3- and 3,4-Bis(2-cyanoethylsulfanyl)thiophenes as Building Blocks for Functionalized Thiophene-Based π-Conjugated Systems

Philippe Blanchard,* Bruno Jousselme, Pierre Frère, and Jean Roncali

Ingénierie Moléculaire et Matériaux Organiques, CNRS UMR 6501, Université d'Angers, 2 Bd Lavoisier, 49045 Angers Cedex, France

philippe.blanchard@univ-angers.fr

Received February 19, 2002

Abstract: The facile access to 3- and 3,4-bis(2-cyanoethylsulfanyl)thiophenes allows the straightforward synthesis of 3-alkylsulfanyl and symmetrical or unsymmetrical 3,4-dialkylsulfanylthiophenes by using a methodology based on a highly efficient sequence of deprotection/alkylation reactions of thiolate group(s).

3-Substituted and 3,4-substituted thiophenes are subject to considerable current interest as basic units of thiophene-based π-conjugated systems[1] usable as organic semiconductors in electronic[2] or optoelectronic[3,4] devices or as electrode materials for energy conversion[5] or sensors.[6]

Among the large number of 3-substituted thiophenes synthesized so far,[7] quite a few can be used as starting compounds for the development of strategies aiming at the synthesis of 3-functionalized polythiophenes (PTs). Initial work in that direction used 3-(2-hydroxyethyl)-thiophene[8] or thiophene-3-acetic,[9] whereas chain lengthening required tedious sequences based on malonic synthesis.[10] More recently the synthesis of 3-(ω-haloalkyl)thiophenes[11] with variable chain lengths has given access to a large number of functional PTs in which the problems posed by steric interactions among substituents grafted on adjacent thiophene rings can be resolved by adjusting the length of the alkyl spacer group. Despite its obvious advantages, the use of 3-(ω-haloalkyl)thiophenes presents some inherent limitations, namely, (i) multiple synthetic steps are required, (ii) final deprotection of the halide group requires rather drastic conditions that are not applicable to longer thiophene oligomers, and (iii) this approach is not applicable to alkyl chains containing less that four carbons. In this context, the definition of alternative synthetic approaches for PT functionalization remains a problem of current interest.

As a possible way for PT functionalization, we report here various examples illustrating a new approach in which thiophene derivatization is achieved by formation of a sulfide function at a β-position. Besides its synthetic interest, this method presents the advantage of decreasing the oxidation potential of the polymer and hence improving the stability of the doped state as a result of the electron-donating effect of the sulfide group.[12] In addition, sulfur atoms can contribute to control of the solid-state long range order in the material owing to their propensity to generate intermolecular S···S interactions.[13]

Formation of the sulfide function is achieved by reaction of a functional group bearing a terminal halogenomethyl moiety onto a 3-thiophenethiolate and/or 3,4-thiophenedithiolate. These later intermediate compounds are efficiently produced from 3-(2-cyanoethylsulfanyl)-thiophene **1** and 3,4-bis(2-cyanoethylsulfanyl)thiophene **2**. The straightforward alkylation of the later thiolate intermediates leads to related alkylsulfanylthiophenes in good yields, paving the way for a new approach of functionalization of thiophene-based π-conjugated systems. Moreover, the selective monodeprotection of only one thiolate group of compound **2** gives a ready access to symmetrical or unsymmetrical 3,4-dialkylsulfanylthiophenes.

As demonstrated in tetrathiafulvalene chemistry, the cyanoethyl group is a convenient protecting group of thiolate anion.[14] The protection reaction involves S-alkylation using 3-bromopropionitrile, and regeneration of the thiolate anion is carried out in mild basic conditions with acrylonitrile as side product. Thus, compound **1** (83% yield) was prepared in a one-pot reaction from 3-bromothiophene after lithium−bromine exchange with *n*-butyllithium at low temperature and insertion of

* To whom correspondence should be addressed. Fax 33(0)2 41 73 54 05.

(1) (a) Roncali, J. *Chem. Rev.* **1997**, *97*, 173−205. (b) Bäuerle, P. In *Electronic Materials: The Oligomer Approach*; Müllen, K., Wegner, G., Eds.; Wiley-VCH: Weinheim, 1998; pp 105−197.

(2) (a) Dodabaladpur, A.; Torsi, L.; Katz, H. E. *Science* **1995**, *268*, 270. (b) Katz, H. E. *J. Mater. Chem.* **1997**, *7*, 369. (c) Sirringhaus, H.; Brown, P. J.; Friend, R. H.; Nielsen, M. M.; Bechgaard, K.; Langeveld-Voss, B. M. W.; Spiering, A. J. H.; Janssen, R. A. J.; Meijer, E. W.; Herwig, P.; de Leeuw, D. M. *Nature* **1999**, *401*, 685. (d) Dimitrakopoulos, C. D.; Malenfant, P. R. L. *Adv. Mater.* **2002**, *14*, 99.

