Organic Mass Spectrometry, 1968, Vol. 1, pp. 199 to 204. Heyden & Son Limited. Printed in Northern Ireland

THE PRIMARY FRAGMENTATION STEP OF ISOXAZOLE UPON ELECTRON IMPACT. A CORRELATION WITH PHOTOCHEMISTRY

HISAO NAKATA
Department of Chemistry, Aichi Kyoiku University, Higashi-ku, Nagoya

and

HIROSHI SAKURAI, HIDEO YOSHIZUMI, AKIRA TATEMATSU
Faculty of Pharmacy, Meijo University, Showa-ku, Nagoya

(*Received* 18 *December* 1967: *accepted for publication* 1 *January* 1968)

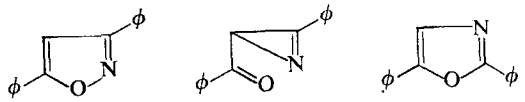
Abstract—Three isomeric compounds, I, II and III, were prepared and their mass spectra recorded. Comparisons of the spectra showed that the fragmentation of I proceeds only by way of II, and that II itself is transformed in part to III upon electron impact. It is suggested that selective ionization of each one of the two isolated functional groups in II may afford two isomeric radical ions, II*a* and II*b*. A possible interrelation to the photochemistry of these compounds is also discussed.

IN RECENT years the correlation between the mass spectral fragmentation of certain organic compounds and their photochemical behaviour has been noted in several laboratories.[1] It would be useful to have such information as an aid to the understanding of the more precise mechanism of electron impact induced reactions. In connection with our recent work on the mass spectra of isoxazoles,[2] the present paper deals with the primary fragmentation step of 3,5-diphenylisoxazole and its possible interrelation to the photochemical isoxazole-oxazole rearrangement.[3]

As we have already pointed out,[2] the first step of the fragmentation of several 3,5-disubstituted isoxazole derivatives is the fission of the N—O bond leading to an azirine intermediate. The lability of the N—O bond in the isoxazole nucleus has not only similarities in chemical reactions in solution[4] but in addition is supported by molecular orbital calculations.[5] Although the carbocyclic analogue of the intermediate of this type has been proposed for fragmentations of various five-membered heteroaromatic compounds,[6] no direct comparison of their spectra has been reported. The formulation of such an intermediate seems to be the only self-consistent rationale for the interpretation of the spectra. Fortunately, however, the corresponding azirine intermediate has been prepared[3] photochemically from 3,5-diphenylisoxazole, and characterized as a relatively stable compound. In view of the external standard method[7] in mass spectra, this key intermediate would provide important information to the fragmentation mechanism. The purpose of the work described below is to prepare this intermediate and to compare its spectrum with those of related compounds.

As has been reported,[3] irradiation of 3,5-diphenylisoxazole (I) in ether solution with <2800 Å light afforded 2-phenyl-3-benzoyl-1-azirine (II) as an oil. The IR, UV and NMR spectra of this compound are identical with those obtained by the previous workers.[3] The mass spectra of the isoxazole I, the azirine II and the

isomeric 2,5-diphenyloxazole (III) were now determined and are shown in Figs. 1, 2 and 3, respectively.



