

<http://www.courses.fas.harvard.edu/~chem206/>

Chemistry 206

Advanced Organic Chemistry

Lecture Number 1

Introduction to FMO Theory

- General Bonding Considerations
- The H₂ Molecule Revisited (Again!)
- Donor & Acceptor Properties of Bonding & Antibonding States
- Hyperconjugation and "Negative" Hyperconjugation
- Anomeric and Related Effects

■ Reading Assignment for week:

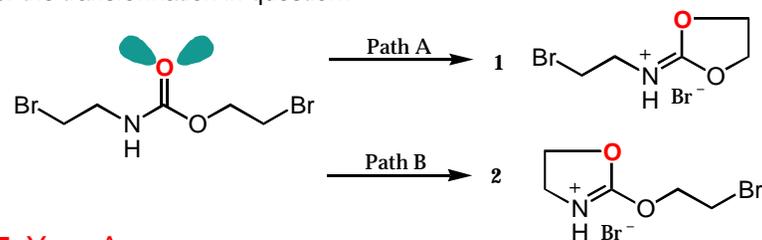
- A. Carey & Sundberg: **Part A**; Chapter 1
- B. Fleming, Chapter 1 & 2
- C. Fukui, *Acc. Chem. Res.* **1971**, *4*, 57.
- D. O. J. Curnow, *J. Chem. Ed.* **1998**, *75*, 910.
- E. J. I. Brauman, *Science*, **2002**, *295*, 2245.

Matthew D. Shair

Wednesday,
September 18, 2002

■ Problem of the Day

The molecule illustrated below can react through either Path A or Path B to form salt **1** or salt **2**. In both instances the carbonyl oxygen functions as the nucleophile in an intramolecular alkylation. What is the preferred reaction path for the transformation in question?



■ Your Answer

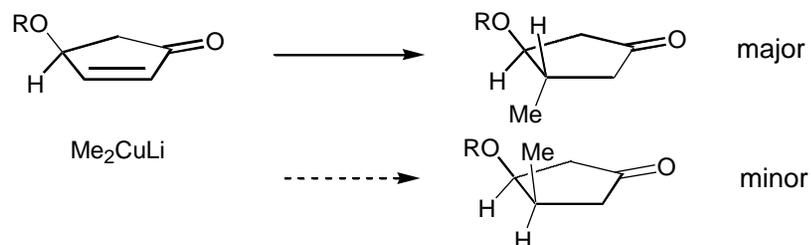
Universal Effects Governing Chemical Reactions There are three:

■ Steric Effects

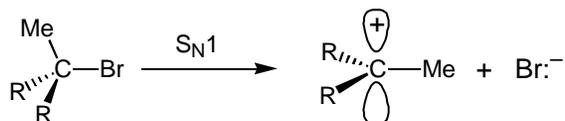
Nonbonding interactions (Van der Waals repulsion) between substituents within a molecule or between reacting molecules



J. I. Brauman, *Science*, **2002**, 295, 2245.



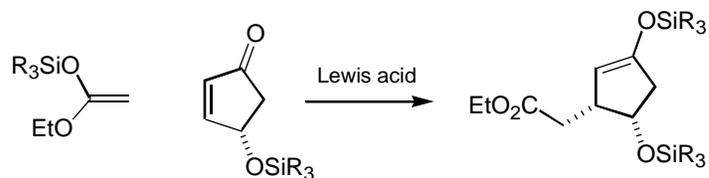
■ Electronic Effects (Inductive Effects):



rate decreases as R becomes more electronegative

Inductive Effects: Through-bond polarization
Field Effects: Through-space polarization

Your thoughts on this transformation



Danishefsky, *JOC* **1991**, 56, 387

diastereoselection >94 : 6

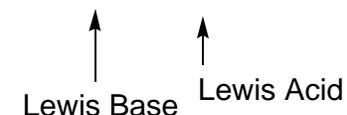
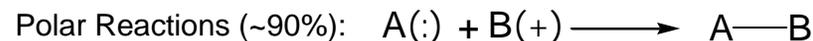
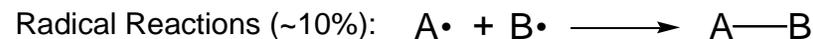
■ Stereoelectronic Effects

Geometrical constraints placed upon ground and transition states by orbital overlap considerations.

Fukui Postulate for reactions:

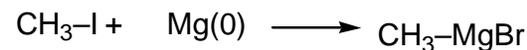
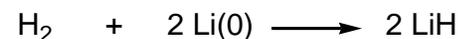
"During the course of chemical reactions, the interaction of the highest filled (HOMO) and lowest unfilled (antibonding) molecular orbital (LUMO) in reacting species is very important to the stabilization of the transition structure."

■ General Reaction Types



FMO concepts extend the donor-acceptor paradigm to non-obvious families of reactions

