

- Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451. (c) Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1968**, *90*, 2622.
2. (a) Buncl, E.; Um, I. H.; Hoz, S. *J. Am. Chem. Soc.* **1989**, *111*, 971. (b) Buncl, E.; Shaik, S. S.; Um, I. H.; Wolfe, S. *J. Am. Chem. Soc.* **1988**, *110*, 1275.
3. (a) Kwon, D. S.; Lee, G. J.; Um, I. H. *Bull. Korean Chem. Soc.* **1990**, *11*, 262. (b) Um I. H.; Jeon, J. S.; Kwon, D. S. *Bull. Korean Chem. Soc.* **1991**, *12*, 406. (c) Um I. H.; Lee, S. J.; Kim, J. J.; Kwon, D. S. *Bull. Korean Chem. Soc.* **1994**, *15*, 473.
4. (a) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1989**, *111*, 2647. (b) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 6362. (c) Bourne, N.; Chrystiuk, E.; Davis, A. M.; Williams, A. *J. Am. Chem. Soc.* **1988**, *110*, 1890.
5. (a) Hengge, A. C.; Hess, R. A. *J. Am. Chem. Soc.* **1994**, *116*, 11256. (b) Hengge, A. C.; Edens, W. A.; Elsing, H. *J. Am. Chem. Soc.* **1994**, *116*, 5045. (c) Hengge, A. C. *J. Am. Chem. Soc.* **1992**, *114*, 6575.
6. (a) Guthrie, P. J. *J. Am. Chem. Soc.* **1991**, *113*, 3941. (b) Yamabe, S.; Minato, T. *J. Org. Chem.* **1983**, *48*, 2972. (c) Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1978**, *100*, 3861. (d) Bentley, J. W.; Koo, I. S. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1385.
7. Tarkka, R. M.; Buncl, E. *J. Am. Chem. Soc.* **1995**, *117*, 1503.
8. Chapman, N. B.; Shorter, J. Eds.; *Advances in Linear Free Energy Relationship*; Plenum: London, 1972.

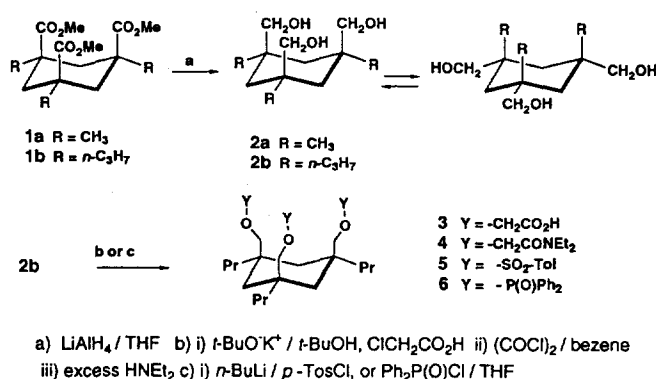
Syntheses of Tripodand and Cage-Type Hosts, and Their Binding Properties with Alkali Metal and Ammonium Ions

Kyu-Sung Jeong*, Joon Woo Nam, and Young Lag Cho

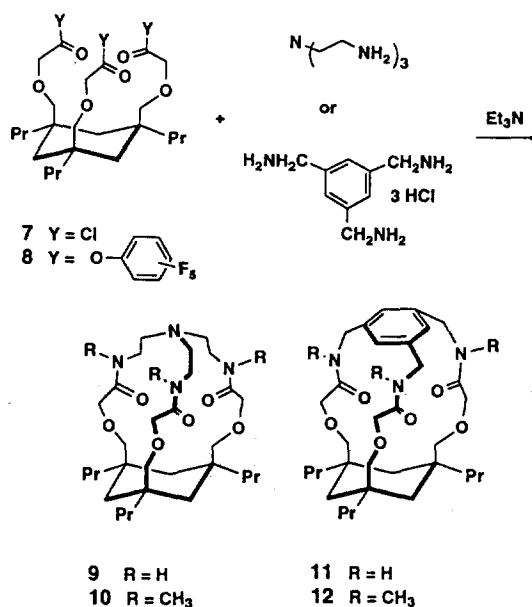
Department of Chemistry, Yonsei University,
Seoul 120-749, Korea

Received April 18, 1995

The construction of a well defined host is the most difficult but important work in molecular recognition chemistry. Design of metal ion host is relatively simple due to the spherical shape of metal ion with the positive charge. Studies for the selective recognition of a metal ion have been focused on the two or three-dimensional cyclic arrangement of electron donor atoms such as oxygen and nitrogen.¹ It has been little studied for the contribution of the donor atom basicity to the stability of complex. We report here syntheses and complexation properties of three tripodands having oxygen atoms with different basicities, that is, amide, sulfonate, and phosphinate groups. In addition, we also describe the syntheses of the cage-type hosts based on a new molecular building block derived from tripropyl Kemp triacid.² Several C₃-symmetric molecules have been employed for the syntheses of cage-type artificial hosts. The representative examples are



Scheme 1.



