Cyclic Host Having Double Bonds as Bridging Units

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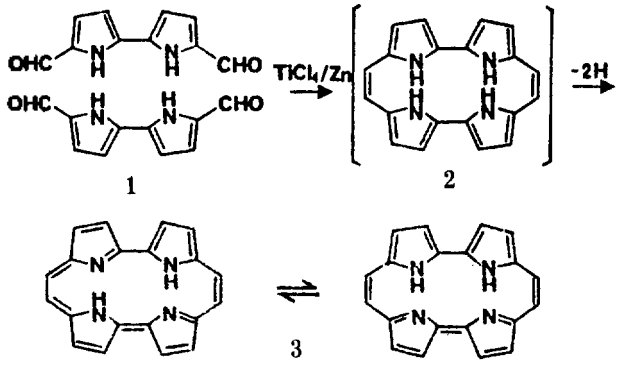
Terphenyl dialdehyde **6** was obtained in 17.4% overall yield through oxidative coupling, methylation, and bisformylation reactions starting from *p*-cresol, and then coupled intermolecularly using McMurry reaction to give 22-membered macrocylic host **7** in 14.4% yield. In crystal structure host **7** has C_{2v} symmetry with *cis-cis* configuration of two double bonds. Four methoxy groups adjacent to double bonds and the other two methoxy groups are directed opposite side, forming a cavity which can nest a guest. The cavity is filled by two inward-turned methyl groups out of four methoxy groups adjacent to double bonds. The kinetically controlled reaction mechanism leading to *cis* product was proposed. The cation binding properties of **7** were obtained using picrate extraction experiment from D_2O into $CDCl_3$ at 25 °C. All the spherical cations (from Li^+ to NH_4^+) are complexed with free energies of 7.3 ± 0.3 kcal/mol.

Introduction

Sterically hindered alkenes have been efficiently obtained by intermolecular carbonyl-carbonyl coupling reaction with *in situ* generated low-valent titanium.[1a-c] Even though the mechanism was extensively studied,[2] the factors leading to *cis vs. trans* olefins as products are not fully understood. The intramolecular version of this reaction gives high yields of cyclic alkenes.[1d-h] McMurry has also used this reaction to form several members of extremely strained polycycloalkenes.[3]

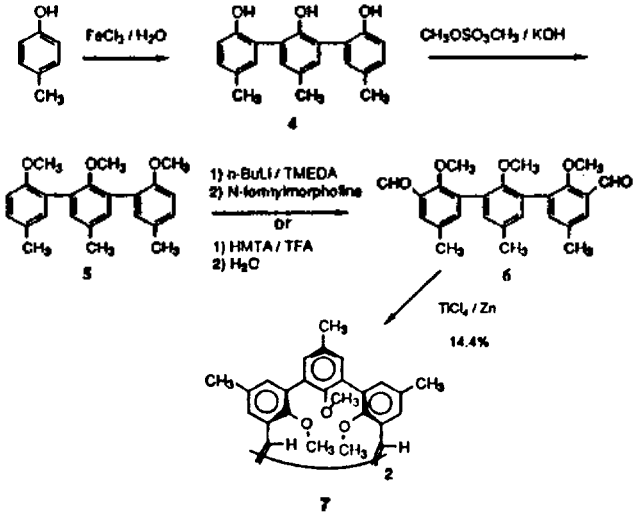
The intermolecular double carbonyl-carbonyl coupling reaction opens new synthetic method for the formation of macrocycles. Vogel *et al.* used this strategy to make porphycens **3**.[4] The intermolecular double carbonyl-carbonyl coupling reaction of dialdehyde **1** gave 2-10% yields of **3** via the spontaneous aromatization of **2**.



In conjunction with above results, the synthesis and characterization of cavitand **7** having two double bond as bridging units were carried through. The results were reported together with the discussion about the competency of the low-valent titanium induced carbonyl-carbonyl reaction as a macrocyclic ring closure method.

