2. J. A. Elvidge and J. H. Golden, J. Chem. Soc., 700 (1957).
3. V. V. Korshak, S. V. Vinogradova, S. A. Siling, and G. A. Fedorov, Dokl. Akad. Nauk SSSR, 195, 1113 (1970).
4. N. Yoda and M. Kurihara, Macromol. Rev., 5, 109 (1971).
5. S. V. Vinogradova, S. A. Siling, V. I. Solov'ev, and V. V. Korshak, Zh. Org. Khim., 10, 2437 (1974).
6. F. Wilig and H. Snaider, Progress in Organic Chemistry [Russian translation], Vol. 1, Inostr. Lit. (1963), p. 45.
7. E. N. Zil'berman, Reactions of Nitriles [in Russian], Khimiya, Moscow (1972), p. 105.
8. G. Rabilloud, B. Sillion, and D. de Gaudemaris, Bull. Soc. Chim. Fr., 171 (1965).
9. M. Kurihara, Macromol. Chem., 105, 84 (1967).
10. H. Budzikiewicz, K. Djerassi, and D. Williams, Interpretation of Mass Spectra of Organic Compounds [Russian translation], Mir, Moscow (1966), p. 214.
11. H. Mehner, J. Prac. Chem., 63, 254 (1902).
12. Dictionary of Organic Compounds [Russian translation], Inostr. Lit., Vol. 1 (1949), p. 168; Vol. 3 (1949), p. 403.

ACTION OF ALKALI METALS IN LIQUID AMMONIA ON SUBSTITUTED THIOPHENES.

VI.* PREPARATION OF DERIVATIVES OF VINYL THIOETHERS

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

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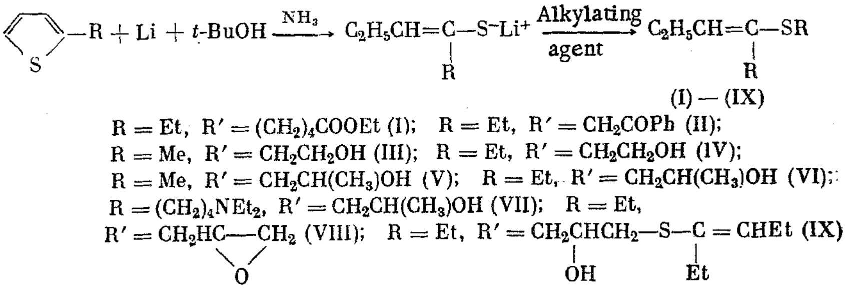
In continuation of our research on the preparation of aliphatic thioethers for substituted thiophenes by reducing the latter with alkali metals and alcohol in liquid ammonia, followed by alkylation [1], we studied the possible use of other alkylating agents in this reaction, with the final aim of synthesizing vinyl thioethers with an additional functional substituent in the molecule.

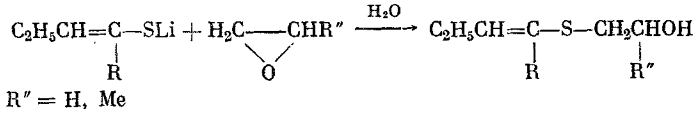


$$\text{—R} + Li + t\text{-BuOH} \xrightarrow{NH_3} C_2H_5CH{=}\underset{R}{C}{—}S^-Li^+ \xrightarrow[\text{agent}]{\text{Alkylating}} C_2H_5CH{=}\underset{R}{C}{—}SR$$

(I) — (IX)

$R = Et$, $R' = (CH_2)_4COOEt$ (I); $R = Et$, $R' = CH_2COPh$ (II);
$R = Me$, $R' = CH_2CH_2OH$ (III); $R = Et$, $R' = CH_2CH_2OH$ (IV);
$R = Me$, $R' = CH_2CH(CH_3)OH$ (V); $R = Et$, $R' = CH_2CH(CH_3)OH$ (VI);
$R = (CH_2)_4NEt_2$, $R' = CH_2CH(CH_3)OH$ (VII); $R = Et$,
$R' = CH_2\underbrace{HC—CH_2}_{O}$ (VIII); $R = Et$, $R' = CH_2\underset{OH}{C}HCH_2—S—\underset{Et}{C}=CHEt$ (IX)

