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Studies on Pyrido[2,3-*d*]pyrimidine 3-Oxide

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The reaction of pyrido[2,3-*d*]pyrimidine (I) with several nucleophilic reagent was carried out.

In the reaction of I with hydrazine reagent added across the 3,4-positions in I to result in the formation of 3-hydroxy-4-hydrazino-3,4-dihydropyrido[2,3-*d*]pyrimidine (V).

In the case of the reaction with acetic anhydride ring fission between the 2- and 3-positions took place and resulted in the formation of 2-aminonicotinonitrile (VI). The similar ring fission also occurred in the use merely alkali hydroxide for I at ordinary temperature to form 2-(formylamino)nicotinoaldehyde oxime (VII).

In the case of the reactions with ethyl cyanoacetate, malononitrile and ethyl acetoacetate without base catalyst the transformation of I into 1,8-naphthyridine derivatives proceeded to result in the formation of ethyl 2-amino-1,8-naphthyridine-3-carboxylate (X), 2-amino-1,8-naphthyridine-3-carbonitrile (XI) and ethyl 2-methyl-1,8-naphthyridine-3-carboxylate (XII), respectively.

In the case of the reaction with symmetric β-diketone without base catalyst 2-substituted-pyrido[2,3-*d*]pyrimidine was formed. Thus the reactions with 2,4-pentanedione and with 1,3-diphenyl-1,3-propanedione gave 1-(2-pyrido[2,3-*d*]pyrimidinyl)-2-propanone (XX) and 2-(2-pyrido[2,3-*d*]pyrimidinyl)acetophenone (XXI), respectively. But in the case of the reaction with asymmetric β-diketone such as 1-phenyl-1,3-butanedione it proceeded in a defferent way from the reaction with symmetric β-diketone and resulted in the transformation of I into 2-phenyl-1,8-naphthyridine (XXVIII).

The possible reaction processes for the reactions described above were also proposed and discussed.

In a series of studies on the chemical properties of the pyrimidine portion in the quinazoline 3-oxide ring system, the present authors and his co-workers had reported the reaction of nucleophilic reagents on quinazoline 3-oxide (II),[2] and gained some interesting observations regarding the properties of the pyrimidine portion such as the facile fission of the ring between the 2- and 3-positions and the transformation of II into quinoline derivatives.

The structure of pyrido[2,3-*d*]pyrimidine 3-oxide (I) is similar to that of II so that the nucleophilic reactivities of the ring carbon atom at the 4-psoition caused by overlapping the polar effect of N-oxide group, together with the effect of ring nitrogen, as well as that of the fused pyridine ring, may be considered to be equal to or greater than that in II. From this point of view, in this paper the reactions of I with several nucleophilic reagents were carried out and the reactions could proceed through A, B, C and D type of the reactions classified according to structures of the reaction products.

Pyrido[2,3-*d*]pyrimidine 3-oxide used in this paper is obtained by condensation-cyclization of 2-aminonicotinoaldehyde oxime (III) and ethyl orthoformate. In general, deoxygenation of heterocyclic N-oxides is effected by application of phosphorous trichloride or tribromide,[3] or by catalytic reduction with Raney nickel.[4] The former reaction is found to proceed and pyrido[2,3-*d*]pyrimidine (IV) is obtained from I. The reaction is also found to

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[1] Location: *2-2-1 Oshika, Shizuoka-shi.*

[2] *a*) T. Higashino, *Chem. Pharm. Bull.* (Tokyo), 9, 635 (1961); *b*) T. Higashino, Y. Nagano and E. Hayashi, *ibid.*, 21, 1943 (1973).

[3] M. Hamana, *Yakugaku Zasshi*, 75, 123 (1955).

[4] E. Hayashi, H. Yamanaka and K. Shimizu, *Chem. Pharm. Bull.* (Tokyo), 7, 141 (1959).

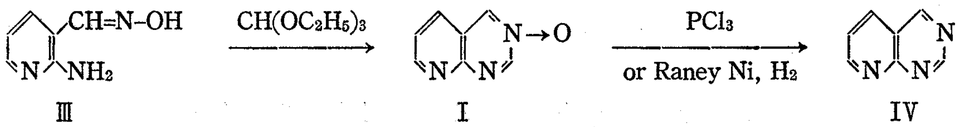

Chart 1

proceed by catalytic reduction over Raney nickel at ordinary temperature resulting in absorption of 1 mole of hydrogen to form IV. These facts show that I should have the N-oxide group.

I. A Type of the Reaction

In A type of the reaction the reagent adds across the 3,4-positions of I to give 4-substituted-3-hydroxy-3,4-dihydropyrido[2,3-*d*]pyrimidine. For example the reaction of I with hydrazine in methanol at ordinary temperature smoothly proceeds and gives 3-hydroxy-4-hydrazino-3,4-dihydropyrido[2,3-*d*]pyrimidine (V).

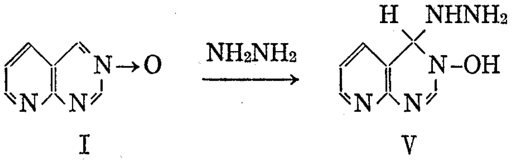

Chart 2

The structure of V is presumed to be 3-hydroxy-4-hydrazino-3,4-dihydropyrido[2,3-*d*]-pyrimidine through the following data. The formation of III and 2-aminonicotinonitrile (VI)[5] from the thermal decomposition of V, shown in Chart 3, may show that oxygen is located at the 3-position's nitrogen atom in V. Under electron impact V gives pyrido[2,3-*d*]-pyrimidine radical ion, *m/e* 131 (77%) through the dissociation pathways involving the first loss of hydrazino radical, hydrazine, hydroxyl radical and water as shown in Chart 4.