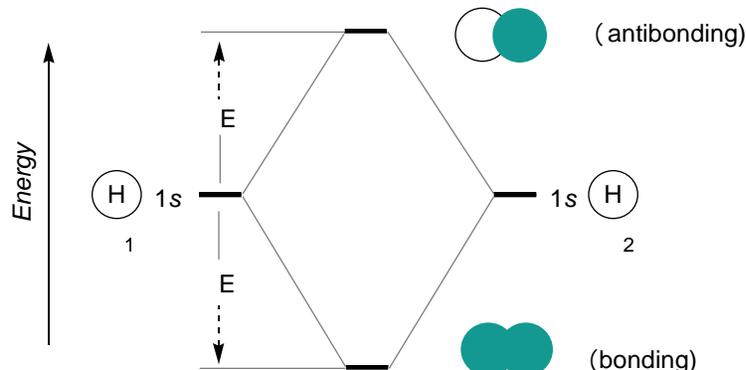
■ Examples to consider



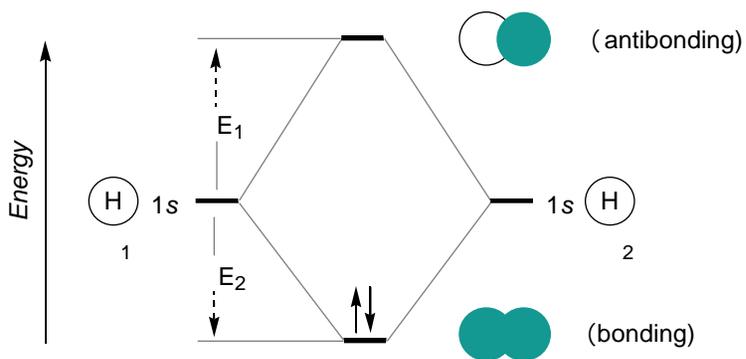
The H₂ Molecule (again!!)

Let's combine two hydrogen atoms to form the hydrogen molecule. Mathematically, linear combinations of the 2 atomic 1s states create two new orbitals, one is bonding, and one antibonding:

■ **Rule one:** A linear combination of n atomic states will create n MOs.



Let's now add the two electrons to the new MO, one from each H atom:



Note that E_1 is greater than E_2 . Why?

Linear Combination of Atomic Orbitals (LCAO): Orbital Coefficients

■ **Rule Two:**

Each MO is constructed by taking a linear combination of the individual atomic orbitals (AO):

$$\text{Bonding MO} = C_1 \psi_1 + C_2 \psi_2$$

$$\text{Antibonding MO} = C_1^* \psi_1 - C_2^* \psi_2$$

The coefficients, C_1 and C_2 , represent the contribution of each AO.

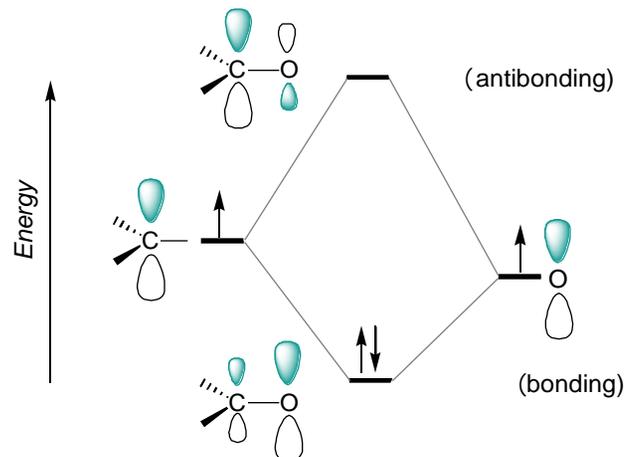
■ **Rule Three:** $(C_1)^2 + (C_2)^2 = 1$

The squares of the C -values are a measure of the electron population in neighborhood of atoms in question

■ **Rule Four:** $\text{bonding}(C_1)^2 + \text{antibonding}(C_1^*)^2 = 1$

In LCAO method, both wave functions must each contribute one net orbital

Consider the pi-bond of a C=O function: In the ground state pi-C=O is polarized toward Oxygen. Note (Rule 4) that the antibonding MO is polarized in the opposite direction.



■ **Bond strengths (Bond dissociation energies) are composed of a covalent contribution (δE_{cov}) and an ionic contribution (δE_{ionic}).**

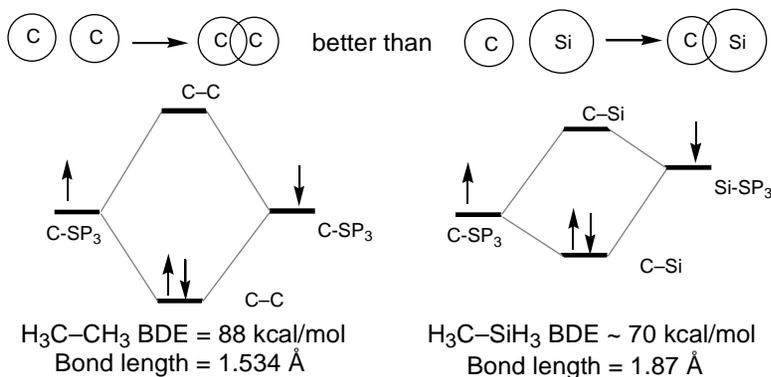
$$\text{Bond Energy (BDE)} = \delta E_{covalent} + \delta E_{ionic} \quad (\text{Fleming, page 27})$$

When one compares bond strengths between C–C and C–X, where X is some other element such as O, N, F, Si, or S, keep in mind that covalent and ionic contributions vary independently. Hence, the mapping of trends is not a trivial exercise.

Useful generalizations on covalent bonding

■ **Overlap between orbitals of comparable energy is more effective than overlap between orbitals of differing energy.**

For example, consider elements in Group IV, Carbon and Silicon. We know that C–C bonds are considerably stronger by Ca. 20 kcal mol⁻¹ than C–Si bonds.



