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Synthesis and Complexing Properties of Four New Tetraamido-type *p-tert*-Butyl Calix[4]arenes Presenting Two Proximal Binding Subunits

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Abstract

The synthesis of four new tetraamido-type *p-tert*-butyl calix[4]arenes presenting two proximal binding subunits is reported. Complexation of alkali metals and zinc picrates with these ligands have been carried out and monitored by ^{1}H-NMR in $CDCl_3$. It is shown that hard cations are included in the tetraamido cavity while the zinc cation is chelated to the pyridine rings of one of the ligands. The formation of a 1:1:1 heterobinuclear complex is also described

Introduction

Much attention has recently been paid to chemical separation techniques and to the design and synthesis of new extraction reagents for metal ions. This attention results in part from environmental concerns, efforts to save energy, and recycling waste metals at the industrial level [1]. Progress in the development of new extractants has resulted from advances in the field of supramolecular chemistry which has provided a variety of new reagents with desired selectivities for chosen cations [1]. In this respect, 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 [2]. Introduction of chosen functionalities on the phenolic OH of *p-tert*-butyl calix[4]arene produces derivatives with different shapes and subsequent selectivities [2]. The family of amide derivatives of calix[4]arenes and their complexes with alkali metal, transition metal, and lanthanide ions have been extensively investigated [3, 4].

In a recent paper we have reported the synthesis and complexing properties of tetra(2- pyridylmethyl)amide *p-tert*-butyl calix[4]arene **2** [5]. Comparison of its complexing properties with related ligand **1** showed that **2** is a *ditopic* receptor [5]. It was shown that the four amido functions delineate a cavity consisting of four carbonyl units and four phenolic oxygens able to complex alkali and alkaline-earth metal cations while the four pyridine moieties are able to complex soft cations such as zinc [5]. At the same time we also observed that although there are two sites of complexation the formation of a 1:1 complex prevents a second cation from entering the ligand [5].

In order to gain more information on this *negative cooperativity* we decided to synthesize related tetraamido-type *p-tert*-butyl calix[4]arenas **3–6** and to investigate their metal-complexing behaviour by the technique of ^{1}H-NMR spectroscopy.

Experimental section

General

The melting points (mps) were taken on a Büchi apparatus in capillaries sealed under nitrogen. ^{1}H-NMR spectra were recorded at 200 MHz in $CDCl_3$ on a Bruker SY200 spectrometer. Chemical shifts δ are given in ppm from $CHCl_3$ at 7.27 ppm. Coupling constants J are given in Hz. FAB(+)MS were obtained on a VG-Analytical ZAB HF. Elemental analyses were performed at the Service de Microanalyse of the Institut de Chimie de Strasbourg.

2-thiophenemethylamine, tetrahydrofurylamine, furfurylamine and 2-(2-aminoethyl)-pyridine and the solvents were commercial reagents and were used without further purification. O-Tetramethylester-*p-tert*-butyl calix[4]arene **7** was prepared according to the literature [6].

Preparation of **3–6**

*Preparation of 5,11,17,23-tetra(*tert*-butyl)-25,26,27,28-tetra(2-ethylpyridine acetamide) calix[4]arene (**3**)*

A mixture of tetramethyl ester calix[4]arene **7** (1.876 g, 2.0 mmol) and 2-(2-aminoethyl)-pyridine (1.038 g, 8.5 mmol), in a 1 : 1 mixture of methanol: : toluene was refluxed for 5 days. Precipitation with acetone gave pure **3** (1.309 g, 51%) as a white solid (mp 224–226 °C).

^{1}H-NMR ($CDCl_3$), 8.37 (t, 4H, J = 6.0 Hz, N-H), 8.31 (d, 4H, J = 5.0 Hz, pyridine-H_6), 7.53 (t, 4H, J = 5.0 Hz, pyridine-H_3), 7.13 (d, 4H, J = 6.0 Hz, pyridine-H_3), 7.04 (t, 4H, J = 6.0 Hz, pyridine-H_4, 6.75 (s, 8H, Ar—H), 4.49 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 4.45 (s , 8H, Ar—O—CH_2), 3.74 (q, 8H, J = 6.5 Hz, CH_2—N), 3.15 (d, 4H, J = 13.0 Hz, AB system Ar-CH_2—Ar), 3.01 (t, 8H, J = 7.0 Hz, CH_2—Py) and 1.07 (s, 36H, t-C_4H_9). MS-FAB positive *m/z* = 1297.50 (calculated 1296.73). Anal. calcd. for $C_{80}H_{96}N_8O_8$, $0.5CH_2Cl_2$: C, 72.15; H, 7.30. Found: C, 72.47; H, 7.63.

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

Using the same procedure as for **3**: calix[4]arene **7** (1.876 g, 2.0 mmol) and 2-thiophenemethylamine (1.358 g, 12.0 mmol) in a 1 : 1 mixture of methanol : toluene was refluxed for 7 days under nitrogen. The solvents were removed by evaporation under reduced pressure. The residue was precipitated with methanol to give pure **4** (1.133 g, 45%) as a white solid (mp = 280–282 °C).

^{1}H-NMR ($CDCl_3$): 7.86 (t, 4H, J = 6.0 Hz, NH), 7.14 (2d, 4H, J = 1.5 Hz; J = 5.0 Hz, thiophene-H_5), 6.86 (m, 8H, thiophene-$H_{3,4}$), 6.75 (s, 8H, ArH), 4.69 (d, 8H, J = 6.0 Hz, CH_2-thiophene), 4.40 (d, 4H, J = 13.0 Hz, AB system, Ar—CH_2—Ar), 4.39 (s, 8H, Ar—O—CH_2), 3.17 (d, 4H, J = 13.0 Hz, AB system, Ar—CH_2—Ar) and 1.06 (s, 36H, t-C_4H_9). MS-FAB positive *m/z* = 1261.30 (calculated 1260.51). Anal. calcd. for $C_{72}H_{84}N_4O_8S_4$: C, 68.54; H, 6.71. Found: C, 68.70; H, 6.59.

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

Using the same procedure as for **3**: calixarene **7** (2.814 g, 3.0 mmol) and 1-(2-tetrahydrofuryl)methylamine (5.057 g, 50.0 mmol), in a 1 : 1 mixture of methanol : toluene was refluxed for 2 days. Precipitation with methanol gave pure **5** (2.100 g; 58%) as a white solid (mp = 260–262 °C).

^{1}H-NMR ($CDCl_3$): 7.75 (broad s, 4H, NH), 6.76 (s, 8H, ArH), 4.71–4.40 (m, 12H, ArCH_2Ar and O—CH_2), 4.20–3.15 (m, 24H, ArCH_2Ar, furfuryl-CH_2 and furfuryl-$H_{2,5}$), 2.10–1.40 (m, 16H, furfuryl-$H_{3,4}$) and 1.07 (s, 36H, t-C_4H_9). MS-FAB positive *m/z* = 1213.90 (calculated 1212.73). Anal. calcd. For $C_{72}H_{100}N_4O_{12}$: C, 71.26; H, 8.31; N, 4.62. Found: C, 71.12; H, 8.55; N, 4.42.