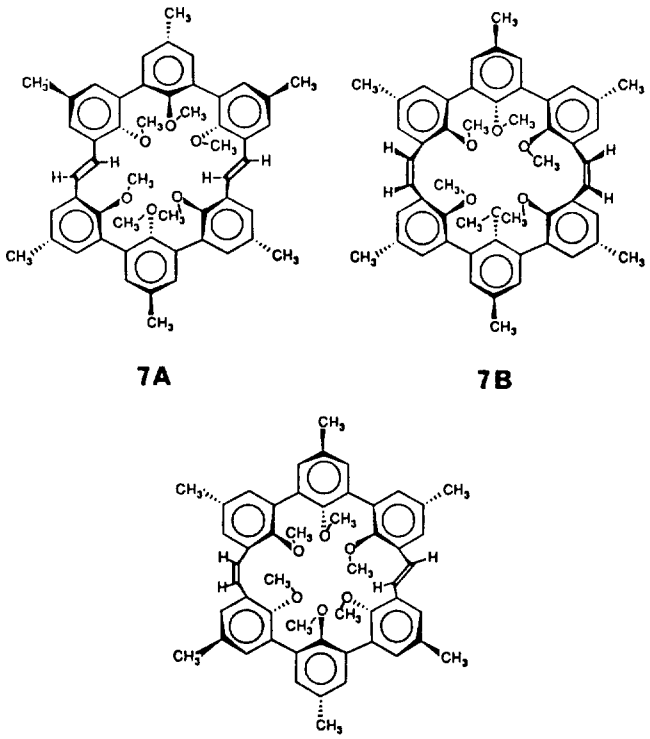
Results and Discussion

Synthesis. The oxidative coupling of *p*-cresol using iron trichloride gave the terphenyl compound **4** in about 35% yield after one month reaction time.[5] Methylation of **4** with dimethyl sulfate gave **5** (80.9%).[5] Compound **6** was prepared by either of two methods. When compound **5** was lithiated with *n*-butyllithium in the presence of TMEDA and quenched with N-formylmorpholine,[6] a mixture of dialdehyde **6** (40%) and corresponding monoaldehyde was obtained. But when compound **5** was treated with hexamethylenetetramine (HMTA) in trifluoroacetic acid (TFA) and subsequently subjected to hydrolysis (Duff reaction),[7] the dialdehyde was obtained exclusively (61.4%). The dialdehyde **6** was intermoleculary coupled using titanium tetrachloride-zinc couple[1a] to give the dimer **7**. The doubly *cis* bridged dimer **7** was obtained in 14.4% yield after recrystallization.



Scheme 1

Configulation and Mechanism Study. CPK model examination shows that the cyclic dimer **7** could have the following configurational isomers: trans-trans **7A**, *cis-cis* **7B**, and trans-*cis* **7C** (Figure 1). Each configurational isomer can exist as one or more conformational isomers which interconvert *via* the successive passage of methoxy group through the 22-membered macroring and/or the rotation of double bonds. In molecular models rotation about the olefin-aryl single carbon-carbon bond appears facile.



7A **7B**

7C

Figure 1.

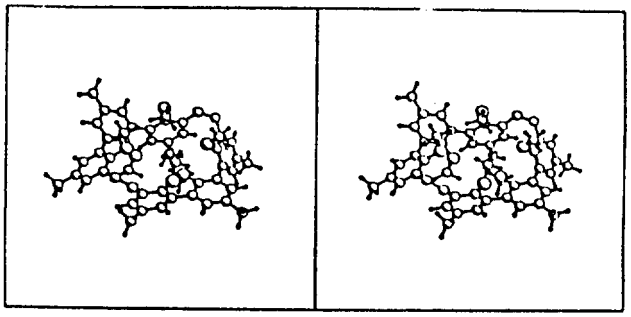


Figure 2. A stereo view of the crystal structure of cavitand 7.

An X-ray quality single crystal of cavitand 7 was grown by slow evaporation of a solution of 7 in a mixture of solvents (1/2 dichloromethane/ethanol). The stereo veiw of the crystal structure of 7 is shown in Figure 2.[8] Host 7 has C_{2v} symmetry with the *cis-cis* configuration (isomer **7B**) of the two double bonds, which is consistent with ^{1}H NMR data showing only one olefinic proton at 6.93 ppm. Four methoxy groups adjacent to double bonds and the other two methoxy groups are directed opposite side, forming a good nest for a guest. The cavity is filled by two inward-turned methyl groups out of four methoxy groups adjacent to double bonds. Thus 7 must undergo considerable reorganization of binding sites during complexation.

