

Chapter 9

Aldehydes and Ketones

Chapter Summary

The **carbonyl group**, $C=O$, is present in both **aldehydes** ($RCH=O$) and **ketones** ($R_2C=O$). The IUPAC ending for naming aldehydes is *-al*, and numbering begins with the carbonyl carbon. The ending for the names of ketones is *-one*, and the longest chain is numbered as usual. Common names are also widely used. Nomenclature is outlined in Sec. 9.1.

Formaldehyde, **acetaldehyde**, and **acetone** are important commercial chemicals, synthesized by special methods. In the laboratory, aldehydes and ketones are most commonly prepared by oxidizing alcohols, but they can also be prepared by hydrating alkynes and by Friedel-Crafts acylation of arenes. Aldehydes and ketones occur widely in nature (see Figure 9.1).

The carbonyl group is planar, with the sp^2 carbon trigonal. The $C=O$ bond is polarized, with C positive and O negative. Many carbonyl reactions are initiated by nucleophilic addition to the positive carbon and completed by addition of a proton to the oxygen.

With acid catalysis, alcohols add to the carbonyl group of aldehydes to give **hemiacetals** [$RCH(OH)OR'$]. Further reaction with excess alcohol gives **acetals** [$RCH(OR')_2$]. Ketones react similarly. These reactions are reversible; that is, acetals can be readily hydrolyzed by aqueous acid to their alcohol and carbonyl components. Water adds similarly to the carbonyl group of certain aldehydes (for example, formaldehyde and chloral) to give hydrates. Hydrogen cyanide adds to carbonyl compounds as a carbon nucleophile to give **cyanohydrins** [$R_2C(OH)CN$].

Grignard reagents add to carbonyl compounds. The products, after hydrolysis, are alcohols whose structures depend on that of the starting carbonyl compound. Formaldehyde gives *primary* alcohols, other aldehydes give *secondary* alcohols, and ketones give *tertiary* alcohols.

Nitrogen nucleophiles add to the carbonyl group. Often, addition is followed by elimination of water to give a product with a $R_2C=NR$ group in place of the $R_2C=O$ group. For example, primary amines ($R'NH_2$) give **imines** ($R_2C=NR'$); **hydroxylamine** (NH_2OH) gives **oximes** ($R_2C=NOH$); and **hydrazine** (NH_2NH_2) gives **hydrazones** ($R_2C=NNH_2$).

Aldehydes and ketones are easily reduced to primary or secondary alcohols, respectively. Useful reagents for this purpose are various metal hydrides such as **lithium aluminum hydride** ($LiAlH_4$) or **sodium borohydride** ($NaBH_4$).

Aldehydes are more easily oxidized than ketones. The **Tollens' silver mirror test** is positive for aldehydes and negative for ketones.

Aldehydes or ketones with an α -hydrogen exist as an equilibrium mixture of **keto** ($H-C_\alpha-C=O$) and **enol** ($C_\alpha=C-OH$) **tautomers**. The keto form usually predominates. An α -hydrogen is weakly acidic and can be removed by a base to produce a resonance-stabilized **enolate anion**. Deuterium exchange of α -hydrogens provides experimental evidence for enols as reaction intermediates.

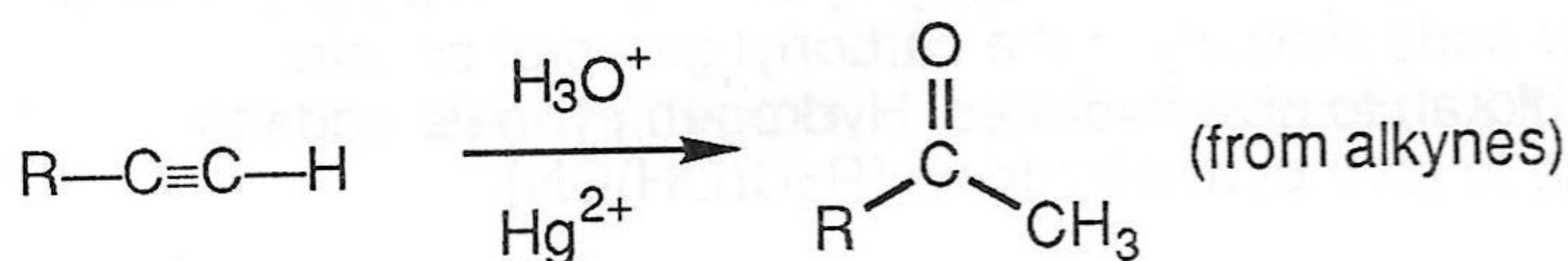
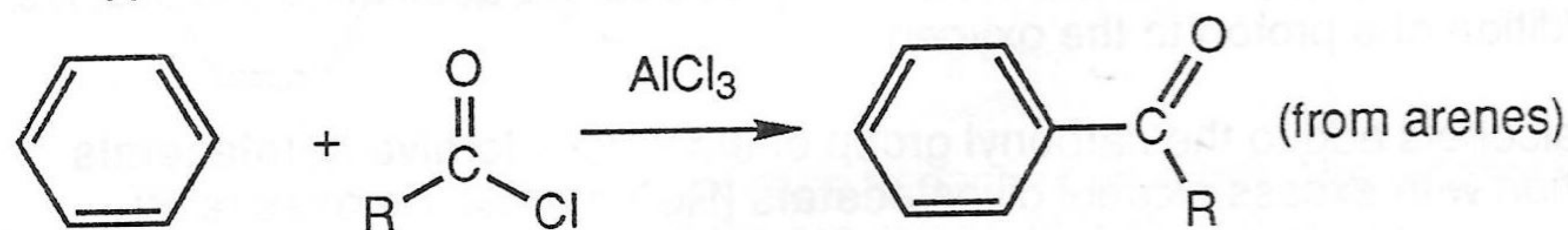
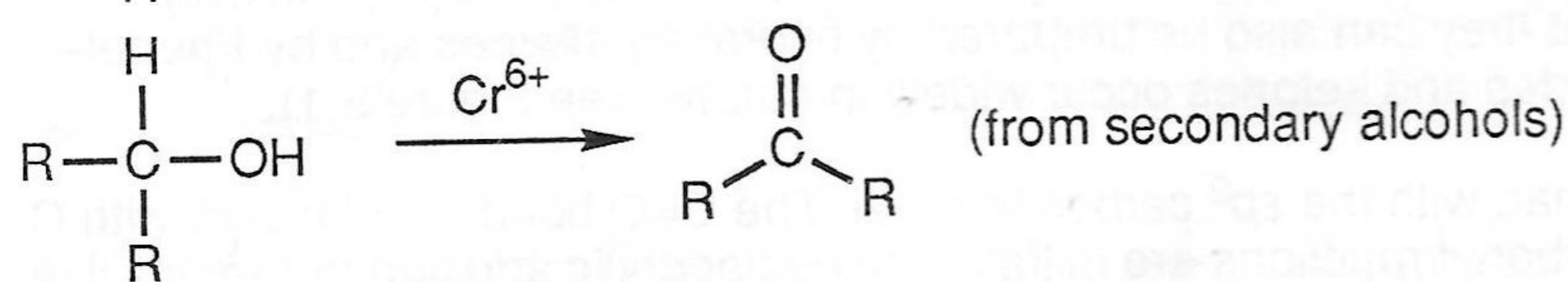
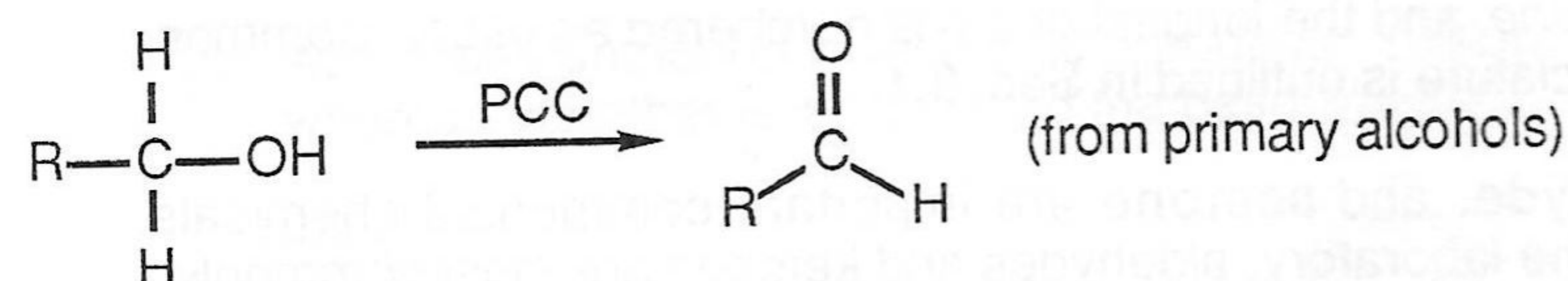
In the **aldol condensation**, an enolate anion acts as a carbon nucleophile and adds to a carbonyl group to form a new carbon-carbon bond. Thus, the α -carbon of one aldehyde molecule becomes bonded to the carbonyl carbon of another aldehyde molecule to form an aldol (a 3-

hydroxyaldehyde). In the **mixed aldol condensation**, the reactant with an α -hydrogen supplies the enolate anion, and the other reactant, usually without an α -hydrogen, supplies the carbonyl group to which the enolate ion adds. The aldol reaction is used commercially and also occurs in nature.

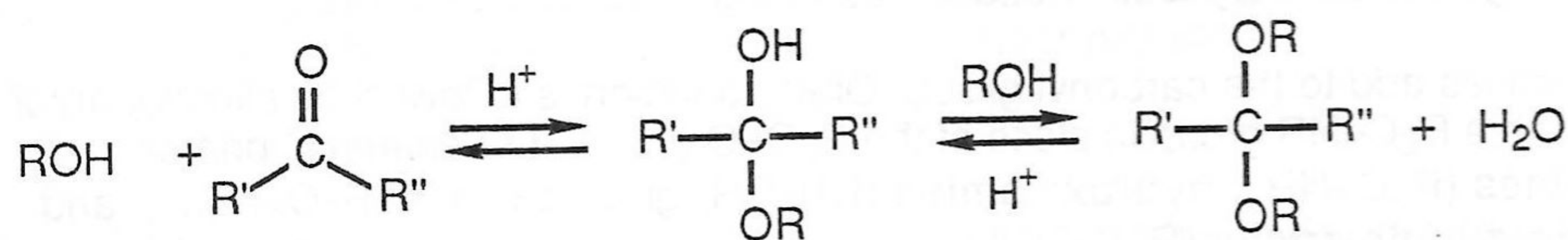
Quinones are cyclic conjugated diketones. They are colored compounds used as dyes. They also play important roles in reversible biological oxidation–reduction (electron-transfer) reactions.

Reaction Summary

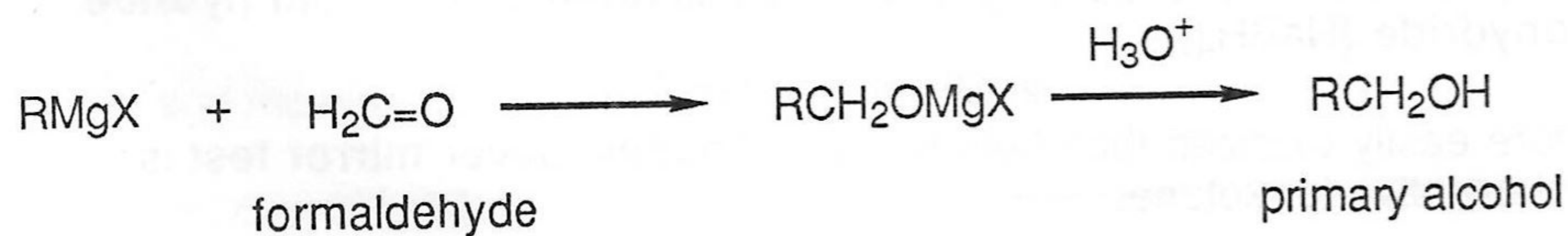
Preparation of Aldehydes and Ketones

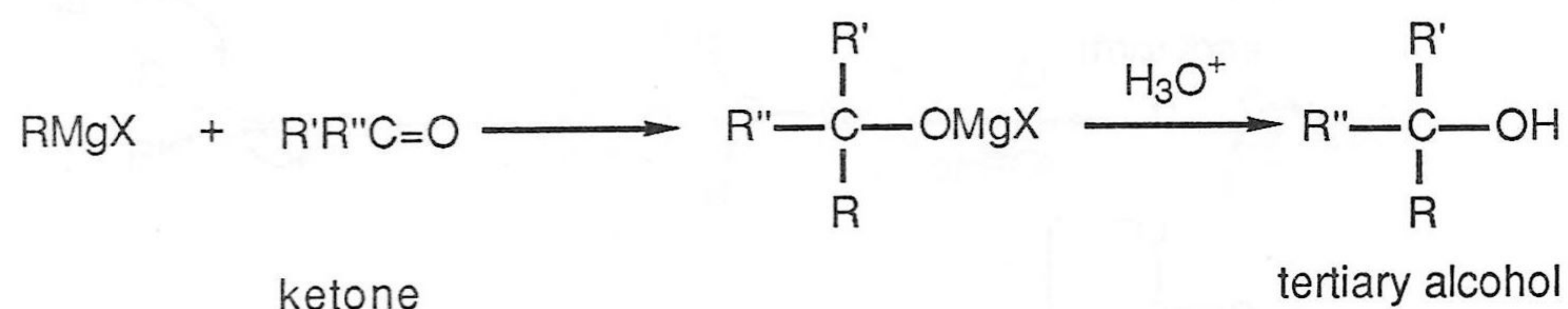
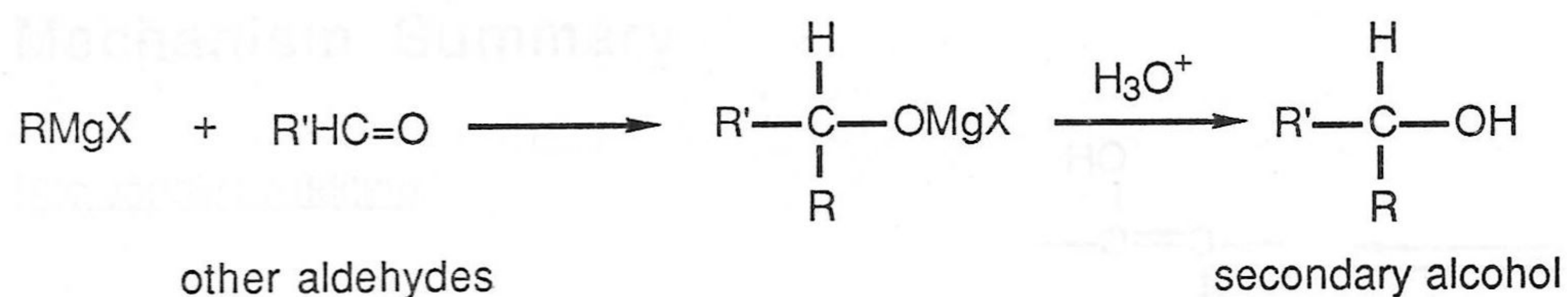
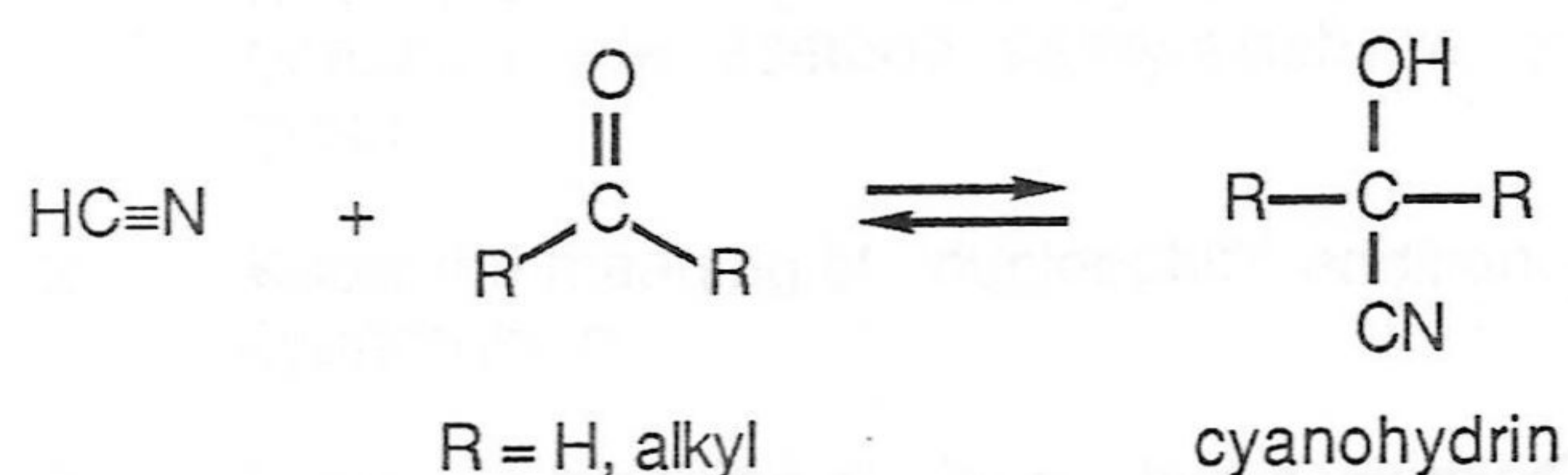
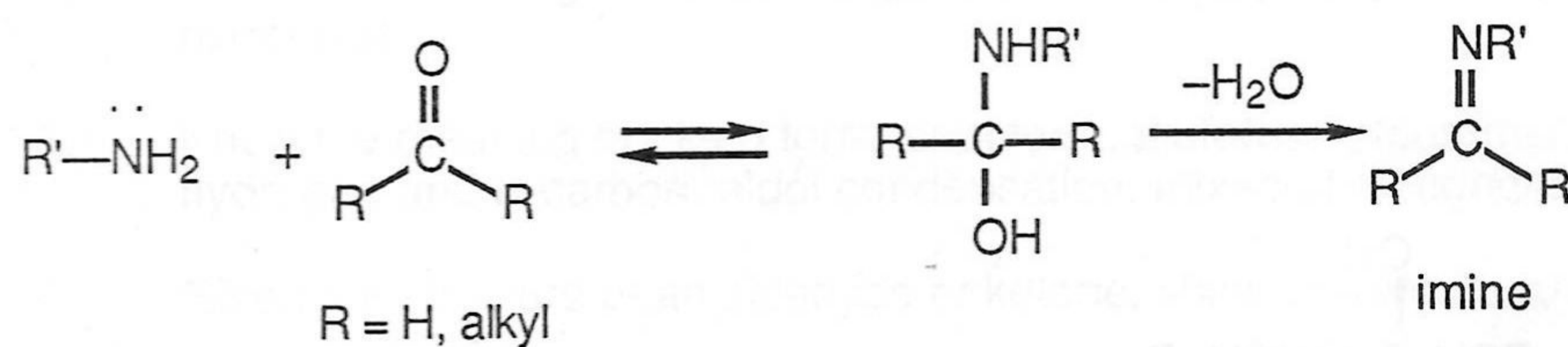
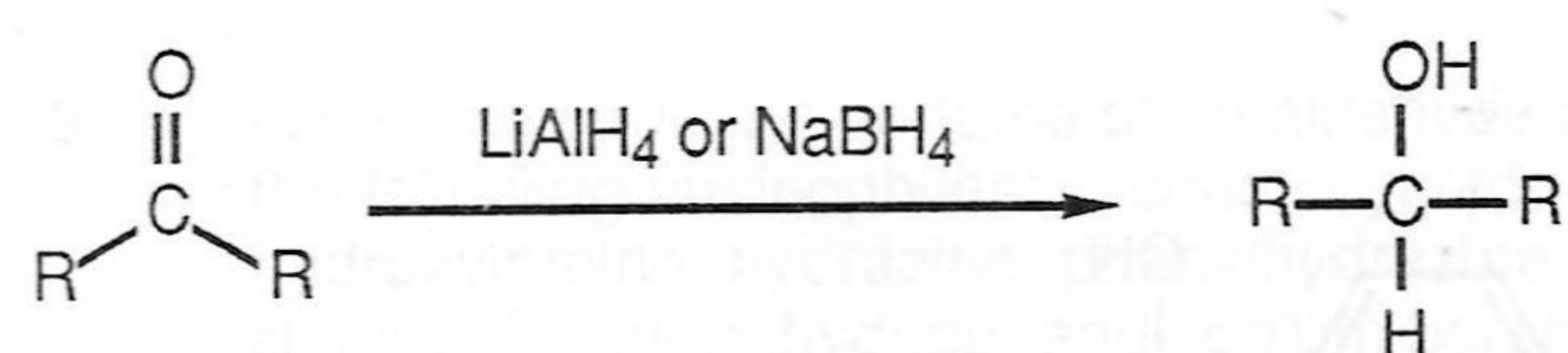
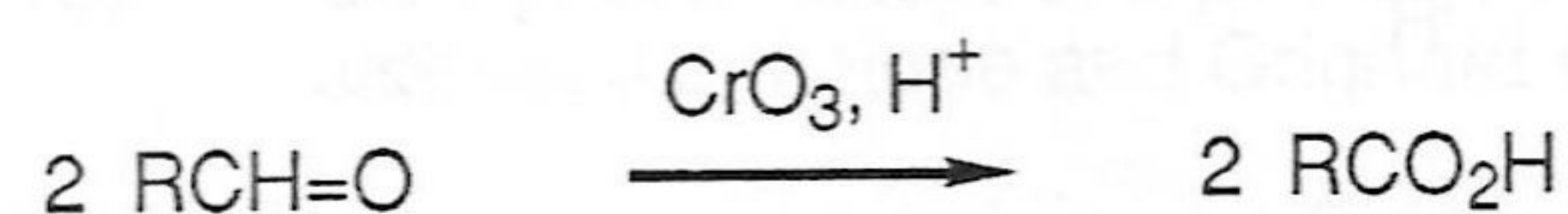
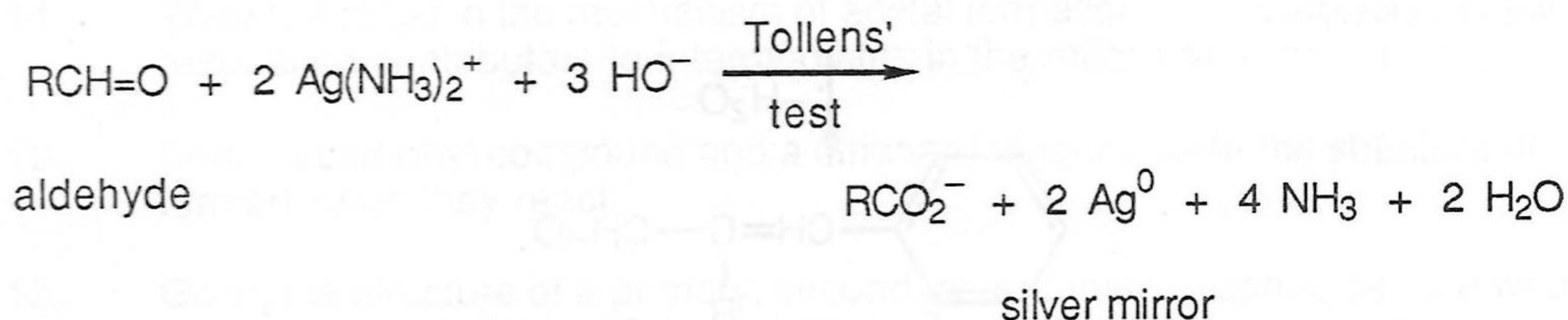


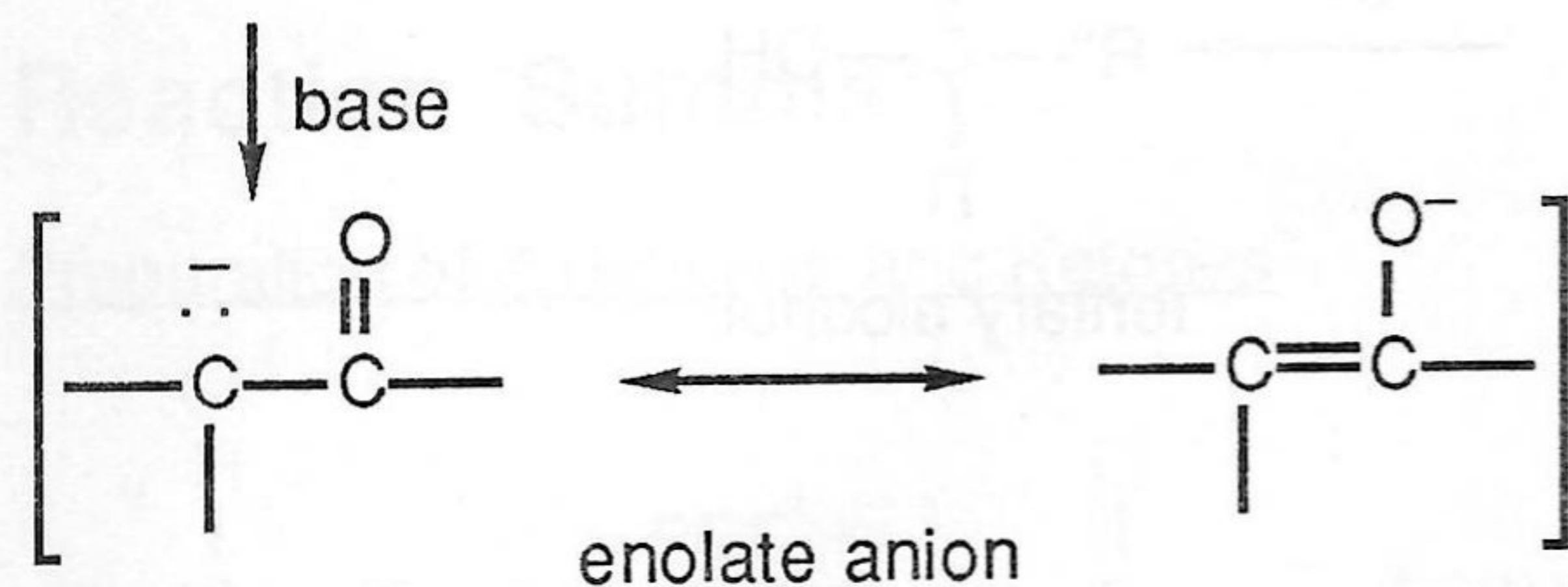
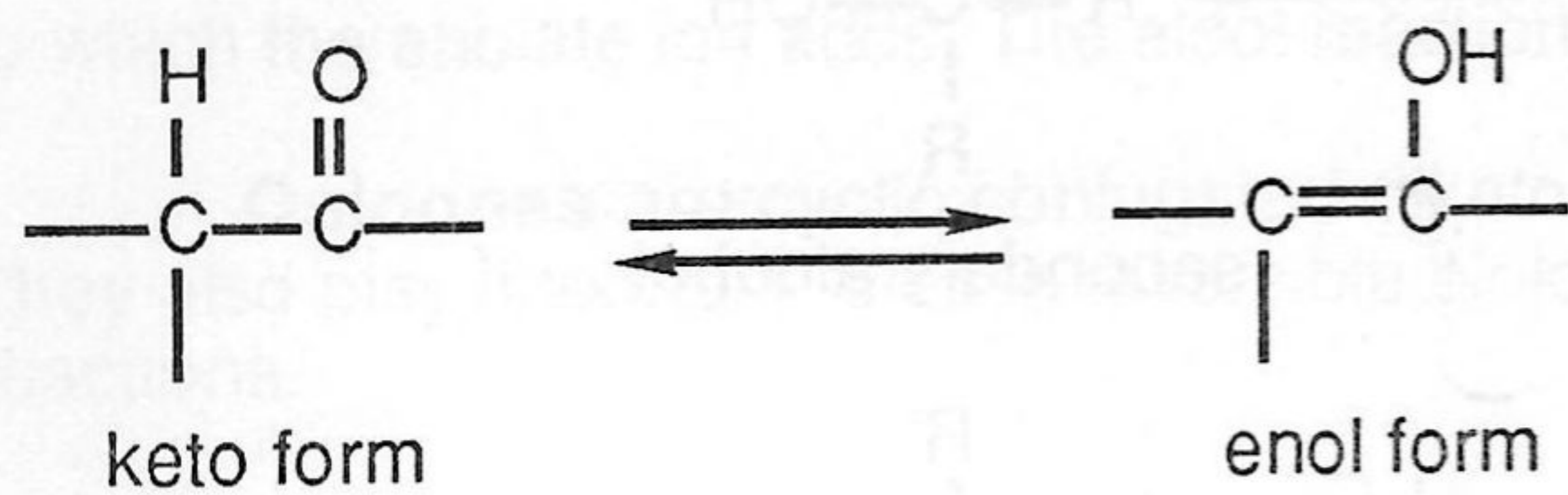
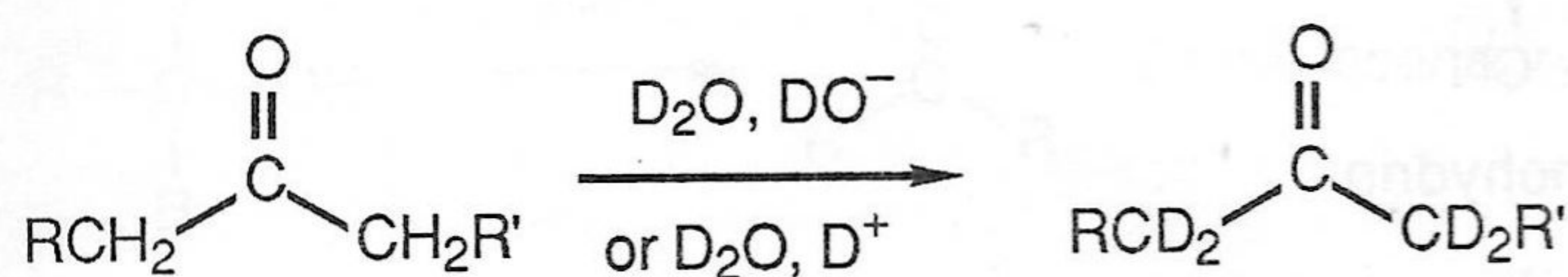
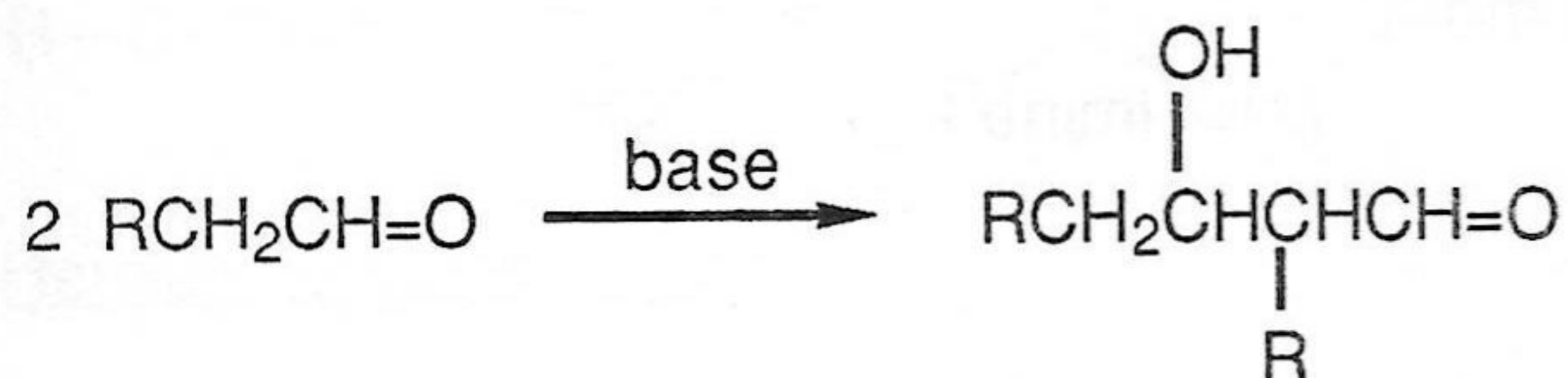
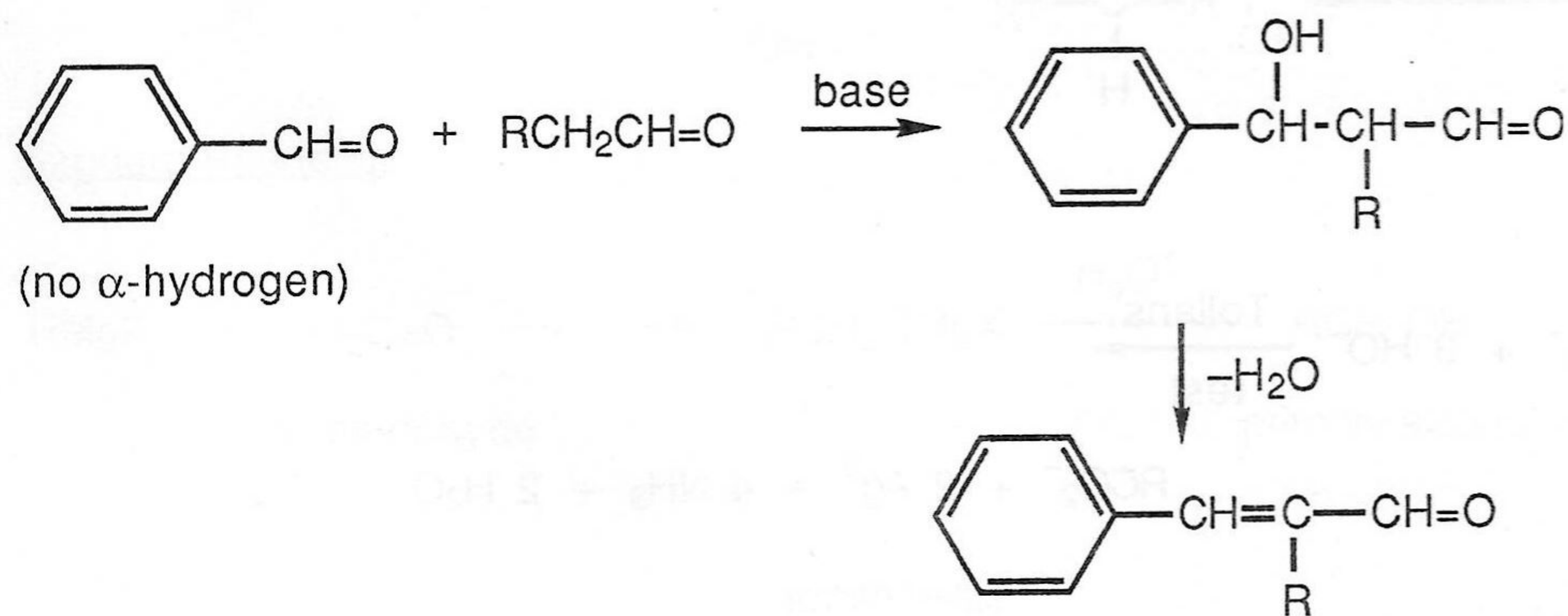
Hemiacetals and Acetals



