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The Thiol−Isocyanate Click Reaction: Facile and Quantitative Access to ω-End-Functional Poly(*N*,*N*-diethylacrylamide) Synthesized by RAFT Radical Polymerization

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ABSTRACT: *N*,*N*-Diethylacrylamide (DEAm) was homopolymerized by reversible addition−fragmentation chain transfer (RAFT) radical polymerization yielding a homopolymer with a calculated degree of polymerization of 30 ($PDEAm_{30}$), as determined by ^{1}H NMR spectroscopic end-group analysis, and a polydispersity index (M_w/M_n) of 1.10. Aminolysis of the dithioester end groups followed by treatment with tris(carboxyethyl)phosphine hydrochloride yielded the corresponding macromolecular secondary thiol ($PDEAm_{30}$-SH). Reaction of $PDEAm_{30}$-SH with a range of commercially available isocyanates, catalyzed by NEt_3, gave the corresponding thiocarbamate end-functional polymers in essentially quantitative yield as determined by a combination of ^{1}H NMR spectroscopy and UV−vis spectrophotometry. These reactions were shown to be rapid as evidenced by the real-time kinetics for the reaction between $PDEAm_{30}$-SH and hexyl isocyanate in the presence of NEt_3. Additionally, these facile reactions were shown to proceed without any apparent detrimental effect/side reactions to the basic polymer structure as evidenced by size exclusion chromatography with all modified polymers retaining their narrow molecular weight distributions. The lower critical solution temperatures (LCSTs) of the resulting ω-modified PDEAm homopolymers were evaluated by turbidimetry. For those samples that were soluble in aqueous media the measured LCSTs were between 3 and 11 °C lower than that determined for $PDEAm_{30}$-SH (34 °C). Such differences were attributed to the hydrophobic nature of the newly introduced end groups—the effect being pronounced given the relatively low molecular weight of the precursor homopolymer. In two instances, and specifically the end-modified PDEAm homopolymers obtained from reaction with 9-isocyanato-9*H*-fluorene and 4-(2-isocyanatoethyl)biphenyl, the resulting materials were not soluble in water even at temperatures approaching 0 °C.

Introduction

As clearly enunciated by Kolb, Finn, and Sharpless,[1] a "click" reaction is one that is modular, wide in scope, (near-) quantitative, generates inoffensive byproducts (if any), is stereospecific, can be conducted with inexpensive, readily available starting materials under solventless conditions or with a benign solvent, and also facilitates simple, nonchromatographic product isolation. Examples of such reactions include the Cu(I)-catalyzed dipolar cycloaddition reaction between an alkyne and an azide (and Diels−Alder reactions in general), nucleophilic substitution chemistry on strained cyclic electrophilic substrates such as epoxides, C=C bond additions, and non-Aldol carbonyl chemistry such as the amine−isocyanate reaction,[1] with extensive focus having been given to the Cu-catalyzed alkyne/azide reaction.[2−5] Several groups have recently investigated the application of other emerging click chemistries in polymer/materials chemistry. In particular, the thiol−ene reaction,[6] in either its radical or nucleophilic forms, has been applied in the materials arena in dendrimer synthesis,[7] convergent star synthesis,[8,9] in the preparation of branched silanes,[10] neoglycopolymer synthesis,[11] the modification of polylactides,[12] in the side-chain modification of polyoxazolines[13] and polybutadienes,[14] in the end-group modification of glycopolymers prepared via catalytic chain transfer polymerization,[15] for stabilizing and functionalizing polymer multilayers/capsules,[16] and as a general means of modifying end groups in RAFT-prepared (co)polymers.[17−20] A sister reaction, the thiol−alkyne (thiol−yne) reaction, bears many similar characteristics to the thiol−ene click reaction in terms of both reaction conditions, yields, rates, and general ease of execution. While barely examined in polymer/materials synthesis, it has impressive potential, and several reports have recently appeared demonstrating the utility of this click-like reaction.[21−24] As recently reported, and related to the amine−isocyanate reaction, the base-catalyzed *thiol−isocyanate* reaction can proceed with the hallmark characteristics of a click reaction and should be considered as such.[25] Indeed, the high reactivity of thiols toward isocyanates under base catalysis, yielding thiocarbamates in high-to-quantitative yields, has been well-known in small molecule organic and polymer chemistry for over half a century.[26−30]

Recently,[24] we described a two-step processes involving sequential thiol−ene/thiol−ene or thiol−ene/thiol−yne reactions as a means of preparing mono- or bis-end-functionalized poly(*N*-isopropylacrylamide)s (PNIPAms) derived from a homopolymer

