Computational Chemistry for Synthetic Chemists

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What is Computational Chemistry?



What is Computational Chemistry?

- Molecular electronic structure methods
- Molecular mechanics/dynamics
- Theoretical quantum chemistry and method development
- Quantitative structure-activity relationships
- Data analysis and extraction

Electronic Structure Theory

 $H_{elec}\{\underline{R}\}\Psi_{elec}\{r,\underline{R}\} = E_{elec}\{\underline{R}\}\Psi_{elec}\{r,\underline{R}\}$



What can be calculated?

- Wavefunction
- Energy inc. thermochemistry
- Structure
- Properties (spectroscopy etc.)
- Reaction mechanisms
- Rate constants
- Pretty much anything...





Predicting Geometries - 2



Roughly n steps



How does it work?

- Analytical solutions: H, H₂⁺
- Exact solutions: 2-electron systems (He, Li⁺, H₂)
- Approximations needed: almost anything else!
- Molecular orbital approximation:

$$\Psi_{\mathsf{approx}}(r_1, r_2, \dots r_n) = \prod_{i=1}^n \psi_i(r_i)$$

Hartree-Fock Method



Molecular Orbitals



Orbitals can give insight into bonding and reactivity...

But they are not physically observable and different calculations can lead to different conclusions.



Basis Sets - Gaussian functions



Basis Sets - Gaussian functions



Basis Sets - Orbital size





H–F H 1s: 1 * 'tight' + 1 * 'medium' + 0.45 * 'loose'

Li–H H 1s: 0.6 * 'tight' + 1 * 'medium' + 0.9 * 'loose'

Basis Sets - Polarisation



Basis Sets - Summary

- Gaussian 'primitives'
- Contracted Gaussian functions = fixed combination of primitives
- Minimal basis = 1 contracted (or primitive) Gaussian per occupied atomic orbital
- Double–ζ (double zeta): 2 Gaussians per occ. AO
- Split-valence: 1 Gaussian per core AO, 2 per valence AO
- Triple zeta: 3 Gaussians per (valence) AO
- Exponents optimized for neutral atoms: additional diffuse functions sometimes needed
- Polarisation functions (*dfgh* for C, N, O, Cl, ... *pdf* for H)

Basis Sets - Heavy atoms

- Core orbitals do not change much with environment
- There can be many core electrons (e.g. U !!)
- Relativistic Effects are very important

$$m_{e} = m_{e,0} \frac{1}{\sqrt{1 - \frac{v^{2}}{c^{2}}}}$$

- Use Effective core potential (ECP)
- Can be Relativistic ECP

Some examples

- **3-21G basis (Pople):**
 - Core orbitals = contracted from 3 Gaussians
 - Split valence. 1 tight function, contracted from 2 Gaussians.
 - 1 looser function, uncontracted
- 6-31G (Pople):
 - Same but 6, 3 primitives
- 6-31G(d) or 6-31G*
 - Identical to 6-31G but 1 d polarisation func on non-H atoms
- 6-31G(d,p) or 6-31G**
 - As 6-31G* but 1 *p* func on H atoms
- 6-311++G(2df,p)
 - Valence triple zeta, diffuse funcs on all atoms, + polarisation
- **aug-cc-pVDZ** similar to 6-31++G(d,p)
- aug-cc-pVQZ large!

Hartree-Fock is not exact

• Electron correlation:



as likely as



- Small effect in absolute terms HF electronic energies within 1% of exact result
- But large in relative terms can *easily* contribute 100 kJ/mol to a bond energy
- In practice, Hartree-Fock is seldom used!
- Correlated methods: MP2, CCSD(T) (can be quite expensive)
- More advanced methods (for experts)

Density Functional Theory

- $E[\rho]$ instead of $E[\Psi]$
- ρ is much more simple (function of three variables) than Ψ (function of $3*n_{el}$ variables)
- In principle, exact: all properties of system can be derived from density (Intuitive proof of HK1)
- In practice, exact DFT functional is not known
- Some functionals give very good results: BP86, BLYP, B3LYP
- Similar cost to HF
- Similar set-up and solutions: MOs, basis sets, programs

