

Electron Impact Induced Rearrangements of Organic Ions. Part III.¹ A Beckmann-like Aryl Migration in Substituted Isoxazol-5(4*H*)-one Molecular Ions

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A novel unimolecular reaction leading to primary amine radical ions occurs in the gas phase decomposition of ions generated from substituted isoxazol-5(4*H*)-ones, upon electron impact. The proposed mechanism implies aryl migration as the first step, and this is unambiguously demonstrated by ¹⁵N and ²H labelling experiments, metastable transition studies, and exact mass measurements. This [1,2] sigmatropic shift is a fast process, as evidenced by a primary kinetic isotope effect on competing metastable transitions. Energetic and electronic factors involved in the process suggest striking similarities to the Beckmann rearrangement in the condensed phase.

THE chemistry of unimolecular reactions of organic ions induced by electron impact has been extensively related to ordinary solution chemistry, and many parallels between the behaviour observed for gaseous cations and that of condensed phase systems have been found.² Striking similarities in the photochemistry of ketones and their mass spectral decomposition are well documented.³

¹ Part II, G. Stagno d'Alcontres, G. Cum, and N. Uccella, *Org. Mass Spectrometry*, in the press.

² M. M. Bursey and F. W. McLafferty, in 'Carbonium Ions,' ed. G. A. Olah, Interscience, London, 1968, vol. 1, p. 257; T. W. Bentley and R. A. Johnstone, in 'Advances in Physical Organic Chemistry,' ed. V. Gold, Academic Press, London, 1970, vol. 8, p. 222.

Rearrangements of carbonium ions have been studied in the metastable regions of a double focusing mass spectrometer by ²H and ¹³C labelling, and have been shown to lead to complete isomerisation of primary, secondary, and tertiary structures, in a manner analogous to the Wagner-Meerwein rearrangements of the corresponding ions in solution.⁴

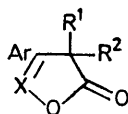
³ F. W. McLafferty, *Analyt. Chem.*, 1952, **31**, 82; J. N. Pitts and A. D. Osborne, *J. Amer. Chem. Soc.*, 1961, **83**, 3011; N. J. Turro, D. C. Neckers, P. A. Leermakers, D. Seldner, and P. D'Angelo, *ibid.*, 1965, **87**, 4097.

⁴ W. C. Cole and D. H. Williams, *Chem. Comm.*, 1969, 784; B. Davis, D. H. Williams, and A. N. H. Yeo, *J. Chem. Soc. (B)*, 1970, 81; G. A. Olah, J. Sommers, and E. Namanworth, *J. Amer. Chem. Soc.*, 1967, **89**, 3579.

Migration of hydrogen upon electron impact is already a well known process and is the most common source of skeletal rearrangements.⁵ Phenyl group migrations to carbonium ion centres have been invoked to interpret the isomerisation reaction of benzenoid $C_9H_{11}^+$ ions.⁶ 3,5-Diphenylisoxazole derivatives decompose on electron impact to generate ions shown to be formed by a phenyl shift, on the basis of deuterium labelling experiments.⁷

We report here the occurrence of a deep-seated rearrangement in isoxazol-5(4*H*)-one molecular ions (I), which involves a carbon to nitrogen aryl migration in the oxime-like system, leading to the formation of primary amine radical ions. This process is analogous to the Beckmann rearrangement in solution chemistry.

Although the mass spectra of isoxazol-5(4*H*)-ones have been previously reported and discussed,⁸ such a fragmentation has not been detected, probably because of the different inlet system used in the previous study.



- (1) Ar = Ph, R¹ = R² = H, X = ¹⁴N
- (2) Ar = Ph, R¹ = R² = H, X = ¹⁵N
- (3) Ar = Ph, R¹ = R² = ²H, X = ¹⁴N
- (4) Ar = Ph, R¹ = H, R² = ²H, X = ¹⁴N
- (5) Ar = *p*-NO₂-C₆H₄, R¹ = R² = H, X = ¹⁴N

The mass spectra of isoxazol-5(4*H*)-ones (1)–(5) have been determined using a double focusing mass spectrometer of 'reversed' Nier–Johnson geometry and the ion kinetic energy (IKE) spectra⁹ of the relevant ions obtained by the direct analysis of daughter ions (DADI) technique.¹⁰ The assignments of parent to daughter ion transitions is somewhat difficult in conventional IKE spectra which must be mass analysed.^{5b} This disadvantage in identifying metastable reactions is overcome when the positions of the magnetic and electric sectors are reversed.¹⁰ In fact, one particular ion can be selected by tuning the magnetic field and the pure metastable spectrum recorded by automatic variation of the electrostatic analyser (ESA) voltage from the initial value (E_0) downwards. Each metastable peak arises from unimolecular decompositions in the second drift region of the reversed geometry instrument and occurs at an ESA voltage, E , which allows the assignment of parent (m_1) and daughter (m_2) mass numbers using the relationship $m_2 = m_1 E / E_0$.

