PROPERTIES OF 3-MERCAPTO-2,2-DIPHENYLPROPIONIC β-THIOLACTONE

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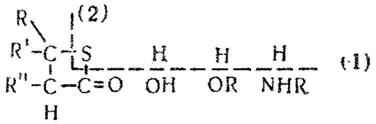
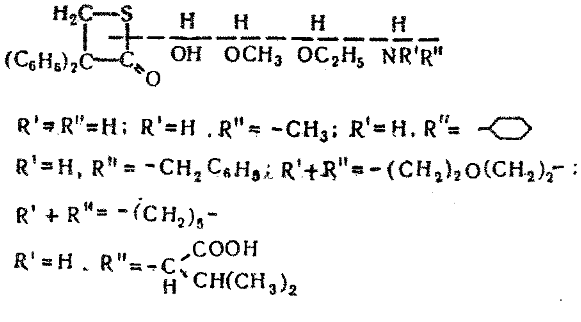
Study of the properties of the thiolactones prepared previously has shown that their hydrolysis, alcoholysis, and aminolysis always proceed in the same direction with scission of the sulfur-carbonyl bond [direction (1)] and formation of the corresponding β-mercapto acids or their derivatives [1-4].



It is known that their oxygen analogs undergo cleavage in a way dependent on the reagent, the solvent, or the order of the addition of the reactants, and that this may occur at the oxygen-carbonyl link [direction (1)], or at the O–C link [direction (2)], or in both directions simultaneously; β-substituents favor cleavage mainly in direction (1) and α-substituents favor cleavage in direction (2), with formation of derivatives of β-hydroxy acids or β-substituted carboxylic acids, respectively. Thus, 3-hydroxy-2,2-diphenylpropionic β-lactone (I) is split by alcohols, amines, and salts mainly in direction (2) with formation of β-substituted acids [5].

In this connection it was of interest to prepare 3-mercapto-2,2-diphenylpropionic β-thiolactone (II), the sulfur analog of (I), and investigate its properties. 3-Mercapto-2,2-diphenylpropionic β-thiolactone was prepared by a previously described method from 3-chloro-2,2-diphenylpropionyl chloride [6]. Study of the reactions of 3-mercapto-2,2-diphenylpropionic β-thiolactone showed that, irrespective of the reaction conditions (order of addition of reactants, solvent), hydrolysis and aminolysis go in one direction only with cleavage of the sulfur-carbonyl bond.



Thus, alkaline hydrolysis of (II) leads to 3-mercapto-2,2-diphenylpropionic acid, and aminolysis to the corresponding 3-mercapto-2,2-diphenylpropionamides; in particular, in the case of valine the product is N-(3-mercapto-2,2-diphenylpropionyl)valine. With more prolonged reaction in excess of amine the amides formed are readily oxidized by air to the corresponding disulfides. Sodium alkoxides split the thiolactone with formation of 3-mercapto-2,2-diphenylpropionic esters, which immediately oxidize in air with formation of the corresponding disulfides.

EXPERIMENTAL

N-Benzyl-3-mercapto-2,2-diphenylpropionamide (III). To 0.96 g (0.004 mole) of (II) we added 3.85 ml (0.036 mole) of benzylamine. The reaction was exothermic. The precipitate formed was filtered off on the next day and washed with dilute hydrochloric acid; yield 1.35 g (97%) of (III). After crystallization from acetic acid: m. p. 176-178°. Found: C 75.13; H 5.83; S 8.67%. $C_{22}H_{21}NOS$. Calculated: C 76.07; H 6.05; S 9.22%.

By the use of different solvents (CH_3CN, C_6H_6) and change in the order of addition, we did not succeed in changing the direction in which the cleavage of (II) occurred. (III) was reaily oxidized with iodine solution to 3,3'-dithiobis(N-benzyl-2,2-diphenylpropionamide), m. p. 130-133° (from petroleum ether). Found: C 76.22; H 5.81; S 8.34%. $C_{44}H_{40}N_2O_2S_2$. Calculated: C 76.30; H 5.78; S 9.24%. On reduction of the latter with zinc dust in acetic acid (III), m. p. 173-175°, was regenerated in quantitative yield. A mixture test with a known sample of (III) showed no depression of melting point.

1-(3-Mercapto-2,2-diphenylpropionyl)piperidine (IV). To 0.96 g (0.004 mole) of (II) we added 2.4 ml (0.024 mole) of piperidine. The solution was boiled for five hours and then left overnight. On addition of dilute hydrochloric acid a precipitate of (IV) was formed; yield 1.25 g (95%). After crystallization from acetic acid: m. p. 199-200°. Found: C 73.65; H 6.63; S 9.65%. $C_{20}H_{23}NOS$. Calculated: C 73.84; H 7.07; S 9.84%.