The predominance of isomer **7B** can be explained by consideration of reaction mechanism.[2] The proposed reaction mechanism of intramolecular carbonyl-carbonyl coupling reaction is shown in Figure 3. The equilibrating ketyl radicals **D** and **D'** are coupled to give the titanium-bound *cis* (**E**) and trans (**E'**) cyclic pinacolate. The subsequent fission of C–O bonds yields the *cis* (**F**) and trans (**F'**) cyclic alkenes. The

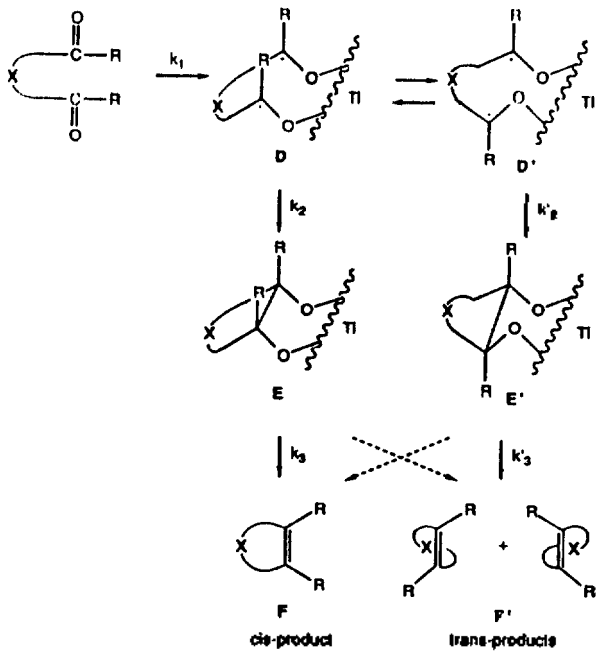


Figure 3. The proposed reaction mechanism of intramolecular dicarbonyl coupling reaction.

Table 1. Association Constants (K_a) and Binding Free Energies ($-\Delta G°$) at 25 °C of Cavitand 7 Binding Alkali and Ammonium Picrates in Water-saturated $CDCl_3$

Cation	Values based on Organic phase		Values based on Aqueous phase	
	K_a (M^{-1})	$-\Delta G°$ (kcal/mol)	K_a (M^{-1})	$-\Delta G°$ (kcal/mol)
Li^+	3.34×10^5	7.53	2.80×10^5	7.43
Na^+	2.81×10^5	7.43	1.97×10^5	7.22
K^+	2.97×10^5	7.46	1.97×10^5	7.22
Rb^+	3.43×10^5	7.55	2.39×10^5	7.33
Cs^+	3.00×10^5	7.47	2.41×10^5	7.34
NH_4^+	1.61×10^5	7.10	1.66×10^5	7.12
$CH_3NH_3^+$	3.91×10^4	6.26	3.40×10^4	6.19
$(CH_3)_3CNH_3^+$	1.49×10^3	4.33	1.61×10^3	4.37

deoxygenation of the *cis* pinacolate is faster than that of the trans pinacolate ($k_3 > k'_3$).[2a] The intermediate **E'** is unfavorable when the main cycle is too rigid or not large enough to adopt a trans configuration. It cannot be ruled out that both the *cis* and trans products can be formed from the same pinacolates *via* the non-concerted C–O fission. The overall reaction goes *via* the route which gives the favorable pinacolate intermediate. In case of intermolecular double carbonyl-carbonyl coupling reaction, possibly the favorable pinacolate for the second radical coupling is **E**, since the uncoupled radicals are oriented in the same direction (favorable for intramolecular coupling to give a cycle), but those of **E'** are oriented in the wrong direction (favorable for intermolecular coupling to give polymer). Thus cavitand 7 becomes the kinetically controlled product. Gandour *et al.* also reported a preference for a *cis*-isomer in the intramolecular ring closure of aromatic bis(carbonyls).[9] The photoisomeri-

