

Ninth Progress Report for the Division of Basic Energy Sciences

Department of Energy, Contract DOE EY 76-S-03-0034, P.A. 218

(includes results of the last three years)

MULTIHETEROMACROCYCLES THAT COMPLEX METAL IONS

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I. Objectives and Background of Research

The overall objective of this research is to design, synthesize, and evaluate cyclic and polycyclic host organic compounds for their abilities to complex and lipophilize guest metal ions, their complexes, and their clusters. Host organic compounds consist of strategically placed solvating, coordinating, and ion-pairing sites tied together by covalent bonds through hydrocarbon units around cavities shaped to be occupied by guest metal ions, or by metal ions plus their ligands. Specificity in complexation is sought by matching the following properties of host and guest: cavity and metal ion sizes; geometric arrangements of binding sites; numbers of binding sites; characters of binding sites; and valences. The hope is to synthesize new classes of compounds useful in the separation of metal ions, their complexes, and their clusters.

The sixth progress report for the Division of Basic Energy Sciences, Department of Energy, summarizes the research done under this contract since its inception. Full-length papers have been published that cover most of the work done during the first five years of this contract. This report covers the results obtained during the seventh, eighth, and ninth years of the contract, with special emphasis on the ninth year, which has not been covered in any previous report. The seventh and eighth reports and published papers for those two years provide more detail. Here we will only summarize the results of the seventh and eighth years. Particularly important among these papers is the 88-page invited review paper, "Concept, Structure and Binding in Complexation," Topics in Current Chemistry, 98, 43-106 (1981) by D. J. Cram* and K. N. Trueblood.

II. Personnel During Last Twelve Months

1. Dr. Donald J. Cram, principal investigator, devoted one full-time

summer month and about 20% of each of the nine academic months to the project.

2. Dr. Roger Helgeson, Assistant Research Chemist, was employed at 99% of full time for 9 months on this project. He has had 13 postdoctoral years of experience in the synthesis of macroring compounds, eight of which were with multiheteromacrocycles.

3. Dr. Takeo Taguchi, Postgraduate Research Chemist I, was employed at 65% of full time for 4 months on this project. Dr. Taguchi has had 2 postdoctoral years of experience in synthetic organic chemistry.

4. Ms. Siew Ho, a Ph.D. degree candidate at UCLA, worked as a Postgraduate Research Chemist III on this project at 49% of full time for 11 months.

5. Mr. Rich Carmack, a Ph.D. degree candidate at UCLA, worked as a Postgraduate Research Chemist III on this project at 49% time for one month.

6. Mr. Mark deGrandpre, a Ph.D. degree candidate at UCLA, worked as a Postgraduate Research Chemist III on this project at 49% time for 11 months.

7. Mr. John Moran, a Ph.D. degree candidate at UCLA, worked as a Postgraduate Research Chemist III on this project at 49% time for 11 months.

8. Ms. Beverly Selle, a third-year undergraduate at UCLA, worked on this contract as a Laboratory Helper on an hourly basis.

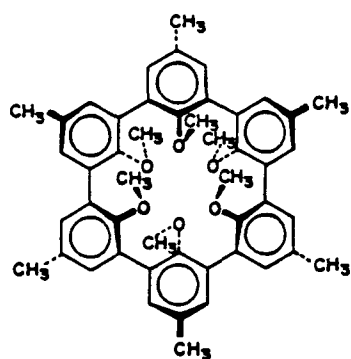
III. Research Results Obtained for the Reporting Period 1 May 1980 through 30 April 1982.

Our efforts have been largely concentrated on the design, synthesis, and metal cation binding properties of the spherands and hemispherands. Spherands are defined as hosts containing cavities lined with binding sites that are organized fully by the support system during synthesis rather than by guests during complexation. Hemispherands are hosts, at least half of whose binding sites are organized by the support system, the others being organized during complexation by the guests. Neither crowns nor cryptands fit these definitions,

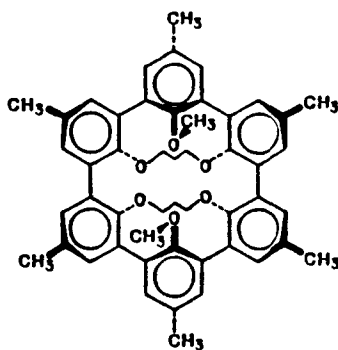
since all of their parts are conformationally mobile and the binding sites are frozen into binding conformations only during complexation!

