Acid-Functionalized Amphiphiles Derived from Polystyrene–Poly(propylene imine) Dendrimers, with a pH-Dependent Aggregation

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The research interest in the area of dendrimers has shifted from the design of new synthetic routes of these well-defined, highly branched macromolecules to their use as building blocks for new functional materials.[1] Recent examples are hybrid block copolymers,[2] new catalytic systems,[3] liquid crystalline dendrimers,[4] unimolecular micelles,[5] hydraamphiphiles,[6] and the dendritic box.[7] We have used the unique hydrophilic character of the poly(propylene imine) dendrimers in the preparation of a new class of amphiphilic block copolymers.[8] These structures, prepared by a divergent dendrimer synthesis onto a primary amine functionalized polystyrene core molecule of $M_n = 3.2 \times 10^3$, possess the size of traditional block copolymers but the shape of low molecular weight amphiphiles. A remarkable generation-dependent aggregation behavior was observed for these new amphiphiles, that qualitatively followed Israelachvili's theory of the relationship between molecular shape and amphiphile aggregation.

The versatility of these amphiphiles, however, is based not only on the ability of variation of head-group size by using different generations of the dendrimer part but also on the possibility of dendrimer modification. Extensive studies on the traditional poly(propylene imines) have provided us with a number of quantitative modification reactions.[9] We report our recent results on acid-functionalized surfactants (PS-*dendr*-(COOH)$_n$) (Figure 1) that contribute to the interesting area of the amphiphilic dendrimers.[2,5,6,8,10] Newkome et al.[11] have already shown the effect of pH on the radii of end-group acid-functionalized unimolecular micelles. Our structures have both carboxylic acid end groups and tertiary amines in the dendritic head group. This can give rise to a pH-dependent behavior, of which the change in amphiphilicity has our special interest.

The PS-*dendr*-(COOH)$_n$ (n = 2, 4, 8, 16, 32) series were synthesized by acid hydrolysis of the corresponding nitrile-functionalized structures (Scheme 1 and Table 1) based on a modification of the procedure developed for the traditional poly(propylene imines).[9]

However, due to the amphiphilic character of our structures, the reaction had to be performed in a toluene-concentrated hydrochloric acid (1:1 by volume) mixture to allow reaction to take place at the interface. PS-*dendr*-COOH could not be prepared from the corresponding nitrile, probably due to the lack of amphiphilic character.

The amphiphiles were obtained after workup in their protonated form as HCl salt. Characterization of the amphiphilic structures proved to be possible with IR, ^{1}H-NMR, and ^{13}C-NMR (DMSO-d_6) spectroscopy.[12] The latter technique also demonstrated the development of amphiphilic behavior as a function of dendrimer generation (Table 1). In CDCl$_3$ only the polystyrene part of PS-*dendr*-(COOH)$_n$ with n = 4–16 was discernible, thereby indicating inverted micellar behavior. The higher generations PS-*dendr*-(COOH)$_n$ with n = 8–32 could easily be dissolved in D$_2$O at high pH. In this solvent only the dendrimer block was visible using ^{13}C-NMR spectroscopy. The polystyrene block was confined inside the aggregates in this solvent and therefore long relaxation times resulted in broad peaks, which made it impossible to identify this part of the amphiphile. This NMR behavior has, for example, also been reported by Gitsov et al. for their hybrid dendrimer–PEG block copolymers.[13]
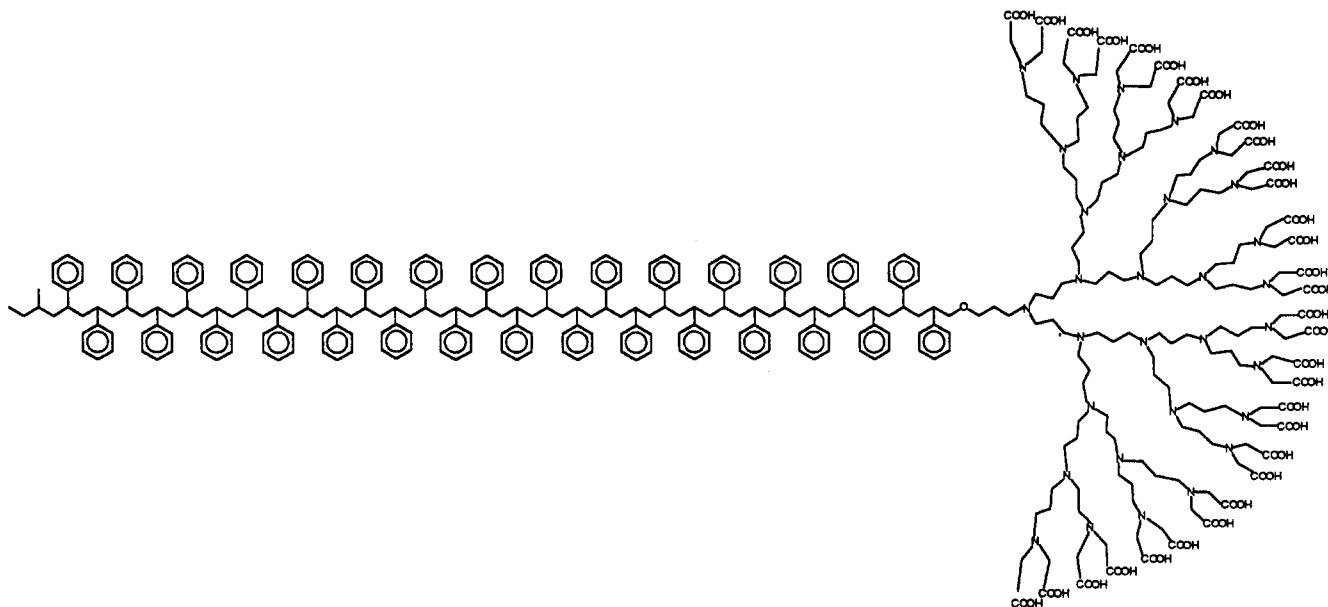

