Efficient One Pot Preparation of Variously Substituted Thieno[2,3-*b*]thiophene

Alain Comel and Gilbert Kirsch*

Laboratoire d'Ingénierie Moléculaire et de Biochimie Pharmacologique, Université de Metz, Ile du Saulcy, 57045 Metz Cedex 1, France

Received December 27, 2000

An efficient one pot access to variously substituted thieno[2,3-*b*]thiophene is described. The title compounds were obtained from 1,3-dicarbonyl or equivalent compounds, carbon disulfide and halomethyl derivatives in good to high yields and fully characterized.

J. Heterocyclic Chem., **38**, 1167 (2001).

Substituted thieno[2,3-*b*]thiophenes and their preparation methods are known since the 1950's. These compounds have been studied and developed for different purposes in the pharmaceutical field and have been tested as, depending on the nature of the substituents, potential antiviral [1], antibiotic [2], antiglaucoma [3], analgesic and antipyretic drugs [4].

Several synthetic methods have been investigated [5]. Among them, two main synthetic pathways are the most used and described.

The first one [6] started from thiophene or a substituted thiophene treated with BuLi, sulfur and an halide in order to obtain a thioalkyl substituent with an activated methylene next to the sulfur atom at the 2-position of the thiophene. The 3-position should be functionalised with a carbonyl group (or a nitrile), if not accurately substituted [3] before the lithiation. The final cyclization step occurs in a basic medium, usually EtONa in ethanol, and leads to poorly substituted thieno[2,3-*b*]thiophenes with modest to good yields.

The second one is based on the cyclization (in basic media) of ketene dithioacetals, obtained from carbon disulfide [7-15]. The first reported synthesis of this type is due to Gompper [7] *et al*., in 1962. A dozen of compounds have been obtained in moderate to good yields (48-78%) following a one pot procedure for the formation of the thienothiophene skeleton and identified by ir and elemental analyses, as well as other substituted thiophenes. Ketene dithioacetals have been prepared from carbon disulfide in a basic medium and allow one to obtain thieno[2,3-*b*]thiophenes directly after the addition of haloacetic acid derivatives. The cyclization is performed or not during the alkylation depending on the nature of the base used.

It is quite surprising that almost nothing on this topic has been done until the works of L. Dalgaard [8] and colleagues in 1973 and M. Augustin [9] and colleagues in 1976. Both reported the formation of thieno[2,3-*b*]thiophenes in poor to moderate yields using a method similar to the one described by Gompper. The choice of the base and the solvent used for the formation of ketene dithioacetals is not discussed and no explanation for the poor yields reported has been given. More recently, better results have been reported [10-12] using similar conditions but the reasons of the improvement are not detailed, not even discussed.

El-Shafei and colleagues [13-15] reported a slight modification of this synthetic pathway and prepared thieno[2,3-*b*]thiophenes in very good yields. The authors claimed that the use of PTC conditions in a one pot reaction was the reason why their results were so good in addition to the fact that they avoid the use of expensive, inconvenient and dangerous reagents and solvents.

The introduction of the thieno[2,3-*b*]thiophene feature in a molecular structure has been described recently [1] but the preparation of 2-bromo-thieno[2,3-*b*]thiophene is well known [16] and Pd-coupling reactions are of no interest in this work because they lead to poorly substituted products.

All the compounds reported in the literature have been identified and characterized by ir and elemental analyses, ^{1}H nmr for the most recent.

The increasing interest for the thieno[2,3-*b*]thiophene skeleton and our continuing synthetic efforts in the condensed thiophene research field [17] prompted us to develop an easy and attractive one pot procedure for the preparation of such compounds.

We propose here a good to high yields access to alkyl, aryl, cyano, amino, hydroxy or carbethoxy thieno[2,3-*b*]thiophene derivatives, fully characterized by ir (KBr), uv (ethanol), ^{1}H, ^{13}C nmr and elemental analyses.

