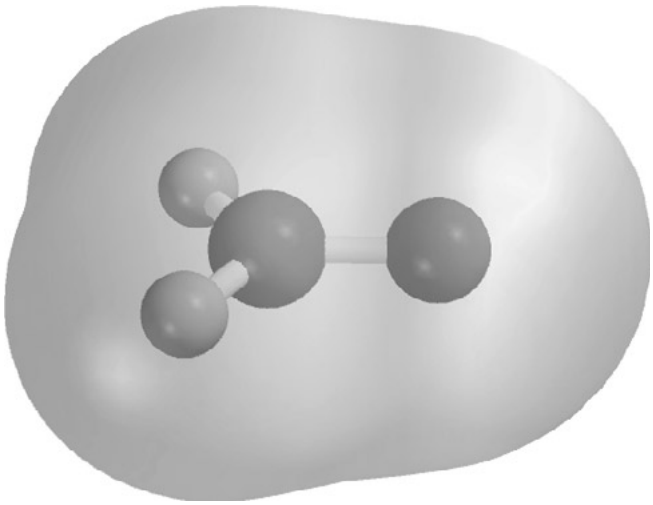
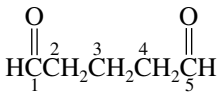


CHAPTER 17

ALDEHYDES AND KETONES: NUCLEOPHILIC ADDITION TO THE CARBONYL GROUP

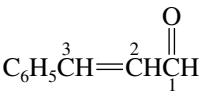
SOLUTIONS TO TEXT PROBLEMS

17.1 (*b*) The longest continuous chain in glutaraldehyde has five carbons and terminates in aldehyde functions at both ends. **Pentanedial** is an acceptable IUPAC name for this compound.



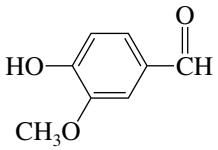
Pentanedial (glutaraldehyde)

(*c*) The three-carbon parent chain has a double bond between C-2 and C-3 and a phenyl substituent at C-3.



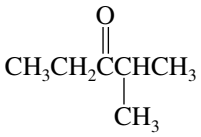
3-Phenyl-2-propenal
(cinnamaldehyde)

(*d*) Vanillin can be named as a derivative of benzaldehyde. Remember to cite the remaining substituents in alphabetical order.



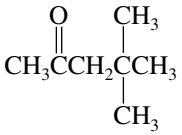
4-Hydroxy-3-methoxybenzaldehyde
(vanillin)

17.2 (*b*) First write the structure from the name given. Ethyl isopropyl ketone has an ethyl group and an isopropyl group bonded to a carbonyl group.



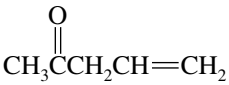
Ethyl isopropyl ketone may be alternatively named 2-methyl-3-pentanone. Its longest continuous chain has five carbons. The carbonyl carbon is C-3 irrespective of the direction in which the chain is numbered, and so we choose the direction that gives the lower number to the position that bears the methyl group.

(*c*) Methyl 2,2-dimethylpropyl ketone has a methyl group and a 2,2-dimethylpropyl group bonded to a carbonyl group.



The longest continuous chain has five carbons, and the carbonyl carbon is C-2. Thus, methyl 2,2-dimethylpropyl ketone may also be named 4,4-dimethyl-2-pentanone.

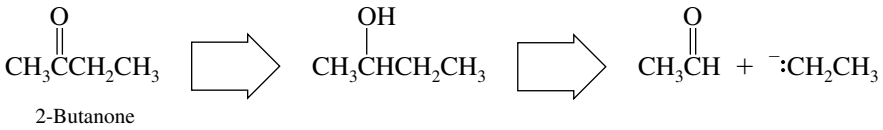
(*d*) The structure corresponding to allyl methyl ketone is



Because the carbonyl group is given the lowest possible number in the chain, the substitutive name is 4-penten-2-one *not* 1-penten-4-one.

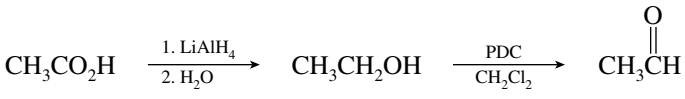
17.3 No. Lithium aluminum hydride is the only reagent we have discussed that is capable of reducing carboxylic acids (Section 15.3).

17.4 The target molecule, 2-butanone, contains four carbon atoms. The problem states that all of the carbons originate in acetic acid, which has two carbon atoms. This suggests the following disconnections:



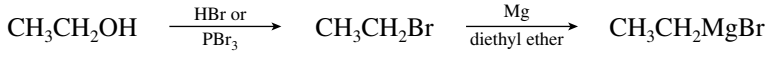
2-Butanone

The necessary aldehyde (acetaldehyde) is prepared from acetic acid by reduction followed by oxidation in an anhydrous medium.



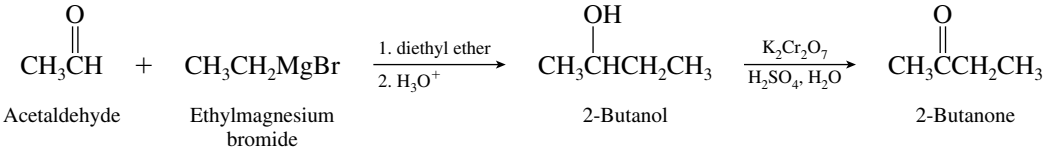
Acetic acid — Ethanol — Acetaldehyde

Ethylmagnesium bromide may be obtained from acetic acid by the following sequence:

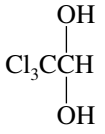


Ethanol (Prepared as previously) — Ethyl bromide — Ethylmagnesium bromide

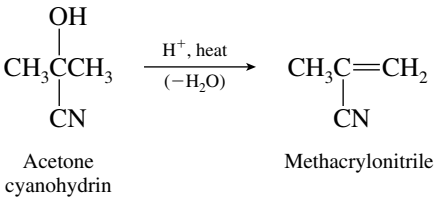
The preparation of 2-butanone is completed as follows:



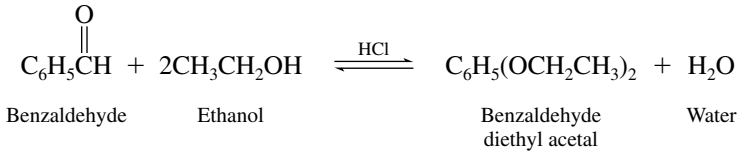
17.5 Chloral is trichloroethanal, CCl_3CH. Chloral hydrate is the addition product of chloral and water.



17.6 Methacrylonitrile is formed by the dehydration of acetone cyanohydrin, and thus has the structure shown.



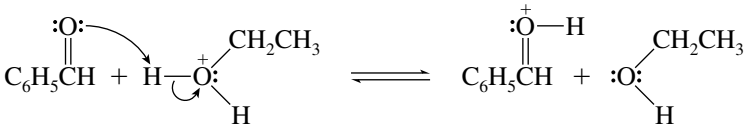
17.7 The overall reaction is



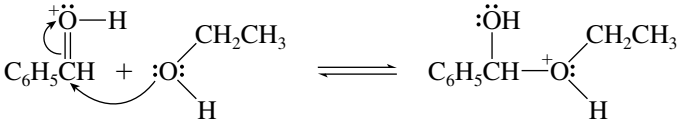
HCl is a strong acid and, when dissolved in ethanol, transfers a proton to ethanol to give ethyloxonium ion. Thus, we can represent the acid catalyst as the conjugate acid of ethanol.

The first three steps correspond to acid-catalyzed addition of ethanol to the carbonyl group to yield a hemiacetal.

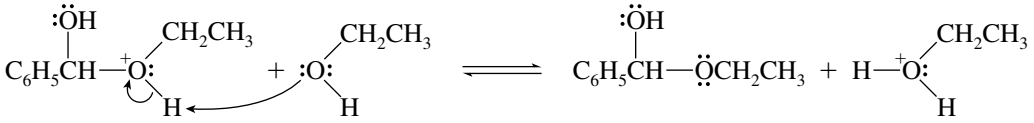
Step 1:



Step 2:



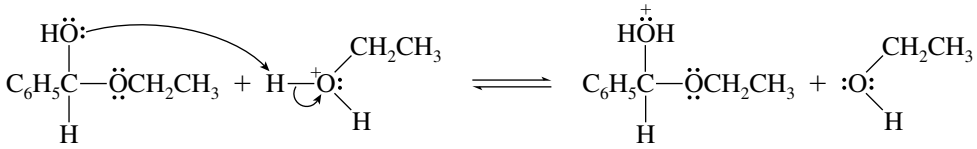
Step 3:



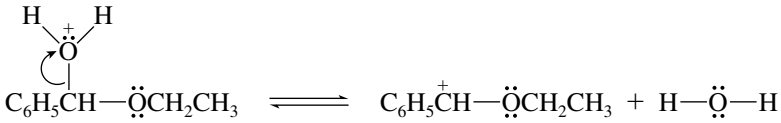
Hemiacetal

Formation of the hemiacetal is followed by loss of water to give a carbocation.

Step 4:

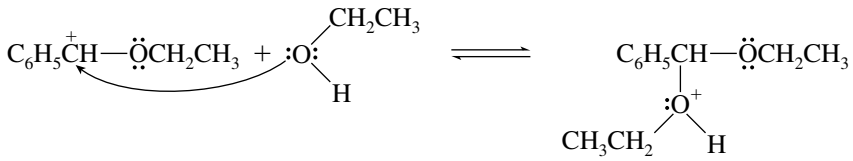


Step 5:

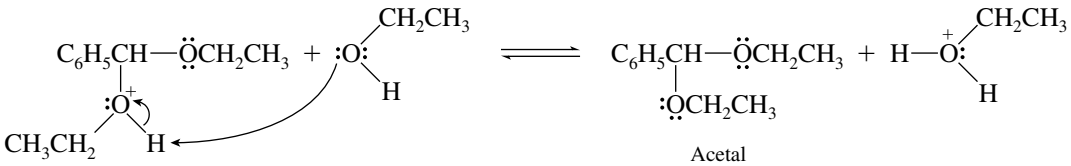


The next two steps describe the capture of the carbocation by ethanol to give the acetal:

Step 6:

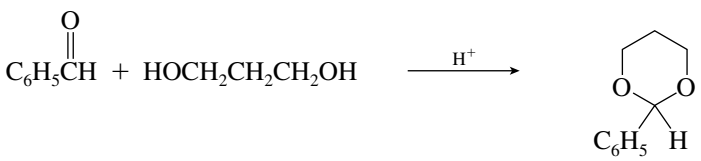


Step 7:



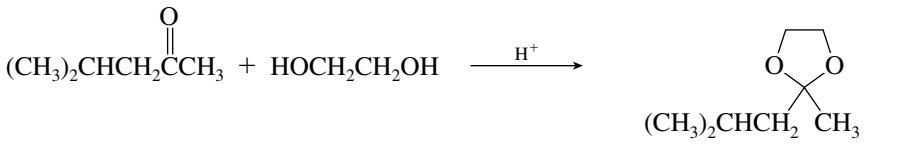
Acetal

17.8 (*b*) 1,3-Propanediol forms acetals that contain a six-membered 1,3-dioxane ring.



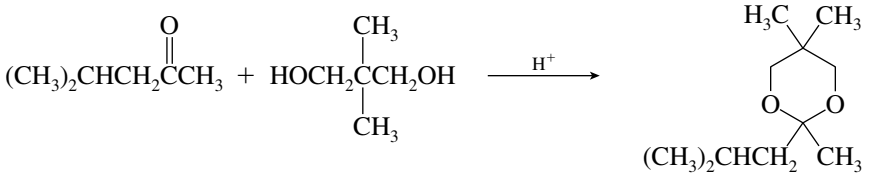
Benzaldehyde 1,3-Propanediol 2-Phenyl-1,3-dioxane

(*c*) The cyclic acetal derived from isobutyl methyl ketone and ethylene glycol bears an isobutyl group and a methyl group at C-2 of a 1,3-dioxolane ring.



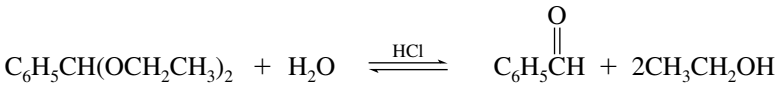
Isobutyl methyl ketone — Ethylene glycol — 2-Isobutyl-2-methyl-1,3-dioxolane

(*d*) Because the starting diol is 2,2-dimethyl-1,3-propanediol, the cyclic acetal is six-membered and bears two methyl substituents at C-5 in addition to isobutyl and methyl groups at C-2.



Isobutyl methyl ketone — 2,2-Dimethyl-1,3-propanediol — 2-Isobutyl-2,5,5-trimethyl-1,3-dioxane

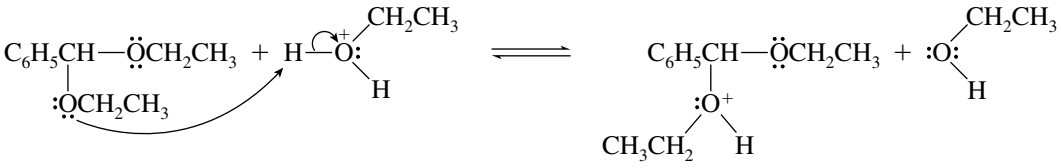
17.9 The overall reaction is



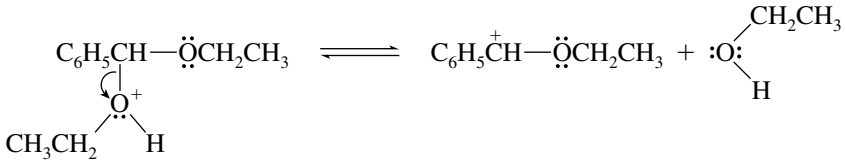
Benzaldehyde diethyl acetal — Water — Benzaldehyde — Ethanol

The mechanism of acetal hydrolysis is the reverse of acetal formation. The first four steps convert the acetal to the hemiacetal.

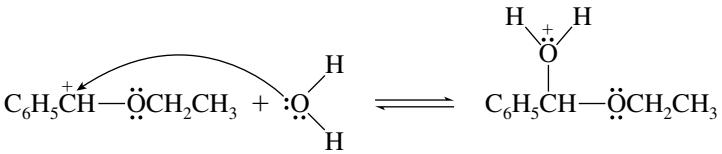
Step 1:



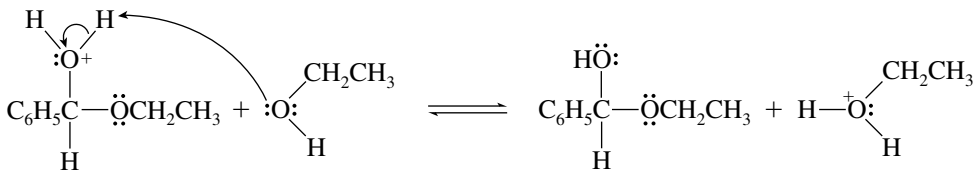
Step 2:



Step 3:

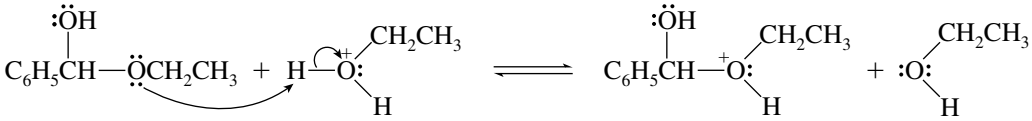


Step 4:

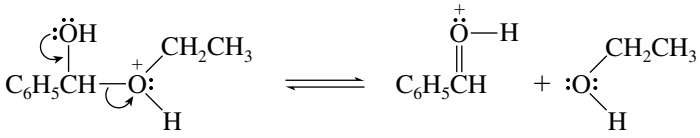


Hemiacetal

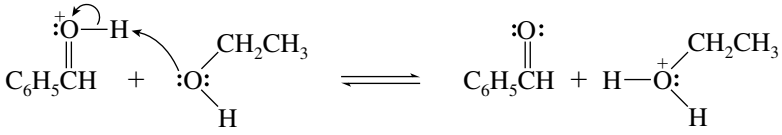
Step 5:



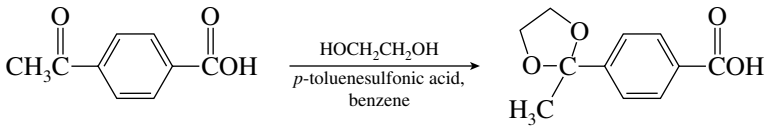
Step 6:



Step 7:

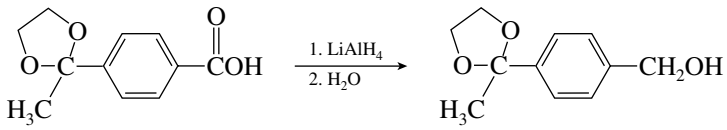


17.10 The conversion requires reduction; however, the conditions necessary ($LiAlH_4$) would also reduce the ketone carbonyl. The ketone functionality is therefore protected as the cyclic acetal.

