TABLE III

3-NITRODIBENZOFURAN-8-SULFONIC ACID AND ITS AMINE SALTS

| | | Free acid | Salts of the free acid<br>2<br>Aniline | <br>3<br>$p$-Toluidine | <br>4<br>$p$-Bromoaniline | <br>5<br>Urea |
|---|---|---|---|---|---|---|
| M.p., °C. | | Chars 240 | 258–260 dec. | 250 dec. | 258–266 dec. | Over 300 dec. |
| Neut. equiv. | Calcd. | 293.2 | | | | |
| | Found | 296.3, 296, 294.2 | | | | |
| N, % | Calcd. | 4.78 | | | | |
| | Found | 4.80, 5.0 | | | | |
| S, % | Calcd. | 10.93 | 8.30 | 8.01 | 6.89 | 9.07 |
| | Found | 10.72 | 8.25 | 8.04 | 6.82 | 9.18 |
| | | 10.62 | 8.40 | | | |

TABLE IV

AMINO ACID SALTS OF 3-NITRODIBENZOFURAN-8-SULFONIC ACID

| Amino acid | M.p., °C. | Sulfur, %<br>Calcd. | Sulfur, %<br>Found |
|---|---|---|---|
| 1-Arginine (di)[a] | 235–236 | 8.43 | 7.98 |
| Creatinine | 258 | 7.89 | 7.82 |
| 1-Cysteine | 219 | 15.47 | 15.60 |
| 1-Cystine (di) | 215 | 15.50 | 15.70 |
| 1-Histidine (di) | 248 | 8.65 | 8.59 |
| *dl*-Iso-leucine | 246 | 7.55 | 7.21 |
| *dl*-Phenyl-alanine | 247 | 7.00 | 7.01 |
| *l*-Leucine | 260–262 dec. | 7.55 | 7.58 |

*dl*-alanine, $\alpha$-aminoisobutyric acid, *dl*-lysine, *dl*-methionine, *dl*-norleucine, *dl*-tryptophan[b] and *dl*-valine formed salts which decomposed without melting in the high range of 250–300°

Glycine, aspartic and glutamic acids, tyrosine, proline and hydroxyproline, threonine, asparagine and serine all failed to precipitate from solution upon addition of the nitrosulfonic acid

[a] All salts were monosulfonates except those marked (di). [b] The tryptophan salt of the acid has a brilliant yellow coloration, which may have diagnostic significance; the others were nearly white or pale yellow.

able and very difficult to dry (indications being that it undergoes some hydrolysis of the sulfonic acid group due to the water present). Consequently the crude product was crystallized from glacial acetic acid. Three crystallizations gave a yellow product which could be dried suitably in a vacuum oven at 70°; it had no definite melting point but charred in the region of 240°. Of the analytical values the neutral equivalent seemed to be most reliable (calcd. 293; found 294 to 297).

This acid was tested as an agent for amines and amino acids, the procedure used being the same as given above. The results are given in Table III which lists properties of the free acid and its salts.

Although the analytical values for the acid itself leave something to be desired, the preparation and analysis of the four additional salts 2, 3, 4 and 5 (which crystallize nicely from ethanol) seem to confirm the constitution of the acid.

The acid is soluble in water, methyl and ethyl alcohols, and insoluble in ether, benzene and other non-polar solvents. It precipitates many metal ions from dilute aqueous solutions, *e.g.*, $Ag^+$, $Cu^{+2}$, $Mg^{+2}$, $Ca^{+2}$, $Zn^{+2}$, $Al^{+3}$, $Pb^{+2}$, $Cr^{+3}$, $Mn^{+2}$, $Ni^{+2}$, $Fe^{+2}$, $Fe^{+3}$, $Co^{+2}$, $Sn^{+2}$ and $Ba^{+2}$. The sodium and potassium salts of the nitro acid seem to be more soluble than those from dibenzofuran-2-sulfuric acid itself, but quantitative studies were not made.

