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Suzuki route to regioregular polyalkylthiophenes using Ir-catalysed borylation to make the monomer, and Pd complexes of bulky phosphanes as coupling catalysts for polymerisation

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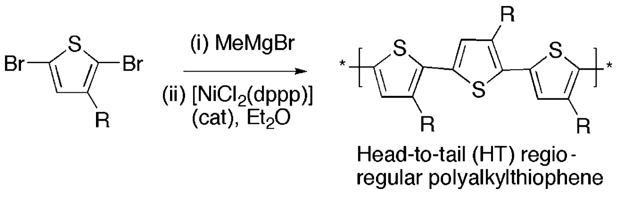
Abstract—We have applied palladium complexes of bulky, electron-rich phosphane ligands as catalysts for the Suzuki synthesis of highly head-to-tail regioregular polyalkylthiophenes from 2-(5-bromo-4-*n*-alkyl-thiophen-2-yl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane. The monomer can be prepared in high yield by Ir-catalysed borylation of 2-bromo-3-hexylthiophene, without the need for organolithium reagents or strong bases.

Polythiophenes have been widely studied as they have potentially useful electronic and optical properties.[1,2] Poly-(3-alkyl)thiophenes are soluble in organic solvents, but early syntheses afforded polymers which had essentially regiorandom relative orientation of the alkyl chains, and these had poor performance in electronic devices. In particular, the field-effect mobility, a key parameter for thin-film transistor devices, was typically $\leqslant 10^{-5}\,\mathrm{cm^2\,V^{-1}\,s^{-1}}$. The threshold for a worthwhile organic semiconductor material is $\geqslant 10^{-2}\,\mathrm{cm^2\,V^{-1}\,s^{-1}}$.[3]

Regioregular (head-to-tail coupled) polyalkylthiophenes were first synthesised in the early 1990s.[4–6] Interest in these materials became intense following the discovery of very high field-effect mobility for solvent-cast films (ca. $0.05\,\mathrm{cm^2\,V^{-1}\,s^{-1}}$).[7] This was attributed to self-assembly of polymer chains during solvent casting, giving a lamellar structure with organised crystalline domains, and unusually favourable π–π stacking interactions between polymer chains that facilitated interchain charge carrier hopping.[8] For the best electrical performance, it is crucial to have very high (>97%) regioregularity and purity.

To date, the most satisfactory route to regioregular polyalkylthiophenes uses [NiCl$_2$(dppp)]-mediated coupling of the Grignard reagent generated by metathesis of 2,5-dibromo-3-alkylthiophene with MeMgBr (Scheme 1).[9,10] Polymers with $\geqslant$98% regioregularity and M_W 25,000, M_N 20,000 can be made reproducibly in moderate yield after purification (60%). However, (i) stoichiometry control in the Grignard metathesis reaction is important to obtain high molar mass material and (ii) Grignard reagents have limited functional group tolerance.

Functionalised polymers have been made using Stille or Rieke chemistry.[11,12] However, stoichiometry control can be difficult when using Rieke chemistry. Although Suzuki couplings have been used to prepare oligothiophenes, in particular using combinatorial methodology,[13–15]



Scheme 1.

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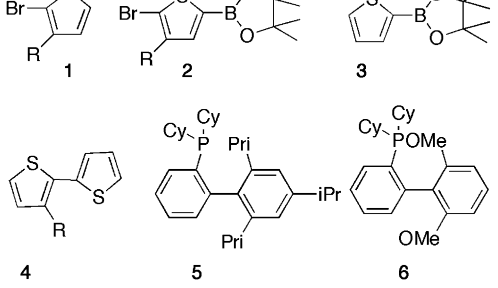
polymerisations have proven more difficult. Where thiophene boronates have been used, deboronation was a problem, as was the termination of polymerisation by aryl group transfer from the PPh_3 ligands employed.[16] A phosphane-free route produced quite high molar mass polymer, but with low regioregularity;[17] in our hands, the yield has also proved capricious.

