Artificial Molecular Machinery

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PART 3
From simple molecules to complex materials

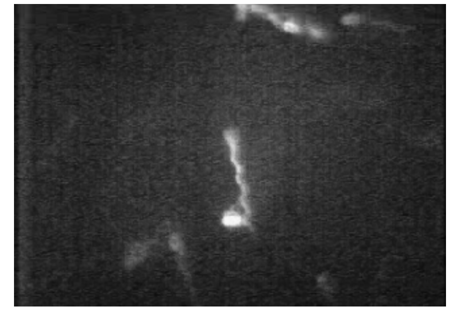
PREMISE : Artificial and Biomolecular Machines are Densely Packed Multicomponent Assemblies (1D, 2D and 3D Crystals)

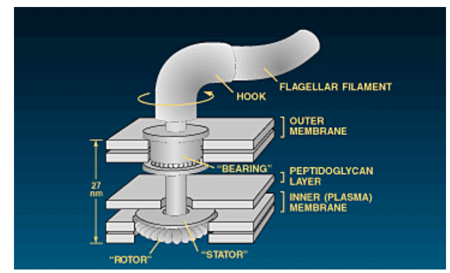
Types of Motion (Periodic)
- ***—Rotary***
- ***—Oscillatory***

Functional Design
- ***—Free Volume***
- ***—Volume Conserving Motions***
- ***—Correlated Motions***

Khuong et al, *Acc. Chem. Res.* **2006**, *39*, 413-422.

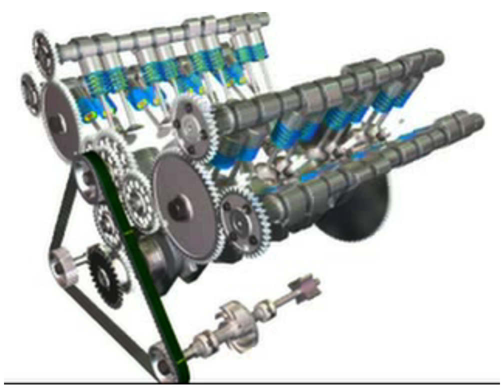
Bacterial flagellum



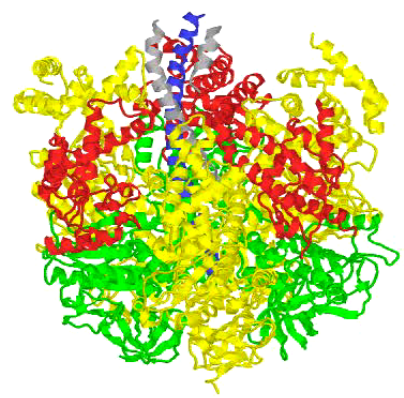


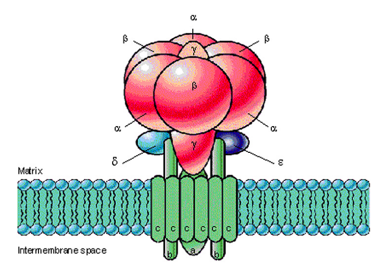
H.C. Berg, Rowland Institute

Internal combustion engine



ATPase



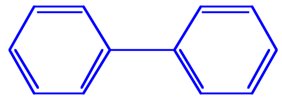


Wang & Oster, UC Berkeley

What Do We Know About Dynamics and Order in Dense Media?

Condensed Phase Matter and Molecular Dynamics (Crystals of molecules with arbitrary shapes)

Diffusion:

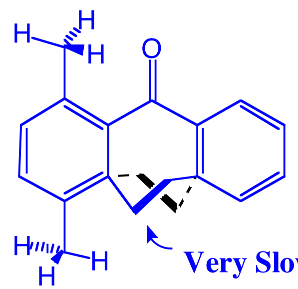


$D = 7 \times 10^{-16}\ m^2\ s^{-1}$

$D = 7 \times 10^{-7}\ nm^2\ ns^{-1}$

Conformational Motions

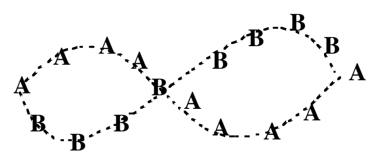
Very fast $>10^9\ s^{-2}$



Very Slow

Phonons: *STATIC:* A B A B A B A B A B A B A B A B A

OPTICAL PHONONS

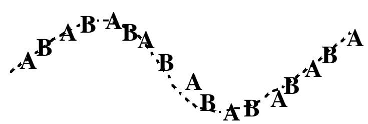


$\lambda \sim 0.01$ cm

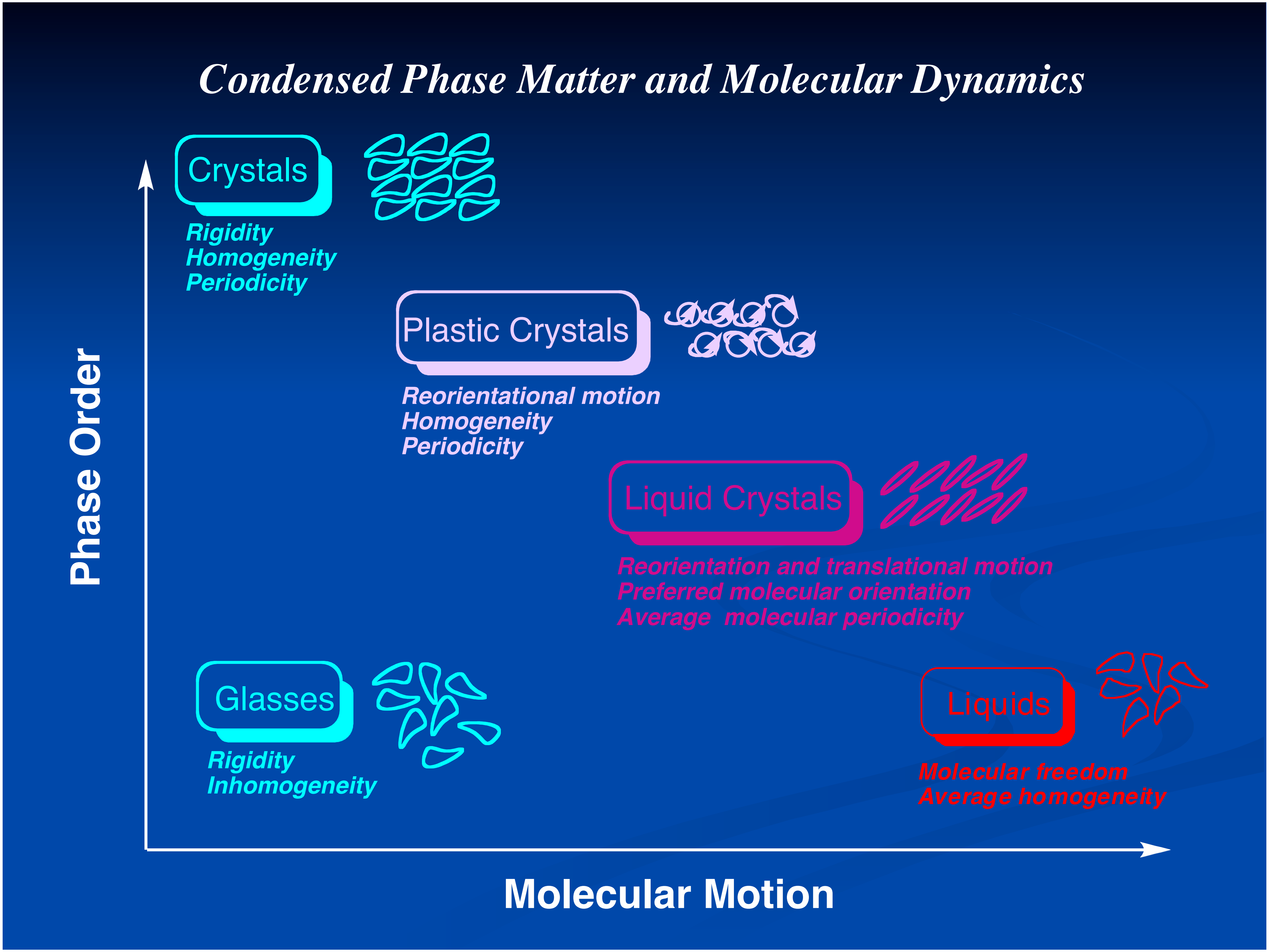
$v \sim 100\ cm^{-1}$

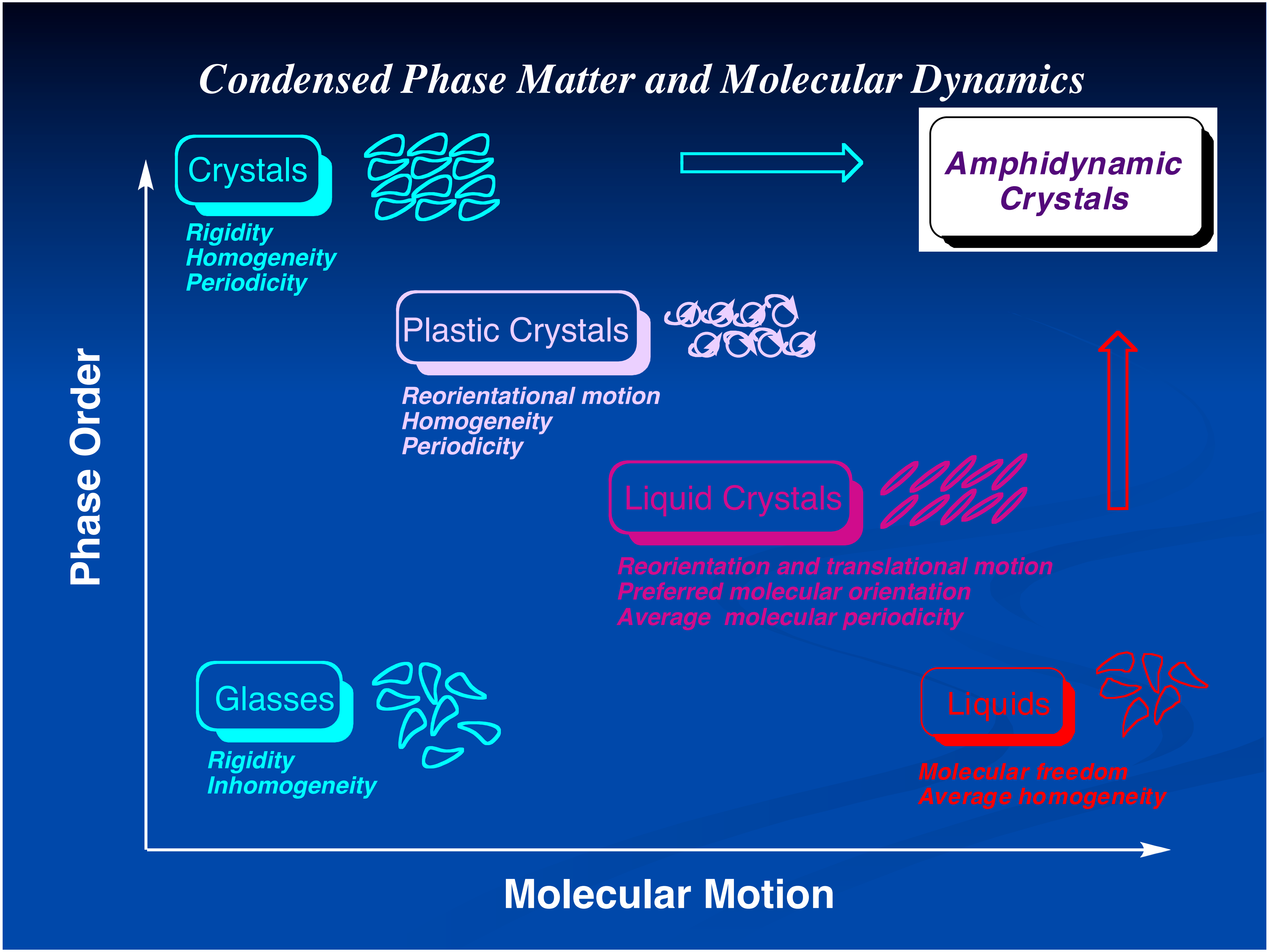
$(\sim 10^{12}\ s^{-1})$

ACOUSTIC PHONONS



Statistical theories of crystal packing


Condensed Phase Matter and Molecular Dynamics
Crystals
Rigidity
Homogeneity
Periodicity
Plastic Crystals
Reorientational motion
Homogeneity
Periodicity
Liquid Crystals
Reorientation and translational motion
Preferred molecular orientation
Average molecular periodicity
Glasses
Rigidity
Inhomogeneity
Liquids
Molecular freedom
Average homogeneity
Phase Order
Molecular Motion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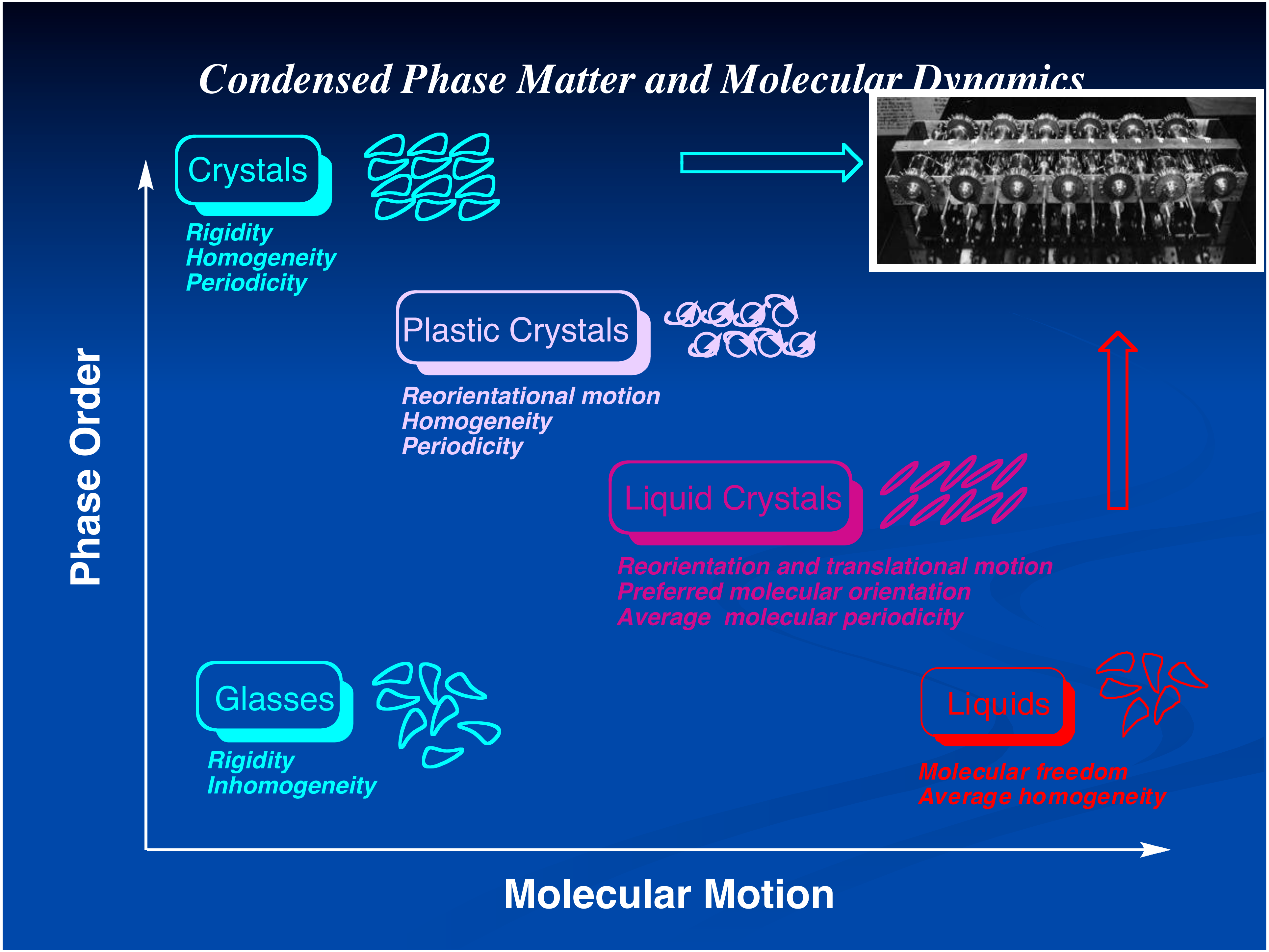
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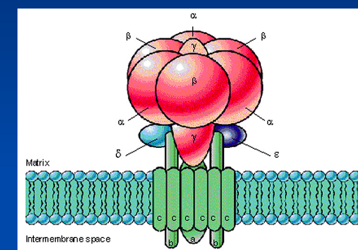
Molecular Motion

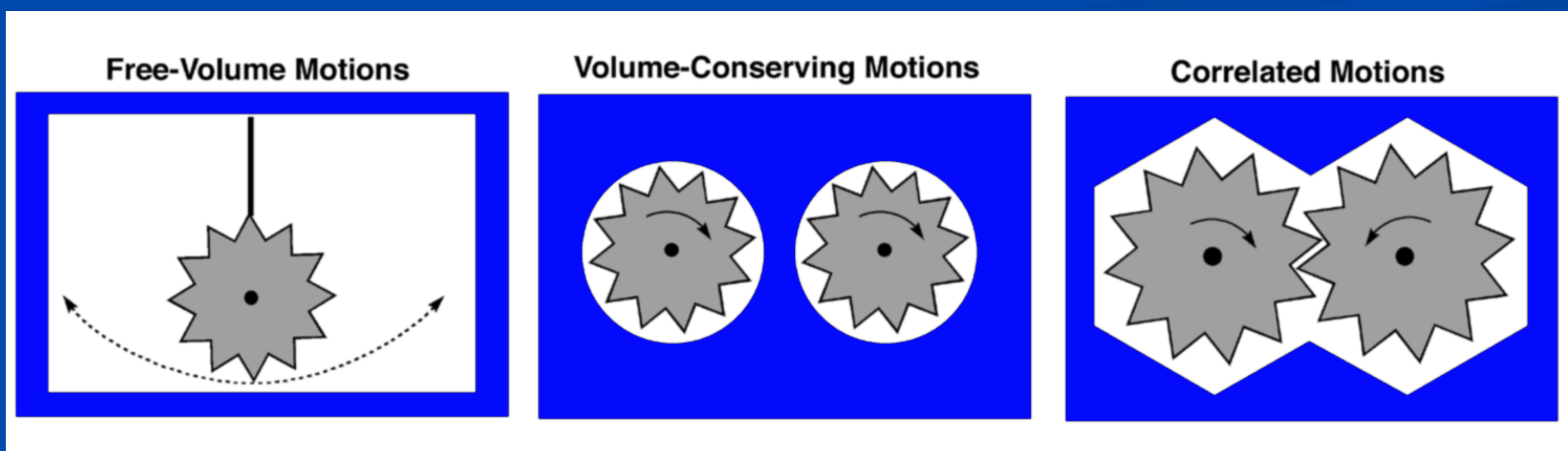
Challenge: Artificial Molecular Machines

I: Emulate structural attributes of macroscopic and biomolecular machines

Motions in dense media demand :
—Free Volume
—Volume-Conserving motions
—Correlated Motions

—Periodic, Rotary, or Oscillatory





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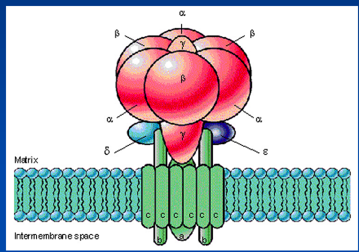


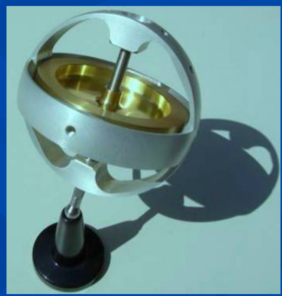
II: Characterize their equilibrium dynamics

—Solid State NMR

—Dielectric spectroscopy

—Electronic, vibrational and microwave spectroscopies

—X-Ray diffraction, Neutron Scattering, computational chemistry, etc.



III: Characterize their dynamics upon external excitation to design input-output processes

Where to Start?

Molecular Rotors!

