[Chem. Pharm. Bull. 20(12)2678—2685(1972)]
UDC 547.821'551.04 : 542.958.1

Syntheses of Nitrogen-containing Heterocyclic Compounds. XIX.[1] Nitration of 2-Anilinopyridine

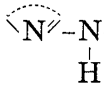
YOSHIO ITO, YOSHIKI HAMADA,[2a] and MINORU HIROTA[2b]

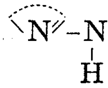
Faculty of Pharmacy, Meijo University,[2a] and Faculty of Engineering, Yokohama National University[2b]

(Received November 22, 1971)

Nitration of 2-anilinopyridine (II) with a mixed acid afforded 2-(2-nitroanilino)pyridine (III), 2-(4'-nitroanilino)pyridine (V), and 2-(2',4'-dinitroanilino)pyridine (VI), in a poor yield, but that with excess nitric acid gave VI alone in a high yield. Nitration of II with acetyl nitrate gave VI, 2-(2',4'-dinitroanilino)-5-nitropyridine (IX), and 2-(2',4'-dinitroanilino)-3,5-dinitropyridine (X).

II showed different reactivity in nitration with a strong acidic medium and a mild medium like nitric acid in acetic anhydride. In order to elucidate the reactivity of II in each case, it was assumed that II takes an anilinopyridinium ion form in a strongly acidic medium and a neutral anilinopyridine form in the mild acidic medium.

In the present series of work designed to examine the chemical nature of compounds having an anilino group bonded to the α-position of a nitrogen-containing hetero ring (compounds of  $\diagdown N /\!\!/ -\underset{H}{N}-Ar$ series), nitration of 2-anilino-4-methylquinoline (I) with three types of acidic medium, mixed acids, nitric acid, and acetyl nitrate, was found to give a specific product in a high yield selectively for each reagent.[3] The product obtained by the use of a mixed acid was 4-methyl-6-nitro-2-(4'-nitroanilino)quinoline, that from nitric acid was 4-methyl-2-(4'-nitroanilino)quinoline, and that from acetyl nitrate was 4-methyl-2-(2'-nitroanilino)quinoline or 2-(2',4'-dinitroanilino)-4-methylquinoline.

I was expected that the quinoline ring-nitrogen and anilino-nitrogen would be protonated in an acidic medium. According to the simple LCAO-MO calculation,[4] electron density of the anilino-nitrogen is likely to be greater than that of quinoline ring-nitrogen. Actually, however, it was found from the active site for a nitration agent (NO_2^+), that anilino-nitrogen is not protonated[5] and that the unshared electrons on the anilino-nitrogen are in conjugation with the π-electrons in the quinoline and benzene rings. In other words, electrophilic activity of the quinoline and benzene rings is increased by the mesomeric effect of the functional group,  $\diagdown N /\!\!/ -\underset{H}{N}-Ar$ in the molecule of I and the polar effect of the functional group.

In the present series of work, reactivity of 2-anilinopyridine (II) with the same nitration reagents was examined for the same purpose, and discussions will be made on this reaction together with observations made in previous works.

---

1) Part XVIII. Y. Hamada and I. Takeuchi, *Chem. Pharm. Bull.* (Tokyo), **19**, 1857 (1971). The title of this series has been changed to this from Quinoline Derivatives, XIV.

2) Location: *a*) *Tenpaku-cho, Showa-ku, Nagoya,* 468, *Japan*: *b*) *Ooka 2-31-1, Minami-ku, Yokohama, 233, Japan.*

3) *a*) Y. Hamada and Y. Ito, *Chem. Pharm. Bull.* (Tokyo), **17**, 2250 (1969). See Experimental part of this reference for the preparation of the reagent. See also F.G. Bordwell and E.W. Garbisch, *J. Am. Chem. Soc.*, **82**, 3588 (1960), for the nature of the nitrating agents. *b*) Y. Hamada, Y. Ito, and M. Hirota, *Chem. Pharm. Bull.* (Tokyo), **18**, 2094 (1970).

4) Y. Hamada, Y. Ito, T. Mizuno, and M. Hirota, *Chem. Pharm. Bull.* (Tokyo), **20**, 2686 (1972).

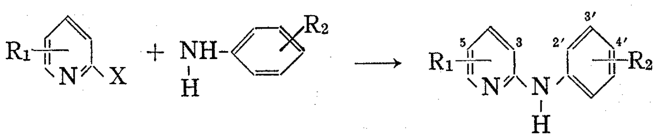
5) Y. Hamada, Y. Ito, H. Yanagawa, T. Mizuno, and M. Hirota, *Nippon Kagaku Zasshi*, **91**, 402 (1970).

