SYNTHESIS AND PROPERTIES OF AZOLES AND THEIR DERIVATIVES.

25.* ELECTRON-IMPACT MASS SPECTRA OF NITRO- AND NITROALKYL-SUBSTITUTED 3-ARYL-Δ^2-ISOXAZOLINES

A. Barańskii and A. I. Mikaya

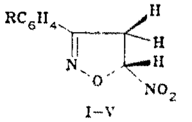
UDC 543.51:786.1

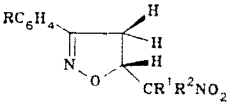
The fragmentation of nitro and nitroalkyl derivatives of 3-aryl-Δ^2-isoxazolines under the influence of electron impact was investigated. It was established that the fragmentation of the molecular ions of these compounds takes place primarily through the nitro- and halogen-containing groups; other pathways of dissociative ionization include the most important pathways of the fragmentation of arylisoxazoles.

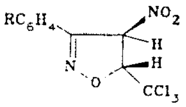
It has been observed that Δ^2-isoxazoline derivatives have a broad spectrum of biological activity [2-6]. Some of them have found application as agents for plant protection [2, 3] and medicinal preparations [4]. Many are used in the synthesis of pharmacologically important products and intermediates [7-10], including those of natural origin.

The present research was devoted to a study of the behavior of nitro- and nitroalkyl-substituted 3-aryl-Δ^2-isoxazolines I-XIII under the influence of electron impact. Compounds that have moderate and high degrees of fungistatic activity against some pathogenic fungi and moderate activity with respect to staphylococcus and the tuberculosis mycobacterium have been previously found [5, 11] among this group of substances.

Depending on the structure and the character of fragmentation under the influence of electron impact, the investigated compounds can be subdivided into three groups, viz., I-V, VI-X, and XI-XIII.


I-V


VI-X


XI-XIII

I, XI R=H; II R=*p*-F; III, XII R=*p*-Cl; IV R=*m*-Cl; V, XIII R=*p*-Br; VI $R=R^1=R^2=H$; VII R=*p-F*, $R^1=R^2=H$; VIII R=Cl, $R^1=R^2=H$; IX R=Br, $R^1=R^2=H$; X R=H, $R^1=NO_2$, $R^2=CH_3$

The mass spectra of 3-aryl-5-nitro-Δ^2-isoxazolines I-V basically coincide with the spectra of the 3,4-diaryl-5-nitro-Δ^2-isoxazolines that we previously investigated [12]. The fragmentation of isoxazolines I-V can be represented by Scheme 1.

The most important peculiarity of the electron-impact mass spectra of I-V (Table 1) is the absence in them of molecular-ion peaks (M^+) which, however, have significant intensities in the case of other derivatives (VI-XIII). Intense peaks of $[M - NO_2]^+$ (F_1), $[M - HNO_2]^+$ (F_2), and $[M - H_2NO_2]^+$ (F_3) ions are observed in the high-molecular-weight region of the spectra of 3-aryl-5-nitroisoxazolines I-V. The formation of F_3 ions as a result of the elimination of a hydrogen radical from the F_2 (F_2') ions is proved by the presence of the corresponding metastable ions in the spectra. The development of F_2 ions can be explained by the detachment of a molecule of HNO_2 from M^+ (from the $C_{(3)}$ and $C_{(4)}$ atoms of the heterocyclic ring) with the formation of pseudomolecular ions of the corresponding 3-arylisoxazoles. This, in particular, is confirmed by comparison of the mass spectrum of 3-phenyl-5-nitro-Δ^2-isoxazoline (I) with the mass spectrum of 3-phenylisoxazole, which is presented in complete form in [13]. It should be noted that the thermal (80-130°C) dehydronitrosation of these compounds also proceeds similarly [14].

---

*See [1] for Communication 24.

