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C−H Functionalization Polycondensation of Chlorothiophenes in the Presence of Nickel Catalyst with Stoichiometric or Catalytically Generated Magnesium Amide

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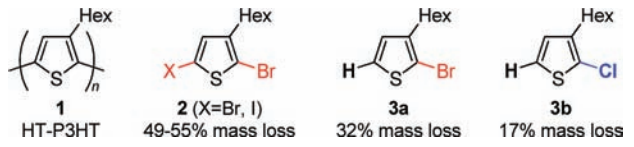
S *Supporting Information*

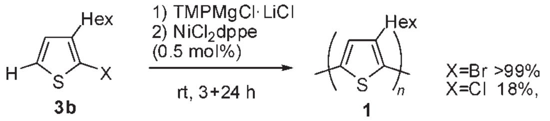
ABSTRACT: Polymerization of 2-chloro-3-substituted thiophenes proceeded with a stoichiometric amount of magnesium amide, TMPMgCl·LiCl, or a combination of a Grignard reagent and a catalytic amount of secondary amine in the presence of a nickel catalyst. Although the nickel-catalyzed polymerization with $NiCl_2$dppe, which exhibited high catalytic activity in the reaction of bromothiophenes, was less effective, use of a nickel catalyst bearing *N*-heterocyclic carbene as a ligand was found to induce polymerization with controlled molecular weight and molecular weight distribution.

Oligothiophenes and polythiophenes have recently attracted considerable attention in materials science. Regioregular thiophenes, which involve head-to-tail (HT) repeating units such as poly(3-hexylthiophene) (HT-P3HT, **1**), are of particular interest since the compounds show remarkable physical properties for uses such as organic thin-film transistors,[1] thin-film organic solar cells,[2] and conductive polymer materials.[3] Development of a practical synthetic method for P3HTs is therefore important in organic synthesis.[4] Dehalogenative polycondensation developed by Rieke,[5] McCullough,[6] and Yokozawa[7] with a Grignard reagent and a nickel catalyst is widely employed for the synthesis of the regioregular polythiophenes. Considering the point of *atom efficiency* in the polythiophene synthesis, the reaction with the loss of two halogen atoms in the thiophene unit is problematic issue; for example, the use of 2,5-dibromo-3-hexylthiophene (**2a**) brings about 49% mass loss in the polymerization. We have recently shown that dehydrobrominative polycondensation with 2-bromo-3-hexylthiophene (**3a**) proceeds with Knochel−Hauser base[8] (chloromagnesium 2,2,6,6-tetramethylpiperidide lithium chloride salt, TMPMgCl·LiCl, **4**), and a nickel catalyst gives highly regioregular HT-P3HT,[9] in which the atom efficiency is improved to 32% mass loss. A more improved efficiency is possible if the polymerization is performed with the corresponding chlorothiophene **3b**, giving only 17% mass loss (Chart 1); however, the reaction of 2-chlorothiophene has been difficult under similar conditions.[10] It is highly intriguing to investigate a novel metal-catalyzed polymerization that can be used for chlorothiophenes as a monomer. Herein, we report that a nickel catalyst bearing *N*-heterocyclic carbene (NHC)[11,12] as a ligand is highly effective for the polymerization of 2-chloro-3-hexylthiophene, affording HT-P3HT. We also describe C−H functionalization with the combination of a Grignard reagent and a catalytic amount of secondary amine in place of Knochel−Hauser base.

Chart 1



Scheme 1



When the polymerization of 2-chloro-3-hexylthiophene (**3b**) was carried out with an equimolar amount of **4** and 0.5 mol % of $NiCl_2$dppe[9a] at 25 °C for 24 h, only 18% of P3HT **1** was obtained, with a much lower $M_n = 4200$ ($M_w/M_n = 1.34$). The result is in sharp contrast to the polymerization with 2-bromo-3-hexylthiophene (**3a**), which brought about complete conversion at room temperature within 24 h, affording **1** with M_n = 45 000 ($M_w/M_n = 1.32$) (Scheme 1).

