Polytopic Coreceptor from Conformationally Stabilized Calix[6]arene for Alkali Metal Ions

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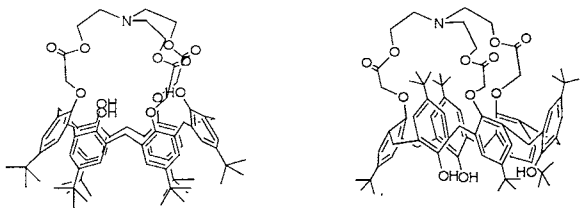
1:4 and 1:3 complexes of a conformationally stabilized calix[6]arene with NaI and KI were detected by matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) for the first time.

When several binding units for specific species are combined together within the same architecture, the so-called polytopic coreceptor system may be constructed. For this system, the discrete binding sub-units contained may cooperate for the simultaneous complexation of several substrates or of multiply bound(polyhapto) polyfunctional species.[1] As for the Na^+-K^+ transport system of the cell, it is believed that the carrier part exists in two major different conformations, one of which shows a high-affinity to Na^+ ion and can selectively bind three Na^+ ions; the other shows a high-affinity to K^+ ion and can selectively bind two K^+ ions.[2] For K^+ ions channel, also it is proved there exists two binding sites.[3,4] The multi-ion binding sites are necessary for these systems to perform information communication and species transfer.[3] To mimic the biological process of nature, considerable recent attention has been focused on supramolecular coreceptor systems that contain several responsive groups as an integral part to perform complicated function.[5-7] Currently, calixarenes have been wildly used as skeletons to construct supermolecular systems that can form complexes with specific molecular targets or metal ions.[10,11] Calix[6]arenes possess a cavity larger than calix[4]arenes, but the conformational freedom limits their application to serve as receptors. Multiple bridges at the lower or upper rim have been used to immobilize the conformation by several groups, [12-14] but the recognition property studies are very scarce. [15,16] The main interests of us are to use calix[6]arene as basic block to construct polytopic coreceptor to metal ions, and to study the cooperation behavior of the sub-units contained in the system. In this communication, we give the first example of the selective, and cooperative complexation to metal ions of a calix[6]arene stabilized by a triple bridge at the lower rim.

Compound (1) was synthesized as follows: 4-*tert*-butyl-calix[6]arene (972 mg, 1 mmol), $(ClCH_2COOCH_2CH_2)_3N$ (260 mg, 1.1 mmol), potassium carbonate(250 mg, 1.8 mmol) and potassium iodide (500 mg, 3 mmol) were added to the flask with 20 ml dried acetonitrile as solvent. The mixture was refluxed with stirring for 12 h. After cooling, 100 ml cold water was added and the solution was extracted with chloroform (3×30 ml). The extraction was dried and concentrated. Compound (1) 310 mg was obtained as a pale yellow powder by column chromatography(chloroform/methanol, 50/1), yield 25%. M.p. > 300°C. IR: 3366,1746,1606,1484. HRMS for $C_{78}H_{99}NO_{12}$, calcd: 1242.6552, found: 1242.8625. ^1H NMR ($CDCl_3/CF_3COOD$): 0.87(br,2H),1.16(s,9H), 1.22(s,9H), 1.26(s,18H), 1.27(s,18H), 3.75(br,8H), 3.91(br,16H), 4.78(br,4H), 7.08(s,2H), 7.09(s,2H), 7.13(s,4H) and 7.15(s,4H).

For supramolecular systems, which contain intermolecular non-covalent interactions, the detection and the elucidation of the composition and structure are still challenging tasks. With the development of soft ionization techniques, such as electrospray ionization (ESI),[17,18] and matrix-assisted laser desorption/ionization (MALDI), [19,20] mass spectrometry(MS) has become an indispensable tool for analysis of non-covalent complexes.[21-23] The MALDI-MS is used in this work, since it enable us to conduct the experiment at relative high concentrations of metal ions.

The mass spectrometer used was a KOMPACT MALDI III laser desorption reflectron time-of-flight instrument (Shimadzu/Kratos). 4-hydroxy-α-cyanocinnamic acid(HCCA) was used as the matrix. Samples were deposited on target surfaces after mixing 100 μl of THF solution of HCCA(10 mg in 1 ml) and 200 μl of acetonitrile solutions of (1)(2.0×10^{-5} M) with metal ion concentrations of 5.0×10^{-4} M for each metal ions. Ionization was achieved using a pulsed nitrogen laser operating at 337 nm. All spectra were obtained in positive-ion reflector mode; 200 single shots were accumulated in order to obtained a good signal-to-noise ratio.



Cone 1,3,5-alternate

(1)

Scheme 1.

