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Characterization of a high resolution drift tube ion mobility spectrometer with a multi-ion source platform

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ABSTRACT

This study presents an atmospheric pressure ionization high resolution ion mobility spectrometer (IMS) equipped with a multi-ion source platform, which together with the design of the drift tube chamber allows the use of various atmospheric pressure ionization (API) methods, namely electrospray ionization (ESI), corona discharge atmospheric pressure chemical ionization (CD-APCI), atmospheric pressure photo ionization (APPI), and radioactive atmospheric pressure chemical ionization (R-APCI). The instrument thus allows one to study samples using the same drift tube with different ionization techniques either in positive or in negative ion mode. The instrument has a high resolving power, around 100, and a reproducible reduced mobility value of ~1.48 $\mathrm{cm^2/Vs}$ (relative standard deviation below 1%) for 2,6-di-*tert*-butylpyridine (2,6-D*t*BP) was obtained with all of the ionization methods. The shape of the ion pulse as a function of gate opening time and how this affect the resolving power is discussed based on the observed differences between calculated and measured resolving power.

1. Introduction

Ion mobility spectrometry (IMS) separates ions, often formed by ion/molecule reactions at atmospheric pressure, according to their mobility in an electrical field at pressures between ~10^2 and 10^5 Pa using either a Faraday cup/plate or mass spectrometer as ion detector. The method is well described in the literature and a number of reviews have been published [1–5]. Traditionally the separation is achieved using a drift tube [1,5], but also aspiration-type [6] and high-field asymmetric waveform ion mobility spectrometers (FAIMS) [5,7] have been used successfully.

Currently, ion mobility spectrometry is widely used for fast detection of explosives and illegal drugs [4,8] because of its significant advantages including compactness of instrumentation, short analysis time and low detection limits (ppt–ppb range [9]). The main drawback of most ion mobility spectrometers is the relatively high probability of false detection caused by insufficient separation efficiency. The selectivity can be improved by increasing separation efficiency of the instrumentation, choosing a different ionization method and/or the use of reagent gasses. Combining IMS with a mass spectrometer (MS) is also an excellent method to increase the selectivity in ion mobility spectrometry and during the resent years the combination IMS-MS has been getting much interest [10].

The resolving power of a single peak in drift tube IMS is defined as [4]:

$$R = \frac{t}{\delta t} \quad (1)$$

where t is the ion drift time and δt is the ion pulse width at the detector measured at half height of the peak maximum. By simple transformations Eq. (1) can be rearranged to

$$R = \frac{K}{\delta K} \quad (2)$$

where K is ion mobility and δK is the mobility range corresponding to the analytical signal peak width at half height. Resolving power reflects the minimal differences in mobility required for compounds to be resolved within a given range of mobility. Thus, resolving power can be considered as a qualitative measure of separation efficiency. Drift tube IMS offers better resolving power than

