

# A New Fluorescent Calix Crown Ether: Synthesis and Complex Formation with Alkali Metal Ions

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**Abstract:** We synthesised a new *N*-benzylaza-21-crown-7 ether **5** with a dihydroxy coumarin as a fluorescence sensor and investigated the binding behaviour towards alkali metal cations in methanol by fluorescence titrations. The association constants are within one order of magnitude, with the exception of sodium. Potassium is the preferred binding partner ( $K_{\text{Na}} = 330 \text{ M}^{-1}$ ;  $K_{\text{K}} = 8600 \text{ M}^{-1}$ ;  $K_{\text{Rb}} = 8200 \text{ M}^{-1}$ ;  $K_{\text{Cs}} = 4400 \text{ M}^{-1}$ ). The corresponding aza-

21-crown-7 ether (**6**) was attached by a methylene unit to a resorcarene to give fluorescent calix crown ether **12**. The binding abilities of the calix crown ether towards alkali metal ions in methanol have also been investigated,

**Keywords:** crown compounds • fluorescence sensors • host–guest systems • sandwich complexes • supramolecular chemistry

and an increasing complex stability, distinct for potassium and rubidium in comparison with **5**, was found:  $K_{\text{Na}} = 440 \text{ M}^{-1}$ ;  $K_{\text{K}} = 110000 \text{ M}^{-1}$ ;  $K_{\text{Rb}} = 63000 \text{ M}^{-1}$ ;  $K_{\text{Cs}} = 20000 \text{ M}^{-1}$ . Like bis-(crown ether)s, a cooperative complexation of the crown ether and the cavitand scaffold can be assumed. The proposed complex geometry is supported by Kohn–Sham DFT calculations for the potassium and caesium complexes.

## Introduction

Resorc[4]arenes are important in the field of supramolecular chemistry and have been the subject of a number of reviews.<sup>[1]</sup> They are used as host systems for noncovalent interactions, and moreover, as building blocks for extended supramolecules like carcerands,<sup>[2,3]</sup> deepened cavitands<sup>[4]</sup> and other large receptor molecules.<sup>[5]</sup> The driving forces for noncovalent interdependence are cation– $\pi$ , CH– $\pi$  and hydrophobic interactions as well as C–H and O–H hydrogen bonds.<sup>[6,7]</sup> The latter might be the most significant driving force, and therefore, the supramolecular chemistry of resorc[4]arenes with unfunctionalised hydroxyl groups differs considerably from functionalised ones, such as the cavitand.<sup>[8]</sup> Owing to the shape of the cavitand, it is highly tempting to expect that a crown ether-like,  $\pi$ -electron-donating all-in-one device, which is suitable for an all-purpose su-

pramolecule will be formed. However, knowledge of interactions of the cavitand with small guest molecules in solution are limited and the strength of the interaction is minor.<sup>[9]</sup> For this reason more sophisticated supramolecules, starting from cavitands, are necessary. Popular examples, analogous to phenol calixarenes,<sup>[10]</sup> are the combination of a cavitand with a crown ether,<sup>[11]</sup> and the incorporation of cavitands in crown ethers.<sup>[12,13]</sup> The binding abilities of crown ethers and aza crown ethers are well-established,<sup>[14]</sup> as is their use as sensors.<sup>[15]</sup>

Herein, we present the synthesis and binding studies of a novel fluorescent *N*-benzylaza-21-crown-7 ether with a dihydroxy coumarin chromophore.<sup>[16–18]</sup> Based on this crown ether, we synthesised the first fluorescent cavitand crown ether and also carried out binding studies in solution. Conformations of the complexes formed were investigated by DFT calculations.

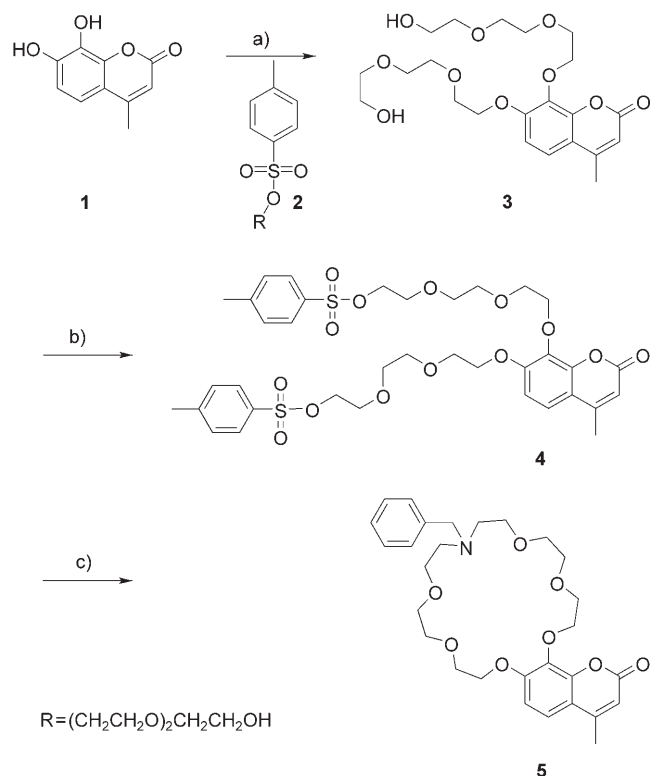
## Results and Discussion

7,8-Dihydroxycoumarin (**1**) was prepared according to a procedure by Sugimo and Tanaka.<sup>[19]</sup> The synthesis of the benzo crown ether was carried out in an analogous manner to that reported by Gokel et al. (Scheme 1).<sup>[20]</sup> Triethylene glycol tolylsulfonyl ether (**2**) was used to attach the glycol units to the coumarin hydroxyl groups to give **3**. Tosylation

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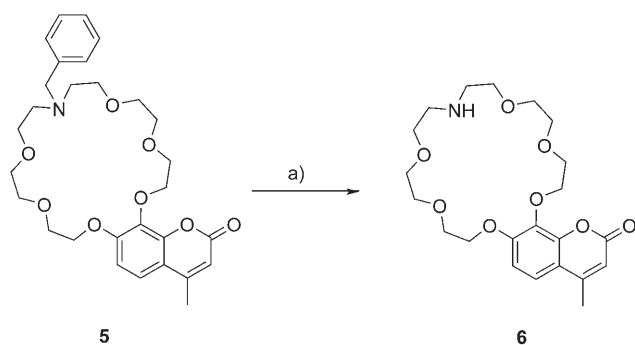
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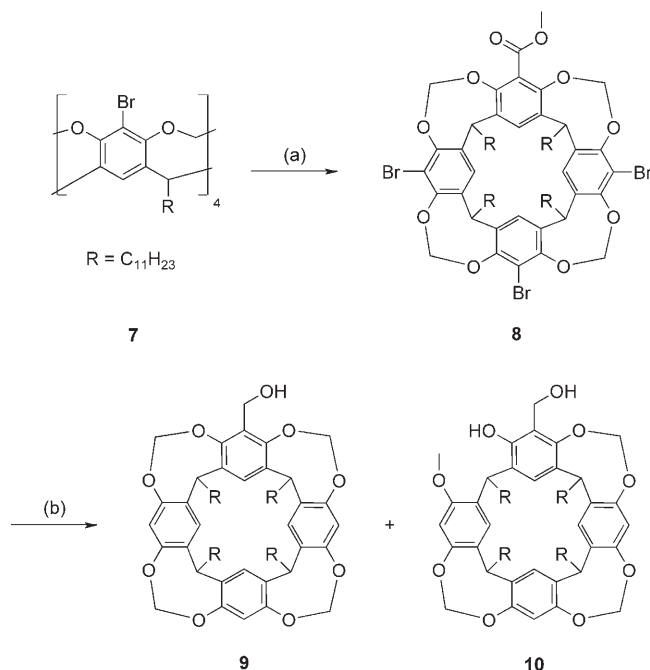
Scheme 1. Synthesis of luminescent crown ether **5**. a)  $\text{K}_2\text{CO}_3$ , DMF; b)  $\text{TsCl}$ ,  $\text{NEt}_3$ ,  $\text{CH}_2\text{Cl}_2$ ; c)  $\text{K}_2\text{CO}_3/\text{Cs}_2\text{CO}_3$ , benzyl amine, MeCN,  $80^\circ\text{C}$ , 39 h.

and cyclisation using benzyl amine finally gave crown ether **5**. For further synthetic steps the benzyl group has to be removed. Benzyl groups are prevailing protecting groups for aza crown ethers and are generally removed by hydrogenation (Scheme 2).<sup>[21]</sup>



Scheme 2. Removal of the benzyl protecting group. a)  $\text{HCl}$ , Pd/C, *i*PrOH,  $50^\circ\text{C}$ , 45 min.

Tetrabromo cavitaand **7**<sup>[22]</sup> was treated with one equivalent of *n*-butyllithium and equilibrated for two hours to control the product distribution to the mono-functionalised species (Scheme 3). Subsequently, methyl chloroformate was added.<sup>[23]</sup> Methyl ester **8** was reduced with  $\text{LiAlH}_4$  in THF.



