CCCLXXXVIII.—*Nitration of 2-, 3-, and 4-Phenylpyridines.*

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FORSYTH, NIMKAR, and PYMAN (this vol., p. 800) suggested as an explanation of the facts that nitration leads mainly to meta-substitution in 2-phenyl-4 : 5-dihydroglyoxaline (I), but mainly to para-substitution in 2-phenylglyoxaline (II), that the effect of the

(I.) $\begin{matrix} CH_2\cdot NH \\ | \\ CH_2—N \end{matrix}\!\!>\!\!C\cdot Ph$ $\qquad$ $\begin{matrix} CH\cdot NH \\ \| \\ CH—N \end{matrix}\!\!>\!\!C\cdot Ph$ (II.)

nitrogen atoms in the latter compound was suppressed, the glyoxalinium ion behaving as an aromatic complex as a whole and having a para-directive effect like the phenyl group in diphenyl. In order to test this hypothesis, the nitration of 2-, 3-, and 4-phenylpyridines was proposed with the view of determining whether the pyridinium residue had mainly an *op*-directive effect in all cases, or, if not, how far the position of the nitrogen atom relative to the phenyl group affected the result. This has now been done by the method used in the previous cases (addition of the nitrate of the base to sulphuric acid), and the yields of pure or nearly pure isomerides isolated were as follows :

	Nitro-derivatives.		
	o.	*m*.	*p*.
2-Phenylpyridine	5·1	34·9	42·3%
3- ,, ...	—*	—*	64·3
4- ,, ...	12·7	28·5	38·0

* Not determined.

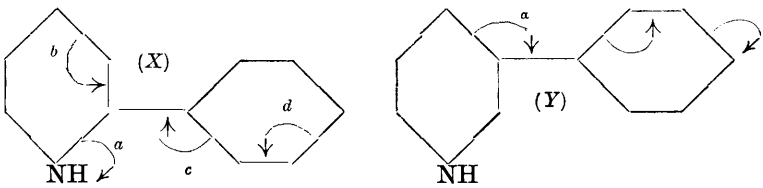
After allowance is made for losses in manipulation, it is clear that *op*-substitution predominates in all cases, although a considerable amount of *m*-substitution occurs in the nitration of 2- and 4-phenylpyridines. Evidence of an alternating effect is seen in the relative yields of the *p*-nitro-compounds. At the Society's meeting on June 17th, one of us invited forecasts of these results, and has received them from three chemists.

Dr. Flürscheim writes : "I predict the following : (1) the percentage of *op*-compound *formed* (calculated on the total $o + p +$

m formed) will be in the order 3>4>2; (2) in 3-phenylpyridine *op*-substitution will be practically exclusive. For the 3-compound, I am able to make this absolute prediction, because here substitution depends practically only on the affinity demand of the 3-carbon atom in the pyridine ring, which is greater than that of hydrogen, both in the free base and in the salt. For the 2- and 4-compounds, I am only able to make the above relative prediction, because here substitution depends both on the degree of hydrolysis and of electrolytic dissociation of the salt, both of which I can foresee relatively, whereas their absolute magnitude is unknown."

Professor Ingold writes: "I would expect the proportion of *meta*- in the mono-nitration product of 2-, 3-, and 4-phenylpyridine to stand in the order 2>4>3. Even in 2-phenylpyridine I would not expect a very large *m*-content, say 50% as a maximum. In the case of the 3-derivative, I should think the *m*-content would be almost zero, or, at any rate, quite small, and I would expect the *para*- to be the main product."

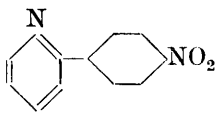
Professor Robinson writes: "The substituting agent is kationoid and consequently the distributed positive charge on the phenylpyridinium ions should reduce the reactivity even of the phenyl group. Substitution in the benzene nucleus, which will obviously be preferentially attacked, should be influenced by (1) the general polar effect of the phenylpyridinium ions, (2) the crotonoid systems in the 2- and 4-phenylpyridines, and (3) butadienoid conjugation of the two nuclei. All these effects are weak; for example, the crotonoid system in 2-phenylpyridine is weak because, as illustrated in the annexed expression (*X*), the original electron displacement (*a*) is doubtless more readily accommodated (*b*) within the nucleus than by the changes (*c*) and (*d*). On the other hand, the butadienoid



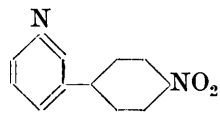
conjugation (*Y*) should be weak because electrons are unlikely to start the process (α) in view of the charge on the pyridine nucleus and the high degree of stability of the aromatic sextet in pyridine. If we consider *m*- as against combined *o*-*p*, then, on account of (1) above, the percentage of *m*-nitrophenylpyridines obtained should be in the order 2->3->4-phenylpyridine. On account of (2), the percentage of *m*-substituted derivatives should be in the order 2->4->3-phenylpyridine, and, finally, the factor (3) gives 2->4->3-

phenylpyridine. Certainly, therefore, the percentage of *m*-nitrophenylpyridine obtained should be highest in the case of the 2-phenylpyridine and probably after this would come 4-phenylpyridine. It is also probable that the gap separating 2- and 4- will be greater than that between 3- and 4-. It is not possible to deduce from the electronic theories what the relation between *m*- and *o*-*p* should be in the individual cases, because pyridyl (β) stands at the end of a series of aromatic groups and the extrapolation involved is scarcely justifiable. Analogies suggest, however, that *o*-*p*-substitution should predominate in 3-phenylpyridine."

