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MASS SPECTRA OF QUINOLINE AND ISOQUINOLINE N-OXIDES

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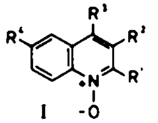
Abstract Mass spectra of a series of quinoline and isoquinoline N-oxides have been recorded. The important fragmentation reactions are discussed with respect to their diagnostic value.

Several papers dealing with the mass spectra of N-oxides have recently been published.[1-4] These investigations were primarily concerned with the diagnostic value for determining the presence of the heteroaromatic N-oxide function associated with the M-16 and M-17 ions (M-O and M-OH respectively) generated upon electron-impact.[1-3] In addition, the occurrence of skeletal rearrangements in the phenazine N-oxide series has also been detected.[4]

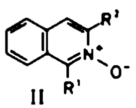
We have investigated the electron-impact behaviour of a series of quinoline and isoquinoline N-oxides in order to determine whether correlations between the mass spectrometric and photochemical[5] processes exist in these series of compounds.

The mass spectra (Figs 1 and 2) of quinoline N-oxide (Ia) and isoquinoline N-oxide (IIa) contain strong molecular ion peaks, while loss of 16 and 17 mass units (M-O and M-OH respectively) generate peaks of less than 12% relative abundance in both series.



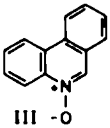
I

	R¹	R²	R³	R⁴
a:	H	H	H	H
b:	Me	H	H	H
c:	Me	Me	H	H
d:	Me	H	Me	H
e:	Me	Me	Me	H
f:	H	H	Me	H
g:	H	H	H	Me
h:	Ph	H	H	H
i:	Ph	Me	H	H



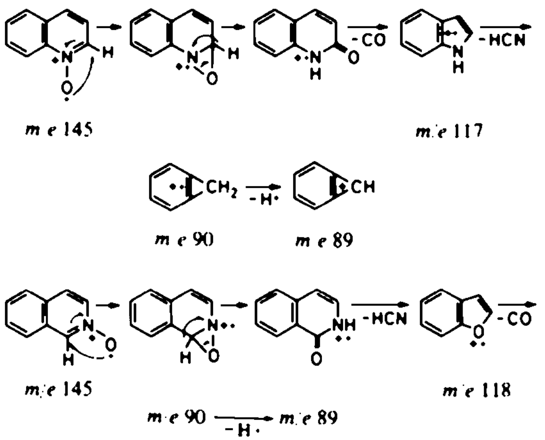
II

	R¹	R²
a:	H	H
b:	Me	H
c:	H	Me
d:	Ph	H



III

Both of the isomers Ia and IIa decompose upon electron impact to yield (Figs 1 and 2) a prominent fragment ion of mass 90. However, the two compounds follow a different pathway to yield this ion. For example, the molecular ion of quinoline N-oxide (Ia) first expels CO[*] to give an ion of mass 117 which further eliminates[*] HCN. In contrast, the molecular ion of isoquinoline N-oxide (IIa) decomposes in the reverse order, with expulsion of HCN[*] preceding that of CO.[*] This difference in the order of expulsion of HCN and CO in quinoline and isoquinoline N-oxides is not only important from an analytical point of view, but also has important mechanistic implications since the two-step breakdown of quinoline N-oxide (Ia) and isoquinoline N-oxide (IIa) appear to follow the same fragmentation routes as their photoisomers, carbostyril and isocarbostyril respectively, upon electron impact.[6,7] The resulting odd electron ion of mass 90 undergoes loss of a hydrogen atom[*] giving the even electron fragment of mass 89. The following mechanistic rationalization (Scheme 1), in which we postulate the rearrangement of the molecular ions of quinoline N-oxide (Ia) and isoquinoline N-oxide (IIa) to carbostyril and isocarbostyril respectively for the principal fragmentation modes of these compounds is consistent with the experimental results.



SCHEME 1

Peaks at M-16 and M-17 appear in the spectra (Figs 1 and 2) of quinoline and isoquinoline N-oxides (Ia and IIa). Although no metastable ions were detected for either process, low voltage measurements strongly indicate, as demonstrated by the increase in abundance of the M-O ion relative to that of the M-OH ion, that the latter is produced by the elimination of a hydrogen atom from the M-16 ion in both isomers. A similar two-step process was proposed previously for benzimidazole N-oxides[3] without the confirmatory evidence of low voltage spectra or metastable ion data. Both the M-16 and M-17 ions fragment in a similar fashion by expulsion of HCN to yield the ion[*] of mass 102 in the spectra (Figs 1 and 2) of Ia and IIa.

