Rearrangement Reactions in Aromatic Systems upon Electron Impact: the Cases of Pyridine and Fluorobenzene

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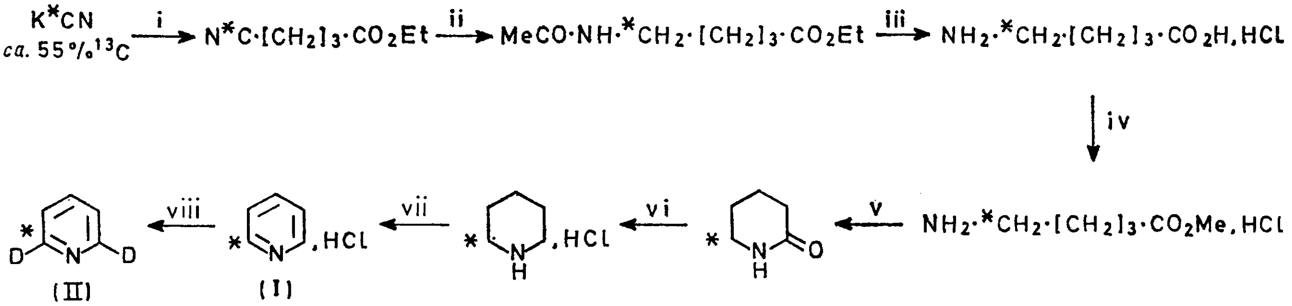
Complete and independent randomisation of the carbon and hydrogen atoms, before fragmentation in the molecular ion of pyridine, and complete randomisation of fluorine and hydrogen atoms in the molecular ion of fluorobenzene, before fragmentation have been demonstrated in the mass spectrometer by isotopic labelling experiments.

INDEPENDENT scrambling of carbon and hydrogen atoms upon electron impact has been shown to occur in benzene.[1] Hydrogen atom scrambling has also been shown to occur in pyridine [2] and fluorobenzene.[3] We now present evidence that independent scrambling of carbon and hydrogen atoms also occurs in pyridine, and that scrambling of hydrogen and fluorine atoms occurs in fluorobenzene, before decomposition, *via* 'metastable transitions'.

[2-^{13}C]Pyridine (I) and [2-^{13}C,2,6-^{2}H$_2$]pyridine (II), required for mass spectral analysis, were prepared by the sequence of reactions outlined in the Scheme. Experimental details for parts of the synthesis have been described,[4-6] although modifications have been made to render them more suitable for the small quantities of material involved in the present work.



SCHEME Reagents: i, I[CH$_2$]$_3$·CO$_2$Et–absolute ethanol; ii, PtO$_2$–H$_2$, Ac$_2$O; iii, conc. HCl, 12 h; iv, MeOH–dry HCl; v, K$_2$CO$_3$–MeOH; vi, LiAlH$_4$ then dry HCl–Et$_2$O; vii, NaOH–20% Pd–C at 250 °C–aq. HCl; viii, K$_2$CO$_3$–D$_2$O

The low-voltage (nominal 16 eV) mass spectrum of (I) showed 54·5% ^{13}C incorporation; it is to be expected that the same isotopic purity with respect to ^{13}C would be obtained from (II). On this basis the isotopic distribution for (II), established from the low-voltage (nominal 12 eV) mass spectrum was D$_1$, 5%; D$_2$, 88%; D$_3$, 7%.

[2-^{13}C]*Pyridine* (I).—The most abundant fragment ion in the 70 eV mass spectrum of pyridine is formed by the loss of hydrogen cyanide from the molecular ion in a one-step process, as indicated by an abundant 'metastable peak' at *m/e* 34·2 (*m/e* 79 → 52). There are much less abundant 'metastable peaks' consistent with the transitions *m/e* 78 → 51 (loss of HCN from the $M^+ - 1$ ion, m^* at *m/e* 33·4) and *m/e* 39 → 37 ($C_3H_3^+ \longrightarrow C_3H^+$, m^* at *m/e* 35·1).

The mass spectrum of (I) shows 'metastable peaks' at *m/e* 33·8 and 35·2 corresponding to the transitions *m/e* 80 → 52 and 80 → 53. If only the hydrogen atoms scrambled, H^{12}CN and H^{13}CN would be lost from *m/e* 80 in equal amounts (on the assumption of no isotope effect).† However, if carbon atom scrambling occurred then the ratio for the loss of H^{12}CN and H^{13}CN would be 4 : 1. Careful measurement of the intensities of these peaks in the second field-free region (Figure 1) indicates that the intensities are in the ratio 4·1 ± 0·2 : 1.

