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ORIGINAL ARTICLE

Synthesis and complexing properties of four imidazolyl acetamido *p-tert*-butylcalix[4]arenes

Najah Cheriaa · Rym Abidi · Jacques Vicens

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Abstract Four imidazolyl acetamido *p-tert*-butylcalix[4]arenes **5–8** have been prepared by reacting the corresponding methyl esters derivatives **1–4** with histamine in 1:1 mixture of methanol:toluene. The yields ranged from 56 to 68%. **5–8** have been shown to be in cone conformation. The complexation behaviour of **5–8** towards monovalent metal picrates M^+Pic^- with $M^+ = Li^+$, Na^+, K^+, Rb^+ and Cs^+ and divalent metal picrates $M^{2+}(Pic^-)_2$ with $M^{2+} = Mg^{2+}$, Ca^{2+}, Sr^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+}, Zn^{2+} and Co^{2+} are given. Tentative localisation of the metal cations in the receptors is given. The binding properties towards these cations have been determined along with stoichiometries of the complexes.

Keywords Calix[4]arenes · Tetraamido · Imidazolyl · Cation complexation

Introduction

The calixarenes prepared by base-catalyzed condensations of *p*-substituted phenols with formaldehyde are attractive matrices, their phenol hydroxy groups being ordered in well shaped cyclic arrays which can be functionalized to give rise to highly selective metal cation receptors [1]. One early studies of calixarene involves derivatives with carbonyl-groups containing substituents on the narrow rim and the realisation that simple ester functions on the rim were effective ligating groups for metal cations led to a comprehensive physicochemical evaluation of factors directing the complexation and the selectivity in complexation [2]. The family of amide calixarenes and their complexes with alkali metal, transition metal, and lanthanide ions have been extensively investigated [1, 2].

We recently reported the synthesis and complexing properties of tetraamido-type *p-tert*-butylcalix[4]arenes presenting two proximal binding subunits [3, 4]. One unit consists of four amido functions delineating a cavity with four carbonyl functions and four phenolic oxygens able to complex hard cations such as alkali and alkaline-earth metal cations. The second cavity is attached to the calix unit through the amido functions and is constructed with heterocycles such as pyridine, thiophene, tetrahydrofurane and furane. Hard and soft cations are complexed in this unit depending on the nature of the heteroatoms. The formation of 1:1:1 hetero complexes has been noted with *negative cooperativity* between the two subunits [3, 4].

As a continuation, in the present work we report the synthesis and complexing properties of related amido-type *p-tert*-butylcalix[4]arenes **5–8** bearing imidazolyl residues (see chart 1). Related-Supramolecular systems have been published based on a *p-tert*-butylcalix[6]arene functionalized in altering positions by three imidazole groups. These systems were mainly designed as mimicks of zinc enzymes [5–7].

Experimental section

General

The melting points (Mps) were determined on an electrothermal apparatus in sealed capillary tubes under nitrogen.

N. Cheriaa (✉) · J. Vicens
Ecole Chimie Polymères Matériaux, Laboratoire de Conception Moléculaire, associé au CNRS, IPHC, LC4, 25, rue Bequerel, 67087 Strasbourg Cédex 2, France
e-mail: najah_cheriaa@yahoo.fr

N. Cheriaa · R. Abidi
Faculté des Sciences, Université de Bizerte, 7021 Zarzouna-Bizerte, Tunisia

^{1}H-NMR spectra were recorded with Bruker SY 300 spectrometer (300 MHz). Chemical shifts δ are expressed in ppm from tms as an internal standard and $CDCl_3$ and CD_3OD as solvents at 7.27 ppm and 3.30 ppm, respectively. Coupling constants J are given in Hz. Elemental analyses were performed at the Service de Microanalyse of the Institut de Chimie de Strasbourg.

Histamine, methyl bromo acetate and the solvents were commercial reagents and were used without further purification. 1,3-Dimethyl ester-[8], trimethyl ester-[8], and tetramethyl ester-[3] *p-tert*-butyl calix[4]arenes were prepared as described in the literature. All the reactions were carried out under nitrogen.

Preparation of **1**

*Preparation of 5,11,17,23-tetra(tert-butyl)-25-monomethyl ester calix[4]arene (**1**)*

p-*tert*-Butyl calix[4]arene (6.489 g, 10.0 mmol), K_2CO_3 (0.719 g, 5.2 mmol) and acetone (250 ml) were stirred at rt for 1 h. Methyl bromo acetate (1.529 g, 10.0 mmol) was added and the reaction mixture was refluxed for 24 h. The solvents were removed under reduced pressure and the residue was treated with dichloromethane and 1 M HCl untill pH = 4. The organic layer was dried over Na_2SO_4. After removal of the solvents, the residue was purified by column chromatography (SiO_2:CH_2Cl_2) to yield **1** (2.002 g, 28%) as a white solid. Mp 148–149°C.

^{1}H-NMR ($CDCl_3$): 10.24 (s, 1H, O*H*), 9.26 (s, 2H, O*H*), 7.12 (s, 2H, Ar*H*), 7.08 (s, 4H, Ar*H*), 7.01 (s, 2H, Ar*H*), 4.93(s, 4H, ArOCH_2), 4.47 (d, 2H, J = 13.2 Hz, AB system, ArCH_2Ar), 4.30 (d, 2H, J = 13.5 Hz, A′B′ system, ArCH_2Ar), 3.95 (s, 3H, OCH_3), 3.49 (d, 2H, J = 13.2 Hz, AB system, ArCH_2Ar), 3.42 (d, 2H, J = 13.5 Hz, A′B′ system, ArCH_2Ar), 1.26 (s, 9H, *tert*-butyl), 1.06 (s, 18H, *tert*-butyl), 0.93 (s, 9H, *tert*-butyl). Anal.calcd. For $C_{50}H_{64}O_8$, 0.5 CH_2Cl_2: C, 78.31; H, 8.39. Found: C, 78.25; H, 8.56.

Preparation of **5–8**

*Preparation of 5,11,17,23-tetra(tert-butyl)-25-mono(4-ethyl imidazole acetamide) calix[4]arene (**5**)*

A mixture of monomethyl ester calix[4]arene **1** (1.441 g, 2.0 mmol) and histamine (0.277 g, 2.5 mmol) in 16 ml of a 1:1 mixture of methanol:toluene was refluxed for 6 days. The solvents were evaporated under reduced pressure. The residue was dissolved in dichloromethane and washed with water. The organic layer was dried over Na_2SO_4. After filtration and evaporation, the resulting oil was purified by chromatography on a column (SiO_2:9:1 CH_2Cl_2–MeOH) to yield **5** (1.053 g, 64%) as a white solid. Mp 148–149°C.

^{1}H-NMR ($CDCl_3$): 9.30 (t, 1H, J = 2.5 Hz, N*H* amide), 7.55 (s, 1H, C*H* imidazolyl-*Ha*), 7.09 (d, 2H, J = 1.0 Hz, Ar*H*), 7.07 (s, 2H, Ar*H*), 7.06 (s, 2H, Ar*H*), 7.02 (d, 2H, J = 1.0 Hz, Ar*H*), 6.93 (s, 1H, C*H* imidazolyl-*Hb*), 4.56 (s, 2H, ArOCH_2), 4.26 (d, 2H, J = 10.1 Hz, AB system, ArCH_2Ar), 4.18 (d, 2H, J = 10.1 Hz, A′B′ system, ArCH_2Ar), 3.50 (d, 2H, J = 10.1 Hz, AB system, ArCH_2Ar), 3.48 (d, 2H, J = 10.1 Hz, A′B′ system, ArCH_2Ar), 3.86 (q, 2H, J = 5.2 Hz, NHCH_2CH$_2$-imidazole), 3.10 (t, 2H, J = 5.2 Hz, CH_2-imidazole), 1.24 (s, 9H, *tert*-butyl), 1.23 (s, 18H, *tert*-butyl), 1.17 (s, 9H, *tert*-butyl). Anal.calcd. For $C_{51}H_{65}O_5N_3$, 2 CH_3OH: C, 73.65; H, 8.52. Found: C, 73.48; H, 8.60.

