Molecular Mechanics

Chem 8711/7711

Some Basic Theory - Energetics

Energies can be calculated at several levels of theory

- *Ab Initio*
  - Most theoretically rigorous
  - Energies calculated from electronic structure
  - Requires no experimental parameters
- Semi-Empirical
  - Simplifying assumptions made
  - Experimental parameters compensate
- Molecular Mechanics
  - Electrons essentially ignored
  - Many experimental parameters required

Reasonable Simplification

- Born-Oppenheimer Approximation:
  - Movements of electrons are so rapid relative to movements of nuclei that they adapt essentially instantly to the nuclear positions - thus the motions of electrons and nuclei can be separated
  - Molecular (classical) mechanics relies on this approximation to the extreme of allowing electrons to be IMPLIED by their associated nuclei

Additional Approximations

- Potential energy can be represented by terms describing deformation from “standard” values
- Deformations from “standard” values can be represented harmonically
- Potential functions and parameters are transferable across molecules

Transferability

- Forcefields are generally parameterized to give accurate relative energies for isomeric structures
- Energy values will not be comparable from one forcefield to another

Exercise

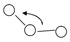
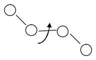
- Build a simple molecule in MOE or Spartan (cyclohexane, an amino acid, a monosaccharide, etc)
- Compute and record its energy using every available forcefield
  - Forcefields can be changed in MOE using the Window->Potential Control dialog box
  - Forcefield control in Spartan is controlled during calculation setup
- What is the range of energies you noted?

Molecular Mechanics - Goals

- To reproduce molecular geometries and RELATIVE energies
  - Bond lengths: ± 0.005 Å
  - Bond angles: ± 1°
  - Torsion angles: ± 5°
  - ΔH_f: ± 0.7 kcal/mol

Molecular Mechanics

- Energy broken down into terms
  - Bond stretching

  - Angle bending

  - Torsional potential

  - Non-bonded interactions
    - Van derWaals, electrostatic, dipolar interactions


Forcefields

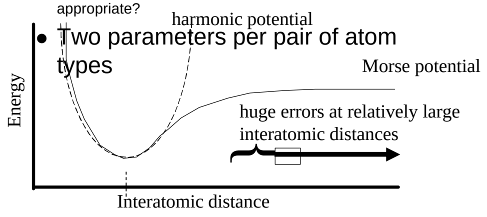
- The combination of mathematical formulae and parameters used to represent the energy of a chemical system
- Different forcefields are optimized for different problems:
  - MMFF94: optimized for small organic compounds - wide structural variety
  - Sybyl: general purpose – reasonable (but not excellent) parameters for wide variety of atom environments
  - AMBER94: optimized for proteins - often missing parameters for other organics
  - PEFSAC95: optimized for carbohydrates
  - UFF: universal forcefield, contains parameters even for metals

Question

1. Sketch the energy as a function of distance (r) between two bonded atoms (start @ r=0 Å)
2. If this interaction is expressed harmonically [$V = k_s (r - r_0)^2$] what will the curve look like?
3. Where will the greatest error be?
4. What chemical process(es) will therefore <u>not</u> be modeled accurately?

Bond Stretching

- Approximated with a harmonic potential
- $V = k_s (r - r_0)^2$ What value of r_0 is appropriate?
- Two parameters per pair of atom types



Experimental Bond Distances

- r_e: equilibrium bond distance - bottom of energy well
- r_{av}: average distance (slightly longer than r_e)
- r_a : thermal average, from electron diffraction radial distribution function
- r_g : derived from r_a (~0.002 Å longer) averaged over all molecular vibrations
- r_α: distance between mean atom positions at a given T
- r_α°: r_α extrapolated to 0 K
- r_o: directly obtained from microwave
- r_s: directly obtained from microwave
- r_z: microwave result with vibrational correction (should agree with r_α°

Experimental Bond Distances

- Electron Diffraction
  - Thermal average of occupied states
  - Gives r_a, r_g, r_α, r_α°
- Microwave
  - Values for the state examined
  - Gives r_o, r_s, r_z
- Molecular Mechanics
  - Usually parameterized to give room-temperature vibrationally-averaged structures: r_α
  - Comparable to x-ray or electron diffraction (usually)
  - NOT identical to *Ab Initio* (which gives r_e)!

Angle Bending

- Treated Harmonically

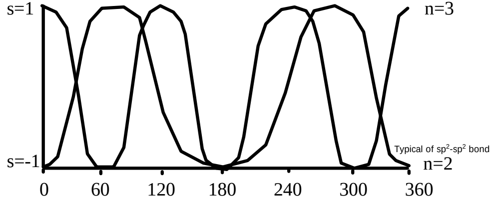
$$E = k\,(\underbrace{\theta - \theta_0}_{\textbf{Displacement from equilibrium bond angle}})^2$$

- Requires two parameters for each combination of three atom types

Question

1. Sketch the energy as a function of rotation around the central bond of butane
2. Draw structures of minimum energy structures and transition structures

Torsional Potential



Eω = Vn (1 + s cos nω)

(Two--fold term added to compensate for non-equivalent minima)

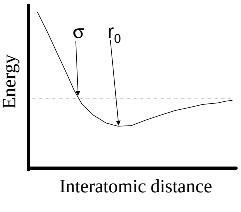
Three parameters needed for each combination of atom types

Question

- What value of n do you expect for an sp^2-sp^3 bond?
- Sketch the energy as a function of distance for non-bonded atoms

Van der Waals

- Usually expressed as a Lennard-Jones potential (6-12 shown):



$$V_{VDW} = 4e\left[\underbrace{\left(\frac{s}{r}\right)^{12}}_{\text{repulsive}} - \underbrace{\left(\frac{s}{r}\right)^{6}}_{\text{attractive}}\right]$$

$$\mathbf{r_0 =}\ 2^{-1/6}\,s$$

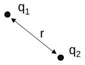
$$V_{VDW} = e\left[\left(\frac{r_0}{r}\right)^{12} - 2\left(\frac{r_0}{r}\right)^{6}\right]$$

Ionic Interactions

- Generally approximated using partial point charges
- Point charges come from
  - Forcefield
  - Quantum mechanics

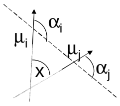
$$V = \frac{q_1 q_2}{Dr}$$

Effective dielectric constant



Dipolar Interactions

- Directional
- Often computed using Jeans' formula



$$V = \frac{m_i m_j}{D r_{ij}^{3}} \left(\cos x - 3 \cos a_i \cos a_j \right)$$

Angle formed by dipole tails

Angles dipoles form with vector between midpoints

Reading

- Required
  - Chapter 1 in Leach (will discuss questions only)
  - Chapter 3 in Leach
- Historical Interest
  - Molecular Mechanics, Burkert and Allinger, ACS Monograph, 1982