# ACTION OF ALKALI METALS IN LIQUID AMMONIA ON SUBSTITUTED THIOPHENES.
# V.* PREPARATION OF ALIPHATIC α,β-UNSATURATED THIOETHERS

Ya. L. Gol'dfarb and E. P. Zakharov

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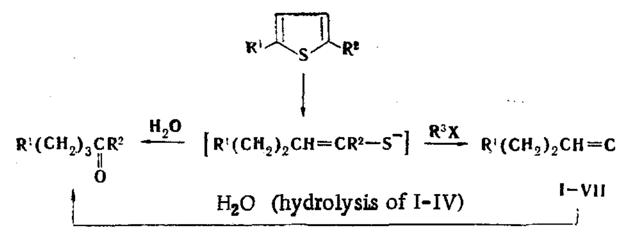
**α,β-Unsaturated thioethers of the aliphatic series were obtained by reduction of α-alkyl- and α-diethylaminoalkylthiophenes with lithium and alcohol in liquid** ammonia and subsequent alkylation of the reduction product with alkyl halides.

We have previously shown [2-4] that functional compounds of the aliphatic series containing a butyryl group in all cases are obtained by the action of alkali metal and alcohol on α-substituted thiophenes in liquid ammonia and subsequent hydrolysis of the reduction product. This process, according to our ideas [3] includes the intermediate formation of an unsaturated thiolate ion (see the reaction scheme below). The latter, as one might have assumed from the literature data [5, 6], should be readily alkylated in liquid ammonia by alkyl halides to give the thioether. In fact, we obtained the expected unsaturated thioether I by carrying out the reduction of 2-nonylthiophene with lithium and tert-butyl alcohol in liquid ammonia and by treating the reaction mixture with methyl iodide. The structure of the product was established by spectroscopic and chemical methods. By changing the composition and length of the side chain in the starting compound and by using different alkyl halides we obtained a number of unsaturated thioethers in high yields (see Table 1).† In most cases distillation of the reaction products gave pure [according to gas—liquid chromatography (GLC)] substances.



X=Br or I; $R^1$=H except for IV, where $R^1=CH_3$); I $R^2=C_9H_{19}$, $R^3=CH_3$; II $R^2=C_9H_{19}$, $R^3=C_4H_9$; III $R^2=R^3=C_2H_5$; IV $R^2=CH_3$, $R^3=C_4H_9$; V $R^2=(CH_2)_2N(C_2H_5)_2$, $R^3=C_4H_9$; VI $R^2=(CH_2)_4N(C_2H_5)_2$, $R^3=C_4H_9$; VII $R^2=(CH_2)_6N(C_2H_5)_2$, $R^3=C_4H_9$

The thioethers obtained are mobile liquids with a sharp odor that turn appreciably yellow on standing in air. Thioethers I-IV were rapidly hydrolyzed by the action of dilute (aqueous or alcoholic) hydrochloric acid to give ketones; the latter were isolated from the reaction mixture in the form of the 2,4-dinitrophenylhydrazones. 4-Tridecanone was regenerated by treatment of the 2,4-dinitrophenylhydrazone obtained from the product of hydrolysis of thioether II with stannous chloride in hydrochloric acid [7]. We also carried out the hydrolysis of thioether II by using an $HgCl_2$—acetonitrile—water system [8]; according to the GLC data, the hydrolysis product contained 4-tridecanone. Unsaturated thioethers V-VII, which contain a nitrogen atom in one of the alkyl groups, were also decomposed by the action of hydrochloric acid solutions, but in this case chromatographic analysis showed that complex mixtures were formed. We were unable to obtain derivatives involving either the carbonyl or amino group from the hydrolysis products in these cases. Attempts to obtain a solid derivative involving the amino group of thioethers V-VII themselves were also unsuccessful.

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*See [1] for communication IV.

†See [1] for the preliminary results.

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N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow 117913. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 337-340, March, 1977. Original article submitted April 2, 1976.

