Starlike Block Copolymers with Amphiphilic Arms as Models for Unimolecular Micelles

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Received December 29, 1998

In this paper, we describe the synthesis of novel, controlled starlike molecular architectures with six and twelve amphiphilic arms, respectively. These molecules form unimolecular micelles in solution, which respond in a unique fashion to the polarity of the solvent by changing their molecular geometry.

Certain amphiphilic block copolymers form micelles in solvents which are selective for either one block or the other.[1−5] These represent supermolecular self-assembled structures composed of individual amphiphiles in a dynamic equilibrium, i.e., exchange of individual components between the micelles and/or the solution occurs readily. The organized structure of polymeric micelles may be stabilized by intramolecular cross-linking.[6] On the other hand, unimolecular micelles cannot participate in such dynamic equilibria since the individual amphiphiles are covalently fixed. Unimolecular micelles have been reported from certain graft copolymers.[7] However, to mimic the fundamental parameters associated with traditional micelles, a very controlled polymeric molecular architecture is required. This is provided, for example, with dendrimers, which display controlled, three-dimensional branched structures. A variety of amphiphilic dendritic unimolecular micelles have been described in the literature.[8−11] Multiarm, starlike block copolymers, on the other hand, present the opportunity for a new class of unimolecular micelles. Fréchet et al. have integrated both approaches by endcapping a hydrophilic 4-arm poly(ethylene glycol) star polymer with hydrophobic dendritic blocks.[12] Our approach to preparing unimolecular micelles involves the design of novel starlike block copolymers with six and twelve arms, respectively. To produce these architectures, we have utilized atom transfer radical polymerization (ATRP)[13,14] in the consecutive polymerization of *tert*-butyl acrylate (tBA) and methyl methacrylate (MMA) from the branched initiators shown in Figure 1. Subsequent selective deprotection of the acrylate block with trifluoroacetic acid leads to a structure with a poly(acrylic acid) (PAA) hydrophilic block,
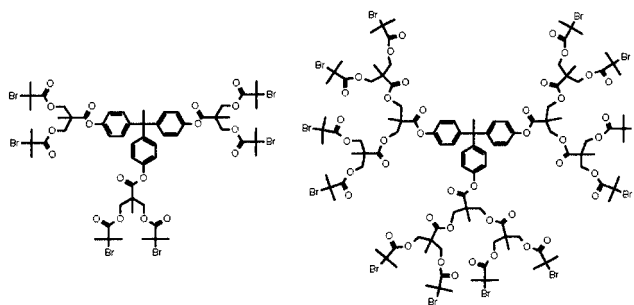

Figure 1. 6- (left) and 12-arm (right) atom transfer radical polymerization (ATRP) initiators.

and PMMA as the hydrophobic component. We recently reported the synthesis and versatility of these starlike initiators in the controlled polymerization of MMA homo and random copolymers.[15,16] Although other research groups have recently reported the synthesis of star-polymers by ATRP techniques,[17,18] to our knowledge this work represents the first preparation of unimolecular micelles using ATRP techniques.

The characteristics of the macroinitiators and the block copolymers are summarized in Table 1.[19,20] When run to less than 60−70% conversion, both 6- and 12-arm PtBAs have a polydispersity <1.1. The molecular weight determined by ^{1}H NMR from the ratio of integrated peak areas of the aromatic signals of the initiator core and the *tert*-butyl ester groups is about 7000 g/mol for the 6-arm polymer (DP ∼ 12 per arm) and 16500 for the 12-arm polymer (DP ∼ 14 per arm), respectively. By using these functionalized PtBA macroinitiators for the subsequent polymerization of MMA, starlike block copolymers could be obtained. The molecular weight of the PMMA block was determined to be 43000 g/mol (6-arm) and 58000 g/mol (12-arm) by ^{1}H NMR analysis of the ratio of the integrated peak areas from the methyl ester groups relative to the initiator cores. Figure 2 shows the GPC traces of both the 6-arm macroinitiators and the resulting block copolymers. The polydispersities of the starlike block copolymers are <1.3 for both examples. Quantitative deprotection of the PtBA block with trifluoroacetic acid in methylene chloride results in the desired amphiphilic block copolymers. By changing the order of monomer addition in the polymerization, the reversed block copolymers, i.e., hydrophobic core with a hydrophilic shell, were obtained with similarly low polydispersities (Table 1, Figure 2).

