Handout IRTG, May 2009

- Jan Reedijk. Leiden Institute of Chemistry
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Bifunctionality in ligands and coordination compounds: application in design of new materials, catalysts and drugs.

IRTG: Spring 2009, Münster

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Lectures overview

- Introduction Ligands (general)
- Introduction Bifunctionality
- Introduction Metal-DNA binding and anticancer drugs, followed by:
  Bifunctionality in M-DNA binding
- **Introduction Materials and Catalysis**
- **Bifunctionality in Molecular Materials and Homogeneous Catalysis**
- Conclusions and Outlook

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Introduction Ligands and Bifunctionality

- Bifunctionality has been applied in our recent work on:
- Rigid Coordination polymers (also called MOFs) and molecular materials
- Oxidation catalysts
- DNA cutting agents based on Cu and Pt
- Pt anticancer drugs (third generation)

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Ligands for metals (introduction at lectures coordination chemistry)

- In coordination chemistry the metals are at the center, some 70 possibilities in the Periodic Table!
- However, with (organic) ligands the possibilities are almost unlimited!!

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Ligands for metals

- Simple ligands (monodentate or bridging)
- Ligands to master the coordination geometry (pre-orientation of donor atoms, through rigid constraints in the ligand)
- Special chelate effects with rigid ligands
- Ligands to control semi-coordination
- **Ligands with groups to control the second coordination sphere (solubility, stacking, recognition, surface attachment)**
- **Ligands with a second chemical function (metal binding, intercalator, switches, …)**

The ligand

- Monofunctionality: Monodentate, bridging
- Bi- and Trifunctionality: Metal binding with other function(s)
- Other functions may include: steric effects (bulky groups), solubilizing effect (hydrophobic, hydrophylic), H-bond donor, H-bond acceptor, intercalator/stacking ligand, bridge to another metal (flexible or rigid bridges)

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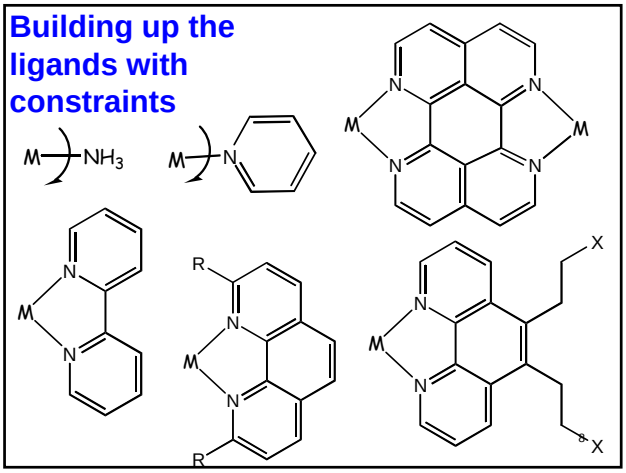
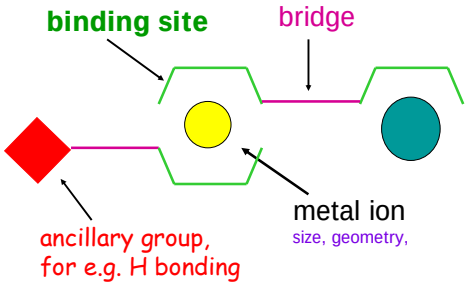
Building up the ligands with constraints



Building up a structure



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Examples for control of coordination geometry

- Ligand bite angle some 120-140 degrees: tetrahedral geometry for Cu(I) and Cu(II)
- Steric bulk in cis position to force tetrahedral rather than square planer geometry
- Pre-orientation of donor atoms in chelating ligands, at rigid positions

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Reducing reactivity of small molecules by encapsulation

- EXAMPLES:
- Dioxygen binding in between 2 or more metals

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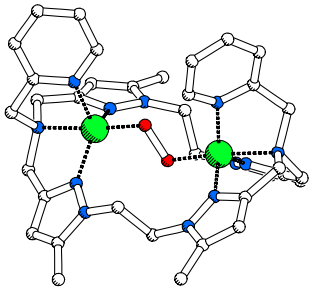
Dinuclear structure for a dicopper peroxide-bridged system



