Electrophilic Aromatic Reactivities *via* Pyrolysis of 1-Arylethyl Acetates. Part X.[1] Pyridine *N*-Oxide

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All three 1-acetoxyethylpyridine *N*-oxides have been prepared and the rates of elimination of acetic acid from these esters and from 1-phenylethyl acetate have been measured over a 50° range for each compound at temperatures between 286 and 402°. The rates lead to σ^+ values of +0·81 and +0·016 for the 3- and 4-positions respectively, in good agreement with both theoretical predictions and the qualitative observations of electrophilic substitution. The reactivity of the 4-position lends strong support to the belief that nitration of pyridine *N*-oxide does not take place on the free base. The 2-compound is very much more reactive than the other isomers (contrary to theoretical prediction) and gives 2-acetylpyridine instead of the expected 2-vinylpyridine *N*-oxide as the elimination product. 2-Acetylpyridine is also obtained on elimination of water from 2-(1-hydroxyethyl)pyridine *N*-oxide which proceeds at almost the same rate as elimination of acetic acid from the acetate. The high reactivity is attributed either to acceleration of the loss of the functional group in the side chain through a neighbouring group effect (followed by rearrangement) or to an initial insertion of the oxygen into the side chain α-C–H bond followed by rapid elimination from the 1,1-diol (and its acetyl derivative). The literature mechanism for the 3-nitration of quinoline *N*-oxide is shown to be highly unlikely, and an alternative is suggested.

THE quantitative electrophilic reactivity of pyridine *N*-oxide has hitherto not been completely evaluated. A number of electrophilic substitutions of the molecule have been carried out and this work has been extensively reviewed.[2-4] One of the main problems has been to decide which of the free base or protonated species is involved in the reaction. Sulphonation,[5] halogenation,[6] and hydrogen exchange (of methylated derivatives)[7] under severe conditions lead to 3-substitution, and the reactions are believed to involve the conjugate acid. The last reaction of substituted pyridine *N*-oxides indicates that for reaction on the free base a value of σ^+ for the 3-position of 0·8 applies. Halogenation under milder conditions and nitration both give 4-substitution, the latter reaction doing so almost exclusively, whereas for the former reaction the yield of product (which includes some 2-substituted material) is very low; for both these reactions the free base has been postulated as the reacting species.[8] In contrast to these reactions, mercuration gives mainly 2-substitution which was attributed to initial co-ordination of the electrophile with the negative oxygen,[9] but an alternative explanation for this 2-substitution is described below.

Although nitration has been considered to occur on the free base, more recent work on pre-exponential functions indicates that this is not the reacting species (and rate profiles show that the conjugate acid is not involved either).[10] The partial rate factor for the 4-position of 2×10^{-3} disagrees markedly with predictions of π-electron densities or localisation energies, and further indicates that reaction does not take place upon the free base.

The difficulty with the above reactions is to produce

[1] Part IX, E. Glyde and R. Taylor, *J.C.S. Perkin II*, 1973, 1632.

[2] E. Ochiai, 'Aromatic Amine Oxides,' Elsevier, Amsterdam, 1967, pp. 210—243.

[3] K. Schofield, 'Heteroaromatic Nitrogen Compounds,' Butterworths, London, 1967, pp. 162—199.

[4] A. R. Katritzky and J. M. Lagowski, 'Chemistry of the Heterocyclic *N*-Oxides,' Academic Press, London, 1971, pp. 231—257.

[5] H. S. Mosher and F. J. Welch, *J. Amer. Chem. Soc.*, 1955, **77**, 2902.

[6] M. van Ammers, H. J. den Hertog, and B. Haase, *Tetrahedron*, 1962, **18**, 227.

[7] G. P. Bean, P. J. Brignell, C. D. Johnson, A. R. Katritzky, and C. J. Ridgewell, *J. Chem. Soc.* (*B*), 1967, 1222.

