

Application of Computer in Chemistry

SSC 3533

MOLECULAR MODELING

Prof. Mohamed Noor Hasan
Dr. Hasmerya Maarof
Department of Chemistry



Outline

- Introduction to Molecular Modeling
- Molecular Mechanics
- Quantum Mechanic methods
- Software Packages
- Comparison

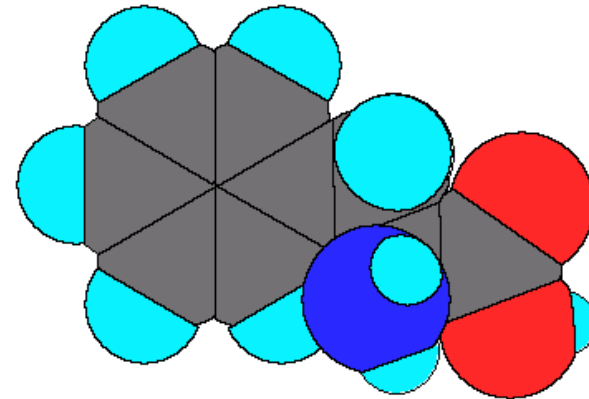
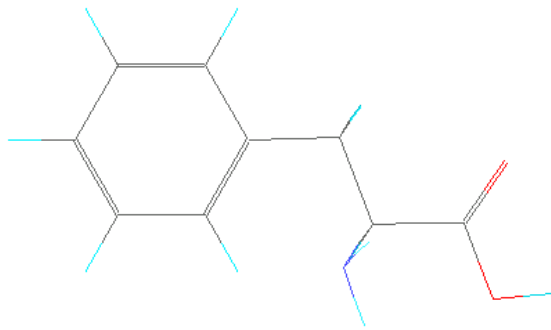
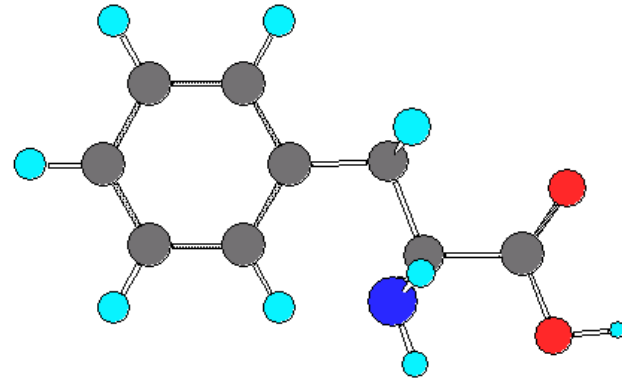
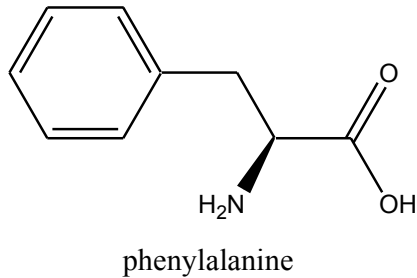
Introduction

- Using computer to construct models of molecular structures
- Involves calculation of preferred (lowest energy) conformation of molecular structures
- Models generated can be used to estimate properties, perform simulation, predict reactions

Why use computer?

- The models produced are flexible
- Models of large molecules can be easily generated
- Size of the models can be modified
- Able to zoom to certain areas of the structure - to study properties, reactions etc.

Molecular Models



Modeling methods

- **Quantum Mechanics**

- **Ab Initio Method**

- Calculation is very intensive because all electrons involved in the formation of bonds are taken into account

- Only suitable for small molecules

- **Molecular Orbital Method**

- Just like ab initio but simpler because only orbitals (valence electrons) are taken into account

Modeling Methods

- **Molecular Mechanics**
- Modeling is based on interactions among atoms – the smallest entity in the model development
- Electrons and orbitals are considered part of the atoms

Molecular Mechanics

- Data for small molecules can be used for large molecules
- A molecule consists of atoms held by elastic/harmonic forces. Law of physics (Hooke's Law) can be applied
- The forces are defined by potential energy function
- Group of forces form force field
- A molecule in the force field will take the conformation with lowest energy