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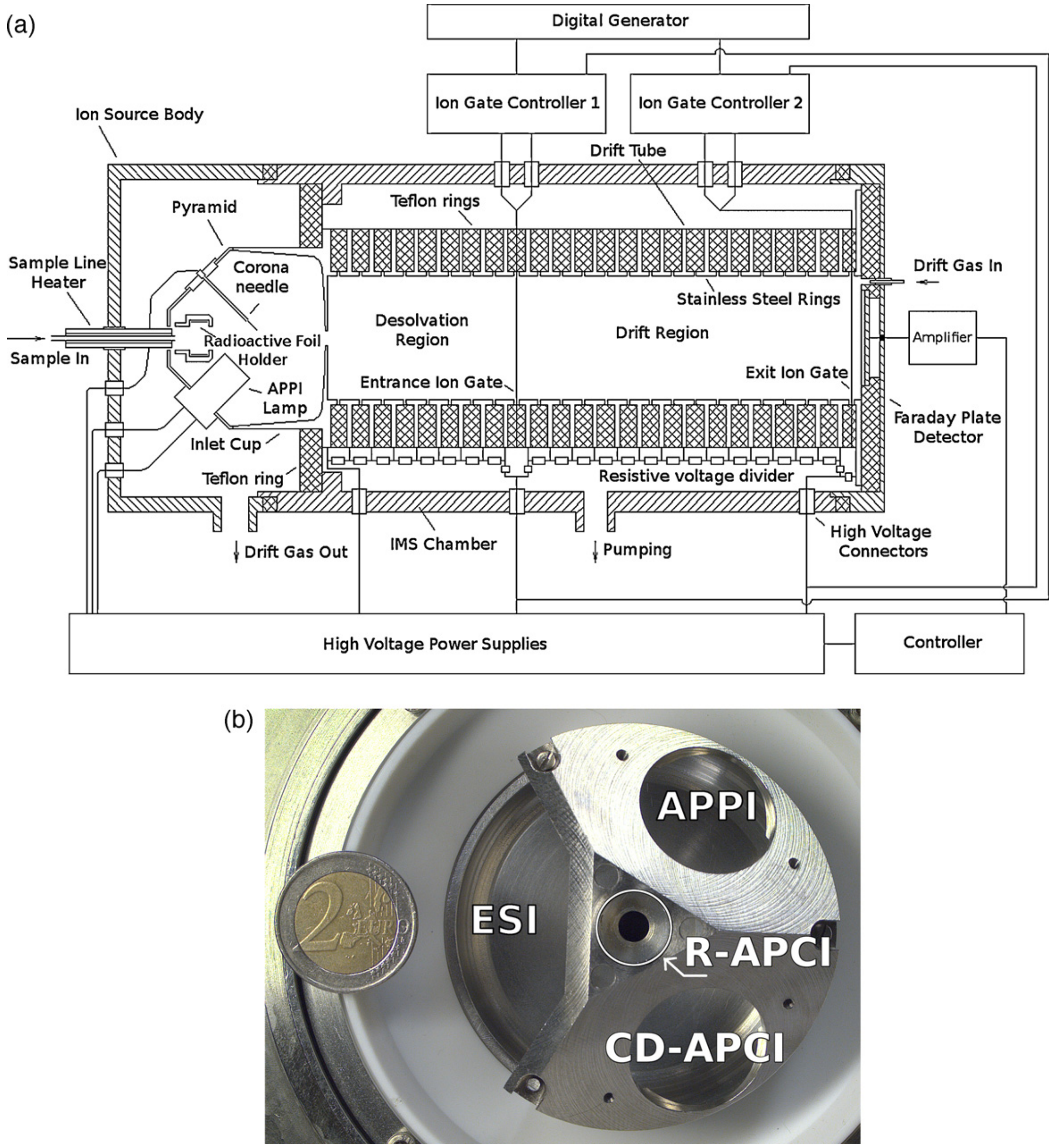

Fig. 1. (a) A schematic diagram of the multi-ion source platform API-IMS instrument with multi-mode ion source body (CD-APCI, APPI and R-APCI) and (b) a picture of multi-mode ion source pyramid.

other kinds of IMS. The resolving power of commercially available drift tube IMS [9] is in the range of 20–60 and resolving powers above 150 have been reported for custom build IMS interfaced with mass spectrometers [11–14].

The choice of ionization is vital for making a good analysis. Different ionization methods have different, and often complementary characteristics, both with respect to which ions are formed and in which abundance [4]. Different ionization techniques such as electrospray ionization (ESI) [4,15–21], corona discharge atmospheric pressure chemical ionization (CD-APCI) [4,22,23], radioactive atmospheric pressure chemical ionization (R-APCI) [4] and atmospheric pressure photo ionization (APPI) [4] have been used together with ion mobility spectrometry for analysis of compounds in gas and/or liquid phase. We have designed and built a high resolution drift tube IMS instrument which allows rapid switching of different atmospheric pressure ionization modes, namely ESI, CD-APCI, APPI and R-APCI. This enables rapid application development, but also offers the possibility to study the fundamental mechanisms of ionization. Operation of the instrument using selected model compounds, of which several, namely 2,6-di-*tert*-butylpyridine (2,6-D*t*BP) and the tetraalkylammonium halides (TAAH), have been proposed as a reference compound for IMS instrumental comparisons [24–26] is discussed.

2. Experimental

The multi-source API-IMS instrument (Fig. 1) consists of three main parts: a multi-ion source platform, a drift tube, and a Faraday cup detector. The drift tube geometry/design is identical to the API-IMS/MS instrument built previously [26,27]. This enables us to use of the same ion sources for both instruments.

