Computational Material Science
Part I

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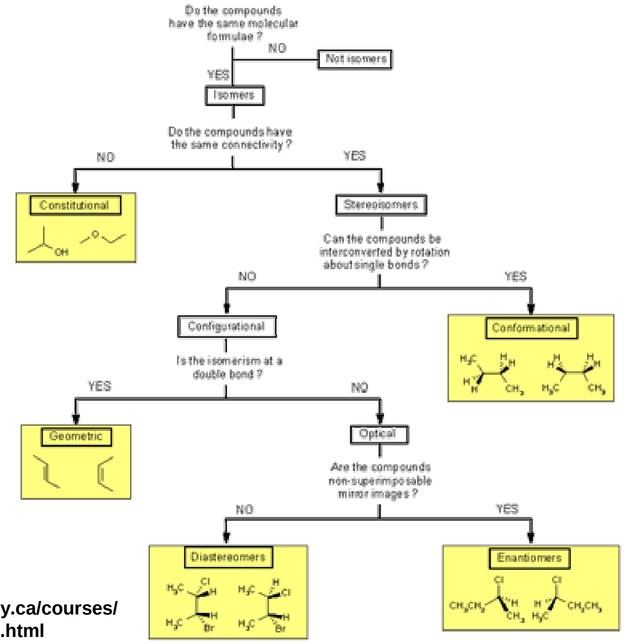
Types of isomers



http://www.chem.ucalgary.ca/courses/351/Carey5th/Ch07/ch7-1.html

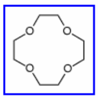
- **Isomers** are compounds with the same molecular formulae but that are structurally different in some way. It is important to be able to recognise isomers because they can have different chemical, physical properties and biological properties.
- **Constitutional** isomers differ in the order in which the atoms are connected so they can contain different functional groups and / or bonding patterns (*e.g.* branching)
- **Stereoisomers** have the same functional groups and connectivities, they differ only in the arrangement of atoms and bonds in space.
- **Conformational** isomers (or **conformers** or **rotational isomers** or **rotamers**) are stereoisomers produced by rotation about Ïƒ bonds, and are often rapidly interconverting at room temperature
- **Configurational** isomers are stereoisomers that do not readily interconvert at room temperature and can (in principle at least) be separated.
- **Geometric** isomers are configurational isomers that differ in the spatial position around a bond with restricted rotation (*e.g*. a double bond)
- **Optical** isomers are configurational isomers that differ in the 3D relationship of the substituents about one or more atoms.
- **Enantiomers** are optical isomers that are non-superimposable mirror images.
- **Diastereomers** are stereoisomers that are not enantiomers

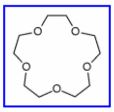
- Do not compare steric energies of compounds that have different atom connectivities

  --energies of constitutional isomers are not comparable….

Applications of MM

- **Design molecules to bind alkali metal cations (Li^+, Na^+, K^+…):**
  - **Salts does not dissolve well in nonpolar solvent, but with the help of crown ether, they can be brought into nonpolar solvent**
  - **Different size of crown ether binds different metal cations**


12-crown-4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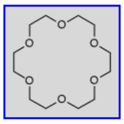
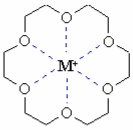
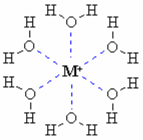

18-crown-6

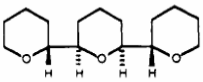


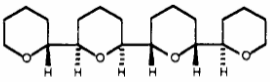
complex



hydration of a metal ion

- **While crown ether binds cations well, acyclic glyme ether, $MeO(CH_2CH_2O)_nMe$, does not bind as well due to entropy reasons.**
- ***Design nonmacrocyclic host; can it compete with cyclic analogs?***


1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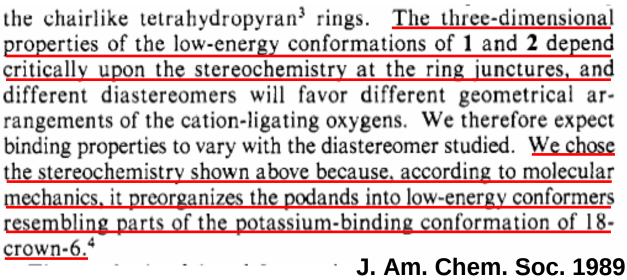
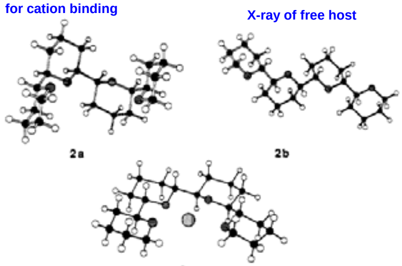

the chairlike tetrahydropyran[3] rings. The three-dimensional properties of the low-energy conformations of **1** and **2** depend critically upon the stereochemistry at the ring junctures, and different diastereomers will favor different geometrical arrangements of the cation-ligating oxygens. We therefore expect binding properties to vary with the diastereomer studied. We chose the stereochemistry shown above because, according to molecular mechanics, it preorganizes the podands into low-energy conformers resembling parts of the potassium-binding conformation of 18-crown-6.[4]