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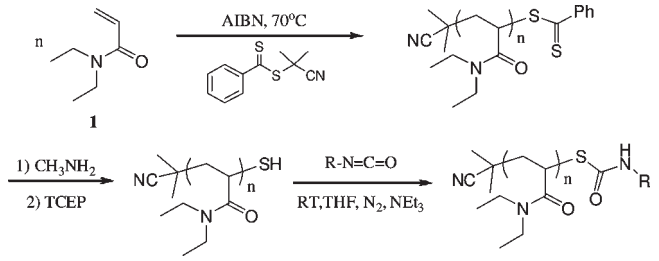
Scheme 1. Outline for the Synthesis of Thiocarbamate End-Functionalized Poly(*N*,*N*-diethylacrylamide) via Dithioester End-Group Cleavage Followed by a Macromolecular Thiol−Isocyanate Click Reaction



prepared via reversible addition−fragmentation chain transfer (RAFT)[31−35] radical polymerization. Specifically, treatment of a thiol-terminated PNIPAm with allyl methacrylate or propargyl acrylate under phosphine catalysis yielded the corresponding allyl or propargyl end-functional NIPAm homopolymers. Subsequent reaction with a variety of thiols, including hydrophilic and hydrophobic species, under photochemical conditions yielded the corresponding mono- and bis-functional thioethers in essentially quantitative yield. Given the low molecular weight of the parent PNIPAm, it was shown that the newly introduced thioether end groups had a measurable impact on the lower critical solution temperature when compared to the unmodified PNIPAm. Such end-group effects have been documented previously.[36,37] Expanding on these facile and versatile chemistries, herein we report the first examples of an alternative, highly efficient route to ω-end-functionalized poly(*N*,*N*-diethylacrylamide) (PDEAm), also prepared by RAFT polymerization. Specifically, such ω-functional polymers are obtained by a NEt_3-catalyzed macromolecular *thiol−isocyanate* reaction (Scheme 1). Given the current, and growing, interest in site-specific functionalization, including bioconjugation and utilization of the masked thiol functionality in RAFT-synthesized (co)polymers as a functional handle for postpolymerization modification, we anticipate that the addition of the thiol−isocyanate reaction to the toolbox of currently employed click chemistries will have a significant impact in many areas of polymer/materials chemistry.

Experimental Section

All reagents were purchased from the Aldrich Chemical Co. Inc. at the highest available purity and used as received unless noted otherwise. *N*,*N*-Diethylacrylamide was purchased from Polysciences Inc., purified by vacuum distillation, and stored in a freezer at −20 °C until needed. 2,2′-Azobis(2-methylpropionitrile) (AIBN) was recrystallized from methanol and stored in a freezer at −20 °C until needed. 1-Cyano-1-methylethyl dithiobenzoate (CPDB) was prepared according to a literature procedure.[32] Hexyl isocyanate was purchased from Acros Organics and used without further purification.

Homopolymerization of *N*,*N*-Diethylacrylamide. *N*,*N*-Diethylacrylamide (10.98 g, 85.55 mmol), CPDB (0.63 g, 2.85 mmol), and AIBN (94.0 mg, 0.57 mmol) were mixed in a round-bottomed flask equipped with a magnetic stir bar. The resulting homogeneous solution was stirred at room temperature while being purged with N_2 for a period of 2 h. The flask was then immersed in a preheated oil bath at 70 °C, and the polymerization was allowed to proceed overnight. The polymerization was quenched by exposure to air while cooling the flask with liquid nitrogen. THF (8.0 mL) was then added to the flask to dilute the monomer/polymer mixture. The polymer was isolated by precipitation into hexanes (600 mL) followed by Buchner filtration and drying in vacuo, yielding 9.82 g of poly(*N*,*N*-diethylacrylamide).

Cleavage of Dithioester End Groups in Poly(*N*,*N*-diethylacrylamide). Poly(*N*,*N*-diethylacrylamide) (5.0 g) and benzene (200 mL) were added to a round-bottomed flask equipped with a magnetic stir bar. The mixture was stirred until a homogeneous solution was obtained. To this solution was added methylamine as a solution in MeOH (2.0 M) (2.00 mL, 4.00 mmol). The resulting solution was stirred at room temperature for 3 h. Subsequently, the solvent was removed using a rotary evaporator. To the residue was added THF, and the resulting solution was loaded to a dialysis bag and dialyzed against THF (800 mL) for 5 days with daily changes of THF. The crude product was isolated by removal of the THF using a rotary evaporator. The polymer was then dissolved in water (200 mL), and then tris(2-carboxyethyl)phosphine hydrochloride (0.50 g, 1.74 mmol) was added to the solution and allowed to stir at room temperature for 2 h. After removal of the bulk of the water under vacuum the polymer was isolated by heating the concentrated aqueous solution to 60 °C—a temperature above the lower critical solution temperature of the homopolymer. After decanting the aqueous phase the product was dried in vacuo to yield 2.76 g of isolated product.

