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RESEARCH ARTICLE

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# Syntheses and metal ions recognition of dendritic calix[*n*]arenes ($n = 6,8$) amide derivative

**Abstract** Dendritic *p*-*t*-butylcalix[*n*]arene amide derivatives with terminal amino groups of the first and second generations were synthesized by using divergent methods from ammonolysis of ethyl calixarylacetate with 1,6-diaminohexane and Michael addition of methyl acrylate. Their structures were confirmed by IR, $^1$H NMR. The recognition properties of these amide derivatives for several kinds of metal ions were studied with UV–Vis spectroscopy. The results showed a great affinity for soft $Ag^+$ and $UO_2^{2+}$ ions and formed 1:2 or 1:3 stoichiometric complexes.

**Keywords** calixarene, dendrimer, amide, ion recognition, UV-Vis spectrum

## 1 Introduction

Known as the third generation of supramolecular receptors, calixarenes play very important roles in the recognition for cations, anions, and neutral molecules [1]. Owing to its easy chemical preparation, persistent shape and size, relatively much more reactive sites, and easy chemical modification, they have been used as a construction platform to prepare versatile receptors with hydrophilic, lipophilic or amphiprotic substituents to recognize metal ions, organic cations, gas molecules, and organic molecules with lower molecular weight as well as anions and chiral molecules [2]. Recently, some new calixarene receptors bearing double functional groups to recognize both cations and anions have been developed [3–5]. On the other hand, calixarene is an ideal candidate for the construction of new types of dendritic molecules, from which high molecular weight of dendrimers can be prepared rapidly [6–9]. Indeed several examples of dendrimer synthesis based on *p*-tert-butylcalix [4] arenes or resorcinarenes have been described in the literature. Dendritic polyamidoamine (PAMAM) have been shown to exhibit interesting complexing, extraction and transport properties towards a great variety of metal ions [10–12]. The results showed that the structural factors of polyamidoamine such as the peripheral functions, generation number and branching derivatization could cause much effect for complexing metal ions. To the best of our knowledge there is no investigation report about the complexing ability of calixarene based dendritic compounds in the literature. In this article, we report a successful rapid synthesis of dendritic *p*-*t*-butylcalix[*n*]arene amide derivatives with terminal amino groups by using divergent methods from ammonolysis of ethyl calixarylacetate with 1,6-diaminohexane and Michael addition of methyl acrylate and their recognition properties for several kinds of metal ions were studied with UV–Vis spectroscopy.

## 2 Experimental

### 2.1 Material and apparatus

Melting points were taken using a hot-plate microscope apparatus. IR spectra were obtained using a Nicolet FT-IR 740 spectrometer (KBr disc). $^1$H NMR spectra were recorded with a Bruker AV-600 spectrometer with DMSO-$d_6$ as solvent and TMS as internal standard. UV–Vis spectra were recorded on Shimadzu UV-2501PC spectrophotometer. 1,6-Diaminohexne, ethyl acrylate, are commercial reagents and used as received. Solvents (acetone, alcohol, and dichloromethane, etc) were purified by standard techniques. The reaction process was monitored by TLC. *p*-tert-Butylcalix[*n*]arenes [13] **1a**–**b** ($n = 6$, 8) and ethyl *p*-tert-butylcalix[*n*]arylacetates [14] **2a**–**b** were prepared according to the published methods.

### 2.2 UV–Vis measurements

UV–Vis titrations were carried at 25°C in ethanol/water ($v/v = 9:1$) using a Shimadzu UV-2501 PC spectrophotometer. Usually 1.0 mL of ligand solution ($5 \times 10^{-5}$ mol·L$^{-1}$) was

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added to the metal ion solution ($5 \times 10^{-5}$ mol·L$^{-1}$) in 10-mL flask and the solution was allowed to equilibrate for 5 min. The spectrophotometric data were collected over the range 220–600 nm.