Recently, Pd complexes with bulky, electron-rich phosphane ligands have been found to be highly active in a range of cross-coupling reactions,[18,19] including Suzuki couplings.[20] These catalysts are extremely reactive towards oxidative addition, so that commercially-available aryl chlorides become suitable substrates, whereas traditional catalysts necessitate the use of more reactive but less available aryl bromides or iodides. We reasoned that since thiophene halides are also poor substrates for oxidative addition (thiophenes are electron-rich aryls), such catalysts might be suitable for the synthesis of polythiophenes using Suzuki chemistry, if the deboronation problem could be overcome. Accordingly, we have investigated a range of these Pd catalysts for the synthesis of regioregular polyalkylthiophenes by the Suzuki reaction (Scheme 2).

We selected as monomer compound **2**, based upon the work of Janssen et al., who showed that, in polymerisations using thiophene boronates, pinacolates gave higher molar mass polymers than other boronate esters.[16] Deprotonation of **1** by LDA, reaction with $B(OMe)_3$, hydrolysis and subsequent reaction of the thiopheneboronic acid in situ with pinacol, gave **2** in 74% yield.[17]

Although this preparation of **2** is satisfactory, the increased functional group tolerance of Suzuki coupling would clearly be of limited use for widening the range of accessible functionalised polyalkylthiophenes if it is necessary to use organolithium reagents to generate the appropriate boronic acid or boronate ester. Recently, there has been much interest in Ir-catalysed borylation of arenes with either (pin)B–B(pin) or HB(pin) (pin = pinacolato), in which an arene C–H bond is activated and undergoes boronation directly.[21] We found that treatment of **1** with 1 equiv of (pin)B–B(pin) in the presence of a catalytic amount (5 mol %) of $[\mathrm{Ir_2}(\mu\text{-Cl})_2(\eta^4\text{-COD})_2]$ (COD = 1,5-cyclooctadiene) and 4,4′-(^{t}Bu)$_2$-2,2′-bipyridine (10 mol %) in refluxing THF for 16 h gave **2** in 97% yield after chromatography.[22]



Scheme 2.

As an initial test of possible polymerisation catalysts, we investigated an analogous dimerisation reaction, the coupling of **1** with **3** to give **4**. For those ligands giving good results, the optimised conditions were then employed to polymerise monomer **2**. The crude polymer was fractionated using successive Soxhlet extraction,[23] which removes by-products and shorter oligomers. The fractions containing polymeric material (in order of increasing M_W: hexane, CH_2Cl_2, THF, $CHCl_3$) were characterised by NMR, GPC and (where possible) MALDI mass spectrometry.

Fu et al. reported that [Pd(^{t}Bu$_3$P)$_2$] was an effective precatalyst for the Suzuki coupling of aryl chlorides.[24] We employed this complex, generated in situ from [$Pd_2(dba)_3$] (dba = dibenzylideneacetone) and the ligand, as a catalyst for the coupling of **1** with **3**. Optimising the conditions (solvent, base, temperature), we found that the conditions previously used for couplings with this system using unactivated aryl chloride substrates (3 mol % Pd, 4.5 mol % ligand, 3.3 mol KF as base, THF at room temperature, 24 h)[24] worked best. This gave the desired unsymmetrical bithiophene **4** in excellent yield (90%) after chromatography. Prior examination of the crude product by ^1H and ^{13}C NMR spectroscopy and mass spectrometry showed that little deboronation had occurred, since unreacted **1** and **3** were the only detectable impurities.

We therefore employed the same reaction conditions in the polymerisation of **2**.[25] After purification,[23] the highest molar mass fraction, extracted by CH_2Cl_2, was obtained in 25% yield (Table 1). This had M_W 9900, M_N 7600, PD 1.30 by GPC against polystyrene standards, and was 98% regioregular (HT) by ^1H and ^{13}C NMR spectroscopy. The hexane fraction (35%) was also polymeric (Table 1). Although the degree of HT regioregularity of the hexane fraction appeared low, GPC exaggerates the molar mass of these materials since they behave more like rigid rods than do the polystyrene calibration standards, and the high proportion of end groups for shorter polymer chains will cause the 'regioregularity' as determined by integration of the arylCH_2– resonances[26] to be artificially low (since the thiophene end groups contribute to the integration of the 'regioirregular' resonances). A MALDI mass spectrum of the hexane fraction showed three series of peaks, corresponding to polymer chains terminated by 2H, HBr and 2Br. The approximate ratio of these peaks was 35:45:20, respectively, at the peak of the distribution (which was at 10 monomer units for all three series). It is likely that the MALDI technique underestimates the average molar mass by preferentially ionising the smaller chains.[26] The likely true mean chain length for this fraction would therefore be somewhere between the 10 units found by MALDI and the 28 found by GPC. Unfortunately, with available equipment we were unable to obtain meaningful MALDI spectra with the higher molar mass fraction.