Reaction of Thiol-Terminated Poly(*N*,*N*-diethylacrylamide) (PDEAm-SH) with Isocyanates. A typical procedure for the reaction between thiol-terminated poly(*N*,*N*-diethylacrylamide) and an isocyanate is as follows:

PDEAm-SH (0.15 g) and the target isocyanate (2 mol equiv based on thiol end groups) were weighed into a 5.0 mL vial equipped with a magnetic stir bar. The vial was capped with a rubber septa, and the solution was purged with N_2 for 2 h. Subsequently, NEt_3 in THF (1.0 mL, 10 g/L) was added to the vial by syringe. The resulting solutions were left to stir overnight at ambient temperature. The product was isolated by precipitation into hexanes (15.0 mL). After being left to stand for 5 h, the liquid phase was decanted and the product dried in vacuo.

Real-Time Reaction Kinetics between $PDEAm_{30}$-SH and Hexyl Isocyanate. Hexyl isocyanate (3.6 mg, 0.028 mmol) and triethylamine (5.0 mg, 0.049 mmol) were dissolved in 0.5 mL of THF, and PDEAm-SH (108 mg, 0.028 mmol) in 0.5 mL of THF was added to the mixture. After mixing, the sample solution was sandwiched between two salt plates sealed with silicon at a thickness of ~0.4 mm and set up immediately in the real-time FTIR spectrometer at 20 °C.

Instrumentation. ^1H and ^{13}C NMR spectra were recorded on a Bruker 300 53 mm spectrometer in appropriate deuterated solvents. Size exclusion chromatographic analysis was performed on a Waters system comprised of a Waters 515 HPLC pump, a Waters 2487 dual λ absorbance detector, and a Waters 2410 RI detector equipped with a PolymerLabs PLgel 5 μm guard column and a PolymerLabs PLgel 5 μm MIXED-C column (molecular weight range: 200−2 000 000 g/mol), in THF stabilized with 281 ppm BHT at a flow rate of 1.0 mL/min. The column was calibrated with a series of narrow molar mass distribution poly(methyl methacrylate) standards. Real-time FTIR spectra were recorded on a modified Bruker 88 spectrometer. UV−vis spectra of the modified polymers were recorded in THF on a Cary 500 Scan UV−vis spectrophotometer at a typical concentration of ~0.2 g/L. In the case of 2-(2-isocyanatoethyl)-1,4-dimethoxybenzene (**Iso5**), a UV−vis calibration curve was generated by measuring the absorbance at 292 nm at concentrations of 0.0208, 0.0312, 0.0416, and 0.0520 g/L. A plot of concentration vs absorbance was linear (see Supporting Information).

Results and Discussion

N,*N*-Diethylacrylamide (DEAm), **1** (Scheme 1), was homopolymerized by RAFT at 70 °C with 1-cyano-1-methylethyl dithiobenzoate (CPDB) as the RAFT agent and 2,2′-azobis(2-methylpropionitrile) (AIBN) as the source of primary radicals at a molar ratio of [DEAm]:[CPDB]:[AIBN] = 150:5:1, for a target DP of 30 (M_n = 3800) at 100% conversion. The polymerization was stopped at ca. 90% conversion to minimize termination reactions and preserve the dithioester end groups. The DEAm homopolymer was isolated by precipitation in hexanes and

