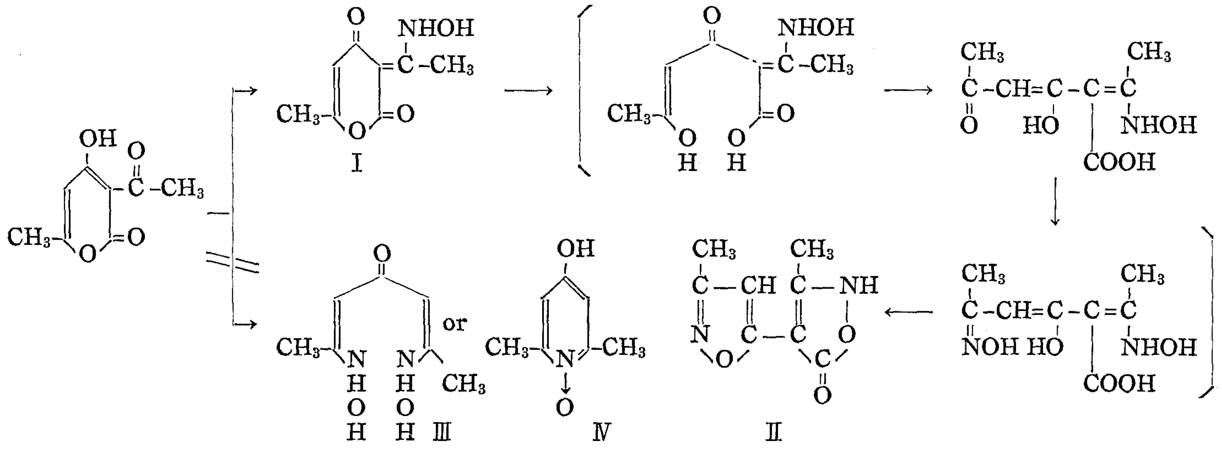
Chem. Pharm. Bull. 12 (3) 381 ~ 383

UDC 547.292-126 : 546.172

On the Reaction of Dehydroacetic Acid to Hydroxylamine

It was reported in the previous papers[1,2] that dehydroacetic acid (DHA) was apt to transform into 4-(1*H*)-pyridones *via* Schiff's base even under a mild condition when it coexisted with ammonia or primary amines in aqueous solution.

In an extension of this work we investigated the reaction between DHA and hydroxylamine, and found that a quite different reaction took place under the similar condition. When DHA reacted with the equivalent mole of hydroxylamine at room temperature, the compound (I), m.p. 171~173° (decomp.), which had been reported as Perkin's oxime,[3] was formed. But the other compound (II), m.p. 165~166° (decomp.), was obtained in the presence of an excess of hydroxylamine at room temperature or when the solution containing the both substances was refluxed. Furthermore, II was also obtained on the additional treatment of I with an excess of hydroxylamine. II gave blue color with ferric chloride solution, whereas I showed violet color. II was neither 2,6-bis(hydroxylamino)-2,5-heptadien-4-one (III) nor 2,6-dimethyl-4-pyridinol 1-oxide (IV), which was first assumed from the reaction as before.[2] In consequence of an elemental analysis, infrared and ultraviolet spectra, the molecular formula of II was $C_8H_8O_3N_2$ and it seemed as the compound which was constructed from one mole of DHA and two moles of hydroxylamine. II was clearly identified as 3-methyl-4-(3-methyl-5-isoxazolyl)-3-isoxazolin-5-one by the perfect agreement in its infrared spectrum with that of the authentic sample synthesized from ethyl acetoacetate and hydroxylamine.[4] Therefore, the reaction should be considered to proceed through the following courses.



The validity of structure of I (Perkin's oxime), which had been described as the ketoxime in the side chain of DHA without a conclusive evidence, was also deduced this time from the determination of the final product (II).

