

ISTCP 2024

Sunday 13th October 2024 Qingdao Huanghai Hotel





IQMOL is an open-source molecular editor and visualization package which runs under Windows, Mac OS X and Linux.

- Wide range of chemical file formats supported
- Free-form molecular builder:
 - Structure optimization using MM
 - Symmetrization of structures
 - Built-in library of molecules
- Analysis features:
 - Animations: reaction pathways and vibrational frequencies
 - Surface plots: MOs and (spin) densities
 - Surface properties: ESP and cube data



IQMOL is a standalone program, but has been optimized to work best in a Q-CHEM work flow:

- Building structures
- Generating Q-Снем input
- Submitting Q-CHEM calculations
- Visualizing results

This is due to several Q-CHEM specific features:

- ► Comprehensive Q-CHEM input file generator
- Embedded Q-CHEM keyword documentation
- Submission of Q-CHEM jobs to local and cloud servers including PBS, SGE and Web-based





Binary packages for IQMOL can be freely downloaded from:

iqmol.org/downloads.html

The Q-CHEM manual is available online via:

manual.q-chem.com

Video resources are available on Q-CHEM's YouTube page:

- ► IQMOL introduction
- Advanced IQMOL usage
- Checkout Q-CHEM's entire webinar series







2-Fluoroethanol









Indole

iso-Indole

- **1.** Build structures for indole and iso-indole. Cleanup your strutures using molecular mechanics and symmetrize.
- 2. Run HF/STO-3G energy calculations to obtain the MOs.
- **3.** Plot the HOMO of each molecule and predict which isomer is the more stable (hint: consider the nodal structure).
- 4. Optimize each structure using HF/6-31G and determine the energy difference. Was your prediction correct?



Indole has fewer nodes and is more stable.





Indole -361.337412 E_h iso-Indole -361.315424 E_h

 $\Delta E = 58$ kJ/mol @ HF/6-31G



In 1952 Kenichi Fukui published his Frontier Molecular Orbital (FMO) theory which provides a qualitative approximation for determining reactivity.

Electrophilic attack is favoured where the HOMO density is largest.





Exercise — Electrophilic Attack







Aniline

Benzoic Acid

Fluorobenzene

- **1.** Build structures for all three systems.
- 2. Run HF/6-31G energy calculations.
- **3.** For each molecule, plot the HOMO and predict whether the NO₂⁺ electrophile is ortho, meta or para directing.
 - ► Hint: increase the surface isovalue to make it clearer where the density is larger.



Results— Electrophilic Attack







Benzoic Acid Ortho 🖌

Meta 🖌 Para X



Fluorobenzene

Ortho 🖌 Meta X Para V

Steric hindrance also plays a role.



Vibrational frequencies can be computed within the harmonic approximation.

 $\hat{\rm V}_{\rm eff}(\textbf{R}) = \textit{V}(\textbf{R}_0) + \textit{V}'(\textbf{R}_0)(\textbf{R}-\textbf{R}_0) + \textit{V}''(\textbf{R}_0)(\textbf{R}-\textbf{R}_0)^2 + \dots$



Meaningful frequencies must be computed at an energy minimum obtained at the same level of theory.











Benzoquinone exists in two isomeric forms:



o-Benzoquinone



p-Benzoquinone

- 1. Optimize both structures at the B3LYP/6-31G* level.
- 2. Compute the harmonic frequencies at the same level.
- **3.** Identify the most intense band for each isomer.
- 4. Characterize the mode that gives the key difference between the isomers.



The following IR spectrum of benzoquinone was obtained from the NIST website:



To which isomer does this spectrum correspond?



- The most intense bands both occur at 1757 cm⁻¹ and correspond to the symmetric (o-benzoquinone) and asymmetric (p-benzoquinone) C=O stretches.
- The out-of-plane wag of o-benzoquinone (742 cm⁻¹) is intense. The corresponding mode in p-benzoquinone is IR silent.
- ► The NIST spectrum is that of p-benzoquinone.







Traditional DFT methods are unsuitable for non-covalent interactions due to the absence of long-range electron correlation.



