

Influence of cluster/de-cluster reactions on ion separation in differential mobility spectrometry (DMS) in dependence of the analyte structure

Florian Stappert¹; Christine Polaczek¹; Walter Wissdorf¹; Hendrik Kersten¹; Thorsten Benter¹;
Bradley B. Schneider²; Tom Covey²



1: Physical & Theoretical Chemistry
Wuppertal, Germany
(Institute for Pure and Applied Mass Spectrometry)
2: SCIEX
Concord, Ontario; Canada

Introduction

Background:

The ion separation in differential mobility spectrometry (DMS) is based on the different mobility of ions under high and low field conditions. Mainly as result of cluster/de-cluster reactions and hard-sphere interactions the mobility depends on the corrected electric field strength E/N . The resulting dependence is described by the "α-function". By adding chemical modifiers to the transport gas the cluster effect can be enhanced, depending strongly on chemical properties of the modifier and the analyte.[1] There is some evidence in the literature for analyte/modifier combinations that allow the prediction of the degree of dispersion in DMS by small structural variations.[2][3] In addition to the steric structure of the substances used, other material properties such as basicity are also important.[3]

Previous results:

The cluster/de-cluster reactions are one major driver of ion separation using DMS, which was shown by suitable simulations of cluster dynamics.[4] This effect depends on the used modifier and the DMS temperature. To check this thesis the dispersions of Substance P signals were examined under varying conditions. The results showed a decreasing cluster effect with increasing temperature, as well as an influence of the modifier structure, which in turn leads to a significant influence of the analyte structure. [5]

Present results:

Results of DMS measurements of various amines and di-amines are presented using typical modifiers to investigate the analyte structure dependence. The same analytes are investigated in supercharging experiments and the results are compared to get a deeper insight into the underlying molecular level processes.

Methods

Instruments:

MS System: 6500 Triple Quad™ (SCIEX)
DMS System: SelexION® DMS (SCIEX)
Ion Source: Turbo V™ (ESI-mode; SCIEX)
Data Processing: Analyst® 1.6.2 (SCIEX)

Chemicals:

Gases: Nitrogen (boil-off from LN₂)
Modifiers: Acetonitrile (ACN; HPLC grade), Methanol (MeOH; HPLC grade), 2-propanol (iso-prop; HPLC grade)
Analytes: Various amines and polyamines
Analyte solutions: 0,1 mmol/L analyte in ACN/H₂O with 0.05 % of formic acid

Experimental parameters:

- Constant DMS-temperature of 150 °C ("Low"-setting)
- Liquid flow of 10 μl/min
- Injection with a 2.5-ml-syringe by use of the built in syringe pump
- Modifier concentration of 3 % ("High"-setting)
- Ion-transfer optimized for each analyte for a maximum signal

Aliphatic and aromatic Amines

Linear aliphatic amines

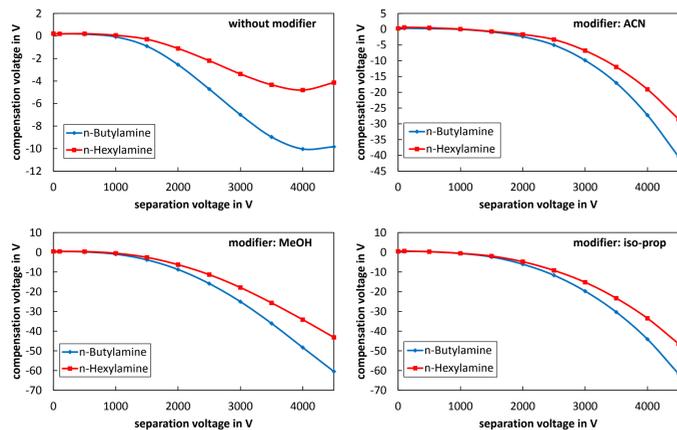


Figure 1: Dispersion plots of protonated n-butylamine and n-hexylamine depending on the modifier present in the DMS transport gas (Nitrogen; N₂): without modifier (100 % N₂), with ACN (3 %), with MeOH (3 %) and with iso-propanol (3 %)

Without modifier present, a positive compensation voltage (CV) is expected. The declining plots (Type B) are normally explained by polarization effects with the nitrogen transport gas. Independently of that, the hard-sphere collision interactions are very weak.

Note the always larger shifts observed for the smaller analytes. This suggests larger average cluster sizes caused by smaller steric hindrances or simply a larger relative change of the impact cross section.

Aromatic amines and di-amines

Similarly to the above results, in the absence of any modifier, hard-sphere collisions are not mainly responsible for the curve shapes. Note the inverse behavior of the two phenylenediamines as compared to the results with modifier present.

