33. *The Structure and Reactivity of 2-Aminopyridine 1-Oxide.*

By A. R. KATRITZKY.

A convenient preparation of 2-aminopyridine 1-oxide is described. A comparison of its ultraviolet spectrum with those of 2-methylamino- and 2-dimethylamino-pyridine 1-oxide and of 2-methylimino- and 2-imino-1-methoxy-1 : 2-dihydropyridine has shown that 2-aminopyridine 1-oxide does not exist mainly in the tautomeric imino-form. The preparation of these reference compounds is described. 2-Aminopyridine 1-oxide is usually acylated in the amino-group, but a labile *O*-benzoate has been obtained. 2-Aminopyridine 1-oxide can be diazotised. The reasons for the different tautomeric composition of 2-amino- and 2-hydroxy-pyridine 1-oxide are discussed.

NONE of the published methods [1-3] is suitable for the preparation of 2-aminopyridine 1-oxide in quantity. It is now shown that crude 2-ethoxycarbonylaminopyridine [3] may be oxidised and the corresponding 1-oxide hydrolysed without isolation to give 2-aminopyridine 1-oxide in 68% yield.

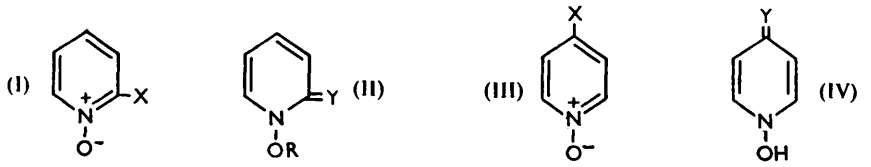
Whereas 2-hydroxypyridine 1-oxide (I; X = OH) exists mainly as the tautomeric 1-hydroxy-2-pyridone (II; R = H, Y = O),[4,5] evidence suggests that neither 4-amino- (III; X = NH_2) nor 4-hydroxy-pyridine 1-oxide (III; X = OH) occurs in the alternative form (IV; Y = NH or O).[6] To determine the precise structure of 2-aminopyridine 1-oxide, methyl derivatives of the two possible forms have been prepared and the ultraviolet spectra compared.

2-Chloropyridine gave the corresponding 1-oxide (isolated as such; contrast the apparently unstable bromo-compound [7]) which was converted by methylamine into 2-methylaminopyridine 1-oxide (I; X = NHMe); the latter gave a strong blue colour

[1] Newbold and Spring, *J.*, 1949, S 133.
[2] Adams and Miyano, *J. Amer. Chem. Soc.*, 1954, **76**, 2785.
[3] Katritzky, *J.*, 1956, 2063.
[4] Shaw, *J. Amer. Chem. Soc.*, 1949, **71**, 67.
[5] Cunningham, Newbold, Spring, and Stark, *J.*, 1949, 2091.
[6] Jaffé, *J. Amer. Chem. Soc.*, 1955, **77**, 4445; but see also Hayashi, *J. Pharm. Soc. Japan*, 1951, **71**, 213.
[7] Shaw, Bernstein, Losee, and Lott, *J. Amer. Chem. Soc.*, 1950, **72**, 4362.

with ferric chloride solution and was acetylated, probably to the *N*-acetyl derivative (I; X = NMeAc); the alternative is an *O*-acetyl structure (II; R = Ac, Y = NMe). Similarly prepared, the oily 2-dimethylaminopyridine 1-oxide (I; X = NMe_2) did not give a colour with ferric chloride; it gave a solid picrate and picrolonate.

2-Amino-, and 2-methylamino-pyridine 1-oxide with methyl toluene-*p*-sulphonate gave 2-amino-1-methoxy- (V; R = Me, R′ = R″ = H) and 1-methoxy-2-methylamino-pyridinium (V; R = R′ = Me, R″ = H) toluene-*p*-sulphonate. Although they could



