Self-assembly of an aminoalkylated resorcinarene in aqueous media: host–guest properties†

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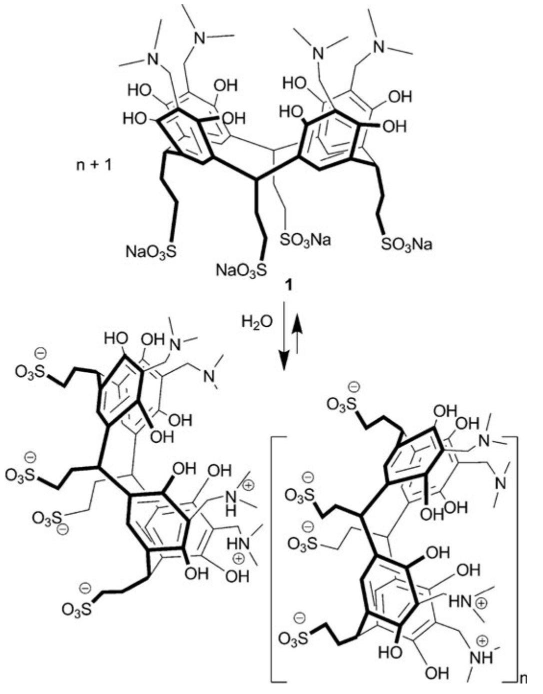
A new water-soluble resorcinarene, with a negatively-charged lower rim and a positively-charged upper rim self-assembles into supramolecular oligomers to bind 1,5-diaminonaphthalene in water.

Recently, dynamic supramolecular assemblies have been of great interest because of their potential application in the construction of new nanoscale materials.[1] A number of dynamic supramolecular systems stabilized by metal–ligand coordination bonds,[2] hydrogen binding,[3] hydrophobic interactions and host–guest complexation[4,5] have been reported over the past decade. Molecules containing both host and guest groups have been employed for the production of self-assembled systems, formed by intermolecular guest–host complexation.[4a–g,5b–d] For example, the pH-controlled aggregation of calixarene with a terminal alkylamino group has been reported.[5b] The host–guest properties of tetraphosphonate cavitands have been effectively employed for the construction of guest-dependent linear or star-branched supramolecular polymers.[5d] Earlier, Mannich base resorcinarenes with *O*-propyl and *O*-butylphosphonatomethylene moieties on the lower rim were shown to produce pH-controlled supramolecular oligomers in aqueous media.[6] By extending this work, we designed a new derivative of resorcinarene, **1**, with sodium sulfonatoethylene groups on the lower rim and aminoalkylated moieties on the upper rim, and have investigated its ability to self-assemble in aqueous media.

Resorcinarene **1** was obtained from sodium sulfonatoethylene resorcinarene[7] by a Mannich reaction with *N*,*N*,*N*′,*N*′-tetramethyldiaminomethane (see the ESI†). In aqueous media, the presence of charged sulfonate groups leads to the formation of a negatively-charged lower rim, giving $\mathbf{1}^{4-}$. The protonation of the amino groups of the upper rim of **1** produces a positively-charged upper rim, the interaction of which with the negatively-charged lower rim generating tail-to-head ensembles (Scheme 1). In this Letter, we report the synthesis of new supramolecular oligomers based on resorcinarene **1** and their host–guest properties towards aromatic amines. 1,5-Diaminonaphthalene (DAN) was chosen as a guest molecule because of its ability to enter the resorcinarene cavity in neutral aqueous media and the potential capacity of its protonated form to interact with the lower rim of **1** in acidic media.

The acid–base properties of **1** were studied using spectrophotometric techniques. The UV spectra of **1** reveal a characteristic absorption band at 287–310 nm at pH 1–9 in aqueous media. The absorption maximum is at 287 nm in acidic media (pH 1–2) and is shifted bathochromically by about 20 nm in basic media (pH 7–8) (see the ESI†). A mathematical treatment of the spectrophotometric data of fully protonated $\mathbf{1}^{4-}\cdot 4H^+$ results in pK_a values for the stepwise dissociation of the $(NMe_2H)^+$ groups.[8] The determined pK_a values for **1** are significantly increased as the concentration of **1** is increased (Table 1). For instance, the pK_a value of the deprotonation of the first $(NMe_2H)^+$ group at a concentration of 0.1 mM is about two times less than that at a concentration of 0.25 mM. The third $(NMe_2H)^+$ group deprotonates with almost identical pK_a values. The change in acid–base properties at different concentrations may be induced by the electrostatic



Scheme 1 The self-assembly of **1** in water.

