The equivalence points on the titration curves and the half-neutralization potentials (E) were found graphically. Benzoic acid, the acidic ionization constant ($pK_a{}^0$) of which in DMSO is 10.9 [7], was used as the standard. The reproducibility of the pK_a values was ±0.1 logarithmic units.

Starting 2-imino-1,3-thiazinoazoles I and III-V were synthesized by the method in [3-5]. The DMSO was purified by vacuum distillation over NaOH.

A 0.08-g (0.3 mmole) sample of 2-imino-4-(1-hydroxy-1-methylethyl)-1,3-thiazino[2,3-b]-benzimidazole (III) was dissolved in 2 ml of DMSO, and 1 ml of a 10% aqueous solution [0.1 g (0.07 mmole)] of tetraethylammonium hydroxide was added.

A 0.1-g (0.4 mmole) sample of III was dissolved in 2-4 ml of DMSO, and 3 ml of a 10% aqueous solution [0.3 g (2 mmoles)] of tetraethylammonium hydroxide was added. The solution heated up and took on a bright-yellow coloration. When the solution was poured into ice water, the yellow coloration vanished, and a white precipitate formed. The precipitate was removed by filtration and washed with water until the wash water was neutral to give 0.08 g of a substance, the melting point and TLC and IR spectral data for which were identical to those for III. Neutralization of the solutions was carried out with 10% HCl.

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POLYFUNCTIONAL MACROHETEROCYCLES.

1. SYNTHESIS OF SULFUR-CONTAINING MACROHETEROCYCLES WITH ENDOCYCLIC AMIDO OR SULFONAMIDO GROUPS

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The reaction of 1,8-diamino-, 1,8-bis(2-carbomethoxyethylamino)-, and 1,8-bis(2-phenylethylamino)-3,6-dithiaoctanes and 1,2-bis(2-aminoethylthiomethyl)-4,5-dimethylbenzene with adipic, phthalic, and terephthalic acid dichlorides leads to the corresponding sulfur-containing macrocyclic diamines. Macrocycles that contain endocyclic sulfonamido groups are formed in the reaction of benzene-1,3-disulfonic acid dichloride with hexamethylenediamine and 1,8-bis(2-carbomethoxyethylamino)-3,6-dithiaoctane. The oxidation of 9,10-benzo-8,11-dioxo-7,12-bis(2-carbomethoxyethyl)-1,4-dithia-7,12-diazacyclotetradec-9-ene with 30% hydrogen peroxide was studied.

Polyfunctional macroheterocycles are currently used as complexones and extractants of transition metals [1-4]. Functional groups in the endo- and exocyclic position in the macrocycle molecule intensify its complexing properties and stabilize the formation of a complex [4]. Compounds of this type are used in the synthesis of new types of crown compounds or to

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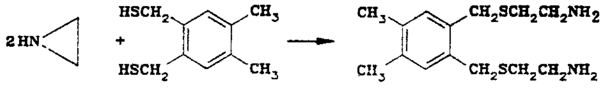
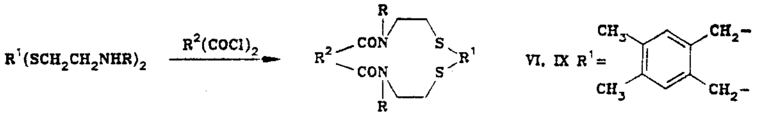
obtain polymeric and immobilized macroheterocycles [4]. Their antidote and antibacterial activity has been studied [5, 6].

In order to obtain new types of macroheterocycles that contain endo- and N-exocyclic functional groups and to investigate their complexing ability and biological activity we studied the reaction of heterochain α,ω-diamines I-IV with dicarboxylic acid dichlorides and benzene-1,3-disulfonic acid dichloride.

The starting 1,8-diamino-, 1,8-bis(2-carbomethoxyethylamino)-, and 1,8-bis(2-phenylethylamino)-3,6-dithiaoctanes I-III were synthesized by a previously described method from the corresponding aziridines and ethane-1,2-dithiol [7, 8]. 1,2-Bis(2-aminoethylthiomethyl)-4,5-dimethylbenzene (IV) was obtained by the reaction of aziridine with 4,5-dimethyl-1,2-di(mercaptomethyl)benzene in 80% yield.

