Rapid flow-based synthesis of poly(3-hexylthiophene) using 2-methyltetrahydrofuran as a bio-derived reaction solvent

James H. Bannock*, Wenmin Xu, Théophile Baïssas, Martin Heeney and John C. de Mello

* j.bannock@imperial.ac.uk

Centre for Plastic Electronics and Department of Chemistry, Imperial College London, Exhibition Road, London. SW7 2AZ UK.

Abstract

We report the synthesis of poly(3-hexylthiophene) (P3HT) by Grignard metathesis (GRIM) polymerization using the bio-derived ‘green’ solvent 2-methyltetrahydrofuran (2-MeTHF). Using a standard flask-based reaction, the molecular weight distribution, regioregularity and product yield were found to be similar to those obtained under equivalent conditions using tetrahydrofuran (THF) as a reaction solvent. The synthesis was subsequently adapted to a novel “tube-in-shell” droplet-based flow reactor, using a newly developed high-solubility catalyst derived from nickel(II) bromide ethylene glycol dimethyl ether complex (Ni(dme)Br₂) and 1,3-bis(diphenylphosphino)propane (dppp). Use of the new catalyst together with an increased reaction temperature of 65 °C (enabled by the higher boiling point of 2-MeTHF) resulted in an approximate four-fold increase in reaction rate compared to a standard THF-based synthesis at 55 °C, with full conversion reached within one minute. The purified flow-synthesized polymer had an Mw of 46 kg mol⁻¹, a low PDI of 1.4, and a regioregularity of 93 %, indicating the suitability of flow-based GRIM polymerization in 2-MeTHF for the high-throughput synthesis of high quality P3HT.

Keywords

semiconducting polymers; poly(3-hexylthiophene); P3HT; flow synthesis; green synthesis;

Introduction

Poly(3-hexylthiophene) (P3HT) is the most widely studied semiconducting polymer in organic electronics research, and, despite the existence of many higher performing alternatives, it remains one of the few materials that can be produced at sufficiently low cost for commercialization of organic photovoltaic devices. [1] There are many synthetic pathways for P3HT, with the Grignard metathesis (GRIM) polymerization route developed by the McCullough Group in 1999 [2] being the most common due to its simplicity, high product
yield, and the ease with which molecular weight may be tuned through simple changes to the reaction conditions. [3,4]

Scheme 1 shows a two-step, one-pot GRIM polymerization route for the preparation of P3HT. In its usual form, 2,5-dibromo-3-hexylthiophene (1) is first activated with one equivalence of a Grignard reagent in an ether-based solvent, typically tetrahydrofuran (THF), yielding a mixture of two thienyl-Grignard regioisomers (2a and 2b). After completion of the initial metathesis, a nickel-diphosphine catalyst, typically [1,3-bis(diphenolphosphinopropane)]-nickel(II) chloride (Ni(dppp)Cl₂), is added to initiate Kumada-Yamamoto cross-coupling – known more widely as Kumada catalyst transfer polymerization (KCTP) – to form the conjugated polymer (3). The polymerization is quenched using a protic (often acidified) non-solvent that also induces precipitation of the polymer, enabling isolation over a filter. When isopropylmagnesium chloride (iPrMgCl) is used as the Grignard reagent, the ratio of 2a to 2b is approximately four to one, [5] with the minority isomer 2b being sterically inactive towards Ni(dppp)Cl₂ and the majority isomer 2a undergoing quasi-living chain-growth to form regioregular P3HT, [2,6] suitable for organic electronics applications. [7,8]

The standard GRIM polymerization synthesis route as described above is effective for the lab-scale synthesis of regioregular P3HT. However, the use of THF as a process solvent presents significant difficulties for larger-scale manufacturing owing to the energy intensive, non-renewable nature of its production. [9] Here we investigate the use of the bio-derived solvent 2-methyltetrahydrofuran (2-MeTHF) as a greener alternative to THF. We show that 2-MeTHF can be used as a direct replacement for THF in the flask-based synthesis of P3HT, yielding polymer with similar material properties under equivalent reaction conditions. We further show that the reaction procedure in 2-MeTHF may be adapted to flow synthesis in a droplet-based microreactor, where the higher boiling point of 2-MeTHF (~80 °C [10]) allows the reaction to be carried out at temperatures of up to 65 °C, leading to substantially faster reaction rates. In combination with a new catalyst derived from nickel(II) bromide ethylene glycol dimethyl ether complex (Ni(dme)Br₂) and 1,3-bis(diphenolphosphino)-propane (dppp), we find that it is possible to achieve full conversion in under one minute, while still achieving regioregularities comparable to those obtained using Ni(dppp)Cl₂. The described modifications to the standard GRIM polymerization route are of direct relevance to the large-scale manufacturing of P3HT, allowing for increased materials throughput whilst at the same time reducing environmental impact.

