in this series, as benzoxazines without the carboxyl group, or with other groups such as the methyl group, have been reported as being of considerable medicinal value.[7]

Summary

3-(α-Bromopropionylamino)-salicylic acid was synthesized and, from this by treatment with alkali, 2-methyl-8-carboxy-3-keto-3,4-dihydro-1,4-benzoxazine. Both of these substances are new compounds.

Neither 2-methyl-8-carboxy-3-keto-3,4-dihydro-1,4-benzoxazine nor 6-carboxy-3-keto-3,4-dihydro-1,4-benzoxazine exerts either antipyretic or analgesic action in various test animals.

(7) F. Hoffman, La Roche & Co. A.-G., British patent 370,375 (Apr. 17, 1931); German patent, 557,111 (Apr. 18, 1931); Preiswerk and Mayer, U. S. patent 1,951,897 (Mar. 20, 1934).

PITTSBURGH, PENNA.
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[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF MARYLAND]

A New Method for the Purification of the Alcoholate of the Trimer of Hydroxypyruvic Aldehyde

BY WILLIAM E. EVANS, JR., C. JELLEFF CARR AND JOHN C. KRANTZ, JR.

Hydroxypyruvic aldehyde is of interest owing to its relationship to the intermediate metabolites of glucose. This compound has been prepared by the oxidation of dihydroxyacetone[1-4] and by the photochemical decomposition of glyoxal.[5] Evans and Waring[1] treated dihydroxyacetone with an excess of cupric acetate and removed the excess of copper by precipitation as sulfide. Friedemann[2] employed the same method but did not separate the compound from solution. This process was objectionable on account of the formation of sulfur derivatives of hydroxymethyl glyoxal which are toxic. Küchlin and Böeseken[3] decomposed the sulfur compounds with an excess of silver acetate at 30° and subsequently removed the excess of silver as chloride. Hynd[4] found that the use of silver acetate caused the formation of a highly polymerized product. He avoided the use of hydrogen sulfide by precipitating the excess copper with barium hydroxide. The barium was then removed as sulfate. Norrish and Griffiths[5] prepared small amounts of glycerosone by the photochemical decomposition of glyoxal and isolated it as the trimer combined with one molecule of alcohol.

Experimental

Preparation of Hydroxypyruvic Aldehyde.—One mol of dihydroxyacetone was dissolved in 10 mols of water and treated at room temperature with 2.25 mols of finely divided crystallized cupric acetate. The mixture was shaken frequently in order to keep the solution saturated with copper acetate. The reaction was allowed to proceed until the calculated amount of cuprous oxide was precipitated. The usual period of time necessary was five to seven days. At this time a grayish-colored precipitate of cupric oxalate began to appear. The excess of Cu^{++} was then precipitated carefully by the addition of a calculated amount of a 10% solution of oxalic acid. After filtering the solution was reduced to a small volume by distilling at 17 mm. at 35°. Successive portions of alcohol were added and the product was reduced to dryness at 17 mm. The residue was then dissolved repeatedly in small amounts of absolute alcohol and precipitated by the addition of ether. The ether–alcohol solutions were worked up later, using the same procedure, to recover some of the product. Substances which were insoluble in water and in absolute alcohol were removed and the product was dried *in vacuo* at 70°. The yield of the product was 87%. After purification for biological use the yield was 64%. The product gave a negative test for Cu^{++} or oxalate. It was obtained as a pale yellow amorphous solid which melted between 155 and 160°. A 1% aqueous solution exhibited a *p*H of 3.12 at 25°. It reduced Fehling's solution and mercuric chloride solution rapidly in the cold. No immediate reaction was obtained when Schiff's reagent was added to the freshly prepared solution but the characteristic color appeared within several minutes.

Anal. Calcd. for $(C_3H_4O_3)_3 \cdot C_2H_5OH$: C, 42.47; H, 5.85; mol. wt., 310. Found: C, 42.57; H, 5.42; mol. wt., 306.

This is in agreement with the results obtained by Norrish and Griffiths.[5]

On account of the ease of depolymerization, molecular weight determinations had to be made with the greatest possible rapidity.

The aqueous solution was depolymerized by long standing or by heating for ten minutes in a water-bath at 60–70°.

Mol. wt. Calcd. for $3C_3H_4O_3 + 1C_2H_5OH$: 77.6. Calcd. for $2C_3H_4O_3 + C_3H_4O_3 \cdot C_2H_5OH$: 103. Found 99.3. These mol. wts. confirm those of Norrish and Griffiths.[5]

Quinoxaline derivative: m. p. 250–251°; reported[5] m. p. 165°.

(1) W. L. Evans and C. E. Waring, THIS JOURNAL, **48**, 2678 (1926).

