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A Novel Type of Hydrogen-Bonded Assemblies Based on the Melamine·Cyanuric Acid Motif

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This paper reports the formation of novel hydrogen-bonded assemblies $\mathbf{1}_3$·CA obtained upon mixing cyanuric acid (CA) with melamine derivatives **1**, in which two of the three possible H-bonding arrays have been blocked. The four components are held together by 9 hydrogen bonds and form a rigid planar structure in which a central CA (three ADA motifs: A = acceptor, D = donor) is hydrogen bonded to three peripheral melamine derivatives (DAD motif). Furthermore, the synthesis and assembly studies are described of hydrogen-bonded assemblies **2**−**4**·CA, comprised of three melamine derivatives that are covalently connected, and CA. The overall thermodynamic stability of assemblies **2**−**4**·CA is superior to $\mathbf{1}_3$·CA ($I_{Tm} = 9$ vs 3.6). The presence of the **2**·CA complex in chloroform was confirmed by ^{1}H NMR spectroscopy and MALDI-TOF mass spectrometry. Substitution of the trimelamines with chiral or fluorescent groups (R^3) enabled the study of the assemblies by CD and fluorescence spectroscopy. Titration experiments revealed strongly enhanced stabilities even in the presence of polar solvents, such as THF and CH_3OH. Depending on the polarity of the solvent, stacking between the planar assembly units was observed.

Introduction

Multiple noncovalent interactions, such as hydrogen-bonding, hydrophobic interactions, metal coordination, and ionic interactions, drive host−guest complexation processes and control the spontaneous aggregation of highly ordered structures in many natural and synthetic systems. Because of the unique properties of hydrogen bonds (directionality, specificity),[1,2] considerable efforts have focused on a complete understanding and full control of this special type of weak interaction.[3,4] Over the years a wide variety of well-defined synthetic supramolecular architectures has been developed.[5−10] In this respect many groups have studied the self-assembly of multicomponent structures based on the cyanuric acid−melamine motif.[11,12] Early work by Whitesides and Lehn has shown that blocking one of the H-bonding arrays of both the cyanuric acid and melamine components leads to the formation of either infinite tapes or cyclic rosette motifs.[11,13] While tape-like structures have been studied merely in the solid state[14,15] and in monolayers,[16,17] the rosette motif has been the major topic of interest in solution-phase studies.[18]

The exclusive formation of a cyclic rosette structure was achieved by covalently connecting three melamine units on a synthetic scaffold.[13,19] The resulting assemblies with single cyanurates exhibit increased thermodynamic stabilities ($I_{Tm} = 6$) in comparison to conventional rosettes ($I_{Tm} = 3.6$) as a result of the reduced number of separate components in the assemblies. The melting point index ($I_{Tm} = HB/(N - 1)$) was defined as a parameter that qualitatively represents the stability of an assembly comprised of N particles held together by HB hydrogen

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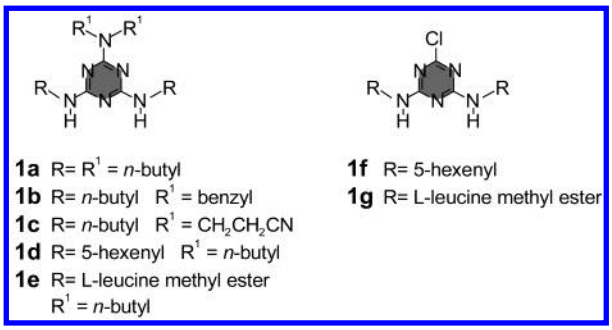
CHART 1



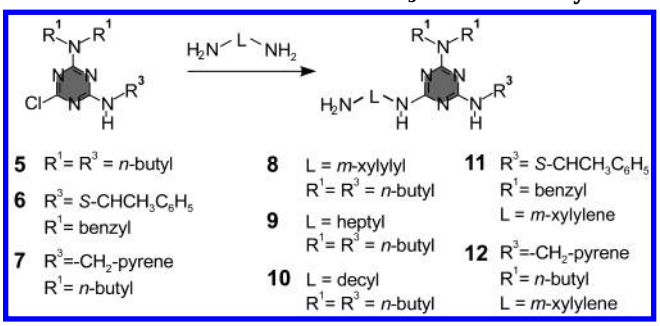
bonds.[20] A different approach toward rosette structures with improved thermodynamic stabilities involves the sideways connection of two or more melamine units into layer-by-layer double rosette ($I_{Tm} = 4.5$),[21,22] tetrarosette ($I_{Tm} = 5.14$),[23] and octarosette ($I_{Tm} = 5.33$) assemblies.[24] In a similar fashion others have used the concepts of cooperativity to improve the stability of different H-bonded structures.[25−30]

In this paper we report on a hitherto unknown substructure of the melamine·cyanuric acid (M·CA) lattice. The structure (**1**$_3$·CA) is obtained when neat cyanuric acid is mixed with 3 equiv of an *N*,*N*′,*N*″,*N*″-tetraalkyl melamine unit **1**. Despite the complete insolubility of CA in chloroform, formation of the **1**$_3$·CA assembly is readily observed as the result of the very strong interaction between cyanurate and melamine units.[31] We further describe the synthesis and formation of assemblies **2**−**4**·CA, which exhibit improved thermodynamic stabilities as the result of covalent preorganization of the melamine units.

Results and Discussion

Synthesis of the Melamine Derivatives. Single *N*,*N*′,*N*″,*N*″-tetraalkylmelamine derivatives **1a**−**e** were synthesized starting from cyanuric chloride by stepwise substitution of the three chloro substituents for either a primary or a secondary amine. Compounds **1a**−**c** were prepared in a one-pot procedure by reaction of cyanuric chloride with 1.0 equiv of either dibutylamine (**a**), dibenzylamine (**b**), or 3,3′-iminodipropionitrile (**c**) at 0 °C in the presence of *N*,*N*-diisopropylethylamine (DIPEA) in THF. Subsequent reaction with an excess of *n*-butylamine at 90 °C gave **1a**−**c** in 80−90% yield. Compounds **1d** and **1e** were prepared in a two-step procedure. First, the chlorotriazines **1f** and **1g** were synthesized by reaction of cyanuric chloride with 2.0 equiv of either 1-amino-5-hexene (**f**) or L-leucine methyl ester (**g**) at room temperature. Conversion into the melamines **1d** and **1e** was achieved by reaction with an excess of dibutylamine in 75−85% yield.

SCHEME 1. Formation of the 1$_3$·CA Assembly[a]



[a] The four components are held together by nine hydrogen bonds ($I_{Tm} = 3$).

Preparation of trimelamines **2a**, **3**, and **4** was carried out in a three-step procedure. In the first step the chlorotriazines **5**, **6**, and **7** (Scheme 1) were synthesized in 85% yield by reaction of cyanuric chloride with 1.0 equiv of the corresponding primary amine (*n*-butylamine, (*S*)-2-methylbenzylamine, and pyrenemethylamine, respectively) at 0 °C, followed by treatment with 2.0 equiv of the secondary amine (dibutylamine, dibenzylamine, and dibutylamine, respectively) at 30 °C. Subsequently, the amino-functionalized melamines **8**−**10** were obtained (80−98% yield) by refluxing the chlorotriazine **5** with a large excess of the corresponding diamine (*m*-xylylenediamine, 1,7-diaminoheptane, and 1,10-diaminodecane, respectively), while melamine **11** and **12** were obtained by refluxing **6** and **7** with *m*-xylylediamine.

In the final step (Scheme 2), the trimelamines **2a**, **3**, and **4** were synthesized by reaction of 0.5 equiv of 2-(*N*,*N*-dibenzylamino)-4,6-dichloro-1,3,5-triazine, obtained by reaction of cyanuric chloride with 1.0 equiv of dibenzylamine at 0 °C, with **8**, **9**, and **10** respectively, in 60−85% yield. For the synthesis of trimelamines **2b** and **2c** a slightly different procedure was followed. The strands **13** and **14** were obtained by a reaction of 2 equiv of the corresponding external melamines **11** and **12** with cyanuric chloride at 30 °C (70% yield). The third chloride of the central melamine was substituted by reaction with an excess of dibutylamine in refluxing THF to give the final compounds **2b** and **2c** in 90% and 80 yield, respectively.

