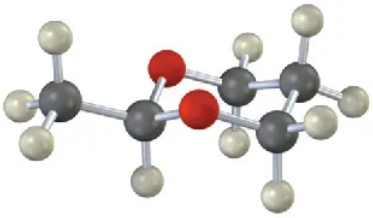
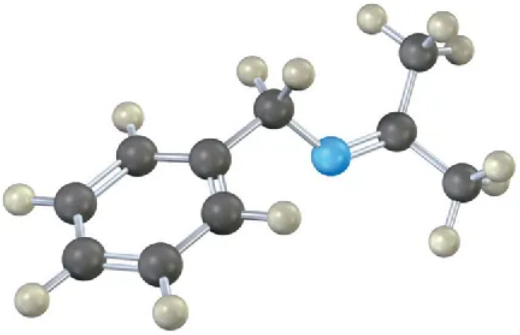
5.16: Additional Problems

Visualizing Chemistry

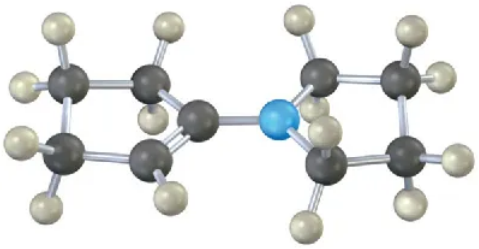
Each of the following substances can be prepared by a nucleophilic addition reaction between an aldehyde or ketone and a nucleophile. Identify the reactants from which each was prepared. If the substance is an acetal, identify the carbonyl compound and the alcohol; if it is an imine, identify the carbonyl compound and the amine; and so forth. (a)



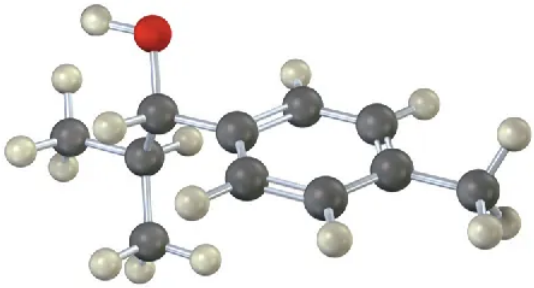
(b)



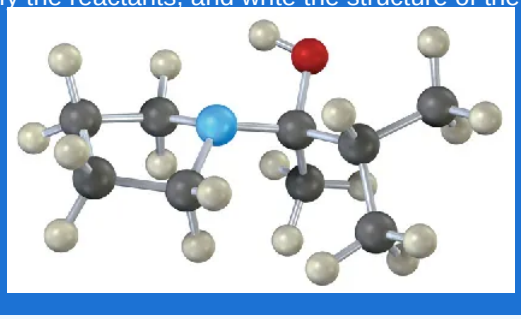
(c)



(d)



The following molecular model represents a tetrahedral intermediate resulting from addition of a nucleophile to an aldehyde or ketone. Identify the reactants, and write the structure of the final product when the nucleophilic addition reaction is complete.



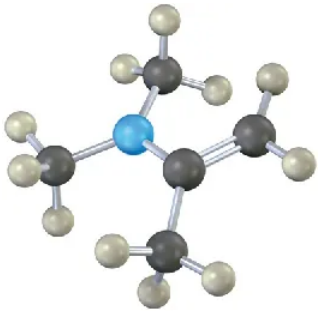
What is the geometry and hybridization of the nitrogen atom?

(b)

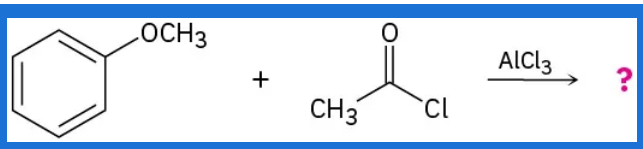
What orbital on nitrogen holds the lone pair of electrons?

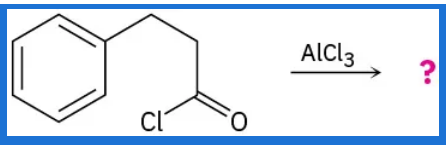
(c)

What is the geometric relationship between the *p* orbitals of the double bond and the nitrogen orbital that holds the lone pair? Why do you think this geometry represents the minimum energy?

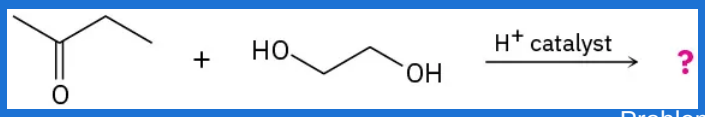


Mechanism Problems



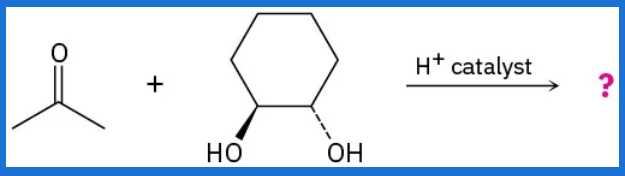


(b)

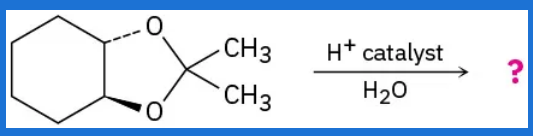


(b)

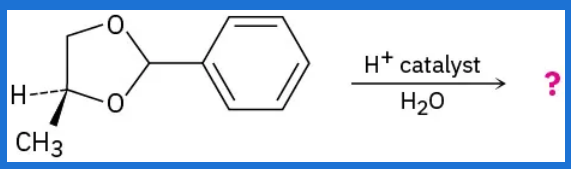
Problem 19-36



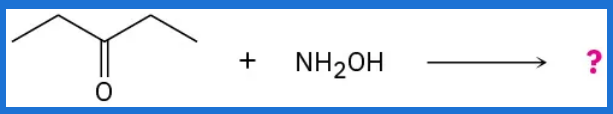
Problem 19-32 Predict the product(s) and propose a mechanism for each of the following reactions: (a)



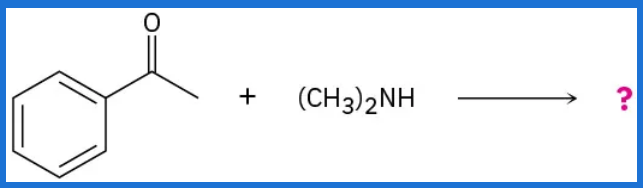
(b)



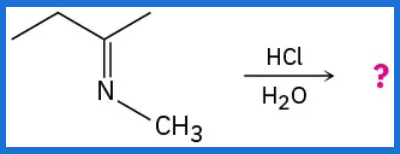
Problem 19-33 Predict the product(s) and propose a mechanism for each of the following reactions: (a)



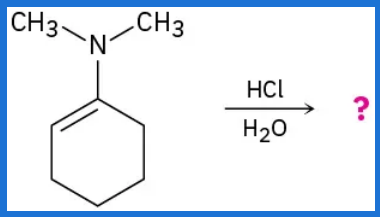
(b)



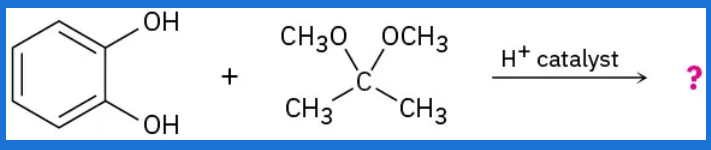
Problem 19-34 Predict the product(s) and propose mechanisms for the following reactions: (a)



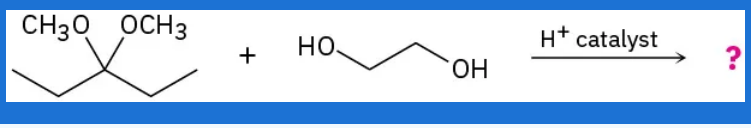
(b)



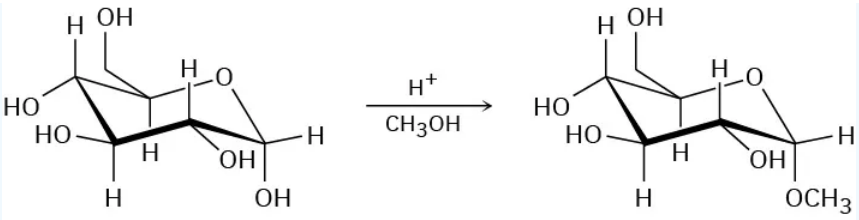
Problem 19-35 The following reaction begins with an acetal and converts it into a different acetal. Predict the product(s) and propose a mechanism. (a)



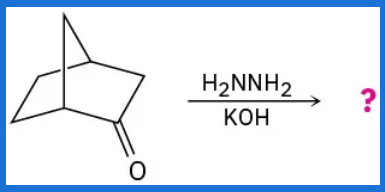
(b)



When α-glucose is treated with an acid catalyst in the presence of an alcohol, an acetal is formed. Propose a mechanism for this process and give the structure of the stereoisomeric acetal that you would also expect as a product.

