ADDITION OF METHYLSULFENYL CHLORIDE TO DIMETHYLACRYLIC ACID AND ITS DERIVATIVES

V. A. Zabelaite, Z. A. Stumbrevichute,
L. P. Rasteikene, M. G. Lin'kova,
and I. L. Knunyants

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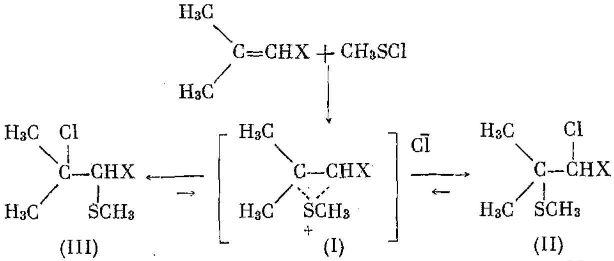
Previously we have studied the addition of methylsulfenyl chloride and β-chloroethylsulfenyl chloride to methacrylic [1] and crotonic acid [2] derivatives. The present paper is devoted to the addition of methylsulfenyl chloride to dimethylacrylic acid, and to its acid chloride, methyl ester, anilide and amide. The addition was run at the lowest possible temperatures in carbon tetrachloride, in the presence of traces of calcium carbonate. The anilide, the methyl ester and dimethylacrylic acid readily form adducts with methylsulfenyl chloride at –15°C. The addition of methylsulfenyl chloride to the acid chloride of dimethylacrylic acid could be accomplished only at room temperature. The NMR spectra were taken of a multiple portion of the reaction mass and of the pure compounds after isolation. By means of the NMR spectra we were able to establish that, the same as in the case of both the acrylic [3, 4] and the crotonic [2] acid derivatives, in the case of dimethylacrylic acid the intermediately formed three-membered episulfonium ring (I) is opened by chloride ion with the preferential formation of the kinetically unstable α-chloro-β-methylmercapto derivatives of isovaleric acid (II). The latter are isomerized much more easily than are the acrylic and crotonic acid derivatives to the more thermodynamically stable derivatives of β-chloro-α-methylmercaptoisovaleric acid (III).



(III) (I) (II)

$X = COOH(a);\ COCl(b);\ COOCH_3(c);\ CONHC_6H_5(d);\ CONH_2(e)$

Thus, for example, in the case of the anilide of dimethylacrylic acid we were able to detect 40% of the unstable isomer (IId) in the reaction mass within 20 min after adding the methylsulfenyl chloride at −25 to −30°. After isolation (either distillation or recrystallization) all of the compounds were the pure (III) isomers (Table 1).

Due to the poor solubility of the amide of dimethylacrylic acid in CCl_4, the addition of methylsulfenyl chloride could be accomplished only in CH_2Cl_2 at 30°. Together with the normal adduct, we isolated a secondary chlorination product, the structure of which was not established. The chemical shifts for compounds (II) and (III) are given in Table 2. It is known that the action of trimethylamine [4] and triethylamine [3, 5] on the α-chloro-β-alkylmercapto derivatives of propionic acid fails to cause isomerization, and leads only to the cleavage of HCl from the already existing β-chloro-α-alkylmercapto isomer.

An attempt to confirm the structure of the (III) compounds obtained by this method proved unsuccessful; triethylamine fails to cleave HCl from the derivatives of β-chloro-α-methylmercaptoisovaleric acid.

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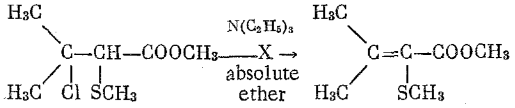
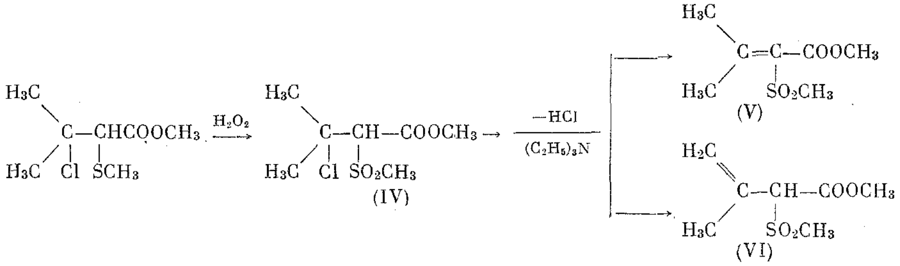
TABLE 1. Addition of CH_3SCl to $(CH_3)_2C = CHCOR$

