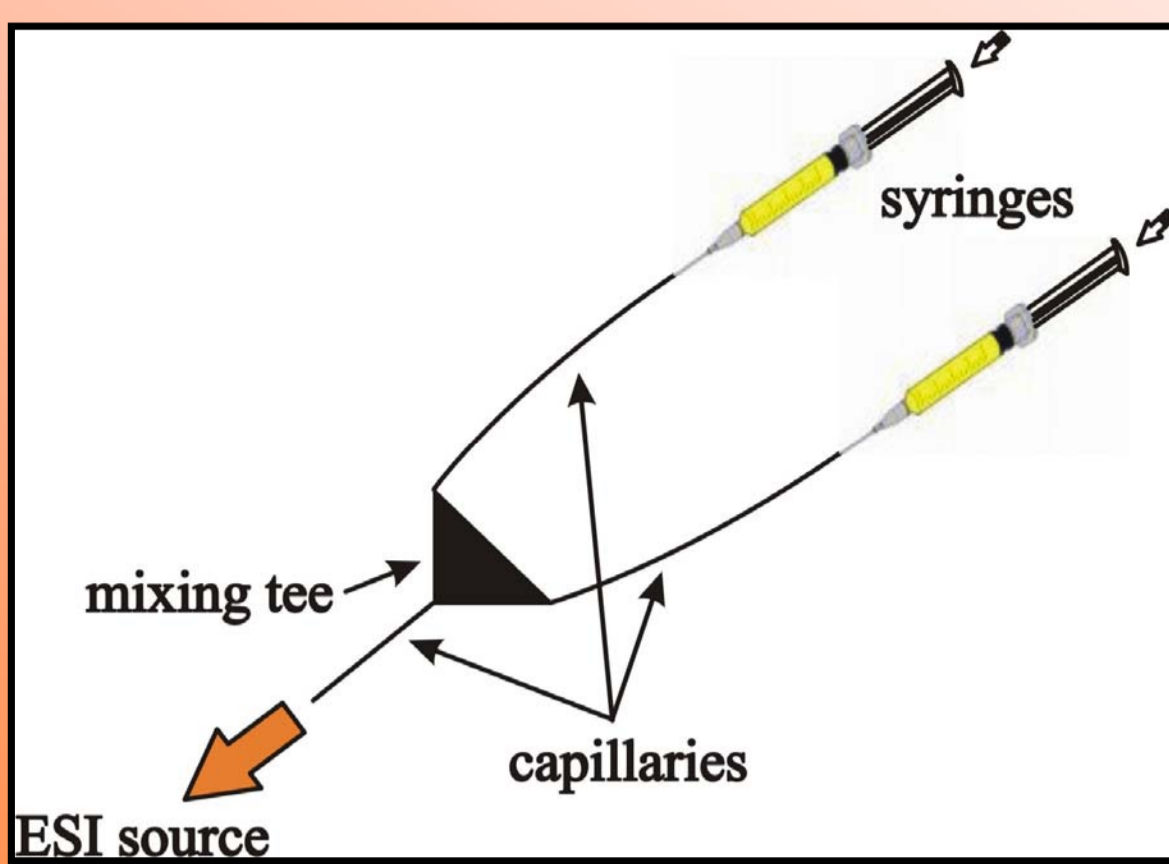


A Mixed-Flow Technique for Mass Spectrometric Analysis of Self-Assembly Mechanisms

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I. The Mass Spectrometric Mixed-Flow Technique



The mass spectrometric on-line microreactor is a tool, which is used to investigate reactions and their mechanisms^[1].

Due to this, we use this tool to explore the mechanisms of self-assembly of metallo-supramolecular systems.

Intermediates of self-assembly processes of at least two different building blocks can be observed with mass spectrometry by using this fast mixed-flow technique.

