Tautomerism in Aromatic Hydroxy *N*-Heterocyclics in the Gas Phase by Metastable Ion Mass Spectrometry

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The kinetic energy release associated with the decomposition of metastable ions has been used to differentiate between the hydroxyquinolines and hydroxypyridines and the corresponding tautomeric quinolinones and pyridinones in the gas phase. It is shown that 2-hydroxyquinoline exists in both tautomeric forms, whereas the other monohydroxyquinolines exist only in the hydroxy forms. The hydroxy forms are also favoured for the hydroxypyridines, but both the 3- and 4-isomers show some tendency to occur as the pyridinones, or, for the 3-isomer, the betaine.

Extensive studies have clearly established that aromatic hydroxy *N*-heterocyclics exist mainly in the keto forms in the solid phase and in solution, whereas studies of gas-phase tautomerism using ultraviolet, infrared, and photoelectron spectroscopy and mass spectrometry have given somewhat ambiguous results. The results of earlier studies, summarized in Table 1, have been reviewed by Katritzky, who concluded that the quinolin-2 or 4(1*H*)-one forms were favoured over 2- and 4-hydroxyquinolines, whereas the hydroxypyridines were favoured over the pyrid-2 or 4(1*H*)-ones.[1] The diverse mass spectrometric (m.s.) techniques that have been used in studying tautomeric equilibria include analysis of peak intensities from electron impact (e.i.) spectra, deuterium isotope effects on fragmentation, measurement of ionization and appearance energies, and chemical ionization followed by collision-induced dissociation (c.i./c.i.d.). These techniques have been reviewed by Maquestiau and Flammang.[2]

In this work we have used differences in the kinetic energy release (KER) associated with the mass spectrometric decomposition of metastable molecular ions to investigate the gas-phase tautomerism of hydroxyquinolines and hydroxypyridines. The release of kinetic energy manifests itself in a broadening of the metastable peaks, and widths of the peaks can be used to calculate the average KERs and the distribution of these energies for a particular fragmentation.[11,12] The loss of CO is a common fragmentation for the molecular ions of phenolic compounds such as phenol itself, giving metastable peaks with large KERs, whereas small KERs are observed for the loss of CO from carbonyl-containing aromatics such as quinones.[13] We have used the shapes of the peaks arising from the loss of CO from the metastable molecular ions of the hydroxyquinolines/quinolinones and hydroxypyridines/pyridinones to determine the tautomers present under the high vacuum gas-phase conditions pertaining in the same spectrometer electron impact ionization source.

Results and Discussion

As a preliminary to studying the hydroxyquinolines and hydroxypyridines, we confirmed the contrasting behaviour of hydroxy- and carbonyl-containing compounds by comparing the metastable peaks for CO loss from the molecular ions of 2-naphthol and 1,4-naphthoquinone. The peaks were studied for fragmentations occurring in the second field-free region of a reverse geometry double-focusing mass spectrometer by mass-analysed ion kinetic energy spectroscopy (MIKES), in which the parent ion is selected by the magnetic field and the daughter ion is scanned by varying the electric sector voltage.[11] The peaks are illustrated in Figure 1(a) and (b), showing the broad dished peak of 2-naphthol compared with the narrow Gaussian shape for CO loss from naphthoquinone ions, the dished shape for 2-naphthol being due to angular discrimination in the mass spectrometer.[11] For a metastable transition $M_1^+ \longrightarrow M_2^+ + M_3$ the KER at half-height ($T_{50\%}$) can be calculated from equation (1),[11] from which the $T_{50\%}$ values for 2-naphthol and 1,4-naphthoquinone were calculated to be 620 and 88 meV respectively, and we have similarly measured $T_{50\%}$ for CO loss from phenol ions as 480 meV, and from 1-naphthol as 502 meV. It should be noted that $T_{50\%}$ values are not absolute as they depend on the geometry of the mass spectrometer and on the operating conditions.

