

0040-4039(95)01816-6

A Facile and Convenient Synthesis of 2-(arylthio)thiophenes, 2-(alkylthio)thiophene, and 2-(thiophenylthio)thiophene

Sang Bok Lee and Jong-In Hong*

Department of Chemistry, Seoul National University, Seoul 151-742, Korea

Abstract: 2-(Arylthio)thiophenes, 2-(alkylthio)thiophene, and 2-(thiophenylthio)thiophene were prepared in high yield by simply mixing 2-iodothiophene and aryl, alkyl, or thienyl thiols at room temperature without solvent, base, and/or catalyst.

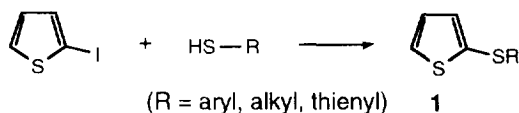
Poly(*p*-phenylene sulfide) (PPS)¹ possesses high crystallinity, poor solvent solubility, good thermal stability, good mechanical strength, chemical resistance, and good electrical characteristics. Poly(2,5-thiophenediyl sulfide) (PTS)² and poly(2-(arylthio)thiophenyl sulfide) (PATS)³ are also expected to have similar or even better physical and chemical properties which may make them an excellent high-performance engineering plastic. While PPS¹ has been studied by several groups, to the best of our knowledge, no research group is currently working on PTS and PATS. In line with our interest in the synthesis of PTS and PATS, we studied on the improved preparation of monomeric units of PTS and PATS. In this report we describe a facile and convenient route to the preparation of 2-(arylthio)thiophenes, 2-(alkylthio)thiophene, and 2-(thiophenylthio)thiophene.

The previous synthesis was generally effected by nucleophilic substitution of halothiophenes by aryl thiolates, alkyl thiolates, or thiophenethiolates. 2,2'-Dithienyl sulfide was prepared in ~ 60% yield by heating 2-thiophenethiol and 2-bromothiophene in DMF at 130 - 140°C for 16 h in the presence of copper(I) oxide (50 mol%) and potassium hydroxide.^{4,5} Aryl 2-thienyl sulfide was prepared by either condensation of 2-iodothiophene with aryl thiolate in the presence of copper in refluxing pyridine (55 ~ 75% yield)⁶ or photostimulated S_{RN1} reactions of halothiophenes with benzenethiolate ion in acetonitrile (10 ~ 52% yield).⁷ 2-*n*-Butylmercaptothiophene was formed in 92% yield by condensation of cuprous *n*-butylmercaptide with 2-bromothiophene at 200°C in a quinoline-pyridine mixture.⁸

In contrast to the former synthesis done under rather harsh conditions, structure **1** can be made very quickly and in high yield by simply mixing 2-iodothiophene and aryl, alkyl, or thienyl thiols at room temperature without solvent, base, and/or catalyst. Table 1 shows simple condensation reactions of 2-iodothiophene with various thiols. In the case of using aryl thiols, the reaction time is in good correlation with the nucleophilicity of the thiol. While the reaction between 2-iodothiophene and 2-methoxybenzenethiol was completed after six to ten hours at 50 °C (~85% yield) in various solvents (DMF, acetone, DMSO, THF, acetonitrile, or *n*-hexane, 5 M concentration each) without base, addition of potassium carbonate to the reaction mixture in DMF decreased

both the reaction rate and the yield.⁹ However, the substitution reaction between 2-iodothiophene and 2-methoxybenzenethiol proceeded faster in acetic acid¹¹ than either in solvent (*vide supra*) without base or in DMF with potassium carbonate as base.⁹ The reaction in the absence of both solvent and base (see Table 1) is faster than the reaction in acetic acid.¹¹ Though there is no direct evidence for the mechanism, the results obtained may be explained assuming that the reactions proceed by the autocatalytic or acid-catalytic S_NAr mechanism.^{12,13,14}

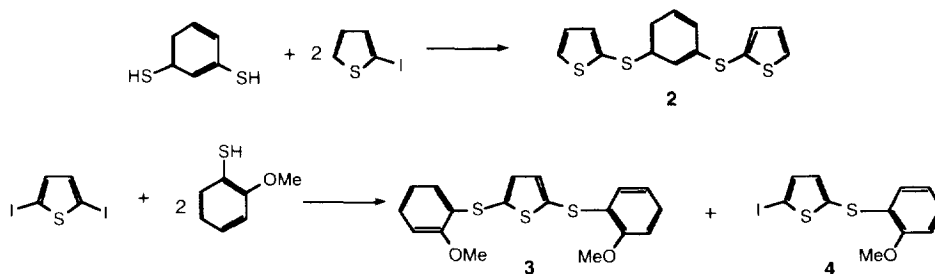
Table 1. Reactions between 2-Iodothiophene and Various Thiols^a



| Thiols ^b | Time (min) ^c | % Isolated yield ¹⁰ |
|-----------------------|-------------------------|--------------------------------|
| 2-thiophenethiol | 5 | 84 |
| 2-methoxybenzenethiol | 1 | 95 |
| thiophenol | 10 | 88 |
| 4-chlorobenzenethiol | 20 | 90 |
| 4-fluorobenzenethiol | 45 | 90 |
| <i>n</i> -butanethiol | 15 | 88 |