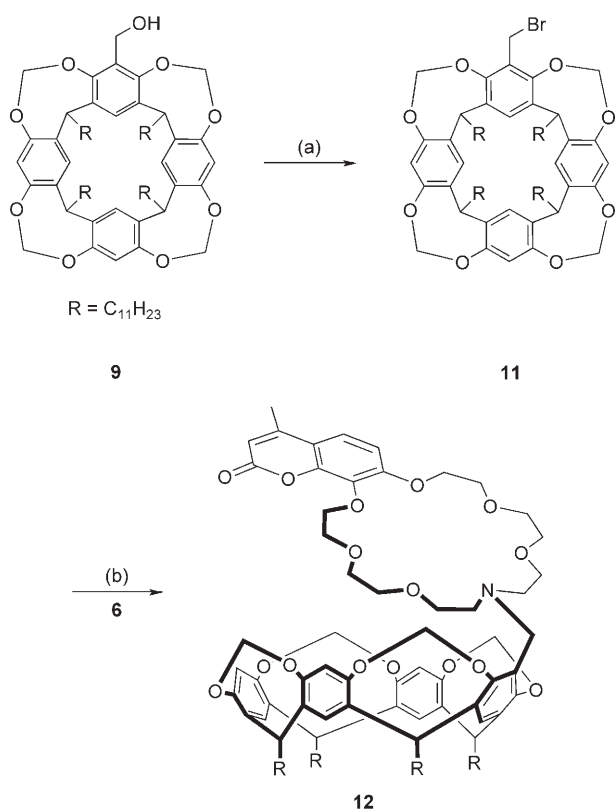
Scheme 3. Monofunctionalisation of the resorcinarene scaffold. a) i) 1 equiv *n*-butyllithium, THF,  $-78^\circ\text{C}$ , 1.5 h; ii) methyl chloroformate, 12 h, RT; b) i)  $\text{LiAlH}_4$ , THF,  $60^\circ\text{C}$ ; ii) 12 h, RT.

This step was the problematic stage of the synthesis. In the simple case with four methyl esters, ambient conditions were sufficient.<sup>[24]</sup> In our case there are three remaining bromines on the resorcinarene moiety. Their removal requires higher reaction temperatures and causes formation of by-product **10**. With increasing reaction time, concurrent bromine removal and opening of the cavitaand can be monitored by MALDI-TOF mass spectrometry. We tried to control the conditions in favour of benzyl alcohol **9**, but so far our endeavours have not been successful.

The reaction was carried out several times with only fair yields of up to 34% of **9**. Treatment of the methyl ester with  $\text{LiAlH}_4$  for only a few minutes followed by removal of bromine in a further reaction by successive addition of *n*-butyllithium and methanol gave the best results. However, formation of byproduct **10** could still not be suppressed completely.

Substitution of the hydroxyl group of **9** proceeds in almost quantitative yield to give benzyl bromide **11**, whereas subsequent substitution to form calix crown ether **12** proceeds with the expected moderate yield for nucleophile substitution reactions with aza crown ethers. In addition, the isolated yield is reduced by the efficient chromatographic workup (Scheme 4).

$^1\text{H}$  NMR spectra of **12** are shown in Figure 1. The spectrum in Figure 1a shows **12** purified by column chromatography on silica gel. Silica gel provides cations on the surface, and hence, broadened resonances of the host protons as a result of complexed ions are observed. Most apparent is the broadening of the signals that belong to the methylene unit located between two phenolic oxygen atoms (arrows at low



Scheme 4. Synthesis of luminescence host **12**. a) PBr<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 1 h, RT; b) Cs<sub>2</sub>CO<sub>3</sub>, DMF, 80 °C, 44 h.

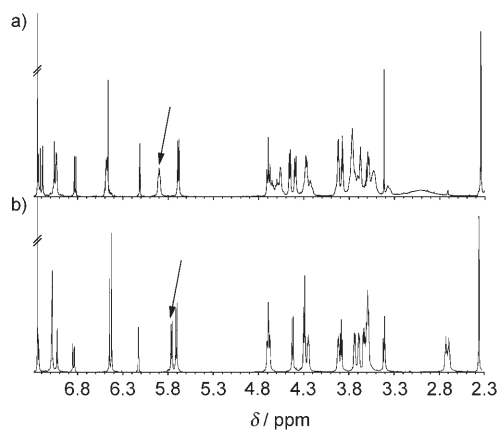


Figure 1. <sup>1</sup>H NMR spectra of **12** in CDCl<sub>3</sub>, 500 MHz. a) Prior to and b) after filtration through basic alumina.

field). In a similar way, but to a lesser extent, most of the other signals are also broadened and/or shifted. After filtration through basic alumina, which is a standard chromatographic procedure in crown ether chemistry, the cations are detached and the resonances are now well resolved (Figure 1b).

Crown ethers that contain a coumarin fluorophore are known as photoinduced-charge-transfer (PCT) cation sensors. Upon cation binding, spectral changes in the emission

spectra appear owing to the change of the excited-state dipole.<sup>[25]</sup> In contrast, dihydroxy coumarin cryptands are reported to act as photoinduced-electron-transfer (PET) sensors.<sup>[16]</sup> Upon cation binding or protonation, these compounds show an enhanced fluorescence intensity. This indicates a PET mechanism by electron transfer from the nitrogen lone pair to the coumarin in the non-complexed form. We investigated the PET activity for our fluorescence systems **5** and **12** by titration with trifluoroacetic acid, which demonstrates the absence of PET. Only minor changes were observed after addition of multiple equivalents of trifluoroacetic acid. It seems that the nitrogen lone pair is too far away from the coumarin unit for an efficient electron transfer. Hence, we assume a PCT mechanism for both host systems.

The absorption spectrum of **5** shows the typical shape of a 7,8-substituted coumarin, with an absorption maximum at 316 nm, a small maximum at 253 nm, and a maximum in the region of aromatic absorbance at 210 nm. The emission maximum is at 452 nm (Figure 2).<sup>[26,27]</sup>

The absorption and emission spectra of calix crown ether **12** is shown in Figure 3. Aside from an absorption at

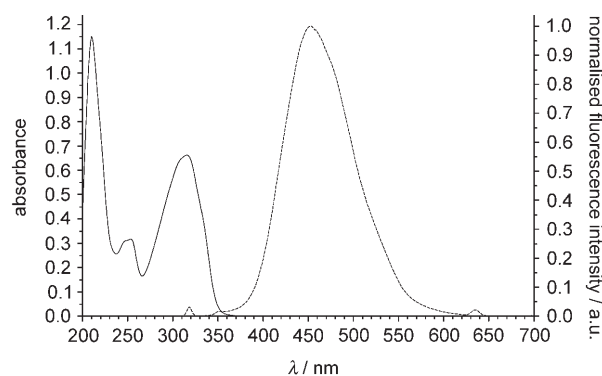


Figure 2. Absorption (—) and emission (----) spectra of coumarin crown ether **5** in methanol ( $c=5 \times 10^{-5}$  M, bandwidth=0.5 nm). Raman and Rayleigh peaks are not removed.

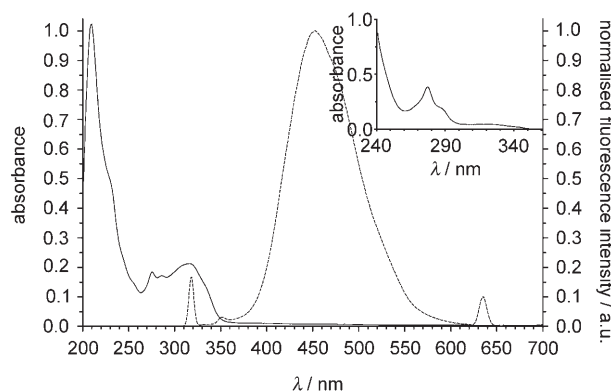


Figure 3. Absorption (—) and emission (----) spectra of calix crown ether **12** in methanol ( $c=1 \times 10^{-5}$  M, bandwidth=0.5 nm). Raman and Rayleigh peaks have not been removed. Inset: Absorption spectrum of C-undecylcalixcavitand in methanol.

316 nm, two poorly resolved absorption bands appear at 286 and 276 nm. These maxima result from the resorcarene moiety, as shown by comparison to the absorption spectrum of an unsubstituted cavitand (Figure 3, inset and the literature<sup>[22]</sup>). The maximum at 452 nm of the emission spectrum is analogous to **5**.

Crown ether **5** and calix crown ether **12** were titrated with solutions that contained different alkali metal acetates to determine binding constants. For example, the emission spectra of **12** recorded after the addition of potassium acetate is shown in Figure 4.

