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# Complexation and transport of transition and heavy metal cations by *p*-*tert*-butyldihomooxacalix[4]arene tetraketones and X-ray crystal structure of the *tert*-butyl ketone derivative

Paula M. Marcos,<sup>\*ad</sup> Sandra Félix,<sup>ab</sup> José R. Ascenso,<sup>c</sup> Manuel A. P. Segurado,<sup>d</sup> Pierre Thuéry,<sup>e</sup> Besma Mellah,<sup>fg</sup> Sylvia Michel,<sup>f</sup> Véronique Hubscher-Bruder<sup>f</sup> and Françoise Arnaud-Neu<sup>\*f</sup>

Received (in Durham, UK) 18th April 2007, Accepted 18th July 2007

First published as an Advance Article on the web 15th August 2007

DOI: 10.1039/b705879a

The binding properties of three *p*-*tert*-butyldihomooxacalix[4]arene tetraketone derivatives (*tert*-butyl **2b**, adamantyl **2c** and phenyl **2d**) in the cone conformation and one derivative (methyl **2a**) in a partial cone conformation, towards transition ( $\text{Mn}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$ ) and heavy ( $\text{Ag}^+$ ,  $\text{Cd}^{2+}$ ,  $\text{Hg}^{2+}$  and  $\text{Pb}^{2+}$ ) metal cations have been established by extraction studies of metal picrates from water into dichloromethane, transport experiments with the same salts through a dichloromethane membrane and stability constant measurements in methanol and acetonitrile. Results concerning the microcalorimetric study of  $\text{Cu}^{2+}$ ,  $\text{Ag}^+$  and  $\text{Pb}^{2+}$  complexes in methanol are presented. The affinity of the ligands for some cations ( $\text{Zn}^{2+}$ ,  $\text{Ag}^+$ ,  $\text{Pb}^{2+}$  and  $\text{Hg}^{2+}$ ) has also been investigated by proton NMR spectrometry. The X-ray crystal structure of *tert*-butylketone **2b** was determined. Towards transition metal cations, ketones **2b**, **2c** and **2d** are reasonable binders, showing in general preference for  $\text{Cu}^{2+}$ . Methylketone **2a** is a poor binder for these cations, due to its partial cone conformation. The three ligands in the cone conformation present a high affinity for the heavy metal cations, with selectivities for  $\text{Ag}^+$  and  $\text{Pb}^{2+}$ . This series of cations is even fairly well complexed by methylketone **2a**, which presents high stability constants for  $\text{Hg}^{2+}$  and  $\text{Pb}^{2+}$ . The cases studied by  $^1\text{H}$  NMR titrations confirm the formation of 1 : 1 complexes between the ketones and the cations, also indicating that they should be located inside the cavity defined by the phenoxy and carbonyl oxygen atoms. Ketones **2b**, **2c** and **2d** show transport rate sequences that follow, in general, the same trends observed in extraction and complexation for transition cations, but they are reversed for the heavy metal cations.

## Introduction

Calixarenes<sup>1,2</sup> are an extremely versatile class of macrocyclic receptors, able to bind and transport selectively ions and neutral molecules, and to serve as building blocks for the design of more elaborate structures. The parent compounds are readily available and can be further upper- and lower-rim functionalised into a large variety of derivatives. In particular, the calix[4]arene derivatives are an important family of host

molecules, mainly due to the features of the cone conformation, that they are able to take.

Intense research work has been devoted to binding studies towards metal ions, predominantly alkali and alkaline earth cations, of calixarene derivatives bearing carbonyl groups at their lower rims.<sup>3,4</sup> Transition and heavy metal cations have been less studied, although lately the study of their interactions with calixarenes has increased considerably.<sup>5–7</sup> The harmful impact that toxic metal ions such as cadmium, mercury and lead can provoke on environmental quality and consequently on human health, can explain that increasing interest. Despite the complexation of transition and heavy metal cations being favoured by the introduction of softer donor atoms (as nitrogen, sulfur and phosphorus),<sup>6</sup> ligands with harder oxygen atoms can also bind these cations. Among these ligands, functionalised calix[*n*]arenes (mainly *n* = 4,<sup>3,8–12</sup> but also *n* = 6<sup>9,11</sup>), biscalix[4]arenes<sup>13,14</sup> and thiacalix[4]arenes<sup>15</sup> with ketone groups have been studied.

Dihomooxacalix[4]arenes with extra oxygen and carbon atoms in the macrocyclic ring are more flexible molecules than calix[4]arenes, but still possess a cone conformation. Thus, they are potential host molecules for larger cations. In the course of the studies of alkali and alkaline earth metal cation

<sup>a</sup> Faculdade de Ciências da Universidade de Lisboa, Departamento de Química/CCMM, Edifício C8, 1749-016 Lisboa, Portugal.

E-mail: pmmarcos@fc.ul.pt

<sup>b</sup> Universidade Atlântica, Antiga Fábrica da Pólvora de Barcarena, 2730-036 Barcarena, Portugal

<sup>c</sup> Instituto Superior Técnico, Complexo I, Av. Rovisco Pais, 1049-001 Lisboa, Portugal

<sup>d</sup> Faculdade de Farmácia da Universidade de Lisboa, Av. Prof. Gama Pinto, 1649-003 Lisboa, Portugal

<sup>e</sup> CEA Saclay, SCM (CNRS URA 331), Bât. 125, 91191 Gif-sur-Yvette, France

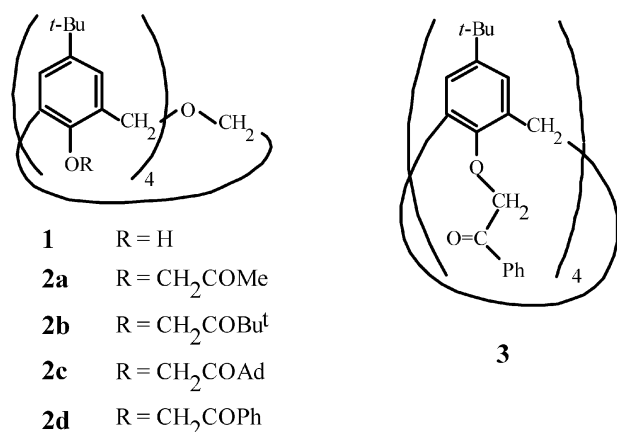
<sup>f</sup> Laboratoire de Chimie-Physique, Département des Sciences Analytiques, Institut Pluridisciplinaire Hubert Curien, ULP, CNRS, ECPM, 25 rue Becquerel, 67087 Strasbourg Cedex 2, France.

