Host-Guest Complexation. 15. Macrocyclic Acetylacetone Ligands for Metal Cations[1,2]

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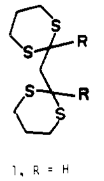
Abstract: Five macrocycles containing 1,5-disubstituted acetylacetone units (AcAc) have been synthesized. Their abilities to complex metal cations in water-dioxane have been compared to those of noncyclic model compounds. The AcAc units were bound together through bridges composed of the following groups: oxa (O), ethylene (E), and 1,3-disubstituted benzene (B). Cycles O(AcAcOEOE)(EOEOE)O (**7**), $(OEOAcAcOE)_2$ (**8**), and $(OEOAcAcOE)_3$ (**9**) were prepared by hydrolysis of rings closed by the reactions of $CH_2[HOCH_2C(SCH_2)_2CH_2]_2$ (**2**) and appropriate polyethylene glycol ditosylates. Ligand systems $O(EAcAcE)_2O$ (**12**) and $B(CH_2AcAcCH_2)_2B$ (**14**) were synthesized in Ca^{2+} or Mg^{2+} templated, two-step sequences involving reactions of HAcAcH dianions with either diethylene glycol ditosylate or *m*-xylyl dibromide, respectively. The preparation of $(CH_2IsCH_2O)_3$ (**17**) is also described, in which Is is the 3,5-disubstituted isoxazole unit. Also described are the preparations of $O(EAcAcH)_2$ (**11**), $B(CH_2AcAcH)_2$ (**13**), and $P(CH_2AcAcH)_2$ (**15**), in which P is 2,6-disubstituted pyridine. The logarithms of the formation constants (log K^{f}_{av}) of the salts of $(OEOAcAcOE)_2$ with 11 divalent metal cations and of $(OEOAcAcOE)_3$ with 3 trivalent cations were 1.8-6.3 units higher valued than for $CH_3OAcAcOCH_3$. The log K^{f}_{av} values for salt formation of $O(EAcAcE)_2O$ and $B(CH_2AcAcCH_2)_2B$ with 10 divalent cations were compared with those of $O(EAcAcH)_2$ and $B(CH_2AcAcH)_2$, respectively, and with HAcAcH itself. Without exception, $O(EAcAcE)_2O > O(EAcAcH)_2 >$ HAcAcH in values of log K^{f}_{av}, the maximum difference being 4.3 for Ca^{2+}. Although both $B(CH_2AcAcCH_2)_2B$ and $B(CH_2AcAcH)_2$ were better ligands than HAcAcH by 1.8-3.9 in Δ log K^{f}_{av} values, the difference between $B(CH_2AcAcCH_2)_2B$ and $B(CH_2AcAcH)_2$ varied between +0.9 and −2.2, depending on the ion. The effects on their binding abilities of gathering, orienting, and constraining acetylacetone units in ring systems are discussed.

Ligand assemblies can be partially structured with covalent bonds prior to their complexation with metal cations by their incorporation into ring systems. The resulting ligand organizations in their metal complexes confer special properties on the systems. The hemes and chlorophylls provide perhaps the most important examples of cyclic ligand assemblies that embrace metal ions. Their survival in evolutionary chemistry and their importance in biological energy transfer and control suggest the possibility that synthetic cyclic ligand assemblies of entirely different structures are worth investigation. The extensively studied porphyrin ring system binds small-diameter metal ions. Its structure provides two negative charges and four convergent nitrogen binding sites.

We report the first synthesis and examination of the binding properties, toward metal cations, of acetylacetone units incorporated in ring systems. The acetylacetonide anion is probably the most ubiquitous of the organic ligand systems. It complexes most metal cations,[3] and each unit supplies one negative charge distributed between two oxygens. The two methyl ends of acetylacetone provide logical covalent bonding sites for elaboration of macroring systems.[4]

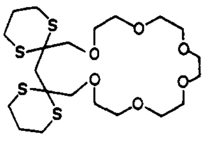
Results and Discussion

Syntheses. Three synthetic strategies were devised. The first utilized the 1,3-dithiacyclohexane unit as a masked ketonic group that forms a nucleophilic anion good for making carbon-carbon bonds. The second involved the dianion of acetylacetone, itself, as a nucleophile for attaching carbon chains. In the third, 3,5-disubstituted isoxazoles served as masked acetylacetone units in assembling the ring system. Of the three approaches, the first two led to the desired products, and the third provided a cyclic precursor containing the masked acetylacetone units.



1, R = H

2, R = CH_2OH



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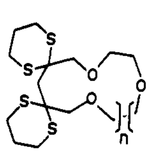
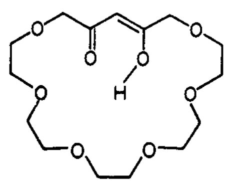
Treatment[5] of **1** with BuLi followed by CH_2O gave the monoalcohol, which with the same reagents gave the diol **2** (45%). With pentaethylene glycol ditosylate,[6] diol **2** and NaH in THF gave cycle **3** (90%). With diethylene glycol ditosylate, **2** and NaH gave a mixture of the three oligomeric cycles (97%), **4–6**. These were separated and identified by osmometric molecular weights. The high yields in these ring closures probably reflect the large steric requirements of the dithiacyclohexane units. Linear polymers could not be constructed with CPK molecular models. Methanolysis of **3** (catalyzed by $HgCl_2$ and $CdCO_3$) gave ethers which when hydrolyzed in acid gave macrocycle **7** (25%). Similar treatment of the mixture of **4–6** and separation of the cyclic components gave **8** (24%) and **9** (16%). The open-chain model compound **10** was prepared from **2** through the dimethyl ether of **2**.



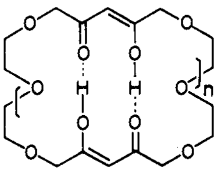
4, n = 1

5, n = 2

6, n = 3

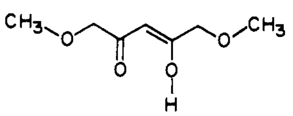


7, O(AcAcOEOE)(EOEOE)O



8, n = 1, $(OEOAcAcOE)_2$

9, n = 2, $(OEOAcAcOE)_3$



10, $CH_3OAcAcOCH_3$

In the second approach, the dianion of acetylacetone was prepared with NaH and BuLi. Treatment of 3 mol of this dianion in THF with either 1 mol of diethylene glycol ditosylate or 1,3-bis(bromomethyl)benzene gave **11** (70%) or **13** (81%), respectively. With CaH_2, **11** in THF and HMPA gave its

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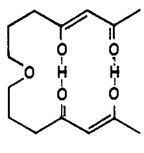
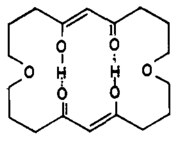
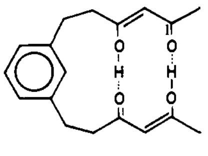


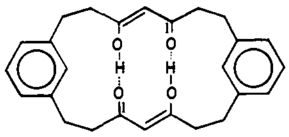
11, $O(EAcAcH)_2$



12, $O(EAcAcE)_2O$



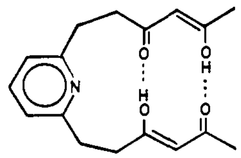
13, $B(CH_2AcAcH)_2$



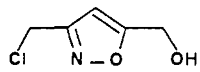
14, $B(CH_2AcAcCH_2)_2B$

calcium salt, which with lithium diisopropylamide in THF and then diethylene glycol ditosylate gave macrocycle **12** (16%), the dimer of **12** (2%), polymer (4%), and 75% of recovered **11**. When the Mg^{2+} complex of **11** was similarly treated, only polymer and the dimer of **12** (15%) were produced. Treatment of the Mg salt of **13** in THF-HMPA with lithium diisopropylamide and 1,3-bis(bromomethyl)benzene gave cycle **14** (13%), the dimer of **14** (12%), polymer (12%), and recovered **13** (35%). When the Ca salt of **13** was used, only polymer and the dimer of cycle **14** (16%) were obtained. Thus cycle **12** was produced from the Ca, but not the Mg, salt of **11**, and **14** was generated from the Mg, but not the Ca, salt of **13**. The disodium salt of **13**, even at high dilution, gave only polymer. These experiments indicate that the cyclization reaction that led to **12** was templated by Ca^{2+}, and that leading to **14** was templated by Mg^{2+}.

In an attempt to prepare the 2,6-dipyridine analogue of cycle **14**, the $NaLi(CH_2COCHCOCH_3)$ salt (see above) was mixed with 2,6-bis(bromomethyl)pyridine in THF to give a 41% yield of **15**. However, attempts to obtain the desired cycle failed, probably because of the pyridine's acidifying effect on the hydrogens of its attached methylene groups.[6]



15, $P(CH_2AcAcH)_2$



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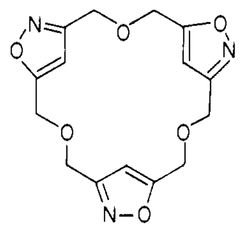
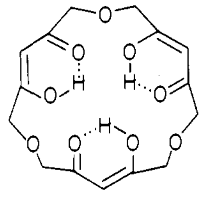


17, $(CH_2IsCH_2O)_3$



18, $(AcAcCH_2O)_3$

In the third approach to macrocycles containing acetylacetone units, isoxazole **16** was prepared by the 1,3-dipolar addition reaction (9%) of propargyl alcohol with chloroacetonitrile oxide[7] prepared in situ by HCl elimination from 1,2-dichloroacetaldehyde oxime.[8] With NaH in THF, **16** cyclized to give a mixture of the three- and four-unit oligomers, of which only **17** was characterized (10%). The completion of the envisioned synthesis involved reduction of **17** with Raney Ni and hydrolysis of the product to **18**.[7] This approach was aborted because of the unpleasant dermatological properties of 1,2-dichloroacetaldehyde oxime.

