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Tri(diethyl)amide with Alkali, Alkaline Earth,
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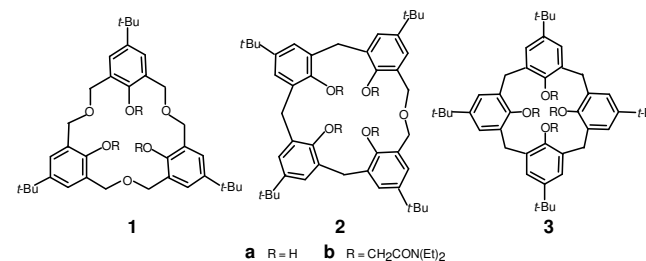
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Graphical Abstract

Binding Properties and Molecular Mechanics Calculations of *p*-*tert*-Butylhexahomotrioxacalix[3]arene Tri(diethyl)amide with Alkali, Alkaline Earth, Transition and Heavy Metal CationsPaula M. Marcos^{a,b,*}, José R. Ascenso^c, Peter J. Cragg^d^aFac. de Ciências da Universidade de Lisboa, Dep. de Química/CCMM, Edifício C8, 1749-016 Lisboa, Portugal^bFac. de Farmácia da Universidade de Lisboa, Av. Prof. Gama Pinto, 1649-003 Lisboa, Portugal^cInstituto Superior Técnico, Complexo I, Av. Rovisco Pais, 1049-001 Lisboa, Portugal^dSchool of Pharmacy and Biomolecular Sciences, University of Brighton, Brighton BN2 4GJ, UK

The binding properties of cone **1b** with alkali, alkaline earth, transition (Mn^{2+} , Fe^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} and Zn^{2+}) and heavy metal (Ag^+ , Cd^{2+} , Hg^{2+} and Pb^{2+}) cations have been assessed by extraction studies of metal picrates and proton NMR titrations. Molecular mechanics calculations were also performed. The results are compared to those obtained with the analogues **2b** and **3b**.



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**Binding Properties and Molecular Mechanics Calculations of
p-tert-Butylhexahomotrioxacalix[3]arene Tri(diethyl)amide with
Alkali, Alkaline Earth, Transition and Heavy Metal Cations**

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Abbreviated title: Metal Binding by Hexahomotrioxacalix[3]arene Tri(diethyl)amide

Abstract

The binding of alkali, alkaline earth, transition (Mn^{2+} , Fe^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} and Zn^{2+}) and heavy metal (Ag^+ , Cd^{2+} , Hg^{2+} and Pb^{2+}) cations by cone *p-tert*-butylhexahomotrioxacalix[3]-arene tri(diethyl)amide (**1b**) has been assessed by extraction studies of metal picrates from water to dichloromethane and proton NMR titration experiments. Molecular modelling techniques were also employed to complement the NMR data. The results are compared to those obtained with the dihomooxacalix[4]arene (**2b**) and calix[4]arene (**3b**) derivative analogues. Triamide **1b** displays a high extracting ability towards Na^+ , Ba^{2+} , Ni^{2+} , Co^{2+} , Ag^+ and mainly Pb^{2+} (80% *E*). However, these values are lower than those obtained with tetraamides **2b** and **3b**, presumably due to the higher conformational flexibility of **1b**. ^1H NMR titrations indicate the formation of 1:1 complexes between **1b** and all the cations studied, and also that they should be located inside the cavity defined by the phenoxy and carbonyl oxygen atoms.

Keywords: Calixarene, Hexahomotrioxacalix[3]arene, Amide derivative, Cation extraction study, ^1H NMR titration, Molecular mechanics calculation

INTRODUCTION

Since the late 1980s calixarene-based molecules [1,2] have been intensively investigated, mainly as host compounds. They represent an extremely versatile class of macrocyclic receptors, able to bind and selectively transport ions and neutral molecules. The parent compounds are readily available and can be further functionalised on the lower and upper

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3 rims to give a variety of derivatives. Thus, in the field of supramolecular chemistry
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5 calixarenes have been increasingly used as platforms for the construction of more elaborate
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7 host molecules.
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10 In parallel with these developments, homooxacalixarenes [3-5], calixarene analogues
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12 in which the CH₂ bridges are partly or completely replaced by CH₂OCH₂ groups, have also
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14 been investigated. Among them, hexahomotrioxacalix[3]arenes have received significant
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16 attention as receptors, mainly due to their structural features [6]: a cavity formed by a 18-
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18 membered ring, only two basic conformations (cone and partial cone) and a C₃-symmetry.
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20 Their ionophoric capabilities towards metal cations [6-8], ammonium ions [9-10] and
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22 fullerenes [11-13] have been investigated, as well as their applications as selective electrodes
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24 [14], biological models [15-17] and molecular capsules [18-20]. In contrast to the numerous
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26 studies of metal ions complexation by calix[4]arene derivatives containing carbonyl groups at
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28 their lower rims, there have been only a few studies on the metal binding ability of the
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30 homooxacalix[3]arene analogues, namely with ester [21,22] and amide [23,24] groups.
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36 For some years, we have been synthesising dihomooxacalix[4]arene derivatives with
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38 carbonyl containing substituents on the lower rim and studying their binding properties
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40 towards alkali, alkaline earth, transition and heavy metal cations [25-27]. In the course of
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42 these studies, we have now extended our research to the study of hexahomotrioxa-
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44 calix[3]arenes.
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48 In the present work we report the binding properties of *p*-*tert*-butylhexahomotrioxa-
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50 calix[3]arene tri(diethyl)amide (**1b**, Fig. 1), in the cone conformation [23,28], towards alkali,
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52 alkaline earth, transition (Mn²⁺, Fe²⁺, Co²⁺, Ni²⁺, Cu²⁺ and Zn²⁺) and heavy metal (Ag⁺, Cd²⁺,
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54 Hg²⁺ and Pb²⁺) cations. This has been assessed by extraction studies with the corresponding
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56 metal picrates from an aqueous solution into dichloromethane and proton NMR titration
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58 experiment. In the absence of X-ray structures, molecular modelling techniques were
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3 employed to complement the information given by the NMR data. Previous experience has
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5 shown that, for supramolecular complexes, excellent agreement can be obtained between
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7 simple solvent free molecular mechanics models and X-ray data [29] or NMR shifts [30]. The
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9 results are compared to those obtained with the dihomooxalix[4]arene (**2b**) and
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11 calix[4]arene (**3b**) derivative analogues (Fig. 1), in order to analyse the effects of the extra
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13 oxygen bridges present in the macrocyclic ring of **1b**, namely on its conformational
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15 flexibility.
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25 RESULTS AND DISCUSSION

