Session 5

Overview:

I.   Electron Densities

II.   Electrostatic Potentials

III. Reactivity Predictions

I. Electron Densities

• Visualization of the electron density gives a better indication of molecular size

Example: Methane
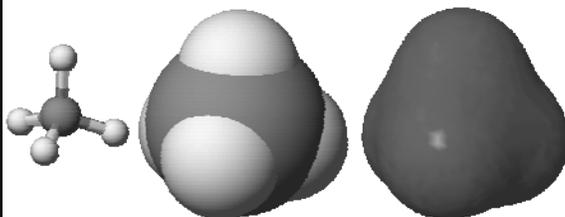
– Electron probability density of $0.01 e^-/Å^3$ similar to conventional (CPK) space filling models

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Electron Density

• Indicates location of electrons in molecules
  – Around atoms; between bonded atoms

Phenylacetylene

1
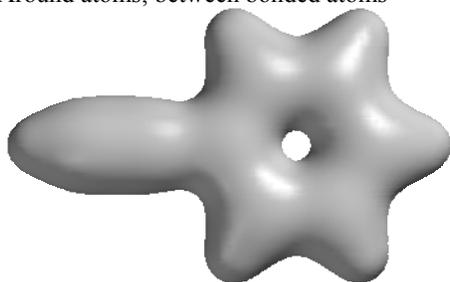
Electron Density Function

- Also called the *electron probability distribution function*: $\rho(r)$

- A 3-D function defined such that $\rho(r)\,dr$ is the probability of finding an electron in a small volume element (dr) at some point in space (r)

$$\int \rho(r)dr = N$$

- Integration of the function over all space must equal the number of electrons (N):

Calculation of Electron Density

- The square of the wavefunction at point (r) is interpreted as a probability

  – For a molecule with n electrons and $n/2$ occupied orbitals, the electron density at point (r) is given by:

$$\rho(r) = 2\sum_{i=1}^{n/2}\left|\psi_i(r)\right|^2$$

  – Recall that M.O.'s (Ψ_i) are expressed as linear combinations of a set of basis functions

Population Analysis

- Mathematical method of partitioning a wave function or electron density into charges on each atom

  – Condenses nuclear charge and e⁻ density into an atomic partial charge
  – Can help understand reactivity, bond orders, etc.
  – Corresponds to chemist's view of bond type (ionic, covalent, polar covalent)
  – Since atomic charge is not a quantum mechanical observable, arbitrary methods used to compute

Mulliken Population Analysis

- Electrons shared between basis functions are *split evenly* between the two atoms involved
  - Relative electronegativity is ignored
- Method is entrenched in software packages due to it's ease of implementation
- For small basis sets:
  - Provides an approximate representation of the 3D charge distribution in a molecule
- For larger basis sets:
  - Can produce unreasonable results
    - (e.g. Orbitals with > 2 electrons)

Löwdin Population Analysis

- Löwdin Method
  - Atomic orbitals are first transformed into an orthogonal set of basis functions
  - MO coefficients are then transformed to give a representation of Ψ using the new basis set

  - Requires more computation
  → No longer have orbitals with > 2 electrons

  - Still have basis set dependent results

Results of Population Analyses

1. Total number of e⁻'s (q_A) "associated" with each atom can be found. Thus, the *total atomic charge* on that atom is calculated via: $A = Z_A - q_A$ (where Z_A is atomic number).

2. The **total overlap population** between two atoms can be determined.
   - Large (+) values reflect strong bonding
   - Large (-) values reflect antibonding

Caveats

1. Total atomic charges and total overlap populations are *strongly* dependent on the basis set used

2. The equal partitioning of electrons between basis sets on different atoms (Mulliken method) is arbitrary, and (often) goes against chemical intuition

→ More complex methods are available
   - NBO, NPA, AIM, etc.