Four competitive unimolecular decompositions are observed in the first and second drift regions from 3-phenylisoxazol-5(4*H*)-one molecular ions (I) (Scheme 1) and their metastable transitions are reproduced in Figure 1.

⁵ I. Howe, in 'Mass Spectrometry,' ed. D. H. Williams, Specialist Periodical Report, The Chemical Society, London; (a) 1971, vol. 1, ch. 2; (b) 1973, vol. 2, ch. 2.

⁶ N. Uccella and D. H. Williams, *J. Amer. Chem. Soc.*, 1972, **94**, 8778.

⁷ B. K. Simons, R. K. M. R. Kallury, and J. H. Bowie, *Org. Mass Spectrometry*, 1969, **2**, 749.

⁸ T. Nishiwaki, *Tetrahedron Letters*, 1969, 2049, 4355; *Tetrahedron*, 1969, **25**, 747.

The fragmentation reaction of interest is that leading to the formation of ions m/e 93 [reaction (a)] and it has been defined by a combination of high resolution

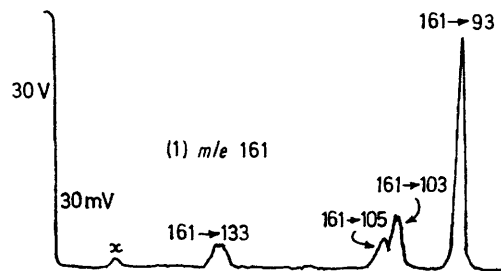
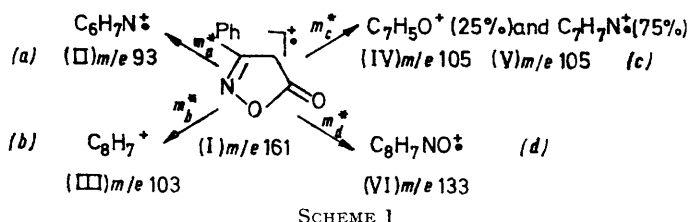


FIGURE 1 DADI spectrum of ions m/e 161, from 3-phenylisoxazol-5(4*H*)-one (1)

measurements, isotope labelling, and energetic inferences. In the mass spectrum of (1) at 70 eV, ion m/e 93 corresponds to 32% of the base peak (m/e 103). At high resolution, the ion under study appears as a singlet of elemental composition $C_6H_7N^+$. By the refocusing mode¹¹ this ion is observed to be uniquely generated from the molecular ion, m/e 161, and measurements using the DADI technique show that reaction (a) carries 60% of the total metastable ion current. These results establish that the rearrangement ion $C_6H_7N^+$ is produced directly from the 3-phenylisoxazol-5(4*H*)-one molecular ion itself (m/e 161 \rightarrow 93, Scheme 1). Independent and unambiguous evidence of the mechanism of this fragmentation is supplied by isotopic labelling studies.

The mass spectrum of 3-phenyl[¹⁵N]isoxazol-5(4*H*)-one (2) shows a peak at m/e 94 (33% of the m/e 103 base peak), and refocusing experiments reveal a unique metastable peak corresponding to the transition m/e 162 \rightarrow 94. In the IKE spectrum of the precursor ion m/e 162 (the molecular ion), four metastable peaks are observed, the most intense being that corresponding to the transition m/e 162 \rightarrow 94 which is 59% of the total metastable abundance.

