STRUCTURE OF THE PRODUCT OF THE REACTION OF 3,6-DIOXA-1,8-(DI-2,3-DICHLOROMALEIMIDO)OCTANE WITH 3,6-DIOXAOCTANE-1,8-DIAMINE

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The reaction of 3,6-dioxa-1,8-(di-2,3-dichloromaleimido)octane with 3,6-dioxaoctane-1,8-diamine gave 7,11-diaza-1,4-dioxa-9-en-7,11-oxo-9-chlorobicyclo-[1.2.9]tridecan-8-one. The steric structure of the last was determined by x-ray structural investigation.

The characteristic direction of the reaction of imides with amines is the cleavage of the imide heterocycle with the formation of the corresponding diamides, or transimidation [1, 2]. In particular, polyoxyethylenediphthalimides form macrocyclic diamides of phthalic acid with polyoxyethylenediamines [3]. The nucleophilic substitution of the chlorine atoms is also characteristic of imides of 2,3-dichloromaleic acid [4].

We established that the reaction of 3,6-dioxa-1,8-(di-2,3-dichloromaleimido)octane (I) with 3,6-dioxaoctane-1,8-diamine (II) occurs with the substitution of the chlorine atom and the formation of 7,11-diaza-1,4-dioxa-9-en-7,11-oxo-9-chlorobicyclo[1.2.9]tridecan-8-one (IV) (Table 1) (see scheme below).

In order to specify the features of the course of the reaction, we carried out the reactor of the model compound N-cyclohexyl-2,3-dichloromaleimide (V) with the primary and secondary amines (VIa-j) of varying structure.

It was established from the disappearance of the imide (V) from the reaction mixture that the reaction is completed in 3-15 min with the primary amines of normal structure (VIa, b) and secondary mesocyclic amines (VIe, h), in 1-1.5 h with the amines of isostructure (VIc, d), and in 1.5 days with the secondary amines diethylamine (VIi) and monoaza-15-crown-5 (VIj). In all cases, the substitution of the chlorine atom occurs with the formation of the imides (VIIa-j). When the primary amines of normal structure are utilized, the diamides (VIIIa, b) are also formed in the molar amount approximately equal to that of the imides (VIIa, b). The four- to fivefold increase in the reaction time by comparison with that indicated above does not lead

TABLE 1. Characteristics of the Synthesized Compounds (I), (IV), (VIIa-j), and (VIIIa, b)

Compound	Empirical formula	mp, °C	R_f	IR spectrum, ν, cm^{-1}		Yield, %
				N—H	C=O	
I	$C_{14}H_{12}Cl_4N_2O_6$	113...114	0,46	Split	1700	55
IV	$C_{10}H_{13}ClN_2O_4$	173...174	0,32	3300	1760, 1710	27
VIIa	$C_{14}H_{21}ClN_2O_2$	103...104	0,64	3400	1770, 1720	38
VIIb	$C_{20}H_{33}ClN_2O_2$	65...66	0,81	3370	1770, 1720	35
VIIc	$C_{13}H_{19}ClN_2O_2$	108...109	0,67	3365	1770, 1720	76
VIId	$C_{16}H_{23}ClN_2O_2$	153...154	0,57	3370	1760, 1710	80
VIIe	$C_{14}H_{19}ClN_2O_2$	150...151	0,58	Split	1760,1695	94
VIIf	$C_{15}H_{21}ClN_2O_2$	76...77	0,76	"	1760,1695	82
VIIg	$C_{16}H_{23}ClN_2O_2$	58...59	0,74	"	1770, 1720	85
VIIh	$C_{14}H_{19}ClN_2O_3$	140...141	0,42	"	1770, 1695	96
VIIi	$C_{14}H_{21}ClN_2O_2$	Oil	0,72	"	1770, 1710	78
VIIj	$C_{20}H_{31}ClN_2O_6$	"	0,10	"	1770, 1720	65
VIIIa	$C_{14}H_{22}Cl_2N_2O_2$	172...173	0,17	3300	1640	40
VIIIb	$C_{20}H_{34}Cl_2N_2O_2$	76...77	0,40	3400	1640	37

