# POLYFUNCTIONAL MACROHETEROCYCLES.
# 4.* SYNTHESIS AND SOME CHEMICAL TRANSFORMATIONS OF NITROGEN- AND SULFUR-CONTAINING CROWN COMPOUNDS WITH EXOCYCLIC METHOXYCARBONYL, CYANO, AND PHENYLETHYL GROUPS

**M. G. Voronkov, V. I. Knutov, and M. K. Butin**

*The acylation of 1,5-diamino-, 1,5-bis(2-phenylethylamino)-, and 1,5-bis(2-methoxycarbonylethylamino)-3-thiapentanes with adipic and phthalic acid dichlorides, as well as oxalyl chloride, leads to, respectively, 13-, 22-, and 18-membered macroheterocycles containing exocyclic methoxycarbonyl and phenylethyl groups. The reduction by* $LiAlH_4$ *of the endocyclic amido groups and exocyclic ester or cyano groups of some nitrogen- and sulfur-containing crown compounds, which are converted to* $CH_2NR_2$, $CH_2OH$, *and* $CH_2NH_2$ *groups, respectively, was studied. A macrobicyclic system containing endocyclic amido groups was synthesized, and its reduction, which leads to the corresponding* $CH_2NR_2$ *derivative, was investigated.*

The synthesis of new polyfunctional macroheterocycles is of interest, since it makes it possible to use them in supramolecular chemistry as endo and exo receptors that selectively tie up cations, anions, and neutral molecules [2, 3].

We have previously obtained crown compounds containing donor nitrogen and sulfur atoms and exocyclic phenylethyl, methoxycarbonylethyl, 1,2-bis(methoxycarbonyl)ethyl, and cyanoethyl groups [4-9]. They were found to be complexones and selective extractants of transition metal ions [10, 11]. Complexes of nitrogen- and sulfur-containing macrocycles with the copper(II) ion have spectral characteristics and redox potentials corresponding to the active centers of "blue" proteins and may be models for the study of metal enzymes [12].


$RNHCH_2CH_2SCH_2CH_2NHR + ClCO(CH_2)_4COCl \xrightarrow[Et_3N]{}$

I-III

IV-VI

I, IV R=H; II, V $R=CH_2CH_2Ph$; III, VI $R=CH_2CH_2COOMe$

For the further investigation of the properties of models of copper proteins we developed a method for the synthesis of 13-, 18-, and 22-membered nitrogen- and sulfur-containing crown compounds with phenylethyl and methoxycarbonylethyl groups near the endocyclic nitrogen atoms of the macroring. The corresponding nitrogen- and sulfur-containing macroheterocycles are formed in high yields in the acylation of $\alpha,\omega$-diamines with dicarboxylic acid dichlorides [4-6, 8, 9]. We previously obtained diamines I-III by the reaction of aziridine and 1-(2-phenylethyl)- and 1-(2-methoxycarbonylethyl)aziridine with hydrogen sulfide [1]. Their cyclization with adipic acid dichloride in benzene under high-dilution conditions is realized via a mechanism of the [1 + 1] type and leads to macroheterocycles IV-VI in 67-70% yields.

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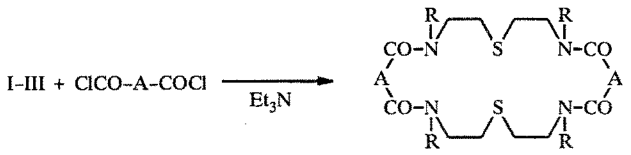
*For Communication 3 see [1].

Irkutsk Institute of Organic Chemistry, Siberian Branch, Russian Academy of Sciences, Irkutsk 664033. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 273-276, February, 1992. Original article submitted February 4, 1991.

TABLE 1. Parameters of the PMR Spectra of Nitrogen- and Sulfur-Containing Macroheterocycles (δ, ppm)

| Compound | $CH_2$ | $CH_2S$ | $CH_2N$ | $COOCH_3$, $COCH_2$ | $CH_2C_6H_5$ | $C_6H_5$, $C_6H_4$ |
|---|---|---|---|---|---|---|
| IV | 1,62 (m) | 2,75 (m) | 2,87 (m) | 3,72 (s) | — | — |
| V | 1,58 (m) | 2,65 (m) | 2,82 (m) | 3,60 (s) | 3,51 (q) | — |
| VI | 1,65 (m) | 2,60 (m) | 2,87 (m) | 3,66 (s); 3,70 (s) | — | — |
| VII | — | 2,89 (m) | 3,32 (m) | — | 3,60 (q) | 7,20 (m) |
| VIII | 2,16 (m) NH | 2,88 (m) | 3,09 (m) | — | — | 7,46—7,74 (m) |
| IX | — | 2,88 (m) | 3,35 (m) | — | 3,63 (q) | 7,22 (m) |
| X | — | 2,67 (m) | 3,10 (m) | 3,60 (s); 3,71 (s) | — | 7,20 (m) |
| XI | 1,38 (m) | 2,70 (m) | 3,20 (m) | 3,60 (m) $OCH_2$ | 4,60 (s) OH | 7,30 (m) |
| XIV | 1,38 (m) | 2,71 (m) | 3,59 (m) | — | — | 7,30 (m) |

