An Overview on Metal Cations Extraction by Azocalixarenes

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Abstract

In this overview, our main aim is to present the design, preparation, characterization, and extraction/sorption properties of chromogenic azocalix[4]arenes (substituted with different groups) toward metal cations. Azocalixarenes, which contain a conjugated chromophore, i.e. azo (-N=N-) group are synthesized in "*one-pot*" procedures in satisfactory yields. A wide variety of applications is expected by the functionalization of the side arms. Some of them are used to complex with metal ions. These macrocycles due to their bowl-shaped geometry are indeed used as hosts allowing ionic or organic guests to coordinate onto their cavity. The azocalixarene based ionophores are generally applied in various fields such as catalyst recovery, power plant, agriculture, metals finishing, microelectonics, biotechnology processes, rare earths speciation, and potable water purification. Besides these, they find applications in the area of selective ion extractions, receptors, optical devices, chemical sensor devices, the stationary phase for capillary chromatography, ion transport membranes, and luminescence probes etc. This survey is focused to provide overview an of the versatile nature of azocalix[*n*]arenes as highly efficient extractants for metal ions treated as pollutants.

Keywords: Calixarene; Azocalixarene; Complexation; Extraction; Transition metals; Host-guest chemistry; Supramolecular chemistry.

Introduction

Heavy metal contamination of various surface waters or groundwater is of great concern because of the toxic effects of there metal ions to plants, animals and human beings [1-4]. Therefore, effective removal of heavy metal ions from water or various industrial effluents is very important and

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has attracted considerable research and practical interest. Several methods, such as chemical precipitation, ion exchange, reverse osmosis and sorption, etc. have been used to remove metal ions from various aqueous solutions [2-4]. Among these methods, sorption has increasingly received more attention in recent years due to simplicity, relatively low-cost and effective in removing toxic ions especially, at medium to low ion concentrations12 [2-5].

The importance of controlling the levels of environmental pollutants has generated increasing interest in the development of novel sensors [6,7]. Moreover, from environmental and economic view point, there remains a need for more selective and effective extractants for toxic and harmful metals from waters and soils [8]. The challenge is to find complexation components that selectively extract those harmful metals from a mixture and allow them to be released in pure form. In this respect, the supramolecular chemistry has provided a much better solution to the search for molecular structures that can serve as building blocks for the production of sophisticated molecules by anchoring functional groups oriented in such a way that they delineate a suitable binding site. As a result, researchers of this area have focused on calixarenes due to their ability to act as preorganized complexing agents, carriers, and potential biomimics as well as their ability to undergo multiple functionalizations [9, 10].

Calixarenes are ideal frameworks for the development of chromogenic ionophores in the molecular recognition of ionic species of chemical and biological interest since the incorporation of a suitable sensory group into the calixarene molecule results in a tailored chromogenic receptor. These compounds have lately attracted considerable attention because of their potential as enzyme mimics [11].

The name "*Calixarene*" was introduced by Gutsche, an American chemist in 1978 to describe a homologous series of macrocyclic oligomers, which are obtained from the condensation of formaldehyde with *p*-alkylphenols under alkaline conditions [9]. The usage of this word ("*Calix*" means "Beaker / Vase" in Latin and Greek) was suggested in particular due to the shape of the

tetramer, which can (and generally does) adopt a bowl or beaker like conformation and indicating the possibility of the inclusion of "Guest" molecules like other macrocyclic compounds (cyclodextrins and crown ethers) (Fig. 1).
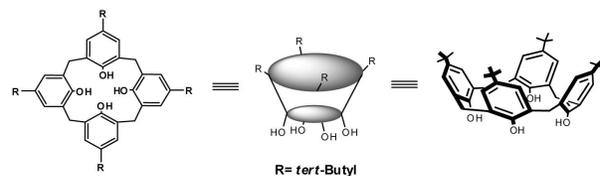

Figure 1. Different structural representations of calix[4]arene.

The chemistry of calix[n]arenes [n = 4-8] is well represented in the literature due to the convenient approach toward their synthesis [12]. Extraction, transport, stability constant and colorimetric measurements, augmented by NMR, X-ray and computer simulation studies provide evidence that many of the *lower rim* derivatives of calixarenes have very significant ionophoric properties for cations, several with good selectivity within groups of metals [13,14].

Much of the interest in the calixarenes has been derived from their promise as selective and useful complexation agents. This depends in part simply on the presence of cavities, but for the more sophisticated applications of complexation and catalysis, it is also necessary that appropriate binding sits should be incorporated onto the backbone of calix moiety. Thus, several novel calixarene derivatives have been synthesized by the modification of *upper* or *lower rims* of these molecules (Fig. 2) [15-17].
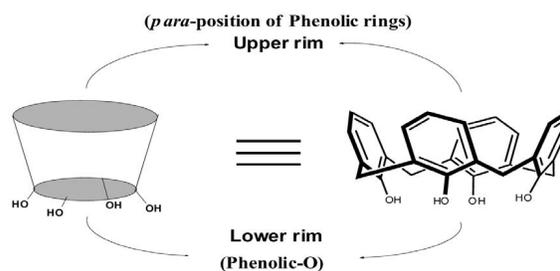

Figure 2. Schematic representation of "*upper*" and "*lower*" rims of calix[4]arene.

Calixarenes derived from phenol can undergo chemical modification by the introduction of various functionalities at the phenolic -OH groups (*lower rim*) [10, 18]. This type of chemical modification was first introduced by Gutsche as part of conformational studies in calix[n]arenes [19], since then this method has been widely used by several research groups to produce pendant ether, carboxylate, ester, amide, phosphine, *vic*-dioxime, and keto derivatives [20-22]. In addition, the easy removal of *ter-butyl* groups attached to phenyl rings at *para*-position makes it possible to affix a large variety of functional groups to the *upper rim* of calixarenes. As expected, most of the reactions that have been carried out on calixarenes are electrophilic substitution reactions (Fig. 3).
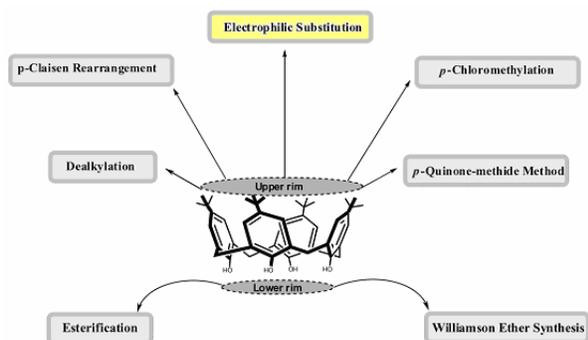

Figure 3. **The derivatization schemes of *p-ter*-butylcalix[4]arene.**

Azocalix[n]arenes are the most widely used class of dyes due to their versatile application in various fields such as the dyeing of textile fibre and the colouring of various materials, and for plastics, biomedical studies, and advanced applications in organic synthesis [23]. Moreover, azo groups bring to calixarenes a chromogenic activity. These compounds are an important class of organic colorants and consist of at least a conjugated chromophore azo (-N=N-) group and two or more aromatic rings. The color properties of organic dyes depend on both the presence of the chromophore groups and the crystallographic arrangement of molecules in the solid state (Fig. 4) [24].

Pertaining to all these subjects, several azocalix[n]arene derivatives have been synthesized [25-27]. It has also been found that these compounds act as excellent host molecules for the selective binding of metal ions. The present initiative is to elaborate and present an overview of those studies dealing with azocalix[n]arenes and related compounds. This is a continuation of our previous articles concerning azocalixarene complexes with transition metal ions and with soft metal ions; where azocalixarene complexes with metal ions are described up to 2005 [28,29]. In this review article the references are cited up to 2010. Since the number of reports concerning azocalixarene complexes with metal ions is enormous, only selected examples are given.
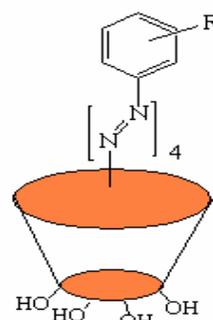

Figure 4. **The derivatization schemes of azocalix[4]arene.**

Design and synthesis of azocalixarene structures

Azocalixarenes, which are generated by the electrophilic substitution reaction of nitrogen atoms at the *p*- position unit of the calixarene structure, have several isomers based on the position of the nitrogen atoms and the ring size. The first reported calix[4]arene diazo coupling involved the reaction of *p*-nitrobenzenediazonium tetrafluoroborate with calix[4] arene [30]. Unexpectedly, it proceeded in an autocatalytic fashion to give **4e** as the almost exclusive product with only small amounts of **4a-d**. *p*-Methyl, *p*-methoxy and *p*-carboxy benzene diazonium chlorides react in comparable fashion to give the corresponding tetrasubstituted compounds **4e** (Fig. 5) [31].

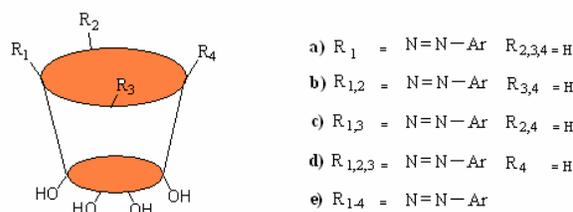a) R_1 = N=N—Ar $R_{2,3,4} = H$

b) $R_{1,2}$ = N=N—Ar $R_{3,4} = H$

c) $R_{1,3}$ = N=N—Ar $R_{2,4} = H$

d) $R_{1,2,3}$ = N=N—Ar $R_4 = H$

e) R_{1-4} = N=N—Ar

Figure 5. **Structures of *mono-*, *di-*, *tri-* and *tetra-* azocalix[4]arenes.**

As a general procedure, *p*- substituted azocalix[n]arenes are obtained by the diazo-coupling reaction. At first, the calix[n]arene is prepared by the debutylation of *p-tert*-butyl calix[n]arene [32]. Then, a solution of diazonium chloride, which was prepared from carbocyclic and heterocyclic amines, water and concentrated hydrochloric acid is heated to 40-45 °C while being stirred until a clear solution is obtained. This solution is cooled down to 0-5 °C, and a solution of sodium nitrite in water is then added dropwise, maintaining the temperature below 5 °C. The resulting solution is stirred for an additional 30 min in an ice bath, before an excess nitrite is destroyed by addition of urea. This solution is buffered with solid sodium acetate [33].

Synthesis and characterization

Calixarenes are often described as "macrocycles with unlimited derivatization possibility" because of their versatility and utility as host molecules, which mostly come from the ease in the synthesis of the basic platform and ready functionalization at *lower* and *upper rims* to construct variously modified three-dimensional structures [11].