Figure 1a-d shows the mass spectra of ligand (1, L) in the presence of LiI, NaI, KI and their mixture with CsI, respectively. For CsI, no complex form can be detected in the mass spectrum. In the experimental condition concerned, no single-charged cations of LM^{1+} can be detected in the mass spectra. In the case of LiI, only doubly charged species LLi^{2+} can be detected (Figure 1a). But when NaI is used, strong peaks at 444.8 and 656.5 appear, which correspond to triply and doubly charged species of LNa_4^{3+} and LNa_3^{2+}, respectively (Figure 1b). For KI, the most abundant species appears at 453.6, which come from the triply charged species LK_3^{3+}(Figure 1c). In the same time, a weak peak at 430.2 can be seen, which should come from the triply charged ion (LK_2^{3+}). In order to determine the selectivity of the system to metal ions, the mass spectrum is measured in the presence of a mixture of metal ion salts mentioned above, the result indicates that the present system has a high selectivity to K^+ ion. Similar with the case of K^+ ion alone, the strongest peak appears at 453.7(Figure 1d). Apart from the weak peak at 447.8, which correspond to a triply charged complex of $LNaK_2^{3+}$, no other complex can be observed in the mass

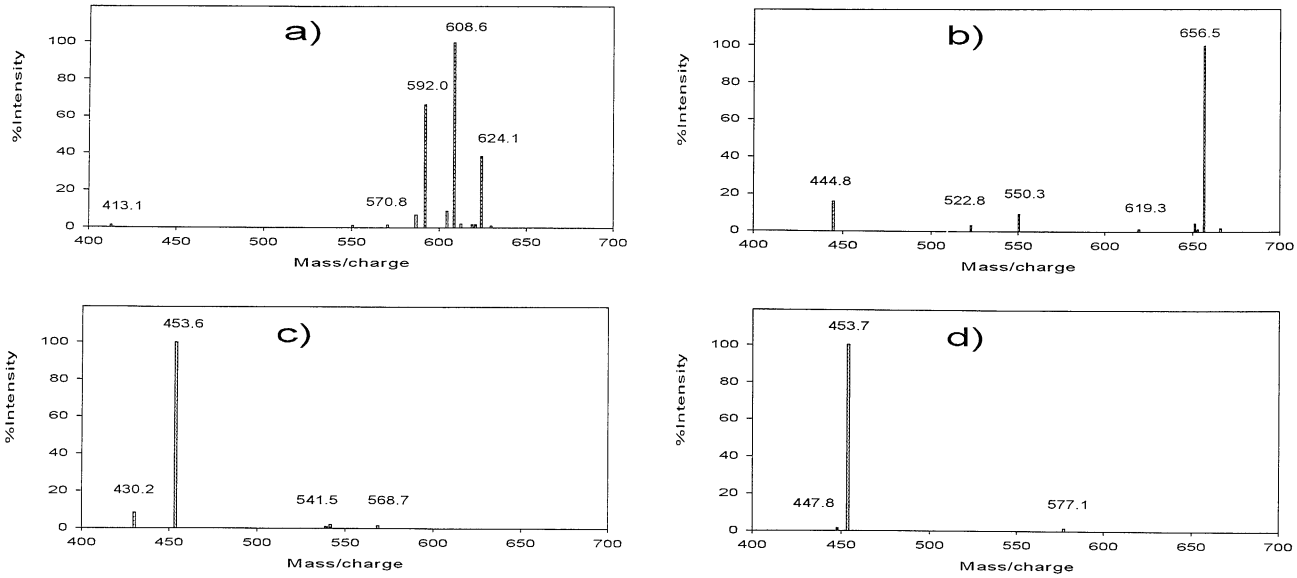
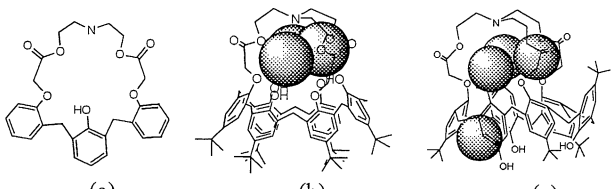


Figure 1. MALDI mass spectra of polytopic coreceptor(1) in presence of alkali metal iodide and their mixture, a). LiI, b). NaI, c). KI, d). their mixture with CsI (more details see the text).

spectrum. Based on these results, we can conclude: Li^+ ion, with a small size, can only form a 1:1 complex with (1), the middle size Na^+ ion can form 3:1 and 4:1 complex with (1), while the larger K^+ ion can form 3:1 complex with (1), no 4:1 complex can be found. Another characteristic is that no counterion is detected in the mass spectra, this indicates that the metal ions in the complexes are located far away each other, no counterion is needed to balance the repulsion interaction between the metal ions. All these properties can be understood in the following way. In the cone conformation (Scheme 1), obviously, the system exists three binding sites, each of them is formed from the sub-units with structure shown in scheme 2a, and the sub-units are somewhat similar to that of 18-crown-6 and other macrocycle system. Each of them may complex a metal ion and then it is easy to understand the formation of 1:3 complexes with K^+ and Na^+ ions and the high selectivity to K^+ ion (Scheme 2b).