^a Reactions were performed by simply mixing two reactants at room temperature. ^b 1.2 Equivalents of thiols were used. ^c Reactions were monitored by ¹H NMR spectroscopy. Samples were taken every minute for the reactions done within 5 min and every 5 min for the reactions done in more than 5 min.

In order to extend the reactions in Table 1 to the synthesis of PTS and PATS, we tried two model reactions as shown in Scheme 1.¹⁵ 1,3-Benzenedithiol reacted smoothly with 2-iodothiophene at 35 °C for 15 min to give rise to **2** in 89% yield.¹⁰ However, treatment of 2,5-diiodothiophene with 2-methoxybenzenethiol at 100 °C for 40 min afforded **3** and **4** in an around 1:5 ratio. The former reaction is applicable to the synthesis of PTS and PATS.



Scheme 1

In conclusion, the reactions described in this paper offer a quick, convenient, mild, and inexpensive alternative to other methods⁴⁻⁸ for the synthesis of 2-(aryltio)thiophenes, 2-(alkyltio)thiophenes, and 2-(thiophenyltio)thiophenes. Extension of the reactions with 2-iodothiophene to those with 2-iodoselenophene will be reported in due course and application of this work to the efficient synthesis of PTS and PATS is currently underway in our laboratory.

Experimental

Synthesis of 2,2'-dithienyl sulfide: A mixture of 2-iodothiophene (0.50 g, 2.40 mmol) and 2-thiophenethiol (0.33 g, 2.88 mmol) was stirred at room temperature for 5 min. The resulting mixture was dissolved in 100 mL of ether and washed three times with 5% aqueous Na₂S₂O₃ solution. The organic extract was diluted with 25 mL of methanol and treated with NaBH₄ (1.8 g, 47.6 mmol). After stirring for 10 min, the mixture was washed three times with 0.1 N NaOH solution and twice with water. The organic layer was dried (MgSO₄) and concentrated at reduced pressure to give 2,2'-dithienyl sulfide as a pale yellow oil (0.4 g, 84% yield).

Note: In the case of large scale reaction, more than one equivalent of 2-iodothiophene is recommended. NaBH₄ reduction used for removing small amount of the disulfide formed during the reaction in the previous case may not be required. Residual 2-iodothiophene can be removed by vacuum distillation.

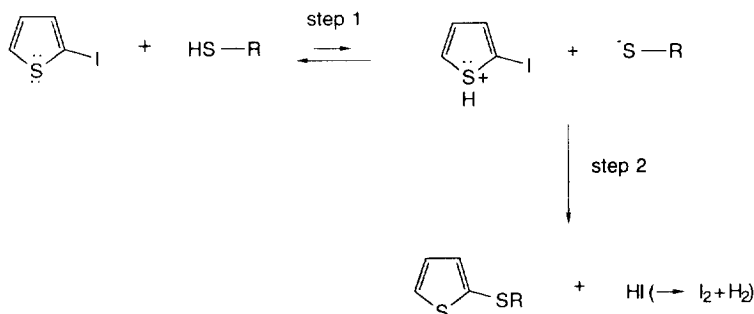
Acknowledgements: This work was supported by the Basic Science Research Institute Program (1994), R.O.K. Ministry of Education and the Organic Chemistry Research Center (KOSEF).