E-mail: farnaud@chimie.u-strasbg.fr

<sup>g</sup> Faculté des Sciences de Bizerte, 7021 Zarzouna-Bizerte, Tunisia

complexation and transport properties of dihomooxalix[4]-arenes bearing carbonyl groups at the lower rim, we have extended our research into transition and heavy metal ions.<sup>16–19</sup>

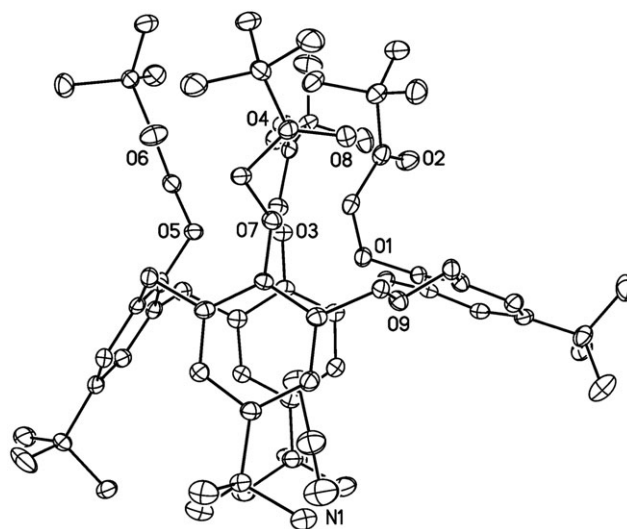
This paper reports the binding properties of four tetraketone (methyl **2a**, *tert*-butyl **2b**, adamantyl **2c** and phenyl **2d**) derivatives of *p-tert*-butyldihomooxalix[4]arene (**1**) towards transition ( $\text{Mn}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$ ) and heavy ( $\text{Ag}^+$ ,  $\text{Cd}^{2+}$ ,  $\text{Hg}^{2+}$  and  $\text{Pb}^{2+}$ ) metal cations. These properties have been assessed by extraction studies of metal picrates from an aqueous solution into dichloromethane, transport experiments with the same salts through a dichloromethane membrane and stability constant measurements in methanol and acetonitrile based on UV absorption spectrophotometry. Thermodynamic parameters of  $\text{Cu}^{2+}$ ,  $\text{Ag}^+$  and  $\text{Pb}^{2+}$  complexation have been determined by microcalorimetric studies. The affinity of the ligands for some cations has also been investigated by proton NMR spectrometry. The X-ray crystal structure of *tert*-butylketone **2b** has been determined. The results are compared to those obtained with closely-related calix[4]arene derivatives and discussed in terms of substituents, size and conformational effects.



## Results and discussion

### X-Ray crystal structure

The conformation of the dihomooxa *tert*-butylketone **2b** is intermediate between a much distorted cone and a flattened partial cone (Fig. 1). One of the aromatic rings, bearing O1, is nearly parallel to the mean plane defined by the four phenolic oxygen atoms O1, O3, O5 and O7. However, it is located on the same side of this plane as the three other rings. The dihedral angles between this mean plane (rms deviation



**Fig. 1** Molecular structure of *tert*-butylketone **2b**. Hydrogen atoms are omitted for clarity. Displacement ellipsoids are drawn at the 30% probability level.

0.193 Å) and the four aromatic rings are 13.59(11), 82.61(8), 65.76(9) and 76.67(8)°. The ether atom O9 is located at 1.140(4) Å from the mean plane and the two C–O9–C<sub>arom</sub> torsion angles in the ether bridge are *anti* [170.6(3) and 176.4(3)°], the C<sub>arom</sub>–CH<sub>2</sub>–O9–CH<sub>2</sub>–C<sub>arom</sub> fragment being thus nearly planar, with O9 pointing towards the dihomooxalixarene cavity. The four *tert*-butylketone substituents are all located on the same side of the dihomooxalixarene and they are roughly parallel to one another. One acetonitrile molecule is included in the dihomooxalixarene cavity, in which it is held by CH<sub>3</sub>···π interactions (shortest H···centroid contact 2.54 Å, C–H···centroid angle 172°).

### Extraction studies

The ionophoric properties of tetraketones **2a**, **2b**, **2c** and **2d** towards transition and heavy metal cations were first investigated by the standard picrate extraction method.<sup>20</sup> The results, expressed as a percentage of cation extracted (% *E*), are collected in Table 1. The corresponding values for *p-tert*-butylcalix[4]arene tetraphenylketone (**3**)<sup>17</sup> are included for comparison. Dihomooxa ketones **2b**,<sup>21</sup> **2c**<sup>21</sup> and **2d**<sup>22</sup> had already been synthesised and obtained in the cone conformation, while methylketone **2a**<sup>21</sup> was obtained in a partial cone conformation.

The data reveal that ketones **2b**, **2c**, **2d** (in the cone conformation) display low to reasonably high extraction levels

**Table 1** Percentage extraction of transition and heavy metal picrates into CH<sub>2</sub>Cl<sub>2</sub> at 25 °C<sup>a</sup>

	$\text{Mn}^{2+}$	$\text{Fe}^{2+}$	$\text{Co}^{2+}$	$\text{Ni}^{2+}$	$\text{Cu}^{2+}$	$\text{Zn}^{2+}$	$\text{Ag}^+$	$\text{Cd}^{2+}$	$\text{Hg}^{2+}$	$\text{Pb}^{2+}$
Ionic radius <sup>b</sup> /Å	0.83	0.78	0.75	0.69	0.73	0.75	1.15	0.95	1.02	1.18
<b>2a</b>	2.9	5.2	2.5	4.2	4.5	3.9	4.4	2.9	4.7	2.0
<b>2b</b>	6.5	11	15	19	45	20	79	13	11	25
<b>2c</b>	7.0	11	5.2	7.0	31	21	80	15	12	43
<b>2d</b> <sup>c</sup>	8.0	11	4.0	5.5	39	19	74	13	10	9.1
<b>3</b> <sup>c</sup>	3.8	7.4	2.3	3.8	28	16	50	9.1	7.6	4.4

<sup>a</sup> Values with uncertainties less than 5%. <sup>b</sup> Ref. 41; data quoted in ref. 42. <sup>c</sup> Data taken from ref. 17.

towards transition metal ions (%  $E$  ranges from 4 to 45).  $\text{Cu}^{2+}$  is the best extracted cation (45, 31 and 39%  $E$ , respectively) followed by  $\text{Zn}^{2+}$  (20, 21 and 19%  $E$ , respectively). Comparing to some thioamides,<sup>3</sup> Schiff base calix[4]arene derivatives bearing oxygen and nitrogen donor atoms<sup>3</sup> and pyridino dihomooxa derivatives,<sup>23,24</sup> these ketones present higher extraction values for  $\text{Cu}^{2+}$ . Towards heavy metal cations, all three ketones show the highest extraction percentages for  $\text{Ag}^+$  (79, 80 and 74%  $E$ , respectively).  $\text{Pb}^{2+}$  is also well extracted by ketone **2c** and, to a lesser extent, by ketone **2b**.

Although ketones **2b**, **2c** and **2d** present similar extraction profiles, the two former are slightly better phase transfer agents than the latter. The higher basicity of the carbonyl oxygens in derivatives **2b** and **2c** due to the presence of the *tert*-butyl and adamantyl groups, respectively, more donating than the phenyl group (ketone **2d**), may account for this difference.

The comparison of phenylketone **2d** with its analogue **3** shows that the former is a better extractant for all the cations, though both compounds exhibit the same extraction profile, with preference for  $\text{Ag}^+$ ,  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$ . Ketones **2c** and **2b** are the best extractants for  $\text{Ag}^+$ , showing the highest values obtained in this work, but phenyl ketones **2d** and **3** display the highest  $\text{Ag}^+/\text{Pb}^{2+}$  selectivities ( $S_{\text{Ag}^+/\text{Pb}^{2+}} = 8.1$  and 11.4, respectively).

