

Some derivatives of Kojic acid

Reactions of Kojic acid with monochloroacetic acid,
monochlorobutylic acid and chloroethyl carbonate

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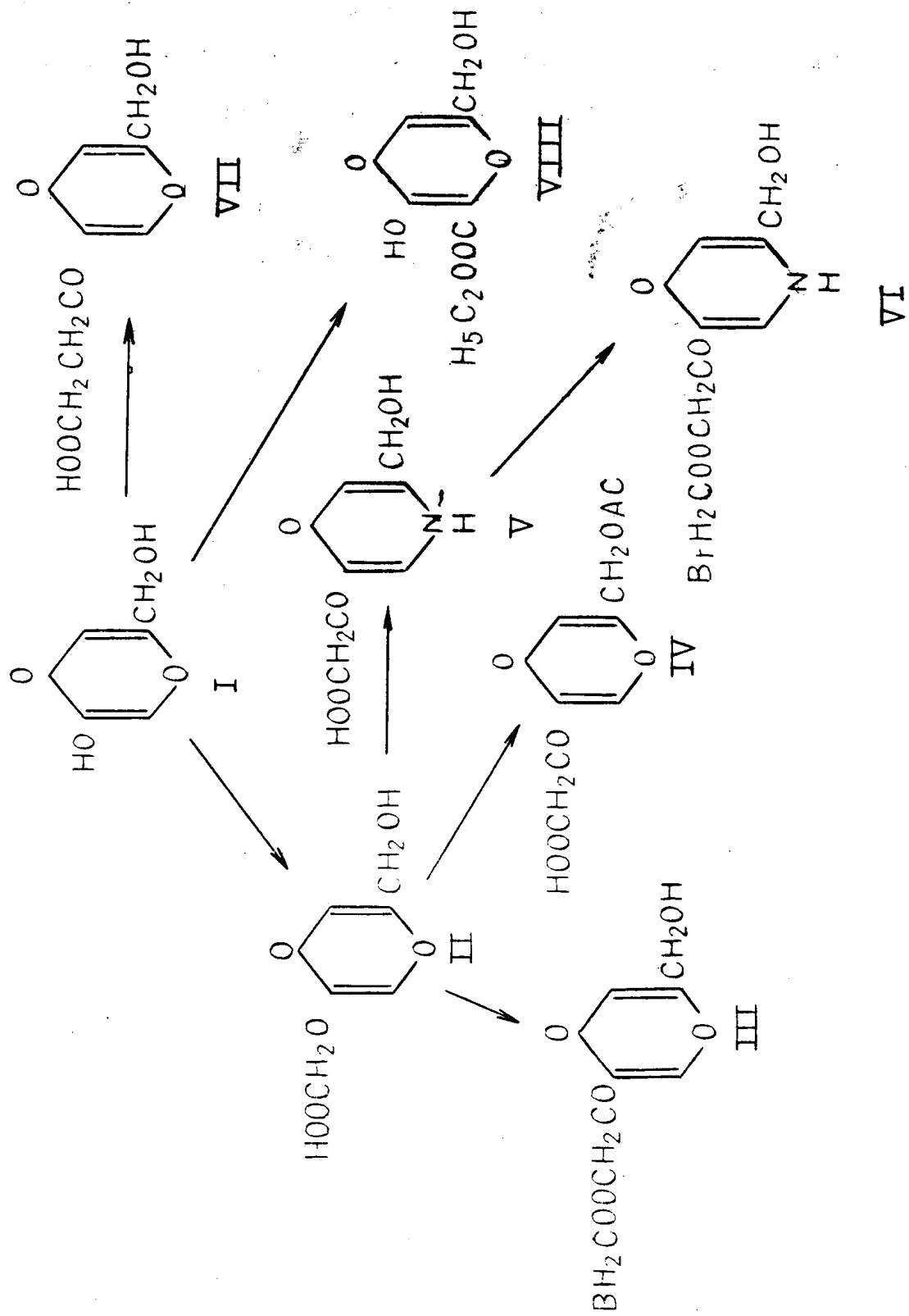
Introduction

Kojic acid (5-hydroxy-2-hydroxymethyl-pyrone) is a crystalline substance which can be produced in good yield by the action of many molds of the *Aspergillus* family on a wide range of carbohydrates or other carbon sources.

Kojic acid was first isolated in 1907 by Saito¹⁾ from *Aspergillus oryzae* grown on steam rice, and then defined its structure in 1924 by Yabuta²⁾.

Kojic acid is an interesting starting material for synthesis, because of having many reactive functional groups. Practically almost of its known derivatives of Kojic acid^{3~4} were formed by the reaction involving the two hydroxy groups.

In this paper, we report several new derivatives of Kojic acid using monochloroacetic acid, monochlorobutylic acid, and chloroethyl carbonate.



Recently, kojiloxycetic acid II was reported by C.D. Hurd and S. Trofimenko,⁵ they obtained II from Kojic acid and monobrom-oacetic acid in dry methanol, which was refluxed for 16 hrs., further they stated that the same product was formed but in lower yield if chloroacetic acid was used instead of bromoacetic acid.

We found that kojiloxycetic acid was easily obtained using chloroacetic acid with potassium hydroxide as a catalyst, but melting point was not identical.

Pyridone, phenacylbromide, and acetyl derivatives of II were obtained by usual manner, but chloro-derivatives were unsuccessful. The esterification of kojic acid with chloroethyl carbonate was failed but obtained unexpected compound. The probable structure of the compound is given in VIII and the reasons for assigning such a structure to the substance were positive to the ferric chloride test and infra-red data.

