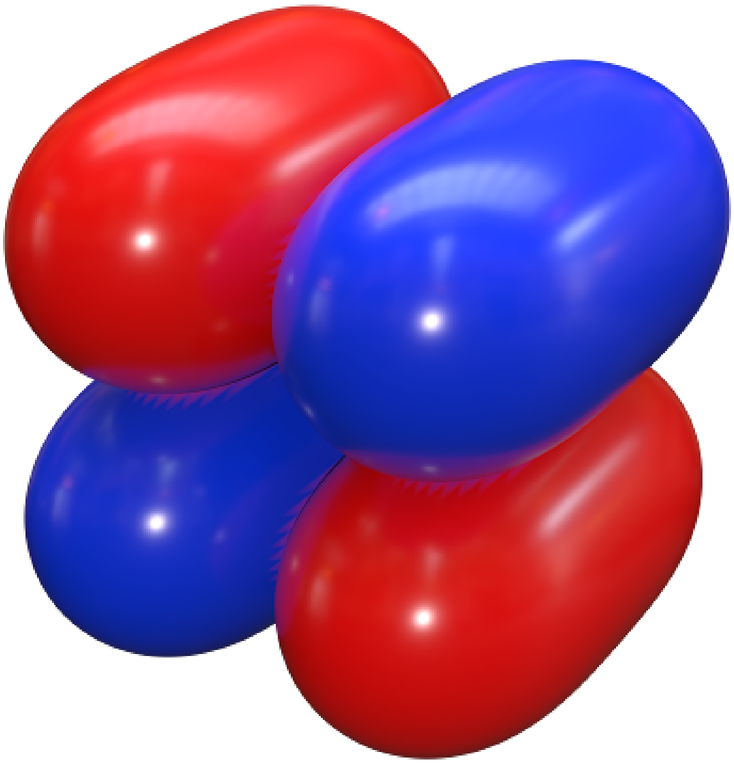
Sakura Science Computational Chemistry Workshop Series:

Reaction Pathway Exploration

February 18, 2025



1 Introduction

In this workshop, we will delve into the exciting world of computational chemistry, focusing on exploring chemical reactions and identifying transition states (TSs). We will use a powerful combination of tools: the xTB path and ORCA 6, which are interfaced through our in-house Swiss-army knife utility, the computational molecular and material environment (CMMDE) code.

The xTB path approach implemented in the XTB program offers a rapid and efficient method for initial transition state allocation. Although finding a transition state structure is sometimes a bit tedious, this approach can decrease the barrier of finding the transition state. This tool uses a metadynamics reaction path finder, which applies a simple metadynamics bias potential to guide the system from reactants to products. The xTB[1–3] method's speed can quickly provide a good estimate of the transition state structure, which can be refined using higher-level methods in ORCA.

By combining the rapid exploration capabilities of the xTB path with the high-accuracy calculations of ORCA, we can efficiently and accurately locate transition states for a wide range of chemical reactions. This approach is particularly powerful for studying complex reactions of large systems where traditional methods might be computationally prohibitive.

Throughout this workshop, you will gain hands-on experience with these tools, learning how to set up calculations, interpret results, and troubleshoot common issues/errors. By the end, you will have a solid foundation in modern computational methods for exploring chemical reactions and identifying transition states. As a case study, we will take an example from our previous work on the single atom catalysis (SAC) system[4]. In the previous work, SAC of nickel and palladium were utilize to catalyze the Suzuki-Miyaura cross-coupling reaction.

2 Prediction of the Prospective Transition States at xTB Level

1. Connect to the SSC workstation by using the user and password from the previous workshop session. You can also see from the following information:

```
address: catalyst.compscience.app
user: ssc
password: sakura
```

2. Make your directory and go into it by typing:

```
mkdir yourname; cd yourname
```

Ensure that you replace `yourname` with your own name. If you made your directory last week, you just need to type:

```
cd yourname
```

3. Copy necessary workshop materials from the resource directory.

```
cp -r /home/ssc/SSC_Workshop/Day3/* .
```

4. Enter the intermediate A directory by typing:

```
cd A
```

5. Inside this directory, you will find `geom.xyz` that contains the molecular structure of the intermediate A as shown in Fig. 1. This structure was optimized at GFN2-xTB level.