Table 1. Results from previous gas-phase studies[a]

	Pyridines			Quinolines		
	2-OH	3-OH	4-OH	2-OH	3-OH	4-OH
e.i. mass spectra[3]	CO	OH	CO			
e.i. mass spectra[4]			CO			
m.s. deuterium isotope effects[5]	OH	OH	OH			
m.s. ionization energies[6]	OH	OH	OH			
c.i./c.i.d. mass spectra[7]			OH	CO		CO
u.v./i.r. spectroscopy[8]	OH		OH			
			CO (30%)			
Photoelectron spectroscopy[9]	OH	OH	OH			
	CO (25%)					
e.i. mass spectra[10]				CO	OH	CO

[a] OH = Hydroxy form; CO = carbonyl form.

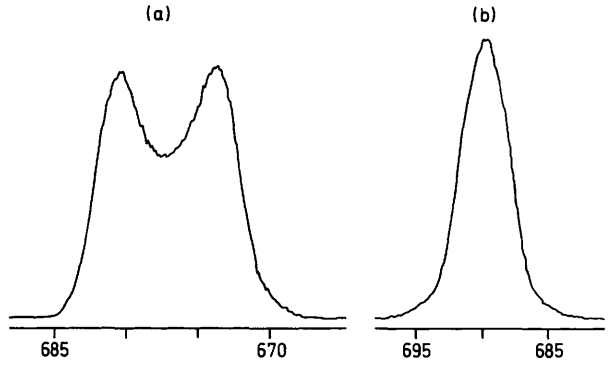


Figure 1. Metastable peaks for CO loss from the molecular ions of (a) 2-naphthol, and (b) 1,4-naphthoquinone, obtained by the MIKES technique. The *x*-axis indicates the electric sector voltage; the peak heights are in arbitrary units

Table 2. Kinetic energy release values ($T_{50\%}$) for hydroxyquinolines

Isomer	3-OH	4-OH	5-OH	8-OH
$T_{50\%}$/meV	571	711	631	801

$$T_{50\%} = \frac{V}{16} \cdot \left(\frac{\Delta E}{E}\right)^2 \cdot \frac{M_1^2}{M_2 M_3} \text{(eV)} \qquad (1)$$

E = Electric sector voltage for transmission of parent ion M_1.
ΔE = Width of metastable peak.
V = Ion accelerating voltage.
(ΔE is corrected for the width of the main beam)[14]

These data confirm the substantially greater KERs for loss of CO from hydroxylated aromatics, which has been explained for phenol ions by Borchers *et al.* as indicating the additional energy requirement for isomerization of the ion to the cyclohexa-2,4-dienone structure, from which CO can be eliminated. This increases the critical energy for the reaction, and part of the additional energy possessed by the reacting ions is released on fragmentation.[15] To confirm that a narrow peak would be shown by a heterocyclic compound containing a carbonyl group without any significant effect from the heteroatom, we studied CO loss from the molecular ion of *N*-propylquinolin-2-(1*H*)-one. This cannot undergo tautomerism, and we obtained a narrow Gaussian peak for which $T_{50\%}$ = 110 meV.

We then determined the peak shapes for CO loss from metastable molecular ions of 2-, 3-, 4-, 5-, and 8-hydroxyquinolines. All but the 2-isomer gave broad peaks typical of phenols, indicating the predominance of the hydroxyquinoline structures over the quinolinones. The $T_{50\%}$ values obtained from these peaks are listed in Table 2.

2-Hydroxyquinoline was exceptional in that it gave a complex peak which appeared to have a narrow component superimposed on a broad peak. This peak is illustrated in Figure 2. The width at half-height of the lowest component measured from the shoulders of the broad peak is very similar to the broad peaks obtained for the other isomers, and indicates that some molecules have the 2-hydroxyquinoline structure, and we assumed that the narrow component was due to ions formed from molecules having the quinolin-2(1*H*)-one structure. To test this a peak profile was generated by summation of the peaks arising from CO loss from 1,4-naphthoquinone and 8-hydroxyquinoline, adjusted for height. This is illustrated in Figure 3. The profile thus produced bears a very close resemblance to that obtained by averaging and smoothing the metastable peak for CO loss from 2-hydroxyquinoline.