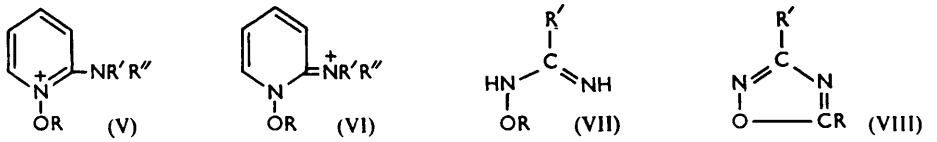
not be isolated, 2-imino- (II; R = Me, Y = NH) and 2-methylimino-1-methoxy-1 : 2-dihydropyridine (II; R = Me, Y = NMe) (or an equivalent quaternary or pseudo-base) were obtained in solution by the action of alkali on these compounds, for from the solution of the imino-compound (II; R = Me, Y = NH) the corresponding picrate and picrolonate were isolated (undoubtedly salts of the ion V; R = Me, R′ = R″ = H). These derivatives were different from those of 2-methylaminopyridine 1-oxide (proving that *O*-methylation had taken place in the reaction of the latter with methyl toluene-*p*-sulphonate) and from those of 2-aminopyridine (so that deoxygenation had not taken place[8]).

The spectra of 2-aminopyridine 1-oxide and its methyl derivatives are shown in Figs. 1 and 2. The curves shown for 1-methoxy-2-methylaminopyridinium toluene-*p*-sulphonate are the measured absorptions less those of an equivalent concentration of toluene-*p*-sulphonic acid in the same solvents. In acid solution (Fig. 1) the spectra are all very similar; mono- and di-*N*-methylation simply shift both maxima to successively higher wavelengths, while *O*-methylation has very little effect. This is understandable, since resonating cations with chief canonical forms (V and VI; R, R′, and R″ = H or Me) would be expected in all cases (from 2-dimethylaminopyridine 1-oxide, etc., by proton addition at the oxygen). In alkaline solution (Fig. 2) the spectra of 2-amino-, 2-methylamino-, and 2-dimethylamino-pyridine 1-oxide are very similar, each showing two maxima and a well-defined inflection, all of which are shifted to higher wavelengths by successive *N*-methylation (except for the higher wavelength maximum on the second methylation, probably due to band overlap). The spectra of 1 : 2-dihydro-2-imino- and 1 : 2-dihydro-2-methylimino-1-methoxypyridine are different, and thus 2-amino- and 2-methylamino-pyridine 1-oxide do not exist in the alternative tautomeric form (II; R = H, Y = NH or NMe) (at least in 0·1N-sodium hydroxide); this conclusion is supported by failure to isolate the *O*-methylated derivatives as the free bases and by further chemical evidence discussed below.

2-Aminopyridine 1-oxide in the tautomeric *N*-hydroxy-form (II; R = H, Y = NH) would be a cyclic amidoxime;[3] some of its reactions have now been compared with those of the amidoximes (VII; R = H).[9] Amidoximes give *O*-acylated derivatives (VII; R = acyl).[9] Benzoylation of 2-aminopyridine 1-oxide in pyridine gave a compound $C_{19}H_{16}O_4N_2$ (compare the formation of a benzamido-benzoate from 2-aminopyridine [10,11]) which with potassium carbonate lost 1 mol. of benzoic acid to give 2-benzamidopyridine 1-oxide, identical with the product obtained on *N*-oxidation of 2-benzamidopyridine. Benzoylation of 2-aminopyridine 1-oxide in acetonitrile gave an isomer of 2-benzamido-pyridine 1-oxide (into which it was slowly converted in ethanol) but with a markedly

[8] Katritzky, *J.*, 1956, 2404.
[9] Tiemann and co-workers; summarising papers, *Ber.*, 1885, **18**, 1060, 2456; 1886, **19**, 1475.
[10] Huntress and Walter, *J. Org. Chem.*, 1948, **13**, 735.
[11] Lur'e, *Zhur. Obshchei Khim.*, 1950, **20**, 195.

