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# Convenient Synthesis of 2,5-Disubstituted Thiophene from 1,6-Dioxo-2,4-Diene

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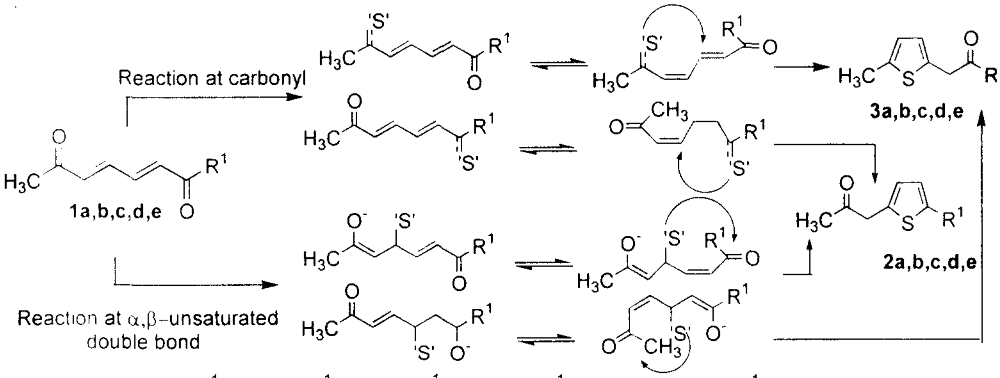
*Abstract:* Reaction of 1,6-dioxo-2,4-diene with $P_2S_5$ and Lawesson's reagent affords the 2,5-disubstituted thiophene. This reaction can take place regioselectively in the presence of $BF_3$-etherate catalysis, useful for the synthesis of arylthiophene. © 1998 Elsevier Science Ltd. All rights reserved.

Our previous studies have demonstrated the use of 1,6-dioxo-2,4-diene derivatives **1**, as versatile intermediates for the synthesis of cyclopentenone[1] and aryl-furan[2] derivatives through an intramolecular process. The important of 1,6-dioxo-2,4-diene moiety is its ability to serve as a four carbon unit which can undergo consecutive nucleophilic addition reaction. Herein, we report our investigation on the addition of sulfur to this four-carbon unit for the synthesis of 2,5-disubstituted thiophenes (Scheme 1).



a : $R^1$=-Me **b** : $R^1$=-Ph **c** : $R^1$=-OEt **d** : $R^1$=-4PhCOOMe **e** : $R^1$=-4PhOMe

The 1,6-dioxo-2,4-diene **1a**, **b**, **c**, **d**, **e** used were synthesized from methylfuran and an appropriate diazoketone according to the method of Wenkert[3]. Treatment of **1a**, **c**, **d**, **e** with $P_2S_5$ or Lawesson's reagent led to the corresponding 2,5-disubstituted thiophenes **2** and **3** in fair to high yield (Table 1). Identification of the structural isomers **2** and **3** were inferred from the IR absorption for unconjugated and conjugated ketone.

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Reaction of **1 c**, **d**, **e** (entries 3-5) with $P_2S_5$ in each case gave a single isomer **3 c**, **d**, **e** respectively, whereas **1b** gave two isomers **2b** and **3b** (entry 2). The reaction carried out with Lawesson's reagent (entries 6-9) gave similar results as for $P_2S_5$, except **1e** with an electron releasing group on benzene was found to give **2e** and **3e** (entry 10). In the case of **1b** with an ester group, the reaction was sluggish under all the reaction conditions.

It has been reported that reaction of compounds having two carbonyl groups can be regioselectively controlled by the use of Lewis acid catalyst.[4] The reaction of 1,6-dioxo-2,4-diene with Lawesson's reagent in the presence of $BF_3$-etherate catalysis in $CH_2Cl_2$ at –78°C to room temperature was thus studied (entries 11-15). Reaction of **1a** was found to give a better yield of **2a**. Reaction of **1b** under this new condition resulted in the regioselective formation of **2b** in near quantitative yield. Furthermore, **1d** having an electron withdrawing group gave **3d** (entry 14); and **1e** having an electron donating group gave **2e** (entry 15). The reaction under this condition was found to be highly regioselective.

| Entry | Compd | $P_2S_5$/EtOH<br>**2** : **3** (Yield %) | Entry | Lawesson's /EtOH<br>**2** : **3** (Yield %) | Entry | Lawesson's /$BF_3$/$CH_2Cl_2$<br>**2** : **3** (Yield %) |
|---|---|---|---|---|---|---|
| 1 | **1a** | Same compd (20) | 6 | Same compd (20) | 11 | Same compd (25) |
| 2 | **1b** | 1.0 : 1.1 (50) | 7 | 1.0 : 1.8 (50) | 12 | 1.0 : 0.0 (93) |
| 3 | **1c** | 0.0 : 1.0 (10) | 8 | - | 13 | 1.0 : 1.0 ( 2) |
| 4 | **1d** | 0.0 : 1.0 (20) | 9 | 0.0 : 1.0 (50) | 14 | 0.0 : 1.0 (30) |
| 5 | **1e** | 0.0 : 1.0 (20) | 10 | 1.0 : 2.0 (60) | 15 | 27.0 : 1.0 (45) |

*a*: Product **2a** is volatile and some might be loss during removal of solvent. *b*: $^1H$ NMR data for all compds. [9]

In summary, we have demonstrated a new methodology for the facile synthesis of arylthiophene.

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3. Wenkert, E.; Guo, M.; Pizzo, F.; Ramachandran, K. *Helv. Chim. Acta*, **1987**, *70*, 1429.
4. Dickinson, R. A.; Kubela, R.; MacAlpine G. A.; Stojanac, Z.; Valenta, Z. *Canad. J. Chem.*, **1972**, *50*, 2377.
5. **2a** : $\delta$ 2.19 (s, 3H), 2.44 (s, 3H), 3.80 (s, 2H), 6.62 (d, 1H), 6.66 (d, 1H). **2b** : $\delta$ 2.22 (s, 3H), 3.77 (s, 2H), 6.29 (d, 1H), 6.60 (d, 1H). 7.33 (m, 3H,) 7.63 (d, 2H). **2e** : $\delta$ 2.21 (s, 3H), 3.75 (s, 2H), 3.83 (s, 3H), 6.25 (d, 1H), 6.46 (d, 1H), 6.90(d, 2H), 7.56(d, 2H). **3b** : $\delta$ 2.43 (s, 3H), 4.39 (s, 2H), 6.60 (d, 1H), 6.69 (d, 1H), 7.50 (m, 3H,) , 8.01 (d, 2H). **3c** : $\delta$ 1.28 (t, 3H), 3.74 (s, 2H), 4.20 (q, 2H), 6.59 (d, 1H), 6.70 (d, 1H). **3d** : $\delta$ 2.44 (s, 3H), 3.05 (s, 3H), 4.42 (s, 2H), 6.60 (d, 1H), 6.70 (d, 1H), 8.11 (q, 4H). **3e** : $\delta$ 2.43 (s, 3H), 3.87 (s, 3H), 4.34 (s, 2H), 6.59 (d, 1H), 6.68 (d, 1H), 6.94 (d, 2H), 8.00 (d, 2H)