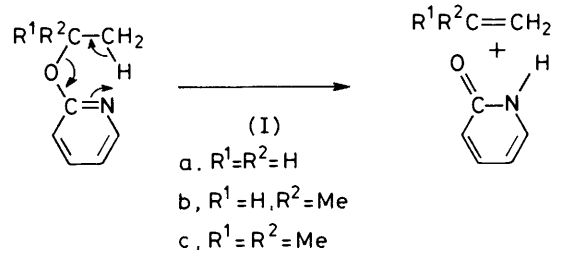
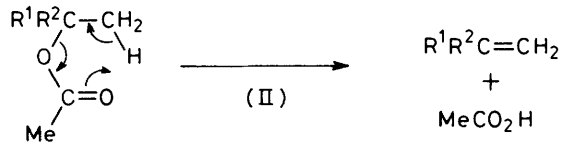
# The Mechanisms of Thermal Eliminations. Part 11.[1] Rate Data for Pyrolysis of 2-Alkoxypyridines to 2-Pyridone, and of 2-Ethoxypicolines to 2-Picolones: Nature and Polarity of the Transition State

By **Nouria Al-Awadi, John Ballam, Paul R. Hemblade,** and **Roger Taylor,*** School of Molecular Sciences, University of Sussex, Brighton BN1 9QJ, Sussex

The rates of thermal elimination of 2-ethoxy-, 2-isopropoxy-, and 2-t-butoxy-pyridine to 2-pyridone and the corresponding alkene, and of the 2-ethoxy derivatives of 3-, 4-, 5-, and 6-methylpyridines to ethylene and the corresponding 2-picolines have been measured over at least 50° for each compound, between 585.1 and 721.1 K. The respective log ($A$/s$^{-1}$) and $E_a$/kJ mol$^{-1}$ values for the former three compounds are 12.20, 196.5; 12.68, 187.6; and 12.33, 161.0, and these are similar to those for the corresponding acetates. The relative rates of the first-order unimolecular decomposition at 600 K are: Et(1.0), Pr$^i$(18.0), Bu$^t$(1 645) compared with 1.0:28.8: 3 316 for the acetates. The polarity of the transition state is thus less than for ester elimination. The difference in the rate ratios $k$(Pr$^i$)/$k$(Et) for alkoxypyridine and acetate pyrolyses is greater than the difference in the $k$(Bu$^t$)/$k$(Pr$^i$) ratios and is interpreted in terms of the difference in polarity of the transition states for primary, secondary, and tertiary elimination. Methyl substituents in the 3-, 4-, 5-, and 6-positions of the pyridine ring change the rate at 600 K by factors of 1.57, 1.02, 0.74, and 1.08, respectively. These show the decomposition does not take place *via* the *N*-alkylpyridone tautomers, and that the reaction is, like ester pyrolysis, sterically accelerated.

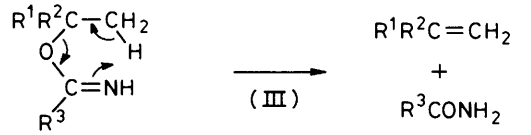
In a preliminary account,[1] one of us described the thermal decomposition of 2-ethoxypyridine to 2-pyridone (I),[2] a reaction which is the nitrogen analogue of ester pyrolysis (I), and is novel in that it involves the



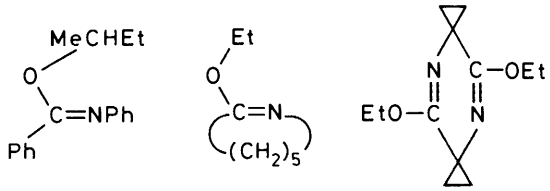




π-electrons of the aromatic ring in the cyclic transition state. Carbocyclic analogues, *e.g.* phenetole are insufficiently polar to undergo a corresponding elimination, but decompose *via* a mechanism which, in part at least, involves radicals. Since this communication appeared, we have learned of an earlier report of the decomposition (in solution) of 2-t-butoxypyridines to 2-pyridones, and the cyclic transition state (I) was proposed for this also.[3]

The elimination (I) is related to iminoether pyrolysis (III) which will be very rapid as here there is no loss of



