[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY, UNIVERSITY OF WISCONSIN]

A SULFUR ANALOG OF GLYCERIC ACID. BETA-THIOGLYCERIC ACID

BY C. FREDERICK KOELSCH

RECEIVED SEPTEMBER 27, 1929 PUBLISHED MARCH 6, 1930

In connection with a study of the oxidation–reduction relations of the sulfhydro group, a compound was needed whose molecule contained, in addition to the sulfhydro group, the carboxyl and hydroxyl groups. This paper describes the preparation of such a compound, β-thioglyceric acid.

Although the disulfide corresponding to this acid is formed by the action of nitrous acid on cystin[1] such a method appeared little suited to the preparation of a comparatively large quantity of the sulfhydro acid.

Several unsuccessful attempts were made to replace the halogen in sodium β-chlorolactate (a) with the sulfhydro group by treatment with sodium hydrosulfide or (b) with the xanthogeno group by treatment with potassium xanthate, according to well-known methods of preparation of mercapto acids.[2] The desired result was finally achieved by allowing ethyl β-chlorolactate to react with an alcoholic solution of potassium hydrosulfide, the resulting ethyl β-thioglycerate being subsequently hydrolyzed to the free acid.

Experimental

β-Chlorolactic Acid.—In a large glass cylinder having an internal diameter of about 5 cm. and fitted with a dropping funnel the lower end of which extended to within 2 mm. of the bottom of the cylinder, was placed a mixture of 250 g. of glycerol α-monochlorohydrin with 250 g. of water. In the dropping funnel was placed 350 g. of nitric acid (sp. gr. 1.42). The nitric acid was allowed to flow into the chlorohydrin–water mixture in portions of about 20 ml., care being taken not to mix the layers formed. The addition was regulated so that there was always a layer of nitric acid at the bottom of the cylinder 5–10 mm. thick. A bright green color developed at the junction of the two layers, and slowly spread throughout the mixture. When all of the nitric acid had been added, which usually required two days, the mixture was allowed to stand until it had become colorless and no more oxides of nitrogen were evolved, requiring some six to eight days longer. (Several experiments designed to shorten the time necessary for the oxidation, in which the reaction mixture was warmed, with stirring, or in which a trace of vanadium pentoxide was added to the nitric acid resulted in the formation of a considerable amount of oxalic acid, with a consequent drop in the yield of β-chlorolactic acid.) The mixture was then transferred to a 1-liter Claisen flask and the water and most of the excess nitric acid were distilled off under reduced pressure (25–30 mm.) from

---

[1] Neuberg and Ascher, *Biochem. Z.*, **5**, 451 (1907); Curtius and Kyriacou, *J. prakt. Chem.*, [2] **95**, 360 (1917).

[2] (a) Klason and Carlson, *Ber.*, **39**, 732 (1906); (b) Holmberg, *J. prakt. Chem.*, [2] **71**, 264 (1905); **75**, 169 (1907); **88**, 590 (1913); Biilman, *Ann.*, **339**, 351 (1905); **348**, 120 (1906); Biilmann and Madsen, *ibid.*, **402**, 331 (1914).

a water-bath. The residue (230–240 g.), which became crystalline on standing, was pure enough for conversion into the ester. In one experiment the oxalic acid was removed by treating with precipitated calcium carbonate. The filtered solution of the calcium salt was mixed with a solution of slightly less than enough oxalic acid to precipitate all of the calcium, the calcium content being determined by analysis of an aliquot. After centrifuging off the calcium oxalate, the acid was extracted with ether. The sirupy residue left after the removal of the ether solidified on standing in a vacuum over sulfuric acid to a mass of thick needles melting at 70–75° and deliquescing on exposure to the air.

Anal. Subs., 0.1474; AgCl, 0.1742. Calcd. for $C_3H_5O_3Cl$: Cl, 28.5. Found: Cl, 29.2. *Neut. equiv.* Subs., 0.2222: 0.0995 *N* NaOH 17.3 ml. Mol. wt., calcd., 125.5. Found: 128.

For further purification the acid was crystallized from hot dry benzene, in which it is difficultly soluble. It separates from this solvent in clusters of fine needles melting at 77°.

Anal. Subs., 0.1884: AgCl, 0.2168. Found: Cl, 28.47.

The ammonium salt was prepared by dissolving 4 g. of the acid in 20 ml. of 95% alcohol, neutralizing with concd. aqueous ammonia, and adding 30 ml. of ether. On standing the solution deposited long thick needles melting, after washing with ether and drying in a vacuum over sulfuric acid, at 141° with decomposition.

