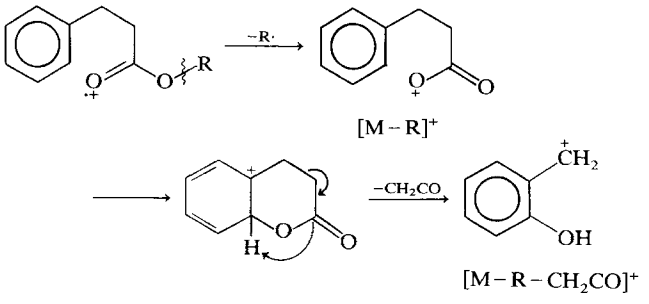
Oxygen Rearrangement of Molecular Ions of 3-Phenylpropionates

Joachim G. Liehr† and Richard M. Caprioli
Analytical Chemistry Center and Department of Biochemistry and Molecular Biology, The University of Texas Medical School at Houston, P, O. Box 20708, Houston, Texas, 77025, USA
John H. Beynon and Roger P. Morgan‡
Royal Society Research Unit, University College of Swansea, Singleton Park, Swansea SA2 8PP, UK
Wilhelm J. Richter
Zentrale Funktion Forschung, Ciba-Geigy AG, Basel, Switzerland

The oxygen rearrangement in molecular ions of 3-phenylpropionates has been investigated with the aid of mass analyzed ion kinetic energy spectra. Elimination of an allyl radical followed by expulsion of ketene from the molecular ion of allyl 3-phenylpropionate is shown to result in formation of protonated benzaldehyde. The oxygen rearrangement has been found to be inoperative in ionized methyl 3-methyl-3-phenylbutyrate. $[M-CH_3-CH_2CO]^+$ ions in the spectrum of the latter compound are formed by elimination of the 3-methyl substituent and subsequent methoxy migration.

INTRODUCTION

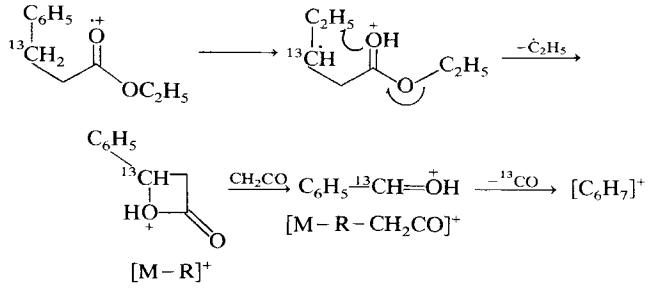
Migrations of carbonyl oxygen have been observed, for instance, in molecular ions of esters,[1-5] acid chlorides[6] and aldehydes.[7,8] Based on substituent and ^{18}O labeling experiments with a variety of esters of different 3-aryl propionates, Kadentsev *et al.*[1-3] were the first to propose a carbonyl oxygen rearrangement as an explanation for ester alkyl losses from molecular ions and subsequent eliminations of ketene to give $[M-R-CH_2CO]^+$ ions (Scheme 1).



Scheme 1

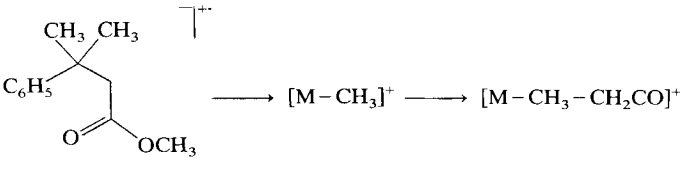
The elimination of ketene was postulated to result from electrophilic substitution of the aromatic moiety by electron deficient carbonyl oxygen and subsequent retro Diels-Alder elimination.

During investigations of oxygen migrations in molecular ions of 3-phenyl-1-nitropropane[9] and carboxylic acid derivatives, such as 3-phenyl propionyl chloride,[6] the problem of oxygen rearrangements in 3-phenyl propionates was investigated to determine the extent of O-migration to the benzylic versus the aromatic *ortho* position. The elimination of ^{13}CO from the rearranged ion $[M-R-CH_2CO]^+$, *m/z* 107, generated from ethyl 3-^{13}C-3-phenylpropionate, led the authors to exclude any involvement of the phenyl ring in oxygen rearrangements. Based on these very elegant experiments, protonated benzaldehyde was postulated to be the product of carbonyl oxygen migration, as shown in Scheme 2.