Results and Discussion

THF is the most widely used solvent for GRIM polymerization, with only a few isolated examples of alternative solvents such as o-dichlorobenzene being used in its place. [11] While THF is an excellent Lewis base for Grignard (and other organometallic) chemistries, its production is highly energy intensive. [9] In recent years there has been a trend towards the use of bio-derived, green solvents as replacements for hazardous and/or
environmentally-damaging solvents. [12] 2-methyltetrahydrofuran (2-MeTHF) is one such solvent that has been developed as a greener alternative to THF. [13] Derived from inedible biomass, 2-MeTHF is a close derivative of THF and is accordingly well-suited to Grignard chemistry. Further advantages of 2-MeTHF include: (i) a higher boiling point (78-80 °C) compared to THF (66-67 °C); (ii) low miscibility with water; (iii) favorable azeotropes with water and alcohols, enabling easier production of anhydrous solvent; and (iv) a favorable preliminary safety assessment. [14,15] 2-MeTHF has been successfully used as a solvent for a range of small molecule chemistries, including organometallic chemistries. [12,14,16] Here we evaluate its suitability for the synthesis of P3HT by Grignard metathesis polymerization, with a view to reducing the environmental impact of P3HT synthesis and exploiting its higher boiling point to achieve higher reaction rates.

To assess the suitability of 2-MeTHF for use as a solvent for P3HT synthesis, we adapted a flask-based synthesis procedure using THF that we had previously optimized for the production of high molecular weight P3HT with weight-average molecular weight (Mw) greater than 100 kg mol⁻¹. [17] (We have recently shown that P3HT prepared using this procedure can yield high performance P3HT:fullerene organic photovoltaic devices with power conversion efficiencies of up to 7 %, using indene-C₆₀ bis-adduct as the fullerene acceptor [18]). Two samples B1 and B2 were prepared under equivalent conditions (see Experimental Methods), using THF and 2-MeTHF respectively. The syntheses were carried out at 55 °C – the highest reaction temperature that can be used with THF without it simmering or boiling in the flask (and thereby causing unwanted quenching of the polymerization on the walls of the flask during the course of the reaction).

After purification, sample B1 was recovered with a yield of 86 % (assuming a four to one ratio of 2a : 2b, with only 2a being active towards the catalyst). Using refractive-index size-exclusion chromatography (RI-SEC), B1 was found to have a Mw of 134 kg mol⁻¹ and a PDI of 1.62, see Table 1 and Figure SI1a. By analyzing the α-methylene region of the ¹H NMR spectrum [19], the regioregularity was determined to be 99 % (see Fig. SI1b) in accordance with the regio-selective nature of the chosen GRIM-based synthesis. [17]

B2 was recovered with a high yield of 94 % after purification (assuming the same four to one ratio of active 2a to inactive 2b). There was only a small difference in the molecular weight distribution compared to B1 (see Figure SI1a), with the Mw and PDI being broadly similar at 137 kg mol⁻¹ and 1.66, respectively. The RR was also similar at 99 %.

The higher boiling point of 2-MeTHF (80 °C) allows the reaction to be carried at higher temperatures of up to 75 °C without simmering or boiling in the flask. A third sample B3 was prepared in 2-MeTHF at 75 °C and recovered at 85 % yield after purification. The Mw and PDI were slightly lower than for B1 and B2 at 118.0 kg mol⁻¹ and 1.53, respectively. The regioregularity was also slightly lower at 98%, consistent with the lower molecular weight.¹²

¹ Full range ¹H NMR spectra for samples B1-3 are shown in Figure SI2.
On the basis of the results above, it is evident that under otherwise identical conditions 2-MeTHF can serve as a direct substitute for THF without substantially affecting the properties or yield of the final product. Moreover, its higher boiling point allows the reaction to be carried out at higher temperatures of up to 75 °C, leading to faster reaction rates and shorter conversion times (see below).

