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NOTE

N-Vinyltriazoles: A New Functional Monomer Family through Click Chemistry

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Introduction

The design of new building blocks and functional units for the construction of macromolecules with novel and/or improved properties is a constant theme in advanced materials.[1] While a goal in itself, an underlying theme in this arena is the development of synthetic strategies for accessing these new building blocks/functional units that are modular and efficient. This allows the efficient incorporation of a wide variety of functional groups and permits a diverse spectrum of researchers to employ these systems. The recent focus on click chemistry has both drawn attention to these concepts as well as facilitated the preparation of a large number of functionalized polymeric materials in an efficient manner.[2] The Cu(I)-mediated azide/alkyne coupling reaction (CuAAC) is the most widely studied click reaction and results in the formation of a 1,4-disubstituted 1,2,3-triazole moiety.[3,4] This triazole core is not simply a passive linker but can present a range of interesting structural and electronic features such as an electron-rich aromatic ring capable of forming $\pi-\pi$ interactions, nitrogen atoms available for metal–ion coordination and hydrogen bonding, and a strong dipole moment. While considering the 1,2,3-triazole moiety as a potential building block for macromolecular synthesis, the regioselectivity of the azide–alkyne coupling chemistry allows a library of different vinyl-based monomers to be envisaged (Scheme 1). These monomers are analogous to the widely used styrene, vinylpyridine, and acrylates considering their aromaticity, presence of heteroatoms, and functional group diversity. In this context, we have previously reported novel 1,4- and 1,5-*C*-vinyltriazole-based monomer families which are readily prepared in multigram quantities.[5−7] These *C*-vinyl systems displayed a range of novel properties while at the same time exhibiting polymerization profiles similar to styrenic/acrylate systems. In this Note, the synthesis, polymerization behavior, and physical properties of a third vinyltriazole monomer family, namely the isomeric 1,4-*N*-vinyltriazoles, are reported.

Results and Discussion

A modular synthetic strategy is established for accessing the desired 1,4-*N*-vinyl-based monomers (Scheme 2). 2-Chloroethanol was treated with sodium azide to give 2-azidoethanol, **1**,[8] followed by conversion of the hydroxyl group in a tosylate or mesylate group. Coupling of the azide **2** with a variety of functionalized acetylene molecules in the presence of a heterogeneous copper (copper-in-charcoal) catalyst under established click conditions leads to the establishment of the trizaole nucleus.[9]

The modularity of this alkyne/azide click reaction allows for incorporation of a library of functional groups while the efficiency and simplified nature of the reaction allow for the preparation of the triazole derivatives on a multigram scale. Finally, base-catalyzed elimination of **3a**–**h** delivers the desired monomer series, **4a**–**h**, in overall yields of 50–70% starting from **1**. Initially, eight monomers carrying diverse functional side chains have been synthesized and characterized by ^{1}H and ^{13}C NMR spectroscopy, ESI mass spectrometry, and IR spectroscopy. The crystalline nature of monomer **4e** also allowed for X-ray analysis, further confirming the isomeric *N*-vinyl structure of these monomers (Figure 1).

The electronic structure of the C=C double bond in the *N*-vinyl monomers differs significantly from the corresponding *C*-vinyl derivatives. Consequently, the vinyl group is not conjugated to a radical stabilizing resonance structure as in the C-vinyl case, but rather to a lone pair bearing nitrogen atom, which results in significantly altered radical polymerization kinetics. To address this issue, xanthate-based reversible addition–fragmentation and transfer (RAFT) procedures have been developed for controlling the polymerization of *N*-vinyl monomers.[10] Initial investigations to determine suitable polymerization conditions for this new class of monomers were conducted with **4a** under a variety of different living free radical polymerization procedures. This includes nitroxide-mediated polymerization[11] as well RAFT procedures in the presence of xanthate-based RAFT agent, **5**, or the commercially available dithiocarbamate derivative **7**[12] with azobis(isobutyronitrile) (AIBN) as the initiator in both RAFT cases (Scheme 3). A detailed screening of the polymerization reaction conditions suggested *N*,*N*-dimethylformamide (DMF) as a good solvent and 60 °C to be an optimal polymerization temperature. The optimal AIBN:**5** ratio was found to be 1:4, which resulted in polymers with moderate polydispersity but failed to yield high molecular weight polymers when compared to the polymers obtained by conventional free radical polymerization using AIBN as an initiator. The latter traditional system consistently gave molecular weights over 50 000 g/mol but resulted in high-polydispersity, bimodal size exclusion chromatography traces. In a further effort to efficiently polymerize *N*-vinyltrizaole systems, substitution of the xanthate, **5**, for the dithiocarbamate, **7**, afforded faster kinetics with the polymerizations reaching 80+% conversion after 6 h (cf. ca. 30% conversion for **5**). The use of **7** allows higher molecular weight, low-polydispersity materials to be obtained.