Scheme 2

Although the ^{13}C labeling experiments lend strong support for the 1,3-oxygen shift to the benzylic position, proposed by Nibbering *et al.*,[5] questions remained as to the applicability of these mechanistic explanations to alkylated analogs, such as is shown in Scheme 3.



Scheme 3

Fragment ions $[M-CH_3]^+$, *m/z* 177 and $[M-CH_3-CH_2CO]^+$, *m/z* 135, from ionized methyl 3-methyl-3-phenylbutyrate have been postulated[4] to arise via the former mechanism proposed by the Russian authors.[1] Unless an improbable 1,4-methyl migration to the carbonyl oxygen takes place as the initial step, oxygen rearrangement to the benzylic position

† Author to whom correspondence should be addressed.
‡ Present address: Shell Research Ltd, Thornton Research Centre, Chester, UK.

CCC-0030-493X/80/0015-0157$02.00

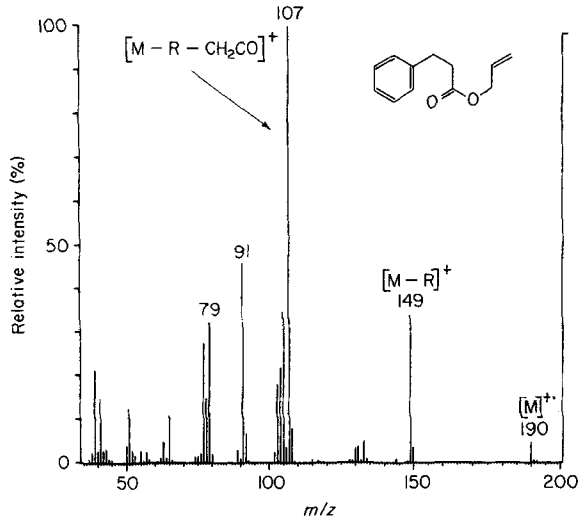


Figure 1. Electron impact mass spectrum of allyl 3-phenylpropionate.

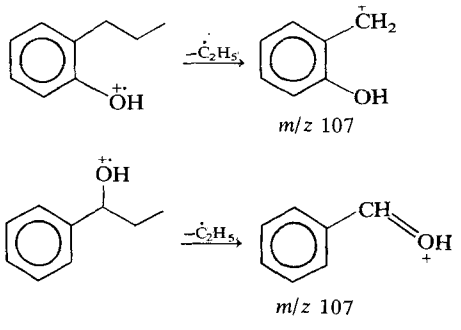
should be inoperative in this case. To distinguish between the two mechanistic proposals or an entirely different route of fragmentation operative for this molecular ion, mass analyzed ion kinetic energy (MIKE) spectroscopy studies of the structures of product ions were undertaken to establish unequivocally the mechanism of oxygen rearrangement. Comparisons of the proposed structures obtained independently from suitable reference materials were expected to shed light on the oxygen rearrangement. The *m/z* 107 ions from allyl 3-phenylpropionate (Fig. 1 shows the mass spectrum) might be typical of ions formed by the mechanism shown in Scheme 2.

RESULTS AND DISCUSSION

The two mechanistic pathways proposed for the oxygen rearrangement lead to different final structures for the product $[M-R-CH_2]^+$. Electrophilic substitution of the aromatic ring system eventually results in an hydroxybenzyl ion.[2] A carbonyl oxygen shift to the benzylic position leads to protonated benzaldehyde.[5]

Each of these same ion species was produced independently and unambiguously by simple α-cleavage reactions from ionized propylphenol and 1-phenylpropanol, respectively (Scheme 4).

