Cooperative Metal Ion Binding by Metal-Organized Crown Ether

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Abstract: Host molecules which satisfy both facile synthesis and strong as well as selective binding of metal ions have been developed by introducing an idea of metal-assisted organization of linear molecules into crown ethers. For this purpose, an oligo(oxyethylene) prehost having two β-diketone units in both terminal positions was synthesized. Intramolecular coordination of the two β-ketones to divalent transition metals, Cu, Zn, or Ni, organized the linear prehost into a macrocyclic pseudo crown structure. The crystal structure of the Cu-organized host and K^+ picrate complex was analyzed by X-ray crystallography. The structure elucidated indicated that the intramolecular coordination of β-ketoenolate oxygens to the transition metal furnished an organized cavity into which the potassium cation was entrapped. The metal-organized crowns showed a good size-fit selectivity, characteristic of macrocycles, and a superior extraction efficiency when compared with dibenzo-18-crown-6 as a reference compound for the picrate extraction of alkali and alkaline earth metal cations. These characteristics have been ascribed to the existence of polar bonds between negatively charged enolate oxygens and transition metals and illustrates the power of the self-organization method in preparing the host.

Introduction

Crown ether chemistry has established the preorganization principle for obtaining host molecules which bind a variety of guests strongly with high selectivities. Preorganized hosts recognizing guest molecules started with a planar macrocyclic structure.[1] The dramatic success in obtaining large stability constants as well as size selectivities directed the molecular design toward a more sophisticated bicyclic structure which wraps guest molecules more completely using a three-dimensional arrangement of coordinating atoms.[2] Conformational restriction of such bicyclic hosts into rigid caged compounds led to a further increase in the stability and selectivity in host−guest molecular recognition [Scheme 1].[3] Such an evolutionary process, for example, a Pedersen−Lehn−Cram route, has formed a clear philosophical backbone for the development of host−guest chemistry. Along this route, the chemistries of crown ether and other macrocyclic and bicyclic molecules have fluorished over the last few decades.[4−7] The synthetic pathway for obtaining better preorganized, i.e., necessarily more and more sophisticated, hosts has proceeded mostly via chemical bond formation. This is understood to be a reasonable selection in view of the recent great advancement of powerful synthetic organic methodology which can synthesize any complex molecule, once the structure has been established.

At the same time, molecules for real use need to be synthesized in the simplest way possible. We therefore started to develop a route,[8,9] in which some critical chemical bonds in the host were substituted by metal−ligand coordination bonds. Since the final host is necessarily the most complicated in the whole course of the synthetic pathway, it seems rational to introduce the metal−ligand coordination bond in the last step of the synthesis. By this substitution, the final host is constructed from the corresponding prehost, the target molecule for the chemical-bond synthesis. If the final host is designed as a bicyclic or a monocyclic molecule, the synthetic target molecule is reduced to a monocyclic or a linear molecule, respectively, and the synthetic burden may be lightened significantly. This situation is illustrated by the inset of Scheme 1.

Such metal-assisted organization is generally applicable to the synthesis of any macrocyclic host for cationic, anionic as well as neutral guests. In this report, the design will be focused on cation-recognizing hosts. Since the resulting metal (M_1) organized hosts are designed to accommodate a second metal cation M_2 into the newly organized cavity, in other words to cooperatively bind M_2 by the introduction of M_1 into the prehost, they must not have an overall positive charge. Since metal−ligand coordination bonds are both strong and inert to exchange, employment of transition metals for M_1 seems advantageous. In this case, the terminal functional groups to accommodate M_1 should consist of anionic chelating units, which neutralize the positive charge of the transition metal M_1 and are further expected to show strong enthalpic stabilization of the binding of M_2. The use of a chelating anion constitutes a basic advantage of the present approach for the cooperative incorporation of the second metal ion and differentiates this method from

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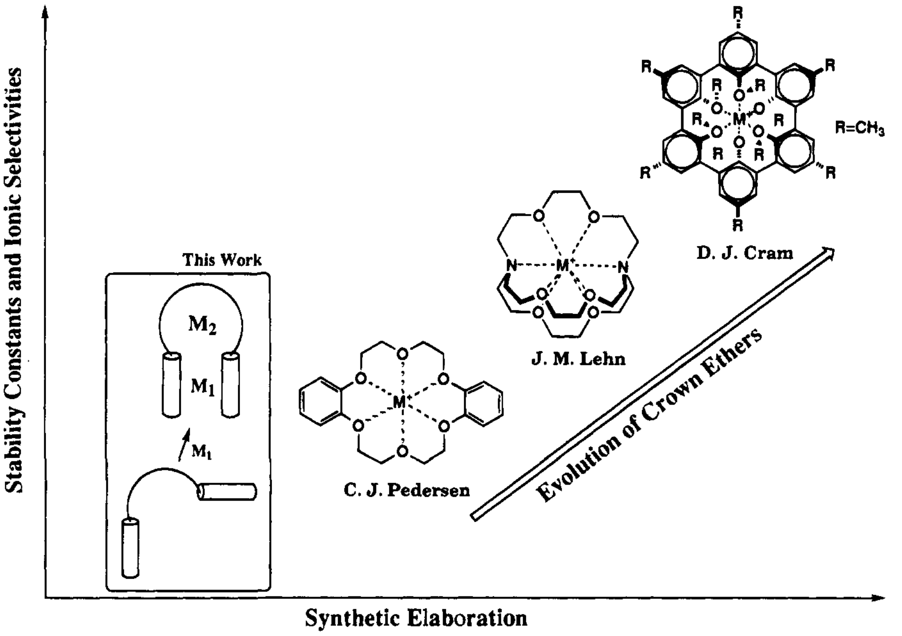
Scheme 1. Evolution of the Concept of Crown Ethers and the Basic Idea for the Organization of Pseudo Crown Ethers by the Metal Coordination



other approaches, where neutral prehost molecules are employed.[10-12] In these cases, the introduction of a positive charge by M_1 resulted in a considerable decrease in the binding of the second metal cation. In other words, negative cooperativity was observed for two cation-binding since Coulombic repulsion overwhelmed the conformational arrangement. Positive cooperativity was observed only for the binding of nonionic metal complexes, where Coulombic repulsion in the complex was eliminated.[13] Alternatively, a cationic organized host was employed for the hydrophobic binding of aromatics in aqueous media.[14] Organization of linear anionic ligands by transition metal cations was applied to the selective binding of alkali metal cations,[15a] but the subsequent structural analysis suggested that the binding mode was different from the expected metal organization.[15b,16] Transition metal complexation of macrocyclic shiff bases afforded heterodinucleating cyclic ligands having sites of two different nature[17] or a binding site for neutral molecules.[18]