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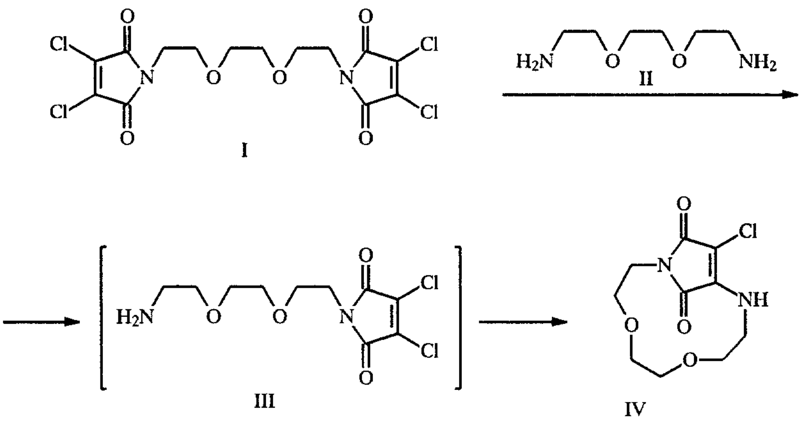
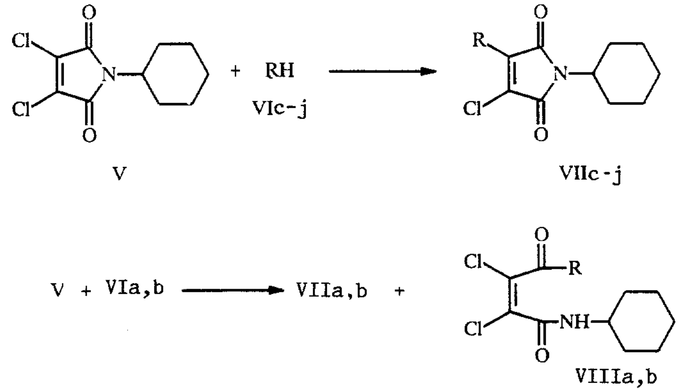


to other reaction products in spite of the excess of the amines (IVa-j). This indicates the stability of the final products — the imides (VIIa-j) and the diamides (VIIIa, b).



VI, VII, VIII a $R=HNC_4H_9$; b $R=HNC_{10}H_{21}$; c $R=HNC_3H_7$-iso d $R=HNC_6H_{11}$-cyclc e $R=N(CH_2)_4$; f $R=N(CH_2)_5$; g $R=N(CH_2)_6$; h $R=N(C_2H_4)_2O$; i $R=N(C_2H_5)_2$; j $R=\overline{NCH_2(CH_2OCH_2)_4CH_2}$

In spite of the fact that the diamine (II) is a structural analog of the monoamines (VIa, b), the bicyclic compound (IV) is formed in the reaction with the diimide (I), and the monocyclic diamide of the type (VIII) could not be detected. The result of the reaction probably depends on the nature of the imides and the amines (I). Since the imides (VIIa-j) and diamides (VIIIa, b) are stable to the action of the amines (VIa, j), it can be assumed that the first stage of the reaction with the diamine (II) proceeds with the cleavage of one of the heterocycles of the diimide (I) according to [1] [the reaction does not occur in the absence of the diamine (II)] and the intermediate formation of the reactive aminoimide (III); the subsequent intramolecular substitution of the chlorine atom by the terminal amino group of (III) leads to the formation of the macrocycle (IV).

We performed an x-ray structural investigation of the compound (IV) in order to explain the steric structure and the factors stabilizing the macrocyclic structure. The steric model of the bicycle (IV) in the projection onto the plane of the heteroatoms of the macrocyclic ring is presented in Fig. 1 with the designation of the atoms; the atomic coordinates, the bond lengths, and the bond angles are presented in Tables 2-4.

In the crystal, the $N_{(1)}...O_{(7)}$ distances of adjacent molecules, equal to 3.082 Å, indicate the formation of the $N_{(1)}$—$H...O_{(7)}$ hydrogen bond with the H...O distance of 2.45 Å (the angle at the H comprises 155°). On account of these hydrogen bonds, the molecules associated with the screw axis of the second order directed along the Z axis of the crystal are assembled in the chain.

The realization of gauche rotamers at the C—C bonds and trans rotamers at the C—O bonds is characteristic of the classical oxygen-containing crown ethers [5]. The conditions of the ring closure lead to one or two of the C—O bonds in the gauche configuration with the formation of an angular fragment of the gauche$^{\pm}$,gauche$^{\mp}$, or gauche$^{\pm}$,gauche$^{\pm}$ type. The first type stabilized the molecule due to the energetically favorable 1,5-C—H...O interactions; the second type destabilizes the molecule leading to the repulsion of the 1,4-CH_2...CH_2 or 1,4-O...O type [6]. The last strained contacts are characteristic of 12- to 15-membered rings [7]; the size of the cavity of these does not allow the introduction of the protons of methylene groups for the formation

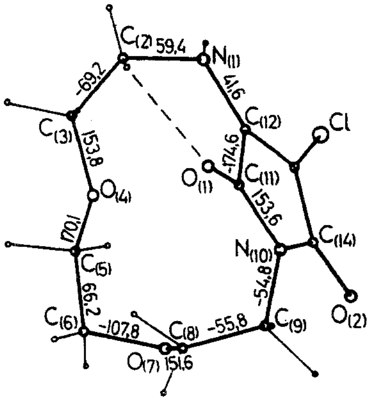


Fig. 1. Molecular structure of the bicycle (IV) in the projection onto the plane of the heteroatoms of the macrocycle.

