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Synthesis of Controlled Structure Water-Soluble Diblock Copolymers via Oxyanionic Polymerization

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Introduction. There is growing interest in hydrophilic−hydrophilic diblock copolymers. Such copolymers can (i) exhibit reversible micellization behavior in aqueous solution,[1−3] (ii) act as dispersants for a wide range of pigments,[4] (iii) influence the crystallization of inorganic materials such as $CaCO_3$,[5] (iv) be utilized for the synthesis of novel shell cross-linked micelles with hydrophilic cores,[6] and (v) have biomedical applications.[7]

We have had a long-standing interest in water-soluble diblock copolymers, particularly those based on 2-(dimethylamino)ethyl methacrylate (DMAEMA).[8−10] We have recently reported several new classes of hydrophilic−hydrophilic block copolymers based on DMAEMA.[9,10] Such copolymers dissolve molecularly as unimers in aqueous solution at 25 °C without the aid of a cosolvent and undergo reversible micellization on altering the solution temperature or pH. A long-term goal of our research program is to study the kinetics of micellization and demicellization of such copolymers.

Recently Nagasaki et al. reported that 2-(di*ethyl*amino)ethyl methacrylate (DEAEMA) can be polymerized at ambient temperature using simple alcoholate initiators such as potassium ethoxide.[11] The Japanese group suggested that the nitrogen heteroatom of the DEAEMA monomer played a crucial role in its polymerization by forming a coordination complex with the potassium cation, thus making the oxyanion more reactive. Although the precise mechanism remains unclear, we have polymerized various tertiary amine methacrylates using functional potassium alcoholate initiators in order to obtain well-defined macromonomers.[12] We have termed this synthetic route "oxyanionic polymerization". Herein we report the use of monohydroxy-capped poly(alkylene oxide)s as macroinitiators for the polymerization of the following tertiary amine methacrylates (see Figure 1): DMAEMA, DEAEMA, 2-(*N*-morpholino)ethyl methacrylate (MEMA), and 2-(di*iso*propylamino)ethyl methacrylate (DPAEMA). This is an attractive synthetic route to novel hydrophilic-hydrophilic diblock copolymers which have interesting aqueous solution properties. Furthermore, other workers have demonstrated that related neutral−cationic block copolymers form colloidal aggregates with DNA and therefore have some potential as novel vectors for gene therapy applications.[13]

Experimental Section. The monohydroxy-capped poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO) were donated by Inspec U.K. GPC analyses gave M_w/M_n's of 1.10 for PEO and 1.17 for the PPO; degrees of polymerization were either 22 or 45 for PEO and 36 for the PPO. In a typical synthesis, PEO (5.0 g) dissolved in 100 mL of dry THF was added to a round-bottomed flask under dry nitrogen. Potassium naphthalene (2.50 mmol) in THF was added via a double-tipped needle, and the reaction solution was stirred at 30 °C for 1−2 h to form the alcoholate macro-initiator. Freshly distilled tertiary amine methacrylate (5−15 mL) was added, and the polymerization was allowed to proceed for 4 h prior to quenching with methanol. In some cases the polymerizations were conducted at 35 or 50 °C. Solvent was removed under vacuum, the copolymer was redissolved in dilute HCl, and the water-insoluble naphthalene was removed by filtration. High yields (95−100%) and good control over copolymer molecular weight were obtained for the polymerization of all four tertiary amine methacrylate monomers.

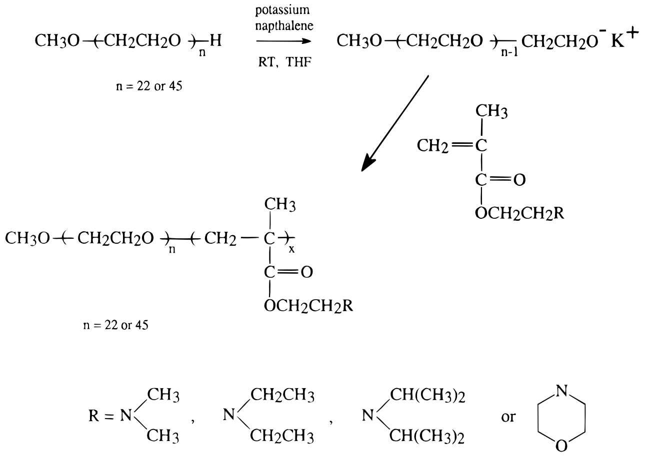

Figure 1. Reaction scheme for the synthesis of poly(ethylene oxide−tertiary amine methacrylate) diblock copolymers.

