envisioned for the (*S*,*S*) complex. Three hydrogen bonds and carboxylate–ammonium ion pairing hold the amino acid to the crown, and carboxyl–carboxyl hydrogen bonding presses the hydrogen of the chiral center of the amino acid to the chiral barrier of the crown. Monoacid **2** binds well to amino acids[3] (see **10**), but the absence of the second carboxyl of the host allows the chiral center of the guest too much conformational flexibility for the diastereomeric complexes to differ much in stability. In models, the hole of **3** is too small for an ammonium ion to penetrate the crown of oxygens and little complexation is observed.[3] Models of amino acid complexes of **4** suggest that the three alternate oxygens remote from the chiral barrier most stably bind the ammonium ion. Thus the two chiral elements are also remote. Complexes of diester **5** are less structured, since they lack two of the three binding features that characterize the complex of diacid **1**. Compound **1** is one of a family of host molecules that promise to be useful in resolution, determination of configuration, and optical purity.

[9] Public Health Service International Postdoctoral Research Fellowship, 1971–1972.

Roger C. Helgeson, Kenji Koga,[9] Joseph M. Timko
Donald J. Cram*
Contribution No. 3089, Department of Chemistry
University of California at Los Angeles
Los Angeles, California 90024

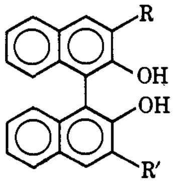
Received December 14, 1972

Structural Requirements for Cyclic Ethers to Complex and Lipophilize Metal Cations or α-Amino Acids[1]

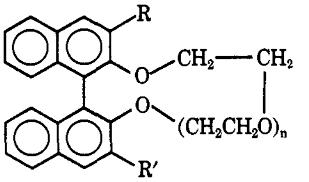
Sir:

Sixteen new multiheteromacrocycles are reported with cavities shaped to complex differentially metal ions and α-amino acids. Cycles **6–21**[2a,b] were prepared from ditosylates of polyethylene glycols and 3,3′-disubstituted-2,2′-dihydroxy-1,1′-binaphthyl compounds **1–5**,[2] which in turn were prepared from 2,2′-dihydroxy-1,1′-binaphthyl (no high dilution). Each unit of **17–21** was designed for a specific role in molecular complexation. The cycles' oxygens provide neutral ligands for metal or ammonium cation complexation.[3] The hole diameters with the oxygens turned inward vary with the naphthyl–naphthyl dihedral angles and the number of ethyleneoxy units. The binaphthyl unit is a chiral steric barrier whose two 3-positions direct attached side chains under or over the hole. The carboxyl groups of the side chains can center above or below the hole, and their anions can provide internal counterions for complexed cations. Amino groups or a second carboxyl attached to the side chain can serve as additional neutral ligands or as sites for hydrogen bonding or ion pairing the carboxyl of complexed amino acids. The binaphthyl and methylene units of the ring and side chain shape the area around the hole and provide a lipophilic skin for the hydrophilic metal or amino acid guest entities.

Complexes **24–32** were examined. Easily visible pmr spectral differences (deuterated solvents, HA-100) of the $ArCH_2$ and $ArOCH_2$ proton signals in complexed and noncomplexed polyethers provided one criterion of complexation in solution. Lipophilization of cat-

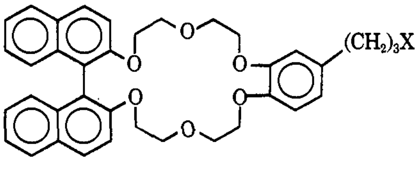


R	R′	mp, °C	%
1, CH_2M	CH_2M	300 dec	75
2, H	CH_2M	226–228	15
3, CH_2OH	CH_2OH	222–224	65
4, CH_2M	CH_2OH	190–192	30
5, H	CH_2OH	206–207	80