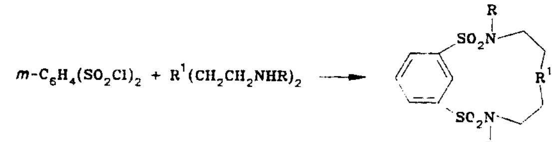

IV

The acylation of α,ω-diamines with dicarboxylic acid dichlorides is most convenient for obtaining macrocyclic diamides [7, 8]. The reaction of diamines I-IV with adipic, phthalic, and terephthalic acid dichlorides in benzene under high-dilute conditions in the presence of triethylamine made it possible to obtain macroheterocycles V-IX in 60-70% yields.


I–IV V–IX

V, VI R=H, VII, IX $R=CH_2CH_2COOCH_3$, VIII $R=CH_2CH_2C_6H_5$; V, VII, VIII $R^1=$ $=CH_2CH_2$; V $R^2=-(CH_2)_4-$, VI $R^2=1,2\text{-}C_6H_4$, VII–IX $R^2=1,4\text{-}C_6H_4$

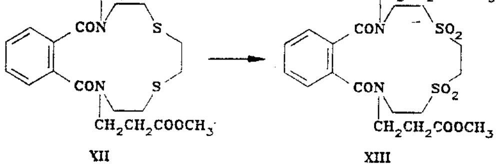
Under high-dilution conditions in benzene, benzene-1,3-disulfonic acid dichloride reacts with hexamethylenediamine and 1,8-bis(2-carbomethoxyethylamino)-3,6-dithiaoctane (II) to give macroheterocycles X (65% yield) and XI (75% yield).


X $R=H$, $R^1=CH_2CH_2$; XI $R=CH_2CH_2COOCH_3$, $R^1=SCH_2CH_2S$

X, XI

The method developed makes it possible to obtain macroheterocyclic compounds that contain N-exocyclic carbomethoxyethyl and phenylethyl groups. The introduction of these groups into crown compounds VII-IX and XI markedly increases their solubility in organic solvents as compared with N-unsubstituted macroheterocycles V, VI, and X.

The sulfur-containing macroheterocyclic diamides that we previously obtained are effective extractants of the transition metal ions Ag(I), Cu(II), Hg(II), and Pd(II) [3]. It is known that macrocycles that contain sulfoxide groups form complexes with alkali metal ions and are used in interphase catalysis [9]. In order to obtain crown compounds that contain sulfoxide groups and to study their complexing properties with alkali and alkaline-earth metal ions we carried out the oxidation of 9,10-benzo-8,11-dioxo-7,12-bis(2-carbomethoxyethyl)-1,4-dithia-7,12-diazacyclotetradec-9-ene (XII) [7] with 30% hydrogen peroxide in acetic acid; macroheterocycle XIII was obtained in 50% yield.


XII XIII

The synthesized macroheterocycles V-XI and XIII are colorless crystalline substances or viscous oils. Compounds VII-IX and XI are soluble in benzene, chloroform, methanol, DMF, and

DMSO, while macroheterocycles V, VI, and X are soluble in methanol, DMF, and DMSO. Crown compound XIII is soluble in chloroform and in hot water.

Absorption bands at 3290-3300 cm^{-1}, which are characteristic for the vibrations of the NH group in secondary amines, are present in the IR spectra of crown compounds V, VI, and X. The frequencies of the vibrations of an ester group in the spectra of VII, IX, XI, and XIII are found at 1715-1735 cm^{-1}. The spectra of macroheterocycles V-IX and XIII contain absorption bands at 1620-1640 cm^{-1} (amide I band) and, in the case of V and VI, at 1550 cm^{-1} (amide II band). The frequencies of the vibrations of the CH_2SCH_2 group in the spectra of V-IX and XI are found at 700-740 cm^{-1}, while the vibrations of the SO_2 group of X, XI, and XIII are found at 1290-1330 and 1160-1180 cm^{-1}.

EXPERIMENTAL

The IR spectra were obtained with a UR-20 spectrometer. The PMR spectra of solutions in $CDCl_3$ and d_6-DMSO were recorded with a Tesla BS-487C spectrometer (80 MHz) with tetramethylsilane (TMS) as the internal standard.

