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 box, 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 whereas some dendrimers have been employed as micellar structures in electrokinetic capillary chromatography.6 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 inverted unimolecular dendritic micelles, by the modification of the end groups of hydrophilic poly(propylene imine) dendrimers6 (DAB-dendr-(NH2)2–64), 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) into their amide analogues with a variety of long-chain alkyl acid chlorides (CICOCO with Cn = (CH2)2n–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(NHOCO)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)2–64, 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 reagents, 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.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(NHOCO)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 low-generations, DAB-dendr(NHOCO)2–16, also showed a concentration dependence of the NHCO position, which was absent for the two higher generations, DAB-dendr(NHOCO)2–64. 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).

(1) Typical preparation and characterization of an alkyl-modified dendrimer, DAB-dendr-palmitoyl: To a solution of 2.5 g DAB-dendr-(NH2)30 (1 equiv, 5.3 mmol) in 50 mL THF, 5.00 g triethylamine and 8.56 g palmitoyl 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. The residue was recrystallized with pivaloyl chloride. To the residue, a solution of 2 g Na2CO3 in 50 mL H2O was added, and the mixture was 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%). 1H-NMR (CDCl3): δ 0.21 equiv 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 13C-NMR (CDCl3): δ 14.10 (CH3), 27.35 (CH2–CO), 29.37–29.73 (CH2–OCH2), 31.93 (H-CHO), 36.75 (N–CH2–CH2–CH2–NH–), 52.20 (N=CH–CH–CH–NH–), 173.59 (NHCO) ppm. IR: amide N–H stretch 3300.2 cm−1, sec. amide N–H 3291.6 cm−1, C–H sat. 2918.1 cm−1, sec. amide C = O 1638.9 cm−1. DSC: phase transition at 74.3 °C. MALDI-TOF: measurement of DAB-dendr(NHOCO)30: 2683 g/mol, calculated 2687 g/mol.

alkylamides, indicating that the first generation is a regular
sured by DSC) that resemble those of the corresponding
generations. Dynamic light scattering (DLS) also confirms the
dependence of the N/YCO NMR resonance of the series, measured
Figure 1. Generation dependence of the NHCO NMR resonance of
DAB-dendr-(NHCO)n series, measured in CDCl3. Inset: Concentra-
tion dependence of the NHCO NMR resonance of the series, measured
in CDCl3 (moles of alkyl amide end groups per liter): ■, n = 4; ●, n = 8; ▲, n = 16; ○, n = 32; *, n = 64.

independent strong intramolecular H-bonding for the higher
generations. Dynamic light scattering (DLS) also confirms the
absence of clustering between DAB-dendr-(NHCO)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-(NHCO)n decreases
from —1 °C for n = 5 to 75 °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-(NHCO)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
bility 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-(NHCO)n 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.
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(11) (a) Percec, V.; Tsuda, Y. Macromolecules 1990, 23, 3509. (b) Percec, 
V; Tomazos, D. Comprehensive Polymer Science: Allen, G., Ed.; Pergamon
(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(yl-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 ε 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
for DAB-dendr-(NHCO)n. The chain-length dependent barrier effect
seems to have its optimum at C6, 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.