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

Using the same procedure as for **3**: calixarene **7** (1.876 g, 2.0 mmol) and 2-furfurylmethyl amine (1.456 g, 15.0 mmol), in a 1 : 1 mixture of methanol : toluene was refluxed for 15 days. Precipitation with methanol gave pure **6** (1.244 g, 52%) as a white solid (mp 258–260 °C).

^{1}H-NMR ($CDCl_3$): 7.80 (t, 4H, J = 5.0 Hz, N-H), 7.27 (d, 4H, J = 2.0 Hz, furfuryl-H_5), 6.75 (s, 8H, Ar—H), 6.27 (t, 4H, J = 2.0 Hz, furfuryl-H_4), 6.19 (d, 4H, J = 2.0 Hz, furfuryl-H_3), 4.55 (d, 8H, J = 5.0 Hz, N—CH_2-furfuryl), 4.43 (s, 8H, Ar—O—CH_2), 4.40 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.17 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar) and 1.06 (s, 36H, t-C_4H_9). MS-FAB positive *m/z* = 1197.60 (calculated 1196.60). Anal. calcd. for $C_{72}H_{84}O_{12}N_4$; $0.5CH_2Cl_2$: C, 70.23; H, 6.91. Found: C, 70.25; H, 6.88.

^{1}H-NMR study of the complexation of metal picrates by **3–6**

$CDCl_3$-solutions of **3–6** (10^{-2} M) were prepared with different solid metal picrates : M^+Pic^- with $M^+ = Li^+$, Na^+, K^+, Rb^+ and Cs^+ and $Zn^{2+}(Pic^-)_2$. The ratio of the extracted cation to ligand in solution was estimated by calculating the integration ratio of the picrate proton resonances *vs* those of the aromatic protons of the calix unit.

Mononuclear complexes

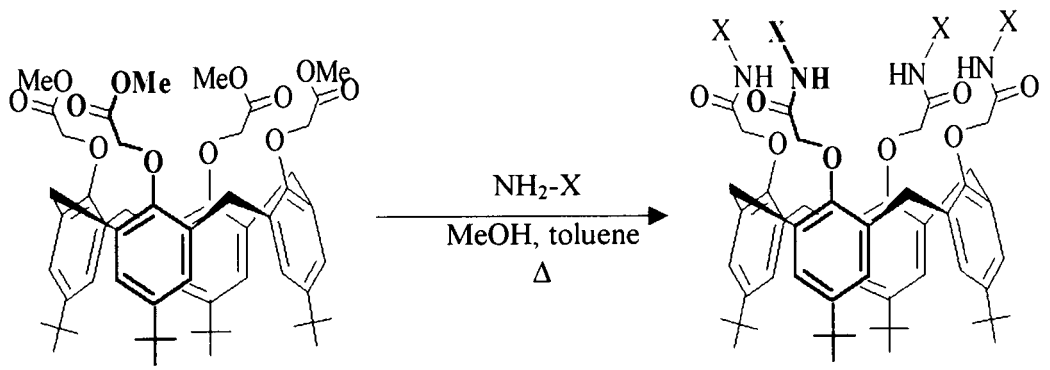
2.Li$^+$Pic$^-$: 8.82 (s, 2H, Picrate) 8.52 (t, 4H, J = 5.5 Hz, NH), 8.38 (d, 4H, J = 4.0 Hz, PyH_6), 7.59 (t, 4H, J = 7.5 Hz, PyH_5), 7.21 (d, 4H, J = 7.5 Hz, PyH_3), 7.11 (t, 4H, J = 6.5 Hz, PyH_4), 6.81 (s, 8H, Ar$H_{\text{metacalix}}$), 4.69 (s, 8H, —CH_2OAr), 4.50 (AB system, 4H, J = 14.0 Hz, ArCH_2Ar), 4.60 (d, 8H, J = 5.5 Hz, —CH_2Py), 3.21 (AB system, 4H, J = 14.0 Hz, ArCH_2Ar), 1.07 (s, 36H, t-C_4H_9).

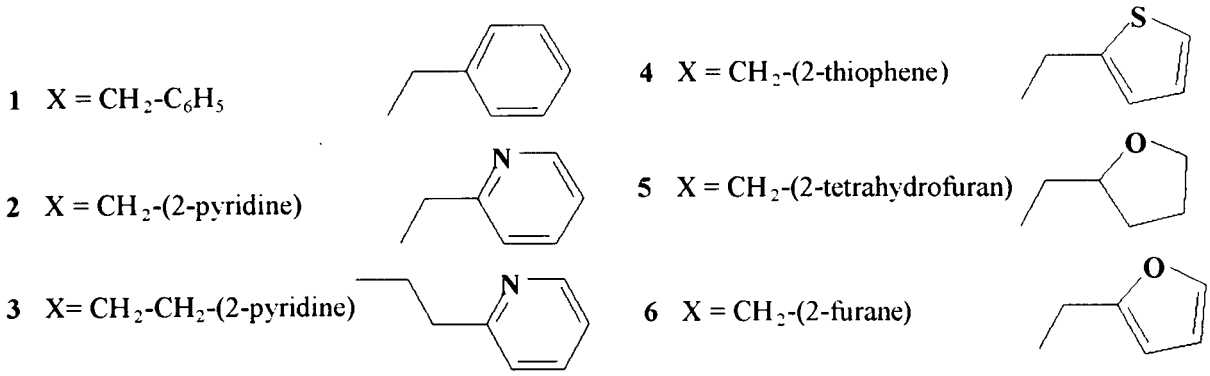
2.Na$^+$Pic$^-$: 8.69 (s, 2H, Pic$^-$), 8.38 (d, 4H, J = 5.0 Hz, PyH_6), 8.32 (t, 4H, J = 5.5 Hz, NH), 7.56 (t, 4H, J = 7.5 Hz, PyH_5), 7.21 (d, 4H, J = 7.5 Hz, PyH_3), 7.12–7.07 (m, 4H, PyH_4), 6.94 (broadening s, 8H, Ar$H_{\text{metacalix}}$), 4.63 (s, 8H, —CH_2OAr), 4.49 (AB system, 4H, J = 13.0 Hz, ArCH_2Ar), 4.57 (d, 8H, J = 5.5 Hz, —CH_2Py), 3.27 (AB system, 4H, J = 13.0 Hz, ArCH_2Ar), 1.09 (s, 36H, t-C_4H_9) [5].