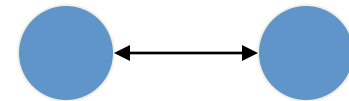
Potential Energy (Strain Energy)

$$E_{str} = E_{bond} + E_{angle} + E_{tor} + E_{nb}$$

- E_{str} - Strain Energy (Potential energy)
- E_{bond} - Bond stretching energy
- E_{angle} - Angle bending energy
- E_{tor} - Torsional angle energy
- E_{nb} - Non-bonded interactions energy

Bond Stretching

$$E_{bond} = \frac{1}{2} \sum_{i=1}^{N_b} k_b (r_i - r_0)^2$$



N_b – number of bonds

C–C – 1.54 Å

k_b – constant

C=C – 1.34 Å

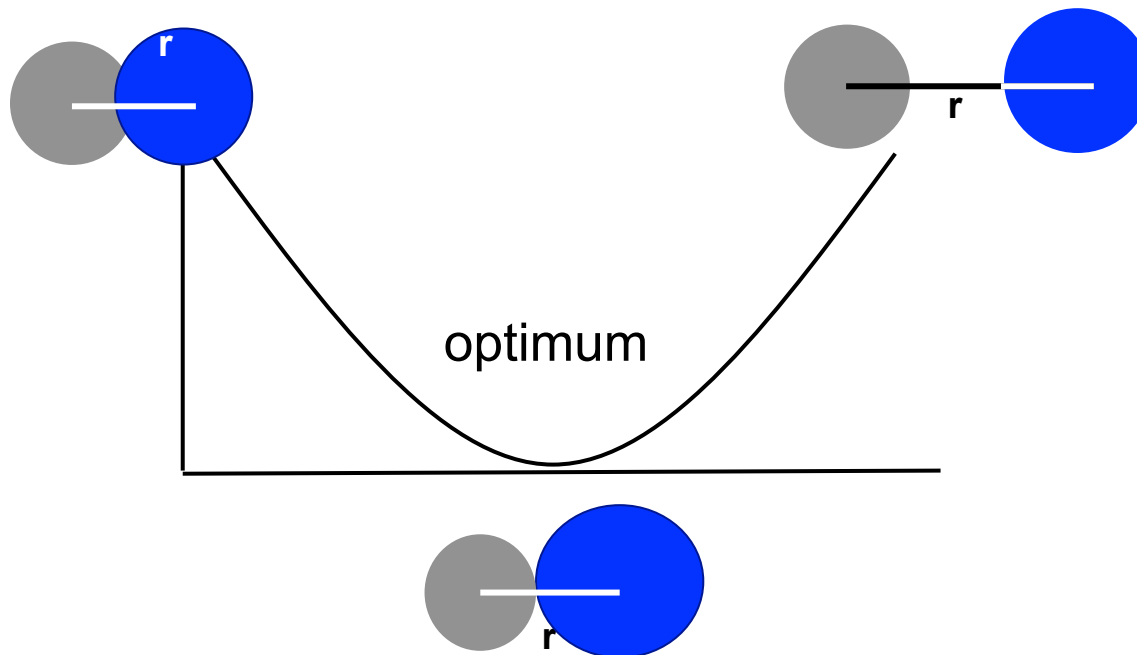
r_i – actual bond length