Furthermore, in a study of the conversion of DHA to N-substituted lutidones by the reaction with the primary amines, 3-(1-alkyliminoethyl)-4-hydroxy-2*H*-2-pyrone and 2,6-bis(alkylamino)-2,5-heptadien-4-one were separated in general and considered to be intermediates, and the reaction process was relative to a general one for the conversion of 4*H*-4-pyrones to 4-(1*H*)-pyridones. But, it is an interesting fact that in the reaction

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[1] S. Iguchi, *et al.* : This Bulletin, **11**, 385 (1963).
[2] *Idem* : *Ibid.*, **11**, 390 (1963).
[3] W. H. Perkin, *et al.* : Ber., **17**, 1522 (1884).
[4] A. Hantzsch : Ber., **24**, 495 (1891).

between DHA and hydroxylamine 3-methyl-4-(3-methyl-5-isoxazolyl)-3-isoxazolin-5-one (Ⅱ) was obtained without 4(1*H*)-pyridones (Ⅳ), showing the quite different process from that of 2,6-dimethyl-4*H*-4-pyrone with hydroxylamine. In the latter case, 4-hydroxylamino-2,6-dimethylpyridine 1-oxide[5,6] was obtained. The details of this work will be reported in the near future.

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Received October 10, 1963

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[5] P. Yates, *et al.*: Can. J. Chem., **40**, 2146 (1962).
[6] F. Parisi, *et al.*: Gazz. chim. ital., **92**, 1138 (1962).

[Chem. Pharm. Bull. 12 (3) 382 ~ 383]

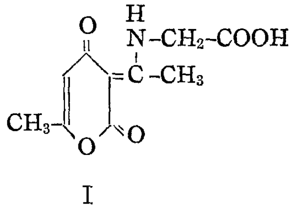
UDC 547.292-126 : 547.466

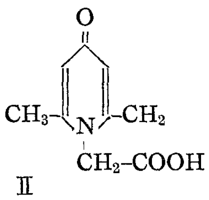
On the Reaction Products between Dehydroacetic Acid and Amino Acids

It was pointed out several times that dehydroacetc acid (DHA) is very reactive with ammonia, primary amines, and some of the compounds possessing amino group, such as sulfanilamides.[1,2] In all cases, the primary reaction product is Schiff's base and the final product 2,6-dimethyl-4(1*H*)-pyridone derivative even under a mild condition.

In an extension of this work to amino acids from the biochemical point of view, we noticed that 2,6-dimethyl-4(1*H*)-pyridone derivative was also formed *via* the primary product Schiff's base under the similar condition.

As soon as DHA was treated with the equivalent mole of glycine at room temperature, the formation of the compound (I), m.p. 247~248° (decomp.), which had been identified already as 3-[1-(carboxymethylimino)ethyl]-4-hydroxy-6-methyl-2*H*-2-pyrone,[3] was recognized by the paper chromatography (Rf 0.61). When the test solution (1%) was kept at room temperature with an excess of glycine, a new spot appeared in the paper chromatogram (Rf 0.43) after 80 days. It was isolated as white prisms, m.p. 229° (decomp.), and identified as 4-oxo-2,6-dimethyl-1,4-dihydro-1-pyridineacetic acid (Ⅱ) in consequence of an elemental analysis, infrared and ultraviolet spectra. Ⅱ was also obtained from the reaction of 2,6-dimethyl-4*H*-4-pyrone with glycine in a small yield.


I


Ⅱ

On the other hand, when DHA reacted with the equivalent mole of a basic amino acid histidine under the similar condition, a new compound (Ⅲ) was detected by the paper chromatography (Rf 0.33), and after 6 days the formation of another compound (Ⅳ) was clearly observed in the test solution (1%) with an excess of histidine (Rf 0.11),

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[1] S. Iguchi, *et al.*: This Bulletin, **11**, 385 (1963).
[2] *Idem*: *Ibid.*, **11**, 390 (1963).
[3] *Idem*: *Ibid.*, **7**, 323 (1959).