Computational NMR spectroscopy with quantum chemistry - A tutorial

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Studies

Born-Oppenheimer approximation

- The most important approximation in chemistry.

- Allows us to think of a molecule as an entity with a structure.

- Then, for a given structure one can study different properties.

- If the property of interest is the total energy (E), plotting E as a function of structural parameters (bond length, angles, etc.) gives us *potential energy curves/potential energy hypersurfaces*.

- Typically, what we call as a molecule corresponds to a minimum on the potential energy surface.

- For applications involving a finite temperature effects, we can Boltzmann-weigh over different minima (*e.g.* conformers).

P. Atkins, R. Friedman, *Molecular Quantum Mechanics*, 2011

Potential energy curves for H_2^+
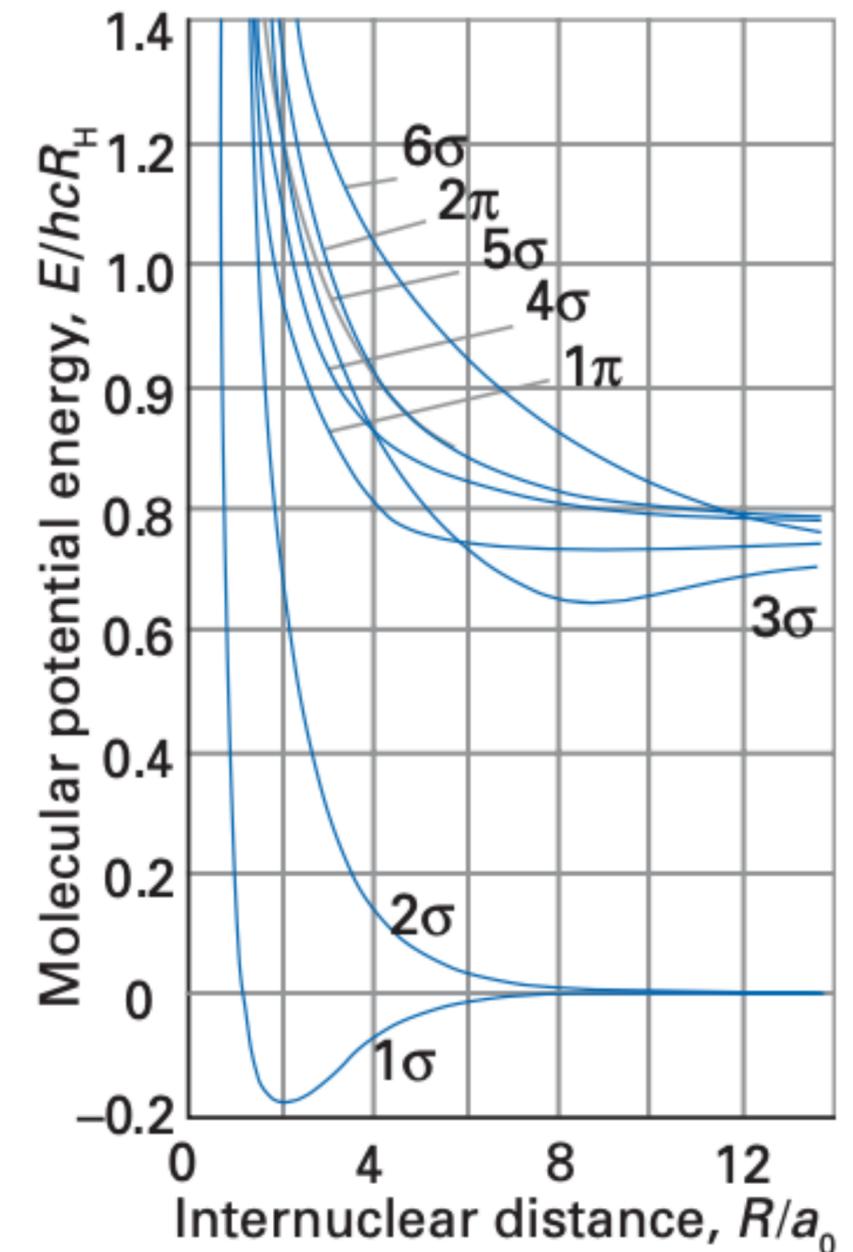
Molecular properties as derivatives of energy

- Molecular properties emerging as a response (of the electron density and nuclei) to an external perturbation (ε) can be represented as a Taylor expansion of the energy around the unperturbed value

$$E(\varepsilon) = E(\varepsilon = 0) + \left.\frac{dE}{d\varepsilon}\right|_{\varepsilon=0} \varepsilon + \frac{1}{2!}\left.\frac{d^2E}{d\varepsilon^2}\right|_{\varepsilon=0} \varepsilon^2 + \ldots$$

- When the external perturbation (ε) is the electric field

$$
\begin{aligned}
\text{dipole moment } (\mu) \quad &\stackrel{\wedge}{=} \quad -\left.\frac{dE}{d\varepsilon}\right|_{\varepsilon=0} \quad &&\text{(first derivative)} \\
\text{polarizability } (\alpha) \quad &\stackrel{\wedge}{=} \quad -\left.\frac{d^2E}{d\varepsilon^2}\right|_{\varepsilon=0} \quad &&\text{(second derivative)} \\
\text{first hyperpolarizability } (\beta) \quad &\stackrel{\wedge}{=} \quad -\left.\frac{d^3E}{d\varepsilon^3}\right|_{\varepsilon=0} \quad &&\text{(third derivative)}
\end{aligned}
$$

J. Gauss, in http://www.fz-juelich.de/nic-series/ (2000)
A. Hinchcliffe, Ab initio determination of Molecular Properties (1987)

Molecular properties as derivatives of energy

$\dfrac{dE}{d\varepsilon_i}$ — dipole moment; in a similar manner also multipole moments, electric field gradients, etc.

$\dfrac{d^2E}{d\varepsilon_\alpha d\varepsilon_\beta}$ — polarizability

$\dfrac{d^3E}{d\varepsilon_\alpha d\varepsilon_\beta d\varepsilon_\beta}$ — (first) hyperpolarizability

$\dfrac{dE}{dx_i}$ — forces on nuclei; stationary points on potential energy surfaces, equilibrium and transition state structures

$\dfrac{d^2E}{dx_i dx_j}$ — harmonic force constants; harmonic vibrational frequencies

$\dfrac{d^3E}{dx_i dx_j dx_k}$ — cubic force constants; vibrational corrections to distances and rotational constants

$\dfrac{d^4E}{dx_i dx_j dx_k dx_l}$ — quartic force constants; anharmonic corrections to vibrational frequencies

$\dfrac{d^2E}{dx_i d\varepsilon_\alpha}$ — dipole derivatives; infrared intensities within the harmonic approximation

$\dfrac{d^3E}{dx_i d\varepsilon_\alpha d\varepsilon_\beta}$ — polarizability derivative; Raman intensities

$\dfrac{d^2E}{dB_\alpha dB_\beta}$ — magnetazibility

$\dfrac{d^2E}{dm_{Kj} dB_\alpha}$ — nuclear magnetic shielding tensor; relative NMR shifts

$\dfrac{d^2E}{dI_{Ki} dI_{Lj}}$ — indirect spin-spin coupling constant

$\dfrac{d^2E}{dB_\alpha dJ_\beta}$ — rotational g-tensor; rotational spectra in magnetic field

$\dfrac{d^2E}{dI_{Ki} dB_\alpha}$ — nuclear spin-rotation tensor; fine structure in rotational spectra

$\dfrac{dE}{dm_{Kj}}$ — spin density; hyperfine interaction constants

$\dfrac{d^2E}{dS_i dB_\alpha}$ — electronic g-tensor

Availability of second derivatives

Gaussian, NWCHEM, GAMESS, Orca, Molpro, and several other programs for molecules

CASTEP, VASP, Quantum Espresso for solids

CFOUR for molecules

Second derivatives	
HF	Pople *et al.* (1979)
DFT	Handy *et al.* (1993), Johnson, Frisch (1994)
MCSCF	Schaefer, Handy *et al.* (1984)
MP2	Handy *et al.* (1985), Bartlett *et al.* (1986)
MP3, MP4	Gauss and Stanton (1997)
CISD	Schaefer *et al.* (1983)
CCSD	Koch, Jørgensen, Schaefer *et al.* (1990)
CCSD(T)	Gauss and Stanton (1997)
CCSDT-n	Gauss and Stanton (2000)

J. Gauss, in http://www.fz-juelich.de/nic-series/ (2000)

Electronic structure: A warm-up problem

For the hydrogen atom, the time-independent non-relativistic Schroedinger equation (in atomic units, where $\hbar = m_e = 1/4\pi\epsilon_0 = 1$) is

$$\left[-\frac{1}{2}\nabla^2(\vec{r}) - \frac{1}{2}\frac{\nabla^2(\vec{R})}{\tilde{M}_p^2} - \frac{1}{|\vec{r} - \vec{R}|} \right]|\Phi\rangle = E|\Phi\rangle,$$

where $\vec{r}$ is the position vector of the electron and $\vec{R}$ is the position vector of the proton. One can write this 2-body problem as two 1-body equations (that of the center of mass and the reduced mass). To a good approximation, we can treat the reduced mass equation as the electronic Schroedinger equation of the H atom.

$$\left[-\frac{1}{2}\nabla^2(\vec{r}) - \frac{1}{r} \right]|\Phi_e\rangle = E_e|\Phi_e\rangle,$$

The exact electronic energy for this problem is -0.5 Hartree (-13.606 eV). Apply variational principle for the trial wavefunction $|\Phi\rangle = N\exp\left(-\alpha r^2\right)$ and determine the variational upper bound to the ground state energy of the Hydrogen atom. What is the best value for α that minimises the energy? In the first computer exercise, you will use this value to calculate the energy with the program Orca.

Electronic structure methods

$$H_{\text{ele}}\Phi_{\text{ele}} = E_{\text{ele}}\Phi_{\text{ele}}$$

Hartree-Fock (HF) approximation

$$|\Phi\rangle \approx |\Psi_0\rangle = \Psi(\mathbf{x_1}, \mathbf{x_2}, \ldots, \mathbf{x_N}) = |\chi_i(\mathbf{x_1})\chi_j(\mathbf{x_2})\ldots\chi_k(\mathbf{x_N})\rangle$$

- Find the best set of spin-orbitals to variationally minimise the total electronic energy.
- Finding the best linear combination of atomic orbitals (LCAO) is a non-linear optimisation problem solved by the self-consistent field (SCF) method.

Configuration Interaction (CI), formally exact approach

$$|\Phi\rangle = c_0|\Psi_0\rangle + \sum_{r,a} c_a^r|\Psi_a^r\rangle + \sum_{r<s,a<b} c_{a,b}^{r,s}|\Psi_{a,b}^{r,s}\rangle + \ldots$$

- Use the coefficients for LCAO from a HF calculation and build singly, doubly, triply, … excited configurations
- Finding the best linear combination (for CI) is a linear optimisation problem

Electronic structure methods

Coupled-cluster approach

$$|\Phi\rangle = e^{\hat{C}}|\Psi_0\rangle \qquad \hat{C} \text{ is the cluster operator, and } e^{\hat{C}} = 1 + \hat{C} + \frac{1}{2!}\hat{C}^2 + \frac{1}{3!}\hat{C}^3 + \dots$$

The effect of the cluster operator is defined as the sum

$$\hat{C}|\Psi_0\rangle = \hat{C}_1|\Psi_0\rangle + \hat{C}_2|\Psi_0\rangle + \dots + \hat{C}_N|\Psi_0\rangle$$

with

$$\hat{C}_1|\Psi_0\rangle = \sum_{a,r} t_a^r |\Psi_a^r\rangle, \quad \hat{C}_2|\Psi_0\rangle = \sum_{a,b,r,s} t_{a,b}^{r,s}|\Psi_{a,b}^{r,s}\rangle$$

where the excitation amplitudes, t, are determined by a non-linear iterative optimisation
- Truncating the sum gives rise to CCSD, CCSDT, etc., approximations. One of the most popular approximations is CCSD(T), where the triples energy correction is estimated using the perturbation theory. CCSD(T) with a large LCAO expansion is commonly used for accurate modelling of spectroscopic properties (very) small molecules.

An example case of CCSD(T) settling the dispute

CCSD(T) calculation of NMR chemical shifts: consistency of calculated and measured ^{13}C chemical shifts in the 1-cyclopropylcyclopropylidenemethyl cation

John F. Stanton [a], Jürgen Gauss [b,c,1], Hans-Ullrich Siehl [d,e,2]

Table 1

^{13}C NMR chemical shifts (in ppm) [a] for **1** with the tzp/dz basis described in Ref. [19] with various treatments of electron correlation. Also included are experimental results from Ref. [3]

	SCF	MBPT(2)	CCSD	CCSD(T)	Expt.
C_α	276.9	211.1	244.4	234.1	234.2
C_β	50.1	53.6	51.7	51.9	51.7
$C_{\beta'}$	12.0	22.6	20.5	22.3	21.2
C_γ	33.3	49.0	43.2	45.4	43.9
$C_{\gamma'}$	34.5	42.3	39.8	41.0	38.9

[a] Relative to TMS. For the conversion of absolute shieldings to relative shifts see footnote 8.