(3) (a) Berggren, M.; Inganäs, O.; Gustafsson, G.; Rasmusson, J.; Andersson, M. R.; Hjertberg, T.; Wennerström, O. *Nature* **1994**, *372*, 444. (b) Mitschke, U.; Bäuerle, P. *J. Mater. Chem.* **2000**, *10*, 1471−1507. (c) Shirota, Y. *J. Mater. Chem.* **2000**, *10*, 1. (c) Segura, J. L. *Acta Polym.* **1998**, *49*, 319.

(4) (a) Wolf, J. J.; Wortmann, R. *Adv. Phys. Org. Chem.* **1999**, *32*, 121−217. (b) Raimundo, J.-M.; Blanchard, P.; Gallego-Planas, N.; Mercier, N.; Ledoux-Rak, I.; Hierle, R.; Roncali, J. *J. Org. Chem.* **2002**, *67*, 205 and references therein.

(5) (a) Sariciftci, N. S.; Smilowitz, A.; Heeger, A. J. *Science* **1992**, *258*, 1474. (b) Sariciftci, N. S.; Heeger, A. J. *Int. J. Mod. Phys. B* **1994**, *8*, 237. (c) Roman, L. S.; Anderson, M. R.; Yohannes, T.; Inganäs, O. *Adv. Mater.* **1997**, *9*, 1164. (d) van Hal, P. A.; Knol, J.; Langeveld-Voss, B. M. W.; Meskers, S. C. J.; Hummelen, J. C.; Janssen, R. A. J. *J. Phys. Chem. A.* **2000**, *104*, 5974.

(6) (a) *Handbook of Conducting Polymers*, 2nd ed.; Skotheim, T. A., Elsenbaumer, R. L., Reynolds, J. R., Eds.; Marcel Dekker: New York, 1998. (b) Roncali, J. *J. Mater. Chem.* **1999**, *9*, 1875. (c) Scheib, S.; Bäuerle, P. *J. Mater. Chem.* **1999**, *9*, 2139. (d) McQuade, D. T.; Pullen, A. E.; Swager, T. M. *Chem. Rev.* **2000**, *100*, 2537.

(7) Schulz, E.; Fahmi, K.; Lemaire, M. *Acros Chimica Acta* **1994**, *1*, 1−16.

(8) (a) Welzel, H. P.; Kossmehl, G.; Schneider, J.; Plieth. W. *Macromolecules* **1995**, *28*, 5575. (b) Welzel, H. P.; Kossmehl, G.; Boettcher, H.; Engelmann, G. *Macromolecules* **1997**, *30*, 7419.

(9) (a) Welzel, H. P.; Kossmehl, G.; Stein, H. J.; Schneider, J.; Plieth, W. *Electrochim. Acta* **1995**, *40*, 577. (b) Millar, D.; Uttamlal, M.; Henderson, R.; Keeper, A. *Chem. Commun.* **1998**, 477.

(10) Lemaire, M.; Garreau, R.; Roncali, J.; Delabouglise, D.; Korri Youssoufi, H.; Garnier, F. *New J. Chem.* **1989**, *13*, 863.

(11) Bäuerle, P.; Würthner, F.; Heid, S. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 419.

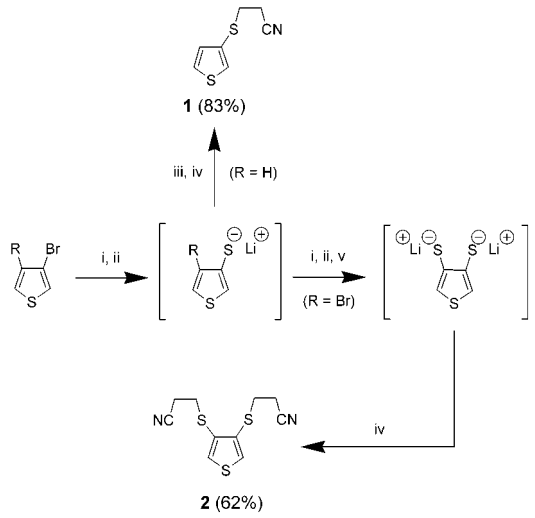
(12) Smie, A.; Synowczyk, A.; Heinze, J.; Alle, R.; Tschuncky, P.; Götz, G.; Bäuerle, P. *J. Electroanal. Chem.* **1998**, *452*, 87−95.

(13) Barbarella, G.; Zambianchi, M.; Di Toro, R.; Colonna, M.; Antonili, L.; Bongini, A. *Adv. Mater.* **1996**, *8*, 327−331.

(14) (a) Svenstrup, N.; Rasmussen, K. M.; Hansen, T. K.; Becher, J. *Synthesis* **1994**, 809. (b) Nielsen, M. B.; Lomholt, C.; Becher, J. *Chem. Soc. Rev.* **2000**, *29*, 153.

