361. N-*Oxides and Related Compounds.*[1] *Part XI.** *Mononitration of 2-, 3-, and 4-Phenyl- and 2- and 4-Benzyl-pyridine 1-Oxide.*

By A. R. HANDS and A. R. KATRITZKY.

The proportions of mononitro-isomers formed from the oxides named in the title have been determined and compared with the data [2,3] for the corresponding pyridines. 2- and 4-Phenylpyridine 1-oxides gave significantly greater proportions of *m*-nitro-compounds than the parent compounds. Substitution in the pyridine oxide ring was never observed. Nitration of 2-phenylpyridine and its oxide in sulphuric acid of varying strengths did not alter the isomer proportions greatly. 2-Phenylpyridine 1-oxide appeared to be nitrated 10—100 times faster than 2-phenylpyridine. It is tentatively concluded that the last two compounds are both nitrated as free base. The results are discussed in terms of differing ease of interaction between a benzene ring and (*a*) an adjacent ring and (*b*) a substituent on an adjacent ring.

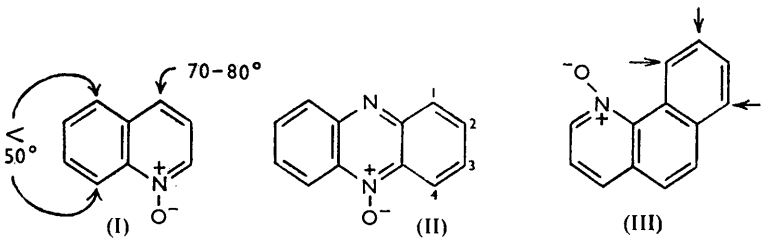
DIPOLE MOMENTS of a series of 4-substituted pyridines and pyridine 1-oxides show [4] that the pyridine 1-oxide ring can create either a deficit or surfeit of electrons at the 4-position, whereas the pyridine ring can create only a deficit; infrared [5] and ultraviolet spectra [6] support this, as do the difficult nitration of pyridines in the 3-position [7] and the easier

* Part X, Katritzky and Monro, *J.*, 1958, 1263.

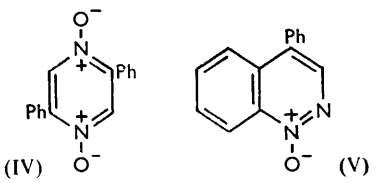
[1] Cf. Katritzky, *Quart. Rev.*, 1956, **10**, 395.
[2] Forsyth and Pyman, *J.*, 1926, 2912.
[3] Bryans and Pyman, *J.*, 1929, 549.
[4] Katritzky, Randall, and Sutton, *J.*, 1957, 1769; Bax, Katritzky, and Sutton, *J.*, 1958, 1254, 1258.
[5] Katritzky, Monro, Beard, Dearnaley, and Earl, *J.*, in the press
[6] Katritzky and Monro, unpublished work.
[7] Schofield, *Quart. Rev.*, 1950, **4**, 382.

nitration of pyridine oxides in the 4-position.[1] The strong directing influence is shown by 2- and 3-methoxypyridine 1-oxide, both being nitrated in the 4-position.[8]

Little is yet known about the transmission of these effects to adjacent rings. Nitration of quinoline 1-oxide is temperature-dependent [cf. (I)].[9] Phenazine 5-oxide (II) on nitration[10] gives 1- and 3-derivatives more quickly than does phenazine, which gives 2(3)-nitrophenazine (however, this may be due to the lower basicity of the oxide; see below), and in the oxide (III) nitration is into the ring furthest from the oxide group.[11]



As a preliminary to physical measurements, we studied the orientation in the mono-nitration of the mono-phenyl- and -benzyl-pyridine 1-oxides, the behaviour of the corresponding pyridines being known.[2,3] The only related work on *N*-oxides showed that 2 : 5-diphenylpyrazine 1 : 4-dioxide (IV) gave[12] the *mm'*-dinitro-derivative (as did the parent pyrazine[12]) and that 4-phenylcinnoline 1-oxide (V) gave four unoriented nitration products.[13]



The preparation[14] of 2-phenylpyridine gave a little by-product, analysis indicating a pyridyldiphenyl or diphenylpyridine. The m. p. (174°) agreed with that[15] (175°) for a "*p*-pyridylphenylbenzene" (a by-product from the action of benzoyl peroxide on pyridine) (promised evidence for the structure has not been traced). *p*-Diphenylylmagnesium bromide is formed as a by-product from bromobenzene and magnesium,[16] but although our picrate agrees in m. p. with that of 2-*p*-diphenylylpyridine,[17] the latter base has m. p. 141—142°; the ultraviolet data also disagree. The m. p.s exclude 2 : 4- and 2 : 6-diphenylpyridine.