- An earlier many-body perturbation theory (MBPT) calculation suggested geometric distortions in the solvent to influence the ^{13}C shift of C_α

Electronic structure methods

Kohn-Sham Density Functional Theory

It is the most popular electronic structure method, founded on the Hohenberg-Kohn existence theorem: The ground state energy and all other ground state properties are uniquely determined by the electron density. So, ground state energy can be written as a functional

$$E\left[\rho\right] = T\left[\rho\right] + V_{\text{Columb}}\left[\rho\right] + \int dr\rho(r)v_{\text{Ne}}(r) + E_{\text{XC}}\left[\rho\right]$$

- The wave function in DFT is also a Slater determinant, but with the molecular orbitals of a hypothetical reference system of non-integrating electrons
- Finding an accurate expression for $E_{\text{XC}}\left[\rho\right]$ is an active area of research
- The domain of applicability and drawbacks of different recipes of $E_{\text{XC}}\left[\rho\right]$ are well known
- In general, for any application, it is recommended to apply different favours of $E_{\text{XC}}\left[\rho\right]$ and rationalise the method selection (method benchmarking)

Why DFT and CCSD(T) are so popular?
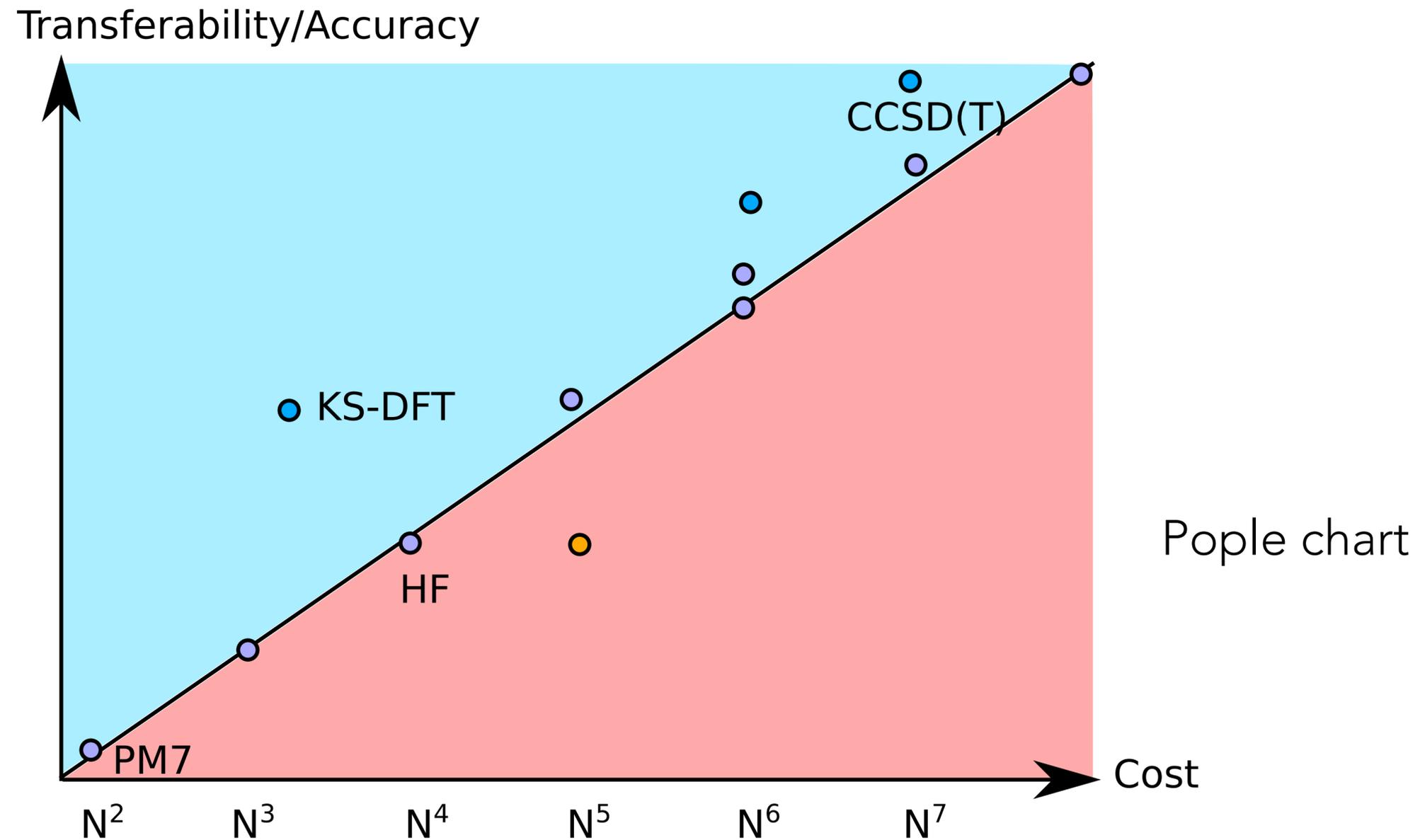
- Majority of the variational/perturbational approximations scale linearly with the system size
- KS-DFT and CCSD(T) scale super linearly, offering better accuracies for the given computational cost compared to other methods of similar computational cost

General information

- It may not be possible to do all the exercises discussed here during the workshop. Go through the exercises quickly and pick the problems that you would like to solve during the workshop. You can also try some of these exercises in the evening, after the lectures, and discuss during the breaks.
- Do the exercises in groups
- The material will be updated in gitlab
  https://gitlab.com/raghurama123/nmrworkshop2022

Software used

- Molecules: Codes using GIAO with Gaussian basis sets
  - ❖ Orca (You can log in to the tutorials server to use the program), Login details have been emailed.
  - ❖ CFOUR (input/output files are provided)

- Structure visualisation
  - ❖ Jmol/Avogadro for molecules
  - ❖ Jmol/Vesta for crystals

First Step: Log in to the workshop server

◉ Connect to VPN

◉ Open a terminal or SSH client

◉ Login to the server with your ID and password.
```
ssh nmrws000@10.10.3.22
```

◉ Once you log in, you should be able see the message like this (or something else)
```
Last login: Mon Dec  5 18:45:42 2022 from 10.1.3.12
nmrws000@expanse:~$
```

Try a few commands quickly

- Check your present working directory
  ```
  nmrws000@expanse:~$ pwd
  /home/nmrws000
  ```

- Check the content of your pwd (you may see more files than shown below)
  ```
  nmrws000@expanse:~$ ll
  total 44
  drwxr-xr-x  9 nmrws000 nmrws000  4096 Dec  5 19:07 ./
  drwxr-xr-x  5 root     root      4096 Nov 28 11:46 ../
  drwxrwxr-x 17 nmrws000 nmrws000  4096 Dec  5 17:10 nmrworkshop/
  ```

- Change the directory
  ```
  nmrws000@expanse:~$ cd nmrworkshop
  ```

Try a few commands quickly

- Check your present working directory
  ```
  nmrws000@expanse:~$ pwd
  /home/nmrws000/nmrworkshop
  ```

- Check the content of your pwd (you may see more files than shown below)
  ```
  nmruser00@expanse:~$ ll
  total 60
  drwxrwxr-x 17 nmrws000 nmrws000  4096 Dec  5 17:10 ./
  drwxr-xr-x  9 nmrws000 nmrws000  4096 Dec  5 19:07 ../
  drwxrwxr-x  3 nmrws000 nmrws000  4096 Dec  4 16:40 exercise_01/
  drwxrwxr-x  3 nmrws000 nmrws000  4096 Dec  4 17:06 exercise_02/
  ```

Warmup exercise

Let's calculate the electronic energy of H atom using the Gaussian function with the optimal α determined from the previous exercise. The figure below shows the content of a typical input file for calculating energy with the Hartree-Fock method.

```
nmrws000@expanse:~/nmrworkshop/exercise_warmup$ cat Hatom.com
! HF                                      ← method details go here

%basis
  newgto H
  S  1
  1  0.28294212  1.00
end
end
                                          ← charge, multiplicity
* xyz 0 2
H  0.0 0.0 0.0                            ← geometry block
*
```

The commands to execute the program Orca are provided in the file `run.sh`. You can execute these commands by typing on your terminal `bash run.sh`. You can find the energy in the output file `Hatom.out`

Solution

You can scroll through the output file `H.out` to find the energy. Does it agree with your analytic result?

```
518 Total SCF time: 0 days 0 hours 0 min 0 sec
519
520 Total time                        ....         0.070 sec
521 Sum of individual times           ....         0.003 sec  (  3.6%)
522
523 Fock matrix formation             ....         0.001 sec  (  0.7%)
524 Diagonalization                   ....         0.000 sec  (  0.0%)
525 Density matrix formation          ....         0.000 sec  (  0.0%)
526 Population analysis               ....         0.000 sec  (  0.6%)
527 Initial guess                     ....         0.001 sec  (  0.8%)
528 Orbital Transformation            ....         0.000 sec  (  0.0%)
529 Orbital Orthonormalization        ....         0.000 sec  (  0.0%)
530 DIIS solution                     ....         0.000 sec  (  0.0%)
531
532 Maximum memory used throughout the entire SCF-calculation: 223.1 MB
533
534 -------------------------         --------------------
535 FINAL SINGLE POINT ENERGY          -0.424413181578
536 -------------------------         --------------------
```

Exercise 01: Generating structures from SMILES

The simplified molecular-input line-entry system (SMILES) is a string-based representation of molecular connectivity. Using SMILES it is very easy to generate thousands of molecular structure without having to draw structures on a graphical users interface (GUI). Here are some examples.

SMILES	Name
C	methane
CC	ethane
CCCCC	pentane
CC(C)CC	isopentane
CC(C)(C)C	neopentane
C1CC1	cyclopropane
C1CCCCC1	cyclohexane
c1ccccc1	benzene

It is also possible to encode stereochemical information (cis/trans, R/S) in SMILES.

Go to the directory, `/home/nmrws000/nmrworkshop/exercise_01`
`cd nmrworkshop/exercise_01`

You can check the content of `structures.smi` using the command
`cat structures.smi`

You can generate the atomic coordinates of all the molecules using the command
`obabel structures.smi -oxyz --gen3d > structures.xyz`

It is also possible to generate 2D cartoons and save them in an svg file.
`obabel -osvg structures.smi > structures.svg`

You can download the content of the entire directory to your caption and use a visualisation software to see the results. The svg file can be visualised on an internet browser.
`scp -r nmrws000@10.10.3.22:/home/nmrws000/nmrworkshop/exercise_01 .`

Exercise 02: Conformer search & Refining geometry

1. Write the SMILES representation for N-methylformamide and save it in a file called, say, `NMF.smi`

2. Generate atomic coordinates as explained in Exercise 01 and save them in the file `NMF.xyz` The command for this step is `obabel -oxyz NMF.smi > NMF.xyz --gen3d`

3. Search for possible conformers of N-methylformamide using `obabel` and visualise them using Avogadro. The command for this step is

`obabel NMF.xyz -O NMF_conformers.xyz --conformer --nconf 10 --score rmsd --writeconformers`
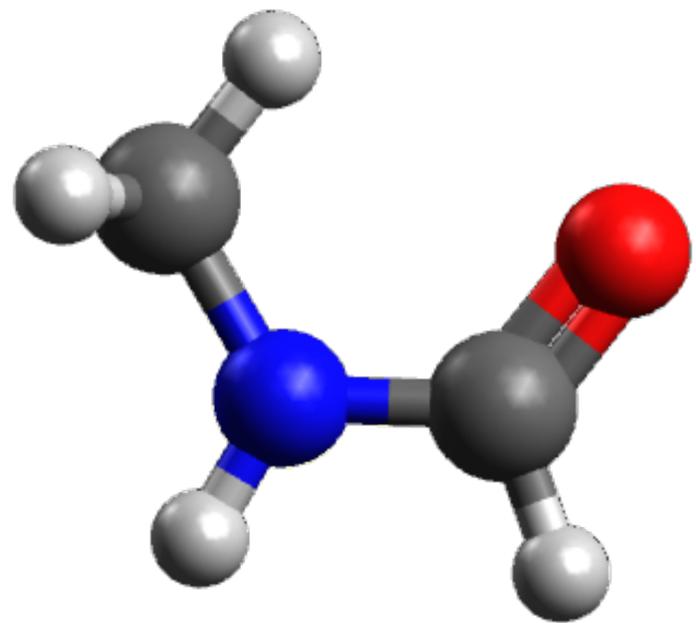
trans-N-methylformamide
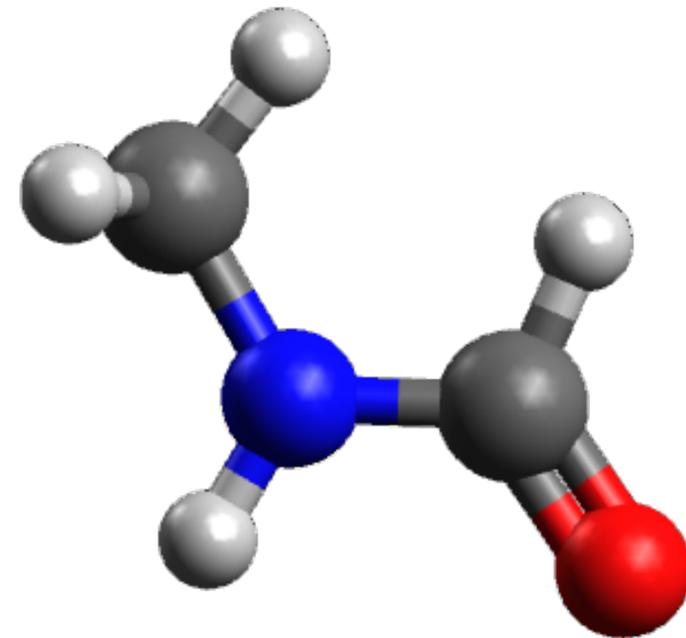
cis-N-methylformamide