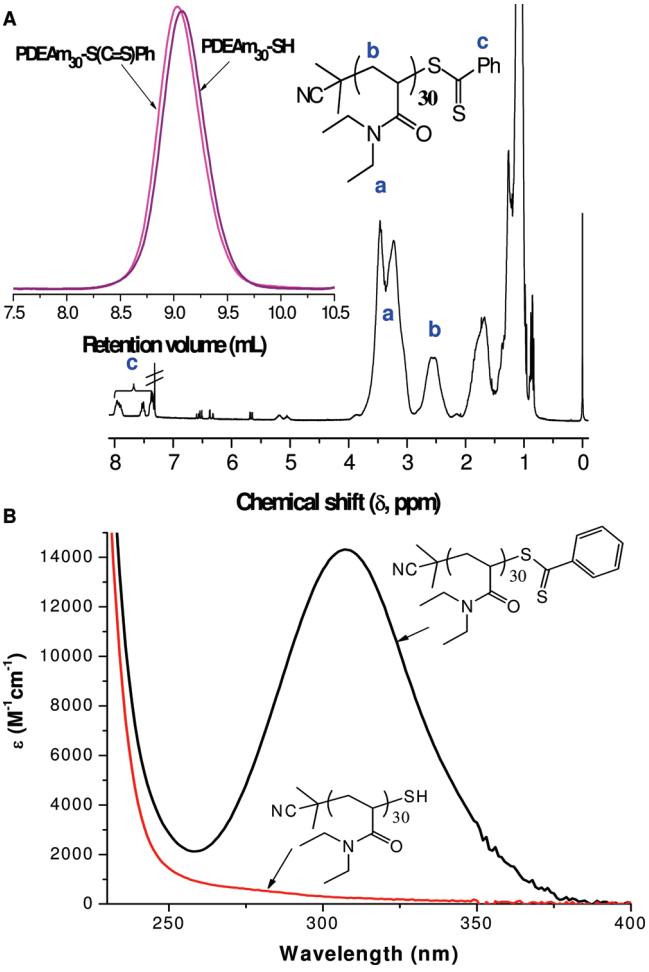


Figure 1. (A) ^{1}H NMR spectrum, recorded in $CDCl_3$, of the parent $PDEAm_{30}$-S(C=S)Ph homopolymer with the size exclusion chromatographic traces (RI signals) of $PDEAm_{30}$-S(C=S)Ph and $PDEAm_{30}$-SH shown (inset) and (B) UV−vis spectra recorded between 240 and 400 cm^{-1} for the parent $PDEAm_{30}$-S(C=S)Ph homopolymer (black trace) and $PDEAm_{30}$-SH (red trace) verifying successful end-group cleavage.

analyzed via a combination of ^{1}H NMR spectroscopy and size exclusion chromatography (SEC) yielding a homopolymer with a narrow molecular weight distribution (M_w/M_n = 1.10) and an M_n, as determined by ^{1}H NMR spectroscopic end-group analysis, of 3800 (DP = 30, $PDEAm_{30}$), close to the predicted value of 3400 (DP = 27) based on the calculated conversion (Figure 1A). Subsequently, the dithioester end groups on the DEAm homopolymer were cleaved by aminolysis[8,9,17,38] by reaction with methylamine followed by treatment with tris(carboxyethyl)-phosphine (TCEP) to yield the macromolecular secondary thiol. Successful, and quantitative, cleavage of the dithioester end groups was verified by a combination of ^{1}H NMR spectroscopy (see Supporting Information) and UV−vis spectroscopy as evidenced by the complete disappearance of the absorbance at 310 nm (Figure 1B) associated with the C=S bond.[39] The absence of any macromolecular disulfide, commonly observed as a shoulder at lower retention time on the main molecular weight distribution and arising from the aerial oxidation of the macromolecular thiol,[9] was confirmed by SEC (Figure 1A inset). Indeed, the chromatogram associated with $PDEAm_{30}$-SH is almost perfectly superimposed on that of $PDEAm_{30}$-S(C=S)Ph and has an identical PDI of 1.10.

With the macromolecular 2° thiol in-hand, the −SH end group was modified, yielding a range of thiocarbamate end-functional

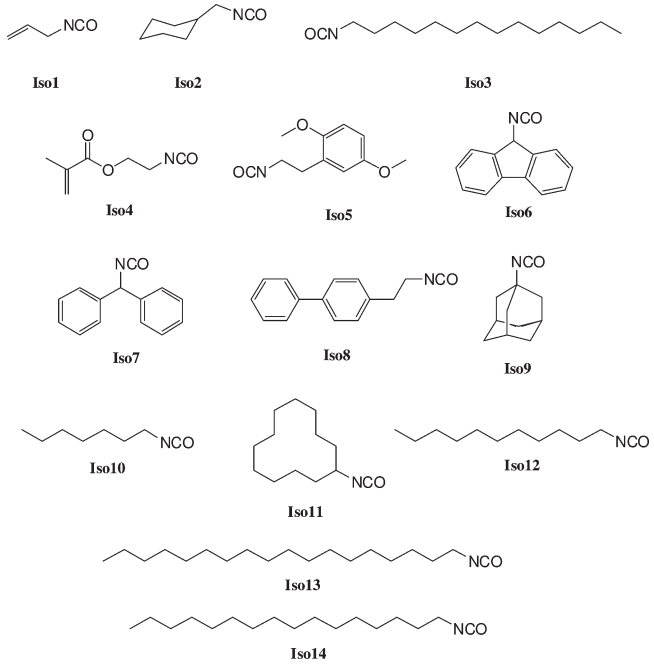


Figure 2. Chemical structures of commercially available isocyanates employed in these studies: allyl isocyanate (**Iso1**), cyclohexylmethyl isocyanate (**Iso2**), tetradecyl isocyanate (**Iso3**), 2-isocyanatoethyl methacrylate (**Iso4**), 2-(2-isocyanatoethyl)-1,4-dimethoxybenzene (**Iso5**), 9-isocyanato-9*H*-fluorene (**Iso6**), isocyanatomethylene dibenzene (**Iso7**), 4-(2-isocyanatoethyl)biphenyl (**Iso8**), adamantly isocyanate (**Iso9**), heptyl isocyanate (**Iso10**), cyclododecyl isocyanate (**Iso11**), undecyl isocyanate (**Iso12**), octadecyl isocyanate (**Iso13**), and hexadecyl isocyanate (**Iso14**).

PDEAm's by reaction with a range of commercially available isocyanates under NEt_3 catalysis (Figure 2).

