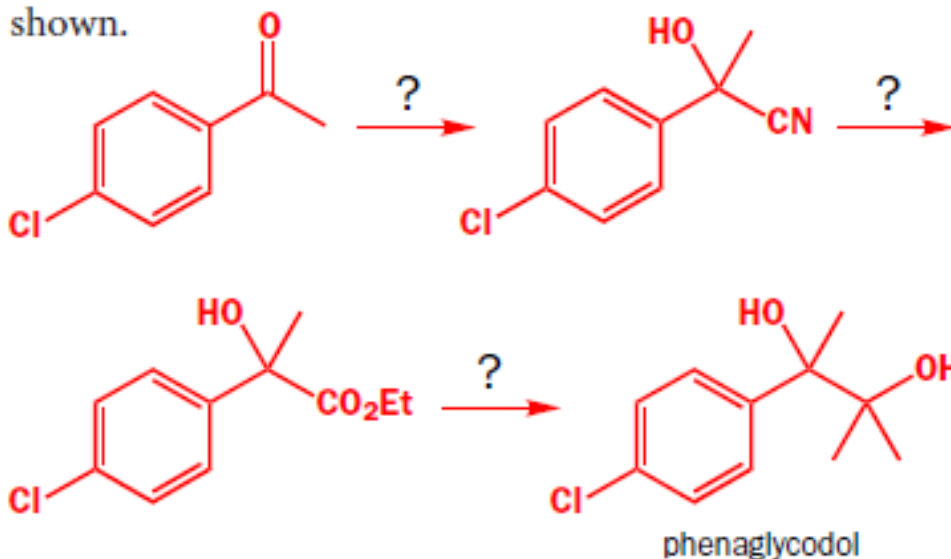


LISTA DE EXERCÍCIOS EXTRA SUBSTITUIÇÃO NUCLEOFÍLICA EM COMPOSTOS CARBONILADOS

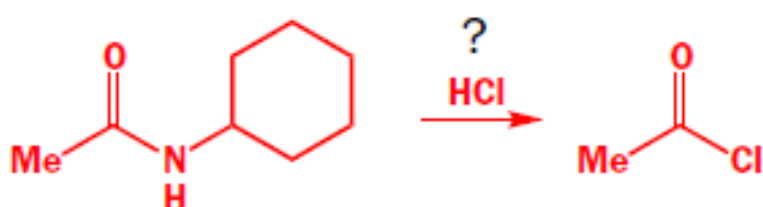
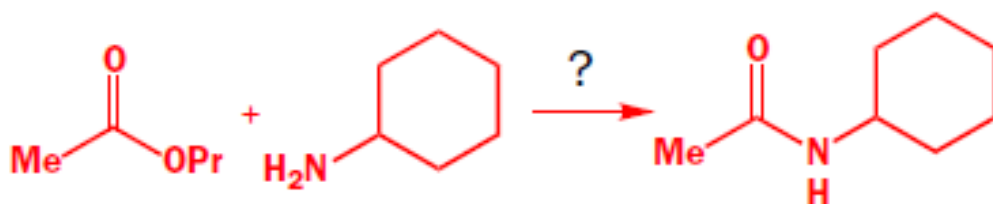
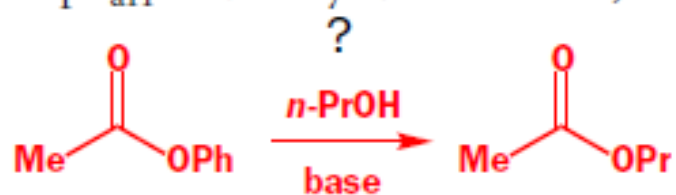
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1. Suggest reagents to make the drug 'phenaglycodol' by the route shown.

