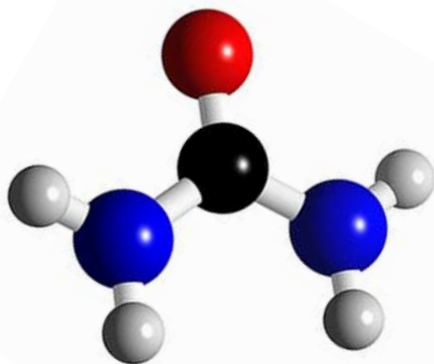
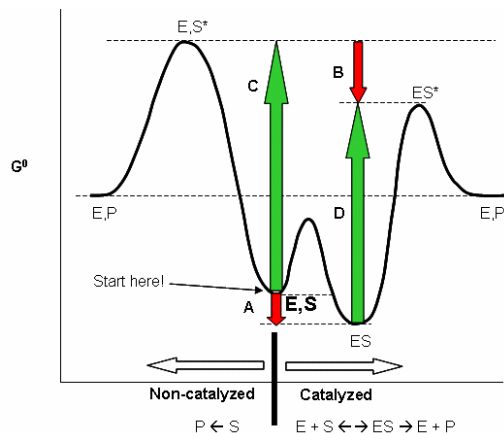


Conceptualizing Reaction Mechanisms using Crystallographic Data



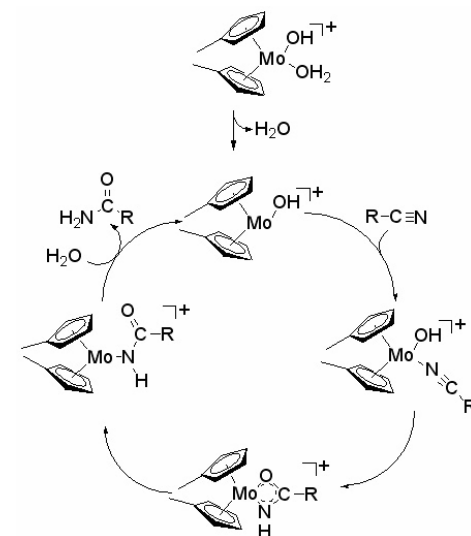
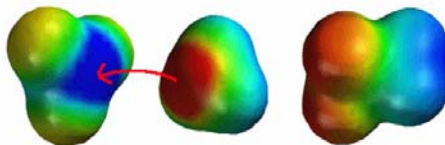
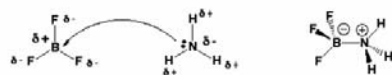
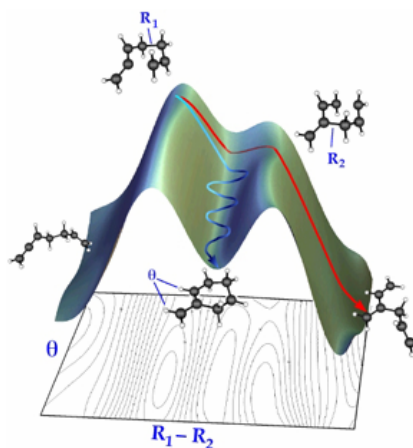
Kraig Wheeler
Department of Chemistry
Eastern Illinois University

Reaction Pathways

Nucleophilic addition to carbonyls
 S_N1 reactions

Reactive Intermediates

Electrophilic Addition to Alkenes
Electrophilic Aromatic Substitutions
Enolate Chemistry



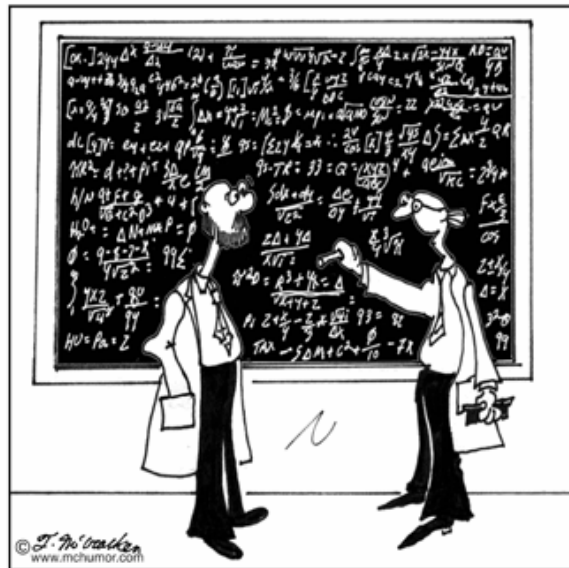
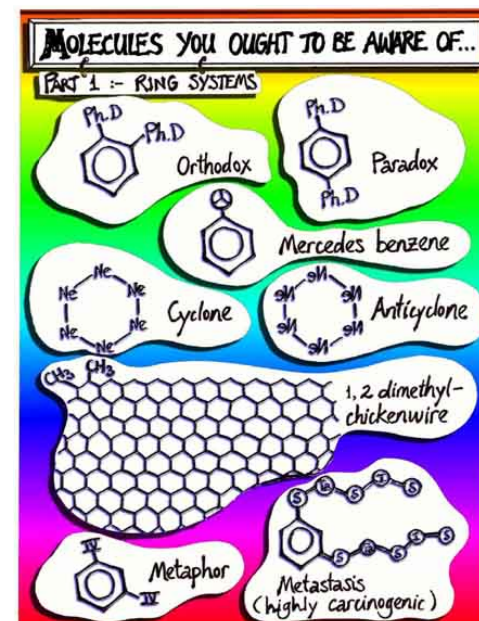
Obstacles to Incorporating Crystallography In Undergraduate Chemistry Courses

Ongoing struggle with course content (What to include?)

- Full Curriculum – American Chemical Society Guidelines
- Complications from Multiple Sections/Multiple Instructors
- Instructor Skill Level/Desire
- Lack of Coverage in Textbooks

Connecting Students with Crystallography

- May require additional instruction
- Noticeable Benefit?
- Low Level use in the classroom
(e.g. proof of bond distances)



“There’s really no need for confusion.
Part 95 of section 33 of article Q
in the formula quite clearly states ...”

Why Use Crystallography in the Classroom?

Now Considered One of the *Essential* Analytical Tools

Depth of Information Gathered From Crystal Structures

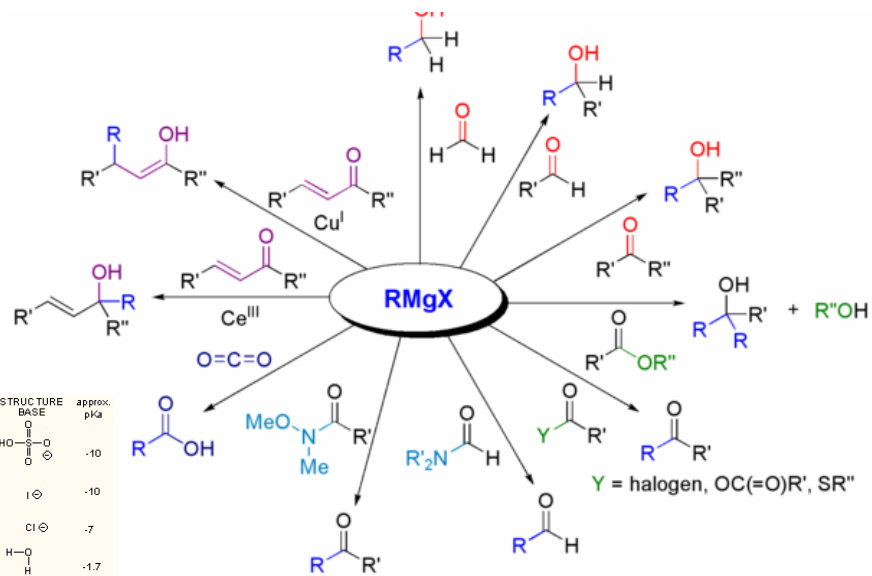
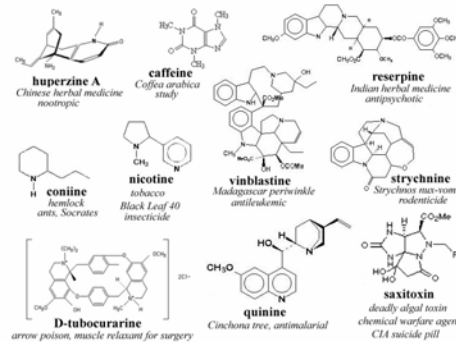
Ease of Access to Crystal Structure Data (>450,000 structures)