26 Extraction Studies

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32 The ionophoric properties of triamide **1b** towards alkali, alkaline earth, transition and heavy
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34 metal cations were first evaluated by the standard picrate extraction method [31]. The results,
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36 expressed as a percentage of cation extracted (% *E*), are collected in Tables 1 and 2 and
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38 illustrated in Figs. 2 and 3. The corresponding values for tetraamides **2b** [26] and **3b** [32,33]
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40 are included for comparison.
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44 The extraction results obtained with derivative **1b** range from 20 to 50% for the alkali
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46 cations and from 17 to 55% for the alkaline earth cations (Table 1). These data indicate that
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48 triamide **1b** is a reasonably good phase transfer agent, displaying a preference for Ba²⁺ (55%)
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50 and Na⁺ (50%), as has already been observed [23]. Triamide **1b** even shows a peak selectivity
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52 for Na⁺, although less sharp than that of tetraamide **3b** (Fig. 2a). These percentages are
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54 significantly lower than those obtained for tetraamides **2b** and **3b**, except in the cases of Rb⁺
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56 and Cs⁺ with **3** and Mg²⁺ with both compounds. Thus, **1b** is a weaker extractant for both kinds
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58 of cations, presumably due to its higher conformational flexibility. The replacement of the
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3 methylene bridges by dimethyleneoxa bridges in triamide **1b** increases its flexibility. The ΔG^\ddagger
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5 barriers for conformational inversion in CDCl_3 are < 9, 12.9 and 15.7 kcal mol⁻¹ for the parent
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7 calixarenes **1a**, **2a** and **3a**, respectively [34]. Moreover, **1b** possesses only three amide groups
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9 and consequently only six donating sites can surround the cations, compared to the eight sites
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11 of the tetraamides.
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15 Towards transition metal cations a similar situation can be observed. The extraction
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17 percentages obtained with triamide **1b** range from 15 to 45% (Table 2), showing a preference
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19 for Ni^{2+} (45%) and Co^{2+} (39%). Again, these percentages are lower than those of tetraamides
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21 **2b** and **3b**, with the exceptions of Co^{2+} with derivative **2b** and Cu^{2+} with **3b**. Triamide **1b**
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23 shows high extraction levels for the soft heavy metal cations (Fig. 3) and the strongest
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25 preference for Pb^{2+} (80%), a Lewis acid of intermediate nature [35]. Although these values
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27 are still lower than those of tetraamides **2b** and **3b**, derivative **1b** is clearly able to
28
29 discriminate between Pb^{2+} and the other heavy metal ions, unlike the tetraamide derivatives.
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31 Compound **1b** also displays the highest $\text{Pb}^{2+}/\text{Zn}^{2+}$ selectivity ($S = 5.3, 2.4$ and 3.5 for
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33 derivatives **1b**, **2b** and **3b**, respectively). As we have previously observed, triamide **1b**, like
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35 other derivatives containing hard oxygen donor atoms [25,26], shows a clear preference for
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37 soft and of intermediate nature Lewis acids.
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44 The extraction of Na^+ , K^+ , Ag^+ and Cu^{2+} cations by triamide **1b** has already been
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46 carried out with metal picrates, but in different experimental conditions [24]. Despite that, the
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48 trends observed in both cases are broadly similar.
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51 52 53 Proton NMR Studies

