

[CO<sup>+</sup>] is negligible in the CAD spectra of these C<sub>2</sub>H<sub>4</sub>O<sup>+</sup> tautomers.<sup>17,18</sup> The lowest energy fragmentations of CH<sub>3</sub>-CH=O lead to <sup>•</sup>CHO or CH<sub>3</sub>CO<sup>•</sup> radicals that easily yield<sup>13</sup> CO<sup>15d,i</sup> and to <sup>•</sup>CH<sub>2</sub>-CH=O ↔ CH<sub>2</sub>=CH-O<sup>•</sup> radicals. The reionization efficiency for producing CO<sup>+</sup> from <sup>•</sup>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.<sup>20,23</sup>

The NR spectra of CH<sub>2</sub>=CH-OH<sup>+</sup> are consistent with its structure. Compared to parts A and D of Figure 2, parts B and E of Figure 2 show lower CH<sub>3</sub><sup>+</sup> and HCO<sup>+</sup> (*m/z* 15 and 29) and higher OH<sup>+</sup> (*m/z* 17; OD<sup>+</sup> from CH<sub>2</sub>=CH-OD<sup>+</sup>) and CH<sub>2</sub>O<sup>+</sup> (also unique in its CAD spectrum)<sup>18</sup> absolute abundances. Neutralization and reionization of CH<sub>2</sub>=CH-OH<sup>+</sup> appear to occur with <<10% direct isomerization of CH<sub>2</sub>=CH-OH to CH<sub>3</sub>-CH=O; the NR spectrum of CH<sub>2</sub>=CD-OH<sup>+</sup> (not shown) indicates a dominant H<sup>+</sup> loss (as does its CAD spectrum) with *m/z* [44]/[45] values of 1.6 and 1.9 for 90% and 30%T, while CH<sub>3</sub>-CD-O<sup>+</sup> shows values of 0.11 and 0.13. Increasing CAD (part E vs. B of Figure 2) increases [OH<sup>+</sup>] via CH<sub>2</sub>=CH-OH → CH<sub>2</sub>=CH<sup>•</sup> + <sup>•</sup>OH, as CH<sub>2</sub>=CH-OH<sup>+</sup> ions do *not* yield OH<sup>+</sup> upon CAD;<sup>17</sup> the counterpart product, C<sub>2</sub>H<sub>3</sub><sup>+</sup>, is reionized less efficiently than <sup>•</sup>OH.<sup>20</sup> The lowest energy dissociation of CH<sub>2</sub>=CH-OH leads to CH<sub>2</sub>=CH-O<sup>•</sup> (Figure 1)<sup>22</sup> which has a poor He reionization cross section;<sup>20</sup> it could contribute to the abundances of C<sub>2</sub>H<sub>3</sub>O<sup>+</sup> (*m/z* 42) and CHO<sup>+</sup> (*m/z* 29) in Figure 2E. The extra collision of part E vs. B of Figure 2 also increases [CO<sup>+</sup>]; it must result from rearrangement, as formation of <sup>•</sup>CHO or CO from CH<sub>2</sub>=CH-OH by simple bond cleavages would require >100 kcal/mol higher energy than CH<sub>2</sub>=CH-O<sup>•</sup> formation. The pathway of this rearrangement is indicated by isotope effects; determined separately under identical experimental conditions, the [CO<sup>+</sup>] increase is very similar (within 5%) for CH<sub>2</sub>=CH-OH and CH<sub>2</sub>=CH-OD but significantly (20% and 50%) smaller for CH<sub>2</sub>=CD-OH and CH<sub>3</sub>-CD=O. For two-fifths of CO loss to proceed by CH<sub>2</sub>=CD-OH → CH<sub>3</sub>-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 CH<sub>2</sub>=CH-OH → CH<sub>3</sub>-C-OH (Figure 1).<sup>24</sup> However, appreciable amounts of nondissociating CH<sub>3</sub>-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.<sup>14</sup> The NR spectra (parts C and F of Figures 2) of stable CH<sub>3</sub>-C-OH<sup>+</sup> ions are dominated by CO<sup>+</sup>, which should *not* result from CH<sub>3</sub>-C-OH → CH<sub>4</sub> + CO, as little CH<sub>3</sub>D is formed from CH<sub>3</sub>-C-OD (*m/z* 12-16 in part I vs. C of Figure 2).<sup>20</sup> The negligible peak at *m/z* 30 (31 in CH<sub>3</sub>-C-OD) indicates little isomerization to CH<sub>2</sub>=CH-OH. The spectra also exhibit abundant molecular ions, but a substantial part appears not to represent reionized CH<sub>3</sub>-C-OH. The lowest energy

