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Fragmentation of Isomeric N-Quinolinyl-phthalimides on Electron Impact Ionization

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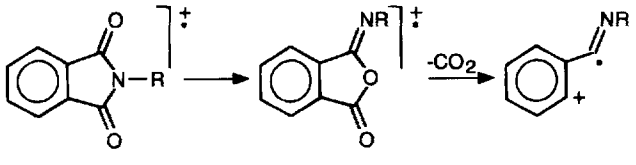
The isomeric 2-, 3-, 5-, 6- and 8-quinolinylphthalimides give rise to different electron impact ionization mass spectra, which permit easy distinction. The specific fragmentation processes are rationalized in terms of proximity effects and stabilization of cyclic ion structures. Collision-induced dissociation spectra were used to support the proposed ion structures of major fragment ions.

KEYWORDS: N-quinolinylphthalimides; electron impact ionization; collision-induced dissociation; positional isomers; fragmentation mechanism

INTRODUCTION

The elimination of CO_2 from the molecular ions of N-methyl-and N-phenylphthalimide under electron impact ionization (EI) was reported in the early days of organic mass spectrometry as an example of an unusual skeletal rearrangement occurring in organic radical cations in the gas phase.[1,2] The mechanism proposed for this process is presented in Scheme 1. It has been noted that the decarboxylation process does not take place in higher N-alkyl-, N-allyl-, N-benzyl- and N-phenylethylphthalimides, which have alternative facile dissociation channels.[2,3] The behavior of other aromatic imides under EI has also been reported.[4–6]

In the process of identifying an unknown contaminant, present in batches of the color additive D&C Yellow No. 10 (Colour Index No. 47005) submitted for certification to the US Food and Drug Administration, five isomeric N-quinolinylphthalimides (**1–5**) were synthesized. The availability of these positional isomers gave us the opportunity to study their behavior under EI and in particular to explore the effect of the distance between the quinoline nitrogen atom and the phthalimido moiety on the relative rate of the decarboxylation reaction versus other possible dissociation processes.



Scheme 1

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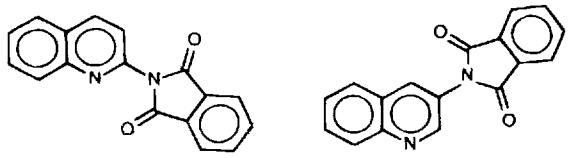
EXPERIMENTAL

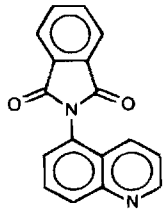
Materials

Compound **1** (m.p. 236–237 °C) was synthesized by following a published procedure.[7] Compounds **2** (m.p.



1

2



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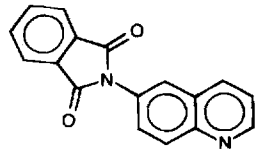

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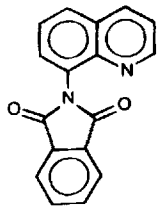


5

213–214 °C), **3** (m.p. 212 °C), **4** (m.p. 221–222 °C, lit.[8] 225 °C) and **5** (m.p. 222–223 °C) were prepared by following the procedure for **1** by condensing the appropriate aminoquinoline with phthalic anhydride in N,N-dimethylaniline at 200–205 °C. Compounds **2–5** were recrystallized from ethanol.

Mass spectrometric analyses

Low-resolution gas chromatographic/mass spectrometric (GC/MS) analyses were performed with an HP-5890 Series 2 gas chromatograph interfaced to an HP-5971 mass-selective detector. EI full-scan data were acquired by scanning from m/z 35 to 600. The gas chromatograph was equipped with an HP-5MS (cross-linked 5% phenyl–methylsilicone) fused-silica capillary column, 30 m × 0.25 mm i.d., 0.25 μm film thickness. The column temperature was programmed from 40 °C, after an initial 5 min hold, to 200 °C at 17 °C min^{-1}, then from 200 to 275 °C at 5 °C min^{-1}. UHP helium was used as the carrier gas. The injection port temperature was 225 °C and the transfer line temperature was 280 °C. The samples were dissolved in anhydrous ethanol.

