ADDITION OF SULFENYL CHLORIDES TO DERIVATIVES OF β,γ-UNSATURATED ACIDS AND HYDROLYSIS OF OBTAINED ADDUCTS

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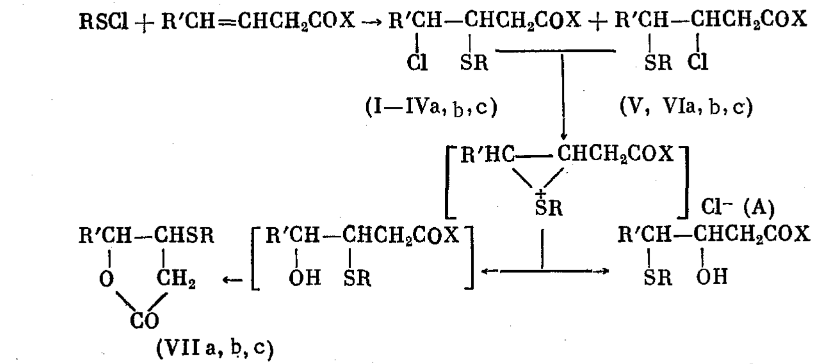
It is assumed that the addition of sulfenyl chlorides to alkenes proceeds via the intermediate episulfonium ion [1, 2]. It was also proved that the nucleophilic substitution of halogen in 2-haloalkyl sulfides also proceeds via the episulfonium ion [1, 3-5]. However, the addition of sulfenyl halides to alkenes and the nucleophilic substitution of halogen, for example, hydrolysis of the C—Cl bond, are accomplished in entirely different media: addition is accomplished in nonpolar solvents, whereas hydrolysis is accomplished in aqueous solutions. It is doubtful that the same intermediate states are formed under different conditions.

We studied the addition of a number of sulfenyl chlorides to derivatives of β,γ-unsaturated acids and the hydrolysis of the C—Cl bond of the obtained adducts. Derivatives of β-alkthio-γ-chlorobutyric acids (R' = H) were obtained previously [6] by the kinetically controlled addition of methane- and benzenesulfenyl chlorides to vinylacetic acid derivatives. They were isomerized to the thermodynamically more stable β-chloro derivatives.

In the present paper, under the same conditions, we obtained the derivatives of β-alkthio-γ-chloro-γ-phenylbutyric acids (I-IVa, b, c) (R' = C_6H_5) by the kinetically controlled addition of the methane-, benzene-, and β-chloroethanesulfenyl chlorides to β-benzalpropionic acid and its methyl ester, anilide, and acid chloride. Only in the case of adding methanesulfenyl chloride to β-benzalpropionic acid anilide was a mixture of the γ-chloro-(IIIa) and β-chloro adducts (VIa) formed in a 1:1 ratio (Table 1).



always R=CH_3 (a), C_6H_5 (b), CH_2CH_2Cl (c); R'=C_6H_5; X=OH (I), OCH_3 (II), (V), NHC_6H_5 (III), (VI), Cl (IV).

The crystalline γ-chloro adducts (I-IVa, b, c) when stored under room conditions were converted to β-alkthio-γ-butyroacetones (VIIa, b, c). However, in the absence of moisture the lactonization failed to occur even when heated to 40°C. Under these conditions the γ-chloro esters (IIa, b) were partially converted to the β-chloro esters (Va, b) and mixtures of isomeric esters (IIa, b) and (Va, b) were obtained (see Table 1). γ-Chloroanilides (IIIa, b) were isomerized to β-chloroanilides (VIa, b) when their solutions in abs. nitromethane were heated in a moisture-free atmosphere; otherwise γ-butyrolactones (VIIa, b) and aniline hydrochloride were obtained.

Hydrolysis of the C—Cl bond in the obtained adducts was run in aqueous dioxane. Here the isomeric β-chloro and γ-chloro compounds were converted to the same products. Thus, from the derivatives of the β-chloro-γ-alkthio- and γ-chloro-β-alkthiobutyric acids (R' = H)

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TABLE 1. Structure of Adducts of Reaction $RSCl+C_6H_5CH=CHCH_2COX$ (obtained under conditions excluding their isomerization) and Their Transformation Products