Experimental

Preparation of II

To a mixture of 14.2g. of kojic acid and 9.6g. of monochloro-acetic acid in 80 ml. of ethyl alcohol was added a solution of 2g. of potassium hydroxide in 20 ml. of water.

This solution was refluxed for 1 hour, on chilling, the potassium salt of II was precipitated, and then was filtered. The salt obtained was dissolved in 30 ml. of water and acidified with hydrochloric acid, with white crystals being precipitated, recrystallized from ethyl alcohol and then from ethylacetate. Yield 9.3g., m.p. 172-173°C. (Hurd, S value was 168°C) The ferric chloride test was negative.

Anal. Calcd. for $C_8H_8O_6$: C, 48.00 H, 4.00

Found: C, 47.84 H, 3.84

Preparation of III

1.5g. of the sodium salt of II were dissolved in 10 ml of water and 1g. of p-bromophenacyl bromide in 30 ml, of ethyl alcohol. This mixture was refluxed for 2 hours and then was treated with a large amount of water. Pale yellow crystals were precipitated, then filtered, recrystallized twice from heptan' yield 0.8g. m.p. 177-178°C.

Anal. Calcd. for $C_{16}H_{13}O_7$: C, 48.36 H, 3.27

Found: C, 49.37 H, 3.09

Preparation of IV

A solution of 2g. of II in 11 ml. of dry pyridine that contained 3 ml. of acetic anhydride was allowed to stand for overnight at room temperature, then it was evaporated in vacuum desiccator at 30°C. the residue was recrystallized twice from acetone, 1g. of white plate crystals of IV was obtained, m.p. 134°C.

Anal. Calc. for $C_{10}H_{10}O_7$: C, 49.60 H, 4.13

Found: C, 49.49 H, 4.21

Preparation of V

The 2-hydroxy-5-oxoacetic acid- γ -pyridone was prepared from II in ammonium hydroxide. 1.5g of II was dissolved in 20 ml. of concentrated ammonium hydroxide allowed to stand for 24 hrs. at room temperature, and was evaporated to dryness, yield 1.3g. Sublimation of a portion of the sample gave white plate crystals, m.p. 140-141°C.

Anal. Calcd. for $C_8H_8O_5N$: N, 7.07

Found: N, 7.14

Preparation of VI

1g. of the crude ammonium salt of V was dissolved in 10 ml. of water and mixed with 1g. of p-bromophenacyl bromide in 30 ml of ethyl alcohol. This mixture was refluxed for one and half hours, and then was treated with a large amount of water. Soft crystals of VI were precipitated, recrystallized from heptane, yield 0.9g. m.p. 111°C.

Anal. Calcd. for $C_{16}H_{14}O_6$ BrN: N, 3.53

Found: N, 3.48

Preparation of VII

A mixture consisting of 14.2g. of kojic acid, 7.5g. of α -Chlorobutylic acid, 1g of potassium hydroxide and 100 ml. of ethyl alcohol containing 20 ml. of water was agitated for one hour at 70°C., on chilling, the potassium salt of VII was precipitated, filtered, then dissolved in 20 ml. of water and acidified with hydrochloric acid with white crystals being precipitated, recrystallized from ethyl alcohol, yield 1.5g. m.p. 168-169°C. The ferric chloride test was negative.

Anal. Calcd. for $C_9H_{10}O_6$: C, 50.47 H, 4.67

Found: C, 50.47 H, 4.79

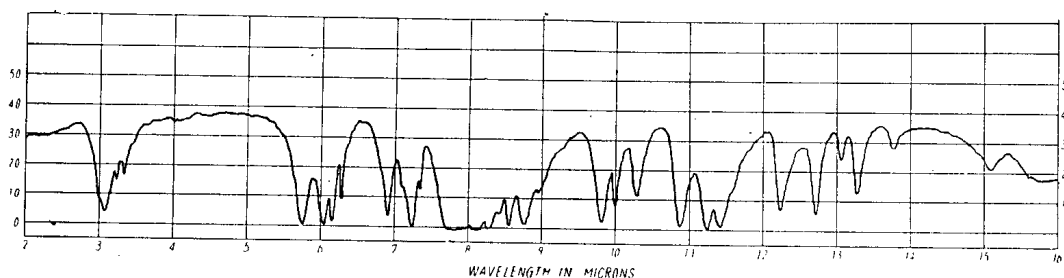
Preparation of VIII

14.2g. of kojic acid dissolved in 80 ml. of ethyl alcohol, 11g. of chloroethylcarbonate and 10g. of potassium hydroxide in 20 ml. of water. This mixture was stirred for one and half hours at 70-80°C., on chilling for overnight in the refrigerator, a white crystalline precipitated, filtered, then recrystallized three times from heptane, yield 9.5g. m.p. 123-124°C. The ferric chloride test was positive.

Anal. Calcd. for $C_9H_{10}O_6$: C, 50.47 H, 4.67

Found: C, 50.62 H, 4.64

Infra-red spectrum was determined on the above compound on a Perkin-Elmer model 21 infrared spectrophotometer using a potassium bromide wafer.



Infra-red spectrum of sample VIII

Acknowledgment

The author wish to thank Dr. L. L. Woods, Texas Southern University, Houston, Texas, for his kind advice.

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