The Conversion of 5-Keto-D-Fructose to Kojic Acid and 5-Oxymaltol

Sir:

In the course of studies on physicochemical properties of 5-keto-D-fructose, we have found that ψ-pyrone derivatives (kojic acid, 5-oxymaltol and an unknown substance) are formed non-microbiologically from 5-keto-D-fructose. Kojic acid (5-hydroxy-2-hydroxymethyl-ψ-pyrone) was first isolated by Saito in 1907 and the chemical structure was determined by Yabuta in 1924. This acid has been found to be produced from a wide range of carbon sources by the action of a variety of microorganisms.

5-Oxymaltol (3,5-dioxy-2-methyl-pyron-1,4) was also found to be produced from fructose, 5-keto-D-fructose and sorbitol as a metabolic product of a number of Acetobactor species together with kojic and 3-oxy-kojic acid.

The conversion of 5-keto-D-fructose to ψ-pyrone derivatives under non-microbial process has been carried out by heating aqueous solution of 5-keto-D-fructose (5~30%) at 100~150°C for 90~120 minutes under pressure (0~70 lb/cm²). The proportion of the conversion to ψ-pyrone derivatives was 60 to 80% of the substrate, 5-keto-D-fructose, in molar bases, determined colorimetrically with ferric sulfates.

ψ-Pyrole derivatives formed were extracted from reaction mixture by chloroform, and the extract was separated into Fraction I (fraction more easily soluble in chloroform, containing ψ-pyrene A and ψ-pyrene B) and Fraction II (fraction subsequently soluble in chloroform, containing ψ-pyrene B only). The yield of crude ψ-pyrene derivatives was 45 to 60%. An unknown substance positive to ferric chloride test remained in the aqueous layer.

ψ-Pyrene A was isolated from the chloroform-residue of Fraction I by repeated crystallization from methanol. It was obtained as rhombic or hexagonal plates freed from the contaminated ψ-pyrene B, and melted at 183.5~184.5°C. The results of its elemental analysis agreed with that of 5-oxymaltol. Anal. Found: C, 50.39; H, 4.27; O, 45.27. Calcd. for C₆H₆O₄: C, 50.71; H, 4.26; O, 45.03%.

From detailed studies on the UV- and IR-absorption spectra and chromatographic behaviors, in addition, it was verified that ψ-pyrene A was 5-oxymaltol. A crystalline material obtained from fraction II was dissolved in water, purified with active carbon, affording long prisms. Its melting point was 152°C and no m.p. depression was observed on mix-

![Fig. 1. Conversion of 5-Keto-D-Fructose to Kojie Acid and 5-Oxymaltol.](image-url)
ing test with authentic kojic acid, and the result of its elemental analysis was identical with that of kojic acid. *Anal.* Found: C, 50.45; H, 4.31; O, 45.24. Calcd. for C₆H₄O₄: C, 50.71; H, 4.26; O, 45.03%.

Its aqueous solution was acidic and showed reddish purple color with ferric chloride. Its IR- and UV-absorption spectra showed good agreement with those of kojic acid. This appears to be the first report of direct conversion of 5-keto-ᴅ-fructose to γ-pyrone derivatives by non-microbial method.

The ratio of kojic acid to 5-oxymaltol was variable according to the reaction condition (i.e., 2.8~6.1). Such phenomena may be attributed to the structural, or conformational change of 5-keto-ᴅ-fructose in the solution. The mechanism of this reaction is under study now, and detailed description will be published later.

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