2.Zn^{2+}(Pic$^-$)$_2$: 9.18 (broad s, 4H, NH), 8.76 (s, 4H, Pic$^-$), 8.48 (d, 4H, J = 4.0 Hz, PyH_6), 7.73 (t, 4H, J = 7.5 Hz, PyH_5), 7.37 (d, 4H, J = 9.0 Hz, PyH_3), 7.20 (t, 4H, J = 5.5 Hz, PyH_4), 6.67 (broadening s, 8H, Ar$H_{\text{metacalix}}$), 4.65 (broad s, 16H, —CH_2OAr and CH_2Py), 4.36 (AB system, 4H, J = 11.5 Hz, ArCH_2Ar), 3.00 (broad s, 4H, ArCH_2Ar), 1.02 (s, 36H, t-C_4H_9) [5].

3.Li$^+$Pic$^-$: 8.83 (s, 2H, picrate) 8.35 (d, 4H, J = 5.0 Hz, pyridine-H_6), 8.22 (t, 4H, J = 6.0 Hz, N—H), 7.55 (t, 4H, J = 5.0 Hz, pyridine-H_5), 7.15 (d, 4H, J = 6.0 Hz, pyridine-H_3), 7.08 (t, 4H, J = 6.0 Hz, pyridine-H_4), 6.80 (s, 8H, Ar—H), 4.54 (s , 8H, Ar—O—C), 4.44 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.74 (q, 8H, J = 6.5 Hz, CH_2—N), 3.17 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.02 (t, 8H, J = 7.0 Hz, CH_2—Py) and 1.07 (s, 36H, t-C_4H_9).

3.Na$^+$Pic$^-$: 8.74 (s, 2H, picrate) 8.36 (d, 4H, J = 5.0 Hz, pyridine-H_6), 8.11 (t, 4H, J = 6.0 Hz, N—H), 7.54 (t, 4H, J = 5.0 Hz, pyridine-H_5), 7.14(d, 4H, J = 6.0 Hz, pyridine-H_3), 7.07 (t, 4H, J = 6.0 Hz, pyridine-H_4), 6.91 (s, 8H, Ar—H), 4.47 (s, 8H, Ar—O—CH_2), 4.39 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.76 (q, 8H, J = 6.5 Hz, CH_2—Py), 3.22 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.02 (t, 8H, J = 7.0 Hz, CH_2—N) and 1.09 (s, 36H, t-C_4H_9).





Scheme 1. Synthesis of **3–6**.

3.Zn^{2+}(Pic^{-})$_2$: 8.81 (s, 4H, picrate) 8.53 (d, 4H, J = 5.0 Hz, pyridine-H_6), 8.34 (broad s, 4H, N—H), 7.75 (t, 4H, J = 5.0 Hz, pyridine-H_5), 7.35 (d, 4H, J = 6.0 Hz, pyridine-H_3), 7.24 (t, 4H, J = 6.0 Hz, pyridine-H_4), 6.81 (s, 8H, Ar—H), 4.58 (s , 8H, Ar—O—CH_2), 4.38 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.78 (broad s, 8H, CH_2—Py), 3.24 (broad s, 12H, Ar—CH_2—Ar and CH_2—N) and 1.09 (s, 36H, t-C$_4$H$_9$).

4.$Li^{+}$$Pic^{-}$: 8.95 (s, 2H, picrate) 7.94 (broad s, 4H, NH), 7.12 (2d, 4H, J = 1.5 Hz; J = 5.0 Hz, thiophene-H_5), 6.86 (m, 8H, thiophene-$H_{3,4}$), 6.80 (s, 8H, ArH), 4.64 (d, 8H, J = 6.0Hz, CH$_2$-thiophene), 4.47 (s, 8H, Ar—O—CH_2), 4.44 (d, 4H, J = 13.0 Hz, AB system, Ar—CH_2—Ar), 3.18 (d, 4H, J = 13.0 Hz, AB system, Ar—CH_2—Ar) and 1.06 (s, 36H, t-C$_4$$H_9$).

4.$Na^{+}$$Pic^{-}$: 8.78 (s, 2H, picrate) 7.85 (t, 4H, J = 6.0 Hz, NH), 7.14 (2d, 4H, J = 1.5 Hz; J = 5.0 Hz, thiophene-H_5), 6.88 (m, 8H, thiophene-$H_{3,4}$), 6.77 (s, 8H, ArH), 4.67 (d, 8H, J = 6.0 Hz, CH$_2$-thiophene), 4.42 (s, 8H, Ar—O—CH_2), 4.38 (d, 4H, J = 13.0 Hz, AB system, Ar—CH_2—Ar), 3.09 (d, 4H, J = 13.0 Hz, AB system, Ar—CH_2—Ar) and 1.07 (s, 36H, t-C$_4$$H_9$).

5.$Li^{+}$$Pic^{-}$: 8.87 (s, 2H, picrate), 7.92–7.54 (m, 4H, NH), 6.81 (s, 8H, ArH), 4.78–4.40 (m, 12H, ArCH_2Ar and O—CH_2), 4.10–3.18 (m, 24H, ArCH_2Ar, tetrahydrofurfuryl-CH_2 and tetrahydrofurfuryl-$H_{2,5}$), 2.08–1.40 (m, 16H, tetrahydrofurfuryl-$H_{3,4}$) and 1.07 (s, 36H, t-C$_4$$H_9$).

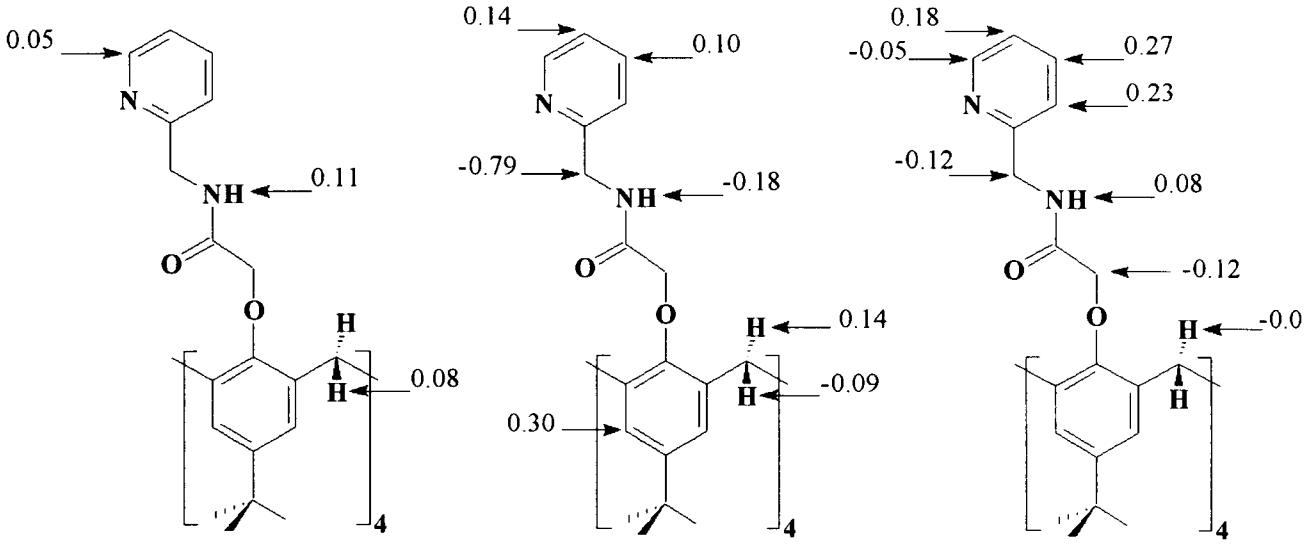
5.$Na^{+}$$Pic^{-}$: 8.83 (s, 2H, picrate), 7.75–7.45 (m, 4H, NH), 6.90 (s, 8H, ArH), 4.67–4.40 (m, 12H, ArCH_2Ar and O—CH_2), 4.03–3.27 (m, 24H, ArCH_2Ar, tetrahydrofurfuryl-CH_2 and tetrahydrofurfuryl-$H_{2,5}$), 2.01–1.49 (m, 16H, tetrahydrofurfuryl-$H_{3,4}$) and 1.08 (s, 36H, t-C$_4$$H_9$).