Scheme 2.

tren, 1,3,5-substituted benzene,³ and cyclotrimeratrylene,⁴ etc.

Syntheses of molecular building blocks **2a**, **2b** and tripodands **4-6** are summarized in Scheme 1. The building blocks **2a**, **2b** were derived from the reduction (85-90% yield) of triesters **1a**, **1b** which were prepared by following a literature procedure² from the commercially available 1,3,5-trimethyl *cis,cis*-cyclohexanetricarboxylate. Reaction of tripropyl triol **2b** with chloroacetic acid in presence of *t*-BuO-K⁺ gave triacid **3** in 61% yield.⁵ Amide tripodand **4** was obtained in 81% yield from activation of **3** with oxalyl chloride followed by treatment with excess diethylamine. Additionally, reaction of tripropyl triol **2b** with *n*-butyllithium / *p*-toluenesulfonyl chloride or diphenylphosphinic chloride afforded the corresponding tripodand **5** (58% yield) or **6** (82% yield), respectively.

Instead of trimethyl triol **2a**, tripropyl triol **2b** has been used for the preparations of hosts in this study by the following reasons. First, tripropyl triol **2b** is highly soluble in organic solvents (CHCl₃, CH₂Cl₂, and EtOAc etc.) but trimethyl triol **2a** is sparingly. Secondly, bulkier propyl group may increase the population of the conformation in which methanolic groups are located in the axial positions.

Syntheses of cage-type hosts **9-12** are outlined in Scheme

Table 1. The Percentages of Liquid-Liquid Extractions of Metal and Ammonium Picrates by Hosts at 290 ± 2 K.*

host	Li ⁺	Na ⁺	K ⁺	NH ₄ ⁺
4	1.1 (3.2)	4.8 (12)	4.1 (6.5)	5.4 (5.7)
5	4.8 (15)	7.1 (18)	8.8 (15)	9.6 (11)
6	26 (130)	16 (51)	17 (37)	20 (30)
9	2.6 (7.6)	2.8 (6.6)	2.7 (4.2)	2.9 (2.9)
10	20 (90)	23 (86)	13 (25)	22 (33)
11	4.1 (12)	2.7 (6.3)	2.1 (3.1)	2.7 (2.7)
12	1.6 (4.5)	2.0 (4.6)	5.1 (8.3)	2.7 (2.7)

*Extractions have been performed by employing 1.5 mL of 0.05 M host in CHCl₃ and 0.3 mL of 0.01 M guest in deionized water. All extractions have been triplicated and the errors in extraction percentages are within 2%. The values in parentheses are the stability constants ($K_a \times 10^{-3}$, M⁻¹) calculated by assuming 1:1 complex of host and guest.

2. The reaction of pentafluorophenol ester **8** with tris(2-aminoethyl)amine (tren) provided host **9** in a surprisingly high yield (60% yield) without a high dilution (~ 0.014 M in THF) and a template assistance.^{6,7} This might be due to the formation of intramolecular hydrogen bonds during the reaction. Once the first amide bond is formed, the resulting amide hydrogen might intramolecularly hydrogen-bond with the oxygen of an adjacent group, and thus two reaction partners of the amine and ester are closely located each other in order to occur an intramolecular reaction. It seems, however, that intramolecular hydrogen bond does not help the formation of **11** on the coupling with more spacious and rigid mesitylenetriamine. Among the various reaction conditions we examined for the preparation of the mesitylene-capped host **11**, the highest yield (21%) was obtained from the reaction of acid chloride **7** with mesitylenetriamine trihydrochloride in presence of excess triethylamine.⁸ Methylation of hosts **9**, **11** was performed with NaH/MeOTs to afford the corresponding hosts **10**, **12**, respectively.

The binding abilities of hosts with alkali metal ions and ammonium ion have been determined by the Cram's liquid-liquid extraction method⁹ and the results are summarized in Table 1.

The phosphinate tripodand **6** extracts much more effectively metal picrates and ammonium picrate from aqueous to chloroform layer than does the amide **4** or sulfonate tripodand **5**. This may reflect the difference in the electron-donating abilities of three functional groups. The three phosphinate groups in **6** may cooperatively bind cations as shown in a proposed structure of complex **14**, in which the metal

ion is completely surrounded by highly hydrophobic attachments. This structure is supported by the fact that the momo-phosphinate analogue **13** does not extract any cation at all under the same condition. It is also worthwhile noting that the phosphinate tripodand **6** shows a moderate selectivity toward lithium cation.