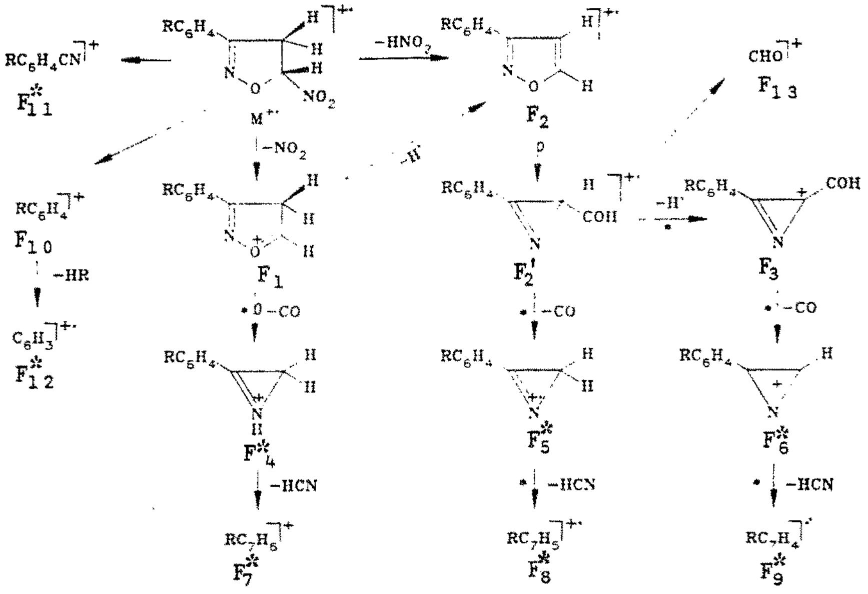
T. Kosciusko Krakow Polytechnical Institute, Krakow 31-155. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 980-983, July, 1990. Original article submitted October 17, 1988; revision submitted January 23, 1989.

TABLE 1. Mass Spectra of I-XIII

Compound	Intensities of the peaks of the characteristic ions (% of the max. peak)																
	M^+	F_1	F_2/F_2'	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}	F_{13}	F_{14}	F_{15}	F_{16}	F_{17}
I	—	33	47	12	27	17	14	13	14	17	100	19	8	6	—	—	—	—
II	—	53	77	60	38	60	34	24	21	27	100	28	51	10	—	—	—	—
III	—	56	100	92	36	41	33	14	10	18	76	30	90	12	—	—	—	—
IV	—	71	81	88	40	29	22	13	8	11	99	48	100	15	—	—	—	—
V	—	70	100	56	33	22	19	7	—	7	33	—	62	13	—	—	—	—
VI	44	56	89	48	17	71	4	14	5	6	100	12	5	7	—	—	—	—
VII	45	43	100	46	22	83	6	22	6	10	65	14	35	15	—	—	—	—
VIII	47	50	100	29	15	72	—	11	—	11	48	10	41	8	—	—	—	—
IX	42	57	100	25	16	68	—	10	—	—	66	10	42	15	—	—	—	—
X	24	41	42	27	18	27	5	13	6	7	100	30	6	11	—	—	—	—
XI	7	30	16	32	—	92	9	—	8	15	100	15	12	5	26	12	28	92
XII	7	16	12	21	—	53	8	—	3	10	33	12	37	3	18	8	20	100
XIII	4	9	9	13	—	29	6	—	—	—	18	5	36	4	9	5	—	100

In the text and in the schemes the ions, the elementary compositions of which for the individual compounds were confirmed by accurate measurement of the masses, are designated by the symbol F_n.

Scheme 1



---

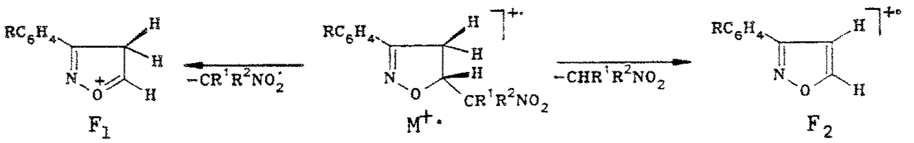
*Metastable transitions determined by the DADI method.

All three fragment ions are capable of subsequently losing a molecule of CO, which leads to the development in the spectra of rather intense peaks of F_4*, F_5*, and F_6* ions, to which, in accordance with the data in [12, 13, 15, 16], azirine ion structures were assigned. Azirine ions readily eject a molecule of HCN to give F_7*, F_8*, and F_9* fragments, respectively; this is in complete agreement with data on the fragmentation of C-aryl-substituted azirines and aziridines [15].

