

Palladium-catalyzed coupling reactions towards the synthesis of well-defined thiophene-oligomers

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Dedicated to Professor J.P. Genêt on the occasion of his birthday.

Abstract

Heck- and Ullmann-type palladium-catalyzed reactions were used in order to perform the synthesis of 3',4"-dioctyl-2,2',5'2",5",2"-tetrathienyl. The desired oligothiophene was synthesized in five steps with a total yield of 38% by a Heck-type reaction of bromo-derivatives and a yield of 45% by an Ullmann-type reaction of iodo-precursors.

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1. Introduction

Thiophene oligomers are starting materials for the preparation of organic conductors [1,2]. The electronic properties of the obtained conjugated polymers are determined by the thorough control of the structural order. Therefore, syntheses leading to regioregular polymers are of utmost importance. Methods involving organometallic compounds for the coupling of arylderivatives [3] have thus been used in the synthesis of poly(alkylthiophenes) and afford high molecular weights and regioregular head-to-tail poly(alkylthiophenes) [4–6]. The main drawbacks of these procedures are the difficult access to the monomer in its highly purified form and the requirement of a stoichiometric amount of the organometallic intermediate. The simple access to well-defined oligomers is also important to mimic, and then predict, the behavior of longer polymers for their various applications. Thus, stepwise syntheses based on the repetitive use of the Stille [7], Suzuki [8] and Kumada [9] coupling reactions were

already reported. We also described the direct arylation of thiophenes in position 2 or 5, using Heck-type reactions [10–12] (Scheme 1).

Then, we successfully applied this method to the polymerization of 2-iodo- and 2-bromo-3-alkylthiophenes in the presence of Pd(OAc)₂ as a catalyst [13,14]. This coupling procedure presents several advantages compared with reported methods such as the use of a catalytic amount of palladium and the easy availability of the functionalized monomers, for example. We also described the efficiency of Pd(OAc)₂ as a catalyst for the synthesis of symmetrical and unsymmetrical biaryls [15,16] in a catalytic version of the Ullmann coupling reaction.

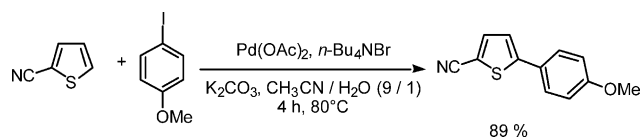
We report here the stepwise synthesis of a tetramer based on the aforementioned Heck- and Ullmann-type reactions.

2. Synthesis

2-Iodo-3-octylthiophene **2** was first regiospecifically synthesized according to a procedure described by Miller and co-workers [17]. This method requires the use of mercuric oxide and iodine in benzene as solvent. A selectivity higher than 95% was obtained for mono-

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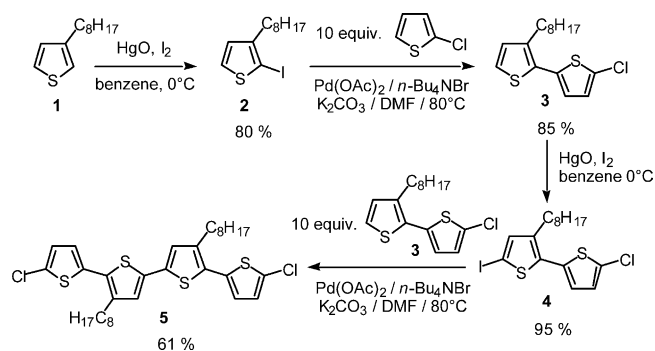
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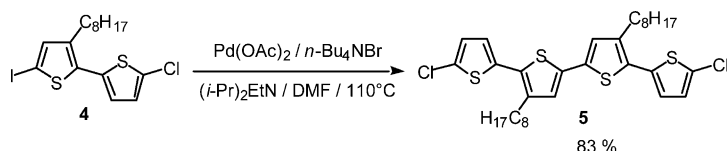
Scheme 1. Arylation of 2-cyanothiophene by 4-iodomethoxybenzene.