II. Electrostatic Potential

- The electrostatic potential surface represents the distance from the molecule at which a (+) test charge experiences a set attraction or repulsion (Not all programs calculate this)

  – Default value (CAChe) = ± 0.03 a.u. (±18 kcal/mol; ± 75 kJ/mol)

- The test charge interacts with *both* the nuclei and the fixed electron cloud (***with zero polarizability***)

Uses of Electrostatic Potential

- What charge distribution does a reactant "see" as it approaches a molecule
- Can rationalize intermolecular interactions (between polar species)
- Helps identify regions of local (-) and (+) potential in a molecule
- Can assist in predicting paths of (charged) reagent approach
  - Potential sites of protonation
  - e.g., electrophiles are attracted to regions of (-) potential

Calculation of Electrostatic Potential

- Usually calculated point-by-point on a set of grid points starting at the van der Waals surface and extending outwards from this surface some distance x

  ~100 grid point per atom typically used

  – The calculation sums the positive charges of nuclei and the amount of electronic charge density

  – Results are color coded for charge

Electrostatic Potential: Examples

- Acetaldehyde

  Red = (+)

  Blue = (-)

  Where is the oxygen?

  Where is the –CH$_3$?

Electrostatic Potential: Examples

- Phenylacetylene: Blue = (-); Red = (+)
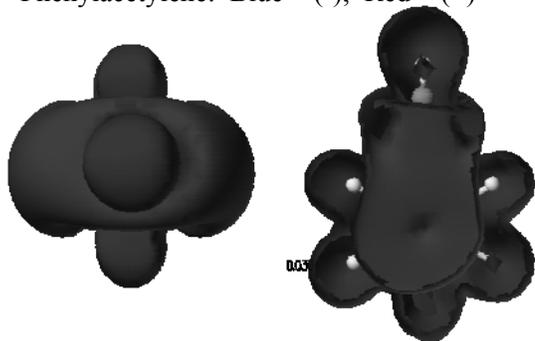
Electron Density + Electrostatic Potential

- The electrostatic potential can be mapped onto the electron density surface ($0.01e^-/Å^3$) using color
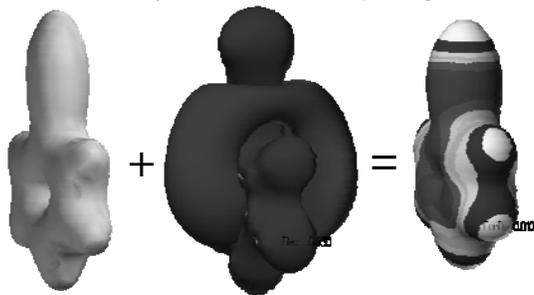
Electron Density + Electrostatic Potential

- 1,1-difluoroethylene
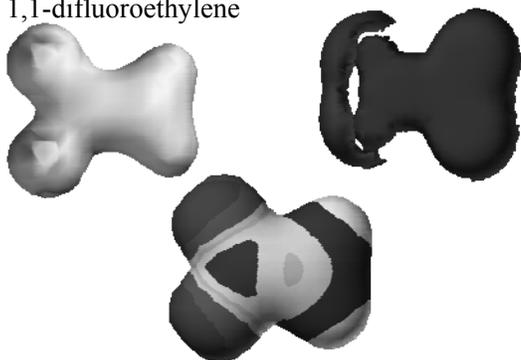
III. Reactivity Predictions

- Various approaches can be used:

  1. Partial charges – Usually found via Mulliken population analysis, so the results can sometimes be misleading
    - Could be helpful in charge-controlled reactions
      – "Hard" electrophiles/nucleophiles
      – Protonations/Deprotonations, for example

  2. Electrostatic Potential – Will reveal possible trajectory for the approach of charged reagents
    – Partial charges more important ("Soft" electrophiles and nucleophiles)

Reactivity Predictions - continued

3. **HOMO/LUMO**: Largest lobes– These can
    sometimes change using different model
    chemistries, so try several methods

    - FMO (Frontier Molecular Orbital) approach is
      well-documented
    - Works best when the HOMO and LUMO are
      well separated in energy from the other orbitals

4. **Reactivity Indices**: Electrophilic,
    Nucleophilic, and Radical Susceptibilities

    - Similar to FMO, but additional orbitals near the
      HOMO and LUMO are also used for a more
      comprehensive indicator

Reactivity Prediction: Examples

Where is the site of protonation in formamide?

