J Incl Phenom Macrocycl Chem (2009) 63:301–308
DOI 10.1007/s10847-008-9523-4

ORIGINAL ARTICLE

Hydrogen bonding receptors of tetraamide derivatives derived from thiacalix[4]arene in cone- and 1,3-alternate conformation

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Received: 12 June 2007 / Accepted: 1 December 2008 / Published online: 17 December 2008

Abstract Novel ditopic receptors of tetraamide derivatives possessing four 2-pyridyl groups derived from thiacalix[4]arene in cone- and 1,3-alternate conformation were prepared. The structure of one of the tetraamide derivatives was confirmed by a single crystal X-ray analysis. The tetrathiacalix[4]arene tetraamides show strong intramolecular hydrogen bonding. The binding behaviour towards Ag^+ and halides has been investigated by ^1H NMR titration experiments.

Keywords Thiacalix[4]arene · *O*-alkylation · Conformation · Ionophores · Hydrogen bond · Metal complexation

Introduction

From both a biological [1, 2] and an environmental [3] viewpoint the synthesis of anion receptors is one of the most intriguing and useful targets in supramolecular chemistry. Calixarenes (For a comprehensive review of all aspects of calixarene chemistry, see Ref [4].) [5, 6] and more recently thiacalixarenes [7, 8] have been widely used in molecular recognition due to their unique three-dimensional structure with almost limitless derivatization possibilities. Despite the importance of the field of molecular recognition of anions, when compared to that of cations, little work has been conducted. The selective complexation of anions is more demanding than that of cations for a number of reasons such as size, charge density, polarizability, solvation energy and pH-dependent acid-base equilibria [9–11].

A number of examples of substituted calixarenes have been utilized for anion complexation [12, 13]. Typically, the introduction of activated amides [14–18], amines [14], urea [19–22], and thiourea [19] into the calixarene platform, led to the receptors which interact with anions. Furthermore such receptors are able to form ditopic systems capable of ion-pair recognition [23–28], which show significant relevance to the selective extraction and/or transport of metals salts across lipophilic membranes. However, thiacalix[4]arene based receptors with multiple their potential binding sites have not to-date been reported.

On progressing from our interest on the synthesis of heteroditopic receptors that function as not only an anion binder but also as a cation binder, we have introduced amides functions into the lower rim of the thiacalix[4]arene. Amide functions have been used as efficient extractants for both cations and anions due to their high stability and hydrophobicity. We report herein, the synthesis and complexation studies of tetraamides of the form **4**, possessing either cone- and 1,3-alternate conformations. The recognition properties of these new tetraamides have been investigated by ^1H NMR experiments in $CDCl_3$.

Experimental

All mps (Yanagimoto MP-S_1) are uncorrected. ^1H NMR spectra (300 MHz) were recorded on a Nippon Denshi

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JEOL FT-300 NMR spectrometer with $SiMe_4$ as an internal reference: *J*-values are given in Hz. IR spectra were measured for samples as KBr pellets in a Nippon Denshi JIR-AQ2OM spectrophotometer. UV spectra were measured by Shimadzu 240 spectrophotometer. Elemental analyses were performed by Yanaco MT-5.

Materials

cone- (*cone*-**2**) and 1,3-*alternate*-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]-2,8,14,20-tetrathiacalix[4]arene (1,3-*alternate*-**2**) were prepared in 76 and 95% according to the reported procedure [29].

*cone-5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis[carboxymethoxy]-2,8,14,20-tetrathiacalix[4]arene (cone-**3**) [30]*

A solution of *cone*-**2** (1.07 g, 1.0 mmol), K_2CO_3 (2.76 g, 20 mmol) in DMSO-water (6:1, 35 mL) was heated at 120 °C for 12 h and then to the cooled mixture was added 2 M HCl (60 mL) in ice-water bath. The precipitate was collected by filtration and washed with water, then dissolved in chloroform. After filtering off the solid residue, the filtrate was evaporated to dryness to obtain *cone*-**3**, which was recrystallized from water-acetone to obtain a pure sample as colorless prisms (750 mg, 85%) as colorless prisms. Mp 333–335 °C. IR *v* (KBr)/cm^{-1} 3480 (OH), 1758 (CO). ^{1}H NMR δ ($CDCl_3$) 1.11(36H, s, *t*Bu), 5.07 (8H, s, OCH_2), 7.38 (8H, s, Ar–*H*). MS *m/z* 975.1 $[M + Na]^+$. Anal. Calcd. For $C_{48}H_{56}O_{12}S_4$ (953.22): C, 60.48; H, 5.92. Found: C, 60.23; H, 5.70%.