6.$Li^{+}$$Pic^{-}$: 8.84 (s, 2H, picrate), 7.74 (t, 4H, J = 5.0 Hz, N—H), 7.26 (d, 4H, J = 2.0 Hz, furfuryl-H_5), 6.79 (s, 8H, Ar—H), 6.26 (t, 4H, J = 2.0 Hz, furfuryl-H_4), 6.19 (d, 4H, J = 2.0 Hz, furfuryl-H_3), 4.52 (d, 8H, J = 5.0 Hz, N—CH_2-furfuryl), 4.48 (s, 8H, Ar—O—CH_2), 4.44 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.19 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar) and 1.07 (s, 36H, t-C$_4$H$_9$).

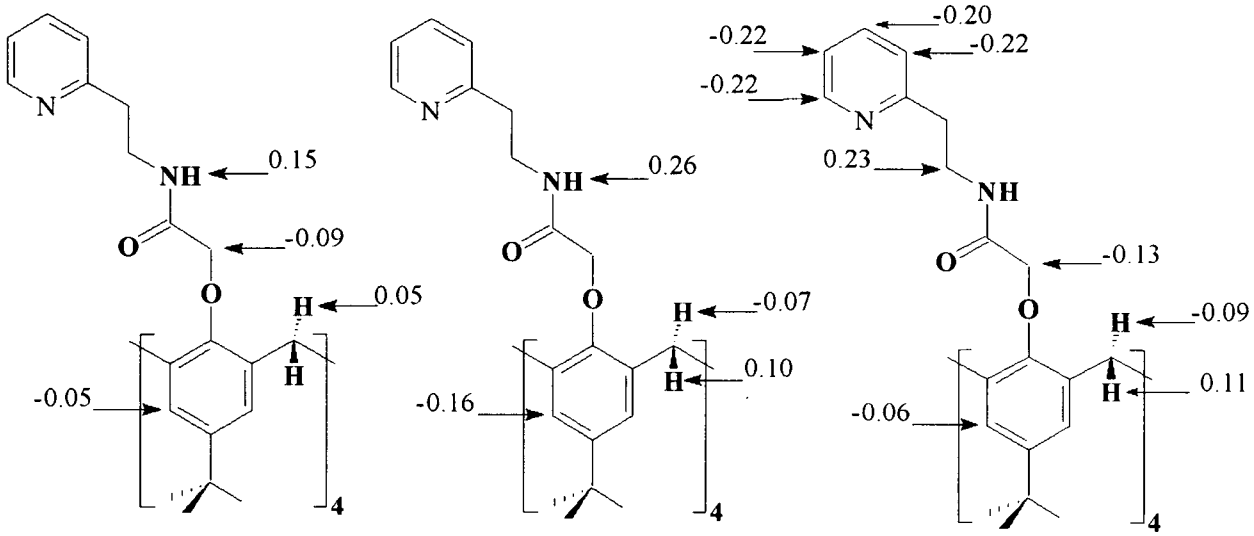
6.$Na^{+}$$Pic^{-}$: 8.70 (s, 2H, picrate), 7.77 (t, 4H, J = 5.0 Hz, N—H), 7.26 (d, 4H, J = 2.0 Hz, furfuryl-H_5), 6.79 (s, 8H, Ar—H), 6.26 (t, 4H, J = 2.0 Hz, furfuryl-H_4), 6.21 (d, 4H, J = 2.0 Hz, furfuryl-H_3), 4.54 (d, 8H, J = 5.0 Hz, N—CH_2-furfuryl), 4.45 (s, 8H, Ar—O—CH_2), 4.38 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.19 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar) and 1.07 (s, 36H, t-C$_4$H$_9$).

Homobinuclear complexes

2.(Li^{+})$_2$(Pic^{-})$_2$: 8.88 (s, 4H, Picrate) 8.61 (t, 4H, J = 5.5 Hz, NH), 8.39 (d, 4H, J = 4.0 Hz, PyH_6), 7.62 (t, 4H, J = 7.5 Hz, PyH_5), 7.26 (d, 4H, J = 7.5 Hz, PyH_3), 7.08 (t, 4H,



2.Li$^+$Pic$^-$ **2.Na$^+$Pic$^-$** **2.Zn^{2+}(Pic$^-$)$_2$**



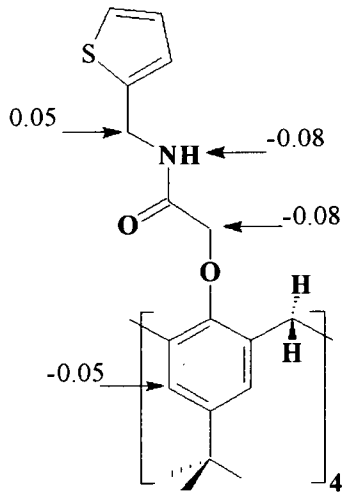
3.Li$^+$Pic$^-$ **3.Na$^+$Pic$^-$** **3.Zn^{2+}(Pic)$_2^-$**

Chart 1. $\Delta\delta$ values for the complexes of **2–6** with different metal picrates.

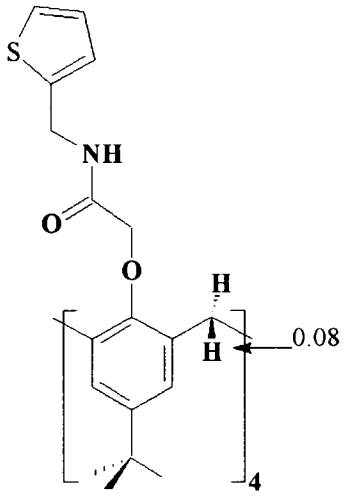
J = 6.5 Hz, PyH_4), 6.79 (s, 8H, Ar$H_{\text{metacalix}}$), 4.78 (s, 8H, —CH_2OAr), 4.41 (AB system, 4H, J = 14.0 Hz, ArCH_2Ar), 4.64 (d, 8H, J = 5.5 Hz, —CH_5Py), 3.23 (AB system, 4H, J = 14.0 Hz, ArCH_2Ar), 1.08 (s, 36H, t-C$_4$H$_9$).