dissociation of both CH<sub>3</sub>-C-OH and CH<sub>3</sub>-C-OH<sup>+</sup> involves loss of the hydroxylic hydrogen atom,<sup>13</sup> so that its substitution with D should decrease its loss. However, in the NR spectrum of CH<sub>3</sub>-C-OD<sup>+</sup> the C<sub>2</sub>H<sub>2</sub>(H,D)<sup>+</sup> signal is increased and C<sub>2</sub>H<sub>3</sub>DO<sup>+</sup> 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,<sup>15h</sup> the [C<sub>2</sub>H<sub>3</sub>DO<sup>+</sup>] decrease suggests that D-substitution slows the isomerization of CH<sub>3</sub>-C-OD to CH<sub>3</sub>-CD=O. The much lower stability of hydroxyethylidene would account for the collisional reduction in the *absolute* abundance of the molecular ion of CH<sub>3</sub>-C-OD (*m/z* 45 in parts I and L of Figure 2), while the tripling of the *absolute* abundance for CH<sub>3</sub>-C-OH (*m/z* 44, parts C and F of Figure 2) is consistent with the presence of the stable CH<sub>3</sub>-CH=O isomer.

Formation of undissociated CH<sub>3</sub>-CH=O from CH<sub>3</sub>-C-OH (Figure 1) requires that the transition-state energy for the isomerization CH<sub>3</sub>-C-OH → CH<sub>3</sub>-CH=O must lie well below 44 kcal/mol (Δ*H*<sub>f</sub> of CH<sub>3</sub><sup>•</sup> + <sup>•</sup>CHO), possibly ~35 kcal/mol. This is also a lower limit for the transition-state energy of the isomerization CH<sub>2</sub>=CH-OH → CH<sub>3</sub>-C-OH leading to the observed CO<sup>+</sup>, as CH<sub>3</sub>-C-OH forms a negligible amount of CH<sub>2</sub>=CH-OH (vide supra). This transition-state energy for the tight complex CH<sub>2</sub>=CH-OH → CH<sub>3</sub>-C-OH isomerization must also be substantially below that<sup>22</sup> for the loose-complex loss of <sup>•</sup>H or possibly ~40 kcal/mol (Figure 1). The direct 1,3 H-rearrangement CH<sub>2</sub>=CH-OH → CH<sub>3</sub>-CH=O is not observed; the predicted transition-state energies of the latter are 36<sup>5</sup>-64 kcal/mol for the symmetry allowed entropically unfavorable antarafacial and 65-75 kcal/mol for the symmetry-forbidden suprafacial isomerization.<sup>1-3</sup>

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

David N. Reinhoudt,\*† Pieter J. Dijkstra,†  
Peter J. A. in't Veld,† Kjell E. Bugge,† Sybolt Harkema,‡  
Rocco Ungaro,§ and Eleonora Ghidini§

Laboratories of Organic Chemistry and  
Chemical Physics, University of Twente  
7500 AE Enschede, The Netherlands  
Institute of Organic Chemistry  
University of Parma, 43100 Parma, Italy

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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<sup>+</sup> or Na<sup>+</sup> cations are complexed with a very high *thermodynamic* stability.<sup>1</sup> Cram and co-workers have shown that these complexes of **1** with Li<sup>+</sup> and Na<sup>+</sup> are also *kinetically* very stable. However, the scope of complexation is