Unfortunately, during the preparation of this paper, a nice work on the same topic has been reported by Mashraqui *et al*., [18], using anhydrous KF as the condensation promoter. Nevertheless, ^{13}C nmr data have not been given by the authors, the yields reported were as good or lower than what we observed and above all our K_2CO_3/DMF cyclization system does not require strictly anhydrous conditions.

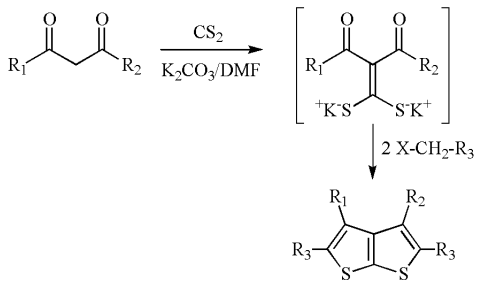
Results and Discussion.

The first part of this paper is dealing with a general synthetic route to tetra- and tri-substituted thieno[2,3-*b*]thiophenes. Our initial goal was to transform 1,3-diketo derivatives into thieno[2,3-*b*]thiophenes, what has been achieved through a one pot reaction from 1,3-diketones, carbon disulfide and accurately substituted halides.

As shown below, the 1,3-diketo compounds were reacted with carbon disulfide in basic media at room temperature to afford the ketene dithioacetals dipotassium salts (Scheme 1).

These intermediates were not isolated but directly treated with 2 equivalents of alkylating agents carrying such activating groups as ester, ketone and nitrile. The resulting disulfides, smoothly undergo Dieckmann type cyclization in basic media at room temperature. The thieno[2,3-*b*]thiophenes were obtained after hydrolysis of the reaction mixtures.

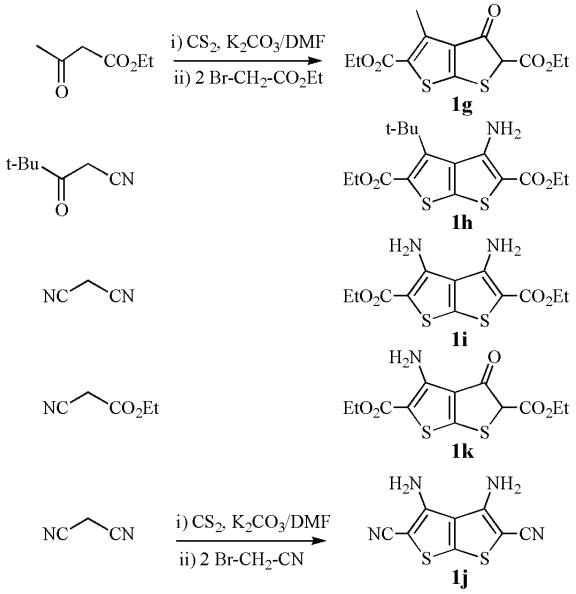
Scheme 1



This protocol using pentan-2,4-dione, 3-oxo-3-phenylpropanal, 1-phenyl-butan-1,3-dione and 1,3-diphenylpropan-1,3-dione and reacting with ethyl bromoacetate, 2-bromoacetone or chloroacetonitrile afforded respectively thieno[2,3-*b*]thiophene **1a** to **1f** in 65 to 92% yields.

In the second part, we describe the extension of this strategy to the synthesis of hydroxy and amino substituted thieno[2,3-*b*]thiophenes. We envisaged the preparation of 3-hydroxy and 3-amino thieno[2,3-*b*]thiophene, by using 1,3-ketoester, malononitrile, 2-ethoxycarbonylacetonitrile or 1,3-ketonitrile as shown in Scheme 2.

