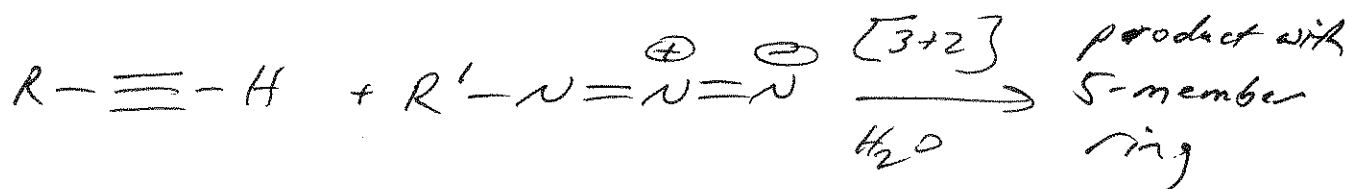


Problem Set 3

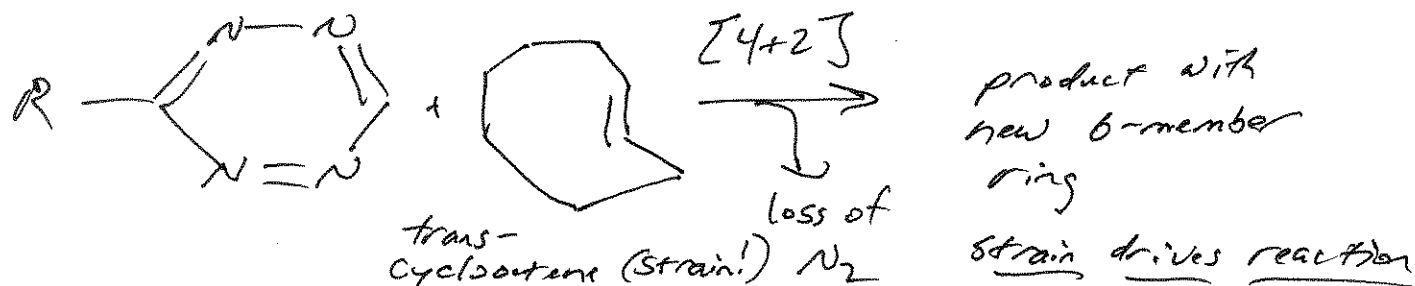
Five points. Monday, March 4, by the start of class.

Provide answers on a separate sheet(s) of paper, stapling together multiple pages.

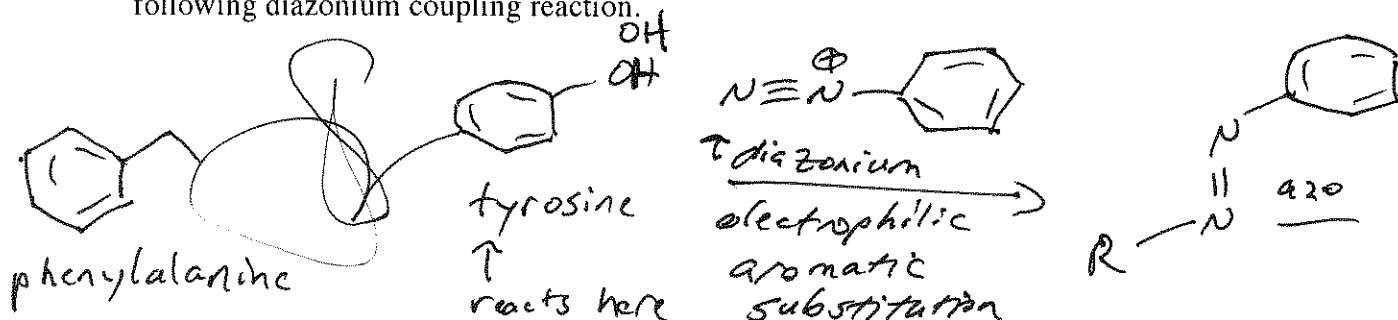
1. A major development in the last decade has been the development of methods of "bioconjugation," mild methods to chemically modify biological molecules (proteins, DNA, RNA, sugars, lipids) that are biocompatible (will not react with regular functional groups of biological molecules), in order to probe and understand the underlying biology. The most common of these reactions, called the click reaction, is between an alkyne and an azide, which undergo [3+2] cycloaddition to form a new 5-membered cyclic product. Provide a mechanism and product for the model click reaction shown below. Why is this reaction so favorable (provide at least 2 reasons)? (You should also be able to provide an orbital description as to why this reaction is allowed.)



2. Another recently described bioorthogonal bioconjugation reaction, developed at the University of Delaware by Professor Fox, is shown below. This is a [4+2] cycloaddition reaction that generates nitrogen gas. Provide a mechanism and product of this reaction.



3. Tyrosine residues will undergo electrophilic aromatic substitution reactions with diazoniums (shown), to generate azo ($\text{R}-\text{N}=\text{N}-\text{R}'$) compounds. These reactions go quickly at pH 10, slowly at pH 8, and not at all at pH 3. They also do not go on phenylalanine residues. Draw a mechanism and product of the following diazonium coupling reaction.



4. Propose syntheses of the following molecules using benzene (or the indicated molecule) as the starting material.

