

# MACROHETEROCYCLES.

## 5.\* SYNTHESIS OF MACROCYCLIC AMIDO ESTERS AND AMIDO THIOESTERS ON THE BASIS OF DERIVATIVES OF $\alpha$ -HYDROXY AND $\alpha$ -MERCAPTO ACIDS

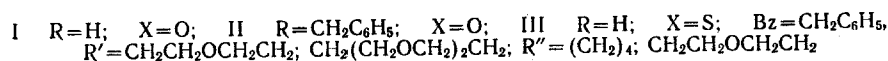
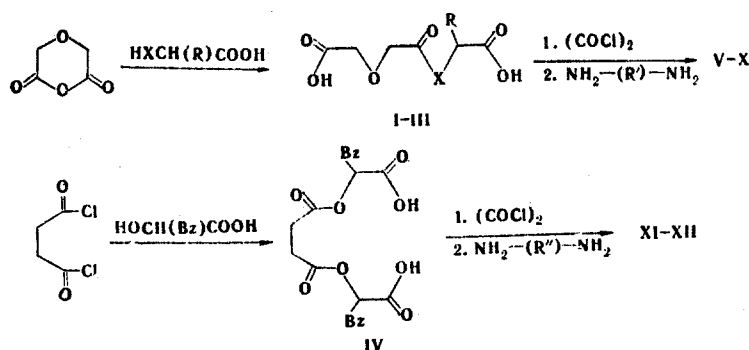
N. G. Luk'yanenko, A. V. Bogat'skii,  
and Yu. A. Popkov

UDC 547.898

3,6-Dioxa-4-keto-, 2-benzyl-3,6-dioxa-4-keto-, and 3-oxa-6-thio-5-ketooctanedioic acids were obtained by the reaction of diglycolic acid anhydride with glycolic,  $\beta$ -phenyllactic, and thioglycolic acids. 2,9-Dibenzyl-3,8-dioxa-4,7-diketodecanoic acid was obtained by the reaction of succinyl chloride with  $\beta$ -phenyllactic acid. Eight macrocyclic amido esters and amido thioesters that are new polydentate macrocyclic ligands were synthesized by the reaction of the chlorides of the acids obtained with 3-oxa-1,5-diaminopentane, 3,6-dioxa-1,8-diaminooctane, and 1,4-diaminobutane.

The ability of macrocyclic polyethers (crown ethers) to highly selectively form complexes with the ions of alkali and alkaline earth metals opens up wide prospects for their use in science and technology [2, 3]. Interest in crown compounds that contain other donor functional groups in addition to ether groups has increased in recent years. In order to study the factors that determine the complexing ability of such compounds, we synthesized a number of new macrocyclic amido esters and amido thioesters (V-XII).

The previously undescribed 3,6-dioxa-4-keto- (I), 2-benzyl-3,6-dioxa-4-keto- (II), and 3-oxa-6-thio-5-ketooctanedioic (III) acids were obtained by the reaction of diglycolic acid anhydride with glycolic,  $\beta$ -phenyllactic, and thioglycolic acids. 2,9-Dibenzyl-3,8-dioxa-4,7-diketodecanedioic acid (IV) was obtained by acylation of  $\beta$ -phenyllactic acid with succinyl chloride.



Intense bands of carboxy and ester carbonyl groups at 1725-1765 cm<sup>-1</sup> are present in the IR spectra of acids I-III. In the spectrum of acid IV the band of a thioester [sic] group appears at 1695 cm<sup>-1</sup>, while the band of a carboxy group appears at 1715 cm<sup>-1</sup>. Signals of all groups of protons with the corresponding intensities are observed in the PMR spectra of acids I-IV (see the experimental section).

Acids I-IV were converted to the corresponding chlorides by the action of oxalyl chloride, and the resulting chlorides were used in the subsequent transformations without additional purification. The reaction of the chlorides of acids I-IV with 3-oxa-1,5-diamino-

\*See [1] for communication 4.

Physicochemical Institute, Academy of Sciences of the Ukrainian SSR, Odessa 270080.  
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 306-309, March, 1980.  
Original article submitted September 25, 1979.