I II III

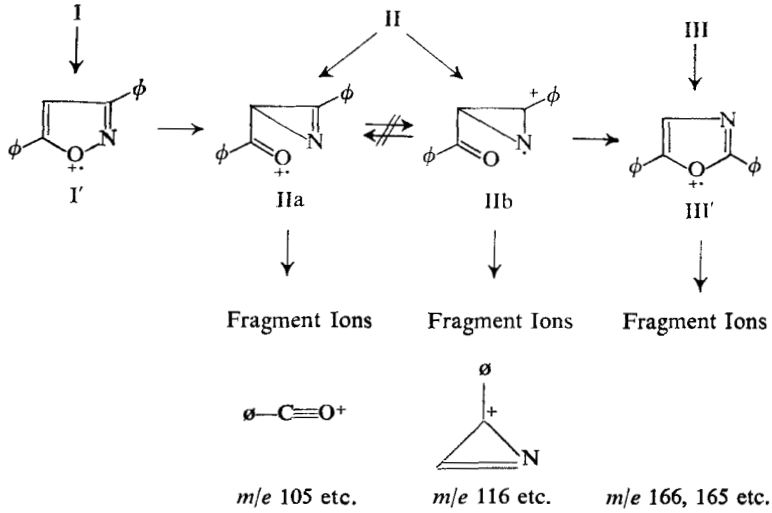
Because the instability of the azirine II upon heating has been noted,[3] an important point must be established prior to discussion of these spectra and their implications. It is to demonstrate that the spectral pattern of II solely derives from the electron impact induced reactions and is not contaminated by any fragment from thermal degradation of the compound. We confirmed the tendency[3] of the thermal conversion of II to the isoxazole I, but further experiments showed that II was essentially unchanged on heating at 200° for 60 minutes in the vapour phase. Transformation of an appreciable amount of II to I required prolonged heating (*ca.* 15 hrs. at 200°). Under reduced pressure at 100° the material could even be distilled without any indication of decomposition. Moreover, conversion of II to the oxazole III upon heating could not be observed in the vapour phase. It is safe, therefore, to assume that no fragment from thermal degradations is involved in the spectrum shown below, which was taken with a direct inlet system heated below 100°.

As can be seen from Figs. 1 and 2, the spectrum of the isoxazole I is very similar to that of the azirine II except for the peaks at *m/e* 166 and 165. These two peaks in II correspond to M − CO − HCN and M − CO − HCN − H respectively, and this indicates that a skeletal rearrangement of II is involved during the fragmentation. On the other hand, these peaks are very prominent in the spectrum of III (Fig. 3). We found that subtraction of these peaks in I from those in II afforded a spectral pattern that was surprisingly similar to the spectrum of III. Although similarities in peak positions and intensities do not always indicate identical ion structures, the above results lead us to present a tentative conclusion that the fragmentation of the isoxazole I takes place only by way of II as suggested previously,[2] and that the azirine (II) is transformed in part to the oxazole III upon electron impact. Further work based on the use of meta-stable ion characteristics[8] is obviously necessary. The fragmentation of the oxazole III may possibly follow the course previously reported.[9]

A point worth comment is the observation that the characteristic peaks of III at *m/e* 166 and 165 do not appear in the spectrum of I despite the fact that reactions I → II and II → III are both possible upon electron impact. The absence of these peaks in I was confirmed by using the *in situ* preparation of I in the mass spectrometer. Thus, after the vapour of II has been left for 15 hours at 200° in the reservoir of the mass spectrometer, the observed spectrum was identical with that of I (since these conditions were known to convert II to I).

This apparent discrepancy would presumably be ascribable to selective ionization of one of two isolated functional groups in the azirine (II). Upon electron impact II would give two isomeric radical ions II*a* and II*b*, which are produced by removal of one electron from the benzoyl and from the ketimine moieties, respectively. If we assume that fragmentation and skeletal rearrangements of these ions proceed more rapidly than charge transfer between the two functional groups, the above results are explained by Scheme I.

