

except that the amount of protein which went into solution in the alcohol was much smaller, possibly not more than five to ten per cent. of the total.

3. **Methylation.**—Reduced protein (10 g.) was treated with benzene (100 cc.) (in which it appears to be slightly soluble) and an excess of methyl iodide (10 g.) was added. This mixture was shaken vigorously, then warmed slightly on the water-bath until it just began to boil. Vigorous shaking was continued. In the course of the reaction, the white sodium salt disappeared and a brown substance separated out. The benzene was poured off and the solid was washed several times with ether, then dissolved in 95% alcohol. The addition of an equal volume of ether precipitated the methylated derivative as an oil. This was thoroughly extracted with ether to remove traces of alcohol, and dried *in vacuo*. It gave a biuret test. It was analyzed for nitrogen and methoxyl.

Anal. (by Research Service Laboratories). 8.855 mg. subs.; 5.595 mg. of AgI; 4.870 mg. subs.: 0.241 cc. N₂ at 26°, 758 mm. Found: OCH₃, 8.34; N, 5.63. (Product contained some sodium iodide.) Ratio OCH₃/N, 0.669.

Summary

1. Proteins are partially ammonolyzed by ammono-bases and ammono-acids in liquid ammonia. The extent of ammonolysis is dependent upon the base and the temperature.

2. Proteins decolorize solutions of sodium and potassium in liquid ammonia, indicating that they are acidic in liquid ammonia. A preliminary study of the reaction or reactions has been made.

3. The reaction of glycyl-*dl*-alanine, glycine ethyl ester hydrochloride, and diketopiperazine with sodium in liquid ammonia has been studied. Other investigations are in progress which we hope will help to throw light on this problem.

CHICAGO, ILLINOIS

[CONTRIBUTION FROM THE INSECTICIDE DIVISION, BUREAU OF CHEMISTRY AND SOILS]

ROTENONE. XV. THE STRUCTURE OF DERRIC ACID

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Derric acid, which is obtained by peroxide oxidation of derrisic acid, is represented by the formula C₁₂H₁₄O₇. It is a dibasic acid containing two methoxyl groups, and it is converted by permanganate into its next lower homolog, which Takei has named rissic acid. Rissic acid readily loses carbon dioxide when heated, yielding decarboxyrissic acid, C₁₀H₁₂O₆.

These facts lead us tentatively to consider derric acid to be a dimethoxyphenylmalic acid, and rissic acid a dimethoxyphenyltartronic acid.¹

Since our last publication on this subject Takei has claimed to have substantiated our formulas and in addition to have placed the methoxy groups in the 2,5-positions.²

¹ LaForge and Smith, *THIS JOURNAL*, **52**, 2878 (1930).

² Takei, *Ber.*, **64**, 248 (1931).

In the meantime we had prepared decarboxyrissic acid and the nitro acid which Takei believed to be dimethoxynitrobenzoic acid.

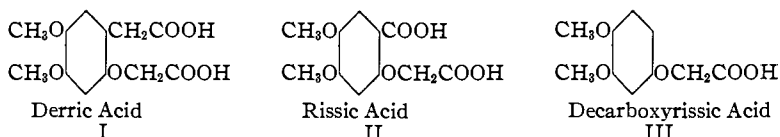
We have also observed a number of new facts which are against the assumption that derric acid is a dimethoxymalic acid and have abandoned this theory for the reasons given below:

Derric acid is very stable when heated and may even be distilled without the formation of an anhydride. It shows none of the properties of the phenylmalic acids which have been so carefully studied by Alexander.³

Derric acid is optically inactive, as are also rissic and decarboxyrissic acids. Attempts to resolve derric acid by means of the brucine salt were unsuccessful.

Decarboxyrissic acid apparently contains no hydroxyl group, as all attempts to prepare acyl derivatives have failed and, in spite of numerous attempts, we have been unable to oxidize it to a benzoic acid derivative. These facts are against the assumption that it is 2,5-dimethoxymandelic acid.² Moreover, we have synthesized 2,5-dimethoxymandelic acid and found it to be different from decarboxyrissic acid.