10.1021/jo025627+ CCC: $22.00
Published on Web 04/25/2002

Scheme 1[a]



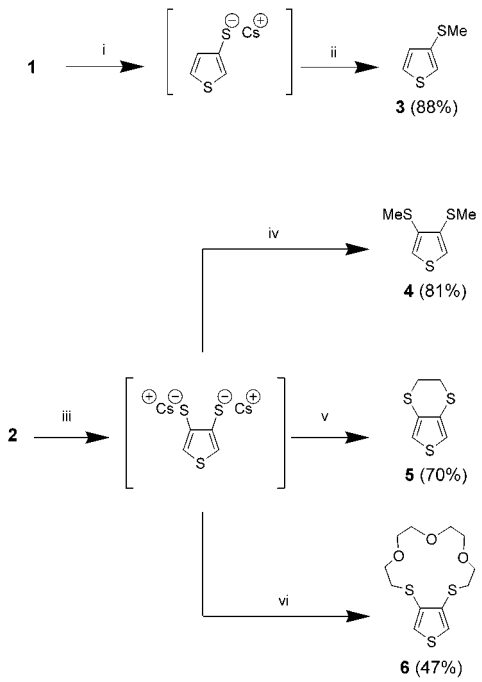
[a] (i) *n*-BuLi (1 equiv) for **1** and *t*-BuLi (1 equiv) for **2**, Et_2O, −78 °C, 30 min; (ii) S_8 (1 equiv), −78 °C, 30 min; (iii) 20 °C, 30 min; (iv) 3-bromopropionitrile, 0 → 20 °C; (v) 20 °C, 2 h.

elemental sulfur generating 3-thiophenethiolate,[15] which was further alkylated using 3-bromopropionitrile (Scheme 1).

The preparation of 3,4-thiophenedithiolate is more delicate[16−18] and implies the preparation of either thieno-[3,4-*d*]-2-thioxo-1,3-dithiole, obtained in low yields (25−33%) from 3,4-dibromothiophene,[16] or thieno[3,4-*d*]-2-oxo-1,3-dithiole by a multistep synthesis.[17] An improved route has been recently proposed by Reynolds et al.,[19] who prepared 3,4-bis(isopropylsulfanyl)thiophene in two steps from 3,4-dibromothiophene. The isopropyl groups were eliminated by treatment with sodium in refluxing pyridine, generating the 3,4-thiophenedithiolate, which was characterized after reaction with MeI.

An important advantage of the cyanoethyl group for thiolate protection lies in the milder deprotection conditions. Thus, by analogy with the initial work of Cowan et. al.,[16a] we prepared the lithium salt of 3,4-thiophenedithiolate starting from 3,4-dibromothiophene. After two successive monolithiations with *tert*-butyllithium and treatment with elemental sulfur at low temperature, the lithium salt of 3,4-thiophenedithiolate was allowed to warm to room temperature. Double S-alkylation was achieved with a slight excess of 3-bromopropionitrile to give **2** (62%) in yields about twice larger than those reported for related precursors.[16] This improved yield can be related to the replacement of *n*-butyllithium by *tert*-butyllithium, which limits the formation of the mono- or dialkylsulfanyl thiophenes observed in significant amounts with *n*-butyllithium, probably because of the easy S_N2 reaction between *n*-bromobutane and lithium thiolate derivatives. On the other hand, an efficient alkylating reagent such as 3-bromopropionitrile allows a better

Scheme 2[a]



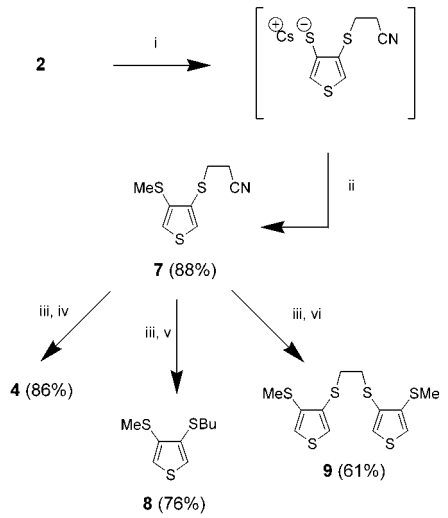
[a] (i) $CsOH·H_2O$ (1.1 equiv), MeOH, DMF, 20 °C, 30 min; (ii) excess of MeI, 20 °C, 2 h; (iii) $CsOH·H_2O$ (2.2 equiv), MeOH, DMF, 0 °C, 5 min; (iv) excess of MeI, 0 → 20 °C, 2 h; (v) 1,2-dibromoethane (1 equiv), 0 → 20 °C, 1 h; (vi) 1,11-diiodo-3,6,9-trioxaundecane (1 equiv), 0 → 20 °C, high dilution.

