POLYFUNCTIONAL MACROHETEROCYCLES. 6*. CROWN ETHERS CONTAINING N AND S WITH EXOCYCLIC METHOXYCARBONYLETHYL, HYDROXY-, OR SULFONATOMETHYL GROUPS

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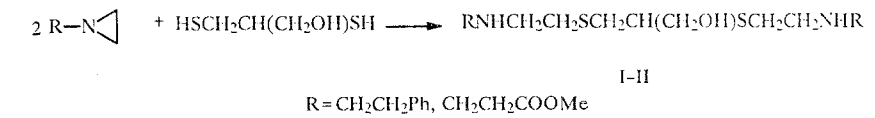
Reaction of 1-phenethyl- and 1-methoxycarbonylethylaziridine with 2,3-dimercaptopropanol gives the corresponding N-substituted (4-hydroxymethyl-1,8-diamino)-3,6-dithiaoctanes. Reaction of aziridine and its 1-substituted derivatives with 2,3-dimercaptopropanesulfonic acid gives the corresponding [1,10-diamino-3-oxa-4,8-dithia-6-(2-aminoethylthio)]decane-4,4-dioxides. Treatment of them with sodium bicarbonate produces the corresponding sodium 2,3-bis(2-aminoethylthio)propanesulfonates. Cyclocondensation of certain synthesized diamines with adipic diazide produces 16-membered macroheterocycles with exocyclic methoxycarbonylethyl, hydroxy-, or sulfonatomethyl groups.

Earlier we developed a synthesis of crown compounds containing N and S with exocyclic phenethyl, methoxycarbonylethyl, 1,2-bis(methoxycarbonyl)ethyl, cyanoethyl, and hydroxy- and aminopropyl groups [2-7]. The resulting polyfunctional macroheterocycles form complexes with cations, anions, or neutral molecules involving donors in the ring and outside it [8, 9]. A study of the spectral and redox properties of their complexes with Cu(II) demonstrates that their properties are identical to those of the blue proteins. Therefore, the synthesized complexes can be used as models for metalloenzymes [10].

We developed syntheses of crown compounds containing N and S with exocyclic hydroxy- and sulfonatomethyl groups in order to obtain new types of macroheterocycles and to use them in supramolecular chemistry to form complexes with organic or inorganic substrates through donors in the ring and outside it.

Previously we used the dichloroanhydride method to synthesize macrocycles containing N and S. Diamines containing a hydroxy or sulfonate group cannot be used as starting materials with this method. Therefore, we developed a diazide method of preparing crown compounds. According to previous data [11], this method enables hydroxyaminoacids to be condensed with carboxylic azides without affecting the hydroxyl.

The corresponding diamines I and II were prepared through reaction of 1-phenethyl- and 1-methoxycarbonylethylaziridine with 2,3-dimercaptopropanol.



$$2\ R{-}N\langle \quad + HSCH_2CH(CH_2OH)SH \longrightarrow RNHCH_2CH_2SCH_2CH(CH_2OH)SCH_2CH_2NHR$$

I-II

R = CH_2CH_2Ph, CH_2CH_2COOMe

*For Communication 5, see [1].

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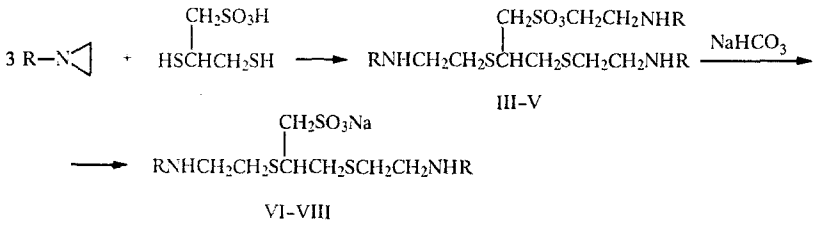
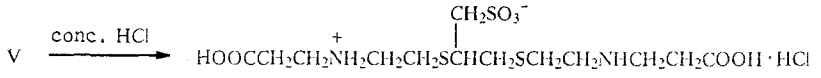
The reaction of 2,3-dimercaptopropanesulfonic acid with aziridine and its 1-substituted derivatives occurs under analogous conditions with a 1:3 ratio of starting reagents.



