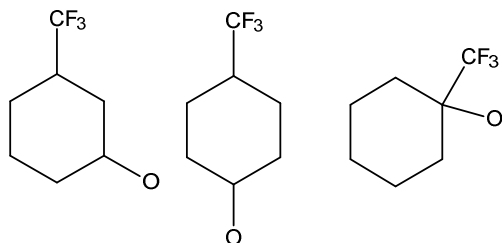


Exercises Topic 8: Reactions in Organic Chemistry

1. Which of the following compounds can exist as *cis-trans* isomers? For each than can, draw both isomers and the two chair conformers formed by interconversion, showing the orientations in space of the $-OH$ and $-CH_3$.



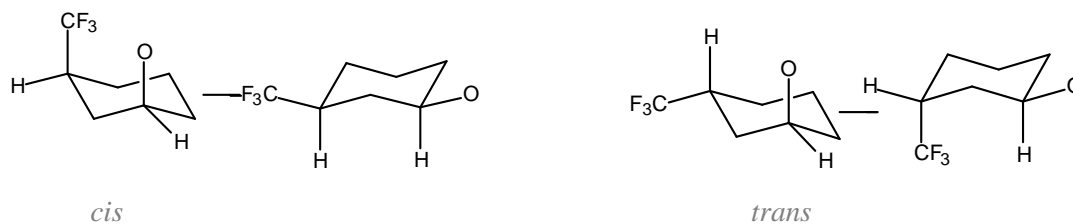
(a)

(b)

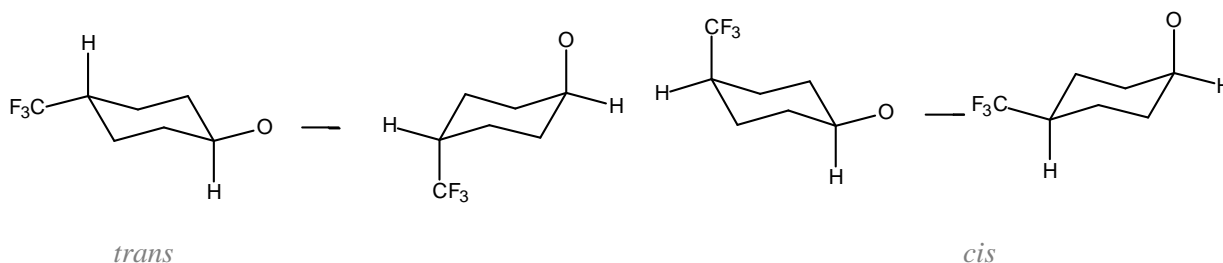
(c)

Solution: Only (a) and (b) will have *cis-trans* isomers

(a)



(b)



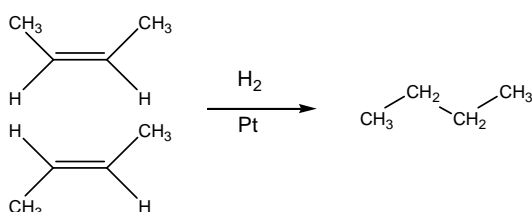
2. Find the molecular structure of lycopene ($C_{40}H_{56}$), a compound partially responsible for the red colour of some fruits (tomatoes) and demonstrate that it is a terpene.

3. Standard hydrogenation enthalpies, ΔH° , for several *cis-trans* alkene isomer pairs are shown in the following Table. (a) Can be used ΔH° values as a measure for the relative stability of the isomers? (b) Can you explain why ΔH° for *trans*-2,2,5,5-tetramethyl-3-hexene is 39 kJ/mol higher than the corresponding *cis* isomer while it is only 4 kJ/mol higher for the *trans*-2-butene?

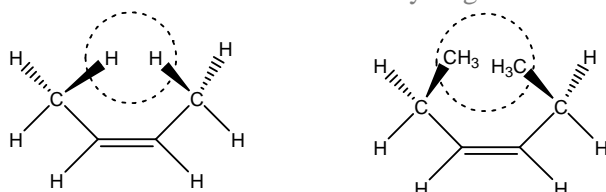
| $\Delta H^\circ_{\text{Hydrog}}$ (kJ/mol) | |
|---|--------|
| <i>cis</i> -2-butene | -119.7 |
| <i>trans</i> -2-butene | -115.5 |
| <i>cis</i> -2,2,5,5,-tetramethyl-3-hexene | -151.5 |
| <i>trans</i> -2,2,5,5,-tetramethyl-3-hexene | -112.6 |

Solution:(a) We know from thermochemistry the relation between enthalpy and internal energy $H=E+pV$. In a chemical process, enthalpy variation is given by $\Delta H=\Delta E+\Delta(pV)$. For constant

pressure processes, which are the majority of the chemical process, in which solids and/or liquids participate, $\Delta(pV) \rightarrow 0$ so $\Delta H \approx \Delta E$. Therefore, we can use reaction enthalpies as a measure of the relative stability of compounds provided that the initial or final states are the same. In the hydrogenation of alkene isomers, the initial states are different but the final states are the same as illustrated in the following scheme for 2-butene isomers



