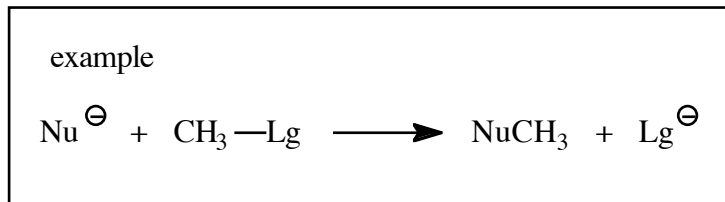
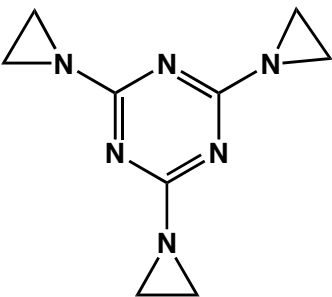
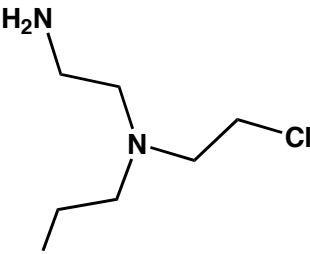
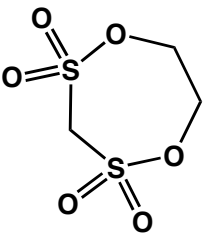


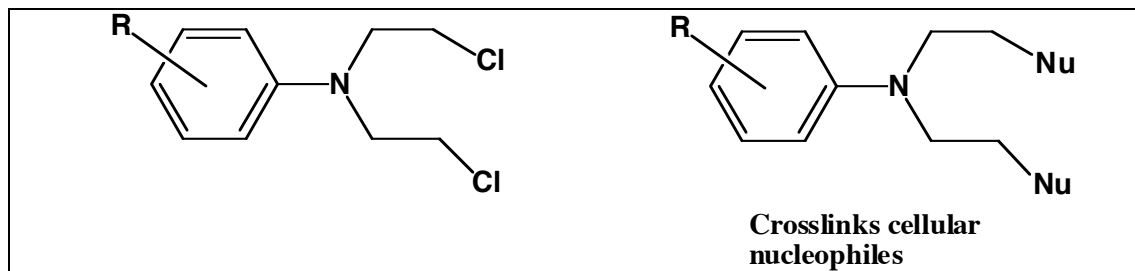
1. The following antitumor agents are under investigation at the National Cancer Institute. For each compound show the structure of the nucleophile substitution product using "Nu-" as your generic nucleophile.



Note that some agents may react with a nucleophile more than once; show the product resulting from nucleophilic reaction at all possible sites. Also show the structure of the leaving group(s) resulting from these reactions.

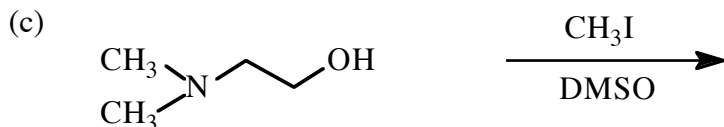
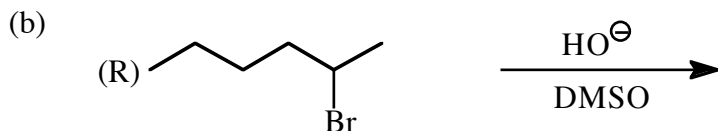
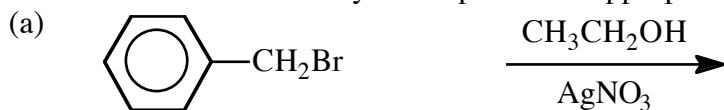
Antitumor Agent	Nucleophile Substitution Product	Leaving Group(s)
 <p>Triethylenemelamine</p>		
 <p>Mustamine</p>		
 <p>Cyclodisone</p>		