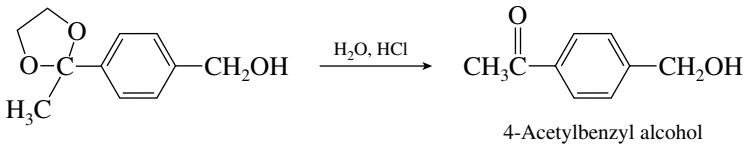


4-Acetylbenzoic acid

Reduction of the carboxylic acid may now be carried out.

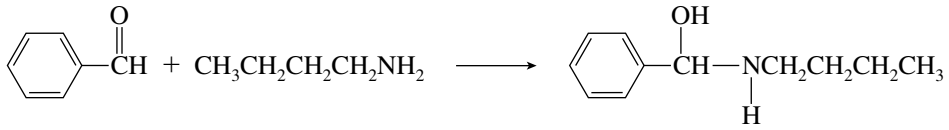


Hydrolysis to remove the protecting group completes the synthesis.



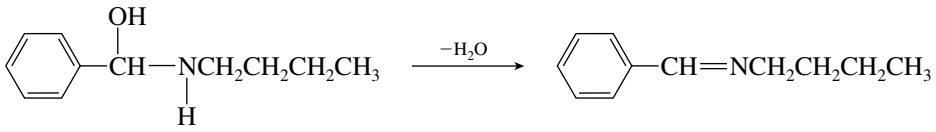
4-Acetylbenzyl alcohol

17.11 (*b*) Nucleophilic addition of butylamine to benzaldehyde gives the carbinolamine.



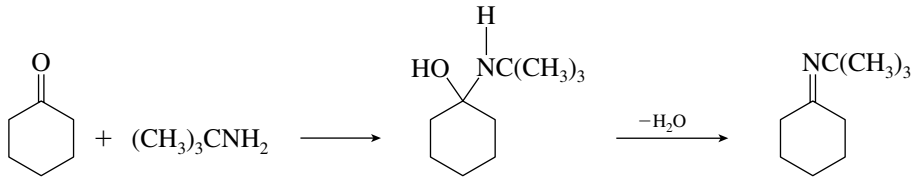
Benzaldehyde Butylamine Carbinolamine intermediate

Dehydration of the carbinolamine produces the imine.



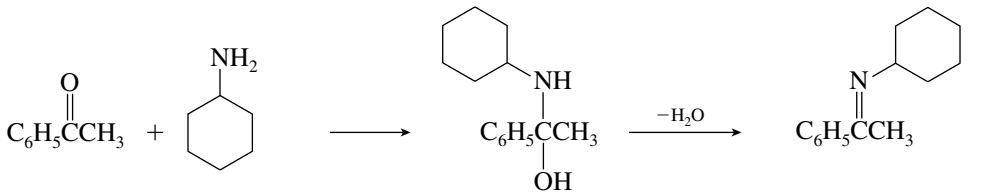
N-Benzylidenebutylamine

(*c*) Cyclohexanone and *tert*-butylamine react according to the equation



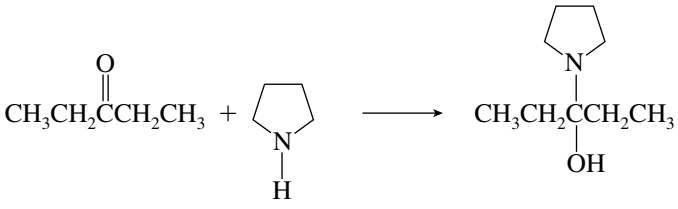
Cyclohexanone *tert*-Butylamine Carbinolamine intermediate *N*-Cyclohexylidene-*tert*-butylamine

(*d*)



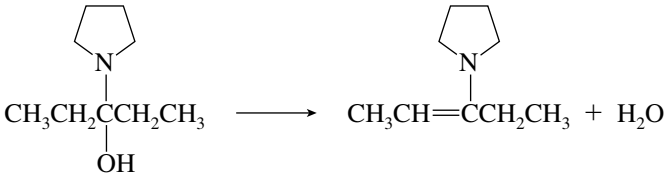
Acetophenone Cyclohexylamine Carbinolamine intermediate *N*-(1-Phenylethylidene)-cyclohexylamine

17.12 (*b*) Pyrrolidine, a secondary amine, adds to 3-pentanone to give a carbinolamine.



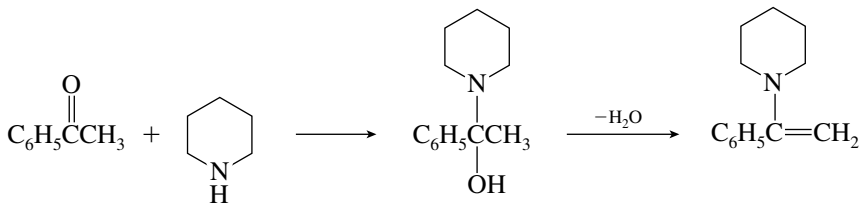
3-Pentanone Pyrrolidine Carbinolamine intermediate

Dehydration produces the enamine.



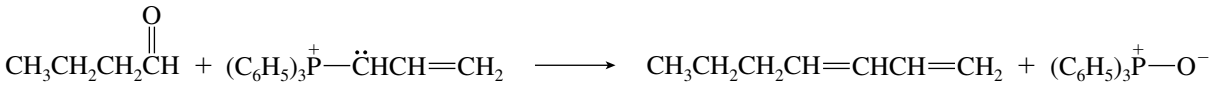
Carbinolamine intermediate 3-Pyrrolidino-2-pentene

(*c*)



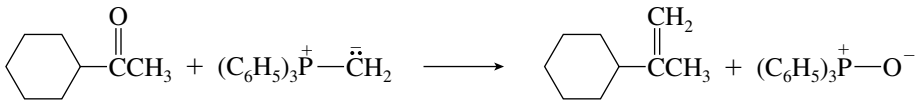
Acetophenone Piperidine Carbinolamine intermediate 1-Piperidino-1-phenylethene

17.13 (*b*) Here we see an example of the Wittig reaction applied to diene synthesis by use of an ylide containing a carbon–carbon double bond.



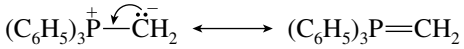
Butanal Allylidenetriphenylphosphorane 1,3-Heptadiene (52%) Triphenylphosphine oxide

(*c*) Methylene transfer from methylenetriphenylphosphorane is one of the most commonly used Wittig reactions.



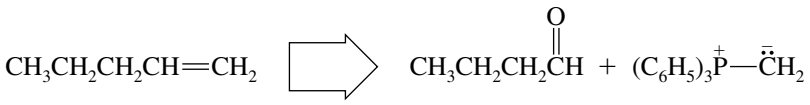
Cyclohexyl methyl ketone Methylenetriphenyl-phosphorane 2-Cyclohexylpropene (66%) Triphenylphosphine oxide

17.14 A second resonance structure can be written for a phosphorus ylide with a double bond between phosphorus and carbon. As a third-row element, phosphorus can have more than 8 electrons in its valence shell.



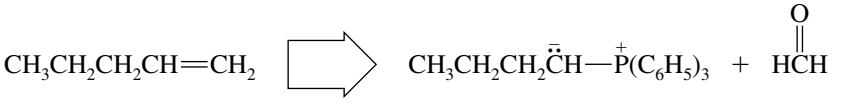
Methylenetriphenylphosphorane

17.15 (*b*) Two Wittig reaction routes lead to 1-pentene. One is represented retrosynthetically by the disconnection



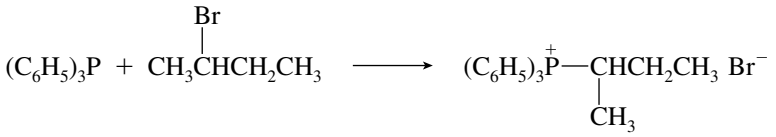
1-Pentene Butanal Methylenetriphenyl-phosphorane

The other route is

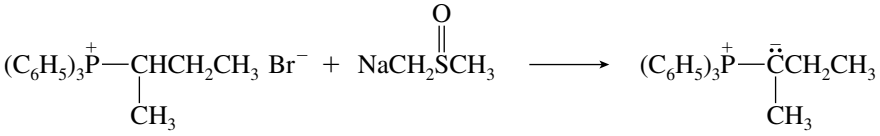


1-Pentene Butylidenetriphenylphosphorane Formaldehyde

17.16 Ylides are prepared by the reaction of an alkyl halide with triphenylphosphine, followed by treatment with strong base. 2-Bromobutane is the alkyl halide needed in this case.

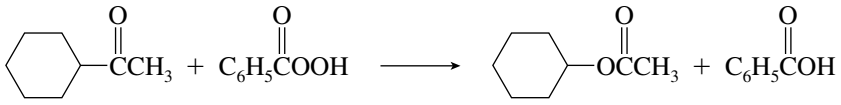


Triphenylphosphine — 2-Bromobutane — (1-Methylpropyl)triphenylphosphonium bromide



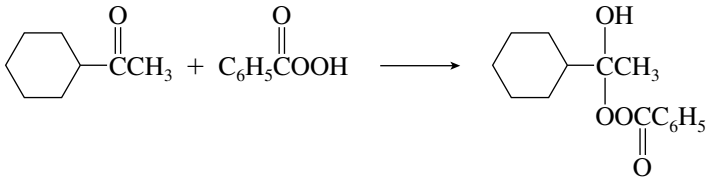
(1-Methylpropyl)triphenylphosphonium bromide — Sodiomethyl methyl sulfoxide — Ylide

17.17 The overall reaction is



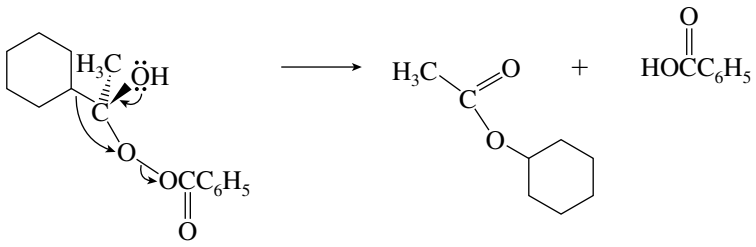
Cyclohexyl methyl ketone — Peroxybenzoic acid — Cyclohexyl acetate — Benzoic acid

In the first step, the peroxy acid adds to the carbonyl group of the ketone to form a peroxy monoester of a *gem*-diol.

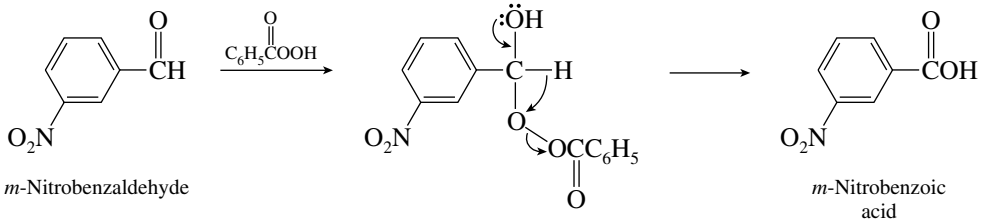


Peroxy monoester

The intermediate then undergoes rearrangement. Alkyl group migration occurs at the same time as cleavage of the O—O bond of the peroxy ester. In general, the more substituted group migrates.

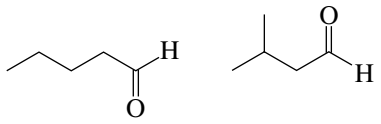


17.18 The formation of a carboxylic acid from Baeyer–Villiger oxidation of an aldehyde requires hydrogen migration.

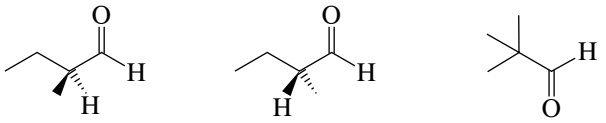


m-Nitrobenzaldehyde — *m*-Nitrobenzoic acid

17.19 (*a*) First consider all the isomeric aldehydes of molecular formula $C_5H_{10}O$.

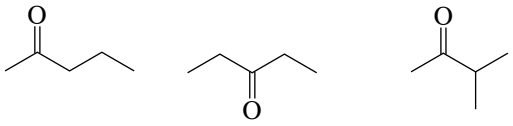


Pentanal 3-Methylbutanal



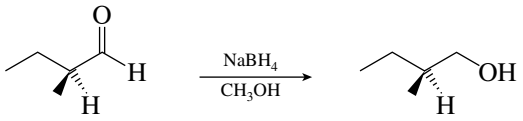
(*S*)-2-Methylbutanal (*R*)-2-Methylbutanal 2,2-Dimethylpropanal

There are three isomeric ketones:

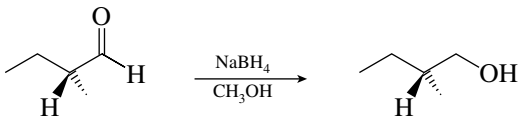


2-Pentanone 3-Pentanone 3-Methyl-2-butanone

(*b*) Reduction of an aldehyde to a primary alcohol does not introduce a stereogenic center into the molecule. The only aldehydes that yield chiral alcohols on reduction are therefore those that already contain a stereogenic center.

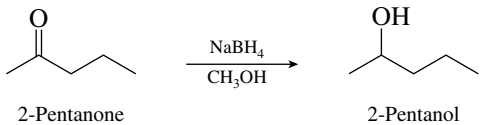


(*S*)-2-Methylbutanal (*S*)-2-Methyl-1-butanol

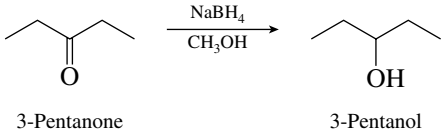


(*R*)-2-Methylbutanal (*R*)-2-Methyl-1-butanol

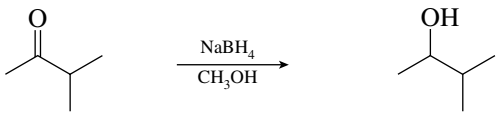
Among the ketones, 2-pentanone and 3-methyl-butanone are reduced to chiral alcohols.



2-Pentanone 2-Pentanol (chiral but racemic)

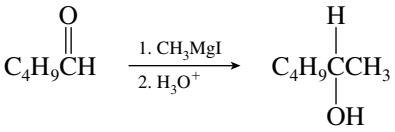


3-Pentanone 3-Pentanol (achiral)

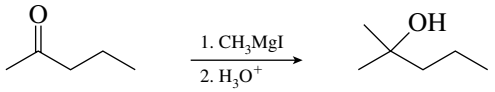


3-Methyl-2-butanone 3-Methyl-2-butanol (chiral but racemic)

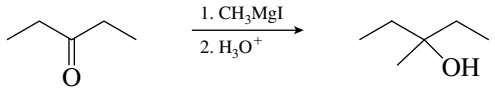
(*c*) All the aldehydes yield chiral alcohols on reaction with methylmagnesium iodide. Thus,



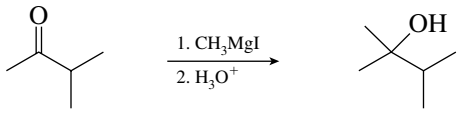
A stereogenic center is introduced in each case. None of the ketones yield chiral alcohols.