To demonstrate that these monomers are amenable to the reliable construction of polymers with advanced architectures, the formation of random and block copolymers using living free radical techniques was examined. Random and block copolymerization,

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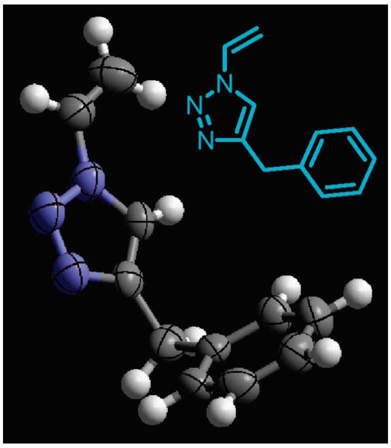
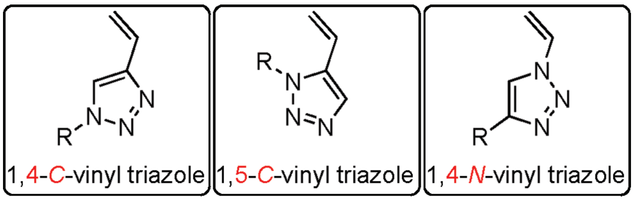
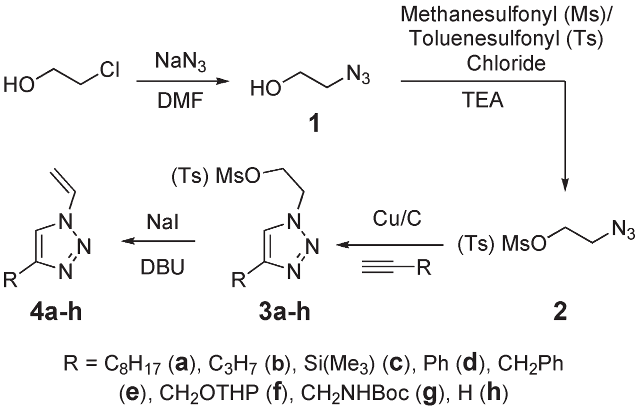


Figure 1. Crystal structure of monomer **4e**.

Scheme 1. Chemical Structures of Three Possible Monomers That Can Be Synthesized by Azide/Alkyne Click Chemistry



Scheme 2. Synthesis of 1,4-*N*-Vinyltriazole Monomer Family



mediated by the alkoxyamines, **8**, showed facile incorporation of the *N*-vinyltrizaole, **4e**, with low polydispersities and high molecular weights being observed for feed ratios of **4e** up to 20 mol %. For example, copolymerization of 500 equiv of a 1:9 molar mixture of **4e** and styrene with the alkoxyamine **8** (R = H) afforded a random copolymer (M_n = 42 000; PDI = 1.17) with the incorporation of the trizaole repeat unit matching the feed ratio (9.5 mol % product ratio compared with 10 mol % feed ratio). At loadings of above 20%, a progressive loss of living character was observed. Similar results were observed for block copolymers derived from alkoxyamine-terminated polystyrene or poly(ethylene glycol) macroinitiators (Scheme 4). Higher levels of *N*-vinyltrizaole incorporation and block copolymers based on trizaole homopolymers could be obtained through RAFT procedures using the dithiocarbamate, **7**, though the polydispersity observed for these materials was increased to ca. 1.4.

