The reactivity of ferrocenylalkyl azoles under the conditions of electrospray ionization

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ABSTRACT

Under the conditions of electrospray ionization of ferrocenylalkyl azoles FcCH(R)X (Fc–η^5-C_5H_5Fe-η^5-C_5H_4, R – H, Me, XH – 2-methyl imidazole, pirazole) the processes of oxidation, protonation, fragmentation and ferrocenylalkylation to form, molecular ions [M]$^+$, protonated molecules [M+H]$^+$, ferrocenylalkyl cations [FcCHR]$^+$ and bisferrocenylalkyl azole cations [(FcCHR)2X]$^+$, respectively, take place. Using special experimental techniques (deuterated solvents, saturation of ionic source of an ESI mass-spectrometer by the vapors of solvents, the experiments under the "inverse" ESI conditions when the solvent is subjected to electrospray in the presence of ferrocenylalkyl derivative vapours) and quantum-chemical calculations at the level of the B3LYP/LanL2DZ theory the scheme of the formation of these ions in a gas phase according to the mechanism of "activating protonation" was suggested. it was found that all these ions are formed through the protonation stage, which is taking place mainly in a gas phase. The key stage is the exothermic process of the protonation of the initial compounds by hydroxonium ions giving rise to protonated [M+H]$^+$ molecules which further oxidize and alkylate ferrocenylalkylazoles to form molecular radical cations and bisferrocenylalkyl azole ions [FcCH(Me)-X-CH(Me)Fc]$^+$. The decomposition of protonated ions with the elimination of the azole molecule gives rise to ferrocenylalkyl cations [FcCHR]$^+$ capable in turn of oxidizing and alkylating the initial compounds.

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1. Introduction

It has been shown recently by us [1,2] that under the conditions of ionization electrospray (ESI) ferrocenylalkyl azoles FcCH(R)X (Fc – η^5-C_5H_5Fe-η^5-C_5H_4, XH – the derivatives of imidazole, pirazole, triazole and their benzo analogs, R = H, Me, Et, Ph) along with the processes typical of this ionization method, such as oxidation, protonation, fragmentation and dimerization to form, respectively, molecular ions [M]$^+$, protonated molecules [M+H]$^+$, ferrocenylalkyl cations [FcCHR]$^+$ ([A]$^+$), ions of dimer [2M]$^+$ and its protonated form [2M+H]$^+$, the ferrocenylalkylation known in the chemistry of solutions [3] giving rise to bisferrocenylalkyl azole cations [(FcCHR)$_2$Az]$^+$ ([MA]$^+$) also takes place (Fig. 1).

The mechanism of ion-formation on electrospray ionization of non-polar substances, unable to form charged species in solution, is still speculative [4]. A concept according to which the ESI ion source is considered as an electrochemical unit and ions in such an ion source result from the redox processes taking place in solution and/or at the solution-capillary interface surface [5–7] is the most widespread. At the same time, the protonation of the analyte neutral molecules under the conditions of ESI may occur in gas phase in the course of ion-molecular reactions. So Amad et al. [8] showed, that on electrospraying of clean water the protonated water clusters (H_2O)$_n$H$^+$ (n = 1–4) are formed. However, on admission of vapors of methanol having higher proton affinity than water to the ion source, the peaks of water cluster ions disappear from the ESI mass-spectrum and the peaks of protonated methanol cluster ions (MeOH)$_n$H$^+$ (n = 1–4) appear, i.e. in this case the protonation of methanol in a gas phase is fulfilled by hydroxonium ions. Recently, [9] it has been discovered by us that the ferrocene molecular ions are formed under the "inverse" ESI conditions when the ferrocene vapors are situated in the ion source, and only clean acetonitrile is subjected to electrospraying. By the help of quantum-chemical calculations it has been found, that under these conditions the ferrocene oxidation occurs in the gas phase according to the scheme of activating protonation, when the protonated molecule is the oxidizer of the initial ferrocene molecule, and the role of electrochemistry in the process of the electrospraying consists in generation of hydroxonium ions, which protonate the ferrocene molecules in the gas phase [9].