Compasses and Gyroscopes

(navigational instruments or “machines”)

—Moment of mass and rotary motion
—Angular Momentum

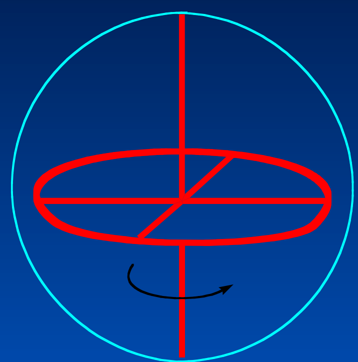
—Magnetic dipole and rotary motion
—Magnetic Moment
—Energy is Orientation Dependent

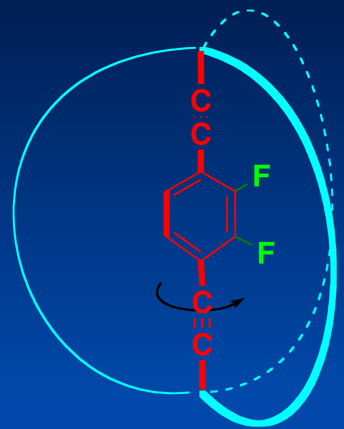
1850’s: Named by Focault
1907: Navigational Machine by H. Anschutz-Kaempfe
1909-1916: Automatic Pilot for ships
… INS in aircraft, missiles, satellites

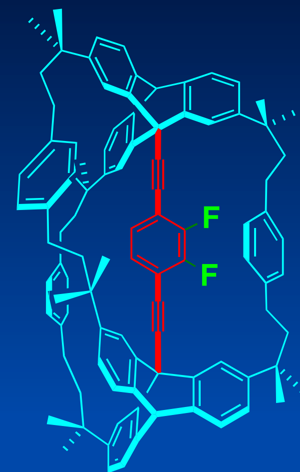
500 BC: First used in china (floating)
700 AC: Needle compass developed
XII AC: First used in Europe
XVII AC: Permanently magnetized steel needles introduced

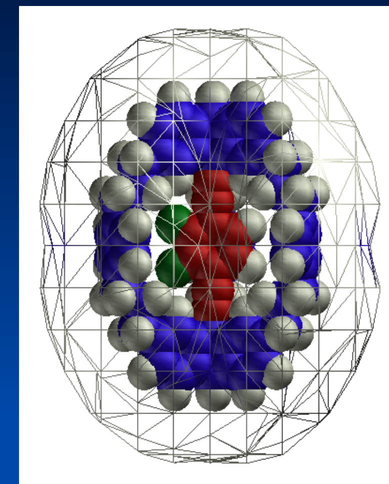
A Promising Model: Gyroscopes and Compasses

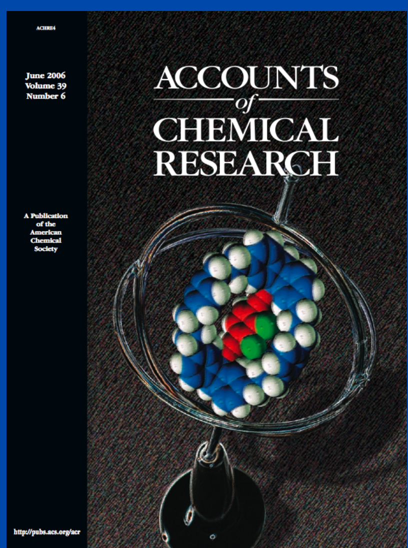
Dynamic Attributes : Free Volume, Volume Conserving, Correlated Processes

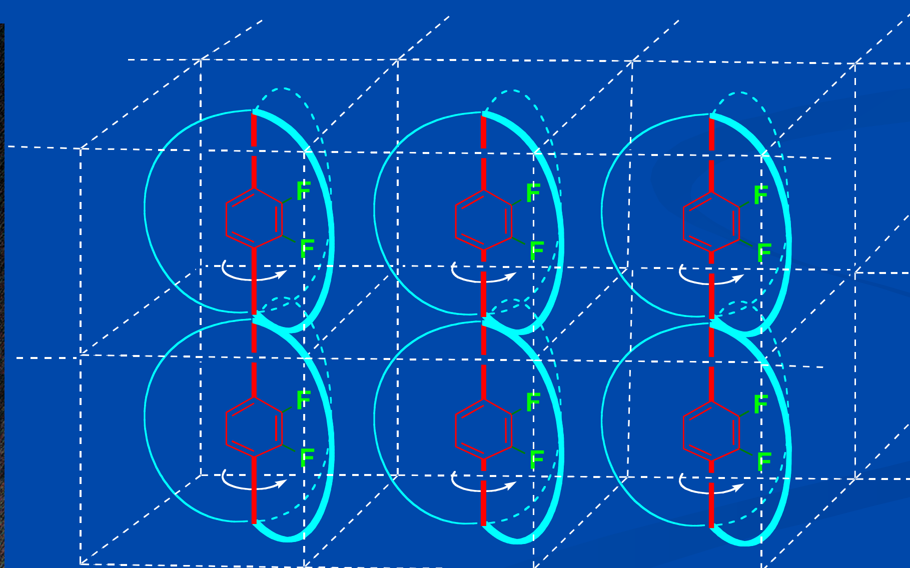












Design Elements (and color code):

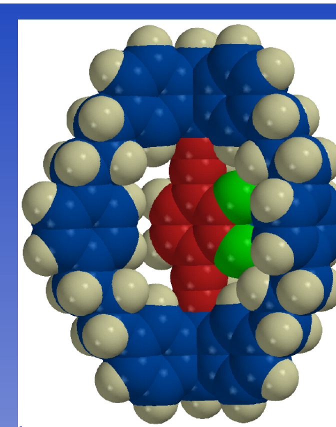
—ROTATOR
(reorienting dipole)

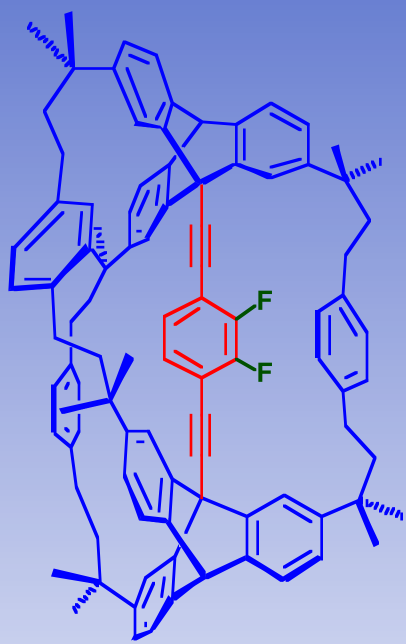
—AXLE
(alkyne linkages)

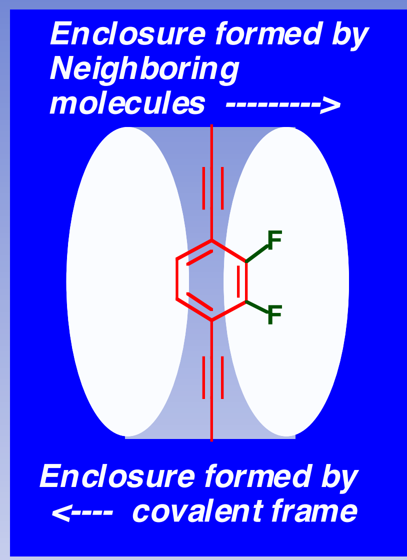
—STATOR
(shielding groups)

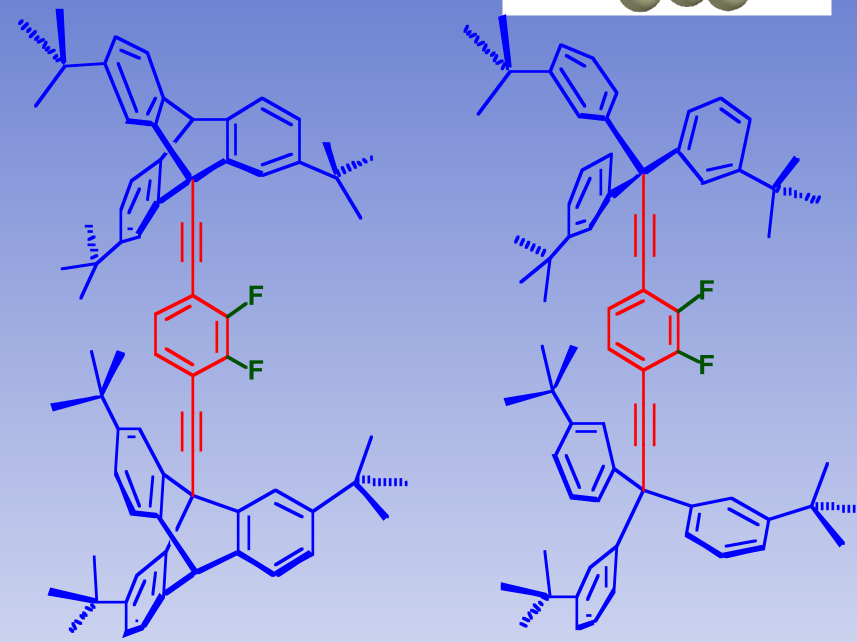
Garcia-Garibay, M. *Proc. Natl. Acad. Sci, USA*, **2005**, *102*, 10771-10776 .
Khuong et al, *Acc. Chem. Res.* **2006**, *39*, 413-422.

Molecular Compasses and Gyroscopes:
STATOR Structures and Topologies





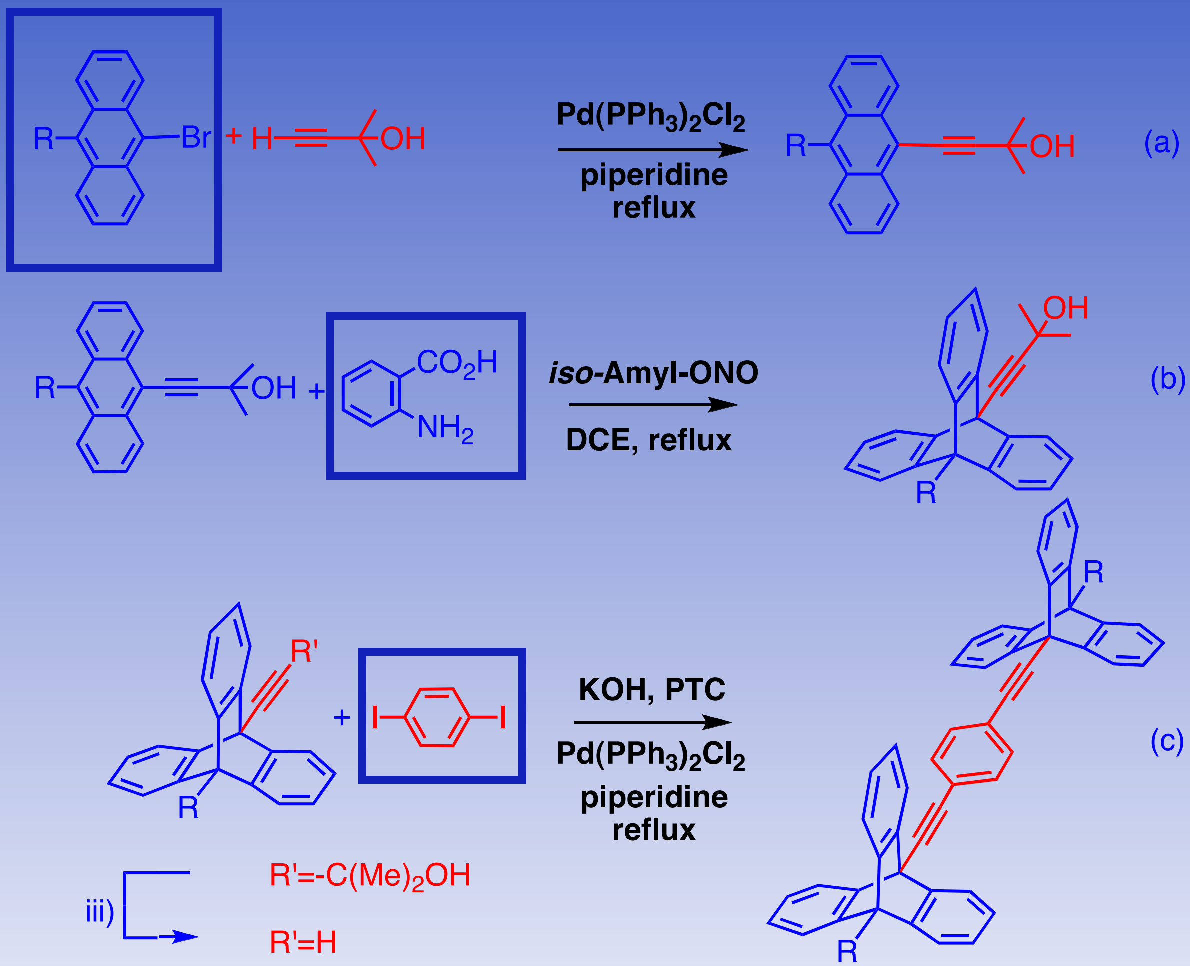


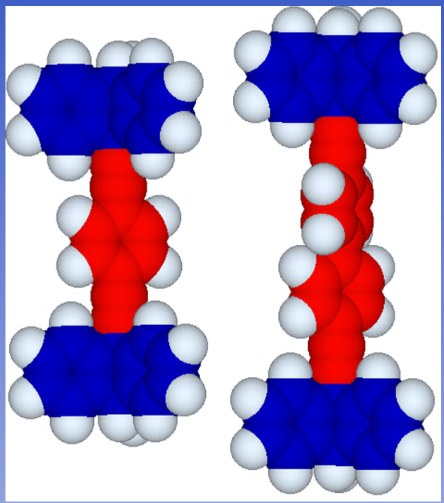


Closed
(triply bridged)

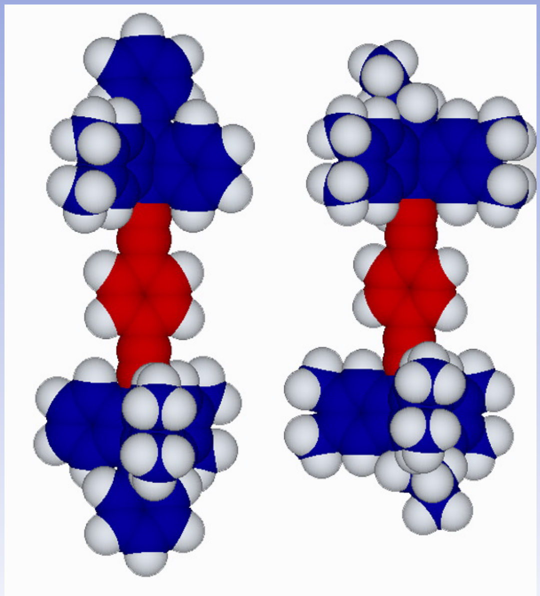
Open
(sterically shielded)

Synthesis of Triptycyl Stators



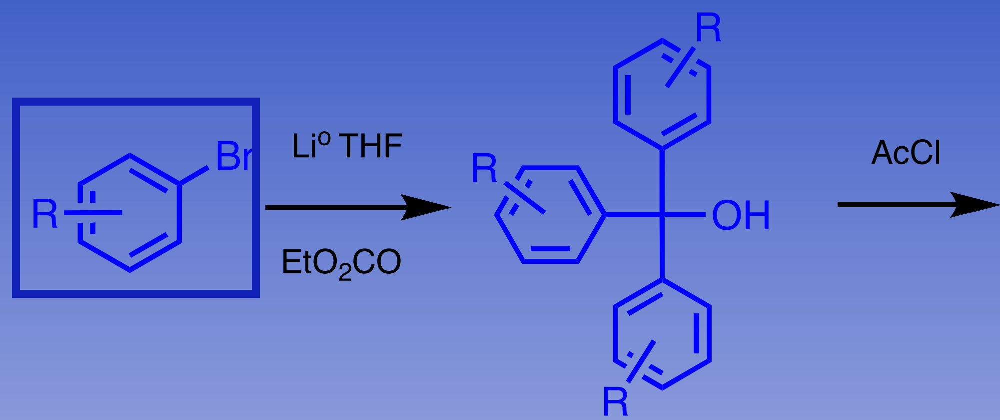


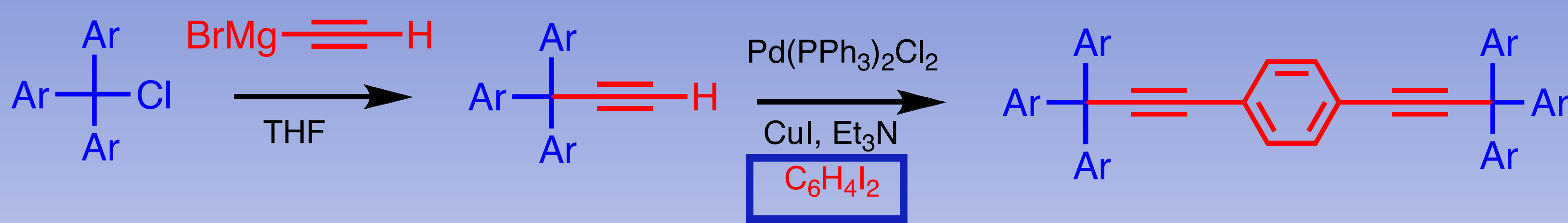
Godinez, Zepeda, Garcia-Garibay
JACS. **2002**, *124*, 4701-4707.

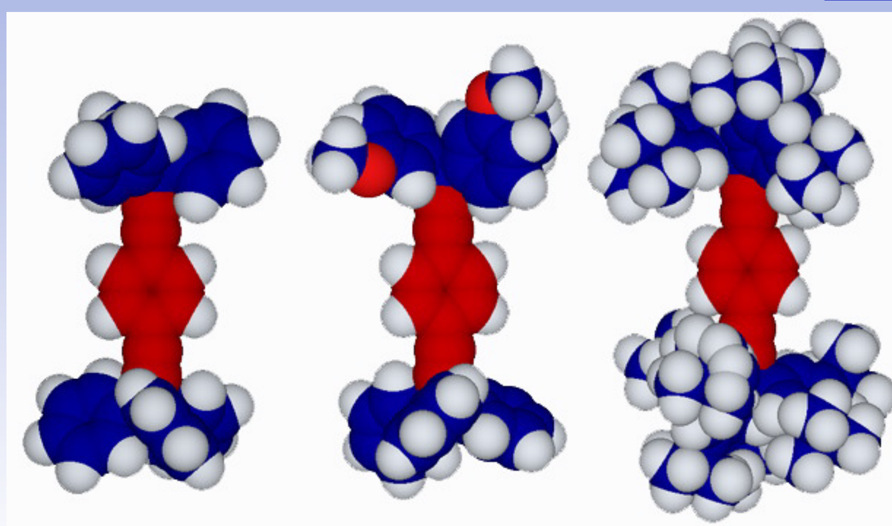


Godinez, Zepeda, Mortko, Garcia-Garibay,
JOC. **2004**, *69*, 1652.

Triarylmethyl Stators





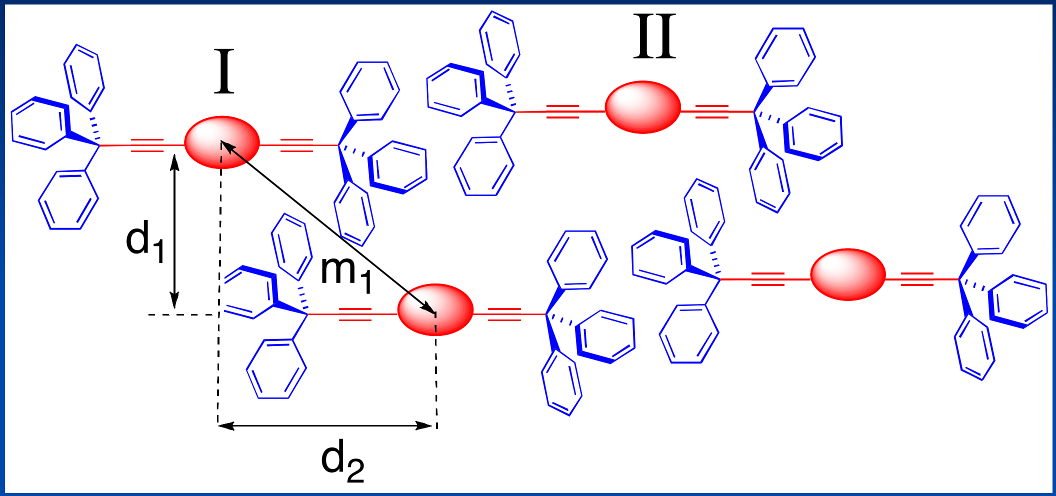


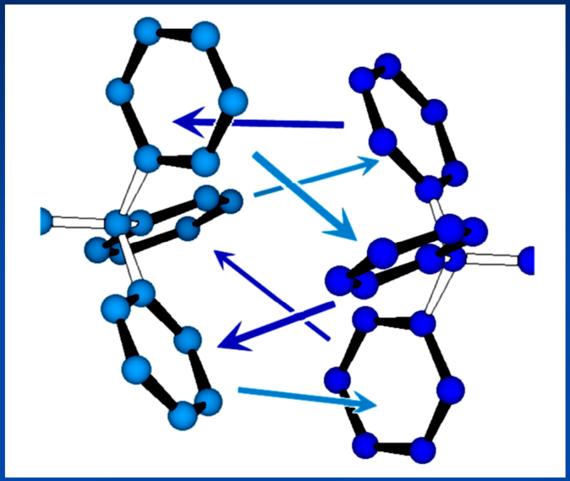
Synthesis:
Dominguez et al. JACS, **2002**, *124*, 2398

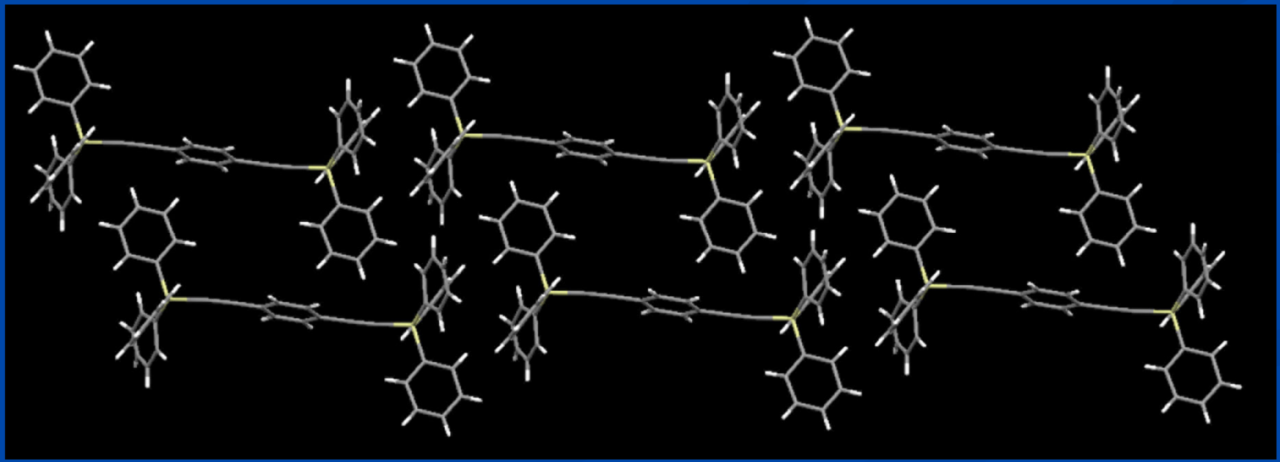
—For analogous structures with Ph_3B- stators:
Gardinier *et al.*, *JACS*. **2005**, *127*, 12448

