IDNM 680: CHEMISTRY PROJECT

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Problem 1. Check the PDB file you obtained or are assigned, report the following information: PDB ID, research article associated with the structure, resolution of the structure, pH at which the crystal was grown, total number of amino acid residues in the structure, total number of crystal water molecules in the structure, active site residues' names and sequence numbers.

- Protein in Question: serine protease: trypsin
- PDB ID: 1FN8
- Research Article: "Fusarium oxysporum trypsin at atomic resolution at 100 and 283 K: a study of ligand binding." Rypniewski, W.R., et al. (2001) Acta Crystallogr D Biol Crystallogr 57: 8-19
- Resolution: 0.81 Angstroms
- Crystal Growth pH: 6
- Total amino acid residues: 227
- Total crystal water molecules: 360 (I think. The article is difficult to understand here, and it appears they used six different models of trypsin.)
- Active site residues names and sequence numbers: SER157, ASP189, HIS57

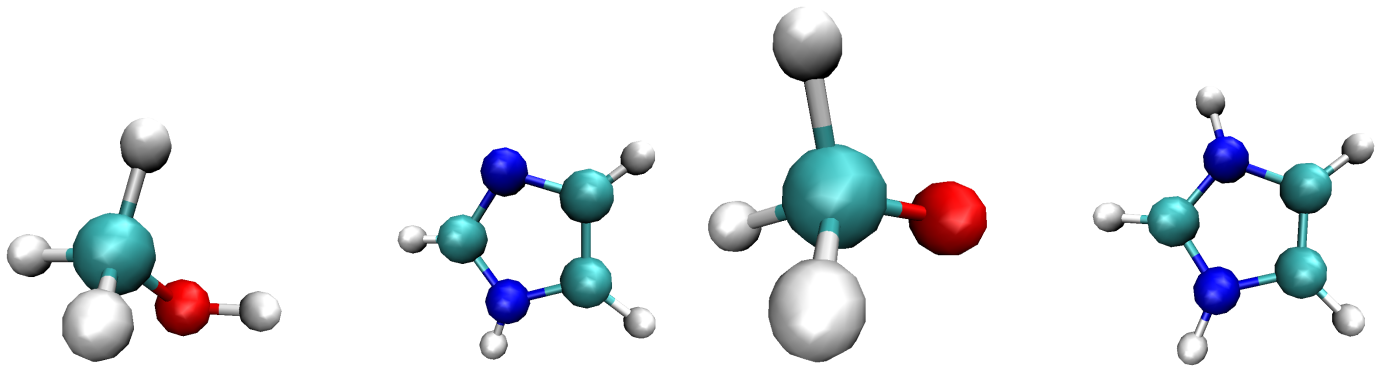
Problem 2. Save the coordinates of the active site serine (Ser), histidine (His), and aspartic (Asp) acid residues in a separate PDB file. Use GaussView to edit the structure and save PDB files for: methanol, imidazole, a complex with methanol and imidazole, and a complex with methanol, imidazole, and acetate.

```
Files sucessfully made!
```

Problem 3. Use the wB97X-D3BJ/6-311+G(d,p) method available in ORCA to optimize the structures of methanol, methanolate, imidazole, and imidazolium. Show the optimized structures and report the reaction energy (ΔE) for the following reaction:

$$\text{methanol (MeOH)} + \text{imidazole} \rightarrow \text{methanolate (MeO)} + \text{imidazolium}$$

Figure 1 shows the MeOH and Imidazole and their product MeO and Imidazolium.



(A) MeOH (B) Imidazole (C) MeO (D) Imidazolium

FIGURE 1

```
#Final Single Point Energy (in atomic Energy units * 627.5096 = kcal/mol):
imidazole = -226.292100663486 * 627.5096
imidazolium = -226.669371503348 * 627.5096
```

Date: Spring 2023.