Formation of the 4-Component Hydrogen-Bonded Assemblies 1$_3$·CA. First we studied the spontaneous formation of the hydrogen-bonded assemblies **1**$_3$·CA that are held together by 9 hydrogen bonds (Scheme 3). Initial extraction experiments showed that the single melamine **1a** ($R^1 = R^2 =$ butyl) can solubilize up to 0.33 equiv of CA in $CDCl_3$, which by itself is completely insoluble in this solvent. ^{1}H NMR spectroscopy gives clear evidence

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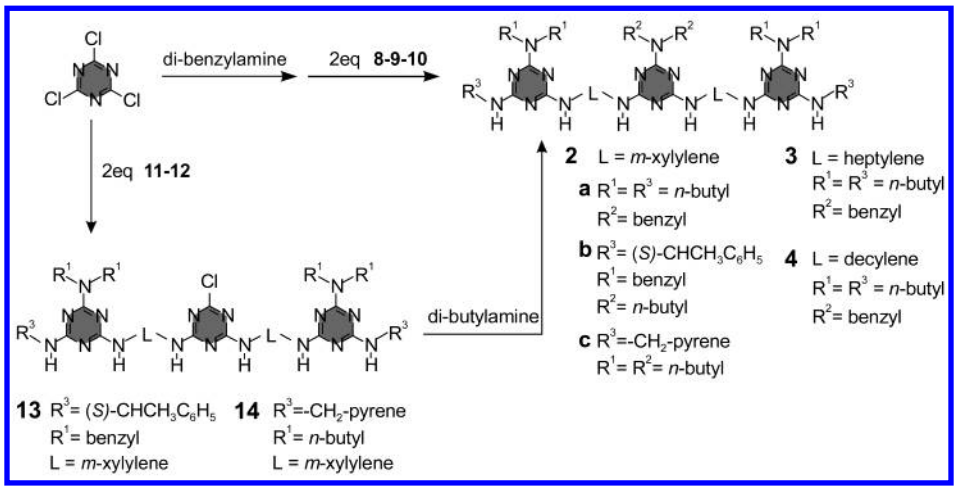
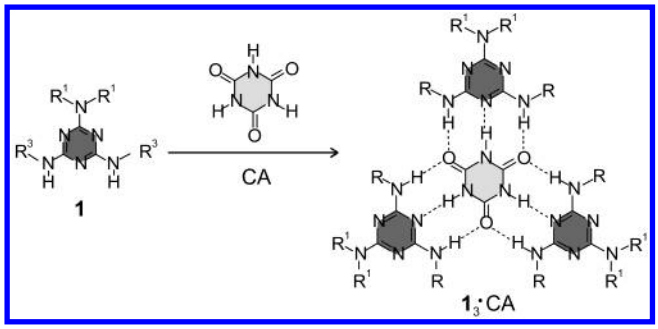
SCHEME 2. Synthetic Scheme for the Melamine Precursors 8−12



SCHEME 3. Synthetic Scheme for the Trimelamines 2−4



for the formation of the anticipated assembly **1a**$_3$·CA. Titration of **1a** with CA causes a strong downfield shift of the broad melamine NH signal at 4.8 ppm as a result of H-bond formation (see Figure 1). With 0.33 equiv of CA present, the melamine NH protons give rise to a single resonance at 7.7 ppm. The signal for the NH protons of CA within the assembly is broad and remains invisible in $CDCl_3$, even at −50 °C. To confirm the 3:1 stoichiometry of the **1a**$_3$·CA assembly, a chloroform solution of **1a** was saturated with CA and after sonication for 2 h the remaining solid was removed via filtration. Upon evaporation of the solvent the mixture was redissolved in DMSO-d_6 and integration of the melamine NHCH_2 and the cyanurate NH proton resonances, clearly visible in this solvent, confirmed the 3:1 ratio.

Formation of the **1a**$_3$·CA assembly in $CDCl_3$ was also observed by means of ^{13}C NMR spectroscopy. The spectrum of free **1a** shows two peaks at 165.3 and 164.6 ppm for the carbons of the triazine ring. In the presence of 0.33 equiv of CA the two peaks shift to 161.7 and 158.0 ppm and an extra signal appears at 163.8 ppm, corresponding to the carbonyl of the complexed CA.

Molecular modeling studies of the **1a**$_3$·CA assembly clearly show that the three melamine units nicely surround the CA unit while forming a well-defined flat triangular structure (Figure 2). The arrangement of the substituents of the three melamine units **1a** is fully compatible with the formation of nine strong hydrogen bonds, without imposing steric hindrance that could possibly destabilize the assembly.

Additional evidence for the formation of the hydrogen-bonded assemblies **1**$_3$·CA was obtained by MALDI-TOF

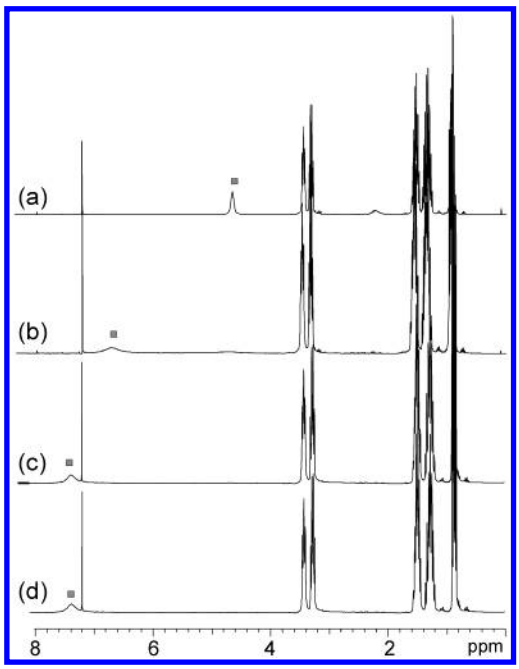


FIGURE 1. ^{1}H NMR titration of melamine **1a** with CA ($CDCl_3$, 25 °C): (a) **1a**/CA = 3:0; (b) **1a**/CA = 3:0.5; (c) **1a**/CA = 3:1; (d) **1a**/CA = 3:2. The melamine NH signal is marked with a square and shifts downfield upon the addition of CA.

mass spectrometry after Ag^+-labeling.[23] This technique was developed in our group for the characterization of neutral hydrogen-bonded assemblies by mass spectrometry. It requires the presence of a (reasonably strong) binding site for Ag^+, like a cyano group or a cleft-like aromatic pocket.[32] Melamines such as **1b** and **1c**, carrying either a dibenzylamino or a cyano group, should be able to bind Ag^+ thus providing the required ionization for detection of the corresponding assemblies **1**$_3$·CA by MALDI-TOF mass spectrometry. Samples of **1b**$_3$·CA treated with 1.5−2.0 equiv of $AgCF_3COO$ in chloroform indeed showed a strong signal at *m/z* 1494.0 (calcd for $C_{78}H_{105}N_{21}O_3$·$^{107}Ag^+$: 1491.8) corresponding to the mono-

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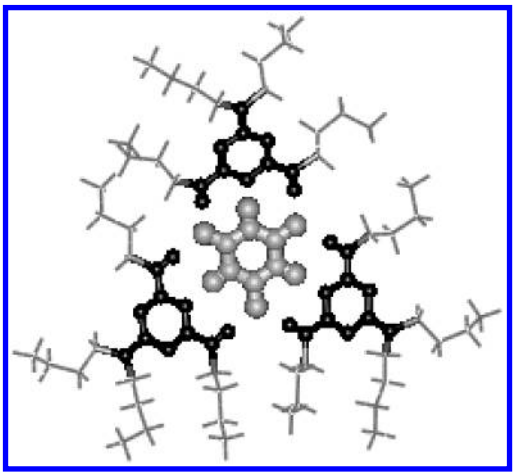

FIGURE 2. Molecular simulation (CHARMm 24.0) of assembly **1a**$_3$·CA.

valent Ag^+-complex of the assembly. Signals for assemblies with different stoichiometries were not detected. Similarly, a sample of assembly **1c**$_3$·CA gave a distinct signal at *m*/*z* 1271.1 (calcd for $C_{54}H_{87}N_{27}O_3$·$^{107}Ag^+$: 1269.5). In this case an additional signal was observed at *m*/*z* 581.3 corresponding to the **1c**·CA·Ag^+-complex (calcd for $C_{20}H_{31}N_{11}O_3$·$^{107}Ag^+$: 580.5).

Formation of assemblies **1b**$_3$·CA and **1c**$_3$·CA in solution was also studied by ^{1}H NMR spectroscopy. The NH signal of melamine **1b** was shifted from 4.8 to 7.3 ppm upon the addition of 0.33 equiv of CA, indicating the formation of assembly **1b**$_3$·CA. The spectra for assembly **1c** were more difficult to interpret. The spectrum of free **1c** gives several broad signals for the NH protons between 4.7 and 5.1 ppm, most likely due to the presence of different conformers resulting from hindered rotation around the C−NH bonds (the same phenomenon was observed for melamine **1a** and **1b** at −50 °C).[33] After the addition of CA to compound **1c** the melamine NH signal shifts downfield to 7.2 ppm and other broad peaks remain between 4.0 and 5.0 ppm. Unfortunately, the relatively low solubility of both assemblies precluded further studies by ^{13}C NMR spectroscopy.

