Noncovalent Assembly of Functional Groups on Calix[4]arene Molecular Boxes

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Abstract: Calix[4]arenes diametrically substituted at the upper rim with two melamine units spontaneously form well-defined box-like assemblies in the presence of two equivalents of 5,5-diethylbarbituric acid. These assemblies, consisting of nine different components, are held together by 36 hydrogen bonds and are stable in apolar solvents at concentrations of up to 10^{-4} M. This paper reports the first X-ray crystal structure, and the MALDI TOF mass spectra together with the complete ^{1}H NMR spectroscopic characterization of these hydrogen-bonded assemblies. The crystal structure clearly shows that the assemblies are stereogenic, as a result of the antiparallel orientation of the two rosette motifs. Furthermore, the synthesis of twelve new 1,3-bis(melamine)calix[4]arenes carrying different numbers and types of functionalities at the upper rim is described. Detailed ^{1}H NMR spectroscopic studies on the assembly behavior of these functionalized calix[4]arenes shows that 1) polar substituents (e.g. nitro, cyano) hardly affect the stability of the hydrogen-bonded assembly; 2) hydrogen bond donating or accepting groups, like amino and acetamido, can disturb assembly of the boxes under certain conditions by destabilizing the calix[4]arene pinched cone conformation as a result of intramolecular hydrogen bond formation; and 3) sterically bulky groups (e.g. *t*Bu) can significantly inhibit the formation of the hydrogen-bonded assembly, but this effect very much depends on the exact positions of the groups.

Keywords
calixarenes · hydrogen bonds · molecular boxes · noncovalent assembly · supramolecular chemistry

Introduction

The unique ability of enzymes,[1] monoclonal antibodies,[2] and T-cell receptors[3] to recognize their targets with exquisite selectivity arises from the cooperative action of a unique set of functional groups in a specific three-dimensional arrangement. Utilizing the highly specific way proteins fold into well-defined three-dimensional structures, nature can generate a large variety of functional group arrays simply by varying the amino acid sequence in the peptide chain. Supramolecular chemists are trying to achieve the same goal in a different way, namely, by anchoring functional groups to synthetic platforms, such as cyclodextrins,[4] calix[4]arenes,[5] resorcinarenes,[6] or a combination thereof,[7] using the stepwise, irreversible formation of covalent bonds. However, for functional group arrays of increasing complexity this approach has severe limitations, such as the time required for syntheses and the yields obtained. As a result, reversible noncovalent assembly is increasingly being considered as a valuable alternative to classical covalent synthesis, because it allows self-correction.[8] Very recently, Kang and Rebek described a unique type of catalysis inside a self-assembled dimeric capsule.[9] Other examples include the noncovalent assembly of dendrimers,[10, 11] tetrahedral cavities,[12] and molecular boxes[13] or squares.[14]

In a previous communication we reported the hydrogen bond directed assembly of calix[4]arene molecular box $(\mathbf{1a})_3\cdot(\mathbf{DEB})_6$ (Scheme 1; **DEB**: 5,5-diethylbarbituric acid),[15] a process that involves the cooperative formation of 36 hydrogen bonds in a rosette motif, which was first described by Whitesides[16] and Lehn.[17] In this assembly six functionalizable sites (R^1 and R^2, see Figure 1) are situated at the periphery of a box-like cavity. In view of our objective to generate functional group diversity in or around noncovalently assembled cavities, we undertook a study of how the nature of the functionality at positions R^1 and R^2 affects the stability of such calix[4]arene box-like assemblies. In this paper we present the first X-ray crystal structure and MALDI TOF mass spectrum of a hydrogen-bonded assembly of this type, and describe ten new molecular boxes carrying different numbers and types of functional groups at the periphery. Furthermore, we show that formation of intramolecular hydrogen bonds in the calix[4]arene units can disturb assembly of the boxes under certain conditions by destabilization of the pinched cone conformation.

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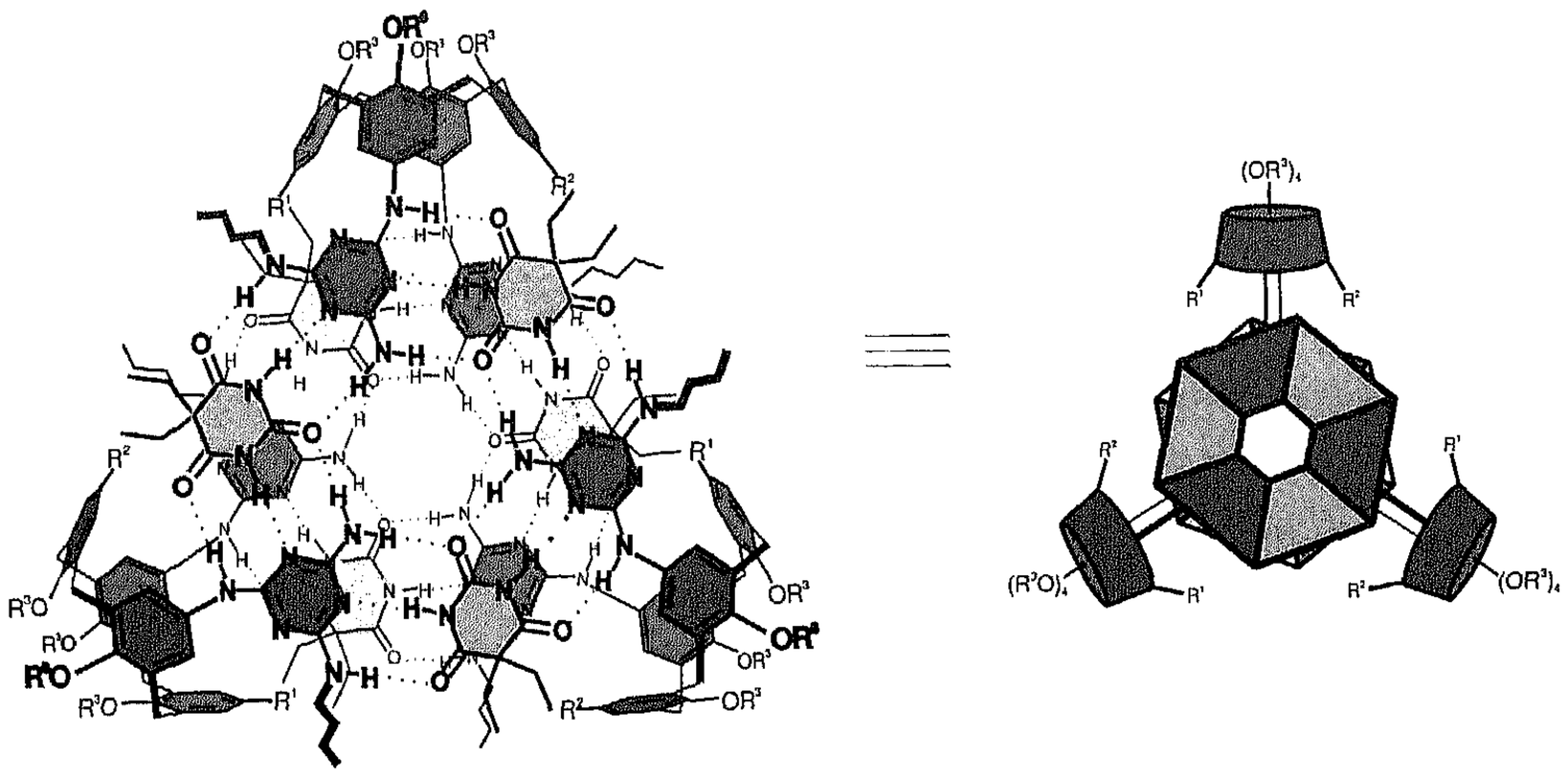


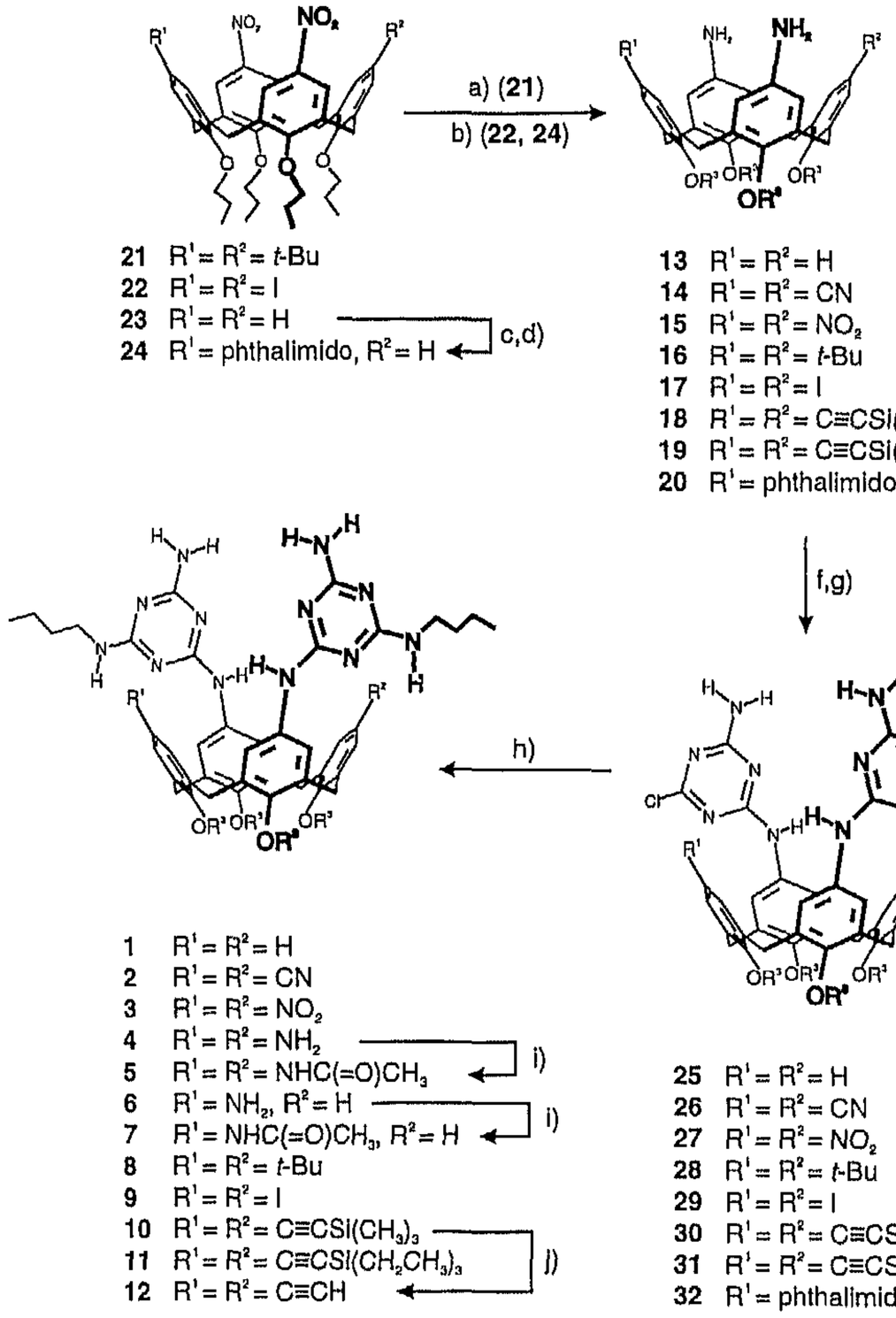
Figure 1. Schematic representation of the noncovalently assembled calix[4]arene molecular boxes $(X)_3 \cdot (DEB)_6$ (X = 1–12).

Results and Discussion

In order to investigate the structure–stability relationship of noncovalently assembled calix[4]arene molecular boxes, we synthesized bis(melamine)calix[4]arenes **1**–**12** carrying a variety of different functionalities at positions R^1 and R^2 (Scheme 1). Using a combination of ^1H NMR spectroscopy, MALDI TOF mass spectrometry, and single crystal X-ray diffraction, we then tested their ability to self-organize into box-like assemblies in the presence of two equivalents of 5,5-diethylbarbituric acid (**DEB**).