SCHEME I



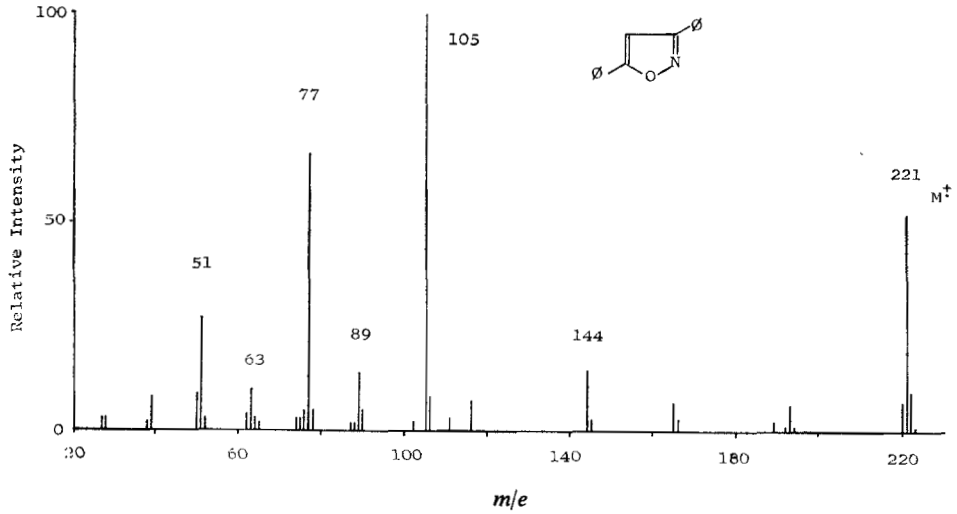


FIG. 1. Mass spectrum of 3,5-diphenylisoxazole (I) by direct-inlet system at 100°.

From the isoxazole I a potential molecular ion I′ will be formed which undergoes the N—O bond fission almost simultaneously to give one of the azirine ions, II*a*, which in turn then yields fragment ions such as *m/e* 105. On the other hand, electron bombardment of II itself may afford two isomeric ion radicals II*a* and II*b*, and only the latter will rearrange to the oxazole ion III′. If the interconversion between II*a* and II*b* is practically impossible for one reason or another, the ion I′ cannot rearrange to III′, and, therefore, the peaks at *m/e* 166 and 165 from III′ will not appear in the spectrum of I.

A similar behaviour of the azirine II upon irradiation has been noted.[3] With >3000 Å light II rearranges to I, while rearrangement to III was observed with 2537 Å light. This wavelength dependence was attributed[3] to selective excitation of

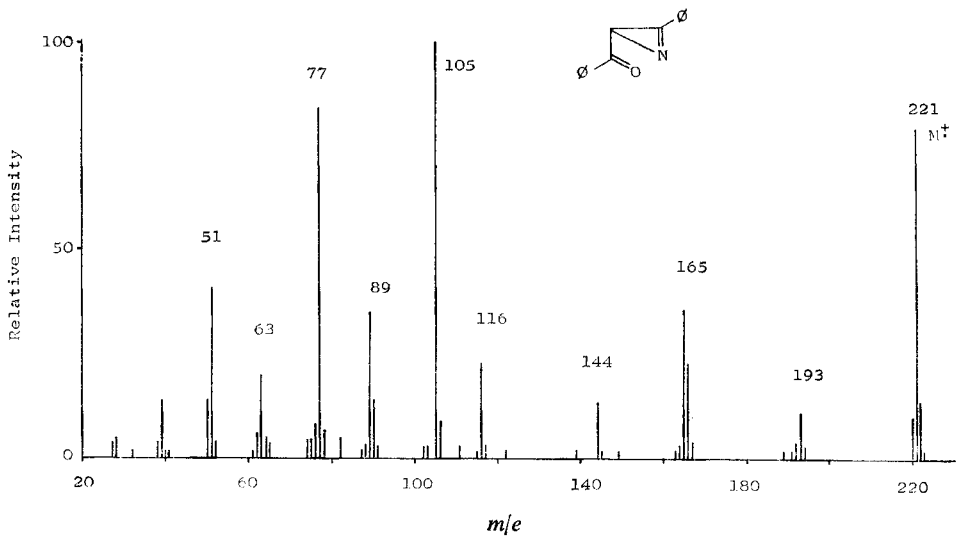


FIG. 2. Mass spectrum of 2-phenyl-3-benzoyl-1-azirine (II) by direct-inlet system at 100°.

