# The chemistry of acyl tellurides: Generation and trapping of acyl radicals, including aryltellurium group transfer

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# Synthesis and Hierarchical Self-Assembly of Cavity-Containing Facial Amphiphiles

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The synthesis and aggregation behavior of cavity-containing facial amphiphiles is described. The molecules consist of a glycoluril-based rigid cavity functionalized with two water-soluble benzoate groups. By specific molecular recognition processes in water, the amphiphilic hosts self-assemble in a hierarchical process to form arrays of molecules. Depending on the counterions, these arrays can be assembled into well-defined aggregates of mesoscopic size. The size and shape of the aggregates can be tuned by variations in the size and substitution pattern of the cavities of the host molecules.

## Introduction

Amphiphilic molecules are essential in the maintenance and function of biological systems, and most of the synthetic amphiphiles that have been studied to mimic these natural systems have the same type of topology: a compact, polar headgroup, to which one or more long hydrophobic hydrocarbon chains are attached.[1] As a result of this topology, amphiphiles readily aggregate in aqueous solutions, in which they expose their headgroups to the water and dehydrate their tails by clustering them together into a hydrophobic environment. Depending on the nature of the headgroup and the number and length of the hydrocarbon tails, the morphology of the supramolecular aggregate that is formed can be in many cases rationally correlated to the topology of the amphiphile.[2] Although these amphiphiles of the "classical type" have received much attention over the past few decades, there recently appears to be increasing interest in the development of amphiphiles with a strongly deviating topology.[3] Kahne et al. were the first to introduce the term "facial amphiphilic" molecules, which are defined as molecules with rigid structures containing separated hydrophilic and hydrophobic "faces".[4] In Nature, helical peptides are known that exhibit this facial amphiphilicity. They bind to membrane interfaces in order to target peptide sequences to membrane-bound receptors.[5] These amphiphiles can also cause membrane fusion[6] and make membranes permeable.[7] In particular Gellman and coworkers have carried out considerable work on determining the factors that govern the self-association of these types of molecules in water[8] and on the ability of the aggregates to include hydrophobic fluorescent probes. However, no aggregate morphology studies of facial amphiphiles have been reported so far. It is, therefore, of general interest to investigate whether these molecules are able to form mesoscopic architectures and, in particular, if their unusual topology can be expressed in a unique morphology of their aggregates.

Recent work in our group has revealed that host molecules based on glycoluril with water−soluble pyridinium groups at their convex side can self-assemble to form well-defined "razorblade-like" aggregates in water.[9] Related hosts with ruthenium-bipyridine groups were found to form rectangular aggregates, which, in a second level of organization self-assembled into "cigar-like" structures.[10] A major driving force for the self-assembly of these types of molecules into nanosized structures is the formation of dimers, in which one cavity side-wall of a host is buried in the cavity of its dimeric partner and vice versa. As an extension of this work we describe in

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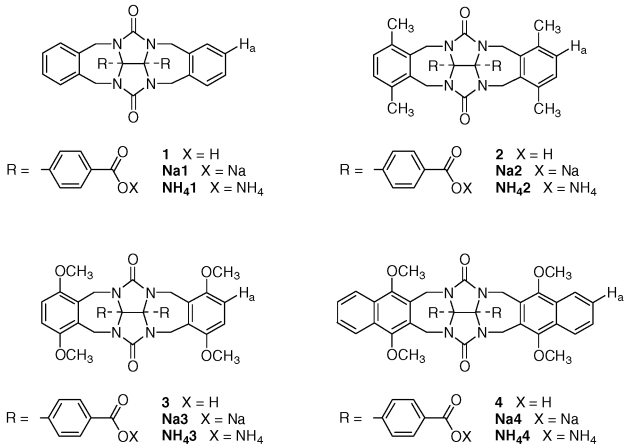
**CHART 1**



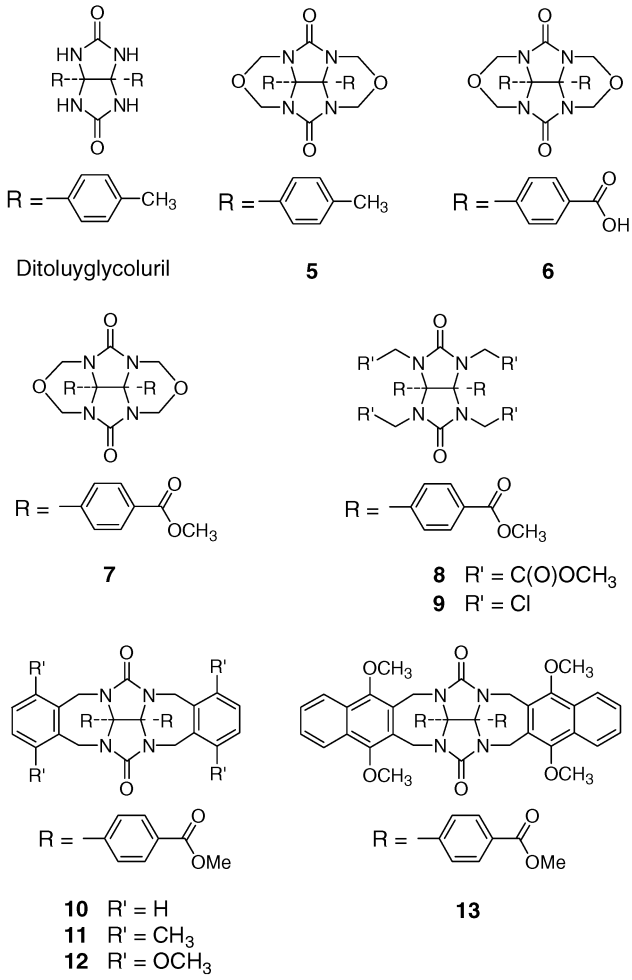

this paper the synthesis and self-assembling properties of benzoic acid-functionalized host molecules **1**−**4** (Chart 1), which vary in cavity size and substitution pattern. It will be shown that, upon deprotonation of the benzoic acid groups, these variations in size and substitution pattern, together with the choice of the counterions, can have a strong influence on the self-assembling behavior of the molecules in water.[11]

## Results and Discussion

**Synthesis.** As starting material for the synthesis of the benzoic acid-functionalized host molecules, cyclic ether **5** was used, which was synthesized by a reaction of ditoluylglycoluril[12] with paraformaldehyde (Chart 2). Its aromatic methyl groups were oxidized with $KMnO_4$ in water to give the dibenzoic acid compound **6** in a yield of 96%. Ureidoalkylation of **6** with *p*-dimethoxybenzene in a mixture of acetic anhydride and trifluoracetic acid afforded the dibenzoic acid-functionalized host **3** in 81% yield. This reaction was only completed after 3 days, which is surprising since the analogous reaction to synthesize a similar host that has phenyl instead of benzoic acid groups just took 1 h.[13] The low reactivity of **6** is attributed to the relatively slow formation of the reactive intermediate, which is believed to be a carbonium-imonium ion.[14] The electron-withdrawing benzoic acid substituents of **6** apparently disfavor the formation of this intermediate.

For reaction of **6** with other aromatic molecules, e.g., benzene, *p*-xylene, and 1,4-dimethoxynaphthalene, it was necessary to replace the relatively stable cyclic ether groups of **6** by better leaving groups. First, the carboxylic acid functions of **6** were protected by esterification in methanol to give dimethyl ester **7** (Chart 2). Apart from the desired compound, considerable amounts of side-products were formed in which one or both of the cyclic ether functions had opened to give compounds with methyl ether groups. Compound **7**, however, could be

**CHART 2**




easily isolated from this mixture by column chromatography (yield 56%). It was also possible to use the crude product mixture in the following step, which is the acid-catalyzed acylation with acetic anhydride to give the tetraacetoxy derivative **8**, which was obtained as a single product (70% yield). This reaction was only completed after 40 h, which is also a much longer time than was needed for the analogous reaction in the case of the diphenylglycoluril-derived compound (3 h). Compound **8** was subsequently treated with thionyl chloride to give the tetrachloride **9** in 84% yield. This activated compound was then used in Lewis acid-catalyzed Friedel−Crafts alkylation reactions with benzene, *p*-xylene, and 1,4-dimethoxynaphthalene as substrates to give host molecules **10**, **11**, and **13** in yields of 36, 34, and 71%, respectively, after purification by column chromatography. The yields of **10** and **11** are relatively low because considerable amounts of single-walled host compounds were present in the reaction mixtures. Prolonged reaction times and variation of the Lewis acid did not improve the yields. Host **12** was synthesized directly from cyclic ether **7** and *p*-dimethoxybenzene in a similar way as described for **3**.