2.1. Multi-ion source platform

The multi-mode ion source consists of a triangular stainless steel pyramid (Fig. 1(a)), which serves as a support for some of the ion

Table 1
Resolving powers measured for TAAH compounds at different gate opening times using ESI-mode. Experimental values are averages of six repetitions measured on the same day. Relative standard deviations are presented in the brackets. Only clearly seen peaks were taken in the calculations. Resolving powers calculated using Eq. (4) are also shown.

Compound	Gate opening time (μs)			
	100	200	300	500
	Experimental/calculated resolving power			
Tetraethylammonium	93(11%)/114	81(10%)/83	69(10%)/62	41(3%)/40
Tetrapropylammonium	111(10%)/119	88(2%)/92	77(5%)/71	51(4%)/47
Tetrabutylammonium	105(11%)/123	93(5%)/99	86(3%)/79	56(4%)/54
Tetrapentylammonium	111(13%)/125	104(16%)/105	91(9%)/86	63(9%)/60
Tetrahexylammonium	Not detected	94(7%)/110	93(3%)/92	71(3%)/66
Tetraheptylammonium	Not detected	97(8%)/113	98(3%)/97	73(3%)/71
Tetraoctylammonium	Not detected	92(13%)/116	100(4%)/101	80(4%)/76
Tetradecylammonium	Not detected	Not detected	90(16%)/107	85(4%)/83
Tetradodecylammonium	Not detected	Not detected	85(15%)/111	91(7%)/88

sources. The pyramid is mounted on the inlet cup of the drift tube, which together define boundaries of the ionization region. There is a hole in the top of the truncated pyramid (Fig. 1(b)), which is both used for sample inlets, which is either a nebulizer or a heatable glass tube for gas samples, and for the radioactive ^{241}Am foil holder (R-APCI mode). One face of the pyramid has a hole for fitting of a corona needle holder (CD-APCI mode) and another face has a hole for fitting a photoionization lamp holder (APPI mode), as seen in Fig. 1(b). The third face has a cut for the needle of an electrospray ion source (ESI-mode, Fig. 1(b)). The cut in the pyramid is such that the electrospray needle can be freely adjusted. This ion source design allows switching between CD-APCI, APPI and ESI modes. Switching to ESI-mode is a simple exchange of ion source housing, because operating with a commercial ESI-source at present. The R-APCI mode requires the corona needle and photoionization lamp to be removed, which is easily done with simple tools. Switching the hardware inside the ion source between different ionization modes is estimated to take around 10–15 min.

The electrospray ion source was a commercial SCIEX Ion Sprayer unit (Applied Biosystems–Sciex, Toronto, Ontario, Canada). The original high voltage connector (10 kV) was replaced by a 20 kV connector, because voltages from 8 to 15 kV are needed for ESI-IMS. Photoionization was done, without dopants, using a Krypton UV lamp with 10 and 10.6 eV photon energies (PKS-100, Cathodeon Ltd., Cambridge, England). The CD-APCI ion source had a stainless steel needle mounted in a teflon holder. The needle was angled 45° relative to the drift tube orifice and the tip of the needle was positioned about 8 mm away from the orifice (diameter is 6 mm). The radioactive ion source consisted of a custom-made cylindrical stainless steel part with 1 cm diameter hole where the sample was carried/blown through. A metal foil coated with ^{241}Am (10 MBq) was placed inside the hole. The distance between the foil and the drift tube orifice was about 26 mm.

2.2. Ion mobility spectrometer

The ion mobility spectrometer (IMS) consists of a drift tube (13.85 cm) and a Faraday cup detector encapsulated in a stainless steel chamber, and electronics in a separate box (Fig. 1(a)). The design is very similar to the IMS described in detail previously [27]. The main difference is the Faraday cup detector with an electrometric amplifier, which is used instead of mass spectrometric detection. The electric field in the drift region [27] and the response time of the Faraday plate detector have been optimized in the design to obtain high resolving power. A membrane pump (MPC201E ILMVAC GmbH, Germany) is connected to the exhaust line to vent the ion source ionization area and the area between the inside chamber and the drift tube electrodes to minimise memory effects. The software for data collection and processing was written using the LabVIEW environment (National Instruments, Austin, US). The program can present data as drift time or mobility distributions and data can be exported to external software (MS Excel, Origin and so on) as a text file.