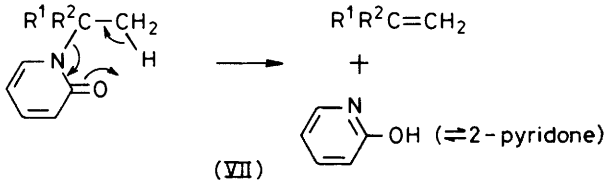

aromaticity in going to the transition state. There have however been no reports of pyrolysis of iminoethers as such, though we are aware of three examples of pyrolysis of the *N*-substituted derivatives. Thus (IV) is reported to be unstable,[4] the rate coefficient for elimination of ethene from *O*-ethylcaprolactam (V) at 558 K has been measured [5] as $5.5 \times 10^{-4}$ s$^{-1}$ (*cf.* $6.4 \times 10^{-7}$ s$^{-1}$ calculated for 2-ethoxypyridine at this temperature), and (VI) readily eliminates ethylene.[6]




(IV) (V) (VI)

In order to learn more about the reaction and in particular the polarity of the transition state, we have prepared, and measured the rates of pyrolysis of 2-ethoxy-, 2-isopropoxy-, and 2-t-butoxy-pyridine. The relative rates of thermal decomposition of the primary, secondary, and tertiary compounds is well documented for a variety of compounds and gives a measure of the reaction polarity.[7]

A decomposition pathway alternative to (I) is *via* the *N*-alkylated pyridone tautomer (VII). Since this is a




substituted amide (and amides are very unreactive towards elimination [8]) this mechanism is very improbable. We have investigated which mechanism operates by measuring the effects of methyl substituents at each

position of the pyridine ring, since these will be quite different for the two pathways.

## RESULTS AND DISCUSSIONS

Each compound gave excellent reproducible first-order kinetics, the rates of which were independent of the initial concentration of compound. However this text for homogeneity is not in our view very reliable, since there have been many reports of compounds satisfying these conditions, yet these compounds have subsequently been found to be undergoing surface-catalysed elimination; a more satisfactory indicator is the complete absence of any deviant runs coupled with normal Arrhenius parameters. [Low log ($A$/s$^{-1}$) values are usually a very strong indicator of surface catalysis as we shall show in a subsequent paper.]

Main features of the results are as follows. (i) The relative rates of elimination of the ethyl, isopropyl, and t-butyl compounds at 600 K are 1.0 : 18.0 : 1 675, and are lower than those obtained for pyrolysis of the corresponding acetates,[7] *viz.* 1 : 28.8 : 3 315. The transition state is thus less polar than for ester pyrolysis.

(ii) The Pr$^i$/Et and Bu$^t$/Pr$^i$ rate ratios for 2-alkoxypyridine pyrolysis are compared with those for ester [7] and halide [9] pyrolysis in Table 2; the polarity of the reaction transition states increases down Table 2. It will be seen that down Table 2 the Pr$^i$/Et rate ratio (A) increases more than does the Bu$^t$/Pr$^i$ rate ratios (B), so that for the bromides the values have become approximately equal (which statistically they should be). This follows from the fact that (with the exception of the bromide pyrolysis) the transition state polarity increases along the series primary < secondary < tertiary. Moreover the fact that (B) is larger than (A) shows that there is a bigger increase in polarity between

TABLE 1

Pyrolysis of 2-alkoxypyridines and 2-ethoxypicolines ($ROC_5H_3NR'$)