3.(Li$^+$)$_2$(Pic$^-$)$_2$: 8.87 (s, 4H, picrate) 8.36 (d, 4H, J = 5.0 Hz, pyridine-H_5), 8.19 (t, 4H, J = 6.0 Hz, N—H), 7.56 (t, 4H, J = 5.0 Hz, pyridine-H_5), 7.14 (d, 4H, J = 6.0 Hz, pyridine-H_3), 7.07 (t, 4H, J = 6.0 Hz, pyridine-H_4), 6.81 (s, 8H, Ar—H), 4.57 (s , 8H, Ar–O–CH_2), 4.41 (d, 4H, J = 13.0 Hz, AB system Ar—C$H2$—Ar), 3.72 (q, 8H, J = 6.5 Hz, CH_2—N), 3.22 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.02 (t, 8H, J = 7.0 Hz, CH_2—Py) and 1.07 (s, 36H, t-C$_4$H$_9$).

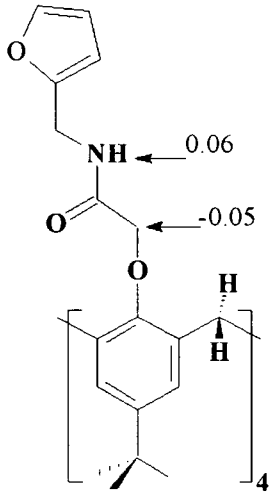
4.(Li$^+$)$_2$(Pic$^-$)$_2$: 8.85 (s, 4H, picrate) 7.71 (t, 4H, J = 6.0 Hz, NH), 7.12 (2d, 4H, J = 1.5 Hz; J = 5.0 Hz, thiophene-H_4), 6.87 (m, 8H, thiophene-$H_{3,4}$), 6.84 (s, 8H, ArH), 4.63 (d, 8H, J = 6.0 Hz, CH_2-thiophene), 4.52 (s, 8H, Ar—O—CH_2), 4.42 (d, 4H, J = 13.0 Hz, AB system, Ar—CH_2—



4.Li$^+$Pic$^-$

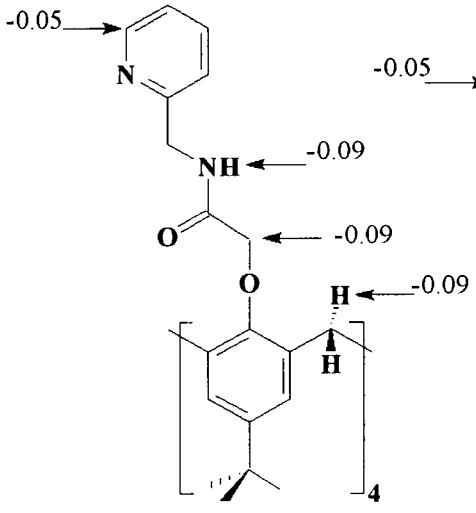


4.Na$^+$Pic$^-$

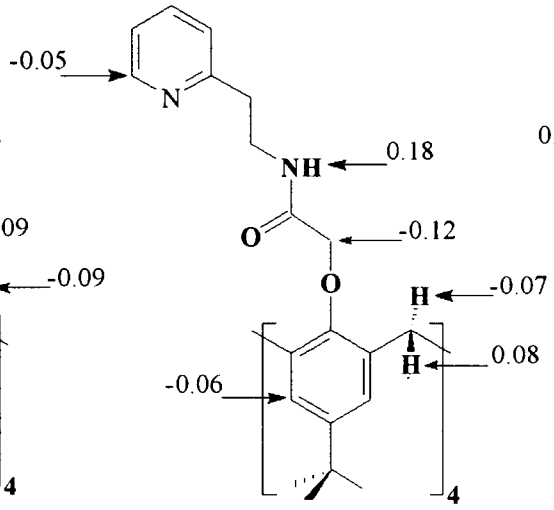


6.Na$^+$Pic$^-$

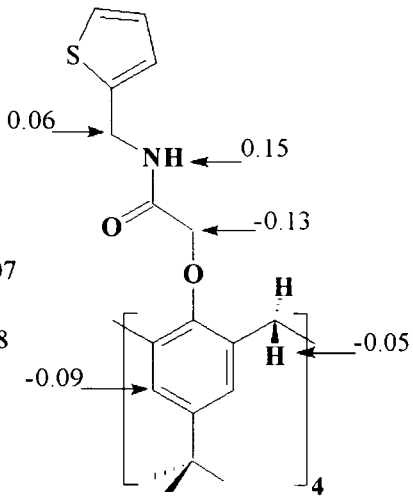
Homobinuclear complexes



2.(Li$^+$)$_2$(Pic$^-$)$_2$



3.(Li$^+$)$_2$(Pic$^-$)$_2$



4.(Li$^+$)$_2$(Pic$^-$)$_2$

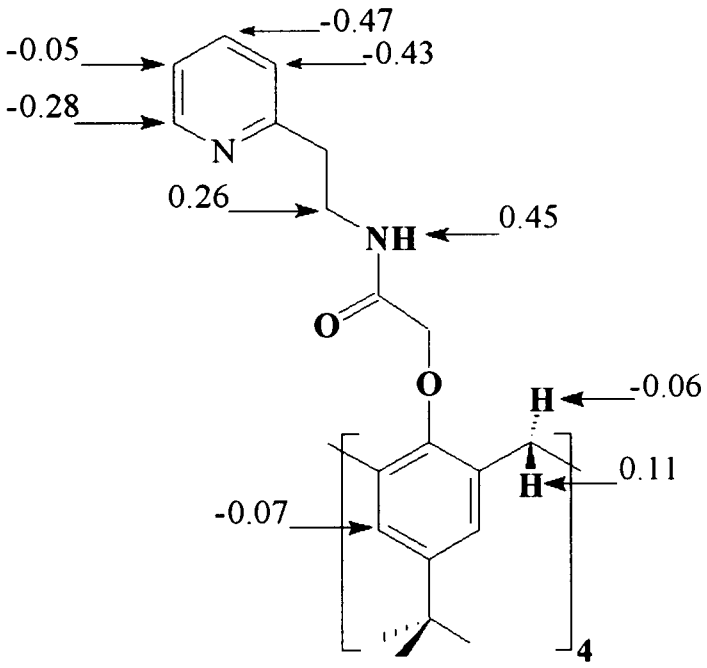
Chart 1. Continued.