quenching of the 3,4-dithiolatethiophene than with CS_2, usually employed for the preparation of thieno[3,4-*d*]-2-thioxo-1,3-dithiole.[16] Finally, the ease of purification of **2** by chromatography on silica gel due to the presence of cyano polar groups and its good stability under atmospheric conditions allow both a preparation at a multigram scale in an efficient one-pot reaction from 3,4-dibromothiophene and its long-term storage.[20]

The versatility of compounds **1** and **2** is demonstrated in Schemes 2 and 3. Upon treatment of a DMF solution of compound **1** (1 equiv) with CsOH (1.1equiv) in methanol, the cyanoethyl group is cleanly eliminated to give the cesium salt of 3-thiophenethiolate. Alkylation with MeI in excess gives 3-methylsulfanylthiophene **3**[21,22] in 88% yield, demonstrating the efficiency of the deprotection/alkylation process (Scheme 2). Similarly, treatment of compound **2** with 2.2 equiv of CsOH and alkylation of the resulting cesium salt with an excess of MeI or 1 equiv of 1,2-dibromoethane gave 3,4-dimethylsulfanylthiophene

(15) Gronowitz, S.; Moses, P. *Acta Chem. Scand*. **1962**, *16*, 155.
(16) (a) Chiang, L.-Y.; Shu, P.; Holt, D.; Cowan, D. *J. Org. Chem*. **1983**, *48*, 4713−4714. (b) Wang, C.; Schindler, J. L.; Kannewurf, C. R.; Kanatzidis, M. G. *Chem. Mater*. **1995**, *7*, 58−68.
(17) Skabara, P. J.; Müllen, K.; Bryce, M. R. R.; Howard, J. A. K.; Batsanov, A. S. *J. Mater. Chem*. **1998**, *8*, 1719.
(18) Skabara, P. J.; Berridge, R.; Prescott, K.; Goldenberg, L. M.; Viruela, Ortí, R.; Pou-Amérigo, R.; Batsanov, A. S.; Howard, J. A. K.; Coles, S. J.; Hursthouse, M. B. *J. Mater. Chem*. **2000**, *10*, 2448−2457.
(19) Reddinger, J. L.; Reynolds, J. R. *J. Org. Chem*. **1996**, *61*, 4833−4834.
(20) A terthiophene bearing two 2-cyanoethylsulfanyl groups at the 3- and 4-positions of the central thiophene ring has been recently prepared by a different synthetic strategy. Pozo-Gonzalo, C.; Roberts, D. M.; Skabara, P. J. *J. Synth. Met*. **2001**, *119*, 115.
(21) (a) Gronowitz, S. *Ark. Kemi* **1958**, *13*, 269. (b) Rossi, R.; Carpita, A.; Ciofalo, M.; Lippolis, V. *Tetrahedron* **1991**, *47*, 8443.
(22) For references on 3-alkylsulfanylthiophenes, see: (a) Gronowitz, S.; Moses, P. *Acta Chem. Scand*. **1962**, *16*, 155. (b) Tourillon, G.; Garnier, F. *J. Electroanal. Chem*. **1984**, *161*, 51. (c) Ruiz, J. P.; Nayak, K.; Marynick, D. S.; Reynolds, J. R. *Macromolecules* **1989**, *22*, 1231. (d) Wu, X.; Chen, T.-A.; Rieke, R. D. *Macromolecules* **1995**, *28*, 2101−2102. (e) Wu, X.; Chen, T.-A.; Rieke, R. D. *Macromolecules* **1996**, *29*, 7671. (f) Bäuerle, P.; Götz, G.; Synowczyk, A.; Heinze, J. *Liebigs Ann*. **1996**, 279−284. (g) Folli, U.; Goldoni, F.; Iarossi, D.; Mucci, A.; Schenetti, L. *J. Chem. Res., Synop*. **1996**, 69. (h) Goldoni, F.; Iarossi, D.; Mucci, A.; Schenetti, L. *Chem. Commun*. **1997**, 2175. (i) Antolini, L.; Goldoni, F.; Iarossi, D.; Mucci, A.; Schenetti, L. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1957. (j) Iarossi, D.; Mucci, A.; Schenetti, L.; Sodini, V. *J. Heterocycl. Chem*. **1999**, *36*, 241−247. (k) Ng, S. C.; Miao, P. *Macromolecules* **1999**, *32*, 5313.

Scheme 3[a]



[a] (i) $CsOH·H_2O$ (1 equiv), MeOH, DMF, 20 °C, 45 min; (ii) excess of MeI, 20 °C, 2 h; (iii) $CsOH·H_2O$ (1.3 equiv), MeOH, DMF, 20 °C, 30 min; (iv) excess of MeI, 20 °C, 1 h; (v) 1-bromobutane (5 equiv), 20 °C, 1 h; (vi) 1,2-dibromoethane (0.5 equiv), 20 °C, 1 h.