| R | R′ | $T$/K | $10^3k$/s$^{-1}$ [a] | log ($A$/s$^{-1}$) | $E$/kJ mol$^{-1}$ | Correlation coefficient | log $k_{rel.}$ at 600 K |
|---|---|---|---|---|---|---|---|
| Et | H | 663.5 | 0.537 | 12.20 | 196.5 | 0.999 62 | 0 |
| | | 668.4 | 0.697 | | | | |
| | | 683.0 | 1.41 | | | | |
| | | 692.4 | 2.26 | | | | |
| | | 697.0 | 2.93(5) | | | | |
| | | 707.6 | 5.10 | | | | |
| | | 709.5 | 5.33 | | | | |
| | | 718.4 | 7.99 | | | | |
| Pr$^i$ | H | 636.4 | 1.80(5) | 12.68 | 187.6 | 0.999 70 | 1.256 |
| | | 651.4 | 4.40 | | | | |
| | | 658.5 | 6.35 | | | | |
| | | 663.5 | 7.90 | | | | |
| | | 672.0 | 12.7 | | | | |
| | | 681.0 | 19.9 | | | | |
| | | 695.1 | 37.6 | | | | |
| | | 702.5 | 51.2 | | | | |
| | | 704.3 | 56.6 | | | | |
| Bu$^t$ | H | 585.1 | 9.05 | 12.33 | 161.1 | 0.999 80 | 3.216 |
| | | 610.8 | 34.3 | | | | |
| | | 626.1 | 77.3 | | | | |
| | | 636.4 | 129 | | | | |
| H | 3-Me | 669.7 | 1.13 | 12.28 | 195.3 | 0.999 99 | 0.196 |
| | | 676.7 | 1.61(5) | | | | |
| | | 692.4 | 3.56 | | | | |
| | | 708.1 | 7.59 | | | | |
| | | 721.1 | 13.7 | | | | |
| H | 4-Me | 663.5 | 0.53 | 12.19 | 196.3 | 0.999 93 | 0.006 |
| | | 680.4 | 1.305 | | | | |
| | | 692.4 | 2.41 | | | | |
| | | 708.1 | 5.08 | | | | |
| | | 721.1 | 9.08 | | | | |
| H | 5-Me | 669.9 | 0.611 | 12.50 | 201.5 | 0.999 99 | −0.131 |
| | | 680.4 | 1.07 | | | | |
| | | 693.0 | 2.04 | | | | |
| | | 708.1 | 4.31 | | | | |
| | | 721.1 | 7.98 | | | | |
| H | 6-Me | 669.9 | 0.789 | 12.55 | 196.7 | 0.999 68 | 0.035 |
| | | 680.4 | 1.41 | | | | |
| | | 693.0 | 2.72 | | | | |
| | | 708.1 | 5.30 | | | | |
| | | 721.1 | 9.90 | | | | |

[a] Average rate coefficient for duplicate runs.

TABLE 2

Rate ratios at 600 K for pyrolysis of various compounds

| Compound | Pr$^i$/Et (A) | Bu$^t$/Pr$^i$ (B) | (B)/(A) |
|---|---|---|---|
| 2-Alkoxypyridines | 18.0 | 91.4 | 5.08 |
| Acetates | 28.8 | 115 | 3.99 |
| Phenylacetates | 32.3 | 121 | 3.74 |
| Benzoates | 36.3 | 125 | 3.44 |
| Phenyl carbonates | 39.8 | 126 | 3.16 |
| Bromides | *ca.* 261 | *ca.* 250 | 0.96 |

the tertiary and secondary compounds than between the secondary and primary compounds. Since the transition states for the tertiary compounds are thus already fairly polar, these transition states will be able to increase their polarity less than will those for the secondary compounds as we go to a reaction for which overall the transition state is more polar.[7,10]

(iii) In Table 3 the Arrhenius parameters for pyrolysis

TABLE 3

Arrhenius parameters for pyrolysis of acetates [a] and 2-alkoxypyridines

| | | Ethyl | Isopropyl | t-Butyl |
|---|---|---|---|---|
| $E$/kJ mol$^{-1}$ | Acetate | 201.04 | 192.25 | 169.60 |
| | Pyridine | 196.5 | 187.6 | 161.1 |
| $\delta E$ | | 4.54 | 4.65 | 8.5 |
| log ($A$/s$^{-1}$) | Acetate | 12.496 | 13.190 | 13.279 |
| | Pyridine | 12.20 | 12.68 | 12.33 |
| $\delta$ log $A$ | | 0.296 | 0.510 | 0.949 |

[a] These values differ very slightly from those given in ref. 7 (see Experimental section).

of the alkoxypyridine are given along with those for the corresponding acetates.[7] In general the activation energies and log $A$ values for the former are slightly less than those for the latter and indeed the differences for each pair of compounds are closely similar. This further confirms the similarity of the reactions and their mechanisms.

