Facile Synthesis of Thiophene Derivatives Using a Cyclopropenyl Cation

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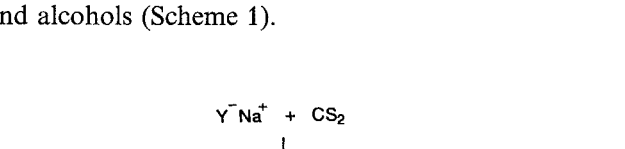
A novel convenient method for the synthesis of thiophene derivatives was developed using a tris(isopropylthio)cyclopropenyl cation, carbon disulfide, and the anions of secondary amines, 2-propanethiol, and ethanol.

The cyclopropenyl cations are attractive as a three-carbon building block in organic synthesis and have been reported to be useful for the synthesis of nitrogen-containing heterocycles[1] such as 1,2-dihydropyridines, pyrrolizines, indolizines, pyrrolo[2,1-*b*]azoles, and pyridines. However, there are few examples of the synthesis of sulfur-containing heterocycles using the cyclopropenyl cations.[1] We now report a novel convenient method for the preparation of thiophene derivatives from tris(isopropylthio)cyclopropenylium perchlorate (**1**) and the compounds **2a–d** with the $-CS-S^-$ moiety, derived easily from carbon disulfide and the anions of amines, thiols, and alcohols (Scheme 1).



Scheme 1

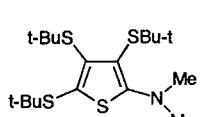
Dithiocarbamates **2a, b** and thiocarbonate **2c** were prepared from carbon disulfide and *N,N*-dimethylamine, *N*-methylaniline, and 2-propanethiol, respectively, in the presence of sodium hydride or sodium hydroxide, and xanthate **2d** from carbon disulfide and sodium ethoxide. The reaction of **1** with **2a–d** was carried out under nitrogen in anhydrous acetonitrile, dichloromethane or benzene at room temperature for 1 hour. The results are summarized in the Table. The homogeneous reaction of **1** with **2a** in acetonitrile gave **3a** in a quantitative yield. The reaction system using dichloromethane and benzene instead of acetonitrile was heterogeneous, since **2a** was insoluble in both solvents and **1** insoluble in benzene. The solution became homogeneous with the passage of time and **3a** was obtained in a high yield. In the reaction with **2b–d**, being insoluble in acetonitrile, **3b, c** were obtained in high yields, but the yield of **3d** became lower because of the formation of unidentified byproducts. In all cases, the structures of **3a–d** were determined by their IR, ^{1}H NMR, ^{13}C NMR, mass spectra and elemental analyses. The ^{13}C NMR spectra showed four signals due to the thiophene ring carbons in the region of δ = 114.2–165.9.

Table. Reactions of **1** with **2a–d**

Y–CS_2^-	Solvent	Yield of **3** (%)[a]
2a	MeCN	99
2a	CH_2Cl_2	93
2a	C_6H_6	97
2b	MeCN	95
2c	MeCN	89
2d	MeCN	54

[a] Isolated yield based on **1**.

Furthermore, the construction of the thiophene framework was established by the X-ray analysis of crystalline thiophene **4** which was synthesized from tris(*tert*-butylthio)cyclopropenylium perchlorate, carbon disulfide, and sodium dimethylamide under similar conditions. The Figure shows the molecular structure of **4**.[2]



4

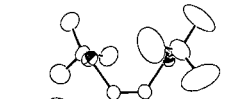
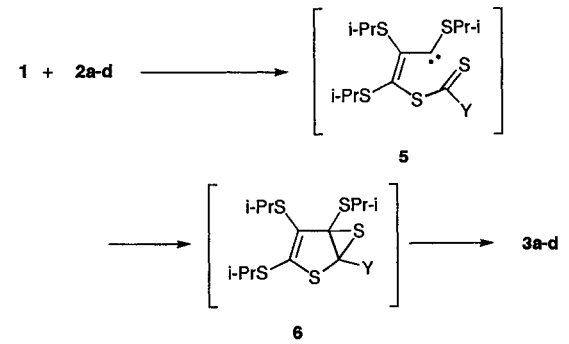


Figure. ORTEP drawing of **4**. Hydrogen atoms are omitted.