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57 To obtain further information on the cation binding behaviour of triamide **1b**, specifically
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59 concerning the binding sites, proton NMR studies were performed. The cations studied were
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3 Na⁺, K⁺, Ca²⁺, Ba²⁺, Zn²⁺, Ag⁺ and Pb²⁺, and in all cases the experimental data were consistent
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5 with the formation of 1:1 complexes only. Variable amounts of the salts were added to **1b** and
6
7 the proton spectra recorded after each addition.
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10 Two different situations were observed after the addition of the salts to ligand **1b**.
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12 These titrations indicate similar behaviour for the divalent cations. With [salt]/[ligand] ratios
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14 lower than 1, both signals of the complexed and uncomplexed ligand are present and sharp in
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16 the spectra (Fig. 4 shows the spectra for Pb²⁺ as an example), indicating that on the NMR time
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18 scale the exchange rate between the two species is slow, at room temperature. This behaviour
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20 reflects the high affinity of ligand **1b** towards these cations, and is consistent with the
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22 extraction results previously obtained, mainly for Pb²⁺. In the case of Zn²⁺ complex, it seems
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24 that it has a higher kinetic stability despite the weak affinity of **1b** for this cation. Upon
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26 reaching 1:1 ratios, all the signals for the free ligand disappear and those of the complexed
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28 ligand remain unaltered after subsequent additions of the salts, indicating a 1:1 metal-to-
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30 ligand stoichiometry. A similar situation was observed for the titration of **1b** with Na⁺,
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32 although with 0.5 equiv of added salt the signals of both species were somewhat broad. In
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34 contrast, titrations of triamide **1b** with K⁺ and Ag⁺ initially induce broadening of the signals
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36 until the [salt]/[ligand] ratio reaches the unity, when the signals become sharp (Fig. 5 shows
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38 the spectra for K⁺ as an example). This indicates a fast exchange rate between the two species
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40 on the NMR time scale, at room temperature. Again, the NMR titration experiments suggest a
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42 1:1 stoichiometry, since no further spectral changes are observed after subsequent additions of
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44 the salts.
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53 Proton NMR data of the free and complexed ligand **1b** are collected in Table 3.
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55 Complexation of the cations affects all the proton chemical shifts in the ligand. The largest
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57 variations are, in general, observed for the aromatic protons and the methylene protons of the
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59 OCH₂CO groups, which move downfield, and by the oxygen bridge equatorial methylene
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3 protons (CH_2OCH_2), which move upfield. The smallest variations are observed for the
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5 protons of the $\text{N}(\text{CH}_2\text{CH}_3)_2$ and *tert*-butyl groups.
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8 It has been observed that the chemical shift changes of the methylene protons of the
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10 OCH_2CO groups in dihomooxalix[4]arene amide [26] and ketones [27,36] derivatives is
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12 upfield for the monovalent and downfield for the divalent cations. A closer examination of the
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14 spectral changes upon complexation indicates that triamide **1b** behaves in a similar way. In
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16 fact, divalent cations (except Ba^{2+}) experience very high downfield shifts, with the highest
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18 value recorded for Pb^{2+} ($\Delta\delta = 0.76$ ppm). The monovalent cations also show downfield
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20 changes, but there are much smaller ($\Delta\delta \leq 0.11$ ppm), and K^+ even shows a small upfield
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22 shift.
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26 For the ArCH_2Ar bridges, the variation in chemical shifts experienced by the
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28 equatorial methylene protons is downfield and much smaller than that of the axial protons, but
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30 the $\text{ArCH}_2\text{OCH}_2\text{Ar}$ bridges behave differently, as reported previously [21,26,27]. The axial
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32 and equatorial methylene protons of the oxygen bridge move upfield and the equatorial
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34 protons experience larger shift variations than the axial ones. The highest differences were
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36 recorded for Pb^{2+} ($\Delta\delta = 0.39$ and 0.10 ppm, respectively) and Ca^{2+} ($\Delta\delta = 0.34$ and 0.05 ppm,
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38 respectively), but in the case of Zn^{2+} these values were practically the same ($\Delta\delta = 0.31$ and
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40 0.28 ppm, respectively). These results suggest that the oxygen bridge conformation changes
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42 significantly upon complexation, with the equatorial protons undergoing a higher shielding
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44 effect. Gutsche [37] has established that the difference in the chemical shifts between the axial
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46 and equatorial protons of the ArCH_2Ar bridges indicates the degree of flattening of the cone
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48 conformation. A value around 0.9 ppm means a regular cone conformation and zero a regular
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50 1,3-alternate conformation. Upon complexation with all cations studied the $\Delta\delta_{\text{Hax-Heq}}$ increases
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52 (see Table 3). If Gutsche's criterion is also applicable to the CH_2OCH_2 bridges, it indicates
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54 that the phenyl groups in triamide **1b** are more flattened than those in calix[4]arenes and
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3 dihomooxacalix[4]arenes and stand up when the cations enter into the ionophoric cavity,
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5 resulting in a more regular cone conformation upon complexation. Again, Pb^{2+} and Ca^{2+}
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7 cations show the highest differences ($\Delta\delta = 0.61$ ppm) and Zn^{2+} the lowest ($\Delta\delta = 0.35$ ppm).
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10 A systematic observation of the data reveals that the complexation with K^+ and Ba^{2+}
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12 produces only small downfield variations on the aromatic protons ($\Delta\delta \leq 0.04$ ppm) compared
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14 to those produced by the other cations ($\Delta\delta \approx 0.25$ ppm). The deshielding effect observed for
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16 the aromatic protons indicates the involvement of the phenolic oxygens in complexation, as
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18 reported previously [38]. Thus, that difference observed among the cations suggests that for
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20 K^+ and Ba^{2+} the contribution of the phenolic oxygens in complexation should be relatively
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22 small and less important than that of the carbonyl oxygens [21]. For example, Ba^{2+} shows a
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24 $\Delta\delta = 0.04$ ppm for the aromatic protons and a $\Delta\delta \approx 0.16$ ppm for the methylene protons of the
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26 $\text{N}(\text{CH}_2\text{CH}_3)_2$ groups (attached to the carbonyl groups). The largest shift changes shown by the
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28 protons adjacent to the oxygen donor atoms can be explained in terms of variations of both
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30 shielding and deshielding effects of the aromatic rings and carbonyl groups upon cation
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32 binding to those donor atoms. Therefore, this suggests that the cations must be inside the
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34 cavity defined by the phenoxy and carbonyl oxygen atoms. The cations should be bound into
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36 that cavity through metal-oxygen interactions, in a geometrical arrangement that should
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38 depend on the nature of each cation.
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45 The magnitude of the chemical shift variations for triamide **1b** follows the order: Pb^{2+}
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47 $> \text{Ca}^{2+} \approx \text{Zn}^{2+} > \text{Na}^+ > \text{Ba}^{2+} \approx \text{Ag}^+ \approx \text{K}^+$. This order seems to indicate a preference for the
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49 divalent cations, independently of their nature and size.
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Molecular Modelling Studies

Solvent free geometry optimised structures of **1b** with metal ions are expected to correlate with solid state structures though not necessarily with extractability from an aqueous solution, as the solvent will have a significant influence on both ligand geometry and ligand - metal interactions. Calculations were therefore restricted to those complexes for which NMR data were collected in non-coordinating CDCl₃ where solvent free calculations should correlate well. Representative binding modes for metal complexes are illustrated in Fig. 6. Closest interactions, distances relative to the plane defined by the three alkyl ether oxygen atoms and distances between aromatic centroids are given in Table 4.

The results of these simulations indicate that K⁺ sits in the plane of the macrocyclic ether interacting with both alkyl and aryl ether oxygen atoms (Fig. 6a). This is not consistent with the NMR data, as K⁺ induces the same type of chemical shifts than do the other cations studied. Na⁺ is held 0.6 Å below this plane (Fig. 6a), but interacts strongly with aryl ether oxygen atoms. The alkali metals impose the flattest macrocycle conformation with distances of 6.6 Å between aromatic ring centroids. Among the cations that display the greatest NMR shifts, Ca²⁺ and Zn²⁺ are predicted to be held tightly and symmetrically within the lower cavity defined by the aryl ether and carbonyl oxygen atoms (Fig. 6b). Both have short oxygen - metal interactions with the lower rim aryl ether, consistent with the significant NMR shifts observed for the ArH and OCH₂CO protons. Interestingly, both Ca²⁺ and Zn²⁺ display anion coordination to perchlorate and triflate oxygen atoms, respectively.

