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Synthesis and caesium complexing properties of water-soluble cavitands

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Abstract

Cs^+–ligand interactions of synthesized hydrosoluble cavitands like tetrol **5**, tetra(carboxymethyl) **11** and tetra-(diethanolaminomethyl) **12** were studied in basic aqueous media by UV–visible analysis. Receptor **5** showed a rather high affinity for the caesium ion. © 1999 Published by Elsevier Science Ltd. All rights reserved.

As a consequence of the development of supramolecular chemistry, a number of hosts and processes for the selective extraction of caesium have been extensively studied. For example, calixarene-bis-crowns have been used in the supported liquid membrane separation technique (SLM)[1] or calix[4]resorcinarene for the extraction of the cation from an aqueous basic solution into benzene solution by flotation.[2] In recent reports, we described the Cs^+/Na^+ selective separation by nanofiltration in basic aqueous media,[3] using calix[4]resorcinarene **1** and its derivatives as hydrosoluble receptors. With regard to the remarkable selective complexing ability of **1** towards Cs^+, we assumed that these properties could be enhanced by rigidifying the cone shape by introducing bridging methylene substituents between the phenol groups. Moreover, resorcinarene **1** was proved to be of little stability in water under basic conditions.[4] Easily available, methylene-bridged resorcinarenes[5] were described as excellent receptors for the specific binding of cations and neutral molecules. This was explained by their rigidity and enforced cavity.[5c,6]

However, to our best knowledge, this rigid molecular platform has not yet been exploited for the design of specific water-soluble ionophores. Moreover, we found only two reports concerning the synthesis of such water-soluble molecules, incorporating water-solubilizing groups at the rim position (R=OH),[7] or into the pendant group ($R'=(CH_2)_3OPO_3H_2$).[8] Therefore, we report here the synthesis of cavitands **9**, **11** and **12** bearing neutral, basic or acidic hydrophilic groups and the preliminary Cs^+ complexing behaviour of the water-soluble cavitands **5**, **11** and **12** (Scheme 1).

Following the procedure described by Sherman et al.,[7] **5** was prepared starting from the known tetrabromo-octol **4**.[5b] Cavitands **9** and **11** were prepared in four steps starting from tetramethylcalix-[4]resorcinarene **2**.[5a] Firstly, the neighbouring hydroxyls were bridged with $BrCH_2Cl$ in DMF using

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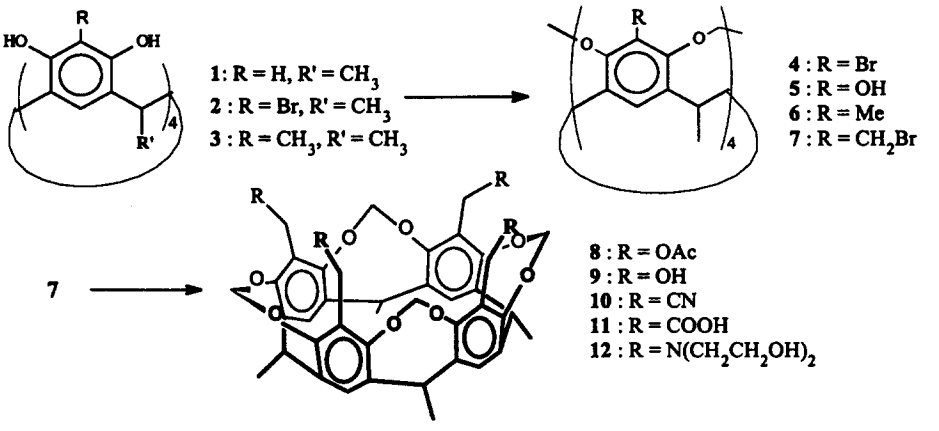

Scheme 1.

