

[CO⁺] is negligible in the CAD spectra of these C₂H₄O⁺ tautomers.^{17,18} The lowest energy fragmentations of CH₃-CH=O lead to [•]CHO or CH₃CO[•] radicals that easily yield¹³ CO^{15d,i} and to [•]CH₂-CH=O ↔ CH₂=CH-O[•] radicals. The reionization efficiency for producing CO⁺ from [•]CHO is nearly as great as from CO, but the reionization efficiencies of the other radicals are at best a few percent of that of CO.^{20,23}

The NR spectra of CH₂=CH-OH⁺ are consistent with its structure. Compared to parts A and D of Figure 2, parts B and E of Figure 2 show lower CH₃⁺ and HCO⁺ (*m/z* 15 and 29) and higher OH⁺ (*m/z* 17; OD⁺ from CH₂=CH-OD⁺) and CH₂O⁺ (also unique in its CAD spectrum)¹⁸ absolute abundances. Neutralization and reionization of CH₂=CH-OH⁺ appear to occur with <<10% direct isomerization of CH₂=CH-OH to CH₃-CH=O; the NR spectrum of CH₂=CD-OH⁺ (not shown) indicates a dominant H⁺ loss (as does its CAD spectrum) with *m/z* [44]/[45] values of 1.6 and 1.9 for 90% and 30%T, while CH₃-CD-O⁺ shows values of 0.11 and 0.13. Increasing CAD (part E vs. B of Figure 2) increases [OH⁺] via CH₂=CH-OH → CH₂=CH⁺ + [•]OH, as CH₂=CH-OH⁺ ions do *not* yield OH⁺ upon CAD;¹⁷ the counterpart product, C₂H₃⁺, is reionized less efficiently than [•]OH.²⁰ The lowest energy dissociation of CH₂=CH-OH leads to CH₂=CH-O[•] (Figure 1)²² which has a poor He reionization cross section;²⁰ it could contribute to the abundances of C₂H₂O⁺ (*m/z* 42) and CHO⁺ (*m/z* 29) in Figure 2E. The extra collision of part E vs. B of Figure 2 also increases [CO⁺]; it must result from rearrangement, as formation of [•]CHO or CO from CH₂=CH-OH by simple bond cleavages would require >100 kcal/mol higher energy than CH₂=CH-O[•] formation. The pathway of this rearrangement is indicated by isotope effects; determined separately under identical experimental conditions, the [CO⁺] increase is very similar (within 5%) for CH₂=CH-OH and CH₂=CH-OD but significantly (20% and 50%) smaller for CH₂=CD-OH and CH₃-CD=O. For two-fifths of CO loss to proceed by CH₂=CD-OH → CH₃-CD=O would require that the major (three-fifths) rearrangement pathway shows no isotope effect, which is not likely for migration of the central hydrogen. Thus, the probable main pathway is the 1,2 H-migration CH₂=CH-OH → CH₃-C-OH (Figure 1).²⁴ However, appreciable amounts of nondissociating CH₃-CH=O are *not* formed through this intermediate, according to the *m/z* [30]/[44] values of parts G vs. H and J vs. K of Figure 2.

This hydroxyethylidene intermediate has also been suggested in the photochemical decarboxylation and the pyrolysis of pyruvic acid.¹⁴ The NR spectra (parts C and F of Figures 2) of stable CH₃-C-OH⁺ ions are dominated by CO⁺, which should *not* result from CH₃-C-OH → CH₄ + CO, as little CH₃D is formed from CH₃-C-OD (*m/z* 12-16 in part I vs. C of Figure 2).²⁰ The negligible peak at *m/z* 30 (31 in CH₃-C-OD) indicates little isomerization to CH₂=CH-OH. The spectra also exhibit abundant molecular ions, but a substantial part appears not to represent reionized CH₃-C-OH. The lowest energy