The thioethers (III)-(VIII) were obtained in high yields (Table 1) from the corresponding α-substituted thiophenes by alkylation of the intermediate enthiolate with epoxy compounds, i.e., ethylene oxide, propylene oxide and epichlorohydrin. In the first two cases, an epoxide ring opening took place with the formation of thiovinyl ethers containing an OH group



$$C_2H_5CH{=}\underset{R}{C}{—}SLi + \underbrace{H_2C—CHR''}_{O} \xrightarrow{H_2O} C_2H_5CH{=}\underset{R}{C}{—}S{—}CH_2\underset{R''}{C}HOH$$

$R'' = H, Me$

The secondary alcohol structure of the product of the alkylation with propylene oxide was confirmed by reductive desulfurization [of the thioether (VI)] with Raney Ni in methanol; isopropanol was detected [n-propanol, according to thin-layer chromatography (TLC) data, was absent]. Thus, the cleavage of the epoxide ring during the reaction of propylene oxide with the thiolate in liquid ammonia takes place selectively. The direction of the opening of the ring coincides with that of similar reaction carried out in different media [3].

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*For communication V, see [1].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
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TABLE 1. Thioethers EtCH=C(R)—SR'

Compound	Name	Yield, %	bp, °C (p, mm Hg)	n^{20}_D	Found, %			Empirical formula	Calculated, %		
					C	H	S		C	H	S
(I)	3-(4-Carbethoxybutylthio)-3-hexene	59*	91–93(0,03)	1,4788	63,87	9,81	13,20	$C_{13}H_{24}O_2S$	63,89	9,89	13,12
(II)	3-(2-Oxo-2-phenylethylthio)-3-hexene	73	115–117(0,3)	1,5588	71,71	7,61	13,57	$C_{14}H_{18}OS$	71,75	7,74	13,68
(III)	2-(2-Hydroxyethylthio)-2-pentene	76	75(0,1)	1,5050	57,22	9,70	21,69	$C_7H_{14}OS$	57,49	9,65	21,92
(IV)	3-(2-Hydroxy ethylthio)-3-hexene	86	82–83(0,1)	1,5000	59,95	10,01	19,96	$C_8H_{16}OS$	59,95	10,06	20,00
(V)	2-(2-Hydroxypropylthio)-2-pentene	89	74–75(0,7)	1,4970	59,75	9,83	19,98	$C_8H_{16}OS$	59,95	10,06	20,00
(VI)	3-(2-Hydroxypropylthio)-3-hexene	81	83–84(0,7)	1,4935	61,81	10,25	18,54	$C_9H_{18}OS$	62,01	10,41	18,39
(VII)	1-Diethylamino-5-(2-hydroxypropylthio)-5-octene	83	119–120(0,03)	1,4963	66,29	11,39	11,56	$C_{15}H_{31}NOS$	65,88	11,43	11,72
(VIII)	3-(2,3-Epoxypropylthio)-3-hexene†	71	97–99(7,0)	1,4951	63,01	9,48	18,77	$C_9H_{16}OS$	62,74	9,36	18,61
(IX)	1,3-bis-[1-(1-Ethyl)-butenylthio]-2-propanol‡	39	112–113(0,02)	1,5223	62,39	9,55	22,10	$C_{15}H_{28}OS_2$	62,44	9,78	22,23

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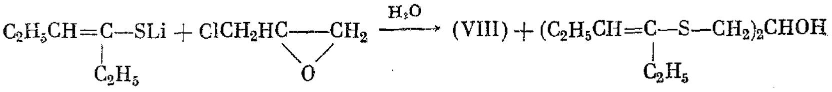
*71%, calculated for ethyl chlorovalerate entering the reaction.

