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Dedicated to Professor Ionel Haiduc
on the occasion of his 65th birthday

CHARACTERIZATION OF THE CHEMICAL WARFARE AGENT SIMULANT METHYL SALICYLATE BY ION MOBILITY SPECTROMETRY / MASS SPECTROMETRY (IMS/MS) AT AMBIENT TEMPERATURE

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ABSTRACT. Ion Mobility Spectrometry (IMS) is one of the most powerful and versatile analytical techniques currently available for the trace detection of chemicals, in the gas phase and at atmospheric pressure. IMS plays an important role in many practical applications, from industrial and environmental monitoring to narcotics and explosive detection. Also, IMS hand-held instrumentation is the backbone of chemical warfare agents (CWA) detection system in the USA and NATO countries. This paper describes the behavior of the CWA simulant methyl salicylate, using IMS and IMS/MS at room temperature in the negative operation mode. Ionic mobility spectra and atmospheric pressure ionization chemistry of methyl salicylate are presented.

1. Short description of Ion Mobility Spectrometry

Ion Mobility Spectrometry (IMS) is a modern analytical technique used to detect ultra-traces (at sub-ppb to ppm levels) of both organic and inorganic compounds in the air and so far quite less known worldwide. This technology emerged in 1970 *[1,2]* and then rapidly developed, especially in the last decade. After a period of slight stagnation in the 1980s a true resurrection of IMS happened, due to the real-time response, to its amazing detection limits and also to several practical considerations concerning the instrumentation (such as great simplicity compared with the complex instruments used in mass spectrometry, reliability, ruggedness and miniaturization) *[3,4,5]*. It must be emphasized here another important advantage: IMS fits perfectly to field and process applications.

IMS is based upon the separation of ions - generated by the ionization of the neutral chemical species in gaseous phase at atmospheric pressure - due to their different mobilities in a relatively weak (<300 V/cm) electric field. Separation of ions occurs because of their mobility differences in a neutral drift (buffer) gas - usually nitrogen or air. In IMS the ions produced are effectively

subjected to atmospheric pressure time-of-flight measurements. Using an ionization source in air, a very complex and fast ion-molecule reaction chemistry leads to the formation of many ion clusters, called reactant ions. Water plays an important role in that atmospheric pressure ion-molecule chemistry, so it is obviously necessary to control its concentration. To obtain an optimum performance, it is best to operate the ion mobility spectrometer with dry air (several ppm water vapor) as drift gas; in that case, the degree of clustering is limited and, most important, kept constant.

Positive reactant ions:	*Negative reactant ions:*
$(H_2O)_xH^+$; $(H_2O)_yNO^+$; $(H_2O)_zNH_4^+$	$(H_2O)_xO_2^-$; $(H_2O)_yO^-$; $(H_2O)_zO_4^-$
predominant species: $(H_2O)_xH^+$	predominant species: $(H_2O)_xO_2^-$

In other words, Ion Mobility Spectrometry is first of all an identification technique of trace vapors by measuring their ionic mobilities in the gaseous phase. IMS provides many possibilities for analysis in a whole variety of fields, and in particular in the chemical warfare agents (CWAs) detection; explosives and narcotics detection, as well as occupational hygiene and environmental spheres, are also the application niches preferred for IMS.

A typical ion mobility spectrometer is illustrated in Figure 1.