2. Results and discussion

In this article, the results of the investigation of mechanisms of ionoformation of 1-ferrocenylmethyl-1*H*-pirazole FcCH$_2$Pz (**1**), 2-methyl-1-(1-ferrocenylethyl)-1*H*-imidazole FcCH(Me)Im (**2**), ferrocenylmethyldimethylamine (**3**) and ferrocenylmethanol FcCH$_2$OH

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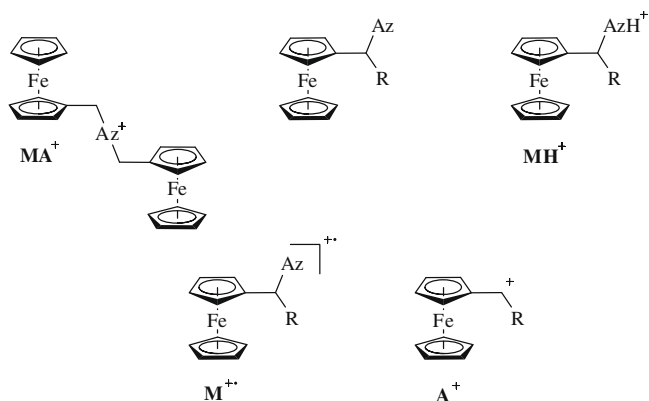(A.N. Rodionov).

Fig. 1. The ions, formed on the electrospray ionization of ferrocenylalkyl derivatives.

(4) under the conditions of the ESI using experimental techniques and quantum-chemical calculations are given. The ESI mass-spectra of the compounds 1 and 2 in acetonitrile solutions (ACN), ACN/H_2O (1:1 w/w) and ACN/D_2O (1:1 w/w) as well as on saturation of ionic source by H_2O, D_2O and CD_3OD vapors were obtained (Table 1). In the last case, the vessel with the corresponding solvent was placed into the ion source.
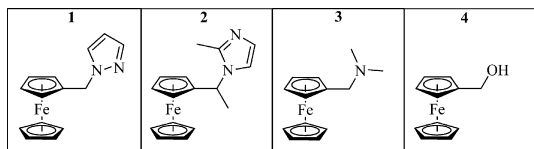
Recently, we have discovered, that the shape of the ESI mass-spectra of ferrocenylalkyl azoles and ferrocenylalkanols essentially depends upon the conditions of the experiment (the analyte concentration, the solvent phase flow rate, solvent, temperature, electric potential) [1,10]. Thus in order to preserve the same ionization conditions the mass-spectra of an equimolar mixture of the compounds 1 and 2 was registered. Under the ESI each of these compounds forms four basic ions: molecular ions $[M]^+$, protonated molecules $[M+H]^+$, ferrocenylalkyl cations $[FcCHR]^+$ ($[A]^+$) and bisferrocenylalkyl azole cat-

ions $[(FcCHR)_2Az]^+$ ($[MA]^+$) (Fig. 2, Table 1; subscript indices 1 and 2 define the compounds 1 and 2, respectively).

Unlike in the control experiments) when the vessel with H_2O was present in the ion source (experiment 2), in the ESI mass-spectra (Table 1), obtained in the presence of D_2O or CD_3OD vapors in the ion source (experiments 3 and 4) the peaks of ions of the protonated molecules $[M_1+H]^+$ (m/z 267) and $[M_2+H]^+$ (m/z 295) was partially shifted for one unit in the direction of higher masses, that is, m/z 268 and m/z 296, respectively, i.e. along with the protonation the deuteron addition takes place. The analysis of the intensity ratio of these peaks showed, that the deuteration occurs for more than 85%. Other ions do not comprise deuterium. Using the mixture ACN/D_2O (1:1 w/w) as a solvent but in the absence of D_2O vapors (experiment 6) also brings to the enrichment of protonated molecules by deuterium $[M_1+H]^+$ and $[M_2+H]^+$ for 72.5% and 87.5%, respectively. However, in the presence of H_2O vapors (experiment 7) the part of ions $[M_1+D]^+$ and $[M_2+D]^+$ reduces to 4.6% and 18.6%, respectively, and once more increases to 80.5% and 92.5% in the presence of D_2O vapors (experiment 8, Table 1).

Two alternative explanations of these results can be suggested: (1) the protonation occurs in solution, and the isotope change of hydrogen takes place in the ions $[M_1+H]^+$ in the gas phase; (2) protonation takes place mainly in the gas phase.

In order to elucidate the possibility of protonation in a gas phase the experiment was made in the "inverse" ESI conditions, when only a solvent was subjected to electrospraying, and the vessel with ferrocenylmethylpirazole was placed in the ion source. In this case, the set of ions formed was the same as was observed in the ESI mass-spectrum, obtained under the usual conditions on electrospraying of solution of this compound (Table 2). However, because of the low volatility of ferrocenylmethylpirazole the intensities of the peaks of these ions were not more than 50 times higher than a background and were two orders lower, than in the spectrum, obtained under usual conditions on electrospraying of solution of this compound in acetonitrile (1 μl of solution with the concentration of 3×10^{-5} mol/l). Thus for more reliable confirmation of the fact of protonation of ferrocenylalkyl derivatives in a gas phase we used the compound ferrocenylmethyldimethylamine 3 as a model possessing higher volatility in comparison with ferrocenylalkyl azoles.