(a) (b) (c)

Scheme 2.

When Li^+ ion is used, the small size of it enables it pass through the cavity of the sub-units mentioned above, and enters into the cavity located at the inner part of the low rim. It will in turn prevent the complex formation between the sub-units and other metal ions, then only 1:1 complex can be observed in the mass spectra. For Na^+ ion, apart from the 3:1 complex, 4:1 complex can also be detected in the mass spectrum. A possible reason for this may be that part of (1) is exist in 1,3,5-alternate conformation (Scheme 1), then apart from the three sub-unites which can complex three metal ions, the fourth metal ion can be complexed by cation-π interaction in the cavity located at the upper rim (Scheme 2c). [24,25] In this conformation the cavities of the three sub-units will be too small to complex K+ ion, then no 4:1 complex can be found for K+ ion.

References

1 J. M. Lehn, *Angew. Chem., Int. Ed. Engl.*, **27**, 89(1988).
2 J.C.Skou, *Angew. Chem., Int. Ed. Engl.*, **37**,2320(1998).
3 D. A. Dougherty and H. A. Lester, *Angew. Chem., Int. Ed. Engl.*, **37**, 2329(1998).
4 H. A. Lester, and D. A. Doughterty, *J. Gen. Physiol*, **111**, 181(1998).
5 R. A. Bissell, E. Cordova, A. E. Kaifer, and J. F. Stoddart, *Nature*, **369**, 133(1994).
6 J.-C. Chambron and J.-P. Sauvage, *Chem. Eur. J.*, **4**, 1362(1998).
7 C. Canevet, J. Libman, and A. Shanzer, *Angew. Chem., Int. Ed. Engl.*, **35**, 2657(1997).
8 J.-P. Sauvage, *Acc. Chem. Res.*, **31**, 611(1998) and references there in.
9 F. Ohseto and S. Shinkai, *J. Chem. Soc., Perkin. Trans.2*, **1995**, 1103.
10 V. Bohmer, *Angew. Chem., Int. Ed. Engl.*, **34**, 713(1998).
11 A. Ikeda and S. Shinkai, *Chem. Rev.*, **97**,1713(1997).
12 R. G. Janssen, W. Verboom, J. P. M. van Duynhoven, E. J. J. van Velzen, and D. N. Reinhoudt, *Tetradron Letters*, **35**, 6555(1994).
13 K. Araki, K. Akao, H. Otsuka, K. Nakashima, F. Inokuchi,and S. Shinkai, *Chem. Lett.*, **1994**, 1251.
14 M. Takeshita, S. Nishio, and S. Shinkai, *J. Org. Chem.*, **59**, 4032(1994).
15 A. Casnati, P. Minari, A. Pochini, R. Ungaro, W. Nijenhuis, F. Jong, and D. N. Reihoudt, *Isr. J. Chem.*, **32**, 79(1992).
16 F. Inokuchi, Y. Shiomi, H. Kawabata, T. Sakaki, and S. Shinkai, *Chem. Lett.*, **1993**, 1595.
17 J. B. Fenn, M. Mann, C.K. Meng, S.F. Wong, and C. M. Whitehouse, *Science*, **246**, 64(1989).
18 J. B. Fenn, M. Mann, C.K. Meng, S.F. Wong, and C. M. Whitehouse, *Mass Spectrom. Rev.*, **9**,37(1990).
19 M. Karas and F. Hillenkamp, *Anal. Chem.*, **60**, 2299(1988).
20 M. Karas, D. Bachmann, U. Bahr, and F. Hillenkamp, *Int. J. Mass. Spectrom. Ion Processes*, **78**, 53(1987).
21 K. C. Russell, E. Leize, A.V. Dorsselaer, and J.-M. Lehn, *Angew. Chem., Int. Ed. Engl.*, **34**, 209(1995).
22 K. Kimura, T. Utsumi, T. Teranishi, M. Yokoyama, H. Sakamoto, M. Okamoto, R. Arakawa, H. Moriguchi,and Y. Miyaji, *Angew. Chem., Int. Ed. Engl.*,**36**, 2452(1997).
23 T. B. Farmer and R. M. Caprioli, *J. Mass Spectrom.*, **33**, 697(1998).
24 A. Ikeda, H. Tsuzuki, and S. Shinkai, *J. Chem. Soc., Perk. Trans.* 2, **1994**, 2073.
25 A. Ikeda and S. Shinkai, *Tetradron Lett.*, **33**, 7385(1992).