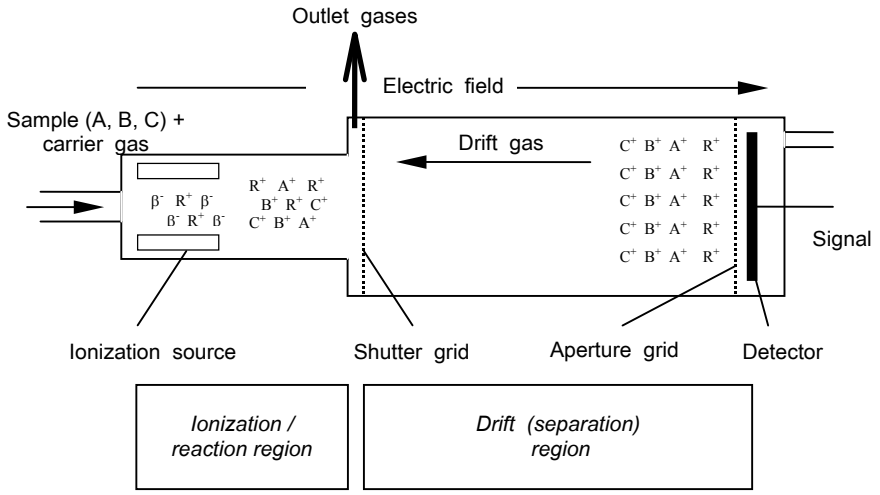

Fig. 1. Schematic of ion mobility spectrometer cell

By applying an electric field, ions of one polarity are extracted from the ionization region before their recombination can occur; these ions are periodically allowed to enter drift region, using a so-called “shutter grid”, periodically triggered open and close by a specialized electronic circuit *[3]*.

Ions migrate towards the detector (a Faraday plate) as a function of their mobility *K*, which is related to mass, size, temperature, pressure and the nature of the neutral species present in the drift region (hence, the drift gas); the Mason-Schamp equation, given below, describes these dependences. Monitoring the ion current in time generates a single ion mobility spectrum; several spectra are averaged to improve the signal to noise ratio, resulting in an ion mobility spectrum (called also plasmagram or IMS signature). After averaging a pre-programmed number of spectra (from 4 to 256, for instance), a processing routine is activated and/or peak measuring programs are used to determine the magnitude of the peaks associated with target analyte. The entire process (data acquisition, averaging and quantitation) can be accomplished in a time interval of 0.5-3 seconds, which means definitely a true real-time response.

The main theoretical issues concerning Ion Mobility Spectrometry are as follows:

- *drift rate equation:* $v_d = K \cdot E = l_d / t_d$ (1)

This proportionality constant ***K*** is exactly *ionic mobility*, v_d is the drift rate, *E* represents the electric field intensity, l_d is the drift length, and t_d is the drift (flight) time of an ion *[1,4]*. The equation (1) describes the behavior of an ion migrating with a constant rate through a neutral drift gas, at atmospheric pressure, under the influence of a relatively weak (with an intensity up to several hundred V/cm) electric field.

- *reduced mobility equation:* $K_0 = (273/T)(P/760)K$ (2)

, where K_0 is the reduced mobility (in $cm^2 \cdot V^{-1} \cdot s^{-1}$), *T* is the absolute temperature of the drift gas, and *P* is the atmospheric pressure *[3,4]*. The role of this particular relationship is to normalize the measured ionic mobilities for temperature and pressure variations.

- *Mason-Schamp equation:* Because the collisions between particles are controlled by forces occurring between them, the mobility should clearly depend on the force between ion and neutral molecule; this dependence appears as an integral of diffusional collision, or the average collision cross section, Ω_D:

$$K = \frac{3}{16} \cdot \frac{q}{N} \cdot \left(\frac{1}{m} + \frac{1}{M} \right)^{1/2} \cdot \left(\frac{2\pi}{kT} \right)^{1/2} \cdot \frac{1}{\Omega_D} \quad (3)$$

Mason-Schamp equation

, where *q* is the electric charge of the ion, *N* is drift gas density, *m* is the mass of the ion, *M* is the mass of drift gas molecule, *k* is the constant of Boltzmann, and *T* is the temperature *[4,5]*.

The samples may be introduced into the ionization/reaction region by using many techniques, but the most common are the semi-permeable membrane inlets (used at ambient temperature, and consequently in the portable hand-held IMS spectrometers) and direct introduction using a heated inlet (used in IMS desktop-sized explosive and narcotics detectors).

The introduction of sample molecules with high proton (or electron) affinity relative to the reactant ions results in the formation of so-called "product ions", which are ions containing one (or more) sample molecules. Product ions are therefore formed in the reaction region, mainly by collisional charge transfer reactions between the reactant ions and analyte neutral molecules from the sample; they could be also generated by attachment reaction of a reactant ion to the neutral species *M* of analyte *[3,4,5]*:

$$(H_2O)_xH^+ + M \longrightarrow (H_2O)_xMH^+ \quad \text{- for positive ions}$$
$$(H_2O)_xO_2^- + M \longrightarrow (H_2O)_xMO_2^- \quad \text{- for negative ions.}$$

Usually, these product ions (very similar to CI-MS secondary ions) are larger and more massive than the original reactant ions. Therefore, they have longer drift times and consequently lower reduced mobilities.

