



Crash course in Comp Chem

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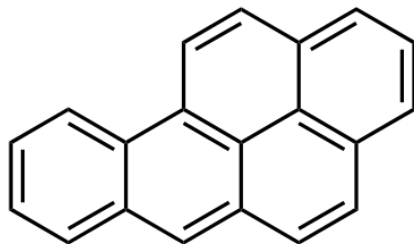
May 2020

Topics overview: 3 webinars

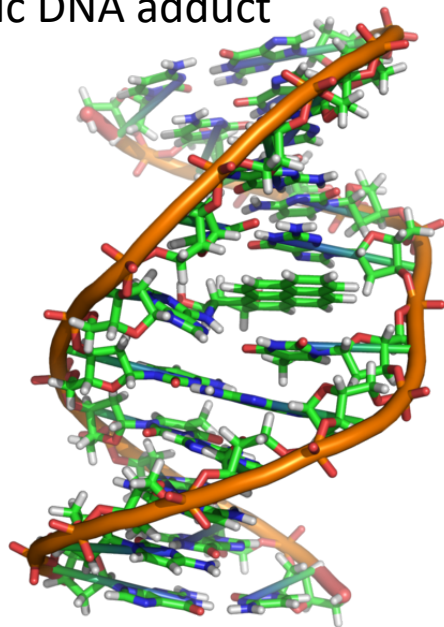
- Building simple structures and modeling organics in their media
- Organic reactions and mechanisms
- Biological systems (dynamics, interactions with xenobiotics and linear response calculations)
- Organometallic systems (Mark Schofield)
- Computational spectroscopy (Mark Schofield)

Central Dogma of Computational Chemistry

benzo[a]pyrene



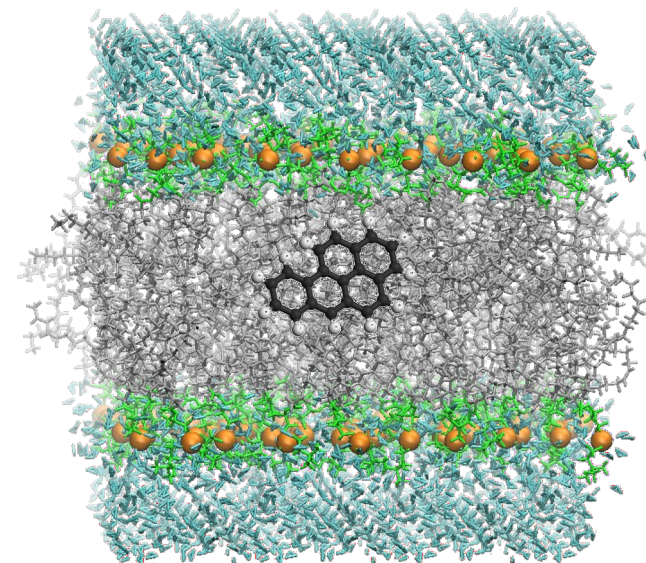
Mutagenic DNA adduct



STRUCTURE

DYNAMICS

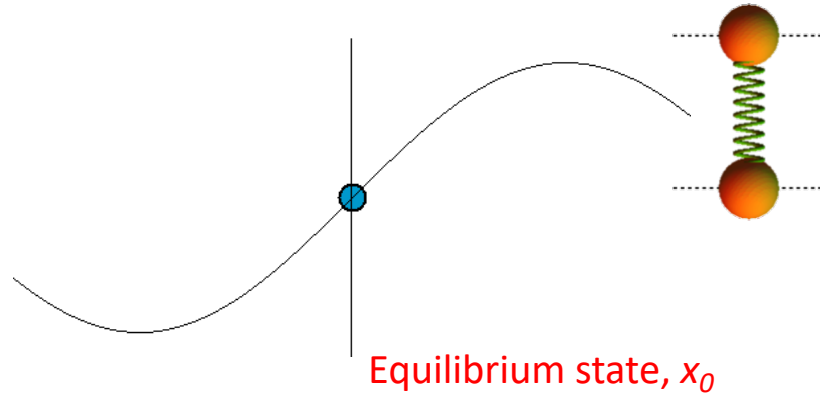
REACTIVITY



Phospholipid bilayer

STRUCTURE

Molecular mechanics

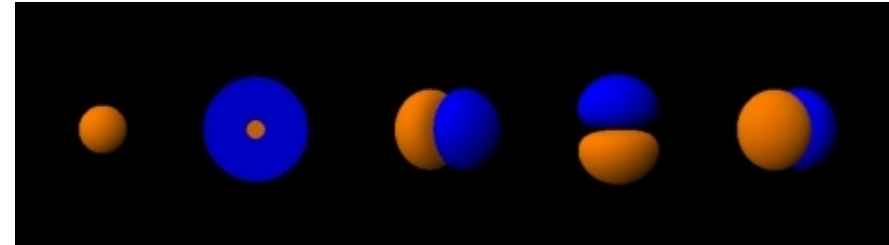


- Employs classical (Newtonian) physics
- Assumes Hooke's Law forces between atoms (discrete masses attached by a spring)
- Energy calculated from **harmonic potential**:

$$E = k(x - x_0)^2$$

- these potential functions are collectively referred to as a *force field*
- **Limited to describing equilibrium states**

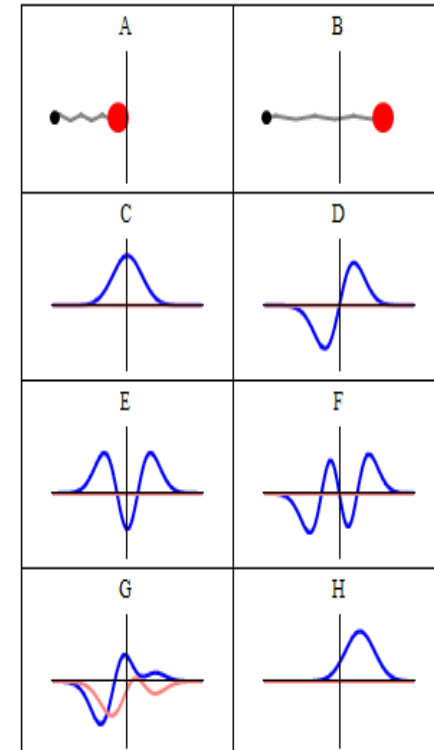
Quantum mechanics



$$E = \Psi H \Psi$$

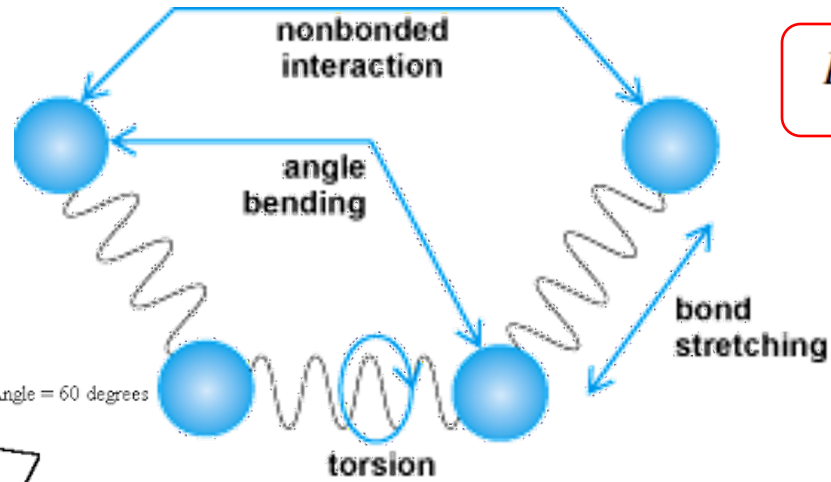
- uses molecular orbital theory: *electrons are treated as moving under the influence of nuclei; orbitals are represented by wave function, $\Psi \Rightarrow$ subatomic level*

→ Can be used to describe non-equilibrium states



MM Calculations: Force field

Not to be confused with:



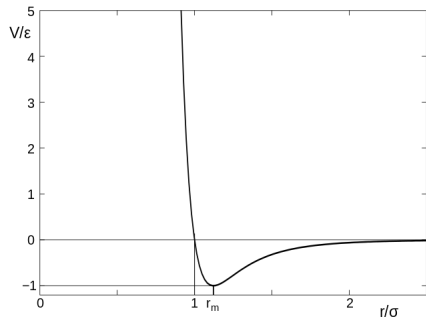
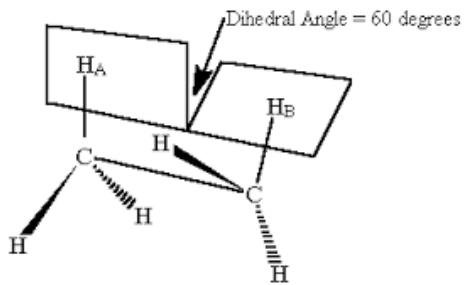
$$E = E_{bond} + E_{angle} + E_{torsion} + E_{nb}$$

$$E_{bond} = \sum_{bonds} k_r (r - r_{eq})^2$$

$$E_{angle} = \sum_{angle} k_\theta (\theta - \theta_{eq})^2$$

$$E_{torsion} = \sum_i \frac{V_1^i}{2} [1 + \cos(\phi_i)] + \frac{V_2^i}{2} [1 - \cos(2\phi_i)] + \frac{V_3^i}{2} [1 + \cos(3\phi_i)]$$

$$E_{nb} = \sum_{i < j} \left\{ \frac{q_i q_j e^2}{r_{ij}} + 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] \right\} + \sum_i^{\in a} \sum_j^{\in b} \left\{ \frac{q_i q_j e^2}{r_{ij}} + 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] \right\}$$



Atomic charges

- Class I-III
 - **Class I:** derived from experimental data (Gasteiger/Marsilli charges – implemented in Marvin)

$$Q_i = \sum_{\alpha} q_i^{<\alpha>}$$

$$q_i^{<\alpha>} = \left(\frac{1}{2}\right)^{\alpha} \sum_{v \in i} \left[\sum_{\mu \in j} \frac{\chi_{j\mu}^{<\alpha>} - \chi_{iv}^{<\alpha>}}{\chi_{iv}^+} + \sum_{\lambda \in k} \frac{\chi_{k\lambda}^{<\alpha>} - \chi_{iv}^{<\alpha>}}{\chi_{k\lambda}^+} \right] - \text{the contribution to the}$$

atomic charge on the a -th step of iteration of charge

$$\chi_{iv} = a_{iv} + b_{iv}Q_i + c_{iv}Q_i^2 - \text{electronegativity of } n\text{-th orbital on } i\text{-th atom}$$

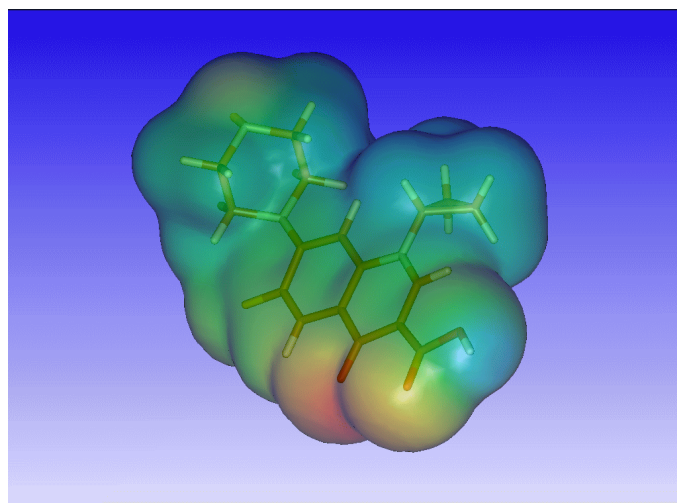
$$a_{iv} = \frac{I_{iv}^0 + E_{iv}^0}{2}$$

$$b_{iv} = \frac{I_{iv}^0 + E_{iv}^+ - E_{iv}^0}{4}$$

$$c_{iv} = \frac{I_{iv}^+ - I_{iv}^0 + E_{iv}^+ - E_{iv}^0}{4}$$

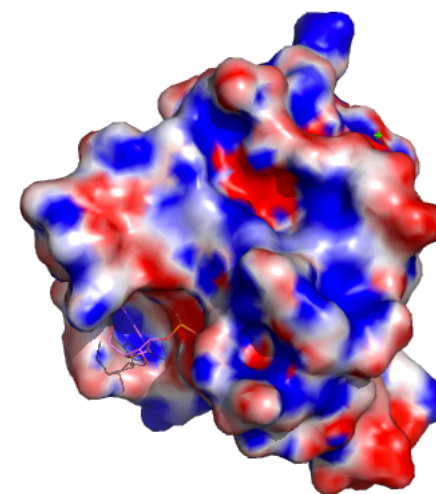
I_{iv}^0 , I_{iv}^+ , E_{iv}^0 , and E_{iv}^+ - the ionization potentials and electron affinities of the neutral atom (superscript 0) and of the positive ion (superscript +), respectively.