Considerable attention was devoted in mid-1990s, and this has continued unabated in the 2000s. This comes as no surprise, because the utility of the azocalixarenes for the majority of potential applications, depend upon suitable modification of the parent azocalix[n]arene compounds. Many papers have been described the synthesis and dyeing properties of *p*-phenylazocalix[n]arene, and several studies are published with respect to *p*-hetaryl azocalix[n]arene. Especially, azocalix[n]arenes based on heterocyclic amines have been developed, and the resultant azocalixarene have been higher tinctorial strength and give brighter dyeing than those derived from aniline-based diazo components [34].

Chawla and coworkers have synthesized and characterized five new chromogenic azocalix[4]arenemonoquinones and examined their interaction with alkali metal cations (Li^+, Na^+, K^+, Rb^+ and Cs^+) by UV-visible spectroscopic and cyclic voltammetric techniques. It has been determined that **5a** selectively exhibits a significant bathochromic shift in its UV-visible spectrum on interaction with potassium ion in comparison to its treatment with other alkali metal cations (Fig. 6) [35].
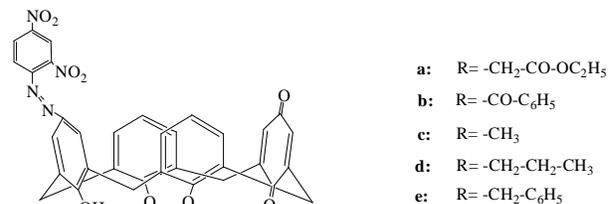

a:	R= -CH$_2$-CO-OC$_2$H$_5$
b:	R= -CO-C$_6$H$_5$
c:	R= -CH$_3$
d:	R= -CH$_2$-CH$_2$-CH$_3$
e:	R= -CH$_2$-C$_6$H$_5$

Figure 6. **Structures of azocalix[4]arenemonoquinones.**

The design and synthesis of abiotic host molecules for recognition of ionic and molecular species constitute important research objectives to resolve complex chemical, biological and environmental issues. In this context, phenolic macrocycles represented by calix[n]arenes [36] occupy a special position due to their unique molecular architecture that can be suitably tailored into potential receptors by facile derivatization [37,38].

Beer and coworkers [39] have reported the synthesis and electrochemical characteristics of various calix[4]quinones possessing ether, ester and amide functionalities. No work have been published on calix[4]arenequinones possessing additional chromogens that can provide unique opto-electrochemical sensing properties for ionic and molecular recognition [40]. Accordingly, they have described the synthesis, characterization and evaluation of a series of chromogenic azocalix[4]arenemonoquinones in the hope to obtain new ionic filters and sensor materials for alkali metal ion recognition.

In Lhotak laboratories, the design of receptors is based on the well-recognized complexation ability of calix[4]arene tetraacetates. If they are immobilized in the *cone* conformation, these compounds exhibit high complexation affinity [41] towards alkali metal cations. To visualize the complexation phenomenon, they appended chromophore groups on the opposite *upper rim* [42]. This functionalization allows the monitoring of complexation using UV-vis spectroscopy.
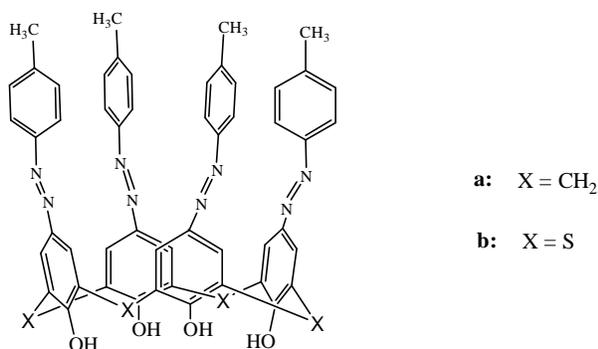
Figure 7. **The derivatization schemes of azocalix[4]arene and thioazocalix[4]arene.**

Figure 8. **The derivatives of azocalix[4]arene 7.**

The synthesis of the receptors was started by a diazo coupling reaction between pristine calix[4]arene **6a** [43] or thiacalix[4]arene **6b** [44] and *p*-methylbenzenediazonium tetrafluoroborate. This reaction proceeded smoothly in a THF solution under pyridine catalysis and yielded the corresponding tetraazo compounds **6a** and **6b** in high yields (Fig. 7). It has been noticed that metal cation used as a base dramatically influences the conformational outcome of the reaction [45]. Hence, the template effect of alkali metal carbonates (Na_2CO_3, K_2CO_3 and Cs_2CO_3) was screened using small scale alkylation of **6a** and **6b** with an excess of ethyl bromoacetate followed by the subsequent ^{1}H NMR analysis of crude reaction mixtures.

Structures of azocalixarenes

Azocalix[4]arenes have been widely used as three-dimentional building blocks for the construction of artificial molecular receptors capable of recognizing neutral molecules, cations and anions as well as determined their thermal behaviours. Thus, having chosen the *p-ter*-butylcalix[4]arene as the basis for derivatization, one of the synthetic schemes as depicted below (Fig. 8) has been developed to enable the derivatization of the molecule. The azocalix[4]arenes were designed to take advantage of the well-established binding interactions of chromogenic molecules and transition metal cations. The syntheses of azocalix[4]arenes **7a**-**7d** were based on the previously published procedures [46].
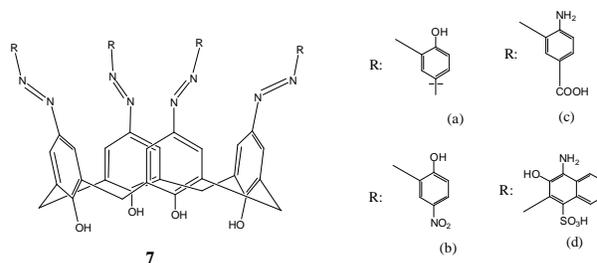
The synthetic utility of the azocalix[4]arene is well known and can be bridged across the *upper rim*. Briefly, calix[4]arene was prepared by debutylation of *p-ter*-butylcalix[4]arene. The coupling reaction of calix[4]arene with 4-carboxyphenyldiazonium chloride in aqueous THF gave *p*-(4-carboxyphenylazo)calix[4]arene in 85% yield. It was confirmed by the appearence of an azo (–N=N–) band at 1470 cm^{-1} in the IR spectra of this compound.

In our laboratory, we synthesized four new diazo coupling calix[4]arene containing two groups in its structure for the recognition of diazo and neighbouring groups (-OH for **7a**, **7b** and **7d**, -NH_2 for **7c**). These groups enable azocalix[4]arenes to be converted to its diazo derivative with phenol derivatives (*p-ter*-butylphenol, *p*-nitrophenol, *p*-aminobenzoic acid and 1-amino-2-hydroxy-4-sulphonic acid) into acetic acid in the presence of $NaNO_2/H_2SO_4$ easily. After 12 h stirring, azocalix[4]arenes **7a-d** were isolated in very high yield, and these four newly synthesized azocalix[4]arenes were characterized by spectroscopic techniques.

The lower field signals of the hydroxyl group of the two azocalix[4]arenes (**7a** and **7b**) resonated at ca. 9.2-10.8 and 8.2-10.2 ppm, respectively and these are typical for intramolecular hydrogen bonding protons as reported in the literature [47]. It was observed that the *ter*-butyl protons of **7a** resonated at 1.3 ppm. Although the compounds have two aromatic rings in different environments, they gave a multiple peak due to overlapping. Also, the phenyl protons were also observed as a multiple at 6.5-7.9 ppm. The peaks of aromatic protons of the azocalix[4]arenes were complicated. The

azocalix[4]arene **7c** showed peaks located in the range of 5.2 ppm, which are attributed to the $-NH_2$ groups. The lower field signals of the carboxyl groups of this compound resonated at ca. 11.0 ppm. On the other hand, **7d** shows a singlet at 5.1 ppm for $-NH_2$ group. It was observed that the $-SO_3H$ protons of 7d resonate at 13.8 ppm.

Recently, a number of chemically modified calixarenes have been synthesized and they can be used as hosts for simple anions [48-51]. Thus, we have targeted the synthesis of an extractant based on the calix[4]arene framework for the dichromate anion [52]. For this purpose, we have designed extractants (**9** and **11**) having a proton-switchable binding moiety for anions. A preliminary evaluation of the binding efficiencies of the extractants **9** and **11** was carried out by solvent extraction of $Na_2Cr_2O_7$ from aqueous solution into dichloro methane at different pH (Fig. 9).
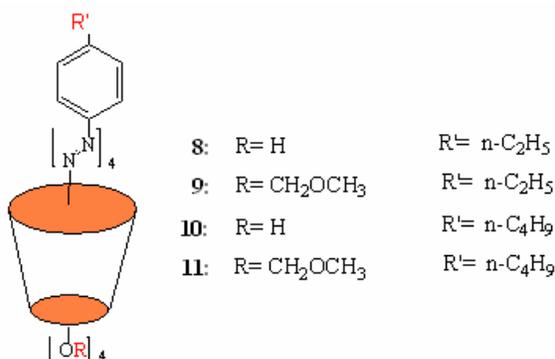

Figure 9. p-Substituted azocalix[4]arenes and their ketone derivatives.

Calix[n]arenes have been widely used as three-dimensional building blocks for the construction of artificial molecular receptors which are capable of recognizing neutral molecules, cations and, more recently, anions [53,54]. In another article, we reported the synthesis of a novel azocalix[4]arene bearing a *di*-acetone azocalix[4]arenes moiety at the *lower rim* and chromogenic azo groups or nitro-, azo-, chloro- and methyl- groups at the *upper rim*. This approach could provide an efficient methodology for improving non-linear optical (NLO) materials and for biologically and/or chemically important cations and amines.

In the field of our investigation, sixteen new *mono-* (**12a-h**) and *di*-substituted (**13a-h**) azocalix[4]arene derivatives were synthesized from 2-, 3- and 4-nitro, 4-phenylazo, 3- and 4-chloro or 2- and 4-methyl aniline and their properties have been investigated. These conversions were carried out by reacting 25,26,27-tribenzoyl oxy-28-hydroxy-5,11,17-tri-(*ter*-butyl)calix[4]arene and 25,27-diacetonyloxy-26,28-dihydroxy-11,23-di-(*ter*-butyl)-calix[4]arene with aryldiazonium salts in DMF/methanol for 2 h at 5 °C (Fig. 10) [55,56].
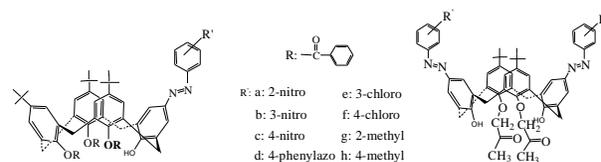

Figure 10. *mono-* **and** *di*-**Substituted azocalix[4]arene derivatives.**

Diazo coupling was accomplished selectively at the *p*-position of calix[4]arene ring to give compounds in moderate to excellent yields. These results which are in accordance with the greater nucleophilicity of the carbocyclic amine ring have been shown earlier in the case of formulation carbocyclic amine derivatives. The structures of the azocalix[4]arenes were unambiguously confirmed by their analytical and spectral data.

