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# A facile synthesis of thienylmethylphosphonates: direct conversion from thiophenes

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## Abstract

An efficient approach to thienylmethylphosphonates has been established through the combination of thienylcoppers with the commercially available diethyl iodomethylphosphonates in a one-pot process. © 2000 Elsevier Science Ltd. All rights reserved.

The growing interest in organic polymeric materials for electro-optic (E-O) device applications has led to the development of highly active π-conjugated chromophore molecules which have large molecular second-order nonlinearity ($\mu\beta$).[1–4] Structure–property relationships that have been established indicate that thiophenes could often be used as π-conjugated units to optimize the conjugation pathway.[5] Thiophene units are generally introduced into the molecular backbone by Horner–Emmons condensation of thienylmethylphosphonates with aldehyde precursors. A general approach to thienylmethylphosphonate compounds involves a number of steps as indicated in Scheme 1 (four steps were required, and the overall yield was less than 50%). Inevitably, multistep procedures lead to low to moderate overall yields and tedious separations.

We have here found it expedient to convert thiophenes directly to thienylmethylphosphonates by combining thienylcoppers with the commercially available diethyl iodomethylphosphonates in a general one-pot process (Scheme 2).

The effectiveness of the reaction was tested in a model system using diethyl iodomethylphosphonate and 3,3′-dihexyl-2,2′-bithiophene (**1a**) under a variety of experimental conditions (Table 1). A higher yield of thienylmethylphosphonate was obtained with the molar ratio of halomethylphosphonate, *n*-butyllithium and cuprous iodide 1.0:1.0:1.0. The use of one equivalent of thiophenes and one equivalent of *n*-butyllithium minimizes bis-metallation of bifunctional thiophenes and warrants an optimal exploitation of starting materials. As shown in Table 1, the amount of CuI significantly affected the outcome of the reaction. If CuI was not employed, no appreciable phosphonate was detected; but an increase in the amount of CuI resulted in a lower yield. In addition, the substitution of *t*-butyllithium for

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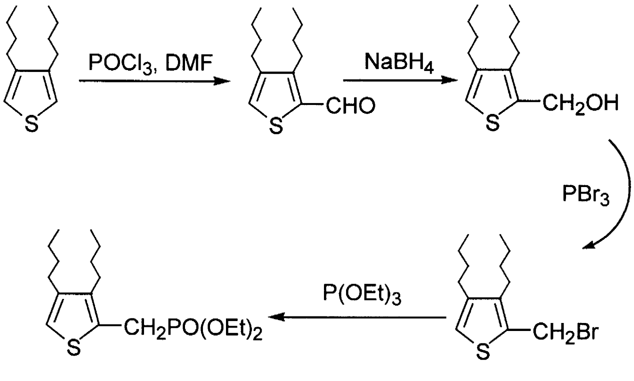
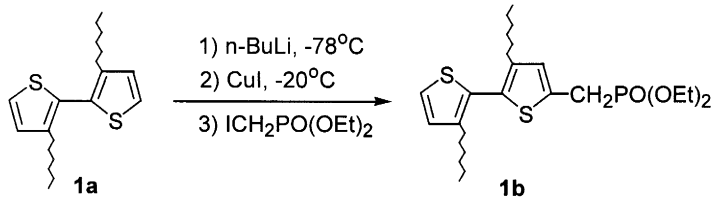


Scheme 1.



**1a** **1b**

Scheme 2.

*n*-butyllithium was found to lower the yield and iodomethylphosphonate proved to be more effective than chloromethylphosphonate.

Table 1
The optimization of reaction conditions in Scheme 2

| Halomethylphosphonate | Thiophene/*n*-BuLi/CuI | Yield / % (**1b**) |
|---|---|---|
| $ClCH_2PO(OEt)_2$ | 1.0:1.0:1.0 | 33 |
| | 1.0:1.0:0[a] | none |
| $ICH_2PO(OEt)_2$ | 1.0:1.0:1.0 | 62 |
| | 1.0:1.0:2.0 | 34 |
| | 1.0:1.0:0[a] | none |
| | 1.0:1.0:1.0[b] | 46 |

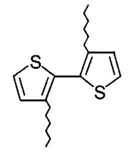
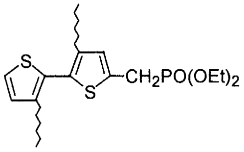
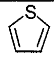
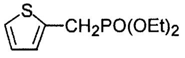
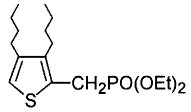
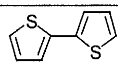
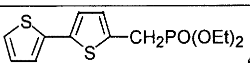
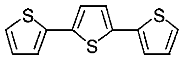
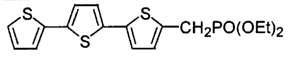
[a]CuI was not employed in this case. [b]*t*-BuLi in place of *n*-BuLi.

From a series of experiments, we also found that the temperature at which thienyllithium is transmetallated with CuI is critical for completion of the reaction. If the temperature is much lower than −20°C, large amounts of starting material is recovered, presumably because the conversion to thienylcopper is incomplete and iodomethylphosphonate protonates thienyllithium. The carbon–carbon coupling reaction takes place slowly at a much lower temperature, so higher termperature (such as room temperature) is necessary to attain desirable rate.