Ar), 3.22 (d, 4H, J = 13.0 Hz, AB system, Ar—CH_2—Ar) and 1.08 (s, 36H, t-C$_4H_9$).

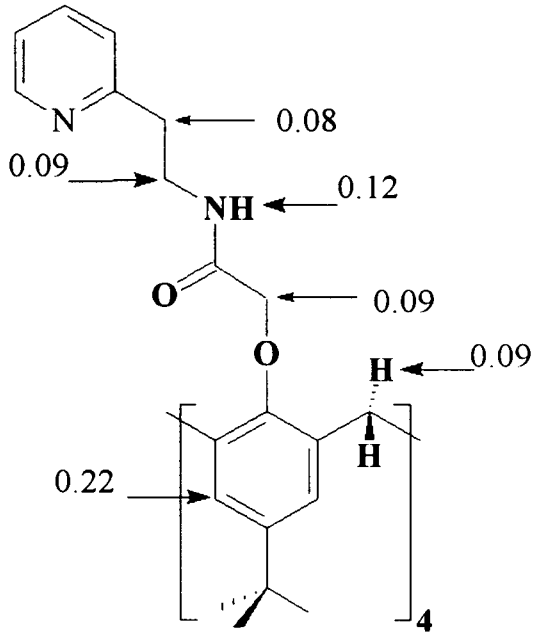
5.(Li$^+$)$_2$(Pic$^-$)$_2$: 8.99 (s, 4H, picrate), 7.90–7.54 (m, 4H, NH), 6.81 (s, 8H, ArH), 4.64–4.49 (m, 12H, ArCH_2Ar and O—CH_2), 4.05–3.22 (m, 24H, ArCH_2Ar, tetrahydrofurfuryl-CH_2 and tetrahydrofurfuryl-$H_{2,5}$), 1.98–1.50 (m, 16H, tetrahydrofurfuryl-$H_{3,4}$) and 1.07 (s, 36H, t-C$_4H_9$.

5.(Na$^+$)$_2$(Pic$^-$)$_2$: 8.83 (s, 4H, picrate), 7.54–7.40 (m, 4H, NH), 6.92 (s, 8H, ArH), 4.65–4.45 (m, 12H, ArCH_2Ar and O—CH_2), 4.07–3.65 (m, 24H, ArCH_2Ar, tetrahydrofurfuryl-CH_2 and tetrahydrofurfuryl-$H_{2,5}$), 1.98–1.50 (m, 16H, tetrahydrofurfuryl-$H_{3,4}$) and 1.09 (s, 36H, t-C$_4H_9$).

6.(Li$^+$)$_2$(Pic$^-$)$_2$: 9.13 (s, 4H, picrate), 7.79 (t, 4H, J = 5.0 Hz, N—H), 7.26 (d, 4H, J = 2.0 Hz, furfuryl-H_5), 6.79 (s, 8H, Ar—H), 6.26 (t, 4H, J = 2.0 Hz, furfuryl-H_4), 6.18 (d, 4H, J = 2.0 Hz, furfuryl-H_3), 4.53 (d, 8H, J = 5.0 Hz, N—



3.Na^{+}.Zn^{2+}(Pic^{-})$_3$



3.Zn^{2+}.Na^{+}(Pic^{-})$_3$

Chart 1. Continued.

C*H*2-furfuryl), 4.47 (s, 8H, Ar—O—CH_2), 4.44 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar), 3.20 (d, 4H, J = 13.0 Hz, AB system Ar—CH_2—Ar) and 1.07 (s, 36H, t-C$_4$H$_9$).

Heterobinuclear complexes

3.Na^{+}.Zn^{2+}.(Pic^{-})$_3$: 8.69 (s, 6H, picrate) 8.59 (d, 4H, J = 5.0 Hz, pyridine-H_6), 7.92 (t, 4H, J = 6.0 Hz, N—H), 7.60–7.40 (m, 12H, pyridine-H_5, pyridine-H_4, pyridine-H_4), 6.98 (broad s, 8H, Ar—H), 4.48 (broad s, 8H, Ar—O—CH_2), 4.28 (broad s, 4H, Ar—CH_2—Ar), 3.76 (broad s, 8H, CH_2—Py), 3.28 (broad s, 12H, Ar—CH_2—Ar, CH_2—N), and 1.07 (s, 36H, t-C$_4$H$_9$).

3.Zn^{+}.Na^{2+}.(Pic^{-})$_3$: 8.79 (s, 6H, picrate) 8.47 (d, 4H, J = 5.0 Hz, pyridine-H_6), 8.22 (t, 4H, J = 6.0 Hz, N—H), 7.72 (t, 4H, J = 5.0 Hz, pyridine-H_5), 7.33(d, 4H, J = 6.0 Hz, pyridine-H_3), 7.24 (t, 4H, J = 6.0 Hz, pyridine-H_4), 6.79 (s, 8H, Ar—H), 4.49 (s , 8H, Ar—O—CH_2), 4.37 (broad s, 4H, Ar—CH_2—Ar), 3.70 (m, 8H, CH_2—Py), 3.15 (broad s, 12H, Ar—CH_2—Ar, CH_2—N) and 1.08 (s, 36H, t-C$_4$H$_9$).

Results and discussion

Preparation of **3–6**

The synthesis of **3–6** was conducted as shown in Scheme 1.

In a general manner tetramethyl ester calixarene **7** was reacted with 4 to 16 equivs of the appropriate methyl amine derivative in a 1 : 1 mixture of methanol : toluene and with reflux from 2 to 15 days. After the removal of the solvents under reduced pressure, the crude residues were precipitated with methanol or acetone to give pure products **3–6** as white solids. The melting points were higher than 220 °C. The yields ranged from 45 to 60%. Table 1 gives selected ^{1}H-NMR chemical shifts δ in ppm for **3–6** and shows that the calix[4]arene is fully substituted due to the presence of singlets for the aromatic protons and the *tert*-butyl groups. Characteristic AB systems were observed for the methylene protons ArCH_2Ar in the macroring leading us to conclude that **3–6** are in the cone conformation. The ^{1}H-NMR spectrum of **5** was complicated due to the asymmetric center at the 2-position of the tetrahydrofuran residue.

Table 1. Selected ^{1}H-NMR chemical shifts in ppm from TMS for **3–6**. Coupling constants are given in Hz in brackets.