2-, 3-, and 4-Phenyl- and 2- and 4-benzyl-pyridine readily gave 1-oxides (characterised as picrates and picrolonates[18]), which were mononitrated with 1·05 equivs. of nitric acid in hot sulphuric acid. Fractional crystallisation of the product was inefficient. The mixture from the nitration of 2-phenylpyridine showed suitable partition between ethyl acetate and water, but no separation in a 40-tube Craig machine. Dewar's method of ultraviolet spectrophotometry[19] gave only approximate results (in agreement with those finally obtained), doubtless because of small amounts of unknown by-products.

[8] den Hertog, Kolder, and Combé, *Rec. Trav. chim.*, 1951, **70**, 591.
[9] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.
[10] Otomasu, *Pharm. Bull.* (*Japan*), 1954, **2**, 283; 1956, **4**, 117.
[11] Iwai, *J. Pharm. Soc. Japan*, 1951, **71**, 1291.
[12] Beech, *J.*, 1955, 3094.
[13] Atkinson and Simpson, *J.*, 1947, 1649.
[14] Evans and Allen, *Org. Synth.*, 1956, Coll. Vol. II, p. 517.
[15] Overhoff and Tilman, *Rec. Trav. chim.*, 1929, **48**, 993.
[16] Manske and Ladingham, *Canad. J. Res.*, 1949, **27***B*, 158.
[17] Heilbron, Hey, and Lambert, *J.*, 1940, 1279.
[18] Katritzky, *J.*, 1956, 2404.
[19] Dewar and Urch, *J.*, 1957, 345.

The mixtures from the nitration of 2-, 3-, and 4-phenylpyridine 1-oxide were separated by deoxygenation with phosphorus trichloride, followed by separation of 2-, 3-, and 4-*x*-nitrophenylpyridine.[2] The products' melting points agreed with those given by Forsyth and Pyman; [2] certain of the salts appeared hydrated.

Much 2- and some 4-*p*-nitrobenzylpyridine 1-oxide crystallised from their respective nitration mixtures. Deoxygenation gave tar in the 4-benzyl series; permanganate oxidation of this tar and of the nitration mixture both failed. Successive deoxygenation and oxidation of the residue in the 2-benzyl series gave mixed 2-(nitrobenzoyl)pyridines, on which we could not repeat Bryans and Pyman's separation.[3] 2-*m*-Nitrobenzoylpyridine, m. p. 117°, isolated in low yield by fractional crystallisation, was identical with an authentic specimen, m. p. 117°, from 2-benzoylpyridine. The earlier workers gave [3] m. p. 122°.

The proportions of isomers found are recorded in Table 1, together with data for the nitration of the parent pyridines.

TABLE 1. *Yields* (%) *of mononitro-compounds in the nitration of phenyl- and benzylpyridines and their* 1-*oxides.*

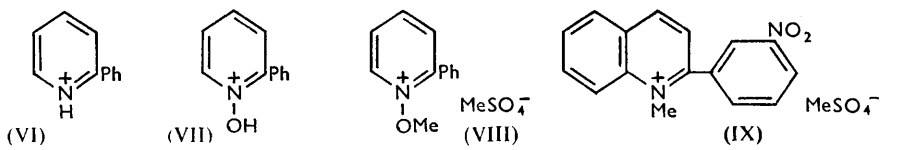
	Pyridine [a]				Pyridine oxide [b]			
Subst.	*o*	*m*	*p*	Total	*o*	*m*	*p*	Total
2-Ph	5	35	42	82	{ 0	58	5	63 }
					{ 3	54	7	64 }
3-Ph	—	—	64	64	—	—	38	38
4-Ph	13	28	38	79	12	51	13	76
2-CH_2Ph	—	10	67	77	—	2	55	57
3-CH_2Ph	—	—	63	63		Not investigated		
4-CH_2Ph	—	5	70	75	—	—	9	9

[a] Refs. 2 and 3. [b] This paper. [c] Duplicate runs.

In 2- and 4-phenylpyridine *para*- is somewhat greater than *meta*-substitution, but in the corresponding 1-oxides *meta*-substitution is much the more important. In the 3-phenyl series, the pyridine undergoes predominant *para*-substitution; *para*-compound was also the only product isolated from the 1-oxide, its yield being lower than from the pyridine, but still more than the *para*-products from the 2- and 4-phenyl oxide. *para*-Substitution predominates for all the benzylpyridines and in 2-benzylpyridine 1-oxide. There is no evidence for substitution into the heterocyclic rings.

Supplementary Experiments.—It is unknown whether the pyridines and their oxides are nitrated as free bases or as conjugate acids or as both in competition. The conjugate acids (as VI and VII) should give more *meta*-isomer, and be more resistant to attack than the free bases, but whether so much more resistant that the small proportion of the free bases in highly acid solution would be preferentially attacked cannot be predicted.