Synthesis of Bis(melamine)calix[4]arenes: Bis(melamine)-calix[4]arenes **1**–**12** were prepared starting from the corresponding calix[4]arene diamines **13**–**20**, some of which (**13**–**15**) had been synthesized previously.[18, 19] Diaminocalix[4]arenes **16** and **17** were prepared from the corresponding 1,3-dinitrocalix[4]arenes **21**[20] and **22**,[19] either by reduction with hydrazine/Raney Ni in MeOH[21] (**16**) or with $SnCl_2$ in EtOH[22] (**17**); both methods gave quantitative yields. The trimethyl- and triethylsilylacetylene functions in **18** and **19** were introduced by means of a Heck-type coupling of 1,3-diiodocalix[4]arene **17** with either trimethylsilylacetylene (yield not determined owing to extensive decomposition during column chromatography) or triethylsilylacetylene (50% yield) in the presence of 5–10 mol% $Pd(PPh_3)_2Cl_2$ and CuI in NEt_3.[23] Monophthalimidocalix[4]arene **24** was prepared in 50% yield by treatment of 1,3-dinitrocalix[4]arene **21**[24] with one equivalent of $AgCF_3COO/I_2$ followed by a Cu^I-catalyzed reaction with phthalimide in refluxing collidine.[25] Finally, reduction of **24** with $SnCl_2$ in EtOH[22] gave diamine **20** in 93% yield.

The melamine units were introduced in **1**–**12** by slightly modifying the procedure reported by Whitesides.[26] 1,3-Diaminocalix[4]arenes **13**–**20** were treated with cyanuric chloride and then NH_3 to afford the bis(chloro-



Scheme 1. For compounds **1**, **13**, and **25**: a, $R^3 = C_{12}H_{25}$; b, $R^3 = C_3H_7$. For compounds **2**–**12**, **14**–**20**, and **26**–**32**: $R^3 = C_3H_7$. Reaction conditions: a) excess hydrazine/Raney Ni in refluxing MeOH, 2 h (>95%); b) $SnCl_2$ (10 equiv), EtOH, reflux, 15 h, acidic workup (>95%); c) $AgCF_3COO$ (1.0 equiv), I_2 (1.0 equiv), $CHCl_3$, reflux, 30 min.; d) phthalimide (1.5 equiv), Cu_2O (0.75 equiv), collidine, reflux, 16 h (overall 50%); e) trimethyl- (**18**) or triethyl- (**19**) silylacetylene (3.0 equiv), $Pd(PPh_3)_2Cl_2$ (10 mol%), CuI (10 mol%), NEt_3, 40–45 °C, 15 h; f) cyanuric chloride (2.5–3.0 equiv), diisopropylethylamine (5–6 equiv), THF, 0 °C, 2 h; g) excess gaseous NH_3, THF, 0 °C, 3 h; h) $nBuNH_2$ (36 equiv), DIPEA (12 equiv), THF, reflux, 5–19 h; i) acetyl chloride (excess), 1 M K_2CO_3, EtOAc/THF, RT, 1 h; j) 1 N NaOH, THF/MeOH (1:1), RT, 1 h.

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triazine)calix[4]arenes **25**–**32** as stable intermediates, the majority of which have very limited solubility in most organic solvents. Compounds **25**–**31** were converted into the corresponding dimelamines **1**–**3** and **8**–**11** in overall yields of between 49 and 100%, by reaction with excess *n*-butylamine in refluxing THF. During the reaction of bis(chlorotriazine) **32** with *n*-butylamine the phthalimide group was partially removed and therefore the product was treated additionally with excess hydrazine in refluxing EtOH to give directly the monoamino dimelamine **6** in 54% yield. Reduction of the nitro groups in **3** with hydrazine/Raney Ni in MeOH[21] gave diamino dimelamine **4** in quantitative yield. Of all the dimelamines synthesized, compound **4** was by far the least soluble; this might be related to the cavity becoming significantly more rigid because of the formation of intramolecular hydrogen bonds (vide infra). Acylation of the amino groups in **4** and **6** with excess acetyl chloride under Schotten–Baumann conditions gave the corresponding dimelamines **5** and **7** in 83 and 65% yield, respectively. The trimethylsilyl groups in **10** were removed with 1 N NaOH to give diacetylene **12** in quantitative yield, as was unambiguously confirmed by the appearance of the acetylene resonance at $\delta = 2.95$ in the ^{1}H NMR spectrum.

Noncovalent Synthesis of Calix[4]arene Molecular Boxes: Titration of dimelamine **1a** with **DEB** in [D_1]chloroform shows several characteristic features (Figure 2). Already at very low concentrations of **DEB** two signals become evident at very low field. These resonances, which remain at $\delta = 14.10$ and 13.32 regardless of the **1a**:**DEB** ratio, are assigned to the hydrogen-bonded NH protons of **DEB** in the complex. These protons are observed at different chemical shifts as a result of the unsymmetrical substitution of the melamine units, which gives the two protons a chemically different environment in the complex. When the amount of **DEB** is increased, the signal corresponding to the NH_2 protons of free **1a** decreases in intensity, but remains at the same position. At the same time, two signals are observed at around $\delta = 6.9$ (c) and 6.7 (d) corresponding to the two NH_2 protons. Two additional signals appear at $\delta = 8.37$ (e) and 7.43 (f), which correspond to the two secondary amine protons of **1a** in the hydrogen-bonded complex. The aromatic protons of the melamine-substituted aromatic rings of calix[4]arene **1a** give rise to signals at $\delta = 7.15$ (g) and 6.03 (h). In free **1a** these protons are observed as broad signals at $\delta = 6.65$–6.05. The resonance at $\delta = 6.03$ is in accordance with a pinched cone structure in which the two melamines approach each other.[27] The fact that the other aromatic proton (g) is observed at significantly lower field is the result of formation of an intramolecular hydrogen bond with a triazene ring nitrogen (N–H distance in crystal structure (vide infra) is 2.23 Å).

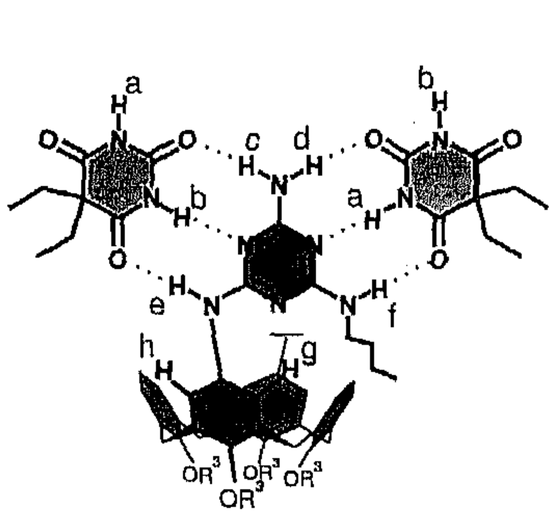

Figure 2. ^{1}H NMR titration (400 MHz) of **1a** (R^1, R^2 = H, $R^3 = C_{12}H_{25}$) with **DEB** in [D_1]chloroform at 25 °C. Separate 10 mM solutions of **1a** and **DEB** were mixed in various ratios.

At a ratio of **1a**:**DEB** of 1:2 the spectrum is sharp; this indicates the absence of free **1a**. The 1:2 ratio is consistent with the box-like assembly that is represented in Figure 1. When more than two equivalents of **DEB** are added, the signal for the NH protons of free **DEB** is observed alongside the two signals for the hydrogen-bonded **DEB**. This indicates that exchange between hydrogen-bonded and free **DEB** is slow on the NMR timescale. The self-assembled calix[4]arene boxes $(\mathbf{1})_3\cdot(\mathbf{DEB})_6$ are stable in apolar solvents like chloroform and toluene. For instance, in [D_1]chloroform $(\mathbf{1b})_3\cdot(\mathbf{DEB})_6$ is the only assembly (>97%) observed in the spectrum over a concentration range of at least 10^{-1}–10^{-4} M (lower limit for ^{1}H NMR spectroscopy). However, their stability progressively decreases when significant amounts (10–20%) of highly polar solvents (like DMSO and methanol) are added.

In order to investigate to what extent functional groups can alter the assembly of the calix[4]arene molecular boxes, we tested the ability of calix[4]arene dimelamines **2**–**12** to self-organize into box-like assemblies in the presence of two equivalents of 5,5-diethylbarbituric acid (**DEB**). The nature of the substituents at positions R^1 and R^2 significantly influences the assembly of the boxes. The results are summarized in Table 1. Diagnostic for the formation of the box-like assemblies is the appearance of the barbituric acid NH signals around $\delta = 14.1$ and 13.3 ([D_1]chloroform) or $\delta = 14.6$ and 13.8 ([D_8]toluene) in the ^{1}H NMR spectra.[15, 26] The introduction of polar substituents at positions R^1 and R^2, such as nitro or cyano, does not influence the stability of the cyclic hydrogen-bonded assembly to any significant extent. Compounds **2** (R^1, R^2 = CN) and **3** (R^1, $R^2 = NO_2$) readily assemble in [D_1]chloroform solution in the presence of **DEB**, and their ^{1}H NMR spectra are virtually identical to that of $(\mathbf{1b})_3\cdot(\mathbf{DEB})_6$ (R^1, R^2 = H), except for the signals of the aromatic protons *ortho* to R^1 and R^2. The titration of **2** with **DEB** clearly proved the 3:6 stoichiometry of the box-like assembly formed.

Recrystallization of the assembly $(\mathbf{3})_3\cdot(\mathbf{DEB})_6$ from toluene gave large single crystals suitable for X-ray diffraction studies. The crystal structure (see Figure 3) provides the first crystallo-

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Table 1. Characteristic ^{1}H NMR resonances for the hydrogen-bonded assemblies obtained by mixing dimelamines **2**–**12** with 2 equiv of **DEB** (overall ±5 mM solutions).

	δ in [D$_1$]chloroform			δ in [D$_8$]toluene		
	Imide NH resonance I	Imide NH resonance II	ArNH resonance	Imide NH resonance I	Imide NH resonance II	ArNH resonance
2	14.0 (s)	13.2 (s)	8.4 (s)	– [a]	– [a]	– [a]
3	13.9 (s)	13.2 (s)	8.4 (s)	14.3 (s)	13.6 (s)	8.8 (s)
4	14.6–14.1 (br m) [b]		9.6–9.4 (br m) [b]	14.6 (s)	13.9 (s)	8.9 (s)
5	14.5–14.0 (br m) [c]		9.6–9.4 (br m)[c]	– [d]	– [d]	– [d]
6	14.2 (br s)	13.5–13.3 (br m)	8.4 (s)	14.8–14.6 (m)	14.1–13.9 (m)	9.0–8.9 (m)
7	14.1 (br s)	13.5–13.2 (br m)	8.4 (s)	14.6 (br s)	13.9–13.7 (m)	8.9–8.7 (m)
8	– [e]	– [e]	9.2–9.4 (br m)	– [a]	– [a]	– [a]
9	14.1 (br s)	13.4 (br s)	8.4 (s)	– [a]	– [a]	– [a]
10	14.1 (br s)	13.4 (br s)	8.35 (s)	– [a]	– [a]	– [a]
11	14.1 (br s)	13.4 (br s)	8.3 (s)	– [a]	– [a]	– [a]
12	14.0 (br s)	13.3 (br s)	8.35 (s)	– [a]	– [a]	– [a]

[a] Not measured. [b] Spectrum recorded at −30 °C. [c] Spectrum recorded at 0 °C. [d] No resonances observed at room temperature owing to very low solubility. [e] No resonances observed at room temperature.

graphic evidence for the formation of this type of molecular box.[28] The structure confirms that the calix[4]arene units are fixed in a pinched cone conformation,[27] which is the only conformation that allows simultaneous participation of the calix[4]arene units in both rosette motifs. The two rosettes tightly stack on top of each other with an interatomic separation of 3.5 Å at the edges and 3.2 Å at the center of the box, which leaves little space for guest molecules. Interestingly, the structure reveals that the two rosette motifs are oriented in an antiparallel fashion[29] (see also Figure 1), which means that the assembly is stereogenic. The enantiomers are expected to have a lifetime of the order of seconds, considering the fact that their racemization requires the simultaneous breakage of at least nine cooperative hydrogen bonds.[30]