The novel approach has been extended to synthesize a variety of thienylmethylphosphonates in order to explore the nonlinear optical properties of variable length thiophene-containing chromophores, and the results are summarized in Table 2. As anticipated, in each case the target compound was obtained with a good yield.

In summary, presented here is an efficient approach to making thienylmethylphosphonates by combining thiophenes with *n*-butyllithium and then cuprous iodide and diethyl iodomethylphosphonate in

Table 2
A test of the effectiveness and the applicability of the approach

| Entry | Thiophenes | Phosphonates[6] | Yield / % |
|---|---|---|---|
| 1 |  **1a** |  **1b** | 62 |
| 2 |  **2a** |  **2b** | 77 |
| 3 |  **3a** |  **3b** | 60 |
| 4 |  **4a** |  **4b** | 67 |
| 5 |  **5a** |  **5b** | 63 |

[a]The starting materials **1a** and **3a** were synthesized by standard procedures.[7]

a one-pot process. This approach provides not only a new category for the expedient synthesis of phosphonates but also a practical solution to alkenes when phosphonates are condensed with carbonyl compounds.

General experimental procedure:

The synthesis of phosphonate (**1b**) is representative. A solution of 2.0g (6 mmol) 3,3′-dihexyl-2,2′-bithiophene (**1a**) in 20 ml of anhydrous THF was added over 15 min under argon at −78°C to a stirred solution of 6 mmol *n*-butyllithium (2.4 ml, 2.5 M, in hexanes) in 25 ml of THF. The solution was stirred for 45 min at −78°C, and then transferred, via cannula, into a flask cooled to −20°C in a dry ice/$CCl_4$ bath, containing 1.14 g CuI (6 mmol). After 2 h, 1.67 g diethyl iodomethylphosphonate (6 mmol) was added in one portion, and the solution was reacted at room temperature overnight. The dark reaction mixture was poured into 100 ml of ether and 100 ml of water, and the organic layer washed successively with 3×100 ml water, 1×100 ml 5% aqueous $NaHCO_3$, 2×100 ml water, and 2×100 ml saturated brine solution. The organic layer was dried ($MgSO_4$), and evaporated. The resulting residue was purified by column chromatography packed with silica gel (1:1 hexanes:ethyl acetate), affording **1b** as a clear yellow viscous oil (1.81 g, 62%).

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## References

1. Burland, D. M.; Miller, R. D.; Walsh, C. A. *Chem. Rev.* **1994**, *94*, 31–75 and references cited therein.
2. Bu, X. R.; Li, H.; Derveer, D. V.; Mintz, E. A. *Tetrahedron Lett.* **1996**, *37*, 7331–7334.
3. Marder, S. R.; Kippelen, B.; Jen, A. K.-Y.; Peyghambarian, N. *Nature* **1997**, *388*, 845–851.
4. Shu, Y.-C.; Gong, Z.-H.; Shu, C.-F; Breitung, E. M.; McMahon, R. J.; Lee, G.-H.; Jen, A. K.-Y. *Chem. Mater.* **1999**, *11*, 1628–1632.
5. (a) Pan, H.; Gao, X.; Zhang, Y.; Prasad, P. N.; Reinhardt, B. A.; Kannan, R. *Chem. Mater.* **1995**, *7*, 816–821. (b) Shu, C.-F.; Tsai, W.-J.; Jen, A. K.-Y. *Tetrahedron Lett.* **1996**, *37*, 7055–7058. (c) Groenendaal, L.; Bruining, M. J.; Hendrickx, E. H. J.; Persoons, A.; Vekemans, J. A. J. M.; Havinga, E. E.; Meijer, E. W. *Chem. Mater.* **1998**, *10*, 226–234. (d) Bosshard, C.; Sutter, K.; Pretre, P.; Hulliger, J.; Florsheimer, M.; Kaatz, P.; Gunter, P. *Organic Nonlinear Optical Materials*; Gordan & Breach: Amsterdam, 1995. (e)Wang, F. Ph.D. Thesis, University of Southern California, 1997.
6. All new compounds were obtained in an analytically pure form and characterized by spectroscopic techniques. Selected data: $^1$H NMR (250 MHz, $CDCl_3$): **1b**, $\delta$ 7.34 (s, 1H), 4.07 (m, 4H), 3.21 (d, $J$=20.5 Hz, 2H), 2.49 (m, 4H), 1.40 (m, 8H), 1.28 (t, 6H), 0.93 (t, 6H): **3b**, $\delta$ 7.26 (d, $J$=5 Hz, 1H), 6.96 (d, $J$=5 Hz, 1H), 6.88 (d, $J$=3.2 Hz, 1H), 4.12 (m, 4H), 3.34 (d, $J$=20.5 Hz, 2H), 2.47 (m, 4H), 1.52 (m, 4H), 1.31 (t, 6H), 1.24 (m, 12H), 0.86 (t, 6H).
7. (a) Gronowitz, S.; Raznikiewicz, T. In *Organic Synthesis*; Parham, W. E., Ed.; John Wiley and Sons: New York, 1964; Vol. 44, pp. 9–11. (b) Van Pham, C.; Mark Jr., H. B.; Zimmer, H. *Synth. Commun.* **1986**, *16*, 689–696.