We then surveyed nickel catalysts with various ligands. Table 1 summarizes the polymerization of 2-chloro-3-hexylthiophene (**3b**) with Knochel−Hauser base **4**. The reaction was slightly improved by the use of $NiCl_2$dppp[9a] (0.5 mol %) as a catalyst to afford the polymer **1** in 57% yield; however, its molecular weight was still low compared with the theoretical M_n (ca. 33 000) based on the ratio of catalyst loading to the monomer. Drastic improvement of the catalytic activity was observed when the catalyst was switched to that bearing PPh_3 and NHC ligands[13a] on the nickel to afford polythiophene with M_n = 27 300 and a relatively narrow polydispersity ($M_w/M_n = 1.27$). As summarized in Figure 1, (a) the average molecular weight was found to decrease by increasing the catalyst loading, while the molecular weight distribution was 1.2 to 1.3, and (b) a linear increase of M_n was observed as consumption of the monomer proceeded.[14] The use of a mixture of $Ni(cod)_2$ and 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr; Ni/L = 1:2) also afforded a polythiophene of high molecular weight and HT selectivity in 41% yield. However, the polydispersity was considerably inferior. Similar reaction with $Ni(cod)_2$

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Table 1. Nickel-Catalyzed Polymerization of Chlorothiophene 3b with Knochel–Hauser Base[a]

catalyst (mol %)	yield, %[b]	M_n (M_w/M_n)[c]	% HT[d]
NiCl$_2$dppe (0.5)	18	4200 (1.34)	91
NiCl$_2$dppp (0.5)	57	9700 (1.39)	98
NiCl$_2$(PPh$_3$)IPr (0.5)	**67 (90)**	**29200 (1.29)**	**99**
NiCl$_2$(PPh$_3$)IPr (1.0)	**(95)**	**17400 (1.31)**	**98**
NiCl$_2$(PPh$_3$)IPr (1.5)	**(99)**	**10700 (1.26)**	**98**
NiCl$_2$(PPh$_3$)IPr (2.0)	**(87)**	**7870 (1.22)**	**97**
NiCl$_2$(PPh$_3$)IPr (3.0)	**(89)**	**5170 (1.15)**	**95**
Ni(cod)$_2$/2IPr (0.5)	41	28400 (1.92)	98
Ni(cod)$_2$/2SIPr (0.5)	70	31900 (6.30)	98

[a] The reaction was carried out with **3b** and 1.0 equiv of TMPMgCl·LiCl **4** in THF for the metalation, and nickel catalyst was employed for the polycondensation. [b] Isolated yield. Conversion (%) of the monomer is shown in parentheses. [c] M_n and M_w/M_n values were estimated by SEC analysis using CHCl$_3$ as an eluent. [d] HT selectivity was estimated by ^{1}H NMR analysis.

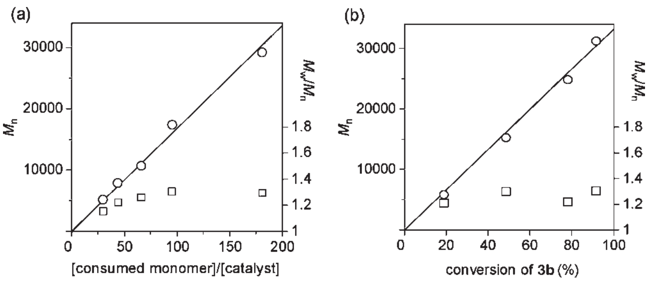


Figure 1. (a) Relationship of [consumed monomer]/[catalyst] feed ratio toward M_n and M_w/M_n in the polymerization of **3b**/**4** with NiCl$_2$(PPh$_3$)IPr after stirring for 24 h. The solid line indicates theoretical molecular weight at each ratio. (b) Relationship of monomer conversion vs M_n, obtained with 0.5 mol % of NiCl$_2$(PPh$_3$)IPr. The solid line indicates theoretical molecular weight at each conversion; ○ and □ show M_n and M_w/M_n, respectively.

and 1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene (SIPr; Ni/L = 1:2) afforded **1** in 70% yield with M_n = 31 900 (M_w/M_n = 6.3).

The reaction was considered to proceed by the C–H functionalization of chlorothiophene **3b** with TMPMgCl·LiCl **4** to form the corresponding thienyl Grignard reagent **A** along with 2,2,6,6-tetramethylpiperidine (TMPH), and the addition of a nickel catalyst induced the polymerization of **A**, as illustrated in Scheme 2. Concerning the *atom efficiency*, the reagent for the generation of the metallic species should also be taken into consideration. Thus, it is intriguing to perform the total polymerization process with catalytic use of the magnesium amide. Since Knochel–Hauser base **4** is prepared by the reaction of 2-propylmagnesium chloride (LiCl salt) with 2,2,6,6-tetramethylpiperidine[8,15] by proton abstraction to form propane, the produced TMPH would be employed for the regeneration of **4**. This suggests that in situ formation of magnesium amide species occurs with a catalytic amount of secondary amine and Grignard reagent. Although metalation of 3-methylthiophene has been shown recently with catalytic TMPH and isopropyl Grignard reagent,[16] it is still unrevealed if the reaction of the Grignard reagent toward the halogen-containing thiophene is applicable.