As a logical next step, we studied the formation of **1**$_3$·CA complexes carrying different functionalities, like amino acid side chains as in **1e**. However, ^{1}H NMR titration experiments of **1e** with CA did not show the expected complexation-induced shifts for the melamine-NH signal, suggesting that the melamine does not interact with CA. Furthermore, the cyanuric acid was not solubilized into chloroform by complexation to the melamine. The very low stability of assembly **1e**$_3$·CA is most likely due to intramolecular H-bond formation between the melamine NH and the ester carbonyl group (Figure 3). The downfield position of the NH proton signals in free **1e** (5.0 and 5.9 ppm) is fully consistent with this hypothesis. CPK model inspections clearly show that the observed low stability cannot be due to steric hindrance between the branched alkyl side chains of the amino acids.

Subsequently, we studied the possibility for covalent capture of the 4-component assembly **1d**$_3$·CA, with the ultimate objective to covalently link the three **1d** units.[34] In this way, the thermodynamic stability is expected to increase significantly, since the number of individual components changes from 4 to 2, and therefore the I_{Tm} from 3 to 9. For this purpose, we used the Grubbs' ring-closing metathesis reaction (RCM) because it is usually quantitative and can be performed under very mild conditions (toluene/dichloromethane, room temperature).[35] Previous work in our group has shown that the RCM reaction is fully compatible with the formation of hydrogen-bonded double rosette assemblies.[36] However, the RCM reaction by adding 0.6 equiv of Grubbs' catalyst to a 5 mM solution of assembly **1d**$_3$·CA in CD_2Cl_2 gave neither the cyclic trimer nor the linear trimer or dimer. This might indicate that assembly **1d**$_3$·CA is significantly less stable and consequently much higher concentrations of free melamine are available for binding to the catalyst and concomitant deactivation.

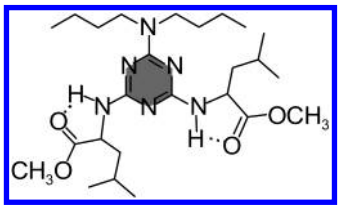

FIGURE 3. Intramolecular H-bonding in melamine **1e**.

Formation of 2-Component Hydrogen-Bonded Assemblies 2a·CA, 3·CA, and 4·CA. The results described above clearly show that single melamines such as **1** form well-defined complexes with CA but the stability of these assemblies is sometimes too low. To enhance the thermodynamic stability of these complexes, we connected the three melamine units via linkers of appropriate size. Thus, trimelamines **2**−**4** are designed to form well-defined 1:1 assemblies with CA (Scheme 4). These assemblies (**2**−**4**·CA) are expected to exhibit increased thermodynamic stabilities as a result of the preorganization of the melamine units within the corresponding complexes (I_{Tm} from 3 to 9).[20]

The three melamine units in **2a** are connected via two relatively rigid *m*-xylylene linkers. Extraction experiments clearly confirmed the formation of 1:1 complex **2a**·CA as up to 1.0 equiv of CA was solubilized in a solution of **2a** in $CDCl_3$ (free CA is completely insoluble in chloroform). ^{1}H NMR titration of trimelamine **2a** with CA showed features characteristic for formation of assembly **2a**·CA. In the presence of 0.5 equiv of CA three broad signals, assigned to the hydrogen-bonded NH protons of melamine **2a** in the assembly, become visible at 8.1, 7.8, and 7.7 ppm in addition to the broad NH signals for free **2a** between 5.3 and 4.8 ppm. The intensity of the three peaks corresponding to the complexed **2a** increases during the titration, while the intensity of the peaks corresponding to the NH protons of free **2a** decreases, indicating that exchange between free **2a** and

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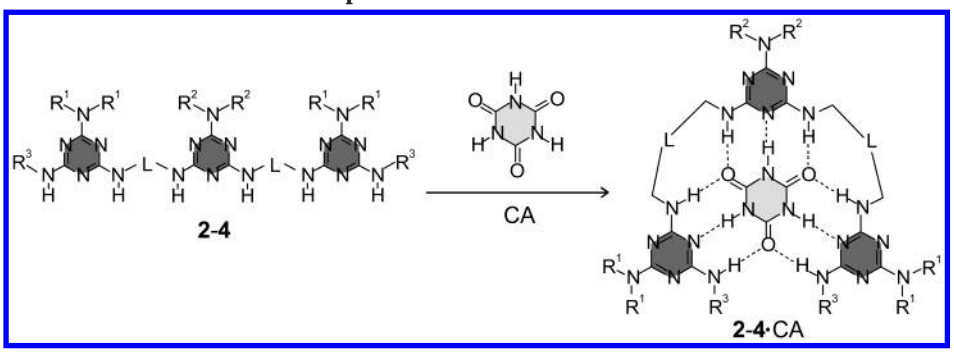
SCHEME 4. Formation of the 2−4·CA Complex[a]



[a] Nine hydrogen bonds are formed between the two species (I_{Tm} = 9).

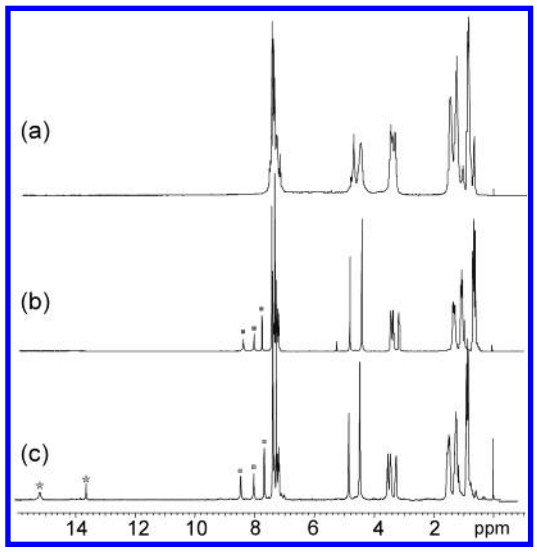


FIGURE 4. ^{1}H NMR titration of melamine **2a** with CA ($CDCl_3$, 25 °C): (a) **2a**/CA = 1:0; (b) **2a**/CA = 1:1; (c) **2a**/CA = 1:1 (at −50 °C). The melamine NH signals are marked with a square and the cyanurate NH signals are marked with stars.

the complex is slow on the NMR time scale. With 1.0 equiv of CA present, the NH signals for free **2a** have completely disappeared and sharp signals for the assembly indicate the exclusive formation of the **2a**·CA assembly (Figure 4). The ^{1}H NMR spectrum of the assembly at −50 °C shows two signals for the hydrogen-bonded NH protons of CA (ratio 1:2). The relatively sharp signal at 13.5 ppm corresponds to the cyanurate NH proton that is hydrogen bonded to the central melamine unit, while the broader signal at 14.5 ppm corresponds to the cyanurate NH protons that are hydrogen bonded to the outer melamine units. Obviously, the difference in peak shape is largely due to differences in exchange rates for these two protons. The cyanurate NH signals are too broad to be observed at room temperature, while all the other peaks remain sharp upon increasing the temperature from −50 to 30 °C. Supporting Information about the stoichiometry of the **2a**·CA complex was obtained by MALDI-TOF mass spectrometry after Ag^+-labeling. The presence of the dibenzyl side chains at the central melamine unit in **2a** allows coordination of Ag^+ ions to this assembly. Consequently, the mass spectrum of a chloroform solution of **2a**·CA after addition with 1.5 equiv of $AgCF_3COO$ showed a strong signal at *m*/*z* 1335.9 (calcd for $C_{66}H_{93}N_{21}O_3{\cdot}^{107}Ag^+$: 1336.4) corresponding to the [**2a**·CA·Ag]$^+$ complex. Signals corresponding to oligomeric species were not observed.

To study the influence of the size and flexibility of the linker on the assembly process, trimelamines **3** and **4**, with heptylene and decylene spacers connecting the individual melamine moieties, were synthesized. ^{1}H NMR titration of free **3** with CA resulted in a gradual disappearance of the broad signal between 4.5 and 4.8 ppm for the NH melamine protons, while three new peaks between 7.0 and 8.5 ppm appeared. With 1.0 equiv of CA, only the three new peaks at 8.5, 7.9, and 7.4 ppm for the three sets of $NH_{melamine}$ protons corresponding to complexed **3** were present. Additional CA was not solubilized in agreement with the expected 1:1 stoichiometry of the complex. Formation of the 1:1 assembly was also confirmed by MALDI-TOF mass spectrometry. Upon addition of 1.5 equiv of $AgCF_3COO$ to a 1:1 mixture of **3**·CA in chloroform an intense signal was observed at *m*/*z* 1324.6 (calcd for $C_{64}H_{105}N_{21}O_3{\cdot}^{107}Ag^+$: 1323.7) corresponding to the [**3**·CA·Ag]$^+$ complex. Again, signals corresponding to higher oligomers were not observed.

