Pergamon

Tetrahedron Letters 43 (2002) 6541–6544

TETRAHEDRON
LETTERS

Rational synthesis of regioregular oligothiophenes via palladium catalyzed coupling reactions

Guillaume Loire,[a,c] Damien Prim,[b] Bruno Andrioletti,[a] Eric Rose,[a,*] André Persoons,[c,*]
Sonja Sioncke[c] and Jacqueline Vaissermann[d]

[a]*Laboratoire de Synthèse Organique et Organométallique UMR 7611, Université P. et M. Curie, Tour 44–45, case 181, 4, Place Jussieu, 75252 Paris cedex 05, France*
[b]*Laboratoire SIRCOB UPRESA 8086, Université de Versailles, 45, Avenue des Etats-Unis, 78035 Versailles cedex, France*
[c]*Laboratory for Chemical and Biological Dynamics, University of Leuven, Celestijnenlaan 200D, B-3001 Heverlee, Belgium*
[d]*LCIM² UA 7071 Université P. et M. Curie, Batiment F, case 42, 4, Place Jussieu, 75252 Paris cedex 05, France*

Received 28 June 2002; accepted 16 July 2002

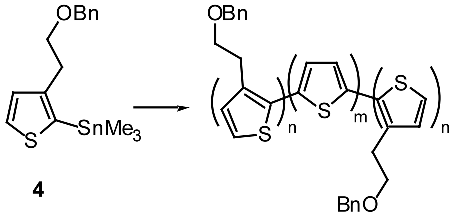
Abstract—The synthesis of bis-, ter-, quater- and sexithiophenes using Stille methodology allows a controlled thiophene chain elongation. © 2002 Elsevier Science Ltd. All rights reserved.

During the last two decades, chemistry of oligothiophenes has received considerable attention. For instance, in June 2002, a SciFinder® Scholar 2001 data search on 'oligothiophenes' revealed 814 hits containing this terminology. Undoubtedly, these ongoing efforts are related to the moderate resonance energy of thiophene that allows a good π-electron delocalization, and explains why polythiophenes are among the best candidates for second-order NLO applications. Recently, we and others have shown that increasing the number of thiophene units in a linker results in a concomitant increase of the β-values of donor–acceptor systems.[1–4] In order to systematically study the influence of oligomerization on the optical properties, we therefore initiated a palladium-based, rational synthetic approach toward well-defined, regioregular oligothiophenes. The synthetic scheme we adopted expands and improves the scope of Barbarella's preliminary approach to bisthiophenes.[5] It consists in employing the key synthon **4** that presents a univocal and suitable functionality for Stille-type palladium couplings.

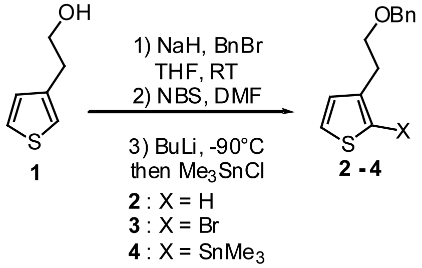
Herein, we wish to report a new, convenient synthesis of regio-controlled poly[*n*]thiophenes ($2 \leq n \leq 6$, Scheme 1).

In particular, we will show how the fine tuning of the experimental conditions allows the selective preparation of bis-, ter-, quater- and sexithiophenes. X-Ray crystal structure of quaterthiophene **7** (Scheme 4) reveals an uncommon symmetry where the thiophene units adopt a *syn–anti–syn* arrangement rather than the more classical all-*anti* (all-*trans*) geometry.[6]

Preparation of thiophene **4** involves *O*-benzylation of commercially available 3-thienylethanol[7] followed by quantitative and selective bromination of the *O*-protected thiophene **2** (Scheme 2).



Scheme 1.



Scheme 2.

---

* Corresponding authors. Tel.: 33(0)1 4427 6235; fax: 33(0)1 4427 5504 (E.R.); tel.: 0 321 632 7445; fax: 0 321 632 7982 (A.P.); e-mail: rose@ccr.jussieu.fr; andre.persoons@fys.kuleuven.ac.be

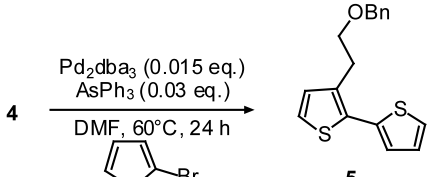
0040-4039/02/$ - see front matter © 2002 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(02)01464-8

Lithium–halogen exchange at −90°C followed by addition of Me_3SnCl afforded the trimethylstannylthiophene **4** in 90% overall yield (three steps). As already reported by others,[8] trialkylstannylthiophenes exhibit low stability upon silica gel chromatography purification. Attempts to purify the raw material only led to destannylation. Fortunately, compound **4** was pure enough to be used in the following step without any additional purification.