Accordingly, we investigated the metalation of 2-chloro-3-hexylthiophene (**3b**) with several Grignard reagents and a catalytic amount of secondary amines to form the corresponding thienyl magnesium reagent. Table 2 summarizes the results. The reaction was examined at 60 °C in THF, and the progress of the reaction was monitored by quenching with iodine to form 2-chloro-3-hexyl-5-iodothiophene (**5**). It was found that combination of several Grignard reagents and 10 mol % of amine was effective. The reaction with a Grignard reagent in the absence of amine afforded **5** in extremely low yield, which suggested that Grignard reagent also abstracted the hydrogen atom, albeit with insufficient efficiency. The reaction with sterically less-hindered ethylmagnesium chloride showed superior reactivity with a hindered secondary amine

Scheme 2

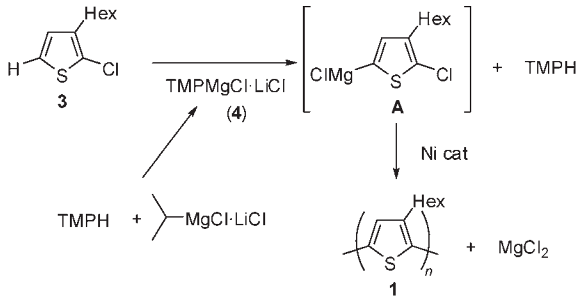
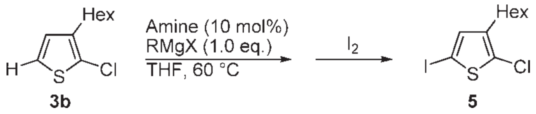


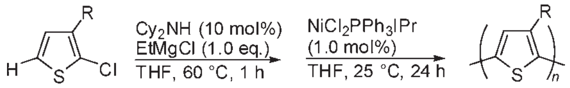
Table 2. Generation of Thienyl Magnesium Species with a Grignard Reagent and a Catalytic Amount of Amine[a]

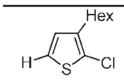
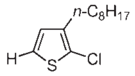
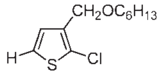


Grignard reagent	amine	time, h	conversion, %[b]
EtMgCl	none	10	26
	Et$_2$NH	2	73
	^{i}Pr$_2$NH	10	85
	Cy$_2$NH	1	85
	TMPH	10	88
	morpholine	10	46
	(Me$_3$Si)$_2$NH	10	17
^{i}PrMgBr	none	10	21
	Et$_2$NH	10	85
	^{i}Pr$_2$NH	5	73
	Cy$_2$NH	2	83
	TMPH	10	35
^{t}BuMgCl	none	10	6
	Et$_2$NH	10	71
	^{i}Pr$_2$NH	10	90
	Cy$_2$NH	10	95
	TMPH	10	5

[a] The reaction was carried out with 2-chloro-3-hexylthiophene (0.5 mmol), Grignard reagent (0.5 mmol), and amine (0.05 mmol) in 0.5 mL of THF at 60 °C. [b] The conversion was estimated by ^{1}H NMR analysis after quenching the reaction mixture with iodine.

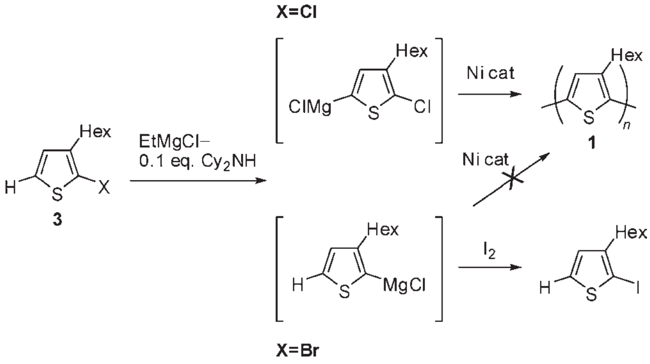
Table 3. Nickel-Catalyzed Polycondensation of 3-Substituted 2-Chlorothiophene Using Grignard Reagent and Catalytic Amine[a]



chlorothiophene		M_n[b]	M_w/M_n[b]	%HT[c]	Yield (%)
	(**3b**)	14900	1.21	98	82
	(**6**)	23100	1.29	99	76
	(**7**)	17000	1.31	99	84