3-Phenyl[4,4-²H₂]isoxazol-5(4*H*)-one (3) decomposes at 70 eV to generate ion m/e 95 which is 15% of the base peak. Refocusing experiments on the daughter ions m/e 95 have again confirmed only one metastable transition leading to its formation (m/e 163 \rightarrow 95), and the pure metastable spectrum of the molecular ion obtained

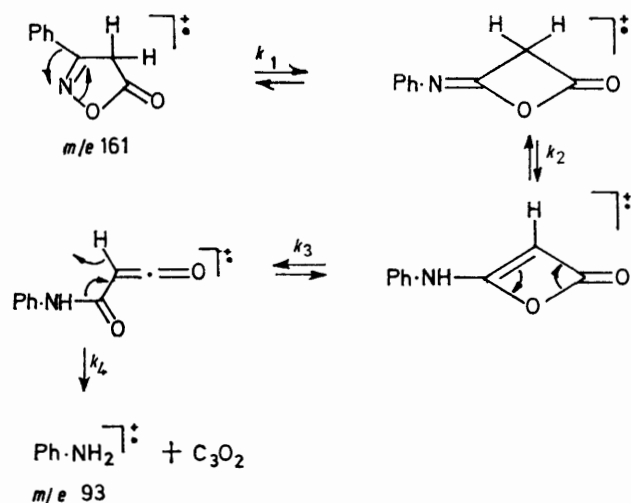
⁹ J. H. Beynon, J. W. Amy, and W. E. Baitinger, *Chem. Comm.*, 1969, 723.

¹⁰ K. H. Maurer, C. Brunnee, G. Kappus, K. Habfast, U. Schröder, and P. Schulze, 19th Annual Conference on Mass Spectrometry, ASTM Committee E-14, Atlanta, Ga., May 1971

¹¹ K. R. Jennings, in 'Some Newer Physical Methods in Structural Chemistry,' eds. R. Bonnett and J. G. Davies, United Trade Press, London, 1967, p. 105.

by electrostatic voltage scanning reveals peaks due to four decomposition processes. The metastable transitions at $E_1 = 294.5$ V (initial voltage $E_0 = 504.4$ V, corresponding to m/e 163 \rightarrow 95) has decreased considerably to 37%, the most abundant peak being that related to the sequence m/e 163 \rightarrow 105 (39%). The relative abundances for the corresponding transitions (*i.e.*, m/e 162 \rightarrow 94 and m/e 162 \rightarrow 104) are 49% and 26% respectively in the DADI spectrum of 3-phenyl-[4- 2 H]isoxazol-5(4H)-one (4).

All these results are in good agreement with the occurrence of a rearrangement process producing ion m/e 93 from the molecular ion *via* the proposed sequence of steps depicted in Scheme 2.



The unimolecular fragmentation of low energy ions (I) leads mainly to the formation of the aniline molecular ion involving an initial [1,2] carbon to nitrogen phenyl migration which is symmetry allowed in the ground state of the carbonium ions,¹² and this is evidenced by 15 N labelling [see compound (2)] and high resolution measurements. The orbital symmetry of ions (I) might be preserved since reaction (a) occurs from low lying energy states, because the lifetimes of ions undergoing decomposition in the second drift region are considerably longer than those of highly excited states.¹³ The fast [1,2] phenyl migration (see below) is favoured because of the appropriate configuration of the initial structure (I), whereby the aromatic group is *anti* to the leaving group (see Scheme 2). This process is then followed by steps involving shifts of the two hydrogen atoms from position 4 as is clearly shown by deuterium labelling [(3) and (4)]. The first is a prototropic shift, and the second is similar to that occurring in the elimination of ketene from acetanilides *via* a four-membered transition

¹² R. B. Woodward and R. Hoffmann, *Angew. Chem. Internat. Edn.*, 1969, **8**, 781.

¹³ R. C. Dougherty, *J. Amer. Chem. Soc.*, 1968, **90**, 5780.

¹⁴ N. Uccella, I. Howe, and D. H. Williams, *Org. Mass Spectrometry*, 1972, **6**, 229.

¹⁵ S. Hammerun and K. B. Tomer, *Org. Mass Spectrometry*, 1972, **6**, 1369.

state.^{14,15} The formation of aniline radical ions and of neutral C_3O_2 (carbon suboxide) molecules are confirmed by refocusing experiments which have revealed the occurrence of the metastable transition m/e 93 \rightarrow 66, as would be expected for the decomposition of the aniline molecular ion.¹⁶

That this decomposition reaction of (1) bears the characteristics of a rearrangement process, *i.e.*, low frequency factor due to entropy requirements and low activation energy, is demonstrated by comparing the ratios of the relative intensities of m/e 93 and m/e 103 ions (Scheme 1) at high and low electron beam energy. The variation of the $[m/e$ 93]/ $[m/e$ 103] ratio with electron energy is shown below for compound (1). It is evident

| eV | 70 | 24 | 18 | 15 | 12 |
|-------------------------|------|------|------|------|------|
| $[m/e$ 93]/ $[m/e$ 103] | 0.33 | 0.33 | 0.45 | 0.90 | 2.00 |

that the $M^{+\cdot} \rightarrow PhNH_2^{+\cdot}$ reaction becomes more prevalent at low molecular ion energies [see also the metastable ratio for compound (1) in the IKE spectrum], showing a low value for both the frequency factor and activation energy of the reaction.

