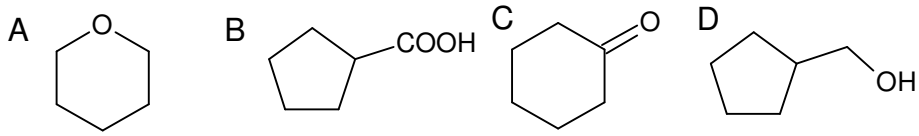
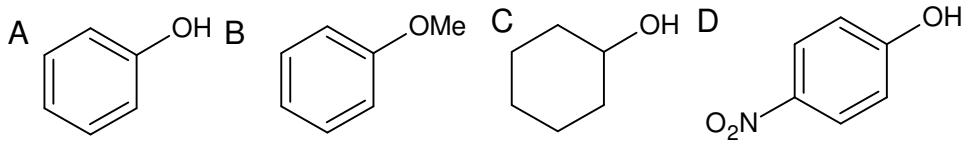
Organic Chemistry Practice Problems:

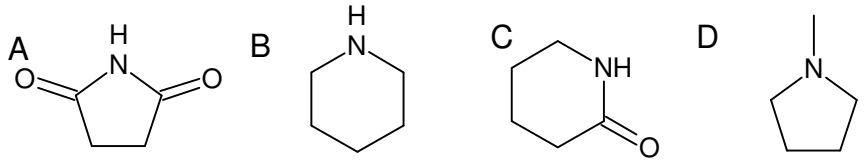
1. Which of the following sets is the strongest and weakest acid?
   a.



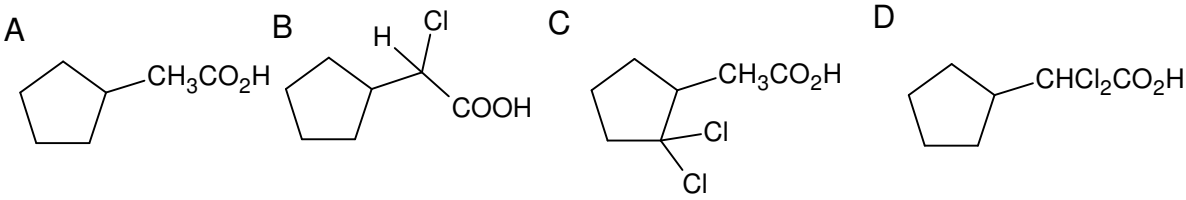
   b.



   c.

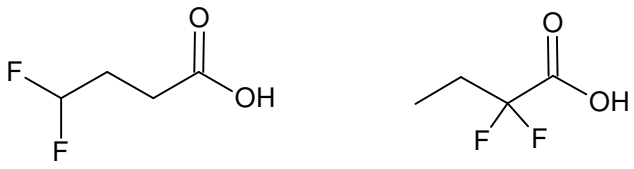


   d.



2. Circle the most acidic and state why:
   a.

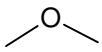
   b.

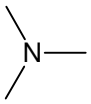


   c.

   d.

e.

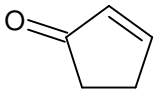




f.

$CHCl_3$ $CHBr_3$

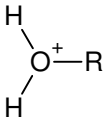
3. Identify the most acidic proton:

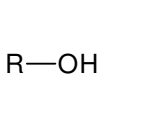


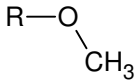
4. Rank the following in order of decreasing nucleophilicity. Explain your choice.

$CF_3CH_2O^-$, $CH_3CH_2O^-$, $CH_3CO_2^-$, $CH_3CH_2S^-$, $(CH_3CH_2)_2O$, CH_3CH_2Li

5. Rank the groups (ie, what is hanging off the R (generic alkyl) group) in order of decreasing leaving group ability. Explain your choice.