Acidities of the Cycles and Their Open-Chain Models. The pK_as of the cyclic β-diketones and their open-chain models were measured in purified dioxane-water (1:1 v) at 24 °C with $HClO_4$ and NaOH solutions. Table I lists the results.

Table I. Acidities of Cyclic β-Diketones and Their Open-Chain Models in Dioxane-Water at 24 °C

compd	structure	pK_a^1	pK_a^2	$pK_a^2 - pK_a^1$
	HAcAcH	9.5		
10	$CH_3OAcAcOCH_3$	8.6		
8	$(OEOAcAcOE)_2$	8.6	11.5	2.9
9	$(OEOAcAcOE)_3$[a]	8.6	11.5	2.9
11	$O(EAcAcH)_2$	9.5	12.6	3.1
12	$O(EAcAcE)_2O$	9.9	13.0	3.1
13	$B(CH_2AcAcH)_2$	9.8	11.8	2.0
14	$B(CH_2AcAcCH_2)_2B$	10.6	13.2	1.6

[a] $pK_a^3 = 13.0$.

The patterns of pK_a relationships provide clues about the conformations and potential transannular hydrogen bonding effects in these compounds. The fact that $pK_a^1 = 8.6$ for $CH_3OAcAcOCH_3$, for $(OEOAcAcOE)_2$ (**8**), and for $(OEOAcAcOE)_3$ (**9**) suggests that intramolecular hydrogen bonding of the type suggested by structural formulas **8** and **9** plays little role in stabilizing the compounds or their monoanions. Evidence for intermolecular hydrogen bonding in $CHCl_3$ for cycles **7–9** was observed when their osmometric molecular weights were determined. At 0.05 M, **8** gave 905, vs. 445 at 0.004 M. Cycle **9**, at 0.007 M, gave 1300, vs. 820 at 0.004 M. In $CDCl_3$ at 40 °C, the ^1H NMR spectrum of **8** and **9** indicated they were not completely in the enol form. Both HAcAcH and $O(EAcAcH)_2$ (**11**) gave $pK_a^1 = 9.5$, a fact which again points to little stabilization of **11** due to transannular hydrogen bonding, either in the acid itself or in its monoanion. To exhibit the type of transannular hydrogen bonding indicated by structure **11**, two unfavorable gauche relationships involving $(CH_2)_3$ groups would be required.

Unlike $O(EAcAcH)_2$ (**11**), $B(CH_2AcAcH)_2$ (**13**) has $pK_a^1 = 9.8$, 0.3 unit higher than HAcAcH. This small effect probably reflects a blend of opposing factors: transannular hydrogen bonding effects that stabilize the acid, and to a lesser degree its monoanion; the unfavorable gauche $ArCH_2CH_2C$ conformations required for transannular hydrogen bonding; and steric inhibition of solvation of the acid and its monoanion by the phenyl group. Cycles $O(EAcAcE)_2O$ (**12**) and $B(CH_2AcAcCH_2)_2B$ (**14**) possess the highest degrees of molecular organization and exhibit the most interesting pK_a relationships. In passing from $O(EAcAcH)_2$ to $O(EAcAcE)_2O$, pK_a^1 increased by 0.4 unit. In passing from $B(CH_2AcAcH)_2$ to $B(CH_2AcAcCH_2B$, pK_a^1 increased by 0.8 unit. This effect is attributed to the presence of intramolecular hydrogen bonding in $O(EAcAcE)_2O$ and $B(CH_2AcAcCH_2)_2B$, as indicated in structures **12** and **14**. One of the hydrogen bonds is lost upon ionization, and external solvation of the resulting anions is sterically inhibited, particularly for the monoanion derived from $B(CH_2AcAcCH_2)_2B$. The ^1H NMR spectra in $CDCl_3$ at 40 °C of **11–14** indicate that they are in their enol forms. Furthermore, isotopic exchange of the vinyl protons in CD_3OD-D_2O is slow (24 h).

The values of $pK_a^2 - pK_a^1$ for **8–12** are very similar and range only from 2.9 to 3.1 pK_a units. The four oxygens that carry partial negative charge in the dianions probably turn outward and away from the centers of the macrocycles, both to minimize repulsion between negative charges and to maximize solvation. Molecular models (CPK) of macrorings **8, 9**, and **12** indicate that they possess enough conformational flexibility to allow the oxygens of the AcAc unit to converge on, or diverge from, the center of the ring.

The $pK_a^2 - pK_a^1$ values for $B(CH_2AcAcH)_2$ (2.0) and $B(CH_2AcAcCH_2)_2B$ (1.6) are considerably smaller than the

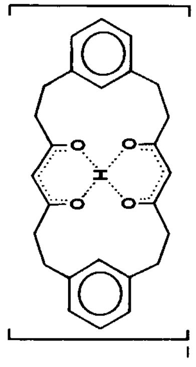
2.9-3.1 values observed in the other systems. More striking is the fact that in the titration of the monoanion of $B(CH_2AcAcCH_2)_2B$ (LH^-) with NaOH solution the ionization rate, in passing from the monoanion to the dianion, was easily observable with the pH meter. This proton transfer is presumed to follow the mechanism of eq 1, in which the rate-determining

$$LH^- + H_2O \overset{slow}{\rightleftharpoons} L^{2-} + H_3O^+$$

$$H_3O^+ + OH^- \overset{fast}{\rightleftharpoons} 2H_2O \qquad (1)$$

step is pseudomonomolecular. This scheme avoids bringing two negatively charged species together (one hindered) in the same transition state, as in mechanism 2. The assumed monomolecular rate constant was estimated to be $4 \times 10^{-4}\ s^{-1}$, which when coupled with the pK_a for LH^- indicates that the reverse reaction is close to diffusion controlled.[9] Proton-transfer rates from oxygen to oxygen rarely are observed on the human time scale.[10] A CPK model of the monoanion of **14** (a tetrahedral nitrogen is substituted for the central hydrogen in the model) provides a spirane internal structure fitted into the macroring. The AcAcH ring systems in the model are somewhat warped from planarity. Formula **19** is a planar projection of the model,

$$LH^- + OH^- \overset{slow}{\rightleftharpoons} L^{2-} + H_2O \qquad (2)$$



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which can be assembled in either a general boat or a general chair conformation. In either conformation, the hydrogen is buried and relatively inaccessible to solvent. In **19**, the negative charge should be highly delocalized. Although unprecedented, **19** might explain the relative kinetic stability of the anion, and it would have to owe its existence to a geometry partially enforced by the macroring system.

Preparation of Salts of Cycle $(OEOAcAcOE)_2$. Three salts of $(OEOAcAcOE)_2$ were prepared in the hope of obtaining materials amenable to X-ray structure determination. Solutions of the macrocycle in $CHCl_3$ were shaken under nitrogen with a fivefold excess of $Cu(OAc)_2$, $Co(OAc)_2$, or $UO_2(OAc)_2$ in water at pH ca. 5. Only $UO_2(OAc)_2$ extracted slowly (5 h). The colored salts obtained were 1:1, and contained no solvent of crystallization. Those of Cu^{2+} and $UO_2{}^{2+}$ were stable, but that of Co^{2+} was air sensitive. None of them gave crystals suitable for X-ray work.

Formation Constants for Salt Complexes. The formation constants (K^f_{av}) were determined for complexes composed by the reactions of HAcAcH, $CH_3OAcAcOCH_3$, $O(EAcAcH)_2$, $B(CH_2AcAcH)_2$, and their cyclic analogues with 12 different metal dianions and 3 different metal trianions. Purified dioxane-water solutions (1:1 v) of the metal nitrate salts, the ligands, $HClO_4$, and $LiClO_4$ were titrated with aqueous NaOH solutions at 24 °C under nitrogen. The K^f_{av} values were calculated at $\bar{n} = 1$ for divalent and $\bar{n} = 3/2$ for trivalent ions in Bjerrum curves.[11] In the calculations of K^f_{av}, 1 mol of the bis-β-diketones was treated as equal to 2 equiv, and 1 mol of the tris-β-diketone as equal to 3 equiv of the mono-β-diketones. Equilibration was essentially instantaneous. Table II reports the results, as well as the ionic diameters, of the metal ions involved.

Correlation between Binding Ability and Structure. The two model ligands, HAcAcH and $CH_3OAcAcOCH_3$, within ex-

Table II. Logarithms of the Formation Constants (log K^f_{av}) for Metal Ions Complexing β-Diketonides in Water-Dioxane (1:1 v) at 24 °C under Nitrogen

no.	ligand structure[a]	Cu^{2+}	$UO_2{}^{2+}$	Ni^{2+}	Co^{2+}	Zn^{2+}	Pb^{2+}	Mg^{2+}	Cd^{2+}	Mn^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}	Ce^{3+}	La^{3+}	Cr^{3+}
	HAcAcH	9.5	8.7		6.3	6.1	5.5	4.5	4.0		3.1	2.7	2.5			
10	$CH_3OAcAcOCH_3$	9.5	8.7	7.0	6.2	6.0		4.5	3.9	3.3	3.1	2.7	2.5	5.1	4.5	5.4
11	$O(EAcAcH)_2$	12.0	11.8		9.2	8.8	8.6	7.1	7.0		7.0	5.3	5.2			
12	$O(EAcAcE)_2O$	12.1	12.5		9.7	9.5	9.1	7.2	7.4		7.4	5.6	5.4			
13	$B(CH_2AcAcH)_2$	11.8	11.4		8.8	8.4	8.1	6.6	6.8		6.3	4.7	4.3			
14	$B(CH_2AcAcCH_2)_2B$	12.0	11.2		8.6	9.0	9.0	5.5	7.5		4.1	2.8	2.5			
8	$(OEOAcAcOE)_2$	11.3	11.0	10.8	9.9	9.7		7.4	7.9	7.6	7.8	6.7	6.4			
9	$(OEOAcAcOE)_3$													11.4	10.4	10.1
pH range used		0.5 2.5	0.5-3.5	2-5	2-6	2.5-7	3.5-7.5	5-12	3-8	3-8	5-12	5-12	5-12	5-8.5	2.3-9	3.5-7
ligands compared								ΔK^f_{av}[b]								
11 − HAcAcH		2.5	3.1		2.9	2.7	3.1	2.6	3.0		3.9	2.6	2.7			
12 − HAcAcH		2.6	3.8		3.4	3.4	3.6	2.7	3.4		4.3	2.9	2.9			
13 − HAcAcH		2.3	2.7		2.5	2.3	2.6	2.1	2.8		3.2	2.0	1.8			
14 − HAcAcH		2.5	2.5		2.3	2.9	3.5	1.0	3.5		1.0	0.1	0			
8 − $CH_3OAcAcOCH_3$		1.8	2.3	3.8	3.7	3.7		2.9	4.0	4.3	4.7	4.0	3.9			
9 − $CH_3OAcAcOCH_3$														6.3	5.9	4.7
M ionic diameters, Å[c]		1.92	1.6-2.0[d]	1.44	1.48	1.48	2.40	1.30	1.94	1.60	1.98	2.26	2.70	2.22	2.30	1.38