1,2-Bis(2-aminoethylthiomethyl)-4,5-dimethylbenzene (IV). A mixture of 4.3 g (100 mmole) of aziridine and 9.9 g (50 mmole) of 4,5-dimethyl-1,2-dimercaptomethylbenzene in 100 ml of methanol was heated for 6 h at 55-60°C, after which the methanol was removed by distillation, and the residue was dissolved in chloroform. Treatment of the solution with petroleum ether in the cold gave 11.4 g (80%) of a viscous oil that was quite soluble in benzene, methanol, chloroform, DMF, and DMSO. IR spectrum: 730 m, 1100 m, 1180 m, 1230 m, 1425 w, 1600 m, 1650 m, 2885 w, 2940 m, 2950 m, 3280 m, 3360 cm^{-1}. PMR spectrum: 2.01 (s, CH_3), 2.99 (m, CH_2N, CH_2S), 3.66 (s, $ArCH_2$), 6.89 ppm (m, C_6H_2). Found, %: C 58.8; H 8.2; N 9.5; S 22.1. $C_{14}H_{24}N_2S_2$. Calculated, %: C 59.1; H 8.4; N 9.8; S 22.5.

8,13-Dioxo-1,4-dithia-7,14-diazacyclohexadecane (V). A solution of 4.5 g (25 mmole) of diamine I in 500 ml of dry benzene and a solution of 4.6 g (25 mmole) of adipic acid dichloride in 500 ml of dry benzene were added simultaneously in the course of 6 h at 20°C with vigorous stirring to 1 liter of dry benzene containing 5.0 g (50 mmole) of triethylamine. The precipitate was removed by filtration, the solvent was removed by distillation at reduced pressure, and the residue was purified by chromatography on aluminum oxide using benzene–methanol (5:1) as the eluent. The solvent was removed by distillation, and the residue was recrystallized from methanol to give 5.0 g (70%) of a product with mp 170-171°C. IR spectrum: 3300 (NH), 1640 (CO), 705 cm^{-1} (CH_2SCH_2). Found, %: C 49.2; H 7.3; N 9.2; S 20.8; M (cryoscopic CH_3COOH) 275. $C_{12}H_{22}N_2O_2S_2$. Calculated, %: C 49.6; H 7.6; N 9.6; S 22.1; M 290.

11,12-Benzo-3,4-(4,5-dimethylbenzo)-10,13-dioxo-1,6-dithia-9,14-diazacyclohexadeca-3,11-diene (VI). This compound was similarly obtained from 8.1 g (0.25 mmole) of diamine IV and 5.0 g (25 mmole) of phthalic acid dichloride. Workup gave 7.7 g (65%) of a product with mp 135-136°C. IR spectrum: 3280 (NH), 1640 (CO), 700 cm^{-1} (CH_2SCH_2). PMR spectrum: 2.40 (s, CH_3), 2.75 (m, CH_2N, CH_2S), 3.75 (s, $ArCH_2$), 7.62 ppm (m, C_6H_2, C_6H_4). Found, %: C 63.3; H 5.8; N 6.4; S 15.1; M 400. $C_{22}H_{26}N_2O_2S_2$. Calculated, %: C 63.7; H 6.2; N 6.7; S 15.4; M 414.

9,12-Benzo-8,13-dioxo-7,14-bis(2-carbomethoxyethyl)-1,4-dithia-7,14-diazacyclohexadeca-9,12-diene (VII). This compound was similarly obtained from 8.8 g (25 mmole) of diamine II and 5.0 g (25 mmole) of terephthalic acid dichloride. Workup gave 8.4 g (70%) of an oil. IR spectrum: 1735 ($COOCH_3$), 1640 (CO), 750 cm^{-1} (CH_2SCH_2). PMR spectrum: 2.85 (m, CH_2N, CH_2S), 3.60 (s, OCH_3), 7.30 ppm (m, C_6H_4). Found, %: C 54.4; H 5.9; N 5.2; S 12.8; M 470. $C_{22}H_{30}N_2O_6S_2$. Calculated, %: C 54.8; H 6.2; N 5.5; S 13.2; M 482.