The same experiments were performed with trimelamine **4**, having two decylene linkers connecting the melamine units. Upon addition of CA to a $CDCl_3$ solution of **4**, a white precipitate was formed and the ^{1}H NMR spectrum showed a decrease of the amount of trimelamine **4** in solution instead of the expected downfield shift of the melamine NH proton signals. When 1.0 equiv of CA was added the proton signals for trimelamine **4** had completely disappeared and no signals for the complex could be seen. Also the MALDI-TOF spectrum did not show any signal related to the 1:1 assembly.

The experiments described above clearly illustrate the crucial role of the linkers in the assembly process.[37] The system should be sufficiently preorganized to form a well-defined hydrogen-bonded structure, otherwise insoluble oligomeric networks are formed.

Subsequently, we investigated the assembly behavior of trimelamines with different R^3 substituents. The functionalities at these positions (R^3) are of particular interest because their environment changes drastically after complexation of CA. Molecular modeling studies suggest that upon formation of assembly **2a**·CA the two R^3 substituents are forced to bend out of the plane of the assembly because of mutual steric hindrance. Therefore, the two R^3 groups are expected to arrange themselves

(37) Tjivikua, T.; Deslongchamps, G.; Rebek, J. *J. Am. Chem. Soc.* **1990**, *112*, 8408−8414.

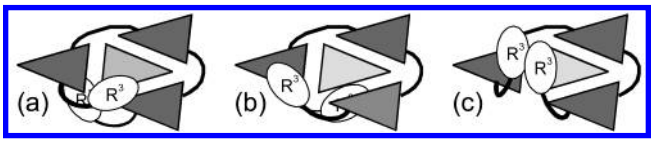


FIGURE 5. Schematic representation of assemblies **2**−**4**·CA. Different diastereoisomers may be formed: (a) the two R^3 groups are on opposite sides of the plane of the assembly, (b) enantiomer of (a), (c) the two R^3 groups are on the same side of the plane of the assembly.

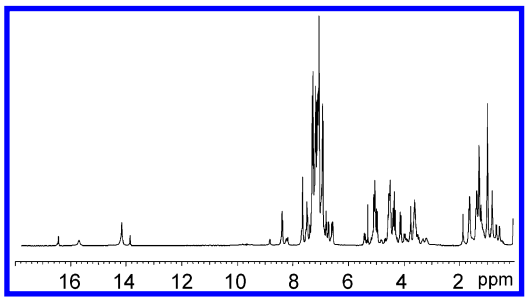


FIGURE 6. ^{1}H NMR spectra of assembly (*S*,*S*)-**2b**·CA ($CDCl_3$, −50 °C). Cyanurate NH signals are observed between 14.5 and 16.5 ppm.

either on the same side of the assembly plane or in a helical fashion (Figure 5). In the second case, the hydrogen-bonded structure can be considered as a non-covalent analogue of helicenes and should be present as a racemic mixture of two enantiomers with either *P*- or *M*-helicity. Introduction of chiral substituents at position R^3 can possibly induce the formation of diastereoisomeric assemblies, exhibiting different ^{1}H NMR and CD spectra.

Therefore, trimelamine (*S*,*S*)-**2b** containing two (*S*)-α-methylbenzylamino substituents was synthesized. In $CDCl_3$ the ^{1}H NMR spectrum of (*S*,*S*)-**2b** in the presence of 1.0 equiv of CA exhibits sharp and well-defined proton signals. Three signals at 7.3, 7.6, and 8.0 ppm are observed for the melamine NH protons. At −50 °C, the ^{1}H NMR spectrum clearly shows the presence of different diastereomeric structures (Figure 6). The signals of the melamine strand split in many small signals and the CA units give rise to four peaks at 16.5, 15.7, 14.2, and 13.8 ppm instead of two as observed with achiral **2a**. The ratio of these peaks (0.9:1.5:4.0:1.1) is difficult to analyze and suggests that all possible conformers are present in solution. Moreover, at low temperatures rotation around the C−N bond in the melamine becomes slow on the NMR time scale, which increases the number of observed signals further. The MALDI TOF mass spectrum measured after treatment of the 1:1 mixture with $AgCF_3COO$ shows only a signal for the (*S*,*S*)-**2b**·CA assembly at *m*/*z* 1500.7 (calcd for $C_{80}H_{89}N_{21}O_3{\cdot}^{107}Ag^+$: 1499.7), which excludes the presence of higher-order assemblies.

As a result of the chirality of trimelamine (*S*,*S*)-**2b**, assembly (*S*,*S*)-**2b**·CA is CD active, which enables us to study its formation and stability by CD spectroscopy. The CD spectrum of free (*S*,*S*)-**2b** shows a weak absorption between 255 and 280 nm with two maxima at 262 and 268 nm ($\Delta\epsilon$ = 2.0 and 1.53 L mol^{-1} cm^{-1}, respectively). However, the CD intensity of the hydrogen-bonded assembly (*S*,*S*)-**2b**·CA is about 10 times larger (Figure 7), and λ_{max} has shifted from 262 to 259 nm ($\Delta\epsilon$ = 12.5 L mol^{-1} cm^{-1}). As expected, assembly of trimelamine (*R*,*R*)-**2b** with two (*R*)-α-methylbenzylamino substituents with CA shows the mirror image CD spectrum.

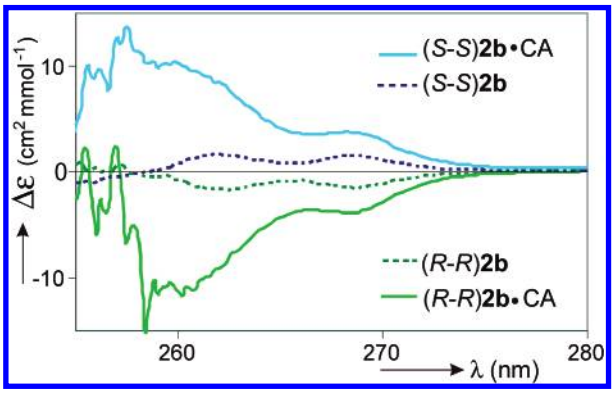


FIGURE 7. CD spectra of (*S*,*S*)-**2b** and (*R*,*R*)-**2b** (dashed lines) and the corresponding assemblies (*S*,*S*)-**2b**·CA and (*R*,*R*)-**2b**·CA (solid line) in $CHCl_3$.

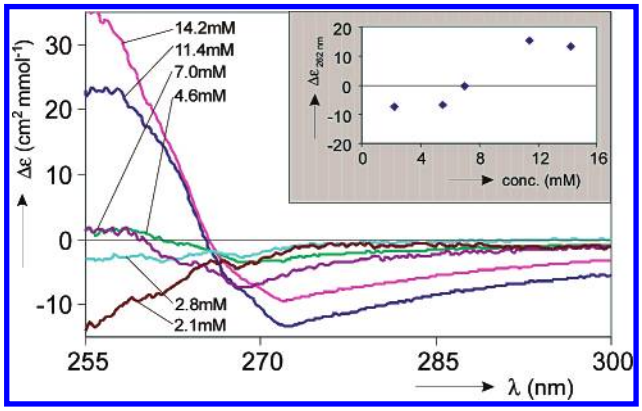


FIGURE 8. CD dilution experiments of assembly (*R*,*R*)-**2b**·CA in $CHCl_3$/THF = 1:1.

CD Titration Experiments: Thermodynamic Stability in Polar Solvents. Subsequently, we studied the thermodynamic stability of assembly (*R*,*R*)-**2b**·CA in chloroform by means of CD titration experiments. A plot of the CD intensity at 259 nm versus the amount of CA added gives a straight line (see Supporting Information, Figure S1), indicating the $K_{ass} > 10^6$ M^{-1}. This is not surprising considering the fact that nine strong hydrogen bonds are formed, while only two different components are brought together (I_{Tm} = 9).

An interesting behavior of assembly (*R*,*R*)-**2b**·CA was observed upon performing dilution experiments in two different solvents. In pure chloroform dilution studies showed a strictly linear relation (see Supporting Information, Figure S2), between the assembly concentration and CD intensity (at λ_{262}). However, the same dilution experiment performed in a 50% THF/$CHCl_3$ solution clearly showed a nonlinear relation, which might suggest that hydrophobic interactions cause stacking of the planar triangular (*R*,*R*)-**2b**·CA assemblies (Figure 8). This phenomenon is currently being studied in detail.