Phenanthridine N-oxide (III), which can be considered as either benzo[c]quinoline

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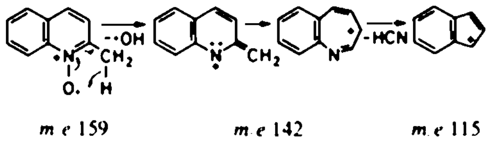
[*] The occurrence of this process is supported by the presence of an appropriate metastable ion in the mass spectrum.

N-oxide or benzo[b]isoquinoline N-oxide, behaves upon electron-impact (Fig. 3) exclusively like quinoline N-oxide (Ia), yielding ions corresponding to M-O, M-CO* and M-CO-HCN.* The ion of mass 140 resulting from consecutive loss of carbon monoxide and HCN then expels a hydrogen atom* to give the even electron species appearing at mass 139. This ion thus has an origin corresponding to the fragment at mass 89 (Scheme 1) in the electron-impact promoted decomposition of quinoline N-oxide.

Methyl substituents adjacent to the N-oxide linkage, in either the quinoline or isoquinoline series, exhibit a dramatic effect on the fragmentation pathways. As in the case of 2-methylpyridine N-oxide,[2] the major fragment ions in the spectra of 2-methylquinoline N-oxide (Ib), 1-methylisoquinoline N-oxide (IIb), and 3-methylisoquinoline N-oxide (IIc) result from the expulsion of OH from the respective molecular ions. An ion due to the loss of oxygen from the molecular ion is present in small abundance in the spectra of Ib, IIb and IIc. The fragment due to the loss of a hydroxyl radical undergoes further decomposition by expulsion of either H_2* or HCN,* the latter elimination being the major one. In the spectrum (Table 1) of 2-methylquinoline N-oxide (Ib) a relatively intense ion at mass 116 is recorded and in the absence of definite metastable data the most likely genesis of this ion is by loss of HCN from the M-O species. No other diagnostically important fragment ions are recorded in the mass spectra of Ib, IIb and IIc. Similar fragmentation patterns as these exhibited by the monomethyl derivatives, Ib, IIb and IIc, of quinoline N-oxide and isoquinoline N-oxide are also shown by the dimethyl derivatives Ic and Id and the trimethyl derivative Ie, although the secondary expulsion of HCN from the M-17 ion is minor in the last example (Table 1). The expulsion of OH is highly dependent on the presence of methyl groups adjacent to the heteratom, and this has been plausibly explained[2, 3] by the operation of an ortho effect. For example, the spectra (Table 1) of 4-methyl- (If) and 6-methylquinoline N-oxide (Ig) show only a minor M-17 peak, as well as an equally minor M-16 peak. In the absence of metastable ions in the spectra of 2-methylquinoline N-oxide (Ib), 1-methylisoquinoline N-oxide (IIb) and 3-methylisoquinoline N-oxide (IIc), it is not clear whether OH is lost in one step (M-OH) or in two (M-O-H). However, low voltage data (Table 1) appear to indicate that the M-OH ion is generated in a fragmentation of the molecular ion, as evidenced by the observation that the abundance of this fragment did not decrease relative to the M-O ion at low electron voltage. The following rationalization (Scheme 2) is proposed for the case of 2-methylquinoline N-oxide (Ib).



SCHEME 2

It is interesting to note that the mass spectra (Table 1) of 4-methylquinoline N-oxide (If) and 6-methylquinoline N-oxide (Ig) show their major fragment ions at mass 130 (M-29), which corresponds to the loss* of CHO. Since an analogous peak

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* See footnote * on p. 3140.

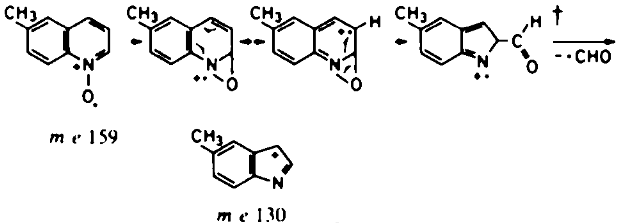
Table 1. Mass spectra of selected ions of alkyl substituted quinoline and isoquinoline N-oxides[a]

