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# The influence of chemical structure of nitrogen-containing heterocyclic compounds on the character of ion mobility spectra

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**Abstract.** In this article, the trace amounts of nitrogen-containing compounds have been examined using ion-mobility spectrometry. Depending on the chemical structure of substances in the row of nitrogen-containing compounds ion-mobility spectra, different types of rules have been stated. The obtained ionograms have been analyzed to determine a probable ion-mobility value for certain functional groups.

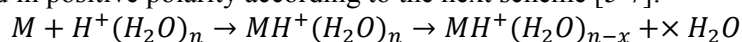
## 1. Introduction

The problem of drug distribution in the modern world is still relevant. There is an urgent need for express analysis and preliminary samples detection due to an increase in synthetic drugs flow. One of the rapid drug detection methods is ion-mobility spectrometry. Ion-mobility spectrometers are mobile, compact; the analysis time takes split second; the well-known drugs such as morphine, amphetamine derivatives can be reliably detected by IMS. Recently, design drugs, e.g., spices, containing different bioactive N-heterocyclic compounds, have become widespread. In this article, the results of ion-mobility spectra analysis are represented for N-heterocyclic compounds. The values of ion-mobility have been found, and the analysis of spectra has been carried out.

## 2. Experimental equipment

Spectrograms were recorded by using KERBER ion-mobility spectrometer. Ionization was carried out by impulse corona discharge via atmosphere pressure chemical ionization (APCI) [1-4]. Detection of the examined substances was carried out in positive polarity due to the basic nature of many drugs.

The ions are formed in positive polarity according to the next scheme [5-7]:



where  $M$  — sample,  $H^+(H_2O)_n$  — reactant ion,  $MH^+(H_2O)_n$  cluster ion,  $MH^+(H_2O)_{n-x}$  product ion,  $\times H_2O$  water.

In this equation, the product ion is called a protonated monomer. A protonated dimer  $MH^+(H_2O)_n$  and other molecular ions are presumed to be formed.

The product ion in this equation is called a protonated monomer. The formation of a protonated dimer  $MH^+(H_2O)_n$  and other molecular ions is possible [8].

Two mechanisms of formation of charged particles in positive polarity under the influence of corona discharge were proposed:

1. Charged particles formation via donor-acceptor interaction between positively charged reactant ion and aromatic system of the examined substances ( $\pi$ -complex).
2. Positively charged ions formation via protonation of basic functional groups and aromatic carbons and heteroatoms.

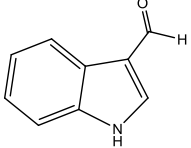
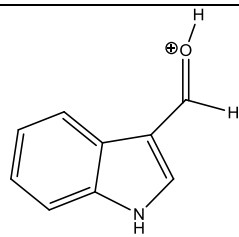
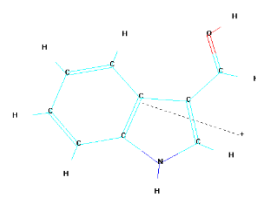
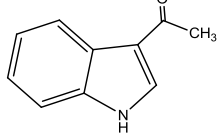
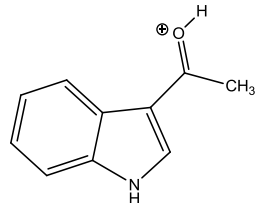
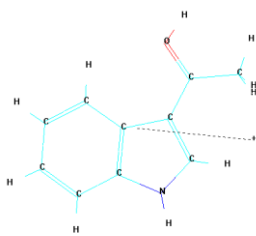
Atom charge calculations were carried out with Hypercube HyperChem 8.0 software using semi-empirical method PM3 to determine a probable protonation site. The electric charge distribution diagram has been constructed. Bond lengths and enthalpies of formations have been calculated for protonated particles. Total ion-dipole moment trend has been demonstrated. A conclusion concerning the molecular ion thermodynamic stability and its orientation in space under the constant electric field gradient in the device drift tube has been made according to this data. PM3 method demonstrates well-reproduced properties of a molecule (ion) such as enthalpy of formation, molecular geometry, which have been used to assume the possibility of ion formation.