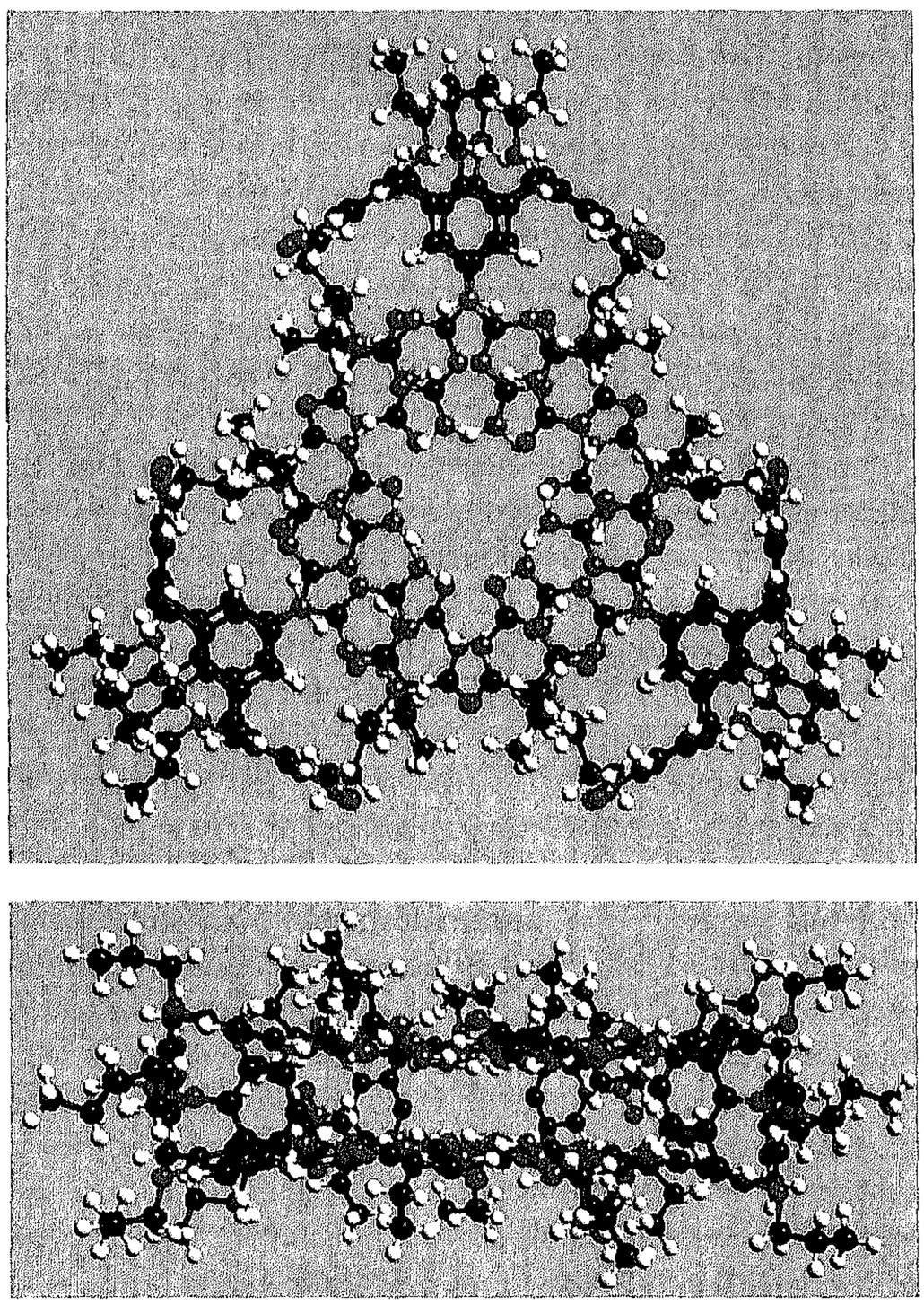

Figure 3. Top (top) and side (bottom) view (some atoms are omitted for clarity) of the X-ray crystal structure of calix[4]arene box-like assembly $(\mathbf{3})_3\cdot(\mathbf{DEB})_6\cdot(\text{toluene})_{12}$ (R^1, $R^2 = NO_2$) obtained by crystallization from toluene (solvent molecules are not shown). Nitrogen atoms are represented in blue, oxygen atoms in red, carbon atoms in black, and hydrogen atoms in white.

The crystals of $(\mathbf{3})_3\cdot(\mathbf{DEB})_6$ belong to the highly symmetric space group $R\bar{3}c$. The box is of trigonal shape (triangle); its sides are approximately 3.2 nm long, and its thickness lies between about 0.7 (center) and 1.3 (periphery) nm. The O–N and the N–N distances in the hydrogen-bonded network forming the rosettes lie between 2.85 and 3.03 Å; the range of values arises because the rosettes in the crystal lattice are slightly unsymmetrical. The crystal packing of the flat boxes is quite remarkable. The boxes are separated by 1.7–1.8 nm, and thus form large cavities accommodating up to 20 toluene sites (Figure 4). Some toluene molecules occupy a single site, while others are disordered over 2–3 locations. Significant disordering of the hydrocarbon chains in the rosette is observed: the propyl chains at the calix[4]arene skeleton are disordered over four sites with the site occupancy varying from 0.1 to 0.4; the *n*-butyl chains connected to the NH groups are disordered over five locations with the site occupancy varying from 0.1 to 0.3.

Evidence for the fact that the solid state structure of $(\mathbf{3})_3\cdot(\mathbf{DEB})_6$ resembles the structure in solution comes from a strong NOE enhancement observed between the NCH_2 protons in **3** and one of the ethyl CH_2 groups of **DEB.** The interatomic distance of these protons within a single rosette is too large (ca. 6.4 Å) to cause the observed NOE connectivity. Therefore, it must arise from a proximity effect between the two rosette motifs, and this puts a limit on the possible orientations that they can adopt relative to one another. In the antiparallel orientation observed in the crystal structure, the two protons are 2.8 Å apart, which is in perfect agreement with the strong NOE observed. The presence of this NOE connectivity provides strong evidence for the fact that the structure in solution closely resembles the solid state structure determined by X-ray crystallography.

Additional evidence for the self-assembly of the boxes was obtained by using MALDI TOF spectroscopy.[31] In the presence of 1.5–2.0 equiv of $Ag^{(I)}CF_3COO$ the assembly $(\mathbf{2})_3\cdot(\mathbf{DEB})_6$ gives rise to an intense signal at an *m*/z of 4220

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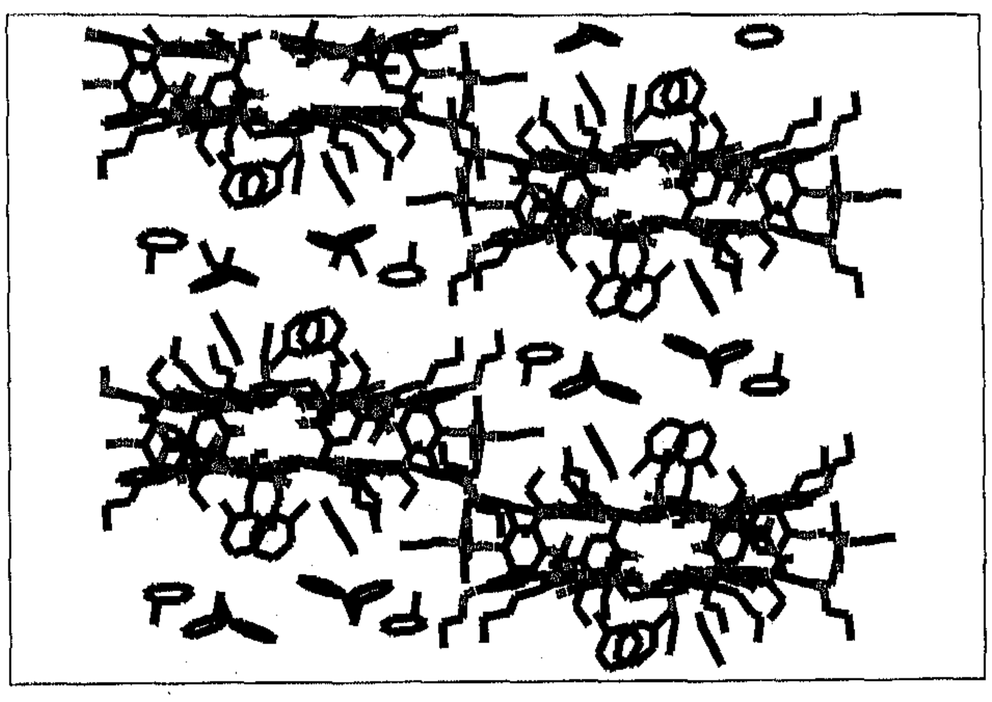
(calcd for $^{13}C_2{}^{12}C_{214}H_{282}N_{54}O_{30}\cdot{}^{107}Ag^{(I)}$ complex: 4219) in the mass spectrum (see Figure 5).[32] Signals corresponding to partially formed aggregates or higher oligomers were not observed in the spectrum. In the absence of $Ag^{(I)}CF_3COO$, none of the assemblies **1**–**3** showed any significant signal in the MALDI-TOF spectrum. Apparently, a Ag^+ ion is coordinated to one of the cyano groups in **2**, giving the assembly an overall positive charge. The applicability of this method for the mass spectrometric detection of other hydrogen-bonded assemblies is currently being investigated.

Surprisingly, the stability of assembly $(\mathbf{4})_3\cdot(\mathbf{DEB})_6$ (R^1, $R^2 = NH_2$) is highly solvent dependent. The ^{1}H NMR spectrum in [D_8]toluene is very well-defined (see Figure 6) and shows two singlets at $\delta = 14.55$ and 13.85 for the magnetically inequivalent barbituric acid NH protons. In [D_1]chloroform, however, the spectrum is very broad and does not show any resonance in the region between $\delta = 13$ and 15 at room temperature; this indicates a preference for nonspecific oligo- or polymer formation in this solvent.[33] The decreased stability of $(\mathbf{4})_3\cdot(\mathbf{DEB})_6$ in the more polar solvent [D_1]chloroform is most probably related to the hydrogen bond donating ability of the two NH_2 groups.

a)



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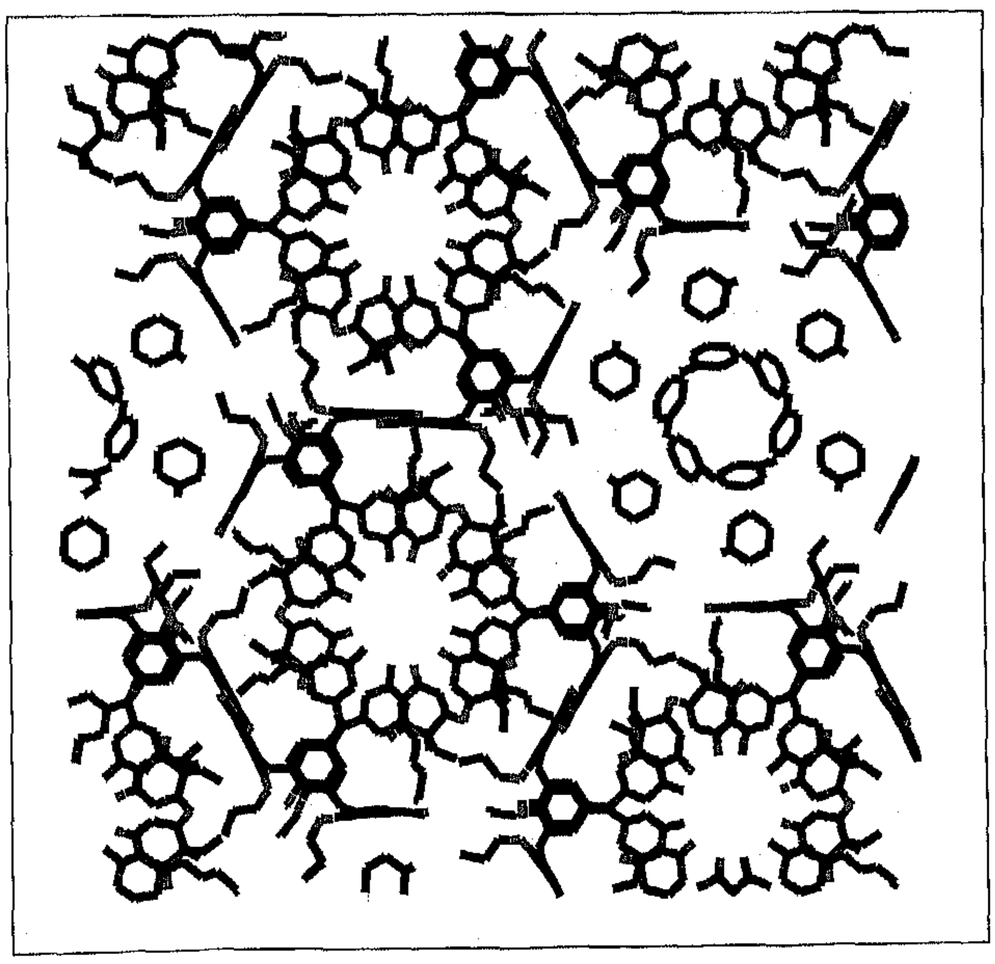

Figure 4. Different views a) and b) of the crystal packing of $(\mathbf{3})_3\cdot(\mathbf{DEB})_6\cdot(\text{toluene})_{12}$ (R^1, $R^2 = NO_2$) showing the positioning of the solvent molecules (disorder as well as 50% of the solvent molecules in view b) are excluded for clarity).

