Chem 106: Computational Handout 2
Transition State for an S_N2 Reaction

Objectives: scan a bond length to locate a transition state, follow the minimum energy path, calculate reaction barriers with and without solvation

In This Exercise: we will locate the transition state for the identity displacement of methyl chloride by chloride using AM1, a standard semi-empirical method. These methods offer rough accuracy at a very small cost (in time). We will also conduct an intrinsic reaction coordinate (IRC) analysis to locate the minimum energy path (MEP) on the potential energy surface (PES).
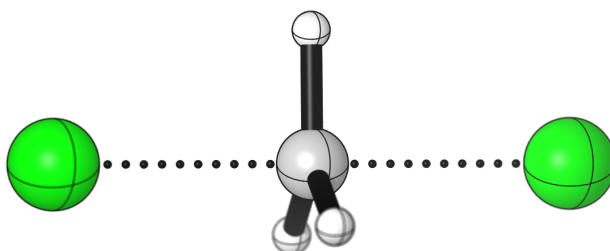
Setup: Login to Odyssey and update your `chem106_calculations` git repository. Locally, start GaussView. For instructions, please see handouts 0 and 1.

Note: All the output files are available in the repository if your jobs do not run in a timely fashion.

Draw Initial Structures

1. Draw methyl chloride in GaussView. Save this file as `MeCl_isolated.gjf`.

2. Edit the file:

```
%mem=1GB
#p am1 opt freq=noraman

isolated MeCl

0 1
 C                  -0.09595300    -0.17418100     0.40262200
 H                   0.96362200     0.15329000     0.42484000
 H                  -0.78057700     0.68297800     0.23830300
 H                  -0.25710300    -0.97071100    -0.35236400
 Cl                 -0.47766800    -0.86708700     2.00425800
```

Remember, at least one blank line is needed at the end of the file. We are using AM1 here, another semi-empirical method ("Austin Model 1").

3. Draw chloride anion in a new file. Save this file as `Cl_isolated.gjf` and edit the file similarly. You will need to set the charge and multiplicity card to `-1 1` this time (negatively charged singlet).

4. Copy these files to Odyssey. You can run them in a new jobs folder if you like. Make a copy of the `jobs_clean` folder in `chem106_calculations`:

```
cp -r jobs_clean new_dir_name
```

5. Submit the jobs: `./submit.sh 1 serial_requeue 5 2000` (1 core, 5 minute limit, 2 GB RAM).

6. Ensure the jobs finish correctly:

```
cd output
tail -n1 *.out
```

If the jobs worked, the last line will say `Normal termination of Gaussian`... If not, then inspect the error message and try again. Download these files to your computer.

Frozen Optimization

To find the transition state for this S_N2 reaction, we need to put the chloride and methyl chloride reactants in the same file.

1. Open `MeCl_isolated.out` in GaussView. View the last geometry.

2. Add a chloride roughly collinear with the existing C–Cl axis. Use the bond distance tool to set the new Cl–C distance to 3.5 Å.

3. Save this geometry as a new input file, `MeCl_freeze.gjf`. Edit the file:

```
%mem=1GB
#p opt=modredundant am1

MeCl + Cl- frozen

-1 1
 C                  0.14333800     0.65469200    -0.23620000
 H                  0.03830800    -0.01714600    -1.11430700
 H                 -0.80355400     0.69290900     0.34294300
 H                  0.98449100     0.32564900     0.41006800
 Cl                -0.56266000    -2.56992200     0.92716700
 Cl                 0.49917300     2.27994700    -0.82254900

 B 1 5 F
```

The `modredundant` option means to optimize this structure with a constraint, which is specified after the geometry specification (separated by a blank line). `B 1 5 F` means to freeze the bond between atoms 1 and 5, but let everything else relax. Although more constraints can be added for more complicated systems, it is generally the case that optimizations will not perform well with more than one constraint.

Perform a Relaxed Scan

Now, we need to gradually move the chloride anion towards methyl chloride. We are looking for the energy to increase and the gradient to decrease in the neighborhood of the transition state.

1. Download the `MeCl_freeze.out` file to your computer. Open the optimized geometry and save it as a new input file, `MeCl_scan.gjf`.