Syntheses of Nitrated 2-Anilinopyridine Derivatives

There seems to be no published report on the syntheses of a series of these compounds. In order to identify the products obtained by nitration of II, as will be described later, synthesis of authentic samples was planned, and 2-bromopyridine or 2-chloro-5-nitropyridine was reacted with nitro-substituted aniline as the nucleophilic reagent, in the presence of a minute amount of pyridine, at 200° for 3—6 hr. II was obtained in a high yield by a slight modification of Fischer's method.[6]

Reaction of 2-chloropyridine and aniline in ethanol, in the presence of anhydrous sodium acetate, by refluxing for 8 hr according to the synthetic method for 2-anilino-3- or -5-nitropyridine[7] failed to afford II. This result is summarized in Table I.

Table I. Syntheses of Nitrated 2-Anilinopyridines



R_1	X	R_2	Product No.	Yield (%)	mp (°C)	IR $\nu_{\max}^{\text{KBr}}$ cm^{-1} (NH)
H	Cl	H	II[a]			
H	Br	H	II	85	102	
3-NO_2	Cl	H	[b]	65	74	3338 3230
5-NO_2	Cl	H	[b]	90	135	3240 3185 3128
H	Br	2′-NO_2	III[c]	trace	58	3300
H	Br	3′-NO_2	IV	60	99	2950 3160 (b)
H	Br	4′-NO_2	V	50	173	3330
H	Br	2′,4′-$(NO_2)_2$	VI	20	155	3100 3280
5-NO_2	Cl	2′-NO_2	non			
5-NO_2	Cl	3′-NO_2	VII	40	225	3310
5-NO_2	Cl	4′-NO_2	VIII	35	275	3330
5-NO_2	Cl	2′,4′-$(NO_2)_2$	non			

a) II did not react by refluxing in ethanol.
b) data of reference 7
c) III was reacted under pressure.

If 2-chloropyridine was considered as *p*-chloronitrobenzene and 2-chloro-5-nitropyridine as 1-chloro-2,4-dinitrobenzene, the carbon atom carrying the chlorine atom would be susceptible to the attack of a nucleophilic reagent. Inversely, in aniline, presence of a nitro group in *ortho* or *para* position of the benzene ring would decrease the electron density of the aminonitrogen. Since 2,4-dinitroaniline is nucleophilically inactive, it is clear that the synthesis of polynitro-substituted compounds of II would be difficult by the above synthetic method, which agreed with the experimental result.

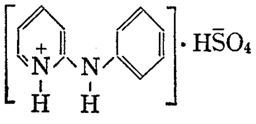
Of the products obtained by nitration of II to be described below, the compounds considered to correspond to those listed in Table I were identified by mixed fusion and comparison of infrared (IR) spectra.

Nitration of 2-Anilinopyridine (II) with Mixed Acid or Nitric Acid

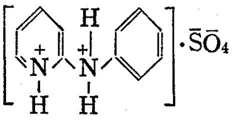
Nitration of II with mixed acid under various conditions generally gives products in a poor yield (Table II). This is considered to be due to the fact that the basic compound (II) is a proton acceptor and protonation is extremely facile by nitration in a strongly acidic medium so that II forms a salt of the form **1**, **2**, or **3**. The conjugated acid of II is likely to

---

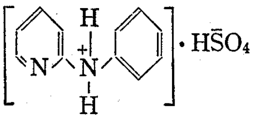
6) O. Fischer, *Chem. Ber.*, 32, 1302 (1899).
7) M. Bell, M. Day, and A. Peters, *J. Chem. Soc.*, C, 132 (1967).



1



2



3

be inactive to electrophilic substitution, and the experimental result clearly indicated the disadvantage of this kind of nitration.

When a large excess of nitric acid alone was used, nitration at room temperature (25°) gave three products (30% of III, 45% of V, and 15% of VI), as in the case of mixed acid, but nitration of II with a large excess of nitric acid alone at 60° for 1 hr resulted in a quantitative formation of VI alone.

According to the simple LCAO-MO calculation[4] of II, electron density of the anilino-nitrogen seems to be greater than that of pyridine-nitrogen. The fact that nitration of II with a strongly acid medium failed to give a product in which the nitro group was introduced into the *meta* position of the anilino moiety seems to suggest that II does not undergo protonation to a salt of **2** and **3** type. Consequently, it seems correct to consider that protonation occurrs only in the pyridine ring-nitrogen since the nitro group was not introduced into the pyridine ring. The prediction by the Hückel molecular orbital calculation of nitration reaction to be reported by us[4] supports this basis grounds of an argument.

