

# Synthesis, nuclear magnetic resonance, and X-ray investigations of 1,10-diazacyclooctadeca-2,9-dione

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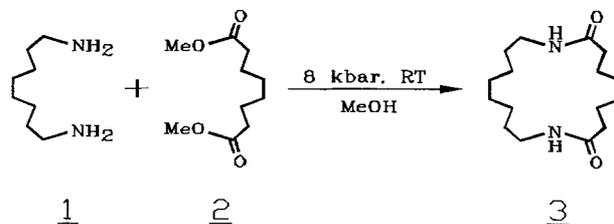
The structure of the title compound has been investigated in the solid state and in solution by X-ray and NMR methods, respectively. The crystals are triclinic, space group  $P\bar{1}$ , with cell dimensions:  $a = 9.616(5)$ ,  $b = 9.923(9)$ ,  $c = 10.21(1)$  Å,  $\alpha = 118.42(4)^\circ$ ,  $\beta = 96.10(5)^\circ$ ,  $\gamma = 94.77(5)^\circ$ . The structure was solved by direct methods, and refined against 3051 unique reflections by a full-matrix, least-squares procedure, giving  $R = 0.049$ . A twofold symmetry element in the molecule, found from  $^1\text{H-NMR}$  investigations, has been established by X-ray investigations to be an approximate twofold symmetry axis, bisecting the C(5)–C(6) and C(14)–C(15) bonds.

## Introduction

Since Pedersen's (1967) investigations on the crown ethers, a growing interest has existed in synthetic macrocyclic molecular potential complexes. The coordination abilities of these compounds depend on the number of hetero-atoms occurring in the macro-rings. Introduction of nitrogen atoms into macrocyclic structures creates an original class of host molecules known as azacoronands. Studies aimed at rational design and synthesis of more elaborate macrocyclic structures with desired complexing properties are now well advanced (Gokel and Korzeniowski, 1982). However, tailored synthesis of polyfunctional azacoronands is calling for further search for more efficient and selective methods (Bradshaw *et al.*, 1989).

Recently (Jurczak *et al.*, 1990), we have developed a new general method of synthesis of diazacoronands, based on intermolecular macrocyclization reaction of  $\alpha,\omega$ -diamines with dimethyl esters of  $\alpha,\omega$ -diacids, carried out in methanol as a solvent.

In this paper we present the application of the above-mentioned method to the synthesis of 1,10-diazacyclooctadeca-2,9-dione using a high pressure technique, necessary to perform the reaction.



We begin a study of the ground-state conformations of hetero-macrocycles (3) by X-ray diffraction methods.

## Experimental

### Synthesis of 1,10-diazacyclooctadeca-2,9-dione (3)

The reaction was carried out in a piston-cylinder type apparatus of a working volume of about 50 ml. The construction details were reported earlier (Jurczak, 1986). The pressure inside the working volume was measured by a calibrated manganin coil. 1,8-Diaminooctane (1) (720 mg, 5 mmol) and suberic acid dimethyl ester (2) (1010 mg, 5 mmol) were dissolved in 50 ml of methanol, placed in a Teflon tube with a screwed cap, and sealed. The sample was kept in the high pressure apparatus under 8 kbar at room tempera-

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ture for 20 hr. After decompression, the reaction mixture was transferred quantitatively to a round-bottomed flask and evaporated after the addition of 10 ml of  $\text{CHCl}_3$ . The crude oil was purified by column chromatography, first on neutral alumina using  $\text{CHCl}_3$  as the eluant, then on silicagel with 2 portions of 5% methanol in  $\text{CHCl}_3$  as the eluant. The solid product obtained was recrystallized from benzene giving 212 mg of **3** (yield 15%) (m.p. 202–203°).

#### Analysis

Calc. for  $\text{C}_{16}\text{H}_{30}\text{N}_2\text{O}_2$ : C, 68.0; H, 10.7; N, 9.9.  
Found: C, 67.7; H, 11.0; N, 9.7.

#### NMR investigations

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured on a Bruker AM-500 spectrometer at 500 MHz and 125 MHz, respectively.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ),  $\delta$ , 5.60 (bt,  $J$  6.0 Hz, 2H,  $\text{NH}$ ); 3.31 (dt,  $J$  5.9 Hz, 4H,  $\text{CH}_2\text{NH}$ ); 2.20 (t,  $J$  6.8 Hz, 4H,  $\text{CH}_2\text{CO}$ ); 1.65 (tt,  $J$  7.4 Hz, 4H,  $\text{CH}_2\text{CH}_2\text{CO}$ ); 1.50 (tt,  $J$  7.0 Hz, 4H,  $\text{CH}_2\text{CH}_2\text{NH}$ ); 1.39 (m, 4H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ); 1.34 (m, 8H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}$ ).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ),  $\delta$ , 173.2, 38.9, 36.3, 29.1, 28.4, 27.5, 25.7, 25.3.