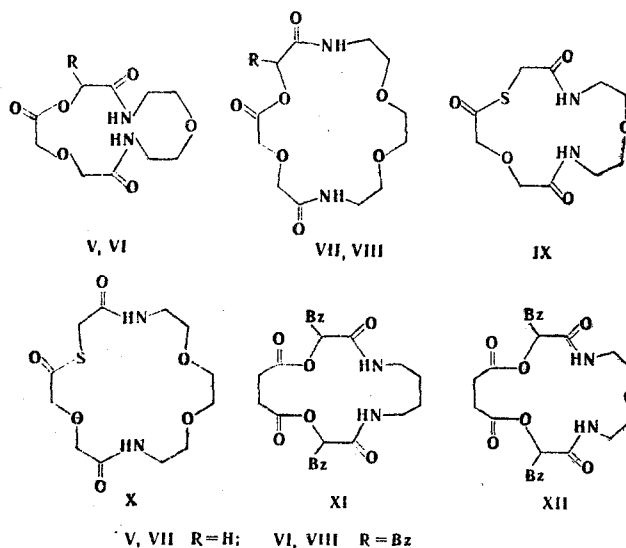
TABLE 1. Characteristics of Crown Compounds V-XII

Com- pound	mp, °C	IR spectrum, cm <sup>-1</sup>		Found, %			Empirical formula	Calc., %			M+	Yield, %
		$\nu_{C=O}$ ester	$\nu_{C=O}$ amide	C	H	N		C	H	N		
V	161—162	1750	1670	45.8	6.4	10.2	C <sub>10</sub> H <sub>16</sub> N <sub>2</sub> O <sub>6</sub>	46.0	6.0	10.4	260	40
VI	148—149	1769	1655	58.0	6.6	7.8	C <sub>17</sub> H <sub>22</sub> N <sub>2</sub> O <sub>6</sub>	58.3	6.3	8.0	350	55
VII	142—143	1745	1670	47.3	6.8	9.1	C <sub>12</sub> H <sub>20</sub> N <sub>2</sub> O <sub>7</sub>	47.4	6.6	9.2	304	40
VIII	132—133	1740	1678	57.7	7.0	7.4	C <sub>19</sub> H <sub>26</sub> N <sub>2</sub> O <sub>7</sub>	57.9	6.6	7.1	394	45
IX	140—141	1690	1645	43.2	6.1	9.8	C <sub>10</sub> H <sub>16</sub> N <sub>2</sub> O <sub>5</sub> S	43.5	5.8	10.1	276	35
X	132—133	1695	1670	44.8	6.5	8.7	C <sub>12</sub> H <sub>20</sub> N <sub>2</sub> O <sub>6</sub> S	45.0	6.3	8.8	320	30
XI	142—143	1715	1670	67.1	6.3	6.1	C <sub>26</sub> H <sub>28</sub> N <sub>2</sub> O <sub>6</sub>	67.2	6.0	6.0	464	40
XII	68—69	1745	1675	64.8	6.0	5.9	C <sub>26</sub> H <sub>28</sub> N <sub>2</sub> O <sub>7</sub>	65.0	5.8	5.8	480	35