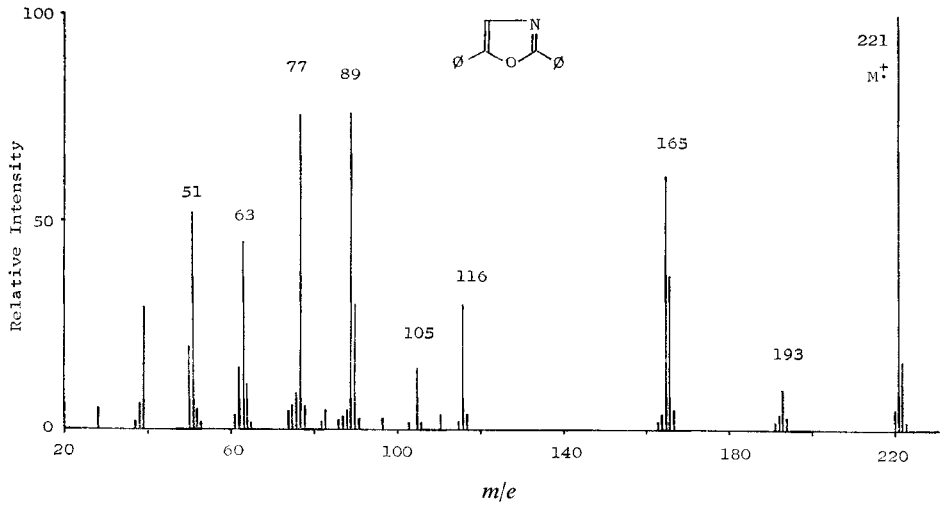


FIG. 3. Mass spectrum of 2,5-diphenyloxazole (III) by direct-inlet system at 100°.

one of two isolated chromophores in II. Thus, the $n \rightarrow \pi^*$ excitation of the benzoyl group with >3000 Å light is probably responsible for the rearrangement to I, and the excitation of the ketimine chromophore with 2537 Å light would lead to the formation of III.

The concept of the localized charge in mass spectral ions[10,11] has been used by a number of workers[6,12,13] to explain specific fragmentation patterns for various organic compounds. Usually it is assumed that, though an electron can be abstracted from any part of a given molecule under the conditions generally employed, a 'cascading'[14] or a 'demotion'[15] of an electron from the highest energy level to the

lower vacant orbital takes place before fragmentation or rearrangements occur. Although recent experimental evidence[16] clearly showed that this is the case even for non-conjugated bifunctional molecules, the isomeric azirine ions II*a* and II*b* above could be an exception in that facile skeletal rearrangements and fragmentations follow preferentially. The conclusions are still tentative, however, and other alternative explanations would be possible. Further work along these lines is now in progress.

EXPERIMENTAL

The mass spectra of the present work were measured by Hitachi double-focusing mass spectrometer RMU-6E, using all-glass inlet system and direct inlet system at 100°. The ionizing energy was kept at 70 eV and the ionizing current at 80 μA.

3,5-*Diphenylisoxazole* (I).[17,18] To a solution of NaOH (11 g) in water (100 ml) and EtOH (60 ml) was added acetophenone (26 g) with stirring. Benzaldehyde (24 g) was then added and the reaction mixture was kept at 25° for 3·5 hours. The resulting oily product was extracted with $CHCl_3$. The chloroform solution was washed with water, dried, and concentrated. An oily residue was crystallized (34·4 g) from EtOH; m.p. 52–54°. This material, benzalacetophenone, (3 g) was dissolved in ether (25 ml) and Cl_2 gas was passed through it for 15 minutes. The product was recrystallized from EtOH to afford α,β-dichlorobenzylideneacetophenone as needles (2·5 g): m.p. 114–115°. (*Anal.*: Calcd. for $C_{15}H_{12}OCl_2$: C, 64·53; H, 4·33. Found: C, 64·88; H, 4·04%.)