The low-resolution product ion EI tandem mass spectra were obtained on a Finnigan-MAT TSQ-46 quadrupole mass spectrometer interfaced to an INCOS 2300 data system. The instrument parameters were source temperature 120 °C, emission current 0.35 mA, ionizing energy 70 eV and conversion dynode −5 kV. The MS/MS collision-induced dissociation (CID) product ion measurements were carried out by using a collision energy of −20 eV and an argon collision gas pressure of 2.6 mTorr (1 Torr = 133.3 Pa). The samples were dissolved in methanol and introduced via the direct chemical ionization (DCI) probe at a heating rate of 50 mA s^{-1}.

High-resolution mass spectral measurements were made on a Fisons Instruments Auto Spec Q mass spectrometer with a VAX 4000 data system. Instrument parameters were electron energy 70 eV, emission current 300 μA, accelerating voltage 8 kV and source temperature 200 °C. The high-resolution data were obtained in the EI mode at 10 000 resolution (10% valley definition) by using voltage scans. Perfluorokerosene was used as the mass reference standard and was added at the beginning of the run, via a heated batch inlet. Samples were introduced by gas chromatography using an HP-5890 Series 2 gas chromatograph on a DB5-MS fused-silica capillary column, 16 m × 0.25 mm i.d., 0.25 μm film thickness. The column temperature was programmed from 80 to 300 °C at 20 °C min^{-1}. Other parameters were injection port temperature 200 °C, transfer line temperature 240 °C and linear velocity (helium) 40 cm s^{-1} at room temperature.

RESULTS AND DISCUSSION

The EI mass spectra of 2-, 3-, 5-, 6- and 8-quinolinylphthalimides (**1–5**, respectively) are shown in

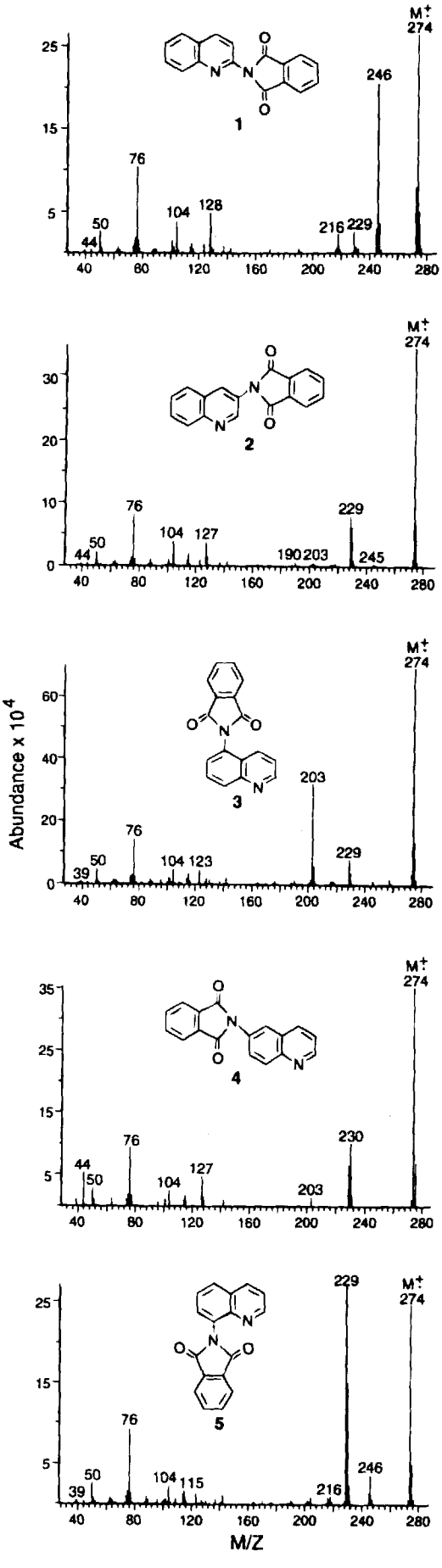


Figure 1. 70 eV EI mass spectra of phthalimidoquinolines **1–5**.