(iv) In analysing the effects of methyl substituents in the pyridine ring (Table 1) we take account of the following factors which apply to ester pyrolysis and should therefore also apply to mechanism (I). (a) Breaking of the $C_\alpha$–O bond is the most important rate-determining step, and electron supply to the acyl carbon (C-2 in alkoxypyridines) retards elimination.[7] (b) Greater basicity in the group which becomes bonded to hydrogen, aids elimination.

Thus according to mechanism (I) a methyl substituent at either the 4- or 6-position, being *meta* to C-2 should retard elimination, and being *para* and *ortho* respectively to the nitrogen, should accelerate elimination. The latter will receive a greater electronic effect than the former, but this will be of lesser importance. The two effects should approximately cancel out, as observed. Moreover the 6-methyl substituent accelerates the reaction slightly more than does the 4-methyl substituent and this is entirely consistent with the n.m.r. shift data (Table 4) which show the stronger interaction between

TABLE 4

$^1$H N.m.r. data for $X$-Me-2-ethoxypyridine [$\delta$($CDCl_3$)]

| | ArH | | | | |
|---|---|---|---|---|---|
| $X$ | 3-H | 4-H | 5-H | 6-H | Me |
| 3 | | 7.33 (d) | 6.72 (t) | 7.99 (d) | 2.15 (s) |
| 4 | 6.54 (s) | | 6.68 (d) | 8.02 (d) | 2.26 (s) |
| 5 | 6.64 (d) | 7.35 (d) | | 7.98 (s) | 2.17 (s) |
| 6 | 6.56 (d) | 7.41 (t) | 6.47 (d) | | 2.39 (s) |

nitrogen and the 6-position for both the aromatic and methyl hydrogens.

If mechanism (VII) applied then similar arguments predict that the elimination should be significantly accelerated by both 4- and 6-methyl substituents, but this is not observed.

Methyl substituents at the 3- and 5-positions have a greater electron supply to C-2 than to the nitrogen, the former being the more important. Elimination should therefore be retarded, as it is by the 5-methyl substituent. However the 3-methyl substituent accelerates the reaction but this is not unexpected since we have previously shown that ester pyrolysis is accelerated by the bulky groups at the acyl carbon which interact with those in the alkyl groups,[11] and in the rigid aromatic ring of the alkoxypyridines, these effects should be larger.

By contrast mechanism (VII) predicts that methyl substituents at the 3- and 5-positions should both produce a modest rate increase with no steric acceleration.

We therefore conclude that mechanism (VII) does not operate and very recent studies on the thermal stability of $N$-alkylpyridones [12] further confirm this.

## EXPERIMENTAL

*2-Ethoxypyridine.*—2-Chloropyridine (0.2 mol) was heated under reflux during 10 h with sodium ethoxide (0.5 mol) in ethanol (100 ml). Normal work-up followed by fractional distillation gave 2-ethoxypyridine (70%), b.p. 159 °C (lit.,[13] 155—156 °C).

*2-Isopropoxypyridine.*—2-Chloropyridine (0.2 mol) was heated under reflux during 24 h with sodium isopropoxide (0.5 mol) in propan-2-ol (100 ml). Normal work-up followed by fractional distillation gave 2-isopropoxypyridine (40%), b.p. 80 °C at 100 mmHg, $n_D^{20}$ 1.4864 (lit.,[14] 90—92 °C at 155 mmHg).

*2-t-Butoxypyridine.*—2-Fluoropyridine (0.03 mol), potassium t-butoxide (0.09 mol), and 2-methylpropan-2-ol (135 ml) were placed in each of four Carius tubes which were sealed and heated at 140 °C during 16 h.[15] The product was poured into water, continuously ether-extracted, and the dried extract fractionally distilled to give 2-t-butoxypyridine (82%), b.p. 88 °C at 100 mmHg, $n_D^{20}$ 1.4850 (lit.,[15] 64—65.5 °C at 13 mmHg, $n_D^{20}$ .1.487). The product forms an azeotrope with water which distils at 60 °C and 100 mmHg, so it is important thoroughly to dry the ether extract in order to obtain the maximum yield. G.l.c. analysis of the product (using a 9 ft column packed with 5% OV101 adsorbed on 100—120 mesh Chromosorb G, operated at 170 °C) indicated it to be 99% pure.