- **Class II:** derived from partitioning of molecular wavefunction (ab initio methods) or electron density (DFT methods) into atomic contributions (Mulliken, Löwdin, natural charges (NPA) and Hirshfeld charges)
- **Class III:** derived from physical observables (such as electrostatic potential), which can be calculated from the molecular wavefunction/ electron density (CHELPG and Merz-Kollman (MK) charge schemes)



Small molecule

vs.



large biomolecule

Useful benchmarking (CM5 model compared to others):

<https://pubs.acs.org/doi/10.1021/ct200866d>

QM calculations:

The time-independent Schrödinger equation

- Developed from DeBroglie's hypothesis of **particle-wave duality** (particle has both wave and particle properties)
- Predicts that wave functions can represent atomic or molecular orbitals

$$E\Psi = \hat{H}\Psi$$
$$E\Psi(\mathbf{r}) = \frac{-\hbar^2}{2m}\nabla^2\Psi(\mathbf{r}) + V(\mathbf{r})\Psi(\mathbf{r})$$

- For multielectron system, this equation cannot be solved analytically \rightarrow variational theorem is used: $\int \phi^* \hat{H} \phi d\tau \geq E_0$

(=the energy predicted from any trial wave function, ϕ , will never be lower than the true ground-state energy)

\rightarrow SE solved iteratively (energy minimization process) \rightarrow it yields **system energy** and other observables (e.g. dipole moment)

- The trial wave functions are defined as a **linear combination of basis functions**, which are usually atomic orbitals.

Basis functions → basis sets

- Used to model atomic orbitals

options: 1. using hydrogen-like WFs (Slater-type orbitals, STO)
2. using Gaussian type functions (GTOs) ...*easier to calculate*

GTOs:

- Typically, several fns represent 1 AO

examples: , 3-21G, 4-31G, 6-31G, 6-31G*, 6-31+G*, etc.

- “*” polarization functions – add to polar bonds (e.g. N-H, O-H, C-O)
- “+” diffuse functions – add to HOMOs of anions and spatially diffuse systems
- **The larger the basis set the greater the computational time!!**



What basis sets are good for what systems?

<https://gaussian.com/basissets/>

***Ab Initio* methods:**

- Solve Schrödinger's equation from mathematical principles
- Do not rely on empirical data
- Use relatively few approximations (depending on the level of theory)
- Can be very accurate but also very costly in computing resources
- => Applicable to small systems only
- Examples: Hartree-Fock (HF) – cheap but no correlation, MP2

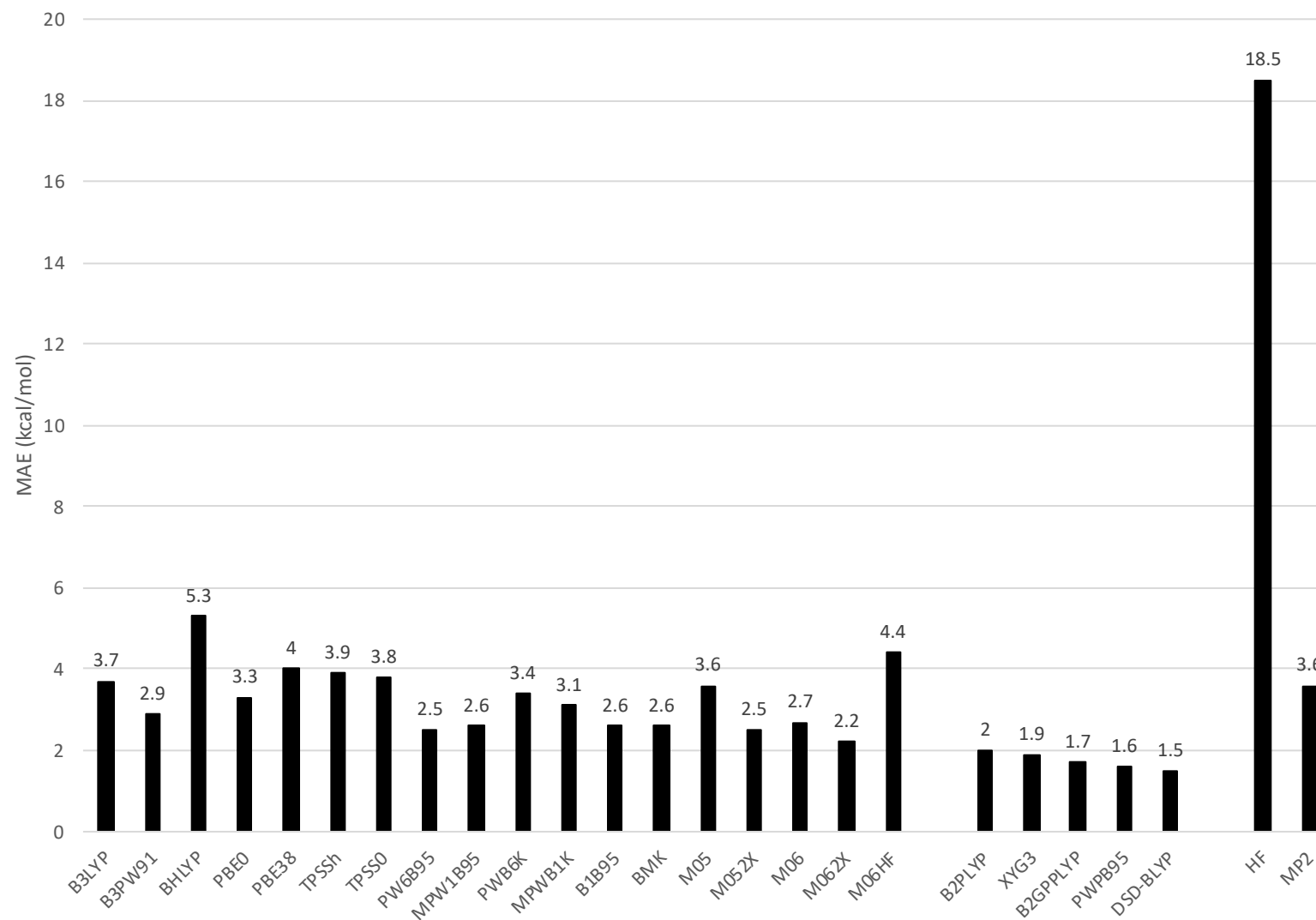
Density functional theory (DFT) methods:

- Like *ab initio* compute the system's energy by iteratively solving Schrödinger's equation
- Instead of wavefunction calculate molecular electronic probability density ρ and calculate the molecular electronic energy from ρ
- Can be very accurate and scale better for larger systems than *ab initio*
- Examples: B3LYP, M06, BMK, PBE

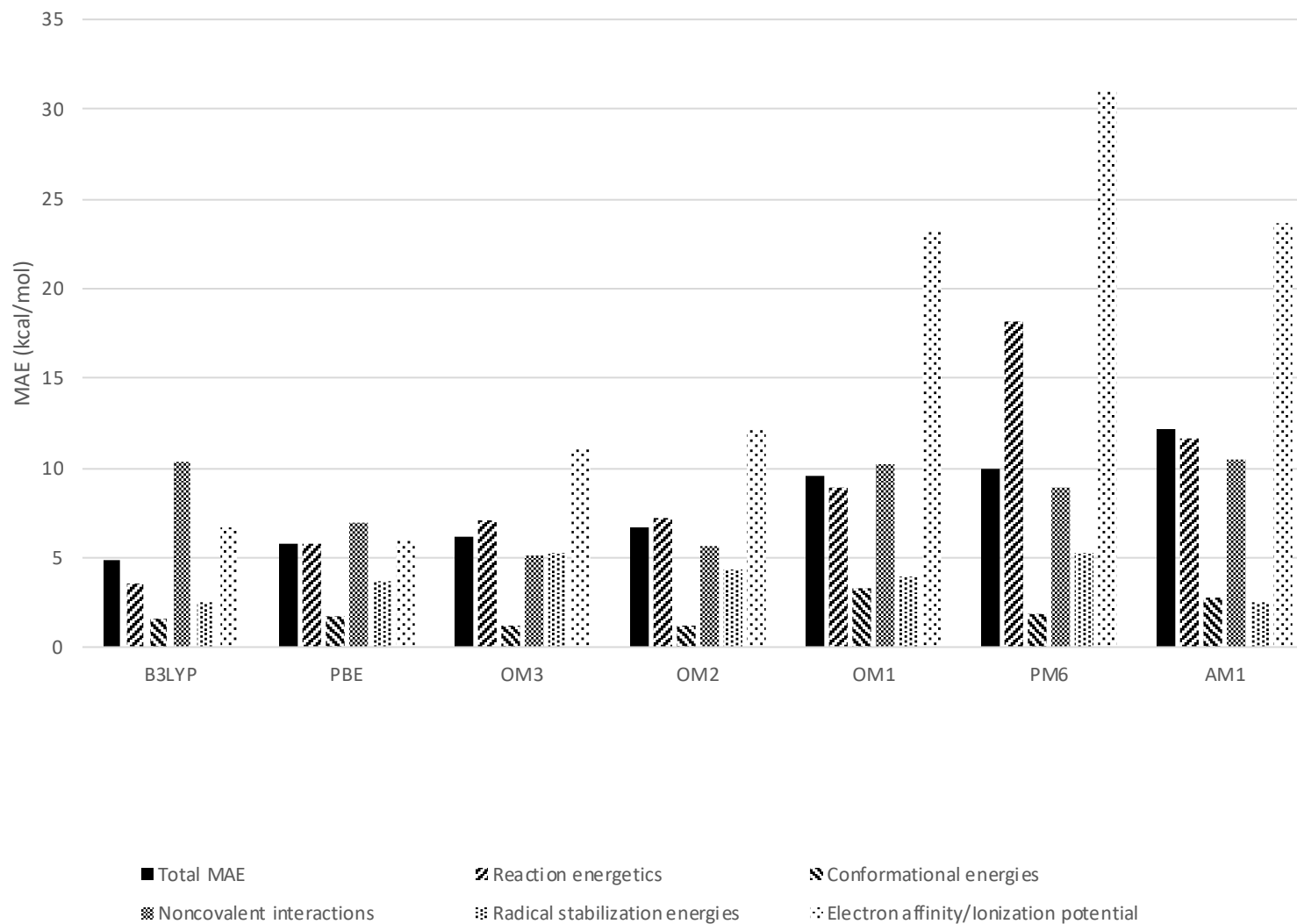
Semiempirical molecular orbital (SMO) methods:

- Hamiltonian operator is much simpler and contains empirical parameters obtained by fitting to experimental or *ab initio* results
- Accuracy relies on parameterization (training set vs. test set)
- Applicable to even very large systems
- Examples: AM1, MNDO, PM3-7, PDDG/PM3

