Facile Synthesis of Well-Defined Hydrophilic Methacrylic Macromonomers Using ATRP and Click Chemistry

Paul D. Topham,*,† Nicolas Sandon,‡ Elizabeth S. Read,‡ Jeppe Madsen,‡ Anthony J. Ryan,‡ and Steven P. Armes‡

School of Chemical Engineering and Applied Chemistry, Aston University, Birmingham, B4 7ET, U.K., and Department of Chemistry, University of Sheffield, Sheffield, S3 7HF, U.K.

Received September 1, 2008; Revised Manuscript Received October 8, 2008

ABSTRACT: A range of well-defined hydrophilic methacrylic macromonomers has been synthesized by the judicious combination of atom transfer radical polymerization (ATRP) and copper-catalyzed 1,3-dipolar cycloaddition (azide−alkyne click chemistry). An azido α-functionalized ATRP initiator was used to produce well-defined homopolymers with terminal azide functionality via ATRP in protic media at 20 °C, with generally good control being achieved over both target molecular weight and final polydispersity ($M_w/M_n = 1.10-1.35$). Suitable methacrylic monomers include 2-aminoethyl methacrylate hydrochloride, 2-(diethylamino)ethyl methacrylate, 2-(dimethylamino)ethyl methacrylate, 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, 2-(methacryloyloxy)ethyl phosphorylcholine, glycerol monomethacrylate, potassium 3-sulfopropyl methacrylate, and quaternized 2-(dimethylamino)ethyl methacrylate. These homopolymer precursors were then efficiently clicked using either propargyl methacrylate or propargyl acrylate to yield near-monodisperse (meth)acrylate-capped macromonomers with either cationic, anionic, nonionic, or zwitterionic character. Moreover, this generic route to well-defined hydrophilic macromonomers is also suitable for "one-pot" syntheses, as exemplified for 2-hydroxyethyl methacrylate and glycerol monomethacrylate-based macromonomers.

Introduction

Macromonomers are polymer chains that contain at least one polymerizable group.[1] Many macromonomers contain a terminal vinylic group that can be (co)polymerized to produce sterically stabilized latexes,[2−4] graft copolymers,[5−9] or "bottle brush" polymers.[10−13] There are two general synthetic routes to vinyl-capped macromonomers: either an appropriate vinyl-functionalized initiator is used or the chain ends are modified after polymerization. The former approach has been exploited by both Nagasaki's group[14] and Lascelles et al.[15] for the synthesis of well-defined styrene-functionalized macromonomers. In both cases oxyanion-initiated polymerization of tertiary amine methacrylates in dry tetrahydrofuran (THF) was conducted using a potassium 4-vinylbenzyl alkoxide initiator. Similar selectivity has also been demonstrated for the atom transfer radical polymerization (ATRP) of both hydrophilic and hydrophobic monomers using allyl-, vinyl acetate-, or vinyl ether-based initiators.[16−18] This approach has the advantage of being a one-step process but is severely limited in the choice of terminal vinyl groups since these moieties must not participate in the in situ polymerization. In principle, postpolymerization modification is much more versatile, allowing access to a large range of different macromonomers. For example, monomethoxy-capped poly(ethylene glycol) monomethacrylate, which is commonly used to prepare sterically stabilized latexes and graft copolymers, is readily prepared on an industrial scale by transesterification using monohydroxy-capped poly(ethylene glycol) and methyl methacrylate. ATRP has also been used to produce macromonomers by reacting terminal bromine atoms with either acrylic or methacrylic groups.[19] An alternative strategy is to use an initiator which contains a functional group that can be reacted to form a polymerizable group after in situ polymerization.[20−25] This usually leads to higher efficiencies than those achieved by substitution of terminal halogen atoms, since the fidelity of the latter functionality is often compromised under monomer-starved conditions. Catalytic chain transfer polymerization (CCTP) based on highly efficient cobalt catalysts can be a very effective and scalable route for the preparation of relatively *polydisperse* macromonomers ($M_w/M_n > 1.77$).[26] Recently ATRP has been combined with CCTP in order to obtain macromonomers with lower polydispersities ($M_w/M_n < 1.5$).[27] However, the terminal methacrylic groups generated by CCTP exhibit nonideal behavior when copolymerized with conventional vinyl monomers and also tend to be prone to fragmentation side reactions.[28]

Click chemistry[29,30] is a set of highly efficient and orthogonal organic reactions that offer high selectivity, excellent tolerance toward functional groups, and no extraneous side products. More specifically, 1,3-dipolar cycloaddition between terminal alkyne and azide groups produces 1,4-disubstituted 1,2,3-triazoles. The extent of reaction can be conveniently monitored by various analytical techniques because the product contains a heteroaromatic ring that is not present in the starting material. There are a plethora of examples of click chemistry now being exploited in polymer science.[30−39] In particular, Vogt and Sumerlin[40] have combined RAFT polymerization with click chemistry to produce a range of new hydrophobic macromonomers. However, there are still very few literature examples of the synthesis of *well-defined macromonomers based on hydrophilic/water-soluble monomers*. This omission is perhaps surprising, since such building blocks are expected to be of particular interest for the synthesis of sterically stabilized latexes with well-defined surface chemistry, which is expected to be a key factor in determining their interfacial activity for the stabilization of emulsions[41] and foams[42−44] and the preparation of colloidosomes.[45]

In the present work we have combined ATRP with click chemistry to yield a wide range of hydrophilic methacrylic macromonomers with either methacrylic or acrylic terminal groups. Thus, the ATRP of 2-aminoethyl methacrylate hydrochloride (AMA), 2-(diethylamino)ethyl methacrylate (DEA), 2-(dimethylamino)ethyl methacrylate (DMA), 2-hydroxyethyl methacrylate (HEMA), 2-hydroxypropyl methacrylate (HPMA), 2-(methacryloyloxy)ethyl phosphorylcholine (MPC), glycerol

* To whom correspondence should be addressed. E-mail: p.d.topham@aston.ac.uk.
† Aston University.
‡ University of Sheffield.

