A New Synthetic Approach to Thiophenes

Mikhail V. Lebedev, Valentine G. Nenajdenko,* Elizabeth S. Balenkova*

Department of Chemistry, Moscow State University, 119899 Moscow, Russia
Fax +7(095)9328846; E-mail: Nen@acylium.chem.msu.ru

Received 27 April 2001; revised 27 July 2001

Abstract: A new simple and efficient way to 3-hydroxy(methoxy)thiophenes is described. The reactions of (ethylsulfanyl)acetyl fluoride/boron trifluoride (**1**) and 2-(ethylsulfanyl)butanoyl fluoride/boron trifluoride (**6**) complexes with acetylenes give rise to the 5-membered cyclic sulfonium salts (**3a–f**). The last ones (**3e**, **3f**) after being refluxed with thiourea in methanol or acetonitrile are converted into 3-methoxythiophenes or 3-(2*H*)-thiophenones respectively. Several 3-methoxythiophenes unsubstituted in the 2-position were obtained by the reactions of **1** with acetylenes. Reactions of **6** with acetylenes allows the synthesis of 2-ethylsubsituted 3-methoxythiophenes. The method allows the synthesis of a variety of mono-, di-, tri- and tetrasubsituted thiophenes.

Key words: acylation, thiophene, acylsulfonium salt, alkynes, electrophilic addition

In our previous work we found that dimethylacylsulfonium salts formed by the reaction of acyltetrafluoroborates with dimethyl sulfide are useful reagents for the synthesis of unsaturated ketones.[1] Certain types of dimethylacylsulfonium salts are milder reagents than the acylium salts which tend to polymerize olefins. Reaction of acylsulfonium salts with alkenes, acetylenes and dienes proceeds as a conjugate addition of the acyl group and dimethyl sulfide to the unsaturated C-C bond and results in the formation of unsaturated ketones. We used this principle further to propose a new trifluoroacylating reagent a complex of dimethyl sulfide borontrifluoride and trifluoroacetic anhydride.[2]

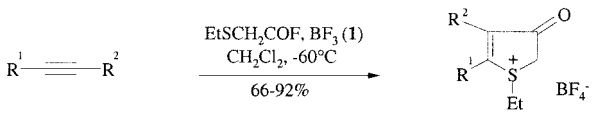
Further work in our group on the intramolecular acylsulfonium salts, resulted in these salts being obtained by the treatment of alkylsulfanyl substituted acyl fluorides with borontrifluoride at –60 °C, significally increased the synthetic applications of acylsulfonium salts.[3] Thus the reactions of β-(ethylsulfanyl)propionyl fluoride·BF_3 complex with alkenes leads initially to the formation of a 6-membered sulfonium salt, which is then converted to the ethylsulfanyl substituted α,β-unsaturated ketone. The complex formed with alkynes gives rise to divinylketones with a sulfide moiety or to the substituted thiapyran-4-ones. Also the complex β-(ethylsulfanyl)propionyl fluoride·BF_3 reacts with various aromatic compounds and could be used for the simple synthesis of aryl vinyl ketones and conjugated thiapyranones.

Synthesis 2001, No. 14, 26 10 2001. Article Identifier:
1437-210X,E;2001,0,14,2124,2128,ftx,en;E03301SS.pdf.

ISSN 0039-7881

The carbonyl group (electrophilic center) linked by two CH_2-groups to the sulfide moiety (nucleophilic center) in the complex β-(ethylsulfanyl)propionyl fluoride·BF_3, made the intramolecular acylsulfonium salts very interesting molecules to study. From this point further investigations of homologous complexes seemed logical.

We have found that the complex ethylsulfanyl acetyl fluoride·BF_3 (**1**) reacts with acetylenes analogously to its homologue, i.e. the reactions proceed as a conjugated addition reaction of acyl and sulfide moeties to the carbon-carbon triple bond. The reaction was carried out in dichloromethane at –60 °C to –40 °C and the cyclic five-membered sulfonium tetrafluoroborates were obtained. They are quite stable pale colored solids or in several cases oils, which can be easily isolated by treatment of the reaction mixture with ether.