We nitrated 2-phenylpyridine and its 1-oxide in sulphuric acid of various strengths (see Table 2). (In the oleum, tar was formed and possibly sulphonation occurred.) The proportion of *m*-isomer does not increase greatly with increasing acid strength; therefore with both 2-phenylpyridine and its 1-oxide the base and conjugate acid are not nitrated significantly in competition.



(VI) (VII) (VIII) (IX)

The metho-salts would presumably behave as the fully protonated compounds. To determine the species reacting, 1-methoxy-2- (VIII) and -4-phenylpyridinium methyl

sulphate were nitrated as before, but the products gave tars with alkali; the action of alkali on 1-methoxypyridinium salts is now known to be complex.[20]

TABLE 2.

c.c.	H_2SO_4 [a] N	H_0 [b]	Time (hr.)	B/BH$^+$ [c]	Product *m*	Product *p*	Total [d]
			2-Phenylpyridine				
15	30	−6·6	72	$10^{-11·6}$	31	26	57
10	37	−9	0·5	10^{-14}	31	29	60
10	45	?	0·5	?	14	22	36
			2-Phenylpyridine 1-oxide				
20	22	−6	72	10^{-7}	45	6	51
15	30	−6·6	24	$10^{-7·4}$	54	11	65
10	37	−9	2	10^{-10}	49	7	56
10	45	?	2	?	20	5	25

[a] For HNO_3 and substrate see main text. [b] The considerable alterations to H_0 made by substrates cannot be estimated but all lie in the same direction. [c] Assumed pK_a: 2-phenylpyridine, 5 (cf. pyridine, 5·29; Golumbic and Orchin, *J. Amer. Chem. Soc.*, 1950, **72**, 4145); its oxide, 0·8 (cf. pyridine 1-oxide, 0·79; Jaffe and Doak, *ibid.*, 1955, **77**, 4441). [d] No attempt made to separate the small amounts of *o*-isomer.

Le Fèvre and Mathur reported [21] that 1-methyl-2-phenylquinolinium methyl sulphate gave the *m*-isomer (IX) in 97% yield (calculated on the yield of picrate of m. p. 162—176°, 77% on that of pure picrate of m. p. 181—182°) on nitration with fuming nitric acid at 0°. This indicates that 2-phenylpyridine is nitrated as the free base, in agreement with the tentative conclusion reached below. We failed to nitrate 1-methyl-2-phenylpyridinium methyl sulphate in concentrated sulphuric acid.

A mixture of one equivalent of 2-phenylpyridine and its oxide was treated with one equivalent of nitric acid: the 2-phenylpyridine was largely (74%) recovered. Deoxygenation of the residue, and separation, gave 61% of *m*- and 10% of *p*-nitro-derivative (calc. on HNO_3) a ratio which also shows that the oxide was preferentially nitrated. Singly, at least 59% of the 1-oxide was unaffected after 5 min., and at least 65% of the pyridine was nitrated after 40 hr. Therefore the oxide is nitrated *ca.* 10—100 times as fast as the pyridine.

ortho-para-Orientation usually occurs together with activation and *meta*-orientation with deactivation; exceptions are substituents (Cl, CH:CH·CO_2Et, etc.) electron-withdrawing by inductive and electron-donating by mesomeric effects.[22] No cases are known of *meta*-substitution with activation. If 2-phenylpyridine were being nitrated as its conjugate acid it would follow that changing a substituent involved increased *meta*-substitution with increased activation: therefore 2-phenylpyridine probably is nitrated as such. If this is so, it is unlikely that the less basic 2-phenylpyridine 1-oxide would be nitrated as the conjugate acid; the tentative conclusion is that both compounds react as free bases. The concentration of the oxide free base is *ca.* 10^4 times that of the pyridine; although the oxide appears to be nitrated some 10—100 times as fast as the pyridine, after allowance for the extent of protonation it reacts at only 0·001—0·01 of the rate for the latter.

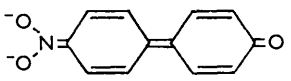
The conclusion that 2-phenylpyridine is nitrated as the free base is unexpected because aniline (of comparable basicity) in excess of concentrated sulphuric acid gives much *m*-nitroaniline [23] by nitration of the cation. The (free) aniline molecule is far more easily substituted electrophilically than the (free) 2-phenylpyridine molecule, and it is hardly to be expected that the 2-phenylpyridine cation would be so much more deactivated than the

[20] Gardner and Katritzky, *J.*, 1957, 4375; Katritzky, unpublished work.
[21] Le Fèvre and Mathur, *J.*, 1930, 2236.
[22] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, Chap. 6.
[23] Hüber, *Annalen*, 1881, **208**, 278.

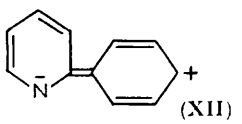
phenylammonium ion as to alter the course of substitution. It is hoped to study these matters further.

