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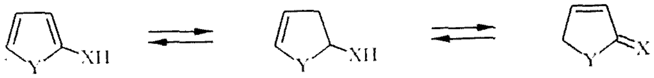
SYNTHESIS AND AUTOCONVERSIONS OF FURANTHIOLS AND -SELENOLS

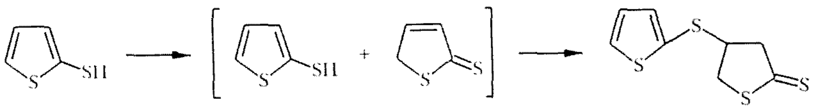
V. Yu. Vvedenskii, E. D. Shtefan, R. N. Malyushenko and É. N. Deryagina

Furanthiols and -selenols have been synthesized by a modified procedure via organolithium derivatives, with the formation of trimethylsilyl ethers as intermediate products. It has been shown that the thiols as well as the selonols undergo autoconversions when standing in air and in the presence of triethylamine with the formation of furylthio-(seleno)-substituted thio-(seleno)-butyrolactones.

It is known that potential 2-hydroxy derivatives of furan, thiophene, and selenophene exist predominantly in the form of unsaturated lactones; on the other hand, for the corresponding thiols no tautomerism has been observed by physicochemical methods in the liquid or in the gaseous phase, or in solutions (IR and PMR spectroscopic data, ionization potentials, and dipole moments were used) [1].



However, the tautomeric form of 2-thiophenethiol has been determined chemically in its autothiylation to 4-(2-thienylthio)tetrahydrothiophene-2-thione [2, 3]:

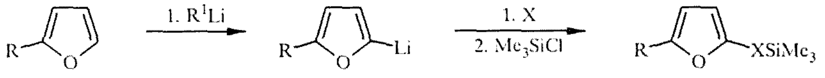


A similar reaction can also take place with 2-thiopheneselenol; however, the C=Se fragment is reduced by the unreacted selenol to the methylene group [4].

Based on the above findings it was of interest to study the analogous autoconversions of 2-furanthiols and -selenols.

5-Methyl-2-furanthiol was prepared for the first time in [1] with a yield of 40% by the subsequent treatment of sylvan with n-butyllithium, sulfur, and an acid. 2-Furanthiol and -selenol were synthesized in the same way [5] by the reaction of furan with phenyllithium, sulfur (selenium), and an acid. The first was obtained in trace quantities; its conversion to a yellow oil was observed when standing in air during the night. The selenol could not be separated.

The low stability of the furanthiols and -selenols forced us to alter the scheme of the synthesis. The basis of the proposed scheme was the treatment of the thiolates and selenolates of lithium with trimethylchlorosilane instead the acid. This made it possible to separate the corresponding thiols and selenols in the form of the stable trimethylsilyl ethers I:



Ia–d

Ia,c R^1 = Ph; Ib,d R^1 = Bu; a R = H, X = S; b R = Me, X = S;
c R = H, X = Se; d R = Me, X = Se

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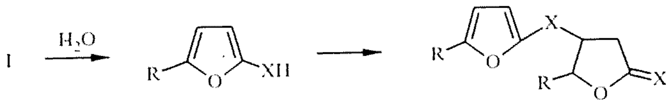
The actual thiols and selenols were then obtained by the hydrolysis of the ethers I by the stoichiometric amount of water. The furanthiols were yellow, while the selenols were bright-red; in the latter case this indicated the presence of their tautomeric forms in the mixture (compounds containing the C=Se group are brightly colored, while for instance selenophenol is virtually colorless). However, the PMR spectra contained only the signals of the selenol form.

The thiols IIa, b and selenols IIc, d are converted instantly to the corresponding dimers III in the presence of catalytic amounts of triethylamine. In the absence of a catalyst the thiols are dimerized completely in about 24 h, the selenols in 1 h.