**Flow Synthesis**

Having confirmed the suitability of 2-MeTHF for the flask-based synthesis of P3HT, we investigated its suitability for use in (droplet-based) flow reactors. Flow synthesis is of significant interest for the synthesis of advanced materials such as conjugated polymers due to its amenability to high volume manufacturing, allowing production rates of a few tens [20] to several hundreds [21,22] of grams per day to be readily achieved in even small lab-scale reactors. [11,20–26]

The majority of reports of polymer synthesis in flow have used commercial single-phase flow reactors, in which the reagents are mixed together and pumped through the reactor in a continuous stream of a single solvent. Such reactors, however, are susceptible to fouling as a result of polymer deposition on the reactor walls. This is a particular issue for industrial manufacturing, where fouling is a major cause of product drift and reactor downtime. We have previously reported the use of droplet-based flow reactors as a means of preventing reactor fouling during the flow synthesis of conjugated polymers. [20,24] In this approach monomer feedstock is injected into a fast-flowing stream of immiscible carrier fluid, forming a stream of near-identical microliter-sized monomer droplets that act as discrete self-contained microliter reaction vessels. The small droplet size ensures rapid equilibration of composition and temperature, and so provides a highly uniform environment for polymerization. Importantly, since materials throughput can be raised independently of droplet volume (by ramping up the rate of droplet generation, while keeping the droplet size fixed), production levels can in principle be scaled-up indefinitely without detriment to product quality.

The carrier fluid is chosen to wet preferentially to the channel walls, ensuring the droplets are kept beneficially isolated from the channel walls and so cannot cause fouling of the reactor. For the work described here perfluorinated polyether (PFPE) was used as the carrier fluid in combination with polytetrafluoroethylene (PTFE) reactor tubing. PFPE wets the PTFE tubing preferentially over most organic solvents, resulting in stable droplet flow over a wide range of temperatures. [27–29] It is not consumed during the flow process and so may be reused, either by recovering it manually from the product at the outlet or by continuously recycling it in-line. [28,30,31]
In the flask-based synthesis of P3HT described above, the catalyst was added in solid form to the thienyl-Grignard. In flow-based syntheses, however, it is preferable to dissolve the nickel catalyst to achieve good control over the molecular weight. At full conversion, the molecular weight average is primarily determined by the initial molar ratio of monomer to catalyst, with each catalyst molecule propagating the growth of an individual chain. Hence, a low monomer to catalyst ratio will lead to a small number of long chains, while a high monomer to catalyst ratio will lead to a large number of short chains. This mechanistic property may be exploited to tune the molecular weight of P3HT in both flask- and flow-based reactions. [3,4,11,20]

While high weight P3HT (as prepared above) is often preferred for small-scale processing from chlorinated solvents, lower molecular weight material (< 50 kg mol⁻¹) is typically preferred for processing from non-chlorinated solvents since it dissolves more readily. Such low weight materials can be difficult to access in flow using the standard Grignard metathesis procedure based on Ni(dppp)Cl₂ since the catalyst is only weakly soluble in ether solvents, exhibiting a room temperature saturation concentration of ~1 mg/mL (1.8 mM) in THF. This limits access to low molecular weight polymers in flow, as a low monomer to catalyst ratio can only be achieved by lowering the monomer concentration, which in turn reduces reactor throughput. The low solubility of Ni(dppp)Cl₂ also risks unwanted precipitation of solid particles during the course of the reaction.

For this work we tested the use of Ni(dppp)Br₂ as an alternative, more soluble catalyst for the GRIM polymerization of P3HT. Ni(dppp)Br₂ may be generated in-situ from nickel(II) bromide ethylene glycol dimethyl ether complex (Ni(dme)Br₂) and 2.5 equivalents of dppp.³⁴ Importantly, Ni(dppp)Br₂ retains the catalytic Ni(0)(dppp) functionality required for KCTP [3,4], with the bromide anions merely acting to improve the solubility of the initial Ni(II) precursor. We have found that the catalyst remains soluble at concentrations up to 26 mM (supported by a proportionate increase of dppp) in THF compared to ~2 mM for Ni(dppp)Cl₂. Although stable in solution under an inert atmosphere, the catalyst rapidly degrades if exposed to air. For the work reported here the catalyst was therefore generated in-situ in an argon atmosphere (see Experimental Methods).