An electron-withdrawing group separated from the benzene ring by a vinyl group (as in cinnamic acid, ω-nitrostyrene, 2- and 4-nitrodiphenyl) gives *ortho*- and *para*-nitration.[22] The pK_a of 4-hydroxy-3'- and -4'-nitrodiphenyl and of 4-hydroxydiphenyl itself are similar (9·14, 8·95, 9·40); the anion canonical form (X) is thus not important [24] in the ground state (ultraviolet evidence [25] indicates considerable conjugation).

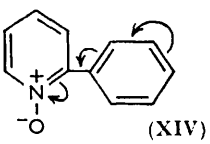
Significantly higher proportions of *para*-isomer isolated in the nitration of 3- than of 2- and 4-phenyl-pyridine and -pyridine oxide (Table 1) indicate that canonical forms of type (XI and XII) *are* important, which is not unexpected for the 2-derivative, as (X) is



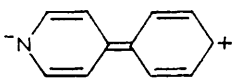
(X)



(XII)



(XIV)



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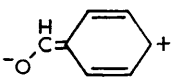
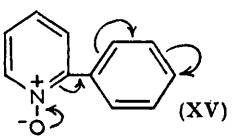


(XIII)



(XV)

similar to the important form (XIII) of benzaldehyde. Shifts of type (XIV) are apparently more important than those of type (XV), *i.e.*, the influence of the nitrogen atom in the ring is greater than that of the oxygen atom outside the ring. This may be compared with the greater influence of nitrogen in the ring in 2- and 4-phenylpyridine than of the nitro-group outside the ring in 2- and 4-nitrodiphenyl.

The comparative ease of electron-donation and electron-withdrawal by an *N*-oxide group appears to depend on distance. At very short distances withdrawal appears to predominate, for nitration rarely takes place into the 2-position of a pyridine 1-oxide.[1] Dipole-moments [4] and easy nitration of the corresponding 4-position [1] show that at medium distances the two effects are comparable; the present work indicates that at larger distances electron-withdrawal again predominates. It is hoped to study these effects further by physical methods.

In the benzylpyridines and their 1-oxides, the difference between the rates of nitration of the bases and the conjugate acids would be expected to be smaller than that in the phenyl compounds. Thus the former may be nitrated as conjugate acids. Little difference in behaviour of the pyridine and the corresponding 1-oxide would be expected, and in the 2-series this is so (Table 1).

In the experimental section details are given of preliminary work on the nitration of 2-styryl- and polynitration of 2-phenyl-pyridine 1-oxide. Some 1-methoxypyridinium iodides are also described.

Experimental

Chloroform extracts were dried over magnesium sulphate.

2-, 3-, and 4-*Phenylpyridine*.—2-Phenylpyridine was prepared [14] in 50% yield. Distillation of the higher-boiling residues gave a *pyridyldiphenyl* (0·2%), plates, m. p. 174° (from methanol) (Found: C, 88·1; H, 5·4; N, 5·8. $C_{17}H_{13}N$ requires C, 88·3; H, 5·7; N, 6·1%), $\lambda_{max.}$ at 270 (ε 26,000) and 286 mμ (ε 28,300) in hexane. The *picrate* formed yellow needles (from ethanol), m. p. 188·5° (Found: C, 60·5; H, 3·7; N, 12·2. $C_{23}H_{16}O_7N_4$ requires C, 60·0; H, 3·5; N, 12·2%). 3- and 4-Phenylpyridine were prepared by known methods (b. p. 136—139°/13 mm. and 77° respectively).

[24] Kreiter, Bonner, and Eastman, *J. Amer. Chem. Soc.*, 1954, **76**, 5770.
[25] Beaven, Hall, Lesslie, and Turner, *J.*, 1952, 854, and references therein.

2- and 4-Benzylpyridine were redistilled commercial products.

2- and 4-Benzyl- and 2-, 3-, and 4-Phenyl-pyridine 1-Oxide.—2-Benzylpyridine (50 g.), 30% aqueous hydrogen peroxide (67 c.c.), and acetic acid (180 c.c.) were kept for 24 hr. at 70—80°; volatile material was removed at 100°/15 mm.; and the residue in hot chloroform (150 c.c.) was digested for 10 min. with potassium carbonate (50 g.). Filtration and evaporation gave *2-benzylpyridine 1-oxide* (51·3 g., 94%), prisms (from benzene), m. p. 100·5° (Found: C, 78·0; H, 6·0; N, 7·5. $C_{12}H_{11}ON$ requires C, 77·8; H, 6·0; N, 7·6%). The *picrate* formed needles (from ethanol), m. p. 119° (Found: C, 52·6; H, 3·6; N, 13·3. $C_{18}H_{14}O_8N_4$ requires C, 52·2; H, 3·4; N, 13·5%). The *picrolonate* formed prisms (from ethanol), m. p. 135·5° (decomp.) (Found: C, 58·5; H, 3·9; N, 15·7. $C_{22}H_{19}O_6N_5$ requires C, 58·8; H, 4·3; N, 15·6%).