The infrared spectra of all the azocalix[4]arenes show broad band within the range 3523-3450 cm^{-1} corresponding to υ_{OH}. The FT-IR spectra also recorded a strong band located at 1495-1480 cm^{-1} which can be assigned to -N=N-. The other υ_{max} values at 1760-1700 cm^{-1} and 1268-1250 cm^{-1} can be assigned to $\upsilon_{C=O}$ and υ_{C-O}, respectively.

It can be suggested that these azocalix[4]arenes do not exist in keto-hydrazo form B but as anionic form D in the solid state (Fig. 11). The *mono*-azo substituted calix[4]arenes may exist in four possible tautomeric forms in solutions; namely the azo-phenol form (A), the quinone-hydrazone form (B) and their deprotonated anions C and D, respectively (Fig. 11). The results are in agreement with the work of Ertan, N. and our recent paper [57-59].
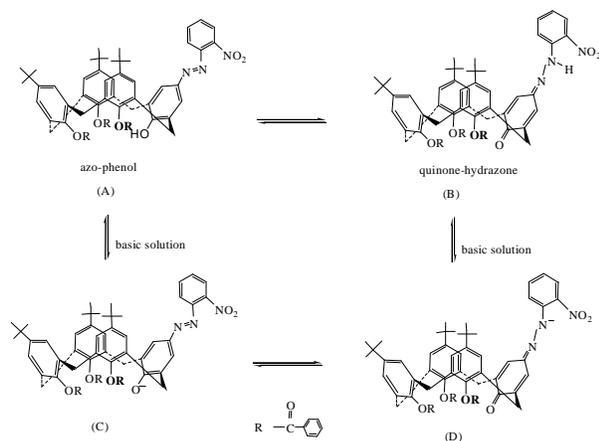
Figure 11. **Tautomeric forms of *mono*-substituted azocalix[4]arene derivative.**

According to ^{1}H NMR in DMSO, the structure of azocalix[4]arene derivatives **12a-h** and **13a-h** do not only impose the *cone* conformation in the liquid state, but also provide evidence for asymmetric structural features. Each of the derivatives had two pairs of doublets around 3.2 - 4.2 and 3.8 - 4.9 ppm (J_{AB} = 12.8 - 13.4 Hz), respectively, which indicates that a *cone* conformation with non-equivalent methylene bridges in the neighboring and remote positions relative to the *p*-substituted arene moiety. Selective *di*-substituted azocalix[4]arenes **13a-h** have been used as precursors for the synthesis of diazo coupled calix[4]arene by electrophilic substitution reactions.

However, *cone* conformation of flexible azocalixarenes (**12a-h**) could be stabilized by intramolecular H-bonding involving OH group. Consecutively, the partial *cone* conformation may be formed with DMSO by breaking the H-bonds resulting a typical AB pattern for the methylene bridge protons (ArCH$_2$Ar) of the azocalix[4]arene moiety. As previously reported [60], this can be explained by the presence of chiral substituents and indicates a significant degree of structural rigidity.

Metal cations extraction by azocalixarenes

Understanding the nature of ion solvation is important to know the relative inclination for a specific ion to cross an aqueous/non-aqueous phase barrier. More directly stated, the higher the energy of hydration for an ion, the more difficult to move this ion into non-polar media where the solvation of ions is ordinarily much weaker. Generally, this trend follows the charge/size ratio; larger the ratio, more difficult to extract an ion from an aqueous solution [61, 62].

The solvation of the host molecule and its complexes play a similar role in terms of the phase barrier, but this is often neglected. The host molecule is solvated in the organic media (diluent) and this solvation is at least partially disrupted by the arrival and coordination of the guest species. This disruption represents an energy penalty that may be more or less compensated by subsequent solvation of the host-guest complex. What if the host molecule contained a volume of space that was inaccessible to solvent molecules, but would allow to guest species? This should enhance the extraction capability towards these guests, as there would be no desolvation required in the protected cavity [63].

Supramolecular chemistry has developed new synthetic methods directed to research areas such as host-guest chemistry, molecular and ionic recognition, supramolecular catalysis, self-organization, aggregation, signal transfer, allosteric effects, etc. Much of the attention has been paid to the search for molecular structures that can serve as building blocks for the production of sophisticated molecules by anchoring functional groups oriented in such a way that they delineate a suitable binding site. This was achieved with the development of macrocyclic molecules such as synthetic crown ethers, cryptants, spherands, cyclophanes, natural cyclodextrins and calixarenes [64].

The interaction between a host and a guest to form a complex can involve one or more of the following features; hydrogen bonding, electrostatic attraction, π - π stacking, van der Waals attraction and charge-transfer interactions. The experimental measure of the collective magnitude of such interactions can be expressed in a variety of ways, including the rate of transport through a membrane (liquid or supported liquid), or the percentage of extraction in phase transfer processes from water into an immiscible solvent.

The actual acquisition of the data of determining complexation capabilities similarly employs a variety of experimental techniques. In addition to the powerful spectrophotometric methods available, most often NMR and/or UV-vis spectrometry various other techniques are also being used [19, 28].

Liquid-liquid extraction of alkali metal cations

Numerous works have been reported concerning calixarene complexes with alkali metal ions; some examples are shown here. The complexation properties of calixarenes **14a–g** toward alkali metal cations have been investigated. Among them calixarenes **14f** and **14g**, each substituted by four identical groups, served for comparison purposes. In experiments, the alkali metal picrates were extracted from water into dichloromethane [65]. One may conclude that the order of decreasing complexing properties with alkali metal ions is: calixarenes with ester groups > calixarenes with methyl groups > calixarenes with benzyl groups (Fig. 12).
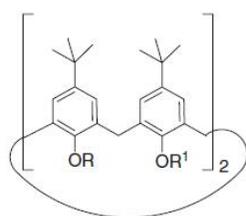

	R	R^1
a	CH$_2$Ph	Me
b	CH$_2$Ph	CH$_2$COOEt
c	CH$_2$Ph	CH$_2$CH$_2$OMe
d	CH$_2$CH$_2$OMe	Me
e	CH$_2$CH$_2$OMe	CH$_2$COOEt
f	Me	Me
g	CH$_2$CH$_2$OMe	CH$_2$CH$_2$OMe

***Figure 12.* Ester, methyl and benzyl group derivatives of calix[4]arene.**

The properties of alkali metal binding of 3,6-*syn* and 3,6-*anti* isomers of calix[6]-bis crown **15** were studied using the metal picrate extraction method, i.e. aqueous solutions of the picrate salts were shaken with chloroform solutions of the receptors. It was found that *syn*- and *anti*-**15** have high extraction ability and selectivity toward Cs$^+$, the Cs$^+$/Na$^+$ selectivity of *syn*-**15** being higher than that of *anti*-**15** (Fig. 13) [66].

Kim and coworkers reported that new chromogenic diazophenylcalix[4]arenes **16** and **17** were synthesized in *cone* conformation (Fig. 14).

Compound **16** with *ortho*-carboxyl groups in CH$_3$CN solution preferentially bind with alkaline earth and transition metal ions, whereas no significant changes in absorption spectra could be observed in the presence of alkali metal ions.
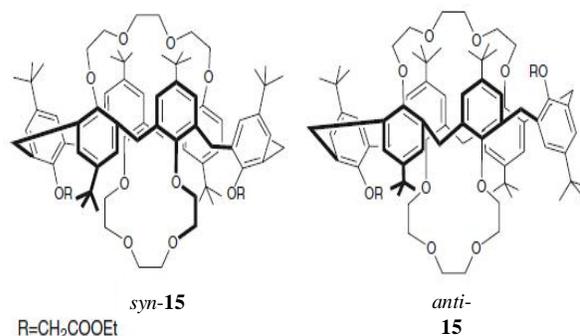

syn-**15**   *anti*-**15**

R=CH$_2$COOEt

***Figure 13.* 3,6-*syn* and 3,6-*anti* isomers of calix[6]-bis crown.**

	R
16	H
17	Et
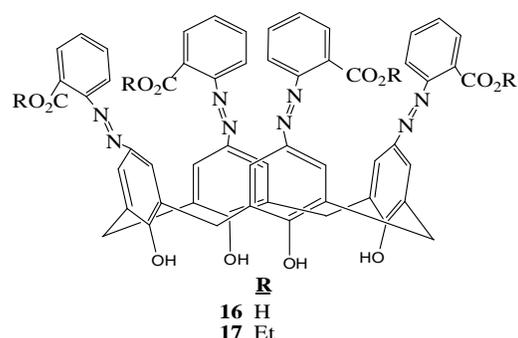
***Figure 14.* Structures of azocalix[4]arene 16 and 17.**

While **17** with the *ortho*-ester groups showed selective complexation properties towards transition metal ions over alkali and alkaline earth metal ions. The detection of metal ions gave rise to bathochromic shifts in the absorption spectra (from orange/yellow to red), which clearly visible even to the naked eye (Fig. 15). According to the selective color changes using both receptors upon cation complexation, one can set up a qualitative analytical routine to screen alkali, alkaline earth, and transition metal ions [67].

Particularly, calixarene chromoionophores have long been studied as specific metal ion indicators since Shinkai and coworkers reported that calix[4]arene having one 4-(4'-nitro phenyl)azophenol unit with three ethyl ester groups shows a Li$^+$ ion selectivity with respect to the UV–

vis band shift [68]. This group has frequently been used in calixarene-based chromoionophores. Because azo group is usually considered to be only a chromogenic center and not a metal-chelating site; to enhance the metal-binding ability, a great number of attempts have been made at the modification of their *lower rim* in azocalix[4]arene. However, azocalix[4]arenes without *lower rim* modification are able to bind transition metal ions effectively [42].