Figure 1. PS-*dendr*-(COOH)$_{32}$. The nomenclature of the poly(propylene imine) dendrimers is as follows: "PS" stands for polystyrene as the core molecule, in this case a PS chain is used with $M_n = 3.2 \times 10^3$ and $M_w/M_n = 1.05$, "(COOH)$_{32}$" describes the number and type of dendrimer end groups. PS-*dendr*-(COOH)$_{32}$ contains a dendrimer of the fifth generation. The term generation refers to the reaction sequence in the dendrimer synthesis. After every sequence the number of end groups is doubled and a new generation is obtained.

Scheme 1. Modification of Nitrile-Functionalized Dendrimers toward Acid Functionalized Structures

PS-*dendr*-CN$_n$ $\xrightarrow[\text{24 h/ RT}]{\text{HCl}}$ PS-*dendr*-(CONH$_2$)$_n$ $\xrightarrow[\text{reflux}]{\text{H}_2\text{O}}$ PS-*dendr*-(COOH)$_n$

Table 1. PS-*dendr*-(COOH)$_n$[a]

product	yield (%)	CDCl$_3$	DMSO-d_6	D$_2$O/NaOD
PS-*dendr*-(COOH)$_2$	95	+	+	−
PS-*dendr*-(COOH)$_4$	93	p	+	−
PS-*dendr*-(COOH)$_8$	85	p	+	d
PS-*dendr*-(COOH)$_{16}$	98	p	+	d
PS-*dendr*-(COOH)$_{32}$	94	−	+	d

[a] Yields after workup of PS-*dendr*-(COOH)$_n$ and characterization with ^{13}C-NMR in different deuterated solvents; +, full characterization, p, only polystyrene-block visible; d, only dendrimer-block visible, −, no characterization possible.

To investigate the influence of head-group modification on the amphiphilic character of the block copolymers, conductivity measurements were used to study their behavior at the interface of a toluene/water system.[14] The results are depicted in Figure 2.

