Dendrimers with Both Hydrophilic and Hydrophobic Chains at Every End

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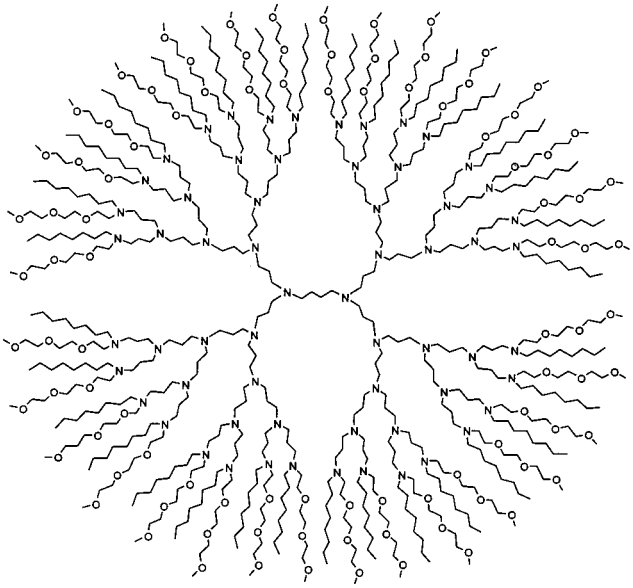
Amphiphilic dendritic polymers can behave as unimolecular micelles that retain their colloidal structures regardless of concentration, ionic strength, and temperature of the solution. Polar end groups make them soluble in water, and their less polar cores and branching units can solvate hydrophobic molecules.[1] These unique properties may enable applications in the areas of molecular encapsulation, membrane transport, and catalysis.[2] Inverted dendritic micelles with hydrophobic C_{16} end groups[3] and stimuli responsive hybrid macromolecules, having a hydrophilic poly(ethylene glycol) star as the core and hydrophobic dendritic groups as chain ends, which can change conformations as the solvent polarity is varied,[4] also have been reported. Here we describe synthetic transformations of poly(propyleneimine) dendrimers to give both hydrophilic triethyleneoxy methyl ether (TEO) and hydrophobic octyl chains on every amine chain end (structure **1**) and the



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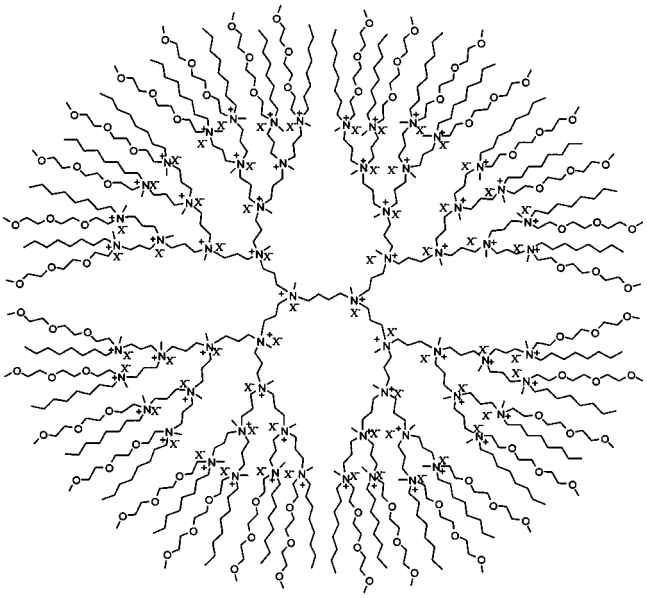
conversion of these dendrimers to completely methylated quaternary ammonium ion derivatives **2**. The aim of mixed end group functionality is to make the dendrimers soluble in a wide range of solvents and, conversely, hosts to a wide range of organic compounds for reactions catalyzed by metal ions bound to the amines and for reactions catalyzed by counterions of the quaternary ammonium ions.

The synthesis of the quaternized amphiphilic dendrimer **2** required five steps from the commercial poly(propyleneimine) dendrimer DAB-*dendr*-$(NH_2)_{32}$. DAB-*dendr*-$(NH_2)_8$ also was transformed using the same procedure. The octyl arms were introduced by amidation



2a X=I
2b X=Cl

of the primary amine groups with octanoyl chloride followed by $LiAlH_4$ reduction, and the TEO arms were introduced by amidation of the resulting secondary amines with $CH_3O(CH_2CH_2O)_2CH_2COCl$ followed by another $LiAlH_4$ reduction to afford polyamine dendrimer **1**.[5] The products were characterized by ^1H and ^{13}C NMR analysis, and the corresponding products from DAB-*dendr*-$(NH_2)_8$ were also characterized by ESI−MS analysis.[6] The formation of the amides and the conversion of the amides to amines were monitored by FT-IR of the amide band at 1650 cm^{-1}. Dendrimer **2a** was synthesized by quaternization of **1** with methyl iodide, and dendrimer **2b** was obtained by ion exchange of iodide for chloride.[7]