TABLE II. Nitration of 2-Anilinopyridine (II) with 1.5 Moles HNO_3 (d. 1.38) in Various Concentration of H_2SO_4

II (g)	Conc. of H_2SO_4 (%)	Temp (°C)	Time (hr)	Yield of product (%)		
				III	V	VI
1	50	60	1	10	20	—
1	80	0	1	20	30	—
2	80	60	1	20	30	5
2	80	80	1	—	trace	—
2	95	0	3	trace	15	10

III: 2-(2′-nitroanilino)pyridine
V: 2-(4′-nitroanilino)pyridine
VI: 2-(2′,4′-dinitroanilino)pyridine

Nitration of 2-Anilinopyridine (II) and Related Nitro Compounds with Acetyl Nitrate in Organic Solvent

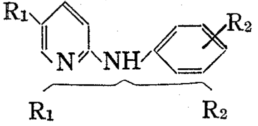
Experimental results obtained under various conditions are summarized in Tables III and IV. The assumed structure of the product (IX) as 2-(2′,4′-dinitroanilino)-5-nitropyridine seems to be correct. IX occurrs as orange-yellow prisms of mp 202—203°; mass spectrum,

TABLE III. Nitration of 2-Anilinopyridine (II) with Acetyl Nitrate Reagent in Organic Solvent

II (g)	Solvent (ml)	$AcONO_2$ (ml)	Temp. (°C)	Time (hr)	Yield of product (%)				
					III	V	VI	VIII	IX
0.5	—	2	25	20	20	trace	15	—	—
0.5	CH_2Cl_2 (5)	2	25	5	50	25	—	—	—
0.5	$CHCl_3$ (5)	2	25	5	45	40	—	—	—
0.5	CCl_4 (5)	2	25	5	43	40	—	—	—
0.5	CH_2Cl_2 (2)	4	25	20	—	—	60	10	30

VIII: 2-(4′-nitroanilino)-5-nitropyridine
IX: 2-(2′,4′-dinitroanilino)-5-nitropyridine

Table IV. Nitration of Nitro Derivatives of 2-Anilinopyridine with Acetyl Nitrate in Dichloromethane

Starting compound  R1	R2	Temp. (°C)	Time (hr)	Yield of product (%) VI	IX	X
H	2′-NO_2	25	10	30	—	—
H	2′,4′-$(NO_2)_2$	25	1[a]	50[b]	—	25
H	4′-NO_2	25	10	80	20	—
NO_2	H	25	3	—	35	50
NO_2	4′-NO_2	25	10	—	—	70

a) time until production of precipitate in the solvent
b) recovery of starting compound
X: 2-(2′,4′-dinitroanilino)-3,5-dinitropyridine

m/e 305 (M^+); and its IR spectrum shows absorptions for NH at 3100 and 3270 cm^{-1} (in KBr pellet). Its nuclear magnetic resonance (NMR) spectrum (in trifluoroacetic acid) is shown in Fig. 1.

The other product (X), $C_{11}H_6O_8N_6$, occurs as pale yellow plates, mp 171—172°; mass spectrum, *m/e* 350 (M^+). Its IR spectrum (in KBr pellet) shows absorptions for NH at 3100 and 3220 cm^{-1}.

NMR spectrum (in pyridine-d_5, Fig. 1) of X was very informative to determine the structure of benzene and pyridine moiety. In the higher field, the benzene protons showed two similar AB system corresponded to the benzene proton signals and coupling constant of IX. The two protons of pyridine ring showed a singlet signal in the lower field, which changed to the doublet-doublet signals centered at 9.40 δ and 9.50 δ by deuterium oxide. This is considered to be due to the fact that an anisotropic effect of pyridine has influence upon the chemical shift of the two protons of 3,5-dinitropyridine moiety so that pyridine and 2-substituted-3,5-di-

