Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2014, **24**, 165–166
Mendeleev Communications

Unusual behavior of benzofuroxans under ESI MS conditions in negative ion mode

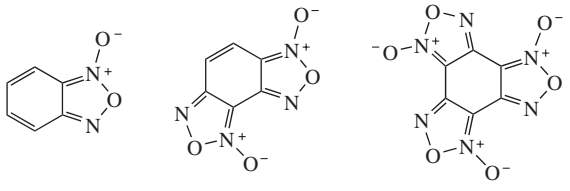
Alexander O. Chizhov, Nina N. Makhova, Ilya V. Kuchurov, Aleksei B. Sheremetev and Sergei G. Zlotin*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 495 135 5328; e-mail: zlotin@ioc.ac.ru

DOI: 10.1016/j.mencom.2014.04.014

The $[M+H]^-$ ion (formal transfer of hydride) was observed for the first time in electrospray ionization (–) mass spectra of benzofuroxans.

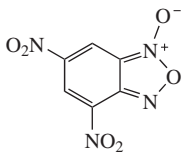
Benzofuroxans (benzo-2,1,3-oxadiazole *N*-oxides) exhibit diverse biological activity depending on the specific substitution within the molecule. They are extensively investigated as NO-releasing agents, calcium channel modulators, monoamine oxidase inhibitors, fungicides, herbicides, *etc*.[1] High-nitrogen benzofuroxan derivatives have been shown to be useful energetic materials.[2] Benzofuroxans are the promising scaffolds for the synthesis of a variety of heteroaromatic and polycyclic heterocyclic systems.[3] It is important to note that benzofuroxans are extremely strong neutral electrophiles in various processes including addition to very weak carbon nucleophiles; for example, π-excessive arenes (anilines, phenols or phenoxide ions) or heteroarenes (pyrroles, indoles, furans) react under smooth conditions with benzofuroxans affording quantitatively stable carbon bonded σ-adducts which are formally the products of S_EAr substitution at the benzene ring.[4] On the other hand, benzofuroxans can serve as organic π-acceptors which have been extensively investigated as highly efficient pairs for charge transfer complex formations.[5] Spectral data of benzofuroxan derivatives are well documented.[2(*h*),3] Several mass spectrometry techniques have been developed to identify benzofuroxan derivatives.[2(*h*),3] Electrospray ionization mass spectrometry (ESI MS) is a useful technique for the analysis of organic compounds; however, it has not been applied to furoxan derivatives yet.



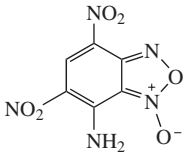
1

2

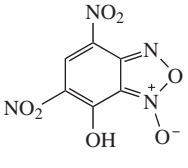
3



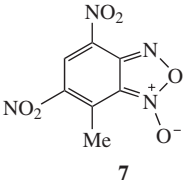
4



5



6



7

Table 1 High-resolution, negative ion mode ESI mass spectrum of BTF **3** (solution in methanol, sodium formate was used for internal calibration).

Entry	*m/z* (experiment)	I_{rel} (%)	Molecular formula of the ion	Origin of the ion	*m/z* (calculated)
1	296.9863	5	$C_7HN_6O_8$	$[M+HCO_2]^-$	296.9861
2	286.9575	4	$C_6N_6O_6Cl$	$[M+Cl]^-$	286.9573
3	266.9880	4	$C_7HN_5O_7$	$[M+HCO_2-NO]^-$	266.9870
4	252.9963	3	$C_6HN_6O_6$	$[M+H]^-$	252.9963
5	251.9887	0.5	$C_6N_6O_6$	M^-	251.9885
6	236.9903	0.5	$C_7HN_4O_6$	$[M+HCO_2-2NO]^-$	236.9891
7	221.9907	100	$C_6N_5O_5$	$[M-NO]^-$	221.9905
8	220.9952	20	$C_7HN_4O_5$	$[M+HCO_2-NO-NO_2]^-$	220.9952
9	206.9914	1	$C_6HN_5O_4$	$[M+H-NO_2]^-$	207.0034
10	205.9953	5	$C_6N_5O_4$	$[M-NO_2]^-$	205.9956
11	193.0002	20	$C_6HN_4O_4$	$[M+H-2NO]^-$	193.0003
12	191.9923	2	$C_6N_4O_4$	$[M-2NO]^-$	191.9925
13	177.0047	2	$C_6HN_4O_3$	$[M+H-NO-NO_2]^-$	177.0054
14	175.9974	4	$C_6N_4O_3$	$[M-NO-NO_2]^-$	175.9976
15	163.0004	0.2	$C_6HN_3O_3$	$[M+H-3NO]^-$	163.0023
16	161.9951	0.3	$C_6N_3O_3$	$[M-3NO]^-$	161.9945
17	147.0072	0.4	$C_6HN_3O_2$	$[M+H-2NO-NO_2]^-$	147.0074
18	145.9995	0.8	$C_6N_3O_2$	$[M-2NO-NO_2]^-$	145.9996
19	133.9996	25	$C_5N_3O_2$		133.9996
20	102.0099	1.5	C_5N_3		102.0098
21	94.0051	3	$C_3N_3O_5$		94.0047
22	90.0101	1.5	C_4N_3		90.0098