R	Initial adducts from the reaction mass, %		Time, min	Yield of (III) after isolation, %
	(II)	(III)		
a OH	42	58	90	100
b Cl	88	12	50	100
c OCH_3	68	32	30	100
d NHC_6H_5	40	60	20	100
e NH_2	—	100	10	100

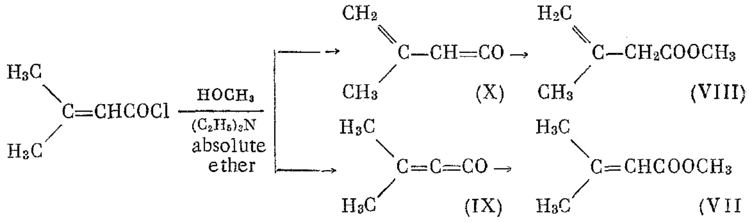


However, the sulfone of the methyl ester of β-chloro-α-methylmercaptoisovaleric acid (IV), obtained by the oxidation of the corresponding sulfide with hydrogen peroxide, easily and quantitatively cleaves HCl under mild conditions. Based on the data of the NMR spectra, the main product (~80%) that is formed here is the sulfone of the methyl ester of α-methylmercaptodimethylacrylic acid (V), contaminated (~15-20%) with the isomeric sulfone of the methyl ester of α-methylmercapto-β-methylvinylacetic acid (VI).



The formation of the latter is probably possible due to the known ease of prototropic rearrangement in dimethylacrylic acid derivatives under the influence of bases [6]. As a result, the structure of the compounds obtained by us was also corroborated chemically.

An attempt to obtain the methyl ester of dimethylacrylic acid from the corresponding acid chloride and absolute methanol, in the presence of triethylamine, in ether solution, led to the formation of a mixture of isomeric esters, which analyzed 55% of the methyl ester of dimethylacrylic acid (VII) and 45% of the methyl ester of β-methylvinylacetic acid (VIII) (chromatographically). The formation of the mixed esters (VII) and (VIII) can be explained by the initial easier formation of the two isomeric ketenes (IX) and (X) from the acid chloride, with a 1–2 and a 1–4 cleavage of hydrogen chloride respectively. An analogous cleavage of HCl by tertiary amine was observed earlier [7]. The subsequent addition of methyl alcohol to the ketenes leads to the mixture of esters. The mixture obtained in this manner could be separated into the pure esters by distillation through a column.



The methyl ester of dimethylacrylic acid was obtained as described in [8].

EXPERIMENTAL METHOD

The NMR spectra were obtained on a Perkin–Elmer P-12 spectrometer with an operating frequency of 60 MHz, in CCl_4 solution, using hexamethyldisiloxane as the internal standard.

α-Methylmercapto-β-chloroisovaleric acid (IIIa). To 2.0 g of dimethylacrylic acid in 8 ml of absolute CCl_4, in the presence of a small amount of $CaCO_3$, was added in drops, with stirring, at −15°, 1.64 g of

TABLE 2. NMR Spectra

Formula	Chemical shift, ppm		
	$\begin{matrix}CH_3\diagdown\\CH_3\diagup\end{matrix}C$	CH	SCH_3
$(H_3C)_2C\ (Cl)\ CH\ (SCH_3)\ COOH$	1,79	3,47	2,32
$(H_3C)_2C\ (SCH_3)\ CH\ (Cl)\ COOH$	1,48	4,34	2,11
$(H_3C)_2C\ (Cl)\ CH\ (SCH_3)\ COCl$	1,76	3,85	2,41
$(H_3C)_2C\ (SCH_3)\ CH\ (Cl)\ COCl$	1,45	4,66	2,13
$(H_3C)_2C\ (Cl)\ CH\ (SCH_3)\ COOCH_3$	1,74	3,44	2,22
$(H_3C)_2C\ (SCH_3)\ CH\ (Cl)\ COOCH_3$	1,42	4,26	2,04
$(H_3C)_2C\ (Cl)\ CH\ (SCH_3)\ CO\underset{\underset{C_6H_5}{\vert}}{N}H$	1,76 1,86	3,42	2,20
$(H_3C)_2C\ (Cl)\ CH\ (SO_2CH_3)\ COOCH_3$	1,96 1,99	4,21	SO_2CH_3 3,10
$(H_3C)_2C\ (Cl)\ CH\ (SCH_3)\ CONH_2$	1,74 1,80	3,42	2,21

CH_3SCl in 3.5 ml of absolute CCl_4. The reaction mixture was kept at −15° for 2 h and then allowed to stand overnight at room temperature. Removal of the CCl_4 in vacuo and subsequent recrystallization of the residue from petroleum ether gave (IIIa) in 58% yield, mp 75-76°. From [9]: mp 73-75°.