X	R	After addition		At 40°C in sealed ampuls		After hydrolysis	
		γ-Cl	β-Cl	γ-Cl	β-Cl	γ-OH (γ-lactone)	β-OH
OH	CH_3	100	–	100	–	100	–
OH	C_6H_5	100	–	100	–	100	–
OH	CH_2CH_2Cl	100	–	100	–	100	–
OCH_3	CH_3	100	–	30	70	100	–
OCH_3	C_6H_5	100	–	40	60	100	–
OCH_3	CH_2CH_2Cl	100	–	100	–		
NHC_6H_5	CH_3	50	50	–		100	–
NHC_6H_5	CH_3				100 *	100	
NHC_6H_5	C_6H_5	100	–	100		100	–
NHC_6H_5	C_6H_5				100 *	100	
NHC_6H_5	CH_2CH_2Cl	100	–	100	–	–	–
Cl	CH_3	100	–	–	–	–	–
Cl	C_6H_5	100	–	–	–	–	–
Cl	CH_2CH_2Cl	100	–	–	–	–	–

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*Obtained after heating the mixture of adducts in abs. nitromethane in a Dry Box at 40° for 5 h.

TABLE 2. Structure of Adducts of Reaction $RSCl+CH_2=CHCH_2COX$ (obtained under conditions excluding their isomerization) and Their Hydrolysis Products [6, 7]

X	R	Ratio of adducts, %		Ratio of hydrolysis products, %	
		γ-Cl	β-Cl	γ-OH (γ-lactone)	β-OH
OH	CH_3	50	50	–	–
OH	CH_3	–	–	80 *	20
OH	C_6H_5	100	–	60	40
OH	C_6H_5	–	–	60 *	40
OCH_3	CH_3	60	40	70	30†
OCH_3	C_6H_5	100	–	60	40†
NHC_6H_5	CH_3	100	–	80	20
NHC_6H_5	CH_3	–	–	80 *	20
NHC_6H_5	C_6H_5	100	–	70	30

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*After hydrolysis of the β-chloro derivative, which was obtained by isomerizing the original γ-chloro adduct.

†β-Hydroxy-γ-methyl(or phenyl)thiobutyric acid.

TABLE 3. Rate Constants for Hydrolysis of Derivatives of β(γ)-Chloro-γ(β)-alkthiocarboxylic Acids in Aqueous Dioxane (6:5 ml) at 40°C

Starting compounds	$10^3 \cdot K^{40°}$, min^{-1}
$C_6H_5CH(SCH_3)CH(Cl)CH_2CONHC_6H_5$	28,1
$C_6H_5CH(SC_6H_5)CH(Cl)CH_2CONHC_6H_5$	6,6
$C_6H_5CH(Cl)CH(SCH_3)CH_2COOCH_3$	9454 *
$C_6H_5CH(Cl)CH(SC_6H_5)CH_2COOCH_3$	3424 *
$CH_2(SCH_3)CH(Cl)CH_2CONHC_6H_5$	16,9†
$CH_2(SC_6H_5)CH(Cl)CH_2CONHC_6H_5$	2,6†
$CH_2(Cl)CH(SC_6H_5)CH_2COOH$	23,0†
$CH_2(SCH_3)CH(Cl)CH_2COOH$	14,8†
$CH_2(SC_6H_5)CH(Cl)CH_2COOH$	1,8†

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*Reaction temperature 10°.

†See [7].

were obtained mixtures of the β- and γ-hydroxy derivatives (Table 2), while from the derivatives of the β-chloro-γ-alkthio- and γ-chloro-β-alkthio-γ-phenylbutyric acids ($R' = C_6H_5$) or their mixtures were obtained only the γ-hydroxy derivatives (see Table 1), which under the experimental conditions were converted to γ-butyrolactones (VIIa, b, c).

A study of the hydrolysis rate of the C—Cl bond in the synthesized derivatives of β,γ-alkthiochlorocarboxylic acids by the conductometric method, with automatic recording of the change in the electrical conductivity of the solution, disclosed that HCl is formed by the first-order reaction. From the calculated hydrolysis rate constants (Table 3) it can be seen that the sulfur atom activates the hydrolysis process, since the hydrolysis rate of the phenylthio derivatives was several times slower than that of the methylthio derivatives. The γ-chloro isomers were hydrolyzed much faster than the thermodynamically more stable β-chloro isomers. The γ-chloro acids (Ia, b) were hydrolyzed at an especially fast rate, which did not permit us to determine the rate constant of this reaction. The γ-phenylbutyric acid derivatives were hydrolyzed more rapidly than the analogous butyric acid derivatives.