Additional benefits can be expected from the introduction of a transition metal into the host. First, transition metals favor a discrete stereochemical structure, planar, tetrahedral, octahedral, and others. The choice of transition metal and/or the valence state may control the final stereochemical structure of the host. It may also be possible to introduce an additional ligand to M_1 by the use of a vacant coordination site, if any, to control the hydrophilic/hydrophobic character of the host and to supply an incremental unit stabilizing M_1. Once the host accommodates M_2 into the organized central hole, the transition metal may be oxidized to switch off M_2. This may introduce an on-off switching of metal ion binding coupled with electrochemical oxidation-reduction processes.

In previous communications,[8,9] we presented examples of metal-assisted self-organization, where catechol and β-diketone was attached to both terminals of oligo(oxyethylene) as the metal chelating functionality. A high binding efficiency and clear hole size selectivity were observed for the complexation of alkali metal ions. Here we would like to report the synthesis of a new series of pre- and metal-organized hosts and present evidence for the molecular design where the transition metal-assisted macrocycle really *accommodates another metal cation into the newly organized hole of the pseudocrown type host* as illustrated by crystallographic analysis. The advantage of the use of a metal-assisted host over a typical crown host, dibenzo-18-crown-6, will be demonstrated by using Cu, Zn, and Ni-assisted bis(β-diketonate) polyether macrocycles for the selective extraction of alkali and alkaline earth metal cations.

Experimental Section

General Methods. Melting points were determined on a Kofler block and are uncorrected. NMR spectra were recorded for $CDCl_3$ solutions on a JEOL EX 90 or a Hitachi R24 spectrometer with tetramethylsilane (Me_4Si) as an internal standard unless otherwise noted. IR spectra were recorded on a Hitachi 260-50 instrument. Mass spectra were measured on a JEOLJMS DX-300 spectrometer using electron impact via direct inlet or positive-ion fast atom bombardment (FAB) with 3-nitrobenzyl alcohol as a matrix. Dry tetrahydrofuran (THF) and diethyl ether (Et_2O) were freshly distilled from sodium before use.

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NaH was a 55% dispersion in mineral oil and was used as such. Other chemicals were of reagent grade and used without purification. Column chromatography was performed with silica gel 60 (SiO_2, E. Merck, particle size 0.063−0.200 mm, 60−230 mesh).

Preparation of Linear Prehosts. 1,2-Bis(2-(3-methyl-5-isoxazolyl)methoxyethoxy)benzene (1). A NaH dispersion in oil (55%, 0.73 g, 16.7 mmol) was added to a solution of 1,2-bis(2-hydroxyethoxyethoxy)benzene[19] (1.50 g, 7.57 mmol) in dry THF (50 mL), and the mixture was heated under reflux for 1 h. Under reflux, a solution of 5-(chloromethyl)-3-methylisoxazole[20] (2.20 g, 16.7 mmol) in dry THF (15 mL) was added over a period of 30 min. The mixture was heated at reflux for 5 h, and the THF was evaporated under vacuo. A saturated aqueous NaCl solution (10 mL) and ether (30 mL) was added to the product, and the ether layer was separated. The aqueous solution was extracted with ether (5 × 30 mL). The combined ether layer was dried over Na_2SO_4, filtered, and evaporated on a rotary evaporator. The product was recrystallized from Et_2O/hexane to afford a colorless solid (2.45 g, 2.94 g theoretical, 83%): ^1H NMR ($CDCl_3$) δ 6.78 (4H, s, aromatic), 5.97 (2H, s, enolate =C-H), 4.54 (4H, s, CH_2 next to isoxazole), 3.90 (8H, s, CH_2), 2.18 (6H, s, CH_3); UV (EtOH) 235, 277 nm; MS *m/e* 388 (M^+). Anal. Calcd for $C_{20}H_{24}N_2O_6$: C, 61.85; H, 6.23; N, 7.21. Found: C, 62.04; H, 6.28; N, 7.22.

1,2-Bis(8-amino-1,4-dioxa-6-oxo-7-nonenyl)benzene (2). The atmosphere of a flask containing a suspension of PtO_2 (0.08 g) and activated carbon (0.40 g) in EtOH (30 mL) was substituted by H_2, and the suspension was stirred at room temperature for 30 min. To this mixture was added **1** (2.45 g, 6.31 mmol), and the mixture was stirred at room temperature under a H_2 atmosphere. The extent of the hydrogenolysis reaction was monitored by TLC (silica) and UV: The hydrogenolysis products of either and both isoxazole rings appeared at R_f 0.63 (EtOAc) and 0.54 (EtOAc/MeOH = 4/1), respectively. UV absorptions of isoxazole at 235 nm were substituted by those of the β-enaminoketone at 232 and 304 nm in EtOH. After stirring for 5 h, both isoxazoles were completely converted to β-enaminoketones. Filtration followed by evaporation afforded 2.47 g of the crude product, which was employed for the further reaction. A small sample was chromatographed through silica gel column: ^1H NMR ($CDCl_3$) δ 6.80 (4H, s, aromatic), 5.11 (2H, s, enolate =C-H), 4.09−3.65 (12H, m, CH_2), 1.80 (6H, s, CH_3); UV (EtOH) 232, 304 nm.

1,2-Bis(1,4-dioxa-6,9-dioxononyl)benzene (3). To a solution of concentrated HCl (5 mL) in H_2O (10 mL) and EtOH (100 mL) **2** (2.47 g, 6.29 mmol) was added with stirring at room temperature. After stirring overnight, the complete conversion of β-enaminoketone was ascertained from the UV spectrum. The solvent was evaporated, saturated aqueous NaCl solution (10 mL) and $CHCl_3$ (50 mL) were added to the product and the aqueous layer was separated. The $CHCl_3$ solution was washed with saturated NaCl (2 × 10 mL). The $CHCl_3$ layer was dried over anhydrous Na_2SO_4, filtered, and evaporated on a rotary evaporator to leave an oil (2.48 g, 2.48 g theoretical, 100%): ^1H NMR ($CDCl_3$) δ 15.1 (1.5H, br, enol H), 6.61 (4H, s, aromatic), 5.53 (1.5H, s, enolate =C-H), 4.22−3.60 (12H, m, CH_2), 3.91 (0.9H, s, $COCH_2CO$), 2.00 (1.3H, s, diketo-CH_3), 1.87 (4.7H, s, ketoenol-CH_3); UV (EtOH) 233, 276 nm.