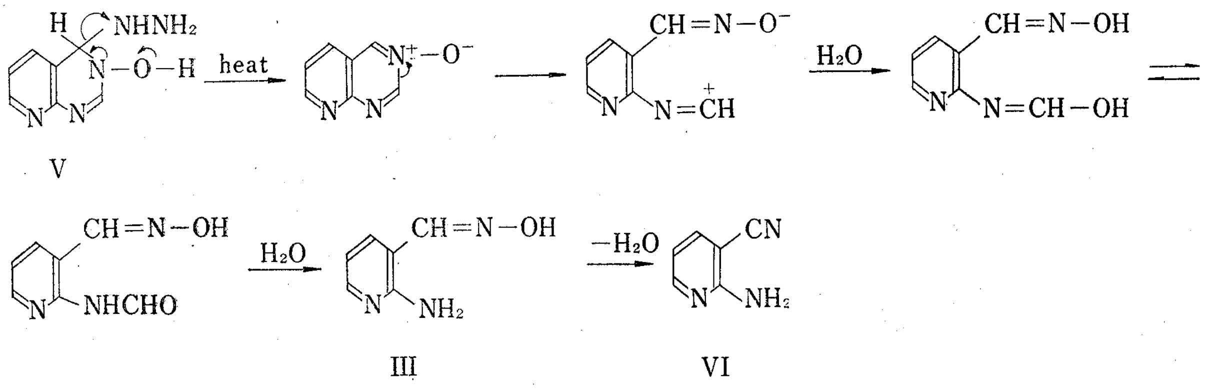

Chart 3

II. B Type of the Reaction

In B type of the reaction excess of reagent attacks the 2-position in an intermediate, formed through the process for A type of the reaction, to form the reaction product being ring fission between the 2- and 3-positions. For example the reaction of I with acetic anhydride gives VI. The similar ring fission occurs in the brief treatment of alkali hydroxide for I at ordinary temperature to form 2-(formamido)nicotinoaldehyde oxime (VII).

The structure of VII is presumed to be 2-(formamido)nicotinoaldehyde oxime through the following experiments. The hydrolysis of VII with alkali hydroxide solution gives III. The thermal decomposition of VII at 175—180° gives VI.

Taking up the reaction of I with alkali hydroxide as a sample, the possible process for B type of the reaction may be considered to be as follows. Hydroxide ion used as nucle-

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[5] E.C. Taylor and A.J. Corvetti, *J. Org. Chem.*, **19**, 1633 (1954).

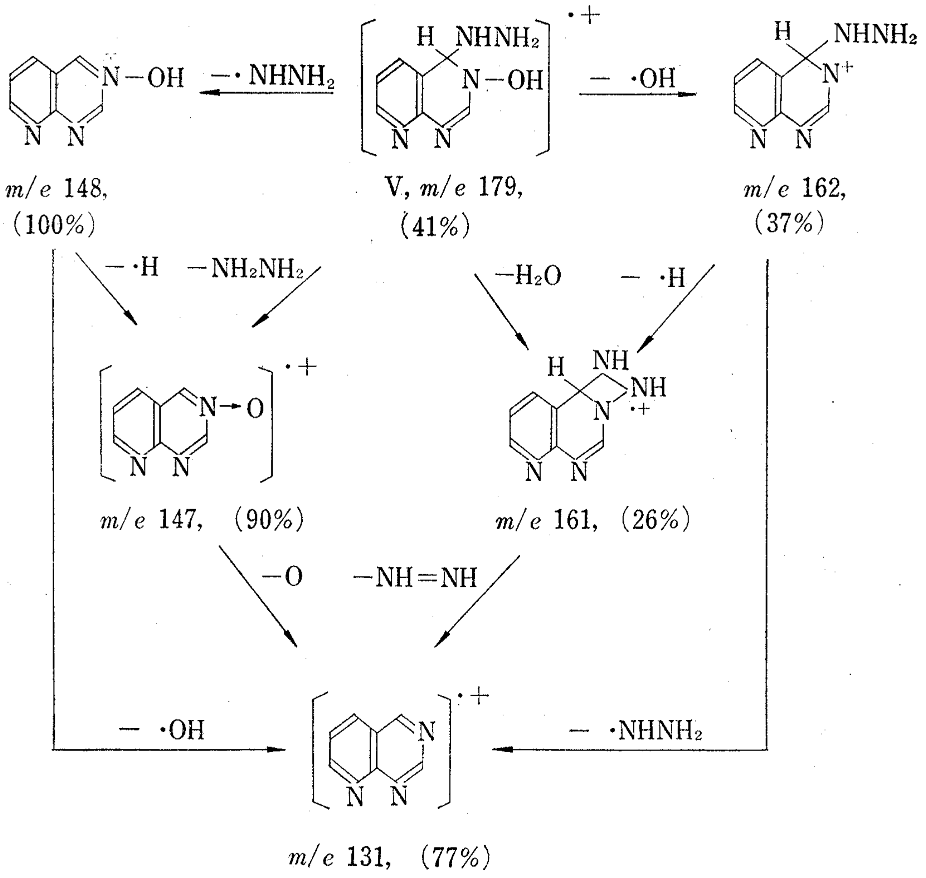

Chart 4. Fragmentation of V under Electron Impact

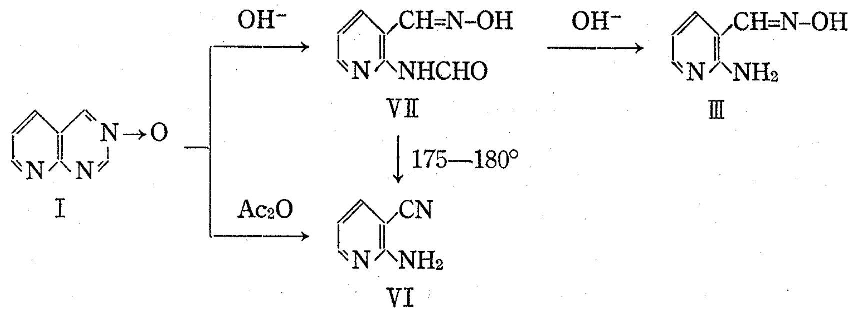

Chart 5

ophilic reagent may attack to the 4-position in I, according to the process for A type of the reaction, to form a type of an intermediate such as 3,4-dihydroxy-3,4-dihydropyrido[2,3-*d*]-pyrimidine. Then excess of hydroxide ion may attack the 2-position in **a** to form an intermediate (**b**). Successive ring fission between the 2- and 3-position in **b** results in the formation of VII accompanied with the elimination of hydroxide ion, as shown in Chart 6.