4. The coordinates can be refined by structure relaxation using a force field molecular model. We will use universal force fields (UFF) and openbabel's minimizer `obminimize`. The command is
`obminimize -oxyz -sd -ff uff NMF_conformers.xyz > NMF_conformers_UFF.xyz`
5. Another popular force fields model for small organic molecules is MMFF94. You can also refine your geometry using this model using the command
`obminimize -oxyz -sd -ff mmff94 NMF_conformers.xyz >`
`NMF_conformers_MMFF94.xyz`
6. Compare the UFF and MMFF94 geometry parameters with the experimental parameters of the *cis* structure (global minimum) collected from NIST: https://cccbdb.nist.gov/expgeom2x.asp

1.114 Å

$\theta(CNC)=121.4°$

1.459 Å   1.366 Å

$\theta(NCO)=124.6°$

1.219 Å

cis-N-methylformamide
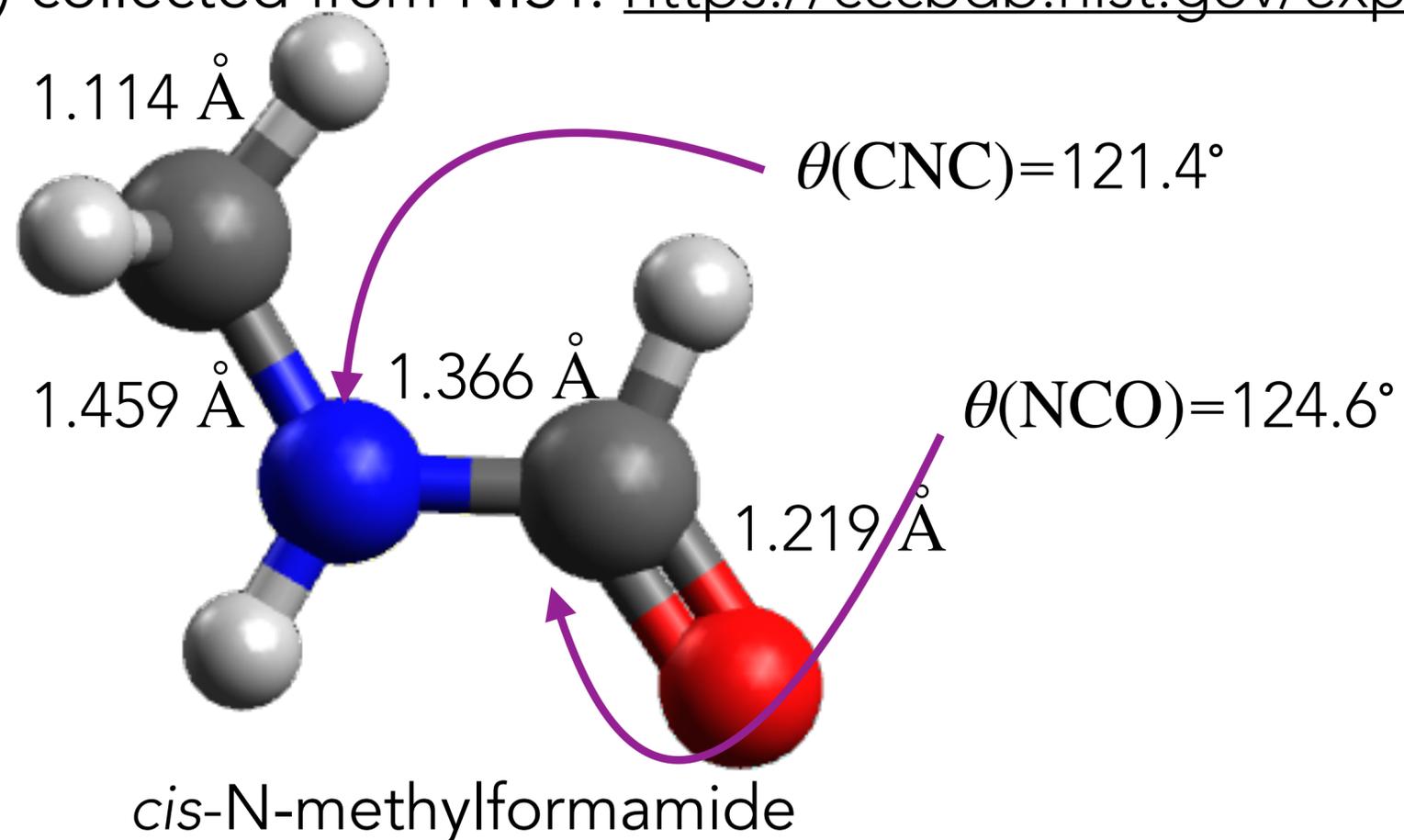
Solution

cis-N-methylformamide

1.093 Å
1.112 Å
1.114 Å

1.361 Å
1.355 Å
1.366 Å

1.223 Å
1.221 Å
1.219 Å

1.438 Å
1.459 Å
1.446 Å

124.3°
121.9°
$\theta(\mathrm{CNC})$=121.4°

122.9°
120.1°
$\theta(\mathrm{NCO})$=124.6°
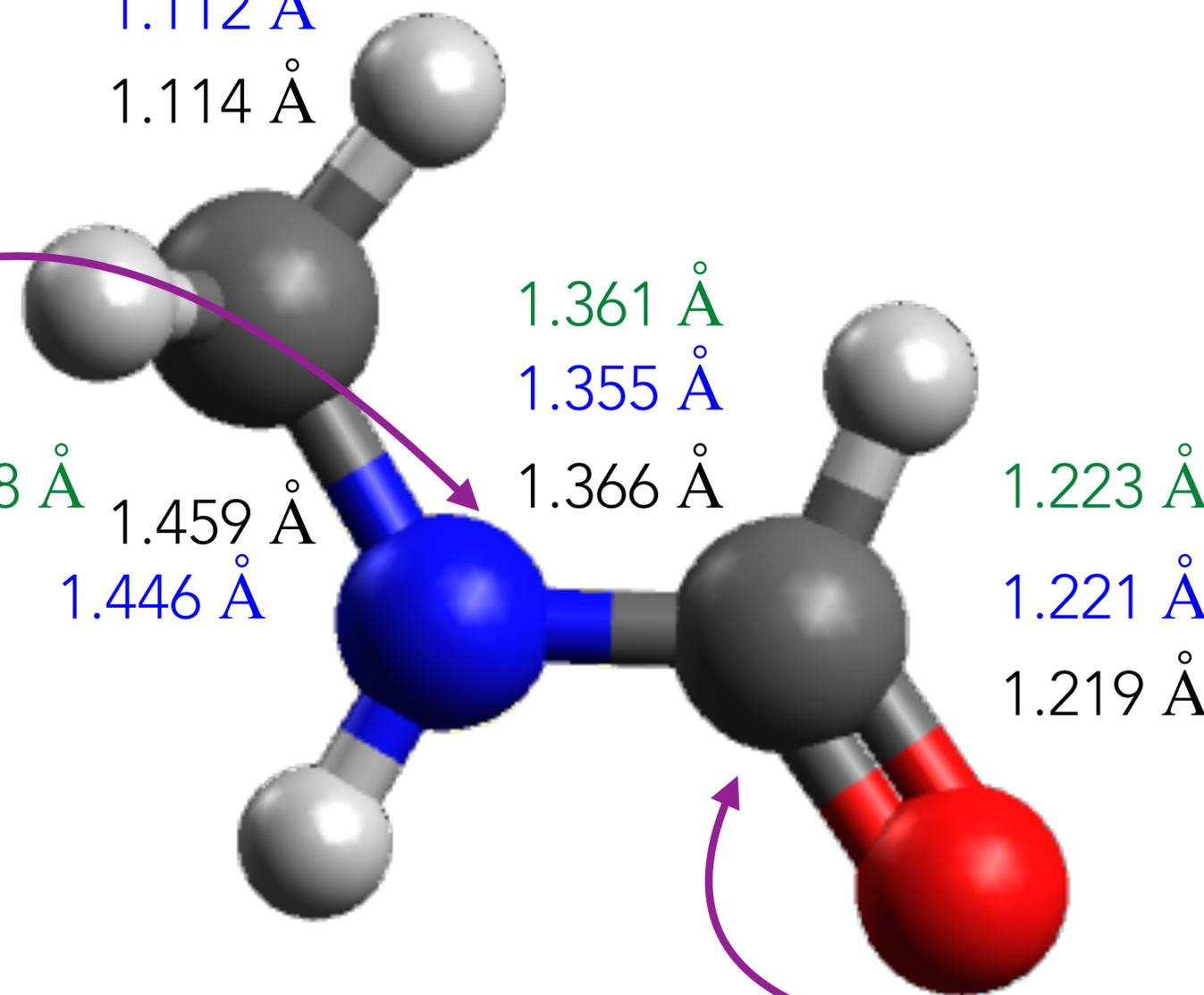
UFF geometry is better than MMFF94 geometry. UFF is trained using experimental geometries, while MMFF94 is parameterised using DFT results. For less conventional geometries, MMFF94 maybe expected to give better results.

Exercise 03: DFT geometry relaxation

Use the UFF-level geometries of cis/trans isomers of N-methylformamide from the previous exercise relax the geometry with the DFT method B3LYP and the basis set def2TZVPP. An empirical dispersion correction has been found to improve geometries of molecules with significant dispersion interactions (which is additive, hence present in all large molecules). Include the D3BJ empirical correction and repeat the geometry relaxation, and compare the results with the experimental geometries.

```
! B3LYP  def2-TZVPP def2/J RIJCOSX Opt

%pal
  nprocs 8
end

* xyzFILE 0 1 cis_NMF_UFF.xyz
```

```
! B3LYP D3BJ def2-TZVPP def2/J RIJCOSX Opt

%pal
  nprocs 8
end

* xyzFILE 0 1 cis_NMF_UFF.xyz
```

UFF geometry file from previous exercise

Approximations to speed up calculation of $E_{\mathrm{XC}}[\rho]$
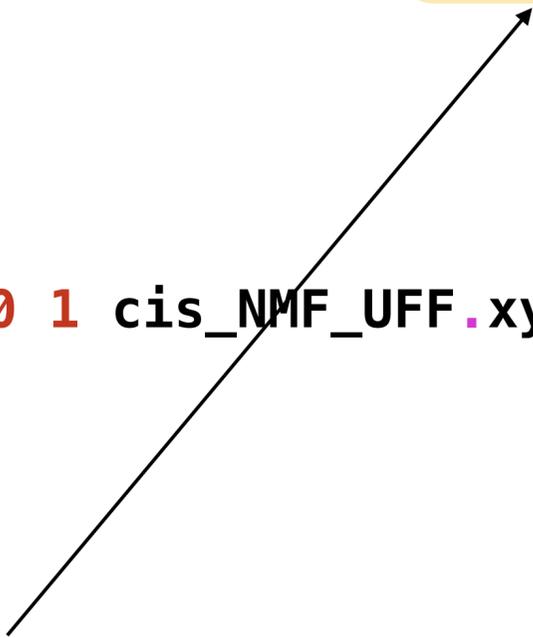
Solution

cis-N-methylformamide

1.089 Å
1.089 Å
1.114 Å

1.356 Å
1.356 Å
1.366 Å

1.212 Å
1.212 Å
1.219 Å

1.448 Å 1.459 Å
1.447 Å

125.0°
124.8°
$\theta(\text{CNC})=121.4°$

125.1°
125.1°
$\theta(\text{NCO})=124.6°$
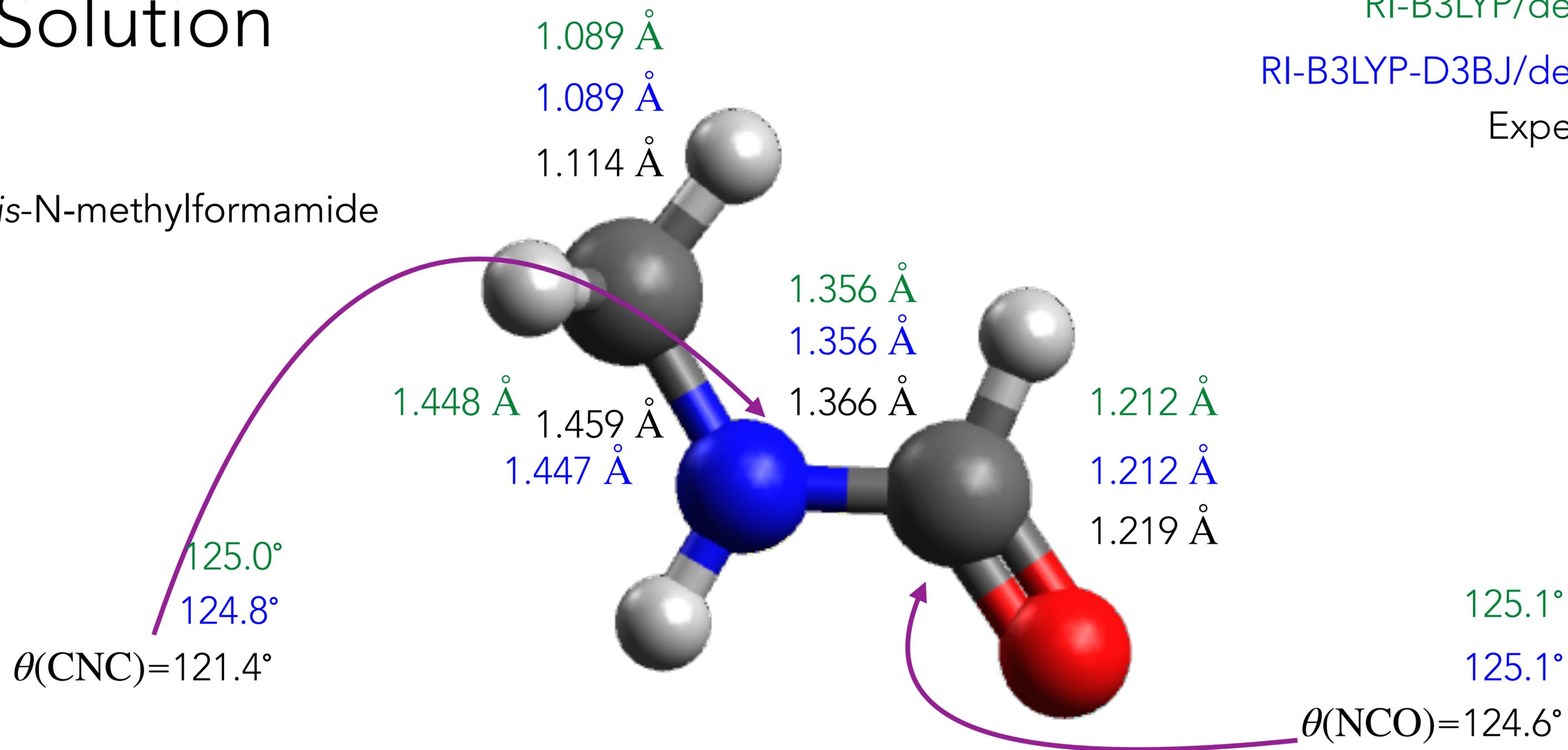
Adding a dispersion correction term (D3BJ) did not affect the results. However, for larger molecules, where dispersion interactions accumulate, D3BJ has been shown to improve geometries.