C≡C – 1.20 Å

r_0 – optimum bond length

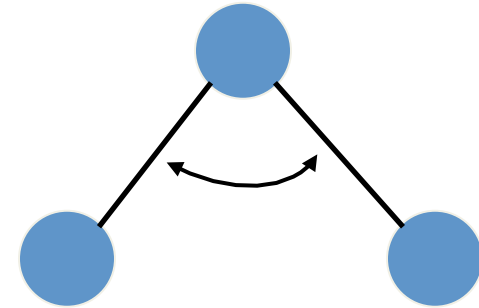
C..C – 1.39 Å

Energy change with bond length



Angle bending

$$E_{angle} = \frac{1}{2} \sum_{i=1}^{N_a} k_{\theta} (\theta_i - \theta_o)^2$$



N_a – Number of angles

k_{θ} - constant

θ_i – actual angle

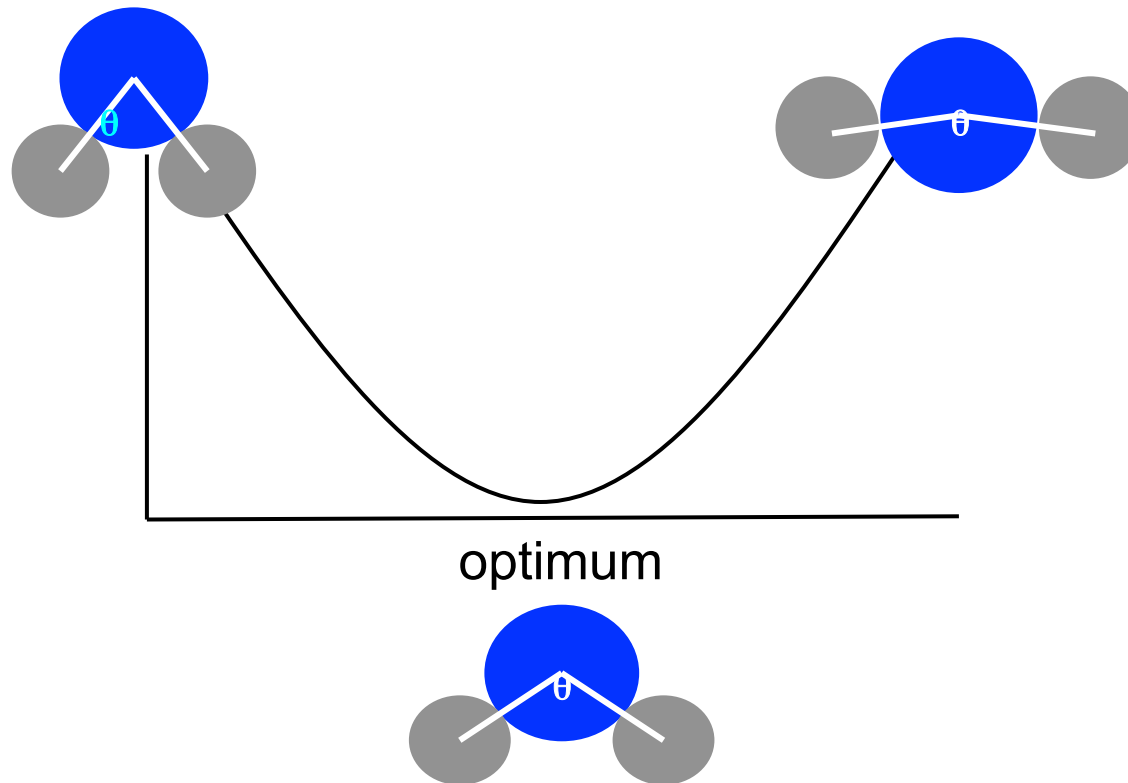
θ_o – optimum angle

$sp^3 - 109.5^\circ$

$sp^2 - 120^\circ$

$sp - 180^\circ$

Energy change with angle



Torsional Angle

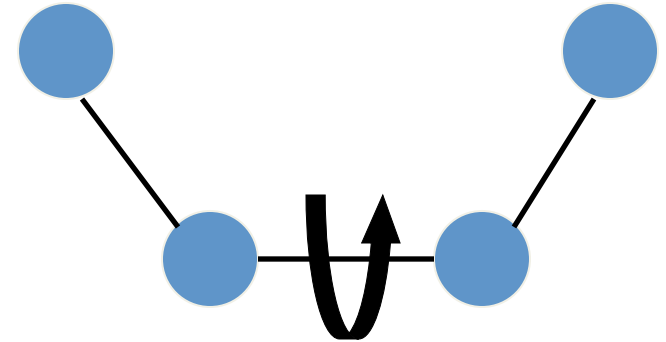
$$E_{\phi} = \frac{V}{2} (1 + \cos(n\phi - \gamma))$$