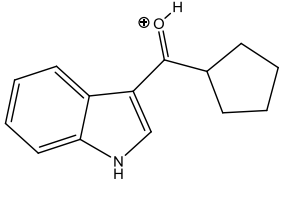
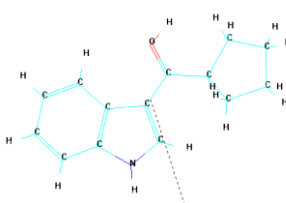
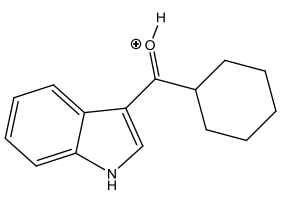
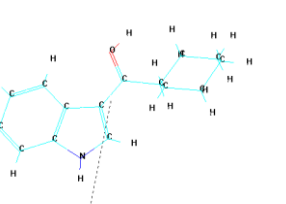
### 3. Experimental results and discussion

The examined substances were divided into three groups.

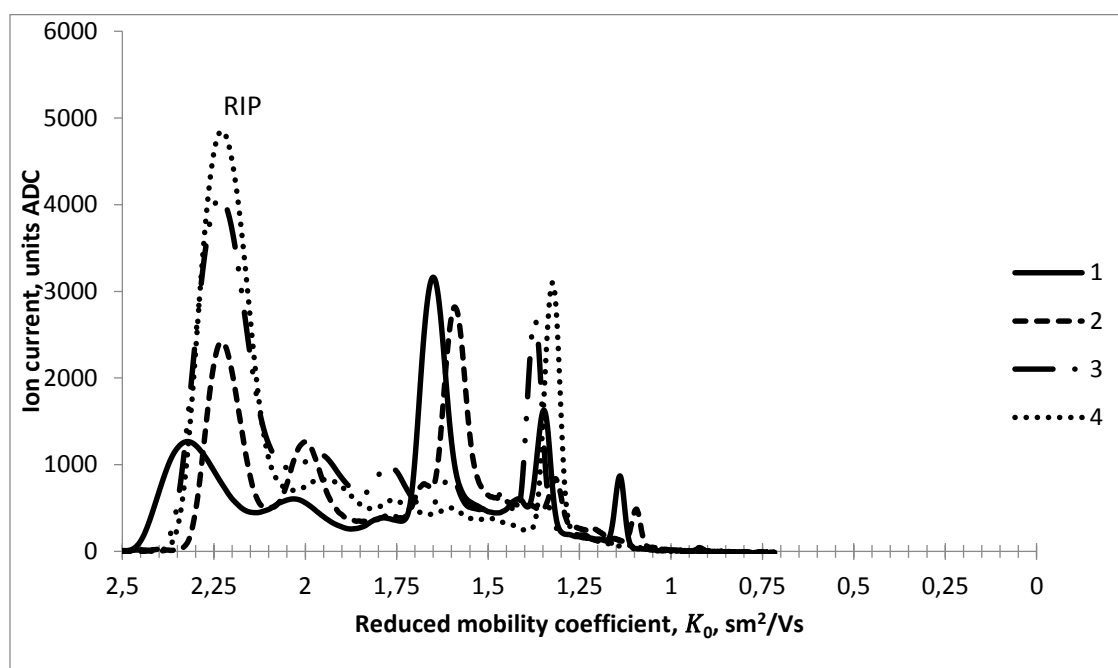
The first group contained indoles with a carbonyl substituent in the position 3 as a privileged scaffold for synthetic cannabinoids (spices). The table 1 represents PM3 method calculation results.

**Table 1.** PM3 method calculation results in synthetic cannabinoids (spices)

Compound	Ion-mobility value $K_0, cm^2 V^{-1} s$	Proposed molecular ion	The direction of the molecular ion-dipole moment vector	Molecular ion enthalpy of formation kcal/mol
Indole-3-carboxaldehyde 	1,627			164,8
3-acetylindole 	1,590			153,38

cyclopentyl(1H-indole-3-yl)methanone	1,377			142,00
cyclohexyl(1H-indole-3-yl)methanone	1,322			136,60

The figure 1 represents the general spectrogram of compounds from the first group.



