Unexpected Structural Integrity of Gas Phase Isoquinoline Cations that Eliminate HCN

Michael A. Baldwin and Jeremy Gilmore
The School of Pharmacy, University of London, 29–39 Brunswick Square, London WC1N 1AX, UK
Margaret N. Mruzek
Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ, UK

^{13}C labelling has been used to study isoquinoline molecular ions undergoing breakdown by HCN elimination in a mass spectrometer. For otherwise stable ions caused to fragment by collisional activation, there is no skeletal rearrangement prior to HCN loss. Of the ions formed by 70 eV electron impact, 69% of those which fragment in the ion source by HCN loss retain their structural integrity, as do 44% of the metastable ions. Of the ions that eliminate HCN without prior arrangement, approximately two-thirds eliminate C-1 and one-third eliminate C-3. Critical energies are reported for the elimination of HCN from pyridine and isoquinoline molecular ions.

INTRODUCTION

The mass spectra of aromatic molecules are characterized by stable molecular ions that undergo little fragmentation but frequently exhibit extensive skeletal rearrangement. For example, D and ^{13}C labelling studies have shown complete and independent loss of positional identity of all carbon and hydrogen atoms in the fragmenting molecular ions of benzene[1] and napthalene.[2]

Aromatic heterocyclics also form stable molecular ions, but the tendency for the heteroatom to initiate well defined reactions, such as the elimination of HCN from ionized pyridine, makes them ideal for the study of scrambling reactions. It has been shown that pyridine cations undergo complete skeletal reorganization before eliminating HCN,[3] metastable quinoline cations losing HCN show complete hydrogen scrambling,[4] and loss of HCN from 2-methylquinoline is preceded by random insertion of the methyl carbon into the ring system.[5] For cyanopyridines the loss of HCN is predominantly from the ring at times $<10^{-6}$ s, but prior to the decomposition of metastable ions the atoms lose their positional identity.[6] It has been suggested that HCN loss from pyridine is via a ring-opened ion,[7] but a more recent study by photoelectron photoion coincidence techniques suggests the elimination is from the cyclic form.[8]

In general it appears that extensive skeletal rearrangement can be anticipated in heterocyclic aromatics, especially if metastable ions are studied. The bicyclic compound indole, for which the heterocyclic ring is not aromatic, shows little scrambling on loss of HCN from the molecular ion, C-2 being the major contributor.[9] In this work we have studied HCN loss from the molecular ions of ^{13}C labelled isoquinolines and have found a surprising degree of structural integrity, with substantial participation of the C-1 and C-3 atoms over a wide range of lifetimes.

RESULTS AND DISCUSSION

We have studied the losses of HCN and $H^{13}CN$ from 1-^{13}C- and 3-^{13}C-isoquinoline molecular ions[4] to determine the extent of any structural rearrangements prior to HCN elimination. The relative abundances of the peaks at *m/z* 102 and 103 corresponding to losses of $H^{13}CN$ and HCN respectively and of associated peaks are listed in Table 1 for 70 eV electron impact (EI) mass spectra. The *m/z* 102:103 ratios in the spectra of the two labelled compounds are very different, so complete carbon randomization has not occurred. After correcting for the various interfering species

Table 1. 70 eV partial mass spectra of isoquinolines[a]

	Relative abundance (%)		
m/z	Unlabelled	1-^{13}C	3-^{13}C
104	0.49	4.7	3.6
103	6.85	14.4	20.6
102	23.1	15.6	11.2
101	5.3	3.5	2.5
100	0.73	0.63	0.67

[a] Averages of several readings taken from the collector meter.

we calculate from the data in Table 1 that 1-^{13}C-isoquinoline loses $H^{13}CN$ to the extent of 50% of total $HCN/H^{13}CN$ loss, and 3-^{13}C-isoquinoline loses 26%. Corrections were made for (i) naturally occurring heavy isotopes, (ii) unlabelled material, (iii) loss of labelled and unlabelled C_2H_2, (iv) loss of labelled and unlabelled H_2CN, and (v) loss of labelled and unlabelled C_2H_3. For (iii) the statistical ratio should be 2:7 for loss of label, but 3-^{13}C- showed indications of enhanced loss of label of approximately 3:2. For (iv) the statistical ratio should be 1:8 but indications of enhanced loss of approximately 3:2 and 2:3 were