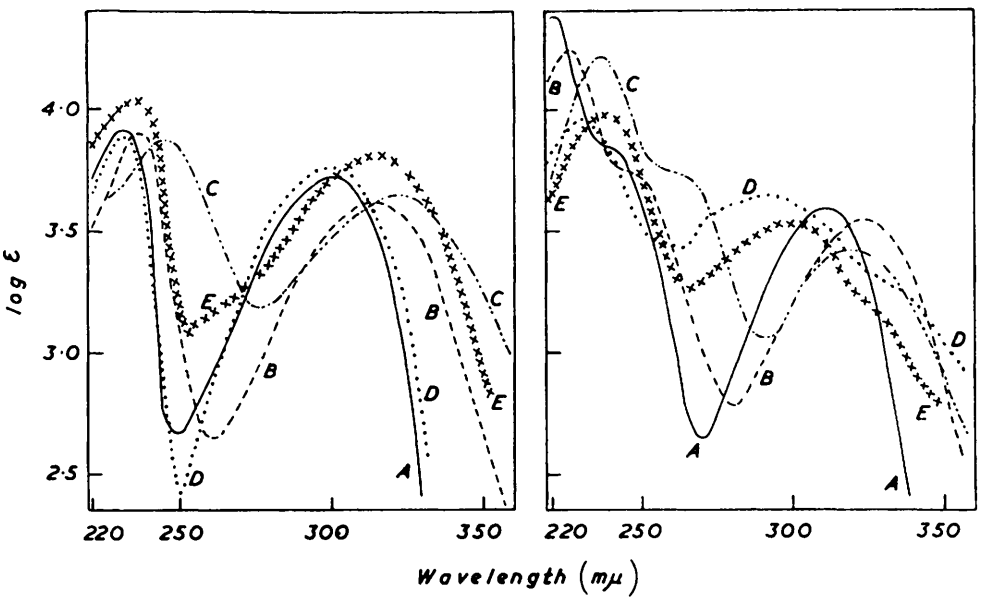
different infrared spectrum. This is probably 1-benzoyloxy-1 : 2-dihydro-2-iminopyridine (II; R = Bz, Y = NH); it gave no colour with ferric chloride. The rearrangement is analogous to that of a benzoyloxy-amine to the corresponding *N*-benzoate,[12]



and to the formation of azoximes (VIII; R = alkyl) from *O*-acylamidoximes (VII; R = acyl).[9]

FIG. 1. *Solvent*: 0·1N-*hydrochloric acid.*

FIG. 2. *Solvent*: 0·1N-*sodium hydroxide.*



A, ———— 2-*Aminopyridine* 1-*oxide* (I; X = NH_2).
B, – – – – – – 2-*Methylaminopyridine* 1-*oxide* (I; X = NHMe).
C, — ·· — ·· — 2-*Dimethylaminopyridine* 1-*oxide* (I; X = NMe_2).
D, ... 2-*Amino*-1-*methoxypyridinium perchlorate* (V; R = Me, R′ = R″ = H).
E, × × × × 1-*Methoxy*-2-*methylaminopyridinium toluene*-p-*sulphonate* (V; R = R′ = Me, R″ = H) (corrected).

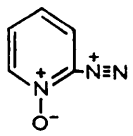
2-Aminopyridine 1-oxide was also acylated by ethyl chloroformate, acetic anhydride, phenyl *iso*cyanate, ethyl oxalate, and 3 : 5-dinitrobenzoyl chloride. In each case a single product was obtained; the first four were identical with the products of *N*-oxidation of, respectively, 2-ethoxycarbonylamino-, 2-acetamido-, and 2-*N*′-phenylureido-pyridine, and *NN*′-di-2-pyridyloxamide and were therefore *N*-acyl derivatives (for a rearrangement in the latter reaction seems unlikely). The structure of 2-(3 : 5-dinitrobenzamido)pyridine 1-oxide was assumed by analogy. Mechanistically, it is likely that the acylations go *via* labile *O*-acyl compounds which isomerise to *N*-acyl derivatives before isolation.

Amidoximes are weakly acidic, and are alkylated in alkaline solution to *O*-alkyl derivatives (VII; R = alkyl).[9] 2-Aminopyridine 1-oxide was recovered after treatment with sodium ethoxide–benzyl chloride, although it was methylated under neutral conditions (see above).

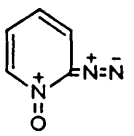
2-Aminopyridine 1-oxide can be diazotised and coupled with β-naphthol in the same

[12] *E.g.*, Grob and Wagner, *Helv. Chim. Acta*, 1955, **38**, 1699.