iodination with regards to diiodination. The addition of this iodothiophene on 2-chlorothiophene under Heck-type coupling conditions led to the dimer **3** with a good yield. It is important to note that the Heck-type coupling of the chlorinated derivatives does not take place under our conditions. Furthermore, to avoid polymerization of 2-iodo-3-octylthiophene under these conditions, 2-chlorothiophene was added in a ten-fold excess. The coupling of the thiophene rings was performed in DMF using 2.5 M equivalents of base, 1 M equivalent of tetra-*n*-butylammonium bromide and palladium acetate (5 mol%) as a catalyst. The palladium atom is selectively inserted into the C–I bond, and the chloride plays the role of a protecting group, preventing a coupling reaction in position 2. Excess of 2-chlorothiophene is efficiently removed by vacuum evaporation. Subsequent iodination is then regioselectively performed in position 5 of dimer **3** giving product **4**. An excess of mercuric oxide ensures a complete reaction, avoiding a purification stage, since 3-octyl-5'-chloro-2,2'-bithiophene **3** and product **4** are not easily separable. The tetrathiophene **5** was finally obtained with a yield of 61% by another Heck-type coupling reaction involving dimer **3** (Scheme 2).

Alternatively, an Ullmann-type coupling of 5-iodo-3-octyl-5'-chloro-2,2'-bithiophene **4** also afforded the tetramer **5** with 83% yield (Scheme 3) by using Pd(OAc)₂–*n*-Bu₄NBr as catalytic system in the presence



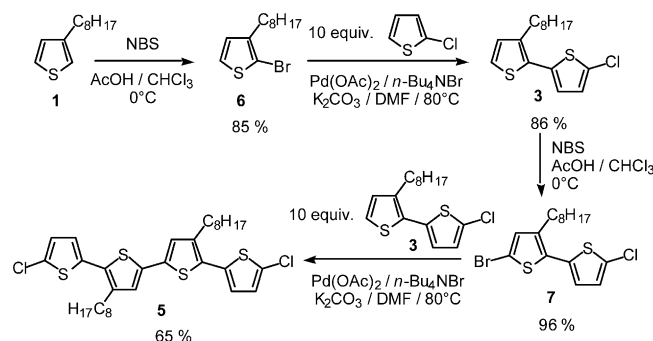
Scheme 2. Synthesis of 3',4''-dioctyl-5,5''-dichloro-2,2':5',2'':5'',2'''-tetrathiényl by Heck-type reactions of iodinated derivatives.



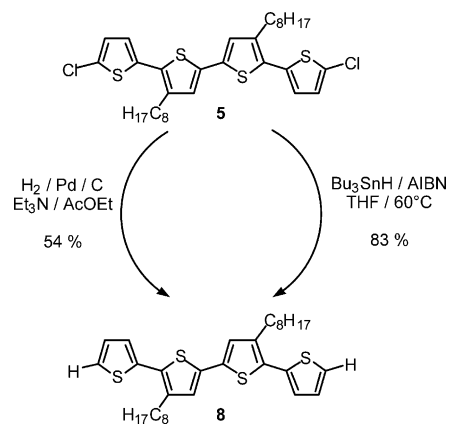
Scheme 3. Synthesis of 3',4''-dioctyl-5,5''-dichloro-2,2':5',2'':5'',2'''-tetrathiényl by an Ullmann-type reaction.

of an organic base, i.e. *N,N*-diisopropylethylamine instead of potassium carbonate. We previously synthesized a series of symmetrical functionalized bithiophenes in good to excellent yields [15] under these Ullmann-type coupling conditions.

The undesirable use of highly toxic products such as mercuric oxide during the iodination step justified the test of analogous brominated derivatives. 2-Bromo-3-octylthiophene **6** was thus regioselectively synthesized starting from 3-octylthiophene by using *N*-bromosuccinimide in a mixture of acetic acid and chloroform [8,18]. The addition reaction between 2-bromo-3-octylthiophene **6** and 2-chlorothiophene was carried out under Heck-type coupling conditions leading to bithiophene **3** with a yield of 86%. Similarly as observed for iodinated derivatives, 2-chlorothiophene was introduced in excess to avoid the homopolymerization reaction of 2-bromo-3-octylthiophene **6**. This coupling was performed in 4 h



Scheme 4. Synthesis of 3',4''-dioctyl-5,5''-dichloro-2,2':5',2'':5'',2'''-tetrathiényl by Heck type reactions of brominated derivatives.



Scheme 5. Dehalogenation of 3',4''-dioctyl-5,5''-dichloro-2,2':5',2'':5'',2'''-tetrathiényl.

with iodinated derivatives and 5 mol% of catalyst, but it lasted 40 h and required 10 mol% of Pd(OAc)₂ to allow a total conversion of the brominated derivative **6**. Bithiophene **3** was then selectively brominated in position 5. Using another Heck-type coupling reaction between **3** and **7**, the tetrathiophene **5** was obtained with 65% yield (Scheme 4).