Combined benchmarking metrics



Some benchmarking for semiempirical methods

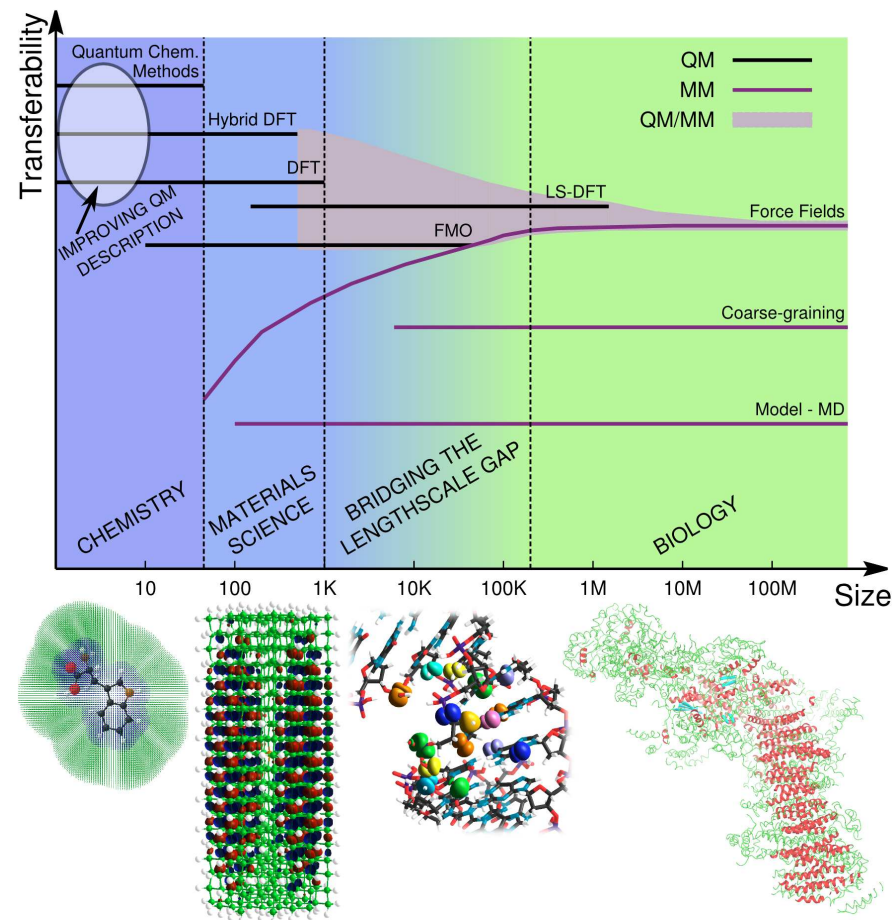
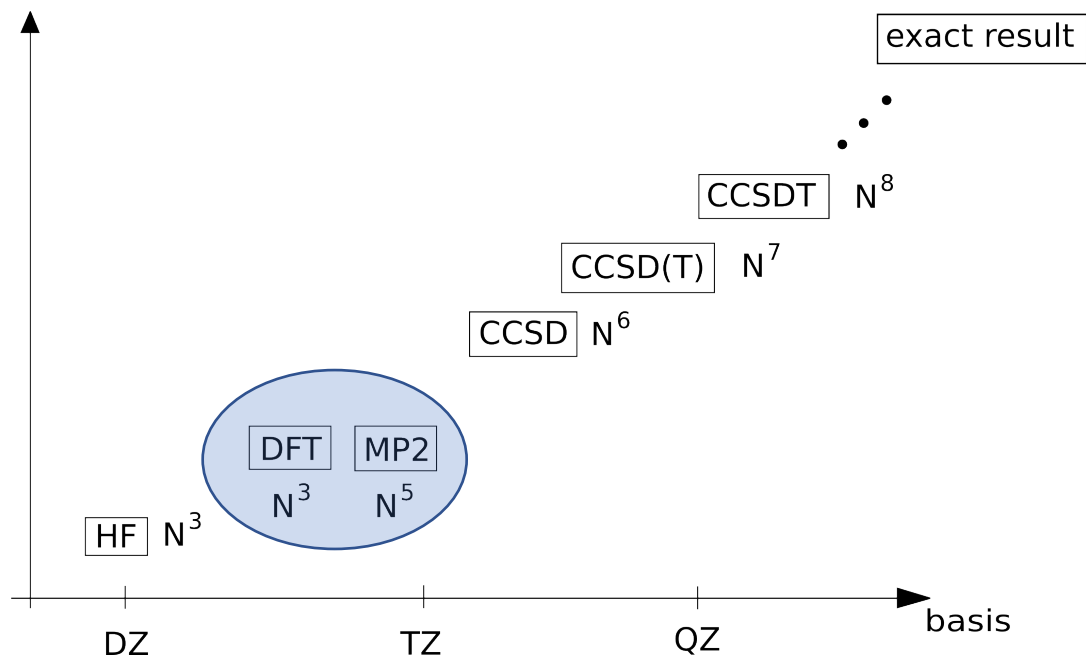


Computational cost

- More accurate methods (and larger basis sets) are more expensive in terms of computing requirements

“Pople Diagram”

quality of method
computational effort

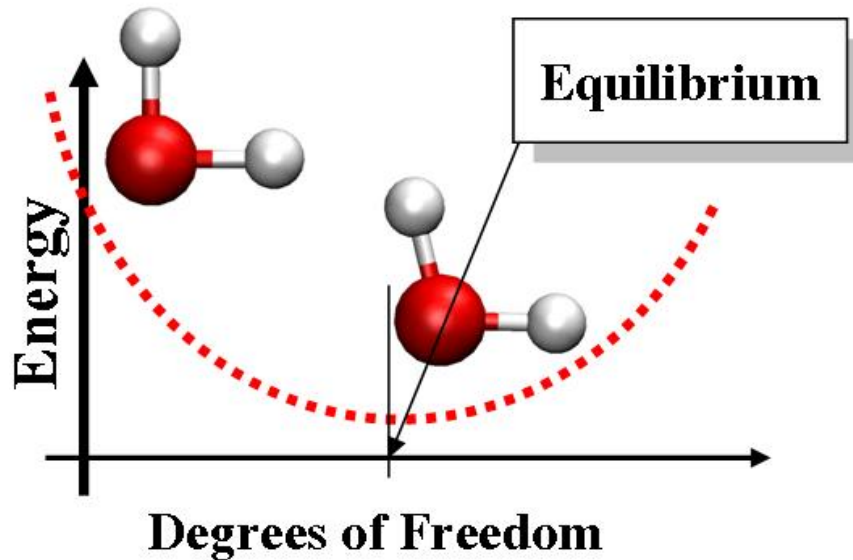


More benchmarking references

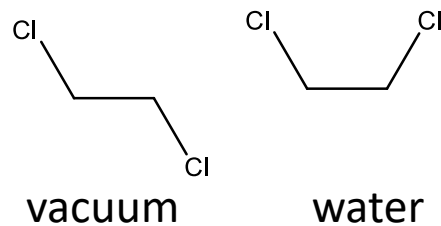
- **Various chemical reactions:** *J. Chem. Theory Comput.* 2007, 3, 2, 569–582: <https://pubs.acs.org/doi/10.1021/ct600281g>
- **Various nonbonded interactions:** *J. Chem. Theory Comput.* 2005, 1, 3, 415–432: <https://pubs.acs.org/doi/10.1021/ct049851d>

Geometry Optimization (Energy Minimization)

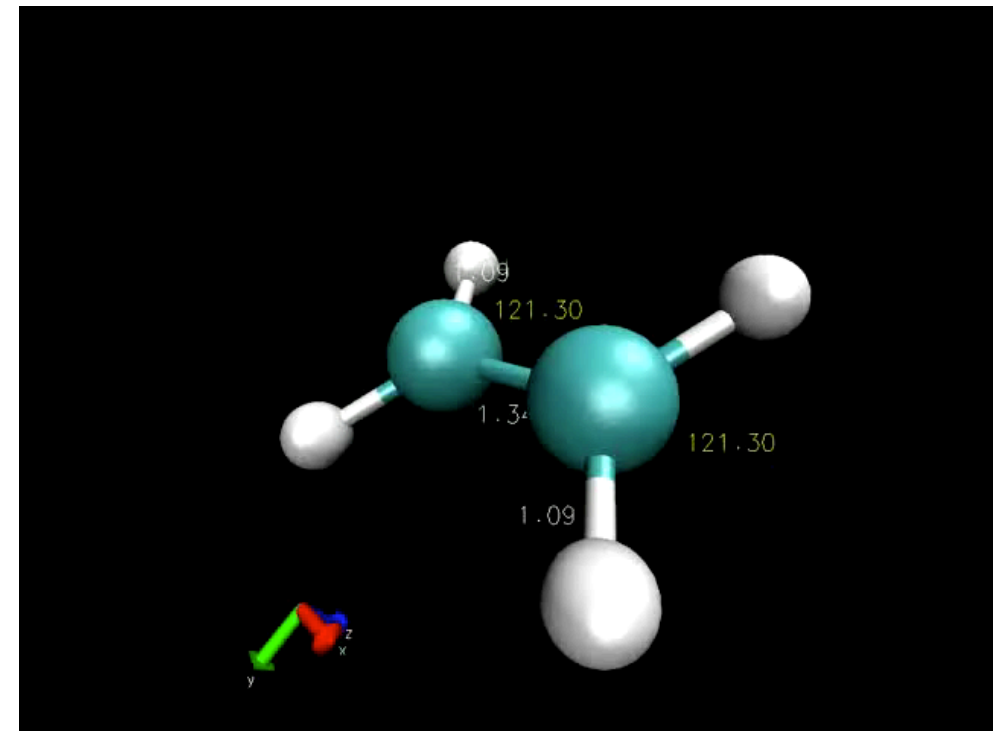
= procedure for finding the equilibrium geometry corresponding to the **local** energy (QM or MM) minimum by optimizing internal degrees of freedom
Real molecules exist in their equilibrium structures



equilibrium structures: $\frac{\partial^2 E}{\partial r_i \partial r_j} > 0$

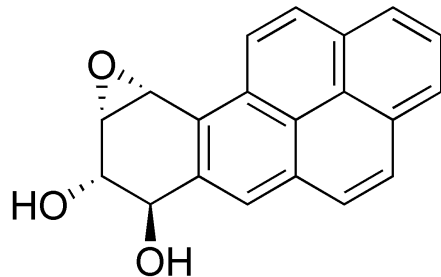


Ethylene in triplet state (QM)

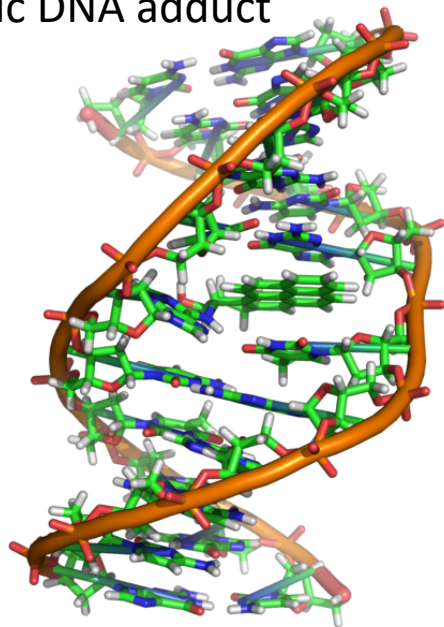


Central Dogma of Computational Chemistry

benzo[a]pyrene diol epoxide



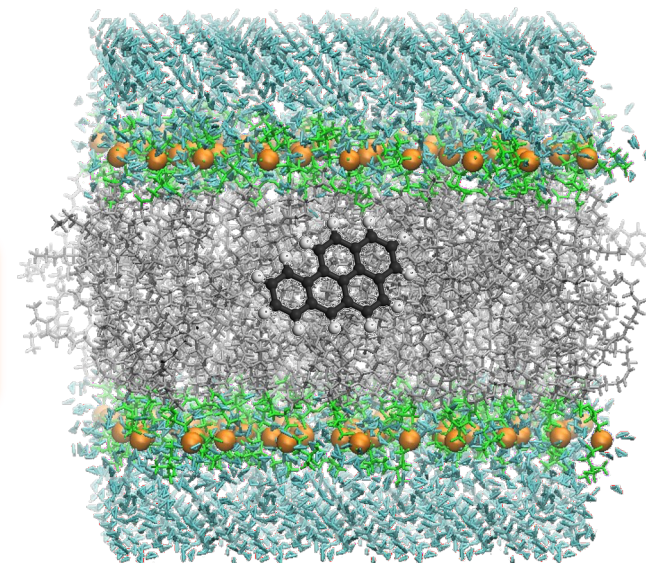
Mutagenic DNA adduct



STRUCTURE

DYNAMICS

REACTIVITY

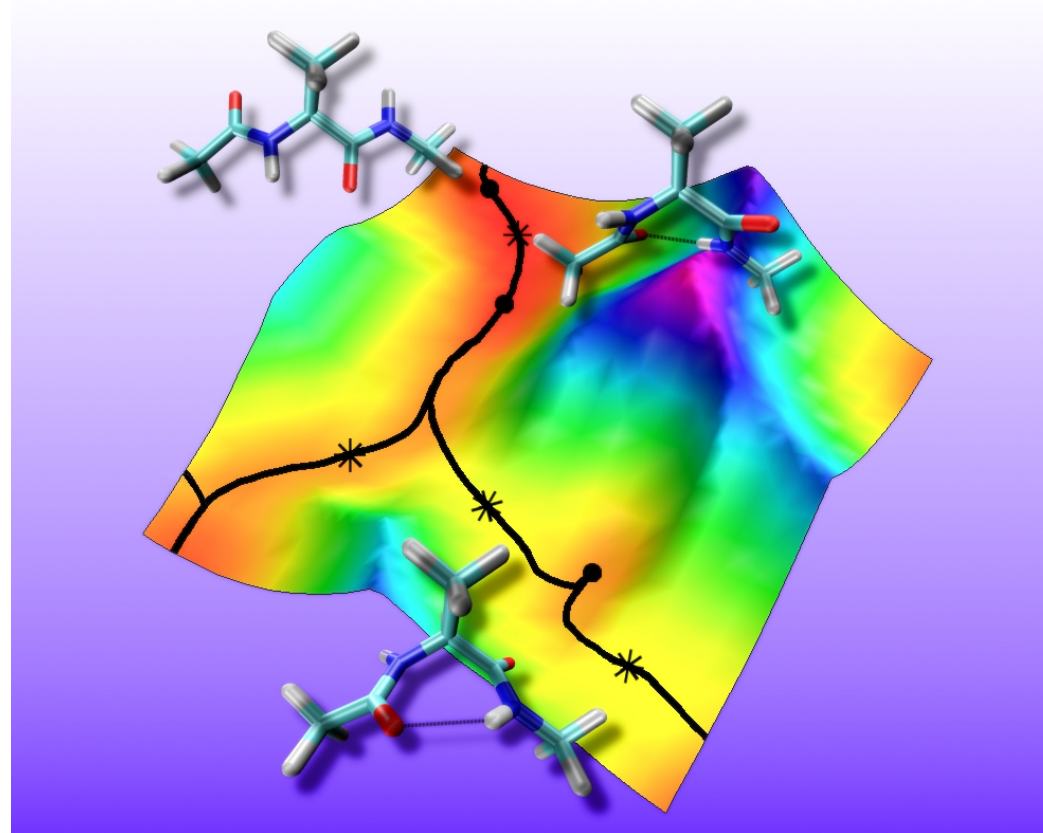


Phospholipid bilayer

DYNAMICS

- molecules rarely exist in a single equilibrium state/conformation, but rather an **“ensemble of states”**
- distribution of these states is guided by the **potential energy surface of the molecule (defined by intramolecular forces and imposed conditions/environment)**

