

Study of Hydantoin. III [1]. Mass Spectrometric Behaviour in the Electron Impact of 2-Imino-4-thiazolidinone Derivatives

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The mass spectral decomposition modes of a series of 2-imino-4-thiazolidinone derivatives are reported and discussed. The fragmentation patterns and mechanisms postulated have been confirmed by the analysis of the MIKE spectra and using DADI technique and the effects of heteroatoms and substituents on the MIKE spectrum of these compounds are compared with that of 3-substituted hydantoins.

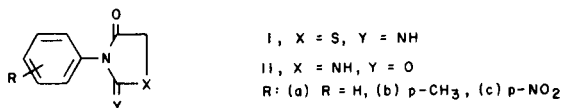
J. Heterocyclic Chem., **20**, 1725 (1983).

It is well established [2-5] that unimolecular decompositions of organic ions in the gas phase can be thoroughly investigated by means of systematic MIKE/DADI mass spectrometry. Application of the above mentioned technique is illustrated by the determination of decomposition pathways occurring from 2-imino-4-thiazolidinone derivative (Ia-c).

A number of 2-imino-4-thiazolidones (pseudohydantoins) were synthesized earlier [6-10] and some of them showed interesting physiological activity [11-13].

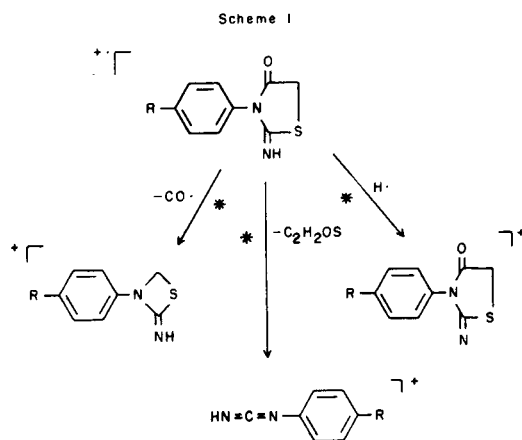
However, very limited mass spectral data [14-15] are available for these compounds. The mass spectra of 2-imino-4-thiazolidinone and its derivatives have not been reported.

Recently we studied the electron impact mass spectra of some 3-substituted hydantoins [1] and rearrangement of protonated arylisocyanate ions induced from hydantoins (IIa-c) using MIKE spectrum. Now we report the 70 eV electron impact spectra of 2-imino-4-thiazolidone derivatives (Ia-c) and compare with the unimolecular reaction of hydantoins (IIa-c) in the gas phase, in order to study the effects of the heteroatoms and the substituents on the MIKE spectrum (metastable transition patterns).

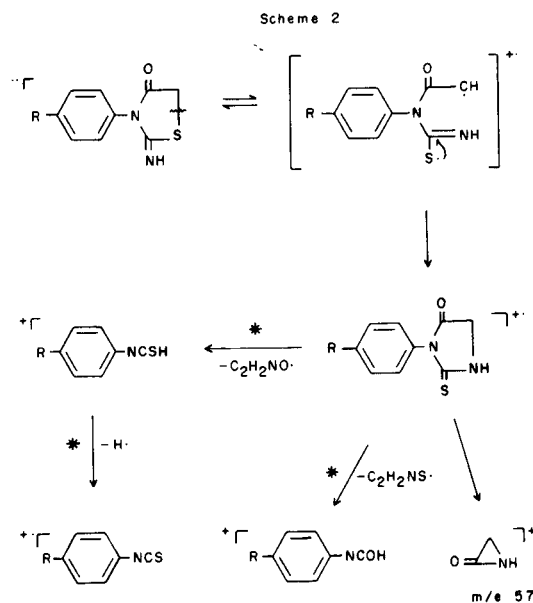


The fragmentation patterns of thiazolidinone derivatives I are reproduced in Scheme 1.

The mass spectra of hydantoins are reported and characterized by the α -fission at the carbonyl group with loss of C=O [16-18]. In the unimolecular reaction of thiazolidinone derivatives, we also observe that the loss of carbonyl radical is one of major pathways, but ($M^+ - CO$) ion formation is little affected by substituents. These results are



different from that of 3-arylsubstituted hydantoins. On the MIKE spectrum of hydantoins, the loss of a carbonyl



group is the most dominant process in the case of an electron withdrawing group substituted on the *meta*- or *para*-position. With an electron donating group (such as methyl or methoxy) substituted on the *meta*- or *para*-position, the loss of C_2H_2NO is the dominant pathway.