This trend is even more dramatic with pi-bonds:

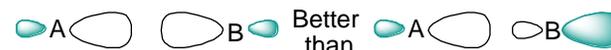
$$\text{C–C} = 65 \text{ kcal/mol} \quad \text{C–Si} = 36 \text{ kcal/mol} \quad \text{Si–Si} = 23 \text{ kcal/mol}$$

■ **Weak bonds will have corresponding low-lying antibonds.**

Formation of a weak bond will lead to a corresponding low-lying antibonding orbital. Such structures are reactive as both nucleophiles & electrophiles

■ **Orbital orientation strongly affects the strength of the resulting bond.**

For Bonds:



For Bonds:



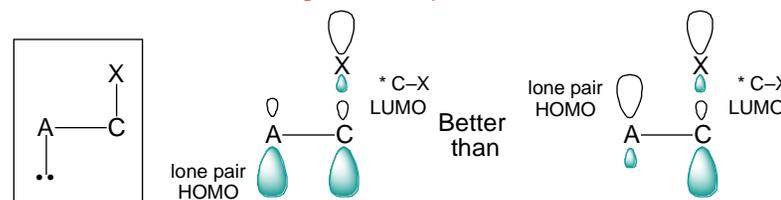
This is a simple notion with very important consequences. It surfaces in the delocalized bonding which occurs in the competing anti (favored) syn (disfavored) E2 elimination reactions. Review this situation.

■ **An anti orientation of filled and unfilled orbitals leads to better overlap.**

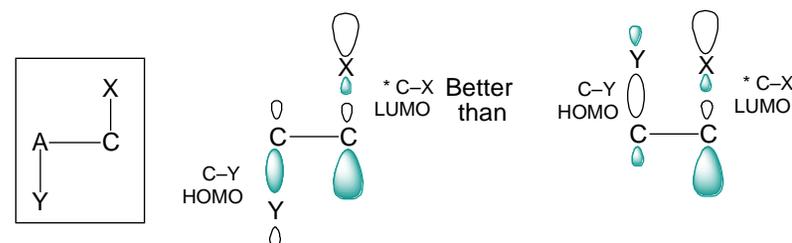
This is a corollary to the preceding generalization.

There are two common situations.

Case-1: Anti Nonbonding electron pair & C–X bond

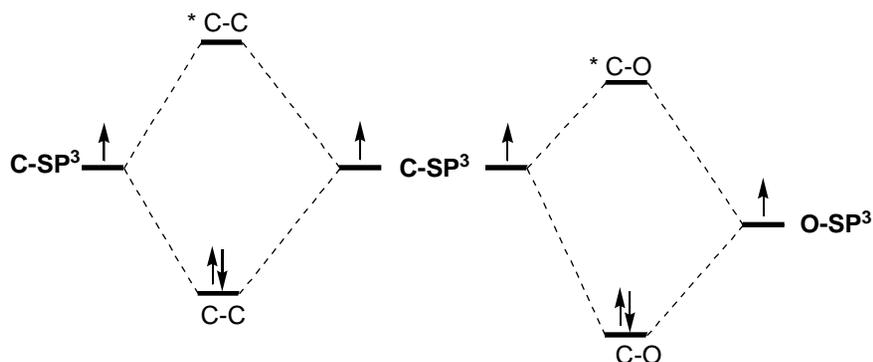


Case-2: Two anti sigma bonds



Donor Acceptor Properties of C-C & C-O Bonds

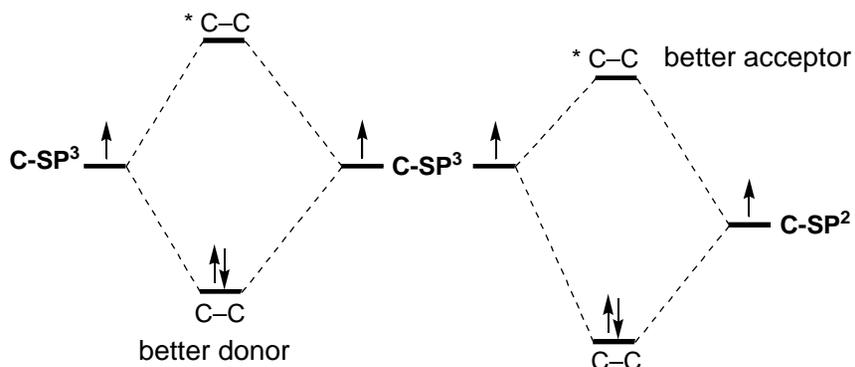
Consider the energy level diagrams for both bonding & antibonding orbitals for C-C and C-O bonds.



■ The greater electronegativity of oxygen lowers both the bonding & antibonding C-O states. Hence:

- C-C is a better donor orbital than C-O
- C-O is a better acceptor orbital than C-C

Donor Acceptor Properties of C_{SP^3} - C_{SP^3} & C_{SP^3} - C_{SP^2} Bonds

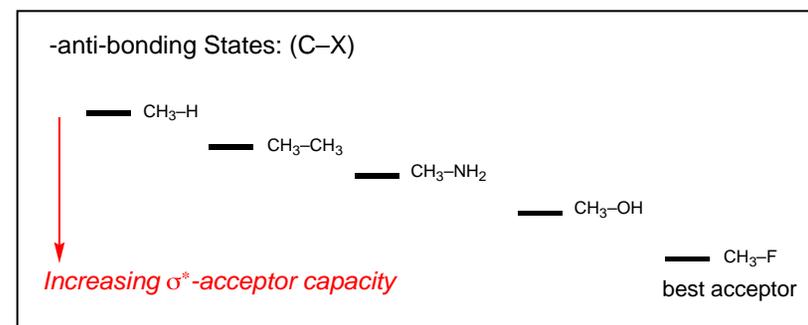
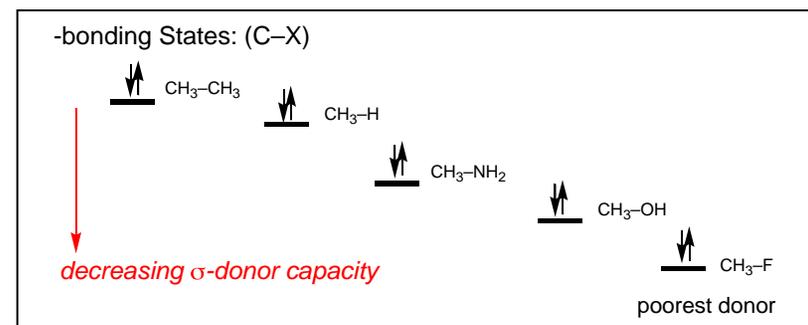


