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Efficient Functionalizations of Heteroatom-Bridged Calix[2]arene[2]triazines on the Larger Rim

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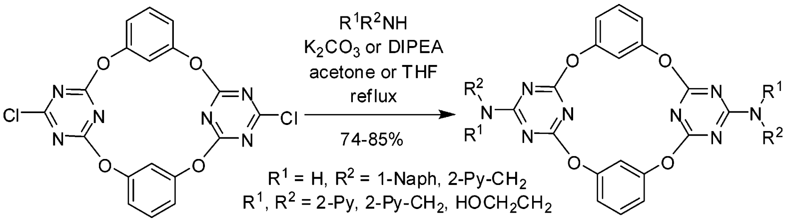

Heteroatom-bridged dichlorinated calix[2]arene[2]triazines, which were synthesized from the fragment coupling reactions of cyanuric chloride and various aromatic dinucleophiles, are a unique type of platform for the construction of functional macrocyclic host molecules. Utilizing a very convenient and straightforward nucleophilic displacement reaction of dichlorinated tetraoxacalix[2]arene[2]triazine by various chelating group-containing amines, a number of functionalized tetraoxacalix[2]arene[2]triazines on the larger rim were efficiently synthesized in good yields. The resulting tetraoxacalix[2]arene[2]-triazines armed with two 2,2′-bi(pyridinyl)amino or two bis(2-pyridinemethyl)amino groups selectively formed 1:1 complexes with Cu^{2+} ion through most probably a chelating interaction effect.

Introduction

Calix[*n*]arenes are an important type of macrocyclic host molecule in supramolecular science owing to their easy availability, unique conformational and cavity structures, and powerful and versatile recognition properties.[1] While the effort in derivatizing the fundamental calix[*n*]arene skeletons is still increasing,[2] one of the recent developments in this area is the construction of new calixaromatics by replacing their phenol units with other (hetero)aromatics, in order to change the cavity and therefore to improve their efficiency and selectivity in recognition of various guest molecules. This has in fact resulted in a few interesting and useful macrocycles such as calixpyrroles,[3] calixpyridines,[4] and other calixheteroaromatic species.[5]

Along with the advances in the field of calix[*n*]arenes and related calix[*n*]aromatics, the heteroatom-bridged calixaromatics (Chart 1) have been attracting considerable attention in recent years.[6−10] In addition to thiacalix[*n*]arenes[7] which have been known for a few years, for example, a number of oxygen[8]- and/or nitrogen[9]-bridged calixaromatics have been prepared very recently through the fragment coupling approach starting from cheap and commercial available materials. Being different from

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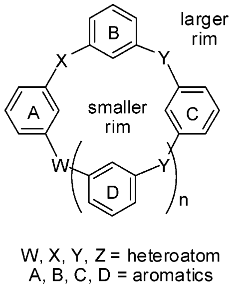
CHART 1. Structures of Heteroatom-Bridged Calixaromatics



the classic calix[*n*]aromatics,[1,2] in which the aromatics are linked by the methylene units and their cavities therefore are only *coarse* tuned by aromatic rings, the heteroatom linked calixaromatics cannot only *coarse* tune the cavity by aromatic rings but also *fine* tune their cavity by the bridging heteroatoms because heteroatoms can adopt different electronic configurations and form various degrees of conjugation with their neighboring aromatic rings. As demonstrated in our previous study,[8a,k] for example, introduction of different numbers of oxygen and/or nitrogen into the bridging positions of calix[2]arene[2]triazines gave a set of macrocyclic molecules of different cavities. Another fascinating example is tetraazacalix[4]pyridine, which has been shown to self-regulate and fine tune its conformation and cavity size when recognizing different guests.[9d−f]

Functionalizations of macrocyclic host molecules are essential in the design of supramolecular systems and applications. Although a few heteroatom-bridged calixaromatics have been synthesized,[6−10] unfortunately, their functionalizations and applications remain largely unexplored. This is most probably due to the difficulty of chemical modifications or elaborations on the macrocyclic rings of most heteroatom-bridged calixaromatics available so far. Very recently, we[8a,k] have synthesized a variety of dichloro-substituted oxygen- and/or nitrogen-bridged calix[2]arene[2]triazines by means of a very efficient, cost-effective, and high-yielding fragment coupling approach from cyanuric chloride and various aromatic dinucleophiles. Since these novel calixaromatics adopt a 1,3-alternate conformation with a tunable cavity size, and they comprise several potential reaction sites on both the rims and the heteroatom bridges, we envisioned that the heteroatom-bridged calix[2]arene[2]triazines might serve as ideal and unique platforms for the construction of functionalized host molecules. Herein we report the efficient functionalizations of dichloro-substituted oxygen- and/or nitrogen-bridged calix[2]arene[2]triazines on the larger rim through very convenient and straightforward nucleophilic displacement reactions of the chlorines by amines that contain chelating groups. We will also show that tetraoxacalix[2]arene[2]triazines armed with pyridine ligands are powerful host molecules able to selectively recognize the Cu^{2+} ion in a mixture of acetonitrile and water.