Grignard Reagents

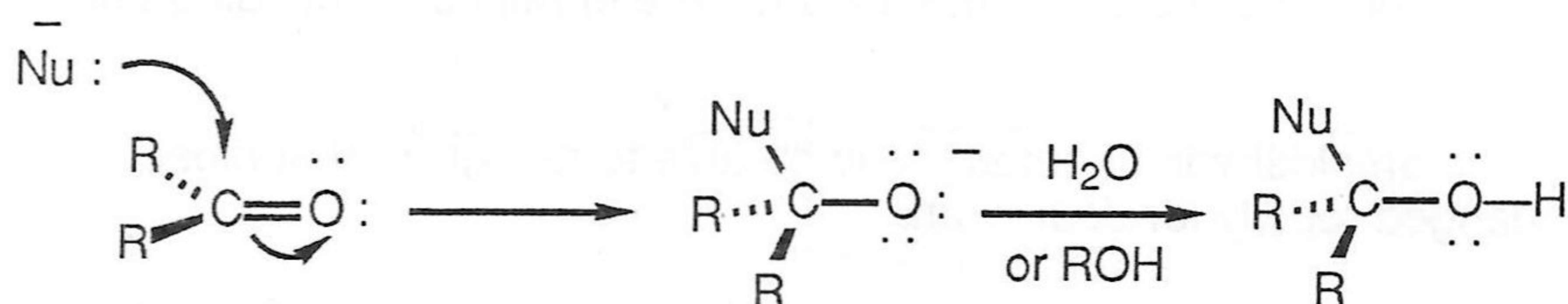


Hydrogen CyanideNitrogen NucleophilesReductionOxidation

TautomerismDeuterium Exchange(only α -hydrogens exchange)Aldol CondensationMixed Aldol Condensation

Mechanism Summary

Nucleophilic Addition



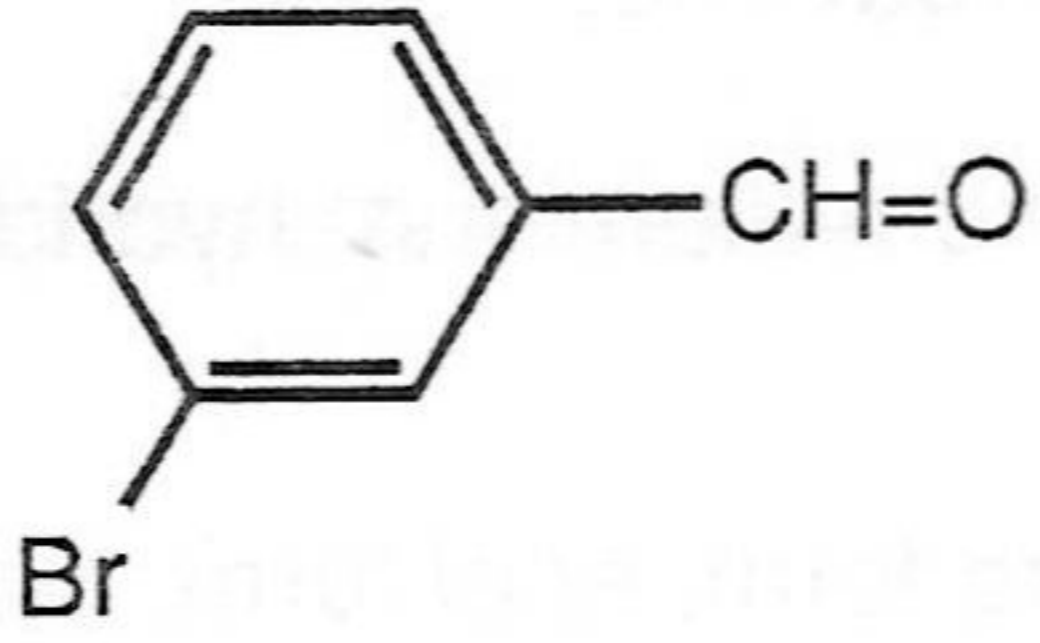
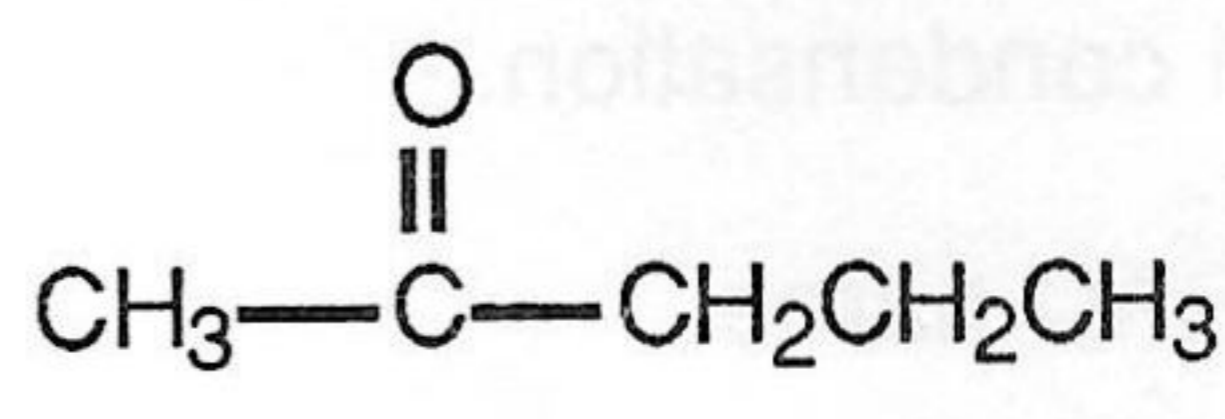
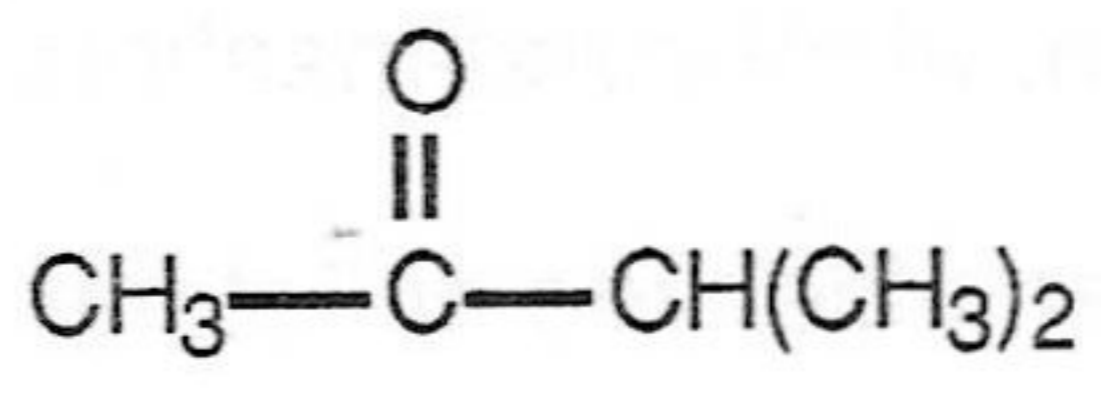
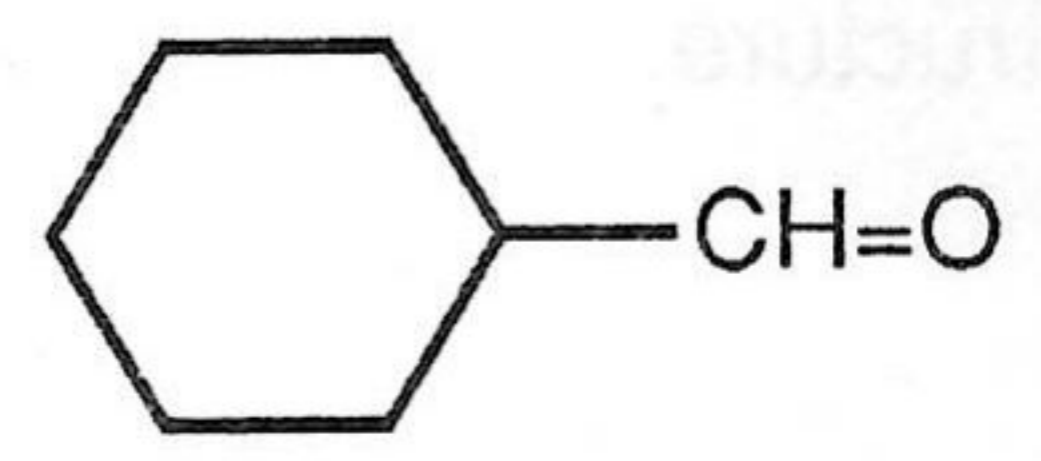
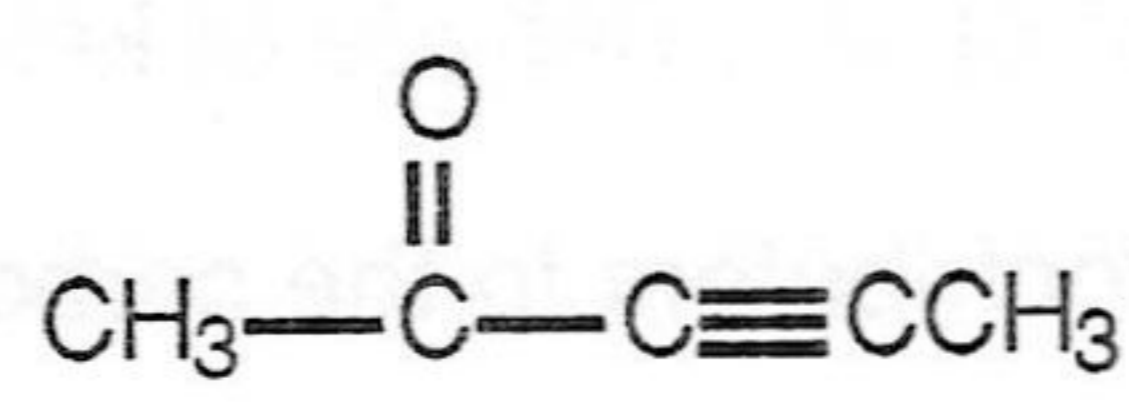
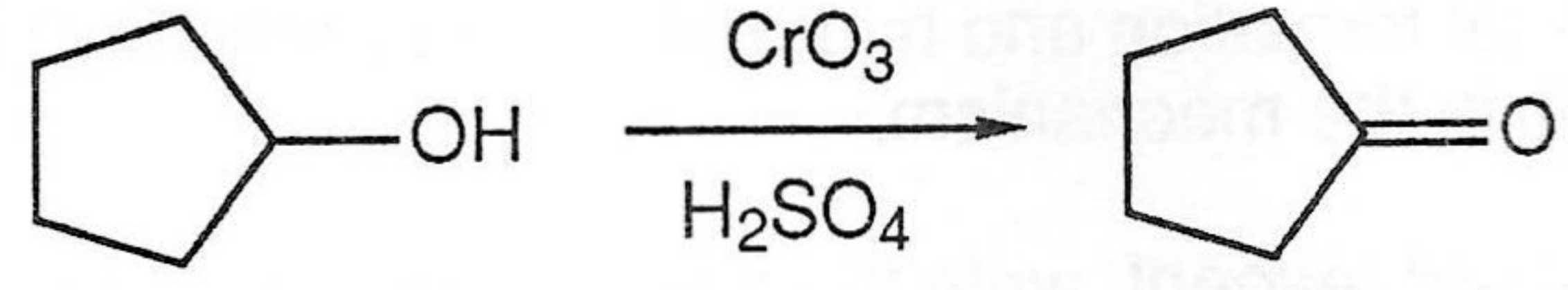
Learning Objectives

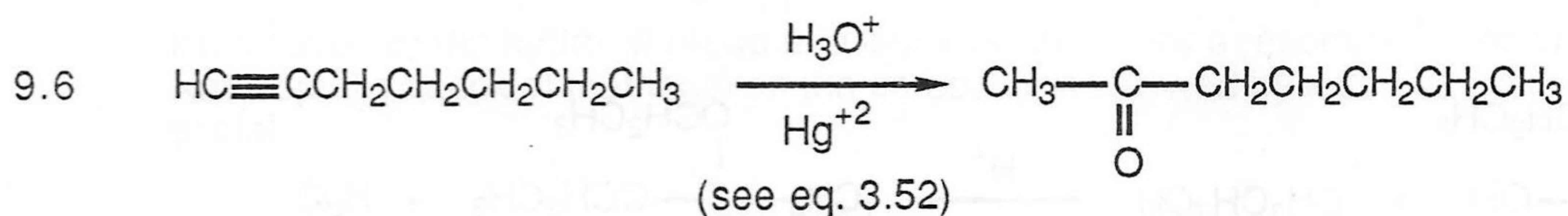
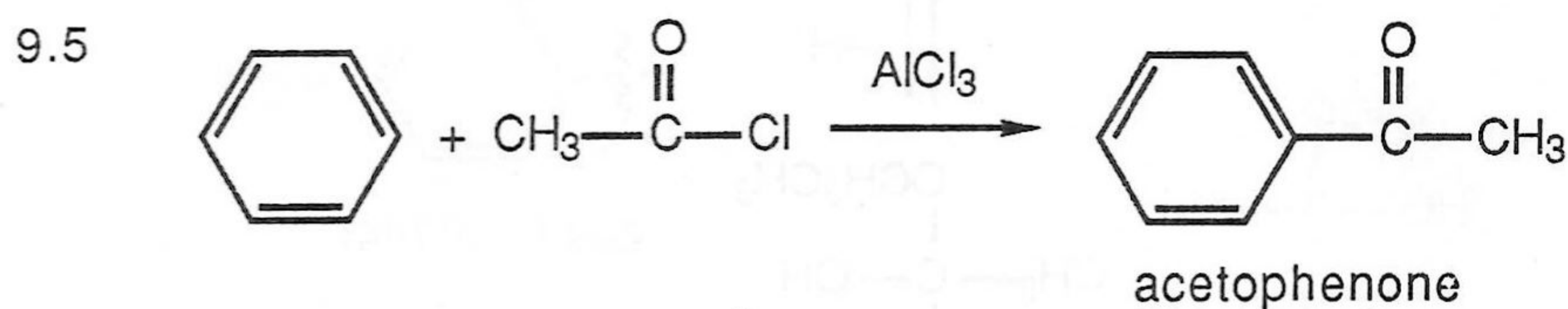
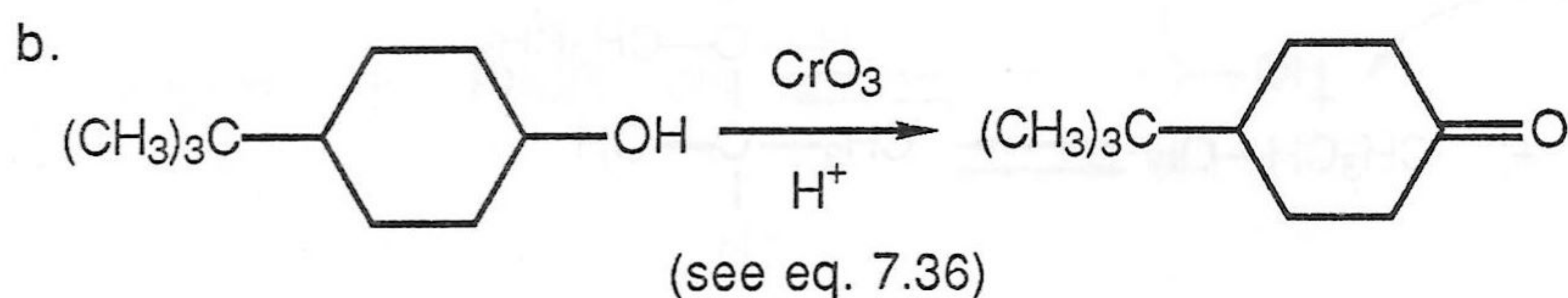
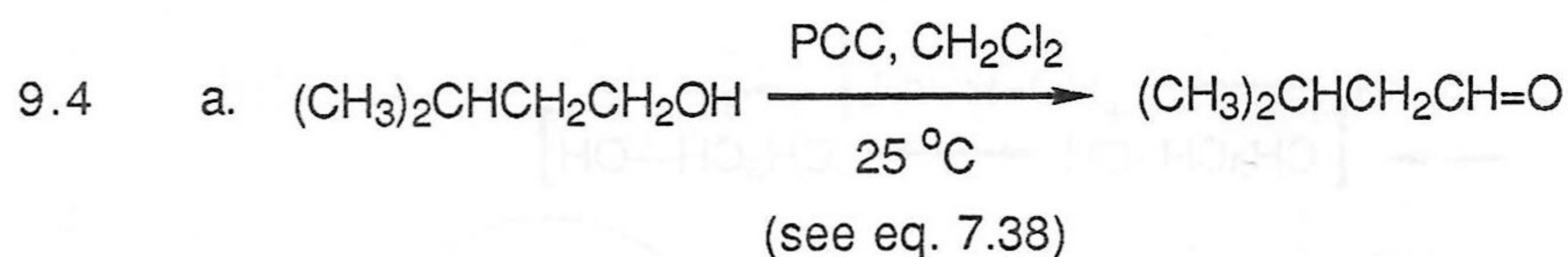
1. Know the meaning of: aldehyde, ketone, carbonyl group, formaldehyde, acetaldehyde, benzaldehyde, acetone, salicylaldehyde, acetophenone, benzophenone, carbaldehyde group.
2. Know the meaning of: nucleophilic addition, hemiacetal and acetal, aldehyde hydrate, cyanohydrin.
3. Know the meaning of: imine, hydroxylamine, oxime, hydrazine, hydrazone, phenylhydrazine, phenylhydrazone, semicarbazone.
4. Know the meaning of: lithium aluminum hydride, sodium borohydride, Tollens' reagent, silver mirror test.
5. Know the meaning of: keto form, enol form, tautomers, tautomerism, enolate anion, α -hydrogen and α -carbon, aldol condensation, mixed aldol condensation.
6. Given the structure of an aldehyde or ketone, state its IUPAC name.
7. Given the IUPAC name of an aldehyde or ketone, write its structure.
8. Write the resonance contributors to the carbonyl group.
9. Given the structure or name of an aldehyde or ketone, write an equation for its reaction with the following nucleophiles: alcohol, cyanide ion, Grignard reagent or acetylide, hydroxylamine, hydrazine, phenylhydrazine, 2,4-dinitrophenylhydrazine, primary amine, lithium aluminum hydride, and sodium borohydride.
10. Explain the mechanism of acid catalysis of nucleophilic additions to the carbonyl group.
11. Write the steps in the mechanism of acetal formation and hydrolysis. Draw the structures of resonance contributors to intermediates in the mechanism.
12. Given a carbonyl compound and a Grignard reagent, write the structure of the alcohol that is formed when they react.
13. Given the structure of a primary, secondary, or tertiary alcohol, deduce what combination of aldehyde or ketone and Grignard reagent can be used for its synthesis.
14. Given the structure of an aldehyde or ketone, write the formula of the alcohol that is obtained from it by reduction.

15. Given the structure of an aldehyde, write the structure of the acid that is formed from it by oxidation.
16. Know which tests can distinguish an aldehyde from a ketone.
17. Given the structure of an aldehyde or ketone, write the structure of the corresponding enol and enolate anion.
18. Identify the α -hydrogens in an aldehyde or ketone, and be able to recognize that these hydrogens can be exchanged readily for deuterium.
19. Write the structure of the aldol formed by the self-condensation of an aldehyde of given structure.
20. Given two reacting carbonyl compounds, write the structure of the mixed aldol obtained from them.
21. Write the steps in the mechanism of the aldol condensation.

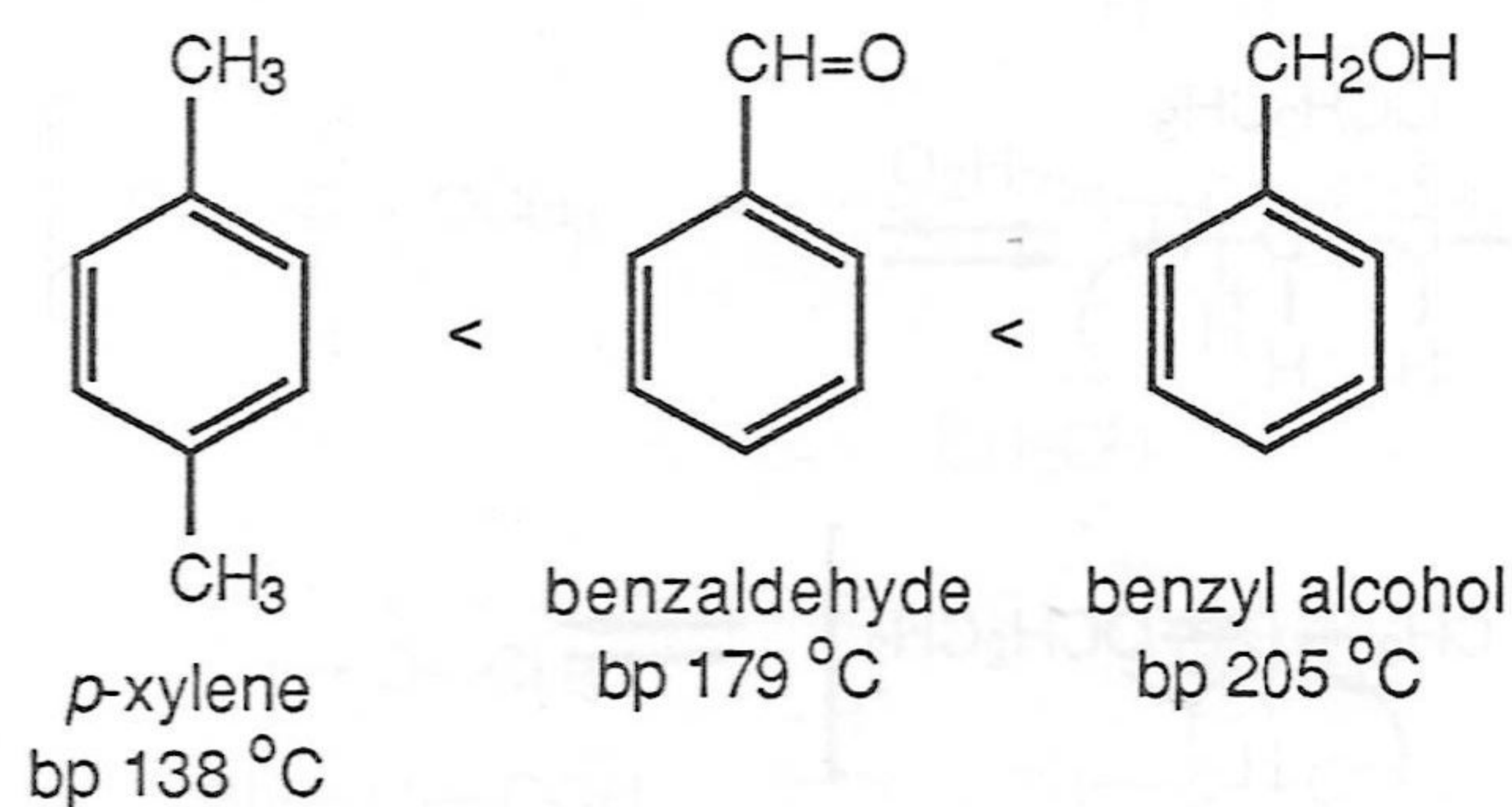
Answers to Problems

Problems Within the Chapter

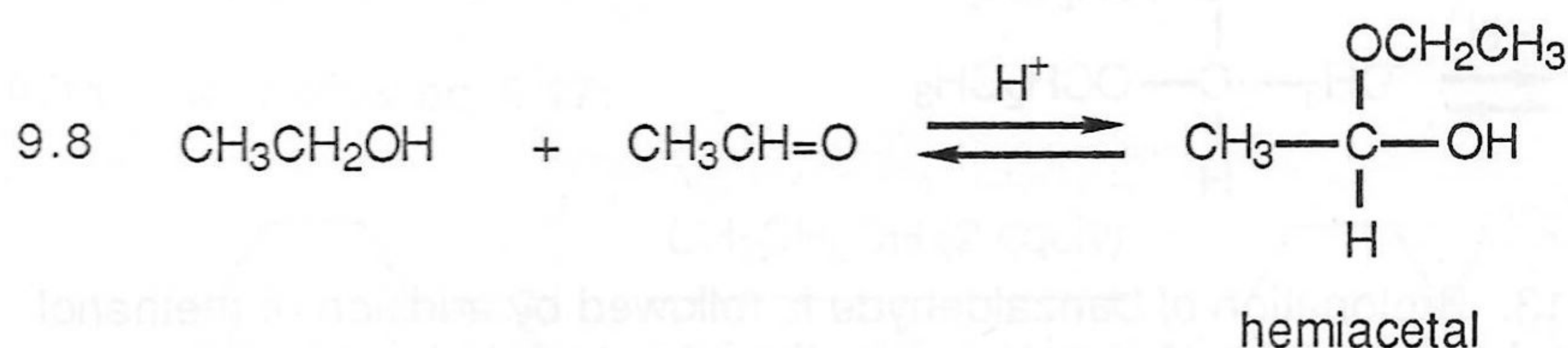
- 9.1
- a. $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}=\text{O}$
 - b. 
 - c. 
 - d. 
 - e. 
 - f. 
- 9.2
- a. 3-methylbutanal
(no number is necessary for the aldehyde function)
 - b. 2-butenal
(the number locates the double bond between C-2 and C-3)
 - c. cyclobutanone
 - d. 3,3-dimethyl-2-butanone or *tert*-butyl methyl ketone
- 9.3
- a. 
 - b. $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} \xrightarrow{\text{PCC}} (\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{CH}_2\text{CH}=\text{O}$

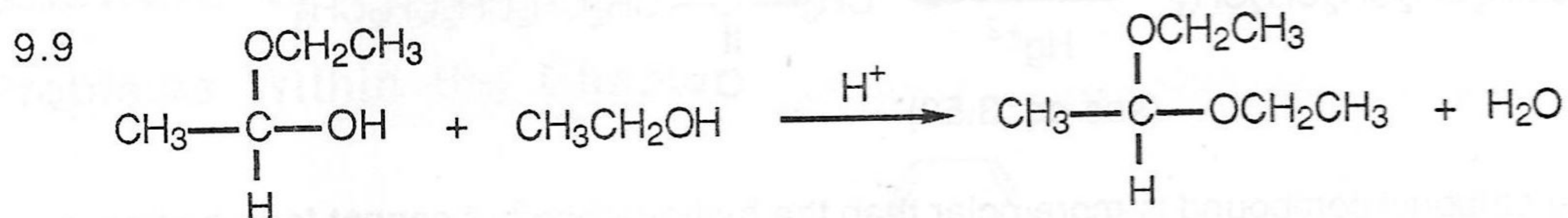
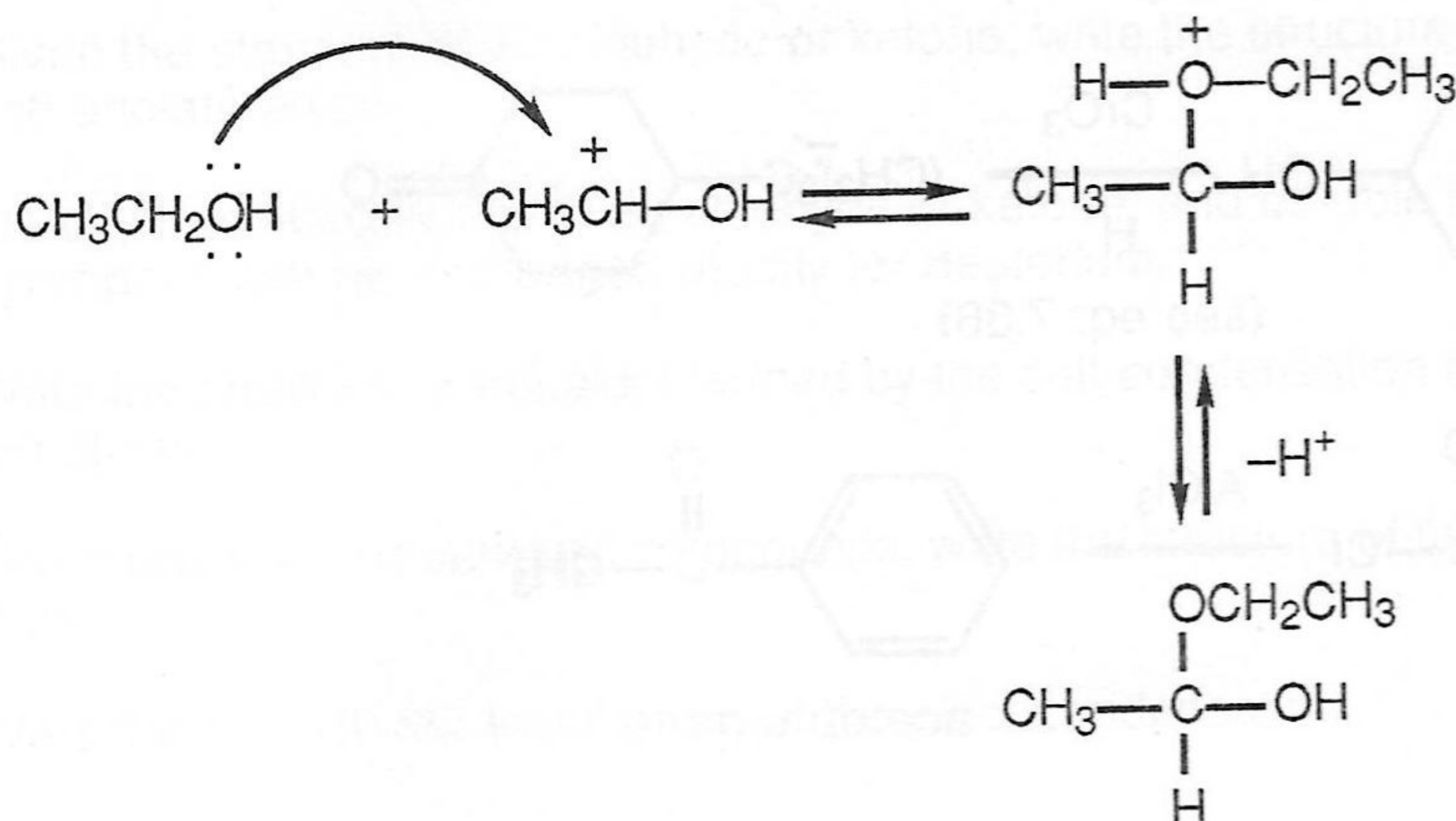
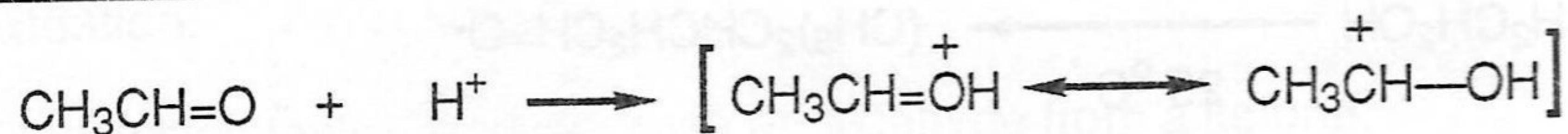
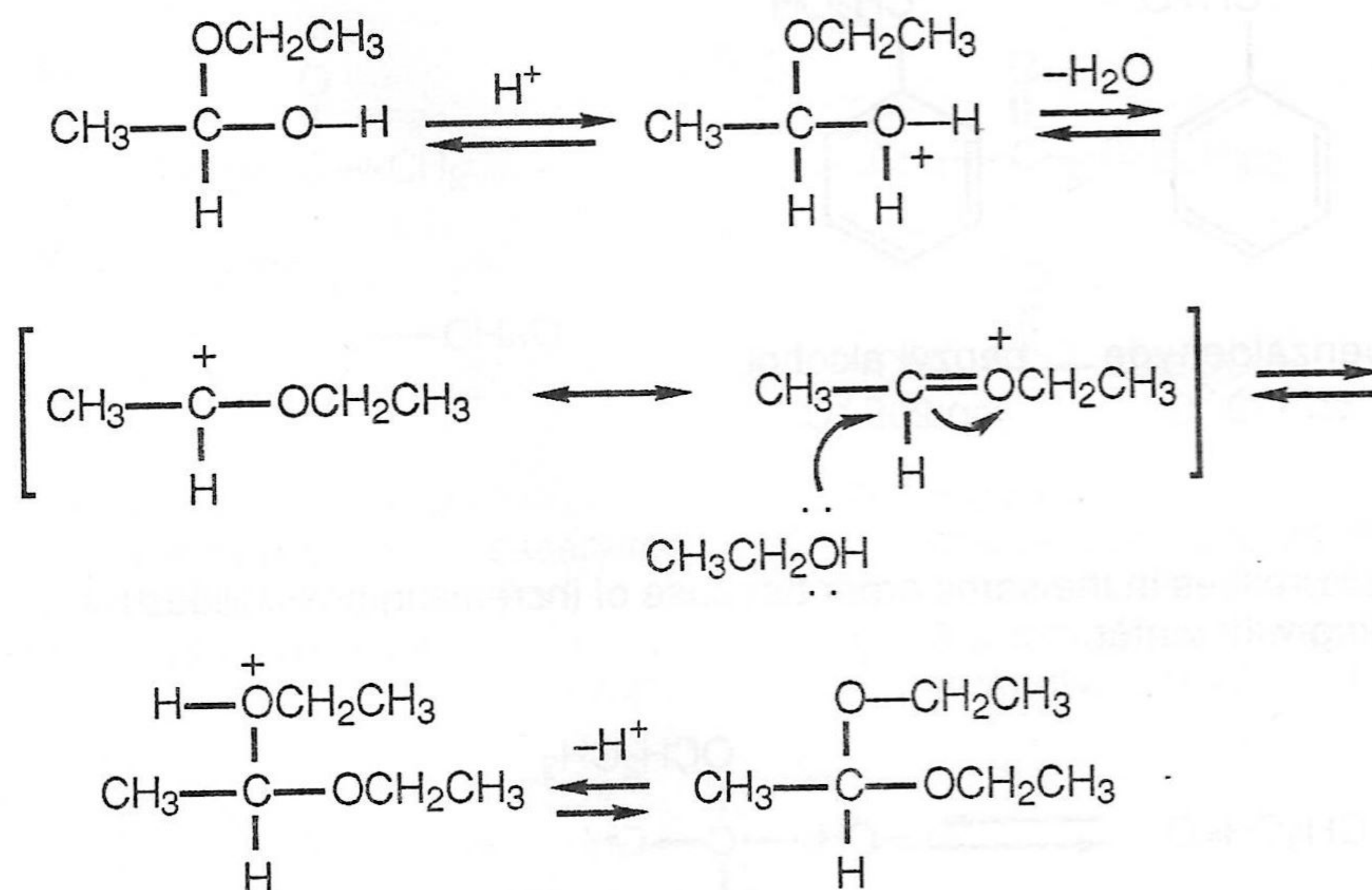


- 9.7 a. The carbonyl compound is more polar than the hydrocarbon but cannot form hydrogen bonds with itself.