■ The greater electronegativity of C_{SP^2} lowers both the bonding & antibonding C-C states. Hence:

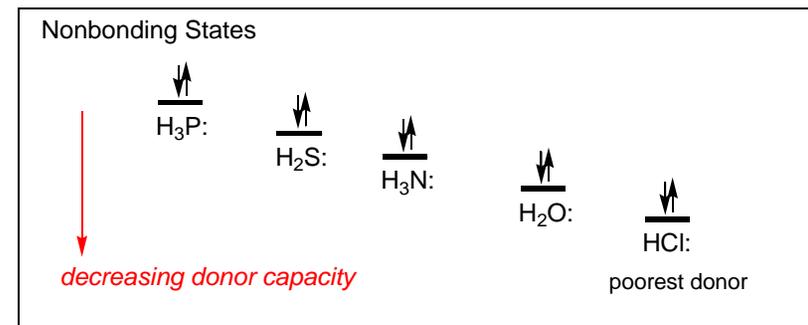
- C_{SP^3} - C_{SP^3} is a better donor orbital than C_{SP^3} - C_{SP^2}
- C_{SP^3} - C_{SP^2} is a better acceptor orbital than C_{SP^3} - C_{SP^3}

Hierarchy of Donor & Acceptor States

Following trends are made on the basis of comparing the bonding and antibonding states for the molecule CH_3-X where $X = C, N, O, F, \text{ \& H}$.

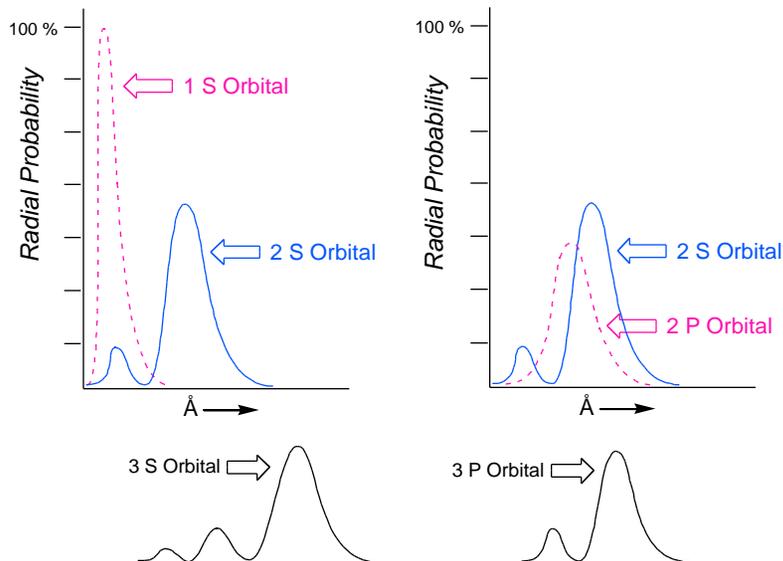


The following are trends for the energy levels of *nonbonding states* of several common molecules. Trend was established by photoelectron spectroscopy.



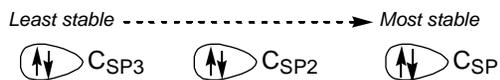
Electrons in 2S states "see" a greater effective nuclear charge than electrons in 2P states.

This becomes apparent when the radial probability functions for S and P-states are examined: The radial probability functions for the hydrogen atom S & P states are shown below.



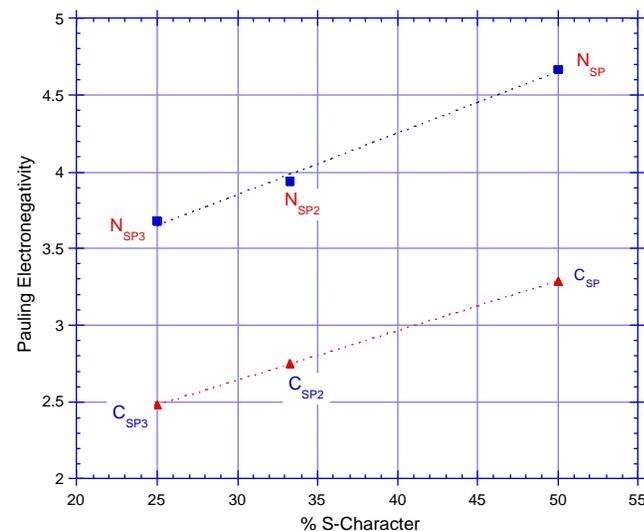
S-states have greater radial penetration due to the nodal properties of the wave function. Electrons in S-states "see" a higher nuclear charge.