[a] The reaction was performed with monomer (1.0 mmol), Cy$_2$NH (0.1 mmol), EtMgCl (1.0 mmol), and NiCl$_2$(PPh$_3$)IPr (1.0 mol %) in 10 mL of THF at 60 °C for 1 h (metalation) and at room temperature for 24 h (polymerization). [b] Estimated by SEC analysis using CHCl$_3$ as an eluent. [c] Estimated by ^{1}H NMR.

Scheme 3



such as dicyclohexylamine (Cy$_2$NH) and 2,2,6,6-tetramethylpiperidine (TMPH), although diethylamine Et$_2$NH was less effective. On the other hand, hindered Grignard reagents ^{i}PrMgBr and ^{t}BuMgCl also showed excellent formation of the metallic species with Et$_2$NH, while hindered amine TMPH did not undergo metalation efficiently.

With the method for catalytic generation of metallic species **A** (in Scheme 2) in hand, the reaction of **3b** was carried out with EtMgCl and 10 mol % of Cy$_2$NH at 60 °C for 1 h. After the mixture cooled to room temperature, the nickel catalyst NiCl$_2$(PPh$_3$)IPr (1.0 mol %) was added. Polymerization was initiated, and, after stirring for 24 h, P3HT was obtained in 82% yield. M_n and M_w/M_n of the polymer were found to be 14 900 and 1.21, respectively, with high HT selectivity as shown in Table 3. It should be pointed out such polymerization with a Grignard reagent and a catalytic amount of amine was specifically achieved with chlorothiophene **3b**, whereas the reaction with bromothiophene **3a** under similar conditions did not afford P3HT at all. Indeed, the reaction of **3a** with EtMgCl and 10 mol % of Cy$_2$NH underwent halogen−metal exchange of the bromine atom for magnesium, leading to 2-thienyl Grignard reagent.[17] Thus, quenching of the metalated species with iodine afforded 2-iodo-3-hexylthiophene exclusively (Scheme 3).

With the polymerization conditions determined for **3b**, several other chlorothiophenes were converted to poly-3-substituted thiophenes, as shown in Table 3. Monomers **6** and **7** were synthesized in a similar manner to that of **3b**. Polymerization of **6** and **7** also proceeded to afford the corresponding polymers highly efficiently.

In conclusion, 2-chloro-3-subsituted thiophenes were revealed to polymerize with magnesium amide and a nickel catalyst. The polymerization shows remarkable synthetic advantage in atom efficiency, giving only 17% mass loss comparing with those (49−55%) of existing dehalogenative methods with 2,5-dihalothiophenes. The reaction using catalytically generated magnesium amide with Grignard reagent and catalytic secondary amine is also worth mentioning from a mechanistic point of view as well as for the practical synthetic efficiency of the total process. The established new concept opens further improvement toward various transition metal-catalyzed coupling reactions as well as the related cross-coupling polycondensation reactions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Experimental details and characterization of new compounds and polymers. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) (a) Sirringhaus, H.; Tessler, N.; Friend, R. H. *Science* **1998**, *280*, 1741. (b) Sirringhaus, H.; Brown, P. J.; Friend, R. H.; Nielsen, M. M.; Bechgaard, K.; Langeveld-Voss, B. M. W.; Spiering, A. J. H.; Janssen, R. A. J.; Meijer, W. W.; Herwig, P.; deLeeuw, D. M. *Nature* **1999**, *401*, 685. (c) Kim, Y.; Cook, S.; Tuladhar, S. M.; Choulis, S. A.; Nelson, J.; Durrant, J. R.; Bradley, D. D. C.; Giles, M.; McCulloch, I.; Ha, C.-S.; Ree, M. *Nat. Mater.* **2006**, *5*, 197. (d) Woo, C. H.; Thompson, B. C.; Kim, B. J.; Toney, M. F.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2008**, *130*, 16324.

(2) (a) Roncali, J. *Chem. Rev.* **1997**, *97*, 173. (b) Günes, S.; Neugebauer, H.; Sarisiftci, N. S. *Chem. Rev.* **2007**, *107*, 1324. (c) Cheng, Y.-J.; Yang, S.-H.; Hsu, C.-S. *Chem. Rev.* **2009**, *109*, 5868.