Packing Rigid Rods with a Six-Fold Phenyl Embrace

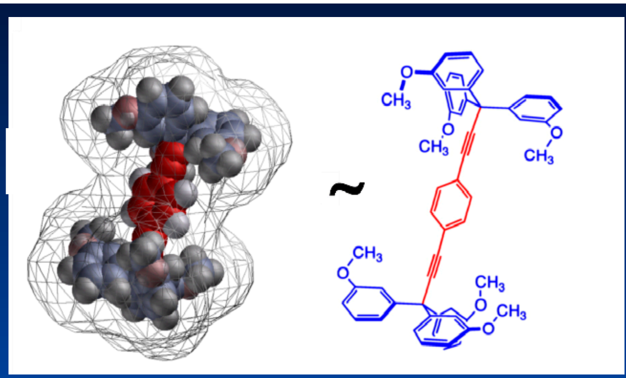
Complementary edge-face interactions

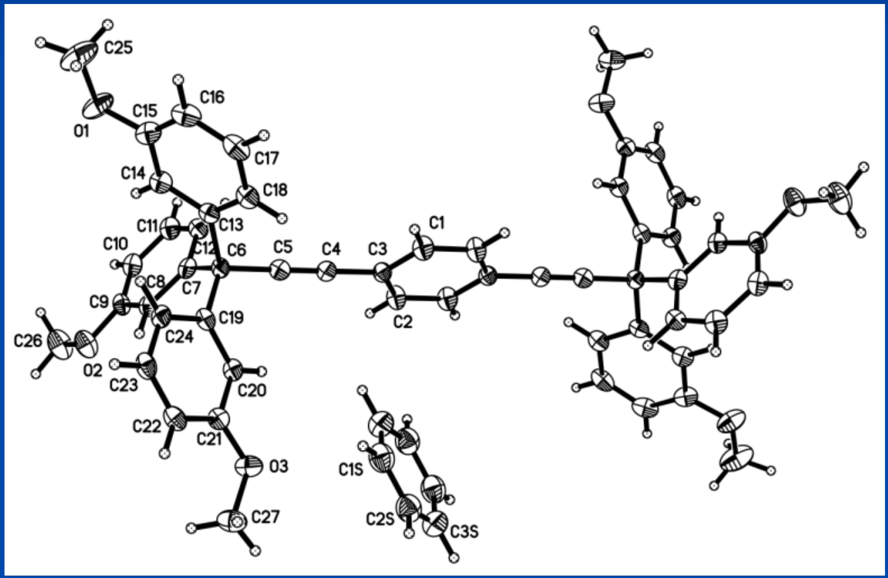






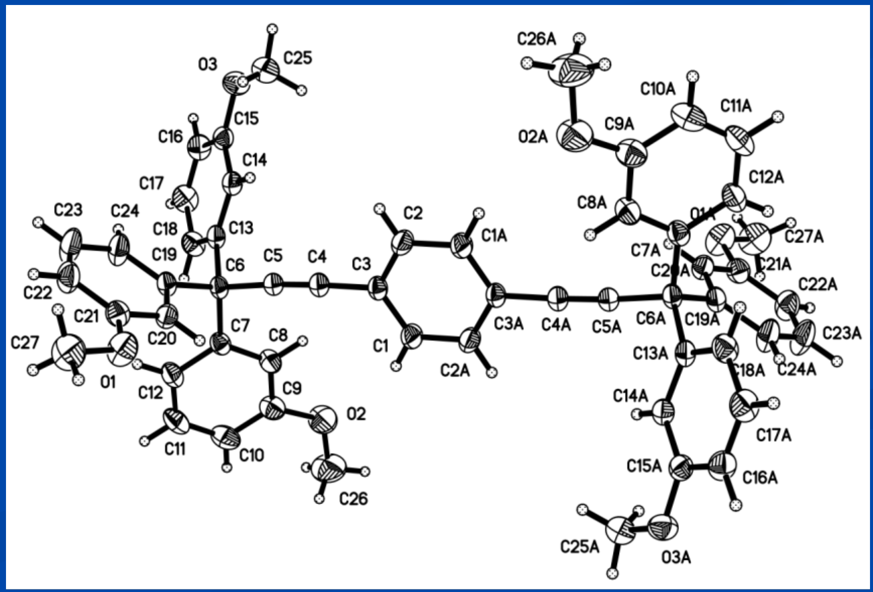
Conformational Diversity and Crystal Forms





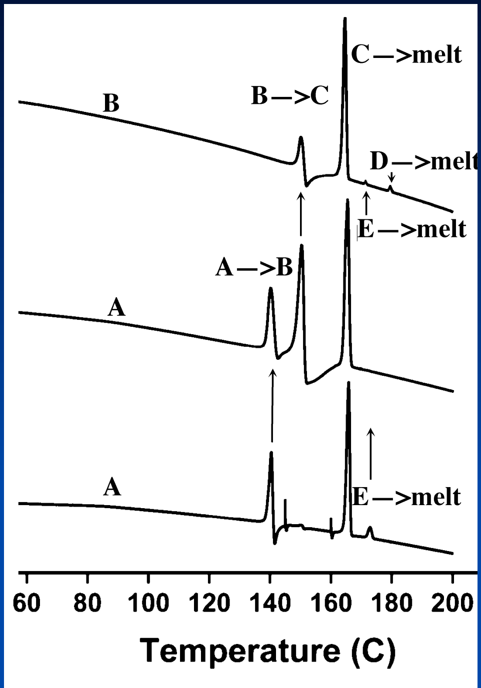
From C_6H_6

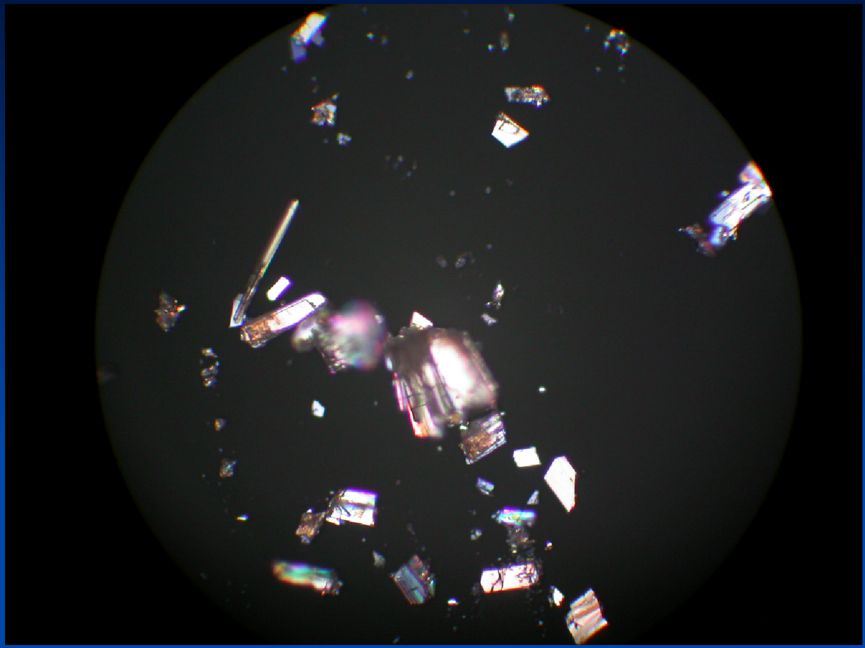
Crystallization from solvents at 298 K
Yields different polymorphs

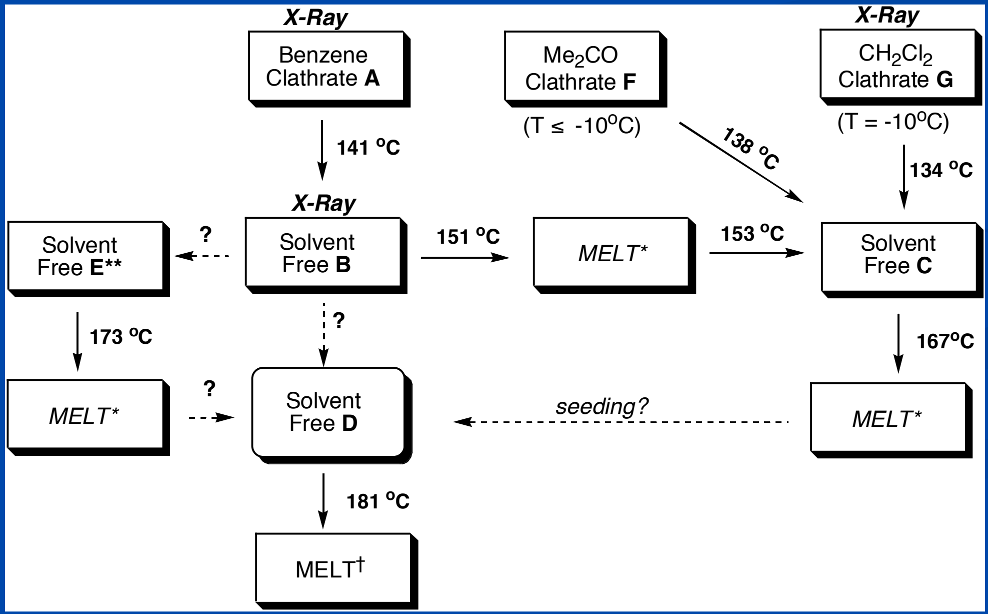


From CH_2Cl_2

DSC, TGA, Thermal microscopy

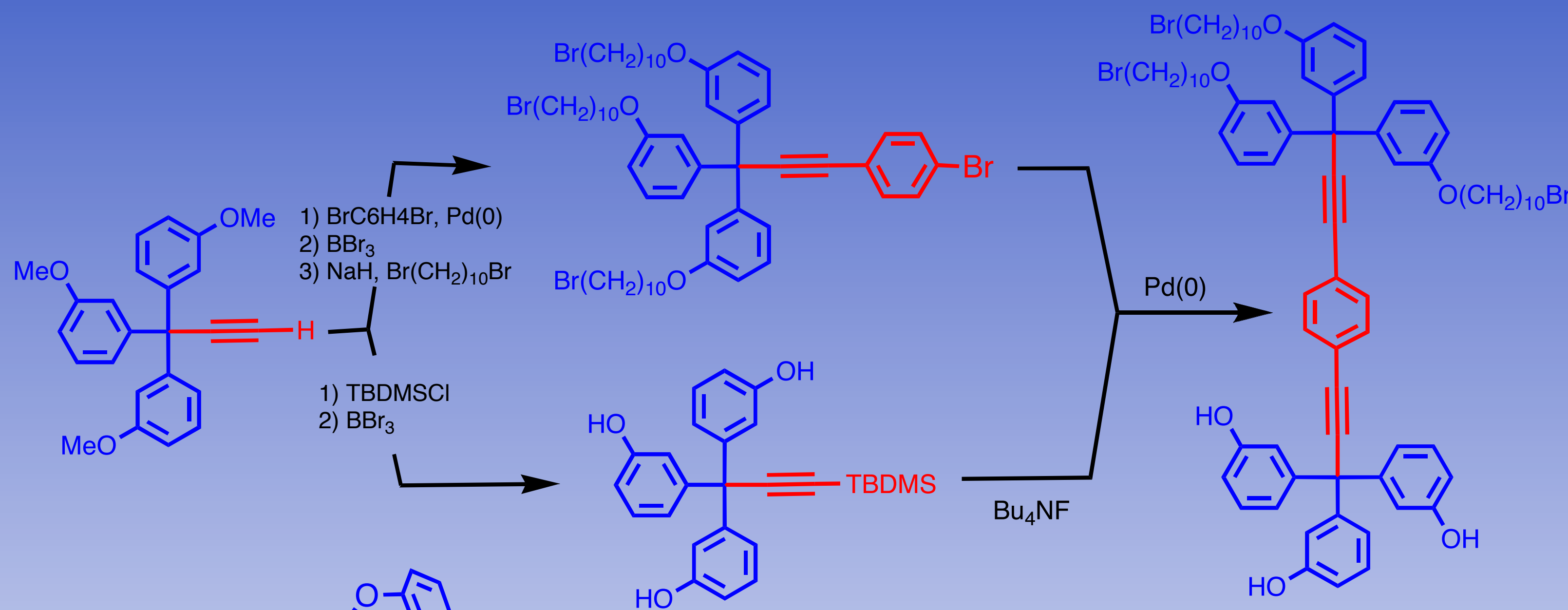


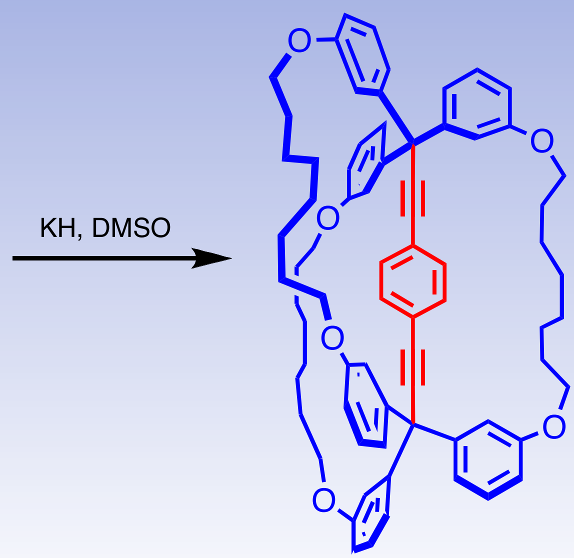




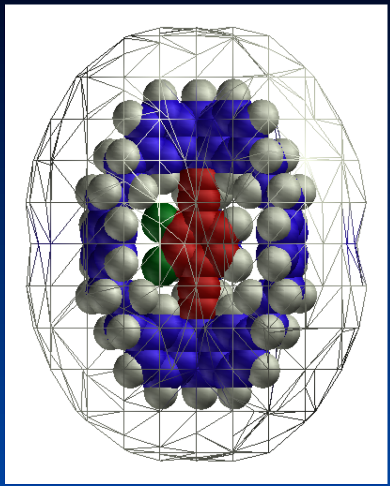
Nuñez, et al. *Cryst. Growth & Design*, **2006**, *6*, 866-873.

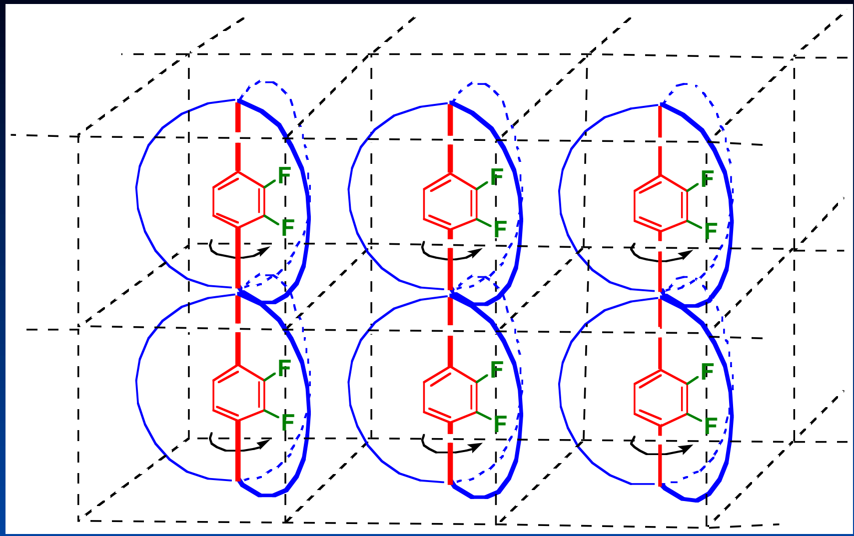
Closed Topologies …

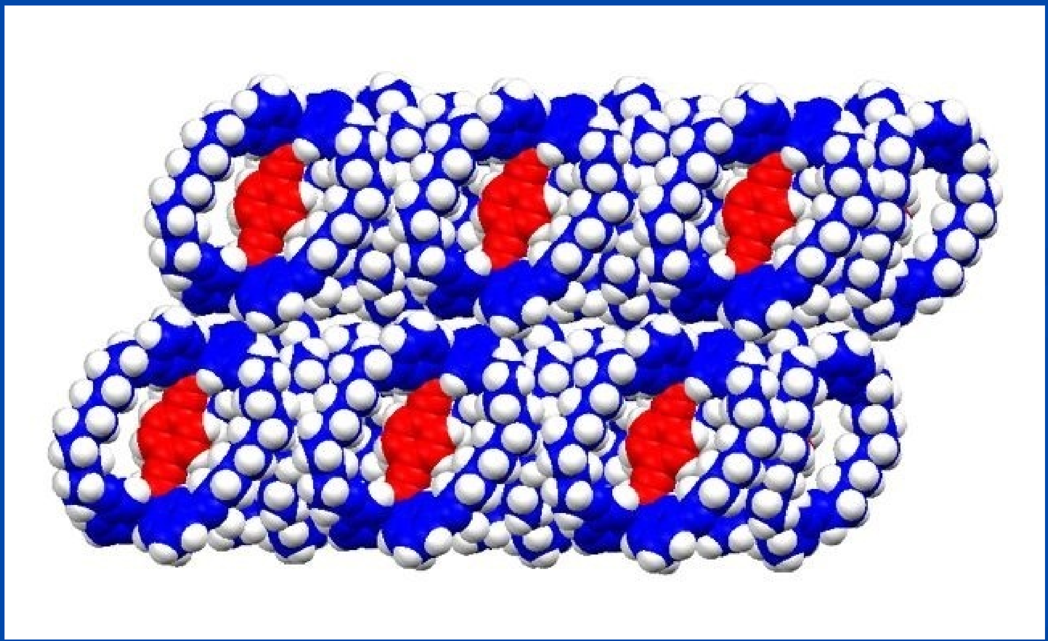




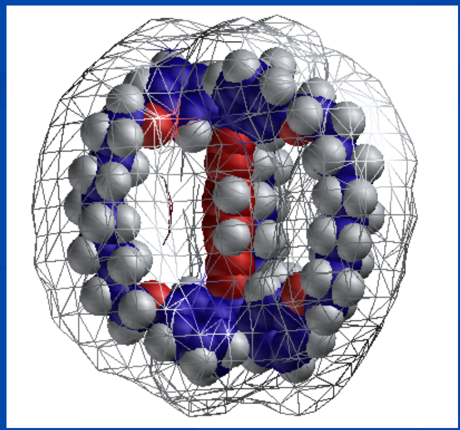
J. Nuñez Org. Letters **2007**, *9*, 3559





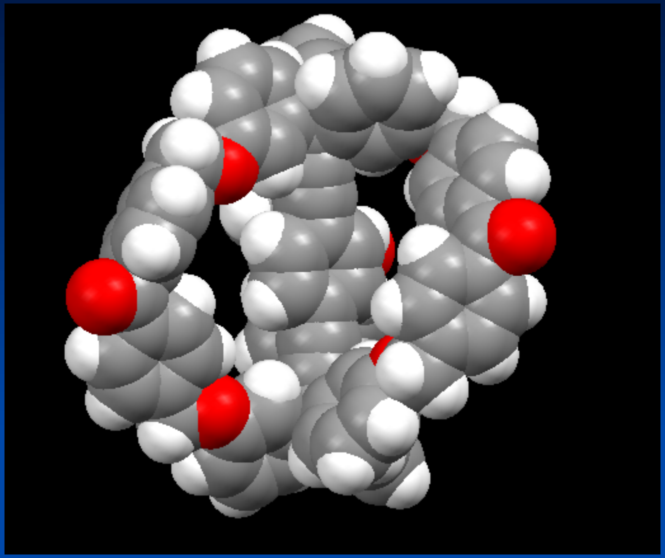


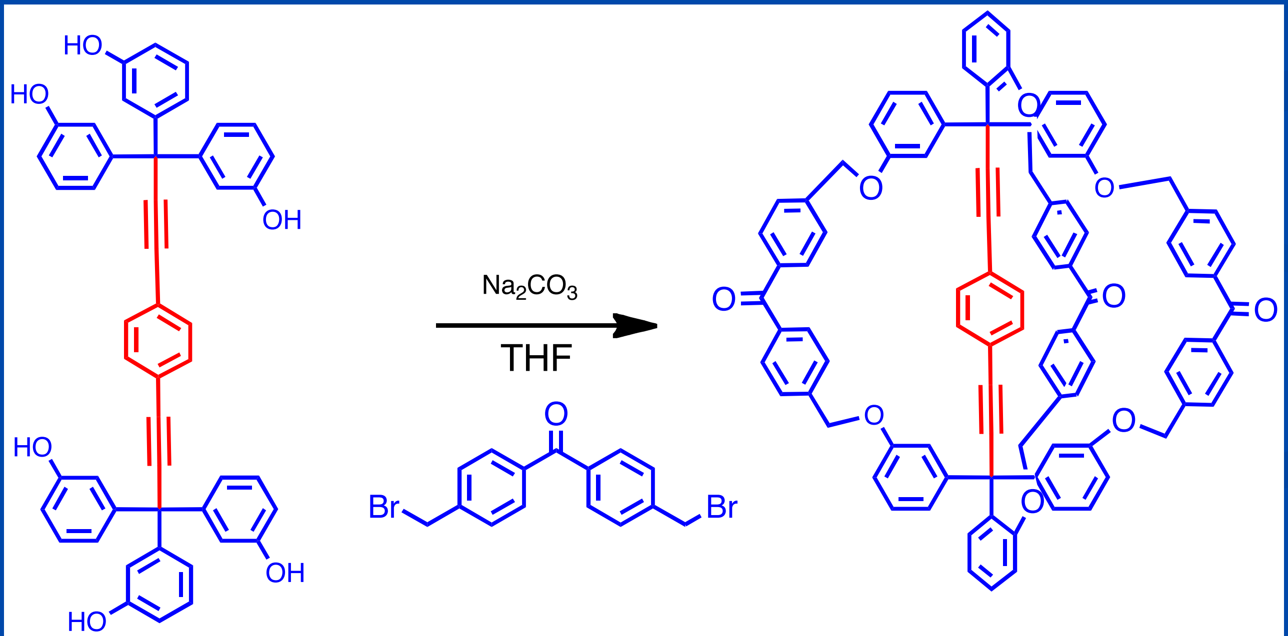
X-Ray



NEED "THICKER" BRIDGES

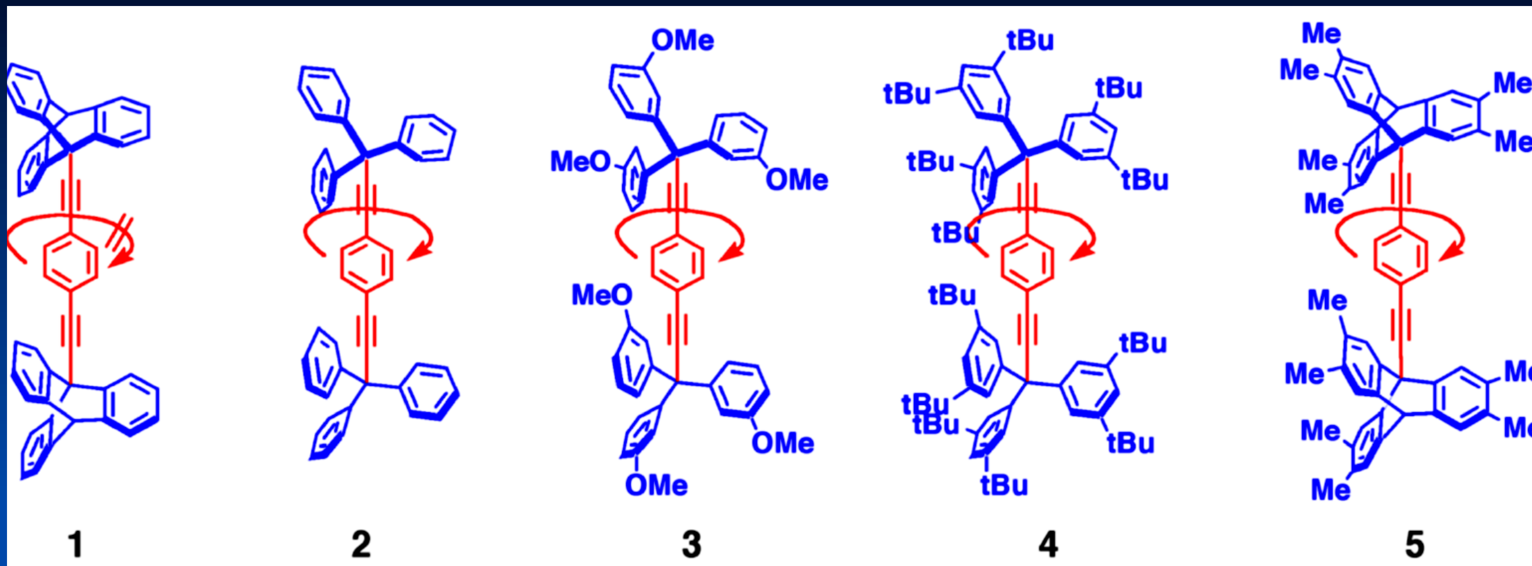
One-Step Synthesis of Triply-Bridged Gyroscopes





Pat Commins

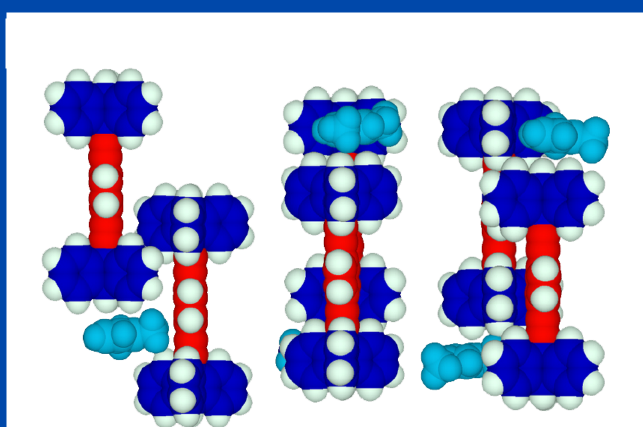
Stator Effects by SSNMR (ca. 0-10^{10} s^{-1})



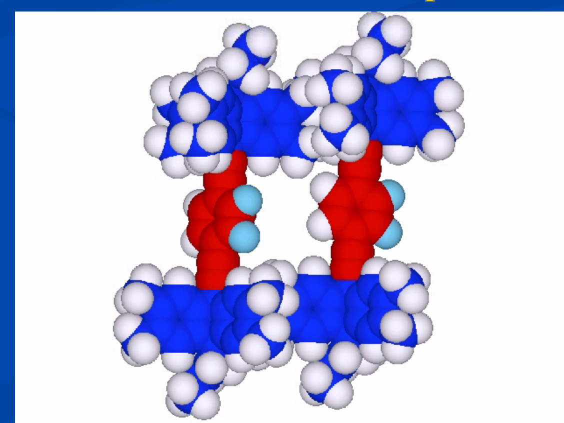
	1	2	3	4	5
k (298)		800 s^{-1}	6000 s^{-1}	> 100x10^{6} s^{-1}	1.11x10^{9} s^{-1}
E_a (kcal/ mol)	>> 20	11.3	10.5	< 5	4.3

This Mac has a 2 GHz processor

1



5

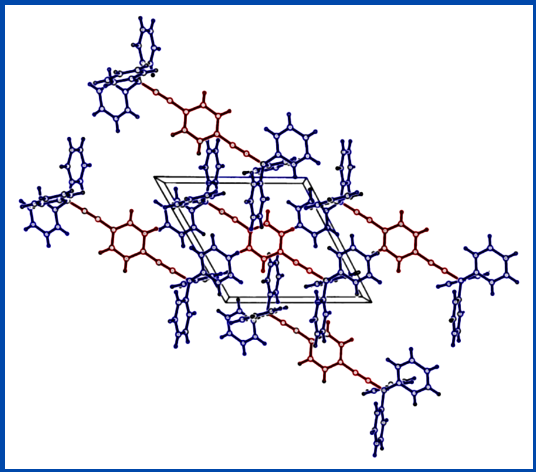


Godinez, et al., *JACS*. **2002**, *124*, 4701-4707.