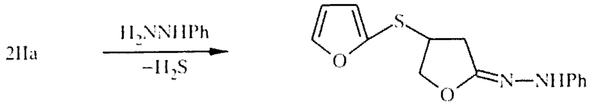
II

III

The position of the equilibrium in the monomer–dimer system for 2-thiophenethiol is such, that the concentration of the monomeric thiol is equal only to a few percent [2]. Besides this, the formation of 4-(2-thienylthio)-tetrahydrothiophene-2-thiol is accompanied by the formation of 2,2'-dithienyl sulfide. 5-methyl-2-thiophenethiol does not form a dimer even in the presence of triethylamine. However, in the instance of furanthiols IIa, b the autothiylation proceeds spontaneously and is not accompanied by side processes. Its equilibrium is strongly shifted toward dimer formation, since no free thiols were detected in the PMR spectra. The strong shift of the thiol ⇄ dimer equilibrium to the right side evidently also explains the relative stability of the 4-(2-furylseleno)tetrahydrofuran-2-selenones IIIc, d: the absence of free selenol in the reaction mixture prevents the reduction of the C=Se group to CH_2 (see above).

Thus, the 2-furanchalcogenols are more inclined to autoconversions into the dimers III than their thiophene analogs.

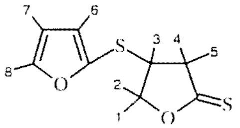
The reaction of 2-furanthiol with phenylhydrazine also proceeds much more easily than in the instance of 2-thiophenethiol [6]:



IV

Although the analogous reaction of 2-furanselenol IIc proceeds extremely vigorously, it does not lead to compound IV, but is accompanied by the formation of unsaturated compounds (signals at 6.98, 5.23, and 4.48 ppm in the PMR spectrum). We intend to investigate further this reaction.

In the PMR spectra of the dimers III all five protons of the tetrahydrofuran fragment are magnetically noequivalent, due to the nonplanar structure of the ring and the presence in it of an asymmetrical center; this manifests itself in the spectrum in the form of combinations: d.d (5-H), d.d (4-H), m (3-H), d.d (20H), d.d (1-H) (in the order of increasing δ):



Thanks to the presence of a methyl group the dimers IIIb,d can exist as cis- and trans-forms; however, only one of them is formed preferably, while the content of the other does not exceed 5%.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra (if not indicated otherwise) were recorded on a Bruker WP-200 SV spectrometer, the GC–MS spectra on a LKB-2091 instrument (70 eV, capillary column 25 m, coated with SE-30, temperature program from 135-240°C, 8 deg/min).

2-Trimethylsilylthiofuran (Ia, $C_7H_{12}OSSi$). A solution of 0.3 mole PhLi in 200 ml ether is treated dropwise with 10 g (0.147 mole) furan and the mixture refluxed for 4 h. It is then cooled to −60°C and treated with 4.48 g (9.14 mole) of sulfur, and the temperature allowed slowly to rise to room temperature. A strong thickening of the mixture is observed already at −25°C, caused by the precipitation of lithium furylthiolate. After the addition of 16.3 g (0.15 mole) Me_3SiCl (at −30°C) the mixture is allowed to stand overnight. Evaporation of the ether, filtration, and vacuum distillation (bp 65-70°C/15 mm Hg) yielded 13.6 g (54%) of compound Ia. PMR spectrum (JEOL FX-90 spectrometer, $CDCl_3$): 0.29 (9H, $SiMe_3$), 6.31 (1H, 3-H), 6.31 (1H, 4-H), 7.41 (1H, 5-H).

5-Methyl-2-trimethylsilylthiofuran (Ib, $C_8H_{14}OSSi$). A solution of n-BuLi (0.12 mole) in 100 ml ether is cooled to −5°C and treated during 15 min with 9.8 g (0.12 mole) freshly distilled sylvan. The cooling is stopped and the mixture refluxed for 4 h; the mixture is cooled again to −5°C and treated during 30 with 3.8 g sulfur. The mixture is refluxed for 1 h to dissolve the sulfur, cooled to −5°C, treated with 14 g (0.13 mole) Me_3SiCl, and again refluxed for 1 h. The ether is then evaporated and the mixture distilled in vacuum after filtration. Yield 7 g (31%) of compound Ib (bp 67-72°C at 7 mm Hg), n_D 1.4960. PMR spectrum ($CDCl_3$): 0.28 (9H, s, SiMe), 2.24 (3H, 5-Me), 5.91 (1H, 4-H), 6.18 (1H, 3-H). Mass spectrum (m/z (fragment, I_{rel}, %)): 186 (M^+, 44) 73 (Me_3Si, 100).