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interaction between the ammonium groups of the upper rim and the sulfonate groups of the lower rim. According to the distribution diagram (Fig. 1), resorcinarene **1** exists in mono- and double-protonated forms in neutral media at a concentration of 0.25 mM. Thus, even in neutral media, the upper rim of **1** is positively-charged and must interact with the sulfonate groups of the lower rim in order to give associates. Indeed, in the UV spectrum of **1**, an increase in concentration at pH 2, 4 and 7 leads to a bathochromic shift of the absorption maximum, indicating the formation of aggregates. Besides, the absence of a linear relationship between concentration and absorbance (the Beer–Lambert law) is observed at 287–300 nm, suggesting the formation of supramolecular polymers, both in acidic and neutral media (Fig. 2). Due to the fact that the driving force behind the association is an electrostatic interaction, the increase of concentration does not lead to a significant shift of the proton signals of **1** in its ^{1}H NMR spectrum. Therefore, NMR diffusivity measurements were carried out at different concentrations (Fig. 3). As the concentration of **1** is increased at pH 4 and 7, the diffusion coefficient (D) decreases, indicating that the size of the associates formed by **1** increases. At pH 4, the aggregates are larger than those at pH 7 due to the additional positive charge on the upper rim of **1**. It was impossible to measure D at pHs below 4 because of the low solubility of **1** in acidic media. The limit of solubility concentration of **1** at pH 2 is only 2 mM, but the coagulation of **1** is observed at even lower concentrations. In acidic media, the negative charge of the lower rim is possibly fully compensated by the positive charge of the upper rim, leading to the formation of linear polymers with an uncharged surface. These polymers are unstable in aqueous media and precipitate from it.

Further evidence of the formation of aggregates of **1** was provided by dynamic light scattering (DLS) measurements in water at pH 7 (Fig. 4). In number distribution, an aqueous solution of **1** showed a peak centered at around 21 nm at a concentration of 1 mM. At a concentration of 5 mM, the average size of the particles increased up to 90 nm. Following increases in concentration did not result in significant changes to the average size distribution. The volume distribution indicates the presence of various aggregates with hydrodynamic diameters of about 25, 120 and 220 nm. The number of larger oligomers increases with increasing concentration of **1**. Thus, the NMR diffusivity and DLS data indicate that **1** forms supramolecular aggregates in water. It is difficult to estimate the sizes and molecular weights of the aggregates of **1** obtained from the DLS and NMR measurements. The sizes calculated from the diffusional properties are the sizes of the dynamic solvated aggregates. Moreover, the exchange between associated and free resorcinarene **1** is fast on the NMR timescale, therefore the weighted-average D is observed.

Table 1 The determined pK_{an} values for the stepwise deprotonation of **1**·4HCl in aqueous media

C/mM	pK_{a1}	pK_{a2}	pK_{a3}	pK_{a4}
0.1	1.9 ± 0.3	4.6 ± 0.2	6.8 ± 0.2	9.8 ± 0.3
0.25	3.5 ± 0.1	5.7 ± 0.2	7.4 ± 0.3	11.7 ± 0.3

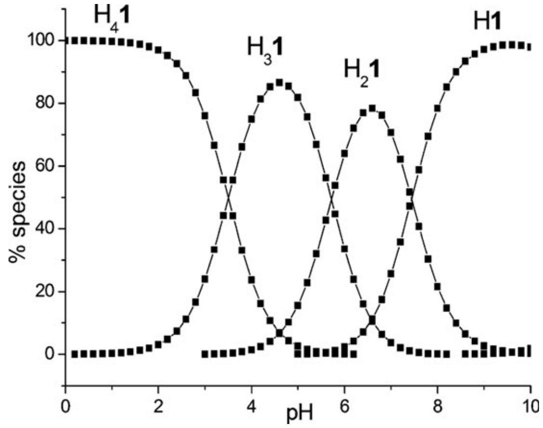


Fig. 1 Distribution diagram of the protonated species of **1** as a function of pH.

