

Anion complexation by amido derivatives of *p*-*tert*-butyl calix[4]arene

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Abstract The binding properties of 1,2,3,4-amido derivatives of *p*-*tert*-butyl calix[4]arene (**4–6**) towards various anions (spherical halides, planar trigonal nitrate and tetrahedral hydrogen sulphate) as their tetrabutyl ammonium (TBA) salts have been studied by ^1H NMR technique and using Equi Chem program. The stability constants, $\log K_{\text{ass}}$, varying from 0.76 ± 0.10 to 2.13 ± 0.04 have been determined for the mononuclear complexes.

Keywords Calixarenes · Anion complexation · ^1H NMR

In 2003, a special issue of Coordination Chemistry Reviews [1] has celebrated the 35th anniversary of Park and Simmons' seminal publication [2] on the complexation of anions by artificial receptors and the search for anionic recognition by specific receptors is still developing in the field of supramolecular chemistry [3]. The rapid growth in this area comes in part from many natural anions binding systems observed in biology to achieve specific works [4]. Types of interactions for anions binding are electrostatic interactions, hydrogen-bonding and coordination to Lewis-acidic metals [5]. Anion recognition is associated with the shape of the anions. Apart from spherical halides, PO_4^{3-} and

SO_4^{2-} are tetrahedral, NO_3^- is trigonal planar, SCN^- and N_3^- are linear and each anions requires a receptor with specific size and shape. Calixarenes, [6] with their multiple sites used in selective functionalisation on a conformationally restricted, macrocyclic scaffold, are obvious starting materials for preparing chosen derivatives with a precise function to be done. The synthesis and binding properties of calix-based anion receptors have been collected in a recent review [7]. They are of three types: inorganic-based receptors, organic-based receptors and ditopic receptors able to complex ion-pairs [7].

We recently reported ^1H NMR studies of the complexation of selected anions (spherical halides, planar trigonal nitrate and tetrahedral hydrogen sulphate) by a series of amido derivatives of *p*-*tert*-butyl calix[4]arenes (organic-based type) and more particularly with **2** and **3** [8]. **2** was shown to do not complex these anions while the following logarithmic association constants were found in CDCl_3 for **3**: 1.20 ± 0.02 (Cl^-), 1.11 ± 0.03 (Br^-), 0.78 ± 0.02 (I^-), 0.99 ± 0.01 (NO_3^-), 1.19 ± 0.02 (HSO_4^-).

In this paper, we present a subsequent study on the complexation of F^- , Cl^- , Br^- , I^- , NO_3^- et HSO_4^- by the 1,2,3,4-tetra-methylfurane amido *p*-*tert*-butylcalix[4]arene (**4**), 1,2,3,4-tetra-methylthiophene amido *p*-*tert*-butylcalix[4]arene (**5**) and 1,2,3,4-tetra-ethoxy-ethanol amido *p*-*tert*-butylcalix[4]arene (**6**) in order to evidence the influence of the residues attached to the calix unit by amido functions.

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Experimental

General. For the synthesis

Uncorrected melting point (Mp), Büchi 500. ^1H NMR, Bruker SY 200 (300 MHz, δ in ppm from tms, J in Hz in

CDCl_3 or CD_3CN , TMS as standart). FAB (+) mass spectrum, Biflex Bruker. The reaction was run under N_2 atmosphere. SiO_2 (Geduran 1.11567) was used for column chromatography. All reagents and solvents were commercial and used without further purification.

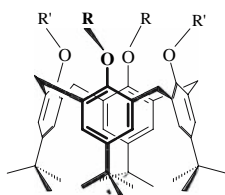
Ligands **1–5** were prepared as described in the literature [9, 10]. Ligand **1** [10] results from a tetra-O-alkylation of a calix[4]arene in acetone, when **2–5** derivatives [9] were obtained by amidation of 1,2,3,4-tetra methyl amine in a mixture of methanol/toluene. ^1H NMR data were in agreement with a cone conformation [9].

For complexation studies, CDCl_3 solutions (10^{-2} M) of ligands were mixed with increasing quantities of anions salts: TBA(tetrabutylammonium)F, TBACl, TBABr, TBANO_3 and TBAHSO_4 . The ratio between TBA anion salts and the ligands was determined directly on the ^1H NMR spectra by using the integration ratio of the triplet of CONH protons of the ligand/the quintuplet of $\text{N}^+(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_4$ protons of added TBA anion salts.