10.1021/ma8019656 CCC: $40.75
Published on Web 11/14/2008

monomethacrylate (GMA), potassium 3-sulfopropyl methacrylate (KSPMA), and methyl chloride-quaternized 2-(dimethylamino)ethyl methacrylate (QDMA) was conducted in turn in protic media at room temperature using an azido-functionalized initiator, and the resulting nine homopolymer precursors were then reacted with propargyl (meth)acrylate to afford the desired well-defined methacrylic macromonomers.

Experimental Section

Materials. AMA monomer, 3-azidopropyl 2-bromoisobutyrate (APBIB) ATRP initiator, and propargyl methacrylate were each synthesized as described in the literature.[39,46,47] DEA (99%) and DMA (98%) (both purchased from Aldrich) were passed through a basic alumina column prior to use. HEMA, HPMA, and GMA were kindly provided by Cognis Performance Chemicals U.K. Ltd. MPC (99.9%) was donated by Biocompatibles Ltd., U.K. 4-Hydroxy-TEMPO was donated by A. H. Marks, Bradford, U.K. 2,2-Diphenyl-1-picrylhydrazyl (DPPH), copper(I) bromide (Cu(I)Br, 99.999%), copper(I) chloride (Cu(I)Cl, 99.995%), 2,2′-bipyridine (bpy, 99+ %), *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDETA, 99%), methanol (MeOH, anhydrous grade, 99.8%), KSPMA (98%), propan-2-ol (iPA, anhydrous grade, 99.5%), and propargyl acrylate (98%) were all purchased from Aldrich. Copper powder (99+ %) was purchased from Alfa Aesar, and methyl chloride-quaternized QDMA was provided as a 75 w/w % concentrated aqueous solution by Elf Atochem, France. Regenerated cellulose dialysis membrane (1000 MWCO) was purchased from Spectra/Por, and silica gel 60 (0.063−0.200 mm) was obtained from E. Merck, Germany. All chemicals were used as received. Deionized water was used in all experiments. NMR solvents (CD_3OD and D_2O) were purchased from Fisher.

ATRP Protocol. The following example describes the synthesis of an azide-functionalized poly(2-(diethylamino)ethyl methacrylate) [$PDEA_{10}N_3$] precursor; this protocol is representative of all other homopolymerizations. APBIB (135 mg, 1.0 equiv) was added to a clean, dry flask equipped with a magnetic follower and a rubber septum. Methacrylic monomer (10−100 mol equiv relative to APBIB corresponding to the target degree of polymerization, D_p) and bpy (169 mg, 2.0 equiv) were added to this flask, which was then evacuated and purged with nitrogen three times prior to the addition of dry solvent (iPA, 1.4 mL, 50% w/v). The vessel was purged with nitrogen for a further 5 min, then either Cu(I)Cl (53 mg, 1.0 equiv) or Cu(I)Br (77 mg) was introduced to begin the polymerization. After the appropriate polymerization time, termination was achieved by adding excess MeOH. Various purification protocols were examined to remove the spent ATRP catalyst due to the wide range of different macromonomers. PAMA, PGMA, and PQDMA homopolymers were dissolved in MeOH and subsequently dialyzed against water. After 72 h, the aqueous polymer solutions were freeze-dried overnight. Reaction solutions for the other homopolymers were diluted with MeOH (or water, in the case of PKSPMA) and purified using silica chromatography.

Click Chemistry Protocol. The following example describes the click reaction between $PDEA_{10}N_3$ and propargyl methacrylate; this is representative of all other "two-pot" macromonomer syntheses. Azide-functionalized polymer (1.0 g, 1.0 equiv), 4-hydroxy-TEMPO (90 mg, 1.1 equiv), and Cu(I)Br (136 mg, 2.0 equiv) were added to a clean, dry flask equipped with a magnetic follower and a rubber septum. The flask was then evacuated and purged with nitrogen three times, before anhydrous MeOH (4.5 mL) was added to give a 25 w/v % solution, and the vessel was purged with nitrogen for a further 5 min. Once complete dissolution had been achieved, PMDETA (238 μL, 2.4 equiv) was introduced to the reaction vessel via the rubber septum using a syringe, followed by propargylmethacrylate (60 μL, 1.1 equiv). The reaction solution was stirred under a positive nitrogen pressure. After 24 h, Cu(0) (60 mg, 2.0 equiv) was added to the reaction mixture, which was then stirred for a further 24 h. Methanol was added to quench the reaction, and the crude product was then dialyzed against water for 72 h. This cleanup protocol was sufficient for most of the macromonomers. However, PHEMA, PHPMA, and PKSPMA macromonomers required further purification by silica chromatography, using MeOH eluent (or water, in the case of the PKSPMA macromonomer). Overall gravimetric yields ranged from 86% to 98%.

"One-Pot" Macromonomer Synthesis. The following example describes the synthesis of $PHEMA_{10}$ methacrylate ($PHEMA_{10}MA$); this is representative of the "one-pot" macromonomer syntheses (the other example being) ($PGMA_{10}MA$). APBIB (192 mg, 1.0 equiv) was added to a clean, dry flask equipped with a magnetic follower and a rubber septum. Methacrylic monomer (1.00 g; 10 mol equiv relative to APBIB, corresponding to a target D_p of 10) and bpy (240 mg, 2.0 equiv) were added to this flask, which was then evacuated and purged with nitrogen three times prior to the addition of dry solvent (MeOH, 1.5 mL, 50% w/v). The vessel was purged with nitrogen for a further 5 min, then Cu(I)Br (110 mg, 1.0 equiv) was introduced to begin the polymerization. After 5 h, a 100 μL aliquot was extracted for gel permeation chromatography (GPC) and ^{1}H NMR analyses before 4-hydroxy-TEMPO (146 mg, 1.1 equiv) and anhydrous MeOH (3.0 mL, 25% w/v total solution) were added under nitrogen. Propargyl methacrylate (159 μL, 1.1 equiv) was added via syringe, and the click reaction was allowed to proceed at 20 °C for 48 h. Cu(0) (49 mg, 1 equiv) was added after 24 h. Each of these macromonomers was purified as described in the "two-pot" protocol described above. In the case of the GMA-based macromonomer, the catalyst was Cu(I)Cl.

