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Poly(vinyl acetate-*b*-vinyl alcohol) Surfactants Derived from Poly(vinyl ester) Block Copolymers

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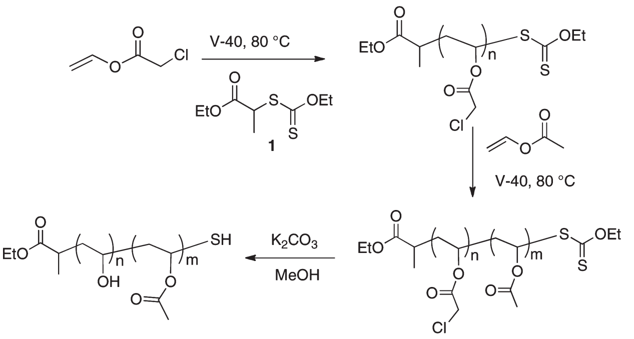
Amphiphilic block copolymers (ABCs) are useful materials in many applications, including the templating and patterning of mesoporous materials and nanomaterials,[1] as rheological modifiers for personal care products[2] and enhanced oil recovery,[3] and in drug delivery.[4−6] Comprised of a hydrophilic block conjoined with a hydrophobic segment, polymer amphiphiles adopt micellar morphologies in dilute solutions that balance the interfacial energies of the solvated polar headgroup and the hydrophobic tail.[2,7] Aqueous dispersions of ABCs adopt myriad complex structures including spherical and disklike micelles, tubular and branched tubular micelles, vesicles, and compound vesicles.[2,5,8,9] Micellar morphologies depend sensitively on the overall polymer molecular weight and polydispersity, composition, functionality, solvent conditions, and the method of dispersion preparation.[5] The minuscule critical micelle concentrations of ABCs kinetically trap persistent micellar aggregates, which dramatically alter the wetting properties and viscosities of the solvent, thus forming the basis of their utility in many applications.

The development of nontoxic and biocompatible ABCs having precisely programmed degradation profiles may unlock their further use in drug delivery, tissue scaffolding, and "green chemistry" applications.[10] The most widely studied nonionic block copolymer surfactants are comprised of a hydrophobic block (e.g., poly(propylene oxide)[11] or polybutadiene[9,12]) and a hydrophilic poly(ethylene oxide) (PEO) block, both of which are not degradable. On the other hand, poly(vinyl acetate) (PVAc) and poly(vinyl alcohol) (PVA) are commodity polymers[13,14] that degrade under environmental and *in vivo* conditions,[15] where PVA exhibits water solubility over a large temperature range[16] and the ability to resist nonspecific protein adsorption in biological environments.[17,18] In spite of these attractive properties, fully degradable block copolymer amphiphiles of the type PVAc-*b*-PVA are unknown due to synthetic complexities associated with incorporating PVAc and PVA into block copolymers.[11,19−29] In this Communication, we describe straightforward syntheses of PVAc-*b*-PVA ABCs with variable compositions and narrow polydispersities and we demonstrate their micellization in aqueous media.