Previously, it has been reported that the reaction of thiolates with the cyclopropenyl cations gives the allene derivatives through the formation of the vinylcarbene intermediates[3] and that the reaction of carbenes with the thiocarbonyl compounds gives alkenes through the formation of the thiirane ring followed by desulfurization.[4] On the basis of these results, the reaction pathway for the formation of thiophenes **3a–d** is proposed in Scheme 2. The ring opening of **1** by **2a–d** gives vinylcarbene intermediates **5a–d**, which are converted into **3a–d** probably through the intermediary formation of the thiirane derivatives **6a–d**. In summary, a new synthesis of the thiophene ring system has been achieved by the reaction of the cyclopropenyl cation **1** with the compounds **2a–d** prepared from carbon disulfide and the anions of amines, thiols, and alcohols.

Melting points were determined with a Yanaco MP-S3 melting point apparatus and are uncorrected. The IR spectra were obtained on a Perkin-Elmer Model 1600 (FT) spectrophotometer. All ^{1}H NMR (270 MHz) and ^{13}C NMR (68 MHz) spectra were measured on a JEOL JNM-GX 270 FT NMR spectrometer using $CDCl_3$ as a solvent and chemical shifts were reported in ppm downfield from TMS as an internal standard. Mass spectra were obtained at 70 eV with a Finnigan mat TSQ 70 spectrometer. Elemental analyses were per-



Scheme 2

formed by a Yanaco CHN CORDER MT-3. Column chromatography was performed on silica gel (Wakogel C-300).

Compounds **3a–d** and **4** gave C, H, N analysis ±0.30%.

Sodium *N,N*-Dimethyldithiocarbamate (2a):
To a solution of *N,N*-dimethylamine hydrochloride (100 mg, 12.0 mmol) in MeOH (20 mL) were added CS_2 (0.6 mL, 10.0 mmol) and 1 M aq NaOH (30 mL). After stirring at r.t. for 3 h, the precipitate was filtered off and dried in vacuo to give **2a** as a colorless solid; yield: 1.43 g (100%).

^{1}H NMR (DMSO-d_6): δ = 3.40 (s, 6H, $N(CH_3)_2$).

Sodium *N*-Methyl-*N*-phenyldithiocarbamate (2b):
To a suspended solution of NaH (60% dispersion in mineral oil, 80 mg, 2.0 mmol) in benzene (5 mL) were added CS_2 (0.14 mL, 2.2 mmol) and *N*-methylaniline (0.28 mL, 2.0 mmol). After stirring at 0°C for 1.5 h under N_2, the precipitate was filtered off, washed with Et_2O, and dried in vacuo to give **2b** as a colorless solid; yield: 377 mg (92%).

^{1}H NMR (DMSO-d_6): δ = 3.83 (s, 3H, NCH_3), 7.16–7.40 (m, 5H, ArH).

Sodium *O*-Ethyl Dithiocarbonate (2d):
To a solution of CS_2 (6.0 mL, 100 mmol) in anhyd EtOH (20 mL) was added Na (2.3 g, 100 mmol). The mixture was stirred under N_2 at r.t. for 3 h and refluxed for 6 h. The precipitate was filtered off and dried in vacuo to give **2d** as a colorless solid; yield: 9.07 g (63%).

^{1}H NMR (DMSO-d_6): δ = 1.18 (t, 3H, J = 6.7 Hz, CH_2CH_3), 4.22 (dd, 2H, J = 14.0, 6.7 Hz, CH_2CH_3).

2-(Dimethylamino)-3,4,5-tris(isopropylthio)thiophene (3a):
Table, Solvent; MeCN: A solution of tris(isopropylthio)cyclopropenylium perchlorate (**1**) (180 mg, 0.5 mmol) in anhyd MeCN (2 mL) was added dropwise to a solution of **2a** (72 mg, 0.5 mmol) in anhyd MeCN (2 mL) and the mixture was stirred at r.t. under N_2. After 1 h, the solvent was evaporated in vacuo and the residue was purified by column chromatography on silica gel using hexane/CH_2Cl_2 (4 : 1) as an eluent to give **3a** as a yellowish oil; yield: 173 mg (99%).