To demonstrate the feasibility of applying Ni(dppp)Br₂ to the flow synthesis of low molecular weight P3HT in 2-MeTHF, a flow synthesis was carried out using 3.1 mM Ni(dppp)Br₂ – approximately twice the concentration that can be achieved using standard Ni(dppp)Cl₂. Figure 1 shows a schematic of the experimental set up. Separate solutions of

³ As we have previously reported for Ni(dppp)Cl₂ [23], Ni(dppp)Br₂ requires an excess of 1,3-bis(diphenylphosphino)propane (dppp) to inhibit catalyst deactivation via ligand dissociation. Addition of excess dppp to Ni(dme)Br₂ in solution results in an immediate color change from pink to brown – indicative of the Ni(dppp)Br₂ species forming.

⁴ In early stage tests we found a strong correlation between the [dppp]:[Ni] ratio and the molecular weight distribution of the polymer up to 2.1 equivalences. Above 2.1 equivalences the molecular weight distribution was found to be insensitive towards the ratio of [dppp]:[Ni]. A value of 2.5 equivalences is chosen in order to be safely above the threshold.
thienyl-Grignard (0.25 M) and Ni(dppp)Br₂ (3.1 mM) were prepared in anhydrous 2-MeTHF as described under Experimental Methods. After cooling to room temperature, the solutions were transferred into separate oven-dried 10 mL gas-tight syringes (Hamilton) and sealed prior to use. A third 50 mL gas-tight syringe (SGE) was filled with argon-sparged PFPE (Galden HT-170, Solvay Solexis) and sealed prior to use. The three fluids were connected to a three-inlet/one-outlet PTFE droplet generator, fabricated using a four-axis milling machine to a previously reported design (Fig. 1a). [32] In use, the droplet generator produces a stable stream of near-identical droplets, as shown in the inset photograph of Figure 1. (Note that the droplet generator shown in the photograph was machined from translucent polychlorotrifluoroethylene (PCTFE) to allow optical inspection of the inner channels). The two reagent syringes were connected to the droplet generator using 10 cm segments of 0.3 mm inner diameter (ID) PTFE tubing (Upchurch) and flangeless microfluidic fittings (Upchurch). The PFPE syringe was connected to the droplet generator using a 10 cm segment of 1 mm ID PTFE tubing (Polyflon). Each syringe was mounted on a separate syringe pump (Pump 11+, Harvard Apparatus), allowing the flow-rate of each fluid to be independently controlled.

The flow synthesis was carried out using a novel “tube-in-shell” reactor that allowed the droplet stream to be heated without recourse to a cumbersome oil-bath (Fig. 1b). The reactor was formed from two coaxial tubes of approximate length 1 m: the droplet stream from the droplet generator was injected into the central tube (ID 1 mm, ~785.4 µL), while an outer jacket of temperature-controlled water was constantly recirculated through the void between the outer wall of the central tube and the inner wall of the outer tube (ID 3 mm). The water jacket was maintained at a constant temperature of approximately 65 °C using a small recirculating water heater that kept the water in rapid circulation via a pair of junctions at each end of the reactor (see schematic in Fig. 1c). With a pump speed of several hundred milliliters per minute, the temperature difference between the inlet and the outlet was much less than 1 °C, ensuring virtually constant heating along the full length of the reactor. On exiting the central capillary, the droplet stream was passed into a methanol-filled collection vessel to quench the reaction (Fig. 1d). Complete details of the reactor design can be found in SI Section E.

In initial testing it was determined that using 2-MeTHF as the reaction solvent allowed the tube-in-shell reactor to be operated at a maximum temperature of 65 °C, a 10 °C increase on THF. (Above 65 °C vapor-filled bubbles of 2-MeTHF formed around the liquid droplets, causing the droplet flow to become unstable). By varying the total flow rate of the three fluids from 785.4 to 78.5 µL min⁻¹, while maintaining a volumetric flow-rate ratio of 2:1:1 PFPE : Ni(II) catalyst solution : thienyl-Grignard solution, four polymer samples, F1-4, were collected at reaction times of 60, 150, 300 and 600 s. (Due to the fixed flow-rate ratio, the thienyl-Grignard concentration and catalyst loading remained the same in all four cases at 0.125 M and 1.2 mol%, respectively). After setting each flow-rate, the flow was allowed to stabilize fully before collecting 4 mL of eluent into a methanol-filled vial (to quench the reaction and
precipitate the polymer). Crude samples were analyzed by RI-SEC to determine their molecular weight distributions.