6. For each of the following pairs, which would react more rapidly with CH_3OTs (where OTs is the tosyl group: a phenomenal leaving group)? Why?
   a. CH_3OH and CH_3O^-
   b. H_2O and HI

7. For each of the following pairs, which would undergo nucleophilic substitution more rapidly with a nucleophile such as CH_3OH? Why?
   a. $C_6H_6CH_2OTs$ and $C_6H_6CH_2OH$
   b. $CH_3CH_2OH_2^+$ and $CH_3CH_2NH_2$
   c. CH_3Br and CH_3OH

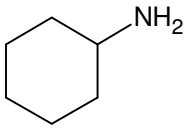
8. For the following reaction, would the rate increase or decrease for each of the following changes? Why?

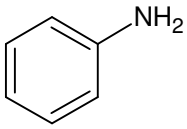
$$CH_3CH_2Br + CH_3COOH \rightarrow ?$$

   a. Replace CH_3CH_2Br with $(CH_3)_3CH_2Br$
   b. Replace CH_3CH_2Br with CH_3CH_2OTs
   c. Replace CH_3COOH with H_2O

9. What products do you expect to get for question 8? What do you expect for the conditions of parts a-c? Give mechanisms.

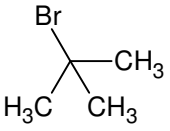
10. Explain why cyclohexylamine (A) is more reactive than aniline (B) towards methyl iodide.

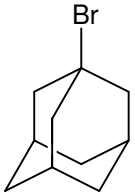
A) 

B) 

(Hint: Think carefully about what the nucleophile is, and what the electrophile is. What changes the strength of the nucleophile? Could electron availabililty be an influence?)

11. Explain the relative reactivity of the following alkyl bromides towards hydrolysis in aqueous ethanol solution:





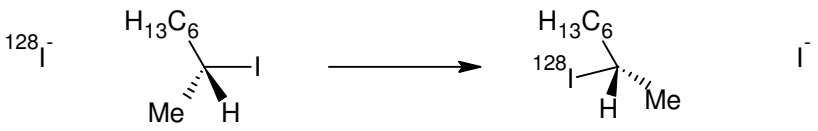
Relative rates: 1 10^{-3} 10^{-6}

(Hint: S_N1 or S_N2?)

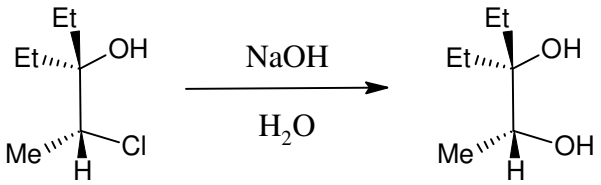
12. Arrange the compounds in each set in order of reactivity towards S_N2 displacement:
    a. 2-bromo-3-methylbutane, 1-bromopentane, 2-bromopentane
    b. 1-bromo-3-methylbutane, 2-bromo-2-methylbutane, 3-bromo-2-methylbutane
    c. 1-bromobutane, 1-bromo-2,2-dimethylpropane, 1-bromo-2-methylbutane, 1-bromo-3-methylbutane

13. Arrange the compounds in order of reactivity towards S_N1 reactivity:
    a. Question 12 a
    b. Question 12 b

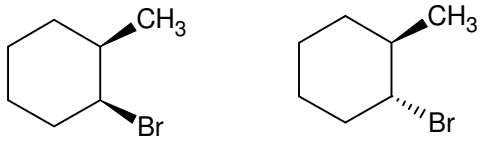
14. In a classic organic chemistry experiment, the rate of the substitution reaction of radioactive iodide (isotope = 128) on (+)-(R)-2-iodooctane as investigated, (see below). The chemists measured the initial rate of reaction for the incorporation of the iodine isotope and also followed the progress of the reaction polarimetrically (ie – they tracked how the polarisation of light changed over time). It was found that the initial rate of racemisation was twice the initial rate of iodine incorporation. By considering S_N1 and S_N2 mechanisms, explain these experimental observations.



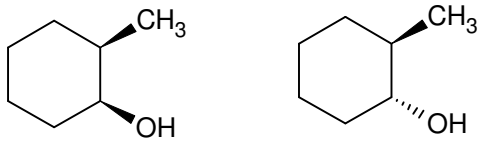
15. The base catalysed hydrolysis of the 1,2-chlorohydrin shown below is found to yield the 1,2-diol with retention of configuration. Suggest a mechanism that is consistent with this observation.