TABLE 1. Thioethers $R^1(CH_2)_2CH = CR^2 - SR^3$

| Compound | bp, °C (mm) | $n_D^{20}$ | mp of the derivative,[a] °C | Found, % |  |  |  | Empirical formula | Calc., % |  |  |  | PMR spectra (δ, ppm)[b] | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | C | H | N | S |  | C | H | N | S |  |  |
| I | 84—85 (0,02) | 1,4750 | —[c] | 73,3 | 12,3 | — | 14,2 | $C_{14}H_{28}S$ | 73,6 | 12,4 | — | 14,0 | 5,43 (1H, t, J=7 Hz)<br>4,99 (traces, t, J=7 Hz) | 81 |
| II | 101—102 (0,03) | 1,4730 | — | 75,4 | 12,6 | — | 11,9 | $C_{17}H_{34}S$ | 75,5 | 12,7 | — | 11,9 | 5,50 (1H, t, J=7 Hz) | 89 |
| III | 91 (50) | 1,4754 | 144—145[11] | 66,6 | 11,3 | — | 22,3 | $C_8H_{16}S$ | 66,6 | 11,2 | — | 22,2 | 5,54 (1H, t, J=7 Hz) | 90 |
| IV | 67 (0,9) | 1,4760 | 107—108[12] | 69,7 | 11,7 | — | 18,5 | $C_{10}H_{20}S$ | 69,7 | 11,7 | — | 18,6 | — | 92 |
| V | 113—114 (0,7) | 1,4796 | —[d] | 69,4 | 12,1 | 5,8 | 12,9 | $C_{14}H_{29}NS$ | 69,1 | 12,0 | 5,8 | 13,1 | — | 89 |
| VI | 107—109 (0,02) | 1,4803 | — | 71,0 | 12,1 | 5,3 | 11,8 | $C_{16}H_{33}NS$ | 70,8 | 12,2 | 5,2 | 11,8 | 5,50 (1H, t, J=7 Hz) | 94 |
| VII | 126—128 (0,03) | 1,4798 | — | 72,2 | 12,3 | 5,1 | 11,2 | $C_{18}H_{37}NS$ | 72,2 | 12,5 | 4,7 | 10,7 | — | 89 |

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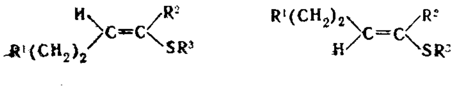
[a] This is the 2,4-dinitrophenylhydrazone of the ketone formed in the hydrolysis of the α,β-unsaturated thioether. [b] In addition to the CH signals presented, the spectra contain groups of lines (multiplets) related to methyl and methylene protons. [c] The 2,4-dinitrophenylhydrazones of the ketones from I and II are liquids at room temperature. [d] We were unable to obtain 2,4-dinitrophenylhydrazones from the products of hydrolysis of thioethers V-VII.



Z (95-100%) E (0-5%)

The PMR spectra of the thioethers contain a signal at 5.43-5.54 ppm (t, J = 7 Hz) related to the proton attached to a double bond. In the case of I we noted a low-intensity signal in the same region (4.99 ppm, t, J = 7 Hz), which can be ascribed [8] to the vinyl proton of the E form of the unsaturated thioether. A comparison of the intensities of the signals and the application of the known correlation methods make it possible to assume with sufficient definitiveness that all of the unsaturated thioethers obtained in this research have Z isomer structures.

The IR spectra of all of the synthesized compounds contain the band at 1627 $cm^{-1}$ characteristic for $\alpha,\beta$-unsaturated sulfides [8]. Molecular ions peaks were recorded in the mass spectra; in the case of amino sulfides V-VII the maximum intensity invariably corresponded to the peak with m/e 86, which was ascribed to the product of $\alpha$ cleavage at the nitrogen atom (effective stabilization of the charge of the $[CH_2{=}N(C_2H_5)_2]^+$ immomium structure). In the mass spectra of sulfides I-IV the most intense peaks correspond to fragments formed by cleavage of the $C{-}R^2$ and C—S bonds ("resonance" stabilization of the charge [9]). The other intense signals characterize subsequent fragmentation of the hydrocarbon chains of the molecule. Thus the assigned structures were confirmed by various methods of investigation of the compounds obtained in this research.

We have previously shown [2] that the yields of products drop sharply in the preparation of amino ketones from $\alpha$-dimethylaminoalkylthiophenes if the number of methylene groups between the thiophene ring and the nitrogen atom of the side chain in the starting compound is reduced to two. We can now assert on the basis of data on the yields of amino sulfides V-VII that the noted unfavorable effect of shortening of the methylene bridge is manifested only in the hydrolysis step, since the reduction step is common to the synthesis of the amino ketone and the amino sulfide.

