ADDITION OF BENZENESULFENYL CHLORIDE TO DIMETHYLACRYLIC ACID AND ITS DERIVATIVES

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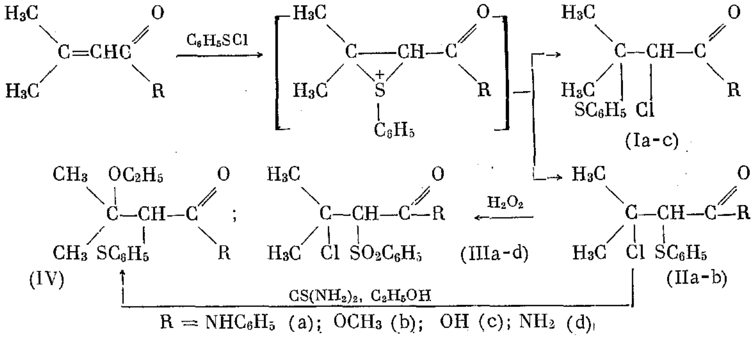
We have previously reported the addition of methanesulfenyl chloride to derivatives of dimethylacrylic acid [1, 2]. In the present work we have studied the addition of benzenesulfenyl chloride to dimethylacrylic acid and its derivatives.

In CCl_4 solution in the presence of traces of $CaCO_3$, benzenesulfenyl chloride adds to dimethylacrylic acid and its methyl ester (at ~20°) with the formation of a mixture of the adducts (Ia-c) and (IIa-c). The addition of benzenesulfenyl chloride to the anilide of the acid takes place most readily (at ~0°). Because of the poor solubility of dimethylacrylamide in CCl_4, its reactions with benzenesulfenyl chloride were performed in CH_2Cl_2 at 37-40°, which led to the formation of a single isomer (IId). Benzenesulfenyl chloride does not add to dimethylacryloyl chloride in CCl_4 at 20°.



The structures of the isomeric adducts and their ratios were shown by their PMR spectra and by a number of chemical transformations (Tables 1-3).

Compounds (Ia-c) isomerize into the stable adducts (IIa-c) at different rates and with much greater difficulty than the α-chloro-β-methylthioisovaleric acid derivatives described previously [2]. In the case of (Ia) at ~20°, isomerization is complete after 14 h. The isomerization of (Ib, c) requires a longer time at ~20° (see Table 1). In this case, the isomerization of (Ia-c) into (IIa-c), taking place through an intermediate episulfonium ion, is retarded by the decrease in the nucleophilicity of the sulfur atom, the unshared pair of electrons of which is conjugated with the π-electrons of the phenyl nucleus. The H_2O_2 oxidation of (IIa-d) (Table 4) forms the corresponding sulfones (IIIa-d) (Table 5).

The ease of the nucleophilic replacement of the chlorine atoms in derivatives of β-chloro-α-methylthioisovaleric acid has been shown previously [3]. The present investigation has shown that the halogen atoms in compounds (IIa-d) or in their mixtures with (Ia-c) are also replaced by hydroxy or methoxy groups on heating in aqueous dioxane or methanol at 60-70° with the formation of derivatives of β-hydroxy-α-phenylthio- or β-methoxy-α-phenylthioisovaleric acids, respectively. At room temperature, in contrast to the derivatives of β-chloro-α-methylthioisovaleric acid, complete replacement of halogen did not take place. The rate of hydrolysis of the chlorine atom in β-chloro-α-phenylthioisovaleranilide (IIa) in aqueous dioxane is given in Table 2.

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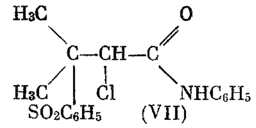
TABLE 1. Addition of C_6H_5SCl to $(CH_3)_2C=CHCOR$, Accompanied by the Isomerization (I) → (II)

Compound	Reaction time	T., °C	Yield of adduct,%	Ratio of the adducts, %	
				(I)	(II)
Ia	40 min	0	100	17	83
	14 h	20	—	—	100
Ib	17 h	20	58	49	51
	74 h	20	90	—	95
Ic	17 h	20	82	23	77
	74 h	20	95	—	100
Id	30 min	37	100	—	95

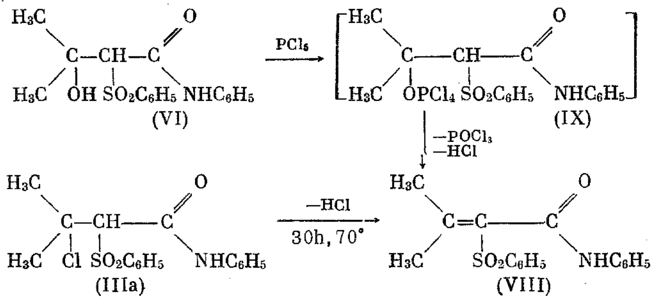
Heating (IIa) with thiourea in ethanol unexpectedly led to the replacement of the chlorine not by a thiourea residue but by an ethoxy group with the formation of β-ethoxy-α-phenylthioisovaleranilide (IVa).