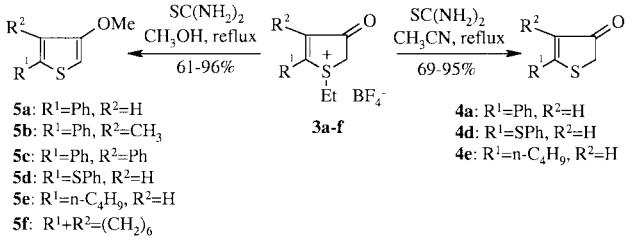
2a: R^1=Ph, R^2=H
2b: R^1=Ph, R^2=CH_3
2c: R^1=Ph, R^2=Ph
2d: R^1=SPh, R^2=H
2e: R^1=n-C_4H_9, R^2=H
2f: R^1+R^2=$(CH_2)_6$

3a: R^1=Ph, R^2=H
3b: R^1=Ph, R^2=CH_3
3c: R^1=Ph, R^2=Ph
3d: R^1=SPh, R^2=H
3e: R^1=n-C_4H_9, R^2=H
3f: R^1+R^2=$(CH_2)_6$

Scheme 1

To investigate a broad range of acetylenes which could undergo reaction with complex **1** we carried out several reactions with a variety of terminal and non-terminal acetylenes **2a–f**, bearing both alkyl and aryl substituents, including cyclooctyne and phenylsulfanyl acetylene. In all cases the formation of five-membered sulfonium salts **3a–f** was observed (Scheme 1). The reactions proceeded regiospecifically, in good yields and without significant amounts of side products forming. Unfortunately, the acetylenes with electron withdrawing substituents could not react with complex **1** in this manner; even the propargyl chloride remained unreacted after several hours at –40 °C due to the deactivating -I-effect.

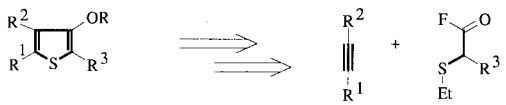
The synthesis of the corresponding thiophene derivatives from the cyclic sulfonium salts was achieved using thiourea as a dealkylating agent. However, after the reaction of **3a** with thiourea in methanol we have isolated the 3-methoxythiophene **5a**, instead of expected thophenone **4a**. Replacing methanol with acetonitrile allowed the isolation of thiophenone **4a** (Scheme 2).



Scheme 2

The observed difference in the reaction products obtained in acetonitrile and methanol proved to be true also for the other sulfonium salts **3a–f**. The products are the derivatives of 3-(2*H*)-thiophenone (**4a, 4d, 4e**) in the first case and 3-methoxythiophenes (**5a–f**) in the second case. The most common and frequently used synthetic methods for substituted 3-hydroxythiophenes is the Fiesselmann condensation and its different modifications.[4] The thiophenes synthesized by those methods usually contain electron withdrawing substituents.

It should also be noted that few examples of the thiophene ring synthesis from the C-C-S and C-C fragments (see Scheme 3) are known at the present time.[5] In our method the C-C-S fragment is derived from the fluoroanhydride of ethylsulfanylacetic acid and the C-C fragment is a triple bond of acetylene.



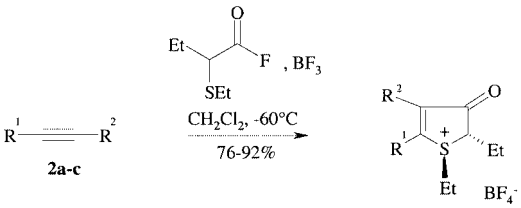
Scheme 3

Thus, we present a new synthetic approach to the thiophene ring construction, the key step of which is the reaction of complex **1** with acetylenes. It opens a simple way to various 4- and 5-substituted 3-(2*H*)-thiophenones and 3-hydroxythiophenes. Both, the first step, acylation of acetylene and the second, dealkylation of the initially formed sulfonium salt, proceed under very mild conditions in good to excellent yields.