The optimised geometries of the Pb²⁺, Ba²⁺ and Ag⁺ complexes (Fig. 6c) show the cations weakly bound within the lower macrocyclic cavity and closer to the carbonyl oxygen atoms. In the case of Ba²⁺, this is consistent with its location indicated by the NMR shifts. The NMR data also corroborate the weak interaction of **1b** with Ba²⁺ and Ag⁺, but the model does

not satisfactorily explain the behaviours of Pb^{2+} and K^+ , in terms of strength of interaction and location inside the cavity, respectively.

CONCLUSIONS

Extraction studies with metal picrates from an aqueous solution into CH_2Cl_2 have shown that, for all cations studied, triamide **1b** is in general a good extracting agent. **1b** displays a preference for Na^+ , Ba^{2+} , Ni^{2+} , Co^{2+} , Ag^+ and the highest extraction percentage (80%) for Pb^{2+} . However, the comparison with the tetraamides **2b** and **3b** indicates that **1b** is a weaker extractant, presumably due to its higher conformational flexibility. Triamide **1b**, like analogues **2b** and **3b** that contain hard oxygen donor atoms, shows a clear affinity for soft metal cations and those of intermediate nature, such as Ag^+ and Pb^{2+} , respectively. NMR studies indicate that **1b** forms 1:1 complexes with all the cations studied. The structures of these complexes show that the cations should be encapsulated in the cavity composed of the phenoxy and carbonyl oxygen atoms. In general, a good agreement was obtained between molecular mechanics models and the NMR data.

MATERIALS AND METHODS

Extraction Studies

Equal volumes (5 mL) of aqueous solutions of metal picrates (2.5×10^{-4} M) and solutions of the calixarenes (2.5×10^{-4} M) in CH_2Cl_2 were vigorously shaken for 2 min, and then

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3 thermostated in a water bath with mechanical stirring at 25 °C overnight. After complete
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5 phase separation, the concentration of picrate ion in the aqueous phase was determined
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7 spectrophotometrically ($\lambda_{\max} = 354$ nm). For each cation-calixarene system the absorbance
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9 measurements were repeated at least four times. Blank experiments showed negligible picrate
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11 extraction in the absence of a calixarene. The details of metal picrate preparation have already
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13 been described [25,39].
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20 **Proton NMR Titration Experiments**

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25 Several aliquots (up to 2-3 equiv) of the salt solutions (0.5 M) in CD₃OD were added to
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27 CDCl₃ solutions (1×10^{-2} M) of ligand **1b** directly in the NMR tube. The salts used were Na
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29 and K thiocyanates, Ca and Pb perchlorates, and Ba, Ag and Zn triflates. The spectra were
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31 recorded on a Varian Unity 300 Spectrometer after each addition of the salts. The temperature
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33 of the NMR probe was kept constant at 22 °C.
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39 **Molecular Modelling Studies**

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44 Energy minimised structures were calculated for complexes of **1b** with dissociated metal salts
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46 to mirror those used in the NMR experiments (NaSCN, KSCN, Ca(ClO₄)₂, Ba(CF₃SO₃)₂,
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48 Zn(CF₃SO₃)₂, AgCF₃SO₃ and Pb(ClO₄)₂). The coordinates of the ligand and a cation held
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50 within the cavity defined by the amide groups were taken from an X-ray structure [15]. The
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52 initial structure for each complex was generated by systematically changing the cation. An
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54 unconstrained geometry optimisation was then carried out on each structure using the Merck
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56 Molecular Force Field (MMFF94) within the Spartan '04 software suite [40].
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Table 1. Percentage extraction of alkali and alkaline earth metal picrates into CH₂Cl₂ at 25 °C^a

	Li ⁺	Na ⁺	K ⁺	Rb ⁺	Cs ⁺	Mg ²⁺	Ca ²⁺	Sr ²⁺	Ba ²⁺
Ionic radius ^b /Å	0.78	0.98	1.33	1.49	1.65	0.78	1.06	1.27	1.43
1b	25	50	32	27	20	17	34	41	55
2b^c	71	96	99	92	66	14	93	90	91
3b^d	63	95.5	74	24	12	9	98	86	74

^a Values with uncertainties less than 5 %.

^b V. M. Goldschmidt, *Skrifter Norske Videnskaps-Akad. Oslo, I, Mat.-Naturv. Kl*, **1926**; data quoted in I. Marcus, *Ion Properties*, Marcel Dekker, New York, 1997, pp 46-47.

^c Data taken from Ref. [26].

^d Data taken from Ref. [32].

Table 2. Percentage extraction of transition and heavy metal picrates into CH₂Cl₂ at 25 °C^a

	Mn ²⁺	Fe ²⁺	Co ²⁺	Ni ²⁺	Cu ²⁺	Zn ²⁺	Ag ⁺	Cd ²⁺	Hg ²⁺	Pb ²⁺
Ionic radius ^b /Å	0.83	0.78	0.75	0.69	0.73	0.75	1.15	0.95	1.02	1.18
1b	19	19	39	45	24	15	40	37	31	80
2b^c	76	43	35	50	48	39	98	88	74	92
3b^d	–	–	–	–	14	28	99	97	–	97

^a Values with uncertainties less than 5 %.

^b R. D. Shannon and C. T. Prewitt, *Acta Cryst.* **1969**, B25, 925; **1970**, B26, 1046; data quoted in I. Marcus, *Ion Properties*, Marcel Dekker, New York, 1997, pp 46-47.

^c Data taken from Ref. [26].

^d Data taken from Ref. [33].

