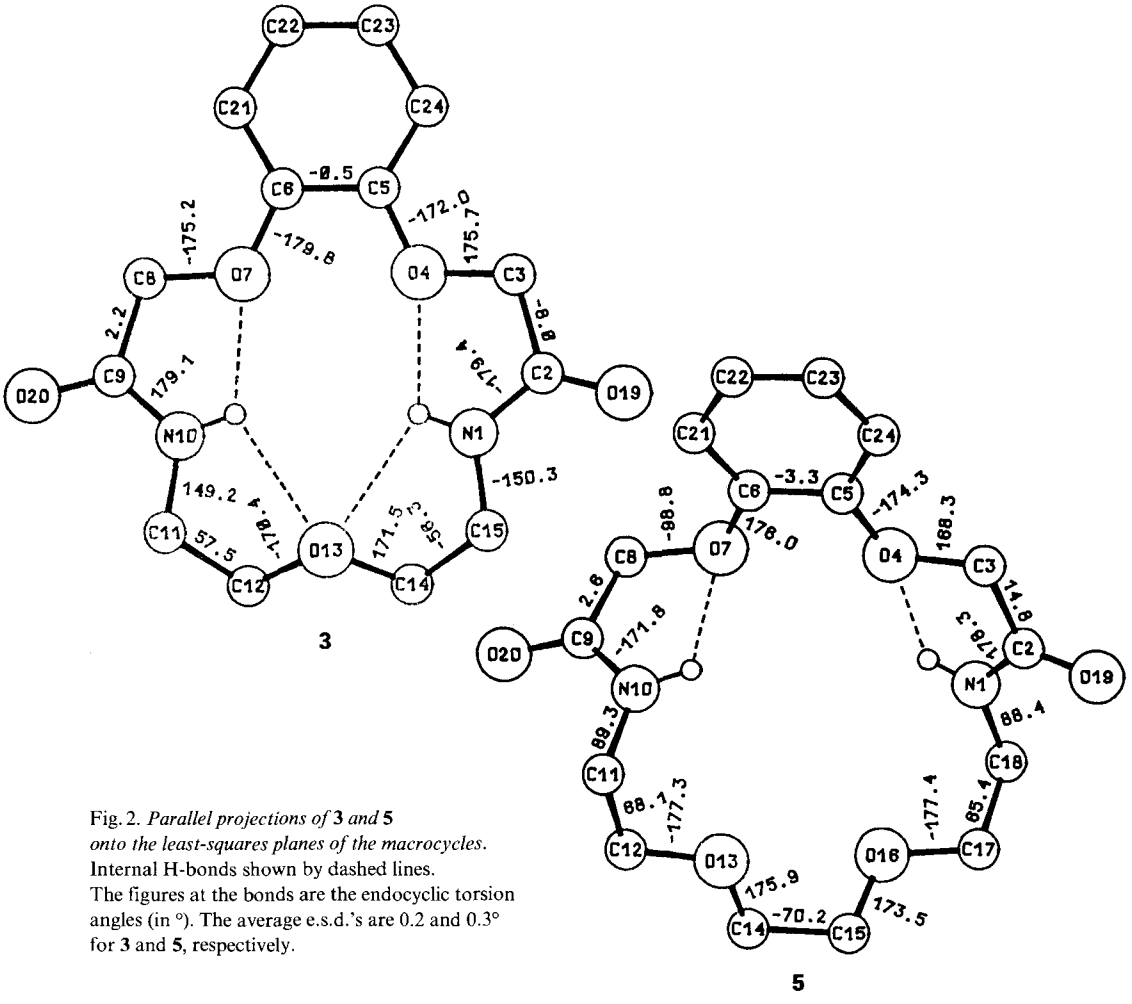


Fig. 2. *Parallel projections of* **3** *and* **5** *onto the least-squares planes of the macrocycles.* Internal H-bonds shown by dashed lines. The figures at the bonds are the endocyclic torsion angles (in °). The average e.s.d.'s are 0.2 and 0.3° for **3** and **5**, respectively.

symmetry relationships are obeyed. The macrocycle conformations may be defined according to the *Boeyens*-and-*Dobson* convention [12] as [1,2,3,4,2,3] for **3** and as [1,2,3,3,4,3,2] for **5**.

The above findings have their consequences for the H-bond formation in the crystal structures. In the structure of **3**, four intramolecular H-bonds are found, involving both amide groups as donors. They are of bifurcated character, thus creating four chelate five-membered rings inside of the macrocycle. Another situation is found for the structure of **5** where only two intramolecular H-bonds are found, but also one H-bond of inte-

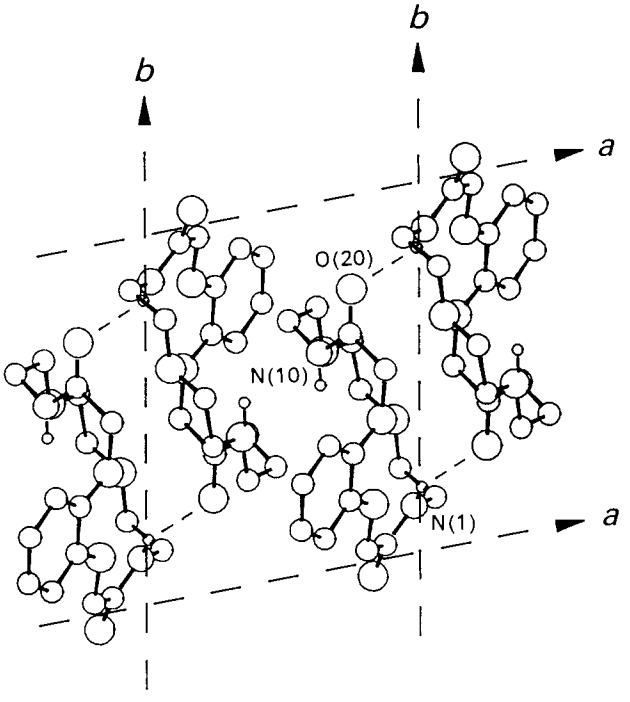


Fig. 3. *A parallel projection of molecules in the structure of* **5** *along the* c *axis of the crystal showing the intermolecular H-bond system* (– – –). Crystal axes *a* and *b* (— — —) show the outline of the cell unit.

Table 2. *Intra- and Intermolecular H-Bonds Observed in* **3** *and* **5** (*D* = donor, *A* = acceptor)

	D···*A* [Å]	*D*–H [Å]	H···*A* [Å]	*D*–H···*A* [°]	Acceptor symmetry
3					
N(1)–H(1)···O(4)	2.559	0.85	2.13	110	*x*, *y*, *z*
N(1)–H(1)···O(13)	2.743	0.85	2.41	104	*x*, *y*, *z*
N(10)–H(10)···O(7)	2.565	0.87	2.11	112	*x*, *y*, *z*
N(10)–H(10)···O(13)	2.745	0.87	2.42	103	*x*, *y*, *z*
5					
N(1)–H(1)···O(4)	2.649	0.83	2.26	109	*x*, *y*, *z*
N(10)–H(10)···O(7)	2.690	0.87	2.25	111	*x*, *y*, *z*
N(1)–H(1)···O(20)	2.899	0.83	2.21	141	2-*x*, 1-*y*, 1-*z*

molecular nature, linking two enantiomeric molecules into dimeric aggregates (*Fig. 3*). *Table 2* shows geometrical details of H-bonds in both compounds.

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