Saponification of the methyl ester-protected hosts **10**−**13** proceeded smoothly in a mixture of dioxane, methanol, and aqueous 4 N NaOH (15:4:1, v/v/v),[15] affording the

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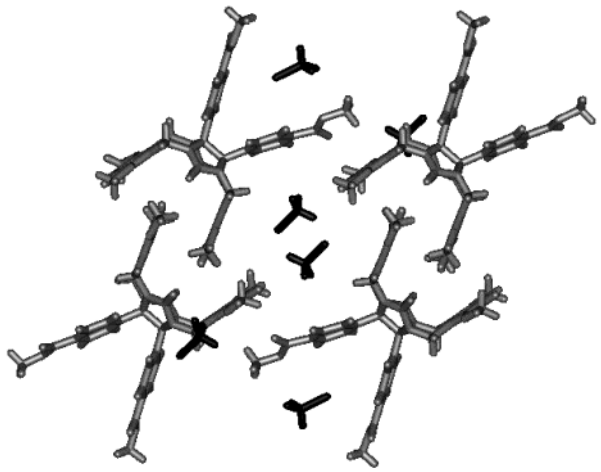

**FIGURE 1.** X-ray crystal structure of **12** (four molecules, with four $CH_2Cl_2$ solvent molecules included), showing the arrangement of the host molecules in dimers, in which the cavity of one host is filled by a side-wall of its neighbor and vice versa.

crude carboxylate disodium salts as precipitates. These could be dissolved in water, whereupon protonation with aqueous 37% HCl gave the benzoic acid-functionalized hosts **1**−**4** as precipitates in nearly quantitative yields. The sodium salts of compounds **1**−**4**, **Na1**−**4**, were prepared by suspension of the former compounds in demineralized water, to which 2 equiv of sodium hydroxide were added. Upon stirring, the compounds completely dissolved, whereafter they were lyophilized. The ammonium salts of **1**−**4**, **$NH_4$1**−**4**, were prepared by suspension of the former compounds in aqueous ammonia (30%). Again, the compounds dissolved upon stirring, whereupon the excess ammonia was evaporated and the products were lyophilized. The sodium and ammonium salts turned out to be very hygroscopic and were therefore stored under nitrogen at −18 °C.

**NMR Dilution Experiments.** The self-association properties of the benzoate-functionalized hosts in water were investigated by $^1$H NMR dilution studies. There appeared to be large solubility differences between the sodium and the ammonium salts of the molecules, i.e., the sodium salts were soluble in water up to relatively high concentrations (>30 mM), whereas the ammonium salts hardly dissolved at all. For this reason, reliable NMR dilution titrations could only be carried out on the sodium salts. For compounds **Na1**−**4**, $^1$H NMR spectra were recorded of samples of at least 10 different concentrations varying between 0.2 and 10 mM. In this concentration range, for all compounds, only the signals of the protons of the cavity side-walls and of their 1,4-attached substituents displayed significant upfield shifts (>0.05 ppm). Increasing the temperature or the addition of acetone caused a decrease in these shifts. The concentration-dependent changes in the NMR spectra are in line with the formation of dimeric structures. An example of such a dimeric arrangement is depicted in Figure 1, which shows the crystal structure[16] of host **12**.

In water, for hosts **Na1**−**4,** average signals were observed for protons in the monomer and the dimer, indicating their fast exchange on the NMR time scale. Only in the case of **Na4** were the shifting resonances somewhat broadened at concentrations above 5 mM. The signals of the side-wall protons $H_a$ (see Chart 1) were monitored versus the concentration, and the titration curves thus obtained were fitted to an equation governing the self-association of two molecules. The calculated dimerization constants ($K_{dimer}$) and the complexation-induced shift (CIS) values of the shifting proton signals are summarized in Table 1.

**TABLE 1. Dimerization Constants and CIS Values of Compounds Na1−4 in $D_2O$ at 298 K**

| compound | $K_{dimer}$ ($M^{-1}$) | $\Delta G$ (kJ/mol) | CIS (ppm)[a] |
|---|---|---|---|
| **Na1** | <5[b] | *b* | *b* |
| **Na2** | 145[c] | −12.3 | −1.38 |
| **Na3** | 630[c] | −16.0 | −1.29 |
| **Na4** | $1.45 \times 10^4$ [d] | −23.7 | −1.60 |

[a] Value calculated for the side-wall protons $H_a$ (see Chart 1). [b] Dimerization was too weak to determine a reliable value. [c] Estimated error = 10%. [d] Estimated error = 20%.

The results show that the dimerization becomes stronger when substituents are introduced at the cavity side-walls, i.e. when the hydrophobic surface of the cavity becomes larger.[17] Without any substituents, dimerization is negligible (cf. the $K_{dimer}$ of **Na1**). The extremely strong dimerization of **Na4** is attributed to the presence of a large hydrophobic cleft formed by the naphthalene side-walls. For hosts **Na1**−**3**, the observed trend in dimerization strength is similar to that of related substituted hosts in chloroform.[18] In water, however, the intermolecular interactions are generally much stronger due to the hydrophobic effect.[19] This is further reflected in the large CIS values of the $H_a$-protons, which indicate that the side-walls of the molecules are inserted more deeply within the cavity of their dimeric partner than in the case of their chloroform-soluble analogues.[18]

Although the strength of dimerization of the ammonium salts **$NH_4$1**−**4** could not be determined by dilution titrations, $^1$H NMR spectra of low-concentration solutions of these compounds (<0.2 mM) in water showed shifts of the cavity side-wall proton signals that were comparable to those of their sodium salt analogues. This indicates that in the case of both salts, self-assembly of the cavities of the molecules occurs.

**Fluorescence Dilution Experiments.** Due to the very low solubility of the ammonium salts **$NH_4$1**−**4** in water, their self-association behavior could not be investigated by NMR techniques, and instead fluorescence spectroscopy was used. The fluorescence dependence of **$NH_4$1** on the concentration of this compound in water is shown in Figure 2. Upon excitation of the $\pi \rightarrow \pi^*$ transition band of the aromatic rings in the molecule (at 290 nm in the UV−vis spectrum), a broad emission

(15) Tesser, G. I.; Bolvert-Geerts, I. C. *Int. J. Pept. Protein Res.* **1975**, *7*, 295.

(16) (a) Holder, S. J.; Elemans, J. A. A. W.; Barberá, J.; Rowan, A. E.; Nolte, R. J. M. *Chem. Commun.* **2000**, 355. (b) Holder, S. J.; Elemans, J. A. A. W.; Donners, J. J. J. M.; Boerakker, M. J.; de Gelder, R.; Barberá, J.; Rowan, A. E.; Nolte, R. J. M. *J. Org. Chem.* **2001**, *66*, 391.

(17) Similar results have been obtained for dimerization of related facial amphiphiles in buffered aqueous solution; see: Isaacs, L.; Witt, D.; Fettinger, J. C. *Chem. Commun.* **1999**, 2549.

(18) Reek, J. N. H.; Elemans, J. A. A. W.; de Gelder, R.; Rowan, A. E.; Nolte, R. J. M. *Tetrahedron* **2003**, *59*, 175.

(19) Tanford, C. In *The Hydrophobic Effect*, 2nd ed.; Wiley: New York, 1980.

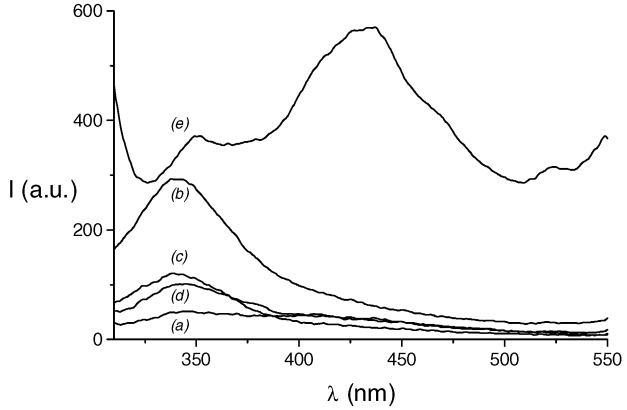


**FIGURE 2.** Selected fluorescence emission spectra ($\lambda_{ex} = 290$ nm) of **$NH_4$1** in water at concentrations of (a) $10^{-8}$, (b) $10^{-6}$, (c) $5 \times 10^{-6}$, (d) $2 \times 10^{-5}$, and (e) $10^{-4}$ M.

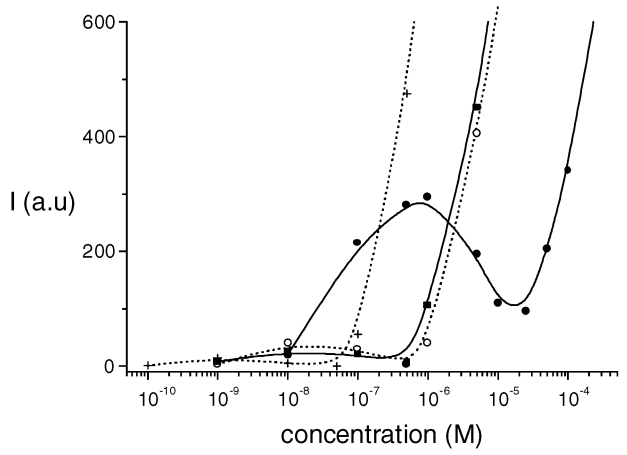


**FIGURE 3.** Fluorescence dilution curves ($\lambda_{em} = 345$ nm) of compounds **$NH_4$1** (●, solid line), **$NH_4$2** (○, dashed line), **$NH_4$3** (■, solid line), and **$NH_4$4** (+, dashed line) in water at 298 K.

between 300 and 400 nm was observed, the intensity of which increased until the concentration was raised to $10^{-6}$ $M^{-1}$. A clear drop in intensity was then observed until a minimum was reached at a concentration of approximately $2 \times 10^{-5}$ $M^{-1}$, whereupon the emission started to quickly increase again. This increase coincided with the evolvement of turbidity in the solution. At the same time, in addition to the emission at ~345 nm, a new, longer-wavelength emission in the fluorescence spectrum became evident. The evolvement of this broad emission between 400 and 450 nm is attributed to the formation of excimers. A similar formation of excimers, although from a different compound, viz., poly-(*S*)-tyrosine, with $\lambda_{em} = 420$ nm has been reported in the literature and has been taken as evidence for the stacking of *p*-hydroxyphenyl rings.[20] The dilution titration curve of **$NH_4$1** ($\lambda_{em} = 345$ nm), which is composed from the data presented in Figure 2, is shown in Figure 3. The maximum and minimum emission are clearly visible at concentrations of $10^{-6}$ ($I = 300$ au) and $2 \times 10^{-5}$ M ($I = 95$ au) of **$NH_4$1**, respectively. When the temperature was increased, this maximum and minimum were found to shift to higher concentrations, and simultaneously the emission intensity of the maximum increased. The observed concentration and temperature effects on the fluorescence spectra of **$NH_4$1** point to the formation of assemblies, which have their aromatic rings in close proximity, resulting in their mutual quenching. At concentrations higher than $5 \times 10^{-4}$ $M^{-1}$, scattering occurs due to the formation of larger aggregates. A similar fluorescence behavior has been reported for the self-assembly of bis(phenylglycine) oxalyl amides in water.[21]

(20) Lehrer, S. S.; Fasman, G. D. *Biopolymers* **1964**, *2*, 199.