The amphiphilic dendrimers **1, 2a**, and **2b** are soluble in toluene, ether, THF, chloroform, acetone, and methanol. Dendrimer **2b** is also readily soluble in water, but can be extracted quantitatitively from water by dichloromethane and chloroform. We expected that, in chloroform, both the TEO and the octyl arms would be solvated and, in polar solvents such as methanol and water, the alkyl arms would contract, leaving the hydrophilic TEO chain ends at the surface of the dendrimer. This prediction is supported by both ^1H NMR spectra and ^{13}C relaxation time (T_1) measurements in solvents of different polarity. The ^1H NMR spectrum of polyamine **1** in $CDCl_3$ has sharp peaks for both the CH_3 and the $(CH_2)_n$ of the octyl arms and the OCH_3 and OCH_2 peaks of the TEO arms, while in CD_3OD the TEO peaks remain sharp and the alkyl peaks are broader as shown in Figure 1. The ^{13}C NMR T_1 values of the TEO arms of **1** and **2a** increase and the T_1 values of the octyl arms decrease when the solvent changes from $CDCl_3$ to CD_3OD (Figure 2). Also the T_1 values of TEO chain ends in **2a** are significantly less than those in **1** in both $CDCl_3$ and CD_3OD, which indicates there is a strong interaction of the TEO arms with the internal quaternary ammonium sites in **2a**. The lesser T_1 values in both cases could be due either to molecular conformations that reduce chain motion

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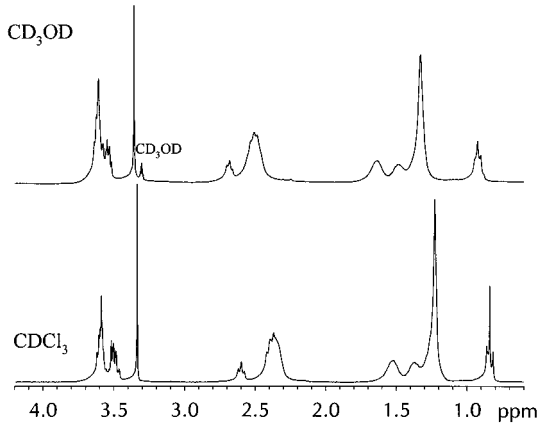

Figure 1. ^{1}H NMR spectra of polyamine **1** in $CDCl_3$ and CD_3OD (20 mg mL^{-1} at 22 °C).

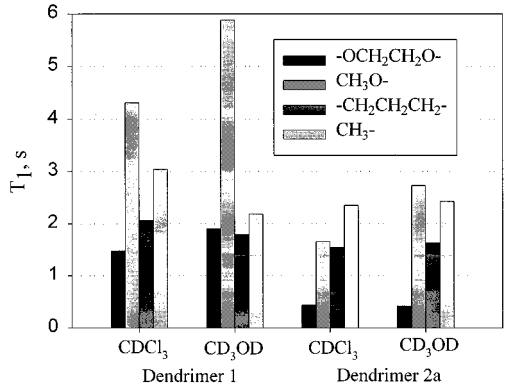

Figure 2. ^{13}C relaxation times (T_1) of **2a** and **1** in $CDCl_3$ and CD_3OD (158 mg mL^{-1} of **2a** and 135 mg mL^{-1} of **1** at 22 °C).

or to aggregation of the dendrimer. In THF and in methanol at concentrations of 30 mg mL^{-1} the hydrodynamic diameters of polyamine **1** determined by dynamic light scattering were 4.8 and 3.5 nm respectively. (THF was used as the less polar solvent, because in chloroform **1** gave weak signals due to insufficient difference of refractive index between dendrimer and solvent). In methanol the hydrodynamic diameter of poly(quaternary ammonium iodide), **2a**, was 5.1 nm. For comparison, the diameter of models of monomeric **1** was 3.4 nm.[8] Thus, the dendrimers are not highly aggregated in solution, and the ^{13}C T_1 differences are due to slower chain motions in the quaternary ammonium than in the tertiary amine dendrimer.

The lipophilic octyl arms make the dendrimers soluble in organic solvents, which facilitates the synthesis and purification, and they can adsorb lipophilic compounds from aqueous solutions. We used the water-insoluble solvatochromic pyridinium-*N*-phenoxide betaine **3** (Reichardt's dye), whose charge-transfer band λ_{max} ranges from 452 nm in water to 810 nm in diphenyl ether,[9] as a probe to test the solvating behavior of dendrimer **1b** in aqueous solution. Dye **3** forms a stable and clear aqueous solution in the presence of dendrimer **2b**. The UV−vis spectrum of this solution is compared with those of the dye in aqueous cetyltrimethylammonium chloride (CTACl) solution and in pure benzyl alcohol in Figure 3. The longer λ_{max} at 576 nm in the presence dendrimer **2b** than in CTACl micelles (542 nm) means that the dye binding site in the unimolecular micelle is less polar that the binding site in the dynamically aggregated CTACl micelle, even though CTACl has C_{16} chains and **2b** has only C_8 chains. The similarity of