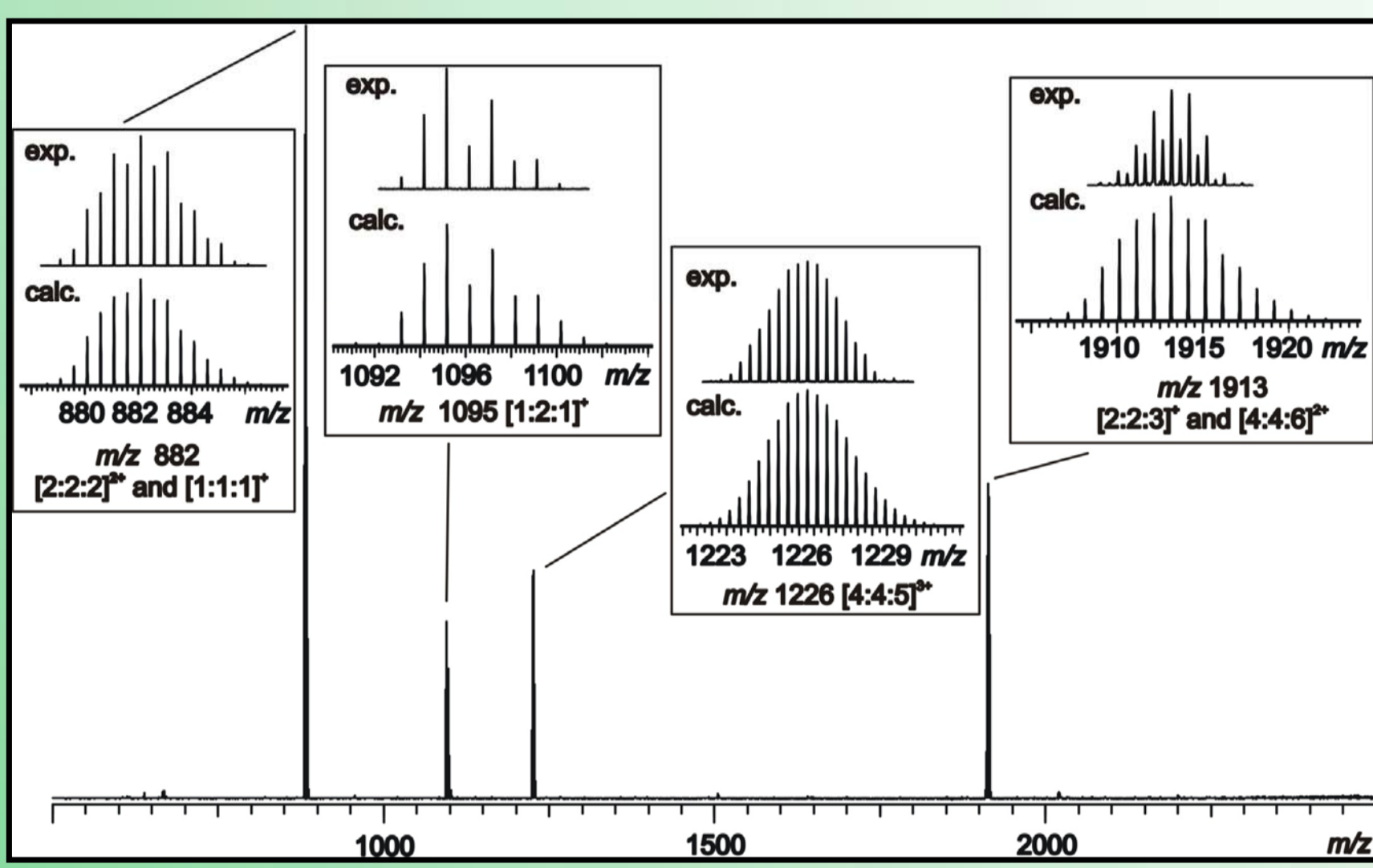
In this experiment, solutions of the building blocks have to be separated in different syringes. The solutions were pressed into capillaries and mixed in a microreactor (or mixing tee). The mixture of the building blocks is transported by another capillary to the ESI source of an ESI FT-ICR mass spectrometer to measure the mixed sample solution after a defined time.

A defined reaction time is essential for mechanistic studies. Otherwise, it would be difficult to identify different mechanistic steps and intermediates.

The reaction time of the building blocks can be influenced by changing the following experimental parameters:

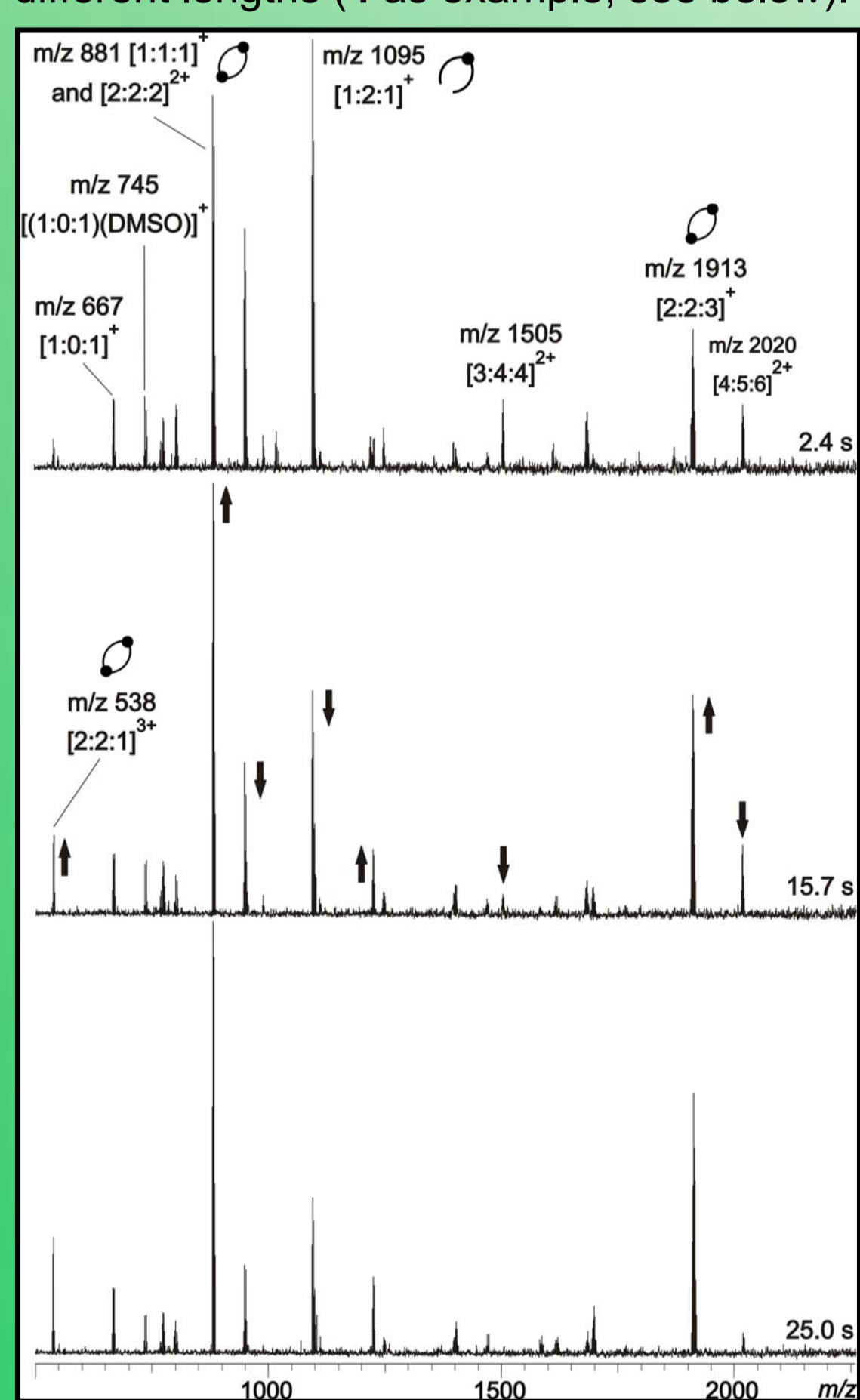
- capillary length and size
- flow rate of the solvents