Data Mining Capability of the CSD

Student Exposure/Training

- Undergraduate Research
- Preparation for Professional Careers

An Assortment of Alkaloids

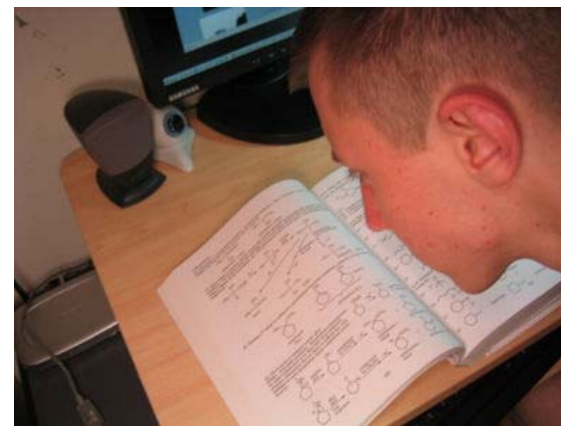
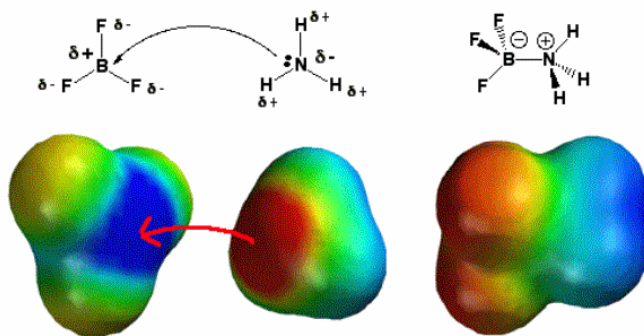
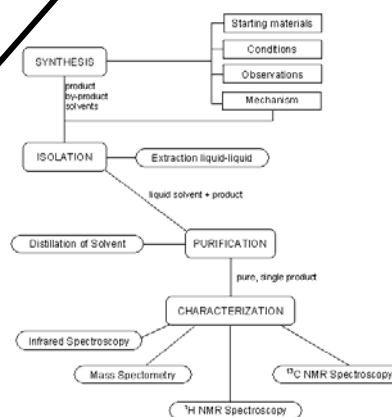


COMPOUND	STRUCTURE ACID	STRUCTURE BASE	approx. pKa
sulfuric acid	<chem>HO-S(=O)(=O)-OH</chem>	<chem>HO-S(=O)(=O)-O-</chem>	-10
hydroiodic acid	<chem>H-I</chem>	<chem>I-</chem>	-10
hydrochloric acid	<chem>H-Cl</chem>	<chem>Cl-</chem>	-7
hydronium ion	<chem>H-O-H</chem>	<chem>H-O-H</chem>	-1.7
acetic acid	<chem>H3C-C(=O)-OH</chem>	<chem>H3C-C(=O)-O-</chem>	5
ammonium	<chem>H-N-H</chem>	<chem>H-N-H</chem>	9
phenol	<chem>c1ccccc1O</chem>	<chem>c1ccccc1[O-]</chem>	10
acetone enol	<chem>CC(=O)C</chem>	<chem>CC(O)=C</chem>	11
methanol	<chem>H3C-OH</chem>	<chem>H3C-O-</chem>	15.5
water	<chem>H-O-H</chem>	<chem>H-O-</chem>	15.7
acetaldehyde	<chem>CC=O</chem>	<chem>CC(O-)=O</chem>	17
t-butanol	<chem>CC(C)(C)O</chem>	<chem>CC(C)(C)[O-]</chem>	18
acetone	<chem>CC(=O)C</chem>	<chem>CC(O-)=O</chem>	19
ammonia	<chem>H-N-H</chem>	<chem>H-N-</chem>	38
methane	<chem>H-C-H</chem>	<chem>H-C-</chem>	48

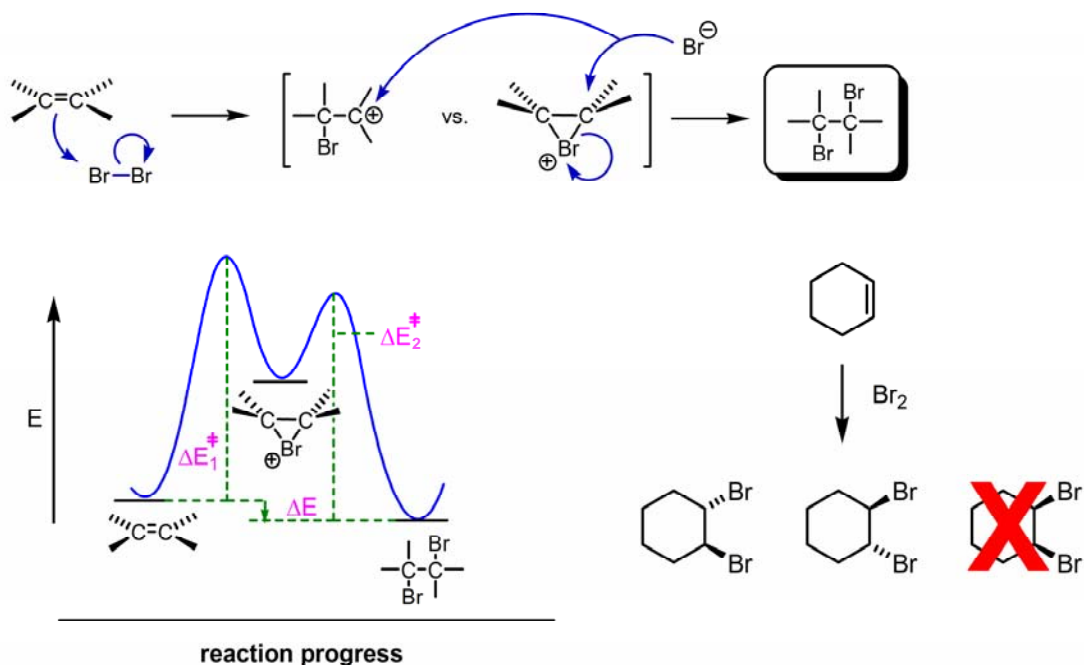
Memory-Based

Student Comprehension of Organic Chemistry

Discovery/Cooperative/Problem-Based



Addition of Halogen to an Alkene

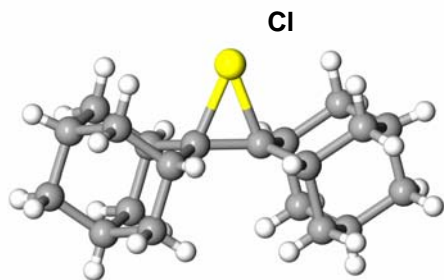
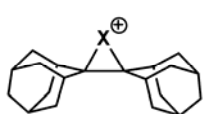


Excerpt from a Professional exam service

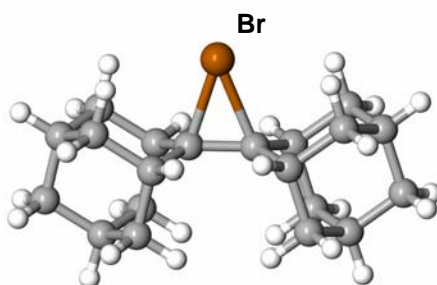
Warning! There are two versions of the ethene / bromine mechanism in common use, and you **must** know which your **examiners** will accept. One version is simplified to bring it into line with the other alkene electrophilic addition mechanisms. You will probably find that your examiners will accept this one, but you must find out to be sure.

Teaching Goals

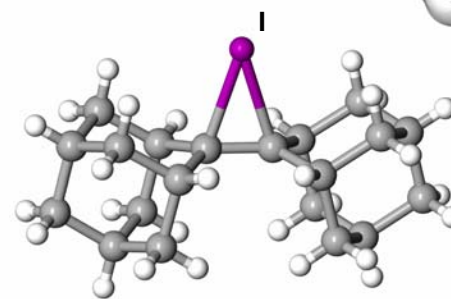
- Reaction outcomes (regio- and stereoselectivity)
- Evidence for cyclohalonium ions? (crystal structure data)
- Why adamantane and not other substrates in the CSD?



