

Mass Spectrometry as a Tool in Supramolecular Chemistry

Christoph A. Schalley

Institut für Chemie und Biochemie der Freien Universität Berlin, Takustr. 3, D-14195 Berlin, email: schalley@chemie.fu-berlin.de

I. The Promise of Mass Spectrometry for Supramolecular Chemistry

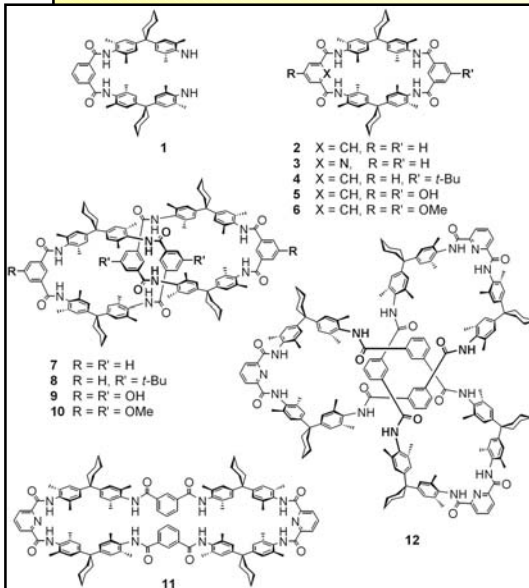
Mass spectrometry analyzes isolated molecules and complexes in the high vacuum of a mass spectrometer under environment-free conditions. Soft ionization methods (ESI, MALDI) permit to intactly ionize non-covalent species.

Beyond analytical characterization (exact mass, charge state, isotope pattern, elemental composition, stoichiometry), mass spectrometry provides insight into

- the secondary structures of non-covalent complexes including chiral recognition and the identification of zwitterionic species
- the reactivity of non-covalent complexes in solution covering the dynamic processes occurring in supramolecules (e.g. ligand exchange reactions)
- the reactivity in the gas phase excluding dynamic processes thus providing a completely different view on the reactivity of weakly bound species
- thermodynamic and kinetic data which in comparison to solution-phase data allows the chemist to extract information on the effects of the environment

Reviews: C. A. Schalley, *Mass Spectrom. Rev.* 2001, 20, 253-309; B. Baytekin, H. T. Baytekin, C. A. Schalley, *Org. Biomol. Chem.* 2006, 2828-2841.

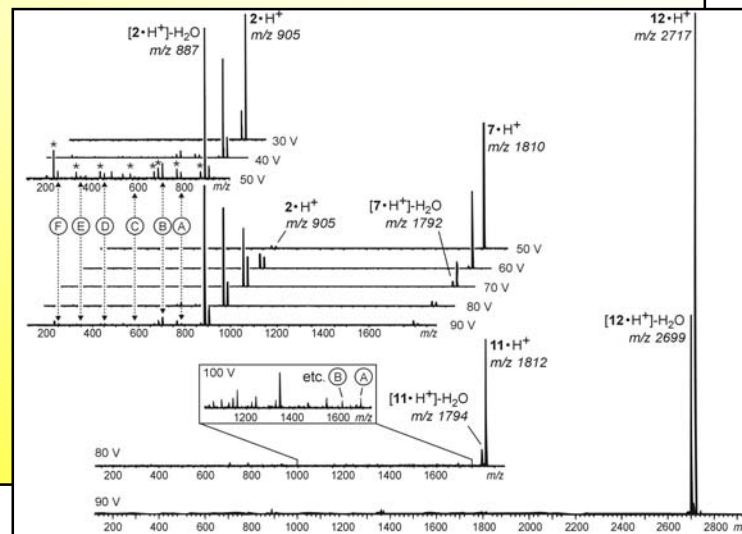
II. Mechanical Bonds: Distinguishing Molecular Topologies



Amide catenanes can be distinguished from simple octalactam macrocycles by collision-induced dissociation through their unique fragmentation patterns

The energy demand for backbone fragmentation of catenanes is lower than that of the octalactam macrocycle, since only one covalent bond needs to be broken

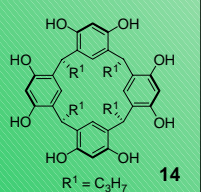
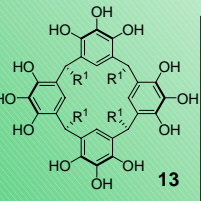
Similar arguments hold for rotaxanes and catenanes in the negative mode and other classes of catenanes



