# Kinetically Controlled Self-Assemblies in a Dynamic Combinatorial Library of Metallo-Supramolecular Cages

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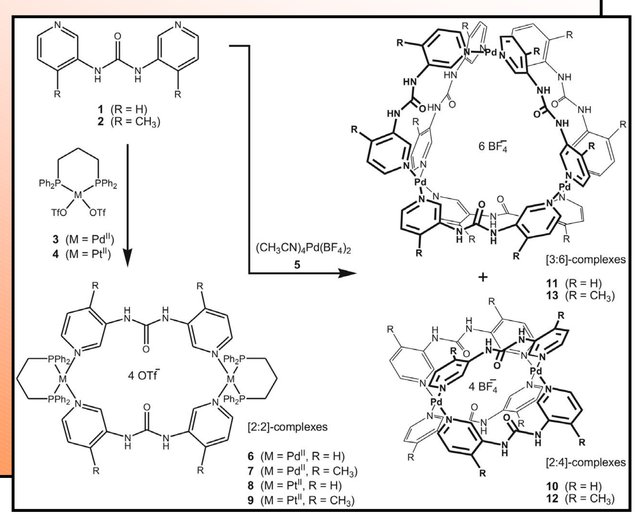
## I. Self-Assembly of Metallo-Supramolecular Complexes[1]

The metallo-supramolecular complexes **6** - **13** are built by the self-assembly of various building blocks:

- self-assembly of equimolar amounts of the ligands (**1**, **2**) with the Stang corners (**3**, **4**) leads to the [2:2]-complexes **6** - **9**
- equilibria between cross-like [2:4]-complexes (**10**, **12**) and double bridged triangle-like [3:6]-complexes (**11**, **13**) are observed, if tetrakis-(acetonitrilo)palladium(II) tetrafluoroborate **5** is used with the ligands (**1**, **2**) in a molecular ratio of 1:2



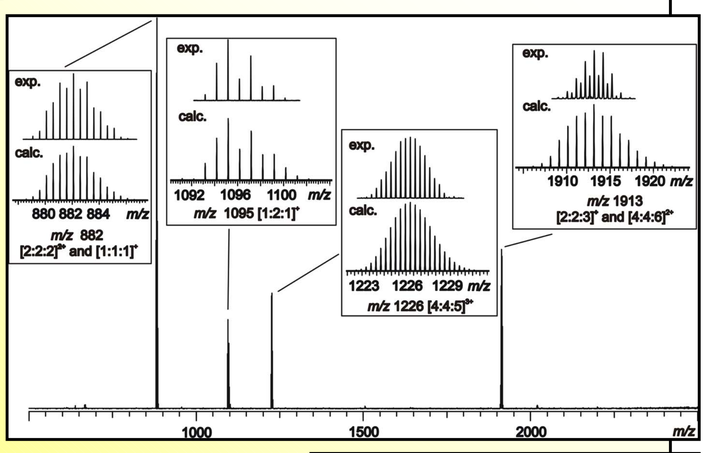

## II. [2:2]-Complexes

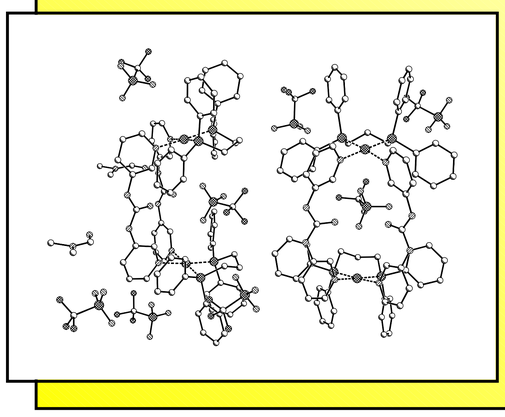
The [2:2]-complexes **6** - **9** were characterized by various analytical methods.

$^{1}$H- and $^{31}$P-NMR spectroscopy showed only one species to exist in solution.

In the ESI-FT-ICR mass spectra, [2:2]-complexes were observed (see for example the mass spectrum of **6**). Other peaks observed in there, were identified by aggregation or fragmentation of these complexes.

A crystal structure analysis of **8** is shown in here.