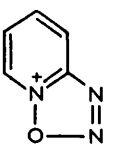
way as the 4-isomer.[13] The far greater stability of (pyridine 1-oxide)-2- and -4-diazonium ions than of pyridine-2- and -4-diazonium ions is doubtless due to canonical forms such as (IX) and (X) both contributing to the resonance hybrid. The (pyridine 1-oxide)-2-diazonium ion may also show valency-bond tautomerism[14] with the ion (XI); the reactions of the latter are under investigation.



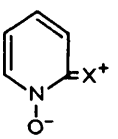
(IX)



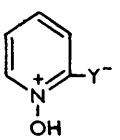
(X)



(XI)



(XII)



(XIII)

The difference in the structure of 2-hydroxy- and 2-amino-pyridine 1-oxides is clarified by considering the mesomerism of the two possible tautomers. In the *N*-oxide the chief canonical forms are (I; X = OH and NH_2) and (XII; X = OH and NH_2); in the *N*-hydroxy-tautomer they are (II; Y = O and NH) and (XIII; Y = O and NH). The contribution from the canonical form (XII) will be more important when X = NH_2 than when X = OH, and conversely that from (XIII) when Y = O than when Y = NH, which explains the differences in precise structure actually found. The 2-acylaminopyridine 1-oxides occupy an intermediate position for in donor power NH_2 > NHAcyl > OH, and in acceptor power :NH < :NAcyl < :O. The structures of some of these compounds are under investigation.

Experimental

0·1N-Sodium hydroxide and -hydrochloric acid for spectral results refer to aqueous solutions.

2-Aminopyridine 1-Oxide.—Crude 2-ethoxycarbonylaminopyridine[3] (36 g.), acetic acid (72 c.c.), and hydrogen peroxide (30% aqueous solution; 43 c.c.) were kept at 70° overnight; the solid which separated on cooling was filtered off. Volatile material was removed from the filtrate at 100°/20 mm., and the residue, together with the solid that had been filtered off, refluxed with concentrated hydrochloric acid (40 c.c.) overnight. Volatile material was removed at 100°/20 mm., and ethanol (50 c.c.) and then ethanolic sodium ethoxide (from 6 g. of sodium and 150 c.c. of ethanol) were added, followed by small pieces of solid carbon dioxide until the solution was no longer strongly alkaline. Filtration, evaporation of the filtrate, and crystallisation of the residue (21 g.) from ethanol–ethyl acetate gave 2-aminopyridine 1-oxide (16·1 g.; 68%), m. p. 157—162°. Further recrystallisation raised the m. p. to 163—164° (lit.,[1,2] 161—163°, 164—165°). Light absorption: max. at 231, 301 mμ (ε 8080, 5230) in 0·1N-hydrochloric acid; max. at 221, 310 mμ (ε 23,300, 3900), infl. at 239 mμ (ε 6900) in 0·1N-sodium hydroxide; max. at 227, 251, 321 mμ (ε 25,000, 5740, 4610) (the trough between the first two maxima is very shallow) in ethanol [lit.;[1] max. at 226, 319 mμ (ε 21,000, 5000), infl. at 248 mμ (ε 4000) in ethanol].

2-Chloropyridine 1-Oxide.—2-Chloropyridine (22·6 g.), acetic acid (150 c.c.), and 30% aqueous hydrogen peroxide (50 c.c.) were heated overnight at 80°. Volatile material was removed at 100°/20 mm., chloroform (140 c.c.) added, and the mixture digested with potassium carbonate (17 g.) at 65° for 5 min. Solid was filtered off and washed with chloroform (60 c.c.); evaporation of filtrate and washings gave the *oxide* (19·75 g., 77%) in prisms (from ethyl acetate), m. p. 67—68·5° (Found: C, 46·5; H, 3·3. C_5H_4ONCl requires C, 46·3; H, 3·1%).