1. Partial charges (B88-LYP/DZVP)
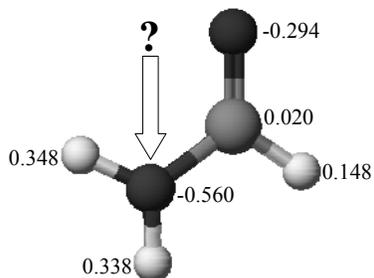
?

-0.294

0.020

0.348

0.148

-0.560

0.338

Reactivity Prediction: Examples

Where is the site of protonation in formamide?

2. Electrostatic potential (B88-LYP/DVZP)
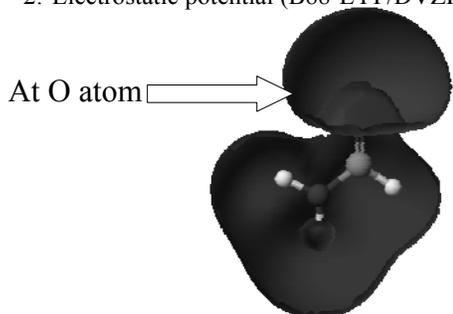
At O atom

Reactivity Prediction: Examples

Where is the site of protonation in formamide?

3. Position of HOMO (B88-LYP/DZVP)
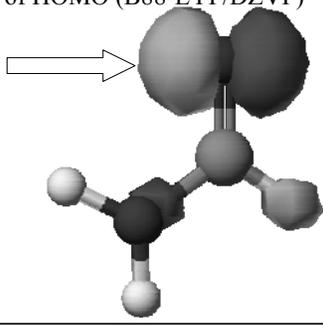
Reactivity Prediction: Examples

Where is the site of protonation in formamide?

4. Electrophilic Susceptibility (B88-LYP/DZVP)

"Bullseye"
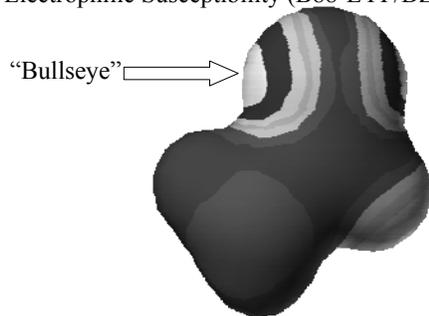
Frontier Orbital Theory

- HOMO/LUMO overlap between molecules is the governing factor
  - Predict stereochemistry with "soft" nucleophiles and electrophiles (charge less important)
  - Example:

Phenylbutadiene

+   [4+2]   ?
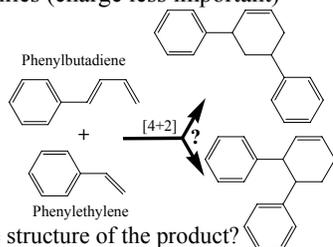
Phenylethylene

- What is the structure of the product?

Frontier Orbital Theory

- Look at HOMO of the phenylbutadiene and the LUMO of the ethylene:

Largest lobe of the HOMO is on the terminal C

These two interact

Largest lobe of the LUMO is on the terminal C
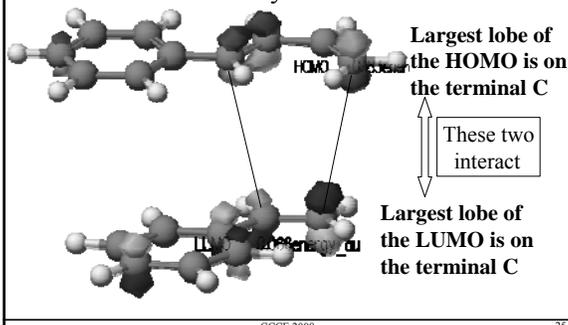
Frontier Orbital Theory