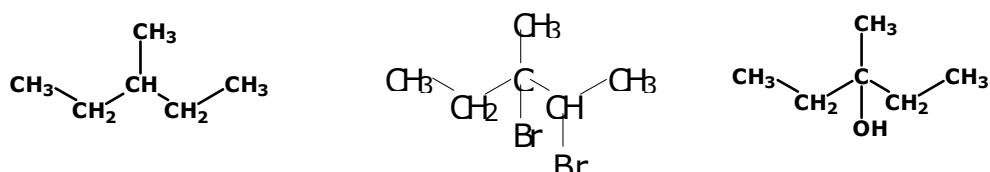
(b) The reason why *cis* isomers are less stable than *trans* is the steric stresses induced by the substituents of the double bond. This is illustrated in the following scheme. Hydrogen atoms in the *cis*-2-butene are in the same region of space creating thus a repulsive stress. This phenomenon is more intense in *cis*-2,2,5,5,-tetramethyl-3-hexene since there are methyl groups which are more voluminous than hydrogen atoms



4. Analyze the following electrophilic addition reactions to 3-methyl-2-pentene:

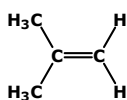
- H_2/Pt .
- $Br_2/CINa$.
- H_2SO_4 cc followed by addition of H_2O .

Solution:



5. Product **B** discolors aqueous solutions of $KMnO_4$. When **B** is treated with O_3 followed by Zn/CH_3-COOH , it is transformed into acetone and formaldehyde. Deduce the structure of **B**.

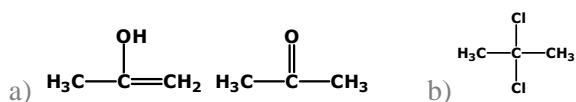
Solution:



6. Which are the reaction products when propine is treated with?:

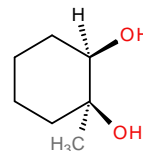
- Water in the presence of H_2SO_4 and $HgSO_4$
- ClH in excess

Solution:

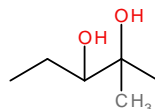


7. Which are the alkenes you will select as starting molecules to obtain the following compounds? :

a. (1S,2R)-1-methylcyclohexane-1,2-diol

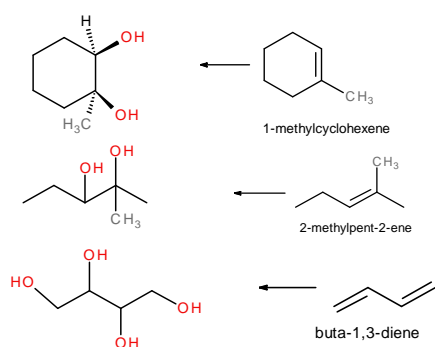


b. 2-methylpentane-2,3-diol



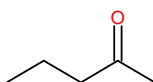
c. butane-1,2,3,4-tetrol

Solution:

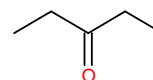


8. Which are the alkynes you will select to prepare the following ketones?

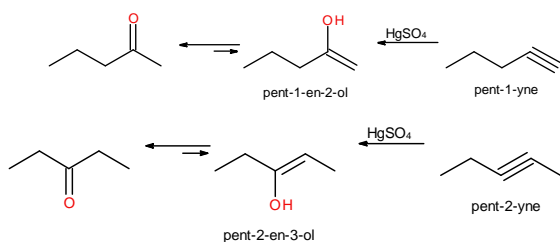
a. pentan-2-one



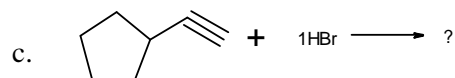
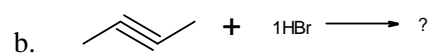
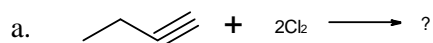
b. pentan-3-one



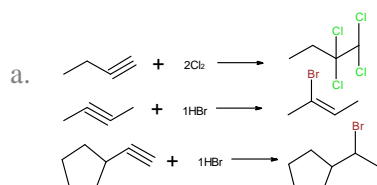
Solution:



9. Which are the expected products for the following reactions?



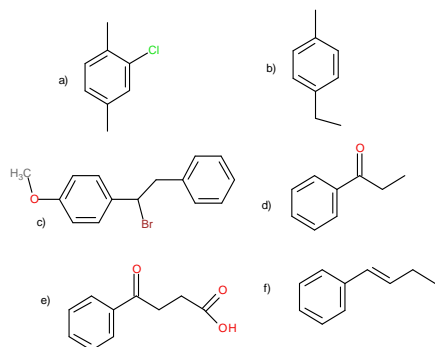
Solution:



10. Which are the expected products for the following reactions?

- p-Xylene (1,4-dimethylbenzene) + Cl_2/Fe
- Toluene + $\text{CH}_3\text{-CH}_2\text{Cl} + \text{AlCl}_3$
- p- $\text{CH}_3\text{O-C}_6\text{H}_4\text{-CH=CH-C}_6\text{H}_5 + \text{HBr}$
- Benzene + $\text{CH}_3\text{-CH}_2\text{-COCl} + \text{AlCl}_3$
- Benzene + succinic anhydride + AlCl_3
- 1-phenyl-1,3-butadiene + 1 mol $\text{H}_2 + \text{Ni}/30^\circ\text{C}/2 \text{ atm}$

Solution:



11. Which are the main products in the mononitration of

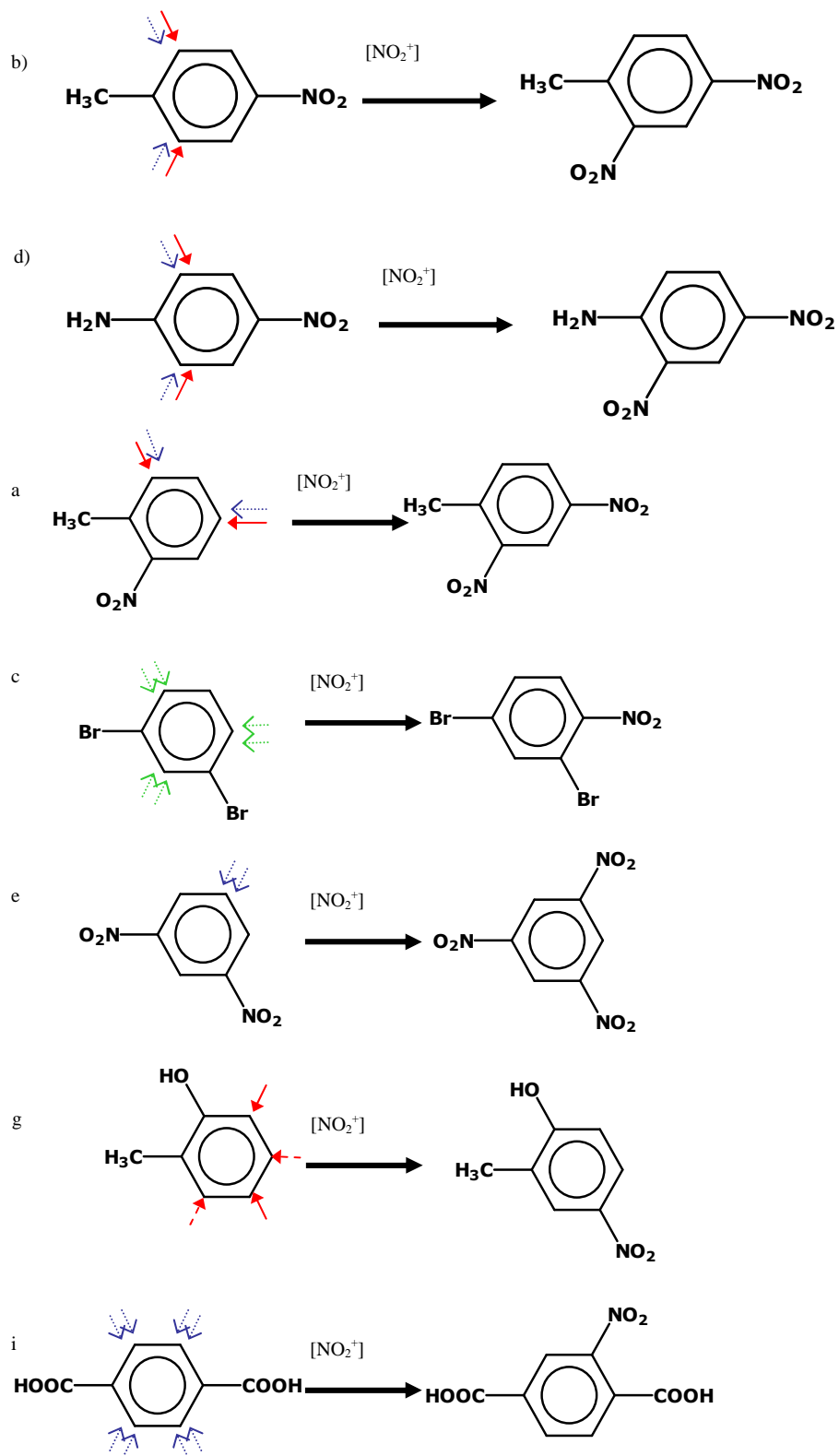
- | | |
|--|--|
| a. o-nitrotoluene | g. o-cresol |
| b. p-nitrotoluene | h. p-cresol |
| c. m-dibromobenzene | i. p- $\text{C}_6\text{H}_4\text{-(COOH)}_2$ |
| d. p-nitroaniline | (tereftalic acid), |
| e. m-dinitrobenzene | j. p-xylene |
| f. m-cresol (3- $\text{CH}_3\text{-C}_6\text{H}_4\text{-OH}$) | |

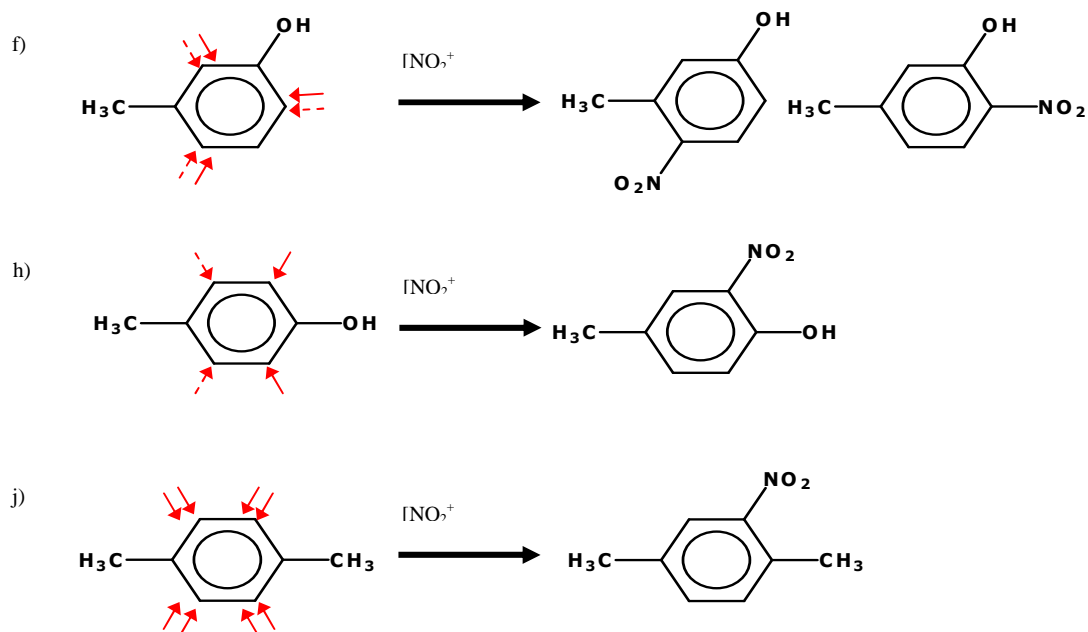
Solution:

Chemistry for Biomedical Engineering. Exercises Topic 8

Open Course Ware Universidad Carlos III de Madrid. 2012/2013

Authors: Juan Baselga & María González





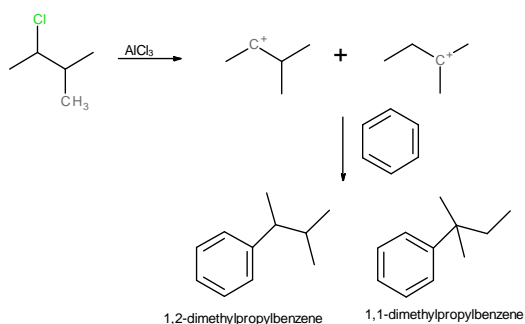
12. Design a synthetic route to obtain the following products starting from benzene

- p-nitrotoluene
- m-nitrophenylmethylketone
- m-nitrotoluene
- p-bromonitrobenzene

Solution: a) Alkylation with CH_3Cl followed by nitration; b) Acylation with CH_3COCl followed by nitration; c) Nitration followed by acylation with CH_3Cl ; d) Bromination followed by nitration

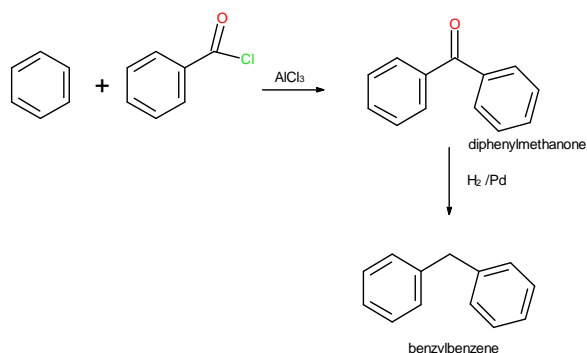
13. The Friedel-Crafts electrophilic substitution of benzene with 2-chloro-3-methylbutane gives two products, being one of them the most abundant. Explain the structures of both.

Solution:



14. How can you prepare diphenylmethane starting from benzene and an adequate acyl chloride?

Solution:



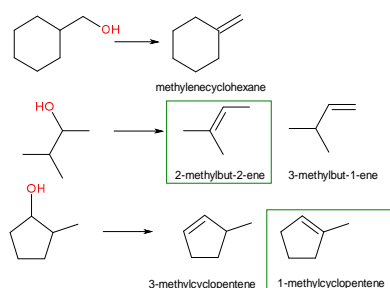
15. Order the following alcohols according to their acidity: Phenol, *p*-methylphenol, *p*-(trifluoromethyl)phenol. Is *p*-cyanophenol more acid than phenol?

Solution:

p-(trifluoromethyl)phenol > Phenol > *p*-methylphenol
p-cyanophenol is more acid than phenol

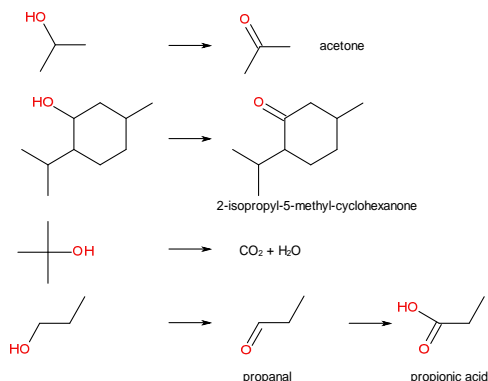
16. Draw the structural formulas for the alkenes formed by dehydration of the following alcohols: (a) 3-methyl-2-butanol; (b) 2-methylcyclopentanol; (c) cyclohexylmethanol

Solution:



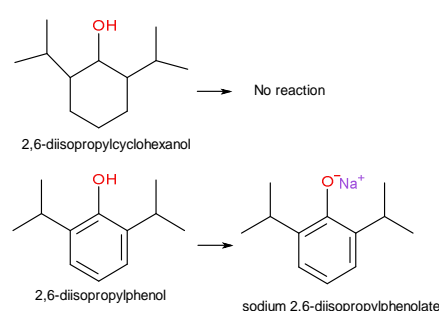
17. Draw the structural formulas for the intermediate and final compounds when the following alcohols are treated with a strong oxidant: (a) *isopropanol*; (b) menthol; (c) 2-methylpropan-2-ol; (d) 1-propanol.