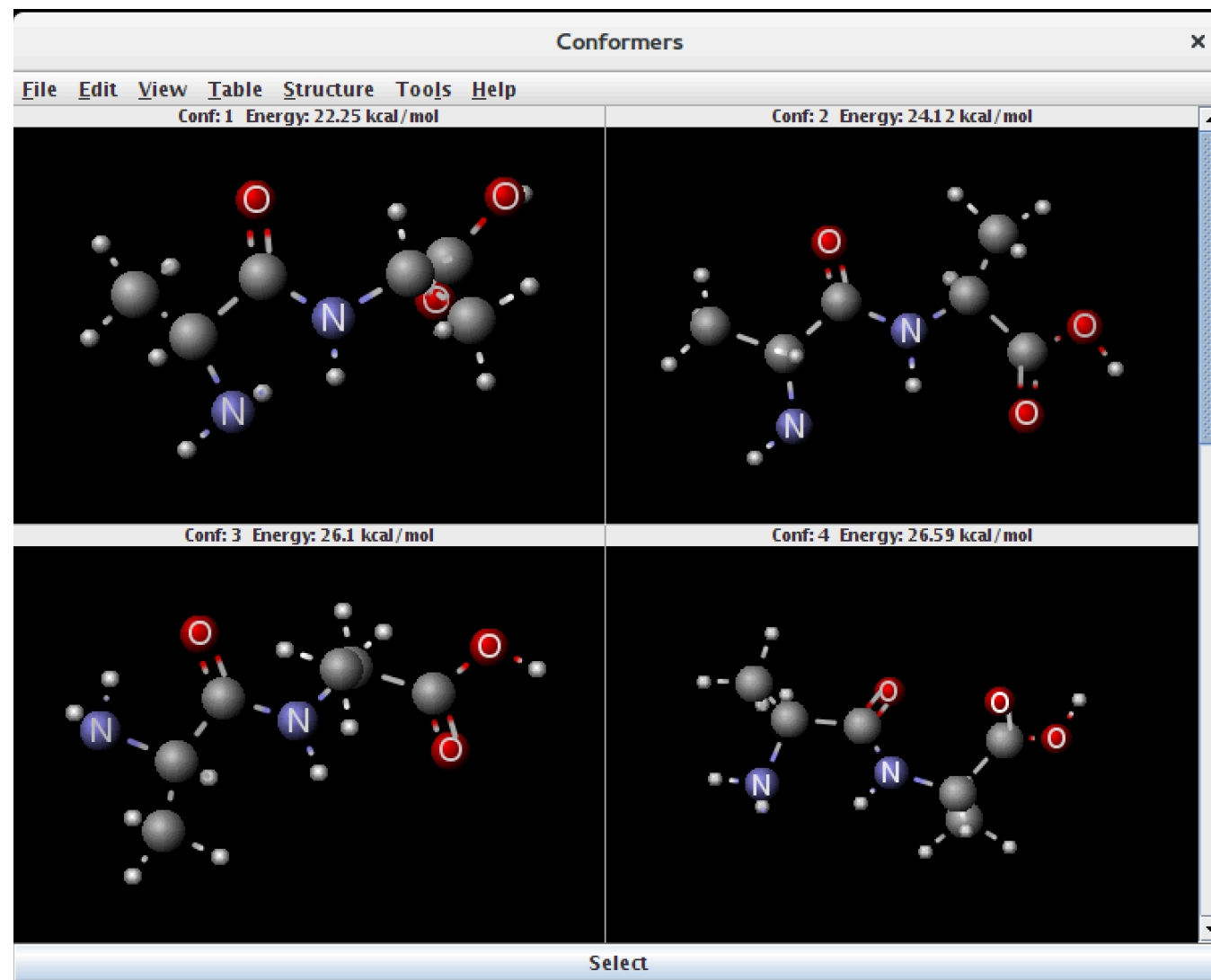
**Different conformers
= different properties**



Dialanine potential energy surface in water

Conformational search (torsion angle driving)

- Single (small) molecule approach

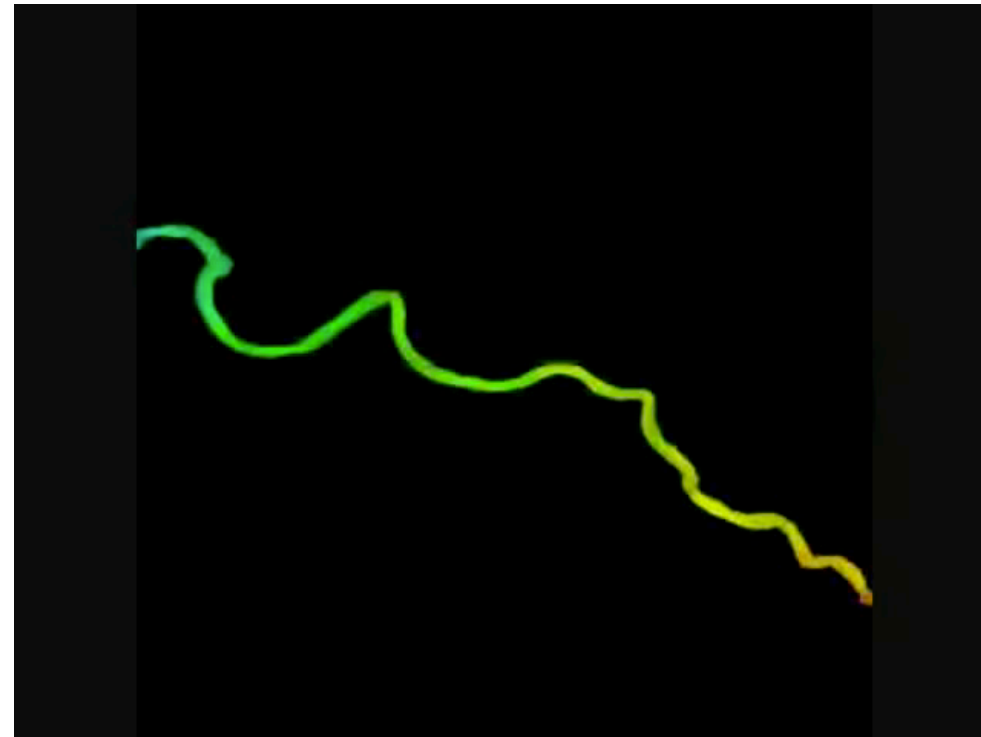
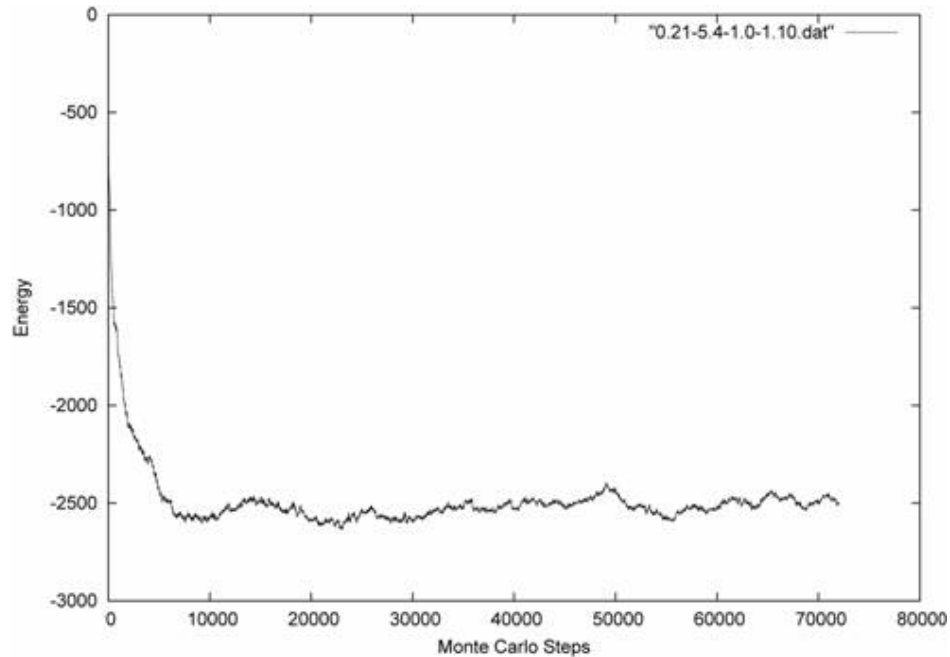


Sampling methods to find global minimum

Molecular dynamics: simulation of physical movements of atoms and molecules according to Newton's equations of motion

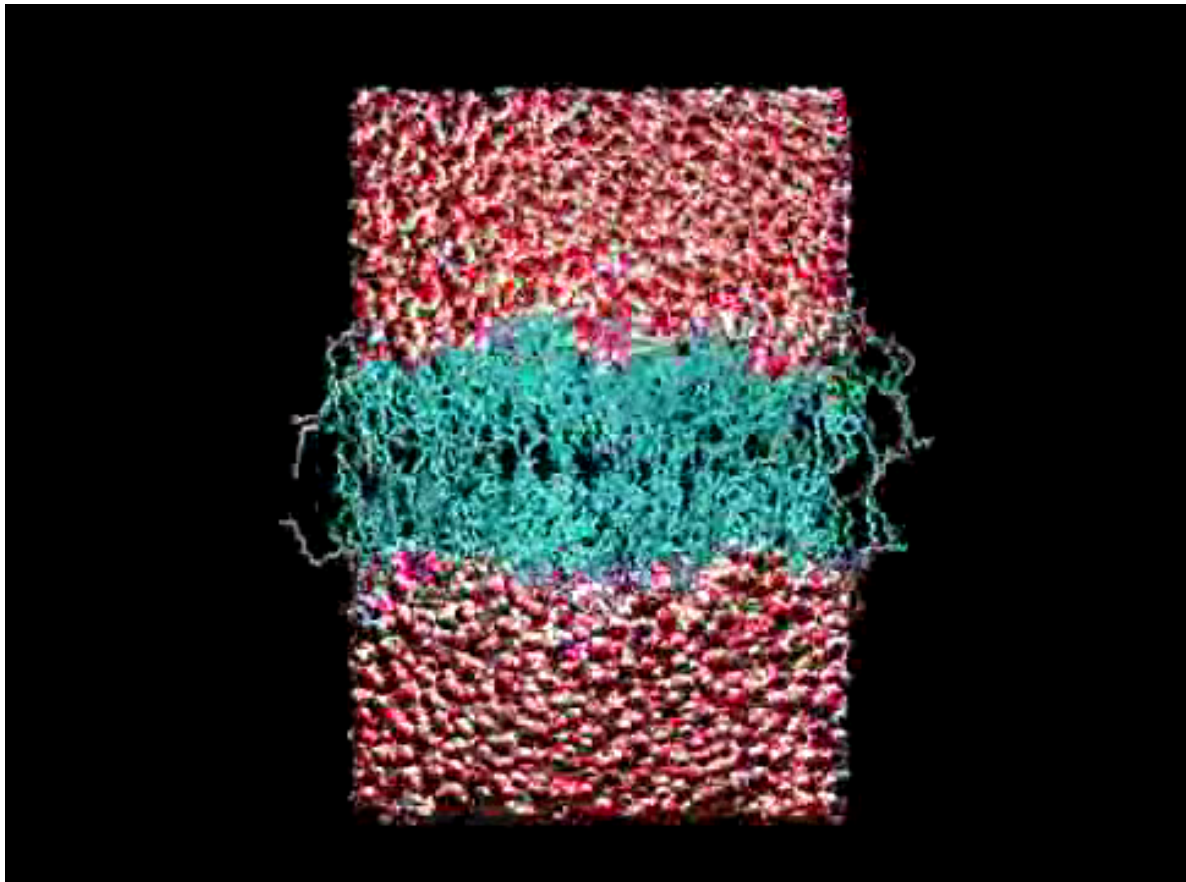
(Metropolis) Monte Carlo: simulation producing configurations with a probability proportional to their Boltzmann factors based on random moves