Fluorescence Studies with Hydrogen-Bonded Assembly 2c·CA. Introduction of two pyrene moieties at positions R^3 of trimelamine **2c** (Scheme 5) enabled us to study the stability of the assembly by fluorescence spectroscopy.[38] As for the other trimelamines, formation of the complex with CA was confirmed by ^{1}H NMR

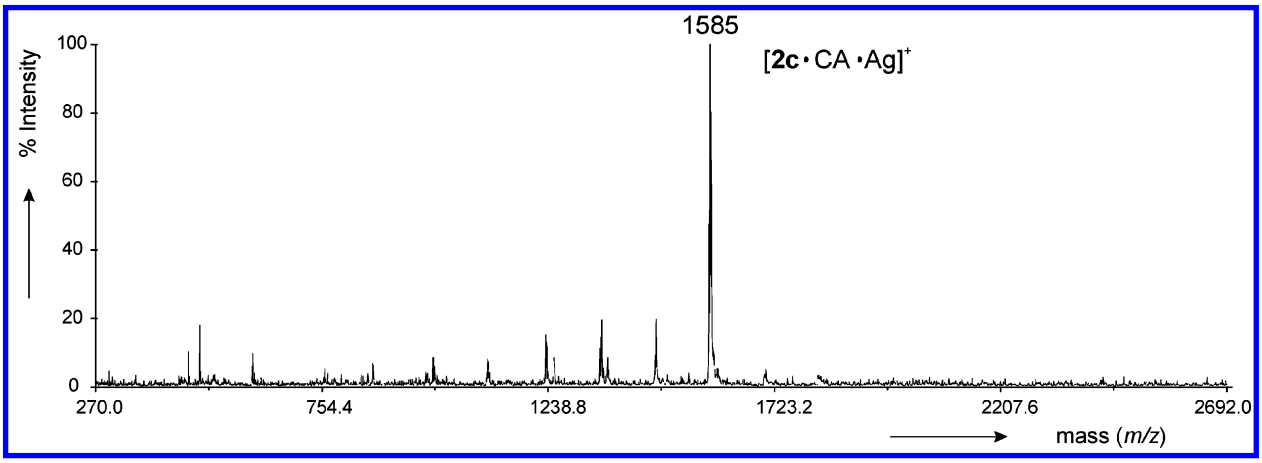
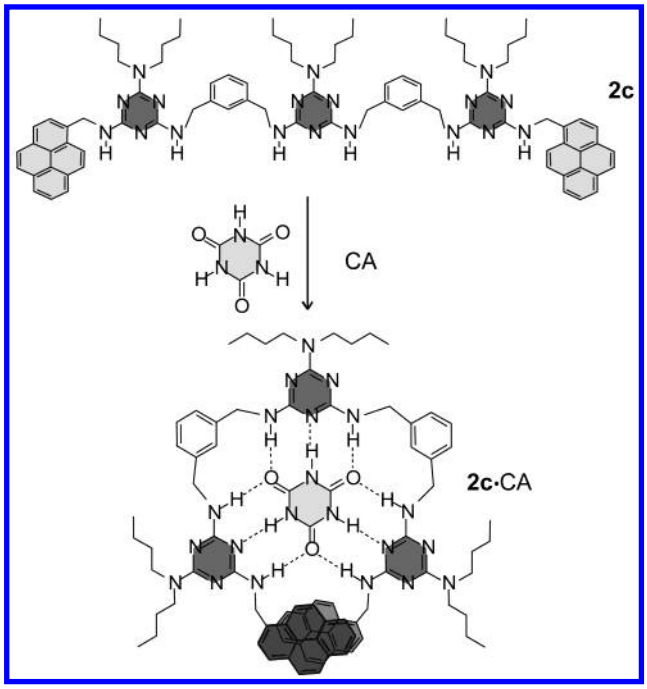


FIGURE 9. MALDI TOF mass spectrum of assembly **2c**·CA after treatment with $AgCF_3COO$ for 24 h at room temperature.

SCHEME 5. Schematic Representation of the Assembly Formed upon Mixing CA and Trimelamine 2c



spectroscopy. In the presence of 1.0 equiv of CA, all the proton signals are sharp.[39] Even though trimelamine **2c** does not carry dibenzyl groups, it was found to be able to coordinate to Ag^+, most likely via the two pyrene units. An intense signal at *m*/*z* 1585.2 (calcd for $C_{86}H_{101}N_{21}O_3$·$^{107}Ag^+$: 1583.9) is present in the MALDI-TOF spectrum (Figure 9), which corresponds to the **2c**·CA·Ag^+ complex.

Both free **2c** and **2c**·CA give nearly identical UV spectra; however, the fluorescence spectra are clearly different (Figure 10, $\lambda_{exc} = 350$ nm). The spectrum of free **2c** shows two fluorescent emission bands, i.e., the pyrene emission at about 375 and 400 nm, and the excimer band at 480 nm. Upon the addition of CA to this solution, the

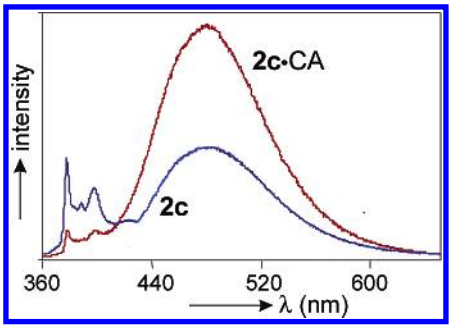


FIGURE 10. Fluorescence spectra of compound **2c** (dashed line) and the corresponding assembly **2c**·CA (solid line) in chloroform ($\lambda_{exc} = 350$ nm).

pyrene emission almost disappears and the excimer band at 480 nm drastically increases, indicating that more of the excimer is present in the complex. This is consistent with the fact that upon formation of the assembly the trimelamine is folded around the CA unit, which brings the chromophores much closer together (Scheme 5).

To estimate the association constant for assembly formation, a fluorescence titration experiment with trimelamine **2c** and CA was carried out in a mixture of chloroform and THF (4:1), ($\lambda_{exc} = 350$ nm) (see Supporting Information, Figure S3), which allows the addition of up to 3.0 equiv of CA. Fitting of the data to a 1:1 binding model gave an association constant of 10^5−10^7 M^{-1}, which represents a remarkably high stability considering the large amount (20%) of THF, a solvent that competes with hydrogen bond formation.

We also studied the stability of the 1:1 assembly via addition of different amounts of CH_3OH and THF to a 0.05 mM solution of **2c**·CA in chloroform.[40,41] Since a change in solvent polarity is also expected to influence the molar absorption coefficient of the chromophores, it is impossible to quantify the obtained results. Instead, we calculated the ratio between excimer intensity (480 nm) and the intensity for free pyrene (400 nm), assuming that both molar absorption coefficients are affected in a similar manner by the solvent polarity change. This

(38) Aoki, I.; Harada, T.; Sakaki, T.; Kawahara, Y.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1992**, 1341−1345.
(39) Only one peak is observed for the melamine NH protons at 8.7 ppm, since the other two peaks are masked by the aromatic proton signals between 8.1 and 7.5 ppm.
(40) Wuerthner, F.; Thalacker, C.; Sautter, A.; Schaertl, W.; Ibach, W.; Hollricher, O. *Chem. Eur. J.* **2000**, *6*, 3871−3886.
(41) Sautter, A.; Thalacker, C.; Heise, B.; Wuerthner, F. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4993−4996.

assumption was supported by the fact that for free **2c** both intensities were equally affected. A plot of the ratio I_{480}/I_{400} versus the percentage of THF shows a clear change in the stability of the complex (manifested as an increase of the amount of the monomer) only at 50% THF/chloroform (see Supporting Information, Figure S4). In the presence of 90% of THF, a significant amount of assembly **2c**·CA is still present, judging from the clear spectral difference for free **2c** and **2c**·CA complex. Similar results were obtained with methanol, with the difference that the spectra of the complex and the free melamine become almost equal at 50% of CH_3OH in chloroform.

Conclusions

Single *N*,*N*′,*N*″,*N*″-tetraalkylmelamines, in which two of the three DAD H-bonding arrays have been crippled, spontaneously form planar 3:1 hydrogen-bonded assemblies $\mathbf{1}_3$·CA upon mixing with 0.33 equiv of cyanuric acid (CA). The assemblies, consisting of 4 components that are held together by 9 H-bonds, are stable in apolar solvents such as chloroform and can be conveniently characterized by MALDI-TOF MS. The thermodynamic stability can be significantly improved when the three melamines are covalently connected to give the 1:1 complex **2**·CA. Titration studies by NMR, CD, and fluorescence spectroscopy confirm the much higher stability of the 1:1 complex, particularly in the presence of the more polar solvent THF. Additionally, the planar assemblies show a strong tendency to form larger aggregates, presumably via stacking, upon increasing the composition of the solvent from pure $CHCl_3$ to $CHCl_3$/THF = 1:1.