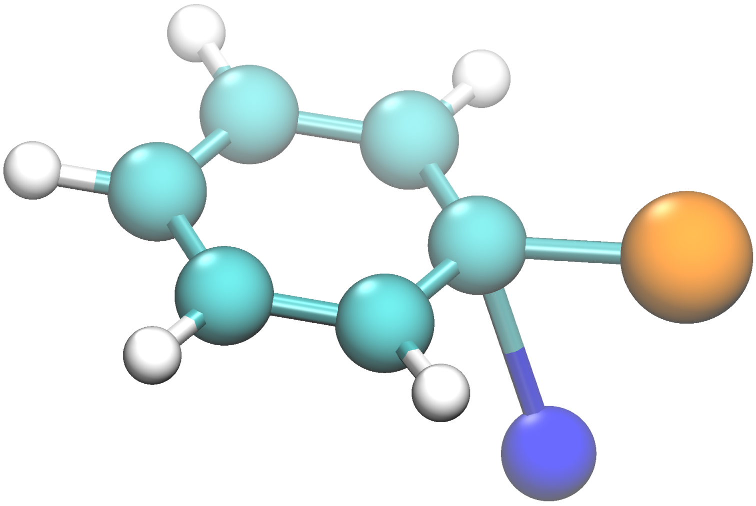


Figure 1: Optimized structure of intermediate A at GFN2-xTB level. The green, blue, orange, and white colors denote carbon, nickel, chlor, and hydrogen atoms, respectively.

6. Optimize the structure as well as calculate its vibrational frequencies by typing:

```
cmmde.py -i geom.xyz -j opt,freq
```

Note that in this case, CMMDE calls the ORCA program to perform the geometry optimization, where the XTB code will be called for each optimization cycle. After confirming the optimization cycle convergency, the Hessian calculation will be performed to obtain the vibrational frequencies of the intermediate A.

7. The output should be in the `cmmd.out` file. You can obtain the details of thermochemistry information for each intermediate by typing:

```
cmmdepost.py -j thermo
```

So that it will display:

```
######INFORMASI ENERGI HOMO & LUMO######
Energi HOMO = -388.25 eV
Energi LUMO = -301.45 eV
Gap HOMO-LUMO = 86.79 eV

######INFORMASI ENERGI ELEKTRONIK & KOREKSI TERMAL######
Energi elektronik = -24.71285646 Hartree = -64883.60463573 kJ/mol
Zero point energy (ZPE) = 0.08625301 Hartree = 226.457277755 kJ/mol
Koreksi termal vibrasi = 0.00534062 Hartree = 14.021797809999999 kJ/mol
Koreksi termal rotasi = 0.00141627 Hartree = 3.7184168850000003 kJ/mol
Koreksi termal translasi = 0.00141627 Hartree = 3.7184168850000003 kJ/mol
Total koreksi termal = 0.00817316 Hartree = 21.458631580000002 kJ/mol

######INFORMASI BESARAN TERMOKIMIA######
Entalpi (H) = -24.61748608 Hartree = -64633.20970304 kj/mol
Energi bebas Gibbs (G) = -24.66042854 Hartree = -64745.95513177 kJ/mol
```

At this point, however, you should not care about the physical meaning of the above-mentioned quantities. They can have the physical meaning if you subtract the values with another chemical species with the same number of atoms.

8. Enter the intermediate B directory and do the same thing.

```
cd ../B
```

```
cmmde.py -i geom.xyz -j opt,freq
```

If you want, but it maybe unnecessary, you can also type:

```
cmmdepost.py -j thermo
```

You can also download `cmmd.xyz` file that contains the optimized structure of intermediate B at GFN2-xTB level. As usual, you can download it by using the SFTP method in the Termius or scp by using your favorite terminal/console or its emulator. The optimized structure of intermediate B is shown in Fig. 2.

