NEW METHOD FOR THE SYNTHESIS OF THIOGLYCIDIC ACIDS AND THEIR DERIVATIVES

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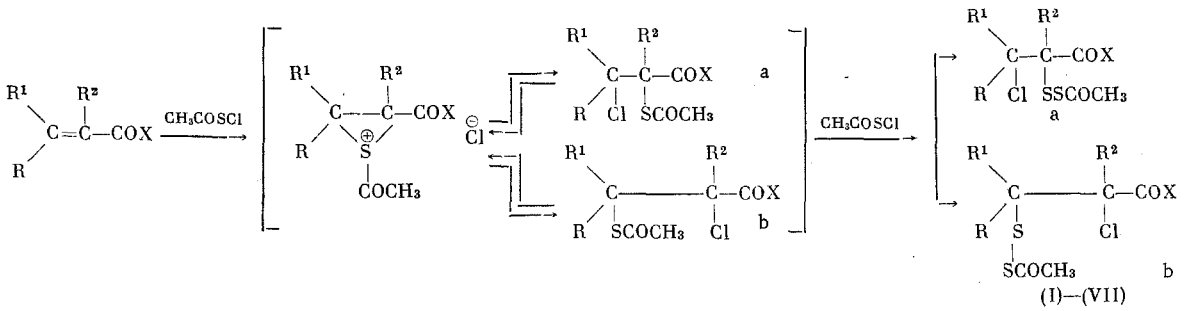
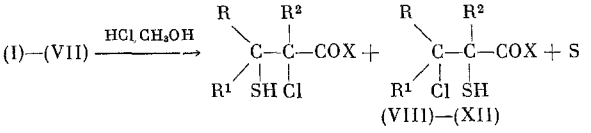
It is known that acetylsulfenyl chloride adds easily to olefins [1] and α,β-unsaturated acids [1, 2] with the formation of the isomeric α,β-chloro S-acetyl disulfides (a, b).



In the present paper we studied the effect of the position and accumulation of methyl groups in some α,β-unsaturated acids, and specifically the acrylic, methacrylic, crotonic and β,β-dimethylacrylic acids, on the ratio of the (a) : (b) isomers in the reactions with acetylsulfenyl chloride. The ratio of the isomeric α,β-chloroacetylthiocarboxylic acids (a) : (b), established by the NMR method, and the yields and constants of the obtained compounds (I)-(VII), are given in Table 1.

As can be seen from the data in Table 1, a mixture of isomeric disulfides is formed when $ClSCOCH_3$ is added to α,β-unsaturated acids. In contrast to the acrylic and methacrylic acids, for crotonic acid the ratio of the (a) : (b) isomers changed toward the formation of the β-S-acetyl disulfide (72%). An exception proved to be the anilide of methacrylic acid and the esters of β,β-dimethylacrylic acid. Only the formation of the α-acetyl disulfide was observed in these cases.

Previously it was shown that S-acetyl sulfides [3] and the S-acetyl disulfide [4], when treated with dry HCl in methanol, are easily converted, respectively, to mercaptans and monohydro disulfides RSSH. The latter compounds are unstable and, depending on the structure, are decomposed either to mercaptans and elemental sulfur, or to polysulfides and H_2S [4]. Instead of the expected RSSH compounds, removal of the $COCH_3$ group under analogous conditions from the acetyl disulfides (I)-(VII) led in high yields to the corresponding α,β-chloromercaptocarboxylic acids (VIII)-(XII).



