76. Nobuo Ikekawa : Studies on Naphthyridines. III.¹⁾ Syntheses of
2,10-Diazaanthracene and 1,7-Naphthyridine.

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It would be natural to expect that the new synthetic method for naphthyridines^{1,2)} may be applied to the syntheses of other aromatic nitrogen compounds by utilizing the reactive methyl group and the carboxy group adjacent to it in the pyridine ring. Such reaction was utilized in the synthesis of 2,10-diazaanthracene.

2,10-Diazaanthracene (2,3-Benzo-1,6-naphthyridine)

As has already been reported,³⁾ reaction of 3-carboxyquinaldine and formaldehyde only gives a condensation product with three moles of formaldehyde, but reaction of sodium salt of 3-carboxyquinaldine led to the product formed with one mole of formaldehyde, as reported in the preceding paper.¹⁾ The lactone (III) was led to the amide (IV) and its oxidation gave 1-hydroxy-2,10-diazaanthracene (V). A chloro compound (VI), obtained by treatment of (V) with phosphoryl chloride, was heated with hydrazine hydrate, but no hydrazino compound precipitated. Catalytic reduction of the 1-chloro compound gave 9,10-dihydro-2,10-diazaanthracene (VII) and its ultraviolet spectrum was similar to that of 9,10-dihydroacridine, as shown in Fig. 1. As the dihydro compound is unstable,⁴⁾ its ultraviolet absorption changed to an intense absorption at 249 mμ, when exposed in the air. It was considered to be oxidized to 2,10-diazaanthracene (VIII), which was isolated by passing the reduction product through alumina column. The ultraviolet spectra are shown in Fig. 2.

1,7-Naphthyridine

Synthesis of 1,7-naphthyridine derivatives has been reported by Baumgarten.⁵⁾ Although Murray and Hauser⁶⁾ reported a synthesis of 4-chloro-1,7-naphthyridine (X) via 4-hydroxy compound, which was obtained from the condensation product of 3-aminopyridine 1-oxide and ethoxymethylenemalononic ester, 1,7-naphthyridine itself has not been produced. In order to compare with other naphthyridines, free 1,7-naphthyridine was synthesized. A facile dechlorination of chloronaphthyridine via hydrazino compound has been described previously.^{1,2)} 4-Chloro-1,7-naphthyridine, synthesized

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1) Part II : This Bulletin, **6**, 269(1958).

2) N. Ikekawa : *Ibid.*, **6**, 263(1958).

3) W. Koenigs, F. Stockhausen : *Ber.*, **34**, 4331(1901); W. Borsche, W. Doeller, M. Wagner-Roemich : *Ibid.*, **76**, 1099(1943).

4) This property is analogous to acridine and phenazine.

5) H.E. Baumgarten, A.L. Krieger : *J. Am. Chem. Soc.*, **77**, 2438(1955); H.E. Baumgarten, K.C. Cook : *J. Org. Chem.*, **22**, 138(1957).

6) J.G. Murray, C.R. Hauser : *J. Org. Chem.*, **19**, 2004(1954).

by the method of Hauser, was led to the 4-hydrazino compound, which was decomposed with copper sulfate to 1,7-naphthyridine (XII), m.p. 57~60°. Ultraviolet spectra of these compounds are shown in Fig. 3.

Unsubstituted 1,8- and 1,5-naphthyridines have been described in literature. Now that 1,6-, 2,7-, and 1,7-naphthyridines have been synthesized, five out of six possible isomers⁷⁾ are known. 2,6-Naphthyridines are not known. These isomers and their alkyl derivatives are summarized in Table I.

TABLE. I.

Compound	m.p. (°C)	Picrate m.p. (°C)	Reference
1,6-naphthyridine	25~27	219~220	2
7-methyl-1,6-naphthyridine	86~87	180~181	2
5-methyl-1,6-naphthyridine	74~75	200~201	2
5,7-dimethyl-1,6-naphthyridine	54	—	9
2,7-naphthyridine	92~94	240	1
3-methyl-2,7-naphthyridine	36~38	220~221	1
1,7-naphthyridine	57~60	205~206	
1,5-naphthyridine	55	206	10, 12
2-methyl-1,5-naphthyridine	62	161	10
2,4-dimethyl-1,5-naphthyridine	40	190	10
1,8-naphthyridine	98~99	207~208	13
4-methyl-1,8-naphthyridine	b.p. _{0.05} 147~148	204~205	11
2,4-dimethyl-1,8-naphthyridine	85~86	204~206	11

Fig. 1. Ultraviolet Spectra (in MeOH)

— 9,10-Dihydro-2,10-diazaanthracene (VII)
 ---- 9,10-Dihydroacridine⁹⁾
 - · - 1-Hydroxy-2,10-diazaanthracene (V)

Fig. 2. Ultraviolet Spectra (in MeOH)

— 2,10-Diazaanthracene (VII)
 ---- 1-Chloro-2,10-diazaanthracene (VI)
 - · - Acridine⁹⁾

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- 8) E.R. Blout, R.S. Corley : J. Am. Chem. Soc., **69**, 763(1947).
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- 12) B. Bobranski, E. Sucharda : Ber., **60**, 1081(1927).
- 13) G. Koller : Ibid., **60**, 1918(1927).