16. What are the major products produced by heating the following isometric alkyl bromides with NaOEt? (Hint: E2)

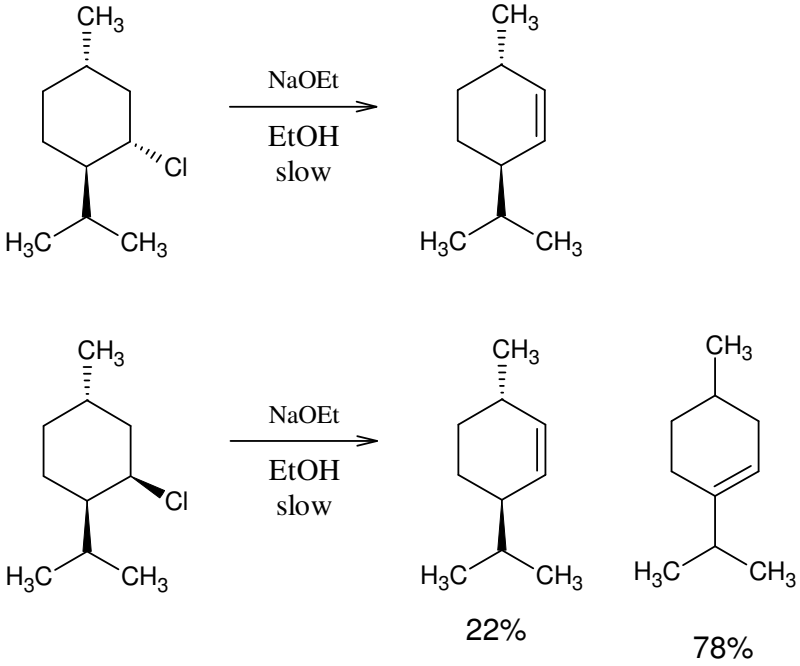


17. What are the major products produced by heating the following isometric alcohols with H_2SO_4?

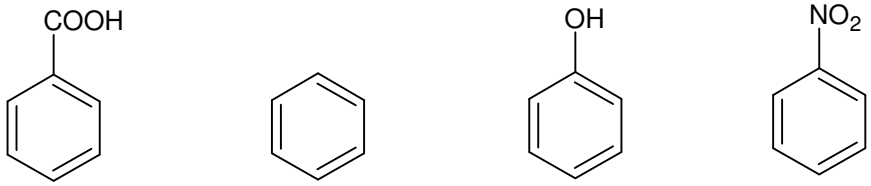


18. Draw Newman projections of product forming steps for cis- and trans-butene from the reaction of 2-bromobutane with NaOEt/EtOH/heat.

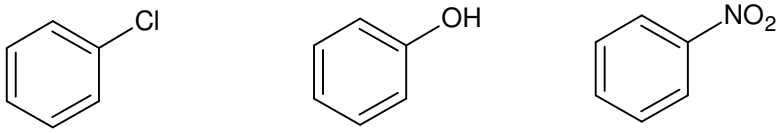
19. Explain the following experimental observation for stereoisomers of methyl chloride:



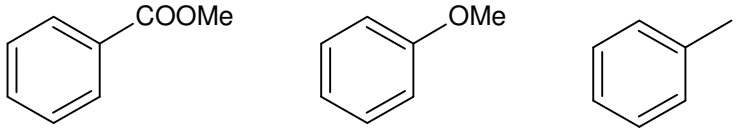
20. Which of the following compounds reacts fastest when treated with a mixture of concentrated nitric and sulphuric acids?



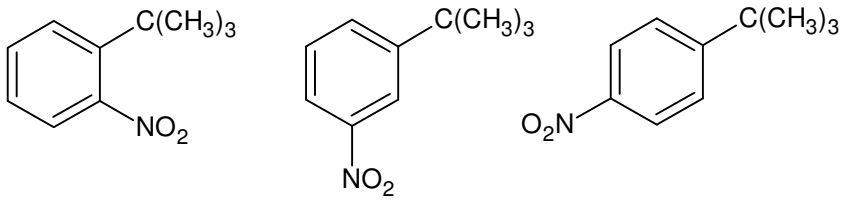
21. Arrange the following according to their reactivity towards Br_2. Explain your reasoning.