Organization by Metal. [1,2-Benzenebis(1,4-dioxanona-6,8-dionato)]copper(II) (3Cu). A solution of prehost **3** (188 mg, 0.477 mmol) in EtOH (480 mL) was added while stirring to a solution of $CuSO_4 \cdot 5H_2O$ (119 mg, 0.477 mmol) in H_2O (minimum amount). After further addition of NaOH (38.1 mg, 0.954 mmol) in a minimum amount of H_2O, the solution was stirred overnight at room temperature. The solvent was concentrated under vacuo, and the remaining solid was dissolved in $CHCl_3$ (ca. 5 mL). The insoluble solid was removed by filtration, and $CHCl_3$ was evaporated under reduced pressure. The material was recrystallized from $CHCl_3$/*n*-hexane to afford green crystals (140.9 mg, 217 mg theoretical, 65%): UV (EtOH) λ_{max}(log ϵ) 238 (4.11), 298 (4.23), 690 (1.9) nm; mp 154−157 °C; FABMS *m/e* 455 (M^+). Anal. Calcd for $C_{20}H_{24}CuO_8$: C, 52.69; H, 5.31. Found: C, 52.44; H, 5.40.

[1,2-Benzenebis(1,4-dioxanona-6,8-dionato)]zinc(II) (3Zn). A solution of prehost **3** (80.5 mg, 0.204 mmol) in EtOH (200 mL) was added with stirring to a solution of NaOH (16.4 mg, 0.410 mmol) in a minimum amount of H_2O. A solution of $ZnSO_4 \cdot 7H_2O$ (58.7 mg, 0.204 mmol) in a minimum amount of H_2O was then added. The solvent was concentrated under vacuo, and the remaining solid was dissolved in $CHCl_3$ (ca. 5 mL). The insoluble solid was removed by filtration, and $CHCl_3$ was evaporated under reduced pressure. The material was recrystallized from $CHCl_3$/*n*-hexane to afford colorless crystals (51.8 mg, 93.0 mg theoretical, 56%): ^1H NMR ($CDCl_3$, 90 MHz) δ 6.89 (2H, s, aromatic C-H), 5.21 (2H, s, enolate =C-H), 4.21−3.97 (12H, m, CH_2), 2.00 (6H, s, CH_3); UV (EtOH) λ_{max}(log ϵ) 231 (3.67), 287 (4.28) nm; FABMS *m/e* 479 (M^+ + Na). Anal. Calcd for $C_{20}H_{24}ZnO_8$: C, 52.47; H, 5.28. Found: C, 52.37; H, 5.35.

[1,2-Benzenebis(1,4-dioxanona-6,8-dionato)]nickel(II) (3Ni). A solution of prehost **3** (81.7 mg, 0.207 mmol) in EtOH (210 mL) was added while stirring to a solution of $NiCl_2 \cdot 6H_2O$ (49.2 mg, 0.207 mmol) in H_2O (minimum amount). An aqueous solution of NaOH (16.6 mg, 0.415 mmol) in a minimum amount of H_2O was added to the solution. The solvent was concentrated under vacuo, and the remaining solid was dissolved in $CHCl_3$ (ca. 5 mL). The insoluble solid was removed by filtration, and $CHCl_3$ was evaporated under reduced pressure. The material was recrystallized from $CHCl_3$/*n*-hexane to afford yellowish green crystals (59.7 mg, 93.4 mg theoretical, 64%): UV (EtOH) λ_{max}(log ϵ) 238 (3.59), 298 (4.16) nm; FABMS *m/e* 450 (M^+). Anal. Calcd for $C_{20}H_{24}NiO_8$: C, 53.25; H, 5.36. Found: C, 53.03; H, 5.45.

Incorporation of Another Metal Ion into Metal-Organized Host. A solution of Cu(II)-organized host **3Cu** (36.3 mg, 0.0796 mmol) in $CHCl_3$ (0.1 mL) was added while stirring to a solution of K_2CO_3 (5.5 mg, 0.0398 mmol) and picric acid (18.24 mg, 0.0796 mmol) in MeOH (100 mL). After the addition, the reaction mixture was concentrated under vacuo and dissolved in $CHCl_3$ (ca. 5 mL). The insoluble material was removed by filtration, and $CHCl_3$ was evaporated under reduced pressure. The material was recrystallized from $CHCl_3$/*n*-hexane to afford green crystals (38.6 mg, 52.5 mg theoretical, 74%): UV ($CHCl_3$) λ_{max} (log ϵ) 250 (4.21), 300 (4.33), 362 (4.14), 418 (3.90), 660 (1.73) nm; mp 210 °C dec.

X-ray Crystallographic Analysis. Under Ar atmosphere, the crude crystals (16.2 mg) obtained above were dissolved in $CHCl_3$ (4.5 mL) and stirred for 30 min to give a yellowish green solution which was then filtered. The filtrate was contained in a glass ampoule, and *n*-hexane was added as a diffusing solvent. After a week, green crystals of K_2(picrate)$_2$(1,2-benzene-bis(1,4-dioxanonyl-6,8-dionate)copper(II))$_2$-($CHCl_3$)$_2$ were obtained.

X-ray Data Collection, Structure Solution, and Refinement: Diffraction data were obtained on a Rigaku AFC6S four-circle diffractometer at ambient temperature. Crystal data and details of measurements for the mixed metal compound, K_2(picrate)$_2$(1,2-benzene-bis(1,4-dioxanonyl-6,8-dionate)copper)$_2$($CHCl_3$)$_2$ are summarized in Table 1. Standard reflections were monitored every 25 measurements, and no decay in their intensities was observed. Reflection data were corrected for Lorentz and polarization effects. Empirical absorption corrections were applied.

