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Molecular Recognition: Comparative Study of a Tunable Host–Guest System by Using a Fluorescent Model System and Collision-Induced Dissociation Mass Spectrometry on Dendrimers

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Abstract: Host–guest interactions between the periphery of adamantylurea-functionalized dendrimers (host) and ureido acetic acid derivatives (guest) were shown to be specific, strong and spatially well-defined. The binding becomes stronger when using phosphonic or sulfonic acid derivatives. In the present work we have quantified the binding constants for the host–guest interactions between two different host motifs and six different guest molecules. The host molecules, which resemble the periphery of a poly(propylene imine) dendrimer, have been fitted with an anthracene-based fluorescent probe. The two host motifs differ in terms of the length of the spacer between a tertiary amine and two ureido functionalities. The guest molecules all contain an acidic moiety (either a carboxylic acid, a phosphonic acid, or a sulfonic acid) and three of them also contain an ureido moiety capable of forming multiple hydrogen bonds to the hosts. The binding constants for all 12 host–guest complexes have been determined by using fluorescence titrations by monitoring the increase in fluorescence of the host upon protonation by the addition of the guest. The binding constants could be tuned by changing the design of the acidic part of the guest. The formation of hydrogen bonds gives, in all cases, higher association constants, demonstrating that the host is more than a proton sensor. The host with the longer spacer (propyl) shows higher association constants than the host with the shorter spacer (ethyl). The gain in association constants are higher when the urea function is added to the guests for the host with the longer spacer, indicating a better fit. Collision-induced dissociation mass spectrometry (CID-MS) is used to study the stability of the six motifs using the corresponding third generation dendrimer. A similar trend is found when the six different guests are compared.

Keywords: dendrimers · fluorescence spectroscopy · mass spectrometry · molecular recognition · supramolecular chemistry

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Introduction

Host–guest chemistry with dendrimers is an area of supramolecular chemistry that has developed fast in recent years.[1–7] With the dendritic box as one of the first examples,[8] the field has developed towards systems that mimick or interact with biological systems, that is, where the host–guest chemistry involves binding to the surface of the dendrimer, so-called *exo* complexation. One of the consequences of having a dendritic architecture is that a large number of groups are presented at the surface of the structure. This situation is well-suited for the study of multivalent interactions in biological systems.[9,10] Some examples of previous work are peptide dendrimers[7,11–13] and glycodendrimers.[7,11,14–16] All of these systems, however, are based on covalent bonding of the surface groups to the dendritic struc-

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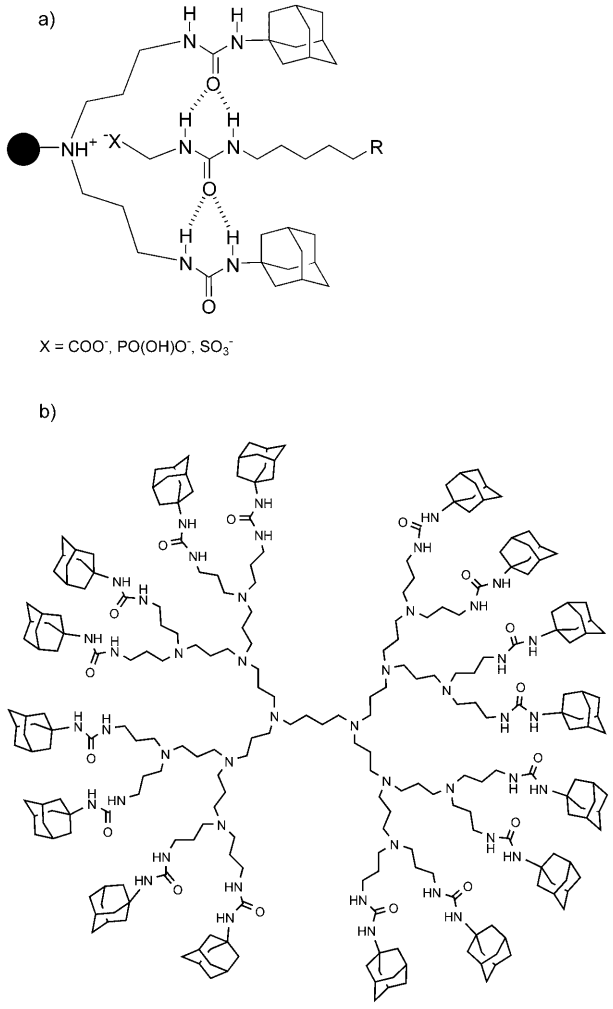
ture. Noncovalent binding to the surface of a dendrimer gives rise to a dynamic system, for which the optimal binding motif for a target can be molded from a dendritic host and an ensemble of guest molecules. An important first step in this direction was the preparation of host–guest complexes between dendrimers and peptides.[17]

Recently a series of new host–guest motifs for *exo* complexation of poly(propylene imine) dendrimers was introduced.[18–22] This design is outlined in Scheme 1, where X is a



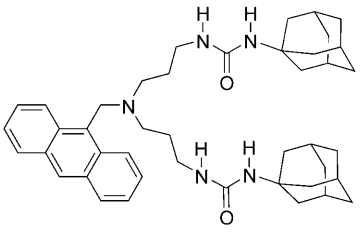
Scheme 1. a) Schematic representation of the host–guest system studied and b) third-generation adamantylurea-terminated poly(propylene imine) dendrimer that is capable of binding eight guest molecules.

carboxylic acid, a phosphonic acid, or a sulfonic acid. The adamantylurea-functionalized poly(propylene imine) dendrimer (with the third generation shown in Scheme 1) serves as a multivalent host for the guest molecules in a very selective manner, thus enabling the isolation of well-defined complexes with one guest per host motif at the periphery of the dendrimer. The complexation is due to a combination of multivalent hydrogen bonding between the urea parts of the guests and the host, and to an electrostatic interaction between the acidic part of the guest and the tertiary amine in the host moiety. These systems were studied in solution by NMR spectroscopy[19,23] and in the gas phase by electrospray mass spectrometry.[21] Determination of the association constants for the different systems would be desirable to gain further insight into the complexation.

However, quantification of the association constants of large dendrimers capable of binding several guest molecules (up to 32 for the fifth-generation poly(propylene imine) dendrimer) is difficult due to multiple equilibrium considerations. A relatively simple solution to this challenge is to quantify the association constants on model host compounds containing only one binding site. This approach furthermore has the advantage that it should allow faster screening of new potential host–guest combinations. Herein we present the quantification of the association constants for the host–guest interactions between two different host motifs that resemble the periphery of a poly(propylene imine) dendrimer and six different guest molecules by attaching a fluorescence probe to the host. Furthermore, these complexes were investigated with collision-induced decomposition mass spectrometry to evaluate their relative stabilities in the gas phase. The difference in solution phase and gas phase stabilities is discussed.

Results and Discussion

Molecular design: In earlier work we observed strong indications, that, in a purely qualitative manner, the binding affinity of the host–guest system is tunable by rational design of the guest molecules.[19–21] As a result, we have designed and synthesized a system in which it is possible to quantify the association constants by fluorescence spectroscopy. We chose to simplify the system, as compared with the multifunctional dendrimer systems, by choosing a model host substrate that only contains one binding site. A well-known, and thoroughly studied, fluorescence probe is the 9-methylanthracenyl moiety. This can conveniently be attached to the host by using the amine functionality in the binding motif. In this way, two different hosts (**1** and **2**) were synthesized with different spacer lengths between the tertiary amine and the ureido moieties. Host **1** is equivalent to the binding motif of the periphery of the poly(propylene imine) dendrimers and host **2** simply has an ethylene spacer replacing the propylene spacer. Host **2** was prepared to study the flexibility of the host-binding motif.