J. Am. Chem. Soc. 1989, 111, 3439

Molecule	(Number of conformers within 3 kcal/mol of global minimum from united AMBER force field calc.)
1	(10)
2	(25)
Diglyme	(80)
Triglyme	(>750)



Low E conformer preorganized for cation binding

X-ray of free host

X-ray of host and sodium

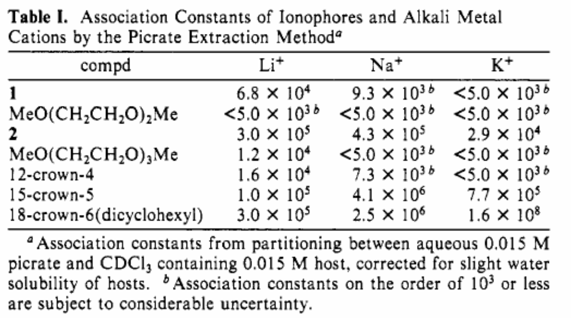


Table I. Association Constants of Ionophores and Alkali Metal Cations by the Picrate Extraction Method[a]

compd	Li^+	Na^+	K^+
1	6.8×10^4	$9.3 \times 10^{3\,b}$	$<5.0 \times 10^{3\,b}$
$MeO(CH_2CH_2O)_2Me$	$<5.0 \times 10^{3\,b}$	$<5.0 \times 10^{3\,b}$	$<5.0 \times 10^{3\,b}$
2	3.0×10^5	4.3×10^5	2.9×10^4
$MeO(CH_2CH_2O)_3Me$	1.2×10^4	$<5.0 \times 10^{3\,b}$	$<5.0 \times 10^{3\,b}$
12-crown-4	1.6×10^4	$7.3 \times 10^{3\,b}$	$<5.0 \times 10^{3\,b}$
15-crown-5	1.0×10^5	4.1×10^6	7.7×10^5
18-crown-6(dicyclohexyl)	3.0×10^5	2.5×10^6	1.6×10^8

[a] Association constants from partitioning between aqueous 0.015 M picrate and $CDCl_3$ containing 0.015 M host, corrected for slight water solubility of hosts. [b] Association constants on the order of 10^3 or less are subject to considerable uncertainty.

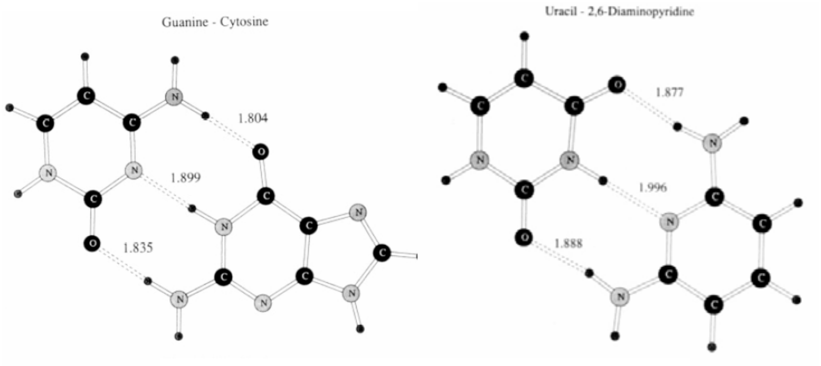
- 1 and 2 bind better than diglyme and triglyme!
- Comparable to crown ether in some cases.

- ***Preorganization desired!***
- ***MM helped with molecular design!***

Additional message

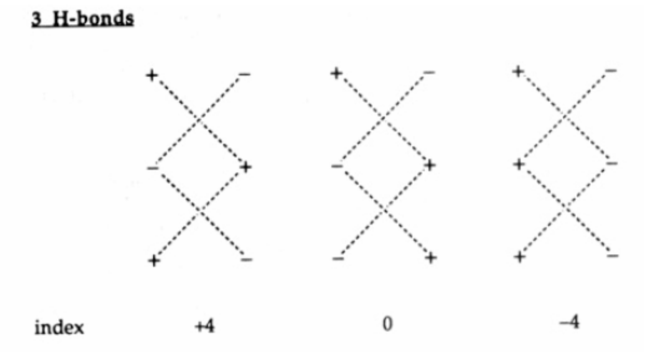
- In the literature, there are ways of systematic and random generation of initial structures.