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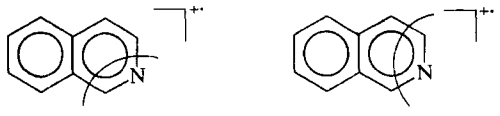
Table 2. Corrected m/z 102:103 peak ratios

	70 eV spectra[a]		Low energy/CAD[b]		m*/FFR1[b]		m*/FFR2[b]	
	1-^{13}C	3-^{13}C	1-^{13}C	3-^{13}C	1-^{13}C	3-^{13}C	1-^{13}C	3-^{13}C
103 (M−HCN)	50±1	74±1	38±2	58±2	64±2	79±2	68±2	76±2
102 (M−H^{13}CN)	50±1	26±1	62±2	42±2	36±2	21±2	32±2	24±2

[a] Estimate of errors arising from uncertainties in corrections for interfering processes.
[b] Measurements were made from UV chart records obtained by scanning slowly over the peaks. At least ten scans were made for each pair of peaks. Errors are standard deviations.

observed for 1-^{13}C- and 3-^{13}C- respectively. The corrections are described in more detail in the Experimental section.

To reduce the effects of interfering ions and to study isoquinoline molecular ions having a range of internal energies, (a) we produced stable molecular ions by low energy EI ionization and subjected these ions to collisions with He to bring about collisionally activated decomposition (CAD), and (b) we studied metastable molecular ions (m^*) in the first and second field free regions (FFR1 and FFR2) of the mass spectrometer (we also attempted to study ions formed by field ionization, but in the absence of collision gas no fragmentation occurred, even when the emitter was heated strongly). The $[M-H^{13}CN]^{+\cdot}$:$[M-HCN]^{+\cdot}$ ratios corrected for any remaining interferences are listed in Table 2.[10] The ions of m/z 102 arising by loss of H^{13}CN are mostly formed by elimination of an intact unit from the molecular ion without skeletal reorganization. It is apparent that for the CAD of stable ions the involvement of C-1 and C-3 constitutes the total carbon participation, and there is no rearrangement of the carbon skeleton prior to HCN elimination. Both C-1 and C-3 are involved in HCN elimination but C-1 participation (mechanism A) is



A ≈ 60% B ≈ 40%

favoured over C-3 (mechanism B). For other fragmenting ions the C-1/C-3 losses compete with rearrangement and participation of other carbon atoms. We envisage a 'random' mechanism C, in which H^{13}CN:HCN losses would be in the statistical ratio 1:8. The m/z 102 peak abundances will have contributions from mechanism C as well as from the specific mechanisms A and B.
Thus:

for 1-^{13}C- [102] = A + C/9 [103] = B + 8C/9
for 3-^{13}C- [102] = B + C/9 [103] = A + 8C/9

These equations have been solved using the data in Table 2 to obtain the relative contributions of pathways A, B and C. The results are given in Table 3.

Table 3. Relative contributions of mechanisms A, B and C to elimination of HCN

	Low energy/CAD	70 eV spectra	m*/FFR1	m*/FFR2	m* mean
A	60±1	46.5±1	30±2	26±2	28
B	40±1	22.5±1	15±2	18±2	16.5
C	0	31±2	55±5	56±5	55.5

CONCLUSIONS

To summarize the labelling results, we find a surprisingly high degree of structural integrity in the molecular ions of isoquinoline which eliminate HCN. Even the long-lived metastable ions show almost 50% specific C-1 and C-3 loss, and when ions of energies below the fragmentation threshold are subjected to CAD there is no skeletal isomerization at all. In each of the three groups of ions studied, (low energy/CAD, 70 eV ions in the normal EI spectrum and metastable ions), mechanism A involving C-1 is more significant than B involving C-3. There is no obvious dependence of the A:B ratio on energy or ion lifetime.

We conclude that the critical energy of isomerization ($\varepsilon_{0_{isom}}$) of isoquinoline molecular ions must be approximately the same as the critical energy of HCN elimination ($\varepsilon_{0_{elim}}$), in contrast to pyridine and other aromatics for which $\varepsilon_{0_{isom}} < \varepsilon_{0_{elim}}$. We have evaluated $\varepsilon_{0_{elim}}$ for pyridine and isoquinoline for HCN loss from FFR2 metastable ions. For pyridine we obtained $\varepsilon_{0_{elim}} = 2.57 \pm 0.1$ eV (0.5–0.7 eV lower than reported previously[8,11]) and for isoquinoline $\varepsilon_{0_{elim}} = 3.94 \pm 0.1$ eV. Thus, for pyridine our results give $\varepsilon_{0_{isom}} < 2.57$ eV, whereas for isoquinoline $\varepsilon_{0_{elim}} \simeq 3.94$ eV. We believe our critical energy values are low because the calibration of the electron energy scale is made with the molecular ion of the compound under investigation. The molecular ion can be formed in a vibrationally excited state by a vertical transition, the excess energy then becoming available for the relatively slow fragmentation of the metastable ions. Nevertheless these data suggest that the energy requirement for isomerization of the bicyclic isoquinoline ion is substantially greater than that of the pyridine ion.