Characterization. For ^{1}H NMR analysis, the homopolymer precursor or macromonomer was dissolved in an appropriate deuterated solvent (10.0% w/w) for subsequent analysis using a 250, 400, or 500 MHz Bruker spectrometer. All chemical shifts refer to samples run in CD_3OD unless otherwise stated. FT-IR spectroscopy studies were conducted using a Perkin-Elmer Spectrum, RX I FT-IR system with a diamond ATR crystal. Absorption spectra were recorded directly from powders (256 scans per spectrum at a resolution of 4 cm^{-1}).

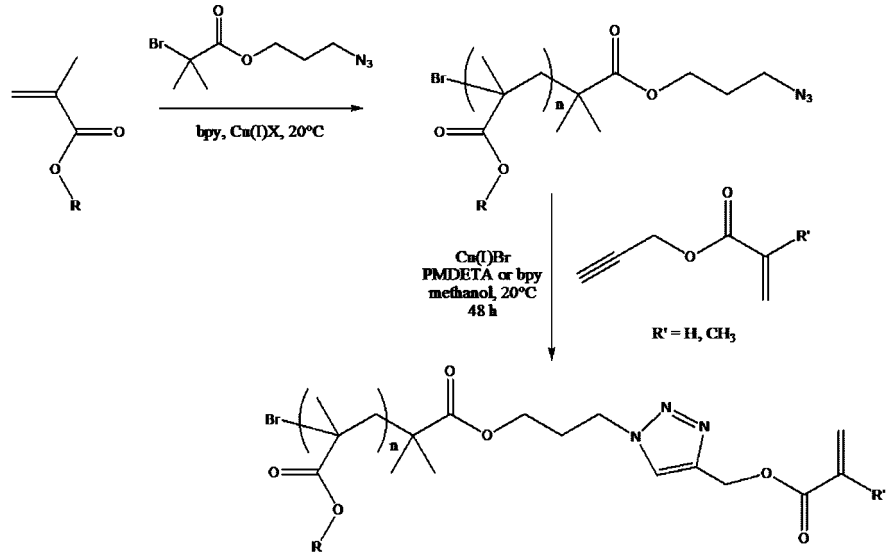
Chloroform/Methanol GPC. The molecular weights (M_n) and polydispersities (M_w/M_n) of PMPC homopolymer precursors and macromonomers were assessed using a Hewlett-Packard HP1090 liquid chromatograph as the pumping unit and two Polymer Laboratories PL Gel 5 μm mixed-C 7.5 mm × 300 mm columns in series with a guard column at 40 °C connected to a Gilson model 131 refractive index detector. The eluent was a 3:1 v/v % chloroform/MeOH mixture containing 2 mM LiBr at a flow rate of 1.0 mL min^{-1}. A series of near-monodisperse poly(methyl methacrylate) (PMMA) standards were used for calibration (M_p = 2000−300 000 g mol^{-1}). Toluene (2 μL) was added to all samples as a flow rate marker.

THF GPC. The molecular weights and polydispersities of PDEA, PDMA, and PHPMA homopolymer precursors and the corresponding macromonomers were assessed by THF GPC. The GPC setup comprised two Polymer Laboratories PL gel 5 μm mixed-C columns. The GPC eluent was HPLC grade THF containing 2.0% (v/v) TEA and 0.05% (w/v) BHT at a flow rate of 1.0 mL min^{-1}. The column temperature was set at 30 °C. Ten near-monodisperse PMMA standards (M_p = 2000−300 000 g mol^{-1}) were used for calibration. The data were analyzed using PL Cirrus GPC software (version 2.0) supplied by Polymer Laboratories.

DMF GPC. The molecular weights and polydispersities of the PGMA and PHEMA homopolymer precursors and the corresponding macromonomers were determined by dimethylformamide (DMF) GPC at 70 °C. The GPC setup comprised three Polymer Laboratories PL gel 10 μm mixed-B columns in series with a Viscotek TriSEC model 302 refractive detector. The flow rate was 1.0 mL min^{-1}, and the mobile phase contained 10 mmol of LiBr. Ten near-monodisperse PMMA standards (M_p = 2000−300 000 g mol^{-1}) were used for calibration. The data were analyzed using Viscotek TriSEC 3.0 software.

Aqueous GPC (Low-pH Buffer). The molecular weights and polydispersities of the PAMA and PQDMA homopolymer precursors and the corresponding macromonomers were determined by aqueous GPC at 35 °C using a PL Aquagel-OH 40 and a PL

Scheme 1. Synthesis of Well-Defined Hydrophilic Macromonomers Using APBIB as an ATRP Initiator, Followed by Click Chemistry with Propargyl(meth)acrylate[a]



R = $CH_2CH_2NH_2$·HCl for AMA, $CH_2CH_2N(CH_3)_2$ for DMA, $CH_2CH_2N^+(CH_3)_3$·Cl^- for QDMA, $CH_2CHOHCH_2OH$ for GMA, CH_2CH_2O-(PO_2^-)-$OCH_2CH_2N^+(CH_3)_3$ for MPC, CH_2CH_2OH for HEMA, $CH_2CH_2CH_2SO_3^-K^+$ for KSPMA, $CH_2CHOHCH_3$ for HPMA and $CH_2CH_2N(CH_2CH_3)_2$ for DEA.

