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Short communication

Mass spectrometric fragmentation pathways of isotope labeled 2,5-disubstituted-1,3,4-oxadiazoles and thiadiazoles

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Abstract

The mass spectrometric decomposition of protonated, lithiated and methylated (quaternary derivatives) 2-(4′-methoxy)phenyl-5-phenyl-1,3,4-oxadiazoles, containing ^{13}C atom at 5 position of oxadiazole ring as well as its thia correspondent is discussed. The electron-donor properties of C-4′ substituent favor cationization of N(3) atom and as a consequence, the losses of HNC(2)O, LiNC(2)O, $CH_3NC(2)O$ molecules are favored over HNC(5)O, LiNC(5)O, $CH_3NC(5)O$ molecules. Analogous results have been obtained for HNCS and CH_3NCS elimination from thiadiazole.

Keywords: 1,3,4-Oxadiazoles; 1,3,4-Thiadiazoles; Mass spectrometric fragmentation pathway; Skeletal rearrangement

1. Introduction

The mass spectrometric fragmentation pathways of 1,3,4-oxadiazoles were studied by electron ionization (EI) [1–3], chemical ionization (CI) [4], electrospray ionization (ESI) [5] and liquid secondary ion mass spectrometry (LSIMS) [5,6].

It has been shown [5,6] that on mass spectrometric dissociation (ESI and LSIMS) protonated 2,5-disubstituted-1,3,4-oxadiazoles lose isocyanic acid (HNCO) and, analogously, lithiated molecules lose lithium isocyanate (LiNCO). In order to better understand this complex skeletal rearrangement the isotope labeled compound was synthesized, namely 2-(4′-methoxy)phenyl-5-phenyl-1,3,4-oxadiazole (**1**), containing ^{13}C atom at 5 position of oxadiazole ring. For comparison its unlabelled correspondent (**2**) was also prepared as well as their thia derivatives, **3** and **4**, (Scheme 1), the *m*/*z* values of fragment ions containing C(5) atom were always one unit lower for **2** and **4**. in comparison to the **1** and **3**, respectively.

2. Experimental

The LSI mass spectra were obtained on an AMD 604 two sector mass spectrometer of the reverse B/E geometry, made by AMD Intectra (Germany). A CsI gun supplied the primary ion beam (12 keV, Cs^+). The secondary ion beam was accelerated to 8 kV. The compounds were dissolved in 3-nitrobenzyl alcohol (NBA) obtained from Aldrich. The metastable decays of the selected ions were analyzed by B/E linked scan mass spectra.

The ESI CID mass spectra of the compounds studied were obtained on a Waters/Micromass (Manchester, UK) ZQ mass spectrometer equipped with a Harvard Apparatus syringe pump. The sample solutions (10^{-5} M) were prepared in methanol/water (1:1). The ESI source potentials were capillary 3 kV, lens 0.5 kV, extractor 4 V and cone voltage value state in the text. The last parameter is important for "in source" fragmentation. The source temperature was 120 °C and the desolvation temperature was 300 °C. Nitrogen was used as the nebulizing and desolvating gas at flow-rates of 100 and 300 l h^{-1}, respectively.

The oxadiazoles were synthesized according to the procedures described elsewhere [7–9]. The isotope labeled compounds **1** and **3** were synthesized using labeled benzoic acid C_6H_5–$^{13}COOH$ (Aldrich).The thiadiazoles were prepared by using Lawsone'a reagent (Aldrich). The quaternary

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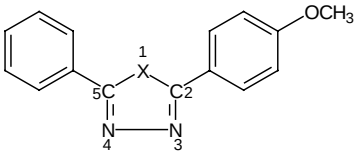


	Comp.
C(5) = ^{13}C, X = O	**1**
C(5) = ^{12}C, X = O	**2**
C(5) = ^{13}C, X = S	**3**
C(5) = ^{12}C, X = S	**4**

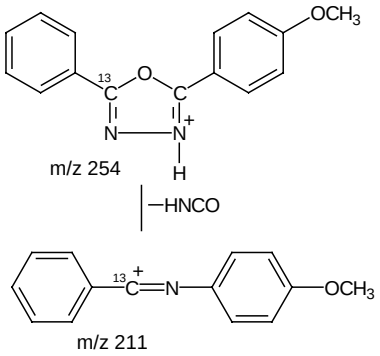
Scheme 1. Compounds studied.

derivatives of compounds studied were performed in acetonitrile by using methyl iodide. The detailed description of the synthesis of compounds studied will be published later.