The specific deuteration of position 4 in compounds (3) and (4) provides the opportunity of investigating the possibility that a carbon-hydrogen bond might be broken in the rate-determining step of the formation of aniline radical ions. Therefore it is useful to correlate the metastable abundance ratio for the reaction involving loss of carbon suboxide [reaction (a)] with that for reaction (b) for compounds (3) and (4), assuming no primary and negligible secondary isotope effects on the latter reaction. The comparison of metastable abundance ratios for compound (3) with those for the unlabelled compound (1) clearly demonstrates that there is an isotope effect operating on the rate of C_3O_2 loss from $M^{+\cdot}$, *i.e.*, $[m_a^*]/[m_b^*]$ is 4.0 ± 0.3 for (1); 0.9 ± 0.1 for (3) ($k_H/k_D = 4.4$). The magnitude of the primary isotope effect decreases from 4.4 to 2.1 in the metastable reactions of compound (4), where $[m_a^*]/[m_b^*] = 1.9 \pm 0.1$, due to direct competition between H and D transfer.

These results establish that a hydrogen atom is transferred in the rate-determining step, preceded by a fast process (k_1) which is the phenyl migration observed, *i.e.*, $k_1 \gg k_2$ and/or k_4 (see Scheme 2). Furthermore, the first hydrogen transfer is probably faster than the second ($k_2 > k_4$), because the competing metastable transitions from compound (4) show a considerable decrease in the formation of aniline radical ions [reaction (a)]. The other alternatives, such as $k_2 \leq k_4$, seem unrealistic on the grounds that previous reports on direct competition between 1 H and 2 H transfer in metastable reactions indicate the operation of primary kinetic isotope effects¹⁵ and no considerable change in the magnitude of these values.^{14,17}

¹⁶ H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Mass Spectra of Organic Compounds,' Holden Day, San Francisco, 1967.

¹⁷ N. Uccella, Ph.D. Thesis, University of Cambridge, 1972; I. Howe, N. Uccella, and D. H. Williams, *J.C.S. Perkin II*, 1973, 76.

An isotope effect is also observed to be operating on the unimolecular decomposition of the more highly energetic ions, which fragment in the mass spectrometer source. For instance, $[m/e\ 93]/[m/e\ 103]$ is 0.33 for (1), but the corresponding ratio $[m/e\ 95]/[m/e\ 105]$ is 0.15 for compound (3). The lower value of the isotope effect ($k_H/k_D = 2.2$), as compared with that reported above for the less energetic metastable ions, is in agreement with the expectations that ions of shorter lifetimes react with a greater excess of energy, and confirms that the process is relatively slow even under these conditions.

The initial [1,2] phenyl shift to an electron deficient centre, induced by partial rupture of the N-O bond, is in strict analogy with the Beckmann rearrangement. Accordingly, electronic factors related to the nature of

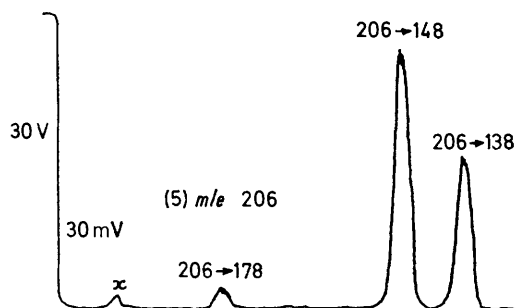
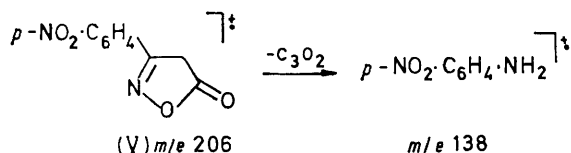


FIGURE 2 DADI spectrum of ions m/e 206, from 3-*p*-nitrophenylisoxazol-5(4*H*)-one (5)

differing migrating groups should cause an alteration of the two-electron Hückel type transition state¹² for the first step of reaction (a) (see Schemes 1 and 2).