On electrospraying of acetonitrile mixtures with H_2O and D_2O (1:1 w/w) in the presence of ferrocenylmethyldimethylamine vapors the set of ions was reliably registered. The same set was observed in the ESI mass-spectrum, obtained under usual

Table 1
The peak intensities (%Σ) and the percentage of deuterated ions on the registration of the ESI mass-spectra of the equimolar mixture of 1-N-(ferrocenylmethyl)pirazole FcCH₂Pz (1), 1-N-(ferrocenylethyl)-2-methyl imidazole FcCH(Me)Im (2) in solutions MeCN, MeCN/H_2O (1:1 w/w) and MeCN/D_2O (1:1 w/w), and also in the presence of vapors of H_2O, D_2O and CD_3OD in the ion source. $C = 3 \times 10^{-5}$ mol/l, $V = 50$ ml/min, $T = 90$ °C, $U = 4.5$ kB, solvent phase MeCN.

Ion	Solvent	ACN	ACN	ACN	ACN	ACN/H_2O	ACN/D_2O	ACN/D_2O	ACN/D_2O
	vapor		H_2O	D_2O	CD_3OD			H_2O	D_2O
	m/z	1	2	3	4	5	6	7	8
$[A_1]^+$	199	0.94	0.77	0.87	6.46	1.13	0.64	0.32	0.44
$[A_2]^+$	213	3.07	1.24	1.49	1.13	3.91	3.46	1.14	1.14
$[M_1]^+$	266	0.30	1.37	0.93	1.90	0.47	0.22	0.48	0.20
$[M_1+H]^+$	267	0.37	12.13	1.37	0.02	3.47	0.64	4.25	0.38
$[M_1+D]^+$	268	0.00	0.00	9.47	0.15	0.00	1.68	0.20	1.54
%D		**0.00**	**0.00**	**87.35**	**88.20**	**0.00**	**72.51**	**4.56**	**80.45**
$[M_2]^+$	294	1.72	1.13	0.80	1.26	1.08	1.36	2.01	1.23
$[M_2+H]^+$	295	50.30	45.67	5.04	6.97	63.86	8.68	59.71	4.95
$[M_2+D]^+$	296	0.00	0.00	36.79	40.40	0.00	60.60	13.68	61.54
%D		**0.00**	**0.00**	**87.96**	**85.29**	**0.00**	**87.47**	**18.64**	**92.55**
$[M_1A_1]^+$	465	11.74	1.52	0.17	0.00	0.27	1.08	0.35	13.17
$[M_2A_1]^+$	493	14.60	21.94	26.92	24.14	0.33	0.82	0.32	0.39
$[M_2A_2]^+$	507	16.96	14.23	16.13	17.60	25.49	20.82	17.54	15.02
	TIC/6	12.7	18.4	10.9	5.1	23.5	23.9	39.0	38.1
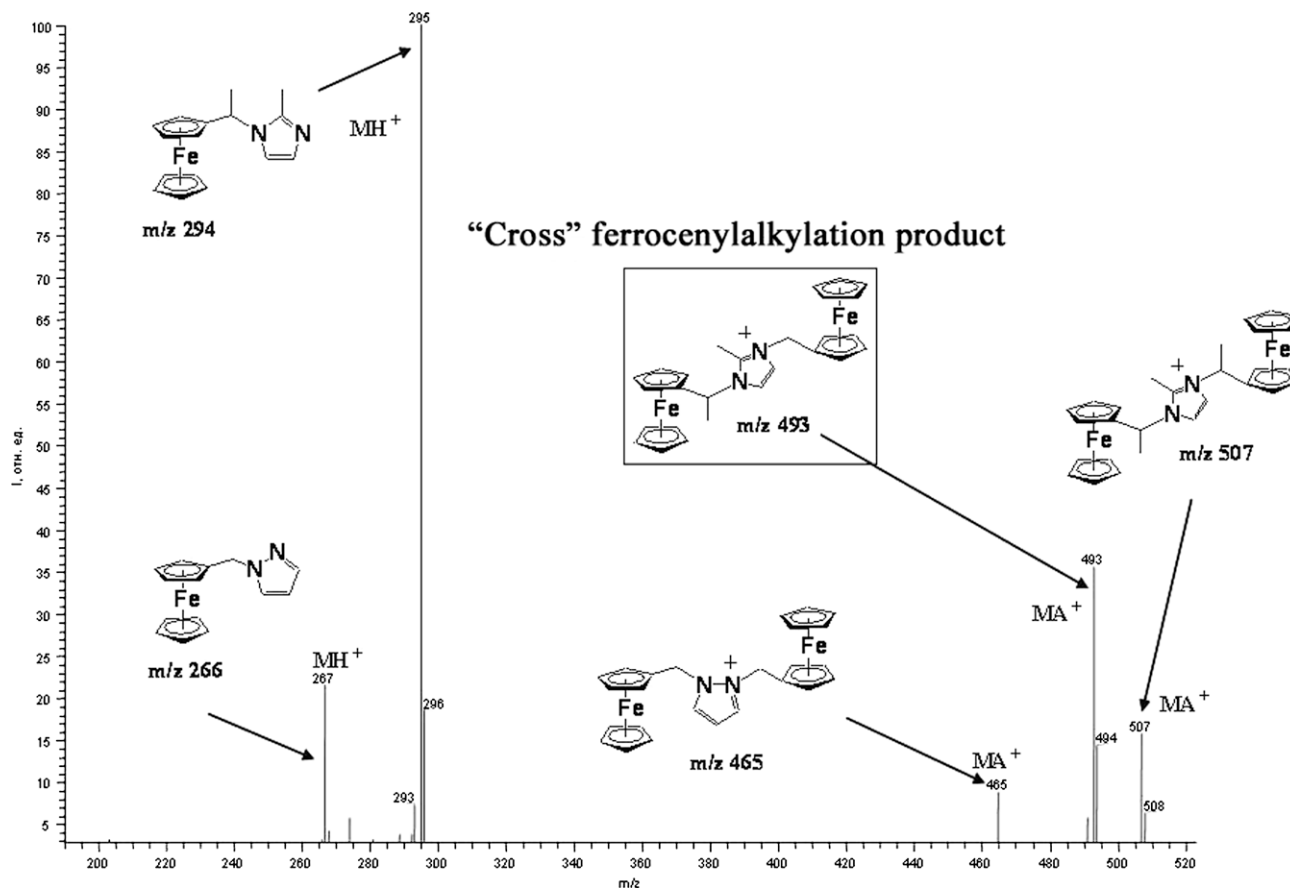
Fig. 2. The ESI mass-spectrum of the equimolar mixture of ferrocenylmethylpirazole (**1**) and 1-(ferrocenylethyl)-2-methyl imidazole (**2**).