Evidently, the presence of two electron-acceptor substituents (COX and Cl) lowers the stability of the intermediately formed RSSH compounds and, with the expulsion of elemental sulfur, they are immediately converted to mercaptans (VIII)-(XII). In this way, the esters of the α,β-chloromercaptopropionic,

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TABLE 1

Compound	R	R^1	R^2	X	Bp, °C (p, mm Hg)	n_D^{20}	Yield, %	Ratio of isomers, (a) : (b), %	Found, %				Empirical formula	Calculated, %			
									C	H	Cl	S		C	H	Cl	S
(I) *	H	H	H	OCH_3	123 (6)	1,5340	82	53 : 47					$C_9H_9ClO_3S_2$				
(II) †	H	H	CH_3	OCH_3	136 (7)	1,5314	89,5	83 : 17					$C_7H_{11}ClO_3S_2$				
(III)	H	H	CH_3	NHPh	‡		92	100 : 0	48,0	4,6	11,8	21,2	$C_{12}H_{14}ClNO_2S_2$	47,5	4,6	11,7	21,1
(IV)	H	CH_3	H	OH	Oil		50	30 : 70									
(V)	H	CH_3	H	OCH_3	116 (3)	1,5292	86	28 : 72	34,4	4,5	14,5	26,8	$C_7H_{11}ClO_3S_2$	34,6	4,5	14,6	26,4
(VI)	CH_3	CH_3	H	OCH_3	137 (3)	1,5294	81	100 : 0	37,1	5,1	13,0	25,8	$C_8H_{13}ClO_3S_2$	37,4	5,1	13,8	25,0
(VII)	CH_3	CH_3	H	OC_2H_5	126 (2)	1,5156	78	100 : 0	39,8	5,3	13,3	24,2	$C_9H_{15}ClO_3S_2$	39,9	5,5	13,1	23,7

*Bp 114° (2 mm); n_D^{21} 1,5330 [2].
† Bp 128° (4 mm); n_D^{21} 1,5312 [2].
‡Bp 74,5° (hexane).

TABLE 2

Compound	R	R^1	R^2	X	Bp, °C (p, mm Hg)	n_D^{20}	Yield, %	Found, %				Empirical formula	Calculated, %			
								C	H	Cl	S		C	H	Cl	S
(VIII)*	H	H	H	OCH_3	54(6)	1,4846	87					$C_4H_7ClO_2S$				
(IX) †	H	H	CH_3	OCH_3	66(10)	1,4825	82	36,4	5,2	19,5	20,0	$C_5H_9ClO_2S$	35,6	5,4	21,0	19,0
(X) †	H	CH_3	H	OCH_3	57(3)	1,4841	81,5	36,2	5,2	19,9	19,4	$C_5H_9ClO_2S$	35,6	5,4	21,0	19,0
(XI)	CH_3	CH_3	H	OCH_3	68(2)	1,4814	76	39,7	6,2	18,8	17,6	$C_6H_{11}ClO_2S$	39,5	6,0	19,4	17,5
(XII)	CH_3	CH_3	H	OC_2H_5	68(2)	1,4746	78	42,8	6,6	18,1	16,1	$C_7H_{13}ClO_2S$	42,8	6,6	18,1	16,3

*Bp 59° (7 mm); n_D^{21} 1,4840 [5].
† The poor results of the analysis are explained by the easy cyclization of the chloro mercaptans to thio epoxides.