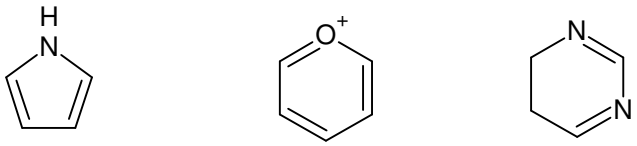
22. Arrange the following according to their relative rate of reaction with ethanoyl chloride/ $AlCl_3$ (or any electrophilic aromatic substitution). Justify the order.



23. Arrange the following products according to the % yield obtained from the nitration of t-butylbenzene. Justify the order.

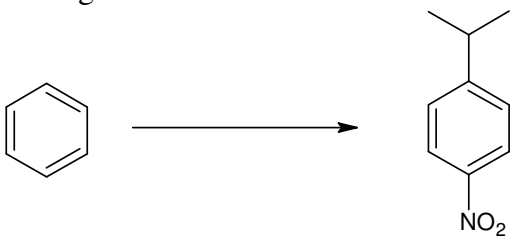


24. Predict whether these molecules would be activated or deactivated compared to benzene. Why?

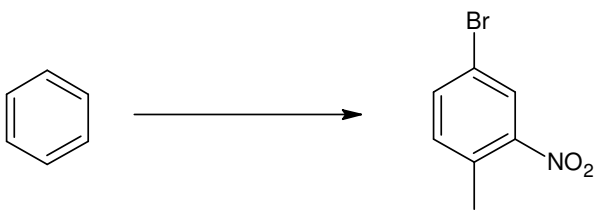


25. Synthesise the following from benzene:

a.

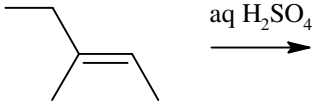


b.



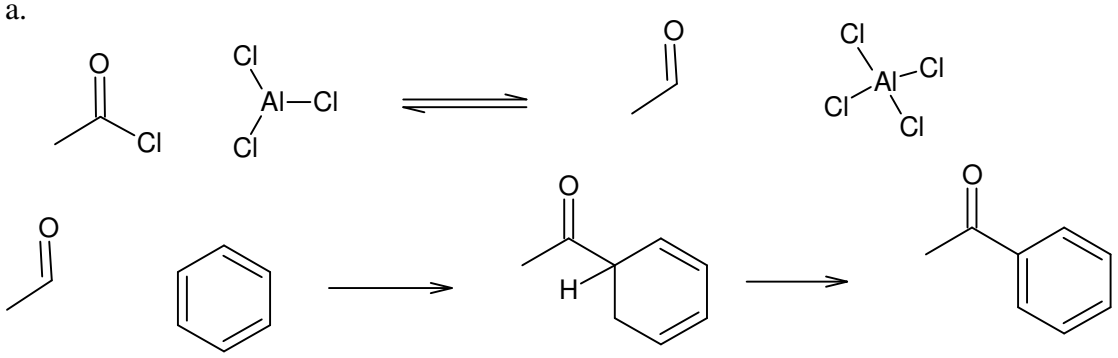
26. Show the major products, with stereochemistry where applicable, for the reactions of:
    a. Propene
    b. Methylcyclohexene
        i. H_2/Pd
        ii. HBr
        iii. Br_2
        iv. H_2SO_4/H_2O