2-Pentanone — 2-Methyl-2-pentanol (achiral)

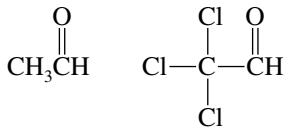


3-Pentanone — 3-Methyl-3-pentanol (achiral)



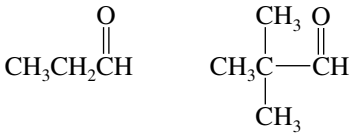
3-Methyl-2-butanone — 2,3-Dimethyl-2-butanol (achiral)

17.20 (*a*) Chloral is the trichloro derivative of ethanal (acetaldehyde).



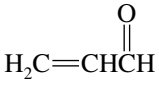
Ethanal — Trichloroethanal (chloral)

(*b*) Pivaldehyde has two methyl groups attached to C-2 of propanal.



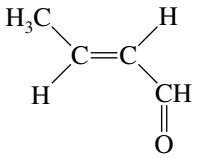
Propanal — 2,2-Dimethylpropanal (pivaldehyde)

(*c*) Acrolein has a double bond between C-2 and C-3 of a three-carbon aldehyde.



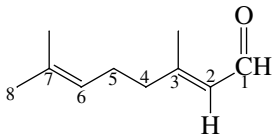
2-Propenal (acrolein)

(*d*) Crotonaldehyde has a trans double bond between C-2 and C-3 of a four-carbon aldehyde.



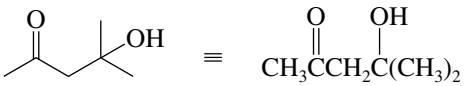
(*E*)-2-Butenal
(crotonaldehyde)

(*e*) Citral has two double bonds: one between C-2 and C-3 and the other between C-6 and C-7. The one at C-2 has the *E* configuration. There are methyl substituents at C-3 and C-7.



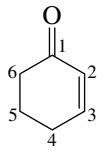
(*E*)-3,7-Dimethyl-2,6-octadienal
(citral)

(*f*) Diacetone alcohol is



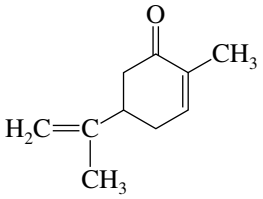
4-Hydroxy-4-methyl-
2-pentanone

(*g*) The parent ketone is 2-cyclohexenone.



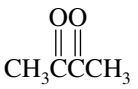
2-Cyclohexenone

Carvone has an isopropenyl group at C-5 and a methyl group at C-2.



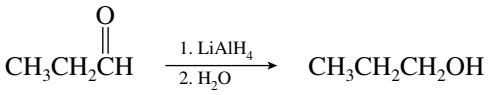
5-Isopropenyl-2-methyl-2-
cyclohexenone (carvone)

(*h*) Biacetyl is 2,3-butanedione. It has a four-carbon chain that incorporates ketone carbonyls as C-2 and C-3.



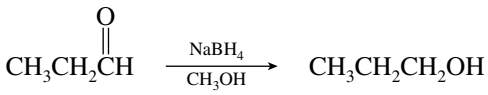
2,3-Butanedione
(biacetyl)

17.21 (*a*) Lithium aluminum hydride reduces aldehydes to primary alcohols.



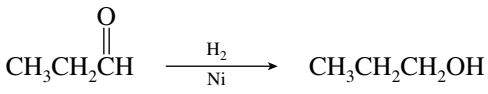
Propanal 1-Propanol

(*b*) Sodium borohydride reduces aldehydes to primary alcohols.



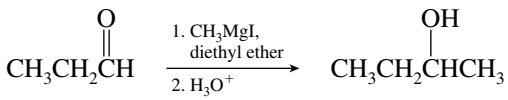
Propanal 1-Propanol

(*c*) Aldehydes can be reduced to primary alcohols by catalytic hydrogenation.



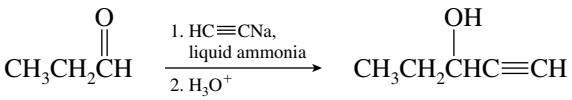
Propanal 1-Propanol

(*d*) Aldehydes react with Grignard reagents to form secondary alcohols.



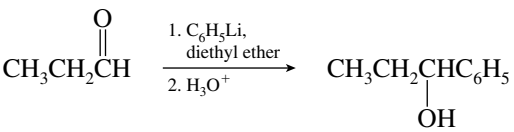
Propanal 2-Butanol

(*e*) Sodium acetylide adds to the carbonyl group of propanal to give an acetylenic alcohol.



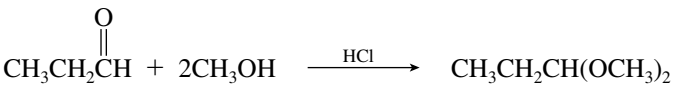
Propanal 1-Pentyn-3-ol

(*f*) Alkyl- or aryllithium reagents react with aldehydes in much the same way that Grignard reagents do.



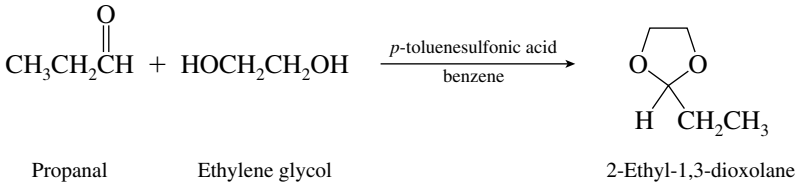
Propanal 1-Phenyl-1-propanol

(*g*) Aldehydes are converted to acetals on reaction with alcohols in the presence of an acid catalyst.



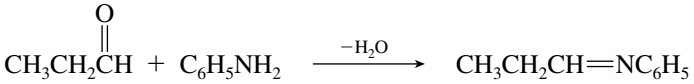
Propanal Methanol Propanal dimethyl acetal

(*h*) Cyclic acetal formation occurs when aldehydes react with ethylene glycol.



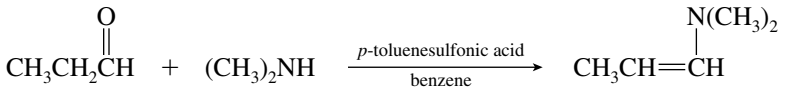
Propanal Ethylene glycol 2-Ethyl-1,3-dioxolane

(*i*) Aldehydes react with primary amines to yield imines.



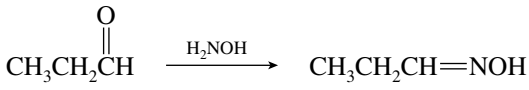
Propanal Aniline *N*-Propylideneaniline

(*j*) Secondary amines combine with aldehydes to yield enamines.



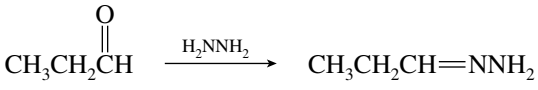
Propanal Dimethylamine 1-(Dimethylamino)propene

(*k*) Oximes are formed on reaction of hydroxylamine with aldehydes.



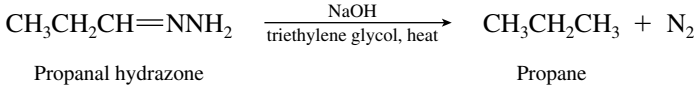
Propanal Propanal oxime

(*l*) Hydrazine reacts with aldehydes to form hydrazones.



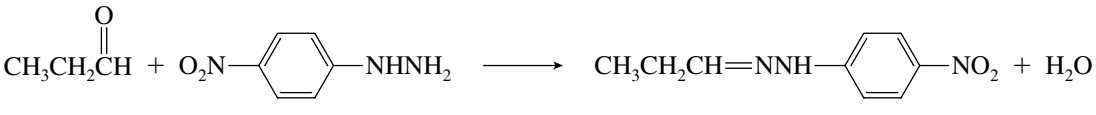
Propanal Propanal hydrazone

(*m*) Hydrazone formation is the first step in the Wolff–Kishner reduction (Section 12.8).



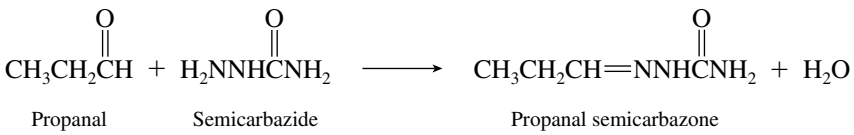
Propanal hydrazone Propane

(*n*) The reaction of an aldehyde with *p*-nitrophenylhydrazine is analogous to that with hydrazine.

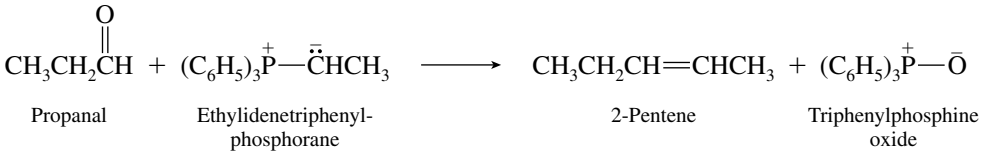


Propanal *p*-Nitrophenylhydrazine Propanal *p*-nitrophenylhydrazone

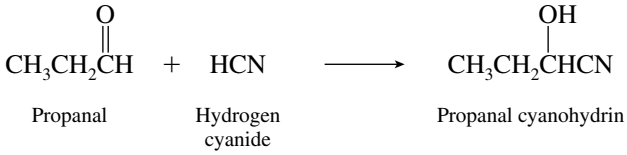
(*o*) Semicarbazide converts aldehydes to the corresponding semicarbazone.



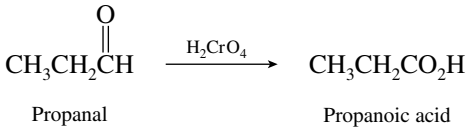
(*p*) Phosphorus ylides convert aldehydes to alkenes by a Wittig reaction.



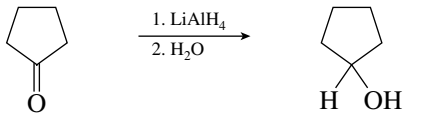
(*q*) Acidification of solutions of sodium cyanide generates HCN, which reacts with aldehydes to form cyanohydrins.



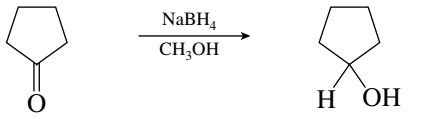
(*r*) Chromic acid oxidizes aldehydes to carboxylic acids.



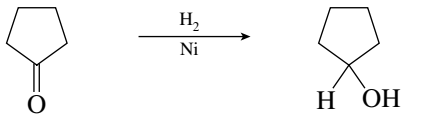
17.22 (*a*) Lithium aluminum hydride reduces ketones to secondary alcohols.



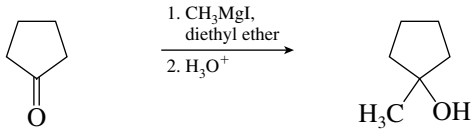
(*b*) Sodium borohydride converts ketones to secondary alcohols.



(*c*) Catalytic hydrogenation of ketones yields secondary alcohols.

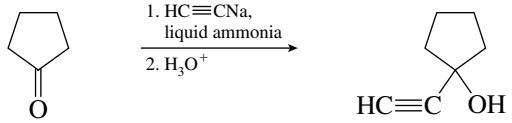


(*d*) Grignard reagents react with ketones to form tertiary alcohols.



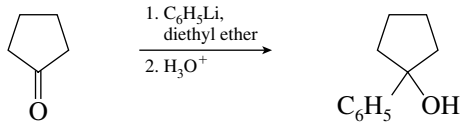
Cyclopentanone 1-Methylcyclopentanol

(*e*) Addition of sodium acetylide to cyclopentanone yields a tertiary acetylenic alcohol.



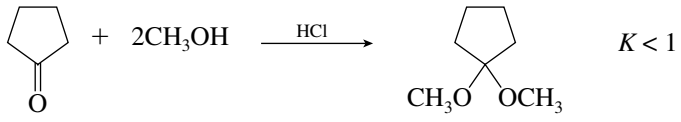
Cyclopentanone 1-Ethynylcyclopentanol

(*f*) Phenyllithium adds to the carbonyl group of cyclopentanone to yield 1-phenylcyclopentanol.



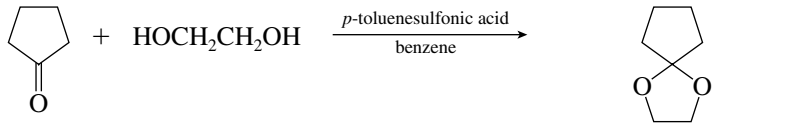
Cyclopentanone 1-Phenylcyclopentanol

(*g*) The equilibrium constant for acetal formation from ketones is generally unfavorable.



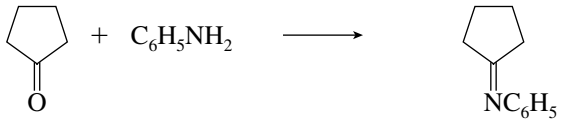
Cyclopentanone Methanol Cyclopentanone dimethyl acetal

(*h*) Cyclic acetal formation is favored even for ketones.



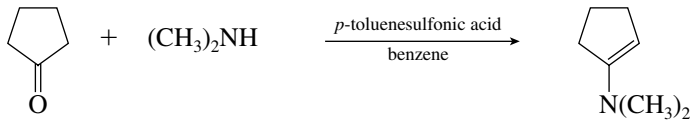
Cyclopentanone Ethylene glycol 1,4-Dioxaspiro[4.4]nonane

(*i*) Ketones react with primary amines to form imines.



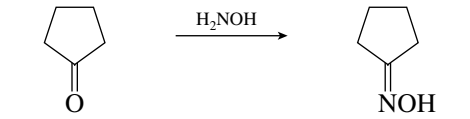
Cyclopentanone Aniline *N*-Cyclopentylideneaniline

(*j*) Dimethylamine reacts with cyclopentanone to yield an enamine.



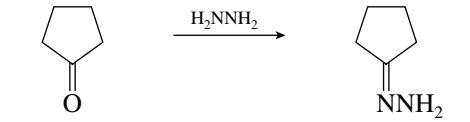
Cyclopentanone Dimethylamine 1-(Dimethylamino)-cyclopentene

(*k*) An oxime is formed when cyclopentanone is treated with hydroxylamine.



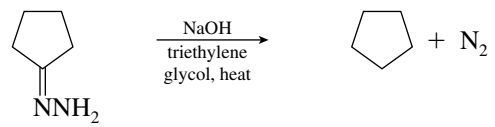
Cyclopentanone — Cyclopentanone oxime

(*l*) Hydrazine reacts with cyclopentanone to form a hydrazone.



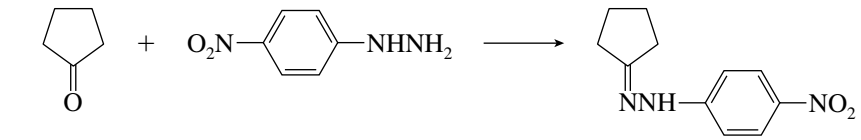
Cyclopentanone — Cyclopentanone hydrazone

(*m*) Heating a hydrazone in base with a high-boiling alcohol as solvent converts it to an alkane.



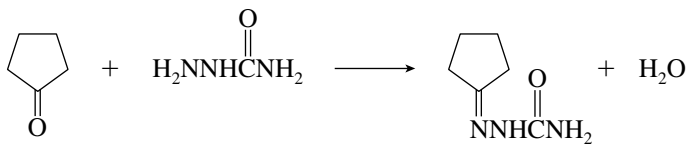
Cyclopentanone hydrazone — Cyclopentane

(*n*) A *p*-nitrophenylhydrazone is formed.