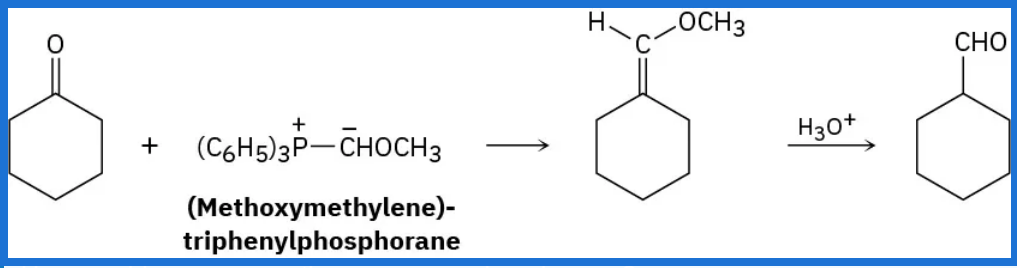


Problem 19-38



(b)

Aldehydes can be prepared by the Wittig reaction using (methoxymethylene)triphenylphosphorane as the Wittig reagent and then hydrolyzing the product with acid. For example,



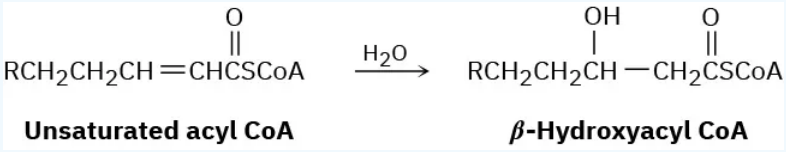
(a)

How would you prepare the necessary phosphorane?

(b)

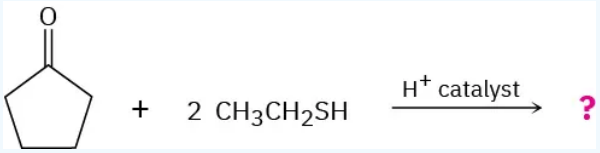
Propose a mechanism for the hydrolysis step.

One of the steps in the metabolism of fats is the reaction of an unsaturated acyl CoA with water to give a β-hydroxyacyl CoA. Propose a mechanism.

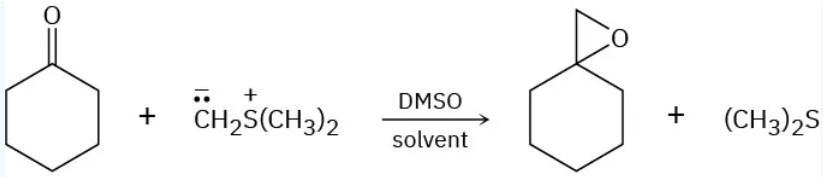


Unsaturated acyl CoA **β-Hydroxyacyl CoA**

Aldehydes and ketones react with thiols to yield *thioacetals* just as they react with alcohols to yield acetals. Predict the product of the following reaction, and propose a mechanism:

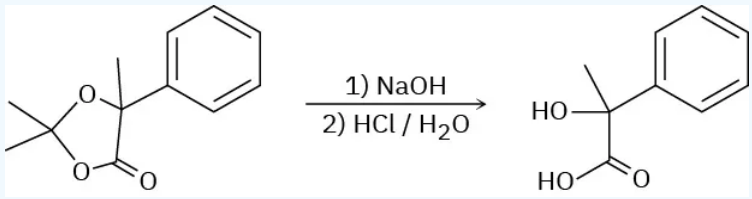


Ketones react with dimethylsulfonium methylide to yield epoxides. Suggest a mechanism for the reaction.

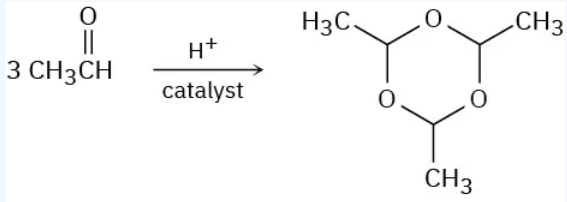


Dimethylsulfonium methylide

Propose a mechanism for the following reaction.

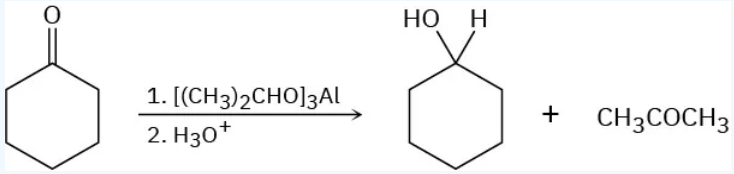


Paraldehyde, a sedative and hypnotic agent, is prepared by treatment of acetaldehyde with an acidic catalyst. Propose a mechanism for the reaction.

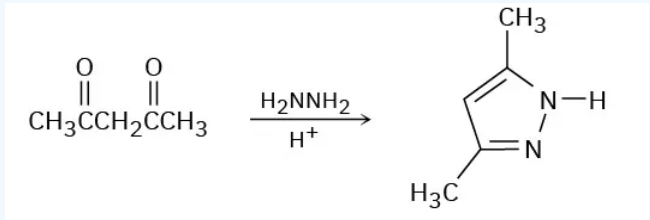


Paraldehyde

The Meerwein–Ponndorf–Verley reaction involves reduction of a ketone by treatment with an excess of aluminum triisopropoxide, $[(CH_3)_2CHO]_3Al$. The mechanism of the process is closely related to the Cannizzaro reaction in that a hydride ion acts as a leaving group. Propose a mechanism.

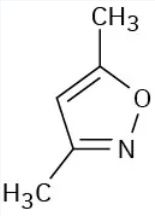


Propose a mechanism to account for the formation of 3,5-dimethylpyrazole from hydrazine and 2,4-pentanedione. What has happened to each carbonyl carbon in going from starting material to product.



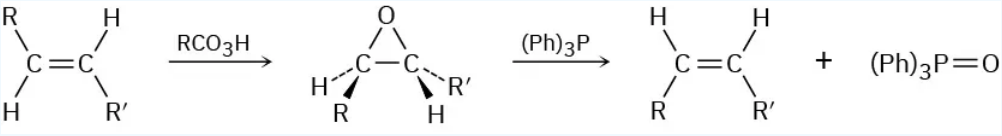
2,4-Pentanedione **3,5-Dimethylpyrazole**

In light of your answer to Problem 19-45, propose a mechanism for the formation of 3,5-dimethylisoxazole from hydroxylamine and 2,4-pentanedione.