27. Give the product and show the mechanism for the following.

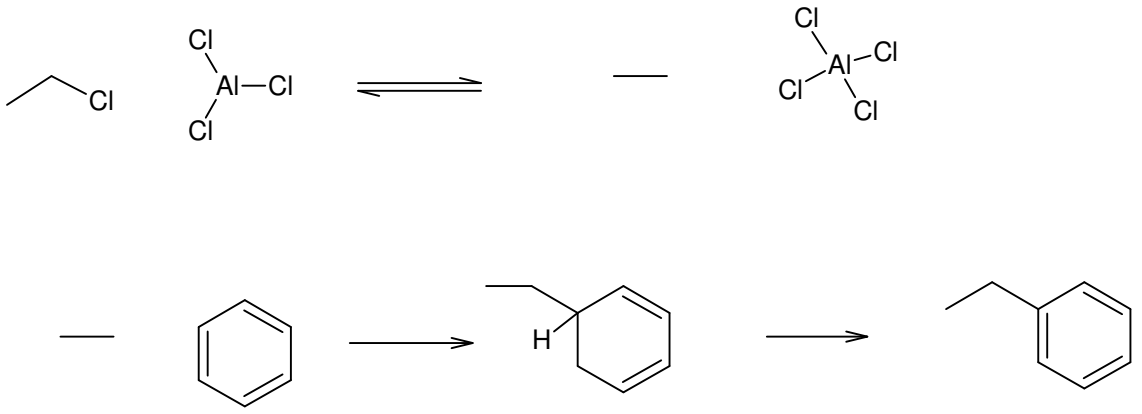


28. Draw in all the mechanistic arrows and any required charges to complete the step-by-step mechanisms for each of the following reaction schemes.

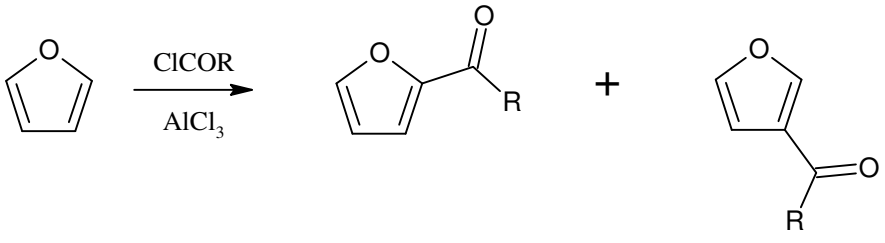
a.



b.

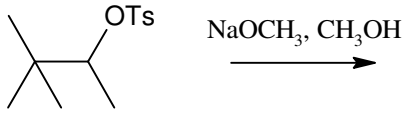


29. When a Friedel-Crafts reaction is performed on furan, two products are possible. Provide mechanisms for both and explain why one is favoured.

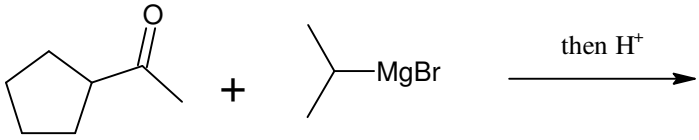


30. Draw the major product (or products) expected from each of the following reactions. Show stereochemistry where appropriate.

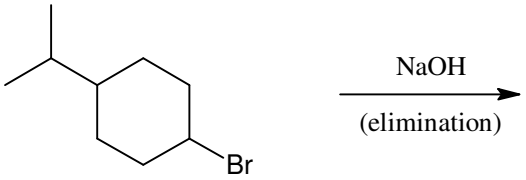
a.



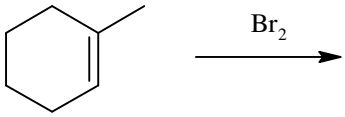
b.



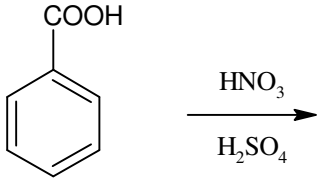
c.



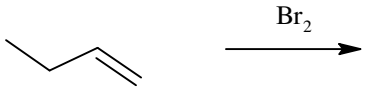
d.



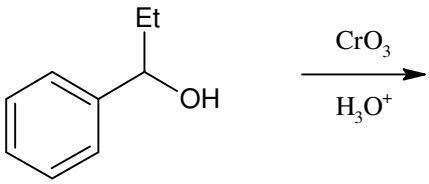
e.



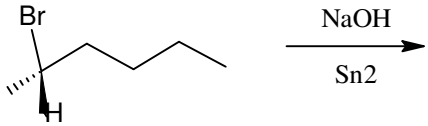
f.



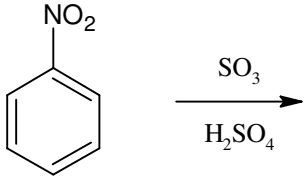
g.



h.