The structures were solved by a direct method[21] and refined anisotropically for non-hydrogen atoms by block-diagonal least-squares calculations. Reliability factors are defined as $R = \sum||F_o| - |F_c||/\sum|F_o|$ and $R_w = [(\sum w|F_o| - |F_c|)^2/\sum wF_o^2)]^{1/2}$. Atomic scattering factors and anomalous dispersion terms were taken from the usual sources.[22] Hydrogen atoms were included as a fixed contribution in the last cycle; their temperature factors were assumed to be isotropic. The calculations were performed on the VAX computer by using the TEXAN program system.[23] The final R and R_w values were 0.059 and 0.066, respectively. The final positional coordinates for non-hydrogen atoms of complexes

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Table 1. Crystallographic Data

formula	$CuKCl_3O_{15}N_3C_{27}H_{27}$
formula wt	842.54
crystal size, mm	0.30 × 0.20 × 0.2
crystal system	triclinic
space group	$P\bar{1}$(no. 2)
a, Å	12.592(4)
b, Å	13.352(3)
c, Å	10.501(2)
α, deg	90.28(2)
β, deg	93.51(2)
γ, deg	89.13(2)
V, Å^3	1762.0(8)
Z value	2
ρ_{calcd} g/cm^{-3}	1.588
T, °C	23
radiation(λ, Å)	Mo Kα(0.71069)
μ, cm^{-1}	10.36
2θ, deg	55.0
F_{000}	858
no. of reflcns measd	8437
no. of unique data used($\|F_1\| > 3\sigma\|F_o\|$)	8069
R^a	0.059
$R_w{}^b$	0.066

[a] $R = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $Rw = [(\sum w(|F_o| - |F_c|)^2/\sum wF_o{}^2)]^{1/2}$. $w = 4F_o{}^2/\sigma^2(F_o{}^2)$.

are given in Table 2. Selected bond angles are given in Table 3. Important bond lengths calculated are shown also in Figures 1 and 2.

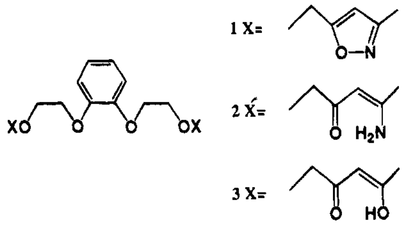
Extraction of Metal Ion. A. Picrate as the Counter Anion. Picric acid was dissolved in water to make a 2.5 × 10^{-4} M solution containing 1.0 M alkali or alkaline earth metal chloride. This was neutralized by the use of LiOH, which is the least extractable alkali metal cation and hardly influences the extraction of other metal cations. The metal-organized hosts in $CHCl_3$ (4.0 × 10^{-5} M, 8 mL) was shaken with the above aqueous solution (0.8 mL). The pH of the aqueous phase was monitored and maintained by readjustment when necessary at 7.0. The two phases were shaken again. This procedure was repeated until the pH settled at 7.0 ± 0.3 after extraction. The picrate absorptions at 358 nm in the aqueous solution before and after the extraction were measured to determine the partition coefficient of metal picrate in chloroform and aqueous phases, $[\text{picrate}]_{CHCl_3}/[\text{picrate}]_{aq}$.

B. 8-Anilinonaphthalene-1-sulfonate (ANS) as the Counter Anion. The metal-organized hosts in $CHCl_3$ (4.4 × 10^{-6} M, 30 mL) were shaken with an aqueous solution of ANS-H (4.0 × 10^{-5} M, 3.0 mL), neutralized with LiOH, containing 0.1 M metal chloride. The same pH adjustment was undertaken. The ANS concentrations in the aqueous solution before and after the extraction were determined by either the absorbance at 350 nm or fluorescence intensity at 468 nm (excitation at 377 nm).

Results and Discussion

Synthesis of Linear Prehosts. Two acetylacetonylmethyl units were connected to both terminal positions of *o*-phenylenedioxybis(ethanol) via ether linkages to form the linear prehost molecule which could be organized via metal coordination. Compared to the compound reported in the preceding paper,[9] the molecule carries the *o*-dioxyphenylene unit, so that it affords higher hydrophobicity for a favorable distribution equilibria in the organic phase in extraction experiments. In addition a favorable geometrical as well as electronic environment toward metal coordination is exhibited. The synthetic route employed the isoxazole unit as the β-diketone synthone[24] as successfully applied in previous preparations.[9] The substituted isoxazoles used as the starting material were obtained easily through regiospecific 1,3-dipolar cycloaddition of the corresponding nitrile oxide and terminal alkynes[20] and stable enough not to suffer from any side reactions under the condition of Williamson's alkylation to afford **1** (Chart 1). The scission of the N–O bond of **1** by hydrogenolysis over PtO_2 catalyst cleanly proceeded to afford the corresponding β-enaminoketone **2**, which was then hydrolyzed to 1,3-diketone **3** quantitatively in mildly acidic conditions. This proved to be an attractive synthetic methodology for the β-diketone, which usually requires an elaborate series of protection and deprotection reactions.[25]

Chart 1. Synthesis of Linear Prehost



Organization by Metal Coordination. Organization of the prehost into the corresponding final host by metal chelation was undertaken at high-dilution to facilitate the participation of the two terminal β-diketones from the same molecule, i.e., intramolecular chelation compared to the intermolecular oligomer formation. Therefore, an equimolar mixture of a linear prehost **3** and transition metal salt, which includes $CuSO_4{\cdot}5H_2O$, $ZnSO_4{\cdot}7H_2O$, or $NiCl_2{\cdot}6H_2O$, was dissolved in ethanol to make a 1 mM solution of each in the presence of 2 equiv of NaOH. After stirring at room temperature, the solvent was evaporated to leave a solid, from which a chloroform soluble material was isolated as the main component. These products gave UV absorptions of β-ketoenolate near at 250 and 300 nm and gave the corresponding parent peaks in their FAB mass spectra. In this way, three transition metal complexes, **3Cu**, **3Zn**, and **3Ni**, were obtained as neutral complexes. Small fractions of the solid material, probably oligomeric mixtures of the intermolecular coordination product, remained insoluble in chloroform.