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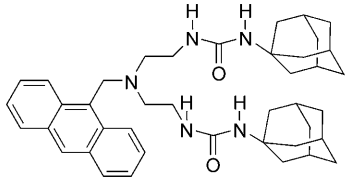


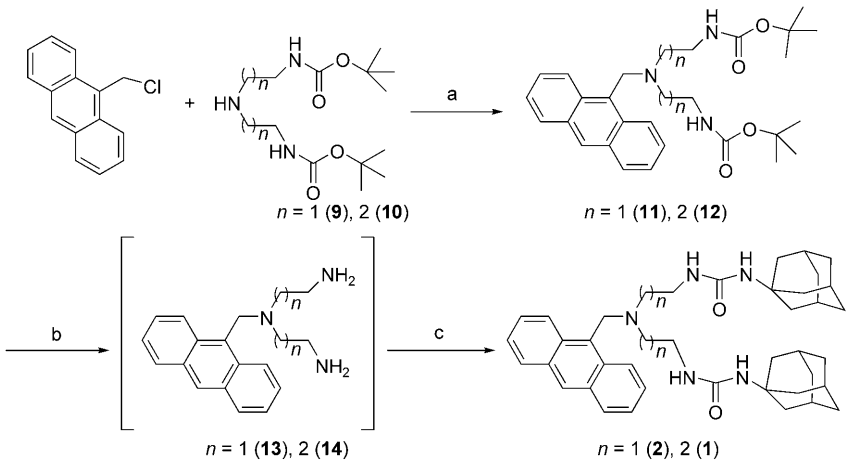
2

The design of the original type of host–guest

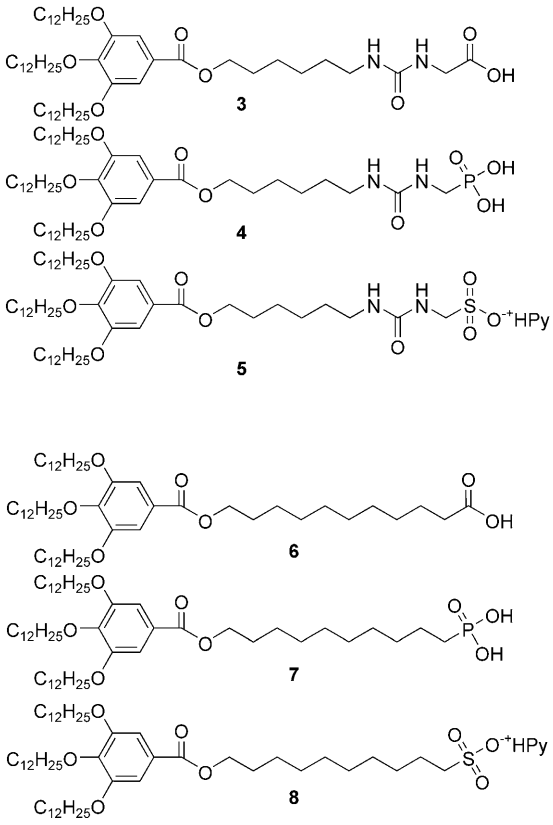
system, in which the guest has an ureido glycine tail that binds to the host, opens the path to several structural modifications. In earlier work it was shown that the ureido glycine part can be substituted for a *C*-terminal peptide (in which the carboxylic acid performs the electrostatic interaction to the host) and the ureido part is replaced by an amide from the peptide (that can form multiple hydrogen bonds to the host). It has also been indicated, in a qualitative fashion, that the binding strength of guests increases for complexes in which the carboxylic acid part is substituted by a phosphonic acid or a sulfonic acid moiety. To study this phenomenon in a systematic manner and to quantify the binding strengths, we prepared a series of chloroform-soluble guest molecules **3**–**5** bearing the above-indicated binding motifs. The attachment of a trisdodecyloxy benzoic acid part to the guest molecules serves only solubility purposes and is identical for all guests in this study.

The guest molecules **6**–**8**, which lack the ureido moiety, and thus the ability to form hydrogen bonds to the ureido part of the hosts, were prepared as reference compounds. The binding properties of these guests rely solely on the electrostatic interaction with the tertiary amine functionality of the host molecules. Thus, this series of guest molecules enables us to investigate the importance of rational design and it makes it possible to rule out that the host–guest interaction is more than merely a H^+ sensor.

Synthesis: The two host molecules **1** and **2** were prepared from the commercially available 9-(chloromethyl)anthracene as outlined in Scheme 2. Reaction of 9-(chloromethyl)-anthracene with the bis-boc-protected triamines[24] **9** and **10** yields, upon treatment with KI and K_2CO_3, the light- and acid-sensitive bis-boc protected triamines **11** and **12** in good yields. Deprotection of the boc protection groups was performed under very mild conditions by treatment with a mixture of phenol and TMSCl in CH_2Cl_2.[25] After the deprotection and a basic workup, the crude triamines **13** and **14** were allowed to react directly with adamantyl isocyanate to yield the target host molecules (**1** and **2**) as white crystalline materials in high yields.



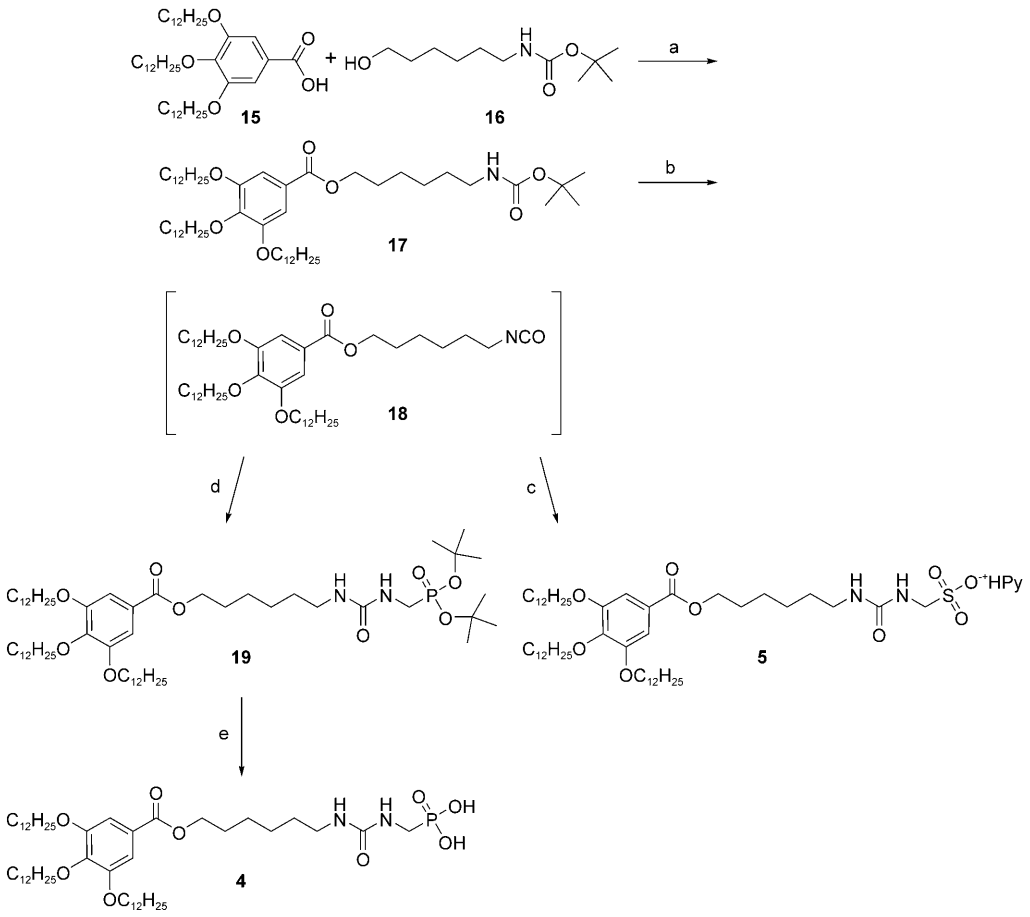
Scheme 2. Synthesis of fluorescent hosts **1** and **2**. Reagents and conditions: a) KI, K_2CO_3, DMF, 68% (**11**), 75% (**12**); b) TMSCl, PhOH, CH_2Cl_2; c) AdNCO, CH_2Cl_2, 60% (**1**), 96% (**2**) (two steps).