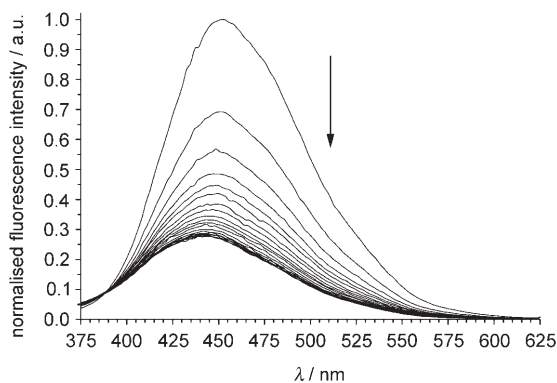


Figure 4. Emission spectra of **12** in methanol upon addition of potassium acetate solution.

The association constants for a 1:1 complex were calculated from non-linear curve fitting by iterative solution of Equation (1):

$$I = I_0 + \frac{I_{\text{lim}} - I_0}{[H]_0} \frac{1}{2} \left( [H]_0 + [G] + K^{-1} - \sqrt{([H]_0 + [G] + K^{-1})^2 - 4[H]_0[G]} \right) \quad (1)$$

Equation (1) gives the relationship between the fluorescence intensity  $I$ , and the association constant  $K$ .  $[H]_0$  is the initial host concentration and  $[G]$  is the guest concentration. The initial fluorescence intensity,  $I_0$ , is measured from the host emission spectra in the absence of guest. The final intensity,  $I_{\text{lim}}$ , was ascertained by measurement of the saturated complex fluorescence intensity or was treated as a floating parameter. A detailed derivation of Equation (1) and further information can be found in the literature.<sup>[28]</sup>

The addition of an alkali metal solution (0.01, 0.05, 0.1 and/or 0.5 M, see Experimental Section) in methanol to a solution of the host system in methanol ( $1.0 \times 10^{-5}$  M) results in a decreasing fluorescence intensity at a given excitation wavelength. The plot of fluorescence intensity of host **12** versus potassium concentration is shown in Figure 5.

A 1:1 complex can be estimated by the shape of the binding isotherm. There was no evidence of a 1:2 (H/G) complex during our work. For example, ESI-MS studies could not

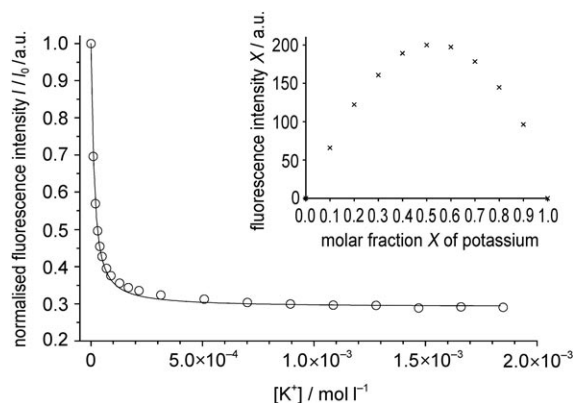


Figure 5. Measured (○) and calculated (—) fluorescence intensity of the potassium complex of **12**. Inset: Job plot for the complex of **12** with potassium ( $c_{\text{overall}} = 1 \times 10^{-5}$  M).

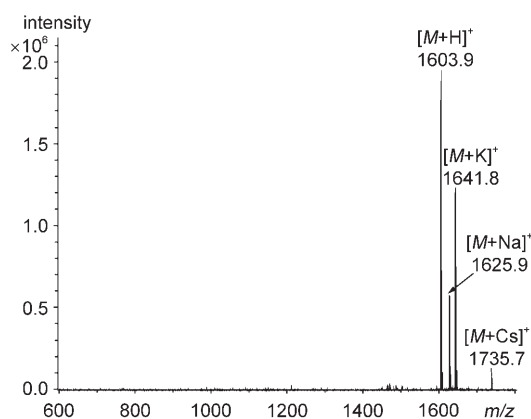


Figure 6. ESI mass spectrum of **12** and sodium, potassium and caesium chlorides in methanol ( $c_{\text{host}} = 1 \times 10^{-5}$  M,  $c_{\text{guest}} = 1 \times 10^{-2}$  M).

give any proof for the formation of a 1:2 complex (Figure 6). A doubly charged 1:2 complex would appear, depending on the guest cations, in the range  $m/z$  810–935. Finally the complex stoichiometry was assured by a representative Job plot<sup>[29]</sup> for the complex of **12** with potassium ( $c_K + 12 = 1 \times 10^{-5}$  M).

## Discussion

The binding constants for various alkali metal complexes with host systems **5** and **12** are summarised in Table 1. For all titration plots the coefficient of determination is higher than 0.99. Alkali acetates were used because of their high solubility. The same results were obtained by using potassium and caesium chlorides, which indicates that the counterion does not have an influence.

The association constant of the potassium complex exceeds the association constant for the other alkali metal complexes for both host systems. The preference of *N*-benzylaza-21-crown-7 for potassium compared with caesium

Table 1. Association constants of **5** and **12** in methanol with various alkali metal acetates at 25 °C.

Compound	Guest	$K$ [ $M^{-1}$ ]	$\log K$	$R^2$
<b>12</b>	$Na^+$	$(4.4 \pm 0.6) \times 10^2$	$2.64 \pm 0.06$	0.994
	$K^+$	$(1.1 \pm 0.2) \times 10^5$	$5.03 \pm 0.08$	0.997
	$Rb^+$	$(6.3 \pm 0.5) \times 10^4$	$4.80 \pm 0.03$	0.997
	$Cs^+$	$(2.0 \pm 0.1) \times 10^4$	$4.29 \pm 0.03$	0.999
<b>5</b>	$Na^+$	$(3.3 \pm 0.6) \times 10^2$	$2.51 \pm 0.06$	0.994
	$K^+$	$(8.6 \pm 1.1) \times 10^3$	$3.93 \pm 0.06$	0.994
	$Rb^+$	$(8.2 \pm 0.8) \times 10^3$	$3.91 \pm 0.04$	0.995
	$Cs^+$	$(4.4 \pm 0.9) \times 10^3$	$3.64 \pm 0.07$	0.991

and sodium has also been reported before by means of calorimetric titrations, and is in very good agreement with our results.<sup>[30]</sup> The caesium ion is not appropriate for the provided coordination sphere, and therefore, weaker complexes are formed. Stronger complexes are formed with potassium and rubidium. Sodium is too small for efficient binding to the crown ether. The results are also in good agreement with the Shannon ionic radii.<sup>[31]</sup> We assume that the slightly smaller association constants for **5** compared with those reported for *N*-benzylaza-21-crown-7 are as a result of the reduced flexibility caused by the incorporated coumarin unit. However, the preference towards potassium and rubidium over caesium and sodium is still confirmed.

The association constants for the alkali metal-calix crown ether complex are one order of magnitude larger than those of the corresponding crown ether complexes, except for the sodium complex. The association constant of the potassium complex noticeably exceeds that of the caesium and rubidium complexes of **12**. In summary, both host systems show the highest selectivity towards potassium and the binding affinity is increased by the attached cavitand. The preference for sodium is only weakly influenced by the cavitand, presumably for the reasons mentioned above.

Sandwich complexes formed from two crown ethers or a bis(crown ether) and one cation are known, especially for big cations.<sup>[32]</sup> For bis(crown ether)s the binding ability towards a cation is enhanced owing to the entropic term by formation of an intramolecular sandwich complex. The observed difference of the binding constants of alkali metal complexes of **5** compared with the alkali metal complexes of **12** are in good agreement with bis(crown ether) complexes.<sup>[33]</sup> From this and the established complex stoichiometry,

we assume that **12** forms a sandwich-like complex geometry with larger alkali metal cations.

In principle, there are two possible enthalpic contributions for an increased binding constant for a calix crown ether sandwich complex: 1) cooperative complexation that involves few or several resorcarene oxygen atoms and crown ether oxygen atoms to form a suitable coordination sphere for the cation, and 2) stabilisation through cation- $\pi$  interactions by the aromatic rings of the resorcarene. To evaluate this and gain further insight into the structural difference of the complexes of **12** formed with different alkali metal ions, we examined selected complexes by structure optimisation and harmonic normal mode analysis in the framework of Kohn-Sham DFT (for details see the Experimental section). Calculations were carried out for the potassium and caesium complexes of **12**, starting from a sandwich-like complex geometry. For the calculations a model compound of **12** was used. The lower rim *n*-undecyl groups were replaced by methyl groups, but this has no influence on the rigid resorcarene cavity. The calculated structures are shown in Figure 7.