2-Methylaminopyridine 1-Oxide.—2-Chloropyridine 1-oxide (7 g.) and 25% aqueous methylamine (40 c.c.) were heated at 140° for 12 hr., potassium carbonate (4 g.) was added, and the whole was evaporated to dryness at 100°/20 mm. The residue was extracted with ethanol, and the extracts evaporated; the *methylamino*-derivative crystallised from ethyl acetate in needles (5·5 g., 82%), m. p. 103—105°, or prisms, m. p. 68—70° (Found: C, 57·8; H, 6·6. $C_6H_8ON_2$ requires C, 58·1; H, 6·4%). The compound gave a dark blue colour with ferric chloride. Light absorption: max. at 236, 314 mμ (ε 7950, 4250) in 0·1N-hydrochloric acid; max. at 226, 324 mμ (ε 18,700, 3640), infl. at 246 mμ (ε 5500) in 0·1N-sodium hydroxide.

The *picrate* formed needles (from ethanol), m. p. 155·5—157° (Found: C, 41·0; H, 3·3.

[13] Ochiai, *J. Org. Chem.*, 1953, **18**, 543.
[14] Baker, "Tautomerism," Routledge, London, 1934, pp. 201—226.

$C_{16}H_{16}O_6N_6$ requires C, 40·8; H, 3·1%). The *picrolonate* separated from ethanol in yellow needles, m. p. 201—203° (Found: C, 49·6; H, 4·0; N, 21·8. $C_{16}H_{16}O_6N_6$ requires C, 49·5; H, 4·1; N, 21·7%). The *hydrochloride* formed needles, m. p. 203—204° (from ethanol) (Found: C, 45·0; H, 5·8; N, 17·4. $C_6H_9ON_2Cl$ requires C, 44·9; H, 5·6; N, 17·4%).

To the 2-methylaminopyridine 1-oxide (0·3 g.) in boiling acetonitrile (3 c.c.), was added acetic anhydride (0·5 c.c.), and the whole left overnight at 18°. Ethanol was added; the whole was evaporated at 100°/20 mm., and treated with chloroform and potassium carbonate. After filtration, evaporation gave the *acetyl derivative* (0·28 g., 70%), hygroscopic prisms, m. p. 95—97° (from ethyl acetate), which gave no colour with ferric chloride (Found: C, 58·2; H, 6·1; N, 17·2. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·0; N, 16·9%).

2-Dimethylaminopyridine 1-Oxide.—Prepared as for the methylamino-analogue, the oily *dimethylamino*-derivative (*ca.* 80%), b. p. 143—145° (bath)/0·25 mm., n_D^{20} 1·6117, gave no colour with ferric chloride (Found: C, 60·9; H, 7·4. $C_7H_{10}ON_2$ requires C, 60·9; H, 7·2%). Light absorption: max. at 243, 320 mμ (ε 7370, 4470) in 0·1N-hydrochloric acid; max. at 236, 319 mμ (ε 16,500, 2690), infl. at 261 mμ (ε 5400) in 0·1N-sodium hydroxide.

The *picrate* (plates from ethanol) had m. p. 142·5—144° (Found: C, 42·4; H, 3·7; N, 19·1. $C_{13}H_{13}O_8N_5$ requires C, 42·5; H, 3·5; N, 19·1%). The *picrolonate* (orange-yellow prisms from ethanol) had m. p. 180—181° (decomp.) (Found: C, 50·5; H, 4·3; N, 21·0. $C_{17}H_{18}O_6N_6$ requires C, 50·7; H, 4·5; N, 20·9%).

Attempted Preparation of 1 : 2-*Dihydro*-2-*imino*-1-*methoxypyridine*.—2-Aminopyridine 1-oxide (5·5 g.) was heated at 100° overnight with methyl toluene-*p*-sulphonate (9·3 g.); the product crystallised from ethanol–ethyl acetate, giving 2-*amino*-1-*methoxypyridinium toluene*-p-*sulphonate* (12·66 g., 85%) as prisms, m. p. 127—129° (Found: C, 53·1; H, 5·5; N, 9·3. $C_{13}H_{16}O_4N_2S$ requires C, 52·7; H, 5·4; N, 9·5%). No colour was given with ferric chloride.