## 2.3 Synthesis of calixarene amide derivatives

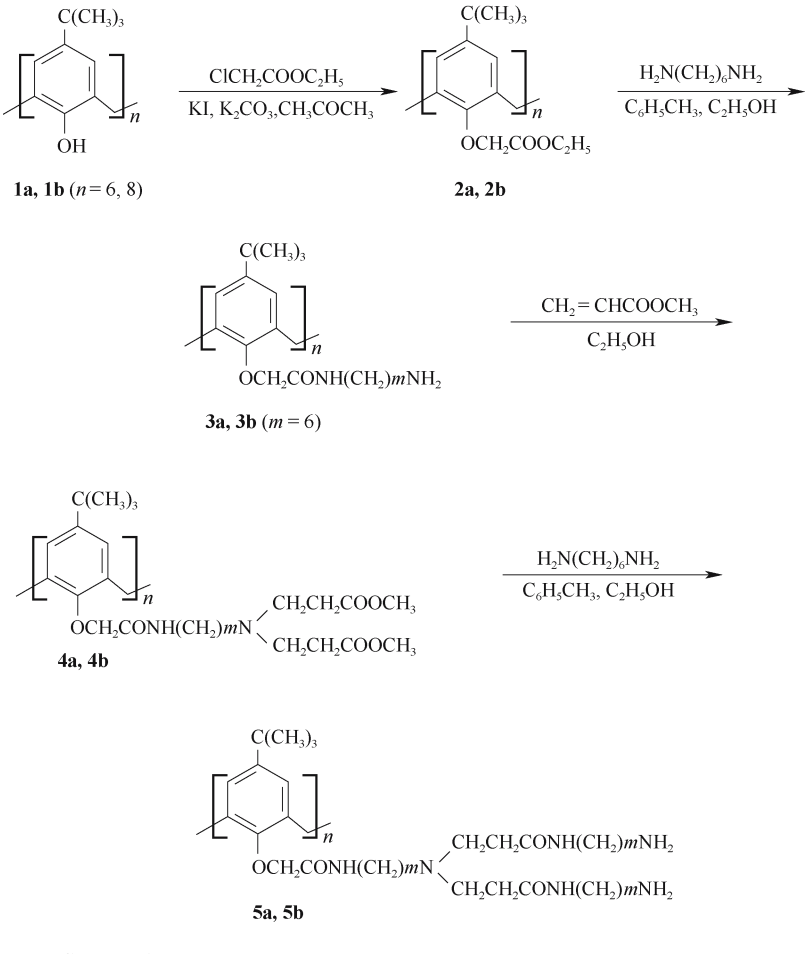
The synthetic routes of the calixarene amide derivatives **3a**–**d** and **5a**–**d** are summarized in Scheme 1.

### 2.3.1 General procedure for the synthesis of first generation amide derivatives (**3a**–**b**)

A mixture of ethyl *p*-tert-butylcalix[6]arylacetate **2a** **(**1.0 mmol, 1.488 g) and 1,6-diaminohexane (10 mL) in ethanol (25 mL) and toluene (25 mL) was refluxed for 24 h. The organic solvent and excess of diamine was removed in vacuum. The residue was washed thoroughly with alcohol to give the white solid as amide derivatives **3a**. 1.379 g (72.3%); mp: >250°C. IR (KBr disc): $\upsilon$ 3281 (w), 3074 (w), 2957 (s), 2860 (m), 1660 (vs), 1543 (s), 1473 (s), 1191 (m), 1115 (m), 1039 (m), 873 (w), 729 (w) cm$^{-1}$. **3b** was prepared in the same way as **3a** using ethyl *p*-tert-butylcalix[8]arylacetate **2b** **(**1.0 mmol, 1.984 g). White solid, 1.954 g (76.5%), mp: >250°C; IR (KBr disc): $\upsilon$ 3295 (m), 3074 (w), 2957 (vs), 2867 (s), 1660 (vs), 1543 (s), 1473 (s), 1356 (m), 1287 (m), 1184 (m), 1115 (m), 873 (w), 715 (w) cm$^{-1}$.

