5.37 Introduction to Organic Synthesis Laboratory
Spring 2009

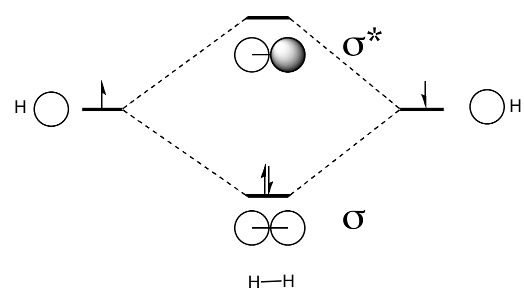
Massachusetts Institute of Technology
Chemistry 5.37
Professor Timothy M. Swager


The Diels-Alder Reaction
Lecture 2: Theory and “Swager Centric” Applications

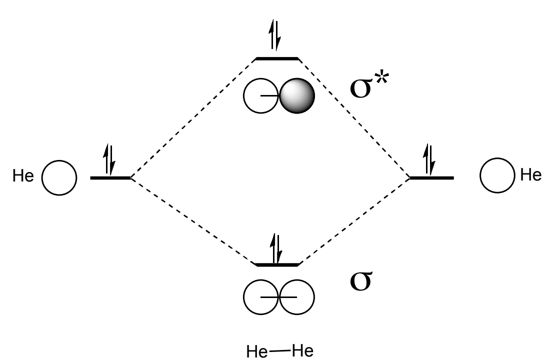
April 7, 2009

First: A Little Review of Simple Bonding

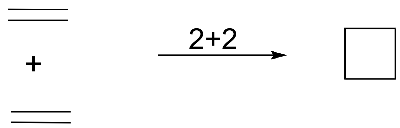
Molecular Hydrogen
Is Stable: Orbital Overlap
Leads to a Net Lowering of Energy



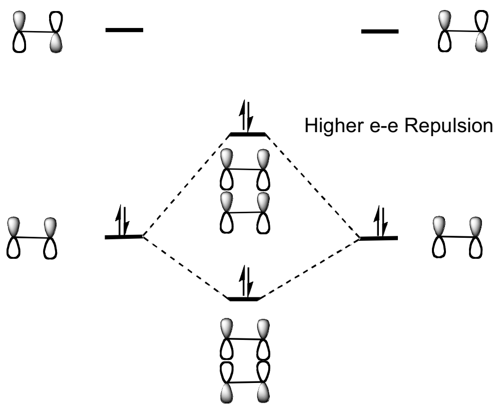
Molecular Helium
Is Unstable: Orbital Overlap
Leads to a Net Increase In Energy
(The σ* is higher than shown due to
e-e repulsion)



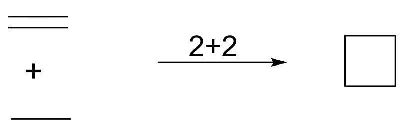
Dimerization of Ethylene



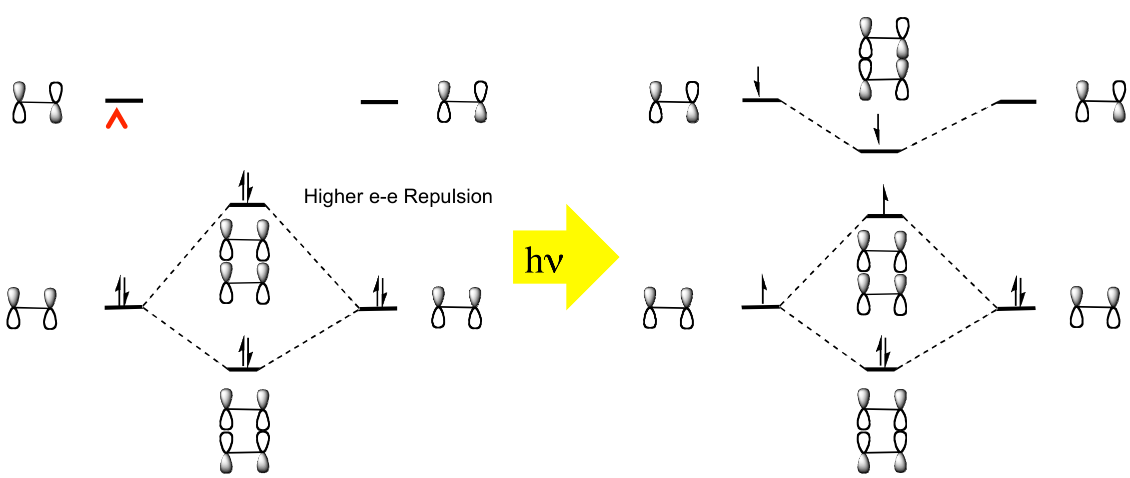
Thermally Forbidden
Photochemically Allowed



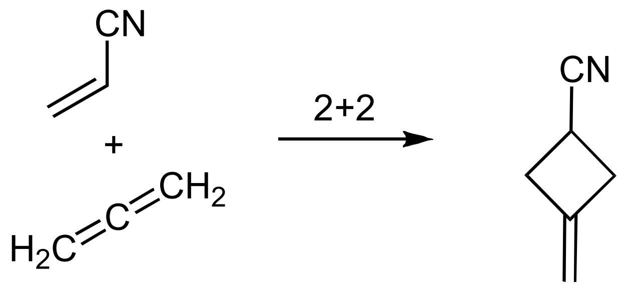
Dimerization of Ethylene



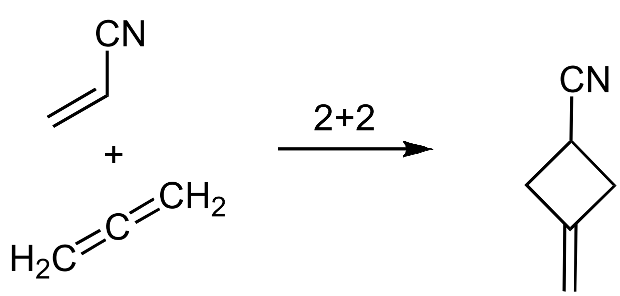
Thermally Forbidden
Photochemically Allowed



