ORIGINAL ARTICLE

Air-tolerant poly(3-hexylthiophene) synthesis via catalyst-transfer polymerization

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Abstract

The discovery of catalyst-transfer polymerization and its further developments have led to unprecedented control over the length and sequence of conjugated polymers. However, the methods themselves are technically challenging to perform due to the air- and moisture-sensitivities of the monomers and catalysts. Herein, we report a catalyst-transfer polymerization method that affords poly(3-hexylthiophene) in high yields without using an inert atmosphere. The synthesis capitalizes on a rapid Negishi cross-coupling using a moisture-tolerant organozinc monomer mediated by an air-stable Pd precatalyst. This simple method should make conjugated polymer synthesis more accessible to a broader range of researchers and may be generalizable to other monomer scaffolds.

KEYWORDS

catalysis, catalyst-transfer polymerization, chain-growth polymerization, conjugated polymers, palladium

1 | INTRODUCTION

Organic conjugated polymers (CPs) have remained fascinating materials for chemists since the Nobel-prize winning observation of their conductivity in 1977.[1] Over the next 40 years, CPs were evaluated as the active materials in transistors,[2] light-emitting diodes,[3] and solar cells.[4] Although research in these traditional areas continues today, new CP-based applications have emerged. For example, in a recent perspective Swager suggested that the future of CPs is in superconductors, magneto-optic materials, and artificial muscles.[5] Around the same time, Seferos and coworkers suggested the future of CPs is in electrical energy storage.[6] Within these evolving contexts, Swager notes that "precision in (CP) synthesis is critical" to enabling these applications.[5]

Most conjugated polymers are still synthesized via step-growth polymerizations involving metal-catalyzed C—C bond forming reactions.[7] This synthetic approach is extremely versatile with respect to monomer structures, but often leads to polymers with broad dispersity and little control over the length, copolymer sequence, or end-groups. An alternative approach, known as catalyst-transfer polymerization, proceeds via a living, chain-growth mechanism.[8–17] As a consequence, specific lengths, copolymer sequences, and end-groups can be targeted, and the resulting polymer's dispersity ($Đ$) is often narrow (<2). Having such exquisite control over polymer architecture has led to numerous advances in the field, including higher performing materials.[15] However, this method works best with only a subset of useful monomers (primarily small, electron-rich aromatic structures). In addition, the synthesis often requires an inert atmosphere due to moisture- and/or air-sensitive catalysts and reagents. As a result, researchers without access to specialized equipment must rely on collaborators or commercial suppliers to make materials, limiting widespread exploration of CPs in electronic applications.

Recognizing this challenge, several recent papers have described a more 'user-friendly' conjugated polymer synthesis, in which the polymerization is performed in air.[18,19] For example, Kanabara and coworkers reported an oxygen- and moisture-tolerant synthesis of thienopyrroledione-based conjugated polymers through a step-growth direct arylation polycondensation, wherein refluxing conditions effectively deoxygenated the solution.[18,20] Most recently, Schoenebeck and coworkers demonstrated CP synthesis in air utilizing the high reactivity of a Pd(I) dimer-based catalyst, which enabled high conversions to be reached before appreciable monomer deactivation via quenching.[19] One limitation of both studies is that control over the molar masses was not achieved, indicating non-living processes. Alternatively, Higashihara and co-workers reported a method for synthesizing regioregular poly(3-hexylthiophene) (**P3HT**) that was tolerant to protic impurities (e.g., MeOH) in the solvent using tBu_4ZnLi_2 and Ni precatalysts. However, the polymerizations still required an inert argon atmosphere presumably due to ligand/catalyst deactivation.[21]

Herein, we describe an air-tolerant, living, chain-growth synthesis of **P3HT** with bench-stable Pd precatalysts and organozinc reagents.[22–24] All reactions were performed in a hood, with commercial reagents used as received, and without using an inert atmosphere. The process begins by generating an organozinc monomer in situ from a Grignard reagent and zinc pivalate.[25–27] The magnesium pivalate byproduct is believed to sequester trace water, serving as a desiccant. Next, the Negishi-based polymerization is mediated by an air-stable Pd precatalyst. This approach was inspired by Knochel and coworkers, who have reported similar open-to-air Negishi cross-couplings of aromatic small molecules.[28–30] The resulting polymers were obtained with narrow dispersity, specified length, and with end-groups consistent with a catalyst-transfer polymerization mechanism.