(3) (a) Chen, F.; Mehta, P. G.; Takiff, L.; McCullough, R. D. *J. Mater. Chem.* **1996**, *6*, 1763. (b) Gangopadhyay, P.; Koeckelberghs, G.; Persoons, A. *Chem. Mater.* **2011**, *23*, 516. (c) McQuade, D. T.; Pullen, A. E.; Swager, T. M. *Chem. Rev.* **2000**, *100*, 2537. (d) Grimsdale, A. C.; Chan, K. L.; Martin, R. E.; Jokisz, P. G.; Holmes, A. B. *Chem. Rev.* **2009**, *109*, 897.

(4) Selected reviews:(a) McCullough, R. D. *Adv. Mater.* **1998**, *10*, 93. (b) Osaka, I.; McCullough, R. D. *Acc. Chem. Res.* **2008**, *41*, 1202.

(5) (a) Chen, T. A.; Rieke, R. D. *J. Am. Chem. Soc.* **1992**, *114*, 10087. (b) Chen, T.-A.; O'Brien, R. D.; Rieke, R. D. *Macromolecules* **1993**, *26*, 3462.

(c) Chen, T. A.; Wu, X.; Rieke, R. D. *J. Am. Chem. Soc.* **1995**, *117*, 233. (d) Wu, X.; Chen, T.-A.; Rieke, R. D. *Macromolecules* **1996**, *29*, 7671.

(6) (a) Loewe, R. S.; Khersonsky, S. M.; McCullough, R. D. *Adv. Mater.* **1999**, *11*, 250. (b) McCullough, R. D.; Lowe, R. D. *J. Chem. Soc., Chem. Commun.* **1992**, *1*, 70. (c) McCullough, R. D.; Lowe, R. D.; Jayaraman, M.; Anderson, D. L. *J. Org. Chem.* **1993**, *58*, 904. (d) Sheina, E. E.; Liu, J.; Iovu, M. C.; Laird, D. W.; McCullough, R. D. *Macromolecules* **2004**, *37*, 3526. (e) Iovu, M. C.; Sheina, E. E.; Gil, R. R.; McCullough, R. D. *Macromolecules* **2005**, *38*, 8649. (f) Jeffries-El, M.; Sauvé, G.; McCullough, R. D. *Macromolecules* **2005**, *38*, 10346. (g) Stefan, M. C. Javier, A. E.; Osaka, I.; McCullough, R. D. *Macromolecules* **2009**, *42*, 30.

(7) (a) Yokoyama, A.; Miyakoshi, R.; Yokozawa, T. *Macromolecules* **2004**, *37*, 1169. (b) Miyakoshi, R.; Yokoyama, A.; Yokozawa, T. *J. Am. Chem. Soc.* **2005**, *127*, 17542. (c) Yokozawa, T.; Yokoyama, A. *Chem. Rev.* **2009**, *109*, 5595. (d) Miyakoshi, R.; Yokoyama, A.; Yokozawa, T. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 753.

(8) (a) Krasovskiy, A.; Krasovskaya, V.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 2958. (b) Lin, W.; Baron, O.; Knochel, P. *Org. Lett.* **2006**, *8*, 5673. (c) Clososki, G. C.; Rohbogner, C. J.; Knochel, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 7681. (d) Rohbogner, C. J.; Clososki, G. C.; Knochel, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 1503. (e) Stoll, A. H.; Knochel, P. *Org. Lett.* **2008**, *10*, 113. (f) Mosrin, M.; Knochel, P. *Org. Lett.* **2008**, *10*, 2497. (g) Piller, F. M.; Knochel, P. *Org. Lett.* **2009**, *11*, 445.

(9) (a) Tamba, S.; Tanaka, S.; Okubo, Y.; Okamoto, S.; Meguro, H.; Mori, A. *Chem. Lett.* **2011**, *40*, 398. See also:(b) Wang, Q.; Takita, R.; Kikuzaki, T.; Ozawa, F. *J. Am. Chem. Soc.* **2010**, *132*, 11420.

