Facile Synthesis of Thiophene Derivatives Using a Cyclopropenyl Cation

Hideo Kojima, Keiichi Nakamura, Kazuhiko Yamamoto, Hiroo Inoue

Laboratory of Organic Chemistry, Osaka Women’s University, Sakai, Osaka 590, Japan
Department of Applied Chemistry, College of Engineering, Osaka Prefecture University, Sakai, Osaka 593, Japan
Fax +81(722)593340
Received 2 February 1996

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 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. We now report a novel convenient method for the preparation of thiophene derivatives from tris(isopropylthio)cyclopropenylum perchlorate (1) and the compounds 2a–d with the \(-\text{CS}–\text{S}^–\) moiety, derived easily from carbon disulfide and the anions of amines, thiois, and alcohols (Scheme 1).

Dithiocarbamates 2a, b and thiocarbonate 2c were prepared from carbon disulfide and \(N,N\)-dimethylamine, \(N\)-methylalanine, 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 \(\delta = 114.2–165.9\).

<table>
<thead>
<tr>
<th>Y – C\text{S}^–</th>
<th>Solvent</th>
<th>Yield of 3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>MeCN</td>
<td>99</td>
</tr>
<tr>
<td>2a</td>
<td>CH(_2)Cl(_2)</td>
<td>93</td>
</tr>
<tr>
<td>2a</td>
<td>C(_2)H(_4)</td>
<td>97</td>
</tr>
<tr>
<td>2b</td>
<td>MeCN</td>
<td>95</td>
</tr>
<tr>
<td>2c</td>
<td>MeCN</td>
<td>89</td>
</tr>
<tr>
<td>2d</td>
<td>MeCN</td>
<td>54</td>
</tr>
</tbody>
</table>

* 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)cyclopropenylum perchlorate, carbon disulfide, and sodium dimethylamide under similar conditions. The Figure shows the molecular structure of 4.

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

Previously, it was reported that the reaction of thiolates with cyclopropenyl cations gives the allenic derivatives through the formation of the vinylicene intermediates and that the reaction of carbones with the thiocarbonyl compounds gives alkynes through the formation of the thirane ring followed by desulfurization. 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 vinylicene intermediates 5a–d, which are converted into 3a–d probably through the intermediary formation of the thirane 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 CDC\(_3\) 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-Dimethylthiocarbamate (2a):**
To a solution of N,N-dimethylaniline hydrochloride (100 mg, 12.0 mmol) in MeOH (20 mL) were added CS₂ (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%).

**Sodium N-Methyl-N-phenylthiocarbamate (2b):**
To a suspended solution of NaN (60% dispersion in mineral oil, 80 mg, 2.0 mmol) in benzene (5 mL) were added CS₂ (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 N₂, the precipitate was filtered off, washed with Et₂O, and dried in vacuo to give 2b as a colorless solid; yield: 377 mg (92%).

**Sodium O-Ethyl Dithiocarbonate (2d):**
To a solution of CS₂ (6.0 mL, 100 mmol) in anhyd EtOH (20 mL) was added Na (2.3 g, 100 mmol). The mixture was stirred under N₂ 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%).

**2-(Dimethylamino)-3,4,5-tris(isopropylthio)thiophene (3a):**
Table; Solvent: MeCN; A solution of tris(isopropylthio)cyclopropenyl 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 N₂. After 1 h, the solvent was evaporated in vacuo and the residue was purified by column chromatography on silica gel using hexane/CH₂Cl₂ (4:1) as an eluent to give 3a as a yellowish oil; yield: 173 mg (99%).

**Thiophenes 3b-d; General Procedure:**
A solution of I (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 N₂ 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/CH₂Cl₂ (4:1) as an eluent.

**2,3,4,5-Tetakis(isopropylthio)thiophene (3c):**
2-Propanethiol (0.056 mL, 0.6 mmol) was added to a suspended solution of NaN (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 I (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/CH₂Cl₂ (4:1) as an eluent gave 3c as a red oil; yield: 169 mg (89%).

**2,3,4,5-Tris(tert-butylthio)-5-(dimethylamino)thiophene (4):**
Thiophene 4 was prepared from tris(tert-butylthio)cyclopropenyl 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 (CDCl₃): δ = 1.20 (s, 18 H, C(CH₃)₃), 1.29 (s, 9 H, C(CH₃)₃), 3.05 (s, 6 H, N(CH₂)₃).

13C NMR (CDCl₃): δ = 31.0 (3 C, C(CH₃)₃), 31.1 (3 C, C(CH₃)₃), 31.3 (3 C, C(CH₃)₃), 44.5 (2 C, N(CH₂)₂), 49.0 (C(CH₃)₃), 49.4 (C(CH₃)₃), 49.7 (C(CH₃)₃), 116.2 (C-4), 123.7 (C-3), 145.4 (C-2), 165.9 (C-5).

MS (EI): m/z = 391 (M⁺).

The present work was supported by the Grant-in-Aid for Scientific Research (No. 05650885) from the Ministry of Education, Science and Culture, Japan. We would like to thank Dr. Tomohiro Adachi and Dr. Akira Sugimoto, University of Osaka Prefecture, for the X-ray structure determination of compound 4.