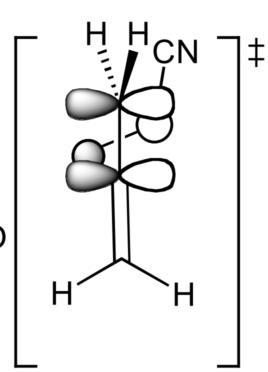
Example of a Thermally Allowed 2+2



Example of a Thermally Allowed 2+2

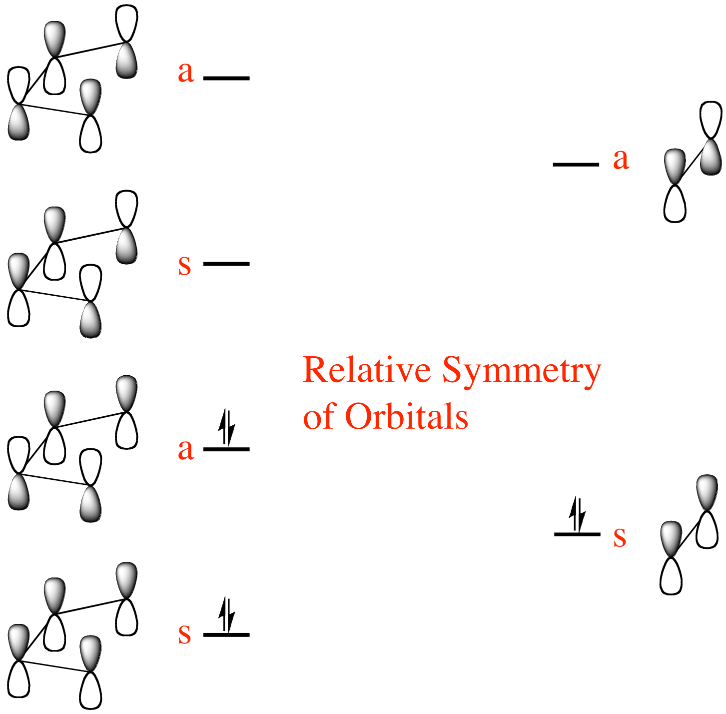


Allene HOMO
Acrylnitrile LUMO

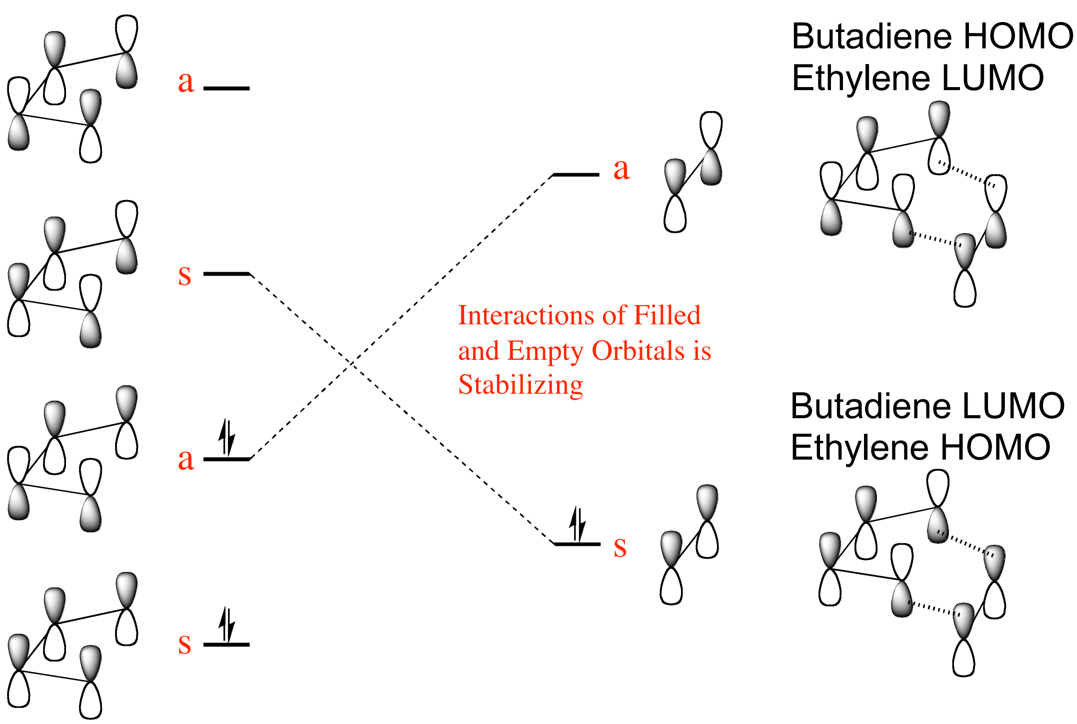


Bonding in the Tranisition State

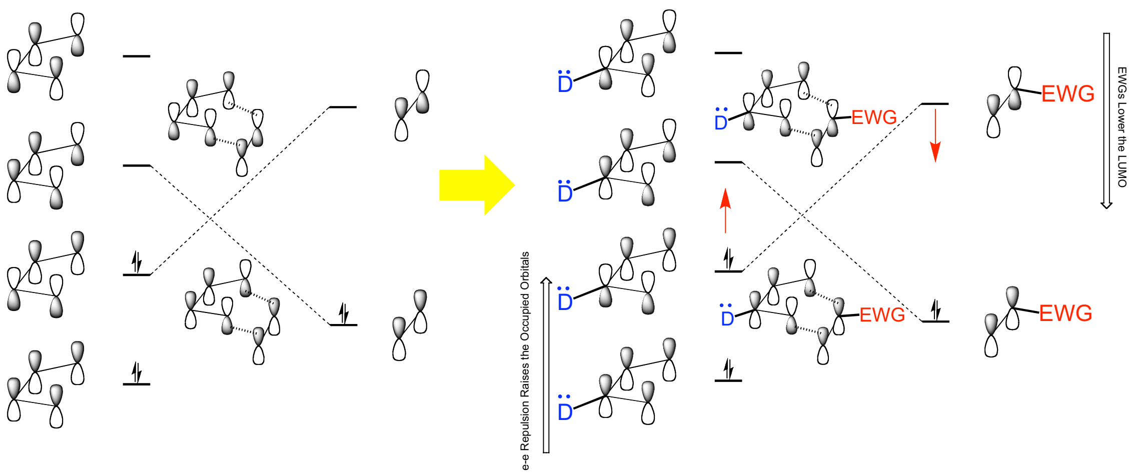
Orbitals of Butadiene and Ethylene



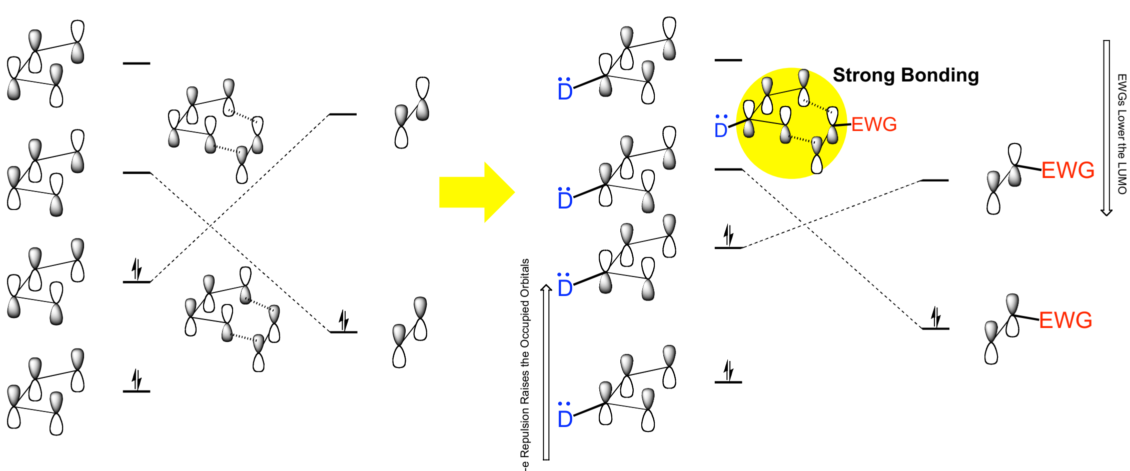
