saturation being due to the action of the strong alkali. Spectroscopic examination of the alcohol produced an absorption curve with a characteristic peak at 2300–2350 Å., where the $E^{1\%}_{1\,cm.}$ was 600. This value, again, is approximately one-half the maximum $E^{1\%}_{1\,cm.}$ reported by Van Der Hulst[8] for 9,11-linoleic acid, in contrast to the negligible absorptive power of 9,12-linoleic acid. Further confirmation of the presence of conjugation was obtained by oxidizing the alcohol with neutral potassium permanganate in acetone[9] to caproic acid and approximately equal parts of azelaic and sebacic acids. It is therefore apparent that the substance is a mixture of octadecadiene-9,12-ol-1 and octadecadiene-10,12-ol-1.

On standing at ice-box temperatures in an evacuated and sealed tube for about a month, the liquid slowly deposited a small amount of a crystalline material melting at 41–42.5° after two crystallizations from methanol, while the freezing point of the mixture rose to 15°. Further investigation of the nature of the crystalline substance was prevented by its rapid conversion, even in highly evacuated containers, into a doughy material, m. p. 128°, insoluble in ligroin, ethyl ether, and methanol.

The effect of sodium butylate on linoleic acid, producing spectroscopic activity, conjugation, and isomerization to crystalline forms will be the subject of a future communication.

(8) Van Der Hulst, *Rec. trav. chim.*, **54**, 641 (1935).

(9) Armstrong and Hilditch, *J. Soc. Chem. Ind.*, **44**, 43T (1925).

Experimental

Eight grams of linoleyl alcohol, prepared essentially as directed by Turpeinen, was dissolved in 200 cc. of purified acetone; 120 g. of powdered potassium permanganate was added carefully, and the mixture finally refluxed on the water-bath for three hours. The acetone was then completely driven off and 450 g. of sodium bisulfite was added. Decolorization was effected by the addition of water and successive small portions of dilute sulfuric acid. The solution was extracted once with ethyl ether and the extract steam distilled. The distillate was extracted with ether, dried over sodium sulfate, and distilled. The volatile portion, weighing 0.8 g., boiled at 200° and had an equivalent of 115.2. (Caproic acid boils at 202°, equiv. 116.1.)

The residue from the steam distillation, after one crystallization from water and charcoal to remove a slight quantity of tarry material, weighed 1 g. and melted at 88–99°. Fractional crystallization yielded 0.2 g. of an acid, equivalent 102.7, m. p. 129–131°, no depression with a sample of authentic sebacic acid, m. p. 132°, equiv. 101.07; and 0.2 g. of azelaic acid, equivalent 95.2, m. p. 97–103°. The intermediate fraction melted at 105–125°.

Summary

1. Linoleyl alcohol prepared by the alcoholic sodium reduction of methyl linoleate was shown to consist of a mixture of octadecadiene-9,12-ol-1 and octadecadiene-10,12-ol-1.

2. The properties of the product were accounted for by the presence of conjugation.

3. The physical properties of the substance were observed to change on prolonged standing in the absence of oxygen.

MINNEAPOLIS, MINN. RECEIVED OCTOBER 27, 1938

[CONTRIBUTION FROM THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, COLUMBIA UNIVERSITY]

The Condensation of α-Keto Acids and Amides. II. Pyruvic Acid and Acetamide[1]

BY ROBERT M. HERBST

When acetamide and pyruvic acid are condensed under the conditions described by Bergmann and Grafe,[2] the principal product is α,α-diacetaminopropionic acid. A small amount of α-acetaminoacrylic acid is also formed and may be separated from the former by its solubility in hot ethyl acetate. The ethyl acetate also removes from the reaction mixture a low melting component which has not been described previously.