Table 2
Total ion current (TIC, arbitrary units of analog-to-digital converter) and the ions peak intensities (%Σ) on the registration of the ESI mass-spectra of ferrocenylmethylpirazole (**1**) under the "inverse" conditions on acetonitrile electrospraying in the presence of vapors of **1** (No. 1) and under usual conditions on electrospraying of solutions of **1** in acetonitrile (1 μl of solution with the concentration of 3×10^{-5} mol/l) (No. 2). $V = 10$ ml/min, $T = 150\,°C$, $U = 4.5$ kV, solvent phase MeCN.

Ion	m/z	1	2
TIC $\times 10^{-4}$		220	1.3
$[A_1]^+$	199	71.4	7.0
$[M]^+$	266	20.1	2.2
$[M+H]^+$	267	6.8	2.8
$[MA]^+$	465	1.8	87.9

Table 3
Total ion current (TIC, arbitrary units of analog-to-digital converter), ions peak intensities (%Σ) and percentage of deuterated ions on the registration of the ESI mass-spectra of ferrocenylmethyldimethylamine (**3**), obtained under the "inverse" conditions on electrospraying of acetonitrile mixtures with H_2O and D_2O (1:1 w/w) in the presence of vapors **3** (Nos. 1 and 2) and under usual conditions on electrospraying of solutions of **3** in acetonitrile (No. 3). $V = 10$ ml/min, $T = 150\,°C$, $U = 4.5$ kV, solvent phase MeCN.

No	Solvent	1	2	3
Ion	m/z	ACN/H_2O	ACN/D_2O	ACN
$[A_1]^+$	199	18.7	20.1	32.8
$[M]^+$	243	0.0	2.2	0
$[M+H]^+$	244	73.6	21.8	53.9
$[M+D]^+$	245	0	48.5	
%D		**0**	**69.0**	
$[2M]^+$	486	1.0	0.5	
$[2M+H]^+$	487	6.7	2.7	0.3
$[2M+D]^+$	488	0	4.2	
%D		**0**	**61.4**	
TIC $\times 10^{-6}$		191	99	473

conditions on electrospraying of solutions of this compound – molecular ions $[M]^+$, protonated molecules $[M+H]^+$, ferrocenylalkyl cations $[FcCH_2]^+$, ions of the dimer $[2M]^+$ and of its protonated form $[2M+H]^+$. Along with this the total ionic current value in spectra, obtained under the "inverse" and usual conditions are comparable within the range of the order of magnitude (Table 3).

