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

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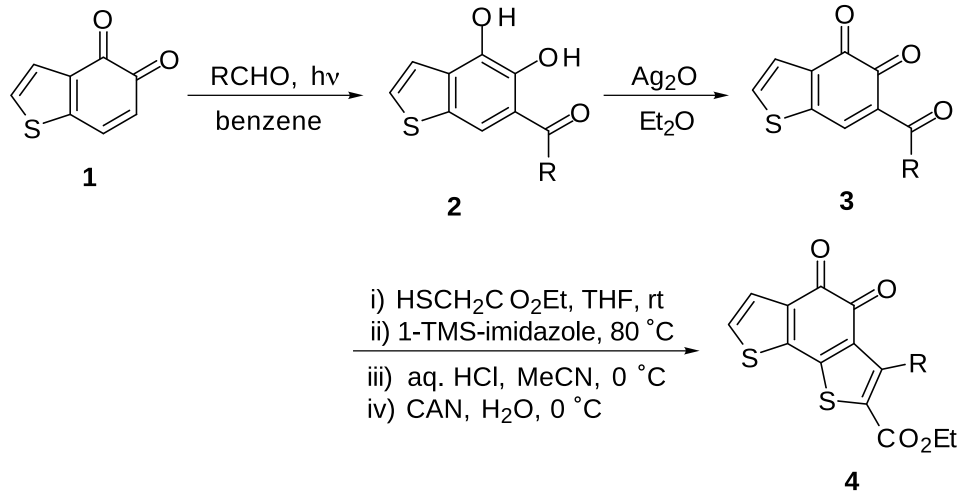
Abstract- The 1-trimethylsilylimidazole-mediated thiophene ring formation from 6-acylbenzo[*b*]thiophene-4,5-diones (**3**), which were prepared utilizing photoacylation of benzo[*b*]thiophene-4,5-dione (**1**) with aliphatic aldehydes, and ethyl mercaptoacetate, followed by acid hydrolysis and oxidation 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 reaction[1] 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*]thiophene[4] in two steps; see Experimental) and aliphatic aldehydes in benzene with Pyrex-filtered light then afforded 6-acyl-4,5-dihydroxybenzo[*b*]-thiophenes (**2**). Although the yields of **2** were less than moderate,[5] oxidation of them with Ag_2O 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



Scheme 1

Table 1: Preparation of 4,5-dioxo-4,5-dihydrobenzo[2,1-*b*:3,4-*b*]dithiophene-2-carboxylates (**4**)

Entry	R	**2** (Yield/%)[a]	**3** (Yield/%)[b]	**4** (Yield/%)[b]
1	Me	**2a** (35)	**3a** (96)	**4a** (80)
2	Et	**2b** (31)	**3b** (99)	**4b** (75)
3	*n*-Pr	**2c** (33)	**3c** (95)	**4c** (81)
4	*i*-Pr	**2d** (33)	**3d** (95)	**4d** (78)
5	*n*-Bu	**2e** (30)	**3e** (99)	**4e** (80)
6	*i*-Bu	**2f** (37)	**3f** (99)	**4f** (72)

[a] Isolated yields by column chromatography on silica gel. [b] Isolated 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 ^1H 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[4] as follows. Thus, 4,5-dimethoxybenzo[*b*]thiophene was treated with BBr_3 in CH_2Cl_2 at 0 ˚C to give benzo[*b*]thiophene-4,5-diol (98%): a white solid; mp 127–128 ˚C (hexane–Et_2O); ν_{max}/cm^{-1} 3425, 1626; δ_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 $C_8H_6O_2S$: 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_2O[6] in Et_2O to give **1** (98%): a dark red solid; mp 115–116 ˚C (hexane–CH_2Cl_2); ν_{max}/cm^{-1} 1684, 1657; δ_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 $C_8H_4O_2S$: 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_2O); ν_{max}/cm^{-1} 3487, 1639; δ_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 $C_{10}H_8O_3S$: 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_2O); ν_{max}/cm^{-1} 3397, 1636; δ_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 $C_{11}H_{10}O_3S$: 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_2O); ν_{max}/cm^{-1} 3441, 1640; δ_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 $C_{12}H_{12}O_3S$: C, 61.00; H, 5.12; S, 13.57. Found: C, 60.98; H, 5.06; S, 13.66.

6-(2-Methylpropanoyl)benzo[*b*]thiophene-4,5-diol (2d): a yellow solid; mp 117–120 ˚C (hexane–Et_2O); ν_{max}/cm^{-1} 3393, 1632; δ_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 $C_{12}H_{12}O_3S$: C, 61.00; H, 5.12; S, 13.57. Found: C, 61.14; H, 5.33; S, 13.55.