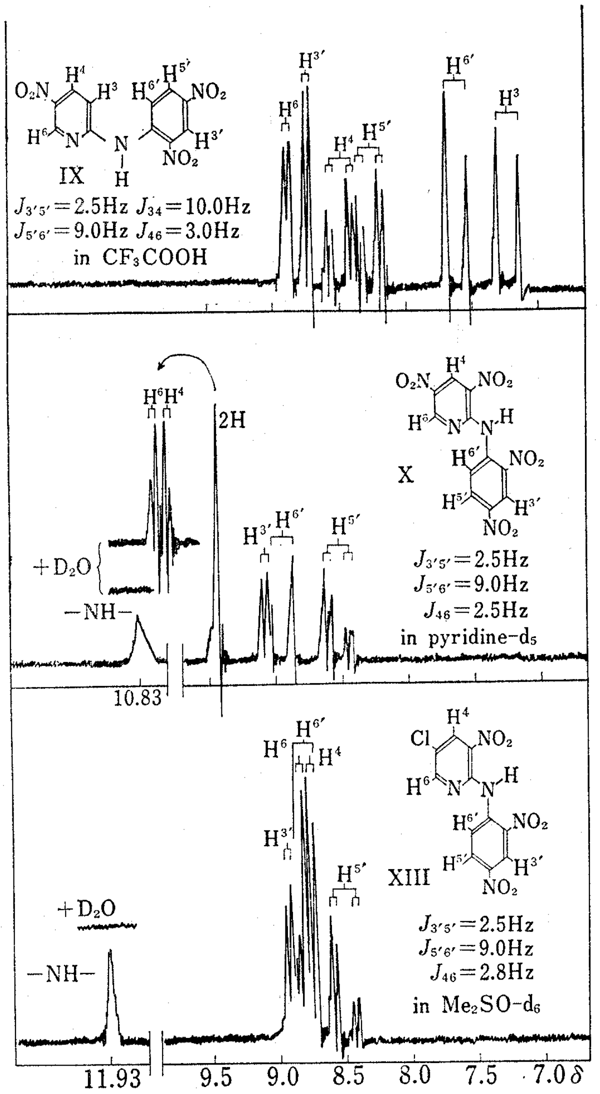


Fig. 1. NMR Spectra of IX, X and XIII Measured at 60 MHz with Tetramethylsilane as an Internal Standard

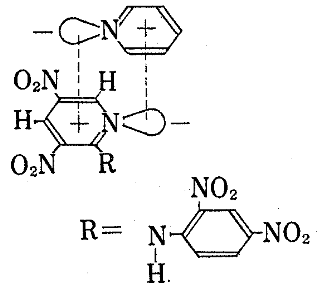
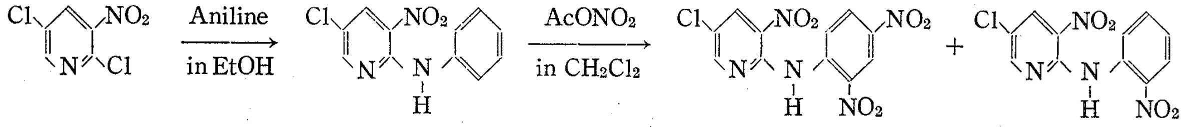


Fig. 2. Dipole Reciprocal Action of Pyridine and 2-Substituted-3,5-dinitropyridine

nitropyridine ring form the dipole–dipole bond by the solvation as shown in Fig. 2. This characteristic anisotropic effect of pyridine decrease to changed to the diluted solution by the addition of deuterium oxide. Comparison of the NMR spectrum of X and that (in Me_2SO-d_6, Fig. 1) of 5-chloro-2-(2′,4′-dinitroanilino)-3-nitropyridine (XIII), an authentic sample obtained by the method to be described below, indicated that this product (X) must be 2-(2′,4′-dinitroanilino)-3,5-dinitropyridine.

XIII was synthesized by the initial formation of 2-anilino-5-chloro-3-nitropyridine[8] (XII) by refluxing 2,5-dichloro-3-nitro-pyridine (XI) and aniline in ethanol, in the presence of sodium acetate, according to the method of Berrie, *et al.*,[9] and nitration of XII with acetyl nitrate, a reliable method of nitrating the 2′- and 4′-positions of the anilino moiety in II as outlined above. In this reaction, 5-chloro-3-nitro-2-(2′-nitroanilino)pyridine (XIV) is also produced. Identity of the structure of XII, XIV, and the following XV will be described in the Experimental part.

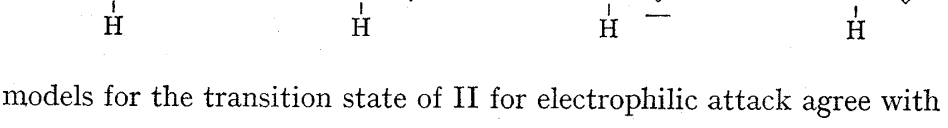


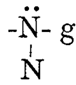
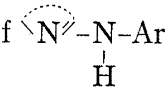
XI XII XIII XIV

Chart 1

Nitration of 2-anilino-5-nitropyridine with a large excess of nitric acid at 60° for 1 hr gives 5-nitro-2-(2′-nitroanilino)-pyridine (XV) in 15% yield and VIII in 50% yield. The fact that IX was not formed under this condition indicates that nitration by acetyl nitrate differs considerably from that with mixed acid or with nitric acid.