### 2.3.2 General procedure for the synthesis of second generation amides (**5a**–**b**)

A mixture of amides **3a** (0.5 mmol) and ethyl acrylate (15 mL) in ethanol (15 mL) were stirred under an atmosphere of nitrogen at 45–50°C for 5 days. Ethanol and excess of ethyl acrylate was removed in vacuo. The residue was crystallized from alcohol/ether to give the ester products **4a**. Then a mixture of **4a** (0.5 mmol) and 1,6-diaminohexane (15 mL) in ethanol (25 mL) and toluene (25 mL) was refluxed for 24 h under an atmosphere of nitrogen. The organic solvent and excess of 1,6-diaminohexane were removed in vacuum. The residue was well washed with alcohol several times to give the amide products **5a**. white solid, 0.969 g (48.9%), mp: 163–165°C. IR (KBr disk): $\upsilon$ 3419 (w), 3288 (m), 2943 (vs), 2860 (m), 1653 (vs), 1549 (s), 1481 (m), 1363 (m), 1294 (m), 1191 (m), 1115 (m), 1039 (m), 873 (w), 715 (w) cm$^{-1}$. $^1$H NMR (DMSO-d$_6$): $\delta$ 7.80–8.10 (br, NH); 6.70–6.90 (m, ArH), 4.00–4.30 (m, OCH$_2$CO), 3.60–3.30 (m, ArCH$_2$Ar, NCH$_2$, NH$_2$), 2.30–2.64 (br, CH$_2$CO), 0.80–1.60 (m, (CH$_2$)$_4$, C (CH$_3$)$_3$).



**Scheme 1** Synthetic routes of calixarene amide derivatives **3a**–**3b** and **5a**–**5b**

**5b** was prepared in the same way as **5a** using **3b**. white solid, 2.954g (56.1%), mp: 147–149°C. IR (KBr disk): $\upsilon$ 3419 (w), 3288 (m), 2943 (vs), 2860 (m), 1653 (vs), 1549 (s), 1481 (m), 1363 (w), 1294 (m), 1191 (m), 1115 (m), 1039 (m), 715 (w) cm$^{-1}$. $^1$H NMR (DMSO-d$_6$): $\delta$ 7.70–8.10 (br, NH); 6.70–6.90 (m, ArH), 3.80–4.30 (m, OCH$_2$CO), 3.60–3.30 (m, ArCH$_2$Ar, NCH$_2$, NH$_2$), 2.30–2.64 (br, CH$_2$CO), 0.80–1.60 (m, (CH$_2$)$_4$, C (CH$_3$)$_3$).

## 3 Results and discussion

### 3.1 Synthesis and characterization of calixarene amide derivatives

The reactions leading to the first and second generation of target Schiff bases **3a**–**b** and **5a**–**b** are shown in Scheme **1**. As shown in Scheme 1, *p*-tert-butylcalix[*n*]arenes [13] **1a**–**b** ($n = 6$, 8) were fully alkylated with ethyl $\alpha$-bromoacetate according to the published procedure [14] with a little deviation to give six or eight ethoxycarbonylmethoxy substituted derivatives **2a**–**b** (**2a**, 86.5%; **2b**, 87.2%). Thus, this kind of activated ester group provides an excellent chance for the chemical modification on the lower rim of calixarene. The esters **2a**–**b** were refluxed with large excess of 1,6-diaminohexane $NH_2(CH_2)_6NH_2$ in a mixture of ethanol and toluene (v/v, 1:1) for about 24 hours to afford corresponding amides **3a**–**b** in high yields (69%–78%). The large excess molar ratio of diamine in the reaction allows mainly monoammonolysis of each diamine and gives the amide product with free terminal amino groups, which greatly prevented the formation of other kind of diamidation or cyclization reactions [19]. Besides being high hydrogynic in air, the amides **3a**–**b** have very poor solubility in common organic solvents such as ether, chloroform, toluene, and acetonitrile, only partially dissolved in hot ethanol, which makes it difficult to get a satisfactory characterization data for them. In order to remove the excess unreacted diamine, the amide product must be crystallized two times and washed thoroughly with alcohol. All amides **3a**–**b** have very similar IR spectra. The absorption of C=O in amide shows a very strong band at 1650–1670 cm$^{-1}$, while the absorption band of C=O in the ester derivatives **2a**–**b** appears at 1760 cm$^{-1}$. This means that all ester groups in **2a**–**b** have transferred to amides. The middle stronger bands at 3300–3500 cm$^{-1}$ belong to the absorption of NH$_2$ or NH groups.

