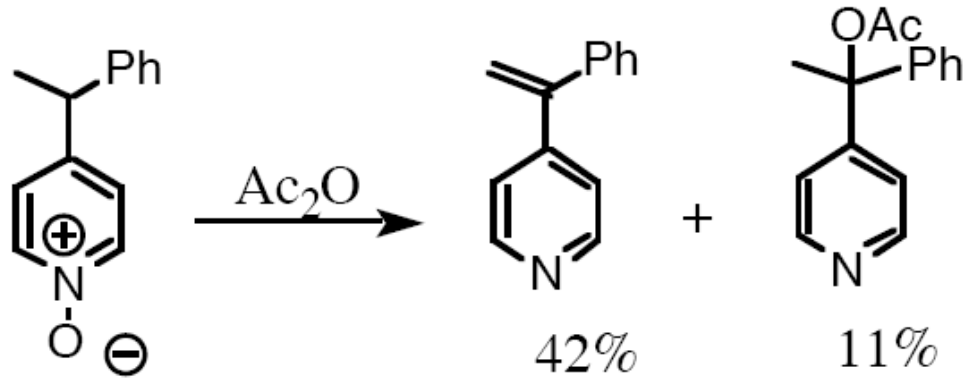
Heterocyclic Chemistry

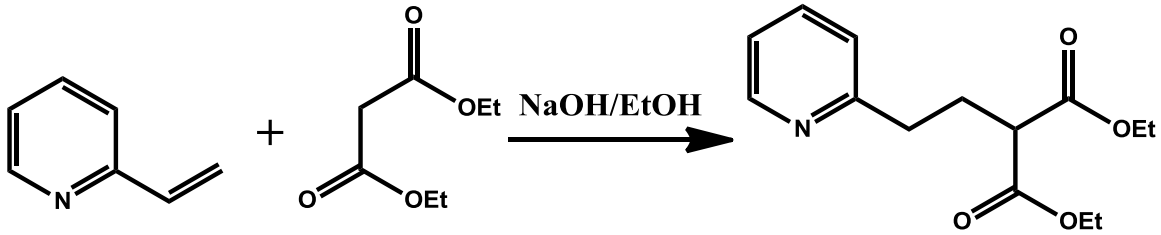
Assignment II

**I. Suggest mechanism for the reactions given below.**

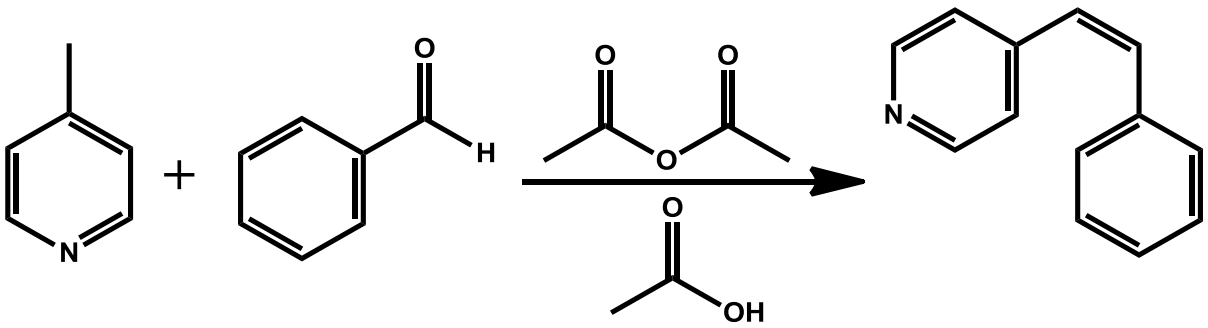
a)