Methylketone **2a** is a very poor phase transfer agent for all the cations, which appears to be due to its conformation. In the partial cone conformation only six donating sites can surround the cation, compared to the eight sites existing in the cone conformation. A similar behaviour was observed by us before towards alkali and alkaline earth metal cations.<sup>19</sup>

These results suggest that the match between the cation and the calixarene cavity dimensions is not an evident factor in selectivity. For example,  $\text{Cu}^{2+}$  being one of the smallest cations is well extracted by the ketones, which showed a strong selectivity for  $\text{Ba}^{2+}$ ,<sup>19</sup> of nearly double size. The hard and soft acids and bases principle<sup>25</sup> does not seem to be an important factor in selectivity, as well. In fact, although these ligands

contain hard oxygen donor atoms, they display a very clear preference for  $\text{Ag}^+$ , a soft Lewis acid and  $\text{Cu}^{2+}$ , of intermediate nature. Moreover, the hard Lewis acid  $\text{Mn}^{2+}$  is one of the least extracted cations. Similar behaviours had already been found for other dihomooxa and calixarene derivatives containing oxygen donor atoms, such as ester<sup>17</sup> and amide.<sup>18</sup>

### Complexation studies

The stability constants  $\beta_{xy}$  of transition and heavy metal complexes were determined in methanol and acetonitrile for ligands **2a**, **2b** and **2d** by UV absorption spectrophotometry from the spectral changes undergone by the ligands upon stepwise addition of the metal ions in solution. Limitations in solubility prevented adamantylketone **2c** from being studied. Table 2 summarizes the results (as  $\log \beta_{xy}$ ) in both solvents.

**Transition metal ions.** In methanol,  $\text{Mn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  cations form 1 : 1 species with both cone *tert*-butyl (**2b**) and phenylketone (**2d**) derivatives, whereas  $\text{Ni}^{2+}$  forms 1 : 1 and 2 : 1 metal to ligand complexes with **2d** and **2b**, respectively (Table 2). In the case of  $\text{Cu}^{2+}$ , the formation of additional species of different stoichiometry is observed, namely a 2 : 1 with **2b** and a 1 : 2 species with **2d**. The spectrophotometric titrations of the partial cone methylketone **2a** with  $\text{Mn}^{2+}$ ,  $\text{Ni}^{2+}$  and  $\text{Zn}^{2+}$  showed very weak spectral changes which could not be interpreted. Only the complexation of  $\text{Co}^{2+}$  and  $\text{Cu}^{2+}$  could be detected, showing the formation of 1 : 1 complexes with the two cations and a 2 : 1 species in the case of  $\text{Cu}^{2+}$ . The stability constants of the 1 : 1 complexes with the three ligands range from 1.38 to 4.63 log units in methanol. Although no data could be obtained for the 1 : 1 complexes of  $\text{Mn}^{2+}$  and  $\text{Zn}^{2+}$  with **2a** and  $\text{Ni}^{2+}$  with **2a** and **2b**, both ligands seem to follow the Irving–Williams rule as far as the most stable complexes are formed with  $\text{Cu}^{2+}$ . In contrast,  $\text{Co}^{2+}$  and  $\text{Ni}^{2+}$  complexes with ligand **2d** are the

**Table 2** Stability constants ( $\log \beta_{xy} \pm \sigma_{N-1}$ ) of transition and heavy metal complexes<sup>a</sup> in methanol and acetonitrile, at 25 °C

Ligand		$\text{Mn}^{2+}$	$\text{Co}^{2+}$	$\text{Ni}^{2+}$	$\text{Cu}^{2+}$	$\text{Zn}^{2+}$	$\text{Ag}^+$	$\text{Cd}^{2+}$	$\text{Pb}^{2+}$	$\text{Hg}^{2+}$
<b>2a</b>	$\log \beta$ (MeOH) <sup>b</sup>		$3.4 \pm 0.2$	<sup>b</sup>	$4.30 \pm 0.02$ $7.36 \pm 0.02$ (2 : 1)	<sup>b</sup>	$3.2 \pm 0.1$	$3.6 \pm 0.2$	$4.4 \pm 0.2$	$4.5 \pm 0.1$
	$\log \beta$ (MeCN)	$4.48 \pm 0.08$	$4.17 \pm 0.04$	$3.14 \pm 0.03$	$5.08 \pm 0.02$ $8.7 \pm 0.2$ (2 : 1)	<sup>a</sup>	<sup>b</sup>	$4.65 \pm 0.07$	$5.11 \pm 0.08$	$5.88 \pm 0.04$
<b>2b</b>	$\log \beta$ (MeOH)	$3.38 \pm 0.04$	$4.04 \pm 0.03$	— $7.05 \pm 0.02$ (2 : 1)	$4.63 \pm 0.04$ $7.4 \pm 0.2$ (2 : 1)	$1.38 \pm 0.09$	$5.36 \pm 0.01$	$3.43 \pm 0.01$	$4.65 \pm 0.02$	$3.1 \pm 0.1$
	$\log \beta$ (MeCN)	$4.63 \pm 0.01$	$1.8 \pm 0.2$	— $7.3 \pm 0.2$ (2 : 1)	$4.5 \pm 0.3$ $8.5 \pm 0.3$ (2 : 1)	$4.28 \pm 0.25$	$5.5 \pm 0.1$	$5.8 \pm 0.1$	$5.18 \pm 0.08$	$3.49 \pm 0.07$
<b>2d</b>	$\log \beta$ (MeOH)	$2.2 \pm 0.2$	$3.5 \pm 0.1$	$3.5 \pm 0.2$	$2.9 \pm 0.3$ $8.27 \pm 0.01$ (1 : 2)	$3.2 \pm 0.2$	$3.4 \pm 0.2$	$4.93 \pm 0.06$	$4.8 \pm 0.3$	$2.7 \pm 0.1$
	$\log \beta$ (MeCN)	$4.49 \pm 0.09$	$3.80 \pm 0.08$	$3.8 \pm 0.2$	$4.23 \pm 0.05$ $8.9 \pm 0.2$ (1 : 2)	$3.9 \pm 0.1$	$3.6 \pm 0.2$	$5.36 \pm 0.07$	$6.4 \pm 0.1$	$4.4 \pm 0.1$

<sup>a</sup> 1 : 1 metal to ligand complexes, unless otherwise stated. <sup>b</sup> Small spectral variations.

most stable. No positive cooperative effect is observed during the formation of binuclear complexes with  $\text{Cu}^{2+}$ . With the cone *tert*-butylketone **2b**, as with the partial cone methylketone **2a**, the formation of the binuclear species is less favoured than that of the 1 : 1 complex. In contrast, the 1 : 2 species observed with  $\text{Cu}^{2+}$  and ligand **2d** is 295 times more stable than the 1 : 1 species ( $\log \beta_{11}(\text{Cu}^{2+}\text{--}2\text{d}) = 2.9$  and  $\log K_2(\text{Cu}^{2+}\text{--}2\text{d}_2) = \log \beta_{21} - \log \beta_{11} = 5.37$ ). Thus, a positive cooperative effect is observed ( $\Delta = \log K_2 - \log \beta_{11} = 2.47$ ).

The complexation of these cations with the three ligands was also followed in acetonitrile. The results (Table 2) show in this solvent (i) the same complex stoichiometries as in methanol; (ii) the higher stability of the complexes with respect to methanol, except with ligand **2b** and  $\text{Co}^{2+}$ , which form a 1 : 1 complex of particularly low stability ( $\log \beta_{11} = 1.8$ ) in acetonitrile; (iii) no particular selectivity in the series, except with ligand **2a** for  $\text{Cu}^{2+}$ . As in methanol, no positive cooperative effect is observed during the formation of the binuclear complexes of  $\text{Cu}^{2+}$  with ligands **2a** and **2b**. The stability of the two 1 : 1 and 1 : 2 complexes of  $\text{Cu}^{2+}$  with **2d** is of the same order of magnitude.