According to Tomalia's synthetic method for dendritic polyamidoamine (PAMAM) dendrimer [15], the second generation of dendritic compounds were constructed by treating amide **3a**–**b** with methyl acrylate in alcohol at 45–50°C for at least 5 days to affirm a complete addition reaction. In this step, amino groups in **3a**–**b** were smoothly added methyl acrylate to yield the corresponding branched methyl aminodiproponate **4a**–**b** (79%–84%). In IR spectra, the new ester groups show very strong C=O absorption at 1731 cm$^{-1}$ with the stronger peak of CONH group at 1654 cm$^{-1}$. Consequently **4a**–**b** were treated with 1,6-diaminohexane again as mentioned in the previous section to transform into the second-generation amide derivatives with free terminal amino groups **5a**–**b**. Similarly, the absorption of C=O at 1675 cm$^{-1}$ and those of NH$_2$ or NH at about 3400 cm$^{-1}$ can be observed in their IR spectrum. **5a**–**b** have good solubility in common organic solvent. In their $^1$H NMR spectra the characteristic absorption peaks overlap heavily and could not evaluate exactly for too many methylene groups of the branching chains.

### 3.2 Binding ability for transition metal ions

The dendritic calixarene amide derivatives **3a**–**b** and **5a–b** have several branched amide chain and terminal amino groups would have stronger complexing ability to metal ions [16]. The binding properties of the target compounds **3a**–**b** and **5a**–**b** to metal ions were studied by UV–Vis spectroscopy. The absorption maxima of the amide derivatives **3a**–**b** and **5a**–**b** appeared at about 270 nm. Upon the addition of alkali and alkaline earth metal salts, no changes of absorption maxima were observed. This indicated the target compounds have negligible binding ability for these kinds of metal ions. When transition metal ions ($Co^{2+}$, $Ni^{+}$, $Cu^{2+}$, $Zn^{2+}$, $Fe^{3+}$, $Cd^{2+}$, $Pb^{2+}$, $Hg^{2+}$) were introduced the absorption maxima shift a little to longer wavelengths ($\Delta\lambda < 10$ nm), which means weak complexation between them. It is very interesting to find that $Ag^+$ and $UO_2^{2+}$ ions cause very large shift of absorption maxim of the target compounds ($\Delta\lambda > 40$ nm). Figure 1 shows the UV–Vis spectra of the host compounds **3a** and **5b** in the presence of $Ag^+$ and $UO_2^{2+}$ ions with the spectra of $Ag^+$ and $UO_2^{2+}$ ions as a reference. Amide derivatives **3a**–**b** and **5a**–**b** have very similar absorption patterns. From Fig. 1 it can be seen that the maxim absorption band of the receptors at about 270 nm was shifted to 423 nm after adding $Ag^+$ ions.