Compound	Accelerating[b] voltage (ev)	M^+	$(M-16)^+$	$(M-17)^+$	$(M-19)^+$	$(M-44)^+$	$(M-29)^+$	$(M-56)^+$
Ib	70	80	3	100	11	47	4	3
Ib	17	100	1	31				-
Ic	70	60	5	100	8	21	2	2
Ic	17	100	1	15			-	-
Id	70	71	8	100	7	18	2	2
Id	17	100	2	37		-		
Ie	70	59	13	100	5	5		
Ie	17	100	9	14				
If	70	100	5	8	4	10	60	11
If	17	100	3	2	-		8	
Ig	70	65	6	15	5	11	100	7
Ig	19	100	1	3		–	30	
IIb	70	100	11	94	6	87		
IIb	19	100	1	23	--	2		
IIc	70	73	14	100	6	45		
IIc	19	100	11	38		5		--

[a] Ion intensities are expressed as percent of base peak and have been corrected for natural abundance of ^{13}C isotope.

[b] Low electron voltages are only nominal values.

is absent in the spectrum of quinoline N-oxide (Ia) it appears that the distant methyl substituents must be influencing the fragmentation process. The fact that the M-29 ion is generated directly from the molecular ion precludes a two-step process in which a hydrogen atom is expelled from the molecular ion as in the case of the corresponding methylquinolines.[8] A minor M-29 peak is also noted in the spectrum of 2,4-dimethylquinoline N-oxide (Id), thereby supporting this hypothesis. Further decomposition of the M-29 ion by expulsion of HCN[*] furnishes an ion of low abundance at mass 103.



Scheme 3

The mass spectra of the three aryl substituted derivatives 2-phenylquinoline N-oxide (Ih), 2-phenyl-3-methylquinoline N-oxide (Ii) and 1-phenylisoquinoline N-oxide (IId) are dominated by an M-1 peak (Table 2). Since Ih and IId contain no

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[*] See footnote [*] on page 3140

[†] Corresponding ring-contractions of pyridine N-oxides to 2-formylpyrroles have been achieved photochemically.[9]

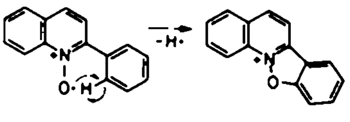
TABLE 2. MASS SPECTRA OF SELECTED IONS OF ARYL SUBSTITUTED QUINOLINE, ISOQUINOLINE AND PYRIDINE N-OXIDES[a]

Compound	Accelerating[b] voltage (ev)	M^+	$(M-1)^+$	$(M-16)^+$	$(M-17)^+$	$(M-28)^+$	$(M-29)^+$	$(M-56)^+$
Ih	70	15	100	7	10	18	27	25
Ih	17	100	42	5		20	6	5
Ii	70	58	100	6	37	5	22	2
Ii	17	100	43	2	7	2	2	
IId	70	59	100	7	42	3	18	4
IId	17	100	51	4	10	2	4	
IV	70	76	100	5	8	20	36	25
IV	17	100	65		1	14	1	

[a] Ion intensities are expressed as percent of base peak and have been corrected for natural abundance of ^{13}C isotope.

[b] Low electron voltages are only nominal values.

aliphatic hydrogens and no other compound employed in this investigation gave an M-1 ion upon electron-impact, it is reasonably assumed that the hydrogen atom is expelled from the phenyl substituent. A possible rationalization for this process is shown below for the formation of the M-1 ion from 2-phenylquinoline N-oxide (Ih). A similar interpretation can be invoked for the analogous process occurring with 1-phenyl-isoquinoline N-oxide (IId).



m/e 221 a, m/e 220

SCHEME 4

An important M-29 peak is noted in the spectra (Table 2) of the three compounds, Ih, Ii and IId, containing an aryl substituent adjacent to the N-oxide linkage. Low voltage measurements clearly indicate that this ion is generated in a secondary process either from the M-1 ion by expulsion of CO or alternatively by elision of a hydrogen radical from the M-CO ion. The loss of CO from *a* may be analogous, in part, to the electron-impact induced expulsion of CO from diphenyl ether.[10] In a tertiary process, the M-29 ion expels HCN to give an M-56 ion.* It is interesting to note that only 2-phenylquinoline N-oxide (Ih) loses CO by a primary process from the molecular ion as indicated from the low voltage spectrum (Table 2) of Ih.

The only other diagnostically important peak appearing in the spectra (Table 2) of Ih, Ii and IId is due to the loss of a hydroxyl radical from the respective molecular ions. Low voltage data (Table 2) indicate that this ion results from a primary reaction in the isoquinoline series (IId) and from a secondary process in the quinoline series (Ih and Ii). Since the spectrum of 2-phenylquinoline N-oxide (Ih) shows a moderately

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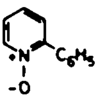
* See footnote * on page 3140

intense M-1 ion, it is proposed that this species then eliminates an oxygen radical to yield the M-17 ion.