Figure 2 shows the molecular weight distributions for the four crude samples, which were virtually identical to each other. The weight-average molecular weights were all approximately 44 kg mol\(^{-1}\) (see Table 2 and inset to Figure 2), consistent with full conversion being reached in less than one minute, i.e. less than one quarter of the time required to achieve full conversion (and a similar Mw) using Ni(dppp)Cl\(_2\) in THF at 55 °C. [20,24] The lower molecular weight of the flow-synthesized samples B1-3 relative to the flask-synthesized samples B1-3 is consistent with the higher concentration of Ni(dppp)Br\(_2\) catalyst used for the reaction (1.2 mol% for F1-4 cf. 0.15 mol% for B1-3). Following purification, polymer F4 had an Mw of 46 kg mol\(^{-1}\), a PDI of 1.4 and a RR of 93 % (see Fig. 2 (red SEC trace) and SI Section F), characteristics that are favorable for processing from non-chlorinated solvents such as o-xylene. [33]

The ability to produce high quality polymers despite a four-fold increase in throughput is highly beneficial from a manufacturing perspective, significantly lowering production costs. When combined with the previously noted environmental advantages, these early results provide a strong case for the use of 2-MeTHF (and related bio-derived solvents) for GRIM-type polymerization chemistry.

**Conclusion**

In this article we have reported the use of 2-MeTHF—a bio-derived alternative to THF—for Grignard metathesis (GRIM) polymerization. Focusing exclusively on the synthesis of poly(3-hexylthiophene), we have shown that 2-MeTHF is a viable alternative to THF that provides comparable performance in terms of molecular weight control, regioregularity and product yield. The reaction can be readily adapted to droplet-based flow synthesis, where the higher boiling point of 2-MeTHF allows the reaction to be carried out at 65 °C, leading to full conversion in under one minute. On the basis of the findings here we conclude that 2-MeTHF is a promising process solvent for the scale-up of P3HT, and other GRIM-type polymerizations.
Experimental Methods

a. Flask Methods

*Flask synthesis of P3HT in THF:* 4 g (12 mmol) of 2,5-dibromo-3-hexylthiophene (Lanzhou Galaxy) was degassed in a 100 mL oven-dried round-bottomed flask under high vacuum and returned to an argon atmosphere. To the flask was added 40 mL of anhydrous THF (Aldrich) followed by drop-wise addition of 5.9 mL (11.8 mmol, 0.98 eq.) 2 M isopropyl magnesium chloride (iPrMgCl) in THF (Aldrich). The solution was heated at 55 °C for 30 minutes to ensure complete conversion of 1 to 2a and 2b. Polymerization was initiated by adding 10 mg (0.15 mol%) of [1,3-bis(diphenylphosphino)propane]nickel(II) chloride (Ni(dppp)Cl$_2$) to the solution under positive flow of argon. The reaction was allowed to proceed for 150 minutes, after which cold methanol was added to the flask to quench the polymerization.

*Adapted flask synthesis of P3HT in 2-MeTHF:* the experimental procedure was carried out as described above, except 1 M iPrMgCl in 2-MeTHF (Alfa Aesar) was substituted for 2 M iPrMgCl in THF and the volume of anhydrous 2-MeTHF (Aldrich) reduced accordingly to maintain a consistent reaction concentration. The solution was heated for 30 minutes at 55 °C (B2) or 75 °C (B3) to ensure complete conversion of 1 to 2a and 2b. The temperature was maintained at the same value (55 °C for B2 and 75 °C for B3) for the polymerization stage.

*P3HT Purification:* all crude polymer samples were purified with acetone and hexane in a Soxhlet extractor for 24 h to remove unreacted monomer, short chain oligomers and salt impurities, following which the polymer was extracted from insoluble impurities using chloroform for c.a. 1 h. The pure polymer solution was concentrated and then re-precipitated by adding cold methanol. The remaining chloroform was removed, followed by the methanol non-solvent to produce a dark purple granular powder with a green/gold shine. Finally, trace solvent was removed by drying in a vacuum oven overnight.

b. Flow Methods

*Preparation of 0.25 M thienyl-Grignard stock solution:* 1.0 g (3.0 mmol, 0.66 mL) of 2,5-dibromo-3-hexylthiophene was degassed in a 50 mL oven-dried round-bottomed flask under high vacuum and returned to an argon atmosphere. Into the flask was added 8.5 mL of anhydrous 2-MeTHF and 2.9 ml (2.9 mmol, 0.97 eq.) of 1 M isopropylmagnesium chloride in 2-MeTHF. The solution was heated at 55 °C for 30 minutes and then allowed to cool to room temperature.