Figure 15. **Color changes of 16 and 17 upon the addition of various metal ions in CH₃CN.**

Many of the Cs-selective ISEs available or reported in literature have limited lifetime of maximum of a couple of months only. One of the investigations [69] was aimed to fabricate an ISE for Cs with a reasonably long life. The 5-(4'-nitrophenylazo)-25,27-bis(2-propyloxy)-26,28-dihydroxycalix[4]arene (Fig. 16) as an ionophore (**18**) was carried out to optimise the membrane composition to obtain the best performance for cesium by varying plasticizers, ion additives and concentration of inner filling solution.
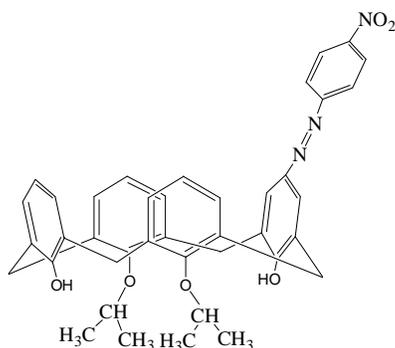

Figure 16. **Structure of 5-(4'-nitrophenylazo)-25,27-bis(2-propyloxy)-26,28-dihydroxycalix[4]arene ionophore.**

Liquid-liquid extraction of alkaline-earth metal cations

Many interesting aspects of complexation of alkali and alkaline earth metal ions were disclosed by studying the absorption behavior of chromophoric groups. However, there are relatively few reports on the design of ionophores for alkaline-earth metal ions. Although, a variety of effective chromogenic ionophores for alkali and alkaline-earth metal cations such as K^+, Ca^{2+}, and Cs^+ have already been developed, those for Ba^{2+} has been rarely reported. Azocalixarenes were particularly attractive for their efficient ionophoric properties towards some of important guest ions such as Ca^{2+} or K^+ ion [70].
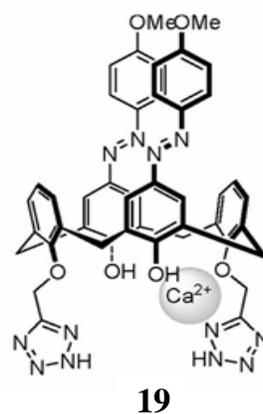
Figure 17. **Structure of 5,17-bis[(4'-methoxyphenyl)azo]-25,27-bis(oxymethyltetrazole)calix[4]arene (19) with Ca²⁺.**

5,17-bis[(4'-methoxyphenyl)azo]-25,27-bis(oxymethyltetrazole)calix[4]arene (**19**) was synthesized by 1,3-dipolar cycloaddition of oxyacetonitrile azocalix[4]arenes activated with trimethylsilyl azide. UV/Vis screening with 14 metal ions showed that **19** is a highly chromogenic sensor for Ca^{2+} (Fig. 17) [71].

Liquid-liquid extraction of transition metal cations

Industrial processes introduce up to a million different pollutants into the atmosphere and the aquatic ecosystem. Heavy metals are one of the groups of these substances, although not all of them are considered harmful to humans. The heavy metal ions are important because of their high toxicity and because of their presence in soils

and waters. The azocalix[4]arene macrocycles could be used effectively in the complexation or extraction of the heavy metals.

A variety of compounds based upon calixarenes having nitrophenylazo, nitro, azo, indophenol and indo-aniline functional groups have been succesfully designed. These compounds exhibited a pronounced chromogenic behaviour toward Na^+, K^+, Cs^+, Ca^{2+}, UO_2^{2+}, and even chiral amines [28]. Shinkai and coworkers have synthesized calix[4]arene with a 4-(4'-nitro phenyl)azophenol and observed the lithium sensitivity of the ionophore [68]. Toth *et al.* also reported the sodium selectivity of related azophenol derivatives [72].

The compounds with diazo groups are not effective for the extraction of Na^+ and K^+. This result has been deduced from the data given in Table 1, it can be seen that compound **20b** exhibits 50.3% extraction of Sr^{2+} cation when the metal nitrate is used. Using metal cations in the hydroxide form causes a decline in metal cation extraction due to higher pH values. Ludwig [73] has observed that the solvent extraction of lantanides is more effective at 2–3.5 pH range.

In the 1960's Pearson explained the differential complexation behavior of metals and ligands (dispersants) in terms of electron-pair accepting Lewis acids [48, 74]. Pearson classified Lewis acids and Lewis bases as being hard soft acid base (HSAB) principle: "*Hard acids prefer to bind to hard bases and soft acids bind to soft bases*".

The compounds **20c** and **20d** show higher selectivity toward Hg^{2+} and Hg^+ than the other compounds do. The above phenomena can be explained by the HSAB principle as -N=N- is a soft base, hence has stronger affinity toward soft than hard metal cations. The strong participation of these compounds containing electron-donating and electron-withdraving groups in complex formation was further confirmed by the results shown in extraction experiments. As compared to other compounds, **20c** is a harder base and prefers Hg^{2+} cation, while **20d** is a softer base and prefers Hg^+ cation (Fig. 18).

In light of our previous experience an extensive survey has been made [46] that pointed out the investigations concerning transition metal binding properties of azocalix[4]arenes **7a-d** (Fig. 8). The aim was to synthesize azocalix[4] arenes with -OH and –NH$_2$ neighbouring to diazo (–N=N–) groups, which may help in solvent extraction. Extraction efficiencies of the azocalix[4]arenes have been carried out by two phase solvent extraction of transition metal picrates (Ag^+, Hg^+, Hg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+}, Zn^{2+}, Al^{3+}, Cr^{3+} and La^{3+}) into chloroform under neutral conditions.

Table 1. **Extraction of metal picrates with ligands.**

Ligand	Picrate salt extracted (%)														
	Na^+	K^+	Sr^+	Ag^+	Hg^+	Hg^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Al^{3+}	Fe^{3+}	Cr^{3+}	La^{3+}
20a	5.8	1.7	-	16.9	51.4	60.2	18.2	1.3	-	5.9	7.1	29.3	-	-	-
20b	-	-	50.3	74.6	72.7	58.6	83.3	81.8	78.9	84.0	84.0	79.1	-	44.7	80.0
20c	-	-	-	-	18.8	51.6	18.4	14.9	12.3	15.4	11.2	19.3	-	-	-
20d	-	-	-	31.0	56.8	35.9	14.3	-	1.3	4.3	-	6.9	-	-	-
21	-	-	-	78.7	76.4	78.0	15.5	-	16.6	-	5.0	-	-	-	-
22	-	3.5	6.2	89.1	72.2	84.2	42.6	6.0	77.3	59.6	5.9	11.8	-	14.1	-
23	-	-	-	10.9	16.0	25.6	8.0	-	2.6	4.3	8.1	-	-	7.1	-

Figure 18. **Structures of substituted azocalix[4]arenes and phenol derivatives.**

Table 2. **Extractions of metal picrates with ligands.**

Ligands	Picrate salt extracted (%)										
	Ag^+	Hg^+	Hg^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Cd^{2+}	Zn^{2+}	Al^{3+}	Cr^{3+}	La^{3+}
7a	66.7	79.0	91.0	11.7	10.9	6.5	9.0	6.0	4.0	11.2	6.0
7b	67.0	68.5	57.1	7.7	10.1	5.7	6.9	2.6	1.2	17.8	5.3
7c	73.0	81.2	65.7	23.4	16.7	8.9	11.4	38.7	3.2	21.8	7.9
7d	-	8.6	9.3	-	-	-	-	-	-	-	-

From the data (Table 2) it can be concluded that azocalix[4]arenes **7a-c** are highy selective for transition metal cations such as Ag^+, Hg^+ and Hg^{2+}. Azocalix[4]arene **7a** containing electron-donating group (*ter*-butyl) is a harder base and prefers the Hg^{2+} cation (91.0%). Azocalix[4]arene **7b** containing electron-withdrawing groups ($-NO_2$) is a softer base and prefers the Hg^+ cation (68.5%).

Figure 19. **Extraction percentage of metal picrates with azocalix[4]arenes.**

Interestingly, it is observed that azocalix[4]arene **7c** shows remarkable change in the extraction of transition metals, especially in the case of Co^{2+} (23.4%), Zn^{2+} (38.7%) and Cr^{3+} (21.8%) due to the presence of $-NH_2$ sites neighbouring to $-N=N-$ groups (Fig. 19). The effectiveness of azocalix[4]arene **7c** in transferring transition metals rather than others indicates that in this case, bridging amine ($-NH_2$) groups appeared to be operative and play an important role at water-chloroform interphase, since the metal ions could possibly be interacted with these soft liganting sites. The other reason for this high binding ability displayed by azocalix[4]arene **7c** may be due to the preorganization and fine tuning of the cation binding sites in the *lower rim* of calixarene moiety, which is immobilized in *cone* conformation possibly prefering such an environment for the complexation of metal cations.

Using the above procedure the deposition of silver from the organic phase is feasible and efficient. An important fact is that calixarenes do not change their extraction properties during electrowinning and can be reused many times. The process is an effective way of electro-reductive stripping, integrating the two separate consecutive operations, i.e. stripping and electrowinning into

one step; in this way the time of the solvent extraction is shorter.

Memon *et al.* has demonstrated [75] a detailed complexation study of calix[4]arene based chemosensor bearing two anthracenyl units as signaling groups on its coordination sphere. The complex formation ability of the chemosensor toward selected transition metals such as Cd(II), Co(II), Cu(II), Ni(II) and Pb(II) has been investigated by UV-visible spectroscopy. Assessment of results reveal that the chemosensor is selective toward Cd(II) and Cu(II). The FT-IR spectroscopic method was applied for further confirmation of the complexation phenomenon. Besides this, a study regarding interference of other metals on complex formation in solution has also supported the efficient binding preference of the chemosensor for Cd(II) and Cu(II). From the results it has been concluded that the chemosensor has compatible coordination sphere to accommodate these metals. The similarities and differences revealed that being soft nature of both metals and because of diagonal relationship in the periodic table their coordination behavior toward N/O-donor ligand may be treated as a test on possibility of the Cu(II) ions to be displaced by Cd(II). It has been expected that the study certainly will help in understanding the hazards of Cd(II) in biological systems.

In our recent study, three series of calixarenes (**24–26**) containing azo groups and functionalized at *lower rim* by acetyl, ketone (**24, 25**) and benzoyl (**26**) groups have been used for the extraction of metal picrates from aqueous solution into chloroform [76]. The functionalization of *lower rim* of calixarenes by these groups was made in order to increase their solubility and their extraction efficiency. All studied compounds have *cone* conformation in solution (Fig. 20). The results are expressed in Table 3 as a percentage of cation extracted (*E%*) and also shown graphically in Fig. 21 and 22.