*1,3-alternate-5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis[carboxy-methoxy]- 2,8,14,20-tetrathiacalix[4]arene (1,3-alternate-**3**)*

A similar procedure to that of *cone*-**2** was carried out affording 1,3-*alternate*-**3** (85%) as an off-white solid. Mp 325-326 °C. IR *v* (KBr)/cm^{-1} 3421 (OH), 1695 (CO). ^{1}H NMR δ ($CDCl_3$) 1.25 (36H, s, *t*Bu), 4.66 (8H, s, OCH_2), 7.39 (8H, s, Ar–*H*). MS *m/z* 975.1 $[M + Na]^+$. Anal. Calcd. For $C_{48}H_{56}O_{12}S_4$ (953.22): C, 60.48; H, 5.92. Found: C, 60.35; H, 5.72%.

*cone-5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis[(2-aminopyridyl)-carbonylmethoxy]-2,8,14,29-tetrathiacalix[4]arene (cone-**4**)*

To a solution of *cone*-**3** (100 mg, 0.105 mmol), 2-aminopyridine (108 mg, 1.14 mmol) and 1-hydroxybenzotriazole (HOBt) (26 mg, 0.17 mmol) in CH_2Cl_2:DMF (4:1, 25 mL) was added drop wise a solution of dicyclohexylcarbodiimide (DCC) (190 mg, 0.92 mmol) in CH_2Cl_2 (5 mL) at 0 °C. After the mixture was stirred for 20 h at room temperature, it was condensed under reduced pressure. The residue was extracted with ethyl acetate (30 mL × 2). The combined extracts were washed with 10% citric acid (20 mL × 2), 5% sodium bicarbonate (20 mL), water (20 mL), saturated brine (20 mL), dried ($MgSO_4$) and condensed under reduce pressure. The residue was recrystallized from methanol affording *cone*-**4** (60 mg, 45%) as colorless prisms. Mp 270–272 °C. IR *v* (KBr)/cm^{-1} 3253 (NH), 1753 (CO). ^{1}H NMR δ ($CDCl_3$) 1.11 (36H, s, *t*Bu), 5.14 (8H, s, OCH_2), 6.92 (4H, dd, *J* = 7.2, 4.8 Hz, Py-H_5), 7.38 (8H, s, Ar–*H*), 7.52 (4H, ddd, *J* = 7.2, 4.8, 1.0 Hz, Py-H_4), 7.96 (4H, d, *J* = 8.4 Hz Py-H_3), 8.24 (4H, dd, *J* = 4.8, 1.0 Hz, Py-H_6), 10.56 (4H, s, N*H*). MS *m/z* 1256 (M^+). Anal. Calcd. For $C_{68}H_{72}N_8O_8S_4$ (1257.62): C, 64.94; H, 5.77; N, 8.91. Found: C, 64.92; H, 5.75; N, 8.90%.

*1,3-alternate-5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis[(2-amino-pyridyl)carbonylmethoxy]-2,8,14,29-tetrathiacalix[4]arene (1,3-alternate-**4**)*

A similar procedure to that of *cone*-**4** was carried out affording 1,3-*alternate*-**4** as colorless prisms in 53% yield. Mp 290–292 °C. IR *v* (KBr)/cm^{-1} 3254 (NH), 1752 (CO). ^{1}H NMR δ ($CDCl_3$) 0.74 (36H, s, *t*Bu), 5.08 (8H, s, OCH_2), 6.98 (4H, dd, *J* = 7.2, 4.8 Hz, Py-H_5), 7.62 (4H, ddd, *J* = 7.2, 4.8, 1.0 Hz, Py-H_4), 7.66 (8H, s, Ar–*H*), 8.25 (4H, d, *J* = 8.7 Hz Py-H_3), 8.27 (4H, dd, *J* = 4.8, 1.0 Hz, Py-H_6), 8.94 (4H, s, N*H*). MS *m/z* 1256 (M^+). Anal. Calcd. For $C_{68}H_{72}O_8N_8S_4$ (1257.62): C, 64.94; H, 5.77; N, 8.91. Found: C, 64.90; H, 5.76; N, 8.90%.