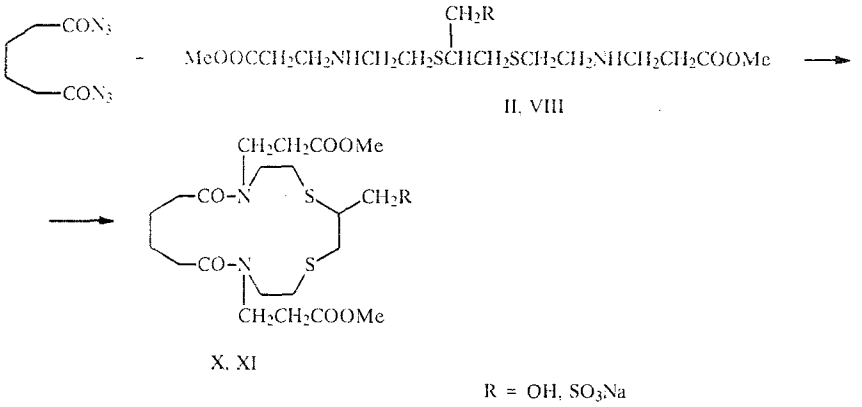
R=H, CH_2CH_2Ph, CH_2CH_2COOMe

The triamines III-V are viscous oils that are very soluble in water and organic solvents (methanol, $CHCl_3$, DMF, DMSO). Treatment of them with an aqueous-methanol solution of $NaHCO_3$ produces sodium 2,3-bis(aminoethylthio)- (VI), 2,3-bis(2-phenethylaminoethylthio)- (VII), and 2,3-bis(2-methoxycarbonylethylaminoethylthio)propanesulfonate (VIII) in yields of 54, 80, and 45%, respectively. Triamine V is hydrolyzed by conc. HCl in acetic acid at 100 °C to form the monohydrochloride of 2,3-bis(2-carboxyethylaminoethylthio)propanesulfonic acid (IX) in 50% yield.



IX

Cyclocondensation of adipic diazide prepared by the literature method [12] with II and VIII occurs under high-dilution conditions.



X, XI

R = OH, SO_3Na

The yield of X and XI is 70-75%.

The IR spectra of I-VIII contain a broad absorption at 3420-3100 cm^{-1} assigned to vibrations of H-bonded OH or NH_2. Vibrations of H-bonded NH are observed at 3200-3100 cm^{-1}. The spectra of II, V, and VIII contain an absorption at 1730 cm^{-1} that is characteristic of the ester. The sulfonate absorptions in the spectra of di- and triamines III-VIII typically have three groups of bands at 1450-1430, 1200-1180, and 1050-1020 cm^{-1}. According to the IR spectra, IX has the betaine structure. The spectrum of this compound contains a broad absorption of the carboxyl at 2800-2400 cm^{-1} and a strong absorption near 1720 cm^{-1}. The vibrations of the $^+NH_2$ group occur at 3010 and 1640 cm^{-1}. The IR spectra of X and XI have absorptions near 1610-1620 and 1720 cm^{-1} from amide and ester groups, respectively. The H-bonded hydroxyl of X appears at 3300 cm^{-1} whereas the sulfonate absorptions of XI are located at 1180 and 1020 cm^{-1}.

EXPERIMENTAL

IR spectra were obtained on a UR-20 instrument (as thin layers and KBr pellets). PMR spectra were recorded on a Tesla BS 487C (80 MHz) spectrometer in D_2O, CD_3OD, and $CDCl_3$ with HMDS internal standard.