Above observation correctly implies that the stability of nonbonding electron pairs is directly proportional to the % of S-character in the doubly occupied orbital

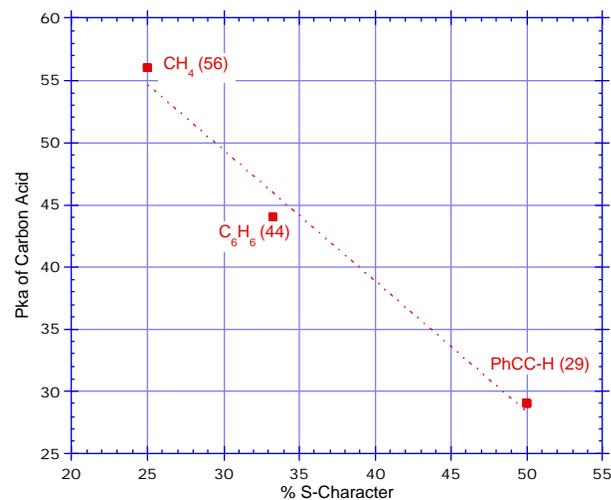


The above trend indicates that the greater the % of S-character at a given atom, the greater the electronegativity of that atom.

There is a linear relationship between %S character & Pauling electronegativity

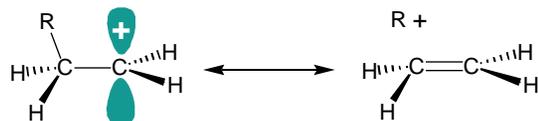


There is a direct relationship between %S character & hydrocarbon acidity



- The interaction of a vicinal bonding orbital with a p-orbital is referred to as hyperconjugation.

This is a traditional vehicle for using valence bond to denote charge delocalization.

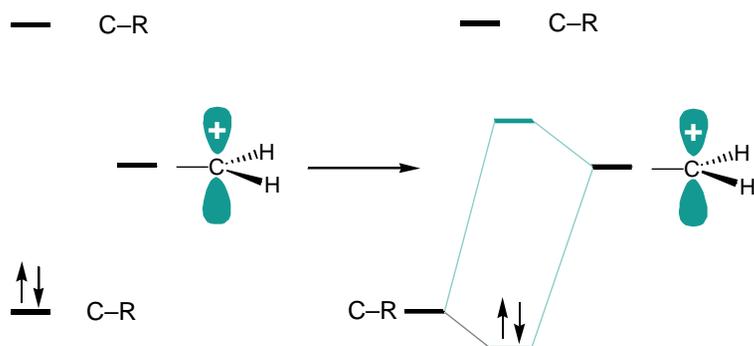


The graphic illustrates the fact that the C-R bonding electrons can "delocalize" to stabilize the electron deficient carbocationic center.

Note that the general rules of drawing resonance structures still hold: the positions of all atoms must not be changed.

**Stereoelectronic Requirement for Hyperconjugation:
Syn-planar orientation between interacting orbitals**

The Molecular Orbital Description



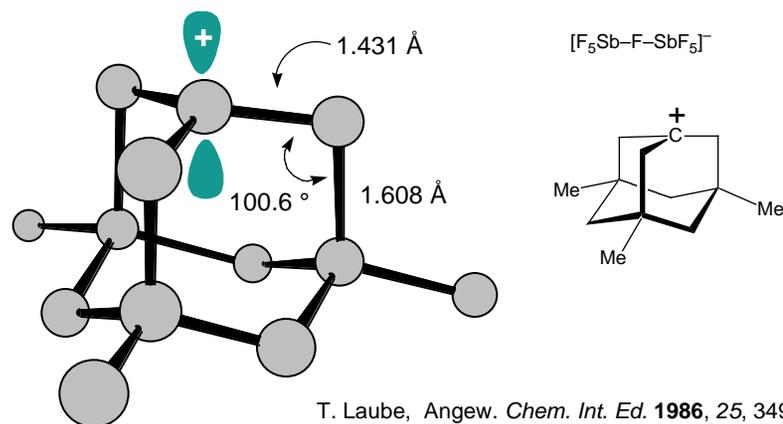
- Take a linear combination of C-R and CSP_2 p-orbital:

The new occupied bonding orbital is lower in energy. When you stabilize the electrons in a system you stabilize the system itself.

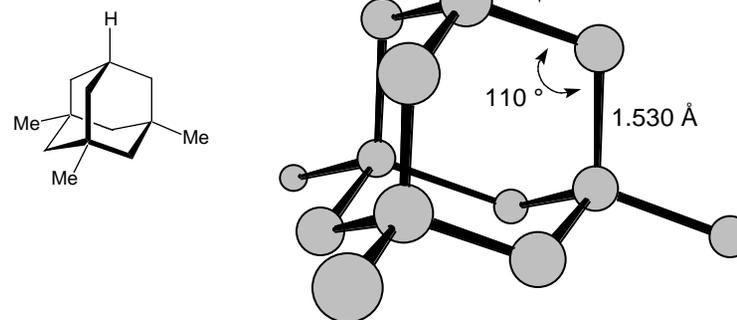
Physical Evidence for Hyperconjugation

- Bonds participating in the hyperconjugative interaction, e.g. C-R, will be lengthened while the $\text{C}(+)\text{-C}$ bond will be shortened.