V – constant

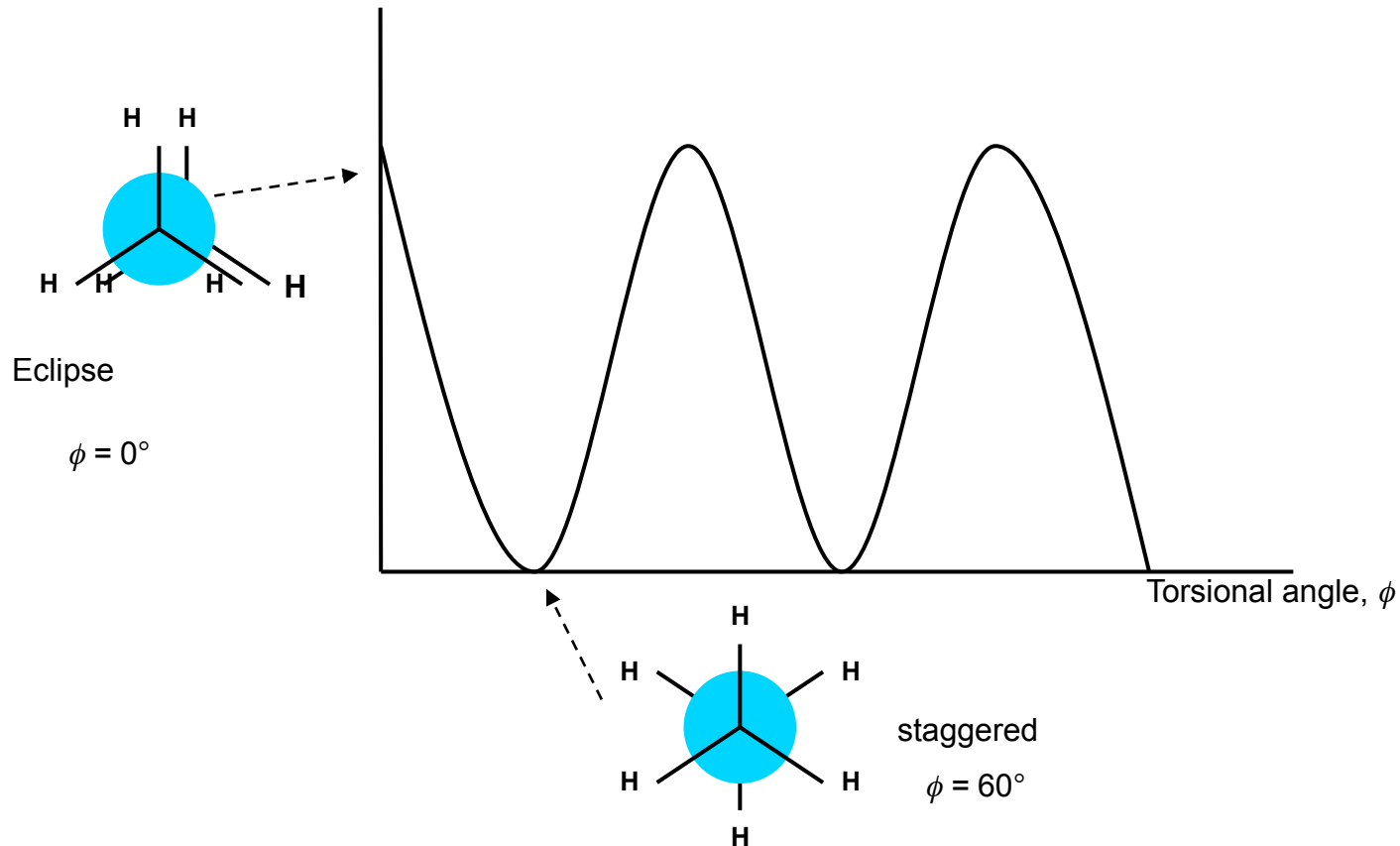
n – number of angles

ϕ – torsional angle

γ – phase factor



Energy change with torsional angle



Non-bonded interactions

E_{nb} = Electrostatic Energy + van der Waals Energy

$$E_s = \frac{q_i q_j}{r_{ij}} \quad E_{vdw} = \epsilon_{12} \left[\left(\frac{R^*}{r_{ij}} \right)^{12} - 2 \left(\frac{R^*}{r_{ij}} \right)^6 \right]$$