(10) (a) Tasler, S.; Lipshutz, B. H. *J. Org. Chem.* **2003**, *68*, 1190. (b) Walla, P.; Kappe, C. O. *Chem. Commun.* **2004**, 564. (c) Xi, Z.; Liu, B.; Chen, W. *J. Org. Chem.* **2008**, *73*, 3954. (d) Zhang, C.; Wang, Z.-X. *Organometallics* **2009**, *28*, 6507. (e) Berding, J.; Lutz, M.; Spek, A. L.; Bouwman, E. *Organometallics* **2009**, *28*, 1845. (f) Ghosh, J.; Sarkar, A. *J. Org. Chem.* **2010**, *75*, 8283. (g) Liu, N.; Wang, Li.; Wang, Z.-X. *Chem. Commun.* **2011**, *47*, 1598. For reviews:(h) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. *Chem. Rev.* **2011**, *111*, 1346. (i) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417.

(11) For reviews:(a) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290. (b) Weskamp, T.; Böhm, V. P. W.; Herrmann, W. A. *J. Organomet. Chem.* **2000**, *600*, 12. (c) Bourissou, D.; Guerret, O.; Gabba, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39.

(12) (a) McGuinness, D. S.; Cavell, K. J. *Organometallics* **1999**, *18*, 1596. (b) Böhm, V. P. W.; Weskamp, T.; Gstöttmayr, C. W. K.; Hermann, W. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 1602. (c) Böhm, V. P. W.; Gstöttmayr, C. W. K.; Weskamp, T.; Hermann, W. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 3387. (d) Sato, Y.; Sawaki, R.; Mori, M. *Organometallics* **2001**, *20*, 5510. (e) Mahandru, G. M.; Liu, G.; Montgomery, J. *J. Am. Chem. Soc.* **2004**, *126*, 3698. (f) Díez-González, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612.

(13) (a) Matsubara, K.; Ueno, K.; Shibata, Y. *Organometallics* **2006**, *25*, 3422. See also:(b) Dorta, R.; Stevens, E. D.; Hoff, C. D.; Nolan, S. P. *J. Am. Chem. Soc.* **2003**, *125*, 10490. (c) Dible, B. R.; Sigman, M. S. *J. Am. Chem. Soc.* **2003**, *125*, 872. (d) Herrmann, W. A.; Gerstberger, G.; Spiegler, M. *Organometallics* **1997**, *16*, 2209.

(14) (a) Bronstein, H. A.; Luscombe, C. K. *J. Am. Chem. Soc.* **2009**, *131*, 12894. (b) Doubina, N.; Ho, A.; Jen, A. K.-Y.; Luscombe, C. K. *Macromolecules* **2009**, *42*, 7670. (c) Boyd, S. D.; Jen, A. K.-Y.; Luscombe, C. K. *Macromolecules* **2009**, *42*, 9387. (d) Lanni, E. L.; McNeil, A. J. *J. Am. Chem. Soc.* **2009**, *131*, 16573. (e) Tkachov, R.; Senkovskyy, V.; Komber, H.; Sommer, J.-U.; Kiriy, A. *J. Am. Chem. Soc.* **2010**, *132*, 7803. (f) Lanni, E. L.; McNeil, A. J. *Macromolecules* **2010**, *43*, 8039. (g) Senkovskyy, V.; Sommer, M.; Tkachov, R.; Komber, H.; Huck, W. T. S.; Kiriy, A. *Macromolecules* **2010**, *43*, 10157. (h) Doubina, N.; Paniagua, S. A.; Soldatova, A. V.; Jen, A. K.-Y.; Marder, S. R.; Luscombe, C. K. *Macromolecules* **2011**, *44*, 512.

(15) (a) Hauser, C. R.; Walker, H. G. *J. Am. Chem. Soc.* **1947**, *69*, 295. (b) Frostick, F. C.; Hauser, C. R. *J. Am. Chem. Soc.* **1949**, *71*, 1350. (c) Eaton, P. E.; Lee, C.-H.; Xiong, Y. *J. Am. Chem. Soc.* **1989**, *111*, 8016.

(16) Asselin, S. M.; Bio, M. M.; Langille, N. F.; Ngai, K. Y. *Org. Process Res. Dev.* **2010**, *14*, 1427.

(17) (a) Shi, L.; Chu, Y.; Knochel, P.; Mayr, H. *Org. Lett.* **2009**, *11*, 3502. (b) Shi, L.; Chu, Y.; Knochel, P.; Mayr, H. *J. Org. Chem.* **2009**, *74*, 2760. (c) Shi, L.; Chu, Y.; Knochel, P.; Mayr, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 202.