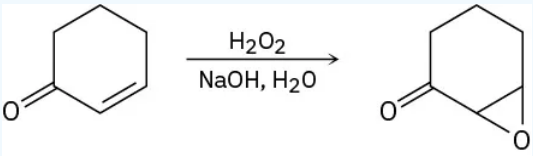


3,5-Dimethylisoxazole

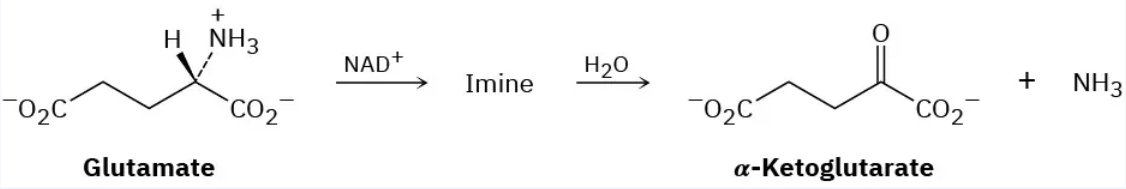
Trans alkenes are converted into their cis isomers and vice versa on epoxidation followed by treatment of the epoxide with triphenylphosphine. Propose a mechanism for the reaction.



Treatment of an α,β-unsaturated ketone with basic aqueous hydrogen peroxide yields an epoxy ketone. The reaction is specific to unsaturated ketones; isolated alkene double bonds do not react. Propose a mechanism.

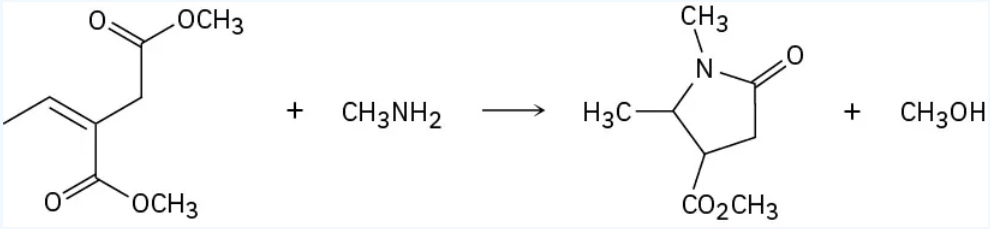


One of the biological pathways by which an amine is converted to a ketone involves two steps: (**1) oxidation of the amine by NAD^+ to give an imine and (2) hydrolysis of the imine to give a ketone plus ammonia. Glutamate, for instance, is converted by this process into α-ketoglutarate. Show the structure of the imine intermediate, and propose mechanisms for both steps.**

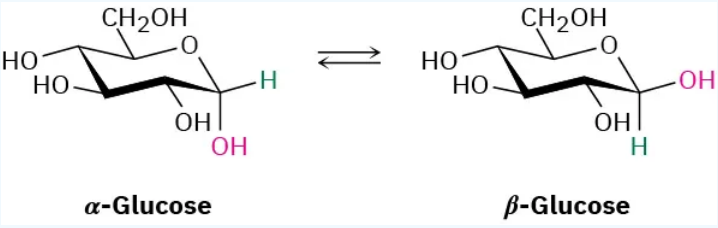


Glutamate **α-Ketoglutarate**

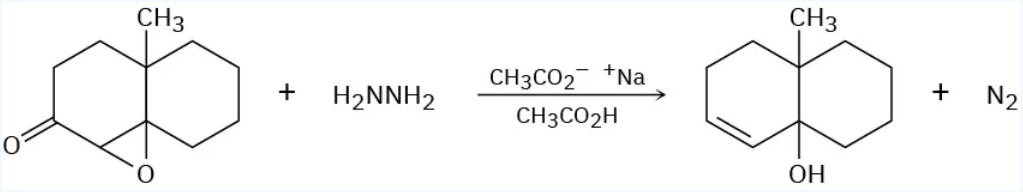
Primary amines react with esters to yield amides: $RCO_2R' + R''NH_2 \rightarrow RCONHR'' + R'OH$. Propose a mechanism for the following reaction of an α,β-unsaturated ester.



When crystals of pure α-glucose are dissolved in water, isomerization occurs slowly to produce β-glucose. Propose a mechanism for the isomerization.



The Wharton reaction converts an epoxy ketone to an allylic alcohol by reaction with hydrazine. Review the Wolff–Kishner reaction in Section 19.9 and then propose a mechanism.

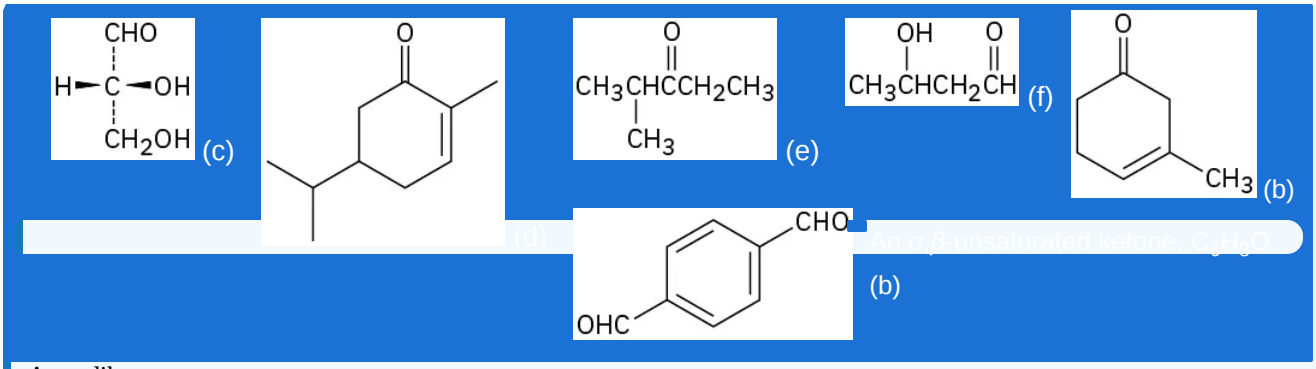


Naming Aldehydes and Ketones

Bromoacetone

(b) (*S*)-2-Hydroxypropanal (c) 2-Methyl-3-heptanone (d) (2*S*,3*R*)-2,3,4-Trihydroxybutanal (e) 2,2,4,4-Tetramethyl-3-pentanone (f) 4-Methyl-3-penten-2-one (g) Butanedial (h) 3-Phenyl-2-propenal (i) 6,6-Dimethyl-2,4-cyclohexadienone (j) *p*-Nitroacetophenone

Draw and name the seven aldehydes and ketones with the formula $C_5H_{10}O$. Which are chiral?

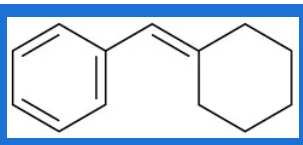


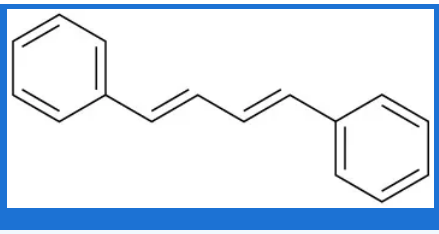
(c) An aromatic ketone, $C_9H_{10}O$ (d) A diene aldehyde, C_7H_8O

Reactions of Aldehydes and Ketones

$NaBH_4$, then H_3O^+

(b) Dess–Martin reagent (c) NH_2OH, HCl catalyst (d) CH_3MgBr, then H_3O^+ (e) 2 CH_3OH, HCl catalyst (f) H_2NNH_2, KOH (g) $(C_6H_5)_3P$ Unexpected text node: ' CH' $_2$ (h) HCN, KCN



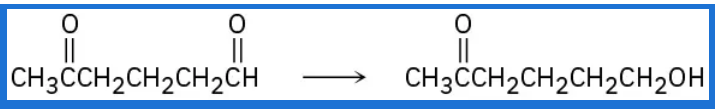


(b)

2-Pentanol

(b)

1-Butanol (c) 1-Phenylcyclohexanol (d) Diphenylmethanol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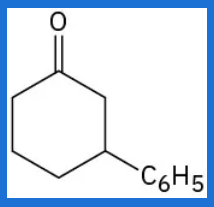
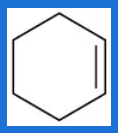