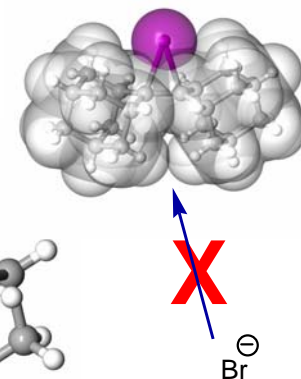
UGIDP



DAKVUG

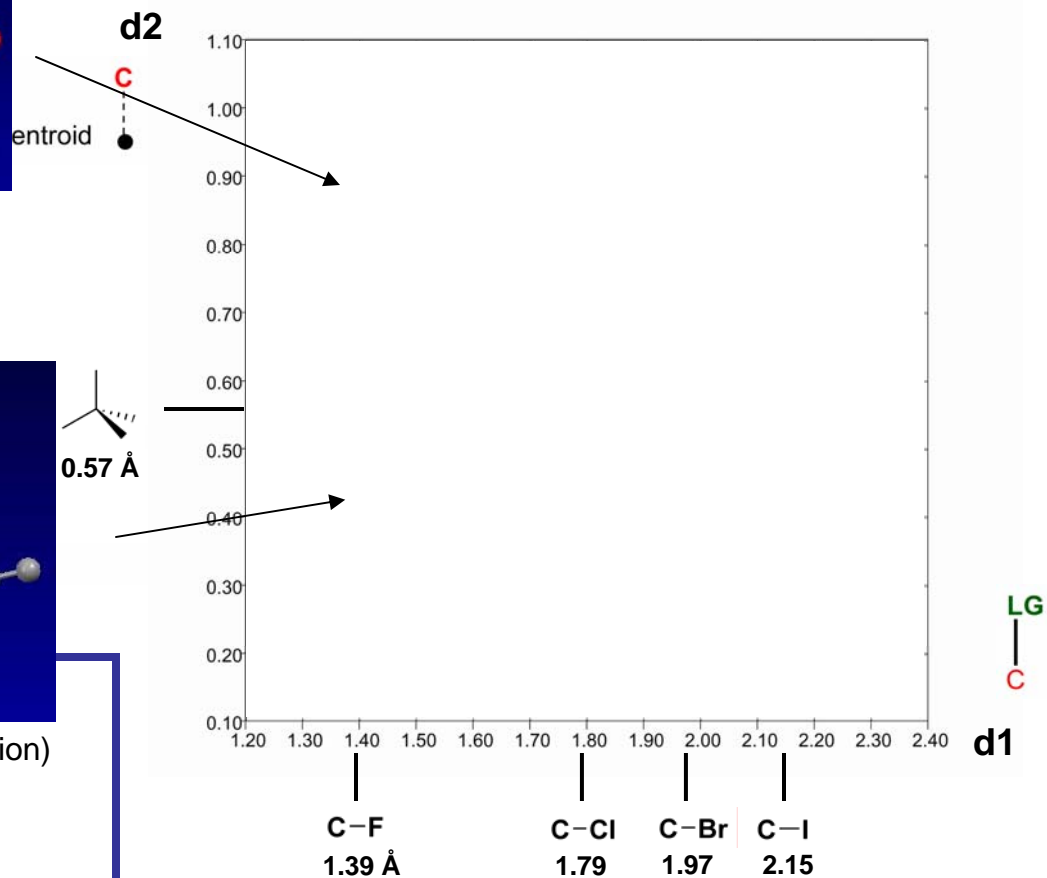
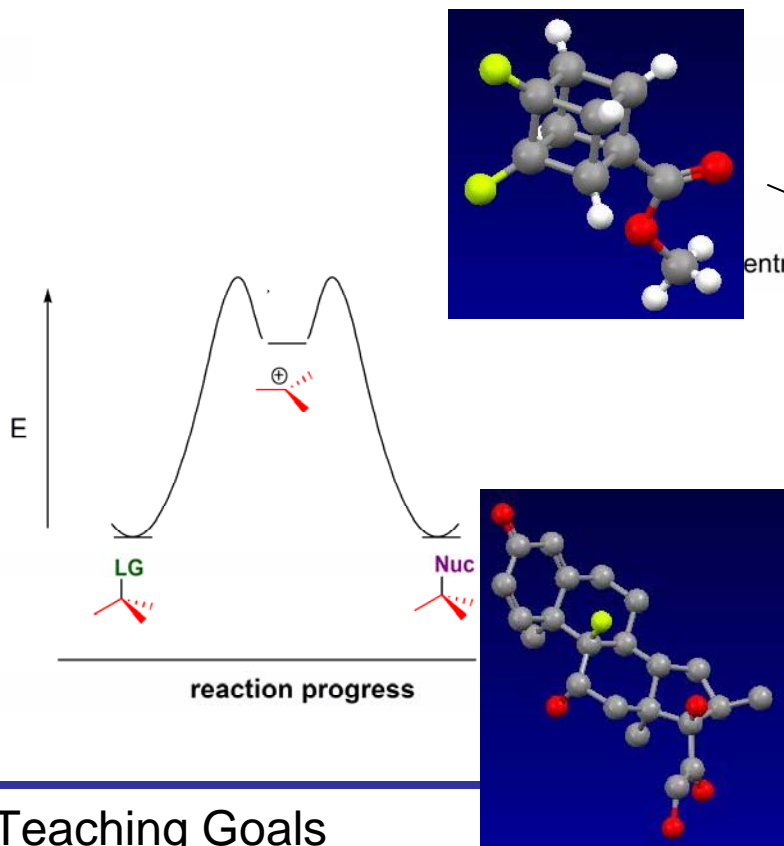
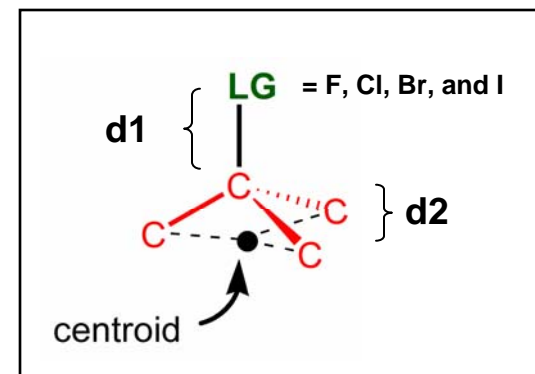
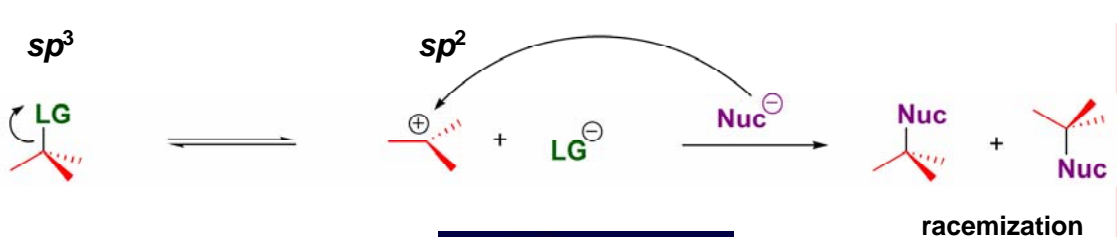


WEVPOC



Substitution – S_N1

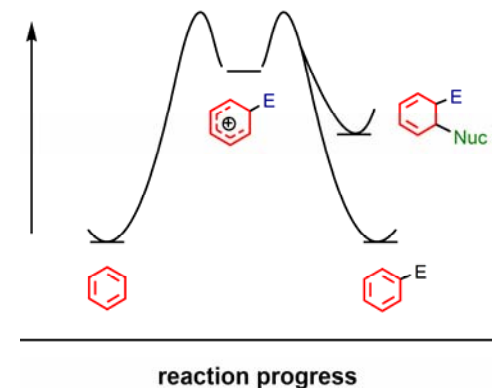
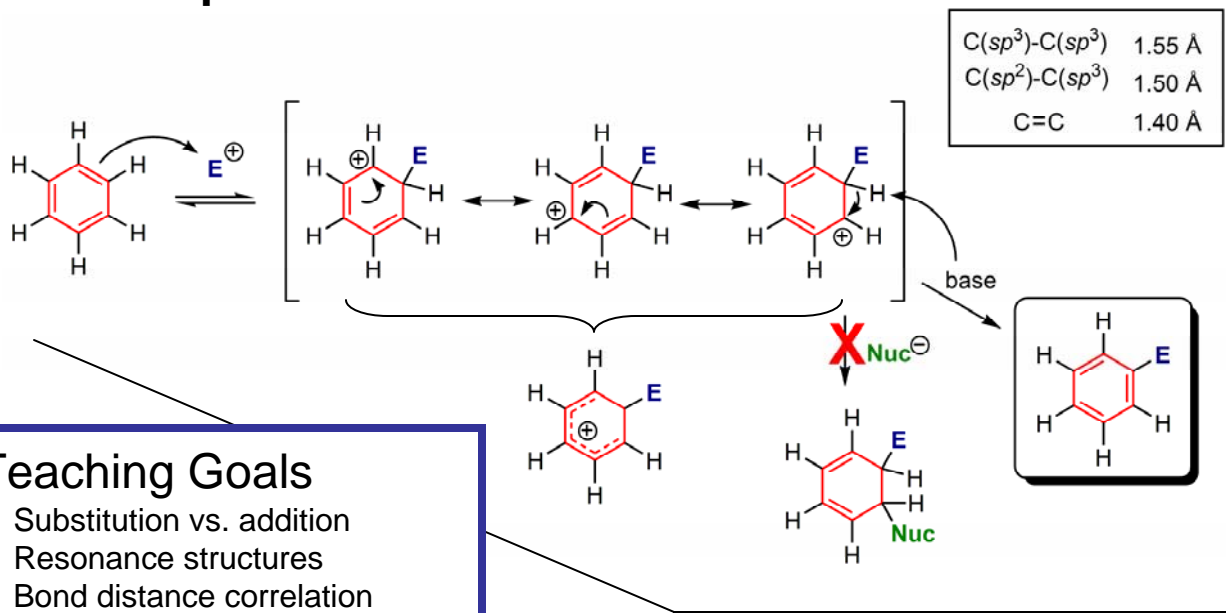
central carbon atom



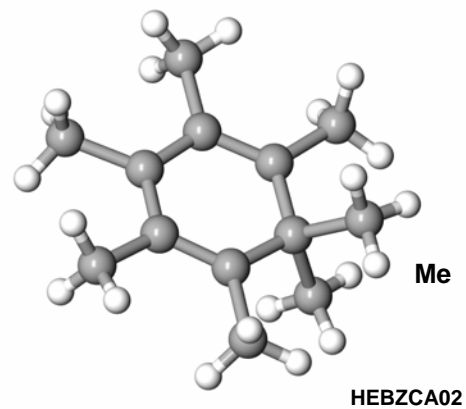
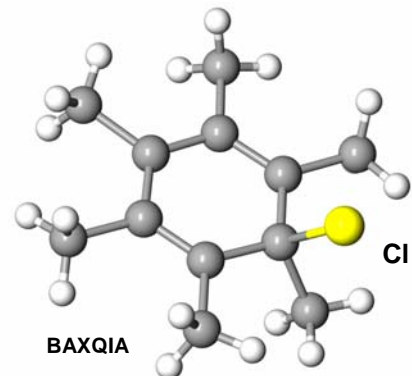
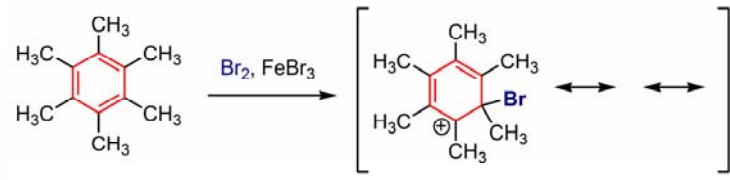
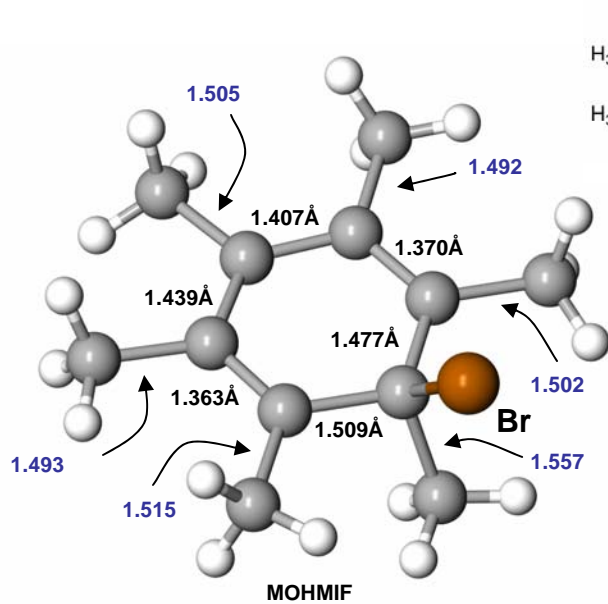
Teaching Goals