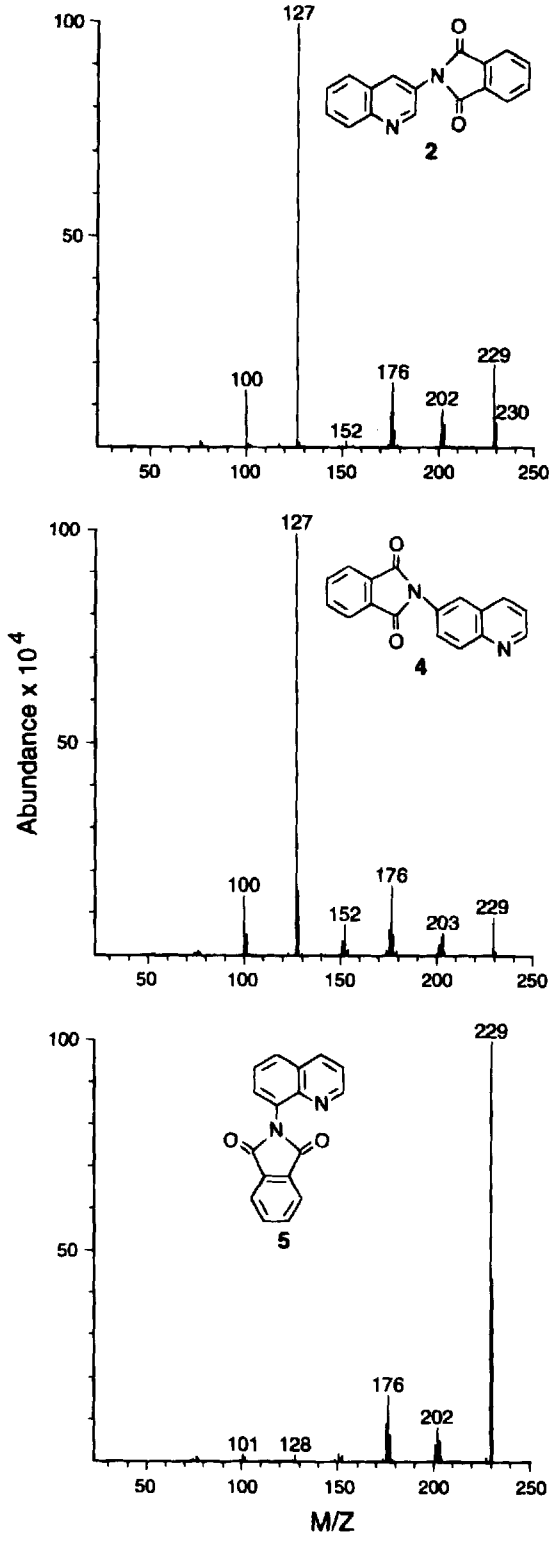
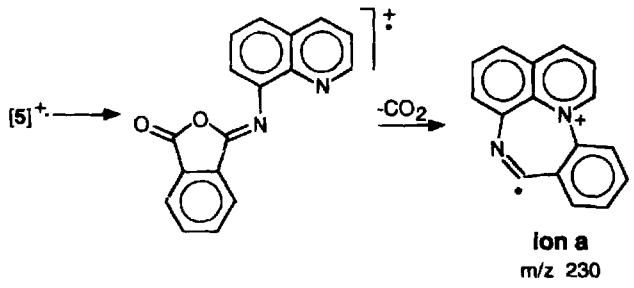


Figure 2. CID mass spectra (−20 eV, collision energy) of the m/z 230 $[M - CO_2]^{+\cdot}$ ion of **2**, **4** and **5**.

Fig. 1. 8-Quinolinylphthalimide (**5**) gives rise to very abundant m/z 230 $[M - CO_2]^{+\cdot}$ (55%) and m/z 229 $[M - HCO_2]^{+}$ (100%) ions. These ions are of considerable abundance in the mass spectra of the 3- and 6-quinolinylphthalimides (**2** and **4**). The 2- and 5-quinolinylphthalimides (**1** and **3**) exhibit only relatively low abundance m/z 229 $[M - HCO_2]^{+}$ ions, while the m/z 230 $[M - CO_2]^{+\cdot}$ ions are negligible.



Scheme 2

High-resolution mass spectral measurements support the assignments of these ions.