Although the ammonium salt of dibenzofuran-2-sulfonic acid is crystalline, the addition of ammonium hydroxide to an aqueous solution of 3-nitro acid gave a slimy stringy mass that resembled a thick soap curd. This curious behavior confirmed the considerable difference in solution characteristics of the two acids.

Twenty-four amino acids were tested for precipitability by 3-nitrodibenzofuran-8-sulfonic acid by the same procedure as given above. Table IV lists the results obtained on the salts.

Since the nitrosulfonic acid failed to precipitate nine of the twenty-four amino acids tested, and under the same conditions dibenzofuran-2-sulfonic acid failed in but three cases (7), the advantage of the latter is obvious.

Although the study of the 3-nitro acid was extended to other amines (salt of $n$-butylamine melted 264°, di-$n$-butylamine 167°, diphenylguanidine 225°) the salts formed in many cases showed decomposition without characteristic melting, hence offered little promise for inclusion in this particular study.

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## 2-Hydroxymethyl-5-hydroxy-6-acetyl-4-pyrone

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In a previous communication,[2] the attempted synthesis of 2-hydroxymethyl-5-hydroxy-6-acetyl-4-pyrone (6-acetylkojic acid) was reported, but a clean-cut reaction was not obtained and an erroneous conclusion as to the nature of the reaction product was made. This was pointed out by Hurd and Sims.[3] However, their confirmation of the fact that kojic acid does react with acetic anhydride under controlled conditions to form a dark mixture which solidifies only upon aging stimulated our further interest in this acetylation, for such behavior could not be attributed to kojic acid diacetate and can only be accounted for by the formation of other substances along with the

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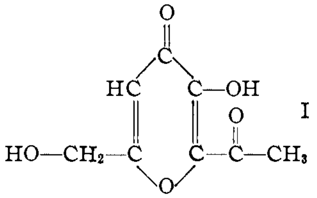
(1) The author wishes to acknowledge the financial assistance given this investigation by the Research Corporation. The kojic acid was furnished through the courtesy of the Corn Products Company.

(2) L. L. Woods, THIS JOURNAL, **70**, 2608 (1948).

(3) C. D. Hurd and R. J. Sims, *ibid.*, **71**, 2440 (1949).

kojic diacetate. Hurd's description of the purification of the reaction product clearly indicates that there is considerable contamination and that kojic acid diacetate is obtained pure only by removing some substance which is considerably more soluble in alcohol. The compound thus removed may have been the desired ketone. Therefore, it was decided that the conditions for creating 6-acetylkojic acid as the major constituent of the reaction product would not be drastically different from those given previously.

Subsequent experiments, which are described in this report, indicate that it is possible to produce 6-acetylkojic acid (I) from kojic acid and acetic anhydride by effecting certain changes in the procedure given originally.[2]



I

## Experimental[4]

A mixture consisting of 28.4 g. of kojic acid and 30 g. of 85% phosphoric acid was heated until practically all the kojic acid had dissolved, placed in an oil-bath at 150° and treated with 40.8 g. of acetic anhydride added slowly from a separatory funnel.

The reaction was allowed to proceed at 150° for 10 hours; following which the excess acetic acid and acetic anhydride was removed under reduced pressure until the flask was heavily fogged with the subliming product. After diluting with water and cooling in the ice chest, the product was collected as brown-purple aggregates, 24.7 g. Extraction of the filtrate with ethyl acetate gave an additional 4.2 g.

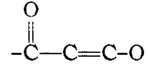
A sample of the crude material from the ethyl acetate was recrystallized from absolute ethanol and sublimed to a white powder. The compound gave a red coloration with ferric chloride solution, m.p. 119–120°. Treating the brown-purple crystals in a similar manner gave the same substance believed to be principally 2-acetoxymethyl-5-hydroxy-6-acetyl-4-pyrone.

*Anal.* Calcd. for $C_{10}H_{10}O_6$: C, 53.10; H, 4.32. Found: C, 52.60; H. 4.60.

