**Synthesis, Characterization, and Computational Modeling of [Co(acacen)L2]+, an Inhibitor of Zinc Finger Proteins**

**Introduction**

This experiment was adapted from “Axial Ligand Exchange of *N*-heterocyclic Cobalt(III) Schiff Base Complexes: Molecular Structure and NMR Solution Dynamics” (Inorg. Chem. 2013, 52, 1069-1076). The Cobalt Schiff base complexes synthesized in this lab will be referred to as [Co(acacen)L2]+, where L represents an axial ligand. By using different axial ligands, a series of complexes can be prepared and characterized. These complexes preferentially bind histidine residues in biological systems. For this reason, they are used as inhibitors of Cys2His2 zinc finger proteins.

**Chemicals Needed (per student)**

2,4-pentanedione (acetylacetone) (5 mL)

Ethanol (5 mL)

Ethylenediamine (1.6 mL)

Diethyl Ether (~20 mL)

Methanol (5mL)

CoBr2•6H2O (0.56 g)

4-Methylimidazole (0.43 g)

OR

7N NH3 in MeOH (750 μL)

**Lab Equipment Needed (per student)**

Round bottom flask

Stir bar

Vacuum filtration system

**Procedure**

1. In a round bottom flask, combine 5.00 mL 2,4-pentanedione and 5 mL ethanol with stirring at room temperature.

2. Add 1.6 mL ethylenediamine dropwise over a period of 5-10 minutes. This reaction will be exothermic.

3. Once the reaction cools to room temperature, store at 4°C overnight to facilitate crystal formation.

4. After 24 hours, vacuum filter the crude solid and wash with ether three times. This yields H2(acacen) as a crystalline white solid.

5. In a separate flask, dissolve 0.56 g (1 molar equivalent) CoBr2•6H2O in 5-10 mL methanol and add 4.1 equivalents axial ligand (4MeIm or ~1mL 7N methanolic NH3). Stir for 5 min under N2 (reaction should turn purple).

6. Open the solution to air and add 1.1 equivalents of H2(acacen). Stir the reaction overnight at room temperature. The reaction should turn brown over time.

7. After 24 hours, purify the product: Make sure that there is enough solvent that the product is clearly in solution (not in a suspension). Slowly add diethyl ether (~1.5 mL at a time) while sloshing around. The pure product (brown solid) should precipitate out. Vacuum filter the product and wash it with cold diethyl ether.

8. Characterize the [Co(acacen)L2]+ complex with UV/Vis (in H2O), 1H NMR (in D2O), and IR Spectroscopy.

9. For each of the complexes synthesized, use an available computational package, such as WebMO and Gaussian 09™, to calculate the following: HOMO, LUMO, vibrational modes, NMR spectra, and UV-Vis spectra. Use the PCM model for water, and a minimum of B3LYP/6-31G(d) level of theory.