[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Mold Metabolites. V. The Stereochemistry and Ultraviolet Absorption Spectrum of Citrinin

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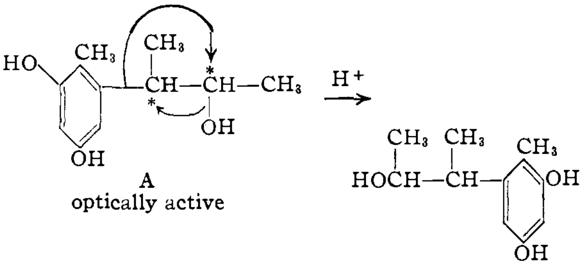
In paper III of this series[1] the syntheses of several degradation products of citrinin were reported as well as a rationalization of the structure of the optically active degradation product, A. The anomalous racemization of A was tentatively explained by assuming that treatment of this molecule with acid produced a Wagner–Meerwein rearrangement involving the aryl group as the migrating species. This explanation of the loss of optical activity has now been substantiated through the study of the behavior of the optical isomers of 3-phenyl-2-butanol under the same conditions. The results of these experiments suggested the series of investigations of the preparation and acetolysis of the *p*-toluenesulfonates of the isomers of 3-phenyl-2-butanol and the subsequent establishment of the relative configurations of these substances, which have been reported elsewhere.[2] The numbering system of the isomeric alcohols has been carried over to the present investigation.



A
optically active

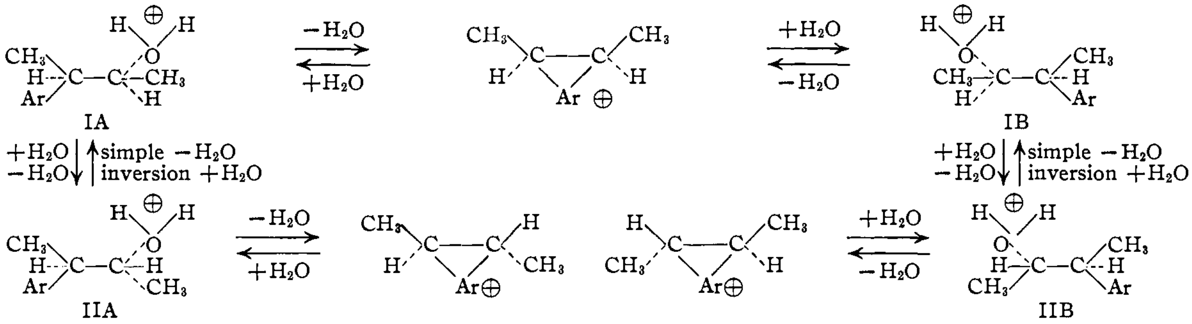
racemic

When IA was heated with strong sulfuric acid and dioxane (the insolubility of IA in water made the addition of dioxane necessary), racemate I was obtained,[3] along with a considerable amount of olefin. When IIA was subjected to the same conditions, most of the starting material was recovered[3] along with a trace of racemate II[4] and a large amount of olefin. A similar treatment of racemate I gave back starting material,[4] a trace of racemate I[3] and olefin.

These results can be interpreted in a fashion analogous to the interpretation given for the acetolysis of the *p*-toluenesulfonates of IA and IIA,[2] the main difference being that the products are just as susceptible to rearrangement or other reactions as are the starting materials. The production of a trace of racemate II from I and the reverse reaction probably takes place through simple inversion of the carbon atom bearing the hydroxyl group by a water molecule. This process can also be used to explain the production of a small amount of IIB from IIA (a trace of II racemate was obtained).

The rapid acid-catalyzed racemization of IA to I is completely analogous to the similar racemization of the degradation product A, obtained from citrinin, and constitutes strong evidence that A possesses the same configuration as either IA or IB[5] (the racemization of IIA under these conditions was negligible).

The recent resynthesis of citrinin from A by Robertson[6] would indicate that the formation of citrinin from A, and the reverse reaction of the conversion of citrinin to A, take place by processes that either leave the configuration of the two asymmetric carbon atoms unchanged, or by processes that are stereochemically the exact reverse of each other. It is likely that both of these processes involve a hemiacetal intermediate, the formation or destruction of which would not result in the breaking of the bond between the oxygen and carbon in the butanol side chain, and that the configurations are maintained



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[1] THIS JOURNAL, **70**, 4245 (1948); **70**, 440 (1948).

[2] Papers I, II, III and IV in the series, Studies in Stereochemistry, THIS JOURNAL, **71**, 3863 (1949).

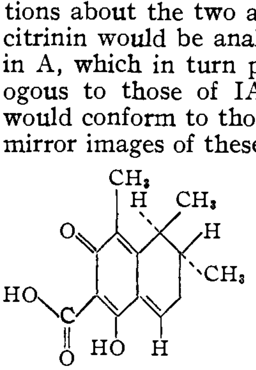
[3] This alcohol was isolated in the form of its crystalline phthalic acid ester.[2]

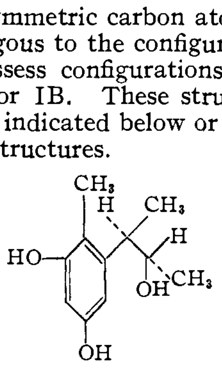
[4] This alcohol was isolated as its crystalline 3-nitrophthalic acid ester.[2]

[5] The strong positive rotations of IA and A suggest an analogous configuration for the two compounds.