Orbitals of the Same Symmetry Can Interact



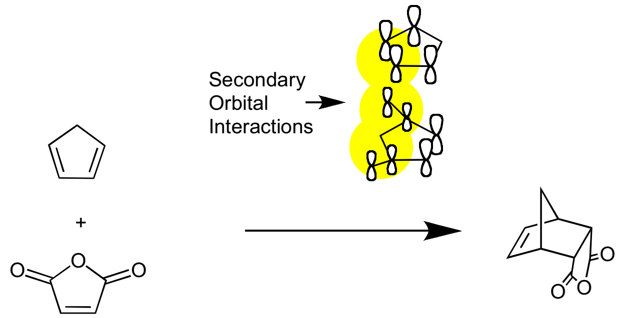
Purturbation Theory:
Orbitals Closer in Energy, Interact Stronger



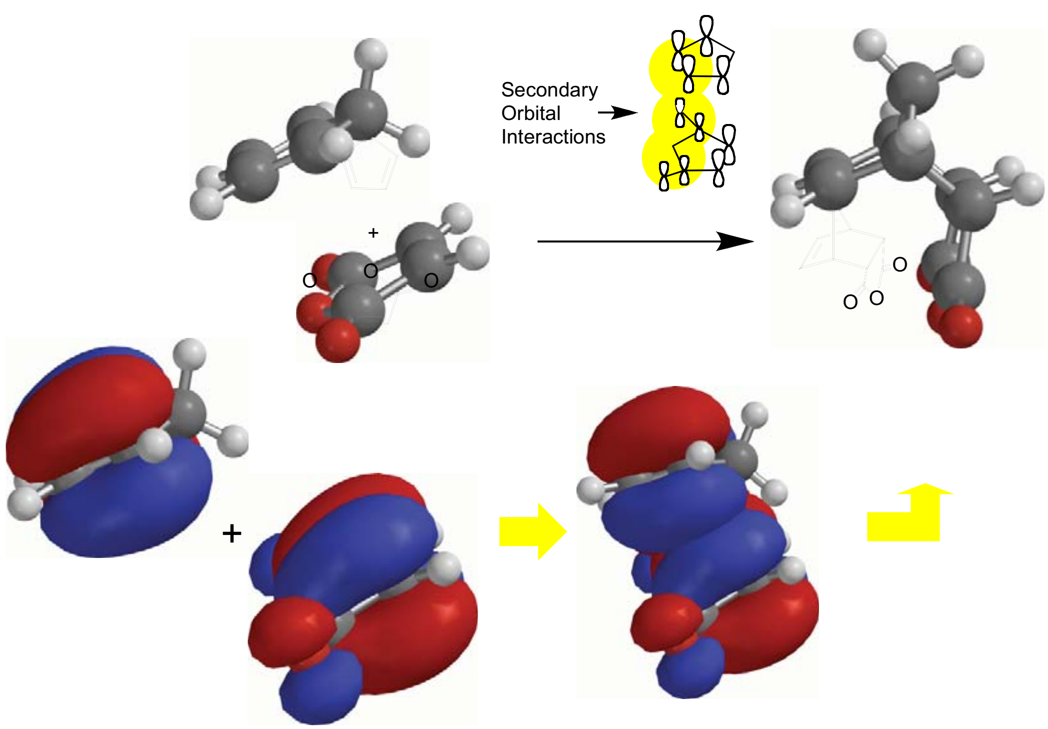
Purturbation Theory:
Orbitals Closer in Energy, Interact Stronger



Alder Endo Rule: Secondary Orbital Interactions



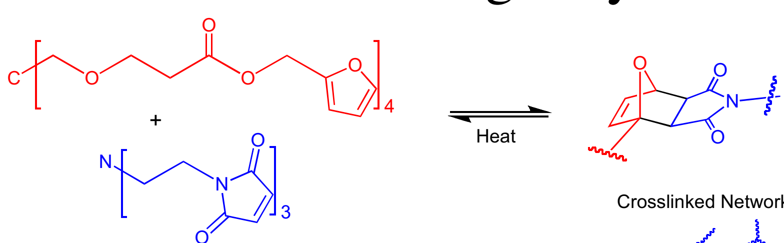
Alder Endo Rule: Secondary Orbital Interactions