Experimental Section

General. THF was freshly distilled from Na/benzophenone, and CH_2Cl_2 from $CaCl_2$. All chemicals were of reagent grade and used without further purification. NMR spectra were recorded at room temperature unless indicated otherwise. Flash column chromatography was performed with silica gel (SiO_2, 0.040−0.063 mm, 230−240 mesh). Compound **1a** was synthesized according to a literature procedure.[31]

General Procedure for the Synthesis of Melamines 1b and 1c. To an ice-cold solution of cyanuric chloride (1.9 g, 10 mmol) and DIPEA (6.6 mL, 50 mmol) in THF (50 mL) was added dropwise the appropriate secondary amine (1.0 equiv) and the solution was stirred for 2 h. Upon increasing the temperature to 30 °C, butylamine (7.2 mL, 74.4 mmol) was added and the solution was stirred for another 24 h at 90 °C. Then, the solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with H_2O and brine and the solvent was removed under reduced pressure. The resulting yellow oil was purified by column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4OH 95/4.5/0.5).

2,4-Bis(*N*-butylamino)-6-*N*,*N*-dibenzylamino-1,3,5-triazine (1b). Compound **1b** was obtained as a transparent oil in 72% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.2−7.1 (m, 10H), 4.68 (br s, 6H), 3.3−3.2(m, 4H), 1.5−1.4 (m, 4H), 1.3−1.2 (m, 4H), 0.8−0.6 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 138.3, 127.8, 127.3, 126.3, 47.5, 39.9, 31.5, 19.5, 13.3. MS (FAB): *m*/*z* 419.3 ([M + H$^+$], calcd. 419.3). Anal. Calcd for $C_{77}H_{86}N_{18}$: C 71.74, H 8.19, N 20.08. Found: C 71.87, H 8.25, N 20.06.

2,4-Bis(*N*-butylamino)-6-(*N*,*N*-bis(cyanoethyl)amino)-1,3,5-triazine (1c). Compound **1c** was obtained as a transparent oil in 74% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.86 (br, 2H), 3.87 (br s, 4H), 3.4−3.3 (m, 4H), 2.8−2.6 (m, 4H), 1.6−1.5 (m, 4H), 1.4−1.3 (m, 4H), 0.96 (t, 6H, J_{HH} = 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 164.2, 118.0, 44.9, 39.9, 31.4, 19.5, 16.5, 13.3. MS (FAB): *m*/*z* 345.4 ([M + H$^+$], calcd 345.2).

General Procedure for the Synthesis of Melamines 1f and 1g. To an ice-cold solution of cyanuric chloride (0.1 g, 0.56 mmol) and DIPEA (12.6 mL, 72 mmol) in THF (80 mL) was added dropwise the appropriate primary amine (4.0 equiv). After the solution was stirred for 24 h at room temperature the solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with H_2O and brine and the solvent was removed under reduced pressure.

2,4-Bis(*N*-(5-hexenyl)amino)-6-chloro-1,3,5-triazine (1f). The resulting yellow solid was purified by column chromatography (SiO_2; CH_2Cl_2) to yield **1f** as a white solid in 84% yield. Mp 128−130. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.8−6.6 (m, 2H), 5.5 and 5.2 (br s, 2H), 5.2−5.0 (m, 4H), 3.4−3.2 (m, 4H), 2.1−1.9 (m, 4H), 1.6−1.5 and 1.5−1.3 (2m, 8H). MS (FAB): *m*/*z* 310.1 ([M + H$^+$], calcd 309.2.

2,4-Bis(*N*-(3-methyl-1-(L)-(methoxycarbonyl)butyl)amino)-6-chloro-1,3,5-triazine (1g). The resulting solid was purified by column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4-OH 95/4.5/0.5) to yield **1g** as a white solid in 75% yield. Mp 160−161 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.9−5.6 (br s, 2H), 4.9−4.6 (m, 2H), 3.8 (s, 6H), 1.8−1.6 (m, 6H), 1.1−0.9 (m, 12H). MS (FAB): *m*/*z* 402.1 ([M + H$^+$], calcd 401.9).

General Procedure for the Synthesis of Melamines 1d and 1e. An excess of dibutylamine (0.9 mL, 5 mmol) was added dropwise to a solution of compound **1f** or **1g** (0.25 mmol) in THF (5 mL) and the solution was refluxed for 20 h at 90 °C. Then, the solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with water and brine and the solvent was removed under reduced pressure.

2,4-Bis(*N*-(5-hexenyl)amino)-6-*N*,*N*-dibutylamino-1,3,5-triazine (1d). The resulting yellow oil was obtained from **1f** and dibutylamine and was purified by flash column chromatography (SiO_2; hexane/AcOEt 4/1). Compound **1d** was obtained as a white solid in 92% yield. Mp 92−95 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.9−5.8 (m, 2H), 5.02 (dd, 2H J_{HH} = 17.1 and 1.8 Hz), 4.96 (dd, 2H J_{HH} = 10.2 and 1.8 Hz), 4.85 (br s, 2H), 3.49 (t, 4H J_{HH} = 7.5 Hz), 3.4−3.3 (m, 4H), 1.6−1.3 (m, 20H), 1.98 (t, 6H J_{HH} = 7.5 Hz). MS (FAB): *m*/*z* 401.3 ([M − H$^+$], calcd 401.3.

2,4-Bis(*N*-(3-methyl-1-(L)-(methoxycarbonyl)butyl)amino)-6-*N*,*N*-dibutylamino-1,3,5-triazine (1e). The resulting yellow oil was obtained from **1g** and dibutylamine and was purified by flash column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4OH 95/4.5/0.5). Compound **1e** was obtained as a white solid in 95% yield. Mp 195−197 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.2 and 5.0 (br s, 2H), 4.7−4.6 (m, 2H), 3.69 (s, 6H), 3.42 (t, 4H J_{HH} = 7.5 Hz), 1.8−1.3 (m, 14H), 1.0−0.9 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 164.9, 164.1, 51.3, 46.3, 40.7, 29.6, 24.2, 22.4, 21.1, 19.7, 13.4. MS (FAB): *m*/*z* 495.3 ([M − H$^+$], calcd 495.4). Anal. Calcd for $C_{25}H_{46}N_6O_4$: C 60.70, H 9.37, N 16.99. Found: C 60.80, H 9.28, N, 16.62.

2-*N*-Butylamino-4-chloro-6-*N*,*N*-dibutylamino-1,3,5-triazine (5). To an ice-cold solution of cyanuric chloride (3.7 g, 3.7 mmol) and DIPEA (12.6 mL, 72 mmol) in THF (80 mL) was added dropwise *n*-butylamine (1.20 g, 12.1 mmol) and the solution was stirred for 2 h at 0 °C. Upon increasing the temperature to 30 °C dibutylamine was added (12.3 mL, 7.2 mmol) and the solution was stirred for another 5 h at room temperature. The solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with H_2O and brine and the solvent was removed under reduced pressure. The resulting yellow solid was purified by column chromatography (SiO_2; CH_2Cl_2) to yield **5** as a transparent oil in 83% yield (3.1 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.4 (br s, 1H, NH), 3.6−3.5 (m, 4H, CH_2NCH_2), 3.4−3.3 (m, 2H, $HNCH_2$), 1.7−1.5 (m, 6H, NCH_2CH_2), 1.4−1.2 (m, 6H, CH_2CH_3), 1.0−0.9 (m, 9H, CH_3).

MS (FAB): *m*/*z* 315.2 ([M + H$^+$], calcd 314.2). Anal. Calcd for $C_{15}H_{28}N_5Cl$: C 57.40, H 8.99, N 22.31. Found: C 57.66, H 8.83, N, 21.60.

General Procedure for the Synthesis of Melamines 8, 9, and 10. To a solution of compound **5** (833 mg, 2.6 mmol) in THF (10 mL) was added dropwise an excess of the appropriate diamine (30 equiv) and the solution was refluxed for 24 h at 90 °C. The solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with water, 1 N NaOH, and brine. The solvent was removed under reduced pressure. The resulting yellow oil was purified by column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4OH 90/8/2).

2-*N*-(3-(Aminomethyl)phenyl)amino-4-*N*-butylamino-6-*N*,*N*-dibutylamino-1,3,5-triazine (8). Compound **8** was obtained from **5** and *m*-xylylene diamine as a transparent oil in 95% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3−7.1 (m, 4H), 5.1 (br s, 1H), 4.72 (br s, 1H), 4.50 (d, 2H, J_{HH} = 6.0 Hz), 3.78 (s, 2H), 3.4−3.3 (m, 4H), 3.3−3.2 (m, 2H), 1.5−1.4 (m, 6H), 1.3−1.2 (m, 6H), 0.9−0.8 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.1, 125.6, 125.5, 125.1, 45.9, 44.0, 39.9, 31.5, 29.6, 19.7, 19.6, 13.4, 13.3. MS (FAB): *m*/*z* 414.3 ([M + H$^+$], calcd 414.3).