In the unimolecular reaction of thiazolidinones Ia-c in the gas phase, the molecular ions are rearranged and followed formation of thiohydantoin derivative ions as an intermediate (Scheme 2).

Arylisocyanate and arylthioisocyanate ions are formed from the thiohydantoin ions [19-21].

The pyrolysis of phenylthiohydantoin yields products, which are the phenylisocyanate and the phenylthioisocy-

anate ion, *etc.*, identified by the combined analysis techniques of pyrolysis/gas chromatography/mass spectrometry [22].

The mass measurements using the MIKE/DADI technique shows that the rearrangement pathway only carries 8-10% of the total metastable transitions current at the spectrum of the molecular ions. The metastable transitions are shown in Figure 1.

The reactivity of the 4-carbonyl group of the hydantoin is worthy of note since the delocalization of the nonbonding electrons of the nitrogen atoms does not extend to that group, and the substituent effects of the aromatic ring is directly affected by the group. In the case of thiazolidinones (Ia-c), the five-membered ring contains a sulfur atom and the 2-carbon atom is bonded to an imino NH group and as a result, the electrophilic reactivity of the carbonyl group at position 4 is decreased. Thus, the nonbonding electrons of the heteroatoms may extend to that group. The results are corroborated with the rearrangement of the molecular ions in the free drift region.

The molecular ions of the thiazolidinones exhibit the same type of metastable transition. The MIKE spectrum for the unimolecular fragmentation, *i.e.*, M-H, M-CO, and M-C₂H₂SO ions with the various relative abundance for the substituents in aromatic rings is shown in Table 1.

In conclusion, the pseudohydantoin rings are open in the α -position to the 4-carbonyl group, and loss of C=O and C₂H₂NS from their molecular ions is observed. The electron impact mass spectra of 2-imino-4-thiazolidinone derivatives are similar to the mass spectra of 3-aryl-4-hydantoin II, however, arylisocyanate ions containing a 4-C=O group are produced from molecular ions which is a contribution of the sulfur atom in the thiazolidinone derivatives.

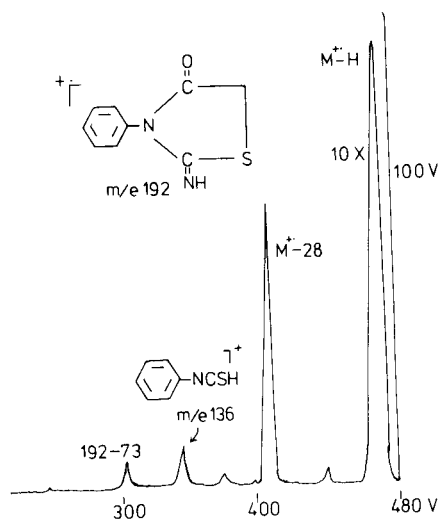

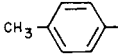
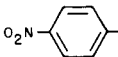



Figure 1. MIKE spectrum of ions m/e 192, from 2-imino-3-phenyl-4-thiazolidinone.

Table 1

EI (70 eV) Mass Spectral Data of 2-Imino-4-thiazolidinones

Compounds	(M · H) ⁺ [a]		(M · CO) ⁺		(M · C ₂ H ₂ OS) ⁺		(XNCS) ⁺ [b]		(XNCO) ⁺	
	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%
	191	100	164	11	118	54	135	8.9	119	31
	205	100	178	5.4	132	43	149	5.6	133	34
	263	86	209	6.4	163	23	180	10	164	25

[a] M: Molecular ion. [b] $x = R$ 

EXPERIMENTAL

Melting points were taken in open capillaries in a Thomas Hoover Mel-Temp apparatus and are uncorrected. The ir spectra were obtained with a Perkin-Elmer Model 283, whereas nmr spectra reported in δ units were taken on a Varian FT-80A spectrometer with TMS as the internal reference. The mass spectra were recorded on a Varian MAT 212 mass spectrometer within an electron beam energy of 70 eV and at a constant acceleration potential of 3 KV and exact mass measurements were obtained from a Spectro System SS MAT 188 computer. Samples were introduced via a direct inlet system at a source temperature of 220-250°. Metastable transitions were determined by automatic variation of electrostatic analyzer (ESA) voltage from initial value (E_0) downwards each metastable peak arises from unimolecular fragmentations in the free drift region of the reversed instrument and occurs at an ESA voltage, E , where allows the assignment of parent (m_1) and daughter (m_2) mass numbers using the relationship $m_2 = m_1 E/E_0$.

The 2-imino-4-thiazolidinone derivatives (Ia-c) were prepared according to well known procedures [6-10].

2-Imino-4-thiazolidinones (Ia-c).