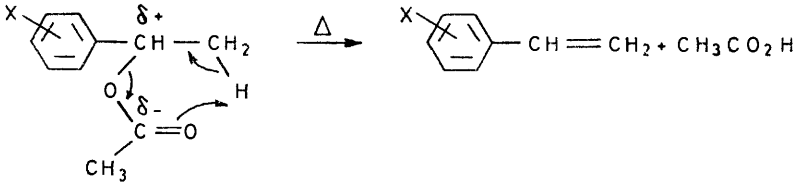
[8] H. C. van der Plaas, H. J. den Hertog, M. van Ammers, and B. Haase, *Tetrahedron Letters*, 1961, 32; E. Ochiai, K. Asima, and M. Ishikawa, *J. Pharm. Soc. Japan*, 1943, **63**, 79; H. J. den Hertog and J. Overhoff, *Rec. Trav. chim.*, 1950, **69**, 468.

[9] M. van Ammers and H. J. den Hertog, *Rec. Trav. chim.*, 1958, **77**, 340; 1962, **81**, 124.

[10] J. T. Gleghorn, R. B. Moodie, E. A. Qureshi, and K. Schofield, *J. Chem. Soc.* (*B*), 1968, 316.

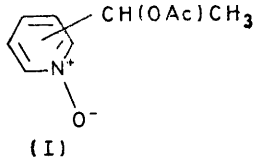
substitution on the unprotonated or unco-ordinated species. Since electrophilic substitutions by definition have positive species in solution, and the negative oxygen has by far the highest electron density in the molecule, co-ordination is obviously very likely! Once co-ordination occurs the reactivity of the molecule becomes so low that accurate quantitative measurement of the reactivity relative to benzene is extremely difficult.

This situation is one where the pyrolysis of 1-arylethyl acetates (Scheme 1) becomes superior to other



SCHEME 1

reactions. The reacting species is unquestionably the free base and the low ρ factor for the reaction (−0·66 at 600 K) allows accurate measurement of widely differing reactivities. The first quantitative measurements of the electrophilic reactivities of the heterocycles furan, thiophen, pyridine, and quinoline[11] have been made using the reaction; we now describe its use in determining the quantitative reactivity of pyridine *N*-oxide through pyrolysis of the esters (I) and comparison of their reactivities with that of 1-phenylethyl acetate.



(I)

RESULTS AND DISCUSSION

Rate coefficients, temperatures at which they were obtained, and the thermodynamic parameters are given in Table 1 together with the log k/k_0 values at 625 K. For the 2-compound the latter value was obtained by a small extrapolation of the Arrhenius plot. The thermodynamic parameters are shown together with the errors for 95% confidence limits. From the log k/k_0 values the σ^+ values were calculated using a ρ factor of −0·63 at 625 K.[11] The 2- and 4-isomers were injected into the reactor as solutions in chlorobenzene since this is known not to affect reaction rates nor to decompose under the reaction conditions. For evaluation of the cause of the very high reactivity of the 2-isomer, kinetic studies were also carried out on the alcohol precursor which was also pyrolysed very rapidly (*ca.* half the rate of the ester). However, the alcohol had to be injected into the reactor in aqueous solution which introduces the possibility that its pyrolysis rate was diminished somewhat through hydrogen bonding. Some indication that this was so was given by the fact that an aqueous solution of the ester gave a pyrolysis rate diminished by 25% so that we are only able firmly to conclude that the alcohol is at *least* half as reactive as the ester.

The first feature of the results is the σ^+ value for the 3-position of +0·81. This is in excellent agreement with the value of 0·8 which has been deduced (for reaction of the free base) from rates of hydrogen exchange of the conjugate acid.[7] It is somewhat lower than the value of 1·18 determined from the carbonyl stretching frequencies of acetylpyridine *N*-oxides.[12] However the latter approach to determining σ^+ values is less well documented than the present method and moreover, a very small error in measuring the frequency leads to a large error in σ^+. This latter work does however indicate that there should be a large difference in the σ^+ values for the 3- and 4-positions (0·95 σ units) and this difference is similar to the value of 0·79 obtained here.