The experimental results have shown that **26c** efficiently extracts Ag^+ and Hg^{2+} ions, **24b** efficiently extracts Ag^+, Hg^{2+}, Cu^{2+} and Cr^{3+}, and all investigated calixarenes except **25c** are good extractants for Hg^{2+} [76].
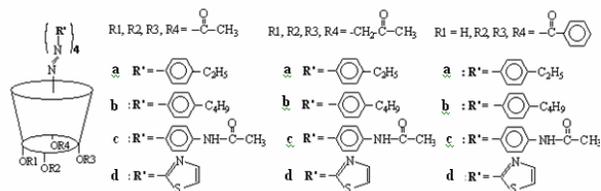

Figure 20. **Ester and Ketone Derivatives of Azocalix[4]arene.**

Table 3. **Extractions of metal picrates with ligands.**

Ligand	Picrate Salt Extracted (%)								
	Sr^{+2}	Ag^+	Hg^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Cr^{3+}
24a	13.0	37.0	69.0	15.0	14.0	34.0	19.0	6.0	39.0
25a	-	28.0	65.0	-	-	1.0	-	-	-
26a	19.0	14.0	67.0	17.0	15.0	32.0	21.0	-	14.0
24b	53.0	87.0	97.0	67.0	44.0	79.0	54.0	60.0	80.0
25b	32.0	55.0	86.0	45.0	26.0	45.0	20.0	18.0	47.0
26b	33.0	58.0	93.0	43.0	35.0	63.0	44.0	48.0	51.0
24c	18.0	52.0	69.0	23.0	24.0	23.0	19.0	23.0	34.0
25c	19.0	68.0	72.0	21.0	15.0	2.0	-	22.0	25.0
26c	17.0	57.0	54.0	21.0	18.0	17.0	17.0	19.0	33.0
24d	23.0	45.0	67.0	22.0	19.0	21.0	22.0	20.0	25.0
25d	15.0	54.0	79.0	24.0	20.0	25.0	30.0	22.0	28.0
26d	21.0	54.0	77.0	20.0	16.0	23.0	20.0	20.0	41.0

Besides a comparison within the data some remarks could be made while looking at the extraction levels of **24b** for Ag^+ (87.0%) and Hg^{2+} (97.0%), which are very superior to others, for Cu^{2+} and Cr^{3+} (79.0% and 80%) are nearly equal and for Co^{2+} (67.0%), Cd^{2+} (60.0%) and mainly for Ni^{2+} (44.0%) are less significant.
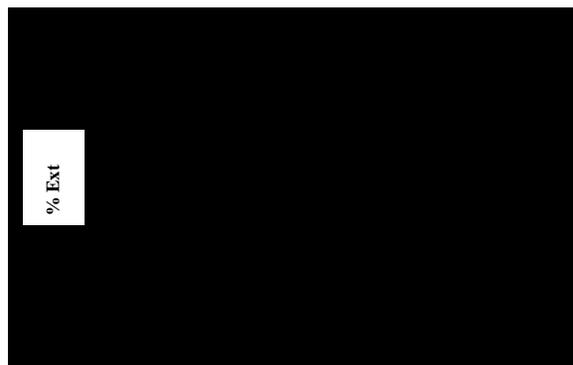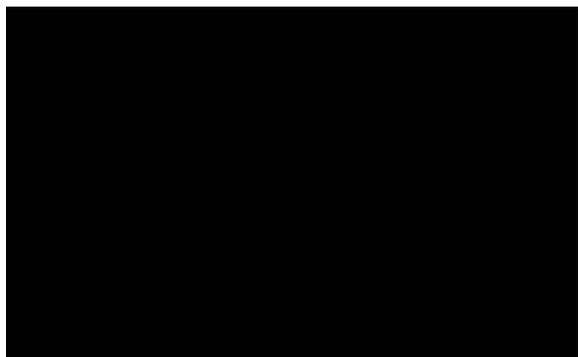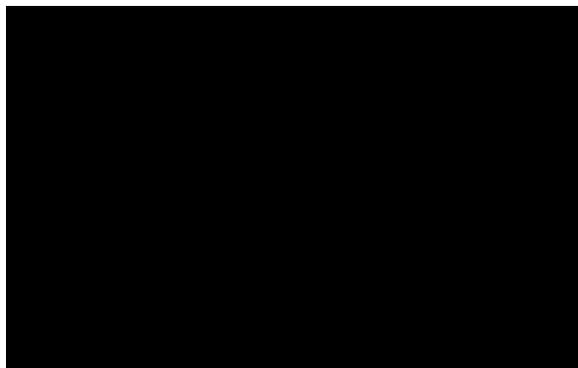
Figure 21. (a) Acetyl, (b) methyl ketone and (c) benzoyl derivatives of azocalix[4]arene extracted (%).
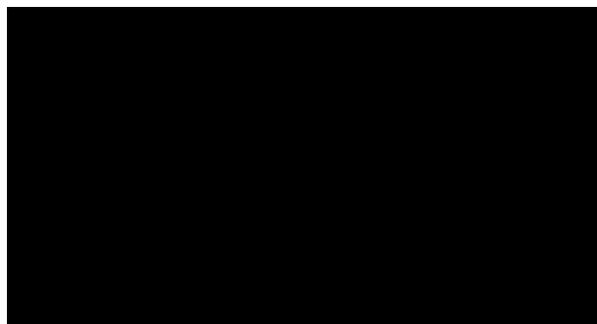

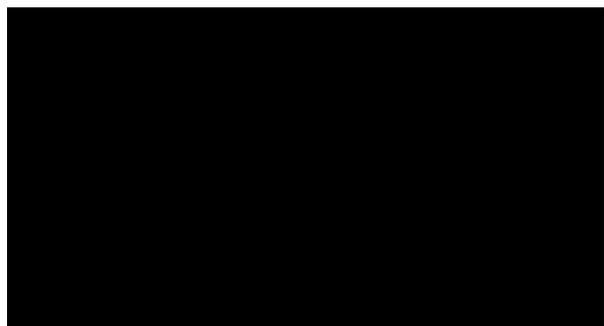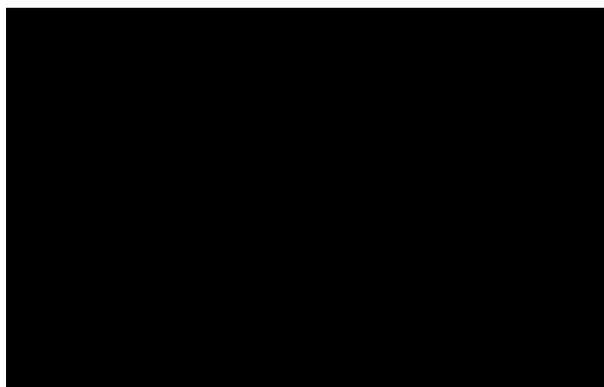**Figure 22.** (a) 4-$\underline{n}$-butyl, (b) 4-asetamid anilin and (c) 2-aminothiazol derivatives of azocalix[4]arene extracted (%).

Our results suggest that the match between the cation and the calixarene cavity dimensions is not an evident factor in selectivity. For example, Co^{2+} and Cu^{2+} have equal ionic radii but both are at the third and last on extractability scale, respectively. Also in case of Zn^{2+} and Cd^{2+} having similar sizes are almost on the opposite ends of that scale for both ketones. With other ester ligands a similar situation is observed for Cu^{2+}, Zn^{2+} and Co^{2+}. Another important remark for one of the smallest cation Cu^{2+} is that it is mostly extracted by ketone **24b**; which also shows strong peak selectivity for Cr^{3+} (80.0%) with nearly double diameter. However, the hard and soft acids and bases (HSAB) principle does not seem to be an important factor in selectivity. Although our ligands contain soft nitrogen donor atoms, they show a very clear preference for Ag^+ a soft Lewis acid and Cu^{2+} of intermediate nature.

Moreover, the soft Lewis acid, Hg^{2+} is one of the most extracted cation. Therefore, no simple explanation for the observed selectivities is apparent from these results, and other factors involving in host and guest phenomenon must be considered. For example, different conformational flexibilities of the calixarenes lead to different arrangements of the donor atoms in the ligating sites and also the cations have different geometrical requirements. Recently, we have investigated the effectivenes of two diazo coupling calix[n]arenes (**27** and **28**), four diazo compounds (phenol derivatives) (**29** - **32**), and three ester derivatives (**33** - **35**) (Fig. 23) in transferring the alkali metal cations (Na^+, K^+) and transition metal cations (Ag^+, Hg^+, Hg^{2+}, Co^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Al^{3+}, Fe^{3+}, Cr^{3+}) from the aqueous phase into the organic phase (Table 4) [77].
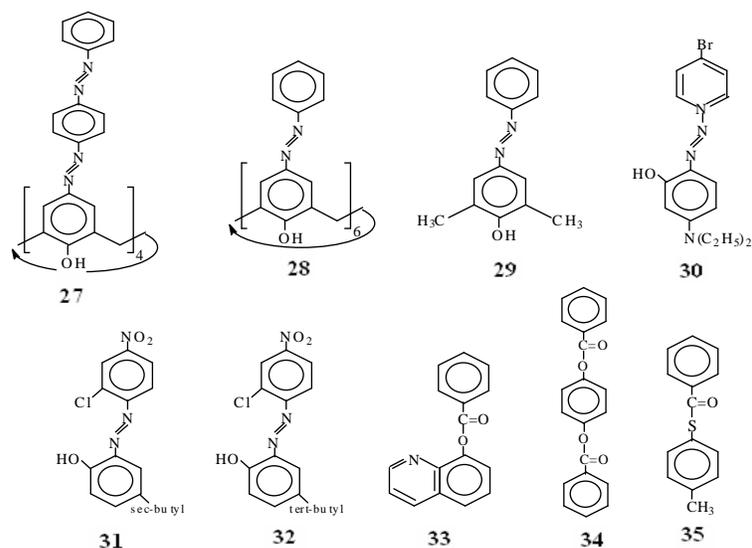
Figure 23. **Calix[n]arenes with different diazo coupling sites.**

Table 4. **Extraction of metal picrates with ligands.**

Ligands	Picrate salt extracted (%)											
	Na^+	K^+	Ag^+	Hg^+	Hg^{2+}	Co^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Al^{3+}	Fe^{3+}	Cr^{3+}
27	-	-	74.6	72.7	58.8	83.3	78.9	84.0	84.0	79.1	-	44.7
28	-	-	22.0	8.0	18.0	-	-	-	-	-	-	-
29	31.0	7.0	23.0	31.0	32.0	-	26.0	24.0	31.0	26.0	-	29.0
30	-	3.5	89.1	72.2	84.2	42.6	77.3	59.6	5.9	11.8	-	14.1
31	-	-	10.9	16.0	25.6	8.0	2.6	4.3	8.1	-	-	7.1
32	-	-	11.2	16.5	12.5	2.0	4.2	-	8.7	-	-	7.4
33	-	-	12.5	8.8	16.8	1.3	2.3	7.1	6.8	12.8	-	9.7
34	-	-	8.1	11.9	18.8	1.4	2.6	1.9	8.1	7.2	-	9.1
35	-	-	2.5	-	8.6	-	2.3	-	-	7.8	-	4.7

Because of the hyperacidity of **27** and **28**, and presence of intramolecular hydrogen bonding the alkali metal cations in acidic media were not extracted as expected. **29-32** contain hydroxy groups at the *para* or *ortho* position. The hydroxy groups at the *ortho* positions form intramolecular hydrogen bonding with diazonium groups thus do not extract alkali metal cations in acidic media. However, **29** extracts lower amounts of alkali metal cations due to the presence of hydroxy groups at *para* positions. The ester compounds were not effective for extracting Na^+ and K^+ cations.
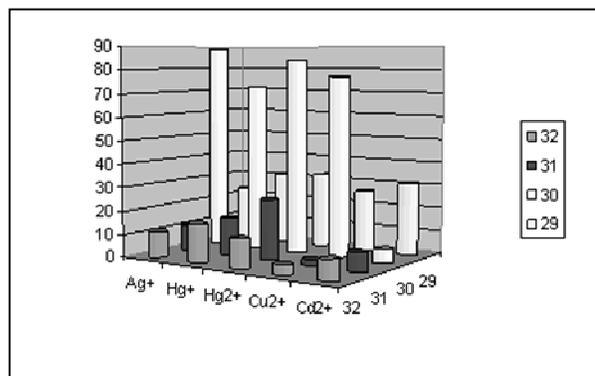

Figure 24. **Extraction percentage of the metal picrates with 29-32 at 25 °C.**

The best extraction efficiency for Ag^+ had been seen with **30** because of more soft ligands (with electron-donating group $-N(C_2H_5)_2$). The extraction efficiency of **31** and **32** was similar because of their similar structure. The extraction efficiency of **29** and **30** was higher than **31** and **32**, which contain electron-withdrawing NO_2 groups (Fig. 24). These groups decreased electron density of diazo goups (-N=N-) and lowered complexation capacity.

