SYNTHESIS OF THIOPHENE-2-THIOL DERIVATIVES

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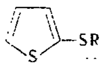
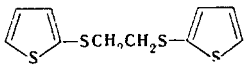
New sulfides of the thiophene series were synthesized by reaction of thiophene-2-thiol with compounds containing active halogen atoms and double bonds. The products were characterized.

A number of studies have been devoted to the synthesis and transformations of thiophenethiols, and the ability of some of their derivatives to form chelate compounds is noted in these studies. A number of thiophenethiol derivatives have biological activity. We have synthesized some new thiophene-2-thiol derivatives by reaction of thiophene-2-thiol with ethylene chlorohydrin, methyl monochloroacetate, allyl bromide, dichloro- and dibromoethane, 3-diethyl- and 3-dibutylaminochloro-1-propanol, and methyl acrylate.



I–IX

I R = H; II R = CH_2CH_2OH; III R = CH_2COOCH_3; IV R = $CH_2CH{=}CH_2$, V R = CH_2CH_2Cl;
VI R = CH_2CH_2Br; VII R = $CH_2CH(OH)CH_2N(C_2H_5)_2$; VIII R = $CH_2CH(OH)CH_2N(C_4H_9)_2$,
IX R = $CH_2CH_2COOCH_3$; X



Compound V was also obtained by reaction of II with thionyl chloride, and X was obtained by reaction of V and VI with sodium thiophenethiolate.

The structures of the compounds were confirmed by alternative syntheses. The individuality of II and III was proved by gas-liquid chromatography (GLC).

EXPERIMENTAL

Gas-liquid chromatographic analysis was accomplished with a Khrom 3-1 chromatograph. The column (240 by 0.6 cm) was filled with N-AW Chromatone impregnated with 15% (by weight) DF-550 silicone. The column temperature was 190°, and the carrier gas (helium) flow rate was 66 cm^3/min. The retention times of II and III were 23.8 and 28.2 min, respectively. The thiophene-2-thiol was prepared by the method in [1] and had bp 44-45°, n_D^{20} 1.6140, and d_4^{20} 1.2450.

2-(β-Hydroxyethylmercapto)thiophene (II). A 4.3-g (0.05 mole) sample of ethylene chlorohydrin was added with stirring at 60° to a mixture of 5 g (0.043 mole) of thiophene-2-thiol (I) and an aqueous solution of 1.9 g (0.047 mole) of sodium hydroxide, after which the mixture was stirred at 60-65° for 2 h. The organic layer was then extracted with ether, washed with water to neutrality, and dried over anhydrous sodium sulfate. The ether was removed by distillation, and the residue was vacuum distilled to give 5.8 g (84%) of a product with bp 94-95° (1.2 mm), n_D^{20} 1.6017, and d_4^{20} 1.2629. Found: C 44.6; H 5.2; S 39.5%; MR_D 43.50. $C_6H_8OS_2$. Calculated: C 44.9; H 5.0; S 40.0; MR_D 44.30.

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The compounds below were similarly synthesized by reaction of I with methyl monochloroacetate and allyl bromide, respectively.

2-(Methoxycarbonylmethylmercapto)thiophene (III). The yield of this compound, with bp 84-85° (0.4 mm), n_D^{20} 1.5655, and d_4^{20} 1.2642, was 5.7 g (70%). Found: C 45.0; H 4.7; S 33.9%; MR_D 48.50. $C_7H_8O_2S_2$. Calculated: C 44.7; H 4.3; S 34.0%; MR_D 49.05.

2-(Allylmercapto)thiophene (IV). The yield of this compound, with bp 73-74° (2.2 mm), n_D^{20} 1.5827, and d_4^{20} 1.1147, was 5.4 g (80%). Found: C 54.3; H 5.7; S 41.2%; MR_D 46.82. $C_7H_8S_2$. Calculated: C 53.8; H 5.2; S 41.0%; MR_D 46.94.