Our interest in benzofuroxan bearing electron-withdrawing groups and/or fusing rings[6] prompted us to investigate the family of compounds **1**–**7**† using ESI MS technique.‡

We found that benzotrifuroxan (**3**, BTF) does not give ions under ESI(+) conditions and the negative mode electrospray mass spectrum [ESI(–)] demonstrates molecular associates of BTF with anions $[M+HCO_2]^-$ (in the presence of sodium formate used as an internal calibrant) and $[M+Cl]^-$ both usual for organic

† Benzofuroxans were synthesized using the reported procedures.[6,9]

‡ High resolution mass spectra were measured on a Bruker maXis instrument. The measurements were performed in a positive ion mode (interface capillary voltage, 4.5 kV) or in a negative ion mode (3.2 kV); ISCID energy, 0.0 eV; quadrupole ion energy, 3.0 eV; scanning mass range from *m/z* 50 to 3000; external calibration was done with Electrospray Tuning MixTM (Agilent) and internal calibration with sodium formate. A syringe injection was used for solutions of BTF (5 μg cm^{-3}) in acetonitrile or methanol (flow rate 3 mm^3 min^{-1}). Nitrogen was applied as a dry gas (4.0 dm^{-3} min^{-1}); interface temperature was set at 180 °C.

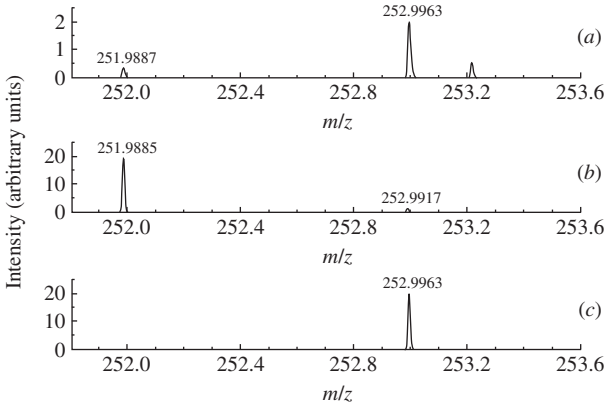


Figure 1 (*a*) The molecular ion area of high resolution ESI(–) mass spectrum of BTF; simulated peaks for (*b*) $C_6N_6O_6^{-\cdot}$ and (*c*) $C_6HN_6O_6^-$. HCOONa was used as an internal calibrant.

compounds (Table 1, entries 1 and 2, respectively). Molecular anion (entry 5) is quite usual for electronegative, nitrogen-rich molecules.[7]

However, the presence of a negatively charged associate with hydrogen $[M+H]^-$ (Table 1, entry 4) is quite unusual and even unbelievable for protic medium (methanol). It was also observed in ESI(–) MS of compound **3** for acetonitrile used as a solvent, and was not observed in APCI(–) MS (see Online Supplementary Materials). To the best of our knowledge, ions $[M+H]^-$ were not previously reported for ESI except $[M+H]^-$ (*m/z* 183) for 2,4-dinitrotoluene detected in cold plasma mass spectrometry.[8]

Associates $[M+H]^-$ were also detected in ESI(–) MS for benzofuroxan **1** (*m/z* 137.0355, calc. *m/z* 137.0357), benzodifuroxan **2** (*m/z* 195.0159, calc. *m/z* 195.0160), and, possibly, for 4,6-dinitrobenzofuroxan **4** (*m/z* 227.0070, calc. *m/z* 227.0058, overlap with isotopic peaks of $[M-H]^-$ and $M^{-\cdot}$). However, for nitrobenzofuroxans bearing additional substituents, *e.g.*, 7-amino-4,6-dinitrobenzofuroxan **5**, 7-hydroxy-4,6-dinitrobenzofuroxan **6** and 7-methyl-4,6-dinitrobenzofuroxan **7**, similar associates ($[M+H]^-$) have not been observed (see Online Supplementary Materials).

