

# A Toolbox of Substituted Molecular Squares for Molecular Recognition

Alexander Rang,<sup>a</sup> Heidi Mansikkamäki,<sup>b</sup> Christoph A. Schalley<sup>\*a</sup>

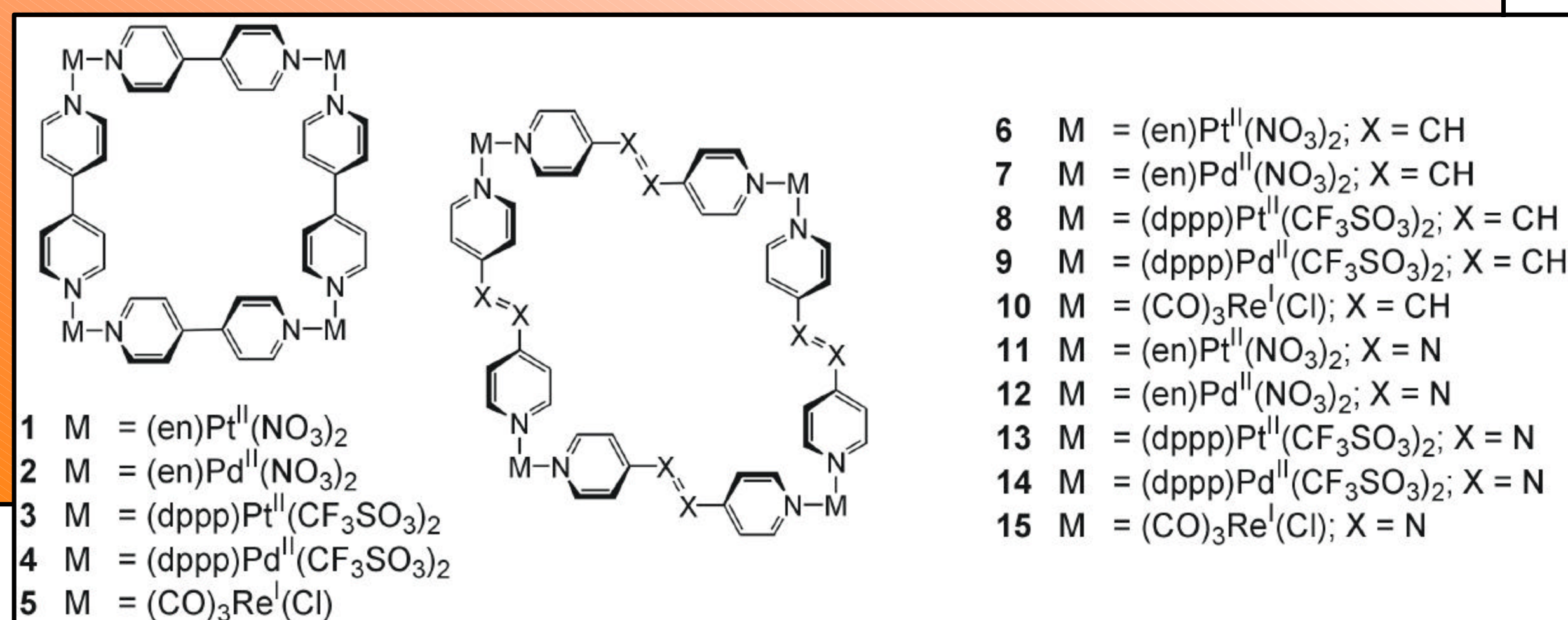
<sup>a</sup> Kekulé-Institut für Organische Chemie und Biochemie, Gerhard-Domagk-Str. 1, D-53121 Bonn, email: c.schalley@uni-bonn.de

<sup>b</sup> Department of Chemistry, University of Jyväskylä, Fin-40014 Jyväskylä

## 1. Introduction

Molecular squares are known since the beginning of the 1990's. Fujita, Stang, Lees and their colleagues introduced the very first examples of these interesting species; applications were developed by the groups of Würthner (electro and photo-chemistry), Hupp (transport) and others. Here we would like to present our approach towards molecular recognition with these squares as hosts.