**TABLE 2. Properties of the Aggregates Formed by Ammonium Carboxylate Hosts in Water**

| compound | CAC (M)[a] | average length (nm)[b] | average width (nm)[b] | aspect ratio (length/width)[b] |
|---|---|---|---|---|
| **$NH_4$1** | $2 \times 10^{-5}$ | 200−250 | 60−80 | $3.5 \pm 1$ |
| **$NH_4$2** | $5 \times 10^{-7}$ | 1500−2500 | 200−400 | $9 \pm 3$ |
| **$NH_4$3** | $3 \times 10^{-7}$ | 1500−2500 | 70−100 | $25 \pm 5$ |
| **$NH_4$4** | $2 \times 10^{-8}$ | *c* | *c* | *c* |

[a] Critical aggregation constant as determined from the fluorescence titrations. [b] Determined from the dimensions of 200−300 unique aggregates obtained from various samples. [c] No well-defined aggregates were observed.

Concentration-dependent fluorescence studies were also carried out with compounds **$NH_4$2**−**4**. In all cases, the same types of plots of concentration versus fluorescence emission were obtained (Figure 3). When the concentration of the amphiphile was increased, a maximum and a subsequent minimum in emission were observed. These maxima and minima shifted to higher concentration values in the order **$NH_4$4** < **$NH_4$3** = **$NH_4$2** < **$NH_4$1**, whereas the degree of quenching decreased in the same order. In addition, the concentration at which scattering occurred increased. The fluorescence titration curves thus give a good indication of the self-association and further aggregation behavior of the ammonium salts of **1**−**4**. A common approach to determine the critical aggregation constant (CAC) of a surfactant is the application of the "pseudo-phase-separation model", which treats the aggregate as a separate phase that is formed in the solution containing the amphiphile.[22] In the case of the ammonium salts **$NH_4$1**−**4**, this occurrence of phase separation coincides with the concentration in the titration curves where the emission reaches a minimum (Figure 3). Hence, these values were taken as the CAC values of the compounds (see Table 2).

**Electron Microscopy Studies.** To investigate if the self-association of the benzoate facial amphiphiles would result in the formation of assemblies on a mesoscopic scale, solutions and dispersions of the compounds in water were investigated with the help of transmission electron microscopy (TEM). None of the sodium salts were found to form large aggregates, as was already expected from the samples used for the NMR dilution studies, which remained clear up to relatively high concentrations. Even when relatively concentrated samples (30 mM) of **Na4** (the molecule that dimerized most strongly) were studied, no nanosized structures were observed. In contrast to this, the turbid dispersions of all the ammonium salts in water (0.1% w/v) indicated

(21) Jokić, M.; Makarević, J.; Žinić, M. *J. Chem. Soc., Chem. Commun.* **1995**, 1723.
(22) Shinoda, K.; Hutchinson, E. *J. Phys. Chem.* **1962**, *66*, 577.

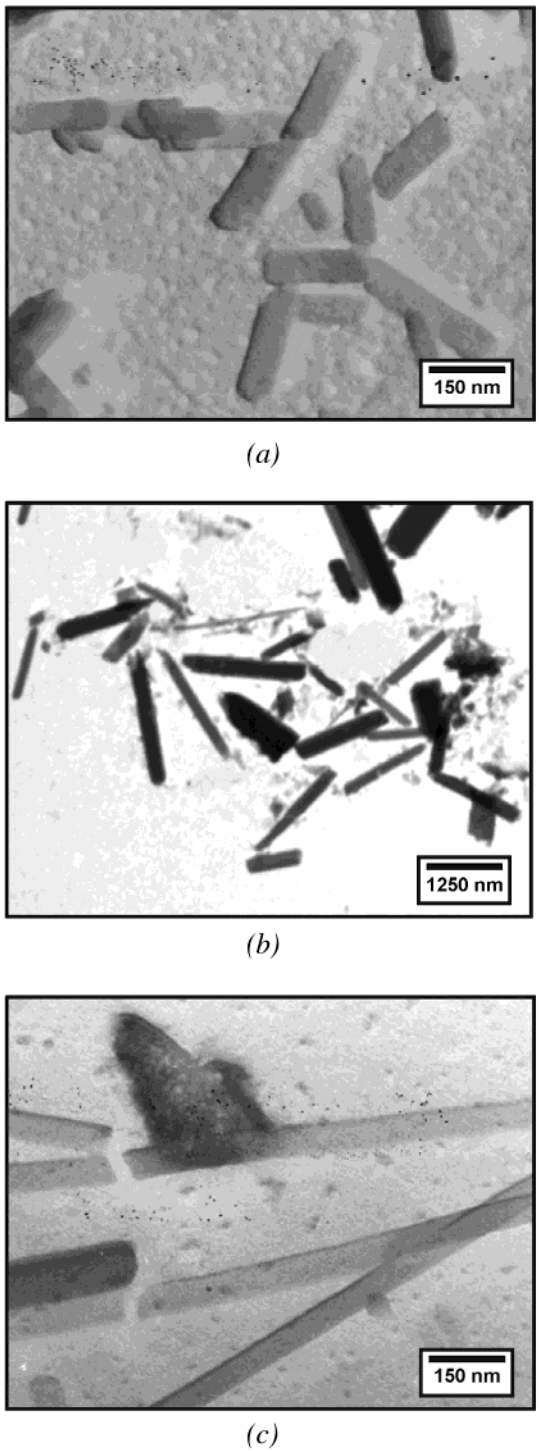


**FIGURE 4.** TEM images of aggregates formed in water by (a) **$NH_4$1**, (b) **$NH_4$2**, and (c) **$NH_4$3**. All samples are platinum shadowed.

the presence of large aggregates. The addition of acetone to these samples led to the formation of clear solutions, apparently as a result of the dissociation of the assemblies.[23] TEM studies revealed that compounds **$NH_4$1−3** indeed formed well-defined aggregates with a uniform, quasirectangular shape and rounded corners (Figure 4). Compound **$NH_4$4** did not form well-defined structures but rather undefined lumps of material. Electron diffraction experiments indicated that none of the structures were crystalline. The typical geometrical features of the observed structures are summarized in Table 2. As can be seen the length/width aspect ratio increases going from **$NH_4$1** to **$NH_4$2** to **$NH_4$3**. These increases are correlated to the increase in self-association strength observed from the fluorescence measurements. The shapes or dimensions of the aggregates were not influenced by changes in concentration of the amphiphile used.

**Infrared Measurements.** The fact that the ammonium salts form nanosized aggregates and the sodium salts do not implies that the ammonium ions in the former salts play an important role in the self-assembly process. It is well-known that these ions can form very strong hydrogen bonds with carboxylate anions.[24] They serve as quadruple hydrogen bond donors, whereas each of the carboxylate groups in principle can act as multiple hydrogen bond acceptors due to the presence of five lone pairs of electrons.[25] To investigate the role of this hydrogen bonding in the self-assembly of the amphiphiles, cast films of aqueous dispersions of both the sodium and ammonium salts were studied by reflectance infrared spectroscopy. Because of charge delocalization, carboxylate anions characteristically exhibit a vibration due to the asymmetrical O−C−O stretching motion between 1600 and 1550 $cm^{-1}$.[26] Indeed, a vibration at approximately 1605 $cm^{-1}$ was present in the spectra of KBr samples of all the sodium salts. In the spectra of the KBr samples of the ammonium salts, however, this asymmetrical O−C−O stretching vibration was absent. Instead, for these compounds a set of superimposed carbonyl vibrations was present between 1740 and 1660 $cm^{-1}$. This is an indication that the carboxylate groups are involved in hydrogen bonding interactions. The N−H stretching vibrations of the ammonium ions were visible as a broad, poorly defined, and intense absorption between 3700 and 2700 $cm^{-1}$. In the cast films of aqueous dispersions (0.5%, w/v) of the sodium salts, no significant shifts in the O−C−O stretching vibrations were observed when compared to the spectra of these compounds in KBr. In cast films of aqueous dispersions (0.5%, w/v) of the ammonium salts, however, the set of superimposed carbonyl vibrations observed in the KBr samples had sharpened and split into two distinct vibrations at approximately 1715 and 1680 $cm^{-1}$, corresponding to the urea carbonyl and carboxylate functions, respectively. In addition, the N−H stretching vibration of the ammonium ions had narrowed considerably to a stretching vibration of relatively low intensity at 3160 $cm^{-1}$. These changes in the infrared spectrum are an indication that in the cast films of aqueous dispersions of the ammonium salts, the hydrogen bonding interactions that are present between the ammonium ions and the carboxylate groups

(23) It is well-known that the addition of acetone or methanol strongly reduces hydrophobic interactions.