The UV–Vis spectra of **3a** with different concentration of $Ag^+$ are shown in Fig. 2. From Fig. 2, an isosbestic point at 345 nm could be obviously observed. It showed again that $Ag^+$ coordinated with **3a** to form a complex [17]. The other three receptors show similar results. Fig. 3 is the UV–Vis spectra of **3b** with different concentration of $UO_2^{2+}$. The

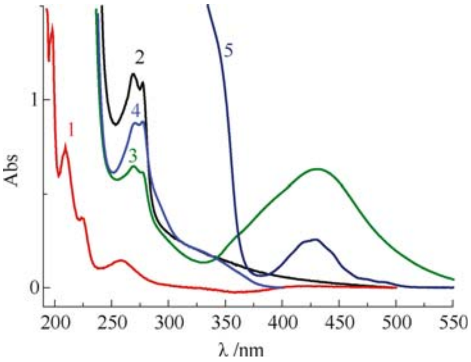


**Fig. 1** UV–Vis Absorption spectra of host **3**a and **5**b in the presence of $Ag^+$ or $UO_2^{2+}$
1. $Ag^+$ (0.2 mmol/L); 2. **3a** (0.2 mmol/L) 3. **3a** + $Ag^+$; 4. **5b** + $UO_2^{2+}$; 5. $UO_2^{2+}$(0.2 mmol/L).

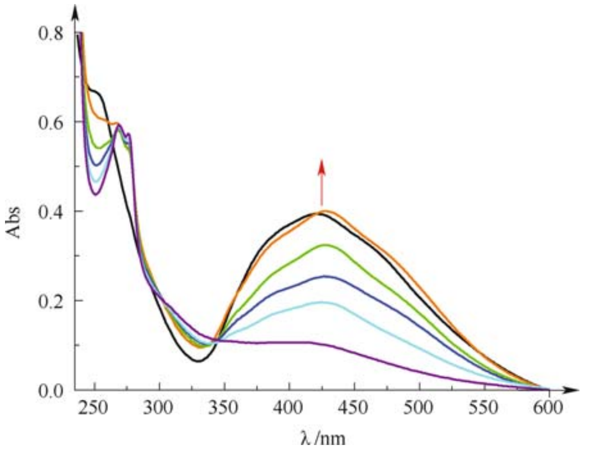


**Fig. 2** UV–Vis absorption spectra of **3a** with different concentration of AgOAc, total concentration of **3a** and AgOAc is keep in 0.2 mmol·L$^{-1}$

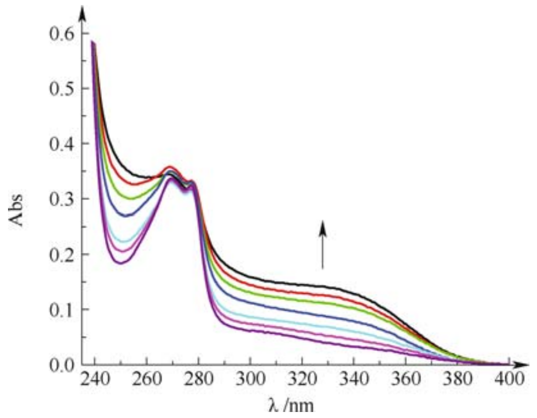


**Fig. 3** UV–Vis absorption spectra of **3b** with different concentration of $UO_2(OAc)$, total concentration of host and $UO_2(OAc)_2$ is keep in 0.2 mmol·L$^{-1}$

isosbestic point appeared at about 275 nm which indicate the formation of at least one metal complex species.

The Job's plot of receptors **3a**–**b**, **5a**–**b** and $Ag^+$ or $UO_2^{2+}$ show the maximum at a molar fraction of 0.2 or 0.33 (Fig. 4 and Fig. 5). These results indicate that the receptors coordinate $Ag^+$ to form 1:2 complexes and coordinate to $UO_2^{2+}$ to form 1:2 or 1:3 complexes. The association constants of receptors for $Ag^+$ and $UO_2^{2+}$ are calculated according to Equation (1), where Cis the total concentration of the receptor and metal ion, $\alpha$ is the dissociation constant, $A$ is the absorbance of host at isosbestic point and $A'$ is the actual absorbance.