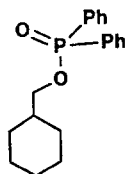
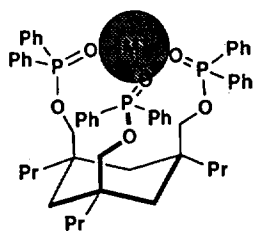
As shown in Table 1, binding affinity of the tren-capped host **9** is negligible probably due to the divergence of three carbonyl oxygens and/or the intramolecular hydrogen bonds between the amide bonds. When the amide NH protons are removed by methylation, the complexation abilities are dramatically increased as shown in host **10**. Compared with the amide tripodand **4**, three amide groups in the methylated host **10** seem to be preorganized for the binding of the metal ions, and entropic penalty is reduced on the binding event. The cage-type host **10** shows much stronger extractabilities of cations than does tripodand host **4**. Finally, mesitylene-capped host **11** and its methylated analogue **12** do not show an appreciable complexation with any cation, suggesting that mesitylene cap is too spacious for the three amide groups to bind cations simultaneously.

In conclusion, the phosphinate tripodand **6** binds most strongly alkali metal ions and ammonium ion among the amide, sulfonate, and phosphinate tripodands. The tren-capped host **9** has been synthesized efficiently and its methylated host **10** binds strongly with Li⁺ and Na⁺ with a moderate selectivity. Further modifications and binding studies of cage-type hosts with other guests are in progress.

Acknowledgment. This work was financially supported by the Korea Science and Engineering Foundation.

References

- (a) *Crown Compounds: Toward Future Applications*; Cooper, S. R., Ed.; VCH: New York, 1992. (b) Okahara, M.; Nakatsuji, Y. In *Crown Ethers and Analogous Compounds*; Hiraoka, M. Ed.; Elsevier: Amsterdam, 1992, Chapter 2.
- (a) Rebek, J., Jr.; Askew, B.; Killoran, M.; Nemeth, D.; Lin, F.-T. *J. Am. Chem. Soc.* **1987**, *109*, 2426. (b) Jeong, K.-S.; Tjivikua, T.; Muehldorf, A.; Deslongchamps, G.; Famulok, M.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 201.
- Berscheid, R.; Luer, I.; Seel, C.; Vögtle, F. In *Supramolecular Chemistry*; Balzani, V.; De Cola, L. Ed.; Kluwer Academic Publishers: Dordrecht, 1992, pp 71-86 and references are therein.
- Collet, A.; Dutasta, J.-P.; Lozach, B.; Canceill, J. *Top. Curr. Chem.* **1993**, *165*, 103.
- Newkome, G. R.; Yao, Z.; Baker, G. R.; Gupta, V. K. *J. Org. Chem.* **1985**, *50*, 2004.
- To a solution of tris(2-aminoethyl)amine (0.12 mL, 0.81 mmol) and Et₃N (1 mL, 9 eq) in dry THF (50 mL), a solution of pentafluorophenyl ester **8** (0.78 g, 0.81 mmol) was dropwise added over 5 min and the solution was stirred for 4 h at rt. After work-up, the crude product was purified by flash chromatography (MeOH/EtOAc 1:8) to afford the host **9** as a white solid (0.27 g, 60%); mp 223-225 °C; IR (KBr) 3434, 3411, 2961, 1681, 1523, 1125 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.86 (t, 3H, $J=5.99$ Hz), 3.93 (s, 6H), 3.19 (m, 6H), 3.15 (s, 6H), 2.47 (m, 6H), 1.82 (d, 3H, $J=14.4$ Hz), 1.51 (m, 6H), 1.22-1.30 (m, 6H),

**13****14**

- 1.10 (d, 3H, $J=14.4$ Hz), 0.89 (t, 9H, $J=7.04$ Hz).
7. When acid chloride **7** was used instead of **8**, yield was dropped to ~20%.
8. To a solution of 1,3,5-mesitylenetriamine trihydrochloride (0.17 g, 0.63 mmol) and Et_3N (1 mL) in dry CH_2Cl_2 (100 mL) at an ice-water bath, a solution of acid chloride **7** (0.33 g, 0.63 mmol) in dry CH_2Cl_2 (10 mL) was dropwise added over 5 min. The solution was stirred for 4 h at an ice-water bath and overnight at rt. After work-up, the crude product was purified by flash chromatography

- ($\text{MeOH}/\text{CH}_2\text{Cl}_2$ 1 : 10) to afford the host **11** as a white solid (74 mg, 21%): mp >300 °C; IR (KBr) 3427, 3289, 2967, 1686, 1098 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.03 (s, 3H), 6.24 (t, 3H, NH, $J=5.60$ Hz), 4.44 (d, 6H, $J=4.20$ Hz), 3.90 (s, 6H), 2.77 (s, 6H), 1.39-1.49 (m, 6H), 1.34 (d, 3H, $J=14.2$ Hz), 1.12-1.28 (m, 6H), 0.86 (t, 9H, $J=7.14$ Hz) 0.49 (d, 3H, $J=14.4$ Hz).
9. Koenig, K. E.; Lein, G. M.; Stuckler, P.; Kaneda, T.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 3553.