Errors in Computational Chemistry

- *All* calculations involve approximations: it is *always* necessary to wonder how accurate a result is
- Most methods give very good geometries
- Bond stretching, bending = stiff; some torsions = soft
- HF method gives poor energies
- For a very similar cost, DFT is very accurate
- E.g. with a TZ+P basis, estimated accuracy on bond energy of 10-20 kJ/mol with BLYP, B3LYP.
- Much of this error is systematic: error cancellation

Errors in Computational Chemistry

Level	E(H)	E(CH ₃)	$E(CH_4)$	BDE(CH ₃ –H)
HF/cc-pVDZ	-0.499278	-39.559639	-40.198711	367.0
BP86/cc-pVDZ	-0.498943	-39.834069	-40.512477	471.2
B3LYP/cc-pVDZ	-0.497858	-39.805323	-40.480369	465.2
MP2/cc-pVDZ	-0.499278	-39.690646	-40.360173	447.0
CCSD(T)/cc-pVDZ	-0.499278	-39.716189	-40.387597	451.9
CCSD(T)/cc-pVTZ	-0.499809	-39.760548	-40.437786	465.8
CCSD(T)/cc-pCVTZ	-0.499809	-39.811080	-40.488591	466.6
CCSD(T)/cc-pVQZ	-0.499945	-39.771956	-40.450511	468.9

Applications. (a) Structure

3-Ethynylcyclopropene: a highly suspicious crystal structure

Steven S. Wesolowski, Jason M. Gonzales, Paul v. R. Schleyer and Henry F. Schaefer III*

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Chem. Commun., 1999, 439–440 439

Baldridge *et al.* recently reported an X-ray crystal structure for 3-ethynylcyclopropene **1** in which the 'curiously short' 1.255 Å double bond is 'the shortest crystallographically observed C=C double bond known in any hydrocarbon.'¹ Their computed



Fig. 1 The structure of 3-ethynylcyclopropene **1** optimized at the TZ2P + f/ CCSD(T) level of theory. Bond lengths are in Å and bond angles are in degrees. Experimental bond lengths and angles are given in brackets.

Chem. Commun., 1999, 439–440 439

Method	$d_{\mathbf{C}=\mathbf{C}}/\mathbf{\hat{A}}$	$d_{\mathbf{C}=\mathbf{C}}/\mathbf{\hat{A}}$
DZP/RHF	1.2841	1.1973
TZ2P + f/RHF	1.2691	1.1840
DZP/BHLYP	1.2904	1.2066
DZP/B3PW91	1.3047	1.2200
DZP/B3LYP	1.3058	1.2207
DZP/MP2	1.3216	1.2387
DZP/CCSD	1.3168	1.2288
DZP/CCSD(T)	1.3233	1.2353
TZ2P/MP2	1.2957	1.2151
TZ2P/CCSD(T)	1.2981	1.2122
TZ2P + f/MP2	1.2939	1.2146
TZ2P(f,d)/MP2	1.2942	1.2145
(cc-pVQZ/TZ)/MP2	1.2899	1.2112
TZ2P + f/CCSD(T) Experiment	1.2957 1.255(2)	1.2112 1.184(2)

Applications. (b) Electronic Structure

The seventeen- and eighteen-electron metallacarbaboranes $[1,1,1-(CO)_3-2-Ph-closo-1,2-MnCB_9H_9]^{n-}$ (n = 1, 2): a structurally characterized, redox-related pair

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Unpaired electron is delocalised