Validation of the coupling method was first carried out using 2-bromothiophene and stannylated thiophene **4**. Combination of Pd_2dba_3 as a catalyst precursor and $AsPh_3$ as ligand was used to generate the catalytic species for the Stille reaction.[9] As shown in Scheme 3, compound **4** smoothly reacted with 2-bromothiophene at 60°C in DMF under the above mentioned catalytic conditions, cleanly affording the monosubstituted bisthiophene **5** in 75% yield. Optimizing the coupling conditions led to the use of low catalyst loading. Indeed, it has been determined that only 1.5% of palladium source and 3% of ligand are sufficient to ensure completion of the coupling reaction. Using the latter conditions, bisthiophene **5** is isolated in 73% yield.

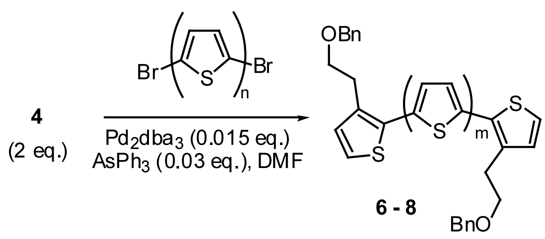
We next examined the formation of ter- and quaterthiophene using the strategy described above.

Coupling 2,5-dibromothiophene with stannane **4** under palladium catalysis readily afforded terthiophene **6** in 60% yield after 24 h under reflux in DMF (Scheme 4). When the same strategy was applied to 5,5′-dibromo-2,2′-bisthiophene and trimethylstannylthiophene **4**, quaterthiophene **7** was isolated in 50% yield.[10] Interestingly, it is worth noting that reaction of 5,5′-dibromo-2,2′-bisthiophene with **4** readily proceeds at room temperature. This enhanced reactivity illustrates the fact that 5,5′-dibromo-2,2′-bisthiophene more likely behaves like two independent 2-bromothiophene units rather than 2,5-dibromothiophene. Surprisingly, traces of a biproduct—namely sexithiophene **8**—were also isolated from the reaction mixture in ca. 3% yield by washings with Et_2O, and characterized by usual methods. The presence of the latter can be explained either by homocoupling of two 5,5′-dibromo-2,2′-bisthiophene units leading to dibromoquaterthiophene prior to bis Stille reactions or a mono Stille reaction affording brominated terthiophene subunit and further dimerization.



5
73 %

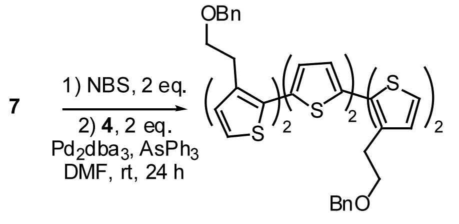
Scheme 3.



6 - 8

6 (n = m = 1) = 60 % (reflux, 24 h)
7 (n = m = 2) = 50 % (rt, 24 h)
8 (n = 2; m = 4) = traces (rt, 24 h)

Scheme 4.



9
60%

Scheme 5.

The strategy presented in this paper allows the selective access to oligothiophenes by iterative increase of the thiophene chain. Thus, sexithiophene **9** was selectively prepared in two steps starting from quaterthiophene **7** (Scheme 5).

Compound **7** was quantitatively brominated in the two unsubstituted α-positions affording the corresponding dibromoquaterthiophene. The latter was then coupled with stannane **4** affording sexithiophene **9** in 60% yield. Once again, the catalyst loading could be lowered to 1.5% of palladium precatalyst and 3% of ligand without visible decrease of the catalytic activity.

A UV–vis study of compounds **1**, **5**–**9** revealed interesting features (Fig. 1). Indeed, in our series, it appears that the absorption coefficient of the oligothiophenes generally linearly varies with the number of thiophene units of the molecule.