- S_N1 reaction outcomes (substitution and racemization)
- Carbocation intermediate - correlation between hybridization and C-LG length
- Bond distances – deviation from average

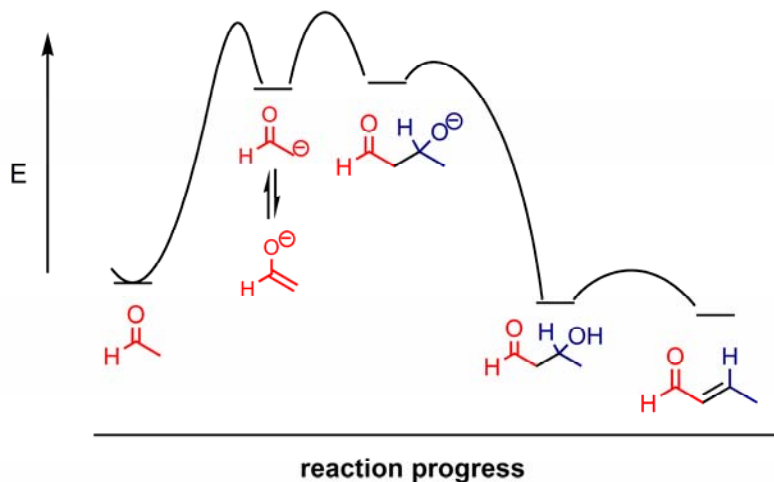
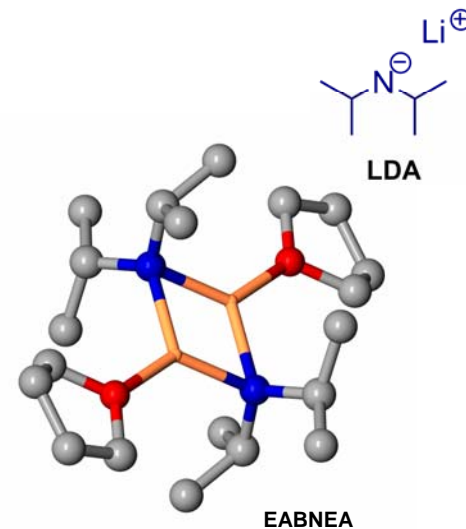
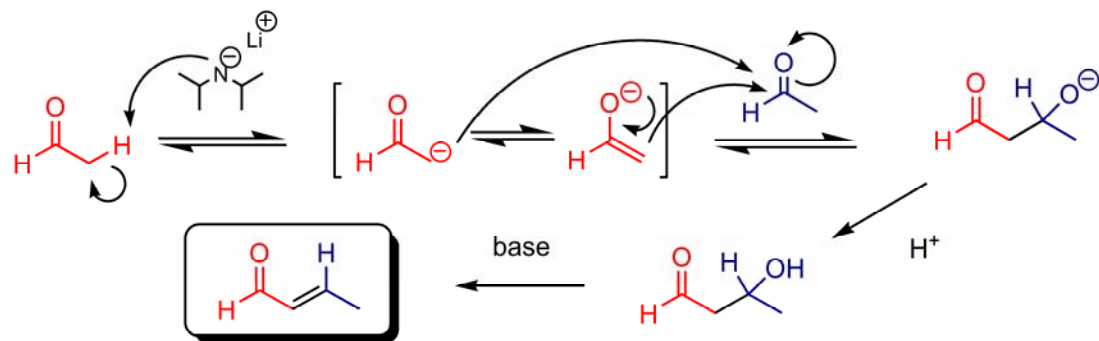
Electrophilic Aromatic Substitution



- Teaching Goals**
- Substitution vs. addition
 - Resonance structures
 - Bond distance correlation



Enolates



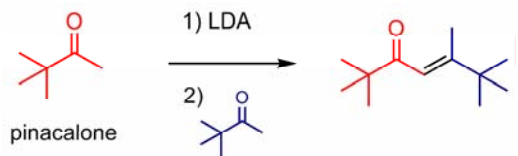
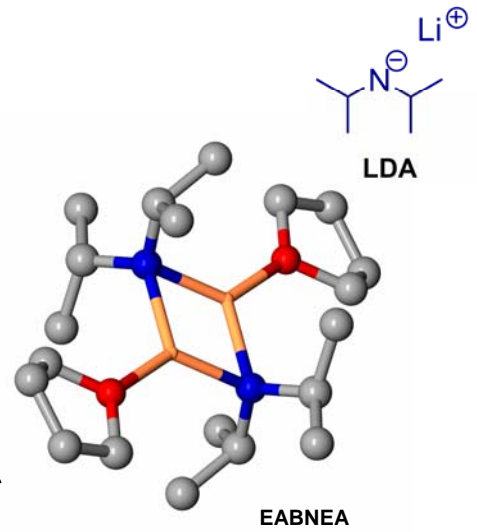
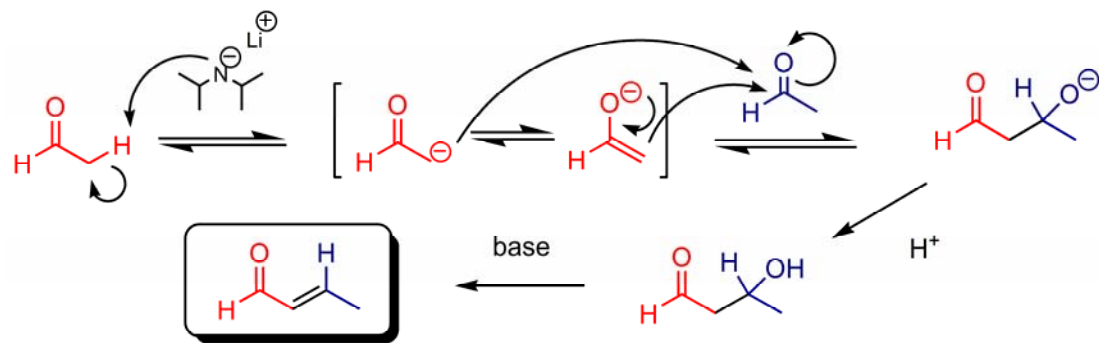
Solvent Choice?

Ligand	Polar:		aprotic		
	protic				
LDA	H ₂ O	AcOH			
	16	4	~60		33
N ⁻	Nonpolar:		aprotic		
	43		~60	(pKa)	

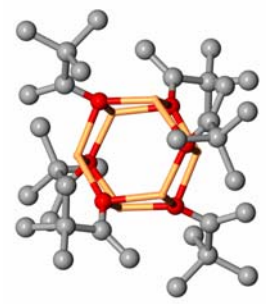
Teaching Goals

- enolate generation
- choice of base and solvent
- reaction driving force
- mechanistic viewpoint