(1) D. J. Cram* and K. N. Trueblood, Topics in Current Chemistry, 98, 43-106 (1981).

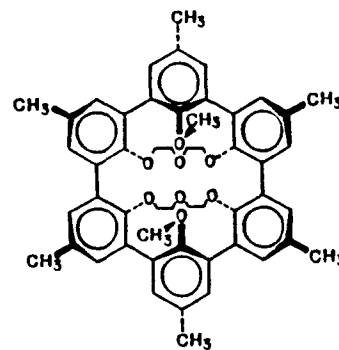
Examples of spherands prepared and studied under these grants are 1-8.



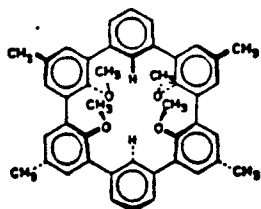
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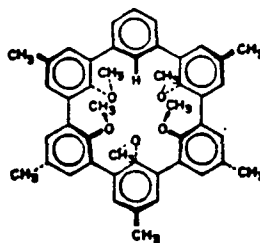
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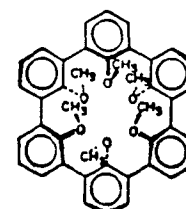
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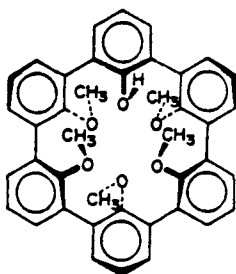
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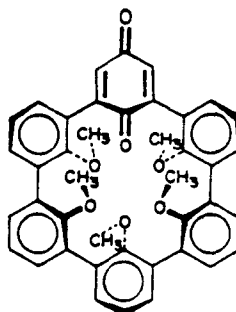
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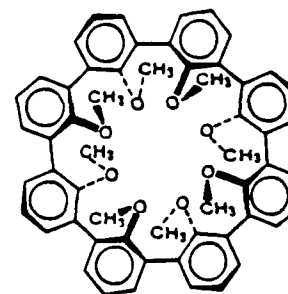
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They differ markedly from any other known ligand systems. For example, 1 binds Li^+ and Na^+ picrates in CDCl_3 at 25°C with $-\Delta G^\circ$ values of > 23 and 19 kcal mol^{-1} , respectively, but bind no other ions detectably.^{2,3} In contrast, 9 binds Cs^+ picrate with $-\Delta G^\circ$ of $11.8 \text{ kcal mol}^{-1}$, $\sim 3 \text{ kcal mol}^{-1}$ better than any other alkali metal ion. Crystal structure determinations of free ligands 1 and 9,

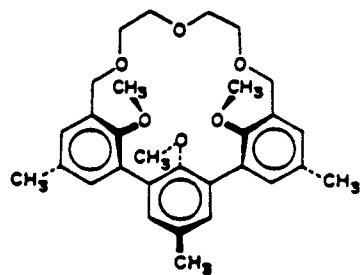
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- (2) D. J. Cram*, G. M. Lein, T. Kaneda, R. C. Helgeson, C. B. Knobler, E. Maverick, and K. N. Trueblood, J. Am. Chem. Soc., 103, 6228-6232 (1981).
 (3) G. M. Lein and D. J. Cram*, J. Chem. Soc. Chem. Commun., 301-304 (1982).

and of metallospherium salt complexes of 1 (both Li^+ and Na^+), of 2, and of 3 prepared under this contract were carried out by Professor K. N. Trueblood (his own NSF grant).⁴ These structure determinations, coupled with NMR spectra

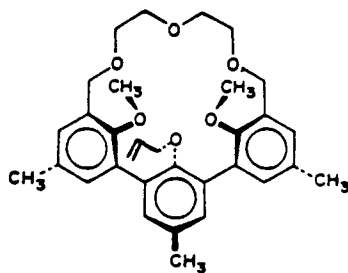
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- (4) K. N. Trueblood, C. B. Knobler, E. Maverick, R. C. Helgeson, S. B. Brown, and D. J. Cram*, J. Am. Chem. Soc., 103, 5594-5596 (1981).

and molecular model determinations demonstrate the preorganization of these spherands.