It should be mentioned that methods for the synthesis of 3-methoxy(hydroxy)thiophenes essentially allows thiophenes with a substituent in the 2-position, while the preparation of 2-unsubstituted heterocycles needs additional steps. In our case, the reaction of the ethylsulfanyl acetyl fluoride·BF_3 complex (**1**) with acetylenes leads to the 3-methoxy derivatives of thiophenes with an unsubstituted 2-position which is additionally activated by the adjacent methoxy-group and could be easy functionalized with different electrophiles.

We have also shown the possibility of introducing the 2-substituent earlier on, in the synthesis of 3-methoxythiophenes. α-Substituted ethylsulfany acetyl fluoride·BF_3 complex undergoes a reaction with acetylenes, which permits the direct synthesis of thiophene derivatives with a substituent in the 2-position.

To illustrate this last hypothesis we have synthesized the fluoroanhydride of 2-ethylsulfanyl butyric acid. This can be viewed as ethylsulfanyl acetyl fluoride with ethyl in the α-position. 2-Ethylsulfanyl butyroyl fluoride reacts with BF_3 to give complex (**6**), the structure of which seems to be analogous to **1**. It is shown (Scheme 4) that complex **6** reacts with acetylenes with the formation of the cyclic sulfonium salts (**7a–c**).



Scheme 4

According to NMR data (^{1}H and ^{13}C), the reaction proceeds diastereospecifically with only one diastereomer of sulfonium salts **7a-c** obtained. In the case of sulfonium salt **7a** the structure was secured by means of X-ray analysis (Figure), with the ethyl-substituents in the *trans*-position relatively to each other.

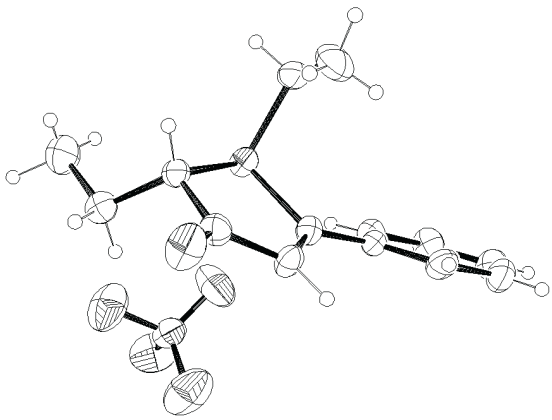
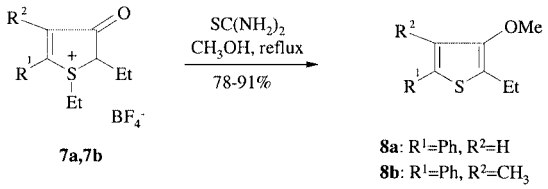


Figure Crystal structure of sulfonium salt **7a**

The dealkylation of sulfonium salts **7a**,**7b** occured in methanol yielding the 2-ethyl-3-methoxy derivatives of thiophene (Scheme 5). 2,3,5-Trisubstituted thiophene (**8a**) was synthesized from phenylacetylene, and the reaction of complex **6** with 1-phenylpropyne-1 furnished the tetra-substituted thiophene (**8b**).



7a,7b

8a: R^1=Ph, R^2=H
8b: R^1=Ph, R^2=CH_3

Scheme 5

Thus, we have proposed a new simple two-step synthetic approach to thiophenes, based on the reaction of boron trifluoride complexes of α-alkylsulfanyl substituted carboxylic acids fluoroanhydrides with acetylenes, which allows the synthesis of various 3-oxygen substituted thiophenes bearing both heteroatoms, alkyl and aryl groups.

Melting points were determined in sealed capillaries. NMR spectra were recorded on Varian VXR-400 and Bruker AM 400C spectrometers in CD_3CN or CD_2Cl_2 for sulfonium salts (**3a-f**, **7a,7b**), $CDCl_3$ for thiophenes (**5a-f, 8a,8b**) and thiophenones (**4a,4d,4e**) and CD_3Cl/CF_3COOH (1/1) for salt **7c** with TMS as an internal standard. The IR spectra were obtained with UR-20 spectrometer. Column chromatography was performed on silica gel (63-200 mesh, Merck). All solvents used were dried and distilled according to the standard procedures. Ethylsulfanylacetyl fluoride was prepared according to the literature procedure from thioglycolic acid (Merck).