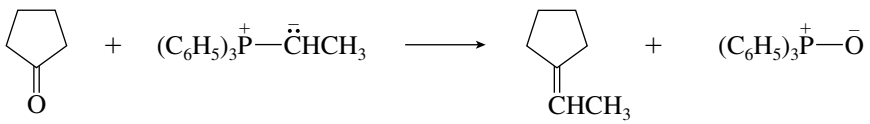
Cyclopentanone — *p*-Nitrophenylhydrazine — Cyclopentanone *p*-nitrophenylhydrazone

(*o*) Cyclopentanone is converted to a semicarbazone on reaction with semicarbazide.



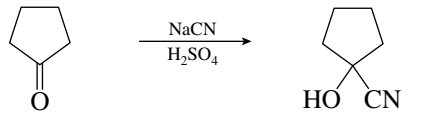
Cyclopentanone — Semicarbazide — Cyclopentanone semicarbazone

(*p*) A Wittig reaction takes place, forming ethylidenecyclopentane.



Cyclopentanone — Ethylidenetriphenyl-phosphorane — Ethylidenecyclo-pentane — Triphenylphosphine oxide

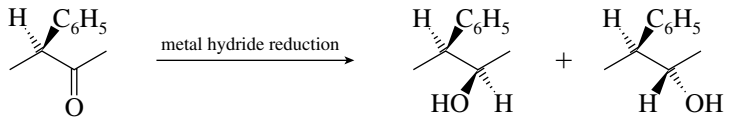
(*q*) Cyanohydrin formation takes place.



Cyclopentanone — Cyclopentanone cyanohydrin

(*r*) Cyclopentanone is not oxidized readily with chromic acid.

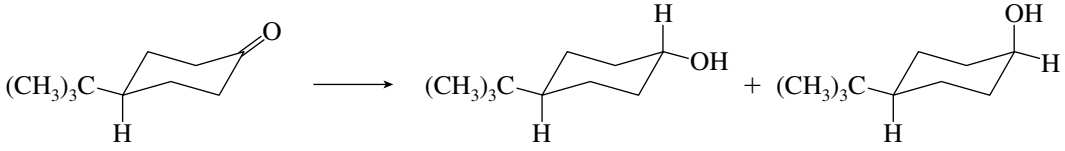
17.23 (*a*) The first step in analyzing this problem is to write the structure of the starting ketone in stereochemical detail.



(*S*)-3-Phenyl-2-butanone — (2*R*,3*S*)-3-Phenyl-2-butanol — (2*S*,3*S*)-3-Phenyl-2-butanol

Reduction of the ketone introduces a new stereogenic center, which may have either the *R* or the *S* configuration; the configuration of the original stereogenic center is unaffected. In practice the 2*R*,3*S* diastereomer is observed to form in greater amounts than the 2*S*,3*S* (ratio 2.5:1 for $LiAlH_4$ reduction).

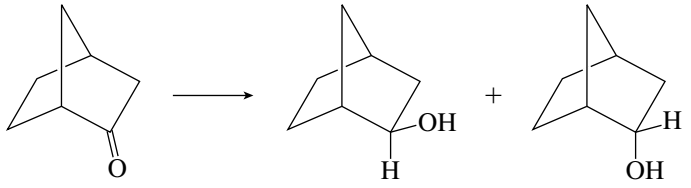
(*b*) Reduction of the ketone can yield either *cis*- or *trans*-4-*tert*-butylcyclohexanol.



4-*tert*-Butylcyclohexanone — *trans*-4-*tert*-Butylcyclohexanol — *cis*-4-*tert*-Butylcyclohexanol

It has been observed that the major product obtained on reduction with either lithium aluminum hydride or sodium borohydride is the trans alcohol (trans/cis ≈9:1).

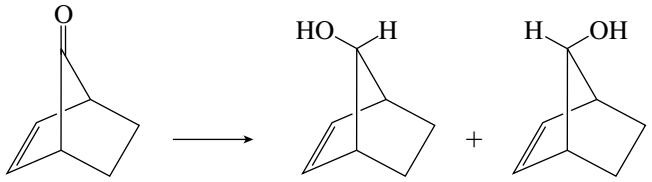
(*c*) The two reduction products are the exo and endo alcohols.



Bicyclo[2.2.1]-heptan-2-one — *exo*-Bicyclo[2.2.1]-heptan-2-ol — *endo*-Bicyclo[2.2.1]-heptan-2-ol

The major product is observed to be the endo alcohol (endo/exo 9:1) for reduction with $NaBH_4$ or $LiAlH_4$. The stereoselectivity observed in this reaction is due to decreased steric hindrance to attack of the hydride reagent from the exo face of the molecule, giving rise to the endo alcohol.

(*d*) The hydroxyl group may be on the same side as the double bond or on the opposite side.



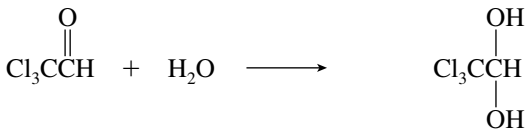
Bicyclo[2.2.1]-hept-2-en-7-one | *syn*-Bicyclo[2.2.1]-hept-2-en-7-ol | *anti*-Bicyclo[2.2.1]-hept-2-en-7-ol

The anti alcohol is observed to be formed in greater amounts (85:15) on reduction of the ketone with $LiAlH_4$. Steric factors governing attack of the hydride reagent again explain the major product observed.

17.24 (*a*) Aldehydes undergo nucleophilic addition faster than ketones. Steric crowding in the rate-determining step of the ketone reaction raises the energy of the transition state, giving rise to a slower rate of reaction. Thus benzaldehyde is reduced by sodium borohydride more rapidly than is acetophenone. The measured relative rates are

$$k_{rel} = \frac{C_6H_5\overset{\displaystyle O}{\overset{\|}{C}}H}{C_6H_5\overset{\displaystyle O}{\overset{\|}{C}}CH_3} = 440$$

(*b*) The presence of an electronegative substituent on the α-carbon atom causes a dramatic increase in K_{hydr}. Trichloroethanal (chloral) is almost completely converted to its geminal diol (chloral hydrate) in aqueous solution.



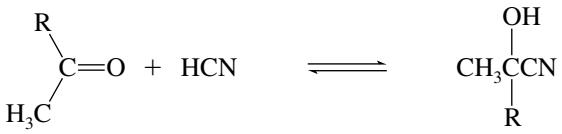
Trichloroethanal (chloral) | 2,2,2-Trichloro-1,1-ethanediol (chloral hydrate)

Electron-withdrawing groups such as Cl_3C destabilize carbonyl groups to which they are attached and make the energy change favoring the products of nucleophilic addition more favorable.

$$K_{rel} = \frac{Cl_3C\overset{\displaystyle O}{\overset{\|}{C}}H}{CH_3\overset{\displaystyle O}{\overset{\|}{C}}H} \approx 20{,}000$$

(*c*) Recall that the equilibrium constants for nucleophilic addition to carbonyl groups are governed by a combination of electronic effects and steric effects. Electronically there is little difference between acetone and 3,3-dimethyl-2-butanone, but sterically there is a significant difference. The cyanohydrin products are more crowded than the starting ketones, and so the

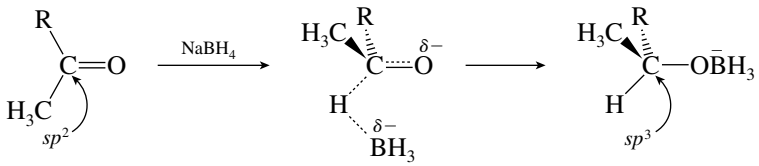
bulkier the alkyl groups that are attached to the carbonyl, the more strained and less stable will be the cyanohydrin.



Ketone — Hydrogen cyanide — Cyanohydrin [less strained for R = CH_3 than for R = $C(CH_3)_3$]

$$K_{rel} = \frac{CH_3CCH_3}{CH_3CC(CH_3)_3} = 40$$

(*d*) Steric effects influence the rate of nucleophilic addition to these two ketones. Carbon is on its way from tricoordinate to tetracoordinate at the transition state, and alkyl groups are forced closer together than they are in the ketone.

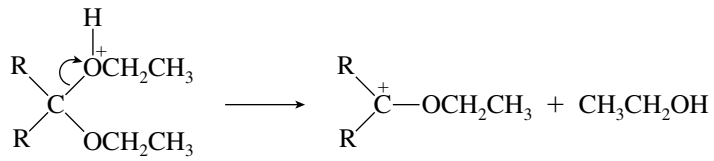


Transition state

The transition state is of lower energy when R is smaller. Acetone (for which R is methyl) is reduced faster than 3,3-dimethyl-2-butanone (where R is *tert*-butyl).

$$k_{rel} = \frac{CH_3CCH_3}{CH_3CC(CH_3)_3} = 12$$

(*e*) In this problem we examine the rate of hydrolysis of acetals to the corresponding ketone or aldehyde. The rate-determining step is carbocation formation.

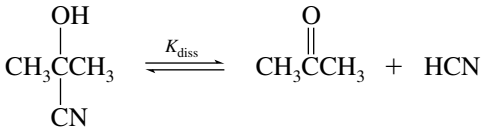


Hybridization at carbon changes from sp^3 to sp^2; crowding at this carbon is relieved as the carbocation is formed. The more crowded acetal (R = CH_3) forms a carbocation faster than the less crowded one (R = H). Another factor of even greater importance is the extent of

stabilization of the carbocation intermediate; the more stable carbocation (R = CH_3) is formed faster than the less stable one (R = H).

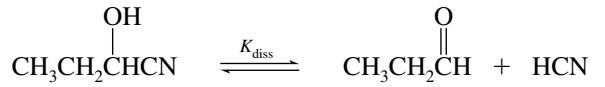
$$k_{rel} = \frac{(CH_3)_2C(OCH_2CH_3)_2}{CH_2(OCH_2CH_3)_2} = 1.8 \times 10^7$$

17.25 (*a*) The reaction as written is the reverse of cyanohydrin formation, and the principles that govern equilibria in nucleophilic addition to carbonyl groups apply in reverse order to the dissociation of cyanohydrins to aldehydes and ketones. Cyanohydrins of ketones dissociate more at equilibrium than do cyanohydrins of aldehydes. More strain due to crowding is relieved when a ketone cyanohydrin dissociates and a more stabilized carbonyl group is formed. The equilibrium constant K_{diss} is larger for



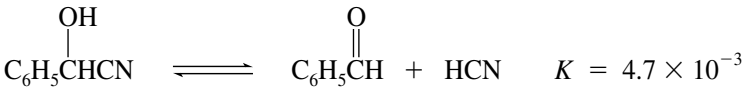
Acetone cyanohydrin — Acetone — Hydrogen cyanide

than it is for

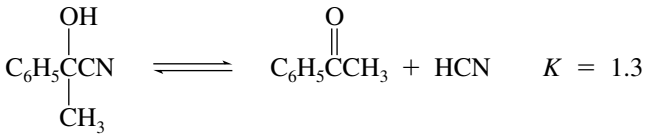


Propanal cyanohydrin — Propanal — Hydrogen cyanide

(*b*) Cyanohydrins of ketones have a more favorable equilibrium constant for dissociation than do cyanohydrins of aldehydes. Crowding is relieved to a greater extent when a ketone cyanohydrin dissociates and a more stable carbonyl group is formed. The measured dissociation constants are

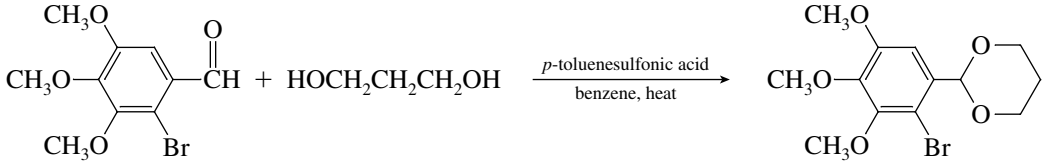


Benzaldehyde cyanohydrin — Benzaldehyde



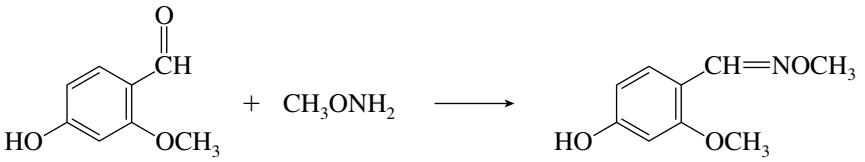
Acetophenone cyanohydrin — Acetophenone

17.26 (*a*) The reaction of an aldehyde with 1,3-propanediol in the presence of *p*-toluenesulfonic acid forms a cyclic acetal.



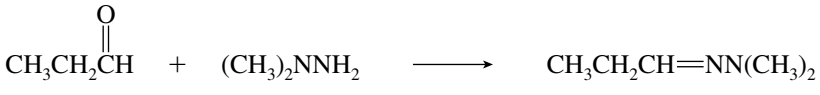
2-Bromo-3,4,5-trimethoxybenzaldehyde — 1,3-Propanediol — 2-(2′-Bromo-3′,4′,5′-trimethoxyphenyl)-1,3-dioxane (81%)

(*b*) The reagent CH_3ONH_2 is called *O*-methylhydroxylamine, and it reacts with aldehydes in a manner similar to hydroxylamine.



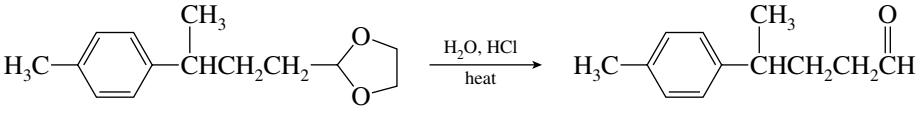
4-Hydroxy-2-methoxybenzaldehyde | *O*-Methylhydroxylamine | 4-Hydroxy-2-methoxybenzaldehyde *O*-methyloxime

(*c*) Propanal reacts with 1,1-dimethylhydrazine to yield the corresponding hydrazone.



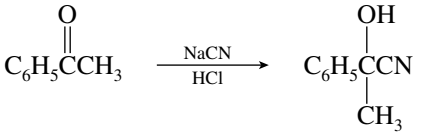
Propanal | 1,1-Dimethylhydrazine | Propanal dimethylhydrazone

(*d*) Acid-catalyzed hydrolysis of the acetal gives the aldehyde in 87% yield.



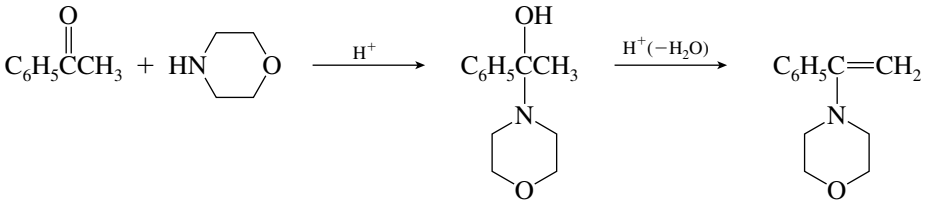
4-(*p*-Methylphenyl)pentanal

(*e*) Hydrogen cyanide adds to carbonyl groups to form cyanohydrins.



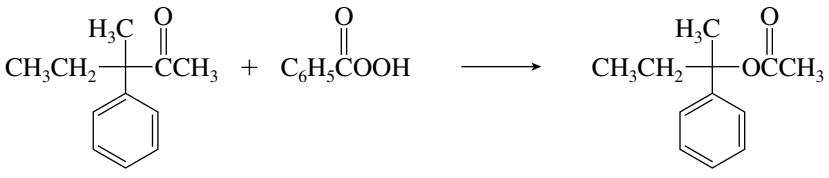
Acetophenone | Acetophenone cyanohydrin

(*f*) The reagent is a secondary amine known as **morpholine.** Secondary amines react with ketones to give enamines.