IR (neat): ν = 2959, 2923, 2862, 2787, 1504, 1448, 1403, 1380, 1364, 1236, 1153, 1118, 1050, 926 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.17 (d, 6H, J = 6.7 Hz, $C(CH_3)_2$), 1.21 (d, 6H, J = 6.7 Hz, $C(CH_3)_2$), 1.26 (d, 6H, J = 6.7 Hz, $C(CH_3)_2$), 2.94 (s, 6H, $N(CH_3)_2$), 3.29 (sep, 1H, J = 6.7 Hz, $CH(CH_3)_2$), 3.54 (sep, 1H, J = 6.7 Hz, $CH(CH_3)_2$), 3.64 (sep, 1H, J = 6.7 Hz, $CH(CH_3)_2$).

^{13}C NMR ($CDCl_3$: δ = 22.7 (2C, $C(CH_3)_2$), 22.9 (2C, $C(CH_3)_2$), 23.0 (2C, $C(CH_3)_2$), 37.3 ($C(CH_3)_2$), 39.3 ($C(CH_3)_2$), 41.4 ($C(CH_3)_2$), 44.4 (2C, $N(CH_3)_2$), 116.8 (C-3), 123.4 (C-4), 140.1 (C-5), 161.3 (C-2).

MS (EI): m/z = 349 (M^+).

Table, Solvent; CH_2Cl_2: A solution of **1** (180 mg, 0.5 mmol) in CH_2Cl_2 (2 mL) was added dropwise to a suspended solution of **2a** (72 mg, 0.5 mmol) in CH_2Cl_2 (2 mL) and the mixture was stirred under N_2 at r.t. for 1 h. Workup described above gave **3a**; yield: 163 mg (93%).

Table, Solvent; benzene: To a suspended solution of **2a** (72 mg, 0.5 mmol) in benzene (4 mL) was added **1** (180 mg, 0.5 mmol) and the mixture was stirred unter N_2 at r.t. for 1 h. Workup described above gave **3a**; yield: 169 mg (97%).

Thiophenes 3b, d; General Procedure:
A solution of **1** (180 mg, 0.5 mmol) in anhyd MeCN (2 mL) was added dropwise to a suspended solution of **2b** or **2d** (0.5 mmol) in anhyd MeCN (2 mL) and the mixture was stirred under N_2 at r.t. for 1 h. After the removal of the solvent in vacuo, **3b** or **3d** was obtained by column chromatography of the residue on silica gel using hexane/CH_2Cl_2 (4 : 1) as an eluent.

2,3,4-Tris(isopropylthio)-5-(methylphenylamino)thiophene **(3b)**:

Yield: 195 mg (95%), a yellowish oil.

IR (neat): ν = 2961, 2924, 2864, 1600, 1580, 1496, 1462, 1448, 1398, 1381, 1364, 1318, 1297, 1234, 1154, 1123, 1051, 887, 749, 693 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.16 (d, 6H, J = 6.7 Hz, $C(CH_3)_2$), 1.26 (d, 6H, J = 6.7 Hz, $C(CH_3)_2$), 1.32 (d, 6H, J = 6.7 Hz, $C(CH_3)_2$), 3.31 (s, 3H, NCH_3), 3.40 (sep, 1H, J = 6.7 Hz, $CH(CH_3)_2$), 3.58 (sep, 1H, J = 6.7 Hz, $CH(CH_3)_2$), 3.68 (sep, 1H, J = 6.7 Hz, $CH(CH_3)_2$), 6.78–6.87 (m, 3H, ArH), 7.19–7.25 (m, 2H, ArH).

^{13}C NMR ($CDCl_3$): δ = 23.06 (2C, $C(CH_3)_2$), 23.10 (2C, $C(CH_3)_3$), 23.2 (2C, $C(CH_3)_2$), 37.6 (NCH_3), 39.3 ($C(CH_3)_2$), 40.2 ($C(CH_3)_2$), 41.0 ($C(CH_3)_2$), 114.5 (2C, ArH), 119.3 (ArH), 128.9 (2C, ArH), 130.6 (C-4), 134.7 (C-3), 136.1 (C-2), 148.3 (Ar), 152.0 (C-5).

MS (EI): m/z = 411 (M^+).

2-Ethoxy-3,4,5-tris(isopropylthio)thiophene **(3d)**:

Yield: 95 mg (54%), an orange oil.