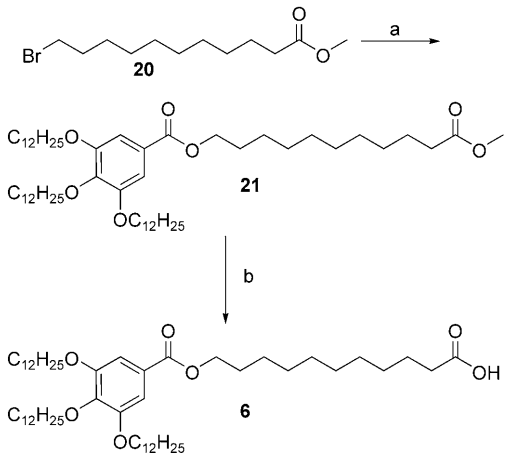
The synthesis of the carboxylic acid guest containing the ureido functionality has been described elsewhere.[19] The syntheses of the phosphonic acid guest **4** and the sulfonic acid guest containing the ureido functionality (**5**) follow the same overall synthetic strategy, and are outlined in Scheme 3.

The syntheses of the guest molecules lacking the ureido functionalities proceeded by different protocols. The synthesis of the carboxylic acid guest without the ureido function (**6**) starts from methyl 11-bromoundecanoate (**20;** Scheme 4),[28] which was treated with the gallic acid derivative[29] **15** to give the diester **21** in high yield. This diester was selectively demethylated to give **6** by using LiI in pyridine.[30,31]

The phosphonic acid guest **7** was prepared via the bromide **23** by an Arbuzov reaction with trimethylphosphite (Scheme 5). The bromide **23** was prepared from the gallic acid precursor **15** via the acid fluoride **22** in a one-pot procedure using fluoro-*N*,*N*,*N*′,*N*′-tetramethylformamidinium hexafluorophosphate (TFFH/4-dimethylaminopyridine



Scheme 3. Synthesis of guests **4** and **5**. Reagents and conditions: a) DCC, DMAP, $CHCl_3$, 67%; b) 1: HCl, diethyl ether, 2: NaOH, 3: tricarbonate; c) aminomethanesulfonic acid, pyridine, 62%; d) di-*tert*-butyl aminomethylphosphonate, $CHCl_3$, 49%; e) TFA, CH_2Cl_2, quant.

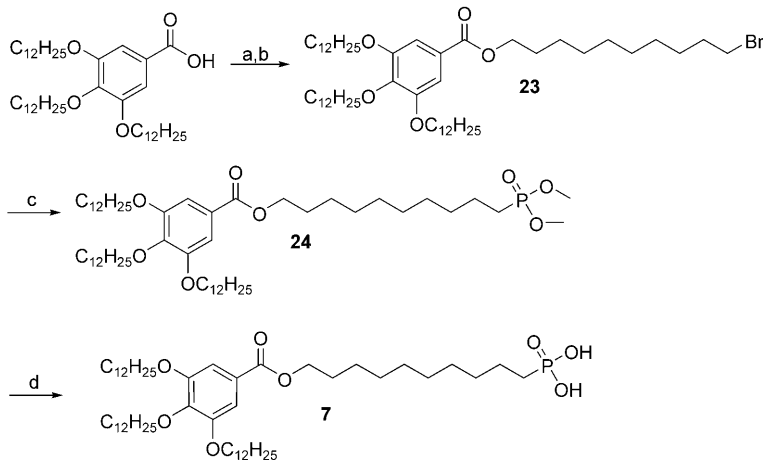


Scheme 4. Synthesis of carboxylic acid guest **6**. Reagents and conditions: a) **15**, K_2CO_3, DMF, 99%; b) LiI, pyridine, 51%.

(DMAP) as the coupling reagents.[32] Demethylation of **24** to yield **7** was carried out using TMSCl and NaI in refluxing CH_3CN.

The sulfonic acid guest **8** was prepared via 10-hydroxydecane-1-sulfonic acid **25** through an ester-formation reaction using TFFH/DMAP[32] in CH_2Cl_2.

Fluorescence: Fluorescence titration experiments are an ideal method to determine the binding constants of the six guest molecules to the two host molecules.[34] These were carried out by increasing the total concentration of the highly soluble (in $CHCl_3$) guest molecules in a solution with a constant total concentration of host molecules and monitoring the increase in the fluorescence intensity. The fluorescence spectra from a titration (between host **1** and guest **3**) are shown in Figure 1. From the fluorescence spectra, we see that the addition of more than 50 equivalents of guest molecules does not lead to a further increase of the fluorescence intensity. Thus, this maximum in intensity (I_{max}) indicates that all the host molecules have bonded guest molecules. Similarly, the lowest intensity measured (I_0) is due only to the host molecule (no guest present). The degree of complexation of host molecules is thus defined as $\alpha=(I-I_0)/(I_{max}-I_0)$ and from this value we can calculate the actual guest concentration in the sample as $[G]=C_G-\alpha C_H$, where C_G is the total guest concentration and C_H is the total host concentration in the sample. By plotting the degree of complexation as a function of the actual guest concentration ([G]) we obtain a Bjerrum *S*-diagram to which we can fit a sigmoidal function and deduce the association constant (see Figure 2). In the analysis described above we have assumed



Scheme 5. Synthesis of phosphonic acid guest **7**. Reagents and conditions: a) TFFH, Et_3N, DMAP, CH_2Cl_2, 87%; b) 1: TFFH, Et_3N, CH_2Cl_2, 2: 10-bromodecanol, DMAP, 90%; c) $P(OEt)_3$, 110°C, three days, 60%; d) TMSCl, NaI, CH_3CN, 89%.

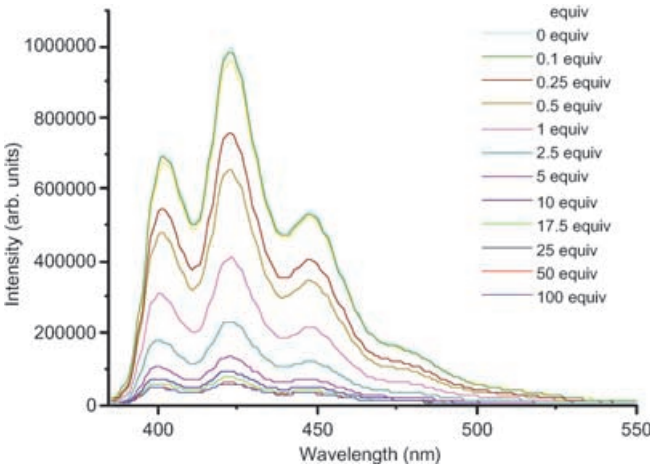


Figure 1. Fluorescence spectra of a titration between host **1** and guest **3**.

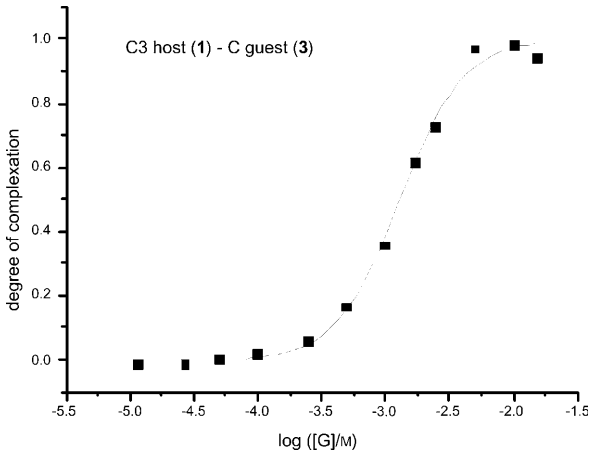


Figure 2. Bjerrum *S*-diagram for the host **1** and carboxylic acid guest **3**.

1:1 stoichiometry between the guest and the host. This assumption is confirmed by the fact that we only observe one equivalence point in the Bjerrum *S*-diagram and the good quality of the sigmoidal fit to the experimental data points (see Figure 2).[18,20]

The association constants for the 12 different complexes were obtained from the sigmoidal curves by fitting a sigmoidal function to the data points using nonlinear regression (see Table 1).

Association constants for the binding of ureido acetic acid guests substituted with oligo(p-phenylene vinylenes) to a methyl-analogue of **2** were reported previously.[22] The association constants (in $CDCl_3$) determined by NMR titration were found to be highly dependent on the length of the oligomer, probably due to self-association of the guests. The K_a values found were in the range from 300 to 13000 M^{-1}.

Table 1. Association constants for the complexes formed between hosts **1–2** and guests **3–8** and the required voltage for the dissociation of the guests from the **G3Ad** dendrimer.