X-ray Structural Analysis (7a):
Empirical formula $C_{14}H_{17}BF_4OS$, formula weight 320.15, orthorhombic, space group $Pna2_1$, wavelength 0.71073 Å, a = 13.486 (3), b = 13.592 (4), 8.493 (1) Å, V = 1554.7 (6) $Å^3$, Z = 4, density (calculated) 1.368 mg/m^3, Reflections collected: 2413, Unique: 2305, R1 = 0.051. Crystallographic data (excluding structure factors) for the structure have been deposited at the Cambridge Crystallographic Data Centre CCDC 163723.

Sulfonium Salts (3); General Procedure
A well-stirred solution of ethylsulfanylacetyl (α-ethylsulfanyl butyroyl) fluoride (0.02 mol) in CH_2Cl_2 (40 mL) was saturated by gaseous BF_3 at –60 °C. A solution of acetylene (0.02 mol) in CH_2Cl_2 (10 mL) was added dropwise. After stirring for 15 min at –40 °C the temperature was allowed to rise to 0 °C and the mixture was stirred for 2 h at this temperature. The reaction mixture was poured into anhyd Et_2O (80 mL). The precipitated sulfonium salt was collected by vacuum filtration, washed with anhyd Et_2O (20 mL), cold MeOH (10 mL), anhyd Et_2O (30 mL) and dried in vacuo.

3-Methoxythiophenes (5); General Procedure
To a solution of sulfonium salt (0.003 mol) in MeOH (15 mL), thiourea (2.3 g, 0.03 mol) and $HClO_4$ (1 mL of 70% aq solution) were added. After 2–24 h (monitored by TLC) at reflux the reaction mixture was poured onto H_2O (100 mL) and extracted with CH_2Cl_2 (4 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated at reduced pressure. The crude product was purified by column chromatography (EtOAc–hexane, 9:1).

3-(2*H*)- Thiophenones 4; General Procedure
The procedure is the same as for 3-methoxythiophenes, except CH_3CN is used as solvent.

3-Oxo-5-phenyl-1-ethyl-2,3-dihydrothiopheniumTetrafluoroborate (3a)
Yield 72%; mp 128–130 °C (dec).

IR (Nujol): 1730, 1610 cm^{-1}.

^{1}H NMR: δ = 7.56–7.31 (m, 5 H), 7.19 (s, 1 H), 4.15 (d, 1 H, *J* = 17.5 Hz), 3.93 (d, 1 H, *J* = 17.5 Hz), 3.42–3.18 (m, 2 H), 1.27 (t, 3 H, *J* = 7.2 Hz).

^{13}C NMR: δ = 192.89, 158.37, 133.82, 130.93, 129.58, 127.39, 126.67, 42.03, 39.01, 7.09.

Anal. Calcd for $C_{12}H_{13}BF_4OS$: C, 49.34; H, 4.49. Found: C, 49.25; H, 4.36.

5-Phenyl-3-(2*H*)-thiophenone (4a)
Yield 69%; mp 75–77 °C, lit.[6] mp 78 °C.

IR (Nujol): 3100–3450, 1700, 1680 cm^{-1}.

^{1}H NMR: ketone: δ = 7.51–7.22 (m, 5 H), 6.36 (s, 1 H), 3.61 (s, 2 H); enol: δ = 6.86 (s, 1 H), 6.11 (s, 1 H); ketone–enol, 10:1.

^{13}C NMR: ketone: δ = 201.22, 177.30, 131.07, 127.41, 124.97 123.60, 116.79, 38.54; enol: δ = 153.27, 131.07, 127.16, 125.83, 123.60, 114.34, 97.41.

Anal Calcd for $C_{10}H_8OS$: C, 68.15; H, 4.58. Found: C, 68.18; H, 4.44.

4-Methoxy-2-phenylthiophene (5a)
Yield 61%; oil.