Structural Elucidation by X-ray Crystallography. The best way to prove that the metal-organized organization has proceeded in the desired fashion is to determine the crystal structure of metal-organized hosts or more favorably of their complexes in which another metal cation is really incorporated allosterically. The former approach was tried first for **3Ni**, **3Zn**, and **3Cu** hosts. However, no single crystal appropriate for the analysis has been obtained so far. On the other hand, the second route was successful for the K(**3Cu**)picrate complex. Potassium picrate was incorporated into a Cu(II)-organized macrocycle **3Cu** by adding the chloroform solution of **3Cu** to a mixture of anhydrous potassium carbonate and picric acid in methanol. The crystals for X-ray analysis were obtained as a **3Cu**-K picrate·$CHCl_3$ complex, whose UV spectrum showed absorptions of picrate at 362 and 418 nm in addition to those of β-ketoenolate near at 240 and 300 nm.

The structure of the K(**3Cu**)picrate complex was shown by X-ray crystallography of the single crystal to consist of a centrosymmetric dimer as shown in Figure 1. The Cu(II) atom is coordinated intramolecularly by two β-diketone units located at both of the terminals of the same molecule in a nearly planar tetradentate structure. By this coordination, four neutral ether oxygens and two β-diketonate oxygen atoms are assembled to constitute a pseudo crown ring, in which the K^+ cation is entrapped. The K^+ cation is not fully buried in this pseudo

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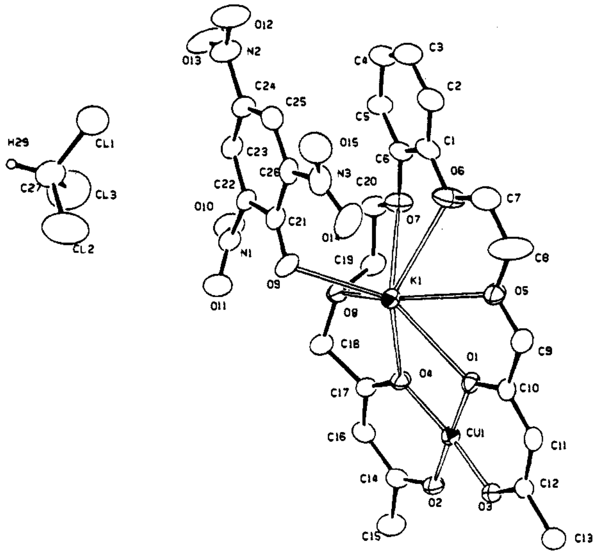
(24) (a) Yates, P.; Hand, E. S. *J. Am. Chem. Soc.* **1969**, *91*, 4749–4760. (b) Auricchio, S.; Ricca, A.; Vajna de Pava, O. *Gazz. Chim. Ital.* **1980**, *110*, 567–569.

(25) (a) Alberts, A. H.; Cram, D. J. *J. Chem. Soc., Chem. Commun.* **1976**, 958–959. (b) Itoh, Sugaya, T.; Nakatsuka, M. Y.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 8366–8367. (c) Tabushi, I.; Kobuke, Y.; Nishiya, T. *Tetrahedron Lett.* **1979**, 3515–3518. (d) Alberts, A. H.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 3545–3553.

Table 2. Positional Parameters of the Atoms and Their Isotropic Vibrational Parameters, *B*(eq)



atom	x^a	y^a	z^a	B(eq)^a	atom	x^a	y^a	z^a	B(eq)^a
Cu(1)	0.88505(5)	0.46542(5)	0.16240(6)	4.26(4)	C(3)	0.4286(7)	0.174(1)	−0.4931(8)	9.7(6)
K(1)	0.6259(1)	0.4078(1)	−0.0499(1)	4.69(7)	C(4)	0.4316(7)	0.0955(7)	−0.4119(8)	8.6(5)
Cl(1)	0.974(3)	0.0154(3)	0.1268(3)	13.2(2)	C(5)	0.4918(6)	0.1024(5)	−0.2984(7)	6.5(4)
Cl(2)	0.1370(4)	0.1509(3)	0.3262(4)	17.1(3)	C(6)	0.5478(5)	0.1875(5)	−0.2670(6)	5.3(3)
Cl(3)	0.1928(3)	−0.0534(3)	0.3587(4)	16.5(3)	C(7)	0.6317(8)	0.4191(8)	−0.4001(7)	9.9(6)
O(1)	0.8257(3)	0.4985(3)	−0.0048(3)	4.5(2)	C(8)	0.705(1)	0.4909(8)	−0.357(1)	13.8(8)
O(2)	0.9494(3)	0.4225(3)	0.3226(4)	5.1(2)	C(9)	0.8101(5)	0.5749(5)	−0.2079(6)	5.7(3)
O(3)	0.9722(3)	0.5809(3)	0.1749(4)	4.8(2)	C(10)	0.8574(4)	0.5691(5)	−0.0733(6)	4.6(3)
O(4)	0.7808(3)	0.3621(3)	0.1566(3)	4.9(2)	C(11)	0.9329(5)	0.6392(4)	−0.0340(6)	4.9(3)
O(5)	0.7395(3)	0.4985(4)	−0.2383(4)	6.4(2)	C(12)	0.9843(5)	0.6441(4)	0.0864(6)	4.8(3)
O(6)	0.6075(5)	0.3477(4)	−0.3154(4)	8.2(3)	C(13)	1.0613(6)	0.7269(5)	0.1179(7)	6.8(4)
O(7)	0.6085(4)	0.2020(3)	−0.1559(4)	6.0(2)	C(14)	0.9165(5)	0.3527(5)	0.3918(5)	5.1(3)
O(8)	0.6239(3)	0.2301(3)	0.1080(4)	5.4(2)	C(15)	0.9803(6)	0.3372(6)	0.5159(6)	7.5(4)
O(9)	0.4194(3)	0.3943(3)	0.0035(5)	6.2(2)	C(16)	0.8274(5)	0.2952(5)	0.3606(6)	5.6(3)
O(10)	0.4111(4)	0.1188(4)	0.1492(5)	7.9(3)	C(17)	0.7640(5)	0.3054(5)	0.2481(6)	5.0(3)
O(11)	0.3974(4)	0.2733(4)	0.2057(5)	7.8(3)	C(18)	0.6607(6)	0.2487(6)	0.2357(6)	6.9(4)
O(12)	0.1158(5)	0.1268(4)	−0.3412(6)	10.1(4)	C(19)	0.6800(5)	0.1539(5)	0.0481(7)	5.6(3)
O(13)	0.1634(5)	0.0227(4)	−0.1933(6)	10.2(4)	C(20)	0.6163(5)	0.1204(5)	−0.0678(7)	5.8(3)
O(14)	0.4118(5)	0.4794(5)	−0.2248(7)	10.2(4)	C(21)	0.3664(4)	0.3294(5)	−0.0538(6)	4.8(3)
O(15)	0.2703(6)	0.4526(4)	−0.3382(6)	9.8(4)	C(22)	0.3442(4)	0.2323(4)	−0.0004(6)	4.4(3)
N(1)	0.3871(4)	0.2072(5)	0.1278(6)	5.6(3)	C(23)	0.2833(5)	0.1610(4)	−0.0624(6)	5.1(3)
N(2)	0.1670(5)	0.1043(5)	−0.2427(7)	7.4(4)	C(24)	0.2351(5)	0.1796(5)	−0.1813(6)	5.3(3)
N(3)	0.3347(6)	0.4292(5)	−0.2544(7)	7.1(4)	C(25)	0.2517(5)	0.2690(5)	−0.2436(6)	5.5(3)
C(1)	0.5473(6)	0.2670(6)	−0.3530(6)	6.1(4)	C(26)	0.3179(5)	0.3384(5)	−0.1823(7)	5.2(3)
C(2)	0.4856(7)	0.2589(7)	−0.4659(7)	7.7(5)	C(27)	0.0987(7)	0.0289(7)	0.2922(9)	9.6(6)