2 | EXPERIMENTAL

All reagents and solvents were used as received and without further purification. All reactions were performed using 8 ml glass vials capped with a rubber septum. The reaction vials and stir bars were dried in an oven overnight and cooled to rt inside a desiccator filled with Drierite granules. All solutions were transferred using disposable plastic syringes and metal needles.

2.1 | Monomer synthesis ($3HT_{Zn}$)

2,5-Dibromo-3-hexylthiophene (0.050 ml, 0.23 mmol) and docosane (internal standard) were added to a vial which was capped with a septum. Then, anhydrous THF

(1.2 ml) and i-PrMgCl (2.0 M in THF, 0.082 ml, 0.16 mmol) were sequentially added. The homogeneous solution was stirred for 10 min at rt. Then, a portion of this Grignard solution (1.0 ml, 0.13 mmol) was added to a separate vial containing $Zn(OPiv)_2$ (36 mg, 0.14 mmol). This solution was stirred for 10 min at rt. The remaining Grignard solution was quenched by adding aq. HCl (1.0 mL, 12 M) and diluting with DI water (2.0 mL). The organics were extracted with DCM (3.0 mL), filtered through a small plug of $MgSO_4$, and analyzed by gas chromatography (GC) with a flame ionization detector (FID).

2.2 | Precatalyst solution

In a separate vial, Pd-PEPPSI-IPent (2.9 mg, 0.0036 mmol) was dissolved in THF (0.8 ml).

2.3 | Polymer synthesis (P3HT)

A portion of the precatalyst solution (0.5 ml, 0.0045 M in THF) was added to the organozinc solution. The reaction was stirred for 10 min at rt. Within the first min, the solution turned dark orange. The polymerization was quenched by adding aq. HCl (1.0 ml, 12 M) and extracted with DCM (2.0 ml). The organic layer was dried and filtered over $MgSO_4$. A portion of this solution was concentrated and then re-dissolved in approx. 1 ml of THF, then analyzed by size-exclusion chromatography (SEC) to determine M_n and $Đ$ and by matrix-assisted laser-desorption time-of-flight mass spectrometry (MALDI-TOF-MS) to determine the end-groups. Another aliquot was diluted with additional DCM and analyzed by GC-FID to determine monomer conversion relative to an internal standard (docosane).

3 | RESULTS AND DISCUSSION

Our synthetic approach is highlighted in Scheme 1. First, 2,5-dibromo-3-hexylthiophene is reacted with i-PrMgCl to generate a Grignard reagent ($3HT_{Mg}$) as a 79:21 mixture of regioisomers, as evidenced by GC analysis (Table S1). After 10 min, an aliquot of the $3HT_{Mg}$ is added $Zn(OPiv)_2$ to generate the zinc-based monomer ($3HT_{Zn}$), with no change in the regioselectivity observed (Table S2). This process generates $Mg(OPiv)_2$ as a byproduct, which has been suggested by others to efficiently sequester adventitious water.[23] Next, the precatalyst (Pd-PEPPSI-IPent) is added to the $3HT_{Zn}$ solution to generate **P3HT**. After 10 min, the polymerization is quenched and the polymer
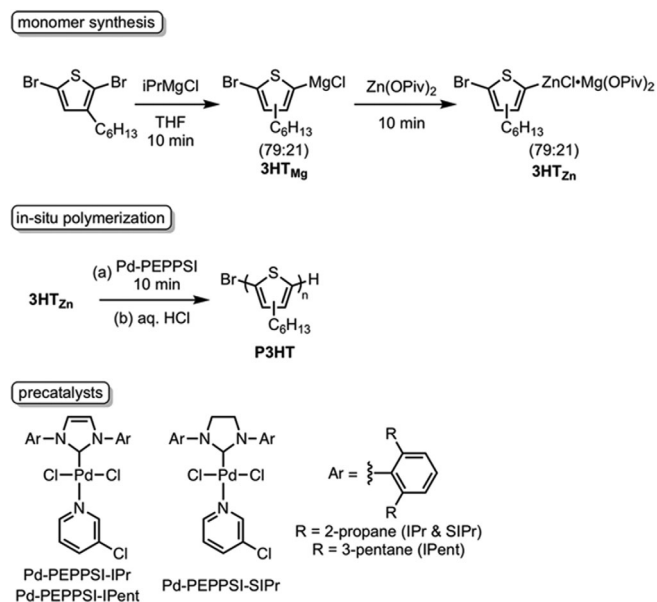
SCHEME 1 Air-tolerant synthesis of poly(3-hexylthiophene) via catalyst-transfer polymerization