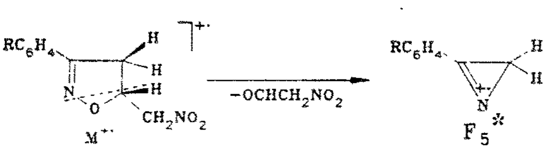
In addition, peaks of $[RC_6H_4]^+$ (F_{10}) and $[RC_6H_4C{\equiv}N]^+$ (F_{11}*) ions, which can arise both from M^+ and from fragment ions, are observed in the mass spectra of compounds of this group. In addition to them, rather intense peaks of $[C_6H_3]^+$ (F_{12}*) ions, which evidently develop from F_{10} ions via elimination of HR, as well as low-intensity peaks of $[CHO]^+$ (F_{13}) ions, the appearance of which may be associated [13, 15] with cleavage of the exocyclic C–CHO bond in the F_2' ion, which arises as a result of skeletal rearrangement of the F_2 ion, are present at times in the low-molecular-weight region of the spectra.

The proposed pathways of fragmentation of the M^+ ions in the mass spectra of I and II are confirmed by the presence of metastable ions for the $F_1 \rightarrow F_4^*$, $F_2 \rightarrow F_5^* \rightarrow F_8^*$, and $F_2^* \rightarrow F_3 \rightarrow F_6^* \rightarrow F_9^*$ transitions, by the precise masses of selected ions in the spectrum of I, and by the corresponding change in the mass numbers of the F_1–F_{11} ions, depending on substituent R.

Fragmentation with the ejection of $NO_2^{\cdot}$ and HNO_2 particles is uncharacteristic for the VI-X group of compounds, which have rather stable M^+ ions (Table 1). The dominating pathway in the dissociative ionization of the M^+ ions of these compounds is splitting out of the nitro-containing substituent; the elimination of $CR^1R^2NO_2$ and $CHR^1R^2NO_2$ particles evidently leads to the formation of F_1 and F_2 ions:



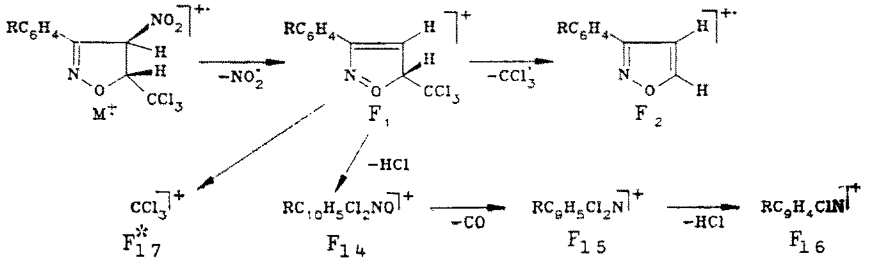
The subsequent fragmentation of these ions proceeds as in the case of the preceding group of compounds and leads to F_3-F_{13} ions (Scheme 1). It should be noted that in the case of VI-XI the F_5 ion may also develop directly from the M^+ ion by the elimination of an $OCHCH_2NO_2$ particle:



The latter process can be considered to be the most likely since, in this case, in contrast to I-V, the peaks that formally correspond to F_5^* ions are very intense. A similar mechanism of dissociative ionization was previously detected [15, 17] for the molecular ions of 3-aryl-Δ^2-isoxazolines and led to $[M - CH_2O]^+$ ions.

A fundamental peculiarity of the fragmentation of the M^+ ions of 3-aryl-4-nitro-5-trichloromethyl-Δ^2-isoxazolines XI-XIII is the facile ejection of an $NO_2^{\cdot}$ radical and complete inhibition of processes associated with the subsequent elimination of one or two hydrogen atoms (Scheme 2).

Scheme 2



The subsequent fragmentation of the $[M - NO_2]^+$ (F_1) ions is also determined by the presence in these molecules of a trichloromethyl substituent, which shows up in the mass spectrum in the form of one of the most intense cations, viz., $[CCl_3]^+$ (F_{17}^*). In particular, the F_1 ions quite readily lose a CCl_3 radical (see Scheme 2) to give, in all likelihood, pseudomolecular ions of the corresponding 3-arylisoxazoles (F_2), and also successively eliminate HCl (F_{14}), CO (F_{15}), and again HCl (F_{16}). The subsequent fragmentation of the F_2 ions proceeds via the pathways that are characteristic for 3-arylisoxazoles [13] and leads to F_5. F_6, F_8, F_9, and F_{13} ions (see Scheme 1). Like the remaining 3-aryl-Δ^2-isoxazolines I-X, XI-XIII to an appreciable extent form $[RC_6H_4]^+$ (F_{10}), $[RC_6H_4C{\equiv}N]^{+\cdot}$ (F_{11}), and $[C_6H_l]^+$ (F_{12}) ions (Table 1).