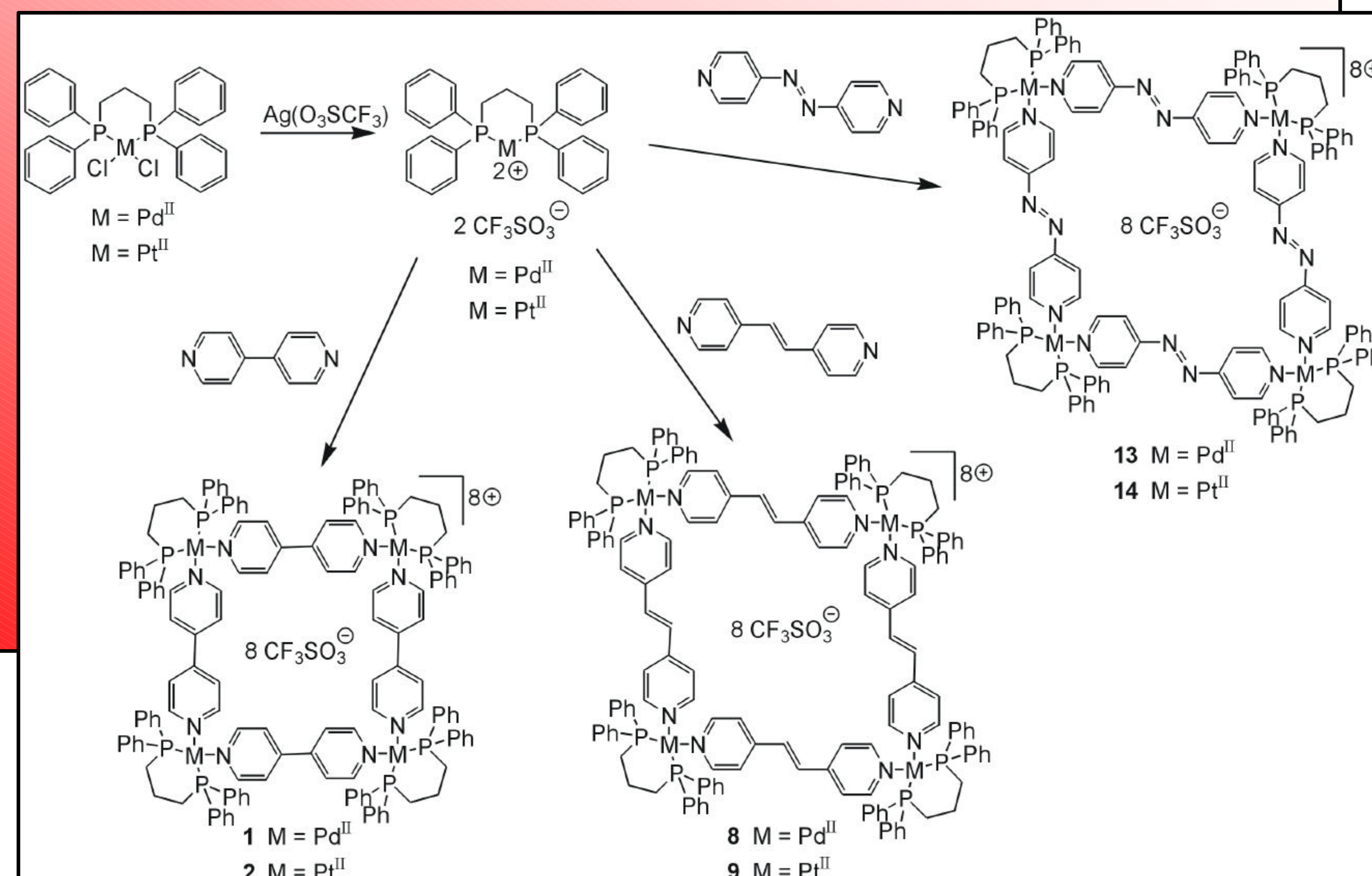
At least five different types of metal-complexes as corner units exist. If one combines this with a number of different ligands, a variety of squares can be made which differ with respect to properties such as solubility, charge, reversibility of their formation and others more. This provides a toolbox of potential hosts for molecular recognition, if the squares are suitably functionalized.