A general procedure is described. To a suspension of 0.01 mole of potassium thiocyanate in 50 ml of acetonitrile, a solution of 0.01 mole of 2-chloroacetaniline was added and the mixture was stirred at room temperature for 6-8 hours. The solvent was evaporated and the crude product was recrystallized from ethanol-chloroform.

The 2-chloro-*N*-phenylacetamide gave 2-imino-3-phenyl-4-thiazolidinone (Ia) in 65% yield, mp 150-151° (lit [6] mp 151°); ir (potassium bromide): 1705, 1690, 1610, 1500, 1405; nmr (deuteriochloroform): δ 4 (s, CH₂, 2H), 7.5-7.2 (m, aromatic, NH, 6H).

2-Imino-3-(4-methylphenyl)-4-thiazolidinone (Ib).

This compound was obtained in a yield of 60%, mp 124-125° (lit [10] 125-126); ir: 1685, 1635, 1600, 1508, 1450, 1400; nmr: δ 2.4 (s, CH₃, 3H), 4 (s, CH₂, 2H), 7.7-7.4 (m, aromatic, NH, 5H).

2-Imino-3-(4-nitrophenyl)-4-thiazolidinone (Ic).

This compound was obtained in a yield of 45%, mp 173-174°; ir: 1755, 1720, 1650, 1505, 1400; nmr δ 4.05 (s, CH₂, 2H), 7.5-8.2 (m, aromatic, NH, 5H).

Anal. Calcd. for C₉H₇N₃O₃S: C, 45.57; H, 2.95; N, 17.75. Found: C, 45.61; H, 3.11; N, 17.73.

REFERENCES AND NOTES

- [1] B. M. Kwon and S. C. Kim, *J. Chem. Soc., Perkin Trans. II*, in press.
- [2] U. P. Schlunegger, *Angew. Chem. Int. Ed. Engl.*, **14**, 679 (1975).
- [3] R. W. Kondraft and R. G. Cooks, *Anal. Chem.*, **56**, 81A (1978).
- [4] J. H. Beynon, R. G. Cooks, J. W. Amy, W. E. Baitinger and T. Y. Ridley, *ibid.*, **45**, 1023A (1973).
- [5] R. P. Morgan, J. H. Beynon, R. H. Bateman and B. N. Green, *Int. J. Mass Spectrom. Ion Phys.*, **28**, 171 (1978).
- [6] H. L. Wheeler and T. B. Johnson, *J. Am. Chem. Soc.*, **24**, 680 (1902).
- [7] S. P. Kharidia, B. K. Raval and J. J. Trivedi, *J. Indian Chem. Soc.*, **39**, 43 (1962).
- [8] E. Akerblom, *Acta Chem. Scand.*, **21**, 843 (1967).
- [9] M. Hauser, *J. Org. Chem.*, **27**, 43 (1962).
- [10] E. Schropf and R. Pohlondk-Fabini, *Pharmazie*, **23**, 638 (1968).
- [11] M. Chaudhary, S. S. Parmar, S. K. Chaudhar, A. K. Chaturvedi and B. V. Ramasastry, *J. Pharm. Sci.*, **65**, 443 (1976).
- [12] K. F. Modi and J. J. Trivedi, *J. Indian Chem. Soc.*, **50**, 564 (1973).
- [13] R. Shyam and I. C. Tiwari, *Agric. Biol. Chem.*, **39**, 715 (1975).
- [14] O. Ceder and U. Stenhede, *Acta Chem. Scand.*, **27**, 1923 (1973).
- [15] R. C. Dougherty, R. L. Flotz and L. B. Kier, *Tetrahedron*, **26**, 1989 (1970).
- [16] R. A. Corral, O. O. Orazi, A. M. Duffield and C. Djerassi, *Org. Mass Spectrom.*, **5**, 551 (1971).
- [17] G. Ruecker, P. N. Natarajan and A. F. Fell, *Arch. Pharm.*, **304**, 833 (1971).
- [18] T. Suzuki and K. Tuzimura, *Agric. Biol. Chem.*, **40**, 225 (1973).
- [19] T. Suzuki, K. D. Song, Y. Itagaki and Tuzimura, *Org. Mass Spectrom.*, **11**, 557 (1976).
- [20] R. E. Ardrey and A. Darbre, *J. Chromatogr.*, **87**, 449 (1973).
- [21] T. Fairwell, S. Ellis and R. E. Lovins, *Anal. Biochem.*, **53**, 115 (1973).
- [22] C. Merritt, Jr., C. Dipietro and D. H. Robertson, *J. Chromatogr. Sci.*, **12**, 668 (1974).