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°: ± 0.7 kcal/mol

Molecular Mechanics

- Energy broken down into terms
  - Bond stretching
  - Angle bending
  - Torsional potential
  - Non-bonded 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 not be modeled accurately?

Bond Stretching

- Approximated with a harmonic potential

Experimental Bond Distances

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

- Electron Diffraction
  - Thermal average of occupied states
  - Gives $r_a$, $r_g$, $r_{\alpha}$
- Microwave
  - Values for the state examined
  - Gives $r_a$, $r_g$, $r_{\alpha}$
  - Molecular Mechanics
  - Usually parameterized to give room-temperature vibrationally-averaged structures: $r_a$
  - Comparable to x-ray or electron diffraction (usually)
  - NOT identical to Ab Initio (which gives $r_e$)!

Angle Bending

- Treated Harmonically
  - $E = k (\theta - \theta_0)^2$
  - Displacement from equilibrium bond angle
- 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

$$E_{\omega} = Vn (1 + s \cos n\omega)$$

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

Three parameters needed for each combination of atom types

Van der Waals

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

$$V_{VDW} = 4\varepsilon \left( \frac{S}{r} \right)^{12} - 2 \left( \frac{S}{r} \right)^6$$

$$r_0 = 2^{1/6} \sigma$$

Van der Waals potential:

- $V_{VDW}$ is repulsive
- $V_{VDW}$ is attractive

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
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

\[ V = \frac{\mu_i \mu_j}{Dr} (\cos x - 3 \cos\alpha_i \cos\alpha_j) \]

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