TABLE 1 Polymerization data with varying reaction conditions

Entry	Precatalyst	Conditions	M_n (kg/mol)	Đ
1	IPent	In air	10.6	1.47
2	IPent	Under N_2	11.2	1.46
3	IPr	Under N_2	10.0	1.87
4	SIPr	Under N_2	17.8	1.81
5	IPent	$ZnCl_2$	6.5	1.46
6	IPent	Without Zn	3.9	1.47

Note: Entries 5–6 were also performed under N_2. M_n (theoretical) = 10 kg/mol for 100% monomer conversion.
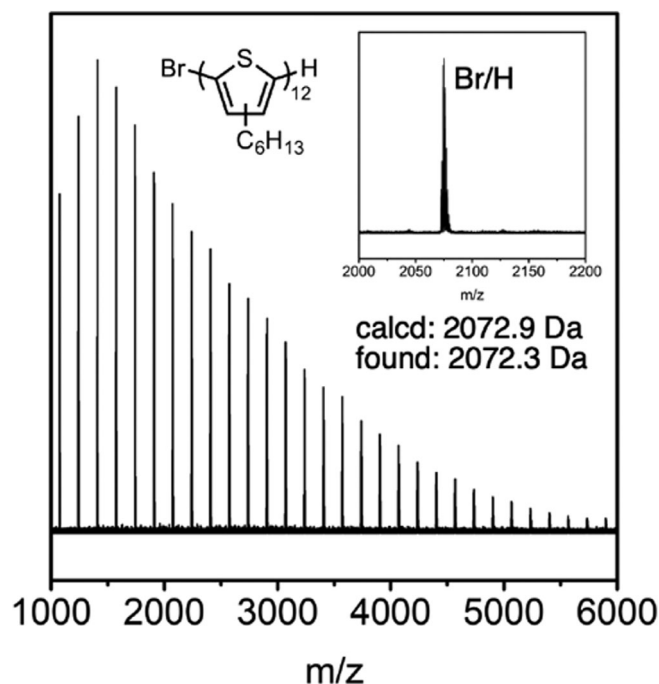

FIGURE 1 Matrix-assisted laser-desorption time-of-flight (MALDI-TOF) mass spectrum of poly(3-hexylthiophene) (**P3HT**) prepared by Pd-PEPPSI-IPent precatalyst

is extracted for analysis. All of the above reactions were performed with solvents used as received and without an inert atmosphere. The reactions were performed in small vials capped with a septum, and the septum is temporarily removed when reagents are added.

^{1}H NMR spectroscopic analysis reveals that the synthesized **P3HT** exhibits 63% regioregularity, indicating that both regioisomers of the 3HT$_{Zn}$ are consumed. Indeed, our GC data reveals high conversions of both regioisomers, with the minor regioisomer having a slightly higher conversion (minor (93%) versus major (87%)), consistent with the low regioregularity. Presumably, switching to the I/Br monomer precursor (i.e., 2-bromo-3-hexyl-5-iodothiophene) would lead to **P3HT** with higher regioregularity, though the reaction temperature may need to be lowered to prevent undesired side-reactions (e.g., HI elimination from the in situ-generated 2-iodopropane.) Analysis by SEC reveals that the number-average molar mass (M_n) is similar to the theoretical M_n, which is calculated based on the initial monomer/catalyst ratio and the monomer conversion (Table 1, entry 1) (Note that SEC measurements relative to PS standards are known to over-estimate the M_n of **P3HT** by a factor of ~1.3).[31,32] Additionally, the resulting polymer sample exhibits moderate dispersity (Đ ≈ 1.5). Combined, these results are consistent with a chain-growth mechanism.