[a] Figures in parentheses are the estimated standard deviations in the last two digits.

Table 3. Selected Values of Intramolecular Bond Angles (deg)

atom	atom	atom	angle^a
O1	Cu1	O3	93.8(2)
O1	Cu1	O4	84.8(2)
O2	Cu1	O3	88.4(2)
O2	Cu1	O4	93.6(2)
Cu1	O1	C10	124.8(4)
Cu1	O2	C14	126.0(4)
Cu1	O3	C12	126.1(4)
Cu1	O4	C17	124.5(4)

[a] Estimated standard deviations in the least significant figure are given in parentheses.

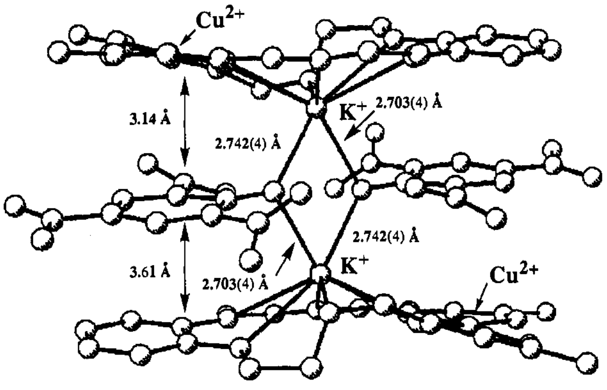


Figure 1. The structure of the copper-organized pseudo crown **3Cu** potassium picrate complex.

crown ring but pulled out of the plane toward two picrate anions with asymmetric bond lengths of 2.703(4) and 2.742(4) Å. Two picrate anions are almost coplanar and inserted between two metal-organized pseudo crown molecules with separation distances of 3.14 and 3.61 Å from the planar Cu-diketonate and dioxybenzo planes, respectively. The dihedral angle between the picrate and benzo groupings is 2.4°, indicating an almost parallel orientation. Two K^+ cations are bridged by two picrate anions to make a "sandwich dimer" structure of 2:2 stoichiometry. A similar 2:2 complex is reported for Cs(dibenzo-18-crown-6)SCN or Cs(18-crown-6)SCN.[4a,6,26]

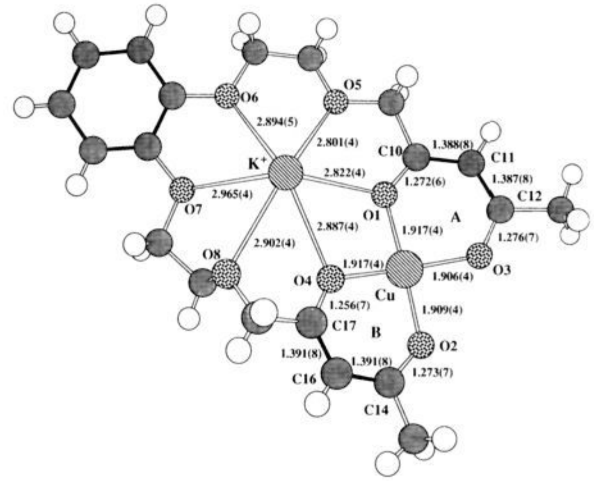


Figure 2. View of Cu(II)-organized pseudo crown ether **3Cu** potassium complex. Picrate and $CHCl_3$ molecules are eliminated for the sake of clarity. Distances related to the complexation of K^+ and Cu^{2+} are marked in Å. Values in parentheses are estimated standard deviations in the last digits.

In order to get more detailed information on the coordination structure, the monomeric unit of the complex is highlighted in Figure 2 illustrating the bond lengths relating to the coordination to Cu(II) and K^+ metal ions. The distances between the central K^+ ion and other ethereal oxygen atoms, O5, O6, O7, and O8, in the pseudo-crown are 2.801(4), 2.894(5), 2.965(4), and 2.902(4) Å, respectively. The K^+ cation appears to be shifted from the center of the ring to the O1, O5, and O6 side, since the mean coordination distance, 2.839(4) Å, is less than that of the O7, O8, and O4 side, 2.918(4) Å. Similarly, the K^+ cation is shifted from the O6 and O7 side to the O1 and O4, since the mean bond length of K−O1 and −O4, 2.854(4) Å is shorter than the mean of K−O6 and −O7, 2.929(5) Å. It is conceivable that such asymmetric disposition of the K^+ cation arises from the stronger coordination of O1 and O4 compared to that of the neutral O6 and O7 atoms. In other words, the β-diketonate oxygens maintain a partial anionic charge even after donation to the Cu(II) center. Although ion−ligand bond lengths in macrocyclic complexes are often highly variable, further support for this hypothesis may be derived from an examination of the Cu−O bonds. Although the difference is not truly statistically significant, the distances between Cu and O1 and O4 (1.917(4) Å each) are slightly greater than those of O2 and O3 (1.909(4) and 1.906(4) Å, respectively). A data accumulation of similar metal organized hosts may be useful for establishing this as a general trend.

