SYNTHESIS OF BENZO[2,1-b:3,4-b']DITHIOPHENE-4,5-DIONE DERIVATIVES

Kazuhiro Kobayashi,* Toshikazu Ogata, Daizo Nakamura, Osamu Morikawa, and Hisatoshi Konishi

Department of Materials Science, Faculty of Engineering, Tottori University, 4-101 Koyama-minami, Tottori 680-8552, Japan

Abstract- The 1-trimethylsilylimidazole-mediated thiophene ring formation from 6-acylbenzo[b]thiophene-4,5-diones (3), which were prepared utilizing photoacylation of benzo[b]thiophene-4,5-dione (1) with aliphatic aldehydes, and ethyl mercaptoacetate, followed by acid hydrolysis and oxidation with cerium(IV) ammonium nitrate (CAN), led to one-pot formation of the 3-substituted ethyl 4,5-dioxo-4,5-dihydrobenzo[2,1-b:3,4-b']dithiophene-2-carboxylates (4) in satisfactory yields.

Our recent success in the one-pot synthesis of thiophene-fused quinone derivatives from acylquinone derivatives and mercaptoacetates utilizing the 1-trimethylsilylimidazole-mediated thiophene ring formation reaction1 suggested that a similar strategy would then lead to the formation of benzo[2,1-b:3,4-b']dithiophene-4,5-dione derivatives from benzo[b]thiophene-4,5-dione. Herein, we wish to demonstrate the results of our investigation which offer a convenient method for the synthesis of benzo[2,1-b:3,4-b']dithiophene-4,5-dione derivatives (4). To the best of our knowledge, only the parent benzo[2,1-b:3,4-b']dithiophene-4,5-dione has been synthesized previously.2,3

Our process for the preparation of ethyl 4,5-dioxo-4,5-dihydrobezo[2,1-b:3,4-b']dithiophene-2-carboxylates (4) is outlined in the Scheme 1. Thus, irradiation of benzo[b]thiophene-4,5-dione (1) (prepared from the known 4,5-dimethoxybenzo[b]thiophene4 in two steps; see Experimental) and aliphatic aldehydes in benzene with Pyrex-filtered light then afforded 6-acyl-4,5-dihydrobenzo[b]-thiophenes (2). Although the yields of 2 were less than moderate,5 oxidation of them with Ag2O gave 6-acylbenzo[b]thiophene-4,5-diones (3) almost quantitatively, as shown in the Table 1. It should be noted that the photoacylation with an aromatic aldehyde, such as benzaldehyde, resulted in the formation of an intractable mixture of products containing a very small quantity of the corresponding desired product.5 These acylquinones (3) were then transformed into the corresponding benzo[2,1-b:3,4-b']-dithiophene-4,5-dione derivatives (4) in good yields in one-pot by addition of ethyl mercaptoacetate
Table 1: Preparation of 4,5-dioxo-4,5-dihydrobenzo[2,1-b:3,4-b]dithiophene-2-carboxylates (4)

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</table>

aIsolated yields by column chromatography on silica gel. bIsolated yields by recrystallization.

and subsequent treatment with 1-trimethylsilylimidazole, followed by acid hydrolysis and oxidation with CAN. These results are also summarized in the Table 1.

In conclusion, by the use of the thiophenequinone synthesis utilizing trimethylsilylimidazole-mediated thiophene ring formation, the previously unknown substituted benzo[2,1-b:3,4-b']dithiophene-4,5-dione derivatives can, thus, be synthesized in one-pot from benzo[b]thiophene-4,5-dione. This procedure may find some value in heterocycle-fused quinone synthesis.

**EXPERIMENTAL**

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were determined with a Shimadzu FTIR-8300 spectrophotometer as KBr disks. The ^1^H NMR spectra were determined in CDCl$_3$ using TMS as an internal reference with a JEOL JNM-GX270 FT NMR spectrometer operating at 270 MHz. J values are given in Hz. Low-resolution MS spectra were measured by a JEOL AUTOMASS 20 spectrometer (Center for Joint Research and Development, this University). TLC was carried out on a Merck Kieselgel 60 PF$_{254}$. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