Results and Discussion

Although dichloro-substituted heteroatom-bridged calix[2]arene[2]triazines seem to be reactive toward aromatic nucleophilic substitution reactions, their reactivity has not been fully explored. For example, the reaction between dichlorodiazadioxacalix[2]arene[2]triazine and di(2-hydroxyethyl)amine proceeded in refluxing tetrahydrofuran (THF) in the presence of di(isopropyl)ethylamine,[8a] whereas the reaction of tetraazacalix[2]arene[2]triazine with dimethylamine took place in the presence of K_2CO_3 in *N*,*N*-dimethylformamide at 130 °C in a sealed tube.[8k] To understand the reactivity of different heteroatom-bridged calix[2]arene[2]triazines, i.e., the effect of the bridging heteroatoms on the reactivity of chloro substituent(s) upon nucleophilic substitution reactions, we first examined their reaction with 8-hydroxyquinoline (8-HQ), a mild nucleophilic reagent. We found the combination of heteroatoms in the bridging positions played an important role in determining the reactivity. In the presence of K_2CO_3 as an acid scavenger, dichlorinated tetraoxacalix[2]arene[2]triazine **1** and diazadioxacalix[2]arene[2]triazine **2** reacted smoothly with 2 equiv of 8-HQ in refluxing acetone to afford product **6** and **7**, respectively, in good yields. The reaction between dichlorinated azatrioxacalix[2]arene[2]triazine **3** and 8-HQ proceeded equally well in refluxing tetrahydrofuran (THF) under similar conditions to give the corresponding dihydroxyquinoline-substituted product **8** in 75% yield. However, under the identical conditions, no reaction

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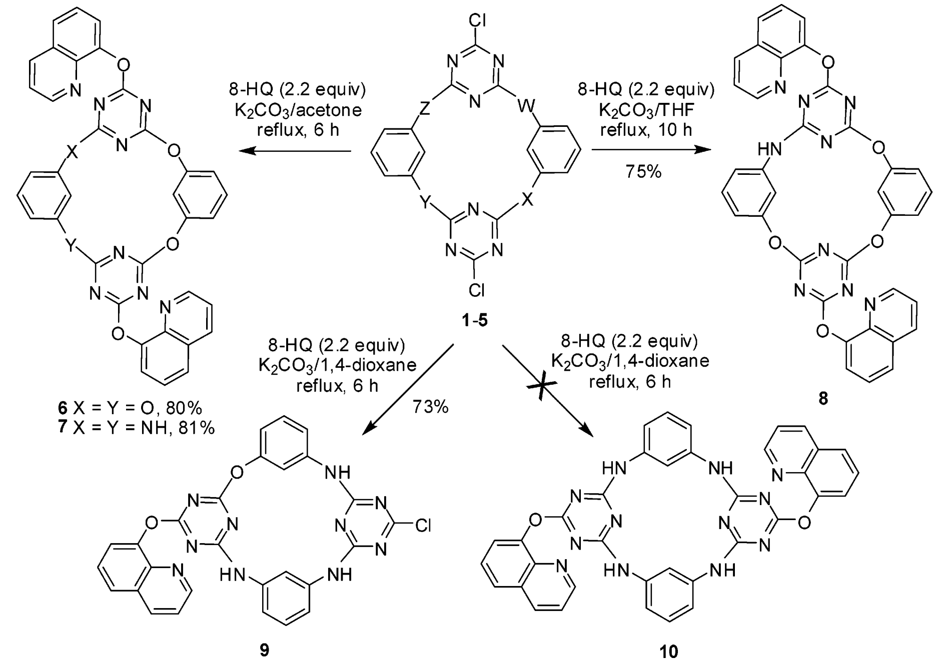
SCHEME 1. Reactivity of Dichlorinated Heteroatom-Bridged Calix[2]arene[2]triazines toward Aromatic Nucleophilic Substitution Reaction with 8-Hydroxyquinoline as a Nucleophile



was observed between oxatriazacalix[2]arene[2]triazine analogue **4** and 8-HQ. Only at an elevated temperature, such as in refluxing 1,4-dioxane, did reaction take place to give the monosubstituted compound **9** as the sole product in 73% yield. No disubstitution product was observed. Dichlorinated tetraazacalix[2]arene[2]triazine **5** did not react with 8-HQ even in refluxing 1,4-dioxane (Scheme 1). The reactions illustrated in Scheme 1 indicated clearly that the more oxygen atoms in the bridge positions, the more reactive the dichloro-substituted calix[2]arene[2]triazines. These different reaction outcomes are not surprising, however. The notable influence of the bridging heteroatom on the reactivity stems obviously from the electronic effect of the heteroatoms. In all heteroatom-bridged calix[2]arene[2]triazines **1**−**5**, heteroatoms such as oxygen and nitrogen are coplanar with their adjacent triazine rings to form strong conjugation systems.[8a,k] Since oxygen is more electronegative than nitrogen, the reactivity of the aromatic nucleophilic substitution reaction of 1,3-diaryloxy-5-chlorotriazine is higher than that of 1-arylamino-3-aryloxy-5-chlorotriazine, followed by the least active 1,3-diarylamino-5-chlorotrizine.

Having established the aromatic nucleophilic substitution reactivity of all heteroatom-bridged dichlorinated calix[2]arene[2]triazines **1**−**5**, we then chose the most reactive tetraoxacalix[2]arene[2]triazine **1** as the macrocyclic platform for further functionalizations. As a demonstration of our strategy, we decided to introduce some strong chelating groups into the larger rim of tetraoxacalix[2]arene[2]triazine. 2,2′-Bipyridylamine[11] and bis(2-pyridinemethyl)amine[12] are powerful bidentate ligands extensively used in coordination chemistry. For example, a few fluorescence-labeled bis(2-pyridinemethyl)amines have been used recently as selective probes to image free Zn^{2+} ion in cells.[12] Our interest in selective recognition of metal ions[9f] led us to synthesize tetraoxacalix[2]arene[2]triazines functionalized with 2,2′-bipyridylamine and bis(2-pyridinemethyl)amine moieties. As a comparison, the synthesis of tetraoxacalix[2]arene[2]triazines bearing respectively two 1-naphthylamino and two di(2-hydroxyethyl)amino groups was also included.