Table 2. Comparison of the Average Binding Free Energies of **7**, **8**,[11] **9**,[12] and **10** ($-\Delta G°$, kcal/mol) Binding Alkali and Ammonium Picrates at 25 °C in Water-saturated $CDCl_3$

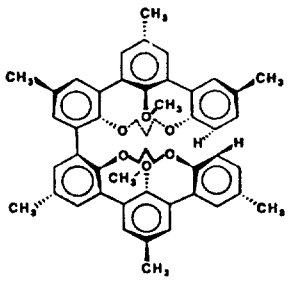
Hcst	Li^+	Na^+	K^+	Rb^+	Cs^+	NH_4^+	$CH_3NH_3^+$	$(CH_3)_3CNH_3^+$
7	7.5	7.33	7.3	7.4	7.4	7.1	6.23	4.35
8	6.0	7.6	7.5	6.6	6.3	5.8	—	—
9	16.8	13.6	—	—	—	—	—	—
10	—	—	—	—	—	—	—	—

—: Below the level of detectability of the extraction experiment ($\ll$ 6 kcal/mol).

zation of cavitand **7B** to isomer **7A** was attempted in THF using an Ace photochemical reaction vessel with a 550 W Canrod-Hanovia lamp. An inseparable mixture of unidentified products was obtained. The addition of a templating agent (KBr) or a sensitizer (benzophenone) gave similar results, which implies that none of the configurational isomers (**7A**, **7B**, and **7C**) has significant thermodynamic stability compared to the others.

Cation Binding Properties of Cavitand 7. The free energies of association for binding alkali and ammonium ions were obtained using the picrate extraction method from D_2O into $CDCl_3$ at 25 °C.[10] The results with cavitand **7** are shown in Table 1. Cavitand **7** does not show noticeable peak binding. It was anticipated that cavitand **7** might bind big cations better than small cations, because it has an elongated binding site due to the two double bonds. But all the spherical cations (from Li^+ to NH_4^+) are complexed with free energies within 0.5 kcal of each other. It seems that the energy consumption required for reorganization of the two inward turned methoxy groups during complexation results in weak and nonselective binding.

Table 2 compares the binding abilities of cavitand **7** with those of analog **8**, and spherand **9**. Compound **8** has a partially organized ligand system bridged with two propylene units. This partial organization of binding sites substantially increased the binding ability of **8** compared to the linear hexamer **10**. This ligand organization effect can be seen by comparing cavitand **7** with spherand **9**. Cavitand **7** and spherand **9** have similar orientations of the ligating oxygens (four up and two down), except that the binding site of cavitand **7** is elongated by two *cis* double bonds. Spherand **9** binds Li^+ (16.8 kcal) and Na^+ (13.6 kcal) far better than cavitand **7** which binds Li^+ (7.48 kcal) and Na^+ (7.33 kcal) rather poorly. This represents a discrimination for Li^+ between **9** and **7** by a factor of 10^7 and for Na^+ by a factor of $10^{4.2}$. This remarkable difference in complexation ability is primary due to the preorganization of the spherand's ligands prior to complexation.[12d,e] Ligand organization of host is also directly related to guest selectivity. Spherand **9** cannot complex K^+ or larger cations. All the alkali metal cations are complexed with cavitand **7** with no ion selectivity. The improved preorganization of the binding site by eliminating two double bonds gives remarkable effects on ion binding energy and selectivity. Cavitand **7** has generally stronger binding properties than compound **8** which has two mobile binding sites.