The range of homopolymers shown in Figure 2 and related random and block copolymers were thoroughly characterized using a combination of analytical techniques. Thermogravimetric analysis (TGA) of all the functionalized polymers demonstrated the influence of the aromatic triazole ring with similar onsets of weight loss around 350 °C, except for polymer **6h**, which shows increased thermal stability (onset temperature = 400 °C). Major property differences for the library of *N*-vinyltriazole polymers, **6a**–**h**, was observed on examination of the glass transition temperature and solubility characteristics. The glass transition temperatures could be tuned depending on the functionality present in the 4-position of the triazole ring. For example, polymer **6a** appended with a long and flexible alkyl chain exhibits the lowest T_g of 70 °C while polymer **6d** bearing a phenyl group shows the highest T_g of 183 °C. The availability of **6a** and **6e** also allowed for a direct comparison of their physical properties with their *C*-vinyl structural isomers reported previously.[7] Interestingly, the T_g's of the newly synthesized poly(1,4-*N*-vinyltriazole)s were found to be higher than the corresponding poly(1,4-*C*-vinyltriazole)s but lower than the poly(1,5-*C*-vinyltriazole)s. The T_g of **6a** is 70 °C while T_g of poly(1-octyl-4-vinyltriazole) and poly(1-octyl-5-vinyltriazole) is 22 and 95 °C, respectively. The influence of the substitution pattern was also observed on the solubility behavior of these polymers. Polymer **6a** shows good solubility in chloroform and tetrahydrofuran (THF) but was insoluble in ethanol, dimethyl sulfoxide (DMSO), and water at room temperature, whereas polymers **6b**–**g** exhibit good solubility

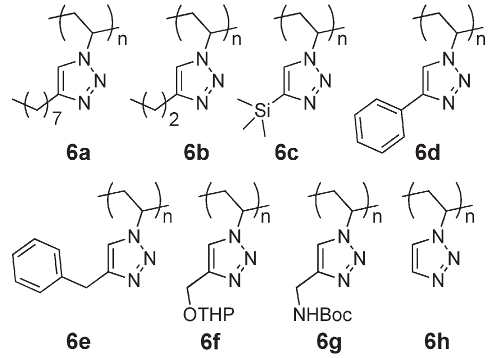
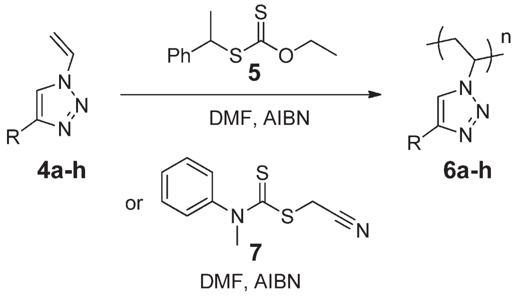
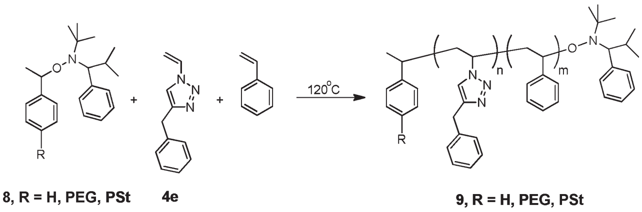


Figure 2. Structure of the *N*-vinyltrizaole homopolymers, **6a**–**h**.

Scheme 3. Polymerization of Monomers 4a–h To Give the Corresponding Polymers 6a–h



Scheme 4. Synthesis of Random and Block Copolymers, 9, Based on the Benzyl-Substituted *N*-Vinyltrizaole, 4e, and Nitroxide-Mediated Polymerization



in almost all solvents except water. Interestingly, polymer **6h** exhibits high solubility in polar solvents such as DMSO and DMF and also in acidic and 5 wt % NaCl aqueous solutions, which suggest the possible use of the parent *N*-vinyltriazole polymer in proton exchange membrane or biomaterial applications. Deprotection of the protected derivatives, **6f** and **6g**, under standard conditions gave the corresponding hydroxymethyl and aminomethyl polymers which proved to have high solubility in water.

Conclusions

In conclusion, we have introduced a new monomer family based on *N*-vinyltriazoles. The modular synthetic strategy allows for incorporation of a variety of groups into the monomer structure with controlled polymerization by either nitroxide or RAFT procedures leading to a library of functionalized macromolecules. The polymer properties are governed by the nature of the functional group present along the backbone with moderate to high glass transition temperatures and variable solubility being observed. The most striking comparison with the corresponding *C*-vinyl systems is the significantly different polymerization behavior, which illustrates the importance of isomer structure in these 1,2,3-trizole-based systems. This study also further demonstrates the use of efficient and modular chemistry for the preparation of novel materials with tunable properties.