It was found that dichlorinated tetraoxacalix[2]arene[2]triazine **1** was highly reactive toward the functionalized amines employed. Under similar conditions for its reaction with 8-HQ, for example, dichlorinated tetraoxacalix[2]arene[2]triazine **1** underwent efficient aromatic nucleophilic displacement with 2 equiv of amines **11a**−**e** to afford the desired difunctionlalized products **12a**−**e** in 74−85% yields. When only 1 equiv of amine **11a**−**c** was used in the reaction, monofunctionalized tetraoxacalix[2]arene[2]triazines **13a**−**c** were obtained as the major products, albeit the disubstitution compounds **12a** and **12c** were also formed in low yields (Scheme 2, Table 1).

All products synthesized were fully characterized on the basis of spectroscopic data and microanalysis. Compound **12a** readily gave X-ray quality single crystals from recrystallization. As revealed by the X-ray diffraction analysis, the macrocyclic ring skeleton of compound **12a** adopts a 1,3-alternate conformation with a C_{2v} symmetry (Figure 1). Careful scrutiny of the bond lengths (caption of Figure 1) showed that all bridging oxygen atoms in **12a** formed conjugations with their neighboring triazine rings rather than with the benzene rings. The two benzenes tended to face-to-face parallel while the two triazine rings were edge-to-edge orientated. The larger rim distances between two benzene rings ($d_{\text{upper-benzene}}$) and between two triazine rings ($d_{\text{upper-triazine}}$) were 6.297 and 8.733 Å, respectively (Figure 1). Compared to the crystal structure of its parent tetraoxacalix[2]arene[2]triazine **1**,[8a] the introduction of the substituents on the

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SCHEME 2. Reaction of Dichlorinated Tetraoxacalix[2]arene[2]triazine 1 with Amines 11a-e

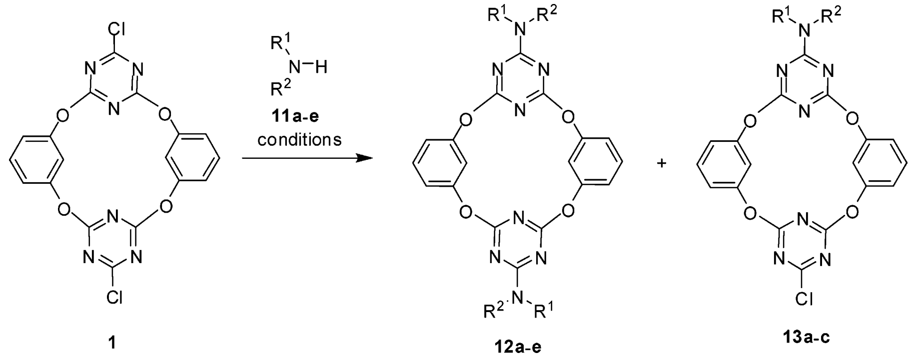

TABLE 1. Synthesis of Functionalized Tetraoxacalix[2]arene[2]triazines 12 and 13

entry	amine	R^1	R^2	conditions	**12** (%)[a]	**13** (%)[a]
1	**11a**	pyridin-2-ylmethyl	pyridin-2-ylmethyl	**11a** (2.2 equiv), K_2CO_3, THF, reflux, 10 h	74	
2	**11a**	pyridin-2-ylmethyl	pyridin-2-ylmethyl	**11a** (1 equiv), K_2CO_3, THF, reflux, 3 h	26	58
3	**11b**	pyridin-2-yl	pyridin-2-yl	**11b** (2.2 equiv), DIPEA, acetone, reflux, 24 h	81	
4	**11b**	pyridin-2-yl	pyridin-2-yl	**11b** (1 equiv), K_2CO_3, THF, reflux, 3 h[b]		26 (70[b])
5	**11c**	pyridin-2-ylmethyl	H	**11c** (2.2 equiv), K_2CO_3, THF, reflux, 12 h	85	
6	**11c**	pyridin-2-ylmethyl	H	**11c** (1 equiv), K_2CO_3, THF, reflux, 3 h	17	53
7	**11d**	1-naphthyl	H	**11d** (2.2 equiv), K_2CO_3, THF, reflux, 24 h	74	
8	**11e**	2-hydroxyethyl	2-hydroxyethyl	**11e** (2.2 equiv), DIPEA, THF, reflux, 12 h	82	

[a] Isolated yield. [b] Chemical yield based on consumed starting **1**.

triazine rings led to a slight distortion of the symmetric conformational structure and a slight change of the cavity or the cleft size. It should be noted that all heteroatom-bridged calix[2]arene[2]triazine products **6**−**9**, **12**, and **13** gave only one set of proton and carbon resonance signals in their ^{1}H and ^{13}C NMR spectra, respectively. This indicated that all functionalized calixaromatics, similar to their parent macrocycles **1**−**4**, are very fluxional in the solution phase. The rate of interconversion of various conformational structures might be very rapid relative to the NMR time scale. Compared to conventional calix[*n*]arenes derived from *p*-*tert*-butylphenol and formaldehyde, the high conformational mobility of the heteroatom-bridged calix[2]arene[2]triazines is most probably due to the lack of steric hindrance and the intramolecular hydrogen bonds, both are key factors in stabilizing conformational structures of calix[*n*]arene in solution.[1,2] Such a molecular flexibility might offer great advantages in the self-regulation of the conformation and cavity through adjusting the bridging atoms' electronic configurations and conjugations dynamically when they are allowed to interact with or recognize the guest species.