Fig. 3. Ultraviolet Spectra (in MeOH)

— 1,7-Naphthyridine (XII)
 ---- 4-Chloro-1,7-naphthyridine (X)
 - · - 4-Hydroxy-1,7-naphthyridine (IX)

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Experimental

2-Hydroxyethyl-3-quinolinecarboxylic Acid Lactone (III)—A mixture of 7 g. of 3-ethoxycarbonyl-quinaldine,¹⁴⁾ 1.8 g. of NaOH, and 25 cc. of water was heated on a water bath for 5 hrs. After evaporating the reaction mixture, the residue was dissolved in 20 cc. of water and the solution was heated with 4 cc. of 30% HCHO in a sealed tube for 15 hrs. at 90°. The resulting mixture was evaporated under a reduced pressure, 50 cc. of 15% HCl was added to the residue, and the mixture was allowed to stand for 1 hr. Recovery of 6 g. of 3-carboxyquinaldine hydrochloride was separated by filtration. The filtrate was made alkaline with Na₂CO₃ and extracted with CHCl₃. After drying, CHCl₃ was distilled off and crude product of (III), m.p. 140~150°, was obtained. Yield, 0.9 g. (14%). The analytical sample was recrystallized from CHCl₃, m.p. 148~150°. *Anal.* Calcd. for C₁₂H₉O₂N: C, 72.30; H, 4.52; N, 7.03. Found: C, 71.96; H, 4.62; N, 6.66.

2-Hydroxyethyl-3-quinolinecarboxamide (IV)—A solution of 1 g. of (III) in 50 cc. MeOH, cooling in ice water, was saturated with NH₃ and allowed to stand over night. After removing the solvent, the residue was recrystallized from CHCl₃-MeOH and white needles of m.p. 179~180° (IV) was obtained. Yield: 0.7 g. (65%). *Anal.* Calcd. for C₁₂H₁₂O₂N₂: C, 66.60; H, 5.56; N, 12.95. Found: C, 66.89; H, 5.63; N, 12.58.

1-Hydroxy-2,10-diazaanthracene (V)—A solution of 0.3 g. of CrO₃ in 30 cc. AcOH was added during a period of 1 hr. into a stirred solution of 0.7 g. of (IV) in 30 cc. AcOH at 40~50°. After 3 hrs., the reaction mixture was concentrated to 5 cc. and made alkaline with aq. NH₃. Yellow crystals (V), 0.4 g., precipitated. Recrystallization from MeOH or sublimation in vacuum gave 0.33 g. (52%) of yellow needles, m.p. 290~305°(decomp.). *Anal.* Calcd. for C₁₂H₈ON₂: C, 73.48; H, 4.08; N, 14.28. Found: C, 73.15; H, 4.13; N, 14.24. U.V. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 231(4.60), 244.5(4.64), 251(4.61), 261.4(4.32), 270.5(4.36), 293(4.12), 378(3.80).

1-Chloro-2,10-diazaanthracene (VI)—A mixture of 0.2 g. of (V) and 10 cc. of POCl₃ was heated in a sealed tube for 10 hrs. at 120°. After removal of POCl₃ in vacuum, ice-water was added to the residue, made alkaline with Na₂CO₃, and extracted with CHCl₃. After drying and removing the solvent, the residue was purified by passing through alumina column using CHCl₃, and 150 mg. (70%) of yellow needles, m.p. 150~152°, was obtained. *Anal.* Calcd. for C₁₂H₇N₂Cl: C, 67.01; H, 3.26; N, 13.05. Found: C, 67.03; H, 3.39; N, 12.81. U.V. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 251(4.89), 330(3.71), 346.5(3.84), 363(3.73), 377(3.74).

2,10-Diazaanthracene (VIII)—Hydrogenation of 50 mg. of (VI) in MeOH over 50 mg. of Pd-CaCO₃ (Pd 15%) catalyst resulted in absorption of 8.5 cc. (1.7 moles) of H₂ during 20 mins. After removal of the catalyst and solvent, the residue was made alkaline with Na₂CO₃ solution and extracted with CHCl₃. Drying of the extract and removal of the solvent left a viscous yellow liquid. U.V. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε), 307(4.18); $\lambda_{\max}^{0.1N \text{ H}_2\text{SO}_4}$ mμ (log ε), 341.5(4.29); $\lambda_{\max}^{0.1N \text{ NaOH}}$ mμ (log ε), 304(4.22).

