Influence of cyclic ion mobility parameters on ion fragmentation and arrival time distribution profiles characteristic of isomers

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1 Introduction

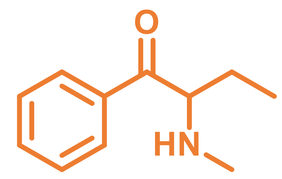
Ion mobility spectrometry–mass spectrometry (IMS-MS) enables separation of isomeric compounds based on differences in ion shape and size [1]. However, resolution can be insufficient for closely related species, such as some new psychoactive substances (NPS), which often exist as structural isomers. One of the possibilities to overcome this limitation can be to use arrival time distribution (ATD) profiles characteristic of isomers [2]. Repeatability of ATDs is crucial for isomer ratio determination. This study explores how tuning IMS parameters affects ATD profiles for selected NPS isomers.

2 Experimental

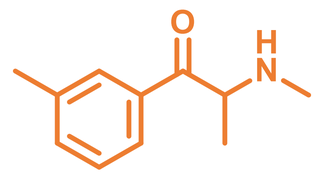
Experiments were performed on a SELECT SERIES Cyclic IMS QTOF (Waters Corp., Wilmslow, UK) equipped with electrospray (ESI) in a positive mode tuned for labile analytes according to Waters recommendations. Effects of injection time and separation time in the cyclic mobility cell on fragmentation were investigated by direct infusion of 4-methylbenzylpyridinium and 4-(trifluoromethyl)benzylamine. Survival yield was calculated from parent ion (I_p) and fragment ion (I_f) mobility peak areas:

$$SY = \frac{I_p}{I_p + I_f}$$

Isomeric new psychoactive substances (3-methylmethcathinone (3-MMC) and buphedrone) were used to evaluate the influence of the reinjection time and activation during the reinjection of ions to the mobility cell on ATD. Samples were introduced by flow injection analysis. Calibration curves were created applying multiple linear regression of ATD profiles [2] in OriginPro 2025 (OriginLab).



Buphedrone



3-methylmethcathinone (3-MMC)

- Injection time
- Separation time
- Reinjection time
- Activation energy

3 Results and Discussion

INJECTION TIME

Increasing the injection time from 5 ms to 15 ms had no effect on the fragmentation of 4-methylbenzylpyridinium ions (critical energy 2.27 eV [3]), whereas for 4-(trifluoromethyl)benzylammonium ions (1.89 eV [4]), a 30 % decrease in survival yield (SY) was observed when the injection time was changed from 5 ms to 10 ms.

SEPARATION TIME

The effect of separation time was evaluated by comparing 0.01 ms (ions did not pass through the cyclic cell) and 2 ms (one pass). The significant fragmentation in the cell was observed for 4-(trifluoromethyl)benzylammonium ions (SY decreased more than 50 %).

REINJECTION TIME & ACTIVATION ENERGY

The reinjection time had no significant effect on fragmentation by itself; however, it amplified the effect of activation energy. The Fig. 1 and 2 represents ATD profiles of buphedrone and 3-MMC standards under different activation energies. Highlighted areas show changes in ATD profiles due to the increasing fragmentation of a protomer. Comparing 0 V and 30 V, the mobilogram intensity decreased for 3-MMC and buphedrone by 30 % and 50 %, respectively. The similar effect was observed for 10 ms reinjection time. However, at 15 ms, any activation voltage (10, 20, 30 V) caused complete loss of signal.

As an example, changes in ATD profiles caused by higher activation voltage (0 V vs. 30 V) affected calibration curves (Fig. 3) by 20% drop of the slope. Slope values decreased for 5 ms reinjection while no trend was observed for 10 ms (Tab.1).

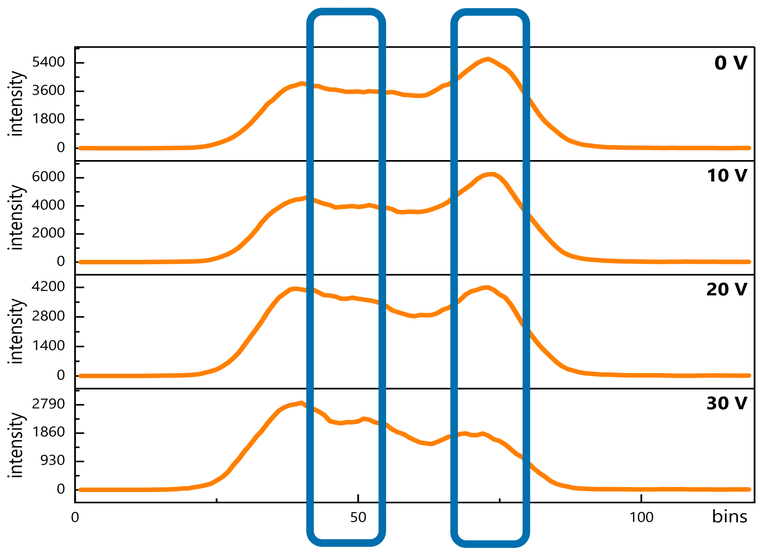


Fig. 1. Buphedrone mobilograms under constant reinjection time 5 ms and increasing activation energies.