The collision induced MIKE spectra of these two ions are shown in Fig. 2 and 3. The interaction of the high kinetic energy ions with the collision gas causes a



Scheme 4

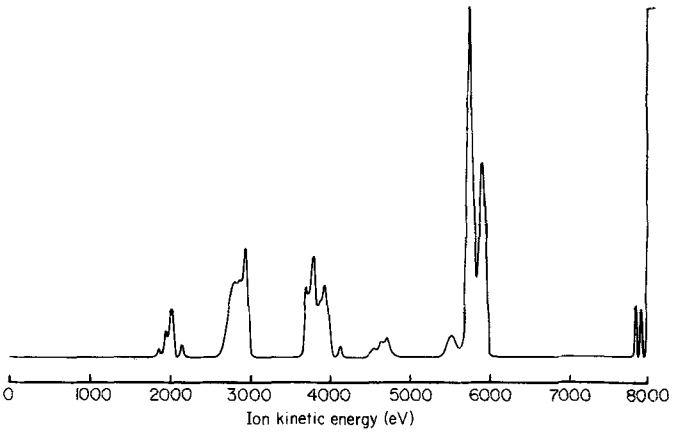


Figure 2. Collision induced MIKE spectrum of ion *m/z* 107 formed by electron impact ionization of propylphenol.

conversion of a portion of the translational energy of the ions into internal energy.[10] The average amount of energy imparted in this way is large compared with the original internal energy distribution of the ion prior to the interaction.[11] Thus, differences in the fragmentation patterns resulting from collision induced MIKE spectra should reflect the differences in structure of the ions rather than differences in the internal energy distribution.[12] It can be seen that the spectrum obtained from the *m/z* 107 ions of propylphenol (Fig. 2) is quite distinct from the spectrum obtained from the *m/z* 107 of 1-phenylpropanol (Fig. 3). Differences are found in intensity of the *m/z* 106 and 105 ions and the group of ions of *m/z* 37, 38 and 39. In addition, in the case of propylphenol the peak due to the formation of the *m/z* 53 daughter ion is quite large, whereas in the 1-phenylpropanol spectrum the corresponding peak is quite small. These results show that two different ion structures are involved.

The collision induced MIKE spectrum of the rearranged *m/z* 107 ion from the allyl 3-phenylpropionate is shown in Fig. 4. If the peaks arising from the processes which also occur unimolecularly (at 5800 and 5900 eV) are excluded, then this spectrum closely resembles the spectrum obtained from the *m/z* 107 ion obtained from 1-phenylpropanol and this result strongly supports the conclusion that the ion has the protonated benzaldehyde structure as proposed by Nibbering *et al.*[5]

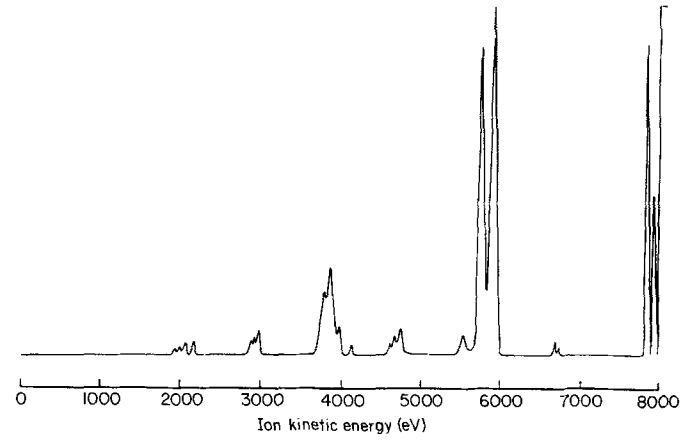


Figure 3. Collision induced MIKE spectrum of ion *m/z* 107 formed by electron impact ionization of 1-phenylpropanol.

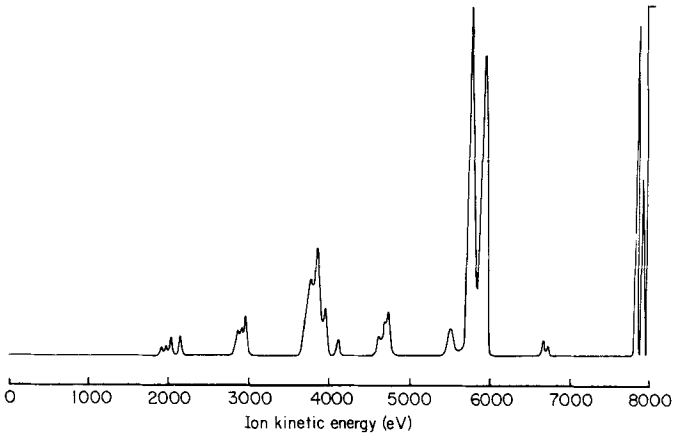


Figure 4. Collision induced MIKE spectrum of ion *m/z* 107 formed by electron impact ionization of allyl 3-phenylpropionate.