## 2. Synthesis of the Unfunctionalized Squares

Mixing equimolar amounts of metal complexes (corners) and organic ligands (edges) results in the desired metallacycles in excellent yields, driven by thermodynamically controlled self-assembling processes.

Self-assembly of the components has the advantage that synthesis of the resulting compounds is kept as simple as possible.



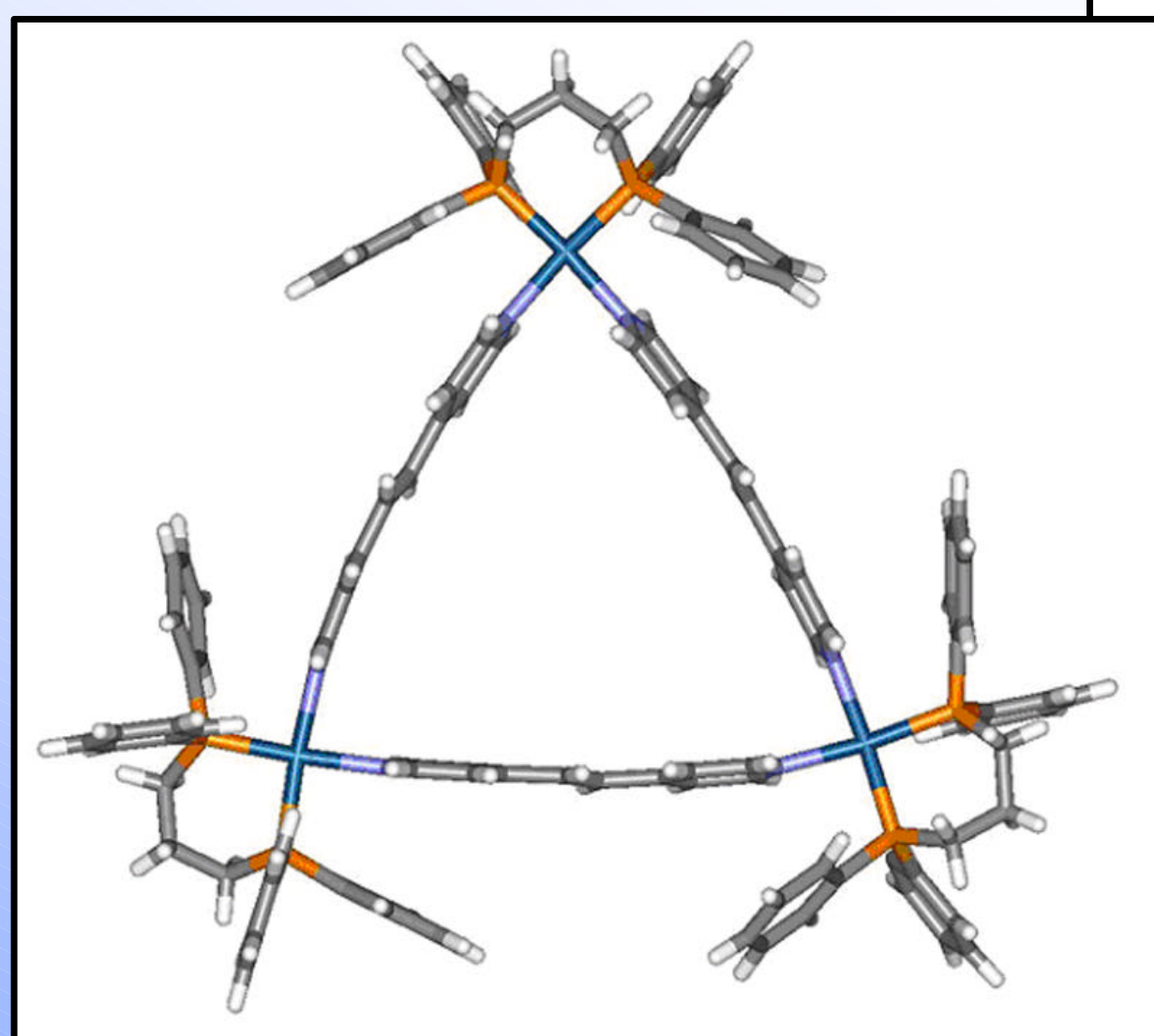
## 3. Characterization of the Unfunctionalized Squares and Triangles