*Preparation of 4-tert-butyl-2,6-dimethyl[(2-pyridylaminocarbonyl)-methoxy]benzene (**6**)*

To a solution of (4-*tert*-butyl-2,6-dimethyl)phenoxyacetic acid **5** [31] (100 mg, 0.43 mmol), 2-aminopyridine (120 mg, 1.28 mmol) and HOBt (26 mg, 0.17 mmol) in CH_2Cl_2 (12 mL) was added dropwise a solution of DCC (190 mg, 0.92 mmol) in CH_2Cl_2 (5 mL) at 0 °C. After the mixture was stirred for 7 h at room temperature, it was condensed under reduced pressure. The residue was extracted with ethyl acetate (30 mL × 2). The combined extracts were washed with 10% citric acid (20 mL × 2), 5% sodium bicarbonate (20 mL), water (20 mL), saturated brine (20 mL), dried (Na_2SO_4) and condensed under reduce pressure. The residue was recrystallized from methanol affording **6** as colorless prisms (86 mg, 65%). Mp 118–120 °C; ν_{max} (KBr)/cm^{-1} 3397, 3323 (NH), 1714 (CO). ^{1}H NMR δ ($CDCl_3$) 1.30 (9H, s, *t*Bu), 2.30 (6H, s, Ph-CH_3), 4.41 (2H, s, ArOCH_2), 7.04 (2H, s, Ar–H), 7.10 (1H, m, pyridine-H_5), 7.75 (1H, m, pyridine-H_4), 8.31(1H,

m, pyridine-H_3), 8.35(1H, m, pyridine-H_6), 9.25 (1H, s, NH). MS m/z 312 (M^+). Anal. Calcd. For $C_{19}H_{24}O_2N_2$ (312.42): C, 73.05; H, 7.74; N, 8.97. Found: C, 73.23; H, 7.35; N, 8.72%.

^{1}H NMR complexation experiments

To a $CDCl_3$ solution (4×10^{-6} M) of **4** in an NMR tube was added 1 to 2 molar molar solution of $AgSO_3CF_3$. The spectrum was recorded after addition and the temperature of the NMR probe kept constant at 27 °C. The ^{1}H NMR data of *cone*-**4** with Ag^+ ion are given below.

cone-**4** ⊃ Ag^+ δ_H ($CDCl_3$:CD_3CN 20:1) 1.11 (36H, s, *t*Bu), 5.12 (8H, s, OCH_2), 7.08 (4H, dd, J = 7.2, 4.8 Hz, Py-H_5), 7.38 (8H, s, Ar–H), 7.71 (4H, ddd, J = 7.2, 4.8, 1.0 Hz, Py-H_4), 7.71 (4H, d, J = 8.4 Hz Py-H_3), 8.33 (4H, dd, J = 4.8, 1.0 Hz, Py-H_6), 10.38 (4H, s, NH).

Stoichiometry of metal complexation

The method of continuous variation was employed to determine the stoichiometry of *cone*-**4** and 1,3-*alternate*-**4** complexes. Two-phase solvent extraction was carried out between aqueous picrates (5 mL, [metal picrate] = 2×10^{-4} M, $AgNO_3$) and **4** (5 mL, [**4**] = 2×10^{-4} M in CH_2Cl_2). The molar ratios of both **4** and metal picrate were varied from 0 to 1, while the total concentration was kept at several constant levels. The two-phase mixture in a glass tube immersed in a thermostated water bath at 25 °C was shaken at 300 strokes per min for 1 h and then kept at the same temperature for 2 h, which allowed for the complete separation of the two phases. The absorbance of each solution was determined by UV spectroscopy (λ = 290 nm) [32]. Job plots were generated by plotting the extracted [Ag^+] versus the mole fraction of metal.