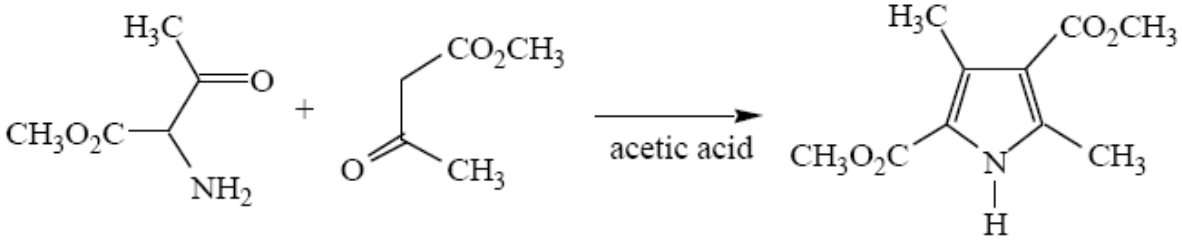

b)



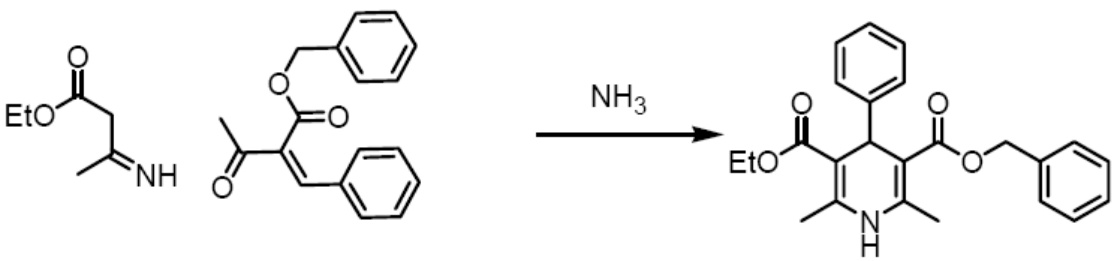

c) The condensation of active methyl groups with aldehydes can be catalyzed with acetic anhydride as well as base. Suggest a possible mechanism?



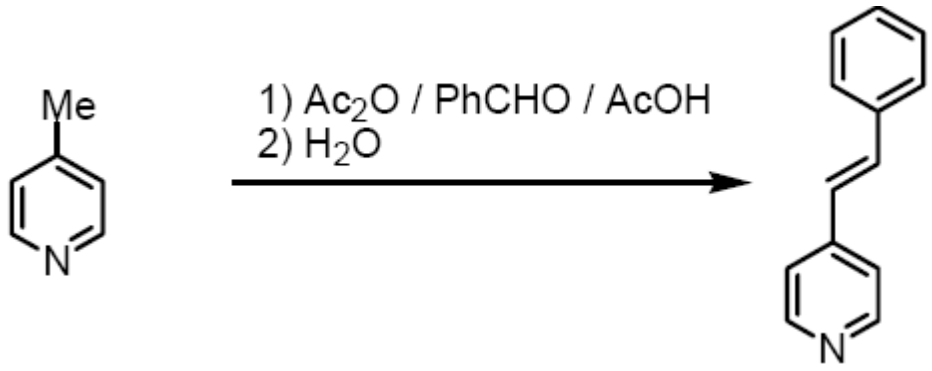

d) Provide a detailed curved-arrow mechanism for this example of the Knorr pyrrole synthesis.



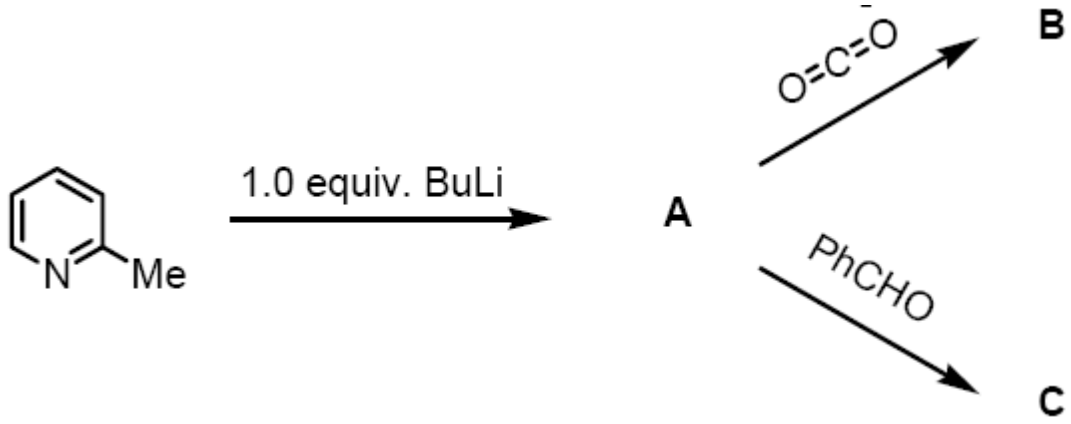

e)