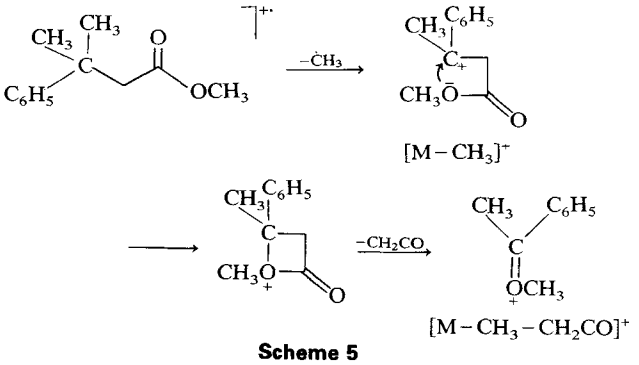
In the molecular ion of methyl 3-methyl-3-phenylbutyrate, migration of carbonyl oxygen to the benzylic portion of the ion is assumed to be inoperative, unless preceding rearrangements clear the benzylic carbon for C—O bond formation. An investigation of the fragmentation with the aid of trideuteriomethyl 3-methyl-3-phenylbutyrate (Table 1) revealed that in the genesis of the $[M-CH_3]^+$ fragment ion, one of the methyl substituents of the acyl portion was eliminated, as shown in Scheme 5.

Benzyl ions of the $[M-CH_3]^+$ structure are known[13] to undergo methoxy migration via a 4-membered ring. Therefore, an analogous mechanistic explanation is advanced for the genesis of the $[M-CH_3]^+$ and $[M-CH_3-CH_2CO]^+$ ions from methyl 3-methyl-3-phenylbutyrate.

These experiments constitute additional evidence in favor of carbonyl oxygen rearrangement to the benzylic position of 3-phenylpropionates, as proposed by Nibbering *et al.*[5] Further 'passive' support for this pathway can be derived from the fact that analogs of this compound, fully substituted on the 3-carbon, fragment via entirely different competing pathways. Therefore, hydrogen abstraction from the 3-C position and formation of a benzyl radical can be regarded as a necessary trigger reaction for the oxygen rearrangement prior to *O*-alkyl cleavage and elimination of ketene.

Table 1. Mass spectra of methyl 3-methyl-3-phenylbutyrate and trideuteriomethyl 3-methyl-3-phenylbutyrate

Compound		m/z (% rel. int.)			
Methyl 3-methyl-3-phenylbutyrate					
192(8)	177(1)	161(1)	145(4)	136(1)	135(12)
118(5)	117(16)	116(1)	115(8)	105(2)	103(5)
91(44)	89(1)	79(4)	78(3)	77(9)	65(2)
120(10)	119(100)				
102(1)	92(3)				
59(2)	51(3)				
Trideuteriomethyl 3-methyl-3-phenylbutyrate					
195(5)	180(1)	161(1)	145(3)	139(1)	138(10)
118(6)	117(19)	116(1)	115(9)	105(1)	103(5)
91(48)	89(1)	79(4)	78(4)	77(11)	65(3)
120(10)	119(100)				
102(1)	92(4)				
62(3)	51(3)				



Scheme 5

EXPERIMENTAL

2-*n*-propylphenol, 1-phenyl-1-propanol and 3-phenylpropionic acid were purchased from Aldrich Chemical Company, Milwaukee, Wisconsin. Allyl 3-phenylpropionate was prepared from 3-phenylpropionic acid, thionyl chloride and allyl alcohol according to standard esterification procedure.[14]

3-Methyl-3-phenylbutyric acid was prepared by condensation of β-dimethylacrylic acid (Aldrich Chemical Company) with benzene in the presence of aluminum chloride.[15] The methyl ester and the trideuteriomethyl ester of this acid were prepared by standard esterification in a methanol/thionyl chloride or tetradeuteriomethanol (99 atom % D enrichment obtained from Merck & Co., Rahway, New Jersey)/thionylchloride mixture respectively.[14]

Electron impact mass spectra were obtained using a Finnigan 3200 gas chromatograph mass spectrometer system with a Finnigan 6000 computer (6 ft × 2 mm glass column, 3% OV 1 on Gas Chrom Q 100/120, initial temperature 100 °C, final temperature 290 °C, 10 °C min^{-1} increase, injector temperature 200 °C, 70 eV).

