UCLA-34P218X1

First Progress Report for AEC Contract AT(04-3)34, P. A. 218

MULTIHETEROMACROCYCLES THAT COMPLEX METAL IONS

PRINCIPAL INVESTIGATOR: Dr. Donald J. Cram, Professor of Chemistry

INSTITUTIONAL AFFILIATION: Department of Chemistry
University of California at Los Angeles
405 Hilgard Avenue
Los Angeles, California 90024

REPORTING PERIOD: 1 May 1974 - 30 April 1975

DATE OF THIS REPORT: 15 January 1975

Prepared for the U. S. Atomic Energy Commission, Division of Physical
Research, under Contract No. AT(04-3)34, Project Agreement No. 218.

RECEIVED
FEB 18 1975
PATENT GROUP

NOTICE
This report was prepared as an account of work sponsored by the United States Government. Neither the United States nor the United States Energy Research and Development Administration, nor any of their employees, nor any of their contractors, subcontractors, or their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness or usefulness of any information, apparatus, product or process disclosed, or represents that its use would not infringe privately owned rights.

MASTER

DISTRIBUTION OF THIS DOCUMENT UNLIMITED

the patent
tion of
ent:
USAEC

Paul H. Leg
May 12 1975

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency Thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

NOTICE

This report was prepared as an account of work sponsored by the United States Government. Neither the United States Atomic Energy Commission nor any of their employees, nor any of their contractors, subcontractors, or their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness or usefulness of any information, apparatus, product or process disclosed, or represents that its use would not infringe privately owned rights.

The 1974-1975 Research Accomplishments

Supported by AEC Contract AT(04-3)34, P. A. 218

Abstract

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 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 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; valences. In the 8.5 months since the inception of this contract (1 May 1974), and in the remaining 3.5 months of this project year, the specific goals and accomplishments are as follows. (1) Feasibility studies have been conducted to incorporate one or more β -diketonide units in macrorings. A "masked" β -diketonide unit has been synthesized, and preliminary ring closures suggest the unit will be useful for the intended synthetic purpose. Acetylacetonide ions are excellent ligands for the lanthanides and other ions. (2) Attempts have been and are being made to synthesize macrorings composed of six 1,3-linked aryl groups, each of which contains a methoxyl or hydroxyl group in the 2-position. The goal is to compose a cage of six oxygens which occupy the apexes of an octahedron, which can contain an adjustable number of negative charges (0-6), and whose cavity is about 1.0 ± 0.1 in radius (that of the lanthanide and actinide ions). Our synthetic approach appears promising. (3) Multiheteromacrocycles have been prepared containing the 2,2'-dioxo-1,1-binaphthyl unit, and the 2,2'-dioxo-1,1-bioctaly unit (outer benzene rings of the binaphthyl unit reduced). Methods have been

developed for preparing starting materials for the synthesis of bicyclic and tricyclic host compounds of various cavity sizes. Model reactions for their syntheses have been carried out.

Personnel

1. The principal investigator (Donald J. Cram) devoted one full-time summer month and 20% of each of the nine academic months to the project.

2. Dr. Roger C. Helgeson, Assistant Research Chemist I, was employed 95% of full time on this project. He has had six postdoctoral years' previous experience in the synthesis of macroring compounds, two of which were with multiheteromacrocycles.

3. Dr. Karl Koenig, Postgraduate Research Chemist I, was employed 88% of full time on this project. He obtained his Ph.D. degree in 1974 at the University of Southern California.

4. Dr. Albert Alberts, Postgraduate Research Chemist I, was employed 88% of full time on this project. He obtained his Ph.D. degree in 1974 at the University of Groningen.

The remaining time of the three postdoctoral research chemists was devoted to attending seminars, auditing courses, and planning their future research careers.

Research Results

A. Syntheses of "Masked" β -Diketonide Units for Incorporation into Multiheteromacrocycles (with Dr. Albert Alberts)

Since β -diketonides are excellent ligands for the lanthanides, the objective was to synthesize a "masked" β -diketonide unit that could be incorporated into multiheteromacrocycles, and then unmasked. Compounds 1 and 2 were chosen as

target units. The ketal or thioketal functional groups are masked ketone units that should withstand the conditions of ring closure, after which those functions could be hydrolyzed to 5-diketonide units. Four possible routes to 1 were explored, and failed. These are outlined.