**Heavy metal ions.** Spectrophotometric titrations in methanol show the formation of 1 : 1 complexes only, with the three ketone derivatives and these cations. In this solvent, stability profiles of the three ligands are different. The *tert*-butylketone **2b** forms the most stable complexes with  $\text{Pb}^{2+}$  and especially with  $\text{Ag}^+$  ( $\log \beta_{11} = 5.36$ ), and the least stable one with  $\text{Hg}^{2+}$ . These results show a high selectivity for  $\text{Ag}^+$  over  $\text{Hg}^{2+}$  ( $S = \beta_{11}(\text{Ag}^+)/\beta_{11}(\text{Hg}^{2+}) = 1.82 \times 10^2$ ), a situation already found in extraction (Table 1). With the phenylketone **2d**,  $\text{Cd}^{2+}$  and  $\text{Pb}^{2+}$  are the best complexed cations, whereas  $\text{Hg}^{2+}$  is again the least complexed one. These results lead to interesting complexation selectivities  $\text{Cd}^{2+}/\text{Hg}^{2+}$  and  $\text{Pb}^{2+}/\text{Hg}^{2+}$  of  $1.7 \times 10^2$  and  $1.3 \times 10^2$ , respectively. Ketone **2d** shows here a different trend from the one found in extraction, where  $\text{Ag}^+$  is the best extracted cation. Contrary to the transition metal cations studied, heavy metal cations are fairly well complexed by methylketone **2a**, in particular  $\text{Hg}^{2+}$  and  $\text{Pb}^{2+}$  ( $\log \beta_{11} = 4.5$  and  $4.4$ , respectively). These results are difficult to interpret, as methylketone **2a** is in a partial cone conformation and

forms more stable complexes than *tert*-butylketone **2b** and phenylketone **2d**, both in the cone conformation, with  $\text{Hg}^{2+}$ .

In acetonitrile, only 1 : 1 stoichiometries were also found, but the complexes show higher stability constants than in methanol. Very weak spectral changes were observed with ligand **2a** and  $\text{Ag}^+$  cation, which may account for the low stability of its complex, possibly due to a competition between the ligand and the solvent molecules. In this solvent, ketone **2b** shows preference for  $\text{Cd}^{2+}$  closely followed by  $\text{Ag}^+$ , whereas **2d** is selective for  $\text{Pb}^{2+}$  and  $\text{Cd}^{2+}$ . Derivative **2a** forms the most stable complexes with  $\text{Hg}^{2+}$  and  $\text{Pb}^{2+}$ , the former complex being 17 times more stable than the  $\text{Cd}^{2+}\text{--}2\text{a}$  complex.

**Microcalorimetric study.** Complexation of  $\text{Cu}^{2+}$ ,  $\text{Ag}^+$  and  $\text{Pb}^{2+}$ , as representatives of the transition and heavy metal ions, with ligands **2a**, **2b** and **2d** has been followed by microcalorimetric titrations in methanol. These experiments have been performed in order to try to confirm the different stoichiometries of the complexes found by spectrophotometry, especially in the case of  $\text{Cu}^{2+}$ , and to determine the thermodynamic parameters of complexation. These data are collected in Table 3.

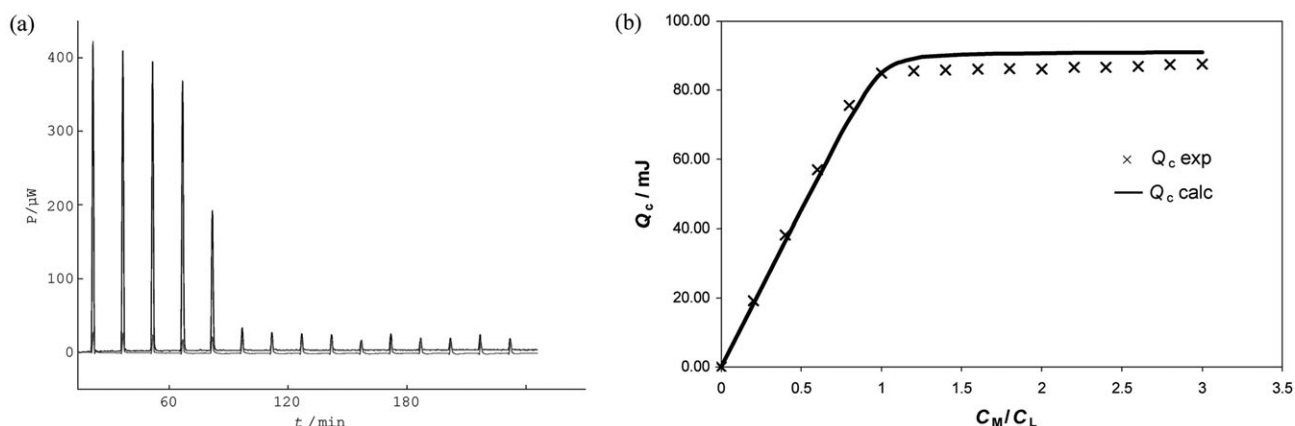
Clear and easily interpretable thermograms, corresponding to strongly exothermic reactions, could be recorded for *tert*-butylketone **2b** with  $\text{Ag}^+$  (Fig. 2). The shape of the curves giving the corrected heat exchanged vs. the  $C_M/C_L$  ratio confirmed the 1 : 1 stoichiometry of the complex formed. The stability constant of the 1 : 1 complex with  $\text{Ag}^+$  obtained by this method ( $\log \beta = 5.4$ ) is in full agreement with the value obtained by spectrophotometry ( $\log \beta = 5.36$ ). The stabilisation of the complex is entirely enthalpically driven ( $-\Delta H = 32 \text{ kJ mol}^{-1}$ ), since the entropy term is close to zero. The measurements with phenylketone **2d** were performed at a lower concentration of the ligand ( $C_L = 10^{-4} \text{ M}$ ), because of its low solubility in methanol. As a consequence, the heat evolved during the titration was much smaller than with **2b**. The shape of the curve was also different and could be interpreted by the formation of two 1 : 1 and 1 : 2 complexes. This additional less stable 1 : 2 complex was not visible in spectrophotometry probably because of spectral similitude with the 1 : 1 complex. The enthalpy change  $-\Delta H$  for the

**Table 3** Thermodynamic overall parameters of complexation<sup>a</sup> of  $\text{Ag}^+$  and  $\text{Pb}^{2+}$  with ligands **2a**, **2b** and **2d** in methanol at 25 °C

Cation		<b>2a</b>	<b>2b</b>	<b>2d</b>
$\text{Ag}^+$	$\log \beta$	$2.4 \pm 0.4$ (3.2) <sup>b</sup>	$5.4 \pm 0.3$ (5.36) <sup>b</sup>	$4.7 \pm 0.1$ (3.4) <sup>b</sup>
	$-\Delta G/\text{kJ mol}^{-1}$	$14 \pm 2$	$31 \pm 2$	$7.9 \pm 0.2$ (1 : 2)
	$-\Delta H/\text{kJ mol}^{-1}$	$2.4 \pm 0.9$	$32 \pm 1$	$26.8 \pm 0.6$
	$T\Delta S/\text{kJ mol}^{-1}$	$12 \pm 3$	$-1 \pm 3$	$45 \pm 1$ (1 : 2)
$\text{Pb}^{2+}$	$\log \beta$	(4.4) <sup>b</sup>	$5.1 \pm 0.3$ (4.65) <sup>b</sup>	$24 \pm 1$
	$-\Delta G/\text{kJ mol}^{-1}$	$25 \pm 1$	$29 \pm 2$	$33 \pm 2$ (1 : 2)
	$-\Delta H/\text{kJ mol}^{-1}$	$1.7 \pm 0.9$ <sup>c</sup>	$24 \pm 4$	$3 \pm 2$
	$T\Delta S/\text{kJ mol}^{-1}$	$23 \pm 2$	$5 \pm 6$	$13 \pm 3$ (1 : 2)

<sup>a</sup> 1 : 1 metal to ligand complexes, unless otherwise stated. <sup>b</sup> Spectrophotometric results. <sup>c</sup> Value derived from the slope of the plot  $Q_c$  vs. the number of moles of metal ion added. <sup>d</sup> Too little heat evolved to be measured.





