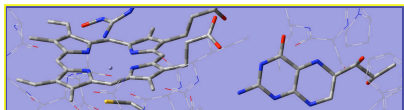


Computational Chemistry: A Practical Guide.

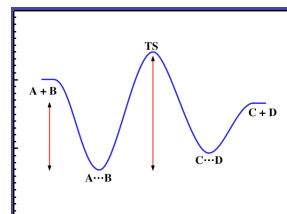


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Why use computational chemistry?

- In general, highly reactive or transient species are as straightforward to study as stable long-lived species.
- Can investigate and predict the properties and reactions of chemical systems.

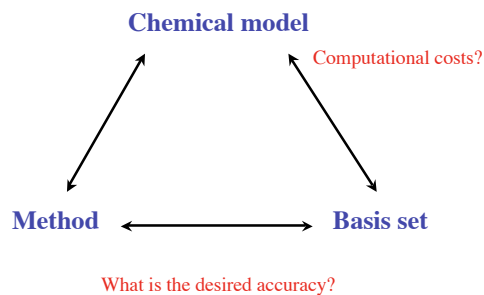


Designing a computational model:

cost versus accuracy

A computational model

What are we investigating?



Part 1: Chemical models

There are a number of things to keep in mind while choosing a chemical model. Two in particular are:

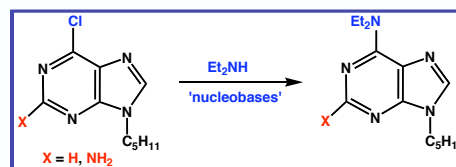
- Replicate or mimic the properties pertinent to the investigation.
- Suitably complete.

In addition, one should always remember, the larger the model, the more expensive the calculation. The largest increase is due to more 'heavy atoms', i.e., non-hydrogen atoms.

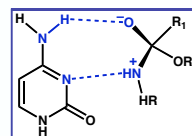
The following example illustrates how carefully choosing your model based on the 'real life' system, can still give reliable results.

However, it is always important to realize and accept any limitations introduced by the model finally used.

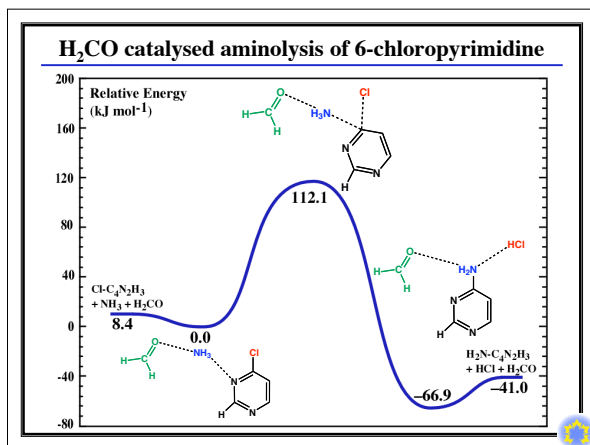
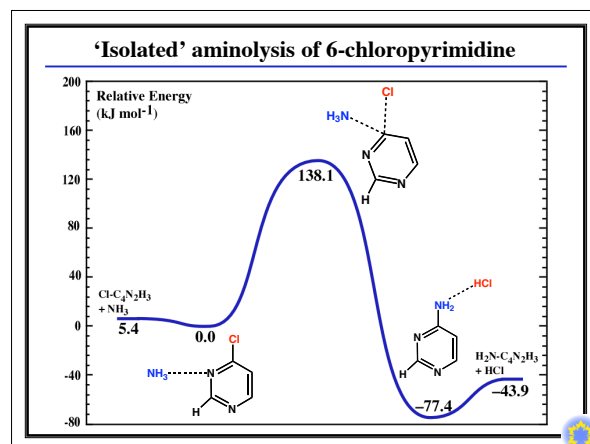
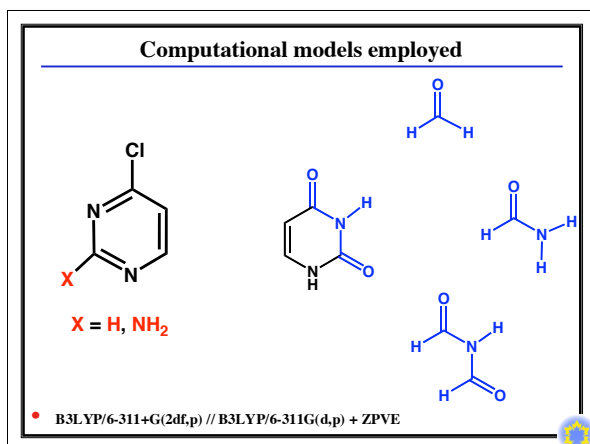
An example: aminolysis of 6-chloropurine