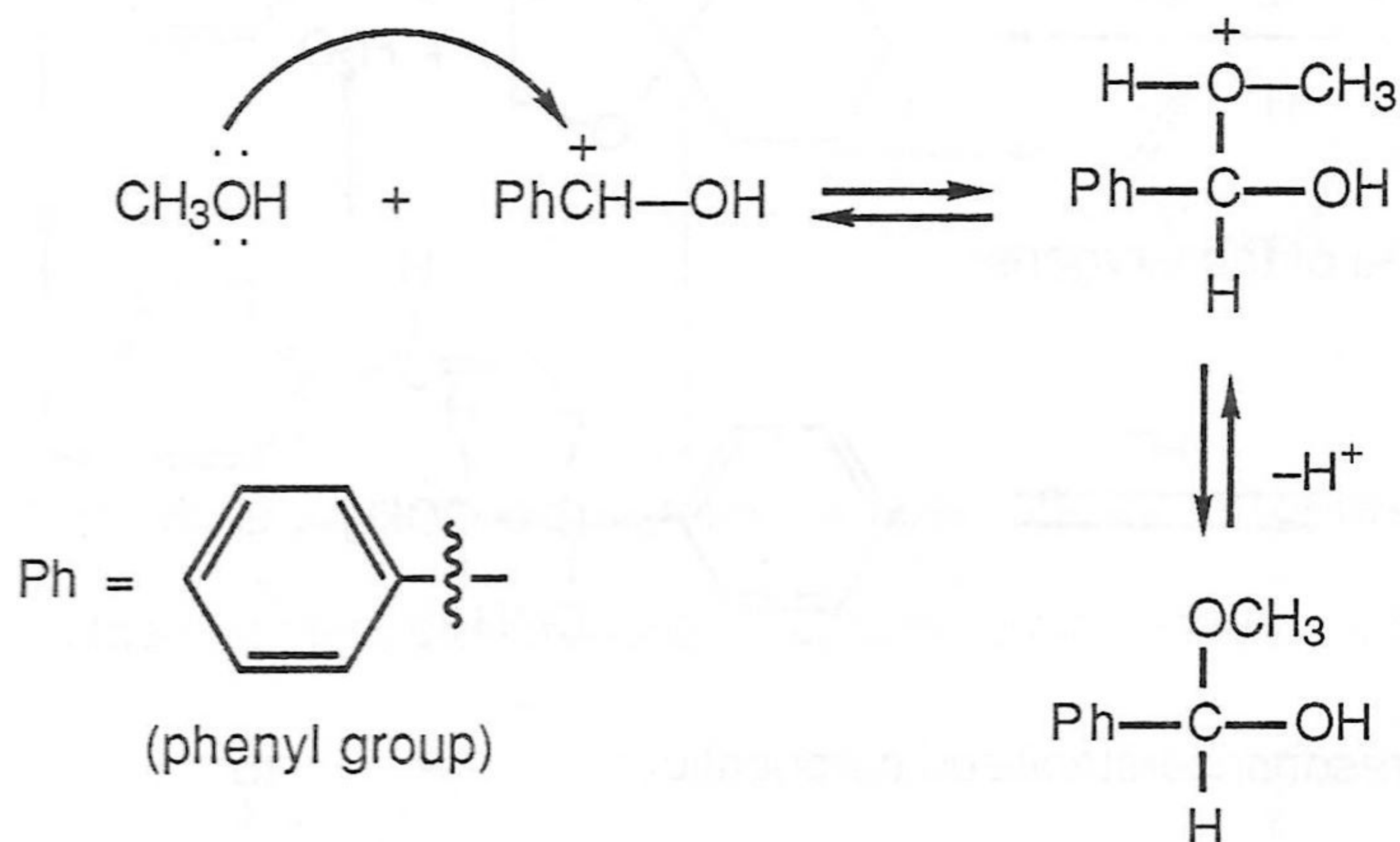
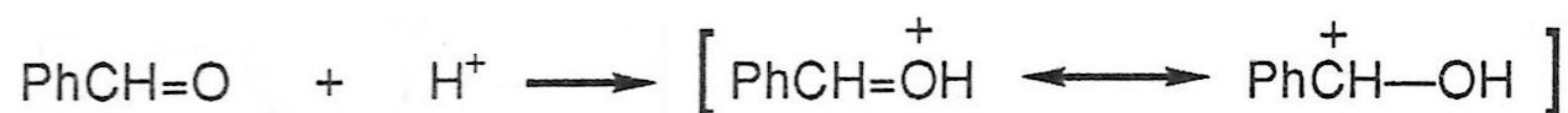


- b. Water solubility increases in the same order because of increasing possibilities for hydrogen bonding with water.

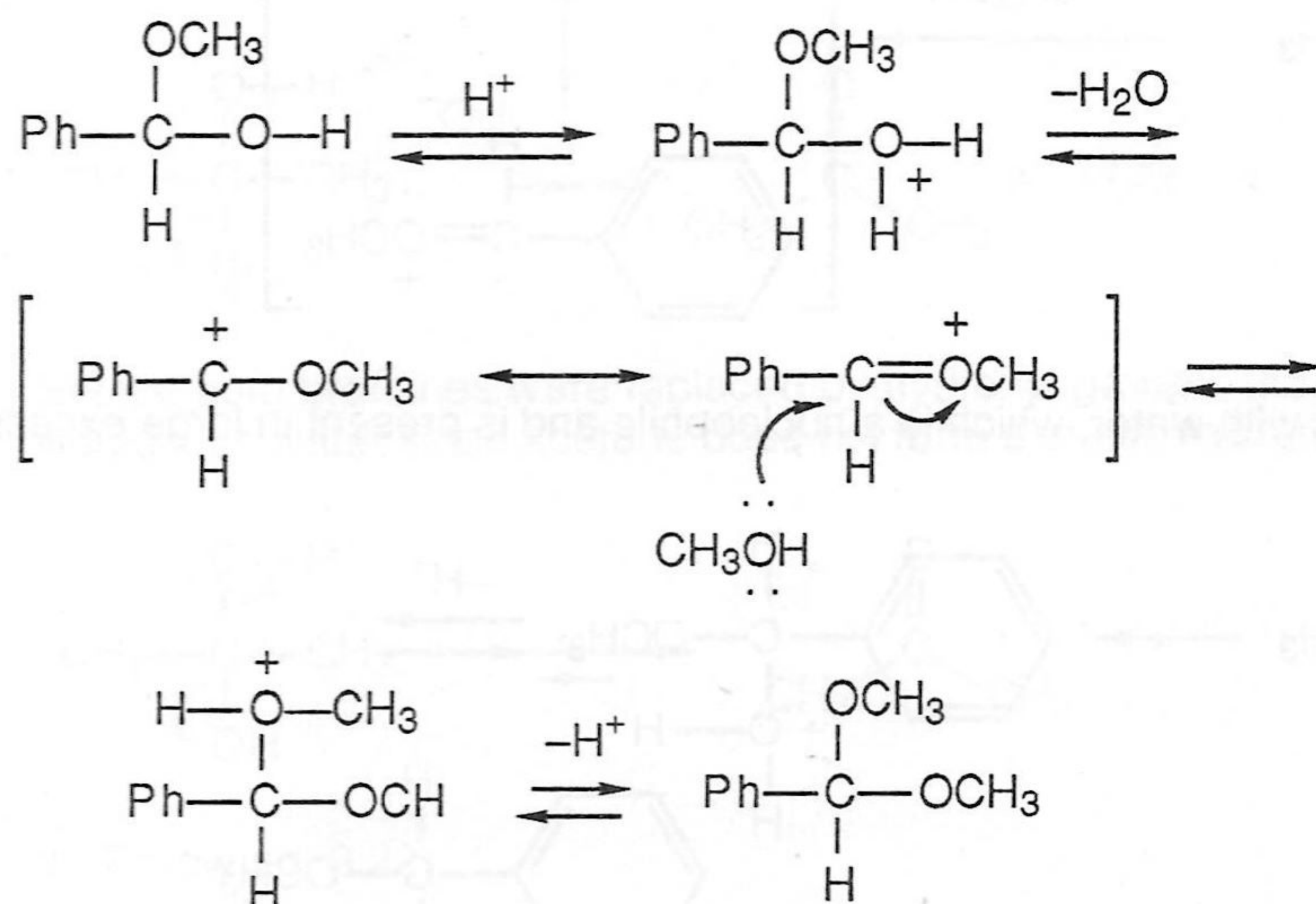


Mechanism:Mechanism:

- 9.10 Follow eqs. 9.11 and 9.13. Protonation of benzaldehyde is followed by addition of methanol to the protonated carbonyl group. Loss of a proton gives the intermediate hemiacetal.

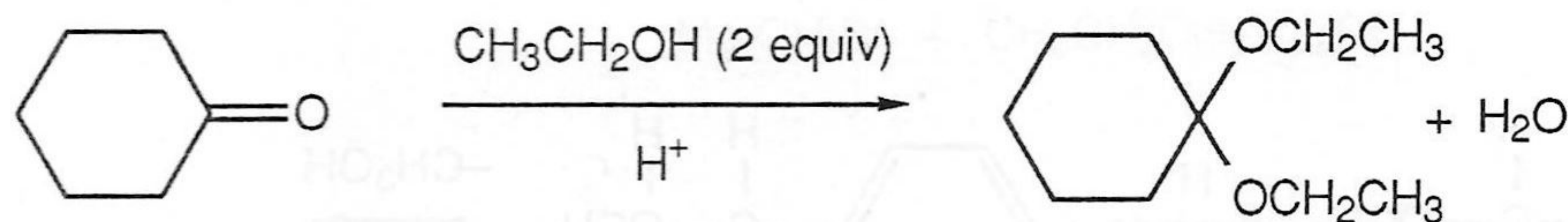


Protonation of the hydroxyl group and loss of water gives a resonance-stabilized carbocation. Nucleophilic attack of methanol on the carbocation followed by loss of a proton gives the acetal.

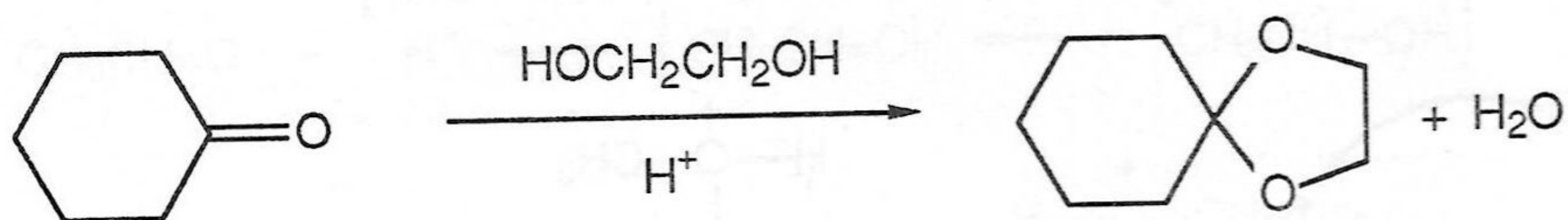


Notice that each step is reversible. The reaction can be driven to the right by removing water as it is formed.

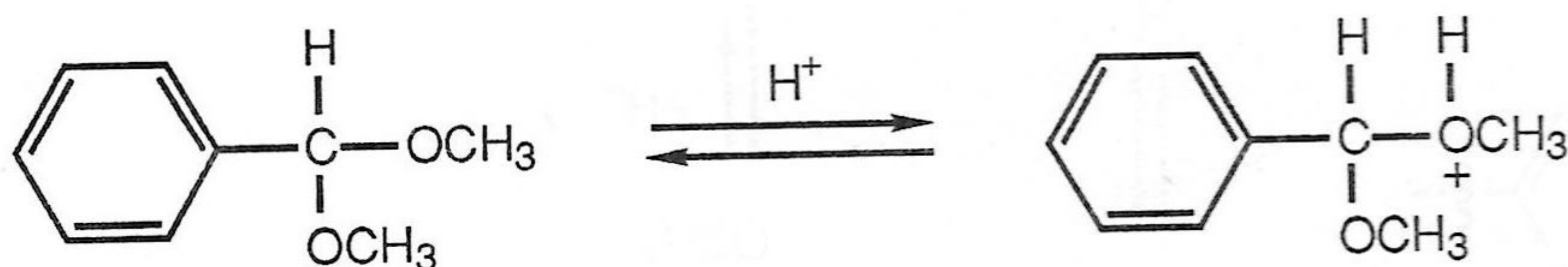
9.11 a. Follow eq. 9.17:



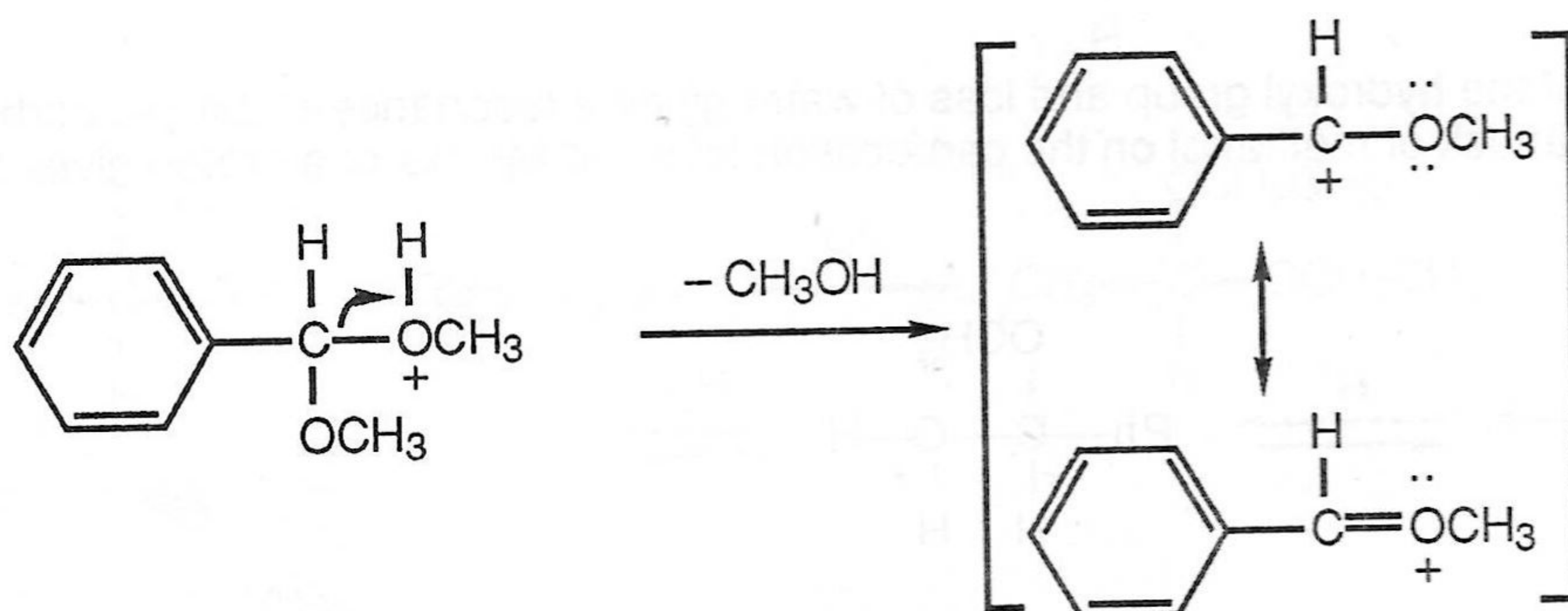
b. Follow eq. 9.16:



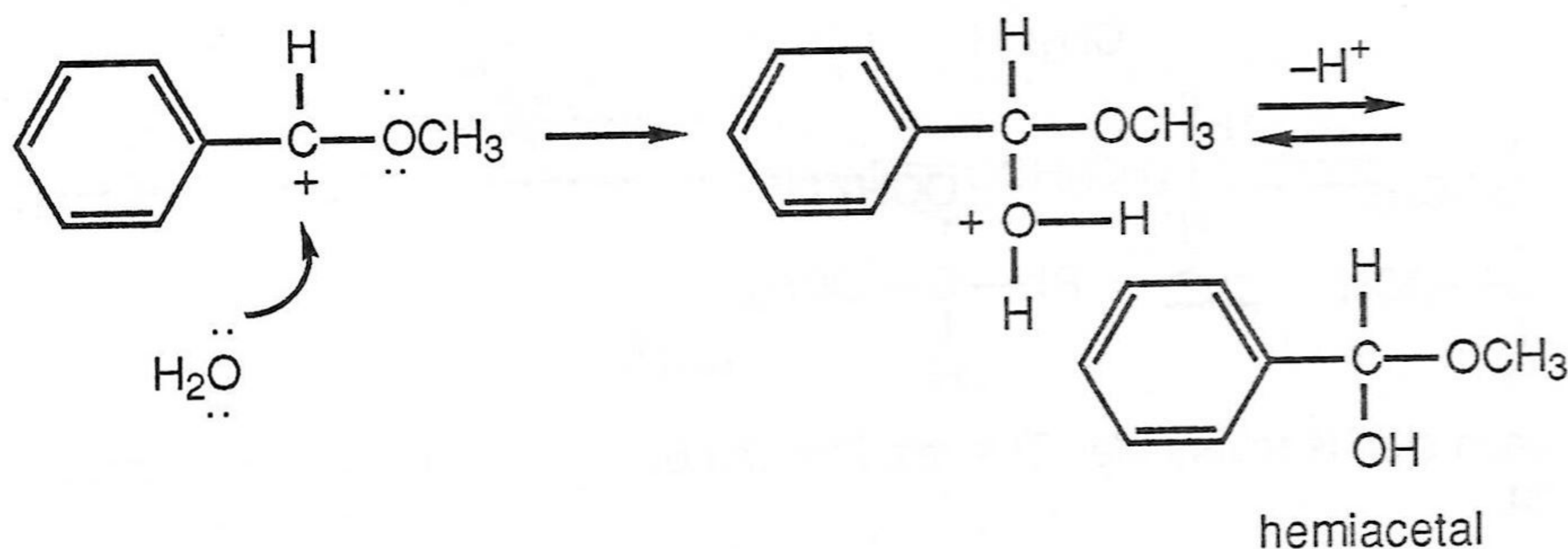
9.12 The proton first adds to one of the oxygens:



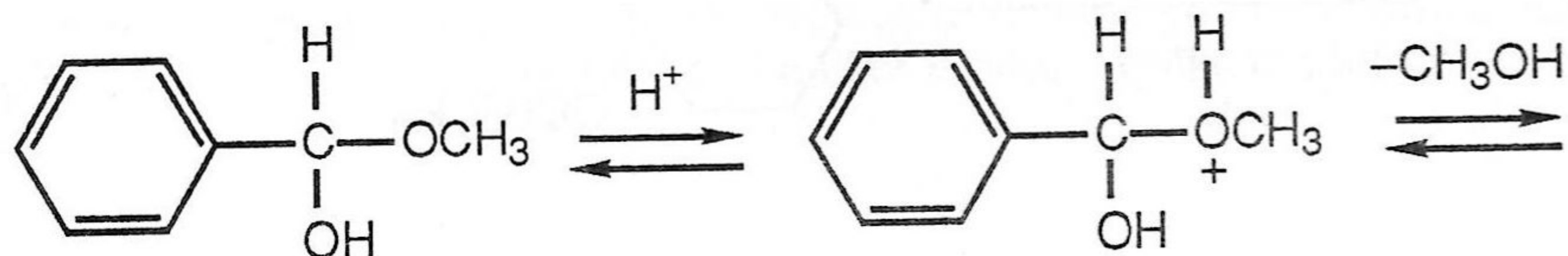
Loss of methanol gives a resonance-stabilized carbocation:

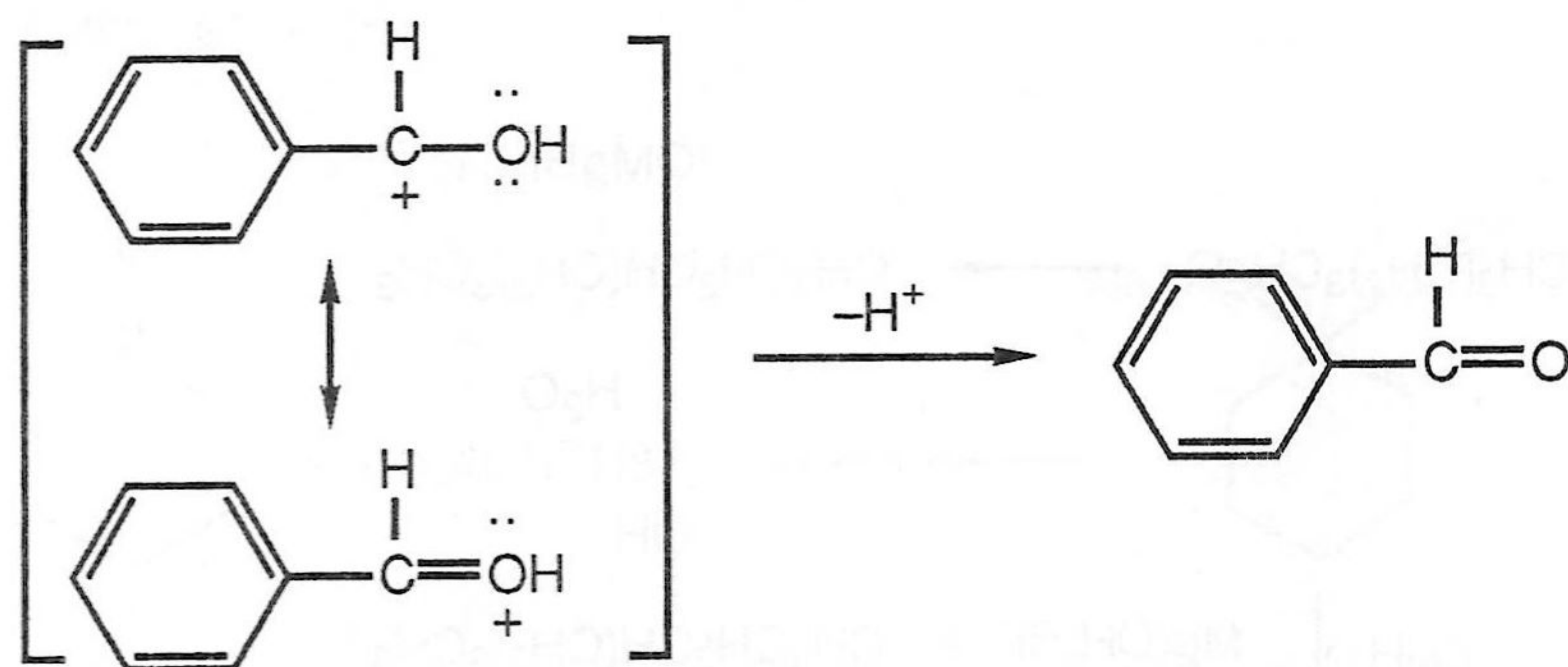


The carbocation reacts with water, which is a nucleophile and is present in large excess:



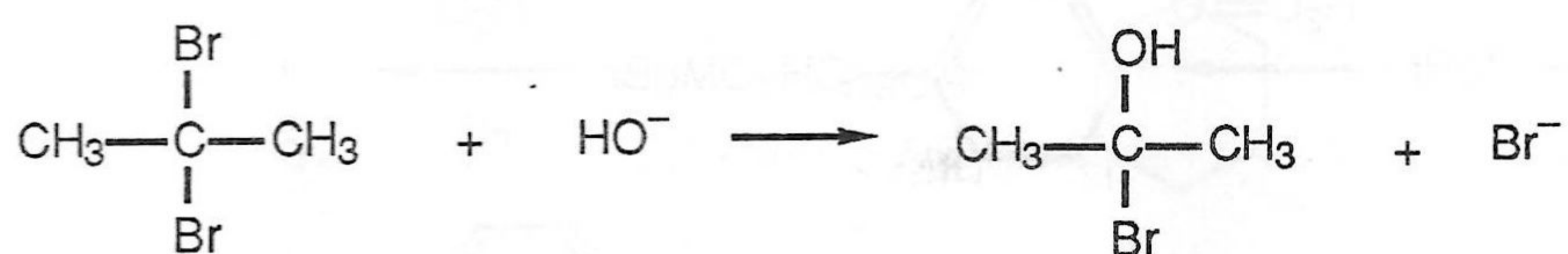
The sequence is then repeated, beginning with protonation of the methoxyl oxygen of the hemiacetal:



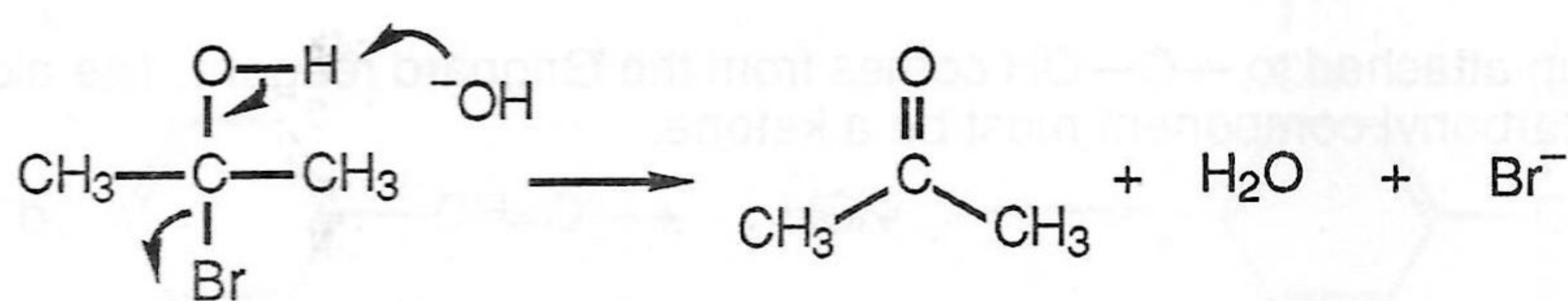


The whole process is driven forward because water is present in excess.

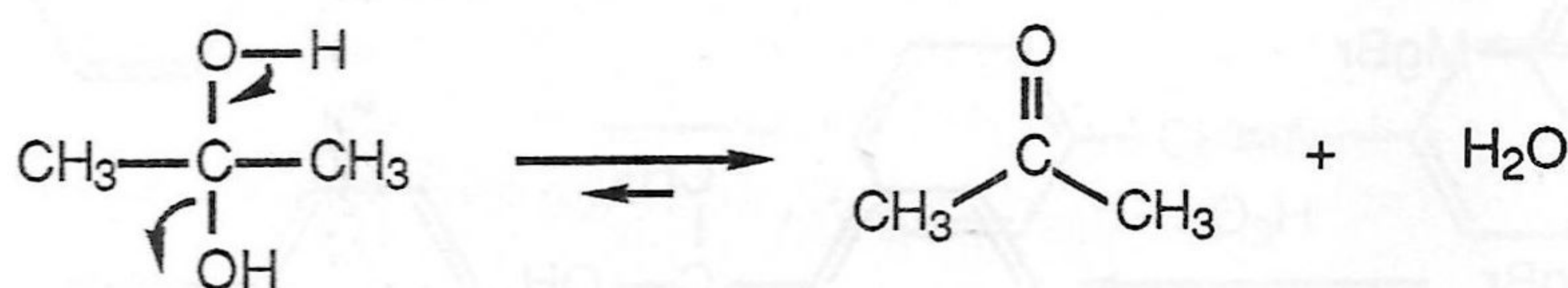
9.13 In the first step, one bromine is replaced by a hydroxyl group:



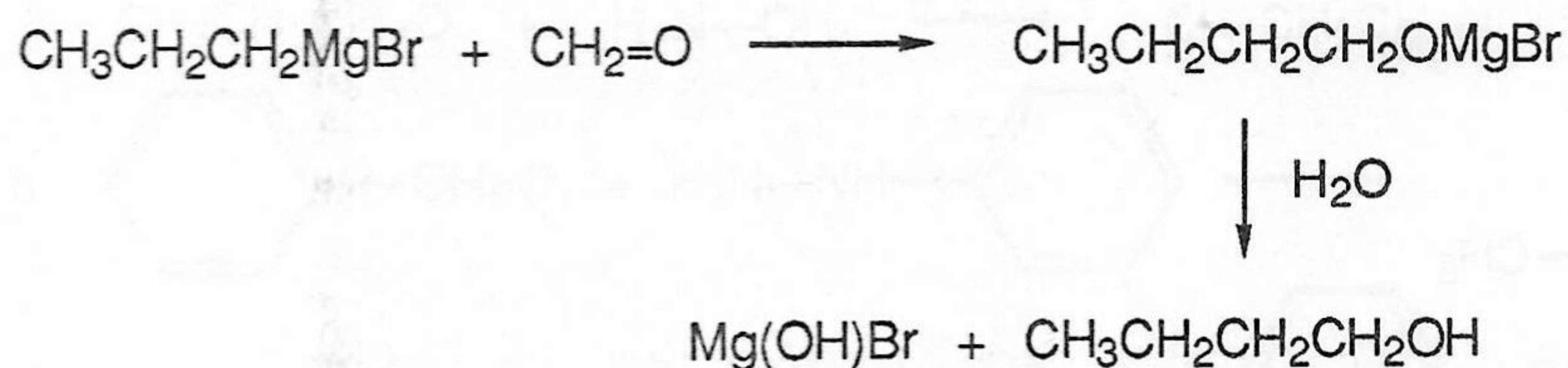
Loss of HBr gives acetone:



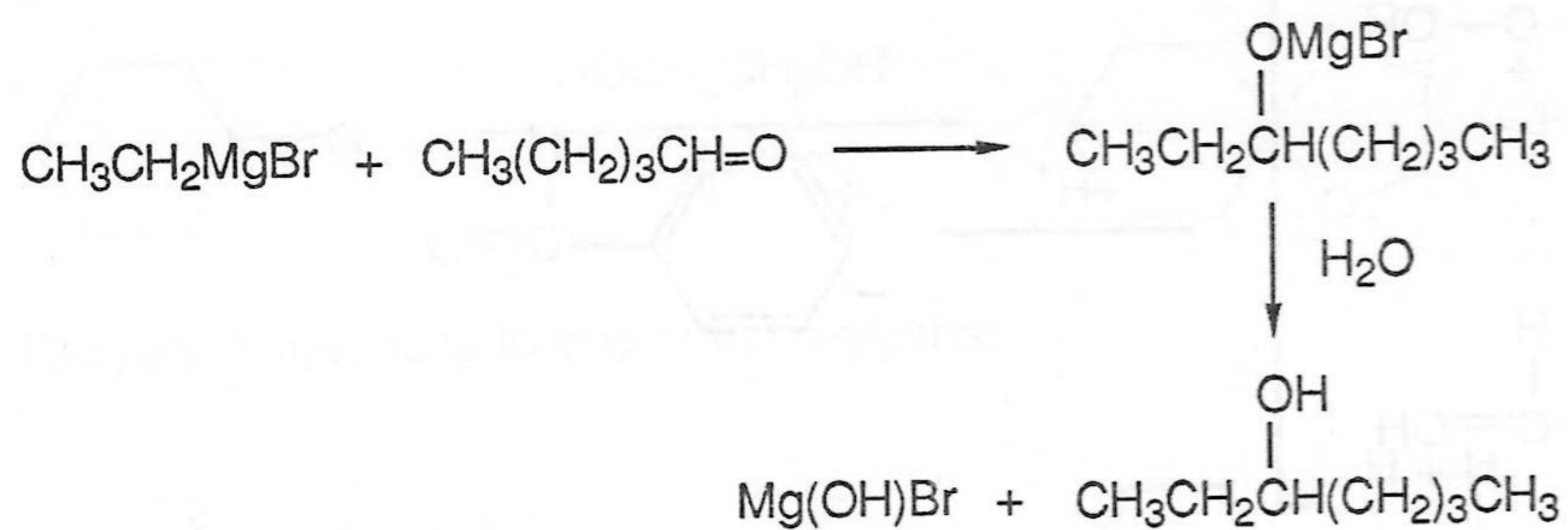
Even if both bromines were replaced by hydroxyl groups, the resulting diol (acetone hydrate) would lose water since acetone does not form a stable hydrate.