It is also known that the applications of acetic anhydride or alkali hydroxide to II result in the formation of *o*-isocyanobenzonitrile (VIII) and 2′-(hydroxyiminomethyl)formanilide (IX), respectively.[2a)]

III. C Type of the Reaction

In C type of the reaction by means of the application of active methylene compound the transformation of I into naphthyridine derivatives proceeds through the process for B type of the reaction. For example the reactions of I with ethyl cyanoacetate, malononitrile and ethyl acetoacetate result in the formation of ethyl 2-amino-1,8-naphthyridine-3-carboxylate

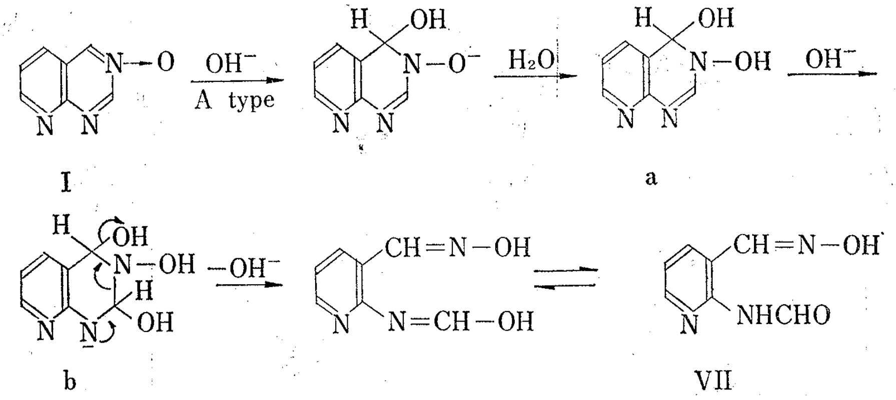

Chart 6

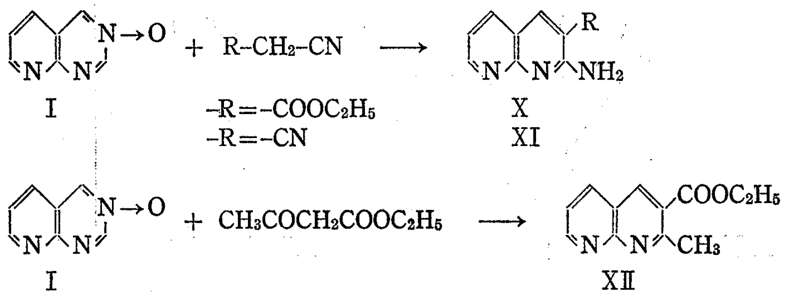

Chart 7

(X), 2-amino-1,8-naphthyridine-3-carbonitrile (XI) and ethyl 2-methyl-1,8-naphthyridine-3-carboxylate (XII), respectively.

The compound XI shows the same decomposition point and absorption peaks in its infrared (IR) and ultraviolet (UV) spectrum as those of 2-amino-1,8-naphthyridine-3-carbonitrile[6a] prepared from the Friedlaender synthesis between 2-aminonicotinoaldehyde (XIII)[7] and malononitrile in the presence of piperidine. These data indicate that XI is to be 2-amino-1,8-naphthyridine-3-carbonitrile. The structure of X is presumed to be ethyl 2-amino-1,8-naphthyridine-3-carboxylate through the presence of the marked absorption peaks at 3420 and 1710 cm^{-1} due to amino and carbonyl group, respectively, in its IR spectrum and the approximation of its UV spectrum to that of XI as shown in Fig. 1. The structure of XII is presumed to be ethyl 2-methyl-1,8-naphthyridine-3-carboxylate through the presence of the marked absorption peak at 1720 cm^{-1} due to carbonyl group in its IR spectrum, the approximation of its UV spectrum to that of 2-methyl-3-acetyl-1,8-naphthyridine (XIV)[6a] prepared from the Friedlaender synthesis by means of XIII and 2,4-pentanedione as shown in Fig. 2, the presence of the absorption bands of AMX pattern due to the protons at the 5-, 6- and 7-positions, of singlet at 1.28 τ due to the proton at the 4-position, of singlet at 6.93 τ due to methyl group at the 2-position, of quartet at 8.54 τ and triplet at 5.53 τ due to ethyl group in ester, in its nuclear magnetic resonance (NMR) spectrum.

The possible reaction process for the transformation of I into 1,8-naphthyridine derivatives, taking up the reaction with malononitrile as a sample, may be considered to be as follows. The reaction through the process for A and B type of the reaction may form **f** type of an intermediate with the elimination of hydroxylamine. The subsequent ring closure with the loss of the cation **h** in **f** may form **g** type of an intermediate which leads to XI. It was shown that the loss of the cation **h** from **f** type of an intermediate was recognized in the trans-

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6) *a*) E.M. Hawes and D.G. Wibbreley, *J. Chem. Soc.*, **1966**, 315; *b*) *Idem*, *ibid.*, **1967**, **1564**.

7) V. Oakes, R. Pascoe and H.N. Ryoon, *J. Chem. Soc.*, **1956**, 1045.