Characterization of the resulting species is possible by standard NMR-techniques (<sup>1</sup>H, <sup>13</sup>C, <sup>31</sup>P-NMR, and DOSY-Spectra (Diffusion Ordered Spectroscopy)) as well as mass-spectrometric and crystal-structure analysis.

ESI-MS spectroscopy of **8**, **9**, **13**, and **14** demonstrates an equilibrium between squares and triangles to exist in solution which depends on the solvent system, concentration, and temperature.

From a solution of **8** which is in equilibrium with the corresponding triangle, we were able to grow single crystals suitable for X-ray crystallography. The crystal structure clearly shows the triangles to preferentially crystallize from the mixture.

These results clearly show that not only squares are formed, but triangles are also found. Both structures have thus been characterized in the solid phase, in solution, and in the gas phase.

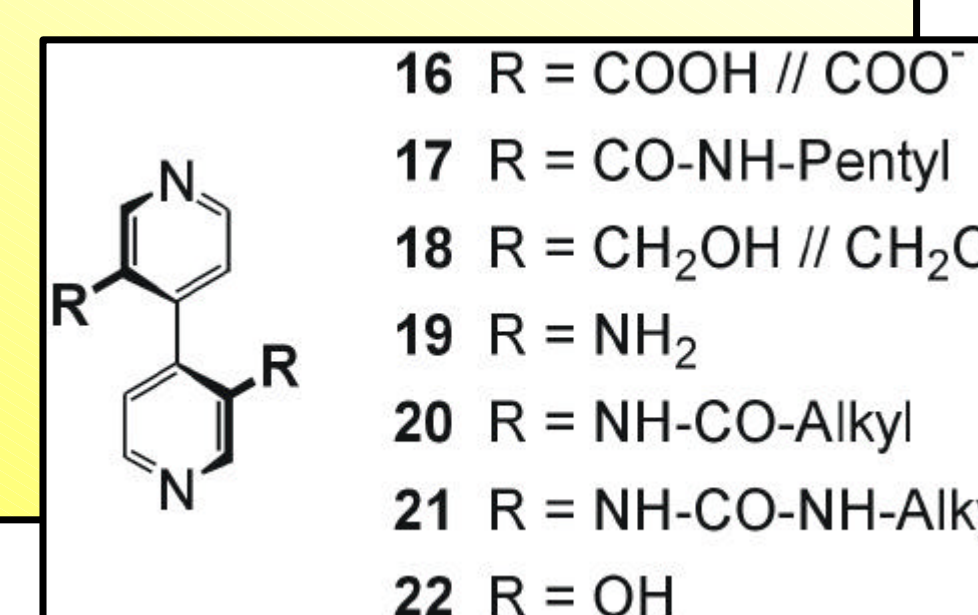
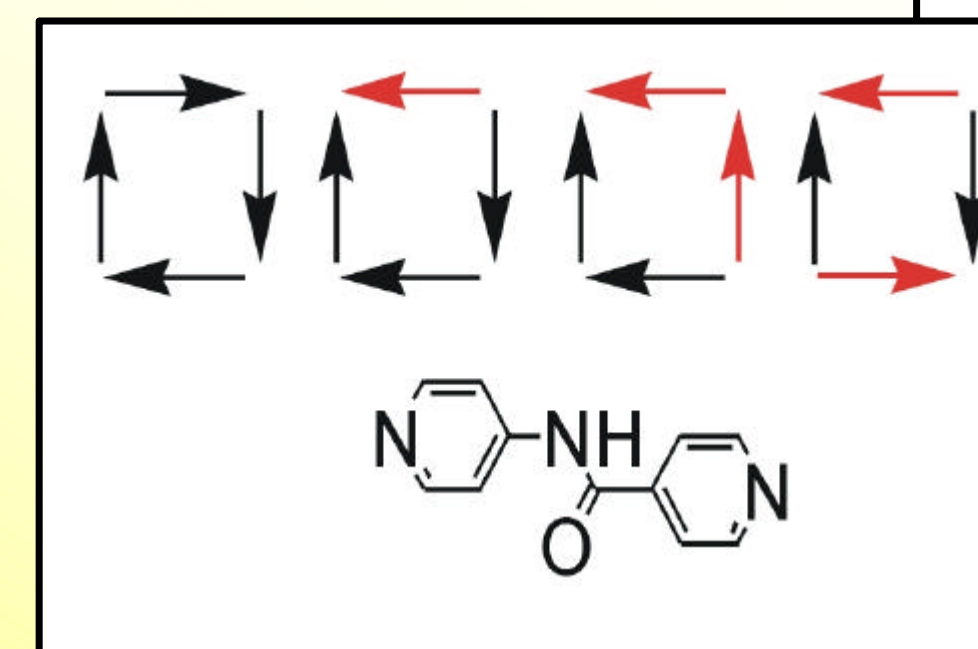