Although the absence of the signal of a H–C–OH proton from the PMR spectra of the β-hydroxy-α-phenylthioisovaleric acid derivatives confirms the structure of the compounds contained, the oxidation of (IVa) with hydrogen peroxide to the sulfone (VI) was performed additionally. Since no isomerization is observed in the sulfones, by the replacement of the OH group in (VI) by an atom of chlorine under the action of PCl_5 we hoped to obtain the sulfone (IIIa) or its isomer (VII), which were synthesized specially by the oxidation of the sulfides (Ia) and (IIa).



(VII)

The sulfone (IIIa) is relatively stable and only on heating is HCl eliminated with the formation of β,β-dimethyl-α-phenylsulfonylacrylanilide (VIII). However, under the action of PCl_5 on the sulfone (VI) at ~20° a molecule of water was unexpectedly split out and the sulfone (VIII) was isolated, apparently having been formed through the intermediate compound (IX).



The splitting out of a molecule of water from the sulfone (VI) under the action of PCl_5 unambiguously confirms the structure of the compounds obtained (IVa-d). The absence of the nucleophilic replacement of the chlorine in the sulfone (IIIa) and in α,β-dichloroisovaleranilide (XI) even under more severe conditions confirms the formation of the intermediate episulfonium ion in these reactions.

Thus, the nucleophilic replacement of the chlorine atoms in (IIa-d) in this case takes place through an intermediate episulfonium ion and also takes place without isomerization.

EXPERIMENTAL METHOD

Benzenesulfenyl chloride was added to the dimethylacrylic acid derivatives, and the resulting adducts were isolated, in a similar manner to that used previously [2]. The reaction temperatures and the yields of the adducts are given in Table 1, and the melting points and analytical results in Table 4.

β-Hydroxy-α-phenylthioisovaleric Acid Derivatives (IVa-d). A mixture of 0.001 mole of a β-chloro-α-phenylthiovaleric acid derivative in 4 ml of aqueous dioxane (1 : 1) was heated at 70° for 0.5 h, diluted with water, and extracted with ether, and the extract was dried with $MgSO_4$ and evaporated in vacuum. The results of the experiments are given in Table 6.

β-Methoxy-α-phenylthioisovaleric Acid Derivatives (IVe-g). A solution of 0.002 mole of a β-chloro-α-phenylthioisovaleric acid derivative in 6 ml of absolute CH_3OH was evaporated in vacuum, and the residue was recrystallized or distilled. The results are given in Table 6.

α-Ethoxy-β-phenylthioisovaleranilide (VIa). a) A solution of 1.6 g of (Ia) and 0.38 g of thiourea in 7 ml of absolute ethanol was boiled for 1 h. The solvent was evaporated off in vacuum, giving an 80% yield of (IVa), mp 84-85°.

TABLE 2. Hydrolysis of (IIa) (10% solution in aqueous dioxane, 3:1, 60°)

Time, min	(IIa), % *	(IVa), % *
10	74	26
20	54	46
30	37	63
40	31	68,5
50	28	71,6
60	26	74
70	20	80
90	19	90

*Ratio of (II) to (IVa) determined from PMR spectra.

b) A solution of 1.0 g of (Ia) in 7 ml of absolute ethanol was boiled for 1 h. Then the ethanol was evaporated off and the residue was recrystallized. Yield of (IVa) 94%, mp 85-85.5° (from aqueous ethanol). Found: C 68.90; H 6.85; S 10.01%. $C_{19}H_{23}NO_2S$. Calculated: C 69.26; H 7.03; S 9.73%. A mixture of the products obtained by the two methods gave no depression of the melting point.

β-Hydroxy-α-phenylsulfonylisovaleranilide (VI). With ice-water cooling, 2 ml of 30% H_2O_2 was added to 0.5 g of β-hydroxy-α-phenylthioisovaleranilide in 6 ml of glacial CH_3COOH and 1.2 ml of $(CH_3CO)_2O$, the mixture was left at ~20° for six days, the solvent was driven off in vacuum, and the residue was recrystallized. The yield of (VI) was 81%, mp 131-132° (from C_6H_6). Found: C 61.66; H 5.60; S 8.40; N 4.35%. $C_{17}H_{19}NO_4S$. Calculated: C 61.24; H 5.74; S 9.61; N 4.20%.