TABLE 2. Coordinates of the Basal Plane Atoms with Standard Deviations × 10^4 in the Structure of the Compound (IV)

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
Cl	1376 (2)	4121 (1)	309 (1)	$C_{(9)}$	7289 (6)	2649 (3)	2417 (3)
$N_{(1)}$	3832 (5)	2364 (2)	-814 (2)	$N_{(10)}$	6307 (5)	3000 (2)	1508 (2)
$C_{(2)}$	3942 (6)	1303 (3)	-935 (3)	$C_{(11)}$	6316(5)	2480 (3)	624 (3)
$C_{(3)}$	2614 (5)	757 (3)	-182 (3)	$C_{(12)}$	4400 (5)	2788 (3)	50 (3)
$O_{(4)}$	3528 (3)	890 (2)	778 (2)	$C_{(13)}$	3606 (6)	3514 (3)	582 (3)
$C_{(5)}$	2052 (6)	800 (3)	1568 (3)	$C_{(14)}$	4648 (6)	3630 (3)	1526 (3)
$C_{(6)}$	3176 (7)	772 (3)	2547 (3)	$O_{(1)}$	7639 (4)	1943 (2)	350 (2)
$O_{(7)}$	4260 (4)	1678 (2)	2769 (2)	$O_{(2)}$	4211 (5)	4148 (2)	2227 (2)
$C_{(8)}$	6479 (7)	1644 (3)	2686 (3)				

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*The numeration of the atoms is presented in Fig. 1.

TABLE 3. Bond Lengths d (Å) in the Compound (IV)

Bond	*d*	Bond	*d*
$N_{(1)}$—$C_{(2)}$	1,471 (5)	$N_{(10)}$—$C_{(11)}$	1,385 (5)
$N_{(2)}$—$C_{(3)}$	1,510 (5)	$C_{(11)}$—$C_{(12)}$	1,529 (5)
$C_{(3)}$—$O_{(4)}$	1,427 (4)	$C_{(12)}$—$N_{(1)}$	1,343 (5)
$O_{(4)}$—$C_{(5)}$	1,428 (5)	$C_{(12)}$—$C_{(13)}$	1,342 (5)
$C_{(5)}$—$C_{(6)}$	1,502 (6)	$C_{(13)}$—$C_{(14)}$	1,440 (5)
$C_{(6)}$—$O_{(7)}$	1,440 (5)	$C_{(14)}$—$N_{(10)}$	1,398 (5)
$C_{(8)}$—$C_{(9)}$	1,505 (6)	$C_{(11)}$—$O_{(1)}$	1,204 (4)
$C_{(9)}$—$N_{(10)}$	1,464 (5)	$C_{(14)}$—$O_{(2)}$	1,218 (5)

of C—H...O interactions in it. In the polyfunctional crown ethers containing ester, amide, and other groups, NH...O, NH...O=C, and C=O...C=O interactions bearing a stabilizing character may arise [8, 9].

The favorable gauche conformation is found in the polyoxyethylene chain of the compound (IV) at the three CH_2—CH_2 fragments. The trans conformation is found at three of the four C—O bonds; the gauche configuration is found for one $O_{(7)}$—$C_{(6)}$ bond. The conformation of the $N_{(1)}$—$C_{(12)}$...$C_{(9)}$ fragment is determined by the rigidity of the conjugated five-membered ring and the axial position of the proton at $N_{(1)}$. Overall, the tetragonal conformation with angles of the gauche±,gauche± and gauche±,gauche∓ type is formed at $N_{(1)}$, $C_{(9)}$ and $C_{(2)}$, $C_{(6)}$ correspondingly. According to Dale [10], this conformation is described as [1 4 $\underline{3}$ $\underline{4}$]. The $C_{(2)}$—H...$O_{(1)}$ intramolecular interaction with the distance of 3.053 Å, which bears a stabilizing character, arises with such a conformation. The angular fragment at the $C_{(6)}$ atom gives the principal possibility of the $C_{(8)}$—H...$O_{(4)}$ interaction. However, the significant deviation of the torsional angle at the $O_{(7)}$—$C_{(6)}$ bond from 60° separates the protons of of the methylene group at $C_{(8)}$ from $O_{(4)}$.