(24) (a) Kinbara, K.; Kai, A.; Maekawa, Y.; Hashimoto, Y.; Naruse, S.; Hasegawa, M.; Saigo, K. *J. Chem. Soc., Perkin Trans. 2* **1996**, 247. (b) Kinbara, K.; Hashimoto, Y.; Sukegawa, M.; Nohira, H.; Saigo, K. *J. Am. Chem. Soc.* **1996**, *118*, 3441. (c) Kinbara, K.; Kobayashi, Y.; Saigo, K. *J. Chem. Soc., Perkin Trans. 2* **2000**, 111. (d) Lee, S. B.; Hong, J.-I. *Tetrahedron Lett.* **1996**, *37*, 8501.

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(26) Rao, C. N. R. In *Chemical Applications of Infrared Spectroscopy*; Academic Press: New York, 1963.

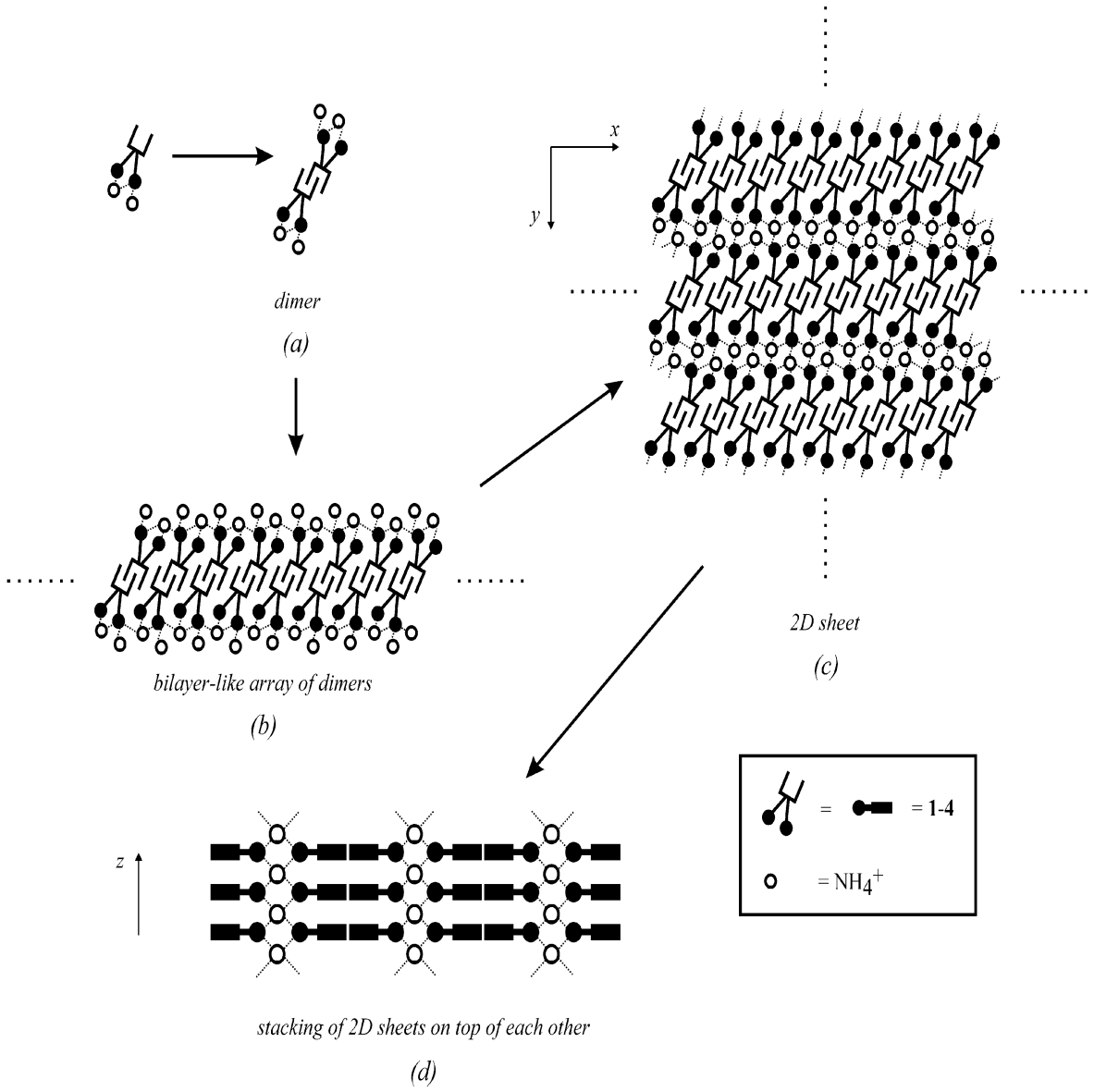


**FIGURE 5.** Schematic representation of the proposed hierarchical self-assembly of facial amhiphiles **$NH_4$1**−**4**. (a) Formation of a dimer. (b) Assembly of dimers in a one-dimensional array. (c) Stitching of bilayers by the $NH_4^+$ ions resulting in the formation of 2D sheets (top view). (d) Stacking of the 2D sheets on top of each other (side-view).

are much better defined than those in the KBr samples of the freshly prepared compound.

**Powder Diffraction Experiments.** To get more information about the precise ordering of compounds **$NH_4$1**−**4** in their aggregates, dried samples of dispersions (0.1%, w/v) of the ammonium carboxylate receptors were investigated by X-ray powder diffraction. For all the compounds, a strong reflection, which can be attributed to a repeating distance of 9.5−9.8 Å, was observed. In addition to this strong reflection, a series of reflections of much lower intensity were observed, which makes the overall interpretation very difficult. It was, however, evident that the diffractogram of each amphiphile displayed reflections at similar 2$\phi$ values, which strongly indicates that the aggregates formed by the ammonium salts are all isomorphic.

**Hierarchical Self-Assembly of the Amphiphiles.** In water, the formation of hydrogen bonds between solutes is highly unfavorable unless a *cooperative* self-assembly process between molecular in sufficiently large aggregates occurs. Considering the various possible interactions, a hierarchical self-assembly[27] model for compounds **$NH_4$1**−**4**, which accounts for such a cooperative process, is proposed (Figure 5). On the basis of the $^1$H NMR data, an essential intermolecular interaction is the "face-to-face" dimerization, in which two receptor cavities are mutually filled (Figure 5a). In a subsequent

(27) For some recent examples of supramolecular architectures that are formed by hierarchical self-assembly, see: (a) Wong, G. C. L.; Tang, J. X.; Lin, A.; Li, Y.; Janmey, P. A.; Safinya, C. R. *Science* **2000**, *288*, 2035. (b) Brunsveld, L.; Vekemans, J. A. J. M.; Hirschberg, J. H. K. K.; Sijbesma, R. P.; Meijer, E. W. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4977. (c) Fenniri H.; Deng, B. L.; Ribbe, A. E. *J. Am. Chem. Soc.* **2002**, *124*, 11064. (d) Petitjean, A.; Cuccia, L. A.; Lehn, J.-M.; Nierengarten, H.; Schmutz, M. *Angew. Chem., Int. Ed.* **2002**, *7*, 1195. (e) Elemans, J. A. A. W.; Rowan, A. E.; Nolte, R. J. M. *J. Mater. Chem.* **2003**, in press.

process, these dimeric units can form long, one-dimensional arrays, in which the hydrophobic aromatic surfaces of the molecules are minimally exposed to the aqueous phase and all the hydrophilic carboxylate groups are directed to the outside. Hence, a bilayer of facial amphiphiles results (Figure 5b). Similar bilayer formation has been observed in the solid state in the case of related receptors functionalized with long aliphatic tails.[16] In a third process, which in principle can occur simultaneously with the growth of the dimeric array, the ammonium cations can act as a "glue" and stitch the bilayers together by the formation of hydrogen bonds to form a 2-dimensional (2D) sheet (Figure 5c). In the case of **Na1**−**4**, this stitching cannot occur, and hence the self-assembly process of these molecules stops at the stage of the dimer or the dimeric array and no aggregates on a mesoscopic scale are formed. Finally, it is proposed that the 2D sheets of the ammonium amphiphiles stack on top of each other to give the aggregates their final 3-dimensional shape.[28] Molecular modeling showed that the thickness of one 2D sheet amounts to approximately 9.2−9.5 Å, a value that corresponds reasonably well with the strong reflection observed in the powder diffractogram of the ammonium benzoate hosts ($d$ = 9.5−9.8 Å). A similar stacking of 2D sheets has been observed before for other related glycoluril-based hosts.[9,16] It is not unlikely that also the 2D sheets of amphiphiles are stitched together by the ammonium ions, which can form, apart from hydrogen bonds between the bilayer arrays, additional hydrogen bonds between the carboxylate functions in different sheets (Figure 5d).