Finally, free-ends tetramer (**8**) was obtained by two dehalogenative procedures. The use of an over-stoichiometric amount of tributyltin hydride in the presence of azobisisobutyronitrile (AIBN), gave the free-ends oligomer with a yield of 83% after 9 h of reaction. Dehalogenation was also alternatively performed by using H₂ over Pd/C in ethylacetate and in the presence of triethylamine, giving **8** in 52% yield in 48 h [8] (Scheme 5).

In summary, we have developed new methodologies for the synthesis of regioregular oligothiophenes with good yields. The reported methods for the synthesis of tetramers were thus improved by using methodologies based on a succession of Heck- and Ullmann-type reactions. These methodologies are economically competitive since they do not require a stoichiometric organometallic intermediate, and the functionalized monomers are easily obtained in their highly purified form.

3. Experimental

3.1. General procedure for Heck-type reactions

A mixture of potassium carbonate (20 mmol), palladium acetate (0.4 mmol), tetra-*n*-butylammonium bromide (8 mmol) and 2-chlorothiophene (80 mmol) or 2-chlorobithiophene (80 mmol) in DMF (18 ml) was stirred under nitrogen atmosphere with a mixture of thiophene iodide (**2** or **4**) or thiophene bromide (**6** or **7**) (8 mmol) in DMF (3 ml). The mixture was maintained at 80 °C for the period of time indicated in the text. After cooling to room temperature, water and ether were added. The organic phase was washed with water and dried over MgSO₄. The solvent was evaporated under vacuum. The crude product was then purified by column chromatography, using silicagel 60 and heptane as the eluent.

3.2. General procedure for Ullmann-type reactions

A mixture of diisopropylethylamine (8 mmol), palladium acetate (0.4 mmol), tetra-*n*-butylammonium bromide (4 mmol) and 5-iodo-3-octyl-5'-chloro-2,2'-bithiophene (8 mmol) in DMF (30 ml) was stirred for 6 h under nitrogen atmosphere at 110 °C. After cooling to r.t., water and ether were added. The organic phase was washed with water and dried over MgSO₄. The

solvent was evaporated under vacuum. The crude product was then purified by column chromatography, using silicagel 60 and heptane as the eluent to give a yellow solid product.

3.3. Analyses

3.3.1. 2-Iodo-3-octylthiophene 2

Prepared according to reference [17]; yield: 80%; b.p. 136–141 °C (4×10^{-4} bar); ¹H-NMR (200 MHz, CDCl₃) δ (ppm): 7.37 (d, 1H, *J* = 5.4 Hz); 6.77 (d, 1H, *J* = 5.4 Hz); 2.56 (t, 2H, *J* = 7.4 Hz); 1.58–1.30 (m, 12H); 0.90 (t, 3H, *J* = 6.4 Hz); ¹³C-NMR (50 MHz, CDCl₃) δ (ppm): 147.2; 130.3; 128.0; 74.0; 32.3; 32.0; 30.1; 29.5; 29.3; 22.7; 18.1; 14.2; MS, *m/z* (%): 322 (65) [M⁺]; 323 (10) [M + 1]; 225 (12); 224 (30); 223 (100); 196 (15); 195 (70); 139 (15); 137 (20); 123 (20).

3.3.2. 2-Bromo-3-octylthiophene 6

Prepared according to references [8,18]; yield: 85%; b.p. 91 °C (3×10^{-2} bar); ¹H-NMR (200 MHz, CDCl₃) δ (ppm): 7.36 (d, 1H, *J* = 5.5 Hz); 6.73 (d, 1H, *J* = 5.5 Hz); 2.53 (t, 2H, *J* = 4.0 Hz); 1.40–1.20 (m, 12H); 0.87 (t, 3H, *J* = 6.4 Hz); ¹³C (50 MHz, CDCl₃) δ (ppm): 141.0; 130.9; 128.7, 109.3; 32.5; 32.4; 30.3; 30.0; 29.9; 23.2; 23.1; 14.0; MS, *m/z* (%): 276 (35) [M + 2]; 274 (20) [M⁺]; 238 (22); 236 (85); 234 (100); 202 (8); 201 (45); 199 (75); 178 (18); 177 (80); 175 (75); 164 (45); 155 (75).