*Preparation of 5,11,17,23-tetra (tert-butyl)-25,27-di(4-ethyl imidazole acetamide) calix[4]arene (**6**)*

Using the same procedure as for **5**: 1,3-dimethyl ester calix[4]arene **2** (1.030 g, 1.3 mmol), histamine (0.288 g, 2.6 mmol) in 16 ml of a 1:1 mixture of methanol:toluene was refluxed for 4 days. The solvents were removed by evaporation under reduced pressure. The residue was dissolved in dichloromethane and washed with water. The organic layer was dried over Na_2SO_4. The residue was precipitated with diethyl ether to give pure **6** (0.751 g, 68%) as a white solid. Mp 154–155°C.

^{1}H-NMR ($CDCl_3$): 9.11 (broad t, 2H, N*H* amide), 7.84 (s, 2H, OH), 7.46 (s, 2H, C*H* imidazolyl-*Ha*), 7.08 (s, 4H, Ar*H*), 6.95 (s, 4H, Ar*H*), 6.77 (s, 2H, C*H* imidazolyl-*Hb*), 4.58 (s, 4H, ArOCH_2), 4.13 (d, 4H, J = 13.3 Hz, AB system, ArCH_2Ar), 3.69 (q, 4H, J = 7.7 Hz, NHCH_2CH$_2$-imidazole), 3.45 (d, 4H, J = 13.3 Hz, AB system, ArCH_2Ar), 2.94 (t, 4H, J = 7.7 Hz, CH_2-imidazole), 1.28 (s, 18H, *tert*-butyl), 1.07 (s, 18H, *tert*-butyl). Anal.calcd. For $C_{58}H_{74}O_6N_6$, CH_3OH: C, 72.05; H, 8.00; N, 8.55. Found: C, 72.43; H, 7.74; N, 8.75.

*Preparation of 5,11,17,23-tetra(tert-butyl)-25,26,27-tri(4-ethyl imidazole acetamide) calix[4]arene (**7**)*

Using the same procedure as for **5**: trimethyl ester calix[4]arene **3** (0.995 g, 1.15 mmol), histamine (0.771 g, 6.94 mmol) in 16 ml of a 1:1 mixture of methanol:toluene was refluxed for 5 days. The solvents were removed under reduced pressure. The residue was dissolved in dichloromethane and washed with water. The organic layer was dried over Na_2SO_4. The residue was precipitated with

hexane-diethyl ether to give pure **7** (0.702 g, 68%) as a white solid. Mp 203–204°C.

^{1}H-NMR ($CDCl_3$): 8.31(broad s, 1H, N*H* amide), 7.93 (broad s, 2H, N*H* amide), 7.45 (broad s, 1H, C*H* imidazolyl-*Ha*), 7.40 (broad s, 2H, C*H* imidazolyl-*Ha*), 7.16 (s, 2H, Ar*H*), 7.07 (s, 2H, Ar*H*), 6.70 (broad s, 1H, C*H* imidazolyl-*Hb*), 6.66 (broad s, 2H, C*H* imidazolyl-*Hb*), 6.59 (s, 2H, Ar*H*), 6.53 (s, 2H, Ar*H*), 6.03 (s, 1H, O*H*), 4.41–4.35 (m, 6H, ArOCH_2), 4.27 (d, 4H, $J = 10.9$ Hz, AB system, ArCH_2Ar), 3.70–3.44 (m, 6H, NHCH_2CH_2-imidazole), 3.24 (d, 4H, $J = 10.9$ Hz, AB system, ArCH_2Ar), 2.89–2.72 (m, 6H, CH_2-imidazole), 1.32 (s, 18H, *tert*-butyl), 0.83 (s, 18H, *tert*-butyl). Anal.calcd. For $C_{65}H_{83}O_7N_9$, 4 CH_3OH: C, 66.86; H, 7.55; N, 11.65. Found: C, 66.86; H, 7.48; N, 10.17.

*Preparation of 5,11,17,23-tetra(tert-butyl)-25,26,27,28-tetra(4-ethyl imidazole acetamide) calix[4]arene (**8**)*

Using the same procedure as for **5**: tetra methyl ester calix[4]arene **4** (0.937 g, 1.0 mmol), histamine (0.889 g, 8.0 mmol) in 16 ml of a 1:1 mixture of methanol:toluene was refluxed for 6 days. The solvents were removed under reduced pressure. The residue was dissolved in dichloromethane and washed with water. The organic layer was dried over Na_2SO_4. The residue was precipitated with hexane to give pure **8** (0.752 g, 56%) as a white solid. Mp $\geq$ 300°C.

^{1}H-NMR (insoluble in chloroform, CD_3OD): 7.56 (s, 4H, C*H* imidazolyl-*Ha*), 6.85 (s, 8H, Ar*H*), 6.77 (s, 4H, C*H* imidazolyl-*Hb*), 4.53 (d, 4H, $J = 13.3$ Hz, AB system, ArCH_2Ar), 4.48 (s, 8H, ArOCH_2), 3.53 (t, 8H, $J = 7.3$ Hz, NHCH_2CH_2-imidazole), 3.23 (d, 4H, $J = 13.3$ Hz, AB system, ArCH_2Ar), 2.82 (t, 8H, $J = 7.3$ Hz, CH_2-imidazole), 1.09 (s, 36H *tert*-butyl). Anal.calcd. For $C_{72}H_{92}O_8N_{12}$, 2 CH_3OH: C, 67.93; H, 7.37; N, 12.82. Found: C, 67.44; H, 7.65; N, 12.76.

^{1}H-NMR study of the complexation of metal picrates by **5–8**

$CDCl_3$-solutions of **5–7** (10^{-2} M) were reacted with different solid metal picrates: M^+Pic^- with $M^+ = Li^+$, Na^+, K^+, Rb^+ and Cs^+, and M^{2+} $(Pic^-)_2$ with $M^{2+} = Ba^{2+}$, Ca^{2+}, Sr^{2+}, Mg^{2+}, Zn^{2+}, Pb^{2+}, Cd^{2+}, Cu^{2+}, and Co^{2+}. The ratio of the extracted cation to ligand in the solution was estimated by calculating the integration ratio of the picrate protons *vs* the aromatic protons of the calix unit. Because insoluble in chloroform, CD_3OD-solutions of **8** (10^{-2} M) were prepared with 1 equiv of the same picrates.