To study the recognition property of the resulting functionalized macrocyclic host molecules, we first chose compounds **6** and **12a**−**e** that contain chelating groups to examine, by means of spectrometric titrations, their interactions with metal ions in the form of perchlorate salts. On the basis of UV−vis titration experiments in a mixture of acetonitrile and water (4:1), no interaction at all took place between **6** or **12a**−**e** and alkali and alkaline earth metal ions (entries 1−6, Table 2). Neither 8-HQ-substituted tetraoxacalix[2]arene[2]triazine **6** nor amino-substituted tetraoxacalix[2]arene[2]triazines **12d**,**e** interacted with metal ions such as Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} (entries 1, 5, and 6, Table 2), suggesting tetraoxacalix[2]arene[2]triazine ring and its derivatives bearing the monodentate ligands were not effective hosts for the metal ions examined. Interestingly, however, tetraoxacalix[2]arene[2]triazines **12a**−**c** armed respectively with two bis(2-pyridinemethyl)amino, 2,2′-bi(pyridinyl)amino, and 2-pyridinemethylamino groups were found highly selective for Cu^{2+} ion binding. As illustrated in Figure 2 and Figures S7 and S13, titrations of **12a**−**c** with $Cu(ClO_4)_2$ led to the variations of the UV−vis spectra of the host molecules, while no interaction was observed between **12a**−**c** and Fe^{2+}, Co^{2+}, Ni^{2+}, or Zn^{2+} ion. The Job plot (Figure 2 as well as Figures S7 and S13 in the Supporting Information) indicated the formation of a 1:1 Cu^{2+}−host complex in all cases. The stability constants (log$K_{1:1}$) for Cu^{2+}−**12a**, Cu^{2+}−**12b**, and Cu^{2+}−**12c** complexes, which were calculated with a Hyperquad2003 program,[13] were 4.43, 4.09, and 4.55, respectively (entries 2−4, Table 2). The species of anion did not affect binding, as the titration of **12a**−**c** with $CuCl_2$ under identical conditions gave almost the same stability constants (log$K_{1:1}$) for all complexes with Cu^{2+} ion (entries 2−4, Table 2). The selective formation of 1:1 complexes of host molecules **12a**−**c** with Cu^{2+} ion appeared intriguing. To shed light on the structure of the complexes, we measured the mass spectra of the complexes after we failed to get X-ray quality single crystals. The electron-spray ionization mass spectra of all complexes gave the mass peaks corresponding to either [Cu-**12**]$^+$ or [Cu_2-**12**$_2$]$^{2+}$ fragment. Careful inspection of the electron spray TOF mass spectra revealed the same isotopic pattern as the theoretical one of the [Cu-**12**]$^+$ fragment (see Supporting Information pp 48−53), indicating a 1:1 stoichiometry of all complexes between **12a**−**c** and the Cu^{2+} ion. To get deeper insight into the mechanism of the recognition of **12a**−**c** toward the Cu^{2+} ion, tetraoxacalix[2]arene[2]triazines **13a**−**c** bearing one pendent chelating group were synthesized (vide supra) and tested.[14] No interaction between **13a** or **13b** and Cu^{2+} was observed from UV−vis titration experiments under identical conditions (Figures S19 and S20 in the Supporting Information; entries 7 and 8 in Table 2). The outcomes demonstrated convincingly that the functionalized tetraoxacalix[2]arene[2]triazines **12a** and **12b**

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(14) We thank one of the referees for this suggestion.

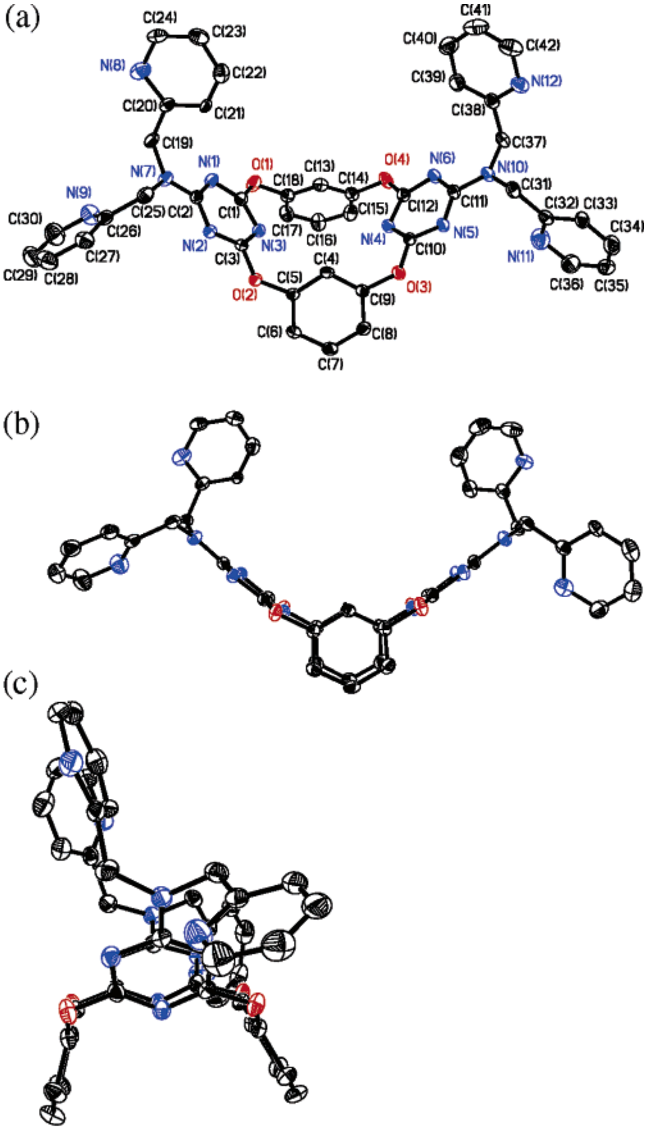

FIGURE 1. Crystal structure of **12a**: top (a) and side (b, c) views. Distances between O(1) and C(1), O(1) and C(18), O(2) and C(3), O(2) and C(5), O(3) and C(9), O(3) and C(10), O(4) and C(12), O(4) and C(14), C(7) and C(16), and C(2) and C(11) are 1.355, 1.404, 1.353, 1.404, 1.399, 1.344, 1.351, 1.401, 6.297, and 8.733 Å, respectively.