Scheme 2

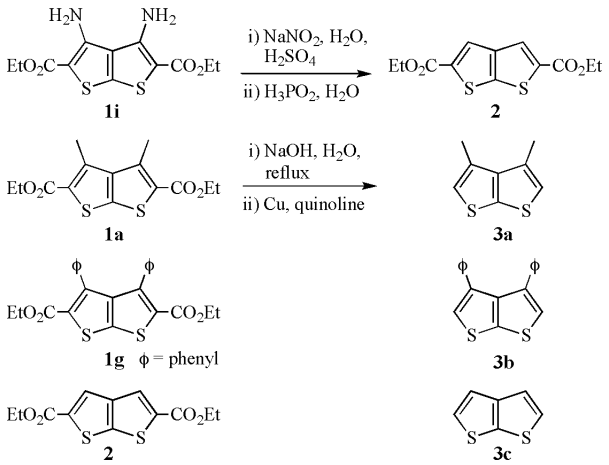


The active methylene starting compounds react in a similar manner to the 1,3-diketones. Variously substituted thieno[2,3-*b*]thiophenes **1g** to **1k** were obtained in 61 to 87% yields. We must note that, in thieno[2,3-*b*]thiophenes **1g** and **1k**, both keto and enol forms are reasonably possible but only the ketone was observed. No trace of an hydroxy group has been detected by ir or ^{1}H and ^{13}C nmr, even though the conjugated aromatic system seems to be more favored than the corresponding ketone.

The preparation of similar compounds has been reported previously [14] and such a behavior has been pointed out (ir and ^{1}H nmr data) but not discussed by the authors. We have actually no explanation for this phenomenon but the δ values of the 2-C for these two compounds allow to confirm unambiguously that the keto form is the only one present.

In the last part of our work, we decided to investigate the reactivity of some of the former synthesized thienothiophenes. For example, compound **2** has been readily obtained from diamino thieno[2,3-*b*]thiophene **1i** in 65% yield. The amino derivative **1i** was treated with 2.3 equivalents of sodium nitrite in presence of aqueous sulfuric acid. The intermediate bisdiazonium salt afforded compound **2** (Scheme 3).

Scheme 3



On the other hand, compounds **1a**, **1g** and **2** were hydrolyzed in order to obtain the corresponding carboxylic acids which were decarboxylated with copper in refluxing quinoline. The 2,5-unsubstituted compounds **3a-c** have been obtained this way in 43 to 61 % yields.

In summary, we succeeded in the preparation of variously substituted thieno[2,3-*b*]thiophenes by an efficient one pot procedure. The peculiar behavior of the 3-hydroxythieno[2,3-*b*]thiophenes has been outlined for the first time and all compounds have been entirely characterized, in particular by ^{13}C nmr.

EXPERIMENTAL

The nmr spectra were recorded using a 250 MHz Brucker spectrometer. δ values are given relatives to internal $CDCl_3$.

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Elemental analyses were performed on a Carlo Erba elemental analyzer. Infra red (ir) were measured on a Perkin-Elmer 881 spectrometer (KBr pellets) and uv spectra were recorded on a Shimadzu 1205 apparatus (solution in ethanol).

General Procedure for the Preparation of Thieno[2,3-*b*]thiophene **1a-f**.

To 0.3 mol (41.5 g) oven dried potassium carbonate in 30 to 40 mL DMF, 0.1 mol of the 1,3-dicarbonyl derivatives dissolved in 10 to 20 mL DMF followed by 0.15 mol (9.0 mL) carbon disulfide were added dropwise under vigorous stirring. After 30 minutes, the mixture was cooled to 0 °C and 0.2 mol of the activated alkylating agents (ethyl bromacetate, chloroacetone or chloroacetonitrile) in 10 mL of DMF was added in 20 minutes. The reaction mixture was then stirred for 3 to 7 hours at room temperature and poured into 200 mL of cold water. The precipitate was collected and washed 3 times with 100 mL of water. The crude thieno[2,3-*b*]thiophenes obtained were purified by crystallization to give **1a** to **1k** in 92 ([15]: 93), 72 ([8]: 35), 86 ([18]: 67), 91 ([7]: 52), 70, 65, 61, 78, 83 ([14]: 88), 87 ([14]: 81) and 66 ([14]: 63) % yield, respectively.

Diethyl 3,4-Dimethylthieno[2,3-*b*]thiophene-2,5-dicarboxylate (**1a**).