4-(3-Mercapto-2,2-diphenylpropionyl)morpholine (V). To 1.1 ml (0.012 mole) of morpholine we added 0.96 g (0.004 mole) of (II). The solution was heated in a water bath for six hours. On addition of water 1.1 g (90%) of (V) separated. After crystallization from petroleum ether: m. p. 167-169°. Found: C 69.65; H 6.58; S 9.29%. $C_{19}H_{21}NO_2S$. Calculated: C 69.72; H 6.42; S 9.78%.

3,3'-Dithiobis(N-cyclohexyl-2,2-diphenylpropionamide) (VI). A solution of 0.96 g (0.004 mole) of (II) in 5 ml of acetonitrile was added to a solution of 1.4 ml (0.012 mole) of cyclohexylamine in 5 ml of acetonitrile, and the mixture was heated in a water bath for six hours. On addition of water 1.3 g (95%) of (VI) separated. After crystallization from petroleum ether: m.p. 116-118°. Calculated: C 74.55; H 7.10; S 9.46%. $C_{42}H_{48}N_2O_2S_2$.

3,3'-Dithiobis(N-methyl-2,2-diphenylpropionamide) (VII). Methylamine was passed for four hours into a solution of 0.96 g (0.004 mole) of (II) in 10 ml of acetonitrile. On the next day the acetonitrile was evaporated off in air, and we obtained 1.05 g (98%) of (VII). After crystallization from aqueous alcohol: m. p. 173-175°. Found: C 71.15; H 5.90; S 11.42%. $C_{32}H_{32}N_2O_2S_2$. Calculated: C 71.11; H 5.92; S 11.85%.

3-Mercapto-2,2-diphenylpropionamide (VIII). Ammonia was passed for three hours into a solution of 0.96 g (0.004 mole) of (II) in 10 ml of acetonitrile. The reaction mixture was warmed, and after 30 minutes it gave a positive reaction for the SH group. After the vaporization of acetonitrile we obtained 1.0 g (97.5%) of (VIII). After crystallization from aqueous alcohol: m. p. 165-167°. Found: C 70.04; H 5.88; S 11.95%. $C_{15}H_{15}NOS$. Calculated: C 70.03; H 5.83; S 12.41%.

N-(3-Mercapto-2,2-diphenylpropionyl)valine (IX). A solution of 0.96 g (0.004 mole) of (II) in 50 ml of alcohol was added to 50 ml of an alcoholic solution of the sodium salt of valine [from 0.7 g (0.006 mole) of valine and 0.24 g (0.006 mole) of sodium hydroxide]. The solution was refluxed for three hours, and alcohol was evaporated off in a stream of nitrogen at low pressure; the dry residue was dissolved in water and acidified. The resulting precipitate (IX) was filtered off, washed with water, and purified by reprecipitation from solution in diethyl ether by petroleum ether; m. p. 93-100° (decomp.); yield 1.2 g (55.6%). Found: C 67.57; H 6.28; S 8.38%. $C_{20}H_{23}NO_3S$. Calculated: C 67.22; H 6.44; S 8.96%.

Dimethyl 3,3'-Dithiobis(2,2-diphenylpropionate) (X). We added 0.96 g (0.004 mole) of (II) to a solution of 0.138 g (0.006 g-atom) of sodium in 5 ml of methanol; after five minutes the mixture gave a positive reaction for the SH group. The solution was heated in a water bath for three hours, and alcohol was evaporated off in the air. The dry residue was extracted with ether. After the evaporation of ether we obtained 1.05 g (96%)

of (X). After crystallization from absolute alcohol: m. p. 120-121°. Found: C 70.38; H 5.18; S 11.81%. $C_{32}H_{30}O_4S_2$. Calculated: C 70.84; H 5.53; S 11.80%. In a similar way we prepared diethyl 3,3'-dithiobis(2,2-diphenylpropionate); yield 88%; m. p. 101-102° (from alcohol). Found: C 72.00; H 6.08; S 11.11%. $C_{34}H_{34}O_4S_2$. Calculated: C 71.92; H 5.94; S 11.22%.

SUMMARY

Under the action of compounds containing a mobile hydrogen atom, 3-mercaptopropionic β-thiolactones undergo cleavage in one direction only with formation of 3-mercaptopropionic acids or their derivatives.

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