Hydrolysis of the above mixture was effected by boiling 21 g. with 100 ml. of water for 24 hours. The solution was cooled, treated with charcoal, and filtered. Upon evaporation of the solution to dryness, 16 g. of crude dark brown 6-acetylkojic acid was obtained.

The analytical sample was obtained by sublimation of the impure ketone to a cream colored powder, m.p. 156.5°.

*Anal.* Calcd. for $C_8H_8O_5$: C, 52.20; H, 4.34. Found: C, 52.21; H, 4.50.

Its infrared spectra (nujol mull) show a sharp absorption band in the C=O region at 1720 cm.$^{-1}$. Another band at 1230 cm.$^{-1}$ may be attributed to the fact that pyrones may be considered to be ester vinylogs.[5] Recently, Zeiss and Tsutsui[6] have shown that the $R_2C{=}C{-}O$ group gives an absorption band at about 1250 cm.$^{-1}$. A  $-\overset{\displaystyle O}{\overset{\|}{C}}-C{=}C{-}O$ group, typical of pyrones, should give a similar absorption band, somewhat displaced.

Five grams of crude 6-acetylkojic acid was treated with 10 ml. of acetic anhydride, diluted with 100 ml. of water, and the free acetic acid neutralized with sodium bicarbonate. Extracting the neutral solution with benzene produced 4.8 g. of the completely acetylated compound. The crystals were yellow prisms which when recrystallized twice from benzene gave a m.p. of 98–99°. A sublimed sample gave the same melting point.

*Anal.* Calcd. for $C_{12}H_{12}O_7$: C, 53.73; H, 4.47. Found: C, 53.90; H, 4.78.

When 6-acetylkojic acid was permitted to react with thionyl chloride, treated with water, and the product recrystallized from benzene, 2-chloromethyl-5-hydroxy-6-acetyl-4-pyrone was formed which gave a strong red purple coloration with ferric chloride and a m.p. of 163–164°.

*Anal.* Calcd. for $C_8H_7C_4Cl$: C, 47.41; H, 3.45. Found: C, 47.14; H, 3.59.

A small amount of 6-acetylkojic acid (1 g.) was dissolved in 10 ml. of water, treated with 10 drops of acetic acid and 40 drops of phenylhydrazine, heated at reflux for 10 minutes, treated with charcoal and filtered while boiling hot. A clear orange solution was obtained which upon cooling deposited a red substance, m.p. 68–70°.

The analytical results indicate clearly that two molecules of phenylhydrazine have combined with the acetyl compound.

*Anal.* Calcd. for $C_{20}H_{18}N_4O_2$: N, 16.18. Found: N, 16.07, 16.20.

Consistent results were not obtained using 2,4-dinitrophenylhydrazine. The nitrogen content of the product was always high (22–24%) but always less than that for the pure 2,4-dinitrophenylhydrazine and slightly less than for its hydrochloride.

Fifteen grams of 6-acetylkojic acid was subjected to the conditions of the Clemmensen reduction for six hours following which the solution was diluted with an equal quantity of water and then extracted with ethyl acetate. The solvent layer was washed twice with water. Upon evaporation of the solvent, 3.3 g. of the reduced compound was obtained.

Sublimation of a portion of the sample gave white needles, m.p. 147–149°.

*Anal.* Calcd. for $C_8H_{10}O_4$: C, 56.47; H, 5.88. Found: C, 56.57; H, 5.69.

The compound gave a dark red coloration with dilute ferric chloride solution.

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(4) Analyses were performed by Dr. Carl Tiedcke, Teaneck, New Jersey, and Clark Micro-analytical Laboratory, Urbana, Illinois. All melting points were determined on a Fisher-Johns melting point assembly. Infrared spectrograms were furnished through the courtesy of Samuel P. Sadtler and Son, Philadelphia, Pennsylvania.

(5) L. F. Cavalieri, *Chem. Revs.*, **41**, 525 (1947).

(6) H. H. Zeiss and M. Tsutsui, THIS JOURNAL, **75**, 897 (1953).