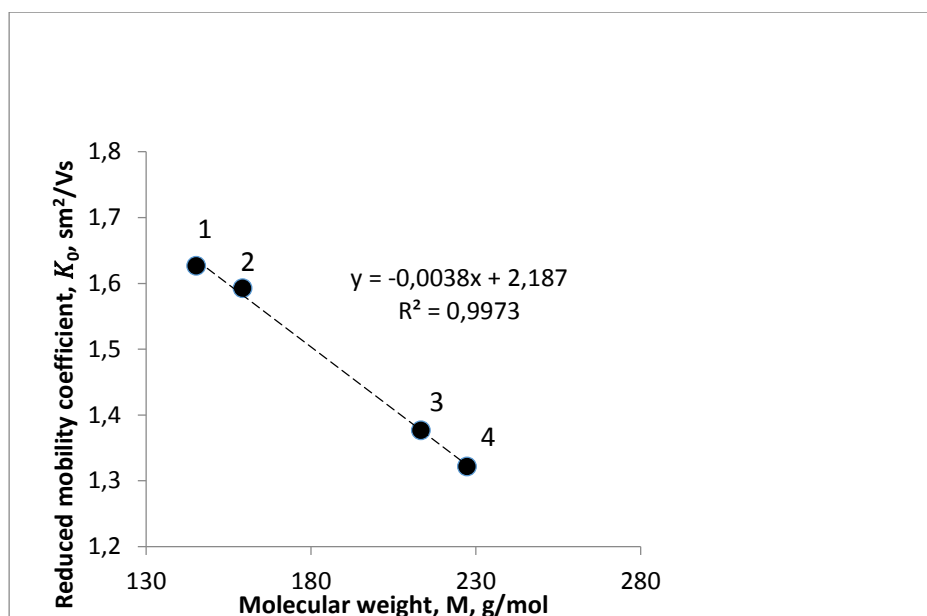
**Figure 1.** General spectrogram of the first group compounds.

1) Indole-3-carboxaldehyde; 2) 3-acetylindole; 3) cyclopentyl(1H-indole-3-yl)methanone; 4) cyclohexyl(1H-indole-3-yl)methanone

The comparison of spectrogram shapes of the first group substances demonstrates a decrease of the ion-mobility values of similar compounds with an increase of carbon atoms number in substituents at the position 3. The most likely protonation site is oxygen according to PM3 semi-empirical calculation data. Besides identification peak, there are two more peaks related to protonated form in the positions 2 and 3 of indole-3-carboxaldehyde and 3-acetylindole. On the contrary, there are no such peaks on the cyclopentyl(1H-indole-3-yl)methanone and cyclohexyl(1H-indole-3-yl)methanone spectra due to steric hindrance in the positions 2 and 3 of the indole fragment.

The reduced ion-mobility dependence on the molecular weight of the compounds has been constructed to corroborate that all of three identification peaks from this group have similar molecular ion structure (Figure 2).

To confirm the thesis that all three identification peaks of this group of substances have the same nature of a molecular ion protonated by the oxygen atom, the dependence of the reduced ion mobility on the molecular weight of the substances was plotted (Figure 2).



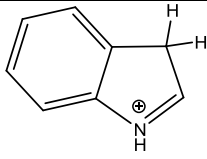
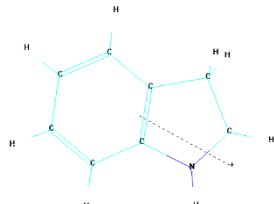
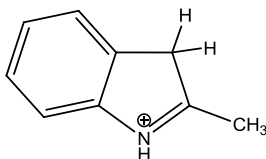
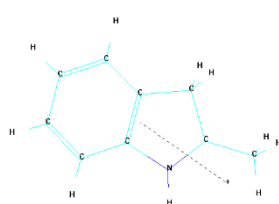
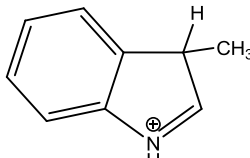
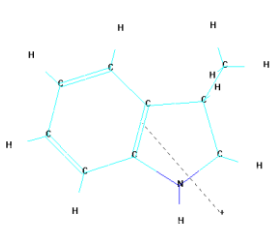
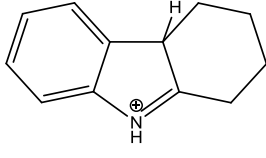
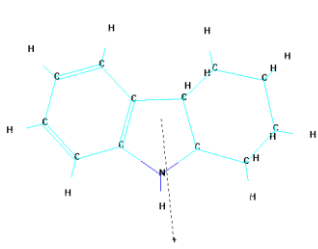
**Figure 2.** The reduced ion mobility dependence on the molecular weights of compounds  
1) Indole-3-carboxaldehyde; 2) 3-acetylindole; 3) cyclopentyl(1H-indole-3-yl) methanone;  
4) cyclohexyl(1H-indole-3-yl)methanone.