By the action of phosphorus pentachloride on decarboxyrissic acid, a monochloro acid is obtained, but it is represented by the formula $C_{10}H_{11}O_5Cl$, which shows that no hydroxyl has been replaced in the process. From these facts it can be assumed that derric, rissic and decarboxyrissic acids contain an indifferent oxygen atom and that they may best be represented by the formulas



The positions of the methoxyl groups follow from the facts brought out in a recent article in which we described the preparation of asaronic acid (2,4,5-trimethoxybenzoic acid) from derritol methyl ether and an hydroxy-dimethoxybenzoic acid from derritol,⁴ which was identical with the acid obtained by Clark from dehydrodeguelin and identified by him as 2-hydroxy-4,5-dimethoxybenzoic acid.⁵

Rissic acid undergoes a very characteristic reaction with dilute nitric acid whereby carbon dioxide is evolved and a nitro group substituted in the molecule. The resulting monocarboxylic acid was believed by Takei² to be a dimethoxynitrobenzoic acid, but according to our analytical data it is nitrodecarboxyrissic acid of formula $C_{10}H_{11}NO_7$.

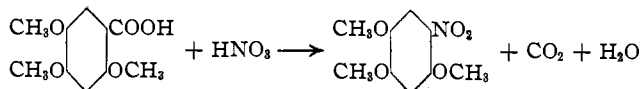
This reaction is strictly analogous to the behavior of asaronic acid,

³ Alexander, *Ann.*, **258**, 67 (1890).

⁴ Smith and LaForge, *THIS JOURNAL*, **53**, 3072 (1931).

⁵ Clark, *ibid.*, **53**, 3431 (1931).

which when treated with nitric acid is converted into 1-nitro-2,4,5-trimethoxybenzene with elimination of the carboxyl group, which is replaced by the nitro group.^{5,6}



Under the same conditions, rissic acid is converted into nitrodecarboxyrissic acid of formula

$$\begin{array}{c} \text{CH}_3\text{O} \\ | \\ \text{C}_6\text{H}_2 \\ | \\ \text{NO}_2 \\ | \\ \text{OCH}_2\text{COOH} \end{array}$$

The analyses of the ethyl ester of the nitro acid agrees for the formula $\text{C}_{12}\text{H}_{15}\text{O}_7\text{N}$.

Finally, we have synthesized the acid of formula III. The method employed was to heat the sodium compound of 1-hydroxy-3,4-dimethoxybenzene with iodoacetic ester. The resulting product, on saponification, yielded 3,4-dimethoxyphenoxyacetic acid, which proved to be identical with decarboxyrissic acid.

The formulas for rissic and derric acids given above follow from analogy. With the structure of these oxidation products established, a number of characteristic reactions of rotenone involving dehydrorotenone and derric acid become intelligible. These relations will be discussed in our next article.

Experimental

Decarboxyrissic Acid.—The rissic acid used in the following experiments was prepared by peroxide oxidation of dehydrihydrorotenonic acid.⁷ Portions of about 0.7 g. of rissic acid were heated to 270° in an atmosphere of carbon dioxide in small distilling flasks by means of a metal bath for about ten minutes. The residue was then distilled over as rapidly as possible under a reduced pressure of about 6 mm. The distillate, which crystallized at once, was removed by breaking the receiver, and several portions were combined and purified by dissolving in benzene and decolorizing with carbon. The substance crystallized in spherical aggregates of prisms, which were then recrystallized from benzene. They melted at 116–117°. The yield was 50%.

Anal. Subs., 0.0634, 0.0680: CO_2 , 0.1320, 0.1401. Calcd. for $\text{C}_{10}\text{H}_{12}\text{O}_5$: C, 56.60; H, 5.66. Found: C, 56.78, 56.19; H, 5.66, 5.46. Subs., 0.0143: cc. of $N/20$ KOH, 1.35. Calcd. mol. wt.: 212. Found: 212.

Chlorodecarboxyrissic Acid.—One gram of decarboxyrissic acid was mixed with 2 g. of finely ground phosphorus pentachloride. Reaction set in at once, with evolution of hydrogen chloride and the formation of a green liquid which was heated for thirty minutes on the steam-bath. Ice was then added, and the resulting green mass was filtered off and recrystallized from 25–30 parts of hot water, from which it separated in long white needles melting at 146°. The yield was 0.9 g.