III. MS of the Self-Assembly of Stang-type [2:2] Complexes

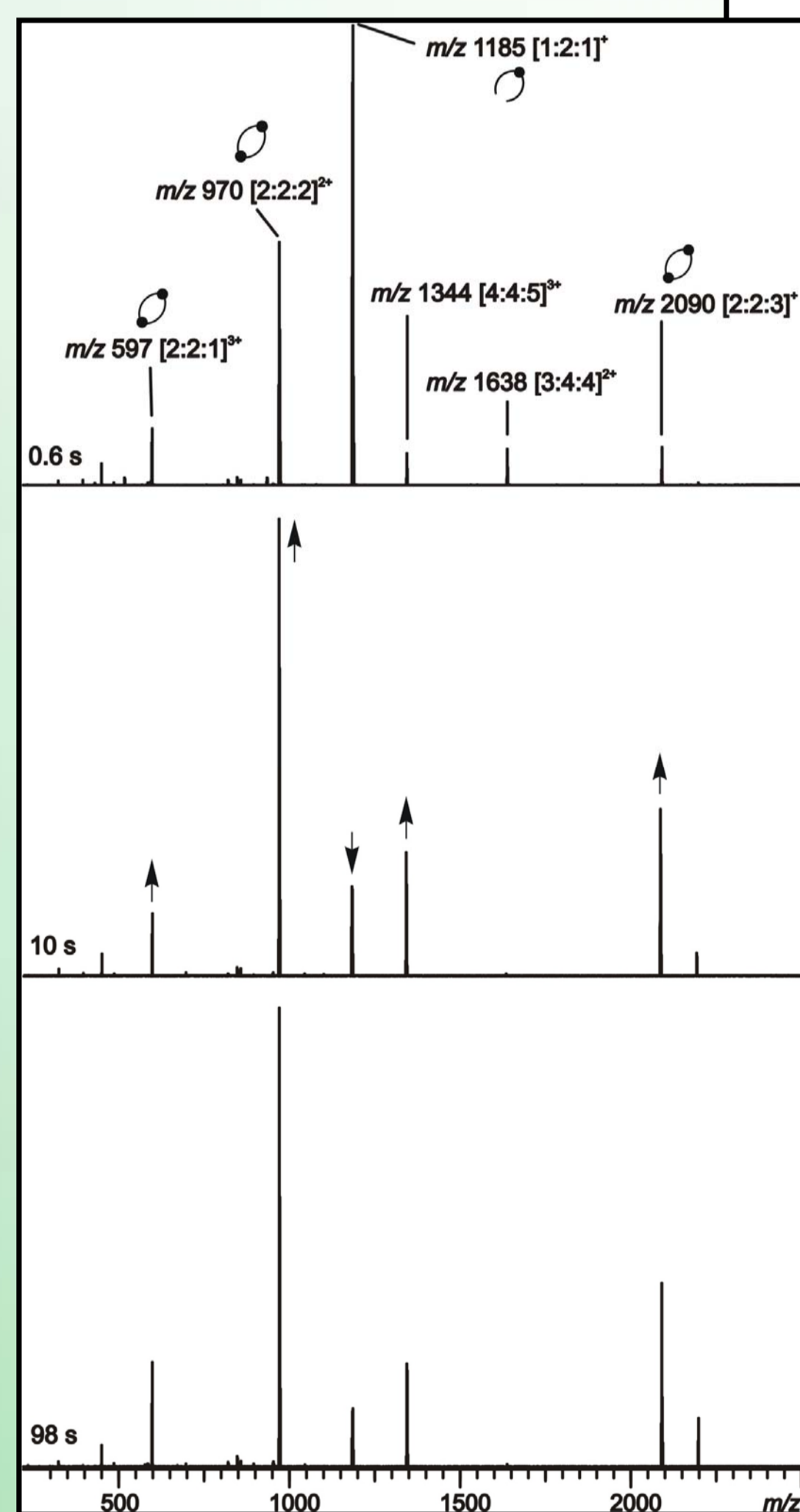


In both cases, mass spectrometry shows several peaks, which can be assigned to the [2:2] complexes, respectively (as shown for complex 4). Furthermore, some peaks for a [4:4] complex are observed. This species can be explained by unspecific aggregation of the [2:2] complexes in the ESI process and though can be identified as dimers. Some fragments like a [1:1] and a [1:2] species are found as well.

In the mixed-flow experiments of these systems, the reaction time was controlled by two different ways. On the one hand the flow rate of the solvents was varied (5 as example, see on the right side). On the other hand the reaction time was controlled by using mixing-capillaries with different lengths (4 as example, see below).