(20) Relative reionization efficiencies were determined for 5 keV CO, OH<sup>+</sup>, CH<sub>3</sub><sup>+</sup>, CH<sub>4</sub><sup>+</sup>, <sup>•</sup>CHO, C<sub>2</sub>H<sub>3</sub><sup>+</sup>, CH<sub>2</sub>=CH=O, CH<sub>2</sub>=CH-OH, CH<sub>3</sub>CO<sup>+</sup>, and CH<sub>2</sub>=CH-O<sup>•</sup>.<sup>15e</sup> The first eight molecules were prepared by charge exchange neutralization from the respective cations while the last two were formed by dissociation from CH<sub>3</sub>COCOCH<sub>3</sub><sup>+</sup> and CH<sub>3</sub>CO<sub>2</sub>CH=CH<sub>2</sub><sup>+</sup>, respectively.<sup>21,22</sup> 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<sup>+</sup>]); OH<sup>+</sup>, 0.60 (1.0); CH<sub>3</sub><sup>+</sup>, 0.48 (1.7); CH<sub>4</sub><sup>+</sup>, 0.015 (1.4); C<sub>2</sub>H<sub>3</sub><sup>+</sup>, 0.035 (0.32); CH<sub>3</sub>-CH=O, 0.032 (0.45); CH<sub>2</sub>=CH-OH, 0.025 (0.26); CH<sub>3</sub>CO<sup>+</sup>, 0.012 (0.061); CH<sub>2</sub>=CH-O<sup>•</sup>, 0.00073 (0.035); <sup>•</sup>CHO, 0.069 (1.3, from which 1.0 is [CO<sup>+</sup>]); note, however, that Franck-Condon factors can increase the extent of fragmentation for species formed by vertical neutralization.<sup>15j</sup>

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(23) In parts G and J of Figure 2 the significant fragments at *m/z* 16, presumably CH<sub>2</sub>D<sup>+</sup>, must originate from dissociation of CH<sub>2</sub>=CD-O<sup>+</sup>, as the complementary reionized product CHO<sup>+</sup> is of minor importance, and the CAD spectrum of CH<sub>3</sub>-CD-O<sup>+</sup> shows a similar *m/z* 16 peak.

(24) An unfavorable isotope effect would be expected for the isomerization CH<sub>2</sub>=CH-OD → <sup>•</sup>CH<sub>2</sub>-CHD-O<sup>•</sup> → CH<sub>3</sub>-CD=O discussed by Splitter et al.<sup>4</sup>

\* Organic Chemistry, University of Twente.

† Chemical Physics, University of Twente.

‡ University of Parma.

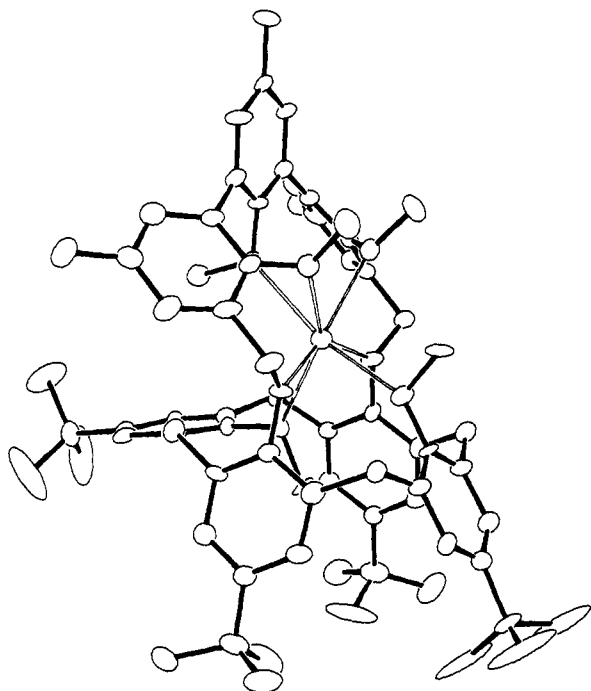
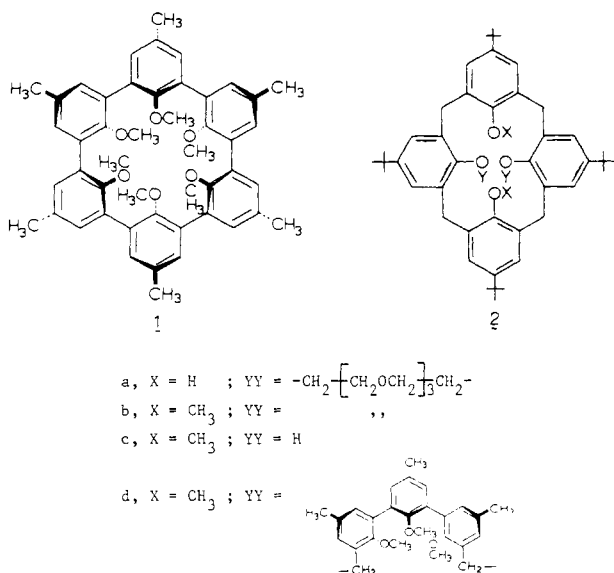