Table 3. Proton chemical shifts (δ , ppm) of ligand **1b** and its 1:1 metal complexes

	<i>t</i> -Bu	NCH ₂ CH ₃		NCH ₂ CH ₃		CH ₂ OCH ₂			OCH ₂ CO	ArH
						eq	ax	$\Delta\delta$		
1b	1.08	1.13	1.16	3.34	3.38	4.62	4.94	0.32	4.57	6.98
1b + Na ⁺	1.21	1.19	1.22	3.19	3.44	4.27	4.73	0.46	4.68	7.20
1b + K ⁺	1.16	1.15	1.20	3.17	3.45	4.33	4.81	0.48	4.53	7.00
1b + Ca ²⁺	1.24	1.23	1.26	3.31	3.52	4.28	4.89	0.61	5.06	7.29
1b + Ba ²⁺	1.15	1.14	1.22	3.14	3.49	4.31	4.88	0.57	4.63	7.02
1b + Zn ²⁺	1.24	1.27	1.28	3.41	3.61	4.31	4.66	0.35	4.98	7.28
1b + Ag ⁺	1.16	1.16	1.21	3.21	3.48	4.39	4.88	0.49	4.60	7.10
1b + Pb ²⁺	1.24	1.28 ^a		3.41	3.58	4.23	4.84	0.61	5.33	7.25

^aTriplets overlapped.

Table 4. Summary of molecular modelling experiments

Complex	Position of cation ^a (Å)	Close M ⁿ⁺ - O interactions ^b (Å)	Aromatic centroid separation (Å)	
1b·Na⁺	-0.61	aryl ether	2.43	6.6
		alkyl ether	2.93	
1b·K⁺	0.24	aryl ether	2.73	6.6
		alkyl ether	2.96	
1b·Ca²⁺	-2.96	carbonyl	2.34	5.4
		perchlorate	2.56	
1b·Ba²⁺	-5.75	carbonyl	6.53	5.4
1b·Zn²⁺	-2.23	triflate	1.96 ^c	5.8
		carbonyl	2.12	
1b·Ag⁺	-6.25	carbonyl	4.47	5.5
1b·Pb²⁺	-5.22	carbonyl	4.05	5.3

^aRelative to the plane defined by the three alkyl ether oxygen atoms in **1b**.

^bMean distance of three closest contacts unless otherwise stated.

^cSingle interaction.

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FIGURE 1 Structural formulae of calixarenes.

FIGURE 2 Percentage extraction (% *E*) of metal picrates into CH₂Cl₂ at 25 °C vs the cation ionic radius (*r*). (a) Alkali and (b) Alkaline earth metals.

FIGURE 3 Percentage extraction (% *E*) of heavy metal picrates into CH₂Cl₂ at 25 °C.

FIGURE 4 300 MHz ¹H NMR spectra of **1b** in CDCl₃ at 22 °C. (a) free ligand, (b) upon addition of 0.5 and (c) 1 equiv of Pb(ClO₄)₂.

FIGURE 5 300 MHz ¹H NMR spectra of **1b** in CDCl₃ at 22 °C. (a) free ligand, (b) upon addition of 0.5 and (c) 1 equiv of KSCN.

FIGURE 6 Representative binding modes determined by molecular mechanics for metal complexes studied by NMR (a) Na⁺, K⁺ (b) Ca²⁺, Zn²⁺ (c) Ba²⁺, Ag⁺, Pb²⁺. Counter ions have been removed for clarity.

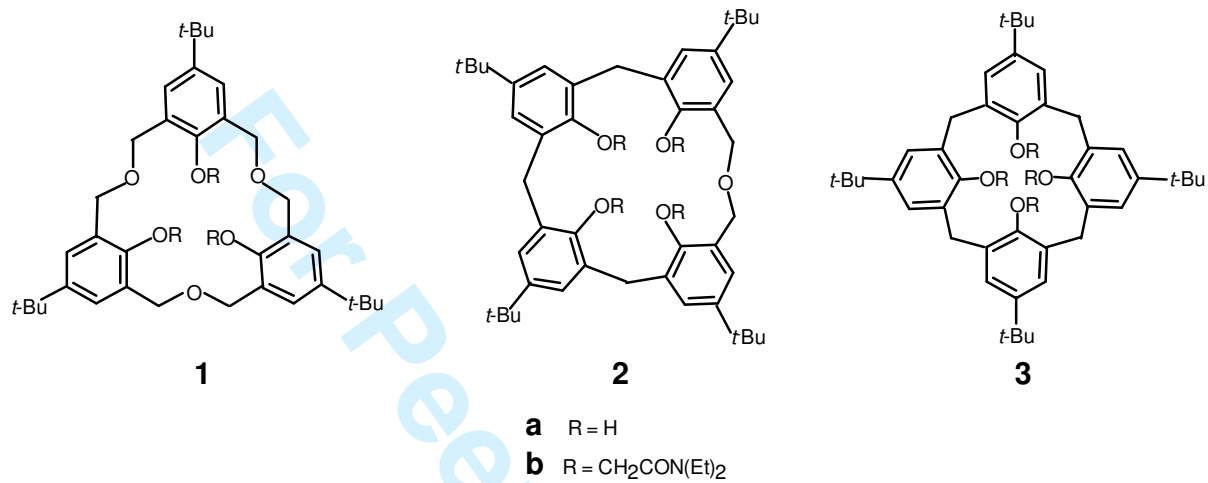
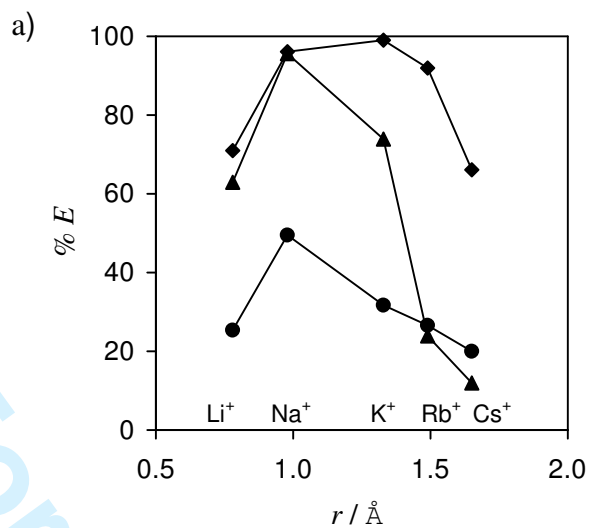
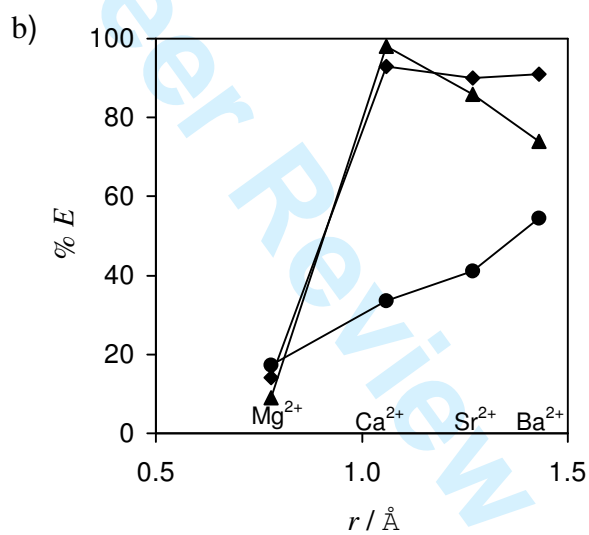