TABLE 4. Bond Angles (deg) in the Structure of the Compound (IV) (standard deviations are in brackets)

Angle	Value	Angle	Value
$C_{(12)}$—$N_{(1)}$—$C_{(2)}$	120,2 (3)	$C_{(9)}$—$N_{(10)}$—$C_{(14)}$	122,5 (3)
$N_{(1)}$—$C_{(2)}$—$C_{(3)}$	111,9 (3)	$C_{(11)}$—$N_{(10)}$—$C_{(14)}$	110,4 (3)
$C_{(2)}$—$C_{(3)}$—$O_{(4)}$	108,3 (3)	$N_{(10)}$—$C_{(11)}$—$O_{(1)}$	126,2 (3)
$C_{(3)}$—$O_{(4)}$—$C_{(5)}$	112,7 (3)	$O_{(1)}$—$C_{(11)}$—$C_{(12)}$	127,7 (3)
$O_{(4)}$—$C_{(5)}$—$C_{(6)}$	109,2 (3)	$N_{(1)}$—$C_{(12)}$—$C_{(13)}$	132,5 (3)
$C_{(5)}$—$C_{(6)}$—$O_{(7)}$	112,4 (3)	$C_{(11)}$—$C_{(12)}$—$C_{(13)}$	105,5 (3)
$C_{(6)}$—$O_{(7)}$—$C_{(8)}$	114,4 (3)	Cl—$C_{(13)}$—$C_{(12)}$	126,1 (3)
$O_{(7)}$—$C_{(8)}$—$C_{(9)}$	107,8 (3)	Cl—$C_{(13)}$—$C_{(14)}$	121,8 (3)
$C_{(8)}$—$C_{(9)}$—$N_{(10)}$	111,1 (3)	$C_{(12)}$-$C_{(13)}$—$C_{(14)}$	111,2 (3)
$C_{(9)}$—$N_{(10)}$—$C_{(11)}$	122,3 (3)	$N_{(10)}$—$C_{(14)}$—$C_{(13)}$	106,3 (3)
$N_{(10)}$—$C_{(11)}$—$C_{(12)}$	105,8 (3)	$N_{(10)}$—$C_{(14)}$—$O_{(2)}$	124,7 (3)
$C_{(11)}$—$C_{(12)}$—$N_{(1)}$	121,8 (3)	$C_{(13)}$—$C_{(14)}$—$O_{(2)}$	128,9 (4)

The donor atoms $N_{(1)}$, $O_{(4)}$, $O_{(7)}$, and $N_{(10)}$ of the structure (IV) are coplanar with the accuracy of ±0.280 Å. The plane of the heteroatoms of the macrocycle with the five-membered flat ring comprises the angle 77.4°. The Cl, $N_{(1)}$, $O_{(1)}$, and $O_{(2)}$ substituents come out of the plane of the five-membered ring by —0.035, —0.141, 0.161, and —0.105 Å correspondingly. The $N_{(10)}$—$C_{(14)}$ and $N_{(10)}$—$C_{(11)}$ distances in the five-membered ring comprise 1.398 and 1.385 Å correspondingly. The length of the $C_{(12)}$—$C_{(13)}$ double bond equals 1.342 Å; the remaining C—C bonds have the lengths 1.529 and 1.440 Å. The latter indicates the nonpolar delocalization of the electron density in the five-membered ring. The $C_{(13)}$—Cl and C=O distances comprise 1.726, 1.204, and 1.218 Å correspondingly. In the macrocyclic ring of the compound (IV), the C—C, C—N, and C—O distances are equal, on average, to 1.506, 1.468, and 1.436 Å correspondingly. The $N_{(1)}$—$C_{(12)}$ bond is not considered in the calculation since it is reduced to 1.343 Å; this may be determined by the delocalization of the electron density in the $C_{(11)}$—$N_{(10)}$—$C_{(14)}$—$C_{(13)}$—$C_{(12)}$—$N_{(1)}$ fragment.

EXPERIMENTAL

The IR spectra were recorded on the IKS-29 spectrophotometer using tablets with KBr. The TLC was performed on plates of Silufol UV-254 using the 4:3 system of ether—hexane; the 1:2 system of acetone—hexane was utilized for the compounds (I) and (IV). Development was performed with UV light and ninhydrin. Column chromatography of the compounds (IV), (VIIa-j), and (VIIIa, b) was carried out on silica gel L 40/100 (Czechoslovakia).