Specifically, the reaction of $PDEAm_{30}$-SH with allyl isocyanate (**Iso1**), cyclohexylmethyl isocyanate (**Iso2**), tetradecyl isocyanate (**Iso3**), 2-isocyanatoethyl methacrylate (**Iso4**), 2-(2-isocyanatoethyl)-1,4-dimethoxybenzene (**Iso5**), 9-isocyanato-9*H*-fluorene (**Iso6**), isocyanatomethylene dibenzene (**Iso7**), 4-(2-isocyanatoethyl)biphenyl (**Iso8**), adamantly isocyanate (**Iso9**), heptyl isocyanate (**Iso10**), cyclododecyl isocyanate (**Iso11**), undecyl isocyanate (**Iso12**), octadecyl isocyanate (**Iso13**), and hexadecyl isocyanate (**Iso14**) was examined. Reactions were conducted at room temperature in THF in the presence of 1−2 wt % NEt_3 as the base catalyst[27] under a nitrogen atmosphere. Reactions were typically left overnight to ensure complete reaction. After work-up the products were analyzed by a combination of ^{1}H NMR spectroscopy and SEC. As representative examples, Figure 3 shows the ^{1}H NMR spectra of the products obtained from the reaction of $PDEAm_{30}$-SH with the fluorene derivative **Iso6** and the methacrylic derivative **Iso4**.

Many of the chosen isocyanates have distinct chemical shifts facilitating straightforward end-group analysis as a means of evaluating the degree of functionalization. For example, in the case of **Iso6** the resonances at ∼7.3−7.8 ppm (aromatic H's, labeled a) can be integrated against the peak labeled b associated with the methylene H's adjacent to the amide N's in the main polymer chain. A comparison of a with b indicates a DP of 30. This agrees perfectly with the calculated DP of the parent DEAm homopolymer and indicates quantitative reaction between $PDEAm_{30}$-SH and **Iso6**. In the case of the reaction between $PDEAm_{30}$-SH and **Iso4** resonances are clearly visible between 5.6 and 6.2 ppm and are attributed to the vinylic protons associated with the methacrylic end group. A ratio of these resonances with those labeled b yields a calculated DP of ∼35. While slightly higher than that calculated for the parent PDEAm homopolymer,

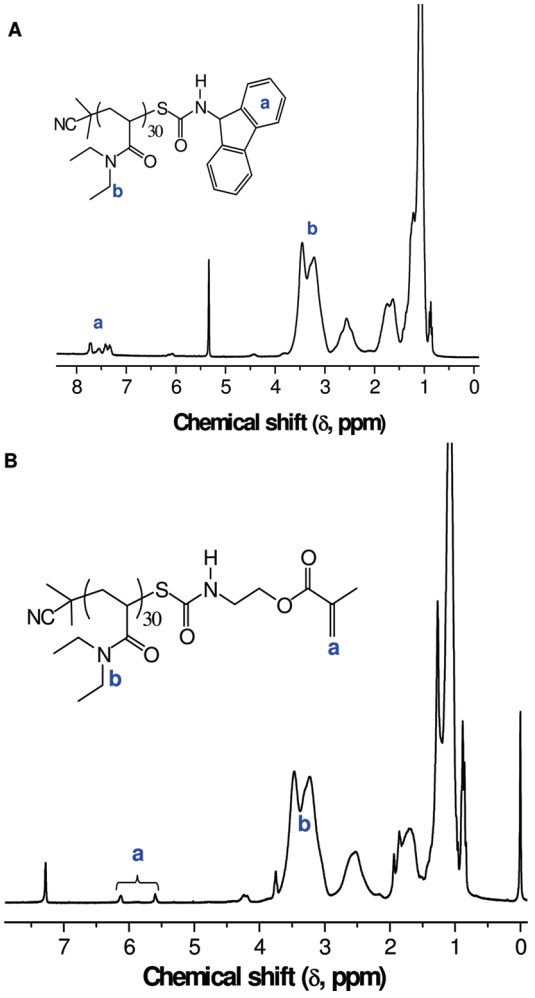


Figure 3. (A) ^{1}H NMR spectrum, recorded in CD_2Cl_2, of the product obtained from the reaction between PDEAm$_{30}$-SH and 9-isocyanato-9*H*-fluorene (**Iso6**). (B) ^{1}H NMR spectrum, recorded in $CDCl_3$, of the product obtained from the reaction between PDEAm$_{30}$-SH and 2-isocyanatoethyl methacrylate (**Iso4**) highlighting the ability to conduct end-group analysis.

it still indicates a very high degree of successful modification which, given the relatively low sensitivity of the NMR technique, is acceptable. Interestingly, it should be highlighted that while the reaction of PDEAm$_{30}$-SH with **Iso4** appears to offer an extremely attractive and facile route to methacrylic macromonomers, we cannot completely dismiss the possibility of a small degree of competing thiol−ene addition, i.e., thiol−Michael addition. Indeed, the occurrence of such a competing reaction would result in a calculated DP somewhat higher than predicted, as was observed. Similar DPs, in the range 25−33, were determined for those isocyanates where distinct, isolated resonances were present facilitating end-group analysis, confirming the high efficiency of the thiol−isocyanate reaction (Table 1). Unfortunately, in the case of the products derived from the reaction of PDEAm$_{30}$-SH with **Iso2**, **Iso3**, and **Iso9**−**Iso14** there were no distinct signals associated with the new end groups that allowed end-group analysis although given the results above it seems reasonable to assume that similar near-quantitative degrees of modification were obtained. Indeed, while not distinct, the end groups were observable in the NMR spectra (see Supporting Information).