Exercise 04: DFT NMR calculation

Use the geometries of cis/trans isomers of N-methylformamide from the previous exercise to calculate the isotropic NMR shielding (σ), which is reported in ppm, using the `B3LYP/def2TZVPP` method. You have to do geometry relaxation (starting with SMILES) of the reference molecule tetramethylsilane (TMS) and calculate the chemical shift as $\delta = \sigma(\text{TMS}) - \sigma$. Compare your results with the low-temperature (in CDCl$_3$) experimental ^{1}H and ^{13}C NMR chemical shifts of NMF given below.
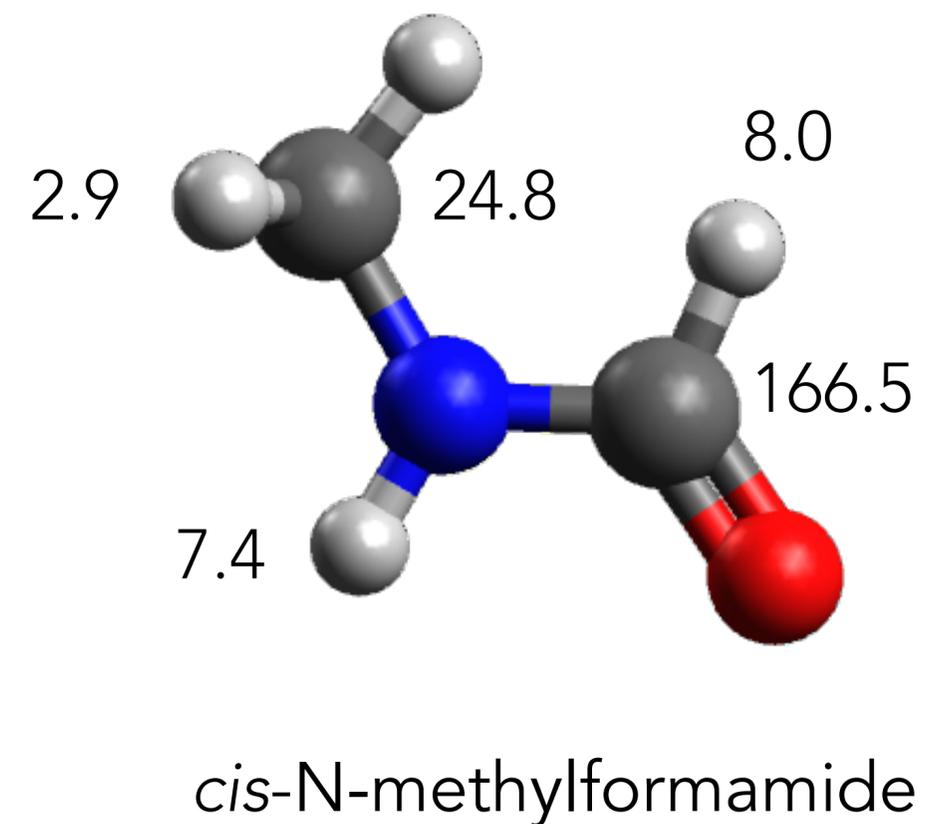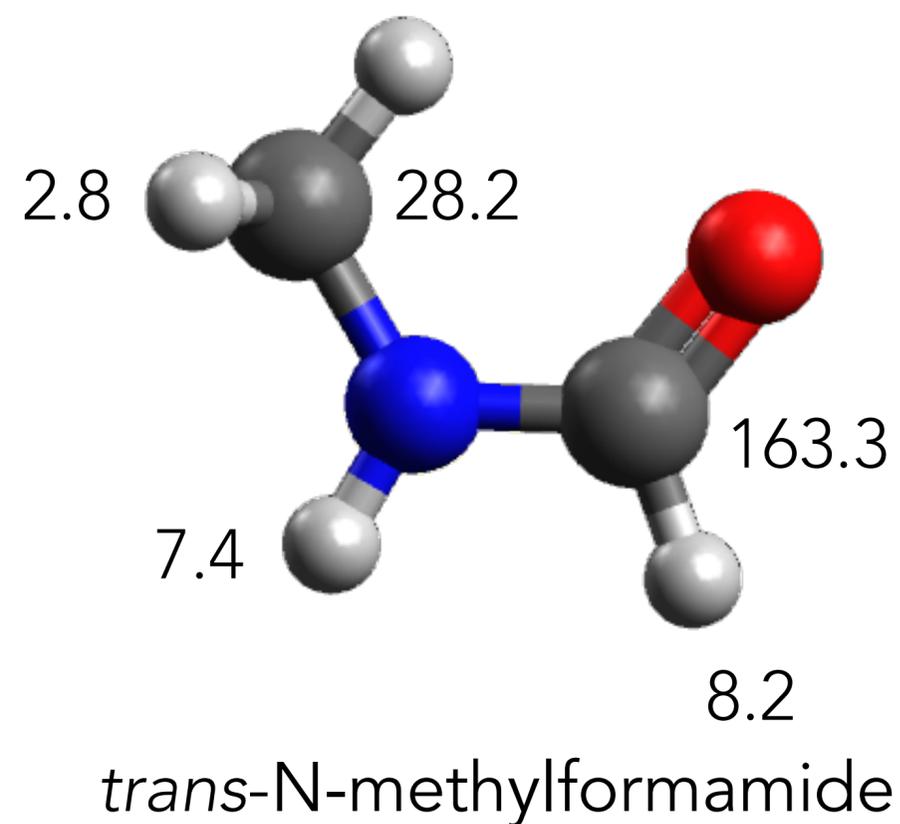
2.8   28.2

163.3

7.4

8.2

trans-N-methylformamide

8.0

2.9   24.8

166.5

7.4

cis-N-methylformamide

You can scroll through the output file `solution/cis_NMF/nmr/nmr.out` to find the energy. Does it agree with your analytic result?

```
1708 --------------------------------
1709 CHEMICAL SHIELDING SUMMARY (ppm)
1710 --------------------------------
1711
1712
1713   Nucleus  Element    Isotropic     Anisotropy
1714   -------  -------   ------------   -----------
1715      4        H         23.483          2.189
1716      5        H         27.376          8.005
1717      6        H         28.504          5.469
1718      7        H         28.970          9.163
1719      8        H         28.968          9.173
1720      0        C         18.877       -118.918
1721      3        C        155.376         46.387
1722      2        N        140.053        142.726
1723      1        O        -79.951       -390.837
```

Solution
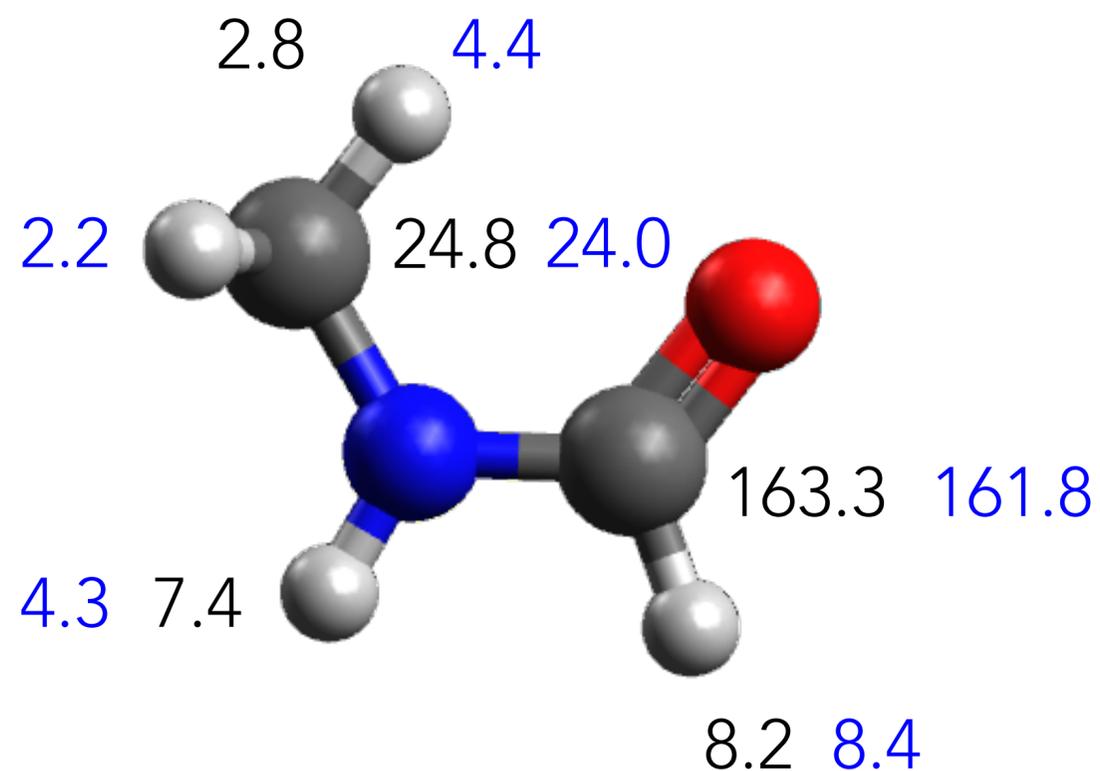
trans-N-methylformamide

MAE=1.2 (^{1}H), 1.1 (^{13}C) ppm
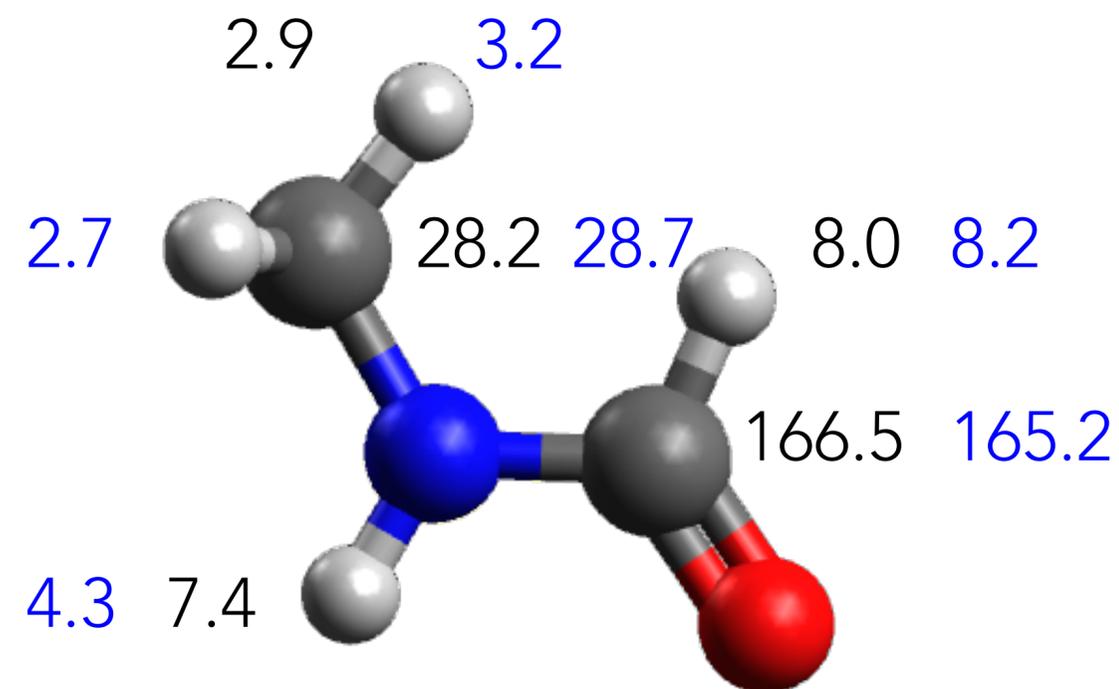
cis-N-methylformamide

MAE=0.8 (^{1}H), 0.9 (^{13}C) ppm

In the rest of the tutorial, we will use "`B3LYP D3BJ def2-TZVPP def2/J RIJCOSX`" for geometry relaxations and "`B3LYP def2-TZVPP def2/J RIJCOSX`" for calculating NMR parameters.