(c)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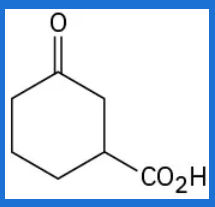
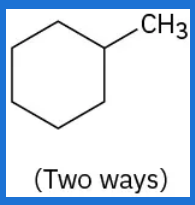
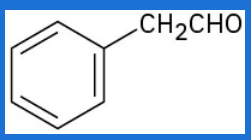
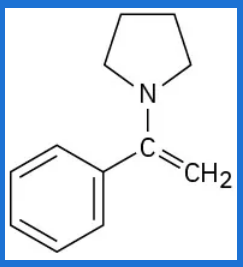
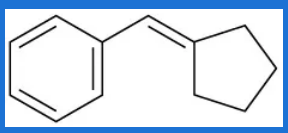

(d)



Problem 19-62 How would you synthesize the following substances from benzaldehyde and any other reagents needed? (a)

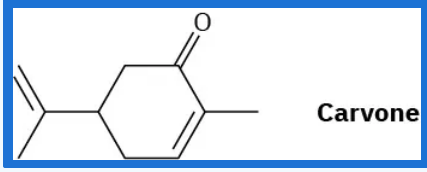

(b)


(c)



Problem 19-63

Carvone is the major constituent of spearmint oil. What products would you expect from reaction of carvone with the following reagents?



(a)

$(CH_3)_2CuLi$, then H_3O^+

(b)

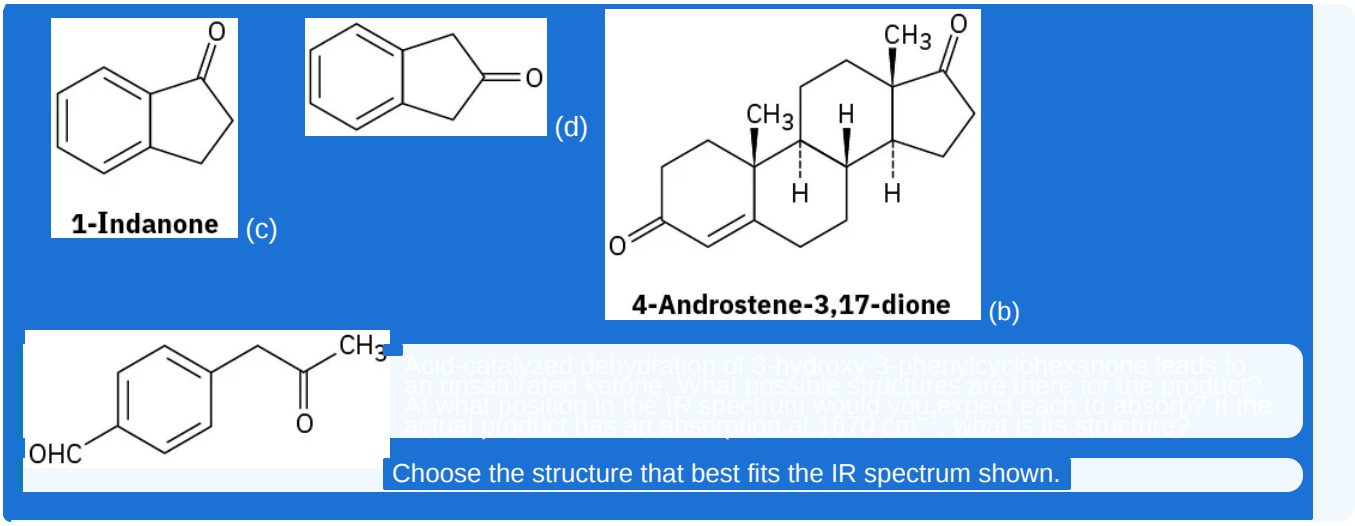
$LiAlH_4$, then H_3O^+

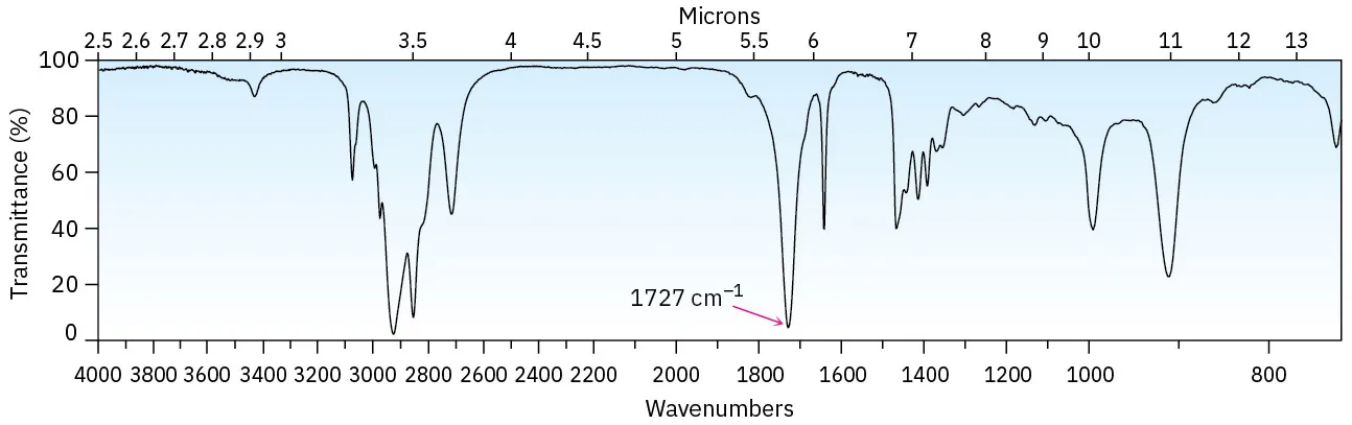
(c) CH_3NH_2 (d) C_6H_5MgBr, then H_3O^+ (e) H_2/Pd (f) $HOCH_2CH_2OH$, HCl (g) $(C_6H_5)_3\overset{+}{P}\overset{-}{C}HCH_3$

1-Methylcyclohexene

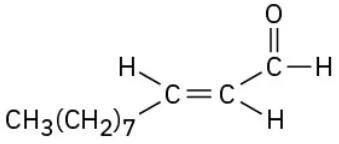
(b) 2-Phenylcyclohexanone (c) *cis*-1,2-Cyclohexanediol (d) 1-Cyclohexylcyclohexanol

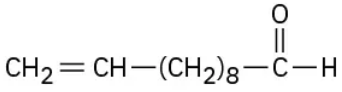
Spectroscopy

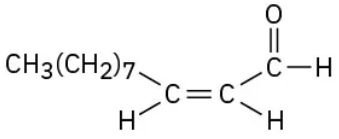


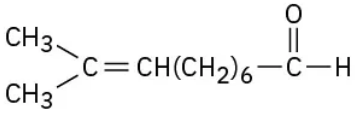


(a)


(b)


(c)


(d)

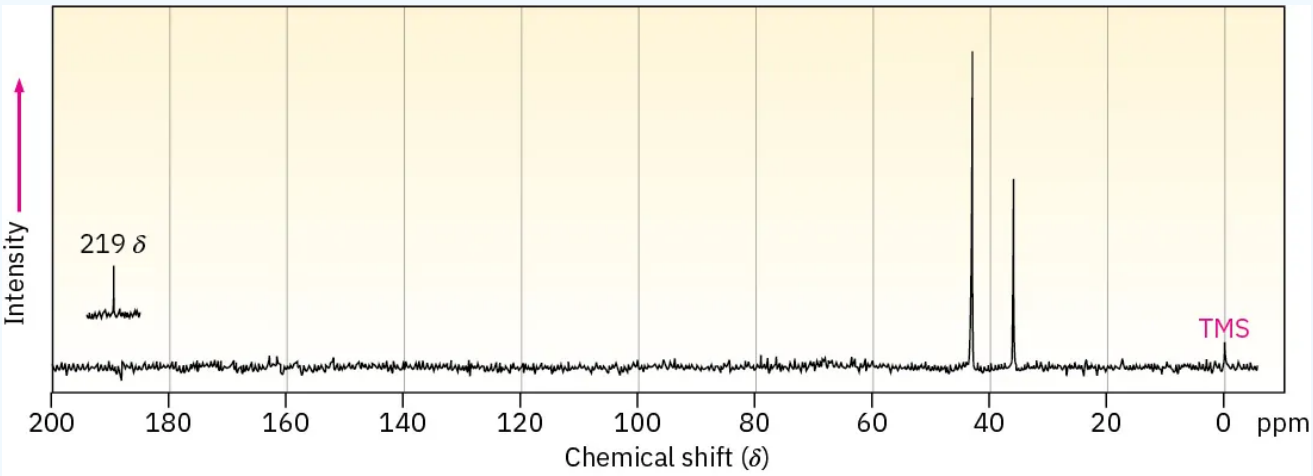


Problem 19-68 Propose structures for molecules that meet the following descriptions. Assume that the kinds of carbons (1°, 2°, 3°, or 4°) have been assigned by DEPT–NMR. (a)