What is unique about the aggregates formed by **$NH_4$1**−**4** is that their growth stops after a certain point, i.e., no infinite assemblies are formed. This effect has been observed before for other aggregates of glycoluril-based receptors in water[9,10] and is believed to be governed by a subtle balance between the enthalpy, i.e., the interaction strength between the molecules that constitute the aggregate, and the entropy of the self-assembly process. After the aggregates have grown to a certain size, the attachment of new monomers to their water-soluble exterior will be energetically no longer favorable. Additional experiments were carried out with dispersions of **$NH_4$1** in water in which the concentrations of the amphiphile were 0.05% and 0.5% w/v, respectively. In both cases, TEM studies showed that the formed aggregates had similar sizes as those formed from the 0.1% w/v dispersions, which strongly suggests that their final structure is controlled by the thermodynamic equilibrium. Another interesting aspect of the aggregates is that their final shape appears to be dependent on the substitution pattern of the cavity side-walls of the amphiphiles. This control over shape and size of self-assembled structures is one of the great challenges of today's supramolecular chemistry.[29] Calculations have shown that the substitution pattern of the receptor cavity has an influence not only on the strength of dimerization but also on the strength of the $\pi-\pi$ interactions between the external faces of thedimers.[18] 1,4-Dimethoxy-substituted side-walled molecules display stronger intermolecular interactions than 1,4-dimethyl-substituted ones, which in turn interact more strongly than unsubstituted benzene side-walls. For the ammonium salts **$NH_4$1**−**4**, these differences in interaction strength are reflected in the fluorescence spectra of the compounds, in which the degree of quenching increases going from **$NH_4$1** to **$NH_4$2** and then to **$NH_4$3**. In line with the differences in interaction strength between the external faces of the dimers, the dimeric array of molecules of **$NH_4$3** in water possibly grows longer than the dimeric array of molecules of **$NH_4$2**, which in turn grows longer than the array formed by **$NH_4$1**. If the growth of the dimeric array occurs in the direction of the long sides of the aggregates (the $x$-direction in Figure 5c), this assumption perfectly explains the differences observed in the lengths of the aggregates formed by the ammonium compounds. The other growth processes, i.e., the stitching of the bilayers in the direction of the short sides of the aggregates (the $y$-direction in Figure 5c), and the stacking of the 2D sheets (the $z$-direction in Figure 5d), are in competition with the growth of the dimeric array. In summary, it is proposed that when the dimerization and subsequent bilayerlike assembly of the hydrophobic faces of the molecules become more favorable, the other growth processes are relatively disfavored, resulting in an increase of the length/width aspect ratio.

## Conclusion

It has been demonstrated that a new series of facial amphiphiles, i.e., rigid receptor cavities functionalized with benzoate groups on their convex sides, can form discrete superstructures on a mesoscopic scale. In water, the hydrophobic cavities of the molecules form dimeric structures, which in a subsequent process are proposed to arrange themselves into bilayerlike arrays in which the hydrophobic parts of the molecules are maximally shielded form the aqueous environment. Further growth of these bilayers into nanosized aggregates appears to be strongly dependent on the countercations of the amphiphiles. When these are sodium ions, no superstructures are formed because the self-assembly stops at the stage of the array of dimers. However, when ammonium ions are used, these form strong hydrogen bonds with the carboxylate anions, and as a result, the bilayers are stitched together to form large architectures. The shape and dimensions of these architectures appear to be directly related to the strength of dimerization of the amphiphiles, which is in turn dependent on the substitution pattern of the cavity side-walls of these compounds. Thus, by introducing small changes in the hydrophobic part of these facial amphiphiles, the size and shape of their final superstructures can be controlled in a fashion similar to crystal engineering.[30]

(28) Heights of the aggregates were estimated to be between 50 and 100 nm from the platinum shadow in the TEM pictures.

(29) (a) Ghadiri, M. R.; Granja, J. R.; Milligan, R. A.; McRee, D. E.; Khazanovich, N. *Nature* **1993**, *366*, 324. (b) Lbotak, P.; Shinkai, S. *Tetrahedron Lett.* **1995**, *36*, 4829. (c) Philp, D.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1155. (d) Vreekamp, R. H.; van Duynhoven, J. P. M.; Hubert, M.; Verboom, W.; Reinhoudt, D. N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1215. (e) Gillard, R. E.; Raymo, F. M.; Stoddart, J. F. *Chem. Eur. J.* **1997**, *3*, 1933. (f) Balagurusamy, V. S. K.; Ungar, G.; Percec, V.; Johansson, G. *J. Am. Chem. Soc.* **1997**, *119*, 1539. (g) Chemseddine, A.; Moritz, T. *Eur. J. Inorg. Chem.* **1999**, 235. (h) Rebek, J., Jr. *Acc. Chem. Res.* **1999**, *32*, 278. (i) Aizenberg, J.; Black, A. J.; Whitesides, G. M. *Nature* **1999**, *398*, 495. (j) Ozin, G. A. *Can. J. Chem.* **1999**, *77*, 2001. (k) Li, M.; Schnablegger, H.; Mann, S. *Nature* **1999**, *402*, 393. (l) Orr, G. W.; Barbour, L. J.; Atwood, J. L. *Science* **1999**, *285*, 1049.

## Experimental Section

**Syntheses: 8b,8c-Di(4-methylphenyl)perhydro-2,6-dioxa-3a,4a,7a,8a-tetraazacyclopenta[*def*]fluorene-4,8-dione (5).** Ditoluylglycoluril (7.3 g, 23 mmol) and paraformaldehyde (3.4 g, 113 mmol) were suspended in DMSO (50 mL). Aqueous 1 N NaOH was added dropwise until a pale yellow solution was obtained, and the mixture was stirred for 16 h. The solution was acidified to pH 1 with aqueous 37% HCl and refluxed for 2 h. After the mixture was cooled, water (10 mL) was slowly added while stirring vigorously and the resulting precipitate was filtered and washed with water (20 mL) and cold ethanol (50 mL). The product was dried under vacuum to give 8.45 g (92%) of **5** as a white powder: $^1$H NMR ($CDCl_3$, 300.13 MHz) $\delta$ 7.04 (d, 4H, $^3J$ = 6.5 Hz), 6.96 (d, 4H, $^3J$ = 6.5 Hz), 5.63 (d, 4H, $^2J$ = 10.6 Hz), 4.54 (d, 4H, $^2J$ = 10.6 Hz), 2.21 (s, 6H) ppm; $^{13}$C{$^1$H} NMR ($CDCl_3$, 75.47 MHz) $\delta$ 159.1, 139.8, 130.2, 129.9, 128.4, 80.1, 72.5, 21.6 ppm.

**4-[8b-(4-Carboxyphenyl)-4,8-dioxoperhydro-2,6-dioxa-3a,4a,7a,8a-tetraazacyclopenta[*def*]fluoren-8-yl]-benzoic Acid (6).** A suspension of **5** (5.0 g, 12.3 mmol) and $KMnO_4$ (10 g, 63 mmol) in water (125 mL) was refluxed for 16 h. After cooling, the brown suspension was filtered over infusorial earth. The residue was washed with aqueous 1 N NaOH (100 mL), and the pale yellow filtrate was acidified to pH 1 with aqueous 37% HCl while stirring vigorously. The precipitate was filtered off, washed with water (200 mL), and dried under vacuum over $P_2O_5$ to give 5.5 g (96%) of **6** as a white powder. A sample was recrystallized from acetic acid for analysis: mp 302 °C (dec); IR (KBr pellet) $\nu$ 3500−3000, 3069, 2938, 1754, 1736, 1702, 1467, 1409, 1385, 1309, 1293, 1252, 1028 cm$^{-1}$; $^1$H NMR ($CDCl_3$/$CD_3OD$ 9:1 (v/v), 300.13 MHz) $\delta$ 7.85 (d, 4H, $^3J$ = 8.2 Hz), 7.30 (d, 4H, $^3J$ = 8.2 Hz), 5.66 (d, $^2J$ = 11.1 Hz), 4.57 (d, 4H, $^2J$ = 11.1 Hz) ppm; $^{13}$C{$^1$H} NMR ($CDCl_3$/$CD_3OD$ 9:1 (v/v), 75.47 MHz) $\delta$ 166.4, 157.3, 136.2, 131.5, 129.3, 127.1, 78.5, 71.3 ppm; FAB-MS *m*/*z* 467 (M + H)$^+$. Anal. Calcd for $C_{22}H_{18}N_4O_8(CH_3COOH)$: C, 54.76; H, 4.21; N, 10.64. Found: C, 54.76; H, 4.50; N, 10.35.