Extraction of Metal Picrates. Picrate extraction experiments have been undertaken using these metal-organized hosts. In order to compare the efficiency of the host according to the present metal-organization method with those of conventional crown ethers, dibenzo-18-crown-6 **4** was chosen as the reference host, and the extraction was compared under identical conditions. The partition coefficient of metal picrate, $[\text{picrate}]_{CHCl_3}/[\text{picrate}]_{aq}$ for **3Cu** and **4** are shown schematically for alkali and alkaline earth metal cations in Figure 3 (A and B, respectively).

The metal-organized host **3Cu** showed a typical characteristic of host−guest molecular recognition, i.e., the complementarity of the self-organized cavity (ca. 1.3 Å in its radius) and cation determined the extraction efficiency,[4−7] since sharp maximum extractions were observed at K^+ (1.33 Å) and Sr^{2+} (1.27 Å) in a series of alkali and alkaline earth metal cations, respectively. In contrast, the prehost **3** itself without Cu(II) metal ion did not show appreciable partitions of any metal picrates under the present partition condition, the coefficients being 0.02−0.05. This may be seen as additional proof that the metal organized host is really the active species for extracting metal ions in solution as well as in the crystalline state.

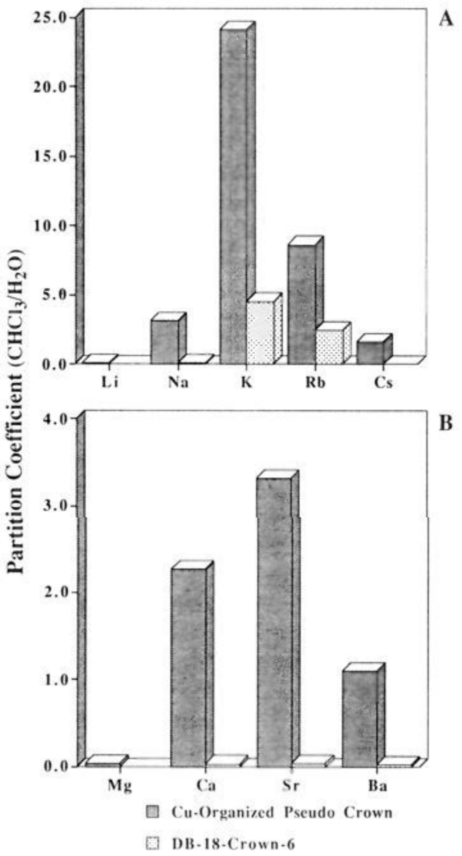


Figure 3. Partition coefficients of alkali (A) and alkaline earth (b) metal picrates by the copper-organized pseudo crown host **3Cu** in comparison to those by dibenzo-18-crown-6 **4**.

Other important behavior in the metal picrate extraction experiments is that the metal-organized host **3Cu** is greatly superior to **4** for all of the alkali and alkaline metal cations examined. The existence of polar bonds between the keto-enolate oxygen atoms and the transition metal cation in the metal-organized host may be of key importance for such enhanced extractabilities of the metal-organized host. Although the metal-organized host is electrically neutral as a whole, the enolate oxygens still keep partial anionic charges and can afford to coordinate to another metal cation. This has already been suggested by the X-ray crystallographic analysis and may also be estimated by measuring the NMR spectrum of the metal-organized host and elucidating the nature of the metal−enolate bond. Despite the fact that the **3Cu** complex is paramagnetic and it is not possible to obtain a high resolution spectrum, it was possible to obtain the NMR spectrum of **3Zn**, whose chemical shift data are given in the Experimental Section. The methyl and methine protons of **3Zn** were shifted on complexing with Zn^{2+} ion to higher fields compared with those in the free keto-enol form by −0.06 and −0.61 ppm, respectively. A similar high-field shift has already been observed for the non-benzo derivative of **3Zn**, (6,9,12,15-tetraoxaeicosa-2,4,17,19-

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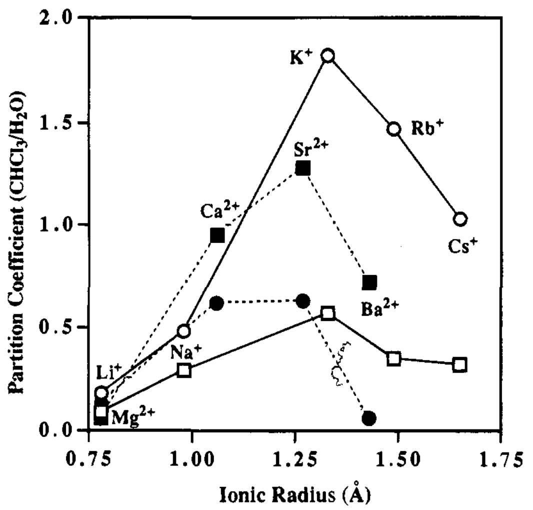

Figure 4. Comparison of partition coefficients towards alkali and alkaline earth metal picrates by zinc and nickel-organized pseudo crown host **3Zn** and **3Ni**, respectively: □; Zn-alkali; ■; Zn-alkaline earth; ○; Ni-alkali; and ●; Ni-alkaline earth metals.

tetraonate)Zn complex, where methyl, methine and α-methylene protons were shifted by −0.108, −0.675, and −0.162 ppm, respectively.[18] These chemical shift data suggest that the anionic charge of the enolate is not fully compensated by the cationic charge of the central transition metal ion but maintained for further delocalization to adjacent atoms of the host. Toward cooperative metal ion binding, the remaining partial negative charge on the enolate oxygen may bring about enthalpic stabilization upon complexation, which should be small in such a neutral crown compound as **4**.

We have employed three different transition metals for the organization of the linear prehost molecule. These metal-organized hosts have also been tested for picrate extraction of alkali and alkaline earth metal cations, and the results were summarized in Figure 4 for **3Zn** and **3Ni**. These hosts also showed maximum extractions at K^+ and Sr^{2+} in the series of alkali and alkaline earth metal ions, respectively, showing the effect of successful organization via intramolecular chelate formation. Compared to **3Cu**, both hosts were much less effective for picrate extraction. Interestingly, **3Ni** showed preference toward the extraction of a series of alkali metal ions in a similar way to **3Cu**, but **3Zn** showed a preference toward a series of alkaline earth metal ions. These phenomena are interesting in view of the fact that control of binding abilities is facilitated by the change of organizing metal ions even starting from the same linear prehost molecule. At this point, however, it is not possible to propose a detailed mechanism for the origin of the change of extractability.