The σ^+ value for the 4-position (+0·016) shows that in electrophilic substitution, the 4-position should not be significantly deactivated. By contrast however, the

TABLE 1

Pyrolysis of pyridine *N*-oxide esters *X*-[MeCH(OAc)]C_5H_4NO

		$10^3k/s^{-1}$			
T/°C	*X*	2	3	4	PhCHMe-(OAc)
286·3		4·12			
293·0		6·29			
310·4		18·6			
321·2		33·6			
331·4		64·0 [a–c]			
337·8		85·0 [a]			
350·7			0·94	3·04	3·13
368·7			2·60	7·50	8·13
384·6			5·68	17·5	18·6
394·8			8·98		30·6
402·2			13·6	40·5	43·7
r		0·9996	0·9996	0·9998	0·9999
log(A/s^{-1})		13·20	12·00	12·29	12·53
		(0·58)	(0·72)	(0·94)	(0·15)
E/kcal mol^{-1}		39·9	42·4	42·2	42·9
		(1·5)	(1·8)	(2·8)	(0·5)
S/cal mol^{-1} K^{-1}		+0·55	−5·1	−3·8	−2·7
		(2·0)	(3·3)	(4·3)	(0·7)
log k/k_0 (at 625 K)		1·73	−0·51	−0·01	0
σ^+		(−2·75)	+0·81	+0·016	0

[a] At these temperatures the rate coefficients (10^3k/s^{-1}) for pyrolysis of the corresponding 1-arylethyl alcohol were 30·2 and 43·5 respectively. [b] An aqueous solution of the ester at this temperature gave a rate coefficient (10^3k/s^{-1}) of 46·0. [c] At this temperature 10^3k/s^{-1} for t-butyl acetate = 48·3; *cf.* 48·45 interpolated from the literature values (E. U. Emovon and A. Maccoll, *J. Chem. Soc.*, 1962, 335).

[11] R. Taylor, *J. Chem. Soc.*, 1962, 4881; *J. Chem. Soc.* (*B*), 1968, 1397; 1971, 2382.

[12] H. Shindo, *Chem. and Pharm. Bull.* (*Japan*), 1958, **6**, 117.

result for nitration (a deactivation by a factor of *ca.* 10^{-3} with almost exclusive 4-substitution [13]) would require a σ^+ value of +0·41 so that this confirms the proposal [13] that nitration does not take place upon the free base. It has been suggested that the nitronium ion co-ordinates with the negative oxygen, subsequent rearrangement (analogous to the nitramine rearrangement) giving the observed substitution pattern.[13] This is possible as is also a mechanism in which a hydrogen-bonded species is involved. This would produce a moderate rate retardation yet might not cause a change in the orientation pattern as would full protonation. For example, in hydrogen exchange in trifluoroacetic acid the methoxy-substituent is hydrogen bonded; the strong *ortho,para*-directing ability is retained, yet the activating effect in the *para*-position is reduced by the equivalent of 0·2 σ units.[14] The oxygen in pyridine *N*-oxide could be expected to be more strongly hydrogen bonded as indeed is indicated by the high water solubility of the molecule.

A particularly significant feature of the reactivities of the 3- and 4-positions is that they are exactly as predicted by π-electron densities (calculated with $\beta_{NO} = 0{\cdot}8\beta_{CC}$) and the reactivity order is correctly given by the localisation energies, though these incorrectly predict that the 4-position should be activated towards substitution (Table 2). It is relevant therefore that we previously found π-electron densities to be the most successful parameters for correlating the reactivities of pyridine and quinoline.[11]

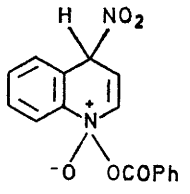
TABLE 2

Predicted [a] and observed reactivities of pyridine *N*-oxide

Position	log k_{rel}	π Electron densities [b]	Localization energies [b]
2	(1·73)	1·011	2·34 β
4	−0·01	0·999	2·42 β
3	−0·51	0·987	2·58 β