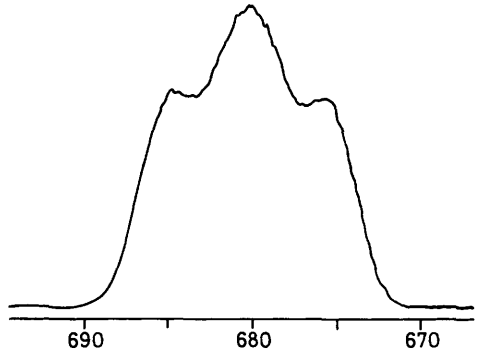


Figure 2. Metastable peak for CO loss from 2-hydroxyquinoline molecular ions.

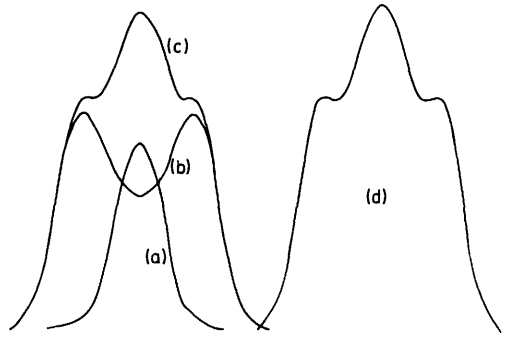


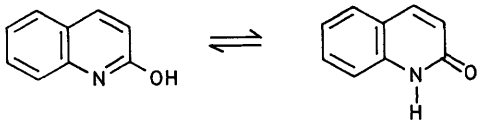
Figure 3. Profile (c) generated by the summation of the height-adjusted CO-loss metastable peaks for 1,4-naphthoquinone (a), and 8-hydroxyquinoline (b), compared with the CO-loss metastable peak for 2-hydroxyquinoline (d)

Subtraction of the height-adjusted 8-hydroxyquinoline metastable peak from the 2-hydroxyquinoline peak gave the profile illustrated in Figure 4, and this was tested for its Gaussian nature by using equation (2) as recommended by Holmes and Terlouw.[12]

$$\ln(h/h_0) = -\ln 2\,(w/w_{0.5})^n \qquad (2)$$

$w_{0.5}$ = peak width at half-height
w = peak width at fraction of peak height h/h_0

For a true Gaussian profile the exponent n in equation (2) should equal 2.0 at all fractions of the peak height. Values of 1.93 and 2.60 were obtained at h/h_0 0.8 and 0.1, indicating some divergence from Gaussian character, whereas the corresponding values for the 8-hydroxyquinoline peak were 2.13 and 2.02 respectively. Nevertheless, this test indicates that the profile obtained in this way is pseudo-Gaussian, and $T_{50\%}$ was calculated to be 77 meV, typical of carbonyl-containing compounds, which indicates the presence of some molecules with the quinolin-2(1*H*)-one structure. From this we conclude that, alone amongst the hydroxyquinolines, the 2-isomer exists in both tautomeric forms in the gas phase at reduced pressure.



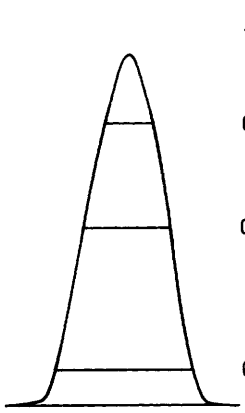


Figure 4. Profile obtained by subtraction of the height-adjusted CO-loss metastable peak for 8-hydroxyquinoline from that of 2-hydroxyquinoline

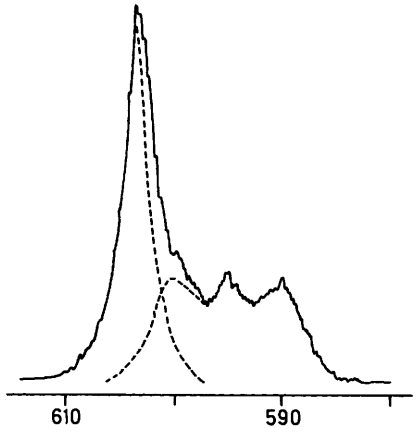


Figure 5. Metastable peak for loss of CO from 3-hydroxypyridine molecular ions. The dotted lines indicate the peak profiles obtained by manual deconvolution, assuming symmetrical peaks

The hydroxypyridines were similarly investigated. 2-Hydroxypyridine gave a broad dished peak ($T_{50\%}$ 497 meV) with no sign of a narrow component, implying that there is no significant amount of the pyridin-2(1*H*)-one form in the gas phase. The 3- and 4-hydroxypyridines both gave very similar CO-loss metastable peaks at $M - 28$ that were unresolved from more intense HCN loss peaks at $M - 27$, as is illustrated for 3-hydroxypyridine in Figure 5. Nevertheless it can be seen that there are narrow components superimposed on the broad components, which implies that both these compounds exist in the pyridinone form to some degree in the gas-phase. In the case of the 3-isomer this could be a zwitterionic betaine form.