After exposure to air over night, its ultraviolet spectrum changed and showed high-intensity absorption at 249 mμ. This material was chromatographed through alumina column and eluted with CHCl₃. The first eluted was a very small amount of 1-chloro compound (VI), and from second portion, 15 mg. of (VIII), m.p. 123~125°, was obtained. *Anal.* Calcd. for C₁₂H₈N₂: C, 80.00; H, 4.45; N, 15.55. Found: C, 79.67; H, 4.70; N, 15.20. U.V. $\lambda_{\max}^{\text{MeOH}}$ mμ (log ε): 249(4.86), 327.5(3.73), 343.5(3.77), 372.5(3.53).

1,7-Naphthyridine (XII)—A mixture of 170 mg. of 4-chloro-1,7-naphthyridine (X) in 1 cc. EtOH and 0.7 cc. of 80% hydrazine hydrate was heated on a steam bath for 10 mins. On cooling, white needles of 4-hydrazino compound (XI), m.p. 200~215°(decomp.), precipitated. A solution of the precipitate in a mixture of 3 cc. water and 1 cc. AcOH was added to 10 cc. of 10% CuSO₄ solution heated on a water bath. After heating for 10 mins., the solution was made alkaline with NaOH and extracted with

14) P. Friedländer, C.F. Gohring: Ber., **16**. 1833(1883).

CHCl_3 . After drying over Na_2SO_4 and removal of the solvent, the residue was purified by passing through alumina column using ether and 90 mg. (67%) of (XII), m.p. $57\sim 60^\circ$, was obtained. *Anal.* Calcd. for $\text{C}_8\text{H}_6\text{N}_2$: C, 73.84; H, 4.61; N, 21.53. Found: C, 73.50; H, 4.64; N, 21.20. U. V. $\lambda_{\text{max}}^{\text{MeOH}}$ $\text{m}\mu$ ($\log \epsilon$): 261 (3.70), 301 (3.46), 313 (3.42).

Picrate: m.p. $205\sim 206^\circ$. *Anal.* Calcd. for $\text{C}_8\text{H}_6\text{N}_2 \cdot \text{C}_6\text{H}_3\text{O}_7\text{N}_3$: C, 46.80; H, 2.51; N, 19.50. Found: C, 46.72; H, 2.60; N, 19.36.

Summary

The reaction of sodium salt of 3-carboxyquinaldine and formaldehyde gave 2-hydroxyethyl-3-quinolinecarboxylic acid lactone, which was led to the amide, and its oxidation gave 1-hydroxy-2,10-diazaanthracene. 2,10-Diazaanthracene was obtained from this 1-hydroxy compound. 1,7-Naphthyridine was synthesized from 4-chloro-1,7-naphthyridine via 4-hydrazino compound.

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77. Nobuo Ikekawa: Studies on Naphthyridines. IV.¹⁾

Infrared Spectra of Naphthyridines.

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Many data on infrared spectra of polymethylnaphthalenes,^{2~4)} polychloronaphthalenes,⁵⁾ and methylquinolines⁶⁾ have been published, but those of naphthyridines have not been reported yet. In the present work, infrared spectra of six 1,6-naphthyridines, four 2,7-naphthyridines, and two 1,7-naphthyridines were determined and the bands of out-of-plane deformation vibration of hydrogen atoms on the naphthyridine ring were compared with those of naphthalenes. Position and intensity of the bands of these compounds are summarized in Fig. 1.

There is little difference between the influence of chlorine atom and of methyl group on the absorption of out-of-plane C-H deformation vibrations, as in the case of naphthalenes.⁵⁾ In the out-of-plane C-H deformation frequencies of alkylpyridines,⁷⁾ the nitrogen in the ring may be considered as a substituent and the band positions are correlated with the number of adjacent hydrogen atoms remaining in the ring. In substituted naphthalenes and quinolines, the bands due to adjacent free hydrogen atoms on each ring can generally be correlated respectively with the strong absorption between 900 and 700 cm^{-1} . It was found, however, that the spectra of some derivatives of fused ring system showed abnormal absorption depending on the position of free hydrogen atoms on the ring.

The spectra of 1,6-naphthyridine and its derivatives (I to VI) show strong bands in the range of $790\sim 760\text{ cm}^{-1}$ corresponding to three adjacent hydrogen atoms on the A-ring. The compounds possessing two adjacent hydrogen atoms on the B-ring (I to III) exhibit the band near 835 cm^{-1} and the bands of isolated hydrogen on the B-ring of the

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7) H. Shindo, N. Ikekawa: *Ibid.*, **4**, 192 (1956).