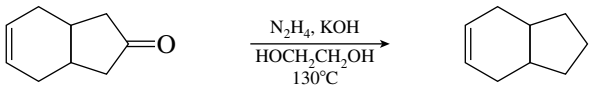
Acetophenone | Morpholine | Carbinolamine intermediate | 1-Morpholinostyrene (57–64%)

(*g*) Migration of the alkyl group in a Baeyer–Villiger oxidation occurs with retention of configuration.



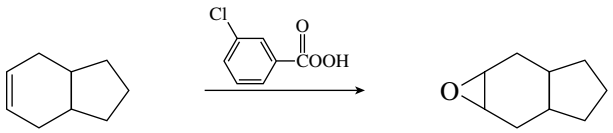
(*R*)-3-Methyl-3-phenyl-2-pentanone | Peroxybenzoic acid | (*R*)-1-Methyl-1-phenylpropyl acetate

17.27 Wolff–Kishner reduction converts a carbonyl group (C═O) to a methylene group (CH_2).



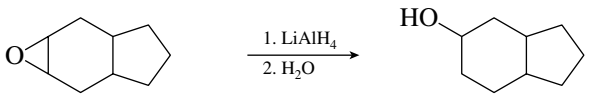
Bicyclo[4.3.0]non-3-en-8-one — Bicyclo[4.3.0]non-3-ene (compound A, 90%)

Treatment of the alkene with *m*-chloroperoxybenzoic acid produces an epoxide, compound B.



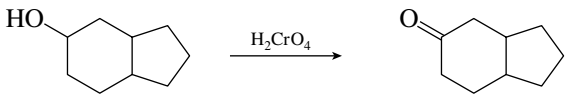
Bicyclo[4.3.0]non-3-ene — 3,4-Epoxybicyclo[4.3.0]nonane (compound B, 92%)

Epoxides undergo reduction with lithium aluminum hydride to form alcohols (Section 16.12).



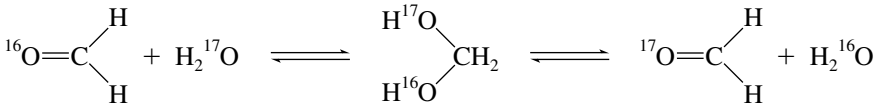
3,4-Epoxybicyclo[4.3.0]nonane — Bicyclo[4.3.0]nonan-3-ol (compound C, 90%)

Chromic acid oxidizes the alcohol to a ketone.



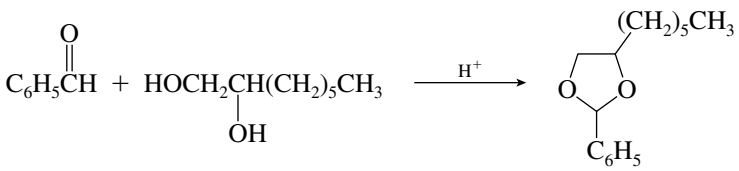
Bicyclo[4.3.0]nonan-3-ol — Bicyclo[4.3.0]nonan-3-one (compound D, 75%)

17.28 Hydration of formaldehyde by $H_2{}^{17}O$ produces a *gem*-diol in which the labeled and unlabeled hydroxyl groups are equivalent. When this *gem*-diol reverts to formaldehyde, loss of either of the hydroxyl groups is equally likely and leads to eventual replacement of the mass-16 isotope of oxygen by ^{17}O.



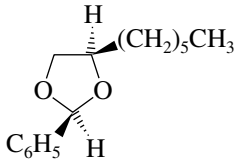
This reaction has been monitored by ^{17}O NMR spectroscopy; ^{17}O gives an NMR signal, but ^{16}O does not.

17.29 First write out the chemical equation for the reaction that takes place. Vicinal diols (1,2-diols) react with aldehydes to give cyclic acetals.

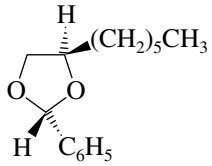


Benzaldehyde — 1,2-Octanediol — 4-Hexyl-2-phenyl-1,3-dioxolane

Notice that the phenyl and hexyl substituents may be either cis or trans to each other. The two products are the cis and trans stereoisomers.

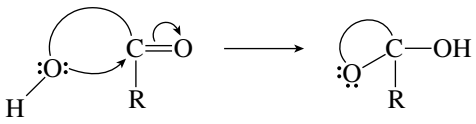


cis-4-Hexyl-2-phenyl-1,3-dioxolane



trans-4-Hexyl-2-phenyl-1,3-dioxolane

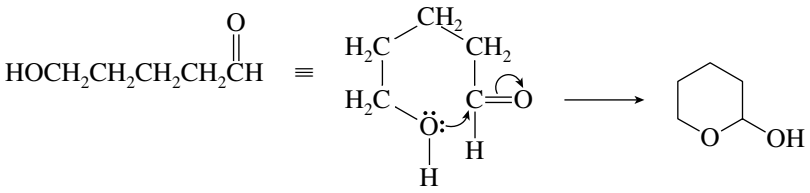
17.30 Cyclic hemiacetals are formed by intramolecular nucleophilic addition of a hydroxyl group to a carbonyl.



Cyclic hemiacetal

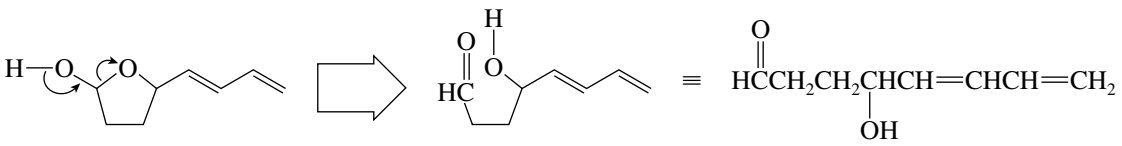
The ring oxygen is derived from the hydroxyl group; the carbonyl oxygen becomes the hydroxyl oxygen of the hemiacetal.

(*a*) This compound is the cyclic hemiacetal of 5-hydroxypentanal.



Indeed, 5-hydroxypentanal seems to exist entirely as the cyclic hemiacetal. Its infrared spectrum lacks absorption in the carbonyl region.

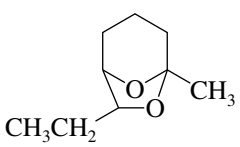
(*b*) The carbon connected to two oxygens is the one that is derived from the carbonyl group. Using retrosynthetic symbolism, disconnect the ring oxygen from this carbon.



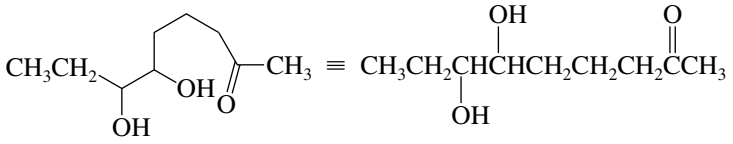
4-Hydroxy-5,7-octadienal

The next two compounds are cyclic acetals. The original carbonyl group is identifiable as the one that bears two oxygen substituents, which originate as hydroxyl oxygens of a diol.

(*c*)

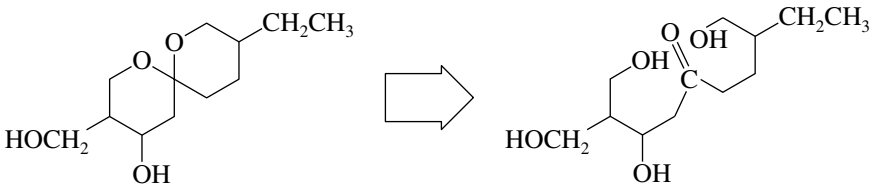


Brevicomin



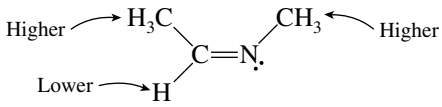
6,7-Dihydroxy-2-nonanone

(*d*)



Talaromycin A — 2,8-Di(hydroxymethyl)-1,3-dihydroxy-5-decanone

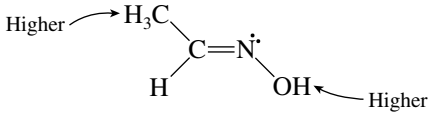
17.31 (*a*) The *Z* stereoisomer of $CH_3CH{=}NCH_3$ has its higher ranked substituents on the same side of the double bond,



(*Z*)-*N*-Ethylidenemethylamine

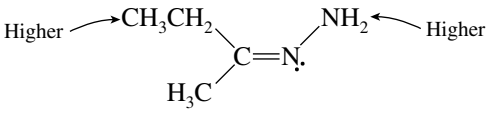
The lone pair of nitrogen is lower in rank than any other substituent.

(*b*) Higher ranked groups are on opposite sides of the carbon–nitrogen double bond in the *E* oxime of acetaldehyde.

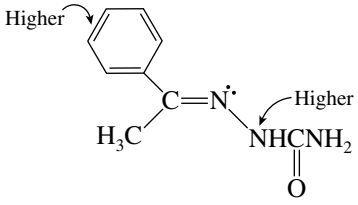


(*E*)-Acetaldehyde oxime

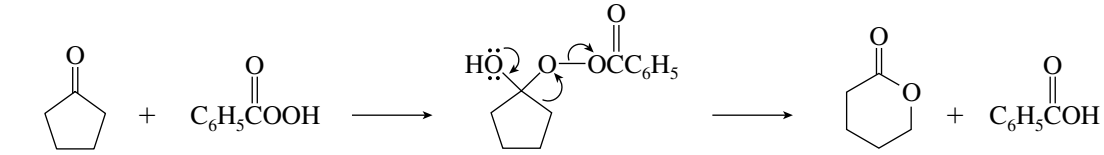
(*c*) (*Z*)-2-Butanone hydrazone is



(*d*) (*E*)-Acetophenone semicarbazone is

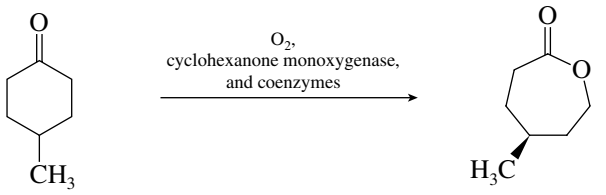


17.32 Cyclopentanone reacts with peroxybenzoic acid to form a peroxy monoester. The alkyl group that migrates is the ring itself, leading to formation of a six-membered lactone.



Cyclopentanone — Peroxybenzoic acid — 5-Pentanolide — Benzoic acid

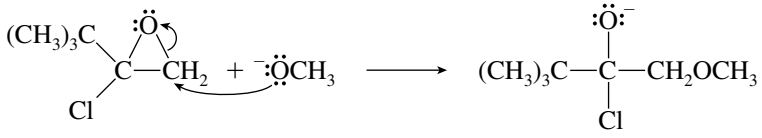
17.33 (*a*) The bacterial enzyme cyclohexanone monooxygenase was described in Section 17.16 as able to catalyze a biological Baeyer–Villiger reaction. Compound A is 4-methylcyclohexanone.



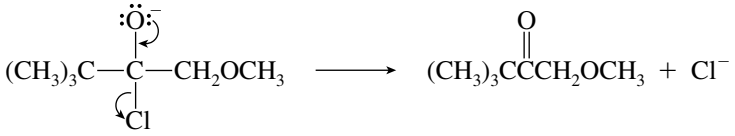
4-Methylcyclohexanone (Compound A) — Compound B

(*b*) The product of Baeyer–Villiger oxidation of 4-methylcyclohexanone with peroxyacetic acid would be the racemic cyclic ester (lactone), not the single enantiomer shown in part (*a*) from the enzyme-catalyzed oxidation.

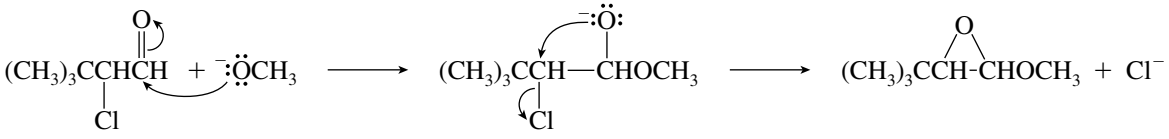
17.34 (*a*) Nucleophilic ring opening of the epoxide occurs by attack of methoxide at the less hindered carbon.



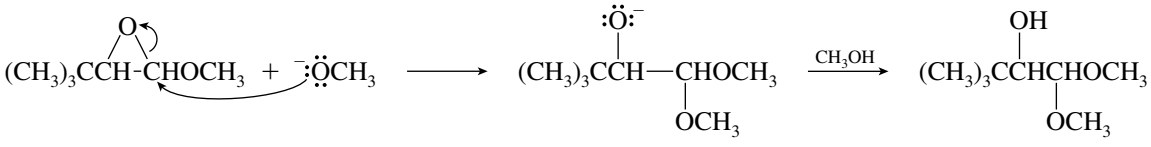
The anion formed in this step loses a chloride ion to form the carbon–oxygen double bond of the product.



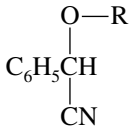
(*b*) Nucleophilic addition of methoxide ion to the aldehyde carbonyl generates an oxyanion, which can close to an epoxide by an intramolecular nucleophilic substitution reaction.



The epoxide formed in this process then undergoes nucleophilic ring opening on attack by a second methoxide ion.

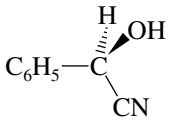


17.35 Amygdalin is a derivative of the cyanohydrin formed from benzaldehyde; thus the structure (without stereochemistry) is



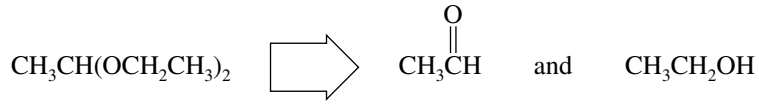
R = H, benzaldehyde cyanohydrin

The order of decreasing sequence rule precedence is HO > CN > C_6H_5 > H. The groups are arranged in a clockwise orientation in order of decreasing precedence in the *R* enantiomer.



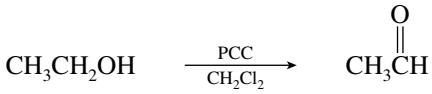
(*R*)-Benzaldehyde cyanohydrin

17.36 (*a*) The target molecule is the diethyl acetal of acetaldehyde (ethanal).



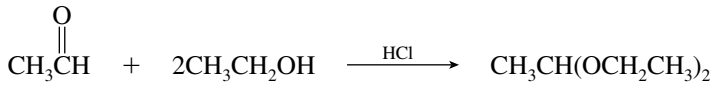
Acetaldehyde diethyl acetal

Acetaldehyde may be prepared by oxidation of ethanol.



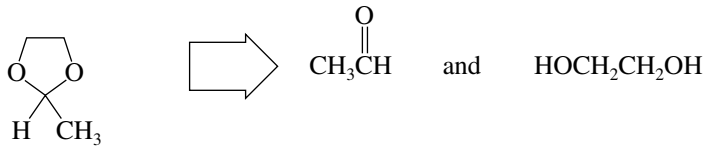
Ethanol Acetaldehyde

Reaction with ethanol in the presence of hydrogen chloride yields the desired acetal.



Acetaldehyde Ethanol Acetaldehyde diethyl acetal

(*b*) In this case the target molecule is a cyclic acetal of acetaldehyde.

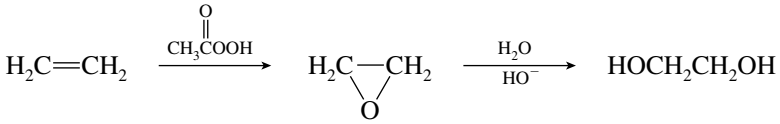


2-Methyl-1,3-dioxolane

Acetaldehyde has been prepared in part (*a*). Recalling that vicinal diols are available from the hydroxylation of alkenes, 1,2-ethanediol may be prepared by the sequence

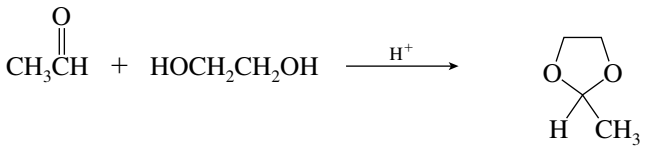
Ethanol Ethylene 1,2-Ethanediol

Hydrolysis of ethylene oxide is also reasonable.



