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β-Terthiophene aldehyde and phosphonate: key building blocks for the synthesis of functionalised conducting polymers

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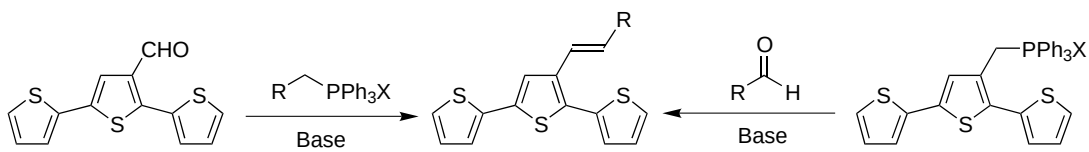
Abstract—A simple and efficient methodology has been developed for the synthesis of β-functionalised terthiophene monomers, conducting polymer precursors. Using a building block approach, the key materials, β-terthiophene aldehyde and phosphonate, were constructed with Suzuki chemistry. Reactions of these building blocks with the appropriate coupling partner under Wittig/Horner–Emmons conditions provides conjugatively-linked functionalised monomers.

1. Introduction

There has been an enormous interest in functionalised conducting polymers over the last thirty years. In particular, derivatised thiophene oligomers have received considerable attention as the chemistry of thiophene allows easy modification at both the α- and β-positions.[1] The many interesting and novel functionalised monomers that have been reported[1–3] commonly require separate synthetic strategies. A general method in which various derivatised monomers can be formed from a key precursor, thereby reducing the number of specific syntheses, has yet to be reported.

We have been interested in synthesising a series of functionalised terthiophene monomers (**1**) for the generation of application-specific conducting polymers. The key to this approach is the facile synthesis, using Wittig chemistry, of the functionalised monomers from the appropriate precursors, the terthiophene aldehyde (**2**) or the terthiophene phosphonium salt (**3**) (Scheme 1). This obviates the need to develop new synthetic methodology for the formation of the terthiophene moiety for each individual monomer (**1**), which contains a different R group. A simple synthetic route to (**2**) was envisioned using metal mediated coupling strategies (Scheme 2). Functional Group Interconversion (FGI) of (**2**) would then provide the phosphonium salt (**3**).

Metal-mediated coupling reactions, such as the Kumada, Suzuki, Stille and Negishi, have become accepted methods for the synthesis of poly-aromatic systems.[4] Of these methods, the Kumada coupling approach is advantageous due to the in-situ formation of Grignard reagents and cheap nickel catalysts employed.[5] With these benefits in mind, we began gram scale coupling of the acetal (**5**) with an excess of the organomagnesium reagent (**4**) in the presence of $NiCl_2$(dppp) (Scheme 2). After an aqueous workup of



(**2**) (**1**) (**3**)

Scheme 1.

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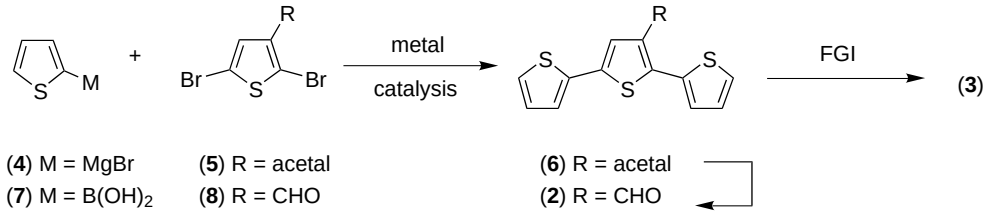


Scheme 2.

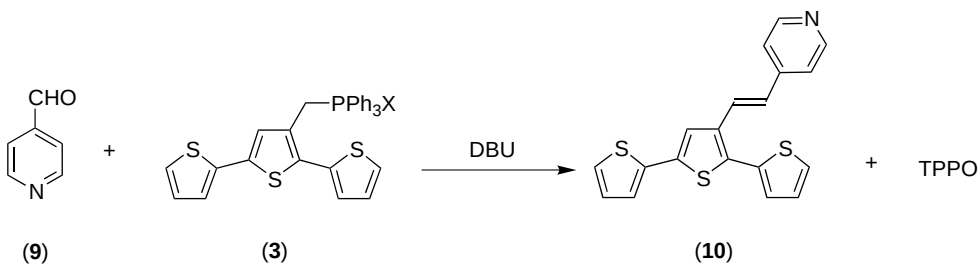
the reaction mixture, followed by chromatography and recrystallisation, the terthiophene acetal (**6**) was obtained in good yield (71%). The acetal group was easily hydrolysed to give the terthiophene aldehyde (**2**)[†] in excellent yield (95%). However, attempts to perform the Kumada reaction on a larger scale were met with incomplete reaction of the dibromide, resulting in poor yields and complications in isolating pure product. To eliminate these problems alternative coupling protocols were considered.