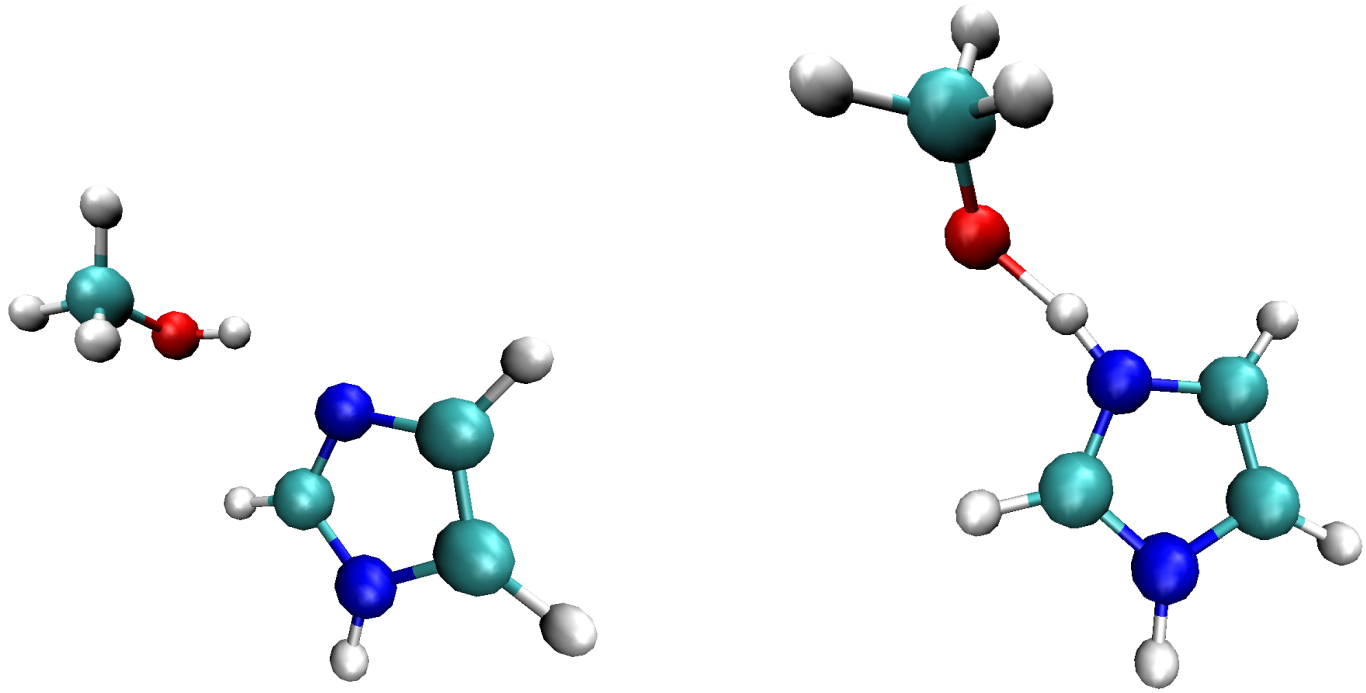
```
meo = -115.160314185684 * 627.5096
meoh = -115.794151194762 * 627.5096

reactants = meoh + imidazole
products = meo + imidazolium

print("The reaction energy is", products-reactants, "kcal/mol.")
```

```
The reaction energy is 160.99773421822465 kcal/mol.
```

Problem 4. Perform a relaxed energy scan using the wB97X-D3BJ/6-311+G(d,p) method available in ORCA for the following reaction to transfer a proton from methanol to imidazole. Show the optimized complex structures at the reactant state and the product state. Show the energy plot along the reaction path and report the reaction energy (ΔE).

Dyad reactant → Dyad Product

Figure 2 shows the Dyad reactant and product, while Figure 3 plots the respective energies and ΔE.



(A) MeOH (B) Imidazole

FIGURE 2

```
import matplotlib.pyplot as plt
import matplotlib


data = [
   (2.21500000, -342.17391514),
   (2.08000000, -342.17457969),
   (1.94500000, -342.17494094),
   (1.81000000, -342.17460359),
   (1.67500000, -342.17286433),
   (1.54000000, -342.16881791),
   (1.40500000, -342.16127686),
   (1.27000000, -342.14989628),
   (1.13500000, -342.13374969),
   (1.00000000, -342.11083414), ]
```

```
x = [point[0] for point in data]
y = [point[1] for point in data]

plt.plot(x, y, 'o-')
plt.xlabel(r'$R_{H-N}(\dot{A})$')
plt.ylabel('E(a.u.)')
plt.grid(True)
x_10, y_10 = data[-1]
x_1, y_1 = data[0]
plt.plot([x_10, x_1],[y_10, y_10], 'r--')
plt.plot([x_1, x_1],[y_10, y_1], 'r--')

plt.annotate(
    r'$\Delta E$',
    xy = (x_1+0.01, -342.14989628),
    xycoords = 'data',
    fontsize = 16,
    horizontalalignment = 'left',
    verticalalignment = 'center',
)

plt.xlim(0.95, 2.3)
plt.ylim(-342.18, -342.1)
plt.gca().invert_yaxis()
params = {'font.size' : 16,
          'figure.figsize':(15.0, 8.0),
          'lines.linewidth': 2.,
          'lines.markersize': 15}

matplotlib.rcParams.update(params)
plt.title('Dyad Distance vs Energies')
plt.show()
```