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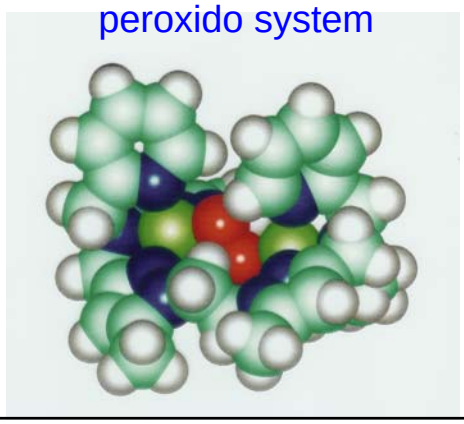
Encapsulation in a dicopper peroxido system



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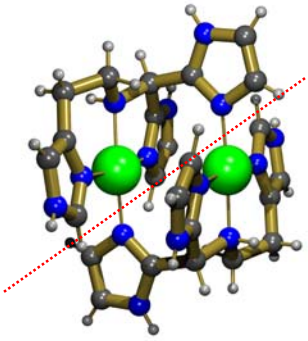
Enforcing a dinuclear Cu(II) species when the ligand cannot chelate



No space for dioxygen in between the Cu ions (Cu--Cu = 350 pm)

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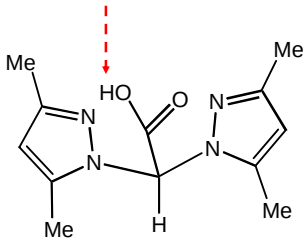
Ligand to control semi-coordination



2 isomeric Cu(II) complexes, each having a different Jahn-Teller axis

Long axis: O-Cu-O and N-Cu-N

HLLL → $Cu(LLL)_2$

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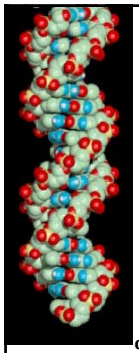

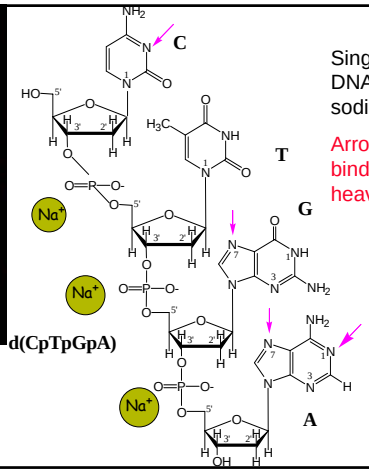

Single-stranded DNA anion with sodium cations;

Arrows are binding sites for heavy metals.

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Interplay of metal binding and hydrogen bonding is important

- Hydrogen-bonding effects often finetune the coordination phenomenon
- In many cases M-L binding is effected by hydrogen bonds.
- In almost all cases of metal-DNA binding, the metal alone cannot be held responsible for binding and stability;
- In very many cases Hydrogen Bonding interferes with M-DNA interactions

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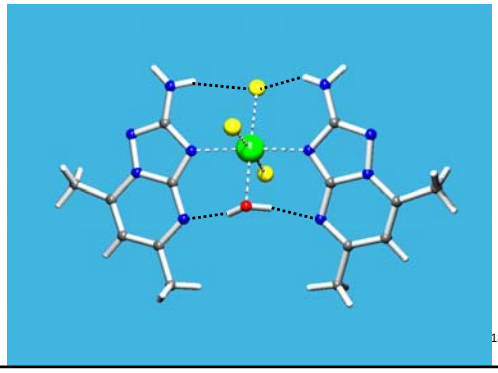
Role of H bonding in Ru-Cl complex