The key advantages of the Suzuki reaction[6] are that the mild conditions favour a large number of functional groups and the by-product from the reaction, boric acid, is non-toxic and easily removed. It was found that reaction of the dibromide (**8**) with an excess of the boronic acid (**7**) under Suzuki conditions[7] gave the target terthiophene aldehyde (**2**) in multigram quantities and in high yield (78%). This aldehyde (**2**) afforded materials of the type (**1**) (Scheme 1) in Wittig reactions with several *p*-substituted aryl ylides. The physical, chemical and electrochemical properties of these materials have been studied and the results of these findings are to be published shortly.[8]

With the ready availability of aldehyde (**2**), it was envisioned that FGI would afford the phosphonium salt (**3**) (Scheme 2). Sodium borohydride reduction of (**2**) gave the corresponding alcohol in excellent yield. Direct treatment of this alcohol with triphenylphosphine hydrogen bromide in refluxing toluene gave the desired phosphonium bromide salt, albeit in low yields (34%). Attempts to obtain greater quantities of the salt (**3**) by converting the alcohol to the halide first and then heating in the presence of triphenylphosphine also proved difficult; the halide precursor was found to be extremely unstable. With sufficient quantities of (**3**) in hand, Wittig condensation using 4-pyridyl carboxaldehyde (**9**) and DBU in THF gave the crude product (**10**) (Scheme 3) as determined by proton NMR. However, attempts to obtain the pure pyridyl derivative (**10**) were thwarted as the by-product, triphenylphosphine oxide (TPPO), could not be easily removed. Given the poor yield of (**3**) and TPPO contamination, an alternative approach using Horner–Emmons chemistry was explored.

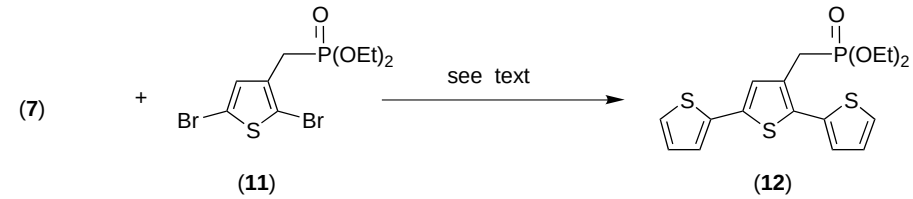
The synthesis of thienylmethylphosphonates is achieved using the Michaelis–Arbuzov rearrangement, which involves reacting halomethylthiophene with triethyl phosphite. This route provides simple access to both α- and β-thiophene methylphosphonates in good yields.[9] To the best of our knowledge, this method has not been used to make the bithiophene and terthiophene homologues. Recently, Dalton and Wang[10] described an efficient facile synthesis of oligothiophene phosphonates. The method involves deprotonation of a thiophene substrate with butyllithium, followed by in-situ formation of an organocuprate species which is then coupled with diethyl iodomethylphosphonate. However, due to the higher reactivity of the α-protons this strategy only allows the formation of phosphonates at this position.

With the successful facile synthesis of β-terthiophene aldehyde, we envisioned a similar approach could be used to form the required β-substituted terthiophene phosphonate (**12**). As depicted in Scheme 4, the target phosphonate (**12**) should be accessible via the coupling of the known dibromide (**11**) with 2-thienylboronic acid (**7**). Given the difficulties of coupling electron rich



Scheme 3.

