

## New Preparative Procedure for the Synthesis of Chloroalkyl Sulfides\*

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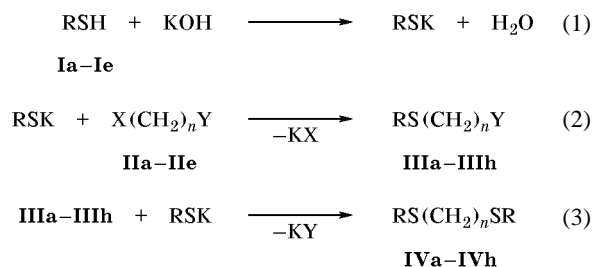
**Abstract**—Reaction of thiols with dihaloalkanes in the system hydrazine hydrate–base leads to alkyl(chloroalkyl) sulfides with different positions of the chlorine atom with respect to sulfur. The developed one-step procedure for the synthesis of such unsymmetrical sulfides is most suitable for arenethiols and alkanethiols having a long polymethylene chain. The reaction mechanism is discussed.

Chloroalkyl sulfides are used as pesticides [1] and intermediate products in organic synthesis [2, 3].  $\alpha$ -Chloroalkyl sulfides available by the Böhme reaction or its modifications were studied to the greatest extent [4].  $\beta$ -Chloroalkyl sulfides were also studied in sufficient detail; they are usually prepared from sulfur dichloride or sulfenyl chlorides and unsaturated compounds [5, 6]. Chloroalkyl sulfides with a longer alkyl chain are synthesized in two steps from thiols and chlorohydrins with subsequent replacement of the OH group by chlorine by the action of sulfuryl chloride [7].

We recently studied the reaction of dihaloalkanes with thiolate ions  $RS^-$  generated by reductive splitting of organic disulfides in the system hydrazine hydrate–alkali, which resulted in formation of bis(alkylthio)alkanes [8]. In most cases, intermediate unsymmetrical sulfides having one chlorine atom were not detected. These were obtained only from diaryl disulfides. In continuation of our studies on reactions of thiolate ions with polyelectrophiles, we examined the behavior of various thiols **I** toward dihaloalkanes **II** in the system hydrazine hydrate–alkali. This system prevents oxidation to disulfides of thiolate ions generated from thiols. It was surprising that, unlike disulfides, thiols **I** reacted with dihalogen derivatives **II** to give unsymmetrical chlorine-containing sulfides **III** even when

the amount of dihaloalkane **II** was less than stoichiometric. In some cases, sulfides **III** were the major products (Scheme 1). Simultaneously, bis-sulfide derivatives **IV** were formed. The reaction conditions and yields of the products are given in Table 1.

### Scheme 1.



**I**, R = Et (**a**), Pr (**b**), Bu (**c**), Ph (**d**), 2-thienyl (**e**); **II**,  $n = 2$ , X = Y = Cl (**a**), Br (**b**);  $n = 3$ , X = Br, Y = Cl (**c**);  $n = 5$ , X = Y = Cl (**d**), Br (**e**); **III** (Y = Cl), **IV**,  $n = 2$ , R = Et (**a**), Pr (**b**), Bu (**c**), Ph (**d**), 2-thienyl (**e**);  $n = 3$ , R = Pr (**g**);  $n = 5$ , R = Pr (**h**).

It is seen that the yield of chloro sulfides **III** from the same dihaloalkane increases as the alkyl chain in the alkanethiol becomes longer: **Ia** < **Ib** < **Ic**. This may be due to decrease of the solubility of the corresponding sulfide **III** in hydrazine hydrate, which changes in the same order. In a similar way (cf. [8]), we can explain the behavior of arenethiols **Id** and **Ie** in reactions (1)–(3). Reaction (3) is hampered by withdrawal of sulfides **III** to the organic phase.

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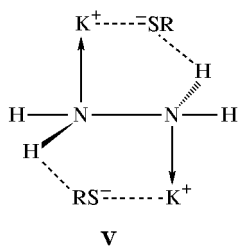
**Table 1.** Reactions of thiols with dihaloalkanes