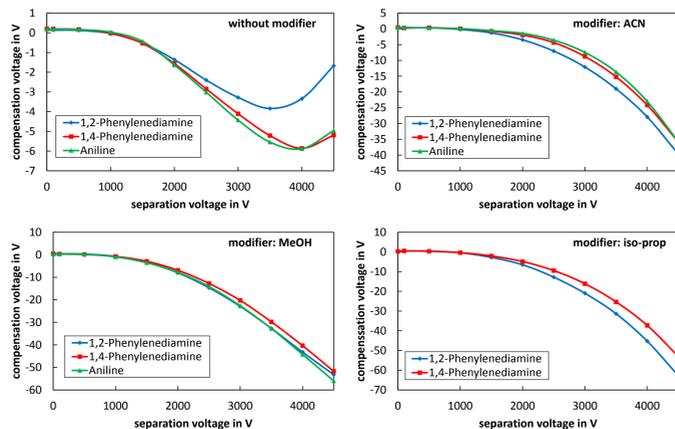


Figure 2: Dispersion plots of protonated 1,2-phenylenediamine, 1,4-phenylenediamine and aniline depending on the modifier present in the DMS transport gas (Nitrogen; N₂): without modifier (100 % N₂), with ACN (3 %), with MeOH (3 %) and with iso-propanol (3 %)

Without additional modifier or with ACN present in the transport gas, aniline behaves as 1,4-phenylenediamine, which indicates a comparable steric surrounding at the protonated site.

Aniline is quantitatively deprotonated with iso-propanol, which is in accord with supercharging experiments, see below.

Comparison with supercharging experiments

Table 1: Main differences of reaction conditions in supercharging and DMS experiments

DMS	Supercharging
ESI	nESI
High temperature	Low temperature
Dynamic processes driven by high/low field conditions	Swift formation of equilibrium cluster distribution at AP

Main issues:

- Are the chemical mechanisms comparable or even identical?
- Note: Much higher collision energies prevailing in DMS

Matching results:

- charge depletion with alcohols
- in general, similar trends in signal distribution
- analyte-dependent ACN cluster distribution
- no double protonation of phenylenediamines observed

• detailed results on poster WP 307: C. Polaczek et al.; *Ion-solvent interactions in nano-ESI-MS: Characterization of Charge Depletion and Charge Conservation (Supercharging) Processes*

Linear Di-amines

Singly protonated [M+H]⁺

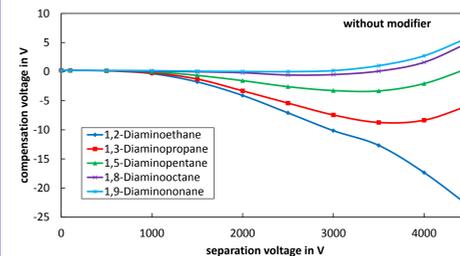


Figure 3: Dispersion plots of single protonated linear di-amines with growing carbon chain without modifier in the DMS transport gas

In absence of a modifier, the low molecular weight di-amines behave like amines and show a CV decline in the plots, while a growing carbon chain leads to a Type C behavior. This effect is explained by a increasing hard-sphere interaction.

Note the qualitatively identical CV behavior for all di-amines with the exception of 1,2-diaminoethane, which shows a turn to smaller CVs at a SV of 3500 V, while all other curves turn upwards to higher CVs at this SV. This very interesting finding is currently under investigation.

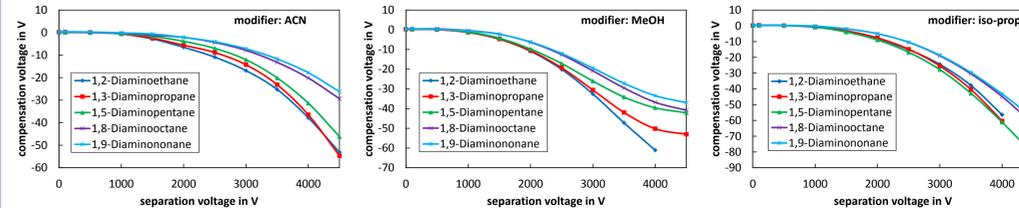


Figure 4: Dispersion plots of singly protonated linear di-amines with growing carbon chain length in dependence of the modifier present in the DMS transport gas: ACN, left (3 %), MeOH, center (3 %), and iso-propanol, right (3 %)

Adding ACN or MeOH as modifier to the transport gas causes an increase of the cluster effect, while the order of the extent of dispersion remains unchanged.

In addition to the possible steric hindrance the increase of the

collision cross section seems to be the most plausible explanation. Analyte overlapping is also evident here as well the higher absolute dispersion with alcohols based on the great basicity of the OH-group. By using large modifiers like

iso-propanol the shift of the small analytes differs from the previous measurements. The collision cross sections of these clusters seem to be especially influenced by the modifier instead of the analyte.