Godinez, et al., *JOC*. **2004**, *69*, 1652.

Feature article: Garcia-Garibay, M. *Proc. Natl. Acad. Sci, USA*, ***2005***, *102*, 10771. .

"Rotation" in the Solid State



Solid State NMR √

- VT ^{13}C CPMAS NMR (~100-1000 Hz)
- VT Quadrupolar Echo ^{2}H NMR (10^{4}-10^{8} Hz)
- VT Spin-Lattice Relaxation

VT X-Ray Diffraction (ADP) √
(≤ 20 kcal/mol)

VT Dielectric Spectroscopy √
(10 Hz - 10^{12} Hz)

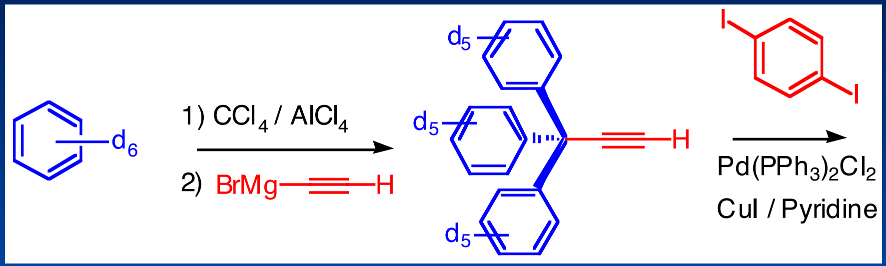
Computer Modeling √

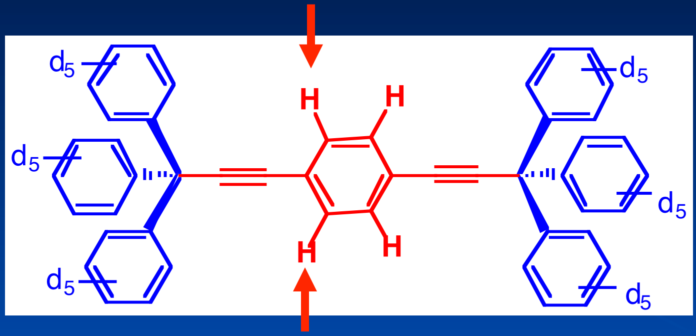
Fluorescence Anisotropy Decay
(10^{8}-10^{11} Hz)

Inelastic Neutron Scattering
(10^{10}-10^{12} Hz)

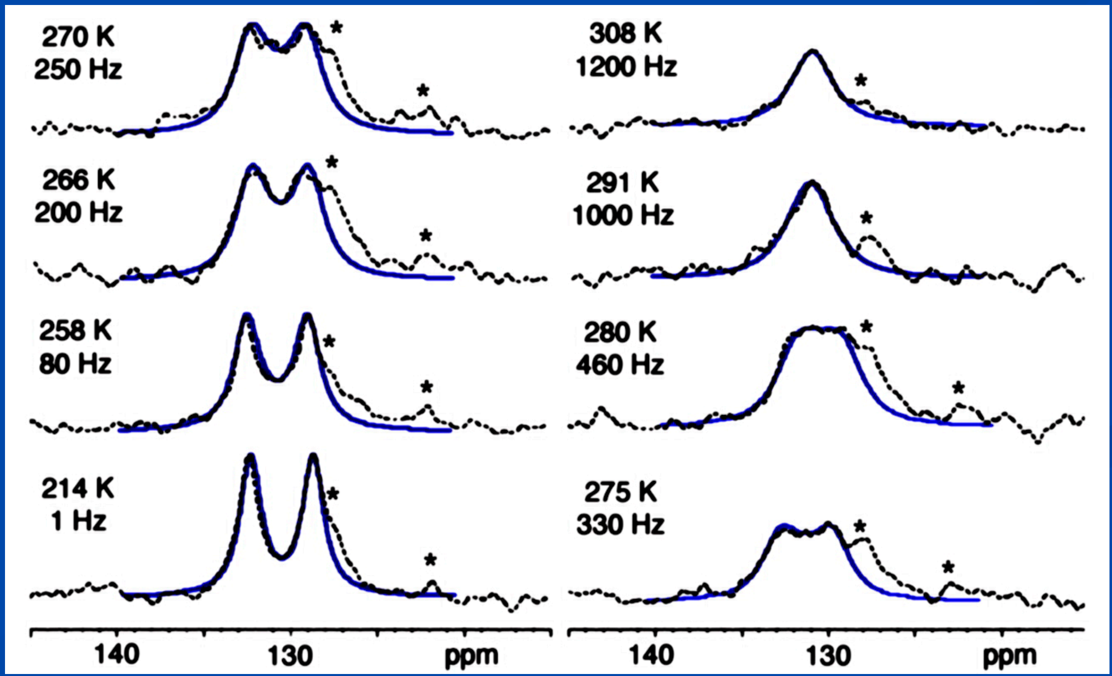
VT 13C CPMAS NMR: Rotation in the Hz-kHz Regimes

(if signals not resolved… use isotopic labeling!





d_{30}- Trityl-h_4-phenylene



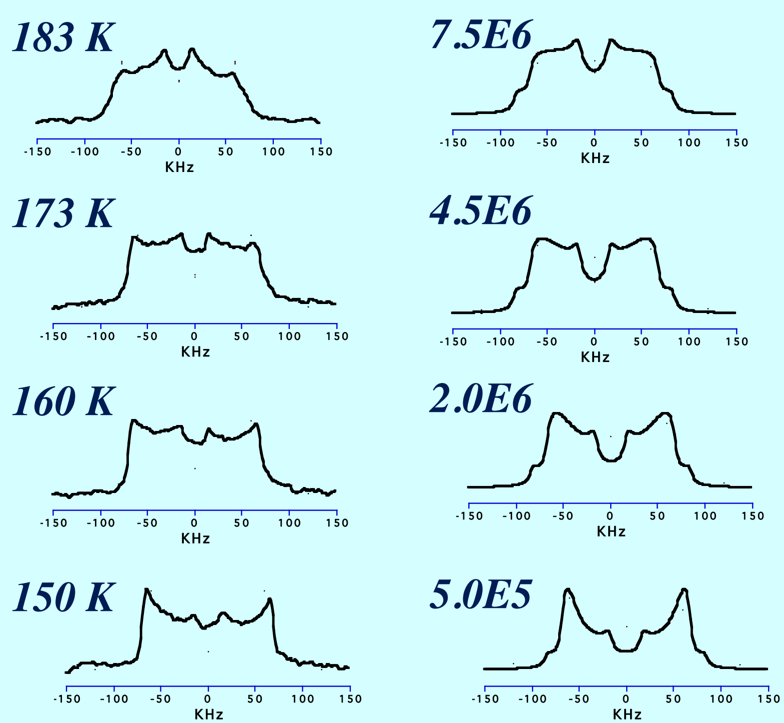
k_{280} = 611.6 Hz

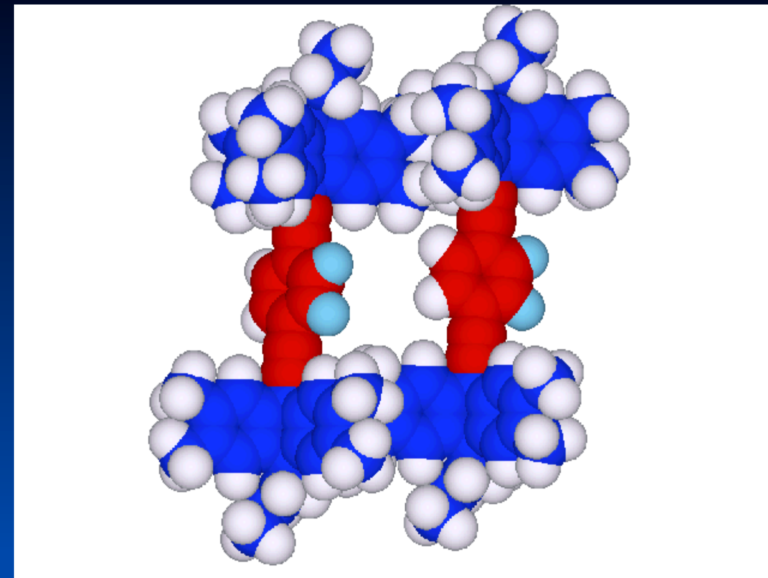
E_a = 12.8 kcal/mol

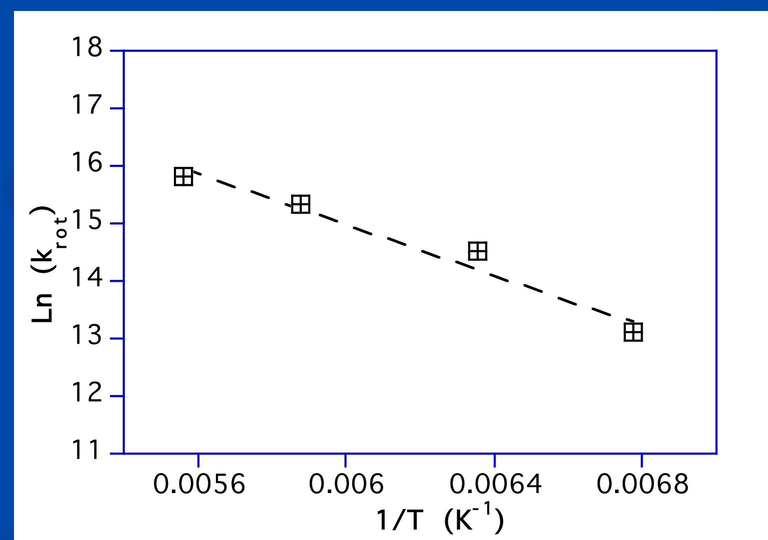
Steve Karlen

Stator Effects on Phenylene Rotation MHz Regime by ^{2}H NMR

$k_{rot} \approx$ 0.1 THz @ 400 K



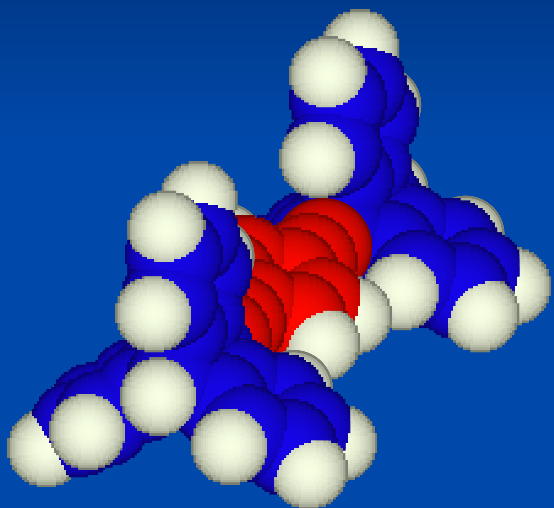


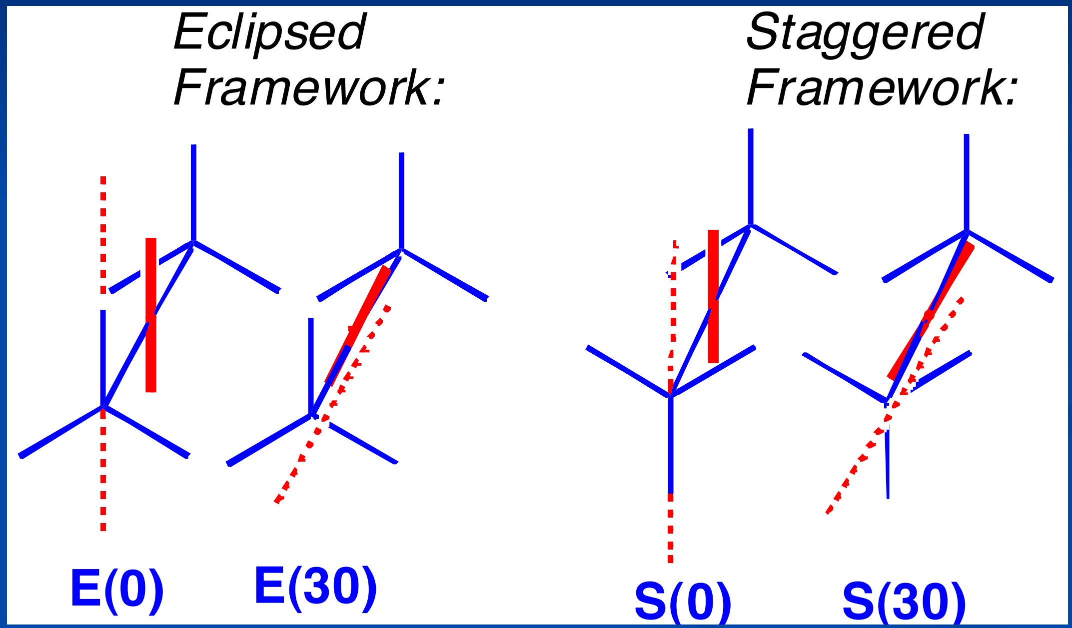


$A = 1.45 \times 10^{12}$; $Ea = 4.3$ kcal/mol

Carlos Godinez

Molecular Compasses and Gyroscopes: Internal Rotation

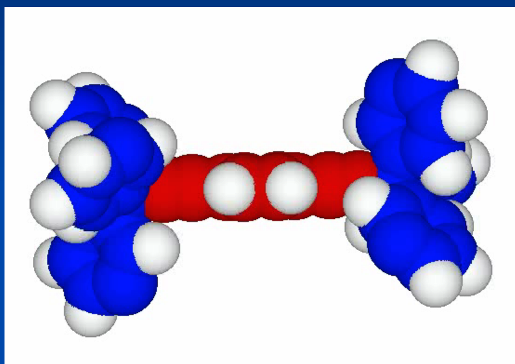




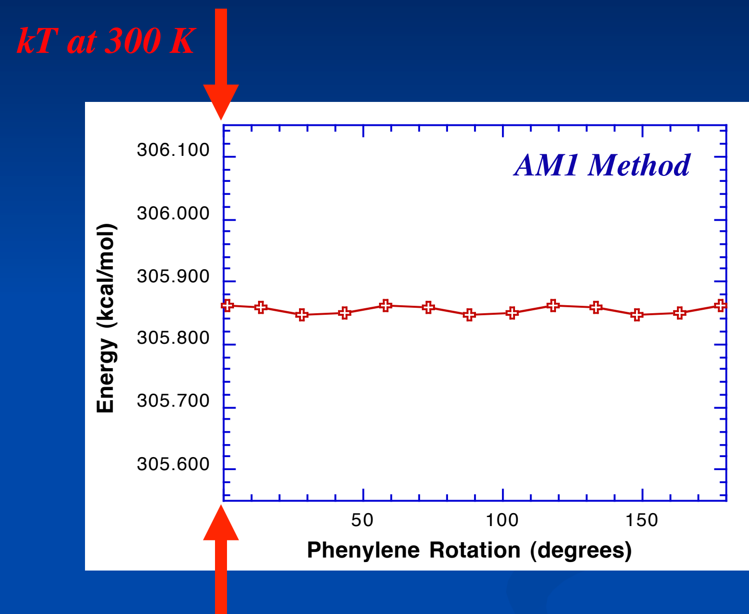
Conformational energy

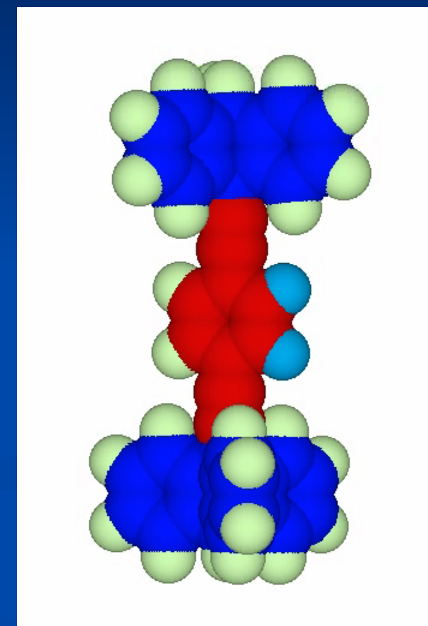
$E(\Theta) \approx S(\Theta)$

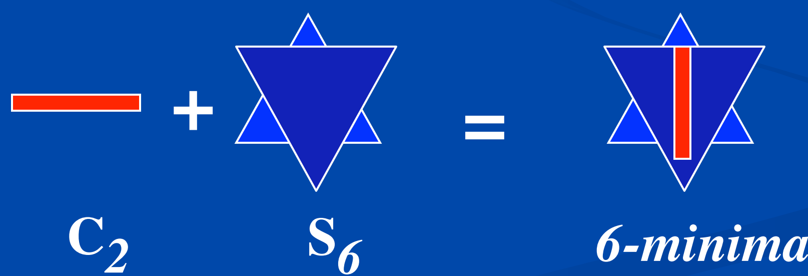
Low barrier (Ea<<kT): Gyroscopic (inertial) motion



Two degenerate states, j=±n, n≠0







Inertial Rotation :[1]
τ_{FR}^{-1} = 2.4 x 10^{12} sec $^{-1}$ at 298 K

[$\tau_{FR} = (2\pi / 9)\,(I/kT)^{1/2}$]

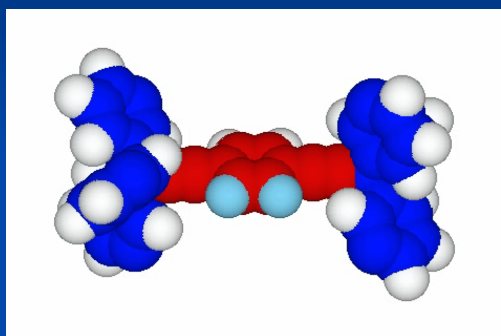
I= moment of inertia of the 1,4-phenylene with respect to the 1,4-axis

"Free Rotation" about sp-sp^n single bonds:
(a) Saebo et al. *J. Mol. Struct.* **1989**, *200*, 361.
(b) Sipachev et al. *J. Mol. Struct.* **2000**, *523*, 1

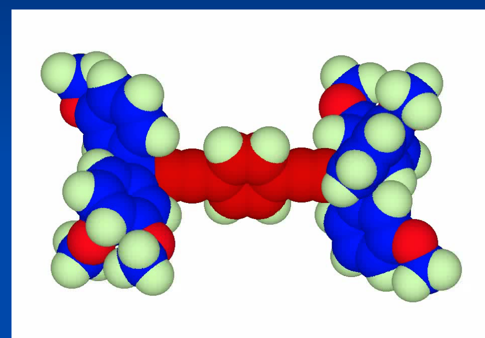
Hindered Rotation (Ea>>kT): Brownian Rotor

Oscillation, jumps, random direction

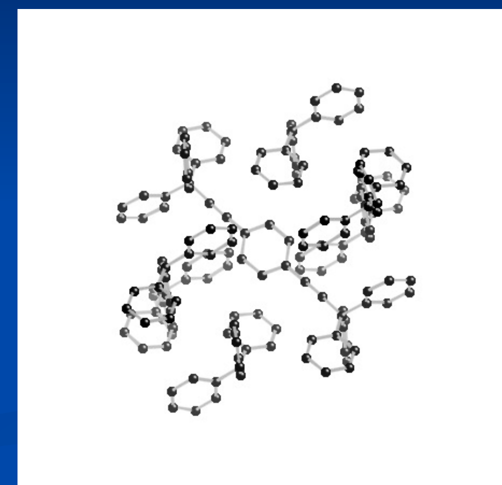
Exchange (NMR)