Static light scattering (SLS) measurements were carried out for the estimation of the average molecular weight (M_w) of the aggregates of **1** at different concentrations in water (pH 7) (Fig. 5). M_w significantly increased as the concentration increased from 1 to 6 mM. In the concentration range from 6 to 10 mM, the M_w slightly increased up to 9700 g mol^{-1}, which corresponds to about 8 associated units of **1**. Thus, the UV, NMR, DLS and SLS data show that resorcinarene **1** self-assembles in aqueous media as a result of tail-to-head interactions of the positively-charged ammonium groups of the upper rim and negatively-charged sulfonate groups of the lower rim.

In neutral media, **1** may bind the aromatic guest DAN, both by its positively-charged upper rim and negatively-charged lower rim. In acidic media, DAN exists in its doubly-deprotonated, positively-charged form, and therefore may be bound only by the negatively-charged lower rim of **1**. The NMR data show that the treatment of DAN with one equivalent of **1** in D_2O (pD 7) results in an upfield shift and broadening of its signals in the ^{1}H NMR spectrum. This result indicates the complexation of DAN inside the cavity of **1**. The Job titration curve for the DAN proton signals reaches its maximum at 0.5 on the abscissa axis ($C_{DAN}/(C_1 + C_{DAN})$), confirming the 1 : 1 complex formation between DAN and **1** (see the ESI†). The addition of an equivalent amount of DAN to a solution of **1** at pD 7 does not lead to significant changes in the D values of **1**. Thus, DAN does not destroy the supramolecular ensembles of **1** (Fig. 3(b)). However, the D of DAN decreases from 7.2 × 10^{-10} to 6.0 × 10^{-10} m^2 s^{-1} with the addition of one equivalent of **1**, confirming the formation of a host–guest complex between DAN and **1**.‡ According to the DLS data (Fig. 4), the addition of 5 mM of DAN to a 5 mM aqueous solution of **1** (pH 7) does not lead to the destruction of the associates of **1**. On the contrary, the size of the associates increases from 90 to 120 nm, which proves the formation more bulky associates in the presence of DAN. From the results of the SLS measurements (Fig. 5), the M_w of the aggregates formed by mixing **1** and DAN is significantly higher than that obtained from **1** itself. The M_w of the aggregates obtained from the mixture of **1** and DAN increases with concentration in the range 1–8 mM and reaches