†The product contained 2.1% of unknown impurity (data of functional analysis [2]).

‡Obtained together with (VIII); yield 41%.

During alkylation with epichlorohydrin, the reaction, in principle, can proceed at the halogen-carrying carbon atom, and with opening of the ring. It is known that at an equimolecular ratio of the reagents, or in the presence of an excess of epichlorohydrin, the last reacts with the thiol only at the chlorine atom [4, 5].* The reaction proceeded similarly in our experiments also: The molecule of the thioether (VIII) formed included a fragment with the epoxide ring being retained. At the same time, if the amount of epichlorohydrin is purposedly insufficient, together with the epoxy sulfide, a product of the ring cleavage of the second molecule of the thiolate is also obtained



Alkylation of the reduction product of 2-ethylthiophene with phenacyl bromide leads to the formation of an oxo-substituted sulfide (II); a sulfide substituted with a carbethoxy group (I) was obtained by the action of ethyl δ-chlorovalerate on the thiolate. The yield in the last case is somewhat too low, which agrees with the lower activity of alkyl chlorides compared with that of bromides and iodides of similar structure.

The structure of the thioethers obtained was confirmed by PMR, IR, and mass spectroscopy.

Thus, using halides carrying functional groups, as well as epoxy compounds as alkylating agents, it is possible to prepare practically in one step unsaturated sulfides of different structures from α-substituted thiophenes.

EXPERIMENTAL

The PMR spectra were run on the DA-60-JL apparatus (60 MHz) in CCl_4 with reference to TMS. The spectra of all the thioethers contained the signals of the vinyl proton (broadened triplet, δ, 5.5-5.7 ppm, J = 7.0-7.1 Hz; 1 H) and of the protons of the ethyl group belonging to the thiolate fragment of the molecule. The spectra also had sharply discernible signals, characteristic of given specific structures [δ (ppm), type of signal, spin–spin-interaction coupling constant (Hz), intensity, and group of protons are given]. (I): 4.06, q, 7.2, 2H, $CH_3\underline{CH_2}O$. (II): 3.83, s, –, 2H, SCH_2CO; 7.91, m, –, 2H, CH aromatic (α, α); 7.37, m, –, 3H, CH aromatic (β, β, γ). (III): 1.87, s, –, 3H, $CH_3C{=}$; 2.74, t, 6.7, 2H $SCH_2\underline{CH_2}$. (IV): 2.59, t, 6.7, 2H, $S\underline{CH_2}CH_2$. (V): 3.65, m, 6.1, 1H, $CH_2\underline{(CH_3)}CHOH$; 2.92, broad s, –, 1H, OH; 2.64, d (split), 6.1, 2H, $S\underline{CH_2}CH$; 1.95, s, –, 3H, $CH_3C{=}$. (VI): 3.62, m, 6.1, 1H, $CH_2(CH_3)\underline{CH}OH$; 2.85, s, –, 1H, OH; 2.54, d (split), 6.1, 2H, $S\underline{CH_2}CH$. (IX): 3.45, m, 5.6, 1H, $CH_2(OH)\underline{CH}CH_2$. In the spectra of (VII) and (VIII), due to overlapping of the signals in the middle section (2-4 ppm), it was not possible to obtain accurate data on the chemical shifts and the spin–spin interaction in addition to those noted above.

The IR spectra were run on the UR-20 spectrometer (in a liquid film, KBr). Besides the lines present in the spectra of all the thioethers obtained, namely at 1620-1630 cm^{-1} (C=CH), as well as the lines corresponding to the CH_3 and CH_2 groups, signals were also observed corresponding to the vibrations of the OH group (3350-3540, 1030-1070 cm^{-1}) in the spectra of (III)-(VII) and (IX), the epoxy group (3000, 3050, 1260 cm^{-1}) in the spectrum of (VIII), the carbonyl group (1735 and 1690 cm^{-1}) in the spectra of (I) and (II), respectively.