TABLE 3

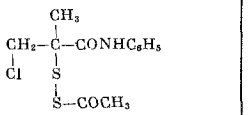
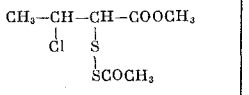
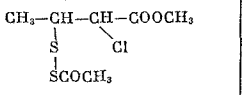
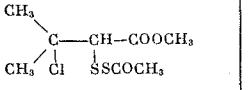
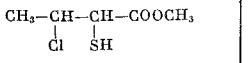
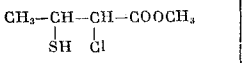
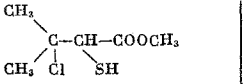
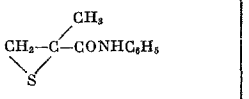
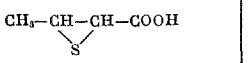
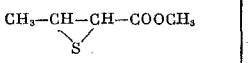
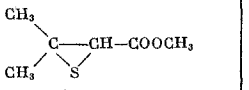
Compound	R	R^1	R^2	X	Bp, °C (p, mm Hg)	n_D^{20}	Yield, %		Found, %			Empirical formula	Calculated, %		
							method A	method B	C	H	S		C	H	S
(XIII)*	H	H	H	OCH_3	58 (12)	1,4875	71	68				$C_4H_6O_2S$			
(XIV) †	H	H	CH_3	OCH_3	52 (10)	1,4855	74,5	70				$C_5H_8O_2S$			
(XV)	H	H	CH_3	NHPh	71(hexane)	—	84	—	61,9	5,8	16,4	$C_{10}H_{11}NOS$	62,2	5,7	16,4
(XVI) ‡	H	CH_3	H	OH	56(hexane)	—	40	—	40,6	4,9	27,3	$C_4H_6O_2S$	40,7	5,1	27,1
(XVII)	H	CH_3	H	OCH_3	55 (5)	1,4795	70	66,5	45,5	6,6	23,6	$C_5H_8O_2S$	45,5	6,8	24,2
(XVIII)	CH_3	CH_3	H	OCH_3	77 (16)	1,4784	65,5	59	49,3	6,9	21,5	$C_6H_{10}O_2S$	49,3	6,9	21,9
(XIX)	CH_3	CH_3	H	OC_2H_5	67 (7)	1,4716	65	58	52,6	7,5	19,4	$C_7H_{12}O_2S$	52,5	7,5	20,0

* Bp 52° (10 mm); n_D^{20} 1,4875 [5].

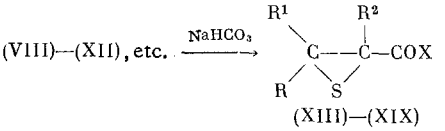
† Bp 54-56° (12 mm); n_D^{20} 1,4850 [6]

‡ Together with the acid, we isolated the methyl ester (XVII), which is formed by the removal of the CH_3CO group from disulfide (IV).

TABLE 4

Compound	Chemical shifts δ, ppm (J, Hz)							
	CH_3C	$\begin{matrix}CH_3\\ \diagdown\\ C\\ \diagup\\ CH_3\end{matrix}$	CH_3CS (=O)	CH_2	CHCH	CHS	$\begin{matrix}CH\\ \vert\\ Cl\end{matrix}$	$\begin{matrix}C\\ \vert\\ SH\end{matrix}$
	1,61		2,41	3,95				
	Doublet 1,75 (6,7)		2,50			Doublet 3,35 (8)	Multiplet 4,30—4,70	
	Doublet 1,42 (6,7)		2,50			Multiplet 3,20—3,50	Doublet 4,55 (8)	
		1,78	2,43			3,62		
	Doublet 1,72 (6,7)					Doublet 3,50 (9,30)	Multiplet 4,10—4,40	Doublet 2,15 (10,7)
	Doublet 1,52 (6,7)					Multiplet 3,35—3,65	Doublet 4,30 (9,3)	Doublet 2,15 (10,7)
		1,78				Doublet 3,60 (10,7)		Doublet 2,22 (10,7)
	1,85			Doublet 2,63 (6,7)				
	Doublet 1,57 (6)				Doublet 3,01 (4,7) Multiplet 3,09—3,49			
	Doublet 1,54 (6)				Doublet 2,98 (4,7) Multiplet 3,09—3,44			
		Two singlets 1,60; 1,64				3,17		

α,β-chloromercaptobutyric, and α,β-chloroisobutyric acids were obtained as a mixture of the isomeric compounds and the esters of α-mercapto-β-chloroisovaleric acid (Table 2). Further studies disclosed that the α,β-chloromercaptocarboxylic acids are easily cyclized under mild conditions to the corresponding thioglycidic acids (XIII)-(XIX)



(XIII)—(XIX)

Due to the quite high nucleophilicity of sulfur, the α- or β-position of the SH group in the starting chloromercaptans fails to have an effect on the yield of the thioglycidic acids (Table 3).