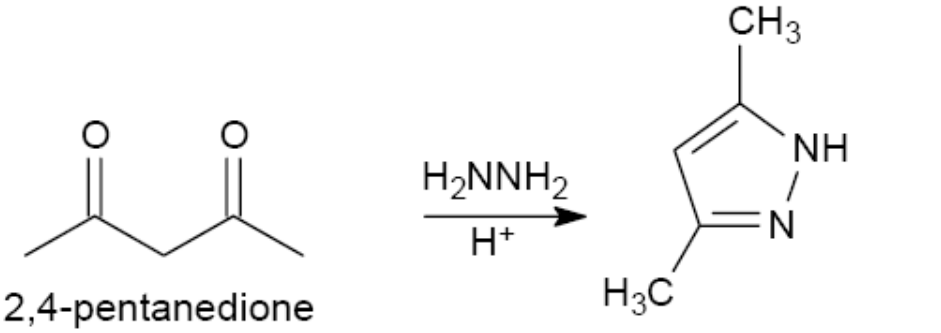
f)




g) Write mechanisms for the reaction and write the products **A**, **B** and **C**



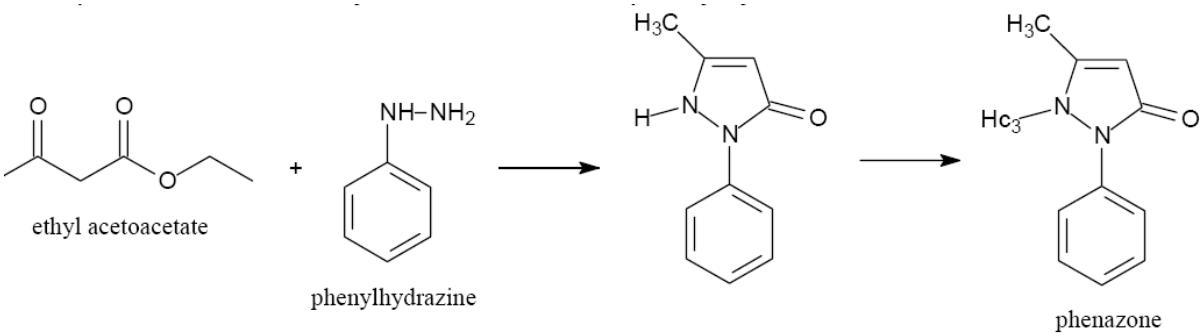

h) Propose a mechanism to account for the formation of 3,5-dimethylpyrazole from hydrazine and 2,4-pentanedione.




2,4-pentanedione

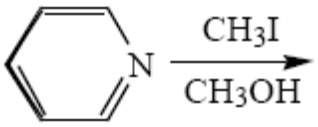
3,5-dimethylpyrazole

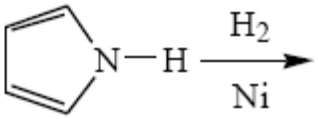
i) Pyrazole derivatives are therapeutically used as analgesics, antipyretics and antirheumatics such as phenazone. Write a detailed mechanism for the formation of phenazone from ethyl acetoacetate and phenylhydrazine.

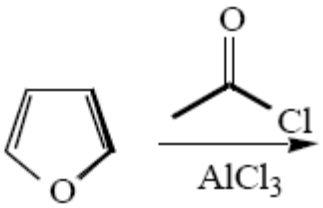



j) Electrophilic attack in pyrroles, thiophenes and furans occur more readily at the α- than β-position. Provide a mechanism for this reaction using the nitration of pyrrole as an example.