TABLE 2. PMR Spectra of Crown Compounds V-XII

Com- pound	Chemical shifts, $\delta$ , ppm
V	7.10 (2H, s, NH); 4.45 (2H, s, COCH <sub>2</sub> OCO); 4.22 (2H, s, COCH <sub>2</sub> O); 3.93 (2H, s, OCH <sub>2</sub> CON); 3.37 (8H, m, CH <sub>2</sub> N, CH <sub>2</sub> OCH <sub>2</sub> )
VI	7.12 (7H, s, NH, C <sub>6</sub> H <sub>5</sub> ); 5.30 (1H, t, CHBz); 4.17 (2H, s, COCH <sub>2</sub> O); 3.88 (2H, s, OCH <sub>2</sub> CON); 3.25 (10H, m, CH <sub>2</sub> N, CH <sub>2</sub> OCH <sub>2</sub> , CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )
VII	7.11 (2H, s, NH); 4.52 (2H, s, COCH <sub>2</sub> OCO); 4.23 (2H, s, COCH <sub>2</sub> O); 3.93 (2H, s, OCH <sub>2</sub> CON); 3.41 (2H, m, CH <sub>2</sub> N, CH <sub>2</sub> OCH <sub>2</sub> )
VIII	7.13 (7H, s, NH, C <sub>6</sub> H <sub>5</sub> ); 5.35 (1H, q, CHBz); 4.13 (2H, s, COCH <sub>2</sub> O); 3.85 (2H, s, OCH <sub>2</sub> CON); 3.41 (12H, m, CH <sub>2</sub> N, CH <sub>2</sub> OCH <sub>2</sub> ); 3.05 (2H, t, CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )
IX	7.01 (2H, s, NH); 4.36 (2H, s, COCH <sub>2</sub> O); 4.00 (2H, s, OCH <sub>2</sub> CON); 3.48 (2H, s, CH <sub>2</sub> SCO); 3.37 (8H, m, CH <sub>2</sub> N, CH <sub>2</sub> OCH <sub>2</sub> )
X	7.03 (2H, s, NH); 4.28 (2H, s, COCH <sub>2</sub> O); 3.98 (2H, s, OCH <sub>2</sub> CON); 3.48 (2H, s, CH <sub>2</sub> SCO); 3.40 (12H, m, CH <sub>2</sub> N, CH <sub>2</sub> OCH <sub>2</sub> )
XI	7.18 (10H, s, C <sub>6</sub> H <sub>5</sub> ); 6.75 (2H, s, NH); 5.05 (2H, q, CHBz); 3.05 (8H, m, CH <sub>2</sub> N, CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> ); 2.51 (4H, s, CH <sub>2</sub> CO); 1.41 (4H, m, CH <sub>2</sub> CH <sub>2</sub> N)
XII	7.15 (12H, t, C <sub>6</sub> H <sub>5</sub> , NH); 5.08 (2H, m, CHBz); 3.10 (12H, m, CH <sub>2</sub> N, CH <sub>2</sub> OCH <sub>2</sub> , CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> ); 2.58 (4H, s, CH <sub>2</sub> CO)

pentane, 3,6-dioxa-1,8-diaminooctane, and 1,4-diaminobutane in benzene under high-dilution conditions leads to crown compounds V-XII:



The compounds obtained are colorless crystalline substances, the properties of which are described in Table 1. The structures of V-XII were confirmed by the results of elementary analysis and data from IR, PMR, and mass spectroscopy. The IR spectra of solid

samples of V-XII contain intense bands of ester and amide carbonyl groups at 1645-1765  $\text{cm}^{-1}$ , as well as bands of an associated NH group at 3330-3490  $\text{cm}^{-1}$ . In addition to the indicated bands, the spectra of V-X and XII contain the band of an ether bond at 1090-1150  $\text{cm}^{-1}$ . Signals of both acid and amine fragments of the molecule are noted in the PMR spectra of V-XII, and this confirms the structure assigned to them (Table 2).

An analysis of Corey-Pauling-Koltun (CPK) models shows that, like crown ethers, V-XII may take on a conformation in which the unshared pairs of electrons of the ester oxygen and nitrogen atoms are directed into the ring, in which case the size of the inner plane of the molecules ranges from 1.7 to 3.5 Å, which makes it possible to assume the possibility of effective interaction of these substances with the ions of alkali and alkaline earth metals.

#### EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Perkin-Elmer 580B spectrometer. The PMR spectra were recorded with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard. The mass spectra were obtained with a Varian MAT CH-5 spectrometer. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates in an acetone-hexane system (1:2).