(5)$_2$ · Zn^{2+} (Pic$^-$)$_2$: 9.62 (broad s, 1H, N*H* amide), 9.37 (broad s, 2H, O*H*), 8.69 (s, 2H, picrate), 8.01 (broad s, 2H, O*H* and C*H* imidazolyl-*Ha*), 7.05 (s, 8H, *ArH*), 6.97 (s, 1H, C*H* imidazolyl-*Hb*), 4.59 (s, 2H, ArOCH_2), 4.08 (broad d, 4H, $J = 12.4$ Hz, AB system, ArCH_2Ar), 3.81 (broad s, 2H, NHCH_2CH_2 imidazole), 3.41 (broad d, 4H, $J = 12.4$ Hz, AB system, ArCH_2Ar), 3.09 (broad s, 2H, CH_2-imidazole), 1.21 (s, 9H, *tert*-butyl), 1.20 (s, 18H, *tert*-butyl), 1.16 (s, 9H, *tert*-butyl). **(5)$_2$ · Cd^{2+} (Pic$^-$)$_2$**: 9.92 (broad s, 1H, N*H* amide), 9.34 (broad s, 2H, O*H*), 8.67 (s, 2H, picrate), 8.14 (s, 1H, *CH* imidazolyl-*Ha*), 7.13 (s, 1H, C*H* imidazolyl *Hb*), 7.01 (s, 6H, *ArH*), 6.95 (s, 2H, *ArH*), 4.61 (s, 2H, ArOCH_2), 4.07 (d, 4H, $J = 13.7$ Hz, AB system, ArCH_2Ar), 3.93 (m, 2H, NHCH_2CH_2-imidazole), 3.40 (d, 4H, $J = 13.7$ Hz, AB system, ArCH_2Ar), 3.13 (sl, 2H, CH_2-imidazole), 1.20 (s, 9H, *tert*-butyl), 1.19 (s, 18H, *tert*-butyl),1.15 (s, 9H, *tert*-butyl). **(6)$_2$ · Mg^{2+}(Pic$^-$)$_2$**: 9.19 (broad s, 2H, N*H* amide), 8.84 (s, 4H, picrate), 7.86 (s, 2H, N*H* imidazole), 7.55 (s, 2H, C*H* imidazolyl-*Ha*), 7.07 (s, 4H, Ar*H*), 6.94 (s, 4H, Ar*H*), 6.78 (s, 2H, C*H* imidazolyl-*Hb*), 4.57 (s, 4H, ArOCH_2), 4.08 (d, 4H, $J = 13.1$ Hz, AB system, ArCH_2Ar), 3.62 (broad s, 4H, NHCH_2CH_2 imidazole), 3.42 (d, 4H, $J = 13.1$ Hz, AB system, ArCH_2Ar), 2.87 (sl, 4H, CH_2-imidazole), 1.26 (s, 18H, *tert*-butyl), 1.05 (s, 18H, *tert*-butyl). **6 · Ca^{2+}(Pic$^-$)$_2$**: 9.49 (broad s, 2H, N*H* amide), 8.71 (s, 4H, picrate), 8.00 (broad s, 2H, N*H* imidazole), 7.40 (s, 2H, C*H* imidazolyl-*Ha*), 7.07 (s, 4H, Ar*H*), 6.95 (s, 4H, Ar*H*), 6.64 (s, 2H, C*H* imidazolyl-*Hb*), 4.61 (s, 4H, ArOCH_2), 4.08 (d, 4H, $J = 12.4$ Hz, AB system, ArCH_2Ar), 3.62 (broad s, 4H, NHCH_2CH_2 imidazole), 3.43 (d, 4H, $J = 12.4$ Hz, AB system, ArCH_2Ar), 2.79 (sl, 4H, CH_2-imidazole), 1.25 (s, 18H, *tert*-butyl), 1.06 (s, 18H, *tert*-butyl). **(6)$_2$ · Sr^{2+}(Pic$^-$)$_2$**: 9.14 (broad s, 2H, N*H* amide), 8.77 (s, 2H, picrate), 7.82 (s, 2H, N*H* imidazole), 7.59 (s, 2H, C*H* imidazolyl-*Ha*), 7.07 (s, 4H, Ar*H*), 6.93 (s, 4H, Ar*H*), 6.81 (s, 2H, C*H* imidazolyl-*Hb*), 4.57 (s, 4H, ArOCH_2), 4.08 (d, 4H, $J = 13.3$ Hz, AB system, ArCH_2Ar), 3.66 (broad s, 4H, NHCH_2CH_2 imidazole), 3.41 (d, 4H, $J = 13.3$ Hz, AB system, ArCH_2Ar), 2.91 (broad s, 4H, CH_2-imidazole), 1.26 (s, 18H, *tert*-butyl), 1.05 (s, 18H, *tert*-butyl). **(6)$_2$ · Ba^{2+}(Pic$^-$)$_2$**: 9.13 (broad s, 2H, N*H* amide), 8.63 (s, 2H, picrate), 7.61 (s, 2H, C*H* imidazolyl-*Ha*), 7.06 (s, 4H, Ar*H*), 6.90 (s, 4H, Ar*H*), 6.78 (s, 2H, C*H* imidazolyl-*Hb*), 4.55 (s, 4H, ArOCH_2), 4.05 (d, 4H, $J = 12.9$ Hz, AB system, ArCH_2Ar), 3.65 (broad s, 4H, NHCH_2CH_2 imidazole), 3.38 (d, 4H, $J = 12.9$ Hz, AB system, ArCH_2Ar), 2.89 (broad s, 4H, CH_2-imidazole), 1.26 (s, 18H, *tert*-butyl), 1.03 (s, 18H, *tert*-butyl). **(6)$_2$ · Zn^{2+}(Pic$^-$)$_2$**: 9.02 (broad s, 2H, N*H* amide), 8.73 (s, 2H, picrate), 7.88 (broad s, 2H, N*H* imidazole), 7.76 (broads, 2H, C*H* imidazolyl-*Ha*), 7.05 (s, 4H, Ar*H*), 6.90 (s, 6H, Ar*H* and C*H* imidazolyl-*Hb*), 4.53 (broad s, 4H, ArOCH_2), 4.10 (d, 4H, $J = 11.8$ Hz, AB system, ArCH_2Ar), 3.64