2-(β-Chloroethylmercapto)thiophene (V). A 30-g (0.3 mole) sample of dichloroethane was added all at once to a mixture of 10 g (0.086 mole) of thiol I and 3.8 g (0.094 mole) of sodium hydroxide (20% aqueous solution), and the mixture was heated at 75-80° for 6 h. The organic layer was extracted with ether, the extract was worked up as described above, and the residue was vacuum distilled to give 9.6 g (62%) of a product with bp 78-79° (0.9 mm), n_D^{20} 1.5950, and d_4^{20} 1.2811. Found: C 41.0; H 4.2; Cl 19.5%; MR_D 47.40. $C_6H_7ClS_2$. Calculated: C 40.3; H 3.9; Cl 19.8%; MR_D 47.65.

2-(β-Bromoethylmercapto)thiophene (VI). This compound was obtained by reaction of thiol I with dibromoethane. Workup of the reaction mixture gave 12.5 g (65%) of a product with bp 95-97° (2 mm), n_D^{20} 1.6327, and d_4^{20} 1.5756. Found: C 31.8; H 3.4; Br 35.4%; MR_D 49.98. $C_6H_7BrS_2$. Calculated: C 32.3; H 3.2; Br 35.8%; MR_D 50.55.

1,2-(Bisthienylmercapto)ethane (X), with bp 165-167° (1.2 mm), n_D^{20} 1.6515, and d_4^{20} 1.2864, was also obtained in the synthesis of V and VI. The yield was 2.8 g (25%). Found: C 46.9; H 4.1; S 49.6%; MR_D 73.41. $C_{10}H_{10}S_4$. Calculated: C 46.5; H 3.9; S 49.6%; MR_D 74.13.

2-(β-Hydroxy-γ-diethylaminopropylmercapto)thiophene (VII). A 20-g (0.12 mole) sample of 3-diethylamino-1-chloro-2-propanol [2] was added dropwise at 80-85° to a mixture of 10 g (0.086 mole) of thiol I and 4 g (0.1 mole) of sodium hydroxide (in a 20% aqueous solution) at 80-85°, after which the mixture was maintained at the same temperature for another 5 h. Water was then added to dissolve the resulting sodium chloride, and the organic layer was extracted with ether. The extract was worked up as described above, and the residue was vacuum distilled to give 16 g (77%) of VII with bp 135-136° (1 mm), n_D^{20} 1.5470, and d_4^{20} 1.0986. Found: C 53.8; H 8.2; N 5.4; S 26.0%; MR_D 70.83. $C_{11}H_{19}NOS_2$. Calculated: C 53.8; H 7.8; N 5.7; S 26.1%; MR_D 71.34.

2-(β-Hydroxy-γ-dibutylaminopropylmercapto)thiophene (VIII). This compound was similarly obtained from thiol I and 3-dibutylamino-1-chloro-2-propanol. The yield of product with bp 155-156° (0.6 mm), n_D^{20} 1.5199, and d_4^{20} 1.0267 was 19 g (73%). Found: C 60.3; H 9.7; N 4.6; S 20.8%; MR_D 89.24. $C_{15}H_{27}NOS_2$. Calculated: C 59.8; H 9.0; N 4.6; S 21.3%; MR_D 89.81.

2-(β-Methoxycarbonylethylmercapto)thiophene (IX). A few drops of diethylamine and 2.8 g (0.03 mole) of methyl acrylate were added to a benzene solution of 5 g (0.043 mole) of thiol I, and the mixture was heated at 65-70° for 2 h. The benzene was removed, and the residue was vacuum distilled to give 6.6 g (76%) of a product with bp 117-118° (1.6 mm), n_D^{20} 1.5782, and d_4^{20} 1.2372. Found: C 47.9; H 4.8; S 31.4%; MR_D 54.27. $C_8H_{10}O_2S_2$. Calculated: C 47.5; H 5.0; S 31.7%; MR_D 53.67.

LITERATURE CITED

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2. R. Rothstein and K. Binovic, Compt. Rend., 236, 1050 (1953): Ref. Zh. Khim., 16219 (1954).