Fragments are easily formed for BTF-derived anions without additional activation. Fragmentation pattern looks like an overlap of decomposition of $[M+HCO_2]^-$, $[M+H]^-$, and $M^{-\cdot}$ anions. Successive loss of NO and NO_2 is well-known for furoxans in ESI(+) mass spectra.[2(*h*)] Analogous processes were also revealed in ESI(–) MS for BTF (Table 1) and other furoxans (Online Supplementary Materials).

The formation of $[M+H]^-$ seems doubtfully to be a primary process. One can suppose that $[M+H]^-$ ion presumably originates by decarboxylation of $[M+HCO_2]^-$ ion; however, this hypothesis is in contradiction with the formation of this anion in the absence of the formate internal calibrant [see Figure S3(*b*), Online Supplementary Materials]. Moreover, fragmentation of $[M+HCO_2]^-$ in the collision cell gives MS^2 spectrum which does not contain $[M+H]^-$ and its lower *m/z* part differs from that expected for decomposition of $[M+H]^-$. This ion possibly originates from $[M+C_2H_3O_3]^-$ [see Figure S8(*a*),(*b*)]. To clarify the mechanism of formation of $[M+H]^-$ further studies are needed.

In conclusion, we observed formation of $[M+H]^-$ ion in ESI(–) mass spectra (formal transfer of hydride) in protic medium for the first time. The fact of observation of $[M+H]^-$ may be useful for ESI(–) MS identification of benzofuroxans, and, hopefully, other high nitrogen compounds.

This work was supported by the Russian Foundation for Basic Research (grant no. 12-03-12012-ofi_m).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2014.04.014.

References

1 (*a*) H. Cerecetto and M. Gonzales, *Top. Heterocycl. Chem.*, 2007, **10**, 265; (*b*) E. M. Gibadullina, E. A. Chugunova, E. V. Mironova, D. B. Krivolapov, A. R. Burilov, L. M. Yusupova and M. A. Pudovik, *Chem. Heterocycl. Compd*., 2012, **48**, 1228 (*Khim. Geterotsikl. Soedin*., 2012, 1318); (*c*) C. Jovene, E. A. Chugunova and R. Goumont, *Mini-Rev. Med. Chem.*, 2013, **13**, 1089; (*d*) L. Wang, C. Li, Y. Zhang, C. Qiao and Y. Ye, *J. Agric. Food Chem*., 2013, **61**, 8632; (*e*) S. D. Jorge, F. Palace-Berl, K. F. Mesquita Pasqualoto, M. Ishii, A. K. Ferreira, C. M. Berra, R. V. Bosch, D. A. Maria and L. C. Tavares, *Eur. J. Med. Chem.*, 2013, **64**, 200; (*f*) I. V. Serkov, E. A. Chugunova, A. R. Burilov, A. D. Voloshina, N. V. Kulik, V. V. Zobov and A. N. Proshin, *Russ. J. Gen. Chem.*, 2013, **83**, 1007 (*Zh. Obshch. Khim*., 2013, **83**, 873).

2 (*a*) *Energeticheskie kondensirovannye sistemy (Energetic Condensed Systems)*, ed. B. P. Zhukov, 2nd edn., Yanus-K, Moscow, 2000 (in Russian); (*b*) J. P. Agrawal and R. D. Hodgson, *Organic Chemistry of Explosives*, John Wiley, New York, 2007; (*c*) V. F. Zhilin, V. L. Zbarsky and N. V. Yudin, *Malochuvstvitel'nye vzryvchatye veshchestva (Insensitive Explosives)*, RKhTU, Moscow, 2008 (in Russian); (*d*) L. Turker and S. Varis, *Polycyclic Aromat. Compd*., 2009, **29**, 228; (*e*) Yu. A. Bogdanova, S. A. Gubin, B. L. Korsunskii and V. I. Pepekin, *Combust. Explos. Shock Waves*, 2009, **45**, 738 [*Fiz. Goren. Vzr*., 2009, **45** (6), 115]; (*f*) V. I. Pepekin, *Russ. J. Phys. Chem. B*, 2010, **4**, 954 [*Khim. Fiz.*, 2010, **29** (12), 8]; (*g*) V. I. Pepekin, *Russ. J. Phys. Chem. B*, 2011, **5**, 41 [*Khim. Fiz.*, 2011, **30** (1), 20]; (*h*) J. Sarlauskas, Z. Anusevicius and A. Misiunas, *Cent. Eur. J. Energ. Mater*., 2012, **9**, 365; (*i*) E. A. Chugunova, R. E. Timasheva, E. M. Gibadullina, A. R. Burilov and G. R. Goumont, *Propellants Explos. Pyrotech*., 2012, **37**, 390.