Exercise 05: Solvent effect

Repeat Exercise 04 by including solvent modelling in your DFT calculations. This can be done by adding the keyword `CPCM(solvent name)`. For advanced options, one must consult the latest Orca manual. In this exercise, we will compare the calculated results using `DMSO`, `Ethanol`, and `Chloroform` with the experimental chemical shifts of NMF (measured in CDCl$_3$). Comment on the solvent effect based on the solvent-polarity.

For keeping the calculations simple, we will use the gas phase geometries of NMF and TMS from previous exercises. As an advanced exercise, you can relax the geometries separately with the solvent model and compare your results with the experimental results.

Exercise 06: Karplus-type relation

Karplus equation, relates the correlation between ^3J-coupling constants and a dihedral torsion angle (about a sigma bond) as $^3J = A\cos^2\theta + B\cos\theta + C$, where θ is the dihedral angle. The constants A, B, and C empirical constants that depend on substituents. For the cis and trans NMF, this analysis was done using the INDO semi-empirical method by Ostlund.
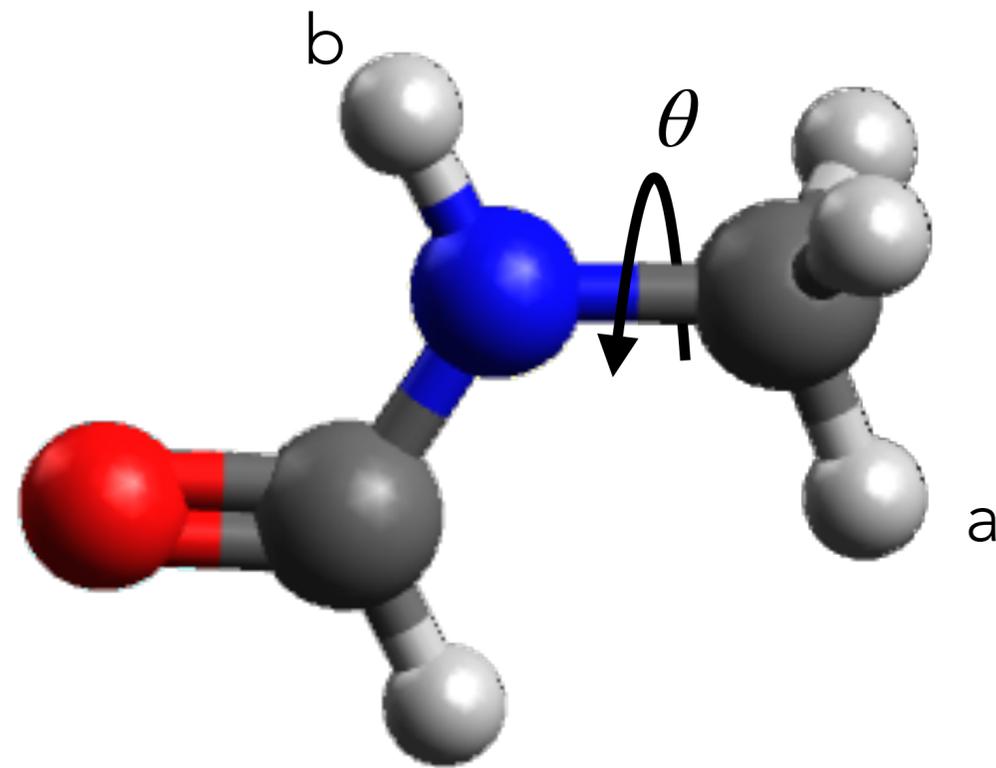

cis-N-methylformamide
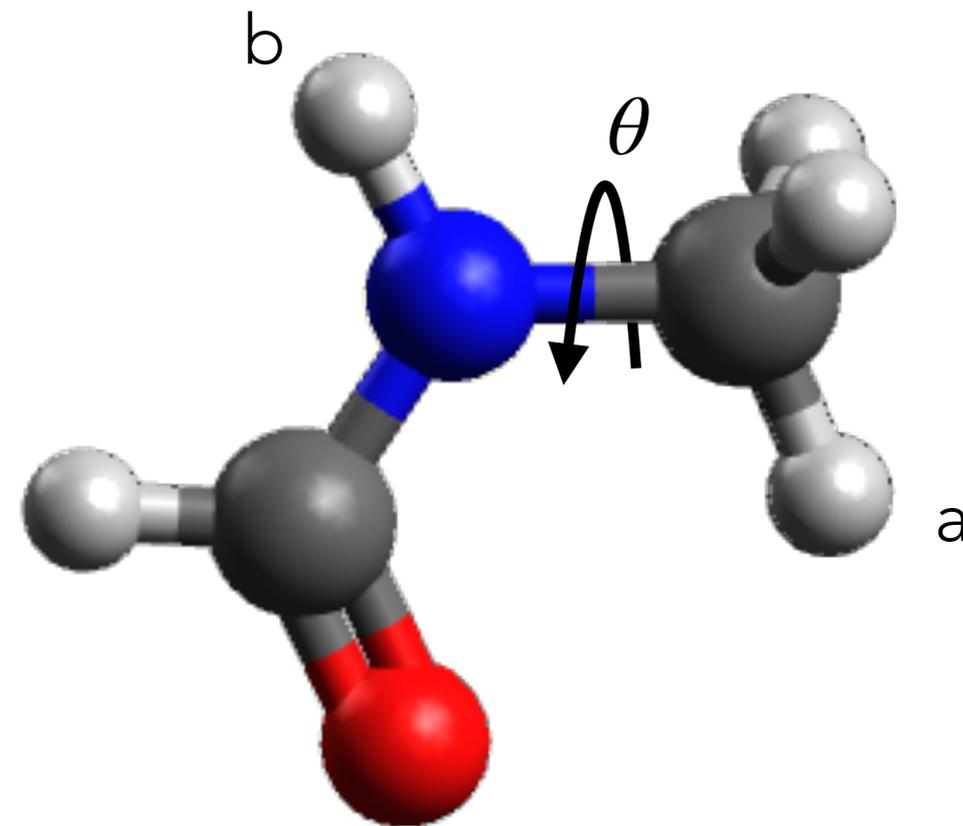
trans-N-methylformamide

1. For both *cis* and *trans* NMF, do relaxed scan optimisations, by fixing the H-C-N-H dihedral angles from 0 to 360 degrees in steps of 10 degrees.

2. For each geometry, perform an NMR calculation by including the keyword `ssall` to calculate the spin-spin coupling constants between all nuclei.

3. Plot the J values for the two protons marked in the previous figure for various angles.

4. Perform the fit and determine the constants A, B, and C. Report the goodness of the fit using the standard deviation between DFT values of J, and the fit.

5. Is it possible to determine the rotation-averaged value of J in terms of the constants A, B, and C?

Solution
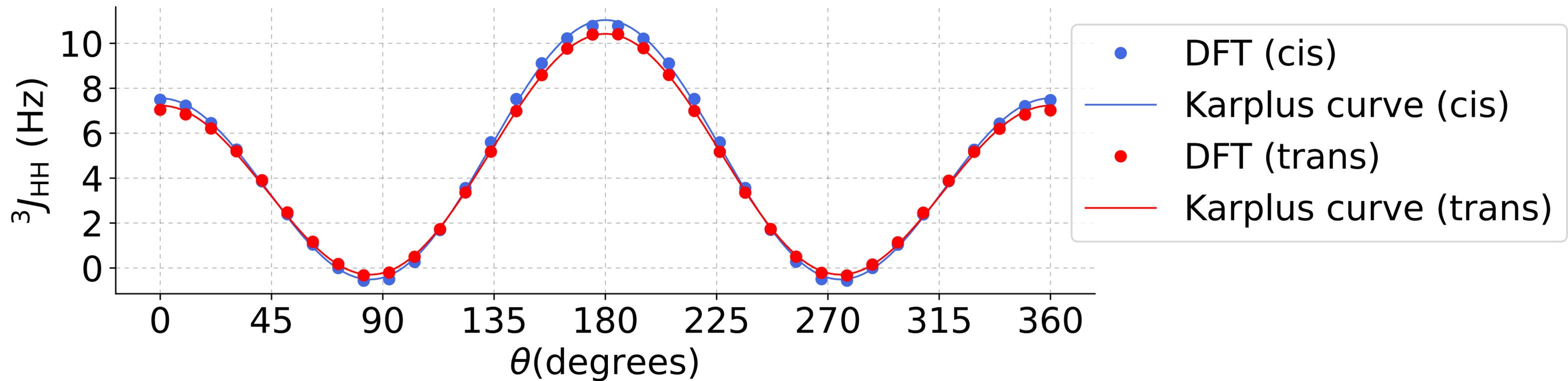
Details of the fit are provided in the Jupyter notebook in the folder Exercise06/ipynb

Exercise 07: Spin-spin coupling constant

Let us calculate the isotropic nuclear spin-spin coupling constant for the diatomic molecule ^1H-^{19}F and compare with the experimentally accepted value, 529 ± 23 Hz.

1. The total J comprises of four contributions, all are due to electron-coupled interaction of nuclei i) J_{FC}, Fermi contact term, ii) J_{SD}, spin-dipole term, iii) J_{PSO}, paramagnetic spin-orbit coupling term, and iv) J_{DSO}, diamagnetic spin-orbit coupling term.

2. Use the experimental bond length, $r = 0.9168 \text{Å}$, and the robust method CCSD(T) with the cc-pVTZ, cc-pVQZ, and cc-pV5Z basis sets. Use the frozen-core approximation and comment on how the different contributions to J are sensitive to the basis set.

3. Compare the best computed result with the experimental value. If there is discrepancy, what are the possible sources of errors in the modelling?

CFOUR input/output files for these calculations are provided.

Solution

	J_{FC} (Hz)	J_{SD} (Hz)	J_{PSO} (Hz)	J_{DSO} (Hz)	J (Hz)
cc-pVTZ	156.8	-7.5	197.4	0.4	347.1
cc-pVQZ	295.2	-7.5	191.8	0.0	479.5
cc-pV5Z	353.3	-5.6	190.7	-0.3	538.1
Exp.					529 ± 23

DFT-level vibrational (harmonic + anharmonic) corrections to J of HF is estimated to be -38 Hz

T.A.Ruden et al., J. Chem. Phys. 118 (2003) 9572
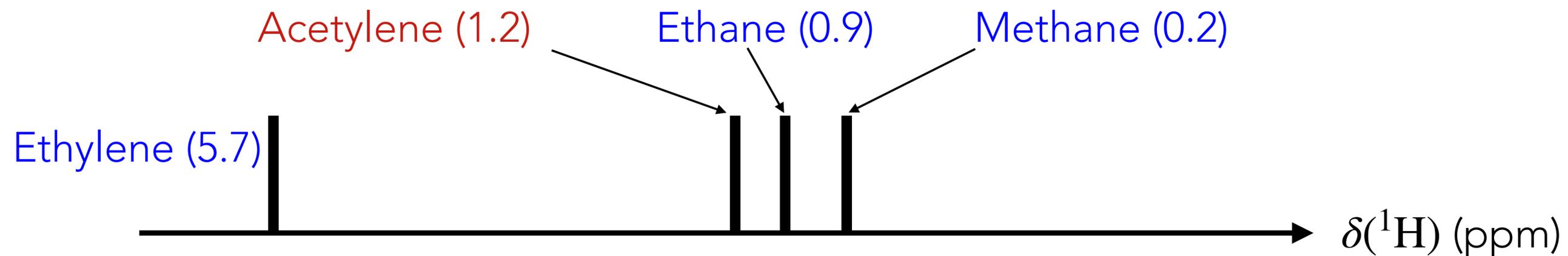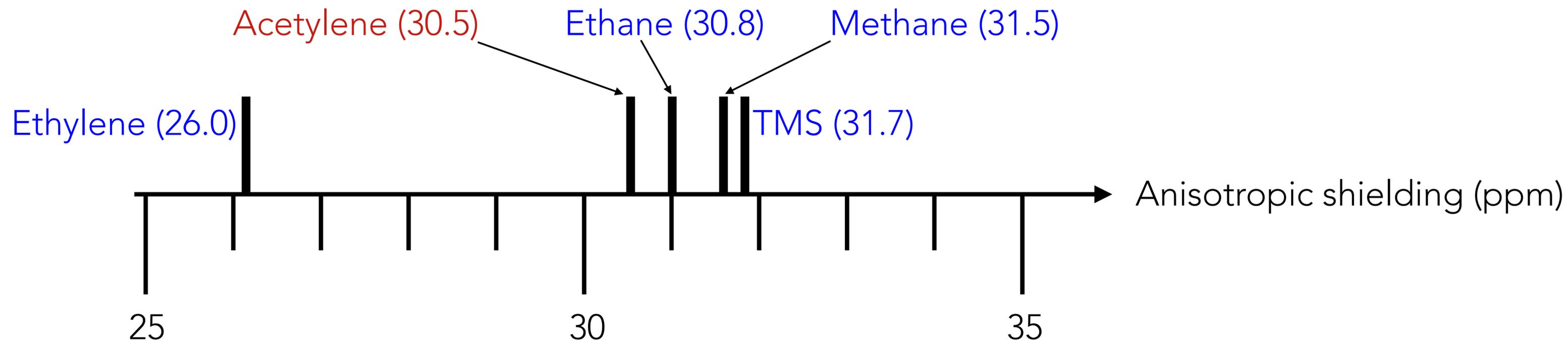
Exercise 08: Acetylene terminal H

The trend in proton shifts of ethane, ethylene, acetylene is $\delta(^1H_{ethylene}) > \delta(^1H_{acetylene}) > \delta(^1H_{ethane})$. If one estimates this trend solely based on the electronegativity (or *s*-character) of the C atoms, the shift of acetylene may be expected at a higher field than ethylene. The following figure shows how the acetylene proton is more shielded as a result of the anisotropy in the magnetic susceptibility of the CC triple bond.
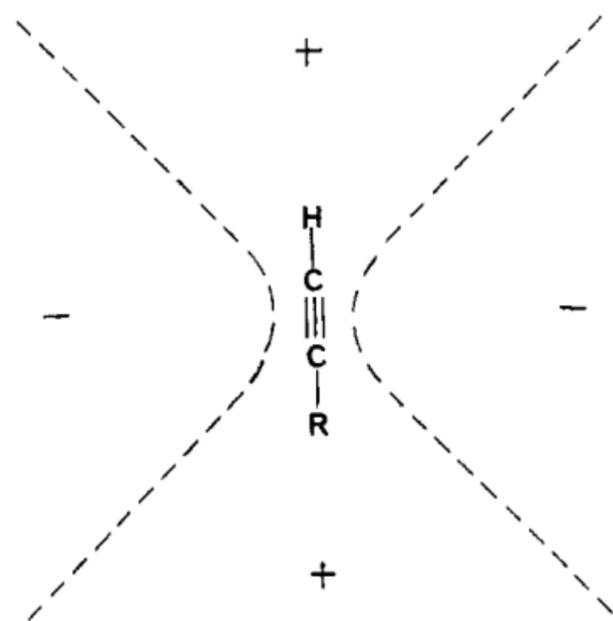
Estimate $\delta(^1H)$ for methane, ethane, ethylene, and acetylene using TMS as the reference.