recognize the Cu^{2+} ion through the formation of a 1:1 chelate complex. However, it should be pointed out that tetraoxacalix[2]arene[2]triazine **13c** armed with one 2-pyridinemethylamino also formed a 1:1 complex with the Cu^{2+} ion, and its binding constant ($\log K_{1:1} = 4.71$) was comparable to that of the Cu^{2+}–**12c** complex according to UV–vis titration data (Figure S21 in the Supporting Information; entry 9 in Table 2). It implied most probably that tetraoxacalix[2]arene[2]triazines functionalized with 2-pyridinemethylamino group(s) interacted with the Cu^{2+} ion in a different model rather than a chelating model.

Conclusion

In summary, we have shown that heteroatom-bridged dichlorinated calix[2]arene[2]triazines, derived from the fragment coupling reactions of cyanuric chloride and various aromatic dinucleophiles, are a type of useful platforms for the construction of functionalized macrocyclic host molecules. A few chelating groups have been introduced efficiently into the larger rim of the heteroatom-bridged calix[2]arene[2]triazines through the straightforward and very convenient aromatic nucleophilic substitution reactions on the chlorotriazine rings. The resulting tetraoxacalix[2]arene[2]triazines bearing two 2,2′-bi(pyridinyl)amino or two bis(2-pyridinemethyl)amino groups exhibited excellent selectivity in the complexation with metal ions in a mixture of acetonitrile and water (4:1). They formed 1:1 complexes with the Cu^{2+} ion through most probably a chelating interaction effect. The strategy demonstrated in the current study provides us with a new avenue for the construction of more sophisticated functional host molecules.

TABLE 2. The Log $K_{1:1}$ for the Complexation of Functionalized Tetraoxacalix[2]arene[2]triazines with Metal Ions[a]

entry	host	alkali	alkaline earth	Fe^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}
1	**6**	[b]						
2	**12a**						4.43 ± 0.01 3.92 ± 0.02[c]	
3	**12b**						4.09 ± 0.01 4.17 ± 0.02[c]	
4	**12c**						4.55 ± 0.01 4.66 ± 0.01[c]	
5	**12d**							
6	**12e**							
7	**13a**	n.d.[d]	n.d.	n.d.	n.d.	n.d.		n.d.
8	**13b**	n.d.	n.d.	n.d.	n.d.	n.d.		n.d.
9	**13c**	n.d.	n.d.	n.d.	n.d.	n.d.	4.71 ± 0.01	n.d.

[a] Perchlorate salts were used as metal ion sources in UV–vis titration experiments. The $\log K_{1:1}$ values were calculated on the basis of UV–vis titration data, using a Hyperquad2003 program. [b] No interaction was observed. [c] $CuCl_2$ was used. [d] Not determined.

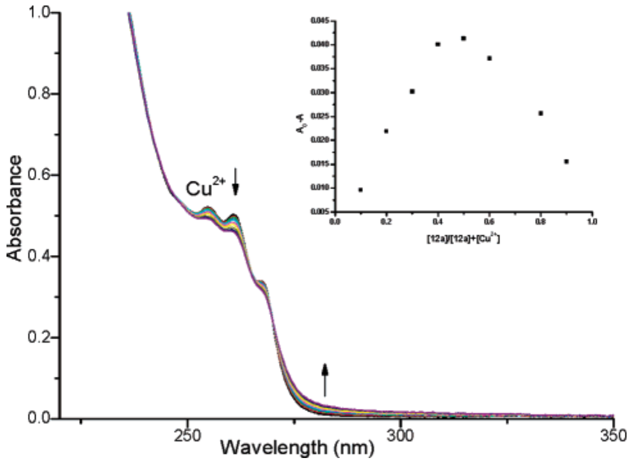

FIGURE 2. UV–vis titration of **12a** (1.728×10^{-5} M) upon the addition of Cu^{2+} in a mixture of acetonitrile and water (4:1). The concentrations of Cu^{2+} are 0, 0.766×10^{-5}, 1.53×10^{-5}, 2.30×10^{-5}, 3.06×10^{-5}, 4.60×10^{-5}, 7.66×10^{-5}, 13.79×10^{-5}, 22.98×10^{-5}, and 32.17×10^{-5} M, respectively. The inset is the Job plot for the complexation of **12a** with Cu^{2+} ion in a mixture of acetonitrile and water (4:1). Total concentration of **12a** and Cu^{2+} is 8×10^{-5} M.

Experimental Section

General Procedure for the Reaction of Heteroatom-Bridged Dichlorinated Calix[2]arene[2]triazines with 8-Hydroxyquinoline or Amines. A mixture of 8-hydroxyquinoline or an amine (1.1 mmol) and a base (K_2CO_3 or diisopropyl(ethyl)amine) (2.2 mmol) in acetone, THF, or 1,4-dioxane (20 mL) was refluxed for 0.5 h. A solution of the heteroatom-bridged dichlorinated calix[2]arene[2]-

triazines **1**−**5** (0.5 mmol) in the same organic solvent (20 mL) as for 8-hydroxyquinoline or amine solution was then added over 0.5 h. For the synthesis of **13a**−**c**, a solution of amine **11a**−**c** (1 equiv) was added over about 1 h to a mixture of **1** and a base in the same organic solvent. The resulting mixture was refluxed for a period of time (Scheme 1 and Table 1). After removal of the solvent, the residue was subjected to silica gel chromatography. For the reactions with K_2CO_3 as a base, the reaction mixture was filtrated, and the filtrate was concentrated under vacuum to give a residue that was subjected to silica gel chromatography to give pure product.