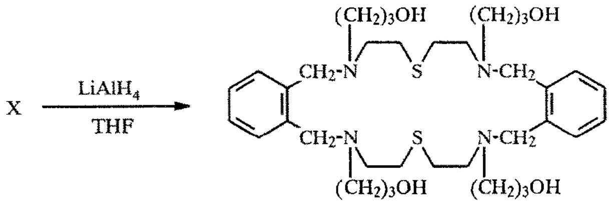
Diamines I-III react with oxalyl chloride and phthalic acid dichloride under similar conditions to give, respectively, dimeric 18- and 22-membered macroheterocycles VII-X. The cyclocondensation in this case proceeds via a mechanism of the [2 + 2] type.



VII-X

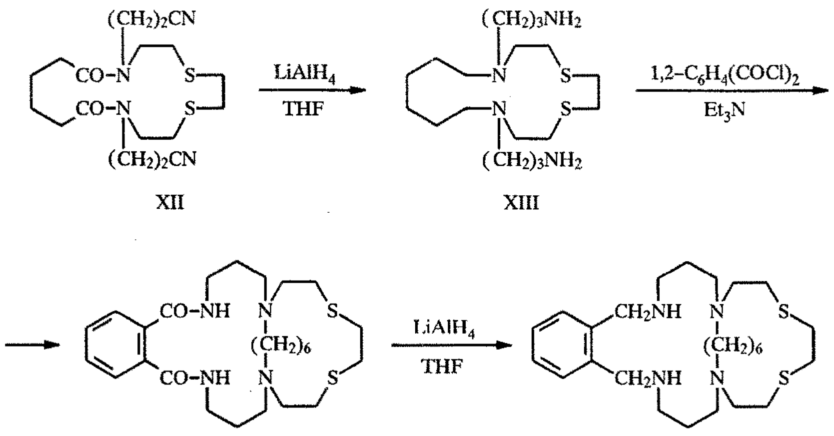
VII $R=CH_2CH_2C_6H_5$, A= VIII R=H, $A=1,2\text{-}C_6H_4$; IX $R=CH_2CH_2C_6H_5$, $A=1,2\text{-}C_6H_4$; X $R=CH_2CH_2COOCH_3$, $A=1,2\text{-}C_6H_4$

The reduction by $LiAlH_4$ of macroheterocycle X, which contains endocyclic amido groups and exocyclic ester groups, was studied. The reaction proceeds at the boiling point of THF in 3 h. The yield of macroheterocycle XI is 80%.



XI

The reduction of the previously obtained [6] macroheterocycle XIII, which contains amido and cyano groups, was carried out similarly. The yield of crown compound XIII is 82%. The cyclocondensation of this macroheterocycle with phthalic dichloride in benzene under high-dilution conditions was studied to obtain macrobicyclic system XIV. The yield of macrobicyclic system XIV is 72%. The reduction of the amido groups with $LiAlH_4$ leads to cryptand XV (in 80% yield).



XII XIII

XIV XV

Frequencies of vibrations of a carbonyl group at 1620-1640 cm$^{-1}$ (amide band I) are observed in the IR spectra of crown compounds IV-X, which contain amido groups. The absorption bands at 3300 and 3050 cm$^{-1}$ are related to stretching vibrations of the NH group of the monosubstituted amide of macroheterocycles IV and VIII. The frequency of a vibration at 1550 and 1540 cm$^{-1}$, respectively, which is characteristic for a carbonyl absorption band (amide II), also shows up in the spectra of IV and VIII. Intense absorption bands of an ester group are observed in the spectra of crown compounds VI and X at 1730 and 1720 cm$^{-1}$, respectively. Frequencies of vibrations of amido, ester, and cyano groups at 1640, 1720, and 2260 cm$^{-1}$, respectively, are absent in the IR spectra of macroheterocycles XI and XIII. There are absorption bands at 3400 and 3340 cm$^{-1}$ and at 3280 cm$^{-1}$, which are characteristic for stretching vibrations of hydroxy and primary amino groups, respectively. Only one absorption band at 3300 cm$^{-1}$, which belongs to a secondary amino group, is present in the IR spectra of macrobicyclic systems XIV and XV. The frequency of the vibration at 1640 cm$^{-1}$ is related to the amido group (amide band I) of macrobicyclic system XIV.

The PMR spectra of IV-XI, XIV, and XV are presented in Table 1.

## EXPERIMENTAL

The IR spectra of KBr pellets and suspensions of the compounds in mineral oil were obtained with a UR-20 spectrometer. The PMR spectra of solutions in $CDCl_3$ were recorded with a Tesla BS 487C spectrometer (80 MHz) with hexamethyldisiloxane (HMDS) as the internal standard.

The results of elementary analysis of IV-XV and their isopiestically determined molecular masses were in agreement with the calculated values.