2. Edit the file, changing the redundant coordinate from a "freeze" (`F`) to a scan (`s`):

```
%mem=1GB
#p am1 opt=modredundant

MeCl scan

-1 1
 C                  -0.09595300    -0.17418100     0.40262200
 H                   0.96362200     0.15329000     0.42484000
 H                  -0.78057700     0.68297800     0.23830300
 H                  -0.25710300    -0.97071100    -0.35236400
 Cl                  0.65193112     1.18342176    -2.73546405
 Cl                 -0.47766800    -0.86708700     2.00425800

B 1 5 S 40 -0.05
```

This means "take 40 steps, shrinking the bond between atoms 1 and 5 by 0.05 Å every step." This will take us from 3.5 Å to 1.5 Å, which is just a bit less than the nominal C–Cl bond length. (When setting up more complex systems, it is worth knowing what the bond length is at your particular level of theory.)

3. Run this job (5 minutes is more than enough). Download the file and view the results in GaussView. Go to Results…Scan and expand the graph:
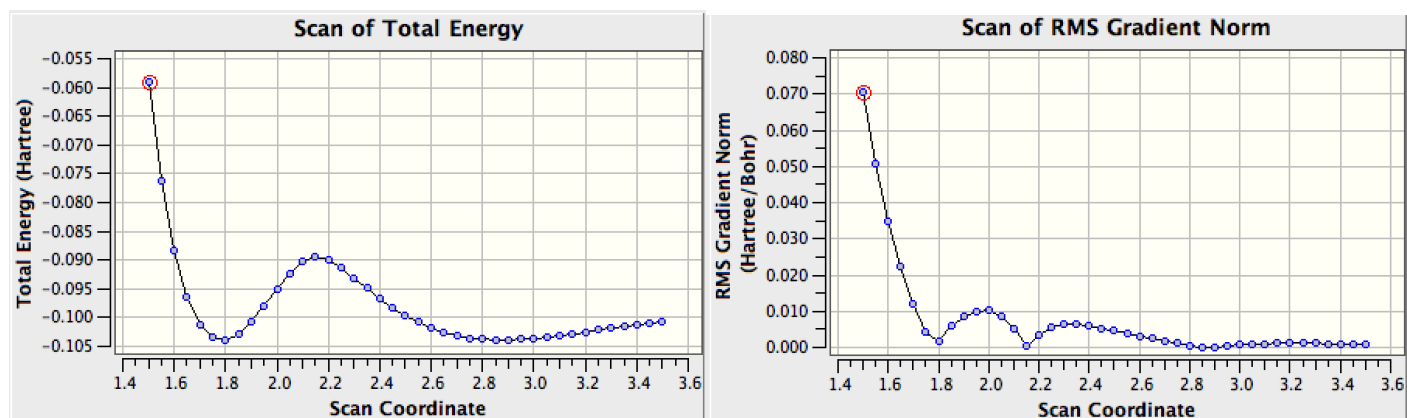
Clicking on any dot will show you the geometry at that scan point. There is an ion-dipole precomplex at around 2.9 Å that is more stable than the isolated reactants, a transition state around 2.2 Å, and an ion-dipole post-complex that is symmetric to the precomplex. These are most likely true stationary points, as judged by the small gradients.

Locate the Transition State

1. Take the scan geometry that is closest to the transition state (i.e., the one with the lowest gradient) and save it as `MeCl_ts.gjf`:

```
%mem=1GB
#p opt=(ts,noeigentest,calcfc) freq=noraman am1

Title Card Required

-1 1
 C                     0.02662000   -0.00020200   -0.00008900
 H                    -0.00315600   -0.94118100   -0.56458200
 H                    -0.00329400   -0.01859200    1.09706500
 H                    -0.00333700    0.95917300   -0.53272700
 Cl                    2.13665400    0.00005600    0.00002400
 Cl                   -2.14547300    0.00005000    0.00002200
```

`opt=(ts,noeigentest,calcfc)` The use of parentheses and commas after a keyword is the standard way to specify more than one option for a particular keyword. This calls for an optimization to a saddle point, rather than a local minimum. Such a search requires the force constant matrix, which we will calculate before proceeding (`calcfc`).
2. Run the job on Odyssey.