4[22f] (81% yield) or 3,4-ethylenedisulfanylthiophene **5**[16,23] (70% yield), respectively. Note that lower yields were obtained, e.g., in the case of the preparation of **4**, when the reaction of double deprotection was performed at 20 °C (54% yield) instead of 0 °C, indicating a significant decrease of stability of 3,4-thiophenedithiolate at 20 °C. For this reason, the synthesis of the oxathia crown ether compound **6** in high dilution conditions was adapted in order to allow the 3,4-thiophenedithiolate to react immediately with the corresponding α,ω-dihalogeno compound. Thus, slow addition of a mixture of **2** and 1,11-diiodo-3,6,9-trioxaundecane to a solution of CsOH in a mixture of MeOH/DMF at 0 °C gave compound **6** in satisfactory yield.

Selective deprotection of only one thiolate group can be readily achieved by treatment of compound **2** with 1 equiv of CsOH (Scheme 3), thus providing direct access to unsymmetrical 3,4-disubsituted thiophenes. For example, subsequent S-alkylation of the later monothiolate intermediate with an excess of iodomethane gave compound **7** (88% yield), which was then deprotected and again S-alkylated with MeI (excess) and 1-bromobutane (5 equiv) or 1,2-dibromoethane (0.5 equiv), leading to the disubstituted compounds **4** (86% yield), **8** (76% yield), and **9** (61% yield), respectively. Compound **4** has already been obtained from 3-bromo-4-methylsulfanylthiophene but in a much lower yield (5%).[22f] Thus, the high yields obtained for the stepwise synthesis of **4** via the intermediate compound **7** show that the above-described stepwise deprotection/S-alkylation sequences can be easily extended to the synthesis of unsymmetrically disubstituted molecular systems, thus opening interesting new routes for the synthesis of functionalized π-conjugated oligomers and polymers.

To summarize, we have shown that 3-(2-cyanoethylsulfanyl)thiophene **1** and 3,4-bis(2-cyanoethylsulfanyl)-thiophene **2** can be prepared in an efficient one-pot reaction. These compounds can be deprotected under mild basic conditions, thus giving a straightforward access to 3-substituted thiophenes and to symmetrical and/or unsymmetrical 3,4-disubstituted thiophenes.

Experimental Section

^1H and ^{13}C NMR spectra were recorded at 500.13 and 125.7 MHz, respectively; δ are given in ppm (relative to TMS) and coupling constants (*J*) are in Hz. IR spectra were recorded by using samples embedded in KBr disks or thin films between NaCl plates. Melting points are uncorrected. Commercial 3-bromothiophene was used as received, and 3,4-dibromothiophene was prepared from tetrabromothiophene after a selective double debromination using Zn/AcOH[24] and then purified by distillation before use.

3-(2-Cyanoethylsulfanyl)thiophene 1. To a solution of 3-bromothiophene (3 mL, 32 mmol) in anhydrous Et_2O (25 mL) under N_2 at −78 °C was added dropwise a solution of *n*-BuLi 2.5 M in hexane (13.4 mL, 1.05 equiv) over a period of 30 min. After 15 min of stirring at −78 °C, the lithiated salt precipitated, and then elemental sulfur (1.05 g, 1.05 equiv) was added in one portion. After 30 min of additional stirring at −78 °C, the reaction mixture was allowed to warm to room temperature and stirred for 30 min. Then the solution was cooled to 0 °C, and 3-bromopropionitrile (8.23 g, 5.1 mL, 2 equiv) was added dropwise. The reaction mixture was stirred for 1 h at room temperature. After careful addition of an aqueous solution of HCl (0.5 M, 40 mL), the mixture was extracted with CH_2Cl_2 (200 mL). The organic phases were dried over Na_2SO_4 and evaporated in vacuo. The excess of 3-bromopropionitrile was separated by distillation (1 mbar, 78 °C) using a Kugelrhor apparatus. The resulting oil was purified by chromatography on silica gel (eluent, CH_2Cl_2/petroleum ether 1:1) to give compound **1** as a slightly yellow oil (4.5 g; 83% yield). ^1H NMR ($CDCl_3$) δ: 2.57 (t, 2H, CH_2−CN, ^3J = 7.2 Hz); 3.02 (t, 2H, CH_2−S, ^3J = 7.2 Hz); 7.08 (dd, 1H, ^3J = 4.9 Hz, ^4J = 1.3 Hz); 7.37 (dd, 1H, ^4J =1.3 Hz, ^4J = 3.0 Hz); 7.38 (dd, 1H, ^4J = 3.0 Hz, ^3J = 4.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 18.4 (CH_2−CN), 31.3 (CH_2−S), 118.0 (CN), 127.1, 128.0, 128.4, 130.6. MS (70 eV, EI) *m*/*z* (I%): 169 ($M^{+\bullet}$, 53), 129 (54), 116 (29), 85 (50), 71 (100). IR (NaCl) ν cm^{-1}: 2249 (C≡N). Anal. for $C_7H_7NS_2$ Found (Calcd): C, 49.20 (49.67); H, 4.22 (4.17); S, 36.54 (37.88); N, 8.10 (8.28).