Very important is the IMS response, which could be briefly defined as the intensity change of the product ions with the modification of analyte concentration. Figure 2 illustrates such a response for an IMS spectrometer equipped with a radioactive ^{63}Ni ionization source.

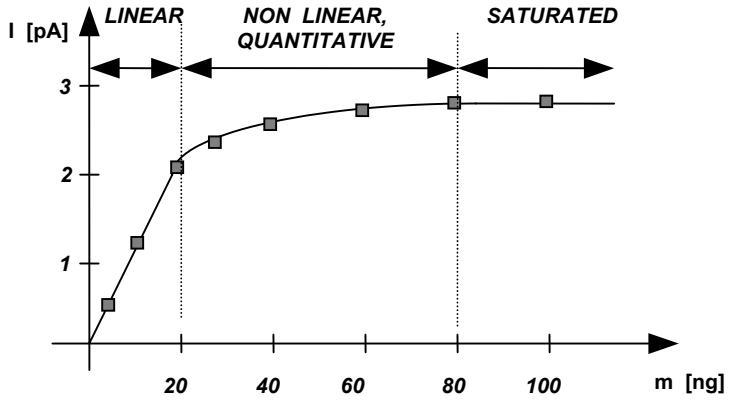

Fig. 2. Typical quantitative IMS response

In the radioactive ionization source the distribution of available charge is done in a competitive way. The consequence is that the appearance of an ion should lead, because of the charge conservation, to a decrease in intensity of another ion (or ions). In a first approximation, the charge seems to be distributed proportionally with the concentration of each component in the sample and according to its proton (or electron) affinity.

In most instances, the charge goes to the neutral with the highest proton/electron affinity and it maybe that only a low concentration will take all this charge. Such happens with CW agents and so, the charge will not distribute to any compound in the vapor sample. In the absence of a high proton affinity

(PA) neutral, lower PA materials can be ionized; thus, if the chemical compounds which compose a given sample have similar proton (or electron) affinities, then the charge will distribute virtually to any compound present in the vapor sample, and this is exactly the cause of the IMS extraordinary versatility. However, because most of commercial drift tubes used currently have a low resolution, they can't be used to separate complex mixtures of ions *[4]*. In conclusion, the specificity of IMS might be said to rely on the various target materials having high PA, such as chemical warfare agents (or electron affinities, in the negative operation mode); when common airborne materials (such as ethanol, aldehydes etc., monitored on NASA International Space Station)) are targeted, one must employ GC-IMS to separate the analytes to achieve specificity.

An ion mobility spectrometer can be successfully used to detect a great range of chemicals, both organic and inorganic. This device was for a long time considered as an ideal detector for organic vapors monitoring, but it can also be used to detect many inorganic gases. As a matter of fact, the applications of Ion Mobility Spectrometry can be grouped into several categories:

- ➲ industrial monitoring and hygiene - organic and inorganic pollutants detection *[6,7,9]*
- ➲ process monitoring *[8,9]*
- ➲ detection of medical related materials (such halogenated anesthetics) and in forensic medicine
- ➲ laboratory applications - ionic mobilities measurements and studies concerning ion structure
- ➲ military applications - detection of chemical warfare agents (both nerve and blister gases)
- ➲ explosives and illicit drugs detection
- ➲ use of IMS spectrometer as a chromatographic detector *[3]*.

Ion Mobility Spectrometry has several important advantages:

- ☺ analytical flexibility, because it can be applied to analyze both organic and inorganic vapors, and also ca be monitored both positive and negative ions.
- ☺ very fast response (the drift times are in the millisecond range); so, a complete analysis cycle can be less than a second - a true real-time response
- ☺ very good sensitivity, in the parts-per-billion and even parts-per-trillion range
- ☺ good selectivity; it can be improved by using dopants and/or different ionization sources
- ☺ the analysis is done at atmospheric pressure, and not in vacuum like in mass spectrometry
- ☺ the instrumentation is very robust (no delicate components, no liquid reagents, few moving parts) and can be easily miniaturized.