The point of phase inversion from water to toluene as a continuous phase is indicated by a conductivity drop to zero. The change of position of this inversion point as a function of pH and dendrimer generation is a measure for the development of polar and amphiphilic properties of the block copolymers. The behavior of PS-*dendr*-(COOH)$_n$ in a 0.01 M KCl solution is comparable to results of earlier measurements of PS-*dendr*-(NH$_2$)$_n$.[8] The apolar PS chain is the dominant block for the low-generation PS-*dendr*-(COOH)$_n$ with n = 2–8. Therefore, there is a strong preference for these structures to stabilize toluene as a continuous phase. For PS-*dendr*-(COOH)$_{16}$ a balance is obtained between the apolar and polar part of the amphiphile, resulting in a strongly increased phase inversion point. This structure is equally capable of stabilizing toluene as water as a dispersing phase. At low and high pH, PS-*dendr*-(COOH)$_n$ with n = 2–8 show, compared to the KCl system, a much better ability to stabilize water as a continuous phase. At low pH the tertiary amines of PS-*dendr*-(COOH)$_n$ are protonated and a polycationic structure is obtained, at high pH the tertiary amines and carboxylic acid end groups are not protonated, resulting in a negative charge on the dendrimer surface. Both processes result in a net charge and hence follow Newkome's observations for spherical, acid functionalized dendrimers of a sharp increase of dendrimeric diameter due to repulsive interactions.[11] Therefore, the measured behavior is in line with the increased polarity of these structures. Because of the already good water-stabilizing properties of PS-*dendr*-(COOH)$_{16}$, its behavior is less influenced by a change of pH. The remarkable upswing in conductivity of PS-*dendr*-(COOH)$_{16}$ in the KCl solution is accompanied by a strong viscosity increase of the system. The conductivity increase can therefore be explained by the formation of a laminar phase, that allows conductivity paths to sustain.

Finally, transmission electron microscopy (TEM) was used to study aggregates of PS-*dendr*-(COOH)$_n$ with n = 8–32, made of samples from aqueous solutions (pH = 14; 3 × 10^{-4} M). Large network structures were observed due to the clustering of the aggregates. Only in the case of PS-*dendr*-(COOH)$_8$ could the single aggregation structures be identified as curved, "worm-like" micelles (Figure 3). This aggregation form is thought to be in between the structures observed for PS-*dendr*-(NH$_2$)$_8$ and PS-*dendr*-(NH$_2$)$_{16}$,[8] that respec-
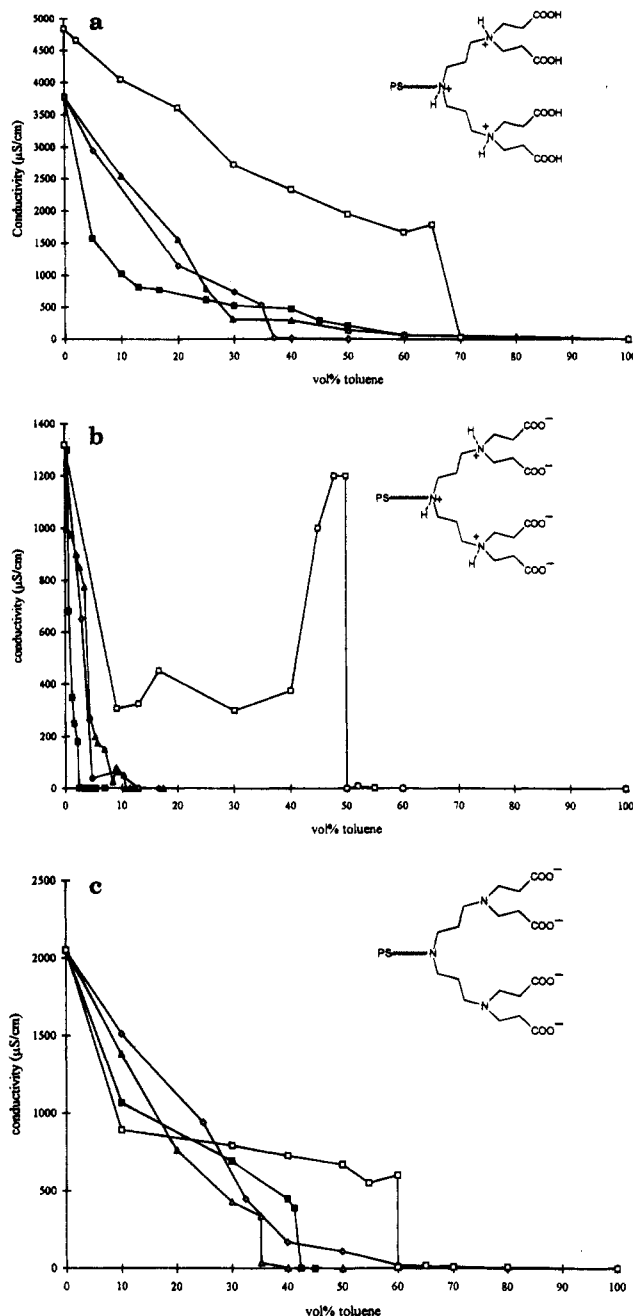
Figure 2. Conductivity measurements of PS-*dendr*-(COOH)$_n$ in toluene/water emulsions at different pH, as a result of different electrolytes used: (a) 0.01 M HCl; (b) 0.01 M KCl; c) 0.01 M KOH. (■) PS-*dendr*-(COOH)$_2$; (△) PS-*dendr*-(COOH)$_4$; (◇) PS-*dendr*-(COOH)$_8$; (□) PS-*dendr*-(COOH)$_{16}$. pH's of PS-*dendr*-(COOH)$_{16}$ in aqueous electrolyte solutions were, in the case of 0.01 M HCl, pH = 1.9, for 0.01 M KCl, pH = 3.5, and for 0.01 M KOH, pH = 9.1.The low pH value at 0.01 M KCl is a result of the fact that PS-*dendr*-(COOH)$_{16}$ is added as the HCl salt in fully protonated form. Because of deprotonation of the carboxylic functions and a H$^+$/K$^+$ exchange, the pH of the solution is lowered.