**Fig. 2** Complexation of  $\text{Ag}^+$  with ketone **2b**. (a) Microcalorimetric titration of 2.7 mL of **2b** ( $C_L = 10^{-3}$  M) by addition of  $15 \times 15 \mu\text{L}$  of  $3.7 \times 10^{-2}$  M  $\text{AgNO}_3$  in methanol at  $25^\circ\text{C}$ . (b) Plot of the corrected heat ( $Q_c$ ) vs. the metal to ligand concentration ratios.

1 : 1 complex was found to be smaller than that for its homologue with ligand **2b**, showing a weaker cation–ligand interaction, in agreement with the electronic properties of the substituents. However, the corresponding entropy change is close to zero and the formation of this complex is still enthalpically driven. In contrast, the formation of the 1 : 2 complex is driven equally by both terms, the corresponding enthalpic and entropic contributions being of the same order of magnitude within the experimental errors. With the quite soluble methylketone **2a** ( $C_L = 10^{-3}$  M), very weak corrected heat changes were observed during the titrations. A stability constant of 2.4 log units, instead of 3.2 obtained from spectrophotometry, was derived as well as a very low complexation enthalpy. This can be explained by weaker interactions between the cation and this ligand in a partial cone conformation, presenting only three arms available for the complexation. The stabilisation of the complex is therefore entropically driven.

The titration of  $\text{Pb}^{2+}$  with ligand **2b** gave also rise to strong signals, confirming the 1 : 1 stoichiometry of the complex. The stability constant obtained ( $\log \beta_{11} = 5.1$ ) is in reasonably good agreement with the spectrophotometric result ( $\log \beta_{11} = 4.65$ ). The enthalpy term is lower ( $-\Delta H = 25 \text{ kJ mol}^{-1}$ ) than that with  $\text{Ag}^+$ , although still strongly negative. This can be explained by the higher solvation of the divalent  $\text{Pb}^{2+}$  as compared to the monovalent  $\text{Ag}^+$  cation. However,  $T\Delta S$  remains close to zero. In the case of ligand **2d** the heat evolved was too weak to allow any interpretation. With ketone **2a**, despite of the weak effects observed, it was possible to determine a low value of the complexation enthalpy ( $-\Delta H = 1.7 \text{ kJ mol}^{-1}$ ). The origin of the relatively high stability of this complex is due to an entropic effect. As mentioned before, this effect is also significant in the case of  $\text{Ag}^+$ , which may indicate deeper conformational rearrangements and/or solvation changes of ligand **2a** upon complexation, compared to those of ketones **2b** and **2d**.

In the case of  $\text{Cu}^{2+}$ , it was not possible as expected to confirm the nature of the complexes with the three ligands and to determine the complexation thermodynamic parameters. The thermograms recorded during the titrations show strongly endothermic effects, becoming slightly exothermic when cor-

rected by dilution effects. In each case, the heat exchanged revealed to be too small to lead to a reliable interpretation or to clearly indicate the stoichiometry of the complex. However, it could be clearly deduced from these thermograms that the stabilisation of these complexes is rather entropically than enthalpically driven.

### Proton NMR studies

To obtain further information on the cation binding behaviour of ketones **2b**, **2c** and **2d**, namely concerning the binding sites, proton NMR studies were performed. The cations studied were  $\text{Zn}^{2+}$ ,  $\text{Ag}^+$ ,  $\text{Pb}^{2+}$  and also  $\text{Hg}^{2+}$  in the case of ketone **2c**. Variable amounts of the salts were added to the calixarenes and the proton spectra recorded after each addition.

Different situations were found after the addition of the salts to the ligands. Very small changes were observed in the case of  $\text{Zn}^{2+}$  with all the ketones, indicating a very weak affinity towards this cation. This behaviour is in agreement with the stability constant values (in methanol), mainly for *tert*-butylketone **2b**. Ketones **2b**, **2c** and **2d** exhibit similar behaviours towards  $\text{Ag}^+$  and  $\text{Pb}^{2+}$ . These titrations show that with [salt]/[ligand] ratios lower than 1, both signals of the complexed and uncomplexed ligands are present in the spectra, indicating that on the NMR time scale the exchange rate between the two species is slow, at room temperature. This reflects a high affinity of these ligands towards  $\text{Ag}^+$  and  $\text{Pb}^{2+}$ , as previously observed. Upon reaching 1 : 1 ratios, all the signals for the free ligands disappear and those of the complexed ligands remain unaltered after subsequent additions of the salts, indicating a 1 : 1 metal-to-ligand stoichiometry. Small differences can, however, be observed between the  $\text{Ag}^+$  and  $\text{Pb}^{2+}$  spectra. The peaks in the methylene region are less overlapped for the latter and the position of the aromatic peaks relative to that of  $\text{CDCl}_3$  peak is also different. A similar monovalent/divalent cation dichotomy has already been observed with diethylamide derivative.<sup>18</sup> The titration of adamantylketone **2c** with  $\text{Hg}^{2+}$  cation initially induces broadening of the signals until the [salt]/[ligand] ratio reaches the unity value, when the signals become sharp. This indicates a

**Table 4** Relevant proton chemical shifts ( $\delta$ , ppm) of ligands **2b**, **2c** and **2d** and its 1 : 1 metal complexes