Yield
equilibrated
structures

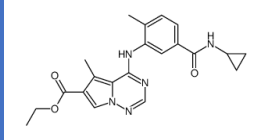


Folding of a globular protein with MC simulations

Sampling molecular energy surface to find average system properties



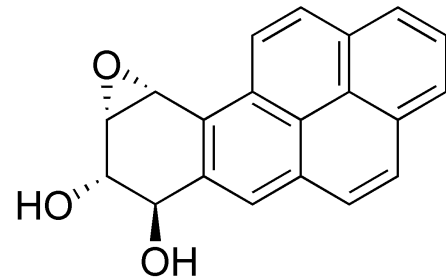
Sampling a phospholipid bilayer in water to get average properties of the system

	Dipole (D)	IP / EA (eV)	SASA (Å ²): Total/ Hydrophilic/ Hydrophobic	Cost (s)
				
AM1/MC simulation	4.3	9.0 / 0.6	754 / 121 / 428	13,266
AM1 minimization	2.9	8.9 / 0.9	735 / 127 / 415	1,670

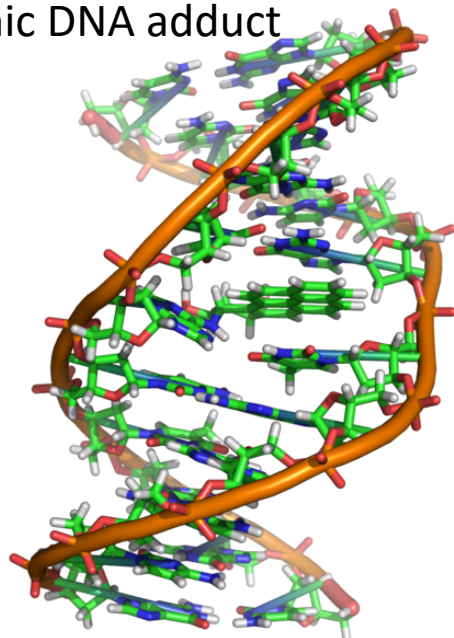
Determining selected physicochemical properties for a clinical prodrug (CAS 623152-11-4) from a **multiple-state simulation versus a simple geometry optimization** using AM1 semiempirical method.

Central Dogma of Computational Chemistry

benzo[a]pyrene diol epoxide



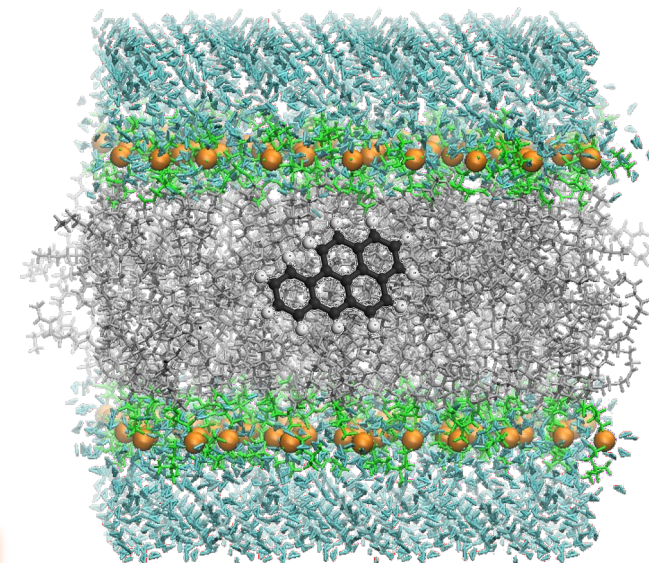
Mutagenic DNA adduct



STRUCTURE

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Phospholipid bilayer

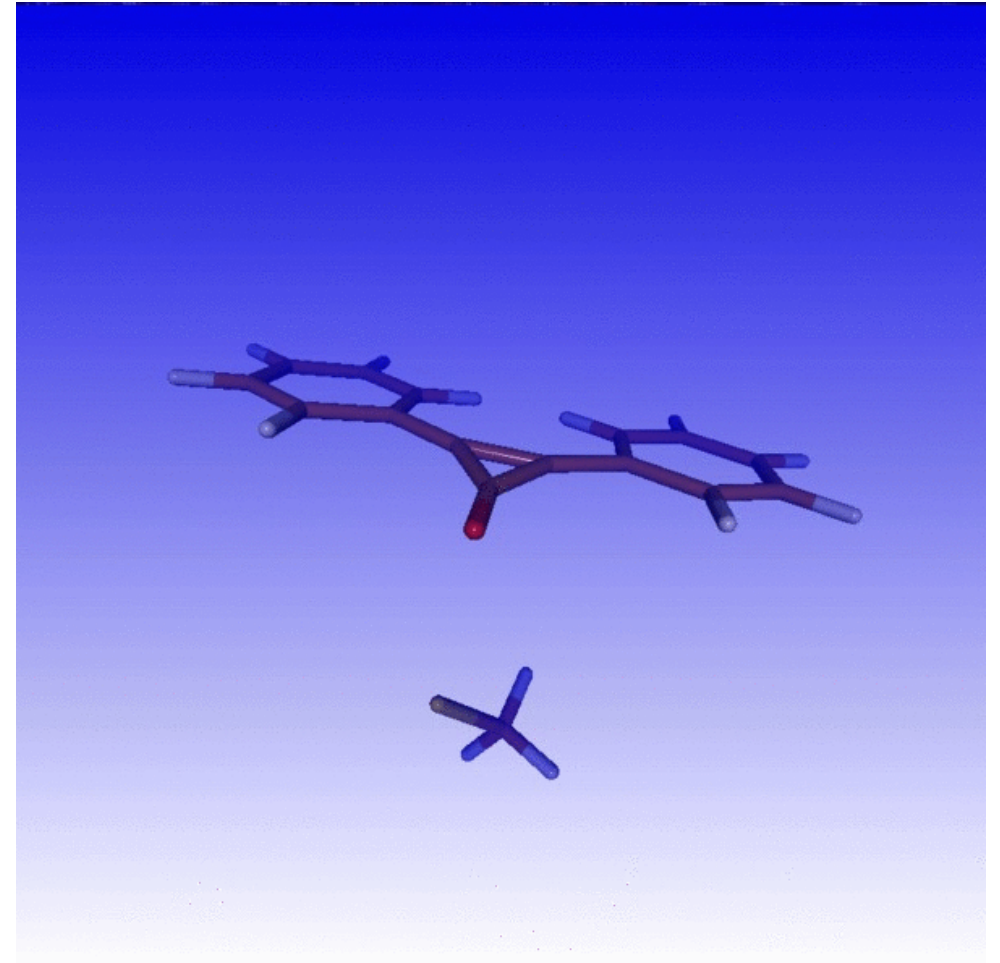
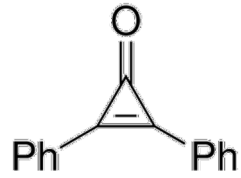
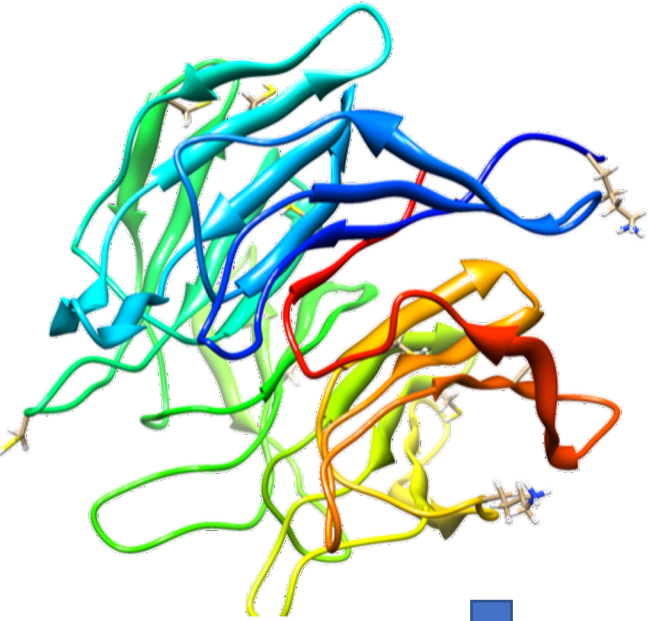
REACTIVITY

= forming/breaking of chemical bonds

= forming of new molecular orbitals

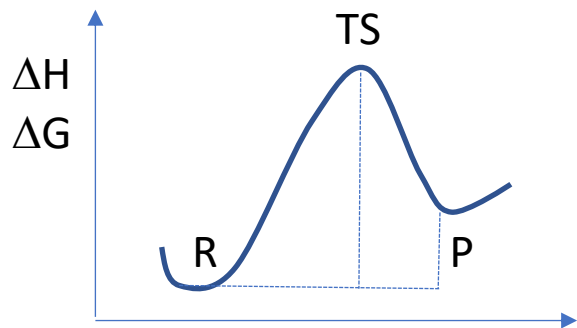
→ **purely a QM domain**

Reactivity of xenobiotics with biol. targets



Example:

Diphenylcyclopropanone (DPCP) reacts with skin proteins



Thermodynamics and kinetics: relating experiment to theory

$$k(T) = \frac{k_B T}{h c^\circ} e^{-\Delta^\ddagger G^\circ / RT}$$

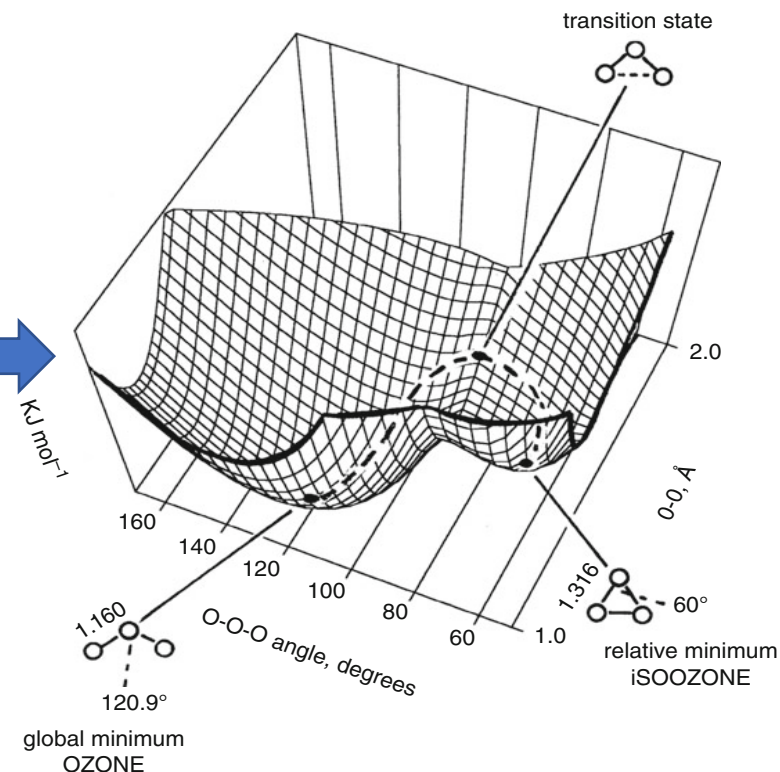
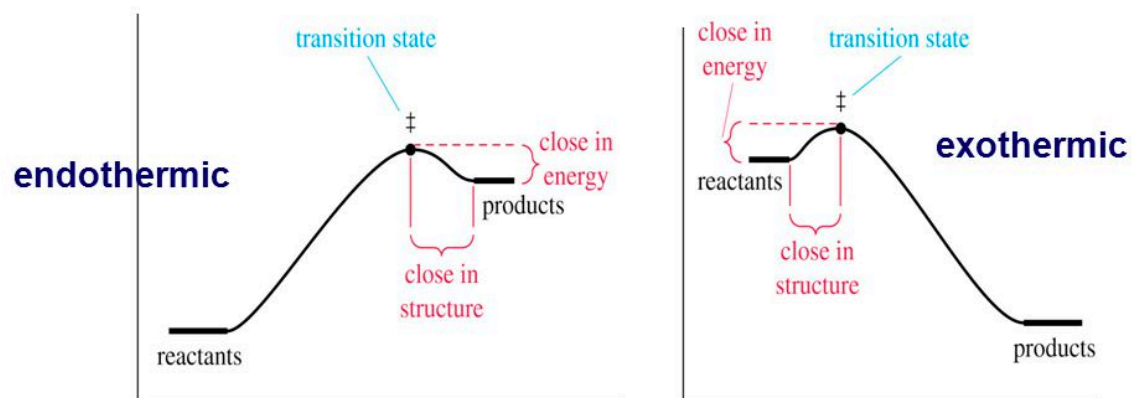
$$\Delta G^\circ = \sum n_p G_f^\circ(\text{each product}) - \sum n_r G_f^\circ(\text{each reactant})$$