Solution

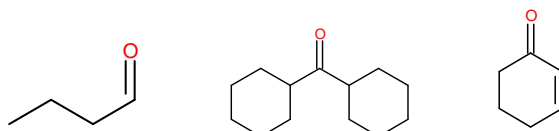


18. What are the reaction products of 2,6-diisopropylcyclohexanol and 2,6-diisopropylphenol with aqueous sodium hydroxide?

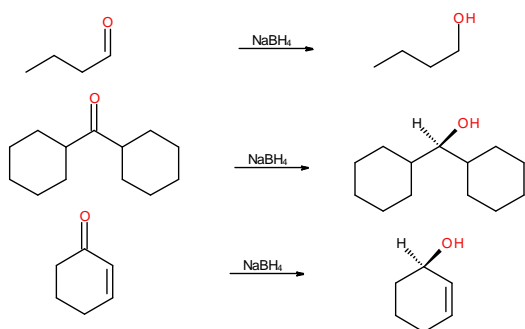
Solution



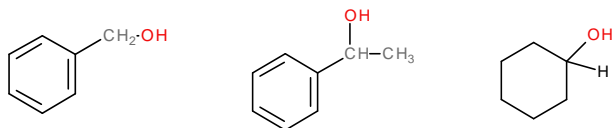
19. Sodium borohydride (NaBH₄) is a common reducing agent in organic chemistry, less reactive than LiAlH₄. Deduce the reaction products when the following molecules are treated with NaBH₄



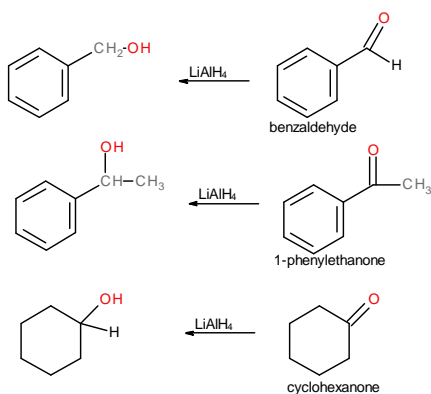
Solution:



20. Deduce the parent carbonyl compounds whose reduction originates the following alcohols

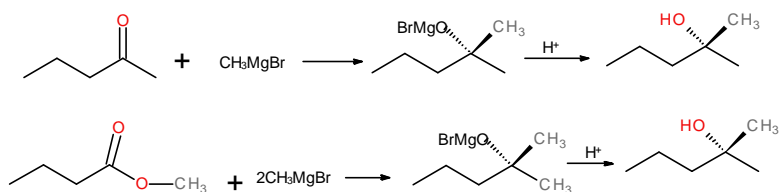


Solution:



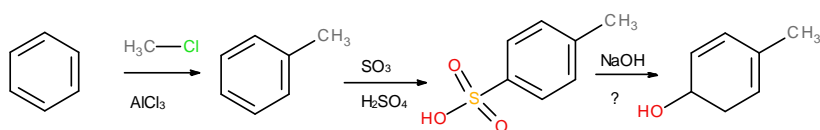
21. 2-methyl-2-pentanol can be synthesized from two carbonyl compounds A and B using methyl magnesium bromide as Grignard reagent. A needs two moles of CH_3MgBr while B only needs one. Deduce the structural formula of A and B.

Solution:

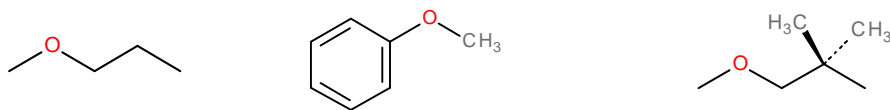


22. Propose a synthetic route to prepare *p*-cresol from benzene (two steps).

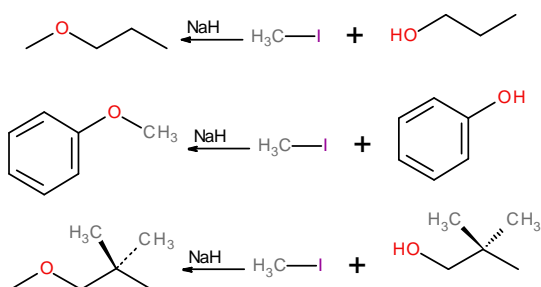
Solution:



23. How would you prepare the following ethers using the Williamson synthesis?



Solution:



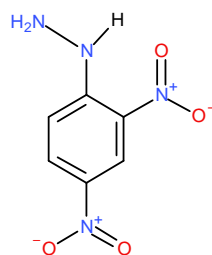
24. Propose the reaction products when acetone is treated with:

a) Hydroxylamine (NH_2OH)