UV−vis spectrophotometry was also examined as a means of verifying the high degree of end-group modification. Such analysis was performed for those materials with aromatic end groups (products from PDEAm$_{30}$-SH with **Iso5-Iso8**) since these

Table 1. Summary of the Calculated Average Degrees of Polymerization (DP), Lower Critical Solution Temperatures (LCST), SEC Determined M_n, and the Corresponding Polydispersity Indices (M_w/M_n)

sample	calcd DP[a]	LCST (°C)[b]	M_n[c]	M_w/M_n[c]
PDEAm-S(C=S)Ph	30	23	2540	1.10
PDEAm-SH		34	2420	1.10
PDEAm-SH + **Iso1**	33	31	2560	1.10
PDEAm-SH + **Iso2**		28	2630	1.10
PDEAm-SH + **Iso3**		27	2750	1.10
PDEAm-SH + **Iso4**	35	34	2620	1.09
PDEAm-SH + **Iso5**	33	28	2600	1.10
PDEAm-SH + **Iso6**	30	XX[d]	2610	1.09
PDEAm-SH + **Iso7**	27	29	2620	1.10
PDEAm-SH + **Iso8**	25	XX[d]	2630	1.10
PDEAm-SH + **Iso9**		27	2840	1.13
PDEAm-SH + **Iso10**		26	2850	1.13
PDEAm-SH + **Iso11**		23	2810	1.15
PDEAm-SH + **Iso12**		24	2930	1.12
PDEAm-SH + **Iso13**		25	3010	1.14
PDEAm-SH + **Iso14**		25	2970	1.14

[a] As determined by ^{1}H NMR spectroscopic end-group analysis. [b] As determined by turbidimetry with 1 wt % aqueous solutions. [c] As determined by size exclusion chromatography in THF. The column was calibrated with a series of narrow molecular weight distribution poly(methyl methacrylate) standards. [d] Not soluble at 1 wt % in water even at temperatures approaching 0 °C.

were the only species that possessed a distinct absorbance that did not overlap with absorbencies associated with other functionality (Figure 4), and within this limited pool PDEAm$_{30}$-SH modified with **Iso5** was the most convenient to evaluate. A solution of the product derived from PDEAm$_{30}$-SH + **Iso5** was prepared at a concentration of 0.5050 g/L, and its UV−vis spectrum was recorded. At this concentration an absorbance of 0.4010 was observed which when fitted to the calibration curve indicated an end-group concentration of 1.24×10^{-4} mol/L. This corresponds to a calculated DP of 32—almost identical to the value of 33 determined by NMR end-group analysis. This serves to further confirm the high efficacy of the base catalyzed thiol−isocyanate reaction.

It should be noted that while the end-group modification reactions were left to react overnight, the macromolecular thiol−isocyanate reactions are, in fact, considerably faster than this. As an example, Figure 5 shows the real-time kinetics, as determined by FTIR spectroscopy, for the reaction between PDEAm$_{30}$-SH and hexyl isocyanate in the presence of NEt_3. Specifically, the decrease in the intensity of the band at 2270 cm^{-1}, associated with the isocyanate functionality, was monitored.

It is clear that such reactions are rapid with, in this case, ~94% conversion being reached in only 15 min. Given that the initial spectra were recorded after premixing of the reagents followed by sandwiching and sealing between salt plates, it is likely that the "real" conversion is higher than this measured value. However, these results clearly highlight the impressive kinetics of the thiol−isocyanate reaction and its high efficiency.

When performing postpolymerization modification reactions aside from desirable quantitative modification, it is important that no other side reactions occur that could lead to a broadening of the molecular weight distribution or result in less-well-defined structures. The measured M_n, as determined by SEC, for the parent PDEAmS(C=S)Ph homopolymer was 2540 while that for PDEAm-SH was 2420 with both exhibiting symmetric, unimodal chromatograms (Figure 1A inset) with polydispersity indices of 1.10. In all instances the thiocarbamate end-functionalized PDEAms possessed near-identical chromatographic characteristics with all polydispersity indices lying in the range 1.09−1.15 with measured M_n's between 2560 and 3010 (Table 1). As representative examples, Figure 6 shows the chromatograms