A successful and practical synthesis of 2 has been developed by the following route, in which 4 is an intermediate. Coupling of two molecules of 4 through an ether linkage should also give a synthetically useful compound (see research plan for 1975-1976).

Three cyclizations have been carried out on a small scale, but the products have not been definitely identified. Their probable structures are formulated.

The acid-catalyzed hydrolysis of compounds 5 and 6 to the β -diketones 7 and 8 (respectively) will be carried out after the two thioketals have been definitely identified.

7

8

9 ?

20%

+

10 ?

25%

The pmr spectra and chromatographic behavior of 9 and 10 are consistent with their assigned structures, but full proof of structure is not yet realized.

3)

2

+

11

20%

+

12

55%

The pmr spectra and chromatographic behavior of 11 and 12 are consistent with the structures drawn, but full proof of structure is not yet in hand.

11 ?

12 ?

If 12 has the structure drawn, its hydrolysis should give a bis-β-diketone, which is designed to complex and lipophilize the uranyl ion, 13, in acid solution. Corey-Pauling-Koltun (CPK) molecular models of 13 indicate the four oxygen ligands of the host occupy a plane perpendicular to the O=U=O axis, and the N-H...O=U=O...H-N assembly is linear. This geometry should be ideal for complexation.

13

B. Attempts to Synthesize Macrorings Composed of Six 1,3-Linked Aryl Groups, Each with a Methoxyl Group in Its 2-Position (with Dr. Karl Koenig)

Aryl groups are resistant to radiation damage. Also phenoxide anions and phenol ethers are good ligands for many metal ions. Molecular models (CPK) of macrorings composed of six 1,3-linked aryl groups, each of which contains a methoxyl or hydroxyl group in the 2-position, indicates the molecule must assume a geometry resembling 14. The six aryl groups are not coplanar, but have an arrangement that places three alternate oxygens above and the other three alternate oxygens below the best plane of the macrocycle. Thus an octahedral cage of oxygen ligands is composed, whose cavity radius is about $1.0 \pm 0.1 \text{ \AA}$, depending on the dihedral angles between the planes of the benzene rings attached to one another. In models these dihedral angles appear somewhat manipulable by substituents in the 4- and 6-positions, and thus the cavity size is subject to some control. The overall valence of the ligand is potentially adjustable (0-6) by control over whether hydrogen or methyl groups are attached to the oxygens. The lanthanides and actinides have valences of +3 to +4, and their ions have atomic radii of about 1.10 ± 0.1 .

14, R = H or CH₃; R' = H, CH₃ or (CH₃)₃C

Attempts have been and are being made to prepare 14 with $R=H$ and $R'=CH_3$ or CH_3CH_2 . A chemical literature search indicated two possible ways (aside from electrochemical, which will also be tried) of coupling aryl residues ortho to a hydroxyl or methoxyl group.

Attempts to couple 15 with $R=CH_3$ gave product coupled ortho to meta, contrary to the literature. Attempts are being made to couple 14 with $R=CH_3CH_2$ (more steric hindrance). Compound 17 ($R=CH_3$) was prepared, and from it, 18 ($R=CH_3$). Attempts will be made to trimerically couple 18 to give 14 ($R=R'=CH_3$). Compound 19 was available from other studies in both racemic and optically pure form. Application of route 2) to 19 in optically pure form should give much more cycle than racemic 19. Only coupling of molecules of identical configuration can lead to cycle, since the ends of the coupled reaction intermediates do not converge on one another unless this condition is met. Coupling of units of unlike configuration leads to open-chain oligomers. Racemic 19 (the cheaper compound) when subjected to coupling conditions gave low yields of what are probably cyclic trimer and tetramer (mass spectra), 20, plus polymer. This cyclization reaction will be conducted with optically active 19, and much higher yields of more easily isolable products should result.

C. Multiheteromacrocycles Containing the 2,2'-Dioxo-1,1-Binaphthyl Unit, and the 2,2-Dioxo-1,1-Bioctalyl Unit (with Dr. Roger C. Helgeson)

Units 21 and 22 possess unique properties for shaping mono-, bi- and tricyclic ligand assemblies. Their aryl groups form a hinge and can rotate with respect to

one another only about 20° from the 90° dihedral angle position. This rotation allows the size of rings attached to the 2,2'-oxygen to vary somewhat. The 3,3'-positions direct attached groups over and under (respectively) macrorings (attached at the 2,2'-positions) that lie in between. In connection with other work, we have learned how to prepare and manipulate multiheteromacrocycles that contain these units, particularly those with certain substituents in the 3-position. The 3,3'-positions make ideal places to close additional rings leading to highly shaped bicyclic and tricyclic systems, illustrated by structure 23, a target compound. The cavity size can be altered by varying the length of the heteroatom-containing bridges.