This compound was obtained as colorless crystals (ethanol), mp 142-143 °C ([15]: 135 °C); ir (potassium bromide): CH_3 2987, 2941, CO 1703 cm^{-1}; uv: λ max 271 nm (ε 25,100); ^1H nmr (deuteriochloroform): δ 1.38 (t, 6H, CH_3, J = 7.1 Hz), 2.86 (s, 6H, CH_3), 4.35 ppm (q, 4H, CH_2, J = 7.1 Hz); ^{13}C nmr: δ 14.4 (2 CH_3), 21.2 (2 CH_3), 61.0 (2 CH_2), 130.7 (2 CAr), 138.9 (CAr), 142.6 (2 CAr), 152.1 (CAr), 176.3 ppm (2 CO_2).

Anal. Calcd. for $C_{14}H_{16}O_4S_2$: C, 53.85; H, 5.13. Found: C, 53.98; H, 5.28.

1-(5-Acetyl-3,4-dimethyl-thieno[2,3-*b*]thiophen-2-yl)-ethanone (**1b**).

This compound was obtained as colorless crystals (ethanol), mp 160-161 °C; ([8]: 157-158 °C); ir (potassium bromide): CH_3 2996, 2962, CO 1671 cm^{-1}; uv: λ max 288 nm (ε 10,100); ^1H nmr (deuteriochloroform): δ 2.57 (s, 6H, $COCH_3$), 2.87 ppm (s, 6H, CH_3); ^{13}C nmr: δ 15.1 (2 CH_3), 30.1 (2 CH_3), 139.9 (2 CAr), 143.6 (CAr), 144.8 (2 CAr), 151.6 (CAr), 191.3 ppm (2 CO).

Anal. Calcd. for $C_{12}H_{12}O_2S_2$: C, 57.14; H, 4.76. Found: C, 57.03; H, 4.81.

3,4-Dimethylthieno[2,3-*b*]thiophene-2,5-dicarbonitrile (**1c**).

This compound was obtained as light brown crystals (ethanol), mp 225 °C; ([18]: 220-222 °C); ir (potassium bromide): CH_3 2964, CN 2213 cm^{-1}; uv: λ max 259 nm (ε 44,200): λ max 222 nm (ε 12,400); ^1H nmr (deuteriochloroform): δ 2.69 ppm (s, 6H, CH_3); ^{13}C nmr: δ 14.8 (2 CH_3), 108.5 (2 CAr), 113.3 (2CN), 134.1 (CAr), 143.1 (2CAr), 150.8 ppm (CAr).

Anal. Calcd. for $C_{10}H_6N_2S_2$: C, 55.04; H, 2.75; N, 12.84. Found: C, 54.82; H, 2.92; N, 12.97.

Diethyl 3-Phenylthieno[2,3-*b*]thiophene-2,5-dicarboxylate (**1d**).

This compound was obtained as colorless crystals (ethanol), mp 106-108 °C ([12] : 94-96 °C); ir (potassium bromide): CH_3 2986, 2942, CO 1735, 1701, CHAr 730, 704 cm^{-1}; uv: λ max 308 nm (ε 3,120): λ max 259 nm (ε 7,960); ^1H nmr (deuteriochloroform): δ 1.33 (m, 6H, CH_3), 4.29 (m, 4H, CH_2), 7.61 (m, 5H, C_6H_5), 7.91 ppm (s, 1H, 4-H); ^{13}C nmr: δ 14.1 (CH_3), 14.3 (CH_3), 61.6 (CH_2), 62.2 (CH_2), 128.6 (2 CAr), 129.1 (2 CAr), 132.4 (CAr), 132.8 (CAr), 135.6 (CAr), 137.1 (CAr), 138.1 (CAr), 143.8 (CAr), 145.1 (CAr), 148.7 (CAr), 169.8 ppm (CO_2), 171.1 ppm (CO_2).