The MeOH fraction from this reaction consisted mainly of unreacted **2**, its deboronation product **1**, and some dimer. Therefore, we conclude that this reaction gives

Table 1. Summary of the results of the Pd-catalysed Suzuki polymerisation with electron-rich bulky phosphane ligands

Ligand	Conditions	Polymer fraction	Yield (%)	RR[a] (%)	M_W	M_N	PD
^{t}Bu$_3$P	1.5 mol % Pd$_2$(dba)$_3$, 4.5 mol % L,	CH$_2$Cl$_2$	25	98	9900	7600	1.30
	KF, THF, 24 h, rt	Hexane	35	88	5500	4600	1.20
^{t}Bu$_3$P	As above, but CsF base	(No extraction)	50[b]	97	11,100	3400	3.30
(o-biphenyl)P^{t}Bu$_2$	2 mol % Pd$_2$(dba)$_3$, 4 mol % L,	CH$_2$Cl$_2$	<5	80	7600		
	CsF, THF, rt, 24 h	Hexane	15	<80	4600		
5	2 mol % Pd(OAc)$_2$, 5 mol % L,	CH$_2$Cl$_2$	17	92	9100	8000	1.14
	K$_3$PO$_4$, THF, 24 h rt, then reflux 3 h	Hexane	<10	86	4500		
6	2 mol % Pd(OAc)$_2$, 5 mol % L, K$_3$PO$_4$,	THF	20	97	16,900	15,300	1.10
	THF, 24 h rt, then reflux 3 h	CH$_2$Cl$_2$	21	95	11,400	10,000	1.14
		Hexane	35	87	5100	4250	1.20

[a] RR = regioregularity, determined by integration of ArCH$_2$ resonances in the ^{1}H NMR spectra.

[b] Reaction performed on 0.25 g monomer **2**; all other reactions on a 2 g scale.

a good yield (60% total) of highly regioregular polymer, albeit with rather low molar mass. Use of the more soluble base CsF resulted in a small but significant improvement in molar mass (M_W 11,500 *without* Soxhlet fractionation; 97% HT regioregularity). Use of isolated [Pd(^{t}Bu$_3$P)$_2$], in place of Pd$_2$dba$_3$/1.5 equiv of ligand, did not make an appreciable difference.

Following our moderate success with ^{t}Bu$_3$P, we next investigated some (o-biphenyl)PR$_2$ ligands.[27] The parent (o-biphenyl)P^{t}Bu$_2$ was unsuccessful, giving low yields of low molar mass material on attempted polymerisation of **2**. More recently, it has been shown that phosphane **5** is successful in Pd-catalysed Suzuki coupling of boronic acids with unactivated aryl sulfonates, which are normally highly unreactive.[28] We therefore employed this ligand in an attempted polymerisation of **2**, using the published optimum conditions (Table 1). Although polymer was obtained in low yield, the regioregularity and molar mass were low (Table 1).

Further improvements in Suzuki coupling with this family of ligands has recently been noted for **6**.[29,30] Accordingly, we employed this ligand in a polymerisation of **2**, using the same conditions as for ligand **5**.[31] We were pleased to find that this system gave excellent results. Firstly, it was the only one to give appreciable amounts (21% yield) of THF-extracted polymer. The latter fraction contained >97% HT polymer with good molecular weight (Table 1). The CH$_2$Cl$_2$ and hexane fractions were also polymeric (Table 1).

The catalyst utilising this ligand therefore gave a total of 73% yield of regioregular, polymeric product. Although the molar mass, and hence the proportion of polymer extracted into the later solvents, was lower than that which we typically obtain for the optimised Grignard coupling chemistry, it is nonetheless very significant that the regioregularity and total yield approaches that of the Grignard metathesis route, yet monomer **2** can be made by Ir-catalysed borylation without the use of strongly-basic or nucleophilic reagents, and can be purified by column chromatography. We are now exploring the application of this chemistry to the syntheses of regioregular polyalkylthiophene derivatives bearing functional groups for various purposes.