\sum = sigma = "sum of"

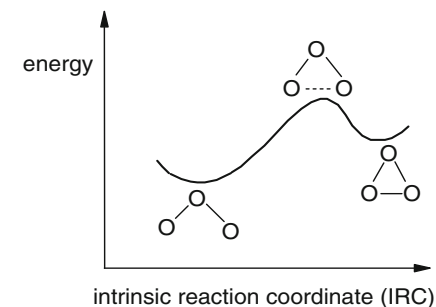
n_p = coefficient of product, n_r = coefficient of reactant

Hammond Postulate

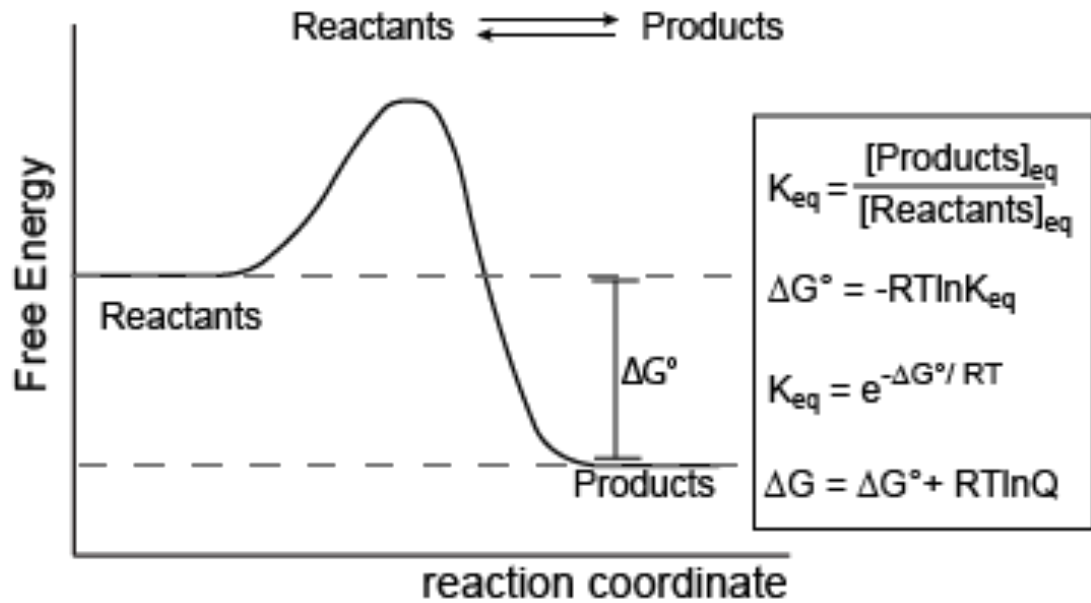
- For an endothermic reaction, the transition state more closely resembles the products.
- For an exothermic reaction, the transition state more closely resembles the reactants.



Transition states are not easy to model for the nonexpert



Thermochemistry in Gaussian comp software



- How do we calculate enthalpy and free energy?



$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

Thermochemistry in Gaussian comp software

$$S = Nk_B + Nk_B \ln \left(\frac{q(V, T)}{N} \right) + Nk_B T \left(\frac{\partial \ln q}{\partial T} \right)_V$$

$$S = R + R \ln(q(V, T)) + RT \left(\frac{\partial \ln q}{\partial T} \right)_V$$

$$= R \ln(q(V, T)e) + RT \left(\frac{\partial \ln q}{\partial T} \right)_V$$

$$= R \left(\ln(q_t q_e q_r q_v e) + T \left(\frac{\partial \ln q}{\partial T} \right)_V \right)$$

$$E = Nk_B T^2 \left(\frac{\partial \ln q}{\partial T} \right)_V$$



$$H_{\text{corr}} = E_{\text{tot}} + k_B T$$

$$G_{\text{corr}} = H_{\text{corr}} - T S_{\text{tot}}$$

Where S/E_{tot} = sum of all contributions,

e.g. $S_{\text{tot}} = S_t + S_r + S_v + S_e$.

Use partition function, q to calculate contributions to **entropy** and **thermal E** from all types of molecular motion (electronic, translations, rotations and vibrations)



Sum of electronic and thermal energies = $\mathcal{E}_0 + E_{\text{tot}}$

Sum of electronic and thermal enthalpies = $\mathcal{E}_0 + H_{\text{corr}}$

Sum of electronic and thermal free energies = $\mathcal{E}_0 + G_{\text{corr}}$

Benchmarking and method validation

- It's important to validate your theoretical approach against experimental data:
 - i) use existing benchmarking studies (look for similar system, similar conditions, similar output – e.g. kinetics vs. thermodynamics)

AND/OR

- ii) Gather some experimental data for your system to do your own validation (e.g. in studying reaction $X \rightarrow Y$ in different media, find exptl yields to relate to your free energies of reaction, or rate constants to relate to free energy barriers, for a subset of similar systems to see if relative trends agree)

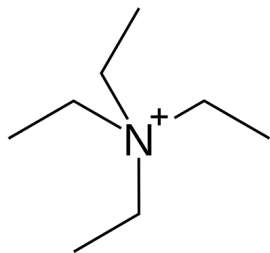


ALWAYS REMEMBER: ABSOLUTE VALUES OF COMPUTED OBSERVABLES (ENERGIES, PHYSICO-CHEMICAL PROPERTIES, ETC) ARE OFTEN MEANINGLESS; FOCUS ON RELATIVE VALUES, I.E. TRENDS GENERATED IN COMPARING ONE SYSTEM TO ANOTHER

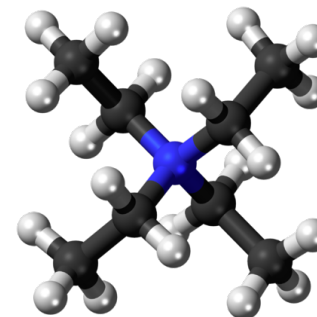
Example 1

- Building a chemical structure and analyzing its properties

Using ChemDraw or MarvinSketch to draw your 2D structure...



Tetraethylammonium (ligand)



...and convert it to a 3D structure....



Save as a 3D coordinate file
(.mol, .sdf, .pdb or similar)



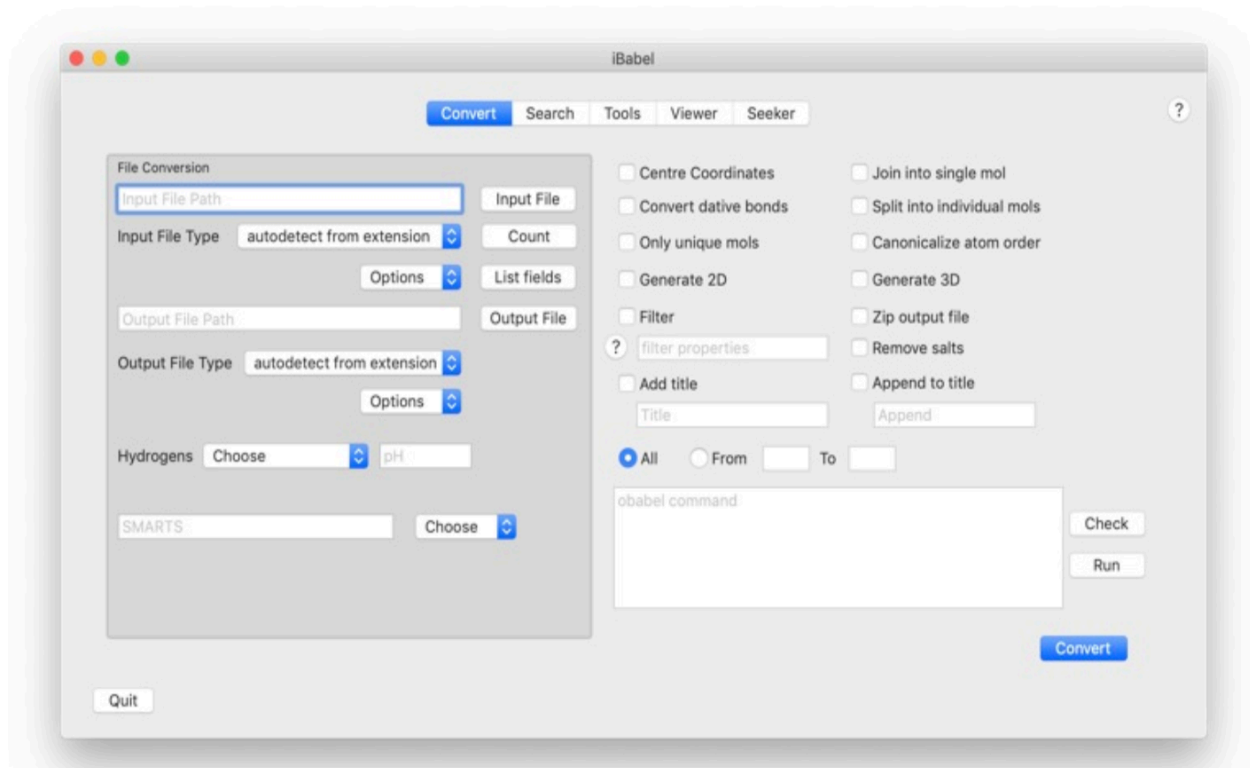
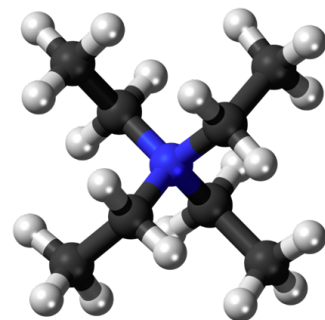
...run a conformational analysis to obtain
global minimum in gas phase...

Live DEMO of previous slide

Example 1

- Building a chemical structure and analyzing its properties

a) Use iBabel (https://www.macinchem.org/ibabel/version4/iBabel4_0.php) to convert 3D xyz file saved in MarvinSketch to .com input file for Gaussian software (Gaussian cartesian input):



Example 1

- Building a chemical structure and analyzing its properties

b) Make your own working directory:

```
mkdir "Yourname"
```

```
cd "Yournamedirectory" (change to your new directory)
```

```
ls
```

```
vi "yourfilename.mol" (open and edit your new file with VIM)
```

```
i (to edit text)
```

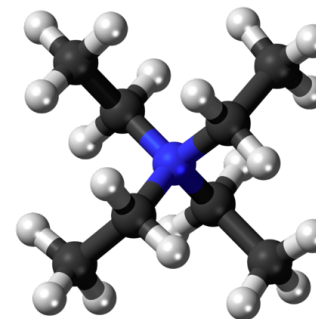
```
copy and paste the content of your 3D structure file (.mol)
```

```
esc (to stop edit mode)
```

```
:wq (save and exit)
```

```
babel -imol yourfilename.mol -ocom yourfilename.com
```

```
vi "yourfilename.com" (edit yourfilename.com)
```



Live DEMO of making Gaussian input files
from Marvin/Chemdraw 3D output (.mol)

Live DEMO of editing Gaussian input files to carry out different calculations:

- Editing checkpoint (%), routing (#) sections and charge and spin multiplicity
- Calculating charges (CHELPG, Hirshfeld, CM5)
- Single point calculations
- Geometry optimization
- Frontier orbital energy calculations (calculating the band gap)
- Frequency calculations for entropy and free energy calculations
- Implicit solvent effects (PCM and SMD models)

```
%chk=filename
# HF/3-21G* opt=z-matrix scf=tight nosymm ginput iop(6/7=3)

job 1

0,1
c
c
c 1 cc2
c 2 cc3 1 ccc3
c 3 cc4 2 ccc4 1 dih4
c 4 cc5 3 ccc5 2 dih5
c 5 cc6 4 ccc6 3 dih6
```

Example 1 – Calculating Charges/Single Point Calculations*

Name checkpoint (chk) file

```
%chk=test
#B3LYP/3-21G* pop=Hirshfeld SCF=tight int=Ultrafine freq
test
1 1
N      1.97510      -0.59920      -0.98240
C      1.53530      -1.92310      -0.35410
C      3.50010      -0.48250      -1.02120
C      1.44520      -0.54060      -2.41650
```

Theory

Basis set

Job name

Charge

Spin multiplicity

= $2S+1$ where S is total spin

*With no optimization keyword, Gaussian will run a single point calculation

pop keyword calculates charges specified by the option (in this case, Hirshfeld population analysis)
Various options for pop keyword found at
<http://gaussian.com/population/>