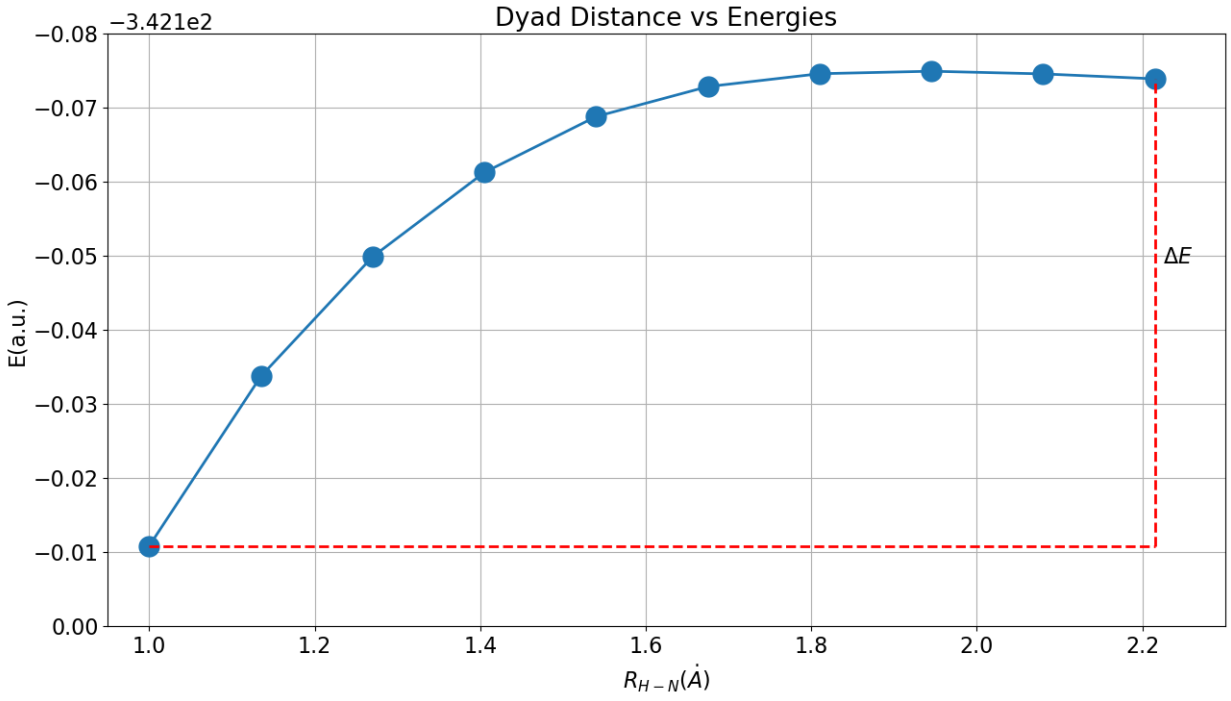


FIGURE 3

```
print("The reaction energy is", (y_10 - y_1) * 627.5096, "kcal/mol.")
```

```
The reaction energy is 39.58393307760693 kcal/mol.
```

Problem 5. Compare the reaction energies (ΔE) calculated from (3) and (4) above, comment on the similarities and differences of these two processes.

The reaction energy of the meoh+imidazole → meo+imidazolium reaction was 160.99773421822465 kcal/mol, while the reaction energy of the dyad process was only 39.58393307760693 kcal/mol. Although our dyad products picture shows the hydrogen bonded to both molecule structures, it should in fact be only part of the imidazolium, but this is the last image that we were given from the output of the dyad bash file. As for their differences chemically, if I remember correctly, the reaction from 3 separated the hydrogen and then bound it in separate steps, while that of 4 used an enzyme to facilitate the hydrogen transfer directly.

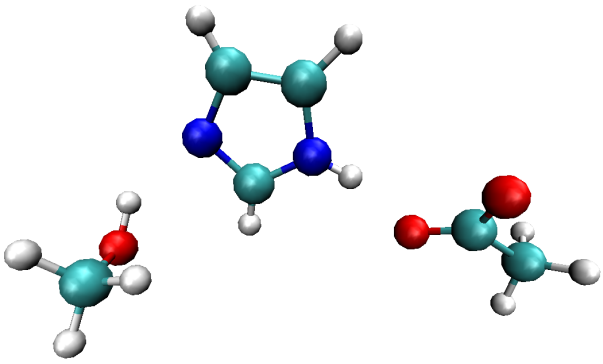
Problem 6. Calculate the energy of the reactant and product state of the following reaction using the wB97X-D3BJ/6-311+G(d,p) method available in ORCA. Show the complex structures at the reactant state and the product state. Determine the reaction energy ΔE.

Triad reactant → Traid Product

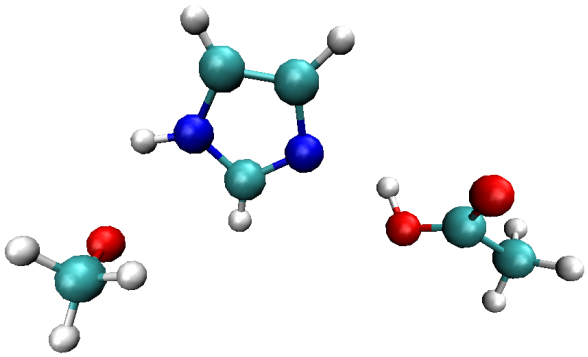
```
#Triad Energies in kcal/mol
TriadProductEnergy = -570.717610388542 * 627.5096
TriadReactantEnergy = -570.792324518118 * 627.5096

print("The reaction energy is", TriadProductEnergy-TriadReactantEnergy, "kcal/mol.")
```

```
The reaction energy is 46.883833564585075 kcal/mol.
```

Figure 4 shows the triad reactant and product respectively.



(A) Triad Reactant



(B) Triad Product

FIGURE 4