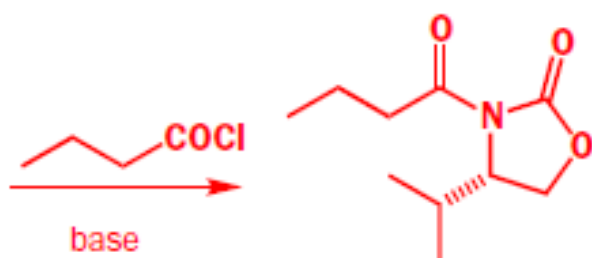
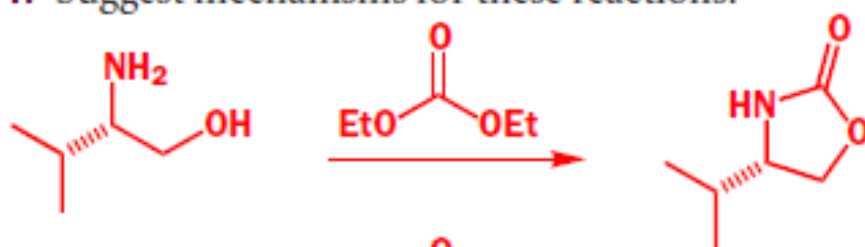


2. Direct ester formation from alcohols (R^1OH) and carboxylic acids (R^2CO_2H) works in acid solution but does not work at all in basic solution. Why not? By contrast, ester formation from alcohols (R^1OH) and carboxylic acid anhydrides, $(R^2CO)_2O$, or acid chlorides, $RCOCl$, is commonly carried out in the presence of amines such as pyridine or Et_3N . Why does this work?

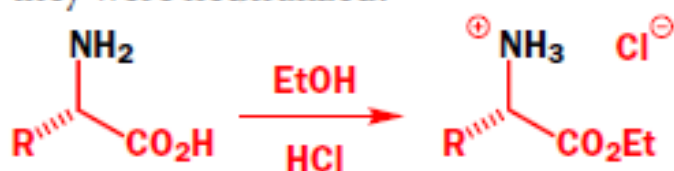
3. Predict the success or failure of these attempted nucleophilic substitutions at the carbonyl group. You should use estimated pK_a or pK_{aH} values in your answer and, of course, draw mechanisms.



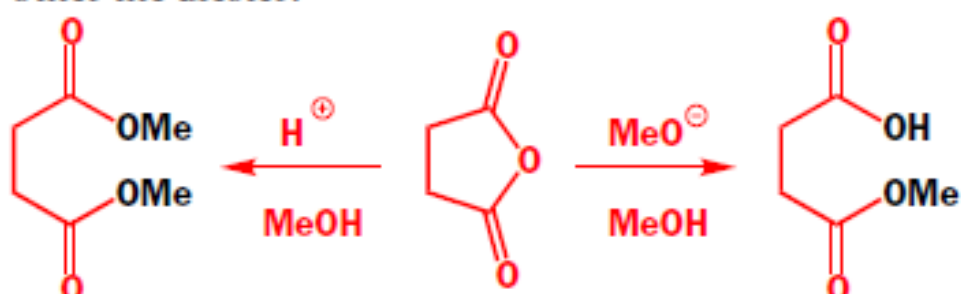
4. Suggest mechanisms for these reactions.



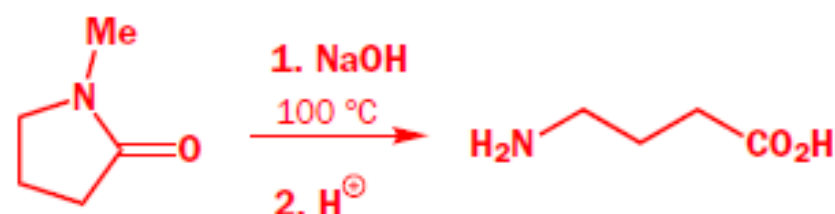
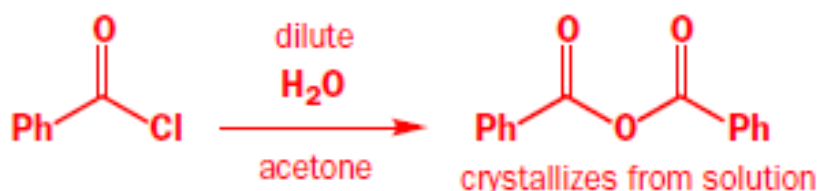
5. In making esters of the naturally occurring amino acids (general formula below) it is important to keep them as their hydrochloride salts. What would happen to these compounds if they were neutralized?