The above toluene-*p*-sulphonate (0·6 g.,) in ethanol was treated with sodium ethoxide (5·5 c.c. of 0·4N-ethanolic solution), solid was filtered off, carbon dioxide was passed into the filtrate, and solid was again filtered off. Addition of picric acid (0·46 g.) in ethanol now gave 2-*amino*-1-*methoxypyridinium picrate* (0·40 g., 56%), yellow needles, m. p. 169·5—171° (from ethanol) (Found: C, 40·9; H, 3·1; N, 19·8. $C_{12}H_{11}O_8N_5$ requires C, 40·8; H, 3·1; N, 19·8%). The infrared spectrum was quite distinct from those of 2-methylaminopyridine 1-oxide picrate (above) and 2-aminopyridinium picrate. The last compound formed needles (from ethanol), m. p. 222—223° (lit.,[15] m. p. 216—217°) (Found: C, 40·9; H, 3·0. Calc. for $C_{11}H_9O_7N_5$: C, 40·9; H, 2·8%).

2-*Amino*-1-*methoxypyridinium picrolonate*, prepared as for the picrate, formed yellow prisms (from ethanol), m. p. 245—247° (decomp.) (Found: C, 49·9; H, 4·0; N, 21·4. $C_{16}H_{16}O_6N_6$, requires C, 49·5; H, 4·1; N, 21·6%). The infrared spectrum was distinct from those of 2-methylaminopyridine 1-oxide picrolonate and 2-*aminopyridinium picrolonate* [yellow prisms, m. p. 269—271° (decomp.), from ethanol] (Found: C, 50·4; H, 3·8; N, 23·6. $C_{15}H_{14}O_5N_6$ requires C, 50·3; H, 3·9; N, 23·5%).

2-Amino-1-methoxypyridinium toluene-*p*-sulphonate (1·48 g.) in ethanol (3 c.c.) mixed with perchloric acid (60%, 0·8 c.c.) gave the corresponding *perchlorate* (0·95 g., 85%), laths (from ethanol), m. p. 182—184° (Found: C, 32·5; H, 4·2. $C_6H_9O_5N_2Cl$ requires C, 32·1; H, 4·0%). Light absorption: max. at 230, 299 mμ (ε 7670, 5870) in 0·1N-hydrochloric acid; max. at 230, 291 mμ (ε 8890, 4400) in 0·1N-sodium hydroxide.

The toluene-*p*-sulphonate (0·6 g.), in pyridine (3 c.c.), and 3 : 5-dinitrobenzoyl chloride (0·46 g.) kept overnight at room temperature and then treated with aqueous sodium hydroxide gave 2-(3 : 5-*dinitrobenzoylimino*)-1 : 2-*dihydro*-1-*methoxypyridine*, pale yellow needles, m. p. 219—220°, from ethanol (Found: C, 49·3; H, 3·3; N, 17·3. $C_{13}H_{10}O_6N_4$ requires C, 49·1; H, 3·1; N, 17·6%).

Attempted Preparation of 1 : 2-*Dihydro*-1-*methoxy*-2-*methyliminopyridine*.—2-Methylaminopyridine 1-oxide (1·24 g.) and methyl toluene-*p*-sulphonate (1·86 g.) when heated for 24 hr. at 100° gave 1-*methoxy*-2-*methylaminopyridinium toluene*-p-*sulphonate*, obtained from acetonitrile–ethyl acetate in prisms (2·33 g., 75%), m. p. 98—100° (Found: C, 53·9; H, 5·9. $C_{14}H_{18}O_4N_2S$ requires C, 54·2; H, 5·8%). Light absorption: max. at 224, 314 mμ (ε 16,400, 6590) in 0·1N-hydrochloric acid; max. at 224, 297, 302 mμ (ε 15,000, 3390, 3370), infl. at 236 mμ (ε 9650) in 0·1N-sodium hydroxide. The absorption of toluene-*p*-sulphonic acid was measured in the same solvent and subtracted from the above figures to give the

[15] Tschitschibabin, *Ber.*, 1924, **57**, 1168.

absorption due to the heterocyclic portion of the molecule. The corrected figures were: max. at 235, 314 mμ (ε 10,900, 6590) in 0·1N-hydrochloric acid; max. at 237, 297, 302 mμ (ε 9400, 3390, 3370) in 0·1N-sodium hydroxide.