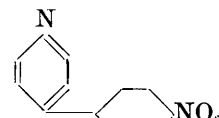
Considerable difficulty was encountered in preparing quantities of the starting materials. 2-Phenylpyridine was first prepared by Skraup and Cobenzl (*Monatsh.*, 1883, **4**, 472) by the decarboxylation of its dicarboxylic acid, which, they state, they obtained by the oxidation of α-naphthaquinoline in the same way as they had prepared its isomeride by the oxidation of β-naphthaquinoline. In our hands, α-naphthaquinoline proved to be very resistant to warm permanganate, and in several experiments a large proportion of this substance was recovered unchanged, but none of the dicarboxylic acid was obtained. Attempts were then made—on the lines of Decker and Pschorr's syntheses (*Ber.*, 1904, **37**, 3397) of 1-alkyl*iso*quinolines—to prepare 2-phenylpyridine methobromide by the action of magnesium phenyl bromide upon *N*-methyl-α-pyridone, but these were unsuccessful. Finally, we had recourse to the method of Kühling (*Ber.*, 1895, **28**, 523; 1896, **29**, 165), who obtained 2-*p*-nitrophenylpyridine in "good yield" by the action of acetic acid and acetyl chloride upon sodium *p*-nitrobenzene*iso*diazotate in pyridine, reduced this to the amine, and eliminated the amino-group by means of nitrous acid and alcohol, when 2-phenylpyridine was obtained. On repeating this work, we found that the crude product from nitrosoamine-salt and pyridine contained a mixture of the three p-*nitrophenylpyridines*, the 2-*isomeride* (III), m. p. 130·5—131·5°, the 3-*isomeride* (IV), m. p. 148—149°, and the



(III.)



(IV.)



(V.)

4-*isomeride* (V), m. p. 123—124°, being isolated in yields of 15, 5, and 2%,* respectively, after a long process of crystallisation as

* For comparison, it may be noted that solid benzenediazonium chloride reacts with excess of pyridine to give 2-phenylpyridine in 18% yield, and a difficultly separable mixture of this with 4-phenylpyridine in 3% yield (Möhlau and Berger, *Ber.*, 1893, **26**, 1994).

base, hydrochloride, and nitrate. The preparation of quantities of the 2-, 3-, and 4-phenylpyridines (VIII), and at the same time the determination of the constitutions of the three nitro-compounds, was effected by reducing each to the amine [2-, 3-, and 4-p-*aminophenylpyridines* (VI)], diazotisation of the amine, and reduction of the diazonium salt to the hydrazine [2-, 3-, and 4-p-*hydrazinophenylpyridines* (VII)], followed by oxidation of the hydrazine with cupric acetate.

$$\underset{\text{(VI.)}}{C_5H_4N\cdot C_6H_4\cdot NH_2} \longrightarrow \underset{\text{(VII.)}}{C_5H_4N\cdot C_6H_4\cdot NH\cdot NH_2} \longrightarrow \underset{\text{(VIII.)}}{C_5H_4N\cdot C_6H_5}$$

The 2- and 3-phenylpyridines were identified by reference to the properties of their salts, and 4-phenylpyridine by direct comparison with a specimen prepared by Hantzsch's method (*Ber.*, 1884, **17**, 1512).

Reference to the melting points given above shows that Kühling's 2-*p*-nitrophenylpyridine, which sintered from 109° and melted, not sharply, at 117°, was a mixture. It doubtless consisted mainly of the 2-isomeride with some of the 3-isomeride, which would not be removed from the first by the methods which he employed. His aminophenylpyridine base has a higher m. p. than pure 2-*p*-aminophenylpyridine, but agrees in m. p. with 3-*p*-aminophenylpyridine containing solvent of crystallisation. The method which he employed for eliminating the amino-group is unsatisfactory in this case, for on boiling 2-*p*-aminophenylpyridine dihydrochloride with alcohol and amyl nitrite, only a poor yield of 2-phenylpyridine is obtained owing to the formation of a considerable quantity of 2-p-*ethoxyphenylpyridine*, $C_5H_4N\cdot C_6H_4\cdot OEt$.