The mass spectra were obtained on the MX-13-03 and Varian CH-6 apparatus. In all cases, the peak of the molecular ion was recorded, with an intensity from 4% (VIII) to 55% (IV) of the maximum. The most intense signals corresponded to the alkyl splitting at the C–S bond, as well as the cleavage of the C–C bond α to the hetero atom (N, O, S).

The gas–liquid chromatographic (GLC) analysis was carried out on the LKhM-8MD chromatograph (flame-ionization detector, gas carrier, helium, 30 ml/min). Column A: 100 × 0.3 cm, 5% Apiezone L on Celite-545, modified with 0.4% Na_3PO_4 (temperature of the column 180-200°C) – for the analysis of (VII) and (IX). Column B: 200 × 0.3 cm, 7% PFMS-5 on a silanized Chromosorb G (160-210°C) – for the analysis of (I)-(VI), (VIII). Column C: 300 × 0.3 cm, otherwise similar to column B (30-50°C) – for the identification of low-molecular-weight products of the reduction desulfurization of (VI) and for controlling the purity of the initial epoxy compounds.

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*The above information refers to reactions carried out in alcohols or without a solvent.

The α-substituted derivatives of thiophene were prepared by methods described in [6, 7]. Alkene oxides, δ-chlorovaleric acid (commercial products), were purified by distillation.

3-(4-Carbethoxybutylthio)-3-hexene (I). Small pieces of lithium (1.39 g, 0.2 g-atom) were added in portions in an inert gas atmosphere, at −40°C, to a stirred solution of 4.48 g (0.04 mole) of 2-ethylthiophene and 14.8 g (0.2 mole) of tert-butanol in 300 ml of liquid ammonia. After stirring (2 h at −40°C), the mixture was cooled to −70°C, and then, 13.1 g (0.08 mole) of ethyl δ-chlorovalerate were added slowly, and then in the course of 30 min, 5 g of NH_4Cl (for neutralization of traces of unreacted metal). Ammonia was evaporated, and the residue diluted with water, and extracted many times with ether. By distillation, 5.75 g (50%) of thioether (I) (see Table 1) and 7.7 g of the starting ethyl chlorovalerate were isolated. Other thioethers were obtained by a similar procedure from 0.02-0.04 mole of the α-substituted thiophene. During the preparation of (VIII), 100 ml of ether, distilled over $LiAlH_4$ immediately before the experiment, served as the cosolvent. In the synthesis of (IX), the molar ratio of the initial 2-ethylthiophene and the alkylating agent was 1:0.9.

Reductive Desulfurization of Thioether (VI). A mixture of 1.25 g of the thioether, 10 g of freshly prepared Raney Ni, and 6 ml of absolute methanol was stirred, with heating, for 4 h. The liquid was decanted from the precipitate, and centrifuged, and then a probe for the GLC analysis was taken.

CONCLUSIONS

Reduction in liquid ammonia of α-substituted derivatives of thiophene, followed by alkylation of the reduction product with organic halides or epoxy compounds, gave unsaturated thioethers, containing various functional groups in the molecule, in high yields.

LITERATURE CITED

1. Ya. L. Gol'dfarb and E. P. Zakharov, Khim. Geterotsikl. Soedin., 337 (1977).
2. W. C. J. Ross, J. Chem. Soc., 2257 (1950).
3. R. Elderfield (ed.), Heterocyclic Compounds [Russian translation], Vol. 1, Inostr. Lit., Moscow (1953), p. 27.
4. Z. I. Mikhailov, N. V. Komarov, L. P. Vakhrushev, and N. F. Chernov, Inv. Cert., No. 330172, July 30, 1970; Byull. Izobr., No. 8, 83 (1972).
5. T. Fujisawa and M. Kakutani, J. Polym. Sci., 12, 557 (1974); Chem. Abstr., 83, 60216y (1975).
6. L. I. Belen'kii, S. Z. Taits, and Ya. L. Gol'dfarb, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 1706 (1961).
7. Ya. L. Gol'dfarb and E. P. Zakharov, Khim. Geterotsikl. Soedin., 1499 (1975).