Molecular modeling studies with monomer **4** suggest that an intramolecular hydrogen bond is formed between the $ArNH_2$ groups and the melamine NH protons, which forces the calixarene to adopt a perfect cone conformation. In the pinched cone conformation observed in the box-like assembly (vide supra) these hydrogen bonds, which lead to an overall decrease in stability of the hydrogen-bonded assembly relative to the monomers, cannot be formed. Supporting evidence for the importance of intramolecular hydrogen bond formation was obtained from the assembly of **6** ($R^1 = NH_2$, $R^2 = H$), which possesses only one of the two $ArNH_2$ groups in **4**. The overall decrease in stability of the hydrogen-bonded assembly $(\mathbf{6})_3\cdot(\mathbf{DEB})_6$ is only half of that in $(\mathbf{4})_3\cdot(\mathbf{DEB})_6$. Both in [$D_8$]toluene and in [$D_1$]chloroform compound **6** forms a stable box-like assembly (see Figure 6c). Apparently, the presence of the additional intramolecular hydrogen bond in calix[4]arene **4** is responsible for the fact that assembly into the box-like aggregate is not observed in the more polar solvent [D_1]chloroform.

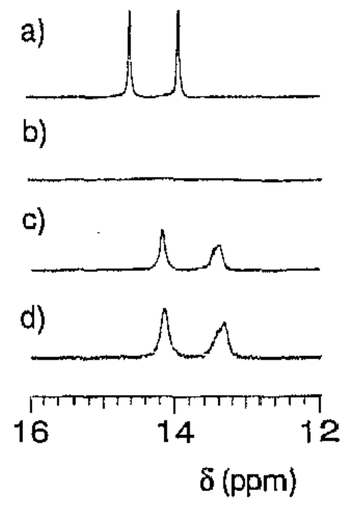

Figure 6. ^{1}H NMR spectra (400 MHz, RT) of calix[4]arene box-like assemblies: a) $(\mathbf{4})_3\cdot(\mathbf{DEB})_6$ (R^1, $R^2 = NH_2$) in [D_8]toluene (5 mM), b) $(\mathbf{4})_3\cdot(\mathbf{DEB})_6$ (R^1, $R^2 = NH_2$) in [D_1]-chloroform (5 mM), c) $(\mathbf{6})_3\cdot(\mathbf{DEB})_6$ ($R^1 = NH_2$, $R^2 = H$) in [D_1]chloroform (5 mM), d) $(\mathbf{7})_3\cdot(\mathbf{DEB})_6$ [$R^1 = NHC(O)CH_3$, $R^2 = H$] in [D_1]-chloroform (5 mM).

Compound **5** [R^1, $R^2 = NHC(O)CH_3$] does not form the box-like assembly in either [D_1]chloroform or [D_8]toluene. Both ^{1}H NMR spectra exhibit broad resonances indicating nonspecific aggregation. Removal of one of the acetamido substituents of **5** fully restores the ability of the system to form the box-like assembly. Compound **7** [$R^1 = NHC(O)CH_3$, $R^2 = H$] gives a well-defined ^{1}H NMR spectrum both in [D_1]chloroform and [D_8]toluene, which is fully in agreement with the formation of the corresponding box-like assembly. Again, the formation of intramolecular hydrogen bonds, namely, between the amide carbonyl and the melamine NH proton, seems to be primarily responsible for preventing the assembly of **5**. Molecular mechanics calculations predict a somewhat stronger intramolecular hydrogen bond for acetamido-substituted calix[4]arene **5** [R^1, $R^2 = NHC(O)CH_3$] than for **4** (R^1, $R^2 = NH_2$);[34] this most probably explains the different assembly behavior of these two compounds in [D_8]toluene.

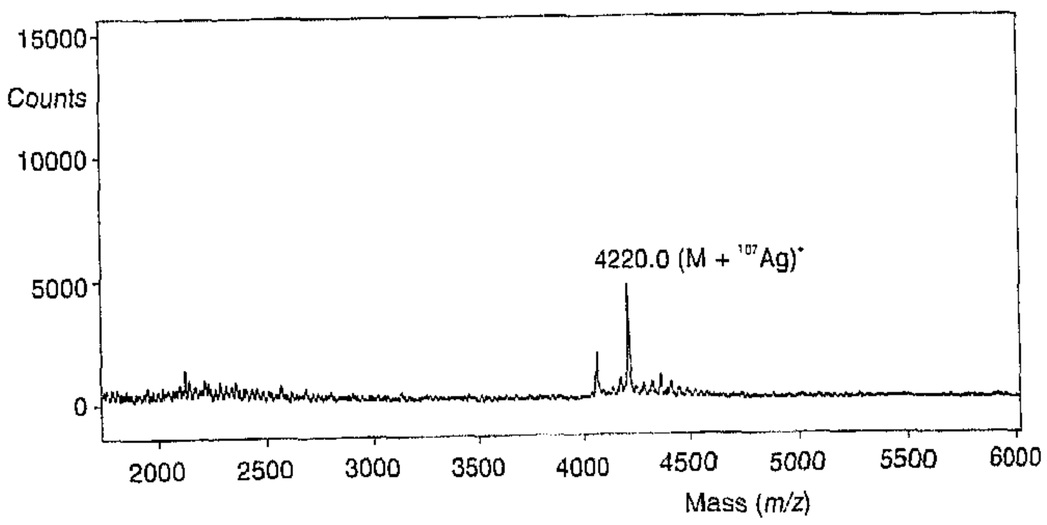

Figure 5. MALDI TOF mass spectrum of calix[4]arene box-like assembly $(\mathbf{2})_3\cdot(\mathbf{DEB})_6$ (R^1, $R^2 = CN$) in the presence of 2 equiv of $Ag^{(I)}CF_3COO$. Dihydroxybenzoic acid (DHB) was used as a matrix.

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Introduction of the bulky iodo substituents at positions R^1 and R^2 in **9** significantly broadens the imide resonances at $\delta = 13.3$ and 14.1; this reflects the reduced stability of the assembly as a result of unfavorable steric interactions. Increasing the steric bulkiness of the substituents further, completely inhibits the assembly into the box-like aggregates. Thus, the ^{1}H NMR spectrum of **8** [R^1, R^2 = *t*Bu] in the presence of two equivalents of **DEB** is extremely broad and poorly defined, and does not show the imide signals at $\delta = 13.3$ and 14.1. In sharp contrast to this, the dimelamines **10** [R^1, $R^2 = C{\equiv}CSi(CH_3)_3$] and **11** [$R^1$, $R^2 = C{\equiv}CSi(CH_2CH_3)_3$], in which the bulky trialkylsilyl substituents are separated from the aromatic rings by an acetylene spacer, do form rosette structures, as judged from the appearance of the somewhat broadened resonances at $\delta = 13.3$ and 14.1. The corresponding free acetylenes give much sharper imide resonances; this proves that the trimethylsilyl substituents also destabilize the assemblies to some extent. The strikingly different behavior of compounds **9** [R^1, $R^2 = C(CH_3)_3$], and **10** [R^1,$R^2 = C{\equiv}CSi(CH_3)_3$] nicely demonstrates that the exact position of the bulky substituents does have a profound effect on the stability of the box-like assemblies.

Conclusions

In this paper we have presented the complete characterization of noncovalently assembled calix[4]arene molecular boxes by ^{1}H NMR spectroscopy, single crystal X-ray diffraction, and MALDI TOF mass spectrometry. The assemblies, which are highly stable in apolar solvents, are stereogenic as a result of an antiparallel orientation of the two rosette motifs. Comparing the stability of the various molecular boxes carrying different types of functionalities at the periphery, we have shown that:

1) Polar substituents, like nitro and cyano groups, hardly influence the stability of the hydrogen-bonded assembly.
2) The exact position of steric bulky groups strongly influences the stability of the corresponding box-like aggregates.
3) intramolecular hydrogen-bond formation can destabilize the pinched cone conformation of the calix[4]arene units and thus prevent assembly of the corresponding box-like aggregates.

We believe that additional conformational constraints at the calixarene skeleton will be required in order to observe the noncovalent assembly of calix[4]arene molecular boxes in the presence of multiple hydrogen bond donating and/or accepting groups.

Experimental Section

General: All experiments were carried out in an argon atmosphere. THF was distilled from Na/benzophenone ketyl, and hexane (referring to petroleum ether fraction with b.p. 60–80 °C), CH_2Cl_2 and EtOAc from K_2CO_3. All chemicals were of reagent grade and used without further purification. NMR spectra were recorded on a Bruker AC250 (^{1}H NMR 250 MHz) or a Varian Unity 400 (^{1}H NMR 400 MHz) spectrometer in [D_1]chloroform at room temperature, unless stated otherwise. Residual solvent protons were used as internal standard, and chemical shifts are given relative to tetramethylsilane (TMS). FAB and EI spectra were measured on a Finnigan MAT90 spectrometer with *m*-nitrobenzyl alcohol (NBA) as a matrix. MALDI-TOF mass spectra were recorded on a PerSpective Biosystems Voyager-DE-RP spectrometer. A 337 nm UV nitrogen laser producing 3 ns pulses was used in the linear and reflectron modes. Melting points were determined with a Reichert melting point apparatus and are uncorrected. Flash chromatography was performed on silica gel (SiO_2, E. Merck, 0.040–0.063 mm, 230–240 mesh). The presence of solvents in the analytical samples was confirmed by ^{1}H NMR spectroscopy. The synthesis of compounds **13a**,[18] **13b–15**,[19] **21**,[20] **23**,[24] and **22**[19] have been described elsewhere.

5,17-Dinitro-11-phthalimido-25,26,27,28-tetrapropoxycalix[4]arene (24): A solution of 1,3-dinitrocalix[4]arene **23** (1.0 g, 1.5 mmol) in $CHCl_3$ (25 mL) was added to a suspension of $AgCF_3COO$ (0.32 g, 1.5 mmol) in refluxing $CHCl_3$ (25 mL), and the cloudy solution was refluxed for 15 min. Then I_2 (0.37 g, 1.5 mmol) was added in portions until the deep purple color was permanent. During the addition, AgI precipitated from the solution as a yellow solid. The reaction mixture was refluxed for another 15 min, filtered over Celite, and evaporated to dryness. The residue was taken up in EtOAc (50 mL), washed with a 10% $Na_2S_2O_3$ solution (10 mL), H_2O (3 × 10 mL), and brine (10 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the crude material refluxed in collidine (25 mL) for 24 h in the presence of phthalimide (0.33 g, 2.2 mmol) and Cu_2O (0.16 g, 1.0 mmol). The reaction mixture was cooled to RT and diluted with CH_2Cl_2 (50 mL). It was then washed with 5% H_2SO_4 (2 × 25 mL), 2N NaOH (10 mL), H_2O (2 × 25 mL), and brine (25 mL), and dried over Na_2SO_4. Evaporation of the solvent gave a black solid material, which was purified by column chromatography (SiO_2, CH_2Cl_2) to give monophthalimide **24** in 50% yield as a yellow solid. M.p. 148–150 °C (CH_2Cl_2/MeOH). ^{1}H NMR: δ = 8.0–7.7 (m, 4H, ArH), 7.7–7.6 (m, 4H, *o*-NO_2ArH), 6.78 (s, 2H, *o*-phthalimidoArH), 6.7–6.4 (m, 3H, ArH), 4.52, 4.49 (2d, 4H, ^2J(H,H) = 13.6 Hz, $ArCH_2Ar$), 4.1–3.9 (m, 4H, OCH_2), 3.86, 3.83 (2t, 4H, ^3J(H,H) = 8.0 and 7.7 Hz, OCH_2), 3.31, 3.28 (2d, 4H, ^2J(H,H) = 13.6 Hz, $ArCH_2Ar$), 2.1–1.8 (m, 8H, OCH_2CH_2), 1.1–0.9 [m, 12H, $O(CH_2)_2CH_3$]. MS (FAB): *m/z* = 828.2 (100) ([*M*+H]$^+$, calcd 828.3). $C_{48}H_{49}N_3O_{10}$: calcd C 69.63, N 5.08, H 5.97; found: C 69.54, N 4.99, H 5.98.