The CID spectra of the m/z 230 $[M - CO_2]^{+\cdot}$ ions obtained from **2**, **4** and **5** are shown in Fig. 2. The CID spectrum obtained from **5** is entirely different from those of **2** and **4**. The most abundant m/z 229 product ion in the CID spectrum of **5** is formed by abstraction of a hydrogen atom, while the other two isomers **2** and **4** give rise to most abundant m/z 127 dehydroquinoline radical cations. The m/z 127 ion is absent in the CID spectrum of **5**. These findings suggest facile cyclization through the quinoline nitrogen atom in the course of decarboxylation of the molecular ion of 8-quinolinylphthalimide (**5**) (resulting in ion a, see Scheme 2), which is not possible in the other isomers.

The data available for the m/z 229 ions do not provide convincing evidence for mechanistic pathways of their formation. The CID spectra of these ions (Fig. 3) show sufficient dissimilarity to allow easy distinction between the five isomers **1**–**5**, but the differences, mainly in relative ion abundances, do not allow reliable assignment of ion structures.

2-Quinolinylphthalimide (**1**) does not undergo the decarboxylation process under EI conditions. The m/z 246 $[M - CO]^{+\cdot}$ ion is the most abundant fragment observed in the mass spectrum of **1**. A plausible mechanism of this decarbonylation process is shown in Scheme 3. Formation of the stabilized cyclic ion b may be the driving force for this decarbonylation process, specific to 2-quinolinylphthalimide (**1**) owing to the proximity of the phthalimido moiety and the quinoline nitrogen atom.

The m/z 246 $[M - CO]^{+\cdot}$ ion is virtually absent in the EI mass spectra of **2**, **3** and **4**, but it is present, although not abundant, in the mass spectrum of 8-quinolinylphthalimide (**5**). The 1,8 relationship of the phthalimido moiety and the quinoline nitrogen atom may explain the occurrence of the decarbonylation process in this isomer. A plausible mechanism for this process is proposed in Scheme 4. It is interesting that ions b and c resulting from the decarbonylation of **1** and **5**, respectively, give rise to entirely different CID spectra, shown in Fig. 4.

5-Quinolinylphthalimide (**3**) gives rise to very low abundance $[M - CO]^{+\cdot}$ and $[M - CO_2]^{+\cdot}$ ions. The most abundant fragment in the mass spectrum of this isomer appears at m/z 203, and it may be formed by the sequential elimination of CO and HNCO, resulting in structure d shown in Scheme 5. The 1,8 relationship between the 5-phthalimido group and position 4, which allows facile cyclization, may be the driving force for the formation of the tetracyclic stabilized aromatic ion d.

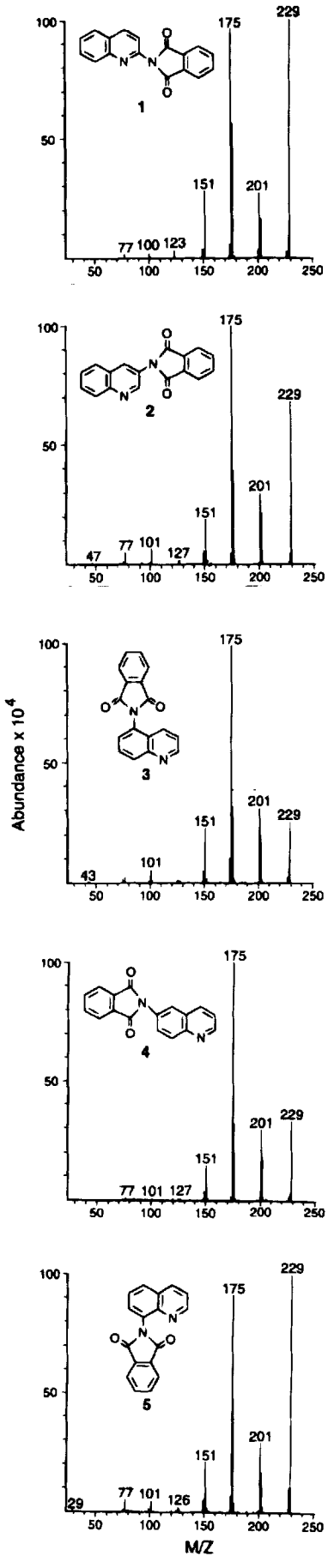
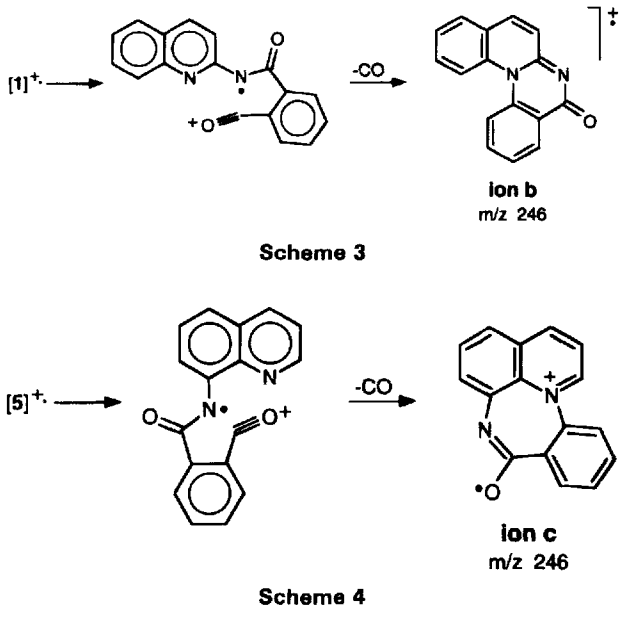