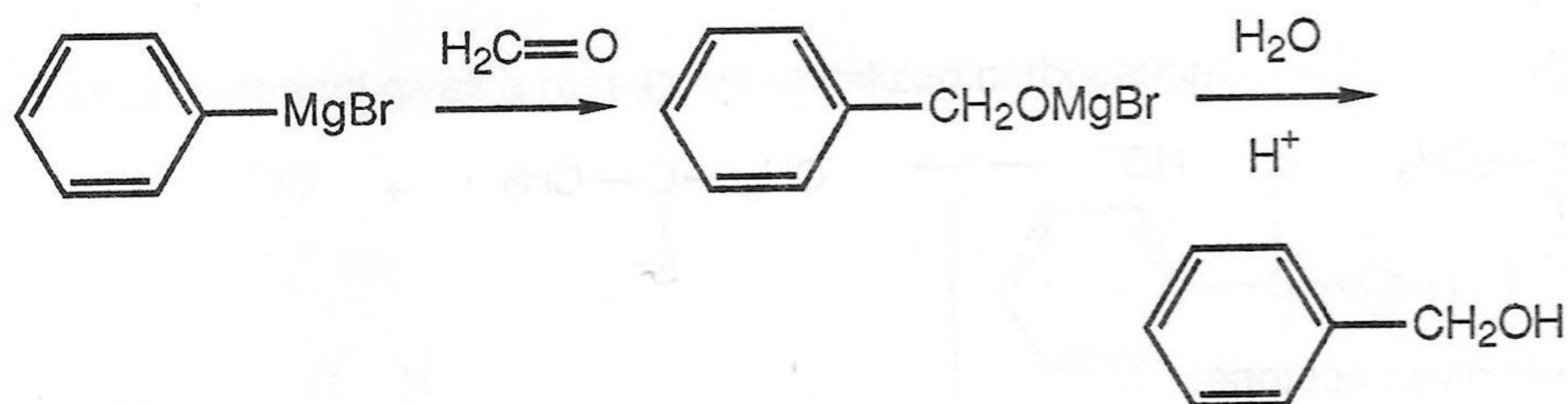
9.14 a. Follow eq. 9.22:



b. Follow eq. 9.23:

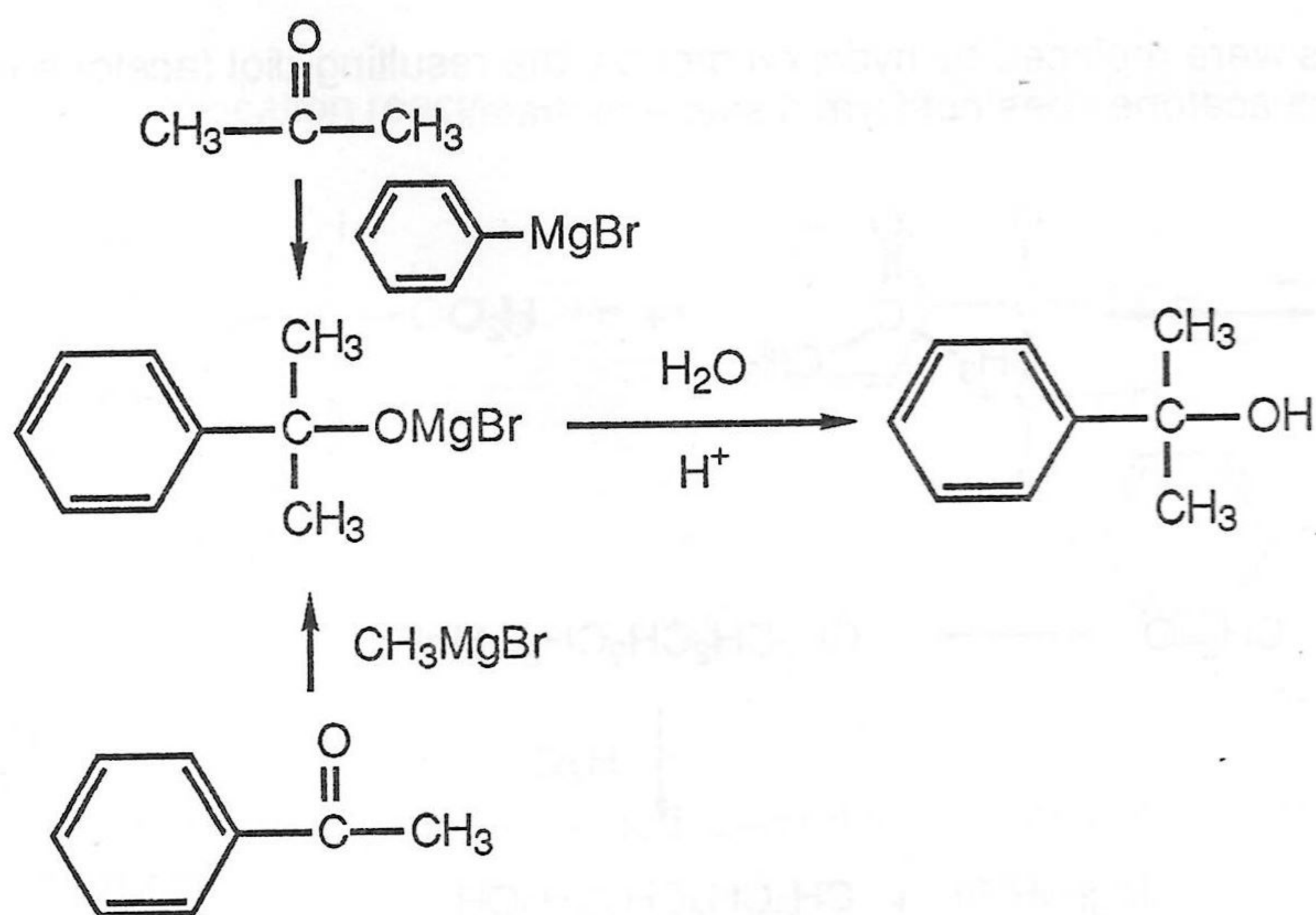


9.15 a. The alcohol is primary, so formaldehyde must be used as the carbonyl component:

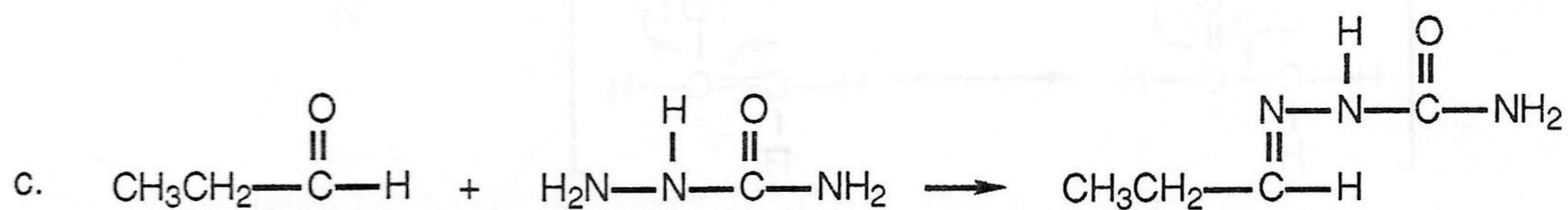
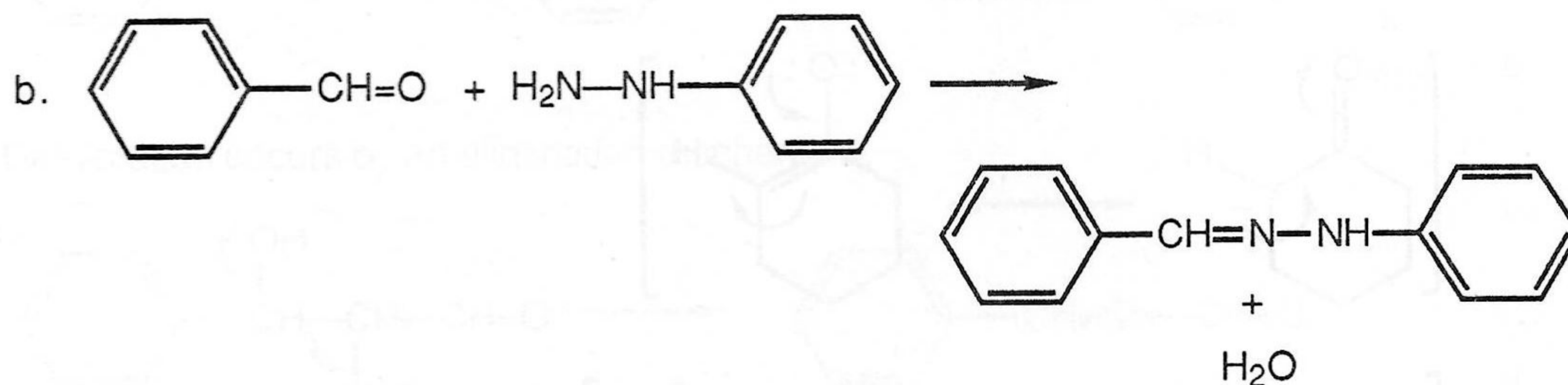
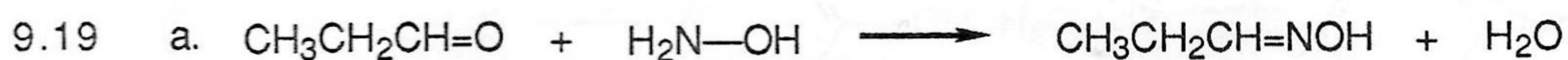
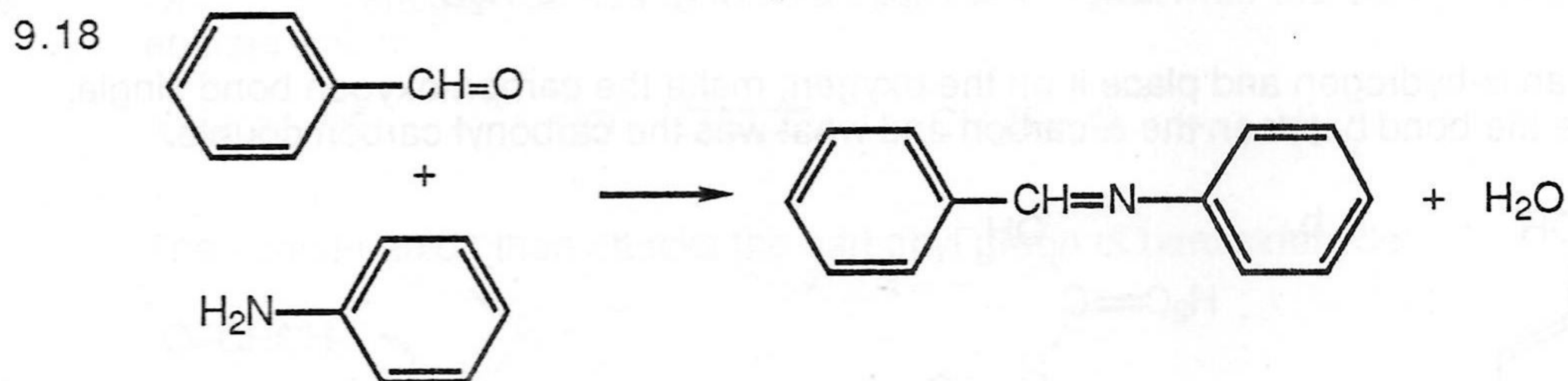
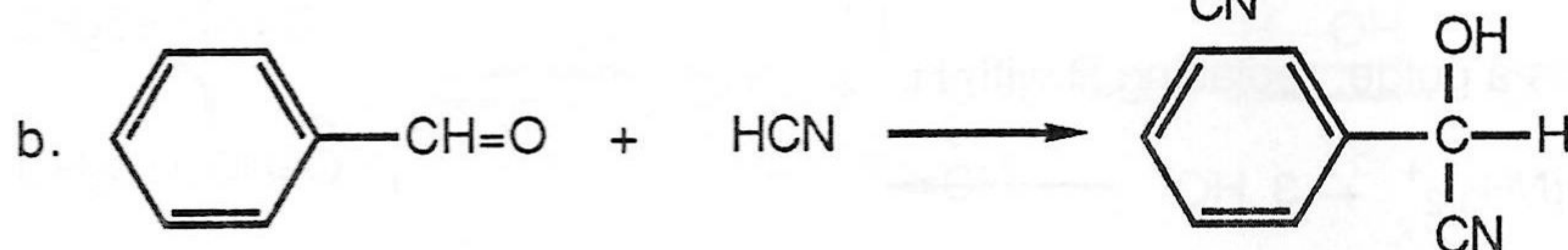
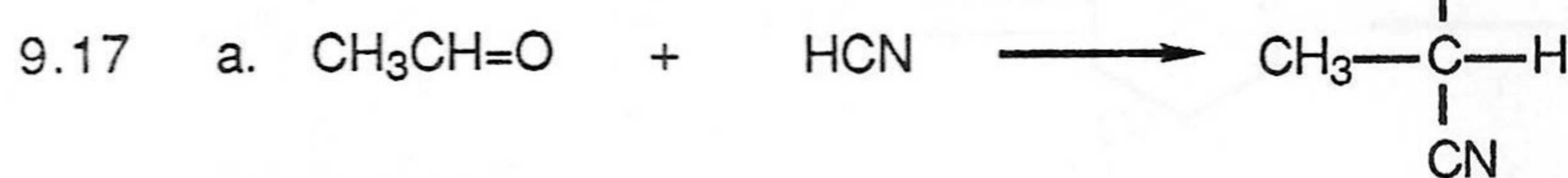
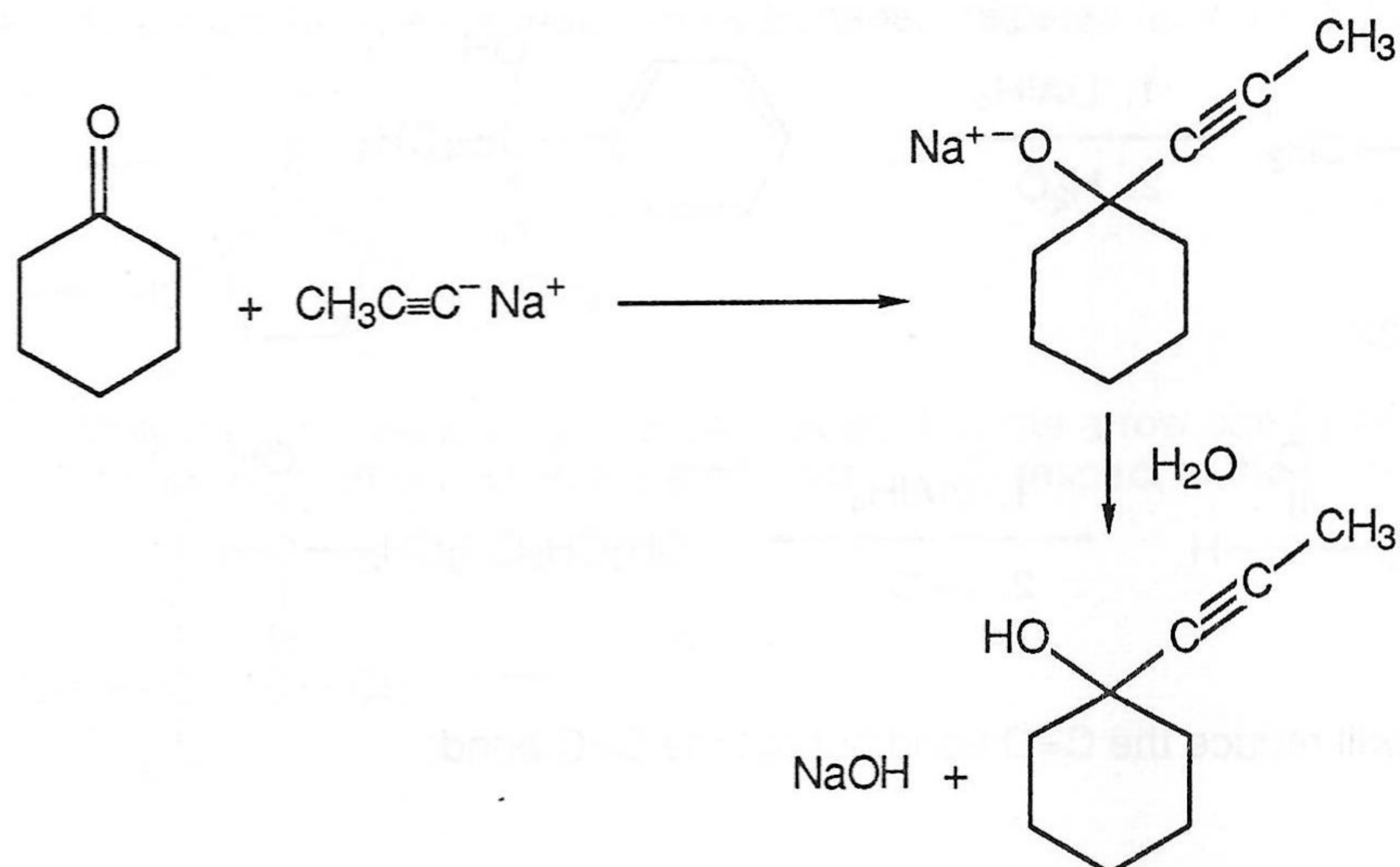


b. Only one R group attached to $-\text{C}-\text{OH}$ comes from the Grignard reagent. The alcohol is tertiary, so the carbonyl component must be a ketone.

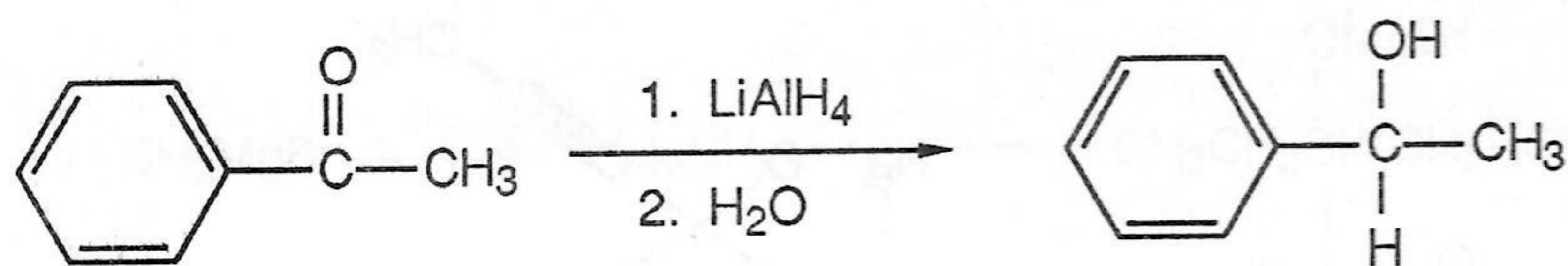
Two possibilities:



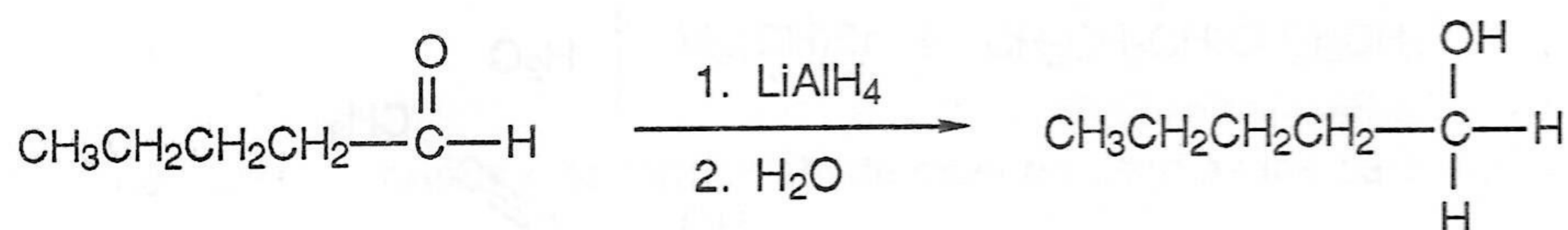
9.16 Follow eq. 9.26:



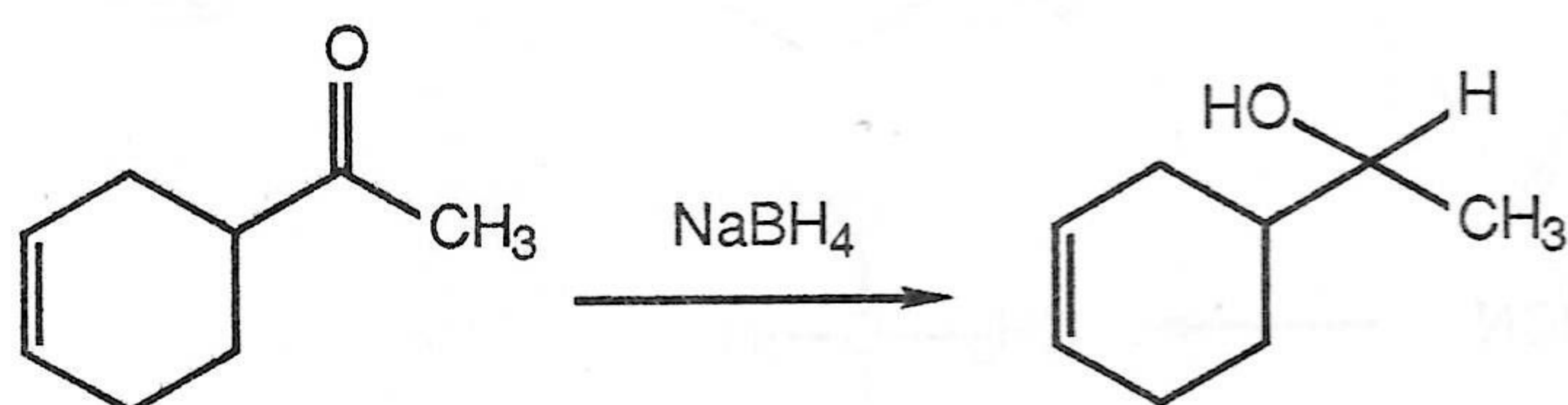
9.20 a. Follow eq. 9.33:



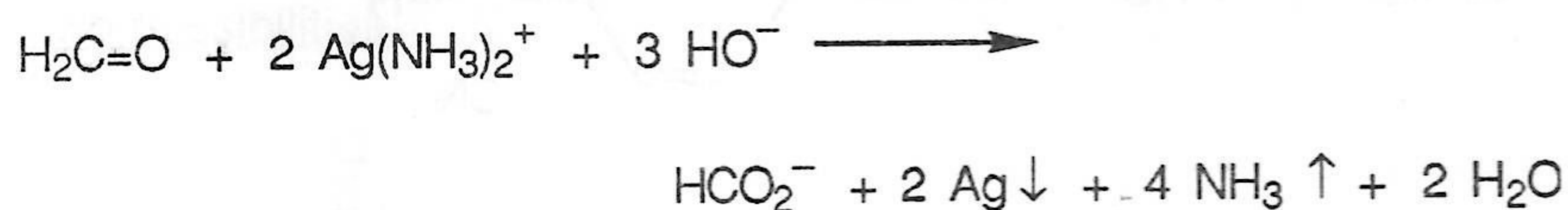
b. Follow eq. 9.33:



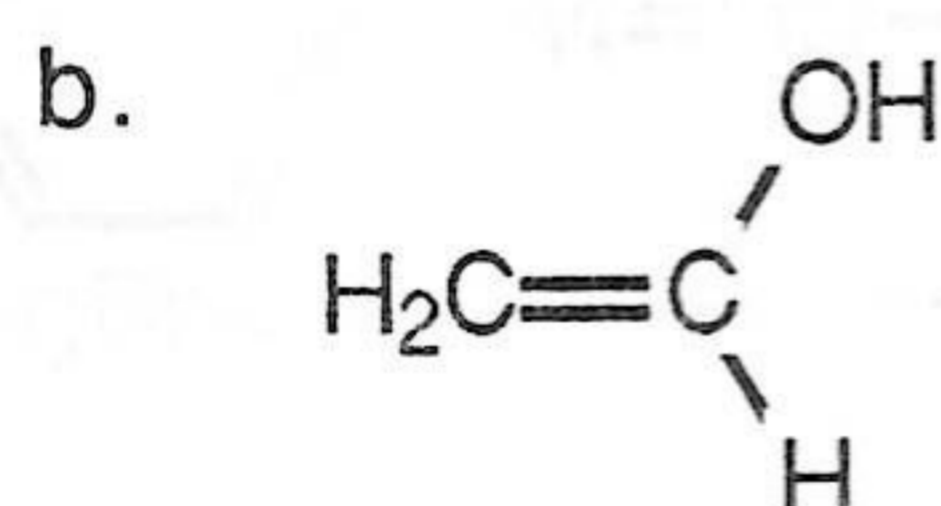
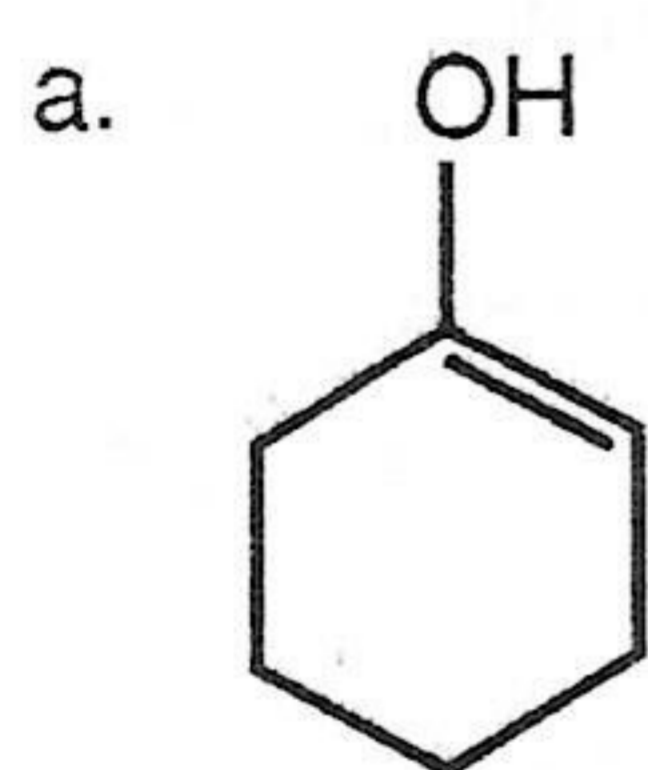
9.21 A metal hydride will reduce the $\text{C}=\text{O}$ bond but not the $\text{C}=\text{C}$ bond:



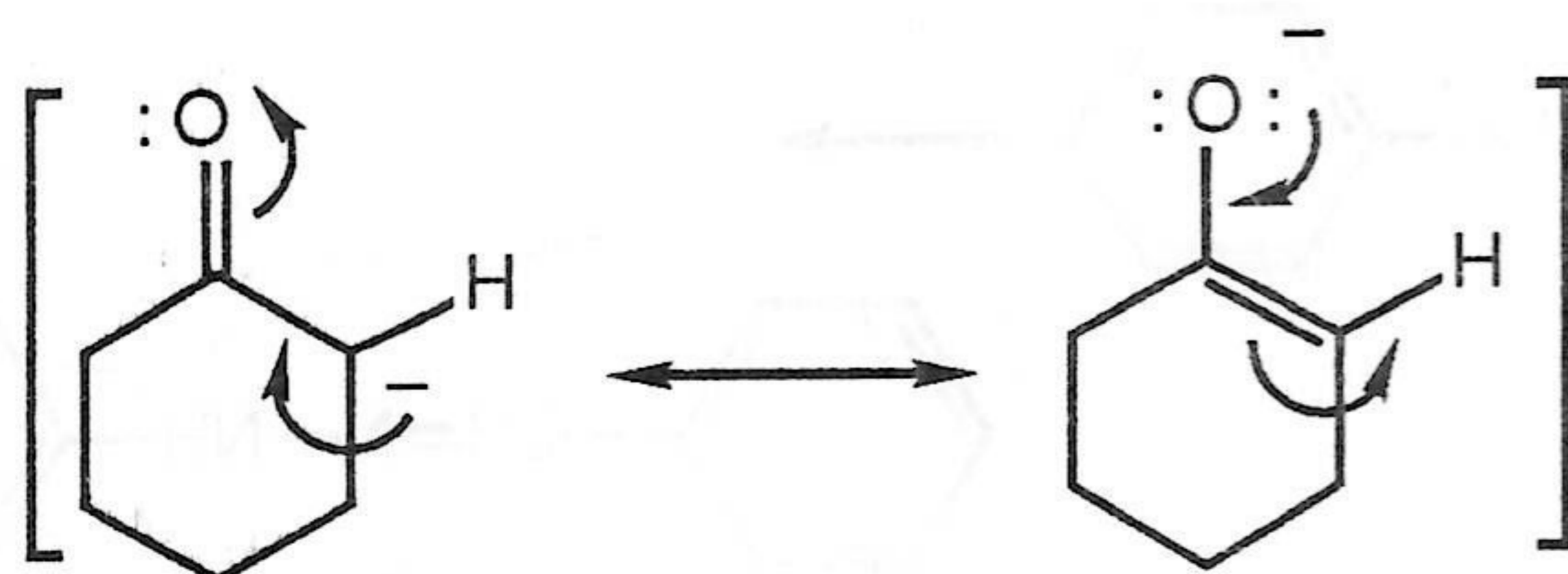
9.22 Follow eq. 9.39 as a guide, replacing R with H:



9.23 Remove an α -hydrogen and place it on the oxygen; make the carbon-oxygen bond single, and make the bond between the α -carbon and what was the carbonyl carbon double.



9.24 a.

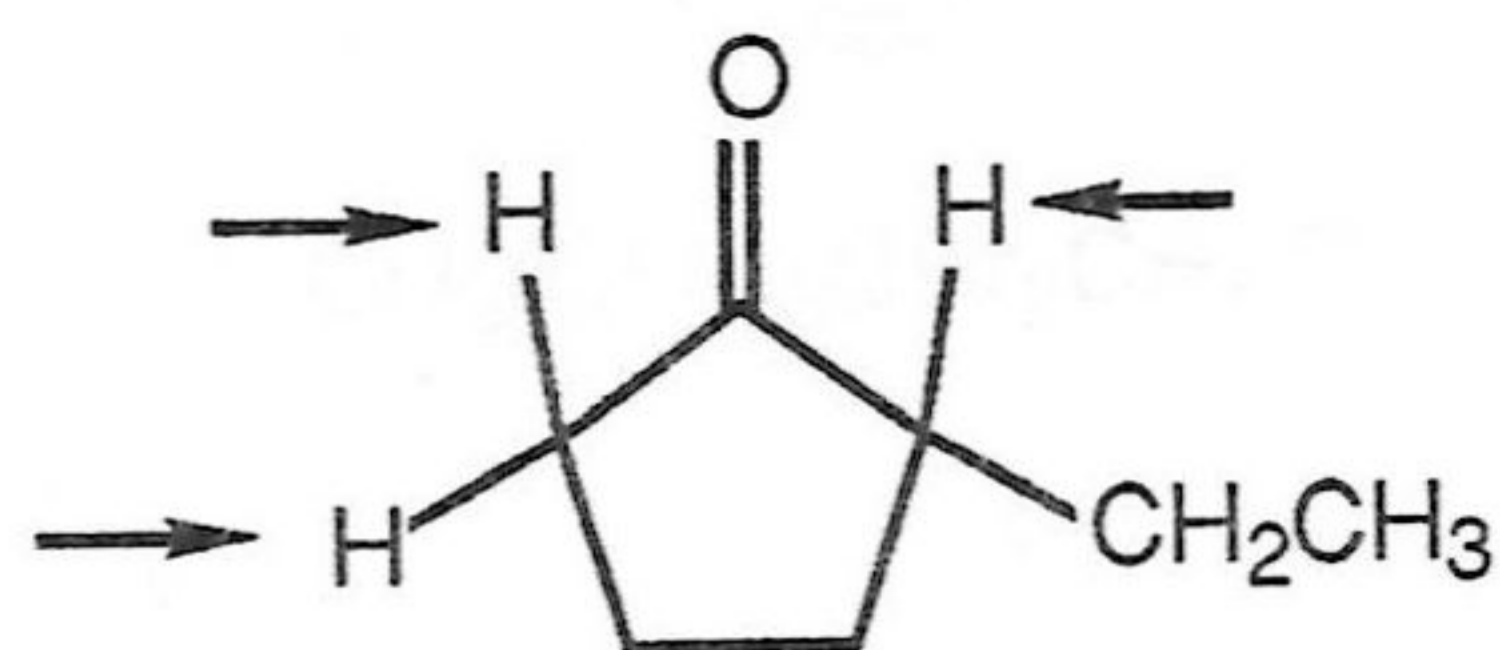


b.

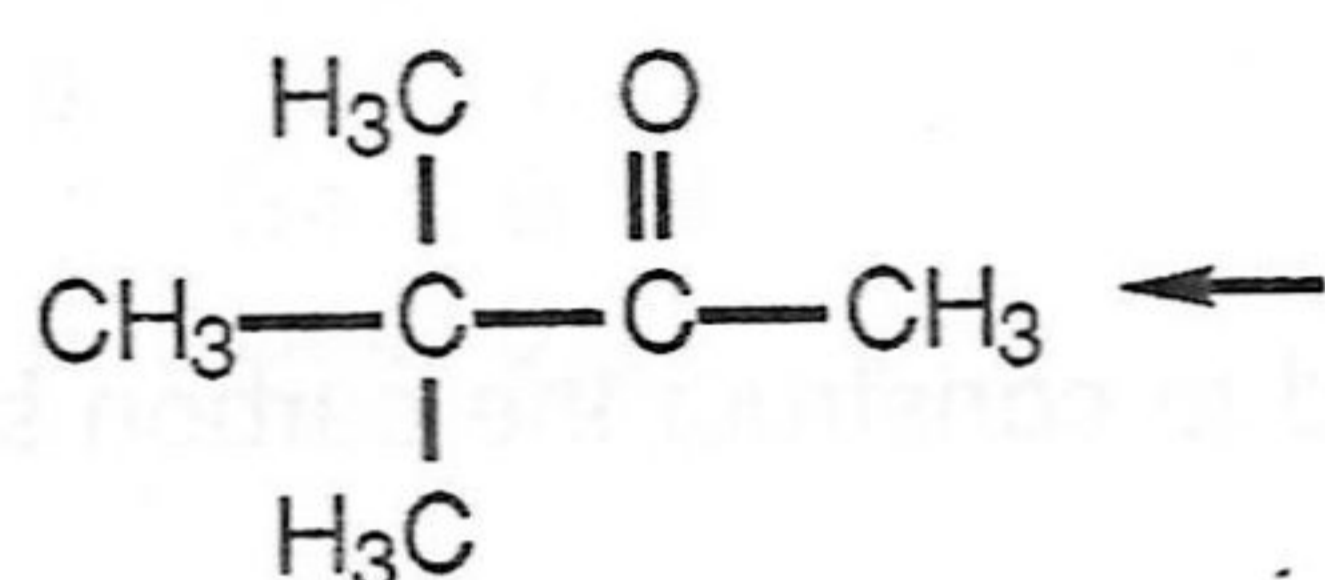


9.25 In each case, only the α -hydrogens can be readily exchanged.

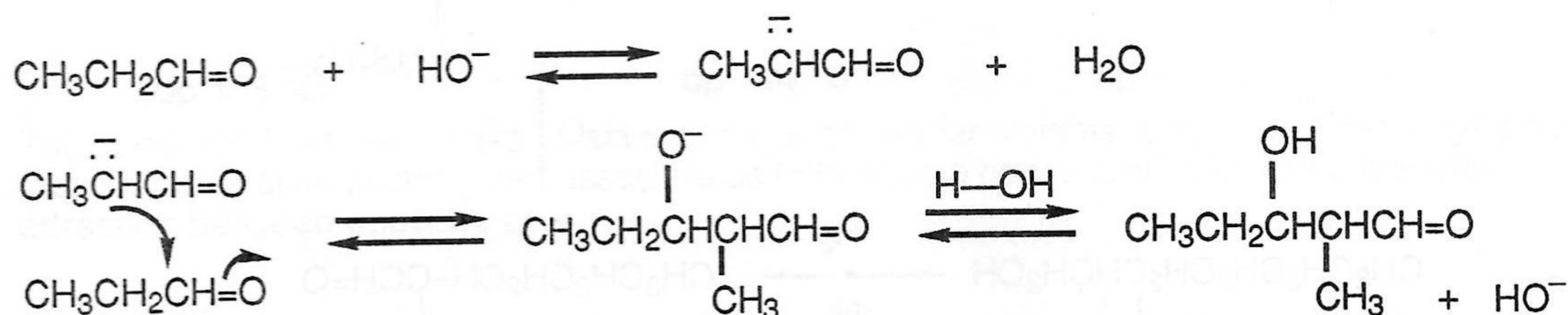
a. There are three exchangeable hydrogens, indicated by the arrows.



b. Only the three methyl hydrogens indicated by the arrow can be readily exchanged. The remaining methyl hydrogens are β , not α , with respect to the carbonyl group.



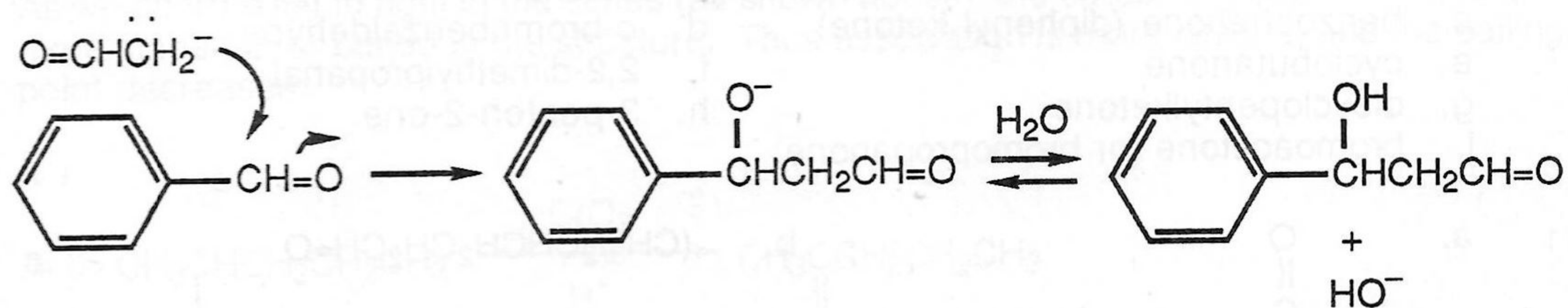
9.26 Follow eqs. 9.51–9.53 as a guide.