q_i – charge on atom i

q_j – charge on atom j

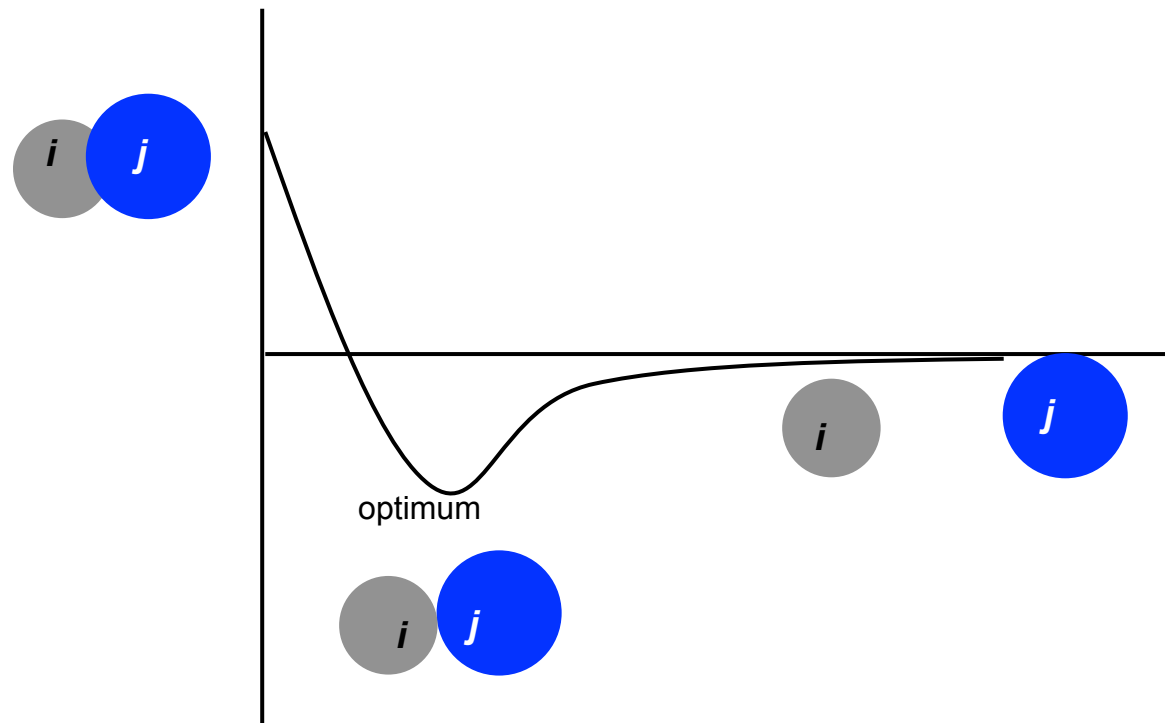
r_{ij} – distance i and j

ϵ – depth of energy well

R^* - van der Waals radius

r_{ij} – distance i and j

Energy change with atomic distance



Method for Energy Minimization

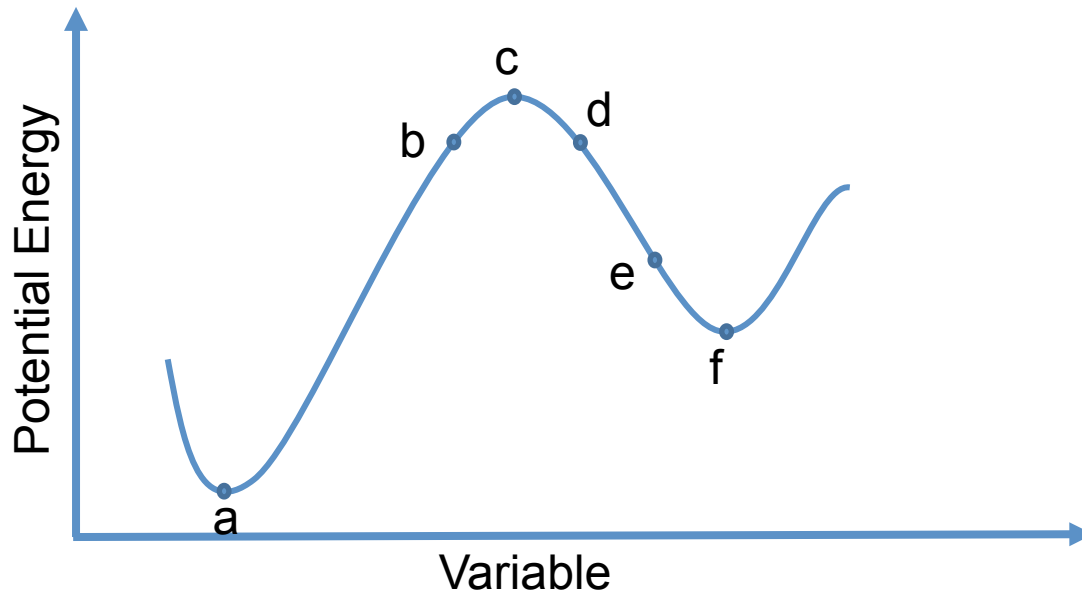
Steepest Decent

1. Move an atom by dx , dy , dz
2. Calculate change of energy per change on coordinate: dE/dx , dE/dy , dE/dz
3. Go back to original position
4. Repeat for all atoms
5. Move the atoms to new positions proportional with the change in energy.
6. Repeat until conformation with minimum energy is reached.

Applications

- Geometry optimization
 - Find conformation with minimum strain energy
- Energy Calculation
 - Energy for certain conformation or plot of potential energy for a particular model
- Estimation of physical/chemical properties
 - Surface area
 - Molecular volume
 - Dipole moment

Global vs. Local Minimum



If optimization starts from point *b*, will achieve minimum energy at *a* – Global minimum

If optimization starts from point *d*, minimum will be found at *f* - Local minimum

Quantum Mechanics

Quantum mechanic methods (*ab initio* and semi-empirical) are based on the following principles:

- Nucleus and electrons are differentiated
- Electron-electron interactions and electron-nucleus interactions are explicit.
- Interactions are controlled by charges on electrons and nucleus (i.e. potential energy) and electron movement
- Interactions determine nuclear and electron distribution and their energies

Schrödinger Equation

- Quantum mechanic methods involve solution of Schrödinger wave equation.

$$H\Psi = E\Psi$$

- H – Hamiltonian Operator: contains information on electrons and nucleus in a system
- Ψ – Wave function: describe electrons in terms of position and movement
- E – Energy related to certain electron

Solution of Schrödinger Equation