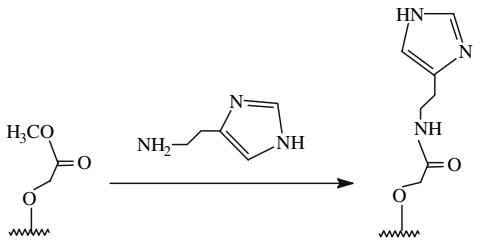
(broad s, 4H, NHCH_2CH$_2$ imidazole), 3.38 (d, 4H, $J = 11.8$ Hz, AB system, ArCH_2Ar), 2.97 (sl, 4H, CH_2-imidazole), 1.25 (s, 18H, *tert*-butyl), 1.02 (s, 18H, *tert*-butyl). **6 · $Pb^{2+}(Pic^-)_2$**: 9.07 (broad s, 2H, N*H* amide), 8.68 (s, 4H, picrate), 8.24 (s, 2H, N*H* imidazole), 7.55 (s, 2H, C*H* imidazolyl-*Ha*), 7.04 (s, 4H, Ar*H*), 6.84 (s, 4H, Ar*H*), 7.14 (broad s, 2H, C*H* imidazolyl-*Hb*), 4.56 (broad s, 4H, ArOCH_2), 4.00 (broad s, 4H, ArCH_2Ar), 3.76 (broad s, 4H, NHCH_2CH$_2$ imidazole), 3.33 (broad s, 4H, ArCH_2Ar), 3.06 (sl, 4H, CH_2-imidazole), 1.24 (s, 18H, *tert*-butyl), 0.97 (s, 18H, *tert*-butyl). **$(6)_2$ · $Cd^{2+}(Pic^-)_2$**: 9.00 (broad s, 2H, N*H* amide), 8.77 (s, 2H, picrate), 7.75 (broad s, 2H, N*H* imidazole), 7.45 (s, 2H, C*H* imidazolyl-*Ha*), 7.05 (s, 4H, Ar*H*), 6.89 (s, 4H, Ar*H*), 6.71 (s, 2H, C*H* imidazolyl-*Hb*), 4.53 (s, 4H, ArOCH_2), 4.10 (d, 4H, $J = 12.9$ Hz, AB system, ArCH_2Ar), 3.59 (sl, 4H, NHCH_2CH$_2$ imidazole), 3.37 (d, 4H, $J = 12.9$ Hz, AB system, ArCH_2Ar), 2.90 (broad s, 4H, CH_2-imidazole), 1.25 (s, 18H, *tert*-butyl), 1.02 (s, 18H, *tert*-butyl). **7 · Na^+Pic^-** : 8.77 (s, 2H, picrate), 8.29 (s, 1H, N*H* amide), 7.97 (s, 2H, N*H* amide), 7.47 (2s, 3H, C*H* imidazolyl-*Ha*), 7.14 (s, 2H, Ar*H*), 7.05 (s, 2H, Ar*H*), 6.69 (s, 3H, C*H* imidazolyl-*Hb*), 6.65 (s, 2H, Ar*H*), 6.60 (s, 2H, Ar*H*), 4.46–4.28 (m, 6H, ArOCH_2), 4.12 (d, 4H, $J = 12.2$ Hz, AB system, ArCH_2Ar), 3.68–3.40 (m, 6H, NHCH_2CH$_2$-imidazole), 3.26 (d, 4H, $J = 12.2$ Hz, AB system, ArCH_2Ar), 2.81 (broad s, 6H, CH_2-imidazole), 1.28 (s, 18H, *tert*-butyl), 0.87 (s, 18H, *tert*-butyl). **7 · $Ca^{2+}(Pic^-)_2$**: 8.73 (s, 2H, picrate), 8.38 (broad s, 1H, N*H* amide), 7.90 (flat s, 2H, N*H* amide), 7.40 (s, 3H, C*H* imidazolyl-*Ha*), 7.13 (s, 2H, Ar*H*), 7.04 (s, 2H, Ar*H*), 6.58 (s, 5H, C*H* imidazolyl-*Hb* and Ar*H*), 6.52 (s, 2H, Ar*H*), 4.48–4.08 (m, 10H, ArOCH_2 and ArCH_2Ar), 3.60–3.45 (m, 6H, NHCH_2CH$_2$-imidazole), 3.25–3.17 (m, 4H, ArCH_2Ar), 2.73 (broad s, 6H, CH_2-imidazole), 1.28 (s, 18H, *tert*-butyl), 0.82 (s, 18H, *tert*-butyl). **7 · $Sr^{2+}(Pic^-)_2$**: 8.71 (s, 4H, picrate), 8.33 (broad s, 1H, N*H* amide), 7.89 (broad s, 2H, *NH* amide), 7.52 (broad s, 3H, C*H* imidazolyl-*Ha*), 7.14 (s, 2H, Ar*H*), 7.04 (s, 2H, Ar*H*), 6.68 (s, 3H, C*H* imidazolyl-*Hb*), 6.60 (s, 2H, Ar*H*), 6.53 (s, 2H, Ar*H*), 4.23–4.38 (m, 10H, ArOCH_2 and ArCH_2Ar), 3.40–3.55 (m, 6H, NHCH_2CH$_2$ imidazole), 3.21 (broad s, 4H, ArCH_2Ar), 2.80 (broad s, 6H, CH_2-imidazole), 1.30 (s, 18H, *tert*-butyl), 0.83 (s, 18H, *tert*-butyl). **$(7)_2$ · $Ba^{2+}(Pic^-)_2$**: 8.63 (broad s, 2H, picrate), 8.33 (broad s, 1H, N*H* amide), 7.83 (broad s, 2H, N*H* amide), 7.48 (broad s, 3H, C*H* imidazolyl-*Ha*), 7.13 (s, 2H, Ar*H*), 7.03 (s, 2H, Ar*H*), 6.64 (broad s, 3H, C*H* imidazolyl-*Hb*), 6.58 (s, 2H, Ar*H*), 6.51 (s, 2H, Ar*H*), 4.46–4.18 (m, 10H, ArOCH_2 and ArCH_2Ar), 3.61–2.51 (m, 16H, NHCH_2CH$_2$ imidazole and ArCH_2Ar and CH_2-imidazole), 1.29 (s, 18H, *tert*-butyl), 0.81 (s, 18H, *tert*-butyl). **7 · $Zn^{2+}(Pic^-)_2$** : 8.73 (s, 4H, picrate), 8.33 (broad s, 1H, N*H* amide), 7.86 (flat s, 2H, N*H* amide), 7.55 (broad s1, 3H, C*H* imidazolyl-*Ha*), 7.14 (s, 2H, Ar*H*), 7.05 (s, 2H, Ar*H*), 6.72 (broad s, 3H, C*H* imidazolyl-*Hb*), 6.58 (s, 2H, Ar*H*), 6.52 (s, 2H, Ar*H*), 4.51–3.12 (m, 6H, ArOCH_2 and ArCH_2Ar), 3.62–3.46 (m, 6H, NHCH_2 CH$_2$ -imidazole), 3.35–3.15 (m, 4H, ArCH_2Ar), 2.82 (s, 6H, CH_2-imidazole), 1.30 (s, 18H, *tert*-butyl), 0.82 (s, 18H, *tert*-butyl). **$(7)_2$ · $Pb^{2+}(Pic^-)_2$**: 8.70 (broad s, 2H, picrate), 8.35 (flat s, 1H, N*H* amide), 7.74 (s, 5H, N*H* amide and 3*H* imidazolyl-*Ha*), 7.14 (s, 2H, Ar*H*), 7.04 (s, 2H, Ar*H*), 6.78 (broad s, 3H, C*H* imidazolyl *Hb*), 6.58 (s, 2H, Ar*H*), 6.53 (s, 2H, Ar*H*), 4.46–4.12 (m, 10H, ArOCH_2 and AB system, ArCH_2Ar), 3.54 (broad s, 6H, NHCH_2CH$_2$-imidazole), 3.24 (broad s, 4H, ArCH_2Ar), 2.85 (broad s, 6H, CH_2-imidazole), 1.28 (s, 18H, *tert*-butyl), 0.82 (s, 18H, *tert*-butyl). **$(7)_2$ · $Cd^{2+}(Pic^-)_2$**: 8.74 (broad s, 2H, picrate), 8.38 (flat s, 1H, N*H* amide), 7.48 (flat s, 3H, C*H* imidazolyl-*Ha*), 7.14 (broad s, 2H, Ar*H*), 7.04 (broad s, 2H, Ar*H*), 6.52 (broad s, 7H, *ArH* and C*H* imidazolyl-*Hb*), 4.49–4.05 (m, 10H, ArOCH_2 and ArCH_2Ar), 3.62–339 (m, 6H, NHCH_2CH$_2$-imidazole), 3.22 (broad s, 4H, AB system, ArCH_2Ar), 2.81 (broad s, 6H, CH_2-imidazole), 1.28 (s, 18H, *tert*-butyl), 0.81 (s, 18H, *tert*-butyl). **8 · Na^+Pic^-** (CD_3OD): 8.75 (s, 2H, picrate), 7.60 (s, 4H, C*H* imidazolyl-*Ha*), 7.29 (s, 8H, Ar*H*), 6.81 (s, 4H, C*H* imidazolyl-*Hb*), 4.46 (s, 8H, ArOCH_2), 4.43 (d, 4H, $J = 12.4$ Hz, AB system, ArCH_2Ar), 3.56 (t, 8H, NHCH_2CH$_2$-imidazole), 3.40 (d, 4H, $J = 12.4$ Hz, AB system, ArCH_2Ar), 2.84 (t, 8H, $J = 7.1$ Hz, CH_2-imidazole), 1.18 (s, 36H *tert*-butyl). **8 · $Ca^{2+}(Pic^-)_2$** (CD_3OD): 8.72 (s, 4H, picrate), 7.88 (s, 4H, C*H* imidazolyl-*Ha*), 7.60 (s, 8H, Ar*H*), 6.85 (s, 4H, C*H* imidazolyl-*Hb*), 4.00 (d, 4H, $J = 12.4$ Hz, AB system, ArCH_2Ar), 4.56 (s, 8H, ArOCH_2), 3.65 (t, 8H, $J = 6.8$ Hz, NHCH_2CH$_2$ imidazole), 3.56 (d, 4H, $J = 12.4$ Hz, AB system, ArCH_2Ar), 2.87 (t, 8H, $J = 6.8$ Hz, CH_2-imidazole), 1.19 (s, 36H *tert*-butyl). **8 · $Sr^{2+}(Pic^-)_2$** (CD_3OD): 8.74 (s, 4H, picrate), 7.60 (broad s, 4H, C*H* imidazolyl-*Ha*), 7.34 (s, 8H, Ar*H*), 6.88 (s, 4H, C*H* imidazolyl-*Hb*), 4.54 (s, 8H, ArOCH_2), 4.06 (d, 4H, $J = 7.5$ Hz, AB system, ArCH_2Ar), 3.68 (sl, 8H, NHCH_2CH$_2$-imidazole), 3.46 (d, 4H, $J = 7.5$ Hz, AB system, ArCH_2Ar), 2.88 (sl, 8H, CH_2-imidazole), 1.17 (s, 36H *tert*-butyl). **8 · $Ba^{2+}(Pic^-)_2$** (CD_3OD): 8.77 (s, 4H, picrate), 7.58 (s, 4H, C*H* imidazolyl-*Ha*), 7.08 (s, 8H, Ar*H*), 6.82 (s, 4H, C*H* imidazolyl-*Hb*), 4.50 (s, 8H, ArOCH_2), 4.33 (d, 4H, $J = 13.0$ Hz, AB system, ArCH_2Ar), 3.58 (t, 8H, $J = 7.1$ Hz, NHCH_2CH$_2$ imidazole), 3.34 (d, 4H, $J = 13.0$ Hz, AB system, ArCH_2Ar), 2.84 (t, 8H, $J = 7.1$ Hz, CH_2-imidazole), 1.13 (s, 36H *tert*-butyl). **8 · $Zn^{2+}(Pic^-)_2$** (CD_3OD): 8.72 (s, 2H, picrate), 8.01 (s, 4H, C*H* imidazolyl-*Ha*), 6.85 (s, 8H, Ar*H*), 7.01 (s, 4H, C*H*-imidazolyl *Hb*), 4.47 (s, 4H, AB system, ArCH_2Ar), 4.47 (s, 8H, ArOCH_2), 3.54 (s, 8H, NHCH_2CH$_2$ -imidazole), 3.24 (d, 4H, $J = 13.3$ Hz, AB system, ArCH_2Ar), 2.87 (s, 8H, CH_2-imidazole), 1.08 (s, 36H *tert*-butyl). **8 · $Pb^{2+}(Pic^-)_2$**