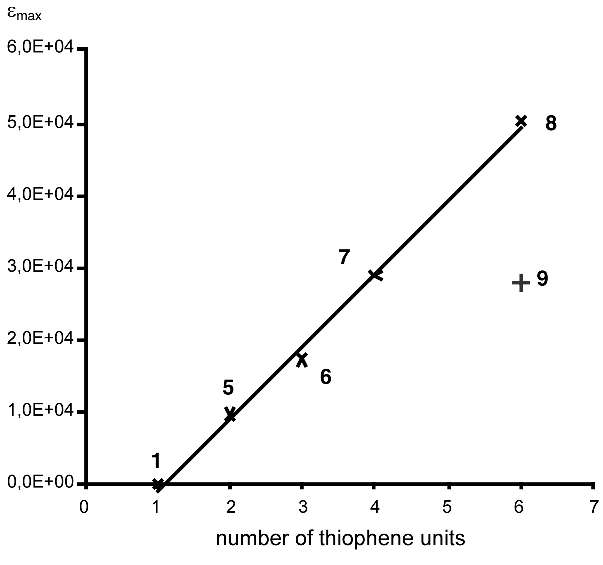


Figure 1.

The only exception concerns sexithiophene **9**. The absorption coefficient ε being closely related to electronic delocalization, it appears that **9** is not as conjugated as sexithiophene **8**. This can be explained by the increased steric bulk of **9** that possesses four chains grafted on four thiophenic β-positions. Thus, **9** probably adopts a twisted conformation that accommodates the steric hindrance at the expense of the conjugation.

Single crystals of **7** suitable for X-ray analyses were obtained by slow diffusion of pentane into a chloroform solution containing the quaterthiophene.[11] The study revealed a C2 symmetrical arrangement (Fig. 2) where the thiophene units adopted a *syn–anti–syn* conformation rather than the expected all-antiplanar symmetry.

Although already reported in the literature,[12–14] such an arrangement remains unusual as the vast majority of X-ray crystal structures reveal the more common all-*anti* conformation in which the sulfur atoms all point inward. A commonly admitted explanation for this peculiar arrangement deals with the minimization of steric energy involving S–S interactions and repulsions due to the presence of the β-substituents. As for the spatial arrangement, the molecule possesses two almost coplanar central thiophenes and two external β-substituted thiophenes slightly twisted—the dihedral angle is ca. 30°—from the main plane.

In conclusion, we have described selective, rational accesses to bis-, ter-, quater- and sexithiophenes.[15] The latter were isolated in moderate to good yields owing to palladium-based couplings between bromothiophenes and stannylated derivatives. The X-ray crystal structure of quaterthiophene **7** showed an unusual *syn–anti–syn* arrangement of the thiophene units.

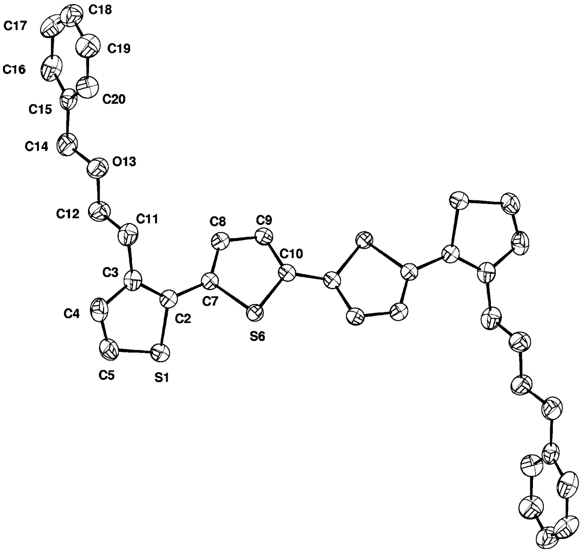


Figure 2.

Acknowledgements

The authors would like to thank the CNRS and the EU Training and Mobility of Researchers Program: 'Organometallic Dipole with NLO Properties' contract # ERBFMRXCT-CT98-0166 and COST D14 for financial support. E.R. and B.A. would like to thank Drs. C. Rolando and G. Ricart (UST Lille, France) for HRMS analyses.