The orientation of the products of nitration of the three phenylpyridines was determined as follows: the three *p*-nitro-compounds were recognised through their identity with products of interaction of sodium *p*-nitrobenzene*iso*diazotate and pyridine, the 2- and 4-m-*nitrophenylpyridines* through the formation of *m*-nitrobenzoic acid on oxidation of their methosulphates by permanganate, and the 2- and 4-o-*nitrophenylpyridines* by difference.

EXPERIMENTAL.

The p-*Nitrophenylpyridines.*—The sodium *p*-nitrobenzene*iso*diazotate from 13·8 g. of *p*-nitroaniline was washed with brine, dried at 100°, finely powdered, and covered with pure pyridine (80 c.c.) in a 1-litre beaker. To the nearly complete, dark brown solution thus obtained, glacial acetic acid (60 c.c.), quickly followed by acetyl chloride (10 c.c.), was added, a vigorous reaction taking place. After a few minutes, the product was diluted with water (1 l.), and the insoluble matter collected. This was extracted with hot

5*N*-hydrochloric acid (500 c.c.), and the extract basified with ammonia; 9·5 g. of crude bases, crystalline but sticky, were then precipitated.

The crude bases (200 g.) prepared in this way from 289·8 g. of *p*-nitroaniline were dissolved in hot 5*N*-hydrochloric acid (1·2 l.) and the solution was digested with charcoal, filtered, and kept; the hydrochlorides of the 2- and 4-isomerides that crystallised were collected, and further crops were obtained by concentration of the mother-liquors (Mother-liquor M). The bases regenerated from the crystalline hydrochlorides were crystallised fractionally from alcohol; the 2-isomeride was then obtained in a nearly pure state. Its purification was completed by further crystallisation as hydrochloride from 5*N*-hydrochloric acid, followed by crystallisation of the base from alcohol. The fraction of the bases most soluble in alcohol gave, on crystallisation from 5*N*-hydrochloric acid, the hydrochloride of the 4-isomeride. After recrystallisation as hydrochloride, and then as base from acetone, the 4-isomeride was obtained in a pure state as regards its m. p., but both the base and the hydrochloride prepared in this way had a deep yellow colour, which was absent from 4-*p*-nitrophenylpyridine, and its hydrochloride, prepared by the nitration of 4-phenylpyridine. The mother-liquor M gave, when basified, a sticky product which was extracted with cold ether, and thus separated into a readily soluble fraction (from which further small quantities of the three isomerides were isolated) and a sparingly soluble crystalline powder, which gave the pure 3-isomeride after crystallisation as base from alcohol, as nitrate from *N*-nitric acid, and again as base from alcohol. After a long process of fractionation on these lines, the 2-, 3-, and 4-*p*-nitrophenylpyridines were isolated in a pure state in quantities of 64·7, 22·2, and 10·3 g., respectively, the yields being 15·4, 5·3, and 2·4%, respectively, of the theoretical yields, calculated on the *p*-nitroaniline used.

2-*Phenylpyridine and its Derivatives.*

2-p-*Nitrophenylpyridine* crystallises from alcohol in nearly colourless needles, m. p. 130·5—131·5° (corr.). It is insoluble in water, sparingly soluble in alcohol, acetone, or ether, but readily soluble in chloroform (Found : C, 66·1; H, 4·2; N, 14·1. $C_{11}H_8O_2N_2$ requires C, 66·0; H, 4·0; N, 14·0%). The *hydrochloride* crystallises from 5*N*-hydrochloric acid in nearly colourless, prismatic needles containing $2H_2O$, which is lost in a vacuum over sulphuric acid. The dried salt has m. p. 185—186° (corr.) (Found : loss, 12·7. $C_{11}H_8O_2N_2,HCl,2H_2O$ requires $2H_2O$, 13·2%. Found, in dried salt : Cl, 15·0. $C_{11}H_8O_2N_2,HCl$ requires Cl, 15·0%). It slowly loses hydrogen chloride at 100° and dissociates on treatment with

water, giving a copious deposit of the base. The latter behaviour is not shown by the nitrate of the 3-isomeride or the hydrochloride of the 4-isomeride, but aqueous solutions of the nitrate of the 3-isomeride give a faint crystalline precipitate.

2-p-*Aminophenylpyridine.*—2-*p*-Nitrophenylpyridine (20 g.) was reduced by tin foil (40 g.) and concentrated hydrochloric acid (120 c.c.). The solution was diluted with water, and concentrated after removal of tin by hydrogen sulphide, 2-*p*-aminophenylpyridine dihydrochloride (20·4 g.; yield, 84%) separating.