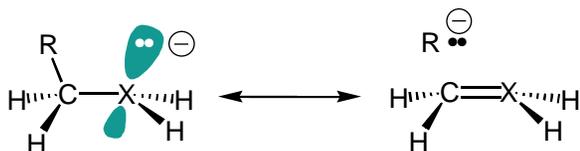
First X-ray Structure of an Aliphatic Carbocation



The Adamantane Reference (MM-2)



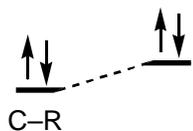
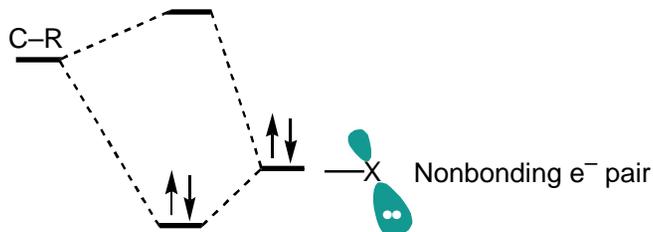
- Delocalization of nonbonding electron pairs into vicinal antibonding orbitals is also possible



This delocalization is referred to as "Negative" hyperconjugation

Since nonbonding electrons prefer hybrid orbitals rather than P orbitals, this orbital can adopt either a syn or anti relationship to the vicinal C-R bond.

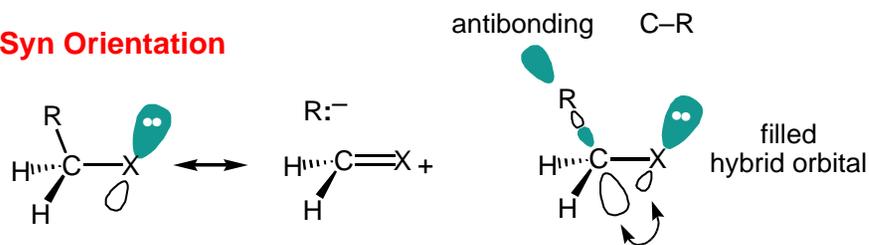
The Molecular Orbital Description



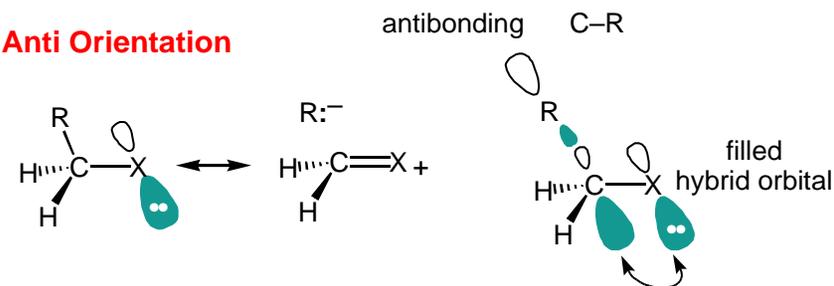
As the antibonding C-R orbital decreases in energy, the magnitude of this interaction will increase

Note that C-R is slightly destabilized

Syn Orientation



Anti Orientation



- Overlap between two orbitals is better in the anti orientation as stated in "Bonding Generalizations" handout.

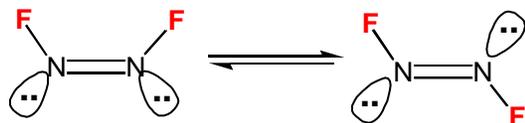
The Expected Structural Perturbations

Change in Structure	Spectroscopic Probe
Shorter C-X bond	X-ray crystallography
Longer C-R bond	X-ray crystallography
Stronger C-X bond	Infrared Spectroscopy
Weaker C-R bond	Infrared Spectroscopy
Greater e-density at R	NMR Spectroscopy
Less e-density at X	NMR Spectroscopy

The interaction of filled orbitals with adjacent antibonding orbitals can have an ordering effect on the structure which will stabilize a particular geometry. Here are several examples:

Case 1: N_2F_2

This molecule can exist as either cis or trans isomers



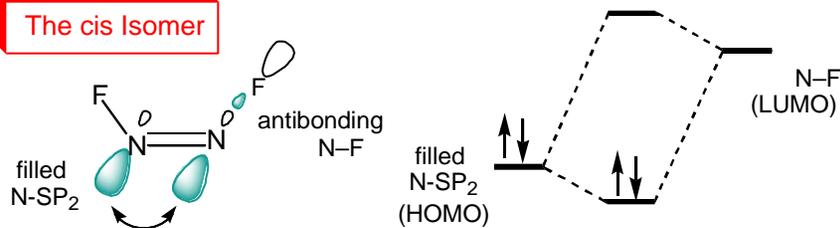
There are two logical reasons why the trans isomer should be more stable than the cis isomer.

- The nonbonding lone pair orbitals in the cis isomer will be destabilizing due to electron-electron repulsion.
- The individual C–F dipoles are mutually repulsive (pointing in same direction) in the cis isomer.

In fact the cis isomer is favored by 3 kcal/ mol at 25 °C.

Let's look at the interaction with the lone pairs with the adjacent C–F antibonding orbitals.

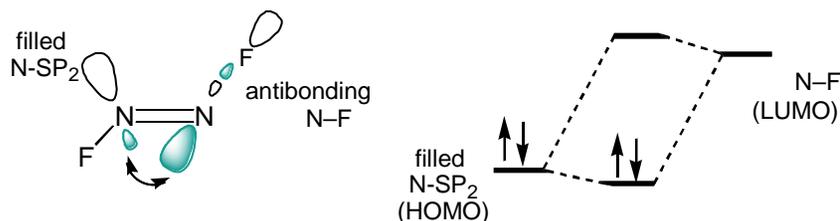
The cis Isomer



- Note that by taking a linear combination of the nonbonding and antibonding orbitals you generate a more stable bonding situation.
- Note that two such interactions occur in the molecule even though only one has been illustrated.