Anal. Calcd. for $C_{18}H_{16}O_4S_2$: C, 60.00; H, 4.17. Found: C, 59.84; H, 4.28.

Diethyl 3-Methyl-4-phenylthieno[2,3-*b*]thiophene-2,5-dicarboxylate (**1e**).

This compound was obtained as colorless crystals (ethanol), mp 128 °C; ir (potassium bromide): CH_3 2986, 2938, CO 1712, 1686, CHAr 717 cm^{-1}; uv: λ max 271 nm (ε 11,900); ^1H nmr (deuteriochloroform): δ 1.13 (t, 3H, CH_3, J = 7.1 Hz), 1.37 (t, 3H, CH_3, J = 7.1 Hz), 2.11 (s, 3H, CH_3), 4.13 (q, 2H, CH_2, J = 7.1 Hz), 4.32 (q, 2H, CH_2, J = 7.1 Hz), 7.29 (m, 2H, C_6H_5), 7.43 ppm (m, 3H, C_6H_5); ^{13}C nmr: δ 13.7 (CH_3), 13.9 (CH_3), 14.1 (CH_3), 60.9 (2 CH_2), 127.2 (2 CAr), 128.1 (CAr), 129.1 (2 CAr), 130.1 (CAr), 131.9 (CAr), 136.8 (CAr), 139.7 (CAr), 142.6 (CAr), 146.6 (CAr), 148.9 (CAr), 161.4 (CO_2), 162.1 ppm (CO_2).

Anal. Calcd. for $C_{19}H_{18}O_4S_2$: C, 60.96; H, 4.81. Found: C, 61.01; H, 4.80.

Diethyl 3,4-Diphenylthieno[2,3-*b*]thiophene-2,5-dicarboxylate (**1f**).

This compound was obtained as light yellow crystals (diethyl ether), mp 174-176 °C; ir (potassium bromide): CH_3 2989, CO 1732, CHAr 694 cm^{-1}; uv: λ max 326 nm (ε 7,030); ^1H nmr (deuteriochloroform): δ 1.08 (t, 3H, CH_3, J = 7.0 Hz), 1.20 (t, 3H, CH_3, J = 7.0 Hz), 4.16 (m, 4H, CH_2), 6.98 ppm (m, 10H, C_6H_5); ^{13}C nmr: δ 13.9 (2 CH_3), 60.7 (2 CH_2), 126.8 (4 CAr), 127.6 (4 CAr), 129.1 (2 CAr), 131.6 (2 CAr), 140.5 (2 CAr), 141.8 (CAr), 149.7 (CAr), 153.5 (2 CAr), 168.6 ppm (2 CO_2).

Anal. Calcd. for $C_{24}H_{20}O_4S_2$: C, 66.05; H, 4.59. Found: C, 65.93; H, 4.77.

Diethyl 4-Methyl-3-oxo-2,3-dihydrothieno[2,3-*b*]thiophene-2,5-dicarboxylate (**1g**).

This compound was obtained as colorless crystals (ethanol), mp 72-74 °C; ir (potassium bromide): CH_3 2984, 2941, CO 1735, 1713, 1693 cm^{-1}; uv: λ max 313 nm (ε 6,940), λ max 247 nm (ε 10,380); ^1H nmr (deuteriochloroform): δ 1.35 (m, 6H, CH_3), 2.72 (s, 3H, CH_3), 3.83 (s, 1H, CH), 4.29 ppm (m, 4H, CH_2); ^{13}C nmr: δ 13.5 (CH_3), 14.2 (CH_3), 15.4 (CH_3), 37.4 (CH), 61.2 (CH_2), 62.1 (CH_2), 136.9 (CAr), 141.5 (CAr), 148.3 (CAr), 151.3 (CAr), 167.6 (CO_2), 168.3 (CO_2), 208.1 ppm (CO).

Anal. Calcd. for $C_{13}H_{14}O_5S_2$: C, 49.68; H, 4.46. Found: C, 49.72; H, 4.59.

