STUDIES ON THE REACTIVITY OF ISOQUINOLINE AND RELATED COMPOUNDS. I. REACTION OF ISOQUINOLINE N-OXIDE WITH DIKETENE.

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The reaction of isoquinoline N-oxide with diketene afforded three products whose structures were assigned 2,6-dimethyl-3-(1-isoquinolyl)-4-pyrone (II), 1-acetonyl-2-acetyl-4-acetoxy-1,2-dihydroisoquinoline (III), and 4-methyl-2-oxo-2H-benzo[a]quinolizine (IV), respectively.

Recently Hamana et al.[1] developed new methods for introducing carbon substituents at the 2-position of the quinoline ring via its N-oxide. Namely, they treated quinoline N-oxide with some enamines in the presence of acylating agents to give the corresponding 2-substituted quinolines. Diketene is considered to have a property as an acylating agent along with a carbanion like character.[2]

From this point of view, the authors[3] investigated the reaction of diketene with quinoline N-oxide in chloroform or acetic acid and found that it gave 2,6-dimethyl-3-(2-quinolyl)-4-pyrone. Our interest was then focused on the reaction of the other

heteroaromatic amine oxide with diketene. This communication deals with the result of the reaction of isoquinoline N-oxide (I).

When I was heated with five molar excess of diketene in glacial acetic acid at 60°, followed by purification of the reaction mixture through extraction with HCl and column chromatography, three products (II, III, IV) were isolated. The empirical formula, mp and yield of the products are as follows;

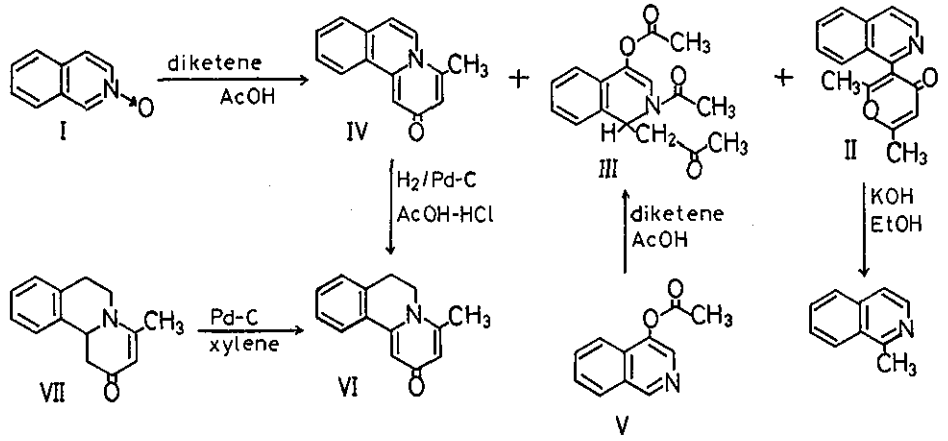
II, $C_{16}H_{13}O_2N$, mp 147-148° colorless prisms (AcOEt), 29.9%

III, $C_{16}H_{17}O_4N$, mp 132-133° colorless prisms (benzene), 13.2%

IV, $C_{14}H_{11}ON$, mp 223-225° (decomp.) colorless prisms (acetone), 9.6%

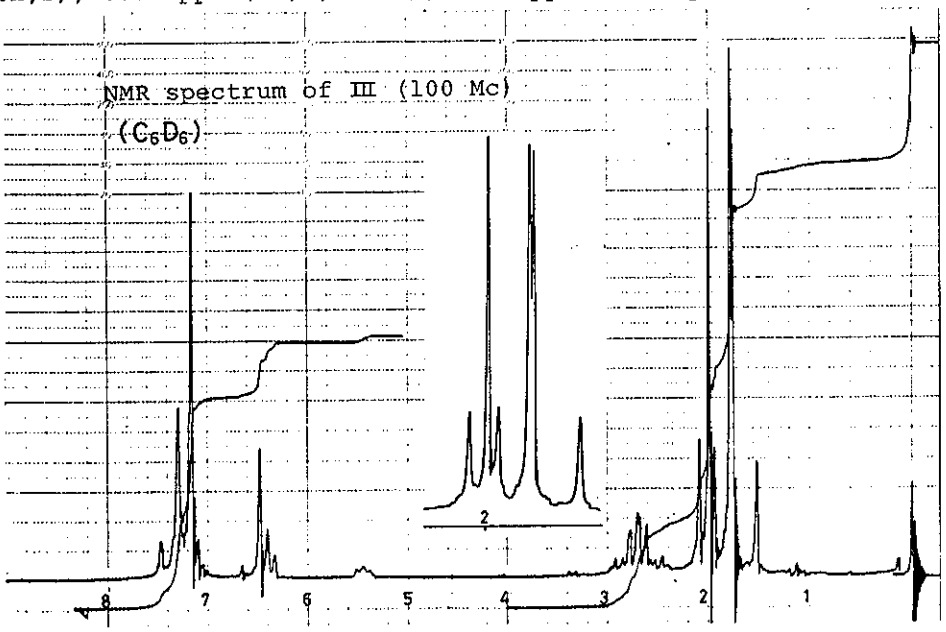
From the spectral data, the main product II was shown to have the 2,6-dimethyl-4-pyrone moiety [NMR($CDCl_3$) ppm: 2.05(3H,s), 2.34(3H,s), 6.24(1H,s); IR($CHCl_3$): 1670cm^{-1}(C=O)]. Alkaline hydrolysis of II gave 1-methylisoquinoline, which proved II being a 1-substituted isoquinoline derivative. From these observations, the structure of II was assigned 2,6-dimethyl-3-(1-isoquinolyl)-4-pyrone.

As shown below, the NMR spectrum of III indicates the presence



of three acetyl methyls and a $-\overset{|}{C}H-CH_2-$ group of which signals are observed as an ABX type multiplet. The somewhat complicated splitting pattern of each signal might be explained by assuming the existence of a pair of rotamers owing to the double bond character of the N-C bond between the ring nitrogen and the amide carbonyl group. The IR spectrum of III ($CHCl_3$) exhibits the characteristic bands of carbonyl groups at 1770, 1720, and 1685 cm^{-1}. Based on the spectral data described above, the structure of III has been assigned as 1-acetonyl-2-acetyl-4-acetoxy-1,2-dihydroisoquinoline. Compound III was also obtained in 28% yield by the reaction of diketene with 4-acetoxyisoquinoline (V)[4] under the identical conditions given for the reaction of isoquinoline N-oxide. This may propose that V is an intermediate in the reaction.

The NMR spectrum of IV (CD_3OD) shows signals at 2.52 ppm (3H,s), 6.51 ppm (1H,d,J=3Hz), 6.88 ppm (1H,ABq,J=7.5Hz), 7.06 ppm



(1H, d, J=3Hz), 7.2-7.55 ppm (3H, m), 7.64 ppm (1H, ABq, J=7.5Hz), and 7.8-8.1 ppm (1H, m). The IR spectrum of IV ($CHCl_3$) shows an absorption band at 1640 cm^{-1} due to the 4-pyridone carbonyl group. From these spectral data, the structure of IV was proposed as 4-methyl-2-oxo-2H-benzo[a]quinolizine. On catalytic hydrogenation in the presence of Pd-charcoal, IV was transformed into its dihydro derivative (VI), $C_{14}H_{13}ON$, mp 168-170° in good yield. Compound VI was identical in every respect with an authentic specimen prepared by dehydrogenation of the known compound VII.[5]

Throughout the course of this work, it was concluded that the reactivity of isoquinoline N-oxide toward diketene was in a striking contrast to that of quinoline N-oxide.

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