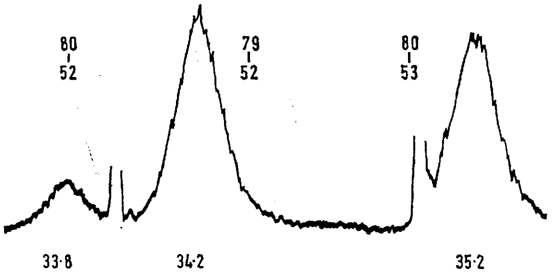


FIGURE 1 [2-^{13}C]Pyridine. Metastable peaks in the second field-free region

The results were confirmed by examining the 'metastable transitions' of the first field-free region using

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† No correction has been made for the small contribution of ^{13}C pyridine to *m/e* 80, associated with the natural abundance of ^{13}C.

[1] (*a*) R. J. Dickinson and D. H. Williams, *J. Chem. Soc.* (*B*), 1971, 249; (*b*) W. O. Perry, J. H. Beynon, W. E. Baitinger, J. W. Amy, R. M. Caprioli, R. N. Renaud, L. C. Leitch, and S. Meyerson, *J. Amer. Chem. Soc.*, 1970, **92**, 7236.

[2] D. H. Williams and J. Ronayne, *Chem. Comm.*, 1967, 1129.

[3] D. H. Williams, S. W. Tam, and R. G. Cooks, *J. Amer. Chem. Soc.*, 1968, **90**, 2150.

[4] M. Rothstein, *J. Amer. Chem. Soc.*, 1954, **76**, 3038.

[5] 'Pyridine and its Derivatives,' Part I, ed. E. Klingsberg, Interscience, New York, 1960, p. 248.

[6] J. A. Zoltewicz and C. L. Smith, *J. Amer. Chem. Soc.*, 1967, **89**, 3358.

' metastable refocusing '[7] with the aid of monitor slits[8] to overcome partial overlap of peaks associated with the transitions *m/e* 80 ⟶ 52 and *m/e* 79 ⟶ 52. This showed a ratio of $H^{12}CN$ to $H^{13}CN$ loss of 3·9 ± 0·2 : 1.

The carbon atom scrambling can be rationalised by postulating randomisation proceeding through valence isomerisation involving such structures as azabenzvalene, azaprismane, and ' Dewar ' pyridine, by analogy with recently reported photochemical transformations,[9] but the relevance of such postulates is questionable, as will be seen from the following discussion. In the light of the foregoing results, the earlier reported[2] occurrence of hydrogen atom scrambling in pyridine could be interpreted in terms of the hydrogen atoms being randomised through scrambling of the carbon atoms without rupture and reformation of the C–H bonds. It was therefore necessary to label pyridine simultaneously with ^{13}C and ^{2}H to determine whether the carbon and hydrogen atoms scramble independently.

[2-^{13}C;2,6-$^{2}H_2$]*Pyridine*.—According to whether carbon and hydrogen atoms scramble independently or not, the abundances of the ' metastable peaks ' for the loss of various hydrogen cyanides from the molecular ion would show two patterns (see Table).*

Relative metastable ion abundances for the loss of hydrogen cyanide from the molecular ion of [2-^{13}C,2,6-$^{2}H_2$]-pyridine (II)

Loss (a.m.u.)	Metastable peak (*m/e*)	Independent scrambling	Carbon atom scrambling alone
27 (HCN)	36·9	12	15
28 (^{2}HCN and $H^{13}CN$)	35·6	11	5
29 ($^{2}H^{13}CN$)	34·2	2	5

Measurement of the intensities of these peaks (Figure 2) shows relative abundances for the loss of 27, 28, and 29 mass units of 11·8 ± 0·2 : 10·6 ± 0·2 : 2·6 ± 0·2. This is consistent with the independent scrambling of all carbon and hydrogen atoms in the molecule. The abundance of the ' metastable peak ' at *m/e* 34·2 (*m/e* 82 ⟶ 53) is inflated by the coincidence of the peak due to the transition *m/e* 40 ⟶ 37 ($C_3H_2D^+ \longrightarrow C_3H^+$).