	N*H*	Ar*H*	NCH_2Y	ArCH_2Y	t-C$_4H_9$
3	8.37	6.75	3.74	4.49 and 3.15	1.07
	(6.0)		(6.5)	(13.0)	
4	7.86	6.75	4.69	4.40 and 3.17	1.06
	(6.0)		(6.0)	(13.0)	
5	7.75	6.76	4.20–3.15	4.71–4.40	1.07
6	7.80	6.75	4.40 and 3.17	1.06	
	(5.0)		(5.0)	(13.0)	

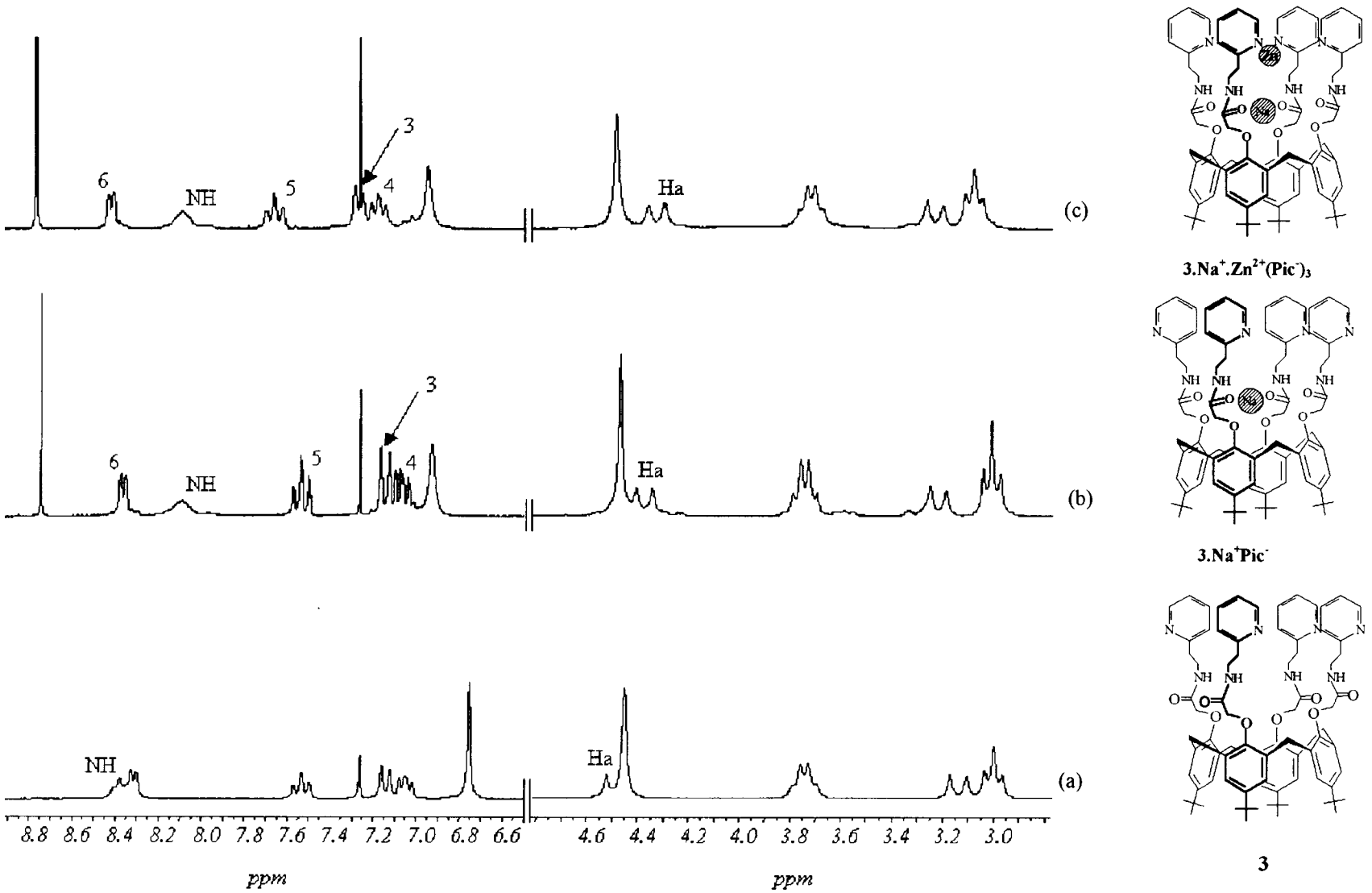


Figure 1. ^{1}H-NMR spectra of (a) ligand **3**, (b) the 1 : 1 **3**.Na^+**Pic**$^-$ complex, (c) the 1 : 1 : 1 **3**.Na^+.Zn^{2+}**Pic**$^-)_3$ complex.