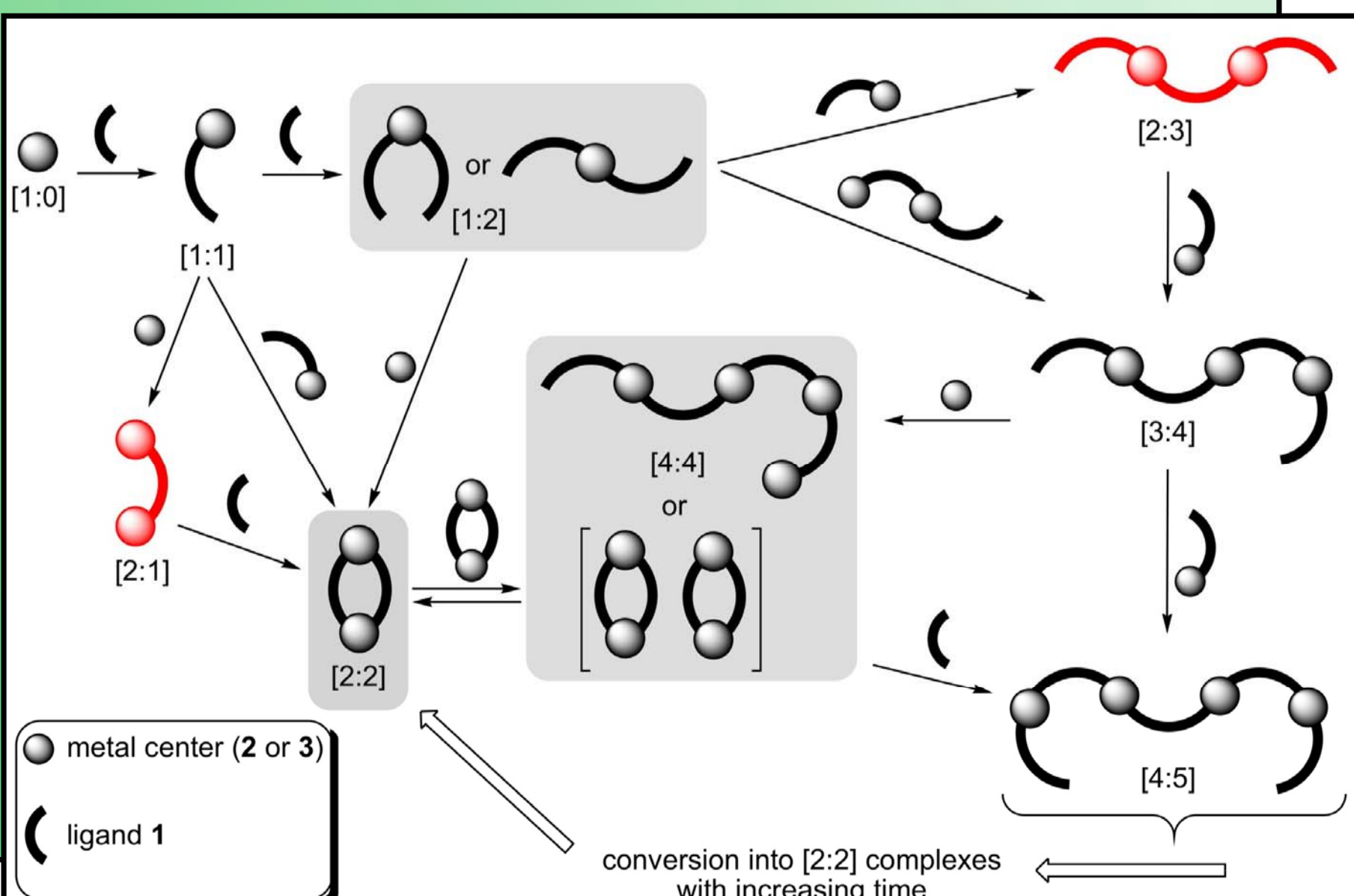
The self-assembly of the [2:2] complexes 4 and 5 seems to be very fast, because peaks for these complexes appear even at very short reaction times (< 1 s). In both cases, [1:2] complexes can be identified as intermediates in the self-assembly process. Additionally to these species, some other peaks can be assigned to complexes which have one ligand more than metal centers ([3:4], [4:5]). These complexes have to be linear, because the metal centers can just coordinate two ligands at once. [1:1] complexes are also observed. They should be intermediates as well.



Solvent molecules also seem to be involved in the self-assembly process (see [(1:0:1)DMSO]⁺).

With increasing reaction times, the signal intensities of the intermediates decrease and those of the [2:2] complexes increase.