2,3-Bis(2-phenethylaminoethylthio)propanol (I, $C_{23}H_{34}N_2OS_2$). A methanol solution (50 ml) of 1-phenethylaziridine (14.7 g, 0.1 mole) was added to a methanol solution (100 ml) of 2,3-dimercaptopropanol (6.2 g, 0.05 mole). The mixture was stirred at 55-60 °C for 6 h. Two thirds of the solvent was evaporated. An oil precipitated in the cold after adding ethyl ether. This was separated and dried under vacuum to give a viscous oil. PMR spectrum, ppm: 2.78 (m, SCH_2, NCH_2), 3.69 (q, $C_6H_5CH_2$), 7.19 (m, C_6H_5). Yield 16.7 g (80%).

2,3-Bis(2-methoxycarbonylethylaminoethylthio)propanol (II, $C_{15}H_{30}N_2O_5S_2$). This was prepared analogously from 2,3-dimercaptopropanol (6.2 g, 0.05 mole) and 1-methoxycarbonylethylaziridine (12.9 g, 0.1 mole) as a viscous oil. PMR spectrum, ppm: 2.48 (m, SCH_2), 2.80 (m, NCH_2), 3.65 (s, OCH_3). Yield 15.8 g (83%).

1,10-Diamino-3-oxa-4,8-dithia-6-(2-aminoethylthio)decane-4,4-dioxide (III, $C_9H_{23}N_3O_3S_3$). This was prepared analogously from 2,3-dimercaptopropanesulfonic acid (3.76 g, 0.02 mole) and aziridine (2.58 g, 0.06 mole) as a viscous oil. PMR spectrum, ppm: 3.30 (m, SCH_2, NCH_2), 3.80 (m, SO_3CH_2). Yield 4.5 g (71%).

1,10-Bis(2-phenethylamino)-3-oxa-4,8-dithia-6-[N-(phenethyl)-2-aminoethylthio]decane-4,4-dioxide (IV, $C_{33}H_{47}N_3O_3S_3$). This was prepared analogously from 2,3-dimercaptopropanesulfonic acid (3.76 g, 0.02 mole) and 1-phenethylaziridine (8.82 g, 0.06 mole) as a viscous oil. PMR spectrum, ppm: 2.77 (m, SCH_2), 2.92 (s, NCH_2), 3.60 (m, SO_3CH_2), 8.38-7.29 (m, C_6H_5). Yield 11.9 g (95%).

1,10-Bis(2-methoxycarbonylethylamino)-3-oxa-4,8-dithia-6-[N-(methoxycarbonylethyl)-2-aminoethylthio]decane-4,4-dioxide (V, $C_{21}H_{41}N_3O_9S_3$). This was prepared analogously from 2,3-dimercaptopropanesulfonic acid (3.76 g, 0.02 mole) and 1-methoxycarbonylethylaziridine (7.74 g, 0.06 mole) as a viscous oil. Yield 8.6 g (75%).

Sodium 2,3-Bis(2-aminoethylthio)propanesulfonate (VI, $C_7H_{17}NaN_2O_3S_3$). A mixture of III (3.17 g, 0.01 mole) and $NaHCO_3$ (0.84 g) in 1:4 aqueous methanol (50 ml) was heated at 60 °C for 6 h. The solvent was distilled off. The residue was recrystallized from hot ethanol with mp 188-190 °C and yield 1.6 g (54%).

Sodium 2,3-Bis(2-phenethylaminoethylthio)propanesulfonate (VII, $C_{23}H_{33}NaN_2O_3S_3$). This was prepared analogously from IV (6.29 g, 0.01 mole) and $NaHCO_3$ (0.84 g) with mp 210-212 °C and yield 3.6 g (80%).

Sodium 2,3-Bis(2-methoxycarbonylethylaminoethylthio)propanesulfonate (VIII, $C_{15}H_{29}NaN_2O_7S_3$). This was prepared analogously from V (5.75 g, 0.01 mole) and $NaHCO_3$ (0.84 g) with mp 260-262 °C and yield 2.1 g (45%).