By the interaction of benzoylformic acid and acetamide, Shemin and Herbst[1] obtained, besides the expected α,α-diacetaminophenylacetic acid, small amounts of α-benzoylaminophenylacetic acid by a reaction apparently analogous to the formation of phenacetylphenylalanine[3] or acetylalanine[4] from ammonia and phenylpyruvic or pyruvic acids, respectively. The low melting by-product of the pyruvic acid–acetamide condensation was found to contain no acetylalanine, but yielded a compound which appeared to be a complex of one molecule of α-hydroxy-α-acet-

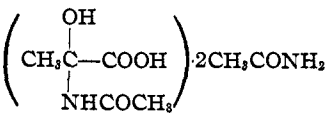
(1) Previous paper, Shemin and Herbst, THIS JOURNAL, **60**, 1954 (1938).

(2) Bergmann and Grafe, *Z. physiol. Chem.*, **187**, 187 (1930)

(3) Erlenmeyer and Kunlin, *Ann.*, **307**, 146 (1899); Erlenmeyer, *ibid.*, **337**, 205 (1904).

(4) De Jong, *Rec. trav. chim.*, **19**, 259 (1900).

aminopropionic acid and two molecules of acetamide.



The isolation of this product supports the mechanism, suggested by Shemin and Herbst,[1] in which the first step of the reaction was assumed to be the addition of acetamide to the carbonyl group of the keto acid.

The same compound is also formed when suitable amounts of the components are allowed to interact in concentrated alcoholic solution or in dry ethyl acetate.

Simple hydroxy-acetamino derivatives have been prepared from aldehydes in which halogen substitution on the carbon atom adjacent to the carbonyl group exerts a stabilizing influence.[5] Free α-hydroxy-α-acetaminopropionic acid seems to be a relatively unstable compound, but the formation of a molecular complex with acetamide provides sufficient stability to permit its isolation.

The tendency of acetamide to form molecular compounds is well known, and the participation of two molecules of acetamide in such combinations is not infrequent. Attempts to replace that portion of the acetamide involved in complex formation in the above compound by other amides such as formamide, propionamide and benzamide were unsuccessful, and it was not found possible to obtain analogous complexes by the interaction of pyruvic acid with these amides.

The equivalent weight of the α-hydroxy-α-acetaminopropionic acid–acetamide complex, when determined by titration, agreed closely with the theoretical value 265. However, the apparent molecular weight, determined cryoscopically in aqueous solution, was 85 when the substance was dissolved in cold water, and 60 after the same solution had been heated for a short time. These values may be explained by assuming dissociation into one molecule of α-hydroxy-α-acetaminopropionic acid and two molecules of acetamide in cold aqueous solution, and into one molecule of pyruvic acid and three molecules of acetamide on heating. The average molecular weights expected under these conditions would be 88 and 66, respectively.

(5) Jacobsen, *et al.*, *Ann.*, **157**, 243 (1871); *Ber.*, **15**, 599 (1882); Pinner, *Ann.*, **179**, 21 (1875); Schiff, *et al.*, *Ber.*, **10**, 1783 (1877); **25**, 1690 (1892); Freundler, *Compt. rend.*, **143**, 682 (1906); *Bull. soc. chim.*, [4] **1**, 200 (1907); Raske, *Ber.*, **45**, 732 (1912); Feist, *ibid.*, **45**, 945 (1912).

The interpretation of the molecular weight determinations is supported by the behavior of the compound in dilute acetic acid solution. On addition of phenylhydrazine to the cold solution pyruvic acid phenylhydrazone begins to separate only after four or five hours at room temperature. However, if the solution is first boiled momentarily and then rapidly cooled to room temperature, subsequent addition of phenylhydrazine causes the immediate precipitation of pyruvic acid phenylhydrazone. Similarly, with 2,4-dinitrophenylhydrazine in alcoholic solution no hydrazone precipitates until the solution is boiled for a few moments after acidification with hydrochloric acid.

