# SYNTHESIS AND STRUCTURE OF 9,10,11,12-DIBENZ[a,c]-7,14-DIAZA-1,4-DIOXACYCLOHEXADECANE-8,13-DIONE

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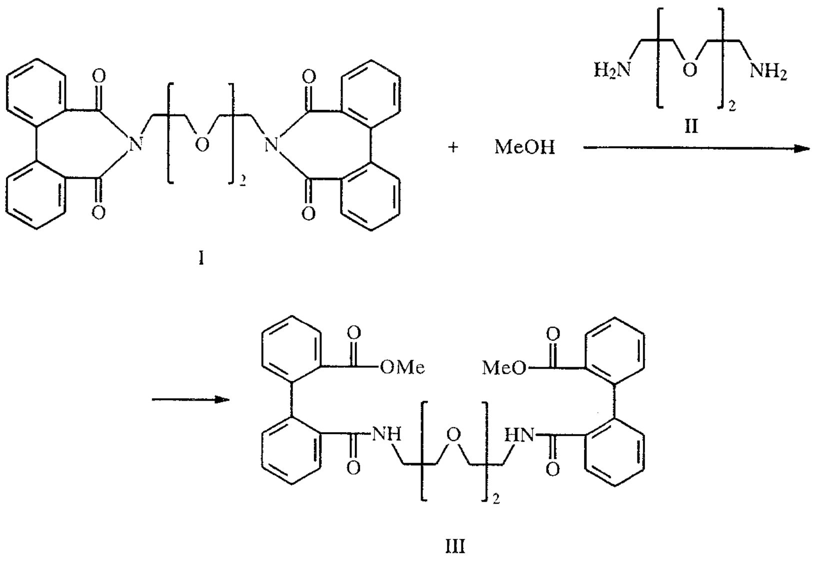
*The reaction of diphenic acid dioxatriethylenediimide with a methanolic solution of amines leads to splitting of the imide heterocyclic ring by methanol with the formation of the corresponding amidoester of diphenic acid. Amines catalyze this reaction. 9,10,11,12-Dibenz[a,c]-7,14-diaza-1,4-dioxahexadecane-8,13-dione was obtained from diphenoyl dichloride and the corresponding diamine. An x-ray diffraction study has been carried out.*

The reaction of polyoxyethylenediamines with polyoxyethylenediphthalimides leads to the formation of macrocyclic diamides, which cannot be obtained by the acid chloride method [1]. In the latter case N-substituted isoimides are formed [2, 3].

To clarify the possibility of the synthesis of a macrocyclic diamide from diphenic acid by the imide method, we carried out the reaction of 3,6-dioxaoctane-18-di(2,2′-diphenyldicarboximide) (I) with a methanolic solution of 3,6-dioxaoctane-1,8-diamine (II). Although the reaction of imides with alcoholic solutions of amines usually results in splitting of the imide heterocyclic ring with the formation of diamides, and not the alcoholysis [4], we obtained the corresponding amidoester of diphenyl-2,2′-dicarboxylic acid (III).



The reaction proceeds in the presence of butyl- and triethylamine, where the formation of diamides is in principle ruled out. This indicates that amines play a catalytic role, and also that the addition of stronger nucleophilic reagents is not always the preferential path of the reaction of imides.

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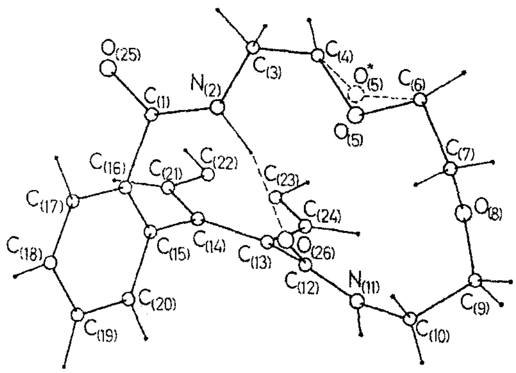


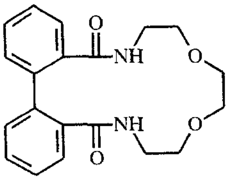
Fig. 1. Steric structure of compound IV.