- Sterically *unfavorable* product forms:

Phenylbutadiene

+ [4+2] →

Phenylethylene
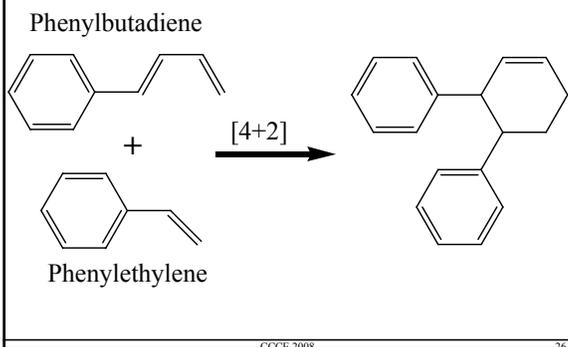
Susceptibilities

- Most useful for larger molecules where the HOMO and LUMO are **not** well separated in energy from the other orbitals – these other orbitals contribute to the reactivity
  - Can calculate electrophilic, nucleophilic, and radical susceptibilities, and map these onto the electron density surface
    - WebMO: Electrophilic (HOMO), Nucleophilic (LUMO), or Radical Frontier Density
    - Each of these is a function of a weighted sum of the squares of the molecular orbital coefficients

Electrophilic Susceptibility

- Orbital Interactions:
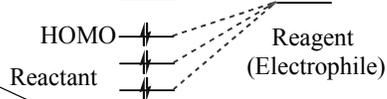
Mathematically:

$$\text{EFonD}(x) = \frac{\displaystyle\sum_{j=1}^{N} \boldsymbol{\nu}_j \boldsymbol{\phi}_j(x)^2 e^{-\boldsymbol{\lambda}(e_{HOMO} - e_j)}}{\displaystyle\sum_{j=1}^{N} \boldsymbol{\nu}_j(x)^2 e^{-\boldsymbol{\lambda}(e_{HOMO} - e_j)}}$$

N = # of orbitals
$\boldsymbol{\nu}_j$ = # e⁻ in orbital

e_j = orbital energy
λ = scaling factor

Nucleophilic Susceptibility

- Orbital Interactions:
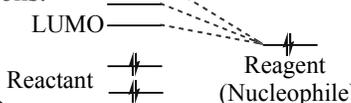
Mathematically:

$$\text{NFonD}(x) = \frac{\displaystyle\sum_{j=1}^{N} (2 - \boldsymbol{\nu}_j)\boldsymbol{\phi}_j(x)^2 e^{-\boldsymbol{\lambda}(e_{LUMO} - e_j)}}{\displaystyle\sum_{j=1}^{N} (2 - \boldsymbol{\nu}_j)(x)^2 e^{-\boldsymbol{\lambda}(e_{LUMO} - e_j)}}$$

N = # of orbitals
$\boldsymbol{\nu}_j$ = # e⁻ in orbital

e_j = orbital energy
λ = scaling factor

Radical Susceptibility

- Orbital Interactions:
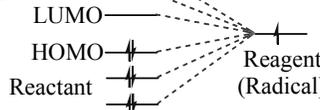
Mathematically:

– An average of electrophilic and nucleophilic susceptibilities

$$\text{RFonD}(x) = \left(\frac{1}{2}\right)\text{EFonD}(x) + \left(\frac{1}{2}\right)\text{NFonD}(x)$$

N = # of orbitals
$\boldsymbol{\nu}_j$ = # e⁻ in orbital

e_j = orbital energy
λ = scaling factor

Reactivity Indices: Which To Use?

- Susceptibilities more widely applicable
  - Should be used in most cases
- As always, try a variety of computational methods, and determine the common thread
- Use known compounds of similar structure whose *reactivity is known* to <u>verify the results</u> of calculations on unknown compounds
- Use your (or a colleagues) chemical intuition
  - Be skeptical: Don't believe the results of all calculations!

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