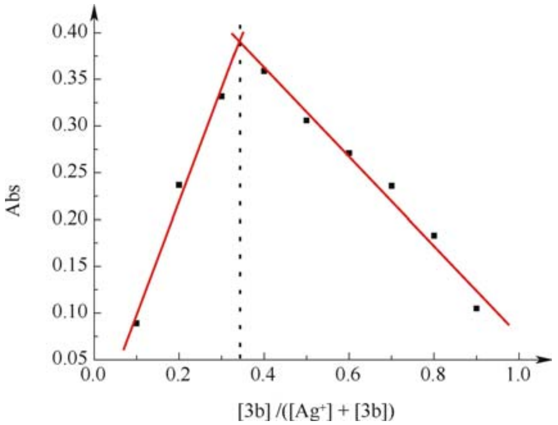


**Fig. 4** Job plot of **3b** and $Ag^+$ at a total concentration of 0.2 mmol·L$^{-1}$

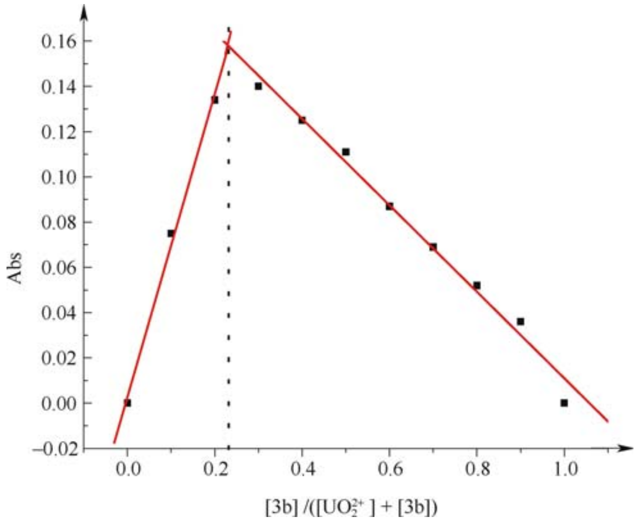


**Fig. 5** Job plot of **5a** and $UO_2^{2+}$ at a total concentration of 0.2 mmol·L$^{-1}$

$$K_{ass}\,(1/\mathrm{mol})=\frac{1-\alpha}{c\alpha^2};\alpha=\frac{A-A'}{A} \tag{1}$$

The association constants of receptors **3a**–**b**, **5a**–**b** for $Ag^+$ and $UO_2^{2+}$ are listed in Table 1. Four receptors are all coordinated with $Ag^+$ to form 1:2 stoichiometric complexes. Receptor **3a** is coordinated with $UO_2^{2+}$ to form 1:2 complex, while the other three receptors are coordinated with $UO_2^{2+}$ to form 1:3 complexes. These results might be attributed to $UO_2^{2+}$ having high coordination numbers.

**Table 1** Association constants and max absorption wavelength of receptors with $Ag^+$ and $UO_2^{2+}$

| Receptor | $Ag^+$ | | | | | $UO_2^{2+}$ | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $K_{ass}/10^{10}$ (l/mol) | $R$ | $\lambda_{max}$/nm | $\varepsilon/10^3$ L/mol·cm | Ratio | $K_{ass}/10^{10}$ (l/mol) | $R$ | $\lambda_{max}$/nm | $\varepsilon/10^3$ L/mol·cm | Ratio |
| **3a** | 3.21 | 0.99542 | 423.0 | 3.65 | 1:2 | 0.23 | 0.99041 | 324.0 | 2.00 | 1:2 |
| **3b** | 0.13 | 0.98118 | 448.0 | 5.20 | 1:2 | 30730 | 0.98325 | 329.0 | 1.96 | 1:3 |
| **5a** | / | / | 442.5 | 1.26 | 1:2 | 1355 | 0.98794 | 329.0 | 1.35 | 1:3 |
| **5b** | 7.69 | 0.99139 | 433.0 | 0.85 | 1:2 | 1937 | 0.99913 | 325.8 | 1.52 | 1:3 |

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