EXPERIMENTAL METHOD

The NMR spectra were taken on a Perkin–Elmer R-12 instrument (60 MHz) in CCl_4 relative to HMDS.

Acetylsulfenyl chloride was obtained by an improvement of the method given in [1], by the reaction of equimolar amounts of thioacetic anhydride and SO_2Cl_2 at −40° in a nitrogen stream in 80% yield. Typical experiments are given below. The constants of the compounds, the yields and the analysis results are given in Tables 1-3, while the chemical shifts of the NMR spectra are given in Table 4.

Method A (without Isolation of the Intermediate Compounds)

Methyl Ester of α-Methylthioglycidic Acid (XIV). With stirring, 22.1 g of CH_3COSCl was added to 10 g of methyl methacrylate at 20°, in 20 min. After 20 h the CH_3COCl was removed in vacuo, and the residue was dissolved in 200 ml of a 1% HCl solution in absolute MeOH and then allowed to stand for 24 h. The sulfur (3.1 g, 97%) was filtered, and the solution was evaporated to 1/3 of the original volume and poured into 100 ml of water; the mixture of isomeric chloromercaptans was extracted with ether. The extract was washed with water, after which it was shaken for 5-10 min with 10% $NaHCO_3$ solution (until the test with I_2 for the SH group was negative) and dried over $MgSO_4$; the solvent was removed, and the residue was distilled. We obtained compound (XIV). Compounds (XIII)-(XIX) were obtained in a similar manner.

Method B (with Isolation of the Intermediate Compounds)

Methyl Ester of β-Chloro-α-acetyldithioisovaleric Acid (VI). A mixture of 11.4 g of methyl β,β-dimethylacrylate and 22.1 g of CH_3COSCl was heated at 50° for 4 h. The CH_3COCl was distilled off in vacuo, and the residue was distilled. We obtained compound (VI). Compounds (I)-(VII) were obtained in a similar manner; reaction temperature for (I)-(III) 20°; time 24 h.

Methyl Ester of β-Chloro-α-mercaptoisovaleric Acid (XI). A solution of 12.8 g of (VI) in 200 ml of a 1% solution of HCl in absolute MeOH was allowed to stand at 20° for 24 h. The sulfur (1.5 g, 94%) was filtered, and the residue was distilled. We obtained compound (XI). Compounds (VIII)-(XII) were obtained in a similar manner.

Methyl Ester of β,β-Dimethylthioglycidic Acid (XVIII). A solution of 3.65 g of (XI) in 50 ml of ether was stirred vigorously with 10% $NaHCO_3$ solution for 15-20 min (until the test with I_2 for the SH group was negative). The ether solution was dried over $MgSO_4$, the solvent was removed in vacuo, and the residue was distilled. We obtained compound (XVIII). Compounds (XIII), (XIV), and (XVII)-(XIX) were obtained in a similar manner.

CONCLUSIONS

A new method was described for the preparation of thioglycidic acids and their derivatives.

LITERATURE CITED

1. H. Böhme, H. Bezzenberger, and H. D. Stachel, Ann. Chem., 602, 1 (1957).
2. M. G. Lin'kova, L. P. Parshina, Z. K. Stumbrevichute, O. V. Kil'disheva, and I. L. Knunyants, Dokl. Akad. Nauk SSSR, 196, 1089 (1971).

3. L. Owen and M. Sultanbava, J. Chem. Soc., 3109 (1949).
4. H. Böhme and G. Zinner, Ann. Chem., 585, 142 (1954); J. Tsurugi and T. Nakabayashi, J. Org. Chem., 24, 807 (1959).
5. L. P. Parshina, M. G. Lin'kova, O. V. Kil'disheva, and I. L. Knunyants, Izv. Akad. Nauk SSSR, Ser. Khim., 931 (1970).
6. M. G. Lin'kova, A. M. Orlov, O. V. Kil'disheva, and I. L. Knunyants, Izv. Akad. Nauk SSSR, Ser. Khim., 1148 (1969).