RMSD over 1744 non-covalent dimers.

Empirical Dispersion corrections, such as Grimme's DFT-D approach, significantly improve DFT calculations.



The D3 correction to KS-DFT relies only on the relative positions of the nuclei:

$$E_{\mathrm{D3}} = -\sum_{A < B}^{\mathrm{atoms}} \sum_{n=6,8} s_n \frac{C_{n,AB}}{R_{AB}^n} f_n(R_{AB})$$

 f_n are damping functions and give rise to the principle differences between the various flavours of D3 corrections.

These are controlled by the DFT_D rem variable:

- D3_ZERO: the original zero damping
- ► D3_BJ: the Becke-Johnson damping
- D3_OP: the 'optimal power' damping by Witte et al.



Basis set superposition error (BSSE) arises from the inconsistent treatment of the monomers and super-system:

$$E_{\text{int}} = E(AB) - E(A) - E(B)$$

The dimer is over-stabilised, leading to over-binding.

- ► For non-covalent interactions def2-QZVPPD roughly represents the CBS limit.
- The performance of aug-triple- ζ (def2-TZVPPD) is close.
- The use of smaller basis sets (e.g. def2-SVPD) can introduce much larger BSSE errors.





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		Setup Advanced	Generated Input Charge and multiplicity
Job Section	Job 1	🖯 Edit 🌸 💻	a 1
Calculate	BSSE Correction	Charge 0 🗘	0 1,7784891
Method E	33LYP	Multiplicity 1 0	0 1 0 -1.75411 0.4298492 -0.1167944
Basis d	ief2-spvd	ECP None	B = -0.3447 0.4652903 0.0005999 B = -1.8949155 0.7343043 Set.d
Exchange		Manually edit Basis to def2-spvd	Manually separa frem Mors = def2-epret frgments with — and add charge
SCF Control			METHOD = POSTY Second Conversion
Algorithm	DIIS	Convergence	Add dispersion from
Guess	SAD	Max Cycles 50 0	the Advanced panel
Second Basi	is None	Guess Mix 0 %	
Unrestric	ted	Dual Basis Energy	
Open-shi	_SCEMAN ell Singlet ROSCE	Generalized Hartree-Fock	
Complex	SCF	Complex Mix 0 %	
			Server Q-Chem G Subm
Wavefunction	Analysis		Reset Disable Controls Cance

You will need to manually edit the fragments in the generated input panel.



Exercise — Water Dimer



- 1. Optimize the structure of the water dimer using BLYP-D3(0) and the def2-SVPD basis.
 - ► Use the MMFF94 forcefield to pre-optimize your structure.
 - ► BASIS=def2-SVPD will need to be manually edited.
 - The checkpoint file should be turned off with GUI=0
 - ► The D3(0) correction can be found in the Advanced panel.
- 2. What length do you get for the hydrogen bond?
- 3. Compute the interaction energy your equilibrium structure using the same level of theory.
 - ► **Use** JOB_TYPE=BSSE
 - You will need to edit the fragments in the QUI panel.
- 4. How does the D3(0) correction affect your results?



Energy decomposition analysis (EDA) can be used to breakdown the binding energy in to physically interpretable components:

- Frozen density (no relaxation)
- Polarization (intrafragment relaxation)
- Charge transfer (interfragment relaxation)
- 1. Use the EDA to determine the breakdown of the binding energy of the water dimer.
- 2. Which component contributes the most to the binding energy?

Note: You will need to specify the separate fragments in the same way as for the BSSE calculation.



Indicative results (depending on initial geometry).

	Units	w/ D3	w/o d3
Hydrogen bond-length	Å	1.9261	1.9353
Binding energy	kJ/mol	-24.491	-21.471
Binding energy (CP)	kJ/mol	-22.589	-19.563
Frozen	kJ/mol	-8.956	-6.315
Dispersion	kJ/mol	-8.153	-4.950
Polarization	kJ/mol	-5.071	-4.944
Charge transfer	kJ/mol	-10.464	-10.212

The bond-length is less effected by dispersion than the energies. Charge transfer gives rise to the largest contribution to binding.