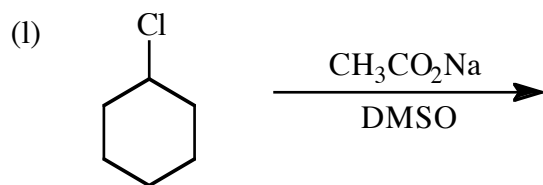
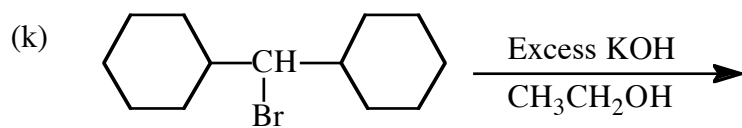
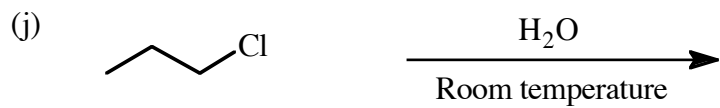
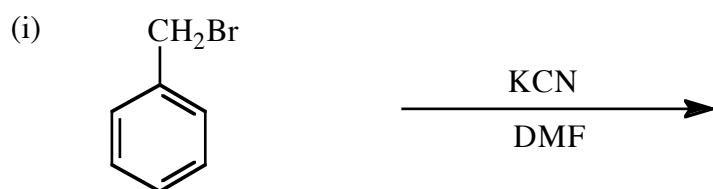
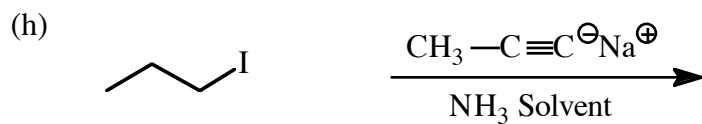
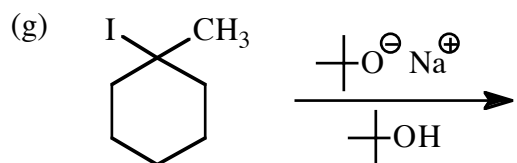
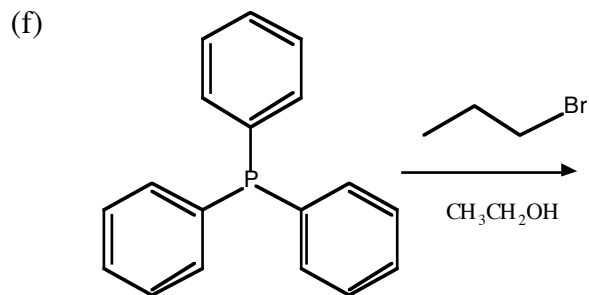
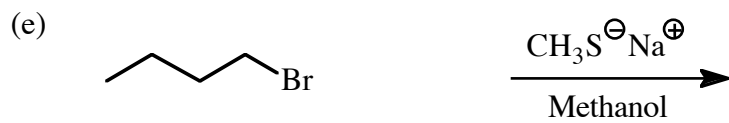
2. Substituent effects applied to drug action. The nitrogen mustard shown below inhibits the growth of hamster ovary cells by a crosslinking alkylation reaction.