The mass spectrum of 2-*n*-propylphenol contained the following ions (*m/z* (% rel. int.)): 137(2), 136(27) $[M]^{+\cdot}$, 108(8), 107(100)$[M-C_2H_5]^+$, 91(4), 79(15), 78(6), 77(28), 65(3), 63(4), 53(3), 52(3), 51(6), 50(3).

The mass spectrum of 1-phenyl-1-propanol contained the following ions: 137(1), 136(14) $[M]^{+\cdot}$ 118(2), 117(4), 115(2), 108(8), 107(100) $[M-C_2H_5]^+$ 106(2), 105(15), 103(2), 91(6), 89(2), 80(5), 79(78), 78(12), 77(52), 76(2), 74(2), 65(2), 63(4), 53(3), 52(4), 51(15), 50(5).

Collision induced mass analyzed ion kinetic energy spectra were obtained in the normal manner[11] using a VG-Micromass ZAB-2F mass spectrometer.[16] The source conditions were as follows: accelerating voltage, 8000 V; trap current, 100 μA; source temperature, 150 °C; electron energy, 70 eV; pressure, 8×10^{-8} Torr as read on the ion gauge situated above the diffusion pump.

Acknowledgments

One of the authors (J.G.L.) gratefully acknowledges support from NATO Scientific Affairs Division and J.H.B. and R.P.M. thank the Royal Society and the Science Research Council for support of this work.

REFERENCES

1. V. J. Kadentsev, B. M. Zolotarev, O. S. Chizov, Ch. Shachidayatov, L. A. Yanovskaya and V. F. Kucherov, *Org. Mass Spectrom.* **1,** 899 (1968).
2. B. M. Zolotarev, V. I. Kadentsev, V. F. Kucherov, O. S. Chizov, Kh. Shakhidayatov and L. A. Yanovskaya. *Izvest. Akad. Nauk SSSR, Ser. Khim.* 1552 (1970).
3. V. I. Kadentsev, O. S. Chizhov, L. A. Yanovskaya and V. F. Kucherov, *Izvest. Akad. Nauk SSSR, Ser. Khim.* 1837 (1971).
4. J. K. MacLeod, *Org. Mass Spectrom.* **2,** 791 (1969).
5. J. J. Resink, A. Venema and N. M. M. Nibbering, *Org. Mass Spectrom.* **9,** 1055 (1974).
6. R. Hittenhausen-Gelderblom, A. Venema and N. M. M. Nibbering, *Org. Mass Spectrom.* **9,** 878 (1974).
7. A. Venema and N. M. M. Nibbering, *Org. Mass Spectrom.* **9,** 628 (1974).
8. C. Fenselau, J. L. Young, S. Meyerson, W. R. Landis, E. Selke and L. C. Leitch, *J. Am. Chem. Soc.* **91,** 6847 (1969).
9. T. A. Molenaar-Langeveld and N. M. M. Nibbering, *Adv. Mass Spectrom.* **6,** 31 (1974).
10. R. G. Cooks, J. H. Beynon, R. M. Caprioli and G. R. Lester, *Metastable Ions* Elsevier, Amsterdam (1973).
11. C. J. Porter, R. P. Morgan and J. H. Beynon, *Int. J. Mass Spectrom. Ion Phys.* **28,** 321 (1978).
12. K. Levsen and U. Schwarz, *Angew. Chem. Int. Ed. Engl.* **15,** 509 (1976).
13. R. G. Cooks and D. H. Williams, *Chem. Commun.* 51 (1967).
14. *Organikum,* VEB Deutscher Verlag der Wissenchaften, Berlin (1971).
15. E. Bergmann, H. Taubadel and H. Weiss, *Ber.* **64,** 1493 (1931).
16. R. P. Morgan, J. H. Beynon, R. H. Bateman and B. N. Green, *Inter. J. Mass Spectrom. Ion Phys.* **28,** 171 (1978).

Received 30 March 1979; accepted 18 October 1979