[a] Both steps can be conveniently conducted in a one-pot synthesis, in which the ATRP catalyst also acts as a click catalyst.

Table 1. Summary of Reaction Conditions, Molecular Weight Data, and Monomer Conversions for the Homopolymerization of Various Methacrylic Monomers Using APBIB as an ATRP Initiator in Protic Media

monomer type	target D_p	solvent composition	catalyst[a]	time h	M_n g mol^{-1}	M_w/M_n	conversion %[b]
MPC	20	MeOH	CuBr	2.5	13 000[c]	1.14[c]	100
MPC	40	MeOH	CuBr	3.0	15 000[c]	1.21[c]	100
AMA[d]	20	4:1 iPA/water	CuBr	7.0	3400[e]	1.14[e]	100
AMA[d]	40	4:1 iPA/water	CuBr	16.0	6500[e]	1.18[e]	100
AMA[d]	50	4:1 iPA/water	CuBr	18.5	6600[e]	1.15[e]	100
DMA	10	iPA	CuBr	7.0	7200[f]	1.20[f]	99
DMA	20	iPA	CuBr	6.25	6900[f]	1.34[f]	100
QDMA	20	3:1 water/MeOH	CuBr	15	4400[e]	1.19[e]	100
GMA	10	MeOH	CuCl	1.33	5500[f]	1.19[f]	100
GMA	40	MeOH	CuCl	5.0	11 000[g]	1.21[g]	96
HEMA	10	MeOH	CuCl	5.0	3000[g]	1.25[g]	98
HEMA	20	MeOH	CuCl	5.0	7000[g]	1.24[g]	98
KSPMA	20	5:2 MeOH/water	CuBr	16.5	20 000[h]	1.18[h]	100
HPMA	20	19:1 iPA/water	CuCl	6.0	5100[f]	1.21[f]	100
DEA	10	iPA	CuCl	8.0	5100[f]	1.19[f]	100
DEA	100	iPA	CuCl	48.0	21 000[f]	1.28[f]	91

[a] bpy was used as the ligand in all cases. [b] Calculated by ^{1}H NMR spectroscopy. [c] 3:1 chloroform/MeOH eluent, 2 mM LiBr, PMMA standards. [d] These three AMA syntheses were conducted at 50 °C; all other polymerizations were conducted at 20 °C. [e] Aqueous eluent comprising 0.5 M acetic acid, 0.3 M NaH_2PO_4 (pH 2), P2VP standards. [f] THF eluent, 2.0% triethylamine, 2.3 mM BHT, PMMA standards. [g] DMF eluent, 10 mM LiBr, PMMA standards. [h] Mixed aqueous eluent comprising 70% aqueous 0.2 M $NaNO_3$/0.01 M NaH_2PO_4 at pH 7 + 30% MeOH cosolvent, PNaStS standards.

Aquagel-OH 30 column connected in series to a Polymer Laboratories ERC-7517A refractive index detector. The eluent was a pH 3.3 buffer solution comprising 0.30 M NaH_2PO_4 and 1.0 M acetic acid at a flow rate of 1.0 mL min^{-1}. Eight near-monodisperse poly(2-vinylpyridine) standards (M_p = 1480−117 000 g mol^{-1}) were used for calibration. The data were analyzed using PL Cirrus GPC software (version 2.0) supplied by Polymer Laboratories.

Aqueous GPC (Neutral pH Buffer). The molecular weights and polydispersities of the PKSPMA homopolymer precursors and the corresponding macromonomers were determined by aqueous GPC using a PL Aquagel-OH 40 and a PL Aquagel-OH 30 column connected in series to a Polymer Labs ERC-7517A refractive index detector. The eluent was 70% 0.2 M $NaNO_3$ and 0.01 M NaH_2PO_4 (adjusted to pH 7 with 5 M NaOH) and 30% MeOH cosolvent at a flow rate of 1.0 mL min^{-1}. The GPC columns were calibrated using ten poly(sodium 4-styrenesulfonate) (PNaStS) homopolymer standards (M_p = 1100−208 000 g mol^{-1}).

Results and Discussion

The overall two-step reaction scheme for the synthesis of the nine hydrophilic methacrylic macromonomers is shown in Scheme 1. Eight methacrylic monomers were polymerized using APBIB and a Cu(I)X/2bpy catalyst in protic media at 20 °C (see Table 1). A ninth monomer (AMA) was polymerized under the same conditions, but at 50 °C.[46] The advantage of using such an azido-functional initiator is that all of the chain ends are guaranteed to be functionalized. In contrast, conversion of terminal halogen atoms to azides[35,48−53] is unlikely to be as effective due to the gradual loss of chain-end functionality under monomer-starved conditions.[54−60]

As expected, Table 1 confirms that all nine monomers were polymerized with good control using the APBIB initiator, with high monomer conversions (≥91%) and low polydispersities (≤1.34) being achieved. Monomers were deliberately chosen

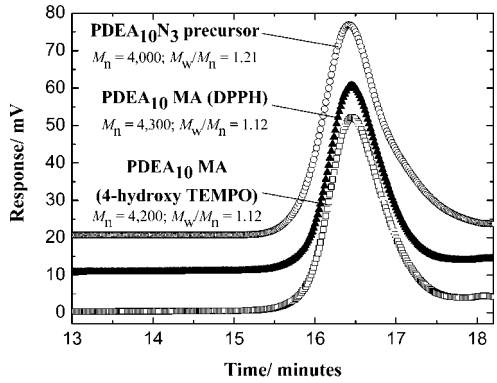


Figure 1. THF GPC chromatograms recorded for (top) azide-functionalized poly(2-(diethylamino)ethyl methacrylate) precursor [$PDEA_{10}N_3$]; (middle) after click reaction with propargyl methacrylate in the presence of DPPH; (bottom) after click reaction with propargyl methacrylate in the presence of 4-hydroxy-TEMPO. The upper two traces have been translated along the response axis to aid comparison.

to include cationic (AMA, DEA, DMA, and QDMA), anionic (KSPMA), zwitterionic (MPC), and nonionic (HEMA, HPMA, and GMA) functionality in order to assess the scope and generality of this synthetic route. These four monomer classes will in turn confer a range of aqueous solution properties on the target macromonomers.