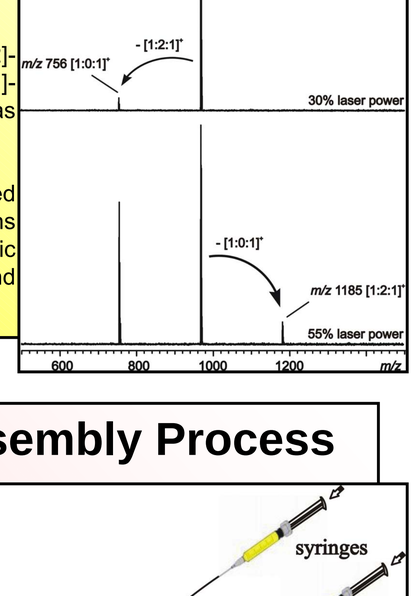


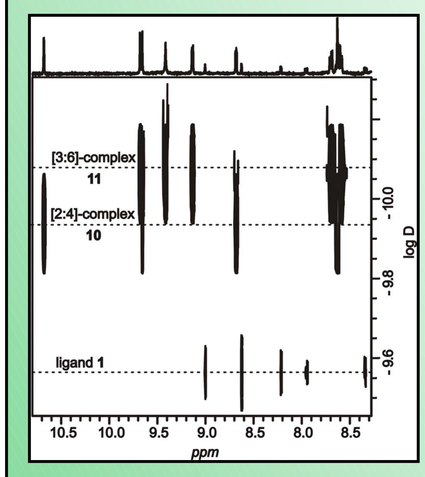
Tandem MS experiments (IRMPD) showed a specific fragmentation of the [2:2]-complexes.

In the case of **8** a [1:2]-complex and no [1:1]-complex is observed as fragment ion.

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




## III. Equilibria between [2:4]- and [3:6]-Complexes

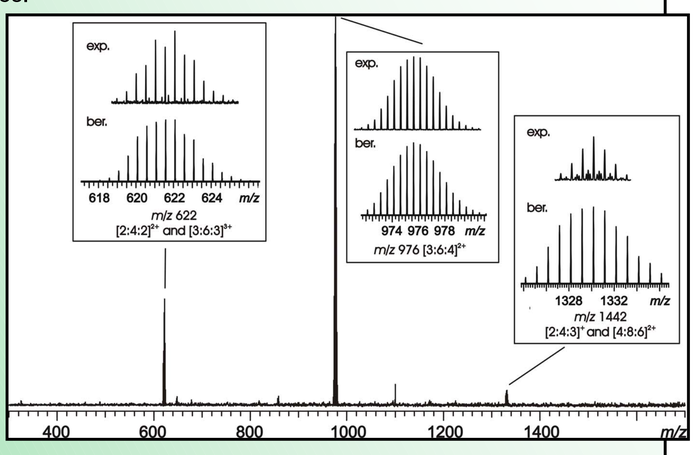


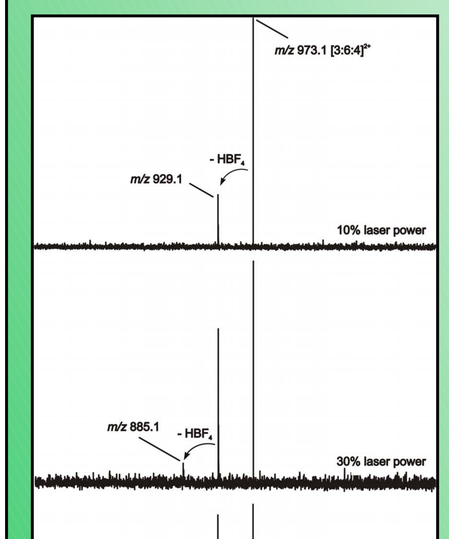

The two systems which contain [2:4]- and [3:6]-complexes were analyzed by the combination of several different analytical methods.

Because of the complexity of the systems, (2D-) DOSY NMR spectroscopy is used to identify the different species in solution (a DOSY NMR spectrum of **10** and **11** is shown as a representative example). The diffusion coefficients of the species were used to calculate the radii of those species[2].

The experimental radii agree well with theoretically calculated ones (molecular modelling) and allow us to identify the [2:4]- and [3:6]-complexes.

The ESI-FT-ICR mass spectra show peaks which could be identified as [2:4]- and [3:6]-complexes. Other peaks are fragments or aggregates of these complexes. Here, the mass spectrum of **10/11** is shown as example.