Complex	Association constant ($\times 10^2$ M^{-1})		Mass spectrometry range in which guest dissociates [V][a]
	2	**1**	**G3Ad**
3	4.66±0.27	7.76±0.43	25–55
6	3.87±0.65	1.64±0.11	–
4	127±9	685±125	40–70
7	62.3±4.3	113±6	30–55
5	864±282	967±57	60–85
8	375±39	253±25	45–65

[a] Required voltage for dissociation of the guests from the **G3Ad** dendrimer.

For the same binding motif, but with a different tail, we find $K_a = 466$ M^{-1}, which is in the interval previously reported.

Mass spectrometry: Recently we observed complexes of a third-generation adamantylurea dendrimer (from now on referred to as **D**) with several guest molecules in the gas phase using electrospray-ionization mass spectrometry.[21] It was also possible to compare the binding strength of different guest molecules in a qualitative manner using collision-induced dissociation. In this technique an ion, consisting of the dendrimer plus two different guest molecules, is selected after it is accelerated. Subsequently the ion enters the collision cell, which contains argon gas. The ion collides with the argon atoms, which, as a fraction of the ion's kinetic energy is transferred into internal energy, results in fragmentation of the supramolecular complex. The guest molecule that dissociates from the dendrimer first is more weakly bound to the dendrimer than the other guest. This methodology is comparable to the kinetic method developed by Cooks and co-workers, which is a procedure for estimating thermochemical information based on the rates of competitive dissociations of mass-selected cluster ions.[35–38] However, in our case, the conversion of collision energy to internal energy is

hard to quantify as multiple collisions occur in the collision cell (see Experimental Section for details). Furthermore, owing to the larger number of degrees of freedom in a larger molecule, it is even more difficult to accurately determine the amount of internal energy upon ion activation.[39,40] However, it is in our view valid to compare the binding of guests **3**–**8** to dendrimer **D** in the gas phase in a qualitative manner.

First, the six different complexes were made, each consisting of four equivalents of guest **3**–**8** added to **D**. All samples, except for guest **6,** give mass spectra that show complexation to the dendrimer, indicating that these complexes are stable enough to be observed in the gas phase. A typical spectrum is shown in Figure 3.

These results show that for the phosphonic and sulfonic acid guests, the urea group is not required to obtain a complex that is stable enough to survive the transfer from solution to the gas phase.

To investigate the influence of the urea groups on the binding strength with **D**, collision-induced dissociation experiments were performed to determine the relative binding strength of **4** versus **7**, and **5** versus **8**. Therefore, a sample containing two equivalents of **4** and two equivalents of **7** added to **D** was prepared. A further sample with two equivalents of **5** and two equivalents of **8** added to **D** in chloroform was also prepared. Both samples gave complexes showing the statistical combinations of guests bound to dendrimer (not depicted). From the first sample, ion $(\mathbf{D}\cdot(\mathbf{4}_1+\mathbf{7}_1))^{3+}$ was selected and subjected to collision-induced dissociation.

The applied voltage is a measure for the kinetic energy of the ion prior to injection into the collision cell. The $(\mathbf{D}\cdot(\mathbf{4}_1+\mathbf{7}_1))^{3+}$ ion remains stable until 25 V, but starts to fragment when the voltage is further increased. The first major product of fragmentation is $(\mathbf{D}\cdot(\mathbf{4}_1))^{3+}$, which has an *m/z* value of 1812.3. This means that **7** dissociates first from the dendrimer as a neutral species and is the weaker binding guest. The dissociation is not 100% selective as the peak of $(\mathbf{D}\cdot(\mathbf{7}_1))^{3+}$ is present at *m/z* 1807.1; however, the intensity of this ion is almost negligible. Guest **4** also starts to dissociate when the voltage is further increased, resulting in bare $(\mathbf{D})^{3+}$ (*m/z* 1508.6) at roughly 70 *V*. This means that guest **4** binds stronger to host **D** than guest **7** in the gas phase. Thus, the urea groups positively influence binding to the dendrimer. Some other peaks are also present in the mass spectra. They correspond to the dendrimer that has lost one to four adamantyl groups. Covalent bond dissociation of host **D** starts to take place at higher voltages, resulting in the peaks with a *m/z* value below 1508.6. Interestingly, covalent bond dissociation can also occur while a guest molecule is still attached. The ion with *m/z* 1761.9 corresponds to $(\mathbf{D}\cdot(\mathbf{4}_1))^{3+}$ which has lost one adamantyl group but still contains a guest. A similar trend is observed for the sulfonic acid guests.

Collision-induced dissociation applied to $(\mathbf{D}\cdot(\mathbf{5}_1+\mathbf{8}_1))^{3+}$ shows that guest **8** dissociates from the dendrimer first, resulting in the ion with *m/z* 1812.3 (Figure 4). Subsequently guest **5** dissociates. This again indicates that the guest molecule without the urea group is the weaker binding guest in the gas phase, which is in agreement with the fluorescence experiments in chloroform. Unfortunately, the technique could not be used to directly compare the difference in binding strength between phosphonic acid guest **4** and sulfonic acid guest **5** (or guest **7** and **8**), as these guest molecules have an almost identical mass. Consequently it is not possible to observe which guest molecule dissociates first. However, there are indications that the sulfonic acid guests bind stronger than the phosphonic acid guests based on the applied voltage. The acceleration voltage required for the ions to start fragmenting is higher for $(\mathbf{D}\cdot(\mathbf{5}_1+\mathbf{8}_1))^{3+}$ than for $(\mathbf{D}\cdot(\mathbf{4}_1+\mathbf{7}_1))^{3+}$. This indicates that sulfonic acid guests **5** and **8** bind stronger to host **D** than phosphonic acid guests **4** and **7**. These observations are further supported by the degree of

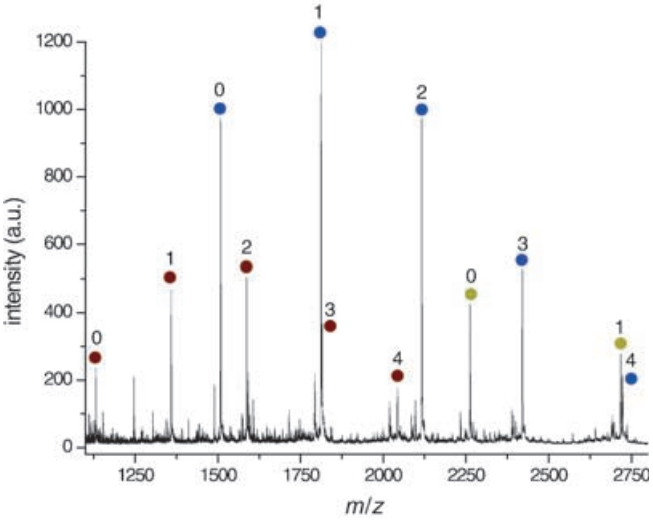


Figure 3. ESI Mass spectrum of a sample containing four equivalents of **5** added to **D** in chloroform. 4+ ions: red, 3+ ions: blue, 2+ ions: green. The number indicates the amount of guest that is bound to the dendrimer.

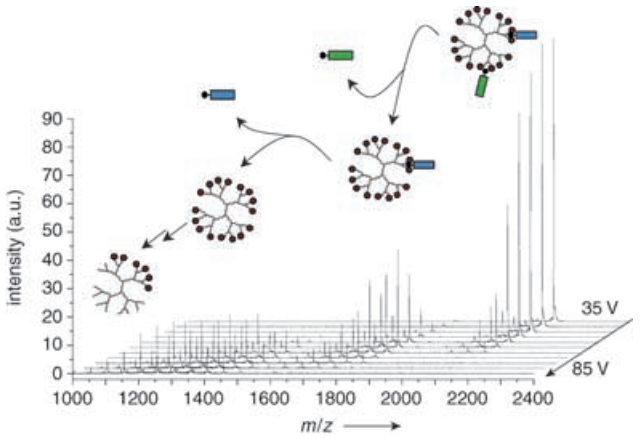


Figure 4. Collision induced dissociation performed on ion $(\mathbf{D}\cdot(\mathbf{5}_1+\mathbf{8}_1))^{3+}$. Guest **8** is depicted in green and guest **5** is depicted in blue. Besides noncovalent fragmentation, severe covalent fragmentation of **D** results in additional ions.

covalent fragmentation. While for the $(\mathbf{D}\cdot(\mathbf{4}_1+\mathbf{7}_1))^{3+}$ ion the adamantyl groups dissociate to some extent, severe covalent dissociation of the adamantyl groups of **D** is observed for $(\mathbf{D}\cdot(\mathbf{5}_1+\mathbf{8}_1))^{3+}$, eventually resulting in host **D** that has lost one to ten adamantyl groups at 85 V. This also indicates that the sulfonic acid guests bind stronger. In conclusion, two general trends are observed from the mass spectrometry measurements. When we compare two guest molecules with identical acid head groups that only differ in the presence of the ureido moiety (**3** versus **6**, **4** versus **7**, **5** versus **8**), the guests with the ureido functionality always bind stronger (Table 1). For guests **3** and **6** this is represented in the fact that no stable complexes are observed for guest **6**. Furthermore, when the acid strength of the guest is increased so that all contain the ureido groups (**3** versus **4** versus **5**), the binding strength also increases.