The compound does not decolorize bromine water. When heated *in vacuo* it decomposes in two ways depending upon conditions: (a) into one molecule each of water, acetamide and α,α-diacetaminopropionic acid, and (b) into two molecules of acetamide and one molecule each of water and α-acetaminoacrylic acid. Attempts to prepare derivatives of the compound by benzoylation or acetylation were unsuccessful; the reagents always caused dehydration with the formation of α-acetaminoacrylic acid. Efforts to prepare the phenylurethan with phenyl isocyanate likewise failed. Treatment with barium hydroxide resulted in complete decomposition of the compound into pyruvate and acetamide.

In the hope of increasing the yield of α-acetaminoacrylic acid in the condensation of pyruvic acid with acetamide the reaction was tried over a wide range of conditions. When equimolar quantities of the reactants were heated at 55–60°, α-acetaminoacrylic acid was formed in greater amount than α,α-diacetaminopropionic acid, but the main product of the reaction was the α-hydroxy-α-acetaminopropionic acid–acetamide complex. Under no conditions could α-acetaminoacrylic acid be made the principal product.

Experimental

α-Hydroxy-α-acetaminopropionic Acid–Acetamide Complex.—The combined ethyl acetate soluble portions of several condensations of acetamide and pyruvic acid performed according to Bergmann and Grafe[2] were fractionally crystallized first from dry ethyl acetate and then from acetone. Most of the α-acetaminoacrylic acid crystallized from the ethyl acetate; the more soluble fraction yielded the α-hydroxy-α-acetaminopropionic acid complex on recrystallization from acetone. The compound separates slowly from either solvent in the form of transparent, colorless prisms, m. p. 115–116° with decomposition.[6]

(6) All melting points are corrected.

The product is easily soluble in cold water, ethyl and methyl alcohol, and is practically insoluble in benzene or petroleum ether.

Anal. Calcd. for $C_6H_{10}N_2O_6$: C, 40.7; H, 7.2; N, 15.8; equiv. wt., 265. Found: C, 40.8; H, 7.0; N, 15.8; equiv. wt., 271.

The molecular weight was determined cryoscopically in aqueous solution. Solutions of 0.4716 and 0.4632 g. of the complex in 17.135 and 17.492 g. of cold water, respectively, showed freezing point depressions of 0.605 and 0.580°, respectively, before heating, and 0.855 and 0.817°, respectively, after heating for ten minutes on a boiling water-bath. The apparent molecular weights calculated from these data are 85 and 85 before heating and 60 and 60 after heating the solutions; those calculated from the empirical formula on the basis of dissociation first into three molecules and then into four (neglecting the ionic dissociation of the carboxyl group) are 88 and 66, respectively.

The same compound was formed on treating a solution of 8.85 g. of acetamide in 15 cc. of absolute alcohol with 4.4 g. of pyruvic acid. Heat was evolved on mixing. After several days at room temperature, the complex precipitated on inoculation. For preparative purposes the use of dry, acid-free ethyl acetate as the medium for the reaction is preferable. The same quantities of reactants in 20 cc. of hot ethyl acetate yielded 10.7 g. of practically pure complex, which was obtained in pure form on recrystallization from acetone.

Behavior toward Phenylhydrazine.—A solution of 265 mg. of the complex in 5 cc. of cold 5% acetic acid was treated with 100 mg. of phenylhydrazine. Crystals of pyruvic acid phenylhydrazone began to appear after about five hours at room temperature. After eight hours these were removed; on recrystallization from 50% alcohol they melted at 191° with decomposition. A similar solution of the complex was boiled for a few minutes and then rapidly cooled to room temperature and treated with phenylhydrazine. Pyruvic acid phenylhydrazone precipitated immediately, and after recrystallization from 50% alcohol melted at 190° with decomposition. The melting point of neither preparation was depressed when mixed with an authentic specimen.[7]