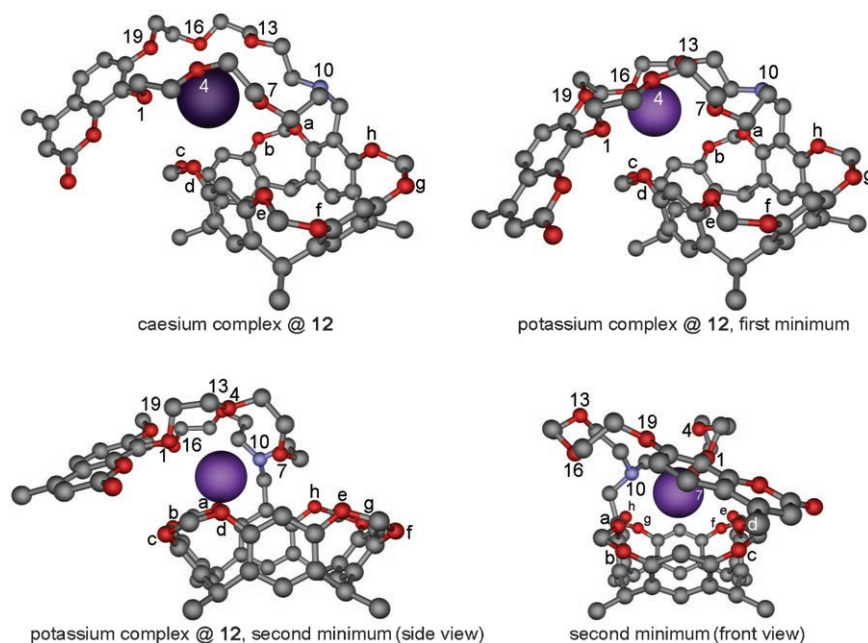


Figure 7. Calculated structures for the potassium and caesium complexes of **12**.

Because van der Waals and other dispersive interactions are not correctly described by the approximate exchange-correlation functionals currently used,<sup>[34]</sup> complexation energies were not calculated. As mentioned above, the measured association constants are in agreement with a sandwich-like complex geometry. Therefore, conformational isomers of **12** whose crown ether covers the resorcarene were chosen. These conformations are energetically most favourable and should be important in solution. The metal cations find many possible coordination sites in these structures, which results in many attracting local minima in structure optimi-



sations. Hence, two coordination isomers were preselected as starting configurations: in the first one the cation was closer to the aza crown ether and in the second isomer it was closer to the resorcarene. For the potassium complex two minima were found, but for the caesium complex only one minimum could be located for coordination by the calix crown ether (Figure 7). For the illustration the Shannon ionic radii for the sixfold coordinated potassium and the eightfold coordinated caesium were used. The resorcarene atoms are displayed in 33% van der Waals radii. The first minimum of the potassium complex is only  $2 \text{ kcal mol}^{-1}$  lower in energy than the second minimum (which includes a zero-point energy correction). The (effective) coordination number for the first minimum is seven and the  $\text{K}\cdots\text{O}$  distances (of coordinating oxygen atoms) range from 282 to 299 pm (oxygen atoms 1, 4, 7, 13, 16, 19, d). For the second minimum the coordination number is six and the  $\text{K}\cdots\text{O/N}$  distances are from 277 to 311 pm (oxygen/nitrogen atoms 1, 4, 7, 10, a, d). This does not prove, but makes plausible, a sixfold coordination in solution. For the caesium complex the coordination number is eight. The  $\text{Cs}\cdots\text{O}$  distances (of coordinating oxygen atoms) range from 311 to 375 pm (oxygen atoms 1, 4, 7, 13, 16, 19, c, d). As is to be expected, in all three compounds the metal cations coordinate to oxygen atoms of the aza crown ether and of the resorcarene. Only a few resorcarene oxygen atoms seem to participate. In summary, the crown ether oxygen atoms and the resorcarene oxygen atoms are able to form different coordination spheres, which are dependent on the size of the guest.

## Conclusions

We have presented the synthesis of a new fluorescence sensing crown ether (**5**) and the first fluorescence sensing calix crown ether (**2**) based on a resorcarene scaffold. The complexation abilities of the host systems towards alkali metal cations in methanol were studied in great detail by fluorescence titration and clearly show a size-dependent selectivity. An incorporation of the cavitand into the supramolecular host system increases the strength of the complexes formed. Based on these results, we assume that there is a cooperative effect in complex formation of **12** by the resorcarene scaffold and the crown ether moiety. This assumption was confirmed by DFT calculations for the complexes of **12** with potassium and caesium.

## Experimental Section

**General procedure for fluorescence titrations:** A solution of the host system was prepared in methanol ( $c = 1.0 \times 10^{-5} \text{ M}$ ). Methanol = 99.9%, A.C.S. spectrophotometric grade, was purchased from Aldrich and used as received. The host solution (1.0 mL) was transferred with a transfer pipette to a PTFE-stoppered  $10 \times 4 \text{ mm}$  half micro quartz cuvette from Hellma. When not in use the cuvette was stored in Caro's Acid. Spectra were recorded three to five times and accumulated. Subsequently, small amounts of alkali metal acetate (caesium acetate 99%, purchased from

Acros Organics; rubidium acetate 99.8%, purchased from Alfa Aesar; sodium and potassium acetate 99%, Merck) solutions in methanol (1 and 2  $\mu\text{L}$  of a 0.01 M solution; 1 and 5  $\mu\text{L}$  of a 0.1 M solution; 1  $\mu\text{L}$  of a 0.5 M solution in the case of sodium to reach complex saturation) were added. This led to a host/guest ratio ranging from 1:1 to at least 1:250 at saturation concentration. The cuvette was shaken for 1 min and was allowed to equilibrate for an additional 1 min. After each addition spectra were recorded until complex saturation was reached. Care was taken to increase the reaction volume less than 6%. The excitation wavelength was 318 nm and the monochromator bandwidth was set to 4 nm for the excitation and the emission monochromator. All spectra were recorded by using a Perkin-Elmer LS50B luminescence spectrometer and a Perkin-Elmer Lambda 40 UV/Vis spectrometer. For Equation (1) integrated fluorescence intensities were used. Integrations were carried out with the software Spekwin32<sup>[35]</sup> from the isoemissive point to the baseline (625 nm). This approach was used for the sake of precision caused by the slight blueshift.

**Details of calculations:** The Kohn-Sham DFT calculations reported herein were performed with the Gaussian 03 program<sup>[36]</sup> using the B3LYP<sup>[37]</sup> hybrid density functional (with the VWN-III, not the VWN-V functional), which is known to give reasonable equilibrium structures and normal mode frequencies for many compound classes<sup>[34]</sup>. To reduce the number of necessary basis functions, effective core potentials (ECP) and corresponding basis sets, of Stevens et al.<sup>[38]</sup> for H (only basis set, no ECP), C, N and O, and of Preuss et al.<sup>[39]</sup> for K and Cs, were used. The basis sets of C, N and O were augmented with polarisation functions (for K and Cs these are already part of the basis sets). For the structure optimisations, an integration grid of 99 radial shells with 590 angular points per shell for all atoms (pruned for nonmetals, unpruned for metals) was used. The threshold for maximum force was  $4.5 \times 10^{-4} \text{ a.u.}$ , the threshold for maximum displacement in internal coordinates was  $1.8 \times 10^{-3} \text{ a.u.}$  This leads to equilibrium structures with energies consistent to  $10^{-7} \text{ a.u.}$  (the same accuracy as for the electronic energy). In the normal mode analyses the integration grid accuracy was reduced to 75 radial shells with 302 angular points per shell (pruned for nonmetals, unpruned for metals). All theoretical structures reported herein were confirmed to be true minima by harmonic normal mode analysis. Throughout this work we used the charge density fitting approximation for Coulomb integrals<sup>[40]</sup> with automatically generated auxiliary basis sets and the Gaussian Fast Multipole Method<sup>[41]</sup> Cartesian coordinates and electronic energies are available in the Supporting Information.

**Toluene-4-sulfonic acid 2-[2-(hydroxy-ethoxy)ethoxy]ethyl ester (2):** *p*-Toluenesulfonic acid chloride (12.88 g, 68 mmol) was added portionwise to a solution of triethylene glycol (40.02 g, 267 mmol) and triethylamine (13.82 g, 137 mmol) in methylene chloride (100 mL) at 0°C. The solution was stirred for 2 h at this temperature. The organic layer was washed with saturated  $\text{NaHCO}_3$  solution and was dried over anhydrous  $\text{MgSO}_4$ . After evaporation the crude product was purified by flash column chromatography ( $\text{SiO}_2$ , chloroform/methanol 98:2) to yield a colourless oil (13.91 g, 46 mmol, 68%).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 500 MHz, 27°C):  $\delta = 7.77$  (d,  $^3J = 8.2 \text{ Hz}$ , 2H; ArH), 7.31 (d,  $^3J = 8.2 \text{ Hz}$ , 2H; ArH), 4.13 (t,  $^3J = 5.2 \text{ Hz}$ , 2H;  $\text{OCH}_2\text{CH}_2\text{OTs}$ ), 3.68 (t,  $^3J = 5.6 \text{ Hz}$ , 2H;  $\text{OCH}_2\text{CH}_2\text{O}$ ), 3.67 (t,  $^3J = 6.3 \text{ Hz}$ , 2H;  $\text{OCH}_2\text{CH}_2\text{O}$ ), 3.57 (brs 4H;  $\text{OCH}_2\text{CH}_2\text{O}$ ), 3.54 (t,  $^3J = 5.2 \text{ Hz}$ , 2H;  $\text{OCH}_2\text{CH}_2\text{O}$ ), 2.41 (s, 3H;  $\text{CH}_3$ ), 2.28 ppm (s, 1H, OH);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 125 MHz, 27°C):  $\delta = 144.8, 132.9, 129.8, 127.9, 72.4, 70.7, 70.2, 69.1, 68.6, 61.7, 21.6 \text{ ppm}$ .