The fact that the same hydrolysis products are obtained from the γ-chloro and β-chloro adducts, and that the sulfur atom takes an active part in the hydrolysis of the C—Cl bond of these compounds, indicates that the hydrolysis proceeds via episulfonium ions, or more accu-

TABLE 4. Structure of Adducts of Reaction of Phenylsulfenyl Chloride with Derivatives of α,β-Unsaturated Acids (under conditions excluding isomerization of the adducts) and Structure of Hydrolysis Products of These Adducts

α,β-Unsaturated acid	X	Adducts, %		Hydrolysis products, %		Literature reference
		α-Cl	β-Cl	α-OH	β-OH	
$CH_2{=}C(CH_3)COX$	OH	25	75	60	40	[9, 10]
The same	OCH_3	35	65	64	36	[9, 10]
»	NHC_6H_5	–	100	70	30	[9, 10]
$CH_3CH{=}CHCOX$	NHC_6H_5	85	15	–	100	[9, 11]
$(CH_3)_2C{=}CHCOX$	OH	25	75	–	100	[9, 12]
The same	OCH_3	60	40	–	100	[9, 12]
»	NHC_6H_5	5	95	–	100	[9, 12]
$C_6H_5CH{=}CHCOX$	OH	–	100	–	100	[13]
The same	OCH_3	100	–	–	100	[13]
»	NHC_6H_5	–	100	–	100	[13]

rately, via dissociated and solvated chlorine and episulfonium ions, as was shown previously in other examples [8].

However, the structure of the reaction adducts from sulfenyl chlorides and vinylacetic acid derivatives does not coincide with the structure of the hydrolysis products of these adducts: the γ-chloro adducts were obtained in the addition reaction, while a mixture of the β- and γ-hydroxy compounds is obtained on hydrolysis (see Table 2). Based on the data of the studies on the addition of sulfenyl chlorides to derivatives of α,β-unsaturated acids and on the hydrolysis of the adducts (Table 4) it can be seen that the structures of the products of these reactions also frequently do not coincide. This indicates different intermediate states in two reactions.

The γ-chloro compounds were obtained when the sulfenyl chlorides are reacted with β-benzalpropionic acid derivatives. The γ-hydroxy derivatives (which converted to γ-butyrolactones) were formed exclusively during their hydrolysis, which proceeds via episulfonium ions. In this case, as in the case of the adducts of sulfenyl chlorides with cinnamic acid derivatives (see Table 4), the structure of the products of both reactions coincided. These reactions were run in media that differed in their polarity, and the same intermediates could not be formed in them. Evidently, the hydrolysis of the C—Cl bond proceeded via the dissociated and solvated complexes of the chlorine and episulfonium ions, but the cyclic episulfonium ions, formed from the derivatives of either the β,γ-alkthiochloro-γ-phenylbutyric acids or the α,β-alkthiochlorohydrocinnamic acids, were opened exclusively at the benzyl carbon, which indicates the carbocation character of the intermediate.

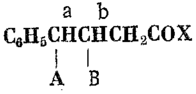
The addition reactions of covalent sulfenyl chlorides to alkenes, as was shown in [14, 15], proceed with involvement of the covalent intermediate of the sulfuran type. However, in the case of adding sulfenyl chlorides to derivatives of unsaturated acids, which contain polar groups at the double bond, more polar intermediate products are probably formed, with a variable delocalization of the positive charge. The rules and regioselectivity of adding sulfenyl chlorides to various unsaturated acids and their derivatives can be explained in this manner.

EXPERIMENTAL

The PMR spectra of the compounds were taken on a Hitachi R-22 spectrometer at an operating frequency of 90 MHz, and using TMS as the standard. The assignment of the β-chloro and γ-chloro isomers was based on the fact that the proton of the CHCl group is less shielded than the proton of the CHS group [1]. The ratio of the isomers in the adduct mixtures was determined by comparing the intensities of the signals of the proton of the CHCl group and the other protons. The parameters of the PMR spectra of the synthesized compounds are given in Table 5.