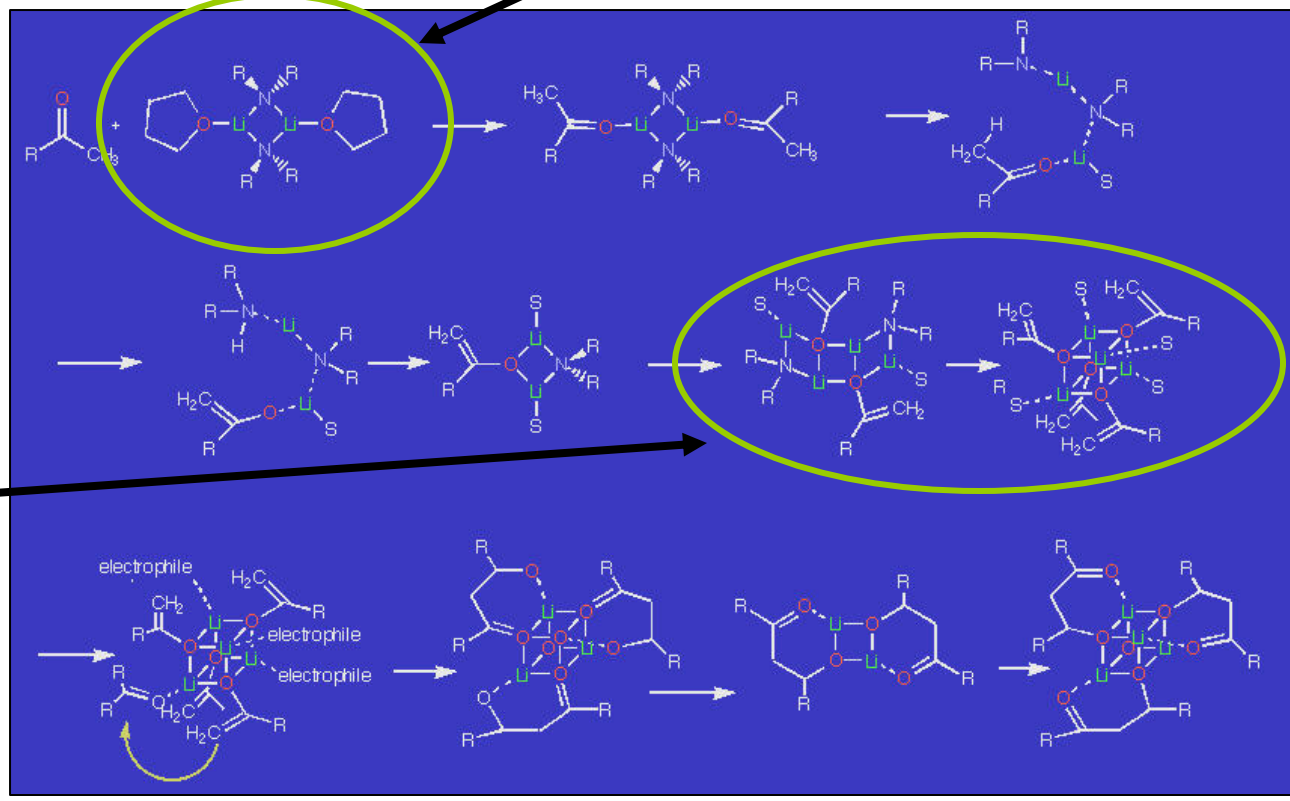
Enolates



J. Am. Chem. Soc., **1993**, *115*, 3380

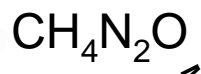
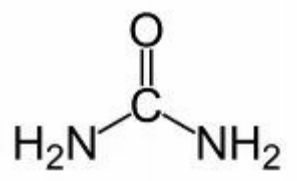
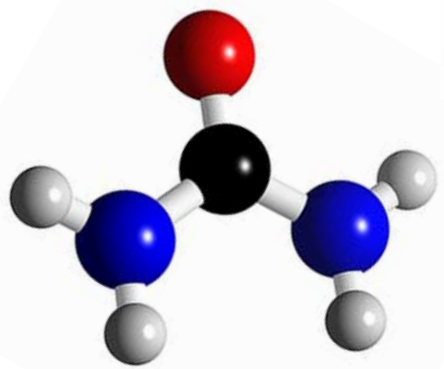


CUYVOH



History of Urea – Production and Mechanism

> 50 participants



1773 – Rouelle (Discovery)
1828 – Wohler (Synthesis)

IONIC
MOLECULAR

Walker – 1895 (1st Kinetics)
Chattaway – 1912

WWI
1913 – Werner
1913 – Wheeler

1932 – Moelwyn-Hughes
1934 – Lowry

Warner and Stitt – 1933
Svibely – 1935-39
Warner and Warrick, Miller

WWII

1949 – Weil and Morris
1952 – Wyatt and Kornberg
Frost and Pearson

1953

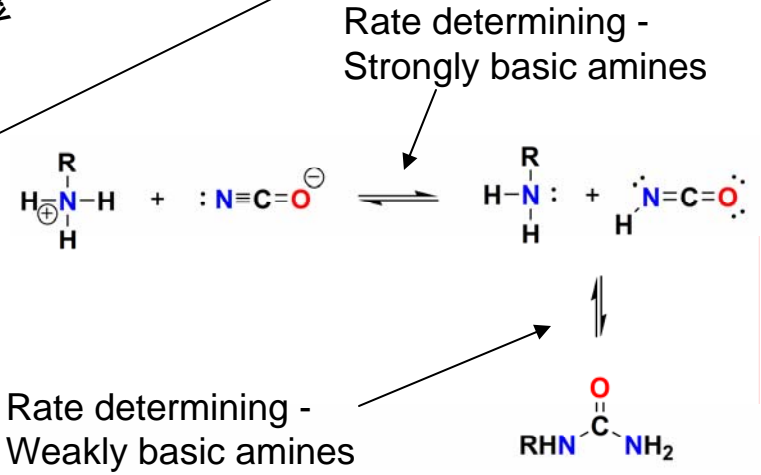
1959-65 – Jensen Stark
Amis

1966

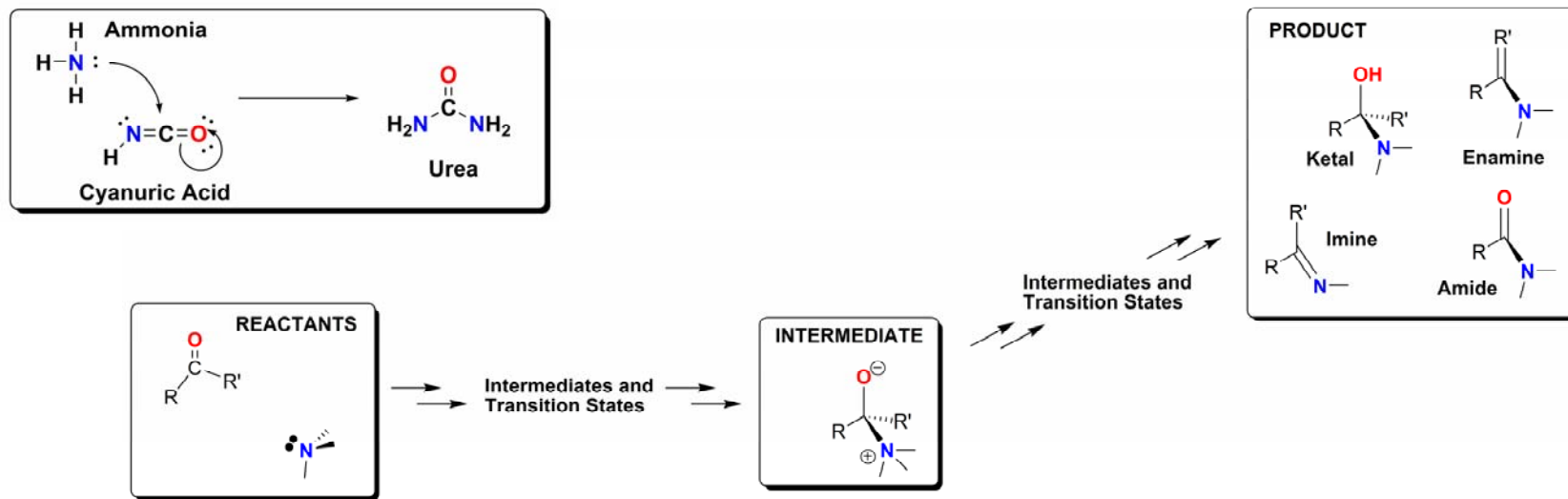
1974 – Williams and Jenks

Williams and Jenks

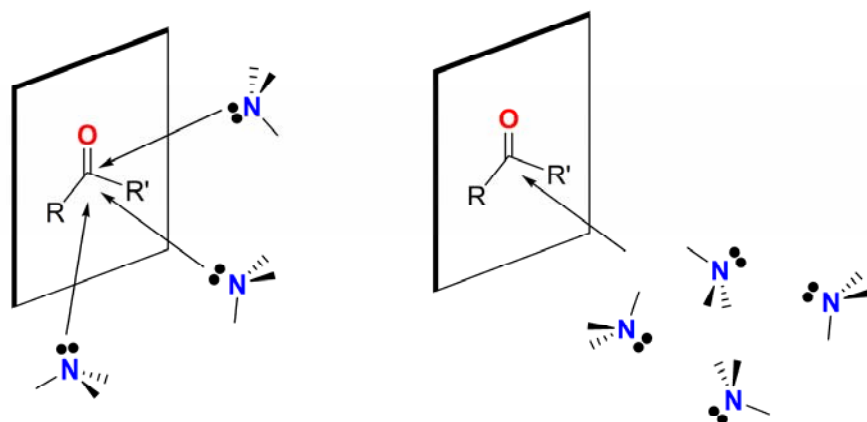
Evidence for Deprotonation!!