Tominaga, M. et al. *J. Am. Chem. Soc.* 1999, 121, 7704.



Melander, C.; Horne, D. A. *J. Org. Chem.* 1996, 61, 8344.



Barrier energies and proton affinities (kJ mol⁻¹)

Base	X = H	X = NH ₂	PA of Base
Isolated	138.1	159.0	—
OCH ₂	112.1	118.0	702.1
OHC-NH ₂	95.4	100.0	808.3
OHC-NH-CHO	100.8	110.5	789.9
1-methyluracil	95.4	103.8	861.5 (831.4)

Part 2: Basis Sets

- ... the set of functions used to describe the molecular orbitals or density.
- minimal:** only atomic orbitals that are occupied in the constituent atoms e.g., H: 1s ; C: 1s, 2s, 2p_x, 2p_y, 2p_z
- split-valence:** each valence atomic orbital of the constituent atoms is described by 2 or more functions
- polarized:** unoccupied higher-angular momentum atomic orbitals

Composition of a basis set

- Pople basis sets: modular.

Core Valence Polarization: heavy atoms

Diffuse Polarization: hydrogen

6-31+ G (d, p)

6-311+ G (d, p)

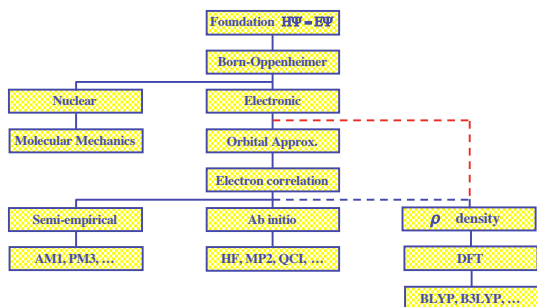
Choosing a basis set

- Interactions and types of reactions.
- *p*-functions on hydrogen:
hydrogen bonds
mechanisms involving H⁺ or H^{*} transfers
- diffuse (+) functions:
long range interactions
anions
cations
weakly bound states
- double-zeta (-31) versus triple-zeta (-311):
increased flexibility of the valence electrons
heavy atom—heavy atom bond making and breaking mechanisms

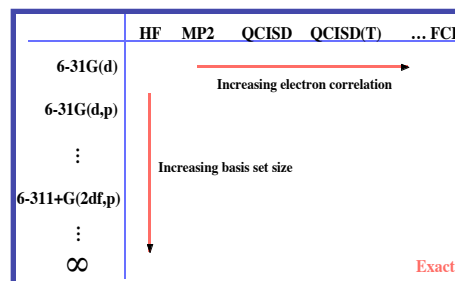
Part 3: theoretical method

- the method chosen to describe how the electrons and their interactions will be treated.
- Molecular mechanics (MM).
- Semi-empirical.
- Ab initio (conventional).
- Density functional theory (DFT).

A general map ...



Ab initio: a hierarchy of methods

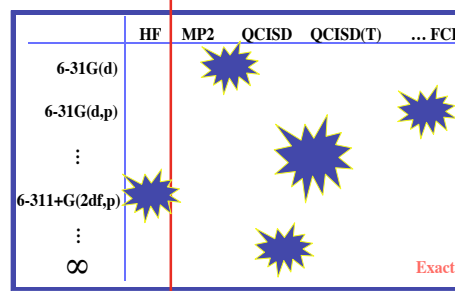


Density functional theory (DFT) methods

- Functional: a function of a function.
- $$E[\rho]$$
- $$E_{\text{exact}}[\rho] = E^T[\rho] + E^V[\rho] + E^J[\rho] + E^{\text{XC}}[\rho]$$
- Functional is composed of 'exchange' and 'correlation' components.
 - Modular.