**7,8-Bis(2-[2-[2-(hydroxyethoxy)ethoxy]ethoxy)-4-methyl-2H-chromen-2-on (3):**  $\text{K}_2\text{CO}_3$  (4.74 g, 34.3 mmol) was suspended in a solution of **1** (3.00 g, 15.6 mmol) and **2** (10.45 g, 34.3 mmol) in *N,N*-dimethylformamide (75 mL). The solution turned yellow and was stirred for 23 h at 80°C under an argon atmosphere. The solvent was removed in vacuo and the residue was dissolved in water (150 mL). The acidity was adjusted to pH 3 with dilute HCl. The aqueous phase was extracted with methylene chloride ( $5 \times 50 \text{ mL}$ ) and the combined organic phase was dried over anhydrous  $\text{MgSO}_4$ . After evaporation the crude product was purified by flash column chromatography ( $\text{Al}_2\text{O}_3$ , methylene chloride/diethyl ether/ethanol 2:2:1) to give a yellowish oil (5.94 g, 13.0 mmol, 83%).  $^1\text{H NMR}$  ( $\text{CD}_3\text{OD}$ , 500 MHz, 27°C):  $\delta = 7.46$  (d,  $^3J = 9.0 \text{ Hz}$ , 1H; ArH), 7.08 (d,

$^3J=9.0$  Hz, 1H; ArH), 6.17 (d,  $^4J=1.3$  Hz, 1H; coumarin), 4.31–4.25 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.93–3.88 (m, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.87–3.83 (m, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.75–3.69 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.67–3.59 (m, 8H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.57–3.50 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.43 (d,  $^4J=1.3$  Hz, 3H; coumarin), 3.54 (t,  $^3J=5.2$  Hz, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 2.41 (s, 3H; CH<sub>3</sub>); <sup>13</sup>C NMR (CD<sub>3</sub>OD, 125 MHz, 27°C):  $\delta=163.0, 156.2, 155.8, 148.9, 136.7, 121.3, 116.1, 112.6, 111.2, 74.0, 73.70, 73.67, 71.83, 71.76, 71.6, 71.53, 71.47, 70.7, 70.1, 62.2, 18.8$  ppm; HRMS (ESI):  $m/z$ : calcd for C<sub>22</sub>H<sub>32</sub>O<sub>10</sub>+H<sup>+</sup> [M+H]<sup>+</sup> 457.20682; found: 457.20655; IR (ATR):  $\bar{\nu}=3253, 2867, 1716, 1605, 1564, 1507, 1448, 1386, 1374, 1299, 1247, 1106, 1064, 936, 880, 860, 848, 806$  cm<sup>-1</sup>.

**7,8-Bis(2-[2-[2-(*p*-tolylsulfonyloxy)ethoxy]ethoxy]ethoxy)-4-methyl-2H-chromen-2-on (4):** A solution of **3** (5.58 g, 12.2 mmol) and triethylamine (4.74 mL, 34.2 mmol) in methylene chloride (50 mL) was cooled to 0°C. *p*-Toluenesulfonic acid chloride (6.52 g, 34.2 mmol) was added rapidly portionwise and the mixture was stirred for 16 h. Water (50 mL) was added and adjusted to pH 3 with dilute HCl. The aqueous phase was extracted with methylene chloride (3 ×) and the combined organic phase was washed with saturated NaHCO<sub>3</sub> solution and dried over anhydrous MgSO<sub>4</sub>. The crude product was purified by flash column chromatography (SiO<sub>2</sub>; i) chloroform, ii) chloroform/methanol 97:3, iii) chloroform/methanol 94:6) to give a yellowish oil (3.37 g, 4.40 mmol, 36%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz, 27°C):  $\delta=7.76$  (d, 4H,  $^3J=8.2$  Hz, Ar<sub>15</sub>H), 7.31 (d, 4H,  $^3J=8.2$  Hz; Ar<sub>7</sub>H), 7.25 (d,  $^3J=8.8$  Hz, 1H; ArH, coumarin), 6.88 (d,  $^3J=8.8$  Hz, 1H; ArH, coumarin), 6.11 (s, 1H; coumarin), 4.27–4.19 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 4.16–4.08 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.87–3.82 (m, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.82–3.77 (m, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.67–3.62 (m, 8H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.60–3.57 (m, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.57–3.53 (m, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 2.40 (s, 6H; CH<sub>3</sub>-Ts), 2.36 ppm (s, 3H; CH<sub>3</sub>, coumarin); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz, 27°C):  $\delta=160.6, 154.6, 152.6, 147.8, 144.84, 144.76, 135.8, 132.9, 132.84, 132.82, 129.82, 129.80, 127.92, 127.90, 119.5, 115.0, 112.4, 109.8, 72.9, 70.8, 70.7, 70.5, 69.6, 69.3, 69.2, 68.9, 68.7, 68.6, 21.6, 18.8$  ppm; HRMS (ESI):  $m/z$ : calcd for C<sub>36</sub>H<sub>44</sub>O<sub>14</sub>S<sub>2</sub>+H<sup>+</sup> [M+H]<sup>+</sup> 765.22452; found: 765.22398; IR (ATR):  $\bar{\nu}=2872, 1725, 1601, 1563, 1506, 1448, 1384, 1352, 1297, 1244, 1174, 1095, 1011, 919, 816, 772, 663, 554$  cm<sup>-1</sup>.

**10-(Benzyl)-22-methyl-2,3,5,6,8,9,11,12,14,15,17,18-dodecahydrochromenon[7,8-b][1,4,7,13,16,19,10]hexaoxaazacycloheptasin-24(8H)-on (5):** A solution of **4** (4.97 g, 6.5 mmol) in dry acetonitrile (100 mL) that contained Cs<sub>2</sub>CO<sub>3</sub> (4.24 g, 13.0 mmol) and K<sub>2</sub>CO<sub>3</sub> (1.80 g, 13.0 mmol) was heated under an argon atmosphere to 80°C. Freshly distilled benzyl amine (0.85 mL, 7.8 mmol) was added and the suspension was heated for additional 39 h. The solvent was removed in vacuo and the residue was dissolved in methylene chloride (10 mL) and water (10 mL). The solution was adjusted to pH 6–7 with dilute HCl. The aqueous phase was extracted with methylene chloride (4 ×) and the combined organic phase was dried over anhydrous MgSO<sub>4</sub>. The solvent was removed in vacuo and the crude product was purified by flash column chromatography (Al<sub>2</sub>O<sub>3</sub>; i) diethyl ether/methanol 99:1, ii) diethyl ether/methanol 97:3) to yield a yellowish oil (0.44 g, 0.83 mmol, 13%). <sup>1</sup>H NMR (CD<sub>3</sub>OD, 500 MHz, 27°C):  $\delta=7.41$  (d,  $^3J=8.8$  Hz, 1H, ArH, coumarin), 7.33–7.16 (m, 5H, Ar<sub>Benz</sub>H), 7.08 (d,  $^3J=8.8$  Hz, 1H; ArH, coumarin), 6.14 (d,  $^4J=1.3$  Hz, 1H; coumarin), 4.29–4.23 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.91–3.86 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.80–3.53 (m, 16H; OCH<sub>2</sub>CH<sub>2</sub>O), 2.79–2.75 (m, 2H; NCH<sub>2</sub>), 2.74–2.70 (m, 2H; NCH<sub>2</sub>), 2.40 ppm (s, 3H; CH<sub>3</sub>, coumarin); <sup>13</sup>C NMR (CD<sub>3</sub>OD, 125 MHz, 27°C):  $\delta=162.9, 156.2, 155.7, 148.8, 136.8, 130.4, 129.2, 128.1, 121.2, 116.0, 112.5, 111.1, 74.1, 72.0, 71.73, 71.67, 71.63, 71.57, 70.6, 70.2, 60.8, 54.8, 54.7, 18.8$  ppm; HRMS (ESI):  $m/z$ : calcd for C<sub>29</sub>H<sub>37</sub>NO<sub>8</sub>+H<sup>+</sup> [M+H]<sup>+</sup> 528.25919; found: 528.25926; IR (ATR):  $\bar{\nu}=2922, 2867, 1724, 1602, 1562, 1506, 1448, 1384, 1369, 1296, 1243, 1202, 1090, 964, 847, 700$  cm<sup>-1</sup>.

