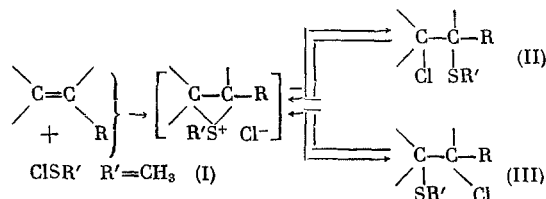


# HYDROLYSIS OF ANILIDES OF $\alpha$ -METHYLTHIO- $\beta$ -CHLORO- AND $\alpha$ -CHLORO- $\beta$ -METHYLTHIOISOBUTYRIC ACIDS

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The kinetic and stereochemical data on the addition of sulfenyl chlorides to olefins make it possible to assume the formation of the intermediate episulfonium ion (I) in these reactions. As a rule, a mixture of adducts (II) and (III) is formed here, which is composed of an unstable isomer, the formation of which can be controlled, and a thermodynamically stable isomer [1]



The initial ratio of the isomeric adducts (II) and (III) is affected by the nucleophilicity of the olefin, the electrophilicity of the sulfenyl chloride, the character of the halogen in the sulfenyl halide, steric factors, polarity of the solvent, and the reaction temperature. The equilibrium is approached via the same intermediate episulfonium ion (I) when varying the conditions for transition of the unstable isomer (II) to the thermodynamically stable (III). The episulfonium ion (I) also takes part in the nucleophilic replacement of the chlorine in  $\beta$ -chloro thioethers, and the formation of the corresponding mixture of isomers is possible in the case of unsymmetrical starting compounds of the (II) or (III) type. Thus, the acetolysis of a mixture [2] of the adducts  $\text{ClCH}_2-\text{CH}(\text{SCH}_3)\text{CH}_3$  and  $\text{CH}_3\text{SCH}_2\text{CHClCH}_3$  (10:90) in which equilibrium had not yet been achieved, as well as the acetolysis of a mixture in which equilibrium had become established (90:10), leads to an initial nonequilibrium mixture of the isomeric  $\beta$ -acetoxy thioethers.

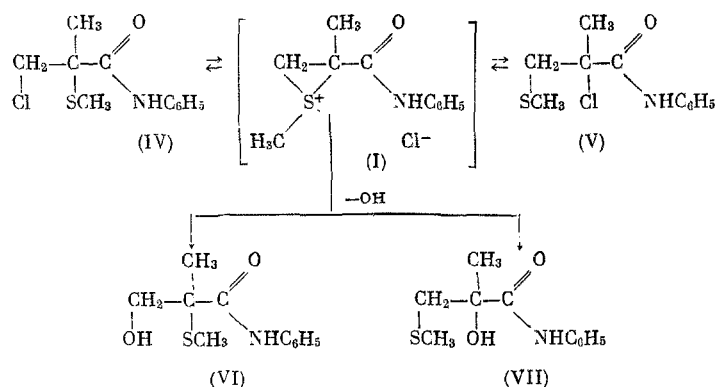
Consequently, the step determining the rate of the reaction, is the formation of the intermediate episulfonium ion (I), and in the kinetically controllable adduct (II) the nucleophilic replacement of chlorine should occur more rapidly than in the thermodynamically stable adduct (III).

The hydrolysis of some isomeric  $\beta$ -chloro thioethers was studied in the present paper. The unstable anilide of  $\beta$ -chloro- $\alpha$ -methylmercaptoisobutyric acid (IV) was obtained previously [3] by the addition of methylsulfenyl chloride to the anilide of methacrylic acid. The thermodynamically stable anilide of  $\alpha$ -chloro- $\beta$ -methylmercaptoisobutyric acid (V) was obtained by the isomerization of (IV), by heating in  $\text{CHCl}_3$  in the presence of traces of  $\text{H}_2\text{SO}_4$ . Based on the data of the NMR spectrum, it contained 5-7% of isomer (IV), which could possibly be the established equilibrium. The reverse isomerization of (V) to (IV) was not observed under the studied conditions.