Anal. Subs., 0.1797: AgCl, 0.1822. Calcd. for $C_3H_8O_3NCl$: Cl, 25.09. Found: Cl, 25.08.

Ethyl β-Chlorolactate.—Crude β-chlorolactic acid freed of water and nitric acid was dissolved in twice its weight of absolute alcohol containing 4% of hydrogen chloride and the solution was refluxed for four hours. The alcohol was distilled off from a water-bath, and the residue was distilled under reduced pressure. After two distillations the ester was obtained as an oil boiling at 106–108° at 25 mm. which soon solidified to a mass of colorless needles melting at 35–37°; yield, 80% of the weight of crude β-chlorolactic acid used.

Anal. Subs., 0.1694: AgCl, 0.1594. Calcd. for $C_5H_9O_3Cl$: Cl, 23.28. Found: Cl, 23.27.

Sodium β-Chlorolactate and Potassium Xanthate.—The reaction between these two substances was carried out in the usual manner. On acidification of the reaction mixture, an oil was precipitated which was identified as carbon bisulfide. Its weight, after purification, indicated that it represented 74% of the sulfur in the potassium xanthate used; the reaction mixture, which could contain at most only a small amount of the expected β-xanthogenolactic acid, was not investigated further.

β-Thioglyceric Ester, $CH_2SHCHOHCOOC_2H_5$.—A solution of 100 g. of potassium hydroxide in 560 ml. of 95% alcohol, contained in a 1-liter 3-necked flask fitted with a stirrer and with a thermometer dipping into the liquid, was saturated at room temperature with hydrogen sulfide. To this was added about 20 ml. of a solution of 150 g. of ethyl β-chlorolactate in 185 ml. of alcohol. The mixture was warmed to 60–65°, at which temperature the reaction started, as was evidenced by the separation of potassium chloride. The temperature of the mixture was kept at 65–70° by the slow addition, with stirring, of the remainder of the ethyl β-chlorolactate solution. When the addition was completed, the mixture was heated at 70° with stirring for thirty minutes. The mixture was then cooled and dry hydrogen chloride was passed in until the mixture was acid to congo red. The potassium chloride was filtered off and the alcohol was distilled from the filtrate. The residue was distilled under reduced pressure, giving

33 g. of ethyl β-thioglycerate boiling at 113–115° at 19 mm.; d_{25}^{25} 1.1779; n_{D}^{25} 1.4754; R_m, calcd., 36.19; obs., 35.88.[3]

Anal.[4] Subs., 0.1799: 0.0917 *N* I_2 soln., 13.1 ml. Calcd. for $C_5H_{10}O_3S$: —SH, 22.0. Found: —SH, 22.0.

Along with the volatile β-thioglyceric ester, 71 g. of a thick oil was obtained which could not be distilled at 5 mm. It was analyzed for sulfur in the hope that this analysis would indicate whether it was principally β,β′-monothiodiglyceric ester or β,β′-dithiodiglyceric ester.

Anal. Subs., 0.2533: $BaSO_4$, 0.3200. Calcd. for $S(CH_2CHOHCOOC_2H_5)_2$, S, 12.0. Calcd. for $S_2(CH_2CHOHCOOC_2H_5)$: S, 21.4. Found: S, 17.36.

The substance showed no reducing properties toward iodine solution and was insoluble in dilute sodium hydroxide. It was not investigated further.

β-Thioglyceric Acid, $CH_2SHCHOHCOOH$.—To 300 ml. of 5% aqueous hydrochloric acid was added 32 g. of ethyl β-thioglycerate, and the mixture was refluxed for seven hours in an atmosphere of carbon dioxide. The solution was concentrated to a volume of about 60 ml. by distillation in a current of carbon dioxide and the residue was placed in a vacuum over sulfuric acid and potassium hydroxide. The sirup remaining after six days was analyzed.

Anal. Subs., 0.3228: 0.0917 *N* I_2 soln., 24.1 ml. Calcd. for $C_3H_6O_3S$: —SH, 26.2. Found: —SH, 22.6.

The acid decomposed when the distillation of a small quantity at 5 mm. was attempted. With ferric chloride in dilute aqueous solution the acid gives a transient blue color.