**22-methyl-2,3,5,6,8,9,11,12,14,15,17,18-dodecahydrochromenon[7,8-b][1,4,7,13,16,19,10]hexaoxaazacycloheptasin-24(8H)-on (6):** *N*-Benzylaza-21-crown-7 ether (**5**) (22 mg, 0.042 mmol) and the same amount in weight of Pd/C (10% Pd) were suspended in 2-propanol (4 mL) and concentrated HCl (0.4 mL) was added. The mixture was heated to 50°C and stirred vigorously under a hydrogen atmosphere. The reaction was monitored by MALDI-TOF and filtered after complete conversion (45 min). The filter

cake was washed with 2-propanol and the solvent was removed in vacuo to yield a yellowish oil (16 mg, 0.038 mmol, 92%). <sup>1</sup>H NMR (CDCl<sub>3</sub>/CD<sub>3</sub>OD 1:1, 500 MHz, 27°C):  $\delta=7.37$  (d,  $^3J=8.8$  Hz, 1H; ArH, coumarin), 6.95 (d,  $^3J=8.8$  Hz, 1H; ArH, coumarin), 6.15 (d,  $^4J=1.3$  Hz, 1H; coumarin), 4.30–4.23 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.93–3.87 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.75–3.70 (m, 4H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.70–3.61 (m, 8H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.03–2.96 (m, 4H; NCH<sub>2</sub>), 2.41 ppm (s, 3H; CH<sub>3</sub>, coumarin); <sup>13</sup>C NMR (CD<sub>3</sub>OD/CDCl<sub>3</sub> 1:1, 125 MHz, 27°C):  $\delta=162.1, 155.1, 154.5, 148.1, 136.0, 120.7, 115.6, 112.6, 110.3, 73.5, 71.09, 71.06, 70.82, 70.76, 70.6, 69.9, 69.2, 68.0, 67.7, 48.0, 18.9$  ppm.

**C-Undecyltribromomethoxycarbonylcavitand (8):** A solution of **7**<sup>[22]</sup> (4.84 g, 3.29 mmol) in anhydrous THF (125 mL) under an argon atmosphere was cooled to –78°C and *n*-butyllithium (2.3 mL of a 1.6 M solution in hexane, 3.68 mmol) was added rapidly. After 1.5 h methyl chloroformate (2 mL, 25.8 mmol) was added and the mixture was allowed to warm to room temperature within 12 h. Methanol (10 mL) was added and the solvent was removed in vacuo. The residue was dissolved in chloroform and the organic layer was washed with water (3 ×) and dried over anhydrous MgSO<sub>4</sub>. Evaporation gave the crude product as a yellow oil. After column chromatography (SiO<sub>2</sub>, cyclohexane/ethyl acetate 9:1) the pure product was obtained as colourless solid (2.6 g, 1.8 mmol, 55%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz, 27°C):  $\delta=7.13$  (s, 1H; ArH), 7.00 (s, 1H; ArH), 7.00 (s, 2H; ArH), 5.92 (d,  $^2J=7.6$  Hz, 2H; OCH<sub>2</sub>O), 5.78 (d,  $^2J=7.6$  Hz, 2H; OCH<sub>2</sub>O), 4.83 (t,  $^3J=8.2$  Hz, 2H; ArCHAr), 4.77 (t,  $^3J=8.2$  Hz, 2H; ArCHAr), 4.46 (d,  $^2J=7.5$  Hz, 2H; OCH<sub>2</sub>O), 4.34 (d,  $^2J=7.5$  Hz, 2H; OCH<sub>2</sub>O), 3.88 (s, 3H; OCH<sub>3</sub>), 2.18–2.11 (m, 8H; CHCH<sub>2</sub>), 1.35–1.20 (m, 72H; CH<sub>2</sub>), 0.86 ppm (t,  $^3J=7.6$  Hz, 12H; CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz, 27°C):  $\delta=166.6, 152.5, 152.1, 150.8, 139.3, 139.1, 138.8, 138.6, 124.0, 121.8, 118.9, 118.8, 113.7, 99.0, 98.4, 53.1, 37.6, 36.9, 31.9, 29.9, 29.7, 29.4, 27.7, 22.7, 14.1$  ppm; HRMS (ESI):  $m/z$ : calcd for C<sub>78</sub>H<sub>111</sub>Br<sub>3</sub>O<sub>10</sub>+Na<sup>+</sup> [M+Na]<sup>+</sup> 1467.56196; found: 1467.55918; IR (KBr):  $\bar{\nu}=2925, 2853, 1744, 1538, 1469, 1453, 1301, 1256, 1142, 1092, 1018, 983, 961, 789, 722, 583$  cm<sup>-1</sup>.

**C-Undecylmonohydroxymethylcavitand (9):** A mixture of **8** (3.82 g, 2.64 mmol) and LiAlH<sub>4</sub> (300 mg, 8 mmol) in anhydrous THF (175 mL) under an argon atmosphere was heated at reflux for 3.5 h and additional LiAlH<sub>4</sub> (150 mg, 2.6 mmol) was added. The mixture was stirred for 12 h at room temperature and treated with methanol (15 mL). Dilute HCl was added until the mixture became acidic. The mixture was extracted with chloroform (3 ×). The organic layer was washed with saturated NaHCO<sub>3</sub> solution and brine, and dried over anhydrous MgSO<sub>4</sub>. After evaporation the crude product was purified by column chromatography (SiO<sub>2</sub>, cyclohexane/ethyl acetate 10:3) to yield a colourless solid (1.07 g, 0.9 mmol, 34%) and byproduct **10** as colourless solid (0.17 g, 0.15 mmol, 5%).

**9:** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz, 27°C):  $\delta=7.12$  (s, 1H; ArH), 7.07 (s, 2H; ArH), 7.07 (s, 1H; ArH), 6.53 (s, 1H; ArH), 6.44 (s, 2H; ArH), 5.80 (d,  $^2J=6.9$  Hz, 2H; OCH<sub>2</sub>O), 5.70 (d,  $^2J=6.9$  Hz, 2H; OCH<sub>2</sub>O), 4.74 (t,  $^3J=8.2$  Hz, 2H; ArCHAr), 4.69 (t,  $^3J=7.9$  Hz, 2H; ArCHAr), 4.66 (d,  $^3J=3.1$  Hz, 2H; ArCH<sub>2</sub>), 4.53 (d,  $^2J=6.9$  Hz, 2H; OCH<sub>2</sub>O), 4.39 (d,  $^2J=6.9$  Hz, 2H; OCH<sub>2</sub>O), 2.28–2.11 (m, 8H; CHCH<sub>2</sub>), 1.67 (t,  $^3J=3.1$  Hz, 1H; OH), 1.48–1.20 (m, 72H; CH<sub>2</sub>), 0.86 ppm (t,  $^3J=6.9$  Hz, 12H; CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz, 27°C):  $\delta=155.0, 154.7, 154.6, 153.8, 138.3, 138.24, 138.17, 138.1, 125.6, 120.5, 120.4, 116.9, 116.5, 99.9, 99.3, 60.4, 55.1, 36.6, 36.3, 31.9, 29.9, 29.84, 29.75, 29.7, 29.4, 27.9, 22.7, 14.1$  ppm; HRMS (ESI):  $m/z$ : calcd for C<sub>77</sub>H<sub>114</sub>O<sub>9</sub>+NH<sub>4</sub><sup>+</sup> [M+NH<sub>4</sub>]<sup>+</sup> 1200.88011; found: 1200.87999; IR (ATR):  $\bar{\nu}=3337, 2919, 2850, 1609, 1578, 1491, 1459, 1420, 1289, 1181, 1078, 1020, 960, 719, 580$  cm<sup>-1</sup>.

**10:** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz, 27°C):  $\delta=7.98$  (s, 1H; ArOH), 7.14 (s, 1H; ArH), 7.12 (s, 1H; ArH), 7.11 (s, 1H; ArH), 7.03 (s, 1H; ArH), 6.50 (s, 1H; ArH), 6.44 (s, 1H; ArH), 6.43 (s, 1H; ArH), 5.83 (d,  $^2J=7.2$  Hz, 1H; OCH<sub>2</sub>O), 5.76 (d,  $^2J=7.2$  Hz, 1H; OCH<sub>2</sub>O), 5.67 (d,  $^2J=7.2$  Hz, 1H; OCH<sub>2</sub>O), 4.75 (dd,  $^3J=8.1$  Hz,  $^3J=8.1$  Hz, 1H; ArCHAr), 4.69 (dd,  $^3J=7.9$  Hz, 1H; ArCHAr), 4.68 (dd,  $^2J=11.9$ ,  $^3J=8.0$  Hz, 1H; ArCH<sub>2</sub>) 4.66 (dd,  $^3J=8.1$ , 8.1 Hz, 1H; ArCHAr), 4.56 (dd,  $^2J=11.9$ ,  $^3J=8.0$  Hz, 1H; ArCH<sub>2</sub>), 4.48 (d,  $^2J=7.2$  Hz, 1H; OCH<sub>2</sub>O), 4.41 (d,  $^2J=7.2$  Hz, 1H; OCH<sub>2</sub>O), 4.37 (d,  $^2J=7.2$  Hz, 1H; OCH<sub>2</sub>O), 4.28 (dd,  $^3J=7.9$ , 7.9 Hz, 1H; ArCHAr), 3.82 (s, 3H; OCH<sub>3</sub>), 2.44 (dd,  $^3J=8.0$ , 1H; CH<sub>2</sub>OH), 2.27–2.10 (m, 8H; CHCH<sub>2</sub>), 1.37–1.16 (m, 72H; CH<sub>2</sub>), 0.87 ppm (t,  $^3J=$