#### X-ray structural investigations

A colorless crystal of **3** (0.32, 0.24, 0.21 mm) was obtained from  $\text{CHCl}_3$ -MeOH. The reflection intensities were collected on an Enraf-Nonius CAD-4 diffractometer, using graphite-monochromated  $\text{Cu K}\alpha$  radiation (1.54178 Å). The cell constants were refined by a least-squares procedure on the setting angles of 25 reflections. The data were collected with the  $\omega/2\theta$  scan technique up to  $2\theta_{\text{max}} = 150^\circ$ .

#### Crystal data

$\text{C}_{16}\text{H}_{30}\text{N}_2\text{O}_2$ ,  $M_r = 282.42$ , triclinic, space group  $P\bar{1}$ ,  $a = 9.616(5)$ ,  $b = 9.923(9)$ ,  $c = 10.21(1)$  Å,  $\alpha = 118.42(4)^\circ$ ,  $\beta = 96.10(5)^\circ$ ,  $\gamma = 94.77(5)^\circ$ ;  $V = 841(1)$  Å<sup>3</sup>,  $Z = 2$ ,  $F(000) = 312$ ,  $D_x = 1.11$  g cm<sup>-3</sup>,  $\mu(\text{Cu K}\alpha) = 5.03$  cm<sup>-1</sup>.

A total of 3663 reflections were collected, of which 3051 were unique, of  $I > 2\sigma_I$ , and thus considered as observed. Lorentz and polarization corrections were applied to the data. Since the linear absorption coefficient and the crystal dimensions were small, no absorption correction was performed.

The phase problem was solved by direct methods

(program SHELXS-86, Sheldrick, 1985) in the space group  $P\bar{1}$ . A total of 40 atoms belonging to two molecules were found in an  $E$ -map. Since the molecules represented enantiomorphs, the average coordinates of the center of symmetry were calculated (individual distribution was small), and the whole structure was shifted to place the center at 0, 0, 0. Then, the average atomic coordinates from each corresponding pair of atoms were used for refinement in the space group  $P\bar{1}$ . Initially, the positional parameters and individual isotropic temperature factors of all nonhydrogen atoms were refined to give  $R = 0.145$  (program SHELX-76, Sheldrick, 1976).

The positions of the hydrogen atoms bonded to carbon atoms were generated from assumed geometries and those of the amino hydrogen atoms were found from a difference Fourier map, and added with isotropic temperature factors to the set of atomic parameters. The refinement of atomic positional and thermal anisotropic parameters (isotropic for H) was performed by the least-squares, full-matrix procedure using SHELX-76.

The refinement converged at  $R = 0.079$ . The  $\Delta F$  map revealed two new electron density peaks both of ca.  $1 \text{ e } \text{Å}^{-3}$  indicating a possible positional disorder of C(5) and C(6) atoms of low population. The disordered atoms were added to the set with isotropic temperature factors and their parameters including the population ratio refined together with the whole molecule. The thermal coefficients of C(5) and C(6) atoms became diminished to a more reasonable values.

The final  $R$  factor was 0.049, (unit weights). The highest peak in the final difference map was  $0.19 \text{ e } \text{Å}^{-3}$ . The refined population ratio of the disordered C atoms was 79:21.

The refined positional parameters for the non-H atoms of **3**, together with their  $B_{\text{eq}}$  values are given in Table 1.

## Results and discussion

NMR spectroscopy results indicate a symmetry element present in the molecule of **3**. Each group of signals shows a double marker of protons attached to respective carbon atoms of similar screening, apparently reflected into themselves. A multiplet with the lowest chemical shift represents protons joined with the four carbon atoms placed in the part of the ring derived from the diaminoctane substrate. These protons are practically undifferentiable in terms of their spectral properties.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra as well as the t.l.c. and elemental analysis confirmed chemical homogeneity and purity of the desired product **3**.