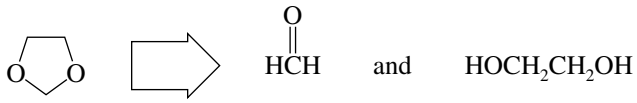
Ethylene Ethylene oxide 1,2-Ethanediol

Reaction of acetaldehyde with 1,2-ethanediol yields the cyclic acetal.



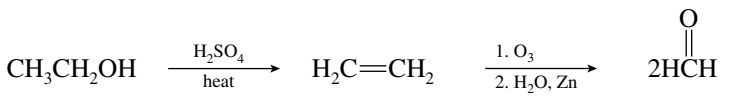
Acetaldehyde 1,2-Ethanediol 2-Methyl-1,3-dioxolane

(*c*) The target molecule is, in this case, the cyclic acetal of 1,2-ethanediol and formaldehyde.



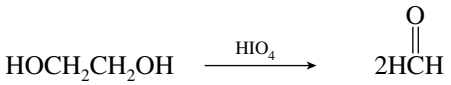
1,3-Dioxolane

The preparation of 1,2-ethanediol was described in part (*b*). One method of preparing formaldehyde is by ozonolysis of ethylene.



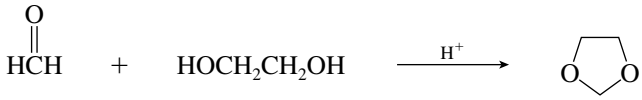
Ethanol Ethylene Formaldehyde

Another method is periodate cleavage of 1,2-ethanediol.



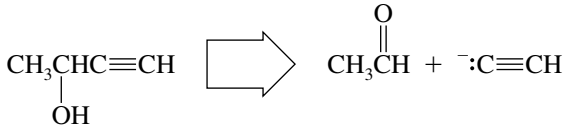
1,2-Ethanediol Formaldehyde

Cyclic acetal formation is then carried out in the usual way.



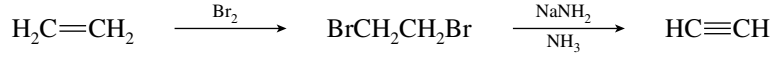
Formaldehyde 1,2-Ethanediol 1,3-Dioxolane

(*d*) Acetylenic alcohols are best prepared from carbonyl compounds and acetylide anions.



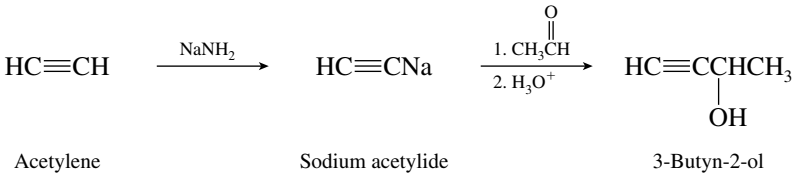
3-Butyn-2-ol

Acetaldehyde is available as in part (*a*). Alkynes such as acetylene are available from the corresponding alkene by bromination followed by double dehydrobromination. Using ethylene, prepared in part (*b*), the sequence becomes

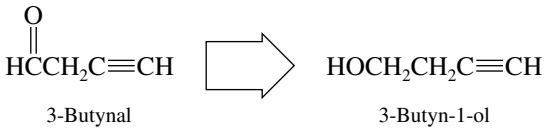


Ethylene 1,2-Dibromoethane Acetylene

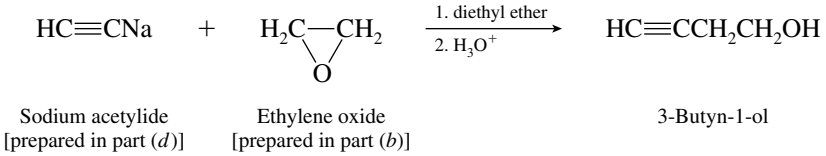
Then



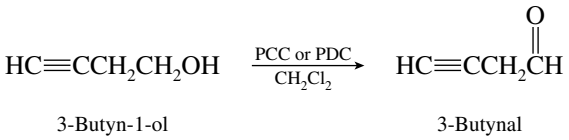
(*e*) The target aldehyde may be prepared from the corresponding alcohol.



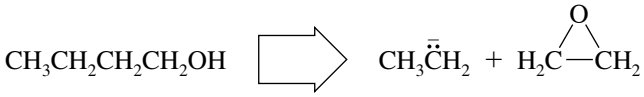
The best route to this alcohol is through reaction of an acetylide ion with ethylene oxide.



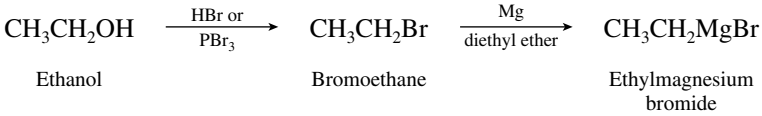
Oxidation with PCC or PDC is appropriate for the final step.



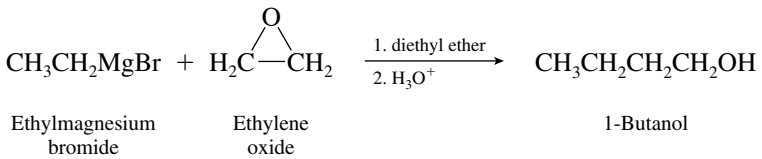
(*f*) The target molecule has four carbon atoms, suggesting a route involving reaction of an ethyl Grignard reagent with ethylene oxide.



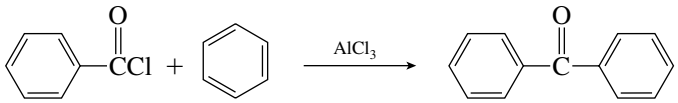
Ethylmagnesium bromide is prepared in the usual way.



Reaction of the Grignard reagent with ethylene oxide, prepared in part (*b*), completes the synthesis.

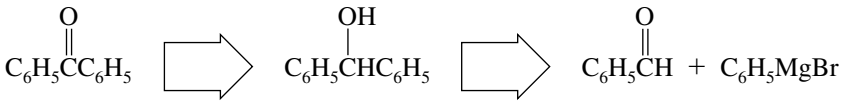


17.37 (*a*) Friedel–Crafts acylation of benzene with benzoyl chloride is a direct route to benzophenone.

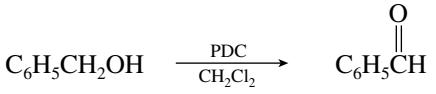


Benzoyl chloride Benzene Benzophenone

(*b*) On analyzing the overall transformation retrosynthetically, we see that the target molecule may be prepared by a Grignard synthesis followed by oxidation of the alcohol formed.

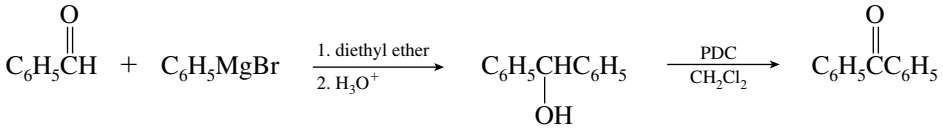


In the desired synthesis, benzyl alcohol must first be oxidized to benzaldehyde.



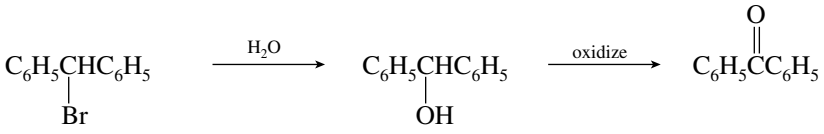
Benzyl alcohol Benzaldehyde

Reaction of benzaldehyde with the Grignard reagent of bromobenzene followed by oxidation of the resulting secondary alcohol gives benzophenone.



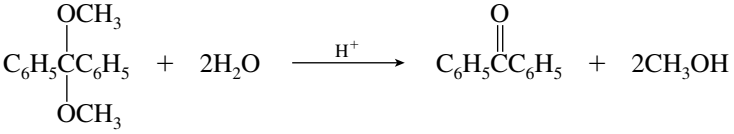
Benzaldehyde Phenylmagnesium bromide Diphenylmethanol Benzophenone

(*c*) Hydrolysis of bromodiphenylmethane yields the corresponding alcohol, which can be oxidized to benzophenone as in part (*b*).



Bromodiphenylmethane Diphenylmethanol Benzophenone

(*d*) The starting material is the dimethyl acetal of benzophenone. All that is required is acid-catalyzed hydrolysis.



Dimethoxydiphenyl-methane Water Benzophenone Methanol

(*e*) Oxidative cleavage of the alkene yields benzophenone. Ozonolysis may be used.

$$(C_6H_5)_2C{=}C(C_6H_5)_2 \xrightarrow[2.\ H_2O,\ Zn]{1.\ O_3} 2(C_6H_5)_2C{=}O$$

1,1,2,2-Tetraphenylethene — Benzophenone

17.38 The two alcohols given as starting materials contain all the carbon atoms of the desired product.

$$CH_3(CH_2)_8CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH{=}CH_2 \Longrightarrow$$

$$CH_3(CH_2)_8CH{=}CHCH_2CH{=}CHCH_2CH_2OH \quad \text{and} \quad HOCH_2CH{=}CH_2$$

3,6-Hexadecadien-1-ol — Allyl alcohol

What is needed is to attach the two groups together so that the two primary alcohol carbons become doubly bonded to each other. This can be accomplished by using a Wittig reaction as the key step.

$$CH_3(CH_2)_8CH{=}CHCH_2CH{=}CHCH_2CH_2OH \xrightarrow[CH_2Cl_2]{PCC} CH_3(CH_2)_8CH{=}CHCH_2CH{=}CHCH_2\overset{O}{\overset{\|}{C}}H$$

3,6-Hexadecadien-1-ol — 3,6-Hexadecadienal

$$H_2C{=}CHCH_2OH \xrightarrow{PBr_3} H_2C{=}CHCH_2Br \xrightarrow{(C_6H_5)_3P} (C_6H_5)_3\overset{+}{P}CH_2CH{=}CH_2\ Br^-$$

Allyl alcohol — Allyl bromide — Allyltriphenylphosphonium bromide

$$\xrightarrow{CH_3CH_2CH_2CH_2Li,\ THF}$$

$$(C_6H_5)_3\overset{+}{P}{-}\ddot{\overset{-}{C}}HCH{=}CH_2$$

Allylidenetriphenylphosphorane

$$CH_3(CH_2)_8CH{=}CHCH_2CH{=}CHCH_2\overset{O}{\overset{\|}{C}}H + (C_6H_5)_3\overset{+}{P}{-}\ddot{\overset{-}{C}}HCH{=}CH_2 \longrightarrow$$

3,6-Hexadecadienal — Allylidenetriphenylphosphorane

$$CH_3(CH_2)_8CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH{=}CH_2$$

1,3,6,9-Nonadecatetraene

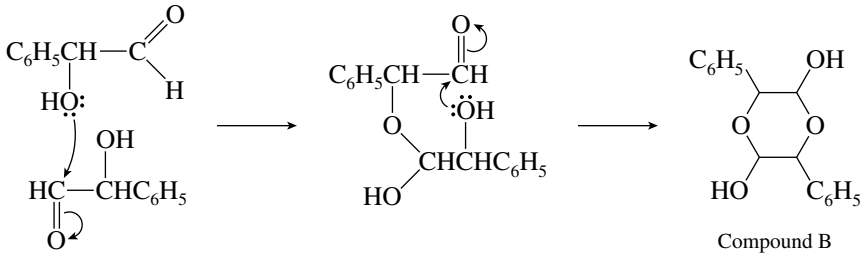
Alternatively, allyl alcohol could be oxidized to $CH_2{=}CHCHO$ for subsequent reaction with the ylide derived from $CH_3(CH_2)_8CH{=}CHCH_2CH{=}CHCH_2CH_2OH$ via its bromide and triphenylphosphonium salt.

17.39 The expected course of the reaction would be hydrolysis of the acetal to the corresponding aldehyde.

$$C_6H_5\underset{OH}{\underset{|}{C}}HCH(OCH_3)_2 \xrightarrow[HCl]{H_2O} C_6H_5\underset{OH}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}H + 2CH_3OH$$

Compound A (mandelaldehyde dimethyl acetal) — Mandelaldehyde — Methanol

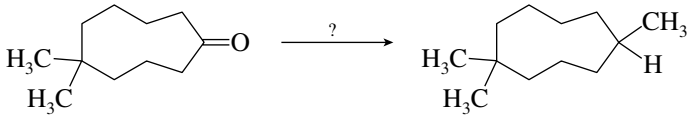
The molecular formula of the observed product (compound B, $C_{16}H_{16}O_4$) is exactly twice that of mandelaldehyde. This suggests that it might be a dimer of mandelaldehyde resulting from hemiacetal formation between the hydroxyl group of one mandelaldehyde molecule and the carbonyl group of another.



Compound B

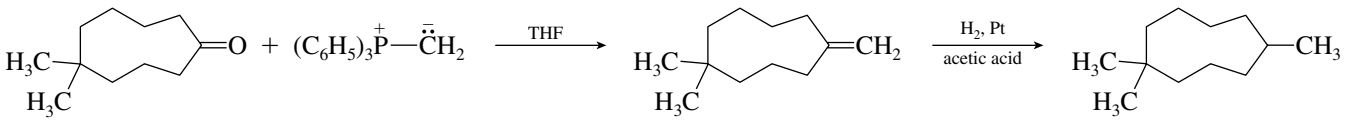
Because compound B lacks carbonyl absorption in its infrared spectrum, the cyclic structure is indicated.

17.40 (*a*) Recalling that alkanes may be prepared by hydrogenation of the appropriate alkene, a synthesis of the desired product becomes apparent. What is needed is to convert —C═O into —C═CH_2; a Wittig reaction is appropriate.



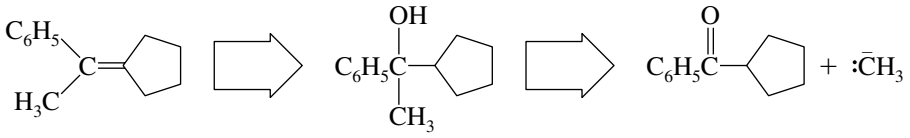
5,5-Dimethylcyclononanone 1,1,5-Trimethylcyclononane

The two-step procedure that was followed used a Wittig reaction to form the carbon–carbon bond, then catalytic hydrogenation of the resulting alkene.

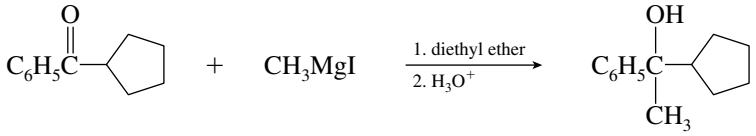


5,5-Dimethylcyclononanone 5,5-Dimethyl-1-methylenecyclononane (59%) 1,1,5-Trimethylcyclononane (73%)

(*b*) In putting together the carbon skeleton of the target molecule, a methyl group has to be added to the original carbonyl carbon.

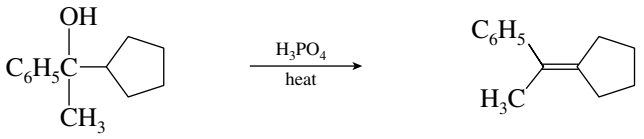


The logical way to do this is by way of a Grignard reagent.



