CONTRIBUTION OF ION MOBILITY FOR STRUCTURAL ANALYSIS AND ANALYTICAL CHEMISTRY: THE USE OF PROBE LIGANDS AND SELECTIVE IMS SHIFT REAGENTS

C. Kune, J. Far, C. Delvaux, G. Eppe, E. De Pauw

Plan:

1/ Concept of specific coordination complex formation with probe ligands

2/ Specificity depending on the presence of chemical function

- Proline/Valine model
- Contaminant of Selenomethionine – intramolecular oxidation

3/ Specificity depending on the steric hindrance

- DAN isomers – Crown ether model
- Isomers ratio determination of two isobaric selenium compounds

4/ Specificity depending on the polarity – differential induce folding

- DAN isomers – Cyclodextrin model

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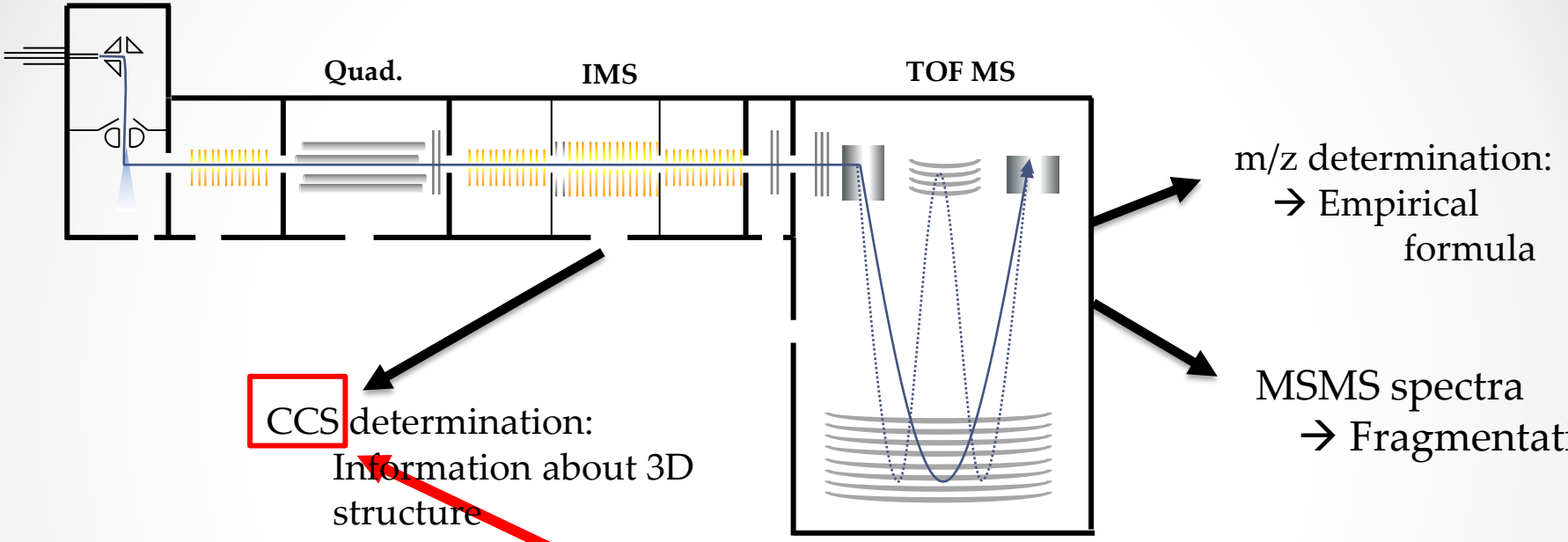
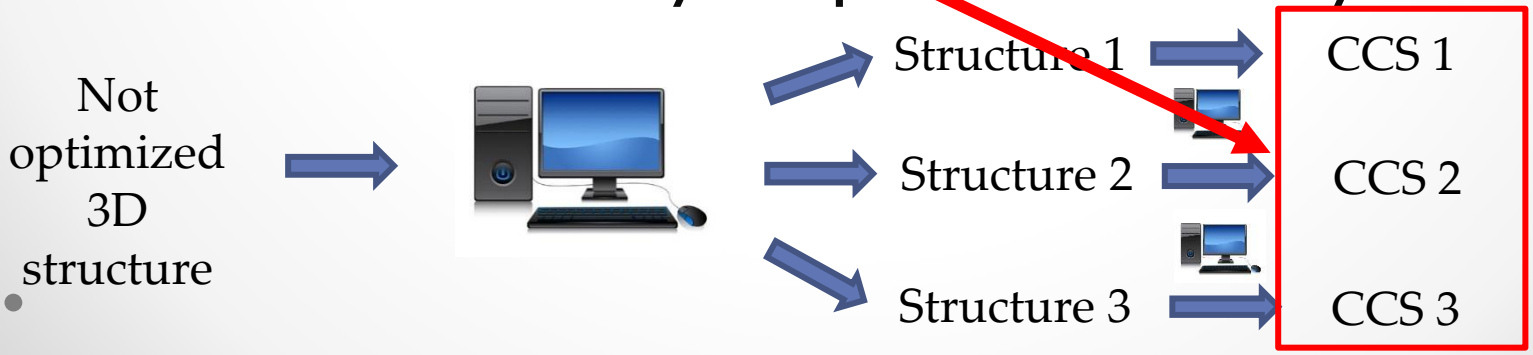
Structural elucidation