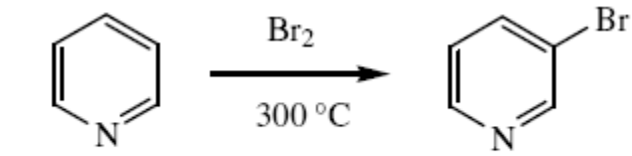
**II. Suggest the organic product(s) of the following reactions.**

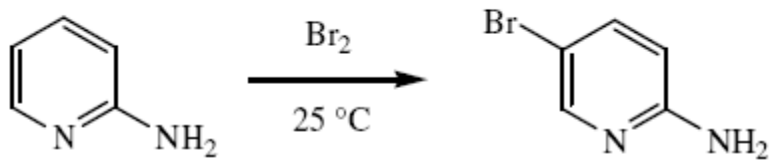
(a) 


(b) 

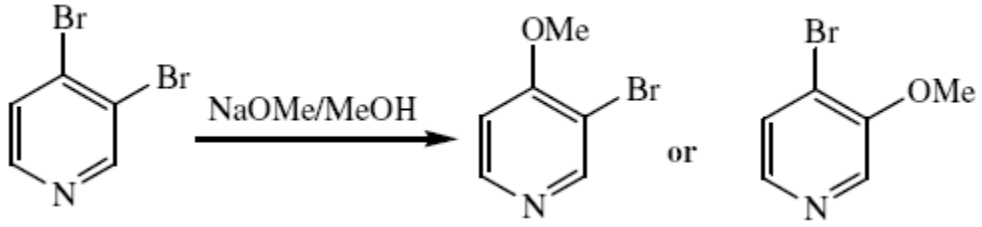

(c) 


III. Explain briefly the differences in the reaction conditions and the orientation of substitution in the two reactions shown below.

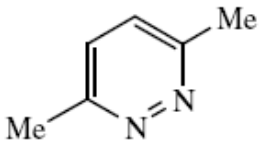


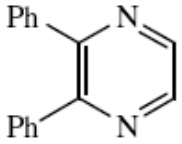
IV. The nucleophilic displacement reaction shown below follows one of the two paths shown (*via* an addition/elimination mechanism). Draw out the structures of the reaction intermediates for each path and thus predict which compound is the product.




V. Suggest synthetic routes to the following compounds from the starting materials shown. In each case outline the mechanisms of the reactions involved and give the structures of any intermediates.