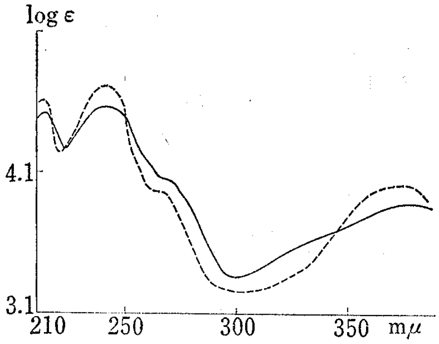

Fig. 1. UV Spectra of X and XI

——: X, - - - -: XI

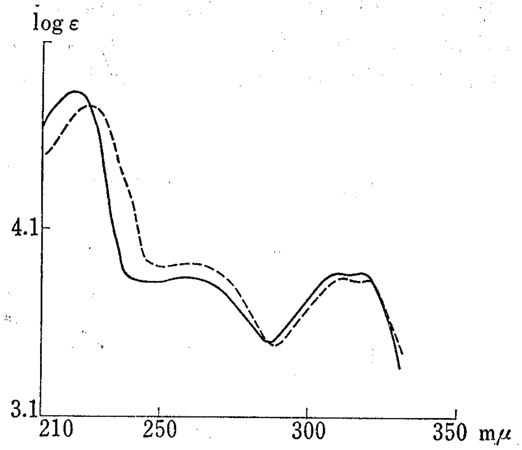

Fig. 2. UV Spectra of XII and XIV

——: XII, - - - -: XIV

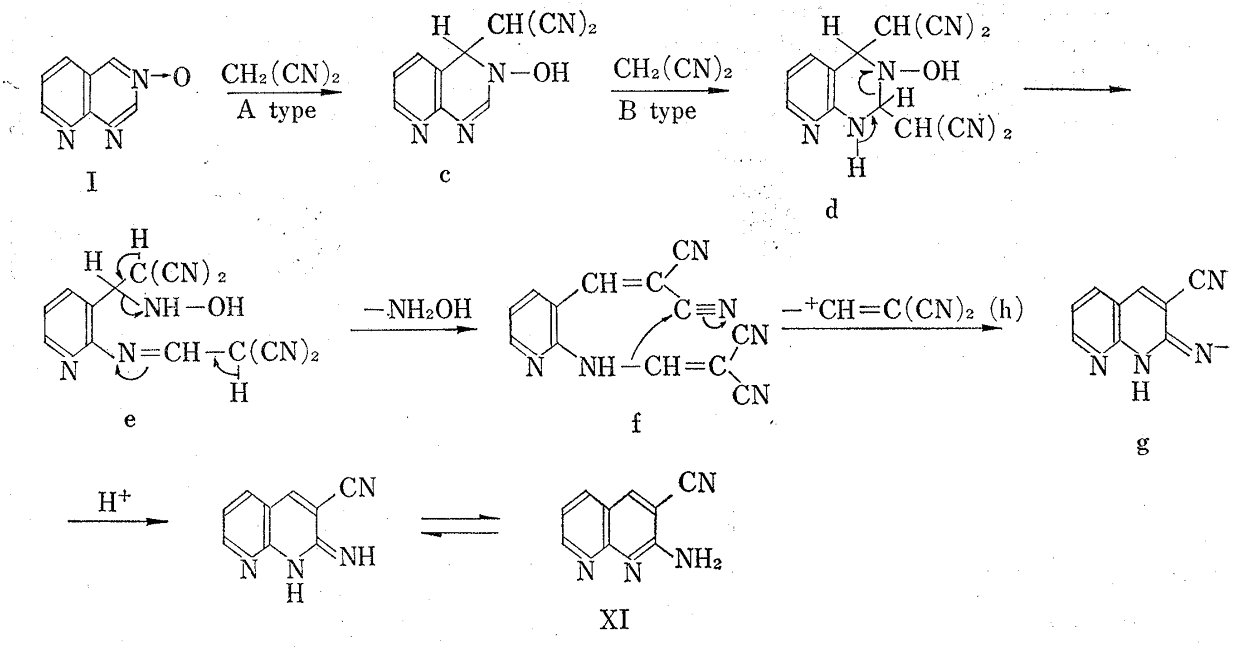

Chart 8

formation of quinazoline (XV) into quinoline derivatives by means of malononitrile.[8] If the reaction process for this transformation is considered to be similar to that of XV, it can be understood that this possible reaction process is well reasoned.

It is also known that the similar transformation takes place in the reaction of II with active methylene compound.[2b] Thus the reaction with malononitrile gives 2-amino-3-quinolinecarbonitrile (XVI), with ethyl cyanoacetate does ethyl 2-amino-3-quinolinecarboxylate (XVII) and with ethyl cyanoacetate does ethyl 2-methyl-3-quinolinecarboxylate (XVIII) and 3-acetylcarbostyrile (XIX), respectively.

IV. D Type of the Reaction

In D type of the reaction by means of the application of symmetric β-diketone 2-substituted pyrido[2,3-*d*]pyrimidines are formed through the process for B type of the reaction. For example the reactions of I with 2,4-pentanedione of 1,3-diphenyl-1,3-propanedione result in the formation of 1-(2-pyrido[2,3-*d*]pyrimidinyl)-2-propanone (XX) and 2-(2-pyrido[2,3-*d*]-

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[8] T. Higashino, H. Ito and E. Hayashi, *Chem. Pharm. Bull.* (Tokyo), **20**, 1544 (1972).

pyrimidinyl)acetophenone (XXI), respectively. But in the case of the reaction with 1-phenyl-1,3-butanedione, it proceeds in a diffrent way from D type of the reaction and results in the transformation of I into 2-phenyl-1,8-naphthyridine (XXVIII).

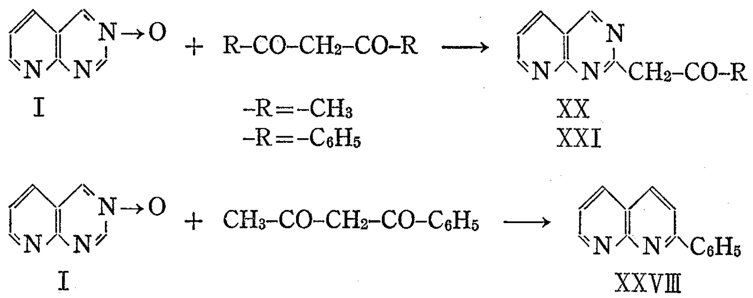

Chart 9

The compound XX shows a split of AMX pattern due to the protons at the 7-, 6- and 5-positions, a singlet at 1.62 τ due to the proton at the 4-position, a singlet at 2.26 τ due to the methylene protons and a singlet at 7.53 τ due to methyl protons of acetyl group in its NMR spectrum. The fragmentation of XX under electron impact proceeds by the two dissociation pathways. One is loss of methyl radical and carbon monoxide from the molecular ion (M^+), in successive step, to lead to pyridodiazatropylium cation,[9] *m/e* 144 (100%). The another is a elimination of acetonyl radical from M^+ to give even-electron pyrido[2,3-*d*] pyrimidium cation,[9] *m/e* 130 (16.3%) as shown in Chart 10. In fact XX does not fail to show any depression of mixed melting point test with 1-(4-pyrido[2,3-*d*]pyrimidinyl)-2-propanone (XXII)[10] prepared from the reaction of 4-chloropyrido[2,3-*d*]pyrimidine (XXIII) with acetone in the presence of sodium amide. From these facts XX is established its structure to be 1-(2-pyrido-[2,3-*d*]pyrimidinyl)-2-propanone.