The following *pyridine 1-oxides* were similarly prepared: *4-benzyl-* (second treatment with more hydrogen peroxide needed for complete oxidation) (96%), deliquescent prisms (from benzene), m. p. 151° (Found: C, 77·7; H, 5·8; N, 7·5%) [*picrate*, yellow needles (from ethanol), m. p. 94° (Found: C, 52·3; H, 3·4%); *picrolonate*, yellow needles (from ethanol), m. p. 185·5° (Found: C, 58·5; H, 4·2%)]; 2-phenyl- (94%), prisms (from benzene), m. p. 157° (lit.,[26] m. p. 155—155·5°) (by-product formed, see below) [picrate (new *polymorph*), orange prisms (from ethanol), m. p. 130—131° (Found: C, 51·2; H, 3·2. $C_{17}H_{12}O_8N_4$ requires C, 51·0; H, 3·0%) (lit.,[26] yellow prisms, m. p. 150—152°); *picrolonate*, brown rhombs (from ethanol), m. p. 141·5—142° (decomp.) (Found: C, 58·3; H, 4·1; N, 16·5. $C_{21}H_{17}O_6N_5$ requires C, 57·9; H, 3·9; N, 16·1%)]; *3-phenyl-* (90%), needles (from benzene), m. p. 119° (Found: C, 77·6; H, 5·3; N, 8·5. $C_{11}H_9ON$ requires C, 77·2; H, 5·3; N, 8·2%) [*picrate*, needles (from ethanol), m. p. 161° (Found: C, 51·0; H, 3·2; N, 14·2%); *picrolonate*, orange prisms (from ethanol), m. p. 152° (decomp.) (Found: C, 58·2; H, 4·0; N, 16·4%)]; *4-phenyl-* (88%), prisms (from benzene), m. p. 152—152·5°, sublimed at 180°/0·05 mm. (Found: C, 76·9; H, 5·2%) [*picrate*, needles (from ethanol), m. p. 173—173·5° (Found: C, 51·1; H, 3·1%); *picrolonate*, orange prisms (from ethanol), m. p. 205° (Found: C, 57·7; H, 4·1%)].

In the preparation of 2-phenylpyridine 1-oxide, a *by-product*, insoluble in chloroform, formed pale yellow needles (from water or ethanol), m. p. 274° (decomp.) (Found: C, 49·5, 49·7; H, 4·8, 4·8; N, 16·9. $C_7H_8O_3N_2$ requires C, 50·0; H, 4·8; N, 16·7%).

General Procedures for Mononitration and Deoxygenation of 1-Oxides.—Procedure A. The oxide (5 g.) was added to a mixture of nitric acid (*d* 1·42; 2·0 c.c., 1·05 mol.) and sulphuric acid (8·5 c.c.) at 0°. The whole was kept for 12 hr. at 100°, poured on ice (20 g.), basified with hydrated sodium carbonate (25 g.), and extracted with chloroform (8 × 75 c.c.). Evaporation of the extracts gave the mixed 2-(nitrophenyl)pyridine 1-oxides.

Procedure B. The mixed nitro-oxides (usually *ca.* 5 g.), chloroform (20 c.c.), and phosphorus trichloride (10 c.c.) were kept for 2 hr. at 75°, poured on ice (20 g.), and basified with 2·5N-sodium hydroxide (200 c.c.). The aqueous layer was extracted with chloroform (3 × 50 c.c.) and all the combined organic layers were evaporated to give the mixed nitro-deoxygenated bases.

Mononitration of 2-Phenylpyridine 1-Oxide.—The product (from procedures A and B) from the oxide (5 g.), recrystallised from 5N-nitric acid, gave 2-*m*-nitrophenylpyridine nitrate (3·47 g.), m. p. 193° (lit.,[2] m. p. 193°). Successive regeneration of the bases (sodium hydroxide solution and chloroform-extraction) and repetition of the above gave two further crops, which, combined and recrystallised from 5N-nitric acid, gave more *m*-isomer nitrate (0·76 g., total yield 54%). Fractional precipitation with aqueous ammonia of the bases remaining gave three crops of 2-*p*-nitrophenylpyridine, which after recrystallisation from ethanol had m. p. 130—131° (lit.,[2] m. p. 130·5—131·5°) (0·38 g., 7%) (Found: C, 65·8; H, 3·9; N, 13·9. Calc. for $C_{11}H_8O_2N_2$: C, 66·0; H, 4·0; N, 14·0%). Evaporation of the mother-liquors and repeated recrystallisation from ether gave 2-*o*-nitrophenylpyridine (0·20 g., 3%), m. p. 59—60° (lit.,[2] m. p. 60—61°). Aqueous sodium hydroxide and chloroform-extraction of the above nitrate gave 2-*m*-nitrophenylpyridine (3·16 g., 54%), m. p. 73° (lit.,[2] m. p. 73—74°) (Found: C, 65·6; H, 4·0; N, 14·1%). In a duplicate run 58% of *m*-, 5% of *p*- but no *o*-isomer were obtained.