- **Structural elucidation by ion mobility mass spectrometry (IMMS):**



Comparison → Structure determination

- **Structural elucidation by computational chemistry**



Structural elucidation with probe ligands

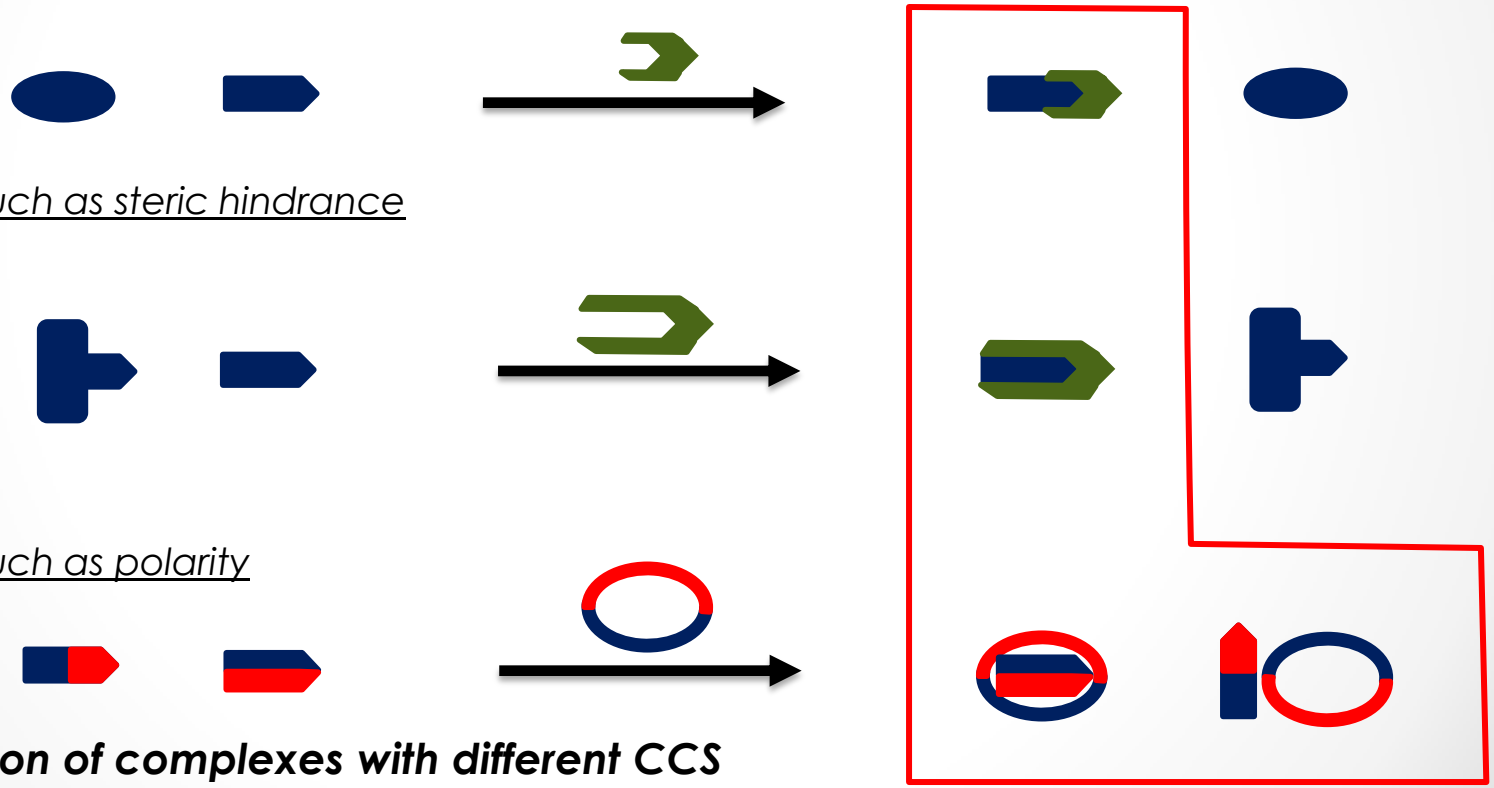
- **Probe ligands :** *Molecules which interact with target ion to form specific complexes depending on their physicochemical properties*

- ***Confirmation of physicochemical properties:***

  Such as the presence of chemical moeities

  Such as steric hindrance

  Such as polarity



- ***Formation of complexes with different CCS***

  → Application as Selective Shift Reagent

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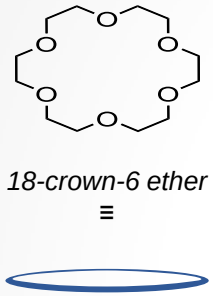
Specific coordination complex depending on the chemical functions: Proline Valine model

Ligand used:



18-crown-6 ether

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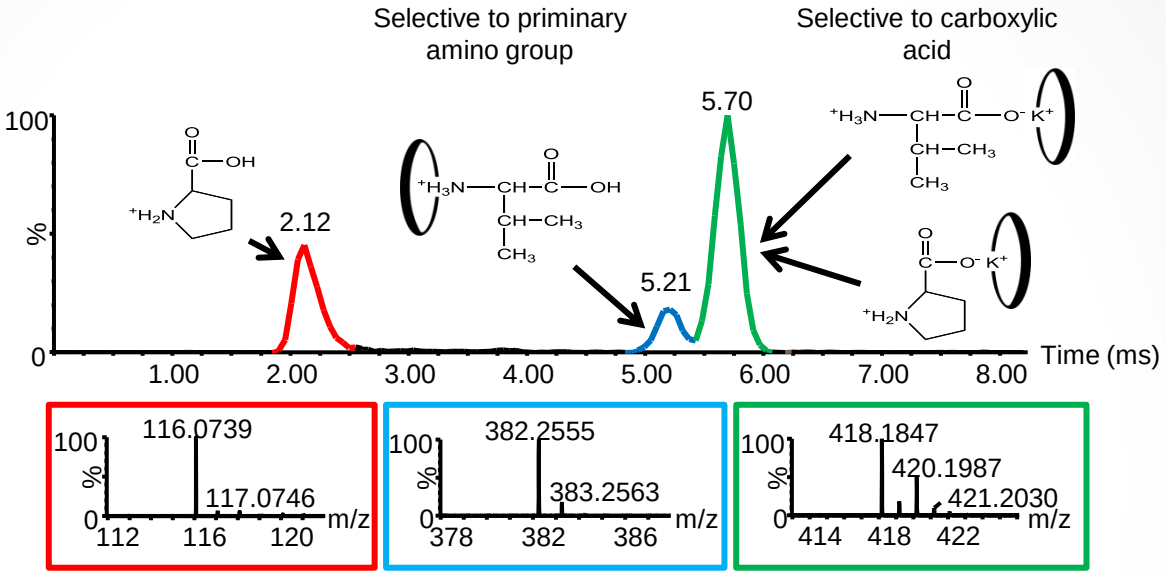
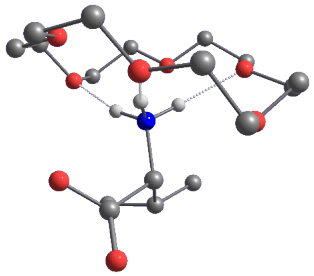
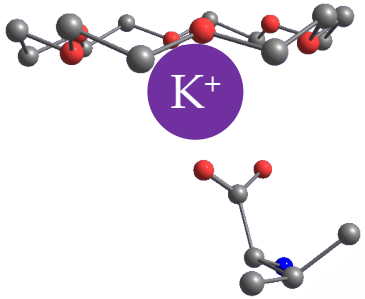


Controlled ligand Specificity:

Crown ether

Selective to primary amino group





Crown ether + K^+

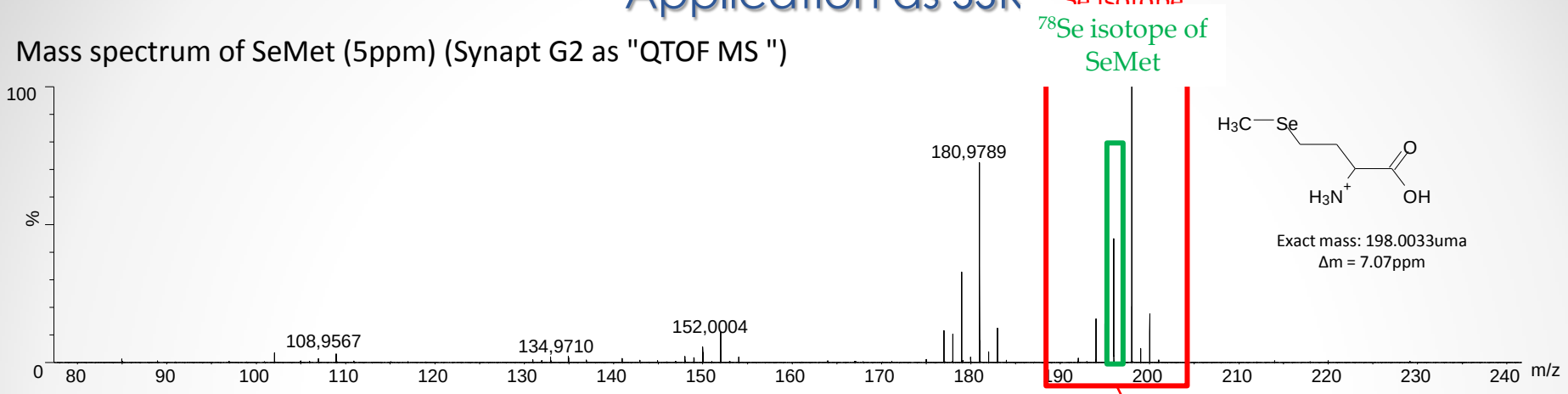
Selective to carboxylate group

Important IMS shift provided by crown ether complexation

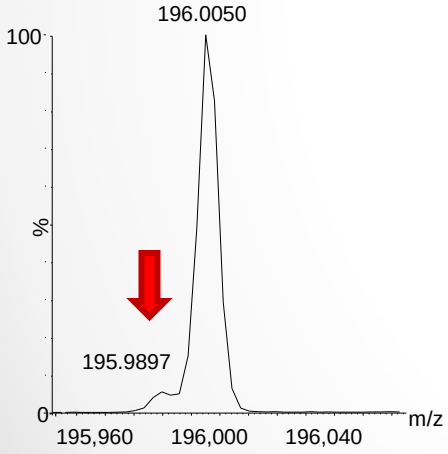
➔ Selective shift Reagent (SSR)