(CD_3OD): 8.72 (s, 4H, picrate), 7.63 (s, 4H, C*H* imidazolyl-*Ha*), 7.29 (s, 8H, Ar*H*), 6.89 (s, 4H, C*H* imidazolyl-*Hb*), 4.57 (s, 8H, $ArOCH_2$), 4.14 (d, 4H, $J = 12.2$ Hz, AB system, $ArCH_2Ar$), 3.69 (t, 8H, $J = 7.1$ Hz, $NHCH_2CH_2$-imidazole), 3.41 (d, 4H, $J = 12.2$ Hz, AB system, $ArCH_2Ar$), 2.89 (t, 8H, $J = 7.1$ Hz, CH_2-imidazole), 1.17 (s, 36H, *tert*-butyl). **8 · $Cd^{2+}(Pic^-)_2$** (CD_3OD): 8.73 (s, 4H, picrate), 7.67(s, 4H, C*H* imidazolyl-*Ha*), 6.87 (s, 8H, Ar*H*), 6.82 (s, 4H, C*H*-imidazolyl *Hb*), 4.47 (d, 4H, $J = 12.4$ Hz, AB system, $ArCH_2Ar$), 4.46 (s, 8H, $ArOCH_2$), 3.50 (t, 8H, $J = 6.8$ Hz, $NHCH_2CH_2$-imidazole), 3.20 (d, 4H, $J = 12.4$ Hz, AB system, $ArCH_2Ar$), 2.81 (t, 8H, $J = 6.8$ Hz, CH_2-imidazole), 1.08 (s, 36H, *tert*-butyl).

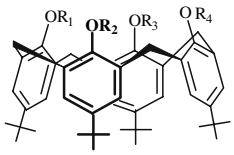
Results and discussion

Preparation of **1**

Mono methyl ester **1** was prepared as it follows: *p-tert*-butylcalix[4]arene was reacted with 1 equiv of $BrCH_2CO_2CH_3$ in the presence of 0.5 equiv. of K_2CO_3 in acetone with reflux for 24 h. The reaction was monitored by TLC. **1** was obtained pure in 28% yield by chromatography on silica column with CH_2Cl_2 as eluent. The fixation of 1 methyl ester and the cone conformation of **1** were deduced from the ^{1}H-NMR of **1** in $CDCl_3$: one singlet was observed at 3.95 ppm for the OCH_3 and two AB systems were found at 3.49 ppm and 4.47 ppm with $J = 13.2$ Hz and 3.42 ppm and 4.30 ppm with $J = 13.5$ Hz characteristic of the $ArCH_2Ar$ in the cone conformation. Three singlets were detected at 1.17, 1.23 and 1.24 ppm in an integration ratio 1:2:1 for the *tert*-butyl groups.



Scheme 1 Amidation of methyl ester function by histamine



1 R_1 = A, $R_2 = R_3 = R_4$ =H
2 $R_1 = R_3$ =A, $R_2 = R_4$ = H
3 $R_1 = R_2 = R_3$ = A, R_4 =H
4 $R_1 = R_2 = R_3 = R_4$ = A

5 R_1 = B, $R_2 = R_3 = R_4$=H
6 $R_1 = R_3$ =B, $R_2 = R_4$ = H
7 $R_1 = R_2 = R_3$ = B, R_4 =H
8 $R_1 = R_2 = R_3 = R_4$ =B

A = $CH_2CO_2CH_3$

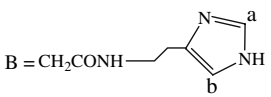


Chart I

Preparation of **5–8**

According to Scheme 1, the synthesis of **5–8** was conducted by amidation of the corresponding methyl ester derivatives **1–4** (see chart 1).

Table 1 Selected ^{1}H-NMR chemical shifts in ppm for **5–8** coupling constants are given in Hz in brackets

	N*H* amide	*Hb*	Ar*H*	*Ha*	$ArCH_2Ar$	CH_2Z	NCH_2Z	t-C_4H_9
5	9.30	7.55	7.09	6.93	4.26 and 4.18	3.86	3.10	1.24
			7.07		3.50 and 3.48	(3.0)	(3.0)	1.23
			7.06		(6.0)			1.16
			7.02					
6	9.11	7.46	7.08	6.77	4.13 and 3.45	3.69	2.94	1.28
			6.95		(8.0)	(4.0)	(4.0)	1.07
7	8.31	7.45	7.16	6.70	4.27 and 3.24	3.55	2.83	1.32
	7.93	7.40	7.07	6.66	(6.0)			0.83
8	–	7.56	6.85	6.77	4.53 and 3.23	3.53	2.82	1.09
					(8.0)	(4.0)	(4.0)	

Table 2 Stoichiometries of complexes **5–7** in $CDCl_3$ and **8** in CD_3OD with metal picrates as estimated by ^{1}H-NMR

Cations	Ligands			
	5	**6**	**7**	**8**
Li^+	a	a	a	a
Na^+	a	a	1:1	1:1
K^+	a	a	a	a
Rb^+	a	a	a	a
Cs^+	a	a	a	a
Mg^{2+}	a	1:2	a	a
Ca^{2+}	a	1:1	1:1	1:1
Sr^{2+}	a	1:2	1:1	1:1
Ba^{2+}	a	1:2	1:2	1:1
Pb^{2+}	a	1:1	1:2	1:1
Cd^{2+}	1:2	1:2	1:2	1:1
Zn^{2+}	1:2	1:2	1:1	1:1
Co^{2+}	b	b	b	b

a: No changes in the spectrum

b: The spectrum was unreadable due to the paramagnetism of the cation but we assumed the extraction