2-Trimethylsilylselenofuran (Ic, $C_7H_{12}OSeSi$). A solution of 0.125 mole PhLi in 200 ml ether is treated dropwise with 8.78 g (0.125 mole) of furan and the mixture refluxed for 4 h; it is then cooled to −60°C and treated with 9.87 g (0.125 mole) selenium; the temperature is slowly raised to room temperature and the solution refluxed again for 30 min. A precipitate of lithium 2-furylselenolate is formed. After the addition of 14.2 g (0.13 mole) Me_3SiCl (−30°C) the mixture is allowed to stand overnight. Evaporation of the ether, filtration, and distillation in vacuum (bp 71.5-80°C at 11 mm Hg) gives 11.75 g of compound Ic (55%). PMR spectrum (JEOL FX-90 spectrometer, $CDCl_3$): 0.36 (9H, $SiMe_3$), 6.34 (1H, 3-H), 6.34 (1H, 4-H), 7.45 (1H, 5H).

5-Methyl-2-trimethylselenofuran (Id, $C_8H_{14}OSeSi$) is obtained in the same way as compound Ib, yield 43%; bp 75-77°C at 7 mm Hg. PMR spectrum ($CDCl_3$): 0.36 (9H, $SiMe_3$), 2.26 (3H, 5-Me), 5.86 (1H, d, J = 2.9, 4-H), 6.24 (1H, d, J = 2.9, 3-H). Mass spectrum: 234 (M^+, 11) 161 (M^+, $SiMe_3$, 7), 73 ($SiMe_3$, 100).

2-Furanthiol (IIa, C_4H_4OS) is obtained in a mixture with hexamethyldisiloxane by the hydrolysis of compound Ia with the stoichiometric amount of water with quantitative yield. PMR spectrum (acetone, D_6): 4.24 (1H, s, SH), 6.42 (1H, d.d, $J_{3,4}$ = 3.3, $J_{4,5}$ = 2.0 Hz, 4-H), 6.5 (1H, d.d, $J_{3,5}$ = 1.0, 3-H), 7.59 (1H, d.d, 5-H).

5-Methyl-2-furanthiol (IIb, C_5H_6OS) is obtained in a mixture with hexamethyldisiloxane with quantitative yield by hydrolysis with the stoichiometric amount of water in the presence of a catalytic amount of HCl (0.01 N solution). PMR spectrum ($CDCl_3$): 2.24 (3-H, m, 5-Me), 3.41 (1H, d.d, $J_{Ch,3}$ = 1.9, $J_{SH,5}$ = 1.0 Hz, SH), 5.94 (1H, d.d, J_{34} = 3.0, J_{45} = 1.0 Hz, 4-H), 6.38 (1H, m, J_{35} = 0.4 Hz, 3-H). Mass spectrum: 114 (M^+, 100), 113 (M^+ -H, 39).

2-Furanselenol (IIc, C_4H_4OSe) is obtained in the same way as compound IIa. PMR spectrum ($CDCl_3$): 1.68 (1H, s, SH), 6.35 (1H, d.d, $J_{3,4}$ = 3.4, J_{45} = 2.0 Hz, 4-H), 6.55 (1H, d.d, J_{35} = 1.0 Hz, 3-H), 7.50 (1H, d.d, 5-H).

5-Methyl-2-furanselenol (IId, C_5H_6OSe) is obtained in the same way as compound IIb. PMR spectrum ($CDCl_3$): 1.53 (1H, SeH), 2.1 (3H, 5-Me), 5.94 (1H, 4-H), 6.44 (1H, 3-H).