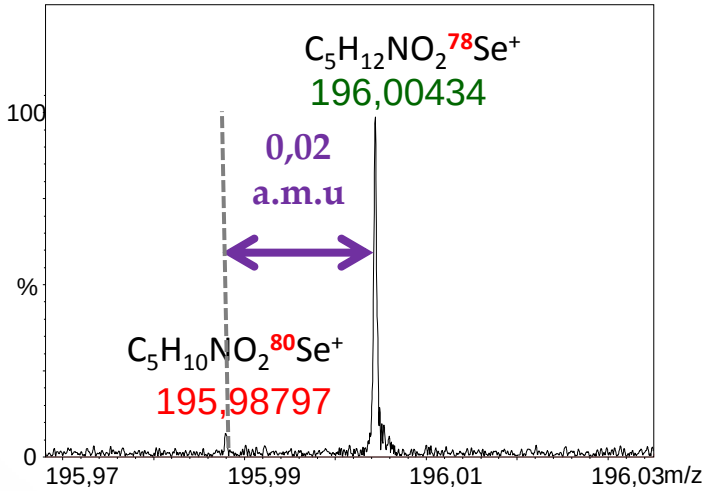
Specific coordination complex depending on the chemical functions: Application as SSR

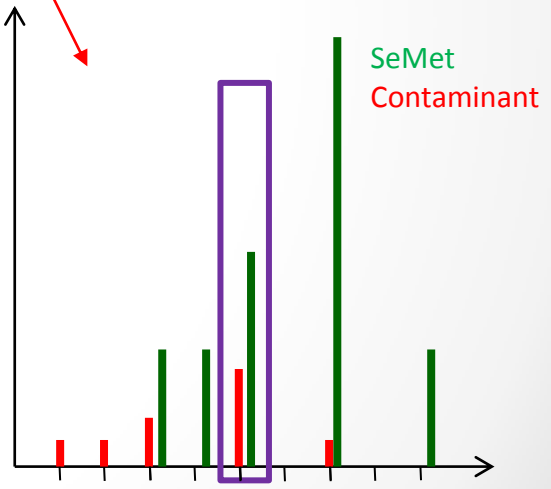
Mass spectrum of SeMet (5ppm) (Synapt G2 as "QTOF MS ")



Detection of isobaric compounds …confirmed by high resolution mass spectrometry …with Se isotopic pattern







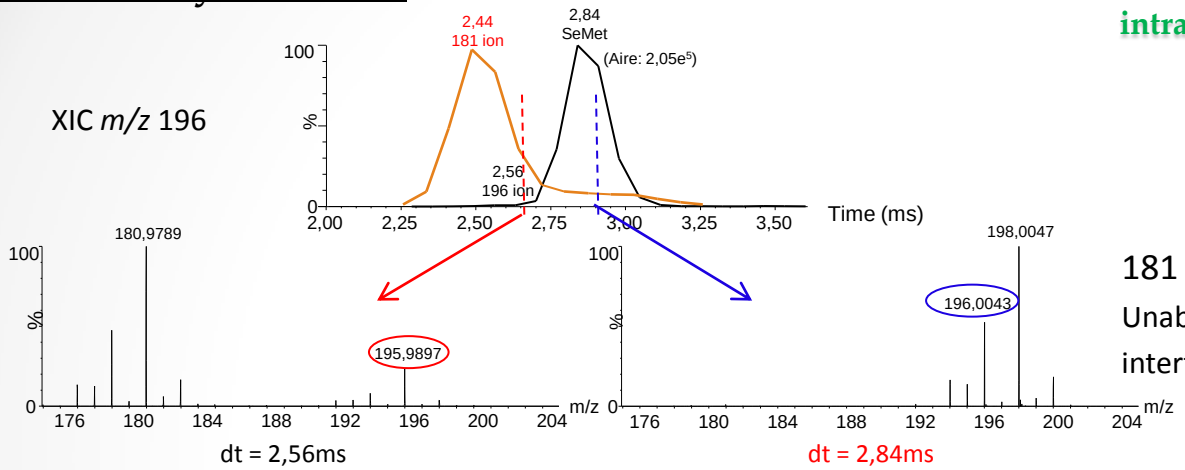
Exact mass → univoque empiric formula for m/z = 196 ion

Higher Double Bound Equivalent (DBE) value → **Double bound or ring formation ?**

- Overlapping on the Se isotopic pattern → Orthogonal separation required

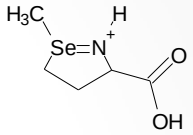
Specific coordination complex depending on the chemical functions: Application as SSR for Selenomethionine

Separation by IMS-MS



Separation by ion mobility spectrometry

intramolecular oxidation hypothesis

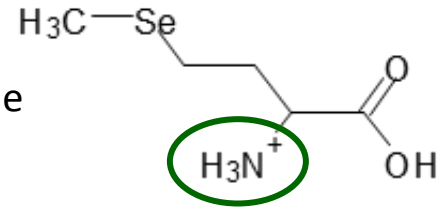


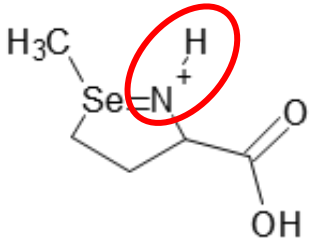
181 ion fragment (ammonium loss)