IMS has also a number of major drawbacks:

- ☹ the theoretical concepts concerning ion mobility spectrometry are not yet perfectly defined
- ☹ there are no comprehensive models for the response characteristics
- ☹ the dynamic range is quite limited, which in turn restricts the quantitation.

The crucial demand by military forces who might be exposed to Chemical Warfare Agents (CWAs) is the ability to detect the presence of these colorless, odorless compounds; this detection must be early enough so that the forces have an opportunity to protect themselves before they are exposed to incapacitating doses of these extremely dangerous materials. Similar situations exist for applications in and around chemical weapons storage and destruction sites. In both situations the primary goal and use of the detector systems is to warn workers or military personnel of imminent danger associated with their possible exposure to toxic chemicals.

Methyl salicylate is an important chemical in IMS technology, since it is being used:

- ❒ As a CWA simulant for blister agents (mustard gas), in the negative operation mode of IMS spectrometer *[9,10]*; methyl salicylate and dipropylene glycol monomethyl ether (DPM) are the materials used to verify in the field that a military hand-held IMS device of CAM type (Graseby Dynamics, Ltd., UK) is operational.
- ❒ As a IMS calibrant standard in the negative mode, when its reduced mobility K_0 is taken exactly as 1.474 $cm^2 \cdot V^{-1} \cdot s^{-1}$ and this way the IMS cell constant may be calculated *[6,9]*.
- ❒ As a dopant used in IMS for the detection of hydrogen fluoride (HF), especially in industrial applications or in the analysis of submarine's recycled air *[8,11]*.

The goal of this paper is the attempt to elucidate the main aspects concerning the ion mobility spectrometric response of methyl salicylate. All experiments were performed at DIAS (Department of Instrumentation and Analytical Science) - UMIST (University of Manchester Institute of Science and Technology).

2. Experimental

Standard atmospheres with known concentrations of methyl salicylate were generated using a thermostated gas rig based on permeation tubes. Methyl salicylate (2-(HO)$C_6H_4COOCH_3$, purity 99+%, MW 152.15, purchased from Aldrich Chemical Ltd., U.K.), was introduced (1 cm^3) in a glass chromatographic vial, and the vial was sealed using a silicone rubber cap. This improvised permeation source was then conditioned at 50°C for 48 hours; by repeatedly measuring the mass of the vial, the permeation source was gravimetrically calibrated and it was found to deliver a concentration of 10 mg m^{-3} of methyl salicylate into a flow of 40 $cm^3 \cdot min^{-1}$ air.

Both IMS drift gas and carrier gas were compressed air, supplied from air cylinders (BOC Gases, UK) and further purified (dried) using molecular sieve filters.

Ion mobility spectrometer - instrument characterization:

- IMS cell: modified CAM (Chemical Agent Monitor), manufactured by Graseby Dynamics Ltd. (Watford, Herts., UK)
- data acquisition card: ASP (Advanced Signal Processing), from Graseby Dynamics Ltd. (Watford, Herts., UK)
- data acquisition software: WASP (Waveform Analysis Signal Processing) - Version 1.35 [1991/1992], also from Graseby Dynamics Ltd. (Watford, Herts., UK)
- hardware control PC: Intel 386 processor, 40 MHz, 4 MB RAM.

IMS cell configuration:

- stacked rings drift tube
- drift length: 4.25 cm
- drift voltage: 850 V
- membrane inlet (dimethylsilicone rubber membrane)
- radioactive ionization source (10 mCi ^{63}Ni)
- operating temperature: room temperature (25°C).

Spectral generation for IMS:

- Averages = 250
- Samples = 1024 per waveform
- Frequency = 50 kHz
- Gating pulse width = 180 μs.

The filters for drift and carrier gases were cartridges containing as filtering material molecular sieve 15A.

Methyl salicylate ($C_6H_4OHCOOCH_3$, with M= 152.15, CAS # 119-36-8, density 1.186, purity 99+%) was purchased from ALDRICH and used as received, without any further purification.

Spectra were recorded in the negative mode of operation.

The diagram of instrumentation for experiments is given in Figure 3.