Acid Chloride of α-Methylmercapto-β-chloroisovaleric Acid (IIb). To 2.37 g of the acid chloride of dimethylacrylic acid in 8 ml of absolute CCl_4, in the presence of a small amount of $CaCO_3$, was added in drops 1.64 g of CH_3SCl in 3.5 ml of absolute CCl_4 at −15°. After adding the CH_3SCl the reaction mixture was allowed to stand at room temperature for 48 h. The yield of (IIb) was 51%, bp 70° (3 mm); n_D^{20} 1.514. From [9]: bp 71-72° (3 mm); n_D^{20} 1.514.

Methyl Ester of α-Methylmercapto-β-chloroisovaleric Acid (IIc). To 2.28 g of the methyl ester of dimethylacrylic acid in 8 ml of absolute CCl_4, in the presence of a small amount of $CaCO_3$, was added at −30°, in drops, with stirring, 1.64 g of CH_3SCl in 3.5 ml of absolute CCl_4. After standing at −30° for 1.5 h the reaction mixture was allowed to stand for 24 h at room temperature. The solvent was removed in vacuo, and the residue was distilled. The yield of (IIc) was 92.9%, bp 75° (4 mm); n_D^{20} 1.4812; d_4^{20} 1.147. Found: C 42.21; H 6.61; Cl 17.82; S 15.82%; MR 48.823. $C_7H_{13}ClO_2S$. Calculated: C 42.74; H 6.66; Cl 18.02; S 16.31%; MR 49.047.

To 0.196 g of (IIc) in 15 ml of absolute ether was added 0.202 g of triethylamine. The mixture was allowed to stand overnight. The ether solution was washed with water. Volhard titration of the water solution gave 0.18% Cl; calculated 18.02% Cl.*

Anilide of α-Methylmercapto-β-chloroisovaleric Acid (IId). To 1.75 g of the anilide of dimethylacrylic acid in 7 ml of absolute CCl_4, in the presence of a small amount of $CaCO_3$, was added in drops, with stirring, at −30°, 0.82 g of CH_3SCl in 1.7 ml of absolute CCl_4. After standing at −30° for 0.5 h the reaction mixture was allowed to stand at room temperature for 0.5 h. The solvent was removed in vacuo, and the precipitate was recrystallized from a mixture of CCl_4 and petroleum ether (4 : 1). After recrystallization the yield of (IId) was 80.5%, mp 112-112.5°. Found: C 55.60; H 6.14; Cl 13.10; N 4.86; S 12.95%. $C_{12}H_{16}ClNOS$. Calculated: C 55.91; H 6.25; Cl 13.75; N 5.43; S 12.43%.

Amide of α-Methylmercapto-β-chloroisovaleric Acid (IIe). To a solution of 3 g of the amide of dimethylacrylic acid in 40 ml of absolute CH_2Cl_2, in the presence of a small amount of $CaCO_3$, was added in drops, with stirring, at 30°, 2.47 g of CH_3SCl. Here the temperature of the reaction mixture rose to 42° and decolorization occurred immediately. After cooling to room temperature the CH_2Cl_2-insoluble precipitate was filtered to give 0.4 g (8%) of material with mp 154° (C_2H_5OH + absolute ether) ($C_6H_{11}ONSCl_2$). The filtrate was evaporated in vacuo and the residue was worked up to give an 88% yield of (IIe); mp 94-95° (CCl_4). Found: C 39.70; H 6.60; Cl 18.83; N 7.70; S 17.68%. $C_6H_{12}ONSCl$. Calculated: C 39.66; H 6.66; Cl 19.51%; N 7.71; S 17.65%. Found: C 33.32; H 5.12; Cl 32.94; S 14.91; N 6.73%. $C_6H_{11}ONSCl_2$. Calculated: C 33.34; H 5.13; Cl 32.81; N 6.48; S 14.83%.