## 4. The Role of the Square/Triangle Equilibrium for Molecular Recognition

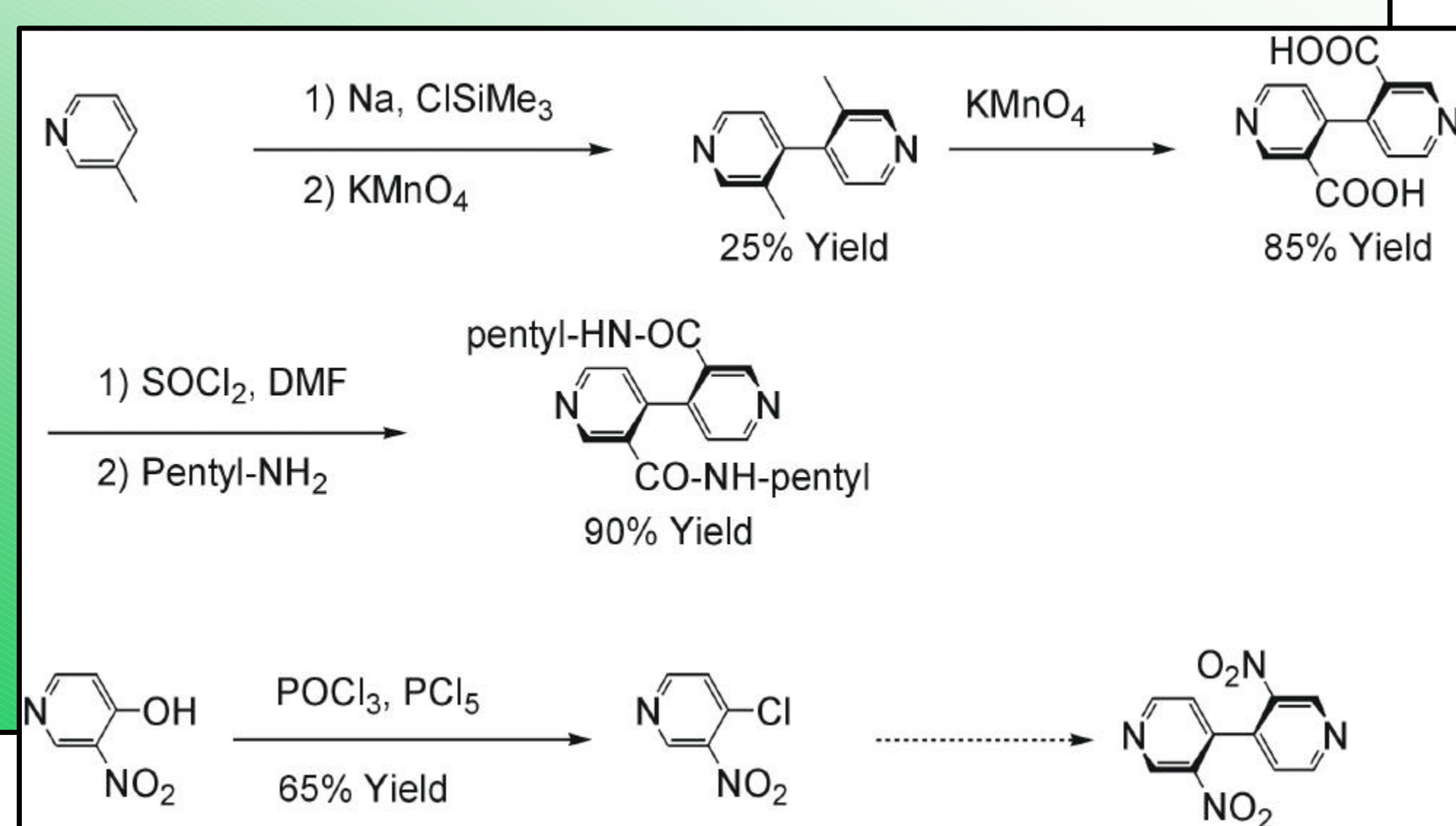
As pre-organization plays an important role in molecular recognition, the discussed equilibrium is a crucial factor for the binding constants of the resulting host-guest-complexes. One should take into account that for best binding constants this equilibrium should be shifted to one side. The host should have a defined structure.

Furthermore, the ligand must not have any sort of directionality. Otherwise a mixture of different squares would be inevitable (see figure).

For those two reasons we decided to use rigid 4,4'-bipyridines as ligands. *Ortho*-substitution relative to the pyridine N atom hampers the formation of squares due to steric hindrance. Instead, 2,2'-disubstituted 4,4'-bipyridines can be synthesized and readily form squares with substituents suitable for host-guest chemistry.