3. Download the file and animate the imaginary mode (Results…Vibrations).

Displace Along the Reaction Coordinate

This structure has a low gradient and one imaginary frequency, so it is a true transition state. But, how do we know it is a transition state that actually connects the starting materials and products? One simple way is to displace along the imaginary mode in both directions and optimize the resulting structures.

1. Return to the Results…Vibrations dialog.

2. Select the imaginary mode and click on "Manual Displacement" at the very bottom. Select a reasonable displacement (in this case, about +0.4), and click "Save Structure…" to make a new input file.

Alert! The sign in the normal mode vector is arbitrary. Positive *might* mean towards product, but it might also mean towards starting material. (In this case, the starting materials and products are symmetric, but they are not the same because each atom is labeled with a unique number.)

3. Save the forward structure as `MeCl_postcomplex.gjf` and the reverse structure as `MeCl_precomplex.gjf`. Edit these files to perform AM1 optimization followed by a frequency job.

Intrinsic Reaction Coordinate Analysis

The method above is relatively inexpensive, but could give misleading results if the minimum energy path "turns" significantly from the imaginary mode vector. A better, but more expensive approach is to follow the minimum energy path in both directions. This is called IRC analysis.

1. Take the transition state geometry and save it as a new input file, `MeCl_ts_IRC_forward.gjf`, and GaussView.

2. Set the route card to the following:

```
#p am1 IRC=(forward,calcfc,maxpoints=300,stepsize=1,recalc=10)
```

This means to follow the minimum energy path in the "forward" (see above) direction up to 300 points, taking steps of 10 units at a time (0.01 $amu^{0.5}$ bohr) and recalculating the Hessian (the second derivative matrix) every 10 steps.

Alert! IRC analysis frequently fails to converge for numerical reasons. The usual culprit is a step size that is too large. For example, this calculation fails with the default step size of 10.

3. Make a copy of this file: `cp MeCl_ts_IRC_forward.gjf MeCl_ts_IRC_reverse.gjf`

4. Edit the second file to say `reverse` instead of `forward` in the route card.

5. Run both jobs and transfer the files back to your computer.

6. Open the files in GaussView. Results…IRC/Path shows the MEP:
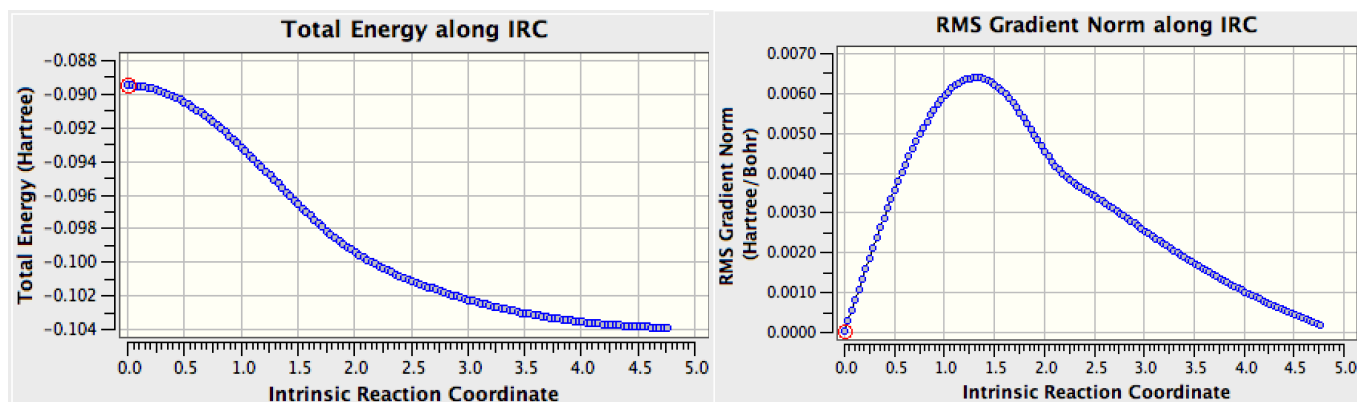
The transition state is located at IRC=0, and there is a corresponding zero in the gradient. The ion-dipole complex is located at IRC=4.3, where there is another zero in the gradient. This analysis verifies that the transition state connects the two minima. While there was not much doubt in this very simple system that this was the case, in more complex systems, such analyses can be very useful.