Unable to obtain **MS² spectra of 196** ion without interference from SeMet or in-source fragment

Use the difference in chemical group → Probe ligands

Selenomethionine



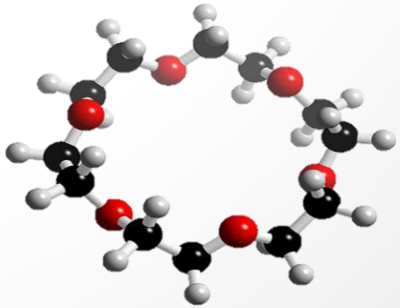


m/z: 196 ion

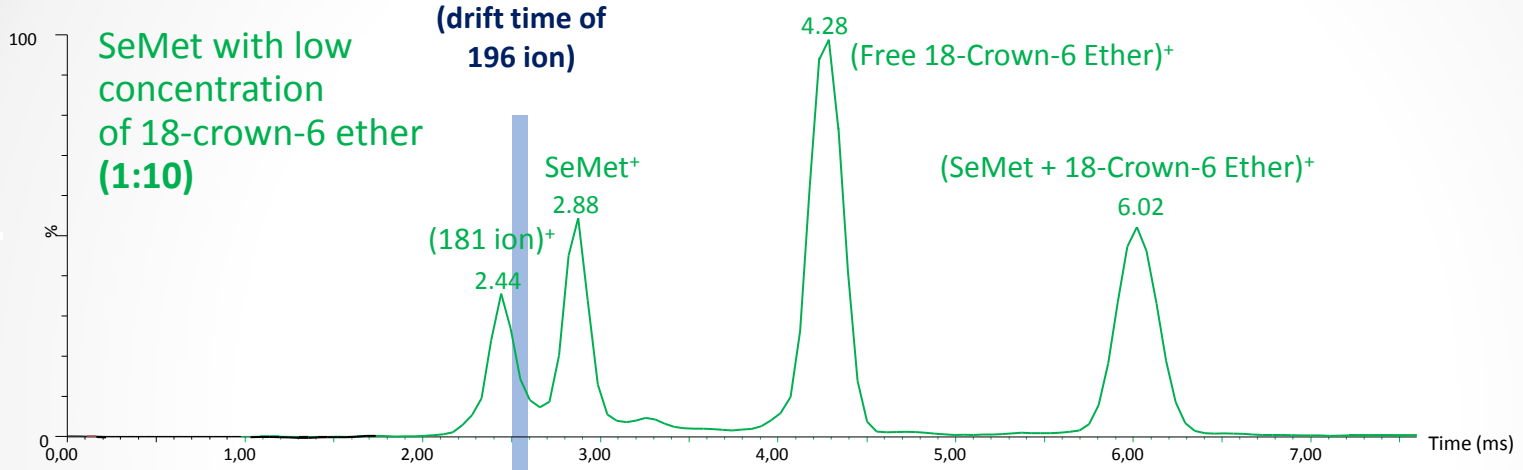
18-Crown-6 Ether ➔ Selective to primary amino group

- Support the expected structure of 196 ion
- Remove the interferences from SeMet

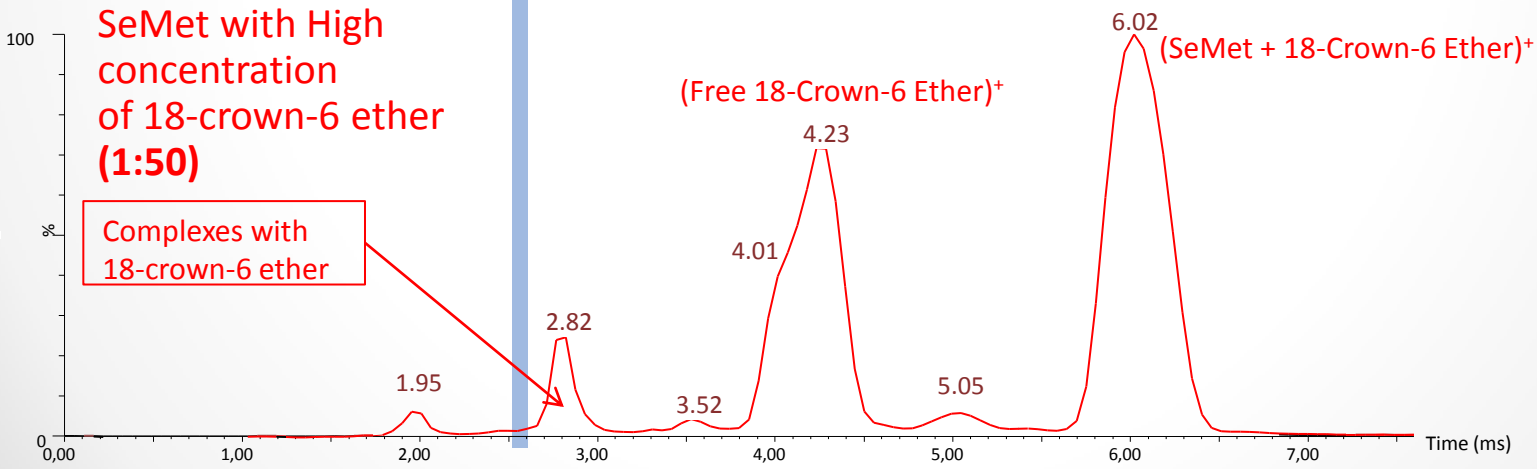
➔ **Free interferences MS² spectra of 196 ion**



