

Name (Print) \_\_\_\_\_

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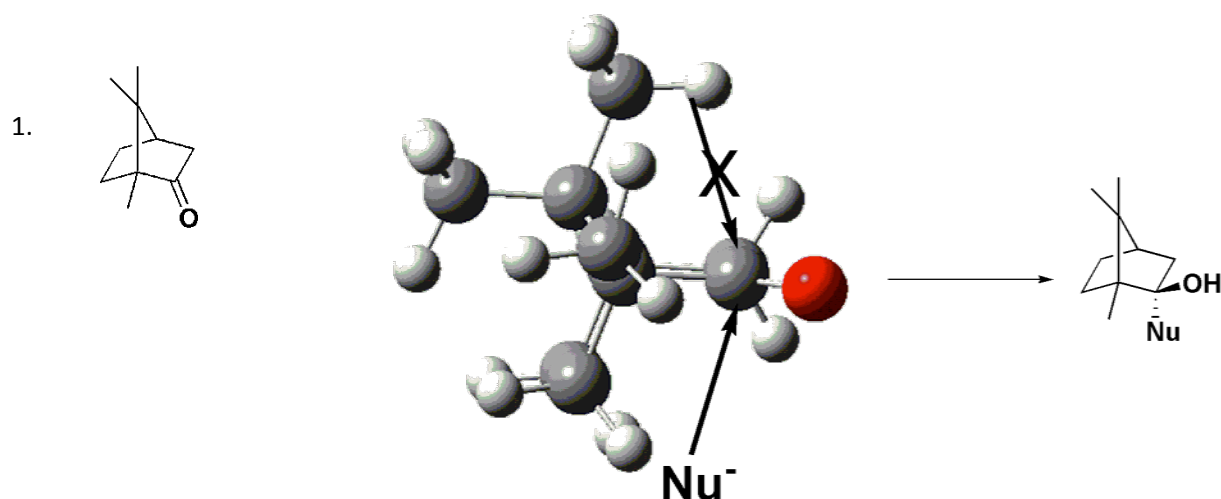
Group # \_\_\_\_\_

**PS #5 – Rigid Bicyclic Compounds and Stereoselectivity**

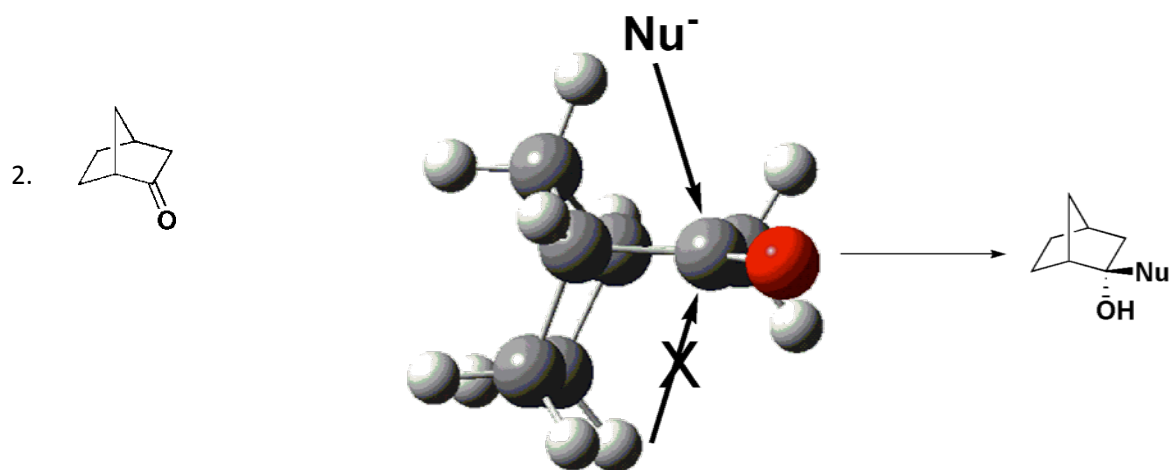
**Part A)** As a group, build 3-D models of the following molecules using the model kits provided. Use the models to answer the following questions for each molecule.

Draw the molecule in 3-D using the model you built as a group. Consider the C=O bond, where is the  $\pi^*$  orbital located? What path does the nucleophile take (use  $\text{Nu}^-$  to represent any nucleophile)? Show the path of nucleophilic attack on your diagram. What is the major product that results from this attack?