Determination of association constants

A solution of the receptor 1,3-*alternate*-**4** was prepared at a concentration typically of the order of 0.01 mol dm^{-3} in $CDCl_3$:CD_3CN 20:1 (v/v). The initial ^{1}H NMR spectrum was recorded, and aliquots of cation ($AgSO_3CF_3$) in the same solvent were added by a microsyringe from a solution made such that from 1 to 2 molar equivalents were added in 20 μL. The association constants (K_{ass}) were calculated by nonlinear least squares fitting [33] by the chemical shift change of NH protons as a function of 1,3-*alternate*-**4** concentration in $CDCl_3$:CD_3CN 20:1 (v/v) at 27 °C.

Crystallographic data for *cone*-4 · 2½H_2O

Diffraction data were collected at Daresbury Laboratory Station 9.8 using synchrotron radiation due to small crystal size, needle habit and weak diffraction. A Bruker APEX II CCD diffractometer was used to collected data to $\theta = 21.3°$ beyond which data were too weak to be observed. The data were twinned via a rotation of 180° about b with the major:minor twin component ratio being 85.1:14.9(3)%. Data were corrected for absorption on the basis of symmetry equivalent and repeated data (min. and max. transmission factors: 0.980, 0.996) and Lp effects. The structure was solved by direct methods and refined on F^2 using all data. H atoms were constrained in a riding model. Further details can be found in Table 1. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 645623. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: 144-1223-3360336033 or e-mail: deposit@ccdc.cam.ac.uk].

Results and discussion

Synthesis

The thiacalix[4]arene tetracarboxylic acid *cone*-**3** was prepared by hydrolysis of *cone*-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]- 2,8,14,20-

Table 1 Crystallographic data and data-collection details for *cone*-**4** · 2½H_2O

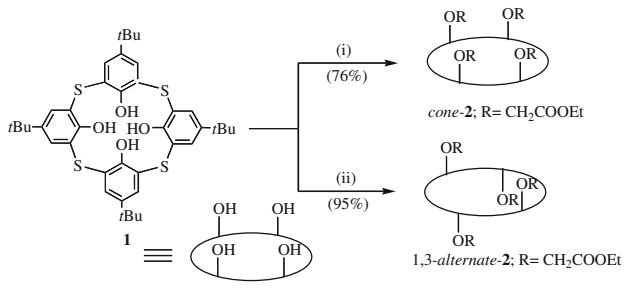
Formula	$C_{68}H_{72}N_8O_8S_4 \cdot 2½H_2O$
FW	1302.62
Crystal size/mm	0.15 × 0.02 × 0.02
Space group	Monoclinic, $P2_1/n$
a/Å	21.199 (7)
b/Å	15.106 (5)
c/Å	21.595 (8)
β/°	90.996 (5)
U/Å^3	6914 (4)
Z	4
ρ_{calcd} g/cm^3	1.251
T/K	120 (2)
Radiation	Synchroton,
λ/Å	0.6893
μ/cm^{-1}	0.200
No. of reflections	38051
Unique reflections	8391
R_{int}	0.105
Reflections with $F^2 > 2\sigma(F^2)$	5608
R ($F^2 > 2\sigma(F^2)$)	0.1162
Rw (all data)	0.3329
S	1.225

tetrathiacalix[4]arene *cone*-**2** [30, 34] with K_2CO_3 aq. in a mixture of DMSO and water, which was prepared by *O*-alkylation of **1** with ethyl bromoacetate in the presence of NaH according to the reported procedures [29, 35] (Scheme 1). Tetrathiacalix[4]arene tetraamide *cone*-**4** was prepared by condensation reaction of *cone*-**3** with 2-aminopyridine in the presence of dicyclohexylcarbodiimide (DCC) and 1-hydroxybenzotriazole (HOBt) at room temperature for 15 h in CH_2Cl_2. Similarly, 1,3-*alternate*-**4** was prepared from the corresponding 1,3-*alternate*-**2** as described above (Scheme 2). The conformational assignments of **4** were not necessary because the tetraacetate **2** was conformationally immobilized in *cone*- and 1,3-*alternate* conformation [29, 35]. The product structures were supported by their spectral and analytical data [29].