**Starting Materials.** Benzo[b]thiophene-4,5-dione (1) was prepared from 4,5-dimethoxybenzo[b]-
thiophene as follows. Thus, 4,5-dimethoxybenzo[b]thiophene was treated with BBr$_3$ in CH$_2$Cl$_2$ at 0 °C to give benzo[b]thiophene-4,5-diol (98%): a white solid; mp 127–128 °C (hexane–Et$_2$O); $\nu_{\text{max}}$/cm$^{-1}$ 3425, 1626; $\delta_\text{H}$ 4.88 (1H, s), 5.49 (1H, s), 6.96 (1H, d, J 8.6), 7.30 (1H, d, J 8.6), 7.37 (1H, d, J 5.6), 7.39 (1H, d, J 5.6). Anal. Calcd for C$_8$H$_6$O$_2$S: C, 57.81; H, 3.64; S, 19.29. Found: C, 57.80; H, 3.62; S, 19.30. This diol was oxidized with Ag$_2$O$_6$ in Et$_2$O to give 1 (98%): a dark red solid; mp 115–116 °C (hexane–CH$_2$Cl$_2$); $\nu_{\text{max}}$/cm$^{-1}$ 1684, 1657; $\delta_\text{H}$ 6.28 (1H, d, J 9.9), 7.40 (1H, d, J 9.9), 7.41 (1H, J 5.3), 7.57 (1H, d, J = 5.3). Anal. Calcd for C$_8$H$_4$O$_2$S: C, 58.52; H, 2.46; S, 19.53. Found: C, 58.16; H, 2.50; S, 19.39.

6-Acetylbenzo[b]thiophene-4,5-diol (2a). Typical Procedure for the Photoacylation of Benzo[b]thiophene-4,5-dione (1). A solution of 1 (0.40 g, 2.4 mmol) and acetaldehyde (1.1 g, 24 mmol) in benzene (120 mL) was irradiated at room temperature under argon with a 500W mercury arc through a Pyrex filter for 10 h. The precipitate was filtered off and the filtrate was evaporated. The residue was purified by column chromatography on silica gel (benzene) to give 2a (0.18 g, 35%) as a yellow solid; mp 159–160 °C (hexane–Et$_2$O); $\nu_{\text{max}}$/cm$^{-1}$ 3487, 1639; $\delta_\text{H}$ 2.72 (3H, s), 6.00 (1H, s), 7.45 (1H, dd, J 5.3, 0.6 Hz), 7.57 (1H, d, J 5.3 Hz), 7.86 (1H, d, J 0.6 Hz), 12.01 (1H, s). Anal. Calcd for C$_{10}$H$_8$O$_3$S: C, 57.68; H, 3.87; S, 15.40. Found: C, 57.42; H, 4.02; S, 15.27.

6-Propanoylbenzo[b]thiophene-4,5-diol (2b): a pale-brown solid; mp 138–140 °C (hexane–Et$_2$O); $\nu_{\text{max}}$/cm$^{-1}$ 3397, 1636; $\delta_\text{H}$ 1.28 (3H, t, J 7.3), 3.13 (2H, q, J 7.3), 6.02 (1H, s), 7.45 (1H, dd, J 5.6, 1.0), 7.56 (1H, d, J 5.6), 7.88 (1H, d, J 1.0), 12.12 (1H, s). Anal. Calcd for C$_{11}$H$_{10}$O$_3$S: C, 59.44; H, 4.53; S, 14.43. Found: C, 59.47; H, 4.67; S, 14.19.

6-Butanoylbenzo[b]thiophene-4,5-diol (2c): a yellow solid; mp 132–134 °C (hexane–Et$_2$O); $\nu_{\text{max}}$/cm$^{-1}$ 3441, 1640; $\delta_\text{H}$ 1.05 (3H, t, J 7.3), 1.82 (2H, sextet, J 7.3), 3.06 (2H, t, J 7.3), 6.00 (1H, s), 7.45 (1H, dd, J 5.6, 1.0), 7.56 (1H, d, J 5.6), 7.89 (1H, d, J 1.0), 12.17 (1H, s). Anal. Calcd for C$_{12}$H$_{12}$O$_3$S: C, 61.00; H, 5.12; S, 13.57. Found: C, 61.14; H, 5.33; S, 13.55.

6-(2-Methylpropanoyl)benzo[b]thiophene-4,5-diol (2d): a yellow solid; mp 117–120 °C (hexane–Et$_2$O); $\nu_{\text{max}}$/cm$^{-1}$ 3393, 1636; $\delta_\text{H}$ 1.30 (6H, d, J 6.6 Hz), 3.71 (1H, septet, J 6.6), 6.02 (1H, s), 7.46 (1H, dd, J 5.6, 1.0), 7.57 (1H, d, J 5.6), 7.92 (1H, d, J = 1.0), 12.17 (1H, s). Anal. Calcd for C$_{12}$H$_{12}$O$_3$S: C, 61.00; H, 5.12; S, 13.57. Found: C, 60.98; H, 5.06; S, 13.66.