3,6-Dioxa-4-ketooctanedioic Acid (I). A 3.8 g (0.05 mole) sample of glycolic acid was added to a suspension of 5.8 g (0.05 mole) of diglycolic acid anhydride in 100 ml of dry benzene, and the mixture was refluxed with stirring for 3 days. It was then cooled, and the precipitated acid was removed by filtration and dried in vacuo to give 6.2 g (65%) of a product with mp 120-122°C. IR spectrum: 1765 (COOR) and 1725  $\text{cm}^{-1}$  (COOH). PMR spectrum: 4.16 (4H, s,  $\text{COCH}_2\text{O}$ ), 4.00 ppm (2H, s,  $\text{OCH}_2\text{CO}$ ). Found: C 37.3; H 4.4%.  $\text{C}_6\text{H}_8\text{O}_7$ . Calculated: C 37.5; H 4.2%.

2-Benzyl-3,6-dioxa-4-ketooctanedioic Acid (II). This compound, with mp 111-112°C, was similarly obtained in 80% yield. IR spectrum: 1765 (COOR) and 1725  $\text{cm}^{-1}$  (COOH). PMR spectrum: 5.26 (1H, q, CHBz), 4.17 (2H, s,  $\text{COCH}_2\text{O}$ ), 4.05 (2H, s,  $\text{OCH}_2\text{CO}$ ), 3.11 (2H, t,  $\text{CH}_2\text{C}_6\text{H}_5$ ), and 7.21 ppm (5H, s,  $\text{C}_6\text{H}_5$ ). Found: C 58.7; H 5.3%.  $\text{C}_{13}\text{H}_{14}\text{O}_7$ . Calculated: C 58.9; H 5.0%.

3-Oxa-6-thia-5-ketooctanedioic Acid (III). This compound, with mp 116-117°C, was similarly obtained in 60% yield by reaction of diglycolic acid anhydride with thioglycolic acid. IR spectrum: 1725 (COOH) and 1695  $\text{cm}^{-1}$  (COSR). PMR spectrum: 4.27 (2H, s,  $\text{COCH}_2\text{O}$ ), 4.23 (2H, s,  $\text{OCH}_2\text{CO}$ ), and 3.51 ppm (2H, s,  $\text{COCH}_2\text{S}$ ). Found: C 34.4; H 4.2; S 15.2%.  $\text{C}_6\text{H}_8\text{O}_6\text{S}$ . Calculated: C 34.6; H 3.9; S 15.4%.

2,9-Dibenzyl-3,8-dioxa-4,7-diketodecanedioic Acid (IV). A 15.5-g (0.01 mole) sample of succinyl chloride was added at -5 to 0°C to a solution of 3.32 g (0.02 mole) of  $\beta$ -phenyllactic acid and 2.02 g (0.02 mole) of triethylamine in 50 ml of dry chloroform, and the mixture was stirred at room temperature for 20 h. The solvent was then removed by vacuum distillation, and the oily residue was dissolved in ether. The ether solution was filtered, the ether was removed from the filtrate by distillation, and the residue was recrystallized from benzene to give 2.5 g (60%) of a product with mp 87-88°C. IR spectrum: 1740 (COOR) and 1730  $\text{cm}^{-1}$  (COOH). PMR spectrum: 5.08 (2H, q, CHBz), 3.09 (4H, s,  $\text{CH}_2\text{C}_6\text{H}_5$ ), 2.51 (4H, s,  $\text{CH}_2\text{CO}$ ), and 7.2 ppm (10H, s,  $\text{C}_6\text{H}_5$ ). Found: C 63.5; H 5.5%.  $\text{C}_{22}\text{H}_{24}\text{O}_8$ . Calculated: C 63.8; H 5.3%.

Dichlorides of Acids I-IV. Two drops of pyridine and 0.04 mole of oxalyl chloride were added to a solution of 0.01 mole of the corresponding acid in 50 ml of dry benzene, and the mixture was stirred at room temperature until it became completely homogeneous. The solvent was then removed by distillation with a rotary evaporator at 40°C. The resulting acid chlorides were used for the synthesis of V-XII without additional purification.