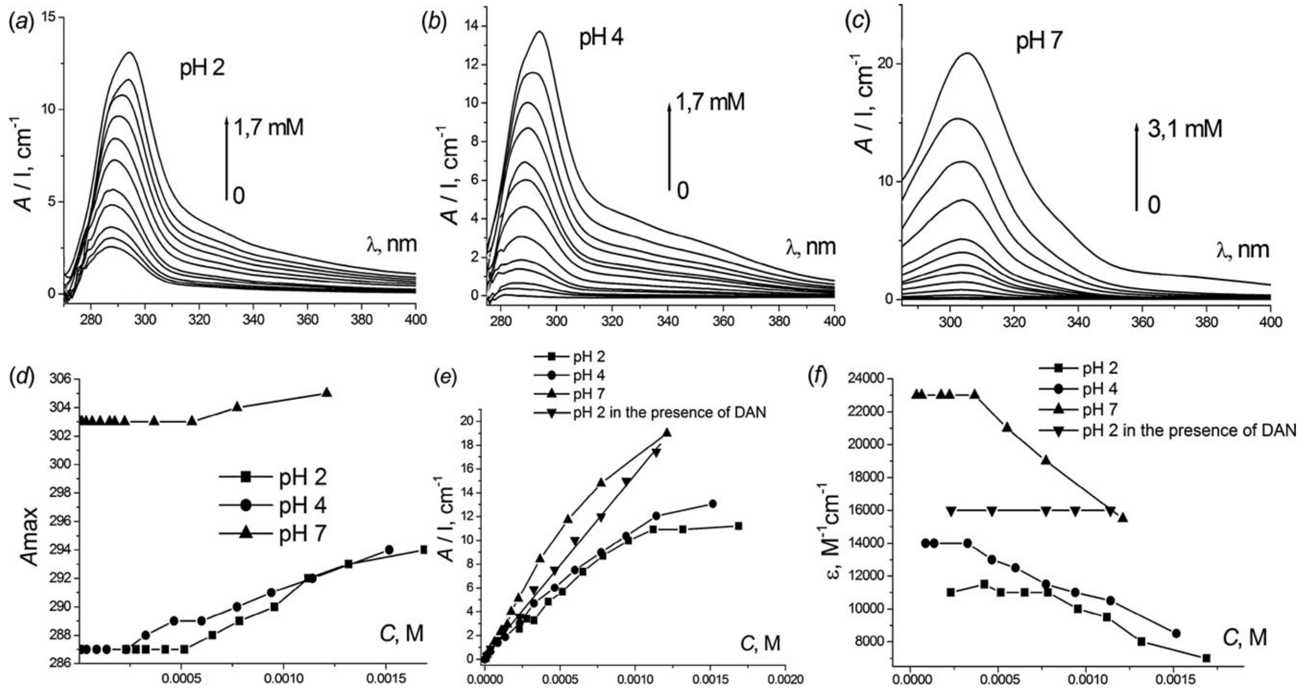


Fig. 2 (a–c) Absorption spectral changes of **1** with increasing concentration at pH 2, 4 and 7. (d) Plots of the concentration-induced shift of the absorption maximum of **1** as a function of concentration at pH 2, 4 and 7. (e) Absorption intensity as a function of the concentration of **1**. (f) The molar extinction coefficient as a function of the concentration of **1** (l = 0.2 cm cell).

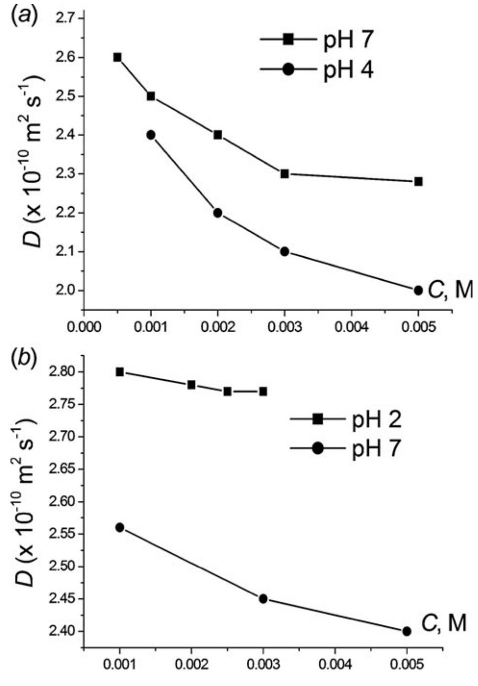


Fig. 3 Plots of the self-diffusion coefficients (D) of (a) **1** and (b) a **1** + DAN mixture obtained by pulsed-field-gradient (PFG) NMR measurements as a function of concentration.

16 000 g mol^{-1}. This approximately corresponds to 12 associated units of a **1** + DAN mixture. Thus, the NMR, DLS and SLS data demonstrate that supramolecular associates formed from **1** bind DAN by the upper rim, forming two-component supramolecular polymers (Scheme 2).

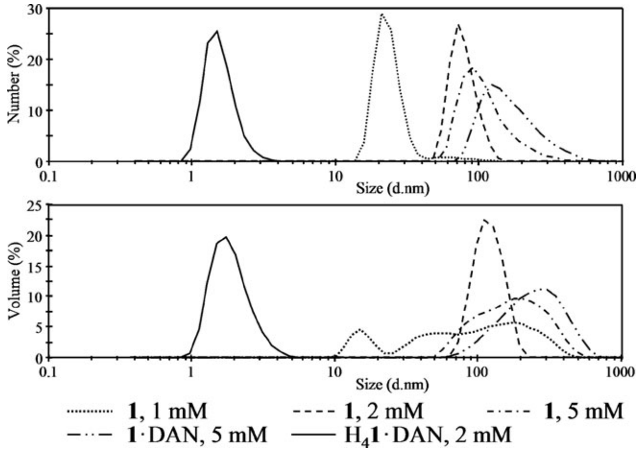


Fig. 4 DLS results for **1** in water in the presence and absence of DAN.

