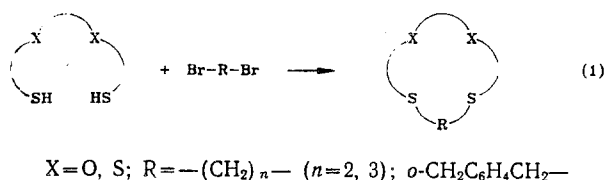


Reaction of 1,8-dimercapto-3,6-dithiooctane with oxa-, aza-, and thiadihaloderivatives under high dilution conditions in the presence of cesium carbonate, which acts as a template for the condensation reaction, produces 15- and 18-membered polythiamacrocylic ligands in yields greater than 50%.

Polythia-, thiaoxa-, and thiaazamacrocyclic ligands are promising complexing agents, extractants, and detoxicants for a number of transition metals [1-3]. Metal complexes of them model the active centers of some enzymes, in particular, the so-called copper-containing blue proteins.

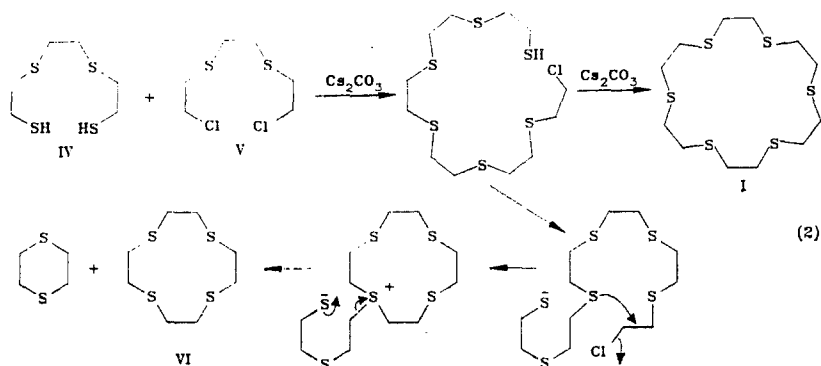
However, synthetic routes to preparation of these compounds has not been as extensively developed as in the case of the polyoxa- and polyazamacrocyclic ligands. The majority of synthetic methods for sulfur-containing macrocycles allows the target product to be obtained only with small yields, except for the Kellog method [4]. Use of this method increases the yields of tetrathia- and oxathiamacrocylic ligands to 60-80%. The cyclization method proposed in [4] consists of the reaction of dithiols containing esters or thioesters with dibromoderivatives in the presence of cesium carbonate, which acts as a template:



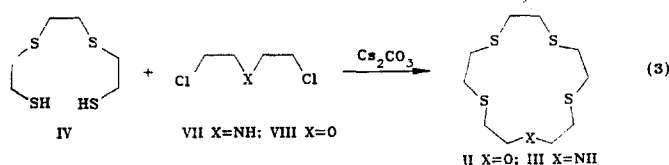
However, macrocyclic compounds containing only four or less sulfur atoms were prepared by this method.

Use in (1) of substituted dihaloderivatives significantly widens the possibilities of the method for synthesis of various sulfur-containing macroheterocycles. This possibility is illustrated by the example of the synthesis of 1,4,7,10,13,16-hexathiacyclooctadecane (hexathia-18-crown-6(I)), 1-oxo-4,7,10,13-tetrathiacyclopentadecane (monooxatetrathia-15-crown (II)), and 1,4,7,10-tetrathia-13-azacyclopentadecane (tetrathiamonoaza-15-crown-5 (III)).

Macrocycle I was synthesized by the method proposed by us through reaction of dithiadithiol IV and dithiadichloro V with 70% yield. Earlier [5], this ligand was prepared with 30% yield. Use of cesium carbonate as a template allows the yield of the target product to be increased more than twice, as in equation (2). A side product isolated was the 12-membered tetrathiamacrocycle VI (1,4,7,10-tetrathiadodecane) with 5% yield. The unexpected formation of macrocycle VI is explained by intramolecular rearrangement with involvement of the sulfonium ion [6].



Use of dihaloderivatives 1,5-dichloro-3-azapentane (VII) and 1,5-dichloro-3-oxapentane (VIII) in the cyclization reaction allows preparation of macrocyclic compounds II and III with yields greater than 50%:



Thus, on the example of the synthesis of macrocycles I-III, the possibility of principle of using the Kellogg method for preparation of polythia-, oxathia-, and thiaazamacrocyclic compounds with more than four donor atoms has been demonstrated.

EXPERIMENTAL

Mass spectra were obtained on a MX-1310 instrument with 5000 resolving power with fast atom bombardment by argon ions with an energy of 3.5 keV [9]. The sample was dissolved or dispersed in a glycerine matrix and placed in an aluminum target supported in the ion source. Dithiadithiol IV was synthesized according to [7], dithiadichloride V was prepared according to [8].