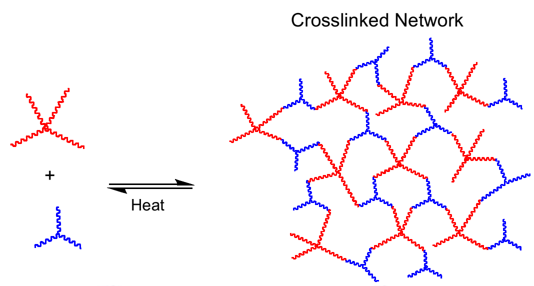


DA Reaction in Materials Chemistry

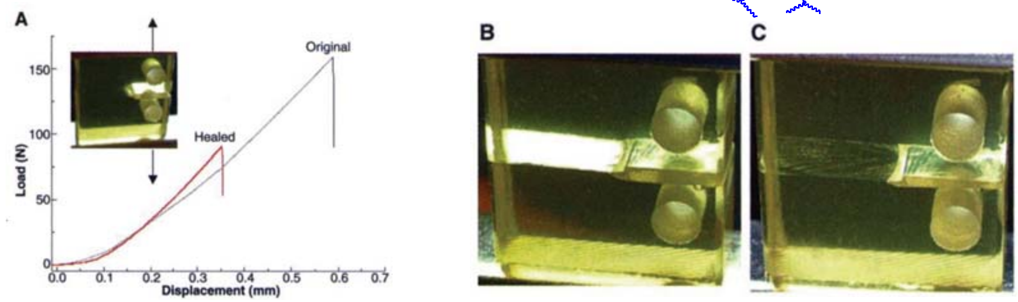
Features:
- Often a Very Clean Reaction
- It can be a Reversible Reaction
- Forms 2 New Bonds at Once
  - Produces Structurally Rigid Stuctures