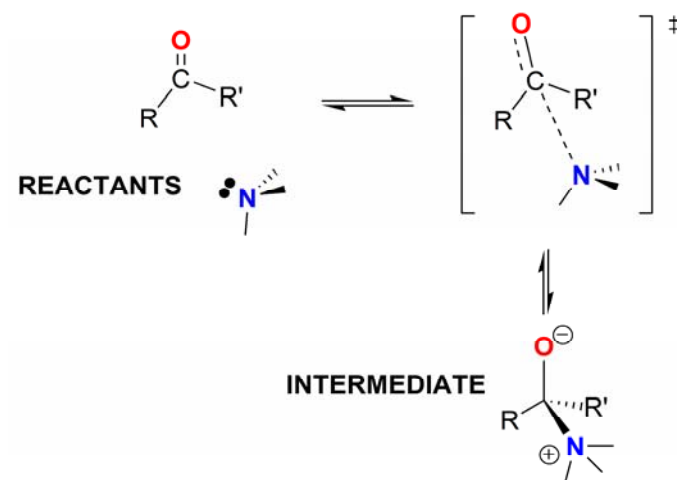
Data Mining Using Crystal Structures



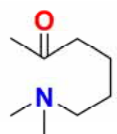
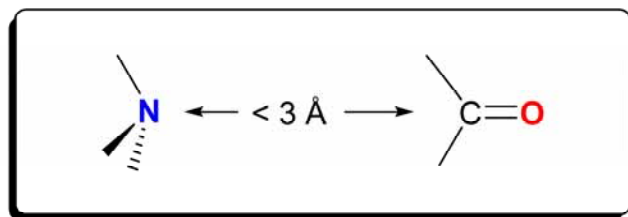
Orientation of Attack



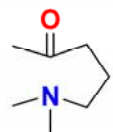
Correlation of Bond Distances



Data Mining Using Crystal Structures

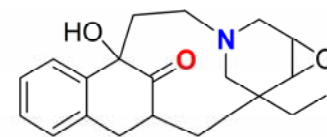
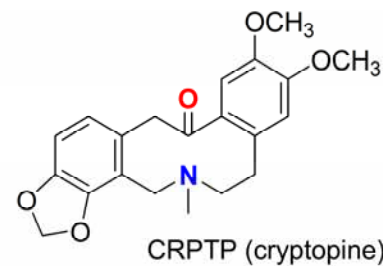


4-Membered Tether
(15 Structures)

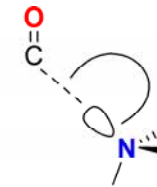
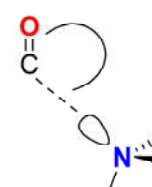
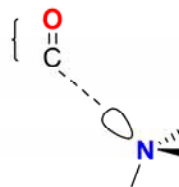
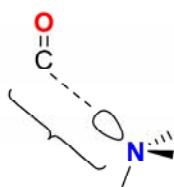
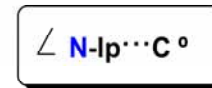
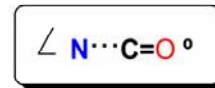
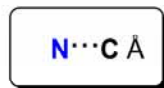
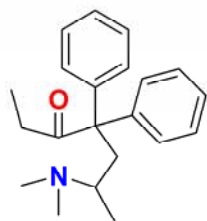
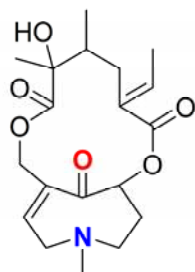
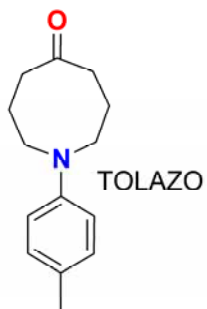


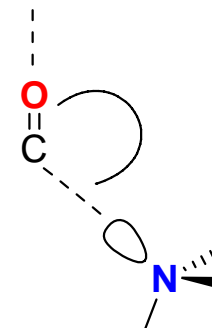
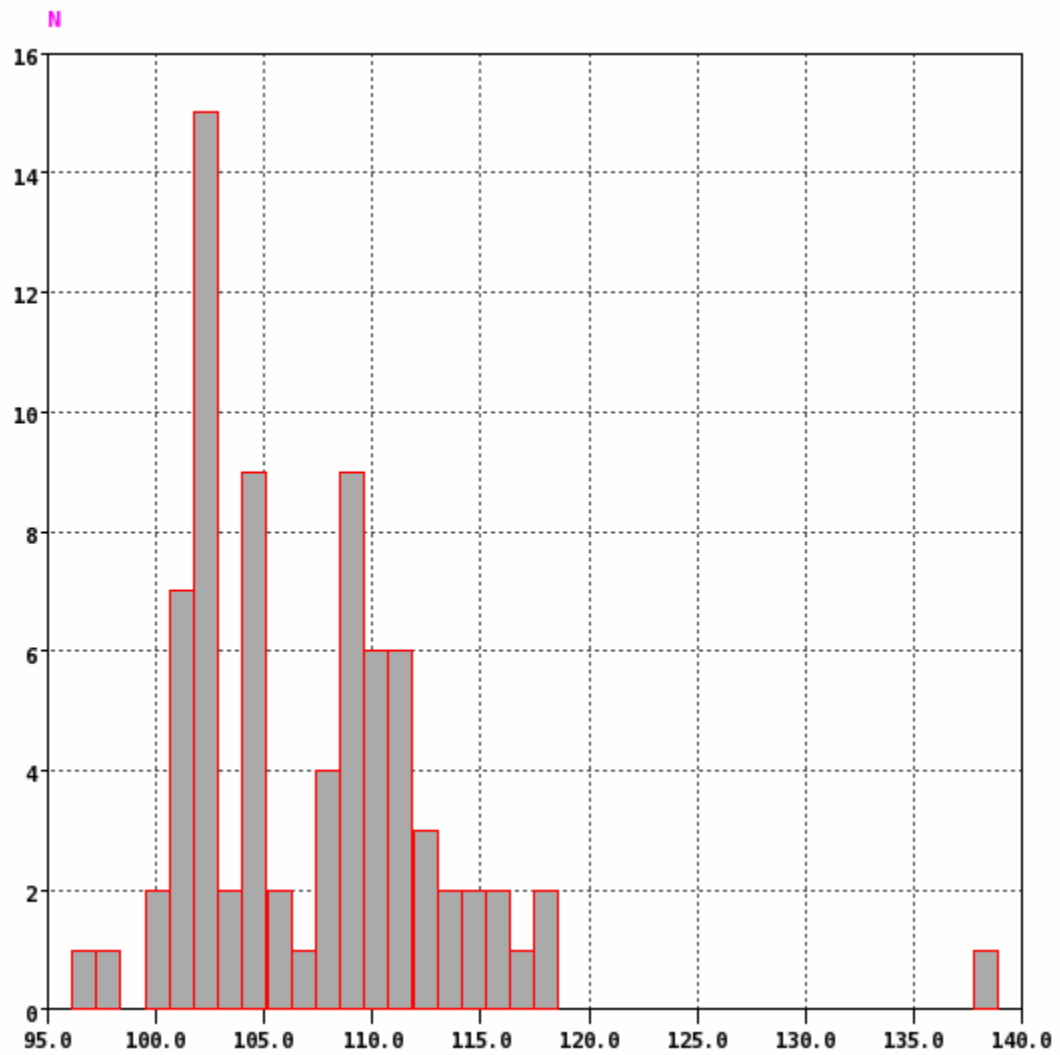
3-Membered Tether
(25 structures)

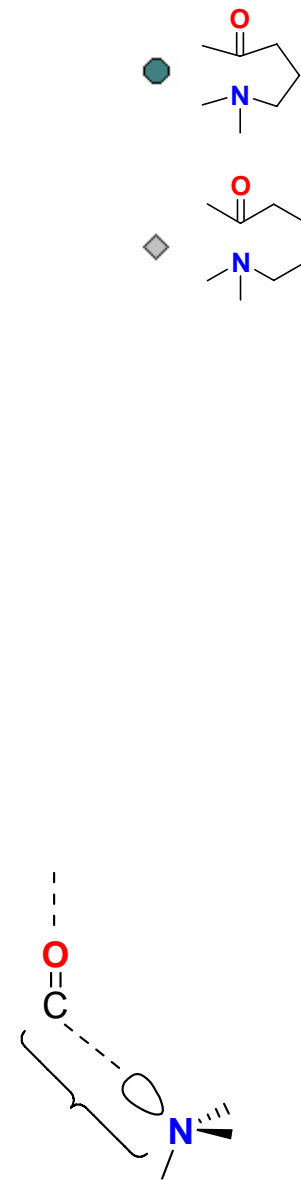
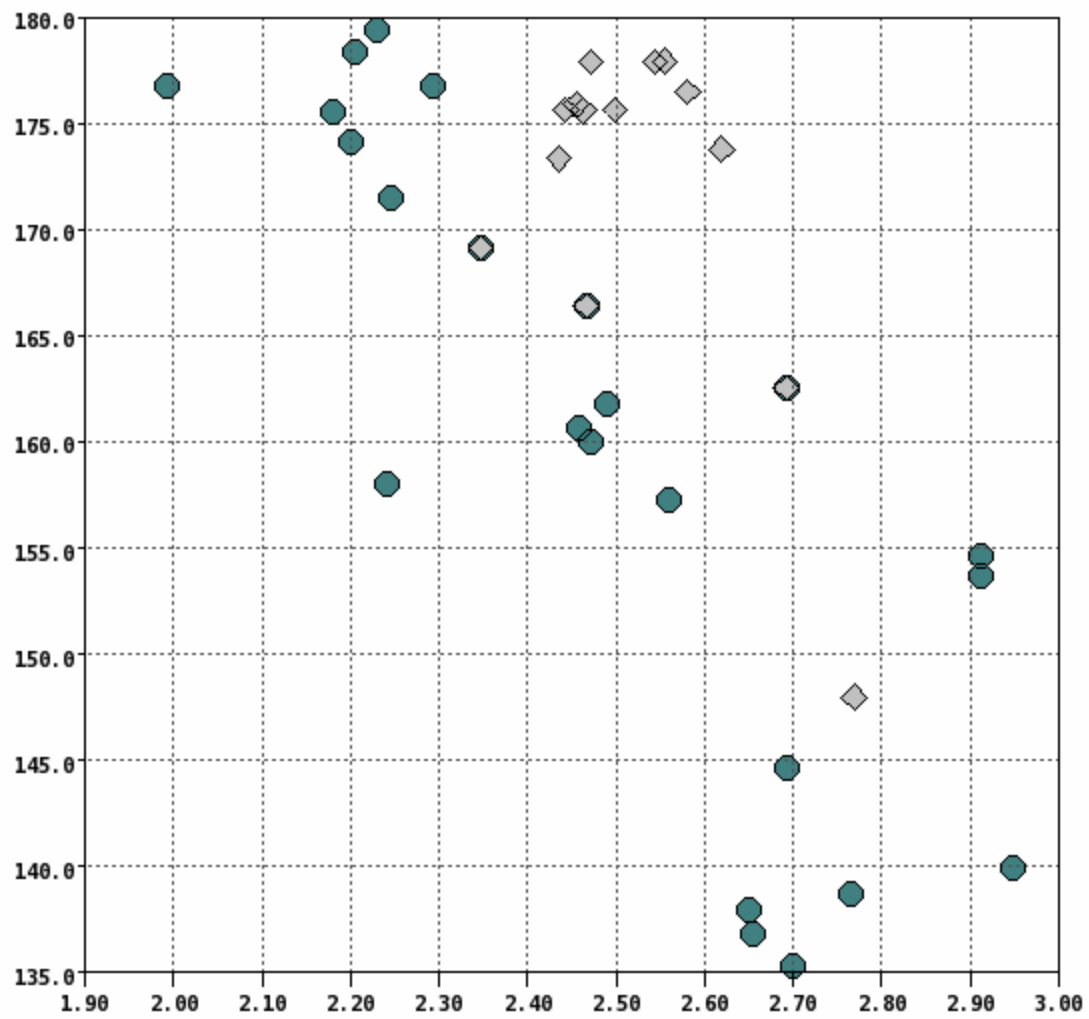
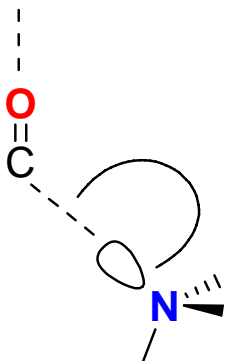
Burgi, Dunitz, and Shefter *JACS* **1973**, *95*, 5065.