3. Results and discussion

Previously performed theoretical calculations have shown that groups like methoxy or amino (electron-donor group) at 4′-position, favor the protonation of N(3) atom [6]. As a result, the eliminated HNCO should contain C(2) atom as shown in Scheme 2 for **1**, according to the earlier proposed mechanism [5].

Fragmentation pattern of **1** obtained upon electrospray ionization (ESI) has shown that elimination of HNC(2)O is strongly favored over elimination of HNC(5)O, as the loss of mass 43 is observed from the ions $[\mathbf{1}+H]^+$ and $[\mathbf{2}+H]^+$, as shown in Fig. 1. If the elimination of HNC(5)O occurred, the loss of mass 44 would be observed for **1**. Under liquid secondary ion mass spectrometric condition, from the $[\mathbf{1}+H]^+$ ion both HNC(5)O and HNC(2)O molecules were lost. Elimination of the latter was favored since the observed ratio of respective fragment ions was 3:2. The ions generated by LSIMS contain more energy than those generated by ESI [10], thus the protonation of N(5) atom is possible under LSIMS condition which leads to the loss of HNC(5)O. Decomposition of the [**1**+Li] ion gives the LiNC(2)O molecule, but not LiNC(5)O one. For lithiated molecule the process discussed is, in general, less efficient [6].



Scheme 2. Loss of HNCO molecule from protonated **1**.

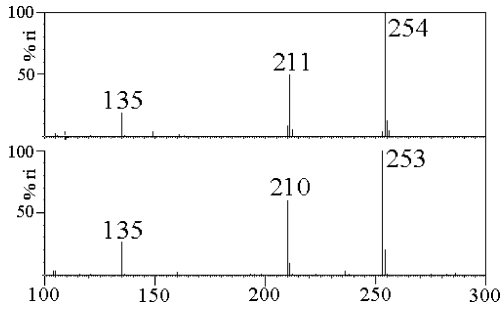


Fig. 1. The ESI CID mass spectra of **1** (top) and **2** (bottom) recorded at cone voltage 50 V.

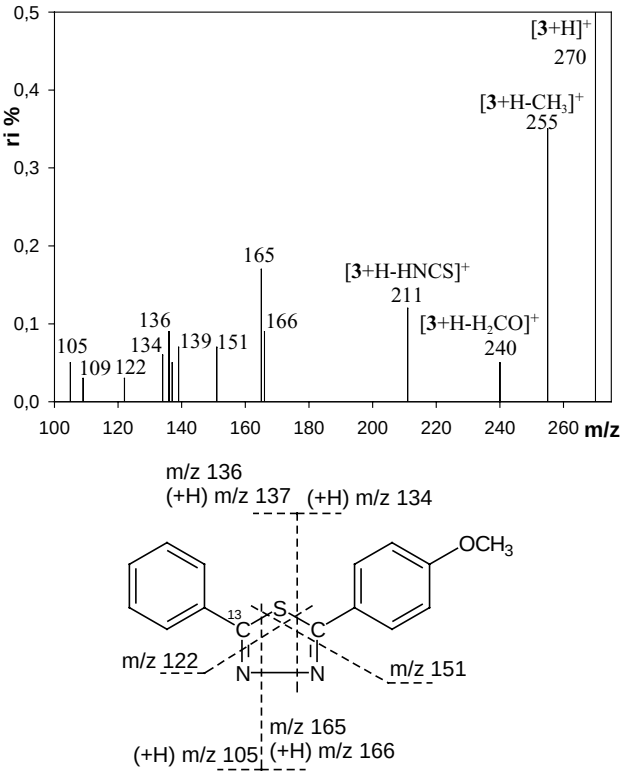


Fig. 2. The LSI B/E mass spectrum of $[\mathbf{3}+H]^+$ ion and fragmentation pathways observed. The peaks at *m/z* 139 and 109 corresponds to the $[H_3CO–C_6H_4–S]^+$ and $[C_6H_5–S]^+$ ions.

For protonated thiadiazole **3**, under both ESI and LSIMS conditions, the loss of isothiocyanic acid containing C(2) atom (HNC(2)S molecule) was found to be strongly favored over the loss of HNC(5)S molecule, analogously as for oxadiazole **1**. Although the isothiocyanic acid is thermodynamically more stable than isocyanic acid [11–13], the rearrangement discussed is less efficient for thiadiazoles than for oxadiazoles. It seems to be reasonable to assume, that other directions of fragmentation pathway observed for **3**, shown in Fig. 2, compete with the HNCS loss making this process less efficient.