To optimize this method, several commercially available, air-stable Pd-PEPPSI precatalysts (where PEPPSI stands for pyridine-enhanced precatalyst preparation, stabilization, and initiation) were screened under an N_2 atmosphere with the primary selection criterion being their ability to generate polymers with exclusively H/Br end groups, as measured using MALDI-TOF-MS. These end-groups are indicative of a living, chain-growth mechanism[33] wherein the precatalyst initiates via two sequential transmetalation reactions and then continues to propagate without termination until quenching with acid. For comparison, the original IPent precatalyst yielded **P3HT** with exclusively H/Br chain ends, as evident in Figure 1. In contrast, both IPr and SIPr precatalysts afforded polymers with multiple chain-end identities, including Br/Br and H/H, as well as the desired H/Br (see SI Figures S2 and S4). These results are consistent with both catalyst disassociation (Br/Br) and the released Pd(0) catalyst undergoing subsequent initiation with monomer (H/H). In addition, although the IPr precatalyst gave polymer with the expected

M_n, the dispersities were broader than with IPent (Table 1, entry 3). In contrast, the SIPr precatalyst gave both a much higher than expected M_n and a broader dispersity (Table 1, entry 4.) Although the mechanistic rationale for the improved results with the sterically demanding but conformationally flexible environment provided by IPent is unclear at this time, we note that Organ and co-workers previously observed that IPent was optimal for sterically congested substrates.[34] For comparison, Ni(dppp)Cl$_2$ gave only oligomers with multiple end-group identities (SI Figure S5). Having identified IPent as a suitable precatalyst, we further probed the impact of the reaction conditions on the polymerization.

Control experiments revealed the importance of using Zn(OPiv)$_2$; for example, using a different zinc reagent (i.e., ZnCl$_2$) or using no zinc reagent resulted in polymers with a significantly lower M_n (Table 1, entries 5 and 6), suggesting a slower polymerization. One hypothesis was that the slower rate might be due to prematurely quenched monomer, which would lower its effective concentration in solution and decrease the polymerization rate. Alternatively, the slower polymerization rate may simply be due to the different nucleophilicities of the organometallic species (**3HT$_{Mg}$** vs. **3HT$_{Zn}$**), either due to the identity of the counterion or their aggregation state. To identify which factor was more important, we monitored the polymerization by periodically quenching aliquots with iodine. This method enabled us to distinguish prematurely quenched monomer (**3HT$_H$**) from unreacted monomer (**3HT$_I$**). The results, highlighted in Figure 2, showed rapid polymerization when Zn(OPiv)$_2$ was added (>90% conversion within 5 min). During this time, only ca. 10% of monomer was prematurely quenched. Without Zn(OPiv)$_2$, the polymerization was much slower (~20% conversion within 5 min) and a similar amount of the monomer was prematurely quenched (10%). Combined, these results suggest that the slower polymerization is not due to monomer quenching with adventitious moisture but instead that the Zn(OPiv)$_2$-based monomer is more nucleophilic, leading to a faster polymerization. The different reactivities of the Zn and Mg monomers may be useful for generating random, gradient, and block copolymers in situ.[35] Our earlier results (Table 1) also indicate that the form of ZnX$_2$ (where X = OPiv or Cl) plays an important, yet still not well-defined role, because the polymerization was slower with ZnCl$_2$. One difference is that upon ZnCl$_2$ addition, the MgCl$_2$ generated is insoluble and precipitates out of solution. In contrast, the generated Mg(OPiv)$_2$ remains in solution, and may form a mixed aggregate with the organozinc monomer.[25]