K_2CO_3 as a base to yield the tetramethyl cavitand **6** in 60% yield.[9] Bromination of **6**, as described by Sorrell and Pigge,[10] gave the tetrakis(bromomethyl)cavitand **7** in 70% yield. Following the same route used by Reinhoudt and colleagues[11] for the preparation of an analogue bearing nonyl chains as pendant groups, hydroxymethyl substituents were introduced by the reaction of **7** with sodium acetate in DMF affording the acetoxymethyl cavitand **8** in 59% yield. This was followed by hydrolysis in a 1:0.5 THF:H_2O mixture with LiOH giving cavitand **9** in 91% yield.[12] Similarly, reaction of **7** with KCN in dry DMSO gave the tetrakis(cyanomethyl)cavitand **10** which was hydrolyzed in an EtOH/H_2O mixture with KOH to give the carboxymethylene analogue **11** in 74% yield.[13] Finally, **12** was prepared by reaction of **7** with diethanolamine in dry DMSO in 88% yield.[14]

The ^1H NMR spectra of compounds **8–12** exhibit the characteristic signals of the aromatic (singlet) and the methyleneoxy-bridged hydrogens (two doublets) for tetrasubstituted cavitands. The chemical shift variations for **8–12** induced by the different substituents at the aromatic ring are, respectively, 7.32, 7.71, 7.80, 7.69 and 7.81 ppm for the aromatic protons. The resonance signals of outer-bridged hydrogens were observed at 5.87, 5.83, 6.05, 5.75 and 6.05 ppm and the inner at 4.36, 4.50, 4.32, 4.77 and 4.40 ppm. The structural assignment of these receptors was confirmed by the observation of typical ^{13}C NMR signals for cavitands and by the characteristic signals of C=O (170.5 ppm) and CH_2OAc (57.02 ppm) for **8**; CH_2OH (53.79 ppm) for **9**; CN (117.8 ppm) and CH_2CN (54.82 ppm) for **10**; COOH (171.9 ppm) and CH_2COOH (31.54 ppm) for **11**; NCH_2CH_2OH and $CH_2N(CH_2CH_2OH)_2$ (56.98, 56.01, 49.38 ppm) for **12**.

Water solubility of **9** and **11** has been studied in basic aqueous media and showed that only **11** was soluble at pH=11, whereas, **9** is insoluble even at pH>12. However, cavitand **12** was soluble both in the neutral and basic aqueous media.

Due to the fact that **5** was also hydrosoluble in basic aqueous solutions,[7] caesium complexing properties of **5**, **11** and **12** could be studied by UV–visible analysis following the same procedure as the one used for the evaluation of Cs^+–ligand interactions for a series of water-soluble calix[4]arene-bis-crown-6 ligands.[15] Absorption changes in the UV range for the ligand were measured in the presence of increasing amounts of CsCl (Fig. 1). The stability constants β_{CsL} for the caesium–ligand complexes were evaluated (Table 1) by using the Forster–Hammick–Wardly method.[16] Interactions of **5**, **11** and **12** with the Cs^+ cation were studied at 276, 275 and 293 nm, respectively. Among the three ligands studied, only **5** showed a significant hyperchromic shift which led to a β_{CsL} value of 35×10^3 for a 1:1 stoichiometry of Cs^+ and **5**. The stoichiometry was obtained from the presence of an isobestic point at 291 nm.

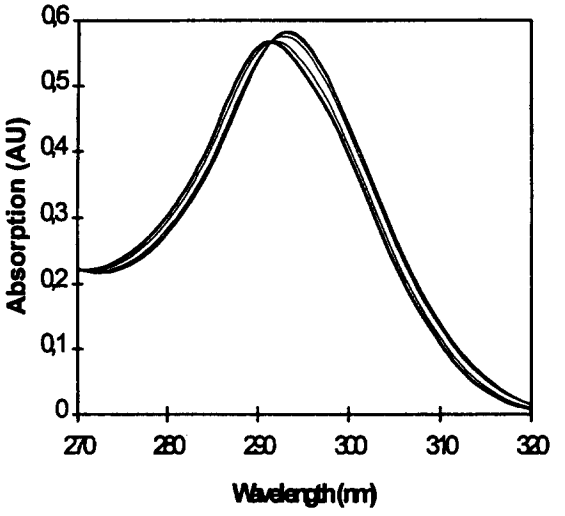

Figure 1. Spectral changes upon the addition of 0 (bold curve), 5, 10, 30 and 40 equiv. of CsCl to an aqueous solution (pH=12) of **5** (5×10^{-5} mol/l) at 25°C

