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Studies on Ketene and Its Derivatives. XXVI.[1] The Structure of the Self-condensation Product of Acetoacetamide (Supplement)[2]

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In a previous paper of this series,[2] we reported the pyrolysis of acetoacetamide (I) to give 2,6-dimethyl-4-pyrimidone (II) as a main product and colorless needles of mp 314—317° (decomp.), $C_8H_{10}O_2N_2$ (III),[4] as a by-product, for which we gave the proper structure of 3-acetyl-4-amino-6-methyl-2-pyridone (IIIa). The structural assignment was made as follows: the hydrolysis of III afforded the known compound, 3-acetyl-4-hydroxy-6-methyl 2-pyridone (IV),[5] therefore, the structure of the precursor should be IIIa taking account of the reaction pathway shown in Chart 1. During the course of the farther investigation of the chemical behaviour of III, it became desirable to correct the structure of III. The present paper describes that the structure of III is not the 4-amino compound (IIIa) but 3-acetimidoyl-4-hydroxy-6-methyl-2-pyridone (IIIb).

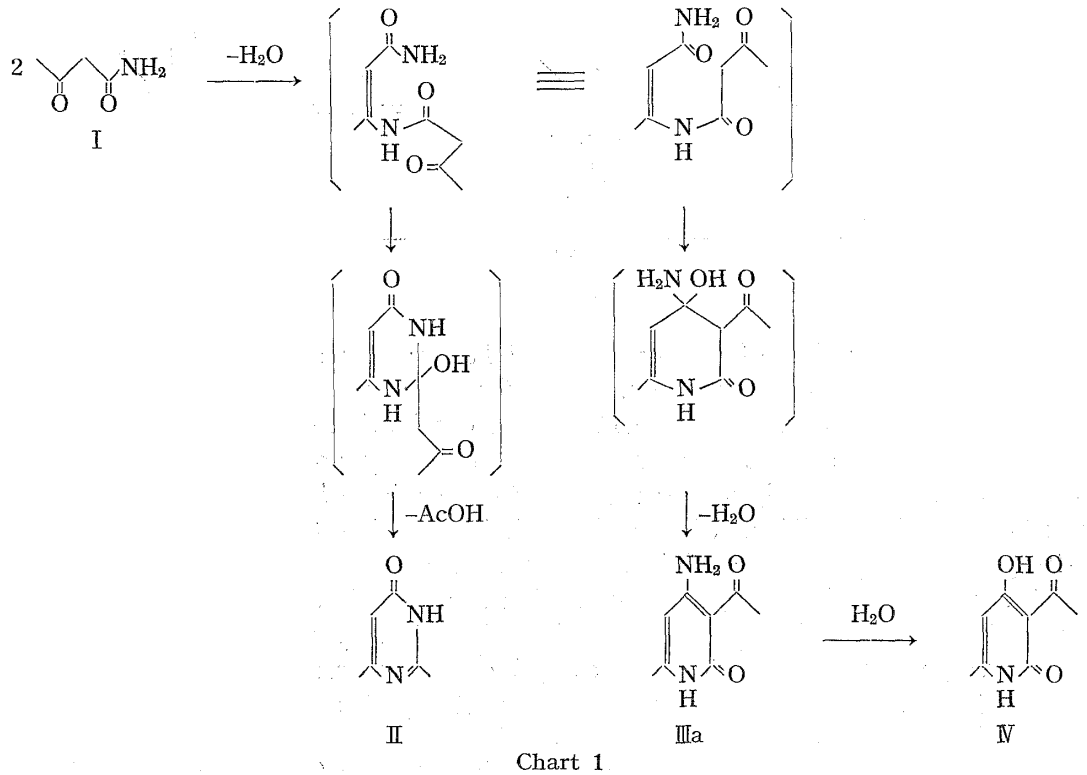

Chart 1

1) Part XXV: T. Kato, J. Kawamata and T. Shibata, *Yakugaku Zasshi*, **88**, 106 (1968).
2) T. Kato, H. Yamanaka, and T. Shibata, *Chem. Pharm. Bull.* (Tokyo), **15**, 921 (1967).
3) Location: *a*) *Kita-4, Sendai*; *b*) *Shinano-machi, Shinjuku-ku, Tokyo.*
4) To this product (III) Claisen gave the structure of 2,4-dimethyl-6-pyridone-5-carbamide (L. Claisen and K. Meyer, *Chem. Ber.*, **35**. 583 (1902)).
5) S. Seto, H. Sasaki, and K. Ogura, *Bull. Chem. Soc. Japan*, **39**, 281 (1966).