The general diagnostic value of the M-1, M-17 and M-29 ions, generated from α-aryl N-oxides, was supported by the mass spectrum of 2-phenylpyridine N-oxide (IV) in which these peaks are the dominant features (Table 2).



IV

In conclusion, mass spectrometry can be of great diagnostic value in the structure determination of heteroaromatic N-oxides. The mass spectra obtained from these compounds depend to a remarkable degree upon the substituents adjacent to the N-oxide group. Thus 2-methylquinoline N-oxide readily eliminates OH whereas the corresponding 2-phenyl compound exhibits a pronounced peak in its mass spectrum due to loss of one hydrogen atom. There also seems to be some similarity between the initial electron-impact promoted processes and those induced by photochemical means.* This latter aspect is being pursued in our laboratories at present.

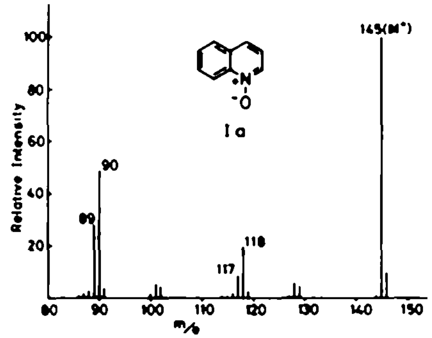


FIG. 1a Mass spectrum of quinoline N-oxide at 70 eV.

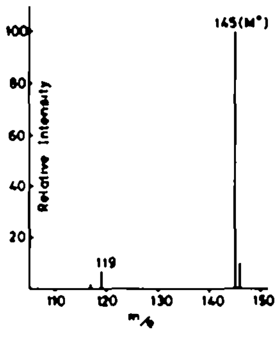


FIG. 1b Mass spectrum of quinoline N-oxide at 19 eV.

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* During the preparation of this manuscript, Kubo *et al.*[11] have reported that 2-cyanoquinoline N-oxide undergoes similar electron-impact and photochemically induced reactions.

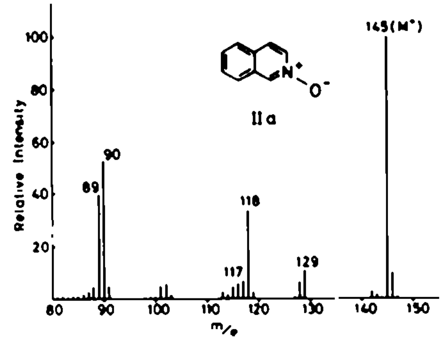

FIG. 2a Mass spectrum of isoquinoline N-oxide at 70 eV.

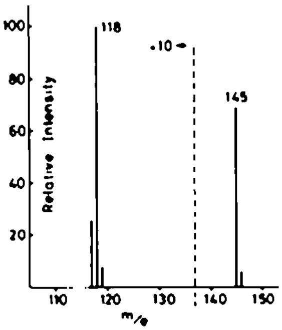

FIG. 2b Mass spectrum of isoquinoline N-oxide at 19 eV.

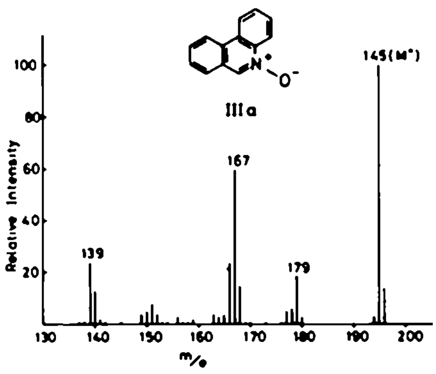

FIG. 3a Mass spectrum of phenanthridine N-oxide at 70 eV.

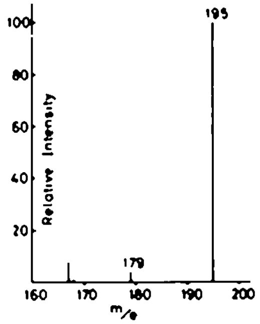

Fig. 3b Mass spectrum of phenanthridine N-oxide at 17 eV.

EXPERIMENTAL

All of the N-oxides were prepared by known procedures.[5,12,13] The mass spectra were determined on an Atlas CH-4 mass spectrometer equipped with the TO-4 ion source. Samples were directly introduced into a relatively cool ion source (70°) and minimum heat applied until vapourization occurred at which time the spectra were determined.

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