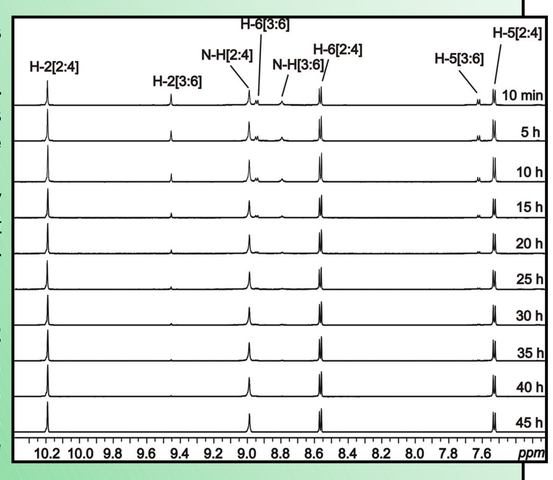




The fragmentation of [2:4]- and [3:6]-complexes were analyzed via IRMPD experiments. It is shown for the example of **11**.

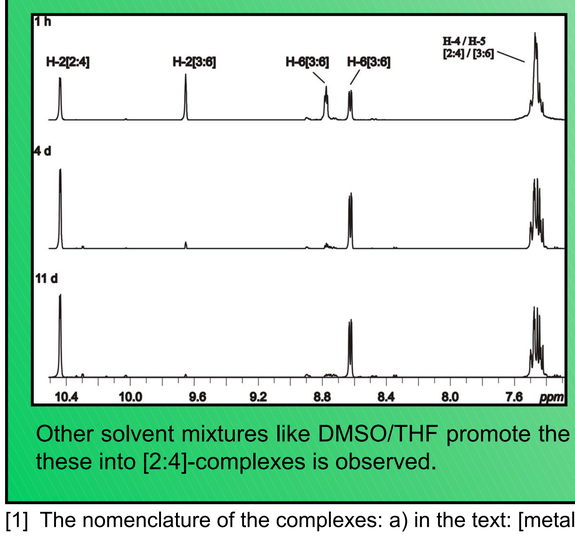
At first, a loss of three $HBF_4$ molecules is observed. Afterwards, a ligand is lost. This can be interpreted by a strong coordinative interaction between the ligand and the metal center.

The $HBF_4$ protons were identified to be the urea-protons of the ligands by deuteration experiments.

The systems changed over time. In the case of **10/11** a new species is observed after five days.
Mass spectrometry indicates that it could be a [4:8]-complex.




In the other system the [3:6]-complex **13** is converted into **12** and after 40 hours no **13** is observed with NMR spectroscopy. This result was verified by ESI-FT-ICR mass spectrometry, wherein a complete conversion was observed after 15 days. This can be interpreted by involving a bite-angle chance caused by the ligand´s methyl groups.




The equilibria between the [2:4]-complexes and the [3:6]-complexes can be influenced by changing the solvent.

A mixture of DMSO and water in the ratio of 3:7 for example leads to a conversion of **11** into **10** which is more or less complete after 11 days.

| solvent mixture (ratio) | ratio [2:4] : [3:6] |
|---|---|
| DMSO/THF (9:1) | 1.00 : 0.88 |
| DMSO/THF (7:3) | 1.00 : 0.79 |
| DMSO/THF (1:1) | 1.00 : 1.39 |
| DMSO/THF (3:7) | 1.00 : 1.85 |
| DMSO/water (9:1) | 1.00 : 0.30 |
| DMSO/water (6:4) | 1.00 : 0.55 |
| DMSO/water (3:7) | 1.00 : 0.39 |

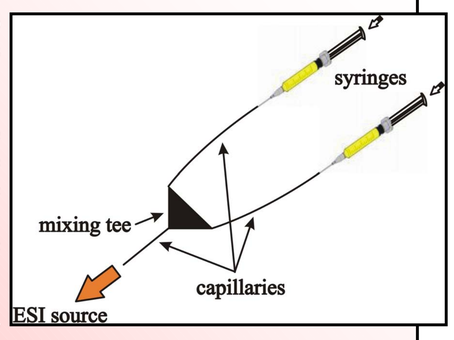
Other solvent mixtures like DMSO/THF promote the building of [3:6]-complexes, but also here a conversion of these into [2:4]-complexes is observed.

