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Improved Synthesis of Functionalized Sexithiophenes

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Abstract. Yields of functionalized sexithiophenes through the Stille reaction are greatly ameliorated using in situ generated $Pd(AsPh_3)_4$ as the catalyst. The regiospecific synthesis of a new head-to-head/tail-to-tail hexa(methylsulfanyl)sexithiophene is reported. All sexithiophenes were distilled under high vacuum to reach the degree of purity required for use in electronic applications. © 1997 Elsevier Science Ltd.

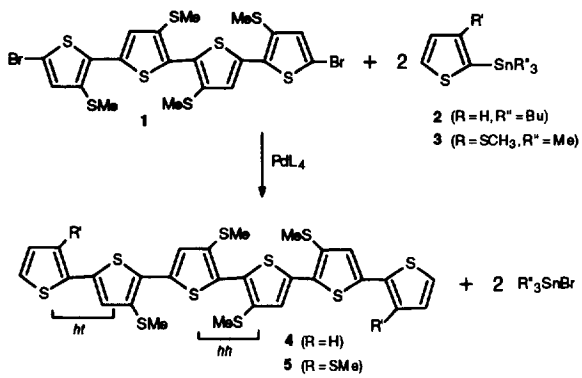
The finding that oligothiophenes are good electroactive materials for applications in organic field effect transistors and electrooptical devices has prompted an increasing need for amelioration of the synthetic procedures for the preparation of these compounds and for more efficient purification and characterization methods.[1-4]

We have recently started a research aimed at achieving the control of both the degree of purity and the solid state organization of oligothiophenes - which are key features in the optimization of electric conductivity and luminescence properties of these compounds - through appropriate functionalization of the aromatic skeleton, which renders the compounds soluble and processable. We report here our results on the effect of the change of palladium(0) catalyst ligands in the preparation of polysubstituted sexithiophenes through the Stille reaction.[6]

To our knowledge, only commercially available $Pd(PPh_3)_4$ has been used so far to prepare oligothiophenes through the Stille coupling and no studies on catalyst tailoring for the synthesis of these compounds have been carried out. An improvement over the typical Stille conditions would be a useful development in the synthesis of oligothiophenes, since the Stille reaction is compatible with a great number of functional groups[6] and functionalizing oligothiophenes in the α or β positions is a way to tailor their properties.[1-4]

The reaction chosen for the study of the Stille coupling in the presence of different catalysts generated *in situ* is shown in Scheme 1. Reaction conditions and yields are reported in Table 1. The palladium catalyzed coupling of the dibromoquaterthiophene **1** with the 2-trialkyltin derivatives **2, 3** was studied in the presence of triphenylphosphine, triphenylarsine and tri-(2-furyl)phosphine as the palladium(0) ligands and with tetrahydrofuran or toluene as solvents at the refluxing temperatures of 65 and 110 °C, respectively. Although iodine is a better leaving group than bromine and consequently should be better suited for the rate determining transmetallation step of the Stille reaction,[6] we preferred to use the dibromo derivative **1** to avoid the risk of polymerization of the substrate. Indeed we found that in the Stille reaction conditions the diiodo derivative of substituted quaterthiophenes - which are easily prepared by reported methods[7,5d] - may give rise to polymerization.

Scheme 1



Synthetic pattern followed for the preparation of β-functionalized sexithiophenes containing one head-to-head (hh) and two or three head-to-tail (ht) junctions between adjacent 3-methylsulfanylthiophene rings.

Table 1. *Yields of the coupling reaction of dibromoquaterthiophene* **1** *with trialkyltin derivatives* **2** *and* **3** *(Scheme 1) in the presence of* Pd_2dba_3 *and of different ligands (Pd:L ratio 1:4) in refluxing tetrahydrofuran (THF) or toluene.*

Ligand	R',R"	Solvent, T (°C)	Yield (%)[a]	*Item*
PPh_3	*H, Bu*	*Toluene, 110*	*65*[b]	**4**
PPh_3	H, Bu	THF, 65	80	**4**
PPh_3	H, Bu	Toluene, 110	75	**4**
TFP	H, Bu	Toluene, 110	80	**4**
$AsPh_3$	H, Bu	THF, 65	95	**4**
$AsPh_3$	H, Bu	Toluene, 110	85	**4**
PPh_3	*SMe, Me*	*Toluene, 110*	*60*[b]	**5**
PPh_3	SMe, Me	Toluene, 110	65	**5**
TFP[c]	SMe, Me	THF, 65	65	**5**
$AsPh_3$	SMe, Me	Toluene, 110	85	**5**

a) From ^1H NMR. *b)* Yield obtained using the commercial catalyst $Pd(PPh_3)_4$. *c)* Tri(2-furyl)phosphine