Diethyl 3-Amino-4-*tert*-butylthieno[2,3-*b*]thiophene-2,5-dicarboxylate (**1h**).

This compound was obtained as light yellow crystals (acetonitrile), mp 124 °C; ir (potassium bromide): NH_2 3489, 3346, 1596, CH_3 2978, 2959, CO 1683, 1665 cm^{-1}; uv: λ max 292 nm (ε 22,800): λ max 230 nm (ε 14,200); ^1H nmr (deuteriochloroform): δ 1.37 (m, 6H, CH_3), 1.61 (s, 9H, $C(CH_3)_3$), 4.36 (m, 4H, CH_2), 6.29 ppm (broad s, 2H, NH_2); ^{13}C nmr: δ 14.1 (CH_3), 14.5 (CH_3), 31.7 (3 $C(CH_3)_3$), 35.3 ($C(CH_3)_3$), 60.3 (CH_2), 61.1 (CH_2), 119.9 (CAr), 134.9 (CAr), 138.5 (CAr), 144.5 (CAr), 145.1 (CAr), 157.7 (CAr), 166.2 (CO_2), 167.3 ppm (CO_2).

Anal. Calcd. for $C_{16}H_{21}NO_4S_2$: C, 54.08; H, 5.91; N, 3.94. Found: C, 53.92; H, 6.01; N, 4.09.

Diethyl 3,4-Diaminothieno[2,3-*b*]thiophene-2,5-dicarboxylate (**1i**).

This compound was obtained as light brown crystals (acetonitrile), mp 203-204 °C ([14] : 201-202°C); ir (potassium bromide): NH_2 3442, 3353, 1622, CH_3 2981, CO 1678 cm^{-1}; uv: λ max 353 nm (ε 1,700): λ max 272 nm (ε 4,870); ^1H nmr (deuteriochloroform): δ 1.12 (t, 6H, CH_3, J = 7.0 Hz), 4.07 (q, 4H, CH_2, J = 7.0 Hz), 6.60 ppm (broad s, 4H, NH_2); ^{13}C nmr: δ 13.6 (2 CH_3), 58.8 (2 CH_2), 98.7 (CAr), 127.6 (CAr), 146.5 (2 CAr), 147.9 (2 CAr), 163.2 ppm (CO_2).

Anal. Calcd. for $C_{12}H_{14}N_2O_4S_2$: C, 45.86; H, 4.46; N, 8.92. Found: C, 45.82; H, 4.52; N, 9.17.

3,4-Diaminothieno[2,3-*b*]thiophene-2,5-dicarbonitrile (**1j**).

This compound was obtained as brown crystals (ethanol), mp 250-253 °C; ([14]: 210 °C); ir (potassium bromide): NH_2 3368, 3314, 1635, CN 2204 cm^{-1}; uv: λ max 347 nm (ε 4,230): λ max 261 nm (ε 18,500); ^1H nmr (deuteriochloroform): δ 5.43 ppm (broad s, 4H, NH_2); ^{13}C nmr: δ 97.9 (CAr), 114.2 (2 CN), 124.7 (2 CAr), 143.8 (CAr), 148.9 ppm (2 CAr).

Anal. Calcd. for $C_8H_4N_4S_2$: C, 43.64; H, 1.82; N, 25.45. Found: C, 43.56; H, 1.82; N, 25.43.

Diethyl 4-Amino-3-oxo-2,3-dihydro-thieno[2,3-*b*]thiophene-2,5-dicarboxylate (**1k**).

This compound was obtained as yellow crystals (ethanol), mp 213 °C ([14]: 275-276 °C); ir (potassium bromide): NH_2 3478, 3364, 1597, CH_3 2984, 2942, CO 1736, 1687, 1664 cm^{-1}; uv: λ max 265 nm (ε 4,750), λ max 214 nm (ε 5,870); ^1H nmr (deuteriochloroform): δ 1.31 (m, 6H, CH_3), 3.91 (s, 1H, CH), 4.26 (m, 4H, CH_2), 6.83 ppm (broad s, 2H, NH_2); ^{13}C nmr: δ 13.3 (CH_3), 13.8 (CH_3), 35.7 (CH), 59.2 (CH_2), 61.4 (CH_2), 113.1 (CAr), 114.1 (CAr), 128.8 (CAr), 154.1 (CAr), 155.9 (CAr), 162.3 (CO_2), 162.8 (CO_2), 206.9 ppm (CO).