2.3. Experimental procedure

The ion mobility spectrometer was operated in single gate mode. The first gate opening time was 100, 200, 300 or 500 μs. The second ion gate was kept open at all times. Mobility distributions were recorded for 50 or 65 ms with repetition rates of 20 or 15.4 Hz, respectively. 500–2000 transients were combined to obtain the analytical signal, i.e., the time required to make a single measurement was 25–130 s. The data was collected at a drift field of 378 V/cm. Reduced mobility was calculated according to Eq. (3) [4] using atmospheric pressure, which varied from 737 to 767 Torr (data from SMEAR III, Helsinki, Finland) depending on the day of experiment:

$$K_0 = K\left(\frac{273}{T}\right)\left(\frac{P}{760}\right) \tag{3}$$

where K is mobility of the ion in units, T is temperature in Kelvin (298 K was used in the calculations, but it was not measured during these experiments) and P is pressure in Torr.

2.4. Samples

Chemicals were purchased from the following suppliers and used as received: methanol (HPLC grade) from Baker (Deventer, Holland), pentane (99%, Labscan, Dublin, Ireland), tetraethylammonium iodide (98%) from Sigma–Aldrich (St. Louis, USA); tetrapropylammonium iodide (purum), tetrabutylammonium iodide (purum), tetrapentylammonium iodide (≥98%), tetraheptylammonium iodide (≥99%), tetradecylammonium bromide (≥99%), and tetradodecylammonium chloride (≥97%) from Fluka (Buchs SG, Switzerland); tetrahexylammonium bromide (99%) from Aldrich (Milw., USA); tetraoctylammonium bromide (98%), 2,6-di-*tert*-butylpyridine (2,6-D*t*BP) (>97%) from Sigma–Aldrich (Steinheim, Germany), and ortho-phthalic acid from Merck (New Jersey, USA).

Gas samples containing 2,6-D*t*BP at a concentration of 800 ppb were analyzed in CD-APCI, APPI and R-APCI modes. Gas samples were prepared using a gas calibrator by injection of a 1% solution of 2,6-D*t*BP in pentane at a constant rate of 50 μl/h into a stream of nitrogen using a syringe pump (MC 789100C, Cole-Parmer Instrument Company, Vernon Hills, IL, USA). The primary flow was further diluted by an additional flow of nitrogen, resulting in a 2,6-D*t*BP concentration of about 800 ppb. The gas flow was then divided into two portions and the amount of gas introduced into the ion source of the ion mobility spectrometer (about 1.5 l min^{-1}) was controlled by a needle valve. All the flows were adjusted using a thermal mass flow meter (TSI 4140, TSI Incorporated, Shoreview, MN, USA). The measurements were taken at ambient pressure and temperature in a thermostatic room. The nitrogen (99.5%) used as drift gas and for dilution was produced from pressurized air using a NGLCMS20 nitrogen generator (Labgas Instrument Co., Espoo, Finland). To keep the humidity constant during the experiments the drift gas was passed through driers and the humidity was measured with a dew-point sensor (Vaisala DMT242; Helsinki, Finland). The drift gas flow rate was 1.5 l/min.

Three different liquid samples were used in ESI-mode: a mixture of tetra alkyl ammonium halides (see Table 1), 2,6-D*t*BP and ortho-phthalic acid solutions, all dissolved in methanol. Concentration of an individual tetra alkyl ammonium halide in solution used was 2 μM, concentration of 2,6-D*t*BP in its methanol solution was 5 μM and concentration of ortho-phthalic acid in its solution 100 μM. The ortho-phthalic acid solution was analyzed in negative ion mode and the other in positive ion mode. The standard solutions were typically infused at a rate of 0.5 ml/h through a fused silica capillary (100/170 μm i.d./o.d.) placed within the electrospray needle.