TABLE 1. Coordinates of Basal Atoms with Standard Deviation (×$10^4$) in Structure of Compound IV

| Atom | x/a | y/b | z/c | Atom | x/a | y/b | z/c |
|---|---|---|---|---|---|---|---|
| $C_{(1)}$ | 5766 (4) | 2040 (5) | -1156 (8) | $C_{(14)}$ | 4027 (4) | 1639 (4) | 480 (7) |
| $N_{(2)}$ | 5360 (4) | 2772 (3) | -1520 (6) | $C_{(15)}$ | 4760 (4) | 1540 (4) | 1508 (8) |
| $C_{(3)}$ | 5429 (5) | 3178 (5) | -3289 (8) | $C_{(16)}$ | 5565 (4) | 1682 (4) | 696 (8) |
| $C_{(4)}$ | 4580 (7) | 3504 (7) | -3628 (9) | $C_{(17)}$ | 6248 (5) | 1478 (5) | 1649 (10) |
| $O_{(5)}$ | 4059 (5) | 3917 (6) | -2215 (12) | $C_{(18)}$ | 6095 (5) | 1181 (4) | 3419 (10) |
| $O^*_{(5)}$ | 4601 (7) | 4294 (7) | -2204 (14) | $C_{(19)}$ | 5293 (5) | 1069 (4) | 4219 (9) |
| $C_{(6)}$ | 4074 (6) | 4918 (6) | -2454 (10) | $C_{(20)}$ | 4604 (5) | 1247 (5) | 3282 (8) |
| $C_{(7)}$ | 3753 (5) | 5328 (5) | -645 (10) | $C_{(21)}$ | 3891 (5) | 940 (4) | -674 (8) |
| $O_{(8)}$ | 2952 (3) | 4979 (3) | -47 (6) | $C_{(22)}$ | 3210 (5) | 979 (4) | -1640 (9) |
| $C_{(9)}$ | 2659 (5) | 5155 (5) | 1764 (10) | $C_{(23)}$ | 2659 (5) | 1702 (5) | -1424 (9) |
| $C_{(10)}$ | 3074 (4) | 4563 (5) | 3058 (9) | $C_{(24)}$ | 2793 (5) | 2396 (4) | -265 (9) |
| $N_{(11)}$ | 3020 (3) | 3627 (4) | 2572 (6) | $O_{(25)}$ | 6267 (3) | 1656 (4) | -2288 (6) |
| $C_{(12)}$ | 3667 (4) | 3198 (4) | 1712 (7) | $O_{(26)}$ | 4400 (3) | 3443 (3) | 1712 (5) |
| $C_{(13)}$ | 3476 (4) | 2371 (4) | 694 (7) | | | | |

**Note.** The $O_{(5)}$ and $O^*_{(5)}$ atoms are distributed statistically in a ratio of 0.55:0.45.

The macrocyclic diamide – 9,10,11,12-dibenz[a,c]-7,14-diaza-1,4-dioxacyclohexadecane-8,13-dione (IV) — was obtained by the reaction of diphenoyl dichloride with diamine II under conditions described in [2], where the formation of isoimides is also possible.



IV

In systems similar to IV, the conformational features of the ring are determined both by the rigid fragments (aromatic rings and the amide groups) and by the ring sizes [5-7].

To determine the steric structure of the macrocyclic compound IV and to discover the reasons for the formation of the macrocyclic 16-membered, and not the 7-membered mesocyclic isoimide system, we carried out an x-ray diffraction study of diamide IV. Its steric model is shown in Fig. 1 (the atom coordinates, the bond lengths between them, and the valence angles are given in Tables 1-3). The separate molecules in the crystal are joined by hydrogen bonds $N_{(11)}-H...O_{25}$ = 2859 Å in the chain, and van der Waals interaction takes place between them. In the macrocyclic compound IV a fairly strained structure is realized. The strains in the molecules are caused by the small size of the ring preventing the occurrence of the C–H...O