**Table 1.** Fractional coordinates ( $\times 10^4$ ) and  $B_{eq}^a$  values for nonhydrogen atoms<sup>b</sup> of **3**

	<i>x</i>	<i>y</i>	<i>z</i>	$B_{eq}$
N(1)	6449(1)	-3619(2)	-3147(1)	4.15(3)
C(2)	5631(1)	-2603(2)	-3123(1)	3.94(3)
C(3)	6311(2)	-1248(2)	-3243(2)	5.12(4)
C(4)	6139(2)	311(2)	-1938(3)	6.53(5)
C(5)	6794(2)	577(3)	-406(2)	5.06(5)
C(5A) <sup>c</sup>	6924(16)	1394(19)	-891(17)	9.4(3)
C(6)	8406(2)	822(3)	-74(2)	5.23(5)
C(6A) <sup>c</sup>	8481(13)	1627(15)	-696(15)	8.1(3)
C(7)	9150(2)	2446(3)	596(3)	6.78(6)
C(8)	8915(2)	3541(2)	2210(2)	5.37(4)
C(9)	9466(1)	3060(2)	3317(2)	4.35(3)
N(10)	8515(1)	2629(1)	3957(2)	4.25(3)
C(11)	8863(2)	2068(2)	5018(2)	5.09(4)
C(12)	7942(2)	563(2)	4600(2)	4.92(4)
C(13)	8065(2)	-769(2)	3069(2)	4.64(4)
C(14)	7243(2)	-2306(2)	2733(2)	4.75(4)
C(15)	7356(2)	-3657(2)	1204(2)	4.94(4)
C(16)	6615(2)	-3588(2)	-150(2)	4.62(4)
C(17)	6764(2)	-4952(2)	-1640(2)	5.03(4)
C(18)	5970(2)	-4977(2)	-3021(2)	4.99(4)
O(1)	4368(1)	-2731(2)	-2994(1)	5.44(3)
O(2)	10738(1)	3043(2)	3623(2)	6.13(4)

**Table 1.** Final hydrogen fractional coordinates ( $\times 10^3$ ) for **3**

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i>
H(1)	727(2)	-348(2)	-325(2)	5.3(4)
H(3A)	583(2)	-134(2)	-420(2)	6.5(4)
H(3B)	731(2)	-130(2)	-327(2)	5.4(4)
H(4A)	506(2)	36(2)	-192(2)	6.7(4)
H(4B)	670(2)	125(2)	-200(2)	7.3(5)
H(5A)	646(2)	155(2)	43(2)	5.9(5)
H(5B)	632(2)	-49(2)	-42(2)	5.8(5)
H(6A)	877(2)	15(2)	-112(2)	6.1(6)
H(6B)	880(2)	47(2)	80(2)	6.2(6)
H(7A)	871(2)	275(2)	-22(2)	7.3(5)
H(7B)	23(2)	246(2)	62(2)	7.4(5)
H(8A)	788(2)	365(2)	223(2)	5.4(4)
H(8B)	942(2)	459(2)	255(2)	6.3(4)
H(10)	765(2)	264(2)	368(2)	5.1(3)
H(11A)	872(2)	287(2)	607(2)	5.8(4)
H(11B)	987(2)	192(2)	497(2)	5.9(4)
H(12A)	691(2)	76(2)	460(2)	6.0(4)
H(12B)	822(2)	25(2)	539(2)	6.4(4)
H(13A)	770(2)	-46(2)	230(2)	5.5(4)
H(13B)	910(2)	-88(2)	301(2)	5.8(4)
H(14A)	620(2)	-218(2)	276(2)	5.4(3)
H(14B)	759(2)	-256(2)	353(2)	5.8(4)
H(15A)	839(2)	-368(2)	111(2)	6.3(4)
H(15B)	697(2)	-465(2)	119(2)	5.6(4)
H(16A)	699(2)	-259(2)	-12(2)	5.2(3)
H(16B)	558(2)	-359(2)	-8(2)	5.4(4)
H(17A)	784(2)	-494(2)	-173(2)	5.8(4)
H(17B)	642(2)	-595(2)	-164(2)	5.9(4)
H(18A)	612(2)	-595(2)	-393(2)	6.1(4)
H(18B)	494(2)	-498(2)	-293(2)	5.2(3)

<sup>a</sup> $B_{eq} = 8\pi^2 \cdot D_u^{1/3}$ , where  $D_u$  is the determinant of the  $U_{ij}$  matrix in orthogonal space.<sup>b</sup>In this and following tables the figures in parentheses are estimated standard deviations.<sup>c</sup>Positionally disordered atoms.

The bonding interatomic distances, and valence angles for **3** are given in Table 2 and 3, respectively. Figure 1 presents a stereoview of **3**.

The positional disorder of two atoms C(5) and C(6) (approximate ratio 4:1) suggests that the 18-membered macrocyclic ring could exist in two conformations.