The catalyst was formed *in situ* using the weakly coordinated tris(dibenzylideneacetone)dipalladium Pd_2dba_3 and four equivalents of ligand for each palladium atom, as described by Farina *et al.* for the reaction between olefinic stannanes and several electrophiles.[7a] However, the formation of the C-C bond between

thienyl bromides and thienylstannanes requires more drastic conditions than are usually applied, in particular elevated temperatures and a greater amount of catalyst (up to 10% molar equivalents, see the experimental section).[5e]

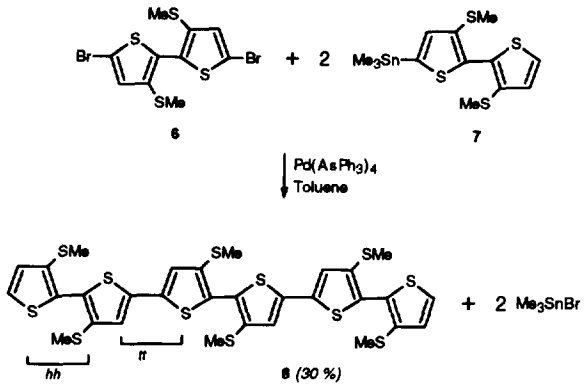
Inspection of table 1 shows that the lowest yields are those obtained using commercial $Pd(PPh_3)_4$ as the catalyst (up to 30% lower). The yields with $Pd(PPh_3)_4$ generated *in situ* are from 5% to 15% greater than those obtained with the commercial catalyst. Tri-(2-furyl)phosphine is a better ligand than triphenylphosphine while triphenylarsine is the best of all ligands. The superiority of triphenylarsine as the ligand is apparent from the data reported in the table and is in line with the results of the above mentioned study on the reaction of olefinic stannanes with electrophiles.[7a] An almost quantitative coupling (95%) is obtained using $Pd(AsPh_3)_4$ generated *in situ* for **4** in refluxing THF and a very high yield (85%) for **5** in refluxing toluene. The acceleration of the C-C bond formation rate on changing PPh_3 for $AsPh_3$ does not exceed a factor 2-4, which is much lower than that (up to three orders of magnitude) observed in other cases.[7a] In our experience, great care must be taken in the addition of the catalyst and it is more convenient to add the total amount of catalyst in more than one step. After usual work up,[5] repeated washing first with pentane then with methanol allowed for the separation of the more soluble reaction products, including trialkyltin bromide and the bithiophenes arising from homocoupling of the tin derivatives. The residual sexithiophenes were pure on the basis of ^1H NMR and were further purified by distillation under vacuum using a home-made 'cold finger' apparatus. This methodology (see experimental section) allows separation of the products not only on the basis of their vapour pressure but also on the basis of their molecular weight[9] and is particularly useful for long oligothiophenes which are contaminated by small amounts of shorter homologues.

Although the Stille reaction has become popular for the synthesis of a large variety of compounds, little is as yet known about the mechanistic effects by which electronic and steric factors affect the rate and the yield of the reaction. That electronic and steric effects play an important role in the reactions of Scheme 1 is shown by the fact that the yields for **5** are generally smaller than those for **4** and that we had to use the trimethyl stannane rather than the more bulky tributylstannane and toluene rather than tetrahydrofuran in the synthesis of **5**, in order to obtain yields comparable to those of **4**.

The synthesis of a hexa(methylsulphanyl)sexithiophene with alternating *head-to-head/tail-to-tail* linkages between adjacent thiophene units is described in Scheme 2. The rationale for wanting this product was the possibility of generating quasi planar arrangements of the aromatic backbone in solid (despite the presence of the β-substituents), owing to the existence of favourable intermolecular S...S interactions among substituents.[5f] It is easily seen that there are not many strategies available for obtaining a sexithiophene with this precise regiochemistry of substitution. The synthetic pattern proposed in Scheme 2 implies the coupling between the dibromo derivative of the 3,3'-bis(methylsulfanyl)-2,2'-bithiophene with the corresponding 2-trimethyl stannane. As shown in Scheme 2, the yield of **8** is 30% hence much lower than that for **4,5**. It is worth noting, however, that this yield is twice that obtained in the synthesis by Grignard coupling of a hexamethylsexithiophene having the same regiochemistry as **8**.[5c] The low yield of formation of **8** in the reaction in Scheme 2 is due to the fact that the homocoupling reaction of stannane **7** (to afford the quaterthiophene having two *hh* and one *tt* junction) was largely competitive with the heterocoupling reaction

which afforded sexithiophene **8** (see the experimental section). Since the homocoupling products were negligible in the synthesis of sexithiophenes **4,5**, this result indicates that when using a bithienylstannane