Reaction of 2-Aminopyridine 1-Oxide with Benzoyl Chloride.—2-Aminopyridine 1-oxide (1 g.), pyridine (6 c.c.), and benzoyl chloride (2·4 c.c.) were kept overnight; addition of water then gave *2-benzamidopyridine 1-oxide benzoate* (1·57 g., 51%), needles, m. p. 94—95°, from 1 : 1-benzene–light petroleum (b. p. 40—60°) (Found: C, 67·8; H, 4·8; N, 8·3. $C_{19}H_{16}O_4N_2$ requires C, 67·8; H, 4·8; N, 8·3%).

This benzoate (0·75 g.) was treated in chloroform with potassium carbonate (1 g.) and the whole filtered. The solid with dilute hydrochloric acid gave benzoic acid (m. p. and mixed m. p. 120—121°). Evaporation of the chloroform solution gave *2-benzamidopyridine 1-oxide* (0·47 g., 98%), laths, m. p. 122—124°, from ethanol (Found: C, 67·2; H, 4·7; N, 13·0. $C_{12}H_{10}O_2N_2$ requires C, 67·3; H, 4·7; N, 13·1%). A red colour was given with ferric chloride.

Benzoyl chloride (0·6 c.c.) and 2-aminopyridine 1-oxide (0·55 g.) in hot acetonitrile (5 c.c.), kept at room temperature overnight, gave *1-benzoyloxy-1 : 2-dihydro-2-iminopyridine* (0·43 g., 40%), needles (from ethanol), m. p. 158—159° (Found: C, 66·9; H, 4·9; N, 12·8. $C_{12}H_{10}O_2N_2$ requires C, 67·3; H, 4·7; N, 13·1%). No colour was given with ferric chloride.

When 1-benzoyloxy-1 : 2-dihydro-2-iminopyridine was recrystallised from ethanol and left in the mother liquor for 4 days, it gradually redissolved and 1-benzamidopyridine 1-oxide separated; this was identical (m. p., mixed m. p., and infrared spectra) with the material described above.

2-Benzamidopyridine [10,11] (0·32 g.), acetic acid (6 c.c.), and hydrogen peroxide (30% aqueous solution; 0·2 c.c.) were kept overnight at 70°; the whole was evaporated, and treated in chloroform with potassium carbonate to give (from the chloroform) the corresponding 1-oxide, identical with the specimens prepared by the two methods described above (m. p., mixed m. p., and infrared spectra).

Reaction of 2-Aminopyridine 1-Oxide with other Acid Chlorides, Anhydride, and Esters.—(i) The amine (0·55 g.) in hot acetonitrile (10 c.c.) was treated with ethyl chloroformate (0·5 c.c.) and kept for 2 days. Evaporation followed by treatment of the residue in chloroform with potassium carbonate, evaporation, and crystallisation from ether gave a low yield of 2-ethoxycarbonylaminopyridine 1-oxide, identical with an authentic specimen [3] (m. p., mixed m. p., and infrared spectra).

(ii) The amine (1·1 g.), acetonitrile (10 c.c.), and acetic anhydride (1 c.c.) were kept overnight, and the mixture treated with potassium carbonate and evaporated. Crystallisation of the residue from ethyl acetate gave 2-acetamidopyridine 1-oxide (0·82 g., 58%), as rods, m. p. 137—140° raised to 140·5—141° by recrystallisation (Found: C, 55·1; H, 5·4. Calc. for $C_7H_8O_2N_2$: C, 55·3; H, 5·3%). (Lit.,[2] m. p. 130—131°.)

Authentic 2-acetamidopyridine 1-oxide was prepared as described by Adams and Miyano,[2] except that the product after evaporation was treated in chloroform with potassium carbonate; it was identical with the specimen described above (m. p. and mixed m. p.). The compound gave a deep red colour with ferric chloride.

(iii) The amine (1 g.) and ethyl oxalate (3 c.c.) were boiled for 10 min. Addition of ethanol to the cooled solution gave *NN'*-di-2-pyridyloxamide 1 : 1'-dioxide (0·2 g., 16%) which separated from acetic acid as the *diacetate*, plates, m. p. *ca.* 270° (decomp.) (varies with rate of heating (Found: C, 48·5; H, 4·6; N, 14·0. $C_{12}H_{10}O_4N_4,2C_2H_4O_2$ requires C, 48·7; H, 4·6; N, 14·2%).