Using the notation of Boeyens and Dobson (1987), which is based on the endocyclic torsion angles (Fig. 2), the forms of these conformations may be defined as 1,3,4,1,1,1,4,3 and 1,3,4,3,4,3 for higher and lower populations, respectively. Both conformers of **3** exhibit an approximate noncrystallographic twofold axis sym-

Table 2. Bond lengths (Å)

C(2)–N(1)	1.322(2)	C(9)–C(8)	1.487(3)
C(18)–N(1)	1.456(3)	N(10)–C(9)	1.332(3)
C(3)–C(2)	1.509(3)	O(2)–C(9)	1.233(2)
O(1)–C(2)	1.238(1)	C(11)–N(10)	1.457(3)
C(4)–C(3)	1.524(2)	C(12)–C(11)	1.513(3)
C(5)–C(4)	1.510(4)	C(13)–C(12)	1.517(2)
C(5A)–C(4)	1.211(13)	C(14)–C(13)	1.521(3)
C(6)–C(5)	1.524(3)	C(15)–C(14)	1.521(2)
C(6A)–C(5A)	1.473(20)	C(16)–C(15)	1.520(3)
C(7)–C(6)	1.494(4)	C(17)–C(16)	1.511(2)
C(7)–C(6A)	1.235(12)	C(18)–C(17)	1.518(3)
C(8)–C(7)	1.536(3)		

Table 3. Valence angles (deg)

N(1)–C(2)–C(3)	116.9(1)	C(7)–C(8)–C(9)	112.9(2)
N(1)–C(2)–O(1)	122.4(2)	C(8)–C(9)–N(10)	116.7(1)
C(2)–N(1)–C(18)	124.0(1)	C(8)–C(9)–O(2)	122.1(2)
N(1)–C(18)–C(17)	112.4(1)	C(9)–N(10)–C(11)	124.0(1)
C(2)–C(3)–C(4)	112.7(2)	N(10)–C(9)–O(2)	121.2(2)
C(3)–C(2)–O(1)	120.7(2)	N(10)–C(11)–C(12)	112.6(1)
C(3)–C(4)–C(5)	113.8(2)	C(11)–C(12)–C(13)	114.0(2)
C(3)–C(4)–C(5A)	135.8(8)	C(12)–C(13)–C(14)	113.2(2)
C(4)–C(5)–C(6)	116.3(2)	C(13)–C(14)–C(15)	114.0(2)
C(4)–C(5A)–C(6A)	126(1)	C(14)–C(15)–C(16)	114.9(2)
C(5A)–C(6A)–C(7)	118(1)	C(15)–C(16)–C(17)	112.8(2)
C(5)–C(6)–C(7)	117.0(2)	C(16)–C(17)–C(18)	114.6(2)
C(6)–C(7)–C(8)	114.6(2)		

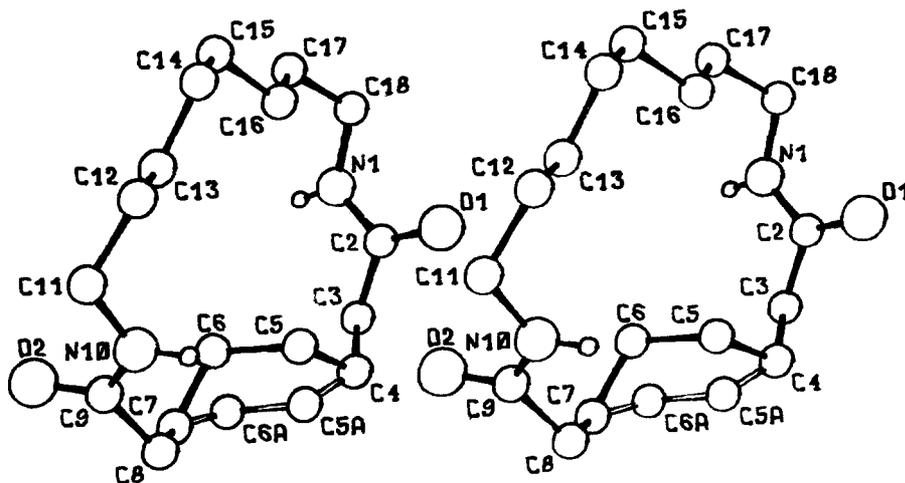


Fig. 1. Stereo-view of **3**, with labelling of atoms. Methylene H atoms are omitted for clarity. Orientation is at optimal viewing.