Figure 3. CID mass spectra (−20 eV, collision energy) of the m/z 229 $[M - CHO_2]^+$ ion of **1**–**5**.



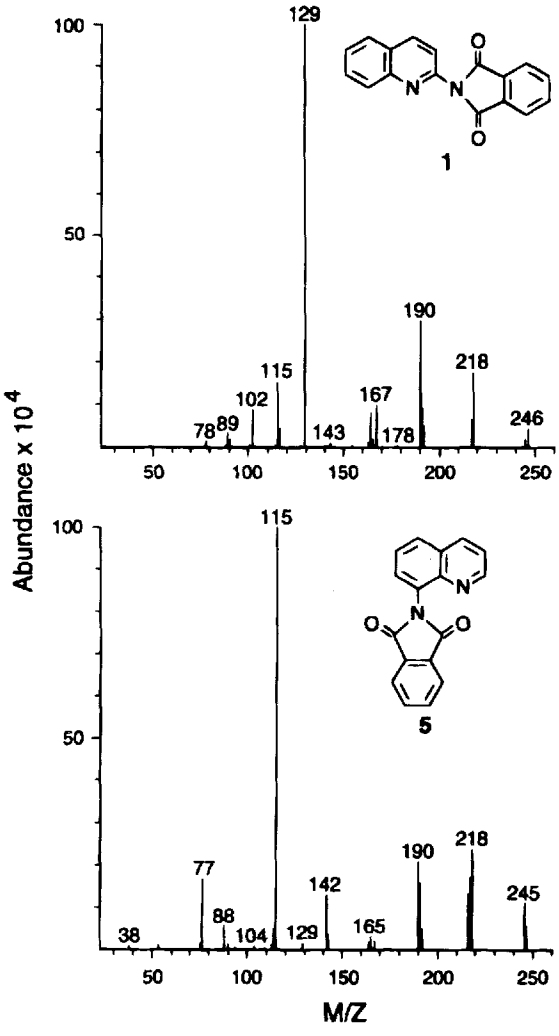
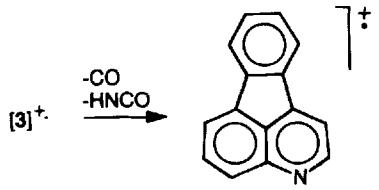


Figure 4. CID mass spectra (−20 eV, collision energy) of the m/z 246 $[M - CO]^{+\cdot}$ ion of **1** and **5**.



Ion d
m/z 203

Scheme 5

has a pronounced effect on the fragmentation pattern under EI conditions. The different behaviors of the positional isomers make mass spectrometry a reliable tool for structural assignments in the quinolinylphthalimide system. The analysis of the mass spectra shows that decarboxylation, which has been shown previously to be a characteristic process in a number of N-substituted phthalimides, is suppressed when structural factors lower the energy of alternative channels.

CONCLUSION

The results of this study show that the site of substitution of the phthalimido group in the quinoline system

Acknowledgement

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