Preparation of 5,11,17,23-tetra(*tert*-butyl)-25,26,27,28-tetra(2-ethoxy)ethanol acetamide calix[4]arene (**6**)

Using the same procedure as **2–5**, tetramethyl ester calix[4]arene (**1**) (3.75 g, 4 mmol) was mixed with and 2-(2-aminoethoxy)ethanol (4.21 g, 40 mmol), in a 1:1 mixture of methanol:toluene and refluxed for 10 days. Precipitation with methanol gave pure **6** (2.80 g, 57%) as a white solid (mp 244–246 °C). ^1H -NMR (CDCl_3), 8.20 (t, 4 H, $J = 5.0$ Hz, NH), 6.80 (s, 8 H, ArH), 4.63 (s, 8 H, ArOCH_2), 4.55 (d, 4 H, $J = 13.0$ Hz, AB system ArCH_2Ar), 3.55 (s, 36 H, $\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OH}$), 3.74 (q, 8 H, $J = 6.5$ Hz, CH_2N), 3.35 (d, 4 H, $J = 13.0$ Hz, AB system ArCH_2Ar), and 1.06 (s, 36 H, $t\text{-C}_4\text{H}_9$). MS-FAB positive $m/z = 1228.70$ (calculated 1229,56). Anal. calcd. for $\text{C}_{68}\text{H}_{100}\text{O}_{16}\text{N}_4$: C, 66,43; H, 8,20. Found: C, 67,89; H, 8,37.

- 1 R = R' = $\text{CH}_2\text{COOCH}_3$
- 2 R = H ; R' = $\text{CH}_2\text{CONH-benzyl}$
- 3 R = R' = $\text{CH}_2\text{CONH-benzyl}$
- 4 R = R' = $\text{CH}_2\text{CONHCH}_2\text{-furane}$
- 5 R = R' = $\text{CH}_2\text{CONHCH}_2\text{-thiophene}$
- 6 R = R' = $\text{CH}_2\text{CONH}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{OH}$



The ^1H NMR studies of the binding properties of **4–6** towards the selected anions were conducted in the same

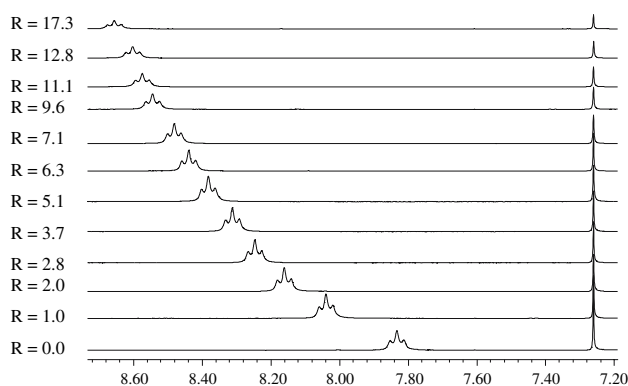


Fig. 1 CONH proton shift changes of the ^1H NMR spectra of **5** with upon addition of increasing amount of TBANO_3 . (R = Concentration of metal/concentration of ligand)

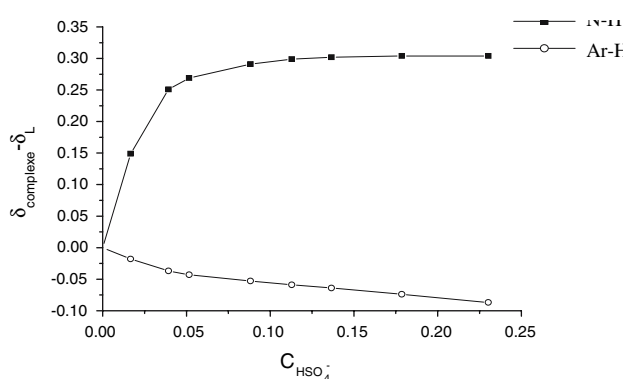


Fig. 2 Variation $\Delta\delta$ ($\delta_{\text{complex}} - \delta_{\text{ligand}}$)_{NH} and ($\delta_{\text{complex}} - \delta_{\text{ligand}}$)_{ArH} of the chemical shifts of ligand **6** as function of HSO_4^- concentration

conditions as indicated for **2** and **3** [8]. CDCl_3 solutions (10^{-2} M) of ligands were mixed with increasing quantities of anions salts: TBA(tetrabutylammonium)F, TBACl, TBABr, TBANO_3 and TBAHSO_4 . The ratio between TBA anion salts and the ligands was determined directly on the ^1H NMR spectra by using the integration ratio of the triplet of CONH protons of the ligand/the quintuplet of $\text{N}^+(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_4$ protons of added TBA anion salts. The addition of TBA anion salts (0 to 30 equivs) provoked significant shifts of CONH protons resulting in titration curves suggesting the formation of H-bonding with the anionic species. Figure 1 shows the ^1H NMR spectra of **5** with upon addition of increasing amount of TBANO_3 with noticeable CONH proton shift changes.

