Synthesis and Binding Property of Tunable Upper-Rim Calix[4]crowns

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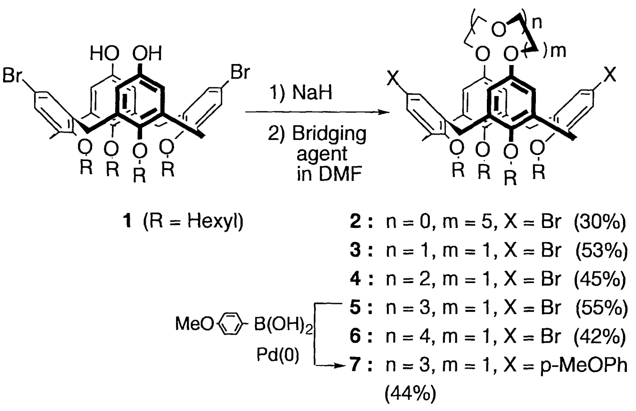
Conformationally stable, tunable upper-rim calix[4]crowns **3** ~ **7** were synthesized in good yields from dibromodihydroxycalix[4]arene hexyl ether **1** and the picrate extraction experiment showed their higher affinities for primary ammonium ions compared to those for alkali metal cations.

Calixarenes have been used as versatile building blocks for the synthesis of numerous hosts for neutral or ionic species.[1] Conformationally stable, cone-structured, upper-rim calix[4]crowns would show interesting binding properties, because they will provide a hydrophobic cavity as well as a hydrophilic binding site for the complexation of cationic organic guests such as alkylammonium ions. Ammonium ion complexing properties were detected in calixarene propyl ether,[2] calix[6]arene hexaester,[3] *p*-sulfonic acid[4] or quinone[5] derivarives, lower-rim calix[4]crowns,[6] and tetraanions of resorcarene,[7] which are binding ammonium ions mainly through charge-dipole or charge-charge interaction. Upper-rim calix[4]crowns in conformational mixtures were synthesized from distal bis(chloromethyl)calix[4]arene methyl ether by Reinhoudt *et al.*, and no binding properties were mentioned.[8]

Recently the regioselective synthesis of a distal dibromodihydroxycalix[4]arene hexyl ether **1** from *p*-bromocalix[4]arene hexyl ether was reported.[9] From this distal diol **1** conformationally stable hosts **2**[9] and **3** ~ **7** were synthesized by introducing alkyl or oligoether bridges on the upper-rim (Scheme 1). Host **3**, **4**, **5** and **6** were obtained in 53%, 45%, 55% and 42% yield respectively by high dilution reaction between diol **1** treated with NaH and the corresponding oligomeric ethylene glycol di-*p*-tosylate in DMF solution.[10] Interesting features of these hosts would arise from the two versatile bromo groups which make the articulate tuning of the host's properties possible. For instane, to enlarge the hydrophobic cavity, two bromo groups of host **5** were substituted by *p*-methoxyphenyl groups using Pd(0)-catalyzed Suzuki reaction,[11] which gave host **7** in 44% yield.



Scheme 1.

^{1}H NMR spectrum of the host **5** shows two singlets for the aromatic protons at δ 7.26 and 5.80, and two doublets (J = 13.3 Hz) for the bridging methylene protons at δ 4.39 (H_{endo}) and δ 3.07 (H_{exo}). Similar patterns which confirm their cone or pinched-cone conformations were observed for all the other hosts.

Molecular recognition properties were investigated by extraction experiment of solid alkali metal or ammonium picrates into chloroform solution of host at 25 °C.[12] Figure 1 shows the extractability spectra of the representative host **5** and **6**. Characteristically host **5** showed much higher extraction efficiencies for primary ammonium ions (e.g., 48% for t-BuNH$_3^+$) compared with those for ammonium or alkali metal cations. It was the common phenomena for hosts **3**, **4** and **7**. The poor extractabilities of ammonium or alkali metal cations (< 5%) are attributable to the fact that those cations could only be bound to partially organized oligoether moiety or to the intrinsically low binding lower-rim alkoxy groups.[13] However, as CPK molecular model study and molecular mechanics calculation (MM+ force field) suggested, primary ammonium ion could be bound to both hydrophobic cavity and hydrophilic oligoether unit of host using each alkyl and ammonium part simultaneously, which results in synergistic affinities. When the bridge becomes longer than that of host **5**, the bridge easily coils, collapsing the cavity and forming pseudocircular crown unit which can accomodate Li$^+$ or Na$^+$. In fact no strong synergistic effect was observed for host **6** which instead showed the highest affinity for lithium picrate (29%).

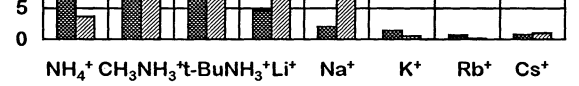


Figure 1. Liquid - solid extractability spectra of host **5** and **6**.

The extractabilites of host **3** ~ **7** for ammonium or primary ammonium ions were compared in Figure 2. The binding tendencies of host **3**, **4** and **5** imply that the longer crown unit better sustained the cone-structured cavity, enabling host to nest larger alkyl ammonium ion. For host **6** the cavity appeared collapsed and for host **7** the hydrophobic binding effect seemed to be tuned optimal (57% for t-BuNH$_3^+$). The extractability of host **5** increases in order of ammonium (8%) < methyl-

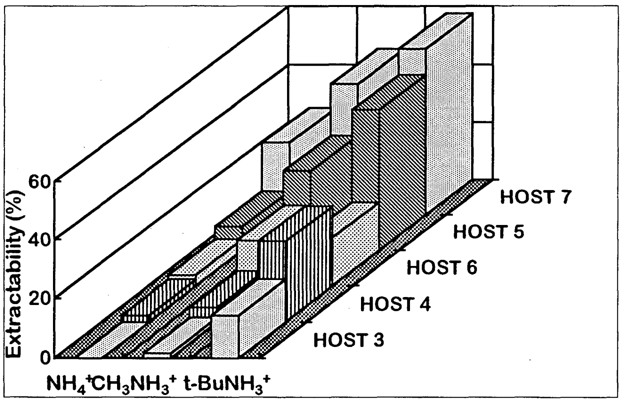


Figure 2. Extractabilities of hosts **3**, **4**, **5**, **6** and **7** for ammonium and alkylammonium ions.

ammonium (27%) < t-butylammonium (48%), showing the importance of size-fit hydrophobic binding. Host **4** was less efficient than host **5**, but gave the highest selectivity (5.6) of t-$BuNH_3^+/MeNH_3^+$. Host **2** and distal diol **1** were subjected to the same extraction experiment, but the extractabilities for all ions were negligible within experimental error.

In conclusion, conformatinally stable upper-rim calix[4]-crowns were prepared in good yields and their synergistic binding efficiencies were confirmed from the high affinities toward primary ammonium ions. Further modifications of bromo groups would give unprecedented calix[4]crowns such as polymeric or lariat-type calix[4]crowns.

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