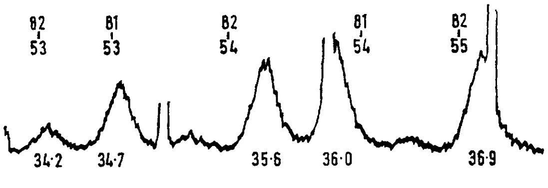

FIGURE 2 [2-^{13}C;2,6-$^{2}H_2$]Pyridine. Metastable peaks in the second field-free region

The results were confirmed by examining the ' metastable transitions ' of the first field-free region (monitor slits being used to overcome partial overlap of peaks associated with the transitions *m/e* 81 ⟶ 54 and 82 ⟶ 54, and 81 ⟶ 53 and 82 ⟶ 53). Experimental results for the loss of 27, 28, and 29 mass units show relative abundance of 11·7 ± 0·2 : 10·95 ± 0·2 : 2·3 ± 0·3. The experimental results thus agree closely with the calculated value for complete and independent scrambling of *both* carbon and hydrogen atoms. While rationalisations involving analogies with photochemical transformations (which result only in re-organisation of C–C bonds) cannot be ruled out, it is now clear that more fundamental rearrangements are taking place.

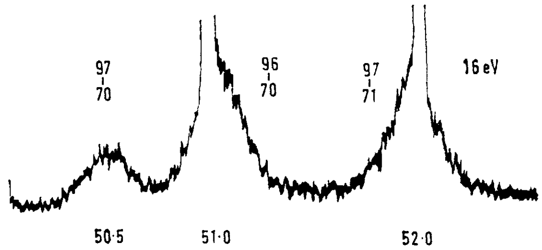

FIGURE 3 [1-^{13}C]Fluorobenzene. Metastable peaks in the second field-free region at 16 eV

[1-^{13}C]*Fluorobenzene* (III).—The most abundant fragment ion in the 70 eV mass spectrum of fluorobenzene is formed by loss of acetylene from the molecular ion in a one-step process as indicated by a ' metastable peak ' at *m/e* 51·0 (*m/e* 96 ⟶ 70).

The mass spectrum of (III) shows ' metastable peaks ' at *m/e* 52·0 and *m/e* 50·5 (corresponding to the transitions *m/e* 97 ⟶ 71 and *m/e* 97 ⟶ 70). The presence of the latter (due to loss of $^{13}C^{12}CH_2$ from the molecular ion) confirms the occurrence of scrambling of fluorine and hydrogen atoms.† If such scrambling was complete, the ratio of intensities for the loss of 26 ($^{12}C_2H_2$) and 27 ($^{13}C^{12}CH_2$) mass units would be 2 : 1. Measurement of the relative intensities of the ' metastable peaks ' (*m/e* 52·0 and 50·5) is rendered difficult by the coincidence of one of these with the normal mass peak. However, careful measurement of the intensities of these two peaks indicates relative abundancies for the loss of 26 and 27 mass units of 2·2 ± 0·4 : 1.

At a lower electron-impact voltage (nominal 16 eV), the normal mass peak at *m/e* 52·0 is considerably less intense (relative to the metastable peak) (Figure 3), and careful measurement of the relative intensities of the two peaks indicates that they are in the ratio 2·1 ± 0·2 : 1.

These results were confirmed by examining the ' metastable transitions ' of the first field-free region (monitor slits being used to overcome partial overlap of peaks associated with the transitions *m/e* 97 ⟶ 70 and 96 ⟶ 70). The relative intensities of the two

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* No correction has been made for the small contributions of [^{13}C;2,6-$^{2}H_2$]pyridine to *m/e* 82, associated with the natural abundance of ^{13}C, or for the small contribution of [2,4,6-$^{2}H_3$]-pyridine.

† No correction has been made for the small contribution of [^{13}C]fluorobenzene to *m/e* 97 associated with the natural abundance of ^{13}C.

[7] K. R. Jennings, in ' Some Newer Physical Methods in Structural Chemistry,' eds. R. Bonnet and J. G. Davis, United Trade Press, London, 1967, pp. 105—109.

[8] J. H. Beynon, A. E. Fontaine, J. A. Hopkinson, and A. E. Williams, *J. Mass Spectrometry and Ion Phys.*, 1969, **3**, 143.

[9] S. Caplain and A. Lablache-Combier, *Chem. Comm.*, 1970, 1247.

transitions (m/e 97 ⟶ 71 and 97 ⟶ 70) were in the ratio 2·2 ± 0·2 : 1.

The experimental results thus agree closely with the calculated value for the randomisation of hydrogen and fluorine atoms with respect to the carbon skeleton of the molecular ion of fluorobenzene before decomposition. It should be emphasised that the experiment does not establish randomisation of carbon atoms with respect to each other, although in all probability this process also occurs.