It is interesting to note that the nitro group was introduced into the 5-position of the pyridine ring by nitration of II with acetyl nitrate in methylene chloride. In an aprotic acid medium like acetic anhydride and methylene chloride, II seems to react as a neutral species with a nitrating reagent as NO_2ONO_2, as will be described below. A neutral reactive species of II would be represented as an anilino form and an imino form which the pyridine ring is predicted to have higher reactivity rather than the pyridine ring of an anilino form, according to the Hückel molecular orbital calculation. In the nitration of II with acetyl nitrate, presence of an imino form as the reactive species cannot be entirely neglected but it seems more appropriate to consider an anilino form as the reactive species.[4,10] The resonance structure of II may be expressed as follows:



Since the models for the transition state of II for electrophilic attack agree with the position of electrophilic substitution in the experimental results described above,  $\underset{\mathrm{N}}{\underset{|}{-\ddot{\mathrm{N}}-}}$ group in compounds of  $\diagdown\mathrm{N}\diagup-\underset{\mathrm{H}}{\underset{|}{\mathrm{N}}}-\mathrm{Ar}$ series are strong electron donating group in pyridine and benzene rings.

Nitration of II with acetyl nitrate[3a] in methylene chloride must be explained by a mechanism slightly different from that with mixed acid or nitric acid as described above. According-

---

[8] Y. Maki, *Gifu Yakka Daigaku Kiyo*, No. **15**, 31 (1965).
[9] A.H. Berrie, G.T. Newbold, and F.S. Spring, *J. Chem. Soc.*, **1952**, 2042.
[10] T. Mizuno, M. Hirota, Y. Hamada, and Y. Ito, *Tetrahedron*, **27**, 6011 (1971).

ing to the conclusion of Ingold and others[11] on the mode of nitration with benzoyl nitrate, a nitrating agent similar to acetyl nitrate, both the nitration with acetyl nitrate and that with nitric acid in acetic anhydride progress with the formation of dinitrogen pentoxide (NO_2ONO_2) and this molecule probably advances the nitration reaction.

We have also considered the attack of a nonionized dinitrogen pentoxide molecule on II for the progress of nitration. Question of the true nitrating species of acetyl nitrate is under investigation at present to obtain a more accurate data.

Experimental[12]

2-Anilinopyridine (II)——A mixture of 18.1 g of aniline, 8 g of ZnCl, 20 g of 2-bromopyrine, and 0.5 g of zinc dust was refluxed in an oil bash at 170—180° for 1 hour. When cooled, the crystalline mass was washed with hot water, made alkaline with 5% NaOH, and extracted with ether. The solvent was dried over anhydrous K_2CO_3 and evaporated. The crude crystals were recrystallized from cyclohexane to obtained 17 g (85%) of II as white scaly crystals, mp 100—102°, which was identified with an authentic sample.[6]

2-(2′-Nitroanilino)pyridine (III)——To a Carius tube (3 × 150 cm) was added 2.0 g of *o*-nitroaniline, 20 g of 2-bromopyridine, 1.0 g of anhydrous K_2CO_3, 0.2 g of copper powder, and 20 ml of EtOH. The tube was sealed and heated on an oil bath at 180° for 15 hr. The cooled tube was opened and the mixture was washed out with EtOH. After removal of the catalyst, the solvent was evaporated to dryness. The residue was dissolved in benzene and the solution was passed through an Al_2O_3 column, which was eluted with the same solvent. The reddish effluent afforded the mixed crystals of III and *o*-nitroaniline, and they was recrystallized from cyclohexane to obtain III as reddish scaly crystals, mp 57—58°. Yield trace. *Anal.* Calcd. for $C_{11}H_9O_2N_3$: C, 61.39; H, 4.22; N, 19.53. Found: C, 61.27; H, 4.09; N, 19.89. Mass Spectrum *m/e*: 215 (M^+), 169 ($M-NO_2$).