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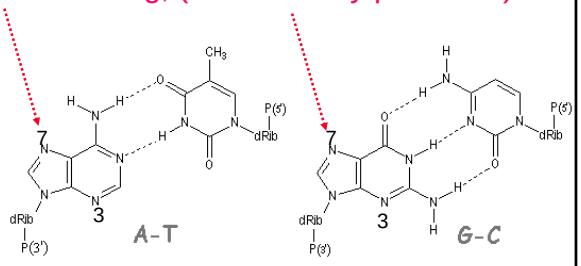
Nucleic acid bases and base pairs: N7 not involved, so it is available for M binding; (N3: sterically protected)



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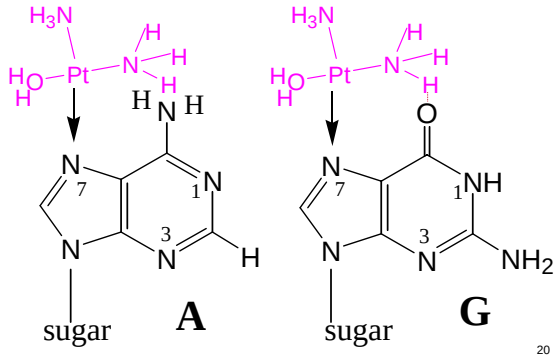
steric repulsion makes A binding weak; H bonding makes G binding strong (200x)



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Ligands for materials science and molecular materials

Use of ligand as building bricks

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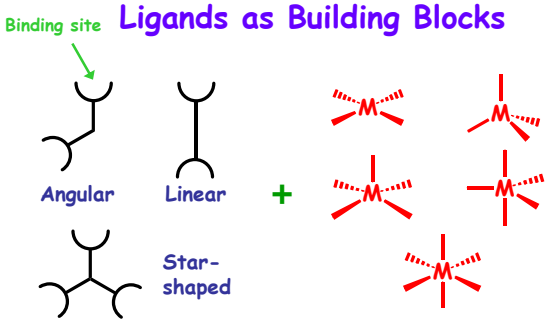
Crystal Engineering: Ligands as Building Blocks



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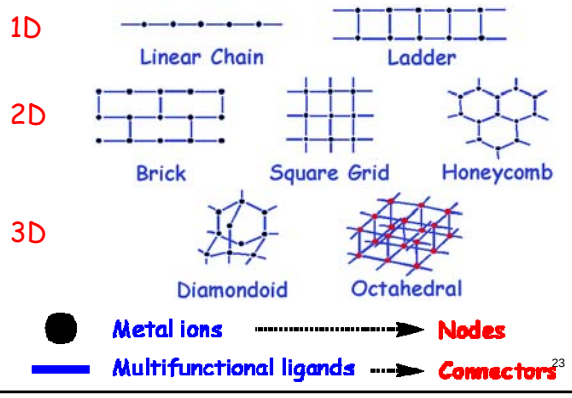
Possible 1D, 2D and 3D Networks



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Ligands to make linear systems: 3, 4, 5, 7, 8 or 9 metals in a row or a cluster

- Semi-Rigid ligands:
- **Examples of structures:**

Too rigid ligand will not for a flexible lattice; too flexible ligands will not form a lattice.

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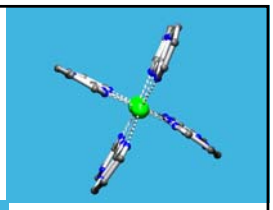
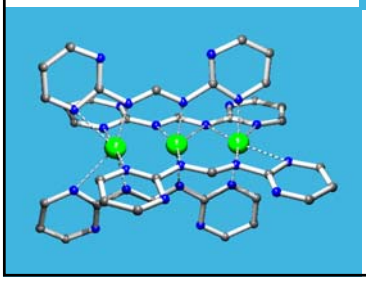
Trinuclear chain