Figure 1. Expected regions of net magnetic shielding (+) and deshielding (−) around a freely tumbling acetylene resulting from circulations of the triple-bond electrons induced by an external magnetic field.

F.B. Mallory, M. B. Baker, *J. Org. Chem.* 49 (1984) 1323

Solution

Acetylene (30.5) Ethane (30.8) Methane (31.5)

Ethylene (26.0) TMS (31.7)

Anisotropic shielding (ppm)

25 30 35

Acetylene (1.2) Ethane (0.9) Methane (0.2)

Ethylene (5.7)

$\delta(^1\mathrm{H})$ (ppm)

36
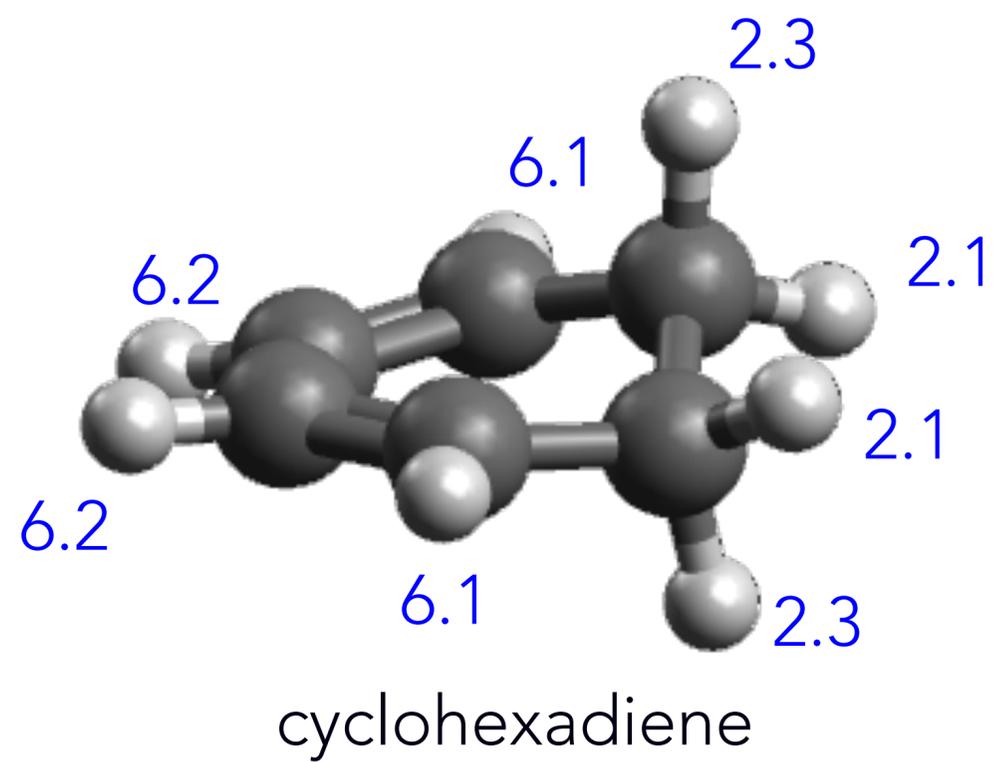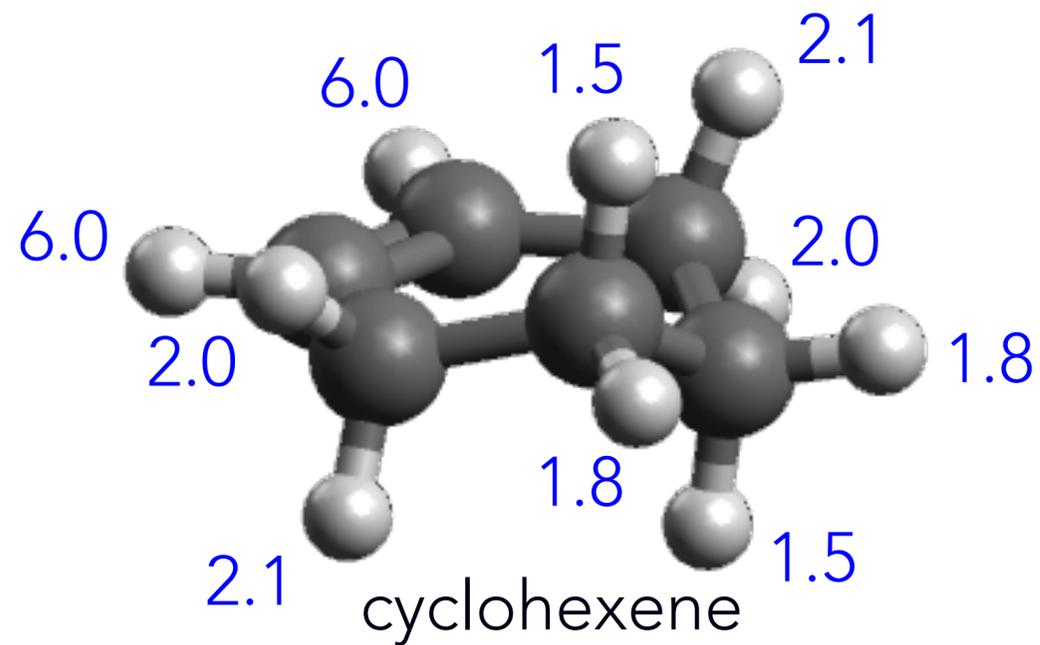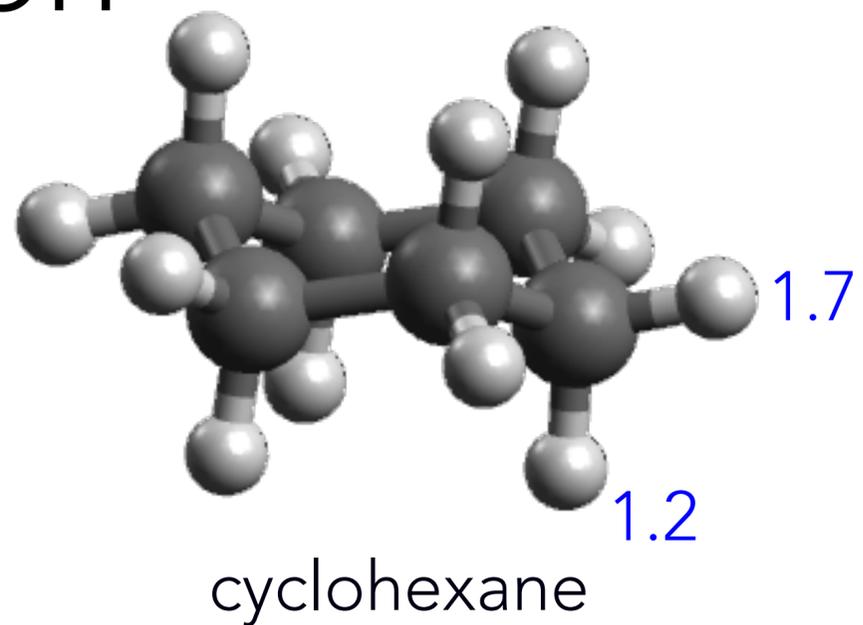
# Exercise 09: Ring current shift

Estimate $\delta(^1\text{H})$ for cyclohexane, cyclohexane, cyclohexadiene, and benzene with the RI-B3LYP/def2TZVPP@ RI-B3LYP(D3BJ)/def2TZVPP model. Can the proton shift in benzene be estimated using addition of contributions per double bond?
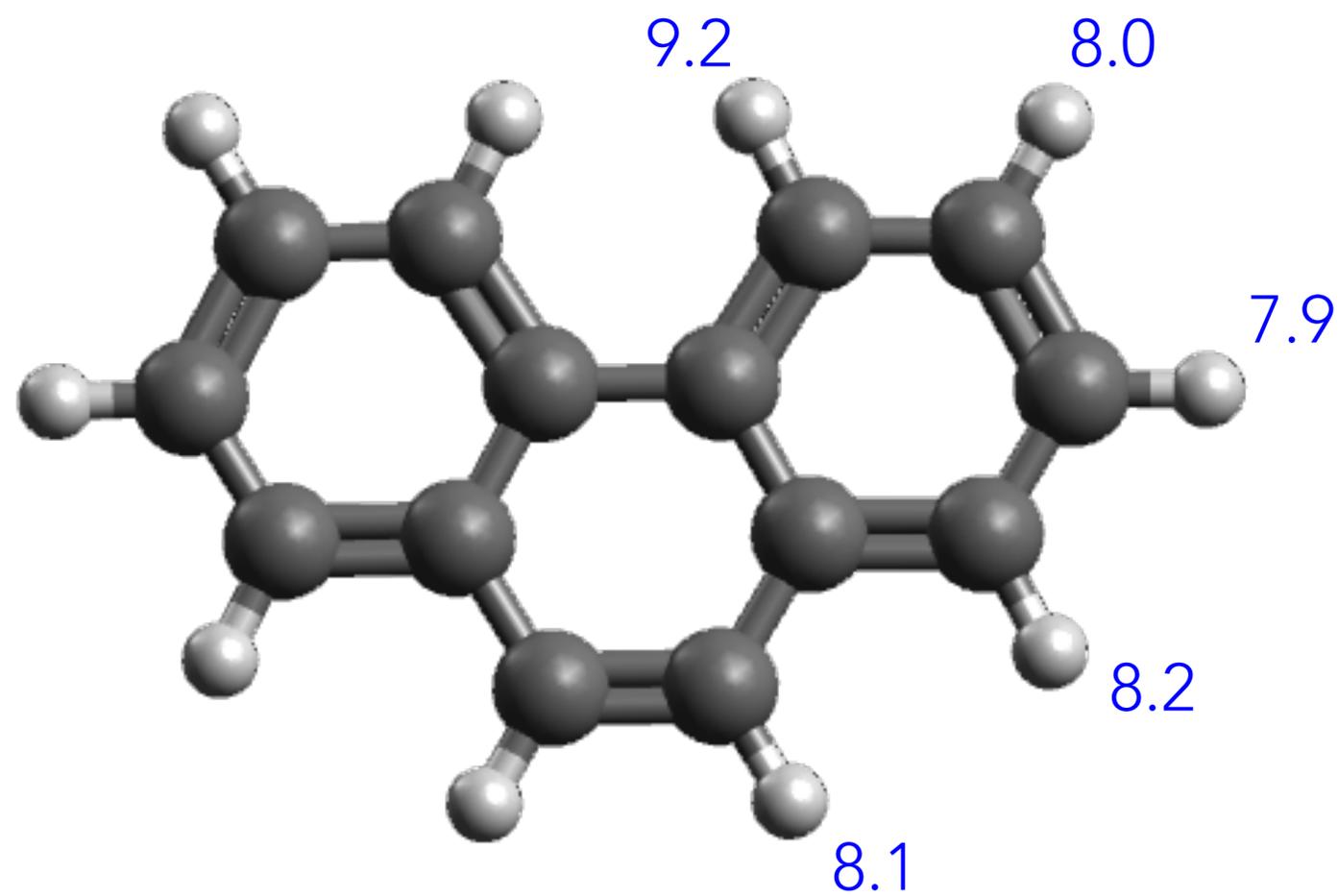
Solution

cyclohexane

1.7
1.2

cyclohexene

6.0
1.5
2.1
6.0
2.0
2.0
1.8
2.1
1.8
1.5

cyclohexadiene

2.3
6.1
6.2
2.1
2.1
6.2
6.1
2.3

benzene

7.6
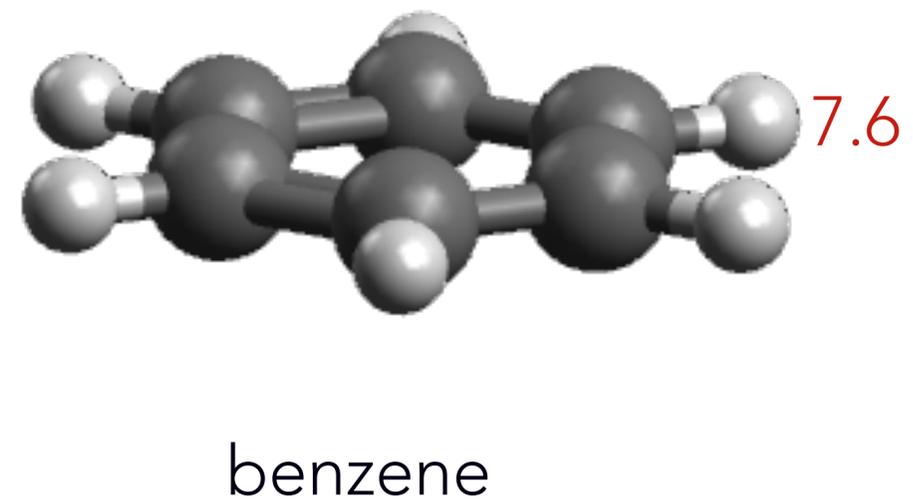
Exercise 10: Anisotropy of CC triple bonds