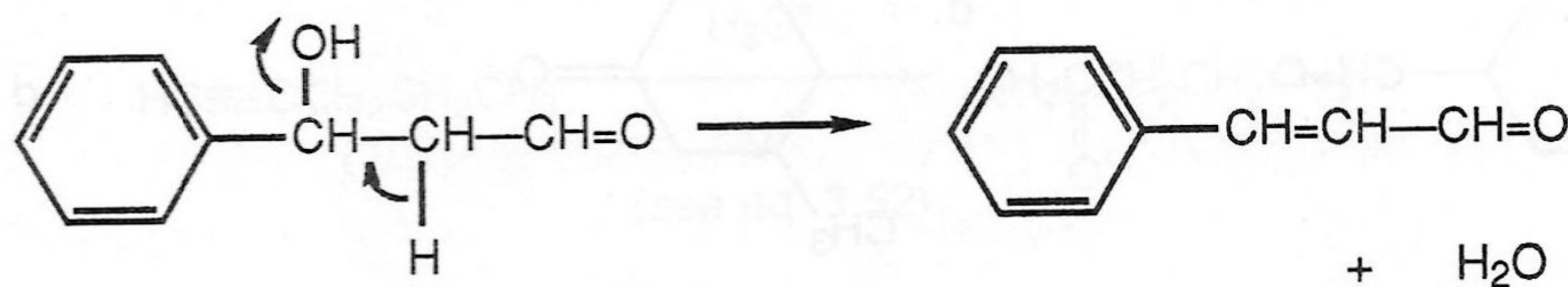
9.27 Only the acetaldehyde has an α -hydrogen, so it reacts with the basic catalyst to produce an enolate anion:



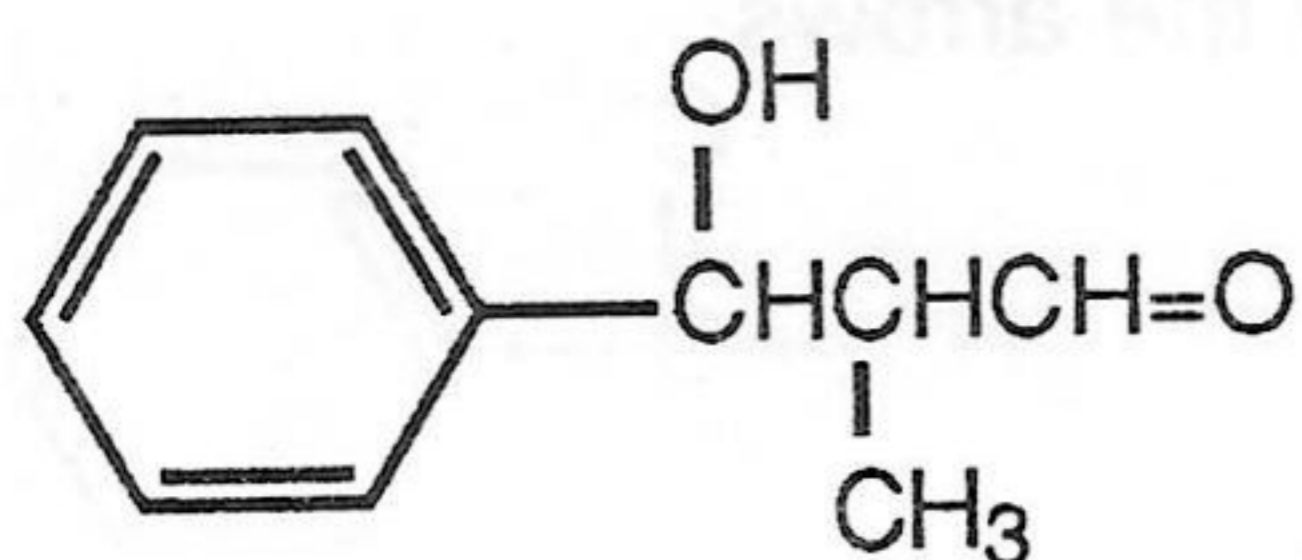
The enolate anion then attacks the carbonyl group of benzaldehyde:



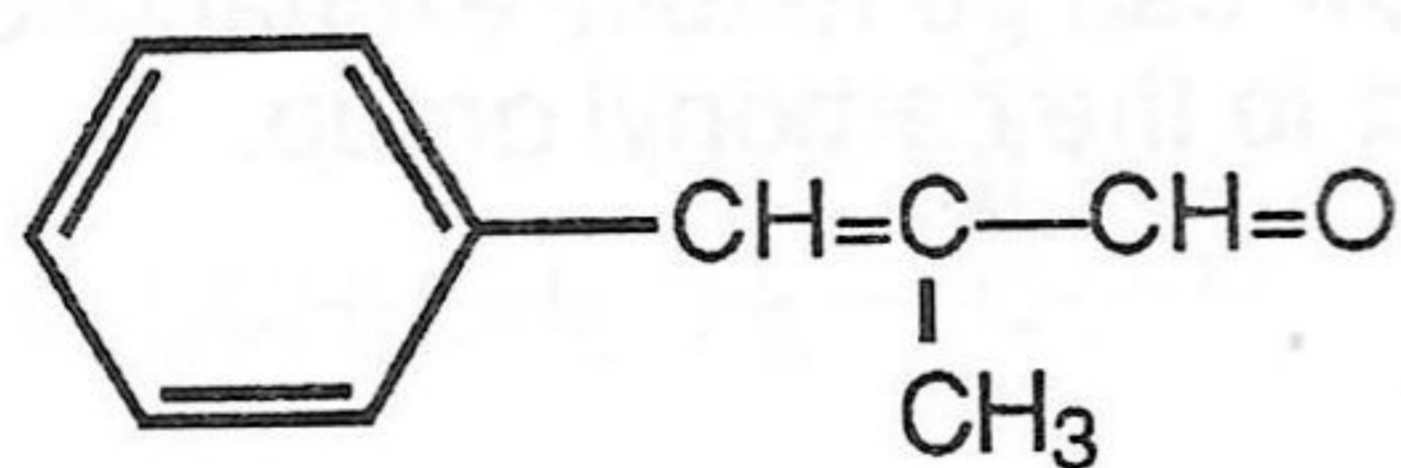
Dehydration occurs by an elimination mechanism:



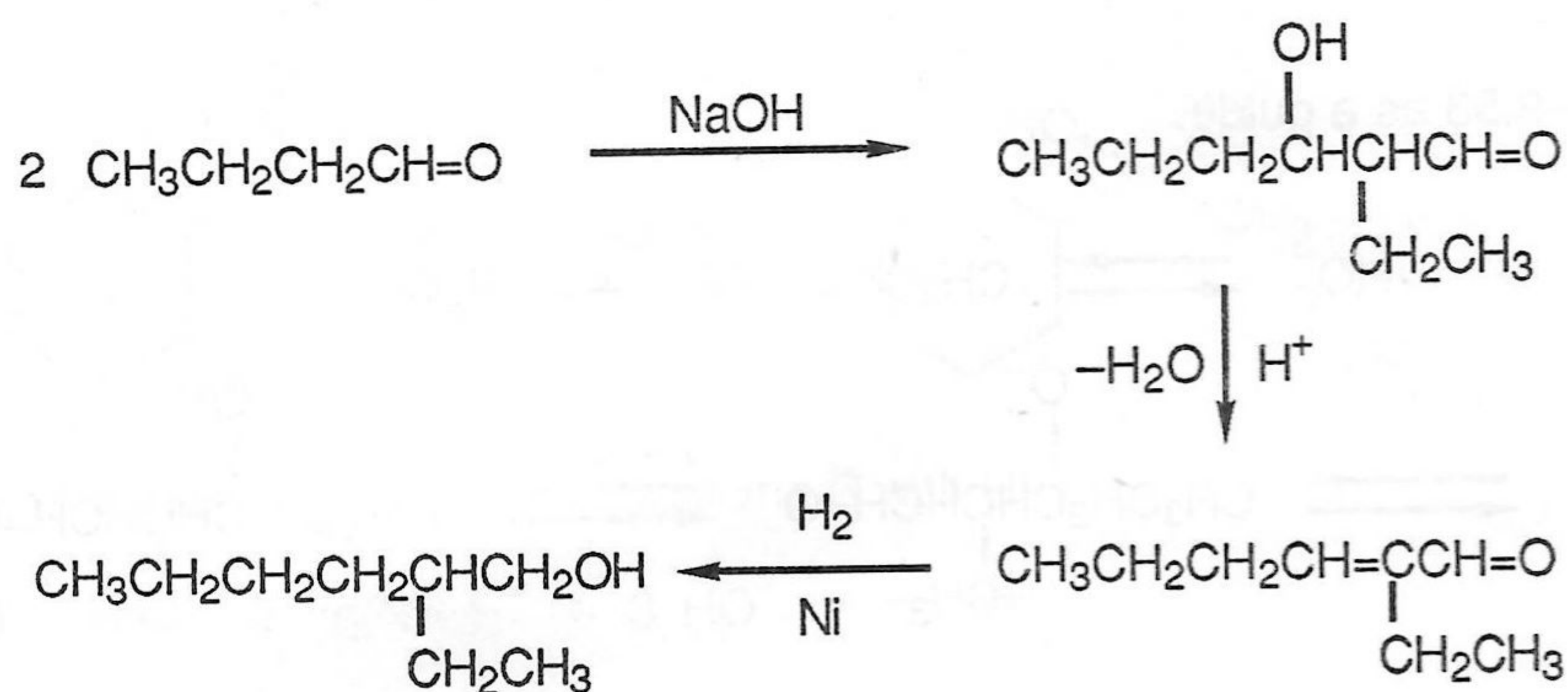
9.28 Propanal has the α -hydrogens. The aldol is



and its dehydration product is



9.29 An aldol condensation–dehydration sequence can be used to construct the carbon skeleton.

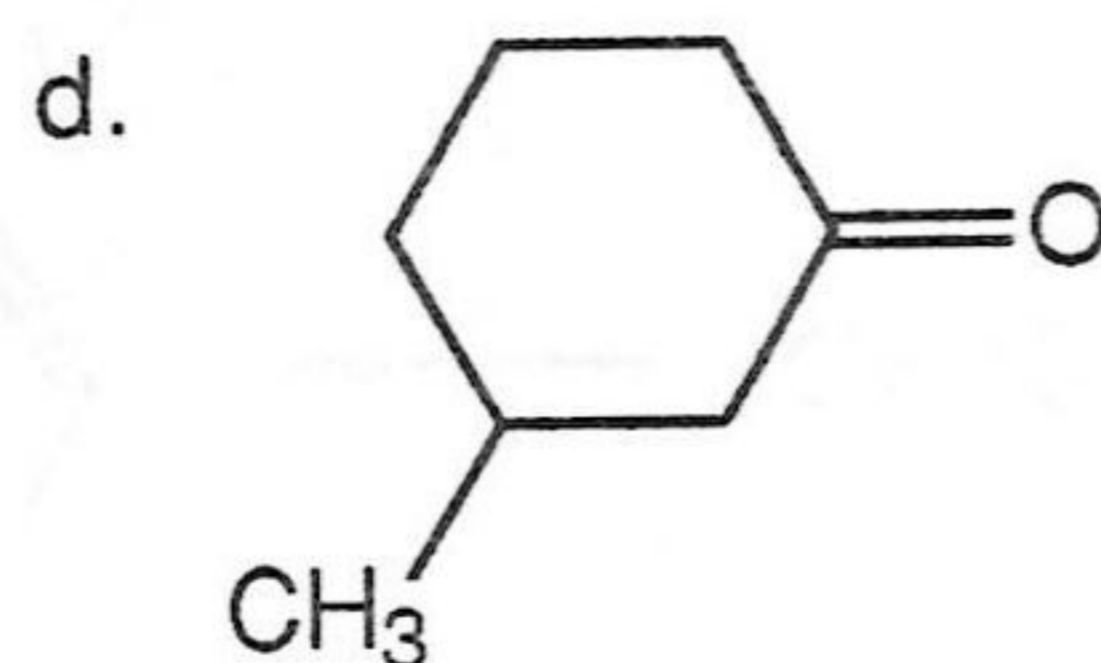
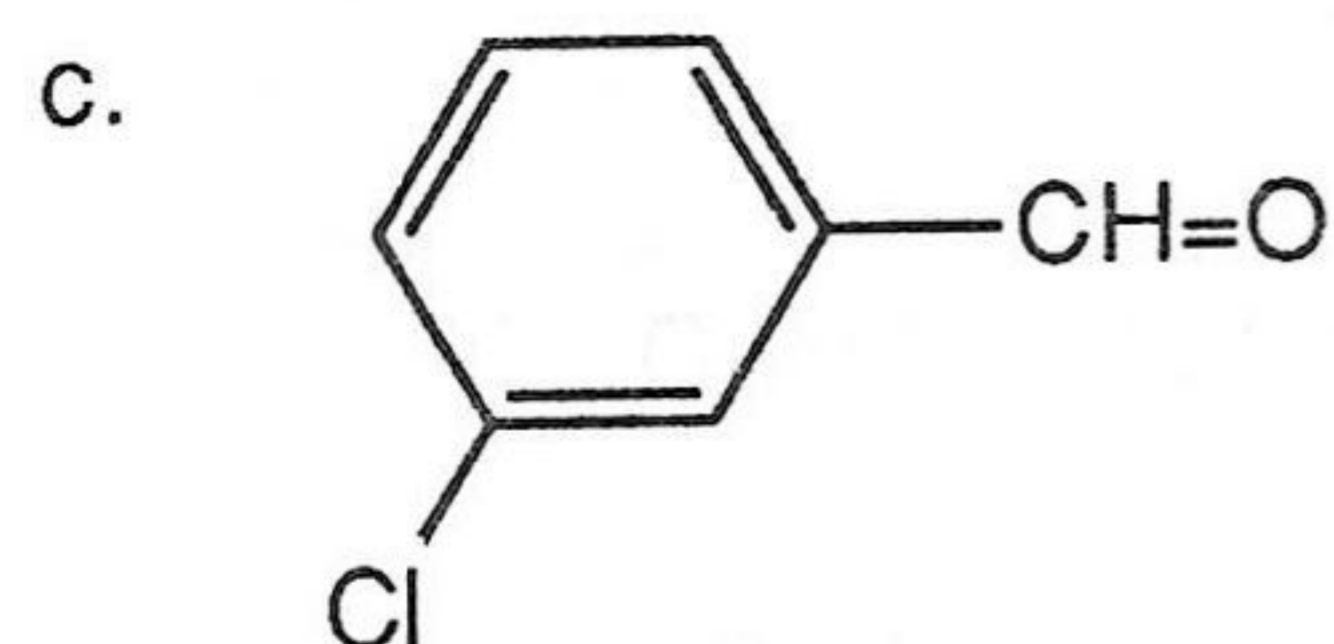
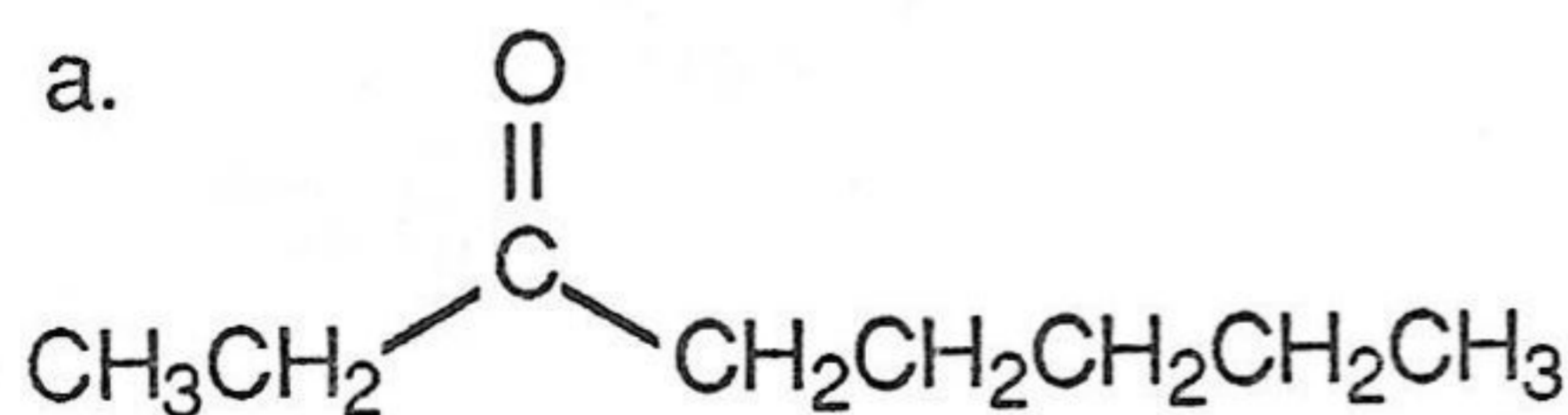


Catalytic hydrogenation of the double bonds completes the synthesis.

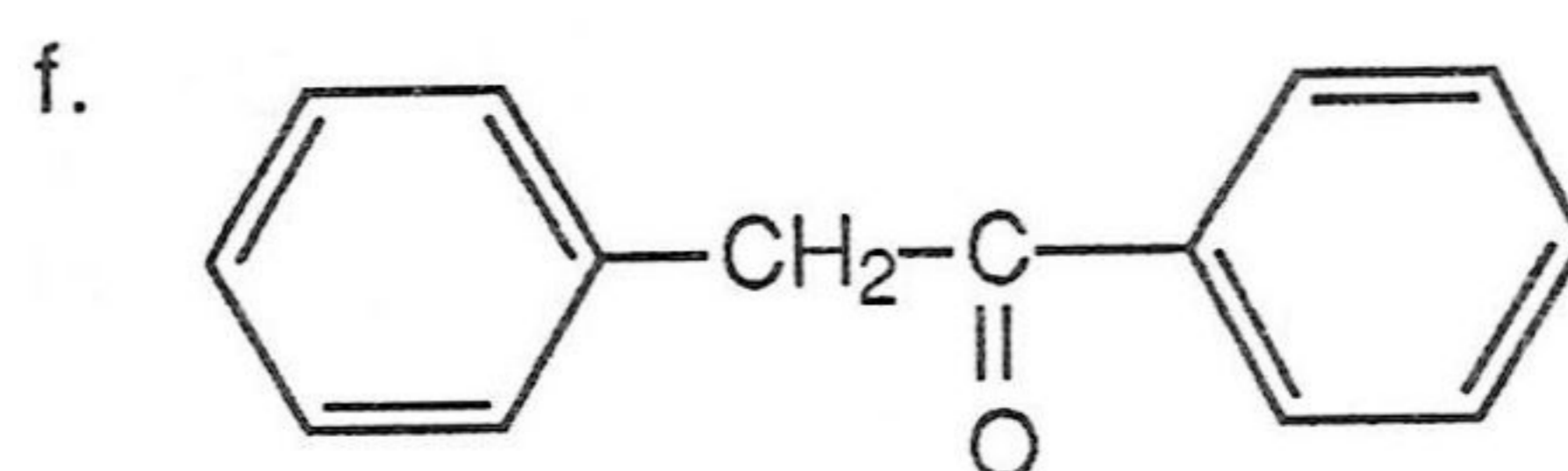
Additional Problems

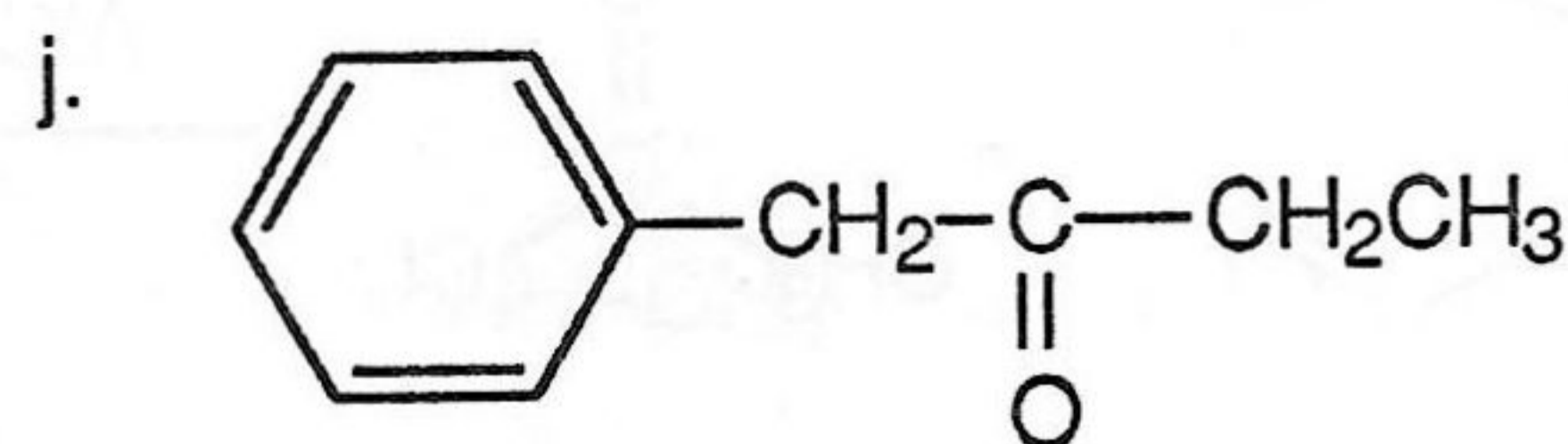
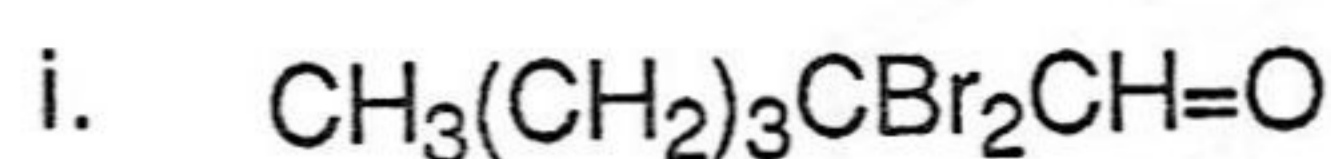
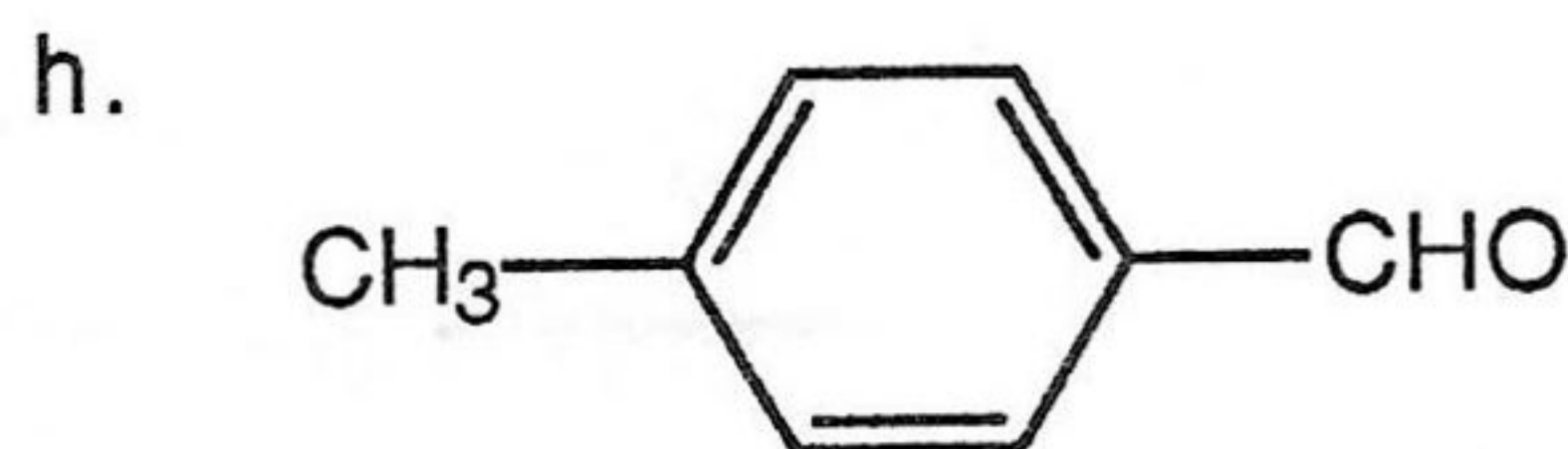
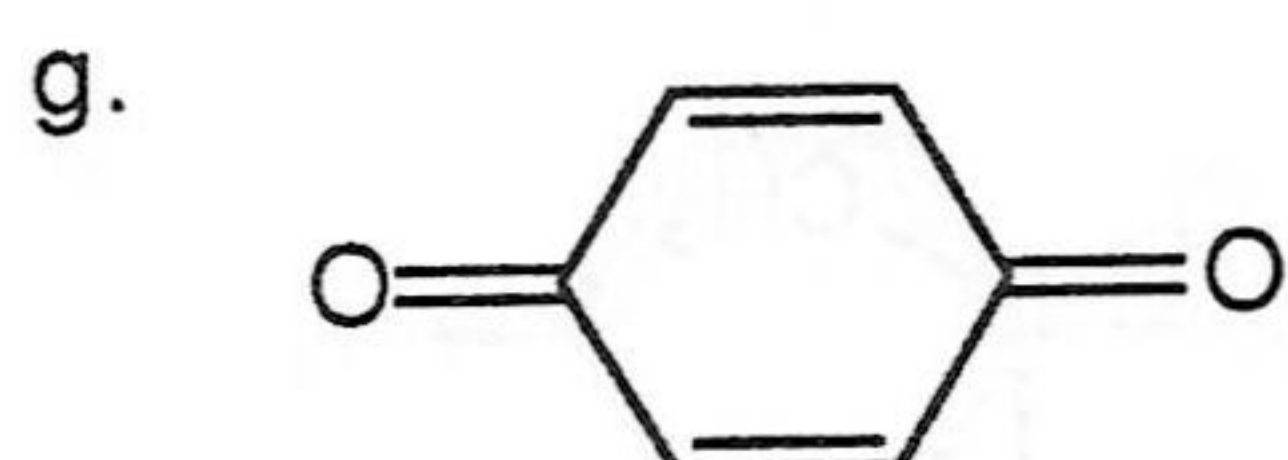
- 9.30
- | | |
|-------------------------------------|--------------------------------|
| a. 3-pentanone | b. octanal |
| c. benzophenone (diphenyl ketone) | d. <i>o</i> -bromobenzaldehyde |
| e. cyclobutanone | f. 2,2-dimethylpropanal |
| g. dicyclopentylketone | h. 3-penten-2-one |
| i. bromoacetone (or bromopropanone) | |

- 9.31
- | | |
|----|--|
| a. | b. $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{CH}=\text{O}$ |
|----|--|



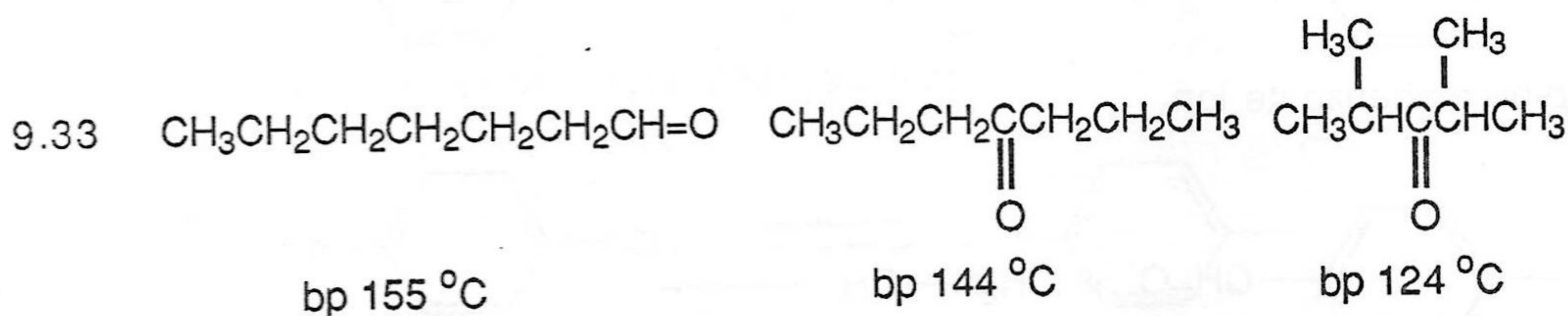
- e. $\text{CH}_3\text{CH}_2\text{CH}=\text{CHCHO}$



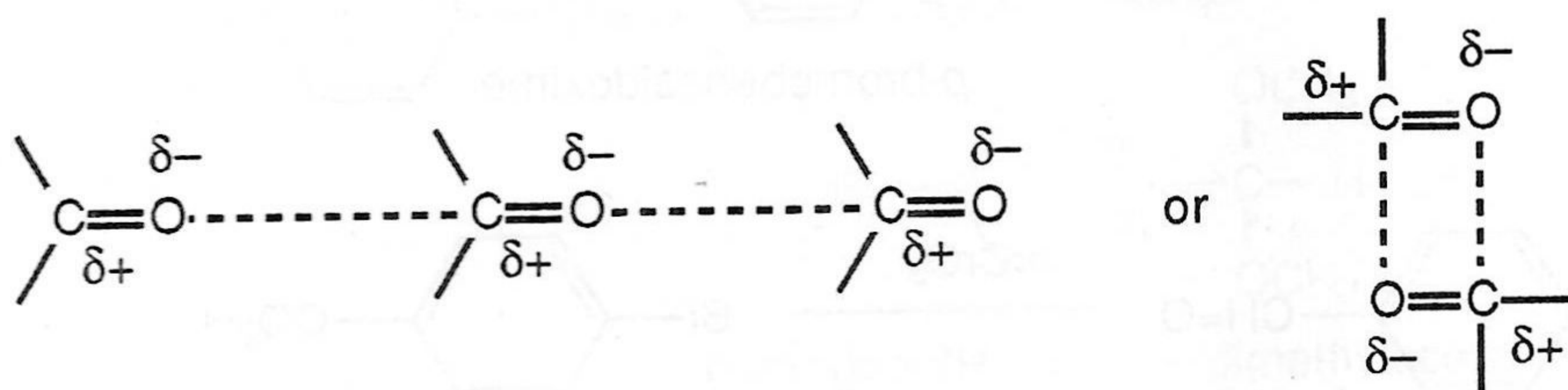


9.32 In each case, see the indicated section of the text for typical examples.

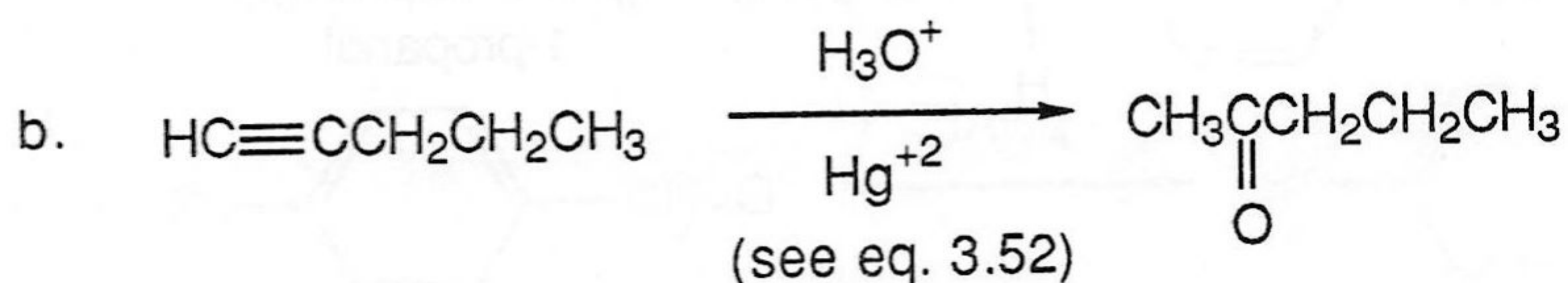
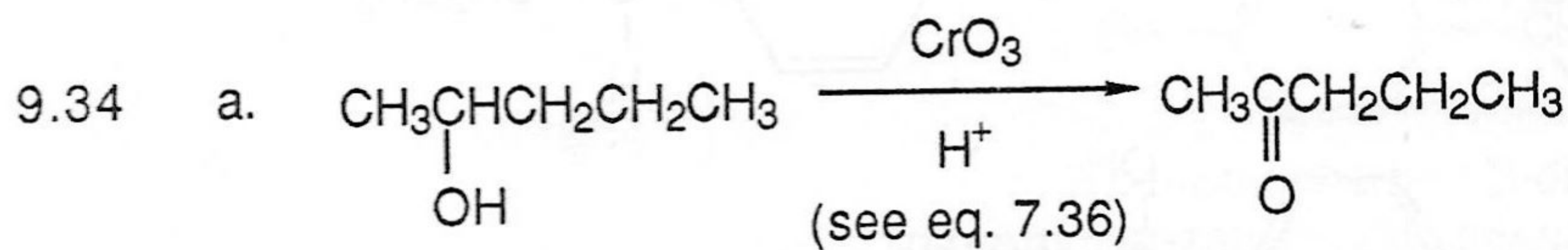
- | | | |
|--------------|------------------------|--------------|
| a. Sec. 9.7 | b. Sec. 9.7 | c. Sec. 9.10 |
| d. Sec. 9.11 | e. Sec. 9.11 | f. Sec. 9.11 |
| g. Sec. 9.14 | h. Secs. 9.14 and 9.18 | i. Sec. 9.15 |
| j. Sec. 9.11 | | |



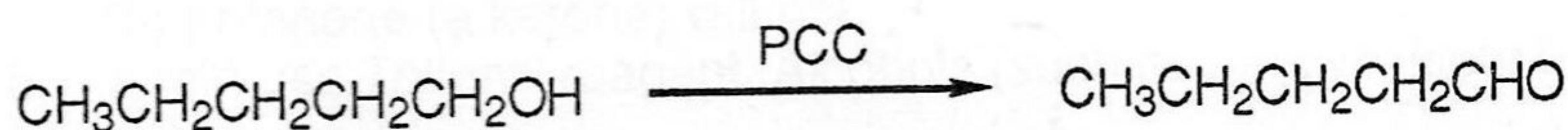
The compounds are isomers and have identical molecular weights. Each has a carbonyl group that, because of its polarity, can associate as follows as a consequence of intermolecular attraction between opposite charges:



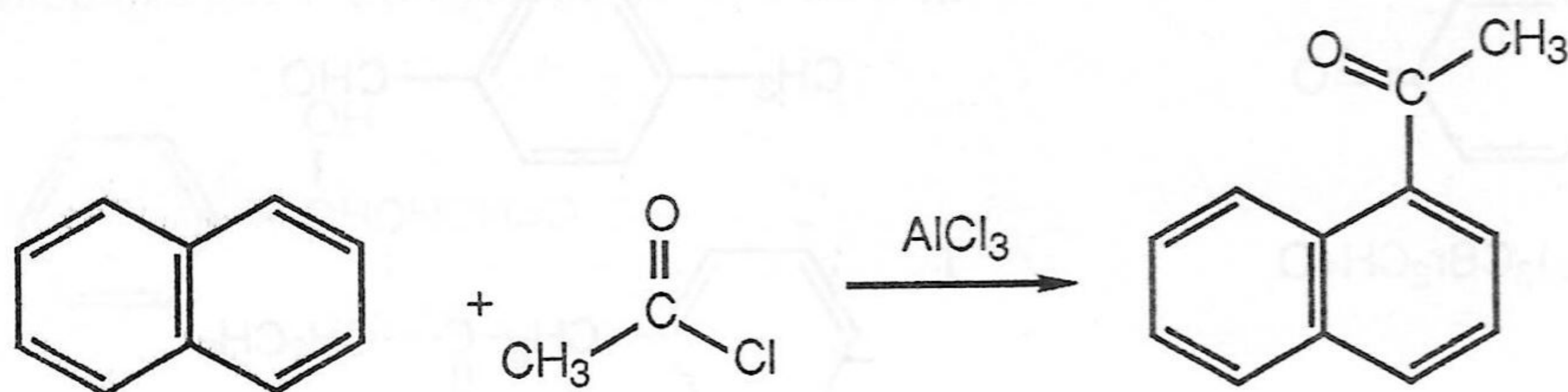
As we go from left to right in the series (as shown above), the carbonyl group is more and more hindered, or buried in the structure. Thus association is more difficult, and the boiling point decreases.