Experimental parameters were as follows:

- Negative mode of operation
- T = 298 K
- P = 722 torr
- Drift flow: 120 cm^3min^{-1}, clean air
- Source (carrier) flow = 200 $cm^3 \cdot min^{-1}$, clean air
- Sample inlet flow = 40 $cm^3 \cdot min^{-1}$, clean air passed through the thermostated holder containing the permeation source

- Emission rate of the permeation source with methyl salicylate: R= 400 ng· min^{-1}
- Methyl salicylate concentration: C = R/Q = 400/40 = 10 mg· m^{-3}

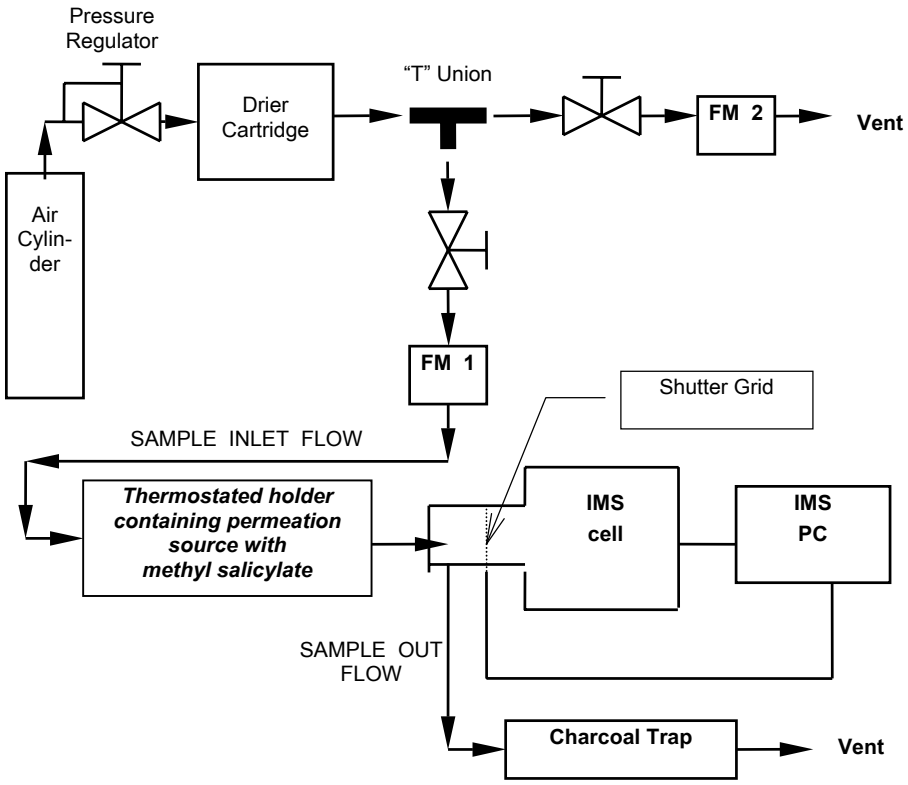

Fig 3. Schematic diagram of instruments for IMS experiments

, where FM = Flow Meter.

3. Results and discussion

Ion mobility spectra were obtained for both clean air (these spectra contain only the negative reactant ion peak RIP) and methyl salicylate at 10 mg· m^{-3}. The IMS spectra are presented in Figures 4 and 5, respectively.

The features seen at the beginning and the end of the ion mobility spectra are the shutter grid pulses.

One can observe that IMS spectra of methyl salicylate were very simple, with only one product ion peak (PIP) at drift time t_d= 8.960 ms.