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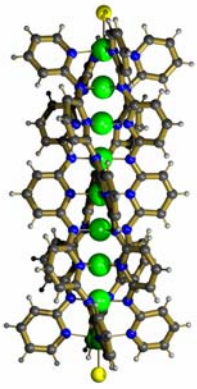
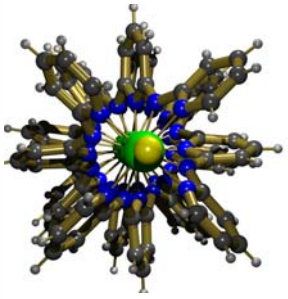
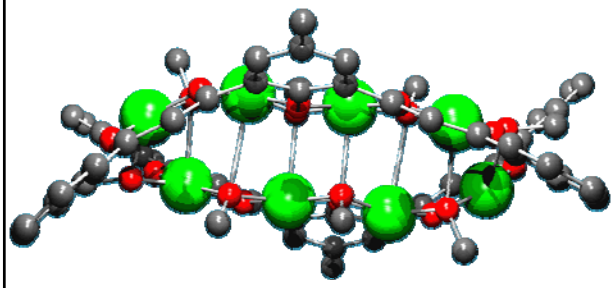
Metals in chains(2)



chain bendings also due to the solid state packing



A new Cu_8 cluster (Aromi et al)



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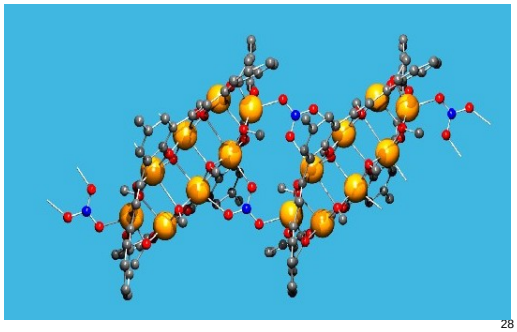
A new double Cu_8 cluster (Aromi)



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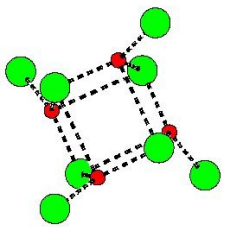
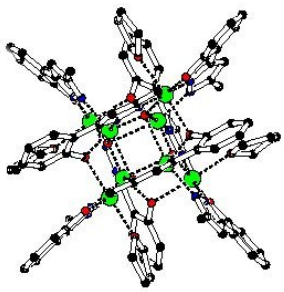
Mn_8 clusters of high symmetry Tanase-Grecea, chem. comm.





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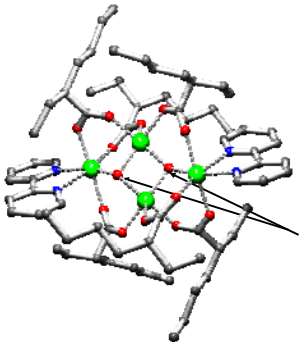
3D structure of $Mn_4O_2(bpy)_2(2\text{-ethylhexanoate})_6$



Mixed valence!

2 Mn^{2+}
2 Mn^{3+}
6 2-ethylhexanoate
2 bipyridine
2 O^{2-}

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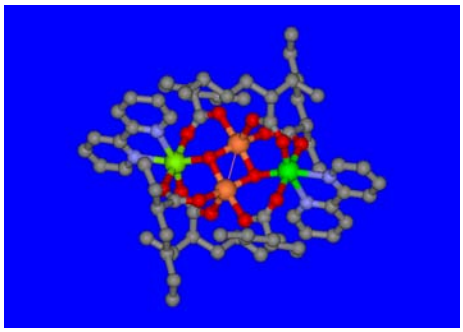
3D structure of $Mn_4O_2(bpy)_2(2\text{-ethylhexanoate})_6$



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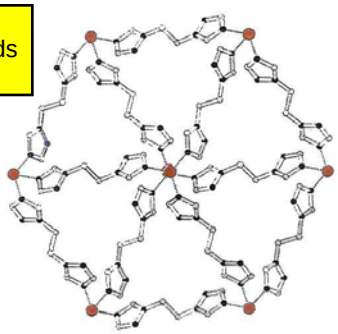
Polymeric 3D systems with bis(azole)alkane bridges