dissociation of both CH₃-C-OH and CH₃-C-OH⁺ involves loss of the hydroxylic hydrogen atom,¹³ so that its substitution with D should decrease its loss. However, in the NR spectrum of CH₃-C-OD⁺ the C₂H₂(H,D)O⁺ signal is increased and C₂H₃DO⁺ decreased (parts I,L vs. C,F of Figure 2). Assuming that the yield for reionization to stable molecular ions is lower for hydroxyethylidene than for ethanal,^{15h} the [C₂H₃DO⁺] decrease suggests that D-substitution slows the isomerization of CH₃-C-OD to CH₃-CD=O. The much lower stability of hydroxyethylidene would account for the collisional reduction in the *absolute* abundance of the molecular ion of CH₃-C-OD (*m/z* 45 in parts I and L of Figure 2), while the tripling of the *absolute* abundance for CH₃-C-OH (*m/z* 44, parts C and F of Figure 2) is consistent with the presence of the stable CH₃-CH=O isomer.

Formation of undissociated CH₃-CH=O from CH₃-C-OH (Figure 1) requires that the transition-state energy for the isomerization CH₃-C-OH → CH₃-CH=O must lie well below 44 kcal/mol (Δ*H*_f of CH₃[•] + [•]CHO), possibly ~35 kcal/mol. This is also a lower limit for the transition-state energy of the isomerization CH₂=CH-OH → CH₃-C-OH leading to the observed CO⁺, as CH₃-C-OH forms a negligible amount of CH₂=CH-OH (vide supra). This transition-state energy for the tight complex CH₂=CH-OH → CH₃-C-OH isomerization must also be substantially below that²² for the loose-complex loss of [•]H or possibly ~40 kcal/mol (Figure 1). The direct 1,3 H-rearrangement CH₂=CH-OH → CH₃-CH=O is not observed; the predicted transition-state energies of the latter are 36⁵-64 kcal/mol for the symmetry allowed entropically unfavorable antarafacial and 65-75 kcal/mol for the symmetry-forbidden suprafacial isomerization.¹⁻³

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Kinetically Stable Complexes of Alkali Cations with Rigidified Calix[4]arenes. X-ray Structure of a Calixspherand Sodium Picrate Complex

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In this communication we describe the synthesis of a novel class of highly preorganized host molecules in which the structural features of the calix[4]arenes and spherands are combined (calixspherand **2d**), together with the complexation with alkali cations.

The hexa-anisyl spherand **1** represents a macrocyclic host with an enforced cavity in which Li⁺ or Na⁺ cations are complexed with a very high *thermodynamic* stability.¹ Cram and co-workers have shown that these complexes of **1** with Li⁺ and Na⁺ are also *kinetically* very stable. However, the scope of complexation is

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(20) Relative reionization efficiencies were determined for 5 keV CO, OH⁺, CH₃⁺, CH₄⁺, [•]CHO, C₂H₃⁺, CH₃-CH=O, CH₂=CH-OH, CH₃CO⁺, and CH₂=CH-O[•].^{15e} The first eight molecules were prepared by charge exchange neutralization from the respective cations while the last two were formed by dissociation from CH₃COCOCH₃⁺ and CH₃CO₂CH=CH₂⁺, respectively.^{21,22} He (90% transmittance) reionization of identical abundances of the above neutral species produces molecular ions (and total ions) with the following intensities relative to the values of CO: CO, 1.0 (1.1 vs. [28⁺]); OH⁺, 0.60 (1.0); CH₃⁺, 0.48 (1.7); CH₄⁺, 0.015 (1.4); C₂H₃⁺, 0.035 (0.32); CH₃-CH=O, 0.032 (0.45); CH₂=CH-OH, 0.025 (0.26); CH₃CO⁺, 0.012 (0.061); CH₂=CH-O[•], 0.00073 (0.035); [•]CHO, 0.069 (1.3, from which 1.0 is [CO⁺]); note, however, that Franck-Condon factors can increase the extent of fragmentation for species formed by vertical neutralization).^{15j}

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(23) In parts G and J of Figure 2 the significant fragments at *m/z* 16, presumably CH₂D⁺, must originate from dissociation of CH₃-CD-O⁺, as the complementary reionized product CHO⁺ is of minor importance, and the CAD spectrum of CH₃-CD-O⁺ shows a similar *m/z* 16 peak.

