Communications to the Editor

Synthesis, Characterization, and Guest-Host Properties of Inverted Unimolecular Dendritic Micelles


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Dendrimers, being well-defined and highly-branched macromolecules, have become the subject of extensive studies,1,2 because their multifunctionality and specific shape have been recognized as powerful tools in the synthesis of new structures. Applications of dendrimers in molecular architectures,2 and the dendritic box,3 show the versatility of these materials. In 1985, the use of dendrimers as unimolecular micelles was already proposed by Newkome.4 Micellar behavior has been demonstrated by dissolving, e.g., organic molecules in dendrimers,5,6 whereas some dendrimers have been employed as micellar structures in electrokinetic capillary chromatography.5-8 In all of these cases, dendrimers are regarded as regular unimolecular structures in which consist of an apolar core and a polar shell. In this communication we report on the synthesis of inverted unimolecular dendritic micelles, by the modification of the end groups of hydrophilic poly(propylene imine) dendrimers6 (DAB-dendr-(NH2)4-64), with hydrophobic alkyl chains.

The modification consists of the conversion (in 60-95% isolated yield) of the 4-64 primary amines of DAB-dendr-(NH2)4-64 into their amide analogues with a variety of long-chain alkyl acid chlorides (C10H21COCl with n = 5, 9-15) in THF and in the presence of Et3N as an external base (Scheme 1). Structural characterization of the dendritic amines (DAB-dendr-(NHCO)4-64) with 1H-NMR, 13C-NMR, IR, and MALDI-TOF spectroscopies showed that all of the dendrimer end groups were amidated.7,8 Most remarkably, when the long-chain alkyl acid chlorides were used in the reaction with an excess of DAB-dendr-(NH2)4-64, two products were always isolated; water-insoluble fully reacted dendrimer (at least 90% of the end groups, as determined by 1H-NMR) and water-soluble, totally unmodified dendrimers (no fatty acid amide functionality is observed by 1H-NMR and IR) were obtained in the correct product ratios.8 This effect proved to be independent with respect to solvent (THF or CH2Cl2), concentration of the reactants and the degree of excess dendrimer used. The water (in)solubility of the products makes the separation and characterization very easy. However, this effect is not found for pivaloyl chloride, with which partially converted structures are prepared.9 A reasonable explanation for the phenomenon observed is lacking at the present time.10

Evidence for the development of dendritic character (i.e., high packing of end groups) by increasing generation from DAB-dendr-(NHCO)4-64 was obtained by 1H-NMR spectroscopy. A significant shift for the NHCO proton to lower fields with increasing generation was observed (Figure 1). The low-generations, DAB-dendr-(NHCO)4-64, also showed a concentration dependence of the NHCO position, which was absent for the two higher generations, DAB-dendr-(NHCO)12-84. The shift of the amide proton is a result of the change from predominantly concentration-dependent, but weak, intermolecular H-bonding for the lower generations to concentration-dependent.

(7) Preparation and characterization of an alkyl-modified dendrimer, DAB-dendr-palmityl: To a solution of 2.5 g DAB-dendr-(NH2)4 (1 equiv, 3.3 mmol) in 50 mL THF, 5.00 g triethylamine and 8.56 g pivaloyl chloride (10 equiv, 28.6 mmol) were added. After the mixture stirred for 20 h at room temperature, the solvent was evaporated. The mixture was then heated under reflux in 50 mL of diethyl ether for 30 min and filtered. The residue was dissolved in acetone and the mixture was filtered. The mixture was then heated under reflux for 6 h, in order to remove residual ammonium salts and to deprotonate the dendrimers. The filtrate was cooled to 4 °C and the product was obtained as a white/yellow solid material (yield 76% of the theoretical yield), as described in the experimental section.11

(8) This phenomenon was observed for reactions between a 2-, 3-, and 4-fold excess of DAB-dendr-(NH2)4-64 based-on the number of primary amine end groups—and palmitoyl and oleoyl chloride. The workup procedure with the Na2CO3 solution resulted in separation between water-soluble DAB-dendr-(NHCO)4-64 and modified DAB-dendr-(NHCO)12-84. Both products were isolated and identified by 1H and 13C-NMR spectroscopy, and the melting points of the amidated products resembled those of the products made by using equimolar amounts of reactants. For experimental details see the Experimental Section.

(9) It was found that 13 out of 64 end groups were amidated by using 0.21 equiv of pivaloyl chloride per equialent end group of DAB-dendr-(NH2)4. Workup was strongly hampered by the formation of emulsions. An alternative reaction procedure was therefore developed. Small amounts of pivaloyl chloride are used, no emulsions were observed, and the fully amidated structure was easily obtained in pure form (i.e., at least 95% of the end groups have reacted).

The first-generation dendrimers showed melting points (measured by DSC) that resemble those of the corresponding generations. Dynamic light scattering (DLS) also confirms the generation dependence of the N/HCO NMR resonance of the series, measured in CDCl₃. Inset: Concentration dependence of the N/HCO NMR resonance of the palmitoyl-modified dendrimers and the yields after workup of all the fully modified structures (14 pages). See any current masthead page for ordering and Internet access instructions.

Evidence for an inverted micellar structure of the alkyl amide-modified dendrimers was obtained by their capability to act as guest–host systems. DAB-dendr(NHCOCH₃)₉₋₁₅, and no odd–even behavior could be detected.¹¹¹²

Supporting Information Available: Synthetic procedures and spectroscopic properties of the palmitoyl-modified dendrimers and the yields after workup of all the fully modified structures (14 pages). See any current masthead page for ordering and Internet access instructions.