Example 1 – Geometry Optimization

- Same process as previous example but add opt keyword
- opt keyword optimizes structure to a local minimum

```
%chk=testOPT
#B3LYP/3-21G* opt=(tight,MaxCycle=100) pop=Hirshfeld SCF=tight int=Ultrafine freq

testOPT

1 1
N      1.97510      -0.59920      -0.98240
C      1.53530      -1.92310      -0.35410
C      3.50010      -0.48250      -1.02120
C      1.44520      -0.54060      -2.41650
C      1.41980       0.54930      -0.13770
```

Example 1 – Implicit Solvent Effects

- SCRF keyword preforms calculation in solvent
 - Gaussian has [common solvents](#) built in to define solvent environment
 - Solvent=[*Common Solvent Name*]
- Polarizable Continuum Model (PCM) or Solvent Density Model (SMD)
 - SMD model better when defining your own solvent
- Defining your own solvent
 - Solvent=Generic
 - Add dielectric constant
 - Add refractive index

Optimizing in common solvent

```
%chk=testOPT
#B3LYP/3-21G* opt=(CalcFC,tight,MaxCycle=100) pop=Hirshfeld SCF=tight
int=Ultrafine freq Guess=Read Geom=AllCheck SCRF=(SMD,Solvent=Ethanol)
~
```

```
%chk=IL4
# M062X/6-31++G(d,p) opt=(tight,MaxCycle=1000) SCF=tight guess=read
geom=AllCheck int=UltraFine freq SCRF=(SMD,Solvent=Generic,Read)
~
```

```
eps=36.47
epsinf=2.127
~
```

Troubleshooting

- *Sometimes adding dielectric constant helps even if using common solvent
- *Make sure there is a blank line at the end of file (this goes for all Gaussian inputs)

Optimizing when defining your own solvent

Running Jobs

- Run Gaussian jobs using “`rung16 filename.com &`”

```
[ox@harlequin samantha]$ rung16 example.com &  
[1] 37046  
[ox@harlequin samantha]$ jobs  
[1]  + Running                rung16 example.com  
[ox@harlequin samantha]$  
[1]  Done                    rung16 example.com  
[ox@harlequin samantha]$
```

Command to run Gaussian job

Job ID

“Jobs” command displays jobs that are currently running

Job will stop with “Done” if finished or “Exit 1” if terminated due to error

Analyzing Jobs

- *Vi filename.log*
 - Running input (com file) generates output (log file)
- Check for normal termination at bottom of file (Shift G)
 - This is also where error will be if there is not normal termination

```
LET US PLACE AT THE END OF EVERY CHAPTER.....THE
TWO LETTERS USED BY THE ROMAN JUDGES WHEN THEY DID
NOT UNDERSTAND A PLEADING.
N. L. -NON LIQUET- IT IS NOT CLEAR.
-- VOLTAIRE
Job cpu time:      0 days  0 hours  0 minutes  3.8 seconds.
Elapsed time:     0 days  0 hours  0 minutes  3.6 seconds.
File lengths (MBytes):  RWF=      6 Int=      0 D2E=      0 Chk=      1
Scr=              1
Normal termination of Gaussian 16 at Thu May 14 16:04:58 2020.
```

- Search for HOMO/LUMO values, charges, enthalpy, free energy, etc.
 - Search keywords with */word* [enter]

Analyzing Jobs (cont.)

- Finding enthalpy, free energy, etc
 - Scroll or search /therm [enter]
 - Units in hartrees
 - Convert to kcal/mol, eV, J, etc.
 - 1 Hartree = 627.509 kcal/mol
- Finding Charges
 - Scroll or search /Hirshfeld [enter]

```
Vibrational temperatures: 836.97 836.97 1863.45 3366.06
(Kelvin)

Zero-point correction= 0.010931 (Hartree/Particle)
Thermal correction to Energy= 0.013644
Thermal correction to Enthalpy= 0.014588
Thermal correction to Gibbs Free Energy= -0.009840
Sum of electronic and zero-point Energies= -187.512703
Sum of electronic and thermal Energies= -187.509990
Sum of electronic and thermal Enthalpies= -187.509046
Sum of electronic and thermal Free Energies= -187.533474
```

	E (Thermal) KCal/Mol	CV Cal/Mol-Kelvin	S Cal/Mol-Kelvin
Total	8.561	7.263	51.412
Electronic	0.000	0.000	0.000
Translational	0.889	2.981	37.270
Rotational	0.592	1.987	13.149
Vibrational	7.080	2.295	0.993
Vibration 1	0.938	1.071	0.482
Vibration 2	0.938	1.071	0.482

```
Hirshfeld charges, spin densities, dipoles, and CM5 charges using IRadAn= 5:
      Q-H      S-H      Dx      Dy      Dz      Q-CM5
1  C   0.321559  0.000000  0.000000  0.000000  0.000000  0.405886
2  O  -0.160780  0.000000 -0.000000 -0.000000 -0.166823 -0.202943
3  O  -0.160780  0.000000 -0.000000  0.000000  0.166823 -0.202943
Tot -0.000000  0.000000 -0.000000  0.000000  0.000000 -0.000000
```

```
Mulliken charges:
      1
1  C   0.819681
2  O  -0.409841
3  O  -0.409841
Sum of Mulliken charges = -0.000000
```

*Mulliken charges calculates automatically in Gaussian without pop keyword

Analyzing Jobs (cont.)

- Finding orbital energies

HOMO energy (hartrees)

Band gap

LUMO energy (hartrees)

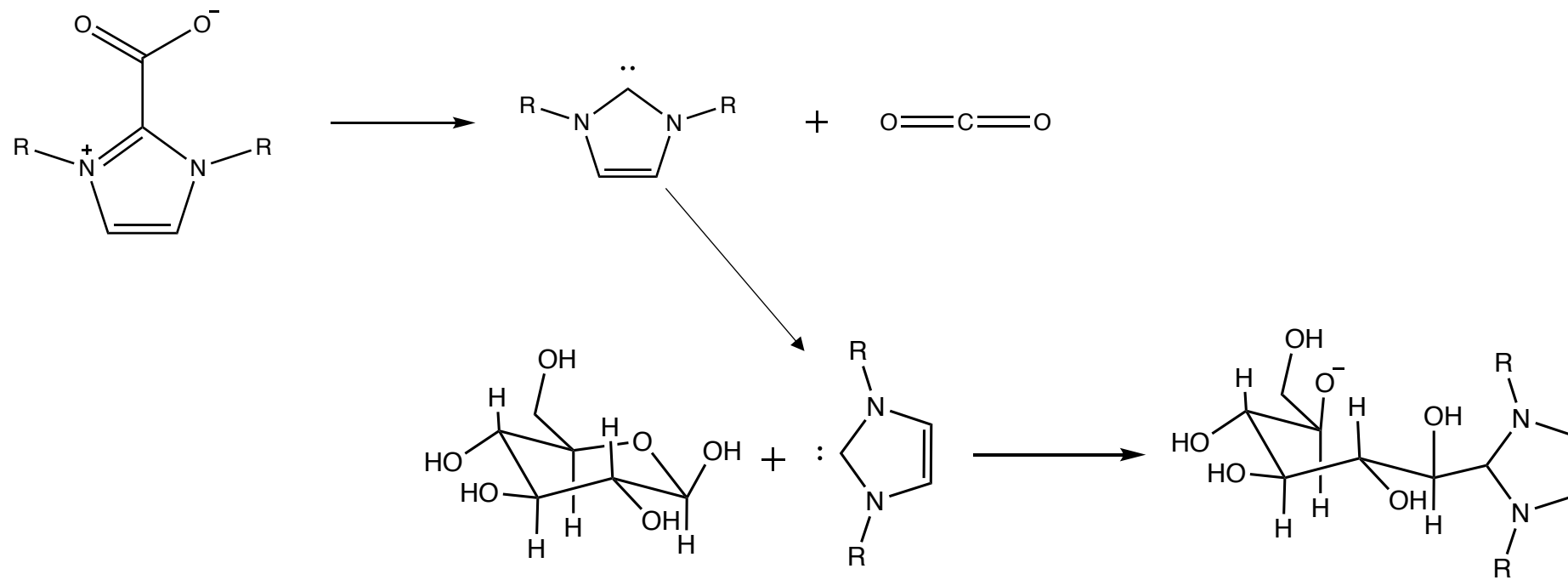
```
Framework group C1[X(C5H100)]
Deg. of freedom 42
Full point group C1 N0p 1
Rotational constants (GHZ): 15.0311875 1.2378469 1.2069508
*****
Population analysis using the SCF density.
*****
Alpha occ. eigenvalues -- -20.46232 -11.27374 -11.18082 -11.17962 -11.17356
Alpha occ. eigenvalues -- -11.16077 -1.40426 -1.09887 -1.02216 -0.90826
Alpha occ. eigenvalues -- -0.81463 -0.79557 -0.67807 -0.64918 -0.62332
Alpha occ. eigenvalues -- -0.60373 -0.58217 -0.54824 -0.52530 -0.50330
Alpha occ. eigenvalues -- -0.48458 -0.47959 -0.46982 -0.40447
Alpha virt. eigenvalues -- 0.16140 0.25466 0.28083 0.29430 0.30532
Alpha virt. eigenvalues -- 0.32835 0.34046 0.34875 0.36205 0.36649
Alpha virt. eigenvalues -- 0.36960 0.41349 0.42416 0.45026 0.51759
Alpha virt. eigenvalues -- 0.55573 0.88766 0.91178 0.93053 0.93893
Alpha virt. eigenvalues -- 0.95249 1.01149 1.03616 1.04468 1.06243
Alpha virt. eigenvalues -- 1.09205 1.14478 1.16234 1.21224 1.23767
Alpha virt. eigenvalues -- 1.26852 1.33569 1.36151 1.36849 1.38713
Alpha virt. eigenvalues -- 1.39162 1.42010 1.42892 1.44576 1.45767
Alpha virt. eigenvalues -- 1.63974 1.75448 1.90656 1.92998 1.96773
Alpha virt. eigenvalues -- 2.04069 2.19748 2.33672 2.64872 3.49712
Molecular Orbital Coefficients:
1 2 3 4 5
0 0 0 0 0
Eigenvalues -- -20.46232 -11.27374 -11.18082 -11.17962 -11.17356
1 1 C 1S 0.00004 -0.00024 -0.00715 -0.00494 -0.00770
2 2S 0.00019 -0.00021 -0.00162 -0.00145 -0.00312
```


Helpful VIM Commands

- Open file with command “vi filename”
- i (enters edit mode)
- [esc] (exits edit mode)
- :wq (saves and quits)
- :q (quits)
- [shift] g (skips to bottom of page)
- [ctrl] b (moves page up)
- [ctrl] f (moves page down)
- /*word* [enter] (searches document for *word*)
- n (moves to next searched *word* in document)

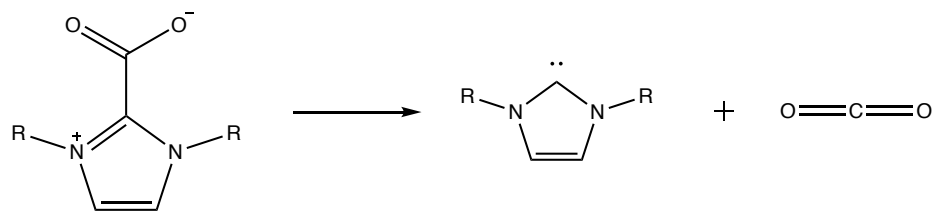
Example 2

- Analyzing a reaction pathway (to obtain rxn energetics and elucidate mechanisms)



Live DEMO of calculating enthalpies and free energies of reactants, intermediates and products to obtain overall energy changes in reaction pathways

Example 2 – Analyzing a Reaction Pathway



$$\Delta H_{rxn} = \sum \Delta H_{products} - \sum \Delta H_{reactants}$$

$$\Delta G_{rxn} = \sum \Delta G_{product} - \sum \Delta G_{reactants}$$

SUM fx `=(M28+M34)-M27`

	K	L	M	N
19	Gas Phase			
20	name	enthalpies(hartrees)	Enthalpy (kCal/mol)	dH kcal.mol
21	IL1	-1155.530459	-725105.7628	22.40269881
22	IL1carbene	-966.994154	-606797.5346	
23	IL2	-1111.918869	-697739.0976	12.65748404
24	IL2carbene	-923.398094	-579440.6146	
25	IL3	-1347.499881	-845568.3028	12.75349292
26	IL3carbene	-1158.978953	-727269.7238	
27	IL4	-493.065546	-309403.0677	M27
28	IL4carbene	-304.543266	-191103.6403	
29	IL5	-493.048366	-309392.2871	22.3744609
30	IL5carbene	-304.512106	-191084.0871	
31	IL6	-610.867432	-383324.8114	14.9278116
32	IL6carbene	-422.343039	-265024.0581	
33				
34	CO2	-188.500604	-118285.8255	