[a] AcAc is $CH_2COCH_2COCH_2$, E is CH_2CH_2, B is 1,3-disubstituted benzene. [b] Log K^f_{av} for first indicated ligand minus log K^f_{av} for the second. [c] Ionic diameters of metal ions. [d] A. F. Trotman-Dickenson, Ed., "Comprehensive Organic Chemistry", Vol. 5, Pergamon Press, Elmsford, N.Y., p 465 ff.

perimental error, had the same log K^f_{av} values for formation of complexes with each of the nine divalent ions examined (Table II). Thus the two methoxyl groups in the latter compound played no visible role in the complexation. The divalent metals in Table II are arranged in the order of their log K^f_{av} values for HAcAcH or $CH_3OAcAcOCH_3$. When these ions gather and orient single β-diketone units, their intrinsic binding power decreases in the order Cu^{2+}, UO_2^{2+}, Ni^{2+}, Co^{2+}, Zn^{2+}, Pb^{2+}, Mg^{2+}, Cd^{2+}, Mn^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}. The values range from a high of 9.5 to a low of 2.5. With 7 interesting exceptions out of 46 adjacent relationships, the same order is followed by the other 5 ligand systems that contain two β-diketone units. Thus the intrinsic affinity of each metal ion for the β-diketonide ligand generally is more important in determining this order than the gathering and partial organization of two β-diketonide units in the same organic compound.

Of the comparisons in Table II between the binding power of the mono-β-diketonides and the bis-β-diketonides for the divalent metal ions, the bis-β-diketonides gave log K^f_{av} values that exceeded those of the mono-β-diketonides (Δ log K^f_{av}) by 4.7–2.0 units in 45 out of the 51 cases examined. In the remaining six comparisons, four exhibited Δ log K^f_{av} values between 1.8 and 1.0 and two comparisons gave values of essentially zero. Of the three comparisons involving trivalent metal ions, the Δ log K^f_{av} values ranged from 6.3 to 4.7. Thus the gathering and partial organization in one molecule of two or three β-diketone units prior to complexation can provide up to about 10^6 increase in complex formation constants over what is observed when the metal ion must gather and organize its own β-diketonide units.

For the mono-β-diketonides, the greatest difference in log K^f_{av} for the different divalent ions was 7.0. For $O(EAcAcH)_2$, it was 6.8; for $O(EAcAcE)_2O$, 6.7; for $B(CH_2AcAcH)_2$, 7.5; for $B(CH_2AcAcCH_2)_2B$, 9.5; and for $O(EOAcAcOE)_2O$, 4.9.

Examination of Corey–Pauling–Koltun (CPK) molecular models of the five bis-β-diketonides demonstrated that the bridges bonding the AcAc moieties in the complexes vary in their conformational adaptability in the order OEOEO > EOE > CH_2BCH_2. The cycles contain two bridges and are much more structured than the open-chain compounds. Of the macrorings, $B(CH_2AcAcCH_2)_2B$ > $O(EAcAcE)_2O$ > $(OEOAcAcOE)_2$ in overall rigidity, whereas with the open-chain systems $B(CH_2AcAcH)_2$ > $O(EAcAcH)_2$. These structural factors correlate with the fact that the cyclic ligands show the greatest overall deviation from HAcAcH in spread of log K^f_{av} values. The largest and most flexible cycle shows the smallest spread, and the smallest and least flexible, the greatest spread.

The effect of organizing two AcAc units across from one another with two bridges to give a macrocycle vs. collecting and partially organizing them with one bridge are visible in comparisons of log K^f_{av} values for $O(EAcAcH)_2$ vs. $O(EAcAcE)_2O$ and $B(CH_2AcAcH)_2$ vs. $B(CH_2AcAcCH_2)_2B$. Formation of the cycles enhances complexation by as much as Δ log K^f_{av} = 0.9, and inhibits it by as much as 2.2.

With the relatively flexible EOE bridges, the cycle $O(EAcAcE)_2O$, without exception, provided a better ligand system than did its open-chain counterpart, $O(EAcAcH)_2$. The difference in log K^f_{av} values for these two systems ranged from 0.1 with Cu^{2+} and Mg^{2+} to 0.7 with UO_2^{2+}. Molecular models (CPK) of complexes that involved these two systems in either square-planar or tetrahedral arrangements of the four AcAc oxygens indicated compatibility with metal ions that ranged in diameter from about 1.4 to 2.1 Å.[12] Formula **20** approximates a reasonable structure for a square-planar complex of $O(EAcAcE)_2O$. The AcAcMAcAc part of complexes of $O(EAcAcE)_2O$ can also assume a tetrahedral arrangement with an internal spirane ring system. The smaller the diameter of M^{2+}, the more planar the AcAcM rings can become. By warping these inner rings, M^{2+} ions of diameters up to 2.7 Å are accommodated by both $O(EAcAcH)_2$ and $O(EAcAcE)_2O$. However, less warping is required by $O(EAcAcH)_2$ than by $O(EAcAcE)_2O$. The diameters of the M^{2+} ions studied ranged from 1.3 to 2.7 Å (Table I).

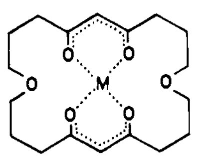
In M^{2+} complexes that involved $B(CH_2AcAcH)_2$ and $B(CH_2AcAcCH_2)_2B$, much more variation was encountered. For Zn^{2+}, Pb^{2+}, and Cd^{2+}, the cycle binds better by 0.9, 0.6, and 0.7 log K^f_{av} units, respectively. For Cu^{2+}, UO_2^{2+}, and Co^{2+}, the open-chain and cyclic ligand systems are within 0.2 unit of each other. For Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}, cyclization inhibits complexation by 1.9, 1.5, 2.0, and 1.8 log units, respectively. Thus the softer metal ions (Zn^{2+}, Pb^{2+}, and Cd^{2+}), with low-order ligand orientational preferences, are favored by the enforced organization of the cycle. The harder ions, with a square-planar ligand preference, trade the general preorganization of the cycle for the more refined ligand alignments available in the complexes of $B(CH_2AcAcH)_2$. The relatively small hard ions, such as Mg^{2+} and Ca^{2+} (1.30 and 1.98 Å, respectively), that prefer a tetrahedral orientation, and the larger ions, such as Sr^{2+} and Ba^{2+} (1.26 and 2.70 Å, respectively), that can accommodate additional solvent ligands, bind the more flexible $B(CH_2AcAcH)_2$ better than the more rigid $B(CH_2AcAcCH_2)_2B$.

Molecular model examination[12] of the complexes of $B(CH_2AcAcCH_2)B$ indicates that the macroring system is least strained with a square planar ligand arrangement. In this configuration, the system, without warping, accommodates ions up to a diameter of about 2.1 Å. The benzene rings prevent the ligand system from going to a completely tetrahedral spirane arrangement in which the AcAc units are not warped, even with an ion as small as Mg^{2+} (1.30 Å). Furthermore, the benzene rings inhibit solvation of the metal ions by water or dioxane, particularly when biased toward a tetrahedral arrangement. These two factors provide a possible explanation for the inhibition which the second CH_2BCH_2 bridge causes in the binding of Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}.

The Δ log K^f_{av} values between the cycles and their open-chain counterparts provide explanations for why some of the ring closures were templated and others were not. The log K^f_{av} value for $O(EAcAcE)_2O$ minus that for $O(EAcAcH)_2$ with Ca^{2+} was 0.4, but with Mg^{2+} was only 0.1. The calcium salt of $O(EAcAcH)_2$ ring closed, but the magnesium salt did not. A better yield of cycle should have been obtained had the zinc salt been used where Δ log K^f_{av} = 0.7. The log K^f_{av} value for $B(CH_2AcAcCH_2)_2B$ minus that for $B(CH_2AcAcH)_2$ with Mg^{2+} was −1.1, but with Ca^{2+} was −2.2. The magnesium salt of $B(CH_2AcAcH)_2$ ring closed, but the calcium salt did not. Had the cadmium salt been used where Δ log K^f_{av} = 0.7, a better yield of cycle should have been realized.

Particularly interesting are the relatively high log K^f_{av} values that result from the reactions of $O(EAcAcE)_2O$ to give neutral complexes of the physiologically important ions. Thus Cu^{2+} gave 12.1; Co^{2+}, 9.7; Zn^{2+}, 9.5; Ca^{2+}, 7.4; and Mg^{2+}, 7.2. Since Na^+ was the reference ion, $O(EAcAcE)_2O$ complexes the above ions many powers of ten better than Na^+.