To support a chain-growth mechanism, the change in the M_n over time was monitored by SEC, which revealed monomodal and symmetric peaks shifting to a lower retention time during the polymerization (e.g., see
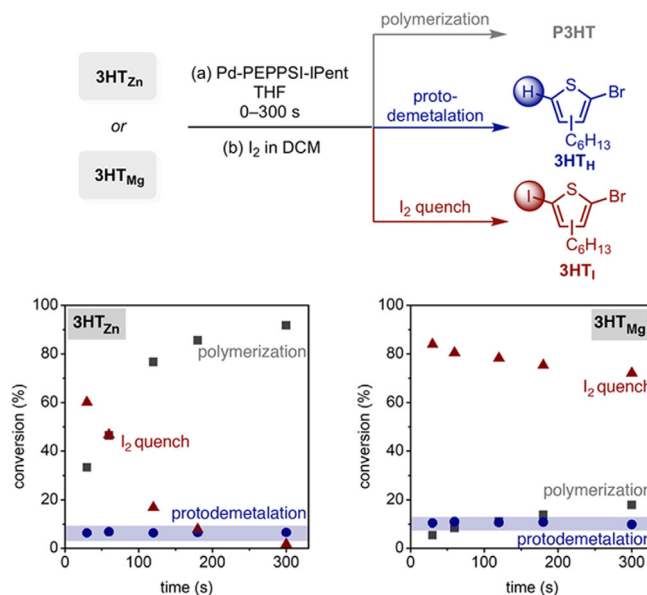

FIGURE 2 Iodine quenching studies for polymerizations with and without Zn(OPiv)$_2$. Plots depict changes in monomer conversion (%) versus time (s) [Color figure can be viewed at wileyonlinelibrary.com]
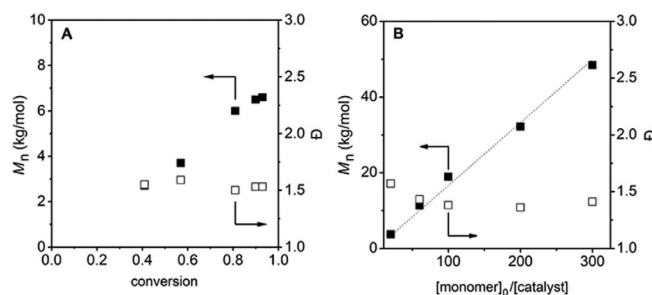

FIGURE 3 Plots of M_n and Đ versus (A) monomer conversion and (B) (monomer)$_0$/(catalyst) ratio

Figure S10). More specifically, a linear increase in M_n versus conversion was observed, along with a constant Đ, both of which are indicative of a chain-growth mechanism (Figure 3(A)). Changing the (monomer)/(precatalyst) ratio enabled us to target specific molar masses ranging from 5 to 50 kg/mol (Figure 3(B)). Combined with the MALDI-TOF-MS study shown above, in which exclusively H/Br end groups are observed, these results are all consistent with a chain-growth polymerization mechanism.

To determine whether our polymerization was living, a simple chain-extension experiment was performed. That is, a second batch of monomer was added after the first batch of monomer had polymerized. SEC analysis before and after the second addition of monomer displayed the expected increase in M_n while maintaining
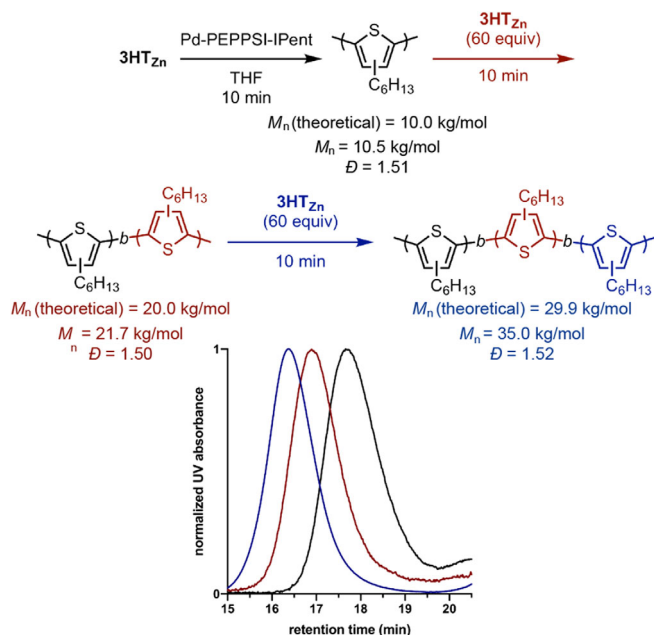
FIGURE 4 Size exclusion chromatography (SEC) traces for the chain extension experiment [Color figure can be viewed at wileyonlinelibrary.com]