The figure below (that was also used in one of the previous exercises) shows that the region perpendicular to the CC triple bond should experience deshielding. Find example molecules where this effect can be realised. Verify your assumption by DFT modelling.
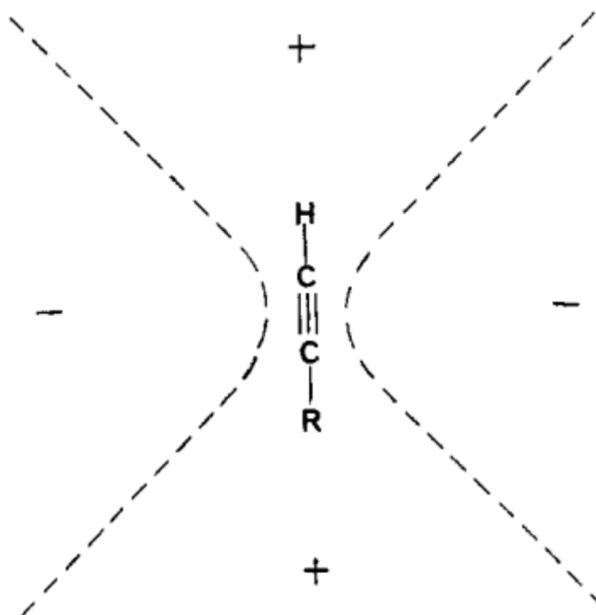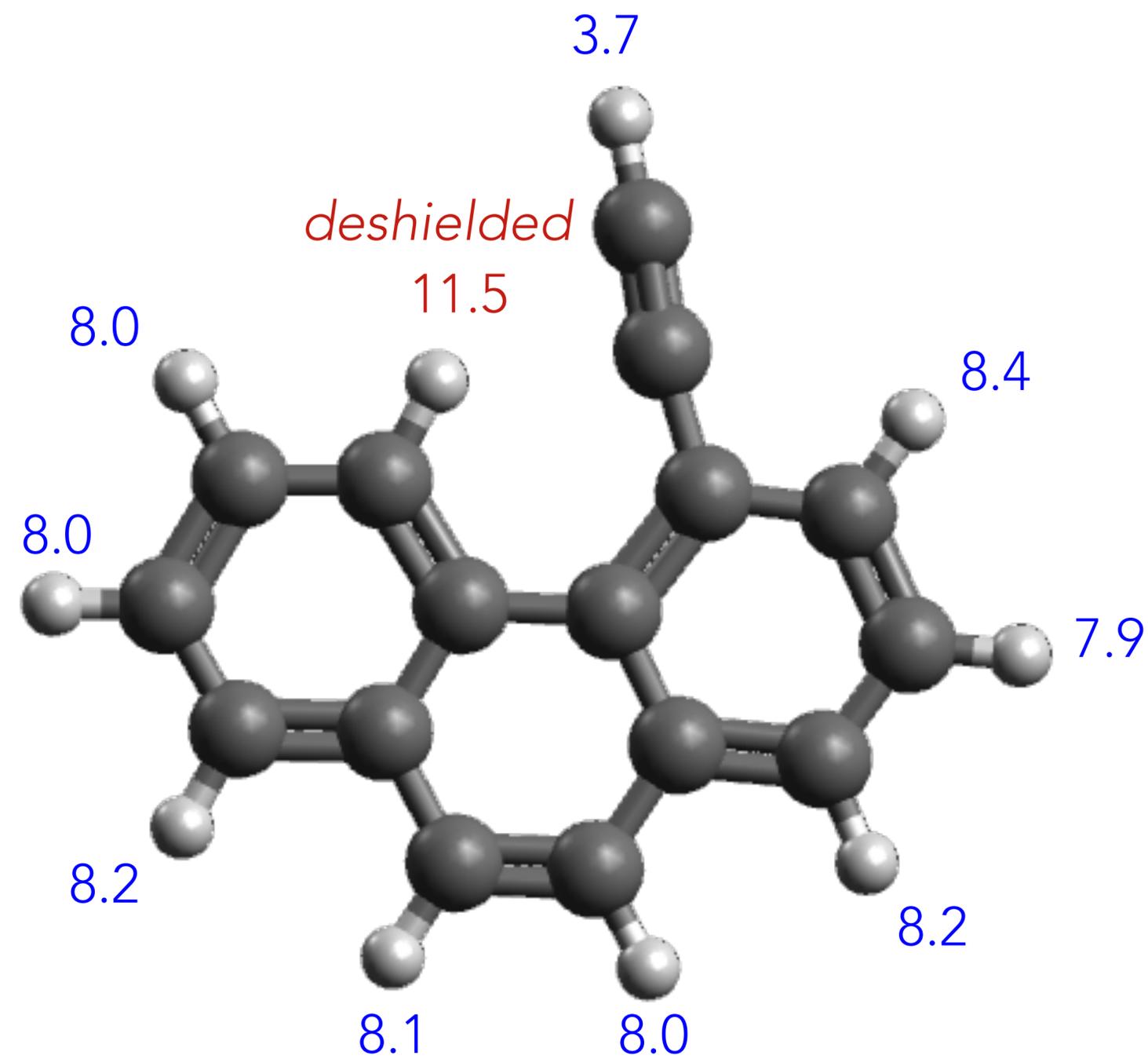

Figure 1. Expected regions of net magnetic shielding (+) and deshielding (−) around a freely tumbling acetylene resulting from circulations of the triple-bond electrons induced by an external magnetic field.

F.B. Mallory, M. B. Baker, *J. Org. Chem.* 49 (1984) 1323
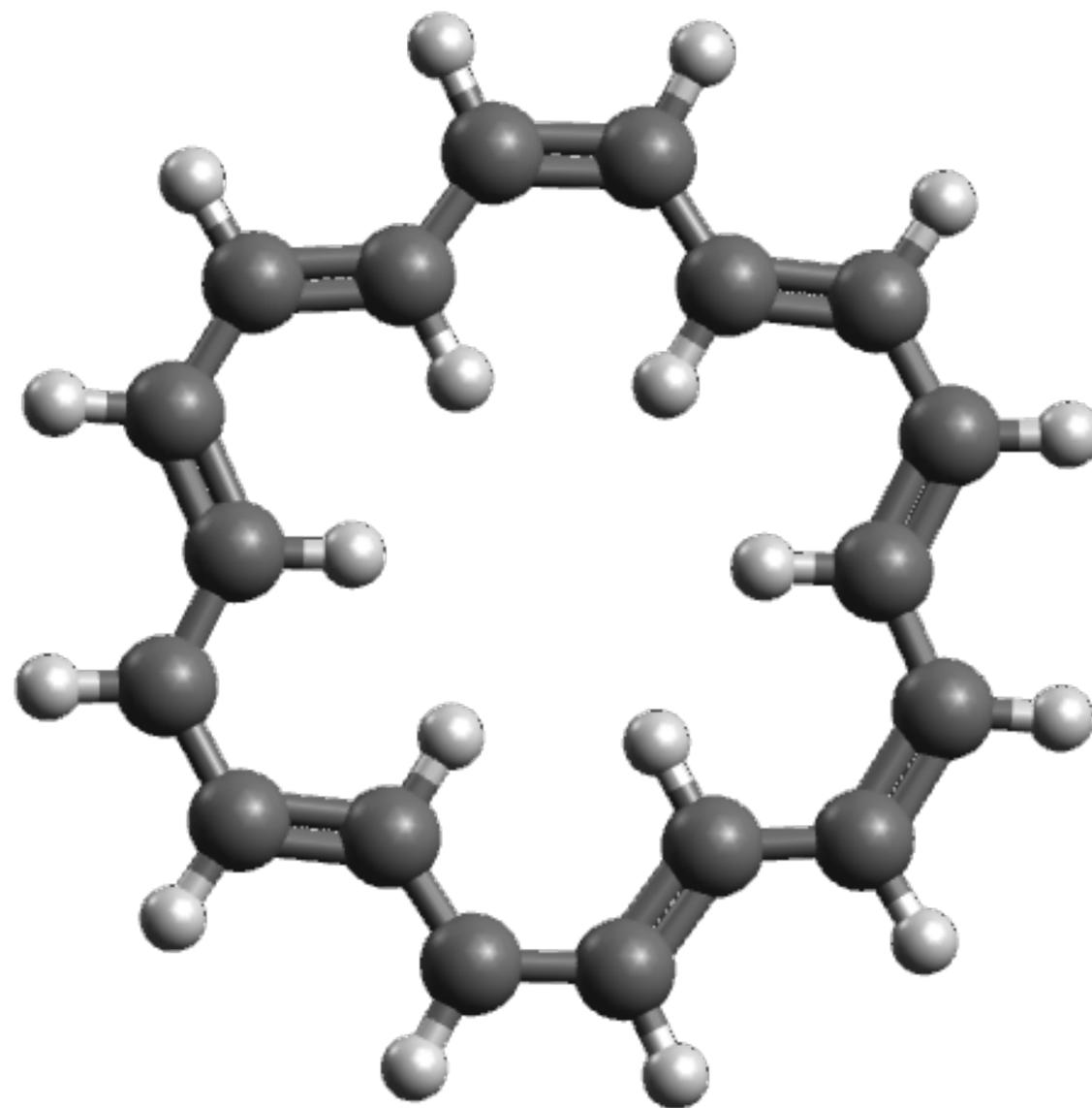
Solution
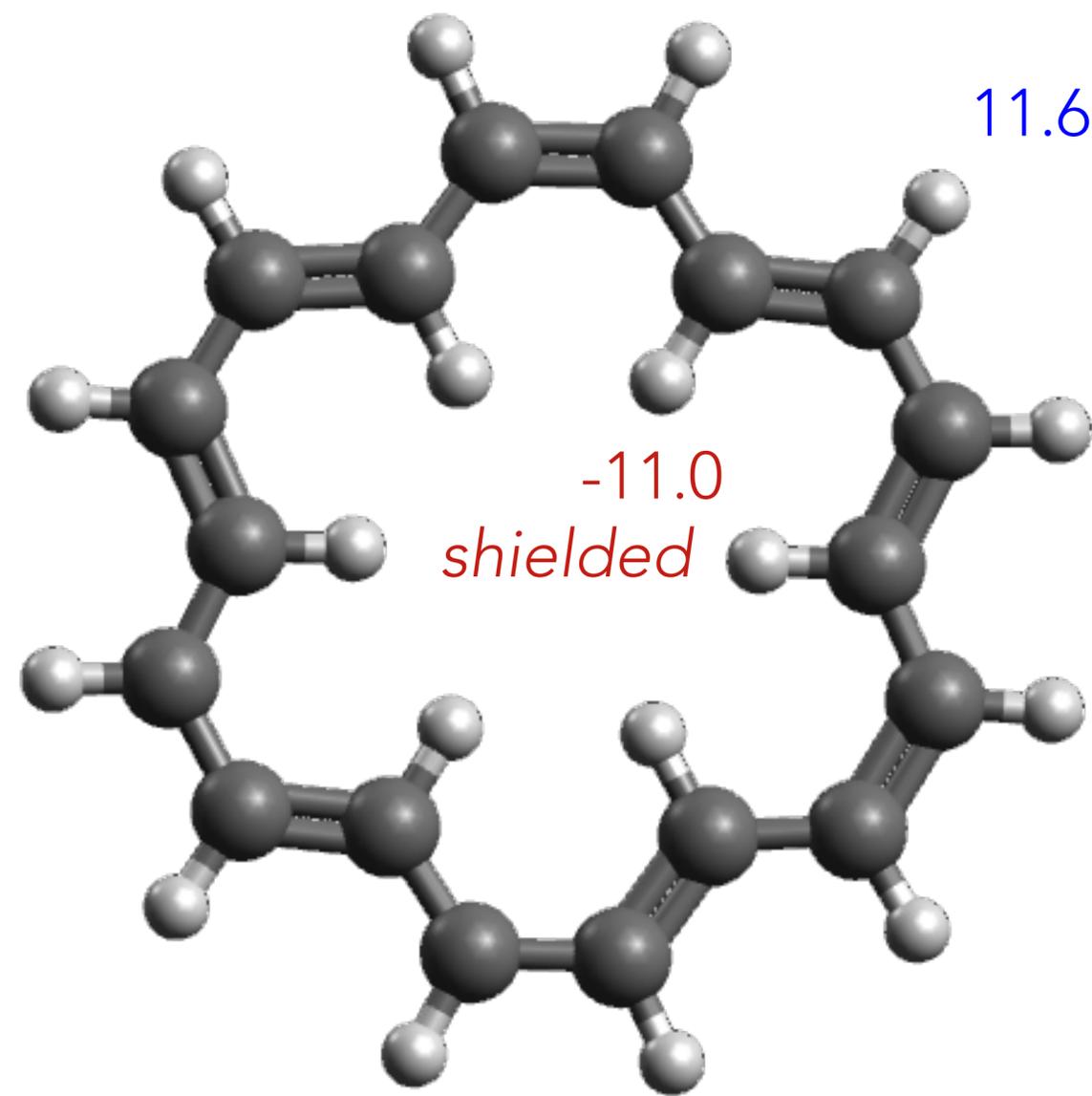