Macrocycle $(OEOAcAcOE)_2$ possesses enough flexibility to adapt even to a nearly octahedral arrangement of ligands in which the oxygens centered in each of the two OEOEO bridges act as two additional ligands (according to molecular models). The EOE bridge is not long enough in $O(EAcAcE)_2O$ for such an arrangement and is only long enough in $(OEOAcAcOE)_2$ when the metal ion is 2 Å in diameter or less (model examination). This flexibility accounts for the relatively lower discriminating character of $(OEOAcAcOE)_2$ in binding M^{2+}. In models, the square-planar arrangement can accommodate ions that range from 1.4 to 2.7 Å. In the tetrahedral arrangement, ions from 1.4 to 2.0 Å fit with minor warping of the



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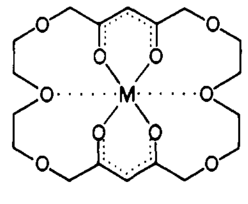

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spirane for the larger ions. In the octahedral arrangement, ions that range from 1.4 to 2.7 Å can be accommodated, with varying degrees of warping of the plane of the AcAcM units.

Formula **21** is a planar arrangement of a hexacoordinate complex of $(OEOAcAcOE)_2$, which can reorganize in any of three ways to provide an octahedral arrangement of oxygens. In two octahedral arrangements, the AcAcMAcAc system is planar. When the bridges are attached syn to one another, a formula is produced whose plane projection describes an S. In this structure, the chain organization resembles seams of a tennis ball. The structure possesses one C_2 axis, one mirror plane, and a center of symmetry. When the bridges are attached anti to one another, the formula produced projects on a plane to give an 8, which is chiral and contains two mutually perpendicular C_2 axes. When the two AcAcM rings are perpendicular to one another, the formula is chiral with no symmetry elements. In models, all three forms look equally feasible from a geometric point of view.

Molecular models of $(OEOAcAcOE)_3$ are so flexible that as many as nine oxygens, in principle, can bind to a metal. One possible arrangement resembles a three-bladed propellor with a C_3 axis, and is chiral. The higher $\Delta \log K^{f}_{av}$ values for Ce^{3+} and La^{3+} (6.3 and 5.9, respectively) compared to that for Cr^{3+} are probably associated with the larger diameters of the former ions (2.22 and 2.3 Å, respectively). The larger ions can make use of more binding sites of the cycle.

This study has demonstrated that collecting and organizing β-diketonide ligands in appropriately sized and shaped macrorings can vary the binding power of these ligands to various metal ions by up to 10^6 in formation constants. The results can be loosely rationalized in terms of complementary relationships between metal ion guests and ligand system hosts.

Experimental Section

General. Dioxane was purified by refluxing over 2 M HCl solution in water under N_2 for 20 h. The aqueous layer was saturated with KOH and separated, and the dioxane was refluxed over Na for 24 h and distilled. Dichloromethane was fractionally distilled before use. Tetrahydrofuran was dried over KOH and distilled from sodium benzophenone ketyl under N_2 just before use. Commercial acetylacetone was distilled before use. Melting points were taken on a Thomas-Hoover apparatus and are uncorrected. Mass spectra were recorded on an AEI Model MS-9 double-focusing spectrometer. The ^1H NMR spectra were taken in $CDCl_3$ at 60 MHz on a Varian T-60 or A-60 spectrometer with chemical shifts given in δ (ppm) with internal Me_4Si as standard. Infrared spectra were recorded on a Beckman 100 spectrometer. Unless noted otherwise, gel permeation chromatograms were run on a 21 ft by 3/8 in. Styragel 100 Å bead (37–70 μm particle size, exclusion limit 1500 molecular weight) column in THF solvent at 200–400 psi (flow rate 3–4 mL/min) with a refractive index detector coupled to a recorder. Sodium hydride was always used as a 50% dispersion in mineral oil.

Bis-2-(2-hydroxymethyl-1,3-dithianyl)methane (**2**). A solution of 105 mL of $BF_3{\cdot}OEt_2$ (freshly distilled), 220 mL of glacial AcOH, and 400 mL of $CHCl_3$ was stirred at reflux while a solution of 78 g (0.48 mol) of 1,1,3,3-tetramethoxypropane (Aldrich) and 102 g (0.98 mol) of 1,3-propanedithiol in 2 L of $CHCl_3$ was added over a period of 12 h. The solution was cooled, washed twice with water, dried ($MgSO_4$), and evaporated under reduced pressure. The residual solid was recrystallized from $CH_3OH-CH_2Cl_2$ to give 92 g of bis-2-(1,3-dithianyl)methane (**1**), mp 100–102 °C (77%). A solution of 36.4 g (0.145 mol) of this material in 500 mL of dry THF was cooled under N_2 to −30 °C, and 0.15 mol of 2.3 M BuLi in hexane was added by syringe. The resulting yellow solution was kept at −20 to −30 °C for 4 h, then cooled to −50 to −60 °C. Gaseous CH_2O (0.3 mol, formed by pyrolysis of 10 g of paraformaldehyde at 150 °C) was carried with a stream of N_2 through the reaction mixture stirred at −50 to −60 °C. The addition took 2 h, and the flow rate of N_2 was adjusted to avoid plugging the inlet tube. The reaction mixture was warmed and decanted from polymerized material, and the solvent was evaporated under reduced pressure. The residue was dissolved in 500 mL of CH_2Cl_2, and the solution was washed with 200 mL of 2 M sulfuric acid and then with 250 mL of water. The organic layer was dried, the solvent was evaporated, and the residue was dried on a rotoevaporator at 50 °C and 0.1 mm pressure for 15 h to give 42 g of a viscous, pale yellow oil whose ^1H NMR spectrum suggested it to be about 96% monoalcohol and 4% diol **2**. This material was dissolved in 500 mL of dry THF and treated with 0.6 mol (2 equiv) of BuLi as before, followed by 15 g of CH_2O, added as before at −50 to −60 °C. The reaction mixture was treated as before, to produce 46 g of thick, yellow oil, which was chromatographed on 1 kg of silica gel (column length 1.2 m). The column was washed with CH_2Cl_2 (1 L), 5% $(CH_3)_2CO$-95% CH_2Cl_2 (v) (3.5 L), and 10% $(CH_3)_2CO$-90% CH_2Cl_2 (v) (2.5 L). The first 2.5 L contained traces of starting material (**1**). The next 1.8 L contained 22 g of the monoalcohol (47%) useful for recycling, and the next 2.5 L contained 25 g of crude diol **2**. This material was crystallized from hexane-CH_2Cl_2 to give 22.8 g (43%) of foul-smelling crystals, mp 112–114 °C. Anal. $(C_{11}H_{20}S_4O_2)$ C, H, S.

15,18,21,24,27,30-Hexaoxa-1,5,9,13-tetrathiadispiro[5.1.5.18]-henetriacontane (**3**). A mixture of 624 mg (2 mmol) of diol **2**, 50 mL of dry THF, and NaH (360 mg, 5 mmol) was stirred under N_2 at 25 °C. Pentaethylene glycol ditosylate[13] (1.3 g, 2 mmol) dissolved in 20 mL of THF was added. The mixture was heated at reflux with stirring under N_2 for 5 h and cooled, and the NaOTs was filtered and washed with THF. The filtrate was evaporated under reduced pressure and chromatographed on alumina. The column was eluted with C_6H_6, CH_2Cl_2, and finally 10% $(CH_3)_2CO-CH_2Cl_2$ (v) to give crude cycle **3** (730 mg). This material was submitted to gel permeation chromatography on an 18 ft by 3/8 in. column of Bio-Rad SX 8 beads (1000 molecular weight exclusion limit), flow rate of THF 3 mL/min. Cycle **3** eluted as a single peak with a retention volume of 190 mL which, after drying at 40 °C for 24 h as a film, weighed 620 mg (78%): ^1H NMR δ 1.9–2.2 and 2.7–3.2 (2 m, $(CH_2)_3$, 12 H), 2.8 (s, $S_2CCH_2CS_2$, 2 H), 3.75 (broad s, OCH_2CH_2O, 20 H), 4.00 (s, OCH_2CS_2, 4 H), M^+ 414. Anal. $(C_{21}H_{38}O_6S_4)$ C, H, S.

15,18,21-Trioxa-1,5,9,13-tetrathiadispiro[5.1.5.9]docosane (**4**), **15,18,21,37,40,43-Hexaoxa-1,5,9,13,24,28,31,35-octathiatetraspiro[5.1.5.9.5.1.5.9]tetratetracontane** (**5**), **and 15,18,21,37,40,-43,59,62,65-Nonaoxa-1,5,9,13,24,28,31,35,46,50,53,57-dodecathiahexaspiro[5.1.5.9.5.1.5.9.5.1.5.9]hexahexacontane** (**6**). A mixture of 3.12 g (10 mmol) of diol **2**, 500 mg of NaH (21 mmol), and 400 mL of dry THF was stirred under N_2. After N_2 evolution stopped, 2.1 g (5 mmol) of diethylene glycol ditosylate[13] was added, and the mixture was stirred at reflux under N_2 for 4 h. According to TLC of the reaction mixture, much **2** remained, whereas ditosylate was consumed (probably by an elimination reaction). An additional 750 mg (31 mmol) of NaH was carefully added, followed by an additional 2.1 g (5 mmol) of diethylene glycol ditosylate. The mixture was stirred at reflux under N_2 for 12 h, cooled, and filtered, and the NaOTs was washed with dry THF. The filtrate was concentrated under vacuum to give 5.5 g of viscous oil, which was chromatographed on a 40 by 3 cm silica gel column in CH_2Cl_2. Material was eluted with 450 mL of CH_2Cl_2, 400 mL of 5% $(CH_3)_2CO-CH_2Cl_2$ (v), 400 mL of 20% $(CH_3)_2CO-CH_2Cl_2$ (v), and 400 mL of 30% $(CH_3)_2CO-CH_2Cl_2$ (v). Fractions of 50 mL were cut. The elution was followed on TLC silica gel plates with 5–10% $(CH_3)_2CO$ in CH_2Cl_2 (v) as developer. The mixture of cycles **4–6** was eluted by the last two solvent mixtures, and was obtained by evaporation under vacuum and drying as a film at 0.1 mm and 40 °C, wt 3.7 g (97%). Anal. $[(C_{15}H_{26}O_3S_4)_n]$ C, H, S. This mixture of cyclic oligomers gave for ^1H NMR spectra δ 1.8–2.1 and 2.8–3.1 (2 m, $(CH_2)_3$, 6 H), 2.8 (s, $S_2CCH_2CS_2$, 2 H), 3.8 (s, OCH_2CS_2, 4 H); M^+ 382 (for **4**) and M^+ 764 (for **5**) A 100-mg portion of this mixture was subjected to gel permeation chromatography in THF at 500 psi (3 mL/min) on a 12 ft by 3/8 in. column of Bio-Rad SX 8 beads. Component **6** (30%) eluted with a 90-mL retention volume, mol wt (osmometric in $CHCl_3$) 1140 (theory 1146); component **5** (60%), retention volume 775 mL, mol wt 775 (theory

764); component 4 (5%), retention volume 150 mL, mol wt 384 (theory 382).