3. Results and discussion

3.1. Electrospray ionization (ESI)

A mixture of aliphatic C_2–C_8, C_{10} and C_{12} tetraalkylammonium halides (a 2 μM equimolar solution) was analysed using positive ion mode ESI-IMS (Fig. 2, Table 1). These compounds were previously suggested as chemical standards for positive ion mode electrospray ionization ion mobility spectrometry/mass spectrometry (ESI(+)-IMS/MS) because of the low clustering tendency [26]. Only a single clearly defined ion mobility peak was observed for each compound. As it was expected sensitivity of analysis depends on the gate opening time. The sensitivity is increasing with longer gate opening times. Thus, at 100 μs only four (C_2–C_5) were clearly observed, whereas at 500 μs all nine tetraalkylammonium halides (C_2–C_8, C_{10} and C_{12}) were seen. An increase in gate opening time increases the amount of ions introduced into the drift tube, which leads to the sensitivity improvement. A resolving power of about 100 can be obtained for many of the alkylammonium compounds with a gate opening time of 100, 200 or 300 μs (Fig. 2 and Table 1). For each compound six repetitions were made at each gate opening time and the measured resolving power values presented in Table 1 are averages of these six repetitions measured on the same day. The relative standard deviations of the measured resolving powers varied from 2% to 17% and the average value of all the relative standard deviations (29 values) was 8%. The measured reduced mobilities in nitrogen were 1.76, 1.47, 1.26, 1.10, 0.97, 0.88, 0.80, 0.70, and 0.64 cm^2/Vs, for C_2–C_8, C_{10} and C_{12} tetraalkylammonium halides, respectively. Relative reduced mobilities (relative to 2,6-D*t*BP) for the same compounds were 1.19, 0.99, 0.85, 0.74, 0,66, 0.59, 0.54, 0.47, and 0.43, respectively. These are in excellent agreement with the previously published values [26].

The resolving power (Table 1) is dependent of both the mobility of the ion and the gate opening time. In general, better resolving powers were observed for shorter gate opening times, as reported also previously [28]. Calculated resolving powers were obtained based on the following equation [28,29]:

$$R_t = \frac{L_d^2/KV_d}{\sqrt{t_g^2 + (16kT\ln 2/V_d ez)\cdot(L_d^2/KV_d)^2}} \qquad (4)$$

where t_g is the initial ion pulse width, k is Boltzman's constant, e is the elementary charge, z is the number of charges on the ion, V_d is the voltage drop across the drift space, K is the mobility of the ion and L_d is the drift length. In our calculations, the K values were replaced with the measured reduced mobility K_0, where pressure and temperature correction is applied.

The experimentally obtained resolving powers are good for a 13-cm drift tube operating at room temperature measurements compared to commercial instruments and in relative good agreement with the calculated limit estimated by the formula (4) (Table 1). Resolving powers for some of the measured peaks exceed the calculated resolving power. Data dispersion is not sufficient for detailed analysis of this phenomenon, but some trends can still be seen. The experimental resolving powers exceeding the calculated value are observed for gate opening times of 300 and 500 μs. For 300 μs gate opening time 6 out of 9 experimental resolving powers exceed the calculated value and for 500 μs gate opening time all the experimental resolving powers exceed the corresponding cal-

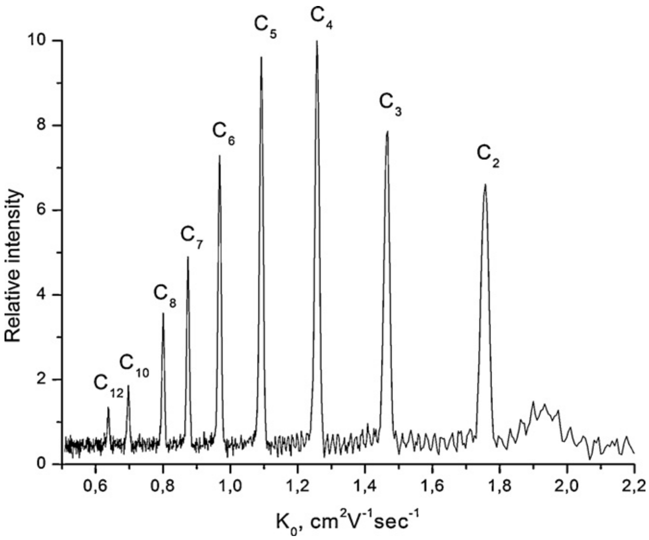

Fig. 2. ESI(+)-IMS spectrum of an equimolar solution (2 μM in MeOH) of aliphatic C_2–C_8, C_{10} and C_{12} tetraalkylammonium halides at 1.5 l/min drift gas flow rate, 378 V/cm drift field, and 300 μs gate opening time.