Behavior toward 2,4-Dinitrophenylhydrazine.—A solution of 100 mg. of the complex in 5 cc. of cold 95% alcohol was treated with a warm solution of 75 mg. of 2,4-dinitrophenylhydrazine in 5 cc. of 95% alcohol to which a drop of concentrated hydrochloric acid had been added. The hydrazine reagent crystallized on cooling the solution and was recovered almost quantitatively. In an experiment identical in other respects the solution of the reactants was boiled for a few minutes. On cooling, pyruvic acid 2,4-dinitrophenylhydrazone separated as yellow needles. After recrystallization from 95% alcohol the product melted at 216° with decomposition and showed no depression when mixed with an authentic sample.[8]

Behavior on Heating.—The α-hydroxy-α-acetaminopropionic acid–acetamide complex (265 mg.) was heated in a long tube at 100° under a pressure of 18–20 mm. for six hours. The loss in weight, probably mainly water, was 21 mg. or 115% of the theoretical amount. The sublimate weighed 73 mg., melted at 81–81.5°, and showed no depression when mixed with acetamide. The residual material (171 mg.) was saturated toward aqueous bromine solution and melted at 189° with decomposition after recrystallization from alcohol. Analysis showed it to be α,α-diacetaminopropionic acid.

Anal. Calcd. for $C_7H_{12}N_2O_4$: N, 14.9. Found: N, 14.8.

When another portion of the complex (265 mg.) was heated at 76° under 0.5 mm. pressure for five hours, the loss in weight was 10 mg., the sublimate weighed 160 mg. and the residue 95 mg. Pure acetamide, m. p. and mixed m. p. 81–82°, was obtained on resublimation of the sublimate. The residual material after recrystallization from acetone absorbed bromine in aqueous solution and melted at 197° with decomposition.[9] Analysis confirmed the identification of the product as α-acetaminoacrylic acid.

Anal. Calcd. for $C_5H_7NO_3$: N, 10.9. Found: N, 11.0.

Behavior toward Barium Hydroxide.—A solution of the complex (265 mg.) in 50% alcohol was treated with the calculated amount of 0.4 *N* aqueous barium hydroxide solution which had been diluted with an equal volume of absolute alcohol. A barium salt (135 mg.) was precipitated almost immediately. However, the product contained no nitrogen, and when dissolved in dilute acetic acid and treated with phenylhydrazine immediately gave a precipitate of pyruvic acid phenylhydrazone, m. p. 189° with decomposition, after recrystallization from 50% alcohol.

Treatment of the complex with cupric, mercuric or lead acetates in water or aqueous alcohol failed to yield insoluble metal salts of the compound.

Condensation of Pyruvic Acid and Acetamide.—In an effort to eatablish conditions under which α-acetaminoacrylic acid would be the major product of the reaction, experiments were carried out over a wide range of conditions. The reactants were heated together without solvent under 15–20 mm. pressure; the temperature of the

TABLE I

CONDENSATION OF PYRUVIC ACID AND ACETAMIDE

Moles pyruvic acid / Moles acetamide	Temp., °C.	Time, hrs.	Yields, %[a] α-Acetaminoacrylic acid	α,α-Diacetaminopropionic acid	Complex[b]
1/2	100	5	3	59	..
1/1.1	80	8	1	26	8
1/1	60–65	7.5	23	27	28
1/1	55–60	9	19	10	52

[a] The yields of α,α-diacetaminopropionic acid and of the α-hydroxy-α-acetaminopropionic acid complex are based on the amount of acetamide, that of the α-acetaminoacrylic acid on the amount of pyruvic acid employed. [b] Complex designates the α-hydroxy-α-acetaminopropionic acid–acetamide compound.

(7) Fischer, *Ber.*, **17**, 572 (1884); Curtius, *ibid.*, **45**, 1057 (1912).

(8) Allen, THIS JOURNAL, **52**, 2955 (1930).

(9) Mixed melting point determinations are not satisfactory for distinguishing between α-acetaminoacrylic acid and α,α-diacetaminopropionic acid. The decomposition of the former varies over a rather wide range dependent upon the rate of heating.

heating bath, the proportions of the reactants and the length of the reaction period were varied as shown in Table I.