4-(2-Furylthio)tetrahydrofuran-2-thion (IIIa, $C_8H_8O_2S_2$). A small amount (1 g or 0.0058 mole) of compound Ia is treated with 52 μl (0.029 mole) of water and a catalytic amount of triethylamine. A violent reaction (hydrolysis and autothiylation) is observed. The mixture separates into layers, whereby the upper layer represents hexamethyldisiloxane and the lower layer (a viscous liquid) represents compound IIIa. Based on the PMR spectrum the yield is virtually quantitative. PMR spectrum (JEOL FX-90 spectrometer, $CDCl_3$): 4.62 (1H, d.d, J_{12} = 10.2, J_{13} = 5.3 Hz, 1-H), 4.85 (1H, d.d, J_{21} = 10.2, J_{23} = 6.3 Hz, 2-H), 3.84 (1H, m, 3-H), 3.03 (1H, d.d, J_{43} = 6.0, J_{45} = 19.0 Hz, 4-H), 3.37 (1H, d.d, J_{53} = 7.9, J_{54} = 19.0 Hz, 5-H), 6.66 (1H, d.d, J_{67} = 3.3, J_{68} = 1.0 Hz, 6-H), 6.41 (1H, d.d, J_{76} = 3.3, J_{78} = 2.0 Hz, 7-H), 7.57 ppm (1H, d.d, J_{86} = 1.0 Hz, J_{87} = 2.0 Hz, 8-H). The reverse reaction (formation of furanthiol) is observed when attempting to distil the obtained compound in vacuum.

4-(5-Methyl-2-Furylthio)-5-methyltetrahydrofuran-2-thion (IIIb, $C_{10}H_{12}O_2S_2$) is prepared in the same way as compound IIIa; bp 145-147°C at 1 mm Hg. PMR spectrum (acetone, D_6): 1.47 (3H, d, J = 65 Hz, 1-CH_3), 4.88 (1H, d.d, J_{21} = J_{23} = 6.55 Hz, 2-H), 3.5 (1H, m, 3-H), 3.02 (1H, d.d, J_{45} = 22.0, J_{43} = 6 Hz, 4-H), 3.5 (1H, d.d, J_{53} = 10.0, J_{54} = 22.0 Hz, 5-H), 6.67 (1H, d, J_{67} = 3.2 Hz, 6-H), 6.12 (1H, d, J_{76} = 3.2 Hz, 7-H), 2.28 ppm (3H, s, 8-CH_3), ^{13}C NMR spectrum ($CDCl_3$): 218.78 (C=S), 157.48 ($C_{(8)}$), 138.16 ($C_{(6)}$) = CO), 122.56 ($C_{(6)}$), 108.18 ($C_{(7)}$), 90.30 ($C_{(3)}$), 50.37 and 49.79 ($C_{(2)}$), and $C_{(4)}$), 18.64 (1-CH_3), 14.09 ppm (8-CH_3). Mass spectrum 228 (M^+, 53%), 113 (5-methylfuryl-2-S^+, 100%).

4-(2-Furylseleno)tetrahydrofuran-2-selenone (IIIc, $C_8H_8O_2Se_2$) is obtained in the same way as compound IIIa. PMR spectrum (acetone, D_6): 4.73 (1H, d.d, J_{12} = 10.4, J_{13} = 4.6 Hz, 1-H), 5.06 (1H, d.d, J_{21} = 10.4, J_{23} = 6.4 Hz, 2-H), 4.12 (1H, m, 3-H), 2.85 (1H, d.d, J_{43} = 4.9, J_{45} = 19.8 Hz, 4-H), 3.16 (1H, d.d, J_{53} = 7.6, J_{54} = 19.8 Hz, 5-H), 6.81 (1H, d.d, J_{76} = 3.4, J_{78} = 2.1 Hz, 7-H), 7.75 ppm (1H, d.d, J_{86} = 0.9, J_{87} = 2.1 Hz, 7-H), 7.75 ppm (1H, d.d, J_{86} = 0.9, J_{87}

= 2.1 Hz, 8-H). ^{13}C NMR spectrum (JEOL FX-90, $CDCl_3$): 227.91 (C=Se), 147.20, 134.72, 121.84, 111.44 (4 arom. carbon atoms), 84.12, 57.00, 35.55 ppm (aliphatic carbon atoms).