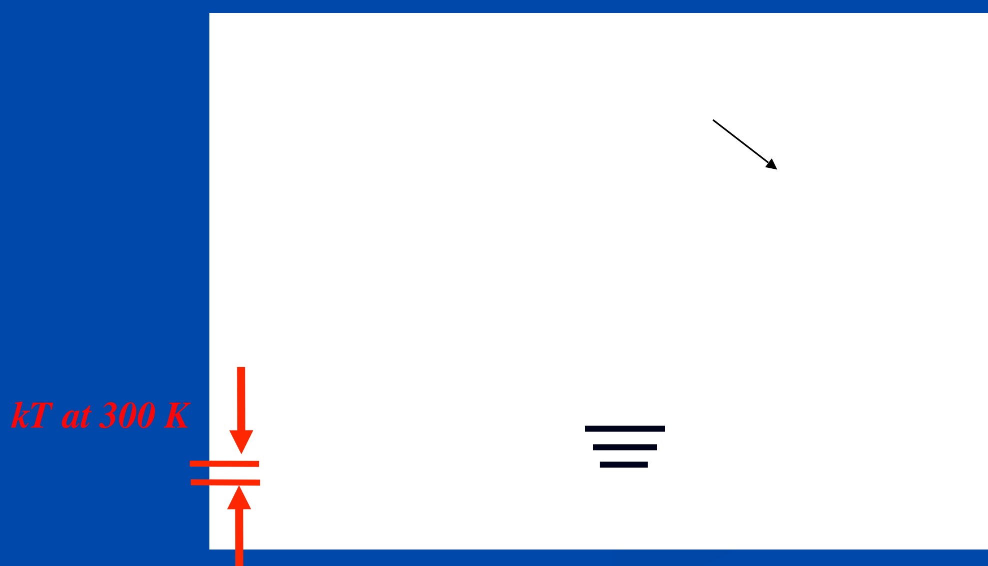


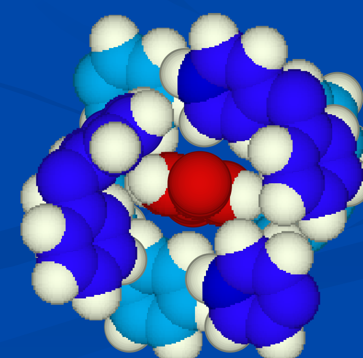
Diffuse e^- density (X-Ray)



Correlated motions (modeling)

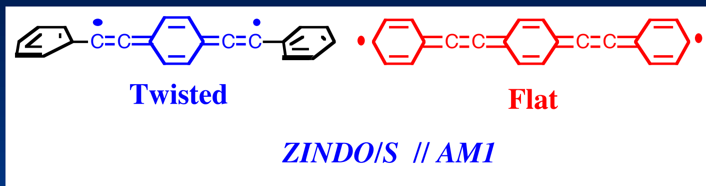


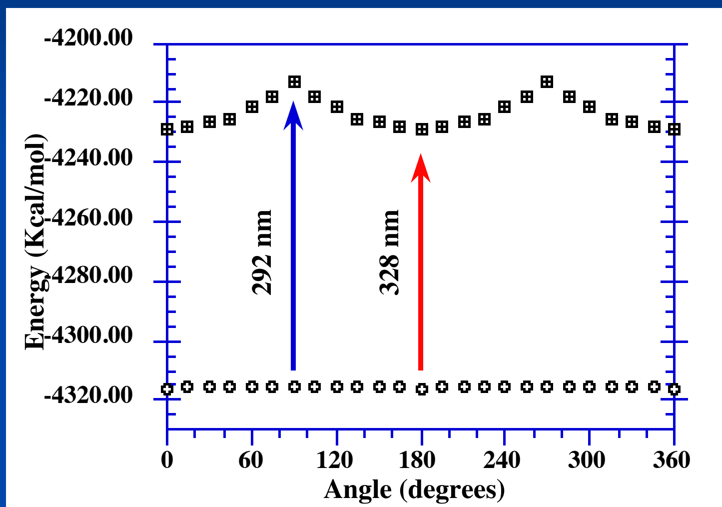




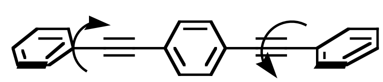
Jarowski et al., *J. Am. Chem. Soc.* **2007**, *129*, 3110**.**

Rotation in the Excited State





Ground State Bariers < 0.4 kcal / mol



Rotation andPlanarization effects on arylene ethynylenes:

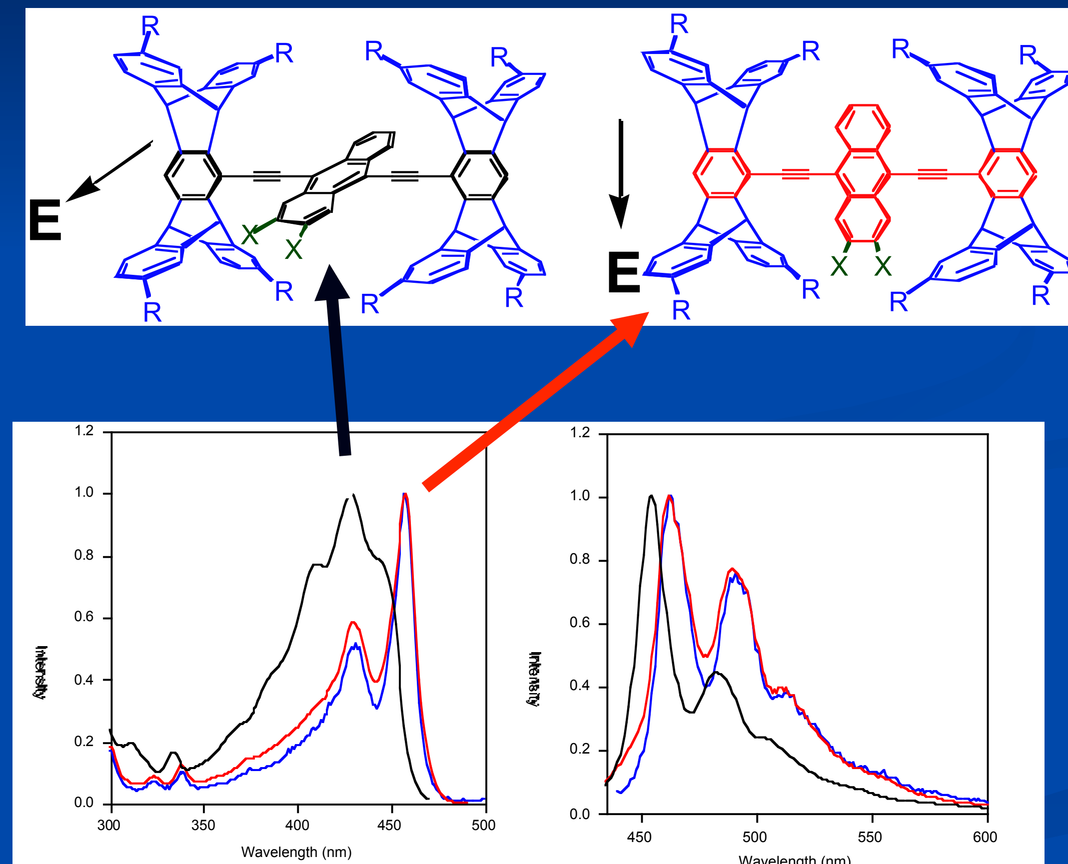
J. Phys. Chem. ***2000****, 104, 8632.*

J. Am. Chem. Soc. ***2001****, 123, 4259;* ***2002****, 124, 8181.*

J. Org. Chem. ***2001****, 66, 4259.*

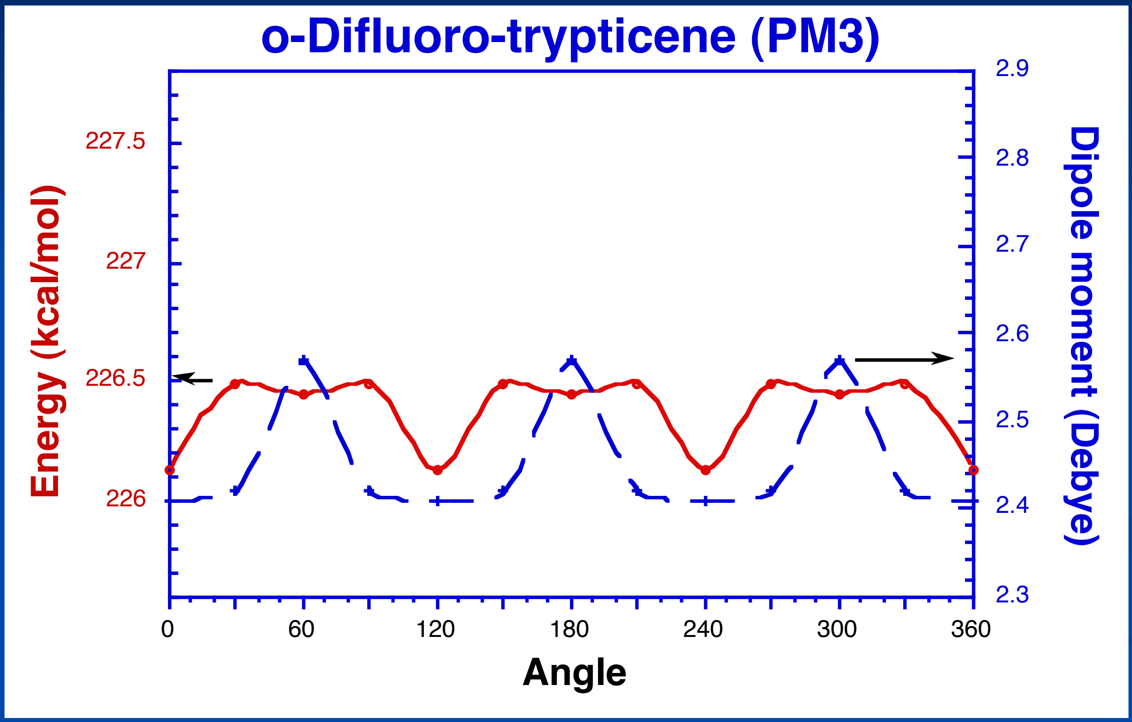
J. Phys. Chem. A, ***2001****, 105, 1551.*

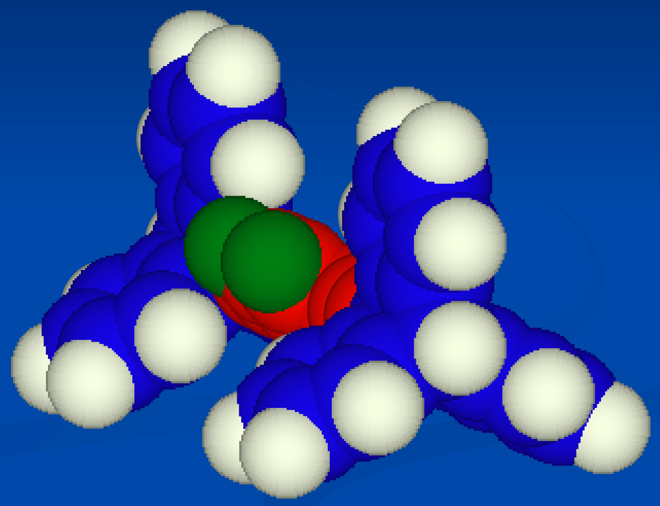
Ultrafast (THz) Electrochromics



Measurements in solution (black) and in stretched polyethylene (red at 300 K and blue at 77K)

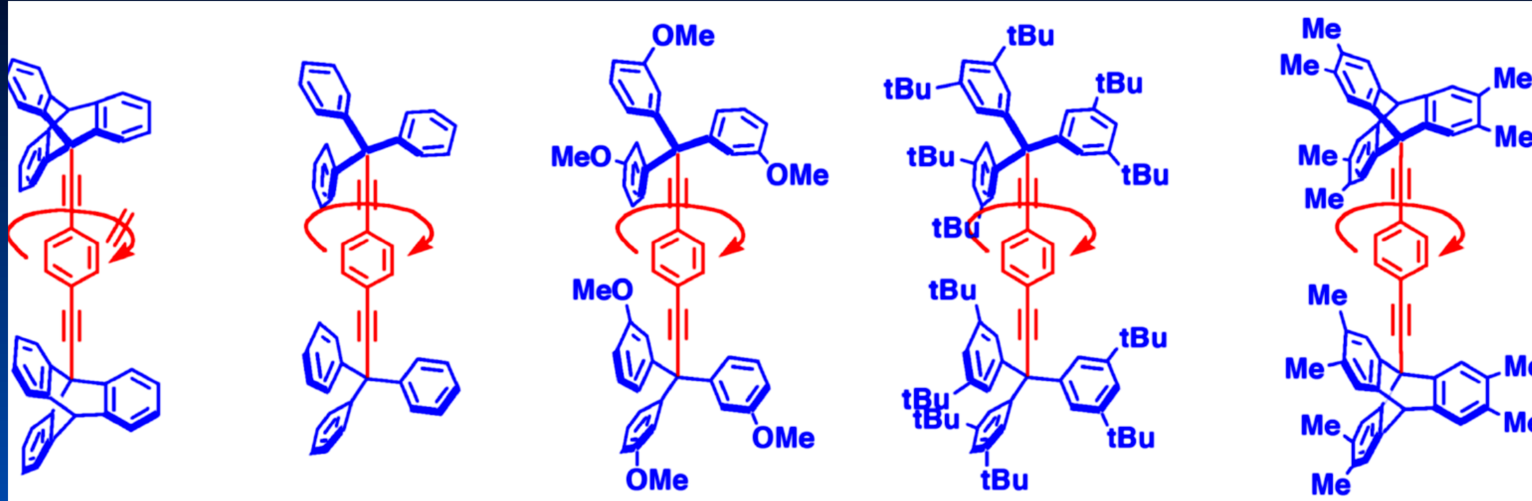
Internal Rotation of Polar Groups





Inertial Rotation : τ_{FR}^{-1} = 2.4 x 10^{12} sec $^{-1}$ at 298 K
[$\tau_{FR} = (2\pi/9)\,(I/kT)^{1/2}$]
I= moment of inertia with respect to the 1,4-axis

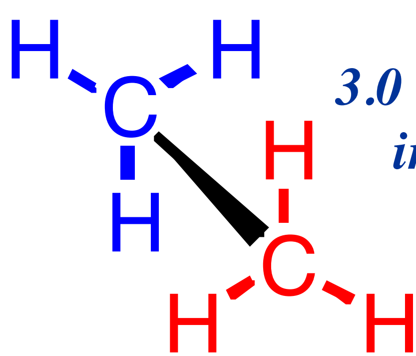
Stator Effects by SSNMR (ca. 0-10^{10} s^{-1})



1 2 3 4 5

	1	2	3	4	5
k (298)	Static	800 s^{-1}	6000 s^{-1}	> 100x10^6 s^{-1}	1.11x10^9 s^{-1}
E_a (kcal/ mol)	>> 20	11.3	10.5	< 5	4.3

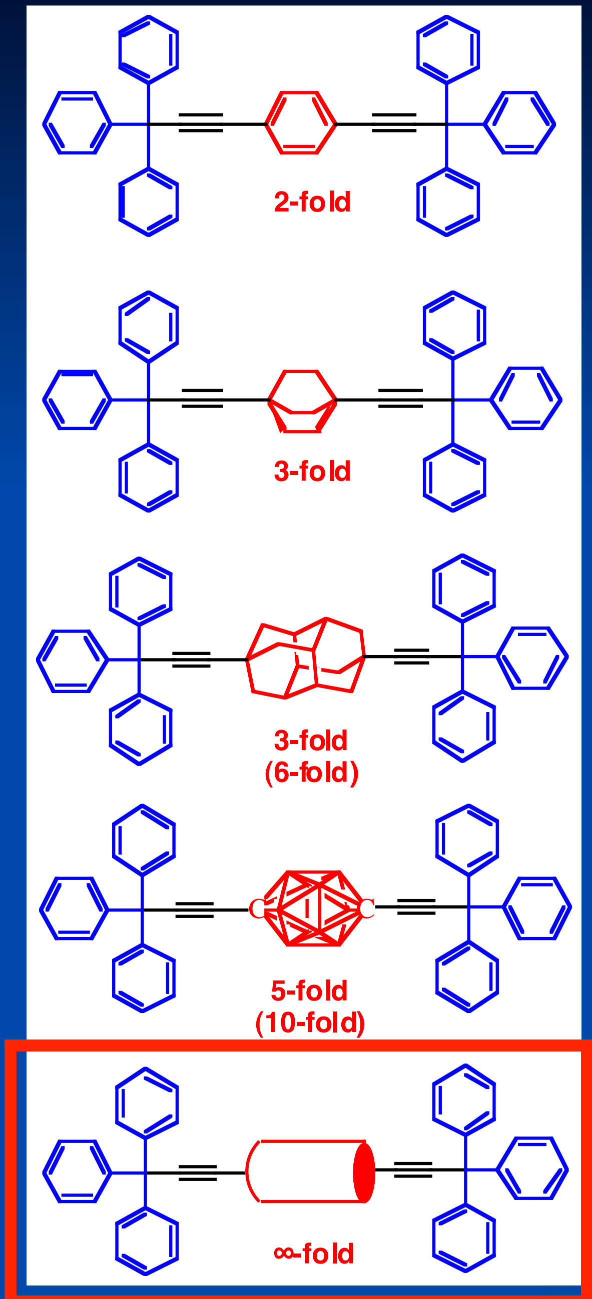
A benchmark…



3.0 kcal/mol in the gas phase!

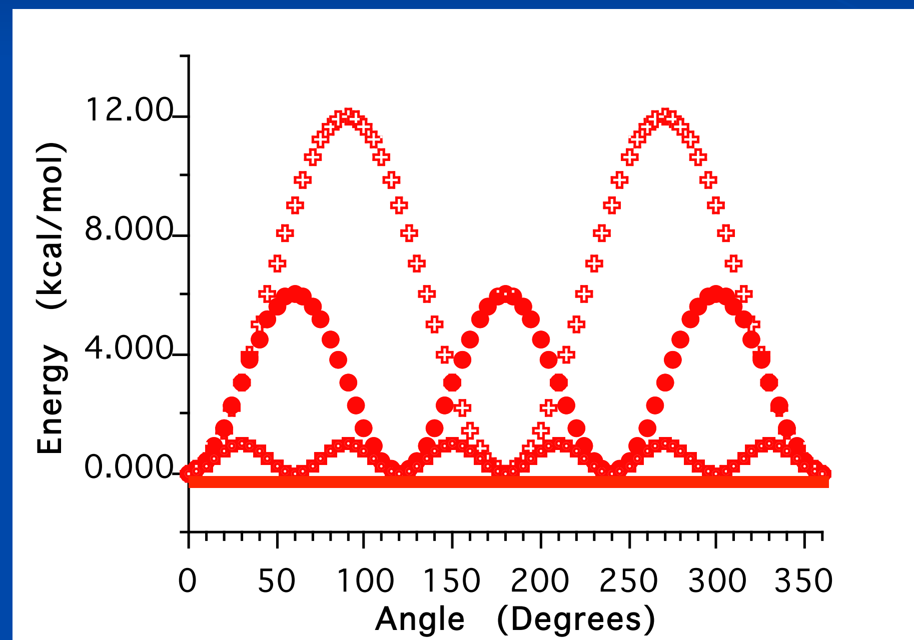
and a target:
Ea << kT (0.6 kcal/mol)

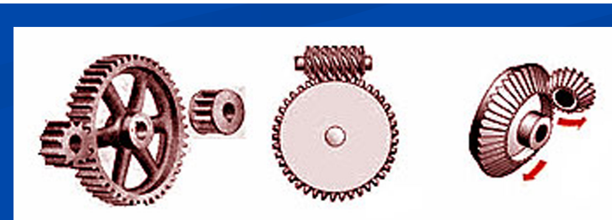
Rotator Effects on Rotary Motion ?



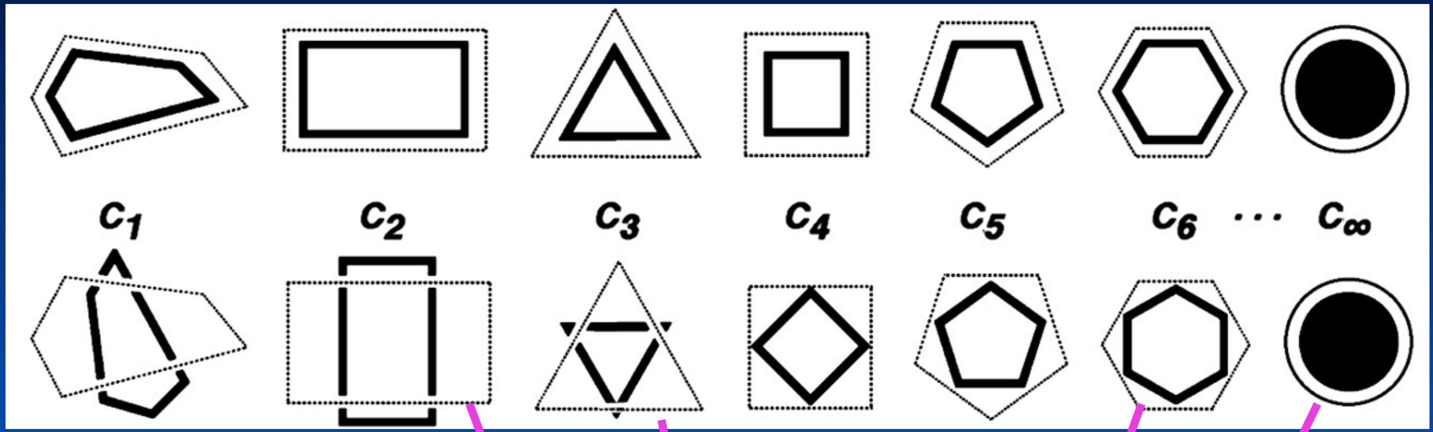
High Symmetry Order Rotors

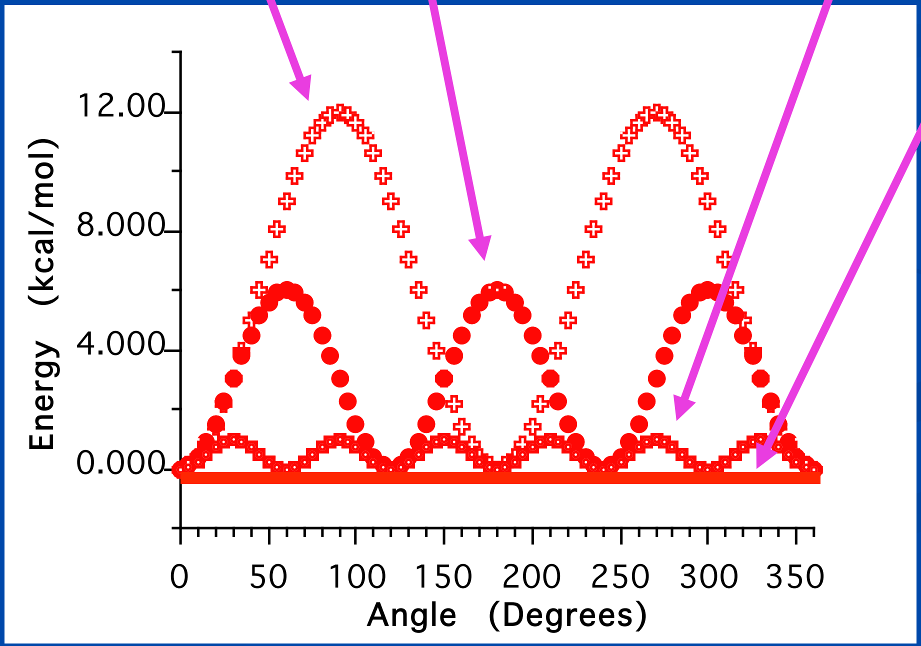
—Low rotational barriers
—High radial resolution (polarity)
—Cogitation (gearing)





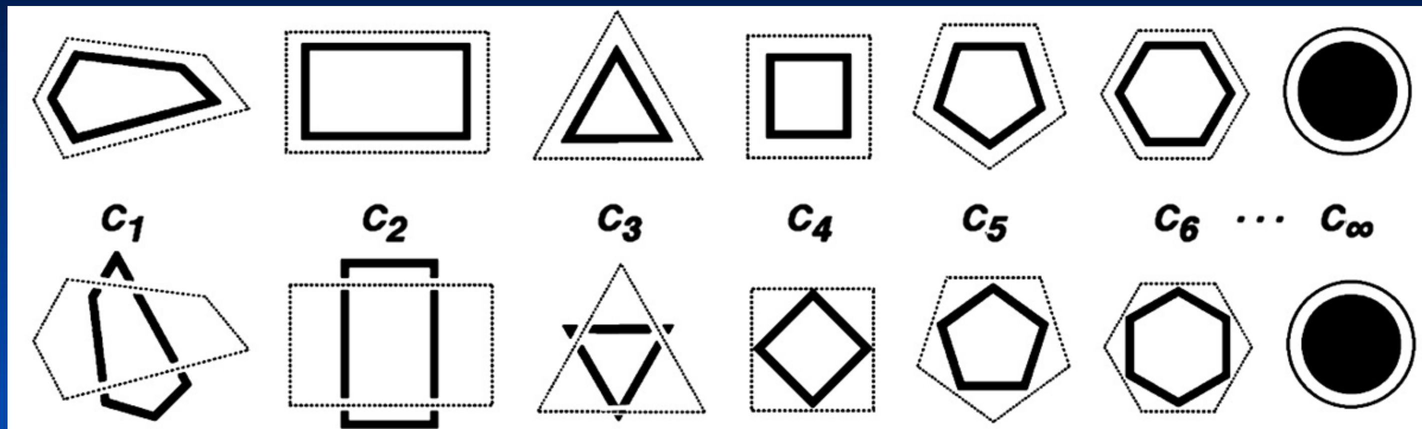
Rotator Effects on Rotary Motion ?