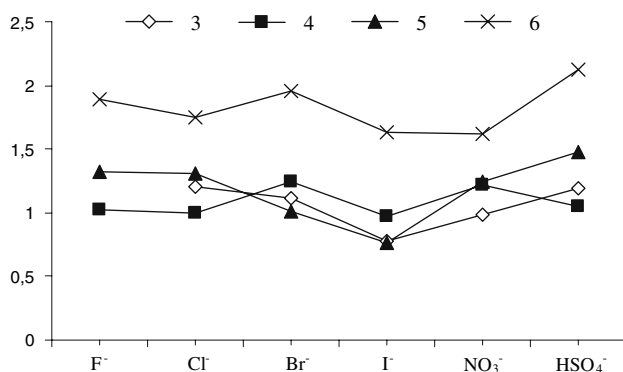
In a general manner we observed a low-field shifts of the NH triplet of **4–6** (Fig. 2) indicating the formation of hydrogen bonding between the anion and the hydrogen of amido groups. Such a behaviour is well know for amide-based ligands [11].

The use of the program EquiChem.¹ shows the formation of 1:1 complexes with logarithmic association

¹ ChemEqui for calculations, V. Solov'ev., e-mail: solvit@ipac.ac.ru.

Table 1 Logarithmic association constants for **3–6** and halides, nitrate, hydrogen sulphate ions in CDCl₃

Ligands	F ⁻	Cl ⁻	Br ⁻	I ⁻	NO ₃ ⁻	HSO ₄ ⁻
3	–	1.20 ± 0.02 ^a	1.11 ± 0.03 ^a	0.78 ± 0.02 ^a	0.99 ± 0.01 ^a	1.19 ± 0.02 ^a
4	1.02 ± 0.05	1.00 ± 0.05	1.25 ± 0.06	0.97 ± 0.04	1.22 ± 0.03	1.05 ± 0.06
5	1.32 ± 0.03	1.31 ± 0.03	1.01 ± 0.03	0.76 ± 0.10	1.24 ± 0.07	1.48 ± 0.11
6	1.89 ± 0.01	1.75 ± 0.08	1.95 ± 0.081	1.63 ± 0.04	1.62 ± 0.01	2.13 ± 0.04

^a Taken from Ref. [8]**Fig. 3** Variations of log K_{ass} of various anions for **3–6** ligands

constants (log K_{ass}) varying from, 0.76 (for **5** with I⁻) to 2.13 (for **6** with HSO₄⁻) (given in Table 1, **3** [8] is considered for comparison), which are low as expected for anion complexes formation. In the halides (or monoatomic) series, I⁻ is generally the less complexed anion probably because of its large size.

Ligand **6**, bearing -CONHCH₂CH₂OCH₂CH₂OH chains, is the best complexant for all anions (Fig. 3). The strongest complex being formed with HSO₄⁻ due probably to the possibility of formation of H-bonds of various types with oxygen O-atoms of the glycolic chains and the OH groups with a needed tetrahedral geometry [11]. Thiophene derivative **5** is also selective for HSO₄⁻. The replacement of thiophenes by furanes makes **4** to be selective for Br⁻ followed by NO₃⁻.

Concerning polyatomic anions (NO₃⁻ and HSO₄⁻), the monoanion complexes of **4** and **5** with NO₃⁻ have similar binding constants. While **3** forms a complex with HSO₄⁻, two times more stable than with **5**.

In comparison tetrabenzyl derivative **3**, also forms monoanion species. The complex with iodine remains the less stable one toward anion series. Logarithmic association constants values remain comparable to those of **4** and **5** suggesting that the anions occupy the cavity delineated by the amide functions.

To conclude, this study shows the formation of monoanion species with ligands **4–6**. The anion being located in the calixarenic cavity near the amido functions. The

logarithmic association constants of anion complexes are weak (between 0.7 and 2), comparing to those of cation complexes (about 4–6) [10]. The complexes obtained with iodine are the less stable in anion series due probably to the large size of this anion. **6** is the best complexant ligand in the series. As ligand **6** the derivative thiophene **5** is selective for HSO₄⁻ in the series of monoatomic anions with probably a formation of hydrogen bonds in the two cases. The derivative furane **4** is selective for Br⁻ and NO₃⁻ explained by an adequacy between the size of the anion and that of the cavity of the ligand.

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