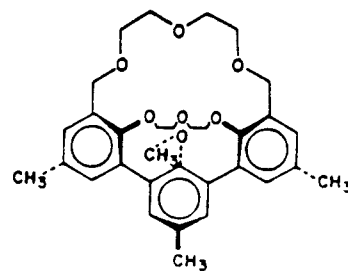
Hemispherands 10-21 have been prepared under this grant. Their binding abilities ($-\Delta G^\circ$ values) of alkali-metal picrate salts at 25°C in CDCl_3 have been examined (see Seventh Progress Report). These compounds generally give $-\Delta G^\circ$ values that range from 5.7 to $14.0 \text{ kcal mol}^{-1}$, and favor Na^+ and K^+ over the other ions. For example, 12 favors K^+ over Na^+ by $1.3 \text{ kcal mol}^{-1}$, and 16 favors Na^+ over K^+ by $1.6 \text{ kcal mol}^{-1}$. Structure-binding correlations have been made (Seventh and Eighth Progress Reports). The crystal structure of 10 and one of its complexes¹ confirmed the expectation that in 10, the



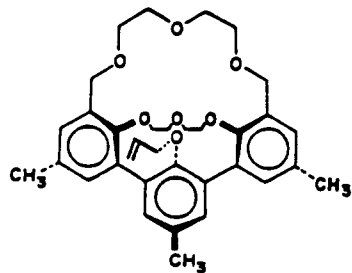
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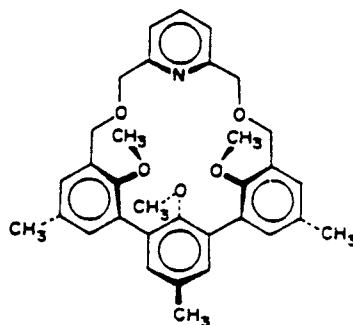
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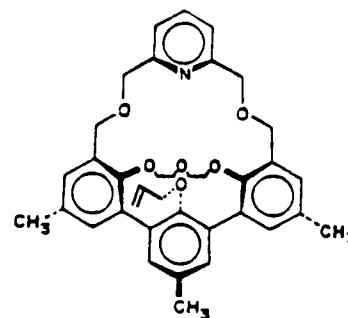
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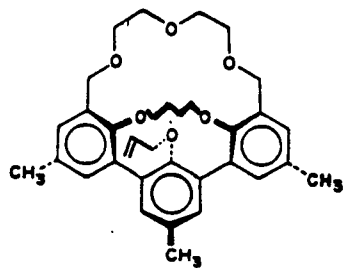
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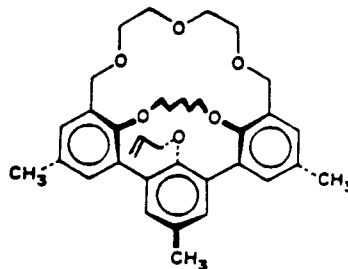
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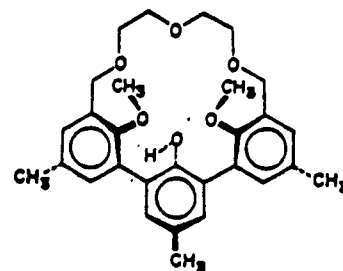
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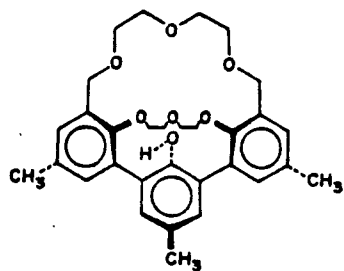
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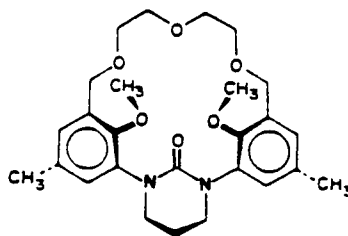
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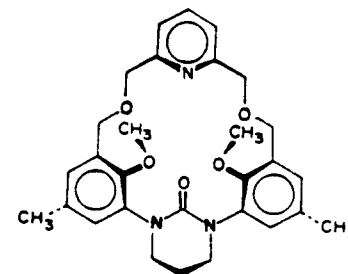
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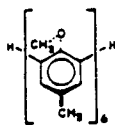
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three methoxyl groups were organized for complexation prior to complexation, but the cavity was filled with the hydrogens of the $(\text{CH}_2\text{OCH}_2)_3$ bridge. This bridge had to reorganize during complexation.