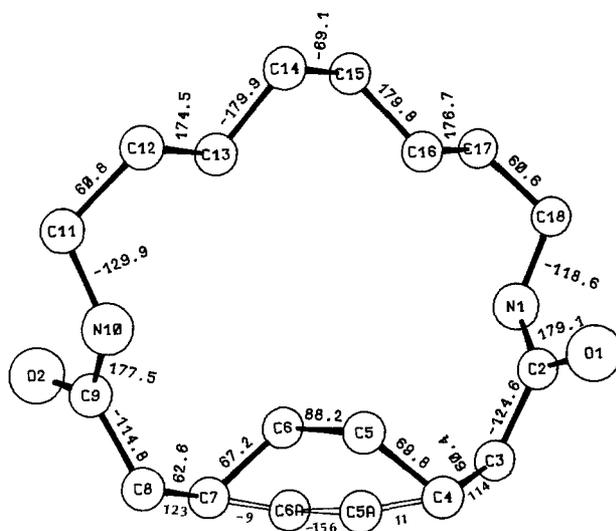


Fig. 2. Projection of the disordered 18-membered ring on to its least-squares plane, showing the twofold symmetry. The figures at the bonds are endocyclic torsion angles (deg). The average esd of the angles is  $0.2^\circ$  ( $2^\circ$  for disordered atoms).

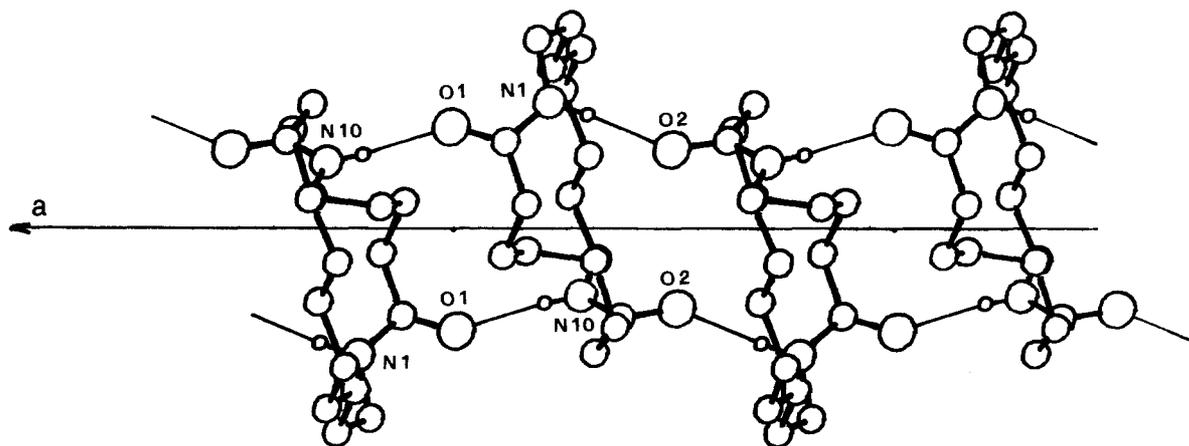


Fig. 3. Infinite chain of hydrogen-bonded molecules of **3** stretched along *a*. Parallel projection on to the *ac* plane of the crystal. Only bonding H atoms are shown; hydrogen bonds are shown by light lines.

metry, the axis bisecting the bonds C(5)—C(6) and C(14)—C(15). The RMS deviations from the ideal  $C_2$  symmetry were estimated (program INERT, Gluźniński, 1988) to be 0.111 and 0.125 Å, for the conformations of higher and lower populations, respectively.

Two species of potential intermolecular hydrogen bonds of medium strength were found in the crystal structure of **3**. The hydrogen bonds involve amino hydrogens and carbonyl oxygens of neighbouring molecules: N(1)—H(1)  $\cdots$  O(2) and N(10)  $\cdots$  O(1) thus forming the infinite chains of doubly bonded molecules, parallel to the *a* axis of the crystal, each chain containing opposite enantiomorphs as neighbouring molecules (Fig. 3). The geometry of the bonds ( $D-H$ ,  $D \cdots A$ ,

$H \cdots A$ , angle at H) is for N(1)—H(1)  $\cdots$  O(2): 0.82, 2.858, 2.04 Å,  $175^\circ$ ; for N(10)—H(10)  $\cdots$  O(1): 0.85, 2.868, 2.01 Å,  $177^\circ$ .

#### Acknowledgment

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Structure factor data have been deposited with the British Library, Boston Spa, Wetherby, West Yorkshire, UK as supplementary publication No. 60714 (20 pages).