The ionophore solvent extraction studies proved **27** to be an efficient extractant and a powerful ligand for alkali and transition metal cations. It is assumed that the double diazo coupling calixarene (**27**) delineating the *upper rim* of the cavity and the aromatic cavity act cooperatively by means of dipole and specific π-interactions for encapsulation for size adapted cationic species. Efficiency for **27** increased in the order $Cr^{3+} < Hg^{2+} < Hg^+ < Ag^+ < Cu^{2+} < Al^{3+} < Co^{2+} < Zn^{2+}, Cd^{2+}$ (Fig. 25).
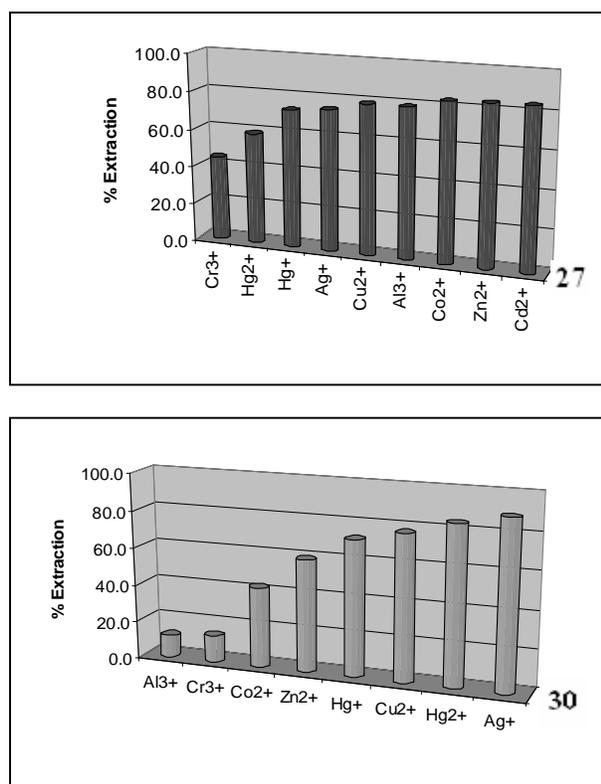

Figure 25. **Efficiency for 27 and 30 increased in the order.**

The most interesting feature of cavitand **27** is its potentiality to form complexes with cationic

guests upon bonding with -N=N- diazo groups via possible participation of π-cation interaction through intra cavity complexation. Strong evidence for complexation of alkali metal and transition metal cations was noted as these salts are readily dissolved in organic solutions of **27**.

The extraction efficiency of **30** was higher than the other compounds due to its soft nature and increased in the order $Al^{3+} < Cr^{3+} < Co^{2+} < Zn^{2+} < Cu^{2+} < Hg^+ < Hg^{2+} < Ag^+$. Generally, hard ligands (hard bases) extract hard cations such as Al^{3+} and Cr^{3+} more effectively; while soft ligands (soft bases) extract soft cations such as Ag^+, Hg^+ and Cd^{2+} (Fig. 25).

In brief, we can say that in these phase transfer experiments the effectiveness of azocalix[n]arenes for transfering the metal cations is reflected by soft π–donor systems and intra-cavity complexation. Generally, a linear relationship between log D *vs* log [L] could be observed with the slope of line suggesting the stoichiometric ratio of calix[n]arene with M^{n+} according to the following equation:

$$M^{n+}{}_{(aq)} + nPic^-{}_{(aq)} + x[L]_{(org)} \rightleftharpoons [M(Pic)_n(L)_x]_{(org)}$$
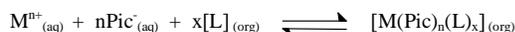
In the case of azocalix[4]arene (**29**) and monomeric diazo derivative of phenol (**30**), the extraction mechanism suggests that metal:ligand ratio is 2:1 for **29** and 1:1 for **30**. Because, **29** has potential to form complexes with cationic guests upon bonding with -N=N- diazo groups with possible participation of π-cation interaction of intra-cavity complexation however, high extraction efficiency of **30** for these cations was obtained because of more soft ligating sites.

Azocalix[4]arenes with linkages at *mono-* and *di-* positions, calix[4]arene derivatives with double methyl ketone and triple benzoyl ester and calix[4]arenes with various connecting chains have been previously reported [55,56]. An alternative pathway has been developed for the synthesis of azocalix[4]arenes in order to increase their affinity toward metal ions and anions. Consequently, two main strategies have been followed. Firstly, different ionophoric groups have been incorporated onto the calixplatform, i.e. 1,3-distal positions on the *lower rim* of calix[4]arenes were substituted

with ester or ketone functionalities. Secondly, the diazotization of calix[4]arene units on the *upper rim* have been performed with different aromatic units containing varying functionalities [78].

Table 5. **Extraction of Metal Picrates with** *Mono-* **and** *Di-* **Azocalix[4]arenas.**

	Picrate Salt Extracted (%)								
Ligand	Sr^{2+}	Ag^+	Hg^+	Hg^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Pb^{2+}	Cr^{3+}
12a	-	-	15.3	6.3	-	-	-	-	6.0
12b	-	-	14.3	12.3	-	-	-	1.2	7.3
12c	-	-	11.3	6.9	-	-	-	-	5.8
12d	-	8.5	47.8	43.1	-	-	-	3.0	19.0
12e	0.9	2.0	18.9	16.4	1.5	4.4	2.8	1.7	5.0
12f	-	-	18.6	11.7	-	-	-	0.3	6.3
12g	1.8	2.0	20.1	16.0	1.2	4.4	2.8	1.5	4.8
12h	1.2	1.8	19.0	15.6	1.5	4.4	2.8	0.9	5.8
13a	-	2.3	22.8	22.0	3.0	4.2	1.0	5.7	11.4
13b	4.0	-	28.0	22.0	2.7	3.6	-	6.7	8.7
13c	-	-	15.6	15.3	0.3	0.6	-	5.4	7.0
13d	1.0	28.0	89.6	89.0	4.0	5.5	12.8	17.0	66.0
13e	2.3	3.6	27.0	23.0	4.6	5.8	-	8.0	8.7
13f	-	4.3	22.0	19.3	5.0	5.5	1.3	4.7	9.0
13g	-	4.6	20.0	19.7	3.7	3.3	-	3.3	7.2

The study was focused on identifying the strategic requirements for the estimation of ionophoric properties of the *upper rim* functionalized azocalix[4]arene derivatives **12a-h** and **13a-h** (Fig. 10) toward selected alkaline-earth and transition metal ions such as Sr^{2+}, Ag^+, Hg^+, Hg^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Pb^{2+} and Cr^{3+}. The extraction properties of azocalix[4]arene derivatives **12a-h** and **13a-h** have been evaluated by solvent extraction of selected metal picrates (Table 5). The results are also shown in bar graphs, which are expressed as a percentage (E%) of cations extracted (Fig. 26a-b).

Unlike the –OH functional groups containing azocalix[4]arene derivatives used in the former studies; the azocalix[4]arene derivatives

contain benzoyl and ketone derivatives are significant in nature mainly due to the positive effect of these functional groups on solubility and leading to higher extraction efficiencies. It could be seen from the data that **13d** has a remarkable extraction efficiency [66.0% Cr^{3+}, 89.6% Hg^+ and 89.0 % Hg^{2+}] as compared to **12d** [19.0% Cr^{3+}, 43.8% Hg^+ and 43.1% Hg^{2+}].
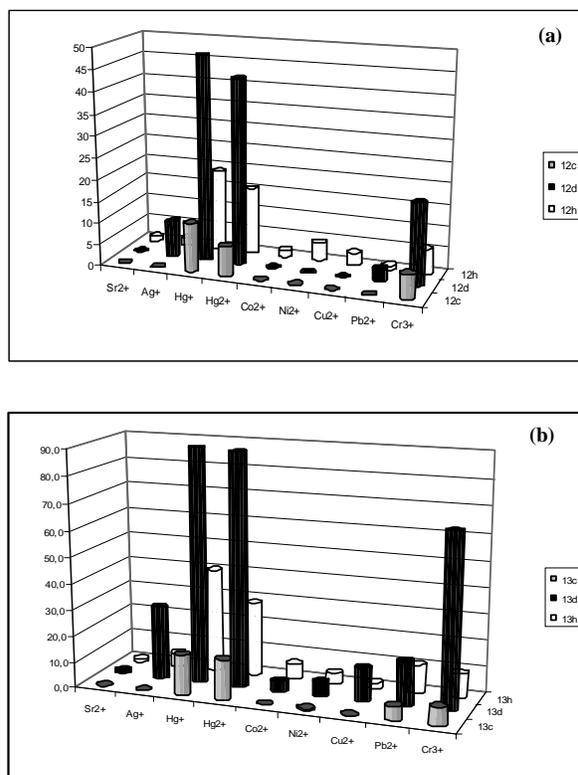
Figure 26. **Extraction percentages of derivatives of** *mono-* **and** *di-* **azocalix[4]arene.**

Phenylazophenylazocalix[4]arenederivativ es **12d** and **13d** displayed different extrac tion behaviors compared to the other substituted azocalix[4]arene moieties. They exhibited poor extraction ability for all metal cations, but they were good extractants for Hg^+ and Hg^{2+}.

In the case of azocalix[4]arenes with *cone* conformation, metal ion is in interaction with the phenol unit of the *upper rim* and azo group(s) in the medium cavity. This arrangement could simultaneously facilitate π-π interactions between metal ions and center of azocalix[4]arene derivatives charged negatively where alkaline-earth or transition metal ions can be bound more

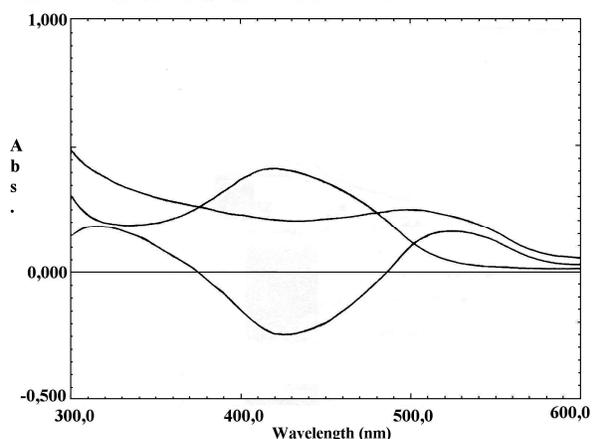strongly into the polar cavity defined by the ester or ketone and azo group(s) [78].