Elemental analyses of macrocycles II-IV for C and H corresponded to those calculated.

Synthesis of Macrocycles I-III. Cesium carbonate (1.43 g, 4.4 mmole) was suspended in 500 ml dry DMF in a two-liter three-necked flask fitted with a stirrer, two synchronous dropping funnels, a system for inert gas entry, and a reflux condenser. The mixture was heated to 50°C and a solution of 0.84 g (4 mmole) dithiadithiol IV in 100 ml DMF and a solution of 4 mmole of the corresponding dihaloderivative V, VII, or VIII in 100 ml DMF were added slowly (~12 h) with vigorous mixing from the dropping funnels. The solution was evaporated to dryness under vacuum, the residue was extracted repeatedly with methylene chloride, and the extract was evaporated to dryness.

For the synthesis of macrocycle I, the residue was a mixture of macrocycles I and VI which was separated on a chromatographic column (2 × 20 cm) filled with silica gel using ethylacetate eluent. In this case, only macrocycle I was eluted. From the upper part of the column, VI was extracted and recrystallized from ethanol (mp 214-215°C, m/z 240). Yield of VI (C₁₂H₂₄S₆) 0.05 g. The eluate (~300 ml) was evaporated to dryness and the residue was recrystallized from 250 ml ethanol. Yield 0.7 g, mp 89-91°C, m/z 359.

For the synthesis of macrocycles II and III, a thick oil was obtained after removal of methylene chloride. This solidified upon trituration with hexane. The solid was recrystallized from ethanol. Yield of II (C₁₀H₂₀OS₄) 0.7 g, mp 94-95°C, m/z 284. Yield of III (C₁₀H₂₁NS₄) 0.6 g, mp 82°C, m/z 285.

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POLYFLUORINATED NITRILE OXIDES

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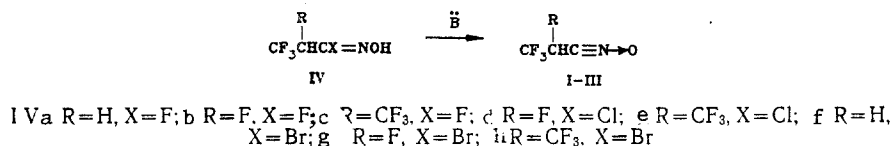
UDC 547.412'239.07

(2+3)-Cycloaddition of polyfluorinated aliphatic nitrile oxides, generated in situ, to donor dipolarophiles takes place regioselectively to give the 5-substituted isoxazolines, and is limited by the donor and steric properties of the dipolarophiles.

The polyfluorinated nitrile oxides which have so far been obtained in situ and characterized by (2+3)-cycloaddition are trifluoroacetonitrile [1-3], 2-hydrotetrafluoropropionitrile [4], and perfluorobenzonitrile oxides [5]. The properties of these compounds differ in many respects from their nonfluorinated analogs, benzonitrile and acetonitrile oxides [6].

We have now examined (2+3)-cycloadditions of 2,2-dihydrotrifluoropropionitrile oxide (I), 2-hydrotetrafluoropropionitrile oxide (II) (for preliminary communication, see [4]), and 2-hydrohexafluoroisobutyronitrile oxide (III).

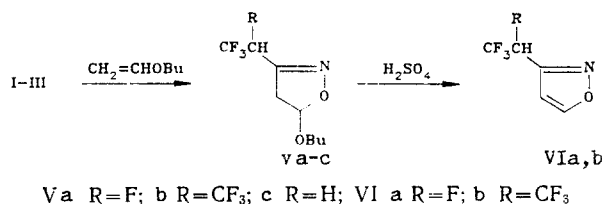
Oxides (I-III) are usually generated by dehydrohalogenation of the appropriate hydroxyamoyl fluorides (IVa-c), chlorides (IVd, e), or bromides (IVf-h).



In this case, the hydroxamoyl fluorides (IVa-c) could not be converted into the oxides (I-III) or their concerted cycloaddition products [7].

However, dehydrochlorination of the hydroamoyl chlorides (IVd, e) takes place even under mild conditions (at -40 to -55°C with triethylamine in ether or other inert solvents). In the presence of vinyl butyl ether at -20°C, 5-butoxy-3-polyfluoroalkyl-1,2-oxazolines (Va) (40%) and (Vb) (23%) were obtained, showing that the oxides (II) and (III) were generated in situ. The spectral data and chromatography showed that the 5-butoxy derivatives (Va) and (Vb) were formed exclusively.

The structures of the oxazolines (Va) and (Vb) were also confirmed by their conversion into the isoxazoles (VIa) and (VIb) by heating in sulfuric acid, as in the case of other 5-alkoxy-1,2-oxazolines [1, 6].



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