Degrees of polymerization were targeted by adjusting the monomer/APBIB molar ratio, affording azide-functional homopolymer precursors of varying chain lengths. The target D_p and experimental D_p (calculated from ^{1}H NMR) data are included as Supporting Information, Table S1. Presence of the terminal azide group was confirmed by a weak band at 2100 cm^{-1} in the corresponding FT-IR spectra (which is available as Supporting Information, see Figures S1−S4). In principle, access to a wide range of macromonomers should allow the synthesis of well-defined sterically stabilized latexes with tunable stabilizer layer thicknesses.

As noted by Mantovani et al.,[39] and more recently by Mespouille et al.,[61] the copper catalyst required for the ATRP of methacrylic monomers is also suitable for the subsequent click reaction. In principle, it is possible for the alkyne (meth)acrylate reagent to act as a vinyl monomer and to simply add to the bromine-capped homopolymer chains, rather than react with the terminal azide group at the opposite chain end in the desired click reaction. However, there is only approximately one alkyne (meth)acrylate per chain, so this reaction is relatively unlikely due to the low monomer concentration. It is also noteworthy that, since the click chemistry is performed in the absence of oxygen, there is some risk of inadvertent in situ radical polymerization of the alkyne (meth)acrylate precursor, or indeed the final macromonomer, even for protocols conducted at ambient temperature. This problem is exemplified in Figure 1, which shows GPC data for the click reaction of an azide-functionalized $PDEA_{10}N_3$ (M_n = 4000; M_w/M_n = 1.21) with propargyl methacrylate in the presence of two radical inhibitors, either 4-hydroxy-TEMPO or DPPH. In the absence of any inhibitor, an insoluble polymeric gel was obtained (thus, no GPC trace was recorded). In contrast, using either 4-hydroxy-TEMPO or DPPH at a level of 1.1 inhibitor molecules per chain led to linear, soluble, well-defined macromonomers being obtained, as judged by THF GPC. In both cases the polydispersities of the final macromonomers are somewhat lower than that of the corresponding homopolymer precursor, presumably due to loss of lower molecular weight chains during dialysis (as discussed later with Table 2). ^{1}H NMR spectroscopy was used to assess the success of the click reaction for both macromonomers. Click efficiencies (calculated by comparing the percentage of polymer chains with methacrylate functionality against the total number of chains), when using DPPH and 4-hydroxy-TEMPO, were 83% and 96%, respectively. As well as its significantly higher click efficiency, the 4-hydroxy-TEMPO inhibitor is also preferred in these macromonomer syntheses because its much higher water solubility allows its facile removal (along with the spent ATRP catalyst) during dialysis.

Table 2. Comparison of GPC Molecular Weight Data Obtained for the Nine Methacrylic Homopolymer Precursors and the Corresponding Hydrophilic Macromonomers after Click Functionalization and Subsequent Purification (See Table 1 for the GPC Protocols Used for Specific Macromonomers)

	before click		after click	
polymer	M_n/g mol^{-1}	M_w/M_n	M_n/g mol^{-1}	M_w/M_n
$PAMA_{20}$ methacrylate	3400	1.14	5300	1.26
$PAMA_{50}$ methacrylate	6600	1.15	8500	1.35
$PDEA_{10}$ methacrylate	4000	1.21	4300	1.12
$PDEA_{10}$ methacrylate	4000	1.21	4200	1.12
$PDEA_{10}$ acrylate	7200	1.21	9400	1.27
$PDEA_{90}$ methacrylate	21 000	1.28	20 000	1.28
$PDMA_{10}$ acrylate	6700	1.18	5200	1.13
$PDMA_{20}$ methacrylate	7800	1.35	7200	1.27
$PQDMA_{20}$ methacrylate	4400	1.19	5800	1.17
$PMPC_{20}$ methacrylate	13 000	1.14	13 000	1.10
$PMPC_{40}$ methacrylate	15 000	1.25	18 000	1.21
$PHEMA_{10}$ methacrylate	3000	1.25	3600	1.18[a]
$PKSPMA_{10}$ methacrylate	14 000	1.15	15 000	1.16
$PGMA_{10}$ methacrylate	5500	1.19	6200	1.16[a]
$PHPMA_{20}$ methacrylate	5100	1.21	4500	1.16

[a] "One-pot" reaction conducted at 20 °C.

^{1}H NMR studies confirmed the success of the click reaction (see Figure 2). The fully assigned spectrum for the propargyl methacrylate reagent is shown in spectrum A. Two features are particularly noteworthy: triplet "a" at 2.95 ppm is due to the terminal alkyne proton and doublet "d" at 4.80 ppm is assigned to the two methylene protons adjacent to the alkyne group. Spectrum B was recorded for the azide-functionalized $PDEA_{10}N_3$ precursor, and spectrum C was obtained for the final clicked macromonomer. Signal "d" in spectrum A is shifted to 5.20 ppm in spectrum C, since these two protons are now adjacent to the aromatic triazole ring. There is no evidence for the original terminal alkyne proton in the latter spectrum due to overlapping homopolymer peaks. However, comparison of signal "d" with the vinyl signals "b" and "c" confirm the expected 2:1:1 integrated intensities (see spectrum C), suggesting that there is no detectable propargyl methacrylate contamination of the macromonomer. Moreover, there is also a new signal at 8.00 ppm, which is assigned to the single triazole proton. FT-IR spectroscopy studies of selected homopolymer precursors and their corresponding macromonomers also confirmed the disappearance of the azide band at 2100 cm^{-1} in each case, as shown in Figure 3 (also see Supporting Information, Figures S1−S4).

