Novel Macrocyclic Carriers
For Proton-Coupled Liquid Membrane Transport

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J.D. Lamb, J.S. Bradshaw, and R.M. Izatt

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Department of Chemistry
Brigham Young University
Provo, Utah 84602

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NOVEL MACROCYCLE CARRIERS
FOR PROTON-COUPLED LIQUID MEMBRANE TRANSPORT

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I. Ligand Synthesis

We have prepared a number of new macrocyclic ligands for transport studies (see Figure 1). The cryptands (*1-9*) were prepared by a new metal carbonate catalyzed one-step method from one mole of the appropriate oligoethyleneoxy diamine and two moles of the dihalide derivative of the appropriate oligoethylene glycol. Although the yields for these reactions were in the 18% to 40% range, this is a convenient way to prepare these compounds. Previous methods take four to six steps giving only 8% to 15% overall yields. The yield of cryptand [3,3,2], when prepared by this method, was only 13% when sodium carbonate was the base. This yield increased to 40% using cesium carbonate indicating a template effect.

Bis-crown ethers *10-13* were isolated in yields of 17% - 30% when the dihalide of tetraethylene glycol was used in the reaction. These materials were formed when the amine reacted with the two end alkyl halides of the same dihalide starting material. A complete report of this work can be found in J. Org. Chem., 57, 3166-3173 (1992).

Cage compounds *14-23* were also prepared during the past year. These materials were prepared in four or five steps from first the reaction of a diaminodiol and a dihalide using a carbonate base. Under these conditions, the amines react giving a diaza-crown containing two N-hydroxyalkyl groups. The resulting dialcohol is further reacted with a dihalide using sodium

hydride as the base to give butterfly-shaped macrotricycles 24-26. These materials have internal secondary amines (25, 26) or two pendant alcohols each of which can react further with a dihalide to form the cage compounds.

These cage compounds interact with various metal ions and protons. The log K for the interaction of 19 with Pb^{2+} was found to be 12.6 while that of 23 with Hg^{2+} was 10.1 in water. These are very strong interactions. More complete details of the synthesis and complexing properties of 14-26 will be found in a paper: H.-Y. An, J.S. Bradshaw, K.E. Krakowiak, C.-Y. Zhu, N.K. Dalley, and R.M. Izatt, J. Org. Chem., in press (October, 1992).

II. Extraction and Liquid Membrane Experiments

Back extraction and dual module hollow fiber membrane separation experiments were performed. Back extraction experiments have been used for monitoring the membrane separation behavior and the membrane experiments to characterize the cation selectivity of new ligands. Details of these experiments are found in the copies of papers appended to this report.

Representative results (Table 1 and Table 2) show that three new crown thioethers (Figure 2) can selectively transport Hg^{2+} and Ag^+ over other cations studied. Since the transport is diffusion limited in the membrane experiment, the selectivity of the extraction system is maintained.

Log K , ΔH , and ΔS values for the interaction of Hg^{2+} with the three ligands have been determined in aqueous and 90% ethanol solutions at 25°C by polarography and calorimetry. The corresponding complex structures were also determined by single-crystal X-ray analysis. The results show that these ligands can strongly bind Hg^{2+} and ΔH values favor the complexation.

The stability of Hg^{2+} complexes is a reflection of the presence of the polarizable sulfur atoms and the formation of stable Hg^{2+} -ligand covalent bonds.

III. Construction of High Temperature Isothermal Flow Calorimeter

Crown ether-cation complex reactions are very temperature dependent and this characteristic can be exploited in making separations. This phase of the project is designed to study these reactions at high temperature. In order to determine the thermodynamic quantities for macrocycle-cation reactions at different temperatures, we have begun construction of an isothermal flow calorimeter. This calorimeter retains all of the desirable operating characteristics and advantages of previous isothermal flow calorimeters, while offering the additional advantages of operation at temperatures from 25°C up to 325°C. It can be operated at pressures from 0.1 to 25.5 MPa, and at solution pH ranging from 3 to 14. The data can be collected and displayed in digital form by a Macintosh Plus computer and/or obtained on a strip chart recorder.

The main components of the calorimeter (Figure 3) are: the reaction vessel, the isothermal cylinder, the thermal shields and insulating container, the fluid delivery system containing the high pressure pumps and pushers, the pressure control system which contains a waste solution container, a pressure gauge, a back pressure regulator with two nitrogen tanks, the temperature control system which contains four Tronac PTC-41 temperature controllers and a Hart Scientific 3704 isothermal control unit, and the data acquisition system which contains a Macintosh Plus computer and an interface between the isothermal control unit and the computer. The Macintosh Plus computer also controls the operation of the pumps. Parts were

ordered and construction began in January 1992. The calorimeter is almost completed and testing should begin in August 1992.