Syntheses of Nitrated 2-Anilinopyridine Derivatives (IV to VIII)——General Procedure: A mixture of 1.0 g of 2-bromopyridine or 2-chloro-5-nitropyridine, 1.0 g aniline (*m*-NO_2, *p*-NO_2, 2,4-$(NO_2)_2$), 0.5 g of copper powder, and 0.1—0.2 ml of pyridine was refluxed in an oil bath at 200° for 3—6 hr. After cooling, the pyridine in the mixture was evaporated with $H_2O+EtOH$ (2:1) *in vacuo*, when, treated with toluene in a similar manner. The residue was dissolved in benzene, and the benzene-soluble portion was passed through an Al_2O_3 column. The benzene-insoluble portion which was removed copper powder was recrystallized from EtOH.

2-(3′-Nitroanilino)pyridine (IV)——The initial effluent eluted with benzene gave IV as bright yellow needles, mp 98—99°. *Anal.* Calcd. for $C_{11}H_9O_2N_3$: C, 61.39; H, 4.22; N, 19.53. Found: C, 61.62; H, 3.93; N, 19.91. Mass Spectrum *m/e*: 215 (M^+), 169 ($M-NO_2$).

2-(4′-Nitroanilino)pyridine (V)——The yellow adsorbed portion on an Al_2O_3 was eluted with EtOH and gave V as yellow needles, mp 172—173°. *Anal.* Calcd. for $C_{11}H_9O_2N_3$: C, 61.39; H, 4.22; N, 1953. Found: C, 61.09; H, 4.51; N, 19.88. Mass Spectrum *m/e*: 215 (M^+), 169 ($M-NO_2$).

2-(2′,4′-Dinitroanilino)pyridine (VI)——The reddish effluent eluted with benzene gave VI as orange prisms, mp 154—155°. *Anal.* Calcd. for $C_{11}H_8O_4N_4$: C, 50.77; H, 3.10; N, 21.53. Found: C, 50.49; H, 2.82; N, 21.97. Mass Spectrum *m/e*: 260 (M^+), 214 ($M-NO_2$), 168 ($M-2(NO_2)$).

2-(3′-Nitroanilino)-5-nitropyridine (VII)——The benzene-insoluble portion was recrystallized from EtOH to obtain VII as reddish yellow prisms, mp 224—225°. *Anal.* Calcd. for $C_{11}H_8O_4N_4$: C, 50.77; H, 3.10; N, 21.53. Found: C, 50.93; H, 3.22; N, 21.81. Mass Spectrum *m/e*: 260 (M^+), 214 ($M-NO_2$), 168 ($M-2(NO_2)$).

2-(4′-Nitroanilino)-5-nitropyridine (VIII)——The benzene-insoluble portion was recrystallized from EtOH to obtain VIII as yellow cotton crystals, mp 274—275°. *Anal.* Calcd. for $C_{11}H_8O_4N_4$: C, 50.77; H, 3.10; N, 21.53. Found: C, 50.51; H, 3.30; N, 21.28. Mass Spectrum *m/e*: 260 (M^+), 214 ($M-NO_2$), 168 ($M-2(NO_2)$). NMR (Me_2SO_4-d_6) δ: 7.06 (H, doublet, $J=9.0$ Hz, C_3-H), 7.99 (2H, doublet, $J=9.0$ Hz, $C_{2'}$ and $C_{6'}$-H), 8.20 (2H, doublet, $J=9.0$ Hz, $C_{3'}$ and $C_{5'}$-H), 8.50 (H, quartet, $J=9.0$ Hz and $J=2.5$ Hz, C_4-H), 8.99 (H, doublet, $J=2.5$ Hz, C_6-H), 10.10 (H, broad signal, N-H).

Nitration of 2-Anilinopyridine (II)——1) With the Mixed Acid of Sulfuric and Nitric Acid: The concentration of sulfuric acid, the reaction temperature and the reaction time are given in Table II. To a solution of 0.5 g of II dissolved in 10 ml of H_2SO_4, 0.3 ml of HNO_3 (sp. gr. 1.38) was added dropwise at room

---

11) V. Gold, E.D. Hughes, and C.K. Ingold, *J. Chem. Soc.*, **1950**, 2467.

12) All melting points were determined using the Yanagimoto melting points test apparatus, and are uncorrected. IR spectra were taken on a Nippon bunko Model IR-S spectrophotometer. NMR spectra were obtained in the specified solvents on a Varian A-60 spectrometer with tetramethylsilane as an internal standard. Mass spectra were determined on a Hitachi RMU-6 spectrometer.

temperature or at 0° (when concentration of sulfuric acid is 80—95%), the mixture was stirred at 0° or 60° for several hours, and poured into ice-water (100—200 ml). The yellow precipitate thereby formed was collected, neutralized with 5% K_2CO_3, washed with H_2O, and dried. The residual acidic solution was neutralized with 10% NaOH and the reddish yellow precipitate formed was collected. These precipitates were dissolved in benzene and the solution was passed through an Al_2O_3 column, which was eluted with the same solvent. The initial reddish yellow effluent afforded III and the next orange effluent gave VI. The yellow absorbed portion was eluted with EtOH and afforded V. Yield of products from these reaction is shown in Table II.