Results and Discussion. GPC analyses (PMMA standards, THF eluent, refractive index detector) of the crude diblock copolymers generally indicated some PEO homopolymer contamination, albeit at a low level (typically 5−10%). However, heating aqueous alkaline solutions (pH 12) of the crude copolymer mixture to 90 °C led to quantitative precipitation of the diblock copolymer, with the PEO homopolymer impurity remaining in solution (verified by control experiments). Subsequent GPC analyses of the purified block copolymers confirmed that the molecular weight distributions were relatively narrow (M_w/M_n = 1.23−1.34) and that the PEO homopolymer had been removed. This cleanup procedure also demonstrated that genuine block copolymer formation had occurred, i.e., that the PEO macroinitiator was covalently attached to the poly(DMAEMA) block. Block copolymer compositions were determined by proton NMR spectroscopy. The peak integral of the signal assigned to the ethylene oxide residues at δ 3.6 (or the terminal methoxy group at δ 3.3) was compared to those due to the oxyethylene protons of the methacrylate residues in order to determine the degree of polymerization of the tertiary amine methacrylate block. Such calculations gave absolute number-average molecular weights, which are compared to the GPC data in Table 1.

The PEO−DMAEMA block copolymers had cloud points in the 60−80 °C range, as indicated by turbidimetry. Prior to precipitation, some of these block copolymers undergo micellization. Variable temperature pro-

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Table 1. Summary of the Molecular Weights, Polydispersities, and Block Copolymer Compositions of a Series of Poly(alkylene oxide−tertiary amine methacrylate)s Synthesized Using Oxyanionic Polymerization

block copolymer	polym temp (°C)	copolym comp[a] theor	copolym comp[a] actual	M_n by ^{1}H NMR	M_n by GPC[b]	M_w/M_n[b]
PEO2000−DMAEMA[c]	35	45−11	45−12	3900	6400	1.23
PEO1000−DMAEMA[c]	35	22−12	22−17	3700	9900	1.34
PEO2000−DMAEMA	30	45−33	45−37	7800	9300	1.24
PEO2000−DMAEMA	30	45−38	45−50	9800	9900	1.33
PEO2000−DEAEMA	35	45−30	45−34	8300	13600	1.33
PEO2000−MEMA	35	45−32	45−38	9600	12400	1.34
PEO2000−DPAEMA	50	45−17	45−19	6000	6900	1.27
PEO2000−DPAEMA	35	45−26	45−37	9900	9400	1.29
PPO2000−DMAEMA	50	33−23	33−28	6400	12000	1.35

[a] Degrees of polymerization of each block (PEO or PPO first). The experimental values were determined by ^{1}H NMR spectroscopy. [b] Calibrated with poly(methyl methacrylate) standards, THF eluent, RI detector. [c] In this case KH was used as the base in the macroinitiator synthesis, rather than the potassium naphthalene complex.

