ISOMERIZATION OF $\beta$-HALO DISULFIDES (ALKYL 2-HALOETHYL DISULFIDES)

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The methyl ester, amide, dimethylamide, and anilide of $\alpha$-methylthioglycidic acid are readily cleaved by methane- and acetylsulfenyl chlorides to give mixtures of the corresponding isomeric cleavage products - vicinal chlorodithio derivatives of isobutyric acid. It is shown that the ratio of isomers obtained depends both on the character of the substituent in the carboxyl group of the isobutyric acid and on the character of the substituent attached to the sulfur atom in the sulfenyl chloride (sulfomonochloride) used. It was found that $\beta$-halo disulfides, like $\beta$-halo sulfides, are capable of isomerization.

It is known that sulfides that contain halogen in the $\beta$ position are capable of isomerization. It is presently established that isomerization proceeds only in those cases in which the formation of an intermediate episulfonium ion is possible [1-3]. In later investigations, it was shown that the rate of isomerization and the resistance to isomerization of $\beta$-halo sulfides depend principally on the nucleophilicity of the sulfur atom. Thus no derivatives of 3-chloro-2-acetylthiobutyric acid isomerize, since the electron-acceptor substituent attached to the sulfur atom - the COCH$_3$ group - markedly lowers its nucleophilicity [4]. At the same time, derivatives of 3-chloro-2-methylthiobutyric acid are readily isomerized to more stable isomers - 2-chloro-3-methylthioisobutyric acid derivatives. In this case, an electron-donor substituent - the CH$_3$ group - increases the nucleophilicity of the sulfur atom and promotes isomerization.

It should be noted that the rate of isomerization also depends on the character of the substituent in the carboxyl group of 3-chloro-2-methylthiobutyric acid. The amides isomerized most readily, the anilide isomerized with somewhat greater difficulty, the esters isomerized considerably more slowly, and, finally, the acid chloride and nitrile were not isomerized [5].

In the cleavage of the methyl ester, amide, dimethylamide, and anilide of $\alpha$-methylthioglycidic acid (2,3-epithioisobutyric acid) with methane- and acetylsulfenyl chlorides, we obtained the corresponding disulfides containing halogen in the $\beta$ position. Since the cleavage of thioepoxides with electrophilic reagents occurs through the formation of an intermediate episulfonium ion [4-6], it was natural to expect the formation of isomeric cleavage products as a result of subsequent attack by chloride ion of both carbon atoms in the episulfonium ion.

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\begin{align*}
\text{CH}_3\text{C}^\text{O}X & \quad \text{RSCI} \\
\text{CH}_3\text{C}^\text{O}X & \quad \text{CI} \quad \text{SSR} \quad \text{Cl}^-
\end{align*}
\]

1, H: a X = NH$_2$, R = CH$_3$; b X = NH$_2$, R = COCH$_3$; c X = N(CH$_3$)$_2$, R = CH$_3$; d X = N(CH$_3$)$_2$, R = COCH$_3$; e X = NH$_2$, R = COCH$_3$; f X = N(CH$_3$)$_2$, R = COCH$_3$; g X = OCH$_3$, R = CH$_3$; h X = OCH$_3$, R = COCH$_3$

It was found that methanal- and acetylsulfenyl chlorides reacted extremely readily with 2,3-epithiosobutyric acid derivatives. The reaction was complete in several minutes at -20 to -40°C in CC14 solution. When the reaction mass no longer gave a qualitative reaction for unchanged sulfenyl chloride, it was analyzed at the same temperature by recording the PMR spectra. It was found that a mixture of isomeric cleavage products - β-halo disulfides with different isomer ratios (I:II) - was obtained in almost quantitative yield; as in the case of the β-halo sulfides mentioned above, the isomer ratio depended on the character of the substituents attached to the sulfur atom in the sulfenyl chlorides and in the carboxyl group, of the α-methylthioglycidic acid (see Table 1).

Further investigations demonstrated that β-halo disulfides, like β-halo sulfides, are capable of isomerization and that the rate of isomerization and the resistance to isomerization depend mainly on the nucleophilicity of the sulfur atom in the investigated disulfides. Thus the isomer ratio (I:II) of the various derivatives of vicinal acetyldithiochloroisobutyric acid remained constant both after prolonged storage at room temperature and after prolonged heating at high temperatures (see Table 1, compounds d, f, and h). At the same time, the isomer ratio (I:II) of derivatives of vicinal methylthiochloroisobutyric acid changed appreciably after heating at 100°C for 10 h (see Table 1, compounds a, c, and e). However, in contrast to β-halo sulfides, the isomerization of β-halo sulfides proceeds considerably more slowly, although the effect of the character of the substituents attached to the sulfur atom and in the carboxyl group is precisely the same (see Table 2). For comparison, Table 2 also contains our isomer ratios (I:II) and isomer ratios (III:IV) reported in [2, 5] before and after isomerization of the analogous vicinal halo mono- and disulfide derivatives of isobutyric acid.

It should be noted that the ready disproportionation of the β-halo disulfides to symmetrical disulfides [7] interfered with observations of their isomerization and isolation in pure form.