Table 2 summarizes the GPC data obtained before and after reacting propargyl (meth)acrylate with a number of azido-functionalized homopolymer precursors prepared by ATRP. The M_n values for the macromonomers are generally higher than their corresponding polymer precursors, which we attribute to the loss of lower molecular weight chains during dialysis. This hypothesis is supported by the observed polydispersities, which are generally lower for the macromonomers (with the exception of the PAMA macromonomers). A tentative explanation for the higher polydispersities observed for PAMA macromonomers is that the hydrophobic methacrylate end-groups may be more prone to adsorb onto the aqueous GPC columns for this low-pH GPC protocol. GPC traces of two PDEA homopolymer precursors and their corresponding macromonomers are shown in Figure 4. Other GPC traces are available as Supporting Information(Figures S5−S10).

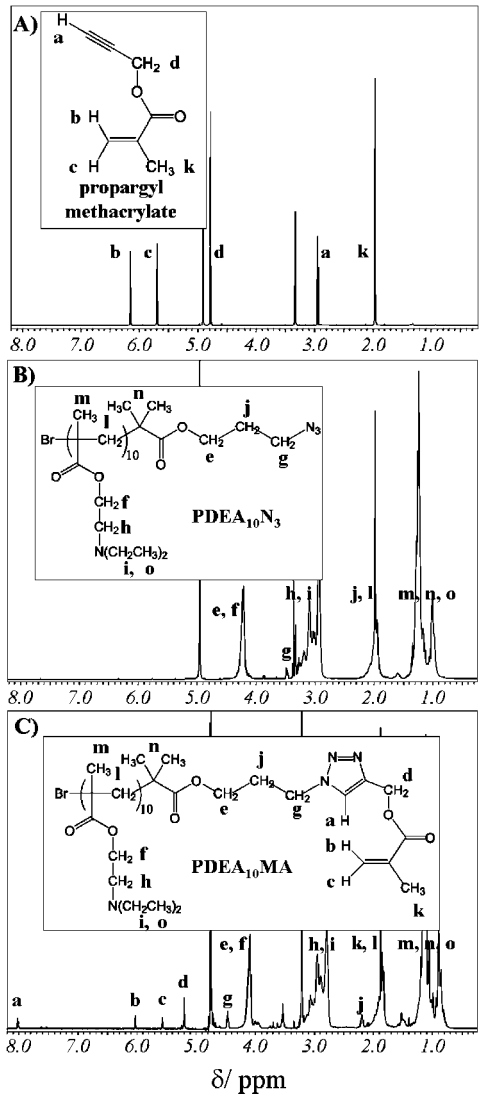


Figure 2. ^{1}H NMR spectra of propargyl methacrylate (A), $PDEA_{10}N_3$ homopolymer precursor (B), and $PDEA_{10}$ methacrylate macromonomer (C).

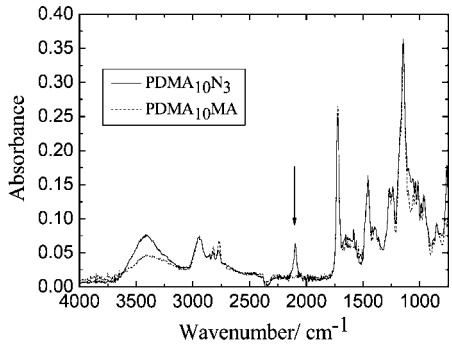


Figure 3. FT-IR spectra of a $PDMA_{10}N_3$ homopolymer precursor and its corresponding methacrylate macromonomer, $PDMA_{10}MA$.

Mantovani et al.[39] have recently demonstrated that a Cu(I) ATRP catalyst prepared using pyridylmethanimine-based ligands is also highly active toward click chemistry. This was exploited for the "one-pot" synthesis of fluorescently labeled PMMA. In view of this prior work, we wished to explore the possibility of similar "one-pot" macromonomer syntheses using the Cu(I)X/2bpy catalyst, which is preferred for the ATRP of various hydrophilic methacrylic monomers at ambient temperature in protic media.[62−66] Thus, HEMA and GMA were homopolymerized to high monomer conversion (98−100%) using APBIB at 20 °C, then clicked in situ with propargyl methacrylate in the presence of 4-hydroxy-TEMPO. After purification, ^{1}H NMR analysis confirmed that both macromonomers possessed terminal vinyl groups and gravimetric yields exceeded 89%.

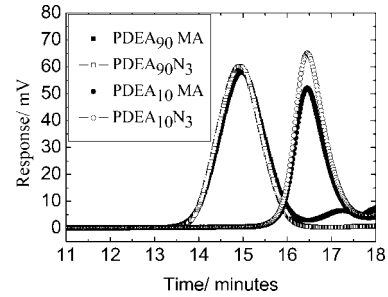


Figure 4. THF GPC traces of two azido-functionalized homopolymers, $PDEA_{10}N_3$ and $PDEA_{90}N_3$, and their corresponding macromonomers, $PDEA_{10}$ methacrylate and $PDEA_{90}$ methacrylate, respectively.

Conclusions

Nine new well-defined hydrophilic methacrylic macromonomers have been synthesized by combining ATRP with click chemistry. These macromonomers have either acrylic or methacrylic chain-end functionality, with polydispersities ranging from 1.10 to 1.35. The presence of a free radical inhibitor is essential to prevent self-polymerization during modification of the homopolymer precursors with propargyl (meth)acrylate. One-pot syntheses have also been demonstrated for selected hydroxyl-functional monomers. It is expected that these new methacrylic macromonomers will prove useful in the preparation of sterically stabilized latexes with tunable surface chemistry.