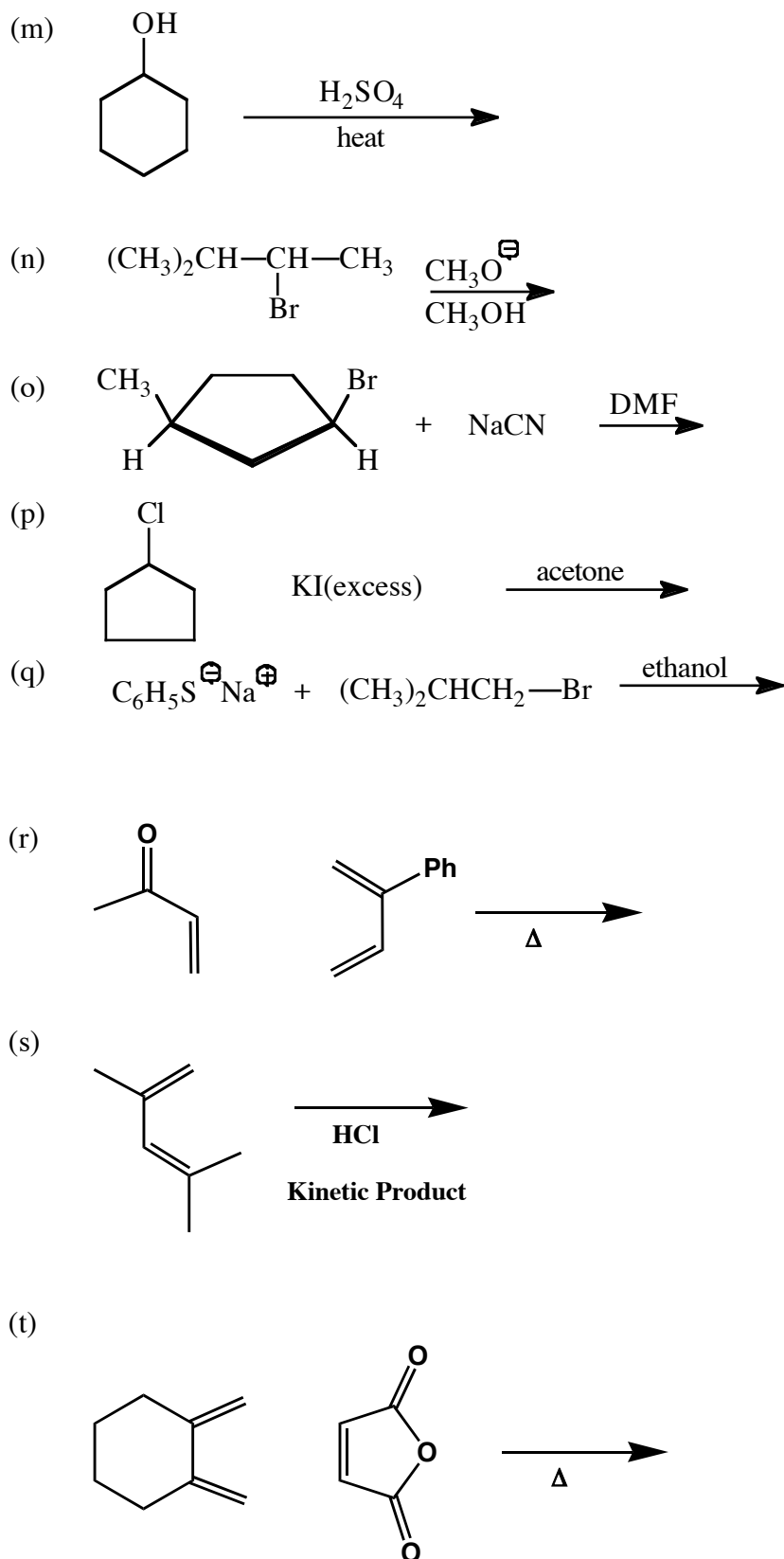


The most active analogue has a *p*-amino substituent and the least active analogue (2450-fold less active) has a *p*-SO₂Me substituent. Explain by providing an alkylation mechanism and resonance structures.

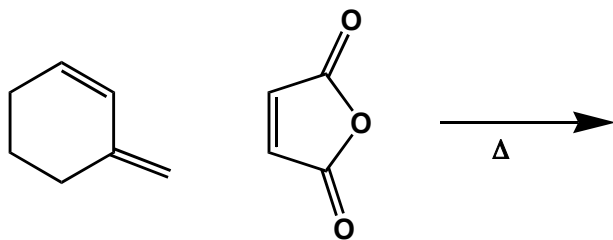
3. Predict the major organic product of the following reactions. If there is no reaction, write "NR" as your answer. Show stereochemistry of the product if appropriate.



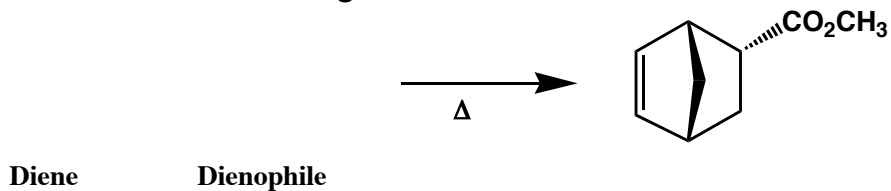




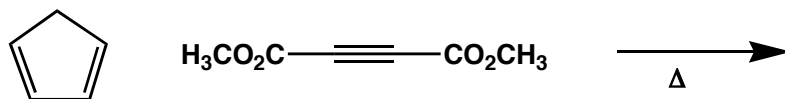
(u)