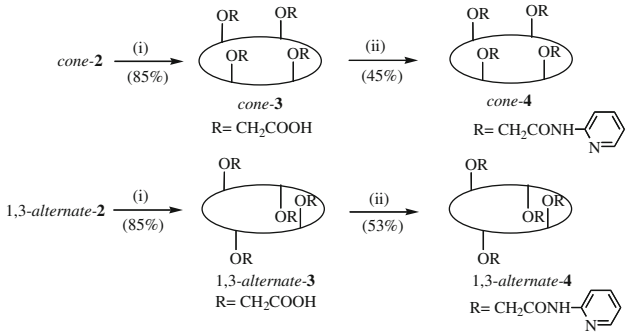
The tetraamide derivative 1,3-*alternate* **4** has, in the first instance, two possible binding sites because of the 1,3-*alternate* conformation [36–38]. Furthermore, the NH group can bind anions by hydrogen bonding, while the carbonyl and phenolic oxygens are also available for cation binding. In particular, receptor **4** with additional binding sites for cations can present higher form of molecular behavior. In other words, their binding sites could participate simultaneously and cooperatively upon ion binding.

Receptors **4** could, in principle, work as a heteroditopic receptor. The presence of the pyridine function might provide the possibility to complex soft cations. Furthermore, the acetate functions of 1,3-*alternate*-**4** could work as a controller for the recognition of cations or anions by the amide function placed at the other site of the thiacalix[4]arene cavity.

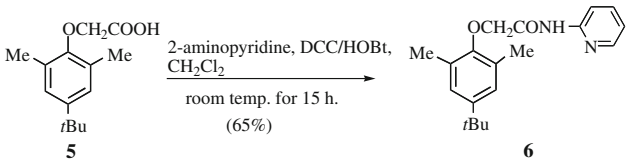
Several examples of the formation of intramolecular hydrogen-bonding among opposing urea groups which can bind anionic species in calix[4]arenes have been reported [39, 40]. As a consequence, intramolecular hydrogen bonding may be foreseen between the NH and CO groups in compounds such as those reported herein. In the case of **4**, additional intramolecular hydrogen bonding between NH and N_{pyr} groups can also be anticipated. In order to investigate the existence of intramolecular hydrogen



Scheme 1 Reagents and conditions: (i) $BrCH_2CO_2Et$, NaH, THF-DMF, reflux for 36 h; (ii) $BrCH_2CO_2Et$, Cs_2CO_3, acetone, reflux for 36 h



Scheme 2 Reagents and conditions: (i) K_2CO_3, DMSO/water, 120 °C for 12 h; (ii) 2-aminopyridine, DCC/HOBt, CH_2Cl_2, room temp. for 15 h



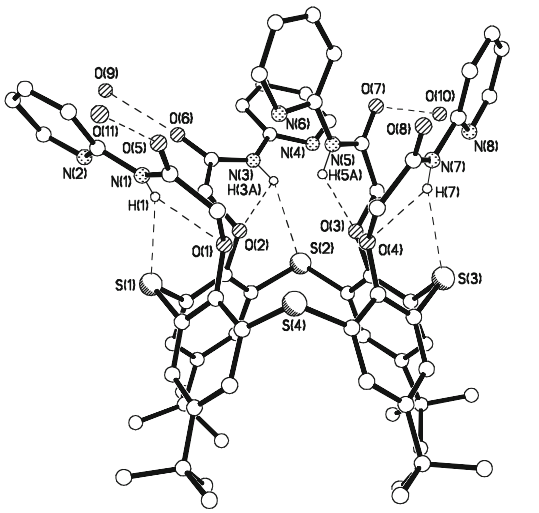
Scheme 3 Synthesis of reference compound **6**