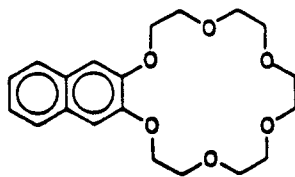
Scales of binding for open-chain model compounds, crowns, cryptands, hemispherands and spherands in CDCl_3 at 25°C towards Li^+ and Na^+ picrates were reported^{1,2,3} (see Eighth Progress Report for discussion). Combinations of techniques were used in developing these scales reported in Charts I and II.

The rates of complexation and decomplexation and equilibrium constants were measured and reported for spherands 1, 2, and 3 complexing lithium and sodium picrates in CDCl_3 as a function of temperature.³ The complexation rate constants varied only from 7.5×10^4 to $1.2 \times 10^6 \text{ mol}^{-1} \text{ sec}^{-1}$, but the decomplexation rate constants varied from 2.2×10^{-4} to $< 1.6 \times 10^{-12}$. These extremes are large indeed. The relatively slow complexation rates and very, very slow decomplexation rates, as well as the large variation in decomplexation rates differentiates the spherands from other classes of binders.³

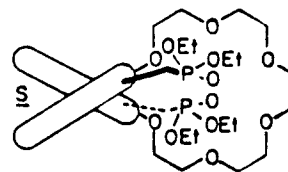
$-\Delta G^0$ (Kcal/mol), CDCl_3 , 25°C , for Complexing Lithium Picrate



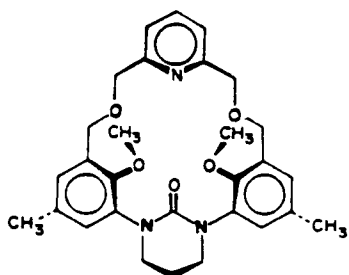
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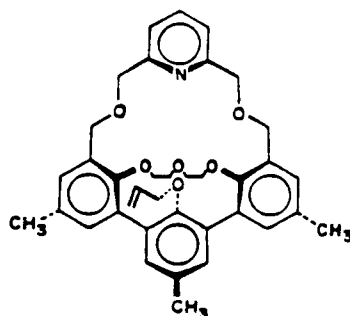
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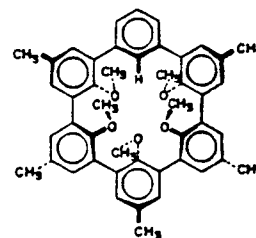
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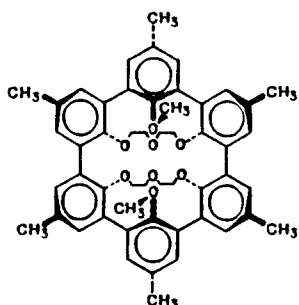
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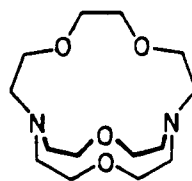
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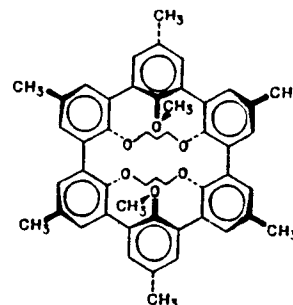
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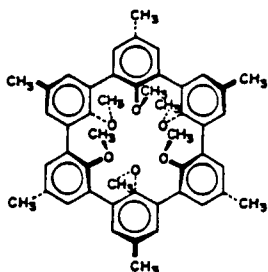
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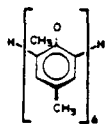