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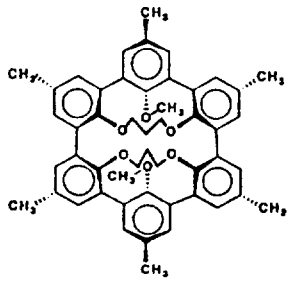

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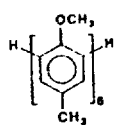

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Experimental

General. All chemicals were reagent grade and purchased from common vendors. Where necessary, chemicals were purified according to procedures reported.[14] Tetrahydrofuran, diethyl ether, and dioxane were freshly distilled from sodium benzophenone ketyl prior to use. All anhydrous reactions were conducted under an argon atmosphere. Flash chromatography was carried out using silica gel 60 (E. M. Merck, Particle size 0.040–0.063 mm, 230–400 mesh ASTM). Gravity columns were packed with silica gel 60 (E. M. Merck, Particle size 0.063–0.200 mm, 70–230 mesh ASTM). Gel permeation chromatography was performed on 20′ by 0.375″ (o.d.) column packed with 200 g of styragel (100 Å, Waters Associates) using methylene chloride distilled twice from calcium hydride as eluent at flow rates of approximately 4.0 m*l* per minute. Thin layer chromatography was conducted on plastic-backed precoated silica gel plates (E. M. Merck, F254, 0.2 mm thickness). Melting points below 240 °C were measured on Thomas-Hoover melting point apparatus. Those above 240 °C were measured on Mel-Temp apparatus. All melting points are uncorrected. Infra-red spectra were obtained on Perkin-Elmer 297 grating spectrophotometer (KBr pellets). Mass spectra were obtained on an AE1 model MS-9 double focusing spectrometer interfaced by Kratos Company to a Data General Nova 3 at 16 or 70 eV at the temperature indicated. Proton NMR spectra were obtained in $CDCl_3$ solution at 200.1 MHz on a Bruker WP-200 spectrometer unless otherwise specified. All proton chemical shifts (δ values) are reported in parts per million using tetramethylsilane at 0.00 ppm. Elemental analyses were performed by Spang Microanalytical laboratory (Eagle Harbor, Michigan).

2,2′,2″-Trimethoxy-5,5′,5″-trimethyl-[1,1′:3′,1″-terphenyl]-3,3″-dicarboxaldehyde, 6. Compound **6** was obtained by two methods.

Method 1; Compound **5** (3.0 g, 8.3 mmol) was dissolved in 100 m*l* of dry ether in a 300 m*l* round-bottom flask flushed with argon. To this solution were added at room temperature 3.0 m*l* (19.9 mmol) of TMEDA and 8.0 m*l* (20.0 mmol) of 2.5 M *n*-butyllithium in hexane. The orange solution was stirred, and a precipitate appeared after 1 hour. After an additional 2 hours stirring, the lithiated solution was cooled to −78 °C and quenched with 10 m*l* of 4-formylmorpholine (dried over activated 4Å molecular sieves for 3 days). The

mixture was stirred for 30 minutes and warmed to 25 °C. After an additional 30 minutes stirring, 30 m*l* of 2 N hydrochloric acid was added. The mixture was stirred for 15 minutes. The organic phase was separated and the aqueous phase was extracted with 30 m*l* of ether. The combined organic extracts were washed with brine and dried over anhydrous magnesium sulfate. The solution was concentrated at reduced pressure and the residue was purified by flash chromatography (silica gel, 5 × 40 cm, dichloromethane and then 5% ethyl acetate in dichloromethane). The fractions corresponding to the product were combined and the solvent was evaporated at reduced pressure. The residue was dissolved in a minimum amount of 95% ethyl alcohol. The product (1.38 g, 40%) was crystallized and collected by filtration.

Method 2; Compound **5** (11 g, 30.4 mmol), trifluoroacetic acid (120 m*l*), and hexamethylenetetramine (14.18 g, 101.1 mmol) were placed in a 500- m*l* round-bottom flask. The mixture was refluxed for 3 days, then cooled to room temperature. The solution was slowly poured into 500 m*l* of water with vigorous stirring. The mixtue was stirred for 3 hours. The crude product (fine yellow powder) was extracted with two 200 m*l* portions of dichloromethane. The organic extracts were washed with water, and then brine. The solution was dried over anhydrous magnesium sulfate and concentrated. The residue was purified by flash column chromatography (5 × 40 cm, dichloromethane and then 5% ethyl acetate in dichlomethane). The fractions corresponding to the product were combined and concentrated. The residue was dissolved in a minimum amount of 95% ethyl alcohol. The precipitate which was formed on standing was collected to give 5.6 g of product. A second crop (2.2 g) was combined with the first to give compound **6** in 61.4% combined yield; mp. 102–104 °C; ^{1}H NMR (200 MHz): δ 2.40 (s, 6H, outer-CH_3), 2.41 (s, 3H, inner-CH_3), 3.18 (s, 3H, inner-OCH_3), 3.63 (s, 6H, outer-OCH_3), 7.21–7.68 (m, 6H, Ar-H), 10.45 (s, 2H, CHO); IR (KBr): 2955, 2900, 1692, 1610, 1480, 1398, 1242, 1013; MS (230 °C, 70 eV): 418 (100, M$^+$); Anal. Calcd for $C_{26}H_{26}O_5$ (MW 418.49): C, 74.62; H, 6.26. Found: C, 74.72; H, 6.30.