Specific coordination complex depending on the chemical functions: Application as SSR for Selenomethionine



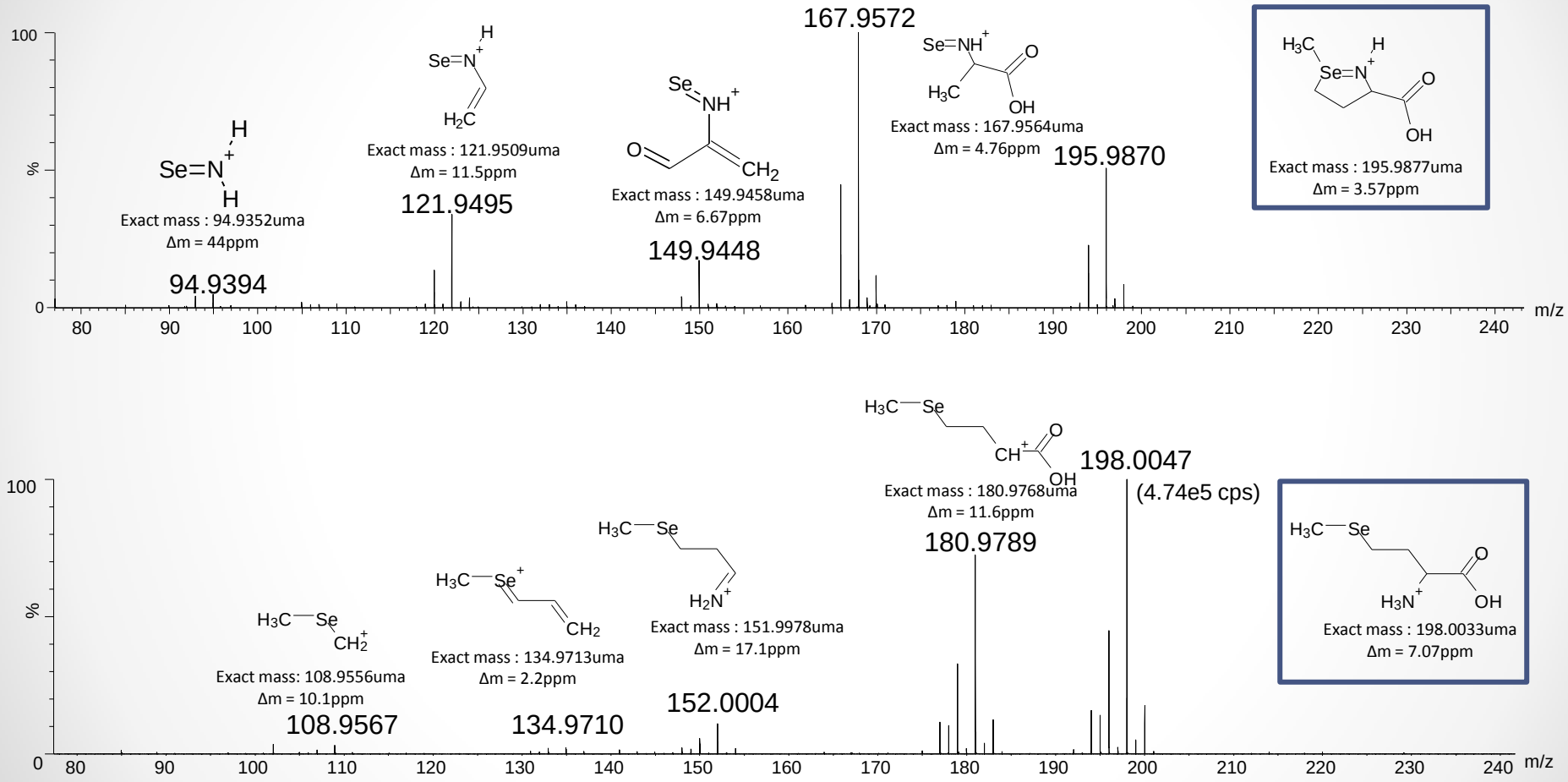
2,55ms: Spectra of 196 ions **and** Fragments of SeMet



2,55ms: Spectra of 196 ions **without interferences**

➔ **Interferences free MS^2 spectra of 196 ion**

Specific coordination complex depending on the chemical functions: Application as SSR for Selenomethionine



- Fragments of 196 ions:
  - Confirme the structure of 196 ion → **Formation of 5-membered ring compounds**
  - Differ from those of SeMet

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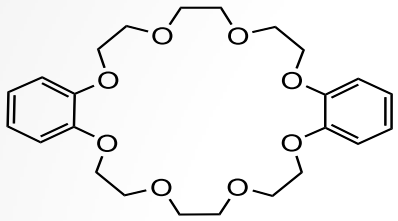
Specific coordination complex depending on the steric hindrance: Diaminonaphtalen isomers / Crown Ethers model

SSR used:



Dibenzo 24-crown-8 ether

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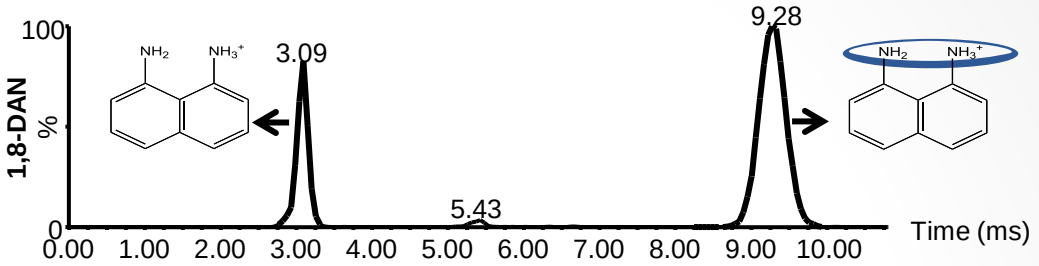
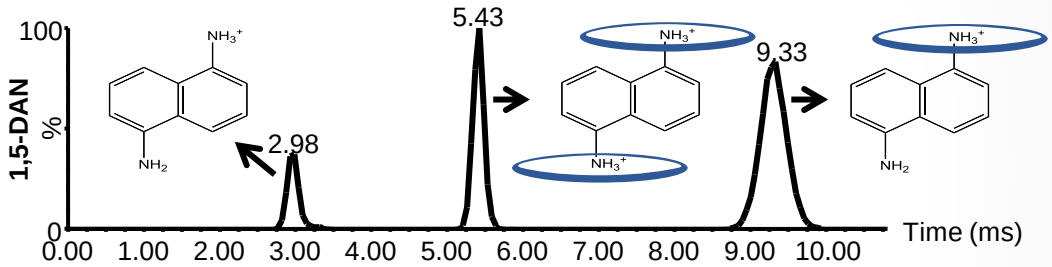
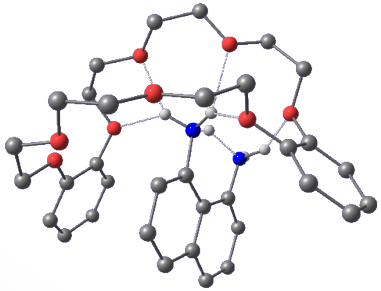
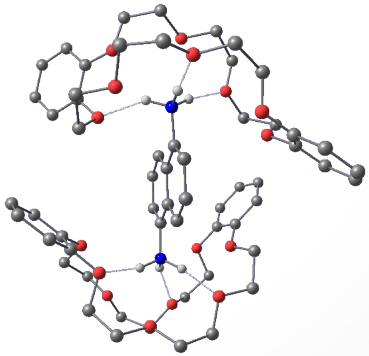




Controlled Stoechiometry:

Only one primary amino group available





2 priminary amino groups available

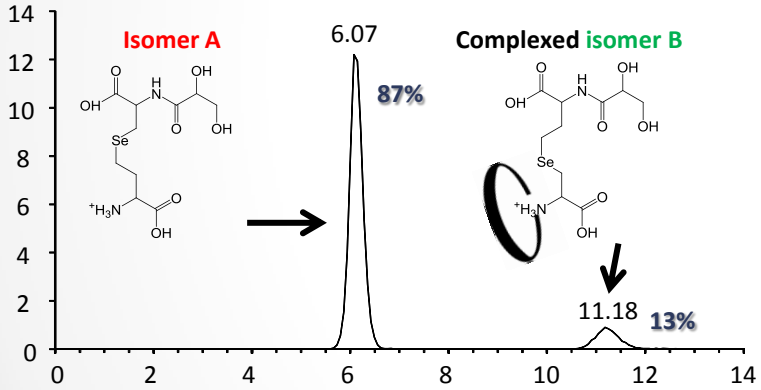
Application as Selective shift Reagent (SSR)

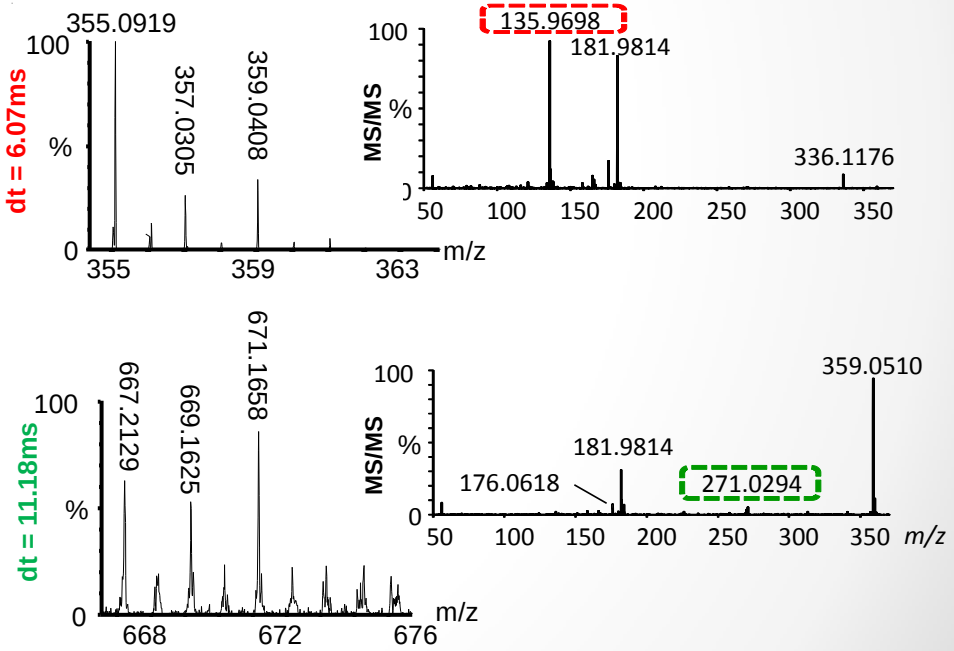
Specific coordination complex:

Travelling wave ion mobility did not successfully separate the native isomers of 2,3-DHP-selenocystathionine

The use of a nitrobenzo 15-crown-5 ether as SSR allowed to perform the separation and quantification of the isomer ratio (**87% - 13%**).

Far and coworkers, Anal. Chem (2014) Vol.86, Issue 22, : 11246-11254





Good agreement with theoretical values obtained by computational chemistry and isomer ratio determined from raw data by Dernovics and coworkers

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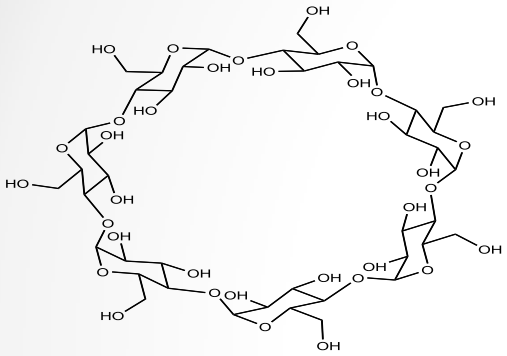
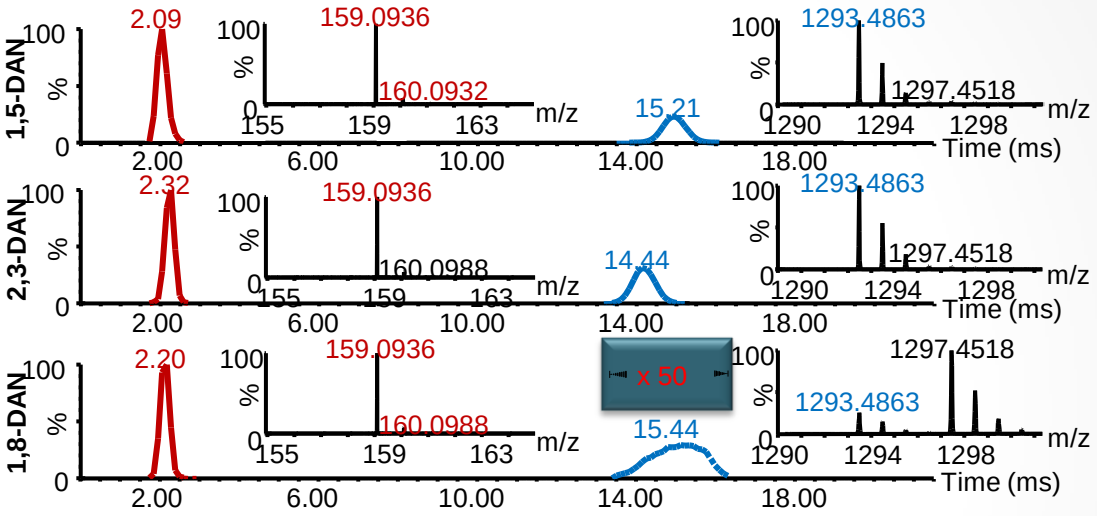
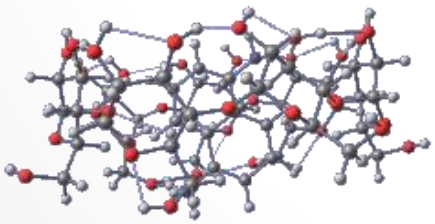
Specific coordination complex depending on the polarity: DAN-Cyclodextrin model

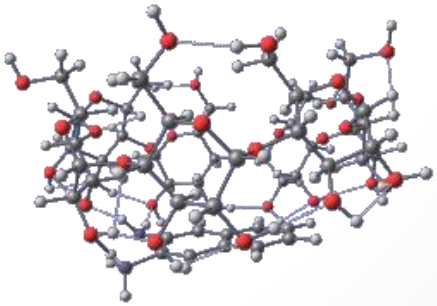




Controlled folding:

1,5-DAN:
Inclusion





2,3-DAN:
Exclusion

Application as Selective Shift Reagent (SSR)

Conclusion and perspectives

- Confirmation of hypothetical structure
  - Probe physicochemical properties
    - As chemical functions, steric hindrance, polarity, pi stacking

- Use as Selective Shift Reagent
  - Allow a control of the arrival time distribution of ion
    - Separation of isomers
    - Obtention of interference free MS^2 spectra

- Perspectives:
  - Use ligands to probe the three dimensional structural of larger (bio)molecules
    - As peptide, protein, DNA

Aknowledgement:

- Laboratory of Mass Spectrometry

  - Docteur Johann Far
  - Cédric Delvaux
  - Professeur Gauthier Eppe
  - Professeur Edwin De Pauw

- Laboratory of Theoritical Physical Chemistry
  - Professeur Françoise Remacle

Thanks for your attention