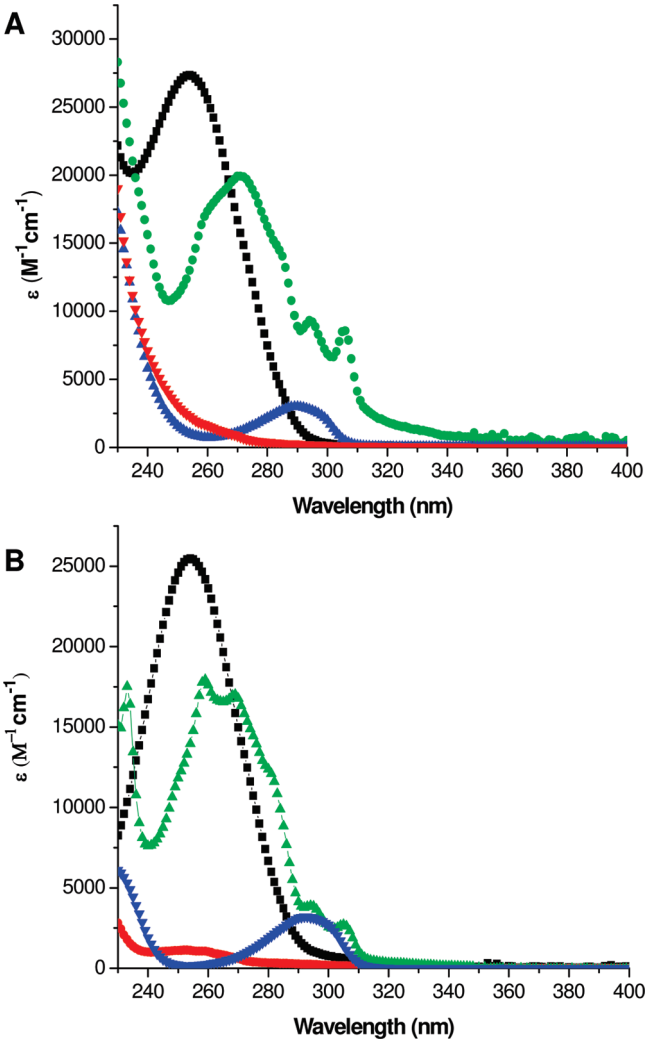


Figure 4. (A) UV spectra of PDEAm-S−CO−NH−$CH(Ph)_2$ (red), PDEAm-S−CO−NH−CH_2CH_2−bisphenyl (black), PDEAm-S−CO−NH−fluorenyl (green), and PDEAm-S−CO−NH−CH_2CH_2−2,5-dimethoxyphenyl (blue). Solvent: THF. (B) UV spectra of isocyanatomethylene dibenzene, **Iso7** (red), 4-(2-isocyanatoethyl)biphenyl, **Iso8** (black), 9-isocyanato-9*H*-fluorene, **Iso6** (green), and 2-(2-isocyanatoethyl)-1,4-dimethoxybenzene, **Iso5** (blue). Solvent: THF.

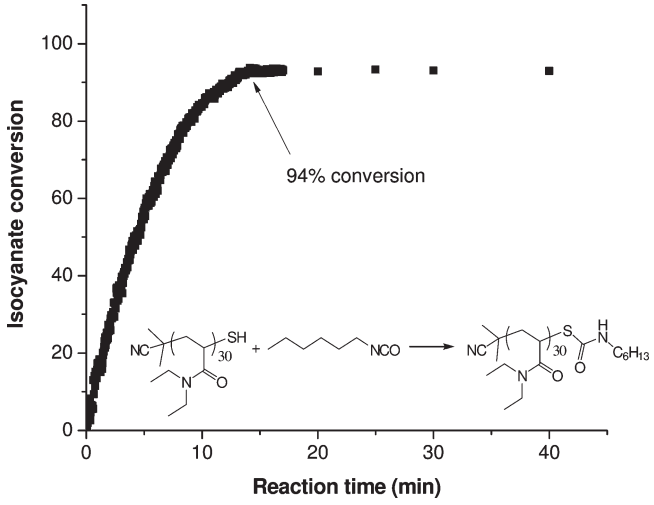


Figure 5. Real-time kinetics, as determined by FTIR spectroscopy, for the reaction between $PDEAm_{30}$-SH and hexyl isocyanate. Conversion was determined by monitoring the decrease in the intensity of the band at 2270 cm^{-1} associated with the isocyanate functional group.