2-p-*Aminophenylpyridine* crystallises from ether in nearly colourless, elongated prisms or from alcohol in quadrilateral prisms, m. p. 97—98° (corr.). It is insoluble in water, sparingly soluble in ether, and easily soluble in alcohol (Found: C, 77·5; H, 5·7. $C_{11}H_{10}N_2$ requires C, 77·7; H, 5·9%). The *dihydrochloride* crystallises from dilute hydrochloric acid in colourless, felted needles, which are readily soluble in water, giving a yellow solution, but very sparingly soluble in alcohol. It is anhydrous and does not melt at 310° (Found: C, 54·3; H, 4·9. $C_{11}H_{10}N_2,2HCl$ requires C, 54·3; H, 4·9%). The *picrate* crystallises from alcohol in elongated plates, m. p. 218—219° (decomp.; corr.).

2-p-*Hydrazinophenylpyridine.*—2-*p*-Aminophenylpyridine dihydrochloride (20 g.) in water (180 c.c.) and concentrated hydrochloric acid (80 c.c.) was diazotised at 15° by sodium nitrite (5·9 g.) in aqueous solution. To this, a cold solution of hydrated stannous chloride (75 g.) in concentrated hydrochloric acid (150 c.c.) was added, and after keeping for 1 hour, the tin was removed by hydrogen sulphide. The solution was concentrated and basified with ammonia; the bulk of the hydrazine (11·7 g.; m. p. 112—113°) then separated as an oil which quickly became crystalline. The filtrate was extracted with ether, and the extract, after being concentrated, deposited a further 0·2 g. of the hydrazine, of which the total yield is thus 78% of the theoretical.

2-p-*Hydrazinophenylpyridine* crystallises from alcohol in clear, nearly colourless, well-formed plates, m. p. 117° (corr.) after softening a few degrees lower. It is insoluble in water, soluble in alcohol, and sparingly soluble in ether (Found: C, 71·5; H, 6·0. $C_{11}H_{11}N_3$ requires C, 71·4; H, 6·0%).

2-*Phenylpyridine.*—To 2-*p*-hydrazinophenylpyridine (11·7 g.; m. p. 112—113°) dissolved in 5*N*-acetic acid (80 c.c.), powdered cupric acetate (27 g.) was added and the product was basified and distilled with steam. Ether extracted from the distillate 2-phenylpyridine (7·3 g.), which was converted into the nitrate and crystallised from absolute alcohol, 10·1 g. of the pure salt being obtained (yield, 73%).

2-*Phenylpyridine nitrate* crystallises from absolute alcohol in large, colourless, elongated prisms, m. p. 115—117° (corr.). It is anhydrous and easily soluble in water, but sparingly soluble in cold absolute alcohol (Found : C, 60·4; H, 4·7. $C_{11}H_9N,HNO_3$ requires C, 60·5; H, 4·6%). 2-Phenylpyridine was identified through its properties and those of its picrate and chloroplatinate. The base was an oil, volatile with steam. The picrate crystallised from alcohol in yellow prisms, m. p. 176—177° (corr.) (Found : C, 52·9; H, 3·1. Calc. : C, 53·1; H, 3·1%). Skraup and Cobenzl (*loc. cit.*) give m. p. 169—172°; Leben (*Ber.*, 1896, **29**, 1673) gives m. p. 175°. The chloroplatinate crystallised from dilute hydrochloric acid in elongated plates, containing $2H_2O$, m. p. (after drying) 209° (decomp.; corr.) (Found, in air-dried salt : loss at 100°, 5·4. Calc. : 4·8%. Found, in dried salt : Pt, 27·2. Calc. : Pt, 27·1%). Skraup and Cobenzl and also Leben state that this salt crystallises with $2H_2O$, and the latter gives m. p. 204°.

2-p-*Ethoxyphenylpyridine.*—Finely-powdered 2-*p*-aminophenylpyridine dihydrochloride (7·5 g.), absolute alcohol (75 c.c.), and amyl nitrite (10 c.c.) were boiled gently on the water-bath during 3 hours, in the course of which another 8 c.c. of amyl nitrite were added. Hydrochloric acid was added, the alcohol distilled off, and amyl alcohol removed in a current of steam. The liquor was then basified and distilled with steam fractionally; mixtures of 2-phenylpyridine with 2-*p*-ethoxyphenylpyridine passed over, the former (liquid) predominating in the earlier runnings and the latter (solid) in the later. Further quantities of 2-*p*-ethoxyphenylpyridine were obtained by extracting the distillation residue with ether, and eventually 1·1 g. (yield 18%) were obtained pure. The 2-phenylpyridine was converted into picrate, and after many crystallisations from alcohol 2·95 g. (yield 25%) of this salt were obtained pure.

2-p-*Ethoxyphenylpyridine* crystallises from ether in large, colourless prisms, m. p. 74—75° (corr.), which are insoluble in water but readily soluble in alcohol or ether (Found : C, 78·2; H, 6·5. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·5%). The *picrate* crystallises from alcohol in yellow, woolly needles, m. p. 168—170° (corr.) (Found : C, 53·3; H, 3·5; N, 13·1. $C_{13}H_{13}ON,C_6H_3O_7N_3$ requires C, 53·3; H, 3·7; N, 13·1%).