**5,10-Dioxo-1-thia-4,11-diazacyclotridecane (IV).** A solution of 6.0 g (0.05 mole) of bis(2-aminoethyl) sulfide (I) in 500 ml of dry benzene and a solution of 9.15 g (0.05 mole) of adipic acid dichloride in 500 ml of dry benzene were added synchronously in the course of 6 h at 20°C with vigorous stirring to 1.0 liter of dry benzene containing 10.1 g (0.1 mole) of triethylamine. The resulting precipitate was removed by filtration, and the solvent was removed by distillation at reduced pressure. The residue was purified chromatographically on aluminum oxide by elution with benzene—methanol (5:1). The solvent was removed by distillation, and the residue was dissolved in chloroform and precipitated in the cold by the addition of petroleum ether. The yield of the product, which was an oil, was 8.05 g (70%).

**4,11-Bis(2-phenylethyl)-5,10-dioxo-1-thia-4,11-diazacyclotridecane (V).** This compound was similarly obtained from 3.28 g (0.01 mole) of bis(2-phenylethylaminoethyl) sulfide (II) and 1.83 g (0.01 mole) of adipic acid dichloride. The yield of the product, which was an oil, was 2.93 g (67%).

**4,11-Bis(2-methoxycarbonylethyl)-5,10-dioxo-1-thia-4,11-diazacyclotridecane (VI).** This compound was similarly obtained from 2.92 g (0.01 mole) of bis(2-methoxycarbonylethylaminoethyl) sulfide (III) and 1.83 g (0.01 mole) of adipic acid dichloride. The yield of the product, which was an oil, was 2.82 g (72%).

**4,7,13,16-Tetrakis(2-phenylethyl)-5,6,14,15-tetraoxo-1,10-dithia-4,7,13,16-tetraazacyclooctadecane (VII).** This compound was similarly obtained from 3.28 g (0.01 mole) of bis(2-phenylethylaminoethyl) sulfide and 1.27 g (0.01 mole) of oxalyl chloride. The yield of the product, which was an oil, was 2.6 g (68%).

**6,7,17,18-Dibenzo-5,8,16,19-tetraoxo-1,12-dithia-4,9,15,20-tetraazacyclodocosa-6,17-diene (VIII).** This compound was similarly obtained from 6.0 g (0.05 mole) of bis(2-aminoethyl) sulfide and 10.15 g (0.05 mole) of phthalic acid dichloride. The product had mp 54-56°C, and the yield was 8.75 g (70%).

**4,9,15,20-Tetrakis(2-phenylethyl)-6,7,17,18-dibenzo-5,8,16,19-tetraoxo-1,12-dithia-4,9,15,20-tetraazacyclodocosa-6,17-diene (IX).** This compound was similarly obtained from 3.28 g of bis (2-phenylethylaminoethyl) sulfide and 2.03 g (0.01 mole) of phthalic acid dichloride. The yield of the product, which was an oil, was 6.3 g (69%).

**4,9,15,20-Tetrakis(2-methoxycarbonylethyl)-6,7,17,18-dibenzo-5,8,16,19-tetraoxo-1,12-dithia-4,9,15,20-tetraazacyclodocosa-6,17-diene (X).** This compound was similarly obtained from 2.92 g (0.01 mole) of bis(2-methoxycarbonylethylaminoethyl) sulfide and 2.03 g (0.01 mole) of phthalic acid dichloride. The yield of the product, which was an oil, was 3.04 g (72%).

**4,9,15,20-Tetrakis(3-hydroxypropyl)-6,7,17,18-dibenzo-1,2-dithia-4,9,15,20-tetraazacyclodocosa-6,17-diene (XI).** An 8.44-g (0.01 mole) sample of macroheterocycle X in 30 ml of dry THF was added slowly to a suspension of 3.8 g (0.1 mole) of $LiAlH_4$ in 60 ml of dry THF, and the mixture was stirred at 55°C for 3 h. It was then cooled, and the excess $LiAlH_4$ was decomposed with water and 15% HCl solution. The resulting mixture was extracted with chloroform, the extract was dried over $MgSO_4$ and filtered, and the product was precipitated by the addition of petroleum ether. The yield of the product, which was an oil, was 5.41 g (80%).

**7,14-Bis(3-aminopropyl)-1,4-dithia-7,14-diazacyclohexadecane (XIII).** This compound was similarly obtained from 3.96 g (0.01 mole) of macroheterocycle XII and 3.8 g (0.1 mole) of $LiAlH_4$. The yield of the product, which was an oil, was 3.08 g (82%).

**13,14-Benzo-12,15-dioxo-1,4-dithia-7,11,16,20-tetraazabicyclo[8.12.6]octacos-13-ene (XIV).** This compound was obtained in the same way as IV from 3.76 g of macrocycle IV and 2.03 g (0.01 mole) of phthalic acid dichloride. The product had mp 193-195°C, and the yield was 3.64 g (72%).

**13,14-Benzo-1,4-dithia-7,11,16,20-tetraazabicyclo[8.12.6]octacos-13-ene (XV).** This compound was obtained in the same way XI from 5.06 g (0.01 mole) of macrobicyclic system XIV and 1.9 g (0.05 mole) of $LiAlH_4$. The yield of the product, which was an oil, was 3.82 g (80%).

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