symmetrical SEC peaks, consistent with a living polymerization (Figure 4). To further challenge the system, a third batch of monomer was added, again showing the expected increase in M_n without any significant broadening of the dispersity. As a consequence, this living polymerization method may be useful to prepare sequenced copolymers, such as block and gradient copolymers.

Until this point, most of the experiments were performed on a small scale (<0.5 mmol monomer), which can be more challenging than larger scales due to quenching with adventitious moisture or contact with air. As a consequence, we scaled the reaction to approx. 5 mmol monomer, which should generate 0.5 g of **P3HT**. As anticipated, the reaction proceeded quite well, giving a M_n close to the theoretical molar masses (9.4 vs. 7.6 kg/mol, respectively) and a narrow dispersity ($Đ = 1.34$). Isolating the polymer was more challenging, however, due to leftover monomer. However, after a series of precipitation steps, pure **P3HT** was isolated in 68% yield. Overall, this method is viable for generating significant quantities of **P3HT** for use in applications.

4 | CONCLUSIONS

A living, chain-growth synthesis of **P3HT** was developed using the air-stable Pd-PEPPSI-IPent precatalyst combined with moisture-tolerant organozinc monomer. Using this approach, polymers with predictable molar masses, moderate dispersities, and high end-group fidelity were obtained. The living, chain-growth nature of this polymerization was corroborated by performing a chain-extension experiment, highlighting the potential of this approach for synthesizing block and gradient copolymers. We anticipate that this method may be useful for other monomer types. In addition, this method should be more accessible to a broader community of researchers due to the air/moisture tolerance and lack of need for specialized equipment. As researchers continue to explore CPs for varied applications, living, chain-growth methods like this one will be at the forefront.

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REFERENCES

[1] H. Shirakawa, E. J. Louis, A. G. MacDiarmid, C. K. Chiang, A. J. Heeger, *J. Chem. Soc., Chem. Commun.* **1977**, 578.
[2] H. Sirringhaus, *Adv. Mater.* **2014**, *26*, 1319.
[3] Y. Tsubata, *Sci. Technol. Adv. Mater.* **2014**, *15*, 034203.
[4] G. Wang, F. S. Melkonyan, A. Facchetti, T. J. Marks, *Angew. Chem. Int. Ed.* **2019**, *58*, 4129.
[5] T. M. Swager, *Macromolecules* **2017**, *50*, 4867.
[6] T. B. Schon, B. T. McAllister, P.-F. Li, D. S. Seferos, *Chem. Soc. Rev.* **2016**, *45*, 6345.
[7] F. Babudri, G. M. Farinola, F. Naso, *J. Mater. Chem.* **2004**, *14*, 11.
[8] A. Yokoyama, R. Miyakoshi, T. Yokozawa, *Macromolecules* **2004**, *37*, 1169.
[9] E. E. Sheina, J. Liu, M. C. Iovu, D. W. Laird, R. D. McCullough, *Macromolecules* **2004**, *37*, 3526.
[10] K. Okamoto, C. K. Luscombe, *Polym. Chem.* **2011**, *2*, 2424.
[11] Z. J. Bryan, A. J. McNeil, *Macromolecules* **2013**, *46*, 8395.
[12] A. Kiriy, V. Senkovskyy, M. Sommer, *Macromol. Rapid Commun.* **2011**, *32*, 1503.
[13] A. K. Leone, A. J. McNeil, *Acc. Chem. Res.* **2016**, *49*, 2822.
[14] M. A. Baker, C.-H. Tsai, K. J. T. Noonan, *Chem. Eur. J.* **2018**, *24*, 13078.
[15] J. P. Lutz, M. D. Hannigan, A. J. McNeil, *Coord. Chem. Rev.* **2018**, *376*, 225.
[16] A. K. Leone, E. A. Mueller, A. J. McNeil, *J. Am. Chem. Soc.* **2018**, *140*, 15126.