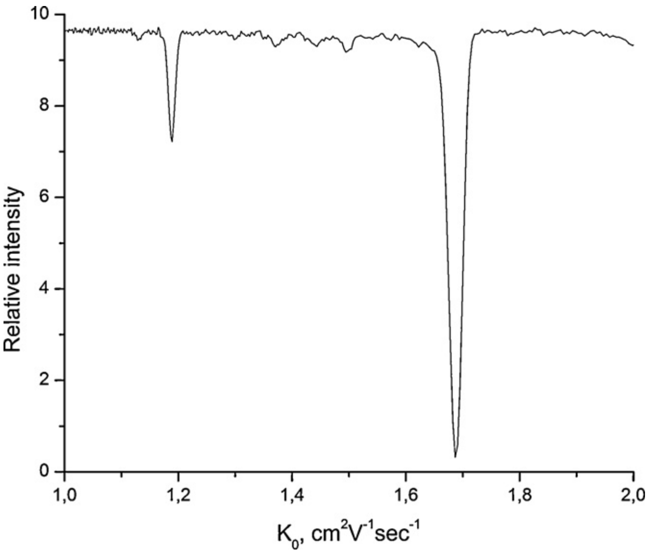

Fig. 3. Negative ion mode electrospray mobility distribution for ortho-phthalic acid (100 μM in methanol) obtained at 1.5 l/min drift gas flow rate, 378 V/cm and 300 μs gate opening time.

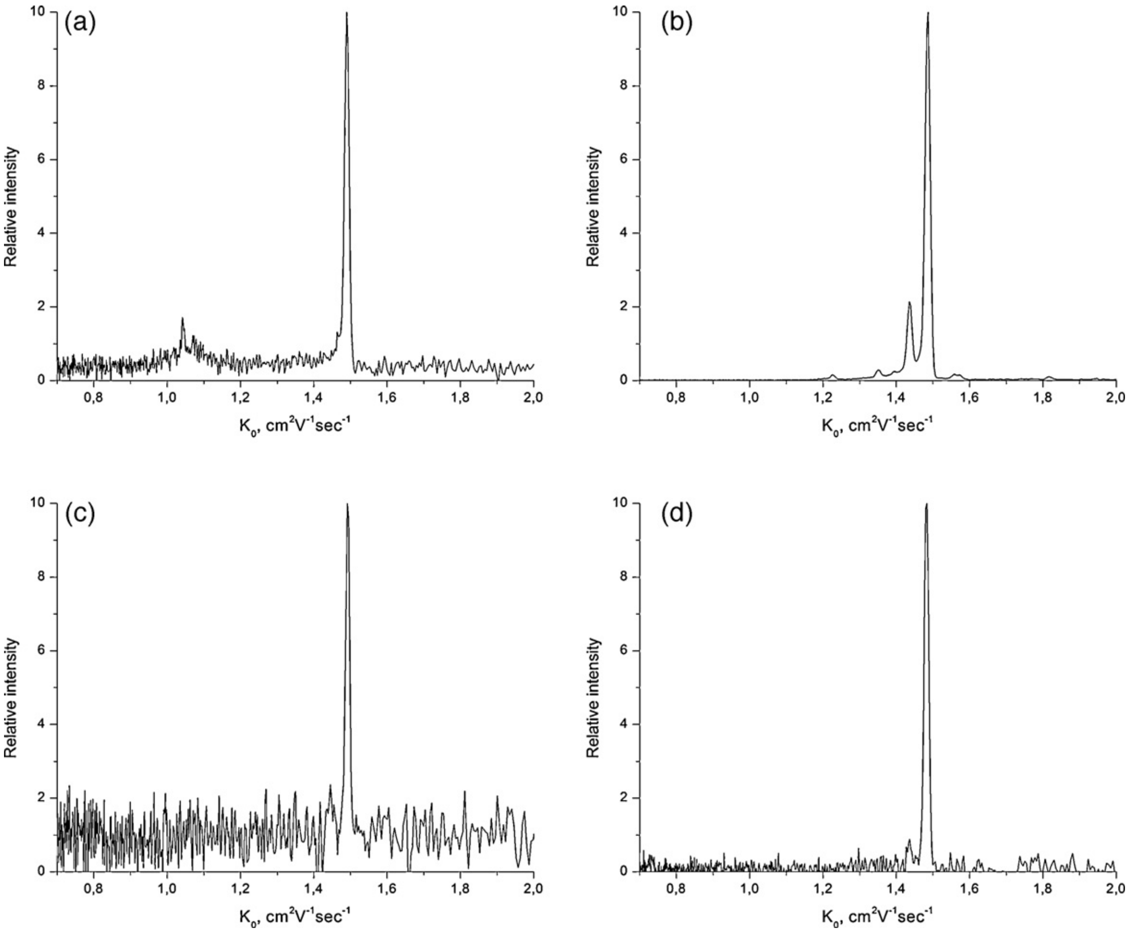

Fig. 4. Mobility distributions of 2,6-D*t*BP samples obtained using (a) ESI, (b) CD-APCI, (c) APPI and (d) R-APCI ion sources, at 1.5 l/min drift gas flow rate, 378 V/cm drift field, and 100 μs gate opening time.

culated values. Whereas for 100 and 200 μs gate opening times all the experimental resolving powers are below the calculated values.