2,3-Bis(2-carboxyethylaminoethylthio)propanesulfonic Acid Hydrochloride (IX, $C_{13}H_{26}N_2O_7S_3 \cdot HCl$). Concentrated HCl (10 ml) was added to an acetic acid solution (50 ml) of V (5.75 g, 0.01 mole). The mixture was heated for 2 h at 100 °C. The solvent was evaporated. The residue was recrystallized from methanol with mp 258-260 °C. PMR spectrum, ppm: 2.92-2.77 (m, SCH_2), 3.43 (m, NCH_2), 9.30 (s, $^+NH_2$), 11.30 (s, CO_2H), Yield 2.3 g (50%).

2-Hydroxymethyl-7,15-bis(2-methoxycarbonylethyl)-8,14-dioxo-1,4-dithia-7,15-diazacyclohexadecane (X, $C_{21}H_{36}N_2O_7S_2$). Dioxane solutions (250 ml each) of adipic diazide (1.96 g, 0.01 mole) and II (3.82 g, 0.01 mole) were added synchronously over 5 h at 20 °C with vigorous stirring to dioxane (500 ml). The solvent was distilled off. The residue was dissolved in methanol and precipitated by ether in the cold. The precipitated oil was separated and dried under vacuum to give a viscous oil. PMR spectrum, ppm: 1.56 (m, CH_2), 2.80 (m, SCH_2), 3.17 (m, NCH_2), 3.68 (s, OCH_3). Yield 3.5 g (70%).

Sodium 2-Sulfonatomethyl-7,15-bis(2-methoxycarbonylethyl)-8,14-dioxo-1,4-dithia-7,15-diazacyclohexadecane (XI, $C_{21}H_{35}NaN_2O_9S_3$). This was prepared analogously from adipic diazide (1.96 g, 0.01 mole) and VIII (4.68 g, 0.01 mole) with mp 220 °C. PMR spectrum, ppm: 2.77 (m, SCH_2), 3.30 (m, NCH_2), 3.67 (s, OCH_3). Yield 4.3 g (75%).

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SYNTHESIS OF 2-(2-SELENIENYL)PYRROLE FROM METHYL-2-SELENIENYLKETOXIME AND ACETYLENE

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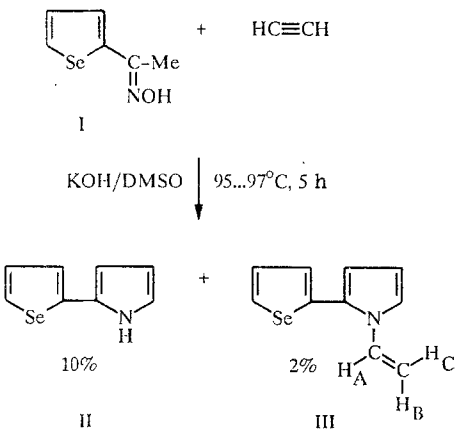
The reaction of methyl-2-selenienylketoxime with acetylene in KOH—DMSO gives 2-(2-selenienyl)pyrrole and its 1-vinyl derivative.

2-Hetarylpyrroles are important starting materials for synthesizing biologically active compounds in addition to interesting models for studying conjugation effects and internal rotation of two different interacting π-systems [1-3]. In 2-(2-furyl)- and 2-(2-thienyl)pyrroles, such conjugation changes the reactivity of the α-positions toward electrophiles by several orders of magnitude compared with that of the corresponding unsubstituted five-membered heterocycles [3]. The limited number of such compounds, in particular the difficultly accessible Se analogs, impedes extended studies in this area.

The goal of the present study was to investigate the possibility of forming pyrrole from methyl-2-selenienylketoxime (I) and acetylene under Trofimov reaction conditions [1] to give 2-(2-selenienyl)pyrrole (II) and 1-vinyl-2-(2-selenienyl)pyrrole (III) and to investigate the spectral properties of the resulting compounds.



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