Figure 27. **Absorption spectra of azocalix[4]arene 12d and its mercury complex. (a) 12d solution against DMF blank; (b) the solution 12d and Hg⁺ against water blank; (c) the solution 12d and Hg⁺ against reagent 12d blank.**

Different functionalized azocalixarenes are potentially excellent starting materials for the selective designing of new materials. In another work, the preparation of *di-* functionalized azocalix[4]arene at the *upper rim* followed by their conversion into the bisazoalkyl benzene has lead to new materials for metal sorption (Fig. 28) [79].
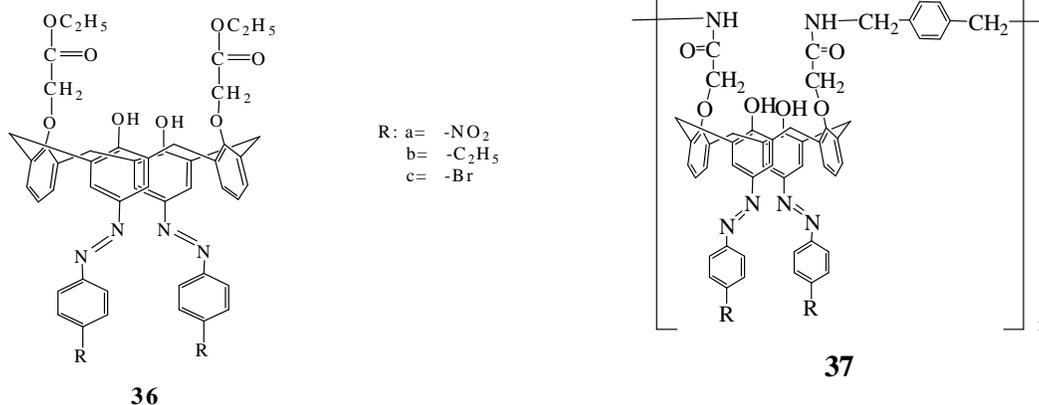
Transport experiments for picrate salts were carried out with a H_2O-$CHCl_3$ system. In liquid-liquid or liquid-solid phase transfer system the diazo coupling calix[*n*]arene and diazo compounds were used as cation carriers. The results of the cation transport experiments were in good agreement with those of the two-phase extraction measurements.

Table 6. **Extraction/Sorption of Metal Picrates with Ligands.**

	Picrate Salt Extraction/Sorption (%)							
Ligand	Ag^+	Hg^{2+}	Hg^+	Co^{2+}	Ni^{2+}	Cu^{2+}	Cd^{2+}	Cr^{3+}
36a	3.39	25.82	21.08	-	2.27	2.56	1.21	18.81
36b	-	28.63	21.17	2.58	3.78	3.74	1.46	18.93
36c	5.27	26.59	15.98	2.14	1.89	3.44	4.39	17.69
37a	74.26	69.91	82.51	67.04	70.01	70.60	71.63	62.50
37b	82.18	76.42	87.83	81.28	77.91	83.74	86.68	74.00
37c	78.50	61.29	66.55	75.21	71.80	70.71	73.41	72.38

The ionophoric properties of monomers **36a-c** as well as oligomers **37a-c** toward the transition metal cations were investigated by the picrate sorption method [36]. The results are expressed as a percentage of cation extraction (E%) or sorption (S%), which are collected in Table 1 and shown graphically in Fig. 29.
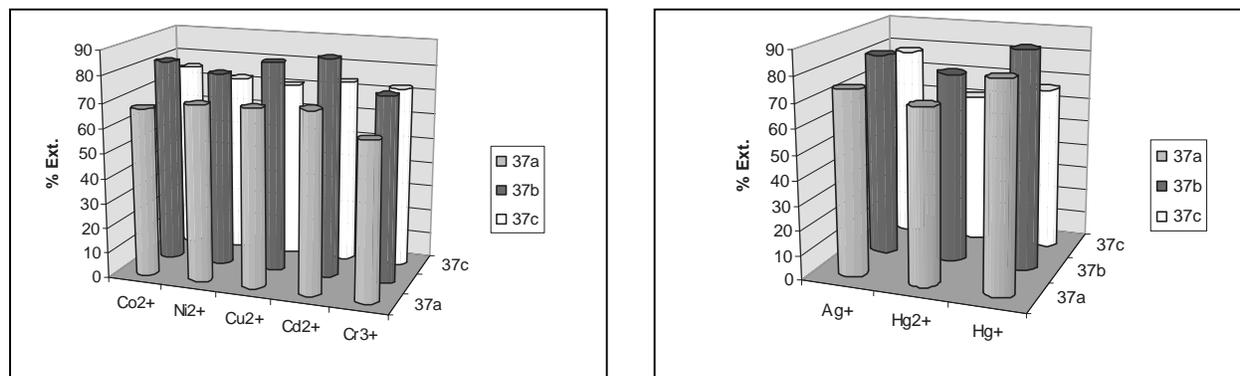

Figure 28. **Sorbants used in this work.**

Figure 29. **Sorption percentage of the metal picrates with 37a–c at 25 ºC.**

From the results, it was observed that oligomers are effective sorbants. The sequence of sorption efficiency of **37b** for heavy metal cations is the order $Cd^{2+} > Cu^{2+} > Co^{2+} > Ni^{2+} > Cr^{3+}$. Consequently, grafting of azo groups with calix[4]arene is useful approach for heavy metal sorption. It was clearly found out that -N=N- group was preferable to complex with more polarizable transition metal ions due to cation-π interactions. Thereafter, it was suggested that this increased binding ability is due to the rigid azo (-N=N-) groups moiety at the upper rim of calix[4]arene in the oligomeric skeleton.

Selective extraction of Fe^{3+} cation

The most important contribution in this field was made by our group and embarked on an ambitious program that focuses on the use of calixarenes and azocalixarenes as selective ligands [80]. A good example, and one that represents an especially interesting study of cation complexation by calixarenes, deals with the selective extraction of Fe^{3+} from an analytical mixture of Cu^{2+}, Ni^{2+}, Co^{2+} and Fe^{3+}. Thus, the extraction of Fe^{3+} from analytical mixture poses a tantalizing challenge, which has been addressed by a number of chemists during the years.

Deligöz et al. [80] have theorized that azocalixarenes might be utilized as selective ionophores for Fe^{3+}. Thus, a strategy was made to make a comparative study between the extractants **2a-d**, **3** and the calix[4]arenes, i.e. *p-tert*-butylcalix[4]arene (**1**), calix[4]arene (**2**),

azocalix[4]arenes and two phenol derivatives (Figure 30) 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol (**38**) (Bromo-PADAP) and 2-hydroxy-5-methylphenylazonapthol (**39**) (HMPAN). The solvent extraction experiments for the selective removal of Fe^{3+} cation with these ligands was carried out in a water/chloroform system at pH 2.2, 3.8, 4.5 and 5.4.

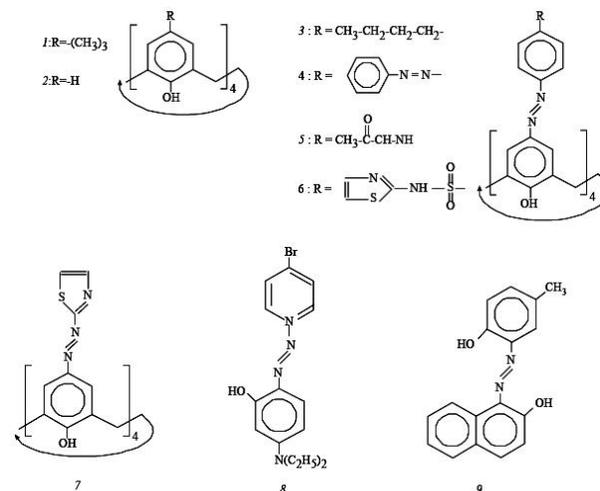*Figure 30.* **Monomer Extractants.**

Table 7 illustrate the effect of pH on the extraction of Fe^{3+} cation with the ligands. The lower extraction recovery of compound **1** containing electron-donating *tert*-butyl group than that of compound **2** lacking this group can be explained by difficulty in removing the -OH proton of compound **1**.

*Table 7.* **Extraction of metal cations with ligands Percent Recovery.**

Ligand	pH 2.2	pH 3.8	pH 4.5	pH 5.4
1	7.0	22.4	46.5	66.0
2	8.4	56.0	57.5	90.0
2a	21.7	38.8	40.9	76.1
2b	31.1	36.9	41.7	78.6
2c	28.3	31.3	36.9	92.4
2d	22.8	35.9	52.5	77.5
3	22.4	28.9	36.6	66.9
38	28.2	30.4	36.5	56.8
39	34.1	44.6	46.0	64.5

Compounds **2a-d** and **3** include both coupled diazo (-N=N-) groups and calix[4]arene. Due to the positive effect of this group on complex formation, higher extraction yields were observed especially at lower pH values. Compounds **38** and **39** are structurally similar to each other. The higher extraction yields have obtained with compound **39** than with compound **38**, though, because of the presence of two –OH groups in ortho position. The decrease in extraction yield can be explained by presence of resonance among the three nitrogen atoms in compound **38** thus lowering the electron-donating capacity of diazo groups. It can be concluded that the extraction yields of azocalix[4]arenes are higher with respect to their monomers.

The UV spectra of compound **2c** and Fe^{3+} at the same concentrations (1.10^{-3} M) were taken in DMF individually or together. The formation of a complex was evident when the color of the mixture solution changed from light brown to dark brown and an absorption inflection appeared at 586 nm. The molar ratio of **2c** to Fe^{3+} ion in the complex was determined by the continuous variation plots (Job's Method). The complex had its maximum absorbance at $[FeCl_3/calix + FeCl_3] = 0.50$. The results indicate that **2c** forms a 1:1 complex with Fe^{3+} in solution.