[6] Robertson, *et al.*, *Nature*, **163**, 94 (1949).

throughout either process. Thus the configurations about the two asymmetric carbon atoms of citrinin would be analogous to the configurations in A, which in turn possess configurations analogous to those of IA or IB. These structures would conform to those indicated below or to the mirror images of these structures.


citrinin


A

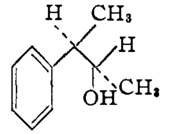

IA

Figure 1 records the ultraviolet absorption spectrum of citrinin.

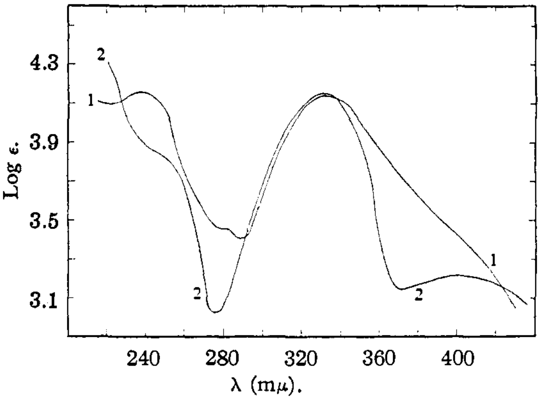


Fig. 1.—Ultraviolet absorption spectra of citrinin (Beckman quartz spectrophotometer): curve 1, in 50% ethanol-50% 0.20 *N* hydrochloric acid; curve 2, in 50% ethanol-50% 0.20 *N* sodium hydroxide.

Experimental

Acid Treatment of IA, IIA, I and II.—A mixture of 1.0 g. of IA[7] ($[\alpha]^{25}D$ 30.9°)[7], 15 ml. of 12 *N* sulfuric acid and 15 ml. of dioxane was heated at reflux for ten hours and cooled (two phases appeared when the mixture was heated and disappeared as the mixture was cooled, thus in effect decreasing the acidity of the medium in which the alcohol was dissolved). This mixture was shaken with petroleum ether and water, the organic layer was washed three times with water, dried and the solvent evaporated. The resulting oil was distilled; wt. 0.79 g., α +1.62° (*l* = 1 dm., λ = D). Conversion of this substance to the phthalic acid ester by the usual method and recrystallization of the product from ethyl acetate and petroleum ether produced 0.43 g. of the ester of I,[7] m. p. 130–131°, not depressed by admixture with an authentic sample. From the filtrates was recovered 0.21 g. of olefin, isolated by distillation of the oil that resulted from the evaporation of the solvent.

Treatment of 1.0 g. of IIA ($[\alpha]^{25}D$ +0.69°)[7] by the procedure recorded above produced 0.85 g. of distilled product (α +0.53°). This material was converted to the acid phthalate to give 0.39 g. of recrystallized product (ethyl acetate and petroleum ether); m. p. 97–99°, $[\alpha]^{25}D$ −61.2°[7] (*c* = 3% in ethanol), m. m. p. with the phthalic acid ester of IIA,[7] 99–101°, (this melting point was depressed by admixture with the acid phthalates of IIB, IA or IB). From the filtrates was isolated less than 0.10 g. of olefin. The material that would not distil was hydrolyzed to the alcohol and this material converted to the 3-nitrophthalic acid ester,[7] wt. of material after three recrystallizations from ethyl acetate and petroleum ether, 10 mg., m. p. 155–156°, m. m. p. with an authentic sample of the 3-nitrophthalic acid ester of II,[7] 156–157°.

Similar treatment of 3.0 g. of I produced 2.25 g. of recrystallized acid phthalate of I,[7] m. p. 130–131°, not depressed by admixture with an authentic sample, and 0.63 g. of olefin. Conversion of the material in the filtrates first to the free carbinol and then to the 3-nitrophthalic acid ester produced 15 mg. of pure 3-nitrophthalic acid ester of II[7] (recrystallized from ethyl acetate and petroleum ether), m. p. 155–156°, not depressed by admixture with an authentic sample.[7]

When 3.0 g. of II was treated in a similar manner, there was obtained 2.35 g. of the 3-nitrophthalic acid ester of II,[7] m. p. 155–156° (not depressed by admixture with an authentic sample), 0.23 g. of olefin and 25 mg. of the acid phthalate of I, m. p. 129–130°, not depressed by admixture with an authentic sample.[7]

Summary

1. The racemization of the degradation product A obtained from citrinin has been shown to take place by means of a Wagner–Meerwein rearrangement through the use of model substances, the optical isomers of 3-phenyl-2-butanol. This racemization process provides evidence for the relative configurations about the two asymmetric carbon atoms of A, which in turn has led to an assignment of the relative configurations to the two asymmetric carbon atoms of citrinin itself.

2. The ultraviolet absorption spectrum of citrinin has been reported.

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[7] These compounds have been reported in paper I of the series, ref. 2.