The hydrolysis of both anilides (IV) and (V) in aqueous dioxane, under the same conditions, gave the same mixture of the isomeric anilides of  $\beta$ -hydroxy- $\alpha$ -methylthio- (VI) and  $\alpha$ -hydroxy- $\beta$ -methylthioisobutyric acid (VII) in equal proportions

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In the NMR spectrum of the hydrolysis products are distinctly present two quadruplets of two methylone groups, at 3.68 and 3.83 ppm,  $J = 12$  Hz (VI), and at 2.64 and 3.06 ppm,  $J = 14$  Hz (VII). Based on the intensities of the signals and the integration, the ratio of the isomers is equal to 1:1. The structure of isomer (VI) as being  $\alpha$ -hydroxy- $\beta$ -methylthioisobutyric acid, and of isomer (VII) as being  $\beta$ -hydroxy- $\alpha$ -methylmercaptoisobutyric acid, was assigned on the basis of the greater shift of the proton downfield under the influence of the oxygen atom than under the influence of the sulfur atom. A study of the hydrolysis rate of anilides (IV) and (V) in aqueous dioxane disclosed that actually the hydrolysis rate of the unstable anilide (IV) greatly exceeds the hydrolysis rate of the stable isomer (V) ( $k_{IV}/k_V \approx 10$ ).

Together with the formation of (VI) and (VII), the partial isomerization of (VI) to (V) was observed when the hydrolysis was followed by means of the NMR spectra. As a result, when (IV) is hydrolyzed in aqueous dioxane the intermediately formed episulfonium ion (I), due to an insufficient concentration of  $\text{OH}^-$  anion, despite the large excess of water, is stabilized by hydrolysis not only in (VI) and (VII), but also in the stable isomer (V).

## EXPERIMENTAL

Anilide of  $\alpha$ -Chloro- $\beta$ -methylthioisobutyric Acid (V). To 3.85 g of the anilide of  $\alpha$ -methylthio- $\beta$ -chloroisobutyric acid (IV) in 30 ml of dry  $\text{CHCl}_3$  was added one drop of conc.  $\text{H}_2\text{SO}_4$ , and the mixture was heated in a flask under reflux at  $65^\circ\text{C}$  for 35 h. The solvent was vacuum distilled, while the residue was dissolved in boiling petroleum ether and allowed to stand in the refrigerator. A small amount of crystals deposited after 7 days. Fractional crystallization from petroleum ether gave (V) in 16% yield; mp  $38\text{--}39^\circ\text{C}$ . Based on the NMR spectrum it contains 5-7% of the starting isomer (IV). Found: C 54.30; H 5.56%.  $\text{C}_{11}\text{H}_{14}\text{ClNO}_2\text{S}$ . Calculated: C 54.21; H 5.75%.

Hydrolysis of Anilide of  $\alpha$ -Methylthio- $\beta$ -chloroisobutyric Acid (IV). A solution of 2 g of (IV) in 25 ml of dioxane and 10 ml of water was heated in a flask under reflux at  $60\text{--}70^\circ\text{C}$  for 8 h. The mixture was extracted with ether and with benzene, and dried over  $\text{MgSO}_4$ . The solvent was vacuum distilled. We obtained a mixture of isomers (VI) and (VII), 1:1 (based on the NMR spectrum), as an oil in 68% yield. Found: C 58.70; H 6.70%.  $\text{C}_{11}\text{H}_{15}\text{NO}_2\text{S}$ . Calculated: C 58.66; H 6.66%.

Hydrolysis of Anilide of  $\alpha$ -Chloro- $\beta$ -methylthioisobutyric Acid (V). The hydrolysis was run in a similar manner, with heating for 12 h. The same mixture of isomers was obtained in 77% yield. Found: C 57.17; H 6.91%.  $\text{C}_{11}\text{H}_{15}\text{NO}_2\text{S}$ . Calculated: C 58.66; H 6.66%.

Study of the Hydrolysis Rate of Anilides (IV) and (V). To a solution of 2.26 mM of the substance in 1 ml of dioxane was added 11 ml of 50% aqueous dioxane. The hydrolysis was run at  $40^\circ\text{C}$ , and the amount of formed HCl was determined conductometrically [4].

## CONCLUSIONS

1. The anilide of  $\beta$ -chloro- $\alpha$ -methylthioisobutyric acid (IV), as well as the anilide of  $\alpha$ -chloro- $\beta$ -methylthioisobutyric acid (V), on hydrolysis forms a mixture of the anilides of the  $\alpha$ - and  $\beta$ -hydroxy acids in equal proportions, namely 1:1.

2. Preliminary data on the hydrolysis kinetics disclosed that the hydrolysis rate of anilide (IV) is approximately 10 times faster than the hydrolysis rate of anilide (V).

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