Table 1

Ligand	**12**	**11**	**5**
[ligand] (mol/l)	10^{-4}	$5\ 10^{-5}$	$5\ 10^{-5}$
pH	11	12	12
λ (maximum absorption)	276 nm	275 nm	293 nm
β_{CsL} (without unit)	low	low	35,000

Further research on the complexation properties of **5** by the nanofiltration–complexation technique is under current investigation and will be presented in due course.

Acknowledgements

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9. Compound **6**: From **2** (2 g, 3.34 mmol), K_2CO_3 (9.6 g, 70 mmol) and $BrCH_2Cl$ (56 mmol) in dry DMF (160 ml) at 70°C for 24 h. Purification: see Ref. 4b. White powder (1.3 g, 60%). Compound **6** has been previously reported by Cram et al.[4b] but was synthesized via another route using DMA in a 3 day reaction time with a similar yield.
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12. Compound **9**: **7** (1.5 g, 1.55 mmol) and AcONa (1.27 g, 15.5 mmol) were stirred in dry DMF (25 ml) for 24 h. The mixture was poured into H_2O and the resulting precipitate filtered, washed with H_2O, dissolved in CH_2Cl_2, dried over $MgSO_4$ and purified on SiO_2 (CH_2Cl_2:MeOH, 98:2) to give **8**. White powder (0.8 g, 59%). ^1H NMR ($CDCl_3$): 7.32 (s, 4ArH), 5.87 (d, *J*=7.2, 4H, outer of OCH_2O), 5.04 (q, *J*=7.6, 4H, CH_3CH), 5.00 (s, 8H, CH_2OAc), 4.36 (d, *J*=7.2, 4H, inner of OCH_2O), 2.02 (s, 12H, CH_3CO), 1.78 (d, *J*=7.4, 12H, CH_3CH); ^{13}C NMR ($CDCl_3$): 170.5 (CO), 153.4, 139.2, 121.7 (ArC), 120.8 (ArCH), 99.68 (OCH_2O), 57.02 (CH_2OAc), 31.2 (CH), 21.08 (CH_3CO), 16.04 (CH_3). ES-MS: 919.3 ($[M+K]^+$), 903.2 ($[M+Na]^+$), $C_{48}H_{48}O_{16}$, 0.5 CH_2Cl_2 (932.15): calcd C, 62.49; H, 5.41; O, 26.32; found C, 62.57; H, 5.62; O, 26.86. Hydrolysis of **8** (0.6 g, 0.68 mmol) in a mixture of THF (50 ml) and 1N LiOH (25 ml) at 40°C for 18 h, followed by evaporation of THF, and filtration of the resulting white precipitate which was washed with H_2O to give **9**. White powder (0.442 g, 91%). For another procedure and analysis, see: Cram, D. J.; Karbach, S.; Kim, Y. H.; Baczynskyj, L.; Marti, K.; Sampson, R. M.; Kalleymeyn, G. W. *J. Am. Chem. Soc.* **1988**, *110*, 2554–2560.
13. Compound **11**: From **7** (1 g, 1.04 mmol), KCN (0.83 g, 12.5 mmol) in DMSO (15 ml) at 85°C for 24 h. After cooling, the mixture was poured into H_2O and acidified with 2N HCl. The resulting precipitate was filtered off, rinsed with H_2O, then stirred in hot MeOH for 1 h. The light brown suspension was filtered off, rinsed with MeOH and Et_2O. Purification on SiO_2 (CH_2Cl_2:MeOH, 