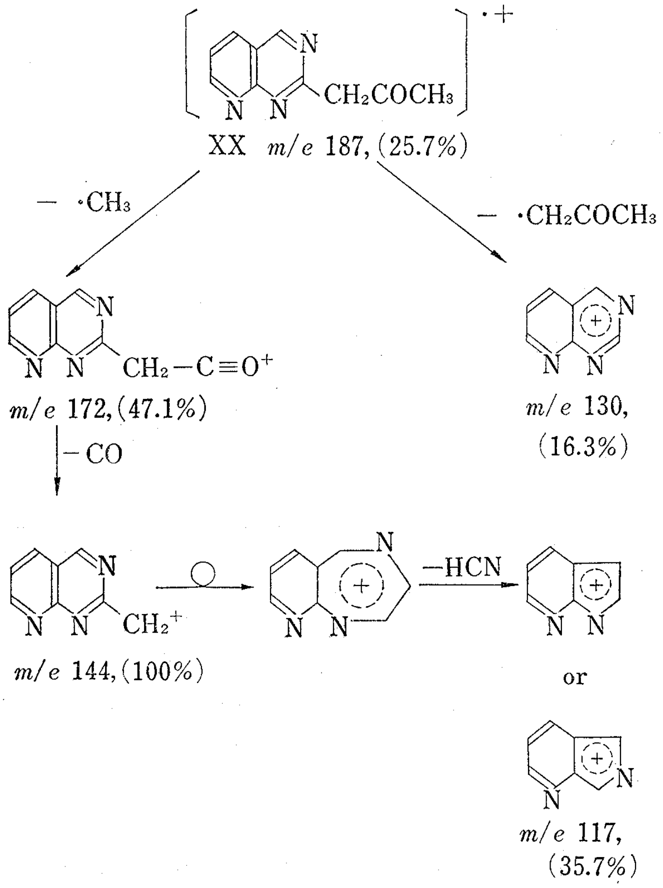

Chart 10. The Fragmentation of XX under Electron Impact.

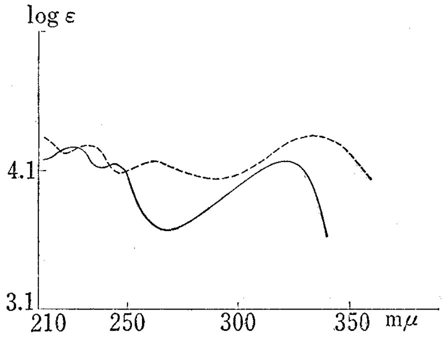

Fig. 3. UV Spectra of XX and XXI
——: XX, ------: XXI

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9) T. Higashino, M. Uchida and E. Hayashi, *Chem. Pharm. Bull.* (Tokyo), **20**, 772 (1972).
10) T. Higashino and E. Hayashi, *Chem. Pharm. Bull.* (Tokyo), **18**, 1457 (1970).

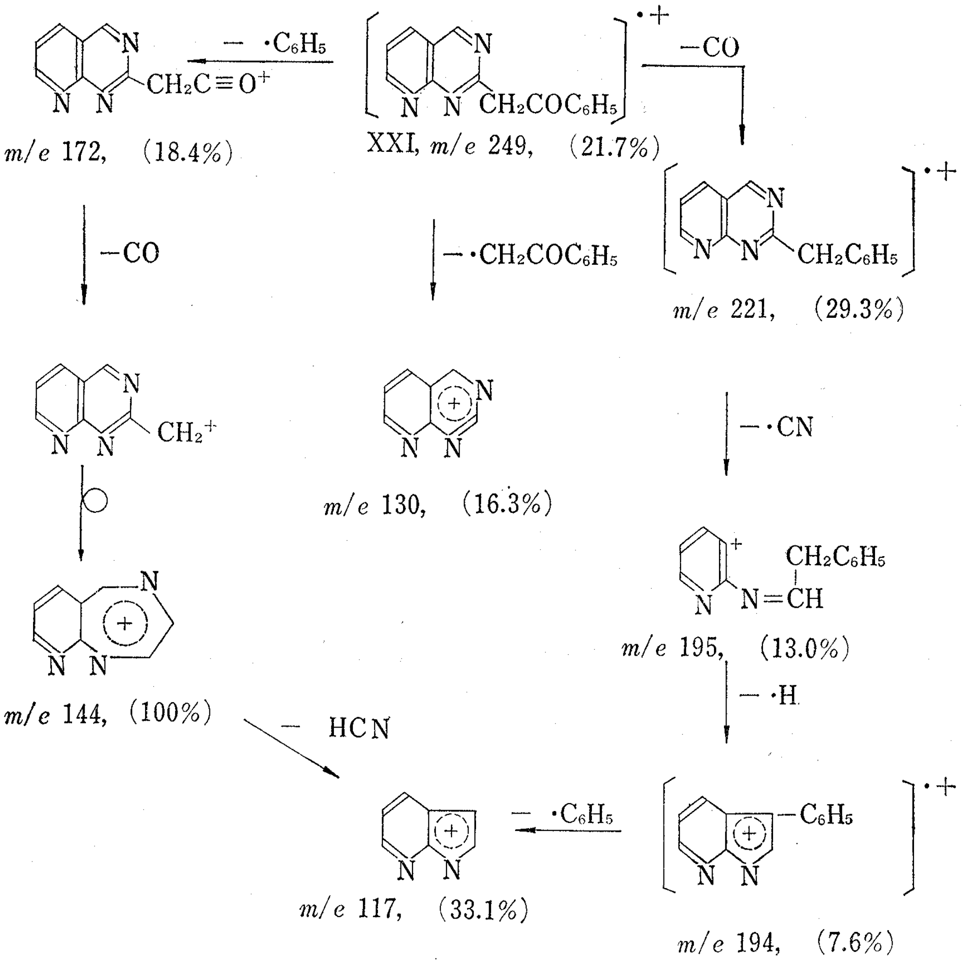

Chart 11. The Fragmentation of XXI under Electron Impact

The compound XXI shows a peak at 1640 cm^{-1} due to carbonyl group in its IR spectrum. Its UV spectrum approximates to that of XX as shown in Fig. 3. In the fragmentation of XXI under electron impact the main dissociation pathway involves loss of phenyl radical and carbon monoxide from M^+, in successive step, to lead pyridodiazatropylium cation, *m/e* 144 (100%). One of other dissociation bypath is loss of phenyl radical to form even-electron pyrido[2,3-*d*]pyrimidinium cation, *m/e* 130 (16.3%) as shown in Chart 11. In fact XXI does not fail to show any depression of mixed melting point test with 2-(4-pyrido[2,3-*d*]pyrimidinyl)acetophenone (XXIV)[10] prepared from another route. These facts described above show that XXI is to be 2-(2-pyrido[2,3-*d*]pyrimidinyl)acetophenone.