Figure 1. X-ray structure of **2d**·Na<sup>+</sup>.<sup>8</sup>

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



Although the calix[4]arenes<sup>3</sup> are flexible molecules, this flexibility can be reduced by derivatization of the phenolic groups.<sup>4,5</sup> 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-5<sup>4</sup> (**2a**) with methyl iodide in 60% yield. The <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) of the free ligand **2b** corresponds to a flattened cone conformation.<sup>3,4</sup> The association constants *K*<sub>a</sub> (M<sup>-1</sup>) and binding

free energies  $-\Delta G^\circ$  (kcal·mol<sup>-1</sup>) for the complexation of alkali picrates<sup>6</sup> showed that host **2b** is an efficient ionophore for K<sup>+</sup> and Rb<sup>+</sup> with  $-\Delta G^\circ$  11.3 and 10.6 kcal·mol<sup>-1</sup>, respectively. The selectivity found for *K<sub>a</sub><sup>K+</sup>*/*K<sub>a</sub><sup>Na+</sup>* was  $2 \times 10^3$  ( $\Delta\Delta G^\circ = 4.5$  kcal·mol<sup>-1</sup>), whereas a substantial decrease in Cs<sup>+</sup>-picrate (Cs·Pic) complexation was found ( $-\Delta G^\circ = 7.8$  kcal·mol<sup>-1</sup>). The <sup>1</sup>H 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**<sup>5</sup> and 3,3''-bis(bromo-methyl)-2,2',2''-trimethoxy-5,5',5''-trimethyl-1,1':3',1''-terphenyl<sup>7</sup> 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).<sup>8</sup> 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<sup>+</sup> distances vary from 2.38 to 2.60 Å giving a cavity diameter of  $\sim 2.2$  Å, larger than the ionic diameter of Na<sup>+</sup> (1.96 Å). The aryl-aryl dihedral angles in the *m*-teranisyl moiety are 54.7°, comparable to those in the anisyl spherands.<sup>1</sup>

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.<sup>1</sup>

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

The <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) of the free ligand corresponds to a partial cone conformation with chemical shifts of the methoxy protons at  $\delta$  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  $\delta$  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  $\delta$  0.14 and 0.23, respectively. The larger ionic radii of K<sup>+</sup> and Rb<sup>+</sup> force the "endo-positioned" methoxy group more out of the calix,<sup>3</sup> compared with the Na<sup>+</sup> 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<sup>+</sup> and Rb<sup>+</sup>.

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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) C<sub>72</sub>H<sub>86</sub>O<sub>7</sub>·Na·C<sub>6</sub>H<sub>5</sub>N<sub>3</sub>O<sub>7</sub>, monoclinic, space group P2<sub>1</sub>/m, *a* = 15.614 (7) Å, *b* = 15.720 (5) Å, *c* = 16.219 (7) Å,  $\beta$  = 112.31 (3)°, *Z* = 2, *D<sub>c</sub>* = 1.17 g·cm<sup>-3</sup>,  $\mu$ (Mo K $\alpha$ ) = 0.8 cm<sup>-1</sup>, number of unique reflections measured 5194 (3° <  $\theta$  < 22.5°), *T* = 100 K. Solution by direct methods, refinement on 3930 reflections (*F<sub>o</sub>*<sup>2</sup> > 1.5 $\sigma$ (*F<sub>o</sub>*<sup>2</sup>)). H atoms not included in structure factor calculations. Final *R* = 11.7%, *R<sub>w</sub>* = 13.3%. Number of variables: 524.

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