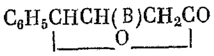
Addition of Methane-, Benzene-, and β-Chloroethanesulfenyl Chlorides to β-Benzalpropionic Acid and Its Derivatives. To a solution of 10 ml of β-benzalpropionic acid or its derivative in 10 ml of abs. CCl_4 at —30° was added in drops an equivalent amount of methane-, benzene-, or β-chloroethanesulfenyl chloride in abs. CCl_4 solution. The reaction mixture was kept for 10-15 h at 0°. The solvent was evaporated in vacuo and the product was recrys-

TABLE 5. Parameters of PMR Spectra in $(CD_3)_2CO$



$C_6H_5\underset{A}{\overset{a}{C}}H\underset{B}{\overset{b}{C}}HCH_2COX$

Compound	A	B	X	Chemical shifts δ, ppm a CH	b CH	CH_2	J, Hz CHCl	CH_2
(Ia)	Cl	SCH_3	OH	5,20 *	3,46 †	2,73; 3,09 ‡	9	4; 9; 16
(Ib)	Cl	SC_6H_5	OH	5,25	4,00	2,85; 3,15	9	4; 9; 17
(IIa)	Cl	SCH_3	OCH_3**	4,90	3,33	2,57; 3,06	9	4; 9; 17
(IIb)	Cl	SC_6H_5	OCH_3**	4,92	3,84	2,58; 3,07	9	4; 10; 16
(IIIa)	Cl	SCH_3	NHC_6H_5	5,28	3,70	2,77; 3,19	8	4; 9; 15
(IIIb)	Cl	SC_6H_5	NHC_6H_5	5,25	4,28	2,90; 3,22	8	4; 9; 15
(IVa)	Cl	SCH_3	Cl**	4,81			9	
(IVb)	Cl	SCH_3	Cl**	4,85	3,81	3,17; 3,58	9	4; 9; 15
(Va)	SCH_3	Cl	OCH_3**	3,95	4,63		7	
(Vb)	SC_6H_5	Cl	OCH_3**	4,40	4,65		8	
(VIa)	SCH_3	Cl	NHC_6H_5	4,23	4,90	2,73; 3,17	7	4; 9; 16
(VIb)	SC_6H_5	Cl	NHC_6H_5	4,81	5,09	2,67; 3,14		4; 9; 16



$\underbrace{C_6H_5CHCH(B)CH_2CO}_{O}$

Compound	A	B	X	a CH	b CH	CH_2	CHCl	CH_2
(VIIa)		SCH_3		5,27	3,56	2,64; 3,01	7	17; 9; 8
(VIIb)		SC_6H_5		5,34	4,09	2,64; 3,11	7	18; 8; 8

*$\overset{a}{CH}$ always a doublet.

†$\overset{b}{CH}$ always a multiplet center

‡CH_2 alwayd d.d; d.d.

**In CCl_4 solution.

tallized. The yields, melting points, and analytical data for the obtained compounds are given in Table 6.

Isomerization of Derivatives of β-Alkyl(phenyl)thio-γ-chloro-γ-phenylbutyric Acids (IIIa, b, c). The experiments were run in a Dry Box. A solution of 0.005 M of γ-chloroanilide (IIIb) or the reaction mixture from the γ-chloro-(IIIa) and β-chloroanilides (VIa) in abs. nitromethane, prepared under absolutely dry conditions, was heated in vacuum-sealed ampuls at 40°. After 3-4 h the ampuls were opened. The solvent was evaporated in vacuo. The anilides of the β-chloro-γ-methyl(phenyl)thio-γ-phenylbutyric acids (IVa, b) were obtained. The properties and microanalysis data are given in Table 6.

When a solution of γ-chloroanilides (IIIa, b, c) in abs. nitromethane is heated either under reflux, or using a condenser capped with a $CaCl_2$ tube, under ordinary laboratory conditions a precipitate of aniline hydrochloride deposits from solution. Evaporation of the solvent in vacuo gave γ-butyrolactones (VIIa, b, c) (see Table 6).

Hydrolysis of C—Cl Bond of Derivatives of γ(β)-Chloro-β(γ)-methyl(or phenyl)thio-γ-phenylbutyric Acids (Ia, b)-(IIIa, b) and (VIa, b). The compound (1 g) was heated in aqueous dioxane at 60° (60 mmoles/liter) until the test for Cl^- ion in the benzene extract was negative. The reaction mixture was extracted with benzene and dried over $MgSO_4$. The solvent was distilled off, and the residue was studied via the PMR spectra and recrystallized. We obtained γ-butyrolactones (VIIa, b) (see Table 6).

A study of the hydrolysis rate of the C—Cl bond of compounds (Ia, b)-(IIIa, b), (VIa, b) was run in a solution composed of abs. dioxane and doubly distilled water (6:5). The initial concentration was 2.26 mmoles/liter. The electrical conductivity measurements and calculation of the hydrolysis rate constant were done as described in [16]. The calculated constants are given in Table 3.