Acidification of a **1** + DAN mixture in water must result in the displacement of the protonated, positively-charged DAN from the positively-charged upper rim of **1** to the negatively-charged lower rim. Indeed, acidification of a D_2O solution of **1** and DAN up to pD 2 results in a downfield shift of the proton signals of the guest and an upfield shift of signals of aromatic protons of **1**. This indicates the formation of a host–guest complex between DAN and the lower rim of **1**. According to the Job titration data, the protonated DAN forms a stable 1 : 1 host–guest complex with **1** (see the ESI†). Increasing the concentration of **1** up to 2 mM in the presence of 4 mM of DAN does not lead to a shift of the absorbance maximum in UV spectra at pH 2, which indicates the lack of aggregate

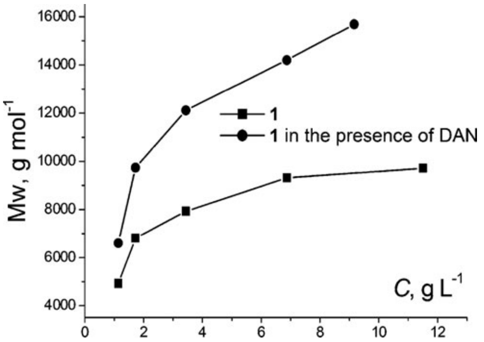
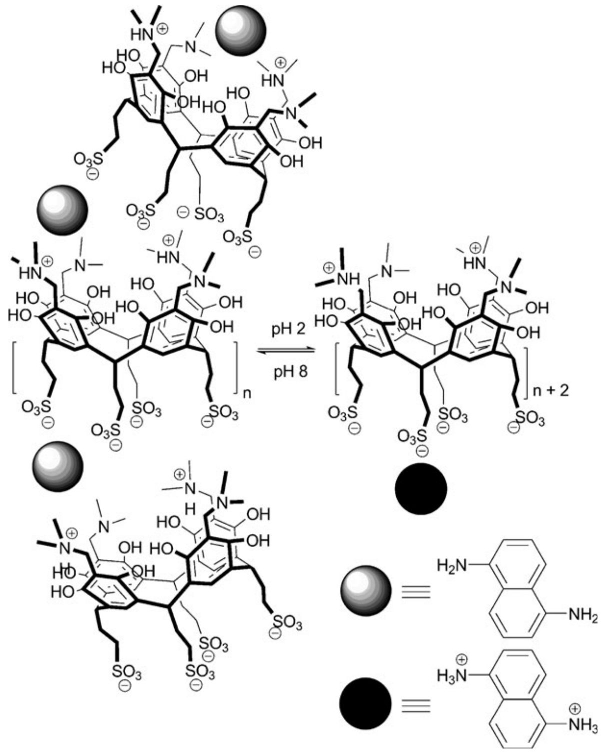


Fig. 5 The concentration dependant molecular weight of aggregates of **1** in the presence and absence of DAN, as observed by SLS measurements.



Scheme 2 pH-controlled assembly/disassembly of **1** in the presence of DAN.

formation of **1** in the presence of DAN in acidic media. Moreover, a linear relationship between concentration and absorbance in the 290–310 nm range confirms the disassembly of **1** by DAN (Fig. 2). The DLS data prove the destruction of the associates of **1** in the presence of DAN in acidic media. In both number and volume distribution diagrams, only a peak around 1.5 nm is observed at pH 2 (Fig. 4); it corresponds to a host–guest complex between protonated **1** and protonated DAN. According to the PFG NMR data, the *D* of the mixture of **1** and DAN in acidic media is higher than that at pD 7, and slightly decreases with increasing concentration of **1**, which indicates the formation of host–guest complexes or small assemblies in acidic media (Fig. 3). Thus, the UV, NMR and DLS data show that acidification of the assemblies between **1** and DAN up to pH 2 results in their destruction and the formation of a host–guest complex between protonated **1** and DAN (Scheme 2).

In conclusion, the self-assembly of **1** in aqueous solution, with the formation of head-to-tail supramolecular oligomers, was shown to bind DAN inside its cavity. In the absence of DAN, a decrease of pH lead to the formation of supramolecular polymers that were insoluble in water. In the presence of DAN, acidification of the aqueous medium destroyed the supramolecular associates and formed a host–guest complex between the protonated DAN and the negatively-charged lower rim of **1**.

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Notes and references

‡ The observed *D* results from the fast exchange between free and complexed DAN. The *D* of DAN in the system DAN + **1** is larger than the *D* of **1**, but less than that of free DAN. It indicates that only a fraction of DAN is complexed in aggregates with **1**.[9]

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