Anal. Subs., 0.0798: CO_2 , 0.1422; H_2O , 0.0322. Subs., 5.238 mg., 5.907 mg., 4.224 mg.: AgCl, 3.169, 3.403, 2.465 mg. Calcd. for $\text{C}_{10}\text{H}_{11}\text{O}_5\text{Cl}$: C, 48.68; H, 4.46;

⁶ Fabinyi and Széki, *Ber.*, **39**, 3681 (1906).

⁷ LaForge and Smith, *THIS JOURNAL*, **52**, 3608 (1930).

Cl, 14.40. Found: C, 48.59; H, 4.48; Cl, 14.73, 14.26, 14.44. Subs., 0.0276: cc. of *N*/20 KOH, 2.29. Calcd. mol. wt. 246.5. Found: 241.

Chlorodecarboxyrissic Acid Ethyl Ester.—This derivative was prepared by adding absolute alcohol to the reaction product of phosphorus pentachloride and decarboxyrissic acid. On addition of water the ester was obtained in needles, which were recrystallized from dilute alcohol. It melts at 83°. The yield is nearly quantitative.

Anal. Subs., 0.0777: CO₂, 0.1494; H₂O, 0.0361. Calcd. for C₁₂H₁₆O₅Cl: C, 52.60; H, 5.46. Found: C, 52.45; H, 5.16.

Nitrodecarboxyrissic Acid.—Two-tenths of a gram of rissic acid was heated to about 100° with 2 cc. of a mixture of one part concentrated nitric acid and three parts of water. Reaction set in very shortly with strong evolution of gas. The reaction product turned yellow without completely dissolving. The heating was continued until no more gas was evolved, after which the product was cooled, filtered and washed with water. The material was recrystallized from water and melted at 214–215°. The yield was about 0.15 g. Subs., 0.0706, 0.0703, 0.0624, 0.0711: CO₂, 0.1220, 0.1206, 0.1078, 0.1226; H₂O, 0.0294, 0.0271, 0.0244, 0.0277. Subs., 0.0258, 0.0325, 0.0236, 0.0358: cc. of *N*/20 HCl (Kjeldahl), 1.97, 2.35, 1.60, 2.55. Subs., 0.0238, 0.0200: AgI, 0.0444, 0.0370. Calculated for C₁₀H₁₁O₇N: C, 46.69; H, 4.28; N, 5.45; 2CH₃O, 24.13. Found: C, 47.12, 46.78, 47.11, 47.02; H, 4.63, 4.28, 4.34, 4.34; N, 5.34, 5.06, 4.74, 4.98; CH₃O, 24.64, 24.50. Subs., 0.0279: cc. of *N*/10 KOH, 1.17. Calcd. mol. wt., 257. Found: 238.

Nitrodecarboxyrissic Acid Ethyl Ester.—Seven-tenths of a gram of the nitro acid was boiled for fifteen minutes with 15 cc. of 7% alcoholic sulfuric acid. The ester crystallized from the solution in pale yellow needles or prisms melting at 164–165°; yield, 0.5 g.

Anal. Subs., 0.0776, 0.0739: CO₂, 0.1449, 0.1364; H₂O, 0.0340, 0.0340. Calcd. for C₁₂H₁₃NO₇: C, 50.52; H, 5.22. Found: C, 50.92, 50.37; H, 4.87, 5.19.

Bromodecarboxyrissic Acid.—Six and one-half cc. of a 5% solution of bromine in carbon tetrachloride was added to 0.4 g. of decarboxyrissic acid in 5 cc. of chloroform. The bromine was consumed, with evolution of hydrogen bromide, and the evaporated solution yielded a colorless sirup which crystallized at once. Recrystallized from benzene it melted at 150°; yield, 0.25 g.

Anal. Subs., 0.0684: CO₂, 0.1045; H₂O, 0.0225. Subs. (mg.), 3.279, 3.069: AgBr, 2.057, 1.885. Calcd. for C₁₀H₁₁O₅Br: C, 41.24; H, 3.78; Br, 27.49. Found: C, 41.66; H, 3.65; Br, 26.70, 26.15. Subs., 0.0314: cc. of *N*/20 KOH, 2.25. Calcd. mol. wt.: 291. Found: 281.