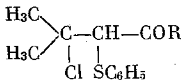
β,β-Dimethyl-α-phenylsulfonylacrylanilide (VIII). a) A solution of 0.1 g of the sulfone (IIIa) in 5 ml of dioxane and 1.5 ml of water was heated at 70° for 30 h. After dilution with water, the mixture was extracted with ether, the extract was dried with $MgSO_4$, the solvent was evaporated in vacuum, and the residue was recrystallized. The yield of (VIII) was 62%, mp 182-184° (from C_6H_6).

b) A mixture of 0.1 g of (VI) and 0.07 g of PCl_5 was ground together and left at 20° for 30 min, after which absolute benzene was added and carefully evaporated off in vacuum. The yield of (VIII) was 52%, mp 182-185° (from C_6H_6). Found: C 64.21; H 5.17; N 4.22; S 10.20%. $C_{17}H_{17}NO_3S$. Calculated: C 64.74; H 5.43; N 4.44; S 10.16%. A mixture of the samples obtained by the two methods gave no depression of the melting point.

TABLE 3. PMR Spectra of the Products Obtained ("Perkin-Elmer R-12" spectrometer, 60 MHz, 5% solution in CCl_4, internal standard HMDS)

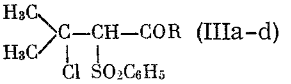
$(CH_3)_2CR^1—CHR^2—COR^3$			Chemical shift, δ, ppm		$(CH_3)_2CR^1—CHR^2—COR^3$			Chemical shift, δ, ppm	
R^1	R^2	R^3	$(H_3C)(H_3C)>C$	CH	R^1	R^2	R^3	$(H_3C)(H_3C)>C$	CH
Cl	SC_6H_5	OH	1,81 1,86	3,87	Cl	$SO_2C_6H_5$	OCH_3	2,04	4,37
SC_6H_5	Cl	OH	1,31 1,54	4,19	OH	SC_6H_5	NHC_6H_5	1,41	3,58
Cl	SC_6H_5	NHC_6H_5	1,77 1,91	3,84	OH	SC_6H_5	OH	1,38 1,40	3,56
SC_6H_5	Cl	NHC_6H_5	1,31 1,43	4,27	OH	SC_6H_5	OCH_3	1,35 1,39	3,58
SC_6H_5	Cl	OCH_3	1,33 1,54	4,23	OCH	SC_6H_5	NHC_6H_5	1,34 1,46	3,55
Cl	SC_6H_5	OCH_3	1,78 1,84	3,)	OCH	SC_6H_5	OCH_3	1,33 1,35	3,78
Cl	SC_6H_5	NH_2	1,75 1,87	3,82	OH	$SO_2C_6H_5$	NHC_6H_5*	1,32 1,42	4,17
Cl	$SO_2C_6H_5$	NHC_6H_5*	1,53 1,69	4,33	Cl	Cl	Cl	1,77 1,83	4,74
$SO_2C_6H_5$	Cl	NHC_6H_5	1,40 1,54	4,49	Cl	Cl	NHC_6H_5	1,75 1,78	4,51
Cl	SO C_6H_5	OH	2,05	4,39		(VIII)		1,76 1,89	—

*5% solution in CF_3COOH

TABLE 4. Melting Points and Elementary Analyses of Compounds  $(H_3C)_2C(Cl)—CH(SC_6H_5)—COR$ (IIa-d)

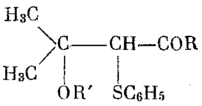
Compound	mp, °C (solvent)	Empirical formula	Found, %					Calculated, %				
			C	H	Cl	N	S	C	H	Cl	N	S
IIa	103.5-104 (CCl₄ and hexane)	$C_{17}H_{18}ClNOS$	63.49	5.65	10.82	4.56	9.92	63.83	5.67	11.08	4.37	10.02
IIb*	—	$C_{12}H_{15}ClO_2S$	55.53	5.83	13.99	—	12.39	55.69	5.84	13.70	—	12.39
IIc	57-58 (petroleum ether)	$C_{11}H_{13}ClO_2S$	54.19	5.37	14.28	—	13.02	53.98	5.35	14.48	—	13.10
IId	90-91 (CCl_4)	$C_{11}H_{14}ClNOS$	54.20	5.58	15.42	5.64	13.20	54.20	5.78	14.54	5.74	13.15

* bp 150°C (5mm); n_D^{20} 1.5495.