TABLE 2. Bonds Lengths d (Å) in the Structure of Compound IV (in brackets — standard deviations)

| Bond | *d* | Bond | *d* |
|---|---|---|---|
| $C_{(1)}$—$C_{(16)}$ | 1,486 (9) | $C_{(1)}$—$N_{(2)}$ | 1,322 (9) |
| $C_{(1)}$—$O_{(25)}$ | 1,239 (8) | $N_{(2)}$—$C_{(3)}$ | 1,450 (8) |
| $C_{(3)}$—$C_{(4)}$ | 1,51 (1) | $C_{(4)}$—$O_{(5)}$ | 1,41 (1) |
| $C_{(4)}$—$O^{*}_{(5)}$ | 1,59 (1) | $O_{(5)}$—$C_{(6)}$ | 1,50 (1) |
| $O^{*}_{(5)}$—$C_{(6)}$ | 1,29 (1) | C(6)—$C_{(7)}$ | 1,51 (1) |
| $C_{(7)}$—$O_{(8)}$ | 1,41 (1) | O(8)—$C_{(9)}$ | 1,406 (9) |
| $C_{(9)}$—$C_{(10)}$ | 1,53 (1) | C(10)—$N_{(11)}$ | 1,452 (9) |
| $N_{(11)}$—$C_{(12)}$ | 1,324 (8) | C(12)—$C_{(13)}$ | 1,505 (8) |
| $C_{(12)}$—$O_{(26)}$ | 1,243 (8) | C(13)—$C_{(14)}$ | 1,409 (9) |
| $C_{(13)}$—$C_{(24)}$ | 1,39 (1) | C(14)—$C_{(15)}$ | 1,502 (9) |
| $C_{(14)}$—$C_{(21)}$ | 1,393 (8) | C(15)—$C_{(16)}$ | 1,383 (9) |
| $C_{(15)}$—$C_{(20)}$ | 1,393 (8) | C(16)—$C_{(17)}$ | 1,42 (1) |
| $C_{(17)}$—$C_{(18)}$ | 1,39 (1) | C(18)—$C_{(19)}$ | 1,36 (1) |
| $C_{(19)}$—$C_{(20)}$ | 1,41 (1) | C(21)—$C_{(22)}$ | 1,39 (1) |
| $C_{(22)}$—$C_{(23)}$ | 1,39 (1) | C(23)—$C_{(24)}$ | 1,38 (1) |

*See note in Table 1.

interactions [8, 9], and also by the steric interaction of two diphenyl systems. The energy of the intramolecular interactions is partially compensated by a hydrogen bond $N_{(2)}-H...O_{(26)}$ = 2.888 Å, while the steric contacts between the two aromatic rings are prevented by their rotation with respect to one another around the $C_{(14)}-C_{(15)}$ bond to an angle 106°C. The aromatic rings deviate substantially from the middle plane of the heteroatoms of the 16-membered macrocyclic ring, forming angles with it of 41 and 110°, respectively. For the phthalic acid diamides the possility was noted of the interaction of the carbonyl groups according to the C═O...C═O principle [5]. In diamide IV shortened contacts between the carbonyl groups were not detected. The distant disposition of the carbonyl groups in the diphenic fragment is possibly the reason for the ruling out of the formation of the 7-membered isoimide system according to the principle described in [10].

As the result of the above indicated strains, the conjugation between the two aromatic rings is disturbed: The distance between them is equal to 1.502 A, while the $C_{(15)}$, $C_{(12)}$ and $C_{(14)}$, $C_{(1)}$ atoms deviate from the plane of the aromatic systems $C_{(13)}-C_{(24)}$ and $C_{(15)}-C_{(20)}$, respectively, which is expressed in the torsional angles at $C_{(13)}-C_{(14)}$ and $C_{(15)}-C_{(16)}$, equal to 12 and 7°, respectively. In the polyoxyethylene chain, gauche-rotamers are realized at the C−C bonds and trans- at the C−O bonds (except for $O_{(8)}-C_{(9)}$). An angular fragment (gauche-, gauche-) is thereby formed at the $C_{(9)}$ atom with a strained intramolecular contact $O_{(8)}...N_{(1)}$. The observed asymmetry of the molecule as a whole is possibly determined by the fact that only one amide group forms an intramolecular hydrogen bond — $N_{(2)}-H...O_{(26)}$. The remaining geometrical parameters of compound IV are typical for macrocyclic compound with amide groups, and do not substantially differ from those found in [5, 11].