6-Pentanoylbenzo[b]thiophene-4,5-diol (2e): a yellow solid; mp 128–130 °C (hexane–Et$_2$O); $\nu_{\text{max}}$/cm$^{-1}$ 3450, 1639; $\delta_\text{H}$ 0.98 (3H, t, J 7.3), 1.45 (2H, sextet, J 7.3), 1.77 (2H, quint, J 7.3), 3.08 (2H, t, J 7.3), 6.00 (1H, s), 7.48 (1H, dd, J 5.6, 0.7), 7.56 (1H, d, J 5.6), 7.89 (1H, s), 12.17 (1H, s). Anal. Calcd for C$_{13}$H$_{14}$O$_3$S: C, 62.38; H, 5.64; S, 12.81. Found: C, 62.24; H, 5.71; S, 12.54.

6-(3-Methylbutanoyl)benzo[b]thiophene-4,5-diol (2f): a yellow solid; mp 103–105 °C (hexane–Et$_2$O); $\nu_{\text{max}}$/cm$^{-1}$ 3450, 1639; $\delta_\text{H}$ 1.04 (6H, d, J 6.8), 2.25–2.45 (1H, m), 2.93 (2H, d, J 6.9), 6.11 (1H, s), 7.45 (1H, dd, J 5.6, 0.8), 7.56 (1H, d, J 5.6), 7.87 (1H, s), 12.24 (1H, s). Anal. Calcd for C$_{13}$H$_{14}$O$_3$S: C, 62.38;
6-Acetylbenzo[b]thiophene-4,5-dione (3a). Typical Procedure for the Ag₂O Oxidation of 6-Acylbenzo[b]thiophene-4,5-diols 2. A solution of 2a (0.14 g, 0.68 mmol) in Et₂O (10 mL) was added to a stirred suspension of Ag₂O [prepared from 0.57 g (3.3 mmol) of silver nitrate by the literature method⁶] in Et₂O (10 mL) in the presence of anhydrous sodium sulfate (3.5 g). After stirring for 15 min, the solid was filtered off and the filtrate was concentrated. The residual solid was recrystallized from Et₂O–hexane to give pure 3a (0.13 g, 96%) as a red solid; mp 125–127 °C (decomp) (hexane–CH₂Cl₂); ν max/cm⁻¹ 1691, 1672, 1645; δ H 2.62 (3H, s), 7.63 (1H, d, J 5.3), 7.66 (1H, dd, J 5.3, 0.7), 8.22 (1H, s). Anal. Calcd for C₁₀H₆O₃S: C, 58.24; H, 2.93; S, 15.55. Found: C, 58.28; H, 2.98; S, 15.50.

6-Propanoylbenzo[b]thiophene-4,5-dione (3b): a red solid; mp 118–120 °C (decomp) (hexane–CH₂Cl₂); ν max/cm⁻¹ 1693, 1674, 1653; δ H 1.15 (3H, t, J 7.3), 3.02 (2H, q, J 7.3), 7.61 (1H, d, J 5.2), 7.65 (1H, dd, J 5.2), 8.20 (1H, s). Anal. Calcd for C₁₁H₈O₃S: C, 59.99; H, 3.66; S, 14.56. Found: C, 59.65; H, 3.72; S, 14.55.

6-Butanoylbenzo[b]thiophene-4,5-dione (3c): a red solid; mp 110–112 °C (decomp) (hexane–CH₂Cl₂); ν max/cm⁻¹ 1695, 1676, 1665, 1647; δ H 0.97 (3H, t, J 7.3), 1.68 (2H, sextet, J 7.3), 2.97 (2H, t, J 7.3), 7.63 (1H, d, J 5.1), 7.64 (1H, dd, J 5.1, 0.7), 8.17 (1H, d, J 0.7). Anal. Calcd for C₁₂H₁₀O₃S: C, 61.52; H, 4.30; S, 13.69. Found: C, 61.47; H, 4.31; S, 13.68.

6-(2-Methylpropanoyl)benzo[b]thiophene-4,5-dione (3d): a red solid; mp 109–111 °C (decomp) (hexane–CH₂Cl₂); ν max/cm⁻¹ 1690, 1668, 1655; δ H 1.14 (6H, d, J 6.9), 3.59 (1H, septet, J 6.9), 7.61 (1H, d, J 5.4), 7.65 (1H, dd, J 5.4, 0.7), 8.23 (1H, d, J 0.7). Anal. Calcd for C₁₂H₁₀O₃S: C, 61.52; H, 4.30; S, 13.69. Found: C, 61.19; H, 4.39; S, 13.47.