TABLE 5. The Sulfones  (IIIa-d)

$(H_3C)_2C(Cl)-CH(SO_2C_6H_5)-COR$

Symbol	Yield, %	mp, °C (solvent)	Empirical formula	Found, %					Calculated, %				
				C	H	Cl	N	S	C	H	Cl	N	S
a	89	160–161 (benzene)	$C_{17}H_{18}ClNO_3S$	58,23	5,02	10,02	4,26	9,11	58,04	5,15	10,07	3,98	9,11
b	90	68–69 (hexane)	$C_{12}H_{15}ClO_4S$	49,39	5,25	11,93	—	11,37	49,57	5,20	12,19	—	11,02
c	74	110,5–111,5 (hexane)	$C_{11}H_{13}ClO_4S$	47,33	4,83	12,57	—	11,60	47,74	4,73	12,81	—	11,58
d	96	174–175	$C_{11}H_{14}ClNO_3S$	47,68	5,03	13,12	5,25	11,80	47,91	5,12	12,85	5,08	11,62

TABLE 6. α-Phenylthioisovaleric Acid Derivatives  (IVa-g)

$(H_3C)_2C(OR')-CH(SC_6H_5)-COR$

Symbol	R′	R	Yield, %	mp, °C (solvent)	Empirical formula	Found, %				Calculated, %			
						C	H	N	S	C	H	N	S
a	H	NHC_6H_5	80,3	95–95,5 (CCl_4 and hexane, 1 : 1)	$C_{17}H_{19}NO_2S$	67,33	6,18	—	10,84	67,74	6,35	—	10,63
b	H	OCH_3	75	bp 134° (4 mm) n_D^{20} 1,5525	$C_{12}H_{16}O_3S$	61,39	6,32	—	14,35	59,97	6,71	—	13,34
c	H	OH	85,7	86–87 (ether and hexane)	$C_{11}H_{14}O_3S$	58,31	6,25	--	13,39	58,38	6,24	—	14,16
d	H	NH_2	94	117–117,5 (ethyl acetate and hexane)	$C_{11}H_{15}NO_2S$	58,24	7,05	6,53	14,37	58,64	6,71	6,22	14,25
e	CH_3	NHC_6H_5	92	109–110 (CCl_4 and hexane, 3 : 7)	$C_{18}H_{21}NO_2S$	68,45	6,70	4,70	10,39	68,53	6,71	4,58	10,16
f	CH_3	OCH_3	76	bp 141° (5 mm) n_D^{20} 1,5456	$C_{13}H_{18}SO_3$	61,86	6,87	—	14,24	61,38	7,13	—	12,60
g	CH_3	NH_2	88	128–129 (ethyl acetate)	$C_{12}H_{17}NO_2S$	60,46	7,13	6,08	13,26	60,22	7,16	5,85	13,39

α,β-Dichloroisovaleroyl Chloride. To 3.0 g of α,β-dichloroisovaleric acid, mp 46° [4], was added 3.1 g of $SOCl_2$, and the mixture was left at ~20°. On the following day, it was heated to 100°, and then the excess of $SOCl_2$ was eliminated in vacuum without heating, and the residue was distilled. The yield of acid chloride was 72%, bp 33° (3 mm); n_D^{20} 1.4720. Found: C 32.82; H 3.75; Cl 54.40%. $C_5H_7Cl_3O$. Calculated: C 31.70; H 3.72; Cl 56.13%. According to the PMR spectra, the substance contained 5% of an impurity, probably α-chloro-β,β-dimethylacryloyl chloride.

α,β-Dichloroisovaleranilide (IX). With stirring at ~20°, 1.86 g of aniline in 15 ml of absolute ether was added dropwise to 1.89 g of α,β-dichloroisovaleroyl chloride in 20 ml of absolute ether. The mixture was left at ~20° for 0.5 h and was then boiled for 0.5 h. The aniline hydrochloride was filtered off, and the ether was evaporated off in vacuum. The yield of (IX) was 82%, mp 107-108° (from CCl_4). Found: C 53.82; H 5.40; Cl 28.74; N 5.72%. $C_{11}H_{13}Cl_2NO$. Calculated: C 53.67; H 5.32; Cl 28.80; N 5.68%.

Attempt at the Hydrolysis of (IX). A solution of 0.5 g of the anilide (IX) in 4.5 ml of dioxane and 3 ml of H_2O was heated at 65° for 2 h and was then diluted with water and extracted with ether. After the evaporation of the ether, the initial anilide with mp 108-109° was recovered. A mixture with authentic (IX) gave no depression of the melting point.

CONCLUSIONS

1. Benzenesulfenyl chloride adds to dimethylacrylic acid and its derivatives with the formation of mixtures of adducts of α-chloro-β-phenylthio- and β-chloro-α-phenylthioisovaleric acids and their derivatives, respectively.

2. α-Chloro-β-phenylthioisovaleranilide readily isomerizes spontaneously at ~20° into β-chloro-α-phenylthioisovaleranilide; α-chloro-β-phenylthioisovaleric acid and its methyl ester isomerize with far greater difficulty.

3. The nucleophilic replacement of the chlorine atoms in β-chloro-α-phenylthioisovaleric acid and its derivatives at high temperatures by OH and OCH_3 groups, which takes place through an intermediate equisulfonium ion, is not accompanied by isomerization.

LITERATURE CITED

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