*Preparation of 3.1 mM Ni(II) catalyst stock solution:* 9.5 mg (31 µmol) of nickel(II) bromide ethylene glycol dimethyl ether complex and 31.4 mg (76 µmol, 2.5 eq.) of 1,3-bis(diphenyl-phosphino)propane (dppp) were degassed in a 50 mL round-bottomed flask and returned to
an argon atmosphere. 10 mL of anhydrous 2-MeTHF was added to the flask, resulting in immediate formation of Ni(dppp)Br₂ by ligand exchange.

*General Flow Procedure:* Flow-synthesized polymers F₁-₄ were prepared at a constant flow-rate ratio of 2:1:1 PFPE : thienyl-Grignard solution (0.25 M) : Ni(II) catalyst solution (3.1 mM), equating to a fixed catalyst loading of 1.2 mol%. The total flow-rate in the 1 m (≈785.4 µL) flow reactor was varied from 785.4 to 78.5 µL min⁻¹, corresponding to reaction times of between 60 and 600 s. At each set of flow conditions, and after allowing the droplet flow to stabilize, 4 mL of eluting fluid was collected into methanol, causing the polymer to precipitate as a deep purple solid. The polymer was isolated and dried over a gravity filter and then rinsed with excess cold methanol and acetone. Subsequent purification of sample F₄ was carried out using the same procedure as for the flask-synthesized polymers.
Acknowledgements

The authors wish to thank Mr. Simon Turner and Mr. Lee Tooley for assistance in construction of prototype flow components. JHB acknowledges financial support from the Royal Commission for the Exhibition of 1851 Industrial Fellowship scheme and the EPSRC Knowledge Transfer Secondments scheme (EP/K503733/1). WX acknowledges financial support from the China Scholarship Council (CSC) grant number 201508060171 and the EPSRC Centre for Doctoral Training in Plastic Electronics (EP/L016702/1). Data underlying this article can be accessed from the Box service at [HYPERLINK TO BE ADDED BEFORE PUBLICATION], and used under the Creative Commons Attribution 4.0 International License.
References

[1] T.P. Oseadach, T.L. Andrew, V. Bulović, Effect of synthetic accessibility on the commercial viability of organic photovoltaics, Energy Environ. Sci. 6 (2013) 711. doi:10.1039/c3ee24138f.

[2] R.S. Loewe, S.M. Khersonsky, R.D. McCullough, A Simple Method to Prepare Head-to-Tail Coupled, Regioregular Poly(3-alkylthiophenes) Using Grignard Metathesis, Adv. Mater. 11 (1999) 250–253. doi:10.1002/(SICI)1521-4095(199903)11:3<250::AID-ADMA250>3.0.CO;2-J.

[3] R. Miyakoshi, A. Yokoyama, T. Yokozawa, Catalyst-transfer polycondensation of Ni-catalyzed chain-growth polymerization leading to well-defined poly(3-hexylthiophene), J. Am. Chem. Soc. 127 (2005) 17542–17547. doi:10.1021/ja0556880.

[4] M.C. Iovu, E.E. Sheina, R.R. Gil, R.D. McCullough, Experimental Evidence for the Quasi-“Living” Nature of the Grignard Metathesis Method for the Synthesis of Regioregular Poly(3-alkylthiophenes), Macromolecules. 38 (2005) 8649–8656. doi:10.1021/ma051122k.

[5] R.C. Hiorns, A. Khourkh, B. Gourdet, C. Dagron-Lartigau, Extremely regio-regular poly(3-alkylthiophene)s from simplified chain-growth Grignard metathesis polymerisations and the modification of their chain-ends, Polym. Int. 55 (2006) 608–620. doi:10.1002/pi.2013.