REFERENCES AND NOTES

- (a) Wang, Z. Y.; Hay, A. S. *Macromolecules*, **1991**, *24*, 333. (b) Yamamoto, K.; Shouji, E.; Nishide, H.; Tsuchida, E. *J. Am. Chem. Soc.* **1993**, *115*, 5819. (c) Yamamoto, K.; Shouji, E.; Suzuki, F.; Kobayashi, S.; Tsuchida, E. *J. Org. Chem.* **1995**, *60*, 452.
- (a) General review for thiophene chemistry; Meth-Cohn, O. In *Comprehensive Organic Chemistry*, 1st ed.; Pergamon Press Ltd.: Oxford, 1979; Vol. 5, pp 789 - 838. (b) Jen, K.-Y.; Benfaremo, N.; Cava, M. P.; Huang, W.-S.; MacDiarmid, A. G. *J. Chem. Soc., Chem. Commun.* **1983**, 633. (c) Jones, E.; Moodie, I. M. *J. Polym. Sci., Polym. Symp.* **1967**, 2881. (d) Voronkov, M. G.; Khalivllin, A. K.; Annenkova, V. Z.; Antonik, L. M.; Kamkina, L. M.; Deryagina, E. N.; Vakul'skaya, T. I. *Dokl. Akad. Nauk SSSR*. **1976**, *228*, 1341. (e) Ford, W. T.; Gutierrez, M.; Pohl, H. A. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1983**, *24*(2), 332.
- Giuffre, L.; Tempesti, E.; Montoneri, E.; Bonfanti, C.; Modica, G. *Int. J. Hydrogen Energy*, **1984**, *9*(11), 907.
- (a) Jones, E.; Moodie, I. M. *Org. Synth., Coll. Vol. 6*, **1988**, 558. (b) Jones, E.; Moodie, I. M. *Tetrahedron*, **1965**, *21*, 2413.
- (a) Challenger, F.; Harrison, J. B. *J. Inst. Pet.* **1935**, *21*, 135. (b) Koft, E. *U.S. Pat.* **1951**, *2*, 571, 370.
- Rajsner, M.; Metysova, J.; Protiva, M. *Coll. Czech. Chem. Comm.* **1970**, *35*, 378.
- Novi, M.; Garbarino, G.; Petrillo, G.; Dell'Erba, C. *J. Org. Chem.* **1987**, *52*, 5382.
- Adams, R.; Ferretti, A. *J. Am. Chem. Soc.* **1959**, *81*, 4927.

9. Treatment of 2-iodothiophene with 2-methoxybenzenethiol and potassium carbonate in DMF at 50°C for 2 days gave 2-(2'-methoxyphenylthio)thiophene in 30% yield.
10. Spectral data: 2,2'-Dithienyl sulfide: $^1\text{H NMR}$ (CDCl_3 , 80 MHz) δ 6.90 (t, $J = 4.4$ Hz, 2 H), 7.09 (d, $J = 3.6$ Hz, 2 H), 7.16 (d, $J = 4.8$ Hz, 2 H); MS (EI) m/z 198 (M^+). 2-(2'-Methoxyphenylthio)thiophene: $^1\text{H NMR}$ (CDCl_3 , 80 MHz) δ 3.84 (s, 3 H), 6.73 ~ 7.58 (m, 7 H); MS (EI) m/z 222 (M^+). 2-(Phenylthio)thiophene: $^1\text{H NMR}$ (CDCl_3 , 80 MHz) δ 6.95 ~ 7.50 (br. m, 8 H); MS (EI) m/z 192 (M^+). 2-(4'-Chlorophenylthio)thiophene: $^1\text{H NMR}$ (CDCl_3 , 80 MHz) δ 7.17 ~ 7.44 (br. m, 7 H); MS (EI) m/z (rel int) 226 (M^+ , 3), 228 (M^+ , 1). 2-(4'-Fluorophenylthio)thiophene: $^1\text{H NMR}$ (CDCl_3 , 80 MHz) δ 6.81 ~ 7.48 (br. m, 7 H); MS (EI) m/z 210 (M^+). 2-(*n*-Butylthio)thiophene: $^1\text{H NMR}$ (CDCl_3 , 80 MHz) δ 0.91 (t, $J = 6.4$ Hz, 3 H), 1.30 ~ 1.65 (m, 4 H), 2.87 (t, $J = 6.8$ Hz, 2 H), 6.86 (t, $J = 4.4$ Hz, 1 H), 7.03 (d, $J = 4.4$ Hz, 1 H), 7.14 (d, $J = 4.4$ Hz, 1 H); MS (EI) m/z 172 (M^+). 1,3-bis-(2'-thienylthio)benzene (**2**): $^1\text{H NMR}$ (CDCl_3 , 80 MHz) δ 6.77 ~ 7.62 (m, 10 H); MS (EI) m/z 306 (M^+).
11. 2-(2'-Methoxyphenylthio)thiophene was obtained in 88% yield from the reaction between 2-iodothiophene and 2-methoxybenzenethiol in acetic acid (5 M) at 50°C for 1.5 h.
12. Illuminati, G. *Advan. Heterocycl. Chem.* **1964**, 3, 285.
13. Similar autocatalytic phenomena were observed in the nucleophilic aromatic substitution of 4-chloroquinoline by piperidine.¹²

14.



Since the second, essentially irreversible, step provides the driving force for this reaction, the presence of a small equilibrium concentration of the conjugate acid of 2-iodothiophene presumably contributes to the rate acceleration of the substitution reaction. Since the acid-catalytic reaction in acetic acid appears to involve the attack of the free thiol on the conjugate acid of 2-iodothiophene, it is slower than the autocatalytic reaction in the absence of solvent and base.

15. We thank the referee for suggesting us to try the model reaction.

(Received in Japan 22 July 1995; revised 18 September 1995; accepted 22 September 1995)