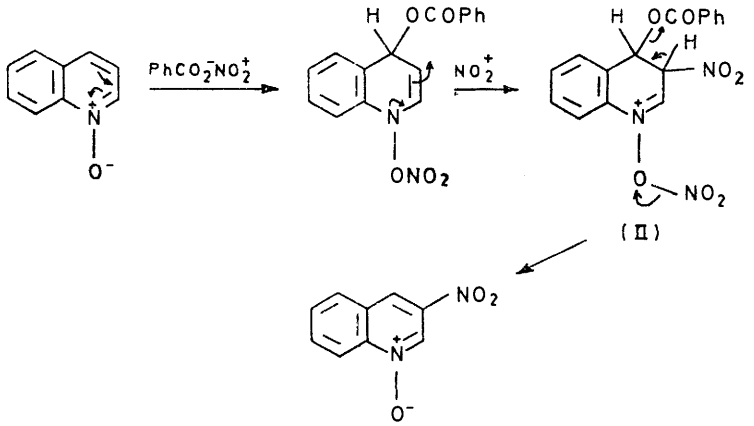
[a] R. A. Barnes, *J. Amer. Chem. Soc.*, 1959, **81**, 1935. [b] For benzene the values are 1·00 and 2·54 β respectively.

Although nitration under acidic conditions occurs at the 4-position, the substitution pattern with acyl nitrates is less clearly defined. Thus pyridine *N*-oxide itself gives the 3-isomer but in low yield, and quinoline *N*-oxide gives 40% of 3-substitution together with a small amount of 6-substitution.[15] A mechanism has been proposed for this latter (Scheme 2),[16] and is almost certainly incorrect. It requires bimolecularity in nitrating species, an eclipsed intermediate (II), and neutralisation of the positive charge on the ring nitrogen through a forbidden $\pi \longrightarrow n$ transition, *i.e.* the mechanism assumes cancellation of a positive charge in a σ orbital by acquisition of a negative charge in a π-orbital, which is probably invalid. A more probable explanation takes account of the very recent observation of rearrangement of adducts formed in nitration under these conditions.[17] In these adducts, the nitro-group becomes initially attached to the point of highest electron density in the ring and subsequently rearranges to an adjacent site. The sites of highest electron density in quinoline *N*-oxide should be the 4- and 5-positions leading to adducts such as (III),



(III)

rearrangement of which would produce 3- and 6-substitution, exactly as observed.



SCHEME 2

[13] J. Gleghorn, R. B. Moodie, K. Schofield, and M. J. Williamson, *J. Chem. Soc.* (*B*), 1966, 870.

[14] R. Taylor, 'Specialist Periodical Report on Aromatic and Heteroaromatic Chemistry,' 1971–1972, The Chemical Society, London, p. 181.

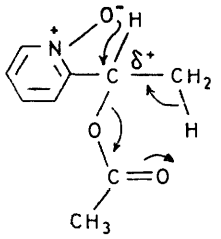
[15] E. Ochiai and C. Kaneko, *Chem. and Pharm. Bull.* (*Japan*), 1951, **5**, 56; 1959, **7**, 191, 195.

[16] E. Ochiai and C. Kaneko, *Chem. and Pharm. Bull.* (*Japan*), 1959, **7**, 267.

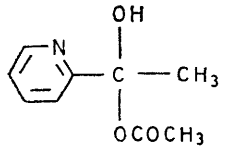
[17] R. Taylor, 'Specialist Periodical Report on Aromatic and Heteroatomic Chemistry,' 1972–1973, The Chemical Society, London, pp. 242—244.