6.9 Hz, 12H; CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz, 27°C): δ = 155.5, 155.0, 154.8, 154.6, 154.4, 153.4, 152.8, 151.3, 138.7, 138.1, 138.0, 137.8, 134.5, 133.3, 129.4, 127.9, 123.1, 121.5, 120.8, 120.3, 120.1, 116.6, 116.5, 106.0, 99.9, 99.5, 99.4, 56.3, 56.0, 36.3, 36.0, 33.7, 33.1, 31.9, 30.3, 29.9, 29.8, 29.7, 29.4, 28.04, 27.98, 27.9, 27.8, 22.7, 14.1 ppm; HRMS (ESI): *m/z*: calcd for C<sub>77</sub>H<sub>116</sub>O<sub>9</sub>+Na<sup>+</sup> [M+Na]<sup>+</sup> 1207.85116; found: 1207.85067; IR (ATR):  $\bar{\nu}$  = 3335, 2920, 2851, 1609, 1592, 1492, 1465, 1420, 1290, 1180, 1068, 1019, 959, 890, 804, 720, 578 cm<sup>-1</sup>.

**C-Undecylmonobromomethylcavitand (11):** A solution of **9** (1.07 g, 0.9 mmol) in dry methylene chloride (25 mL) was treated with phosphonium tribromide (0.28 g, 1.03 mmol). The reaction mixture was stirred for 1 h at room temperature and 2-propanol (5 mL) was added. Diethyl ether (20 mL) was added to the reaction mixture and the solution was washed with saturated NaHCO<sub>3</sub> solution and brine and dried over anhydrous MgSO<sub>4</sub>. Purification by column chromatography (SiO<sub>2</sub>, cyclohexane/ethyl acetate 9:1) yielded a colourless solid (1.11 g, 0.89 mmol, 99%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz, 27°C): δ = 7.10 (s, 1H; ArH), 7.10 (s, 1H; ArH), 7.09 (s, 2H; ArH), 6.52 (s, 1H; ArH), 6.46 (s, 2H; ArH), 5.86 (d, <sup>2</sup>J = 7.5 Hz, 2H; OCH<sub>2</sub>O), 5.72 (d, <sup>2</sup>J = 7.5 Hz, 2H; OCH<sub>2</sub>O), 4.72 (t, <sup>3</sup>J = 8.2 Hz, 2H; ArCHAr), 4.70 (t, <sup>3</sup>J = 8.2 Hz, 2H; ArCHAr), 4.56 (s, 2H; ArCH<sub>2</sub>), 4.56 (d, <sup>2</sup>J = 7.5 Hz, 2H; OCH<sub>2</sub>O), 4.50 (d, <sup>2</sup>J = 7.5 Hz, 2H; OCH<sub>2</sub>O), 2.27–2.12 (m, 8H; CHCH<sub>2</sub>), 1.48–1.18 (m, 72H; CH<sub>2</sub>), 0.86 ppm (t, <sup>3</sup>J = 6.9 Hz, 12H; CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz, 27°C): δ = 154.9, 154.8, 154.6, 153.7, 138.5, 138.4, 138.2, 137.8, 124.3, 121.4, 120.5, 120.4, 116.9, 116.5, 99.3, 70.9, 36.5, 36.3, 31.9, 30.0, 29.9, 29.84, 29.80, 29.7, 29.4, 27.9, 24.0, 22.7, 14.1 ppm; HRMS (ESI): *m/z*: calcd for C<sub>77</sub>H<sub>113</sub>BrO<sub>8</sub>+NH<sub>4</sub><sup>+</sup> [M+NH<sub>4</sub>]<sup>+</sup> 1262.79571; found: 1262.79516; IR (ATR):  $\bar{\nu}$  = 2916, 2849, 1578, 1489, 1464, 1419, 1284, 1261, 1181, 1154, 1093, 1020, 965, 890, 811, 718, 580 cm<sup>-1</sup>.

**C-Undecylmono(aza-21-coumarylcrown-7)cavitand (12):** A mixture of **6** (33 mg, 0.075 mmol), **11** (94 mg, 0.074 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (50 mg, 0.15 mmol) in dry *N,N*-dimethylformamide (5 mL) was stirred for 44 h at 80°C. The solvent was removed in vacuo. The residue was dissolved in methylene chloride and water (1:1) and adjusted to pH 7 with dilute HCl. The organic layer was washed with water (3×) and dried over anhydrous MgSO<sub>4</sub>. Evaporation gave the crude product as a yellow oil. It was purified by column chromatography (SiO<sub>2</sub>; i) chloroform/methanol 97:3, ii) chloroform/methanol 1:1) and the product was filtered through a small amount Al<sub>2</sub>O<sub>3</sub> (chloroform/methanol 1:1) to detach the complexed ions. After evaporation a colourless solid was obtained (12 mg, 0.0075 mmol, 10%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz, 27°C): δ = 7.24 (d, <sup>3</sup>J = 8.8, 1H; ArH, coumarin), 7.09 (s, 1H; ArH), 7.08 (s, 2H; ArH), 7.03 (s, 1H; ArH), 6.85 (d, <sup>3</sup>J = 8.8, 1H; ArH, coumarin), 6.45 (s, 1H; ArH), 6.42 (s, 2H; ArH), 6.13 (d, <sup>4</sup>J = 1.3, 1H; CH, coumarin), 5.76 (d, <sup>2</sup>J = 6.9 Hz, 2H; OCH<sub>2</sub>O), 5.71 (d, <sup>2</sup>J = 6.9 Hz, 2H; OCH<sub>2</sub>O), 4.69 (t, <sup>3</sup>J = 8.2 Hz, 4H; ArCHAr), 4.42 (d, <sup>2</sup>J = 6.9 Hz, 2H; OCH<sub>2</sub>O), 4.29 (d, <sup>2</sup>J = 6.9 Hz, 2H; OCH<sub>2</sub>O), 4.29 (t, <sup>3</sup>J = 5.3 Hz, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 4.25 (t, <sup>3</sup>J = 4.4 Hz, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.92 (t, <sup>3</sup>J = 4.4 Hz, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.88 (t, <sup>3</sup>J = 5.3 Hz, 2H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.78–3.55 (m, 12H; OCH<sub>2</sub>CH<sub>2</sub>O), 3.43–3.38 (m, 2H; ArCH<sub>2</sub>), 2.66–2.76 (m, 4H; NCH<sub>2</sub>CH<sub>2</sub>), 2.36 (s, 3H; CH<sub>3</sub>, coumarin), 2.27–2.08 (m, 8H; CHCH<sub>2</sub>), 1.46–1.16 (m, 72H; CH<sub>2</sub>), 0.86 ppm (t, <sup>3</sup>J = 6.9 Hz, 12H; CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz, 27°C): δ = 169.7, 160.7, 154.9, 154.8, 154.7, 154.2, 152.5, 147.9, 138.4, 138.3, 138.1, 138.0, 135.9, 124.0, 120.63, 120.56, 119.7, 116.6, 116.3, 115.0, 112.5, 109.7, 99.6, 99.5, 72.9, 71.2, 70.8, 70.5, 70.4, 69.6, 69.5, 69.3, 53.3, 48.4, 36.6, 36.3, 31.9, 30.2, 29.9, 29.88, 29.85, 29.7, 29.4, 27.94, 27.89, 22.7, 18.8, 14.1 ppm; HRMS (ESI): *m/z*: calcd for C<sub>99</sub>H<sub>143</sub>NO<sub>16</sub>+H<sup>+</sup> [M+H]<sup>+</sup> 1603.04796; found: 1603.04673; IR (ATR):  $\bar{\nu}$  = 2920, 2851, 1722, 1604, 1579, 1489, 1455, 1383, 1367, 1293, 1180, 1089, 1018, 959, 850, 719, 580 cm<sup>-1</sup>.

## Acknowledgements

Financial support from the Deutsche Forschungsgemeinschaft is gratefully acknowledged. The authors are also grateful to Stefan Vosskötter for his effort on ESI-MS complex studies.