3,5,15,17-Tetraoxo-1,7,10,13,19,22-hexaoxacyclotetracosane (8) and 3,5,15,17,27,29-Hexaoxo-1,7,10,13,19,22,25,31,34-nonaoxacyclohexatriacontane (9). The mixture of cyclic thioketals **6–8** (1.2 g, 3 mmol) was dissolved in 100 mL of THF-MeOH (1:1 by v). The solution was degassed by alternately saturating it with N_2 and then refluxing it under vacuum. Mercuric chloride (6.5 g, fourfold excess per thioketal unit) was introduced under N_2 with stirring. A suspension of mercury-sulfur compounds appeared after 4 min. Cadmium carbonate (or calcium carbonate), 5.2 g (4.5-fold excess per thioketal unit), was added under N_2, and the mixture was heated to reflux with vigorous stirring for 4 h and then filtered while hot. The precipitate was washed with four portions of THF. The filtrate was concentrated to about 5 mL under vacuum (if dried and warmed, the products decompose), and 100 mL of THF was added. The mixture was filtered, and the filtrate was shaken with an equal volume of 5 M NH_4OAc solution in water. The precipitate that formed was collected and washed with THF. The two layers of the filtrate were separated, the aqueous layer was washed with two 50-mL portions of pure ether, and the combined organic layers were washed with 50 mL of a saturated aqueous NaCl solution. The organic layer was concentrated at 25 °C under reduced pressure, the residue was dissolved in CH_2Cl_2 (50 mL), and the solution was washed with 25 mL of water. The organic layer was dried with $MgSO_4$, and the solvent was evaporated to give 600 mg of a yellow, viscous oil. This mixture of products was unstable and had to be either carried to final product or stored under argon at −20 °C. It was dissolved in 100 mL of 10% H_2O-90% CH_3CN (v), and 2 drops of concentrated H_2SO_4 was added. The initially clear solution was refluxed for 2 h, cooled, and filtered, and the CH_3CN was evaporated under vacuum at 25 °C to about 10 mL. The residue was mixed with 100 mL of CH_2Cl_2, and the organic layer was washed with 10 mL of water. The clear yellow solution was shaken with 50 mL of a 0.5 N NaOH solution in water. A reddish-brown emulsion appeared from which the aqueous layer could be removed after 2 h. The organic layer was extracted with three additional 50-mL portions of 0.5 N NaOH solutions in water. The combined light yellow basic extracts were slowly acidified at 0 °C with concentrated H_2SO_4, and the suspension that separated was extracted with four 50-mL portions of CH_2Cl_2. The combined extracts were washed with water, dried, and evaporated under vacuum to give 400 mg (60%) of an impure mixture of cyclic β-diketones. This material was submitted to gel permeation chromatography on the standard 21 ft by $^3/_8$ in. Styragel 100-Å bead column at a THF flow rate of 3–4 mL/min at 300–400 psi. Four fractions were collected: polymeric material, retention volume 120–145 ml; cycle **9**, retention volume 145–155 mL; cycle **8**, retention volume 155–170 mL; trace of monomeric cycle, retention volume 181 mL. Cycles **8** and **9** were again chromatographed to give pure samples, which were dried as films at 25 °C under high vacuum for 24 h. Cycle **8** formed a waxy solid, wt 92 mg (24%): ^{1}H NMR ($CDCl_3$) δ 3.9–4.0 (broad s, OCH_2CH_2O, 16 H), 4.1 (s, =CH–, 2 H, exchangeable with D_2O in CH_3OD), 4.2 (s, OCH_2CO, 8 H), 6.5 (s, OH, 2 H exchangeable with D_2O in CH_3OD); M^+ 404; osmometric molecular weight in $CHCl_3$, 905 at 0.050 M, 445 at 0.004 M. Anal. ($C_{18}H_{28}O_{10}$) C, H.

Cycle **9** was a viscous oil, wt 31 mg (16%): ^{1}H NMR ($CDCl_3$) δ 3.9–4.0 (broad s, OCH_2CH_2O, 24 H), 4.1 (s, =CH–, 3 H, exchangeable with D_2O in CH_3OD), 4.2 (s, OCH_2CO, 12 H), 6.5 (s, OH, 3 H, exchangeable with D_2O in CH_3OD); osmometric molecular weight in $CHCl_3$, 1300 at 0.007 M, 820 at 0.004 M (theory 606). Anal. ($C_{27}H_{42}O_{15}$) C, H.

3,5-Dioxo-1,7,10,13,16,19-hexaoxacycloheneicosane (7). By the same procedure used to convert thianyl cycles **5** and **6** to cyclic β-diketones **8** and **9**, respectively (see above), thianyl cycle **3** (0.50 g) was converted to cyclic β-diketone **7**, wt 0.10 g (25%), as a colorless oil, which was molecularly distilled at 100 °C at 0.005 mm. The compound possesses the following spectra: ^{1}H NMR δ 3.9–4.0 (broad s, OCH_2CH_2O, 20 H), 4.1 (s, =CH–, 1 H), 4.2 (s, OCH_2CO, 4 H), 6.5 (s, OH, 1 H); M^+ 334. Anal. $C_{15}H_{26}O_8$ C, H.

Bis-2-(2-methoxymethyl-1,3-dithianyl)methane. Diol **2**, 2.3 g (7.5 mmol), was mixed under N_2 with 200 mL of dry THF and 1 g (20 mmol) of NaH. The mixture was stirred for 1 h at 20 °C and cooled to 0 °C, and 10 g (80 mmol) of CH_3I was added in one portion. The mixture was stirred under N_2 for 5 h at 25 °C, and 2.0 g of methanol was carefully added. The mixture was filtered, the solvent evaporated under reduced pressure, and the residue chromatographed on 100 g of silica gel-CH_2Cl_2. The product was eluted with 10% $(CH_3)_2C{=}O$-90% CH_2Cl_2 (v), crystallized, and recrystallized from hexane-CH_2Cl_2 to give 2.1 g (83%) of product: mp 82–83 °C; M^+ 340; ^{1}H NMR ($CDCl_3$) δ 2.1–2.4 and 3.0–3.3 (2 m, $(CH_2)_3$, 12 H), 2.8 (s, $S_2CCH_2CS_2$, 2 H), 3.9 (s, OCH_3, 6 H), 4.2 (s, OCH_2CS_2, 4 H). Anal. ($C_{13}H_{24}S_4O_2$) C, H.

1,5-Dimethoxyacetylacetone (10). By the procedure used for converting dithianyl cycles **5** and **6** to cyclic β-diketones **8** and **9**, 2.0 g (5.9 mmol) of 2,4-bis[1,3-dithianyl(2)]-1,5-dimethoxypentane was converted to 0.340 g (52%) of **10** and purified by molecular distillation at 80 °C at 0.01 mm. This material possessed the same properties as reported earlier[14] for this substance.

Preparation of the Salts of 3,5,15,17-Tetraoxo-1,7,10,13,19,22-hexaoxacyclotetracosane (8). The cyclic bis-β-diketone **8** was converted to its salts as follows. A solution of **8**, 40 mg (0.10 mmol), in 2 mL of $CHCl_3$ was shaken with 2 mL of $Cu(OAc)_2$ (91 mg, 0.50 mmol) in water at pH 4.5 (adjusted with $HClO_4$). The organic layer was separated, dried over $MgSO_4$, and evaporated. The green residue was subjected to standard gel permeation chromatography in THF to give a retention volume for the salt of 165 mL and 185 mL for the acetic acid. The column eluate corresponding to the salt peak was evaporated under reduced pressure to give an amorphous, green solid, wt 35 mg (76%), transition point 196 °C dec, IR ($CHCl_3$) C=O stretch at 1580 cm^{-1}; M^+ 466. Anal. ($C_{18}H_{26}O_{10}Cu$) H. C: calcd, 46.40; found, 44.40.

Attempts to form the cupric salt in methanol led to a blue-gray, amorphous precipitate, which is probably polymeric since it was insoluble in hot water, hot pyridine, and all other organic solvents tried.

A solution of **8**, 40 mg (0.10 mmol), in 2 mL of $CDCl_3$ was shaken for 5 h with 2 mL of an aqueous solution of 0.194 g (0.50 mmol) of $UO_2(OAc)_2$ buffered to pH 5.5 with NaOAc. The yellow $CDCl_3$ layer was dried with $MgSO_4$ and evaporated under vacuum. The residue was subjected to standard gel permeation chromatography in THF, and the salt eluted with a retention volume of 165 mL and 185 mL for acetic acid. The column eluate corresponding to the salt peak was evaporated under reduced pressure. It gave an orange, amorphous residue that foamed when dried at 25 °C and 0.01 mm for 24 h to give 51 mg (77%) of salt, transition point 153 °C dec; M^+ 672; IR ($CDCl_3$) (C=O stretch) 1583 cm^{-1}. Anal. ($C_{18}H_{26}O_{12}U$) C, H.