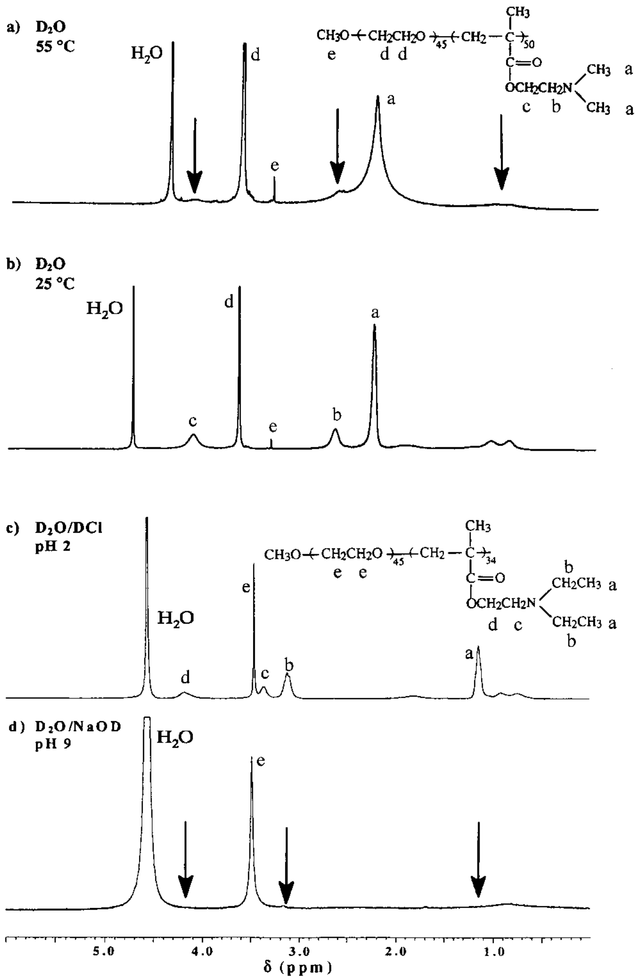

Figure 2. Proton NMR spectra for (a) a micellar solution of a 45−50 PEO−DMAEMA diblock copolymer at 55 °C in D$_2$O, (b) the same PEO−DMAEMA diblock copolymer at 25 °C (note the increased relative intensities of the re-solvated DMAEMA residues), (c) a 45−34 PEO−DEAEMA diblock copolymer in DCl/D$_2$O (pH 2), and (d) a micellar solution of the same copolymer at pH 8 (note the complete disappearance of the DEAEMA residues, indicating fully dehydrated micelle cores).

ton NMR studies of a 45−50 PEO−DMAEMA copolymer (see Figure 2a) confirmed that the signals assigned to the DMAEMA residues (at δ 2.3−2.4, δ 2.6−2.7, and δ 4.1−4.2) broadened at 55 °C and became much less intense relative to the PEO signal (at δ 3.6−3.7). This is consistent with the formation of micelles with DMAEMA cores and PEO coronas. Since the DMAEMA signals do not disappear, the micelles must retain some degree of hydration. When the solution was cooled to room temperature, the original NMR spectrum was observed (see Figure 2b). This confirms that copolymer aggregation is reversible. Similar observations were reported by Lowe et al. for the micellization of DMAEMA−methacrylic acid block copolymers.[10] For the PEO−DEAEMA block copolymers, micellization can be induced at room temperature simply by adjusting the solution pH. A proton NMR spectrum of a 45−34 PEO−DEAEMA block copolymer dissolved in DCl/D$_2$O (pH 2) is shown in Figure 2c. Under these conditions the copolymer is in its "unimer" state: both blocks are solvated since the DEAEMA block is fully protonated and behaves as a cationic polyelectrolyte. However, on adjusting this solution to pH 9 the DEAEMA residues are deprotonated and become hydrophobic. Thus the NMR signals due to this block disappear, indicating formation of fully dehydrated micelle cores (see Figure 2d). Again, similar observations were made for betainized DMAEMA−DEAEMA diblock copolymers by Bütün et al.[3] Dynamic light scattering studies indicate intensity-average micelle diameters of around 20−30 nm for both the PEO−DMAEMA and PEO−DEAEMA block copolymers.

Several research groups have investigated the possibility of using water-dispersible or water-soluble diblock copolymers in place of conventional small-molecule surfactants for latex syntheses via emulsion polymerization.[14] The above observations suggest that the nature of the micelle interior may be an important consideration in such syntheses. Thus, dehydrated micelle cores are likely to be a better locus for the polymerization of relatively hydrophobic, water-insoluble monomers such as styrene or MMA than relatively hydrated micelle cores.

Finally, we note that novel, well-defined DMAEMA−PPO diblock copolymers can also be synthesized by the same synthetic route (see the final entry in Table 1). These new well-defined poly(alkylene oxide−tertiary amine methacrylate)s are interesting polyelectrolytic analogues[15] for the well-known PEO−PPO diblock and triblock copolymers. Initial studies confirm that these new copolymers have interesting aqueous solution properties, e.g., reversible temperature- or pH-induced micellization in aqueous solution.

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