Nitration of 2-Phenylpyridine.—2-Phenylpyridine nitrate (12 g.) was added gradually to concentrated sulphuric acid (24 c.c.) cooled with water. After keeping for 5 minutes, the product was heated for ½ hour at 100°, then diluted with water (120 c.c.) and precipitated fractionally with 5*N*-ammonia. First, pure 2-*p*-nitrophenylpyridine separated from the liquor while still hot in three crops

amounting to 3·95 g., m. p. 130—131°. After cooling and addition of more ammonia, another three crops amounting to 4·07 g., m. p. about 62—64°, separated; the final crop, collected by ether, was 2·75 g., m. p. about 35°. When the 4·07 g. were crystallised from 40 c.c. of 5*N*-nitric acid, the nitrate of the *m*-isomeride separated, and the bases regenerated from the mother-liquors readily gave more of the *p*-isomeride on crystallisation from alcohol. The 2·75 g. also gave a quantity of the nitrate of the *m*-isomeride on crystallisation from 27 c.c. of 5*N*-nitric acid, but the bases regenerated from these mother-liquors contained little of the *p*-isomeride. After the *p*- and *m*-isomerides had been removed as completely as possible by these means, the residual bases were precipitated fractionally from dilute hydrochloric acid by ammonia; mixtures of the *p*- and *m*-isomerides were precipitated first, followed by the crude *o*-base. The *p*-isomeride was finally purified by crystallisation from alcohol; the *m*-isomeride by recrystallisation of its nitrate from 5*N*-nitric acid, followed by crystallisation of the base from alcohol; and the *o*-isomeride by recrystallisation from ether. The yields were as follows: *p*-, 4·61 g. pure + 0·05 g., m. p. 125—128° (42·3%); *m*-, 3·82 g. pure + 0·02 g., m. p. 68—70° (34·9%); *o*-, 0·52 g. pure + 0·04 g., m. p. 57—59° (5·1%). In addition, a final residue of base (0·6 g., m. p. 35—37°, yield 5·4%) doubtless consisted largely of the *o*-isomeride. The *p*-isomeride was identified by comparison and by the mixed-m. p. method with 2-*p*-nitrophenylpyridine prepared from *p*-nitroaniline.

2-m-*Nitrophenylpyridine* crystallises from alcohol in very pale yellow, prismatic needles, m. p. 73—74° (corr.) (Found: C, 65·9; H, 4·0. $C_{11}H_8O_2N_2$ requires C, 66·0; H, 4·0%). It is insoluble in cold water, sparingly soluble in cold alcohol, and soluble in ether. The *nitrate* crystallises from 5*N*-nitric acid in colourless needles, m. p. 193° (corr.) (Found, in air-dried salt: loss at 110°, 2·0%. Found, in dried salt: N, 16·0. $C_{11}H_8O_2N_2,HNO_3$ requires N, 16·0%). The orientation of the nitro-group was determined by heating 2-*m*-nitrophenylpyridine (0·5 g.) with methyl sulphate (0·5 c.c.) for 10 minutes at 100°, and oxidising the methosulphate (which crystallised readily) in alkaline solution with potassium permanganate (2·5 g.); 0·08 g. of *m*-nitrobenzoic acid, m. p. 140—141°, alone or mixed with a genuine specimen, was then obtained.

2-o-*Nitrophenylpyridine* crystallises from ether in large, colourless, quadrilateral tablets, m. p. 60—61° (corr.) (Found: C, 66·0; H, 4·0. $C_{11}H_8O_2N_2$ requires C, 66·0; H, 4·0%). It is insoluble in cold water, but readily soluble in alcohol or ether.

3-Phenylpyridine and its Derivatives.

3-p-*Nitrophenylpyridine* crystallises from alcohol in pale buff needles, m. p. 148—149° (corr.) (Found : C, 66·0; H, 4·1; N, 14·0. $C_{11}H_8O_2N_2$ requires C, 66·0; H, 4·0; N, 14·0%). It is insoluble in water, sparingly soluble in alcohol, acetone, or ether, and readily soluble in chloroform. The *nitrate* crystallises from *N*-nitric acid in anhydrous, cream-coloured, silky needles, m. p. 198° (corr.) (Found : N, 16·0. $C_{11}H_8O_2N_2,HNO_3$ requires N, 16·0%).

3-*p*-Nitrophenylpyridine was converted into 3-phenylpyridine through the amine and hydrazine, the same methods and proportions being used in each operation as in the case of the corresponding 2-isomerides.