Analysis

What is the barrier of the reaction?

1. Define the zero of energy as the sum of the energies of isolated MeCl and Cl⁻:

```
~/chem106_calculations/SN2 $ grep "SCF Done" MeCl_isolated.out
 SCF Done:   E(RAM1) = -0.293874123263E-01 A.U. after    10 cycles
 SCF Done:   E(RAM1) = -0.301434199862E-01 A.U. after    10 cycles
 SCF Done:   E(RAM1) = -0.302377887022E-01 A.U. after    10 cycles
 SCF Done:   E(RAM1) = -0.302439258233E-01 A.U. after     9 cycles
 SCF Done:   E(RAM1) = -0.302439258233E-01 A.U. after     2 cycles

~/chem106_calculations/SN2 $ grep "SCF Done" Cl_isolated.out
 SCF Done:   E(RAM1) = -0.600109765117E-01 A.U. after     2 cycles
 SCF Done:   E(RAM1) = -0.600109765117E-01 A.U. after     2 cycles
 SCF Done:   E(RAM1) = -0.600109765117E-01 A.U. after     2 cycles
```

In English: search for the phrase "SCF Done" in the specified file. There are multiple hits because the energy is calculated once for every step of the geometry optimization.

We can make this simpler by showing only the last hit:

```
~/chem106_calculations/SN2 $ grep "SCF Done" MeCl_isolated.out | tail -n1
 SCF Done:   E(RAM1) = -0.302439258233E-01 A.U. after     2 cycles

~/chem106_calculations/SN2 $ grep "SCF Done" Cl_isolated.out | tail -n1
 SCF Done:   E(RAM1) = -0.600109765117E-01 A.U. after     2 cycles
```

The pipe, |, means "send to." We are sending the output of `grep` to `tail`, and asking for the last line.

Thus, the energy zero is the sum of these two numbers, –0.0902549 hartree.

2. Similarly, get the energy of the transition state. Subtract the energy zero from this number and multiply by 627.509469 to convert from hartree to kcal. What barrier do you get? (I get 0.5 kcal/mol).

3. What is the energy of the precomplex? (I get –8.6 kcal/mol).

4. What does this mean? Open the scan file again and go to Results…Scan. Right-click on the y-axis and select Properties. Set the units to kcal/mol and the zero to -56.6358 (the electronic energy of MeCl and Cl⁻ in kcal/mol).
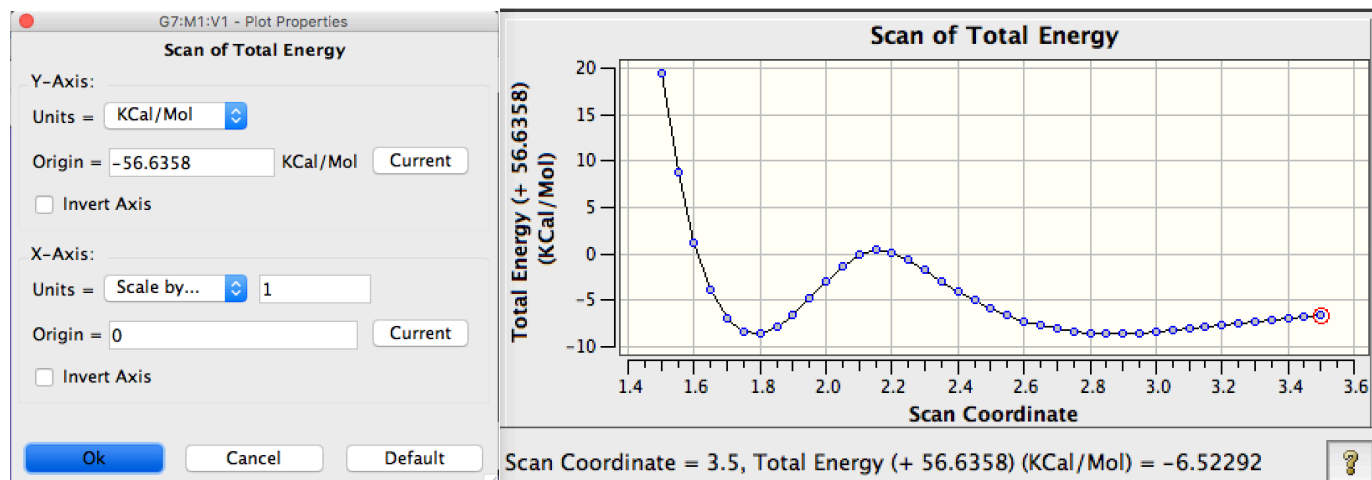
This calculation assumes the reactants are in the gas-phase. It is quite unfavorable to have an isolated chloride anion. As it comes into contact with the methyl chloride, it is "solvated" in an exothermic process. The barrier is approximately 9 kcal/mol above this.