The formation of compound IV may be determined by the specific features of the structure of diphenic acid fragment, which, as noted above, prevents the formation of a 7-membered isoimide, but leaves the possibility of the closing of a 16-membered macroring.

## EXPERIMENTAL

The IR spectra were recorded on an IKS-29 spectrophotometer in tablets with KBr. The PMR spectrum of compound III was run on a Tesla BS-467 spectrometer in $CDCl_3$, using HMDS as internal standard. The mass spectrum of diamide IV was obtained on a Varian-112 MAT-112 spectrometer, at an ionizing voltage of 70 eV, with direct introduction of the sample into the ionic source. The TLC was carried out on Silufol UV-254 plates, using an acetone−hexane (1:1) mixture as eluent. The development was carried out in UV light or with ninhydrin.

For the x-ray diffraction investigation, a single crystal of diamide IV with a prismatic appearance, with linear dimensions of 0.4 × 0.5 × 0.9 mm was selected. A monoclinic crystal with unit cell parameters $a$ = 16.192 (15), b =

TABLE 3. Valence Angles (degrees) in the Structure of Compound IV (in brackets — standard deviations)

| Angle | Value | Angle | Value |
|---|---|---|---|
| $N_{(2)}$—$C_{(1)}$—$C_{(16)}$ | 115,9 (6) | $N_{(2)}$—$C_{(1)}$—$O_{(25)}$ | 122,7 (6) |
| $C_{(16)}$—$C_{(1)}$—$O_{(25)}$ | 121,2 (6) | $C_{(1)}$—$N_{(2)}$—$C_{(3)}$ | 123,6 (6) |
| $N_{(2)}$—$C_{(3)}$—$C_{(4)}$ | 108,9 (6) | $C_{(3)}$—$C_{(4)}$—$O_{(5)}$ | 118,9 (8) |
| $C_{(3)}$—$C_{(4)}$—$O^{*}_{(5)}$ | 91,6 (7) | $C_{(4)}$—$O_{(5)}$—$C_{(6)}$ | 110,2 (8) |
| $C_{(4)}$—$O^{*}_{(5)}$—$C_{(6)}$ | 111,5 (9) | $O_{(5)}$—$C_{(6)}$—$C_{(7)}$ | 107,2 (7) |
| $O^{*}_{(5)}$—$C_{(6)}$—$C_{(7)}$ | 108,6 (8) | $C_{(6)}$—$C_{(7)}$—$O_{(8)}$ | 109,2 (6) |
| $C_{(7)}$—$O_{(8)}$—$C_{(9)}$ | 114,7 (6) | $O_{(8)}$—$C_{(9)}$—$C_{(10)}$ | 112,5 (6) |
| $C_{(9)}$—$C_{(10)}$—$N_{(11)}$ | 110,7 (6) | $C_{(10)}$—$N_{(11)}$—$C_{(12)}$ | 121,3 (5) |
| $N_{(11)}$—$C_{(12)}$—$C_{(13)}$ | 116,3 (5) | $N_{(11)}$—$C_{(12)}$—$O_{(26)}$ | 123,5 (5) |
| $C_{(13)}$—$C_{(12)}$—$O_{(26)}$ | 120,0 (5) | $C_{(12)}$—$C_{(13)}$—$C_{(14)}$ | 121,8 (5) |
| $C_{(12)}$—$C_{(13)}$—$C_{(24)}$ | 117,9 (5) | $C_{(14)}$—$C_{(13)}$—$C_{(24)}$ | 119,6 (6) |
| $C_{(13)}$—$C_{(14)}$—$C_{(15)}$ | 123,2 (5) | $C_{(13)}$—$C_{(14)}$—$C_{(21)}$ | 120,4 (6) |
| $C_{(15)}$—$C_{(14)}$—$C_{(21)}$ | 116,2 (5) | $C_{(14)}$—$C_{(15)}$—$C_{(16)}$ | 121,3 (5) |
| $C_{(14)}$—$C_{(15)}$—$C_{(20)}$ | 117,6 (6) | $C_{(16)}$—$C_{(15)}$—$C_{(20)}$ | 120,9 (6) |
| $C_{(1)}$—$C_{(16)}$—$C_{(15)}$ | 123,2 (6) | $C_{(1)}$—$C_{(16)}$—$C_{(17)}$ | 117,1 (6) |
| $C_{(15)}$—$C_{(16)}$—$C_{(17)}$ | 119,6 (6) | $C_{(16)}$—$C_{(17)}$—$C_{(18)}$ | 119,4 (7) |
| $C_{(17)}$—$C_{(18)}$—$C_{(19)}$ | 120,0 (7) | $C_{(18)}$—$C_{(19)}$—$C_{(20)}$ | 121,4 (7) |
| $C_{(15)}$—$C_{(20)}$—$C_{(19)}$ | 118,4 (6) | $C_{(14)}$—$C_{(21)}$—$C_{(22)}$ | 119,3 (6) |
| $C_{(21)}$—$C_{(22)}$—$C_{(23)}$ | 120,4 (6) | $C_{(22)}$—$C_{(23)}$—$C_{(24)}$ | 120,1 (7) |
| $C_{(13)}$—$C_{(24)}$—$C_{(23)}$ | 120,0 (6) | | |