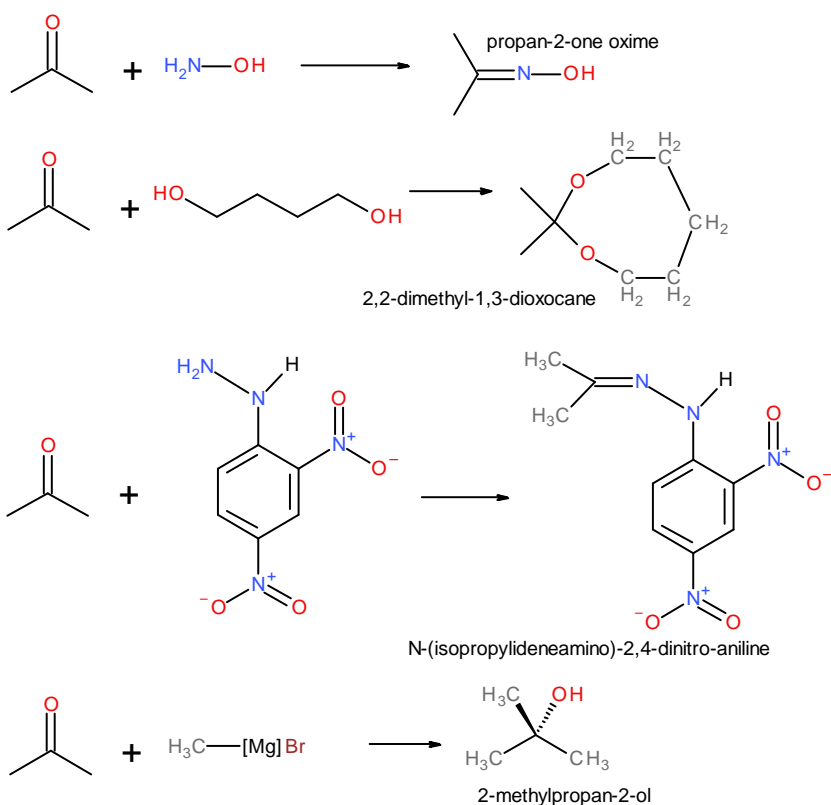
b) Butanediol

c) 2,4-dinitrophenylhydrazine

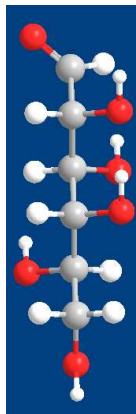
d) Methyl magnesium bromide



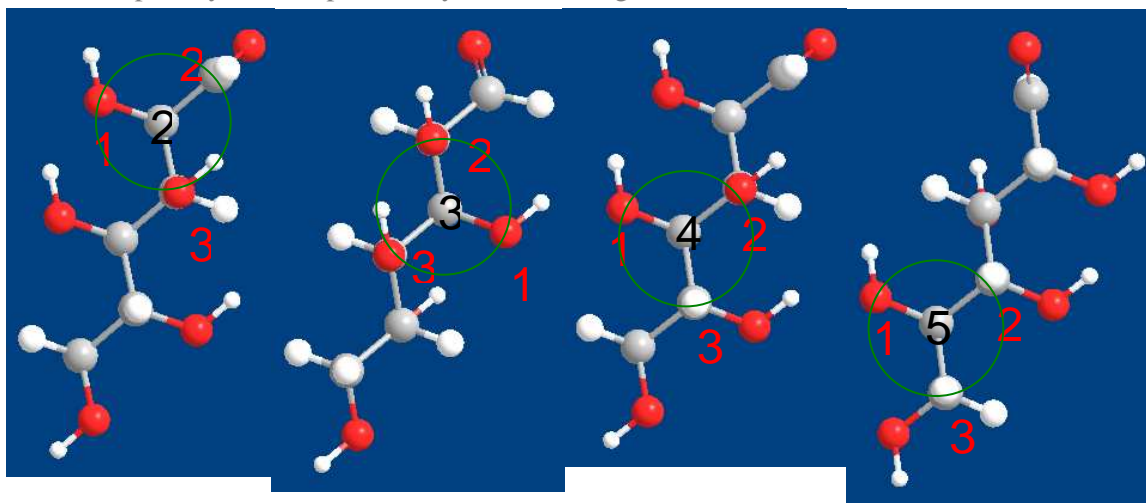
Solution:



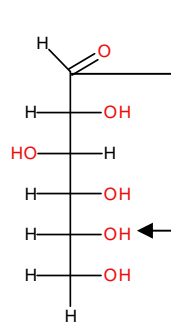
25. Find if the following molecule is D-Glucose. Draw the two possible six membered rings formed by hydroxy addition to the aldehyde.



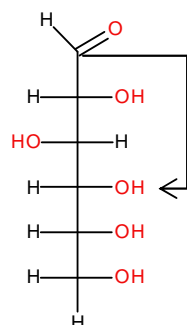
Solution: D-Glucose is (2R,3S,4R,5R)-2,3,4,5,6-Pentahydroxyhexanal. We need to find the R/S configuration of each carbon. Numbers start from the aldehyde (1). We apply Cahn rules to each carbon as shown in the following images. In these, the original image has been rotated to allow the lowest priority atom to point away from the image



Therefore, C2 is R, C3 is S, C4 is R and C5 is also R. Therefore, this molecule is D-glucose. Ring closing can occur by hemiacetal formation between carbon C1 and the hydroxy group either from C4 or C5. If ring closes by C4, a five membered ring is formed. Six membered ring (pyranose) is formed closing by C5. With a Fischer projection it is seen more clearly