cage compounds MOFs



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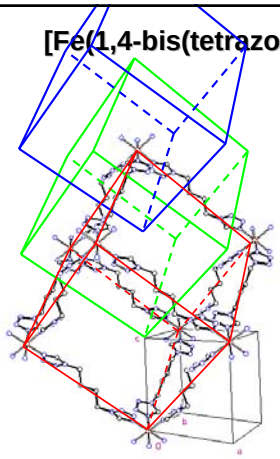
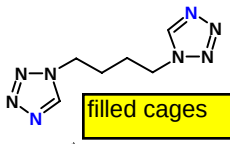
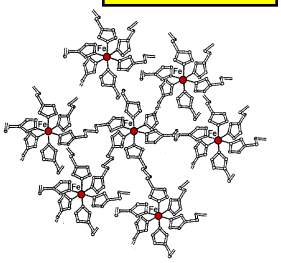
$[Fe(1,4\text{-bis(tetrazol-1-yl)butane})_3](ClO_4)_2$



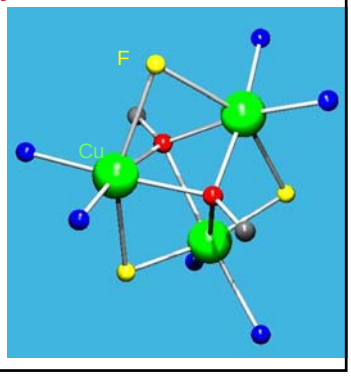


filled cages



Lattice of trinuclear clusters, bridged by F and OMe

N atoms are part of aminopyridazine



Ligands to control the second coordination sphere

- Solubility (in water, or in a hydrophobic medium)
- Stacking with other species in solution, or on a reaction substrate
- Recognition site on a cell surface or a polymer
- Binding to a surface (e.g. electrode)

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Ligands with a second chemical function

- For binding of second (or third) metal,
- Intercalator attachment,
- Recognition site (e.g. at a cell surface),
- Generation of a switch (upon binding, or after an external effect, such as light or redox),
- Several functions in addition, or even in synergy.

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The binding site

- **Stability**: needed to bind metal, control by chelate or macrocyclic effect, ligand type (class A or B)
- **Structure:** control by denticity, steric effects
- **Lability:** decreases with multidentate or macrocyclic ligands, rigid ligands

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The bridge

- Provides a mechanical linkage between sites
- May also provide electronic or magnetic linkage
- Must be flexible enough to allow the formation of the complex
- Must not be too flexible, or chelation may replace bridging, and stereochemical information will be lost

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Ancillary groups may have:

- Structural effects: steric bulk (blocking of conformations), intramolecular attractions
- Links beyond the outer sphere: H-bonding, stacking interactions, coordination
- Solubility enhancement
- Spectroscopic probes – diastereotopic protons, chromophores

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Functions

May be included at any point of the structure

- Chromophores
- Luminophores
- Electrochemical centres
- Reactivity (e.g. hydronation, coordination)
- Magnetism (unpaired electrons)

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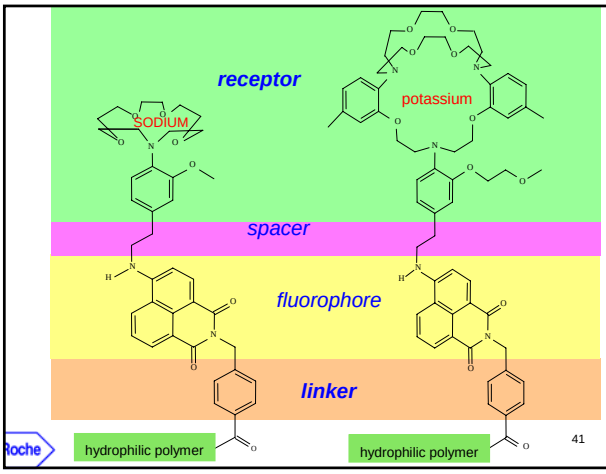

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3 Sections on details

- 1. Metal anticancer and Metal-DNA
- 2. Molecular Materials
- 3. Metal (biomimetic) complexes in catalysis

- (in 3 later, separate handouts as pdf).

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