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

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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,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,3 and the dendritic box4 show the versatility of these materials. In 1985, the use of dendrimers as unimolecular micelles was already5,6 dendritic box recognized as powerful tools in the synthesis of new structures. Because their multifunctionality and specific shape have been proposed by Newkome7,8 groups of hydrophilic poly(propylene imine) dendrimers6 in electrokinetic capillary chromatography.6 In all this communication we report on the synthesis of micelles, which consist of an apolar core and a polar shell. In 1985, (1) (a) Newkome, G. R.; Nayak, A.; Behera, R. K.; Moorefield, C. N.; (b) 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)2-NHCO)2, was obtained by 1H-NMR spectroscopy. A significant shift for the NHCO proton to lower fields with increasing generation was observed (Figure 1). The lower generations, DAB-dendr-(NHCO)2-NHCO)2, also showed a concentration dependence of the NHCO position, which was absent for the two higher generations, DAB-dendr-(NHCO)2-NHCO)2. 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-

alkyl acid chlorides (CICOOCH3 with Ce = (CH2)n−1CH3 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)2) with 1H-NMR, 13C-NMR, IR, and MALDI-TOF spectroscopies showed that all of the dendrimer end groups were amidated.7 Most remarkably, when the long-chain alkyl acid chlorides were used in the reaction with an excess of DAB-dendr-(NH2)3–44, two products were always isolated; water-insoluble fully reacted dendrimer (at least 90% of the end groups, as determined 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

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S0002-7863(95)04207-7 CCC: $12.00
alkylamides, indicating that the first generation is a regular
sured by DSC) that resemble those of the corresponding
ations. Dynamic light scattering (DLS) also confirms the
tion dependence of the \textit{N}/\textit{YCO} NMR resonance of the series, measured
in CDCl$_3$ (moles of alkyl amide end groups per liter): ■, $x = 4$; ♦, $x = 8$; ▲, $x = 16$; ○, $x = 32$; *, $x = 64$.

**Figure 1.** Generation dependence of the \textit{NHC}O NMR resonance of DAB-dendr-(\textit{NHCOC})$_n$ series, measured in CDCl$_3$. Inset: Concentration dependence of the \textit{NHC}O NMR resonance of the series, measured in CDCl$_3$ (moles of alkyl amide end groups per liter). ■, $x = 4$; ♦, $x = 8$; ▲, $x = 16$; ○, $x = 32$; *, $x = 64$.

independent strong intramolecular H-bonding for the higher
generations. Dynamic light scattering (DLS) also confirms the
absence of clustering between DAB-dendr-(\textit{NHCOC})$_n$ molecules: single particle behavior was observed with a
hydrodynamic diameter of 2–3 nm in dichloromethane.

The first-generation dendrimers showed melting points (mea-
sured 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 in-
creasing chain length (mp of DAB-dendr-(\textit{NHCOC})$_n$ varies
from $-1\,^\circ C$ for $n = 5$ to $75\,^\circ C$ for $n = 15$), and no odd–even
behavior could be detected.$^{11,12}$

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-(\textit{NHCOC$_{9,15,64}$})$_n$ 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.$^{13}$ It was possible to strongly improve the compat­
ibility 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-(\textit{NHCOC$_{64}$}) 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.$^{14}$

**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.

JA954207H

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(12) The phase transition is probably due to the melting of small ordered
domains of alkyl chains, as proposed for alkanethiol-stabilized gold clusters
and poly(\textit{l}-glutamates) with long alkyl chains; see e.g.: (a) Watanabe, J.;
Ono, H.; Uematsu, I.; Abe, A. Macromolecules 1985, 18, 2141. (b) Terrill,
Hutchison, J. E.; Clark, M. R.; Wignall, G.; Londono, J. D.; Superfine, R.;

(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 ($n$) of molecules entrapped is found for
DAB-dendr-(\textit{NHCOC$_{64}$}). The chain-length dependent barrier effect
seems to have its optimum at $C_6$, in which case the hydrophobic shell favors
trapping of the dye into the micelle instead of release or exclusion.

(14) Independently, Tomalia et al. prepared guest–host systems based
on inverted unimolecular micelles from PAMAM dendrimers modified with
fatty acids: D. A. Tomalia, personal communication.