Isolating Benzenium Ion Salts

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cation	C ₁ –C ₂ C ₁ –C ₆	C ₂ C ₃ C ₅ C ₆	C ₃ C ₄ C ₄ C ₅	C ₆ – C ₁ –C ₂
benzenium (calcd)	1.473 ^b	1.373	1.413	117.0
	1.461 ^c	1.366	1.406	117.4.0
benzenium (exptl)	1.381(6)	1.345(6)	1.391(6)	119.8(3)
	1.391(6)	1.345(6)	1.381(6)	
toluenium	1.451(8)	1.336(8)	1.394(7)	116.0(5)
	1.448(8)	1.334(8)	1.409(7)	
<i>m</i> -xylenium	1.429(6)	1.376(6)	1.382(6)	119.2(5)
	1.400(8)	1.377(7)	1.427(6)	
mesitylenium	1.414(12)	1.384(11)	1.370(10)	120.6(8)
	1.425(12)	1.387(11)	1.380(10)	

Table 1. Selected Bond Lengths and Angles for Chemically Equivalent Bonds in Arenium Ic



. Frequencies of the C₆H₇⁺ Ion as a Function of Counterie

counterion (or complex)	ν(CH ₂) (average)
none (calcd)	2854, 2850 (2853)
CH ₃ Br (calcd)	2852, 2775 (2813)
N_2^b	2809, 2792, (2801)
$CB_{11}H_6Cl_6^-$	2770, 2720 (2745)
$CB_{11}H_6Br_6^-$	2757, 2714 (2736)
$CB_{11}H_6I_6^-$	2746, 2696 (2721)
$CB_{11}HMe_5Br_6^-$	2700, 2672 (<i>2686</i>), 2785 ^d
CB ₁₁ HMe ₅ Br ₆ ⁻	(2043, 1981) ^e

Table 3. Comparison of Solid-State and Solution ¹³C NMR Spectra of Arenium lons

ion	state	temp (°C)	C_1	C_2	C_3	C_4	C_5	
benzenium ^a	crystalline	-120	52	184	136	176	136	18
benzenium ^b	HSO ₃ /SbF ₅ /SO ₂ ClF	-135	52.2	186.6	136.9	178.1	136.9	18
benzenium ^c	HBr/AlBr ₃ /surface	-195	53	185	138	178	138	18
toluenium ^d	crystalline	25	45	179	126	203	126	1′
toluenium ^d	crystalline	-70	47	180	139	208	139	18
toluenium ^e	HSO ₃ F/SbF ₅	-80	46.7	178.6	138.5	201.0	138.5	1′
\square um ^c	HBr/AlBr ₃ /surface	-195	49	179	139	200	139	1′



Calc: (JNH) C1: 60; C2: 201; C3: 149; C4: 190 B3LYP/6-311G(d)

Applications. (d) Reactivity



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Compound	$k_{\rm exp}/{\rm cm}^3 {\rm \ molecule}^{-1} {\rm \ s}^{-1a}$	$k_{\rm TST}/k_{\rm exp}$	
Methane	6.4×10^{-15}	0.58	
Ethane	$2.4 imes 10^{-13}$	1.0	
Propane	1.1×10^{-12}	1.1	
Cyclobutane	2.03×10^{-12b}	1.7	
Acetone	$1.7 imes 10^{-13}$	0.35	
		$\sim TS - E_{\circ}$	

 $k = \frac{k_B T}{h} \frac{Q^{\mathrm{TS}}}{Q_{\mathrm{R}}} \times e^{-\frac{E_0}{k_B T}}$

A computational study of the atmospheric oxidation of nopinone

Peter J. Lewis,[†] Katherine A. Bennett and Jeremy N. Harvey^{*}

Phys. Chem. Chem. Phys., 2005, 7, 1643-1649

Applications. (d) Reactivity



Applications. (e) Solvation effects



Applications. (e) Solvation effects







Applications: (e) Reactivity in solution

Unraveling the Mechanism of Epoxide Formation from Sulfur Ylides and Aldehydes

Varinder K. Aggarwal,* Jeremy N. Harvey,* and Jeffery Richardson

J. AM. CHEM. SOC. 2002, 124, 5747-5756





B3LYP/6-311+G**//B3LYP/6-31G*(CH₃CN)