A solution of **8**, 40 mg (0.10 mmol), was dissolved in 2 mL of dry methanol. This solution, under N_2, was added slowly, with stirring, to a violet solution of 21 mg (0.21 mmol) of $Co(OAc)_2$ in methanol (2 mL). The red solution was stirred for 5 min, the methanol was evaporated under reduced pressure, and the residue was extracted with dry THF and filtered. The THF solution was evaporated, and the violet residue was extracted with CH_2Cl_2. The mixture was filtered and evaporated under reduced pressure to give a violet, amorphous foam, 25 mg (56%), after drying for 24 h at 0.01 mm. This material gave a transition point at 132 °C dec; IR ($CDCl_3$) (C=O stretch) 1585 cm^{-1} Anal. ($C_{18}H_{26}O_{10}Co$) H. C: calcd, 46.86; found, 44.40. This complex slowly decomposed when exposed to air.

8-Oxo-2,4,12,14-tetraoxapentadecane (11). To a solution of 10 g (0.10 mol) of freshly distilled acetylacetone in 300 mL of dry THF stirred at 0 °C under N_2 was carefully added 5 g (0.10 mol) of NaH. A white precipitate formed immediately. The mixture was stirred for 30 min at 0 °C, and 50 mL of a 2 M solution of BuLi in hexane (0.10 mol) was added through a syringe. The resulting suspension was stirred at 0 °C for 30 min, and 12 g (29 mmol) of diethylene glycol ditosylate[13] in 150 mL of dry THF was added dropwise, with stirring, at 0 °C under N_2. The reaction mixture was stirred for 8 h at 25 °C, ice was carefully added to destroy excess NaH, and the reaction mixture was poured into 500 g of ice and 400 mL of 6 N HCl solution. The aqueous solution was extracted with three portions of ether. The combined ether extracts were washed with 200-mL portions of water, dried with Na_2SO_4, and evaporated. The brownish-yellow residual oil was dried as a film for 24 h under vacuum to remove the excess acetylacetone. It was then dissolved in 250 mL of dry methanol, and this solution was added dropwise with stirring to a solution of 7 g of $Cu(OAc)_2$ in 80% CH_3OH-20% H_2O (v). The light blue precipitate was filtered and washed with methanol. The resulting paste was suspended in 400 mL of dry ether, stirred vigorously, and filtered. This procedure was repeated until the filtrate was colorless. The solid was dried under vacuum for 20 h at 20 °C and pulverized. This powdered copper complex was suspended in 300 mL of warm $CHCl_3$, and the mixture was shaken with 200 mL of 6 N aqueous HCl solution and finally heated and mixed until the suspension dissolved. The organic layer was washed with 200 mL of 6 N HCl solution and 200 mL of water. It was dried with $MgSO_4$ and evaporated under reduced pressure to give a yellow oil, which after film drying at 0.01 mm for 24 h at 25 °C solidified to give 5.4 g (70%) of **11**, sufficiently pure for preparation of **12**. A 1.0-g sample of crude **11** was recrystallized from ether-pentane to give 500 mg (35%) of pure **12**: mp 36-37 °C; osmometric molecular weight in $CHCl_3$ 270 at 0.048 M and 272 at 0.0048 M; M^+ 270; ^1H NMR spectrum ($CDCl_3$) δ 1.9-2.9 (m, $COCH_2CH_2$, 8 H), 2.1 (s, CH_3, 6 H), 3.2-3.4 (t, CH_2OCH_2, 4 H), 5.7 (s, =CH-, 2 H). In 1:1 (v) CH_3OD-D_2O, complete vinyl proton-deuterium exchange took about 20 h at 20 °C. Anal. ($C_{14}H_{20}O_5$) C, H.

***m*-Bis(2,4-dioxo-1-pentyl)benzene (13).** This procedure for the preparation was modeled after that for **11**, except that 15 g (0.15 mol) of acetylacetone, 7.5 g (0.15 mol) of NaH suspension, 60 mL of 2.5 M BuLi (0.15 mol), 13 g (50 mmol) of 2,6-bis(bromomethyl)benzene, and 450 mL of dry THF were used. The initially dried crude product was dissolved in a minimum of benzene and chromatographed on 120 g of silica gel-benzene. The forerun contained mineral oil, and the product eluted with CH_2Cl_2 and 5% $(CH_3)_2CO$-CH_2Cl_2 (v). This material was dissolved in 150 mL of dry methanol and added, dropwise, to a solution of 20 g of $Co(OAc)_2$ in 300 mL of dry methanol. A pink precipitate formed, the mixture was stirred for 2 h and filtered, and the cake was washed with methanol and ether until the washings were colorless. This solid was dried for 20 h at 0.01 mm and 25 °C to give 19 g (95%) of salt. This material was powdered and shaken with 500 mL of $CHCl_3$ and 300 mL of 6 N HCl in water until no solid remained. The organic layer was dried ($MgSO_4$) and evaporated under vacuum, and the residual mobile yellow oil was dried for 20 h at 0.01 mm and 25 °C to give 13.6 g (90%) of crude **13**, suitable for use in the next step. A 1.0-g sample of **13** was chromatographed on the standard gel permeation column to give a retention volume of 173 mL. The final dried product **13** (0.9 g, 81%) was a colorless oil: M^+ 302; osmometric molecular weight in $CHCl_3$ 304 at 0.0320 M and 300 at 0.0032 M; ^1H NMR spectrum ($CDCl_3$) δ 2.1 (s, CH_3, 6 H), 2.6-3.2 (m, $(CH_2)_2$, 8 H), 3.8 (broad s, OH, 2 H), 5.8 (s, =CH-, 2 H), 7.1-7.6 (m, ArH, 4 H). In 1:1 (v) CH_3OD-D_2O at 20 °C, the vinyl protons took about 20 h to completely exchange with deuterium. Anal. ($C_{18}H_{22}O_4$) C, H. Compound **13** readily formed a Cu^{2+} complex in CH_3OH, which was recrystallized from $CHCl_3$-octane (2:1, v), mp 260-261 °C.

Preparation of the Calcium Salts of 11 and 13. The bis-β-diketone **11** or **13** (2-8 g) was dissolved in 100-500 mL of dry THF under N_2, and a large excess of finely ground CaH_2 was added along with 5-10 drops of dry methanol. The heterogeneous reaction mixture was stirred at reflux under N_2 for 20 h and filtered while hot through Celite. The filtrate was evaporated under vacuum, and the residue as a yellow foam was dried at 0.01 mm and 25 °C for 24 h. The two Ca complexes were obtained in essentially quantitative yield and were homogeneous to TLC on silica gel plates (10% $(CH_3)_2CO$-90% CH_2Cl_2, v), and both gave IR spectra ($CDCl_3$) that had no OH band, but C=O bands at 1700 cm^{-1} and C=C bands at 1600-1610 cm^{-1}.

Preparation of Magnesium Salts of 11 and 13. The bis-β-diketone **11** or **13** (2-8 g) was dissolved in 100-500 mL of dry THF under N_2. A large excess of Mg turnings (rubbed in a mortar under dry Et_2O and dried for 1 h at 80 °C under N_2) was added. After addition of 10-20 drops of dry methanol and a crystal of I_2 the mixture was refluxed with stirring for 20 h. The mixture was then filtered while hot, and the solvent was evaporated under vacuum to give a quantitative yield of the Mg salt as a foam, homogeneous by TLC, and characterized by IR spectroscopy ($CDCl_3$): OH bands absent, C=O band at 1705 cm^{-1} and C=C at 1600-1610 cm^{-1}.

1,11-Dioxo-5,7,15,17-tetraoxacycloeicosane (12). To 2.0 g (2.8 mL, 20 mmol) of freshly distilled diisopropylamine in 200 mL of dry THF at 0 °C was added, with stirring under N_2, 8 mL of 2.5 M BuLi (20 mmol) in hexane. The Ca salt of **11** (3 g, 10 mmol) in 200 mL of THF and 100 mL of freshly distilled hexamethylphosphoramide was added with stirring at 0 °C. After 1 h, the homogeneous yellow solution was diluted to 1 L with dry THF, and 4 g (10 mmol) of diethylene glycol ditosylate was added. The mixture was stirred under N_2 for 20 h at 24 °C and poured onto 1 L of ice-6 N HCl mixture. The product was extracted with three 200-mL portions of ether. The combined extracts were washed with two 200-mL portions of water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on 60 g of silica gel-CH_2Cl_2, and the column was washed with 500 mL of CH_2Cl_2, 250 mL of 5% $(CH_3)_2CO$-95% CH_2Cl_2 (v), and 600 mL of 10% $(CH_3)_2CO$-90% CH_2Cl_2 (v). The elution of materials was followed by silica gel TLC. The bis-β-diketones were detected by the color they produced with $FeCl_3$ in methanol. They appeared in the later column fractions. They were evaporated under vacuum and chromatographed on the standard gel permeation column to give, after evaporation of the eluate and drying of the residue's four materials: polymer, retention volume 120 mL (120 mg, 3.5%); the cyclic dimer of **12**, 60 mg (2%), retention volume 150 mL; cycle **12**, 540 mg (16%), retention volume 158 mL; starting material **11**, 2.0 g, retention volume 172 mL. Cycle **12** was rechromatographed to give 500 mg (15%) of material that crystallized after drying at 0.01 mm for 24 h: mp 32-34 °C; M^+ 340; ^1H NMR spectrum ($CDCl_3$) δ 1.9-3.0 (m, $COCH_2CH_2$, 16 H), 3.2-3.8 (t, CH_2OCH_2, 8 H), 5.8 (s, =CH-, 2 H). Anal. ($C_{18}H_{28}O_6$) C, H.

When the Mg salt of **11** was treated by the same procedure, only polymer and the cyclic dimer of **12** (15%) were detected.