2-*N*-(7-Aminoheptyl)amino-4-*N*-butylamino-6-*N*,*N*-dibutylamino-1,3,5-triazine (9). Compound **9** was obtained from **5** and 1,7-diaminoheptane as transparent oil in 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (br s, 2H), 3.48 (t, 2H, J_{HH} = 7.2 Hz), 3.4−3.3 (m, 4H), 2.7 (t, 2H, J_{HH} = 6.9 Hz), 1.6−1.3 (m, 22H), 1.0−0.9 (m, 9H). MS (FAB): *m*/*z* 408.5 ([M + H$^+$], calcd 408.4).

2-*N*-(10-Aminodecyl)amino-4-*N*-butylamino-6-*N*,*N*-dibutylamino-1,3,5-triazine (10). Compound **10** was obtained from **5** and 1,10-diaminodecane as a transparent oil in 99% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.71 (br s, 2H), 3.5−3.4 (m, 4H), 3.4−3.3 (m, 4H), 2.71 (t, 2H J_{HH} = 6.6 Hz), 1.7−1.3 (m, 28H), 1.0−0.9 (m, 9H). MS (FAB): *m*/*z* 450.4 ([M + H$^+$], calcd 450.4).

General Procedure for the Synthesis of Melamines 2a, 3, and 4. To an ice-cold solution of cyanuric chloride (30 mg, 0.16 mmol) and DIPEA (0.27 mL, 1.0 mmol) in THF (10 mL) was dropwise added dibenzylamine (0.031 mL, 0.16 mmol) and the solution was stirred for 2 h at 0 °C. Upon increasing the temperature to 30 °C the appropriate compound **8**, **9**, or **10** was added (4.0 equiv) and the solution was stirred for another 24 h at 90 °C. The solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with H_2O and brine and the solvent was removed under reduced pressure. The resulting yellow oil was purified by column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4OH 98/1.7/0.3).

2-*N*,*N*-Dibenzylamino-4,6-bis[*N*-(3-(*N*-(4-*N*-butylamino-4-*N*,*N*-dibutylamino-1,3,5-triazin-2-yl)aminomethyl)-phenylmethyl)amino]-1,3,5-triazine (2a). Compound **2a** was obtained from **8** as a transparent oil in 74% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4−7.1 (m, 18H), 5.5, 5.1, and 4.8 (3 br s, 6H), 4.7 (s, 4H), 4.5 (br s, 8H), 3.5−3.4 and 3.4−3.3 (2m, 20H), 1.7−1.5 and 1.5−1.2 (2m, 24H), 1.0−0.9 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 165.5, 165.4, 165.3, 164.4, 139.9, 138.5, 128.6, 128.3, 128.2, 127.9, 127.8, 126.9, 48.1, 46.6, 44.7, 44.5, 40.4, 32.0, 30.1, 20.2, 20.1, 14.0, 13.8. MS (FAB): *m*/*z* 1099.8 ([M + H$^+$], calcd 1099.8).

2-*N*,*N*-Dibenzylamino-4,6-bis[*N*-(7-*N*-(4-*N*-butylamino-6-*N*,*N*-dibutylamino-1,3,5-triazin-2-yl)aminoheptyl)amino]-1,3,5-triazine (3). Compound **3** was obtained from **9** as a white solid in 80% yield. Mp 202−203 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.3−7.2 (m, 10H), 4.78 (br s, 6H), 4.76 (s, 4H), 3.5−3.4 (m, 8H), 3.3−3.1 (m, 12H), 1.6−1.5 (m, 20H), 1.3−1.2 (m, 24), 1.0−0.9 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 165.6, 165.4, 164.4, 138.3, 127.8, 127.3, 126.3, 47.5, 45.9, 40.2, 40.1, 39.8, 31.6, 29.7, 29.4, 29.3, 28.6, 26.4, 19.7, 13.5. MS (FAB): *m*/*z* 1087.8 ([M + H$^+$], calcd 1087.9). Anal. Calcd for $C_{61}H_{102}N_{18}$: C 67.37, H 9.45, N 23.18. Found: C 66.91, H 9.26, N, 22.84.

2-*N*,*N*-Dibenzylamino-4,6-bis[*N*-(10-*N*-(4-*N*-butylamino-6-*N*,*N*-dibutylamino-1,3,5-triazin-2-yl)aminodecyl)amino]-1,3,5-triazine (4). Compound **4** was obtained from **10** as a transparent oil in 60% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4−7.2 (m, 10H), 4.9 (br s, 6H), 4.7 (s, 4H), 3.6−3.4 (m, 8H), 3.4−3.3 (m, 12H), 1.7−1.2 (m, 56H), 1.0−0.9 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2, 127.7, 127.3, 126.2, 47.4, 45.8, 40.1, 39.7, 31.4, 29.6, 29.3, 28.8, 28.7, 26.3, 19.6, 19.5, 13.4, 13.2. MS (FAB): *m*/*z* 1171.9 ([M + H$^+$], calcd 1172.0). Anal. Calcd for $C_{67}H_{114}N_{18}$: C 68.68, H 9.81, N 21.52. Found: C 68.34, H 9.60, N, 20.98.

General Procedure for the Synthesis of Melamines 6 and 7. To an ice-cold solution of cyanuric chloride (1.4 g, 7.5 mmol) and DIPEA (5.2 mL, 3.0 mmol) in THF (100 mL) was added dropwise the appropriate primary amine (1.0 equiv) and the solution was stirred for 2 h at 0 °C. Upon increasing the temperature to 30 °C the secondary amine (dibenzylamine and dibutylamine, respectively) was added (4.0 equiv) and the solution was stirred for another 24 h at 90 °C. Then, the solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with H_2O and brine and the solvent was removed under reduced pressure.

2-Chloro-4-*N*,*N*-dibenzylamine-6-*N*-((*S*)-α-methylbenzyl)amino-1,3,5-triazine (6). The resulting yellow solid was purified by flash column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4OH 98/1.7/0.3) to yield **6** as a yellow oil in 84% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4−7.1 (m, 15H), 5.73 (d, 1H, J_{HH} = 6.9 Hz), 5.1−5.0 (m, 1H), 4.9−4.5 (m, 4H), 1.53 (d, 3H, J_{HH} = 6.9 Hz). MS (FAB): *m*/*z* 430.5 ([M + H$^+$], calcd 430.2). Anal. Calcd for $C_{25}H_{24}N_5Cl$: C 69.84, H 5.63, N 16.29. Found: C 69.88, H 5.46, N, 15.89.

2-Chloro-4-*N*,*N*-dibutylamino-6-*N*-(pyrenemethyl)amino-1,3,5-triazine (7). The resulting yellow oil was purified by flash column chromatography (SiO_2; hexane/EtOAc 250/8) to yield **7** as a white solid in 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.5−8.0 (m, 9H), 6.03 (br s, 1H), 5.31 (d, 2H, J_{HH} = 5.4 Hz), 3.6−3.4 (m, 4H), 1.6−0.9 (m, 8H), 1.0−0.7 (m, 6H). MS (FAB): *m*/*z* 472.5 ([M + H$^+$], calcd 472.5). Anal. Calcd for $C_{28}H_{30}N_5Cl$: C 71.25, H 6.41, N 14.84. Found: C 71.36, H 6.26, N 14.51.

General Procedure for the Synthesis of Melamines 11 and 12. An excess of *m*-xylylenediamine (30 equiv) was added dropwise to a solution of the appropriate melamine (**6** or **7**) in THF (10 mL) and the solution was refluxed for 24 h at 90 °C. The solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with H_2O, 1 N NaOH, and brine. The solvent was removed under reduced pressure.

2-*N*-(3-(Aminomethyl)phenylmethyl)amino-4-*N*,*N*-dibenzylamino-6-*N*-((*S*)-α-methylbenzylamino)-1,3,5-triazine (11). The resulting yellow oil was obtained from **6** and *m*-xylylene diamine and was purified by flash column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4OH 92/6/2). Compound **11** was obtained as a transparent oil in 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.2−7.1 (m, 19H), 5.10 (br s, 3H), 4.8−4.6 (br m, 2H), 4.8 (m, 4H), 3.74 (br s, 2H), 1.42 (d, 3H, J_{HH} = 5.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 165.6, 164.8, 144.4, 142.9, 139.5, 138.0, 128.2, 127.9, 127.8, 127.4, 126.4, 126.2, 125.7, 125.5, 125.3, 49.6, 47.5, 45.8, 44.2, 22.4. MS (FAB): *m*/*z* 530.3 ([M + H$^+$], calcd 530.3). Anal. Calcd for $C_{33}H_{35}N_7$: C 74.83, H 6.66, N 18.51. Found: C 74.79, H 6.54, N 18.46.