Acknowledgment. S.P.A. is the recipient of a 5 year Royal Society−Wolfson Research Merit Award.

Supporting Information Available: Additional tabulated data (target D_p vs calculated D_p), FT-IR spectra recorded for homopolymer precursors and the corresponding clicked macromonomers, and various GPC traces. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Yamashita, Y.; Kato, H.; Kojima, S. *Chemistry and Industry of Macromonomers*; John Wiley & Sons: New York, **1993**.
(2) Amalvy, J. I.; Wanless, E. J.; Li, Y.; Michailidou, V.; Armes, S. P.; Duccini, Y. *Langmuir* **2004**, *20*, 8992–8999.
(3) Amalvy, J. I.; Unali, G. F.; Li, Y.; Granger-Bevan, S.; Armes, S. P.; Binks, B. P.; Rodrigues, J. A.; Whitby, C. P. *Langmuir* **2004**, *20*, 4345–4354.
(4) Houillot, L.; Nicolas, J.; Save, M.; Charleux, B.; Li, Y.; Armes, S. P. *Langmuir* **2005**, *21*, 6726–6733.
(5) Cai, Y.; Hartenstein, M.; Mueller, A. H. E. *Macromolecules* **2004**, *37*, 7484–7490.
(6) Gnanou, Y.; Lutz, P. *Makromol. Chem.* **1989**, *190*, 577–588.
(7) Xie, H.; Zhou, S. *J. Macromol. Sci., Chem.* **1990**, *A27*, 491–507.
(8) Radke, W.; Roos, S.; Stein, H. M.; Mueller, A. H. E. *Macromol. Symp.* **1996**, *101*, 19–27.
(9) Hawker, C. J.; Mecerreyes, D.; Elce, E.; Dao, J.; Hedrick, J. L.; Barakat, I.; Dubois, P.; Jerome, R.; Volksen, W. *Macromol. Chem. Phys.* **1997**, *198*, 155–166.
(10) Ito, K.; Tomi, Y.; Kawaguchi, S. *Macromolecules* **1992**, *25*, 1534–1538.
(11) Pantazis, D.; Chalari, I.; Hadjichristidis, N. *Macromolecules* **2003**, *36*, 3783–3785.
(12) Wintermantel, M.; Gerle, M.; Fischer, K.; Schmidt, M.; Wataoka, I.; Urakawa, H.; Kajiwara, K.; Tsukahara, Y.*Macromolecules* **1996**, *29*, 978–983.
(13) Dziezok, P.; Sheiko, S. S.; Fischer, K.; Schmidt, M.; Moller, M. *Angew. Chem.* **1998**, *36*, 2812–2815.