## EXPERIMENTAL

The PMR spectra of $CCl_4$ solutions of the compounds were recorded with a DA-60-JL spectrometer with tetramethylsilane as the standard. The IR spectra of liquid films between KBr plates were recorded with a UR-20 spectrometer. The mass spectra were obtained with MKh-1303 and Varian CH-6 spectrometers. Analysis by gas—liquid chromatography (GLC) was carried out with an LKhM-8 MD chromatograph with a flame-ionization detector and helium as the carrier gas at 130-200°; the stainless steel column was 100 by 0.3 cm, and the stationary phase was Apiezon-L (5%) on celite 545 modified with 0.4% $Na_3PO_4$ or PFMS-4 (7%) on silanized Chromosorb G.

The starting 2-alkyl- and 2-($\omega$-diethylaminoalkyl)thiophenes were prepared by previously described methods [1, 10].

4-Methylthio-3-tridecene (I). Small pieces of lithium [0.69 g (0.1 g-atom)] were added in the course of 5 min at ∿ −40° to a stirred solution of 4.2 g (0.02 mole) of 2-nonylthiophene, 7.4 g (0.1 mole) of tert-butyl alcohol, and 30 ml of distilled (over $LiAlH_4$) diethyl ether in 150 ml of liquid $NH_3$, after which the mixture was stirred for 2 h. It was then treated with 14.2 g (0.1 mole) of methyl iodide, and the ammonia was evaporated. The residue was diluted with water, and the aqueous mixture was extracted repeatedly with ether. Fractionation of the extract yielded 3.7 g (81%) of thioether I (see Table 1).

4-Butylthio-3-tridecene (II), 3-ethylthio-3-hexene (III), 2-Butylthio-2-hexene (IV), 1-Diethylamino-3-butylthio-3-hexene (V), 8-Diethylamino-4-butylthio-3-octene (VI), and 10-Diethylamino-4-butylthio-3-decene (VII). These compounds were obtained as described above from 0.02-0.06 mole of the substituted thiophene (see the reaction scheme above) and the appropriate amount of lithium and absolute ethanol. Preparative thin-layer chromatography (TLC) was used for additional purification of thioethers IV and VII.

4-Tridecanone. A 0.83-g (0.12 g-atom) sample of lithium was added to a stirred solution of 4.2 g (0.02 mole) of 2-nonylthiophene, 8.9 g (0.12 mole) of tert-butyl alcohol, and 40 ml of distilled (over $LiAlH_4$) ether in 250 ml of liquid $NH_3$, after which the mixture was stirred for 2 h. Ammonium chloride (6.5 g) was added, the ammonia was evaporated, and the residue was diluted with water. It was then acidified with hydrochloric acid and extracted repeatedly with ether. Fractionation of the extract gave 3.2 g (80%) of practically pure (according to GLC data) 4-tridecanone [13] with bp 72° (0.02 mm) and mp 16-19°.

Hydrolysis of the Thioethers. A 1.17-g sample of 4-butylthio-3-tridecene (II) was treated with a solution of 1 g of 2,4-dinitrophenylhydrazine in a mixture of 100 ml of methanol and 2 ml of concentrated HCl. At the end of the exothermic reaction, 10.5 ml of 2 M HCl solution was added dropwise until the mixture became turbid. The next day, the 2,4-dinitrophenylhydrazone, which separated in the form of a heavy red oil, was worked up by the method in [7]. Hydrolysis was accomplished by refluxing the mixture for 30 min. Extraction with petroleum ether and removal of the solvent from the extract by distillation yielded 0.6 g of a substance, which, from the GLC data, was identical to the 4-tridecanone obtained by alternative synthesis (see above). Thioethers I, III, and IV were converted to the corresponding ketones by a similar method; the ketones were isolated in the form of their 2,4-dinitrophenylhydrazones (see Table 1).

Thioether II was also hydrolyzed by another method [8]. A mixture of 1.52 g of II, 3.04 g of $HgCl_2$, 42 ml of acetonitrile, and 14 ml of $H_2O$ was heated at 50° until the peak of the starting sulfide disappeared during chromatographic analysis of periodically selected samples of the reaction mixture. The hydrolysis product (1.1 g) was treated with a solution of 2,4-dinitrophenylhydrazine in acidified methanol. The liquid 2,4-dinitrophenylhydrazone obtained in this way was converted to the ketone, which, according to the GLC data, was 4-tridecanone, by the procedure described above.

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