**Part B)** Brainstorm and list all possible carbonyl transformations that might be governed by these rules.

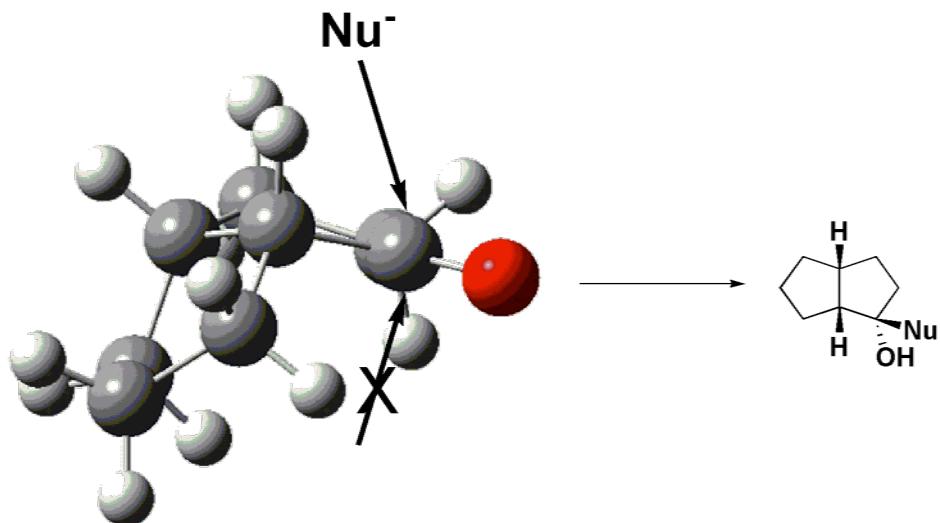
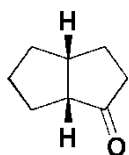


*One of the two methyl groups attached to the five-membered ring sits above the carbonyl carbon and blocks attack on that face. The carbonyl is much less sterically hindered on the bottom face and this is where nucleophilic attack occurs.*



*A one carbon bridge takes up less space than a two carbon bridge. Nucleophilic attack on the side of the molecule with the one carbon bridge is the least sterically hindered path for attack.*

3.



*This fused bicycle is highly curved. The hydrogen are pointing up and leave the top of the molecule relatively open, while the fused five-membered ring curves under blocking the nucleophile from attacking from underneath the carbonyl group.*

**Part B)** *Some nucleophiles that would result in carbonyl transformations governed by these rules:*

*Grignard reagents*

*Lithium reagents*

*Cuprates*

*Alcohols and alkoxides*

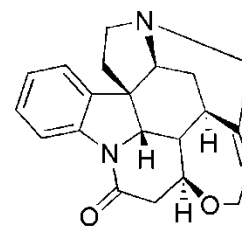
*Amines and amides*

*Thiols and thiolate anions*

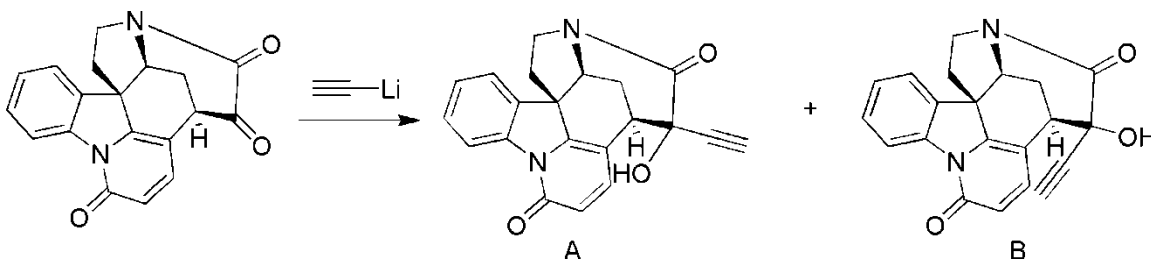
*Cyanide salts*

*Water*

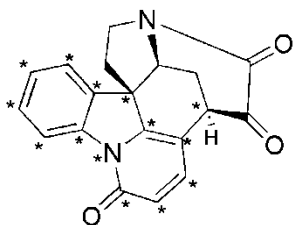
**Part C)** Strychnine is a natural plant toxin that has long been the target by which organic synthetic chemists test their skills. During the synthesis of strychnine, a key bond is formed by the following chemoselective and diastereoselective organometallic addition. The long bonds in the drawings below are telltale signs that this simple 2-D representation is not a good representation of the true structure of the molecule.



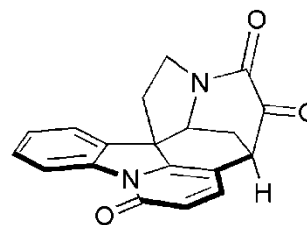
Strychnine  
Woodward, 1954



Work together to arrive at a reasonable understanding of the 3-D structure of the precursor and sketch the molecule in a reasonable 3-D representation (no chair, Newman projection, or any such formalism is required, just a 3-D structure that you will have to be creative about).

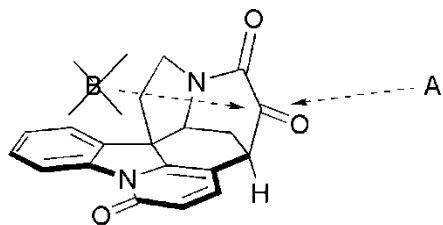


Atoms marked with \* are all part of a conjugated core or connected to  $sp^2$  centres, therefore they are all in the same plane.



The other substituents are all “out of the page,” which in a side-on view is above the plane defined by the flat portion. This molecule is highly curved!

Based on this structure, which product is favored — .



Attack along the Bürgi-Dunitz angle from path **B** (to produce product **B**) would require the nucleophile approaching over the more hindered, concave face of the precursor. This is unfavourable relative to **A** in which the approach from the convex side is completely unencumbered. So product **A** is formed preferentially.