Experimental Section

Materials and Instrumental Details. Unless otherwise stated, ACS reagent grade chemicals and solvents were purchased from Aldrich and used without further purification. All reactions were carried out under ambient conditions unless specified. Analytical thin layer chromatography (TLC) was performed on commercial Merck Plates coated with silica gel GF254 (0.24 mm thick). Flash column chromatography was carried out either by using silica gel (Merck Kieselgel 60 (230−400 mesh, ASTM)) or on Biotage SP1 system using 40+M or 65i columns. ^{1}H NMR (500 and 200 MHz) and ^{13}C NMR (162 and 60 MHz) analyses were done using Bruker AC 500 and 200 spectrometers, respectively, with the chemical shift reported in ppm and referenced to signals from residual protons of the solvents. NMR data were processed on ACD laboratories Version 11 software. Size exclusion chromatography (SEC) was carried out at room temperature on a Waters chromatograph connected to a Waters 410 differential refractometer and six Waters Styragel columns (five HR-5 μm and one HMW-20 μm) using THF as eluent (flow rate: 1 mL/min). A Waters 410 differential refractometer and a 996 photodiode array detector were employed. The molecular weights of the polymers were calculated relative to linear polystyrene standards. Differential scanning calorimetry (DSC) measurements took place using a TA Instruments DCS 2920 at a ramp rate of 10 deg/min. A Mettler TGA/DTA 851e was used for thermal gravimetric analysis (TGA) measurements with the experiments being run under nitrogen at a ramp rate of 10 deg/min. Infrared spectroscopic experiments were completed on a Perkin-Elmer Spectrum 100 Fourier transform infrared spectrometer (FTIR). Typically, 4 scans at a resolution of 4 cm^{-1} were recorded on each sample by using an attenuated total reflection (ATR) apparatus. The crystal structures were determined by mounting crystals on glass fibers and transference to a Bruker CCD platform diffractometer. The SMART1 program was used to determine the unite cell parameters and data collections (15 s/frame, 0.3 deg/frame for a sphere of diffraction data). The data were collected at room temperature with Mo Kα radiation. The raw frame data were processed using the SAINT2 program. Empirical absorption corrections were applied based on Psi scan method. Subsequent calculations were carried out using SHELXTL3 program, and the structures were solved by direct methods and refined on F2 by full-matrix least-squares techniques. Mass spectral data were collected on a Micromass QTOF2 quadrupole/time-of-flight tandem mass spectrometer (ESI-MS)

General Click Procedure: Synthesis of 2-(4-Propyl-1*H*-1,2,3-triazol-1-yl)ethyl Methanesulfonate (3b). Pent-1-yne (1.99 g, 29.2 mmol), 2-azidoethyl methanesulfonate (4.55 g, 27.5 mmol), and triethylamine (2.32 g, 22.9 mmol) were dissolved in 50 mL of 1,4-dioxane. Then 200 mg of Cu/C was added, resulting in the formation of a black suspension. The reaction mixture was heated to 30 °C for 24 h, after which the reaction mixture was filtered through a Celite plug, and solvent was removed using a rotary evaporator to yield 5.30 g (83%) of **3b**. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 (s, 1H), 4.56 (br s, 2H), 4.50 (br s, 2H), 2.96 (s, 3H), 2.55 (t, J = 7.6 Hz, 2H), 1.56 (m, J = 7.6 Hz, 2H), 0.83 (t, J = 7.6 Hz, 3H). ESI-mass spectra for $C_8H_{15}N_3O_3S$: Calculated: 233.29; Found $(M + H)^+$: 234.08. IR (ATR): ν (cm^{-1}) 3445, 2962, 1667, 1552.