The C—Cl bond of γ-chloro acids (Ia, b) was hydrolyzed even at 10° immediately after solution and consequently the reaction rate could not be followed. Lactonization occurred when the C—Cl bond of γ-chloroanilide (IIIb) was hydrolyzed and $C_6H_5NH_2 \cdot HCl$ was formed, which complicated the rate of the process.

TABLE 6. Microanalysis Data and Properties of New Compounds

Compound	Yield, %	mp, °C (solvent)	Found, %					Empirical formula	Calculated, %				
			C	H	Cl	N	S		C	H	Cl	N	S
(Ib)	80	83 (decompn.) (CCl_4)	62,90	5,10	11,32	–	10,21	$C_{16}H_{15}ClO_2S$	62,64	4,92	11,57	–	10,46
(Ic)	95	80 (decompn.) (CCl_4)	49,07	4,69	24,42	–	11,05	$C_{12}H_{14}Cl_2O_2S$	49,14	4,77	24,23	–	10,91
(IIa)	85	47–49 (abs. hexane)	55,63	5,78	13,70	–	12,35	$C_{12}H_{15}ClO_2S$	55,65	5,82	13,72	–	12,41
(IIb)	90	47–49 (abs. hexane)	63,63	5,76	11,18	–	10,09	$C_{17}H_{17}ClO_2S$	63,65	5,33	11,03	–	10,00
(IIc)	85	63–66 (abs. hexane)	50,90	5,28	23,20	–	10,51	$C_{13}H_{16}Cl_2O_2S$	50,81	5,21	23,12	–	10,45
(IIIb)	90	101–103 (CCl_4)	69,14	5,35	9,18	3,71	8,35	$C_{22}H_{20}ClNOS$	69,18	5,29	9,29	3,66	8,40
(IIIc)	70	84–87 (ether–pet. ether)	58,64	5,20	19,08	3,92	8,74	$C_{18}H_{19}Cl_2NOS$	58,69	5,16	19,29	3,80	8,71
(IVa)	80	Oil from abs. hexane	49,99	4,56	26,60	–	12,41	$C_{12}H_{15}ClO_2S$	50,19	4,59	26,93	–	12,19
(IVb)	90	82–84 (abs. hexane)	59,83	4,55	22,06	–	9,72	$C_{16}H_{14}Cl_2OS$	59,08	4,33	21,85	–	9,86
(IVc)	65	41–44 (abs. hexane)	46,29	4,21	31,50	–	10,18	$C_{12}H_{13}Cl_3OS$	46,24	4,20	30,90	–	10,30
(VIa)	30	101–102 (CCl_4)	63,62	5,57	11,00	4,37	9,97	$C_{17}H_{18}ClNOS$	63,85	5,65	11,10	4,41	10,00
(VIb)	40	125–126 (CCl_4)	69,10	5,49	9,43	3,50	8,88	$C_{22}H_{20}ClNOS$	69,18	5,29	9,29	3,66	8,40
(VIIa)	98	28–29 (ether–pet. ether)	63,36	5,86	–	–	14,26	$C_{11}H_{12}O_2S$	63,46	5,81	–	–	15,41
(VIIb)	98	53–55 (ether–pet. ether)	71,41	5,05	–	–	11,76	$C_{16}H_{14}O_2S$	71,11	5,18	–	–	11,87
(VIIc)	95	82 (decompn.) (CCl_4)	56,13	5,17	13,66	–	12,34	$C_{12}H_{13}ClO_2S$	56,13	5,10	13,82	–	12,50

CONCLUSIONS

1. The kinetically controlled addition of alkane (and benzene) sulfenyl chlorides to β-benzalpropionic acid derivatives gave derivatives of β-alkthio-γ-chloro-γ-phenylbutyric acids, which in a moisture-free medium are isomerized to the more stable β-chloro derivatives.

2. The hydrolysis of the C—Cl bond of derivatives of both γ-chloro- and γ-chloro-β(γ)-alkthio-γ-phenylbutyric acids gives β-alkthio-γ-butyrolactones. The hydrolysis proceeds with anchimeric involvement of the sulfur via episulfonium ions.

3. Contrary to the accepted concepts, it is postulated that the addition of sulfenyl chlorides to the derivatives of unsaturated acids and the hydrolysis of the C—Cl bond of the obtained adducts proceed via different intermediates.

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