On electrospraying of the mixture of acetonitrile with D_2O (1:1 w/w) in the presence of ferrocenylmethyldimethylamine vapors the ions $[M+H]^+$ and $[2M+H]^+$ are enriched in deuterium by 69.0 and 61.4%, respectively (experiment 2, Table 3).

Thus, the results obtained using the deuterated solvents and analyte vapors testify, that the protonation of ferrocenylalkyl azoles on the ESI occurs mainly in the gas phase.

To elucidate the mechanisms of the ferrocenylalkyl azole ion-formation under the conditions of the ESI the quantum-chemical calculations of the heats of the possible reactions of the formation of the basic ions observed in the ESI mass-spectra of the com-

pounds **1–4** were made. In this regard, the hydroxonium ion H_3O^+, which is formed on electrospraying of humid solvents, was accepted as a protonating agent.

In order to check up the adequacy of the used quantum-chemical method (at the level of the B3LYP/LanL2DZ theory with the full geometry optimization) to the set problem the calculations of ionization energies (IP) and proton affinities (PA) of some azoles and ferrocene derivatives for which the experimental values of these variables are known [11–13] (Table 2) were made. It follows from the Table 4, that the calculated and the experimental IP values well agree inter se.

Table 4
Ionization energies (IP, eV) and proton affinities (PA, kcal/mol) of some azoles and ferrocene derivatives.

	Compound	IP_{calc} (eV)	IP_{exp} (eV)	PA_{calc} (kcal/mol)	PA_{exp} (kcal/mol)
1	$FcCH_2Im$	6.30		258.47	
2	$FcCH_2Pz$	6.39		266.94	
3	FcCHMeIm	6.48		254.58	
4	ImH	8.88	8.81 [11]	240.50	224.0 [12]
5	PzH	9.23	9.25 [11]	226.72	
6	TzH	9.95	10.06 [11]	225.59	
7	ImMeH	8.36	8.50 [11]	245.92	
8	FcH	6.36	6.75 [11]	214.0	213.0 [13]
9	$FcCHMePzMe_2$	6.4	6.88[6)]		

Table 5
Heats of possible reactions of basic ions formation, observed in the ESI mass-spectra of 1-N-(ferrocenylmethyl)pirazole $FcCH_2Pz$ (**1**), 1-N-(ferrocenylethyl)-2-methyl imidazole FcCH(Me)Im (**2**) and ferrocenylmethanol $FcCH_2OH$ (**3**).