The compound XXVIII is determine its structure to be 2-phenyl-1,8-naphthyridine on admixture with the authentic specimen[6b] prepared from another route.

The possible reaction process for the formation of 2-substituted-pyrido[2,3-*d*]pyrimidine may be considered to be as follows. During the process for B type of the reaction **j** type of an intermediate may occur ring fission between the 2- and 3-positions with an elimination of β-diketone to form **k** type of an intermediate. Successive ring closure of **k** gives **l** type of an intermediate which leads to 2-substituted-pyrido[2,3-*d*]pyrimidines, XX and XXI by hydrolysis as shown in Chart 12.

It is also reported that the reaction of II with β-diketone proceeds in a different way from D type of the reaction and results in the transformation of II into quinoline derivatives.[2b] Thus the reaction of II with 2,4-pentanedione gives methyl 2-methyl-3-quinolyl ketone (XXV) and 4-acetonyl-8-quinolinecarbonitrile (XXVI) and with 1,3-diphenyl-1,3-propanedione or 1-phenyl-1,3-butanedione give 2-phenylquinoline (XXVII), respectively.

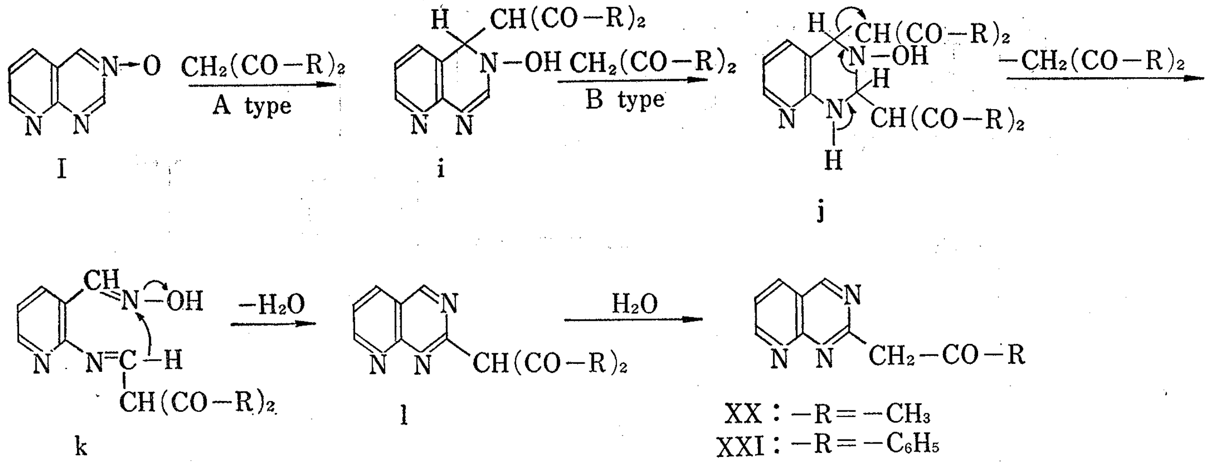

Chart 12

The reaction process for the formation of XXVIII in the reaction of I with 1-phenyl-1,3-butanedione may be considered to be similar to that of C type of the reaction. Thus the formation of **o** type of an intermediate may proceed through the same way as that of **e** type of an intermediate shown in Chart 8. The elimination of acetohydroxamic acid from **o** forms **p** type of an intermediate which lead to **q** type of an intermediate through ring closure accompanied with an elimination of cation **r**. Successive loss of hydroxide ion from **q** gives XXVIII as shown in Chart 13.

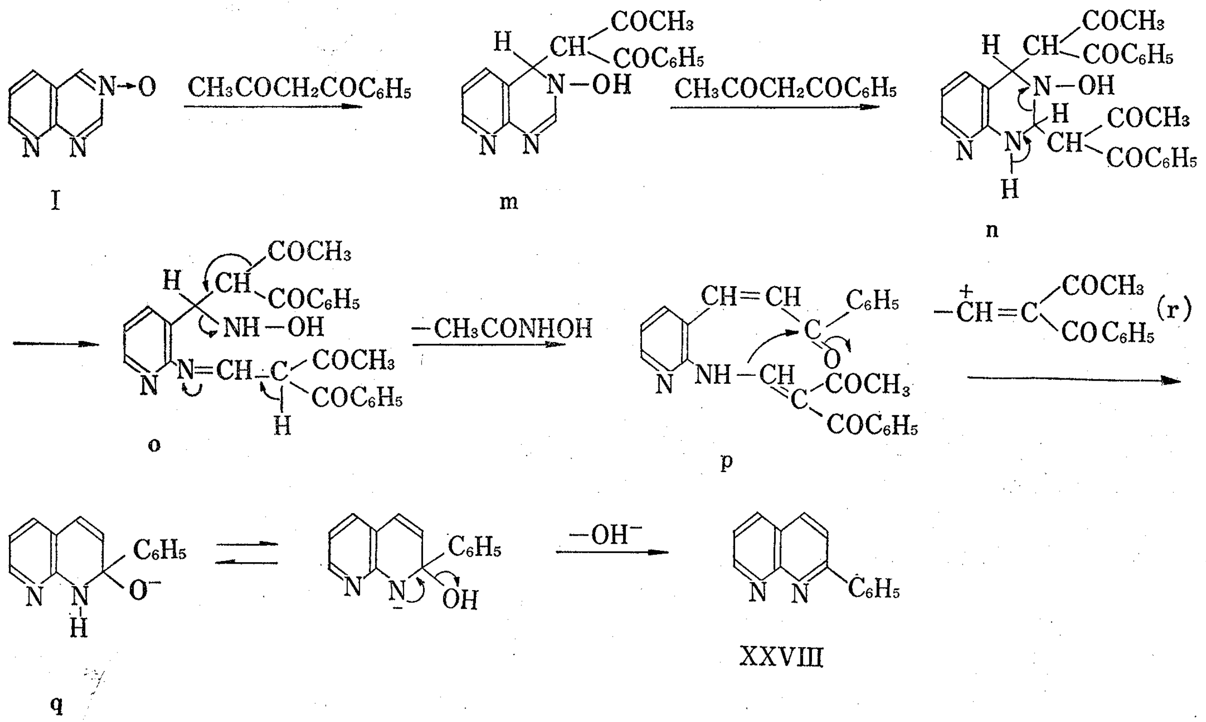

Chart 13

Experimental[11]

UV spectra were measured in 99.5% EtOH on a Hitachi Spectrophotometer Model ESP-2U. IR spectra were recorded with a Jasco Grating Infrared Spectrophotometer Model IRA-1. NMR spectra were measured at 60 Mc and 21° on a Hitachi High Resolution NMR Spectrometer Model R-24. Tetramethylsilane was used as an internal standard.