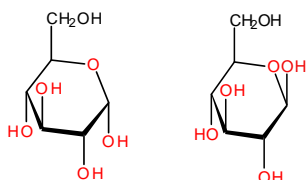


Furanose ring

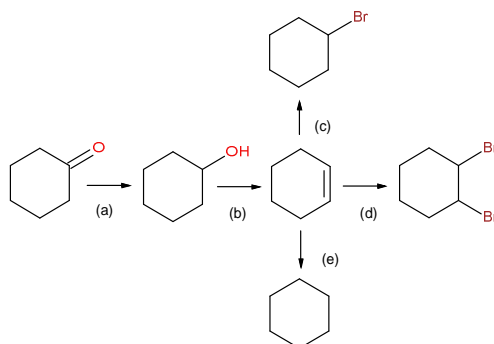


Pyranose ring

Hemiacetal formation transforms carbon C1 into a chiral center since it is bonded to -H, OH, -C and -O. Therefore, there are two ways to locate these four substituents that give rise to the two different optical isomers. To view them more clearly a special projection called Haworth projection is commonly used:



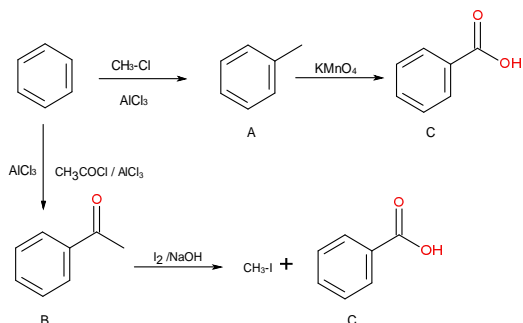
26. Show reagents and experimental conditions to convert cyclohexanone to each of the following compounds



Solution: a) Oxidation with $K_2Cr_2O_7$; b) Dehydration with H_2SO_4 ; c) Addition of HBr ; d) Addition of Br_2 ; e) Hydrogenation with a catalyst as for example Pt .

27. Product **A** is obtained reacting benzene with one mole of CH_3Cl using $AlCl_3$ as catalyst. **A** is subjected to a strong oxidation treatment giving the product **D**. If instead of this route, benzene is treated with acetyl chloride (CH_3COCl) in the presence of $AlCl_3$ and afterwards, with $I_2 / NaOH$ followed by acid treatment, the same final product **D** is obtained. Deduce the structural formulas of all the compounds.

Solution:



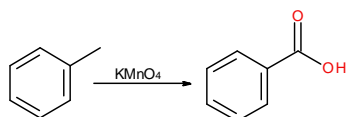
28. Propose synthetic routes to obtain benzoic acid from the following substances:

- Toluene
- Benzonitrile
- Acetophenone

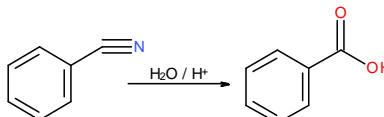
- d) Benzyl alcohol
e) Benzaldehyde

Solution:

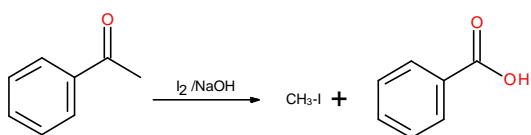
(a)



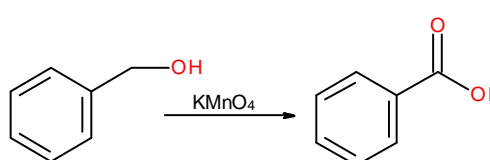
(b)



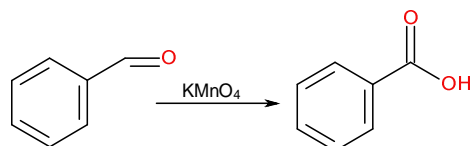
(c)



(d)



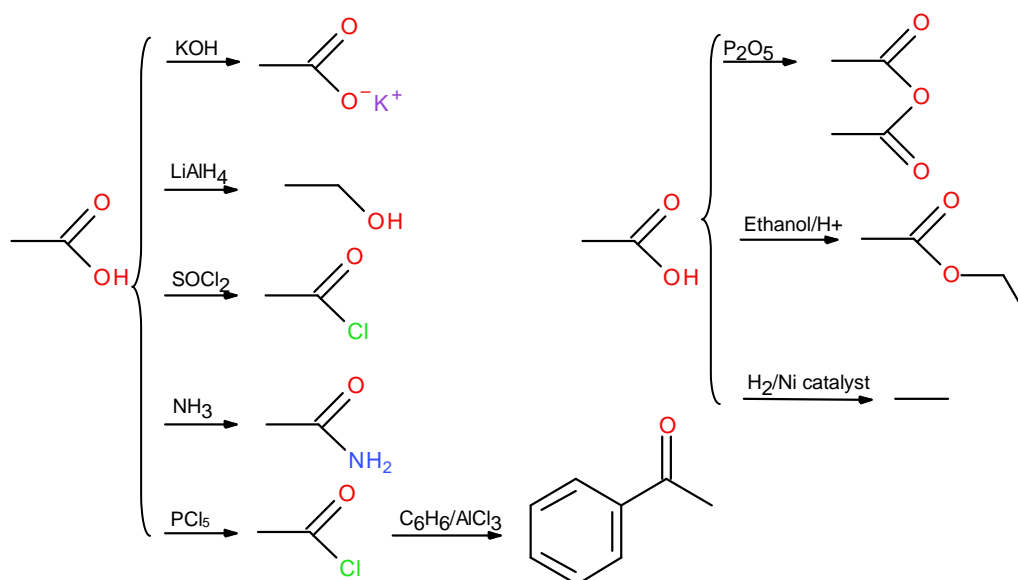
(e)