5,17-Diamino-11,23-bis(1,1-dimethylethyl)-25,26,27,28-tetrapropoxycalix[4]arene (16): A solution of 1,3-dinitro **21** (0.50 g, 0.63 mmol), hydrazine monohydrate (0.50 mL), and a catalytic amount of Raney Ni in MeOH (25 mL) was refluxed for 2 h. After filtering the hot solution over Celite, the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (50 mL), washed with H_2O (2 × 25 mL) and brine (25 mL), and dried over Na_2SO_4. Evaporation of the solvent gave 1,3-diamine **16** as an orange-brown solid in quantitative yield. ^{1}H NMR: δ = 6.98 (s, 4H, *o*-*t*BuArH), 5.39 (s, 4H, *o*-NH_2ArH), 4.32, 2.95 (ABq, 8H, ^2J(H,H) = 13.3 Hz, $ArCH_2Ar$), 3.9–3.8 (m, 4H, OCH_2), 3.54 (t, 4H, ^3J(H,H) = 6.6 Hz, OCH_2), 1.9–1.7 (m, 8H, OCH_2CH_2), 1.30 [s, 18H, $C(CH_3)_3$], 1.01, 0.77 [2t, 12H, ^3J(H,H) = 7.4 Hz, $O(CH_2)_2CH_3$]. ^{13}C NMR: δ = 155.8, 149.3, 144.1, 140.1, 136.1, 134.1, 125.6, 115.8, 34.1, 31.8, 31.4, 23.5, 22.9, 10.9, 9.8. MS (FAB): *m/z* = 735.9 (100) ([*M*+H$^+$], calcd 735.5). $C_{48}H_{66}N_2O_4.0.5\ H_2O$: calcd C 77.48, N 3.77, H 9.08; found: C 77.42, N 3.56, H 8.92.

5,17-Diamino-11,23-diiodo-25,26,27,28-tetrapropoxycalix[4]arene (17): A suspension of 1,3-dinitro **22** (1.16 g, 1.24 mmol) and $SnCl_2 \cdot 2H_2O$ (2.8 g, 12 mmol) in EtOH (50 mL) was refluxed for 15 h, and the hot solution was then poured onto ice. CH_2Cl_2 (100 mL) was added, and the solution stirred at RT for 1 h. This was followed by the addition of 1N NaOH (100 mL) and stirring for another 30 min at RT. The organic layer was washed with H_2O (2 × 25 mL) and brine (25 mL), and dried over Na_2SO_4. Evaporation of the solvent gave pure 1,3-diamine **17** in quantitative yield as a white solid. M.p. > 280 °C (CH_2Cl_2). ^{1}H NMR: δ = 7.16 (s, 4H, *o*-IArH), 5.81 (s, 4H, *o*-NH_2ArH), 4.30, 2.97 (ABq, 8H, ^2J(H,H) = 13.3 Hz, $ArCH_2Ar$), 3.9–3.8 (m, 4H, OCH_2), 3.67 (t, 4H, ^3J(H,H) = 7.2 Hz, OCH_2), 3.1 (br s, 4H, NH_2), 2.0–1.7 (m, 8H, OCH_2CH_2), 0.99, 0.90 [2t, 12H, ^3J(H,H) = 7.5 and 7.4 Hz, $O(CH_2)_2CH_3$]. ^{13}C NMR: δ = 157.4, 149.2, 141.0, 138.6, 137.0, 134.1, 115.7, 85.5, 30.8, 23.3, 23.1, 10.6, 10.1. MS (FAB): *m/z* = 874.3 (100) (M^+, calcd 874.2). $C_{48}H_{66}N_2O_4$: calcd C 54.93, N 3.20, H 5.53; found: C 55.04, N 3.52, H 5.57.

5,17-Diamino-11,23-[(trimethylsilyl)ethynyl]-25,26,27,28-tetrapropoxycalix[4]arene (18): $Pd(PPh_3)_2Cl_2$ (10 mg, 10 mol%), CuI (2 mg, 10 mol%), and trimethylsilylacetylene (50 μL, 0.34 mmol) were added to a thoroughly degassed suspension of 1,3-diamine **17** (0.10 g, 0.11 mmol) in NEt_3 (20 mL).

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The reaction mixture was heated at 40 °C for 16 h. The solvent was removed, and the residue dissolved in CH_2Cl_2 (50 mL), washed with H_2O (2 × 25 mL) and brine (25 mL), and dried over Na_2SO_4. Evaporation of the solvent gave crude 1,3-diamine **18**, which was used as such in further reaction. ^{1}H NMR: δ = 7.16 (s, 4H, *o*-TMSC≡CArH), 5.41 (s, 4H, *o*-NH_2ArH), 4.20, 2.90 (ABq, 8H, ^2J(H,H) = 13.3 Hz, ArCH_2Ar), 3.9–3.8 (m, 4H, OCH_2), 3.45 (t, 4H, ^3J(H,H) = 7.2 Hz, OCH_2), 2.6 (brs, 4H, NH_2), 1.9–1.6 (m, 8H, O$CH_2C\mathit{H}_2$), 0.94, 0.71 [2t, 12H, ^3J(H,H) = 7.4 Hz, O$(CH_2)_2C\mathit{H}_3$], 0.16 [s, 18H, Si$(CH_3)_3$]. MS (70 eV, EI) *m/z* 814.3 (100) (M^+, calcd for $C_{50}H_{66}N_2O_4Si_2$ 814.5).

5,17-Diamino-11,23-bis[(triethylsilyl)ethynyl]-25,26,27,28-tetrapropoxycalix[4]arene (19): $Pd(PPh_3)_2Cl_2$ (50 mg, 20 mol%), CuI (5 mg, 10 mol%), and triethylsilylacetylene (0.19 mL, 1.0 mmol) were added to a thoroughly degassed suspension of 1,3-diamine **17** (0.30 g, 0.34 mmol) in NEt_3 (30 mL). The reaction mixture was heated at 45 °C for 15 h. The solvent was removed, and the residue dissolved in CH_2Cl_2 (50 mL), washed with H_2O (2 × 25 mL) and brine (25 mL), and dried over Na_2SO_4. Evaporation of the solvent gave crude 1,3-diamine, which was purified by column chromatography (SiO_2, 5% MeOH/CH_2Cl_2) to give pure diamine **19** as a foam in 50% yield. ^{1}H NMR: δ = 7.25 (s, 4H, *o*-TESC≡CArH), 5.54 (brs, 4H, *o*-NHArH), 4.33, 3.03 (ABq, 8H, ^2J(H,H) = 13.3 Hz, ArCH_2Ar), 4.1–3.9 (m, 4H, OCH_2), 3.57 (t, 4H, ^3J(H,H) = 6.6 Hz, OCH_2), 2.9 (brs, 4H, NH_2), 2.0–1.7 (m, 8H, O$CH_2C\mathit{H}_2$), 1.2–1.0 [m, 24H, O$(CH_2)_2C\mathit{H}_3$ + Si$(CH_2C\mathit{H}_3)_3$], 0.84 [t, 6H, ^3J(H,H) = 7.4 Hz, O$(CH_2)_2C\mathit{H}_3$], 0.71 [q, 12H, ^3J(H,H) = 7.8 Hz, Si$(C\mathit{H}_2CH_3)_3$]. ^{13}C NMR: δ = 159.0, 137.2, 132.7, 116.0, 107.4, 89.7, 76.6, 31.0, 23.5, 22.9, 10.9, 9.8, 7.6, 4.6. MS (FAB): *m/z* = 899.6 (100) ([*M*+H]$^+$, calcd for $C_{56}H_{78}N_2O_4Si_2$: 899.6).

5,17-Diamino-11-phthalimido-25,26,27,28-tetrapropoxycalix[4]arene (20): A solution of 1,3-dinitro **24** (0.50 g, 0.60 mmol) and $SnCl_2 \cdot 2H_2O$ (1.4 g, 6.0 mmol) in EtOH (50 mL) was refluxed for 13.5 h. The hot solution was then poured onto ice. CH_2Cl_2 (100 mL) was added, and the solution stirred at RT for 1 h. This was followed by the addition of 1 N NaOH (100 mL) and stirring for another 30 min at RT. The organic layer was washed with H_2O (2 × 25 mL) and brine (25 mL), and dried over Na_2SO_4. Evaporation of the solvent gave pure 1,3-diamine **20** in 93% yield as a yellow foam. ^{1}H NMR: δ = 8.0–7.7 (m, 4H, ArH), 6.98 (s, 2H, *o*-phthalimidoArH), 6.87 (d, 2H, ^3J(H,H) = 7.4 Hz, ArH), 6.73 (t, 1H, ^3J(H,H) = 7.4 Hz, ArH), 5.83, 5.76 (2d, 4H, ^4J(H,H) = 2.7 Hz, *o*-NH_2ArH), 4.43, 4.40 (2d, 4H, ^2J(H,H) = 13.3 Hz, ArCH_2Ar), 4.0–3.8 (m, 4H, OCH_2), 3.69 (t, 4H, ^3J(H,H) = 7.1 Hz, OCH_2), 3.09, 3.05 (2d, 4H, ^2J(H,H) = 13.3 Hz, ArCH_2Ar), 3.0 (brs, 4H, NH_2), 2.1–1.8 (m, 8H, O$CH_2C\mathit{H}_2$), 1.04 [t, 6H, ^3J(H,H) = 7.4 Hz, O$(CH_2)_2C\mathit{H}_3$], 1.0–0.9 [m, 6H, O$(CH_2)_2C\mathit{H}_3$]. ^{13}C NMR: δ = 167.6, 157.5, 157.2, 149.3, 140.9, 136.7, 136.1, 134.8, 134.2, 134.0, 132.0, 128.6, 126.4, 125.0, 123.5, 121.8, 115.8, 115.6, 76.7, 76.6, 31.1, 23.4, 23.1 (2×), 10.7, 10.1, 10.0. MS (FAB): *m/z* = 767.5 (100) (M^+, calcd for $C_{48}H_{53}N_3O_6$: 767.4).

General Procedure for the Preparation of Bis(chlorotriazine)calix[4]arenes 25a–32: A solution of the 1,3-diaminocalix[4]arene in THF was added dropwise to an ice-cooled solution of cyanuric chloride (2.5–3.0 equiv) and diisopropylethylamine (DIPEA, 5–6 equiv) in THF. The solution was stirred at 0 °C for 2 h. Then gaseous NH_3 was gently bubbled through the solution for another 3 h, while keeping the temperature at 0 °C. The reaction mixture was subsequently diluted with CH_2Cl_2 (50 mL), washed with H_2O (25 mL) and brine (25 mL), and dried over Na_2SO_4. Evaporation of the solvent gave crude bis(chlorotriazine), which was used without further purification.

5,17-*N*,*N*′-Bis[4-amino-6-chloro-1,3,5-triazin-2-yl]diamino-25,26,27,28-tetrakis(dodecyloxy)calix[4]arene (25a) was prepared from diamine **13a** (1.47 g, 1.30 mmol), cyanuric chloride (0.72 g, 3.9 mmol), and DIPEA (1.35 mL, 7.82 mmol) in THF (30 mL). The yellowish bis(chlorotriazine) **25a** was obtained in 63% yield after trituration with *n*-butanol and *n*-hexane and used without further purification. ^{1}H NMR ([D_6]DMSO) δ = 9.73 (brs, 2H, ArNH), 7.15–6.65 (brm, 6H, ArH), 6.27 (s, 4H, *o*-NHArH), 4.40, 3.19 (ABq, 8H, ^2J(H,H) = 12 Hz, ArCH_2Ar), 4.1–3.85 (brm, 4H, OCH_2), 3.75–3.35 (brm, 4H, OCH_2), 2.0–1.65 (brm, 8H, CH_2), 1.40–1.05 (m, 72H, CH_2), 0.81 (t, 12H, ^3J(H,H) = 6.2 Hz, CH_3). MS (FAB): *m/z* = 1384.5 (100) ([*M*+H]$^+$, calcd for $C_{82}H_{124}{}^{35}Cl_2N_{10}O_4$: 1384.0).

5,17-*N*,*N*′-Bis[4-amino-6-chloro-1,3,5-triazin-2-yl]diamino-25,26,27,28-tetrapropoxycalix[4]arene (25b) was prepared from diamine **13b** (0.50 g, 0.80 mmol), cyanuric chloride (0.45 g, 2.4 mmol), and DIPEA (0.84 mL, 4.8 mmol) in THF (50 mL). Instead of the normal workup, H_2O (100 mL) was added to the reaction mixture, and the resulting suspension stirred for 15 min at RT. The white solid was filtered off and washed successively with H_2O, *n*-butanol, and *n*-hexane. After the solid had been dried under high vacuum, bis(chlorotriazine) **25b** was obtained in 93% yield and used without further purification. ^{1}H NMR ([D_6]DMSO) δ = 9.65 (brs, 2H, ArNH), 7.6–7.3 (m, 6H, ArH), 6.27 (s, 4H, *o*-NHArH), 4.34, 3.12 (ABq, 8H, ^2J(H,H) = 12.9 Hz, ArCH_2Ar), 4.0–3.8 (m, 4H, OCH_2), 3.64 (t, 4H, ^3J(H,H) = 6.5 Hz, OCH_2), 2.0–1.8 (m, 8H, O$CH_2C\mathit{H}_2$), 1.07, 0.90 [2t, 12H, ^3J(H,H) = 7.4 Hz, O$(CH_2)_2C\mathit{H}_3$]. MS (FAB): *m/z* = 878.1 (100) (M^+, calcd for $C_{46}H_{52}{}^{35}Cl_2N_{10}O_4$: 878.4).