(Z,Z)-35,36,37,38,39,40-Hexamethoxy-4,9,16,21,26,33-hexamethylheptacyclo[29.3.1.1$_{2,6}$.1$_{7,11}$.1$_{14,18}$.1$_{19,23}$.1$_{24,28}$]tetraconta-1(35),2,4,6(40),7,9,11(39),12,14,16,18(38),19,21,23(37),24,26,28(36),29,31,33-eicosaene, 7. To a 2-liter three neck round-bottom flask flushed with argon and equipped with a condenser and a reflux-dilution thimble (30 m*l* capacity) was added 1 liter of dry dioxane. Zinc (9.46 g, 144 mmol) and dry potassium bromide (5.0g, 41.7 mmol) were added and the mixture was cooled to 0 °C. Titanium tetrachloride (7.92 m*l*, 72 mmol) was cautiously added. The whole mixture was refluxed for 2 hours and then the solution became black. Meanwhile 4.0 g of dialdehyde **6** was dissolved in 100 m*l* of dry dioxane. The first 50 m*l* of dialdehyde solution was injected to the refluxing balck solution via syringe pump over the course of 24 hours, and the mixture was refluxed for 24 hours. The rest of the dialdehyde solution was then added over the course of 24 hours. The whole mixture was further refluxed for 24 hours, and then cooled to room temperature. The excess reagents were destroyed with 20 m*l* of saturated potassium carbonate solution. The mixture was stirred overnight, during which the black mixture turned to a white suspension. The reaction mixture was filtered through celite and the filtrate was concentrated. The crude mixture was partitioned between 200 m*l* of dichloromethane and 100 m*l* of water. The organic phase was separated and the aqueous phase was extracted with 50 m*l* of dichloromethane. The combined organic extracts were washed with deionized water two times and concentrated to about 15 m*l*. The concentrated solution was washed with deionized water three times by the vortexing (2 min)–centrifuging (2 min) method. The solution was subjected to gel permeation chromatography (2 m*l* for each run). The fractions with a retention volume of 150–170 m*l* were combined and concentrated to about 10 m*l*. To this, 10 m*l* of 95% ethyl alcohol was added and the solution was slowly evaporated. A light brown precipitate (0.71 g, 19% yield) was obtained. It was recrystallized from a mixture of dichloromethane and ethyl alcohol to give the pure product (0.53 g, a white thick needle, 14.3% yield). A single crystal for X-ray structure analysis was grown by slow evaporation of a solution of **7** in a mixture of dichlomethane and ethanol; mp: >294 °C (decompose); ^{1}H NMR (500 MHz): δ 2.22 (s, 12H, side Ar-CH_3), 2.32 (s, 6H, center Ar-CH_3), 2.45 (s, 6H, center OCH_3), 3.17 (s, 12H, side OCH_3), 6.77(s, 4H, Ar-H), 6.93 (s, 4H, olefinic H), 6.94 (s, 4H, Ar-H), 7.04 (s, 4H, Ar-H); MS (270 °C, 70 eV): 772 (M$^+$, 100). Anal. Calcd for $C_{52}H_{52}O_6$ (MW 772.99). C, 80.80; H, 6.78. Found: C, 81.17.; H, 7.06.