S-2,4-Dinitrophenyl-β-thioglyceric Acid, $(NO_2)_2C_6H_3SCH_2CHOHCOOH$.—Since the analysis of the mercapto acid obtained above agreed only approximately with that required by its formula, the S-2,4-dinitrophenyl ether was prepared and analyzed as a derivative characteristic of the sulfhydro group.[5] To a solution of 2.5 g. of β-thioglyceric acid in 70 ml. of 95% alcohol was added 10 g. of anhydrous sodium acetate. The mixture was boiled until most of the salt was dissolved, and the solution was filtered. To this solution was added 5 g. of 2,4-dinitrochlorobenzene. The mixture was boiled under a reflux for five minutes and then allowed to cool to room temperature. The crystalline sodium salt which separated was filtered off, washed with a little alcohol and dissolved in warm water. This solution was acidified with dilute sulfuric acid. The precipitate was filtered off and recrystallized twice from hot water. The acid was obtained thus in very small sulfur-yellow plates melting at 167–168° (uncorr.).

Anal. Subs., 0.2076: $BaSO_4$, 0.1685. Calcd. for $C_9H_8O_7N_2S$: S, 11.11. Found: S, 11.15. *Neut. equiv.* Subs., 0.1503: 0.0802 *N* NaOH, 6.6 ml. Mol. wt., calcd., 288. Found: 284.

Barium β,β′-Dithiodiglycerate, $(—SCH_2CHOHCOO)_2Ba$.—A solution of 19 g. of β-thioglyceric acid in 100 ml. of water was made alkaline with a slight excess of ammonia. A slow current of oxygen was bubbled through the solution until a portion acidified with acetic acid no longer decolorized an aqueous iodine solution. The oxidation was complete in about ten hours. The solution was mixed with a concentrated solution of 20 g. of crystallized barium chloride and a slight turbidity which developed was filtered off. On mixing the solution with an equal volume of alcohol, the barium salt was precipitated

---

[3] Value for atomic refraction of sulfur in C—S—H according to Price and Twiss, *J. Chem. Soc.*, **101**, 1259 (1912).

[4] Klason and Carlson, *Ber.*, **39**, 738 (1906).

[5] Friedländer and Chwala, *Monatsh.*, **28**, 250 (1907).

as a white indistinctly crystalline powder. It was filtered off and allowed to stand in a vacuum over sulfuric acid overnight, when it changed to a thick sirup. This was dissolved in water and reprecipitated with alcohol. The precipitate was allowed to remain in contact with the mother liquor for two days, then filtered off and dried at 40° in air. The barium salt was obtained as a white chalky powder.

Anal. Subs., 0.1540, 0.1681: $BaSO_4$, 0.0943, 0.1034. Calcd. for $C_6H_8O_6S_2Ba$: Ba, 36.34. Found: Ba, 36.03, 36.19.

β,β'-Dithiodiglyceric Acid, $(—SCH_2CHOHCOOH)_2$.—A solution of 3.77 g. of the barium salt in water was treated with the calculated amount of *N* sulfuric acid. The barium sulfate was filtered off and the resulting solution was evaporated to a sirup on a water-bath. After this sirup had stood over sulfuric acid in a vacuum for several days, a thick gum remained, weighing 2.30 g. (calcd., 2.42 g.).

Anal. Subs., 0.1397: $BaSO_4$, 0.2676. Calcd. for $C_6H_{10}O_6S_2$: S, 26.45 Found: S, 26.31.

The acid was easily soluble in water and in ethyl acetate; it was precipitated from its solution in the latter solvent by chloroform as a sticky gum.

The writer wishes to express his appreciation of the assistance and advice offered by Professor S. M. McElvain.

Summary

1. A new method of preparation of β-chlorolactic acid has been described.

2. β-Thioglyceric acid and a few of its derivatives have been prepared from ethyl β-chlorolactate.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE WILLIAM H. CHANDLER CHEMISTRY LABORATORY OF LEHIGH UNIVERSITY AND THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY]

THE PREPARATION OF PRIMARY AMINES FROM ALDEHYDES AND MONOCHLORO-AMINE

BY CHARLES R. HAUSER

RECEIVED SEPTEMBER 30, 1929 PUBLISHED MARCH 6, 1930

In view of the fact that oximes have been reduced to primary amines, it would seem possible that chloro-imines could be reduced in a similar manner. Thus primary amines might be prepared from aldehydes and monochloro-amine by the reduction of the intermediate chloro-imine, as represented by the equation

$$RCH{=}O + H_2NCl \xrightarrow{-H_2O} RCH{=}NCl \xrightarrow{+\ 4H} RCH_2NH_2HCl$$

With the exception of methylene chloro-imine,[1] apparently no chloro-imine prepared by this method has been isolated. However, there is evidence that benzalchloro-imine is the condensation product of benzaldehyde and monochloro-amine. Forster[2] reported that benzonitrile and

---

[1] Cross, Bevan and Bacon, *J. Chem. Soc.*, **97**, 2404 (1910).

[2] Forster, *ibid.*, **107**, 265 (1915).