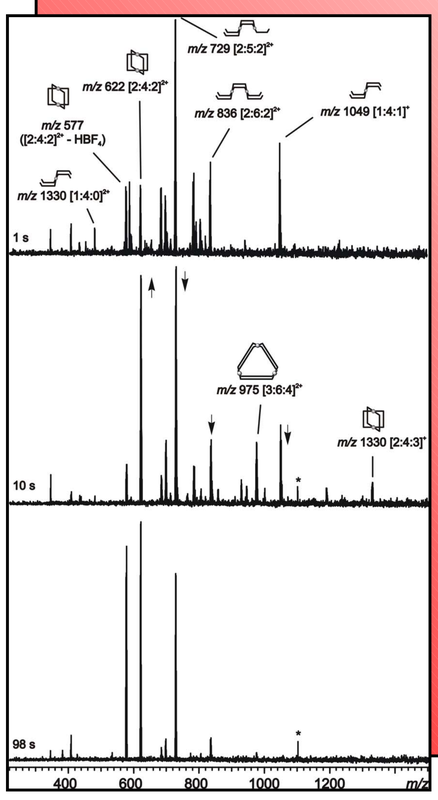
## IV. Intermediates in the Self-Assembly Process

Intermediates of self-assembly processes of at least two different building blocks can be observed with mass spectrometry by using a fast double-syringe mixing experiment.

In this experiment, solutions of the building blocks have to be seperated in different syringes. The solutions were pressed into capillaries and mixed in a 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.

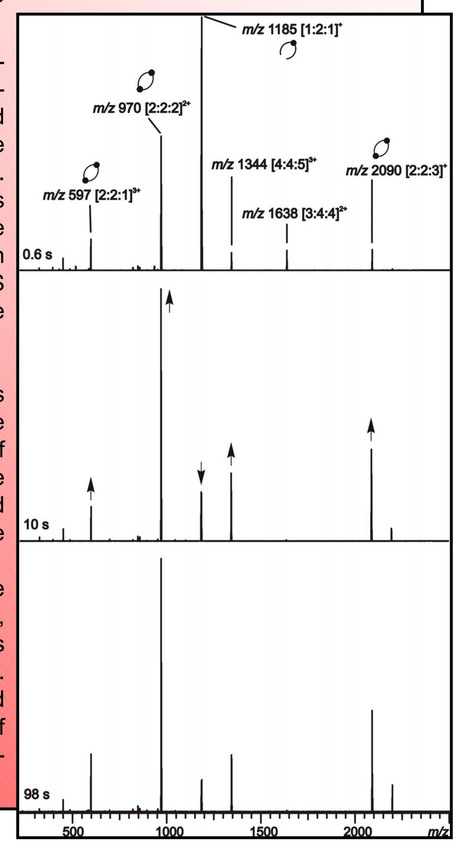
The reaction time of the building blocks can be influenced by changing the experimental parameters of capillary length, size of the syringes and velocity of the solvents.




In the case of [2:2]-complex **8**, a [1:2]-complex can be identified as an intermediate in the self-assembly process. No [1:1]-complex was found as intermediate which is consistent with the tandem MS experiments on these complexes.

A [1:4]-complex was detected as intermediate in the building process of **10/11**. Other chain-type complexes ([2:5] and [2:6]) were observed to be intermediates.
[2:4]-complexes were detected quite well, whereas [3:6]-complexes were observed irregularly. This could be explained by the influence of concentration on the self-assembly process.




## V. Conclusions

The dipyridyl urea ligands **1** and **2** are well-suited building blocks which self-assemble with metal centers to complexes like [2:2]-, [2:4]- and [3:6]-complexes. The [2:4]- and [3:6]-complexes have two shells with different polarity which is caused by the directed dipyridyl urea ligands. This feature can be used for molecular recognition and host-guest chemistry.

The equilibria between [2:4]- and [3:6]-complexes is influenced by the bite angle of the ligands as shown for **12/13**. The self-assembly of [3:6]-complexes is affected by the solvent. The [2:4]-complex is thermodynamically more stable than the [3:6]-complex which is converted to the [2:4]-complex under kinetic control. The building process of [3:6]-complexes is depending on the concentration of the starting materials which is observed in the double-syringe experiments.

The double-syringe mixing experiment proves to be well-suited to study self-assembly processes which could help to understand them much better. The [1:2]-complex which is found to be an intermediate for **8** is favoured over the [1:1]-complex. This is explainable by π-π interactions between the aromatic rings in this compound.

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

[2] Y. Cohen, L. Avram, L. Frish, *Angew. Chem.* **2005**, *117*, 524; *Angew. Chem. Int. Ed.* **2005**, *44*, 520.

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