bonding in **4**, the reference compound **6** was synthesized (Scheme 3). On comparison of the chemical shift of the N*H* proton of **6** (δ 9.25 ppm, $CDCl_3$) with that observed for *cone*-**4**, we observe that N*H* proton in *cone*-**4** is shifted downfield shift (δ 10.56 ppm; *i.e.* $\Delta\delta = +1.31$ ppm) indicative of the strong intramolecular hydrogen-bonding between NH and neighboring C=O moities. On the other hand, the pyridyl protons in *cone*-**4** and compound **6** show similar chemical shift (*i.e.* H_6 $\delta = 8.24$ and 8.36, respectively), which suggests that there is a lack of an intramolecular hydrogen bond between N*H* and N_{py} groups. In contrast, the N*H* protons of 1,3-*alternate*-**4** shows an upfield shift (δ 8.94 ppm; *i.e.* $\Delta\delta = -0.31$ ppm), which suggests that the steric hindrance of the *tert*-butyl groups hinders the formation of intramolecular hydrogen bonding.

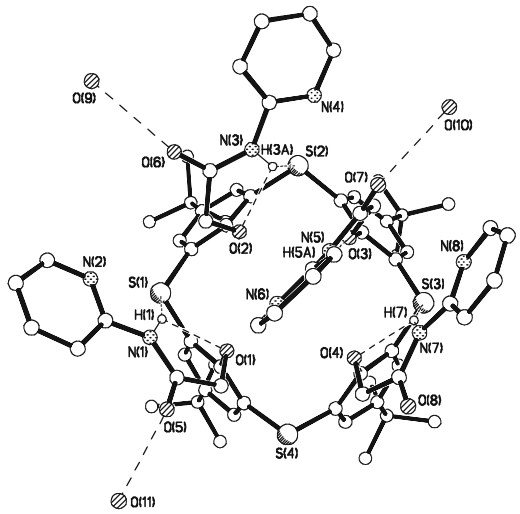
The chemical shift of the N*H* protons of *cone*-**4** did not change in ^{1}H NMR dilution studies due to the presence of concentration-independent intramolecular hydrogen-bonding. The presence of the NH groups can also lead to intermolecular hydrogen-bonding involving the solvent. The compound *cone*-**4** was dissolved in the strongly hydrogen-bonding solvent DMSO-d_6. A slight downfield shift of N*H* protons ($\Delta\delta = +0.12$ ppm) of *cone*-**4** in DMSO-d_6 was observed, suggestive of the braking of the intramolecular hydrogen-bonding and the formation of new intermolecular hydrogen-bonding.

Fortunately, recrystallization from MeOH and $CHCl_3$ (3:1 v/v) produced small X-ray quality colorless crystals of *cone*-**4** suitable for single crystal X-ray diffraction using synchrotron radiation. The structure of of *cone*-**4** is shown

in Fig. 1. In the solid state, it is clear that compound *cone*-**4** adopts a "*cone* conformation" and the orientations of the carbonyl oxygens of the amide are outwardly orientated with respect to the cavity because of the electron repulsion between oxygens. Interestingly, the structure of *cone*-**4** reveals the existence of intramolecular hydrogen bonding between three of the sulfur atoms in the bridges and NH protons (S···HN, range: 3.269(10)–3.459(11) Å), and between the phenolic oxygens and the NH protons (ArO···HN, range: 2.628(12)–2.730(12) Å). Each molecule of *cone*-**4** is linked to approx 2½ water molecules of crystallization via H-bonds to thicalix[4]arene C=O groups. Neighbouring molecules of *cone*-**4** are linked together via these H-bonded water molecules which act as bridges.



side view



top view

Fig. 1 Ball and stick drawing of *cone*-**4** · 2½H_2O. Oxygen atoms O(9), O(10) and O(11) are water molecules of crystallization with O(11) modelled with 50% occupancy. The dashed lines indicate hydrogen bonding

Binding studies

The recognition properties of receptors *cone*-**4** and 1,3-*alternate*-**4** were investigated by ^{1}H NMR titration experiments in $CDCl_3$:CD_3CN (20:1) using selected anions (tetrabutylammonium (TBA) chloride and bromide) and cations (silver and potassium trifluoromethanesulfonate). In general, the titration experiments were carried out by the increasing addition of ion (0.1 mol dm^{-3}) into 5×10^{-6} mol of the receptor in 0.5 mL of $CDCl_3$:CD_3CN (20:1). The association constants (K_{ass}) were calculated by nonlinear least squares fitting [33], and the stoichiometry was determined by using Job's method.