The 2-isomer possesses an anomalously high reactivity (an indication of which is the fact that a σ^+ value of −2·75 would be required to correlate the reactivity in linear free energy terms). At first we believed this enhancement to arise from a direct field effect since this is particularly effective in side-chain reactions.[18] Furthermore the kinetics of the elimination are first order and lead to Arrhenius parameters commensurate with those obtained from the other isomers. However, product analysis revealed the presence of 2-acetylpyridine instead of the expected 2-vinylpyridine *N*-oxide. The possibility that the latter isomerises to the former under the reaction conditions was discounted by the following. (i) The literature contains many accounts of reactions performed with 2-vinylpyridine *N*-oxide with no reference to isomerisation.[19] (ii) Test tube pyrolyses of the ester in diphenyl ether gave 2-acetylpyridine (and acetic acid) but no 2-vinylpyridine *N*-oxide, whereas pyrolyses of 2-(2-hydroxyethyl)pyridine *N*-oxide under the same conditions revealed the latter but no trace of the former, *i.e.* under the conditions which produce 2-acetylpyridine, 2-vinylpyridine *N*-oxide does not isomerise.

By contrast 2-(1-hydroxyethyl)pyridine *N*-oxide, the precursor of the ester also produces only 2-acetylpyridine by the same treatment and at almost the same rate as does the ester. This immediately disposes of



(IV)



(V)

the possibility that the ester decomposes *via* nucleophilic attack of the negative oxygen upon the carbonyl group in the ester followed by rearrangement. Two possibilities therefore remain. (i) A neighbouring group participates in stabilising the intermediate incipient carbonium ion as in (IV) followed by rearrangement giving 2-acetylpyridine after or concurrent with the loss of acetic acid.* This could proceed *via* shift of the hydrogen at the α-side-chain carbon atom concurrent with breaking of the N–O bond to give the intermediate vinyl alcohol which would then isomerise to 2-acetylpyridine. Although the formation of an incipient carbonium ion has yet to be shown for alcohol pyrolysis there can be no doubt that it is formed and the mechanisms would therefore be essentially the same. (ii) Alternatively, reaction could proceed *via* prior and rate-determining insertion of oxygen into the side chain α-C–H bond to give the intermediate (V) which would undergo rapid 1,1-elimination; for the alcohol the intermediate would be the corresponding 1,1-diol, the difference in rate arising from the different ease of this oxygen insertion. Although this oxygen insertion is a well known reaction of pyridine *N*-oxide, it has hitherto been observed only in the presence of acid anhydrides,[20,21] or by u.v. irradiation in the gas phase.[22] We were unable to induce this insertion (at least with 5-hydroxy-2-methylpyridine *N*-oxide) by heating in diphenyl ether in the absence of acetic anhydride and we do not favour this mechanism by virtue of this observation and the fact that all three isomers give similar Arrhenius parameters suggesting a fairly similar elimination mechanism. The close similarity of the rates of elimination from the 2-substituted *N*-oxide ester and the alcohol precursor contrasts with the wider reactivity difference usually found between these two classes of compounds, but this is not unreasonable in view of the extreme activation of both compounds which could be expected to be accompanied by a decrease in the reactivity difference.

Two other points are relevant. First, if a neighbouring group activation is involved, some idea of its effectiveness can be gauged from the fact that the 2-ester *N*-oxide is pyrolysed faster than the tertiary ester, t-butyl acetate (Table 1), and only the tertiary ester, 1-cyclopropyl-1-methylethyl acetate, is significantly more reactive.[23] (The temperature corrected rate for 1-methyl-3-oxobutyl acetate given in ref. 23 is miscalculated with *ca.* 100-fold error from the published Arrhenius data. This compound is in fact less reactive than the 2-ester *N*-oxide.) Secondly, migration of the hydrogen from the side-chain α-carbon presupposes that it is subject to a considerable field effect from the oxygen. Some indication that this is so comes from the fact that the n.m.r. frequency for this hydrogen is shifted by the large amount of 0·53 p.p.m. downfield relative to that for the corresponding hydrogen in 1-phenylethyl acetate. By contrast the shifts for the other isomers are a trivial 0·08 p.p.m. upfield. (These results relate to a constant 3·6% solution in deuteriochloroform to nullify the solvent dependence of shifts which is marked for *N*-oxides.[24]) By contrast the shifts for the α-hydrogens in all three methylpyridine *N*-oxides are closely similar and differ by not more than 0·11 p.p.m. in carbon tetrachloride.[25]

Finally, in electrophilic mercuration, the predominance of 2-substitution of pyridine *N*-oxide and of 8-substitution of quinoline *N*-oxide [9,26] has been

* It may be supposed that the neighbouring group effect of the positive nitrogen should cancel that of the negative oxygen but this is not so because the former charge is nuclear whereas the latter is peripheral.