Scheme 2



Synthetic pattern followed to synthesize a β-functionalized sexithiophene containg alternating head-to-head (hh) and tail-to-tail (tt) junctions between adjacent 3-methylsulfanylthiophene rings.

the rate of the slow transmetallation step in the catalytic cycle[6,7a] is much lower than in the case of thienylstannanes. Consequently, the use of bithienylstannanes should be avoided when alternative synthetic strategies are allowed. The high yield (40%) of homocoupling product was a drawback of the reaction reported in Scheme 2, since the quaterthiophene produced in this way was very difficult to separate from the sexithiophene, either by crystallization or chromatography. Only after accurate distillation under vacuum were we able to obtain **8** in the very pure form needed for electronic applications.

It is worth noting that in our experience the stability and the reactivity of thienylstannanes are greatly variable. For example, **2** can be purified by distillation but **7** decomposes during distillation or chromatography on silica gel and has to be used as soon as it is prepared, as is the case for other stannanes obtained from functionalized bithiophenes.[5e]

In conclusion, we have demonstrated that use of *in situ* generated $Pd(AsPh_3)_4$ instead of commercial $Pd(PPh_3)_4$ as the catalyst in the Stille reaction between thienylstannanes and thienyl bromides leads to higher reaction yields and to acceleration of the reaction rates. Taking into account that the Stille reaction is efficient in the presence of a great variety of electron-donating or electron-withdrawing substituents[7] this result offers excellent opportunities for the synthesis of polyfunctional oligothiophenes.

Experimental Section

General procedures. $Pd(PPh_3)_4$, Pd_2dba_3, $AsPh_3$, PPh_3, BuLi, Me_3SnCl, 2-tributiltinthiophene were purchased from Aldrich. Tri-(2-furil)phosphine was purchased from Acros Organics. All solvents used in reactions and chromatographies were dried by standard procedures. Flash chromatographies were carried out using silica gel (230-400 mesh ASTM) and analytical thin layer chromatographies (TLCs) using 0.2 mm silica gel plates (Merk). The visualization in TLC was accomplished by UV light.

The synthesis of compounds **4** and **5** using the commercial catalyst $Pd(PPh_3)_4$ and the synthesis of intermediates **1-3** have already been described.[5a] The typical improved procedure followed to synthesize **4** and **5** with the catalyst generated *in situ* is described below for **4** using $AsPh_3$ as the ligand and THF as the solvent.

***4',4'',3''',3''''-tetra(methylsulfanyl)-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':sexithiophene*, 4.** 15.5 mg(0.05 molar eq) of tris(dibenzylideneacetone)dipalladium, Pd_2dba_3, were dissolved in 20 mL of freshly distilled tetrahydrofuran and 18.4 mg (0.20 molar eq) of $AsPh_3$ were added. The solution was stirred for about 30 minutes, then 400 mg (0.60 mmoles) of *5,5'''-dibromo-3,4',3'',3'''-tetra(methylsulfanyl)-2,2':5',2'':5'',2'''- quaterthiophene* **1**[5a] and 0.56 g (1.50 mmoles) of commercial *2-tributyltinthiophene* **3** (95 % pure from ^1H NMR) were added. The reaction was followed by thin layer chromatography (TLC) using petroleum ether:ethyl acetate 80:20 as the eluent. The mixture was allowed to reflux (65 °C) and after 24 hours additional 20 mL of THF containing 15.5 mg of Pd_2dba_3 and 18.4 mg of $AsPh_3$ were added. After 24 more hours the temperature was decreased to ambient, 30 mL of 2N HCl were added, the solution neutralized with saturated $NaHCO_3$, washed twice with brine, dried with $MgSO_4$ and evaporated. The crude product (374 mg) was washed three times with MeOH and three times with CH_2Cl_2. ^1H NMR showed that the solid contained only hexamer **4** (93% yield).[5a] The product was distilled under high vacuum using a home-made 'cold finger' apparatus similar to those commonly used for sublimation. 50 mg of the solid were deposited on the pot, then the finger cooled with liquid nitrogen was inserted and a 10^{-4} mm Hg vacuum was created in the apparatus. The sample was slowly heated at a temperature higher than the melting point. After melting, high-vacuum distillation occurred and the distilled compound was deposited on the surface of the cold finger. A red violet microcrystalline material (m.p. 163°C) was recovered.