Preliminary ^{1}H NMR investigations show that either block can be selectively collapsed by changing solvent as indicated schematically in Figure 3. Unfortunately for the protiated monomers, the signals of the main chain protons of the PMMA block (δ 0.5−2 ppm) overlap those of the PAA block. Consequently, changes in the micellar molecular geometry cannot be determined directly from these overlapping proton signals. However, the aromatic signals of the initiator core are easily monitored by ^{1}H NMR. This provides an indirect reporter for the solvation of the block directly attached to the core. In a nonselective solvent like acetone which solvates both blocks, the signals of the initiator

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(1) Munk, P.; Prochazka, K.; Tuzar, Z.; Webber, S. E. *Chemtech* **1998**, *October*, 20−28.
(2) Halperin, A. *Macromolecules* **1991**, *24*, 1418−1419.
(3) Ma, Y.; Cao, T.; Webber, S. E. *Macromolecules* **1998**, *31*, 1773−1778.
(4) Zhang, L.; Eisenberg, A. *J. Am. Chem. Soc.* **1996**, *118*, 3168−3181.
(5) Pispas, S.; Poulos, Y.; Hadjichristidis, N. *Macromolecules* **1998**, *31*, 4177−4181.
(6) Thurmond, K. B., II; Kowalewski, T.; Wooley. K. L. *J. Am. Chem. Soc.* **1997**, *119*, 6656−6565.
(7) Kikuchi, A.; Nose, T. *Macromolecules* **1996**, *29*, 6770−6777.
(8) Hawker, C. J.; Wooley, K. L.; Fréchet, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1287.
(9) Newkome, G. R.; Morrefield, C. N.; Baker, G. R.; Saunders, M. J.; Grossman, S. H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1178−1180.
(10) Tomalia, D. A.; Berry, V.; Hall, M.; Hedstrand, D. M. *Macromolecules* **1987**, *20*, 1164−1167.
(11) Stevelmans, S.; van Hest, J. C. M.; Jansen, J. F. G. A.; Van Boxtel, D. A. F. J.; de Brabander-van den Berg, E. M. M.; Meijer, E. W. *J. Am. Chem. Soc.* **1996**, *118*, 7398−7399.
(12) Gitsov, I.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1996**, *118*, 3785−3786.
(13) Patten, T. E.; Matyjaszewski, K. *Adv. Mater.* **1998**, *10*, 901−915.
(14) Matyjaszewski, K. *Controlled Radical Polymerization*; Matyjaszewski, K., Ed.; ACS Symp. Ser. No. 685; American Chemical Society: Washington, D.C., 1998.

(15) Heise, A.; Hedrick, J. L.; Trollsås, M.; Miller, R. D.; Frank, C. W. *Macromolecules* **1999**, *32*, 231−234.
(16) Heise, A.; Hedrick, J. L.; Trollsås, M.; Miller, R. D.; Frank, C. W. *Polym. Prepr.* **1998**, *39*, 627.
(17) Angot, S.; Murthy, K. S.; Tanton, D.; Gnanou, Y. *Macromolecules* **1998**, *31*, 7218−7225.
(18) Ueda, J.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1998**, *31*, 6762−6768.
(19) Hedrick, J. L.; Trollsås, M.; Hawker, C. J.; Atthoff, B.; Claesson, H.; Heise, A.; Miller, R. D.; Mecerreyes, D.; Jérôme, R.; Dubois, Ph. *Macromolecules* **1998**, *31*, 8691.
(20) Coca, S.; Davis, K.; Miller, P.; Matyjaszewski, K. *Polym. Prepr.* **1997**, *38*, 689−690.

Table 1.

polymer	block-1 PtBA		block-2 PMMA		block copolymer P(tBA-*b*-MMA)
	$M_n{}^a$ (g/mol)	$M_w/M_n{}^b$	$M_n{}^a$ (g/mol)	$M_w/M_n{}^b$	$M_n{}^c$ (g/mol)
6-arm	6800	1.05	43000	1.29	49800
12-arm	16500	1.04	58000	1.23	74500

polymer	block-1 PMMA		block-2 PtBA		block copolymer P(MMA-*b*-tBA)
	$M_n{}^a$ (g/mol)	$M_w/M_n{}^b$	$M_n{}^a$ (g/mol)	$M_w/M_n{}^b$	$M_n{}^c$ (g/mol)
6-arm	15000	1.13	7000	1.23	22000

[a] M_n for PMMA blocks was determined from the ratio of integrated peak areas of initiator peaks around 7 ppm and the methyl ester peaks around 3.5 ppm in the ^{1}H NMR spectrum. M_n of the PtBA blocks was determined accordingly from the *tert*-butyl ester peak around 1.4 ppm. [b] Derived from size exclusion chromatography (SEC) calibrated with polystyrene. [c] Represents the sum of values of the single blocks determined by ^{1}H NMR.
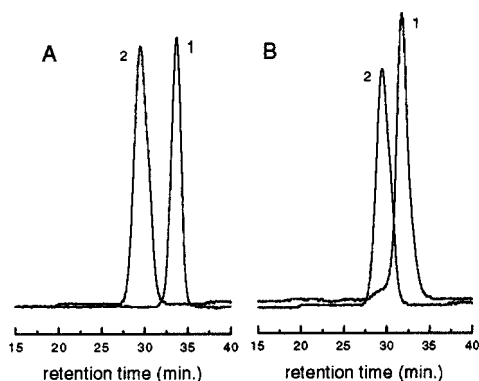