Discussion and Conclusions

The results of the fluorescence studies in chloroform depicted in Table 1 clearly show that the guest molecules containing the urea functionality bind stronger to both host molecules (**1** and **2**) than the guest molecules lacking the urea functionality. Thus, from these results we conclude that we actually observe molecular recognition and not just differences in pK_a values among the guests. Also, it is evident from the results in Table 1 that the three designed guests (**3**, **4**, and **5**) bind slightly stronger to host **1** than to host **2**, though these differences are minor. The effect is most pronounced for the phosphonic acid guest **4** that binds approximately five times stronger to host **1** than to host **2**.

In general, the gain in binding strength, when going from the guests lacking the urea functionality (**6**–**8**) to the guests having the urea function incorporated (**3**–**5**), is larger for host **1** than for host **2**. For host **1** (the host containing propyl spacers) the association constants are 4–5 times higher for the guests with the urea functionality but only 1–2 times higher in the case of host **2** (the host containing ethyl spacers). This, combined with the fact that the binding strength in general is slightly higher, strongly suggest that guests fit better with the cavity of host **1** than the cavity of the host **2**. This conclusion can be drawn because the gain in association constant has an entropy and an enthalpy contribution, and we assume that the enthalpies are comparable, which is reasonable because the main contribution to the enthalpy term is the electrostatic interaction. As the host–guest complexes represent a more highly ordered state than the guest and the host on their own, the entropy of the reaction will constitute a negative contribution to the association constant. This cost of entropy is larger for the host with the longer spacer groups because it has more degrees of freedom, and this must mean that the gain in binding strength is due to a better fit.

An important point to note is that the two sulfonic acid guests **5** and **8** are present as their pyridinium salts. This makes the pyridinium ion the acidic part of the guest and not the sulfonic acid. This provides strong evidence for the fact that the association constants for the urea-modified guests are due to a better recognition of the guest and not merely a matter of the acidic moiety being more acidic when a urea function is present at the β-carbon atom to the acidic function.

In our attempts to fully understand the dendrimer-based multivalent supramolecular complexes, we studied the gas-phase stabilities of the complexes as well. It is tempting to compare these results with the fluorescence model studies in solution. However, discrepancies between gas-phase binding and binding strengths in aqueous media have often been observed.[41,42] The main reasons are that electrostatic interactions and dipolar noncovalent interactions are strengthened in the absence of solvent shielding, while hydrophobic interactions become less important in the absence of solvent.[41] In our case we compare the gas-phase experiments to those in chloroform instead of aqueous media. Chloroform is an aprotic solvent, and a non-competing solvent to acid–base and hydrogen-bonding interactions due to the low dielectric constant.[43–46] Therefore, some comparisons between chloroform and the gas phase can be made. With this in mind we find that the mass spectrometry results in the gas phase are in reasonable agreement with the fluorescence experiments in chloroform. In all cases the guest molecules with urea groups bind stronger than the guest molecules without urea groups. Furthermore, an increase in binding strength is observed when the acidity of the head group becomes stronger.

In conclusion, we have presented design and synthetic procedures for a series of novel guest molecules for supramolecular functionalization of specific host molecules. Also, two novel piner-type fluorescence host molecules have been designed and synthesized. Finally, we have presented a simple method for evaluating a new host–guest system based on a combination of noncovalent interactions using a simple fluorescent probe. The host–guest system is highly flexible with respect to the host motif, and the association constants can be tuned by varying the design of the guest. The relatively high association constants of this all-organic host–guest system makes it an appealing alternative in the construction of supramolecular materials that can compete with metal-based and natural supramolecular materials.

The results presented herein complement earlier findings for this host–guest motif in large dendrimers both in solution and in the gas phase.

Experimental Section

General methods: Solvents were HPLC grade and were used as received. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 300 MHz NMR (Varian) apparatus (300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR) or on a 400 MHz NMR (Bruker) apparatus (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR). Proton chemical shifts are reported in ppm downfield from tetramethylsilane (TMS) and carbon chemical shifts in ppm downfield of TMS using the resonance of the deuterated solvent as internal standard. Melting points were measured on a Büchi B-140 appa-

ratus and are uncorrected. Elemental analysis was performed by Mrs Karin Linthoe on a Perkin-Elmer Series II, 2400 elemental analyser. Fast-atom bombardment (FAB) mass spectra were recorded on a Jeol JMS-HX 110A Tandem Mass Spectrometer in the positive ion mode using m-NBA as the matrix. HRMS were recorded on a Micromass Q-TOF apparatus using the electrospray ionization (ESI) technique. All column chromatography was performed on Merck Kiselgel 60 (0.015–0.040 mm) using the dry column vacuum chromatography (DCVC) technique.[49] All fluorescence measurements were performed by using Spectrosolve grade solvents and the solutions were degassed for 15 min prior to use. Emission spectra were measured on a FLS920 spectrometer from Edinburgh Instruments. The instrument is fitted with a 450-W Xe lamp for steady-state measurements. The detecting system comprises a single-photon-counting PMT detector in a Peltier cooled housing. All spectra were measured in a perpendicular geometry using 1-cm quartz cuvettes.

The ESI mass spectra of the dendrimer complexes were recorded with a Q-Tof Ultima GLOBAL mass spectrometer (Micromass, Manchester, UK) equipped with a Z-spray source. The samples (10 μL) were injected in the flow injection analysis (FIA) mode. The HPLC-grade chloroform was pumped with a Shimadzu LC-10 ADvp at a flow rate of 30 $\mu L\,min^{-1}$. Electrospray ionization was achieved in the positive-ion mode by application of 5 kV on the needle. The source block temperature was maintained at 60 °C and the desolvation gas was heated to 60 °C. Argon collision gas was introduced into the central hexapole collision cell of the mass spectrometer in collision-induced dissociation (CID) experiments. The pressure in the collision cell corresponds to approximately 0.8 mTorr (1×10^{-6} bar). With a collision cell length of 18.5 mm, multiple collisions occur in the collision cell.[39,47,48]

For the regular mass spectrometry experiments all complexes were prepared by adding four equivalents of guest to the dendrimer in a total concentration of 1 $mg\,mL^{-1}$ in chloroform. To 400 μL of each of these solutions was added 100 μL of a 1% acetic acid in chloroform solution. For the MS/MS experiments, two equivalents of each guest molecule were added to the dendrimer in a total concentration of 1 $mg\,mL^{-1}$ in chloroform. To 400 μL of these solutions was added 100 μL of a 1% acetic acid in chloroform solution. This mixture was immediately injected in the mass spectrometer. The small amount of acetic acid is used to protonate the dendrimer interior. When no acetic acid is used, no ions are observed in the mass spectrum. When too much acetic acid is used, the solvent destroys the supramolecular aggregate and only bare dendrimer **D** is observed. Under these conditions, we mostly observed the 4+ and 3+ ions as well as small amounts of the 2+ ion. As the 3+ ions are often the predominant species, all MS/MS experiments were performed with this ion. MS/MS experiments performed on the 2+ ion gave different voltages of dissociation, but never changed the order of dissociation when two different guests were compared when bound to the same dendrimer.