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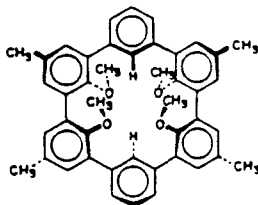


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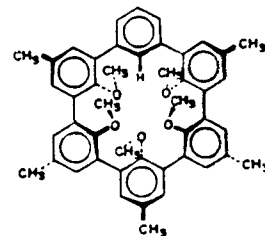
$-\Delta G^{\circ}$ (Kcal/mol), CDCl_3 , 25°C , for Complexing Sodium Picrate



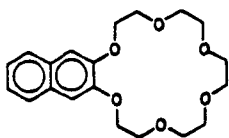
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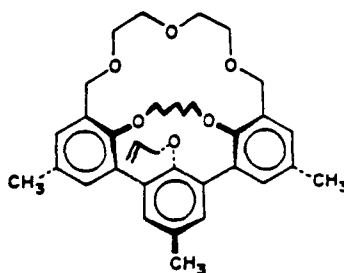
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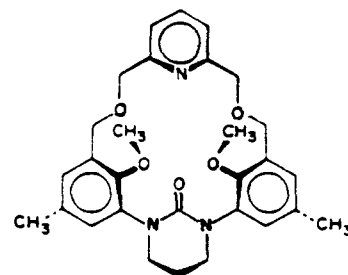
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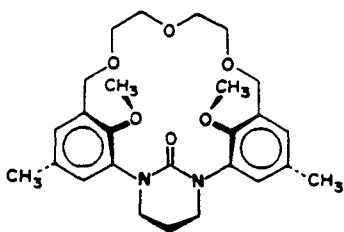
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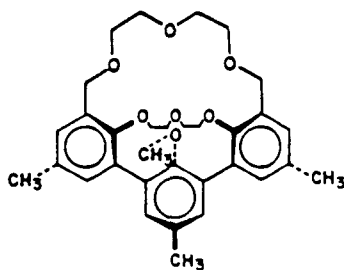
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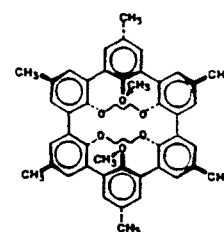
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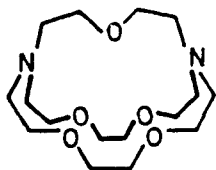
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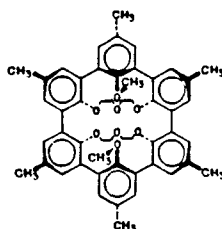