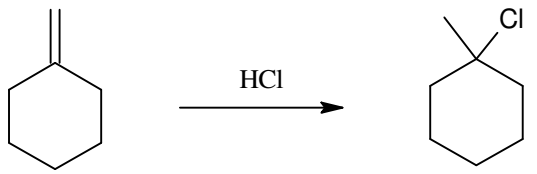


i.

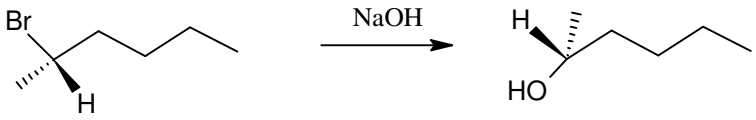


31. Give the mechanism for the following reactions:

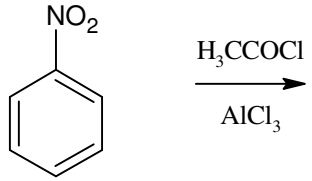
a.



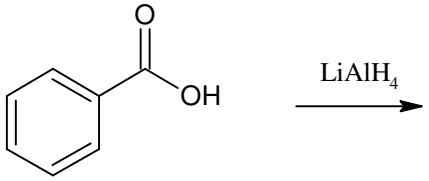
b.



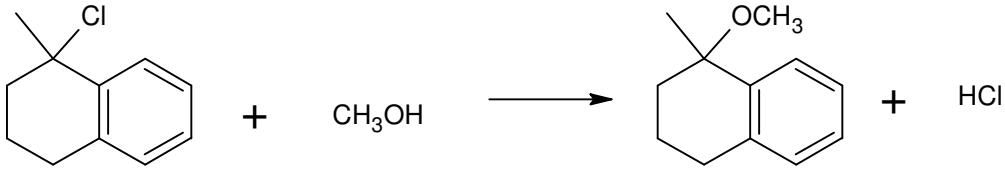
32. What is the most likely product from the following reaction?



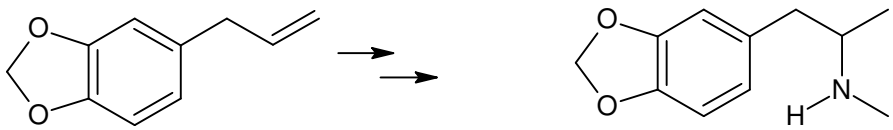
33. What is the most likely product of the following reaction?



34. What mechanism does the following reaction probably proceed via?



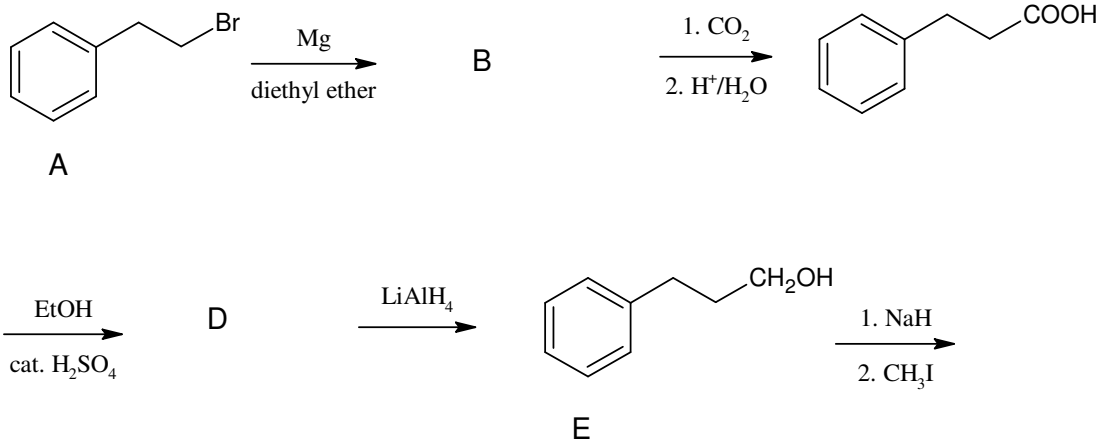
35. Safrole is a key ingredient of "oil of sassafras" and was readily available from health food shops until the early 1990s. Using functional group transformations that you have studied in your lectures and tutorials, suggest a synthesis of ecstasy from safrole.