As described before,[2] the hydrolysis of III gave readily the 4–hydroxy compound (IV). However, when IV was treated with ammonia, the starting material (III) was generated *in situ*. This observation suggests that the structure of III should be rather the 3–acetimidoyl derivative (IIIb) than the 4–amino derivative (IIIa) by the following reason; that is, if the structure of III is the 4–amino compound (IIIa), the ammonolysis mentioned above seems to be unusual, because, in the amination reaction of the similarly structural compound such as dehydroacetic acid (V), the acetyl group reacts usually to give the acetimidoyl derivatives (VI).[6]

Finally, a more direct basis for the structural assignment was made by the comparison of III with an authentic 3–acetimidoyl compound (IIIb) prepared from 3–acetyl–6–methyl–4–hydroxy–2–pyridone oxime (VII).

As reported in the previous paper,[1] 3–acetyl–6–methyl–4–hydroxy–2–pyridone (IV) reacted with hydroxylamine to give the oxime, for which we assigned the structure as 3–(N–hydroxyacetimidoyl)–4–hydroxy–6–methyl–2–pyridone (VII),[1] and upon catalytic reduction with Raney Ni, VII absorbed an equimolar amount of hydrogen and was reduced to the amino derivative (IIIb), whose infrared spectrum was uniquely identical in every respect with the pyrolyzed product (III).

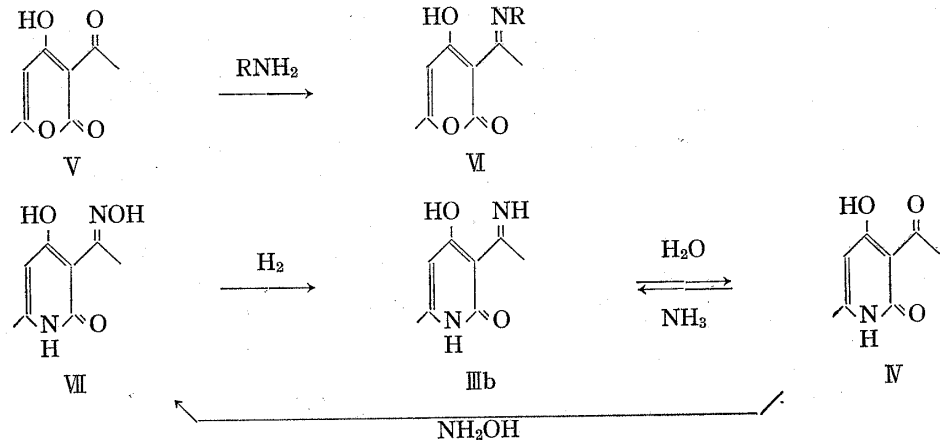

Chart 2

Although the mechanism of the formation of IIIb from I still obscure for the present, two probable pathways will be proposed. The first one pathway A, is shown in Chart 3; the intermediate of this reaction will be IV by the elimination of water and ammonia, and the next stage might well involve the ammonolysis of the acetyl group to give IIIb. Concerning this mechanism, Zymalkowski, *et al.*[7] reported the reaction of the primary enamine of 1–ethoxypentane–2,4–dione (VIII), with malondinitrile to give 3–cyano–4–ethoxymethyl–6–methyl–2–pyridone (IX). They explained this reaction as shown in Chart 3, in which they proposed the mechanism involving the elimination of ammonia and the ammonolysis.

As reported in the previous paper,[2] the yield of III is very poor under ordinary pressure (3%). However, when this reaction was carried out under reduced pressure, the yield of III increased (45%). From this observation, the pathway A seems to be in doubt because ammonia eliminated seems to react hardly again *in vacuo*.

Therefore, we propose the pathway B, which is shown in Chart 4, as more likely one; that is, the first stage of this reaction is the formation of the eight membered ring to give the diazocine derivative (X), and the next stage might well involve the transannular rearrangement to give IIIb.

6) *e.g.*, A. Oppenheim, H. Precht, *Chem. Ber.*, **9**, 1100 (1876).
7) F. Zymalkowski and P. Messinger, *Archiv der Pharm.*, **300**, 168 (1967).