	<i>t</i> -Bu	ArCH <sub>2</sub> Ar		CH <sub>2</sub> OCH <sub>2</sub>		OCH <sub>2</sub> CO	ArH
		eq	ax	eq	ax		
<b>2b</b>	0.96, 1.16	3.28, 3.28	4.63, 4.72	4.68	4.84	4.62, 4.86, 5.17, 5.21	6.73, 6.86, 6.97, 7.09
<b>2b</b> + Zn <sup>2+</sup>	0.98, 1.17	3.30, 3.30	4.64, 4.64	4.64	4.89	4.69, 4.90, 5.16, 5.22	6.80, 6.91, 7.00, 7.06
<b>2b</b> + Ag <sup>+</sup>	1.18, 1.25	3.44, 3.44	4.31, 4.35	4.21	4.50	4.84, 4.87, 4.91, 4.96	7.10, 7.21, 7.29, 7.46
<b>2b</b> + Pb <sup>2+</sup>	1.18, 1.22	3.76, 3.74	4.05, 3.92	4.28	4.51	5.11, 5.32, 5.35, 5.54	7.15, 7.38, 7.40, 7.57
<b>2c</b>	0.95, 1.15	3.27, 3.27	4.61, 4.71	4.69	4.85	4.63, 4.83, 5.15, 5.16	6.70, 6.84, 6.94, 7.08
<b>2c</b> + Zn <sup>2+</sup>	0.99, 1.18	3.33, 3.34	4.53, 4.53	4.57	4.97	4.78, 4.93, 5.10, 5.11	6.81, 6.90, 6.99, 7.05
<b>2c</b> + Ag <sup>+</sup>	1.18, 1.24	3.42, 3.41	4.30, 4.34	4.19	4.48	4.82, 4.84, <sup>a</sup> 4.93	7.09, 7.20, 7.28, 7.44
<b>2c</b> + Pb <sup>2+</sup>	1.17, 1.22	3.73, 3.69	4.01, 3.85	4.28	4.46	5.07, 5.22, 5.28, 5.50	7.14, 7.37, 7.38, 7.55
<b>2c</b> + Hg <sup>2+</sup>	1.10, 1.25	3.43, 3.42	4.77, 4.69	4.46	4.86	4.76, 4.87, 4.98, 5.08	7.04, 7.23, 7.29, 7.39
<b>2d</b>	1.07, 1.14	3.41, 3.42	5.10, 5.05	4.57	5.08	5.21, 5.48, 5.67, 5.72	6.91, 6.94, 6.95, 7.08
<b>2d</b> + Zn <sup>2+</sup>	1.07, 1.15	3.41, 3.41	5.09, 5.00	4.56	5.10	5.26, 5.48, 5.67, 5.74	6.94, 6.96, 6.97, 7.07
<b>2d</b> + Ag <sup>+</sup>	1.22, 1.28	3.57, 3.55	4.63, 4.79	4.29	4.86	5.40, 5.43, 5.46, 5.52	7.17, 7.29, 7.38, 7.56
<b>2d</b> + Pb <sup>2+</sup>	1.22, 1.25	3.86, 3.76	4.42, 4.20	4.31	4.83	5.67, 5.78, 6.07, 6.11	7.19, 7.45, 7.48, 7.64

<sup>a</sup> Singlet corresponding to four protons.

fast exchange rate between the free and complexed ligand on the NMR time scale, at room temperature, and consequently a weak affinity of ligand **2c** towards Hg<sup>2+</sup>.

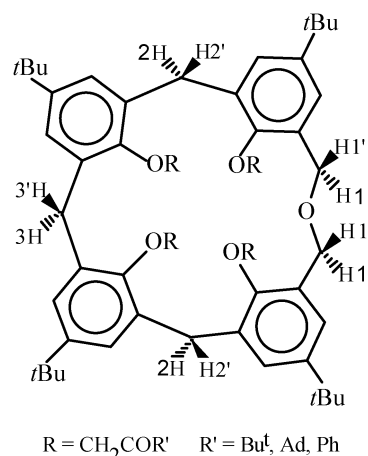
Proton NMR data of the free and complexed ligands are collected in Table 4. Complexation of the cations affects all the proton chemical shifts in the ligands, except in the case of Zn<sup>2+</sup> that produces only minor variations, as already mentioned. The most pronounced shift changes are observed for the bridging axial methylene protons (ArCH<sub>2</sub>Ar) and the oxygen bridge equatorial and axial methylene protons (CH<sub>2</sub>OCH<sub>2</sub>), which move upfield, and by the aromatic protons, which move downfield. The methylene protons of the OCH<sub>2</sub>CO groups undergo also large shift variations, being upfield in the case of Ag<sup>+</sup> and downfield for the divalent cations, mainly for Pb<sup>2+</sup>. Similar observations have been made for dihomooxa diethylamide<sup>18</sup> and closely related calix[4]arene derivatives.<sup>9,12,26</sup>

A closer examination of the spectral changes upon complexation indicates that the difference in the chemical shifts between the two *t*-Bu groups decreases significantly in the case of ketones **2b** and **2c** and, to a lesser extent, for ketone **2d**. Moreover, the differences in the chemical shifts between the axial and the equatorial protons of the ArCH<sub>2</sub>Ar bridges in the ligands ( $\Delta\delta$  = 1.35, 1.44 ppm for ketone **2b**, for example) also decrease, being closer to 0.9 ppm<sup>27</sup> for Ag<sup>+</sup> ( $\Delta\delta$  = 0.87, 0.91 ppm for ketone **2b**), suggesting that the ligands adopt a more symmetrical cone conformation upon complexation. In fact, the solid state structure of the free ligand **2b** had already shown a much distorted cone conformation. For Pb<sup>2+</sup> the chemical shift separations are much lower than 0.9 ppm ( $\Delta\delta$  = 0.29, 0.18 ppm for ketone **2b**), indicating that upon complexation with this cation the pendant arms of the ligands move closer together to a larger extent, resulting in a more flattened cone conformation.

A systematic observation of the data reveals that the axial methylene protons of both ArCH<sub>2</sub>Ar groups (H2 and H3, Scheme 1) experience similar upfield shifts for Ag<sup>+</sup> ( $\Delta\delta$   $\approx$  0.35 ppm), but the upfield shift experienced by H3 is significantly higher ( $\Delta\delta$   $\approx$  0.84 ppm) than that experienced by H2 ( $\Delta\delta$   $\approx$  0.62 ppm) for Pb<sup>2+</sup> cation. Similar results

were found before with these ligands and the monovalent alkali and the divalent alkaline earth cations, respectively.<sup>19</sup> As observed for other calixarenes, the variation in chemical shift experienced by the equatorial methylene protons (ArCH<sub>2</sub>Ar) is downfield and much smaller than that of the axial protons. Again, Pb<sup>2+</sup> cation produces higher downfield shift changes ( $\Delta\delta$   $\approx$  0.44 ppm) than Ag<sup>+</sup> ( $\Delta\delta$   $\approx$  0.15 ppm). The CH<sub>2</sub>OCH<sub>2</sub> resonances behave differently, as reported before.<sup>18,19</sup> Both axial and equatorial methylene protons of the oxygen bridge move upfield, and with approximately the same value. These results suggest that the oxygen bridge conformation changes significantly upon complexation, with both CH<sub>2</sub> groups undergoing similar shielding effects.

The deshielding effect observed for the aromatic protons indicates the involvement of the phenolic oxygens in complexation.<sup>28</sup> The largest shift changes shown by the protons adjacent to the oxygen donor atoms can be explained in terms of variations of both shielding and deshielding effects of the aromatic rings and carbonyl groups upon cation binding to those donor atoms. Therefore, this suggests that the cations must be inside the cavity defined by the phenoxy and carbonyl oxygen atoms.

**Scheme 1**

**Table 5** Transport rate ( $V/\mu\text{mol h}^{-1}$ ) of transition and heavy metal picrates through a  $\text{CH}_2\text{Cl}_2$  liquid membrane at  $25^\circ\text{C}^a$ 

	$\text{Mn}^{2+}$	$\text{Co}^{2+}$	$\text{Ni}^{2+}$	$\text{Cu}^{2+}$	$\text{Zn}^{2+}$	$\text{Ag}^+$	$\text{Cd}^{2+}$	$\text{Hg}^{2+}$	$\text{Pb}^{2+}$
<b>2a</b>	0.05	0.026	0.034	0.23	0.07	1.6	0.07	1.3	0.22
<b>2b</b>	0.016	0.017	0.026	0.08	0.016	0.38	0.029	2.1	1.1
<b>2c</b>	0.040	0.018	0.022	0.11	0.05	0.18	0.08	0.61	0.27
<b>2d<sup>b</sup></b>	0.046	0.023	0.032	0.21	0.049	0.76	0.08	0.77	1.0
<b>3<sup>b</sup></b>	0.032	0.016	0.029	0.09	0.033	0.48	0.035	1.7	1.0

<sup>a</sup> Reproducibility of  $\pm 10\%$ . <sup>b</sup> Data taken from ref. 17.