$C_6H_{12}O$; IR: 1715 cm^{-1}; ^{13}C NMR: 8.0 δ (1°), 18.5 δ (1°), 33.5 δ (2°), 40.6 δ (3°), 214.0 δ (4°) (b)

$C_5H_{10}O$; IR: 1730 cm^{-1}; ^{13}C NMR: 22.6 δ (1°), 23.6 δ (3°), 52.8 δ (2°), 202.4 δ (3°) (c) C_6H_8O; IR: 1680 cm^{-1}; ^{13}C NMR: 22.9 δ (2°), 25.8 δ (2°), 38.2 δ (2°), 129.8 δ (3°), 150.6 δ (3°), 198.7 δ (4°)

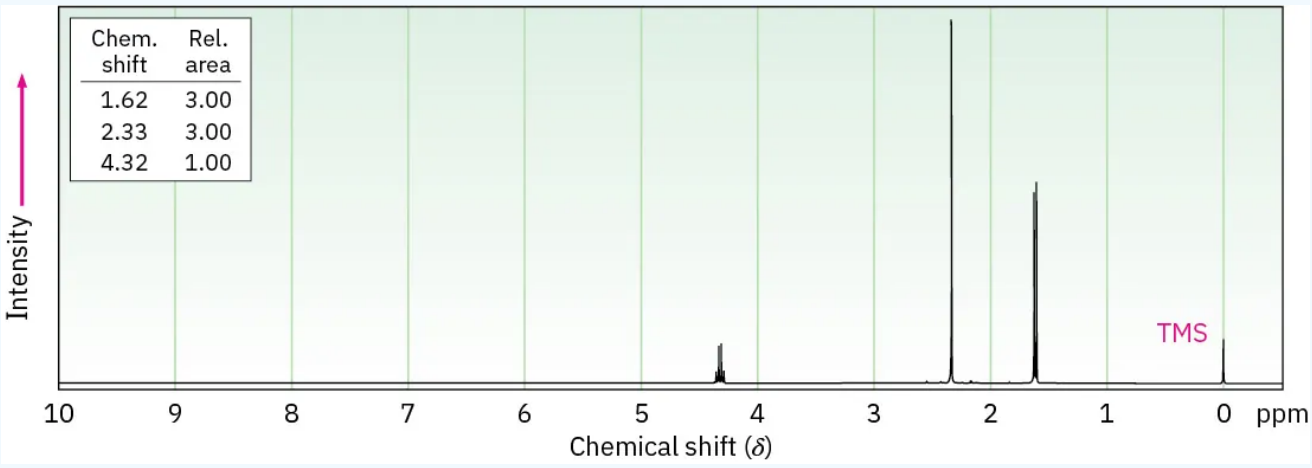
Compound **A**, $C_8H_{10}O_2$, has an intense IR absorption at 1750 cm^{-1} and gives the ^{13}C NMR spectrum shown. Propose a structure for **A**.



1H NMR spectra: (a)

C_4H_7ClO

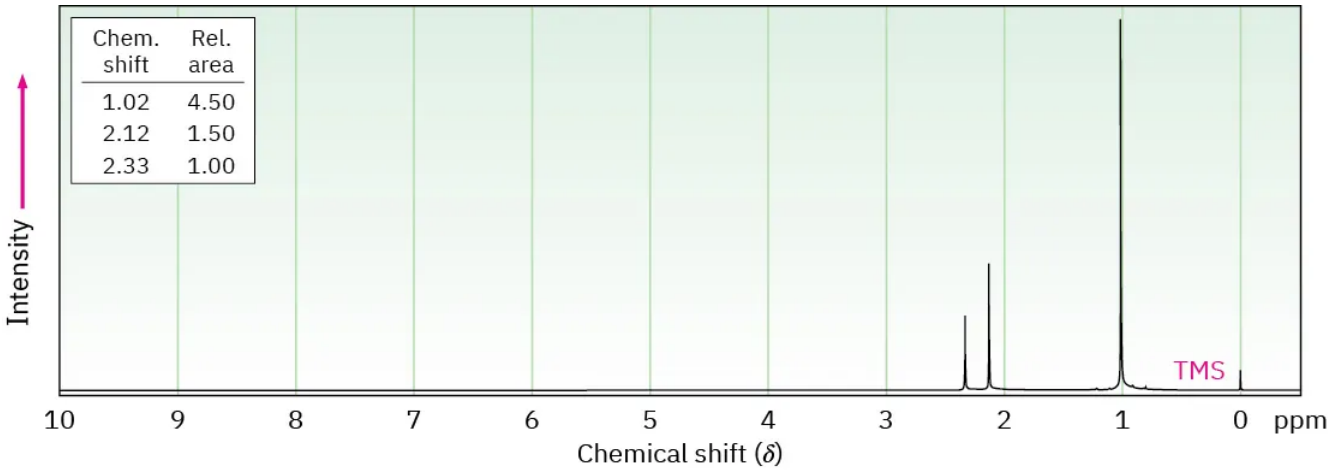
IR: 1715 cm^{-1}



(b)

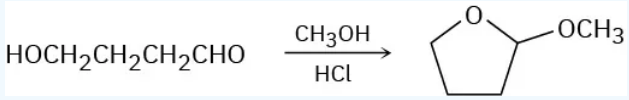
$C_7H_{14}O$

IR: 1710 cm^{-1}



General Problems

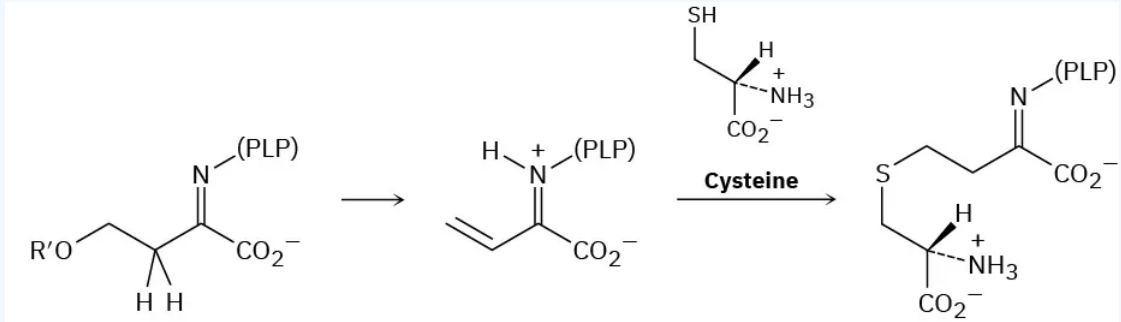
When 4-hydroxybutanal is treated with methanol in the presence of an acid catalyst, 2-methoxytetrahydrofuran is formed. Explain.



The S_N2 reaction of (dibromomethyl)benzene, $C_6H_5CHBr_2$, with NaOH yields benzaldehyde rather than (dihydroxymethyl)benzene, $C_6H_5CH(OH)_2$. Explain.