3 (*a*) A. J. Boulton and P. B. Ghosh, *Adv. Heterocycl. Chem*., 1969, **10**, 2; (*b*) A. Gasco and A. J. Boulton, *Adv. Heterocycl. Chem*., 1981, **29**, 251; (*c*) R. M. Paton, in *Comprehensive Heterocyclic Chemistry II*, eds. A. R. Katritzky, C. W. Rees and E. F. V. Scriven, Pergamon Press, Oxford, 1996, vol. 4, p. 229; (*d*) L. I. Khmel'nitskii, S. S. Novikov and T. I. Godovikova, *Khimiya furoksanov. Struktura i sintez (Chemistry of Furoxans, Structure and Synthesis)*, 2nd edn., Nauka, Moscow, 1996 (in Russian); (*e*) L. I. Khmel'nitskii, S. S. Novikov and T. I. Godovikova, *Khimiya furoksanov. Reaktsii i primenenie (Chemistry of Furoxans. Reactions and Applications)*, 2nd edn., Nauka, Moscow, 1996 (in Russian); (*f*) G. Nikonov and S. Bobrov, in *Comprehensive Heterocyclic Chemistry III*, eds. A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor, Elsevier, Amsterdam, 2008, vol. 5, p. 315; (*g*) A. S. Bailey, C. W. Gutch, J. M. Peach and W. A. Waters, *J. Chem. Soc. (C)*, 1969, 681.

4 (*a*) E. Buncel and F. Terrier, *Org. Biomol. Chem.*, 2010, **8**, 2285; (*b*) F. Terrier, J. M. Dust and E. Buncel, *Tetrahedron*, 2012, **68**, 1829.

5 (*a*) G. Berionni, A.-M. Gonsalves, C. Mathieu, T. Devic, A. Etcheberry and R. Goumont, *Phys. Chem. Chem. Phys*., 2011, **13**, 2857; (*b*) Z. Yang, H. Li, X. Zhou, C. Zhang, H. Huang, J. Li and F. Nie, *Cryst. Growth Des*., 2012, **12**, 5155; (*c*) C. Guo, H. Zhang, X. Wang, X. Liu, Y. Liu and J. Sun, *Chin. J. Energ. Mater.*, 2012, **20**, 503; (*d*) H. Zhang, C. Guo, X. Wang, J. Xu, X. He, Y. Liu, X. Liu, H. Huang and J. Sun, *Cryst. Growth Des*., 2013, **13**, 679.

6 (*a*) A. B. Sheremetev, N. S. Aleksandrova, N. V. Ignat'ev and M. Schulte, *Mendeleev Commun*., 2012, **22**, 95; (*b*) N. V. Pyatakova, Yu. V. Khropov, I. V. Ovchinnikov, I. S. Severina and N. N. Makhova, *Biochemistry (Moscow)*, 2000, **65**, 547 (*Biokhimiya*, 2000, **65**, 540).

7 M. Wood, M. Laloup, N. Samyn, M. del Mar Ramires Fernandes, E. A. de Brujin, R.A.A. Maes and G. De Boeck, *J. Chromatog. A*, 2006, **1130**, 3.

8 J. F. Garcia-Reyes, J. D. Harper, G. A. Salazar, N. A. Chairpar, Z. Ouyang and R. G. Cooks, *Anal. Chem.*, 2011, **83**, 1084.

9 E. Leyva, S. Leyva, R. M. González-Balderas, D. de Loera and R. Jiménez-Cataño, *Mendeleev Commun*., 2013, **23**, 217.

Received: 7th October 2013; Com. 13/4221