21

22

23

Feasibility studies in synthesizing monocycles with 21 and 22 as starting materials have been carried out. The reactions serve as models for preparing the bicyclic and tricyclic systems, provide starting materials for closing the additional rings, and give compounds interesting as ligand assemblies in their own right.

1. Monocycles Closed on Units Containing Carboethoxy, Aldehyde and Carboxamido Groups in the 3-Position

Since carboethoxy, aldehyde and carboxamido groups are synthetically useful, it was important to see if ring closures could be performed in their presence. The following reactions proved successful.

2. Synthesis of Key Intermediates

Several key intermediates have been prepared for the future syntheses of bicyclic and tricyclic systems (see renewal proposal for 1975-1976). Compound 26 is such a system. Another is 28, which is the starting point for preparing 23, and several other bi- and tricyclic systems (see renewal proposal for 1975-1976).

3. Exploratory Synthesis of Bicyclic Systems

To test the feasibility of closing rings leading to bicyclic systems, the already available compound 29 was converted successfully to 30.

4. Exploratory Synthesis of a Ligand Assembly Containing Inward-Turned Aryloxy Groups

Molecular models (CPK) of compounds such as 32 indicate that the six oxygens can provide a square bipyramidal arrangement of ligands. Due to the acidity of phenolic hydroxyl groups, up to four negative charges can be incorporated into the ligand to match the valence of metal ion guests. Attempts to prepare 32 are in progress from the already available compound, 31. Hopefully the sulfide nucleophile will react in preference to the phenoxide nucleophile.

Reaction has been run, and products are being isolated.

Cooperation with Other AEC Contractors

The principal investigator contacted by letter the following people who are engaged in AEC work related to our research: Dr. Charles F. Coleman, Oak Ridge Laboratory, Dr. B. E. Jepson, Mound Laboratories, Dr. Walter Stevens, University of Utah and Dr. E. P. Horwitz, Argonne National Laboratory. As a result, the principal investigator visited Oak Ridge Laboratory, gave an informal seminar, learned much about their problems and about possible applications of our research to solutions to their problems. As a result of this visit, three compounds were supplied them, 33, 34 and 35, small amounts of which had been prepared before the start of our AEC contract in connection with other studies. The larger samples of 34 and 35 were prepared particularly to be sent to Oak Ridge.

33

10g

34

5g

35

5g

A further result of these contacts was a visit to our laboratories by Dr. B. E. Jepson of Mound Laboratories, with whom we spent a mutually profitable day consulting. As a result of this visit, we synthesized a larger sample of compound 36, a substance prepared earlier in smaller amounts in connection with other studies and sent it to him for possible use in calcium isotope fractionation.

36
~~

0.7g

We anticipate sending small samples of other compounds in the future to these groups, and to Dr. Walter Stevens for those preliminary tests that we are not able to do here. Because of limitations in the size of our equipment, and our commitment to research and the teaching of research, we are not able to carry out large-scale syntheses for other groups. We are very pleased to supply our procedures for these syntheses to other groups, so they can make or have made desired compounds in laboratories organized for that purpose.

Educational Profit from this Contract

A new field of organic host-inorganic guest chemistry is being developed under this contract. Three carefully chosen postdoctoral research chemists and the principal investigator are learning the science and art of multiheteromacrocyclic synthesis, and enough inorganic chemistry to design our ligand assemblies. As time goes on, the same group will develop new test systems to determine the complexing properties of the systems synthesized. A whole new way of thinking about organic-inorganic chemistry is evolving, and it is our belief that we are cultivating a field that will attract many other research groups. Another twelve coworkers, who are primarily graduate students, are also learning this field by association with those who are creating this field. By the third year, graduate students are expected to join in this effort.

Publications

No publications based on this work have yet been submitted or have appeared, since the work has not much more than been started. Programs of this degree of difficulty and complexity take several years to mature.