The CH_3NCO molecule (methyl isotiocyanate) eliminated from quaternary derivatives **1**–**2** (methylated) also contained C(2) atom. For quaternary derivatives, the process discussed depends on which nitrogen atom was methylated. Therefore, the conclusion can be drawn that N(3) atom is more prone for methylation than N(4) atom. For oxadiazoles the loss

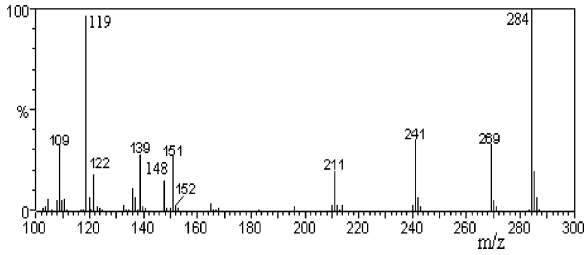


Fig. 3. The ESI CID mass spectrum of methylated **3** recorded at cone voltage 80 V.

of CH_3NCO molecule was the only fragmentation pathway observed in both LSI and ESI mass spectra. However, for thiadiazoles, besides $CH_3NC(2)S$ loss, other fragmentation also proceeded as shown in Fig. 3.

In order to generate the abundant fragment ions from thiadiazoles the cone voltage should be increased to 70–80 V (Fig. 3), since for oxadiazoles 50 V was enough (Fig. 1). It seems to be reasonable that the higher collision energy enables other dissociation to take place. The abundant $[C_6H_5–^{13}CN–CH_3]^+$ ion (*m*/*z* 119) seems to contradict the above conclusion that N(3) atom was methylated. The $[H_3CO–C_6H_4–CN–CH_3]^+$ ion was also formed (*m*/*z* 148). There are examples of methyl group transfer on mass spectrometric dissociation [14–16], therefore, it is most probably also in this case.

4. Conclusion

The data obtained are in agreement with the results of the theoretical calculations performed for protonated oxadiazoles and support the previously suggested mechanism of HNCO elimination [5,6]. The C-4′ substituent strongly affects this process. Its electron-donor properties enable protonation of N(3) atom and as a consequence the loss HNC(2)O molecule is favored over HNC(5)O molecule. The same effect is observed for LiNCO and CH_3NCO elimination from lithiated and quaternary derivatives. Analogous results have been obtained for HNCS (or CH_3NCS) elimination from thiadiazoles. However, the exchange of oxygen for sulfur enables the fragmentation pathways not observed for oxadiazoles, e.g., rearrangements leading to the formation of $[H_3CO–C_6H_4–S]^+$ and $[C_6H_5–S]^+$ ions.

References

[1] L.I. Balen'kii, S.I. Luiksaar, I.S. Poddubnyi, M.M. Krayushkin, Izv. Akad. Nauk Ser. Khim. 11 (1998) 2309.
[2] R. Frański, K. Eitner, G. Schroeder, V. Rybachenko, Eur. J. Mass Spectrom. 8 (2002) 295.
[3] K. Eitner, R. Frański, G. Schroeder, V. Rybachenko, O.P. Szwajka, Pol. J. Chem. 76 (2002) 761.
[4] A.M. Seldes, N. D'Accorso, M.F. Souto, M.M. Alho, C.G. Arabehety, J. Mass Spectrom. 36 (2001) 1069.
[5] R. Frański, G. Schroeder, V. Rybachenko, O.P. Szwajka, Rapid Commun. Mass Spectrom. 16 (2002) 390.
[6] R. Frański, K. Eitner, G. Schroeder, O.P. Szwajka, J. Am. Soc. Mass Spectrom. 14 (2003) 289.
[7] A.P. Grekov, O.P. Szwajka, Zh. Obshch. Khim. 30 (1960) 3082 (in Russian).
[8] O.P. Szwajka, T.P. Mnacakanova, V.G. Golovatyi, L.G. Schevchuk, Chem. Heter. Comp. 2 (1970) 300 (in Russian).
[9] Z. He, T.R. Burke Jr., Tetrahedron 53 (1997) 4219.
[10] R.B. Cole, J. Mass. Spectrom. 35 (2000) 763.
[11] M. Gosselin, J. Chim. Phys. Phys. Chim. Biol. 66 (1969) 769.
[12] T.A. Spiglanin, R.A. Perry, D.W. Chandler, J. Phys. Chem. 90 (1986) 6184.
[13] S.S. Brown, H.L. Berghout, F.F. Crim, J. Chem. Phys. 105 (1996) 8103.
[14] S. Tajima, A. Fujizuka, O. Sekiguchi, Rapid Commun. Mass Spectrom. 13 (1999) 669.
[15] P.R. Tiller, C. Raab, C.E.C.A. Hop, J. Mass Spectrom. 36 (2001) 344.
[16] H. Keck, P. Tommes, J. Mass Spectrom. 34 (1999) 44.