Mononitration of 3-Phenylpyridine 1-Oxide.—The product from the oxide (3·42 g.) was twice recrystallised from ethanol, to give 3-*p*-nitrophenylpyridine (1·52 g., 38%), m. p. 148° (lit.,[2] m. p. 148—149°) (Found: C, 65·9; H, 4·3; N, 13·9%). A brown oil remained.

Mononitration of 4-Phenylpyridine 1-Oxide.—The product from the oxide (5·25 g.) was twice recrystallised from 5N-nitric acid, giving 4-m-*nitrophenylpyridine nitrate hemihydrate* (total yield

[26] Gilman and Edward, *Canad. J. Chem.*, 1953, **31**, 457.

4·30 g., 52%), prisms, m. p. 215° (decomp.) [Found (after drying 100°): C, 48·7; H, 3·6. $C_{11}H_9O_5N_3,\frac{1}{2}H_2O$ requires C, 48·5; H, 3·7%] [lit.,[2] m. p. for anhydrous salt 222° (decomp.)].

The bases were regenerated from the mother-liquors and twice crystallised from 5N-hydrochloric acid, giving 4-p-*nitrophenylpyridine hydrochloride monohydrate* (total yield, 1·13 g., 13%), needles, m. p. 241—242° [Found (after drying at 100°/14 mm.): C, 51·6; H, 4·7; N, 10·7; Cl, 13·6. $C_{11}H_9O_2N_2Cl,H_2O$ requires C, 51·9; H, 4·4; N, 11·0; Cl, 13·9%].

The base were again regenerated from the mother-liquor and the above process was repeated twice. The bases regenerated from the final mother-liquor gave, with picric acid (1 g.) in ethanol, 4-*o*-nitrophenylpyridine picrate (1·72 g., 13%), m. p. 177° after two recrystallisations from this solvent.

Basification of the above salts and chloroform-extraction gave: 4-*m*- (3·10 g., 51%), m. p. 110° (lit.,[2] m. p. 109—110°) [*picrate*, needles (from ethanol), m. p. 210° (decomp.) (Found: C, 48·0; H, 2·5. $C_{17}H_{11}O_9N_5$ requires C, 47·6; H, 2·6; N, 16·3%)]; 4-*p*- (0·80 g., 13%), m. p. 123° (lit.,[2] m. p. 123—124°) [*picrate*, yellow needles (from ethanol), m. p. 220° (Found: C, 47·4; H, 2·7; N, 16·3%)]; and 4-*o*-nitrophenylpyridine (0·76 g., 12%) (from ether), m. p. 50—52° (lit.,[2] m. p. 51—52°).

Mononitration of 2-Benzylpyridine 1-Oxide.—The oxide (5·5 g.), nitrated by procedure A, gave mixed nitro-derivatives (6·7 g., 98%), m. p. 131—148°. Two recrystallisations from ethanol gave 2-p-*nitrobenzylpyridine 1-oxide* (3·71 g., 55%) as needles, m. p. 166·5—167° (Found: C, 62·9; H, 4·5. $C_{12}H_{10}O_3N_2$ requires C, 62·6; H, 4·4%) [*picrate*, needles (from ethanol), m. p. 134—134·5° (Found: C, 46·8; H, 2·8; N, 14·9. $C_{18}H_{13}O_{10}N_5$ requires C, 47·1; H, 2·8; N, 15·2%)].

Deoxygenation (procedure B) of 2-*p*-nitrobenzylpyridine 1-oxide (1 g.) gave 2-*p*-nitrobenzylpyridine (0·87 g., 94%), m. p. 80° (lit.,[3] m. p. 81°) (Found: C, 67·6; H, 4·9; N, 13·0. Calc. for $C_{12}H_{10}O_2N_2$: C, 67·3; H, 4·7; N, 13·1%). The picrate had m. p. 185—186° (lit.,[3] m. p. 185—187°). 2-*p*-Nitrobenzylpyridine (1 g.), boiled for 1 hr. with aqueous potassium permanganate (1·5 g. in 200 c.c.) and decolorised with sulphur dioxide, gave on cooling 2-*p*-nitrobenzoylpyridine (0·8 g., 52%), m. p. 104° after one recrystallisation from ethanol (lit.,[3] m. p. 105°).

Evaporation of the ethanolic mother-liquors from the 2-*p*-nitrobenzylpyridine 1-oxide, and successive deoxygenation (procedure B) and oxidation (with permanganate as above but product separated with chloroform) of the residue, gave mixed 2-(nitrobenzoyl)pyridines (0·90 g., 13%), m. p. 99—101°. Three recrystallisations from water gave 2-*m*-nitrobenzoylpyridine (0·15 g., 2%), needles, m. p. and mixed m. p. 117° (lit.,[3] needles, m. p. 122°).