The trans Isomer

Now carry out the same analysis with the same 2 orbitals present in the trans isomer.



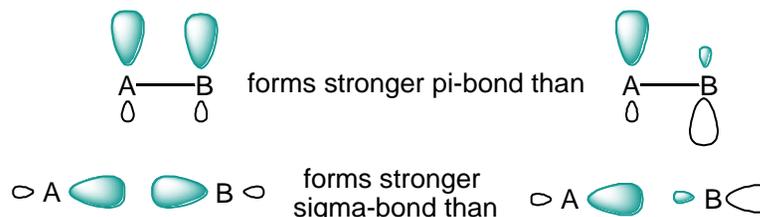
- In this geometry the "small lobe" of the filled N- SP_2 is required to overlap with the large lobe of the antibonding C–F orbital. Hence, when the new MO's are generated the new bonding orbital is not as stabilizing as for the cis isomer.

Conclusions

- Lone pair delocalization appears to override electron-electron and dipole-dipole repulsion in the stabilization of the cis isomer.
- This HOMO-LUMO delocalization is stronger in the cis isomer due to better orbital overlap.

Important Take-home Lesson

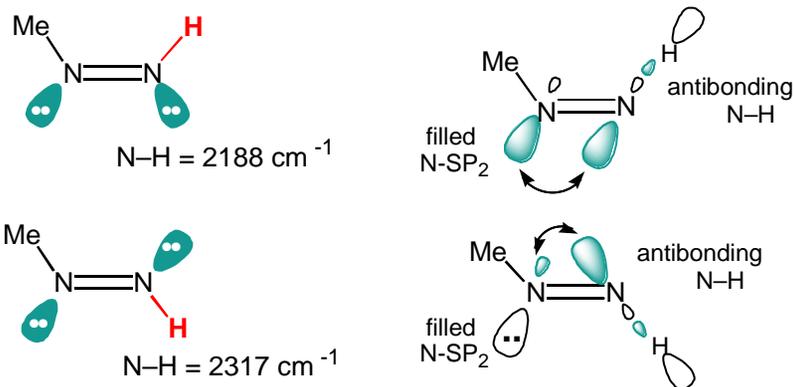
Orbital orientation is important for optimal orbital overlap.



This is a simple notion with very important consequences. It surfaces in the delocalized bonding which occurs in the competing anti (favored) syn (disfavored) E2 elimination reactions. Review this situation.

Infrared evidence for lone pair delocalization into vicinal antibonding orbitals.

The N–H stretching frequency of cis-methyl diazene is 200 cm^{-1} lower than the trans isomer.

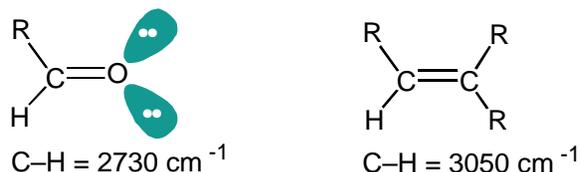


■ The low-frequency N–H shift in the cis isomer is a result of N–H bond weakening due to presence of the anti lone pair on the vicinal nitrogen which is interacting with the N–H antibonding orbital. Note that the orbital overlap is not nearly as good from the trans isomer

N. C. Craig & co-workers *JACS* **1979**, *101*, 2480.

Aldehyde C–H Infrared Stretching Frequencies

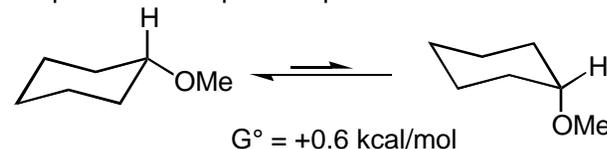
The IR C–H stretching frequency for aldehydes is lower than the closely related olefin C–H stretching frequency. For years this observation has gone unexplained.



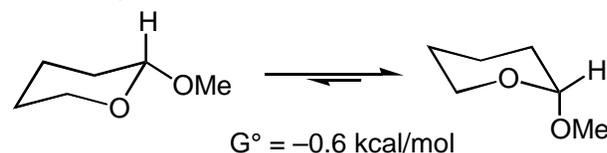
■ We now conclude that this is another example of the vicinal lone pair effect.

The Anomeric Effect

It is not unexpected that the methoxyl substituent on a cyclohexane ring prefers to adopt the equatorial conformation.

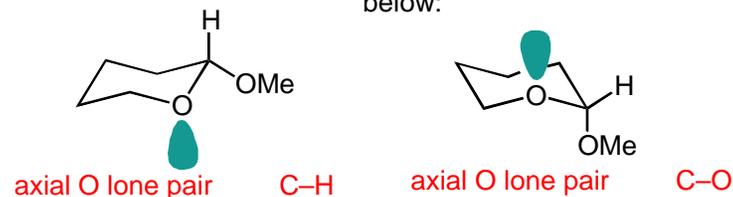


What is unexpected is that the closely related 2-methoxytetrahydropyran prefers the axial conformation:



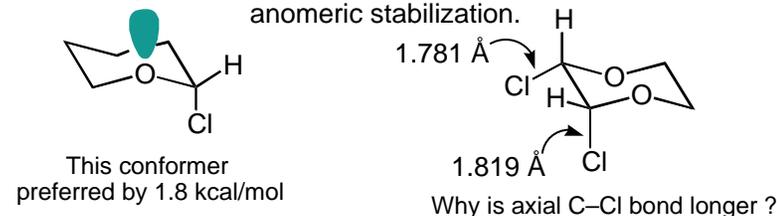
■ That effect which provides the stabilization of the axial OR conformer which overrides the inherent steric bias of the substituent is referred to as the anomeric effect.