General Elimination Procedure: Synthesis of 1-Ethenyl-4-propyl-1*H*-1,2,3-triazole (4b). In a 500 mL round-bottom flask equipped with cooling condenser was added **3b** (10.6 g, 45.3 mmol) and NaI (2.00 g, 13.6 mmol) in 250 mL of dimethoxyethane, followed by DBU (13.8 g, 90.8 mmol). After addition of all the reagents, the mixture was heated to 130 °C for 1 h and the dimethoxyethane removed under reduced pressure. The crude product was then dissolved in CH_2Cl_2 and washed with water. The aqueous layer was extracted three times with CH_2Cl_2, the organic fractions were collected, and the crude product was absorbed on silica gel. This crude product was then purified via flash column chromatography (2:3 ethyl acetate:hexanes) to yield 4.04 g (65%) of **4b**. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.53 (s, 1H), 7.15−7.20 (dd, J = 15.76, 8.83 Hz, 1H), 5.50 (dd, J = 15.76, 1.89 Hz, 1H), 4.92−4.96 (m, 1H), 2.54−2.57 (t, 2H), 1.52−1.60 (m, 3H), 0.81−0.83 (t, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.3, 130.2, 117.7, 103.8, 27.4, 22.4, 13.5. IR (ATR): ν (cm^{-1}) 3137, 2961, 1647, 1043, 959, 715. ESI-mass spectra for $C_7H_{11}N_3$: Calculated: 137.10; Found $(M + H)^+$: 138.11.

General Polymerization Procedure Using CTA 5. Ampules equipped with a magnetic stirring bar, monomer **4**, CTA **5**, AIBN (CTA:AIBN = 4:1), and DMF (10 wt % monomer concentration) were subjected to four cycles of freeze−pump−thaw and then sealed under vacuum. The monomer (typically 200 mg) to initiator ratio was 200:1. In a typical run, polymerization reaction was conducted at 60 °C for 6 h. The viscous reaction mixture was then cooled to room temperature, and monomer conversion was calculated by using ^{1}H NMR spectroscopy. Polymers were then precipitated in ethanol or diethyl ether as a white solid. The polymers were dried under vacuum at 50 °C for 12 h. Raft polymerizations with the dithiocarbamate, **7**, were conducted under the same procedure.

General Polymerization Procedure Using AIBN. Free radical polymerization was carried out in 1:1 vol % DMF:DMSO using AIBN as an initiator in ampules equipped with magnetic stirring bar. AIBN to monomer ratio was kept 1:200 for all the polymerizations. In a typical polymerization run, the ampules were subjected to four cycles of freeze−pump−thaw then sealed under vacuum and then placed in an oil bath at 60 °C. The run were generally completed in 2 h with almost complete consumption of the monomers.

General Polymerization Procedure Using Alkoxyamine. Nitroxide-mediated radical polymerizations were performed using the alkoxyamines, **8**, under standard conditions. In a typical polymerization run, the ampules were subjected to four cycles of freeze−pump−thaw, then sealed under vacuum, and placed in an oil bath at 120−125 °C. The polymerizations were generally completed in 12 h.

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Supporting Information Available: Synthetic procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) For a comprehensive review please see: Iha, R. K.; Wooley, K. L.; Nyström, A. M.; Burke, D. J.; Kade, M. J.; Hawker, C. J. *Chem. Rev.* **2009**, *109*, 5620–5686 and references therein . (b) Hawker, C. J.; Wooley, K. L. *Science* **2005**, *309*, 1200–1205. (c) Leibfarth, F. A.; Kang, M.; Ham, M.; Kim, J.; Campos, L. M.; Gupta, N.; Moon, B.; Hawker, C. J. *Nat. Chem.* **2010**, *2*, 207–212.

(2) (a) Lutz, J. F.; Pfeifer, S.; Zarafshani, Z. *QSAR Comb. Sci.* **2007**, *26*, 1151–1158. (b) Killops, K. L.; Campos, L. M.; Hawker, C. J. *J. Am. Chem. Soc.* **2008**, *130*, 5062–5064. (c) Campos, L. M.; Meinel, I.; Guino, R. G.; Schierhorn, M.; Gupta, N.; Stucky, G. D.; Hawker, C. J. *Adv. Mater.* **2008**, *20*, 3728–3733. (d) Campos, L. M.; Killops, K. L.; Sakai, R.; Paulusse, J. M. J.; Damiron, D.; Drockenmuller, E.; Messmore, B. W.; Hawker, C. J. *Macromolecules* **2008**, *41*, 7063–7070. (e) Gu, W.; Chen, G.; Stenzel, M. H. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 5550–5556. (f) Li, C.; Ge, Z.; Liu, H.; Liu, S. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 4001–4013. (g) Yu, B.; Chan, J. W.; Hoyle, C. E.; Lowe, A. B. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 3544–3557. (h) Gacal, B. N.; Koz, B.; Gacal, B.; Kiskan, B.; Erdogan, M.; Yagci, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 1317–1326.