5,17-*N*,*N*′-Bis[4-amino-6-chloro-1,3,5-triazin-2-yl]diamino-11,23-dicyano-25,26,27,28-tetrapropoxycalix[4]arene (26) was prepared from diamine **14** (0.90 g, 1.3 mmol), cyanuric chloride (0.74 g, 4.0 mmol), and DIPEA (1.4 mL, 8.0 mmol) in THF (50 mL). Bis(chlorotriazine) **26** was obtained in 61% yield after trituration with EtOH and used without further purification. ^{1}H NMR: δ = 7.45 (s, 4H, *o*-CNArH), 6.4 (brs, 4H, *o*-NHArH), 4.45, 3.22 (ABq, 8H, ^2J(H,H) = 13.3 Hz, ArCH_2Ar), 4.2–4.0 (m, 4H, OCH_2), 3.8–3.5 (m, 4H, OCH_2), 2.0–1.7 (m, 8H, O$CH_2C\mathit{H}_2$), 1.06, 0.90 [2t, 12H, ^3J(H,H) = 7.4 Hz, O$(CH_2)_2C\mathit{H}_3$]. MS (FAB): *m/z* = 929.5 (100) ([*M*+H$^+$], calcd for $C_{48}H_{50}{}^{35}Cl_2N_{12}O_4$: 929.3).

5,17-*N*,*N*′-Bis[4-amino-6-chloro-1,3,5-triazin-2-yl]diamino-11,23-dinitro-25,26,27,28-tetrapropoxycalix[4]arene (27) was prepared from diamine **15** (0.40 g, 0.56 mmol), cyanuric chloride (0.32 g, 1.7 mmol), and DIPEA (0.60 mL, 3.4 mmol) in THF (25 mL). Bis(chlorotriazine) **27** was obtained in 86% yield after recrystallization from DMSO/CH_2Cl_2. ^{1}H NMR ([D_6]DMSO) δ = 9.9 (brs, 2H, ArNH), 7.8–7.4 (m, 8H, *o*-NO_2ArH + NH_2), 6.89 (s, 4H, *o*-NHArH), 4.35, 3.30 (ABq, 8H, ^2J(H,H) = 13.6 Hz, ArCH_2Ar), 4.3–4.1 (m, 4H, OCH_2), 3.92, 3.74 (2t, 8H, ^3J(H,H) = 6.3 Hz, OCH_2), 1.9–1.8 (m, 8H, O$CH_2C\mathit{H}_2$), 1.09, 0.86 [2t, 12H, ^3J(H,H) = 7.4 Hz, O$(CH_2)_2C\mathit{H}_3$]. MS (FAB): *m/z* = 969.5 (100) ([*M*+H$^+$], calcd for $C_{46}H_{50}{}^{35}Cl_2N_{12}O_8$: 969.4).

5,17-*N*,*N*′-Bis[4-amino-6-chloro-1,3,5-triazin-2-yl]diamino-11,23-bis(1,1-dimethylethyl)-25,26,27,28-tetrapropoxycalix[4]arene (28) was prepared from cyanuric chloride (0.38 g, 2.0 mmol), DIPEA (0.71 mL, 4.0 mmol), and diamine **16** (0.50 g, 0.68 mmol) in THF (25 mL). Crude **28** was obtained as an orange solid in quantitative yield and used without further purification. ^{1}H NMR: δ = 7.04 (s, 4H, *o*-*t*BuArH), 6.1–5.8 (m, 6H, *o*-NHArH + NH_2), 4.38, 3.06 (ABq, 8H, ^2J(H,H) = 13.5 Hz, ArCH_2Ar), 4.0–3.9 (m, 4H, OCH_2), 3.58 (t, 4H, ^3J(H,H) = 6.5 Hz, OCH_2), 2.0–1.7 (m, 8H, O$CH_2C\mathit{H}_2$), 1,30 [s, 18H, $C(CH_3)_3$], 1.02 [t, 6H, ^3J(H,H) = 7.4 Hz, N$(CH_2)_3C\mathit{H}_3$], 1.03, 0.79 [2t, 12H, ^3J(H,H) = 7.4 Hz, O$(CH_2)_2C\mathit{H}_3$]. MS (FAB): *m/z* = 991.5 (100) ([*M*+H$^+$], calcd for $C_{54}H_{68}{}^{35}Cl_2N_{10}O_4$: 991.5).

5,17-*N*,*N*′-Bis[4-amino-6-chloro-1,3,5-triazin-2-yl]diamino-11,23-diiodo-25,26,27,28-tetrapropoxycalix[4]arene (29) was prepared from 1,3-diamine **17** (0.88 g, 1.0 mmol), cyanuric chloride (0.56 g, 3.0 mmol), and DIPEA (1.0 mL, 6.0 mmol) in THF (50 mL). Crude bis(chlorotriazine) **29** was obtained as a white solid in quantitative yield and used without further purification. ^{1}H NMR: δ = 8.3 (brs, 1H, NH), 7.43 (s, 4H, *o*-IArH), 6.3 (brs, 4H, *o*-NHArH), 5.3 (brs, 1H, NH), 4.31, 3.01 (ABq, 8H, ^2J(H,H) = 13.4 Hz, ArCH_2Ar), 4.0–3.9 (m, 4H, OCH_2), 3.54 (t, 4H, ^3J(H,H) = 6.6 Hz, OCH_2), 2.0–1.7 [m, 8H, O$CH_2C\mathit{H}_2$], 1.01, 0.81 [2t, 12H, ^3J(H,H) = 7.4 Hz, O$(CH_2)_2C\mathit{H}_3$]. MS (FAB): *m/z* = 1131.2 (100) ([*M*+H$^+$], calcd for $C_{46}H_{50}{}^{35}Cl_2I_2N_{10}O_4$: 1131.1).

5,17-*N*,*N*′-Bis[4-amino-6-chloro-1,3,5-triazin-2-yl]diamino-11,23-bis(trimethylsilylethynyl)-25,26,27,28-tetrapropoxycalix[4]arene (30) was prepared from crude diamine **18** (125 mg, 0.114 mmol), cyanuric chloride (63 mg, 0.34 mmol), and DIPEA (0.12 mL, 0.69 mmol) in THF (15 mL). Crude **30** was obtained quantitatively and used without further purification. ^{1}H NMR: δ = 7.32 (s, 4H, *o*-TMSC≡CArH), 6.3 (brs, 4H, *o*-NHArH), 5.3 (brs, 2H, NH_2), 4.39, 3.11 (ABq, 8H, ^2J(H,H) = 13.3 Hz, ArCH_2Ar), 4.1–3.9 (m, 4H, OCH_2), 3.63 (t, 4H, ^3J(H,H) = 6.6 Hz, OCH_2), 2.0–1.7 (m, 8H, O$CH_2C\mathit{H}_2$), 1.10, 0.89 [2t, 12H, ^3J(H,H) = 7.3 Hz, O$(CH_2)_2C\mathit{H}_3$], 0.20 [s, 18H, Si$(CH_3)_3$]. MS (FAB): *m/z* = 1073.1 (100) ([*M*+H$^+$], calcd for $C_{56}H_{68}{}^{35}Cl^{37}ClN_{10}O_4Si_2$: 1073.4).

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5,17-*N,N'*-Bis[4-amino-6-chloro-1,3,5-triazin-2-yl]diamino-11,23-bis(triethylsilylethynyl)-25,26,27,28-tetrapropoxycalix[4]arene (31) was prepared from cyanuric chloride (55 mg, 0.30 mmol), DIPEA (0.11 mL, 0.60 mmol), and diamine **19** (90 mg, 0.10 mmol) in THF (15 mL). Crude **31** was obtained as an off-white solid in quantitative yield and used without further purification. ^{1}H NMR: δ = 7.32 (s, 4H, *o*-TESC≡CArH), 6.3 (brs, 4H, *o*-NHArH), 5.3 (brs, 2H, NH_2), 4.39, 3.11 (ABq, 8H, ^2J(H,H) = 13.3 Hz, $ArCH_2Ar$), 4.1–3.9 (m, 4H, OCH_2), 3.63 (t, 4H, ^3J(H,H) = 6.6 Hz, OCH_2), 2.0–1.7 (m, 8H, OCH_2CH_2), 1.2–1.0 [m, 24H, $O(CH_2)_2CH_3$ + $Si(CH_2CH_3)_3$], 0.87 [t, 6H, ^3J(H,H) = 7.3 Hz, $O(CH_2)_2CH_3$], 0.69 [q, 12H, ^3J(H,H) = 7.8 Hz, $Si(CH_2CH_3)_3$]. MS (FAB): *m/z* = 1155.6 (100) ([*M*+H$^+$], calcd for $C_{62}H_{80}{}^{35}Cl_2N_{10}O_4Si_2$: 1155.5).

5,17-*N,N'*-Bis[4-amino-6-chloro-1,3,5-triazin-2-yl]diamino-11-phthalimido-25,26,27,28-tetrapropoxycalix[4]arene (32) was prepared from diamine **21** (0.43 g, 0.56 mmol), cyanuric chloride (0.26 g, 1.4 mmol), and DIPEA (0.49 g, 2.8 mmol) in THF (25 mL). Crude **32** was obtained in 70% yield and used without further purification. ^{1}H NMR ([D$_4$]methanol/[D$_1$]chloroform 1:9): δ = 7.6–7.4 (m, 4H, ArH), 6.95 (d, 2H, ^3J(H,H) = 7.4 Hz, ArH), 6.85–6.75 (m, 1H, ArH), 6.2 (brs, 2H, *o*-NHArH), 4.39 (d, 4H, ^2J(H,H) = 13.4 Hz, $ArCH_2Ar$), 4.0–3.8 (m, 4H, OCH_2), 3.64 (t, 4H, ^3J(H,H) = 6.9 Hz, OCH_2), 3.2–3.0 (m, 4H, $ArCH_2Ar$), 2.0–1.7 (m, 8H, OCH_2CH_2), 1.01 [t, 6H, ^3J(H,H) = 7.3 Hz, $O(CH_2)_2CH_3$], 0.9–0.8 [m, 6H, $O(CH_2)_2CH_3$]. MS (FAB): *m/z* = 1063.4 (40) ([*M*+H^{37}Cl+H]$^+$), 1042.3 (100) ([*M*+NH$_4$]$^+$), 1024.4 (50) ([*M*+H]$^+$, calcd for $C_{54}H_{55}{}^{35}Cl_2N_{11}O_6$ 1024.4].

General Procedure for the Preparation of Bis(melamine)calix[4]arenes 1–3, 6, and 8–11: A solution of the bis(chlorotriazine), *n*-butylamine (36 equiv), and DIPEA (12 equiv) in THF (25–50 mL) was refluxed for 5.5–19 h. The mixture was then evaporated to dryness. The residue was dissolved in CH_2Cl_2 (50 mL), washed with H_2O (3 × 25 mL) and brine (25 mL), and dried over Na_2SO_4. Evaporation of the solvent gave the crude calix[4]arene dimelamine as a white solid, which was further purified when necessary.

5,17-*N,N'*-Bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-25,26,27,28-tetrakis(dodecyloxy)calix[4]arene (1a) was prepared from bis(chlorotriazine) **13a** (1.0 g, 0.72 mmol), *n*-butylamine (2.5 mL, 25 mmol), and DIPEA (1.5 mL, 8.7 mmol) in THF (250 mL). Crude dimelamine **1a** was triturated with acetone and recrystallized from EtOAc and CH_2Cl_2 to give pure dimelamine **1a** in 74% yield. ^{1}H NMR: δ = 7.05–6.7 (br m, 6H, ArH), 6.65–6.05 (br m, 6H, *o*-NHArH + NH), 5.25–4.7 (br m, 6H, NH), 4.42, 3.11 (ABq, 8H, ^2J(H,H) = 13.3 Hz, $ArCH_2Ar$), 4.1–3.9 (br m, 4H, OCH_2), 3.8–3.6 (m, 4H, OCH_2), 3.4–3.2 (m, 4H, NCH_2), 2.0–1.75 (m, 8H, OCH_2CH_2), 1.6–1.15 (m, 72H, CH_2), 1.0–0.8 (m, 12H, CH_3). MS (FAB): *m/z* = 1458.4 (100) ([*M*+H$^+$], calcd 1458.1). $C_{90}H_{144}N_{12}O_4$: calcd C 74.14, N 11.53, H 9.95; found: C 74.29, N 11.60, H 10.26.