Addition of 1 equivalent of KSO_3CF_3 into either *cone*-**4** and 1,3-*alternate*-**4** solutions did not cause significant chemical shift change (*i.e.* greater than 0.01 ppm) even in the presence of an excess of K^+ ion. In contrast, upon titration of *cone*-**4** and 1,3-*alternate*-**4** with $AgSO_3CF_3$ moderate chemical shift changes were observed. In fact, titration of *cone*-**4** with 1 equivalent $AgSO_3CF_3$ caused dramatic chemical shift change not only in the pyridine protons ($\Delta\delta = +0.09$, $+0.16$, $+0.19$ and -0.25 ppm for H_6, H_5, H_4 and H_3, respectively)[1] but also in the N*H* protons ($\Delta\delta = -0.18$ ppm) (Fig. 2).

The upfield shift of the N*H* protons strongly suggests that the intramolecular hydrogen bonding between the NH and neighbouring C=O groups might be broken upon complexation of Ag^+ ion as shown in Fig. 3. It was also found that the original C_4-symmetry has been retained following complexation of *cone*-**4** with Ag^+. Similar phenomena were also observed in the titration of 1,3-a*lternate*-**4** with 1 equivalent $AgSO_3CF_3$. Interestingly, further chemical shift changes were observed upon the addition of an extra equivalent of Ag^+ into the solution containing 1,3-*alternate*-**4** $\supset$ Ag^+, supporting the 1:2 complexation stoichiometry ($Ag^+ \subset$1,3-*alternate*-**4** $\supset$ Ag^+). The association constants (K_{ass}) were calculated by nonlinear least squares fitting [33] by the chemical shift change of N*H* protons as a function of 1,3-*alternate*-**4** concentration in $CDCl_3$:CD_3CN 20:1 (v/v) at 27 °C. Theassociation constants K_{ass} of both amide sites are quite similar ($K_{ass} = 2.62 \times 10^2$ M^{-1} and $K_{ass} = 2.37 \times 10^2$ M^{-1}), suggesting that the two amide sites work independently. These findings suggest that the Ag^+ must be coordinated by two pyridine nitrogens and the CO oxygens to saturate the requirements of the Ag^+ coordination sphere [41]. It is worth mentioning that the complexation of 1,3-*alternate*-**4** with the first Ag^+ ion did not affect the induced-fit recognition of the second Ag^+ ion which implies a positive cooperativity between the two sides which favoring the formation of the 1:2 complex (Fig. 4).

[1] A minus sign (−) denotes a shift to higher magnetic field and a plus sign (+) denotes a shift to down field

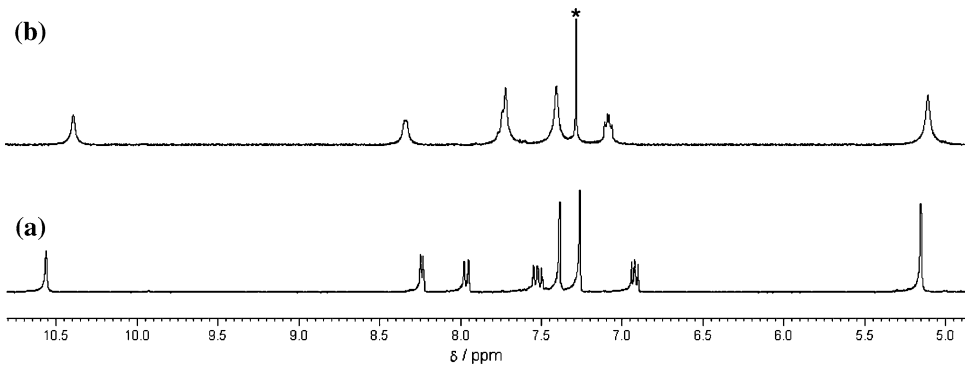


Fig. 2 Partial ^{1}H NMR of *cone*-**4** (5×10^{-6} M) at 300 MHz in $CDCl_3$:CD_3CN 20:1 (v/v) at 27 °C) **a** Free ligand, **b** in the presence of 1 equiv. of $AgSO_3CF_3$. *Denotes solvent signal