3-p-*Aminophenylpyridine* was isolated as dihydrochloride in 89% yield. The base crystallises from moist alcohol in colourless plates, m. p. 102—104° (corr.), containing solvent of crystallisation, and after drying at 100° (loss, 9·9, 10·2. $C_{11}H_{10}N_2,H_2O$ requires H_2O, 9·6%) has m. p. 118—120° (corr.) (Found, in dried base : C, 77·6; H, 5·9. $C_{11}H_{10}N_2$ requires C, 77·7; H, 5·9%). The *dihydrochloride* crystallises from dilute hydrochloric acid in small, colourless needles, m. p. *ca.* 310° (decomp.; corr.). It is readily soluble in water, and sparingly soluble in alcohol (Found, in air-dried salt : loss at 110°, 3·7. $C_{11}H_{10}N_2,2HCl,\frac{1}{2}H_2O$ requires H_2O, 3·6%. Found, in dried salt : Cl, 29·1. $C_{11}H_{10}N_2,2HCl$ requires Cl, 29·2%). The *picrate* is precipitated in yellow needles, m. p. 185—188°, when alcoholic solutions of the base (1 mol.) and picric acid (2 mols.) are mixed, but when this product is boiled with much alcohol it is converted into orange needles, m. p. 219—220° (corr.), which are very sparingly soluble in hot alcohol and presumably represent a monopicrate.

3-p-*Hydrazinophenylpyridine* was isolated as base, m. p. 153—154°, in 70% yield. It crystallises from alcohol in colourless, anhydrous leaflets, m. p. 156—157° (corr.) (Found : C, 71·2; H, 6·1. $C_{11}H_{11}N_3$ requires C, 71·4; H, 6·0%). It is insoluble in water and sparingly soluble in ether or cold alcohol. 3-Phenylpyridine was isolated in 74% yield. It was identified through its properties and those of its picrate. The base was an oil volatile with steam, whilst the picrate crystallised from alcohol in woolly, yellow needles, m. p. 162—164° (corr.). Skraup and Cobenzl (*loc. cit.*) give m. p. 161—163·5°; Ciamician and Silber (*Ber.*, 1887, **20**, 191) give m. p. 162—163°. The *nitrate* crystallises from absolute alcohol in colourless, anhydrous prisms, m. p. 78—80° (corr.) (Found : N, 13·1, 13·0. $C_{11}H_9N,HNO_3$ requires N, 12·8%). It is very easily soluble in water or hot alcohol.

Nitration of 3-Phenylpyridine.—3-Phenylpyridine nitrate (6·1 g.) was added gradually to concentrated sulphuric acid (12·5 c.c.), cooled with water. After being kept for 5 minutes, the product was heated for ½ hour at 100°, then diluted with water and precipitated fractionally with ammonia. First, 3·5 g. of pure 3-*p*-nitrophenylpyridine were obtained, m. p. 148—149° alone or mixed with a specimen prepared (as above) from *p*-nitroaniline. Then a sticky precipitate was obtained, from which a further 0·1 g. of the above compound, m. p. 147—148°, was obtained by washing with ether and crystallising from alcohol, followed by an oil which was collected by ether. This, together with the residues from the mother-liquors of the 0·1 g. mentioned above, gave an oily residue (1·65 g.), which became mainly crystalline. Since no pure base could be isolated from it, it was converted into methosulphate and oxidised with permanganate; a mixture of acids not wholly nitrobenzoic acids was then obtained. The most sparingly soluble barium salt prepared from this mixture gave a trace of a crude acid, melting at about 130°, and at about 135° if mixed with *m*-nitrobenzoic acid. The total yield of the *p*-isomeride, 3·6 g., is 64·3% of the theoretical.

4-Phenylpyridine and its Derivatives.

4-p-*Nitrophenylpyridine* crystallises from acetone in nearly colourless, prismatic needles, m. p. 123—124° (corr.). It is insoluble in water, sparingly soluble in ether, and readily soluble in alcohol, acetone, or chloroform (Found: C, 65·9; H, 3·8; N, 14·0. $C_{11}H_8O_2N_2$ requires C, 66·0; H, 4·0; N, 14·0%). The *hydrochloride* crystallises from 5*N*-hydrochloric acid in nearly colourless, elongated prisms containing $3H_2O$, which are lost at 100°. The salt then has m. p. 255° (corr.) (Found, in air-dried salt: H_2O, 18·7. $C_{11}H_8O_2N_2,HCl,3H_2O$ requires $3H_2O$, 18·6%. Found in dried salt: C, 55·9; H, 4·1; Cl, 14·8. $C_{11}H_8O_2N_2,HCl$ requires C, 55·8; H, 3·8; Cl, 15·0%).