2a) With Nitric Acid at 20—25°: A solution of 1.0 g of II dissolved in 5 ml of HNO_3 (sp. gr. 1.38) at room temperature, was maintained for 24 hr, when, the reddish brown reaction mixture was poured into ice-water (200 ml). The reddish yellow precipitate thereby formed was treated as in 1), affording 0.3 g (30%) of III, 0.5 g (45%) of VI, and 0.15 g (15%) of V.

2b) With Nitric Acid at 60°: A solution of 0.5 g of II dissolved in 10 ml of HNO_3 (sp. gr. 1.38) with stirring under ice chilling was maintained for 10 min., heated to 60°, and stirred 1 hour at that temperature. The light yellow reaction mixture was poured into 200 ml of ice-water, the yellow precipitate thereby formed was collected by filtration, neutralized with 5% Na_2CO_3, washed with water, and dried. The crude orange crystals were recrystallized from benzene to obtain 0.5 g (90%) of VI.

3a) With Acetyl Nitrate ($AcONO_2$) in CH_2Cl_2, $CHCl_3$, and CCl_4: To a solution of II in organic solvent under ice chilling, $AcONO_2$ was added dropwise and the mixture was maintained under reaction conditions listed in Table III. The reddish brown mixture was treated in order to evaporate the solvent and acetic anhydrate under a reduced pressure at room temperature, poured into ice-water, and treated as in 1). Yield of III, V, and VI from these reaction is shown in Table III.

3b) With $AcONO_2$ in CH_2Cl_2: To a solution of 0.5 g of II in 2 ml of CH_2Cl_2 under ice chilling, 4 ml of $AcONO_2$ was added dropwise. The yellow crystals (IX) formed in the reaction mixture which was maintained under reaction conditions listed Table III, were collected by filtration, washed with a small amount of CH_2Cl_2, and dried. The residual solution was treated as in 3a) and 1).

The initial yellowish green effluent and brown adsorbed band gave VI, and the reddish brown adsorbed band gave IX. The yellowish brown adsorbed portion was eluted with EtOH and afforded VIII. Yield of products from this reaction is shown in Table III.

The structures of III, V, VI, and VIII from nitrations of II, were identified by mixed melting test with authentic samples through the independent synthesis, and comparison of their infrared spectra. The assumed structure of the other product (IX) seems to be 2-(2′,4′-dinitroanilino)-5-nitropyridine. *Anal.* Calcd. for $C_{11}H_7O_6N_5$: C, 43.28; H, 2.31; N, 22.91. Found: C, 43.50; H, 2.12; N, 22.41. Mass Spectrum (direct inlet system) *m/e*: 305 (M^+), 259 ($M-NO_2$), 213 ($M-2(NO_2)$), 167 ($M-3(NO_2)$).

Nitration of Nitro Derivatives of 2-Anilinopyridine (III and V) with $AcONO_2$ in CH_2Cl_2——To a solution of 0.3 g of starting compounds in 2 ml of CH_2Cl_2 under ice chilling, 4 ml of $AcONO_2$ was added dropwise. The mixture was maintained under reaction conditions (see Table IV), and treated as in 3b), affording VI and IX.

Nitration of Nitro Derivatives of 2-Anilinopyridine (VI, VIII, and 5-NO_2 of Pyridine Moiety Derivative) with $AcONO_2$ in CH_2Cl_2——In a similar manner as above, the mixture which was maintained under reaction conditions listed in Table IV, was treated in order to evaporate the solvent and acetic anhydrate under a reduced pressure at room temperature, and poured into water. The crude yellowish brown crystals formed were collected, neutralized with 5% K_2CO_3, washed with water, dried, and recrystallized from benzene. IX was obtained by concentration of the solution, and the insoluble portion was recrystallized from EtOH. X was obtained from the solution. Yield of products from the nitration of derivatives of II is shown in Table IV.