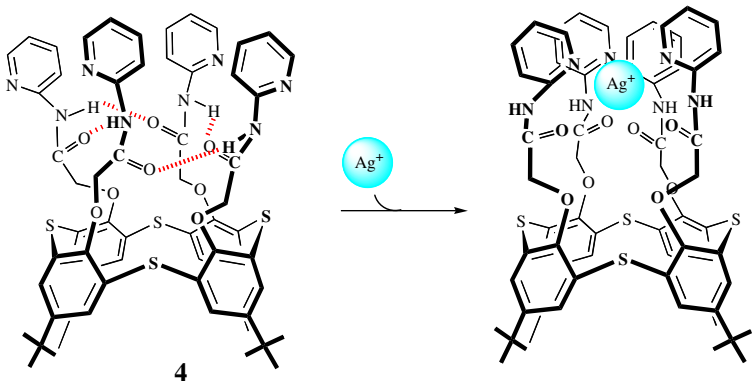


Fig. 3 Binding mode and chemical shift changes of *cone*-**4** upon complexation with Ag^+ [300 MHz, in $CDCl_3$:CD_3CN 20:1 (v/v) at 27 °C]

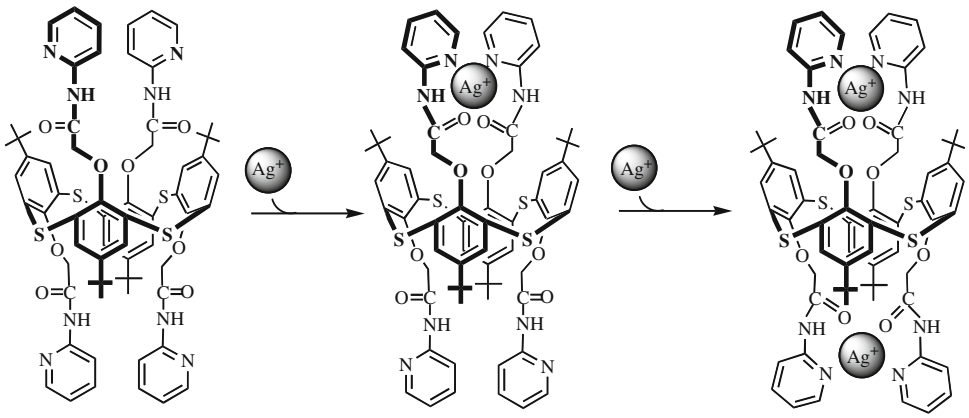


Fig. 4 Binding mode and chemical shift changes of 1,3-*alternate*-**4** upon complexation with Ag^+ [300 MHz, in $CDCl_3$:CD_3CN 20:1 (v/v) at 27 °C]

Disappointingly, during the titration of *cone*-**4** and 1,3-*alternate*-**4** with 1 equivalent or even excess of TBACl or TBABr no significant shifts were observed indicating that there is little or no interaction between these molecules and the anionic species. This implies that the present hydrogen-bonding systems are not strong enough to form tight complexes with anionic species.

Conclusion

Novel receptors thiacalix[4]arene tetraamides possessing four 2-pyridyl groups with either a *cone*- or a 1,3-*alternate* conformation have been prepared. In the thiacalix[4]arene tetraamide derivative *cone*-**4,** the existence of two different intramolecular hydrogen bonds between the sulfur atom on the bridge and NH proton (S···HN), and between the phenolic oxygen and the NH proton (ArO···HN) was confirmed by single crystal X-ray analysis. The presence of the pyridine function allows for high affinity toward Ag^+ ion complexation. However, the affinities for K^+ and halide anions are quite small in both thiacalix[4]arene tetraamide derivatives *cone*-**4** and 1,3-*alternate*-**4**. Further studies on the synthesis of anion receptors based on thiacalix[4]arenes are now in progress.

Acknowledgments We would like to thank the OTEC at Saga University for financial support and the EPSRC UK National

Crystallography Service at Southampton University and Daresbury Laboratory.

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