Doubly protonated [M+2H]²⁺

With growing carbon chain length, the fraction of doubly charged ions [M+2H]²⁺ increases, which are favorably stabilized by clustering with e.g. ACN (see supercharging) used as solvent. However, in this case ACN is present only below 2 · 10⁻⁷ %.

When using ACN as modifier all di-amines shows a clear cluster effect. The CV trends are similar to the trends observed for singly protonated species. Note that the cluster effect increases with increasing length of the carbon chain.

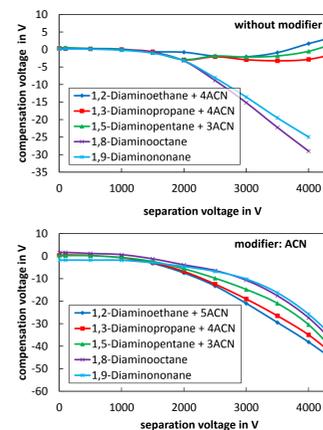


Figure 5: Dispersion plots of doubly protonated linear di-amines with growing carbon chain without and with modifier (ACN, 3%) present in the DMS transport gas. Note: For the short chain di-amines mass signals of the smallest detectable ACN-clusters were recorded, because the bare [M+2H]²⁺ ions were below the low mass cut-off of the set-up

Effect of the presence of a secondary amine group

Without modifier present the effect of an additional secondary amine group is barely noticeable.

In the presence of modifiers the qualitative trends are comparable to those observed with the di-amines. The absolute values, however, show pronounced differences as the result of distinctively different clustering properties, attributed to a largely different gas phase basicity as well as structural properties.

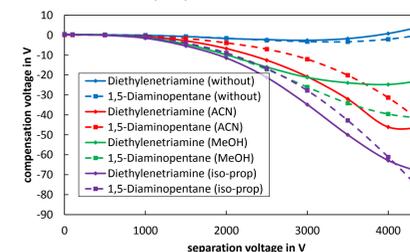


Figure 6: Dispersion plots of diethylenetriamine and 1,5-Diaminopentane in dependence of the used modifier

Conclusions

- Both the modifier and analyte structural properties are of importance for the extent of the cluster effect on CV values. Self clustering (i.e. formation of multimers) in addition to clustering with modifiers needs to be taken into account.
- The cluster effect on CV values becomes increasingly important with decreasing molecular size of the analyte, as the relative change in the collision cross section due to clustering/de-clustering increases.
- Larger molecular weight analytes tend to exhibit hard-sphere collision behavior.
- The size ratio between analyte and modifier determines, which of the two species has the larger impact on the extent of dispersion.
- For the investigated analytes the indirect consequences of any structural changes (e.g. basicity, relative collision cross section, ...) seem to be more important than changing steric properties alone.
- The general observations and results of the supercharging experiments are in very good agreement with the DMS experiments despite the largely different experimental set-ups used.

Outlook

- More experiments on structural dependencies are underway. For example chiral analytes may be dispersed in a DMS cell using chiral modifiers (enantiomeric separation).
- Further comparisons between DMS and supercharging experiments are currently carried out to arrive at a deeper understanding of the DMS gas phase cluster chemistry.

Literature

- Schneider, B. B.; Nazarov, E. G.; Lounry, F.; Vouros, P.; Covey, T. R.; Differential mobility spectrometry/ mass spectrometry history, theory, design optimization, simulations, and applications; Mass Spectrometry Reviews; 35; 687-737 (2015)
- Campbell, J. L.; Zhu, M.; Hopkins, W. S.; Ion-Molecule Clustering in Differential Mobility Spectrometry: Lessons Learned from Tetraalkylammonium Cations and their Isomers; J. Am. Mass Spectrom.; 25; 1583-1591 (2014)
- Auerbach, D.; Aspenleiter, J.; Volmer, D.; Description of gas-phase ion/neutral interactions in differential ion mobility spectrometry: CV prediction using calibration runs; J. Am. Mass Spectrom.; 25; 1610-1621 (2014)
- Wissdorf, W.; Schneider, B. B.; Covey, T.; Hager, J.; Benter, T.; Is differential mobility chemically driven? Evidence and simulations for chemical effects as a primary separation factor in DMS; 64th ASMS Conference on Mass Spectrometry and Allied Topics; San Antonio, Texas, USA; (2016).
- Stappert, F.; Schneider, B. B.; Thinius, M.; Wissdorf, W.; Kersten, H.; Covey, T.; Hager, J.; Benter, T.; Effects of chemical dynamics and clustering reactions of chemical modifiers with analyte ions in differential mobility spectrometry (DMS); 65th ASMS Conference on Mass Spectrometry and Allied Topics; Indianapolis, Indiana, USA; (2017).

Acknowledgement

Financial and technical support by SCIEX (Concord, Canada) is gratefully acknowledged.