**4-[13b-(4-Carboxyphenyl)-1,4,8,11-tetramethoxy-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,6a,12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo[*f*]azulen-13-yl]benzoic Acid (3): Method A.** Compound **6** (650 mg, 1.39 mmol) and *p*-dimethoxybenzene (580 mg, 4.18 mmol) were dissolved in a mixture of acetic anhydride (1.5 mL) and trifluoroacetic acid (1.5 mL). The mixture was heated at 100 °C for 64 h. After the mixture was cooled, methanol (6 mL) was added dropwise and the precipitate was filtered off and washed with methanol (50 mL) and diethyl ether (50 mL) to yield 800 mg (81%) of **3** as a white solid. **Method B.** Starting from **12** (120 mg, 0.16 mmol), this compound was synthesized as described for **1**: yield, 112 mg (97%) of **3** as a white solid; mp 309 °C (dec); IR (KBr pellet) $\nu$ 3500−3300, 3046, 2937, 2915, 2837, 1727, 1702, 1678, 1484, 1467, 1427, 1413, 1360, 1305, 1261, 1225, 1080 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$, 300.14 MHz) $\delta$ 7.74 (d, 4H, $^3J$ = 8.4 Hz), 7.20 (d, 4H, $^3J$ = 8.4 Hz), 6.86 (s, 4H), 5.43 (d, 4H, $^2J$ = 16.0 Hz), 3.75 (s, 12H), 3.72 (d, 4H, $^2J$ = 16.0 Hz) ppm; $^{13}$C{$^1$H} NMR (DMSO-$d_6$, 75.47 MHz) $\delta$ 170.6, 160.5, 154.6, 142.1, 134.8, 133.5, 132.3, 131.3, 116.1, 88.2, 60.6, 40.3 ppm; FAB-MS *m*/*z* 707 (M + H)$^+$. Anal. Calcd for $C_{38}H_{34}N_4O_{10}$: C, 64.58; H, 4.85; N, 7.93. Found: C, 64.64; H, 4.80; N, 7.82.

**Methyl 4-8b-[4-(Methoxycarbonyl)phenyl]-4,8-dioxoperhydro-2,6-dioxa-3a,4a,7a,8a-tetraazacyclopenta-[*def*]-fluoren-8-ylbenzoate (7).** Compound **6** (5.4 g, 11.6 mmol) was suspended in methanol (300 mL); 98% $H_2SO_4$ (0.25 mL) was added, and the mixture was refluxed for 16 h. After the mixture was cooled, the solvent was evaporated. The residue was dissolved in $CH_2Cl_2$ (200 mL), and the organic layer was washed with a saturated aqueous $NaHCO_3$ solution (200 mL) and with water (200 mL), dried ($MgSO_4$), filtered, and evaporated to dryness. Purification by column chromatography (silica, eluent 1% MeOH in $CHCl_3$, $R_f$ = 0.16) afforded 3.2 g (56%) of **7** as a white solid: mp 221 °C; IR (KBr pellet) $\nu$ 3048, 2960, 2927, 2854, 1748, 1736, 1714, 1475, 1451, 1389, 1212, 1290, 1254, 1178, 1110, 1020 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300.13 MHz) $\delta$ 7.82 (d, 4H, $^3J$ = 8.0 Hz), 7.28 (d, 4H, $^3J$ = 8.0 Hz), 5.68 (d, 4H, $^2J$ = 10.7 Hz), 4.52 (d, 4H, $^2J$ = 10.7 Hz), 3.87 (s, 6H) ppm; $^{13}$C{$^1$H} NMR ($CDCl_3$, 75.47 MHz) $\delta$ 165.9, 158.1, 137.5, 131.4, 130.0, 127.9, 79.1, 72.1, 52.3; EI-MS *m*/*z* 494 (M)$^+$. Anal. Calcd for $C_{24}H_{22}N_4O_8$: C, 58.30; H, 4.48; N, 11.33. Found: C, 58.86; H, 4.03; N, 11.22.

**Methyl 4-1,3,4,6-Tetra[(acetyloxy)methyl]-6a-[4-(methoxycarbonyl)phenyl]-2,5-dioxoperhydroimidazo[4,5-*d*]-imidazol-3-ylbenzoate (8).** Compound **7** (3.9 g, 7.9 mmol) and *p*-toluenesulfonic acid monohydrate (0.40 g, 2.1 mmol) were suspended in acetic anhydride (15 mL), and the mixture was stirred at 110 °C for 40 h. After cooling, the dark solution was poured into aqueous 1 N NaOH (300 mL) and the product was extracted with $CH_2Cl_2$ (100 mL). The organic layer was washed with a saturated aqueous NaCl solution (200 mL) and with water (200 mL), dried ($MgSO_4$), and evaporated to dryness. The residue was dissolved in a minimal amount of $CHCl_3$, and this solution was added dropwise to stirred diethyl ether. After filtration, 3.9 g (70%) of **8** was obtained as an off-white powder: mp 269 °C; IR (KBr pellet) $\nu$ 3050, 2925, 2854, 1744, 1616, 1437, 1410, 1367, 1285, 1220, 1114, 1019 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300.13 MHz) $\delta$ 7.75 (d, 4H, $^3J$ = 8.5 Hz), 6.97 (d, 4H, $^3J$ = 8.5 Hz), 5.68 (d, 4H, $^2J$ = 11.6 Hz), 5.28 (d, 4H, $^2J$ = 11.6 Hz), 3.89 (s, 6H), 2.03 (s, 12H) ppm; $^{13}$C{$^1$H} NMR ($CDCl_3$, 75.47 MHz) $\delta$ 169.7, 165.5, 156.1, 135.7, 131.7, 129.6, 128.3, 86.6, 66.7, 52.4, 20.7 ppm; FAB-MS *m*/*z* 721 (M + Na)$^+$. Anal. Calcd for $C_{32}H_{34}N_4O_{14}$: C, 55.01; H, 4.91; N, 8.02. Found: C, 54.91; H, 4.79; N, 8.12.

**Methyl 4-1,3,4,6-Tetra(chloromethyl)-6a-[4-(methoxycarbonyl)phenyl]-2,5-dioxoperhydroimidazo[4,5-*d*]imidazol-3-ylbenzoate (9).** Compound **8** (400 mg, 0.66 mmol) was suspended in thionyl chloride (2 mL). One drop of water was added, and the mixture was stirred under argon for 20 h. Diethyl ether (10 mL) was added, and the white suspension was stored at 4 °C for 2 h. The precipitate was filtered off and dried under vacuum to give 290 mg (84%) of **9** as a white, very hygroscopic powder: mp 258 °C (dec); IR (KBr pellet) $\nu$ 3052 (ArH), 2955, 1749, 1729, 1451, 1438, 1410, 1317, 1282, 1115 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300.13 MHz) $\delta$ 7.85 (d, 4H, $^3J$ = 8.6 Hz), 7.07 (d, 4H, $^3J$ = 8.6 Hz), 5.35 (d, 4H, $^2J$ = 11.4 Hz), 5.27 (d, 4H, $^2J$ = 11.4 Hz), 3.90 (s, 6H) ppm; $^{13}$C{$^1$H} NMR ($CDCl_3$, 75.47 MHz) $\delta$ 165.5, 153.9, 133.7, 132.5, 130.1, 128.7, 86.8, 66.7, 52.5 ppm; FAB-MS *m*/*z* 642 (M + H)$^+$. Anal. Calcd for $C_{24}H_{22}N_4O_6Cl_4$: C, 47.70; H, 3.67; N, 9.27. Found: C, 47.91; H, 3.58; N, 9.15.

**Methyl 4-13b-[4-(Methoxycarbonyl)phenyl]-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,6a,12a,13a-tetraazabenzo-[5,6]azuleno[2,1,8-*ija*]benzo[*f*]azulen-13-ylbenzoate (10).** A mixture of **9** (1.50 g, 2.48 mmol) and $AlCl_3$ (2.31 g, 17.3 mmol) in benzene (20 mL) was refluxed under nitrogen for 120 h. After the mixture was cooled, aqueous 6 N HCl (20 mL) was added and the mixture was refluxed for 1 h. To the dark yellow solution was added $CH_2Cl_2$ (100 mL), and the organic layer was washed with water (2 × 200 mL) and evaporated to dryness. The product was purified by column chromatography (silica, $CH_2Cl_2$/MeOH 197:3, v/v, $R_f$ = 0.30) to yield 650 mg (36%) of **10** as a white powder: mp 315 °C (dec); IR (KBr pellet) $\nu$ 3050, 2956, 2921, 1722, 1454, 1422, 1283, 1115 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300.13 MHz) $\delta$ 7.83 (d, 4H, $^3J$ = 8.6 Hz), 7.24 (d, 4H, $^3J$ = 8.6 Hz), 7.29−7.23 (m, 4H), 7.16−7.09 (m, 4H,), 4.81 (d, 4H, $^2J$ = 15.8 Hz), 4.11 (d, 4H, $^2J$ = 15.8 Hz), 3.87 (s, 6H) ppm; $^{13}$C{$^1$H) NMR (75.47 MHz, $CDCl_3$) $\delta$ 166.8, 157.5, 138.7, 136.3, 130.8, 130.1, 129.5, 128.2, 128.0, 84.9, 52.1, 45.3

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ppm; FAB-MS *m/z* 615 $(M + H)^+$. Anal. Calcd for $C_{36}H_{30}N_4O_6$: C, 70.35; H, 4.92; N, 9.12. Found: C, 70.73; H, 4.89; N, 8.77.