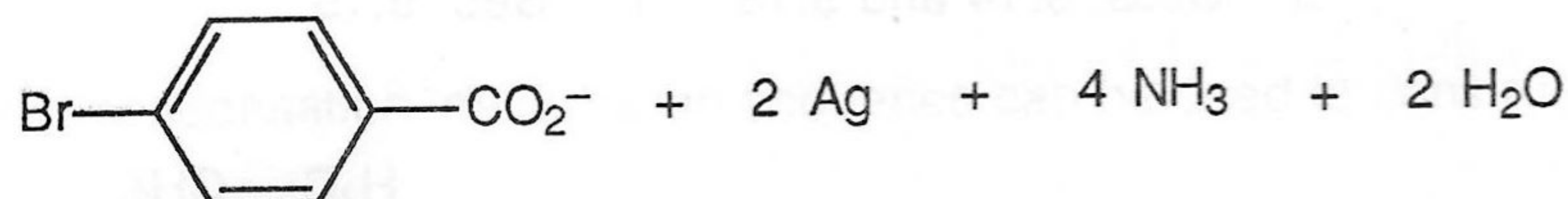
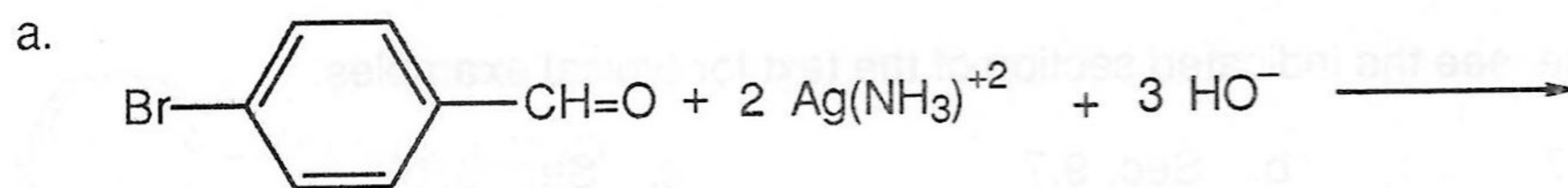
9.35 Use eq. 7.38 as a guide:



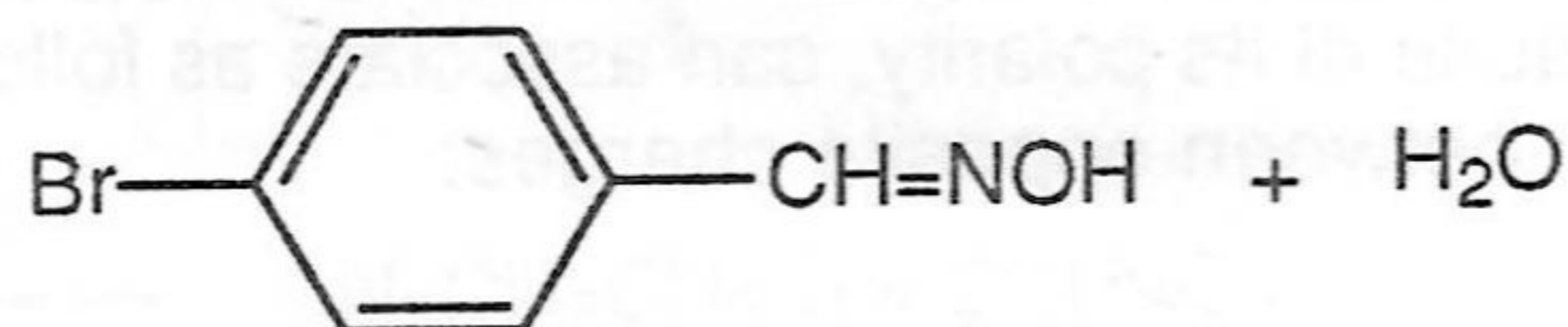
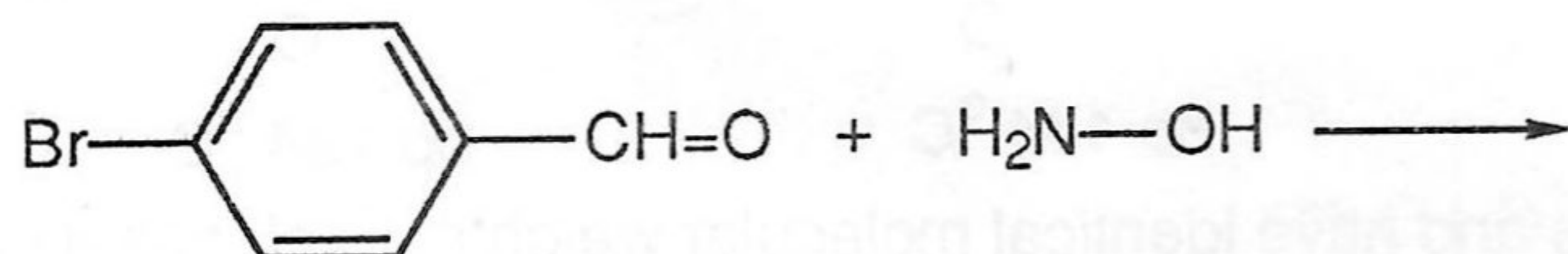
9.36



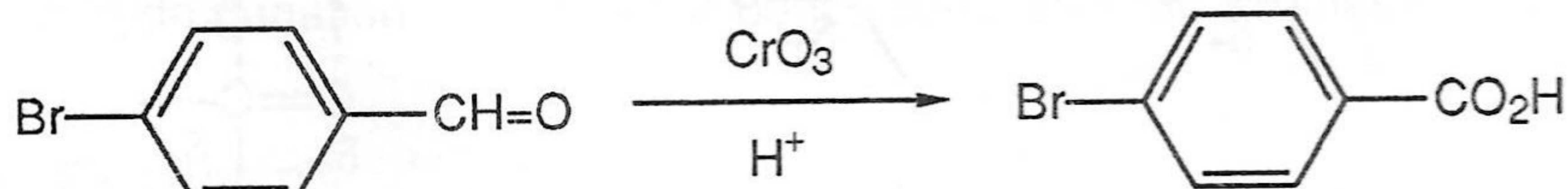
9.37

*p*-bromobenzoate ion

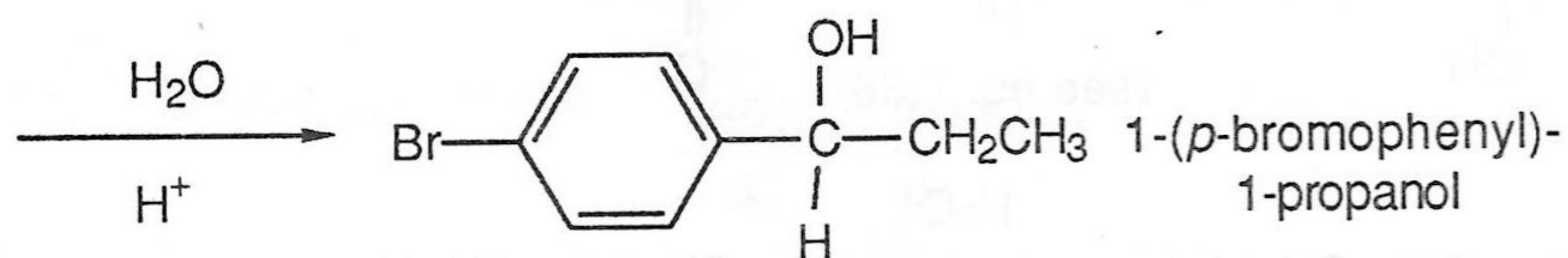
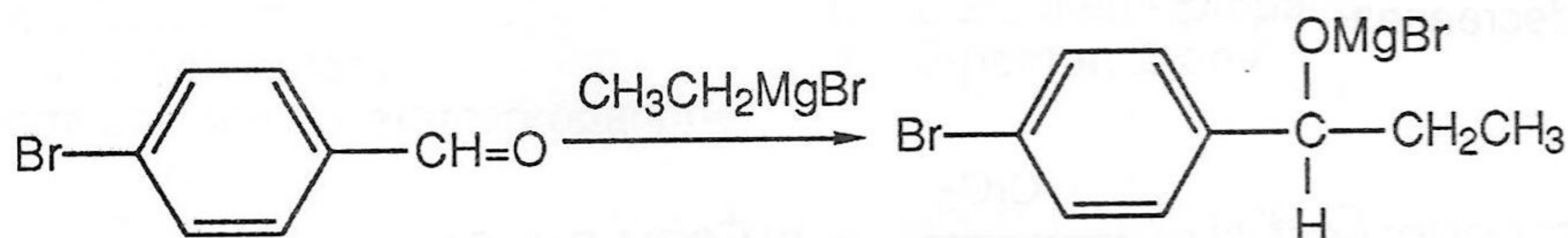
b.

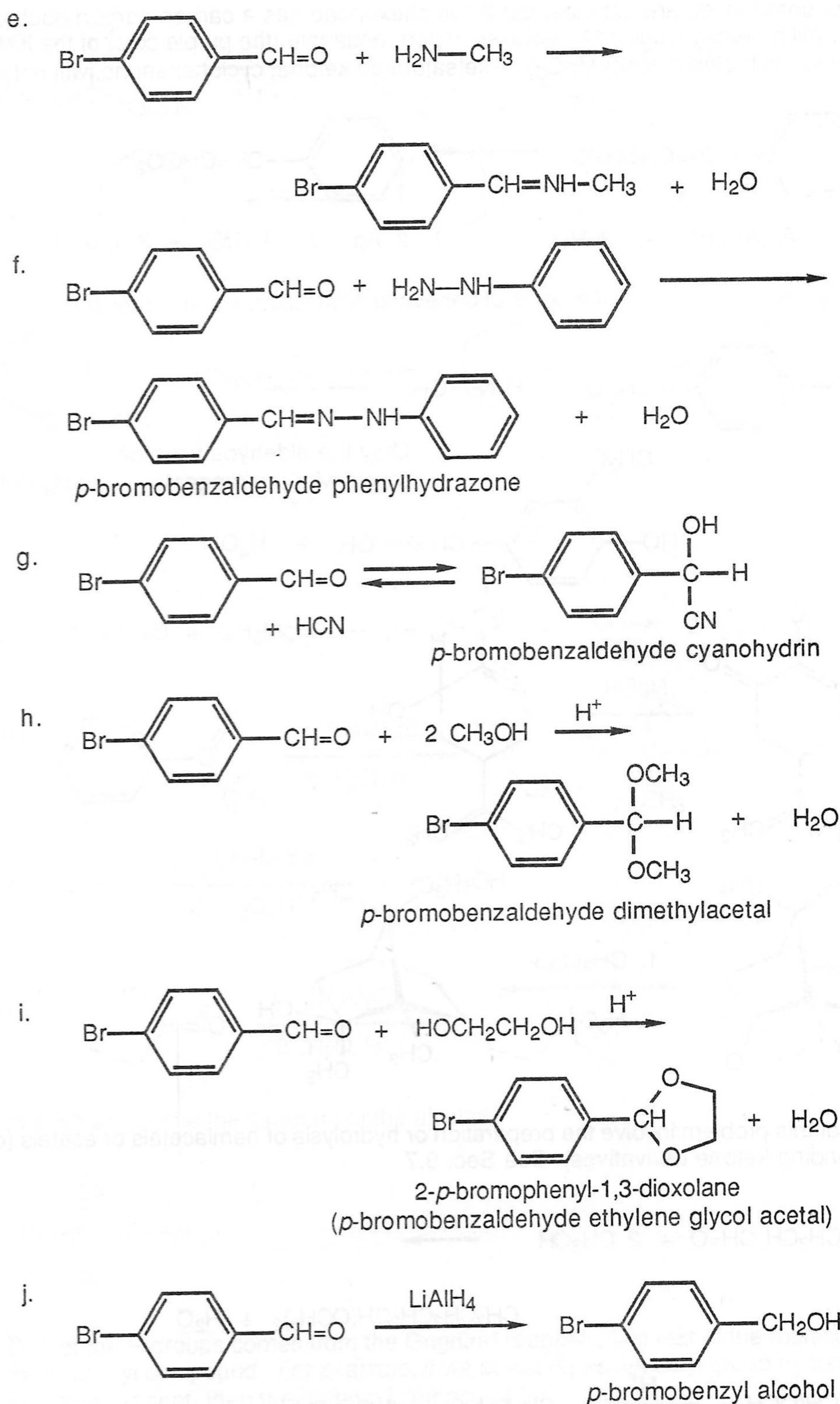
*p*-bromobenzaldoxime

c.

*p*-bromobenzoic acid

d.

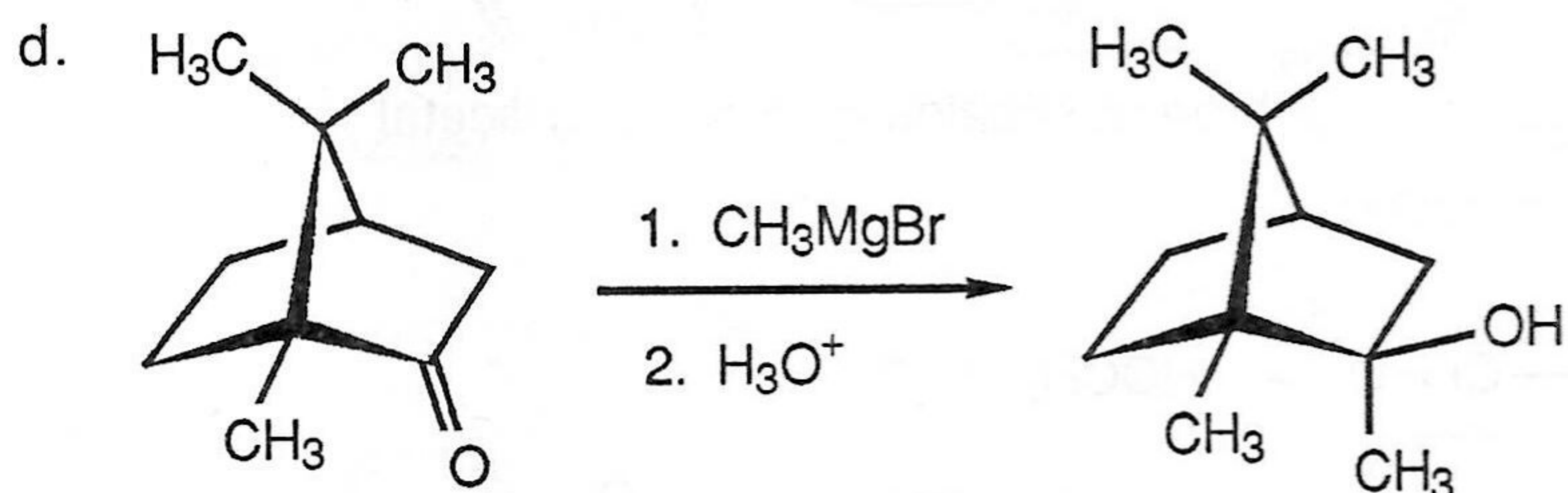
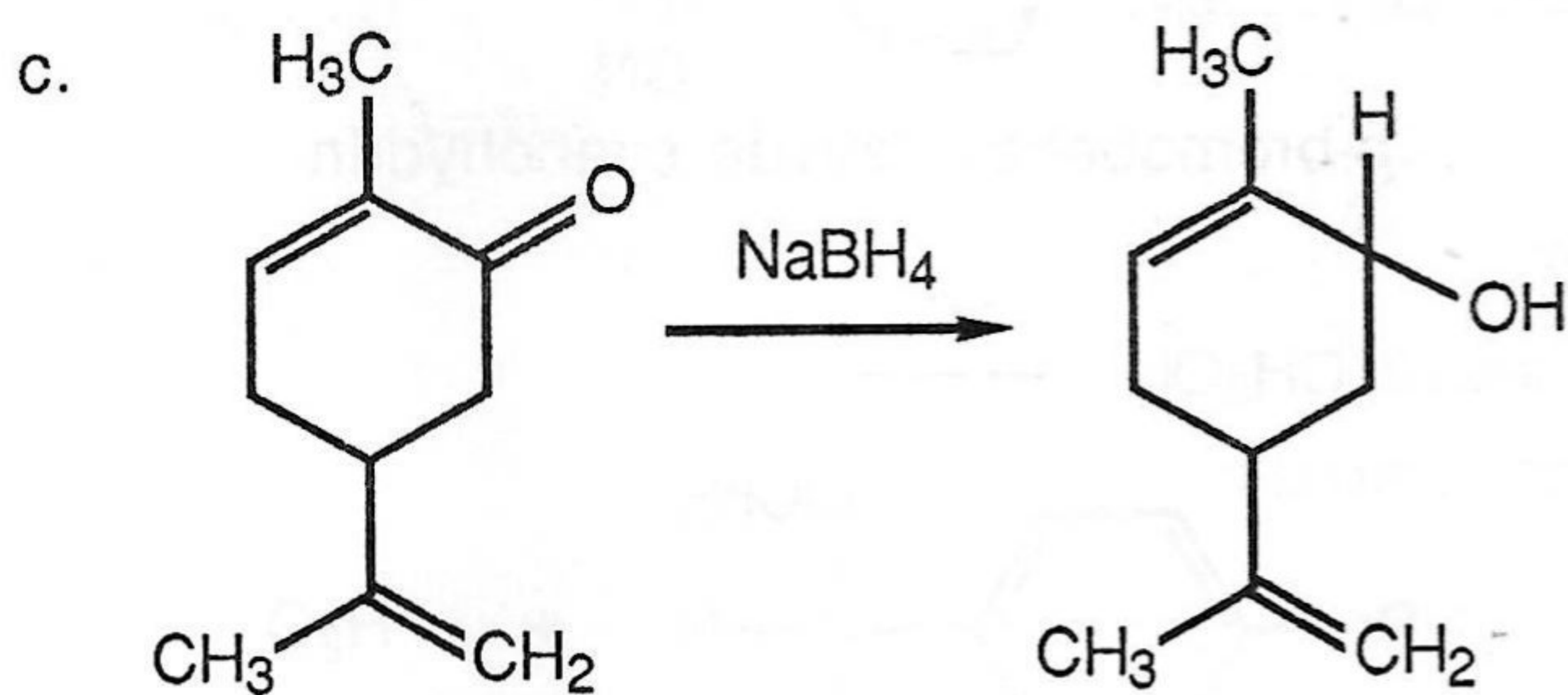
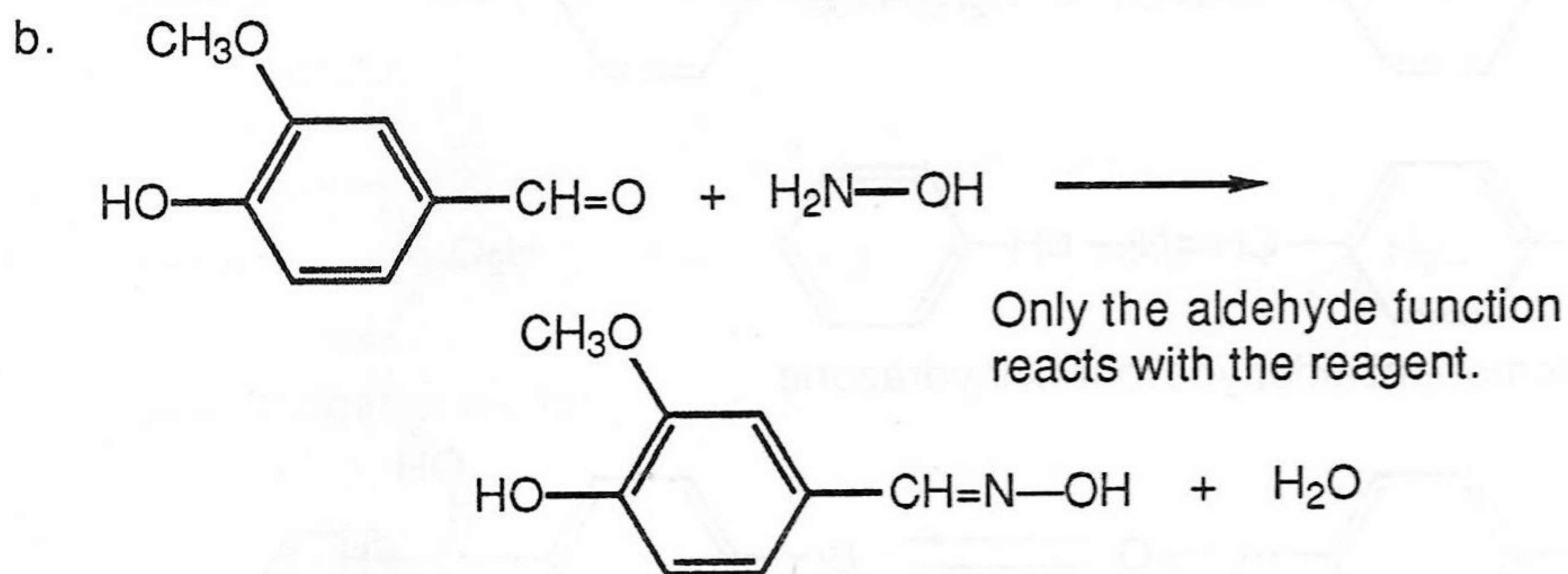
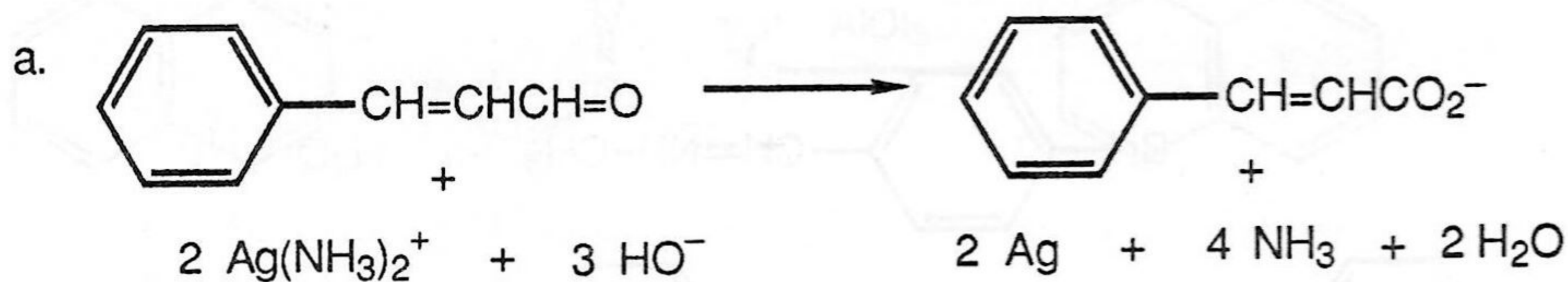




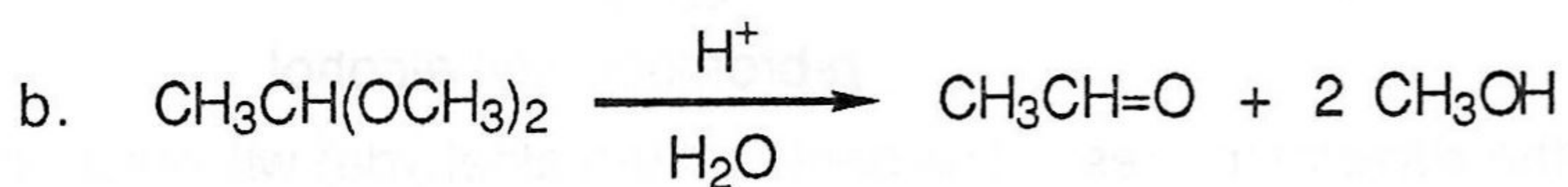
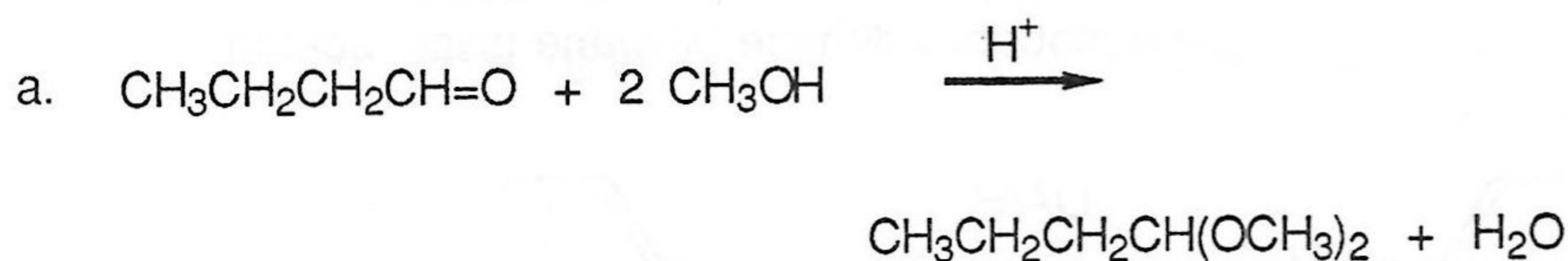
- 9.38 a. Use Tollens' reagent (the silver mirror test). The pentanal (an aldehyde) will react, whereas 2-pentanone (a ketone) will not.
- b. Again use Tollens' reagent. Alcohols (such as benzyl alcohol) do not react.

- c. Both compounds are ketones, but 2-cyclohexenone has a carbon-carbon double bond and will be easily oxidized by potassium permanganate (the purple color of the KMnO_4 will turn to the brown color of MnO_2). The saturated ketone, cyclohexanone, will not react.

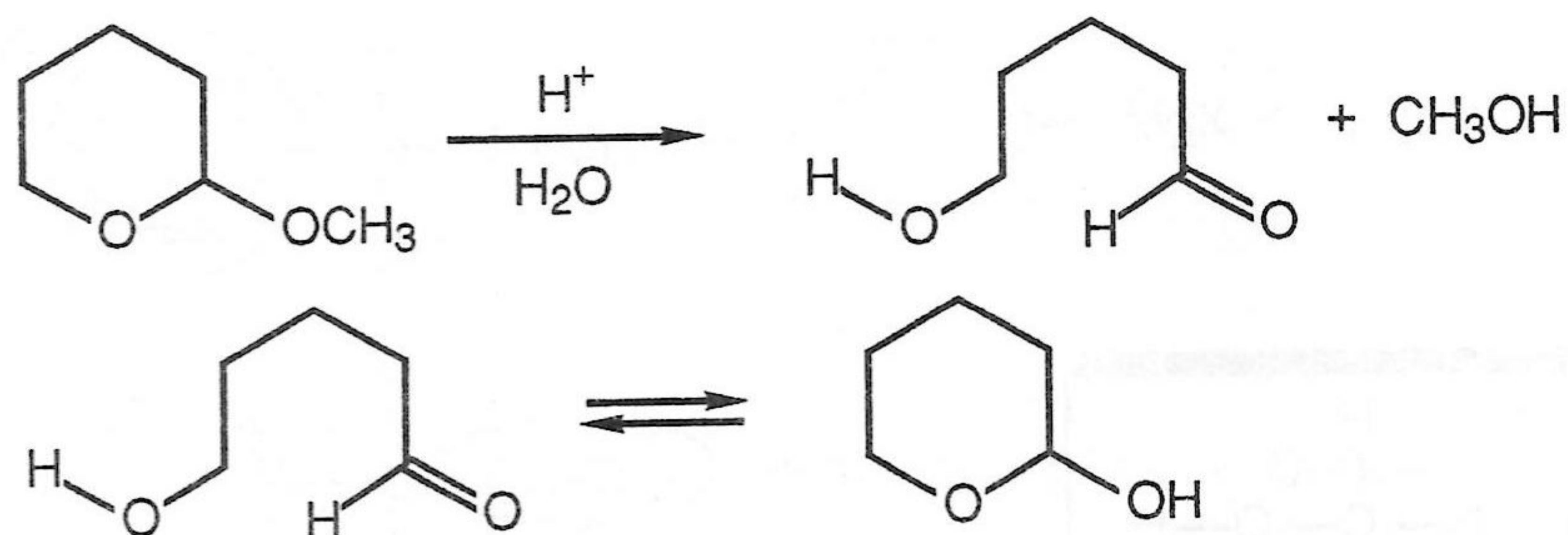
9.39



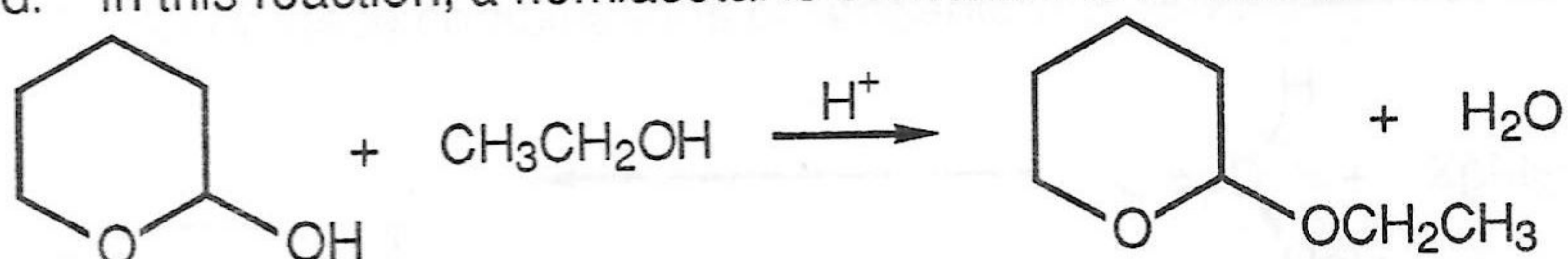
- 9.40 All parts of this problem involve the preparation or hydrolysis of hemiacetals or acetals (or the corresponding ketone derivatives). See Sec. 9.7.



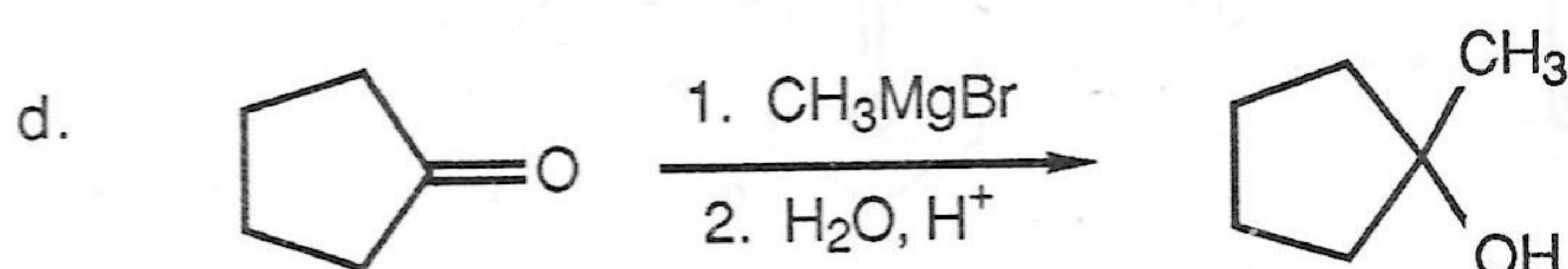
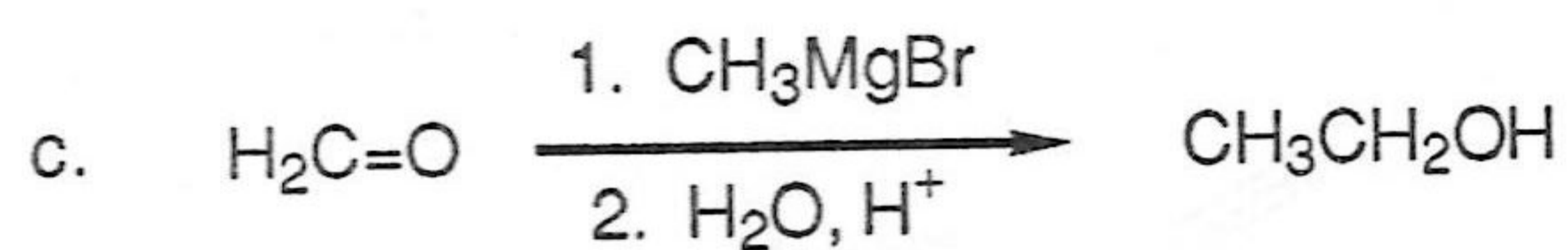
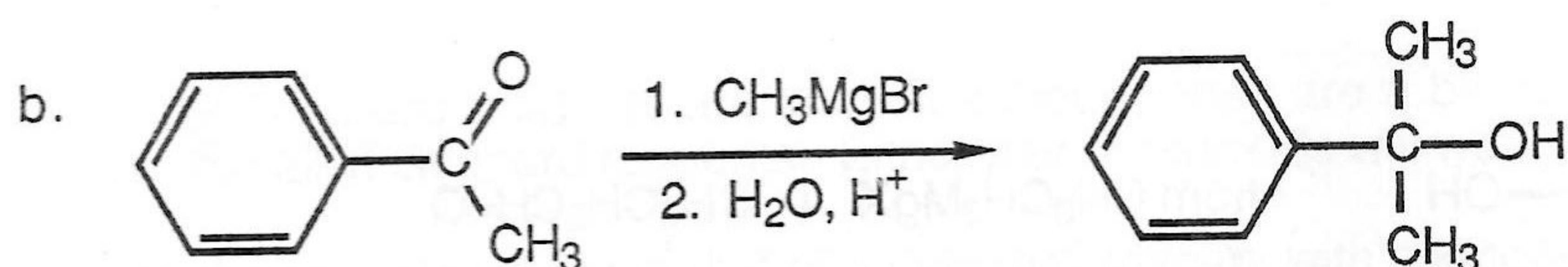
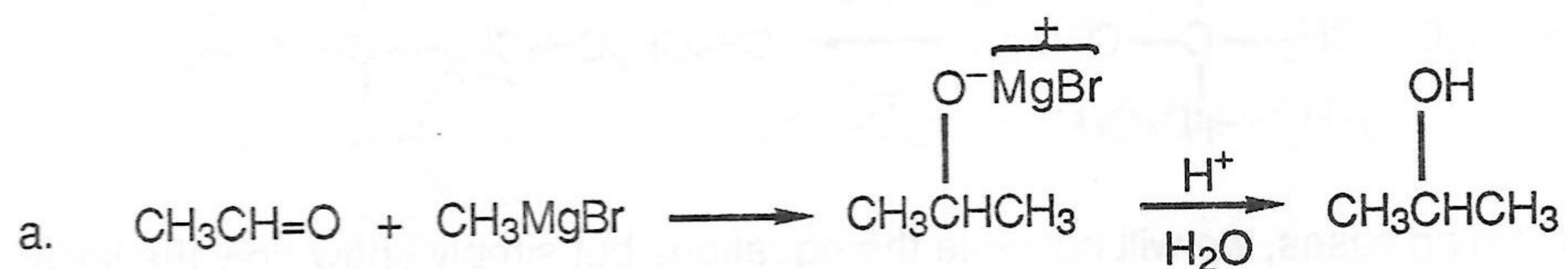
- c. In this case, the acetal is cyclic, and the product is a hydroxy aldehyde, which may exist in its cyclic hemiacetal form.



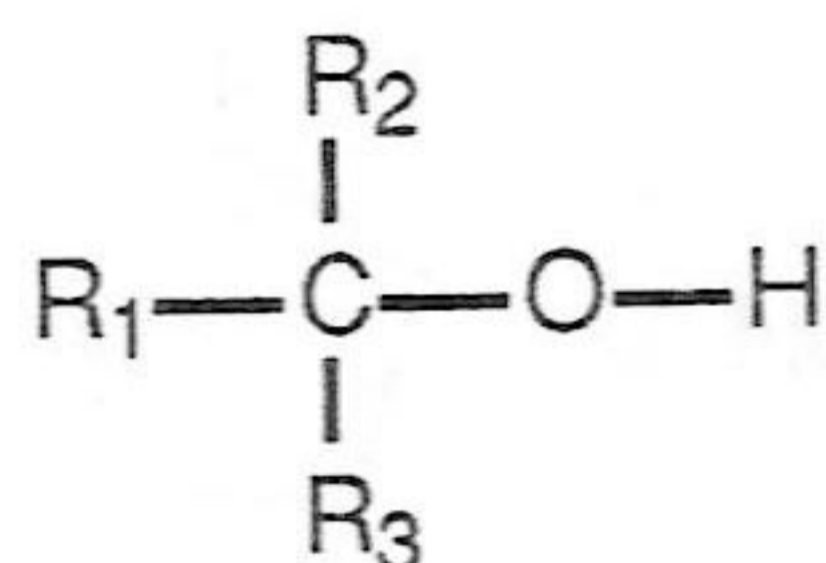
d. In this reaction, a hemiacetal is converted to an acetal.