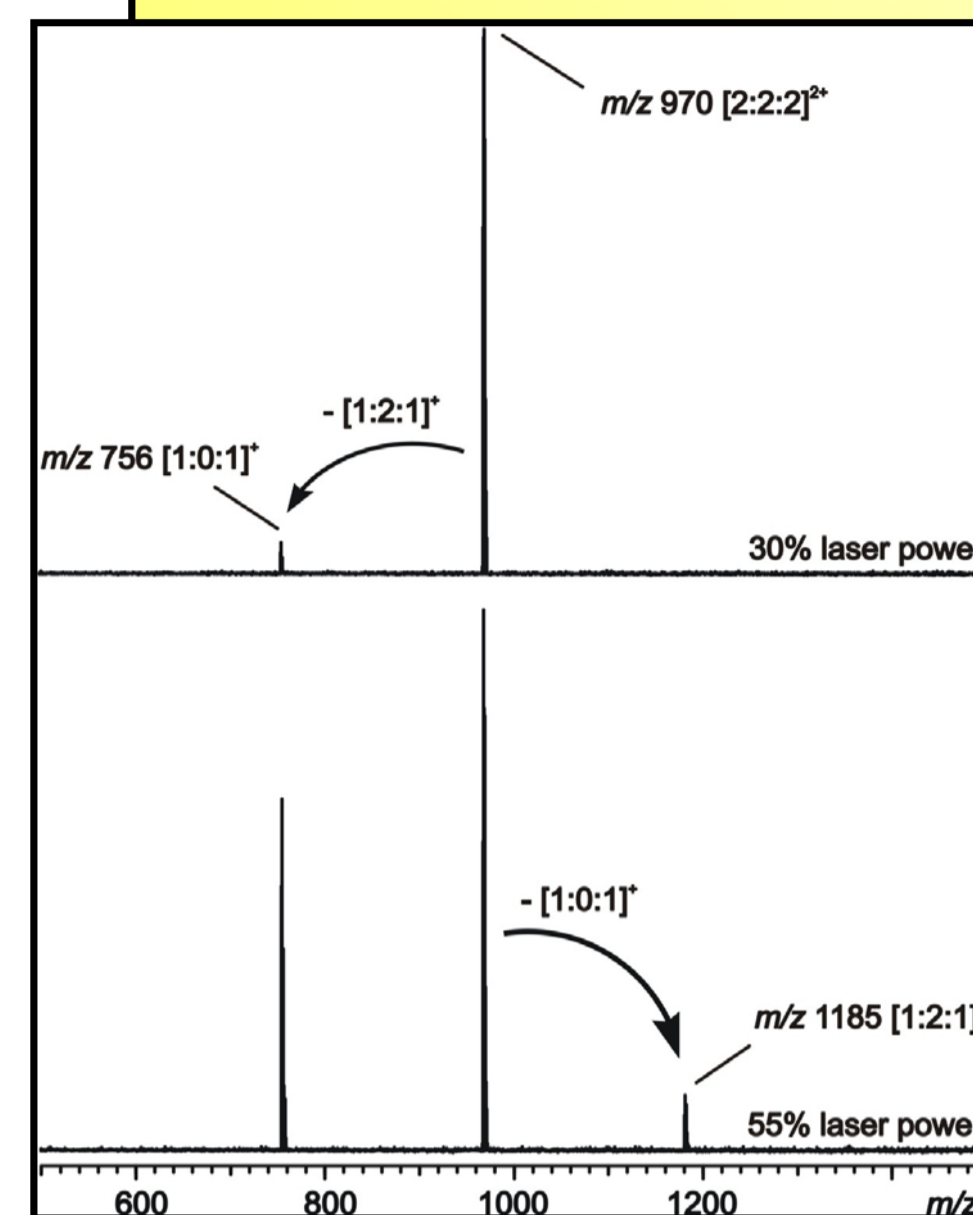
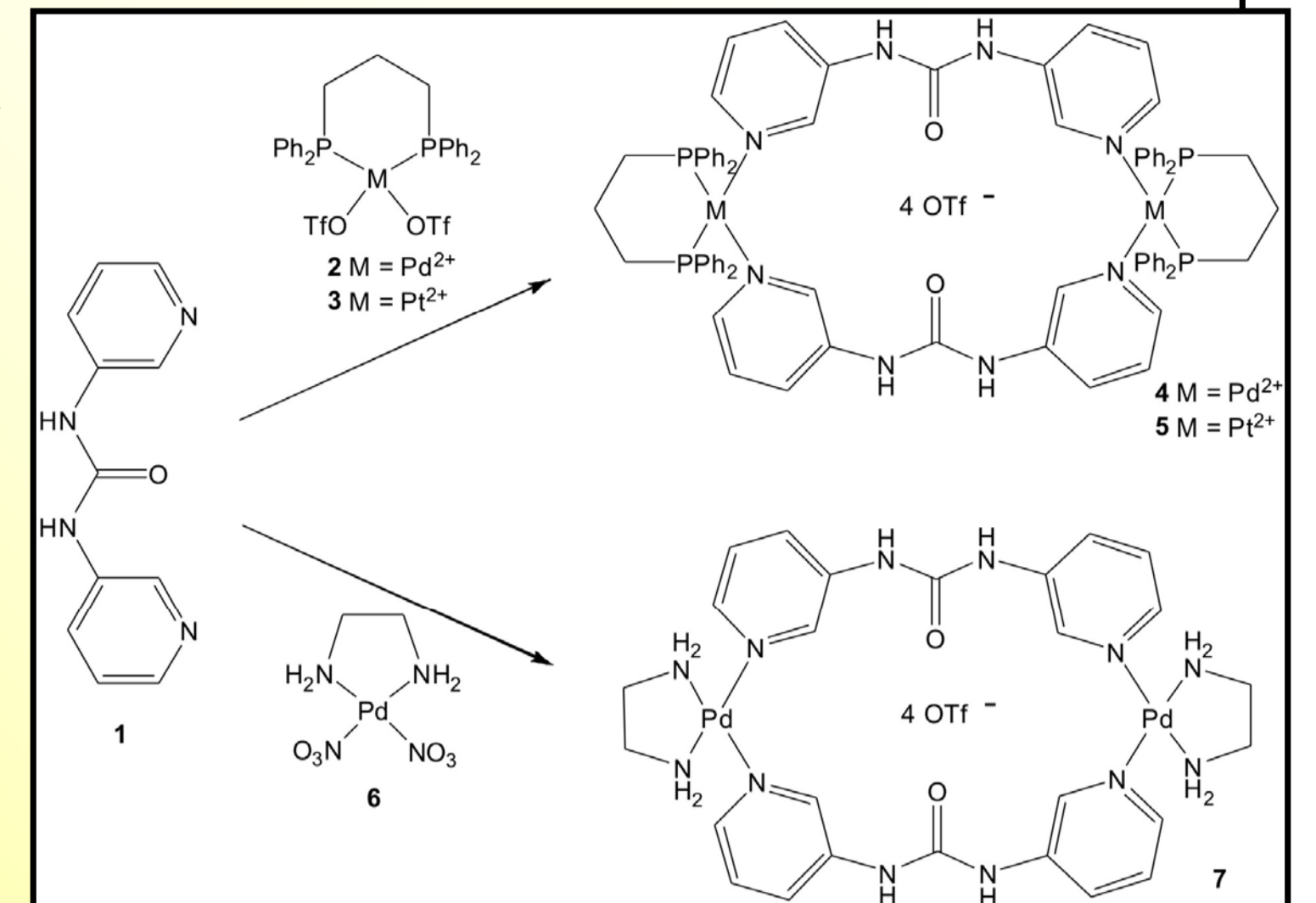
All observations can be used to discuss different pathways of the self-assembly-mechanism for the building of [2:2] complexes with Stang-type metal centers. In the beginning many different and mostly linear complexes are build, which undergo some kind of conversion into [2:2] complexes with increasing time. In all experiments no [2:1] complex was observed.