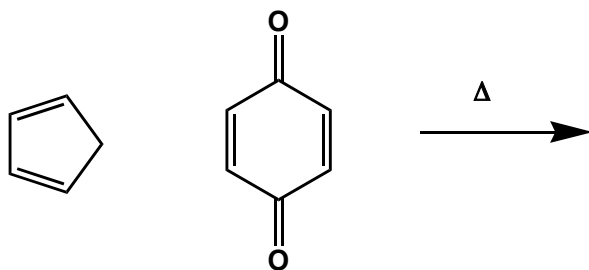
(v)



(w)

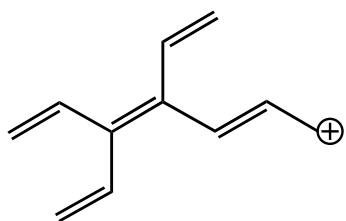


(x)

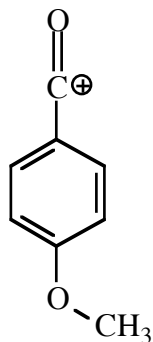


4. Show all charge delocalization structures for the following charged species. Include all degenerate structures.

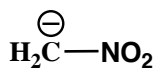
a)



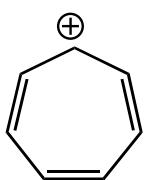
b)



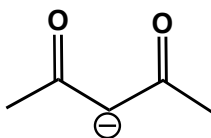
c)



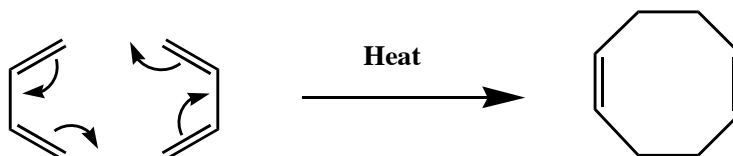
d)



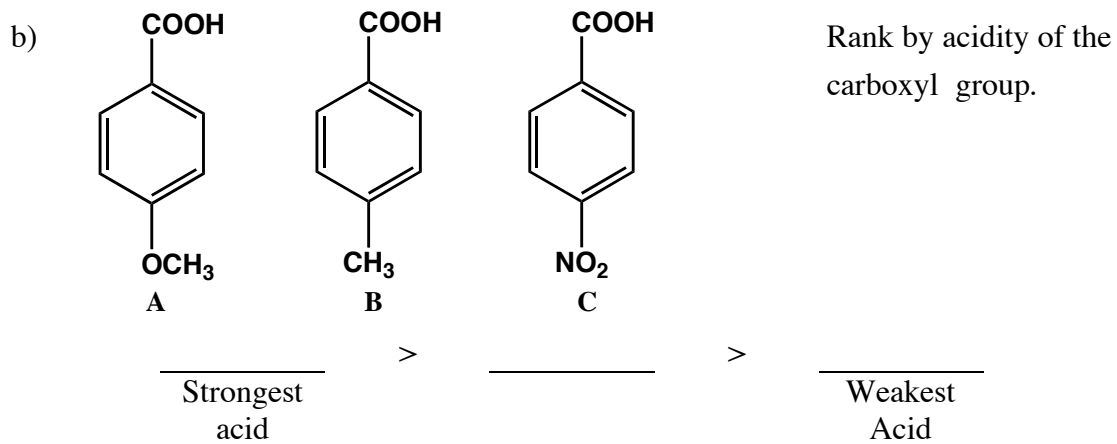
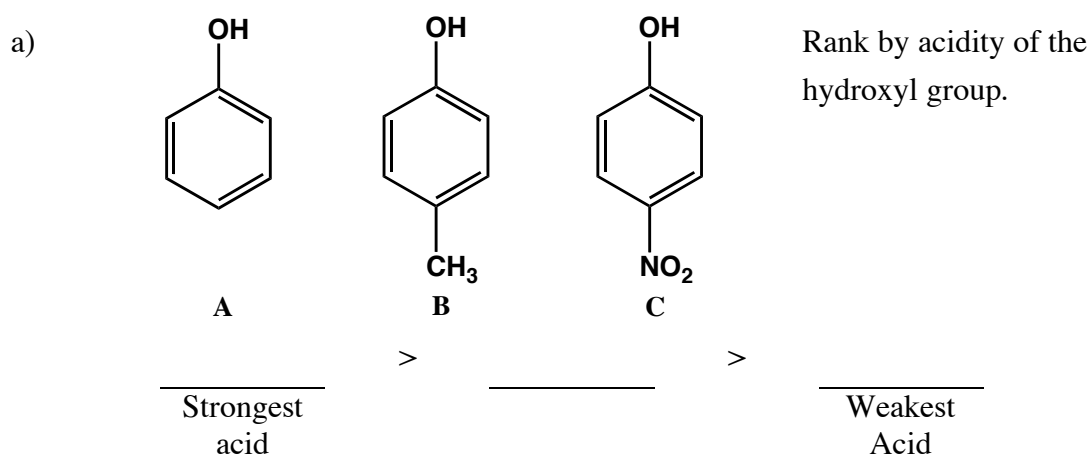
e)