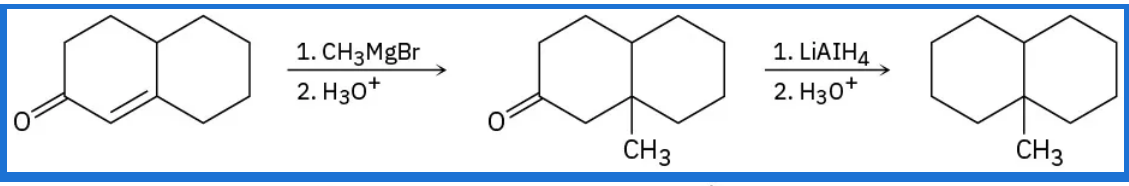
Reaction of 2-butanone with HCN yields a chiral product. What stereochemistry does the product have? Is it optically active?

The amino acid methionine is biosynthesized by a multistep route that includes reaction of an imine of pyridoxal phosphate (PLP) to give an unsaturated imine, which then reacts with cysteine. What kinds of reactions are occurring in the two steps?

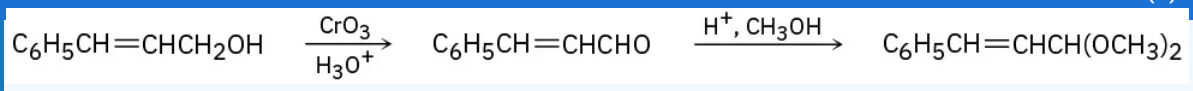


***O*-Succinylhomoserine–PLP imine**

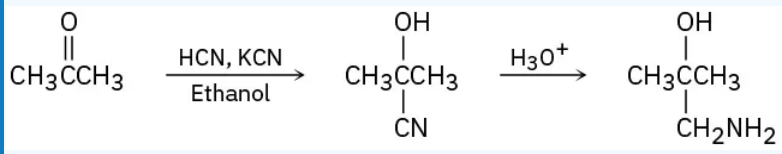
Unsaturated imine



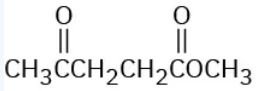
(b)



(c)

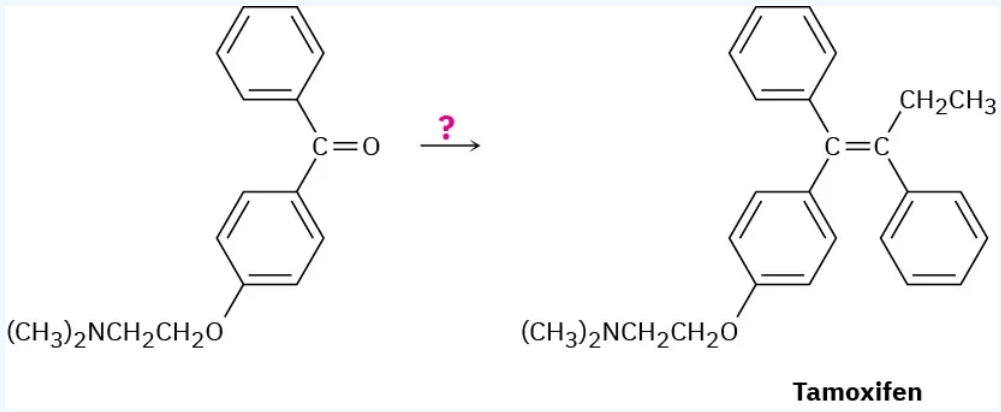


6-Methyl-5-hepten-2-one is a constituent of lemongrass oil. How could you synthesize this substance from methyl 4-oxopentanoate?



Methyl 4-oxopentanoate

Tamoxifen is a drug used in the treatment of breast cancer. How would you prepare tamoxifen from benzene, the following ketone, and any other reagents needed?

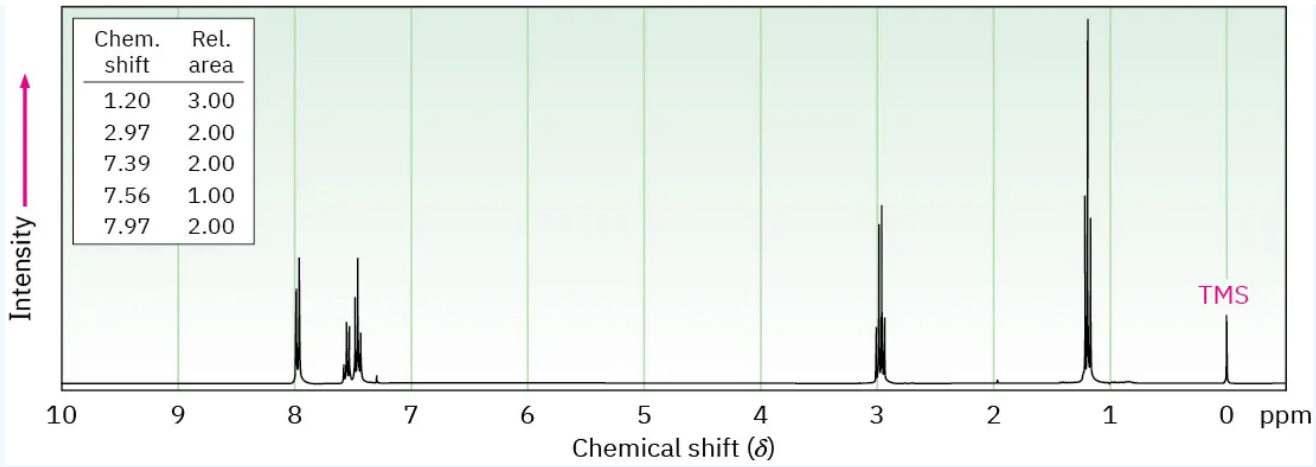


Tamoxifen

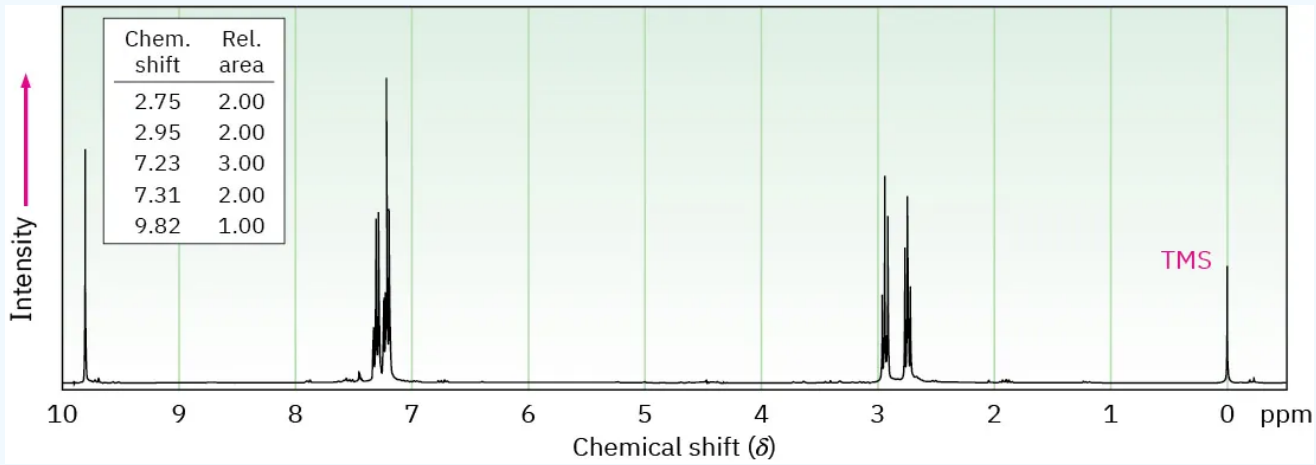
Compound **A**, MW = 86, shows an IR absorption at 1730 cm^{-1} and a very simple ^1H NMR spectrum with peaks at 9.7 δ (1 H, singlet) and 1.2 δ (9 H, singlet). Propose a structure for **A**.