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Supplementary data

Scans of ^{1}H and ^{13}C NMR spectra and mass spectra for compound **2**, and of ^{1}H and ^{13}C NMR spectra for the high molecular weight polymer fractions, are available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.05.063.

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22. Into a flame dried three-neck flask equipped with a condenser, **1** (0.5 g, 2.02 mmol), di-μ-chloro-bis(η^4-1,5-cycloctadiene)diiridium (0.07 g, 0.101 mmol), 4,4′-di-*tert*-butyl-2,2′-dipyridyl (0.054 g, 0.202 mmol) and 4,4,5,5-tetramethyl-[1,3,2]-dioxaborane (0.30 cm^3, 2.07 mmol) were added and the flask was purged with N_2. Anhydrous THF (20 cm^3) was added and the reaction was refluxed for 16 h. After cooling and quenching with water (15 cm^3), the product was extracted into diethyl ether (5 × 20 cm^3). The combined organic extracts were then washed with brine (2 × 50 cm^3), dried over anhydrous $MgSO_4$, filtered, and the solvent removed in vacuo. The pure product was obtained after column chromatography (dichloromethane; Et_3N-treated silica; 0.747 g, 97%). Found: C, 51.59; H, 7.13; S, 8.34. $C_{16}H_{26}SO_2BBr$ requires C, 51.50; H, 7.02; S, 8.59. NMR data identical with lit.[16]
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25. To KF (2.0 g, 34 mmol) and [$Pd_2(dba)_3$] (0.095 g, 0.103 mmol), in a Schlenk flask under argon, was added **2** (3.88 g, 10.4 mmol) in THF (20 cm^3), and a solution of P^tBu_3 in THF (2.2 cm^3 of 0.12 M, 0.264 mmol). The reaction was stirred for 24 h at room temperature. The solution was then poured into MeOH (200 cm^3) to yield a purple precipitate, which was then filtered through a Soxhlet thimble. The precipitate was Soxhlet-extracted with, successively, MeOH, acetone, hexane, CH_2Cl_2 and THF. The hexane, CH_2Cl_2 and THF fractions were separately evaporated to small volume and poured into MeOH, and the precipitates were filtered off and dried in vacuo. Yield (hexane fraction) 0.605 g, 35%, (CH_2Cl_2 fraction) 0.356 g, 21% (THF fraction) 0.04 g of regioregular poly-3-hexylthiophene. Found: C, 71.5; H, 8.00; S, 18.5; Br, 2.1. $\{C_{10}H_{14}S\}_\infty$ requires C, 72.23; H, 8.49; S, 19.28. Selected ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm (J Hz): 6.98 (s, 1H, HT alkylthiophene 4-H), 2.79 (br t, 2H, J 6.3, arylCH_2–). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ ppm: 139.0, 132.8, 129.6, 127.7 (thiophene C, HT monomer unit). GPC: $M_W = 9900$, $M_N = 7600$, PD = 1.30 (all data for CH_2Cl_2 fraction).
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31. Into a flame-dried Schlenk flask was placed anhydrous K_3PO_4 (3.4 g, 16.1 mmol), $Pd(OAc)_2$ (0.024 g, 0.107 mmol), **2** (2.00 g, 5.36 mmol) and 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (**6**; 0.044 g, 0.107 mmol) under Ar. Anhyd THF (50 cm^3) was added and the reaction was stirred at room temperature for 16 h. It was then brought to reflux for a further 3 hours, allowed to cool to room temperature, and poured into MeOH (200 cm^3). The precipitate formed was filtered through a Soxhlet thimble, and worked up as described above.[25] Yield (CH_2Cl_2) 0.174 g, 21% (THF) 0.175 g, 20%, (hexane) 0.287 g, 33%. From ^{1}H NMR data (determined as above[25]), CH_2Cl_2 fraction: 95% HT regioregularity, GPC (in THF) $M_W = 11400$, $M_N = 10000$, PD = 1.14. Data for THF fraction: >97% HT regioregularity. Found: C, 71.2; H, 7.98; S, 19.1; Br, 1.9. $\{C_{10}H_{14}S\}_\infty$ requires C, 72.23; H, 8.49; S, 19.28. $M_W = 16900$, $M_N = 15300$, PD = 1.10.