Poly(vinyl ester) block copolymers are differentially protected PVA segments that provide synthetic entry into PVA-based block copolymer surfactants: if the ester moieties in one block are more easily hydrolyzed than in the second block, the more labile esters may be selectively cleaved to unmask a latent PVA block while maintaining the integrity of the second poly(vinyl ester) segment. On this basis, we have extended recent studies of sequential reversible addition−fragmentation chain transfer (RAFT) block copolymerizations of vinyl esters[30,31] to vinyl acetate (VAc) and the electron-deficient vinyl chloroacetate (VClAc) to generate copolymer precursors to PVAc-*b*-PVA (Scheme 1). RAFT polymerization of VClAc at 80 °C in the presence of xanthate **1** using V-40 as a thermal initiator yields relatively monodisperse xanthate-terminated PVClAc-RAFT (M_w/M_n = 1.29−1.41), when [**1**] ~ 55.0 mM and [**1**]:[V-40] ~ 10:1 (Table 1, samples 3−7). RAFT homopolymerizations of VClAc conducted at 60 °C using AIBN initiation were severely retarded as compared to conventional free radical polymerizations, whereas RAFT reactions conducted at 70−80 °C using V-40 initiation resulted in controlled polymerizations with lower observed polydispersities at higher reaction temperatures. We ascribe this behavior to slow fragmentation of the tertiary carbon-centered radical intermediate derived from polymer chain addition to the RAFT agent combined with its "hybrid behavior";[32] similar effects were previously observed in vinyl benzoate RAFT polymerizations.[30] The polydispersity of the resulting PVClAc further decreases with increasing concentration of **1** due to the increased rate of degenerate transfer, also consistent with prior observations for vinyl ester RAFT polymerizations (see Supporting Information Table S1 for representative data).[30] Chain extension RAFT block copolymerization of VAc using the PVClAc macromolecular chain transfer agent proceeds with control at 70−80 °C in $ClCH_2CH_2Cl$ with [PVClAc-RAFT] ~ 5−15 mM, [V-40] ~ 0.3−1.5 mM as a thermal initiator, and [PVClAc-RAFT]:[V-40] ≥ 8.6:1 to yield PVClAc-*b*-PVAc diblock copolymers (Table 1 and Supporting Information Table S2 and Figure S1). Lower polydispersities were generally achieved in these block copolymerizations by increasing [PVClAc-RAFT] and decreasing [V-40] at a reaction temperature of 80 °C, in accord with predictions from known kinetic models of RAFT processes.[33] We found that sequential block copolymerization of VAc followed by VClAc also yields PVAc-*b*-PVClAc diblock copolymers, albeit with slightly broader polydispersities due to the relatively electron-rich nature of the PVAc-RAFT agent that slows macromolecular chain transfer agent initialization (Table 1, entries 1 and 2, and Supporting Information Table S2).[30] Representative size exclusion chromatography (SEC) traces of PVAc-*b*-PVClAc-**2** and PVClAc-*b*-PVAc-**4** demonstrate that these highly efficient chain extension reactions produce unimodal polymers with relatively narrow molecular weight distributions (Supporting Information Figure S1).

Scheme 1. Synthesis of PVA-*b*-PVAc via Selective Hydrolysis of PVClAc-*b*-PVAc



Selective and mild hydrolysis of the chloroacetate esters of the PVClAc-*b*-PVAc and PVAc-*b*-PVClAc diblock copolymers is readily achieved using wet MeOH/K_2CO_3 at 22 °C to yield PVAc-*b*-PVA block copolymers; the rate of chloroacetate ester cleavage is known to be 760 times faster than acetate ester

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Table 1. PVAc/PVA Block Copolymers Synthesized by Selective Hydrolysis of PVAc/PVClAc

	PVAc/PVClAc block copolymers					PVAc/PVA block copolymers	
	initial block[a]		block copolymer			after hydrolysis	
sample[a]	M_n (kg/mol)[b]	M_w/M_n[c]	$M_{n,total}$ (kg/mol)[d]	M_w/M_n[c]	[VClAc][d]	[VA][d]	$M_{n,\,total}$ (kg/mol)[d]
PVAc-*b*-PVClAc-**1**	13.2	1.21	15.1	1.31	0.196		
PVAc-*b*-PVClAc-**2**	10.8	1.23	19.9	1.46	0.375	0.254	12.7
PVClAc-*b*-PVAc-**3**	7.73	1.38	14.2	1.66	0.461	0.390	9.54
PVClAc-*b*-PVAc-**4**	5.48	1.29	9.47	1.31	0.495	0.399	5.48
PVClAc-*b*-PVAc-**5**	9.34	1.34	14.5	1.45	0.565	0.478	7.36
PVClAc-*b*-PVAc-**6**	7.71	1.41	9.81	1.45	0.725		
PVClAc-*b*-PVAc-**7**	9.34	1.31	10.1	1.40	0.901		

[a] Samples are named in the order in which monomers were sequentially block copolymerized by RAFT; see text and Supporting Information for synthetic details. [b] Determined by SEC (see Supporting Information for details). [c] Determined by SEC against poly(styrene) standards. [d] Polymer composition (mol %) calculated from quantitative ^{1}H NMR spectra of the diblock copolymers and the initial block M_n.