Comparable spectral changes were observed for *tert*-butyl, adamantyl and phenyl ketones, although the latter has shown slight differences relative to the others. The magnitude of the chemical shift variations for the three ketones follows the order:  $\text{Pb}^{2+} > \text{Ag}^+ \gg \text{Zn}^{2+}$  (or  $\text{Pb}^{2+} > \text{Ag}^+ > \text{Hg}^{2+} > \text{Zn}^{2+}$ , when  $\text{Hg}^{2+}$  was also studied). This preference of the ligands seems to be the result of the combination of two main factors affecting complexation: size and charge of the cations. The trend observed in complexation is approximately the same that was observed in extraction, mainly for ketones **2b** and **2c**. However, ketone **2d** behaves slightly different, since  $\text{Pb}^{2+}$  is well complexed but only weakly extracted by this ligand.

### Ion transport

Transport experiments were carried out in a  $\text{CH}_2\text{Cl}_2$  liquid membrane system, similar to that employed by Lamb *et al.*<sup>29</sup> The transport rate  $V$ , in  $\mu\text{mol h}^{-1}$  for ketones **2a**, **2b**, **2c** and **2d**, are presented in Table 5. The data for ketone **3** are included for comparison.

Table 5 shows that the four dihomooxa ligands are inefficient neutral carriers for the transition metal cations ( $V$  ranging from 0.02 up to  $0.23 \mu\text{mol h}^{-1}$ ). It is interesting to point out that methylketone **2a** is now the best carrier in contrast to the binding process, where it was the worst binder, although presenting transport rate values only slightly higher than those presented by the other ligands. Due to its partial cone conformation, it is expected that **2a** rapidly releases the cations at the interface with the receiving phase, being a better carrier than receptor. The trend found in transport for these ligands follows, in general, that of extraction and stability constants.

Towards heavy metal cations, the ketones display reasonable transport rates, except for cadmium.  $\text{Hg}^{2+}$  and  $\text{Pb}^{2+}$  are the fastest carried cations, with **2b** showing the highest transport rate value ( $2.1 \mu\text{mol h}^{-1}$  for  $\text{Hg}^{2+}$ ). The trend found in transport seems now the reverse of that observed in extraction and for the stability constants. For example, while  $\text{Hg}^{2+}$  is one of the most carried cations with ketones **2b**, **2c** and **2d**, it is only modestly bound by these ligands. This behaviour was already found towards alkali and alkaline earth metal cations.<sup>19</sup> It is perhaps worthwhile to point out that the higher transport rates obtained with  $\text{Hg}^{2+}$  can be related with its large extent of hydrolysis.

Comparing phenylketones **2d** and **3** it is possible to observe that the former is a slightly better carrier than the latter, except for  $\text{Hg}^{2+}$ . However, ketone **3** shows a higher  $\text{Pb}^{2+}/\text{Zn}^{2+}$  transport selectivity, although the highest selectivity is shown by ketone **2b** ( $S = 20, 30$  and  $69$ , respectively).

According to the different behaviours of the ligands, Lehn<sup>30</sup> characterized them as selective carriers (the most efficiently bound cation is also the fastest transported) or selective receptors (the best bound cation is the most slowly transported one). Based on this classification, ketones **2b**, **2c** and **2d** may be considered as selective receptors for the heavy metal cations, but as selective carriers for the transition cations.

### Conclusions

Extraction studies from an aqueous solution into  $\text{CH}_2\text{Cl}_2$  and stability constant measurements in methanol and acetonitrile have shown that ketones **2b**, **2c** and **2d**, in the cone conformation, are reasonable binders for the transition cations, displaying preference for  $\text{Cu}^{2+}$ . With this cation, besides 1 : 1 complexes, other species of different metal : ligand stoichiometries (2 : 1 and 1 : 2) were formed with all the ketones. Methylketone **2a** is a poor binder for these cations, due to its partial cone conformation. Towards heavy metal cations, the ketones in the cone conformation are stronger binders, showing a high affinity for  $\text{Ag}^+$  and  $\text{Pb}^{2+}$ . This series of cations is even fairly well complexed by methylketone **2a**, which exhibits high  $\log \beta$  values for  $\text{Hg}^{2+}$  and  $\text{Pb}^{2+}$ .  $\text{Ag}^+$  complexes with *tert*-butyl and phenyl ketones are stabilised by the enthalpy changes, which are higher for the former derivative. The same stabilisation is observed for  $\text{Pb}^{2+}$  with the **2b**. In contrast, the formation of the corresponding complexes with methylketone **2a** is governed by the entropy changes. The nature of the substituents attached to the ketone function has some influence on their binding properties, with phenylketone **2d** being a slightly weaker binder than ketones **2b** and **2c**, according to the basicity of their carbonyl oxygens. The results have shown that, although these ligands bear hard oxygen donor atoms, they display a clear affinity for soft Lewis acids as  $\text{Ag}^+$ , and also for Lewis acids of intermediate nature as  $\text{Pb}^{2+}$  and  $\text{Cu}^{2+}$ . For the cases studied, the NMR titrations confirmed the formation of 1 : 1 complexes between the ketones and the cations, also suggesting that they should be encapsulated into the cavity composed by the phenoxy and carbonyl oxygen atoms. All the ketones are weak neutral carriers for the transition cations, but they display reasonable transport rates towards the heavy metal ions (except for  $\text{Cd}^{2+}$ ). The comparison of phenylketone **2d** with its analogue **3** shows that the former is a better extractant and carrier (except for  $\text{Hg}^{2+}$ ) for all the cations, although less selective. Nevertheless, both compounds exhibit the same extraction and transport profiles.

## Experimental

### Crystallography

The crystal structure of compound **2b** was determined by single crystal X-ray diffraction. The data were collected at 100(2) K on a Nonius Kappa-CCD area detector diffractometer using graphite-monochromated Mo-K $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ).<sup>31</sup> The data were processed with HKL2000.<sup>32</sup> The structure was solved by direct methods with SHELXS-97 and subsequent Fourier-difference synthesis and refined by full-matrix least-squares on  $F^2$  with SHELXL-97.<sup>33</sup> No absorption correction was done. All non-hydrogen atoms were



refined with anisotropic displacement parameters. Hydrogen atoms were introduced at calculated positions and were treated as riding atoms with a displacement parameter equal to 1.2 (CH, CH<sub>2</sub>) or 1.5 (CH<sub>3</sub>) times that of the parent atom. The molecular plot was drawn with SHELXTL.<sup>34</sup>

**Crystal data and refinement details for 2b.** C<sub>71</sub>H<sub>101</sub>NO<sub>9</sub>,  $M_r$  = 1112.53, orthorhombic, space group *Pbca*,  $a$  = 19.0372(7),  $b$  = 22.9422(7),  $c$  = 30.2456(13) Å,  $V$  = 13209.9(8) Å<sup>3</sup>,  $Z$  = 8,  $D_c$  = 1.118 g cm<sup>-3</sup>,  $\mu$  = 0.072 mm<sup>-1</sup>,  $F(000)$  = 4848. Refinement of 755 parameters on 12 490 independent reflections out of 142 525 measured reflections ( $R_{int}$  = 0.062) led to  $R_1$  = 0.078,  $wR_2$  = 0.218,  $S$  = 1.026,  $\Delta\rho_{max}$  = 0.53,  $\Delta\rho_{min}$  = -0.32 e Å<sup>-3</sup>.