Compound VI was identified by mixed melting test with authentic sample through the independent synthesis, and comparison of its infrared spectra. Compound IX was identified with the sample through the synthesis of 3b) as above. The assumed structure of the other compound (X) seems to be 2-(2′,4′-dinitroanilino)-3,5-dinitropyridine. *Anal.* Calcd. for $C_{11}H_6O_8N_6$: C, 37.73; H, 1.73; N, 24.00. Found: C, 36.76; H, 1.38; N, 23.21. Mass Spectrum (direct inlet system) *m/e*: 350 (M^+), 304 ($M-NO_2$), 258 ($M-2(NO_2)$), 212 ($M-3(NO_2)$), 166 ($M-4(NO_2)$).

Nitration of 2-Anilino-5-nitropyridine with Nitric Acid at 60°——In a similar manner as above and as discribed in 2b), the mixture was treated. After drying, the crystalline product was recrystallized from benzene. XV was obtained from the solution and VIII from the benzene-insoluble portion. Yield of 0.3 g (50%) of VIII and 0.1 g (15%) of XV.

Compound VIII was identified with authentic sample. The assumed structure of compound XV seems to be 2-(2′-nitroanilino)-5-nitropyridine. *Anal.* Calcd. for $C_{11}H_8O_4N_4$: C, 50.77; H, 3.10; N, 21.53. Found: C, 50.55; H, 3.35; N, 21.25. Mass Spectrum *m/e*: 260 (M^+), 214 ($M-NO_2$), 168 ($M-2(NO_2)$). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3100 and 3270 (N-H). NMR (Me_2SO-d_6) δ: 7.05 (H, doublet, $J=9.0$ Hz, C_3-H), 8.37 (H, quartet, $J=9.0$ Hz and $J=2.5$ Hz, C_4-H), 8.91 (H, doublet, $J=2.5$ Hz, C_6-H), and 7.40—8.90 (4H, multiplet, benzene ring protons), 10.38 (H, broad signal, NH).

2-Anilino-3-nitro-5-chloropyridine (XII)——0.5 g of 2,5-dichloro-3-nitropyridine and 0.5 g of aniline were heated under reflux in 10 ml of EtOH in the presence of 0.5 g of anhydrous sodium acetate for 5 hr. After cooling, the crude reddish crystals form were collected by filtration, washed with water, dried, and recrystallized from EtOH to obtained 0.5 g (90%) of XII as reddish needles, mp 85.0—85.5°, which was identified with an authentic sample.[8]

Nitration of 2-Anilino-3-nitro-5-chloropyridine (XII) with $AcONO_2$ in CH_2Cl_2——To a solution of 0.3 g of XII in 2 ml of CH_2Cl_2 under ice chilling, 4 ml of $AcONO_2$ was added dropwise. The mixture which was maintained at room temperature (20°) for 7 hr, was treated in order to evaporate the solvent and acetic anhydrate under a reduced pressure at room temperature, and poured into ice-water. The yellow precipitate formed was collected, neutralized with 5% K_2CO_3, washed with water, and dried. The crude reddish yellow crystals were dissolved in benzene and solution was passed through an Al_2O_3 column, which was eluted with the same solvent. The initial yellow effluent afforded 0.1 g (25%) of XIII as yellow prisms, mp 188—190°, and the next orange effluent 0.3 g (85%) of XIV as orange scaly crystals, mp 135—136°.

The assumed structures of XII and XIV seem to be 2-(2′,4′-dinitroanilino)-3-nitro-5-chloropyridine and 2-(2′-nitroanilino)-3-nitro-5-chloropyridine.

XIII: *Anal.* Calcd. for $C_{11}H_6O_6N_5Cl$: C, 38.89; H, 1.78; N, 20.62·Found: C, 38.57; H, 1.82; N, 20.46. Mass Spectrum *m/e*: 339 (M^+), 293 ($M-NO_2$), 247 ($M-2(NO_2)$), 201 ($M-3(NO_2)$).

XIV: *Anal.* Calcd. for $C_{11}H_7O_4N_4Cl$: C, 44.84; H, 2.39; N, 19.01. Found: C, 45.10; H, 2.01; N, 18.62. Mass Spectrum *m/e*: 294 (M^+), 248 ($M-NO_2$), 202 ($M-2(NO_2)$). IR ν_{max}^{KBr} cm^{-1}: 3100 and 3220 (N-H). NMR (Me_2SO-d_6) δ: 7.30—8.30 (4H, multiplet, benzene ring protons), 8.63 (H, doublet, $J=2.8$ Hz, C_4-H), 8.69 (H, doublet, $J=2.8$ Hz, C_6-H), 11.42 (H, broad signal, NH).

Acknowledgement The authors are indebted to the members of the Analysis Center of this University for elemental analyses and spectral determinations.