II. Self-Assembly and properties of the [2:2] Complexes

The self-assembly of equimolar amounts of dipyriddy urea ligand 1 and the metal centers 2, 3 and 6 in DMSO or DMF leads to the [2:2] complexes 4, 5 and 7.^[2]

In case of the systems with Stang type metal centers 2 and 3, another species is observed. This species could not be identified explicitly up to now, but it should reasonably be [3:3] complexes.

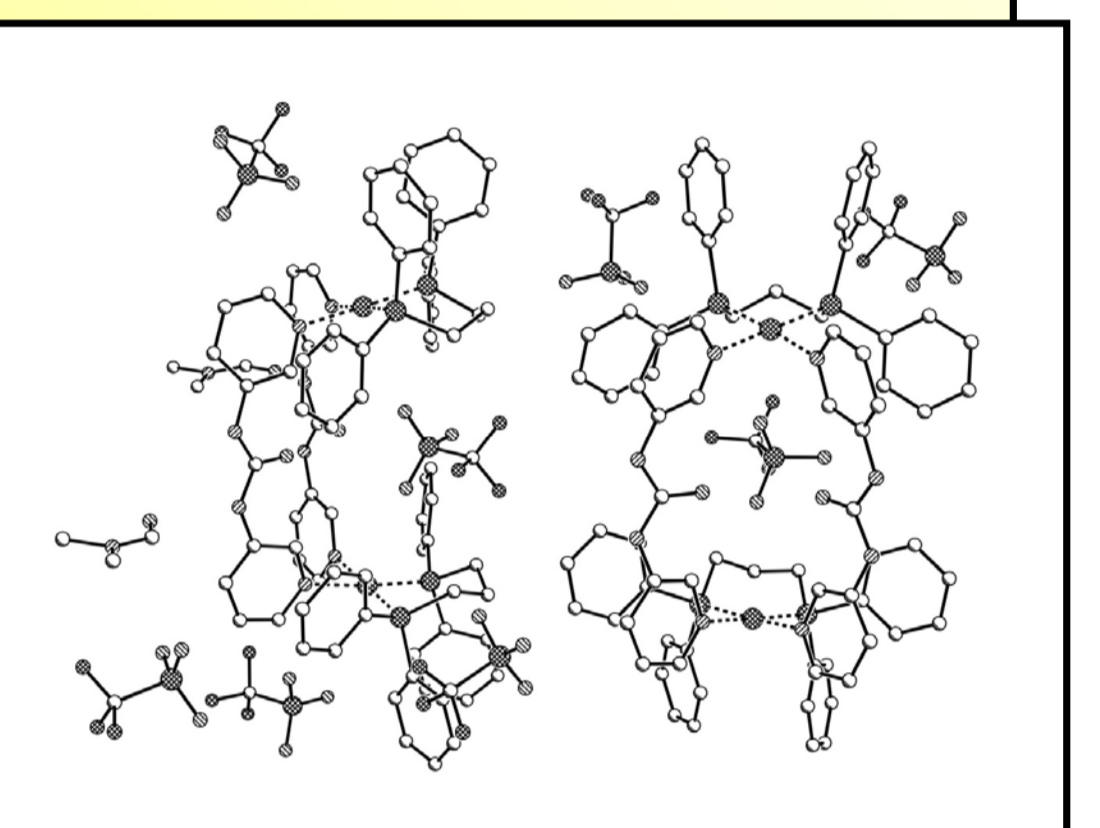


The [2:2]-complexes were characterized by various analytical methods.

¹H and ³¹P and (2D-) DOSY NMR spectroscopy showed two species to be present in solution for the mixtures of 1 and 2 or 3. One species was identified as [2:2] complex and the second species should be a [3:3] complex.

In the ESI-FT-ICR mass spectra of 4, 5 and 7, [2:2] complexes were observed. Other peaks observed therein, were identified by aggregation or fragmentation of these complexes. No other species could be identified herein.