The yellow monocrystal of prismatic appearance with the linear dimensions 0.5 × 0.4 × 0.7 mm was selected for the x-ray structural analysis of compound (IV). The parameters of the elementary cell were as follows: $a = 6.460(1)$, $b = 13.734(4)$, and $c = 13.420(4)$ Å; $\gamma = 91.78(3)°$. The space group of symmetry was $P2_1/n$, $Z = 4$; the composition was $C_{10}H_{13}ClN_2O_4$, $d_{calc} = 1.454$ g/cm^3. The experimental material was obtained on the RÉD-4 diffractometer with the MoK_α radiation. In all, 1445 reflections were registered; 1331 of them with the $I \geq 3\sigma(I)$ were utilized for the determination of, and the specification of, the structure. The structure was resolved by the direct method in the framework of the XTL CM complex [11], and was specified using the anisotropic variant for the C, N, O, and Cl atoms, and the isotropic variant for H. The H atoms were found objectively from different Fourier syntheses. The final R-factor was equal to 0.059; it was 0.063 taking into account the experimental weight scheme.

The compounds (I) and (V) were obtained according to [4]; the compound (II) was obtained according to [12].

7,11-Diaza-1,4-dioxa-9-en-7,11-oxo-9-chlorobicyclo[1.2.9]-tridecan-8-one (cf. Table 1). To the solution of 2.2 g (4 mmole) of the diimide (I) in 200 ml of methanol is added, with stirring in the course of 1 h, the solution of 1.5 g (10 mmole) of the diamine (II) dropwise. The mixture is maintained at 20°C for 1 h. The compound (IV) is isolated by column chromatography; the elution is performed with the mixture utilized for the TLC. Crystals for the x-ray structural analysis are obtained by recrystallization from acetone.

N-Cyclohexylimides of 2-Alkylamino-3-chloromaleic Acid (VIIa-j) and N-Alkyl-N′-cyclohexyldiamides of 2,3-Dichloromaleic Acid (VIIIa, b) (cf. Table 1). To the solution of 0.5 g (2 mmole) of the imide (V) in 50 ml of methanol is added the solution of 10 mmole of the corresponding amine (VIa-j) in 15 ml of methanol; the mixture is left at 20°C until the complete conversion of the imide (V) is shown by TLC. The compounds (VIIe, h) are isolated by crystallization from the reaction medium at —15 °C; the remaining compounds are isolated by column chromatography on silica gel with the elution by the mixture utilized for TLC and the subsequent concentration of the eluent.

LITERATURE CITED

1. F. S. Spring and J. C. Woods, *Nature,* **158**, 754 (1946).
2. M. K. Hargreaves, J. G. Pritshard, and H. R. Dave, *Chem. Rev.,* **70**, 439 (1970).
3. É. V. Ganin, B. V. Rozynov, V. F. Anikin, and G. L. Kamalov, *Khim. Geterotsikl. Soedin.,* No. 8, 1048 (1984).
4. E. L. Martin, C. L. Dickinson, and J. R. Poland, *J. Org. Chem.,* **26**, 2032 (1961).
5. Yu. G. Ganin, Yu. A. Simonov, and T. I. Malinovskii, *Izv. Akad. Nauk Mold. SSR, Ser. Fiz.-Tekh. Mat. Nauk,* No. 1, 18 (1985).
6. P. Flory, *Statistical Mechanics of Chain Molecules* [Russian translation], Mir, Moscow (1972).
7. R. M. Izatt and J. J. Christensen, *Synthetic Multidentate Macrocyclic Compounds,* Academic Press, New York (1978).
8. Yu. A. Simonov, S. T. Malinovskii, and N. G. Luk'yanenko, *Dokl. Akad. Nauk SSSR,* 294, 871.
9. S. T. Malinovskii, Yu. A. Simonov, and N. G. Luk'yanenko, *Izv. Akad. Nauk Mold. SSR, Ser. Fiz.-Tekh. Mat. Nauk,* No. 1, 29 (1989).
10. J. Dale, *Acta Chem. Scand.,* **27**, 1115 (1973).
11. V. K. Pecharskii, P. Yu. Zavalii, and L. G. Aksel'rud, *Vestn. L'vov. Univ., Ser. Khim.,* No. 25, 9 (1984).
12. V. F. Anikin, É. V. Ganin, B. V. Rozynov, R. M. Zakharova, and G. L. Kamalov, *Khim. Geterotsikl. Soedin.,* No. 2, 246 (1982).