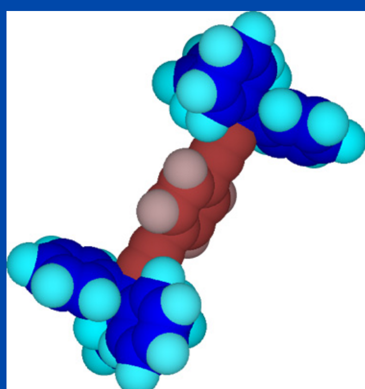


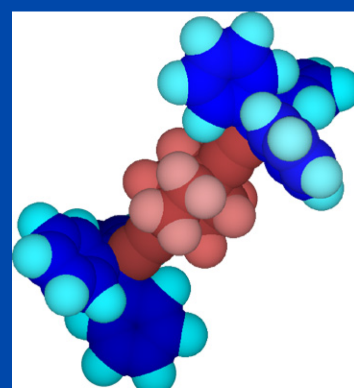
Rotator Effects (keep stator constant)

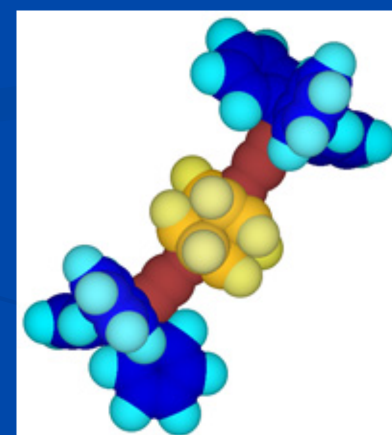
Faster ? →



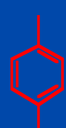
A Constant Stator : Ph_3Si-





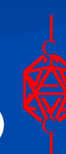


Phenylene
2-Fold



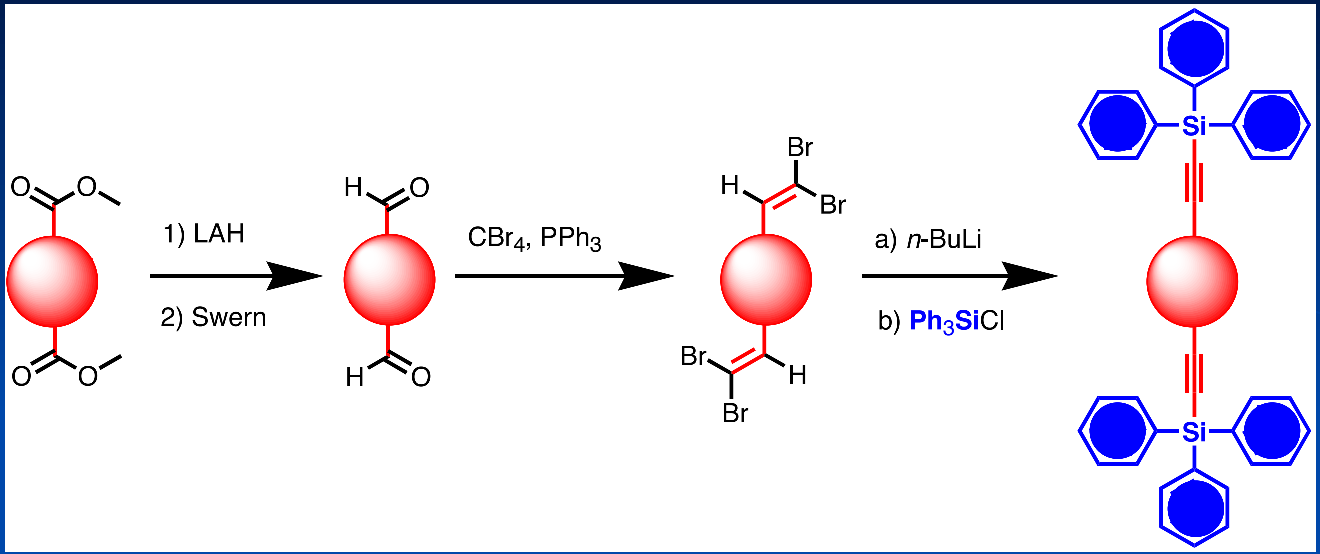
Bicyclo[2,2,2]octane
3-Fold (6-fold)

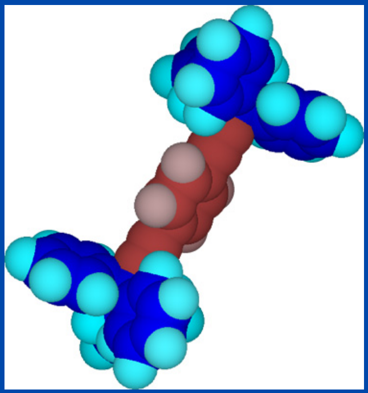
p-Carborane
5-Fold (10-Fold)



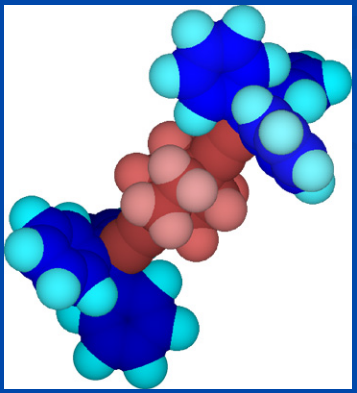
Garcia-Garibay and Karlen, unpublished

Synthetic Strategy

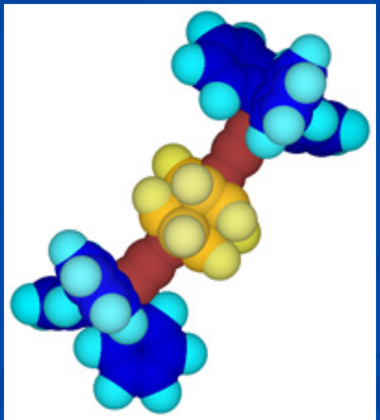




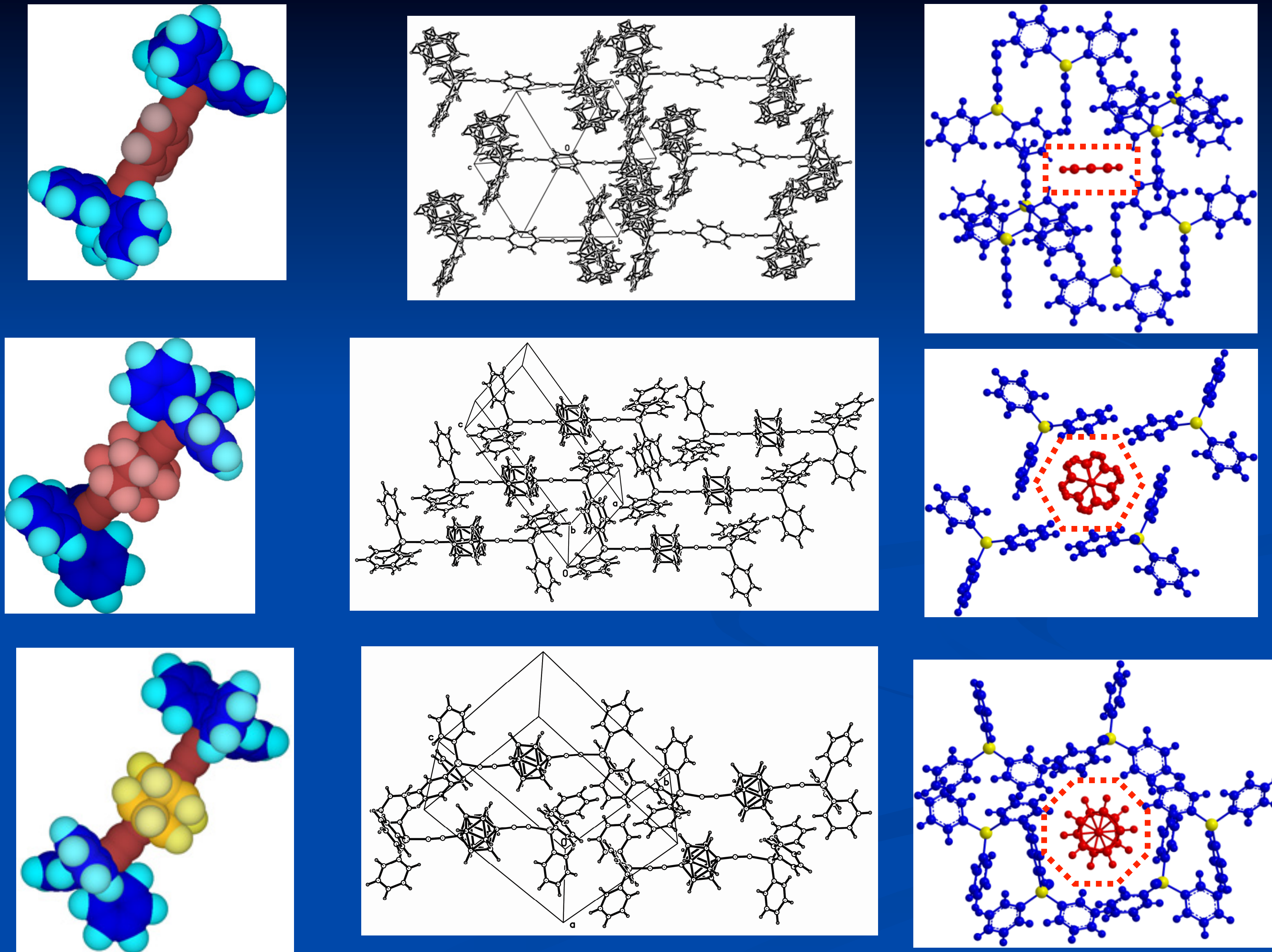
Phenylene
2-Fold



Bicyclo[2,2,2]octane
3-Fold (6-fold)



p-Carborane
5-Fold (10-Fold)



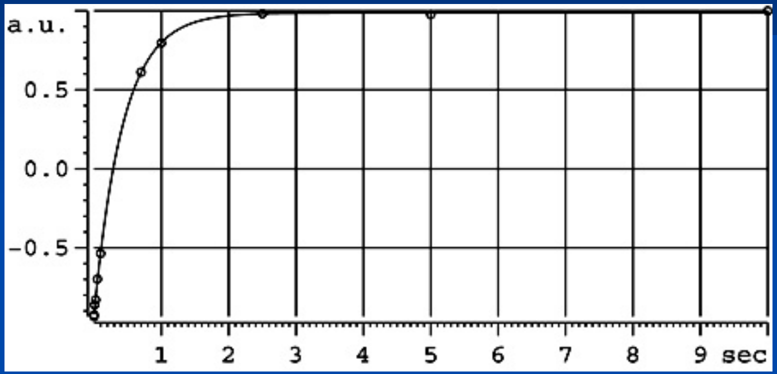
Determine rotational correlation times by ^{1}H T_1 at $\nu_L = 300$ MHz

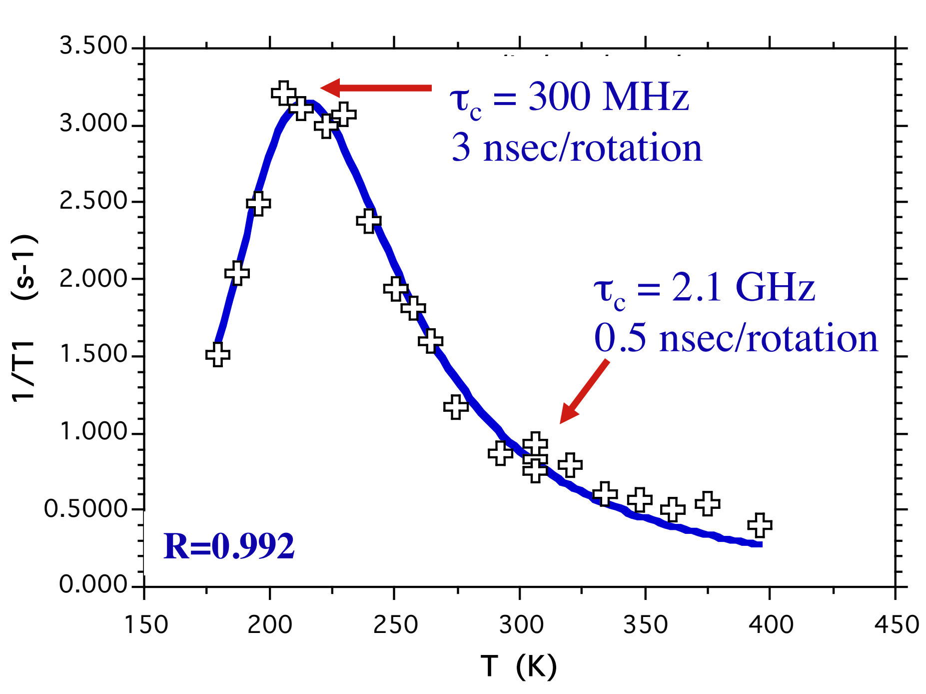
Very Low Rotational Barrier in Crystals!

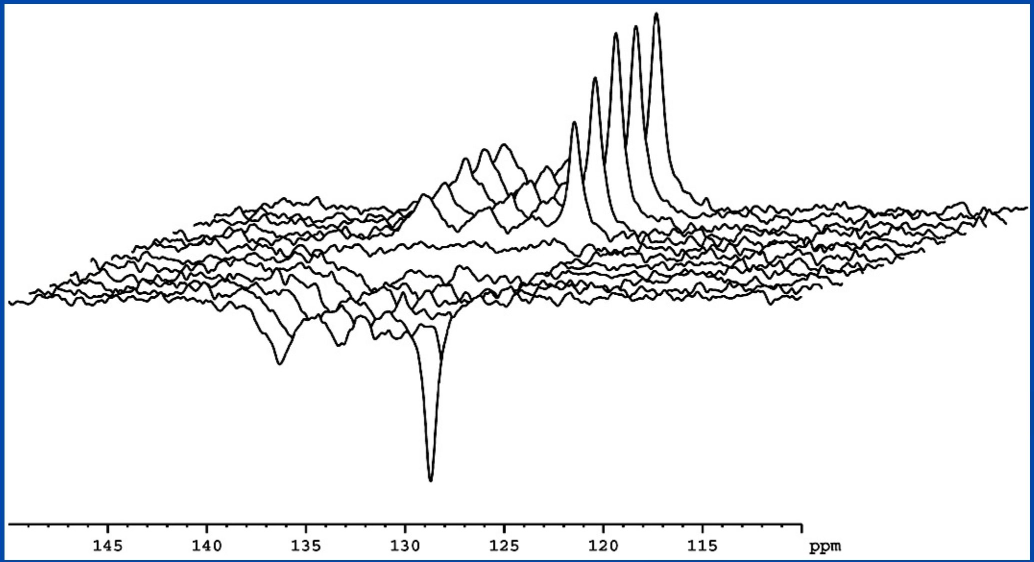
Kubo and Tomita relaxation expression:

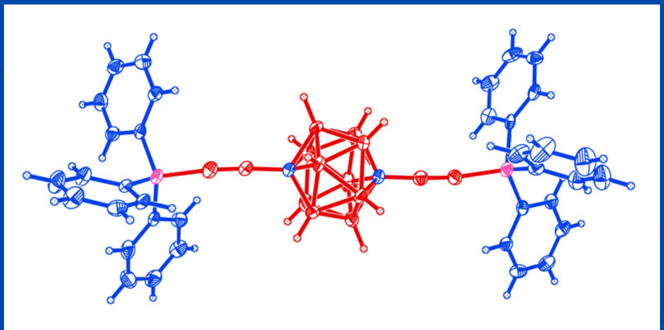
$$T_1^{-1} = C\ [t_c\,(1 + w^2 t_c^2)^{-1} + 4\,t_c\,(1 + 4\,w^2 t_c^2)^{-1}]$$

$$t_c = t_o \exp(Ea/RT)$$





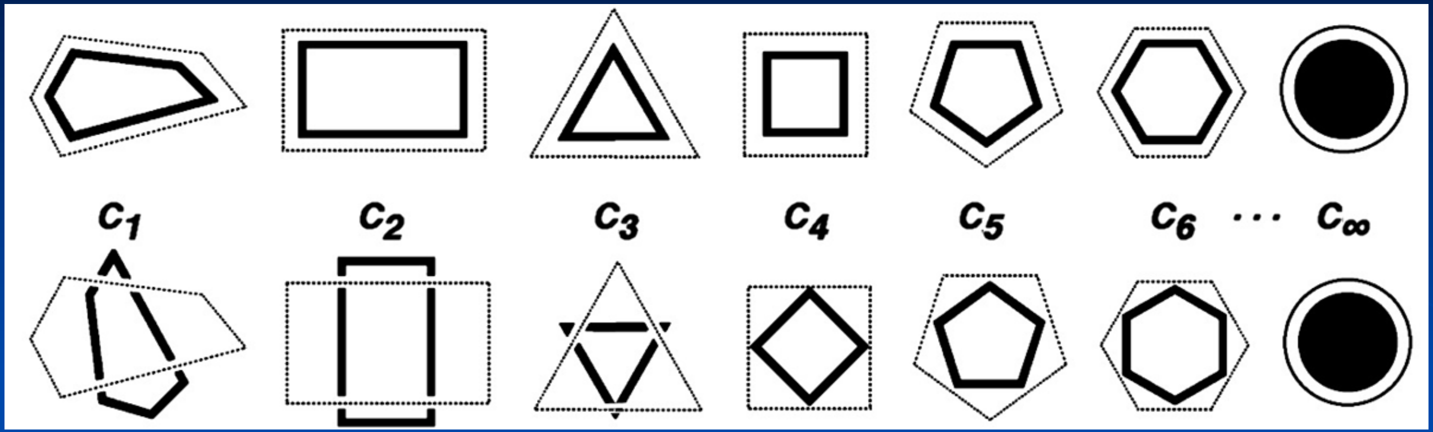


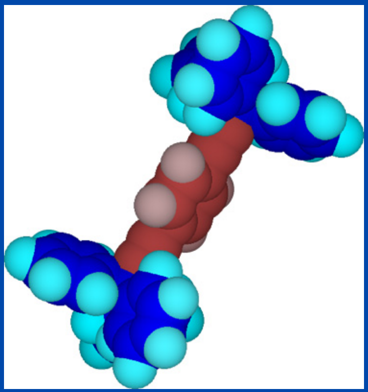


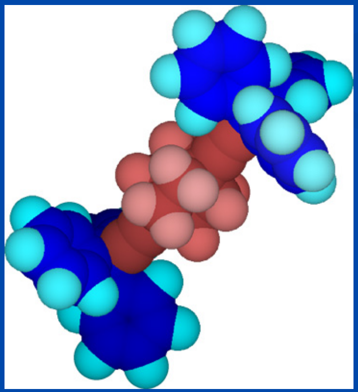
Ea = 2.92 kcal/mol

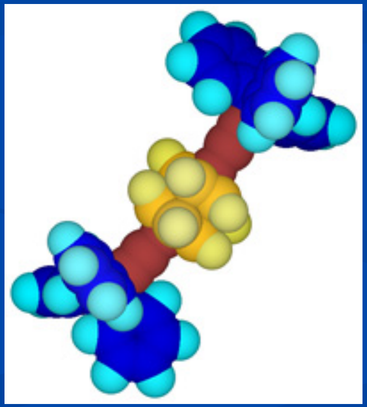
$\tau_o = 2.7 \times 10^{11}\ s^{-1}$

High Rotational Symmetry Rotators







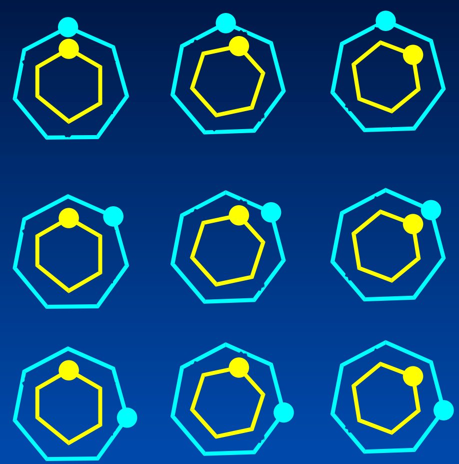


Phenylene
$E_a \approx 8$ *kcal/mol*

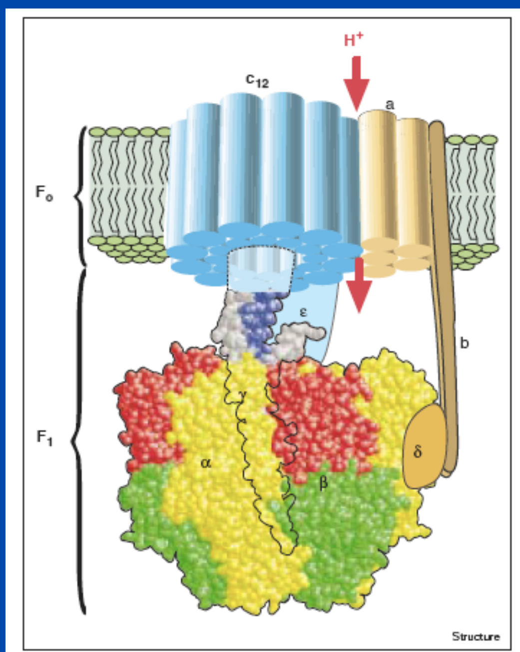
Bicyclo[2,2,2]octane
$E_a = 3.57$ *kcal/mol*