NN'-Di-2-pyridyloxamide, prepared as given by Tschitschibabin,[15] had m. p. 161—163·5° (lit.,[15] 161—162°). The oxamide (1·2 g.), acetic acid (4·5 c.c.), and hydrogen peroxide (1·4 c.c.), when kept overnight at 70°, gave the corresponding 1 : 1'-dioxide diacetate, identical with the specimen described above (infrared spectra).

(iv) Phenyl *iso*cyanate (0·6 c.c.) was added to 2-aminopyridine 1-oxide (0·55 g.) in hot acetonitrile (10 c.c.). After 2 days at room temperature solid was filtered off; it was separated by fractional crystallisation from ethanol into carbanilide, and (less soluble) *2-N'-phenylureidopyridine 1-oxide* (0·52 g., 45%), needles the m. p. of which varied from 212—213° to 220—220·5° according to the rate of heating (Found: C, 63·1; H, 4·9; N, 17·9. $C_{12}H_{11}O_2N_3$ requires C, 62·9; H, 4·8; N, 18·3%).

2-*N'*-Phenylureidopyridine was prepared by Camps's method; [16] it formed needles, m. p.

[16] Camps, *Arch. Pharm.*, 1902, **240**, 345.

188—190° (lit.,[16] m. p. 180°) (Found: C, 67·4; H, 5·2. Calc. for $C_{12}H_{11}ON_3$: C, 67·6; H, 5·2%).

2-*N'*-Phenylureidopyridine (1 g.), acetic acid (2 c.c.), and hydrogen peroxide (0·5 c.c.) were kept overnight at 70°; evaporation at 100°/20 mm. and treatment of the residue in chloroform with potassium carbonate gave the corresponding 1-oxide, identical with the specimen described above (m. p., mixed m. p., and infrared spectra).

(v) 3 : 5-Dinitrobenzoyl chloride (1·15 g.) was added to the amine (0·55 g.) in hot acetonitrile (10 c.c.); a vigorous reaction ensued. After 3 hr. at room temperature the mixture was poured into aqueous sodium carbonate to give 2-(3 : 5-*dinitrobenzamido*)*pyridine* 1-*oxide* (0·98 g., 65%), which separated from acetic acid as the *acetate*, needles, m. p. 216—217° (Found: C, 46·3; H, 3·4; N, 15·5. $C_{12}H_8O_6N_4,C_2H_4O_2$ requires C, 46·2; H, 3·3; N, 15·4%). Reaction in pyridine solution gave the same product.

(vi) After 2-aminopyridine 1-oxide had been refluxed with ethyl carbonate for 8 hr., 90% was unchanged. Heating 2-aminopyridine 1-oxide with phthalic anhydride gave a tar. 2-Aminopyridine 1-oxide did not react smoothly with α-naphthyl thiocyanate or carbon disulphide.

2-Ethoxycarbonylaminopyridine (1·66 g.) was refluxed for 18 hr. with morpholine (0·9 c.c.). The mixture solidified on cooling, and crystallisation from benzene–light petroleum (b. p. 40—60°) gave 2-*morpholinocarbonylaminopyridine* (1·05 g., 52%) as needles, m. p. 86—91° raised by recrystallisation to 91—92·5° (Found: C, 57·7; H, 6·2. $C_{10}H_{13}O_2N_3$ requires C, 58·0; H, 6·3%).

2-(2-*Hydroxy*-1-*naphthylazo*)*pyridine* 1-*Oxide*.—To 2-aminopyridine 1-oxide (1·1 g.) in concentrated hydrochloric acid (2 c.c.) was added ice (4 g.) followed by aqueous potassium nitrite (0·9 g. in 5 c.c.) dropwise. The mixture was gradually added to β-naphthol (1·44 g.) in aqueous sodium hydroxide (10%; 12 c.c.) and ice (6 g.) The *azo-oxide* (1·15 g., 44%) separated from ethanol in crimson plates; it had m. p. 215—216° (decomp.) (Found: C, 68·1; H, 4·5; N, 15·6. $C_{15}H_{11}O_2N_3$ requires C, 67·9; H, 4·2; N, 15·8%). Light absorption: max. at 225, 292, 466 mμ (ε 12,100, 5800, 5600) in ethanol.

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