| RSH | X(CH <sub>2</sub> ) <sub>n</sub> Y | Amount, mol |     |                                    | Yield, <sup>a</sup> % |        |
|-----|------------------------------------|-------------|-----|------------------------------------|-----------------------|--------|
|     |                                    | RSH         | KOH | X(CH <sub>2</sub> ) <sub>n</sub> Y | III                   | IV     |
| Ia  | IIa                                | 1           | 1.5 | 0.5                                | 2                     | 45     |
| Ia  | IIa                                | 1           | 1.5 | 1.0                                | 6                     | 68     |
| Ia  | IIa                                | 1           | 1.0 | 0.5                                | 2                     | 41     |
| Ib  | IIa                                | 1           | 1.5 | 0.5                                | 36                    | 12     |
| Ib  | IIb                                | 1           | 1.2 | 0.5                                | –                     | 78     |
| Ib  | IIc                                | 1           | 1.5 | 0.5                                | 72                    | 10     |
| Ib  | IIc                                | 1           | 1.3 | 1.0                                | 84                    | Traces |
| Ib  | IId                                | 1           | 1.5 | 0.5                                | 19                    | 32     |
| Ib  | IIe                                | 1           | 1.5 | 0.5                                | –                     | 48     |
| Ic  | IIa                                | 1           | 1.2 | 0.5                                | 76                    | 10     |
| Ic  | IIa                                | 1           | 1.5 | 0.5                                | 76                    | Traces |
| Ic  | IIb                                | 1           | 1.5 | 1.0                                | –                     | 88     |
| Id  | IIa                                | 1           | 1.5 | 0.5                                | 12                    | 36     |
| Ie  | IIa                                | 1           | 1.5 | 0.5                                | 87                    | Traces |

<sup>a</sup> The yields were calculated on the initial thiol on the basis of GLC data.

In all cases, the bromine atoms in dibromoalkanes are replaced completely. From dibromo derivatives **IIb** and **IIe** we obtained only bis-sulfides **IV**, and mixed 1-bromo-3-chloropropane (**IIc**) gave rise to unsymmetrical sulfide **IIIg** having only the chlorine atom. These results support the previous observation that bromoalkanes react more effectively with organic chalcogenide ions (RS<sup>–</sup>, RSe<sup>–</sup>, RTe<sup>–</sup>). On the other hand, chloroalkanes react more rapidly than analogous bromoalkanes with unsubstituted chalcogenide ions (S<sup>2–</sup>, Se<sup>2–</sup>, Te<sup>2–</sup>) [9, 10].

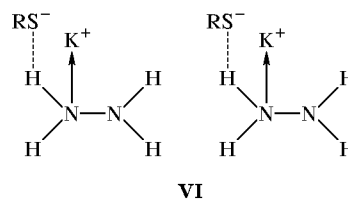
A question arises as to why thiolate ions generated by reductive splitting of dialkyl disulfides react with dichloroalkanes mainly with replacement of both chlorine atoms and formation of the corresponding bis-sulfides, while those generated from thiols under similar conditions are capable of replacing only one chlorine atom to give in many cases chloroalkyl sulfides as the major products. Most probably, hydrazine participates in formation of solvate complexes with thiolate ions generated from disulfides or thiols



(presumably, through hydrogen bonding N–H...<sup>–</sup>SR). Reduction of one disulfide molecule R<sub>2</sub>S<sub>2</sub> with hydrazine hydrate in the presence of alkali gives two thiolate ions RS<sup>–</sup> which may be solvated by one hydrazine molecule, thus forming bridged complex **V** whose structure is shown above. Complex **V** is likely to be stabilized by additional coordination of the nitrogen atom to potassium cation.

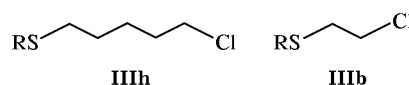
The reaction of dihalogen derivative **II** with one thiolate moiety in complex **V** gives unsymmetrical sulfide **III** in which the remaining chlorine atom appears spatially close to the sulfur atom of the other thiolate moiety in complex **V**. Such orientation is favorable for the subsequent fast replacement of the second chlorine atom and formation of bis-sulfide **IV**.

Thiolate ions generated from thiols according to reaction (1) (Scheme 1) are independent species. They also form solvate complexes with hydrazine, but these complexes have no bridged structure.



In this case, the reaction of complex **VI** with dihaloalkane leads primarily to unsymmetrical sulfide **III**. The possibility for the latter to react with another thiolate ion is controlled by diffusion factor, reactant concentrations, and solubility of sulfide **III** in hydrazine hydrate.

When a dihaloalkane has a long polymethylene chain, it reacts with complex **VI** at a higher rate and at both independent halogen atoms (as with mono-haloalkanes). Therefore, the corresponding unsymmetrical sulfide is formed in the reaction of propanethiol (**I**) with 1,2-dichloroethane in a greater yield than in the reaction with 1,5-dichloropentane (**IId**) (Table 1). In the latter case, unsymmetrical sulfide **IIIh** has a longer “tail” (as compared to sulfide **IIIb**), at which the attack of another thiolate ion is more facile (diffusion factor).