Figure 1



1b(●) 2b(◆) 3b(▲)



51 **Figure 2**

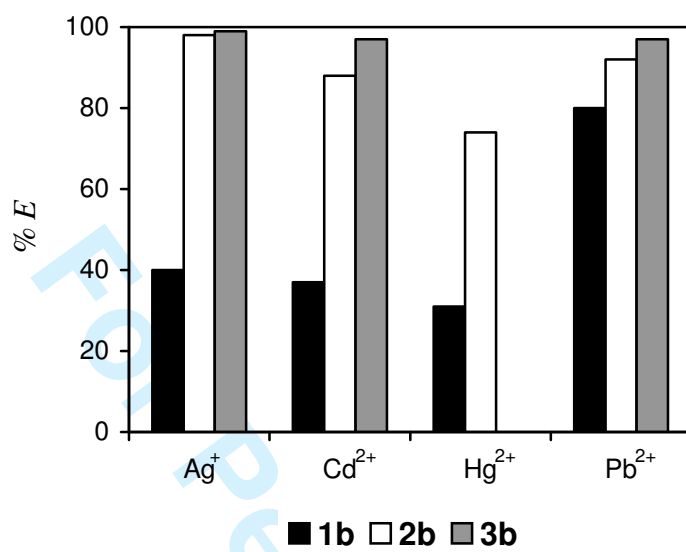


Figure 3

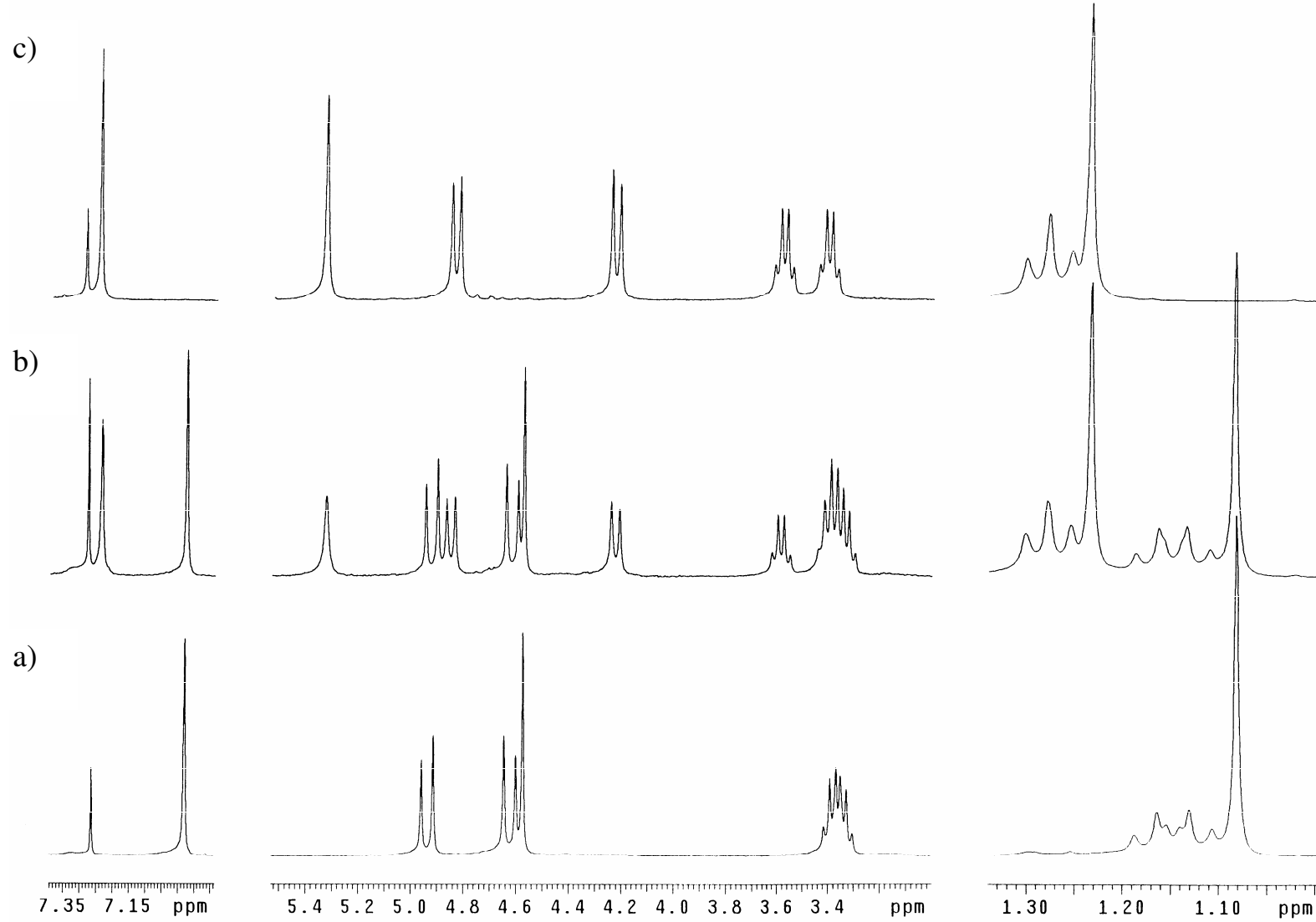


Figure 4

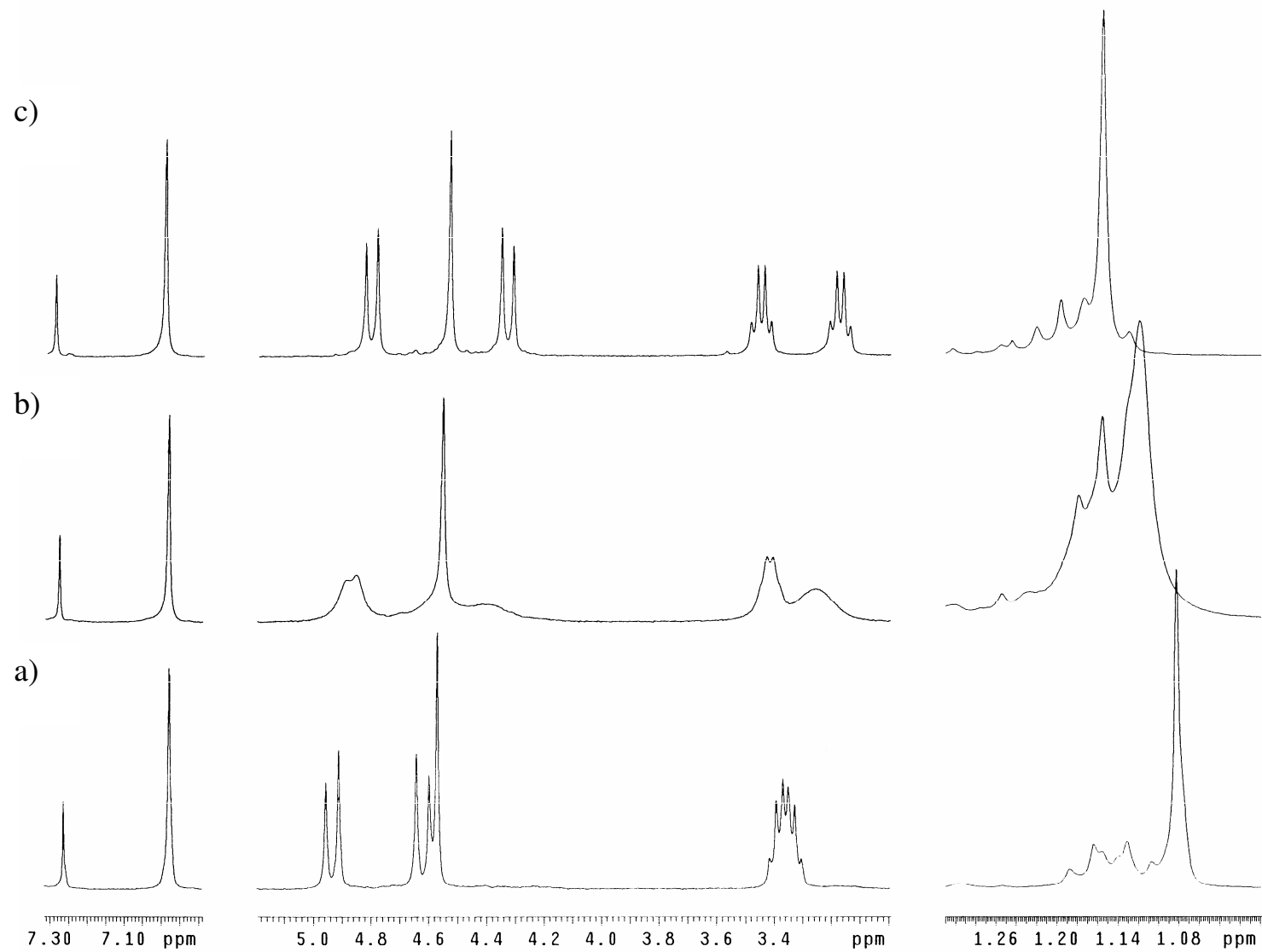