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11) All melting points were not corrected.

Mass spectra were recorded on a Hitachi RMS-4 single focusing mass spectrometer. The ionisation energy normally used was 80 eV. Samples were vaporised in all glass inlet system for compound having melting point below 150° and direct inlet system for the above 150°.

2-Aminonicotinoaldehyde Oxime (III)——To a solution of 1000 mg of $NH_2OH \cdot HCl$ and 331 mg of Na dissolved in 10 ml of MeOH 1500 mg of 2-aminonicotinoaldehyde (XIII)⁷⁾ was added and the reaction mixture was allowed to stand at room temperature overnight. MeOH was removed under reduced pressure and H_2O was added to a residue which was extracted with $CHCl_3$ and dried over anhyd. Na_2SO_4. Evaporation of $CHCl_3$ from the extract gave III as white needles, mp 165° from H_2O, in 71.3% yield (1200 mg). *Anal.* Calcd. for $C_6H_7ON_3$ (2-aminonicotinoaldehyde oxime): C, 52.54; H, 5.15; N, 30.64. Found: C, 55.02; H, 5.38; N, 30.71. Mass Spectrum *m/e*: 137 (M^+).

Pyrido[2,3-*d*]pyrimidine 3-Oxide (I)——The mixture of 400 mg of III and 5 ml of $CH(OC_2H_5)_3$ was heated at 140—145° for 1 hr. After cooling the separated crystals were collected by suction and washed with benzene. Recrystallization from benzene gave I as slightly yellow needles, mp 216° (decomp.) in 32.6% yield (140 mg). *Anal.* Calcd. for $C_7H_5ON_3$ (pyrido[2,3-*d*]pyrimidine 3-oxide): C, 57.14; H, 3.43; N, 28.56. Found: C, 57.00; H, 3.65; N, 28.36. Mass Spectrum *m/e*: 147 (M^+).

Catalytic Reduction of I with Raney Ni——Raney Ni prepared from 1000 mg of Ni-Al alloy was added to 300 mg of I in 25 ml of MeOH and the mixture was shaken in H_2 stream. The reaction was stopped when 1 mole of H_2 had been absorbed. The catalyst was filtered off, the filtrate was evaporated and the residue was extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4, the extract was passed through a column of alumina to remove impurities. Evaporation of $CHCl_3$ gave IV, mp 106—107° from petr. ether in 19.9% yield (53 mg). This compound was undepressed on admixture with pyrido[2,3-*d*]pyrimidine¹⁰⁾ prepared from another route.

Reaction of I with PCl_3——To a solution of 300 mg of I dissolved in 20 ml of $CHCl_3$ a solution of 900 mg of PCl_3 dissolved in 5 ml of $CHCl_3$ was added with shaking under cooling. The reaction mixture was refluxed for 1 hr. The reaction mixture was then poured into excess of NH_4OH-ice mixture and extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4 the extract was passed through a column of alumina to remove impurities. Evaporation of $CHCl_3$ gave IV, mp 106—107° as colorless needles from peter. ether in 35.2% yield (94 mg). This compound was undepressed on admixture with IV¹⁰⁾ prepared from another route.

Reaction of I with NH_2NH_2——To a solution of 300 mg of I dissolved in 20 ml of MeOH, 600 mg of 80% $NH_2NH_2 \cdot H_2O$ was added and the reaction mixture was allowed to stand overnight at room temperature. The separated crystals were recrystallized from MeOH to give V, mp 159° (decomp.) as orange plates in 37.8% yield (138 mg). *Anal.* Calcd. for $C_7H_9ON_5$ (3-hydroxy-4-hydrazino-3,4-dihydropyrido[2,3-*d*]pyrimidine): C, 46.92; H, 5.06; N, 39.09. Found: C, 47.10; H, 5.28; N, 39.50.

Thermal Decomposition of V——In a test tube 200 mg of V was heated at 160° for 1 hr. The reaction mixture obtained was extracted with 2N HCl. The HCl layer was neutralized with K_2CO_3 and extracted with $CHCl_3$. The extract was passed through a column of alumina to separate VI and III. The elution with $CHCl_3$ gave VI, mp 131° as slightly yellow scaly crystals from petr. ether in 25.4% yield (34 mg). This compound was undepressed on admixture with 2-aminonicotinonitrile⁵⁾ prepared from another route. The elution with MeOH gave III, mp 165° as white needles from H_2O in 14.8% yield (23 mg).

Reaction of I with Ac_2O——A mixture of 300 mg of I and 5 ml of Ac_2O was heated at 95—100° for 3 hr. After cooling Ac_2O was removed under reduced pressure and the residue was extracted with 2N HCl. The HCl layer was neutralized with K_2CO_3 and extracted with $CHCl_3$. The extract was passed through a column of alumina by using benzene–$CHCl_3$ mixture (9: 1) to gave VI, mp 131° from petr. ether in 3.7% yield (9 mg).

Reaction of I with Alkali Hydroxide——A solution of 300 mg of I and 2 ml of 2N NaOH was allowed to stand at room temperature for 10 min. The reaction mixture was carefully neutralized with AcOH under cooling to separate crystals which were extracted with large amount of $CHCl_3$. After drying over anhyd. Na_2SO_4 evaporation of $CHCl_3$ gave VII, mp 167° (decomp.) as slightly yellow scaly crystals from MeOH in 76.0% yield (256 mg). *Anal.* Calcd. for $C_7H_7O_2N_3$ (2-(formamido)nicotinoaldehyde oxime): C, 50.91; H, 4.27; N, 25.45. Found: C, 50.99; H, 4.37; N, 25.71. Mass Spectrum *m/e*: 165 (M^+).

Hydrolysis of VII——A mixture of 200 mg of VII and 20 ml of 2N NaOH was heated at 90—95° for 1 hr. The reaction mixture was neutralized with AcOH and extracted with large amount of $CHCl_3$ to give III, mp 165° as white needles from H_2O in 23.0% yield (38 mg).