- [1] a) P. Timmerman, W. Verboom, D. N. Reinhoudt, *Tetrahedron* **1996**, *52*, 2663–2704; b) E. van Dienst, W. I. Iwema Bakker, J. F. J. Engbersen, W. Verboom, D. N. Reinhoudt, *Pure Appl. Chem.* **1993**, *65*, 387–392; c) V. Böhmer, *Angew. Chem.* **1995**, *107*, 785–818; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713–745; d) B. Botta, M. Cassani, I. D'Acquarica, D. Misi, D. Subissati, G. Delle Monache, *Curr. Org. Chem.* **2005**, *9*, 337–355.
- [2] J. C. Sherman, C. B. Knobler, D. J. Cram, *J. Am. Chem. Soc.* **1991**, *113*, 2194–2204.
- [3] R. Warmuth, J. Yoon, *Acc. Chem. Res.* **2001**, *34*, 95–105.
- [4] D. M. Rudkevich, J. Rebek, Jr., *Eur. J. Org. Chem.* **1999**, 1991–2005.
- [5] I. Higler, P. Timmerman, W. Verboom, D. N. Reinhoudt, *Eur. J. Org. Chem.* **1998**, 2689–2702.
- [6] a) H.-J. Schneider, U. Schneider, *J. Inclusion Phenom. Mol. Recognit. Chem.* **1994**, *19*, 67–83; b) C. L. D. Gibb, E. D. Stevens, B. C. Gibb, *J. Am. Chem. Soc.* **2001**, *123*, 5849–5850.
- [7] a) M. C. Letzel, C. Agena, J. Mattay, *J. Mass Spectrom.* **2002**, *37*, 63–68; b) A. B. Rozhenko, W. W. Schoeller, M. C. Letzel, B. Decker, C. Agena, J. Mattay, *J. Mol. Structure: Theochem.* **2005**, *7–20*; c) A. B. Rozhenko, W. W. Schoeller, M. C. Letzel, B. Decker, C. Agena, J. Mattay, *Chem. Eur. J.* **2006**, *12*, 8995–9000.
- [8] J. R. Moran, S. Karbach, D. J. Cram, *J. Am. Chem. Soc.* **1982**, *104*, 5826–5828.
- [9] J. A. Tucker, C. B. Knobler, K. N. Trueblood, D. J. Cram, *J. Am. Chem. Soc.* **1989**, *111*, 3688–3699.
- [10] a) H. Yamamoto, T. Sakaki, S. Shinkai, *Chem. Lett.* **1994**, 469–472; b) H. Yamamoto, K. Ueda, K. R. A. S. Sandanayake, S. Shinkai, *Chem. Lett.* **1995**, 497–498; c) Q.-Y. Zheng, C.-F. Chen, Z.-T. Huang, *Tetrahedron* **1997**, *53*, 10345–10356; d) A. Casnati, A. Pochini, R. Ungaro, F. Ugozzoli, F. Arnaud, S. Fanni, M.-J. Schwing, R. J. M. Egberink, F. de Jong, D. N. Reinhoudt, *J. Am. Chem. Soc.* **1995**, *117*, 2767–2777.
- [11] F. Hamada, S. Ito, M. Narita, N. Nashirozawa, *Tetrahedron Lett.* **1999**, *40*, 1527–1530.
- [12] I. Higler, H. Boerrigter, W. Verboom, H. Kooijman, A. L. Spek, D. N. Reinhoudt, *Eur. J. Org. Chem.* **1998**, 1597–1607.
- [13] A. Kang, S. K. Kim, K. Nakamura, J. H. Park, Y. J. Yoon, K. D. Lee, J. Yoon, *Tetrahedron Lett.* **2005**, *46*, 245–248.
- [14] a) R. M. Izatt, J. S. Bradshaw, S. A. Nielsen, J. D. Lamb, J. J. Christensen, D. Sen, *Chem. Rev.* **1985**, *85*, 271–339; b) R. M. Izatt, K. Pawlak, J. S. Bradshaw, R. L. Bruening, *Chem. Rev.* **1991**, *91*, 1721–2085; c) R. M. Izatt, K. Pawlak, J. S. Bradshaw, R. L. Bruening, *Chem. Rev.* **1995**, *95*, 2529–2586; d) G. W. Gokel, W. M. Leevy, M. E. Weber, *Chem. Rev.* **2004**, *104*, 2723–2750.
- [15] a) J. F. Callan, A. P. de Silva, D. C. Magri, *Tetrahedron*, **2005**, *61*, 8551–8588; b) B. Valeur, I. Leray, *Coord. Chem. Rev.* **2000**, *205*, 3–40; c) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher, T. E. Rice, *Chem. Rev.* **1997**, *97*, 1515–1566.
- [16] K. Golchini, M. Mackovic-Basic, S. A. Gharib, D. Masilamani, M. E. Lucas, I. Kurtz, *Am. J. Physiol.* **1990**, *258*, F438–443.
- [17] D. Masilamani, M. E. Lucas, G. S. Hammond, US-A 5,136,033, 1992.
- [18] A. Goçmen, M. Bulut, Ç. Erk, *Pure Appl. Chem.* **1993**, *65*, 447–450.
- [19] T. Sugino, K. Tanaka, *Chem. Lett.* **2001**, 110–111.
- [20] A. R. Katritzky, O. V. Denisko, S. A. Belyakov, O. F. Schall, G. W. Gokel, *J. Org. Chem.* **1996**, *61*, 7578–7584.
- [21] G. W. Gokel in *Monographs in Supramolecular Chemistry* (Ed.: J. F. Stoddard), RSC Publishing, Cambridge, **1991**, pp. 45–49.
- [22] J. L. Irwin, M. S. Sherburn, *J. Org. Chem.* **2000**, *65*, 602–605.
- [23] J. L. Irwin, M. S. Sherburn, *Org. Lett.* **2001**, *3*, 225–227.
- [24] J. A. Bryant, M. T. Blanda, M. Vincenti, D. J. Cram, *J. Am. Chem. Soc.* **1991**, *113*, 2167–2172.
- [25] B. Valeur, *Molecular Fluorescence*, Wiley-VCH, Weinheim, **2001**, p. 287–315.
- [26] R. Giri, S. S. Rathi, M. K. Machwe, V. V. S. Murti, *Spectrochim. Acta A*, **1988**, *44*, 805–807.
- [27] R. M. Christie, C.-H. Lui, *Dyes and Pigments*, **1999**, *42*, 85–92.



- [28] a) K. A. Connors, *Binding Constants, The Measurement of Molecular Complex Stability*, Wiley, New York, **1987**; b) J. Bourson, J. Pouget, B. Valeur, *J. Phys. Chem.* **1993**, *97*, 4552–4557; c) K. Hirose, *J. Inclusion Phenom. Macrocyclic Chem.* **2001**, *39*, 193–209.
- [29] P. Job, *Ann. Chim.-Paris*, **1928**, *9*, 113–203.
- [30] Y. Liu, B.-H. Han, Y. Inoue, M. Ouchi, *J. Org. Chem.* **1998**, *63*, 2144–2147.
- [31] R. D. Shannon, *Acta Crystallogr., Sect. A* **1976**, *A32*, 751–767.
- [32] M. Bourgoïn, K. H. Wong, J. Y. Hui, J. Smid, *J. Am. Chem. Soc.* **1975**, *97*, 3462–3467.
- [33] Y. Inoue, T. Hakushi, Y. Liu, L.-H. Tong, J. Hu, G.-D. Zhao, S. Huang, B.-Z. Tians, *J. Phys. Chem.* **1988**, *92*, 2371–2374.
- [34] W. Koch, M. C. Holthausen, *A Chemist's Guide to Density Functional Theory*, Wiley-VCH, Weinheim, **2001**.
- [35] F. S. Menges, [http://www.agdal.chemie.uni-konstanz.de/menges/spekwin/index\\_en.html](http://www.agdal.chemie.uni-konstanz.de/menges/spekwin/index_en.html), **2006**.
- [36] Gaussian 03, Revision C.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cio-slawski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, Gaussian, Inc., Wallingford CT, **2004**.
- [37] a) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B: Condens. Matter Mater. Phys.* **1988**, *37*, 785–789; b) D. Becke, *Phys. Rev. A* **1988**, *38*, 3098–3100.
- [38] a) W. J. Stevens, H. Basch, M. Krauss, *J. Chem. Phys.* **1984**, *81*, 6026–6033; b) W. J. Stevens, M. Krauss, H. Basch, P. G. Jasien, *Can. J. Chem.* **1992**, *70*, 612–630.
- [39] a) A. Bergner, M. Dolg, W. Kuechle, H. Stoll, H. Preuss, *Mol. Phys.* **1993**, *80*, 1431–1441; b) T. Leininger, A. Nicklass, W. Kuechle, H. Stoll, M. Dolg, A. Bergner, *Chem. Phys. Lett.* **1996**, *255*, 274–280.
- [40] a) B. I. Dunlap, *J. Chem. Phys.* **1983**, *78*, 3140–3142; b) B. I. Dunlap, *J. Mol. Struct.* **2000**, *529*, 37–40.
- [41] a) M. C. Strain, G. E. Scuseria, M. J. Frisch, *Science* **1996**, *271*, 51–53; b) J. C. Burant, M. C. Strain, G. E. Scuseria, M. J. Frisch, *Chem. Phys. Lett.* **1996**, *248*, 43–49.

Received: July 4, 2007

Published online: November 19, 2007