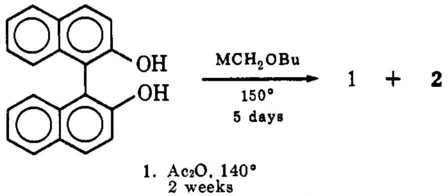
n	R	R′	mp, °C	%
6, 4	CH_2M	CH_2M	Oil	65
7, 4	CH_2OH	CH_2OH	132–134	60
8, 4	H	CH_2OH	136–137	50
9, 4	CH_2M	CH_2OH	Oil	55
10, 3	CH_2OH	CH_2OH	Oil	10
11, 5	CH_2OH	CH_2OH	Oil	50
12, 4	CH_2E	CH_2E	Oil	60
13, 4	H	CH_2E	Oil	70
14, 4	CH_2M	CH_2E	Oil	35
15, 3	CH_2E	CH_2E	Oil	55
16, 5	CH_2E	CH_2E	Oil	50
17, 4	CH_2A	CH_2A	Oil	80
18, 4	H	CH_2A	Oil	70
19, 4	CH_2M	CH_2A	Oil	65
20, 3	CH_2A	CH_2A	Oil	85
21, 5	CH_2A	CH_2A	Oil	75
22, 4	H	H	130–130.5	60

M = $N(CH_2CH_2)_2O$; E = $OCH_2CO_2CH_3$; A = OCH_2CO_2H; Ts = $SO_2C_6H_4CH_3$-*p*



23a, X = OH
23b, X = CO_2H, oil, 70%

Conversions



$$\mathbf{1}\text{ or }\mathbf{2}\xrightarrow[\text{2. LiAlH}_4]{\text{1. Ac}_2\text{O, 140° 2 weeks}}\mathbf{3},\mathbf{4}\text{, or }\mathbf{5}$$

$$\mathbf{1},\mathbf{3},\mathbf{4}\text{, or }\mathbf{5}\xrightarrow[\text{2KO-}t\text{-Bu, THF}]{\text{Ts(OCH}_2\text{CH}_2)_{n-1}\text{OTs}}\mathbf{6},\mathbf{7},\mathbf{8},\mathbf{9},\mathbf{10}\text{, or }\mathbf{11}$$

$$\mathbf{7},\mathbf{8},\mathbf{9},\mathbf{10}\text{, or }\mathbf{11}\xrightarrow{\text{BrCH}_2\text{CO}_2\text{CH}_3}\mathbf{12},\mathbf{13},\mathbf{14},\mathbf{15}\text{, or }\mathbf{16}$$

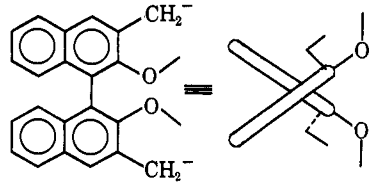
$$\mathbf{12},\mathbf{13},\mathbf{14},\mathbf{15}\text{, or }\mathbf{16}\xrightarrow[\text{2. H}^+]{\text{1. OH}^-}\mathbf{17},\mathbf{18},\mathbf{19},\mathbf{20}\text{, or }\mathbf{21}$$

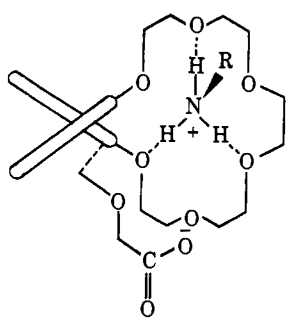
---

[1] This work was supported by U. S. Public Health Service Research Grant No. GM 12640-08 from the Department of Health, Education and Welfare, and by a grant from the National Science Foundation.

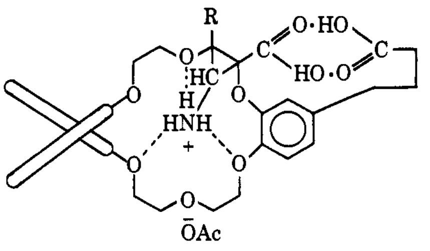
[2] (a) Carbon and hydrogen analyses were within 0.30% of theory. Pmr spectra were consistent with assigned structures. (b) Mass spectra exhibited molecular ions. (c) Metal salt analyses were within 1.00% of theory.