In order to evaluate the electronic effect of the aryl group transferred on the kinetics of the reaction leading to the formation of the primary amine ion from 3-aryl-isoxazol-5(4*H*)-one molecular ion, the mass spectrum and the metastable transitions from M^{++} of 3-*p*-nitrophenylisoxazol-5(4*H*)-one (5) have been determined. The IKE spectrum of ions m/e 206 from compound (5) is reproduced in Figure 2. The aryl migration observed in compound (1) is present also in compound (5). In fact m/e 138 ($C_7H_6N_2O_2$) is 6% of the base peak m/e 148. In the second drift region the transition:



corresponds to 36% of the total metastable ion abundance, but the most intense reaction leads to the formation of ions m/e 148 ($C_8H_6NO_2$). The results clearly demonstrate that the activation energy for *p*-nitrophenyl migration in (5) has increased relative to that for phenyl

migration in (1), as would be predicted on the grounds of destabilisation of the transition state due to the electron withdrawing group. This behaviour is analogous to the lower migratory aptitude of the *p*-nitrophenyl group in the Beckmann rearrangement.

EXPERIMENTAL

All mass spectra were determined on a Varian MAT-CH5 DF double focusing mass spectrometer of 'reversed' Nier-Johnson geometry. The spectra were run at 70 eV (nominal) and 3 kV accelerating voltage, except in the observation of the metastable transitions in the first drift region using the 'refocusing technique',¹¹ when accelerating voltages in the range 1–3 kV were used. Metastable transitions in the second drift region were observed at a nominal 3 kV, varying the electrostatic analyser voltage according to the DADI technique.¹⁰

Samples were introduced *via* the direct inlet system with cooled sample probe. Source temperatures were $\leq 80^\circ\text{C}$. The instrument was saturated with D_2O to prevent back exchange of compound (3).

High resolution mass measurements were performed at 10,000 resolving power (10% valley definition).

Unlabelled compounds (1) and (5) were synthesised by literature methods.

3-Phenyl[^{15}N]isoxazol-5(4*H*)-one (2).—The method of Hantzsch¹⁸ was followed, using [^{15}N]hydroxylamine hydrochloride (110 mg) and ethyl benzoylacetate (300 mg). The isotopic purity of the product [m.p. 152° (decomp.), 80% yield] was [$^{15}\text{N}_1$] 97%; [$^{15}\text{N}_0$] 3%.

3-Phenyl[4,4- $^2\text{H}_2$]isoxazol-5(4*H*)-one (3).—Ethyl benzoylacetate (1 g) in dry THF (2 ml) was added with stirring to a slurry of NaH (260 mg, *ca.* 5 mmol from a 50% suspension in oil, washed with light petroleum) in dry THF (3 ml), at room temperature. After 15 min, the reaction mixture was carefully neutralised with D_2SO_4 (1.35*N* in D_2O), then washed with D_2O and dried ($MgSO_4$). The product was isolated by removing the solvent under vacuum, to give the expected ethyl [2,2- $^2\text{H}_2$]benzoylacetate (isotopic purity [$^2\text{H}_2$] 98% by n.m.r.) in 85% yield.

The deuteriated acetate (300 mg) in excess of MeOD was added to a solution of $H_2NOH\cdot HCl$ (110 mg) in excess of D_2O ; the reaction mixture was heated on a water-bath for 0.5 h, and the product separated upon cooling. Recrystallisation from EtOD gave (3) in 80% yield, m.p. 125° (decomp.), [$^2\text{H}_2$] 90%, [$^2\text{H}_1$] 8%, [$^2\text{H}_0$] 2%.

3-Phenyl[4- ^2H]isoxazol-5(4*H*)-one (4).—Ethyl [2- ^2H]benzoylacetate was prepared by partial exchange of ethyl benzoylacetate with D_2SO_4 (0.9*N* in D_2O).

The procedure described above was used to obtain (4) in 82% yield, m.p. 152° (decomp.), [$^2\text{H}_2$] 30%, [$^2\text{H}_1$] 65%, [$^2\text{H}_0$] 5%.

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¹⁸ A. Hantzsch, *Ber.*, 1891, **24**, 495.