References

1. (a) T. Mukaiyama, T. Sato, and J. Hanna, *Chem. Lett.*, 1041 (1973); (b) J. E. McMurry and M. P. Fleming, *J. Am. Chem. Soc.*, **96**, 4078 (1974); (c) D. Lenoir, *Synthesis*, 553 (1977); (d) A. L. Baumstark, C. J. McCloskey, and K. E. Witt, *J. Org. Chem.*, **43**, 3609 (1978); (e) J. E. McMurry and K. L. Kees, *Ibid.*, **42**, 2655 (1977); (f) F. E. Ziegler and H. Lim, *Ibid.*, **47**, 5229 (1982); (g) J. A. Marshall and K. E. Flynn, *J. Am. Chem. Soc.*, **106**, 723 (1984); (h) J. E. McMurry and C. N. Hodge, *Ibid.*, **106**, 6450 (1984); (i) E. Vogel, W. Puttmann, W. Duchatsch, T. Schieb, H. Schmickler, and J. Lex, *Angew. Chem. Int. Ed. Engl.*, **25**, 720 (1986); (j) Y. H. Lai, *Org. Prep. Proc. Int.*, **12**, 361 (1980).
2. (a) J. E. McMurry, M. P. Fleming, K. L. Kees, and L. R. Krepski, *J. Org. Chem.*, **43**, 3255 (1978); (b) J. E. McMurry, *Acc. Chem. Res.*, 405 (1983); (c) R. Dams, M. Malinowski, I. Westdorp, and H.Y. Geise, *J. Org. Chem.*, **47**, 248 (1982).
3. (a) J. E. McMurry, G. J. Haley, J. R. Matz, J. C. Clardy, G. V. Duyne, R. Gleiter, W. Schafer, and D. H. White, *J. Am. Chem. Soc.*, **108**, 2932 (1986); (b) J. E. McMurry, G. J. Haley, J. R. Matz, J.C. Clardy, and G. V. Duyne, *Ibid.*, **106**, 5018 (1984); (c) J. E. McMurry, G. J. Haley, J. R. Matz, J. C. Clardy, and J. Mitchell, *ibid.*, **108**, 515 (1986).
4. (a) E. Vogel, M. Kocher, H. Schmickler, and J. Lex, *Angew. Chem. Int. Ed. Engl.*, **25**, 257 (1986); (b) E. Vogel, M. Balci, K. Pramod, P. Koch, J. Lex, and O. Ermer, *Ibid.*, **26**, 928 (1987).
5. K. E. Koenig, G. M. Lein, P. Stucker, T. Kaneda, and D. J. Cram, *J. Am. Chem. Soc.*, **101**, 3553 (1979).
6. G. A. Olah, L. Ohannesian and M. Arranaghi, *J. Org. Chem.*, **49**, 3856 (1984).
7. (a) J. C. Duff and E. J. Bills, *J. Chem. Soc.*, 1305 (1934); (b) W. E. Smith, *J. Org. Chem.*, **37**, 3972 (1972); (c) The

authors warmly thank Professor D. N. Reinhoudt for the details of this reaction procedures in closely related systems.
8. The authors thank to Dr. C. B. Knobler for the X-ray crystal structure resolution.
9. J. Tirado-Rives, M. A. Oliver, F. R. Fronczek, and R. D. Gandour, *J. Org. Chem.*, **49**, 1627 (1984).
10. (a) K. E. Koenig, G. M. Lein, P. Stuckler, T. Kaneda, and D. J. *Cram, J. Am. Chem. Soc.*, **101**, 3553 (1979); (b) K. E. Koenig, R.C. Helgeson, and D. J. Cram, *Ibid.*, **98**, 4018 (1976).
11. S. P. Artz, M. P. deGrandpre, and D. J. Carm, *J. Org. Chem.*, **50**, 1486 (1985).
12. (a) D. J. Cram, T. Kaneda, R. C. Helgenson, and G. M. Lein, *J. Am. Chem. Soc.*, **101**, 6752 (1979); (b) K. N. Trueblood, C. B. Knobler, E. Maverick, R. C. Helgeson, S. B. Brown, and D. J. Cram, *Ibid.*, **103**, 5593 (1981); (c) D. J. Cram, T. Kaneda, R. C. Helgeson, S. B. Brown, C. B. Knobler, E. Maverick, and K. N. Trueblood, *Ibid.*, **107**, 3645 (1985); (d) D. J. Cram, *Angew. Chem. Int. Ed. Engl.*, **25**, 1039 (1986); (e) K. S. Paek, "Host-Guest Chemistry", Progress in Chemistry and Chemical Industry, Korea, **29**, No, 10, 654 (1989).
14. D. D. Perrin, D. R. Perrin and W. L. F. Armarego, Purification of Laboratory Chemicals, 2nd ed.; Pergamon Press: N. Y., 1980.