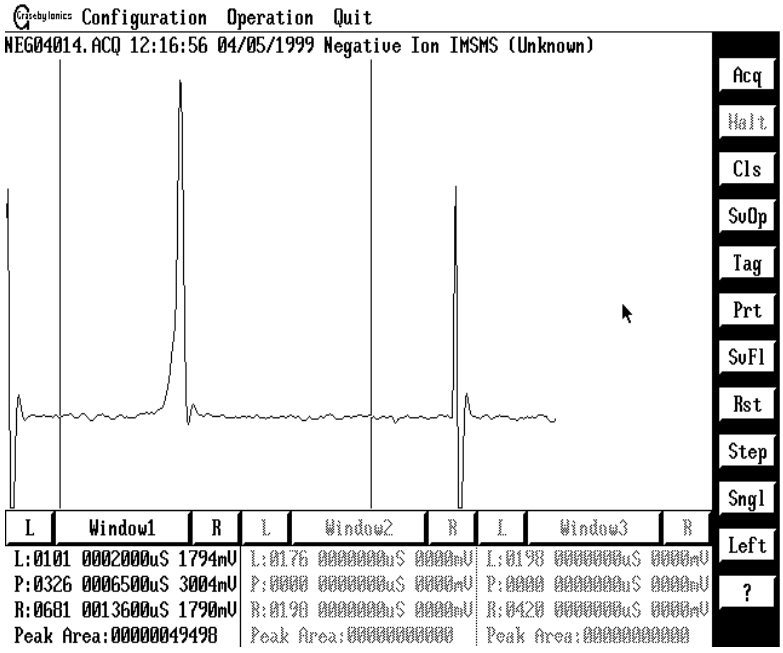

Fig. 4. IMS spectrum for clean air, negative mode

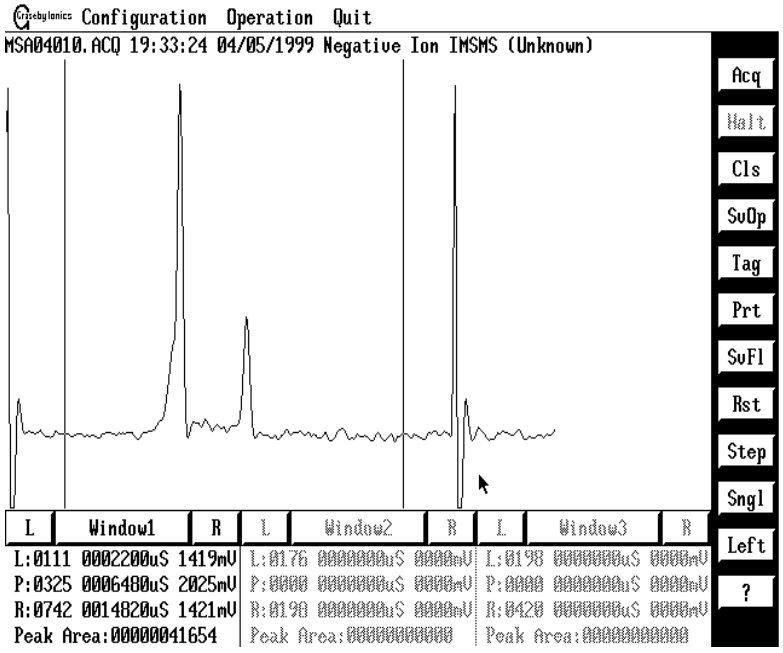

Fig. 5. IMS spectrum for methyl salicylate, 10 mg m^{-3}, negative mode

The atmospheric pressure ionization of methyl salicylate has been investigated successfully by using IMS/MS technique, where the IMS spectrometer was coupled to a quadrupole MS spectrometer (EXTREL C-150, Extranuclear Laboratories, Pittsburgh, USA). This way total atmospheric pressure chemical ionization (APCI) spectra (with the IMS shutter grid fully open), as well as "tuned" ion mobility spectra (when the mass filter allows only a selected m/z value to be detected) were gathered. A total APCI mass spectrum for methyl salicylate is given in Figure 6.