IR (neat): ν = 2960, 2923, 2863, 1498, 1468, 1446, 1383, 1364, 1237, 1215, 1153, 1050, 1037, 886 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.20 (d, 6H, J = 6.7 Hz, $C(CH_3)_2$), 1.21 (d, 6H, J = 6.7 Hz, $C(CH_3)_2$), 1.26 (d, 6H, J = 6.7 Hz, CH_2CH_3), 1.47 (t, 3H, J = 6.7 Hz, CH_2CH_3), 3.28 (sep, 1H, J = 6.7 Hz, $CH(CH_3)_2$), 3.43 (sep, 1H, J = 6.7 Hz, $CH(CH_3)_2$), 3.70 (sep, 1H, J = 6.7 Hz, $CH(CH_3)_2$), 4.20 (dd, 2H, J = 14.0, 7.3 Hz, CH_2CH_3).

^{13}C NMR ($CDCl_3$): δ = 14.9 (CH_2CH_3), 22.9 (2C, $C(CH_3)_2$), 23.0 (2C, $C(CH_3)_2$), 23.1 (2C, $C(CH_3)_2$), 38.6 ($C(CH_3)_2$), 39.4 ($C(CH_3)_2$), 41.6 ($C(CH_3)_2$), 70.2 (CH_2CH_3), 114.2 (C-3), 121.4 (C-4), 140.3 (C-5), 165.9 (C-2).

MS (EI): m/z = 350 (M^+).

2,3,4,5-Tetrakis(isopropylthio)thiophene (3c):
2-Propanethiol (0.056 mL, 0.6 mmol) was added to a suspended solution of NaH (60% dispersion in mineral oil, 24 mg, 0.6 mmol) in anhyd MeCN (2 mL) and the mixture was stirred under nitrogen at r.t. for 1.5 h. A solution of **1** (180 mg, 0.5 mmol) in anhyd MeCN (2 mL) was added dropwise to the mixture. After stirring for 1 h, the solvent was removed in vacuo and the column chromatography of the residue on silica gel using hexane/CH_2Cl_2 (4 : 1) as an eluent gave **3c** as a red oil; yield: 169 mg (89%).

IR (neat): ν = 2961, 2924, 2864, 1461, 1442, 1381, 1365, 1237, 1154, 1050, 929, 879, 668 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.20 (d, 12H, J = 6.7 Hz, $C(CH_3)_2$), 1.32 (d, 12H, J = 6.7 Hz, $C(CH_3)_2$), 3.43 (sep, 2H, J = 6.7 Hz, $CH(CH_3)_2$), 3.67 (sep, 2H, J = 6.7 Hz, $CH(CH_3)_2$).

^{13}C NMR ($CDCl_3$): δ = 23.08 (4C, $C(CH_3)_2$), 23.12 (4C, $C(CH_3)_2$), 39.4 (2C, $C(CH_3)_2$), 41.0 (2C, $C(CH_3)_2$), 138.6 (2C, C-2, C-5), 139.6 (2C, C-3, C-4).

MS (EI): m/z = 380 (M^+).

2,3,4-Tris(*tert*-butylthio)-5-(dimethylamino)thiophene (4):
Thiophene **4** was prepared from tris(*tert*-butylthio)cyclopropenylium perchlorate (201 mg, 0.5 mmol) and **2a** (72 mg, 0.5 mmol) in MeCN in a similar manner as described in the preparation of **3a**.
Yield: 135 mg (69%), a yellowish solid; mp 76–77°C.

IR (KBr): ν = 2974, 2978, 2958, 2918, 2893, 2857, 1501, 1472, 1457, 1424, 1394, 1364, 1261, 1162, 1117, 1050, 1022, 1009, 926, 874, 685, 669 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.20 (s, 18 H, $C(CH_3)_3$), 1.29 (s, 9 H, $C(CH_3)_3$), 3.05 (s, 6 H, $N(CH_3)_2$).

^{13}C NMR ($CDCl_3$): δ = 31.0 (3 C, $C(CH_3)_3$), 31.1 (3 C, $C(CH_3)_3$), 31.3 (3 C, $C(CH_3)_3$), 44.5 (2 C, $N(CH_3)_2$), 49.0 ($C(CH_3)_3$), 49.4 ($C(CH_3)_3$), 49.7 ($C(CH_3)_3$), 116.2 (C-4), 123.7 (C-3), 145.4 (C-2), 165.9 (C-5).

MS (EI): m/z = 391 (M^+).

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