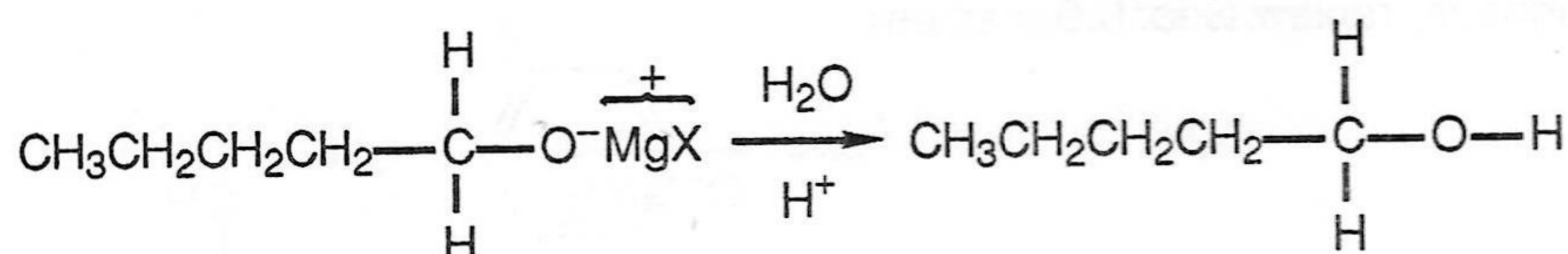
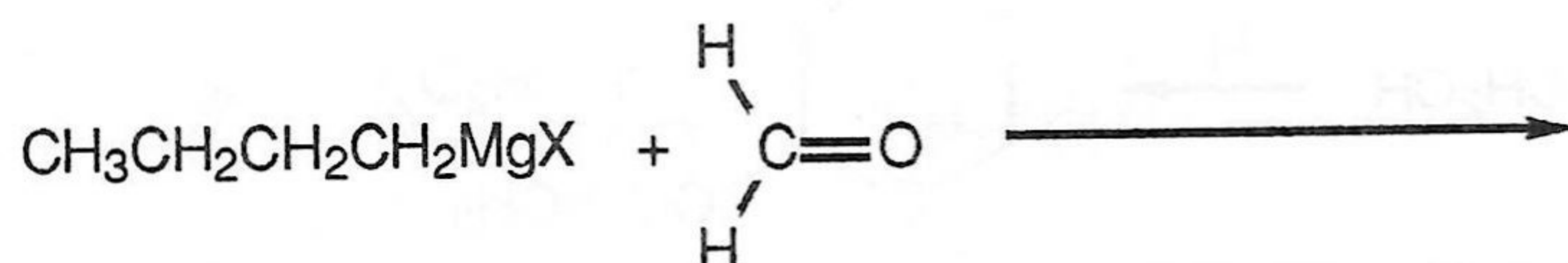
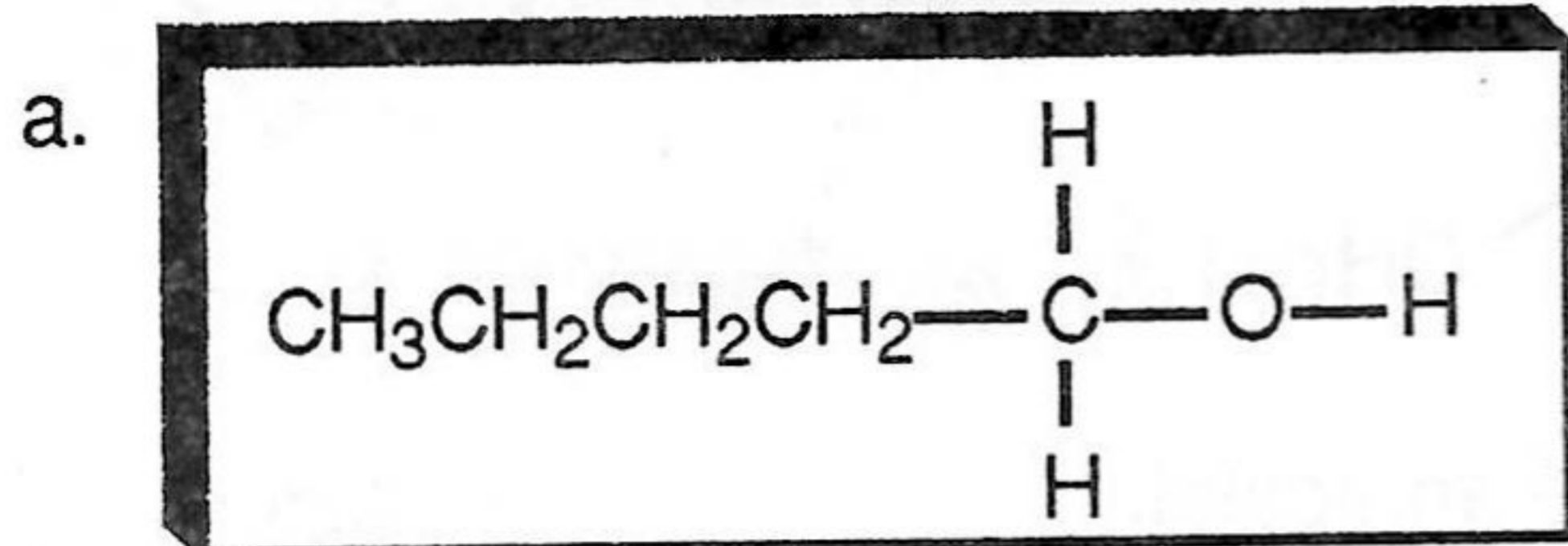
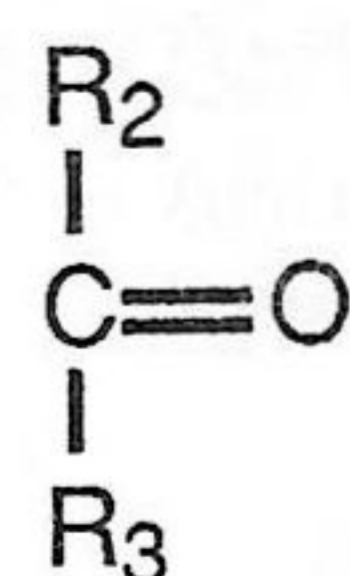
9.41 For guidance, review Sec. 9.9.



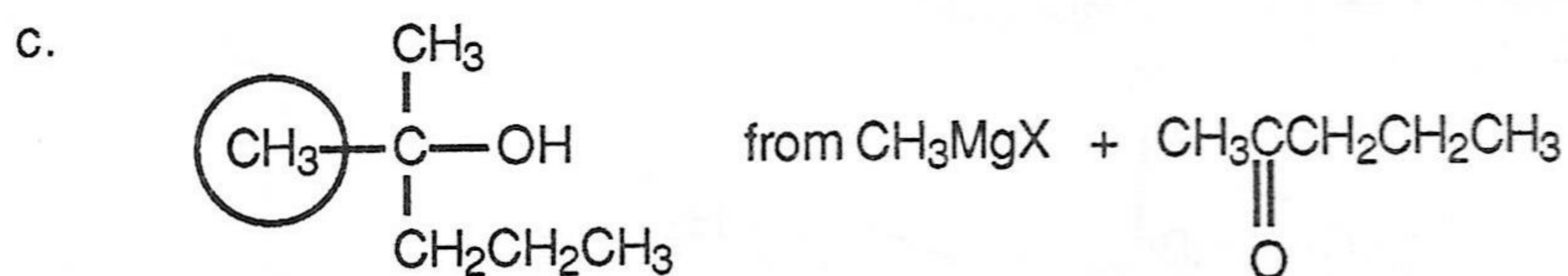
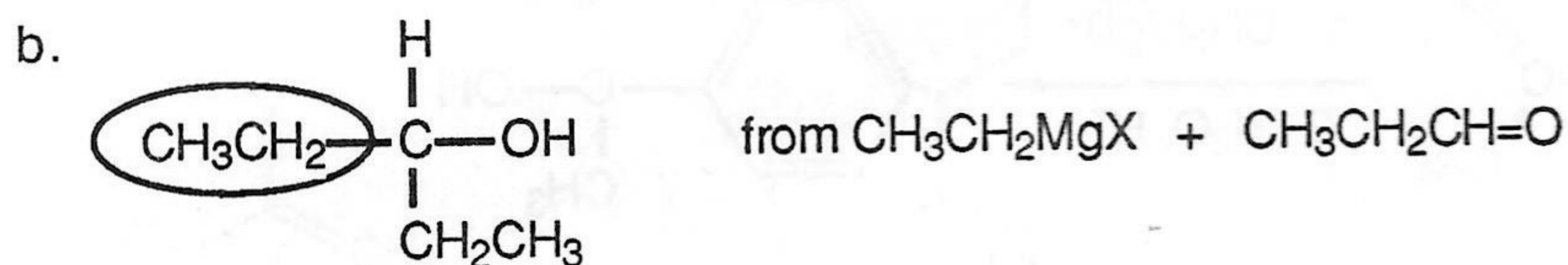
9.42 In each case write the structure of the alcohol:



One of the R groups comes from the Grignard reagent. The rest of the molecule comes from the carbonyl compound. For example, if we select R_1 as the alkyl group to come from the Grignard reagent, then the carbonyl compound is:



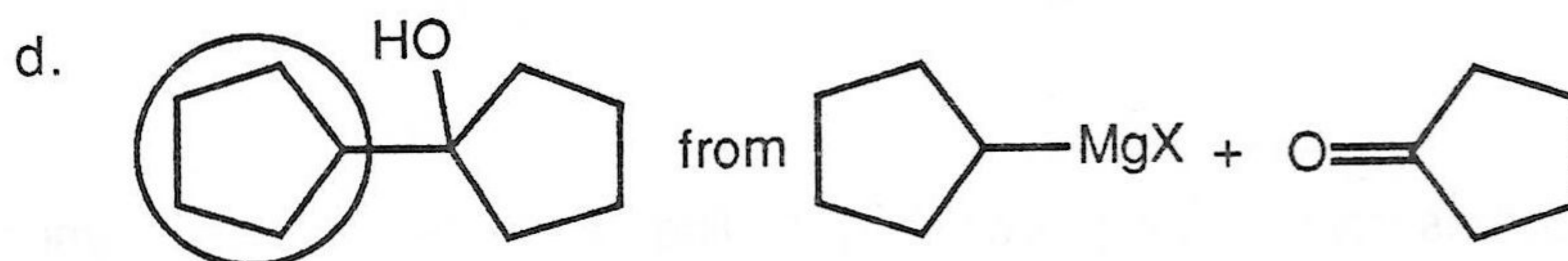
For the remaining cases, we will not write the equations but simply show how the initial reactants are derived.



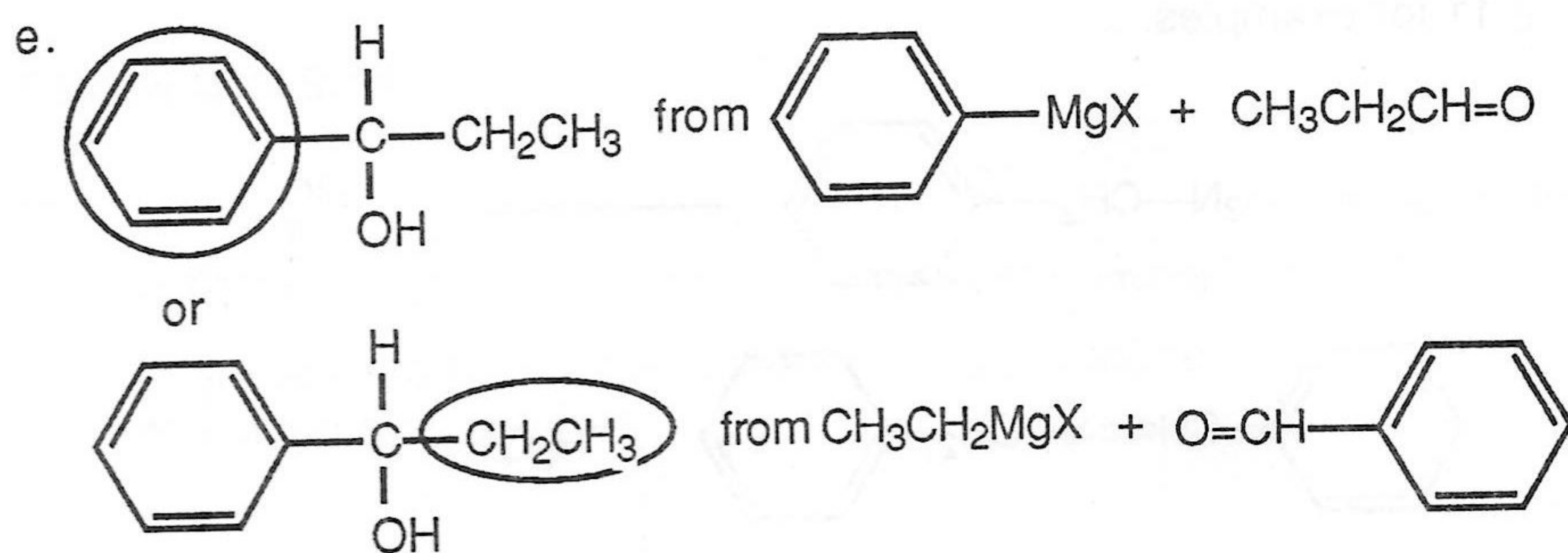
or



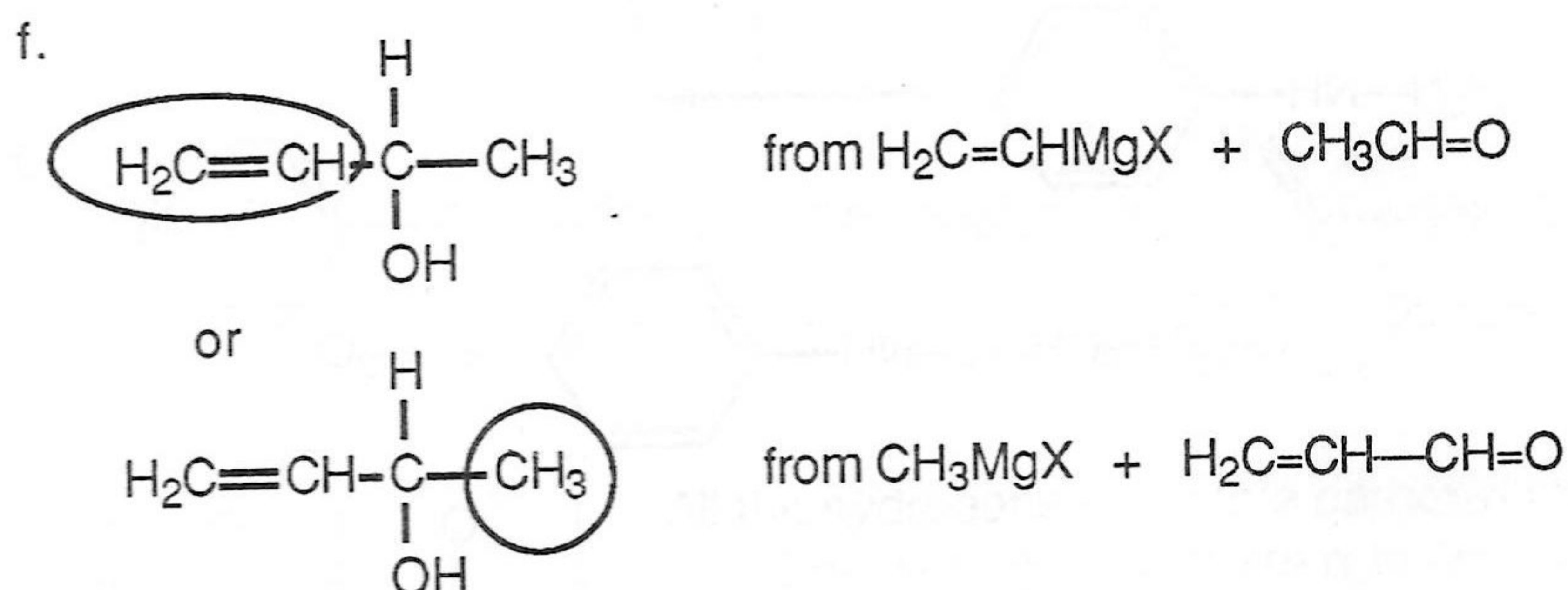
Either of these combinations of reagents will work.



In this case, the "free-standing" R group is selected to come from the Grignard reagent.



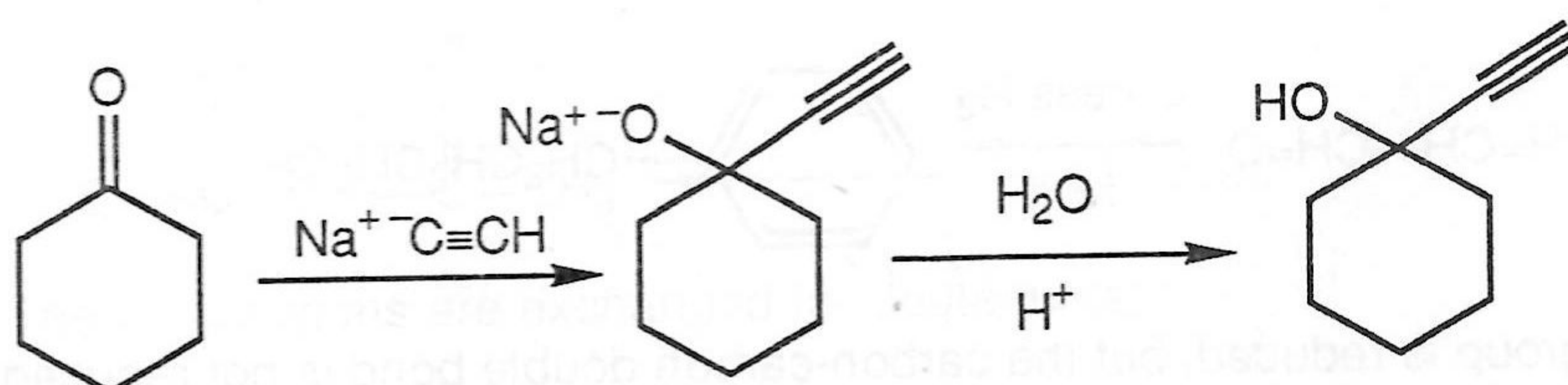
Either of these combinations of reagents will work.



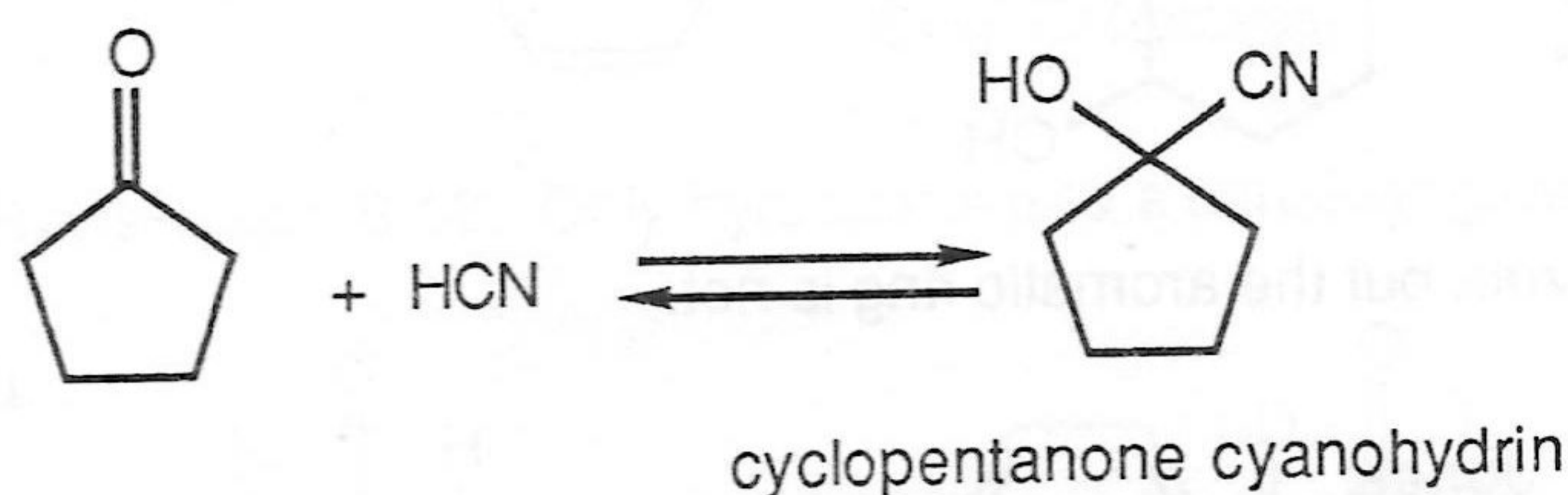
Either of these combinations of reagents will work.

Vinyl Grignard reagents are known, although they are a bit more difficult to prepare than simple alkyl Grignard reagents. Either pair of reagents will work.

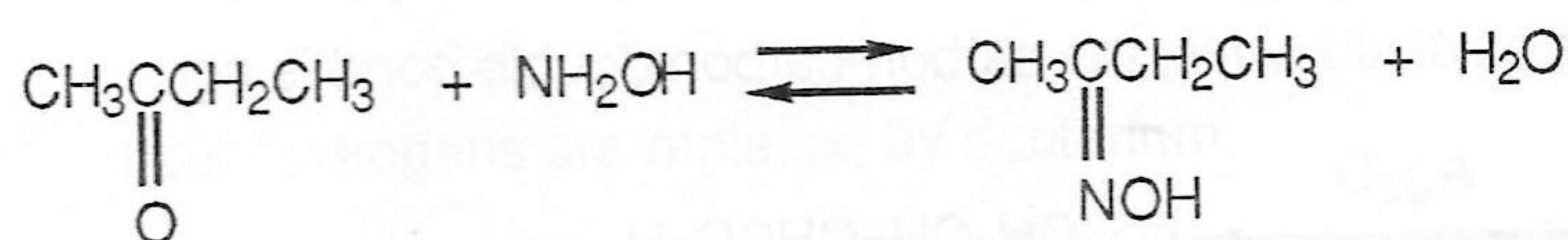
- 9.43 a. The reaction is similar to that of a Grignard reagent with a ketone (see eq. 9.24). Also see eq. 9.26.



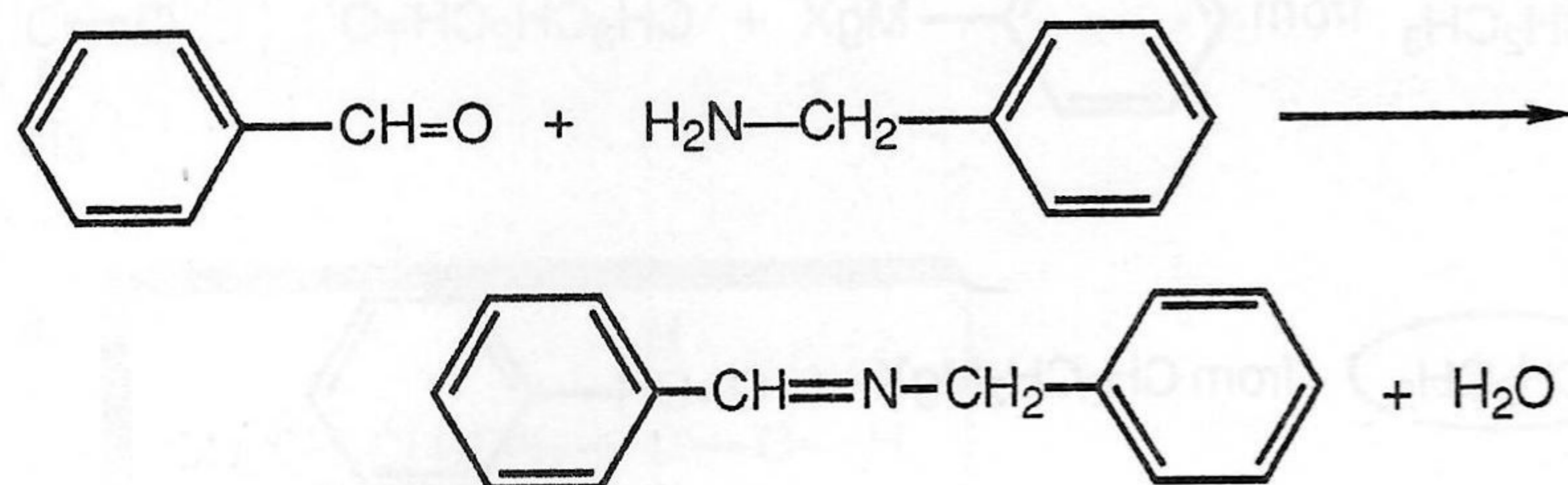
- b. See eq. 9.28 for guidance.



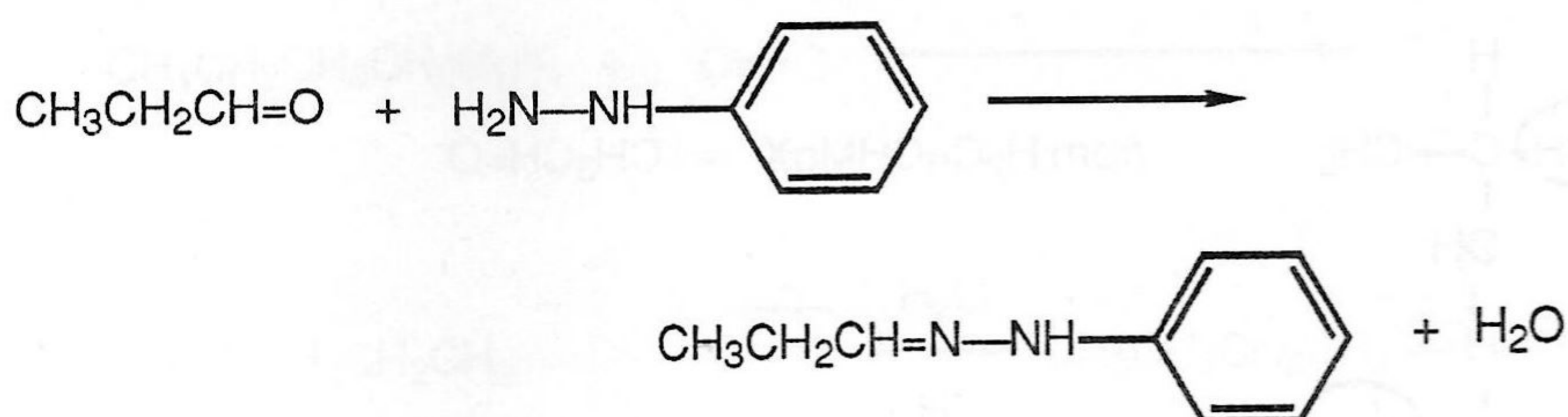
- c. See Table 9.1 for guidance.



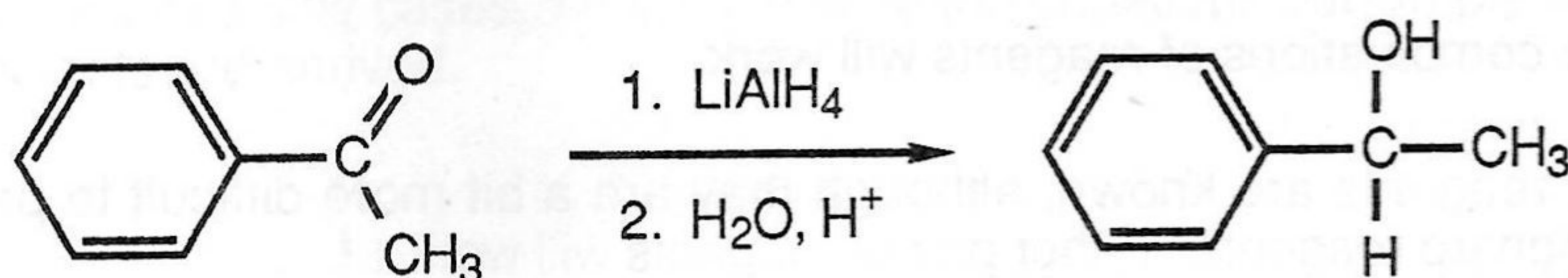
d. See Sec. 9.11 for examples.



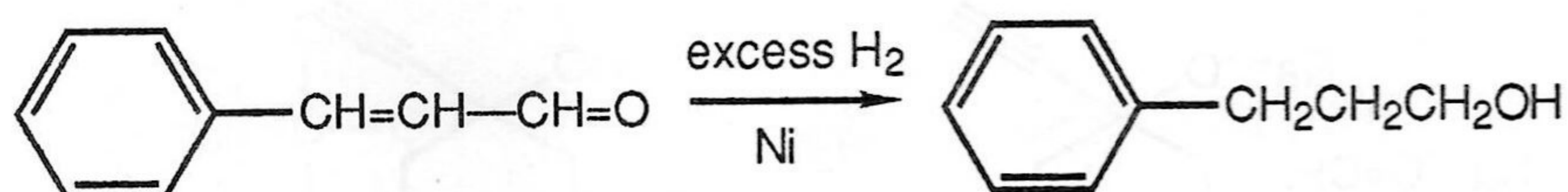
e. See Table 9.1.



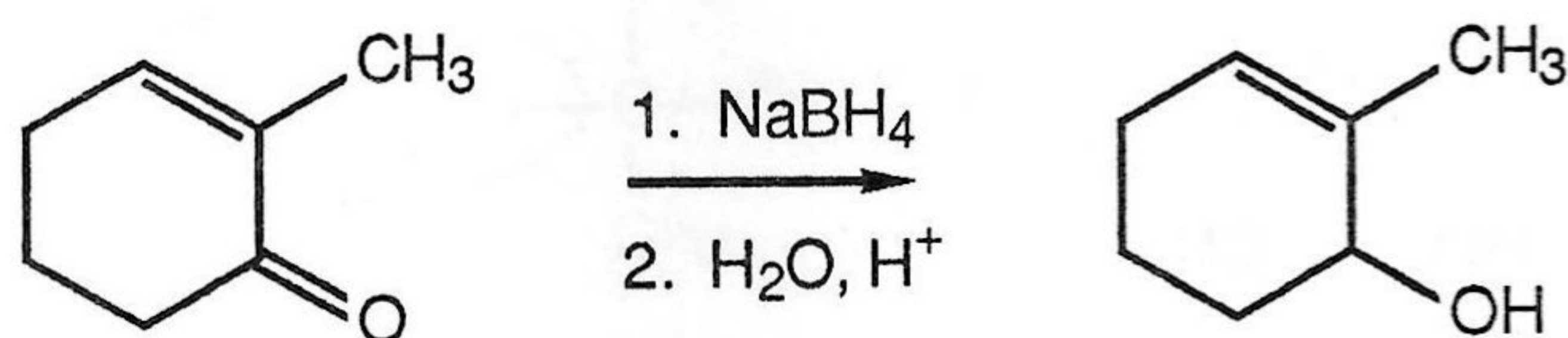
9.44 a. See Sec. 9.12.



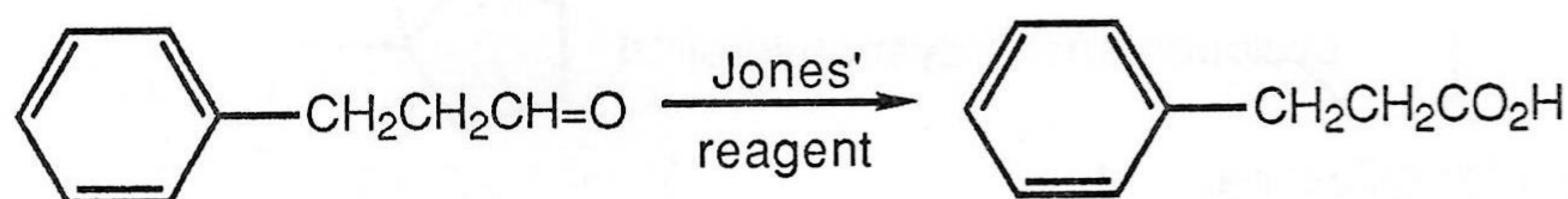
b. See Sec. 9.12. Usually the aromatic ring will not be reduced, although under certain reaction conditions even this is possible.



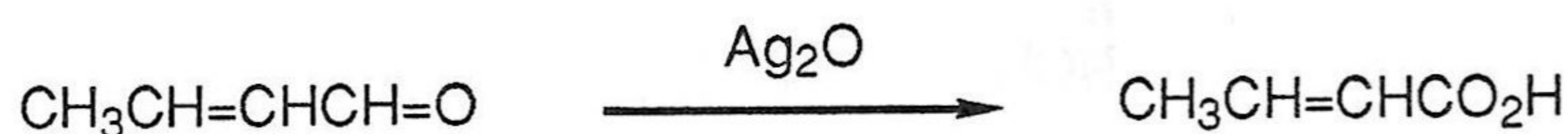
c. The carbonyl group is reduced, but the carbon-carbon double bond is not reduced.



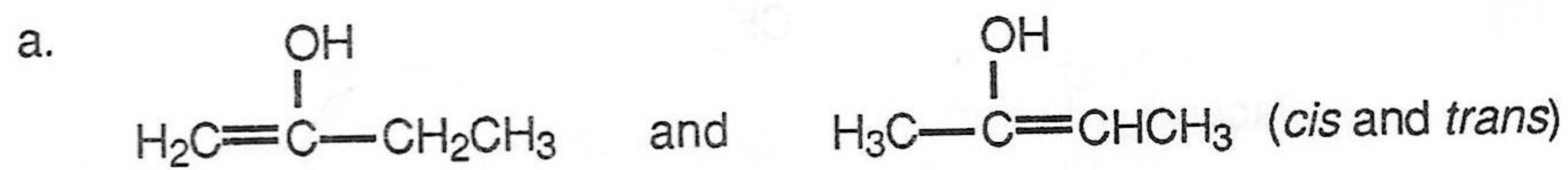
d. The carbonyl group is oxidized, but the aromatic ring is not.