(2) T. E. Friedemann, *J. Biol. Chem.*, **73**, 331 (1927).

(3) A. T. Küchlin and J. Böeseken, *Rec. trav. chim.*, **47**, 1011 (1928).

(4) A. Hynd, *Biochem. J.*, **25**, 1 (1931).

(5) R. G. W. Norrish and J. G. A. Griffiths, *J. Chem. Soc.*, 2829 (1928).

Phenylglycerosazone: m. p. 132°; reported[1,5] m. p. 132°.

Hydroxymethylglyoxime: m. p. 134–135°. Reported[5] m. p. 168°.

Anal. Calcd. for $C_3H_6O_3N_2$: N, 23.7. Found: N, 23.4.

An aqueous solution of the dioxime gave a red color with cobalt acetate in the presence of sodium acetate. On careful addition of dilute sodium hydroxide to this solution a green base was precipitated.

Summary

1. The alcoholate of the trimer of hydroxypyruvic aldehyde was prepared free from sulfur derivatives.

2. The quinoxaline derivative, phenylosazone, and dioxime were prepared.

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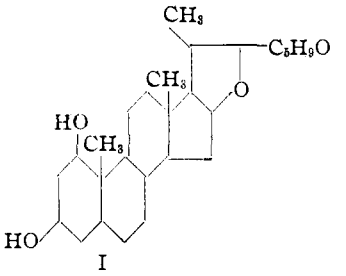
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

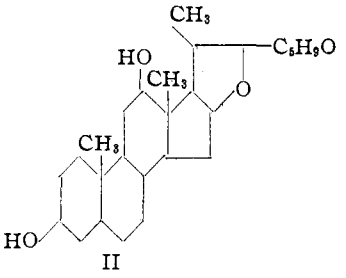
Saponins and Sapogenins. VI. Surface Films of Chlorogenin and Derivatives

BY C. R. NOLLER

In the last paper of this series[1] the tentative formulas, I and II, based on chemical evidence,



I



II

were proposed for chlorogenin. Formula II was favored because the ketodibasic acid obtained on oxidation did not appear to be either an α- or a β-keto acid as would be required by formula I. The second hydroxyl group was assigned to position 12, since the diketone forms a dioxime which would not be expected if the hydroxyl group is at position 11.

Recent work on the surface films of structurally related compounds[2] indicates that those molecules having one or two hydroxyl groups in the end-ring give incompressible films in which the molecules stand on end and occupy an area that is predicted by models of the compounds. Cholestanol-6 and $\Delta^{4,5}$-cholestenol-7 (ψ-cholesterol) having hydroxyl groups in the second ring give highly compressible films indicating that the molecules are tilted or lying flat at low pressures.[3] Hence it was expected that if formula II is a possibility for chlorogenin, the molecules in surface films would lie flat at low pressures and give a highly compressible film. The data plotted in curve I show that this is actually the case. The molecules occupy at low pressures an even larger area than ψ-cholesterol, the film being gaseous at very low pressures. At higher pressures the curve appears as if it will coincide with that for gitogenin

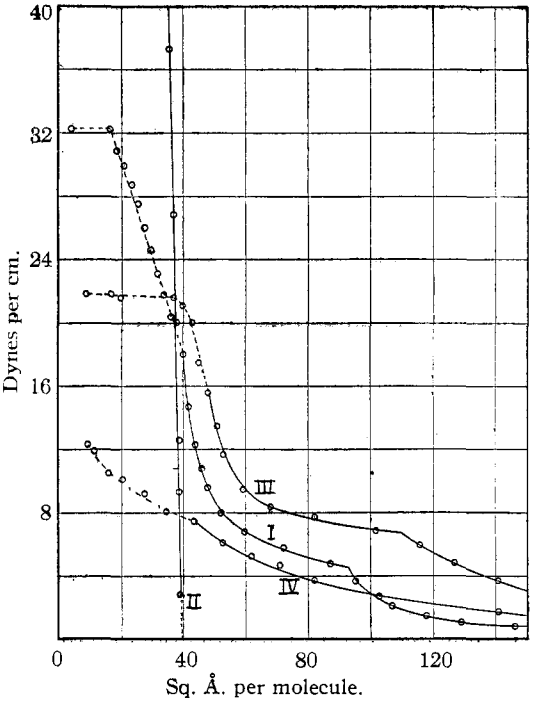


Fig. 1.—Pressure-area curves for surface films of: I, chlorogenin; II, gitogenin; III, chlorogenin diacetate; IV, diketone from chlorogenin.

(1) Noller, THIS JOURNAL, **59**, 1092 (1937).

(2) Askew, Farmer and Kon, *J. Chem. Soc.*, 1399 (1936).

(3) Adam, Askew and Danielli, *Biochem. J.*, **29**, 1786 (1935).