Anal. Calcd. for $C_{12}H_{13}NO_5S_2$: C, 45.71; H, 4.13; N, 4.44. Found: C, 45.47; H, 4.17; N, 4.40.

Diethyl Thieno[2,3-*b*]thiophene-2,5-dicarboxylate (**2**).

At 0 °C, 25 mL of 75% sulfuric acid was added to 10 mmol (3.14g) compound **1i**. 23 mmol (1.6g) of sodium nitrite dissolved in 10 mL of water was added dropwise. The reaction mixture was then stirred for 30 minutes at 0 °C and added dropwise to 50 mL of 50% hypophosphorous acid. After 2 hours at room temperature, 100 mL of ice cold water was added. The precipitate was collected by filtration and crystallized from ethanol to yield 1.85 g (65 %), mp 274-276 °C; ir (potassium bromide): CH_3 2980, CO 1700, CHAr 754 cm^{-1}; uv: λ max 266 nm (ε 42,600); ^1H nmr (deuteriochloroform): δ 1.39 (t, 6H, CH_3, J = 7.1 Hz), 4.38 (q, 4H, CH_2, J = 7.1 Hz), 7.96 ppm (s, 2H, 3-H and 4-H); ^{13}C nmr: δ 14.2 (2 CH_3), 61.6 (2 CH_2), 126.6 (2 CAr), 128.9 (2 CAr), 137.5 (CAr), 145.1 (CAr), 161.8 ppm (2 CO_2).

Anal. Calcd. for $C_{12}H_{12}O_4S_2$: C, 50.70; H, 4.22. Found: C, 50.61; H, 4.43.

General Procedure for the Preparation of Thieno[2,3-*b*]thiophene **3a**, **3b** and **3c**

Compound **1a**, **1f** or **2** (10 mmol) is heated at reflux for 2 hours with 11 mmol of sodium hydroxide (0.44 g) in 50 mL of ethanol and 10 mL of water. After removal of the solvent, the residue is taken up in water, the solution filtered through a celite pad and acidified. The crude carboxylic acid is filtered and dried overnight. The crude acid is then decarboxylated by heating at reflux in 12.5 mL of quinoline in the presence of 0.25 g of copper bronze for 1 hour. After cooling at room temperature, the solution is poured into 50% hydrochloric acid and stirred for 1 hour. Dichloromethane is added, and the solution is filtered. The organic layer is then separated, washed with water, dried with sodium sulfate and evaporated. Compounds **3a**, **3b** and **3c** were obtained in 61, 43, 56% yield respectively.

3,4-Dimethylthieno[2,3-*b*]thiophene (**3a**).

This compound was obtained as colorless crystals (hexane), mp 74 °C; ir (potassium bromide): CH_3 2950, CHAr 720 cm^{-1}; uv: λ max 224 nm (ε 8,100); ^1H nmr (deuteriochloroform): δ 2.51 (s, 6H, CH_3), 6.90 ppm (s, 2H, 2-H and 5-H); ^{13}C nmr: δ 15.2 (2 CH_3), 123.1 (2 CAr), 130.7 (2 CAr), 141.8 (CAr), 146.1 ppm (CAr).

Anal. Calcd. for $C_8H_8S_2$: C, 57.14; H, 4.76. Found: C, 56.98; H, 4.83.

3,4-Diphenylthieno[2,3-*b*]thiophene (**3b**).