4-(5-Methyl-2-furylseleno)-5-methyltetrahydrofuran-2-selenone (IIId, $C_{10}H_{12}O_2Se_2$) is prepared in the same way as compound IIIa. PMR spectrum ($CDCl_3$): 1.6 (3H, d, J = 6.5 Hz, 1-CH_3), 4.78 (1H, d.d, J_{21} = 6.5, J_{23} = 8.5 Hz, 2-H), 3.20 (1H, m, 3-H), 2.50 (1H, d.d, J_{43} = 10.0, J_{45} = 19.0 Hz, 4-H), 3.37 (1H, d.d, J_{53} = 8.0, J_{54} = 19.0 Hz, 5-H), 6.59 (1H, d, J_{67} = 3.0 Hz, 6-H), 6.00 (1H, d, J_{76} = 3.0 Hz, 7-H), 2.32 ppm (3H, s, 8-CH_3).

4-(2-Furylthio)-2-phenylhydrazonotetrahydrofuran (IV, $C_{14}H_{14}N_2O_2$). A sample of 0.48 g (2.8 mmole) of ether Ia is treated with 25 μl (1.4 mmole) water and 0.14 g (1.4 mmole) phenylhydrazine. The violent reaction leads to the formation of a light-yellow crystalline substance. PMR spectrum (Varian VXR-500 spectrometer, acetone, D_6): 4.22 (1H, d.d, J_{12} = 9.4, J_{13} = 4.2 Hz, 1-H), 4.56 (1H, J_{21} = 9.4, J_{23} = 5.9 Hz, 2-H), 3.94 (1H, m, 3-H), 2.60 (1H, d.d, J_{43} = 4.7, J_{45} = 16.7 Hz, 4-H), 3.06 (1H, d.d, J_{53} = 7.7, J_{54} = 16.7 Hz, 5-H), 6.74 (1H, d.d, J_{67} = 3.3, J_{68} = 0.9 Hz, 6-H), 6.50 (1H, d.d, J_{76} = 3.3, J_{78} = 2.0 Hz, 7-H), 7.71 (1H, d.d, J_{86} = 0.9, J_{87} = 2.0 Hz, 8-H), 6.65 (1H, phenyl p-H), 7.01 (2H, phenyl o-H), 7.12 ppm (phenyl m-H).

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REFERENCES

1. B. Cederlund, R. Lantz, A. B. Hernfeldt, O. Thornstad, and K. Undheim, Acta. Chem. Scand. B, **31**, 198 (1977).
2. V. Yu. Vvedenskii, S. V. Zinchenko, T. A. Shkarupa, N. A. Korchevin, E. N. Deryagina, and M. G. Voronkov, Dokl. Akad. Nauk SSSR, **305**, 624 (1989).
3. G. S. Ponticello, C. N. Habecker, S. L. Varga, and S. M. Pitzenberger, J. Org. Chem., **54**, 3223.
4. V. Yu. Vvedenskii, S. V. Zinchenko, E. D. Shtefan, M. V. Ul'ev, A. R. Zhnikin, T. A. Shkarupa, E. N. Deryagina, and M. G. Voronkov, Dokl. Akad. Nauk SSSR, **320**, 96 (1991).
5. E. Niwa, H. Aoki, H. Tanaka, K. Munakata, and M. Namiki, Chem. Ber. **99**, 3215 (1966).
6. V. Yu. Vvedenskii, T. A. Shkarupa, S. V. Zinchenko, A. R. Zhinkin, E. N. Deryagina, and M. G. Voronkov, Zh. Org. Khim., **26**, 2237 (1990).