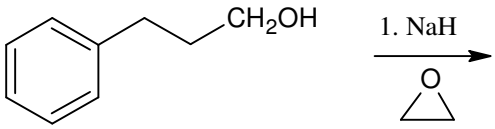
Safrole

Ecstasy

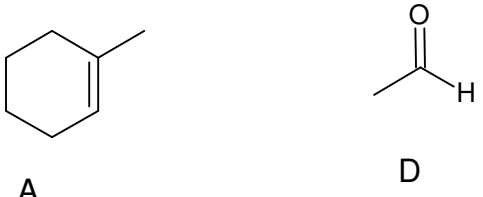
36. Reaction of phenethyl bromide (A) with magnesium metal in diethyl ether gave a reagent (B). This reagent was reacted with carbon dioxide and then treated with aqueous acid to give a carboxylic acid (C). C was treated with ethanol and catalytic concentrated sulphuric acid to afford an ester (D), which was then treated with lithium aluminium hydride to give an alcohol (E). Finally, the alcohol (E) was treated with the strong base sodium hydride to generate an alkoxide salt, which was then reacted with methyl iodide (CH_3I) to afford an ether (F).



a. What are the structures of B, D and F?
b. What would be the product of elimination of phenethyl bromide (A) upon treatment with the base potassium hydroxide?
c. What would be the structure of the product that results from the reaction of phenethyl bromide (A) with sodium cyanide?
d. *Bonus question:* What would be the product of the reaction of alcohol (E) with the strong base sodium hydride and ethylene oxide (below)?



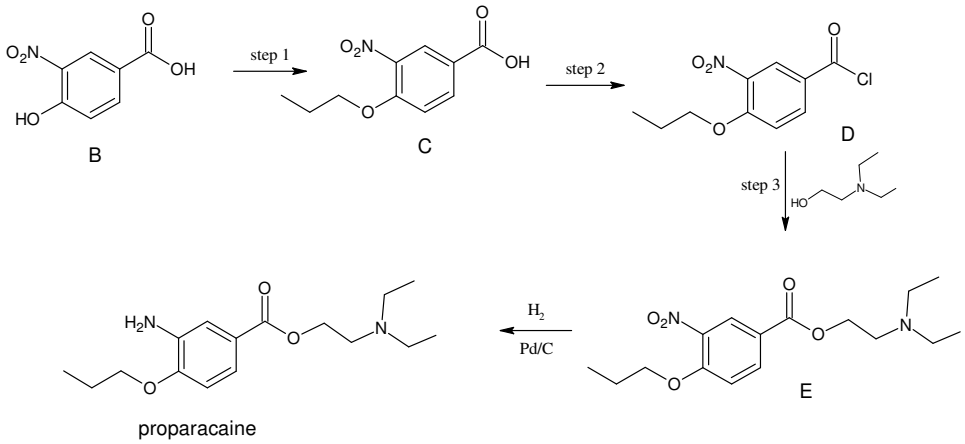
37. Reaction of 1-methylcyclohexene (A) with hydrogen bromide (HBr) gave a compound B with molecular formula $C_7H_{13}Br$. Reaction of B with magnesium metal provided a reagent C that was immediately allowed to react with acetaldehyde (D), followed by aqueous acid, to deliver E with molecular formula $C_9H_{18}O$. Reaction of E with chromium trioxide (CrO_3) gave compound F with molecular formula $C_9H_{16}O$, which displayed an intense absorption at 1700cm^{-1} in its infrared spectrum.



A D

Draw plausible structures for compounds B, C, E and F.

38. The following questions relate to the industrial synthesis of proparacaine (depicted below), a local anaesthetic:



a. Identify the most basic functional group in proparacaine
b. The industrial synthesis of the aromatic ring of proparacaine commences from B above. What type of new functional group is formed in step 1 above? Suggest reagents for this transformation.
c. Step 2 of the industrial synthesis involves converstion of C → D. Suggest reagents for this transformation.

39.