[18] R. Taylor, *J. Chem. Soc.* (*B*), 1971, 622, 1450.
[19] F. E. Cislak, U.S.P. 2,749,349 (*Chem. Abs.*, 1957, **51**, 4442).
[20] Ref. 4, pp. 353—365.
[21] Ref. 2, pp. 290—302.
[22] N. Hata, *Bull. Chem. Soc. Japan*, 1961, **34**, 1440, 1444; *J. Chem. Phys.*, 1961, **36**, 2072.
[23] G. G. Smith and F. W. Kelly, *Progr. Phys. Org. Chem.*, 1971, **8**, 95.
[24] Ref. 4, p. 16.
[25] R. A. Abramovitch and J. B. Davis, *J. Chem. Soc.* (*B*), 1966, 1137.
[26] Ref. 2, p. 243.

explained in terms of co-ordination of the electrophile with the negative oxygen though there is no reason why this should be specific for this electrophile. However we may alternatively consider the field effect of this oxygen to be sufficient to produce this result. Large electrophiles as in mercuration, should, when within the field of the negative oxygen, be sufficiently close to the ring carbon for bond formation to be assured whereas this may not necessarily be so for small electrophiles.

EXPERIMENTAL

1-*Phenylethyl Acetate*.—This was available from previous studies.[1]

2-(1-*Acetoxyethyl*)*pyridine* N-*Oxide*.—1-(2-Pyridyl)ethyl acetate [11] (16·5 g, 0·1 mol) was heated with 1·7 equiv. of 30% hydrogen peroxide in glacial acetic acid at 70° during 12 h. The mixture was evaporated and the residue was fractionally distilled to give a very viscous oil, b.p. 112° at 0·3 mmHg. This partly crystallised and crystallisation was aided by the addition of acetone. Recrystallisation from benzene gave white needles, m.p. 95—97°. N.m.r. analysis showed this product to be not the expected ester, but the 1-arylethyl alcohol, *viz.* 2-(1-hydroxyethyl)pyridine *N*-oxide, confirmed by mass spectrometry (*m/e* 139) and elemental analysis (Found: C, 60·6; H, 6·55; N, 10·1. Calc. for $C_7H_9NO_2$: C, 60·4; H, 6·55; N, 10·1%).

G.l.c. of the alcohol at 200° showed it to be unstable under the column conditions (SE30 on Chromosorb G) and this provided an early indication of the very high reactivity towards elimination of the alcohol and the ester derivative.

The pure alcohol was acetylated with acetic anhydride in pyridine. Work-up (involving liquid–liquid extraction of the ester with chloroform) and fractional distillation gave a yellow oil, b.p. 112° at 0·4 mmHg. This partly crystallised and recrystallisation from acetone gave pure 2-(1-*acetoxyethyl*)*pyridine* N-*oxide* (4·3 g, 24% overall), m.p. 70—72°, *m/e* 181 (Found: C, 59·8; H, 6·1; N, 7·74. $C_9H_{11}NO_2$ requires C, 60·1; H, 6·5; N, 7·95%), τ ($CDCl_3$), 1·8 and 2·7 (4H, m, ArH), 3·57 (q, CH), 7·87 (s, $COCH_3$), and 8·40 (d, CH_3). This compound darkens very slowly in light.

3-(1-*Acetoxyethyl*)*pyridine* N-*Oxide*.—1-(3-Pyridyl)ethyl acetate was treated as for the 2-isomer except that the intermediate alcohol was not isolated in a pure state, but was directly acylated to give after similar work-up, 3-(1-*acetoxyethyl*)*pyridine* N-*oxide*, b.p. 140° at 0·4 mmHg, a viscous, almost colourless oil, n_D^{20}, 1·5507, *m/e* 181 (Found: C, 59·65; H, 6·4; N, 7·56%), τ ($CDCl_3$), 1·8 and 2·72 (4H, m, ArH), 4·18 (q, CH), 7·88 (s, $COCH_3$), and 8·43 (d, CH_3). This compound darkens rapidly in light.

