

# Dynamic Combinatorial Libraries of Self-Assembled Metallo-Supramolecular Dendrimers

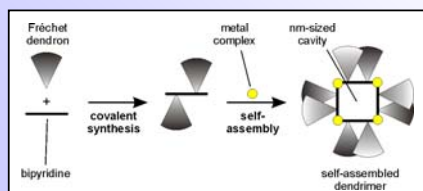
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## I. Self-Assembled Metallo-Supramolecular Dendrimers

Self-assembly of 4,4'-bipyridines connected to Fréchet-dendrons (G0 to G3) through amide bonds leads to metallo-supramolecular squares that

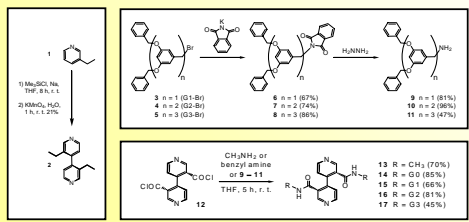
- reduce the synthetic effort needed by replacing covalent synthesis through non-covalent, thermodynamically controlled reaction steps
- bear a nanometer-sized cavity as their cores for guest binding
- carry eight hydrogen-bonding sites along the seam of the cavity
- provide a special microenvironment through the dendritic shell surrounding the functionalized cavity



## II. Covalent Synthesis

Bipyridine building blocks are prepared in a convergent manner by

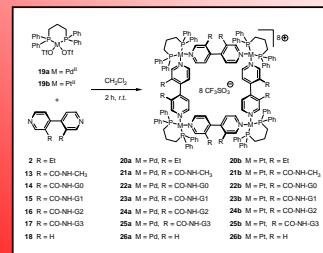
- synthesis of G1 to G3 dendrons using Fréchet's original procedure [1] followed by Gabriel synthesis for the conversion of bromides to amines
- preparation of 4,4'-bipyridine-3,3'-dicarboxylic acid [2] through coupling of two picolines followed by oxidation
- amide-bond formation with methylamine, benzylamine (G0), or G1 to G3 amines



## III. Self Assembly

Self assembly of equimolar amounts of (dppp)M(OTf)<sub>2</sub> corners (M = Pd or Pt) and bipyridines [3][4] has the following advantages:

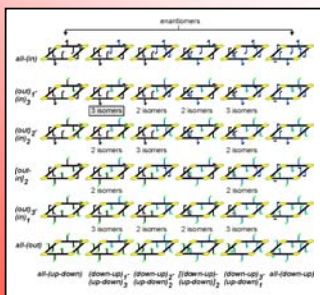
- reversibility and error correction ("smart" materials)
- reduces the synthetic effort
- thermodynamically controlled; **high yields of 85% to 95%**



## IV. Dynamic Combinatorial Libraries

conformation of molecular squares

- each bipyridines can be oriented in an up-down or down-up fashion in the square (six different arrangements)
- towards or outwards from cavity of the square (indicated by small flags)
- superposition of both types of isomerism yields a total of 54 different isomers
- adaptability not proven so far



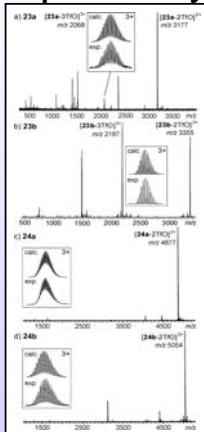
Each compound constitutes a dynamic combinatorial library.

## V. ESI - FTICR Mass Spectrometry

mass spectrometric experiments provide information on size of assemblies [5]

- ions are formed by consecutively stripping away counterions
- 200 μM sample concentrations from acetone
- compounds **25a** and **25b**: (molecular masses of more than 18,000 Da) too heavy to be investigated with our instrument
- compounds **20a/b** – **24a/b**: +2 and +3 charge states of squares most prominent peaks; isotope patterns (insets) match those calculated on basis of natural abundances

only squares are formed; no triangles, larger polygons, or open chain oligomers are observed



## VI. Mixing Experiments

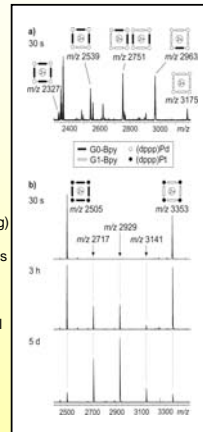
a) mixing two equimolar solutions of two different Pd squares (G0 and G1) showed signals for all possible combinations (ca. 30 s)

- signals intensities close to statistical ratio 1:4:6:4:1; intensities did not change any further; mixture fully equilibrated after ca. 30 s

b) Pt squares only signals for homotetrameric compounds (after mixing)

- expected signals for mixed compounds after 3 h at 22°C (intensities are far from statistical ratio)
- 5 days at room temperature: statistical ratio is reached

ligand exchange in Pt squares is feasible, but significantly slower than that of Pd squares



## VIII. NMR - Spectroscopy

rather complex NMR spectra due to dynamic combinatorial libraries expected

- <sup>1</sup>H and <sup>31</sup>P NMR: chemical shifts and Pt-P-Coupling as expected
- one set of averaged signals (interconversion quickly on NMR time scale); large number of sets of signals with closely similar chemical shift values (interconversion slowly)
- RT <sup>1</sup>H NMR spectra of dendritic Pd squares: sharp signals; broadened RT <sup>31</sup>P NMR signals (indicating isomer equilibrium)
- G3: an all-in isomer highly unfavorable due to steric congestion: complexity of NMR spectra reduced
- <sup>1</sup>H and <sup>31</sup>P spectra sharpen with dendron size with decreasing numbers of possible isomers

## VII. VT - NMR - Spectroscopy

- at low temperature, multiple sets of signals are visible: indication of library formation; spectra sharpens at higher temperatures
- both squares behave similarly, but in different temperature ranges (Pt 60 K higher)
- processes are faster for Pd squares as compared to Pt squares

interconversion of isomers requires more energy in Pt case as compared to Pd squares; in agreement with different ligand exchange rates observed in mass spectrometric experiments

Do exchange processes involve cleavage of M-N bonds, ligand exchange or a combination of both?

## IX. Conclusion

- MS: only squares formed, no other polygons observed
- NMR: in agreement to previously published results
- self-assembled metallo-supramolecular dendrimers can be obtained by this procedure in high yields
- VT-NMR and mixing experiments: interconversion processes are faster for Pd squares than for Pt analogues
- each compound constitutes a dynamic combinatorial library
- nanometer-sized cavity in dendrimers cores for guest binding will be investigated in the near future

## X. Literature

- [1] Hawker, C. J.; Fréchet, J. M. J., *J. Am. Chem. Soc.* **1990**, *112*, 7638.
- [2] J. Rebek, T. Costello, R. Wattle, *J. Am. Chem. Soc.* **1985**, *107*, 7487.
- [3] M. Fujita, J. Yazaki, K. Ogura, *J. Am. Chem. Soc.* **1990**, *112*, 5645.
- [4] P. J. Stang, B. Olenyuk, *Acc. Chem. Res.* **1997**, *30*, 502.
- [5] C. A. Schalley, T. Müller, P. Linnartz, M. Witt, M. Schäfer, A. Lützen, *Chem. Eur. J.* **2002**, *8*, 3538.

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