	R X	H Pz **1**	Me Im **2**	H NMe_2 **3**	H OH **4**
	Protonation reaction				
1	$FcCH(R)X + H_3O^+ \rightarrow FcCH(R)XH^+ + H_2O$	−64.76	−73.67	−67.27	−37.71
	Oxidation reaction				
2	$FcCH(R)X + H_3O^+ \rightarrow FcCH(R)X^{+\cdot} + H_2O + H\cdot$	16.24	21.07	9.74	10.09
2'	$FcCH(R)X + H_3O^+ \rightarrow FcCH(R)X^{+\cdot} + H_3O\cdot$	16.13	20.96	9.62	9.98
3	$FcCH(R)XH^+ + FcCH(R)X \rightarrow FcCH(R)X^{+\cdot} + FcCH(R)X + H\cdot$	81.00	91.91	77.00	47.81
3'	$FcCH(R)XH^+ + FcCH(R)X \rightarrow FcCH(R)X^{+\cdot} + FcCH(R)XH\cdot$	31.12	49.51	33.89	4.83
4	$FcCH(R)X + FcCH(R)^+ \rightarrow FcCH(R)X^{+\cdot} + FcCH(R)\cdot$	6.46	14.56	−0.06	0.31
1.3		16.24	18.24	9.73	10.10
1.3'		−33.64	−24.16	−33.38	−32.88
1.7.4		−25.66	−20.20	−27.48	−29.68
	Reactions of ferrocenylalkyl cation formation				
5	$FcCH(R)X^{+\cdot} \rightarrow FcCH(R)^+ + X\cdot$	79.38		60.30	74.18
2'.5		95.51		69.92	84.16
6	$FcCH(R)X \rightarrow FcCH(R)^+ + X^-$	172.72		209.71	
7	$FcCH(R)XH^+ \rightarrow FcCH(R)^+ + XH$	32.64	38.91	39.85	7.72
1.7		−32.12	−34.76	−27.42	−29.99
	Ferrocenylalkylation reactions				
8	$FcCH(R)XH^+ + FcCH(R)X \rightarrow FcCH(R)\text{-}X\text{-}CH(R)Fc^+ + XH$	−14.37	−5.27	−0.56	6.59
1.8		−79.13	−78.94	−67.83	−31.12
9	$FcCH(R)^+ + FcCH(R)X \rightarrow FcCH(R)\text{-}X\text{-}CH(R)Fc^+$	−47.00	−44.17	−40.41	−1.19
1.7.9		−79.12	−78.93	−67.83	−31.18
10	$FcCH(R)X^{+\cdot} + FcCH(R)X \rightarrow FcCH(R)\text{-}Az\text{-}CH(R)Fc^+ + X\cdot$	27.92		19.89	
2'.10		44.05		29.51	
1.7.4.10		2.26		−7.59	
1.3'.10		−5.72		−13.49	
11	$FcCH_2^+ + PzH \rightarrow FcCH_2\text{-}PzH^+$			−32.63	−32.63
12	$FcCH_2OH_2^+ + PzH \rightarrow FcCH_2\text{-}PzH^+ + H_2O$			7.22	−24.84
1.7.11				−60.05	−62.62
1.12				−60.05	−62.55
	"Cross" ferrocenylalkylation reaction				
13	$FcCH_2PzH^+ + FcCH(Me)Im \rightarrow FcCH(Me)\text{-}Im\text{-}CH_2Fc^+ + PzH$	−17.01			
1.13		−81.77			
14	$FcCH_2PzH^+ + FcCH(Me)Im \rightarrow FcCH_2\text{-}Pz\text{-}CH(Me)Fc^+ + ImH$	−10.54			
1.14		−75.30			
15	$FcCH_2^+ + FcCH(Me)Im \rightarrow FcCH(Me)\text{-}Im\text{-}CH_2Fc^+$	−49.64			
1.7.15		−81.76			
16	$FcCH(Me)ImH^+ + FcCH_2Pz \rightarrow FcCH_2\text{-}Pz\text{-}CH(Me)Fc^+ + ImH$		−3.70		
1.16			−77.37		
17	$FcCH(Me)ImH^+ + FcCH_2Pz \rightarrow FcCH(Me)\text{-}Im\text{-}CH_2Fc^+ + PzH$		8.09		
1.17			−65.58		
18	$FcCH(Me)^+ + FcCH_2Pz \rightarrow FcCH_2\text{-}Pz\text{-}CH(Me)Fc^+$		−42.61		
1.7.18			−77.37		

Ferrocenylalkyl derivatives **1–4** have high proton affinity and their protonation by the hydroxonium ion H_3O^+ is an exothermic process with ΔH from −37.71 to −73.67 kcal/mol (reaction 1, Table 3). Just this fact plays the main role in the ion-formation processes of these compounds on the electrospray ionization. In particular, oxidation of molecules to form molecular ions $[M]^+$ may occur by the help of hydroxonium ions (reactions 2 and 2'), by protonated molecule (reactions 3 and 3') or by ferrocenylalkyl cation (reaction 4). It follows from Table 5, that the oxidation by the hydroxonium ion needs essential energy input (from 9.98 to 21.07 kcal/mol), while the reaction sequence 1 and 3' (protonation to form ion $[M+H^+]$, which is further oxidizing the initial molecule), presents an exothermic process (ΔH = from −24.16 to −33.64 kcal/mol). The reaction sequences 1.7.4 (ΔH from −20.20 to −29.68 kcal/

mol) is also possible. In this case, ferrocenylalkyl cation is an oxidizer, which is formed on decomposition of protonated molecules.

Thus, the oxidation of the initial molecule by its protonated form [M+H]$^+$ and(or) by ferrocenylalkyl cation is the most energetically beneficial process for the formation of the molecular ions of ferrocenylalkyl derivatives under the ESI conditions.

From the three possible ways of formation of ferrocenylalkyl cation, namely: fragmentation of molecular ion with the elimination of azole radical, as it takes place under the conditions of ionization by electrons [14] (reaction 5), heterolytic decomposition of a neutral molecule with the elimination of the azolyl anion (reaction 6) and protonation with the following release of an azole molecule (sequence reactions 1 and 7) the last process is the most energetically beneficial with ΔH from -29.99 to -34.76 kcal/mol. Hence, the ferrocenylalkyl cation only formally can be assigned to the products of the molecular ion fragmentation, while in fact it is formed through the stage of protonation of the initial molecule.

The ferrocenylalkylation giving rise to bisferrocenylalkyl azole cations FcCHR-Az-CHRFc$^+$ may occur by three ways being the result of the interaction of the initial ferrocenylalkyl azole molecules: (1) with their protonated form (reactions 1 and 8), (2) with ferrocenylalkyl cation (reactions 1, 7 and 9) or (3) with molecular ion (reactions 2′.10; 1.3′.10 and 1, 7, 4, 10). It can be seen from Table 5, that the first two processes are energetically beneficial with ΔH from -31.12 to -79.13 kcal/mol, which have the same heat effect in accordance with the Hess law. Which one possibility will be realized in fact depends upon the corresponding activation energy values.