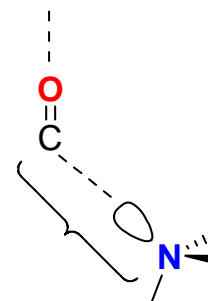
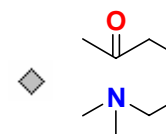
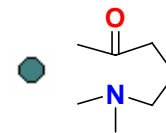
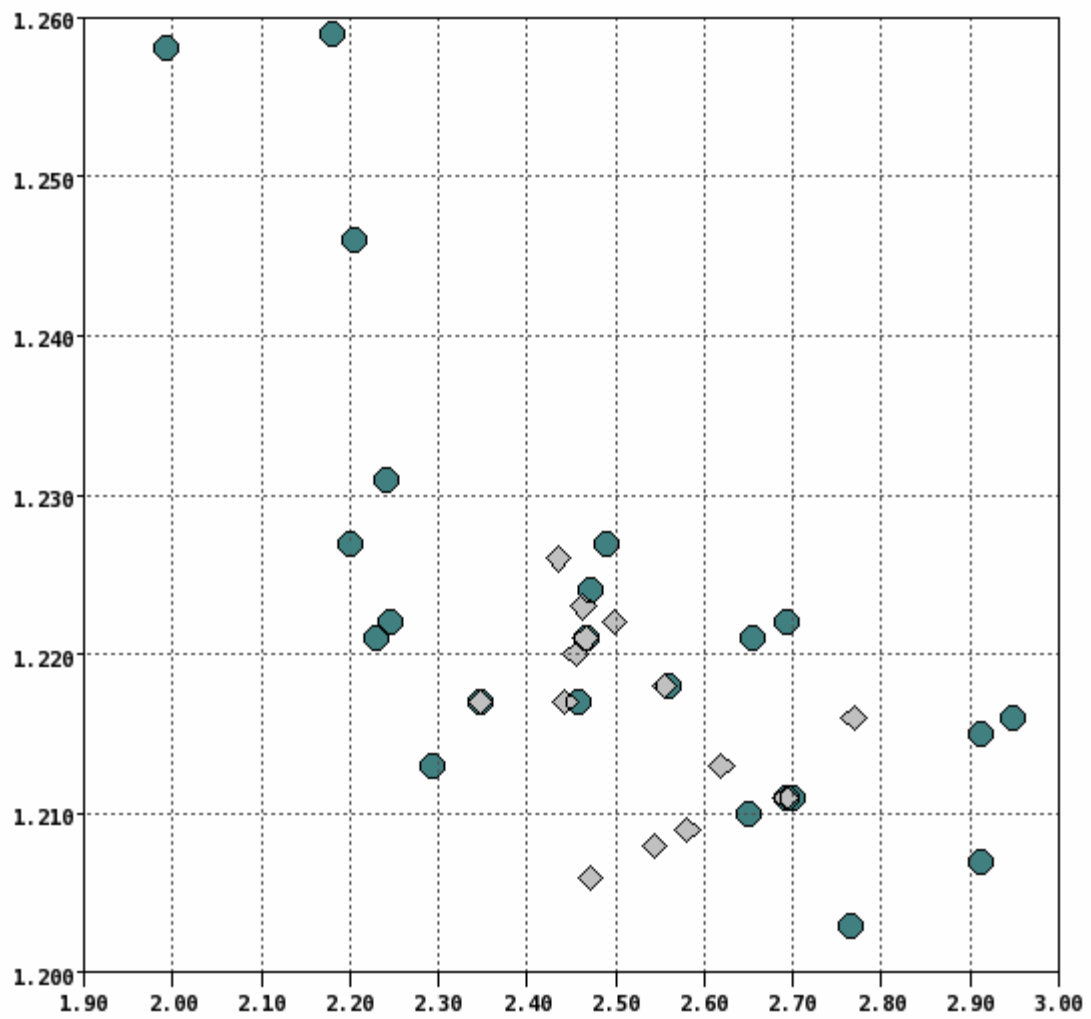
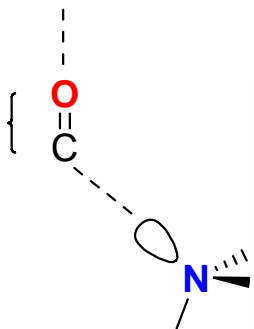


Which Structural Parameters Should We Tabulate?

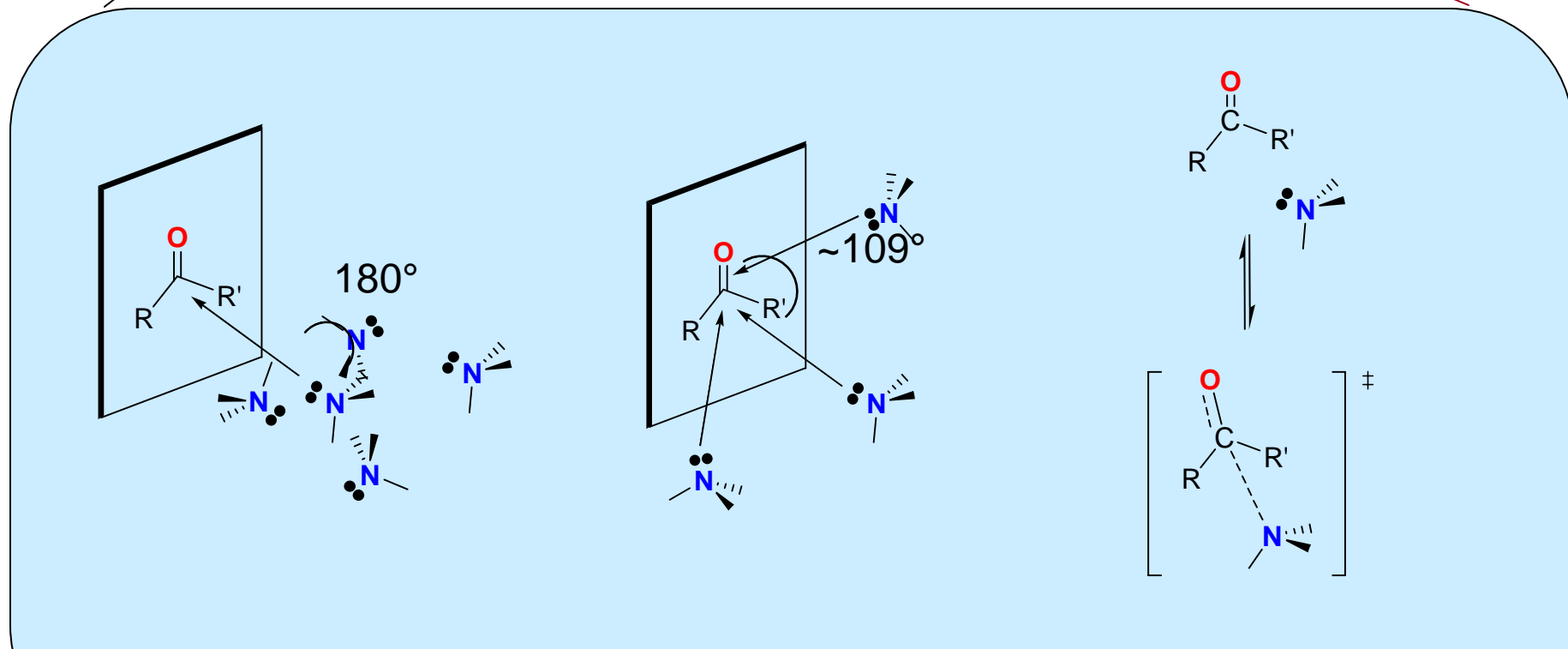
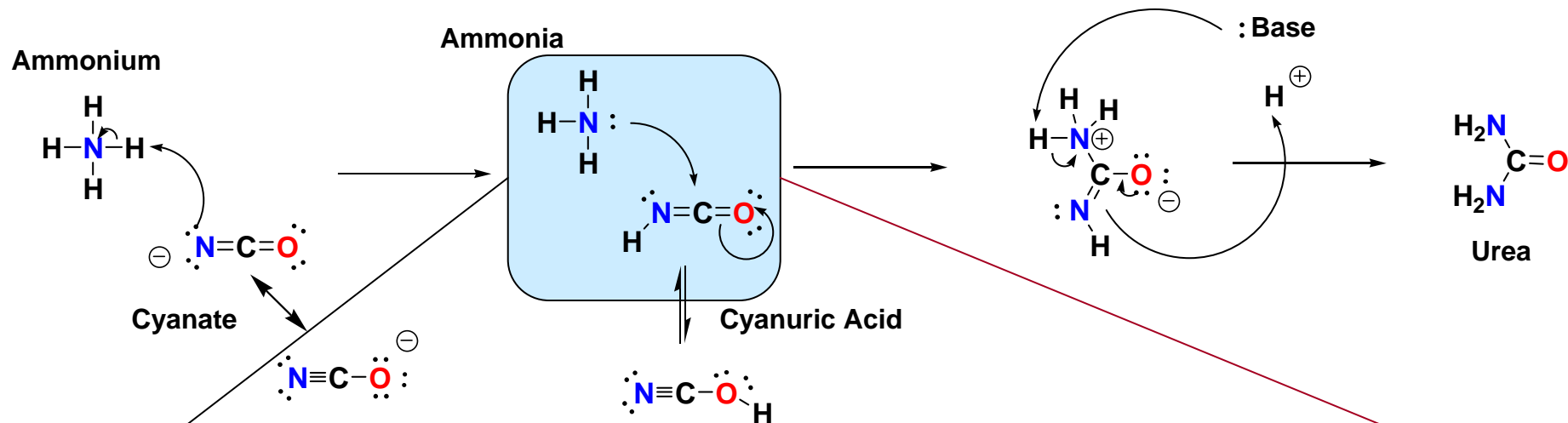