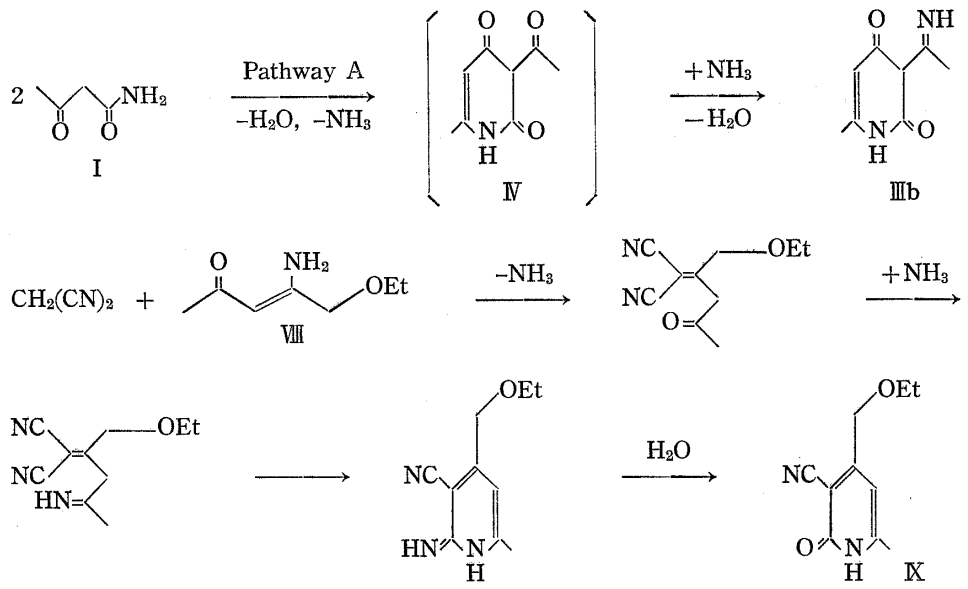

Chart 3

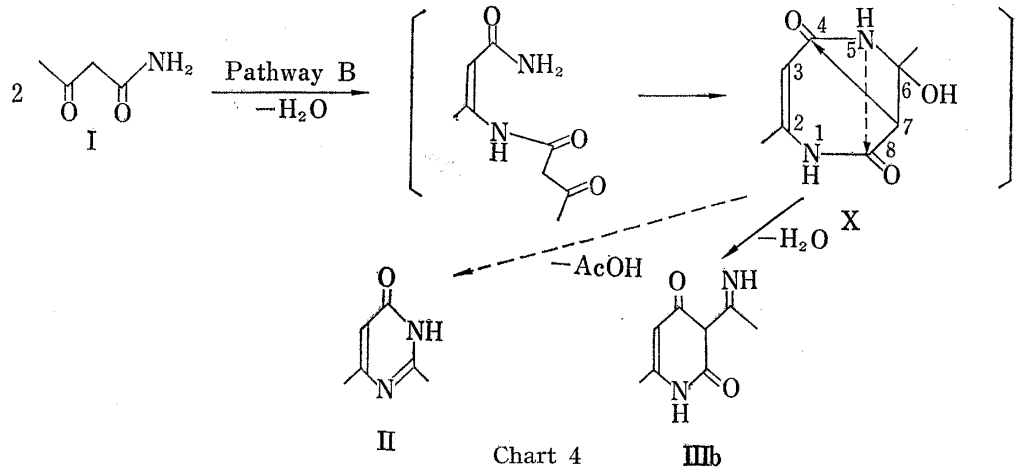

Chart 4

On the other hand, concerning the formation of the pyrimidone derivative (II), the mechanism which is shown in Chart 1 was proposed in the previous paper.[2] However, the pathway B also interprets the formation of II, that is, if the rearrangement occurs between the nitrogen at the 5 position and the carbon at the 8 position, the resulted compound will be the pyrimidone derivative, which eliminates acetic acid giving II.

Experimental

Reaction of 3-Acetyl-4-hydroxy-6-methyl-2-pyridone (IV) with Ammonia——A mixture of IV (0.5 g) and 24% NH_4OH (20 ml) was placed in a sealed glass tube, and warmed in a water bath at 50° for a day. After cooling, the reaction mixture was condensed to give a semi-solid. This was purified by recrystallization from EtOH to afford colorless prisms of mp 314—317° (decomp.), whose infrared (IR) spectrum was identical in every respect with that of an authentic sample of III.

Reduction of 3-Acetimidoyl-4-hydroxy-6-methyl-2-pyridone (V)——A solution of IV-oxime (V) in 20 ml, of MeOH was placed in a reduction vessel, Raney Ni prepared from 1.5 g of Ni-Al alloy was added, and the mixture was shaken in H_2 untill 66 ml of H_2 had been absorbed. The catalyst was filtered off and the filtrate was condensed *in vacuo* to give a crystalline solid. Recrystallization from EtOH gave colorless prisms of mp 314—317° (decomp.), which were identified as III by the comparison of the IR spectrum with that of an authentic sample. Yield, 0.3 g (66%).

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