Recently, we have shown, that under the conditions of the ESI on electrospraying of the mixture of azole AzH and ferrocenylmethanol FcCH$_2$OH the ferrocenylalkylation known from the "wet" chemistry, resulting in the formation of the protonated ferrocenylmethylazoles FcCH$_2$AzH$^+$ occurred [2]. The calculations showed this reaction also to be an energetically beneficial process and to possibly take place as the interaction of pirazole with protonated ferrocenylmethanol molecule [FcCH$_2$OH$_2$]$^+$ (reaction 11), as well as with ferrocenylmethylcation FcCH$_2^+$ (reaction 12), resulting from the dehydration of the protonated molecule [FcCH$_2$OH$_2$]$^+$ (reactions 1.7).

On the ESI of the equimolar mixture of ferrocenylmethylpirazole 1 FcCH$_2$Pz and ferrocenylethyl(2-methyl imidazole) 2 FcCH(Me)Im, along with the bis-ferrocenylalkyl azole ions of each component [FcCH$_2$-Pz-CH$_2$Fc]$^+$ and [FcCH(Me)-Im-CH(Me)Fc]$^+$, respectively, also the formation of two products of "cross" ferrocenylalkylation FcCH(Me)-Im-CH$_2$Fc$^+$ (reactions 13, 15 and 17) and FcCH$_2$-Pz-CH(Me)Fc$^+$ (reactions 14, 16 and 18) is possible. Each one of these products may arise by three ways in dependence from the alkylating agent, which can be presented by one of two protonated ions FcCH$_2$PzH$^+$ (reactions 13 and 14) and FcCH(Me)ImH$^+$ (reactions 16 and 17) or ferrocenylalkyl cations FcCH$_2^+$ (reaction 15) and FcCH(Me)$^+$ (reaction 18). It follows from Table 2, that the reaction sequences 1.13 or 1.7.15 ($\Delta H = -81.77$ kcal/mol) giving rise to the ion FcCH(Me)-Im-CH$_2$Fc$^+$ are more energetically beneficial which is in a good agreement with the experiment, as in the ESI mass-spectrum of the equimolar mixture of the compounds 1 and 2 only the product of this reaction is present (Fig. 2).

Fig. 3. The scheme of formation of ferrocenylmethylpirazole basic ions under the conditions of the electrospray ionization ferrocenylalkyl derivatives according to the mechanism of "activating protonation".

As a result, the following scheme of the formation of basic ions on electrospraying of ferrocenylalkyl azoles (Fig. 3) can be suggested. The key stage consists in the exothermal process of protonation of the initial compounds by hydroxonium ions resulting in the protonated molecules [M+H]$^+$ the decomposition of which with the elimination of an azole molecule brings to ferrocenylalkyl cations [FcCHR]$^+$. On the next stages ferrocenylalkyl cations oxidize and alkylate ferrocenylalkyl azoles giving rise to molecular radical cations and bisferrocenylalkyl azole ions [FcCH(Me)-X-CH(Me)Fc]$^+$. These ions can be formed also on the interaction of the initial molecules directly with protonated molecules [M+H]$^+$.

The comparison of the intensities of peaks of ions [M$_1$]$^+$, [A$_1$]$^+$, [M$_1$A$_1$]$^+$ of the compound 1 and of the peaks of ions [M$_2$]$^+$, [A$_2$]$^+$, [M$_2$A$_2$]$^+$ of the compound 2 in the ESI mass-spectrum of their equimolar mixture with the heats of the most energetically beneficial reactions giving rise to these ions (Table 6) show that, these values, as expected, are in an antibate dependence (Eqs. (1) and (2)), i.e. the lower the reaction heat is, the higher the yield of the corresponding ion is. Along with this the total intensity of the peaks of ions of the compounds 1 and 2 in the ESI mass-spectrum of their equimolar mixture depends upon ΔH of protonation of molecules and falls from 72.1% for the compounds 2 ($\Delta H = -73.67$ kcal/mol) to 13.4% for the compounds 1 ($\Delta H = -46.76$ kcal/mol). Thus, the calculation data completely agree with the experiment, allowing to suggest the following scheme of the formation of the main ions under the electrospaying of ferrocenylalkylazoles, following the mechanism of "activating protonation" (рис.3). The key stage is the exothermic process of the protonation of the initial compounds by hydroxonium ions giving rise to protonated [M+H]$^+$ molecules which further oxidize and alkylate ferrocenylalkylazoles to form molecular radical cations and bisferrocenylalkyl azole ions [FcCH(Me)-X-CH(Me)Fc]$^+$. The decomposition of protonated ions with the elimination of the azole molecule gives rise to ferrocenylalkyl cations capable in turn of oxidizing and alkylating the initial compounds.