IV. A. Papers Published Since the Last Progress Report

1. U. Olsher, K.E. Krakowiak, N.K. Dalley, and J.S. Bradshaw, "SynBishydroxymethyl-14-Crown-4: A Possible Pre-organized Molecule for Simultaneous Lithium Complexation and Anion Solvation," Tetrahedron, **47**, 2947-2956 (1991).
2. U. Olsher, R.M. Izatt, J.S. Bradshaw and N.K. Dalley, "Coordination Chemistry of Lithium Ion: A Crystal and Molecular Structure Review," Chem. Rev., **91**, 137-164 (1991).
3. J.S. Bradshaw, K.E. Krakowiak, P. Huszthy and R.M. Izatt, "Proton-Ionizable Crown Compounds. 20. The Synthesis of Polyazatriazolo-, Polyazabistriazolo- and Bispyridino-Crown Ligands Containing Lipophilic Hydrocarbon Substituents," J. Heterocyclic Chem., **28**, 773-775 (1991).
4. G. Wu, W. Jiang, J.D. Lamb, J.S. Bradshaw and R.M. Izatt, "High-Specificity Thiacycrown Ether Reagents for Silver(I) over Bivalent Mercury and Lead. Thermodynamic and ^{13}C NMR Relaxation Time Studies," J. Am. Chem. Soc., **113**, 6538-6541 (1991).
5. R.M. Izatt, K. Pawlak, J.S. Bradshaw and R.L. Bruening, "Thermodynamic and Kinetic Data for Macrocyclic Interactions with Cations and Anions," Chem. Rev., **91**, 1721-2085 (1991).
6. K.E. Krakowiak, J.S. Bradshaw, N.K. Dalley, C.-Y. Zhu, G.-L. Yi, J.C. Curtis, D. Li and R.M. Izatt, "Preparation and Cation Complexing Properties of Some Macropolycyclic Ligands," J. Org. Chem., **57**, 3166-3173 (1992).
7. H.-Y. An, J.S. Bradshaw and R.M. Izatt, "Macropolycyclic Polyethers (cages) and Related Compounds," Chem. Rev., **92**, 543-572 (1992).

IV. B. Papers in Press or Submitted

1. R.M. Izatt, J.D. Lamb, R.L. Bruening, C. Wang, N. Edge and J.S. Bradshaw, "Cation Separations Using a Proton-Ionizable Macrocyclic in a Dual Module Hollow Fiber Membrane System," Sep. Sci. Technol., in press (10/31/91).

2. J.S. Bradshaw, K.E. Krakowiak, H.-Y. An, T.-M. Wang, C.-Y. Zhu and R.M. Izatt, "A Novel Two-step Method to Prepare New Unsymmetrical Cryptands," Tetrahedron Lett., in press (3/28/92).
3. H.-Y. An, J.S. Bradshaw, K.E. Krakowiak, C.-Y. Zhu, N.K. Dalley and R.M. Izatt, "Synthesis and Complexation Properties of Suitcase-Shaped Macrotricyclic and Butterfly-Shaped Macrobicyclic Polyether Ligands," J. Org. Chem., in press (4/18/92)

Table 1. Extraction Equilibrium Constants (2-octanone) for Interaction of some Thiamacrocyces with Heavy Metal Cations

Macrocycle	Cations	K _{ex}			
BDT18C6	Ag ⁺ Pb ²⁺ Cd ²⁺ Hg ²⁺	0.216	0.017	0.003	5.613
BDT15C5	Ag ⁺ Pb ²⁺ Cd ²⁺ Hg ²⁺	0.247	0.021	0.022	15.76
Jaws Ligand (3rd ligand Figure 3)	Ag ⁺ Pb ²⁺ Cd ²⁺ Hg ²⁺	0.446	0.023	0.013	36.31

Table 2. Flux values for Hg²⁺ in a Dual Modul Hollow Fiber System

Ligand	Slope	Flux
Bdt 15Crown5	8.279 x 10 ⁻⁴ μmoles/sec	.1167 μmoles/m ² sec
Bdt 18Crown6	6.68 x 10 ⁻⁴ μmoles/sec	8.46 x 10 ⁻² μmoles/m ² sec
Jaws Ligand	1.52 x 10 ⁻³ μmoles/sec	.2143 μmoles/m ² sec

*all three ligands were run at the same experimental conditions which are stated below.

Source Phase: .5mM Hg(NO₃)₂, 1mM Ag(NO₃)₂, 1mM Cd(NO₃)₂ in .02M HNO₃

Receiving Phase: .02M HCl

Organic Phase: The ligand in 2-Octanone

Figure 1. New Macrocyclic Ligands

- 1) R = H; n = 2; p = 2 [2Pr₂.2.2]
 2) R = H; n = 2; p = 3 [2Pr₂.3.3]
 3) R = H; n = 3; p = 2 [3Pr₂.2.2]
 4) R = H; n = 3; p = 3 [3Pr₂.3.3]

- 5) p = 2
 6) p = 3

7
 Dithia[2Pr₂.2.2]

8

9

- 10) m = 0; n = 2; z = 1
 11) m = 1; n = 2; z = 1
 12) m = 1; n = 3; z = 1
 13) m = 1; n = 2; z = 0

- 14) n = 1
 15) n = 2

24

25

26

Figure 2. Schematic Diagram of the Main Components of the Calorimeter. 1. Pump, 2. Pusher, 3. Outer Can, 4. Insulating Container, 5. Insulation, 6. Outer Shield, 7. Inner Shield, 8. Reaction Vessel, 9. Isothermal Cylinder, 10. Waste Solution Container, 11. Nitrogen Tank, 12. Pressure Gauge, 13. Back Pressure Regulator, 14. Macintosh Plus Computer, 15. Computer Interface, 16. Tronac PTC-41 Temperature Controller, 17. Hart Scientific 3704 Isothermal Control Unit.

Fig 3.

BDT-18-Crown-6

BDT-15-Crown-5

bis-(1,4 - dioxo - 7,11 - dithiacyclotridecen -9-yl) glutarate

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