[†] Selected data of (**2**): mp 68°; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.08 (s, 1H, CHO); 7.57 (s, 1H, H 4′); 7.51 (dd, 1H, J=5.1, 1.2 Hz, H 5); 7.32 (dd, 1H, J=3.6, 1.2 Hz, H 3); 7.30 (dd, 1H, J=5.1, 1.2 Hz, H 5″); 7.23 (dd, 1H, J=3.6, 1.2 Hz, H 3″); 7.17 (dd, 1H, J=5.1, 3.6 Hz, H 4); 7.06 (dd, 1H, J=5.1, 3.6 Hz, H 4″); ^{13}C NMR (67.8 MHz): δ 184.9, 145.8, 137.5, 136.7, 135.4, 132.0, 129.1, 128.6, 128.2, 127.9, 125.7, 124.9, 122.3; Anal. calcd for $C_{13}H_8OS_3$: C, 56.49; H, 2.92. Found: C, 56.73; H, 2.75.



Scheme 4.

halides with boronic acids, a number of catalysts and conditions were studied.‡ Three of these catalyst systems afforded significant quantities of the terthiophene phosphonate (methods 1, 5 and 6). The best conditions, using $Pd_2(dba)_3$ catalyst system, gave short reaction times and clean reaction mixtures. A typical reaction was performed on a gram scale with the gradual addition of an excess of boronic acid and monitoring by HPLC to ensure that all the phosphonate (**11**) had been consumed. After an aqueous workup, the crude oil was purified by high vacuum distillation to give the terthiophene (**12**)§ as a viscous bright yellow oil in 70% yield. Horner–Emmons reaction of the pyridine aldehyde (**9**) with (**12**) then gave, after a simple aqueous workup and recrystallisation, the desired pure product (**10**) in good yield as a yellow microcrystalline solid.[14]

In conclusion, by using Suzuki coupling methodology, we have established a synthetic route to the key building blocks, β-terthiophene aldehyde (**2**) and phosphonate (**12**). Wittig or Horner–Emmons condensation of these substrates with the appropriate coupling partner allows ready access to conjugatively linked novel functionalised terthiophene monomers. Recent research has been directed towards using this method to synthesise functionalised terthiophene monomers to produce conducting polymers for application in the areas of photovoltaics, bio-sensors, metal-ion detectors and electro-catalysis. The results from some of this work will be published elsewhere in the near future.

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14. All new compounds obtained have been fully characterised by elemental analysis, mass spectrometry, NMR, UV–vis and IR spectroscopy.

‡ (1) $Pd(PPh_3)_4$/1 M Na_2CO_3/DME;[7] (2) Pd/C/aq. Na_2CO_3/isopropanol;[11] (3) $Pd(PPh_3)_4/K_3PO_4$/toluene;[12] (4) $PdCl_2(PPh_3)_2/K_3PO_4$/toluene;[4] (5) $Pd(PPh_3)_4/NEt_3$/DMF[12] and (6) $Pd_2(dba)_3/P(Bu^t)_3/K_3PO_4$/THF.[13]

§ Selected data of (**12**) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (dd, 1H, $J=5.2$, 1.2 Hz, H 5); 7.32–7.30 (m, 1H, H 3); 7.23 (s, 1H, H 4′); 7.23 (dd, 1H, $J=5.1$, 1.1 Hz, H 5″); 7.18 (dd, 1H, $J=3.6$, 1.1 Hz, H 3″); 7.10 (dd, 1H, $J=5.2$, 3.6 Hz, H 4); 7.02 (dd, 1H, $J=5.1$, 3.6 Hz, H 4″); 4.07 (q, 4H, $OC\mathbf{H_2}CH_3$); 3.31, (d, 2H, $J_{H,P}=21.3$ Hz, $ThC\mathbf{H_2}P$); 1.28, (bt, 6H, $OCH_2C\mathbf{H_3}$). ^{13}C NMR (100.6 MHz): δ 136.7, 135.9 (d, $J_{C,P}=2.3$ Hz), 131.9 (d, $J_{C,P}=11.5$ Hz), 128.2 (d, $J_{C,P}=9.4$ Hz), 127.8, 126.8 (d, $J_{C,P}=2.8$ Hz), 126.2, 124.7, 123.9, 62.3 (d, $J_{C,P}=6.6$ Hz), 27.4 (d, $J_{C,P}=141.5$ Hz), 16.4 (d, $J_{C,P}=6.1$ Hz). HRMS EI (M+) calcd for $C_{17}H_{19}O_3PS_3$ 398.0234. Found 398.0230.