Figure 5

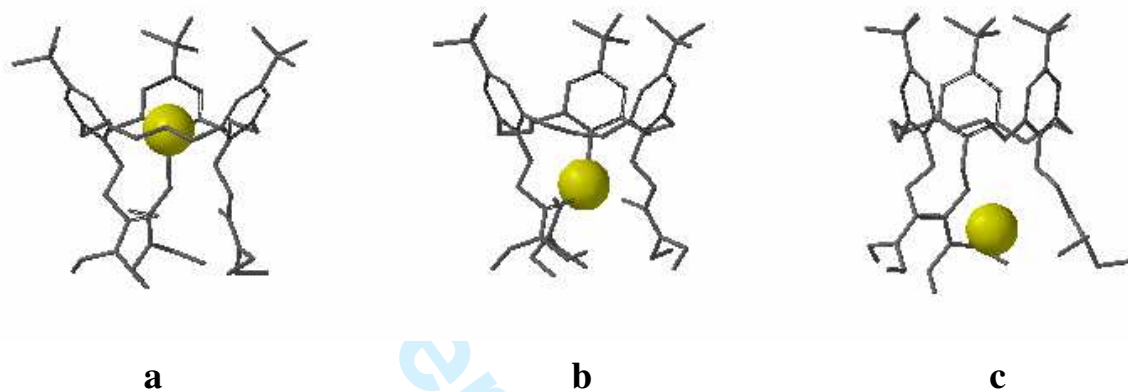


Figure 6

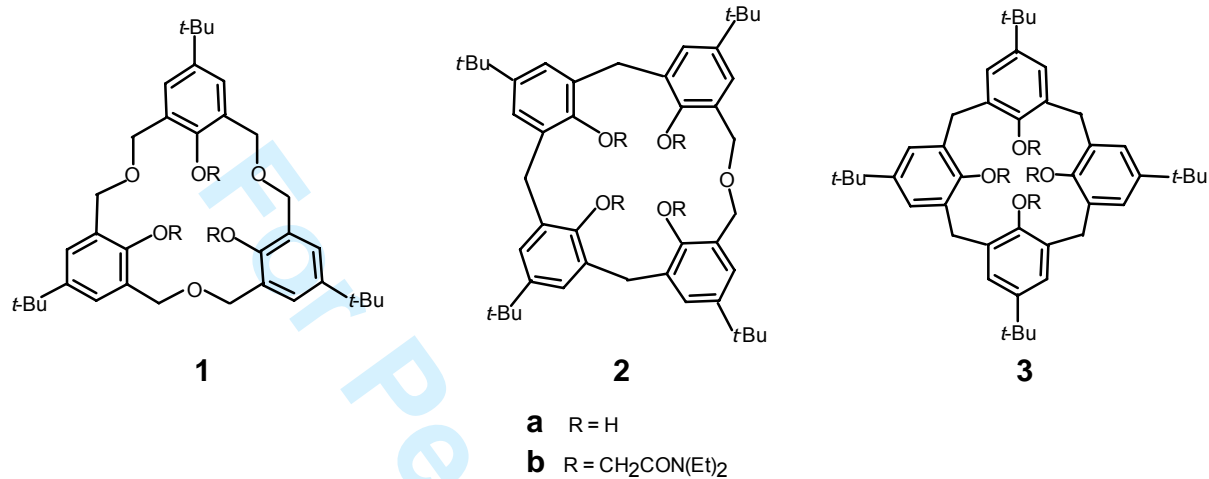
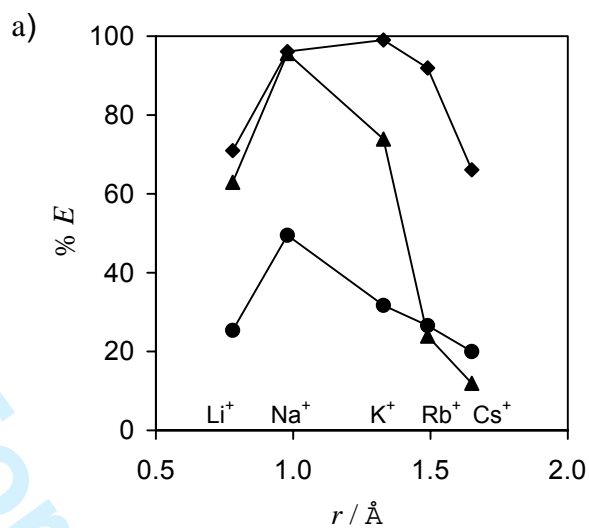


Figure 1