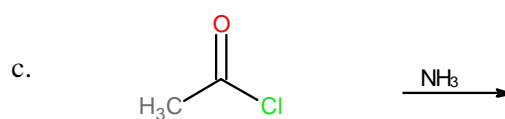
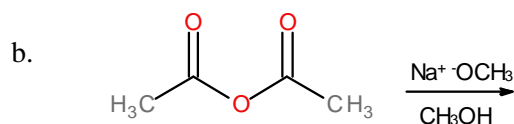
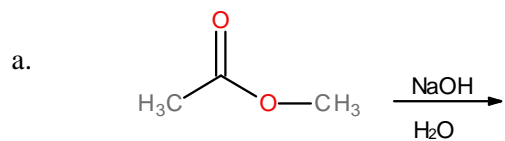
29. Write the reactions of acetic acid with:

- a) KOH ,
b) LiAlH_4 ,
c) SOCl_2 ,
d) NH_3 ,
e) PCl_5 and subsequently with $\text{C}_6\text{H}_6/\text{AlCl}_3$
f) P_2O_5
g) Ethanol/ H^+ ,
h) H_2/Ni catalyst

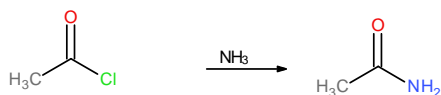
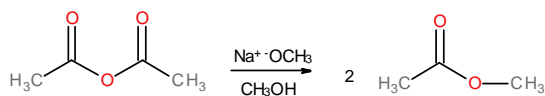
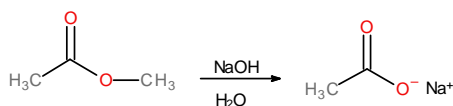
Solution:



30. Propose the reaction products for the following acyl nucleophilic substitution reactions:



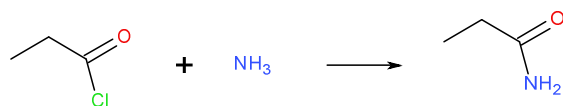
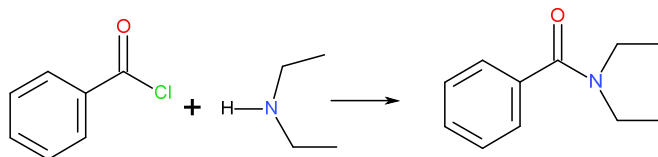
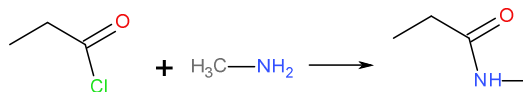
Solution:



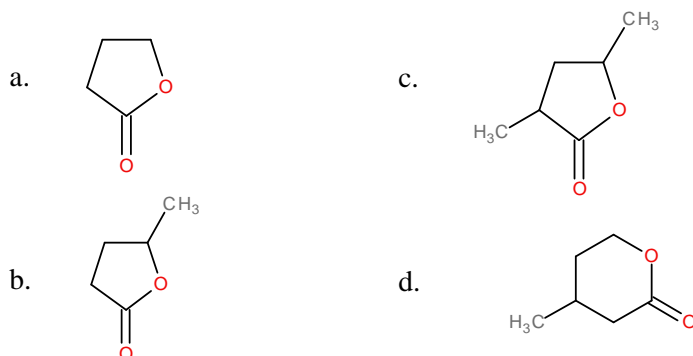
31. Using an acid chloride and an amine or ammonia, propose a synthetic route to obtain:

- $\text{CH}_3\text{-CH}_2\text{-CONH-CH}_3$
- N,N-diethylbenzamide
- Propanamide

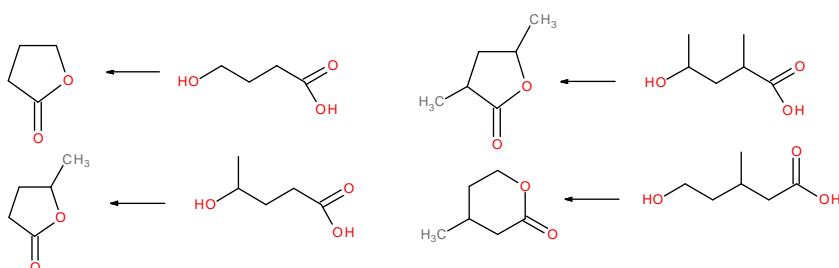
Solution:



32. Hydroxyacids are molecules that behave as acids and alcohols. When the two functionalities are separated an appropriate distance the molecule loses spontaneously a water molecule by intramolecular esterification forming a cyclic compound named lactone. Five member rings are called γ -lactones and six member rings δ -lactones. Find the corresponding hydroxyacids from which the following lactones are formed:



Solution:



33. A given compound **A** ($C_2H_4O_2$) is divided in three portions. The first one is treated with thionyl chloride giving **B** which reacts with methylamine to give **C**. **C** is reduced with $LiAlH_4$ to give **D**, a secondary amine (C_3H_9N). The second portion is treated with P_2O_5 to give **E** which is treated with **D** to give two products, **F**, an amide ($C_5H_{11}NO$), and **A**. The third portion is treated with methanol in acid media to give **G**; **G** is treated with ammonia giving **H**, which is reduced with $LiAlH_4$ to give a primary amine **I** (C_2H_7N). Deduce the structural formulas of compounds **A** to **I**.

Solution: The reactions that give **B**, **E** and **G** products are typical nucleophilic substitutions. **A** must be an acid. There is only one acid with two carbon atoms: acetic acid.