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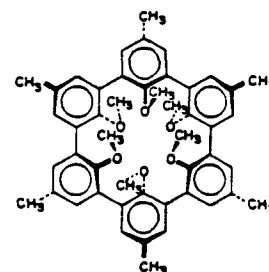
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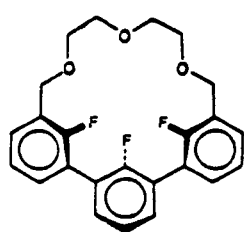
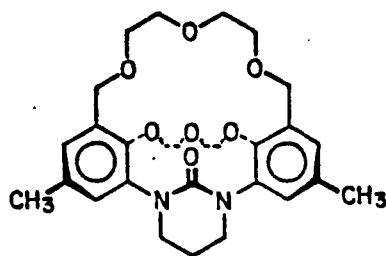
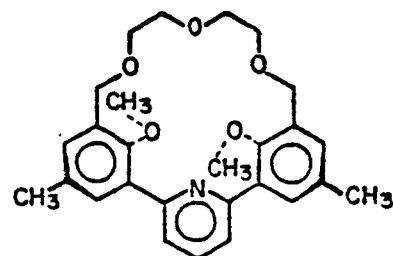
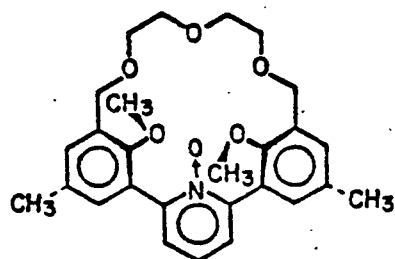
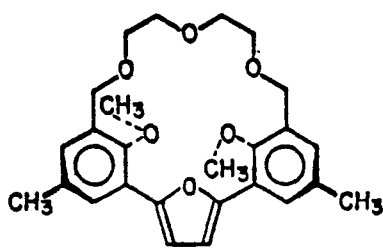
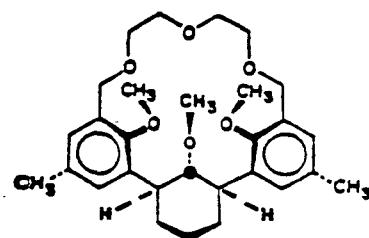
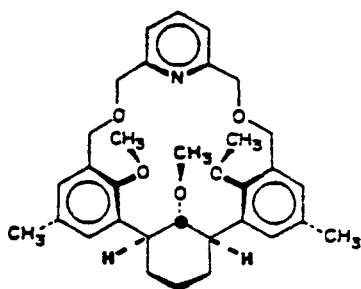
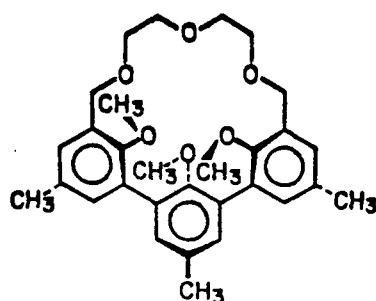
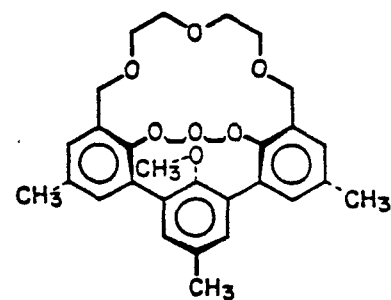
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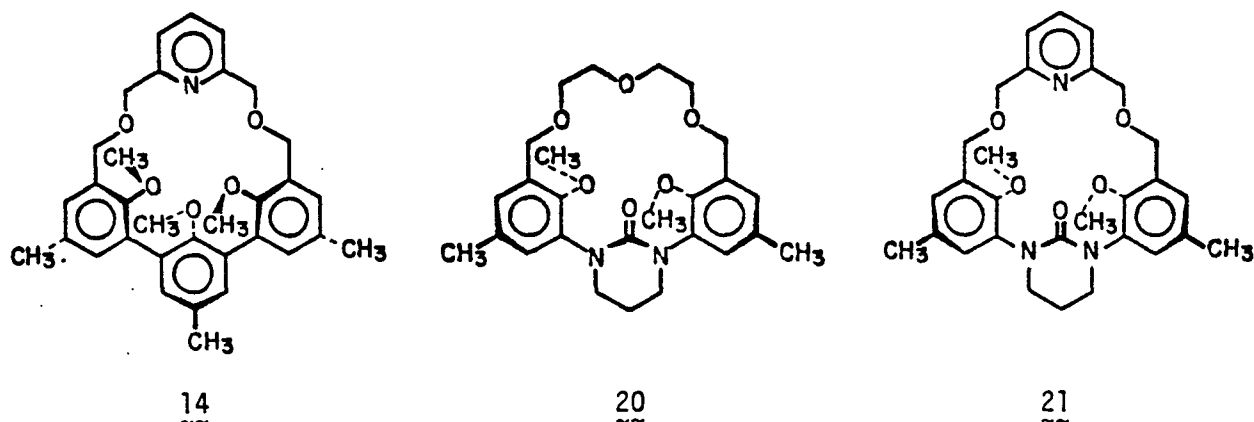


19.2

IV. Research Results Obtained for the Reporting Period 1 May 1982 through 30 April 1983.

Seven new hemispherands, 22-28, have been synthesized as part of our evaluation of various potential binding units for metal ions complexing power and selectivity. These compounds have been compared with 10, 12, 14, 20, and 21 mentioned under III.