(24) An unfavorable isotope effect would be expected for the isomerization CH₂=CH-OD → [•]CH₂-CHD-O[•] → CH₃-CD=O discussed by Splitter et al.⁴

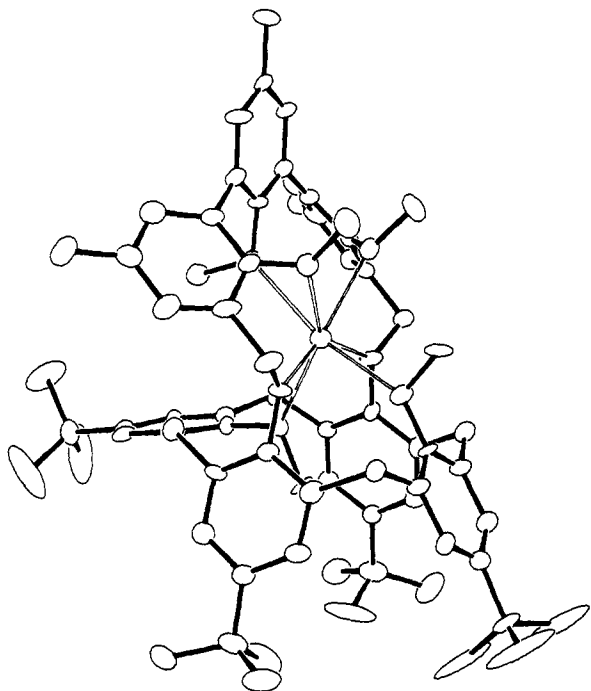
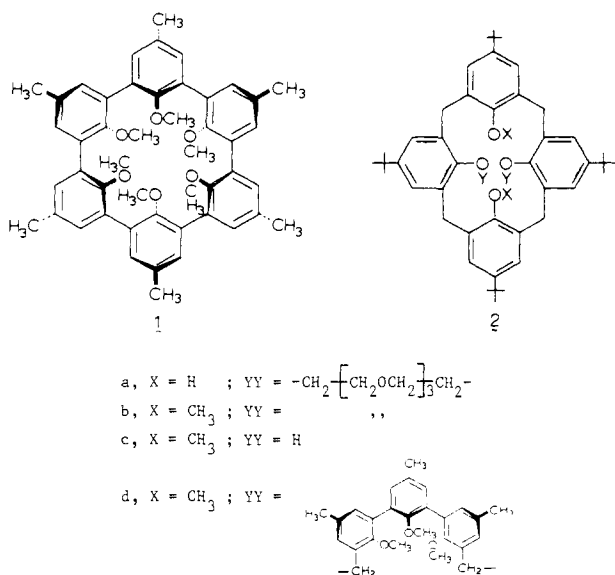


Figure 1. X-ray structure of $2d \cdot Na^+$.⁸

limited, because the rigid cavity is not accessible to larger cations. We are currently interested in complexes of similar kinetic stability with Rb^+ in relation to the application of $^{81}Rb^+$ in organ imaging.²



Although the calix[4]arenes³ are flexible molecules, this flexibility can be reduced by derivatization of the phenolic groups.^{4,5} CPK models indicate that the 26,28-bridged 25,27-dialkoxy-calix[4]arenes should have well-defined molecular cavities.

The macrobicyclic crown ether **2b** (All new compounds, including the complexes, gave elemental analysis in agreement with the molecular (C, H, N, Na \pm 0.3%) composition.) was synthesized by methylation of the *p-tert*-butylcalix[4]arene-crown-5⁴ (**2a**) with methyl iodide in 60% yield. The ¹H NMR spectrum (CDCl₃) of the free ligand **2b** corresponds to a flattened cone conformation.^{3,4} The association constants K_a (M⁻¹) and binding

free energies $-\Delta G^\circ$ (kcal·mol⁻¹) for the complexation of alkali picrates⁶ showed that host **2b** is an efficient ionophore for K^+ and Rb^+ with $-\Delta G^\circ$ 11.3 and 10.6 kcal·mol⁻¹, respectively. The selectivity found for $K_a^{K^+}/K_a^{Na^+}$ was 2×10^3 ($\Delta\Delta G^\circ = 4.5$ kcal·mol⁻¹), whereas a substantial decrease in Cs^+ -picrate (Cs^+ -Pic) complexation was found ($-\Delta G^\circ = 7.8$ kcal·mol⁻¹). The ¹H NMR spectra of the K^+ -Pic and Rb^+ -Pic complexes showed a predominant partial cone conformation of the calix[4]arene moiety.