It is also noteworthy that we were unable to distinguish any difference in $\varepsilon_{0_{elim}}$ for losses of HCN and H^{13}CN from metastable ions of 1-^{13}C-isoquinoline.

EXPERIMENTAL

All data were obtained using a VG ZAB 1F reverse geometry double focusing mass spectrometer. FFR1 ions were studied by linked (B/E) scanning, FFR2 ions by mass analysed ion kinetic energy spectrometry. CAD spectra were obtained for FFR1 collisions at 50% transmission. Critical energies were measured by the technique described previously.[12] Calibration was with pyridine (ionization energy 9.23 eV) and isoquinoline (ionization energy 8.55 eV). The molecular and fragment ion curves were parallel over the region 1.0% to 0.01% of the 50 eV normalized ion currents

to within ±0.05 eV. 0.01% corresponds to the limit of detection for the metastable ions so the results are independent of whether the semi-log plot or the initial onset technique is used for treatment of the data.[13]

Materials

1-^{13}C-isoquinoline and 3-^{13}C-isoquinoline were prepared via a Bischler–Napieralski cyclization. Benzyl bromide reacted with ^{13}C-potassium cyanide in dimethyl sulphoxide[14] to yield 8-^{13}C-benzyl cyanide, which was reduced to the corresponding 1-^{13}C-phenethylamine with sodium trifluoroacetoxyborohydride.[15] Condensation of the amine with formic acid and cyclization in polyphosphoric acid[16] to the 3-^{13}C-3,4-dihydroisoquinoline, followed by dehydrogenation with 10% palladium on charcoal and cyclohexene in boiling toluene, yielded the 3-^{13}C-isoquinoline (purified as the hydrochloride). 1-^{13}C-isoquinoline was prepared by a similar procedure from phenethylamine and ^{13}C-formic acid. The samples were introduced into the mass spectrometer as the hydrochlorides using the direct insertion probe. Low energy EI mass spectra showed (m/z %):

1-^{13}C-, 129/9.5, 130/100, 131/9.2
3-^{13}C-, 129/9.6, 130/100, 131/9.35

Corrections to the 70 eV partial mass spectra

(i) The contribution to each peak by naturally occurring heavy isotopes was subtracted from the spectra of the unlabelled compound and the two labelled compounds.

(ii) The spectrum of the unlabelled material was subtracted from the spectra of the two labelled compounds, the proportion of unlabelled material present having been determined by low ionizing energy.

(iii) The m/z 101 peak in the corrected unlabelled spectrum (5.07%) was assumed to be entirely due to $[M-H_2CN]^+$. The corresponding ions with and without label in the spectra of the labelled compounds occur at m/z 102 and 101 respectively. The m/z 101 peak must have been entirely due to this species, and the balance of the 5.07% was subtracted from m/z 102.

(iv) The m/z 103 peak in the unlabelled spectrum (4.86%) was assumed to be entirely due to $[M-C_2H_2]^{+\cdot}$. The corresponding ions with and without label in the spectra of the labelled compounds occur at m/z 104 and 103 respectively. The m/z 104 peak must have been entirely due to this species, and the balance of the 4.86% was subtracted from m/z 103.

(v) The remaining ion current at m/z 103 and 102 would have contributions from labelled and unlabelled $[M-C_2H_3]^+$. High resolution studies (resolving power 10 000) on m/z 102 in the unlabelled spectrum showed $[M-HCN]^{+\cdot}$: $[M-C_2H_3] \approx 95:5$. To make the corrections it was assumed that 5% of the combined m/z 102 and 103 ion current was due to loss of labelled and unlabelled C_2H_3, in the ratio 2:7.

The balance of the peaks at m/z 102 and 103 was assumed to be due entirely to $[M-H^{13}CN]^{+\cdot}$ and $[M-HCN]^{+\cdot}$ respectively.

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