Compound **B** is isomeric with **A** (Problem 19-78) and shows an IR peak at 1715 cm^{-1}. The ^1H NMR spectrum of **B** has peaks at 2.4 δ (1 H, septet, J = 7 Hz), 2.1 δ (3 H, singlet), and 1.2 δ (6 H, doublet, J = 7 Hz). What is the structure of **B**?

The ^1H NMR spectrum shown is that of a compound with the formula $C_9H_{10}O$. How many double bonds and/or rings does this compound contain? If the unknown compound has an IR absorption at 1690 cm^{-1}, what is a likely structure?

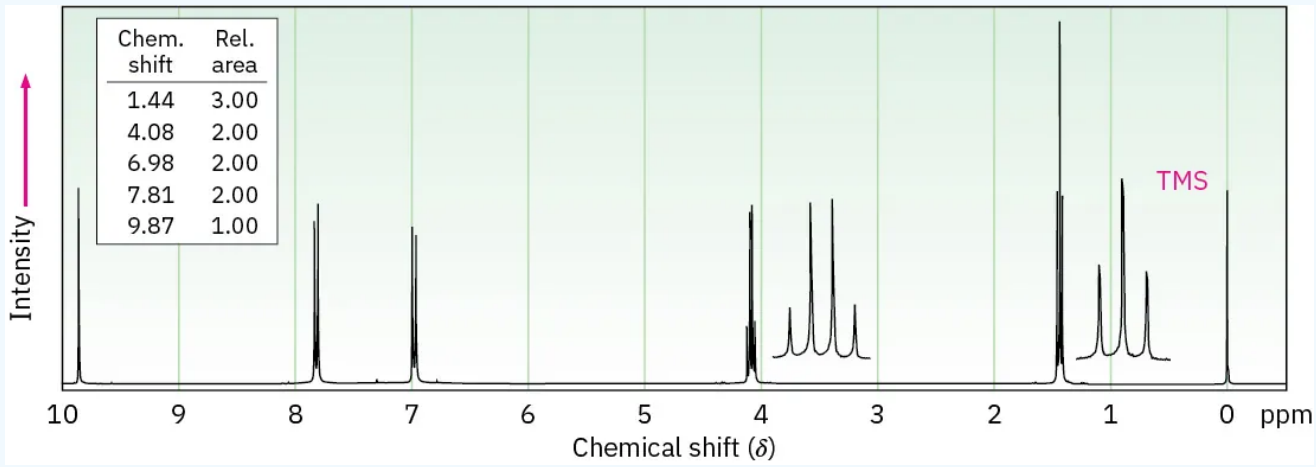


The ^{1}H NMR spectrum shown is that of a compound isomeric with the one in Problem 19-80. This isomer has an IR absorption at 1730 cm^{-1}. Propose a structure. [*Note:* Aldehyde protons (CHO) often show low coupling constants to adjacent hydrogens, so the splitting of aldehyde signals is not always apparent.]



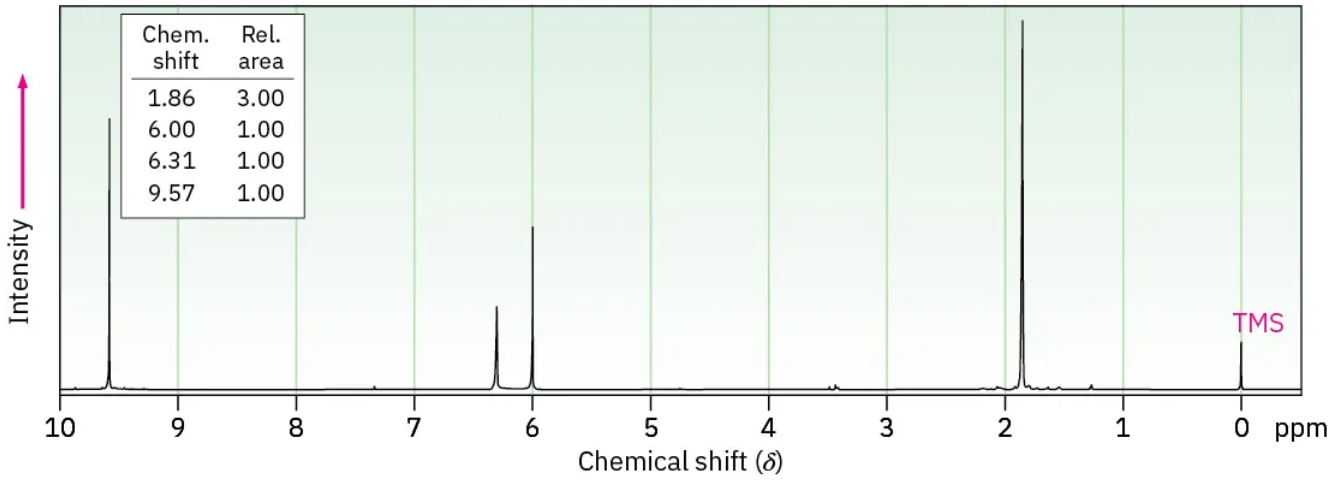
1H NMR spectra: (a)

$C_9H_{10}O_2$: IR: 1695 cm^{-1}



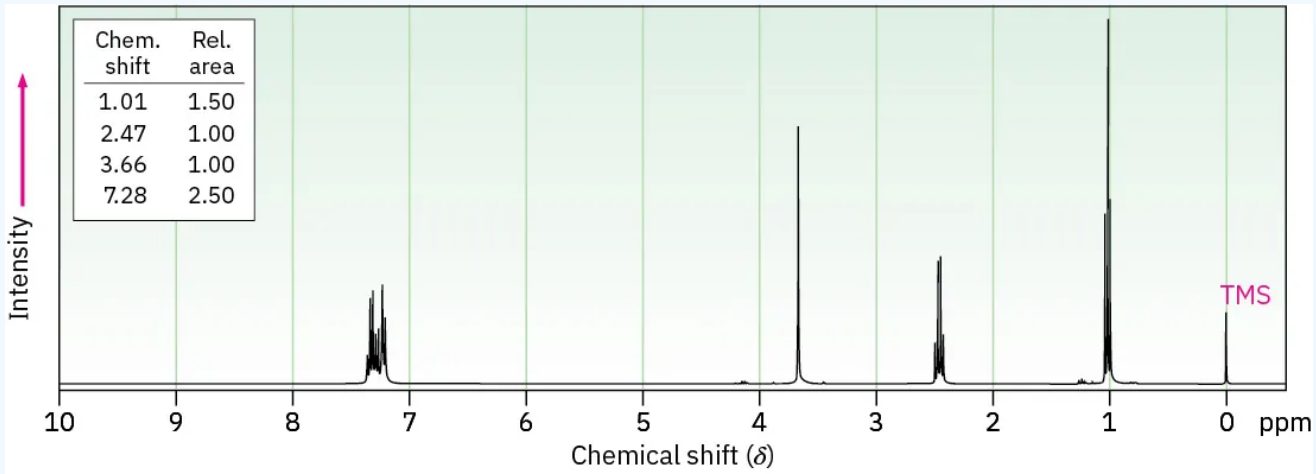
(b)