[3] See C. J. Pedersen, *J. Amer. Chem. Soc.*, **89**, 2495, 7017 (1967), for first observations.

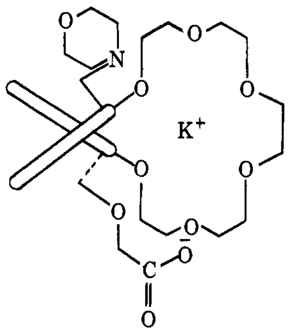




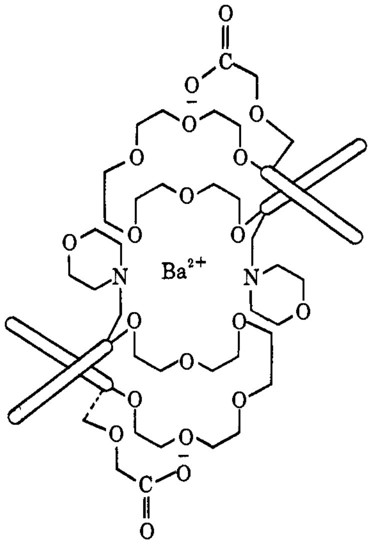
24, R = C_6H_5, $(CH_3)_3C$, or $(CH_3)_2CHCO_2H$



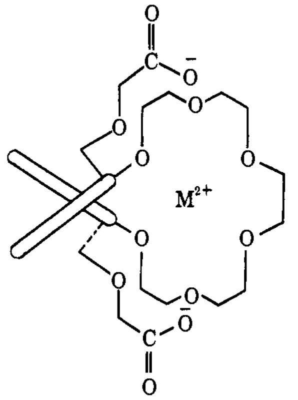
25



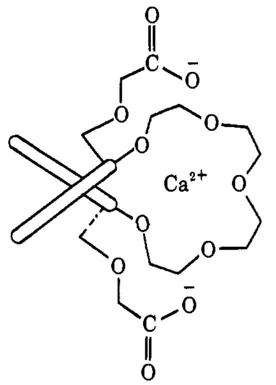
26



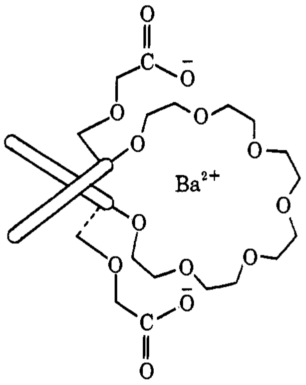
27



28, M = Sr
29, M = Ba
30, M = Ca



31



32

ions provided a second. The stability of some of the salts to experimental manipulation served as a third. Monoacid **18** complexed (one-to-one) aniline and *tert*-butylamine in chloroform, and valine in 80% acetic acid–20% water (by volume) (see **24**). Parent cycle **22**[4a] complexed anilinium and *tert*-butylammonium salts in chloroform,[4b] but lost them when their solutions were shaken with water. Acid **23b**[2a,b] (prepared by conventional reactions from alcohol **23a**[4a]) failed to complex valine under the conditions that acid **18** complexed valine well. Unlike the carboxyl of **18**, that of **23b** cannot reach a position directly below the hole to act as a contact counterion for the ammonium ion. The carboxyls of either **18** or **23b** (see **25**) are positioned to potentially hydrogen bond the carboxyl group of a complexed valine. Thus contact ion pairing of ammonium and carboxylate appears more important to amino acid complexation than is carboxyl–carboxyl hydrogen bonding. Valine is complexed less well by parent cycle **22**, diol **7** and diester **12**, and not at all by diamine **6** in acetic acid–water. The crown-separated amino acid (**19**) complexed valine well in 60% acetic acid–40% water. The three dicarboxylic acids complexed valine in 80% acetic acid–20% water in the order of strength, **17** $\gtrsim$ **21** $\gg$ **20**, as predicted from molecular models.[5]

---

(4) (a) E. P. Kyba, M. G. Siegel, L. R. Sousa, G. D. Y. Sogah, and D. J. Cram, *J. Amer. Chem. Soc.*, **95**, 2691 (1973); (b) E. P. Kyba, K. Koga, L. R. Sousa, M. G. Siegel, and D. J. Cram, *ibid.*, **95**, 2692 (1973).