2-m-*Nitrobenzoylpyridine.*—Nitric acid (*d* 1·42; 1·8 c.c.) in sulphuric acid (3 c.c.) was added to 2-benzoylpyridine [b. p. 106—110°/0·2 mm. (lit.,[27] b. p. 170—172°/10 mm.); prepared from 2-benzylpyridine [27]] in sulphuric acid (7 c.c.) at 0°. The whole was kept for 1½ hr. at 100°, added to ice (50 g.), and basified with sodium carbonate (23 g.), to give the nitro-derivative (6·5 g., 94%), needles (from ethanol), m. p. 117° unchanged by further recrystallisation (Found: C, 62·9; H, 3·2. Calc. for $C_{12}H_8O_3N_2$: C, 63·2; H, 3·5%).

Mononitration of 4-Benzylpyridine 1-Oxide.—The oxide (5·5 g.), nitrated by procedure A, gave a brown oil. Three recrystallisations from ethyl acetate gave 4-p-*nitrobenzylpyridine 1-oxide* (0·63 g., 9%) as prisms, m. p. 165·5—166° (Found: C, 62·2; H, 4·3; N, 11·9. $C_{12}H_{10}O_3N_2$ requires C, 62·6; H, 4·4; N, 12·2%). The *picrate* formed needles (from ethanol), m. p. 156—156·5° (Found: C, 47·1; H, 2·8. $C_{18}H_{13}O_{10}N_5$ requires C, 47·1; H, 2·8%).

Deoxygenation (procedure B) of the oxide (0·5 g.) gave 4-*p*-nitrobenzylpyridine (0·42 g., 90%), m. p. 74° (lit.,[3] m. p. 74°) (Found: C, 67·2; H, 4·8; N, 12·8. Calc. for $C_{12}H_{10}O_2N_2$: C, 67·3; H, 4·7; N, 13·1%).

Attempted deoxygenation (procedure B) of the total product of nitration gave tar only. Attempted oxidation (permanganate, as above) also failed.

Nitration in Sulphuric Acid of Various Strengths.—2-Phenylpyridine (3·10 g.) or 2-phenylpyridine 1-oxide (3·42 g.) was heated at 100° with nitric acid (0·84 c.c.; *d* 1·5) and sulphuric acid. The time of heating and amount and concentration of the sulphuric acid are given in Table 2.

In the 1-oxide experiments the product was isolated and deoxygenated as in procedures A and B. In all experiments the isomers were separated as described above. The proportions of isomers isolated are recorded in Table 2.

[27] Crook and McElvain, *J. Amer. Chem. Soc.*, 1930, **52**, 4006.

Competitive Nitration of 2-Phenylpyridine and its 1-Oxide.—2-Phenylpyridine (3·10 g.) and its oxide (3·42 g.) were added to nitric acid (*d* 1·5; 1·26 g.) in concentrated sulphuric acid (7 c.c.) at 0°. After 5 min., the mixture was heated for 30 min. at 100°, poured on ice (50 g.) and sodium carbonate (20 g.), and steam-distilled. Saturation of the distillate with sodium chloride, extraction with ether, evaporation of the ether, and admixture with picric acid (4 g.) in ethanol gave 2-phenylpyridine picrate (5·47 g., 74%), m. p. and mixed m. p. 175° (lit.,[28] m. p. 175°).

Chloroform-extraction of the residue from the steam-distillation, followed by deoxygenation (procedure B) of the material obtained from the extracts gave mixed 2-nitrophenylpyridines, which were separated by the method given above to give the *m*- (61%) and the *p*-isomer (10%) (calc. on HNO_3).

Nitration of 2-Styrylpyridine 1-Oxide.—Nitration of this oxide (5·75 g.) by procedure A and recrystallisation of the product from ethanol gave *x* : *y-dinitro-2-styrylpyridine 1-oxide* (1·96 g., 23%) as orange prisms, m. p. 195°, or yellow needles, m. p. 193—194° (Found: C, 54·9; H, 3·2; N, 14·5. $C_{13}H_9O_5N_3$ requires C, 54·4; H, 3·1; N, 14·6%).

Attempted Dinitrations of 2-Phenylpyridine 1-Oxide.—The oxide (9 g.) was added to nitric acid (*d* 1·42; 12 c.c.) and sulphuric acid (15 c.c.) at 0°. The whole was kept for 12 hr. at 100°, poured on ice (70 g.), and extracted with chloroform (3 × 100 c.c.). Evaporation of these extracts gave product C (5·7 g.). The aqueous solution, when basified with sodium carbonate (50 g.) and again extracted with chloroform (3 × 100 c.c.), gave (from the chloroform) product D (3·35 g.).