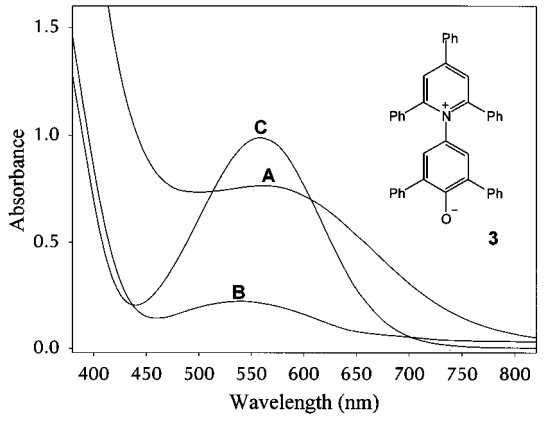

Figure 3. UV−vis spectra of **3** in (A) an aqueous solution of dendrimer **2b** (7.0×10^{-4} M, 36 mg/3.20 mL; 9.6×10^{-4} M **3**), (B) an aqueous solution of CTACl (3.5×10^{-3} M, 3.7 mg/3.20 mL; 9.6×10^{-4} M **3**), and (C) benzyl alcohol (neat; 3.2×10^{-4} M **3**).

λ_{max} of **3** in the aqueous solution of **2b** and in benzyl alcohol suggests that the hydrogen-bonding and polarity of the two media are similar, and the much broader absorption bands in the dendrimer and surfactant solutions suggest a wide range of environments of the dye in the colloidal solutions.

These novel quaternary ammonium ion dendrimers having both octyl and TEO groups on each chain end will be tested as catalysts of organic reactions in aqueous solutions.

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(5) The amidations of both the primary and secondary amines were carried out in anhydrous DMF at 70 °C for 36 h using triethylamine as external base, and the $LiAlH_4$ reductions of both the secondary and tertiary amides were performed in anhydrous THF at reflux for 24 h. The dendrimers were purified by column chromatography over basic alumina, and the purity was confirmed by ^{1}H and ^{13}C NMR and ESI−MS analysis. The polyamine dendrimer **1** was obtained as light yellow thick oil in 40% overall yield from DAB-AM-32. ^{1}H NMR ($CDCl_3$, δ): 0.84 (t, CH_3CH_2), 1.16−1.36 (m, CH_2CH_2), 1.36−1.70 (m, $NCH_2CH_2CH_2N$), 2.30−2.50 (m, $NCH_2CH_2CH_2N$), 2.61 (t, NCH_2CH_2O), 3.34 (s, CH_3O), 3.50 (m, OCH_2CH_2O), 3.62 (m, OCH_2CH_2N and OCH_2CH_2O). ^{13}C

NMR ($CDCl_3$, δ): 14.02 (alkyl C-1), 22.55 (alkyl C-2), 24.5br ($CH_2CH_2CH_2$), 27.03 (alkyl C-6), 27.47 (alkyl C-7), 29.26 (alkyl C-5), 29.52 (alkyl C-4), 31.78 (alkyl C-3), 51.90 (alkyl C-8), 52.7−53.4 (CH_2N), 54.78 (NCH_2CH_2O), 58.96 (CH_3O), 69.87 (OCH_2CH_2N), 70.40 (OCH_2CH_2O), 70.50 (OCH_2CH_2O), 70.60 (OCH_2CH_2O), 71.90 (CH_2OCH_3).

(6) ESIMS of the analogue of **1** having 8 tertiary amine end groups: calcd for $C_{160}H_{336}N_{14}O_{24}$ 2838.55; found *m*/*z* 1420.8 $[M + 2H]^{2+}$, 947.6 $[M + 3H]^{3+}$, 710.8 $[M + 4H]^{4+}$, 568.8 $[M + 5H]^{5+}$.

(7) The quaternization of **1** with a 10-fold excess of CH_3I was conducted in a sealed tube at 100 °C for 48 h to give **2a** as yellow powder. The iodide dendrimer **2a** was converted to the chloride by a column of Amberlite IRA 402 strongly basic anion-exchange resin (Sigma) using 1.2:1 MeOH:H_2O as eluant. The eluate was evaporated to a gum, dissoved by stirring in 1:3 methanol:saturated aqueous NaCl over 3 days, evaporated to a solid, dissolved in water, and extracted with dichloromethane. The organic phase was dried over anhydrous sodium sulfate and evaporated to give **2b** as light yellow powder. ^{1}H NMR showed the absence of the NCH_2 and NCH_2CH_2O peaks of **1** at 2.4 and 2.62 ppm and the presence of a new $OCH_2CH_2N^+$ peak at 4.32 ppm that integrated correctly with respect to the alkyl CH_3 peak at 0.84 ppm. ^{1}H NMR ($CDCl_3$, δ): 0.84, 1.21−1.42, 1.60−1.78, 2.58, 3.32, 3.34−4.18, 4.22−4.42. ^{13}C NMR ($CDCl_3$, δ): 13.99, 17−18, 22.53, 26.36, 29.11, 29.20, 31.67, 48.5−50.0, 57−62, 58.90, 64.78, 70.23, 71.73.

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