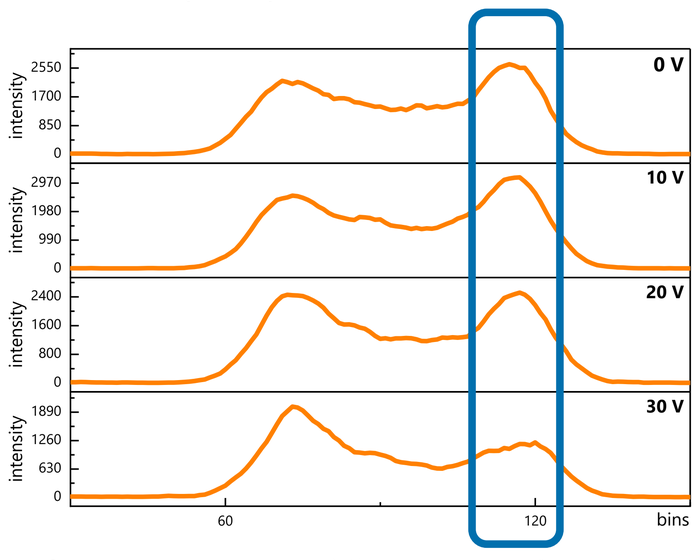


Fig. 2. 3-MMC mobilograms under constant reinjection time 5 ms and increasing activation energies.

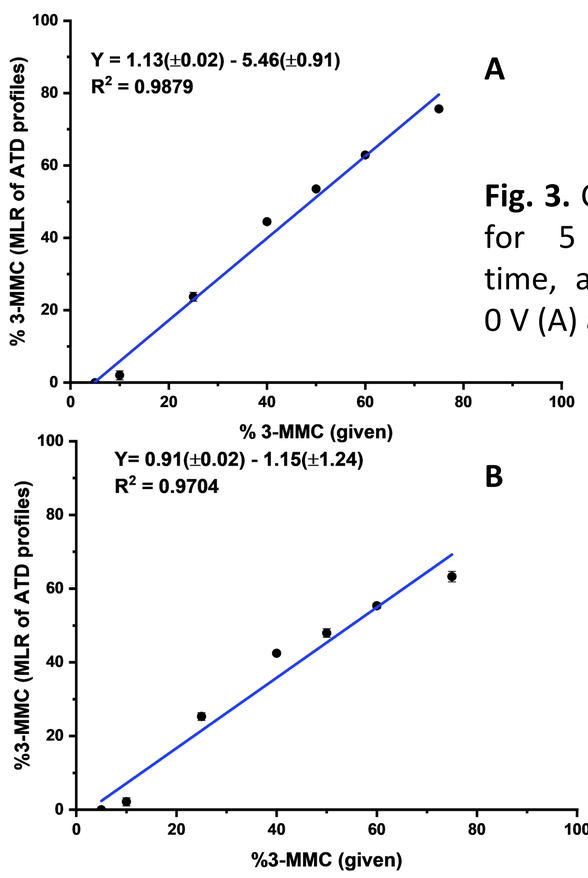


Fig. 3. Calibration curves for 5 ms reinjection time, activation voltage 0 V (A) and 30 V (B).

4 Conclusion

- Increasing the **injection time** and **separation time** can induce fragmentation in the mobility cell, especially for analytes with lower critical energies.
- The **reinjection time** did not contribute to a greater fragmentation by itself, however amplified the effect of activation energies.
- High **activation energy** has a significant effect on fragmentation and can even lead to a complete loss of signal.
- The **reinjection time** and **activation energy** influence calibration curves, e.g. cause changes in slopes.
- **Proper adjustment of instrumental parameters is required to control fragmentation and preserve ATD profiles unchanged, which is more critical for labile ions.**

Activation energy (V)	Reinjection time (ms)	
	5	10
0	y=1.13(±0.02)x - 5.46(±0.91)	y=0.88(±0.03)x-1.80(±1.44)
10	y=0.9878(±0.02)x-2.61(±1.30)	y=0.84(±0.03)x-1.53(±1.74)
20	y=0.936(±0.02)x-2.01(±1.16)	y=0.94(±0.019)x-4.41(±0.94)
30	y=0.91(±0.02)x-1.15(±1.24)	y=0.96(±0.02)x-3.38(±0.97)

Tab. 1. Calibration curves for different reinjection times and activation voltages.

References: [1] F. Lanucara, et al. Nat. Chem., 6 (2014) 281-294. [2] M. Nytka, et al. J. Am. Soc. Mass. Spectrom., 35 (2024) 1733−1742. [3] C. Ieritano, et al. J. Am. Soc. Mass. Spectrom., 31 (2020) 582-593. [4] D. Asakawa, K. Saikusa, J. Am. Soc. Mass. Spectrom., 33 (2022) 1548-1554.

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