References

1. Rao, V. P.; Jen, A. K.-Y.; Wong, K. Y.; Drost, K. J. *Tetrahedron Lett.* **1993**, *34*, 1747–1750.
2. Kim, O.-K.; Fort, A.; Barzoukas, M.; Blanchard-Desce, M.; Lehn, J.-M. *J. Mater. Chem.* **1999**, *9*, 2227–2232.
3. Garcia, M. H.; Royer, S.; Robalo, M. P.; Romão Dias, A.; Tranchier, J.-P.; Chavignon, R.; Prim, D.; Auffrant, A.; Rose-Munch, F.; Rose, E.; Persoons, A.; Asselberghs, I. *Eur. J. Inorg. Chem.*, submitted for publication.
4. Nalwa, H. S.; Watanabe, T.; Miyata, S. In *Nonlinear Optics of Organic Molecules and Polymers*; Nalwa, H. S.; Miyata, S., Eds.; CRC Press: New York, 1997.
5. Barbarella, G.; Zambianchi, M. *Tetrahedron* **1994**, *50*, 11249–11256.
6. Siegrist, T.; Kloc, C.; Laudise, R. A.; Katz, H. E.; Haddon, R. C. *Adv. Mater.* **1998**, *10*, 379–382.
7. Lemaire, M.; Garreau, R.; Delabouglise, D.; Roncali, J.; Youssoufi, H. K.; Garnier, F. *New J. Chem.* **1990**, *14*, 359–364.
8. Miller, L. L.; Yu, Y. *J. Org. Chem.* **1995**, *60*, 6813–6819.
9. (a) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585–9595; (b) Farina, V.; Krishnan, B.; Marshall, D. R.; Roth, G. P. *J. Org. Chem.* **1993**, *58*, 5434–5444; (c) Prim, D.; Tranchier, J.-P.; Rose-Munch, F.; Rose, E.; Vaissermann, J. *Eur. J. Inorg. Chem.* **2000**, *5*, 901–905.
10. **Typical experimental procedure**: To a solution of [3-(2-benzyloxy-ethyl)-thiophen-2-yl]-trimethyl-stannane **4** in DMF, was added a solution of 0.5 equiv. of 2,5-dibromothiophene (resp. 5,5′-dibromo-2,2′-bisthiophene), 0.015 equiv. of Pd_2dba_3 and 0.03 equiv. of $AsPh_3$ in DMF. The mixture was stirred for 24 h at appropriate temperature. The reaction mixture was then poured into cold water, extracted three times with ether, washed with water and dried over $MgSO_4$ before being concentrated under reduced pressure. The crude oil was then purified on a silica gel column chromatography and eluted with an increasing amount of dichloromethane in cyclohexane affording the bis-coupled compounds in 50–73% yield as orange solids.
11. **Crystallographic data for 7**: Orange yellow plate, monoclinic, space group $P2_1/n$, $Z=2$, $a=5.653(1)$, $b=7.780(2)$, $c=34.013(13)$ Å, $\beta=91.44(2)°$, $V=1495.4(8)$ Å^3, $\rho_{\text{calcd}}=1.33$ g cm^{-3}, $F(000)=628$, $\mu=0.33$ mm^{-1}. A total of 4264 reflections were measured (range 1–28°), 3614 unique ($R_{\text{int}}=0.05$), on an Enraf–Nonius MACH-3 diffractometer using graphite monochromatized Mo K_α radiation ($\lambda=0.71069$ Å) at room temperature. The structure was refined on F to $R=0.0553$, $Rw=0.0736$ (2045 reflections with $I>3\sigma(I)$), and a goodness of fit = 1.01 for 182 refined parameters. The molecule lies on a crystallographic inver-