1-(3-{Anthracen-9-ylmethyl-[3-(3-adamantyl-ureido)propyl]amino}propyl)-3-adamantylurea (1): Compound **12** (2.65 g, 5.16 mmol) dissolved in dry CH_2Cl_2 (50 mL) was added to a mixture of TMSCl (5.61 g, 6.55 mL, 51.63 mmol) and phenol (4.86 g, 51.63 mmol) in dry CH_2Cl_2 (50 mL). This reaction mixture was stirred overnight under an N_2 atmosphere at room temperature. Water (50 mL) was added and the mixture was acidified with aqueous HCl (2 M). After vigorous stirring for 1 h, the phases were separated and the aqueous phase was washed with CH_2Cl_2 (2× 75 mL). The aqueous phase was made strongly alkaline by addition of aqueous NaOH (12 M) and extracted with CH_2Cl_2 (3×75 mL). The organic phases were concentrated in vacuo to yield the crude deprotected triamine as a slightly yellow oil. This was redissolved in dry CH_2Cl_2 (50 mL) and adamantyl isocyanate (1.92 g, 10.84 mmol) was added and the reaction mixture was stirred overnight at room temperature under N_2. The resulting precipitate was filtered off, washed with cold CH_2Cl_2, and recrystallized from EtOH to yield **1** as a white solid. Yield 3.30 g, 96%; m.p. 156–158 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.25–8.35 (m, 3H), 7.90–7.95 (m, 2H), 7.40–7.50 (m, 4H), 4.80 (br s, 2H), 4.45 (s, 2H), 4.20 (br s, 2H), 2.95–2.98 (m, 4H), 2.57–2.62 (m, 4H), 1.95–1.98 (m, 6H), 1.88–1.92 (m, 12H), 1.80–1.86 ppm (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9, 131.5, 129.4, 126.5, 125.0–125.4, 124.8, 55.5, 51.4, 50.9, 42.7, 38.2, 36.7, 29.9, 27.0 ppm; MS (positive-ion mode FAB): m/z: 676.9 $[M+H]^+$; elemental analysis (%) calcd for $C_{43}H_{57}N_5O_2$: C 76.41, H 8.50, N 10.36; found: C 76.20, H 8.61, N 10.36.

1-(2-{Anthracen-9-ylmethyl-[2-(3-adamantylureido)ethyl]amino}ethyl)-3-adamantylurea (2): Synthesized as compound **1** from precursor **11**. The product was purified by dry column vacuum chromatography (from heptane to EtOAc with 20% increments, followed by EtOAc to 20% MeOH in EtOAc with 3% increments) to yield **2** as an off-white solid. Yield 0.62 g, 60%; m.p. 140–142 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.25–8.38 (m, 3H), 7.94–7.98 (m, 2H), 7.40–7.55 (m, 4H), 4.50 (br s, 2H), 4.42 (br s, 2H), 4.05 (br s, 2H), 3.05–3.10 (m, 4H), 2.57–2.62 (m, 4H), 1.95–1.98 (m, 6H), 1.88–1.92 (m, 12H), 1.8–1.86 ppm (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9, 131.6, 129.4, 128.0, 126.5, 125.4, 125.3, 125.1, 125.0, 54.9, 51.2, 50.9, 42.6, 38.1, 36.7, 29.8 ppm; MS (positive-ion mode FAB): m/z: 648.9 $[M+H]^+$; elemental analysis (%) calcd for $C_{41}H_{53}N_5O_2$: C 76.01, H 8.25, N 10.81; found: C 76.21, H 8.41, N 10.66.

6-(3-Phosphonomethylureido)hexyl 3,4,5-tris-dodecyloxybenzoate (4): Compound **19** (0.400 g, 0.39 mmol) was dissolved in dry dichloromethane (10 mL) and trifluoroacetic acid (TFA; 10 mL) was added under a nitrogen atmosphere to the stirring solution using a syringe. After the reaction mixture had been stirred for 3 h at room temperature, the solvent was removed in vacuo. The resulting off-white solid was dried in a vacuum oven at 70 °C overnight; yield 0.355 g (100%); m.p. 206–208 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22 (s, 2H), 4.25 (m, 2H), 3.99 (m, 6H), 3.57 (m, 2H), 3.15 (m, 2H), 1.69–1.84 (m, 8H), 1.40–1.54 (m, 8H), 1.24–1.38 (m, 52H), 0.84–0.91 ppm (t, J = 5.8 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.0, 160.5, 153.2, 142.7, 125.0, 108.5, 73.8, 69.5, 65.2, 40.8, 32.2, 30.6, 30.0, 29.95, 29.90, 29.85, 29.70, 29.60, 28.9, 26.6, 26.4, 26.3, 25.7, 23.0, 14.4 ppm; elemental analysis (%) calcd for $C_{51}H_{95}N_2O_9P$: C 67.20, H 10.52, N 3.07; found: C 67.47, H 10.19, 3.02; MS (negative-ion mode FAB): m/z: 910 $[M-H]^-$.

Pyridinium {3-[6-(3,4,5-tris-dodecyloxybenzoyloxy)hexyl]ureido}methanesulfonate (5): *tert*-Butyl protected amine **17** (1.0 g, 1.1 mmol) was dissolved in anhydrous CH_2Cl_2 (15 mL) and a solution of HCl in diethyl ether (5 mL, 1 M) was added. The solution was stirred for 1 h at room temperature. The mixture was made strongly alkaline with aqueous NaOH (30 mL, 2 M) and the organic phase was separated. The aqueous phase was extracted with chloroform (2×30 mL), and the combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The crude amine was redissolved in anhydrous chloroform (10 mL) and a solution of di-*tert*-butyl tricarbonate[27] (0.30 g, 1.1 mmol) dissolved in anhydrous chloroform was added. This was stirred at room temperature overnight (a characteristic peak at 2250 cm^{-1} in the IR spectrum of the crude mixture confirmed the presence of an isocyanate). The reaction mixture was concentrated under reduced pressure. The crude isocyanate was redissolved in pyridine (10 mL), and aminomethane sulfonic acid (134 mg, 1.2 mmol) was added to the reaction mixture. This reaction mixture was heated to 60 °C for 36 h. The reaction mixture was concentrated under reduced pressure. The crude product was redissolved in chloroform and filtered. The mother liquor was concentrated under reduced pressure yielding a white solid that was fractionally recrystallized from ethanol to yield **5** as a white solid. Yield 0.70 g, 62%; M.p. 158–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.05 (d, J = 4.9 Hz, 2H), 8.39 (t, J = 7.8 Hz, 1H), 7.94 (t, J = 7.8 Hz, 2H), 7.22 (s, 2H), 4.37 (br s, 2H), 4.23 (t, J = 6.8 Hz, 2H), 3.96–4.02 (m, 8H), 3.09 (t, J = 6.8 Hz, 2H), 1.67–1.84 (m, 8H), 1.41–1.51 (m, 6H), 1.20–1.39 (m, 54H), 0.87 ppm (t, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.7, 159.3, 153.1, 145.7, 142.9, 142.5, 127.2, 125.2, 108.2, 73.7, 69.4, 65.2, 57.7, 40.6, 32.2, 30.6, 30.1, 30.0, 29.95, 29.9, 29.8, 29.7, 29.6 (2×), 28.9, 26.7, 26.4, 26.3, 25.8, 23.0, 14.4 ppm; MS (negative-ion mode FAB): m/z: 910 $[M-\text{pyridinium}]^-$; elemental analysis (%) calcd for $C_{56}H_{99}N_3O_9S$: C 67.89, H 10.09, N 4.24; found: C 67.53, H 9.92, N 3.91.

10-Carboxydecyl 3,4,5-tris-dodecyloxybenzoate (6): LiI (0.57 g, 4.2 mmol, dried in vacuo overnight at 170 °C) was co-evaporated twice with dry pyridine (25 mL). The resulting anhydrous LiI was redissolved in pyridine (25 mL), and ester **21** (0.50 g, 0.57 mmol) was added to the solution. The reaction mixture was heated to reflux for 48 h. After the reaction mixture was cooled to room temperature, water (50 mL) was added and acidification performed with aqueous HCl (4 M). This was extracted with CH_2Cl_2

(3×50 mL) and the combined organic phases were evaporated to dryness in vacuo and purified by dry column vacuum chromatography (heptane to 1:1 heptane/EtOAc with 5% increments) to yield **6** as a white solid. Yield 0.25 g, 51%; m.p. 55–57°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.22 (s, 2H), 4.24 (t, 2H), 3.97 (t, 6H), 2.31 (t, 2H), 1.68–1.78 (m, 8H), 1.58–1.62 (m, 2H), 1.41–1.45 (m, 8H), 1.23–1.40 (m, 58H), 0.83 ppm (t, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=177.5, 166.4, 152.7, 142.3, 124.94, 107.9, 73.4, 69.1, 65.0, 33.5, 31.8, 30.2, 28.6–29.6, 25.9, 24.6, 22.6, 14.0 ppm; MS (negative-ion mode FAB): *m/z*: 857.3 [*M*−H]$^-$; elemental analysis (%) calcd for $C_{54}H_{98}O_7$: C 75.47, H 11.49; found: C 75.37, H 11.69.