Sulfone of Methyl Ester of α-Methylmercapto-β-chloroisovaleric Acid (IV). To 0.78 g of (IIc) in 6 ml of glacial acetic acid and 1.2 ml of acetic anhydride was added in drops, with cooling in ice water, 2

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* These percentages are as given in the Russian original. Presumably they should read 18.0% and 18.02%, respectively – Consultants Bureau.

ml of 30% hydrogen peroxide solution. The solvent was evaporated in vacuo, while the precipitate was recrystallized from a mixture of ether and petroleum ether. The yield of (IV) was 82%, mp 62-63°. Found: C 36.38; H 5.55; Cl 14.48; S 13.94%. $C_7H_{13}ClO_4S$. Calculated: C 36.79; H 5.73; Cl 15.51; S 14.02%.

Sulfone of Methyl Ester of α-Methylmercaptodimethylacrylic Acid (V). To 0.35 g of (IV) in 10 ml of absolute ether was added 0.42 ml of triethylamine and the mixture was allowed to stand at room temperature for 15 min. The precipitate of triethylamine hydrochloride was removed by washing well with water. The ether solution was dried over $MgSO_4$ and then evaporated in vacuo. The yield of (V) was 93%, bp 120° (7 mm). Found: C 43.73; H 6.23; S 16.67%. $C_7H_{12}O_4S$. Calculated: C 43.74; H 6.29; S 16.68%.

Volhard titration of the water solution gave 15.56% Cl; calculated 15.55% Cl. The NMR spectrum disclosed a mixture of isomers: (IV) ($\delta_{(CH_3)_2C=}$ 1.95 and 2.23 ppm, $\delta_{SO_2CH_3}$ 2.97 ppm, δ_{COOCH_3} 3.80 ppm) and the sulfone of the methyl ester of α-methylmercapto-β-methylenebutyric acid (δ_{CH_3} 2.01 ppm, δ_{CH_2} 4.23 ppm, δ_{CH} 5.32 ppm, $\delta_{SO_2CH_3}$ 2.97 ppm, δ_{COOCH_3} 3.80 ppm).

Reaction of Acid Chloride of Dimethylacrylic Acid with Methanol in the Presence of $(C_2H_5)_3N$. A solution of 34 g of the acid chloride of dimethylacrylic acid in 150 ml of absolute ether was mixed with 14.4 g of absolute methanol at room temperature. Then to the stirred mixture was added in drops a solution of 30 g of triethylamine in 75 ml of absolute ether. The mixture was stirred at room temperature for 2 h, and then it was heated on the water bath for 0.5 h. The triethylamine hydrochloride was filtered, and the filtrate was washed with water, dried over $MgSO_4$, and the solvent was removed in vacuo. We obtained 23.1 g (70% yield) of a mixture of the (VII) and (VIII) isomers in a ratio of 45 and 55%, respectively (by chromatographing), bp 35-40° (22 mm); n_D^{20} 1.4270.

We were able to obtain the methyl ester of β-methylvinylacetic acid slightly contaminated with (VII), bp 36° (22 mm); n_D^{20} 1.4170; d_4^{20} 0.9314. Found: C 63.13; H 8.80%; MR 30.81. $C_6H_{10}O_2$. Calculated: C 63.13; H 8.83%; MR 31.10. From [10]: bp 41° (27 mm); n_D^{20} 1.4168; d_4^{20} 0.931. The methyl ester of dimethylacrylic acid was obtained slightly contaminated with (I), bp 42° (22 mm); n_D^{20} 1.4319; d_4^{20} 0.9392. Found: MR 31.51. Calculated: MR 31.10. From [11]: $n_D^{20.3}$ 1.432; d_4^{20} 0.9373; MR 31.57.

CONCLUSIONS

1. The addition of methylsulfenyl chloride to dimethylacrylic acid derivatives initially leads to the formation of the unstable α-chloro-β-methylmercapto derivatives, which are very easily isomerized to the stable β-chloro-α-methylmercapto derivatives of isovaleric acid.

2. The derivatives of β-chloro-α-methylmercaptoisovaleric acid, in contrast to the derivatives of β-chloro-β-methylmercaptopropionic acid, do not cleave hydrogen chloride when treated with triethylamine.

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