Summary

1. A compound which appears to be a complex of one molecule of α-hydroxy-α-acetaminopropionic acid and two molecules of acetamide has been isolated as a by-product of the condensation of pyruvic acid and acetamide.

2. A method of preparing the complex in good yield from pyruvic acid and acetamide is described; it indicates that the complex probably represents the first step in the condensation reaction.

3. Attempts to modify the conditions of the condensation of pyruvic acid and acetamide in such a way as to make α-acetaminoacrylic acid the principal product were not successful.

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[CONTRIBUTION FROM THE BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE, U. S. DEPARTMENT OF AGRICULTURE]

Crystalline Solvates of Inactive Deguelin

BY LYLE D. GOODHUE AND H. L. HALLER

Extractives prepared from derris and cube contain, besides rotenone, principally deguelin. Certain types of derris also contain considerable amounts of toxicarol and some sumatrol.[1] Deguelin and tephrosin have never been obtained by direct crystallization, but are only obtained in the inactive form[2] when the extractives are treated with mild alkali.

Rotenone crystallizes from certain organic liquids with a definite molecular ratio of rotenone to solvent of crystallization. A number of these solvates have been investigated,[3,4] primarily because of their possible use in methods for the determination of rotenone. The solvates formed with carbon tetrachloride and dichloroacetic acid have been shown to be of value in the analysis of derris and other rotenone-bearing plants, and under the conditions employed rotenone is the only compound that separates when extractives of these plants are treated with these solvents. Deguelin probably occurs in the plant in the levo form,[5] and solvates, if formed during the determination of rotenone, are either too soluble or their melting points too low for ready crystallization.

It has now been found that racemic deguelin forms definite stable solvates with a number of solvents, and several of these are reported in this paper.

After it was observed that inactive deguelin separated from chloroform as the solvate, all the readily available solvents were examined for solvate formation with this compound. It was found that carbon tetrachloride, chloroform, bromoform, and ethylene bromide form definite stable solvates in a ratio of 1 mole of deguelin to 1 of solvent. Although no definite data have yet been obtained, it is evident that the carbon tetrachloride solvate is the least soluble and, just as in the determination of rotenone, it would be the most suitable for deguelin. The solvate with bromoform would be excellent because of its high molecular weight, but it is too soluble to crystallize without the addition of petroleum ether.

In a comparison of the liquids that form solvates with rotenone and deguelin it is interesting to note that, so far as is shown, only carbon tetrachloride and chloroform are capable of forming solvates with both these closely related compounds. Rotenone forms solvates with many organic acids and benzene, but not with bromobenzene, chlorobenzene, or ethylene bromide, whereas deguelin forms solvates with the last three and not with organic acids or benzene. Neither rotenone nor deguelin was found to form solvates with aliphatic hydrocarbons, alcohols, ketones, and ethers. Little is known about solvate formation but with the rotenone group of compounds it appears that solvate formation is more likely to occur when the solvent molecule possesses a negative substituent. Not all compounds containing such a substituent, however, form solvates. This generalization is a useful working tool in the search for new solvates.

The methods for the determination of rotenone depend upon the formation of a sparingly soluble

(1) Cahn and Boam, *J. Soc. Chem. Ind.*, **54**, 42T (1935).

(2) Clark, THIS JOURNAL, **53**, 313 (1931).

(3) Tattersfield and Roach, *Ann. Appl. Biol.*, **10**, 1 (1923); Jones and Smith, THIS JOURNAL, **52**, 2554 (1930); Jones, *ibid.*, **53**, 2738 (1931); Jones, U. S. Patent 1,942,104 (Jan. 2, 1934).

(4) Jones, U. S. Patent 2,103,195 (Dec. 21, 1937); Jones, *Ind. Eng. Chem., Anal. Ed.*, **10**, 684 (1938).

(5) Haller and LaForge, THIS JOURNAL, **56**, 2415 (1934).