^{1}H NMR: δ = 7.61–7.28 (m, 5H), 7.03 (d, 1 H, *J* = 1.8 Hz), 6.23 (d, 1 H, *J* = 1.8 Hz), 3.79 (s, 3 H).

^{13}C NMR δ = 158.63, 142.86, 134.27, 128.78, 127.72, 125.44, 115.32, 96.19, 57.14.

Anal Calcd for $C_{11}H_{10}OS$: C, 69.44; H, 5.30. Found: C, 69.30; H 5.38.

4-Methyl-3-oxo-5-phenyl-1-ethyl-2,3-dihydrothiopheniumTetrafluoroborate (3b)
Yield 77%; oil.

IR (Nujol): 1720, 1620 cm^{-1}.

^{1}H NMR: δ = 7.69–7.66 (m, 5 H), 4.39 (d, 1 H, *J* = 17.8 Hz), 4.21 (d, 1 H, J = 17.8 Hz), 3.53–3.30 (m, 2 H), 2.15 (s, 3 H), 1.20 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR: 193.93, 150.61, 143.60, 133.22, 130.56, 129.14, 128.53, 42.17, 39.86, 12.70, 8.65.

Anal Calcd for: $C_{13}H_{15}BF_4OS$: C, 51.01; H, 4.94. Found: C, 49.86; H, 5.10.

3-Methyl-4-methoxy-2-phenylthiophene (5b)
Yield 84%; mp 41–43 °C.

^{1}H NMR: δ = 7.45–7.24 (m, 5 H), 6.16 (s, 1 H), 3.82 (s, 3 H), 2.15 (s, 3 H).

^{13}C NMR: δ = 157.07, 136.86, 135.06, 128.73, 128.45, 127.30, 124.83, 94.53, 56.92, 11.68.

Anal Calcd for $C_{12}H_{12}OS$: C, 70.58; H, 5.88. Found: C, 70.97; H, 5.80.

3-Oxo-4,5-diphenyl-1-ethyl-2,3-dihydrothiopheniumTetrafluoroborate (3c)
Yield 80%; mp 149–153 °C (dec.).

IR (Nujol): 1720, 1620 cm^{-1}.

^{1}H NMR: δ = 7.61–7.09 (m, 10 H), 4.62 (d, 1 H, *J* = 17.9 Hz), 4.40 (d, 1 H, *J* = 17.9 Hz), 3.56–3.29 (m, 2 H), 1.19 (t, 3 H, *J* = 7.2 Hz).

^{13}C NMR: δ = 193.15, 153.41, 144.38, 133.67, 131.74, 131.57, 130.77, 130.24, 129.93, 129.66, 128.85, 43.51, 40.57, 9.08.

Anal Calcd for: $C_{18}H_{17}BF_4OS$: C, 58.72; H, 4.65; Found: C, 58.40; H, 4.70.

4-Methoxy-2,3-diphenylthiophene (5c)
Yield 79%; mp 108–111 °C.

^{1}H NMR: δ = 7.38–7.21 (m, 10 H), 6.35 (s, 1 H), 3.75 (s, 3 H).

^{13}C NMR: δ = 161.41, 139.00, 134.72, 134.31, 130.44, 129.59, 128.89, 128.26, 128.03, 127.33, 127.00, 95.62, 57.15.

Anal Calcd for $C_{17}H_{14}OS$: C, 76.66; H, 5.30. Found: C, 76.69; H, 5.24.

3-Oxo-5-(phenylsulfanyl)-1-ethyl-2,3-dihydrothiopheniumTetrafluoroborate (3d)
Yield 92%; mp 89–92 °C.

IR (Nujol): 1720 cm^{-1}.

^{1}H NMR: δ = 7.72–7.45 (m, 5 H), 6.39 (s, 1 H), 4.45 (d, 1 H, *J* = 17.6 Hz), 4.17 (d, 1 H, *J* = 17.6 Hz), 3.84–3.56 (m, 2 H), 1.46 (t, 3 H, *J* = 7.2 Hz).

^{13}C NMR: δ = 190.46, 164.06, 135.02, 132.50, 131.28, 130.25, 125.85, 43.94, 40.61, 7.81.