2,3-Dimethoxymandelic Acid.—One and one-half g. of 2,3-dimethoxybenzaldehyde was melted and shaken with 5 cc. of saturated bisulfite solution. The bisulfite compound was filtered off and suspended in 6 cc. of water, and 1.2 g. of potassium cyanide dissolved in 3 cc. of water was added. The separated nitrile was extracted with a small amount of ether, and the ethereal solution added to 5 cc. of concentrated hydrochloric acid; the ether was boiled off and the solution heated under reflux for twenty minutes. The solution was cooled and extracted with ether and the acid removed from the solvent by shaking with bicarbonate solution. After acidification and decolorizing with carbon, the acid was again extracted with ether, leaving a colorless glassy mass, which crystallized after several days. It was recrystallized from butyl ether and then from benzene. It melted at 96°; yield, 0.5 g.

Anal. Subs., 0.0721: CO₂, 0.1497; H₂O, 0.0367. Calcd. for C₁₀H₁₂O₅: C, 56.60; H, 5.66. Found: C, 56.62; H, 5.66. Subs., 0.0262: cc. of *N*/20 KOH: 2.45. Calcd. mol. wt.: 212. Found: 214.

2,5-Dimethoxymandelic Acid.—2,5-Dimethoxybenzaldehyde was prepared from hydroquinone and chloroform by the method of Tieman and Müller.⁸ It was methylated by dissolving 1.8 g. in 5 cc. of 33% sodium hydroxide and 15 cc. of water and adding slowly 5 cc. of dimethyl sulfate with agitation by a turbine. Two cc. more of the 33% sodium hydroxide was then added, and the reaction was continued for three hours. The 2,5-dimethoxybenzaldehyde was isolated by steam distillation and melted at 52°.

For the preparation of 2,5-dimethoxymandelic acid, the procedure was the same as for the 2,3-dimethoxymandelic acid described above. The final product crystallized in a few minutes, but the crystals contained a sirupy impurity. It was therefore extracted with several portions of ligroin, from which the acid crystallizes in spherical aggregates of needles. For analysis it was again recrystallized from benzene. It melts at 101°, after softening at 90°. In crystal form it was quite different from decarboxyric acid.

Anal. Subs. (mg.), 4.001, 4.043: CO₂, 8.389, 8.446. Calcd. for C₁₀H₁₂O₆: C, 56.60; H, 5.66. Found: C, 57.17, 56.98; H, 5.70, 5.52.

1-Hydroxy-3,4-dimethoxybenzene.—This compound has been described by Clark,⁵ who prepared it by decarboxylation of 2-hydroxy-4,5-dimethoxybenzoic acid⁹ obtained by oxidation of dehydroguaielin. We have found that the same method used in the preparation of decarboxyric acid is applicable to 2-hydroxy-4,5-dimethoxybenzoic acid. Nine-tenths of a gram of the acid was heated in a small flask to 230° in an atmosphere of carbon dioxide until the gas evolution had ceased, after which the phenol was distilled in vacuum. The nearly colorless distillate crystallized on seeding. The yield was 0.5 g.

Synthesis of Decarboxyric Acid.—Five-tenths of a gram of 1-hydroxy-3,4-dimethoxybenzene was dissolved in 3 cc. of absolute alcohol containing 0.08 g. of sodium. The alcohol was expelled by boiling to dryness in a current of air on the steam-bath with two additions of a few cc. of toluene. The amorphous sodium compound was heated with 1 g. of iodoacetic ester for one hour at 140–150°. Four cc. of 2.5% sodium ethylate solution was then added, and the solution was boiled for about twenty minutes. Two or three volumes of water was added, the alcohol expelled, and the solution was acidified and extracted with ether. On seeding with decarboxyric acid, the ether residue crystallized. The crystals were pressed between filter paper to remove adhering oil and then twice recrystallized from benzene. They melted sharply at 116–117°, and the melting point was not depressed when the synthetic material was mixed with decarboxyric acid. In crystal form the two products were identical.