Self Healing Polymers

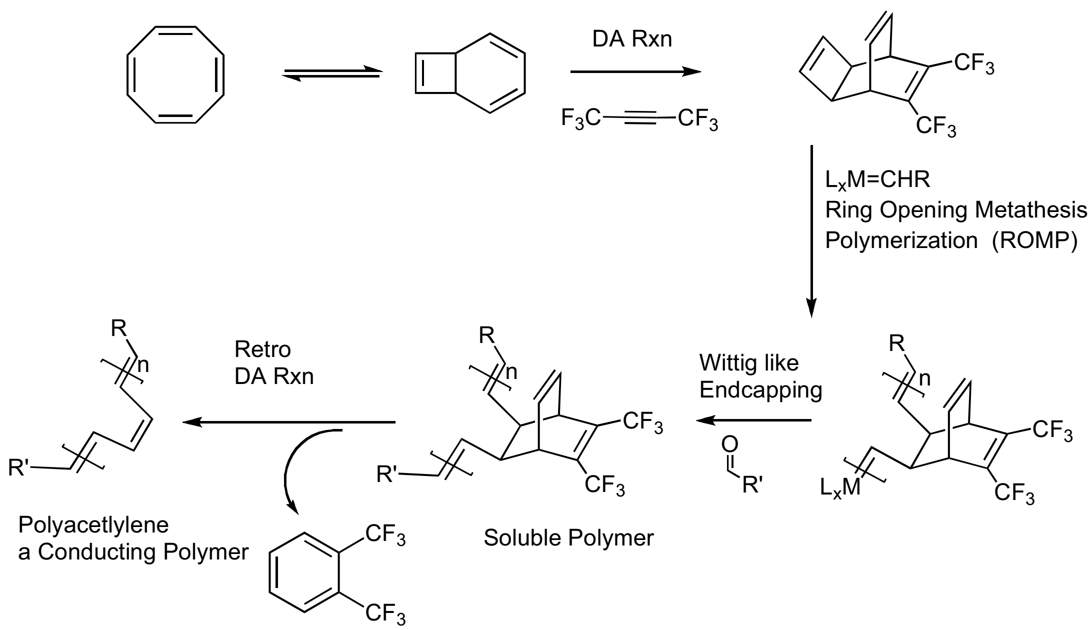




Wudl and coworkers
Science **2002**, 295, 1698

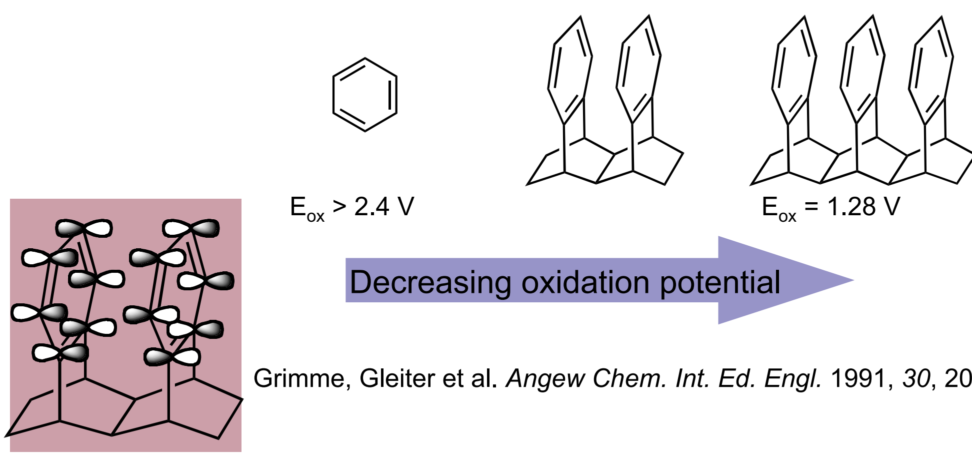


Retro-DA to Form an Organic Metal



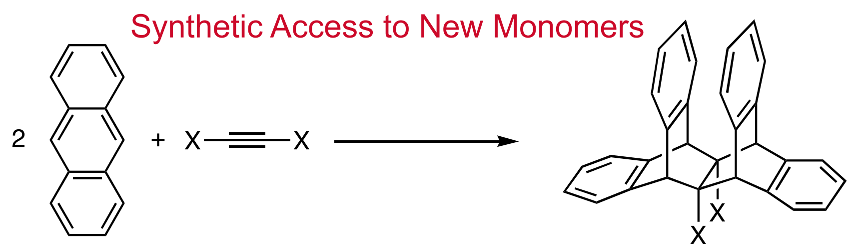
James Feast (Durham U.) Cira 1983

Through Space π-Interactions

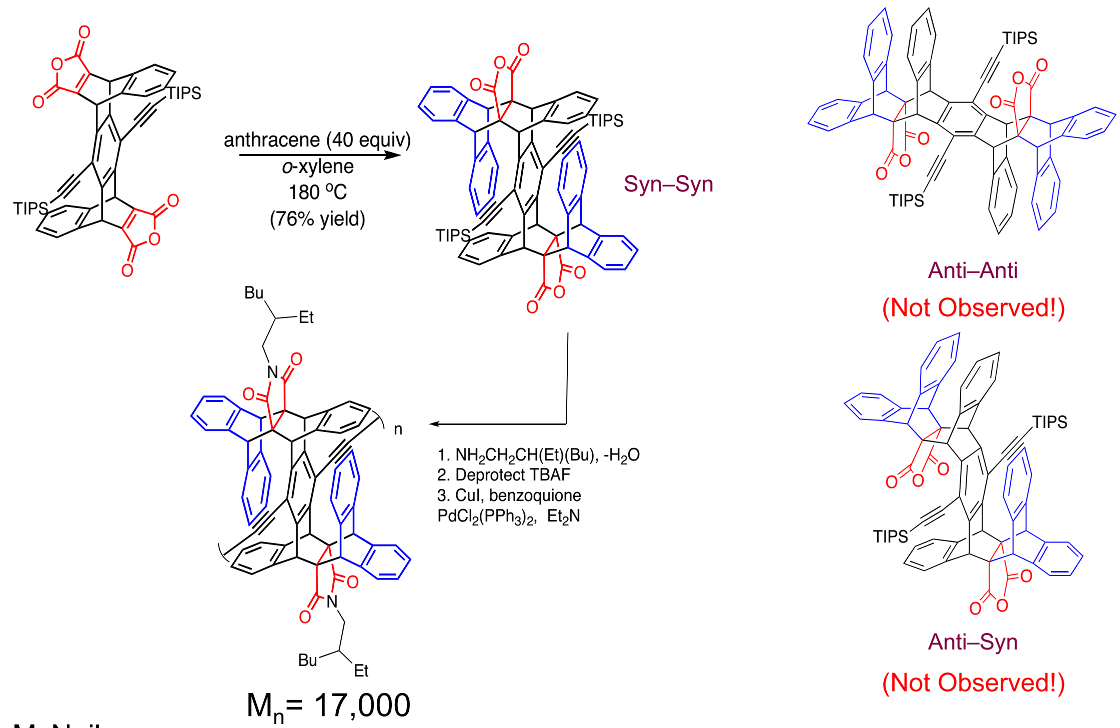


Grimme, Gleiter et al. *Angew Chem. Int. Ed. Engl.* 1991, *30*, 205-207.