Anal Calcd for $C_{12}H_{13}BF_4OS_2$: C, 44.46; H, 4.04. Found: C, 44.87; H, 4.23.

5-(Phenylsulfanyl)-3(2*H*)-thiophenone (4d)
Yield 70%; oil.

IR (Nujol): 1680, 1660 cm^{-1}.

^{1}H NMR: δ = 7.62–7.33 (m, 5 H), 5.86 (s, 1 H), 3.62 (s, 2 H).

^{13}C NMR: δ = 198.65, 183.45, 135.28, 130.77, 129.57, 127.56, 117.12, 41.41.

Anal Calcd for $C_{10}H_8OS_2$: C, 57.66; H, 3.87. Found: C, 57.91; H, 4.06.

4-Methoxy-2-(phenylsulfanyl)-thiophene (5d)
Yield 84%, oil.

^{1}H NMR: δ = 7.28–7.12 (m, 5 H), 6.92 (d, 1 H, *J* = 2.0 Hz), 6.33 (d, 1 H, *J* = 2.0 Hz), 3.75 (s, 3 H).

^{13}C NMR: δ = 157.81, 137.86, 130.78, 128.94, 127.50, 127.09, 126.25, 102.37, 57.07.

Anal Calcd for $C_{11}H_{10}OS_2$: C, 59.43; H, 4.53. Found: C, 59.20; H, 4.77.

5-Butyl-3-oxo-1-ethyl-2,3-dihydrothiopheniumTetrafluoroborate (3e)
Yield 76%; oil.

IR (Nujol): 1730, 1610 cm^{-1}.

^{1}H NMR: δ = 6.92 (s, 1 H), 4.16 (d, 1 H, *J* = 18.0 Hz), 4.02 (d, 1 H, *J* = 18.0 Hz), 3.70–3.51 (m, 2 H), 2.81–2.60 (m, 2 H), 1.79–1.58 (m, 2 H), 1.50–1.35 (m, 2 H), 1.32 (t, 3 H, *J* = 7.2 Hz), 0.92 (t, 3 H, *J* = 7.2 Hz).

^{13}C NMR δ = 195.08, 165.65, 135.80, 43.10, 39.98, 31.33, 30.15, 22.62, 13.19, 8.64.

Anal Calcd for $C_{10}H_{17}BF_4OS$: C 44.14, H 6.30; Found: C 43.88, H 6.21.

5-Butyl-3-(2*H*)-thiophenone (4e)
Yield 95%; oil.

IR (Neat): 1690, 1660 cm^{-1}.

^{1}H NMR: 6.01 (br s, 1 H), 3.62 (s, 2 H), 2.65–2.55 (m, 2 H), 1.7–1.5 (m, 2 H), 1.45–1.25 (m, 2 H), 0.9 (t, 3 H, *J* = 7.2 Hz).

^{13}C NMR: 202.82, 185.73, 120.69, 40.67, 33.50, 30.51, 22.08, 13.61.

Anal Calcd for $C_8H_{12}OS$: C, 61.50; H, 7.74. Found: C, 61.24; H, 7.73.

2-Butyl-4-methoxythiophene (5e)
Yield 96%; n_D^{16} 1.4110.

^{1}H NMR: δ = 6.48 (s, 1 H), 6.03 (s, 1 H), 3.78 (s, 3 H), 2.8–2.6 (m, 2 H), 1.73–1.55 (m, 2 H), 1.51–1.25 (m, 2 H), 0.93 (t, 3 H, *J* = 7.2 Hz).

^{13}C NMR: δ = 157.64, 144.95, 116.61, 93.57, 56.94, 33.38, 30.21, 22.14, 13.80.

Anal Calcd for $C_9H_{14}OS$: C, 63.49; H, 8.29. Found: C, 63.13; H, 7.98.

3-Oxo-1-ethyl-2,3,4,5,6,7,8,9-Octahydrocycloocta-[*b*]-thiophenium Tetrafluoroborate (3f)
Yield 85%, mp 110-112 °C.

IR (Nujol): 1720, 1630 cm^{-1}.

