PDF hosted at the Radboud Repository of the Radboud University Nijmegen

The following full text is a publisher's version.

For additional information about this publication click this link.
http://hdl.handle.net/2066/17430

Please be advised that this information was generated on 2018-06-09 and may be subject to change.
Synthesis, Characterization, and Guest–Host Properties of Inverted Unimolecular Dendritic Micelles


Laboratory of Organic Chemistry
Eindhoven University of Technology
P.O. Box 513, 5600 MB Eindhoven, The Netherlands
DSM Research, P.O. Box 18
6160 MD Geleen, The Netherlands

Received December 15, 1995
Revised Manuscript Received June 4, 1996

Dendrimers, being well-defined and highly-branched macromolecules, have become the subject of extensive studies because their multifunctionality and specific shape have been recognized as powerful tools in the synthesis of new structures. Applications of dendrimers in molecular architectures, and the dendritic box, show the versatility of these materials. In 1985, the use of dendrimers as unimolecular micelles was already proposed by Newkome. Micellar behavior has been demonstrated by dissolving, e.g., organic molecules in dendrimers, whereas some dendrimers have been employed as micellar structures in electroluminescent capillary chromatography. In all of these cases, dendrimers are regarded as regular unimolecular micelles, which consist of an apolar core and a polar shell. In this communication we report on the synthesis of unimolecular dendritic micelles, by the modification of the end groups of hydrophobic poly(propylene imine) dendrimers (DAB-dendr-(NHCO)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-(NH3) into their amide analogues with a variety of long-chain alkyl acid chlorides (CICOCO2H with Cn = (CH2)n−1−CH3 with n = 5, 9−15) in THF and in the presence of Et3N as an external base (Scheme 1).

Structural characterization of the dendritic amides (DAB-dendr-(NHCO)n) with 1H-NMR, 13C-NMR, IR, and MALDI-TOF spectroscopy showed that all of the dendrimer end groups were amidated. Most remarkably, when the long-chain alkyl acid chlorides were used in the reaction with an excess of DAB-dendr-(NH3)−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 ratio. 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-insolubility 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. A reasonable explanation for the phenomenon observed is lacking at the present time.

Evidence for the development of dendritic character (i.e., high packing of end groups) by increasing generation from DAB-dendr-(NHCO)n, as 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)n−1, also showed a concentration dependence of the NHCO position, which was absent for the two higher generations, DAB-dendr-(NHCO)n≥4. 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) Typical preparation and characterization of an alkyl-modified dendrimer, DAB-dendr-(palmityl)4. To a solution of 2.5 g DAB-dendr-(NH3)4 in 50 mL THF, 5.00 g triethylamine and 8.56 g pivaloyl chloride (1.10 equiv, 28.6 mmol) were added. After the mixture stirred for 20 h at room temperature, the solvent was evaporated. The mixture was heated under reflux in 50 mL of diethyl ether for 30 min and filtered. To the residue, 60 mL of acetic acid was added and heated under reflux for 6 h, in order to remove residual ammonium salts and to deprotonate the dendrimers. The mixture was filtered, the residue was dried in vacuo at 40 °C, and the product was obtained as a white/yellow solid material (yield 76%).

(8) This phenomenon was observed for reactions between a 2−3, and 4-fold excess of DAB-dendr-(NH3)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 the separation between water-soluble DAB-dendr-(NHCO)n−1 and modified DAB-dendr-(NHCO)n. Both products isolated were unambiguously identified by IR and NMR spectroscopy and the melting points of the amidated products resembled those of the products made by using equimolar amounts of reagents. 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 equivalent group of DAB-dendr-(NH3)4. Workup was strongly hampered by the formation of emulsions, and the major fraction (60%) of the amidated end groups 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).

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-(NHCOC$_n$)$_{54}$ were used as dynamic hosts for guest molecules like Bengal Rose. The hydrophilic dye was trapped into the inverted unimolecular micelles by first dissolving micelle and dye in ethanol, allowing the dye to enter the dendritic core. Precipitation of the complex in acetonitrile, followed by an extensive washing procedure with acetonitrile until no coloration of solvent occurred, resulted in the removal of untrapped and adhered dye. The $x = 64$ compounds were further purified by dialysis with water. The number of dye molecules trapped (varying from an average of 1 for $x = 8$ to 7 for $x = 64$) was determined with UV spectroscopy. It was possible to strongly improve the compatibility between Bengal Rose and an apolar solvent such as $n$-hexane by first encapsulating the dye into the inverted micelle. It was impossible to release the dye from the solution by washing with water; however, the addition of toluene to Bengal Rose@DAB-dendr-(NHCOC$_n$)$_{64}$ in $n$-hexane released the dye from the micelle. These guest–host systems also open routes toward compatibilization of apolar and polar materials using nanoscopic phase separation, as a result of the unique properties of dendritic macromolecules.

**Supporting Information Available:** Synthetic procedures and spectroscopic properties of the palmityol-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.

JA954207H


(13) It is assumed that the absorption coefficients $\epsilon$ of “free” and encapsulated Rose Bengal, both measured in ethanol, are identical. The load of the dye is strongly dependent on both generation and fatty acid chain length. The highest number (seven) of molecules entrapped is found with increasing chain length (mp of DAB-dendr-(NHCOC)$_n$$_{64}$ varies from $-1^\circ C$ for $n = 5$ to $75^\circ C$ for $n = 15$), and no odd–even behavior could be detected.11,12

The first-generation dendrimers showed melting points (measured by DSC) that resemble those of the corresponding alkylamides, indicating that the first generation is a regular organic compound. Phase transitions observed for the higher generation dendrimers were independent of the number of end groups and fully determined by the alkyl chain length. The phase transition temperature increased continuously with increasing chain length (mp of DAB-dendr-(NHCOC)$_n$$_{64}$ varies from $-1^\circ C$ for $n = 5$ to $75^\circ C$ for $n = 15$), and no odd–even behavior could be detected.$^{11,12}$

**Supporting Information Available:** Synthetic procedures and spectroscopic properties of the palmityol-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.

JA954207H


(13) It is assumed that the absorption coefficients $\epsilon$ of “free” and encapsulated Rose Bengal, both measured in ethanol, are identical. The load of the dye is strongly dependent on both generation and fatty acid chain length. The highest number (seven) of molecules entrapped is found with increasing chain length (mp of DAB-dendr-(NHCOC)$_n$$_{64}$ varies from $-1^\circ C$ for $n = 5$ to $75^\circ C$ for $n = 15$), and no odd–even behavior could be detected.$^{11,12}$

**Supporting Information Available:** Synthetic procedures and spectroscopic properties of the palmityol-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.

JA954207H