Table 3 $\Delta\delta$ (ppm) value for the complexes of **5–7** in $CDCl_3$ and of **8** in CD_3OD with different metal picrates

	NH_{amid}	NH_{hist}	CH_{his}	CH_{his}	$ArOCH_2$	$ArCH_2Ar$	CH_2	NCH_2
δ (ppm) **5**	9.30	–	7.55	6.93	4.56	4.26; 3.50 4.18; 3.84	3.86	3.10
$\Delta\delta$ $(\mathbf{5})_2 \cdot Zn^{2+}(Pic^-)_2$	−0.32	*	−0.46	*	*	0.16; 0.43	*	*
$\Delta\delta$ $(\mathbf{5})_2 \cdot Cd^{2+}(Pic^-)_2$	−0.62	*	−0.59	−0.20	*	0.19; 0.44	−0.07	*
δ (ppm) **6**	9.11	7.84	7.46	6.77	4.58	4.13; 3.45	3.69	2.94
$\Delta\delta$ $(\mathbf{6})_2 \cdot Mg^{2+}(Pic^-)_2$	−0.08	*	−0.09	*	*	*	0.07	0.07
$\Delta\delta$ $\mathbf{6} \cdot Ca^{2+}(Pic^-)_2$	−0.38	−0.56	0.06	0.13	*	*	0.07	0.15
$\Delta\delta$ $(\mathbf{6})_2 \cdot Sr^{2+}(Pic^-)_2$	−0.06	*	−0.13	*	*	*	0.07	0.06
$\Delta\delta$ $(\mathbf{6})_2 \cdot Ba^{2+}(Pic^-)_2$	*		0.15	*	*	0.06	*	0.06
$\Delta\delta$ $(\mathbf{6})_2 \cdot Zn^{2+}(Pic^-)_2$	0.09	*	−0.30	−0.13	*	*	*	*
$\Delta\delta$ $\mathbf{6} \cdot Pb^{2+}(Pic^-)_2$	*	0.40	0.09	0.37	*	−0.13; −0.12	0.07	0.12
$\Delta\delta$ $(\mathbf{6})_2 \cdot Cd^{2+}(Pic^-)_2$	0.11	0.09	*	0.06	*	*	0.10	*
δ (ppm) **7**	8.31	7.93	7.45; 7.40	6.70; 6.66	4.37	4.27; 3.24	3.55	2.83
$\Delta\delta$ $\mathbf{7} \cdot Na^+Pic^-$	*	*	*	*	0.09	0.10	*	*
$\Delta\delta$ $\mathbf{7} \cdot Ca^{2+}(Pic^-)_2$	−0.07	*	*	0.12	−0.15	*	*	0.10
$\Delta\delta$ $\mathbf{7} \cdot Sr^{2+}(Pic^-)_2$	*	*	−0.07	*	*	−0.09	*	*
$\Delta\delta$ $(\mathbf{7})_2 \cdot Ba^{2+}(Pic^-)_2$	*	0.10	*	*	0.08	*	0.06	0.06
$\Delta\delta$ $\mathbf{7} \cdot Zn^{2+}(Pic^-)_2$	*	0.07	−0.10	0.07	*	*	*	*
$\Delta\delta$ $(\mathbf{7})_2 \cdot Pb^{2+}(Pic^-)_2$	*	−0.19	0.30	0.12	*	0.09	*	*
$\Delta\delta$ $(\mathbf{7})_2 \cdot Cd^{2+}(Pic^-)_2$	*		−0.09	0.18	0.07	*	−0.06	*
	NH	CH_{his}	ArH	CH_{his}	$ArOCH_2$	$ArCH_2Ar$	CH_2	NCH_2
δ (ppm) **8**	–	7.56	6.85	6.77	4.48	4.53; 3.23	3.53	2.82
$\Delta\delta$ $\mathbf{8} \cdot Na^+Pic^-$	–	*	−0.44	*	*	0.10; −0.17	*	*
$\Delta\delta$ $\mathbf{8} \cdot Ca^{2+}(Pic^-)_2$	–	−0.32	−0.75	−0.08	−0.08	0.53; −0.33	−0.12	−0.06
$\Delta\delta$ $\mathbf{8} \cdot Sr^{2+}(Pic^-)_2$	–	*	0.49	0.11	0.09	−0.47; 0.23	0.15	0.07
$\Delta\delta$ $\mathbf{8} \cdot Ba^{2+}(Pic^-)_2$	–	*	−0.23	*	*	0.20; −0.11	*	*
$\Delta\delta$ $\mathbf{8} \cdot Zn^{2+}(Pic^-)_2$	–	−0.45	*	−0.24	*	0.06	*	*
$\Delta\delta$ $\mathbf{8} \cdot Pb^{2+}(Pic^-)_2$	–	0.07	*	0.12	0.09	−0.39; 0.18	0.16	0.07
$\Delta\delta$ $\mathbf{8} \cdot Cd^{2+}(Pic^-)_2$	–	−0.11	*	−0.08	*	0.06	*	*

*$\Delta\delta \leq 0.05$

– Does not appear in the NMR spectrum

In a general manner **1–4** were reacted with 4–8 equivs of histamine in 1:1 mixture of methanol:toluene and with reflux from 4 to 6 days. After the removal of the solvents, **6–8** were precipated pure from the crude residues with hexane or diethyl ether while **5** was obtained by chromatography on column of silica with a 9:1 CH_2Cl_2–MeOH as eluent. The yields ranged from 56 to 68%. The cone conformation was maintained during amidation and Table 1 gives selected ^{1}H-NMR chemical shifts δ in ppm for **5–8**.

Study by ^{1}H-NMR of Metal complexation in $CDCl_3$

The suitability of **5–8** as potential ligands able to form metal–ion complexes was demonstrated by the use of ^{1}H-NMR spectroscopy. We have studied the behavior of **5–7** in the presence of various metal picrates. For this purpose $CDCl_3$-solutions of **5–7** (10^{-2} M) were reacted with monovalent metal picrates M^+Pic^- with $M^+ = Li^+$, Na^+, K^+, Rb^+ and Cs^+ and divalent metal picrates $M^{2+}(Pic^-)_2$ with $M^{2+} = Mg^{2+}$, Ca^{2+}, Sr^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+}, Zn^{2+} and Co^{2+}. The ratio of the extracted cation to ligand was estimated by integration of the picrate proton resonances vs. those of the aromatic protons of the calix unit. The results are given in Table 2. For ligand **8**, which is unsoluble in $CDCl_3$, we mixed it with 1 equiv of metal picrates in CD_3OD (10^{-2} M).

Table 2 indicates that 1:1 complexes are observed for **7–8** and sodium with probable inclusion of this cation in the tri- and tetra-amido cavity. Ligands **6–8** complex alkaline-earth metals with the formation of biligand and mononuclear complexes. This can be explained by the need of cavity to entrap these cations. With **6**, biligand complexes are generally formed to satisfy magnesium,

strontium and barium coordination. Derivatives **7** and **8** form 1:1 complexes with zinc cation. The presence of nitrogen atoms of histamine moieties may form a good chelating site, able also to adopt a tetrahedral geometry needed for Zn^{2+} coordination. **6** and **8** form also 1:1 complexes with lead. Biligand complexes are observed with **5** and **6** and cadmium and zinc because the formation of mononuclear species may need more then two imidazolyl moieties.