This compound was obtained as colorless crystals (diethyl ether), mp 160 °C; ir (potassium bromide): CHAr 744, 696 cm^{-1}; uv: λ max 230 nm (ε 13,100); ^1H nmr (deuteriochloroform): δ 6.90 (s, 2H, 2-H and 5-H), 7.14 ppm (m, 10H, C_6H_5); ^{13}C nmr: δ 125.6 (2 CAr), 128.3 (4 CAr), 131.8 (CAr), 135.1 (CAr), 136.9 (2 CAr), 146.7 ppm (2 CAr).

Anal. Calcd. for $C_{18}H_{12}S_2$: C, 73.97; H, 4.11. Found: C, 73.74; H, 4.07.

Thieno[2,3-*b*]thiophene (**3c**).

This compound was obtained as a yellow oil; ir (potassium bromide): CHAr 730 cm^{-1}; uv: λ max 223 nm (ε 17,700); ^1H nmr (deuteriochloroform): δ 7.28 (d, 2H, $H_{Ar.}$, J = 5.4 Hz), 7.38 ppm (d, 2H, $H_{Ar.}$, J = 5.4 Hz); ^{13}C nmr: δ 125.3 (2 CAr), 128.3 (2 CAr), 137.1 (CAr), 146.8 ppm (CAr).

Anal. Calcd. for $C_6H_4S_2$: C, 51.43; H, 2.86. Found: C, 51.27; H, 3.01.

REFERENCES AND NOTES

[1] D. Peters, A. B. Hörnfeldt and S. Gronowitz, *J. Heterocyclic Chem.*, **27**, 2165 (1990).

[2] S. Kukolja, S. E. Draheim, B. J. Graves, D. C. Hunden, J. L. Pfeil, R. D. G. Cooper, J. L. Ott and F. T. Couter, *J. Med. Chem.*, **28**, 1896 (1995).

[3] J. D. Prugh, G. D. Hartman, P. J. Mallorga, B. M. McKeever, S. R. Michelson, M. A. Murcko, H. Schwam, R. L. Smith, J. M. Sondey, J. P. Springer and M. F. Surgrue, *J. Med. Chem.*, **35**, 1805 (1991).

[4] J. L. Fabre, D. Farge and C. James, German Patent 2,703,624 (1976); *Chem. Abstr.*, **87**, 168000v.

[5] V. P. Litvinov and Y. A. L., Gol'dfarb, Advances in Heterocyclic Chemistry, Vol. **19**, A. R. Katrizky and A. J. Boulton, eds, Academic Press, Inc., New York, 1976, p 123.

[6] A. Bugge, *Acta Chem. Scand.*, **25**, 27 (1971).

[7] R. Gompper, E. Kutter and W. Töpfl, *Liebigs Ann. Chem.*, **659**, 90 (1962).

[8] L. Dalgaard, L. Jensen and S. O. Lawesson, *Tetrahedron*, **30**, 93 (1974).

[9] M. Augustin, W. D. Rudorf and U. Schmidt, *Tetrahedron*, **32**, 3055 (1976).

[10] D. Briel, *Pharmazie*, **45**, 895 (1990).

[11] D. Wobig, *Liebigs Ann. Chem.*, 115 (1990).

[12] W. D. Rudorf, J. Köditz, A. Tersakian and S. K. Chatterjee, *Liebiegs Ann. Chem.*, 387 (1992).

[13] A. K. El-Shafei, A. M. M. El-Saghier, A. Sultan and A. M. Soliman, *Phosphorus Sulfur*, **72**, 73 (1992).

[14] A. K. El-Shafei, A. H. Abdel-Ghany, A. Sultan and A. M. M. El-Saghier, *Phosphorus Sulfur*, **73**, 15 (1992).

[15] A. M. M. El-Saghier, *Bull. Chem. Soc. Jpn.*, **66**, 2011 (1993).

[16] A. Bugge, *Acta Chem. Scand.*, **23**, 2704 (1969).

[17] D. Prim and G. Kirsch, *J. Chem. Soc., Perkin Trans. 1*, 2603 (1994).

[18] S. H. Mashraqui, H. Hariharasubrahmanian and S. Kumar, *Synthesis*, 2030 (1999).