3,4,5-Tris-dodecyloxybenzoic acid 10-phosphonodecyl ester (7): Compound **24** (0.923 g, 1.0 mmol) and NaI (0.30 g, 2.0 mmol) was suspended in CH_3CN (10 mL) and TMSCl (0.25 mL, 1.96 mmol) was added under N_2 at room temperature using a syringe. The reaction mixture was heated to 50°C for 15 min, water (50 mL) was added and the reaction mixture was stirred vigorously for 5 h. The reaction mixture was then extracted with CH_2Cl_2 (3×50 mL) and the combined organic phases dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was recrystallized from acetone to yield a white solid. Yield 0.80 g, 89%; m.p. 62–64°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=10.42 (br s, 2H), 7.24 (s, 2H), 4.27 (t, 2H), 4.00 (t, 8H), 1.75–1.83 (m, 12H), 1.40–1.46 (m, 8H), 1.26–1.35 (m, 56H), 0.87 ppm (t, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 152.7, 142.3, 124.9, 108.0, 73.4, 69.1, 65.0, 31.8, 30.2, 29.6, 29.55, 29.5, 29.4, 29.35, 29.3, 29.2, 29.0, 28.7, 26.1, 26.0, 25.9, 22.6, 14.0 ppm; MS (negative-ion mode FAB): *m/z*: 893.6 [*M*−H]$^-$; elemental analysis (%) calcd for $C_{53}H_{99}O_8P$: C 71.10, H 11.15; found: C 70.81, H 11.22.

Pyridinium 10-(3,4,5-tris-dodecyloxybenzoyloxy)-decane-1-sulfonate (8): Carboxylic acid **15** (1.40 g, 2.07 mmol) and TFFH[50] (0.55 g, 2.07 mmol) were suspended in CH_2Cl_2 (50 mL), and Et_3N (1.44 mL, 10.3 mmol) was added using a syringe. The reaction mixture was stirred for 30 min and then alcohol **25** (0.50 g, 2.10 mmol) and DMAP (50 mg) was added. The reaction mixture was stirred overnight and was then evaporated to dryness in vacuo. Water (50 mL) was added and acidified by addition of concentrated HCl, and the mixture was then extracted with CH_2Cl_2 (3×60 mL). The combined organic phases were evaporated to dryness and recrystallized from acetone. This yielded the free sulfonic acid, which was converted to the corresponding pyridinium salt by dissolving it in pyridine (25 mL) and evaporating to dryness in vacuo. The resulting oil was crystallized from acetone to yield **8** as a white solid. Yield 1.72 g, 85%; m.p. 49–52°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.88–8.92 (m, 1H), 8.38–8.42 (m, 1H), 8.18–8.22 (m, 1H), 7.94–7.97 (m, 1H), 7.24 (br s, 2H), 6.63–6.68 (m, 1H), 4.21 (t, 2H), 3.98 (t, 6H), 3.16 (br s, 1H), 3.05–3.10 (m, 2H), 2.95 (t, 2H), 1.67–1.80 (m, 10H), 1.20–1.35 (m, 64H), 0.85 ppm (t, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.1, 153.0, 142.6, 140.1, 127.2, 125.6, 108.4, 106.8, 73.8, 69.5, 65.3, 52.0, 46.3, 40.4, 32.2, 30.5, 29.5–30.0, 29.0, 28.9, 26.5, 25.0, 23.0, 14.7 ppm; MS (negative-ion mode FAB): *m/z*: 894.4 [*M*−HPy]$^-$; elemental analysis (%) calcd for $C_{58}H_{103}NO_8S$: C 71.48, H 10.65, N 1.44; found: C 71.67, H 10.74, N 1.45.

***tert*-Butyl {2-[Anthracen-9-ylmethyl-(2-*tert*-butoxycarbonylaminoethyl)-amino]ethyl}carbamate (11)**: 9-(Chloromethyl)-anthracene (0.50 g, 2.21 mmol), boc-protected triamine **9**[24] (0.74 g, 2.43 mmol), KI (0.37 g, 2.21 mmol), and K_2CO_3 (0.31 g, 2.21 mmol) was suspended in dry DMF (25 mL) and stirred overnight at room temperature under N_2. Water (40 mL) was added and the mixture was extracted with CH_2Cl_2 (2×50 mL). The combined organic layers were evaporated to dryness and purified by dry column vacuum chromatography (heptane to 1:1 EtOAc/heptane with 5% increments) to yield **11** as a pale yellow solid. Yield 0.81 g, 75%; m.p. 138–140°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.31–8.36 (m, 3H), 7.92–7.95 (m, 2H), 7.36–7.49 (m, 4H), 4.55 (br s, 1H), 4.50 (s, 2H), 3.01–3.09 (m, 2H), 2.56–2.63 (m, 2H), 1.29 ppm (br s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=155.8, 131.3, 131.0, 129.3, 129.1, 127.7, 125.9, 124.8, 124.3, 78.8, 53.4, 51.1, 38.3, 28.3 ppm; MS (positive-ion mode FAB): *m/z*: 494.7 [*M*+H]$^+$; elemental analysis (%) calcd for $C_{29}H_{39}N_3O_4$: C 70.56, H 7.96, N 8.51; found: C 70.40, H 8.13, N 8.46.

***tert*-Butyl {3-[Anthracen-9-ylmethyl-(3-*tert*-butoxycarbonylaminopropyl)amino]propyl}carbamate (12)**: 9-(Chloromethyl)-anthracene (0.50 g, 2.21 mmol), boc-protected triamine **10**[24] (0.804 g, 2.43 mmol), K_2CO_3 (0.31 g, 2.21 mmol) and KI (0.367 g, 2.21 mmol) was suspended in dry DMF (15 mL) under N_2. The reaction mixture was stirred overnight at room temperature. Water (40 mL) was added and the reaction mixture was extracted with CH_2Cl_2 (2×50 mL). The combined organic phases were evaporated to dryness and purified by dry column vacuum chromatography (heptane to 50% EtOAc in heptane with 5% increments) to yield **12** as a pale yellow solid. Yield 0.782 g, 68%; m.p, 113–115°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.38–8.44 (m, 3H), 7.98–8.02 (m, 2H), 7.40–7.44 (m, 4H), 4.63 (br s, 2H), 4.48 (s, 2H), 2.94–2.97 (m, 4H), 2.56–2.60 (m, 4H), 1.63 (t, 4H), 1.40 ppm (br s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=156.3, 134.3, 131.6, 131.5, 129.4, 127.4, 126.2, 125.2, 124.9, 79.0, 51.6, 51.5, 39.1, 28.6, 27.2 ppm; MS (positive-ion mode FAB): *m/z*: 522.5 [*M*+H]$^+$; elemental analysis (%) calcd for $C_{31}H_{43}N_3O_4$: C 71.37, H 8.31, N 8.05; found: C 71.42, H 8.51, N 7.70.

6-*tert*-Butoxycarbonylaminohexyl 3,4,5-tris-dodecyloxybenzoate (17): *tert*-Butyl (6-hydroxyhexyl)carbamate[26] (5.0 g, 23.0 mmol), 3,4,5-tridodecyloxybenzoic acid **15**[29] (15.5 g, 23.0 mmol), and DMAP (1.0 g, 8.2 mmol) were dissolved in anhydrous chloroform (250 mL). DCC (5.0 g, 24.2 mmol) was added and the reaction mixture was stirred for three days at room temperature. TLC (dichloromethane, R_f=0.3) showed the formation of a new adduct that was both UV and ninhydrin active. Dicyclohexylurea (DCU) was removed by filtration, and the mixture was concentrated in vacuo. The product was purified by column chromatography (Silica Gel) using dichloromethane as eluent; yield 13.5 g (67%) of a white solid. M.p. 44–45°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.24 (s, 2H), 4.51 (br s, 1H), 4.28 (t, *J*=6.6 Hz, 2H), 4.01 (t, *J*=5.9 Hz, 6H), 3.11 (m, 2H), 1.70–1.85 (m, 8H), 1.44 (s, 9H), 1.24–1.27 (m, 60H), 0.88 ppm (t, *J*=6.6 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 166.7, 156.2, 153.0, 142.6, 125.2, 108.2, 73.7, 69.4, 65.2, 40.7, 32.2, 30.6, 30.2, 30.0, 29.9, 29.85, 29.8, 29.65, 29.6, 29.55, 28.9, 28.6, 26.7, 26.35, 26.3, 25.9, 22.9, 14.3 ppm; MS (positive-ion mode FAB): *m/z*: 874 [*M*+H]$^+$; elemental analysis (%) calcd for $C_{54}H_{99}NO_7$: C 74.16, H 11.43, N 1.60; found: C 74.51, H 11.09, N 1.68.