3,4-Bis(2-cyanoethylsulfanyl)thiophene 2. To a solution of 3,4-dibromothiophene (7.12 g, 29.4 mmol) in anhydrous Et_2O (40 mL) cooled at −78 °C under a nitrogen atmosphere was dropwise added a solution of *t*-BuLi (1.5 M in pentane, 19.6 mL, 1 equiv)[25] over a period of 20 min, and the mixture was stirred at −78 °C for 0.5 h. Elemental sulfur (0.94 g, 1 equiv) was then added in one portion, and stirring was maintained at −78 °C for an additional 0.5 h. An additional 1 equiv of *t*-BuLi (1.5 M in pentane, 19.6 mL) was dropwise added over a period of 15 min, and the solution was stirred at −78 °C for 0.5 h before addition of 1 equiv of elemental sulfur (0.94 g) in one portion. After stirring for 0.5 h at −78 °C, the reaction mixture was allowed to warm to 20 °C and stirred at this temperature for 2 h. A solution of 3-bromopropionitrile (5.5 mL, 66.3 mmol) was slowly added to the mixture cooled at 0 °C, which was then left under stirring overnight at 20 °C. After addition of water (50 mL), the mixture was extracted with CH_2Cl_2 (3 × 100 mL), and the organic phases were gathered and washed with water (3 × 75 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The resulting yellow-brown oil was purified by chromatography on silica gel (eluent, CH_2Cl_2/petroleum ether 1:1 and then CH_2Cl_2) to give 3,4-bis(2-cyanoethylsulfanyl)thiophene **2** (4.64 g, 62% yield) as an oil that slowly crystallized affording a beige solid. Crystallization of the oil in a mixture of solvents (CH_2Cl_2/MeOH/pentane) was also possible after cooling with liquid nitrogen to give 3.43 g of white powder, mp 61−64 °C. ^1H NMR ($CDCl_3$) δ: 7.44 (s, 2H); 3.11 (t, 4H, ^3J = 7.1); 2.62 (t, 4H, ^3J = 7.1). ^{13}C NMR ($CDCl_3$) δ: 131.25; 129.48; 117.75; 30.20; 18.22. FAB MS: 255.06 ($[M + H]^+$); 254.05 ($M^{+\bullet}$). IR (KBr) ν cm^{-1}: 2249 (C≡N). Anal. for $C_{10}H_{10}N_2S_3$ Found (Calcd): C, 47.54 (47.22); H, 3.96 (3.96); N, 10.75 (11.01); S, 36.58 (37.81).

(23) Goldoni, F.; Langeveld-Voss, B. M. W.; Meijer, E. W. *Synth. Commun.* **1998**, *28*, 2237−2244.

(24) Zhang, Q. T.; Tour, J. M. *J. Am. Chem. Soc.* **1998**, *120*, 5355.

(25) The conventional halogen−lithium exchange using 2 equivalents of *t*-BuLi per bromine atom instead of 1 led to lower yield in compound **2** (45%).

3-Methylsulfanylthiophene 3. Under a nitrogen atmosphere, a solution of $CsOH·H_2O$ (0.50 g, 1.2 equiv) in nitrogen-degassed MeOH (7 mL) was dropwise added over a period of 5 min to a nitrogen-degassed solution of compound **1** (0.42 g, 2.48 mmol) in dimethylformamide (25 mL) at 20 °C. After 30 min of additional stirring, an excess of methyl iodide (0.62 mL, 9.94 mmol) was added in one portion, and the reaction mixture was left under stirring for 1 h at 20 °C. After addition of Et_2O (150 mL), the organic phase was washed with a 1 M aqueous solution of HCl (4 × 50 mL) in order to get rid of DMF and then dried over $MgSO_4$. Et_2O was evaporated, and the resulting residue was purified by chromatography on silica gel (eluent, petroleum ether/CH_2Cl_2 7:3) leading to a slightly yellow oil (0.28 g, 88% yield) after evaporation of the eluent under reduced pressure (150 mbar at 40 °C). ^{1}H NMR ($CDCl_3$) δ: 7.34 (dd, 1H, ^3J = 5.1 and ^4J = 3.0); 7.01 (dd, 1H, ^3J = 5.1 and ^4J = 1.4); 6.98 (dd, 1H, ^4J = 3.0 and ^4J = 1.4); 2.48 (s, 3H).