6-Pentanoylbenzo[*b*]thiophene-4,5-diol (2e): a yellow solid; mp 128–130 ˚C (hexane–Et_2O); ν_{max}/cm^{-1} 3450, 1639 ; δ_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 $C_{13}H_{14}O_3S$: 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_2O); ν_{max}/cm^{-1} 3450, 1639; δ_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 $C_{13}H_{14}O_3S$: C, 62.38;

H, 5.64; S, 12.81. Found: C, 62.24; H, 5.68; S, 12.82.

6-Acetylbenzo[*b*]thiophene-4,5-dione (3a). Typical Procedure for the Ag_2O Oxidation of 6-Acylbenzo[*b*]thiophene-4,5-diols 2. A solution of **2a** (0.14 g, 0.68 mmol) in Et_2O (10 mL) was added to a stirred suspension of Ag_2O [prepared from 0.57 g (3.3 mmol) of silver nitrate by the literature method[6]] in Et_2O (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 Et_2O–hexane to give pure **3a** (0.13 g, 96%) as a red solid; mp 125–127 ˚C (decomp) (hexane–CH_2Cl_2); 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 $C_{10}H_6O_3S$: 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–CH_2Cl_2); 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, d, *J* 5.2), 8.20 (1H, s). Anal. Calcd for $C_{11}H_8O_3S$: 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–CH_2Cl_2); 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 $C_{12}H_{10}O_3S$: 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–CH_2Cl_2); 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 $C_{12}H_{10}O_3S$: 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–CH_2Cl_2); 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 $C_{13}H_{12}O_3S$: 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–CH_2Cl_2); 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 $C_{13}H_{12}O_3S$: 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

mL) 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–CH_2Cl_2 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 $C_{14}H_{10}O_4S_2$: 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–CH_2Cl_2); 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 $C_{15}H_{12}O_4S_2$: C, 56.23; H, 3.78; S, 20.20. Found: C, 56.17; H, 3.71; S, 20.21.

Ethyl 4,5-Dioxo-3-propyl-4,5-dihydrobenzo[2,1-*b*:3,4-*b'*]dithiophene-2-carboxylate (4c): a red solid; mp 133–134 ˚C (hexane–CH_2Cl_2); ν_{max}/cm^{-1} 1712, 1695, 1666; δ_H 1.03 (3H, t, *J* 7.3), 1.41 (3H, t, *J* 7.3), 1.59 (2H, sextet, *J* 7.3), 3.37 (2H, t, *J* 7.3), 4.38 (2H, q, *J* 7.3), 7.31 (1H, d, *J* 5.3), 7.53 (1H, d, *J* 5.3); MS *m/z* 334 (M^+, 100). Anal. Calcd for $C_{16}H_{14}O_4S_2$: C, 57.47; H, 4.22; S, 19.18. Found: C, 57.57; H, 4.45; S, 19.09.

Ethyl 3-(1-Methylethyl)-4,5-dioxo-4,5-dihydrobenzo[2,1-*b*:3,4-*b'*]dithiophene-2-carboxylate (4d): a red solid; mp 196–198 ˚C (hexane–CH_2Cl_2); ν_{max}/cm^{-1} 1715, 1672, 1645; δ_H 1.37 (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* 334 (M^+, 50), 288 (100). Anal. Calcd for $C_{16}H_{14}O_4S_2$: C, 57.47; H, 4.22; S, 19.18. Found: C, 57.68; H, 4.48; S, 18.99.

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–CH_2Cl_2); ν_{max}/cm^{-1} 1705, 1674, 1651; δ_H 0.96 (3H, t, *J* 7.0), 1.41 (3H, t, *J* 7.3), 1.45–1.6 (4H, m), 3.37 (2H, t, *J* 7.3), 4.40 (2H, q, *J* 7.3), 7.31 (1H, d, *J* 5.5), 7.53 (1H, d, *J* 5.5); MS *m/z* 348 (M^+, 100). Anal. Calcd for $C_{17}H_{16}O_4S_2$: C, 58.60; H, 4.63; S, 18.41. Found: C, 58.49; H, 4.78; S, 18.69.

Ethyl 3-(2-Methylpropyl)-4,5-dioxo-4,5-dihydrobenzo[2,1-*b*:3,4-*b'*]dithiophene-2-carboxylate (4f): a red solid; mp 122–123 ˚C (hexane–CH_2Cl_2); ν_{max}/cm^{-1} 1714, 1666, 1650; δ_H 0.96 (6H, d, *J* 6.6), 1.41 (3H, t, *J* 7.3), 1.8–2.0 (1H, m), 3.31 (2H, d, *J* 7.3), 4.37 (2H, q, *J* 7.3), 7.31 (1H, d, *J* 5.3), 7.53 (1H, d, *J* 5.3); MS *m/z* 348 (M^+, 81), 302 (100). Anal. Calcd for $C_{17}H_{16}O_4S_2$: C, 58.60; H, 4.63; S, 18.41. Found: C, 58.58; H, 4.77; S, 18.29.

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