5,17-*N,N'*-Bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-25,26,27,28-tetrapropoxycalix[4]arene (1b) was prepared from bis(chlorotriazine) **13b** (0.50 g, 0.57 mmol), *n*-butylamine (2.0 mL, 21 mmol), and DIPEA (1.2 mL, 6.8 mmol) in THF (50 mL). Crude dimelamine **1b** was absorbed on silica gel by addition of silica gel (5% of dry weight used for column) to a solution in THF (10–15 mL) followed by careful removal of the solvent and drying under high vacuum. Subsequent purification by column chromatography (SiO_2, 10% MeOH/CH_2Cl_2) and recrystallization from EtOAc gave dimelamine **1b** as a light orange solid in 74% yield. M.p. 175–180 °C. ^{1}H NMR: δ = 7.0–6.7 (br m, 6H, ArH), 6.6–6.2 (br m, 4H, *o*-NHArH + NH), 5.0–4.8 (br m, 6H, NH), 4.43, 3.11 (ABq, 8H, ^2J(H,H) = 13.3 Hz, $ArCH_2Ar$), 4.1–3.9 (m, 4H, OCH_2), 3.69 (t, 4H, ^3J(H,H) = 6.7 Hz, OCH_2), 3.31 (q, 4H, ^3J(H,H) = 6.5 Hz, NCH_2), 2.0–1.7 (m, 8H, OCH_2CH_2), 1.6–1.3 (m, 8H, $NCH_2CH_2CH_2$), 1.06 [t, 6H, ^3J(H,H) = 7.4 Hz, $O(CH_2)_2CH_3$], 1.0–0.8 [m, 12H, $N(CH_2)_3CH_3$ + $O(CH_2)_2CH_3$]. MS (FAB): *m/z* = 954.0 (100) ([*M*+H$^+$], calcd 953.6). $C_{54}H_{72}N_{12}O_4$.0.5EtOAc: calcd C 67.43, N 16.86, H 7.68; found: C 67.31, N 16.98, H 7.52.

5,17-*N,N'*-Bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-11,23-dicyano-25,26,27,28-tetrapropoxycalix[4]arene (2) was prepared from bis(chlorotriazine) **26** (0.76 g, 0.82 mmol), *n*-butylamine (2.9 mL, 29 mmol), and DIPEA (1.7 mL, 9.8 mmol) in THF (50 mL). Crude dimelamine **2** was absorbed on silica gel by addition of silica gel (5% of dry weight used for column) to a solution in THF (10–15 mL) followed by careful removal of the solvent and drying under high vacuum. Subsequent purification by column chromatography (SiO_2, 10% MeOH/CH_2Cl_2) and recrystallization from CH_2Cl_2/MeOH gave bismelamine **2** as a light brown solid in 49% yield (based on diamine **14**). M.p. 231–233 °C. ^{1}H NMR: δ = 7.2–7.0 (br m, 4H, *o*-CNArH), 6.7–6.2 (br m, 6H, *o*-NHArH + ArNH), 5.0–4.7 (br m, 6H, NH), 4.35, 3.09 (AB q, 8H, ^2J(H,H) = 13.6 Hz, $ArCH_2Ar$), 4.0–3.8 (m, 4H, OCH_2), 3.75–3.55 (m, 4H, OCH_2), 3.28 (q, 4H, ^3J(H,H) = 6.6 Hz, NCH_2), 2.0–1.7 (m, 8H, OCH_2CH_2), 1.6–1.2 (m, 8H, $NCH_2CH_2CH_2$), 1.0–0.8 [m, 18H, $O(CH_2)_2CH_3$ + $N(CH_2)_3CH_3$]. MS (FAB): *m/z* = 1003.4 (100) ([*M*+H$^+$], calcd 1003.6). $C_{56}H_{70}N_{14}O_4$.0.5MeOH: calcd C 66.60, N 19.25, H 7.12; found: C 66.18, N 19.52, H 7.08.

5,17-*N,N'*-Bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-11,23-dinitro-25,26,27,28-tetrapropoxycalix[4]arene (3) was prepared from bis(chlorotriazine) **27** (4.6 g, 4.8 mmol), *n*-butylamine (17.0 mL, 171 mmol), and DIPEA (10.0 mL, 57.0 mmol) in THF (100 mL). The residue was recrystallized from CH_2Cl_2/EtOH to give pure dimelamine **3** as a yellow solid in 81% yield. M.p. 185–190 °C. ^{1}H NMR: δ = 7.7 (brs, 4H, *o*-NO_2ArH), 6.7–6.2 (m, 4H, *o*-NHArH + ArNH), 5.2–4.7 (m, 6H, NH), 4.39, 3.17 (AB q, 8H, ^2J(H,H) = 13.6 Hz, $ArCH_2Ar$), 4.1–3.9 (m, 4H, OCH_2), 3.8–3.6 (m, 4H, OCH_2), 3.3–3.1 (m, 4H, NCH_2), 2.0–1.6 (m, 8H, OCH_2CH_2), 1.6–1.2 (m, 8H, $NCH_2CH_2CH_2$), 1.1–0.8 [m, 18H, $O(CH_2)_2CH_3$ + $N(CH_2)_3CH_3$]. MS (FAB): *m/z* = 1044.3 (100) ([*M*+2H$^+$], calcd 1044.6). $C_{54}H_{70}N_{14}O_8$·EtOH: calcd C 61.74, N 18.00, H 7.03; found: C 61.67, N 18.23, H 7.12.

5,17-Diamino-11,23-*N,N'*-bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]-diamino-25,26,27,28-tetrapropoxycalix[4]arene (4): Excess hydrazine monohydrate (1.0 mL) and a catalytic amount of Raney Ni were added to a suspension of 1,3-dinitro **3** (0.50 g, 0.48 mmol) in THF/MeOH (100 mL, 1:1 *v/v*). The mixture was refluxed for 2 h. Then the suspension was filtered immediately over Celite and evaporated to dryness to give pure diamine **4** as a white solid in quantitative yield. M.p. 175–180 °C (MeOH). ^{1}H NMR: δ = 6.6–6.2 (m, 10H, ArH + NH), 5.1–4.8 (m, 6H, NH), 4.35, 2.97 (AB q, 8H, ^2J(H,H) = 13.0 Hz, $ArCH_2Ar$), 3.9–3.6 (m, 8H, OCH_2), 3.34 (q, 4H, ^3J(H,H) = 6.5 Hz, NCH_2), 2.0–1.3 [m, 16H, OCH_2CH_2 + $NCH_2CH_2CH_2$], 1.04 [t, 6H, ^3J(H,H) = 7.2 Hz, $O(CH_2)_2CH_3$], 1.0–0.8 [m, 12H, $N(CH_2)_3CH_3$ + $O(CH_2)_2CH_3$]. MS (FAB): *m/z* = 983.9 (100) ([*M*+H$^+$], calcd 983.6). $C_{54}H_{74}N_{14}O_4$·2H_2O: calcd C 63.62, N 19.24, H, 7.71; found: C 63.76, N 19.00, H, 7.52.

5,17-Bis(acetamido)-11,23-*N,N'*-bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-25,26,27,28-tetrapropoxycalix[4]arene (5): K_2CO_3 (1 M) was added to a turbid solution of 1,3-diamine **4** (100 mg, 0.102 mmol) in THF/EtOAc (40 mL, 1:1 *v/v*), which rapidly clarified. Excess acetyl chloride (0.3 mL) was then added, and the two-phase solution was vigorously stirred for 1 h, after which TLC analysis showed the complete disappearance of starting material. The reaction mixture was washed with H_2O (3 × 25 mL) and brine (25 mL) and dried over Na_2SO_4. Removal of the solvent and recrystallization from $CHCl_3$/hexane gave pure **5** as an off-white solid in 83% yield. M.p. 258–260 °C. ^{1}H NMR ([D$_4$]methanol/[D$_1$]chloroform 1:9) δ = 7.0 (brs, 4H, ArH), 6.4 (brs, 4H, ArH), 4.32, 3.03 (ABq, 8H, ^2J(H,H) = 13.2 Hz, $ArCH_2Ar$), 4.0–3.8 (m, 4H, OCH_2), 3.56 (t, 4H, ^3J(H,H) = 6.6 Hz, OCH_2), 3.4–3.2 (m, 4H, NCH_2), 2.0–1.7 (m, 8H, OCH_2CH_2), 1.84 [s, 6H, $C(O)CH_3$], 1.6–1.2 (m, 8H, $NCH_2CH_2CH_2$), 1.00 [t, 6H, ^3J(H,H) = 7.3 Hz, $O(CH_2)_2CH_3$], 1.0–0.7 [m, 12H, $N(CH_2)_3CH_3$ + $O(CH_2)_2CH_3$]. MS (FAB): *m/z* = 1068.1 (100) ([*M*+H]$^+$, calcd 1067.6). $C_{58}H_{78}N_{14}O_6$·0.25$CHCl_3$·0.5*n*-hexane: calcd C 64.52, N 17.20, H 7.54; found: C 64.58, N 17.48, H 7.53.

11-Amino-5,17-*N,N'*-bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-25,26,27,28-tetrapropoxycalix[4]arene (6) was prepared from monophthalimide **32** (0.20 g, 0.20 mmol), *n*-butylamine (0.7 g, 7.0 mmol), and DIPEA (0.49 g, 2.8 mmol) in THF (25 mL). The crude material was refluxed for 2 h in EtOH/THF (30 mL, 5:1) in the presence of excess hydrazine (0.20 mL). After evaporation of the solvents, the residue was dissolved in CH_2Cl_2 (50 mL), washed with 1 N NaOH (2 × 25 mL), H_2O (2 × 25 mL), and brine (25 mL), and dried over Na_2SO_4. Removal of the solvent gave crude dimelamine **6**, which was recrystallized from CH_2Cl_2/hexane to give pure **6** in 54% yield. M.p. 150–155 °C (slow phase transition). ^{1}H NMR: δ = 7.0–6.1 (m, 9H, ArH), 4.9 (brs, 6H, NH), 4.41, 4.35 (2d, 4H, ^2J(H,H) = 13.5 and 13.2 Hz, $ArCH_2Ar$), 4.0–3.6 (m, 8H, OCH_2), 3.5–3.2 (m, 6H, NCH_2 + NH_2), 3.09, 2.96 (2d, 4H, ^2J(H,H) = 13.4 and 13.3 Hz, $ArCH_2Ar$),

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2.0–1.8 (m, 8H, OCH_2CH_2), 1.6–1.3 (m, 8H, $NCH_2CH_2CH_2$), 1.04 [t, 6H, ^3J(H,H) = 7.4 Hz, $O(CH_2)_2CH_3$], 1.0–0.8 [m, 12H, $O(CH_2)_2CH_3 + N(CH_2)_3CH_3$]. MS (FAB): m/z = 968.8 (100) ($[M+H]^+$, calcd 968.6). $C_{54}H_{73}N_{13}O_4 \cdot 0.6CH_2Cl_2 \cdot 0.25n$-hexane: calcd C 64.74, N 17.50, H 7.52; found: C 64.61, N 17.54, H 7.48.

11-Acetamido-5,17-*N,N'*-bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-25,26,27,28-tetrapropoxycalix[4]arene (**7**): The reaction was carried out according to the procedure described for compound **5**, by using monoamine **6** (50 mg, 52 μmol) and excess acetyl chloride (0.10 mL) in a mixture of EtOAc/1 M K_2CO_3 (20 mL, 1:1), to give monoamide **7** in 65% yield after recrystallization from CH_2Cl_2/hexane. M.p. 150–155 °C (slow phase transition). ^{1}H NMR: δ = 7.0–6.1 (m, 9H, ArH), 5.1 (brs, 6H, NH), 4.41, 4.38 (2d, 4H, ^2J(H,H) = 13.1 and 13.2 Hz, $ArCH_2Ar$), 4.0–3.6 (m, 8H, OCH_2), 3.5–3.2 (m, 4H, NCH_2), 3.09, 3.07 (2d, 4H, ^2J(H,H) = 13.3 and 12.9 Hz, $ArCH_2Ar$), 2.06 [s, 3H, $C(O)CH_3$], 2.0–1.7 (m, 8H, OCH_2CH_2), 1.6–1.2 (m, 8H, $NCH_2CH_2CH_2$), 1.01 [t, 6H, ^3J(H,H) = 7.3 Hz, $O(CH_2)_2CH_3$], 0.92 [t, 12H, ^3J(H,H) = 7.1 Hz, $O(CH_2)_2CH_3 + N(CH_2)_3CH_3$]. MS (FAB): m/z = 1011.0 (100) ($[M+H]^+$, calcd 1010.6). $C_{56}H_{75}N_{13}O_5 \cdot 0.5CH_2Cl_2 \cdot 0.5n$-hexane: calcd C 65.21, N 16.62, H 7.30; found: C 65.22, N 16.64, H 7.47.