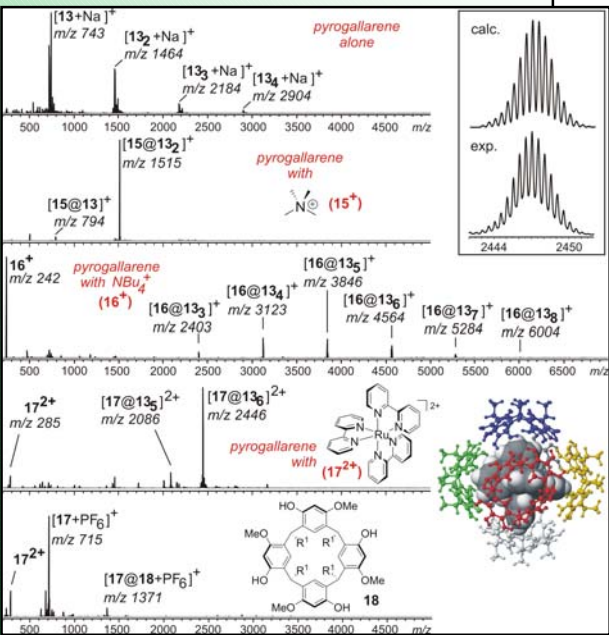
C.A. Schalley, J. Hoemschemeyer, X.-y. Li, G. Silva, P. Weis, *Int. J. Mass Spectrom.* 2003, 228, 373; C.A. Schalley, P. Ghosh, M. Engeser, *Int. J. Mass Spectrom.* 2004, 232-233, 249; M. Amman, A. Rang, C. A. Schalley, P. Bäuerle, *Eur. J. Org. Chem.* 2006, 1940; M. Hutin, C. A. Schalley, G. Bernardinelli, J. R. Nitschke, *Chem. Eur. J.* 2006, 12, 4069.

III. Hydrogen Bonding: Hexameric Pyrogallarene Capsules

Mass spectra of pyrogallarenes and resorcinarenes show the unspecific formation of oligomeric clusters. Only with the appropriate templating guest, a capsule is formed and survives its transfer into the gas phase. Size, shape, and symmetry of the guest are important factors for capsule formation.



Control experiments with tetramethylresorcinarene do not result in capsule formation. Hydrogen bonding involves thus all pyrogallarene or resorcinarene OH groups.

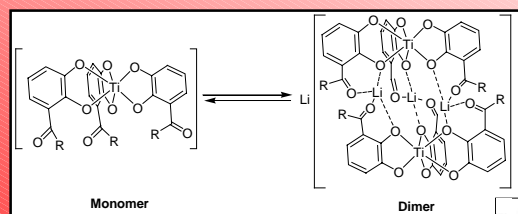


N. K. Beyeh, M. Kogej, A. Ahman, K. Rissanen, C.A. Schalley, *Angew. Chem.* 2006, 118, 5339; *Angew. Chem. Int. Ed.* 2006, 45, 5214

IV. Metal Coordination: Ligand Exchange in Dimeric Helicates

Ligand exchanges on non-covalent helicates do not occur on the lithium-bridged dimer, but on the monomer after dissociation of the dimer

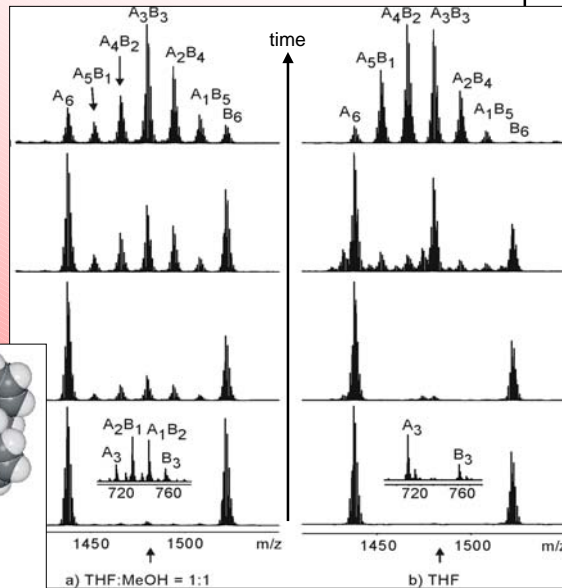
Depending on the solvent, dimer dissociation and monomer exchange have different relative rates and mass spectrometry provides semiquantitative information on these mechanistic features.



Exchange of single ligands on the dimer without dissociation into monomers would result in a U-shaped distribution of signals at intermediate reaction times and finally evolves into a statistical distribution. This is not observed.

Protic solvents speed up the ligand exchange on monomers leading to a statistical distribution of heterodimers growing between the homodimers.

In THF, monomer exchange is faster than the exchange of single ligands.



M. Albrecht, S. Mirtschin, M. de Groot, I. Janser, J. Runsink, G. Raabe, M. Kogej, C.A. Schalley, R. Fröhlich, *J. Am. Chem. Soc.* 2005, 127, 10371

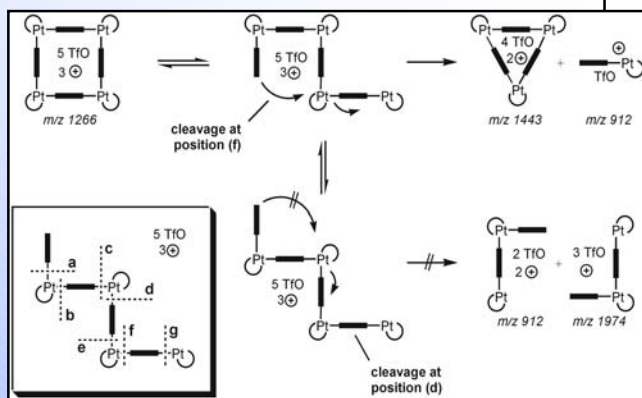
V. Metal-Coordination: A Supramolecular „Neighbor Group“ Effect

Self-assembling squares can be ionized by ESI-MS through stripping away counterions.