(3) (a) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004–2021. (b) Tornoe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057–3064. (c) Lutz, J.-F. *Angew. Chem., Int. Ed.* **2007**, *46*, 1018–1025. (d) Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun.* **2007**, *28*, 15–54. (e) Fukukawa, K. I.; Rossin, R.; Hagooly, A.; Pressly, E. D.; Hunt, J. N.; Messmore, B. W.; Wooley, K. L.; Welch, M. J.; Hawker, C. J. *Biomacromolecules* **2008**, *9*, 1329–1339. (f) Wu, P.; Malkoch, M.; Hunt, J. N.; Vestberg, R.; Kaltgrad, E.; Finn, M. G.; Fokin, V. V.; Sharpless, K. B.; Hawker, C. J. *Chem. Commun.* **2005**, 5775–5777. (g) Tsarevsky, N. V.; Bernaerts, K. V.; Dufour, B.; DuPrez, F. E.; Matyjaszewski, K. *Macromolecules* **2004**, *37*, 9308–9313. (h) Opsteen, J. A.; Hest, J. C. M. *Chem. Commun.* **2005**, 57–59.

(4) (a) Wu, P.; Feldman, A. K.; Nugent, A. K.; Hawker, C. J.; Scheel, A.; Voit, B.; Pyun, J.; Frechet, J. M. J.; Sharpless, K. B.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2004**, *43*, 3928–3932. (b) Vestberg, R.; Malkoch, M.; Kade, M.; Wu, P.; Fokin, V. V.; Sharpless, K. B.; Drockenmuller, E.; Hawker, C. J. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 2835–2846. (c) Antoni, P.; Hed, Y.; Nordberg, A.; Nystrom, D.; von Holst, H.; Hult, A.; Malkoch, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2126–2130. (d) Liu, J.; Nie, Z.; Gao, Y.; Adronov, A.; Li, H. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 7187–7199. (e) Vogt, A. P.; Sumerlin, B. S. *Macromolecules* **2006**, *39*, 5286–5292. (f) Mantovani, G.; Ladmiral, V.; Tao, L.; Haddleton, D. M. *Chem. Commun.* **2005**, 2089–2091. (g) Sumerlin, B. S.; Tsarevsky, N. V.; Louche, G.; Lee, R. Y.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 7540–7545. (h) Parrish, B.; Breitenkamp, R. B.; Emrick, T. *J. Am. Chem. Soc.* **2005**, *127*, 7404–7410.

(5) Thibault, R. J.; Takizawa, K.; Lowenheilm, P.; Helms, B.; Mynar, J. L.; Fréchet, J. M. J.; Hawker, C. J. *J. Am. Chem. Soc.* **2006**, *128*, 12084–12085.

(6) Takizawa, K.; Nulwala, H.; Thibault, R. J.; Lowenhielm, P.; Yoshinaga, K.; Wooley, K. L.; Hawker, C. J. *J. Polym. Sci., Part A: Chem.* **2008**, *46*, 5506–5517.

(7) Nulwala, H.; Takizawa, K.; Odukale, A.; Khan, A.; Thibault, R. J.; Taft, B. R.; Lipshutz, B. H.; Hawker, C. J. *Macromolecules* **2009**, *42*, 6068–6074.

(8) Bräse, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188–5240.

(9) Lipshutz, B. H.; Taft, B. R. *Angew. Chem., Int. Ed.* **2006**, *45*, 8235–8238.

(10) (a) Chiefari, J.; Chong, Y. K.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P. T.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules* **1998**, *31*, 5559–5562. (b) Maki, Y.; Mori, H.; Endo, T. *Macromolecules* **2007**, *40*, 6119–6130.

(11) (a) Rodlert, M.; Harth, E.; Rees, I.; Hawker, C. J. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 4749–4763. (b) Stehling, U. M.; Malmstrom, E. E.; Waymouth, R. M.; Hawker, C. J. *Macromolecules* **1998**, *31*, 4396–4398. (c) Hawker, C. J.; Barclay, G. G.; Dao, J. L. *J. Am. Chem. Soc.* **1996**, *118*, 11467–11471.

(12) The dithiocarbamate, **7**, is commercially available from Aldrich, cat. no. 723002; CAS 76926-16-4.