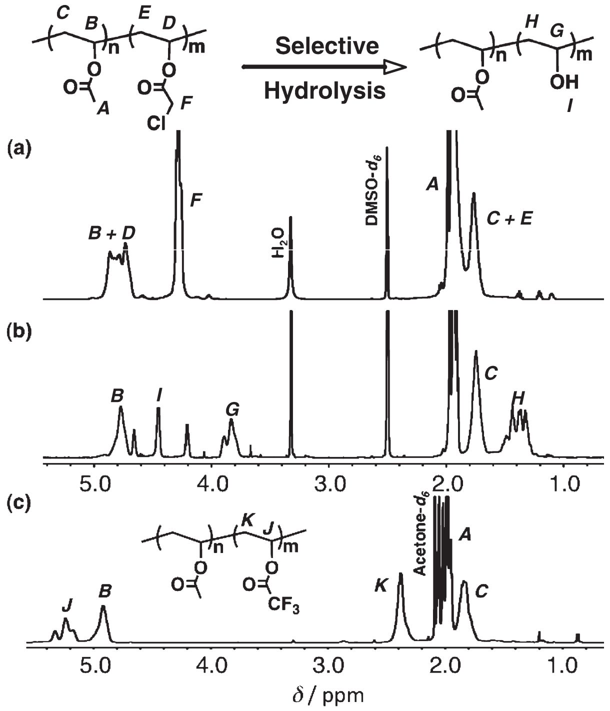

Figure 1. ^{1}H NMR spectra of (a) PVClAc-*b*-PVAc-**5** in DMSO-d_6, (b) PVA-*b*-PVAc-**5** resulting from selective hydrolysis of the vinyl chloroacetate esters in the block copolymer precursor in DMSO-d_6, and (c) PVTFAc-*b*-PVAc-**5** in acetone-d_6 resulting from exhaustive trifluoroacetylation of PVA-*b*-PVAc-**5** using trifluoroacetic anhydride.

cleavage for small molecules.[34] ^{1}H NMR spectra of the initial PVClAc-*b*-PVAc-**5** and the resulting PVA-*b*-PVAc-**5** in DMSO-d_6 indicate quantitative removal of the chloroacetate esters (δ 5.10 and 4.09 ppm) with the appearance of new resonances at δ 4.18, 4.43, and 4.63 ppm associated with the atactic PVA hydroxyl hydrogens (*rr*, *mr*, and *mm* triads), δ 3.81 ppm for the PVA backbone methine hydrogens, and δ 1.40 ppm for the backbone methylene hydrogens (Figure 1a,b).[23] In order to assess the integrity of the PVAc block and to confirm that random hydrolysis of the acetate esters had not occurred, we treated the PVA-*b*-PVAc-**5** with trifluoroacetic anhydride to trifluoroacetylate all hydroxyl functionalities in the polymer. If random hydrolysis of the PVAc occurred, we would expect the trifluoroacetylated polymer to contain random vinyl acetate/vinyl trifluoroacetate comonomer sequences having unique ^{1}H and ^{13}C NMR signatures. ^{1}H NMR spectra of the resulting poly(vinyl trifluoroacetate-*b*-vinyl acetate) (PVTFAc-*b*-PVAc-**5**) in acetone-d_6 clearly resolve the polymer backbone methine protons associated with the PVAc block (δ 4.92 ppm) and the PVTFAc block (δ 5.24 ppm), while *no* peaks having intermediate chemical shifts arising from methine hydrogens associated with vinyl acetate/vinyl trifluoroacetate random copolymer sequences are observed (Figure 1c). Note that the ^{1}H NMR methine hydrogen resonances of the PVTFAc block appear as three peaks due to the atactic polymer stereochemistry (*rr*, *mr*, and *mm* triads), indicating that the polymer tacticity is not altered by trifluoroacetylation. Quantitative inverse-gated decoupled ^{13}C NMR spectroscopy of the PVTFAc-*b*-PVAc also reveals only resonances associated with the constituent homopolymer blocks, confirming our structural assignment. SEC analyses of the trifluoroacetylated polymers using in-line viscometry detection further indicate that the PVAc-*b*-PVTFAc materials are unimodal and that chain scission has not occurred (see Supporting Information Figure S2).