3,4-Dimethylsulfanylthiophene 4. Bisdeprotection. Under a nitrogen atmosphere, a solution of $CsOH·H_2O$ (0.63 g, 3 equiv) in nitrogen-degassed MeOH (10 mL) was dropwise added over a period of 5 min to a nitrogen-degassed solution of compound **2** (0.32 g, 1.26 mmol) in dimethylformamide (30 mL) at 0 °C. After 5 min of additional stirring at 0 °C, a solution of iodomethane (0.50 mL, 6 equiv) was added to the reaction mixture, which was then left under stirring for 20 min at 0 °C and then 1 h at 20 °C. After evaporation of the solvents in vacuo and subsequent addition of CH_2Cl_2 (100 mL), the solution was washed with water (3 × 50 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by chromatography on silica gel (eluent, CH_2Cl_2/petroleum ether 1:1) led to a yellow-orange oil (0.18 g, 81% yield). **Monodeprotection.** Under a nitrogen atmosphere, a solution of $CsOH·H_2O$ (0.20 g, 1.3 equiv) in nitrogen-degassed MeOH (5 mL) was dropwise added over a period of 5 min to a nitrogen-degassed solution of compound **7** (0.20 g, 0.93 mmol) in dimethylformamide (15 mL) at 20 °C. After 30 min of additional stirring, an excess of methyl iodide (0.25 mL, 4.02 mmol) was added in one portion, and the reaction mixture was left under stirring for 1 h at 20 °C. After evaporation of the solvents in vacuo and subsequent addition of CH_2Cl_2 (100 mL), the solution was washed with water (2 × 75 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by chromatography on silica gel (eluent, cyclohexane/CH_2Cl_2 8:2) led to a slightly yellow oil (0.14 g, 86% yield). ^{1}H NMR ($CDCl_3$) δ: 7.01 (s, 2H); 2.46 (s, 6H). ^{13}C NMR ($CDCl_3$) δ: 134.70; 121.20; 17.38. EI MS *m*/*z* (I%): 176 ($M^{+\bullet}$, 61); 161 (8); 97 (17); 58 (50); 43 (100).

3,4-Ethylenedisulfanylthiophene 5. Under a nitrogen atmosphere, a solution of $CsOH·H_2O$ (0.46 g, 2.2 equiv) in nitrogen-degassed MeOH (10 mL) was dropwise added over a period of 5 min to a nitrogen-degassed solution of compound **2** (0.32 g, 1.26 mmol) in dimethylformamide (30 mL) at 0 °C. After 5 min of additional stirring at 0 °C, a solution of 1,2-dibromoethane (0.11 mL, 1 equiv) was added dropwise to the reaction mixture, which was then left under stirring for 20 min at 0 °C and then 1 h at 20 °C. After evaporation of the solvents in vacuo and subsequent addition of CH_2Cl_2 (100 mL), the solution was washed with water (3 × 30 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by chromatography on silica gel (eluent, cyclohexane/CH_2Cl_2 7:3) led to a beige oil (0.15 g, 70% yield). ^{1}H NMR ($CDCl_3$) δ: 6.97 (s, 2H); 3.22 (s, 4H). ^{13}C NMR ($CDCl_3$) δ: 125.23; 118.10; 28.03. EI MS *m*/*z* (I%): 174 ($M^{+\bullet}$, 100); 159 (82); 146 (32).

3,4-(4,7,10-Trioxa-1,13-dithiatridecane-1,13-diyl)thiophene 6. Under a nitrogen atmosphere, a mixture of compound **2** (0.51 g, 2.00 mmol) and 1,11-diiodo-3,6,9-trioxaundecane (0.83 g, 2.00 mmol) in dimethylformamide (25 mL) was dropwise added over a period of 30 min to a nitrogen-degassed solution of $CsOH·H_2O$ (1.00 g, 5.95 mmol) in a mixture of solvents (MeOH/DMF, 10 mL/50 mL) cooled to 0 °C. The reaction mixture was then allowed to warm to 20 °C and stirred again for 1 h. After evaporation of the solvents in vacuo and subsequent addition of EtOAc (100 mL), the solution was washed with brine (3 × 50 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by chromatography on silica gel (eluent, CH_2Cl_2/EtOAc 95:5) led to a yellow oil (0.29 g, 47% yield). ^{1}H NMR ($CDCl_3$) δ: 7.21 (s, 2H); 3.76 (t, 4H, ^3J = 6.5); 3.63−3.59 (m, 8H); 3.10 (t, 4H, ^3J = 6.5). ^{13}C NMR ($CDCl_3$) δ: 134.2; 125.5; 71.0; 70.5; 69.6; 35.2. EI MS *m*/*z* (I%): 306 ($M^{+\bullet}$, 74); 174 (80); 159 (84); 146 (80). Anal. for $C_{12}H_{18}O_3S_3$ Found (Calcd): C, 46.78 (47.03); H, 5.89 (5.92); O, 15.58 (15.66).