Table 3 reports the $\Delta\delta$ values as ($\delta_{\text{free ligand}}-\delta_{\text{complex}}$) for 1:1 mononuclear and for 1:2 (metal:ligand) complexes classified according to the complexation of the metal. Only $\Delta\delta$ values >0.05 ppm in absolute value are given. Large $\Delta\delta$ values were assumed to be indicative of the cation location in the receptor.

The study of solid-liquid extraction, followed by ^{1}H-NMR spectroscopy, of alkali and alkaline-earth picrates by ligands **5–8** show that the cations are probably localised in

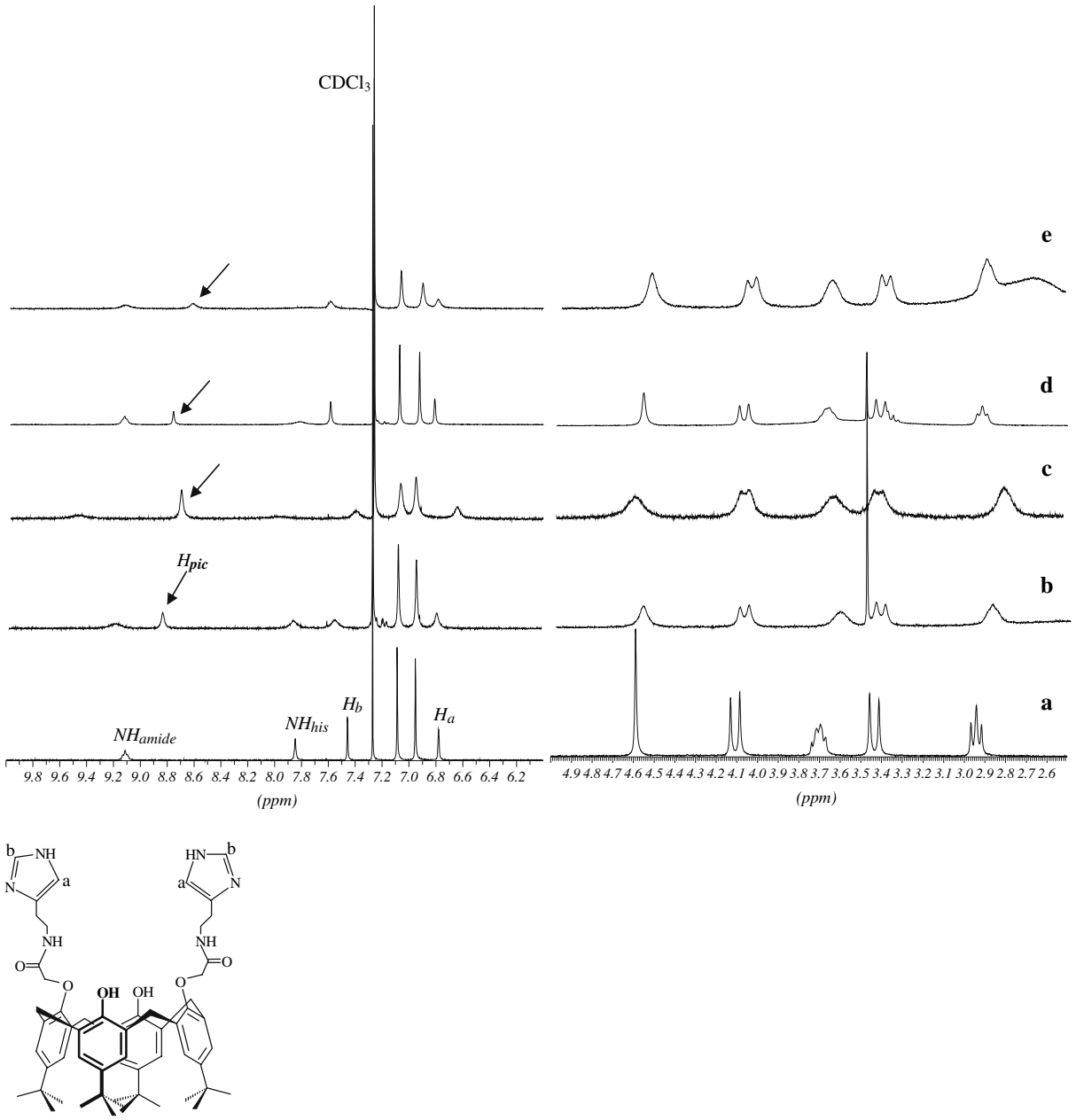
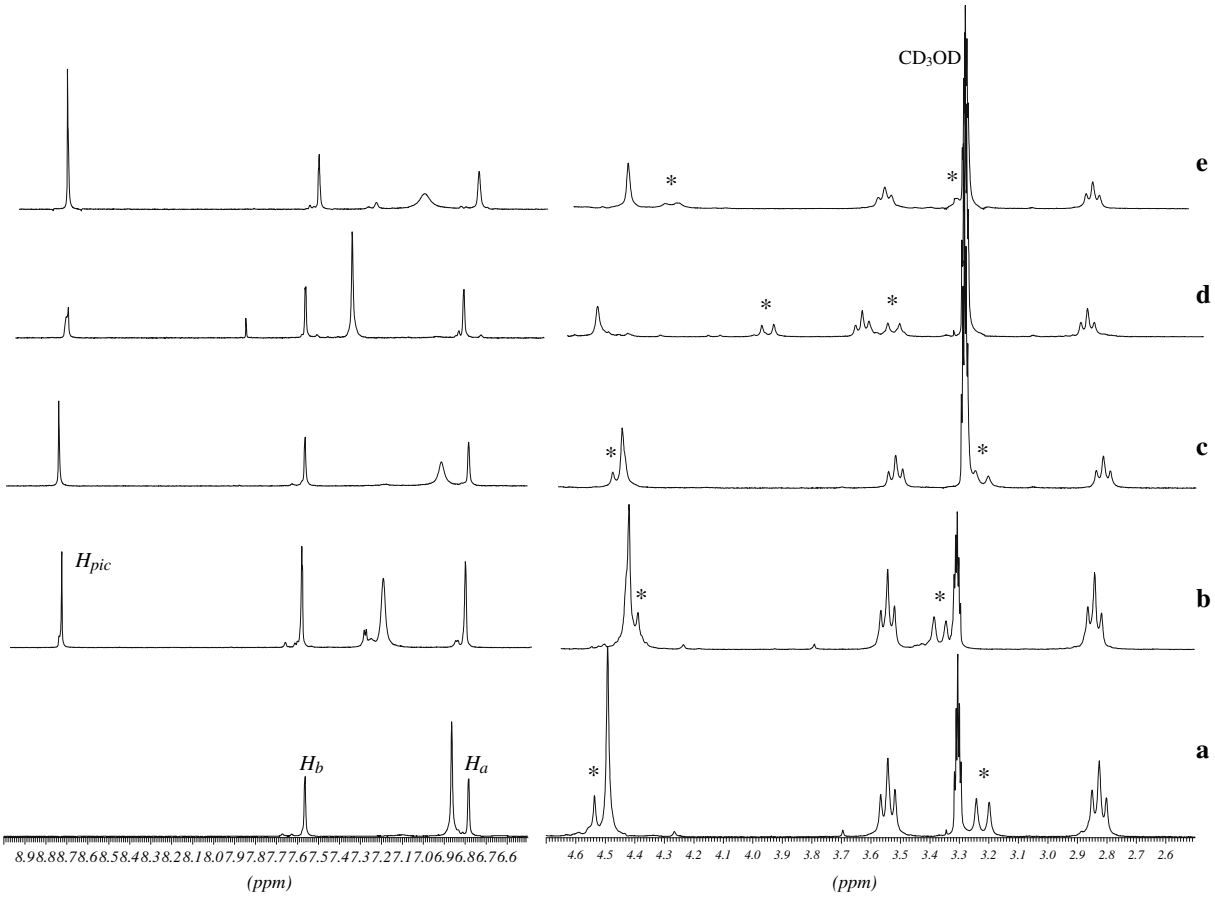