- Exact solution of Schrödinger equation is only for 1 electron – 1 nucleus system.
- The solution describe allowed states of an electron
- $$\int \Psi^2(r) dr = 1$$

$r = \text{radius } (x, y, z)$
- Solution of this probability function is called orbital, i.e. the probability of finding electrons for that atom

Semi-empirical method

- In a semi-empirical method experimental data (parameter) is used to simplify calculations

Examples

- CNDO (Complete neglect of differential overlap)
- MNDO (Modified neglect of diatomic overlap)
- AM1 (Austin Model 1)
- PM3 (Parameterization method 3)

Example Software Packages

- MOPAC (Molecular Orbital Package)
 - Originally free, now a commercial product
 - Also bundled with other software packages
- GAMESS (General atomic and molecular atomic structure system)
 - ab initio method
 - Freely available
- Gaussian
 - ab initio method

Software packages

- Alchemy
 - MM3 and MOPAC
- Chem3D
 - MM2 and MOPAC
- CHARMM
 - Molecular mechanics for large molecules (macromolecule)
- HyperChem
 - MM, semi-empiric and *ab initio*

Method Comparison: MM

- Calculation is fast: time $\propto N^2$
- Concept easy to understand
- Can be used for large molecules (thousands of atoms)
- Cannot calculate charge
- Requires parameters from experimental data
- Easily trapped in local minima

Method comparison: Semi-empirical

- Calculation is faster than *ab initio*: time $\propto N^3$
- Can calculate transition states and excited states
- Can be used to model moderately large molecules (hundreds of atoms)
- Calculation does not require very high CPU time

Method Comparison: ab initio

- Does not depend on experimental data
- Can calculate transition states and excited states
- Calculation results are accurate
- Calculations are a bit slow: time $\propto N^4$
- Theory is difficult to understand
- Limited to small molecules (tens of atoms)