The linear dependence states that all three molecular ions form in a similar way.

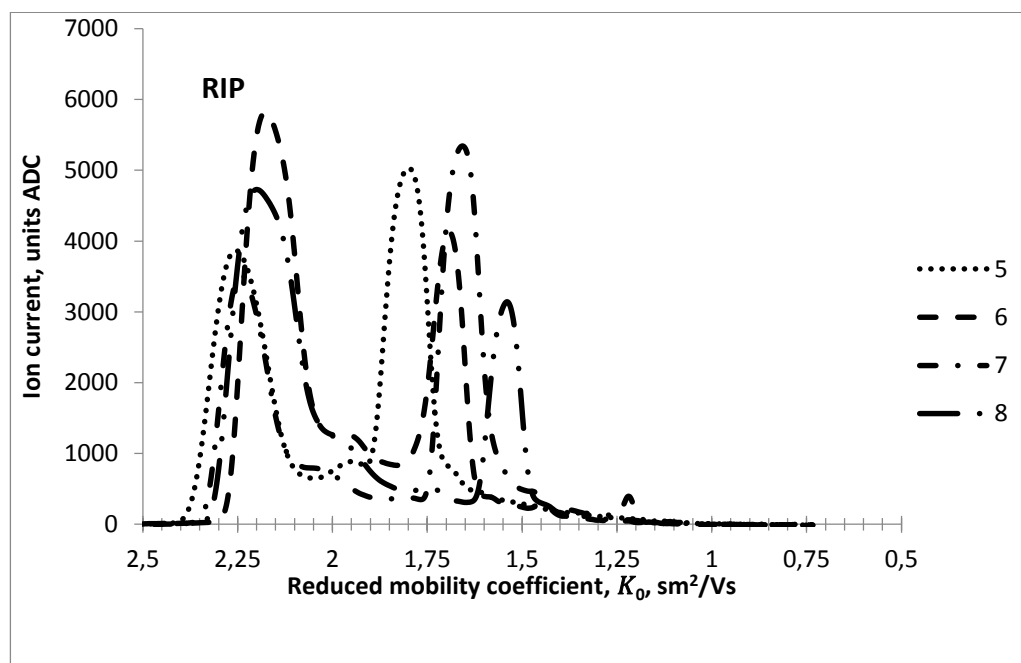
We have suggested that the motion of the ion in the tube depends not only on its charge value but also on the spatial orientation along the electric field. The directions of the total dipole moment vector of protonated ions from this group have been determined to estimate the correlation factor by PM3 method (table 1).

The dipole moment vector spatial orientation allows suggesting that indole-3-carboxaldehyde and 3-acetylindole ions will move from drift tube to collector faster than cyclopentyl(1H-indole-3-yl)methanone and cyclohexyl(1H-indole-3-yl)methanone. Alkylindoles represent the second group of the examined substances. The PM3 method calculation results for this group are shown in table 2.

**Table 2.** PM3 method calculation results for Alkylindoles

Compound	Ion-mobility value $K_0, \text{cm}^2 \text{V}^{-1} \text{s}$	Proposed molecular ion	Direction of the molecular ion-dipole moment vector	Molecular ion enthalpy of formation kcal/mol
indole	1,776			268,1
2-methylindole	1,640			184,74
3-methylindole	1,685			193,30
2,3,4,9,-tetrahydro-1H-carbazole	1.534			177.2

The Figure 3 represents general spectrogram of compounds from the second group.



**Figure 3.** General spectrogram of the second group compounds.  
5) Indole; 6) 3-methylindole; 7) 2-methylindole; 8) 2,3,4,9-tetrahydro-1H-carbazole

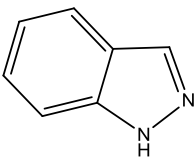
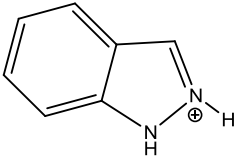
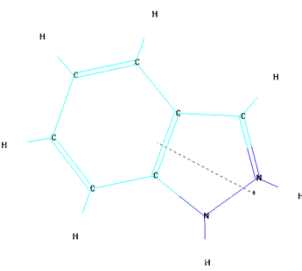
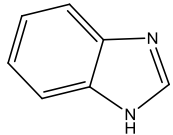
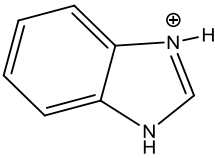
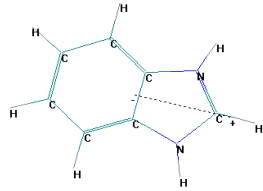
The spectrogram analysis demonstrates that structural isomers 2-methylindole and 3-methylindole have different ion-mobility values in spite of spectra curves similarity. Furthermore, the indole ion-mobility is slightly different from 2-methylindole and 3-methylindole. This agrees with the fact that the dipole moment vectors of these compounds are almost the same. 2,3,4,9-tetrahydro-1H-carbazole molecular ion-dipole moment vector is different from the rest of the group hence it moves through the drift tube as a “flat” particle showing less ion-mobility value (table 2).