3.3.3. 3-Octyl-5'-chloro-2,2'-bithiophene 3

Following the general procedure for Heck-type reactions; yield: 86%; ¹H-NMR (200 MHz, CDCl₃) δ (ppm): 7.2 (d, 1H, *J* = 5.2 Hz); 6.9 (d, 1H, *J* = 5.2 Hz); 6.8 (s, 2H); 2.7 (t, 2H, *J* = 4.0 Hz); 1.6 (m, 2H); 1.3 (m, 10H); 0.9 (t, 3H, *J* = 6.4 Hz); ¹³C (50 MHz, CDCl₃) δ (ppm): 140.2; 135.3; 133.6; 130.0; 129.6; 126.6; 125.2; 124.3; 32.2; 31.0; 30.2; 29.8; 29.4; 23.1; 22.8; 14.5; MS, *m/z* (%): 314 (30) [M + 2]; 312 (80) [M⁺]; 215 (60); 213 (95); 180 (15); 179 (25); 178 (100); 147 (8); 134 (35).

3.3.4. 5-Iodo-3-octyl-5'-chloro-2,2'-bithiophene 4

Prepared according to reference [17]; yield: 95%; ¹H-NMR (200 MHz, CDCl₃) δ (ppm): 7.10 (s, 1H); 6.87 (d, 1H, *J* = 3.9 Hz); 6.81 (d, 1H, *J* = 3.9 Hz); 2.60 (t, 2H, *J* = 4 Hz); 1.50 (m, 2H); 1.30 (m, 10H); 0.90 (t, 3H, *J* = 6.4 Hz); ¹³C (50 MHz, CDCl₃) δ (ppm): 152.7; 142.1; 139.7; 135.6; 133.5; 130.2; 126.6; 73.0; 32.0; 31.5; 30.8; 29.5; 29.3; 23.5; 22.8; 14.3; MS, *m/z* (%): 440 (35) [M + 2]; 438 (100) [M⁺]; 341 (15); 339 (45); 304 (70); 213 (20); 178 (20).

3.3.5. 5-Bromo-3-octyl-5'-chloro-2,2'-bithiophene 7

Prepared according to references [8,18]; yield: 96%; ¹H-NMR (200 MHz, CDCl₃) δ (ppm): 6.90 (s, 1H); 6.85 (d, 1H, *J* = 3.9 Hz); 6.81 (d, 1H, *J* = 3.9 Hz); 2.60 (t, 2H, *J* = 7.4 Hz); 1.20–1.40 (m, 12H); 0.88 (t, 3H, *J* = 7.0

Hz); ^{13}C (50 MHz, CDCl_3) δ (ppm): 143.0; 140.9; 135.1; 133.9; 129.4; 124.0; 121.3; 113.8; 33.3; 32.5; 30.3; 30.0; 29.9; 23.7; 23.1; 14.0; MS, m/z (%): 394 (15) [$\text{M}+2$]; 392 (55) [M^+]; 294 (20); 292 (90); 291 (55); 213 (40); 178 (25); 177 (100).

3.3.6. 3',4''-Dioctyl-5,5'''-dichloro-2,2':5',2'':5'',2'''-tetrathienyl 5

Following the general procedure for Heck- and Ullmann-type reactions; yield: 83%; ^1H -NMR (200 MHz, CDCl_3) δ (ppm): 7.0 (s, 2H); 6.9 (d, 4H); 2.7 (t, 4H); 1.6 (m, 4H); 1.3 (m, 20H); 1.0 (t, 6H, $J = 6.4$ Hz); ^{13}C (50 MHz, CDCl_3) δ (ppm): 143.4; 142.8; 138.0; 134.4; 129.0; 126.3; 124.0; 121.3; 33.4; 32.5; 30.3; 30.0; 29.9; 24.7; 23.1; 14.0; HRMS Calc. for $\text{C}_{32}\text{H}_{40}\text{Cl}_2\text{S}_4$ 622.1390, Found 623, 1468.

3.3.7. 3',4''-Dioctyl-2,2':5',2'':5'',2'''-tetrathienyl 8

Prepared according to reference [8]; yield: 83%; ^1H -NMR (200 MHz, CDCl_3) δ (ppm): 7.35 (d, 2H, $J = 5.0$ Hz); 7.32 (d, 2H, $J = 5.0$ Hz); 7.15 (dd, 2H, $J = 5.0$ Hz, $J = 3.5$ Hz); 7.10 (s, 2H); 2.80 (t, 4H, $J = 4.0$ Hz); 1.70–1.20 (m, 24H); 0.90 (t, 6H, $J = 6.4$ Hz); ^{13}C (50 MHz, CDCl_3) δ (ppm): 140.4; 136.1; 135.0; 129.6; 127.5; 126.4; 125.8; 125.3; 33.4; 32.5; 30.3; 30.6; 29.8; 29.6; 23.1; 14.0.

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