p - Carborane
$E_a = 2.92$ *kcal/mol*

Subtleties about Rotational Potentials



7-fold x 6 fold = 42



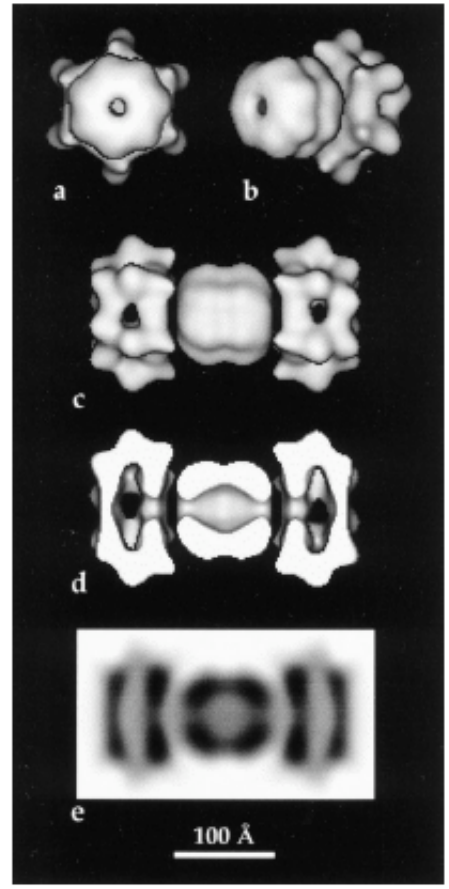
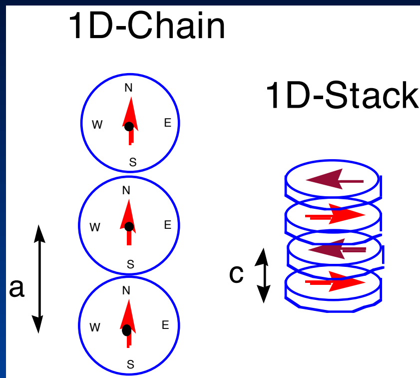


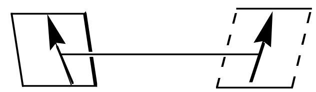
FIG. 6. Three-dimensional model of the ClpAP complex. ClpA was reconstructed from cryo-electron micrographs (see Results), whereas the model of ClpP was obtained by taking the atomic coordinates of the high-resolution structure of Wang *et al.* (1997) and band-limiting this structure to the same resolution as ClpA (~ 30 Å). The proteins have been docked according to the interaction angle determined in the analysis shown in Fig. 5b. (a) Axial view of ClpA (front) and ClpP (rear); (b) oblique view of a 1:1 complex of ClpP with ClpA; (c) side view of the 2:1 complex (ClpAP), with a ClpA hexamer mounted on each face of the ClpP tetradecamer; (d) cutaway view of the ClpAP complex, revealing the internal cavities; (e) averaged side projections of the ClpAP complex. To obtain (e), a total of 186 projections were averaged, with the long axis being rotated in 2° increments through ± 30° in and out of the plane perpendicular to the line of sight: at each such position, the map was rotated through 50° in 10° increments about its long axis. As a byproduct of this simulation, it appears that the apparent concavity of the ClpA striations seen in averaged side views arise mainly from out-of-plane tilt (e.g., Fig. 2d).

Potential Short Term Applications

Molecular Compasses



$$E_{dd} = \mu_i \mu_j / \varepsilon(r_{ij})^3 \, [\cos X - 3\cos\alpha_1 \cos\alpha_2]$$

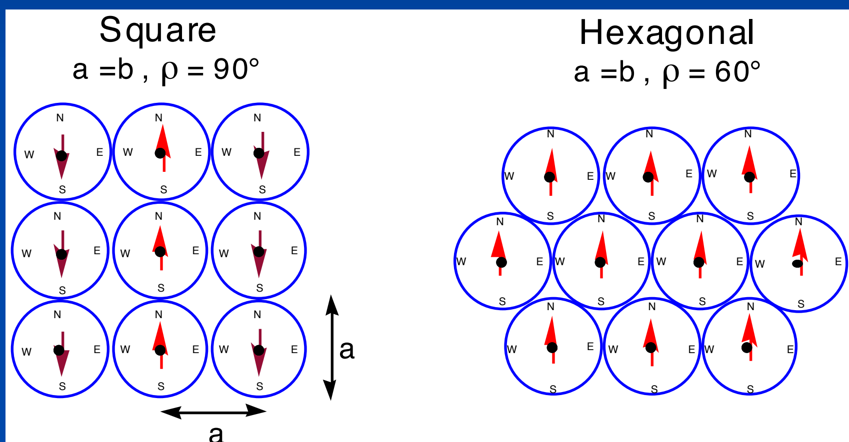


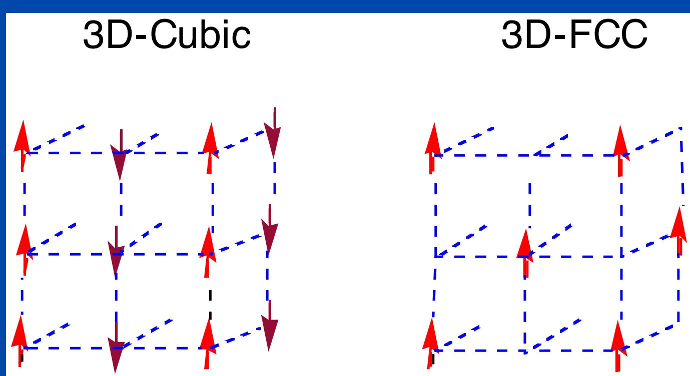
ε=dielectric constant

X=dihedral angle between dipoles

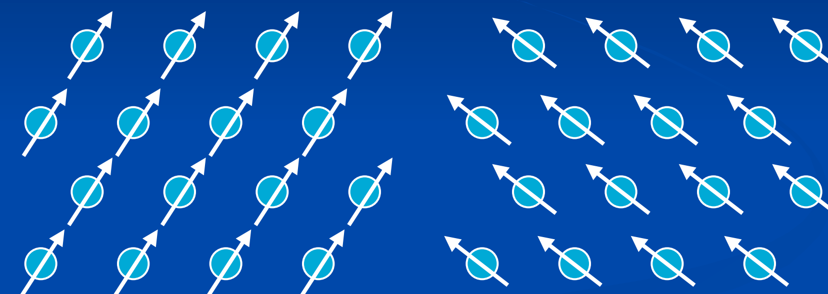
α_1, α_2 =angle between dipole vector and line

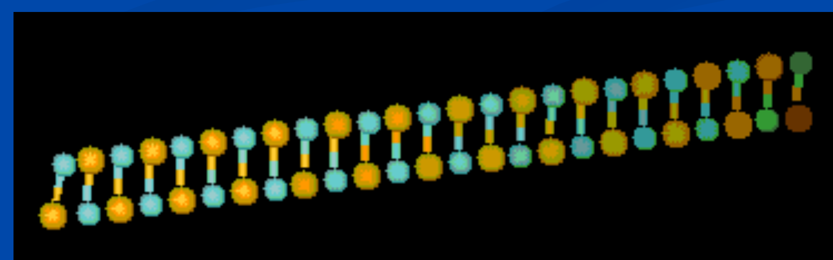
R_{ij} = distance between dipoles





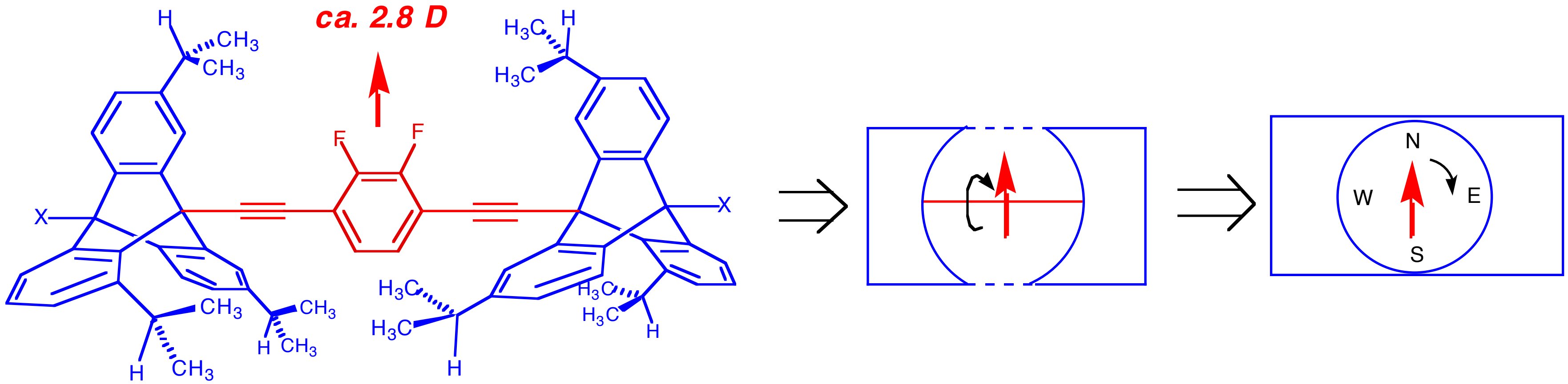
Hexagonal Lattice



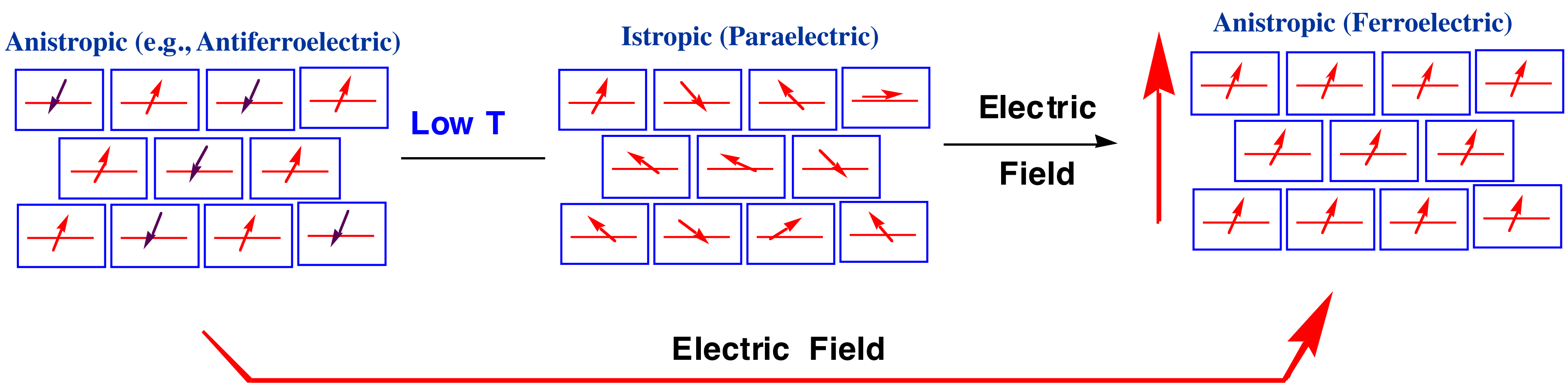


High symmetry lattices have an 'acoustic' mode with very low frequency at k=0 (Goldstone mode). V. Rozenbaum, et al. *Sov. Phys. Usp*. 1991, *34*, 883.

Molecular Compasses

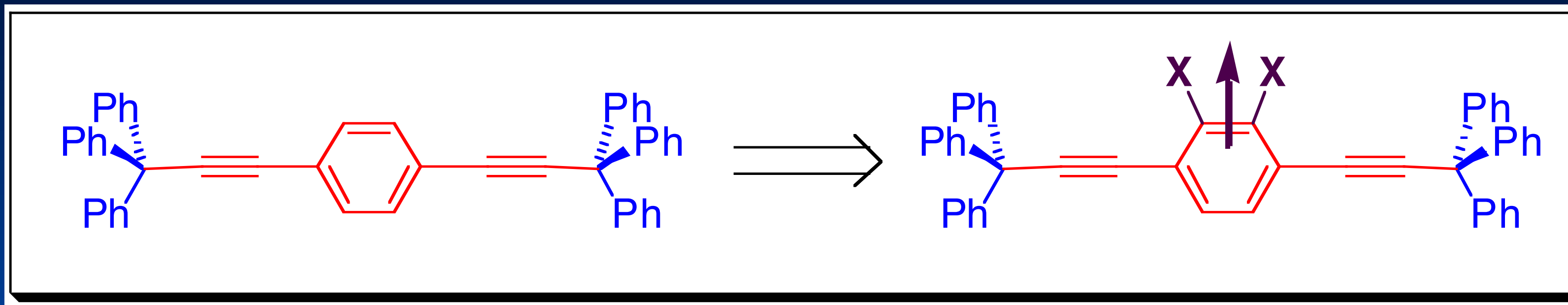


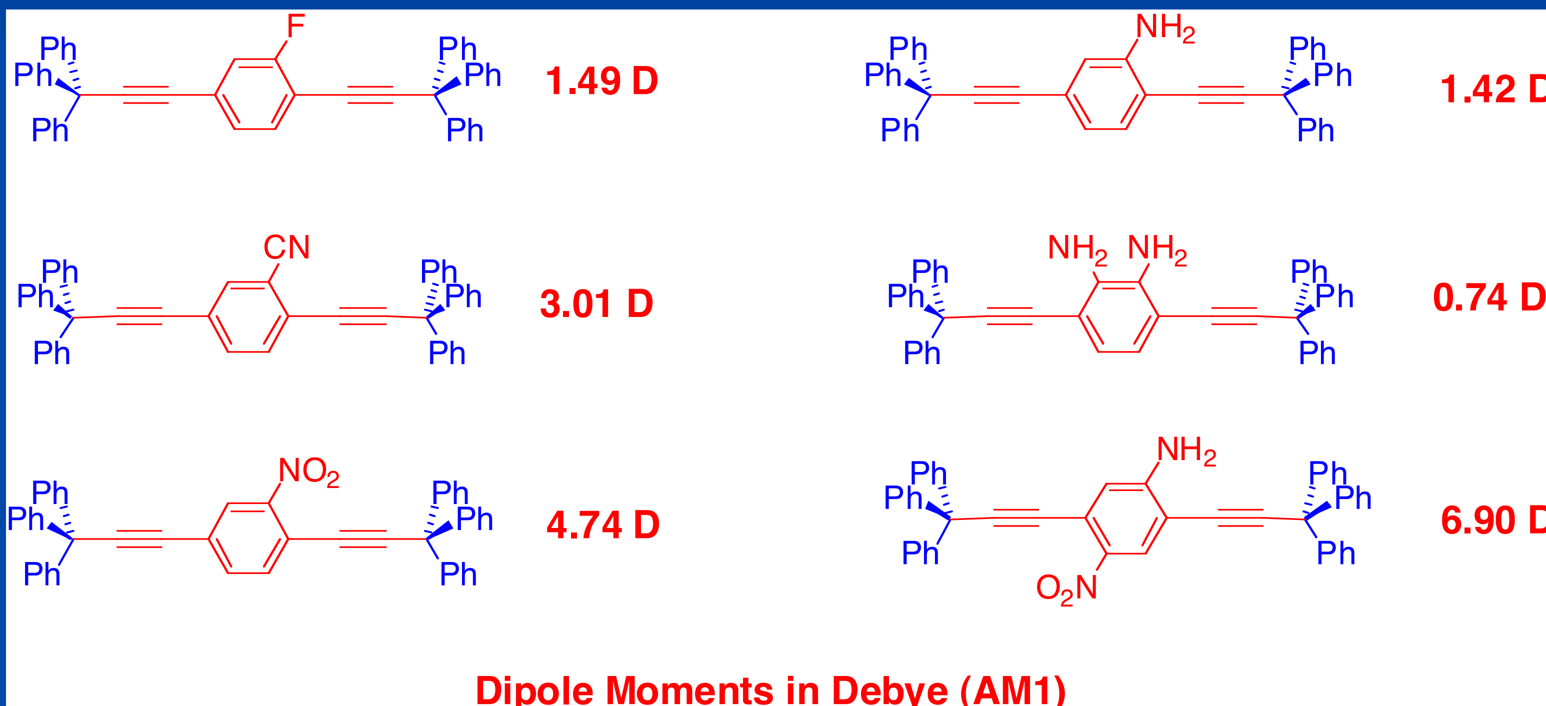
Photonic Materials



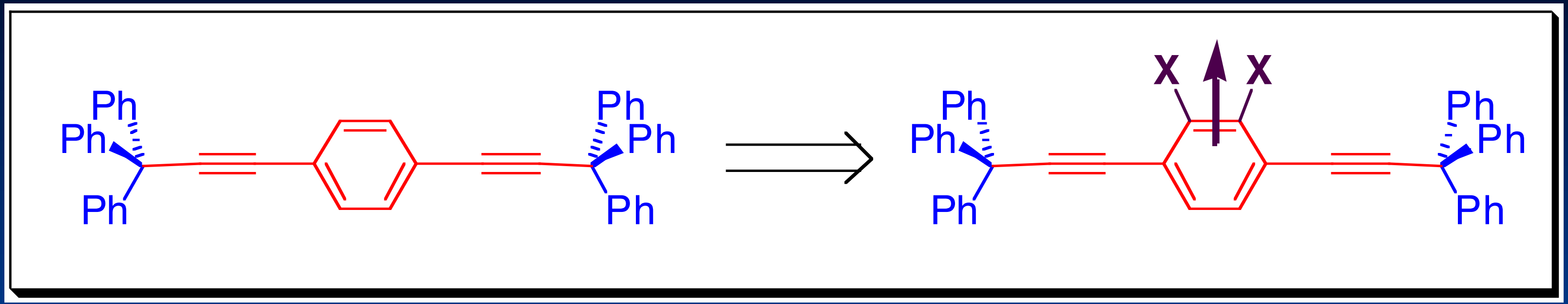
-Dichroism
-Birefringence
-NLO

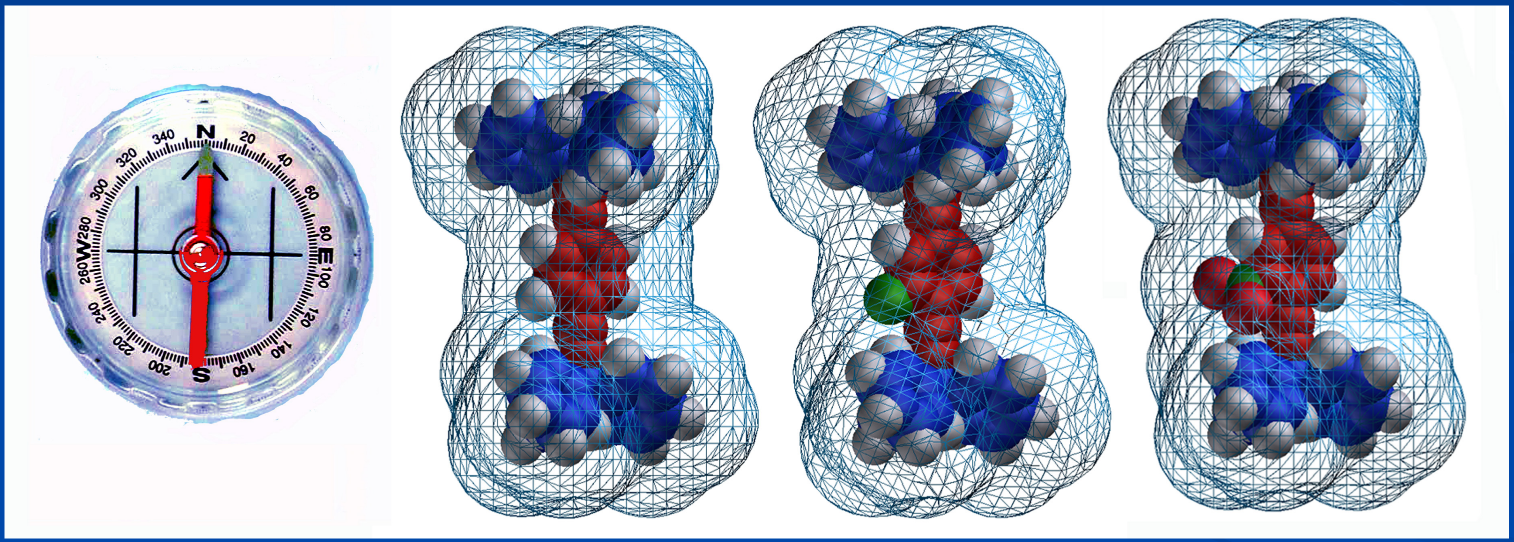
Polar Rotors



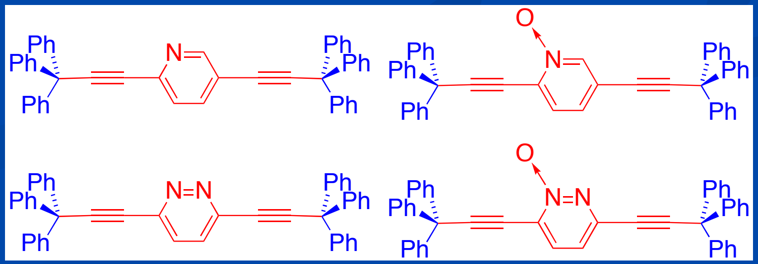


Dominguez, Khuong, Dang, Sanrame, Nuñez, Garcia-Garibay, JACS, ***2003,*** *125, 8827.*