*Anal.*¹⁰ Subs. (mg.), 3.845, 3.315: CO₂, 7.996, 6.892; H₂O, 1.988, 1.764. Calcd. for C₁₀H₁₂O₅: C, 56.60; H, 5.66. Found: C, 56.72, 56.69; H, 5.74, 5.91.

Natural Decarboxyric Acid from Benzene

Synthetic Decarboxyric Acid from Benzene

Both these compounds were found to be identical in so far as the optical crystallographic data were concerned. The following data were obtained by the optical immersion method. Both substances in ordinary light were found to consist of lath-like

⁸ Tieman and Müller, *Ber.*, **14**, 1992 (1881).

⁹ This acid has since been obtained by Haller in this Laboratory by permanganate oxidation in acetone solution of dehydrorotenone or any other compound of this type as will be described in a subsequent article

¹⁰ The micro-analyses were made by J. R. Spies of this Division. The crystallographic examination was by Mr. George L. Keenan of the Food and Drug Administration, for which services we express our thanks.

rods, many with six-sided outline, and fibrous fragments. In parallel polarized light (crossed nicols), the extinction is inclined and the sign of elongation negative; the rods do not extinguish sharply with crossed nicols, many of them remaining essentially bright when the stage is rotated. In convergent polarized light (crossed nicols), biaxial interference figures are common, these showing one optic axis up or slightly inclined. The refractive indices are: n_{α} , 1.506; n_{β} , 1.655; n_{γ} , 1.685; all ± 0.003 .

Summary

Rissic acid which is obtained by oxidation of derric acid is converted into decarboxyrissic acid with elimination of one carboxyl group. Nitro-decarboxyrissic acid is formed by the action of dilute nitric acid on rissic acid. Chlorodecarboxyrissic acid results from the action of phosphorus pentachloride on decarboxyrissic acid. Decarboxyrissic acid is shown by synthesis to be 3,4-dimethoxyphenoxyacetic acid. The 2,5-dimethoxy-mandelic acid which was claimed to be identical with decarboxyrissic acid was also prepared synthetically. The formulas for derric and rissic acid are established by analogy.

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY, NATIONAL TSINGHUA UNIVERSITY]

ALKYL OXALATES AND OXAMATES

BY PETER P. T. SAH AND SHIH-LIANG CHIEN

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Among the known di-alkyl oxalates¹ described in the literature, the methyl and ethyl esters have been thoroughly studied. Regarding the higher homologs, however, very few data can be found even for their simple physical constants. With the calculated amount of ammonia, these esters were reported to give crystalline partial amides, alkyl esters of oxamic acid.² Here, again, only the ethyl derivative was studied in full detail. For the rest, their melting points were not given.

By direct esterification of anhydrous oxalic acid in the presence of hydrogen chloride, we have successfully prepared six alkyl oxalates in a very pure condition and carefully determined their simple constants. By allowing these esters to react with the calculated amount of ammonium hydroxide in alcoholic solution, beautiful crystals of alkyl oxamates were isolated and further purified by recrystallization. Their melting points were carefully

¹ (a) Beilstein, "Handbuch der organischen Chemie," Band II, pp. 534-540 (1920); (b) *ibid.*, Band II (suppl.), pp. 231-234 (1929).

² (a) Dumas and Boullay, *Ann. chim. phys.*, [2] 37, 38 (1828); (b) Dumas, *ibid.*, [2] 54, 241 (1833); *Ann.*, 10, 292 (1834); (c) Liebig, *ibid.*, 9, 131 (1834); (d) Dumas and Peligot, *Ann. chim.*, [2] 58, 60 (1835); *Ann.*, 15, 46 (1835); (e) Balard, *ibid.*, 52, 314 (1844); (f) Cahours, *Comptes rendus de l'Académie des Science*, 77, 746, 1408 (1873); *Bull. soc. chim.*, [2] 21, 77, 358 (1874); (g) Weddige, *J. prakt. Chem.*, [2] 10, 196 (1874); *ibid.*, 12, 435 (1875); (h) Wallach and Liebermann, *Ber.*, 13, 507 (1880).