2-*N*-(3-(Aminomethyl)phenylmethyl)amino-4-*N*,*N*-dibutylamino-6-*N*-(pyrenemethyl)amino-1,3,5-triazine (12). The resulting yellow oil was obtained from **7** and *m*-xylylene diamine and was purified by column chromatography (SiO_2; hexane/EtOAc 250/8) to yield **12** as a white solid in 80% yield. Mp 118−122 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (d, 1H, J_{HH} = 9.8 Hz), 8.19 (d, 1H, J_{HH} = 10.0 Hz), 8.1−8.0 (m, 7H), 7.3−7.2 (m, 4H), 5.29 (br, 2H), 5.28 (br s, 2H), 5.31 (br s, 2H), 3.84 (s, 2H), 3.5−3.4 (m, 4H), 1.6−0.4 (br m, 4H), 1.3−1.1 (br m, 4H), 0.9−0.7 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5,

165.4, 164.6, 143.3, 139.7, 132.3, 130.8, 130.2, 128.3, 128.1, 127.2, 126.9, 126.6, 125.9, 125.6, 125.5, 125.3, 125.2, 124.5, 124.3, 124.2, 122.6, 46.1, 45.9, 44.1, 42.4, 29.7, 19.7, 13.4. MS (FAB): *m*/*z* 573.0 ([M + H^+], calcd 573.3). Anal. Calcd for $C_{36}H_{41}N_7$: C 75.62, H 7.23, N 17.15. Found: C 75.80, H 7.06, N 16.52.

General Procedure for the Synthesis of Melamines 13 and 14. To an ice-cold solution of cyanuric chloride (1.9 g, 10 mmol) and DIPEA (6.6 mL, 50 mmol) in THF (50 mL) was added dropwise the appropriate amino-functionalized single melamine (**11** or **12**) (3.0 equiv) and the solution was stirred for 2 h at 0 °C. Upon increasing the temperature to 30 °C the solution was stirred for another 24 h at room temperature. Then the solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with H_2O and brine and the solvent was removed under reduced pressure.

2-Chloro-4,6-bis[*N*-(3-(*N*-(4-*N*,*N*-dibenzylamino-6-*N*-((*S*)-α-methylbenzyl)amino-1,3,5-triazin-2-yl)aminomethyl)-phenylmethyl)amino]-1,3,5-triazine (13). The resulting yellow oil was obtained from **11** and cyanuric chloride and was purified by column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4-OH 95/4.5/0.5) to yield **13** as a transparent oil in 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.2−6.9 (m, 38H), 5.2−4.2 (br m, 18H), 5.1−5.0 (m, 1H), 4.9−4.5 (m, 8H), 1.29 (br s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 165.2, 164.9, 144.5, 139.7, 137.9, 128.2, 127.8, 127.5, 126.4, 126.2, 125.5, 49.5, 47.5, 44.2, 22.3. MS (FAB): *m*/*z* 1170.7 ([M + H^+], calcd 1170.6).

2-Chloro-4,6-bis[*N*-(3-(*N*-(4-*N*,*N*-dibutylamino-6-*N*-(1-pyrenemethyl)amino-1,3,5-triazin-2-yl)aminomethyl)-phenylmethyl)amino]-1,3,5-triazine (14). The resulting yellow solid was obtained from **12** and cyanuric chloride and was purified by column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4OH 95/4.5/0.5) to yield **14** as a white solid in 65% yield. Mp 196−198 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.1−7.8 (m, 18H), 7.0−6.8 (m, 8H), 6.4, 5.9, 5.6, 5.2, and 4.9 (5 br s, 10H), 4.3 (br s, 8H), 3.3 (br s, 8H), 1.4−0.9 (br m, 16H), 0.7 and 0.5 (2 br s, 12H). MS (FAB): *m*/*z* 1254.6 ([M + H^+], calcd 1254.7.

General Procedure for the Synthesis of Melamines 2b and 2c. An excess of dibutylamine (0.9 mL, 5 mmol) was added dropwise to a solution of the appropriate trimelamine (**13** or **14**) (0.5 mmol) in THF (5 mL) and the solution was refluxed for 24 h at 90 °C. Then, the solvent was removed under reduced pressure and the residue was partitioned between CH_2Cl_2 and 1 N HCl. The organic layer was washed with H_2O and brine and the solvent was removed under reduced pressure.

2-*N*,*N*-Dibutylamino-4,6-bis[*N*-(3-(*N*-(4-*N*,*N*-dibenzylamino-6-*N*-((*S*)-α-methylbenzyl)amino-1,3,5-triazin-2-yl)aminomethyl)phenylmethyl)amino]-1,3,5-triazine (2b). The resulting solid was obtained from **13** and dibutylamine and was purified by flash column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4OH 98/1.7/0.3) to yield **2b** as a white solid in 95% yield. Mp 215−216 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.2−7.0 (m, 38H), 5.2, 5.1, and 4.7 (3 br s, 8H), 4.4 (m, 8H), 3.32 (t, 4H, J_{HH} = 6.7 Hz), 1.7−1.6 (m, 4H), 1.4−1.3 (m, 4H), 0.86 (t, 6H, J_{HH} = 7.8 Hz). MS (FAB): *m*/*z* 1263.4 ([M + H^+], calcd 1261.7). Anal. Calcd for $C_{77}H_{86}N_{18}$: C 73.19, H 6.86, N 19.95. Found: C 73.19, H 6.82, N 19.87.

2-*N*,*N*-Dibutylamino-4,6-bis[*N*-(3-(*N*-(4-*N*,*N*-dibutylamino-6-*N*-(pyrenemethyl)amino-1,3,5-triazin-2-yl)aminomethyl)phenylmethyl)amino]-1,3,5-triazine (2c). The resulting oil was obtained from **14** and dibutylamine and was purified by column chromatography (SiO_2; CH_2Cl_2/MeOH/NH_4-OH 98/1.7/0.3) to yield **2c** as a white solid in 78% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.3−7.9 (m, 18H), 7.3−7.1 (m, 8H), 5.2 (br s, 10H), 4.5 (br s, 8H), 3.5 (br s, 12H), 1.6−1.2 (m, 24H), 1.0−0.8 (m, 6H). MS (FAB): *m*/*z* 1347.9 ([M + H^+], calcd: 1347.8). Anal. Calcd for $C_{83}H_{98}N_{18}$: C 73.97, H 7.33, N 18.71. Found: C 73.21, H 7.79, N 19.04.

Assembly Preparation. Typically, 4.0 mM solutions of assemblies were prepared by sonicating the melamine and cyanuric acid (in excess) for 1 h in THF (5 mL). After evaporation of the solvent and drying under high vacuum, the assemblies were dissolved in $CDCl_3$ (5 mL) and excess of CA was removed by filtration.

General Procedure for MALDI-TOF Characterization. The samples for the MALDI TOF were prepared adding 1.5−2.0 equiv of $AgCF_3COO$ to a 5 mM solution of the assembly in chloroform. Subsequently the suspension was stirred for a couple of minutes. MALDI-TOF measurements were performed according to literature procedures.[32]

General Procedure for CD Measurements. All the measurements were performed using a 0.1-mm cell, to minimize solvent effects. The concentration of the melamines in the samples was kept constant at 7 mM. The titration of compound (*R*,*R*)-**2b** with CA was performed by mixing solutions of melamine (*R*,*R*)-**2b** and assembly (*R*,*R*)-**2b**·CA in different ratios.

In the dilution experiments, the higher limit (14.2 mM) was determined by the solubility of the assemblies, and the lowest (2.1 mM) by the S/N ratio of the CD spectrum.

General Procedure for Fluorescence Studies. The emission spectra were recorded using a 1.0 mm cell with λ_{exc} = 350 nm. The melamine concentration of the samples was 0.5 or 0.05 mM. Dilution experiments showed that in this range the emission of the pyrene moieties was independent from the concentration. The titration experiments were performed maintaining a constant concentration of trimelamine **2c**, applying the same procedure used for the CD measurements.

Supporting Information Available: CD titration of (*R*,*R*)-**2b** with CA; CD dilution experiments of (*R*,*R*)-**2b**·CA; fluorescence titration of trimelamine **2c** with CA; plot of the ratio I_{480}/I_{410} vs percent of THF for free **2c** and **2c**·CA. This material is available free of charge via the Internet at http://pubs.acs.org.

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