98:2) afforded pure **10**. White powder (0.4 g, 51%). ^1H NMR ($(CD_3)_2SO$): 7.80 (s, 4ArH), 6.05 (d, *J*=7.6, 4H, outer of OCH_2O), 4.83 (q, *J*=6.95, 4H, CH_3CH), 4.32 (d, *J*=7.2, 4H, inner of OCH_2O), 3.73 (s, 8H, CH_2CN), 1.86 (d, *J*=6.95, 12H, CH_3CH); ^{13}C NMR ($(CD_3)_2SO$): 151.8, 139.2, 118.2, 117.8 (ArC and CN), 121.5 (ArCH), 99.28 (OCH_2O), 54.82 (CH_2CN), 31.32 (CH), 15.84 (CH_3). ES-MS: 771.3 ($[M+Na]^+$). $C_{44}H_{36}O_8N_4$, 1.75 CH_2Cl_2 (896.75): calcd C, 61.19; H, 4.43; O, 14.25; N, 6.23; found C, 60.97; H, 4.52; O, 14.27; N, 6.20. Compound **10** (0.5 g, 0.667 mmol) was hydrolyzed in a refluxing 1:1 EtOH:H_2O mixture (30 ml) with KOH (0.75 g, 13.3 mmol) for 48 h. After cooling, the mixture was acidified (2N HCl) and the resulting suspension was extracted with AcOEt. The organic layer was washed with H_2O until pH 7, dried over $MgSO_4$ and removed. The brownish residue was stirred in $CHCl_3$ and the residual precipitate was filtered off to give pure **11**. White powder (0.407 g, 74%). ^1H NMR ($(CD_3)_2SO$): 12.20 (s, bd, COOH), 7.69 (s, 4ArH), 5.75 (d, *J*=6.2, 4H, outer of OCH_2O), 4.20–4.29 (m, bd, 4H, CH_3CH), 4.77 (d, *J*=6.2, 4H, inner of OCH_2O), 3.32 (s, bd, 8H, CH_2COOH), 1.86 (s, bd, 12H, CH_3CH); ^{13}C NMR ($(CD_3)_2SO$): 171.9 (COOH), 152.4, 138.3, 122.7 (ArC), 119.7 (ArCH), 98.82 (OCH_2O), 31.54 (CH_2COOH), 31.19 (CH), 16.6 (CH_3). ES-MS: 862.3 ($[M+K]^+$), 846.1 ($[M+Na]^+$), 824.1 ($[M+H]^+$). $C_{44}H_{40}O_{16}$, 2.3 $CHCl_3$ (1098.86): calcd C, 50.61; H, 3.98; O, 23.31; found C, 50.75; H, 4.33; O, 23.67.
14. Compound **12**: From **7** (3 g, 3.11 mmol), diethanolamine (9.83 g, 93 mmol) in dry DMSO (20 ml) at 50°C for 24 h. DMSO was removed in vacuo and the residue dissolved in MeOH (20 ml). Pure **12** was precipitated by addition of $CHCl_3$ (200 ml) and collected by filtration. White powder (2.9 g, 88%). ^1H NMR (D_2O): 7.81 (s, 4ArH), 6.05 (d, *J*=7.06, 4H, outer of OCH_2O), 4.96 (q, *J*=7.2, 4H, CH_3CH), 4.40 (d, *J*=7.06, 4H, inner of OCH_2O), 4.07 (s, 8H, $ArCH_2N$), 3.87 (t, *J*=5.2, 16H, CH_2OH), 3.25 (t, *J*=5.2, 16H, NCH_2), 1.89 (d, *J*=7.2, 12H, CH_3CH); ^{13}C NMR (D_2O): 153.7, 140.3, 123.8 (ArC), 129.2 (ArCH), 100.3 (OCH_2O), 56.98, 56.01, 49.38 (NCH_2CH_2OH and CH_2N), 30.65 (CH), 15.81 (CH_3). ES-MS 1083.4 ($[M+Na]^+$); 1061.5 ($[M+H]^+$). $C_{56}H_{76}O_{16}N_4$, $2H_2O$, 1.5 $CHCl_3$ (1264.36): calcd C, 54.53; H, 6.48; O, 22.78; N, 4.43; found C, 54.60; H, 6.47; O, 22.84; N, 4.53.
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