BLYP
B3LYP
B3P86

Comparison of DFT



What do I do if my 'method/basis set' fails?

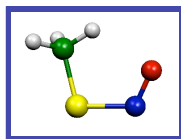
- If your method/basis set choice fails to accurately and/or reliably describe the system being investigated, there are several things one can do ...
- **Ab initio methods.**
For ab initio methods there are several things one can try, including:
(i) changing the basis set,
(ii) increasing the method slightly, e.g., if MP2 fails, try MP3 or QCISD.
- **DFT methods.**
For DFT methods, the options are little more limited. All one can simply try is:
(i) changing the basis set.
- It should be noted that another option that is sometimes possible is to alter the chemical model being used.

Accurate and reliable structures:

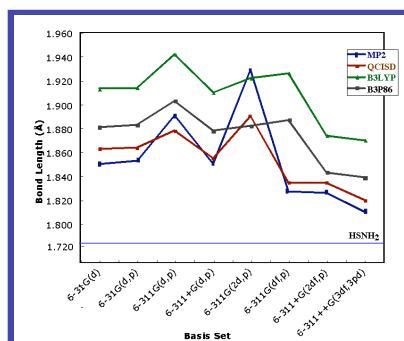
S-nitrosothiols (RSNOs)

Performance of basis sets: an example

- Bond lengths: $\pm 0.01 \text{ \AA}$; Angles: $\pm 1 - 2^\circ$; Dihedrals: $\pm 5^\circ$
- **RSNOs:**
proposed: the S—N bond has considerable double-bond character
previous studies: 3-21G, 6-31G(d)
optimized bond lengths for some species: $1.75 \text{ \AA} - 2.05 \text{ \AA}$



Optimized S—N Bond Lengths for *trans*-HSNO



Some key points: methods and basis sets

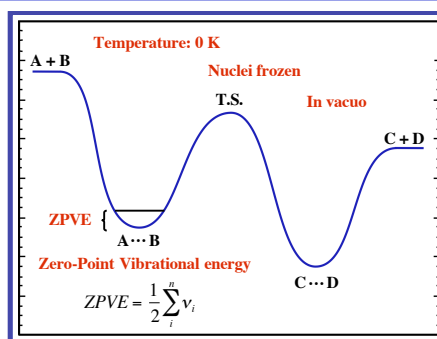
- Choose appropriate basis sets.
Try more than one basis set.
- Use chemical intuition: both in design and interpretation.
- **DFT:** try more than one method.
- **DFT:** tends to give looser transition structures
MP2: tends to overestimate effects of electron correlation; bonds too long, complexes too tight.

Potential energy surfaces (PESs)

Optimized geometries of chemical interest

- **Stationary points:** chemically important structures
 - local minima: correspond to equilibrium structures
 - first-order saddle points: correspond to transition structures
- **Minima:** have all real frequencies.
- **Transition structures (T.S.):** have exactly one imaginary frequency. Corresponds to the reaction coordinate.

Schematic maps of the energy



Reliable relative energies:

Single points and compound methods

Reliable structures vs. Accurate energies

- Chemical accuracy: $\pm 10 \text{ kJ mol}^{-1}$

	HF	MP2	QCISD	QCISD(T)	... FCI
6-31G(d)					
6-31G(d,p)					
⋮					
6-311+G(2df,p)					
⋮					
∞					Exact

Structures (circled in red)
Energies (circled in blue)

S.P.'s: terminology and assumptions

A single point, energy only, calculation performed at ...

Method 1/Basis set 1 // Method 2/Basis set 2

Geometry optimized at ...