[6] R.S. Loewe, P.C. Ewbanks, J. Liu, L. Zhai, R.D. McCullough, Regioregular, Head-to-Tail Coupled Poly(3-alkylthiophenes) Made Easy by the GRIM Method: Investigation of the Reaction and the Origin of Regioselectivity, Macromolecules. 34 (2001) 4324–4333. doi:10.1021/ma001677+.

[7] F. Gu, F. Jérôme, Bio-based solvents: an emerging generation of fluids for the design of eco-efficient processes in catalysis and organic chemistry, Chem. Soc. Rev. 42 (2013) 9550. doi:10.1039/c3cs60241a.

[8] C.P. Ashcroft, P.J. Dunn, J.D. Hayler, A.S. Wells, Survey of Solvent Usage in Papers Published in Organic Process Research & Development 1997–2012, Org. Process Res. Dev. 19 (2015) 740–747. doi:10.1021/op500276u.

[9] V. Pace, P. Hoyos, L. Castoldi, P. Domínguez de María, A.R. Alcántara, 2-Methyltetrahydrofuran (2-MeTHF): A Biomass-Derived Solvent with Broad Application in Organic Chemistry, ChemSusChem. 5 (2012) 1369–1379. doi:10.1002/cssc.201100780.

[10] J.H. Bannock, N.D. Treat, M. Chabinyc, N. Stingelin, M. Heeney, J.C. de Mello, The influence of polymer purification on the efficiency of poly(3-hexylthiophene):fullerene organic solar cells, Sci. Rep. 6 (2016) 23651. doi:10.1038/srep23651.
[19] M. Sato, H. Morii, Nuclear magnetic resonance studies on electrochemically prepared poly(3-dodecylthiophene), Macromolecules. 24 (1991) 1196–1200. doi:10.1021/ma00005a035.

[20] J.H. Bannock, S.H. Krishnadasan, A.M. Nightingale, C.P. Yau, K. Khaw, D. Burkitt, et al., Continuous Synthesis of Device-Grade Semiconducting Polymers in Droplet-Based Microreactors, Adv. Funct. Mater. 23 (2013) 2123–2129. doi:10.1002/adfm.201203014.

[21] A. Kumar, J. Hasan, A. Majji, A. Avhale, S. Gopinathan, P. Sharma, et al., Continuous-Flow Synthesis of Regioregular Poly(3-Hexylthiophene): Ultrafast Polymerization with High Throughput and Low Polydispersity Index, J. Flow Chem. 4 (2014) 206–210. doi:10.1556/JFC-D-14-00009.

[22] M. Helgesen, J.E. Carlé, G.A. dos Reis Benatto, R.R. Søndergaard, M. Jørgensen, E. Bundgaard, et al., Making Ends Meet: Flow Synthesis as the Answer to Reproducible High-Performance Conjugated Polymers on the Scale that Roll-to-Roll Processing Demands, Adv. Energy Mater. 5 (2015) n/a–n/a. doi:10.1002/aenm.201401996.

[23] H. Seyler, D.J. Jones, A.B. Holmes, W.W.H. Wong, Continuous flow synthesis of conjugated polymers., Chem. Commun. (Cambridge U. K.). 48 (2012) 1598–1600. doi:10.1039/c2cc16514b.

[24] J.H. Bannock, M. Al-Hashimi, S.H. Krishnadasan, J.J.M. Halls, M. Heeney, J.C. de Mello, Controlled synthesis of conjugated random copolymers in a droplet-based microreactor, Mater. Horiz. 1 (2014) 214–218. doi:10.1039/c3mh00066d.

[25] F. Grenier, B.R. Aïch, Y. Lai, M. Guérette, A.B. Holmes, Y. Tao, et al., Electroactive and Photoactive Poly[Isindigo -alt- EDOT] Synthesized Using Direct (Hetero)Arylation Polymerization in Batch and in Continuous Flow, Chem. Mater. 27 (2015) 2137–2143. doi:10.1021/acs.chemmater.5b00083.

[26] G. Pirotte, J. Kesters, P. Verstappen, S. Govaerts, J. Manca, L. Lutsen, et al., Continuous Flow Polymer Synthesis toward Reproducible Large-Scale Production for Efficient Bulk Heterojunction Organic Solar Cells, ChemSusChem. 8 (2015) 3228–3233. doi:10.1002/cssc.201500850.