Fig. 1 ^{1}H-NMR spectra ($CDCl_3$) of (**a**) ligand **6**, (**b**) the 1:2 $[Mg \cdot (\mathbf{6})_2]^{2+}(pic^-)_2$ complex, (**c**) the 1:1 $[Ca \cdot (\mathbf{6})]^{2+}(pic^-)_2$ complex, (**d**) the 1:2 $[Sr \cdot (\mathbf{6})_2]^{2+}(pic^-)_2$ complex, (**e**) the 1:2 $[Ba \cdot (\mathbf{6})_2]^{2+}$ $(pic^-)_2$ complex



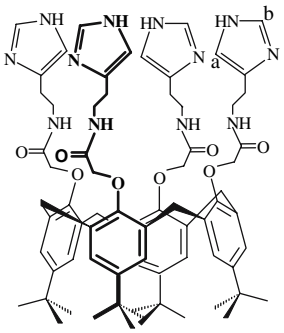


Fig. 2 ^{1}H-NMR spectra (MeOD) of (**a**) ligand **8**, (**b**) the 1:1 [Na · (**8**)]$^{+}$(pic^{-}) complex, (**c**) the 1:1 [Cd · (**8**)]$^{2+}$(pic^{-})$_2$ complex, (**d**) the 1:1 [Pb · (**8**)]$^{2+}$(pic^{-})$_2$ complex, (**e**) the 1:1 [Zn · (**8**)]$^{2+}$ (pic^{-})$_2$ complex

the amido cavity. Indeed, the classification of Pearson [8] (HSAB model: Hard and soft Acids and Bases), proves that hard acids prefer interact with hard bases and soft acids with soft bases and confirms our proposition. In this case, larger $\Delta\delta$ shifts of signals corresponding to the 'histamine' moiety leading to the conclusion that anion (picrate) is located close to the N*H* and C*H* protons forming the soft site. Indeed, several studies show that the presence of N*H* and C*H* supports the complexation of anions [9, 10].

The complexation of transition and heavy metals (soft cations) show that these cations are probably located in the 'histamine' site. In fact, studies published by the team of Olivia Reinaud show that these metals are located in this site which was confirmed by crystalline structure [11–13]. $\Delta\delta$ shifts were observed for the amide and calixarenes moiety leading to the conclusion that anion is probably located in the amido cavity. The presence of N*H* may form a good chelating site for this anion [15] (Figs. 1, 2).

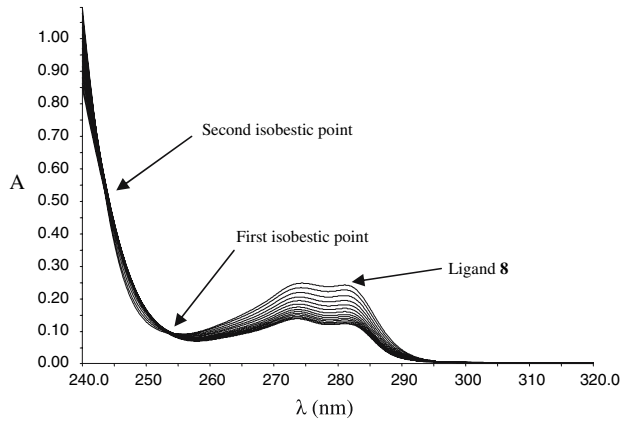


Fig. 3 Changes in the UV-Vis absorption spectrum of ligand **8** upon addition of $SrCl_2$ in methanol; $C_L = 10^{-4}$ M, $0 \leq R_{ML} \leq 1.4$, concentration of $NEt_4Cl = 0.01M$

Study of complexing properties followed by UV-Visible spectrophotometry

We evaluated the stability constants of **5–8** complexes in homogeneous medium limited to methanol because of low solubility of **8** in the usual solvents. The stability constants in methanol were determined by UV absorption spectrophotometry at 20°C. The procedure consisted of adding increasing amounts of metallic perchlorates to a solution of **5–8**. The resulting spectral changes (see Fig. 3) were analysed by Letagrop-Spefo program [14].

The values of the corresponding stability constants, as $\log\beta_{ij}$, are given in Tables 4 and 5 along with the assumed stoichiometries of the complexes.

Table 4 shows the formation of mononuclear species with Na^+, K^+, Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+} and **6–8,** except Na^+ and Mg^{2+}, which form a binuclear complexes with **8** showing up the affinity of this ligand for these two cations. The opportunity to form such species in the case of **8**, is supported by the presence of four arms which are able to shape two independent cavities. Otherwise no complexation was observed for Na^+ and K^+ with ligands **5** and **6** in agreement with the extraction indications.

Selectivities are observed, along the complexation of alkaline-earth cations $S_{Ca^{2+}/Ba^{2+}} = 160$, $S_{Ca^{2+}/Sr^{2+}} = 35$ with ligand **8** and $S_{Sr^{2+}/Mg^{2+}} = 112$ with ligand **6**. The weak affinity of **5–8** for alkali cations, observed previously in the extraction experiment, is generally confirmed by UV spectrophotometry study. The more efficient complexant in the considered series is the tetrasubstituted **8**.

In the case of transition and heavy metals, only 1:1 species have been observed with **5–8** calixarenes. The calculated stability constants suggest a particular affinity of mono-, di-, tri- and tetra-substituted for Cd^{2+} cation. It is evident from Table 5 that the stability of the complexes increases with the number of introduced arms onto the calixarene, except for Zn^{2+} for which the logarithm of stability constants increases from mono- to disubstituted-derivative, and then decreases for the trisubstituted to increase again for tetrasubstituted calixarene. The number of soft and hard binding sites present in those ligands, provided by nitrogen and oxygen atoms, gives the same chance to s- and d-elements to be complexed, since the stability constants are comparable.

Table 4 Logarithm of stability constants corresponding to alkali and alkaline-earth metals complexation with **5–8** in methanol at 20°C, $C_L = 10^{-4}$M, $I = 10^{-2}$M

Cations	Metal:Ligands stoichiometries	**5**	**6**	**7**	**8**
Na^+	1:1	a	a	3.45 ± 0.12	
	2:1				7.74 ± 0.09
K^+	1:1	a	a	3.25 ± 0.06	3.55 ± 0.07
Mg^{2+}	1:1	a	3.78 ± 0.06	4.10 ± 0.01	
	2:1				7.98 ± 0.07
Ca^{2+}	1:1	3.99 ± 0.01	4.20 ± 0.02	4.29 ± 0.12	6.21 ± 0.05
Sr^{2+}	1:1	3.86 ± 0.03	5.83 ± 0.07	4.18 ± 0.09	4.66 ± 0.01
Ba^{2+}	1:1	3.98 ± 0.02	4.15 ± 0.08	4.45 ± 0.07	4.00 ± 0.01

a : No change in the spectrum

Table 5 Logarithm of stability constants corresponding to transition metals complexation with **5–8** in methanol at 20°C, $C_L = 10^{-4}$M, $I = 10^{-2}$M

Ligands	Metal:Ligands stoichiometries	Zn^{2+}	Co^{2+}	Pb^{2+}	Cd^{2+}
5	1:1	4.19 ± 0.04	a	3.43 ± 0.06	4.36 ± 0.01
6	1:1	4.84 ± 0.01	3.79 ± 0.06	3.76 ± 0.05	4.70 ± 0.08
7	1:1	3.95 ± 0.09	4.34 ± 0.01	3.82 ± 0.04	4.83 ± 0.11
8	1:1	4.60 ± 0.01	4.47 ± 0.05	5.12 ± 0.05	5.56 ± 0.07

a: No change in the spectrum

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