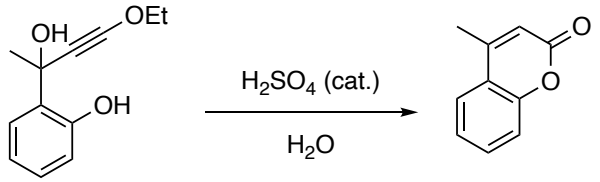
CHEM 8321/4321 **December 4, 2023**

Problem Set #12 **T. R. Hoye**

Due in class, December 11, 2023

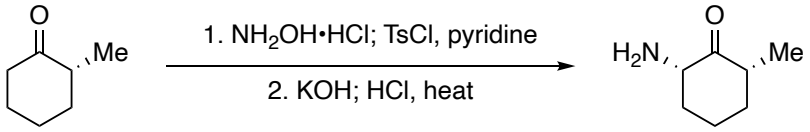
Detailed Mechanism Provide a detailed mechanism [i.e., *explicitly* show (using curly arrows) *EVERY* intermediate, formal charge (where relevant), equilibrium, and bond-making and -breaking step] to account for the following transformations:

1. The conversion of propargyl alcohol **1** to coumarin **2** after treatment with catalytic sulfuric acid in water (notice that this substrate reacts differently than a normal Rupe reaction propargylic alcohol).



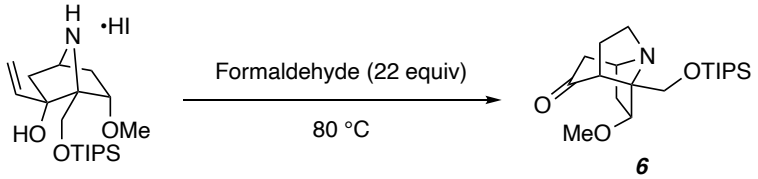
1 ***2***

2. The reaction of the cyclohexanone **3** to form the α-amino cyclohexanone **4**.



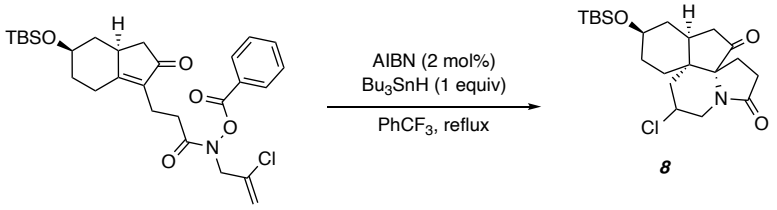
3 ***4***

3. The tandem aza-Cope rearrangement/Mannich cyclization (Overman) of the bicyclic amine **5** and formaldehyde to form the tricyclic amine **6**.



5 ***6***

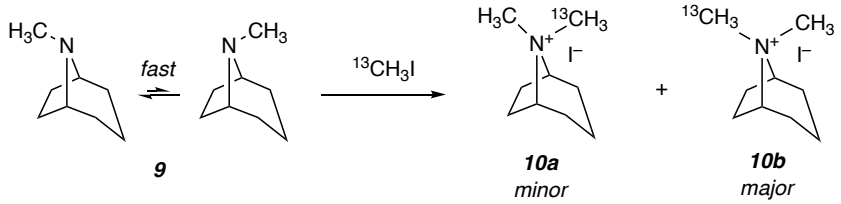
4. The radical cyclization of the enone **7** to form the tetracyclic amide **8**.



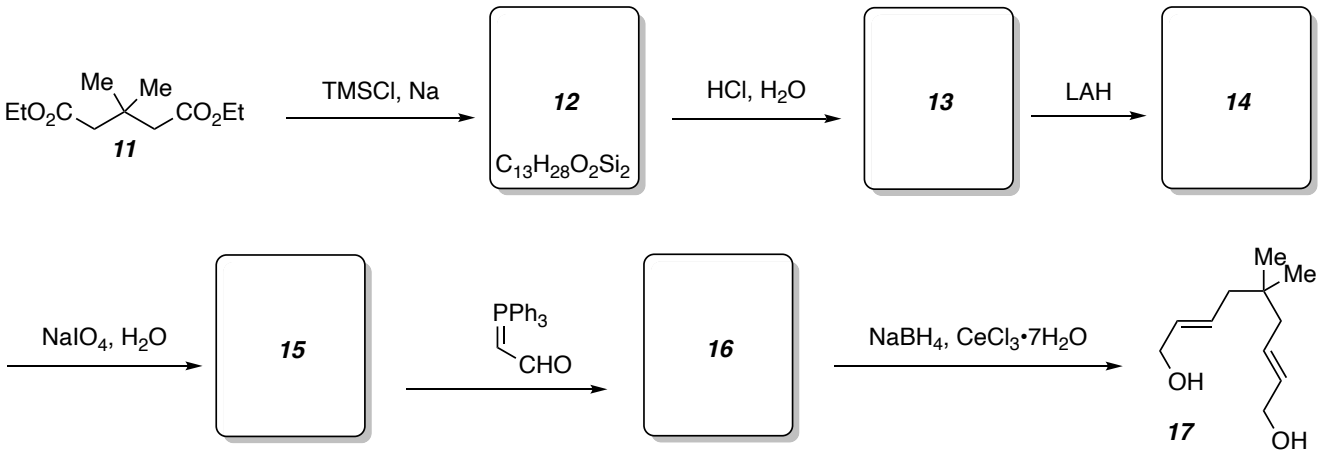
7 ***8***

Other Problems

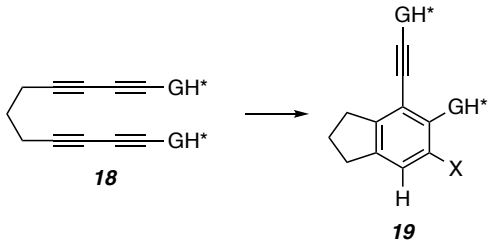
1. In the methylation of the bicyclic tertiary amine **9** using isotopically-labeled methyl iodide, the major product is the ammonium iodide **10b**. Rationalize this observation using a reaction coordinate diagram that includes all four species shown below. (*hint: this is an example of a Curtin-Hammett controlled process)*



2. Provide the structures of compounds **12**-**16**, intermediates in a synthesis of the diol **17**. (*hint: the first step is a silylative acyloin condensation*)



3. Reaxys Database Search



a. According to the Reaxys database, how many single-step transformations convert any tetrayne containing a three-sp^3-carbon-atom tether like that shown in **18** to a benzenoid product like **19** where X = N, O, or S?

b. How many of these reactions were reported in any publication in 2017?