Experimentally, it is found that gas-phase S_N2 reactions are very fast. This reaction is estimated to have a barrier of approximately 1 kcal/mol and a precomplex energy of –10 kcal/mol, in reasonable agreement with these calculations. In *solution*, S_N2 reactions have considerably higher barriers because desolvation is unfavorable.

5. Re-compute isolated chloride, isolated methyl chloride, and the SN2 transition state *in water* by taking the gas phase geometries and making new input files. Add this line to the route card:

```
scrf=(pcm,solvent=water)
```

The polarizable continuum model (PCM) is a standard way to account for solvation that includes the energetics of solute-solvent electrostatics, dispersion, and cavitation. Note that this method cannot account for any specific interactions such as hydrogen-bonding.

Note: In general, PCM solvation improves the quality of calculations significantly at little computational cost. The SMD model is another common alternative (change `pcm` to `smd` in the `scrf` keyword list). For a complete list of possible solvents and models, see:

http://gaussian.com/scrf/

6. Compute the new barrier:

```
~/chem106_calculations/SN2 $ grep "SCF Done" *pcm.out
Cl_isolated_pcm.out: SCF Done:  E(RAM1) = -0.180337956435      A.U. after    2 cycles
Cl_isolated_pcm.out: SCF Done:  E(RAM1) = -0.180337956435      A.U. after    2 cycles
Cl_isolated_pcm.out: SCF Done:  E(RAM1) = -0.180337956435      A.U. after    2 cycles
MeCl_isolated_pcm.out: SCF Done:  E(RAM1) = -0.318621362219E-01 A.U. after   12 cycles
MeCl_isolated_pcm.out: SCF Done:  E(RAM1) = -0.320101271619E-01 A.U. after   10 cycles
MeCl_isolated_pcm.out: SCF Done:  E(RAM1) = -0.319278402571E-01 A.U. after    9 cycles
MeCl_isolated_pcm.out: SCF Done:  E(RAM1) = -0.320193274552E-01 A.U. after    7 cycles
MeCl_isolated_pcm.out: SCF Done:  E(RAM1) = -0.320744467127E-01 A.U. after   10 cycles
MeCl_isolated_pcm.out: SCF Done:  E(RAM1) = -0.320744467126E-01 A.U. after    2 cycles
MeCl_ts_pcm.out: SCF Done:  E(RAM1) = -0.178768297999      A.U. after   12 cycles
MeCl_ts_pcm.out: SCF Done:  E(RAM1) = -0.178785222415      A.U. after    7 cycles
MeCl_ts_pcm.out: SCF Done:  E(RAM1) = -0.178785222415      A.U. after    2 cycles
```

(You can use a wildcard with `grep`, but `tail` no longer works as it would only show the last line over all three files.)

From this, we see the barrier is now much higher: 21.1 kcal/mol!

7. Neither of these calculations accounts for the entropy of bringing together two reactants. Recompute the barriers with free energies (instead of electronic energies as in the above). The free energy is found in each file on a line that contains "`thermal Free Energies`" (note the case). I get 7.2 (gas phase) and 27.7 kcal/mol (water).

Eugene Kwan
March 2017