**Methyl 4-13b-[4-(Methoxycarbonyl)phenyl]-1,4,8,11-tetramethyl-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,-6a,12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo[*f*]-azulen-13-ylbenzoate (11).** Compound **9** (240 mg, 0.40 mmol) was suspended in 1,2-dichloroethane (10 mL). *p*-Xylene (2.5 mL) and $SnCl_4$ (0.5 mL, 4 mmol) were added, and the mixture was refluxed under nitrogen for 64 h. After the mixture was cooled, aqueous 6 N HCl (15 mL) was added and the mixture was refluxed for 1 h. After the mixture was cooled, $CH_2Cl_2$ (100 mL) was added, and the organic layer was washed with water (2 × 100 mL) and evaporated to dryness. After purification by column chromatography (silica, $CH_2Cl_2$/MeOH 397:3, v/v, $R_f = 0.21$), 60 mg (23%) of **11** was obtained as a white powder: mp 354 °C (dec); IR (KBr pellet) $\nu$ 3054, 2952, 2930, 1726, 1713, 1458, 1422, 1408, 1288, 1117 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400.13 MHz) $\delta$ 7.78 (d, 4H, $^3J = 8.6$ Hz), 7.23 (d, 4H, $^3J = 8.6$ Hz), 6.85 (s, 4H), 5.06 (d, 4H, $^2J = 15.7$ Hz), 3.86 (s, 6H), 3.85 (d, 4H, $^2J = 15.7$ Hz), 2.46 (s, 12H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.61 MHz) $\delta$ 166.2, 157.7, 139.9, 135.4, 134.6, 130.5, 129.9, 128.2, 84.6, 52.2, 40.6, 20.2 ppm; FAB-MS *m/z* 671 $(M + H)^+$. Anal. Calcd for $C_{40}H_{38}N_4O_6$: C, 71.63; H, 5.71; N, 8.35. Found: C, 71.51; H, 5.62; N, 8.18.

**Methyl 4-1,4,8,11-Tetramethoxy-13b-[4-(methoxycarbonyl)phenyl]-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,6a,12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo-[*f*]azulen-13-ylbenzoate (12).** Starting from **7** (310 mg, 0.63 mmol) and *p*-dimethoxybenzene (220 mg, 1.59 mmol) in a mixture of acetic anhydride (1 mL) and trifluoroacetic acid (1 mL), this compound was synthesized as described for **6** to yield 375 mg (81%) of **12** as a white solid. Single crystals of **12** were obtained by slow diffusion of diethyl ether in a solution of the compound in dichloromethane: mp 336 °C (dec); IR (KBr pellet) $\nu$ 3010, 2955, 2923, 2851, 1729, 1719, 1486, 1465, 1445, 1307, 1298, 1281, 1262, 1121, 1078 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300.13 MHz) $\delta$ 7.76 (d, 4H, $^3J = 8.5$ Hz), 7.17 (d, 4H, $^3J = 8.5$ Hz), 6.43 (s, 4H), 5.54 (d, 4H, $^2J = 15.9$ Hz), 3.85 (s, 6H, 3.75 (s, 12H), 3.72 (d, 4H, $^2J = 15.9$ Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75.47 MHz) $\delta$ 166.2, 157.6, 150.9, 139.3, 130.4, 129.8, 128.17, 126.8, 111.8, 84.9, 56.6, 52.2, 36.9 ppm; FAB-MS *m/z* 735 $(M + H)^+$. Anal. Calcd for $C_{40}H_{38}N_4O_{10}$: C, 65.39; H, 5.21; N, 7.63. Found: C, 65.62; H, 5.12; N, 7.55.

**Methyl 4-5,9,14,18-Tetramethoxy-16b-[4-(methoxycarbonyl)phenyl]-7,16-dioxo-6,8,15,16b,16c,17-hexahydro-6a,7a,15a,16a-tetraazanaphtho[2′,3′:5,6]azuleno[2,1,8-*ija*]-naphtho[2,3-*f*]azulen-16-ylbenzoate (13).** Compound **9** (560 mg, 0.93 mmol) and 1,4-dimethoxynaphthalene (520 mg, 2.8 mmol) were dissolved in 1.2-dichloroethane (10 mL). $SnCl_4$ (1.5 mL, 12 mmol) was added, and the mixture was refluxed under nitrogen for 40 h. After the mixture was cooled, aqueous 6 N HCl (10 mL) was added and the mixture was refluxed for 1 h. After the mixture was cooled, $CH_2Cl_2$ (50 mL) was added and the organic layer was washed with water (2 × 100 mL) and evaporated to dryness. After purification by column chromatography (silica, $CH_2Cl_2$/ MeOH 99:1, v/v, $R_f = 0.08$), 550 mg (71%) of **13** was obtained as an off-white solid: mp 337 °C (dec); IR (KBr pellet) $\nu$ 3018, 2954, 2848, 1728, 1718, 1488, 1460, 1296, 1280, 1074 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300.13 MHz) $\delta$ 8.00−7.94 (m, 4H), 7.86 (d, 4H, $^3J = 8.5$ Hz), 7.45−7.39 (m, 4H), 7.31 (d, 4H, $^3J = 8.5$ Hz), 5.76 (d, 4H, $^2J = 15.9$ Hz), 4.03 (s, 12H), 3.89 (s, 6H), 3.86 (d, 4H, $^2J = 15.9$ Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75.47 MHz) $\delta$ 166.5, 156.2, 149.4, 138.0, 130.4, 129.6, 128.0, 127.3, 127.1, 122.3, 84.1, 62.6, 52.4, 38.9 ppm; FAB-MS *m/z* 835 $(M + H)^+$. Anal. Calcd for $C_{48}H_{42}N_4O_{10}$: C, 69.06; H, 5.07; N, 6.71. Found: C, 68.88; H, 5.05; N, 6.97.

**4-[13b-(4-Carboxyphenyl)-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,6a,12a,13a-tetraazabenzo[5,6]azuleno-[2,1,8-*ija*]benzo[*f*]azulen-13-yl]benzoic Acid (1).** Compound **10** (85 mg, 0.14 mmol) was stirred in a mixture of dioxane, methanol, and aqueous 4 N NaOH (15:4:1, v/v/v, 8 mL) for 16 h. The precipitate was filtered off, dried, and redissolved in water (2 mL). Aqueous 1 N HCl was slowly added until pH = 1 while stirring the mixture vigorously. The formed precipitate was filtered off (small G3 filter, without the application of vacuum), washed with water (1 mL), and dried under vacuum over $P_2O_5$ to yield 75 mg (95%) of **1** as a white solid: mp 380 °C (dec); $^1H$ NMR (DMSO-$d_6$, 300.13 MHz) $\delta$ 7.83 (d, 4H, $^3J = 8.6$ Hz), 7.24 (d, 4H, $^3J = 8.6$ Hz), 7.29−7.23 (m, 4H), 7.16−7.09 (m, 4H), 4.81 (d, 4H, $^2J = 15.8$ Hz), 4.11 (d, 4H, $^2J = 15.8$ Hz) ppm; $^{13}C\{^1H\}$ NMR (75.47 MHz, $CDCl_3$) $\delta$ 166.8, 157.5, 138.7, 136.3, 130.8, 130.1, 129.5, 128.2, 128.0, 84.9 (N*C*(Ar)N), 52.1 (C(O)O*C*$H_3$), 45.3 ppm; FAB-MS *m/z* 587 $(M + H)^+$. Anal. Calcd for $C_{34}H_{26}N_4O_6$: C, 69.62; H, 4.46; N, 9.55. Found: C, 69.87; H, 4.76; N, 9.37.

**4-[13b-(4-Carboxyphenyl)-1,4,8,11-tetramethyl-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,6a,12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo[*f*]azulen-13-yl]benzoic Acid (2).** Starting from **11** (80 mg, 0.12 mmol), this compound was synthesized as described for **1**: yield, 74 mg (96%) of **2** as a white solid; mp > 400 °C (dec); IR (KBr pellet) $\nu$ 3182, 2048, 2959, 2924, 1727, 1694, 1674, 1475, 1449, 1413, 1308, 1266, 1221, 1141 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$, 300.13 MHz) $\delta$ 7.77 (d, 4H, $^3J = 8.3$ Hz), 7.34 (d, 4H, $^3J = 8.3$ Hz), 6.90 (s, 4H), 4.95 (d, 4H, $^2J = 16.0$ Hz), 3.90 (d, 4H, $^2J = 16.0$ Hz), 2.43 (s, 12H) ppm; $^{13}C\{^1H\}$ NMR (DMSO-$d_6$, 75.47 MHz) $\delta$ 170.6, 160.9, 143.0, 140.4, 137.8, 135.0, 133.5, 132.5, 88.1, 42.2, 23.7 ppm; FAB-MS *m/z* 643 $(M + H)^+$. Anal. Calcd for $C_{38}H_{34}N_4O_6$: C, 71.01; H, 5.33; N, 8.72. Found: C, 71.21; H, 5.55; N, 8.32.

**4-[16b-(4-Carboxyphenyl)-5,9,14,18-tetramethoxy-7,-16-dioxo-6,8,15,16b,16c,17-hexahydro-6a,7a,15a,16a-tetraazanaphtho[2′,3′:5,6]azuleno[2,1,8-*ija*]naphtho[2,3-*f*]-azulen-16-yl]benzoic Acid (4).** Starting from **13** (65 mg, 0.078 mmol) this compound was synthesized as described for **1**: yield, 60 mg (96%) of **4** as a white solid; mp 360 °C (dec); $^1H$ NMR (DMSO-$d_6$, 300.14 MHz) $\delta$ 7.98−7.92 (m, 4H), 7.82 (d, 4H, $^3J = 8.4$ Hz), 7.55−7.49 (m, 4H), 7.39 (d, 4H, $^3J = 8.4$ Hz), 5.58 (d, 4H, $^2J = 16.0$ Hz), 4.02 (d, 4H, $^2J = 16.0$ Hz), 3.96 (s, 12H) ppm; $^{13}C\{^1H\}$ NMR (DMSO-$d_6$, 50.32 MHz) $\delta$ 166.7, 156.6, 149.4, 138.2, 130.1, 129.7, 128.6, 127.5, 126.8, 122.7, 84.2, 62.5, 38.2 ppm; FAB-MS *m/z* 829 $(M + Na)^+$. Anal. Calcd for $C_{46}H_{38}N_4O_{10}$: C, 68.48; H, 4.75; N, 6.94. Found: C, 68.58; H, 4.79; N, 6.81.