sion center. CCDC-188181 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

12. Barbarella, G.; Zambianchi, M.; Del Fresno, I.; Marimon, M.; Antolini, L.; Bongini, A. *Adv. Mater.* **1997**, *9*, 484–487.
13. Mitzi, D. B.; Chondroudis, K.; Kagan, C. R. *Inorg. Chem.* **1999**, *38*, 6246–6256.
14. Muguruma, H.; Kobiro, K.; Hotta, S. *Chem. Mater.* **1998**, *10*, 1459–1467.
15. Selected characterization. Compound **5**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (m, 5H), 7.3 (dd, $J=5.2$, 1.2 Hz, 1H), 7.19 (d, $J=5.2$ Hz, 1H), 7.12 (dd, $J=3.6$, 1.2 Hz, 1H), 7.05 (dd, $J=5.2$, 3.6 Hz, 1H), 7.0 (d, $J=5.2$ Hz, 1H), 4.53 (s, 2H), 3.71 (t, $J=7.1$ Hz, 2H), 3.1 (t, $J=7.1$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 138.4, 135.8, 135.6, 131.8, 130.1, 128.4, 127.6, 127.5, 127.4, 126.3, 125.6, 124.0, 72.9, 70.1, 29.6; MALDI-TOF HRMS calcd for $C_{17}H_{16}OS_2$: $(M+Na)^+$ 323.0549. Found 323.0535; UV–vis ($CHCl_3$) nm: λ_{max} $(\varepsilon)=293$ (8614). Compound **6**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30 (m, 10H), 7.20 (d, $J=5.1$ Hz, 2H), 7.05 (s, 2H), 7.00 (d, $J=5.1$ Hz, 2H), 4.53 (s, 4H), 3.72 (t, $J=6.9$ Hz, 4H), 3.11 (t, $J=6.9$ Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 138.4, 136.0, 135.9, 131.6, 130.3, 128.4, 127.7, 126.7, 124.2, 73.0, 70.2, 29.8; MALDI-TOF HRMS calcd for $C_{30}H_{28}O_2S_3$: 516.1423. Found 516.1246; UV–vis ($CHCl_3$) nm: λ_{max} $(\varepsilon)=334$ (17 000). Compound **7**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.34 (m, 10H), 7.20 (d, $J=5.2$ Hz, 2H), 7.01 (d, $J=5.2$ Hz, 2H), 7.12 (d, $J=3.9$ Hz, 2H), 7.05 (d, $J=3.9$ Hz, 2H), 4.56 (s, 4H), 3.75 (t, $J=6.9$ Hz, 4H), 3.14 (t, $J=6.9$ Hz, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): 138.5, 137.1, 135.9, 135.1, 131.7, 130.5, 128.6, 127.8, 127.1, 124.3, 124.2, 73.1, 70.2, 30; MALDI-TOF HRMS calcd for $C_{34}H_{30}O_2S_4$: 598.1123. Found 598.1044; UV–vis ($CHCl_3$) nm: λ_{max} $(\varepsilon)=377$ (28 000). Compound **8**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.31 (m, 10H), 7.19 (d, $J=5.1$ Hz, 2H), 7.10 (d, $J=3.9$ Hz, 2H), 7.08 (s, 4H), 7.03 (d, $J=3.9$ Hz, 2H), 7.0 (d, $J=5.1$ Hz, 2H), 4.54 (s, 4H), 3.72 (t, $J=6.9$ Hz, 4H), 3.11 (t, $J=6.9$ Hz, 4H); ^{13}C NMR (50 MHz $CDCl_3$): 139.0, 137.1, 136.6, 136.3, 136.2, 135.4, 131.7, 130.8, 128.6, 127.9, 127.8, 127.3, 124.8, 124.8, 124.5, 73.2, 70.4, 30.1; MALDI-TOF HRMS calcd for $C_{42}H_{34}O_2S_6$: $(M+H)^+$ 762.0883. Found 761.9950; UV–vis ($CHCl_3$) nm: λ_{max} $(\varepsilon)=428$ (50174). Compound **9**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (m, 20H), 7.20 (d, $J=5.1$ Hz, 2H), 7.10 (d, $J=3.6$ Hz, 2H), 7.09 (d, $J=3.6$ Hz, 2H), 7.08 (s, 2H), 7.02 (d, $J=5.1$ Hz, 2H), 4.58 (s, 4H), 4.56 (s, 4H), 3.78 (t, $J=7.1$ Hz, 4H), 3.76 (t, $J=7.1$ Hz, 4H), 3.16 (t, $J=7.1$ Hz, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): 138.5, 138.4, 137.1, 136.3, 135.9, 134.7, 134.3, 131.7, 131.7, 130.4, 129.5, 128.5, 127.7, 126.9, 126.8, 124.2, 124.1, 73.1, 73.1, 70.2, 70.0, 30.1, 29.9, 29.8; MALDI-TOF HRMS calcd for $C_{60}H_{54}O_4S_6$: 1030.2316. Found 1030.2341; UV–vis ($CHCl_3$) nm: λ_{max} $(\varepsilon)=411$ (27 292).