Hydroxylamine hydrochloride (10 g) was added to the solution of the above product (5 g) in hot EtOH (400 ml). Sodium hydroxide (20 g) in water (50 ml) was poured into the solution and the mixture was refluxed for 35 minutes. The mixture was cooled and poured into *ca.* 400 ml of water. The crystals thus appeared were collected and recrystallized from EtOH to give pure 3,5-diphenylisoxazole (3·5 g): m.p. 140–141°. (*Anal.*: Calcd. for $C_{15}H_{11}ON$: C, 81·43; H, 5·01; N, 6·33. Found: C, 81·41; H, 4·99; N, 6·21%.) UV: λ_{max}^{EtOH} 245 mμ (log ε = 4·32), 267 mμ (log ε = 4·38).

2-*Phenyl*-3-*benzoyl*-1-*azirine* (II).[3] 3,5-Diphenylisoxazole (I) (500 mg) in ether (400 ml) was irradiated for 25 minutes with a mercury lamp* through a cobalt sulphate filter solution.[19] Ether was evaporated and the residue was chromatographed on silica gel (20 g) using carbon tetrachloride and 5% ether–CCl_4. 3,5-Diphenylisoxazole (I), 2,5-diphenyloxazole (III), and 2-phenyl-3-benzoyl-1-azirine (II) were eluted in this order. UV: λ_{max}^{EtOH} 254 mμ (log ε = 4·45); NMR: 3·76 ppm 1 H, s,† 7·30–8·20 ppm 10 H, m;† IR: 3050, 1775, 1673, 1599, 1579, 1232 cm^{-1}.

2,5-*Diphenyloxazole* (III).[20,21] To a solution of sodium bisulphite (11 g) in water (30 ml) was added benzaldehyde (10 ml) with mechanical stirring. After the mixture was cooled to room temperature, KCN (14 g) was added to it and the stirring continued for 15 minutes. The oily product was extracted with ether (25 ml) and the ether extracts were washed with water and with saturated NaCl solution. Benzaldehyde (10 ml) was dissolved in this ether solution and HCl gas was passed through the solution for 1 hour with stirring. The crystalline 2,5-diphenyloxazorid-4-one was filtered and was recrystallized from MeOH (13 g): m.p. 190·5–191·5°. (*Anal.*: Calcd. for $C_{15}H_{13}O_2N$: C, 75·31; H, 5·44; N, 5·86. Found: C, 75·32; H, 5·51; N, 5·91%.)

The above product (2 g) was heated with $POCl_3$ (10 ml) at 75–80° for 45 minutes. After $POCl_3$ had been removed under reduced pressure, the solid residue was triturated with ether containing a small amount of HCl. The material was shaken with water (50 ml) and ether (150 ml), and the ether layer was separated. The dried ether solution on evaporation gave 2,5-diphenyloxazole (1·65 g), which was recrystallized from aq. MeOH; m.p. 70·5–71°. (*Anal.*: Calcd. for $C_{15}H_{11}ON$: C, 81·45; H, 4·98; N, 6·33. Found: C, 81·41; H, 4·88; N, 6·26%.) UV: λ_{max}^{EtOH} 304 mμ (log ε = 4·31).

Thermal behaviour of 2-*phenyl*-3-*benzoyl*-1-*azirine* (II). The compound (II) had been placed in the sealed end of a glass tube and this portion of the tube was warmed at 100° for 15 hours under reduced pressure (5 mm Hg). The open end of the tube was kept at room temperature. The sample had been protected from light during heating. Distillation occurred in the tube and oily drops appeared on the wall of the tube. These oily drops have the same UV spectrum as the initial material.

After the vapour of the compound was placed for 60 minutes at 200° in a reservoir of the mass

* Halōs, PIH-100s, Eiko-sha, Japan.

† s: singlet, m: multiplet.

spectrometer, the observed mass spectrum was essentially identical with that of the initial material. When the compound was kept for 15 hours under the same conditions, however, a spectrum which was essentially the same as that of 3,5-diphenylisoxazole was obtained.

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