Thus the reaction of thiols with difunctional electrophiles in the system hydrazine hydrate–base may be regarded as a convenient preparative route to alkyl chloroalkyl sulfides with different positions of the

**Table 2.** Boiling points, elemental analyses, and  $^1\text{H}$  NMR spectra of compounds **IIIb–IIIe**, **IIIg**, **IIIh**, **IVa–IVd**, **IVg**, and **IVh**

| Comp. no.    | bp, °C<br>(p, mm) | Found, % |       |       |       | Formula                                | Calculated, % |       |       |       | Reference |
|--------------|-------------------|----------|-------|-------|-------|--|---------------|-------|-------|-------|-----------|
|              |                   | C        | H     | S     | Cl    |  | C             | H     | S     | Cl    |           |
| <b>IIIb</b>  | 75 (25)           | 43.42    | 8.06  | 23.40 | 25.75 | $\text{C}_5\text{H}_{11}\text{ClS}$    | 43.17         | 7.91  | 23.02 | 25.90 | –         |
| <b>IIIc</b>  | 90 (5)            | 47.13    | 8.63  | 21.40 | 23.04 | $\text{C}_6\text{H}_{13}\text{ClS}$    | 47.21         | 8.52  | 20.98 | 23.28 | [7]       |
| <b>III d</b> | 100 (7)           | 55.45    | 5.31  | 19.03 | 20.03 | $\text{C}_8\text{H}_9\text{ClS}$       | 55.63         | 5.22  | 18.55 | 20.58 | [1]       |
| <b>IIIe</b>  | 110 (5)           | 40.15    | 3.78  | 35.96 | 20.11 | $\text{C}_6\text{H}_7\text{ClS}_2$     | 40.34         | 3.92  | 35.85 | 19.89 | [1]       |
| <b>IIIg</b>  | 85–87 (17)        | 46.94    | 8.71  | 20.54 | 23.12 | $\text{C}_6\text{H}_{13}\text{ClS}$    | 47.21         | 8.52  | 20.98 | 23.28 | –         |
| <b>IIIh</b>  | 105 (10)          | 53.62    | 9.43  | 18.04 | 19.43 | $\text{C}_8\text{H}_{17}\text{ClS}$    | 53.18         | 9.42  | 17.53 | 19.67 | –         |
| <b>IVa</b>   | 115 (35)          | 47.61    | 9.65  | 43.14 | –     | $\text{C}_6\text{H}_{14}\text{S}_2$    | 48.00         | 9.33  | 42.67 | –     | [1]       |
| <b>IVb</b>   | 104 (5)           | 53.77    | 9.98  | 36.25 | –     | $\text{C}_8\text{H}_{18}\text{S}_2$    | 53.93         | 10.11 | 35.96 | –     | [1]       |
| <b>IVc</b>   | 140 (5)           | 58.07    | 10.43 | 30.32 | –     | $\text{C}_{10}\text{H}_{22}\text{S}_2$ | 58.25         | 10.68 | 31.07 | –     | –         |
| <b>IVd</b>   | 65 (3)            | 68.85    | 5.95  | 25.56 | –     | $\text{C}_{14}\text{H}_{14}\text{S}_2$ | 68.29         | 5.69  | 26.02 | –     | –         |
| <b>IVg</b>   | 180 (5)           | 56.11    | 10.47 | 33.18 | –     | $\text{C}_9\text{H}_{20}\text{S}_2$    | 56.25         | 10.42 | 33.33 | –     | –         |
| <b>IVh</b>   | 130 (3)           | 60.14    | 10.98 | 28.87 | –     | $\text{C}_{11}\text{H}_{24}\text{S}_2$ | 60.00         | 10.91 | 29.09 | –     | –         |