Crystal structures could be obtained from 4 and 5.



Tandem MS experiments (IRMPD) of 4 and 5 showed a specific fragmentation of the [2:2] complexes. The [2:2] complex fragment into a [1:2] complex and a free Stang corner (shown here for 5). Neither a [1:1] nor a [2:1] complex is observed as a fragment ion.

This can be rationalized by the π-π interactions between the aromatic rings in the ligands and the metal corners.

IV. MS of the Self-Assembly of Fujita-type [2:2] Complexes

In the mixed-flow experiments of system 7, the reaction time was controlled by using mixing-capillaries with different lengths.

The self-assembly of ligand 1 and the Fujita-type metal center 6 is a very fast process. Even at very short reaction times the [2:2] complex 7 is observed as one of the main species.

Several peaks observed in the mass spectrometric experiments could be assigned to intermediates in the self-assembly process. The [1:1] species seems to be the prominent intermediate. Another small intermediate is a [1:2] species, which is just observed at very short reaction times. A [2:1] species is not observed.

Furthermore, some bigger species like [2:3], [3:4] and [4:5] complexes are observed as well. Due to the limited coordination sites of the metal centers, all of these species should be somehow linear and open-ended complexes.

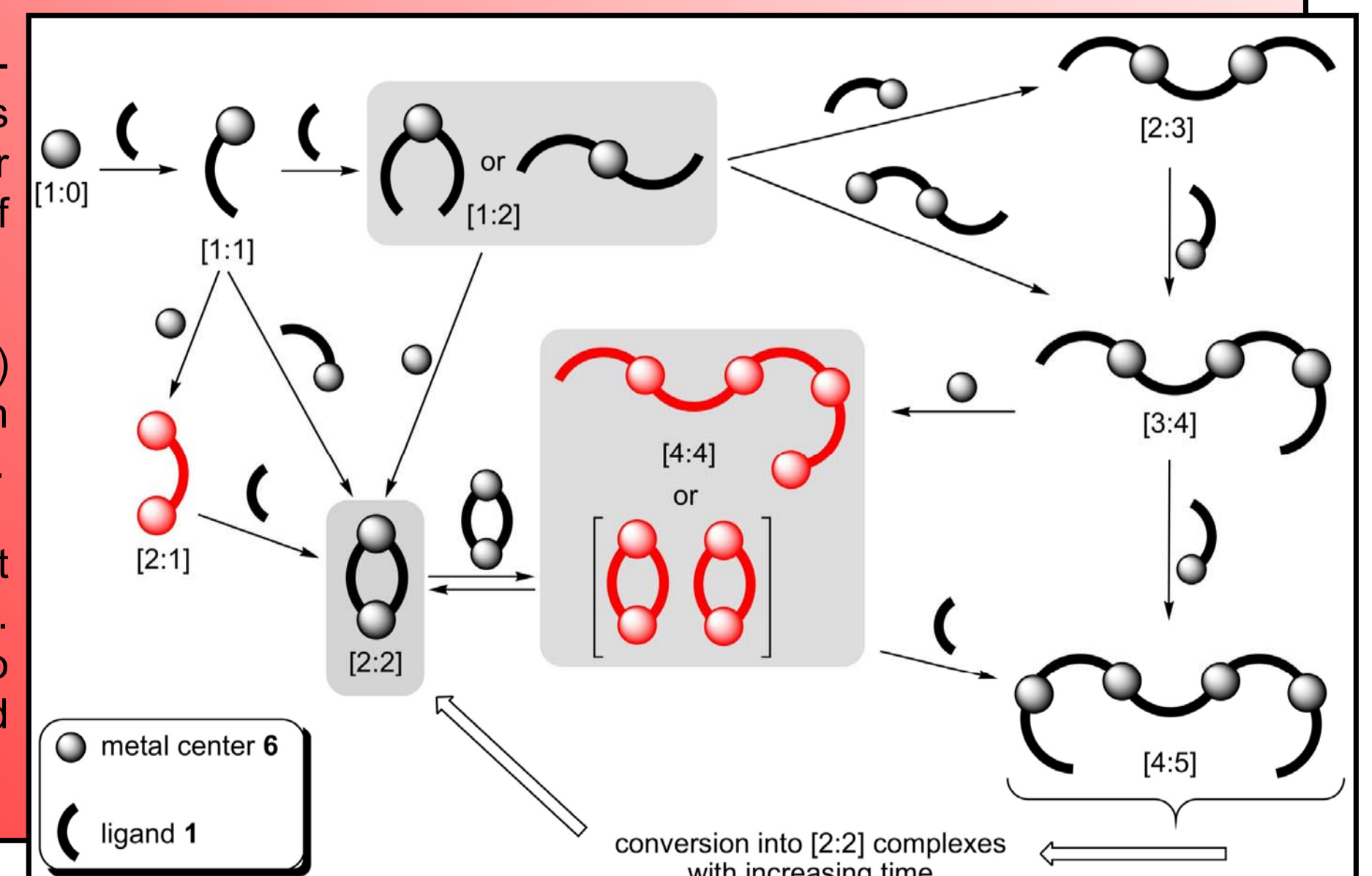
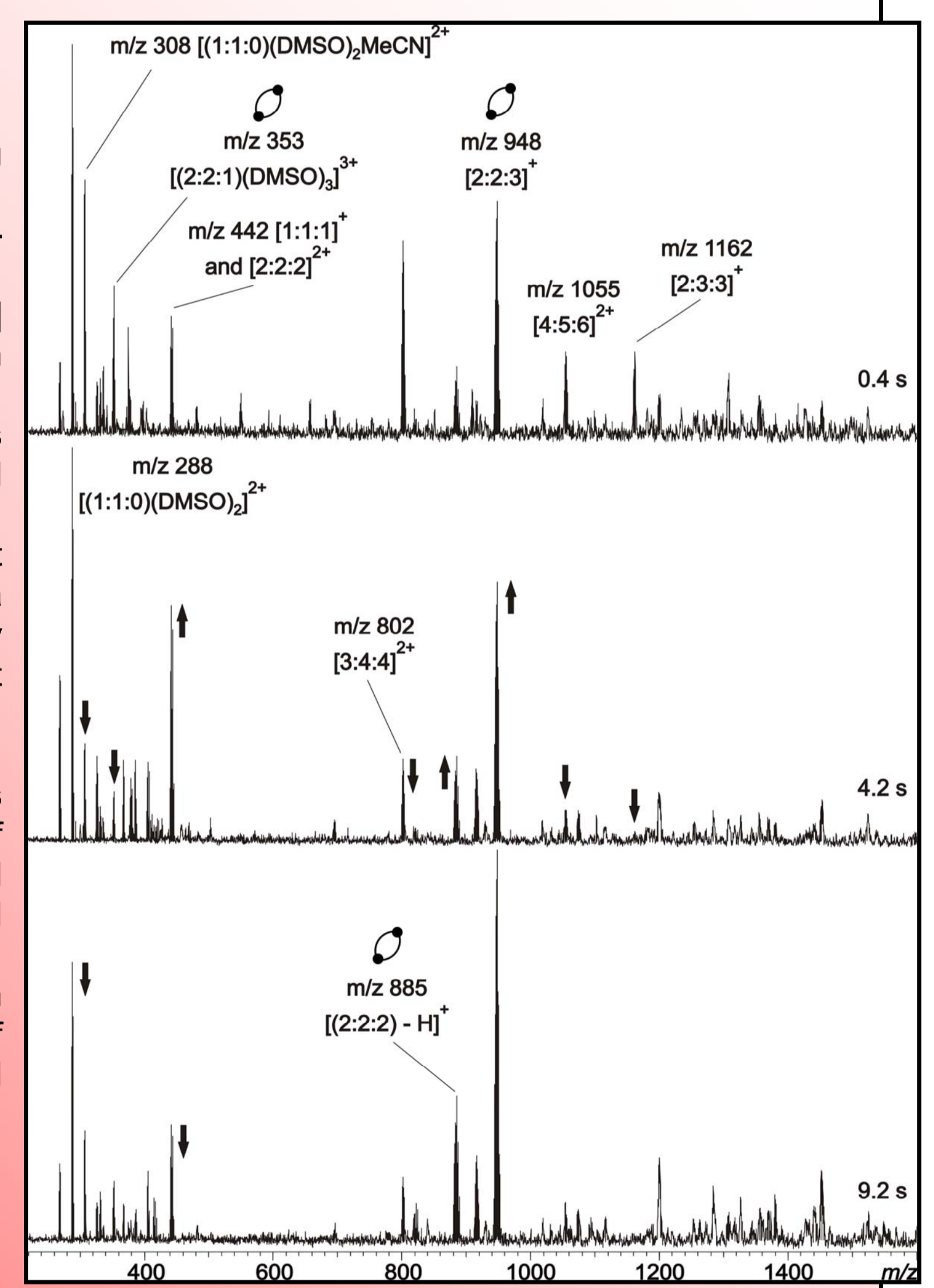
Solvent molecules also play a certain role in here. This can be explained by coordination of the solvent molecules to the metal and interaction with the urea ligands.