9,12-Benzo-8,13-dioxo-7,14-bis(2-phenylethyl)-1,4-dithia-7,14-diazacyclohexadeca-9,12-diene (VIII). This compound was similarly obtained from 9.7 g (25 mmole) of diamine III and 5.0 g (25 mmole) of terephthalic acid dichloride. Workup gave 9.1 g (70%) of a product with mp 230°C. IR spectrum: 1640 (CO), 3030, 1600 (=CH), 730 cm^{-1} (CH_2SCH_2). PMR spectrum: 2.80 (m, CH_2N, CH_2S), 3.65 (m, $C_6H_5CH_2$), 7.20 ppm (m, C_6H_5, C_6H_4). Found, %: C 69.3; H 6.8; N 5.5; S 12.3; M 490. $C_{30}H_{34}N_2O_2S_2$. Calculated, %: C 69.4; H 6.6; N 5.4; S 12.3; M 518.

11,14-Benzo-3,4-(4,5-dimethylbenzo)-10,15-dioxo-9,16-bis(2-carbomethoxyethyl)-1,6-dithia-9,16-diazacyclooctadeca-3,11,14-triene (IX). This compound was similarly obtained from 11.2 g (25 mmole) of diamine IV and 5.0 g (25 mmole) of terephthalic acid dichloride. Workup gave 8.5 g (60%) of an oil. IR spectrum: 1735 ($COOCH_3$), 1640 (CO), 740 cm^{-1} (CH_2SCH_2). Found, %: C 61.1; H 6.1; N 4.6; S 10.5; M 550. $C_{30}H_{38}N_2O_2S_2$. Calculated, %: C 61.4; H 6.4; N 4.8; S 10.9; M 586.

2,2,11,11-Tetraoxo-2,11-dithia-3,10-diazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (X). This compound was similarly synthesized from 1.16 g (10 mmole) of hexamethylenediamine and 2.75 g (10 mmole) of benzene-1,3-disulfonic acid dichloride. Workup gave 2.0 g (65%) of a product with mp 150°C. IR spectrum: 3290 (NH), 1320, 1160 cm^{-1} (SO_2). PMR spectrum: 1.37 (m, CH_2), 2.95 (m, CH_2N), 7.87 ppm (m, C_6H_4). Found, %: C 45.1; H 5.2; N 8.4; S 19.7. $C_{12}H_{18}N_2O_4S_2$. Calculated, %: C 45.3; H 5.6; N 8.8; S 20.1.

3,12-Bis(2-carbomethoxyethyl)-2,2,13,13-tetraoxo-2,6,9,13-tetrathia-3,12-diazabicyclo-[12.3.1]octadeca-1(18),14,16-triene (XI). This compound was similarly synthesized from 3.52 g (10 mmole) of diamine II and 2.75 g (10 mmole) of benzene-1,3-disulfonic acid dichloride. Workup gave 2.98 g (75%) of an oil. IR spectrum: 1730 ($COOCH_3$), 1320, 1160 (SO_2), 750 cm^{-1} (CH_2SCH_2). PMR spectrum: 2.65 (s, CH_2CO), 2.78-3.25 (m, CH_2N, CH_2S), 3.38 (s, OCH_3), 7.45 m d (m, C_6H_4). Found, %: C 43.1; H 5.1; N 4.8; S 22.7. $C_{20}H_{30}N_2O_8S_4$. Calculated, %: C 43.3; H 5.4; N 5.1; S 23.1.

9,10-Benzo-1,1,4,4,8,11-hexaoxo-7,12-bis(2-carbomethoxyethyl)-1,4-dithia-7,12-diazacyclotetradeca-9-ene (XIII). A solution of 1.0 g of XII and 3.3 ml of 30% H_2O_2 in 10 ml of acetic acid was heated for 2 h at 90°C, after which the solution was cooled and poured over ice. The aqueous mixture was extracted with chloroform, the solvent was evaporated in vacuo, and the residual white crystals were washed with methanol and dried to give 0.55 g (50%) of a product with mp 215-216°C. IR spectrum: 1715 ($COOCH_3$), 1620 (CO), 1290, 1180 cm^{-1} (SO_2). Found, %: C 48.7; H 5.8; N 4.8; S 11.2. $C_{22}H_{30}N_2O_{10}S_2$. Calculated, %: C 48.3; H 5.5; N 5.1; S 11.7.

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