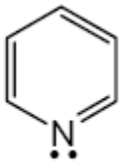



from $H_2NNH_2$

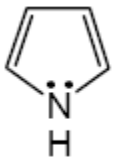



from $H_2NCH_2CH_2NH_2$

VI. Which of the nitrogen-containing heterocycles **A** and **B** is more basic? Why?

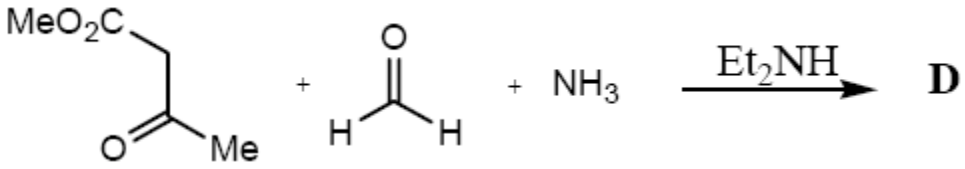



**A**



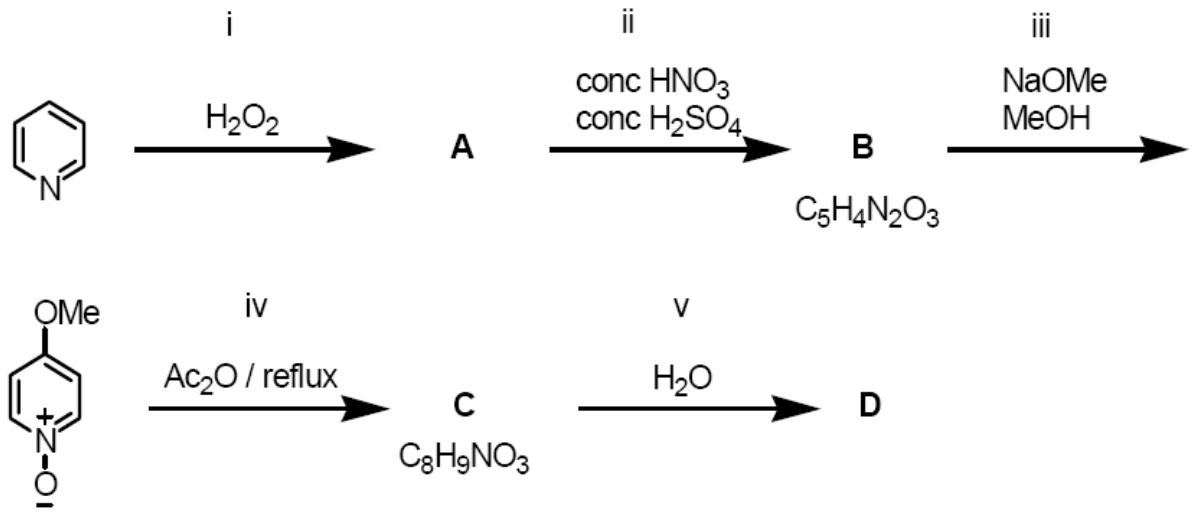

**B**

VII. By proposing a mechanism for the following reaction, suggest a structure for the heterocycle **D**. What final transformation is required to convert **D** into an aromatic heterocycle?



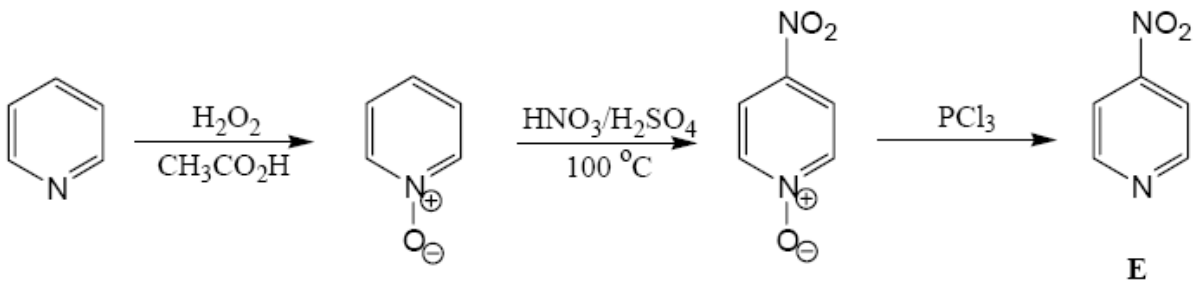

VIII. What is the relative reactivity of bromobenzene, 2-bromopyridine, 3-bromopyridine towards replacement of the halide with ethoxide on treatment with NaOEt?

IX. Write the structures of **A**, **B**, **C** and **D**.

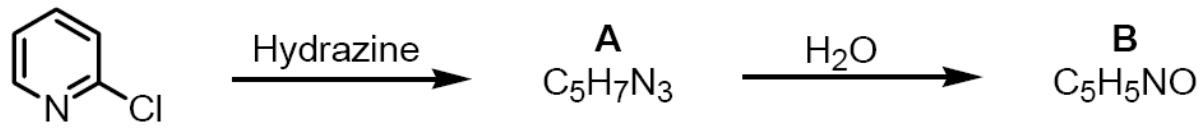



Write a mechanism for step iv.

X. Explain why this apparently circuitous route is used to make the substituted pyridine **E**.



XI. Deduce the structure of the products **A** and **B** formed by the sequence:




XII. Deduce the structures **A**, **B** and **C**.


XIII. Provide an explanation for the following observation. Treatment of 4-chloropyridine with ammonia gives 4-aminoaminopyridine, but treatment of 3-chloropyridine under the same conditions gives no reaction.

XIV. Outline a synthesis for the following compound from methyl-pyridine and any other reagents.