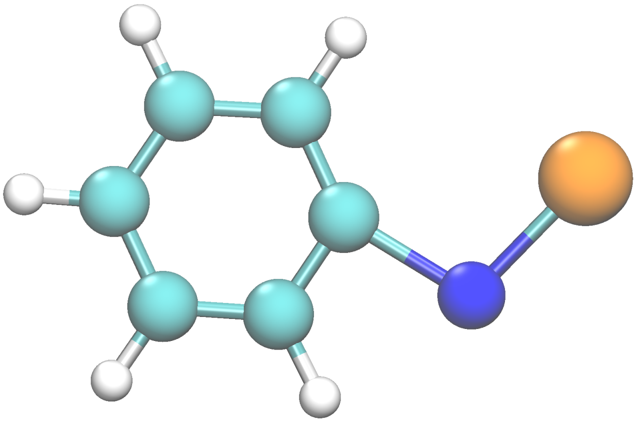


Figure 2: The optimized structure of intermediate B at GFN2-xTB level. The green, blue, orange, and white colors denote carbon, nickel, chlor, and hydrogen atoms, respectively.

9. Make a directory to predict the prospective TS structure.

```
cd ../; mkdir path_A_B; cd path_A_B
```

10. Perform the reaction path prediction by typing:

```
cmmde.py -s xtb -j path -i ../A/cmmd.xyz -produk ../B/cmmd.xyz
```

11. Download all output files to your local computer. If you want, visualize the reaction path animation (`xtbpath.xyz`) by using VMD or Avogadro. The candidate for transition state structure will be `xtbpath_ts.xyz`. Sometimes, this structure is good, but occasionally, it is not good enough for further transition state search.

12. Reoptimize the obtained `xtbpath_ts.xyz` by using the saddle point finder implemented in the ORCA 6. You can simply type:

```
cd ../; mkdir TS_A_B; cd TS_A_B
```

and

```
cmmde.py -j ts,freq -i ../path_A_B/xtbpath_ts.xyz
```

To check whether you got a true TS structure, you should have the imaginary frequency (usually, many programs represent this as the negative frequency) by typing:

```
grep imaginary cmmd.out
```

It will display something like:

```
6: -177.72 cm**-1 ***imaginary mode***
```

The first number (6) represents the vibrational mode index. A large negative value (usually more than 100 cm^{-1}) indicates you successfully obtained a good transition state structure. If you want to plot the vibrational mode of this TS, you can simply type:

```
/opt/orca6/orca_pltvib cmmd.out 6
```

Note that 6 in this case is the vibrational mode index. You can have different indexes depending on the optimized TS structure. You can download the resulted `cmmd.out.v006.xyz` file to your local computer and visualize it by using VMD or Avogadro.

13. Visualize your TS structure (`cmmd.xyz`) by using VMD or Avogadro. The optimized TS structure for A to B transformation is shown in Fig. 3.

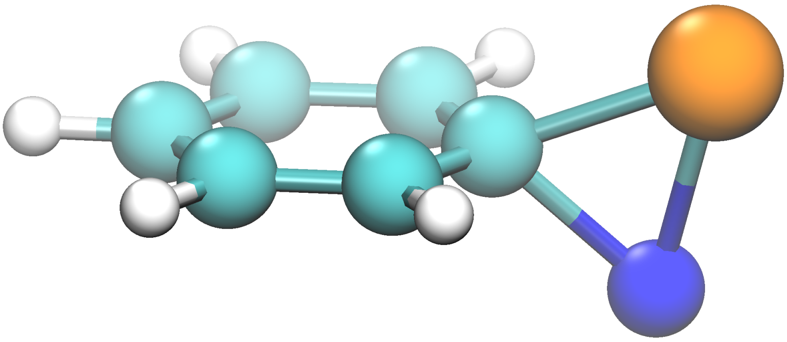


Figure 3: Optimized TS structure for A to B transformation. This is the first elementary step of the Suzuki-Miyaura cross-coupling reaction.

14. Assume that you are still in the `TS_A_B` directory, check the activation and reaction energies by typing:

```
cd ../
```

```
cmmdepost.py -j ts -irx "1A->1TS_A_B->1B"
```

This command will display the following output:

```
Delta_H_forward* = 2.34 kJ/mol

Delta_H_backward* = 42.00 kJ/mol

Delta_G_forward* = 4.11 kJ/mol

Delta_G_backward* = 45.65 kJ/mol

Delta_S_forward* = -5.93 J/(mol K)

Delta_S_backward* = -12.24 J/(mol K)
```

Based on the present GFN2-xTB calculation, the transformation of A to B will require a relatively small energy of 4.11 kJ/mol to proceed at 298.15 K. Note that this temperature is the default in the ORCA program for frequency calculation. You can specify the temperature by using the `-t` or `--temp` option followed by a number in the CMMDE calculation.

3 Additional Task

1. Recalculate the $\Delta G^\ddagger$ at DFT level.

   You can make a separate folder to run the DFT calculation. Copy the previous `cmmd.xyz` file to your new directory and rename it as `geom.xyz`. Here is a hint for the DFT calculation using the CMMDE:

   ```
   cmmde.py -i geom.xyz -j opt,freq -m "B3LYP␣def2-TZVP"
   ```

   The above command is used if you want to perform your calculation by using the B3LYP functional[5] with the basis set of def2-TZVP.

2. Try different metals other than nickel and see how the Gibbs activation energies change upon changing the metals.

References

[1] Sebastian Ehlert et al. “Robust and Efficient Implicit Solvation Model for Fast Semiempirical Methods”. In: *Journal of Chemical Theory and Computation* 17.7 (July 2021), pp. 4250–4261. ISSN: 1549-9618. DOI: `10.1021/acs.jctc.1c00471`. URL: `https://doi.org/10.1021/acs.jctc.1c00471` (visited on 03/14/2024).

[2] Stefan Grimme, Christoph Bannwarth, and Philip Shushkov. “A Robust and Accurate Tight-Binding Quantum Chemical Method for Structures, Vibrational Frequencies, and Noncovalent Interactions of Large Molecular Systems Parametrized for All spd-Block Elements (Z = 1–86)”. In: *Journal of Chemical Theory and Computation* 13.5 (May 2017), pp. 1989–2009. ISSN: 1549-9618. DOI: `10.1021/acs.jctc.7b00118`. URL: `http://dx.doi.org/10.1021/acs.jctc.7b00118` (visited on 10/10/2017).

[3] Christoph Plett and Stefan Grimme. “Automated and Efficient Generation of General Molecular Aggregate Structures”. en. In: *Angewandte Chemie International Edition* 62.4 (2023), e202214477. ISSN: 1521-3773. DOI: `10.1002/anie.202214477`. URL: `https://onlinelibrary.wiley.com/doi/abs/10.1002/anie.202214477` (visited on 06/03/2024).

[4] Laila Roikhatul Jannah et al. “Exploring the energetics of Suzuki cross-coupling reaction: A computational study of palladium and nickel catalysts”. In: *Molecular Catalysis* 560 (May 2024), p. 114103. ISSN: 2468-8231. DOI: `10.1016/j.mcat.2024.114103`. URL: `https://www.sciencedirect.com/science/article/pii/S2468823124002864` (visited on 02/16/2025).

[5] A. D. Becke. “Density-functional exchange-energy approximation with correct asymptotic behavior”. In: *Physical Review A* 38.6 (Sept. 1988), pp. 3098–3100. DOI: `10.1103/PhysRevA.38.3098`. URL: `http://link.aps.org/doi/10.1103/PhysRevA.38.3098` (visited on 08/29/2015).