(5) R. C. Helgeson, K. Koga, J. M. Timko, and D. J. Cram, *J. Amer. Chem. Soc.*, **95**, 3021 (1973).

Hydrolysis of amino ester **14** with potassium hydroxide in methanol–water followed by acidification with hydrochloric acid and extraction into chloroform gave metal salt **26**,[2] whose mass spectrum contained the molecular ion of the salt. When barium hydroxide was substituted for potassium hydroxide and after the chloroform-extracted product was chromatographed on silica gel, a complex of the composition of **27**[2a,b] was isolated. A solution of **27** in methanol when treated with sulfuric acid did not give a precipitate. When a tenfold excess of barium hydroxide 0.8% in strontium hydroxide was used to hydrolyze **12**, strontium ion was scavenged and carried into the chloroform with diacid **17**. The mass spectrum of the mixture produced a parent ion for **28**. Salts **28–32**[2] were prepared by neutralizing their acids with appropriate bases in methanol and evaporating the resulting homogeneous solutions to give powders. Salts **28–32** analyzed for one-to-one compositions.

Thus acids **17**, **19**, **20**, and **21** bind and lipophilize metal ions. When the average hole size of the host matches the ionic diameter of the guest ion and the number of carboxyl groups of the host equals the number of positive charges of the guest ion, stable one-to-one complexes form. The hole diameters (Å) are estimated from CPK models to vary with naphthyl–naphthyl dihedral angles (45–135°) as follows: [17]crown-5, 1.7–2.2; [20]crown-6, 2.4–3.1; [23]crown-7, 3.4–4.1. The most probable diameters (Å) in ionic crystals of metals used here are[6] Na$^+$, 2.24; K$^+$, 2.88; NH$_4^+$, 3.32; Ca^{2+}, 2.36; Sr^{2+}, 2.64; and Ba^{2+}, 2.98. To our knowledge, no one has introduced before the counterions into the host ethers and varied their number.[7] Proper design of hole size, heteroatom type, and the number of "built-in" counterions should provide host molecules with a wide range of differential complexing abilities of many of the metal cations of the periodic table. Ion lipophilization is important to ion transport through membranes, to homogeneous catalysis, and to inorganic reagent design for use in organic solvents.

---

(6) M. F. C. Ladd, *Theor. Chim. Acta*, **12**, 333 (1968).

(7) C. J. Pedersen, *J. Amer. Chem. Soc.*, **92**, 386 (1970), and ref 3, and H. K. Frensdorff, *ibid.*, **93**, 600 (1971), correlated hole size of crown ethers with ionic diameters of complexing metal cations.

Roger C. Helgeson, Joseph M. Timko, Donald J. Cram*
Contribution No. 3088, Department of Chemistry
University of California at Los Angeles
Los Angeles, California 90024

Received December 14, 1972

Thermal Rearrangement of Dewar Benzenes to Benzene Triplet States. Examples of Spin Forbidden Nonadiabatic Pericyclic Reactions

Sir:

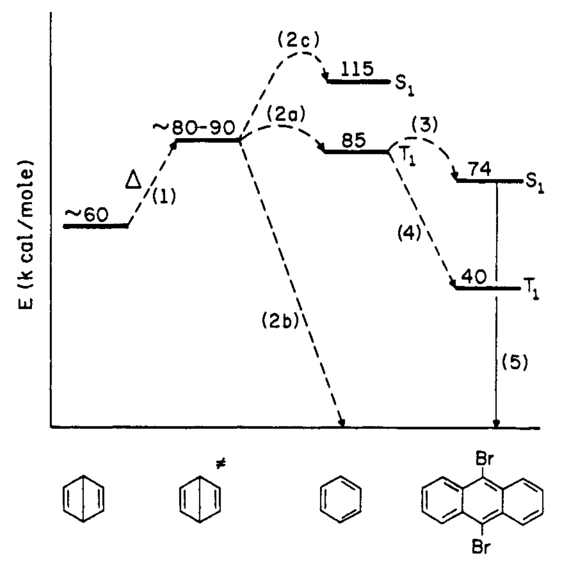
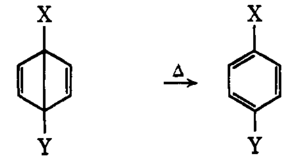


Figure 1. Schematic description of the energy levels involved in the Dewar benzene to benzene rearrangement. The ground-state enthalpy for the rearrangement is estimated to be ~ −60 kcal/mol and the activation enthalpies (step 1) are ~20–30 kcal/mol. From the transition state(s) of 1, 2, and 3 the major deactivation path is 2b, direct formation of ground-state benzene. Path 2c is a very minor path and path 2a, formation of benzene triplets, is a significant process, whose occurrence is monitored by the sequence 3 followed by 5, *i.e.*, triplet to singlet transfer followed by fluorescence. Path 4 is, in fact, the major path of quenching of benzene triplets but is not directly detectable under our conditions.

Thermal rearrangements of Dewar benzenes (**D**) to benzenes (**B**) are exothermic by about 60 kcal/mol.[1] These valence isomerizations also have substantial activation energies,[2,3] *e.g.*, $\Delta H^{\ddagger}$ equals 19, 23, and 30 kcal/mol for the Dewar benzene series **1D**, **2D**, and **3D**,



(1)

1D, X = Cl; Y = H — **1B**
2D, X = Y = H — **2B**
3D, X = Y = Cl — **3B**

respectively. Figure 1 shows that the total transition state energy (as enthalpy relative to ground state benzenes) for the **D** → **B** rearrangement is comparable to the electronic excitation energy required to produce benzene triplet states[4] but is clearly less than the electronic excitation energy required to produce benzene singlets. Thermal population of benzene triplets in **D** → **B** rearrangements thus seems to be energetically feasible and might occur if a mechanism were available which allows a spin flip to occur along the reaction coordinate. Such a process is particularly intriguing because it has important implications with respect to theories of orbital symmetry control of electrocyclic reactions[5] (orbital symmetries do not allow a smooth and facile thermal **D** → **B** conversion) and to ideas con-

---

(1) (a) W. Schaffer, *Angew. Chem., Int. Ed. Engl.*, **5**, 669 (1966); (b) J. F. M. Oth, *ibid.*, 7, 646 (1968); (c) H. C. Volger and H. Hogeveen, *ibid.*, 87, 1185 (1968); (d) W. Adam and J. C. Chang, *Int. J. Chem. Kinet.*, 1, 487 (1969); (e) A. H. Schmidt, unpublished results.

(2) R. Breslow, J. Napierski, and A. H. Schmidt, *J. Amer. Chem. Soc.*, **94**, 5906 (1972).

(3) In the case of hexamethyl(Dewar benzene) a range of values for $\Delta H^{\ddagger}$ have been reported; see ref 1.

(4) A similar analysis suggested that the singlet state of hexamethylbenzene might be energetically accessible from the transition state for thermolysis of hexamethyl(Dewar benzene): C. C. Wamser, F. H. Dorer, L. T. Spada, and G. D. Pfeiffer, Abstracts, 164th National Meeting of the American Chemical Society, New York, N. Y., Aug 1972, ORGN 35. Attempts to observe excited state formation from this system were negative, however.

(5) (a) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970; (b) for a discussion of orbital symmetry disallowed, but energetically concerted reactions, see J. E. Baldwin, A. H. Andrist, and R. K. Pinschmidt, *Accounts Chem. Res.*, **5**, 402 (1972).