4-*p*-Nitrophenylpyridine was converted into 4-phenylpyridine through the amine and hydrazine, the same methods and proportions being used in each operation as in the case of the corresponding 2-isomerides, except that the 4-phenylpyridine was isolated in a different way, since it is scarcely volatile with steam. 4-p-*Aminophenylpyridine* was isolated as base in 89% yield. It crystallises from alcohol in large, well-formed, nearly colourless plates, m. p. 232—234° (corr.). It is insoluble in water, and sparingly soluble even in hot alcohol or ether. Consistent but low results were found on analysis (Found, in air-dried base: loss at 100°, 0·6. Found in dried base: C, 76·6, 76·5, 76·7; H, 5·7, 5·7, 5·9. $C_{11}H_{10}N_2$ requires C, 77·7; H, 5·9%). The *dihydrochloride* crystallises from dilute

hydrochloric acid in anhydrous, prismatic needles, m. p. 312° (decomp.; corr.) after darkening from about 240° (Found : Cl, 29·2. $C_{11}H_{10}N_2$,2HCl requires Cl, 29·2%).

4-p-*Hydrazinophenylpyridine* is precipitated in an amorphous form on the addition of ammonia to an aqueous solution of its hydrochloride, but crystallises from alcohol in wedge-shaped bundles of nearly colourless needles, m. p. 205—207° (corr.). It is almost insoluble in water or ether and sparingly soluble in alcohol. The *dihydrochloride* crystallises from dilute hydrochloric acid in well-formed prisms, m. p. 272° (decomp.; corr.) (Found, in air-dried salt : loss at 100°, 6·6. $C_{11}H_{11}N_3$,2HCl,H_2O requires H_2O, 6·5%. Found, in dried salt : Cl, 27·3. $C_{11}H_{11}N_3$,2HCl requires Cl, 27·5%).

4-*Phenylpyridine* was prepared by oxidising the crude hydrazine with cupric acetate, removing copper by hydrogen sulphide, basifying the solution and collecting the product by ether, the yield being 24% of the theoretical calculated on the amine from which the hydrazine was prepared. After purification by distillation, conversion into the nitrate, and regeneration from the pure salt, it melted at 74° (corr.), alone or mixed with a specimen prepared by Hantzsch's general method. The preparation by this method has been described partly by Hantzsch (*Ber.*, 1884, **17**, 1512) and partly by Schiff and Piluti (*Ber.*, 1883, **16**, 1607). Since the latter authors especially give few details and the yield is not stated numerically in any of the various stages, the following supplementary information is given. Benzaldehyde (53 g.), ethyl acetoacetate (130 g.), aqueous ammonia (80 c.c., *d* 0·88), and alcohol (150 c.c.) were boiled under reflux, and after 2 hours another 20 c.c. of aqueous ammonia were added. After boiling for another 5 hours and keeping, the dihydro-ester (104 g.) was collected. The mother-liquor and alcoholic washings were mixed with another 20 c.c. of aqueous ammonia, boiled for 6 hours, and concentrated; more of the dihydro-ester then separated. The combined crops, after crystallisation from alcohol, gave ethyl 4-phenyl-2 : 6-dimethyl-1 : 4-dihydropyridine-3 : 5-dicarboxylate (120 g., yield 73%) in colourless prisms, m. p. 158—159° (corr.). Schiff and Piluti give m. p. 156—157°.

The dihydro-ester (104 g.), partly dissolved and partly suspended in ether (1 l.), was subjected to the action of nitrous acid, generated from a lower layer of aqueous sodium nitrite and sulphuric acid (the method of Rupe; compare Henle, "Anleitung für das organisch-chemische Praktikum," 1921, p. 180), until after 4 days no suspended matter remained and brown fumes were observed. The ethereal solution was washed with aqueous sodium carbonate, dried, and distilled, and the residue crystallised from alcohol; ethyl 4-phenyl-2 : 6-dimethylpyridine-3 : 5-dicarboxylate was then obtained in

88·4% yield. It formed large, hexagonal plates, m. p. 62—63·5° (corr.), from alcohol. Schiff and Piluti give m. p. 66—67°.

This ester (30 g.) was heated with potassium hydroxide (15 g.) in absolute alcohol (45 c.c.), and the alcohol was then removed by distillation, eventually from an oil-bath at 130° and by adding water to the residue and again distilling. The product was oxidised in boiling aqueous solution by potassium permanganate (57 g.), an operation which took some 40 hours. Monopotassium 4-phenylpyridinetetracarboxylate was isolated by Hantzsch's method and recrystallised from water, 22 g. (yield 62%) being isolated in dense prisms. On concentrating the mother-liquors, needles separated and these were reoxidised with an equal weight of permanganate; a further quantity of the required salt was thus obtained in the characteristic dense prisms, the total yield being 72%.

On distilling this salt (161 g.) with lime and working up the product by Hantzsch's method, 41 g. of distilled 4-phenylpyridine were obtained. The yield in this operation was 61%, and the overall yield of this base from benzaldehyde was 28·3%. 4-Phenylpyridine distilled at 282—284° (corr.)/762 mm. (Hantzsch gives b. p. 274—275° uncorr.), but the base melts at 74° (corr.), not at 77—78° as stated by Hantzsch. The m. p. remained at 74° (corr.) both after the base had been crystallised from ether and after it had been converted into the nitrate and regenerated from the pure salt.