This behaviour can be explained by the contribution of the initial shape of the bundle of ions injected to the drift region and the diffusion broadening of the bundle as it travels through the drift tube to the collector. For the shorter gate opening time signal shape is more dependent on diffusion (Eq. (4)), the model and experimental values are mainly in agreement. But for the longer gate opening times signal shape is expected to be more dependent on initial shape of the bundle of ions admitted to the drift region, because the first term t_g^2 inside the square root in Eq. (4) dominates over the second term $(16kT\ln 2/Vdez)(Ld^2/KVd)^2$. In operation, the repulsive field of the Bradbury–Nielsen ion gate causes depletion of ions in the vicinity of the entrance gate. Therefore, when the entrance gate is opened, the ion packet introduced into the drift region is slightly narrower than the ion gate opening time. The model does not take into account ion depletion at the vicinity of ion gates, and therefore slightly higher resolving powers than predicted from theory are often observed at larger gate opening times.

Negative ion mode operation was demonstrated by analysis of ortho-phthalic acid (100 μM in methanol) with electrospray ionization, resulting in two peaks (Fig. 3). An intense peak (the monomer) with a reduced mobility of 1.69 cm^2/Vs and a less intense peak (the dimer) with a reduced mobility 1.19 cm^2/Vs with corresponding resolving powers of 59 and 85, respectively were observed. The measured reduced mobility for the monomer peak is in relative good agreement with the reported value of 1.77 cm^2/Vs for $[M{-}H_2O]^-$ ion of ortho-phthalic acid [30].

3.2. Operation of other ionization techniques

2,6-D*t*BP was used as a standard compound to demonstrate the operation of the other ionization techniques (CD-APCI, APPI, R-APCI) and compare them to ESI in positive mode. Four measurements for each ionization mode were done in a single day but all the ionization modes were not used during the same day. The reduced mobility spectra for all four ionization modes are shown in Fig. 4 and the reduced mobility, signal-to-noise ratio, measured

Table 2
The reduced mobility, signal-to-noise ratio, resolving power and concentration of 2,6-D*t*BP measured with four different ionization methods. The experimental data is average values of the four measurements made.

	K_0 (cm^2/Vs)	S/N ratio	Measured resolving power	Calculated resolving power	Concentration
ESI	1.48	30	95	116	5 μM in MeOH
CD-APCI	1.47	470	92	117	800 ppb in nitrogen
R-APCI	1.47	20	100	116	800 ppb in nitrogen
APPI	1.48	8	101	116	800 ppb in nitrogen

and calculated resolving power and concentration are listed in Table 2. 2,6-D*t*BP yielded typically a single peak with high resolving power and the same reduced mobility with all ionization modes. The relative standard deviation for the 2,6-D*t*BP reduced mobility determinations made on a single day with different ionization modes was below 1%. The highest S/N ratio, 470, was obtained in CD-APCI mode, while the corresponding values for ESI, R-APCI and APPI were 30, 20 and 8, respectively. Note that for the APPI mode, it is expected that the use of a dopant could increase the sensitivity [31]. The higher sensitivity of CD-APCI compared R-APCI was expected due to the higher reactant ion density of CD-APCI [32].

4. Conclusions

A high resolution atmospheric pressure ionization IMS instrument with a multi-ion source platform was developed. The design of the front end of the drift tube chamber and the multi-ion source platform enabled fast and easy changing between four different atmospheric pressure ionization methods: electrospray ionization, radioactive chemical ionization, corona discharge chemical ionization, and photoionization, which can be operated in both positive and negative detection modes. This allows measurement of a very wide range of analytes, since ESI is well suitable for ionic compounds, APPI and CD-APCI are generally suitable for neutral compounds. Excellent reproducibility for reduced mobility values and a resolving power of about 100 were obtained with all ionization techniques for 2,6-D*t*BP at atmospheric pressure and room temperature.

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