5,17-*N,N'*-Bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-11,23-bis(1,1-dimethylethyl)-25,26,27,28-tetrapropoxycalix[4]arene (**8**) was prepared from crude bis(chlorotriazine) **28** (0.57 g, 0.57 mmol), *n*-butylamine (2.0 mL, 21 mmol), and DIPEA (1.2 mL, 6.9 mmol). Calix[4]arene dimelamine **8** was obtained as an orange oil in 97% overall yield (based on diamine **16**). ^{1}H NMR: δ = 6.97 (s, 4H, *o*-*t*BuArH), 6.2–5.8 (m, 4H, *o*-NHArH), 5.5–4.8 (m, 6H, NH), 4.34, 3.03 (ABq, 8H, ^2J(H,H) = 13.3 Hz, $ArCH_2Ar$), 4.0–3.8 (m, 4H, OCH_2), 3.57 (t, 4H, ^3J(H,H) = 6.6 Hz, OCH_2), 3.19 (q, 4H, ^3J(H,H) = 6.5 Hz, NCH_2), 2.0–1.7 (m, 8H, OCH_2CH_2), 1.5–1.2 (m, 8H, $NCH_2CH_2CH_2$), 1.25 [s, 18H, $C(CH_3)_3$], 1.02, 0.78 [2t, 12H, ^3J(H,H) = 7.4 Hz, $O(CH_2)_2CH_3$], 0.84 [t, 6H, ^3J(H,H) = 7.2 Hz, $N(CH_2)_3CH_3$]. HRMS (FAB): m/z = 1065.7 (100) ($[M+H^+]$, calcd for $C_{62}H_{88}N_{12}O_4$: 1065.7).

5,17-*N,N'*-Bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-11,23-diiodo-25,26,27,28-tetrapropoxycalix[4]arene (**9**) was prepared from crude bis(chlorotriazine) **29** (1.3 g, 1.0 mmol), *n*-butylamine (4.0 mL, 40 mmol), and DIPEA (2.3 mL, 13 mmol). Crude calix[4]arene dimelamine was mixed with 2 equiv of DEB and subsequently purified by flash column chromatography (SiO_2, MeOH/CH_2Cl_2 10:90). The product containing fractions were washed with 1 N NaOH (3 × 25 mL), H_2O (3 × 25 mL), and brine (25 mL), and dried over Na_2SO_4. Evaporation of the solvent in vacuo gave pure dimelamine **9** as a yellow solid in a 75% overall yield (based on 1,3-diamine **17**). M.p. 185–187 °C (CH_2Cl_2). ^{1}H NMR: δ = 7.35 (s, 4H, *o*-IArH), 6.6–6.1 (m, 6H, *o*-NH_2ArH + NH), 4.9 (brs, 6H, NH), 4.35, 3.05 (ABq, 8H, ^2J(H,H) = 13.3 Hz, $ArCH_2Ar$), 4.0–3.9 (m, 4H, OCH_2), 3.64 (t, 4H, ^3J(H,H) = 6.9 Hz, OCH_2), 3.34 (q, 4H, ^3J(H,H) = 6.5 Hz, NCH_2), 2.0–1.8 (m, 8H, OCH_2CH_2), 1.7–1.3 (m, 8H, $NCH_2CH_2CH_2$), 1.1–0.8 [m, 18H, $O(CH_2)_2CH_3 + N(CH_2)_3CH_3$]. MS (FAB): m/z = 1205.6 (100) ($[M+H^+]$, calcd 1205.4). $C_{54}H_{70}I_2N_{12}O_4$: calcd C 53.82, N 13.95, H 5.86; found: C 53.95, N 13.93, H 6.00.

5,17-*N,N'*-Bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-11,23-bis[(trimethylsilyl)ethynyl]-25,26,27,28-tetrapropoxycalix[4]arene (**10**) was prepared using crude bis(chlorotriazine) **30** (110 mg, 0.114 mmol), *n*-butylamine (0.41 mL, 4.1 mmol), and DIPEA (0.24 mL, 1.4 mmol) in THF (20 mL). The crude material was purified by flash column chromatography (SiO_2, 5% MeOH/CH_2Cl_2) to give pure dimelamine **10** as a colorless sticky solid in 46% overall yield (based on 1,3-diamine **18**). ^{1}H NMR: δ = 7.19 (s, 4H, *o*-TMSC≡CArH), 6.3–6.0 (m, 6H, *o*-NHArH + NH), 5.3–4.7 (brm, 6H, NH), 4.30, 3.01 (ABq, 8H, ^2J(H,H) = 13.4 Hz, $ArCH_2Ar$), 4.0–3.9 (m, 4H, OCH_2), 3.55 (t, 4H, ^3J(H,H) = 6.7 Hz, OCH_2), 3.25 (q, 4H, ^3J(H,H) = 6.5 Hz, NCH_2), 1.9–1.7 (m, 8H, OCH_2CH_2), 1.5–1.2 (m, 8H, $NCH_2CH_2CH_2$), 1.01 [t, 6H, ^3J(H,H) = 7.4 Hz, $O(CH_2)_2CH_3$], 0.9–0.7 [m, 12H, $O(CH_2)_2CH_3 + N(CH_2)_3CH_3$], 0.21 [s, 18H, $Si(CH_3)_3$]. MS (FAB): m/z = 1145.7 (100) ($[M+H^+]$, calcd 1145.7). $C_{64}H_{88}N_{12}O_4Si_2 \cdot 1.5H_2O$: calcd C 65.55, N 14.33, H 7.82; found: C 65.62, N 14.39, H 7.63.

5,17-*N,N'*-Bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-11,23-bis[(triethylsilyl)ethynyl]-25,26,27,28-tetrapropoxycalix[4]arene (**11**) was prepared from crude bis(chlorotriazine) **31** (90 mg, 0.10 mmol), *n*-butylamine (0.36 mL, 3.6 mmol), and DIPEA (0.21 mL, 1.2 mmol) in THF (15 mL). Pure dimelamine **11** was obtained as a colorless foam in quantitative yield. ^{1}H NMR: δ = 7.19 (s, 4H, *o*-TESC≡CArH), 6.3–6.1 (m, 6H, *o*-NHArH + NH), 4.9 (brs, 4H, NH_2), 4.7 (brs, 2H, NH), 4.30, 3.02 (ABq, 8H, ^2J(H,H) = 13.4 Hz, $ArCH_2Ar$), 4.0–3.9 (m, 4H, OCH_2), 3.55 (t, 4H, ^3J(H,H) = 6.6 Hz, OCH_2), 3.24 (q, 4H, ^3J(H,H) = 6.5 Hz, NCH_2), 1.9–1.7 (m, 8H, OCH_2CH_2), 1.5–1.2 (m, 8H, $NCH_2CH_2CH_2$), 1.1–1.0 [m, 24H, $O(CH_2)_2CH_3 + Si(CH_2CH_3)_3$], 0.86 [t, 6H, ^3J(H,H) = 7.1 Hz, $N(CH_2)_3CH_3$], 0.79 [t, 6H, ^3J(H,H) = 7.5 Hz, $O(CH_2)_2CH_3$], 0.63 [q, 12H, ^3J(H,H) = 7.8 Hz, $Si(CH_2CH_3)_3$]. MS (FAB): m/z = 1229.9 (100) ($[M+H^+]$, calcd 1229.8). $C_{70}H_{100}N_{12}O_4Si_2 \cdot H_2O$: calcd C 67.37, N 13.47, H 8.24; found: C 67.28, N 13.47, H 8.41.

5,17-*N,N'*-Bis[4-amino-6-(butylamino)-1,3,5-triazin-2-yl]diamino-11,23-diethynyl-25,26,27,28-tetrapropoxycalix[4]arene (**12**): To a solution of calix[4]arene dimelamine **11** (33 mg, 29 μmol) in THF/MeOH (10 mL, 1:1 *v*/*v*) was added 1 N NaOH (1–2 mL), and the mixture was stirred at RT for 1 h. After removal of the solvent, the residue was taken up in CH_2Cl_2 (25 mL), washed with H_2O (3 × 10 mL) and brine (10 mL), and dried over Na_2SO_4. Evaporation of the solvent gave diacetylene **13** as a colorless solid in quantitative yield. M.p. 165–180 °C (slow phase transition). ^{1}H NMR: δ = 7.16 (s, 4H, *o*-HC≡CArH), 6.5–6.1 (brm, 6H, NH/ArH), 5.2–4.8 (brm, 6H, NH), 4.32, 3.02 (ABq, 8H, ^2J(H,H) = 13.5 Hz, $ArCH_2Ar$), 4.0–3.9 (m, 4H, OCH_2), 3.57 (t, 4H, ^3J(H,H) = 6.7 Hz, OCH_2), 3.24 (q, 4H, ^3J(H,H) = 6.5 Hz, NCH_2), 2.95 (s, 2H, ArC≡CH), 2.0–1.7 (m, 8H, OCH_2CH_2), 1.6–1.2 (m, 8H, $NCH_2CH_2CH_2$), 1.0 [t, 6H, ^3J(H,H) = 7.4 Hz, $O(CH_2)_2CH_3$], 0.9–0.7 [m, 12H, $O(CH_2)_2CH_3 + N(CH_2)_3CH_3$]. MS (FAB): m/z = 1002.1 (100) ($[M+H^+]$, calcd 1001.6). $C_{58}H_{72}N_{12}O_4 \cdot 0.5H_2O$: calcd C 68.95, N 16.64, H 7.28; found: C 68.65, N 16.62, H 7.27.

Rosette Formations: Calix[4]arene dimelamine **2**–**12** (10 mg) were each mixed with 2 equiv of **DEB** and suspended in [D_1]chloroform or [D_8]toluene. The resulting mixtures were stirred until all solid material had dissolved. In cases where the material did not dissolve, addition of 10% methanol was usually sufficient to rapidly dissolve the solid material. The resulting solution was then evaporated to dryness, and the residue redissolved in [D_1]chloroform or [D_8]toluene to give clear solutions of the corresponding hydrogen-bonded assemblies.

MALDI-TOF Mass Spectra: The samples were prepared by stirring a solution of 10 mg of $(2)_3 \cdot (DEB)_6$ and ±1.0 mg (1.0 equiv) of $Ag^{(I)}CF_3COO$ in 1.0 mL of $CHCl_3$ until all solid material had dissolved. 10 μL of this solution was then mixed with 20 μL of a solution containing 3 mg L^{-1} of 2,5-dihydroxybenzoic acid in nitromethane. 1 μL of the resulting solution was finally loaded on the gold sample plate and submitted for the MALDI-TOF measurement.

Single Crystal X-Ray Diffraction: Crystal data and structure refinement for $(3)_3 \cdot (DEB)_6 \cdot (toluene)_{20}$ ($C_{350}H_{442}N_{54}O_{42}$); crystal size = 0.60 × 0.60 × 0.50 mm, M_r = 6077.58, rhombohedral crystal system, space group $R\bar{3}c$, a = 38.7950(4), c = 42.0004(9) Å, γ = 120°, V = 54743.9(14) Å^3, Z = 6, ρ_{calcd} = 1.106 Mg m^{-3}. The diffraction data were collected with $Mo_{K\alpha}$ radiation (λ = 0.71073 Å, $2\theta_{max} \leq 40°$, ω scan mode, absorption coefficient = 0.066 mm^{-1}) and a graphite monochromator on a Siemens SMART diffractometer equipped with a CCD detector. Reflections collected 90185, independent reflections 5693 (R_{int} = 0.0478). The structure was solved by direct methods using the SHELXTL suite of programs.[35] All non-hydrogen atoms on the host were refined anisotropically; those of the guest (solvent) molecules were refined isotropically by full-matrix least-squares on F^2; hydrogen atoms were placed in calculated positions and allowed to ride on the parent atoms. No corrections were made for polarization or absorption. Data/restraints/parameters 5151/93/611, goodness-of-fit on F^2 = 1.090, final R indices [$I > 2.5\sigma(I)$]: R_1 = 0.1236, wR_2 = 0.3359, R indices (all data) R_1 = 0.1641, wR_2 = 0.4331, extinction coefficient 0.00051(11), largest diff. peak and hole 0.515 and −0.352 Å^{-3}.

The crystals are very sensitive to the absence of the solvent and are destroyed by exposure to air within several seconds. Selection of crystals to be introduced into the capillary was carried under the solvent. After the crystal was placed inside the capillary, a small amount of solvent was added and the capillary sealed.

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Experiments were carried out on the same crystal at two temperatures; −150 °C and +20 °C. At a temperature of approximately −60 °C, the reflection widths broadened by several orders of magnitude, indicating a change in the crystal. Therefore the experimental errors at −150 °C were much more significant. However, the low-temperature experiment made it possible to observe the toluene molecules and these coordinates were used as the starting points for the refinement of their locations for the experiment at +20 °C.

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100561. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK (Fax: Int. code +(1223)336-033; e-mail: deposit@ccdc.cam.ac.uk).

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