phenanthrene

4-ethynyl-phenanthrene

Exercise 11: Ring current vs. shielding

Estimate $\delta(^1\mathrm{H})$ for [18]-annulene shown below with the `RI-B3LYP/def2TZVPP@RI-B3LYP(D3BJ)/def2TZVPP` model, and compare the values with that of benzene
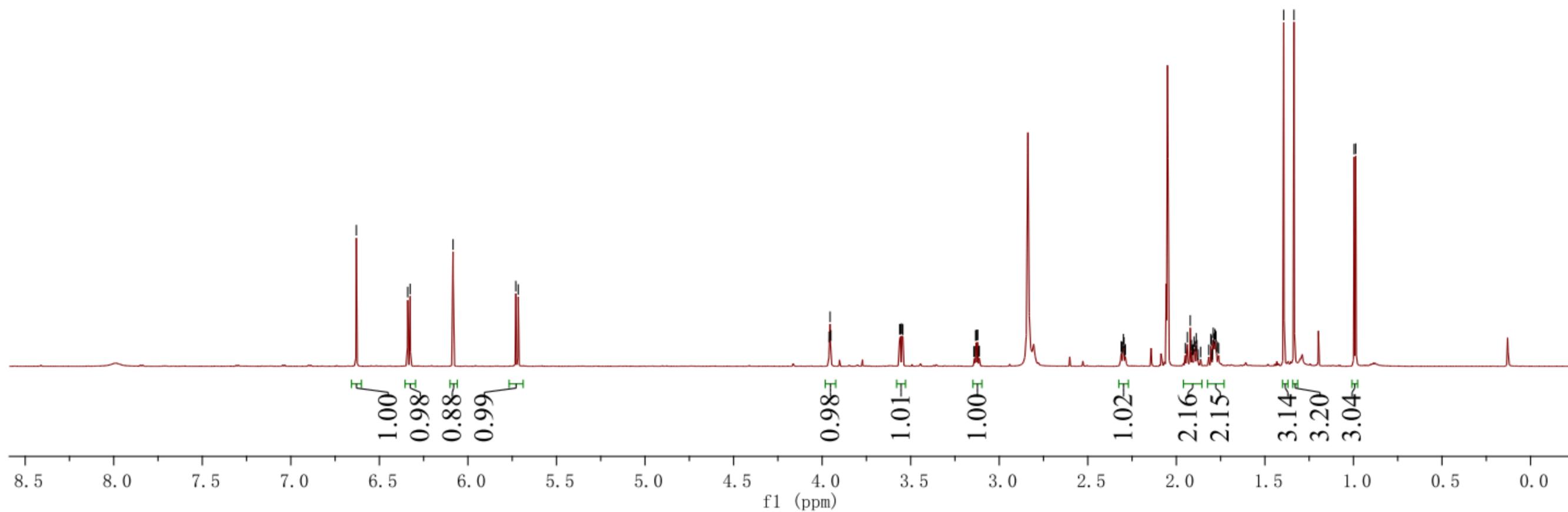

[18]-annulene

Solution

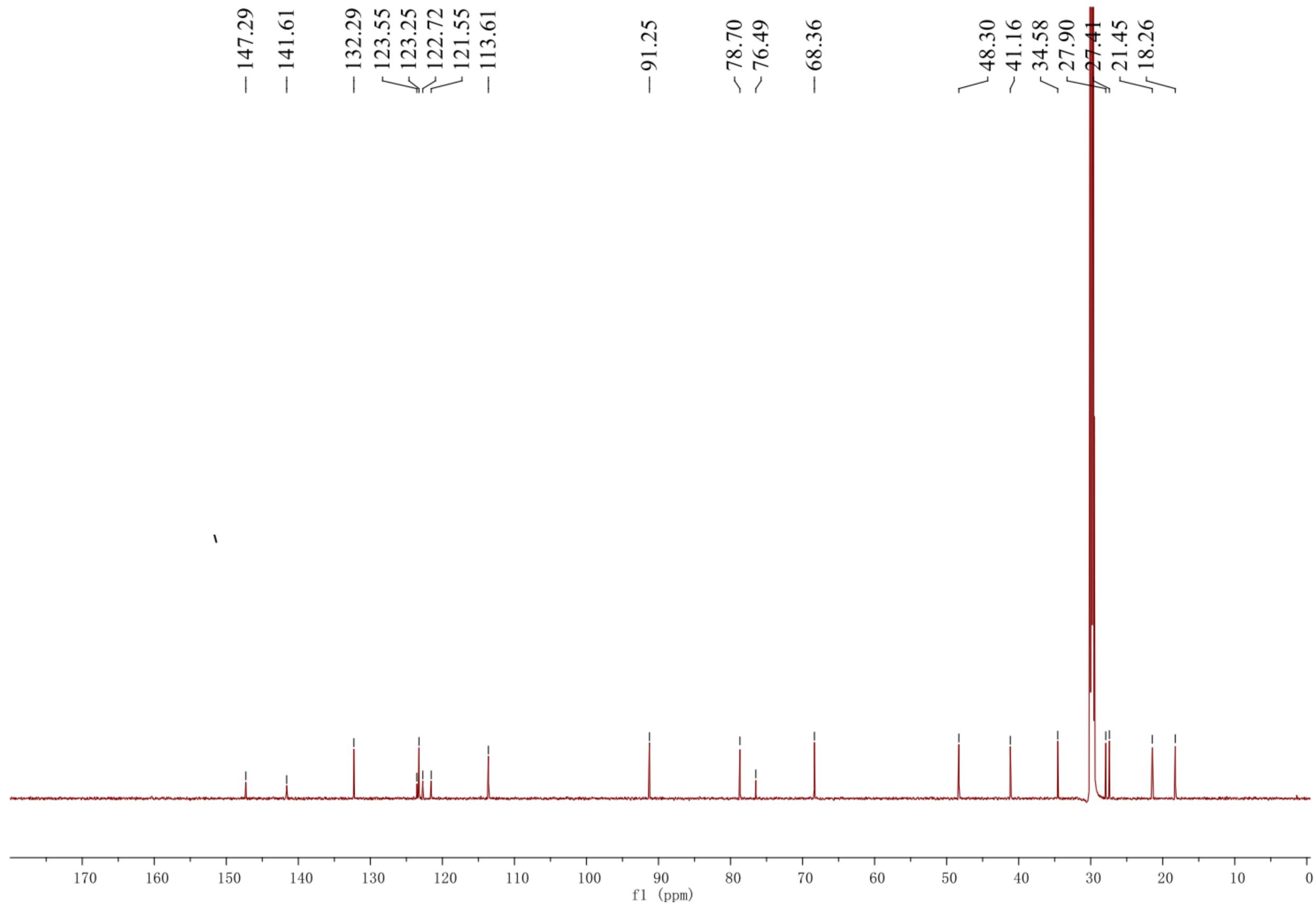11.6

-11.0
shielded

[18]-annulene

Exercise 12: Assign an experimental spectrum

Experimental NMR data, [1]H (700 MHz, in acetone-d6) and [13]C (175 MHz, in acetone-d6), of an organic compound, Euroticin A, extracted from the fungus Eurotium, are given in the next two slides. Compare these chemical shifts to results with the `RI-B3LYP/def2TZVPP@RI-B3LYP(D3BJ)/def2TZVPP` model and assign the experimental data.
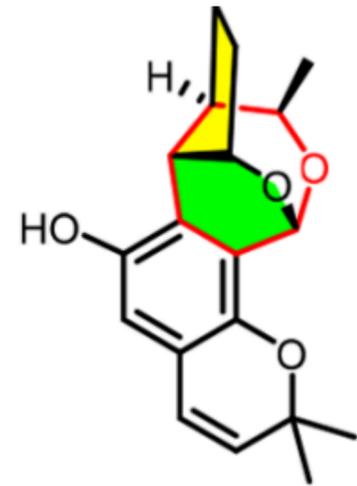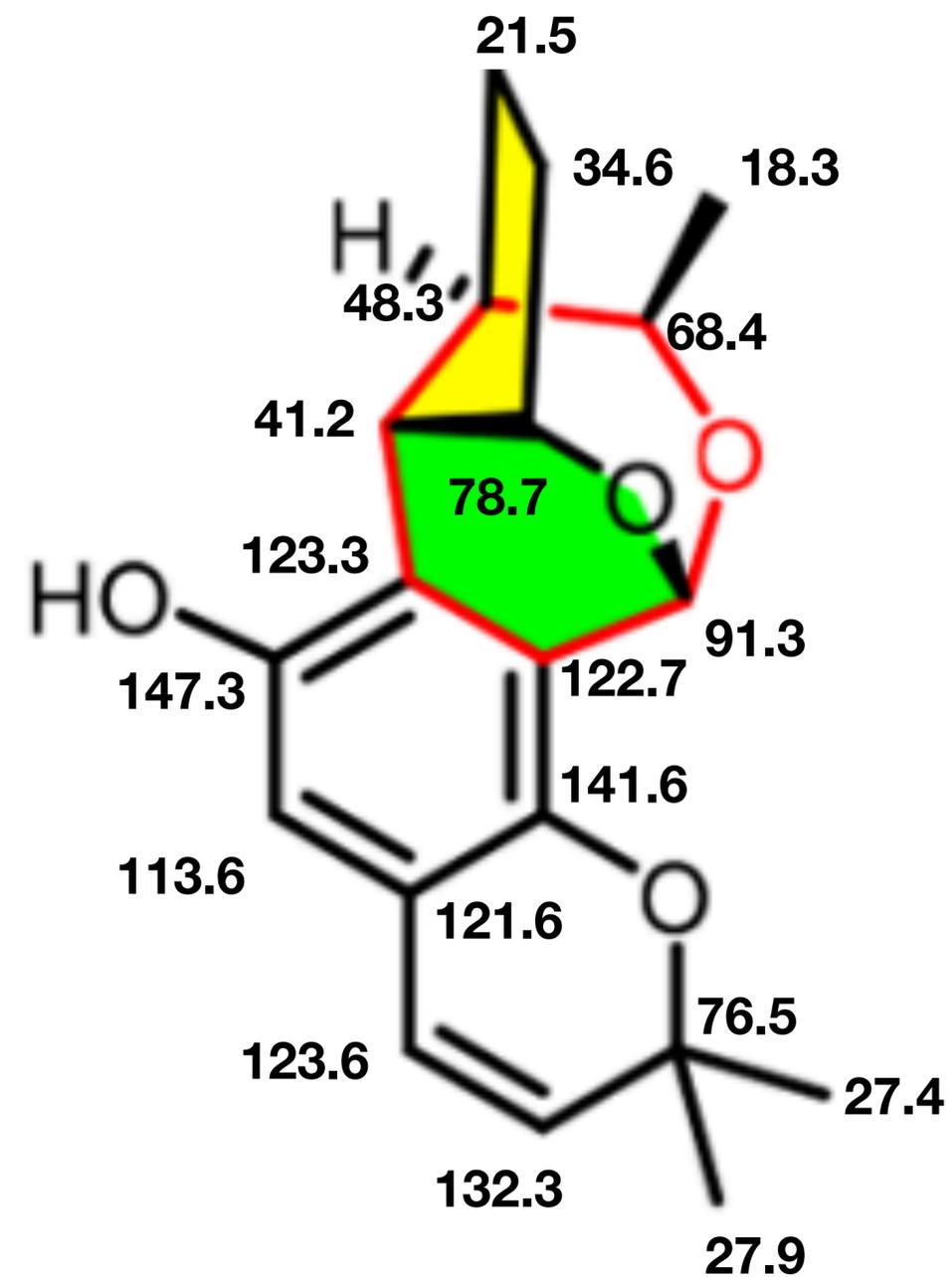

Euroticin A

If there is at least 1 line in the experimental and calculated spectrum that can be unambiguously assigned, then we can use it as an *internal reference* to correct for any systematic error in DFT calculations. Compare the DFT results after correcting using an internal reference.

147.29
141.61
132.29
123.55
123.25
122.72
121.55
113.61
91.25
78.70
76.49
68.36
48.30
41.16
34.58
27.90
27.41
21.45
18.26

f1 (ppm)

Solution

Exp	DFT	DFT (shifted)
147.3	155.4	147.3
141.6	150.3	142.3
132.3	141.2	133.3
123.6	131.2	123.1
123.3	131	122.9
122.7	130.3	122.2
121.6	130	121.9
113.6	117.6	109.5
91.3	99.9	91.8
78.7	87.2	79.1
76.5	85.5	77.4
68.4	75.9	67.8
48.3	54.9	46.8
41.2	47.4	39.3
34.6	38.8	30.7
27.9	30.5	22.5
27.4	27	19.0
21.5	25.6	17.5
18.3	20	11.9
Mean error	6.3	2.2

Happy computing!