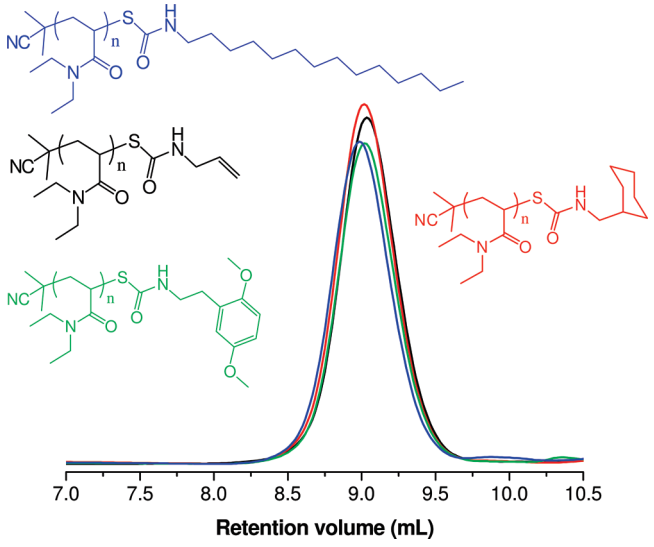


Figure 6. Size exclusion chromatographic traces (RI signal) of the macromolecular thiocarbamate products obtained from the reaction of $PDEAm_{30}$-SH with tetradecyl isocyanate (**Iso3**, blue line), allyl isocyanate (**Iso1**, black line), 2-(2-isocyanatoethyl)-1,4-dimethoxybenzene (**Iso5**, green line), and cyclohexylmethyl isocyanate (**Iso2**, red line).

(RI signals) for four of the thiocarbamate products demonstrating the well-defined nature of the products and the apparent lack of any detrimental effects associated with such end-group modifications.

PDEAm exhibits thermoresponsive properties in aqueous media and, according to the literature, possesses a lower critical solution temperature (LCST), or cloud point (T_{cp}), of ~33 °C—essentially identical to that of the more commonly studied poly(*N*-isopropylacrylamide).[40] It is well-known that the T_{cp} of such stimulus-sensitive (co)polymers is dependent on a variety of structural features including the DP,[41] topology,[42] the hydrophilic/hydrophobic characteristics of comonomers in statistical or block copolymers,[43−45] and in (co)polymers of sufficiently low molecular weight the hydrophilic or hydrophobic characteristics of end groups can become important.[24,46] Given the low molecular weight of the parent PDEAm homopolymer, it was anticipated that the subsequent end-group modifications would have a discernible effect on the T_{cp}. The T_{cp} values were measured via simple turbidimetry on 1 wt % aqueous solutions and are listed in Table 1. The parent $PDEAm_{30}S(C{=}S)Ph$ possessed an experimentally determined T_{cp} of 23 °C, 10 °C lower than that previously reported, whereas the thiol-terminated species, $PDEAm_{30}$-SH, had a measured value of 34 °C, in good agreement with the literature value. Presumably, the low T_{cp} for the parent homopolymer is due to the hydrophobic phenyldithioester end group with its effect being more pronounced given the low DP. This appears to be borne out given the measured T_{cp} for the thiol-terminated species, i.e., after removal of the dithioester group. A cursory inspection of the R groups of the isocyanates in Figure 2 reveals them all to have hydrophobic character. The effect of these introduced hydrophobic end groups is also seen in the measured T_{cp} values. With the exception of the product obtained from $PDEAm_{30}$-SH and **Iso4** all the measured T_{cp} values were <31 °C with typical experimentally determined values between 23 and 28 °C. In the extreme, the thiocarbamate products derived from $PDEAm_{30}$-SH and **Iso6** and **Iso8** were insoluble as 1 wt % solutions even at temperatures approaching 0 °C. Clearly, the thiol−isocyanate reaction represents a facile and convenient route for tuning T_{cp} values in such thermoresponsive (co)polymers and, we argue, is a faster and more

straightforward approach than tuning T_{cp} via the preparation of a range of statistical copolymers of varying molar composition of hydrophilic and hydrophobic comonomers.

Summary and Conclusion

Herein we have highlighted the highly efficient NEt_3-mediated thiol−isocyanate click reaction as a facile means of preparing ω-modified poly(*N*,*N*-diethylacrylamide) (PDEAm). Treatment of a thiol-terminated PDEAm, obtained via the aminolysis of a precursor DEAm homopolymer synthesis via RAFT with a dithioester mediating agent, with a range of commercially available hydrophobic isocyanates under NEt_3 catalysis yields the corresponding thiocarbamate-ω-functional homopolymers under facile conditions essentially quantitatively as verified by a combination of ^{1}H NMR spectroscopy and UV−vis spectrophotometry. Employing real-time FTIR spectroscopy, it was demonstrated that the reaction between $PDEAm_{30}$-SH and hexyl isocyanate was rapid with ∼95% conversion being attained in 15 min. In all instances the modified homopolymers retained their low polydispersities with no evidence of any coupled species as determined by size exclusion chromatography. The introduction of the hydrophobic end groups was shown to have a discernible effect on the aqueous solution properties of the PDEAm homopolymer with the lower critical solution temperature being depressed by between 3 and 11 °C after thiol−isocyanate coupling. Given the current, widespread interest in click chemistries, we believe that the thiol−isocyanate reaction will have a significant impact in polymer/materials synthesis and represents an interesting addition to other thiol-based click and click-like reactions such as the thiol−ene and thiol−yne processes.

Supporting Information Available: Figures showing a series of ^{1}H NMR spectra of end-group-modified poly(*N*,*N*-diethylacrylamide) and UV−vis calibration curve. This material is available free of charge via the Internet at http://pubs.acs.org.

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