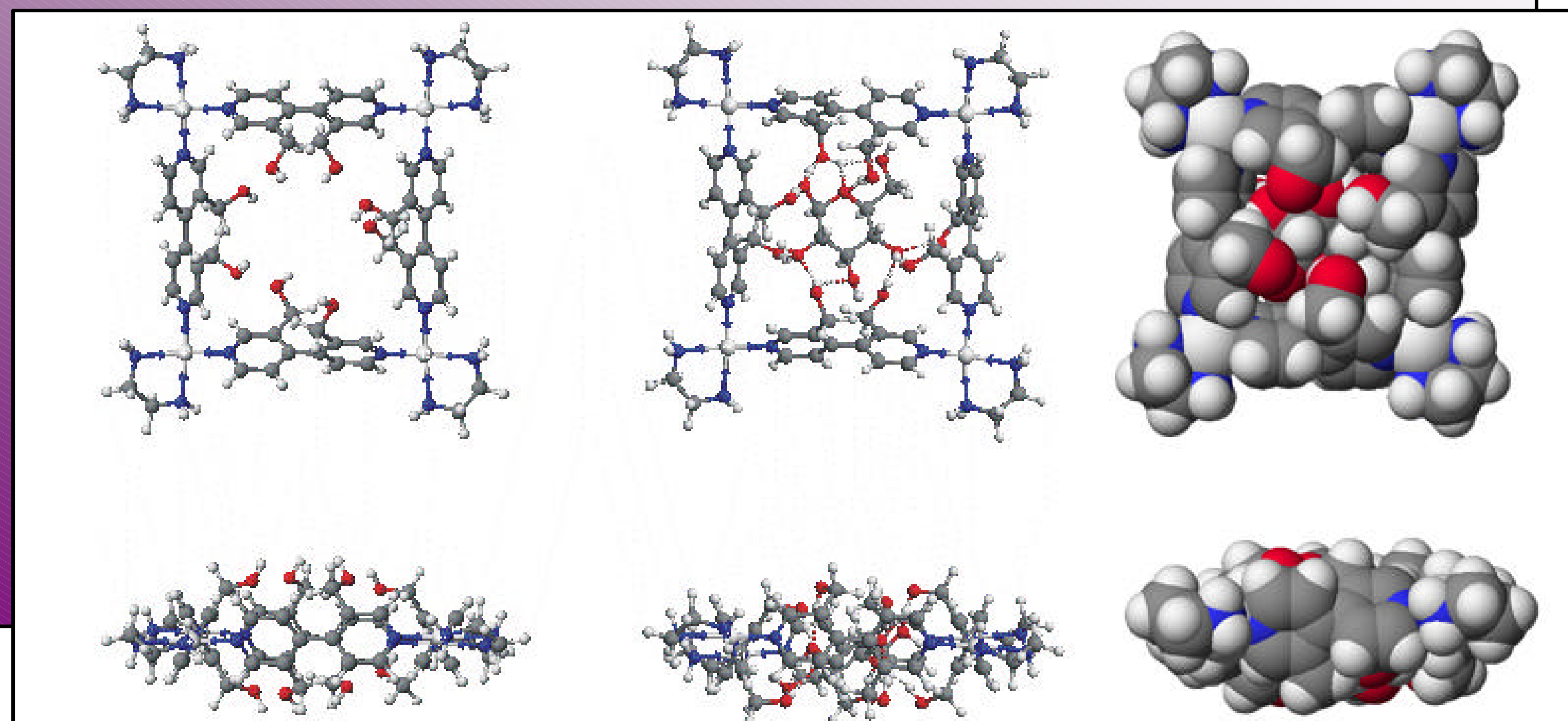


## 5. Synthesis of 2,2'-Disubstituted 4,4'-Bipyridines



## 6. Molecular Modeling of the Resulting Host-Guest-Complexes

The molecular modeling of ((en)Pt<sup>II</sup>(NO<sub>3</sub>)<sub>2</sub>)[**22**]<sub>4</sub> as host – minimized with the MM2 force field implemented in the CACHE 5.0 program package for Windows (Fujitsu Ltd. 2001, Krakow, Poland) – shows the possibility of up to twelve hydrogen bonds binding glucose as guest. The space filling model on the right side demonstrates that there is not much space inside the cavity left, so that disaccharides will not be as suitable as guest, because they are too large.



## 7. Outlook

The preparation and characterization of unfunctionalized squares has been fully developed. The synthesis of 2,2'-disubstituted 4,4'-bipyridines is underway so that functionalized squares should be accessible soon. Molecular modeling suggests that the chosen hosts fit nicely to mono-saccharides. Di- or even poly-saccharides are likely to large for these sorts of hosts.

As chirality plays an important role in saccharide chemistry, chiral hosts should be considered in future work. 2,2',6,6'-tetrasubstituted 4,4'-bipyridines may provide suitable ligands for the self-assembly of chiral receptors.

## Acknowledgement

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