MP2/6-311+G(2df,p) // B3LYP/6-31G(d,p)

- **Assumptions:**
method 2/basis set 2 gives structures in close agreement with what would be obtained at method 1/basis set 1

Compound methods

- **Basis set effects:**
generally additive

$$\left. \begin{aligned} E[6-31G(d,p)] - E[6-311G(d,p)] \\ E[6-31G(d,p)] - E[6-31+G(d,p)] \end{aligned} \right\} \approx E[6-31G(d,p)] - E[6-311+G(d,p)]$$

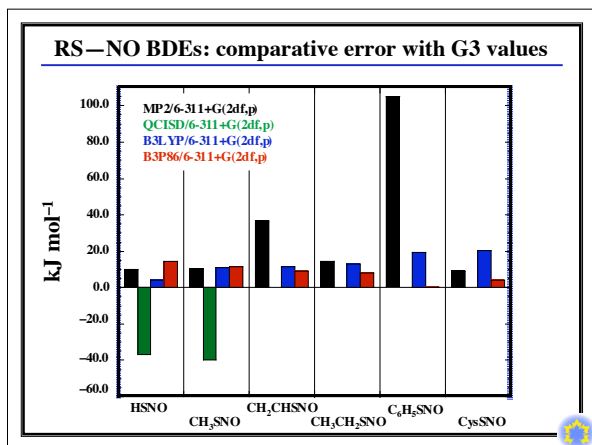
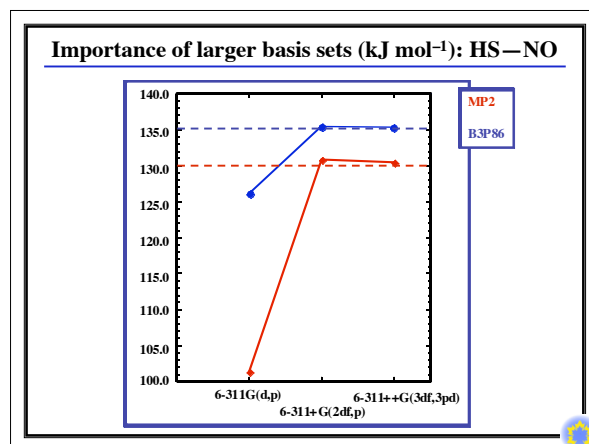
- GX, CBS-X ...
- G3: additional corrections give best fit to a set of highly accurate data

Automation of compound methods: GX

- First step: HF/6-31G(d) optimization and frequency
- Second step: MP2/6-31G(d) optimization starts from HF/6-31G(d) optimized structure **no frequencies calculated** at the MP2/6-31G(d) level
- All additional steps: use the MP2/6-31G(d) optimized structure

conventional hemi-bonded distonic

MP2/6-31G(d): all exist HF/6-31G(d): hemi-bonded do not exist



Spin contamination

- S(S + 1)
 Closed-shell (singlet): 0.000
 Radical (doublet): 0.750
 Biradical (triplet): 2.000
- Contributions from higher excited states, e.g., quartets etc.

Restricted (R) Unrestricted (U) Restricted-open (RO)

Some key points

- Large basis sets - more reliable and accurate energies
 Single points: cheaper, yet usually reliable.
- Use chemical intuition: both in design and interpretation.
- DFT: barrier heights too low.
 MP2: barrier heights too high.
- Automated G3 etc.: use with care.

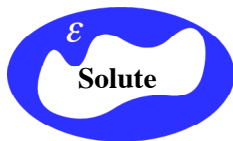
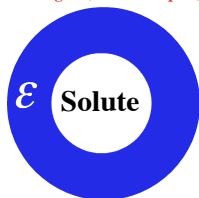
Accounting for environmental effects

Two approaches

- Explicit inclusion of environment molecules.
– can be expensive.
- General environment effects: included using a ‘solvation’ method.

Onsager (SCRF = Dipole)

Fitted, e.g., density



- Note: the SCRF method is the most robust, but the simplest.

Useful resources

- Computational chemistry. A practical guide for applying techniques to real world problems.
David Young (Wiley Interscience)
- Exploring chemistry with electronic structure methods.
James Foresman and Aileen Frisch (Gaussian Inc.)
- Your local friendly computational chemist.

Summary

- Computational chemistry: useful complementary tool.
- Chemical model, computational method and basis set:
cost versus accuracy.
- Keep in mind the chemistry being investigated.
- Give it a go.