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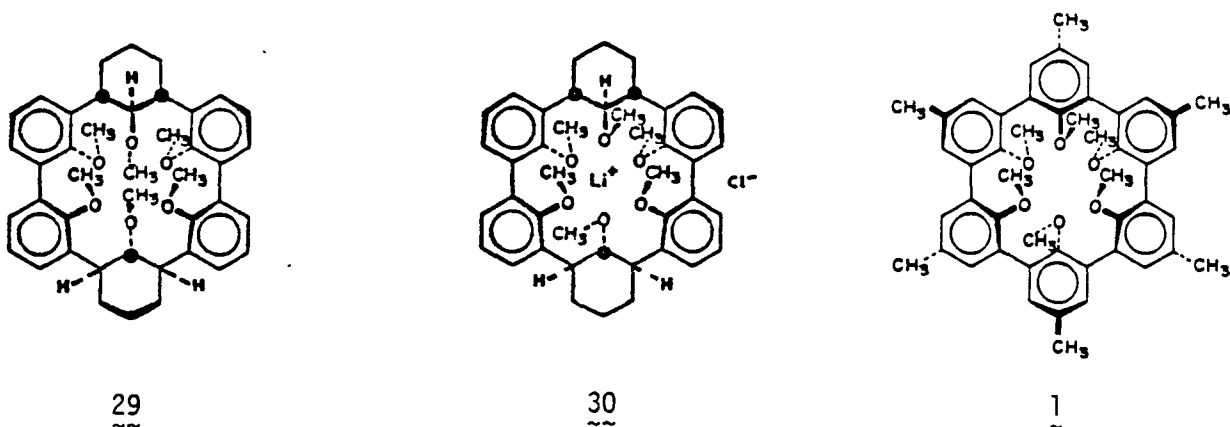


Compound 22 is such a poor binder as to be off scale. Thus, even when forced together, the three fluorines show no indication of behaving as ligands. In molecular shape, binding power and ion selectivity, 23 and 12 resemble one another. Similarly, 25, 10, and 20 resemble one another, as do 14 and 21. Thus the anisyl, pyridine oxide, and cyclic urea units appear interchangeable when located in a central position between two anisyl units which enforce its conformation. These correlations greatly strengthen the thesis that preorganization is of paramount importance in the phenomenon of noncovalent binding. The interchangeability of these units provides versatility, both in the design of hosts themselves in their syntheses. All of these hemispherands are both stronger and more ion selective binders than the crowns, and are more chemically stable than the cryptands. They undoubtedly bind a variety of ions not yet studied, and should provide the starting point for many interesting studies of ion selectivity, conformational analysis, and kinetics. Their syntheses are well worked out, and now are not difficult.

As expected from molecular model examination, 24 and 26 are much poorer and less selective binders. Of the two, 24 is better than 26. We were surprised to find that 27 was a considerably poorer binder than 10, and 28 than 14. The crystal structures of 28, and of its $\text{NaB}(\text{C}_6\text{H}_5)_4$ complex (courtesy of

Professor K. N. Trueblood, separate grant), coupled with ^1H NMR spectral studies provided the reason. In 27 and 28, the methyl groups attached to the cyclohexyl oxygens occupy the cavity, and must be forced into a divergent conformation during complexation. This conformational reorganization that occurs during complexation decreases the free energy of binding. As a result, 27 and 28 are little better than the crowns in their binding power, which also have to be conformationally structured during complexation.