6-[3-(Di-*tert*-butoxyphosphorylmethyl)ureido]hexyl 3,4,5-tris-dodecyloxybenzoate (19): To a solution of crude isocyanate **18**, prepared from compound **17** (1.0 g, 1.1 mmol) as described for compound **5**, was added a solution of di-*tert*-butyl aminomethylphosphonate[50] (0.3 g, 1.3 mmol) in chloroform (5 mL). After 1 h the isocyanate peak in the IR spectrum had disappeared. The reaction mixture was concentrated in vacuo and the crude product was purified by column chromatography (silica gel) using ethyl acetate as eluent. The product **19** (R_f=0.5) was isolated as a white solid; yield 0.552 g (49%); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.23 (s, 2H), 5.50 (m, 1H), 5.45 (m, 1H), 4.27 (t, *J*=6.6 Hz, 2H), 4.00 (t, *J*=6.6 Hz, 6H), 3.51 (dd, *J*=5.9 Hz and *J*(H,P)=11.7 Hz, 2H), 3.16 (m, 2H), 1.68–1.84 (m, 8H), 1.41–1.52 (m, 8H), 1.21–1.37 (m, 70H), 0.88 ppm (t, *J*=7.3 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=166.7, 158.5, 153.0, 142.7, 125.2, 108.2, 73.7, 69.5, 65.2, 53.6, 40.5, 38.8, 32.2, 31.2, 30.7, 30.6, 30.55, 29.95, 29.90, 29.85, 29.80, 29.65, 29.60, 29.55, 26.8, 26.3, 26.2, 25.9, 22.9, 14.4 ppm; elemental analysis (%) calcd for $C_{59}H_{111}N_2O_9P$: C 69.22, H 10.95, N 2.74; found: C 68.87, H 10.66, N 2.67.

10-Methoxycarbonyldecyl 3,4,5-tris-dodecyloxybenzoate (21): Carboxylic acid **15**[29] (2.08 g, 3.08 mmol), methyl 11-bromoundecanoate (**20**)[28] (0.860 g, 3.08 mmol) and K_2CO_3 (0.47 g, 3.4 mmol) was suspended in DMF (50 mL) and heated to 100°C for 18 h. After cooling the reaction mixture to room temperature, it was poured into ice water (100 mL). This was extracted with petroleum ether (b.p.<50°C, 2×50 mL), dried over Na_2SO_4 and evaporated to dryness yielding a white solid material. Recrystallization from acetone yields the title compound as a white crystalline material. Yield 2.67 g, 99%; m.p. 42–43°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.20 (s, 2H), 4.25 (t, 2H), 3.95 (t, 6H), 3.62 (s, 3H), 2.25 (t, 2H), 1.68–1.76 (m, 8H), 1.58–1.62 (m, 2H), 1.41–1.46 (m, 8H), 1.23–1.40 (m, 58H), 0.88 ppm (t, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=174.1, 166.4, 152.6, 142.2, 124.9, 107.9, 73.4, 69.1, 65.1, 54.3, 34.0, 31.8, 30.2, 29.0–29.6, 28.6, 26.0, 25.9, 24.8, 22.6, 14.0 ppm; MS (positive-ion mode FAB): *m/z*: 872.8 [*M*+H]$^+$; elemental analysis (%) calcd for $C_{54}H_{98}O_7$: C 75.64, H 11.54; found: C 75.40, H 11.56.

10-Bromodecyl 3,4,5-tris-dodecyloxybenzoate (23): Carboxylic acid **15**[29] (27.04 g, 40.05 mmol) and TFFH[50] (11.64 g, 40.06 mmol) was dissolved in CH_2Cl_2 (300 mL) and Et_3N (12.16 g, 16.70 mL, 120.2 mmol) was added by

using a syringe to the stirring solution under N_2. The reaction mixture was stirred for 30 minutes and then 10-bromo-1-decanol (11.40 g, 48.06 mmol) was added followed by DMAP (10%, 0.48 g, 4 mmol). The reaction mixture was stirred overnight, and water (400 mL) was added. The phases were separated and the organic phase was dried (Na_2SO_4), filtered, and evaporated to dryness. The product was purified by filtering through a plug of silica with CH_2Cl_2 as eluent. Yield 32.2 g, 90%; m.p. 34–35 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.24$ (s, 2H), 4.28 (t, 2H), 4.01 (t, 6H), 3.40 (t, 2H), 1.70–1.90 (m, 10H), 1.45–1.50 (m, 10H), 1.26–1.30 (m, 56H), 0.88 ppm (t, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 166.4$, 152.7, 142.3, 125.0, 107.9, 73.4, 69.1, 65.0, 33.9, 32.7, 31.8, 30.2, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 28.6, 28.0, 26.0, 25.9, 22.6, 14.0 ppm; MS (DI): m/z: 893.5 ($[M]^+$); elemental analysis (%) calcd for $C_{53}H_{97}BrO_5$: C 71.19, H 10.93; found: C 70.88, H 11.03.

10-(Dimethoxyphosphoryl)decyl 3,4,5-tris-dodecyloxybenzoate (24): Bromide **23** (5.0 g, 5.59 mmol) was dissolved in $P(OMe)_3$ (10 mL) in a round bottomed flask fitted with a Claisen-type condenser and heated to 110 °C for three days. All volatiles were evaporated in vacuo and the product purified by dry column vacuum chromatography (heptane to EtOAc with 5% increments). Yield 3.10 g, 60% as a white solid material. M.p. 34–35 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.23$ (s, 2H), 4.20 (t, 2H), 3.95 (m, 8H), 3.38 (d, 6H), 1.63–1.75 (m, 12H), 1.38–1.43 (m, 8H), 1.20–1.30 (m, 56H), 0.82 ppm (t, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 166.4$, 152.7, 142.3, 124.9, 108.0, 74.0, 69.0, 65.0, 52.2, 31.8, 30.2, 29.6, 29.55, 29.5, 29.4, 29.2, 29.1, 29.0, 28.7, 28.5, 26.1, 26.0, 25.9, 22.6, 14.0 ppm; MS (positive-ion mode FAB): m/z: 923.8 $[M+H]^+$; elemental analysis (%) calcd for $C_{55}H_{103}O_8P$: C 71.54, H 11.24; found: C 71.21, H 11.35.

10-Hydroxydecane-1-sulfonic acid (25): 10-Bromo-1-decanol[33] (2.25 g, 9.49 mmol) was dissolved in EtOH (96%, 40 mL) and a solution of Na_2SO_3 (1.79 g, 14.2 mmol) in water (10 mL) was added. This mixture was refluxed for three days. The clear solution was concentrated in vacuo to yield a white solid material that was redissolved in 2 M HCl (40 mL) and evaporated to dryness in vacuo. The resulting white solid material was extracted with hot EtOH, evaporated to dryness and the residue recrystallized from EtOH. Yield 1.47 g, 75%. M.p. 230–232 °C; ^{1}H NMR (400 MHz, D_2O): $\delta = 3.50$ (t, 2H), 2.81 (t, 2H), 1.64 (m, 2H), 1.45 (m, 2H), 1.22–1.32 ppm (m, 12H); ^{13}C NMR (100 MHz, D_2O): $\delta = 61.6$, 50.8, 31.0, 28.3, 28.2, 27.9, 27.4, 24.7, 23.7 ppm; MS (negative-ion mode FAB): m/z: 237.2 $[M-H]^-$.

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