Chiral Host. Attempted Synthesis Using McMurry Reaction as a Final Ring Closure Method

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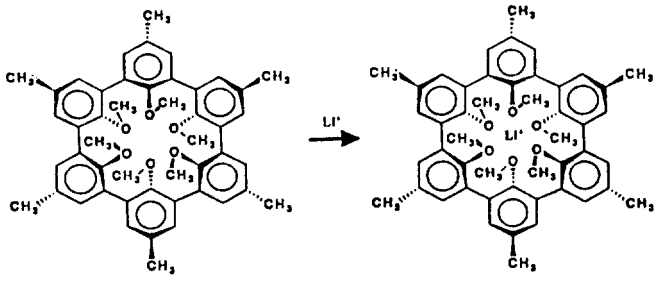
Using the low valent titanium induced carbonyl-carbonyl coupling reaction, it was attempted to synthesize sterically hindered 17-membered cyclic chiral host **2**. The semifinal dialdehyde **12** was obtained through 11 step reactions beginning from *p*-tert-butylphenol and dibenzofuran. When dialdehyde **12** was treated with $TiCl_3$-Zn/Cu, only intermolecularly coupled dimer **14** was obtained instead of intramolecularly coupled cyclic alkene **2**. The mechanistic consideration leading to **14** was discussed and the cation binding properties of dimer **14** and dicarboxylic intermediate **13** was reported, which implies the significance of the principle of preorganization of host's binding sites prior to complexation.

Introduction

Spherands, of which **1** is the first and the ultimate example, have remarkable binding properties arising from the self-organization of the binding sites prior to complexation (Principle of Preorganization.[1] Even though anisole oxygens are known to be intrinsically weak ligands, their perfect preorganization into an octahedral binding site makes **1** the strongest known host for alkali metal ions ($-\Delta G°_{Li^+} > 23$ kcal/mol and $-\Delta G°_{Na^+} = 19.2$ kcal/mol, picrate salts in D_2O-saturated $CDCl_3$ at 25 °C). The crystal structures of spherand **1** and spheraplexes **1**·Na^+ and **1**·Li^+ show almost identical conformations for free and complexed host.[1c]



Spherand **1** Spheraplex **1**·Li^+

Spherand **1** also shows the greatest selectivity toward alkali metal ions. It only binds Li^+ or Na^+. Larger alkali metal ions cannot be incorporated into the binding site (the Principle of Complementarity).[2] This unique selectivity has been applied to a sodium and lithium-selective colorimetric host[3] which changed from yellow to deep blue as it went from its free state to its sodium or lithium complex in 80% dioxane-20% water (v/v). It remains uncomplexed (yellow) in the presence of potassium salts. This chromogenic ion-selective indicating system is capable of detecting Li^+ and Na^+ at concentrations as low as 10^{-8} M in the presence of other common ions.

A desirable goal is the design and synthesis of chiral hosts which mimic the exceptional binding properties of spherand **1**. Chiral crown ethers were used as asymmetric catalysts for Michael additions,[4a] addition of alkyllithiums to aldehydes,[4b] and anionic methacrylate polymerizations.[4c] The tetraphenyl hemispherand systems with various bridges were studied extensively.[5] They are chiral, having C_2 symmetry, but their barrier to racemization is less than 27 kcal/mol. This low energy barrier made it impractical to resolve them at room temperature. The inversion of chirality, which occurs by successive passage of the methoxy groups through the center of