Figure 2. GPC traces of 6-arm starlike block copolymers: A, (1) block poly(*tert*-butyl acrylate) and (2) poly(*tert*-butyl acrylate-*block*-methyl methacrylate); B, (1) poly(methyl methacrylate) and (2) poly(methyl methacrylate-*block*-*tert*-butyl acrylate).
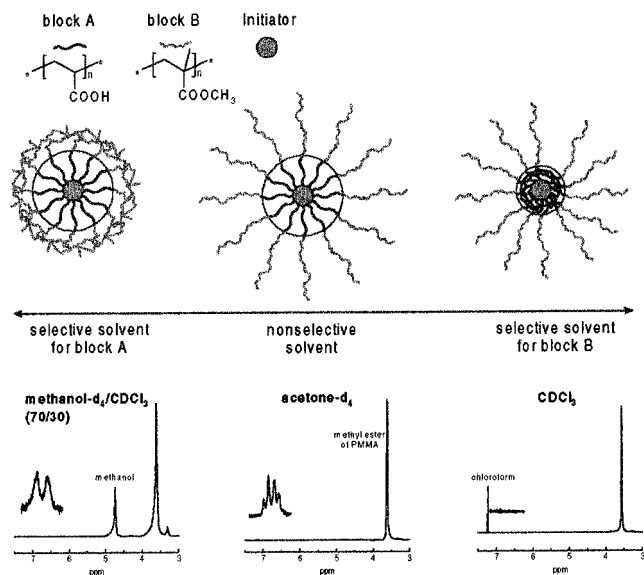

Figure 3. ^{1}H NMR spectra of the starlike poly(acrylic acid-*block*-methyl methacrylate) in different solvents and the schematic description of the proposed changes in molecular geometry of 12-arm starlike polymer in response to the polarity of the solvent. The expanded region of the aromatic protons of the initiator core is shown in the inset.

core as well as a sharp methyl ester peak for the PMMA block can be observed Figure 3. This indicates that both blocks form relatively undisturbed fully extended and solvated conformations. The supermolecular structure of the micelle is, however, preserved

by the covalent attachment of the chains to the initiator core. Chloroform, on the other hand, is a good solvent for the PMMA block, but a poor solvent for the PAA block. Whereas the PMMA block is readily soluble in this solvent and remains in an extended conformation, the signals of the initiator core disappear completely. This effect can be rationalized by the collapse of the PAA block limiting the rotational and diffusional mobility of the protons of the initiator core. By adding about 10 vol % methanol to this solution, one can again restore the core signals in the spectrum. In this solvent mixture, the methanol represents a good solvent for the hydrophilic PAA block, but a poor solvent for the PMMA. Consequently the gradual addition of more methanol causes the PMMA block to begin to collapse whereas the hydophilic PAA block continues to extend. As a result, we observe a significant broadening of the signals assigned to the PMMA block supporting the proposed change in the molecular geometry.[21] Further evidence for the proposed changes in molecular geometry was obtained from similar amphiphilic block copolymers comprising a deuterated PMMA block (MMA-d_5; the methoxycarbonyl substituent is undeuterated). Since the polymer main chain signals of the PMMA block of the deuterated samples are not observed in the ^{1}H NMR spectrum, the signals of the PAA block can be observed directly for this copolymer. In agreement with the earlier interpretation of the change in molecular shape in different solvents based on the initiator core signals, the PAA mainchain resonances can be detected in a solvent mixture of methanol-d_5/CDCl$_3$ (δ 1−2 ppm), whereas in pure CDCl$_3$ these signals are not detectable. In solution, conventional dynamic micelles derived from linear amphiphilic diblock copolymers would be expected to respond to such changes in solvent polarity by forming the reverse micelle. Here, however, the chains are anchored to the core and an inversion of the geometry is impossible.

Preliminary results from light-scattering studies on the amphiphilic star polymers (6-arm: block 1, PAA; block 2, PMMA) are consistent with a unimolecular micelle structure, in the solvents used for the NMR investigation. In these solvents, the hydrodynamic radius (R_H) of the macromolecule ranged from 6 to 7.4 nm with no evidence of formation of higher molecular weight aggregates.

Preliminary results on starlike block copolymers with a reversed arrangement of the amphiphilic blocks also show the expected NMR responses to changes in solvent polarity. The respective 6-arm polymer described in Table 1 which, after deprotection, now comprises a hydrophobic core and a hydrophilic shell is soluble in methanol/chloroform (95/5). In this solvent mixture, no core signals are observed in the ^{1}H NMR spectrum and the methyl ester side chain signals broaden significantly indicating the collapse of the PMMA block. Upon addition of more chloroform, the PMMA block extends as evidenced by the reappearance of the core signals, and the PAA block presumably collapses. However, for this particular polymer configuration, light scattering shows a bimodal size distribution with some evidence of limited aggregate formation (R_H = 140 nm) in addition to the unimolecular micelles (R_H = 7.3 nm).

In conclusion, we have described the synthesis of novel starlike amphiphilic block copolymers with 6- and 12-arms, respectively, with low polydispersities. These polymers show a unique response of the molecular geometry to the polarity of the solvent as indicated by ^{1}H NMR spectroscopy.

(21) The widths at half-height (fwhh) of the methyl ester peak of PMMA block: CDCl$_3$, 4.6 Hz; acetone-d_6, 7.8 Hz; methanol-d_4/CDCl$_3$ (70/30), 13 Hz.