6-Pentanoylbenzo[b]thiophene-4,5-dione (3e): a red solid; mp 121–124 °C (decomp) (hexane–CH₂Cl₂); ν max/cm⁻¹ 1688, 1668, 1657; δ H 0.93 (3H, t, J 7.3), 1.38 (2H, sextet, J 7.3), 1.63 (2H, quint, J 7.3), 2.99 (2H, t, J 7.3), 7.62 (1H, d, J 5.1), 7.64 (1H, dd, J 5.1, 0.7), 8.17 (1H, d, J 0.7). Anal. Calcd for C₁₃H₁₂O₃S: C, 62.88; H, 4.87; S, 12.91. Found: C, 62.65; H, 5.04; S, 12.77.

6-(3-Methylbutanoyl)benzo[b]thiophene-4,5-dione (3f): a red solid; mp 100–103 °C (decomp) (hexane–CH₂Cl₂); ν max/cm⁻¹ 1693, 1665, 1643; δ H 0.96 (6H, d, J 6.8), 2.16 (1H, nonet, J 6.8), 2.87 (2H, d, J 6.8), 7.61 (1H, d, J 5.1), 7.64 (1H, dd, J 5.1, 0.7), 8.17 (1H, d, J 0.7). Anal. Calcd for C₁₃H₁₂O₃S: C, 62.88; H, 4.87; S, 12.91. Found: C, 62.85; H, 5.01; S, 12.75.

Ethyl 3-Methyl-4,5-dioxo-4,5-dihydrobenzo[2,1-b:3,4-b’]dithiophene-2-carboxylate (4a). A Typical Procedure for the Preparation of Benzodithiophenequinone Derivatives 4. To a stirred solution of 3a (90 mg, 0.44 mmol) in THF (0.8 mL) was added ethyl mercaptoacetate (53 mg, 0.44 mmol). After confirmation of the absence of the starting material using a TLC analysis (1:3 EtOAc-hexane) (ca. 5 min). THF was removed under reduced pressure. To the residue was added 1-trimethylsilylimidazole (0.31 g, 2.2 mmol) and the mixture was heated at 80 °C for 2 h. After cooling to 0 °C, acetonitrile (1.8
and 10% hydrochloric acid (0.9 mL) were added. The mixture was stirred at the same temperature for 40 min and then treated with CAN (0.48 g, 0.88 mmol) in water (2.6 mL) for 10 min. The precipitate was collected and recrystallized from hexane–CH₂Cl₂ to give pure 4a (0.11 g, 80%) as a dark-red solid; mp 217–220 °C; ν_max/cm⁻¹ 1720, 1666, 1643; δ_H 1.41 (3H, t, J 7.3), 2.86 (3H, s), 4.38 (2H, q, J 7.3), 7.31 (1H, d, J 5.3), 7.53 (1H, d, J 5.3); MS m/z 306 (M⁺, 100). Anal. Calcd for C₁₄H₁₀O₄S₂: C, 54.89; H, 3.29; S, 20.93. Found: C, 54.75; H, 3.33; S, 20.78.

Ethyl 3-Ethyl-4,5-dioxo-4,5-dihydrobenzo[2,1-b:3,4-b’]dithiophene-2-carboxylate (4b): a red solid; mp 188–189 °C (hexane–CH₂Cl₂); ν_max/cm⁻¹ 1712, 1668, 1643; δ_H 1.21 (3H, t, J = 7.3 Hz), 1.41 (3H, t, J 7.3), 3.40 (2H, q, J 7.3), 4.38 (2H, q, J 7.3), 7.31 (1H, d, J 5.1), 7.53 (1H, d, J 5.1); MS m/z 320 (M⁺, 100). Anal. Calcd for C₁₅H₁₂O₄S₂: C, 56.23; H, 3.78; S, 20.20. Found: C, 56.17; H, 3.71; S, 20.21.

Ethyl 3-Butyl-4,5-dioxo-4,5-dihydrobenzo[2,1-b:3,4-b’]dithiophene-2-carboxylate (4e): a red solid; mp 185–186 °C (hexane–CH₂Cl₂); ν_max/cm⁻¹ 1705, 1674, 1651; δ_H 0.96 (6H, d, J 6.9), 1.41 (3H, t, J 7.3), 4.38 (2H, q, J 7.3), 4.51 (1H, septet, J 6.9), 7.30 (1H, d, J 5.3), 7.52 (1H, d, J 5.3); MS m/z 348 (M⁺, 100). Anal. Calcd for C₁₇H₁₆O₄S₂: C, 58.60; H, 4.63; S, 18.49. Found: C, 58.49; H, 4.78; S, 18.69.

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REFERENCES AND NOTES


5. The preparation of 3-acyl-1,2-naphthalenediols by photoacylation of 1,2-naphthoquinone with aliphatic aldehydes up to 24% yield has been reported by Takuwa, who did not give any statements about the reaction with aromatic aldehydes. Takuwa, Bull. Chem. Soc. Jpn., 1976, 49, 2790.