[17] S. Ye, S. Cheng, A. A. Pollit, M. W. Forbes, D. S. Seferos, *J. Am. Chem. Soc.* **2020**, *142*, 11244.

[18] A. Ichige, H. Saito, J. Kuwabara, T. Yasuda, J.-C. Choi, T. Kanbara, *Macromolecules* **2018**, *51*, 6782.

[19] G. Magnin, J. Clifton, F. Schoenebeck, *Angew. Chem., Int. Ed.* **2019**, *58*, 10179.

[20] J. Kuwabara, T. Kanabara, *Bull. Chem. Soc. Jpn.* **2019**, *92*, 152.

[21] T. Higashihara, E. Goto, M. Ueda, *ACS Macro Lett.* **2012**, *1*, 167.

[22] M. G. Organ, S. Avola, I. Dubovyk, N. Hadei, E. A. B. Kantchev, C. J. O'Brein, C. A. Valente, *Chem. Eur. J.* **2006**, *12*, 4749.

[23] C. Valente, M. E. Belowich, N. Hadei, M. G. Organ, *Eur. J. Org. Chem.* **2010**, *2010*, 4343.

[24] C. Valente, S. Çalimsiz, K. H. Hoi, D. Mallik, M. Sayah, M. G. Organ, *Angew. Chem., Int. Ed.* **2012**, *51*, 3314.

[25] A. Hernán-Gómez, E. Herd, E. Hevia, A. R. Kennedy, P. Knochel, K. Koszinowski, S. M. Manolikakes, R. E. Mulvey, C. Schnegelsberg, *Angew. Chem., Int. Ed.* **2014**, *53*, 2706.

[26] Y.-H. Chen, M. Ellwart, V. Malakhov, P. Knochel, *Synthesis* **2017**, *49*, 3215.

[27] M. Ellwart, Y.-H. Chen, C. P. Tüllmann, V. Malakhov, P. Knochel, *Org. Syn.* **2018**, *95*, 127.

[28] S. Bernhardt, G. Manolikakes, T. Kunz, P. Knochel, *Angew. Chem., Int. Ed.* **2011**, *50*, 9205.

[29] C. I. Stathakis, S. Bernhardt, V. Quint, P. Knochel, *Angew. Chem., Int. Ed.* **2012**, *51*, 9428.

[30] S. M. Manolikakes, M. Ellwart, C. I. Stathakis, P. Knochel, *Chem. Eur. J.* **2014**, *20*, 12289.

[31] M. Wong, J. Hollinger, L. M. Kozycz, T. M. McCormick, Y. Lu, D. C. Burns, D. S. Seferos, *ACS Macro. Lett.* **2012**, *1*, 1266.

[32] K. Gu, J. Onorato, S. S. Xiao, C. K. Luscombe, Y.-L. Loo, *Chem. Mater.* **2018**, *30*, 570.

[33] A. K. Leone, P. K. Goldberg, A. J. McNeil, *J. Am. Chem. Soc.* **2018**, *140*, 7846.

[34] M. G. Organ, S. Çalimsiz, M. Sayah, K. H. Hoi, A. J. Lough, *Angew. Chem., Int. Ed.* **2009**, *48*, 2383.

[35] T. Hardeman, G. Koeckelberghs, *Polym. Chem.* **2017**, *8*, 3999.

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