6: Silica gel column chromatography with a mixture of petroleum ether and acetone as an eluant gave white solids (264 mg, 80%); mp 209−211 °C; ^{1}H NMR (DMSO-d_6/300 MHz) δ 8.92 (d, J = 3.9 Hz, 2H), 8.53 (d, J = 8.3 Hz, 2H), 8.03 (dd, J = 7.0, 2.3 Hz, 2H), 7.65−7.77 (m, 6H), 7.32 (t, J = 8.1 Hz, 2H), 7.12 (t, J = 2.0 Hz, 2H), 6.99 (dd, J = 8.1, 2.0 Hz, 4H); ^{13}C NMR (75 MHz/DMSO-d_6) δ 174.8, 173.2, 151.9, 151.3, 147.7, 140.6, 136.8, 130.9, 129.8, 127.1, 122.8, 121.8, 119.3, 116.8; IR (KBr) 1579, 1566 cm^{-1}; MS (MALDI-TOF) m/z 660.9 (M + 1)$^+$, 682.8 (M + Na)$^+$, 698.8 (M + K)$^+$. Anal. Calcd for $C_{36}H_{20}N_8 \cdot 0.5H_2O$: C, 64.57; H, 3.16; N, 16.73. Found: C, 64.53; H, 3.13; N, 16.43.

7: Silica gel column chromatography with a mixture of petroleum ether and acetone as an eluant gave white solids (265 mg, 81%); mp >300 °C; ^{1}H NMR (DMSO-d_6/300 MHz) δ 9.93 (s, 2H), 8.91 (dd, J = 6.6, 1.6 Hz, 2H), 8.47 (dd, J = 8.4, 1.6 Hz, 2H), 7.97 (dd, J = 6.9, 2.8 Hz, 2H), 7.74−7.61 (m, 6H), 7.43−7.30 (m, 3H), 7.12 (t, J = 8.0 Hz, 1H), 6.94 (dd, J = 8.1, 2.2 Hz, 2H), 6.68 (dd, J = 8.0, 1.9 Hz, 2H); ^{13}C NMR (75 MHz/DMSO-d_6) δ 173.0, 172.6, 166.5, 166.4, 152.2, 151.1, 148.2, 141.2, 138.2, 138.1, 136.7, 130.9, 129.8, 129.2, 127.1, 126.6, 122.6, 122.0, 119.9, 119.0, 118.2; IR (KBr) 1583, 1566 cm^{-1}; MS (FAB) m/z 659 (M + 1)$^+$, 658 (M$^+$). Anal. Calcd for $C_{36}H_{22}N_{10}O_4 \cdot$hexane: C, 67.73; H, 4.87; N, 18.81. Found: C, 67.31; H, 4.49; N, 19.03. Exact mass for $C_{36}H_{22}N_{10}O_4 + H^+$ 659.1904, found 659.1879.

8: Silica gel column chromatography with a mixture of petroleum ether and acetone as an eluant gave white solids (247 mg, 75%); mp 235−236 °C; ^{1}H NMR (DMSO-d_6/300 MHz) δ 9.97 (s, 1H), 8.91 (d, J = 4.0 Hz, 2H), 8.49 (dd, J = 12.6, 8.4 Hz, 2H), 7.94−8.03 (m, 2H), 7.60−7.75 (m, 6H), 7.21−7.31 (m, 4H), 6.90−7.00 (m, 3H), 6.79 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz/DMSO-d_6) δ 174.3, 172.9, 172.8, 172.0, 166.9, 166.8, 152.0, 151.5, 151.1, 150.8, 150.6, 147.8, 147.3, 140.7, 140.3, 138.1, 138.0, 136.4, 136.3, 130.4, 129.7, 129.3, 126.6, 126.1, 122.3, 122.1, 121.5, 121.4, 119.5, 118.9, 118.1, 117.7, 116.9; IR (KBr) 1561 cm^{-1}; MS (FAB) m/z 660 (M + 1)$^+$. Anal. Calcd for $C_{36}H_{21}N_9O_5 \cdot CH_3COCH_3$: C, 65.27; H, 3.79; N, 17.56. Found: C, 65.31; H, 3.61; N, 17.71. Exact mass for $C_{36}H_{21}N_9O_5 + H^+$ 660.1744, found 660.1735.

9: Silica gel column chromatography with a mixture of petroleum ether and acetone as an eluant gave white solids (200 mg, 73%); mp >300 °C; ^{1}H NMR (DMSO-d_6/300 MHz) δ 10.03 (s, 1H), 9.97 (s, 1H), 9.90 (s, 1H), 8.90 (dd, J = 4.2, 1.5 Hz, 1H), 8.47 (dd, J = 8.4, 1.5 Hz, 1H), 7.96 (dd, J = 7.1, 2.5 Hz, 1H), 7.60−7.73 (m, 4H), 7.49 (s, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.17 (t, J = 8.0 Hz, 1H), 6.89 (t, J = 8.3 Hz, 2H), 6.73−6.76 (m, 2H); ^{13}C NMR (75 MHz/DMSO-d_6) δ 172.5, 171.5, 168.2, 166.2, 166.1, 165.2, 165.1, 164.2, 164.1, 151.4, 150.6, 147.8, 140.7, 138.0, 137.9, 137.8, 136.2, 129.7, 129.3, 128.8, 126.6, 126.1, 122.1, 121.6, 120.7, 119.3, 119.0, 118.4, 118.3, 117.9; IR (KBr) 1577 cm^{-1}; MS (FAB) m/z 551 (M + 1 + 2)$^+$, 549 (M + 1)$^+$. Exact mass for $C_{27}H_{17}N_{10}O_2Cl + H^+$ 549.1303, found 549.1300.