After considerable effort, new ligand system 29 and its LiCl salt complex 30 were prepared. A preliminary examination of the system suggests the following



conclusions. (1) Complex 30, which is prepared from nonmacroyclic starting materials, appears to decomplex much more slowly than the corresponding complex of 1. (2) Host 29 in CDCl_3 complexes $\text{Li}^+ \text{ClO}_4^-$ and $\text{Na}^+ \text{ClO}_4^-$ slowly enough for the rate to be on the human time scale ($k \approx 10^{-2} \text{ sec}^{-1} \text{ mol}^{-1}$). (3) Free host 29 possesses a different conformational organization than either 30 or 1 for the positions of its two methyls attached to the two cyclohexyl oxygens. In 29, these two methyls converge on one another and occupy the cavity (crystal structure, courtesy of Professor K. N. Trueblood, different grant, and ^1H NMR). In contrast, 30 and the LiCl complex of 1 resemble one another in conformational organization. (4) Thus, to complex, two 180° rotations around two C-O bonds must occur in 29, but not in 1. This slows down the complexation and

decomplexation rates for 29-30 by a factor of about six powers of ten. Since 29 does not contain an enforced cavity, it is not a spherand. (5) Free host 29, like 1, shows no tendency to complex K^+ .

V. Educational Profit from this Contract

A new field of organic host-inorganic guest chemistry is being developed under this contract. One or two carefully chosen postdoctoral research chemists, several graduate students, and the principal investigator are learning the science and art of multiheteromacrocyclic synthesis and enough inorganic chemistry to design new ligand assemblies. We are developing entirely new classes of compounds whose binding properties are entirely different from any heretofore available. New synthetic methods are being developed. A new way of thinking about organic-inorganic chemistry is evolving. This research group is cultivating a field that is attracting many others.

VI. Research Publications Resulting from Work Done Under this Contract During the Grant Period from 1 May 1980 to 30 April 1983.

A. Papers published during this three-year reporting period (two reprints are being sent to you under separate cover).

1. "Concept, Structure, and Binding in Complexation," Topics in Current Chemistry, 98, 43-106 (1981), by D. J. Cram* and K. N. Trueblood.

2. "Spherands, the First Ligand System Fully Organized During Synthesis Rather Than During Complexation," J. Amer. Chem. Soc., 103, 5594-5596 (1981), by K. N. Trueblood, C. B. Knobler, E. Maverick, R. C. Helgeson, S. Bruce Brown, and D. J. Cram*.

3. "Augmented and Diminished Spherands and Scales of Binding," J. Amer. Chem. Soc., 103, 6228-6232 (1981), by D. J. Cram*, G. M. Lein, T. Kaneda, R. C. Helgeson, C. B. Knobler, E. Maverick, and K. N. Trueblood.

4. "Spherand Complexation and Decomplexation Rates with Sodium and Lithium Picrates, and Activation Parameters for Decomplexation," J. Chem. Soc. Chem. Commun., 301-304 (1982), by G. M. Lein and D. J. Cram*.

B. Paper already accepted during reporting period (two preprints are attached).

1. "Hemispherands Containing Cyclic Urea and Anisyl Units," J. Amer. Chem. Soc., 104, 0000-0000 (1982), by D. J. Cram*, I. B. Dicker, G. M. Lein, C. B. Knobler, and K. N. Trueblood.

C. Besides the above papers, three others are being written, and will be submitted before the end of 1982, some of which should be published by 30 April 1983. Preprints will be sent as they become available.

1. "Host-Guest Complexation 25. Stereoelectronic Substituent Effects on the Complexing Properties of Chorands," to be submitted to J. Amer. Chem. Soc., by T. W. Bell, G. M. Lein, H. Nakamura, and D. J. Cram*.

2. "Hemispherands Containing the Methyl Cyclohexyl Ether Unit," to be submitted to J. Chem. Soc. Chem. Commun., by D. J. Cram*, J. Moran, C. B. Knobler, and K. N. Trueblood.

3. "Effects on Binding of Spherands when Two Anisyls are Converted to Methyl Cyclohexyl Ether Units," to be submitted to J. Chem. Soc. Chem. Commun., by D. J. Cram, J. Moran, C. B. Knobler, and K. N. Trueblood.