The Structure of Stipitatonic Acid, a Mould Metabolite from Penicillium[1]

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Stipitatonic acid, a mould tropolone, $C_9H_4O_6$, m. p. 237~237.5° (decomp.) has been isolated from *Penicillium Stipitatum*

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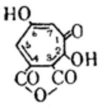
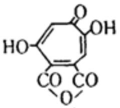
Thom. by Segal and the structure A has been assigned to it rather than the alternative isomer B[2]. We now wish to show evidence which permits the assignment of structure B to stipitatonic acid contrary to that proposed before[2].



(A)



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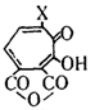

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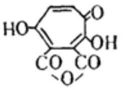

(D)

6-Hydroxytropolone-3, 4-dicarboxylic anhydride(A) and its two isomers concerning with hydroxyl group were synthesized by the following methods and these anhydrides were compared with stipitatonic acid.

Bromination of tropolone-3, 4-dicarboxylic anhydride (C:X=H), an oxidation product of purpurogallin[3] gave 7-bromo compound (C:X=Br), m. p. 198°C[4]. It has been reported[5] that liquid phase hydrolysis of 3-bromotropolone afforded 4-hydroxytropolone, and a minute amount of 3-hydroxytropolone. Application of this reaction to the 7-bromo compound (C:X=Br) gave 7-hydroxy compound (C:X=OH) in 40% yield and a hydroxytropolone-3, 4-dicarboxylic anhydride, m. p. 237°C (*not decomp.*), yellow needles, in 6% yield. *Anal.* Found: C, 51.94; H, 1.86. Calcd. for $C_9H_4O_6$: C, 51.93; H, 1.94%. Ultraviolet maxima, mμ(log ε) in methanol: 272(4.46), 345(3.90), 363 (3.92).

The latter anhydride, m. p. 237°C underwent decarboxylation to give stipitatic acid, m. p. 279 ~280°C[6] whose identity was confirmed by ultraviolet and infrared spectra, *Anal.* Found: C, 52.43; H, 3.47. Calcd. for $C_8H_6O_5$; C, 52.75; H, 3.32%. Therefore the structure of the anhydride, m. p. 237°C. also has to be the structure A. Persulfate oxidation of the anhydride (C:X=H) gave 7- and 5-hydroxy compounds (C:X=OH and D). *Anal.* Found: (5-hydroxy compound, m. p. 250°C): C, 51.79; H, 1.68%. The structure of the 5-hydroxy compound was supported by the decarboxylation to give 5-hydroxytropolone, m. p. 250°C (decomp.)[7].

Any hydroxy compound of the tropolone-3, 4-dicarboxylic anhydride mentioned above was not identical with natural stipitatonic acid which was kindly spared by Dr. Segal. The proof to support the structure A for stipitatonic acid rather than the structure B has been based on the submission to azo-coupling but no detail on the azo compound is mentioned[2]. It seems to us that unless a true azo-coupling compound is produced, the test for the vacant *p*-position can be misleading because even *p*-substituted tropolones show red coloration with aryl diazonium salts.

The difference, $\Delta\nu$ between two carbonyl frequencies of anhydride group of almost all derivatives of tropolone-3, 4-dicarboxylic anhydride in infrared spectra in 60±2 cm^{-1}, while $\Delta\nu$ of stipitatonic acid is 78 cm^{-1} [2].

Therefore the above results and evidence that decarboxylation of stipitatonic acid gave stipitatic acid[2] suggest that *the structure of stipitatonic acid is not A but B.*

When this manuscript was completed, one of us (Y. K.) received a letter from Dr. Segal on August 6, in which he described that his observation on a potash fusion of stipitatonic acid was in complete agreement with our belief regarding the structure.

The authors wish to thank Professor T. Toriumi of this Institute for his encouragement and Dr. W. Segal for a supply of stipitatonic acid.

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[2] W. Segal, *Chem. and Industry*, **1957**, 1040.

[3] W. D. Crow, R. D. Haworth and P. R. Jefferies, *J. Chem. Soc.*, **1952**, 3705.

[4] T. Nozoe, K. Doi and T. Hashimoto, to be published.

[5] Y. Kitahara, *Science. Repts. Tôhoku Univ., First Ser.*, **39**, 258 (1956).
The mechanism may be explained by benzyne* type process (dehydrotropolone).
* J. D. Roberts, H. E. Simmons, Jr., L. A. Carlsmith and C. W. Vanghan, *J. Am. Chem. Soc.*, **75**, 3290 (1953) and subsequent papers.

[6] R. B. Johns, A. W. Johnson and M. Tišler, *J. Chem. Soc.*, **1954**, 4605.

[7] T. Nozoe, S. Seto, S. Ito, M. Sato and T. Katono, *Science Repts. Tôhoku Univ., First Ser.*, **37**, 191 (1953).