CCDC reference number 656213.

For crystallographic data in CIF or other electronic format see DOI: 10.1039/b705879a

### Extraction studies

Equal volumes (5 mL) of aqueous solutions of metal picrates ( $2.5 \times 10^{-4}$  M) and solutions of the calixarenes ( $2.5 \times 10^{-4}$  M) in CH<sub>2</sub>Cl<sub>2</sub> were vigorously shaken for 2 min and then thermostated in a water bath with mechanical stirring, at 25 °C overnight. After complete phase separation, the concentration of picrate ion in the aqueous phase was determined spectrophotometrically ( $\lambda_{max}$  = 354 nm). For each cation–calixarene system the absorbance measurements were repeated, at least, four times. Blank experiments showed negligible picrate extraction in the absence of a calixarene. The details of metal picrate preparation have already been described.<sup>17</sup>

### Determination of stability constants

The stability constants  $\beta_{xy}$  defined as the concentration ratio  $[M_xL_y^{n+}]/([M^{n+}]^x[L]^y)$  (where  $M^{n+}$  = cation and L = ligand) were determined in methanol (Carlo Erba, 99.9%) and acetonitrile (Riedel–deHaën, analytical reagent) used without further purification by UV absorption spectrophotometry, at 25 °C and constant ionic strength provided by 0.01 M Et<sub>4</sub>N-ClO<sub>4</sub> (Fluka, *purum*), Et<sub>4</sub>NCl (Fluka, *purum*) or Et<sub>4</sub>NNO<sub>3</sub> (Acros) according to the procedure already described.<sup>35</sup> A typical experiment consisted in adding increasing amounts of the metal salt to 2 mL of a ligand solution ( $C_L$  ca.  $5.0 \times 10^{-5}$ – $2.0 \times 10^{-4}$  M) directly in the spectrophotometric cell of 1 cm pathlength. The spectra corresponding to each addition were recorded between 250 and 300 nm using a Shimadzu UV-2101-PC or a Perkin Elmer Lambda 11 spectrophotometer. They were then treated with the numerical programs Letagrop<sup>36</sup> and/or Specfit.<sup>37</sup>

The metal salts used were chlorides, perchlorates or nitrates according to their solubilities in the solvents used. The following salts were employed in methanol: ZnCl<sub>2</sub>, CoCl<sub>2</sub>, CuCl<sub>2</sub> and Ni(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O (Fluka), MnCl<sub>2</sub>·4H<sub>2</sub>O, Cd(NO<sub>3</sub>)<sub>2</sub>·4H<sub>2</sub>O and Pb(NO<sub>3</sub>)<sub>2</sub> (Merck, p.a.), HgCl<sub>2</sub> (Prolabo), AgNO<sub>3</sub> (Strem Chemicals). In acetonitrile the following perchlorates and nitrates were used: Co(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Ni(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O and Hg(NO<sub>3</sub>)<sub>2</sub> (Fluka, *purum*), Zn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O and Pb(ClO<sub>4</sub>)<sub>2</sub> (Johnson Matthey Alfa Products), AgNO<sub>3</sub> (Strem Chemicals), Cd(NO<sub>3</sub>)<sub>2</sub>·4H<sub>2</sub>O and Mn(NO<sub>3</sub>)<sub>2</sub>·4H<sub>2</sub>O (Merck). All these salts were dried under

vacuum for at least 24 h before use. The concentrations of their stock solutions (except for Ag<sup>+</sup>) were standardized by complexometry using the appropriate coloured indicators.<sup>38</sup> The concentration of the Ag<sup>+</sup> solution was determined by potentiometric titration against NaCl.

### Microcalorimetric measurements

Microcalorimetric experiments were performed using the 2277 Thermal Activity Monitor Microcalorimeter (Thermometric). Titrations were carried out at 25 °C on 2.7 mL of ca.  $10^{-4}$ – $10^{-3}$  M solutions of the ligands in methanol using a glass cell of 4 mL. The heats of formation of the complexes were measured after addition of  $15 \times 15$  µL aliquots of  $10^{-3}$ – $4 \times 10^{-2}$  M of M(ClO<sub>4</sub>)<sub>*n*</sub> ( $M^{n+}$  = Cu<sup>2+</sup>, Ag<sup>+</sup> and Pb<sup>2+</sup>) in the same solvent. Chemical calibration was made by determination of the complexation enthalpy of Ba<sup>2+</sup> with 18C6 in water or of Rb<sup>+</sup> with 18C6 in methanol, as recommended.<sup>39</sup> Values of the enthalpies of complexation and stability constants were refined simultaneously from these data using the ligand binding analysis program DIGITAM version 4.1<sup>40</sup> and after correction for the heat of dilution of the metal salt determined in separate titrations without the ligands. The values of the corresponding entropies of complexation were then calculated from the expression  $\Delta G = \Delta H - T\Delta S$ , knowing  $\Delta G = -RT \ln \beta$  and  $\beta$  from spectrophotometry or microcalorimetry. In the case of very stable 1 : 1 complexes ( $\log \beta_{11} > 5$ ), assumed to be totally formed at each addition of metal salt before the 1 : 1 stoichiometry, the values of the enthalpies of complexation were also obtained with a good agreement from the slopes of the linear plots of the corrected cumulated heats exchanged against the number of moles of metal ions added until the 1 : 1 stoichiometry.

### Proton NMR titration experiments

Several aliquots (up to 2–3 equiv.) of the salt solutions (0.5 M) in CD<sub>3</sub>OD were added to CDCl<sub>3</sub> solutions ( $1 \times 10^{-2}$  M) of the ligands directly in the NMR tube. The salts used were Ag and Zn triflates, and Hg and Pb perchlorates. Due to the low solubility of Hg perchlorate in MeOH, it was necessary to decrease the concentration of the ligand ( $0.5 \times 10^{-3}$  M) and of the salt ( $5 \times 10^{-3}$  M). In this case, the ligand was dissolved in a mixture CDCl<sub>3</sub>–CD<sub>3</sub>OD (4 : 1, v/v). The spectra were recorded on a Varian Unity 300 Spectrometer after each addition of the salts. The temperature of the NMR probe was kept constant at 22 °C.

### Transport experiments

The ion transport across a liquid membrane was done using an apparatus similar to that employed by Lamb *et al.*<sup>29</sup> The membrane phase (50 mL of a  $7 \times 10^{-5}$  M solution of the calixarene in CH<sub>2</sub>Cl<sub>2</sub>), the receiving phase (25 mL of doubly distilled and deionised water) and the source phase (7 mL of a  $5 \times 10^{-3}$  M aqueous solution of metal picrate), were placed in a thermostated vessel. The apparatus was maintained at 25 °C and the phases stirred at 150 rpm. The experiments were repeated, at least, three times. The appearance of the picrate ion in the receiving phase was followed by UV spectrophotometry at regular time intervals. Experiments with no carrier

present were performed, yielding negligible transport rates, except in the cases of copper, lead and mercury, which were probably due to the formation of neutral complexes of these cations with picrate anion. The experimental procedure has already been described in detail elsewhere.<sup>17</sup>

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