Thus an analysis of the mass spectra of I-XIII showed that the fragmentation of the molecular ions of these substances includes the elimination of the nitro substituent and the most important features of the dissociative ionization of 3-arylisoxazoles [13, 15, 18]. The electron-impact mass spectra are of practical interest for the identification of such compounds and their isoelectronic analogs.

EXPERIMENTAL

The mass spectra were obtained with an LKB-9000S spectrometer using a system for the direct introduction of the samples into the ion source; the ionizing-electron energy was 70 eV, the emission current was 50 μA, and the temperature of the ion source was 250°C. To avoid thermal decomposition, the spectra of I-V were recorded at the vaporization temperatures of the samples (25-55°C), and the spectra of VI-XIII were recorded at 50-80°C. According to the results of thermogravimetric analysis, the compounds investigated in our research are completely stable over the 25-150°C range. The high-resolution spectra were obtained with MKh-1320 and MAT-311A spectrometers.

The methods used for the synthesis of the compounds investigated in this research and their physicochemical characteristics are presented in [14, 19-21].

LITERATURE CITED

1. A. Barański *Zh. Vses. Khim. Obshch.* (in press).
2. Yu. A. Baskov, *Zh. Vses. Khim. Obshch.*, **39**, 22 (1984).
3. A. F. Grakov and N. M. Mel'nikov, *Zh. Vses. Khim. Obshch.*, **39**, 40 (1984).
4. W. Kurylowicz, *Antybiotyki, Aktualny Stan Wiedzy*, PZWL, Warsaw (1979), p. 101.
5. A. Barański Selected Works in the Field of Chemistry: Monograph No. 55, Cracow Techn. Univ. (1987), p. 43.
6. Lu. Jingjong and M. J. Wehrmeister, US Patent No. 4,593,023; *Chem. Abstr.*, **105**, 97462 (1986).
7. V. Jager, H. Grund, V. Buss, W. Schwab, I. Muler, and R. Schohe, *Bull. Soc. Chim. Belges*, **92**, 1039 (1983).
8. A. P. Kozikowski, *Acc. Chem. Res.*, **17**, 410 (1984).
9. A. P. Kozikowski, *Comprehensive Heterocyclic Chemistry*, A. R. Katritzky (ed.), Pergamon Press, Oxford (1984).
10. A. A. Akhrem, F. A. Lakhvich, and V. A. Khripach, *Khim. Geterotsikl. Soedin.*, No. 9, 1155 (1981).
11. A. Barański and E. Cholewka, *Abstracts of Polish Chemical Society Meeting*, Lódz (1988), p. A-11.
12. A. Barański and A. I. Mikaya, *Khim. Geterotsikl. Soedin.* [sic].
13. J. H. Bowie, R. K. M. Kallury, and R. G. Cooks, *Aust. J. Chem.*, **22**, 563 (1968).
14. A. Barański and G. A. Shvekhgeimer, *Pol. J. Chem.*, **56**, 459 (1982).
15. Q. N. Porter, *Mass Spectrometry of Heterocyclic Compounds*, 2nd edn., Wiley, New York (1985), p. 851.
16. P. B. Terent'ev and A. P. Stankyavichyus, *Mass Spectrometric Analysis of Biologically Active Nitrogen Bases* [in Russian], Mokslas, Vilnius (1987), p. 161.
17. G. F. Benetti and S. Facchetti, *Org. Mass Spectrom.*, **9**, 753 (1974).
18. N. S. Vul'fson, V. G. Zaikin, and A. I. Mikaya, *The Mass Spectrometry of Organic Compounds* [in Russian], Khimiya, Moscow (1986), p. 145.
19. G. A. Shvekhgeimer, A. Barański and M. Grzegożck, *Synthesis*, 612 (1976).
20. A. Barański G. A. Shvekhgeimer, and N. I. Kirillova, *Pol. J. Chem.*, **54**, 23 (1980).
21. A. Barański *Pol. J. Chem.*, **56**, 257 (1982).