^{1}H NMR: δ = 4.54 (d, 1 H, *J* = 18.4 Hz), 4.29 (d, 1 H, *J* = 18.4 Hz), 4.02–3.70 (m, 2 H), 3.13–2.69 (m, 4 H), 2.19–1.65 (m, 8 H), 1.58 (t, 3 H, *J* = 7.4 Hz).

^{13}C NMR: 193.39, 155.17, 149.11, 41.95, 38.60, 29.11, 28.38, 27.75, 25.53, 25.51, 27.78, 8.44. Anal Calcd for $C_{12}H_{19}BF_4OS$: C, 48.34; H, 6.42. Found: C, 48.01; H, 6.36.

3-Methoxy-4,5,6,7,8,9-hexahydrocycloocta-[*b*]-thiophene (5f)
Yield 92%, oil.

^{1}H NMR: δ = 5.96 (s, 1 H), 3.80 (s, 3 H), 2.81–2.67 (m, 4 H), 1.70–1.35 (m, 8 H).

^{13}C NMR: δ = 156.06, 137.48, 129.38, 92.26, 57.10, 31.96, 29.35, 27.79, 26.07, 25.50, 23.51.

Anal Calcd for$C_{11}H_{16}OS$: C, 67.30; H, 8.21. Found: C, 67.55; H, 7.95.

3-Oxo-5-phenyl-1,2-diethyl-2,3-dihydrothiophenium Tetrafluoroborate (7a)
Yield 82%; mp 153–156 °C (dec).

IR (Nujol): 1720, 1610 cm^{-1}.

^{1}H NMR: δ = 7.90–7.45 (m, 5 H), 7.40 (s, 1 H), 4.48 (dd, 1 H, *J* = 5.4, 8.2 Hz), 3.70–3.46 (m, 2 H), 2.35–2.05 (m, 2 H), 1.23 (t, 3 H, *J* = 7.2 Hz), 1.11 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR: δ = 196.36, 158.28, 135.52, 132.75, 131.56, 129.17, 128.14, 63.21, 41.26, 23.62, 11.74, 9.18.

Anal Calcd for $C_{14}H_{17}BF_4OS$: C, 52.52; H, 5.35. Found: C, 52.77; H, 5.51.

4-Methyl-3-oxo-5-phenyl-1,2-diethyl-2,3-dihydrothiophenium-Tetrafluoroborate (7b)
Yield 76%; mp 123–126 °C (dec).

IR (Nujol): 1710, 1630 cm^{-1}.

^{1}H NMR: δ = 7.70–7.55 (m, 5 H), 4.48 (dd, 1 H, *J* = 4.8, 7.3 Hz), 3.52–3.45 (m, 2 H), 2.50–2.14 (m, 2 H), 2.14 (s, 3 H), 1.24 (t, 3 H, *J* = 7.1 Hz), 1.12 (t, 3 H, *J* = 7.2 Hz).

^{13}C NMR: δ = 195.23, 149.07, 143.86, 133.21, 130.42, 129.08, 127.89, 62.59, 40.60, 22.85, 13.06, 11.34, 9.33.

Anal Calcd for $C_{15}H_{19}BF_4OS$: C, 53.91; H, 5.73. Found: C, 54.12; H, 5.82.

3-Oxo-4,5-diphenyl-1,2-diethyl-2,3-dihydrothiopheniumTetrafluoroborate (7c)
Yield 92%; mp 205–210 °C (dec).

IR (Nujol): 1720, 1620 cm^{-1}.

^{1}H NMR: δ = 7.39–7.20 (m, 10 H), 4.48 (m, 1 H), 3.42–3.24 (m, 2 H), 2.33–2.04 (m, 2 H), 1.14 (t, 3 H, *J* = 7.2 Hz), 0.98 (t, 3 H, *J* = 7.2 Hz).

^{13}C NMR: δ = 194.64, 150.60, 143.67, 133.82, 131.03, 130.37, 129.50, 129.21, 129.04, 128.00, 127.06, 63.34, 40.29, 22.97, 10.80, 8.55.