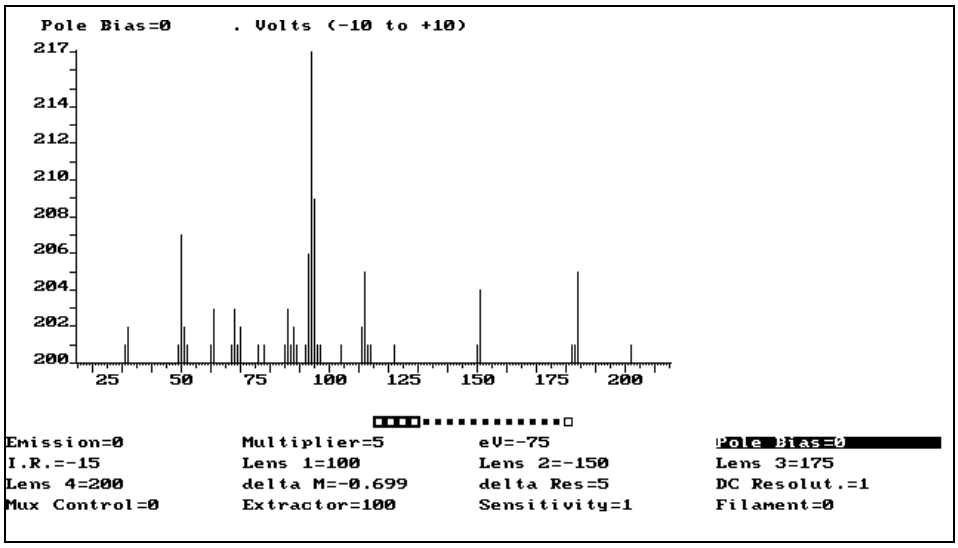

Fig. 6. Total mass spectrum for methyl salicylate (at 10 mg m^{-3})

By using the mass-resolved IMS spectra, it has been clearly demonstrated that ions with m/z 151, 184 and 202 may be assigned to methyl salicylate and that all these ions have the same drift time, corresponding to the second peak in the IMS spectrum (at 8.960 ms - the product ion peak). All the other peaks in the mass spectrum may be assigned to the negative reactant ion species; these are mainly ions of type $(H_2O)_n(CO_2)_mO_2^-$ and $(H_2O)_n(CO_2)_mCO_4^-$.

As a consequence, the ionization chemistry at atmospheric pressure for the target analyte was summarized in Table 1 below.

Table 1

Ionization chemistry for methyl salicylate

Ion species	*Ion identity*	*Reaction type*	*Drift time in IMS spectrum*
m/z 151	$(MSAL - H)^-$	Hydride abstraction (from the phenolic -OH group): $MSAL + O_2^- \longrightarrow (MSAL - H)^- + O_2H$	8.960 ms
m/z 184	$(MSAL)\cdot O_2^-$	Charge transfer reactions: $MSAL + O_2^- \longrightarrow (MSAL)\cdot O_2^-$	8.960 ms
m/z 202	$(MSAL)(H_2O)O_2^-$	Charge transfer with clustering: $MSAL + O_2^- \longrightarrow (MSAL)\cdot O_2^- + H_2O \longrightarrow (MSAL)(H_2O)O_2^-$	8.960 ms

, where MSAL is methyl salicylate molecule.

3. Conclusions

This paper aims to demonstrate the advantages of Ion Mobility Spectrometry and its diversity of applications, including here the detection of a chemical warfare agent simulant for blister agents - methyl salicylate.

Methyl salicylate generates simple ion mobility spectra in the negative mode of operation, which contain only one product ion peak having a drift time of 8.960 milliseconds and a reduced mobility $K_0 = 1.474\ cm^2\ V^{-1}\ s^{-1}$.

One may observe that at the concentration of 10 mg m^{-3} methyl salicylate the reactant ions were preserved, so these measurements fall in the linear range of the IMS response curve (see Figure 2). The limits of detection were not approached, being beyond the scope of this study, but they were previously estimated by other authors to be in the low ppb range - 5 ppb *[12]*; 20 ppb *[13]*; 0.27 mg m^{-3} *[14]*.

Using IMS/MS investigations, it has been found that the ion species that form the unique product ion peak are the following: $(MSAL-H)^-$ with m/z 151; $(MSAL)O_2^-$ with m/z 184, and $(MSAL)(H_2O)O_2^-$ with m/z 202. Therefore, ionization chemistry of this analyte has been elucidated. These findings agree very well with the results of Spangler *[15]*, which observed in the negative mode of operation (by IMS/MS) product ions of hydride abstraction type (m/z 151) and clusters of MSAL with O_2^- and N_2 (m/z 184, 212, 240, and 268).

We are sure that IMS will become very soon a common, widely accepted analytical technique, especially in several particular niches. In fact, it is obvious that the latest trends in IMS field predict a very interesting evolution, especially if the IMS experts and users collaborate to solve the remaining problems.

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