What About Double DA Adducts?
Synthetic Access to New Monomers

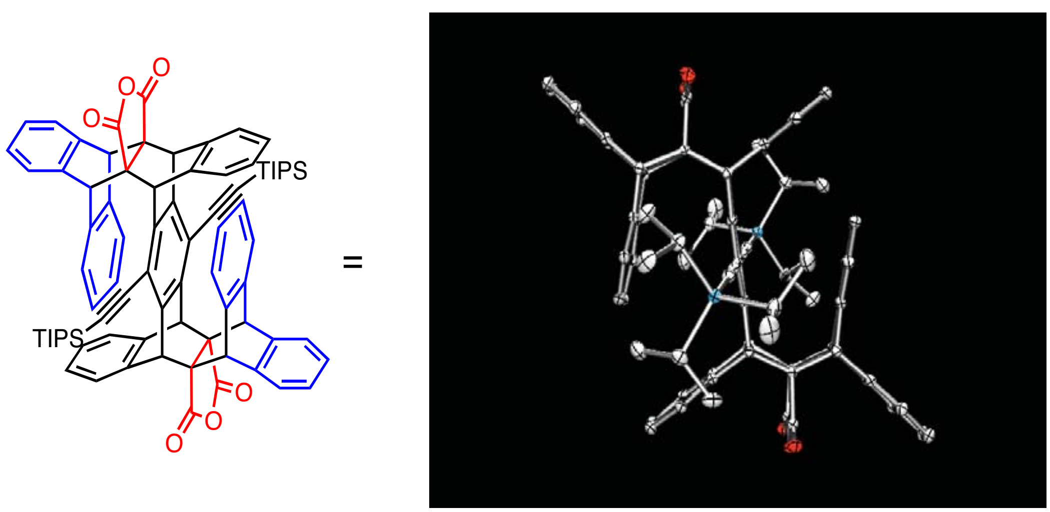


Monomer and Polymer Synthesis

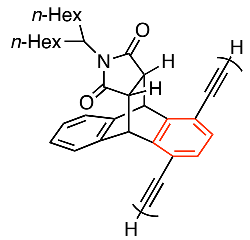


A. McNeil

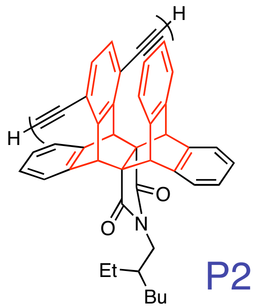
X-ray Crystallography



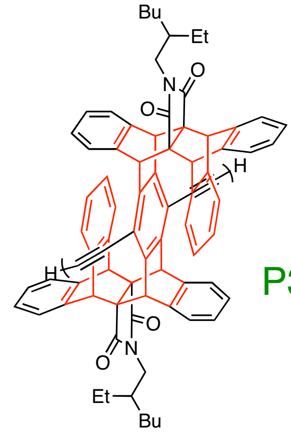
Photobleaching Studies: Thin Films



P1

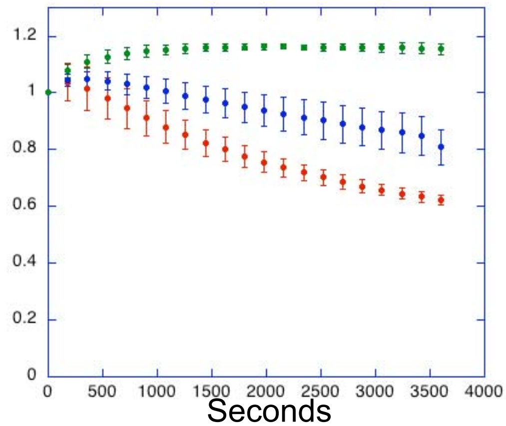


P2



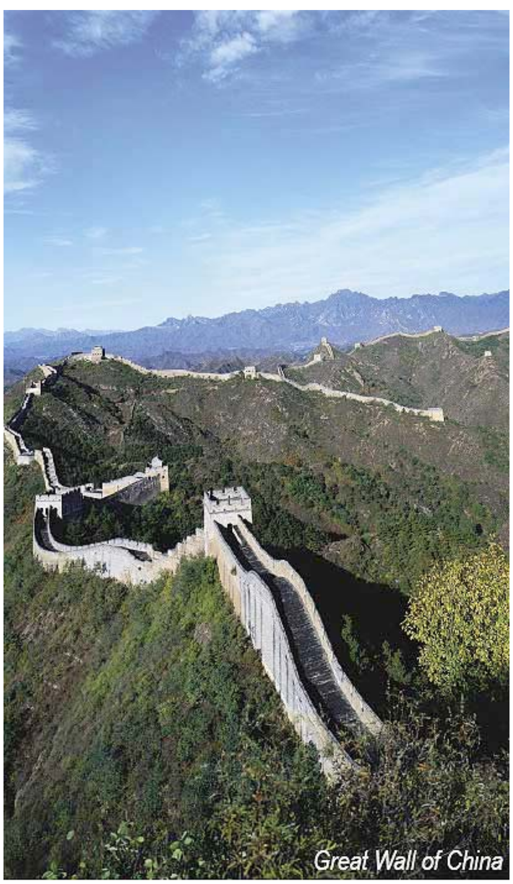
P3

UV Exposure at λ_{max}
With 20nm Slit Width
Matched Optical Densities

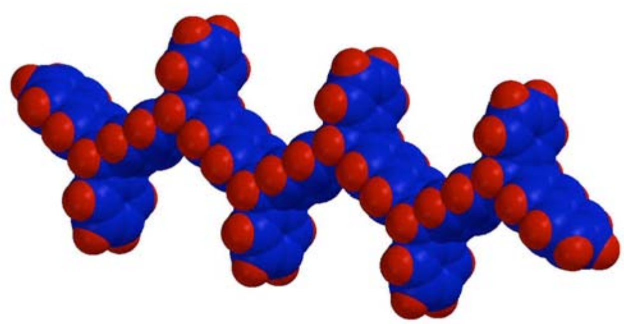


Increased Stability by Design:
1. No Reactive α-Protons
2. Stabilized Cations by Through Space π-Interactions
3. Arene Faces Blocked
4. 3-D Non-Aggregating Structure

A. McNeil

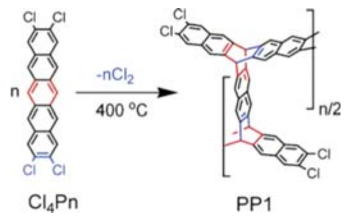


Synthesis of a Poly(iptycene) Ladder Polymer

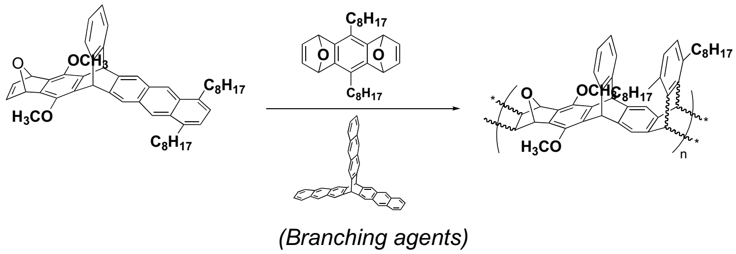


Zhihua Chen
PhD 200

Poly(iptycene)

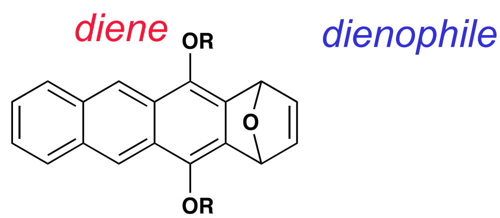


Wudl, F. et al *JACS*, 2003, *125*, 10190



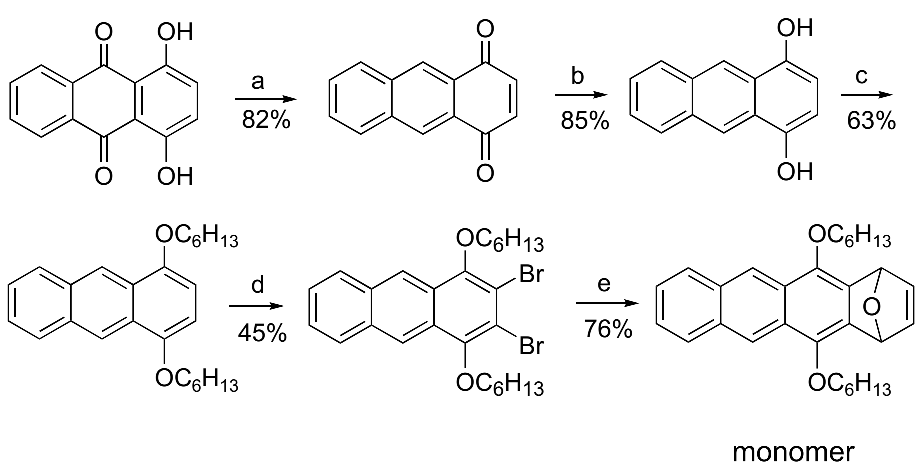
Thomas S. M. et al *JACS*, 2005,*127*, 17976

A simple approach:



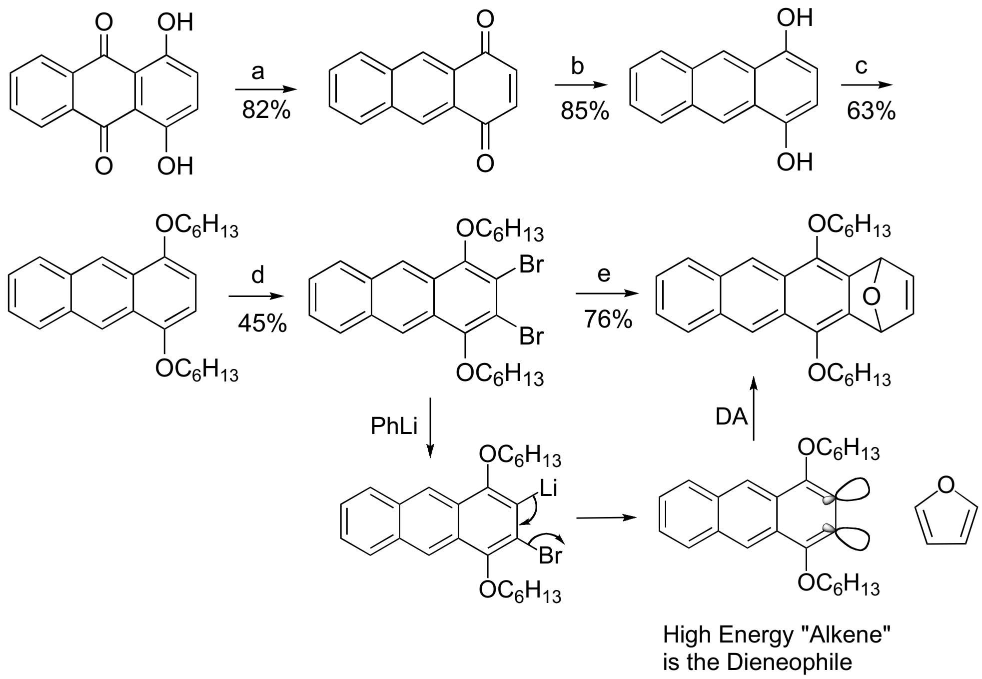
To improve solubility

Synthesis of Monomer

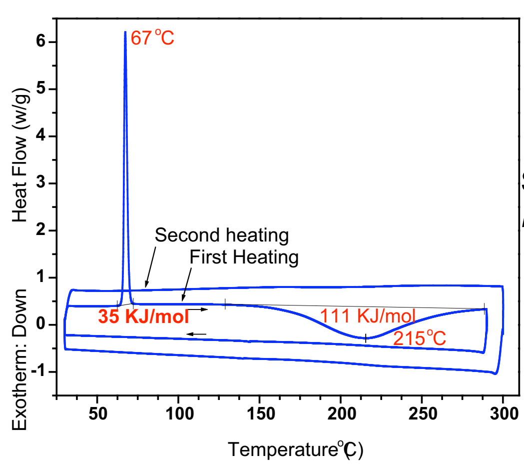


Reagents and conditions: (a) (1) $NaBH_4$, MeOH, rt-reflux; (2) HCl, rt. (b) $Na_2S_2O_4$, *p*-dioxane, H_2O, rt; (c) $C_6H_{13}Br$, K_2CO_3, KI,18-crown-6, DMF, 85 °C; (d) NBS, DMF, rt; (e) furan, THF, PhLi, 0 °C.

Synthesis of Monomer



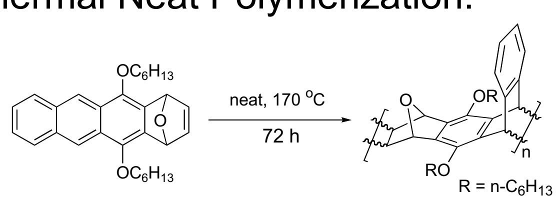
Differential Scanning Calorimetry



Sample after DSC study:

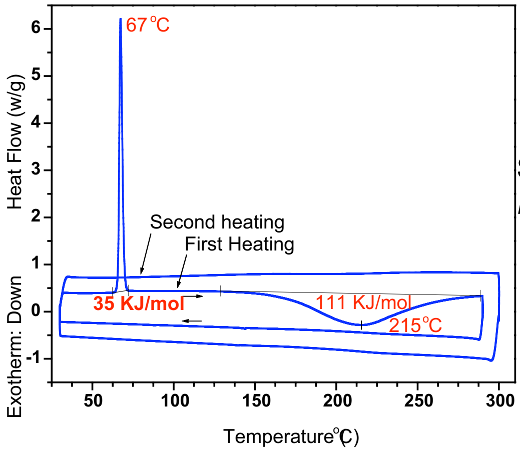
Mn=2.8KDa, PDI =2.8

Thermal Neat Polymerization:



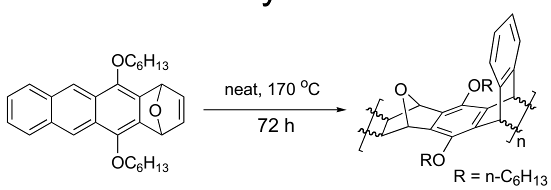
Low MW! Mn = 5~6 KDa

Differential Scanning Calorimetry



Sample after DSC study:
Mn=2.8KDa, PDI =2.8

Thermal Neat Polymerization:

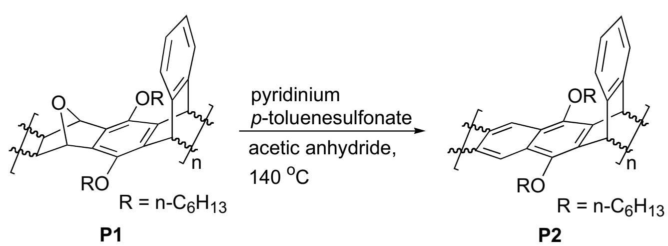


Low MW! Mn = 5~6 KDa

Diels-Alder reactions can be accelerated by the application of high pressure, because the transition state of D-A reaction has a net contraction in volume.

$$\Delta V^{\ddagger} = -RT(\partial \ln k/\partial P)_T$$

Synthesis of Poly(iptycene) Dehydration Reaction



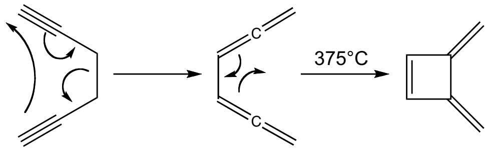
Summary of the synthesis of P1 and P2

entry	[M][a] (M)	Temperature (°C)	Time (h)	Pressure (psi)	P1 M_n[b] (Da)	P1 PDI	P2 M_n[b] (Da)	P2 PDI
1	0.50	145	5	128,900	6,100	2.2	n/a	n/a
2	0.88	145	5	139,600	9,400	2.7	10,900	2.4
3	1.01	145	5	145,800	11,100	3.3	12,600	2.6
4	1.50	145	5	145,800	16,400	3.6	16,300	2.5

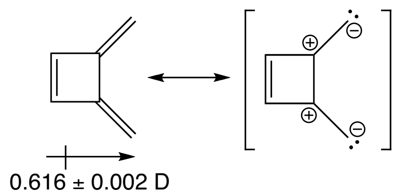
[a] Monomer concentration. [b] Molecular weights determined by GPC in THF against polystyrene standards.