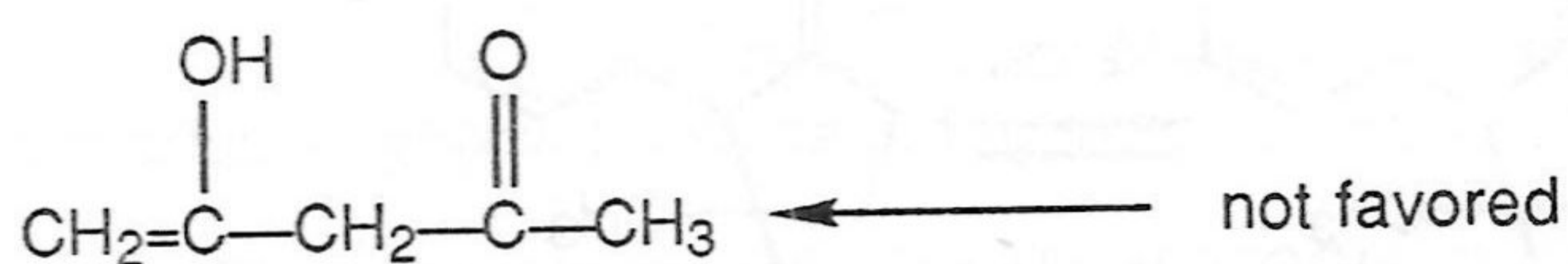
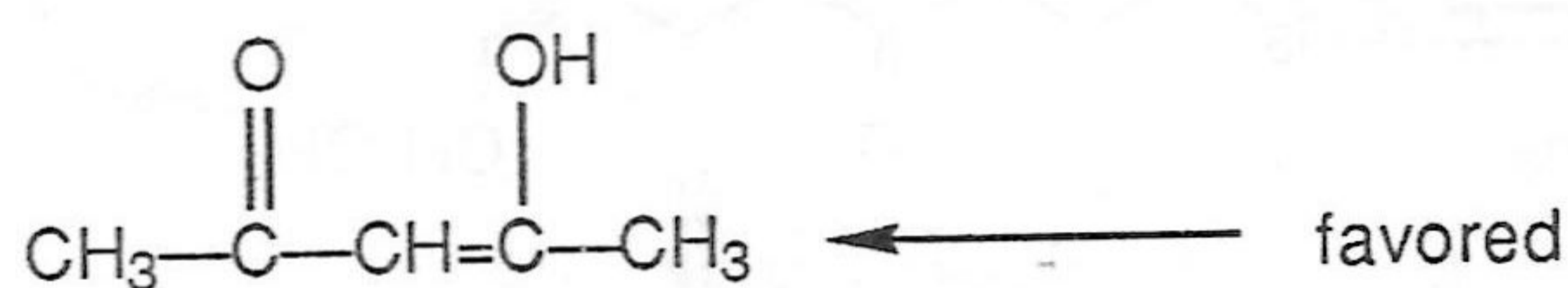
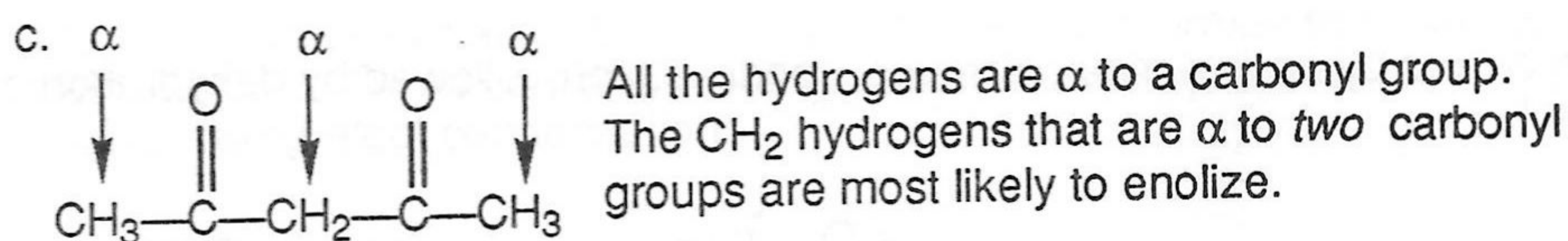
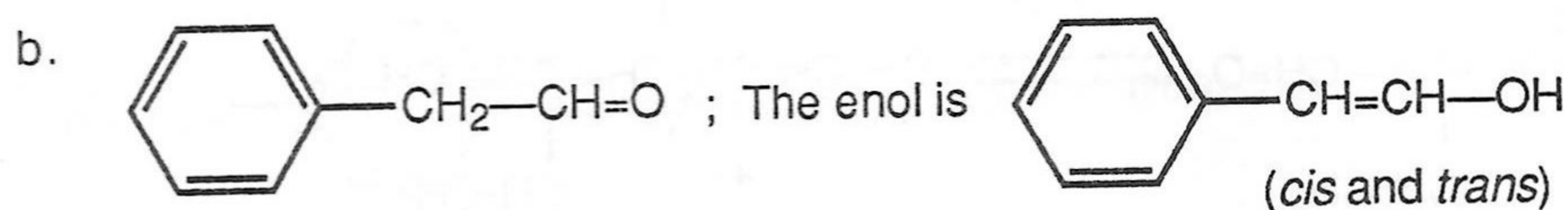
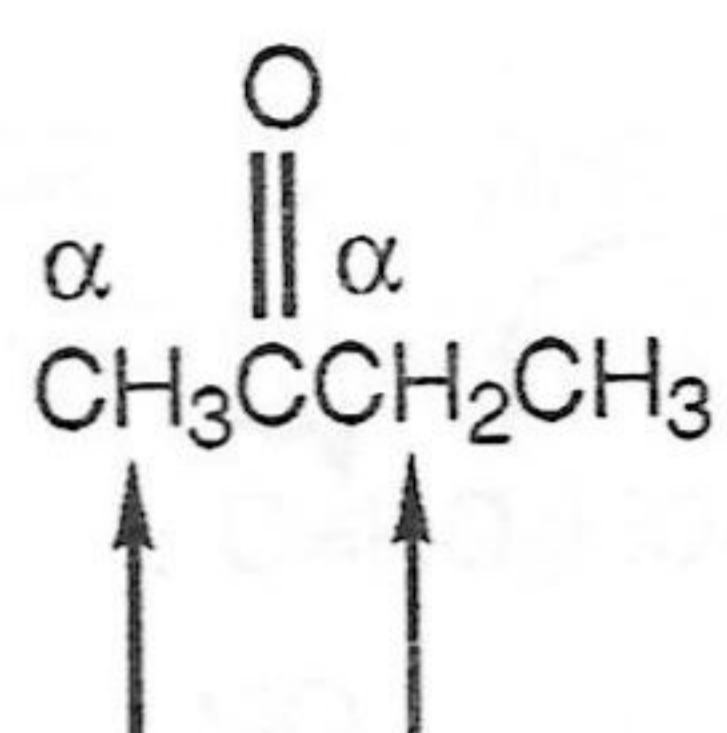
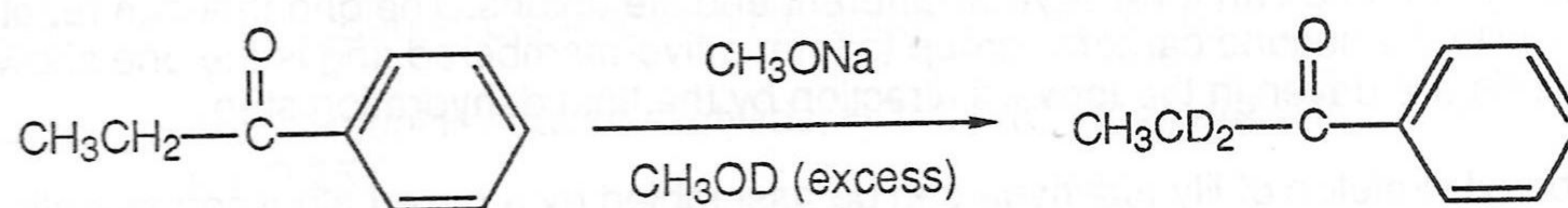
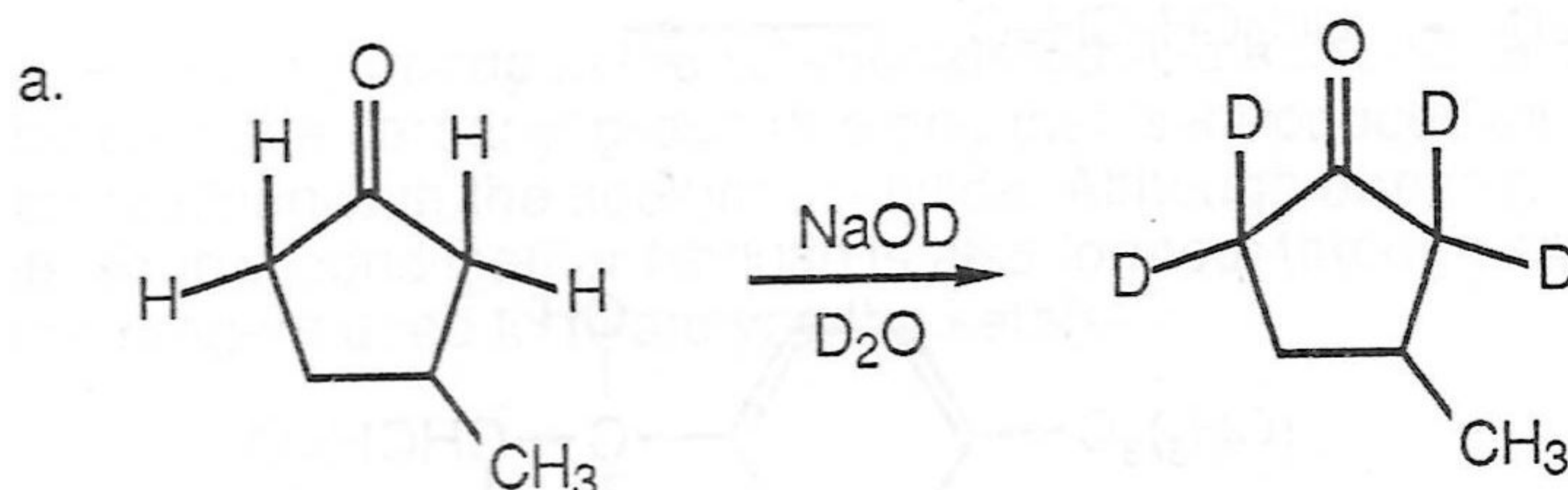
e. The carbonyl group is oxidized, while the carbon-carbon double bond is not.



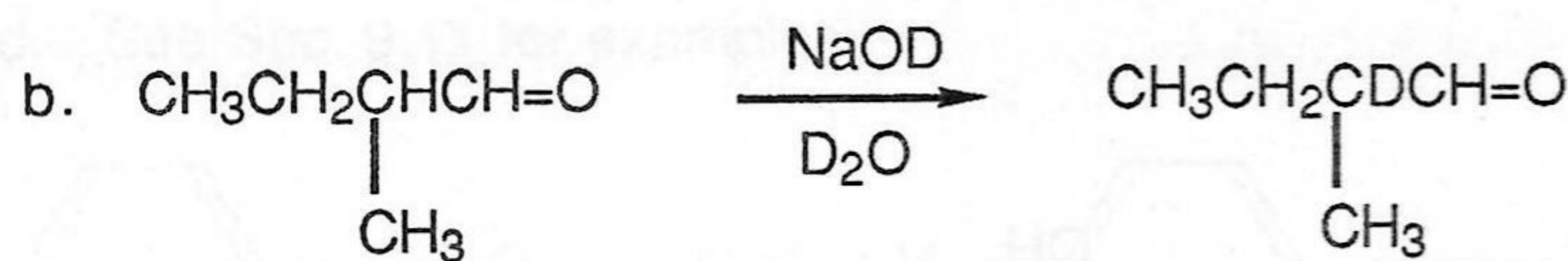
9.45 Review Sec. 9.14.



There are two types of α -hydrogens in 2-butanone, and either may enolize:

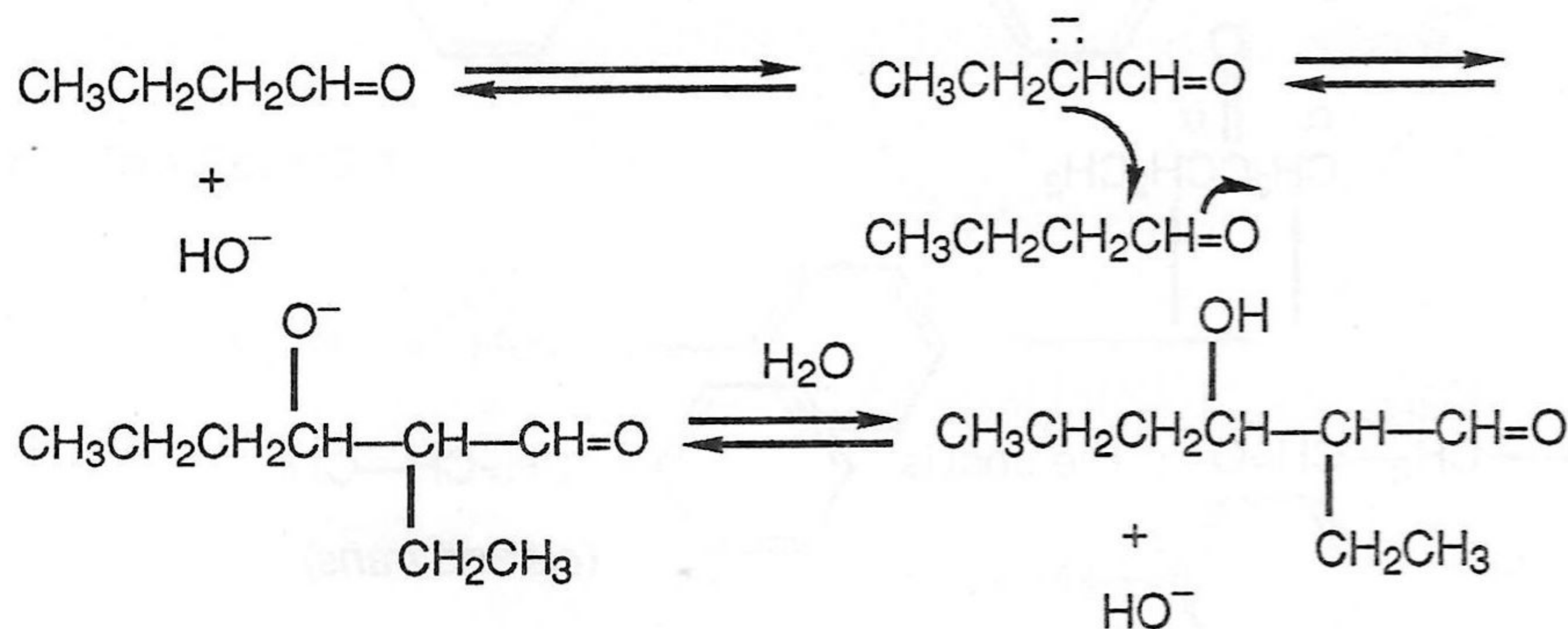
9.46 The α -hydrogens are exchanged for deuteriums:9.47 Review Sec. 9.16. Only hydrogens α to a carbonyl group will be replaced by deuterium.

Four hydrogens are replaced by deuterium.

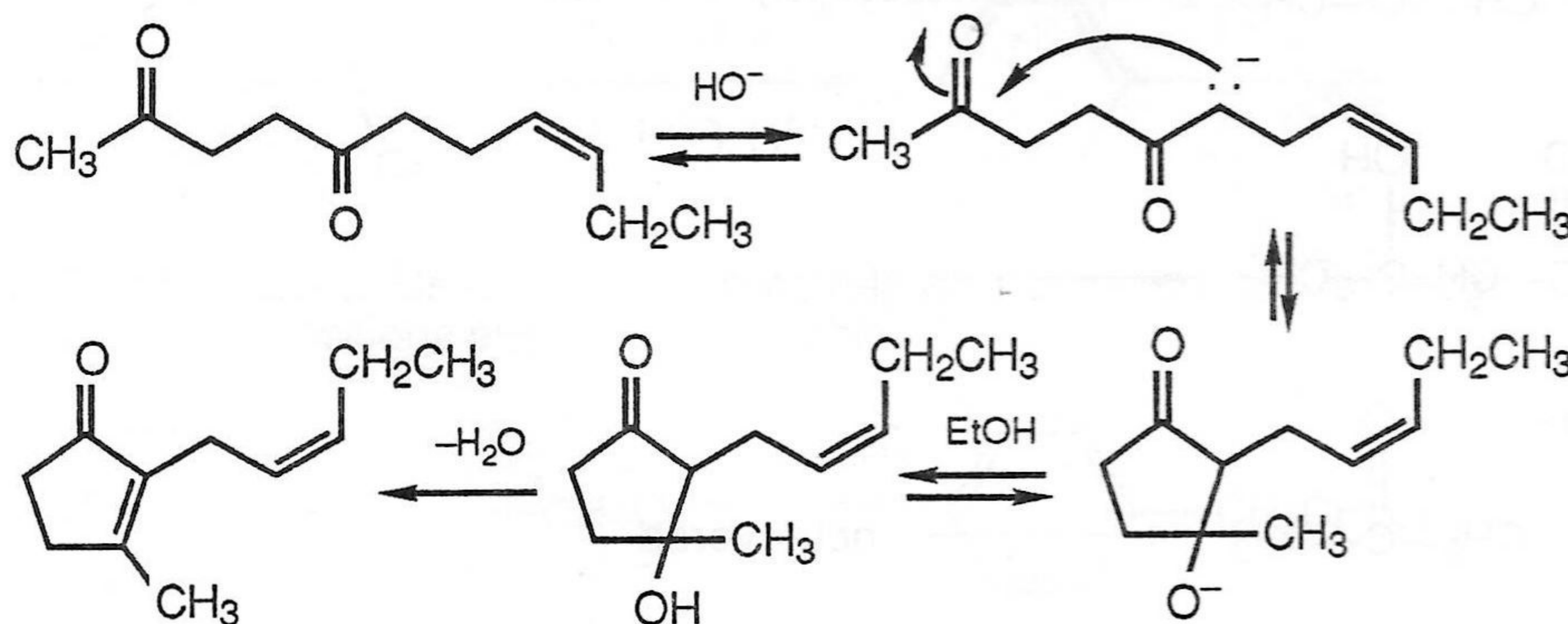


One hydrogen is replaced by deuterium.

9.48 Follow eqs. 9.51–9.53. The steps in the mechanism are as follows:

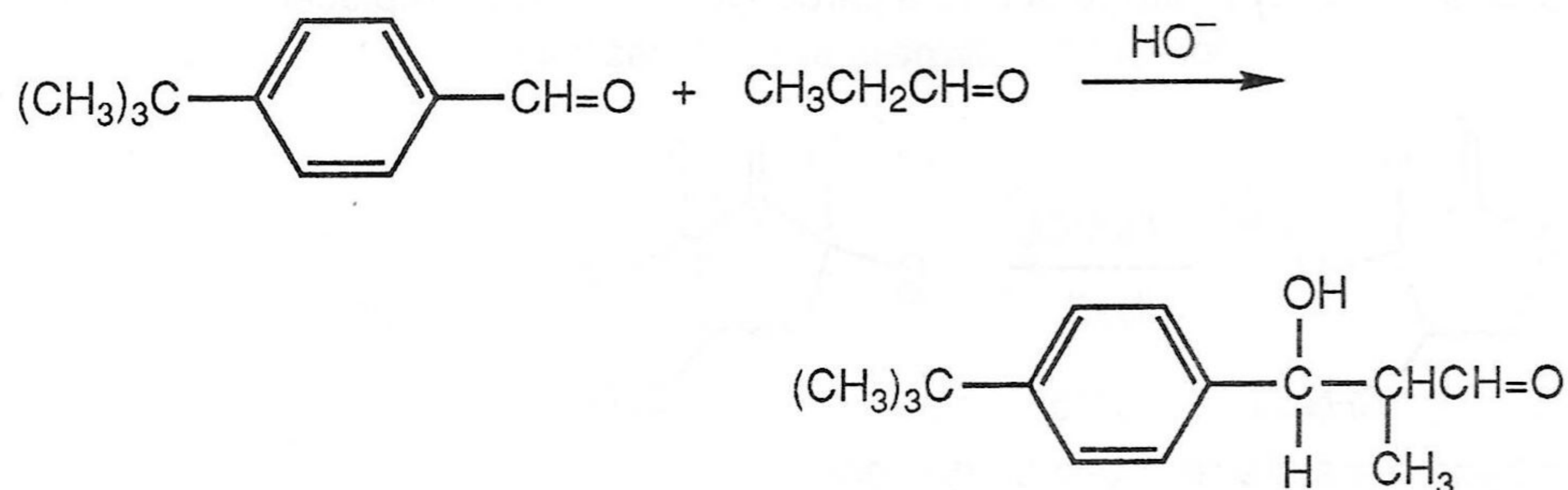


9.49 The reaction occurs by an *intramolecular* aldol condensation, followed by dehydration of the resulting aldol:

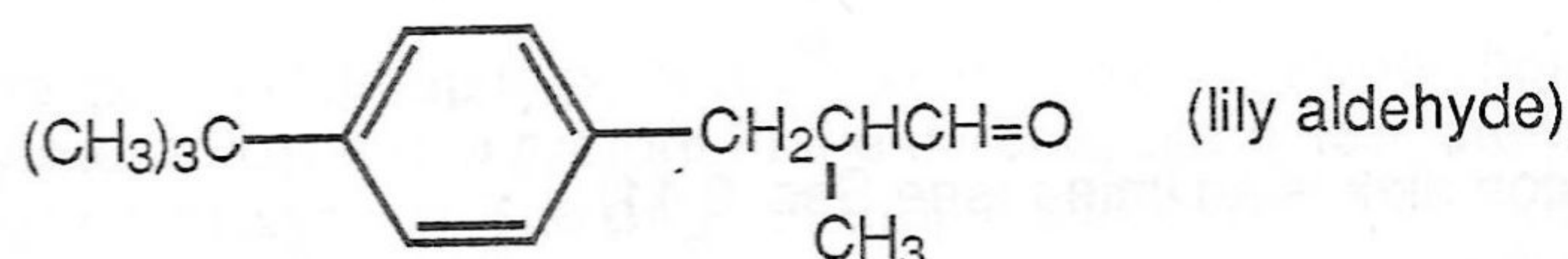
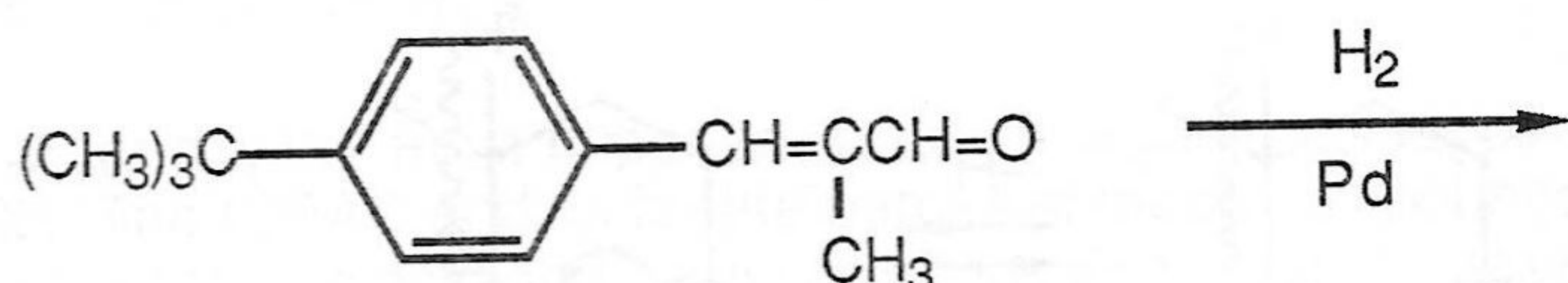
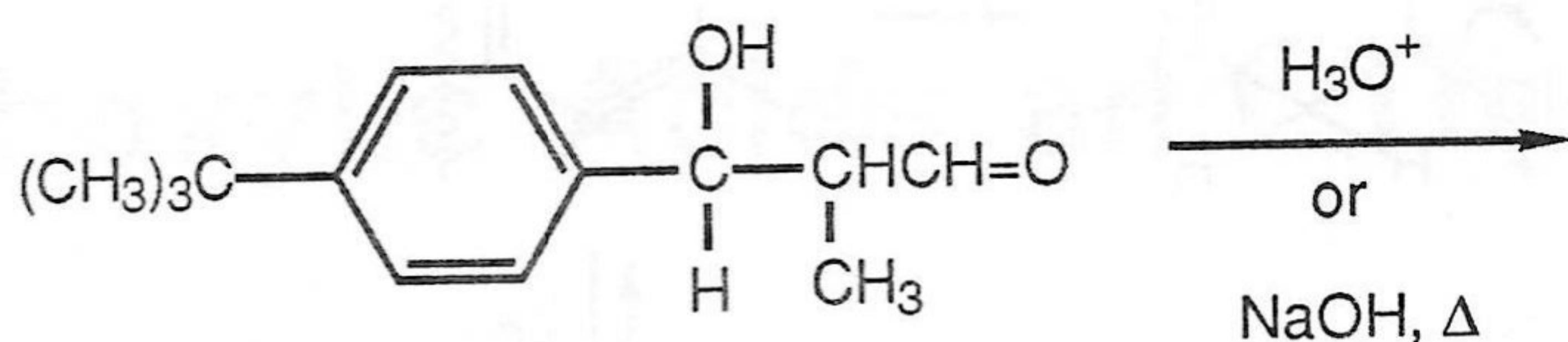


The starting diketone can form several different enolate anions. The one that can react most favorably with the second carbonyl group to form a five-membered ring is the one shown. All the equilibria are driven in the forward direction by the final dehydration step.

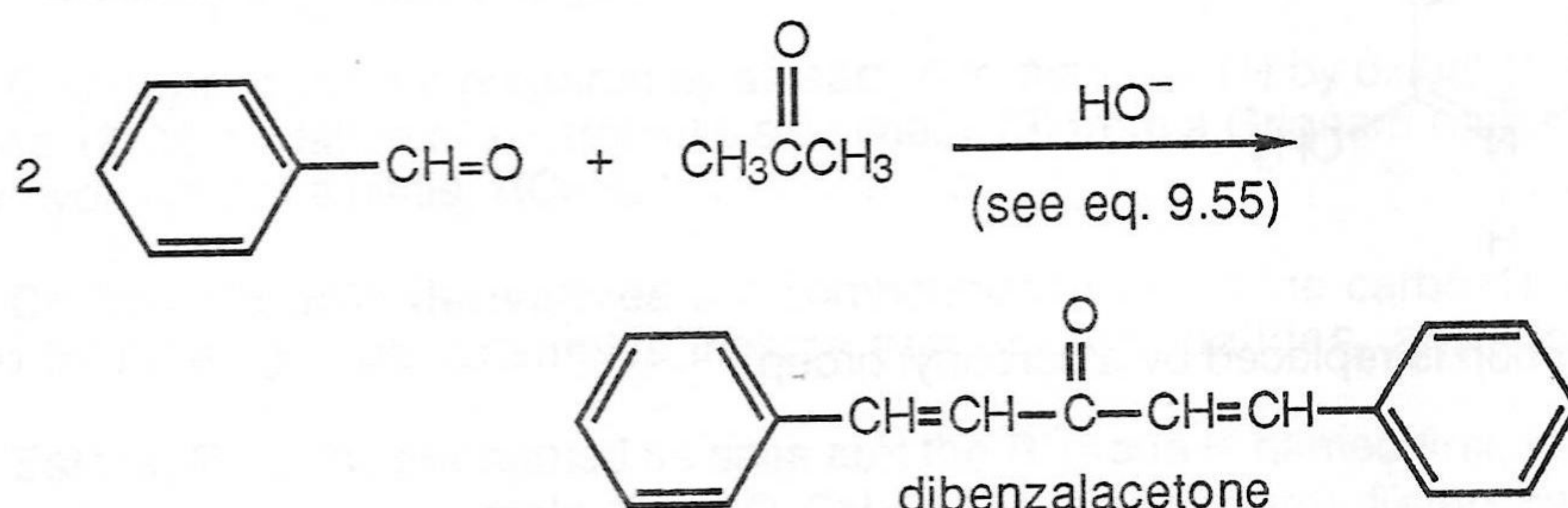
9.50 The carbonyl skeleton of lily aldehyde can be assembled by a mixed aldol condensation between propanal and the nonenolizable aldehyde, 4-*tert*-butylbenzaldehyde:



Dehydration and reduction of the carbon-carbon double bond completes the synthesis of lily aldehyde.



- 9.51 The product has 17 carbons, which suggests that it is formed from two benzaldehyde molecules ($2 \times 7 = 14$ carbons) + one acetone molecule (3 carbons). The product forms by a double mixed aldol condensation:



The product is yellow because of the extended conjugated system of double bonds.

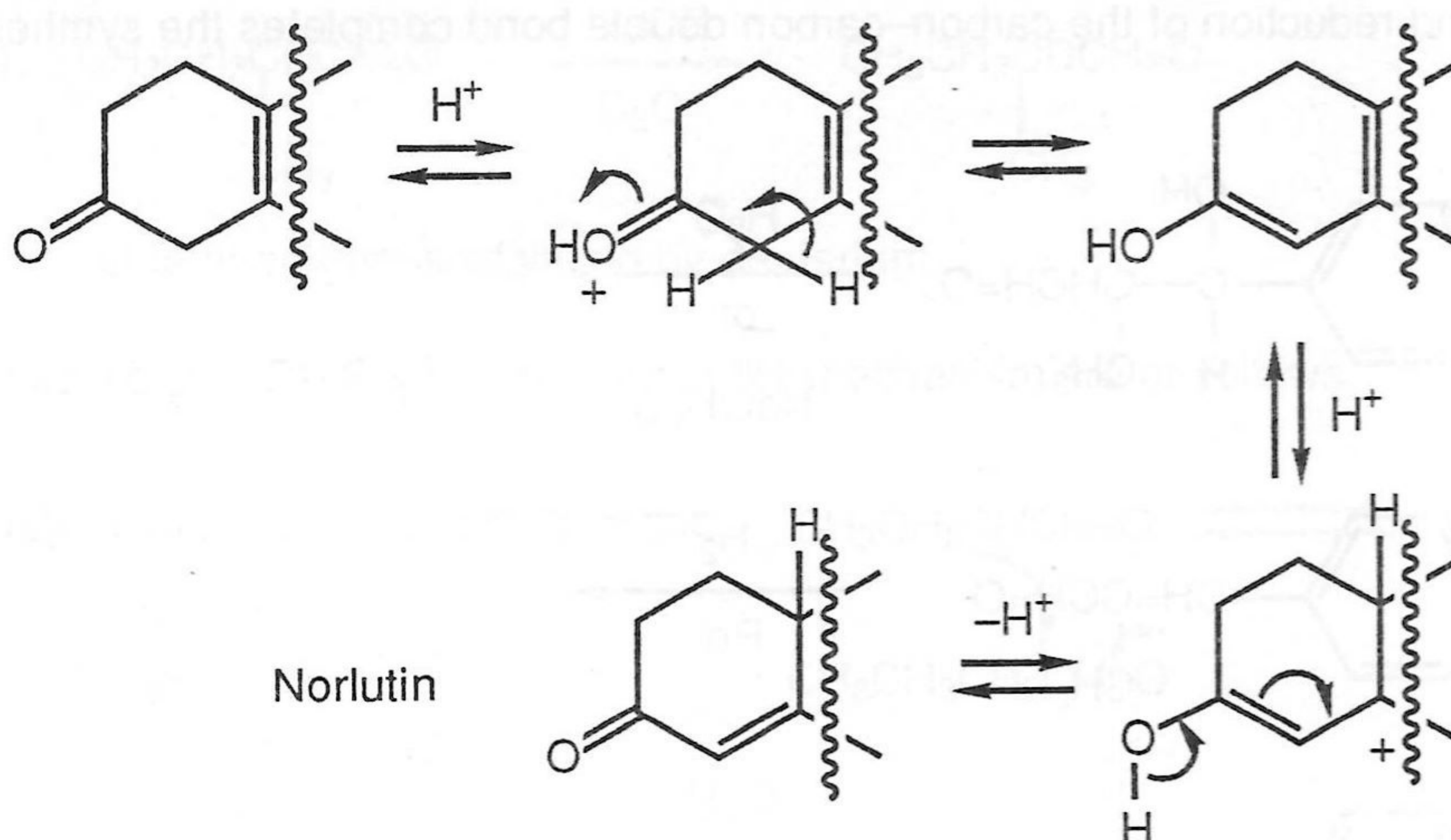
- 9.52 Step A: The reagents are ethylene glycol ($\text{HOCH}_2\text{CH}_2\text{OH}$) and H^+ (compare with eq. 9.16).

Step B: The reagent is chromic acid (compare with eq. 7.36).

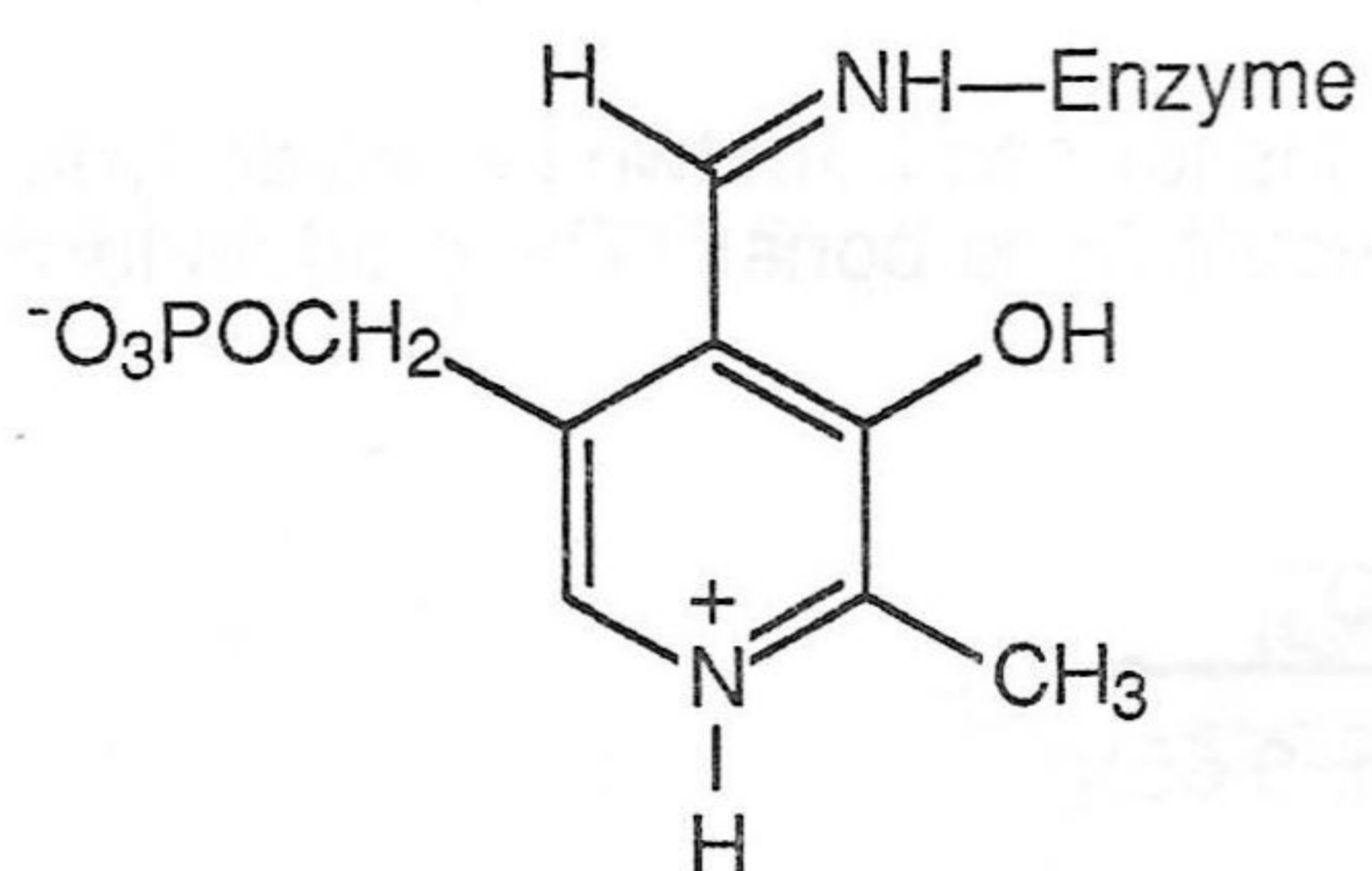
Step C: The reagent is sodium acetylide, $\text{HC}\equiv\text{C}^-\text{Na}^+$ (compare with eq. 9.26).

Step D: The reagent is dilute acid, to hydrolyze the ketal (compare with eq. 9.19).

The carbonyl group in the six-membered ring must be "protected" so that in step C there will be only one carbonyl group (the one that is introduced into the five-membered ring) available for reaction with the sodium acetylide. Although one might expect only Enovid to be formed, its double-bond isomer Norlutin is also formed, through an acid-catalyzed enolization (acid is the reagent used to hydrolyze the ketal):



9.53 a. The vitamin B₆-enzyme complex is an imine (see Sec. 9.11):



b. The amino group is replaced by a carbonyl group:

