

Summary of how to find the free energy of reaction and activation energy barrier:  
For a generic reaction  $R1 + R2 \rightarrow P1 + P2$  that goes through transition state TS

### For R1, R2, P1 and P2:

On your laptop, after building your molecule in Maestro,

- Click on Tasks > Single Point Energy (Jaguar)
- DON'T RUN the job. Instead change the Job Name to something short that makes sense to you, then click the gear icon on the right and select **Write**.
- The program saves the relevant files in the subdirectory **jobname** in your local home directory. The file you're interested in is **jobname/jobname.in**

Everything else is done on saber3:

- Copy your **template.in** file to a new input file, e.g. **R1.in**
- Replace (e.g. cut and paste) the coordinates from your locally created **jobname/jobname.in** to **R1.in** and do be careful of extraneous spaces, blank lines, etc, that might cause problems. Jaguar is very fussy about formatting!
- Now you can run the job. If the input file is called **R1.in**, type: **jrun R1.in**  
[ Technically, **\$SCHRODINGER/jaguar run filename.in -args** (see alias in *.bashrc* file) ]
- When job is finished, record the final electronic energy from the end of **R1.log**, let's call it  $E_{elec}(R1)$ . It will be in atomic units.

\*Always: (1) Read the end of the log file to see if the job completed normally and there were no errors. (2) It's also good to copy the .01.in file (or the coordinates) to your laptop to verify it looks OK on Maestro.

- Starting from the completed **R1.01.in**, create the files **R1\_solv.in** and **R1\_afreq.in**
  - Remove the first line that begins with MAEFILE
  - For the solvation calculation, replace *igeopt=1* with *isolv=2*
  - For the analytical frequency calculation, replace *igeopt=1* with *ifreq=1* and also delete *ip11=2* and *icfit=1*
  - You can now run these Jaguar jobs (**jrun R1\_solv.in** and **jrun R1\_afreq.in**)
- When the solvation calculation is finished, record the solvation energy from the end of **R1\_solv.out** (you'll see 'sfinal') and let's call it  $E_{solv}(R1)$ . It will be in kcal/mol.
- When the frequency calculation is finished, you will find the enthalpy and free energy corrections. At the end of **R1\_afreq.out**, you will see values for  $H_{tot}$  and  $G_{tot}$ .
  - For R1,  $H_{corr}(R1) = H_{tot} - E_{elec}(R1)$  and  $G_{corr}(R1) = G_{tot} - E_{elec}(R1)$
- Repeat all this for R2, P1 and P2. When you're done, you will have  $E_{elec}$ ,  $E_{solv}$ ,  $H_{corr}$  and  $G_{corr}$  for all four molecules. [An Excel spreadsheet will simplify this process!]
- Now you will calculate the CHANGE in energy for the reaction, and remember change is always products minus reactants:
  - $\Delta E_{elec} = \{ E_{elec}(P1) + E_{elec}(P2) \} - \{ E_{elec}(R1) + E_{elec}(R2) \}$
  - $\Delta E_{solv} = \{ E_{solv}(P1) + E_{solv}(P2) \} - \{ E_{solv}(R1) + E_{solv}(R2) \}$
  - $\Delta H_{corr} = \{ H_{corr}(P1) + H_{corr}(P2) \} - \{ H_{corr}(R1) + H_{corr}(R2) \}$
  - $\Delta G_{corr} = \{ G_{corr}(P1) + G_{corr}(P2) \} - \{ G_{corr}(R1) + G_{corr}(R2) \}$
  - Convert anything in a.u. to kcal/mol by multiplying 627.5096
  - Calculate the entropy correction,  $-0.5T\Delta S = 0.5 \times \{ \Delta G_{corr} - \Delta H_{corr} \}$
- The final change in free energy of the reaction in solution at 298K can now be calculated using  $\Delta G_{298} = \Delta E_{elec} + \Delta E_{solv} + \Delta H_{corr} - 0.5T\Delta S$

### For TS:

- After building the transition state as best you can in Maestro with appropriate transition state distances, you will create a Jaguar file, let's call it **TS\_con.in**
- Re-read this Jaguar input file into Maestro and turn on the atom labels. (Be sure you're using the Custom label "Maestro Atom Name")
- Prepare the bond constraints in **TS\_con.in** by adding the &coord section  
e.g. 

```
&coord  
O8 H9 # 1.25  
C4 O8 # 1.80  
&
```
- Now you can run this Jaguar job: You are performing a constrained geometry optimization where you optimize the structure within the imposed constraints.
- When job is finished, you will now need to set up the actual transition state calculation. Starting from the completed TS\_con.01.in, create a new file let's call it TS1.in
  - Remove the first line that designates the Maestro file
  - Replace each constrained value in the &coord section with #active  
e.g. O8 H9 #active
  - Change *igeopt=1* to *igeopt=2*
  - Run the Jaguar job.
- When job is finished, record the final electronic energy from the end of **TS1.log**, let's call it  $E_{\text{elec}}(\text{TS})$ . It will be in atomic units
- Starting from TS1.01.in, create the files TS1\_solv.in and TS1\_afreq.in the same way as described in the previous section and run the Jaguar jobs.

\* Transition states are harder to optimize. Always:

(1) Read the end of the log file to check that the job completed without error or running out of cycles (the default is 99).

(2) Look at your structure in Maestro to verify that it looks like a transition state and has not fallen to reactants or products. If it looks good, sketch the TS in your notebook and write down the distances of all bonds involved in the making-and-breaking process. (These should correspond to "transition" distances)

(3) Check the last several eigenvectors in the TS.out file to make sure at least some of them match the bonds involved in (2).

- When the solvation calculation is finished, record the solvation energy from the end of **TS\_solv.out**, and when the frequency calculation is finished, calculate  $H_{\text{corr}}(\text{TS})$  and  $G_{\text{corr}}(\text{TS})$  from the **TS\_afreq.out** file.

\*\*Check the **TS\_afreq.out** file to make sure there is one large negative frequency and record this value next to your structure.

- You can calculate the barrier in the same way as previously mentioned. Typically you compare the barrier to the reactants and any added "catalyst" molecules [From TS theory, we assume:  $E_a \sim \Delta G_{\text{barrier},298} = \Delta E_{\text{elec}} + \Delta E_{\text{solv}} + \Delta H_{\text{corr}} - 0.5T\Delta S$ ]