tively form flexible bilayers and micellar rods. Preliminary results on critical aggregation concentrations (CAC) of PS-*dendr*-(COOH)$_8$, PS-*dendr*-(COOH)$_{16}$, and PS-*dendr*-(COOH)$_{32}$ gave values of 10^{-6}–10^{-7} M and were determined with pyrene fluorescence probe techniques.[15] Maybe the concentrations used for the TEM measurements enforce the observed clustering, however, the problem of extreme clustering of aggregates did not occur for the PS-*dendr*-(NH$_2$)$_n$ series. A stronger electrostatic interaction between the acid-functionalized

500 nm

Figure 3. TEM picture of PS-*dendr*-(COOH)$_8$, prepared by a Pt-shadowing technique. The used enlargement was 23 000×.

dendrimer head groups, therefore, also has to be taken into account.

In conclusion, we have shown that head-group modification of amphiphilic polystyrene–poly(propylene imine) dendrimers is possible and that pH-dependent amphiphilic behavior can be observed. The versatility of the dendrimer provides us with a new class of amphiphilic block copolymers of which the properties can be varied by changing both head-group size and polarity.

References and Notes

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(12) Characterization of PS-*dendr*-(COOH)$_{32}$: ^{13}C-NMR (DMSO-d_6) δ 17.8 (30 C, NCH$_2$CH$_2$CH$_2$N), 28.6 (32 C, NCH$_2$CH$_2$-COOH), 39–45.0 (CH_2CHPh), 48.1 (32 C, NCH$_2$CH$_2$COOH), 49.3 (61 C, NCH$_2$CH$_2$CH$_2$N), 125.7 (CH$_2$CHPh$_{para}$), 127.2–128.8 (CH$_2$CHPh$_{ortho+meta}$), 145.5 (CH$_2$CHPh$_{ipso}$), 171.6 (32 C, COOH); IR: $\nu_{C=O}$ 1706 cm^{-1}.
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(14) The experiments were performed batchwise at 20 °C, using a Philips PW9550 conductivity cell. The total amount of solvent (H$_2$O and toluene) was 23 mL, containing 3 × 10^{-4} M amphiphile. The same stirring speed was used for all experiments; measurements were performed after 2 min of equilibration time. The pH-dependent amphiphilic behavior of PS-*dendr*-(COOH)$_n$ ($n = 2-32$) was investigated using three different electrolytes: 0.01 M KCl, 0.01 M HCl, and 0.01 M KOH. PS-*dendr*-(COOH)$_{32}$ is left out of the figures, because this structure did not show amphiphilic behavior and a dilution curve was measured instead of a phase inversion. Conductivity measurements of toluene/water mixtures without the addition of amphiphile were not possible, because in these cases no stable emulsions were formed.
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