3,5,16,18-Tetraoxo[7.7]metacyclophane (14). To a solution of 1.65 g (1.2 mL, 15 mmol) of diisopropylamine (freshly distilled from CaH_2) in 100 mL of dry THF stirred at 0 °C under N_2 was added slowly 6 mL of a 2.5 M solution of BuLi in hexane (15 mmol). The mixture was stirred for 30 min at 0 °C. To this material was added, with stirring under N_2 at 0 °C, 2.4 g (7.5 mmol) of the Mg salt of **13** dissolved in 100 mL of THF and 100 mL of hexamethylphosphoramide freshly distilled from CaH_2, followed by 500 mL of dry THF. To the resulting solution was added with stirring under N_2 at 20 °C 2.1 g (9 mmol) of 1,3-bis(bromomethyl)benzene. The reaction mixture was stirred for 20 h at 20 °C, mixed with 1 L of an ice-6 N HCl mixture, and extracted with three 300-mL portions of ether. The combined extracts were washed twice with 200 mL of water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on 60 g of silica gel as was done in the isolation of **12**, the bis-β-diketones being recognized by their $FeCl_3$ color tests. The diketonide products were submitted to standard gel permeation chromatography to give four fractions: polymer, 350 mg (12%), retention volume 127 mL; the cyclic dimer of **14**, 350 mg (12%), retention volume 149 mL; cycle **14**, 390 mg (13%), retention volume 157 mL; starting material **13**, 800 mg (35%), retention volume 172 mL. Cycle **14** was rechromatographed to give 350 mg (12%) of **14** as a glass after film drying for 24 h at 25 °C: M^+ 404; ^1H NMR ($CDCl_3$) δ 2.4-3.2 (m, CH_2CH_2, 16 H), 5.4 (s, =CH-, 2 H), 6.8-7.4 (m, ArH, 8 H). Anal. ($C_{26}H_{28}O_4$) C, H.

When the calcium salt of **12** was submitted to the above procedure, only polymer and the cyclic dimer of **14** (16%) could be detected.

2,6-Bis(3,5-dioxo-1-hexyl)pyridine (15). This procedure was modeled after that for preparation of **11**, except that the materials used were 15 g (0.15 mol) of acetylacetone, 7.5 g (0.15 mol) of NaH suspension, 62.5 mL (0.15 mol) of BuLi (2.4 M in hexane), 600 mL of dry THF, and 13.25 g (0.05 mol) of 2,6-bis(bromomethyl)pyridine.[15] At the end of the reaction, the reaction mixture was poured onto 1 L of ice water and brought to pH 8 with aqueous $NaHCO_3$ solution. The aqueous phase was extracted with three 250-mL portions of ether. The combined organic layers were washed with 100 mL of water, dried (Na_2SO_4), and evaporated under reduced pressure. The yellow oil produced was chromatographed on 120 g of silica gel-benzene. The product that eluted with 9:1 (v) CH_2Cl_2-Et_2O was chromatographed on the standard gel permeation chromatographic column, except that CH_2Cl_2 was the solvent. Product **15** eluted with a retention volume of 190 mL to give, after drying as a film, 6.2 g (41%) as an oil. An analytical sample was molecularly distilled at 140 °C (0.05 Torr): M^+ 303; ^1H NMR spectrum ($CDCl_3$) δ 2.02 (s, enol CH_3), 2.20 (s, ketone CH_3), 2.53-3.30 (m, CH_2CH_2, 8 H), 3.70 (s, $COCH_2CO$), 5.50 (s, =CH-), 6.83-7.60 (m, ArH, 3 H), 13-14 (broad s, OH); IR (neat) C=O stretch, 1695, 1715 cm^{-1} (shoulder). From the integrations of the CH_3, $COCH_2CO$, and =CH- protons, the β-diketones appeared to be about two-thirds enolized. Anal. ($C_{17}H_{21}NO_4$) C, H.

When shaken with a $CDCl_3$-D_2O mixture, the OH, =CH-, and $COCH_2CO$ protons of **15** were exchanged.

The magnesium salt of **15** was prepared (as was that of **13**), M^+ 325, mp 220-230 °C dec. Attempts to ring close **15** through the reaction of its dianion with 2,6-bis(bromomethyl)pyridine led to a mixture of C- and O-alkylation products.

3-Chloromethyl-5-hydromethylisoxazole (16). A solution of 50 g (0.40 mol) of 1,2-dichloroacetaldehyde oxime[8] (made and purified without delay, and used either immediately or stored at −20 °C) in 300 mL of propargyl alcohol was cooled to 0 °C. Triethylamine (30 g, 0.4 mol) was added dropwise with stirring, and the homogeneous solution was allowed to warm to 24 °C over a 12-h period. The solution was poured onto a mixture of 700 g of ice and 2 N H_2SO_4, and the resulting mixture was extracted with three portions of ether, 250 mL each. The combined organic layers were washed with water (twice, 200 mL each), dried, and evaporated under vacuum, finally on a rotavap at 60 °C and 1 mm to evaporate the excess propargyl alcohol. The residue was chromatographed on 1 kg of silica gel, which was washed with benzene-$CHCl_3$ mixtures that ranged from 4:1 to 1:4 (v), then CH_2Cl_2, then 1:20 $(CH_3)_2CO$-CH_2Cl_2 (v), and finally 1:10 $(CH_3)_2CO$-CH_2Cl_2 (v). The isoxazole product was eluted in the last fractions, which were evaporated under vacuum to give 21 g (35%) of **16** as an oil, usable in the next step. A small amount of this sample was molecularly distilled at 80 °C and 0.1 mm. Anal. ($C_5H_6NO_2Cl$) C, H. Both 1,2-dichloroacetaldehyde oxime and **16** cause skin rashes on repeated exposure and should be handled with great care.

3,6,10,13,17,20-Hexaoxo-7,14,21-triazatetracyclo[17.2.1^{5,8}.1^{12,15}]-tetracosa-1(21),5(23),7,12(24),14,19(22)-hexaene. Chloro alcohol **16**, 500 mg (3.2 mmol), was dissolved in 50 mL of dry THF. To this solution stirred under N_2 was added 300 mg of NaH, and the mixture was stirred at reflux for 3 h. The mixture was filtered, and the filtrate was evaporated under reduced pressure. The residue was chromatographed on 30 g of silica gel, and material was eluted with 300 mL of CH_2Cl_2 and 500 mL of 1:20 (v) $(CH_3)_2CO$-CH_2Cl_2. Evaporation of the column eluates gave 100 mg of material that was submitted to standard gel permeation chromatography. Three bands were collected: polymer, retention volume 125-155 mL; tetrameric cycle, retention volume 155-165 mL; trimeric cycle (**17**), retention volume 165-175 mL. The cyclic trimer crystallized, and then was recrystallized from hexane-CH_2Cl_2 to give 38 mg (10%) of **17**, mp 67-68 °C, M^+ 333. Anal. ($C_{15}H_{15}N_3O_6$) C, H. The cyclic tetramer (10%) was characterized only by its mass spectrum of M^+ 444.

Determination of pK_a Values of β-Diketones.[11b] A stock solution was prepared 0.050 M in $NaClO_4$ and 0.0200 M in $HClO_4$ in 1:1 (v) water-dioxane. The water used was deionized and free of CO_2, and the dioxane carefully purified (see General section). The pH measurements were made with a 0-14 rugged pH glass electrode (Corning) with a calomel reference electrode and Beckman Model H2 pH meter. The meter was calibrated with the stock solution at pH 1.7. Titrations of a 25-mL aliquot of 0.020 M $HClO_4$ in CO_2-free water alone compared to those in 1:1 (v) water-dioxane showed no difference in pH readings. A stock solution of 1.00 N NaOH in CO_2-free water was prepared and was added via a 2-mL Koch buret accurate to 0.01 mL. All measurements of pH in this and the next section were done at 24 ± 0.1 °C under a N_2 atmosphere. Particular care was taken to exclude CO_2 in the titration of the monoanion of $B(CH_2AcAcCH_2)_2B$ and to exclude O_2 in the titrations that involved Co^{2+} and Ni^{2+} ions. In the pK_a determinations, a weighed amount of material to be titrated, about 1 mmolar equiv of β-diketone unit (e.g., 0.33 mmol of $(OEOAcAcOE)_3$, 0.50 mmol of $(OEOAcAcOE)_2$, or 1.00 mmol of $CH_3OAcAcOCH_3$), was dissolved in 0.30 mL of purified dioxane and added to 10 mL of the acidic stock solution, which was titrated with the stock basic solution. The pH and the volume of titrant added were recorded for 20-30 points. The average number of protons attached to the ligand, $\bar{n}_H = [NaOH]/C_L$ (where C_L = concentration of β-diketone unit equivalent used), was tabulated and plotted against pH. At $\bar{n}_H = 0.5$, $pK_a^1 = pH$; at $\bar{n}_H = 1.5$, $pK_a^2 = pH$; at $\bar{n}_H = 2.5$, $pK_a^3 = pH$. For example, with acetylacetone, 100 mg (1 mmol) was titrated and the pK_a was obtained from the midpoint of the titration curve. Table I records the pK_a values obtained for the eight β-diketones studied.

In the titrations, equilibration was instantaneous in all cases except for the loss of the second proton from $B(CH_2AcAcCH_2)_2B$ (**14**). It took about 1 h to establish equilibrium after adding 1 drop of base. A crude estimate of an assumed monomolecular rate constant for the reaction ($LH^- + H_2O \rightleftarrows L^{2-} + H_3O^+$) is $4 \times 10^{-4}\ s^{-1}$.