Energetics.—The rearrangements in the pyridine molecular ion indicate a lower energy of activation for isomerisation than for fragmentation. Ionisation and appearance potentials are available for the relevant ions, and from these a maximum limit can be placed on the activation energy for the rearrangement process. The ionisation potential for the $C_5H_5N^{+\cdot}$ ion derived from pyridine is 9·45 ± 0·2 eV,[10] and the appearance potential for the $C_4H_4^{+\cdot}$ ion derived from pyridine is 12·6 ± 0·3 eV.[11] For consistency, both figures refer to electron-impact measurements; the appearance potential measurement was carried out on the ' metastable peak ' for the $C_5H_5N^{+\cdot} \longrightarrow C_4H_4^{+\cdot}$ transition so as to eliminate part of the kinetic shift.[11] These figures imply a maximum activation energy for the isomerisation of the pyridine molecular ion of 3·15 ± 0·4 eV.

The rearrangements in the molecular ion of fluorobenzene similarly indicate a lower energy of activation for isomerisation than for fragmentation. The relevant ionisation and appearance potentials are 9·3 ± 0·2 eV [12] for the $C_6H_5F^{+\cdot}$ ion derived from fluorobenzene, and 14·8 ± 0·3 eV [13] for the $C_4H_3F^{+\cdot}$ ion derived from fluorobenzene. These figures imply a maximum activation energy for the isomerisation of the fluorobenzene molecular ion of 5·5 ± 0·4 eV.

EXPERIMENTAL

Mass spectra were recorded on an AEI MS9 instrument at a beam energy of 70 eV (except where otherwise stated). In each case, the heated inlet system was used. In the case of the deuteriated pyridine, the source temperature was kept at less than 150 °C, to minimise the possibility of back exchange.

Previously reported syntheses [14] of [3-^{13}C]pyridine and [2,6-$^{13}C_2$]pyridine were not used because of the poor yields involved. Experimental details have been given for a synthesis of 5-amino[5-^{14}C]valeric acid,[4] dehydrogenation of piperidine,[5] and deuteriation of pyridine.[6]

Ethyl [4-^{13}C]*Cyanobutyrate*.—Potassium cyanide (0·4 g, *ca.* 55% ^{13}C) and ethyl 4-iodobutyrate (2·25 g, 50% excess) were heated under reflux for 60 h in absolute ethanol. The resulting solution was evaporated to dryness and the residue extracted with ether, and the ether extract evaporated. The organic residue was dissolved in ethanol and heated under reflux with excess of silver nitrate (1·5 g) overnight (to remove all traces of iodide which would otherwise poison the catalyst for the next stage). The organic fraction was then re-isolated in the same manner as before.

5-Amino[5-^{13}C]valeric acid hydrochloride (0·62 g), prepared by literature methods,[4] was esterified with methanol (50 cm^3) and dry hydrogen chloride. The ester hydrochloride (0·54 g; from 0·66 g in all, 64% yield based on added cyanide) was dissolved in dry methanol and stirred with anhydrous potassium carbonate (0·54 g) for 24 h, and the ether soluble fraction isolated. The crude piperidone was then reduced with lithium aluminium hydride, and the piperidine isolated as the hydrochloride (0·20 g; yield for the last two stages 55%). The free base was generated with aqueous sodium hydroxide and extracted into benzene.

[2-^{13}C]*Pyridine*.—Trial experiments showed that good yields (>80%) of almost pure pyridine (95%) could be obtained by use of a 20% Pd–C catalyst in the gas phase at 250 °C, with benzene as a carrier for the small quantities involved. However, at the first attempt the reaction failed, and recycling with a fresh catalyst reduced the yield for this stage to 40%. [2-^{13}C]Pyridine was isolated as its hydrochloride (0·080 g).

[2-^{13}C;2,6-$^2H_2$]*Pyridine*.—[2-^{13}C]Pyridine hydrochloride (0·040 g) was dissolved in deuterium oxide (1 cm^3), and the solvent evaporated. The product was re-dissolved in deuterium oxide (5 cm^3) and anhydrous potassium carbonate (0·025 g) added. This solution was heated at 200 ± 10 °C in a sealed tube for a week, and the product isolated as the hydrochloride.

In each case the free bases (I) and (II) were generated by addition of anhydrous potassium carbonate to the heated inlet tube of the MS9 mass spectrometer.

[1-^{13}C]*Fluorobenzene* (III).—Our synthesis of [1-^{13}C]-aniline hydrochloride (55% ^{13}C) has been described previously.[1a] [1-^{13}C]Aniline hydrochloride (0·05 g) was converted into the diazonium fluoroborate (0·05 g; 75% yield) by the literature method.[15] The salt was then decomposed in the heated inlet system of the mass spectrometer.

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[11] J. H. Beynon, J. A. Hopkinson, and G. R. Lester, *J. Mass Spectrometry and Ion Phys.*, 1969, **2**, 291.

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