4-(1-*Acetoxyethyl*)*pyridine* N-*Oxide*.—Two attempts to prepare this compound from 1-(4-pyridyl)ethyl acetate by the above route were unsuccessful, and our attempt to reduce 4-acetylpyridine *N*-oxide [27] appeared to give the required intermediate alcohol which however exploded on fractional distillation, possibly owing to the presence of traces of peracetic acid. The required product was successfully prepared by reduction of 4-acetylpyridine (60 g, 0·5 mol) with sodium borohydride. Work-up and fractional distillation gave 1-(4-pyridyl)ethyl alcohol, b.p. 92° at 0·6 mmHg, which solidified; m.p. 59—60°. This alcohol was dissolved in acetic acid (500 ml) to which hydrogen peroxide (140 ml; 30%) was added, the whole being heated for 10 h at *ca.* 80°. Work-up with liquid–liquid extraction (chloroform) of the concentrated and neutralised reaction product gave 4-(1-*hydroxyethyl*)*pyridine* N-*oxide* (27 g, 39% overall), m.p. 75—76° (from benzene), *m/e* 139. The yield could if necessary be increased considerably as there was a large amount of semi-pure product. Handling of this alcohol requires considerable care as it is extremely hygroscopic. Acetylation with acetic anhydride in pyridine gave, after work-up with liquid–liquid extraction (chloroform), 4-(1-*acetoxyethyl*)*pyridine* N-*oxide* (18 g, 51%), m.p. 74° (from toluene), *m/e* 181 (Found: C, 60·0; H, 6·4; N, 7·8%), τ ($CDCl_3$) 1·8 and 2·73 (4H, d, ArH), 4·18 (q, CH), 7·88 (s, $COCH_3$), and 8·47 (d, CH_3). Unlike the alcohol precursor, this compound was not hygroscopic, and only slowly darkened in light.

2-(2-*Hydroxyethyl*)*pyridine* N-*Oxide*.—This was prepared according to the literature procedure.[28]

Kinetics.—The kinetic method has been described previously [11] and in the present work the 2- and 4-isomers were injected into the reactor as solutions in chlorobenzene. With each ester a secondary decomposition (most probably deoxygenation) occurred but this was considerably slower than the primary decomposition. Thus after 10 half-lives at which point reaction should cease a small pressure increase continued to take place. For the 2- and 3-esters this was trivial and we believe it to cause an insignificant error in the observed rate coefficients. For the 4-ester the decomposition was more serious and the observed rate coefficients are considered to be accurate to only ±5% as a result. Each run was duplicated and carried out at four different temperatures over a 50° range. The relative reactivities are deduced from the Arrhenius plots and consequently the error in k_{rel} is considerably less than that possible in a given run.

Test tube pyrolyses were carried out in diphenyl ether as a solvent (in the absence of this explosive decomposition tended to occur, probably through local overheating). The acetylpyridine product from pyrolysis of the 2-ester and alcohol was identified by comparison (i.r. and n.m.r. spectra and g.l.c. retention time) with an authentic sample, and most characteristically by its unmistakable odour; acetic acid and water respectively were identified from these pyrolyses by standard procedures. Similar treatment of the 3- and 4-esters produced less decomposition because of their greater stability, but only the normal elimination products, *viz.* acetic acid and the appropriate vinylpyridine *N*-oxide, were evident (together with unchanged starting material and diphenyl ether) in the n.m.r. spectra.

[4/1437 *Received*, 15*th July*, 1974]

[27] S. Kanno, *J. Pharm. Soc. Japan*, 1953, **73**, 120 (*Chem. Abs.*, 1953, **47**, 11,154).

[28] V. Bokelheide and W. Feely, *J. Amer. Chem. Soc.*, 1958, **80**, 2217.