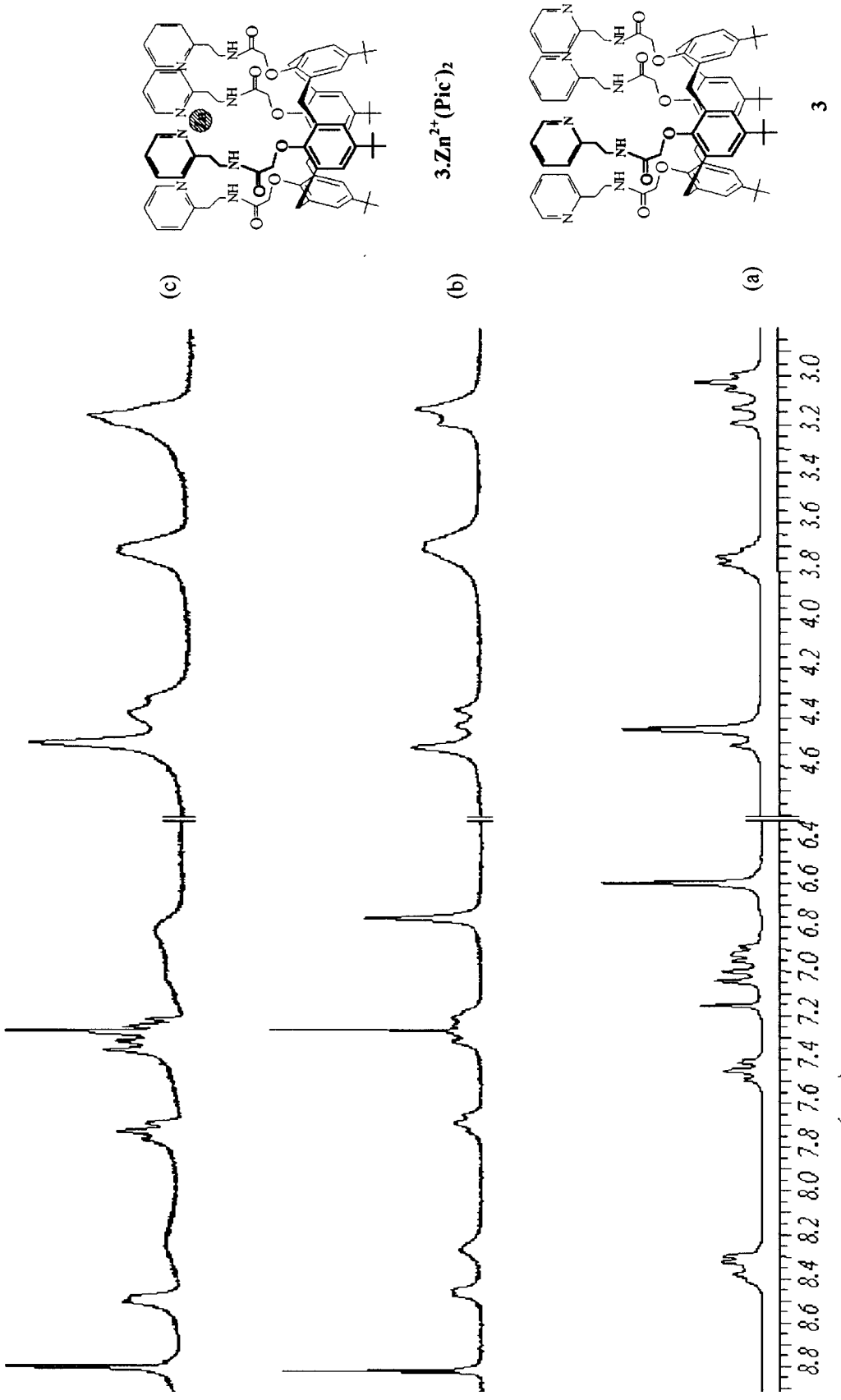


Figure 2. ^{1}H-NMR spectra of (a) ligand **3**, (b) the 1 : 1 **3**.$Zn^{2+}(Pic^-)_2$ complex, (c) unknown.

Table 2. Stoichiometries of complexes of **1–6** with metal picrates as detected by ^{1}H-NMR.

	Li	Na	K	Rb	Cs	Zn
1 [5]	1 : 1	1 : 1	[a]	[a]	[a]	[a]
2 [5]	1 : 1	1 : 1	[a]	[a]	[a]	1 : 1
	1 : 2					
3	1 : 1	1 : 1	[a]	[a]	[a]	1 : 1
	1 : 2					
4	1 : 1	1 : 1	[a]	[a]	[a]	[a]
	1 : 2					
5	1 : 1	1 : 1	[a]	[a]	[a]	[a]
	1 : 2	1 : 2				
6	1 : 1	1 : 1	[a]	[a]	[a]	[a]
	1 : 2					

[a] No evidence of complexation.

Metal ion complexation

The suitability of **3–6** as potential ligands able to form mononuclear and homo- and/or heterobinuclear complexes was demonstrated by the use of ^{1}H-NMR spectroscopy. We have studied their reactions with hard cations (alkali metals) and one soft cation (zinc). For this purpose $CDCl_3$-solutions of **3–6** (10^{-2} M) were reacted with the different solid metal picrates, M^+Pic^- with $M^+ = Li^+$, Na^+, K^+, Rb^+ and Cs^+ and $Zn^{2+}(Pic^-)_2$. The ratio of the extracted cation to ligand in solution 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 along with previous results [5] on **1** and **2**.

Table 2 indicates that **2–6** form 1 : 1 and 1 : 2 complexes with lithium while **1** only forms 1 : 1 complexes. This can be explained by the absence of additional hetero atoms in receptor **1**. 1 : 1 Complexes are observed for **1–6** and sodium with probable inclusion of this cation in the tetraamido cavity as already observed in very similar cases [3, 4]. **5** is the only ligand to form a 1 : 2 complex with sodium cation. It is well known that tetrahydrofuran forms good solvated species with sodium cations with a tetrahedral arrangement of the O-donor atoms [7]. Then, we can assume that the tetrahydrofuran moieties in **5** are mobile enough to have the required geometry around the sodium. Probably one sodium is in the tetraamido cavity while the second is in the tetrahydrofuran site. **2** and **3** form 1 : 1 complexes with zinc cation. The presence of the four nitrogen atoms of the pyridine moieties may form a good chelating site for this cation able also to adopt a tetrahedral geometry needed for Zn^{2+} coordination.

Chart 1 reports the $\Delta\delta$ values as ($\delta_{\text{freeligand}} - \delta_{\text{complex}}$) for 1 : 1 complexes and ($\delta_{1:1\text{complex}} - \delta_{2:1\text{complex}}$) for 2 : 1 complexes of **2–4** with Li^+, Na^+ and Zn^{2+}. Only $\Delta\delta \geq$ 0.05 ppm in absolute value are given. Large $\Delta\delta$ values were assumed to be indicative of the cation location in the receptor. For the 1 : 1 species, **2.Li$^+$Pic$^-$**, **2.Na$^+$Pic$^-$**, **3.Li$^+$Pic$^-$**, **3.Na$^+$Pic$^-$**, **4.Li$^+$+Pic$^-$**, **4.Na$^+$Pic$^-$** and **6.Na$^+$Pic** the alkali cation is located in the tetraamido cavity as already deduced from Table 2. For the 1 : 1 species **2.Zn^{2+}(Pic$^-$)$_2$** and **3.Zn^{2+}(Pic$^-$)$_2$** we can observe the larger $\Delta\delta$ for the proton of the pyridine probably induced by a chelation of the zinc cation with the nitrogen atoms of the pyridine. For the 1 : 2 complexes **2.(Li$^+$Pic$^-$)^2**, **3.(Li$^+$Pic$^-$)$_2$** and **4.(Li$^+$Pic$^-$)$_2$**, the largest $\Delta\delta$ being for those protons near the amido cavity we deduced both cations to be in this cavity. We were also especially concerned with 2 : 1 complexes formed by 3 and sodium and zinc. The 1 : 1 : 1 complex, **3.Na$^+$Zn^{2+}(Pic$^-$)$_3$**, was obtained by reacting **3.Na$^+$Pic$^-$** with $Zn^{2+}(Pic^-)_2$ in the same conditions as previously described. We deduced from the $\Delta\delta$ value that the zinc cation comes into the pyridine cavity of **3.Na$^+$Pic$^-$**. The ^{1}H-NMR spectra of **3**, **3.Na$^+$Pic$^-$** and **3.Na$^+$Zn^{2+}(Pic$^-$)$_3$**, are shown in Figure 1. We assumed the sodium to be located in the tetraamido cavity and the zinc to be in the pyridine site due to the similarity of the spectra of **3.Na$^+$Pic$^-$** and **3.Na$^+$Zn^{2+}(Pic$^-$)$_3$**. When reacting **3.Zn^{2+}(Pic$^-$)$_2$** with Na^+Pic^- a different spectrum (see Figure 2) was obtained which could not be rationalized. These results are reminiscent of similar observations made by Shinkai et al. [8] on a related $EtS(CH_2)NHCOCH_2$—O-calix[4]arene containing both hard and soft cation-sites which are observed along with larger aggregated species depending on the nature and the added quantity ratio of the soft metal cation.

Work is in progress to determine the stability, the thermodyanamic parameters of the different formed complexes and to detect an allosteric effect during the complexation of zinc in the presence of sodium cation [8].

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