We concluded that the *p-tert*-butylcalix[4]arene is a suitable building block for rigid hosts, providing the mobility of the aryl rings could be further reduced by steric barriers which will force the calix[4]arene moiety into a rigid binding conformation.

Host **2d** was synthesized by reacting **2c**⁵ and 3,3''-bis(bromo-methyl)-2,2',2''-trimethoxy-5,5',5''-trimethyl-1,1':3',1''-terphenyl⁷ with sodium hydride in THF under high dilution conditions. Calixspherand **2d** was obtained as the sodium bromide complex (10%). Anion exchange of **2d**·NaBr to **2d**·NaPic afforded suitable crystals that allowed X-ray analysis (Figure 1).⁸ The structure shows the sodium ion encapsulated in a cavity formed by an alternating arrangement of the three methoxy oxygen atoms of the *m*-teranisyl moiety and by the four oxygen atoms of the *p-tert*-butylcalix[4]arene moiety, forced into a partial cone conformation. The O-Na⁺ distances vary from 2.38 to 2.60 Å giving a cavity diameter of ~ 2.2 Å, larger than the ionic diameter of Na⁺ (1.96 Å). The aryl-aryl dihedral angles in the *m*-teranisyl moiety are 54.7°, comparable to those in the anisyl spherands.¹

Decomplexation of **2d**·NaBr only succeeded by heating in a 1:4 methanol water mixture at 120 °C in a sealed ampule. Obviously, the driving force of decomplexation is the crystallization of **2d** from the medium.¹

Extraction experiments with alkali picrates showed large differences in rates of complexation (Rb^+ , $Cs^+ \leq 6$ h; $K^+ \geq 12$ h; $Na^+ \geq 48$ h) indicating complete desolvation prior to complexation.⁹ The binding free energies $-\Delta G^\circ$ have been determined by the picrate extraction method⁶ (Na^+ 13.6, K^+ 14.0, Rb^+ 12.0, Cs^+ 9.8 kcal·mol⁻¹ \pm 0.2).

The ¹H NMR spectrum (CDCl₃) of the free ligand corresponds to a partial cone conformation with chemical shifts of the methoxy protons at δ 3.81 (3 H), 3.49 (6 H), 2.93 (3 H), and 1.06 (3 H). The methoxy protons in the Na-Pic complex were found at δ 4.20 (3 H), 3.59 (6 H), 1.50 (3 H), and -0.04 (3 H), and this indicates minor conformational changes. The high field absorption most likely corresponds to the "endo-positioned" methoxy group. In the K^+ -Pic and Rb^+ -Pic complex this signal is present at δ 0.14 and 0.23, respectively. The larger ionic radii of K^+ and Rb^+ force the "endo-positioned" methoxy group more out of the calix,³ compared with the Na^+ complex. This shows that the structure of these complexes in solution is similar as in the solid state (Figure 1).

We conclude that host **2d** represents an important extension of the spherand principle to the complexation of the larger alkali cations K^+ and Rb^+ .

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Supplementary Material Available: Tables containing listings of positional and thermal parameters, bond lengths, and bond angles (4 pages). Ordering information is given on any current masthead page.

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(8) C₂₇H₃₆O₇·Na·C₆H₂N₃O₇, monoclinic, space group P2₁/m, $a = 15.614$ (7) Å, $b = 15.720$ (5) Å, $c = 16.219$ (7) Å, $\beta = 112.31$ (3)°, $Z = 2$, $D_c = 1.17$ g·cm⁻³, μ (Mo K α) = 0.8 cm⁻¹, number of unique reflections measured 5194 ($3^\circ < \theta < 22.5^\circ$), $T = 100$ K. Solution by direct methods, refinement on 3930 reflections ($F_o^2 > 1.5\sigma(F_o^2)$). H atoms not included in structure factor calculations. Final $R = 11.7\%$, $R_w = 13.3\%$. Number of variables: 524.

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