➢ Importance of secondary interactions in triply hydrogen bonded complexes: Gaunine-Cytosine vs Uracil-2,6-Diaminopyridine



Exptl.		
Association constant:	10^4 M^{-1}	10^2 M^{-1}
Calcd.		
Binding energy:	-22.1 kcal mol^{-1}	-11.4 kcal mol^{-1}

- Rationalization based on electrostatic interactions

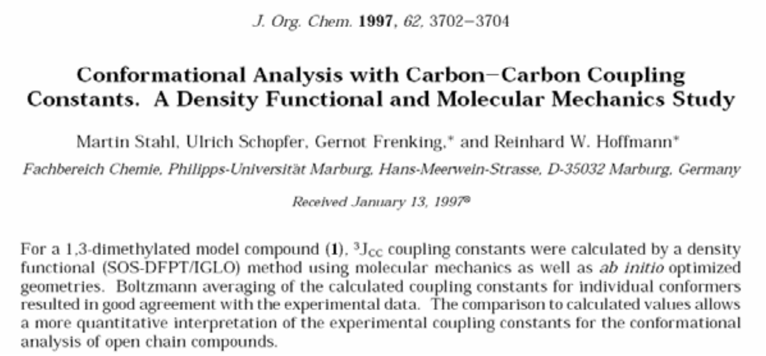


repulsive **attractive**

U ••• D **G ••• C**

➢Getting results in line with experimental results is only the first step. Analysis and rationalization are important!

➢ Decipher spectral information using MM and Boltzmann averaging



J. Org. Chem. **1997**, *62*, 3702–3704

Conformational Analysis with Carbon–Carbon Coupling Constants. A Density Functional and Molecular Mechanics Study

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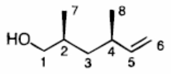
Received January 13, 1997[⊗]

For a 1,3-dimethylated model compound (**1**), $^3J_{CC}$ coupling constants were calculated by a density functional (SOS-DFPT/IGLO) method using molecular mechanics as well as *ab initio* optimized geometries. Boltzmann averaging of the calculated coupling constants for individual conformers resulted in good agreement with the experimental data. The comparison to calculated values allows a more quantitative interpretation of the experimental coupling constants for the conformational analysis of open chain compounds.



1

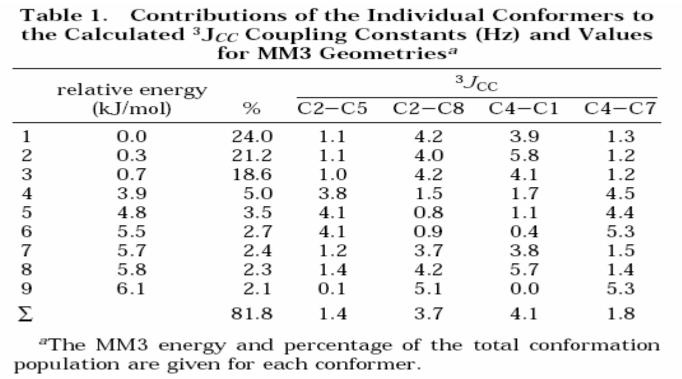


Table 1. Contributions of the Individual Conformers to the Calculated $^3J_{CC}$ Coupling Constants (Hz) and Values for MM3 Geometries[a]

	relative energy (kJ/mol)	%	$^3J_{CC}$			
			C2–C5	C2–C8	C4–C1	C4–C7
1	0.0	24.0	1.1	4.2	3.9	1.3
2	0.3	21.2	1.1	4.0	5.8	1.2
3	0.7	18.6	1.0	4.2	4.1	1.2
4	3.9	5.0	3.8	1.5	1.7	4.5
5	4.8	3.5	4.1	0.8	1.1	4.4
6	5.5	2.7	4.1	0.9	0.4	5.3
7	5.7	2.4	1.2	3.7	3.8	1.5
8	5.8	2.3	1.4	4.2	5.7	1.4
9	6.1	2.1	0.1	5.1	0.0	5.3
Σ		81.8	1.4	3.7	4.1	1.8

[a] The MM3 energy and percentage of the total conformation population are given for each conformer.

Experimental	**1.4**	**3.3**	**3.8**	**2.2**

- ➢ **If different configurational isomers (stereoisomers) are calculated, the results will help to assign the absolute configuration of a molecule**