4-*Phenylpyridine dinitrate* crystallises from fairly concentrated nitric acid in colourless needles, m. p. 114—115° (corr.) (Found, in air-dried salt: C, 46·9; H, 4·2. $C_{11}H_9N,2HNO_3$ requires C, 47·0; H, 3·9%). When this salt is crystallised from absolute alcohol, 4-*phenylpyridine mononitrate* separates in colourless plates, m. p. 140° (corr.) (Found, in air-dried salt: C, 60·5; H, 5·0. $C_{11}H_9N,HNO_3$ requires C, 60·5; H, 4·6%). Both salts are easily soluble in water.

Nitration of 4-*Phenylpyridine.*—4-Phenylpyridine mononitrate (10 g.) was added to concentrated sulphuric acid (20 c.c.) cooled by water, and heated for ½ hour at 100°. The product was basified with ammonia, and the bases were collected partly by filtration and partly by extraction with ether. They were dissolved in hydrochloric acid (50 c.c. of 5*N*- + 10 c.c. of conc. acid); the hydrochloride of the *p*-nitro-derivative (4·35 g., m. p. 250°) then separated. The base regenerated from the mother-liquors was recrystallised from 5*N*-nitric acid (30 c.c.), the nitrate of the *m*-nitro-derivative (3·55 g., m. p. 215°) separating. The base from this mother-liquor was converted into hydrochloride, and gave another 1·2 g., m. p. 251°, of the *p*-salt. The further manipulation of the mother-liquors

consisted of fractional precipitation of the bases; the earlier fractions were crystallised as hydrochloride or nitrate (according to whether they were mainly *p* or *m*), and the later fractions were crystallised from 5*N*-nitric acid, yielding the well-crystallised nitrate of the *o*-isomeride. The three salts were then crystallised until pure from the appropriate 5*N*-acid, and the mother-liquors worked up by the above method. The final yields were 4-*p*-nitrophenylpyridine hydrochloride (+ $3H_2O$), 4·8 g. pure + 0·26 g., m. p. 246° (yield 38%); 4-*m*-nitrophenylpyridine nitrate, 3·37 g. pure + 0·07 g., m. p. 212° (yield 28·5%); and 4-*o*-nitrophenylpyridine nitrate, 1·53 g. pure (yield 12·7%).

The *p*-isomeride was identified as base and hydrochloride by comparison and by the mixed-m. p. method with 4-*p*-nitrophenylpyridine and its hydrochloride prepared (as above) from *p*-nitroaniline. 4-m-*Nitrophenylpyridine* crystallises from acetone in long, cream-coloured needles, m. p. 109—110° (corr.). It is insoluble in cold water, sparingly soluble in ether or hot water, but fairly easily soluble in alcohol or acetone (Found: C, 65·8; H, 3·9. $C_{11}H_8O_2N_2$ requires C, 66·0; H, 4·0%). The *nitrate* crystallises from 5*N*-nitric acid in anhydrous, cream-coloured needles, m. p. 222° (decomp.; corr.). (Found: C, 50·1; H, 3·4. $C_{11}H_8O_2N_2,HNO_3$ requires C, 50·2; H, 3·4%). It is very sparingly soluble in cold 5*N*-nitric acid. The orientation of the nitro-group was determined by heating 4-*m*-nitrophenylpyridine (0·5 g.) with methyl sulphate (0·5 c.c.) for 10 minutes at 100°, and oxidising the methosulphate in hot aqueous solution by permanganate; 0·12 g. of *m*-nitrobenzoic acid, m. p. 140—141° (alone or mixed with a known specimen), was thus obtained.

4-o-*Nitrophenylpyridine* crystallises from ether in colourless, elongated plates, m. p. 51—52° (corr.) to a turbid liquid, containing rather more than $1H_2O$. After drying in a vacuum over sulphuric acid, it retains $\frac{1}{2}H_2O$ (Found, in air-dried base: C, 59·7; H, 4·3; H_2O, 5·5. $C_{11}H_8O_2N_2,H_2O$ requires C, 60·5; H, 4·6; loss of $\frac{1}{2}H_2O$, 4·1%. Found, in dried base: C, 63·1; H, 4·2. $C_{11}H_8O_2N_2,\frac{1}{2}H_2O$ requires C, 63·2; H, 4·3%). The *nitrate* crystallises from 5*N*-nitric acid in large, nearly colourless, elongated prisms, m. p. 178—179° (corr.) (Found, in air-dried salt: loss at 100°, 2·1. Found in dried salt: C, 50·0; H, 3·4. $C_{11}H_8O_2N_2,HNO_3$ requires C, 50·2; H, 3·4%).

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