The existence of polar metal−enolate bonds in the host molecule is favorable for cooperative metal ion binding due to their strong Coulombic interaction as shown in the extraction experiments. The polar bond, on the other hand, may provide an unfavorable factor for metal ion extraction, since the extraction depends on the distribution coefficient of the complex between organic and aqueous phases as well as the metal binding constant. In fact, the **3Cu**·metal picrate complex was distributed to some extent into the aqueous phase on complex formation when alkaline earth metal cations were employed. It thus seems possible to improve the extraction efficiency by employing more hydrophobic counter anions. Therefore, 8-anilino-1-naphthalenesulfonate anion (ANS) was substituted for picrate in the extraction of K^+ and Sr^{2+} cations. Due to the lower solubility of ANS in aqueous solution compared to picrate, this series of experiments were undertaken at lower host concentration (4.4×10^{-6} M) than the picrate case (4.4×10^{-5} M), and therefore the values of Kpartition listed in Table 4 are uniformly smaller than those in Figure 3. Even so, the effect of anion substitution was clearly observed, and the partition coefficients for the series of **3Cu** host were increased for the extraction of both K^+ and Sr^{2+} but more significantly for Sr^{2+} by a factor of 26. When **4** was employed, in contrast, the values were hardly increased by this substitution even for Sr^{2+}, the enhancement factor being only 2. As a result, the metal-organized host **3Cu** is more efficient for the extraction of K^+ and Sr^{2+} than dibenzo-18-crown-6 **4** by factors of 14 and 24, respectively, when ANS was employed as the counter anion. These results are fully compatible with the idea that the metal-organized host becomes hydrophilic and leaks partially into the aqueous phase on complexing, while the dibenzo crown-metal ion complex is sufficiently hydrophobic and slightly affected by use of the more hydrophobic counter anion. Only the complex **3Cu** was influenced by the nature of the counter anion. This is more obvious for Sr^{2+} than K^+ complexation.

Table 4. Effect of Counter Anion on the Extraction of K^+ and Sr^{2+} by Metal Organized Host **3Cu** and Dibenzo-18-crown-6 **4**[a]

		Kpartition	
M^+	counter anion	**3Cu**	**4**
Sr^{2+}	Pic	0.09	0.05
	ANS	2.36	0.10
K^+	Pic	1.67	0.22
	ANS	4.34	0.31

[a] Extraction conditions: aqueous solution (3 mL) containing 0.1 M metal chloride and 4.0×10^{-5} M lithium picrate (Li Pic) or lithium anilinonaphthalene sulfonate (Li ANS) was shaken with chloroform solution (30 mL) containing 4.4×10^{-6} M metal organized host **3Cu** or dibenzo-18-crown-6 **4**.

Table 5. Comparison of Metal Organized Host **3Cu** and Dibenzo-18-crown-6 **4** for the Extraction of Trace K^+ Ion by Using Anilinonaphthalene Sulfonate as the Counter Anion[a]

	Kpartition	
K^+ [M]	**3Cu** 4.4×10^{-6} M	**4** 4.4×10^{-6} M
10^{-1}	4.34	0.31
10^{-2}	1.31	0.25
10^{-3}	0.15	0.18
10^{-4}	0.12	0.12

K^+ [M]	Kpartition **3Cu** 4.0×10^{-5} M
10^{-3}	1.16
10^{-4}	0.21
10^{-5}	0.08

[a] Extraction condition: aqueous solution (3 mL) containing $0.1-1 \times 10^{-5}$ M KCl and 4.0×10^{-5} M lithium anilinonaphthalene sulfonate was shaken with chloroform solution (30 mL) containing 4.4×10^{-6} M or 4.4×10^{-5} M metal organized host **3Cu** or dibenzo-18-crown-6 **4**.

The improved extractability of metal ions and the high metal ion selectivity by **3Cu** in the combined use with hydrophobic anions may afford an interesting possibility to use it as a sensor to detect trace concentrations of metal ions in aqueous solution. Therefore, a chloroform solution containing **3Cu** was shaken with an aqueous solution of various KCl concentrations in the presence of ANS. The partition coefficients of ANS were determined by absorption spectrometry and listed in Table 5 along with the data obtained by the use of **4**. The Cu-organized host **3Cu** exhibited a sensitive response to the variation of KCl concentrations in the range $10^{-1}-10^{-3}$ M. In contrast, the partition coefficients by **4** were much smaller over the whole KCl concentration range and insensitive toward its variation. When the host **3Cu** concentration was increased to 4.0×10^{-5}

M, the sensitive response range was further extended to the range $10^{-4}-10^{-5}$ M. Since ANS is fluorescent, the partition could be detected not only by absorption spectrum but also by fluorescence at 468 nm (excitation at 377 nm) with high precision even in the $10^{-4}-10^{-5}$ M range. This is thought to be an interesting fluorescent sensor detecting trace amount of K^+.[27,28]

Summary and Conclusion

In order to obtain host molecules which satisfy the requirements of both facile synthesis and strong as well as selective binding of metal ions, we have developed an idea of metal-organized crown ethers. For this purpose, an oligoether prehost having two β-diketones in both of the terminal positions was synthesized. Intramolecular coordination of two β-ketoenolates to transition metals, Cu, Zn, or Ni formed the metal-organized real hosts. The structure of the Cu-organized host, analyzed by X-ray crystallography, was shown to consist of intramolecular coordination of β-ketoenolate oxygens to the transition metal which furnished the cavity into which the potassium cation was entrapped. These metal-organized crowns showed a similar size fit selectivity to macrocycles and also remarkable binding abilities in terms of efficiency when compared with dibenzo-18-crown-6 as the reference compound in the picrate extraction of alkali and alkaline earth metal cations. These superior characteristics have been ascribed to the existence of polar bonds between negatively charged enolate oxygens and transition and illustrates the power of the self-organization method in preparing the host.

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