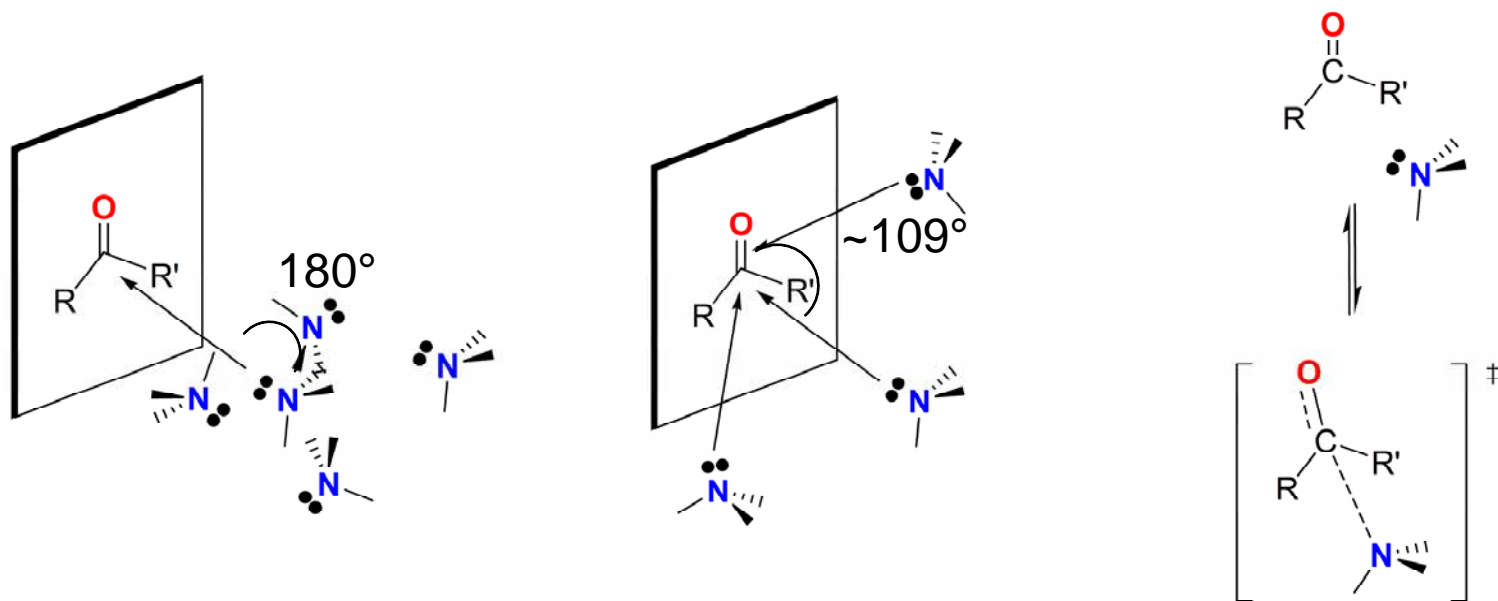
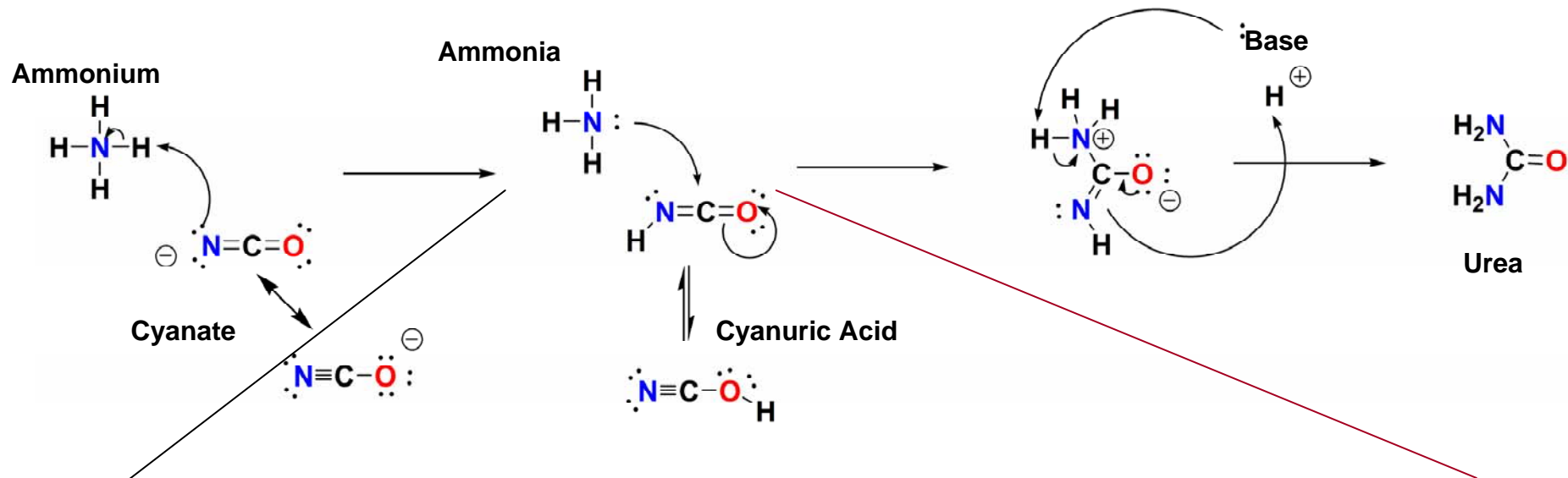




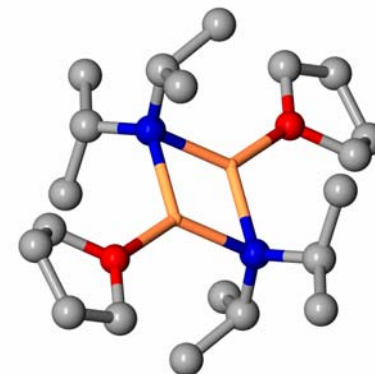
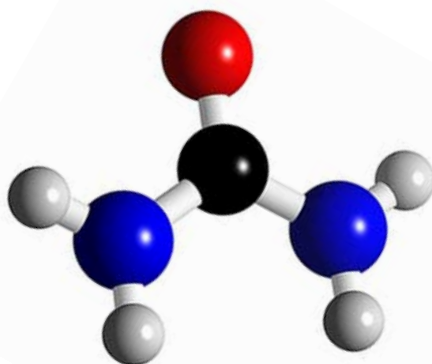
Conclusions Concerning The Reactivity Ammonium Cyanate



Conclusions Concerning The Reactivity Ammonium Cyanate



Conclusions



Crystallographic data in the classroom provides opportunities to:

- **visually explore chemical structures**
- **identify structural trends (e.g. bond distances and angles)**
- **investigate the structural details of chemical reactions**