12a: Silica gel column chromatography with a mixture of petroleum ether and acetone as an eluant gave white solids. Recrystallization from a mixture of *n*-hexane and dichloromethane gave colorless prisms (243 mg, 74%); mp 129−131 °C; ^{1}H NMR (DMSO-d_6/300 MHz) δ 8.55 (d, J = 4.6 Hz, 4H), 7.79 (dt, J = 7.7, 1.7 Hz, 4H), 7.26−7.39 (m, 10H), 6.99 (d, J = 2.1 Hz, 2H), 6.91 (dd, J = 8.1, 2.1 Hz, 4H), 5.06 (s, 8H); ^{13}C NMR (75 MHz/DMSO-d_6) δ 171.4, 168.5, 156.6, 151.8, 149.2, 136.9, 130.0, 122.5, 121.5, 118.3, 116.6, 51.8; IR (KBr) 1586, 1526 cm^{-1}; MS (MALDI-TOF) m/z 769.0 (M + 1)$^+$, 791.0 (M + Na)$^+$. Anal. Calcd for $C_{42}H_{32}N_{12}O_4$: C, 65.62; H, 4.20; N, 21.86. Found: C, 65.78; H, 4.27; N, 21.60. Crystal data for **12a**: $C_{42}H_{32}N_{12}O_4$, colorless prism, M_r = 768.80, crystal size 0.73 × 0.38 × 0.03 mm^3, monoclinic, space group $P2(1)/c$, a = 22.9892(7) Å, b = 14.1850(7) Å, c = 11.4255(11) Å, α = 90.00°, β = 90.1570(19)°, γ = 90.00°, V = 3725.9(4) Å^3, Z = 4, ρ_{calcd} = 1.371 g cm^{-3}, T = 293(2) K. A total of 8476 reflections and 3458 parameters were used for the full-matrix, least-squares refinement on $F2$. $R_1 = 0.0606$ [$I > 2\sigma(I)$], $R_1 = 0.1596$ (all data), $wR_2 = 0.1502$ [$I > 2\sigma(I)$], $wR_2 = 0.1905$ (all data).

12b: After reaction, the product precipitated as white solids. Filtration and repeated washing with acetone gave pure product (288 mg, 81%); mp 218−220 °C; ^{1}H NMR (DMSO-d_6/300 MHz) δ 8.43 (d, J = 3.3 Hz, 4H), 7.96 (dt, J = 7.7, 1.8 Hz, 4H), 7.66 (d, J = 8.0 Hz, 4H), 7.37−7.30 (m, 6H), 7.07−6.91 (m, 6H); ^{13}C NMR (75 MHz/DMSO-d_6) δ 172.0, 169.1, 154.3, 151.9, 148.9, 137.9, 129.8, 122.9, 122.2, 118.8, 116.8; IR (KBr) ν 1575, 1568, 1540 cm^{-1}; MS (MALDI-TOF) m/z 712.4 (M$^+$). Anal. Calcd for $C_{38}H_{24}N_{12}O_4 \cdot H_2O$: C, 62.46; H, 3.59; N, 23.00. Found: C, 62.76; H, 3.40; N, 23.05.

12c: Silica gel column chromatography with a mixture of petroleum ether and acetone as an eluant gave white solids. Recrystallization from a mixture of *n*-hexane and dichloromethane gave colorless prisms (249 mg, 85%); mp 266−267 °C; ^{1}H NMR ($CDCl_3$/300 MHz) δ 8.58 (dt, J = 4.7 Hz, 2H), 7.70 (t, J = 8.5, 1.3 Hz, 2H), 7.33 (d, J = 7.8 Hz, 2H), 7.15−7.28 (m, 4H), 7.12 (t, J = 5.1 Hz, 2H), 6.81 (t, J = 7.9 Hz, 4H), 6.68 (t, J = 8.0 Hz, 2H), 4.87 (d, J = 5.1 Hz, 2H); ^{13}C NMR (75 MHz/$CDCl_3$) δ 172.4, 171.8, 168.7, 155.8, 152.0, 149.1, 136.6, 129.5, 122.3, 121.6, 118.8, 117.0, 45.8; IR (KBr) 3264, 3149, 1608, 1581 cm^{-1}; MS (MALDI-TOF) m/z 586.3 (M + 1)$^+$, 608.2 (M + Na)$^+$, 624.1 (M + K)$^+$. Anal. Calcd for $C_{30}H_{22}N_{10}O_4$: C, 61.43; H, 3.78; N, 23.88. Found: C, 61.26; H, 3.84; N, 23.77.

12d: Silica gel column chromatography with a mixture of petroleum ether and ethyl acetate as an eluant gave white solids. Recrystallization from a mixture of *n*-hexane and ethyl acetate gave colorless prisms (243 mg, 74%); mp >300 °C; ^{1}H NMR (DMSO-d_6/300 MHz) δ 10.46 (s, 2H), 8.02 (dd, J = 6.2, 2.2 Hz, 4H), 7.92 (d, J = 7.3 Hz, 2H), 7.58−7.65 (m, 8H), 7.28 (br, 2H), 6.92 (br, 6H); ^{13}C NMR (75 MHz/DMSO-d_6) δ 172.1, 169.4, 152.4, 134.3, 133.5, 130.5, 129.8, 128.6, 127.1, 126.8, 126.7, 126.1, 124.8, 123.4, 118.9, 117.1; IR (KBr) 3237, 3116, 1634, 1597, 1567 cm^{-1}; MS (FAB) m/z 656 (M$^+$). Anal. Calcd for $C_{38}H_{24}N_8O_4$: C, 69.51; H, 3.68; N, 17.06. Found: C, 69.42; H, 3.87; N, 16.70.