The pH of the 10^{-2} M *p*-(4-acetanilidazo) calix[4]arene in DMF was 3.95 and the pH of the 10^{-2} M Fe^{3+} in DMF was 2.65. After the complexation, the pH has decreased to 2.48. The decrease in pH is due to the H^+ liberated (Eq.1.),

after the complex is formed between **2c** and Fe^{3+} in DMF.

$$Fe^{3+} + HL \rightleftharpoons LFe^{2+} + H^+ \quad (1)$$
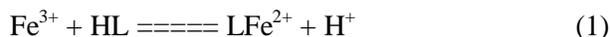
The extraction reaction of the present system can be expressed by Eq.2.,

$$M^{n+}_{(aq)} + [LH_m]_{(org)} \rightleftharpoons [MLH_{m-n}]_{(org)} + nH \quad (2)$$
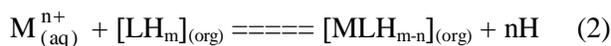
(where aq and org denote the species in the aqueous and the organic phase, respectively).

$$D = [MLH_{m-n}]_{(org)} / [M^{n+}]_{aq} \quad (3)$$

The extraction equilibrium constant (K_{ex}) is given by,

$$K_{ex} = \frac{[MLH_{m-n}][LH_m]}{[H^{n+}]_{aq}[lH_m]_{org}} \quad (4)$$

$$\log D = n\,pH + \log K_{ex} + \log[LH_m]_{org} \quad (5)$$

Eq.5 indicates that the slope n for the log D versus pH plot corresponds to the number of protons released upon extraction.

The results indicate that in the two-phase solvent extraction with **2c** the dissociation of one proton (i.e., an exchange between Fe^{3+} and Na^+ or H^+) takes place at water-chloroform interface. The logarithmic extraction constant, log K_{ex}, for the Fe(III)-compound **2c** complex corresponding to Eq.5 is found to:

$$\log K_{ex} = 1.74 \pm 0.15$$

The solvent extraction processes with azocalixarenes are similar. In our recent work [43], it was shown that the solvent extraction mechanism was the same when calixarenes containing different functional groups was used. The solvent extraction mechanism with the calixarenes and the phenols are shown in (Fig. 32).

Aqueous phase	Organic phase
Fe^{3+}	LH_nNa^+
Na^+	LH_nFe^{3+}
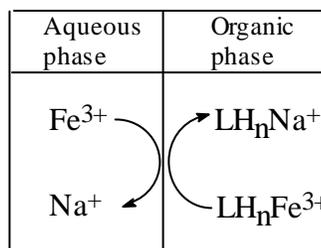
Figure 32. **Extraction mechanism proposed for 2c.**

Discovery of more selective and effective extractants for Fe(III) metal ion from water and soil has become an environmental and economical necessity. During the past two decades much of research effort has focused on embellishing calixarene frameworks with functional groups for the recognition of cations. Oxygen containing macrocycles are effective extractants for alkali and alkaline-earth metals in general. Contrastly, nitrogen containing calixarenes have become an important class of compounds in selective extraction of soft heavy metal ions against alkali, alkaline-earth, or other hard metal ions. Additionally, nitrogen atoms can easily be protonated and hydrogen bonded to Fe^{3+} metal ions. In summary, azocalix[n]arenes, azo-derivatized functionalities, potentially meet the requirements of extractants by being multidentate preorganized macrocyclic type ligands with appended functionalities [79].

A calix[6]arene epoxide extracts Cu(II), Ni(II), Co(II) and Fe(III) with the latter being the least extracted. By contrast, a polymeric polyether with an epoxy group at the end of the chain selectively extracts Fe(III) in the presence of Cu(II), Ni(II) and Co(II). The calix[4]arene with a polystyrene attached on its *lower rim* (i.e., close OH side), takes *cone* conformation, in which metal cations can easily be transported from aqueous to organic phase [19].

In order to extract Fe^{3+} cation, chromogenic *mono-* (**12a,b**) and *di-* (**13a-g**) substituted of azocalix[4]arene analogues with multi azo groups are used. In order to compare the complexation characteristics of the azocalix[4]arene derivatives, the solvent extraction of Fe^{3+} cation were carried out in a water/chloroform system at pH 2.2, 3.8, 4.5 and 5.4 with them (Table 8).

The extraction of Fe^{3+} cation with all ligands substituted with azocalix[4]arene containing multi azo groups occured between 60.8 and 67.4% at pH 2.2. Introduction of phenylazo groups has increased the extraction ratio significantly (Fig.33).

Table 8. Extraction of Fe^{3+} cation with ligands.

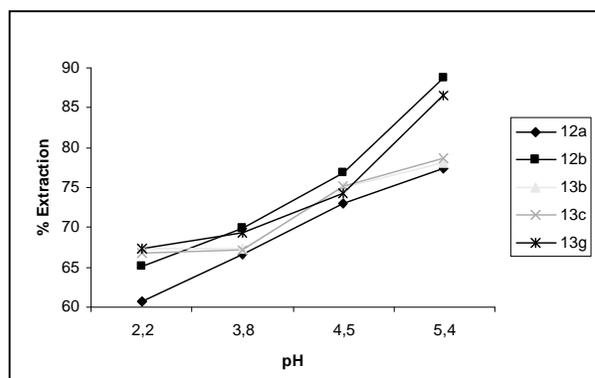| Ligand	pH			
	2.2	**3.8**	**4.5**	**5.4**
12a	60.8	66.5	72.9	77.3
12b	65.2	69.8	76.9	88.8
13a	66.5	68.7	74.8	78.4
13b	67.3	67.4	75.0	78.2
13c	66.8	67.1	75.1	78.6
13d	65.9	66.1	74.4	80.0
13e	65.0	68.9	74.9	80.1
13f	66.5	68.5	74.0	87.4
13g	67.4	69.4	74.2	86.6

Figure 33. Effects of pH on Fe^{3+} cation extraction.

The UV absorption spectra of azocalix[4]arene **12b** and **12b**-iron(III) complex in the wavelength range of 300-700 nm were measured in DMF solutions and shown in Figure 34. The azocalix[4]arene **12b** gave bimodal absorption maxima at 287 and 425 nm, referring a $\pi \rightarrow \pi^*$ and a $n \rightarrow \pi^*$ transitions of the –N=N– bond, respectively.
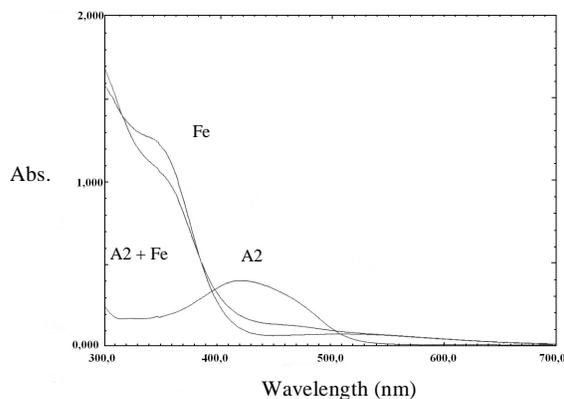

Figure 34. Absorption spectra of azocalix[4]arene 12b and its iron(III) complex.

The UV spectrum of azocalix[4]arene in DMF did not exhibit an absorption maximum above 400 nm. The formation of complex was formed between azocalix[4]arene **12b** and Fe^{3+} cation in DMF did not causes the release of hydronium ions and did not decreased its pH. The formation of complex in solution medium results from ion-dipole interaction. The extraction reaction of the present system can be expressed by:
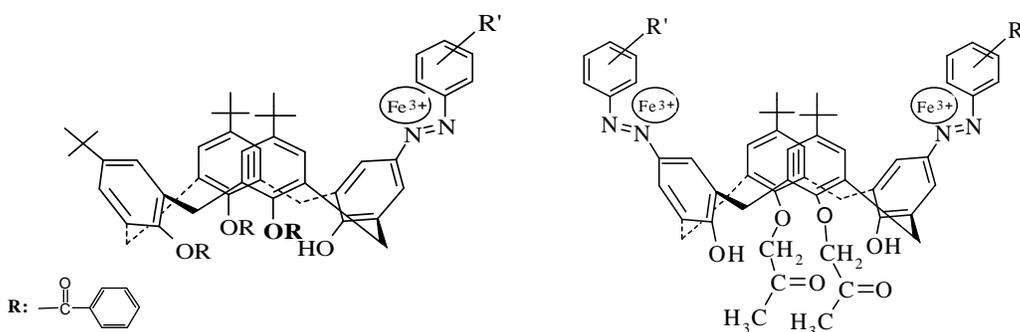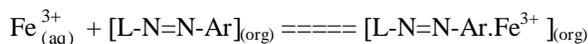
$$Fe^{3+}_{(aq)} + [L-N=N-Ar]_{(org)} ===== [L-N=N-Ar.Fe^{3+}]_{(org)}$$

The extraction processes of chromogenic *mono-* (**12a-b**) and *di-* (**13a-13g**) substituted azo calix[4]arenes are similar. Even with different chelating agents the solvent extraction mechanism of azocalix[4]arenes were all same. The extraction mechanism with the azocalix[4]arenes are shown in (Fig. 35) [80].

Figure 35. **Structure proposed for azocalix[4]arenes-iron(III) complex.**

Conclusions

- The important features of azo functions are related to the electronic structures of possesing lone pair electrons and vacant 3d electrons, suggesting the binding ability of azocalix[*n*]arenes to metal ions.
- Solvent extraction study has shown that azocalix[4]arenes can extract transition metal ions.
- Conventional calix[4]arenes cannot extract them at all, substantiating that the bridging azo plays some important roles in the recognition of metal ions.
- The chemistry of azocalix[4]arene has just been started, its ready availability in substantial quantities and the presence of azo moiety instead of methylene would surely give this new member of the calix family azo unlimited applications in quite near future.

- The goal of this work is to condition a new chromogenic azocalix[n]arene molecule to elaborate an ion selective electrode (ISE) able to detect to this type of pollutant.
- The feasible of extractants based on chromogenic azocalix[4]arene molecules for heavy metal ion detection was shown.
- The new diazo coupling calix[4]arene compounds can be successfully used for the extraction of the Fe^{3+} cation.
- The selectivity of azocalixarenes is the same as its monomeric compounds, but azocalixarenes shows different binding ability.
- The effectiveness of diazo derivatives of calixarenes for transfering the metal cations is reflected by the soft π–donor systems and intra cavity complexation.
- The presence of multi azo units in one azocalix[4]arene has improved the inclusion ability and other azocalix[4]arene related capabilities of the azocalix[4]arene itself.

Acknowledgement

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Biographies

H. Deligoz was born (1965) in Denizli', Turkey. He did Ph.D. from Department of Chemistry, Selcuk University, Konya-Turkey in 1994 with Professor Mustafa Yilmaz and worked on the topic, "Synthesis of New Calix[n]arenes and Investigation of Some Properties". He then moved to Department of Chemistry, Pamukkale University, Denizli-Turkey. Presently, he is working as an Associate Professor in the same University. His main research interests have been in the areas of organic synthesis associated with the preparation of azocalixarenes: synthesis, characterization, complexation, extraction, absorption properties and thermal behaviours as well as their application in various fields of analytical/material science. Other major research interests are in the fields of polymer chemistry, environmental/analytical chemistry, nano/bio-materials, membrane technology, phase transfer reactions, toxic ion remediation, enantiomeric separations, sensor technology and green chemistry, textiles chemistry, dyes and pigment, separation and purification.