Principal HOMO-LUMO interaction from each conformation is illustrated below:



■ Since the antibonding C–O orbital is a better acceptor orbital than the antibonding C–H bond, the axial OMe conformer is better stabilized by this interaction which is worth ca 1.2 kcal/mol.

Other electronegative substituents such as Cl, SR etc. also participate in anomeric stabilization.

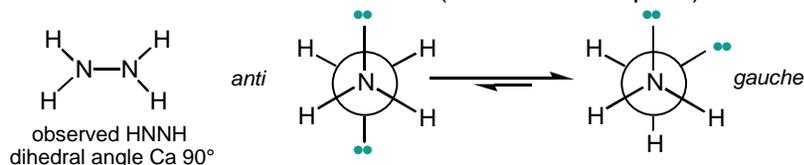


The interaction of filled orbitals with adjacent antibonding orbitals can have an ordering effect on the structure which will stabilize a particular conformation.

Here are several examples of such a phenomenon called the gauche effect:

Hydrazine

Hydrazine can exist in either gauche or anti conformations (relative to lone pairs).

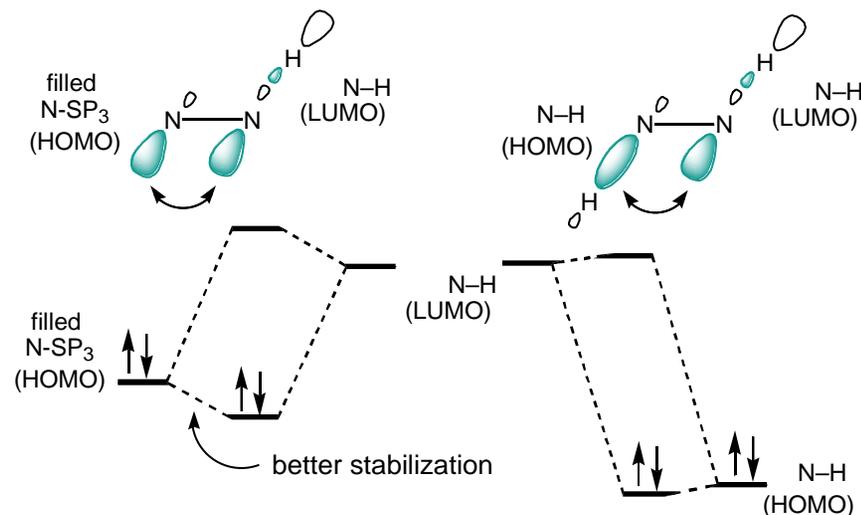


There is a logical reason why the anti isomer should be more stable than the gauche isomer. The nonbonding lone pair orbitals in the gauche isomer should be destabilizing due to electron-electron repulsion.

In fact, the gauche conformation is favored. Hence we have neglected an important stabilization feature in the structure.

HOMO-LUMO Interactions

Orbital overlap between filled (bonding) and antibonding states is best in the anti orientation. HOMO-LUMO delocalization is possible between: (a) N-lone pair N-H; (b) N-H N-H



The closer in energy the HOMO and LUMO the better the resulting stabilization through delocalization.

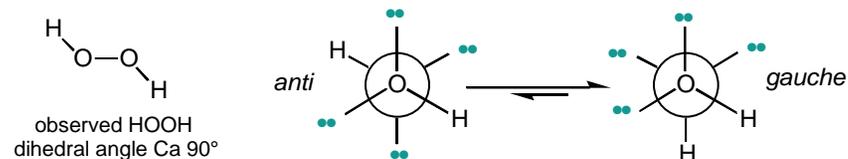
■ Hence, N-lone pair N-H delocalization better than N-H N-H delocalization.

■ Hence, hydrazine will adopt the gauche conformation where both N-lone pairs will be anti to an antibonding acceptor orbital.

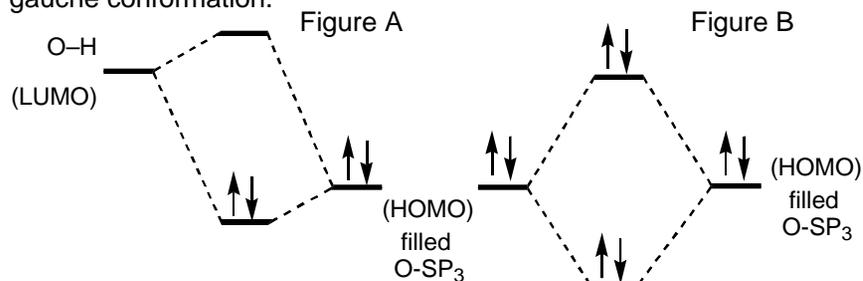
The trend observed for hydrazine holds for oxygen derivatives as well

Hydrogen peroxide

H₂O₂ can exist in either gauche or anti conformations (relative to hydrogens). The gauche conformer is preferred.



■ Major stabilizing interaction is the delocalization of O-lone pairs into the C-H antibonding orbitals (Figure A). Note that there are no such stabilizing interactions in the anti conformation while there are 2 in the gauche conformation.



■ Note that you achieve no net stabilization of the system by generating molecular orbitals from two filled states (Figure B).

Problem: Consider the structures XCH₂-OH where X = OCH₃ and F. What is the most favorable conformation of each molecule? Illustrate the dihedral angle relationship along the C-O bond.