***3,3',4'',3''',4'''',3''''':hexa(methylsulfanyl)-2,2':5',2'':5'',2''':5''',2'''':5'''',2''''':sexithiophene*, 8.** 22 mg (0.05 molar eq) of tris(dibenzylideneacetone)dipalladium Pd_2dba_3 were dissolved in 10 mL of freshly distilled toluene and 26.2 mg (0.20 molar eq) of $AsPh_3$ were added. The solution was stirred for 30 minutes at room temperature while the deep violet colour slightly changed to light yellow-violet. 0.39 g (0.85 mmoles) of *2,5'-dibromo-3,3'-bis(methylsulfanyl)-2,2'-bithiophene* (**6**, 90% pure from ^1H NMR),[2a] followed by 0.79 g (1.69 mmoles) of *2-trimethyltin-3,3'-bis(methylsulfanyl)-2,2'-bithiophene* (**7**, 90% from ^1H NMR) were added to this solution at room temperature. Then the temperature was slightly increased to 100°C and the course of the reaction was monitored by TLC using cyclohexane and methylene chloride as the eluent. After about 23 hours, 10 ml of toluene containing 22 mg of Pd_2dba_3 and 26.2 of $AsPh_3$ were added again and the mixture was allowed to react for 48 more hours. The mixture was quenched (at room temperature) with 30 mL of 2N HCl, neutralized with saturated $NaHCO_3$ and washed twice with brine, dried with $MgSO_4$ and evaporated. The product was then dissolved at room temperature with toluene and cooled at 0°C until a precipitate was formed. The precipitate, which contained mostly hexamer **7**, was washed twice with ethyl acetate, evaporated and 190 mg (30% yield) of hexamer **7** were obtained, which were distilled under high vacuum (see above). Orange-red solid, m.p. 165-166 °C. Anal. Calcd.for $C_{30}H_{24}S_{12}$: C, 46.72; H, 3.40. Found: C, 46.83; H, 3.45. λ_{max} = 420 nm ($CHCl_3$). MS, *m/e* 770 ($M^{\oplus\bullet}$). ^1H NMR ($CDCl_3$, TMS/ppm): 7.41 (d, 2H, J_{AB} = 5.0 Hz), 7.18 (s, 2H), 7.17 (s, 2H), 7.10 (d, 2H, J_{AB} = 5.0 Hz), 2.50 (s, 6H), 2.46 (s, 6H), 2.45 (s, 6H). ^{13}C NMR (APT, $CDCl_3$, TMS/ppm): 136.7, 136.5, 134.5,

134.3, 133.8 (in phase signals, more intense), 130.2, 130.1, 129.9 (in phase signals, less intense), 129.6, 126.5, 126.3, 126.2 (CH, reversed phase signals), 18.9, 18.8, 18.7 ($\underline{C}H_3$, reversed phase signals).

The filtrate was evaporated and 210 mg of a solid containing mostly *3,3',4'',3'''-tetra(methylsulfanyl)-2,2':5',2'':5'',2'''-quaterthiophene*[5a] (40 % yield) were recovered.

***2-trimethyltin-3,3'-bis(methylsulfanyl)-2,2'-bithiophene*, 7.** 0.67 mg (1.89 mmoles) of 2-bromo-3,3'-bis(methylsulfanyl)-2,2'-bithiophene[5f] were dissolved in 7 mL of anydrous tetrahydrofuran and 0.80 mL (1.99 mmoles) of 2.4 M BuLi were added dropwise at -65°C. The solution initially became green, then orange-red while a white suspension was formed. The mixture was stirred for about one hour at -65°C, then the temperature was increased to -40°C for 30 minutes and to 0°C for 5 minutes, again decreased to -65°C and 0.40 g (1.99 mmoles) of Me_3SnCl were added dropwise. The solution became orange and the white suspension disappeared. The mixture was stirred for one hour at -55°C, then quenched with distilled water, extracted with anhydrous ethyl ether, washed with brine, dried on $MgSO_4$ and evaporated. 0.79 g (100% yield) of a white oil were recovered which were used without further purification. From ^1H NMR the crude product was estimated to contain ≥ 95% of **7**. ^1H NMR ($CDCl_3$, TMS): 7.53 (d, 1H, J_{AB} = 5.5 Hz), 7.15 (d, 1H, J_{AB} = 5.5 Hz), 2.40 (s, 6H), 0.41(s, 9H) ppm. ^{13}C NMR (APT, $CDCl_3$, TMS): 140.6, 135.9, 134.6 (in phase signals, more intense), 136.5, 135.4 (in phase signals, less intense), 138.2, 130.2, 127.3 (CH, reversed phase signals). MS, *m/e* 337 ($M^{\oplus\bullet}$).

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