14.959(15), c = 7.501 (6) Å, $\gamma$ = 82.66 (2)°, V = 1802.0 (9) Å$^3$; symmetry space group P$2_1$/n, Z = 4, having the composition of $C_{20}H_{22}N_2O_4$, $d_{calc}$ 1.306 g/cm$^3$. The experimental material was obtained on a DAR-UMB diffractometer with an M-6000 computer control, using the combination $\omega-\theta/2\theta$ method on monochromatized Cu$K_\alpha$ radiation. A total of 2897 reflections with I > 3$\sigma$(I) were used for the determining and refining the structure. The structure was resolved directly within the scope of the SHELX-CM complex [12] and refined to an R factor = 0.097. (The increased value of the R factor is due to the quality of the crystal, in which a statistical disorderliness was found in one of the oxyethylene fragments. The crystallochemical criteria and localization of the H atoms in disordered parts confirm that the structural parameters of compound IV were found correctly.)

The data of the elemental analysis of compounds III, IV correspond to the calculated values.

**Amidoester of Diphenyl-2,2′-dicarboxylic Acid (III, $C_{36}H_{36}N_2O_8$).** A 5.1-g portion (10 mmoles) of imide I was added to a mixture of 100 ml of methanol and 1.6 g (11 mmoles) of diamine II (or 30 mmoles of butylamine or triethylamine), and the mixture was heated at 55°C for 3 h to the complete conversion of diimide I (according to TLC). Methanol was distilled off, and the amidoester was separated by column chromatography on silica gel, eluting with an acetone–hexane (1:1) mixture. mp 108-110°C, $R_f$ 0.25. IR spectrum: 3390 (N–H), 1720 (C═O ester), 1665 cm$^{-1}$ (C═O amide). PMR spectrum, $\delta$: 3.13 (s, $CH_2$), 3.58 (s, $CH_3O$), 6.50 (br. s, NH), 6.83-7.77 ppm (m, Ar). Yield 5.9 g (94%).

**9,10,11,12-Dibenz[a,c]-7,14-diaza-dioxacyclohexadecane-8,13-dione (IV, $C_{20}H_{22}N_2O_4$).** Solutions of 1.4 g (5 mmoles) of diphenoyl dichloride in 200 ml of absolute chloroform and 1.5 g (10 mmoles) of diamine II in 200 ml of chloroform were simultaneously added dropwise to 200 ml of stirred chloroform in the course of 1 h. The reaction mixture was filtered from the filtrate, diamide IV was separated by column chromatography on silica gel, eluting with an acetone–hexane (1:1) mixture. mp 233-234°C. $R_f$ 0.19. IR spectrum: 3300 (N–H), 1620 cm$^{-1}$ (C═O). Mass spectrum, *m/z* (I, %): 104 (92), 152 (52), 180 (100), 181 (98), 195 (84), 209 (74), 222 (50), 250 (30), 266 (28), 354 (34, M$^+$). The sample was prepared for x-ray diffraction examination by recrystallization from methanol. Yield, 1.1 g (62%).

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