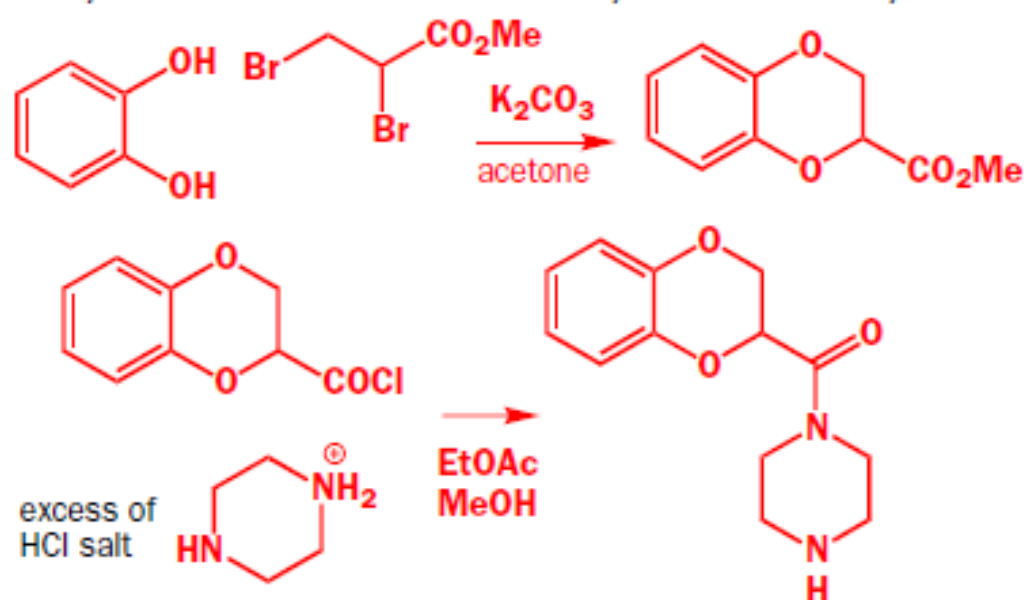
6. It is possible to make either the diester or the monoester of butanedioic acid (succinic acid) from the cyclic anhydride as shown. Why does the one method give the monoester and the other the diester?



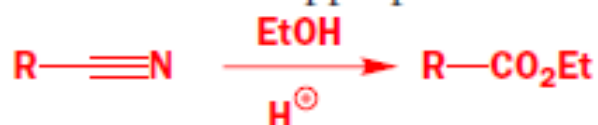
7. Suggest mechanisms for these reactions, explaining why these particular products are formed.



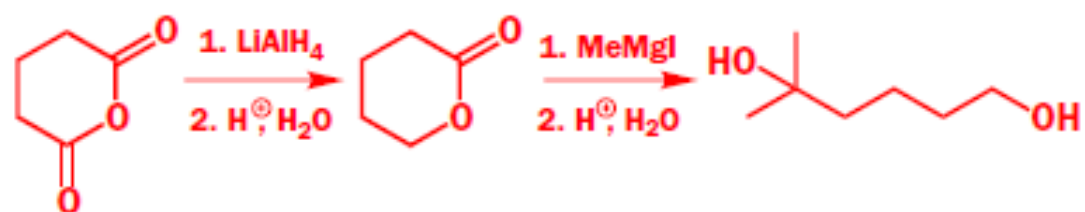
8. Here is a summary of part of the synthesis of Pfizer's heart drug Doxazosin (Cordura®). The mechanism for the first step will be a problem at the end of Chapter 17. Suggest reagent(s) for the conversion of the methyl ester into the acid chloride. In the last step, good yields of the amide are achieved if the amine is added as its hydrochloride salt in excess. Why is this necessary?



9. Esters can be made directly from nitriles by acid-catalysed reaction with the appropriate alcohol. Suggest a mechanism.



10. Give mechanisms for these reactions, explaining the selectivity (or lack of it!) in each case.



11. This reaction goes in one direction in acidic solution and in the other direction in basic solution. Draw mechanisms for the reactions and explain why the product depends on the conditions.