Dimethylene Cyclobutene

- 3,4-Bismethylenecyclobutene (3,4-BMCB) is an isomer of benzene produced by flash vacuum pyrolysis of 1,5-hexadiyne



- Reactivity and electronic structure largely influenced by energetic cost of antiaromatic cyclobutadiene formation

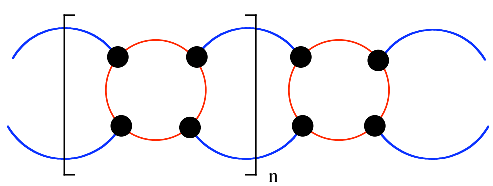


  - For this reason, s-*cis* diene formed by exocyclic methylene groups is *not* reactive in Diels-Alder chemistry

Coller, *Aust. J. Chem.,* **1968**, *21*, 1807.

Ladder Polymers

- Polymers consisting of cyclic subunits connected by two links that do not merge or cross

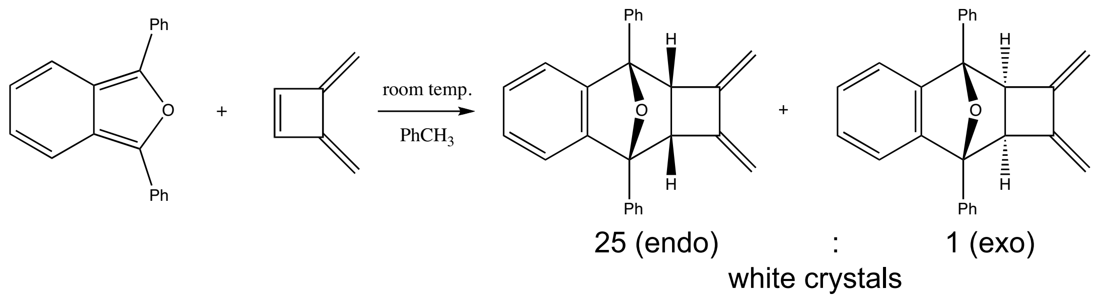


- Molecular weight remains constant when one bond is broken
  - Potential for high-strength materials
- Difficulty of synthesis and processing prevented first generation ladder polymers from gaining industrial importance
- Two main obstacles to ladder polymer synthesis
  - Rigid backbone leads to inherent insolubility
  - Side reactions can lead to cross-linking and defects

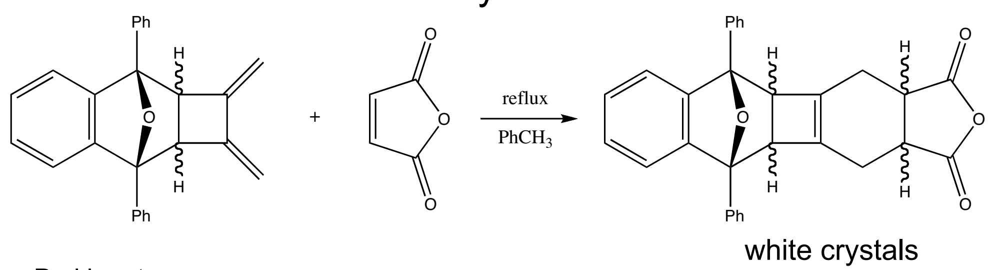
Schluter, A.D. *Materials Science and Technology.,* 1999, **20**, 459.

Diels-Alder of 3,4-Bis(methylene)cyclobutene

• Used 1,3-diphenylisobenzofuran as diene

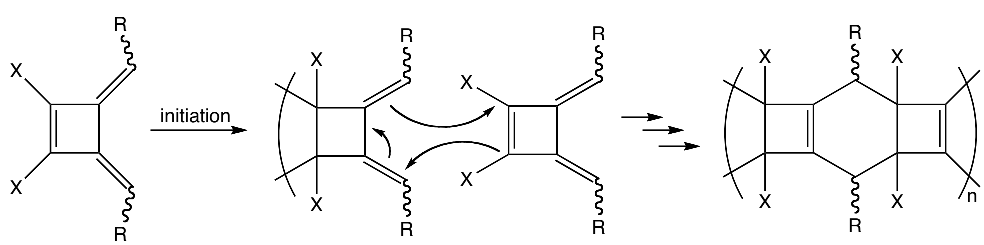


• Reaction with maleic anhydride

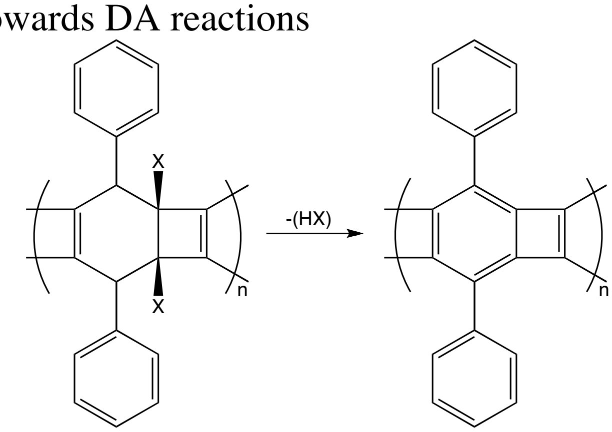


Becca Parkhurst

Towards Conjugated Ladder Polymers



• Using an electron-withdrawing group as "X" sould increase reactivity towards DA reactions



Becca Parkhurst

Diels Alder Reaction

The most powerful reaction in organic chemistry

- Stereochemistry
- Multiple bonds produced
- Products with confomational rigidity
- High yeild and reversible

Applications in synthesis, from nature product synthesis to materials science