(14) Nagasaki, Y.; Sato, Y.; Kato, M. *Macromol. Rapid Commun.* **1997**, *18*, 827–835.
(15) Lascelles, S. F.; Malet, F.; Mayada, R.; Billingham, N. C.; Armes, S. P. *Macromolecules* **1999**, *32*, 2462–2471.
(16) Wang, X. S.; Lascelles, S. F.; Jackson, R. A.; Armes, S. P. *Chem. Commun.* **1999**, 1817–1818.
(17) Matyjaszewski, K.; Gaynor, S. G.; Kulfan, A.; Podwika, M. *Macromolecules* **1997**, *30*, 5192–94.
(18) Matyjaszewski, K.; Beers, K. L.; Kern, A.; Gaynor, S. G. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, *36*, 823–830.
(19) Muehlebach, A.; Rime, F. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 3425–3439.
(20) Schoen, F.; Hartenstein, M.; Mueller, A. H. E. *Macromolecules* **2001**, *34*, 5394–5397.
(21) Ishizu, K.; Tahara, N. *Polymer* **1996**, *37*, 2853–2856.
(22) Ishizu, K.; Yamashita, M.; Ichimura, A. *Polymer* **1997**, *38*, 5471–5474.
(23) Ishizu, K.; Yamashita, M.; Ichimura, A. *Macromol. Rapid Commun.* **1997**, *18*, 639–642.
(24) Uchida, T.; Furuzono, T.; Ishihara, K.; Nakabayashi, N.; Akashi, M. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 3052–3058.
(25) Bon, S. A. F.; Morsley, S. R.; Waterson, C.; Haddleton, D. M. *Macromolecules* **2000**, *33*, 5819–5824.
(26) Haddleton, D. M.; Maloney, D. R.; Suddaby, K. G.; Clarke, A.; Richards, S. N. *Polymer* **1997**, *38*, 6207–6217.
(27) Norman, J.; Moratti, S. C.; Slark, A. T.; Irvine, D. J.; Jackson, A. T. *Macromolecules* **2002**, *35*, 8954–8961.
(28) Huybrechts, J.; Bruylants, P.; Kirshenbaum, K.; Vrana, J.; Snuparek, J. *Prog. Org. Coat.* **2002**, *45*, 173–183.
(29) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem.* **2001**, *40*, 2004–2021.
(30) Dirks, A. J.; Van Berkel, S. S.; Hatzakis, N. S.; Opsteen, J. A.; Van Delft, F. L.; Cornelissen, J. J. L. M.; Rowan, A. E.; Van Hest, J. C. M.; Rutjes, F. P. J. T.; Nolte, R. J. M. *Chem. Commun.* **2005**, 4172–4174.
(31) Jiang, X.; Lok, M. C.; Hennink, W. E. *Bioconjugate Chem.* **2007**, *18*, 2077–2084.
(32) De Geest, B. G.; Van Camp, W.; Du Prez, F. E.; De Smedt, S. C.; Demeester, J.; Hennink, W. E. *Chem. Commun.* **2007**, 190–192.
(33) Fischler, M.; Sologubenko, A.; Mayer, J.; Clever, G.; Burley, G.; Gierlich, J.; Carell, T.; Simon, U. *Chem. Commun.* **2007**, 169–171.
(34) Lutz, J.-F.; Boerner, H. G. *Prog. Polym. Sci.* **2008**, *33*, 1–39.
(35) Lutz, J.-F.; Boerner, H. G.; Weichenhan, K. *Macromolecules* **2006**, *39*, 6376–6383.
(36) Agut, W.; Taton, D.; Lecommandoux, S. *Macromolecules* **2007**, *40*, 5653–5661.
(37) Ladmiral, V.; Mantovani, G.; Clarkson Guy, J.; Cauet, S.; Irwin Jacob, L.; Haddleton David, M. *J. Am. Chem. Soc.* **2006**, *128*, 4823–4830.
(38) Fernandez-Megia, E.; Correa, J.; Riguera, R. *Biomacromolecules* **2006**, *7*, 3104–3111.
(39) Mantovani, G.; Ladmiral, V.; Tao, L.; Haddleton, D. M. *Chem. Commun.* **2005**, 2089–2091.
(40) Vogt, A. P.; Sumerlin, B. S. *Macromolecules* **2006**, *39*, 5286–5292.
(41) Dupin, D.; Armes, S. P.; Connan, C.; Reeve, P.; Baxter, S. M. *Langmuir* **2007**, *23*, 6903–6910.
(42) Fujii, S.; Iddon, P. D.; Ryan, A. J.; Armes, S. P. *Langmuir* **2006**, *22*, 7512–7520.
(43) Fujii, S.; Ryan, A. J.; Armes, S. P. *J. Am. Chem. Soc.* **2006**, *128*, 7882–7886.
(44) Dupin, D.; Howse, J. R.; Armes, S. P.; Randall, D. P. *J. Mater. Chem.* **2008**, *18*, 545–552.
(45) Dinsmore, A. D.; Hsu, M. F.; Nikolaides, M. G.; Marquez, M.; Bausch, A. R.; Weitz, D. A. *Science (Washington, DC, U.S.)* **2002**, *298*, 1006–1009.
(46) He, L.; Read, E. S.; Armes, S. P.; Adams, D. J. *Macromolecules* **2007**, *40*, 4429–4438.
(47) Liu, Q.; Chen, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 6103–6113.
(48) Golas, P. L.; Tsarevsky, N. V.; Sumerlin, B. S.; Matyjaszewski, K. *Macromolecules* **2006**, *39*, 6451–6457.
(49) Coessens, V.; Matyjaszewski, K. *J. Macromol. Sci., Pure Appl. Chem.* **1999**, *A36*, 667–679.
(50) Coessens, V.; Pintauer, T.; Matyjaszewski, K. *Prog. Polym. Sci.* **2001**, *26*, 337–377.
(51) Lutz, J.-F.; Boerner, H. G.; Weichenhan, K. *Macromol. Rapid Commun.* **2005**, *26*, 514–518.
(52) Whittaker, M. R.; Urbani, C. N.; Monteiro, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 11360–11361.
(53) Laurent, B. A.; Grayson, S. M. *J. Am. Chem. Soc.* **2006**, *128*, 4238–4239.
(54) Bednarek, M.; Biedron, T.; Kubisa, P. *Macromol. Chem. Phys.* **2000**, *201*, 58–66.
(55) Jackson, A. T.; Bunn, A.; Priestnall, I. M.; Borman, C. D.; Irvine, D. J. *Polymer* **2006**, *47*, 1044–1054.
(56) Sadhu, V. B.; Pionteck, J.; Voigt, D.; Komber, H.; Fischer, D.; Voit, B. *Macromol. Chem. Phys.* **2004**, *205*, 2356–2365.
(57) Barner-Kowollik, C.; Davis, T. P.; Stenzel, M. H. *Polymer* **2004**, *45*, 7791–7805.
(58) Matyjaszewski, K.; Jo, S. M.; Paik, H.-J.; Gaynor, S. G. *Macromolecules* **1997**, *30*, 6398–6400.
(59) Matyjaszewski, K.; Jo, S. M.; Paik, H.-J.; Shipp, D. A. *Macromolecules* **1999**, *32*, 6431–6438.
(60) Lutz, J.-F.; Matyjaszewski, K. *Macromol. Chem. Phys.* **2002**, *203*, 1385–1395.
(61) Mespouille, L.; Vachaudez, M.; Suriano, F.; Gerbaux, P.; Coulembier, O.; Degee, P.; Flammang, R.; Dubois, P. *Macromol. Rapid Commun.* **2007**, *28*, 2151–2158.
(62) Save, M.; Weaver, J. V. M.; Armes, S. P.; McKenna, P. *Macromolecules* **2002**, *35*, 1152–1159.
(63) Ma, I. Y.; Lobb, E. J.; Billingham, N. C.; Armes, S. P.; Lewis, A. L.; Lloyd, A. W.; Salvage, J. *Macromolecules* **2002**, *35*, 9306–9314.
(64) Weaver, J. V. M.; Bannister, I.; Robinson, K. L.; Bories-Azeau, X.; Armes, S. P.; Smallridge, M.; McKenna, P. *Macromolecules* **2004**, *37*, 2395–2403.
(65) Robinson, K. L.; Khan, M. A.; de Banez, M. V.; Wang, X. S.; Armes, S. P. *Macromolecules* **2001**, *34*, 3155–3158.
(66) Vo, C.-D.; Schmid, A.; Armes, S. P.; Sakai, K.; Biggs, S. *Langmuir* **2007**, *23*, 408–413.

MA8019656