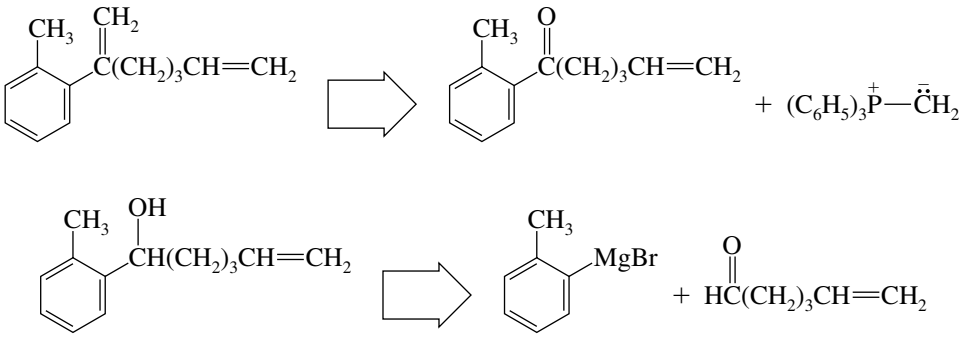
Cyclopentyl phenyl ketone Methylmagnesium iodide 1-Cyclopentyl-1-phenylethanol

Acid-catalyzed dehydration yields the more highly substituted alkene, the desired product, in accordance with the Zaitsev rule.

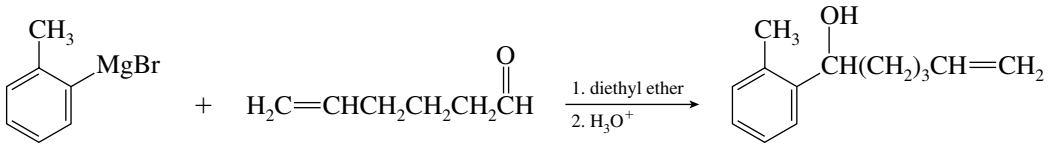


1-Cyclopentyl-1-phenylethanol (1-Phenylethylidene)cyclopentane

(*c*) Analyzing the transformation retrosynthetically, keeping in mind the starting materials stated in the problem, we see that the carbon skeleton may be constructed in a straightforward manner.

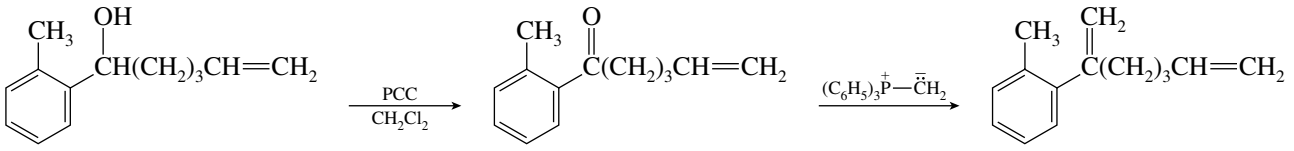


Proceeding with the synthesis in the forward direction, reaction between the Grignard reagent of *o*-bromotoluene and 5-hexenal produces most of the desired carbon skeleton.



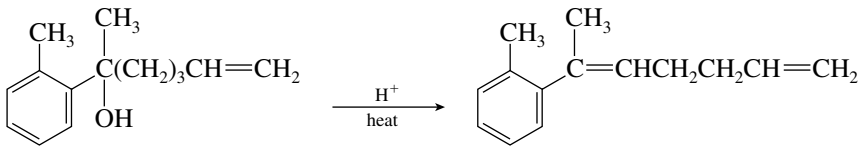
o-Methylphenylmagnesium bromide 5-Hexenal 1-(*o*-Methylphenyl)-5-hexen-1-ol

Oxidation of the resulting alcohol to the ketone followed by a Wittig reaction leads to the final product.



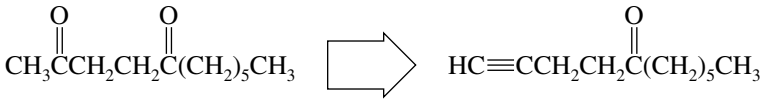
1-(*o*-Methylphenyl)-5-hexen-1-ol 1-(*o*-Methylphenyl)-5-hexen-1-one 2-(*o*-Methylphenyl)-1,6-heptadiene

Acid-catalyzed dehydration of the corresponding tertiary alcohol would *not* be suitable, because the major elimination product would have the more highly substituted double bond.

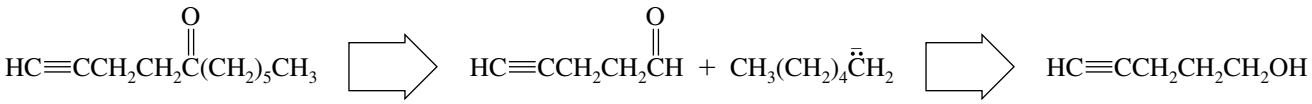


2-(*o*-Methylphenyl)-6-hepten-2-ol 6-(*o*-Methylphenyl)-1,5-heptadiene

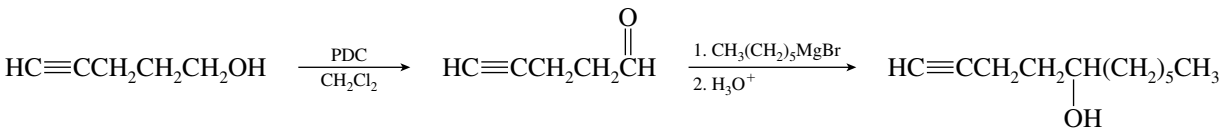
(*d*) Remember that terminal acetylenes can serve as sources of methyl ketones by hydration.



This gives us a clue as to how to proceed, since the acetylenic ketone may be prepared from the starting acetylenic alcohol.

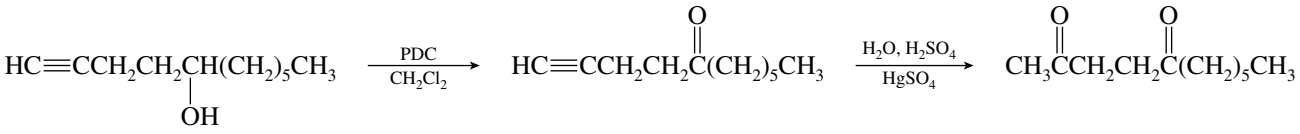


The first synthetic step is oxidation of the primary alcohol to the aldehyde and construction of the carbon skeleton by a Grignard reaction.



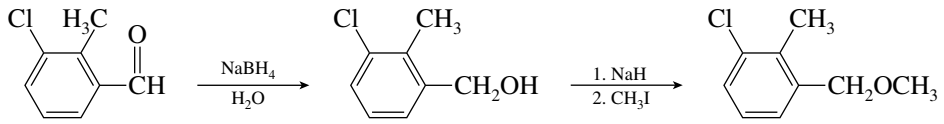
4-Pentyn-1-ol 4-Pentynal 1-Undecyn-5-ol

Oxidation of the secondary alcohol to a ketone and hydration of the terminal triple bond complete the synthesis.

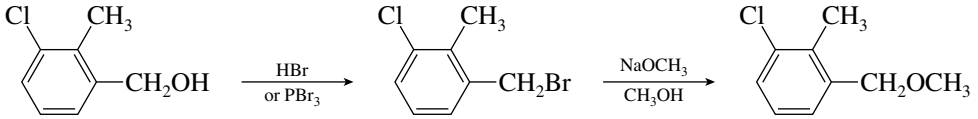


1-Undecyn-5-ol 1-Undecyn-5-one 2,5-Undecanedione

(*e*) The desired product is a benzylic ether. To prepare it, the aldehyde must first be reduced to the corresponding primary alcohol. Sodium borohydride was used in the preparation described in the literature, but lithium aluminum hydride or catalytic hydrogenation would also be possible. Once the alcohol is prepared, it can be converted to its alkoxide ion and this alkoxide ion treated with methyl iodide.

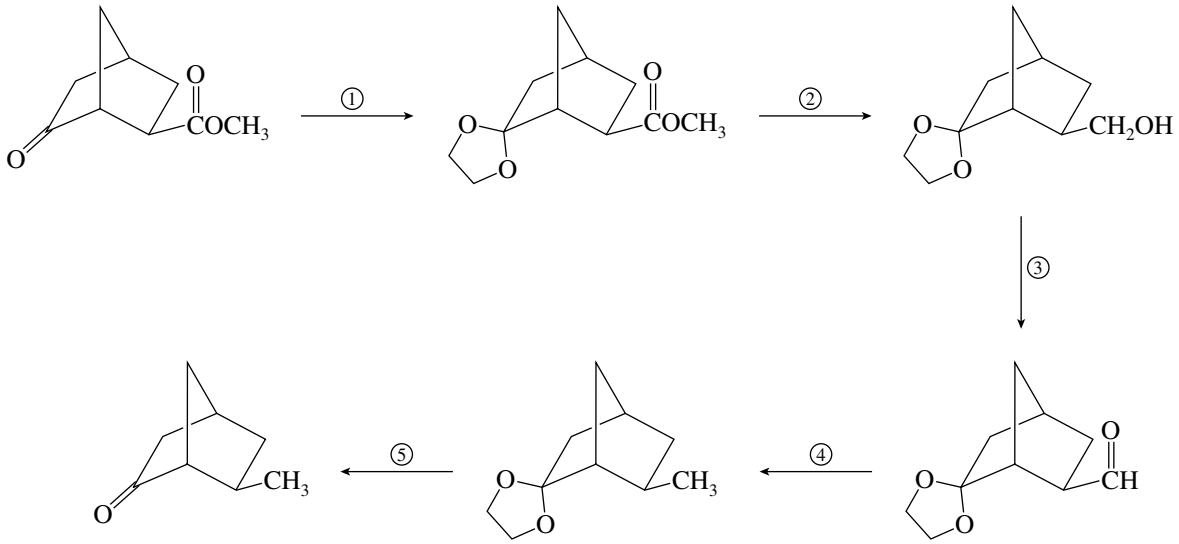


Alternatively, the alcohol could be treated with hydrogen bromide or with phosphorus tribromide to give the benzylic bromide and the bromide then allowed to react with sodium methoxide.

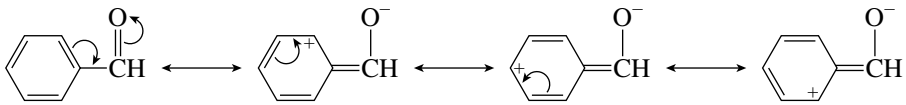


17.41 Step 1 of the synthesis is formation of a cyclic acetal protecting group; the necessary reagents are ethylene glycol ($HOCH_2CH_2OH$) and *p*-toluenesulfonic acid, with heating in benzene. In step 2 the ester function is reduced to a primary alcohol. Lithium aluminum hydride ($LiAlH_4$) is the reagent of choice. Oxidation with PCC in CH_2Cl_2 converts the primary alcohol to an aldehyde in step 3.

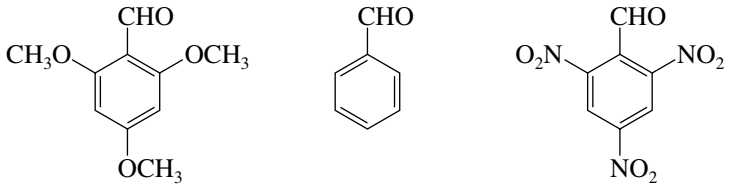
Wolff–Kishner reduction (N_2H_4, KOH, ethylene glycol, heat) converts the aldehyde group to a methyl group in step 4. The synthesis is completed in step 5 by hydrolysis (H_3O^+) of the acetal-protecting group.



17.42 We need to assess the extent of resonance donation to the carbonyl group by the π electrons of the aromatic rings. Such resonance for benzaldehyde may be written as

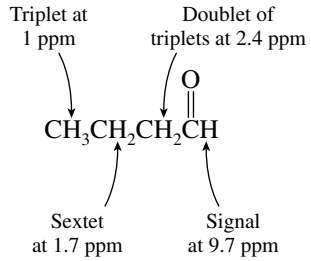


Electron-releasing groups such as methoxy at positions ortho and para to the aldehyde function increase the "single-bond character" of the aldehyde by stabilizing the dipolar resonance forms and increasing their contribution to the overall electron distribution in the molecule. Electron-withdrawing groups such as nitro decrease this single-bond character. The aldehyde with the lowest carbonyl stretching frequency is 2,4,6-trimethoxybenzaldehyde; the one with the highest is 2,4,6-trinitrobenzaldehyde. The measured values are

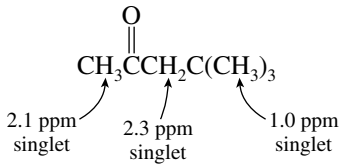


2,4,6-Trimethoxybenzaldehyde ($1665\ cm^{-1}$) | Benzaldehyde ($1700\ cm^{-1}$) | 2,4,6-Trinitrobenzaldehyde ($1715\ cm^{-1}$)

17.43 The signal in the ^1H NMR spectrum at δ 9.7 ppm tells us that the compound is an aldehyde rather than a ketone. The 2H signal at δ 2.4 ppm indicates that the group adjacent to the carbonyl is a CH_2 group. The remaining signals support the assignment of the compound as butanal.



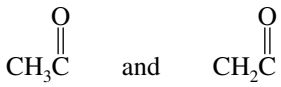
17.44 A carbonyl group is evident from the strong infrared absorption at 1710 cm^{-1}. Since all the ^1H NMR signals are singlets, there are no nonequivalent hydrogens in a vicinal or "three-bond" relationship. The three-proton signal at δ 2.1 ppm, and the 2-proton signal at δ 2.3 ppm can be understood as arising from a $CH_2\overset{\overset{O}{\|}}{C}CH_3$ unit. The intense 9-proton singlet at δ 1.0 ppm is due to the three equivalent methyl groups of a $(CH_3)_3C$ unit. The compound is 4,4-dimethyl-2-pentanone.



4,4-Dimethyl-2-pentanone

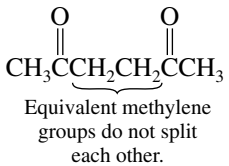
17.45 The molecular formula of compounds A and B ($C_6H_{10}O_2$) indicates an index of hydrogen deficiency of 2. Because we are told the compounds are diketones, the two carbonyl groups account for all the unsaturations.

The ^1H NMR spectrum of compound A has only two peaks, both singlets, at δ 2.2 and 2.8 ppm. Their intensity ratio (6:4) is consistent with two equivalent methyl groups and two equivalent methylene groups. The chemical shifts are appropriate for



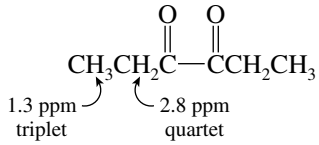
The simplicity of the spectrum can be understood if we are dealing with a symmetric diketone.

The correct structure is



2,5-Hexanedione (compound A)

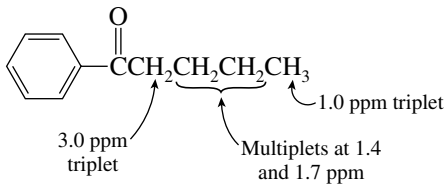
Compound B is an isomer of compound A. The triplet–quartet pattern in the ^1H NMR spectrum is consistent with an ethyl group and, because the triplet is equivalent to 6 protons and the quartet to 4, it is likely that two equivalent ethyl groups are present. The two ethyl groups account for four carbons, and because the problem stipulates that the molecule is a diketone, all the carbons are accounted for. The only $C_6H_{10}O_2$ diketone with two equivalent ethyl groups is 3,4-hexanedione.



3,4-Hexanedione (compound B)

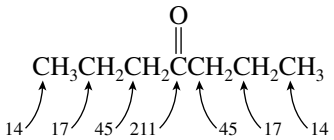
17.46 From its molecular formula ($C_{11}H_{14}O$), the compound has a total of five double bonds and rings. The presence of signals in the region δ 7 to 8 ppm suggests an aromatic ring is present, accounting for four of the elements of unsaturation. The presence of a strong peak at 1700 cm^{-1} in the infrared spectrum indicates the presence of a carbonyl group, accounting for the remaining element of

unsaturation. The highest field peak in the NMR spectrum is a 3-proton triplet, corresponding to the methyl group of a CH_3CH_2 unit. The 2-proton signal at δ 3.0 ppm corresponds to a CH_2 unit adjacent to the carbonyl group and, because it is a triplet, suggests the grouping $CH_2CH_2C{=}O$. The compound is butyl phenyl ketone (1-phenyl-1-pentanone).