**Disodium-4-[13b-(4-carboxylatophenyl)-6,13-dioxo-5,7,-12,13b,13c,14-hexahydro-5a,6a,12a,13a-tetraazabenzo-[5,6]azuleno[2,1,8-*ija*]benzo[*f*]azulen-13-yl]benzoate (Na1).** To a suspension of compound **1** (100 mg, 0.17 mmol) in water (10 mL) was added an aqueous NaOH solution (5 mL containing 0.34 mmol of NaOH). The mixture was stirred overnight, whereafter it was lyophilized to yield 108 mg (100%) of **Na1** as a very hygroscopic white foam, which was stored under nitrogen at −18 °C: mp > 400 °C (dec); IR (KBr pellet) $\nu$ 3050, 2922, 1714, 1684, 1605, 1558, 1471, 1445, 1428, 1407, 1309, 1260 $cm^{-1}$; $^1H$ NMR ($D_2O$, 500.13 MHz, 6.0 mM) $\delta$ 7.56 (d, 4H, $^3J = 7.9$ Hz), 7.20 (d, 4H, $^3J = 7.9$ Hz), 7.18 (br s, 4H), 7.05 (br s, 4H), 4.58 (d, 4H, $^2J = 16.1$ Hz), 4.20 (d, 4H, $^2J = 16.1$ Hz) ppm.

**Disodium-4-[13b-(4-carboxylatophenyl)-1,4,8,11-tetramethyl-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,6a,-12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo[*f*]azulen-13-yl]benzoate (Na2).** Starting from **2** (100 mg, 0.156 mmol), this compound was synthesized as described for **Na1**: yield, 107 mg (100%) of **Na2** as a very hygroscopic white foam; mp 390 °C (dec); IR (KBr pellet) $\nu$ 3048, 2924, 1715, 1682, 1605, 1557, 1475, 1449, 1428, 1405, 1308, 1258 $cm^{-1}$; $^1H$ NMR ($D_2O$, 500.13 MHz, 3.6 mM) $\delta$ 7.54 (d, 4H, $^3J = 8.3$ Hz), 7.16 (d, 4H, $^3J = 8.3$ Hz), 6.33 (s, 4H), 4.84 (d, 4H, $^2J = 16.2$ Hz), 3.82 (d, 4H, $^2J = 16.2$ Hz), 2.20 (s, 12H) ppm.

**Disodium-4-[13b-(4-carboxylatophenyl)-1,4,8,11-tetramethoxy-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,-6a,12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo[*f*]-azulen-13-yl]benzoate (Na3).** Starting from **3** (100 mg, 0.142 mmol), this compound was synthesized as described for **Na1**:

yield, 106 mg (100%) of **Na3** as a very hygroscopic white foam, which was stored under nitrogen at −18 °C; mp 321 °C (dec); IR (KBr pellet) $\nu$ 3047, 2927, 2841, 1726, 1701, 1603, 1558, 1472, 1438, 1308, 1258, 1080 cm$^{-1}$; $^1$H NMR ($D_2O$, 500.13 MHz, 5.2 mM) $\delta$ 7.53 (d, 4H, $^3J$ = 8.2 Hz), 7.13 (d, 4H, $^3J$ = 8.2 Hz), 5.94 (s, 4H), 5.24 (d, 4H, $^2J$ = 16.3 Hz), 3.69 (d, 4H, $^2J$ = 16.3 Hz), 3.45 (s, 12H) ppm.

**Disodium-4-[13b-(4-carboxylatophenyl)-1,4,8,11-tetramethoxy-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,-6a,12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo[*f*]-azulen-13-yl]benzoate (Na4).** Starting from **4** (100 mg, 0.124 mmol), this compound was synthesized as described for **Na1**: yield, 105 mg (100%) of **Na4** as a very hygroscopi white foam, which was stored under nitrogen at −18 °C; mp > 400 °C (dec); IR (KBr pellet) $\nu$ 3053, 2927, 2839, 1729, 1707, 1603, 1559, 1467, 1439, 1392, 1306, 1258, 1077 cm$^{-1}$; $^1$H NMR ($D_2O$, 300.13 MHz, 2.9 mM) $\delta$ 7.63 (d, 4H, $^3J$ = 7.2 Hz), 7.31 (d, 4H, $^3J$ = 7.2 Hz), 6.98 (br s, 4H), 6.05 (br s, 4H), 5.40 (d, 4H, $^2J$ = 15.8 Hz), 4.03 (d, 4H, $^2J$ = 15.8 Hz), 3.65 (s, 12H) ppm.

**Diammonium-4-[13b-(4-carboxylatophenyl)-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,6a,12a,13a-tetraazabenzo-[5,6]azuleno[2,1,8-*ija*]benzo[*f*]azulen-13-yl]benzoate ($NH_4$-1).** Compound **1** (100 mg, 0.17 mmol) was dissolved in aqueous ammonia (5 mL, 30%). The mixture was stirred overnight; the excess ammonia was evaporated, and the residue was lyophilized to yield 106 mg (100%) of **$NH_4$1** as a very hygroscopic white foam, which was stored under nitrogen at −18 °C: mp 380 °C (dec); IR (KBr pellet) $\nu$ 3700−2700, 2939, 1740−1675, 1468, 1426, 1312, 1280, 1220 cm$^{-1}$; $^1$H NMR ($D_2O$, 300.13 MHz, 0.8 mM) $\delta$ 7.58 (d, 4H, $^3J$ = 8.0 Hz), 7.19 (d, 4H, $^3J$ = 8.0 Hz), 7.18 (m, 4H), 7.03 (m, 4H), 4.57 (d, 4H, $^2J$ = 16.0 Hz), 4.14 (d, 4H, $^2J$ = 16.0 Hz) ppm.

**Diammonium-4-[13b-(4-carboxylatophenyl)-1,4,8,11-tetramethyl-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,-6a,12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo[*f*]-azulen-13-yl]benzoate ($NH_4$2).** Starting from **2** (100 mg, 0.156 mmol), this compound was synthesized as described for **$NH_4$1** to yield 105 mg (100%) of **$NH_4$2** as a very hygroscopic white foam, which was stored under nitrogen at −18 °C: mp > 400 °C (dec); IR (KBr pellet) $\nu$ 3700−2700, 2947, 1730−1670, 1471, 1448, 1422, 1406, 1311, 1218 cm$^{-1}$; $^1$H NMR ($D_2O$, 400.13 MHz, 0.8 mM) $\delta$ 7.60 (d, 4H, $^3J$ = 8.0 Hz), 7.25 (d, 4H, $^3J$ = 8.0 Hz), 6.63 (s, 4H), 4.95 (d, 4H, $^2J$ = 16.3 Hz), 3.91 (d, 4H, $^2J$ = 16.3 Hz), 2.32 (s, 12H) ppm.

**Diammonium-4-[13b-(4-carboxylatophenyl)-1,4,8,11-tetramethoxy-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,6a,12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo-[*f*]azulen-13-yl]benzoate ($NH_4$3).** Starting from **3** (100 mg, 0.142 mmol), this compound was synthesized as described for **$NH_4$1** to yield 105 mg (100%) of **$NH_4$3** as a very hygroscopic white foam, which was stored under nitrogen at −18 °C: mp 309 °C (dec); IR (KBr pellet) $\nu$ 3700−2700, 2933, 1730−1670, 1485, 1465, 1427, 1407, 1353, 1299, 1259, 1077 cm$^{-1}$; $^1$H NMR ($D_2O$, 400.13 MHz, 0.7 mM) $\delta$ 7.58 (d, 4H, $^3J$ = 8.1 Hz), 7.18 (d, 4H, $^3J$ = 8.1 Hz), 6.14 (s, 4H), 5.29 (d, 4H, $^2J$ = 16.1 Hz), 3.76 (d, 4H, $^2J$ = 16.1 Hz), 3.54 (s, 12H) ppm.

**Diammonium-4-[13b-(4-carboxylatophenyl)-1,4,8,11-tetramethoxy-6,13-dioxo-5,7,12,13b,13c,14-hexahydro-5a,6a,12a,13a-tetraazabenzo[5,6]azuleno[2,1,8-*ija*]benzo-[*f*]azulen-13-yl]benzoate ($NH_4$4).** Starting from **4** (100 mg, 0.124 mmol), this compound was synthesized as described for **$NH_4$1** to yield 104 mg (100%) of **$NH_4$4** as a very hygroscopic white foam, which was stored under nitrogen at −18 °C: mp 360 °C (dec); IR (KBr pellet) $\nu$ 3700−2700, 2931, 2852, 1730−1670, 1460, 1427, 1409, 1356, 1306, 1047 cm$^{-1}$; $^1$H NMR ($D_2O$, 300.13 MHz, 0.4 mM) $\delta$ 7.72 (d, 4H, $^3J$ = 7.8 Hz), 7.40 (d, 4H, $^3J$ = 7.8 Hz), 7.20 (br s, 4H), 6.35 (br s, 4H), 5.49 (d, 4H, $^2J$ = 15.8 Hz), 4.16 (d, 4H, $^2J$ = 15.8 Hz), 3.75 (s, 12H) ppm.

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**Supporting Information Available:** General experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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