N27 fx `=(M28+M34)-M27`

	K	L	M	N
19	Gas Phase			
20	name	enthalpies(hartrees)	Enthalpy (kCal/mol)	dH kcal.mol
21	IL1	-1155.530459	-725105.7628	22.40269881
22	IL1carbene	-966.994154	-606797.5346	
23	IL2	-1111.918869	-697739.0976	12.65748404
24	IL2carbene	-923.398094	-579440.6146	
25	IL3	-1347.499881	-845568.3028	12.75349292
26	IL3carbene	-1158.978953	-727269.7238	
27	IL4	-493.065546	-309403.0677	13.60188508
28	IL4carbene	-304.543266	-191103.6403	
29	IL5	-493.048366	-309392.2871	22.3744609
30	IL5carbene	-304.512106	-191084.0871	
31	IL6	-610.867432	-383324.8114	14.9278116
32	IL6carbene	-422.343039	-265024.0581	
33				
34	CO2	-188.500604	-118285.8255	

Delta H values for proposed rxn w/ 6 different R-groups

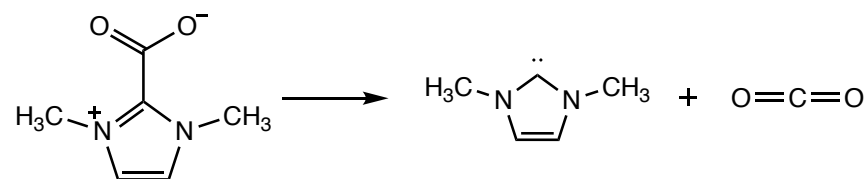
All extracted from log files of Gaussian jobs optimizing specified structure

Converted from hartrees to desired unit

Products - Reactants

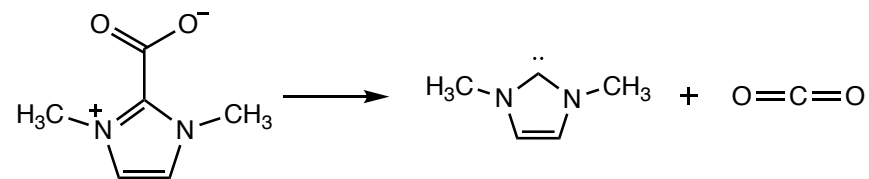
Example 2 – Analyzing a Reaction Pathway

*Comparing Solvents



In Ethanol

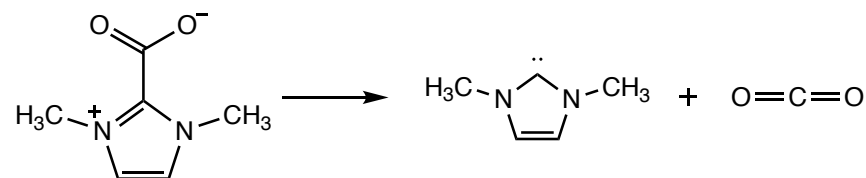
$\Delta H = 31.5$ kcal/mol



In Acetonitrile

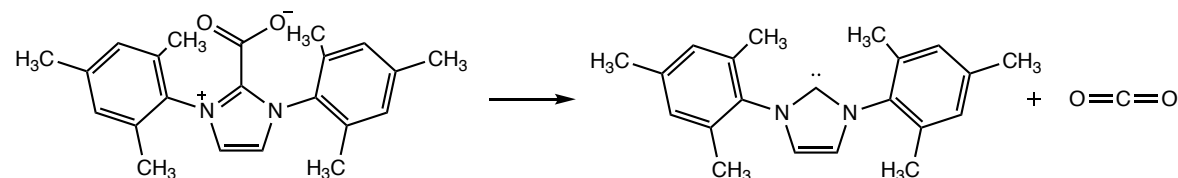
$\Delta H = 22.4$ kcal/mol

*Comparing R-Groups



In Ethanol

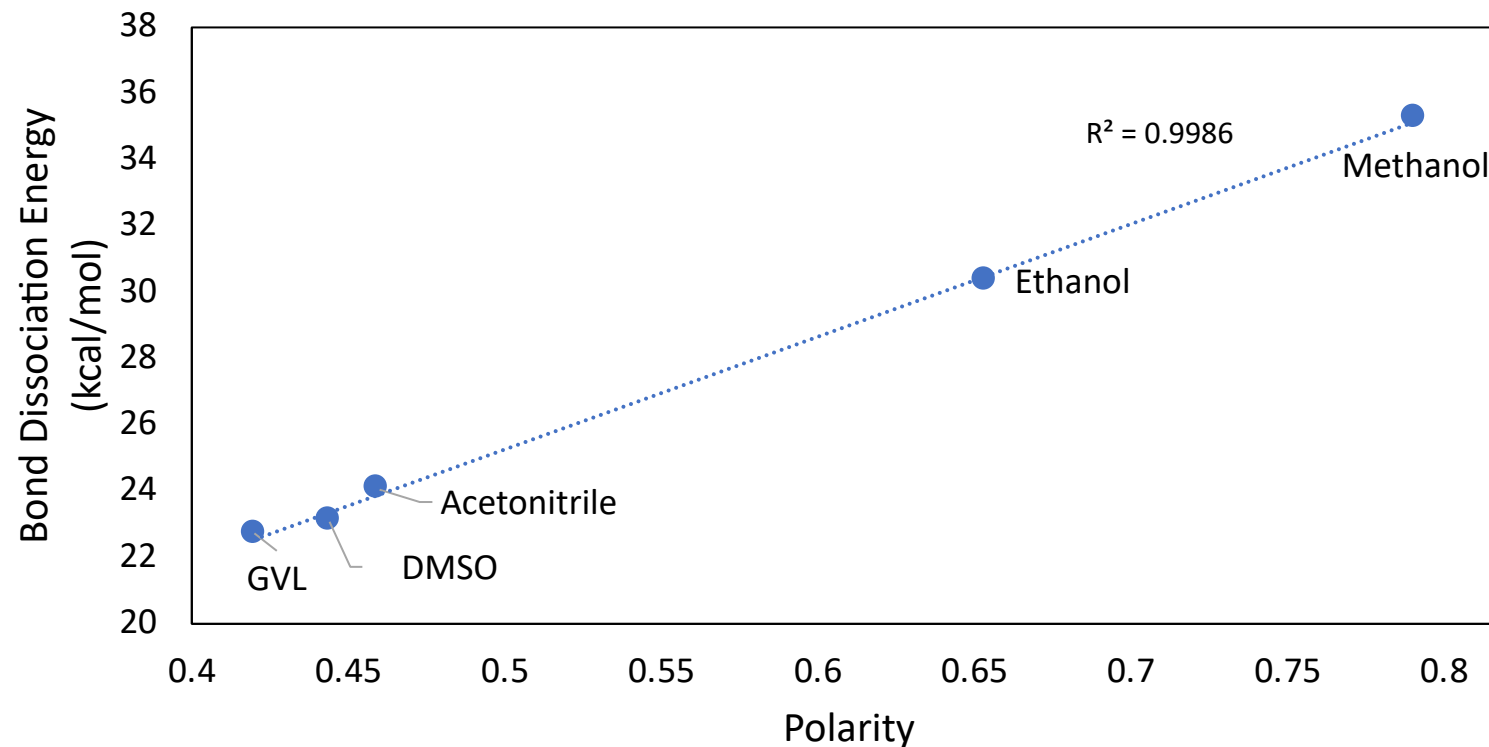
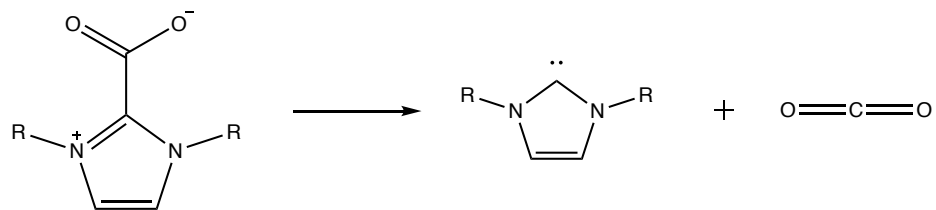
$\Delta H = 31.5$ kcal/mol



In Ethanol

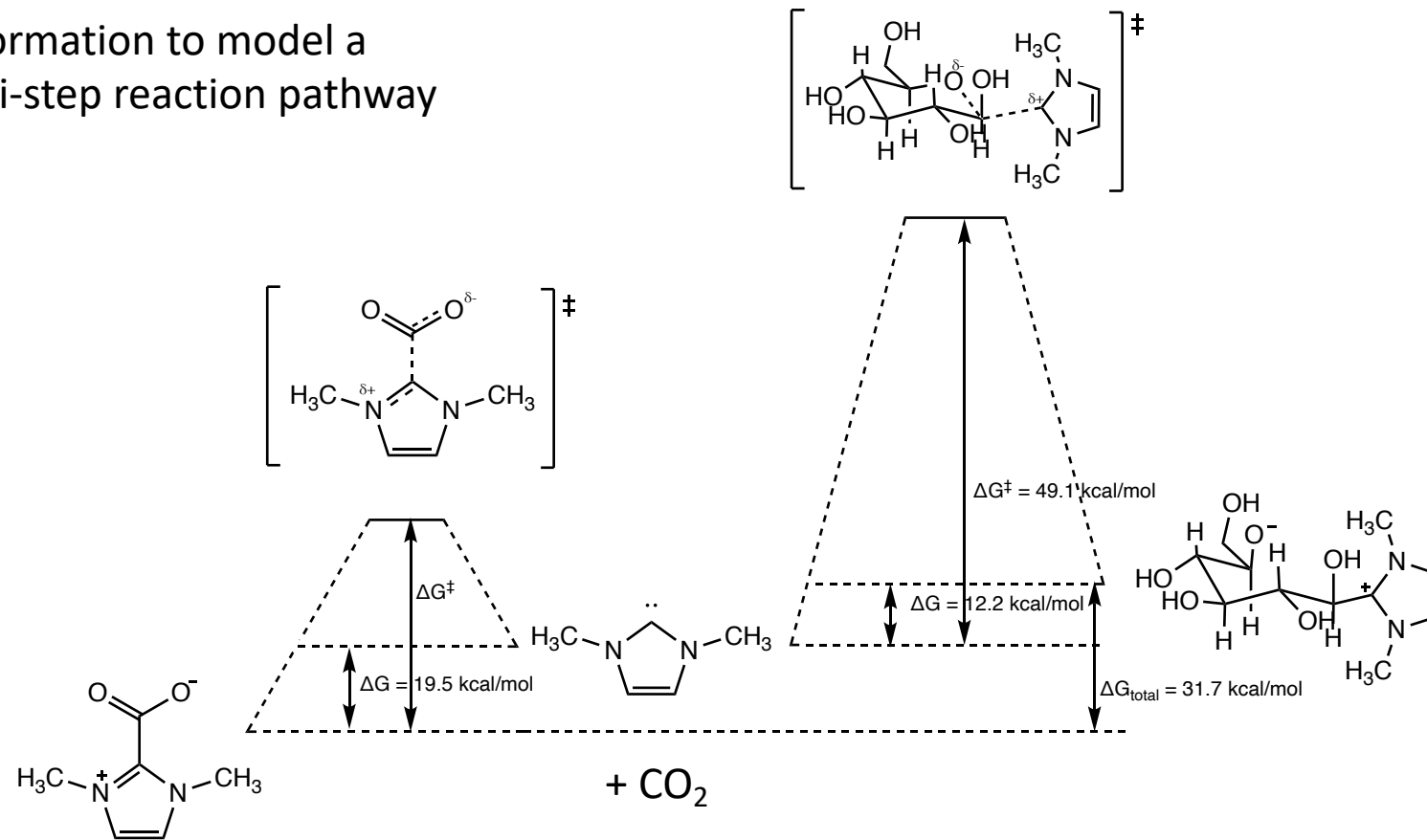
$\Delta H = 29.2$ kcal/mol

Example 2 – Analyzing a Reaction Pathway



Example 2 – Analyzing a Reaction Pathway

Combining information to model a proposed multi-step reaction pathway



Additional resources

- Gaussian manual: <https://gaussian.com/man/>
- Gaussian input keywords: <https://gaussian.com/keywords/>
- Thermochem in Gaussian: <https://gaussian.com/wp-content/uploads/dl/thermo.pdf> (with worked-out examples)
- Atomic charges: <https://gaussian.com/population/>
- Gaussian tutorials:
<https://barrett-group.mcgill.ca/tutorials/Gaussian%20tutorial.pdf>
https://www.tau.ac.il/~ephraim/Gaussian_manual.pdf
<https://www.msi.umn.edu/sites/default/files/IntroToGaussian09.pdf>
- GW VPN: <https://gwu-myit.onbmc.com/dwp/app/#/knowledge/KBA00001158/rkm>
- Implicit Solvation: Common Solvents
http://wild.life.nctu.edu.tw/~jsyu/compchem/g09/g09ur/k_scrf.htm