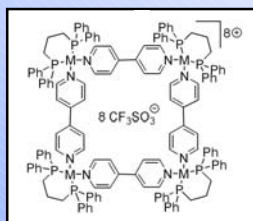
In an IRMPD (infrared multiphoton dissociation) experiment, mass-selected triply charged squares fragment to yield doubly charged triangles.

No splitting into two half squares is observed. As a rationalization, a supramolecular „neighboring group assistance“ mechanism is suggested.

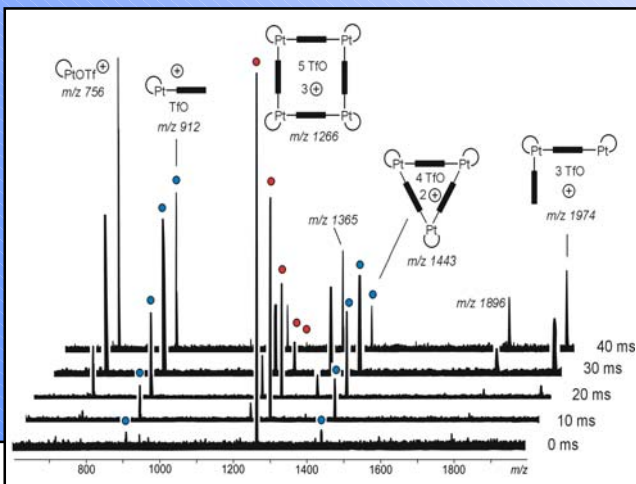
In line with this interpretation, squares in their charge state +5 dissociate specifically into quadruply charged triangles and 1:1 edge-corner complexes.



Due to the absence of dynamic processes in the gas phase, new mechanistic details can be obtained from such gas phase experiments; no such analysis is possible in solution, because exchange processes complicate the situation.



C.A. Schalley, T. Müller, P. Linnartz, M. Witt, M. Schäfer, A. Lützen, *Chem. Eur. J.* 2002, 8, 3538; M. Engeser, A. Rang, M. Ferrier, A. Gutiérrez, C. A. Schalley, *Int. J. Mass Spectrom.*, in press

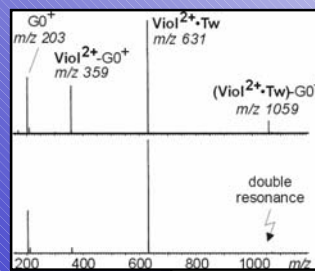


VI. π-Stacking: Gas-Phase Host-Guest Chemistry of Dendrimer-Tweezer Complexes

Kläerner tweezers form host-guest complexes with dendritic viologens which can easily be ionized by ESI-MS

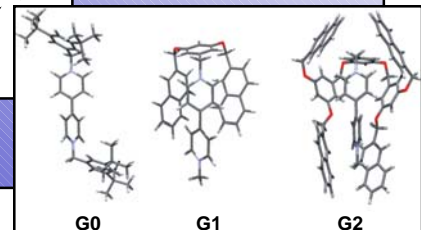
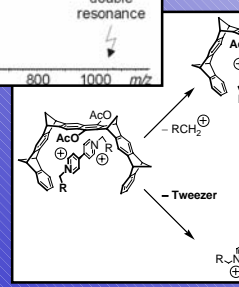
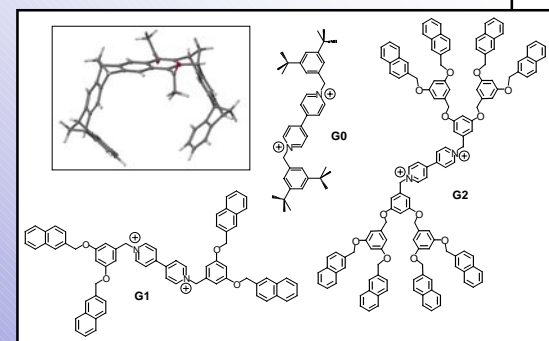
Collision-induced dissociation of mass-selected complex dication shows a remarkable switch in fragmentation pathways:

G0/G1-tweezer complexes fragment by benzyl cation loss followed by tweezer loss



G2-tweezer complexes lose the tweezer first generating a viologen dication which can then fragment by cleavage of the benzyl-N bond.

These findings can be rationalized by invoking a competition between tweezer binding to the dication and dication stabilization of the dication through backfolding dendrimer branches.



C. A. Schalley, C. Verhaelen, F.-G. Klärner, U. Hahn, F. Vögtle, *Angew. Chem.* 2005, 117, 481; *Angew. Chem. Int. Ed.* 2005, 44, 477