1b(●) 2b(◆) 3b(▲)

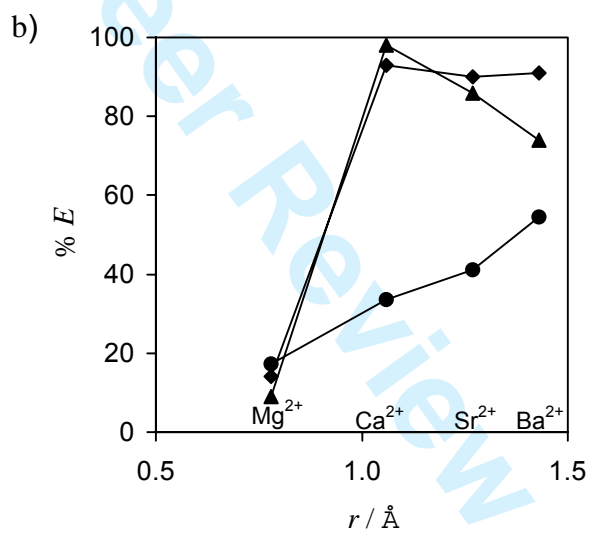


Figure 2

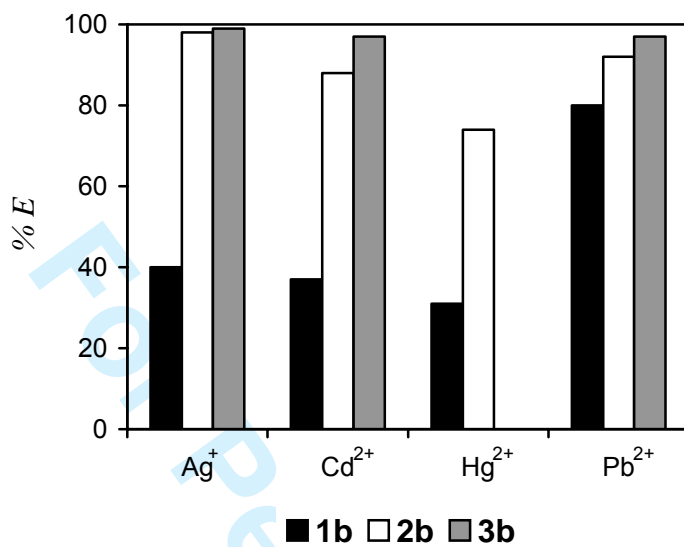


Figure 3

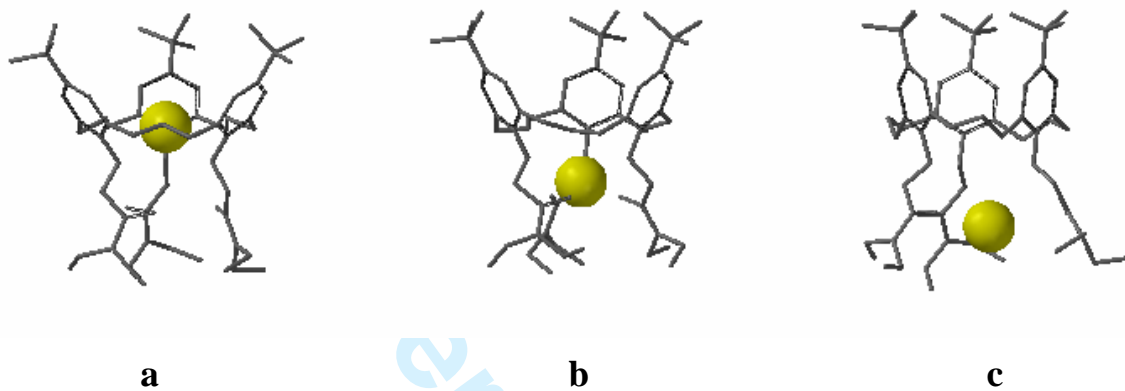


Figure 6