With increasing reaction times the signal intensities of the intermediates decrease and those of the [2:2] complexes increase.

Interestingly, at m/z 802 a [(2:2:2) - H]⁺ complex is observed. The loss of an H⁺ was already observed for in the fragmentation process of other Fujita-type complexes.^[3]

The small species ([1:1] and [1:2]) can act directly as intermediates in the formation of the [2:2] complex 7.

The bigger linear species can not directly form [2:2] complexes. These complexes have to undergo some kind of conversion to yield [2:2] complexes.



V. Conclusion

The mixed-flow technique seems to be a good tool to analyse self-assembly processes in supramolecular chemistry.

The experiments showed, that the self-assembly of metallo-supramolecular complexes is very fast – at least for small complexes.

Due to this, it is difficult to say, if all intermediates can be detected.

A lot of intermediates in the self-assembly process of different [2:2] complexes were identified.

A [1:1] and a [1:2] species were identified as key intermediates, which can self-assemble with other building blocks to yield in [2:2] complexes directly.

In all cases, no [2:1] species was observed, which should be a key intermediate as well.

Instead of this, a lot of bigger complexes were observed. They are formed very fast and change into [2:2] complexes with increasing time.

[1] L. S. Santos, L. Knaack, J. O. Metzger, *Int. J. Mass. Spectrom.* **2005**, *246*, 84-104.

[2] The nomenclature of the complexes: a) in the text: [metal:ligand]; b) in the mass spectra: [metal:ligand:counter ion]^{charge}.

[3] K. S. Jeong, S. Y. Kim, U.-S. Shin, M. Kogej, N. T. M. Hai, P. Broekmann, N. Jeong, B. Kirchner, M. Reiher, C. A. Schalley, *J. Am. Chem. Soc.* **2005**, *127*, 17672-17685.

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