$$I_1 = -0.220\Delta H - 5.707, \quad R^2 = 0.996, \tag{1}$$

$$I_2 = -0.272\Delta H - 4.903, \quad R^2 = 0.975. \tag{2}$$

It is important to note, that the process of protonation and, hence, subsequent interconversions takes place mainly in a gas phase, as is testified by the experiments with the deuterated solvents, as well as by the mass-spectra of ferrocene [9] and ferrocenylmethyldimethylamine, obtained under the "inverse" ESI

Table 6
The ions peak intensities (%Σ) in the ESI mass-spectrum of equimolar mixture of 1-N-(ferrocenylmethyl)pirazole FcCH$_2$Pz (1), 1-N-(ferrocenylethyl)-2-methyl imidazole FcCH(Me)Im (2) in MeCN solution ($C = 3 \times 10^{-5}$ mol/l, $V = 50$ ml/min, $T = 90$ °C, $U = 4.5$ kV, mobile phase MeCN) and heats of formation of the corresponding ions ΔH (kcal/mol).

Ion	[M$_1$]$^+$	[A$_1$]$^+$	[M$_1$+H]$^+$	[M$_1$A$_1$]$^+$	[M$_2$A$_1$]$^+$	[M$_2$]$^+$	[A$_2$]$^+$	[M$_2$+H]$^+$	[M$_2$A$_2$]$^+$
m/z	266	199	267	465	493	294	213	295	507
%Σ	0.30	0.94	0.37	11.74	14.60	1.72	3.07	50.30	16.96
ΔH (kcal mol^{-1})	−25.66	−32.12	−64.76	−79.12	−81.76	−20.20	−34.76	−73.67	−78.93

conditions, when the vapors of the studied compounds are situated in the ESI ion source, and only the solvent is subjected to electrospraying.

3. Summary

Using special experimental techniques: registration of ESI mass-spectra of ferrocenylalkylazoles in deuterated solvents, and under the saturation of ionic source of an ESI mass-spectrometer by the vapors of heavy water, as well as under the "inverse" ESI conditions when the solvent is subjected to electrospray in the presence of ferrocenylalkyl derivative vapours it was found out that the formation of protonated molecules $[M+H]^+$ takes place in a gas phase.

Basing upon quantum-chemical calculations of the heats of possible reactions of the formation of the main ions observed in the ESI mass-spectra of ferrocenylalkylazoles the scheme of ion-formation according to the mechanism of "activating protonation" was suggested. The key stage is the exothermic process of the protonation of the initial compounds by hydroxonium ions giving rise to protonated $[M+H]^+$ molecules which further oxidize and alkylate ferrocenylalkylazoles to form molecular radical cations and bis-ferrocenylalkyl azole ions $[FcCH(Me)-X-CH(Me)Fc]^+$. The decomposition of protonated ions with the elimination of the azole molecule gives rise to ferrocenylalkyl cations $[FcCHR]^+$ capable in turn of oxidizing and alkylating the initial compounds.

4. Experimental

The ESI mass-spectra were registered on the Finnigan LCQ Advantage tandem dynamic mass-spectrometer (USA), equipped by octapole ion trap mass analyzer with the Surveyor MS pump and the nitrogen generator Schmidlin-Lab (Germany). The data collection and treatment was fulfilled using the program *X Calibur* version 1.3.

The temperature of the heated capillary was 150 °C, electric potential 4.5 kB, the solvent phase flow rate was 10 mkl/min, nitrogen was the spraying and drying gas. Acetonitrile of the Merck company was used for the gradient analysis.

The "inverse" ESI conditions consisted in the following: 400 mg of a substance was poured in a thin layer into a glass Petri dish having 3 cm in diameter, which was then placed into the ion source of the ESI mass-spectrometer under the temperature of approximately 60 °C. Only a solvent was subjected to electrospraying.

The ESI mass-spectra were reduced to monoisotropic form using the AELITA program [15]. Quantum-chemistry calculations were made by the Bekke-Lee-Yang-Parr method of the electron density energy functional (B3LYP) [16,17]. The optimization of the geometrical structure of molecular systems was made using the LanL2DZ atomic basis sets [18]. The programs GAUSSIAN 98W and GAUSSIAN 03W [19] were used for calculations on a two processor minisupercomputer SC760-D.

The compounds **1**, **2**, **3** and **4** were obtained according to the techniques [3], [1] and [20], respectively.

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