3-(2-Cyanoethylsulfanyl)-4-methylsulfanylthiophene 7. Under a nitrogen atmosphere, a solution of $CsOH·H_2O$ (0.47 g, 1 equiv) in nitrogen-degassed MeOH (9 mL) was dropwise added over a period of 10 min to a nitrogen-degassed solution of compound **2** (0.70 g, 2.76 mmol) in dimethylformamide (30 mL) at 20 °C. After 45 min of additional stirring, an excess of methyl iodide (0.7 mL, 11.24 mmol) was added in one portion, and the reaction mixture was left under stirring for 2 h at 20 °C. After evaporation of the solvents in vacuo and subsequent addition of CH_2Cl_2 (150 mL), the solution was washed with water (2 × 75 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by chromatography on silica gel (eluent, CH_2Cl_2/petroleum ether 1:1) led to a beige oil (0.52 g, 88% yield). ^{1}H NMR ($CDCl_3$) δ: 7.51 (d, 1H, ^3J = 3.2); 6.88 (d, 1H, ^3J = 3.2); 3.03 (t, 2H, ^3J = 7.2); 2.56 (t, 2H, ^3J = 7.2); 2.48 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 138.32; 131.23; 127.35; 118.73; 117.92; 30.12; 18.28; 16.67. EI MS *m*/*z* (I%): 215 ($M^{+\bullet}$, 100); 162 (52); 160 (38). IR (NaCl) ν cm^{-1}: 2251 (C≡N). Anal. for $C_8H_9N_1S_3$ Found (Calcd): C, 44.54 (44.62); H, 4.04 (4.21); N, 6.40 (6.50); S, 45.10 (44.66).

3-*n*-Butylsulfanyl-4-methylsulfanylthiophene 8. Under a nitrogen atmosphere, a solution of $CsOH·H_2O$ (0.51 g, 1.3 equiv) in nitrogen-degassed MeOH (15 mL) was dropwise added over a period of 10 min to a nitrogen-degassed solution of compound **7** (0.50 g, 2.32 mmol) in dimethylformamide (30 mL) at 20 °C. After 30 min of additional stirring, an excess of *n*-bromobutane (1.25 mL, 11.63 mmol) was added in one portion, and the reaction mixture was left under stirring for 1 h at 20 °C. After evaporation of the solvents in vacuo and subsequent addition of CH_2Cl_2 (200 mL), the solution was washed with water (2 × 75 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by chromatography on silica gel (eluent, cyclohexane) led to a colorless oil (0.39 g, 76% yield). ^{1}H NMR ($CDCl_3$) δ: 7.18 (d, 1H, ^4J = 3.2); 6.91 (d, 1H, ^4J = 3.2); 2.85 (t, 2H, ^3J = 7.3); 2.46 (s, 3H); 1.64−1.58 (m, 2H); 1.46−1.42 (m, 2H); 0.91 (t, 3H, ^3J = 7.3).^{13}C NMR ($CDCl_3$) δ: 136.67; 132.27; 124.96; 119.43; 34.48; 31.25; 21.84; 17.10; 13.59. EI MS *m*/*z* (I%): 218 ($M^{+\bullet}$, 89); 162 (100). Anal. for $C_9H_{14}S_3$ Found (Calcd): C, 49.45 (49.50); H, 6.44 (6.46); S, 43.56 (44.04).

1,2-Bis[4-(methylsulfanyl)-3-thienylsulfanyl]ethane 9. Under a nitrogen atmosphere, a solution of $CsOH·H_2O$ (0.19 g, 1.3 equiv) in nitrogen-degassed MeOH (5 mL) was dropwise added over a period of 5 min to a nitrogen-degassed solution of compound **7** (0.18 g, 0.84 mmol) in dimethylformamide (15 mL) at 20 °C. After 30 min of additional stirring, a solution of 1,2-dibromoethane (36 μL, 0.5 equiv) was added dropwise to the reaction mixture, which was then left under stirring for an additional 1 h at 20 °C. After evaporation of the solvents in vacuo and subsequent addition of CH_2Cl_2 (100 mL), the solution was washed with water (3 × 30 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by chromatography on silica gel (eluent, cyclohexane/CH_2Cl_2 8:2) led to a white solid (0.09 g, 61% yield), mp 84−86 °C. ^{1}H NMR ($CDCl_3$) δ: 7.22 (d, 2H, ^3J = 3.2); 6.88 (d, 2H, ^3J = 3.2); 2.98 (s, 4H); 2.45 (s, 6H). ^{13}C NMR ($CDCl_3$) δ: 137.45; 129.96; 127.52; 119.06; 33.95; 16.96. EI MS *m*/*z* (I%): 350 ($M^{+\bullet}$, 43); 189 (100); 175 (37); 161 (69); 160 (35); 97 (57). Anal. for $C_{12}H_{14}S_6$ Found (Calcd): C, 41.26 (41.11); H, 4.10 (4.02); S, 54.21 (54.87).

Acknowledgment. The authors thank the SCAS of the University of Angers for analytical characterizations.

JO025627+