Anal Calcd for $C_{20}H_{21}BF_4OS$: C, 60.62; H, 5.34. Found: C, 60.27; H, 5.55.

3-Methoxy-5-phenyl-2-ethylthiophene (8a)
Yield 78%; oil.

^{1}H NMR: δ = 7.55–7.20 (m, 5 H), 7.03 (s, 1 H), 3.84 (s, 3 H), 2.75 (q, 2 H, *J* = 7.5 Hz), 1.24 (t, 3 H, *J* = 7.5 Hz).

^{13}C NMR: δ = 153.10, 137.74, 134.69, 128.70, 127.07, 124.90, 124.03, 112.90, 59.01, 19.19, 15.57. Anal Calcd for $C_{13}H_{14}OS$: C, 71.52; H, 6.46. Found: C, 71.18; H, 6.62.

3-Methyl-4-methoxy-2-phenyl-5-ethylthiophene (8b)
Yield 91%; oil.

^{1}H NMR: δ = 7.50–7.20 (m, 5 H), 3.79 (s, 3 H), 2.82 (q, 2 H, *J* = 7.6 Hz), 2.21 (s, 3 H), 1.31 (t, 3 H, *J* = 7.6 Hz).

^{13}C NMR: δ = 152.38, 135.29, 129.48, 129.43, 128.75, 127.38, 126.87, 100.13, 61.25, 19.55, 15.57, 12.24.

Anal Calcd for $C_{14}H_{16}OS$: C, 72.37; H, 6.94. Found: C, 72.33; H, 7.11.

Acknowledgement

Financial support from Russian Fundamental Investigation Foundation (Grant N 00-03-32763a) is gratefully acknowledged.

References

(1) (a) Vertelezkij, P. V.; Balenkova, E. S. *Zh. Org. Khim.* **1990**, *26*, 2446. (b) Vertelezkij, P. V.; Nenajdenko, V. G.; Balenkova, E. S. *Vestnik MGU. Ser. 2. Khim.* **1996**, 540. (c) Nenajdenko, V. G.; Lebedev, M. V.; Shevchenko, N. E.; Balenkova, E. S. *Zh. Org. Khim.* **1998**, *34*, 1026. (d) Kiselyov, A.; Harvey, R. *Tetrahedron Lett.* **1995**, *36*, 4005.
(2) (a) Nenajdenko, V. G.; Balenkova, E. S. *Zh. Org. Khim.* **1992**, *28*, 600. (b) Nenajdenko, V. G.; Balenkova, E. S. *Zh. Org. Khim.* **1993**, *29*, 687. (c) Nenajdenko, V. G.; Leshcheva, I. F.; Balenkova, E. S. *Tetrahedron* **1994**, *50*, 775. (d) Nenajdenko, V. G.; Gridnev, I. D.; Balenkova, E. S. *Tetrahedron* **1994**, *50*, 11023. (e) Nenajdenko, V. G.; Balenkova, E. S. *Tetrahedron* **1994**, *50*, 12407. (f) Nenajdenko, V. G.; Sanin, A. V.; Balenkova, E. S. *Zh. Org. Khim.* **1994**, *30*, 531.
(3) (a) Nenajdenko, V. G.; Lebedev, M. V.; Balenkova, E. S. *Tetrahedron Lett.* **1995**, *36*, 6317. (b) Nenajdenko, V. G.; Lebedev, M. V.; Balenkova, E. S. *Synlett* **1995**, 1133. (c) Lebedev, M. V.; Nenajdenko, V. G.; Balenkova, E. S. *Tetrahedron* **1998**, 5599. (d) Lebedev, M. V.; Nenajdenko, V. G.; Balenkova, E. S. *Synthesis* **1998**, 89.
(4) Lissavetzky, J.; Manzanares, I. *Heterocycles* **1996**, *43*, 775.
(5) Coppola, G. M.; Damon, R. E.; Yu, H. *J. Heterocyclic Chem.* **1996**, *33*, 687.
(6) Kosak, A. I.; Palchak, R. J. F.; Steele, W. A.; Selwitz, C. M. *J. Am. Chem. Soc.* **1954**, *76*, 4450.