*3-, 4-, 5-, and 6-Methyl-2-ethoxypyridines.*—2-Amino-3-, 4-, 5-, and 6-methylpyridines were converted to the corresponding bromo-compounds by the general method of Craig.[16] Each bromo-compound was in turn heated under reflux during 12 h with excess of sodium ethoxide in ethanol to give after work up and fractional distillation, 3-methyl-2-ethoxypyridine, b.p. 32—33 °C at 2.0 mmHg, $n_D^{20}$ 1.4933 (lit.,[17] 59—61 °C at 9 mmHg, $n_D^{15}$ 1.4981); 4-methyl-2-ethoxypyridine, b.p. 35—36 °C at 2.0 mmHg, $n_D^{20}$ 1.5021 (lit.,[17] 70 °C at 10 mmHg, $n_D^{16}$ 1,5005); *5-methyl-2-ethoxypyridine*, b.p. 32 °C at 0.8 mmHg, $n_D^{20}$ 1.4948 (Found: C, 70.2; H, 8.0. $C_8H_{11}NO$ requires C, 70.0; H, 8.1%); 6-methyl-2-ethoxypyridine, b.p. 39 °C at 1.6 mmHg, $n_D^{20}$ 1.4939 (lit.,[17] 59—60 °C at 10 mmHg, $n_D^{14}$ 1.4997).

*Kinetic Studies.*—The general kinetic method has been

described previously.[18] Since the preliminary account of the kinetics for 2-ethoxypyridine was published,[2] the reactor thermocouples have been recalibrated to the highest N.P.L. standard available, and the most representative point within the thermal gradient of the reactor has been reassessed. Consequently the temperatures given previously for the kinetics on 2-ethoxypyridine have been modified slightly as are the Arrhenius data. Additional runs were performed on 2-ethoxypyridine to ensure absolute accuracy in the overall rate ratios; these new data fitted perfectly the original Arrhenius line given by the earlier rates. The temperature correction also produced a similar amendment to the Arrhenius parameters previously published for the alkyl acetates.[7]

We thank Professor G. R. Newkome, Louisiana State University, for helpful correspondence concerning the preparation of 2-t-butoxypyridine.

[2/037 *Received*, 8*th January*, 1982]

REFERENCES

[1] Part 10, R. Taylor, *J. Chem. Res.*, 1981, 250.
[2] R. Taylor, *J. Chem. Soc., Chem. Commun.*, 1978, 732.
[3] G. R. Newkome, J. Broussard, S. K. Staires, and J. D. Sauer, *Synthesis*, 1974, 707.
[4] K. B. Wiberg and B. L. Rowland, *J. Am. Chem. Soc.*, 1955, **77**, 2207.
[5] J. W. Ralls and C. A. Ellinger, *Chem. Ind.* (*London*), 1961, 20. We thank Dr. A. E. A. Porter for drawing our attention to this reference.
[6] A. E. A. Porter, personal communication.
[7] R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1025.
[8] C. H. DePuy and R. W. King, *Chem. Rev.*, 1960, **60**, 431.
[9] Ref. 8, Table 13 and references therein.
[10] R. Taylor, 'The Chemistry of the Functional Groups, Supplementary Volume B. Acid Derivatives,' ed. S. Patai, Wiley, London, 1979, p. 892.
[11] R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1978, 1255.
[12] L. B. Kasunic, I. L. Evoy, and C. N. Sukenik, *J. Org. Chem.*, 1981, **46**, 1970.
[13] H. von Pechmann and O. Baltzer, *Ber.*, 1891, **24**, 3148.
[14] G. C. Hopkins, J. P. Jonak, H. J. Minnemeyer, and H. Tieckelmann, *J. Org. Chem.*, 1967, **32**, 4040.
[15] W. J. Van Zoest, Doctoral Thesis, Landbouwhogeschool, Wageningen, 1975.
[16] L. C. Craig, *J. Am. Chem. Soc.*, 1934, **56**, 231.
[17] K. C. Cunningham, G. T. Newbold, F. S. Spring, and J. Stark, *J. Chem. Soc.*, 1949, 2091.
[18] R. Taylor, *J. Chem. Soc. B*, 1971, 2382.