[27] A.M. Nightingale, S.H. Krishnadasan, D. Berhanu, X. Niu, C. Drury, R. McIntyre, et al., A stable droplet reactor for high temperature nanocrystal synthesis., Lab Chip. 11 (2011) 1221–1227. doi:10.1039/c0lc00507j.

[28] A.M. Nightingale, J.H. Bannock, S.H. Krishnadasan, F.T.F. O'Mahony, S.A. Haque, J. Sloan, et al., Large-scale synthesis of nanocrystals in a multichannel droplet reactor, J. Mater. Chem. A. 1 (2013) 4067–4076. doi:10.1039/c3ta10458c.

[29] A.M. Nightingale, T.W. Phillips, J.H. Bannock, J.C. de Mello, Controlled multistep synthesis in a three-phase droplet reactor, Nat. Commun. 5 (2014) 3777. doi:10.1038/ncomms4777.

[30] J.H. Bannock, T.W. Phillips, A.M. Nightingale, J.C. deMello, Microscale separation of immiscible liquids using a porous capillary, Anal. Methods. 5 (2013) 4991. doi:10.1039/c3ay41251b.

[31] T.W. Phillips, J.H. Bannock, J.C. de Mello, Microscale extraction and phase separation using a porous capillary, Lab Chip. 15 (2015) 2960–2967. doi:10.1039/C5LC00430F.

[32] J.H. Bannock, S.H. Krishnadasan, M. Heeney, J.C. de Mello, A gentle introduction to the noble art of flow chemistry, Mater. Horiz. 1 (2014) 373. doi:10.1039/c4mh00054d.

[33] M. Koppe, C.J. Brabec, S. Heiml, A. Schausberger, W. Duffy, M. Heeney, et al., Influence of Molecular Weight Distribution on the Gelation of P3HT and Its Impact on the Photovoltaic Performance, Macromolecules. 42 (2009) 4661–4666. doi:10.1021/ma9005445.
Scheme 1: Synthesis of regioregular poly(3-hexylthiophene) by Grignard metathesis (GRIM) polymerization.
Table 1: Molecular weight averages, regioregularity and yield data for flask-synthesized P3HT (B1-3). ([a] polydispersity (= Mw/Mn); [b] regioregularity, calculated by integration of the α-methylene region of the $^1$H NMR spectrum (see SI Section C and D); [c] maximum yield of 1.63 g, calculated on the basis of an assumed 4:1 ratio of 2a : 2b, with 2b being inactive towards the catalyst.

| Sample | Solvent    | T / °C | Mn / kg mol$^{-1}$ | Mw / kg mol$^{-1}$ | PDI$^a$ | RR$^b$ / % | Yield$^c$ / % |
|--------|------------|--------|--------------------|--------------------|---------|------------|---------------|
| B1     | THF        | 55     | 83                 | 134                | 1.62    | 99         | 86            |
| B2     | 2-MeTHF    | 55     | 83                 | 137                | 1.66    | 99         | 94            |
| B3     | 2-MeTHF    | 75     | 77                 | 118                | 1.53    | 98         | 85            |
Figure 1: Schematic of the droplet-flow reactor used for the preparation of P3HT, comprising: (a) a three-input/one-output PTFE droplet generator into which the PFPE carrier fluid, Ni(II) catalyst solution and thienyl-Grignard solutions are injected; (b) a 1 m (~785.4 µL) tube-in-shell reactor held at a constant temperature of 65 °C; (c) schematic of 3D-printed housing used to start and terminate the tube-in-shell reactor by bringing heated water into and out of the reactor, see SI Section E for full details; and (d) a collection vessel containing cold methanol to quench the polymerization and precipitate the polymer. Inset photograph shows a translucent PCTFE-variant of the droplet generator, producing a stream of near-uniform droplets in PFPE.
Figure 2: Molecular weight distributions of samples F1-4 before purification (black lines) and sample F4 after purification by Soxhlet extraction (red line), as determined by RI-SEC. Inset figure shows the variation of the weight-average molecular weight (Mw) of the crude samples with time.
**Table 2:** Weight-average molecular weights for flow-synthesized crude samples (F1-4).

| Sample | Time / s | Mw / kg mol$^{-1}$ |
|--------|----------|---------------------|
| F1     | 60       | 43                  |
| F2     | 150      | 44                  |
| F3     | 300      | 44                  |
| F4     | 600      | 44                  |