Thermal Decomposition of VII——In a test tube 50 mg of VII was heated at 175—180° for 15 min. The reaction mixture was dissolved in MeOH and treated with charcoal. Evaporation of MeOH gave VI, mp 131° as pale yellow scaly crystals from petr. ether in 63.9% yield (23 mg).

Reaction of I with Ethyl Cyanoacetate——A mixture of 300 mg of I and 5 ml of ethyl cyanoacetate was heated at 150° for 1 hr. The reaction mixture was dissolved in $CHCl_3$ and extracted with 2N HCl. The extract was neutralized, salted out with K_2CO_3 and extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4 the extract was passed through a column of alumina to give X, mp 187—189° (decomp.) as orange yellow needles from benzene in 6.1% yield (27 mg). *Anal.* Calcd. for $C_{11}H_{11}O_2N_3$ (ethyl 2-amino-1,8-naphthyridine-3-carboxylate): C, 60.82; H, 5.10; N, 19.35. Found: C, 60.42; H, 5.54; N, 19.61. Mass Spectrum *m/e*: 217 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3420 ($-NH_2$), 1710 ($=C=O$). UV λ_{max}^{EtOH} mμ (log ε): 214 (4.42), 241 (4.47), 270 (3.94, shoulder), 379 (3.77).

Reaction of I with Malononitrile——A solution of 300 mg of I and 600 mg of malononitrile dissolved in 20 ml of MeOH was refluxed for 2.5 hr. The solvent was removed under reduced pressure and the residue was extracted with 2N HCl. The HCl layer was neutralized, salted out with K_2CO_3 and extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4 solvent was removed to give XI, mp 260—265° (decomp.) as orange yellow needles from MeOH in 3.5% yield (12 mg). IR ν_{max}^{KBr} cm^{-1}: 3470 (-NH_2), 2240 (-CN). UV λ_{max}^{EtOH} mμ (log ε): 213 (4.50), 240 (4.62), 267 (3.86, shoulder), 375 (3.90).

Reaction of I with Ethyl Acetoacetate——A mixture of 300 mg of I and 1.5 g of ethyl acetoacetate was heated at 140° for 2 hr. Benzene was added to the reaction mixture which was extracted with 2N HCl. The HCl layer was neutralized with K_2CO_3 and extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4 the extract was passed through a column of alumina. The elution with benzene–$CHCl_3$ mixture (8: 2) gave XII, mp 90—91° from petr. ether in 5.9% yield (26 mg). *Anal.* Calcd. for $C_{12}H_{12}O_2N_2$ (ethyl 2-methyl-1,8-naphthyridine-3-carboxylate): C, 66.65; H, 5.59; N, 12.96. Found: C, 66.73; H, 5.31; N, 13.18. Mass Spectrum *m/e*: 216 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1720 (=C=O). UV λ_{max}^{EtOH} mμ (log ε): 221 (4.75), 259 (3.75), 309 (3.78), 320 (3.77). NMR (in $CDCl_3$): 0.88 (1H, quartet, $J_{6-7}=3.9$ cps, $J_{5-7}=1.8$ cps, H-7), 1.28 (1H, singlet, H-4), 1.76 (1H, quartet, $J_{5-6}=7.8$ cps, H-5), 2.54 (1H, quartet, H-6), 5.53 (2H, quartet, $J=7.5$ cps, -OCH_2-Me), 6.93 (3H, singlet, Ar-CH_3), 8.54 (3H, triplet, -CH_3).

Reaction of I with 2,4-Pentanedione——A mixture of 300 mg of I and 1.5 ml of 2,4-pentanedione was heated at 135—140° for 1 hr. Benzene was added to the reaction mixture and extracted with 2N HCl. The HCl layer was neutralized with K_2CO_3 and extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4 the extract was passed through a column of alumina. From the first fraction XX, mp 166—167° as white needles from petr. ether was obtained in 6.0% yield (23 mg). *Anal.* Calcd for $C_{10}H_9ON_3$ (1-(2-pyrido[2,3-*d*]-pyrimidinyl)-2-propanone): C, 64.16; H, 4.85; N, 22.45. Found: C, 64.51; H, 5.23; N, 22.44. UV λ_{max}^{EtOH} mμ (log ε): 228 (4.17), 244 (4.04), 321 (4.06). NMR (in $CDCl_3$): 1.40 (1H, quartet, $J_{5-7}=1.5$ cps, $J_{6-7}=6.3$ cps, H-7), 1.62 (1H, singlet, H-4), 2.26 (2H, singlet, Ar-CH_2-CO-), 2.35 (1H, quartet, $J_{5-6}=6.3$ cps, H-5), 2.92 (1H, triplet, H-6), 7.53 (3H, singlet, -CO-CH_3).

Reaction of I with 1,3-Diphenyl-1,3-propanedione——A mixture of 441 mg of I and 1628 mg of 1,3-diphenyl-1,3-propanedione was heated at 140—145° for 4 hr. Treatment of the reaction mixture according to that of the reaction of I with 2,4-pentanedione gave XXI, mp 151° as white needles from MeOH in 9.1% yield (68 mg). *Anal.* Calcd. for $C_{15}H_{11}ON_3$ (2-(2-pyrido[2,3-*d*]pyrimidinyl)acetophenone): C, 72.27; H, 4.45; N, 16.86. Found: C, 72.44; H, 4.56; N, 16.82. IR ν_{max}^{KBr} cm^{-1}: 1640 (=C=O). UV λ_{max}^{EtOH} mμ (log ε): 234 (4.17), 262 (4.05), 333 (4.25).

Reaction of I with 1-Phenyl-1,3-butanedione——A mixture of 441 mg of I and 1170 mg of 1-phenyl-1,3-butanedione was heated at 140—145° for 4 hr. The reaction mixture was dissolved in $CHCl_3$ and extracted with 2N HCl. The HCl layer was neutralized with 2N NaOH and extracted with $CHCl_3$. The extract was passed through a column of alumina. The elution with benzene–$CHCl_3$ mixture (2: 1) give XXVIII, mp 117—118° as white needles from petr. ether in 4.5% yield (28 mg). *Anal.* Calcd. for $C_{14}H_{10}N_2$ (2-phenyl-1,8-naphthyridine): C, 81.53; H, 4.89; N, 13.58. Found; C, 81.51; H, 4.84; N, 13.62.

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