| Comp. no.    | $^1\text{H}$ NMR spectrum, $\delta$ , ppm  |
|--------------|--|
| <b>IIIb</b>  | 0.99 t ( $\text{CH}_3$ ), 1.62 m ( $\text{CCH}_2\text{C}$ ), 2.54 t ( $\text{ClCH}_2\text{S}$ ), 2.85 t ( $\text{SCH}_2\text{CCl}$ ), 3.62 t ( $\text{CH}_2\text{Cl}$ )  |
| <b>IIIc</b>  | 0.93 t ( $\text{CH}_3$ ), 1.40 m ( $\text{CCH}_2\text{C}$ ), 1.56 m ( $\text{CH}_3\text{CCH}_2$ ), 2.54 t ( $\text{CCCCH}_2\text{S}$ ), 2.81 t ( $\text{SCH}_2\text{CCl}$ ), 3.58 t ( $\text{CH}_2\text{Cl}$ ) |
| <b>III d</b> | 3.2 t ( $\text{CH}_2\text{S}$ ), 3.57 t ( $\text{CH}_2\text{Cl}$ ), 7.26 m ( $\text{H}_{\text{arom}}$ )  |
| <b>IIIe</b>  | 3.01 t ( $\text{CH}_2\text{S}$ ), 3.61 t ( $\text{CH}_2\text{Cl}$ ), 6.90–7.38 m (thienyl)   |
| <b>IIIg</b>  | 0.98 t ( $\text{CH}_3$ ), 1.58 m ( $\text{CCH}_2\text{C}$ ), 2.06 m ( $\text{CCH}_2\text{CCl}$ ), 2.49 t ( $\text{CCCH}_2\text{S}$ ), 2.65 t ( $\text{SCH}_2\text{CCCl}$ ), 3.64 t ( $\text{CH}_2\text{Cl}$ )  |
| <b>IIIh</b>  | 0.98 t ( $\text{CH}_3$ ), 1.54 m ( $\text{CH}_2$ ), 1.78 m ( $\text{CH}_2\text{CCl}$ ), 2.48 t ( $\text{CH}_2\text{S}$ ), 3.42 t ( $\text{CH}_2\text{Cl}$ )  |
| <b>IVa</b>   | 1.25 t ( $\text{CH}_3$ ), 2.52 q ( $\text{CCH}_2\text{S}$ ), 2.72 s ( $\text{SCH}_2\text{CH}_2\text{S}$ )  |
| <b>IVb</b>   | 0.98 t ( $\text{CH}_3$ ), 1.60 m ( $\text{CCH}_2\text{C}$ ), 2.51 t ( $\text{CCCH}_2\text{S}$ ), 2.70 s ( $\text{SCH}_2\text{CH}_2\text{S}$ )  |
| <b>IVc</b>   | 0.91 t ( $\text{CH}_3$ ), 1.41 m ( $\text{CCH}_2\text{C}$ ), 1.58 m ( $\text{CH}_3\text{CCH}_2$ ), 2.54 t ( $\text{CCCCH}_2\text{S}$ ), 2.70 s ( $\text{SCH}_2\text{CH}_2\text{S}$ )                           |
| <b>IVd</b>   | 3.06 s ( $\text{SCH}_2\text{CH}_2\text{S}$ ), 7.26 s ( $\text{H}_{\text{arom}}$ )  |
| <b>IVg</b>   | 0.98 t ( $\text{CH}_3$ ), 1.54 m ( $\text{CCH}_2\text{C}$ ), 2.50 m ( $\text{CH}_2\text{S}$ )  |
| <b>IVh</b>   | 0.98 t ( $\text{CH}_3$ ), 1.50 m ( $\text{CCH}_2\text{CC}$ ), 1.58 m ( $\text{CCH}_2\text{C}$ , $\text{SCCH}_2\text{CCH}_2\text{CS}$ )   |

chlorine atom with respect to sulfur. The proposed one-step procedure for preparation of sulfides **III** is most suitable for arenethiols and long-chain alkane-thiols. All the products were isolated from the reaction mixtures by fractional distillation under reduced pressure; their boiling points, elemental analyses, and  $^1\text{H}$  NMR spectra are given in Table 2. Some compounds were synthesized for the first time.

#### EXPERIMENTAL

The  $^1\text{H}$  NMR spectra were recorded on a Bruker DPX-400 spectrometer (400 MHz) in  $\text{CDCl}_3$  using HMDS as internal reference. The progress of reactions and the purity of products were monitored by GLC on

an LKhM-80 chromatograph (2000×3-mm column packed with 5% of XE-60 on Chromaton N-AW-HMDS, carrier gas helium, linear oven temperature programming at a rate of 12 deg/min). Gas chromatographic–mass spectrometric analysis was performed using a Hewlett–Packard HP 5972A mass-selective detector (PONA capillary column, 50 m×0.2 mm×0.5  $\mu\text{m}$ , carrier gas helium, linear temperature programming at a rate of 12 deg/min).

#### Reaction of thiols **I** with dihaloalkanes **II**.

A four-necked flask equipped with a stirrer, reflux condenser, thermometer, and adapter for loading the reactants was charged with required amounts of alkali, hydrazine hydrate, and appropriate thiol (see Table 1). The mixture was vigorously stirred for 1 h, a required

amount of dihaloalkane was added, the mixture was heated to 50°C, kept for 2 h at that temperature, and cooled, and the organic phase was separated and dried over CaCl<sub>2</sub>. The product yields were calculated from the GLC data (Table 1). The products were isolated by vacuum distillation. Compound **IVe** was isolated by recrystallization from ethanol. Ethyl 2-chloroethyl sulfide (**IIIa**) was identified solely on the basis of the GC-MS data: *m/z* 124 (*M*<sup>+</sup>, <sup>35</sup>Cl). The other products are characterized in Table 2.

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