The third group is represented by unsubstituted heterocycles.

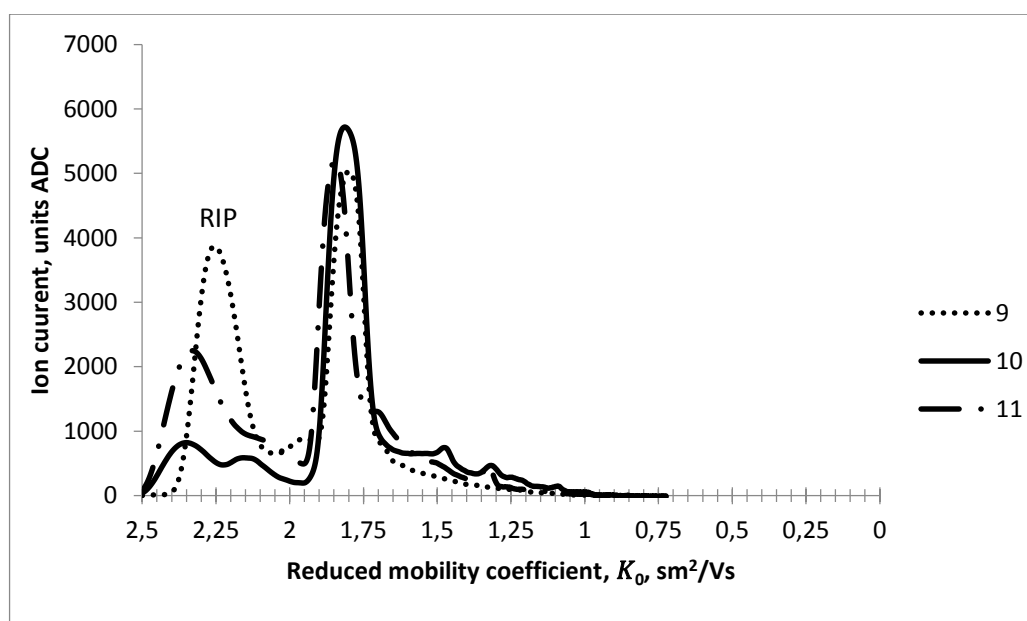
The table 3 shows PM3 method calculation results for the third group.

**Table 3.** PM3 method calculation results for heterocycles

Compound	Ion-mobility value $K_0, \text{cm}^2 \text{V}^{-1} \text{s}$	Proposed molecular ion	Direction of the molecular ion dipole moment vector	Molecular ion enthalpy of formation kcal/mol
indole	1,776			268,1

indazole	1,719				228.38
benzimidazole	1,783				190.98

The Figure 4 represents general spectrograms of compounds from the third group.



**Figure 4.** General spectrogram of the third group compounds  
9) indole; 10) indazole; 11) benzimidazole.

All benzannelated heterocycles show protonated ion signals in a limited range of ion mobility.

Protonated heterocycles calculation results demonstrate that dipole moment vectors have almost the same values. This agrees with the ion-mobility values on the spectrograms of these substances (table 3).  
]

#### 4. Conclusion

Systematic detection of ion-mobility signals of N-heterocyclic compounds of similar in structure and chemical properties has been carried out. A PM3 semi-empirical method was employed to account for spectra character. The probable direction and calculated dipole moment vector values for protonated molecules have been obtained by using this method. A correlation between the ion-mobility and dipole moment vector has been made. The dependence of reduced ion-mobility on dipole moment vector



direction and on the spatial orientation of cation generated in the drift tube is observed in the row of examined substances. The dependence of ion mobility values on the molecular weight of ion is noted among heterocyclic ketones **1-4** (Figure 2).

## 5. References

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