12e: Silica gel column chromatography with a mixture of ethyl acetate and methanol as an eluant gave white solids. Recrystallization from a mixture of *n*-hexane and ethyl acetate gave colorless prisms (220 mg, 76%); mp 163−165 °C; ^{1}H NMR (DMSO-d_6/300 MHz) δ 7.22 (t, J = 8.0 Hz, 2H), 6.93 (d, J = 1.8 hz, 2H), 6.87 (dd, J = 8.1, 1.9 Hz, 4H), 3.68 (d, J = 5.4 Hz, 8H), 3.61 (d, J = 5.1 Hz, 8H); ^{13}C NMR (75 MHz/DMSO-d_6) δ 171.6, 168.7, 152.4, 130.4, 118.8, 117.2, 58.7, 50.8; IR (KBr) ν 1590 cm^{-1}; MS (FAB) m/z 581 (M + 1)$^+$. Anal. Calcd for $C_{26}H_{28}N_8O_8$: C, 53.79; H, 4.86; N, 19.30. Found: C, 53.83; H, 4.87; N, 19.30.

13a: After reaction of **1** (1 mmol) with **11a** (1 equiv), silica gel column chromatography with a mixture of petroleum ether and acetone gave **12a** (101 mg, 26%) and **13a** as pale yellow powers (349 mg, 58%); mp 146−148 °C; ^{1}H NMR ($CDCl_3$/300 MHz) δ 8.57 (d, J = 4.5 Hz, 2H), 7.67 (dt, J = 7.7, 1.7 Hz, 2H), 7.33 (d, J = 7.8 Hz, 2H), 7.26−7.18 (m, 4H), 6.87 (dd, J = 8.0, 1.9 Hz, 2H), 6.81 (dd, J = 8.0, 2.1 Hz, 2H), 6.68 (t, J = 2.2 Hz, 2H), 5.14 (s, 4H); ^{13}C NMR (75 MHz/$CDCl_3$) δ 174.3, 172.6, 172.2, 169.1, 156.6, 152.5, 151.4, 149.5, 136.7, 130.1, 122.4, 122.1, 120.0, 118.4, 116.5, 51.8; IR (KBr) 1588, 1549 cm^{-1}; MS (MALDI-TOF) m/z (%) 606.4 (M$^+$ + 1, 100), 607.5 (34), 608.4 (34), 609.4 (9), 610.4 (3), 628.4 (M + Na)$^+$. Exact mass (EI) m/z 605.1332. $C_{30}H_{20}N_9O_4Cl$ requires 605.1327.

13b: After reaction of **1** (1 mmol) with **11b** (1 equiv), silica gel column chromatography with a mixture of petroleum ether and acetone gave **13b** as white solids (75 mg, 26%); mp 204−206 °C; ^{1}H NMR (CDCl$_3$/300 MHz) δ 8.51 (dd, $J = 4.8$, 1.4 Hz, 2H), 7.84 (dt, $J = 7.8$, 1.9 Hz, 2H), 7.62 (d, $J = 8.0$ Hz, 2H), 7.26−7.20 (m, 4H), 6.87−6.80 (m, 4H), 6.65 (t, $J = 2.2$ Hz, 2H); ^{13}C NMR (75 MHz/CDCl$_3$) δ 174.4, 172.6, 172.2, 169.3, 154.3, 152.3, 151.5, 149.3, 138.3, 130.3, 123.0, 122.4, 119.9, 118.6, 116.4; IR (KBr) 1589, 1544 cm^{-1}; MS (MALDI-TOF) *m*/*z* (%) 578.7 (M$^+$ + 1, 100), 579.7 (32), 580.7 (37), 581.7 (11), 582.7 (3), 600.7 (M + Na)$^+$, 616.6 (M + K)$^+$. Exact mass (EI) *m*/*z* 577.1016. $C_{28}H_{16}N_9O_4Cl$ requires 577.1014.

13c: After reaction of **1** (1 mmol) with **11c** (1 equiv), silica gel column chromatography with a mixture of petroleum ether and acetone gave **12c** (51 mg, 17%) and **13c** as pale yellow powers (275 mg, 53%); mp >300 °C; ^{1}H NMR (CDCl$_3$/300 MHz) δ 8.58 (d, $J = 4.3$ Hz, 1H), 7.74 (t, $J = 7.6$ Hz, 1H), 7.49 (t, $J = 5.1$ Hz, 1H), 7.39 (d, $J = 7.8$ Hz, 1H), 7.29−7.19 (m, 2H), 6.88−6.81 (m, 4H), 6.68 (d, $J = 8.1$ Hz, 2H), 4.89 (d, $J = 5.2$ Hz, 2H); ^{13}C NMR (75 MHz/CDCl$_3$) δ 174.3, 172.5, 172.4, 171.8, 168.8, 155.6, 152.4, 151.4, 148.5, 137.5, 130.2, 122.7, 122.2, 120.0, 119.9, 118.45, 118.4, 116.5, 45.6; IR (KBr) 3271, 3149, 1590, 1550 cm^{-1}; MS (MALDI-TOF) *m*/*z* (%) 515.4 (M$^+$ + 1, 100), 516.4 (28), 517.4 (35), 518.4 (8), 519.4 (3), 537.4 (M + Na)$^+$. Exact mass (EI) *m*/*z* 514.0910. $C_{24}H_{15}N_8O_4Cl$ requires 514.0905.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all products, X-ray crystal structure of **12a** (CIF), UV−vis titrations, and ESI MS spectra of the complexes between **12a**−**c** and Cu^{2+}. This material is available free of charge via the Internet at http://pubs.acs.org.

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