Conclusion

The origin of composite metastable peaks in mass spectrometry has been considered by Holmes and Terlouw, who identified three situations in which they might arise: (i) when two ions of different structure both lose a fragment of the same mass, (ii) when a common parent ion forms fragment ions of two different structures, and (iii) when a common parent ion can fragment by two different pathways to give a common daughter ion.[12] In the present case there is no particular reason to suspect that either (ii) or (iii) is occurring, whereas there is very good reason to attribute the composite peaks to (i), as we are dealing with known tautomeric forms.

As a general principle, the absence of a metastable peak cannot be taken to prove the absence of a certain structure. However, as was demonstrated with the test compounds, strong metastable peaks are generally observed for CO loss from the molecular ions of phenolic and aromatic carbonyl compounds, and we consider the presence or absence of peaks of the appropriate width highly significant in this case. Where composite peaks are observed, no firm conclusions can be drawn from the relative metastable peak heights concerning the proportions of the two forms present, but from our results it is reasonable to infer that the quinolin-2(1*H*)-one is present in significant amounts relative to 2-hydroxyquinoline, and the 3- and 4-hydroxypyridines show some tendency to occur as the oxo tautomers.

Our findings that 2-hydroxyquinoline and quinolin-2(1*H*)-one both exist in the gas phase in the ion source of a mass spectrometer, whereas the hydroxy forms are favoured for the other positional isomers, is at variance with the findings of Clugston and MacLean.[10] They used $(M - CO)^{+\cdot}$ peak intensities in the 70 eV electron impact mass spectra to argue that the quinolinone forms were favoured over the 2-, 4-, and 8-hydroxyquinolines. It may be significant that they introduced the samples through a heated reservoir where there could have been some pyrolysis, and which could have provided the opportunity for intermolecular processes. In the present study we have evaporated the samples directly from the solid phase into a high vacuum in which there was little chance of intermolecular reactions. Although we observed similar trends we found the fragment peak intensities to be considerably less than those reported by Clugston and MacLean, even over a wide range of ion chamber temperatures.

The gas-phase behaviour of the hydroxypyridines/pyridinones has been subject to more study than the quinoline system, and using a wider variety of techniques. The weight of evidence from earlier studies favours the hydroxy forms with small amounts of the pyridinones, and our conclusions are in broad agreement with this.

Experimental

These experiments were carried out using a VG Analytical Ltd., ZAB-1F reverse-geometry double-focusing mass spectrometer. Samples were introduced into the ion source with an unheated direct-insertion probe, the source temperature being about 200 °C, and the pressure being about 1×10^{-6} Torr. Ionization was by electron impact with 70 eV electrons. The ion accelerating voltage was 8 kV, and the electric sector voltage for transmission of the parent ions was 842 V. The daughter ions from the decomposition of the metastable ions in the second field-free region were transmitted at reduced electric sector voltage, which was scanned to obtain the peak shapes. The peaks were recorded on a u.v. oscillograph, and the peaks illustrated in Figures 1, 2, and 5 are single scans across the peak.

The majority of the materials used were of commercial origin and were characterized by mass spectrometry. 3-Hydroxyquinoline was synthesized by diazotization of 3-aminoquinoline.[16] *N*-Propylquinolin-2(1*H*)-one was prepared by propylation of 2-hydroxyquinoline, and separated by thin-layer chromatography from the other isomeric product, 2-propoxyquinoline. Both products gave excellent matches with the corresponding mass spectral reference spectra from the NBS library as supplied by the mass spectrometer data system.*

* VG Analytical Ltd, Manchester M23 9LE.

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Received 13*th April* 1987; *Paper* 7/648