1,7-Diaza-4,10,13-trioxacyclopentadecane-8,12,15-trione (V). Solutions of 4.58 g (0.02 mole) of the chloride of acid I and 4.16 g (0.04 mole) of 3-oxa-1,5-diaminopentane in 200 ml of dry benzene each were added simultaneously from separate dropping funnels, with stirring at room temperature, in the course of 3 h to 500 ml of dry benzene, after which the mixture was stirred for 24 h. It was then filtered, and the filtrate was subjected to vacuum distillation to remove the solvent. The residue was recrystallized from acetone.

Compounds VI-X were similarly obtained.

8,15-Dibenzyl-1,6-diaza-9,14-dioxacyclohexadecane-7,9,13,16-tetraone (XI). This compound was similarly obtained and was recrystallized from carbon tetrachloride.

9,16-Dibenzyl-1,7-diaza-4,10,15-trioxaheptadecane-8,10,14,17-tetraone (XII). This compound was similarly obtained from the chloride of acid IV and 3-hydroxy-1,5-diaminopentane. After removal of the solvent by distillation, the reaction product was isolated by column chromatography on silica gel [acetone-hexane (1:2)].

#### LITERATURE CITED

1. A. V. Bogat'skii, N. G. Luk'yanenko, V. A. Shapkin, M. S. Salakhov, M. U. Mamina, and D. Taubert, Zh. Org. Khim., 16 (1980, in press).
2. J. J. Christensen, D. J. Eataugh, and R. M. Izatt, Chem. Rev., 74, 351 (1974).
3. R. E. Asay, J. S. Bradshaw, S. F. Nielsen, M. D. Thompson, J. W. Snow, D. R. K. Masihdas, R. M. Izatt, and J. J. Christensen, J. Heterocycl. Chem., 14, 85 (1977).

#### NEW METHOD FOR THE SYNTHESIS OF TETRACHLOROTHIOPHENE\*

M. G. Voronkov, É. N. Deryagina,  
and V. I. Perevalova

UDC 547.732.07:542.915

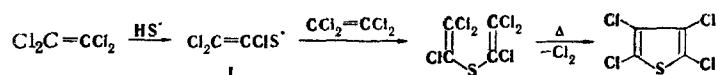
The reaction of tetrachloroethylene with hydrogen sulfide at 450–500°C leads to the formation of tetrachlorothiophene as the principal product, along with hexachlorobutadiene, the yield of which increases as the reaction temperature is raised.

The previously investigated [2] reaction of vinyl chloride with hydrogen sulfide takes place at 530–550°C and leads to the formation of thiophene. It seemed of interest to use a similar scheme involving tetrachloroethylene to obtain tetrachlorothiophene, which is usually obtained by the reaction of sulfur with hexachlorobutadiene at 160–300°C [3] or with tetrachloroethylene at 150–600°C at high pressure [4].

Tetrachloroethylene reacts with hydrogen sulfide in a flow system at a lower temperature (450–500°C) than vinyl chloride and at a slower rate; its conversion per pass is 10–15%, and the reaction was therefore investigated in a flow-recirculation system by the method in [5]. The principal reaction product is tetrachlorothiophene, which is obtained in 75% yield [6]. The possible intermediates, viz., tetrachlorovinylthiol and tetrachlorovinyl sulfide, were not detected in the products of the reaction of hydrogen sulfide with tetrachloroethylene, since, if they were formed, they would be continuously recirculated in the reaction zone, thereby undergoing conversion to the final product.

The temperatures of the formation of the thiylation products from vinyl chloride and tetrachloroethylene are inversely related to their nuclear quadrupole resonance (NQR) frequencies (33.411 and 38.684, respectively); as in the case of aromatic derivatives, this is associated with the strengths of the C–Cl bonds.

The lower reactivity of tetrachloroethylene as compared with vinyl chloride is evidently explained by the greater possibility of stabilization of the intermediate thiyl radical (I) responsible for the chain process [7] due to additional p–π conjugation of the chlorine atoms with the double bond:



\*Communication 15 from the series "High-Temperature Organic Synthesis." See [1] for communication 14.

Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Irkutsk 664033. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 310–311, March, 1980. Original article submitted January 31, 1979.