From C, 34-fractional crystallisation from ethanol gave, from the less soluble fractions, x : y-*dinitro-2-phenylpyridine 1-oxide* (0·1 g., 1%), yellow needles (from ethyl acetate), m. p. 190·5° (Found: C, 50·8; H, 2·8. $C_{11}H_7O_5N_3$ requires C, 50·6; H, 2·7%), and a substance (0·001 g.), yellow plates, insoluble in ethyl acetate, m. p. 189°.

From the more soluble fractions of C, 2-m-*nitrophenylpyridine 1-oxide nitrate* (0·12 g., 1%) crystallised as orange prisms, m. p. 154—157° (decomp.) (Found: C, 47·9; H, 3·0. $C_{11}H_9O_6N_3$ requires C, 47·3; H, 3·3%). Basification gave 2-*m*-nitrophenylpyridine 1-oxide, m. p. and mixed m. p. 178° (see below).

From D, 29-fractional crystallisation from water gave, from the less soluble fractions, 2-m-*nitrophenylpyridine 1-oxide* (0·78 g., 7%) as pale yellow needles, m. p. 178° (Found: C, 60·9; H, 3·5; N, 13·2. $C_{11}H_8O_3N_2$ requires C, 61·1; H, 3·7; N, 13·0%). The *hemi-picrate* formed prisms (from ethanol), m. p. 151—152° (Found: C, 50·7; H, 2·7; N, 14·3. $C_{11}H_8O_3N_2,\frac{1}{2}C_6H_3O_7N_3$ requires C, 50·8; H, 2·9; N, 14·8%). Deoxygenation (procedure B) of the 1-oxide (0·5 g.) gave 2-*m*-nitrophenylpyridine (0·45 g., 97%), m. p. and mixed m. p. 73°.

From the more soluble fractions of D, 2-p-*nitrophenylpyridine 1-oxide* (0·02 g., 0·2%) separated as yellow needles, m. p. 216° (Found: C, 61·3; H, 3·6; N, 12·8%). The *picrate* formed needles (from ethanol), m. p. 162° (Found: C, 46·3; H, 2·6. $C_{17}H_{11}O_{10}N_5$ requires C, 45·8; H, 2·5%). Deoxygenation (procedure B) of the 1-oxide gave 2-*p*-nitrophenylpyridine m. p. and mixed m. p. 130°, identical with the specimen described above.

Oxidation (as above) of 2-*p*-nitrophenylpyridine gave the 1-oxide (77%), m. p. 216°, identical with the specimen described above.

Nitrated with fuming nitric acid, 2-phenylpyridine 1-oxide gave a trace of a x : y : *z-trinitro-derivative*, pale yellow prisms (from ethanol), m. p. 245° (decomp.) (Found: C, 43·2; H, 2·0; N, 18·7. $C_{11}H_6O_7N_4$ requires C, 43·1; H, 2·1; N, 18·3%).

1-*Methoxypyridinium Iodides.*—The following were made by refluxing the oxide with excess of methyl iodide overnight in the dark and evaporating excess of the latter: 1-*methoxy-4-phenyl-* (98%), pale yellow needles, deliquescent and light-sensitive, m. p. 99° (decomp.) (Found: C, 46·1; H, 3·7; I, 40·6. $C_{12}H_{12}ONI$ requires C, 46·0; H, 3·9; I, 40·5%); 1-*methoxy-4-styryl-* (92%), yellow light-sensitive needles, m. p. 118° (decomp.) (Found: C, 50·1; H, 4·2. $C_{14}H_{14}ONI$ requires C, 49·6; H, 4·2%); and 1-*methoxy-pyridinium iodide* (97%), pale yellow deliquescent needles, rapidly darkening in light, m. p. 90° (decomp.) (Found: C, 31·0; H, 3·5; I, 54·1. C_6H_8ONI requires C, 30·4; H, 3·4; I, 53·6%).

2-Phenylpyridine oxide was recovered unchanged; the products from 2- and 4-benzylpyridine oxide decomposed during their preparation.

4-Phenylpyridine 1-oxide (3·4 g.), heated with dimethyl sulphate (1·9 c.c.) for 12 hr. at 100°, then twice crystallised from ethanol, gave 1-*methoxy-4-phenylpyridinium sulphate* (3·92 g., 66%),

[28] Marvel, Brace, Miller, and Johnson, *J. Amer. Chem. Soc.*, 1949, **71**, 34.

needles, m. p. 100·5° (Found: C, 61·3; H, 5·2; N, 6·0; S, 6·6. $C_{24}H_{26}O_6N_2S$ requires C, 61·5; H, 5·6; N, 6·0; S, 6·8%). The compound gave a precipitate with barium chloride. The product from the 2-analogue was very deliquescent, and was used without characterisation (see above).

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