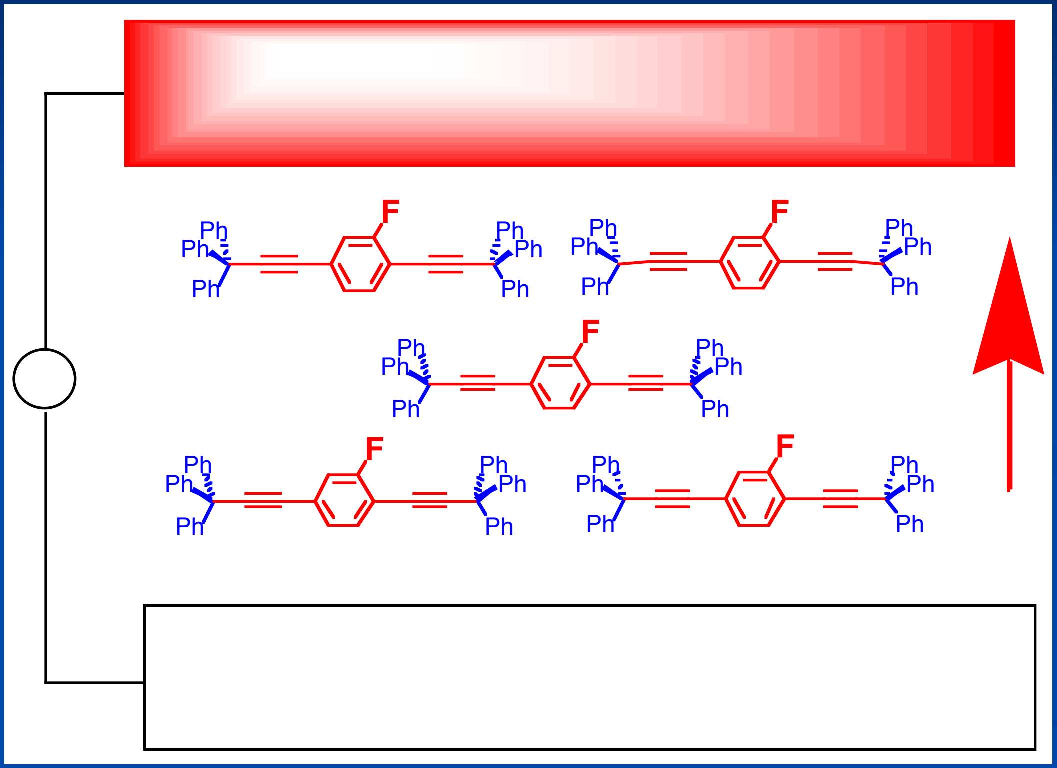




Isomorphous Crystals
—X-Ray
—DSC
—TGA
—Photophysics

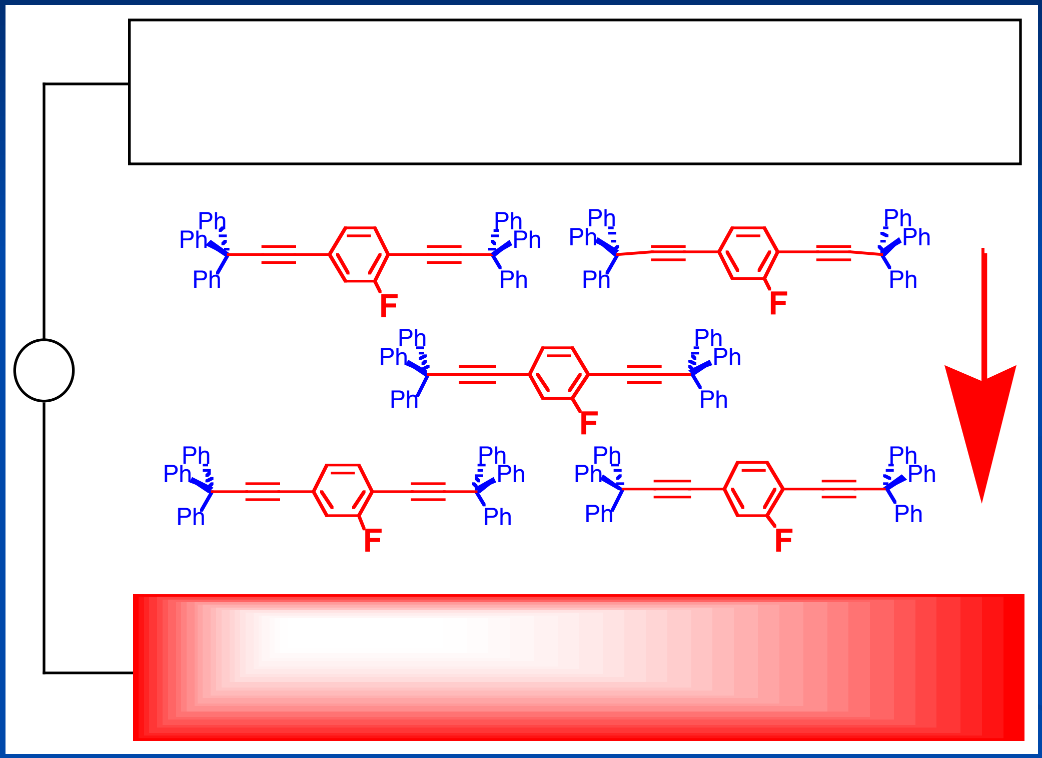


Dielectric Measurements



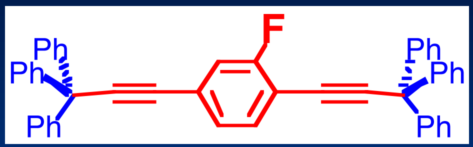
(Electric Energy is Dissipated when AC Frequency Matches that of the Internal Dipole Dynamics)

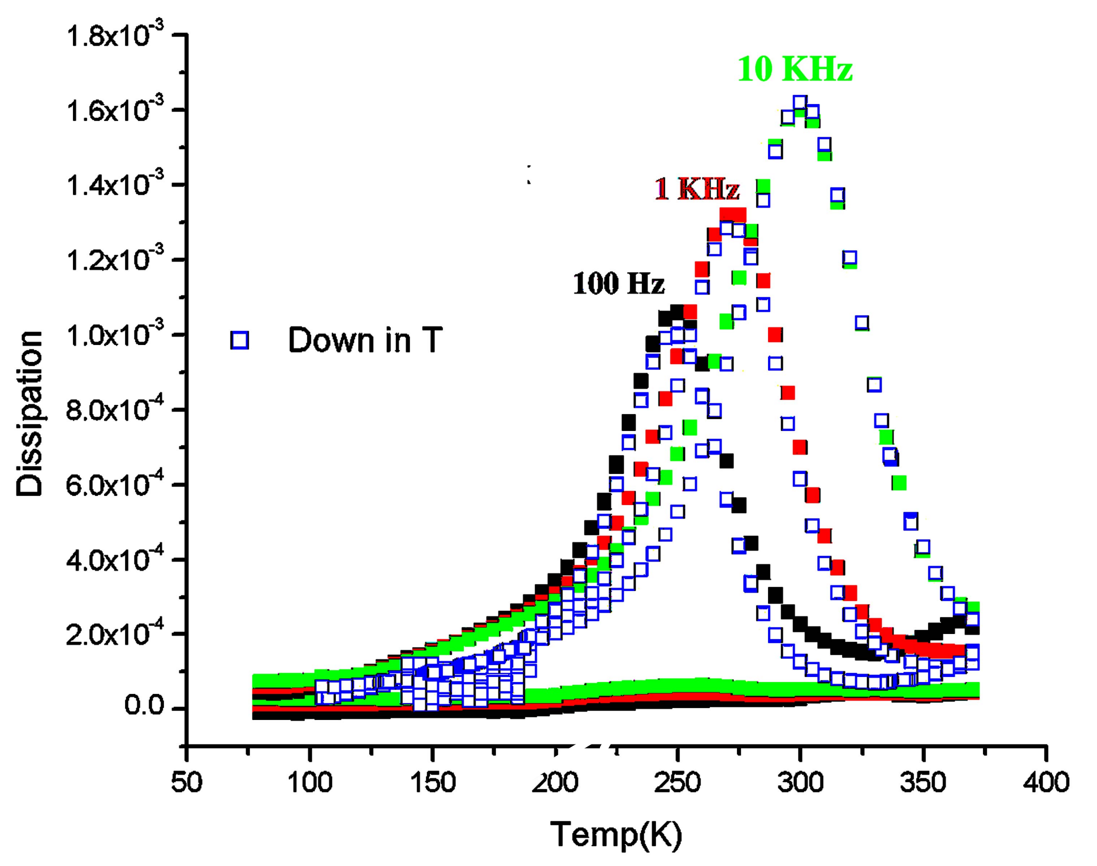
Dielectric Measurements

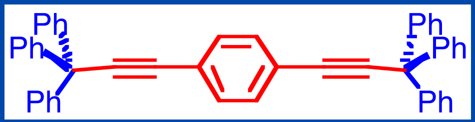


(Electric Energy is Dissipated when AC Frequency Matches that of the Internal Dipole Dynamics)

Frequency-Dependent Dielectric







$$\frac{1}{\tau} = \omega_0 \exp\left(\frac{-E_B}{kT}\right)$$

$$\tan(\delta) = \frac{C_R}{C_0}\frac{\omega\tau}{1+\omega^2\tau^2}$$

$$C_R = \frac{\epsilon_R + 2}{3}\frac{Np_0^2}{3kTL^2}\cosh^{-2}\left(\frac{S}{2kT}\right)$$

a) Non-Polar Rotor Gives Baseline

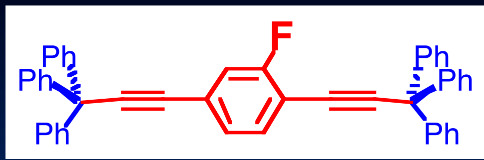
b) Reversible on Heating and cooling cycles

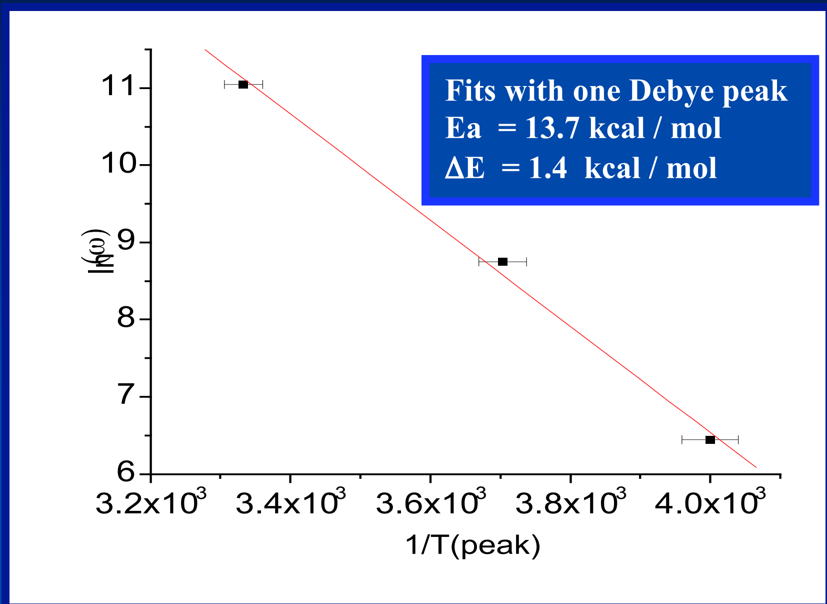
c) Peak Position Depends on AC Freq.

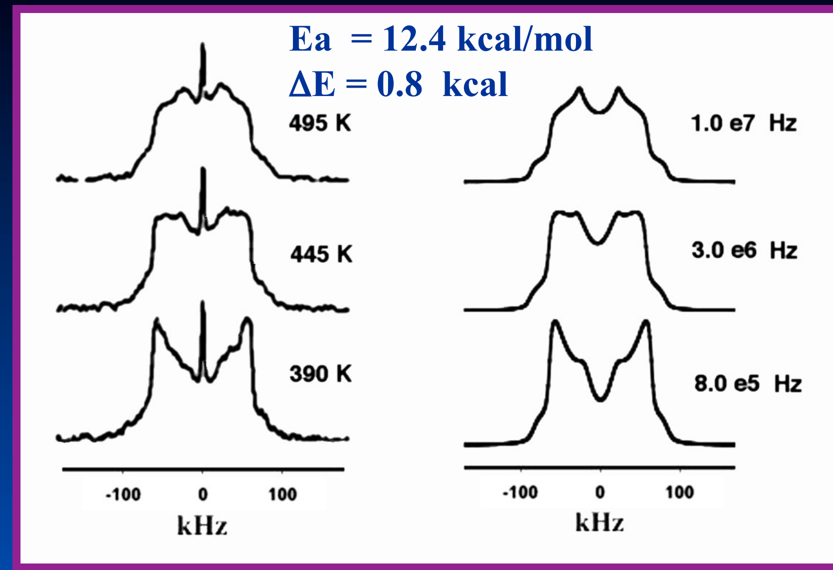
d) Signal Intensity Increases With Temp.

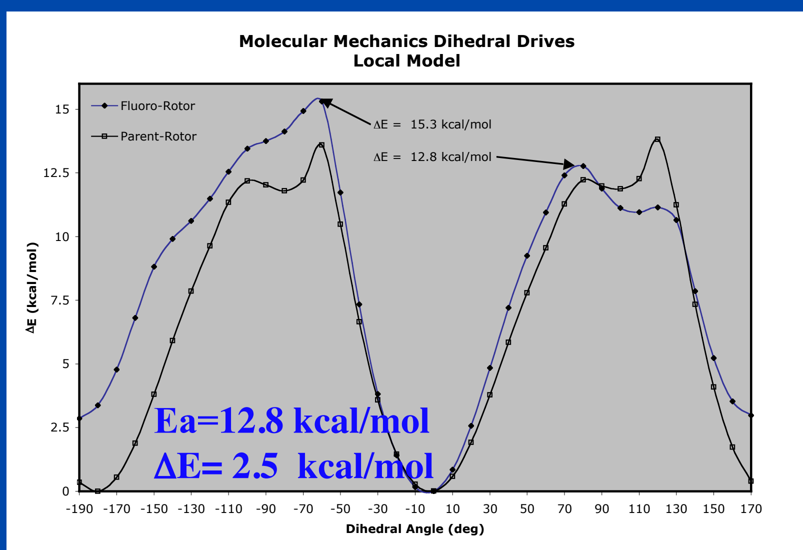
e) Barrier matches that of ^2H and ^{13}C NMR and Force Field calculations

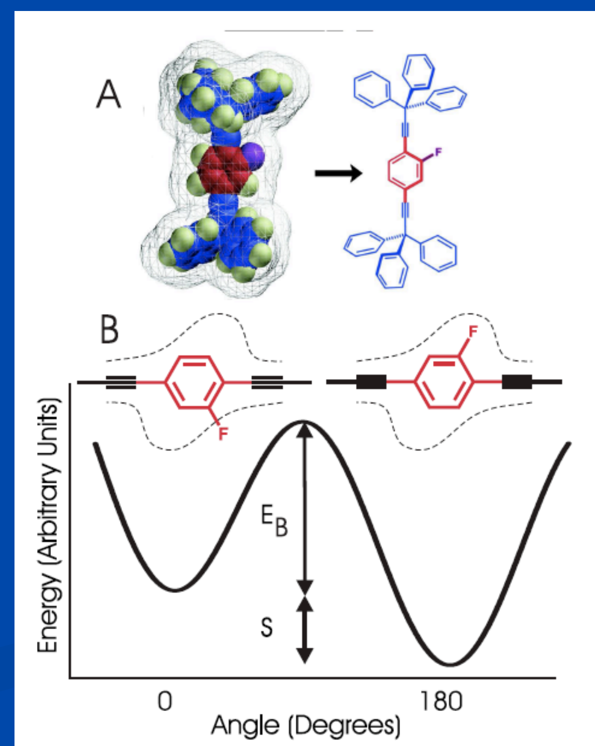
Horansky, Clarke, Price, Khuong, Jarowski, Garcia-Garibay, *Phys. Rev. B* **2005**, *72*, 014302.





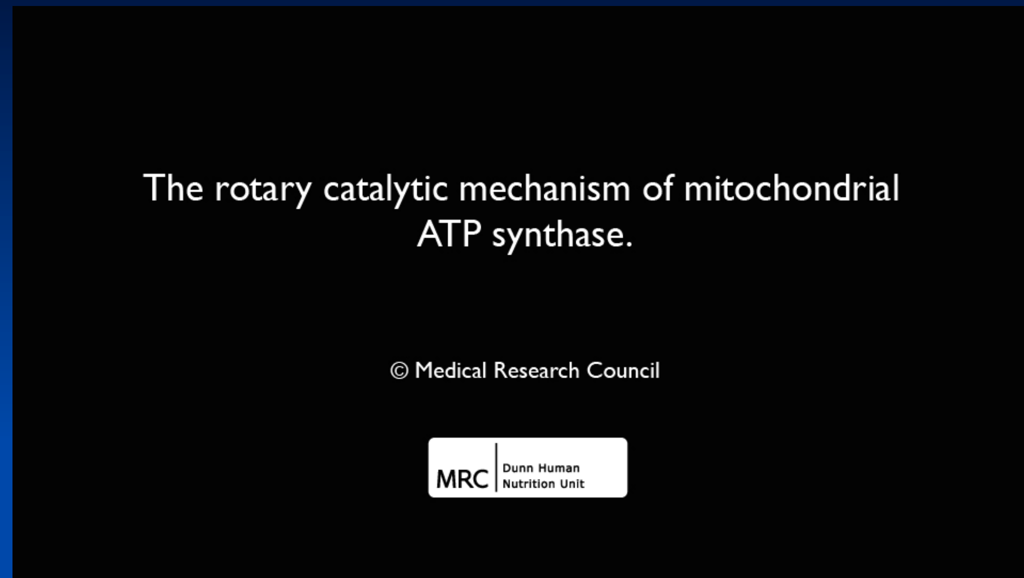






Horansky, Clarke, Price, Khuong, Jarowski, Garcia-Garibay, *Phys. Rev. B* **2005**, *72*, 014302 and *Phys. Rev. B.*, **2006**, *74*, 054306.

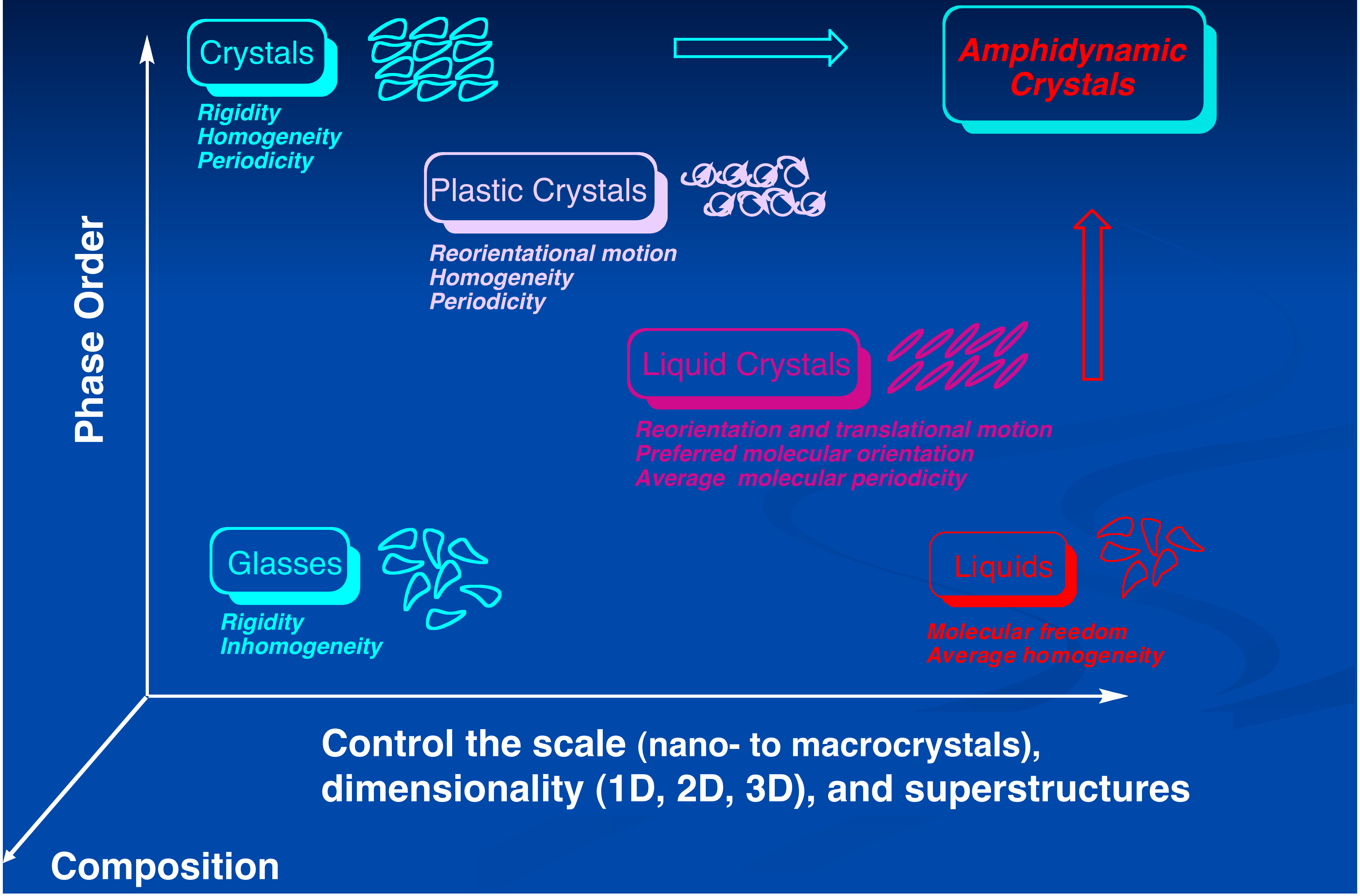
Macroscopic Vs Molecular Machines: Things to Keep in Mind



- **Newtonian Mechanics**
- **Rigid parts**
- **Arbitrary sizes and shapes**
- **Joint parts carry no DOF**
- **Structure's Tm >> T**
- **Thermal energy dissipation (vibr) is decoupled from function**
- **States of absolute rest**
- **Inertia rules (Large R)**
- **Need energy for motion and action**

- **Statistical and Quantum Mechanics**
- **Non rigid parts**
- **Limited shapes (structural theories)**
- **Every part added carries additional DOF's**
- **Structure's Tm ≈ T**
- **Thermal energy dissipation (vibr, rot, conf, coll.) is part of its function**
- **Never "rest" (zero point energies)**
- **Viscous forces rule (small R)**
- **Need energy to change state of motion for action**

Conclusions : Much Remains to be Done



Artificial Molecular Machines

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