Composition analyses of the resulting PVAc-*b*-PVA copolymers by ^{1}H NMR show that the PVA contents of these amphiphiles are systematically 18−25% *lower* than expected based on the copolymer precursor composition (Table 1). We speculated that VClAc polymerization proceeds with some degree of chain transfer to monomer or polymer $-CH_2Cl$ side chains to yield branched polymers, where the branches are cleaved under our hydrolysis conditions. By analogy to previous studies interrogating the extent of branching in PVAc homopolymers,[33] we assessed the veracity of this hypothesis by studying the hydrolysis of PVClAc homopolymers produced from xanthate-mediated RAFT polymerization of VClAc. A PVClAc homopolymer with M_n = 7.9 kg/mol (degree of polymerization N = 66) and M_w/M_n = 1.43 was hydrolyzed using K_2CO_3/MeOH at 22 °C, and the resulting polymer was then exhaustively acetylated with acetic anhydride to produce PVAc.[35] Absolute molecular weight SEC analysis of this PVAc reveals a major peak associated with a PVAc homopolymer having M_n = 4.4 kg/mol (N = 56) with M_w/M_n = 1.45 and a low molecular weight tail attributable to low molecular weight PVAc oligomers (Supporting Information Figure S3). The observed 17% reduction in the degree of polymerization on transforming PVClAc to PVAc by ester hydrolysis and reacetylation coupled with the appearance of lower molecular weight oligomers suggests that the PVClAc is branched.[36] Various groups have previously suggested the possibility of chain transfer to polymer/monomer chloromethyl groups in free radical polymerizations of VClAc. However, these reports are conflicted in their assessments of the extent of branching;[36−38] our studies are the first to use hydrolytic methods to assess the extent of branching in PVClAc. Attempts to quantify the number of branches using ^{13}C NMR spectroscopy by analogy to previous work on branching in PVAc homopolymers[39] have been thus far unsuccessful. Nonetheless, we attribute the systematically lower than expected PVA content of the PVAc-*b*-PVA block copolymers to chain transfer to polymer during block copolymerization and subsequent hydrolysis of the branches.

Preliminary studies of aqueous dispersions of PVAc-*b*-PVA block copolymers show that they micellize to form unusual

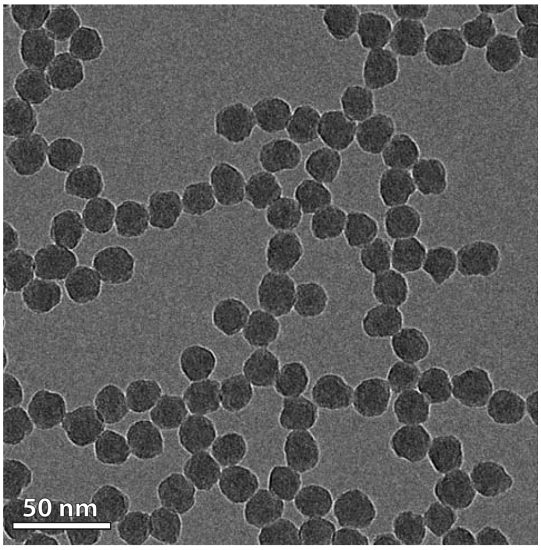

Figure 2. Cryo-TEM image of a solution of 1.0 wt % PVA-*b*-PVAc-**3** in water, indicating the formation of monodisperse irregularly shaped "spherical" micelles with an average diameter d = 18 nm.

morphologies as compared to known PEO-based nonionic surfactants. In order to form a block copolymer micelle dispersion, we added water dropwise to a rapidly stirred methanol solution of PVA-*b*-PVAc-**3** at 22 °C and dialyzed the resulting 1.0 wt % polymer solution to remove the organic solvent as previously reported.[40] Cryogenic transmission electron microscopy (cryo-TEM) imaging of this vitrified micellar dispersion revealed the formation of irregularly shaped micelles (Figure 2). We hypothesize that the observed irregular structures result from strong hydrogen bonding and local crystallization of the hydrophilic PVA corona blocks at the block interface that help to shield the hydrophobic PVAc micellar core. Since the micelles appear to aggregate into strands, dynamic light scattering studies are underway to ascertain whether or not these aggregates persist in solution by virtue of intermicellar hydrogen bonding between PVA corona blocks.

In summary, we have described a straightforward synthesis of well-defined, fully degradable block copolymer amphiphiles comprised of a hydrophobic PVAc block and a hydrophilic PVA segment by exploiting the differential hydrolytic stability of various vinyl ester homopolymer segments in poly(vinyl ester) block copolymers. Poly(vinyl ester-*b*-vinyl alcohol) block copolymers self-assemble in aqueous media to form micellar aggregates with somewhat irregular shapes, likely as a result of hydrogen bonding in the corona segments of these macromolecular amphiphiles. We are currently studying the phase behavior of these poly(vinyl ester-*b*-vinyl alcohol) diblock copolymers in order to understand the morphological consequences of strongly hydrogen bonding hydrophilic blocks, while also exploring their potential for micellar aggregation and supramolecular self-assembly.

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Supporting Information Available: Detailed polymerization and characterization procedures and sample SEC traces. This material is available free of charge via the Internet at http://pubs.acs.org.

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