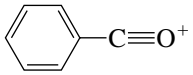
Butyl phenyl ketone

17.47 With a molecular formula of $C_7H_{14}O$, the compound has an index of hydrogen deficiency of 1. We are told that it is a ketone, so it has no rings or double bonds other than the one belonging to its $C{=}O$ group. The peak at 211 ppm in the ^{13}C NMR spectrum corresponds to the carbonyl carbon. Only three other signals occur in the spectrum, and so there are only three types of carbons other than the carbonyl carbon. This suggests that the compound is the symmetrical ketone 4-heptanone.



4-Heptanone
(all chemical shifts in ppm)

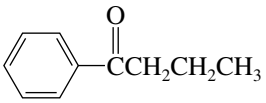
17.48 Compounds A and B are isomers and have an index of hydrogen deficiency of 5. Signals in the region 125–140 ppm in their ^{13}C NMR spectra suggest an aromatic ring, and a peak at 200 ppm indicates a carbonyl group. An aromatic ring contributes one ring and three double bonds, and a carbonyl group contributes one double bond, and so the index of hydrogen deficiency of 5 is satisfied by a benzene ring and a carbonyl group. The carbonyl group is attached directly to the benzene ring, as evidenced by the presence of a peak at *m/z* 105 in the mass spectra of compounds A and B.



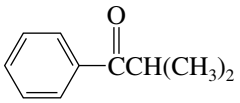
m/z 105

Each ^{13}C NMR spectrum shows four aromatic signals, and so the rings are monosubstituted.

Compound A has three unique carbons in addition to $C_6H_5C{=}O$ and so must be 1-phenyl-1-butanone. Compound B has only two additional signals and so must be 2-methyl-1-phenyl-1-propanone.



Compound A



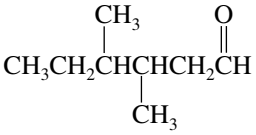
Compound B

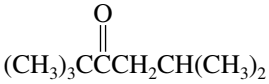
17.49–17.50 Solutions to molecular modeling exercises are not provided in this *Study Guide and Solutions Manual*. You should use *Learning By Modeling* for these exercises.

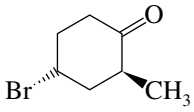
SELF-TEST

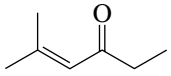
PART A

A-1. Give the correct IUPAC name for each of the following:

(*a*) 

(*b*) 

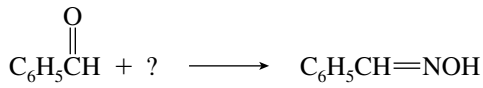
(*c*) 

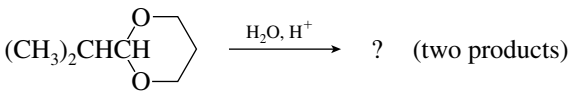
(*d*) 

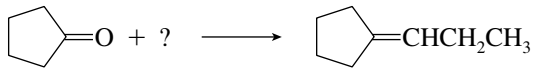
A-2. Write the structural formulas for
(*a*) (*E*)-3-Hexen-2-one
(*b*) 3-Cyclopropyl-2,4-pentanedione
(*c*) 3-Ethyl-4-phenylpentanal

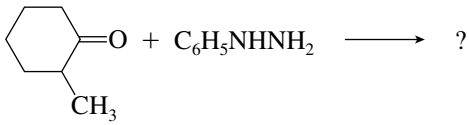
A-3. For each of the following reactions supply the structure of the missing reactant, reagent, or product:

(*a*) 

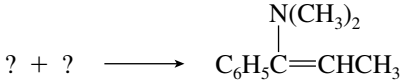
(*b*) 

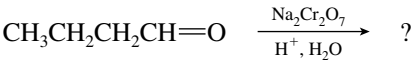
(*c*) 

(*d*) 

(*e*) 

(*f*) 

(*g*) 

(*h*) 

A-4. Write the structures of the products, compounds A through E, of the reaction steps shown.

(*a*) $(C_6H_5)_3P + (CH_3)_2CHCH_2Br \longrightarrow A$

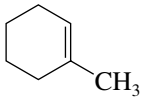
$A + CH_3CH_2CH_2CH_2Li \longrightarrow B + C_4H_{10}$

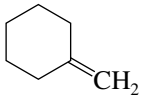
$B + \text{benzaldehyde} \longrightarrow C + (C_6H_5)_3\overset{+}{P}—O^-$

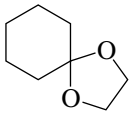
(*b*) $C_6H_5CH_2\underset{\displaystyle OH}{\underset{|}{C}}HCH_3 \xrightarrow[CH_2Cl_2]{PCC} D$

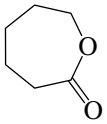
$D + CH_3\overset{\displaystyle O}{\overset{\|}{C}}OOH \longrightarrow E + CH_3\overset{\displaystyle O}{\overset{\|}{C}}OH$

A-5. Give the reagents necessary to convert cyclohexanone into each of the following compounds. More than one step may be necessary.

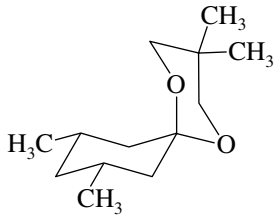
(*a*) 

(*b*) 

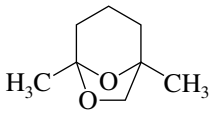
(*c*) 

(*d*) 

A-6. (*a*) What two organic compounds react together (in the presence of an acid catalyst) to give the compound shown, plus a molecule of water?

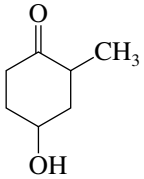
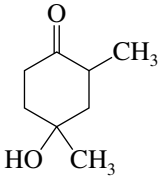


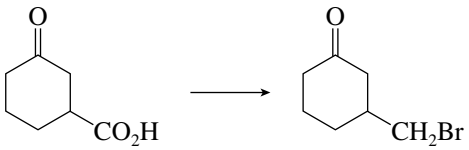
(*b*) Draw the structure of the open-chain form of the following cyclic acetal:



A-7. Outline reaction schemes to carry out each of the following interconversions, using any necessary organic or inorganic reagents.

(*a*) $(CH_3)_2C{=}O$ to $(CH_3)_2\underset{\displaystyle O}{\underset{\diagdown\,/}{C}}—CHCH_3$

(*b*)  to 

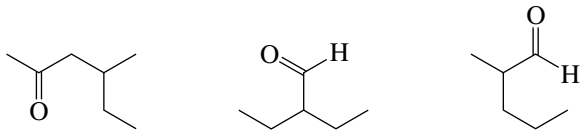
(*c*) 

A-8. Write a stepwise mechanism for the formation of $CH_3CH(OCH_3)_2$ from acetaldehyde and methanol under conditions of acid catalysis.

A-9. Suggest a structure for an unknown compound, $C_9H_{10}O$, that exhibits a strong infrared absorption at 1710 cm^{-1} and has a ^1H NMR spectrum that consists of three singlets at δ 2.1 ppm (3H), 3.7 ppm (2H), and 7.2 ppm (5H).

PART B

B-1. Which of the compounds shown is (are) correctly named as pentane derivatives, either as pentanals or pentanones?



1 2 3

(*a*) 1 only (*b*) 2 only (*c*) 3 only (*d*) 1 and 3 (*e*) None of them

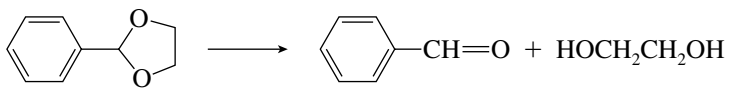
B-2. The compound shown is best classified as a(an)

$$(CH_3)_3CCH_2CH{=}NCH_3$$

(*a*) Carbinolamine
(*b*) Enamine
(*c*) Hydrazone
(*d*) Imine
(*e*) Oxime

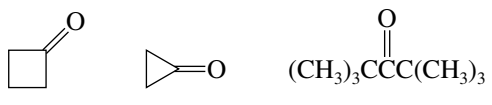
B-3. When a nucleophile encounters a ketone, the site of attack is
(*a*) The carbon atom of the carbonyl
(*b*) The oxygen atom of the carbonyl
(*c*) Both the carbon and oxygen atoms, with equal probability
(*d*) No attack occurs—ketones do not react with nucleophiles.

B-4. What reagent and/or reaction conditions would you choose to bring about the following conversion?



(*a*) 1. $LiAlH_4$, 2. H_2O
(*b*) H_2O, NaOH, heat
(*c*) H_2O, H_2SO_4, heat
(*d*) PCC, CH_2Cl_2

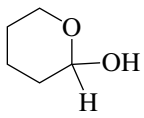
B-5. Rank the following in order of increasing value of the equilibrium constant for hydration, K_{hyd} (smallest value first).



1 2 3

(*a*) 1 < 2 < 3 (*b*) 3 < 1 < 2 (*c*) 2 < 1 < 3 (*d*) 2 < 3 < 1

B-6. The structure



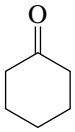
would be best classified as a(n)

(*a*) Acetal
(*b*) Hemiacetal
(*c*) Hydrate
(*d*) Cyanohydrin

B-7. Which of the following pairs of reactants is most effective in forming an enamine?

(*a*) $CH_3CH_2\overset{\overset{O}{\|}}{C}H + [(CH_3)_2CH]_2NH$

(*b*) $(CH_3)_3\overset{\overset{O}{\|}}{C}CH + (CH_3)_2NH$

(*c*)  $+ (CH_3)_3CNH_2$

(*d*) None of these forms an enamine.

B-8. Which of the following species is an ylide?

(*a*) $(C_6H_5)_3\overset{+}{P}CH_2CH_3\ Br^-$

(*b*) $(C_6H_5)_3\overset{+}{P}\overset{-}{\ddot{C}}HCH_3$

(*c*) $(C_6H_5)_3P(-O-CH_2)-CHCH_3$

(*d*) None of these

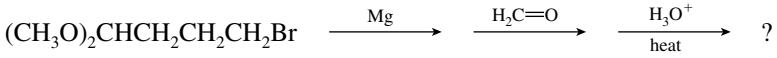
B-9. Which pair of the following compounds could serve as the reagents X and Y in the following reaction sequence?

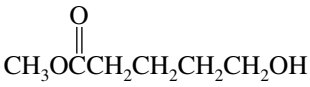
$$X \xrightarrow{(C_6H_5)_3P} \xrightarrow{CH_3CH_2CH_2CH_2Li} \xrightarrow{Y} (CH_3)_2CHCH{=}C(CH_3)(CH_2CH_3)$$

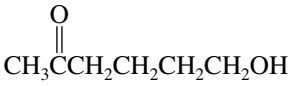
$(CH_3)_2CHCH_2Br$ (1) $(CH_3)_2CHBr$ (2) $CH_3CH_2\underset{\underset{CH_3}{|}}{C}HBr$ (3) $(CH_3)_2CH\overset{\overset{O}{\|}}{C}H$ (4) $CH_3\overset{\overset{O}{\|}}{C}CH_3$ (5)

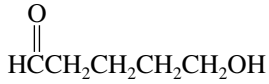
	X	Y
(*a*)	1	5
(*b*)	1	4
(*c*)	2	4
(*d*)	2	5
(*e*)	3	4

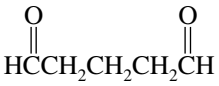
B-10. The final product of the following sequence of reactions is.



(*a*) 

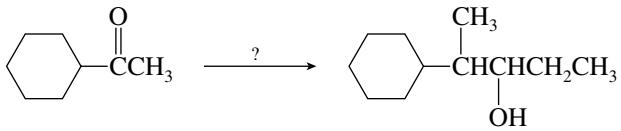
(*b*) 

(*c*) 

(*d*) 

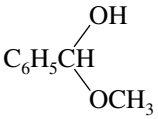
(*e*) 

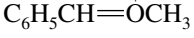
B-11. Which of the following sets of reagents, used in the order shown, would successfully accomplish the conversion shown?

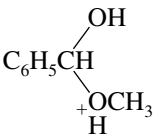


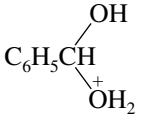
(*a*) $CH_3CH_2CH_2MgBr$; H_3O^+; PCC, CH_2Cl_2
(*b*) $CH_3CH_2CH_2MgBr$; H_3O^+; H_2SO_4, heat; PCC, CH_2Cl_2
(*c*) $(C_6H_5)_3\overset{+}{P}—\ddot{\overset{-}{C}}HCH_2CH_3$; B_2H_6; H_2O_2, HO^-
(*d*) $(C_6H_5)_3\overset{+}{P}—\ddot{\overset{-}{C}}HCH_2CH_3$; H_2SO_4, H_2O

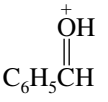
B-12. Which of the following species is the conjugate acid of the hemiacetal formed by reaction of benzaldehyde with methanol containing a trace of acid?

(*a*) 

(*b*) 

(*c*) 

(*d*) 

(*e*) 

B-13. Which sequence represents the best synthesis of hexanal?

$CH_3CH_2CH_2CH_2CH_2CH{=}O$

Hexanal

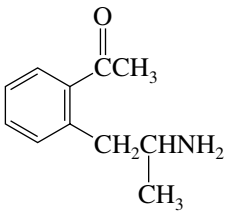
(*a*) 1. $CH_3CH_2CH_2CH_2Br + NaC{\equiv}CH$
2. H_2O, H_2SO_4, $HgSO_4$

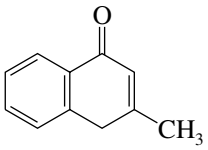
(*b*) 1. $CH_3CH_2CH_2CH_2C(=O)CH_3$
2. $CH_3C(=O)OOH$
3. $LiAlH_4$
4. H_2O
5. PCC, CH_2Cl_2

(*c*) 1. $CH_3CH_2CH_2CH{=}CH_2 + CH_3C(=O)OOH$
2. CH_3MgBr, diethyl ether
3. H_3O^+
4. PCC, CH_2Cl_2

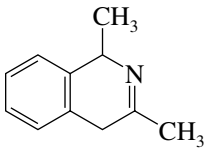
(*d*) 1. $CH_3CH_2CH_2CH_2MgBr + H_2C\text{—}CH_2$ (epoxide, O)
2. H_3O^+
3. PCC, CH_2Cl_2

B-14. The amino ketone shown undergoes a spontaneous cyclization on standing. What is the product of this intramolecular reaction?

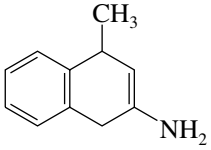




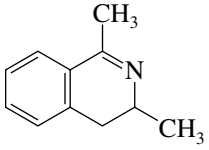
(*a*)



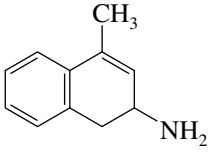
(*d*)



(*b*)

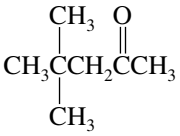


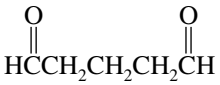
(*e*)

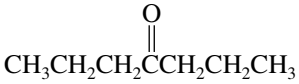


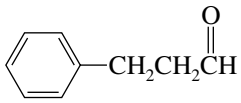
(*c*)

B-15. Which of the following compounds would have a ^{1}H NMR spectrum consisting of three singlets?

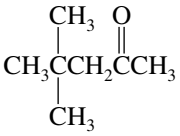
(*a*) 

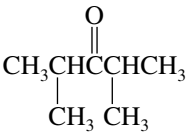
(*c*) 

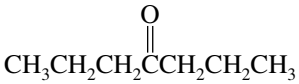
(*b*) 

(*d*) 

B-16. Which of the following compounds would have the fewest number of signals in its ^{13}C NMR spectrum?

(*a*) 

(*c*) 

(*b*) 

(*d*)