5. The following 4+4 cycloaddition does not occur thermally. Provide two explanations referring to the aromaticity of the transition state and HOMO-LUMO interactions.

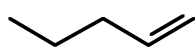


6. Rank each of the following groups of compounds as instructed. Provide an explanation for your ranking along with supporting resonance structures.

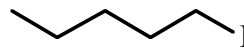


7. Show how the starting material on the left could be converted to the product on the right. Show intermediate compounds along with all necessary reagents and conditions.

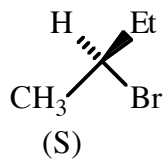
(a)



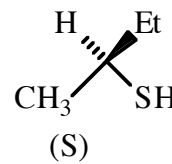
To



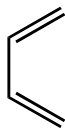
(b)



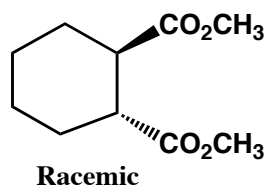
to



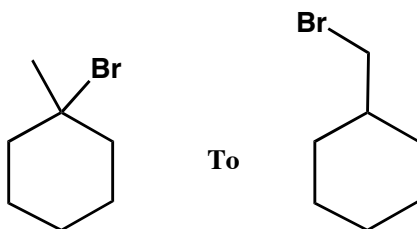
(c)



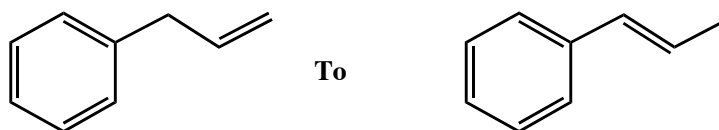
To



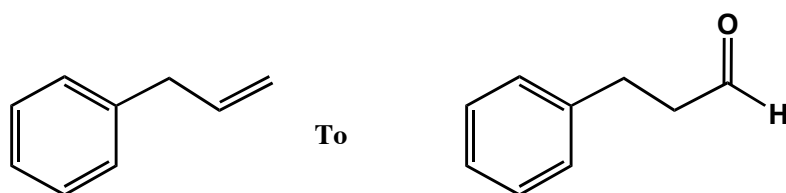
(d)



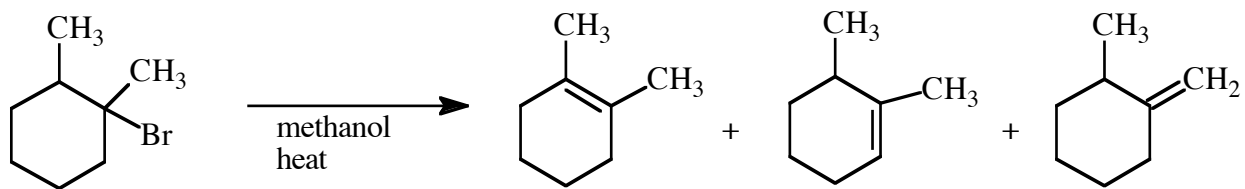
(e)



(f)

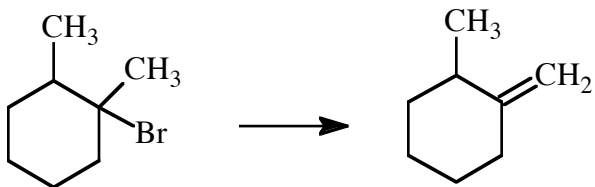


8. Provide a mechanism, which explains the formation of the solvolysis products shown below.



Which of the above alkenes is the major solvolysis product?

Suppose you wanted to carry out the transformation shown below in high yield. How would you do it?



9. Mechanisms. Provide a mechanism for the following reactions. Show intermediates present in the reaction along with curved arrows and proton transfers.