Determination of Formation Constants (K^f_{av}) for the Metal β-Diketonide Complexes. The method used is essentially that which Calvin and Wilson[11a] used for the determination of the average stability constants, as defined in eq 3-5, in which L stands for β-diketonide units and M stands for divalent metals.[11a,b] Those for the trivalent ions are defined by eq 6-9. The average formation constants (K^f_{av}) for the complexes are related to the stability constants by eq 10.

$$ML_2 \rightleftarrows ML^+ + L^- \qquad K^M_1 \tag{3}$$

$$ML^+ \rightleftarrows M^{2+} + L^- \qquad K^M_2 \tag{4}$$

$$ML_2 \rightleftarrows M^{2+} + 2L^- \qquad K^M_{av} \tag{5}$$

$$ML_3 \rightleftarrows ML_2^+ + L^- \qquad K^M_3 \tag{6}$$

$$ML_2^+ \rightleftarrows ML^{2+} + L^- \qquad K^M_4 \tag{7}$$

$$ML^{2+} \rightleftarrows M^{3+} + L^- \qquad K^M_5 \tag{8}$$

$$ML_3 \rightleftarrows M^{3+} + 3L^- \qquad K^M_{av} \tag{9}$$

$$K^f_{av} = 1/K^M_{av} \tag{10}$$

Stock solutions of the metal nitrates that were 0.020 M were prepared in 250-mL volumetric flasks by dissolving 5 mmol of the salt in 250 mL of a 1:1 (v) purified dioxane-water mixture that was 0.020 M in $HClO_4$ and 0.050 M in $NaClO_4$. A 25.0-mL aliquot of this solution was pipetted into a 40-mL flask that was maintained at 24 °C and fitted with a magnetic stirrer. A 1 mmol β-diketone equiv of cycle or open-chain model was added dissolved in 0.30 mL of purified dioxane. This solution was titrated with a 1.00 N NaOH solution in CO_2-free water, as in the pK_a determinations. The pH and the amount of titrant were recorded, as in the pK_a determinations. Equilibria were established essentially instantaneously in these titrations.

The parameter $\bar{n}$ (average number of ligands around the central ion) was calculated from eq 11.[11a,b] In this equation, [NaOH] was

$$n = \frac{[NaOH] + [H^+] - C_{HClO_4}}{C_M}$$

$$\bar{n} = \frac{[NaOH] - C_{HClO_4}}{C_M} \text{ (at pH >3.3)} \tag{11}$$

obtained from the increments of base solution which were introduced, and C_{HClO_4} and C_M were concentrations of the perchloric acid and metal salt used, respectively; $[H^+]$ was neglected at pH >3.3. No volume corrections were made for the small amounts of NaOH and β-diketone solutions that were added. This neglect introduced small errors into the absolute value of K^f_{av}, but should not affect their relative values. Values of $-(\log a)$ (a is the free ligand concentration) for the divalent ions were calculated from eq 12.[11a,b] Equation 13 was

$$-\log a = pK_a^2 - pH - \log (C_L - \bar{n}C_M) \tag{12}$$

$$-\log a = pK_a^3 - pH - \log (C_L - \bar{n}C_M) \tag{13}$$

used for the trivalent ions. In these equations, C_L is the concentration of β-diketone equivalents used in the experiments. Bjerrum curves of $\bar{n}$ plotted against $-(\log a)$ were prepared. Values of $-\log K^M_{av}$ were determined at $\bar{n} = 1$ for the divalent and at $\bar{n} = 3/2$ for the trivalent metal ions. Values of $\log K^f_{av}$ were calculated from $-\log K^M_{av}$ values and eq 10. Table II records the $\log K^f_{av}$ values for the di- and trivalent metal salts and the various ligand systems examined.

After a determination of K^f_{av}, the titrated solution was carefully acidified with concentrated $HClO_4$ solution to about pH 1, and 50 mL of water was added. The ligand was extracted with four portions of CH_2Cl_2. The combined organic layers were washed with 25 mL of water, dried over $MgSO_4$, and evaporated to give a nearly quantitative recovery of ligand. All recovered ligands were subjected to standard gel permeation chromatography, gave the same retention volumes as the original pure samples, and were free of impurities.

References and Notes

(1) The authors thank the Division of Basic Energy Sciences of the Department of Energy for a contract (AT(04-3)34, P.A. 218), which supported this research.

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(6) We are grateful to Dr. Peter Stückler, who prepared **15** and carried out the attempted ring closures.

(7) We warmly thank Dr. Robert Stevens for this suggested synthesis.

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Host–Guest Complexation. 16. Synthesis and Cation Binding Characteristics of Macrocyclic Polyethers Containing Convergent Methoxyaryl Groups[1,2]

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Abstract: The syntheses and free energies of association of 12 new macrocyclic ligand systems (hosts) with alkali metal and ammonium and alkylammonium picrates in $CDCl_3$ are reported at 25 °C. Ten of the hosts were composed of 4-methylanisole units (abbreviated AN) incorporated into the macroring by substitution at their 2,6 positions by CH_2O (MO) units, or by direct attachment to other AN units at *their* 2,6 positions. The macrorings were completed with CH_2CH_2 (E) units and additional ether oxygens (O). Their structures were AN(MOEO)$_2$E (**22**), AN(MOEOE)$_2$O (**23**), AN(MOEOEO)$_2$E (**24**), AN(MOEOM)$_2$AN (**31**), AN(MOEOEOM)$_2$AN (**32**), ANAN(MOEO)$_2$E (**33**), ANAN(MOM)$_2$ANAN (**35**), ANAN(MSM)$_2$ANAN in which S is sulfur (**36**), ANANAN(MOE)$_2$O (**37**), and ANANAN(MOM)$_2$AN (**38**). The other two ligand systems were (AN)$_2$**DP**(OEOEO)$_2$E (**39**) and DP(OEOEO)$_2$E (**40**), in which DP = 5,5′-dimethyldiphenyl substituted in the 2,2′ positions with O and the 3,3′ positions with either H or 2-methoxy-5-methylphenyl (AN) groups. These systems were compared with model macrocyclic ethers not containing anisole units. Generalizations are as follows. The $-\Delta G_{av}°$ of association of hosts (kcal/mol) in $CDCl_3$ with Li^+, Na^+, K^+, Rb^+, Cs^+, and NH_4^+ picrates allowed the hosts to be graded as general ligand systems as follows: ANANAN(MOE)$_2$O (10.2); dicyclohexano-18-crown-6 (9.3); (AN)$_2$DP(OEOEO)$_2$E (9.0); 2,3-naphtho-18-crown-6 (8.7); ANAN(MOEO)$_2$E (8.2); DP(OEOEO)$_2$E (7.1); AN(MOEOE)$_2$O (7.0); AN(MOEOEO)$_2$E (6.6); ANANAN(MOM)$_2$AN (5.8); 1,3-benzo-18-crown-5 (5.7); AN(MOEO)$_2$E (5.5); AN(MOEOEOM)$_2$AN (5.0); AN(MOEOM)$_2$AN (4.5); ANAN(MOM)$_2$ANAN (4.4); ANAN(MSM)$_2$ANAN (4.1). General ion selectivity of each ligand system was measured by the difference in free energies between the best and poorest bound of the picrate salts, $-\Delta(\Delta G_{max})$ (kcal/mol). The order was as follows: ANANAN(MOE)$_2$O (5.3), $Na^+ > Li^+$; (AN)$_2$DP(OEOEO)$_2$E (4.8), $K^+ > Li^+$; 2,3-naphtho-18-crown-6 (4.8), $K^+ > Li^+$; 1,3-benzo-18-crown-5 (4.2), $NH_4^+ > Li^+$; dicyclohexano-18-crown-6 (4.1), $K^+ > Li^+$; ANANAN(MOM)$_2$AN (3.8), $Na^+ > Li^+$; ANAN(MOEO)$_2$E (3.3), $K^+ > Li^+$; AN(MOEOEO)$_2$E (3.2), $Cs^+ > Li^+$; AN(MOEOE)$_2$O (3.1), $K^+ > Li^+$; DP(OEOEO)$_2$E (2.6), $K^+ > Li^+$; AN(MOEOEOM)$_2$AN (1.6), $K^+ > Li^+$; ANAN(MSM)$_2$ANAN (1.1), $K^+ > NH_4^+$; AN(MOEO)$_2$E (1.0), $K^+ > Li^+$; AN(MOEOM)$_2$AN (0.9), $K^+ > Li^+$. These results demonstrate that, when the oxygens of anisole units are held in sterically enforced conformations which make the unshared electron pairs provide the lining of partially spherical cavities, the anisole units become better and more selective complexers of anions than the now classic crown ether compounds. Such conformations are observed only when *m*-teranisyl units are incorporated in macroring systems.

Aryl units possess certain properties useful in the design and synthesis of host compounds. Aromatic nuclei and their attached atoms ordinarily are coplanar and tend to rigidify molecules of which they are a part. They possess many substitutable positions for placement of functional groups in desired positions of hosts. The electronic character of aromatic systems can be varied over a wide range by attachment of appropriate substituents. Aryl units provide hosts with physical properties that aid experimental manipulation and detection. Their magnetic ring currents are sometimes useful in the determination of the structures of complexes in solution. Aryl-aryl bonds are stable to most chemical reagents and to irradiation. Appropriately substituted polyaryl units possess enforced conformations that provide hosts with desired symmetry properties. Polyaryl units incorporated in macrocycles can be used to prevent cavities designed for guest complexation from being blocked by flexible chains folding back on themselves.

This paper reports the synthesis and ligand properties of 12 new hosts designed to bind metal and ammonium cations. The binding sites are $ArOCH_3$ and CH_2OCH_2 units strung together in various combinations that provide differing degrees of enforced molecular organization. The overall goal of the research was to identify structural parameters that control the complementary relationships between potential ligand systems and metal, ammonium, and alkylammonium cations. A second goal was to develop feasible methods of synthesizing rigid polyaryl systems, and a third was to determine the utility of Corey–Pauling–Koltun (CPK) molecular models in predicting and correlating the binding properties of molecules.

Results

Design and Synthesis of Ligand Systems. The new macrocycles studied all contain one to four 4-methylanisole groups incorporated into the major ring system by substitution in their

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