C_4H_6O: IR: 1690 cm^{-1}



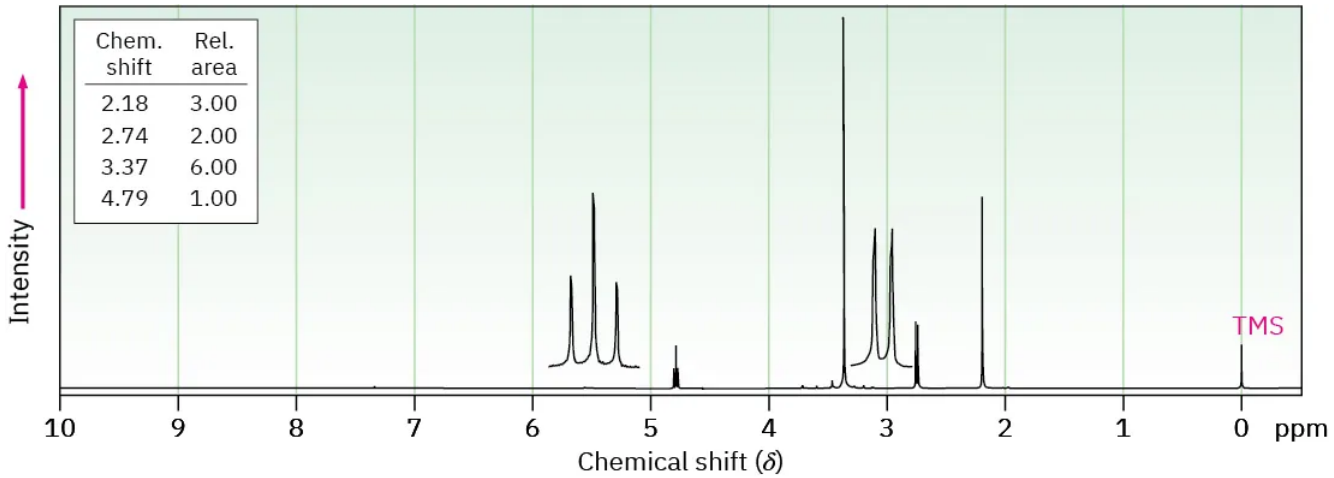
1H NMR spectra. (a)

$C_{10}H_{12}O$: IR: 1710 cm^{-1}

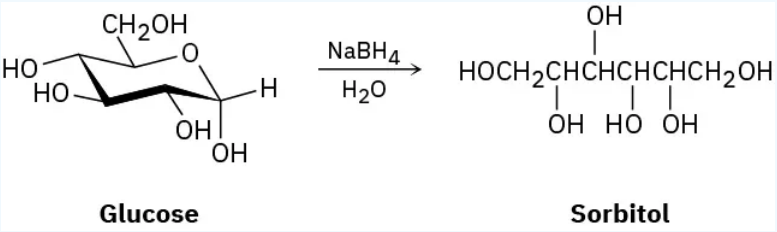


(b)

$C_6H_{12}O_3$: IR: 1715 cm^{-1}

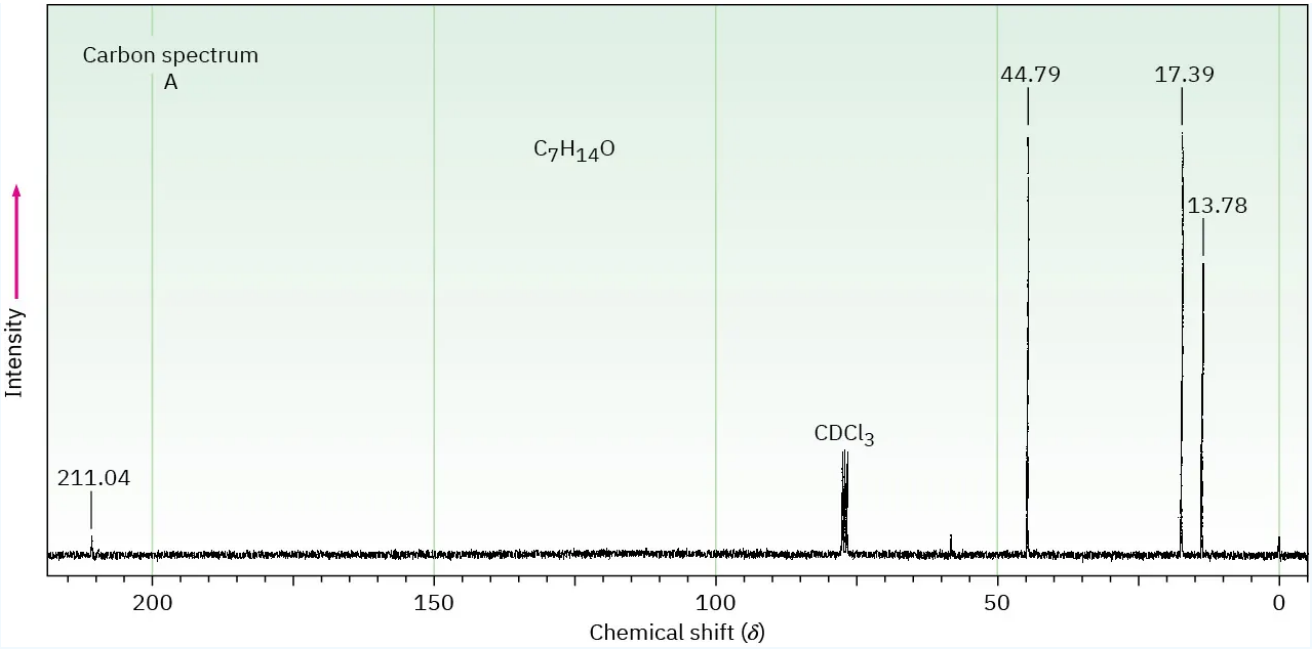


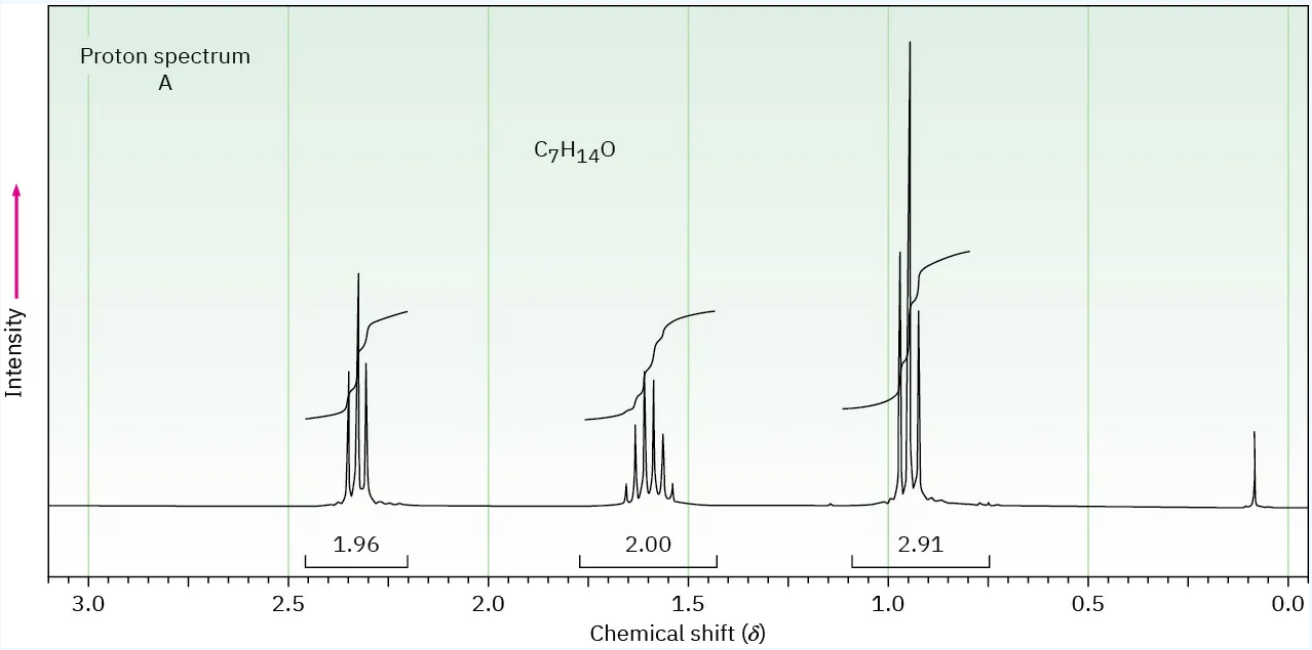
When glucose (Problem 19-51) is treated with $NaBH_4$, reaction occurs to yield *sorbitol*, a polyalcohol commonly used as a food additive. Show how this reduction occurs.

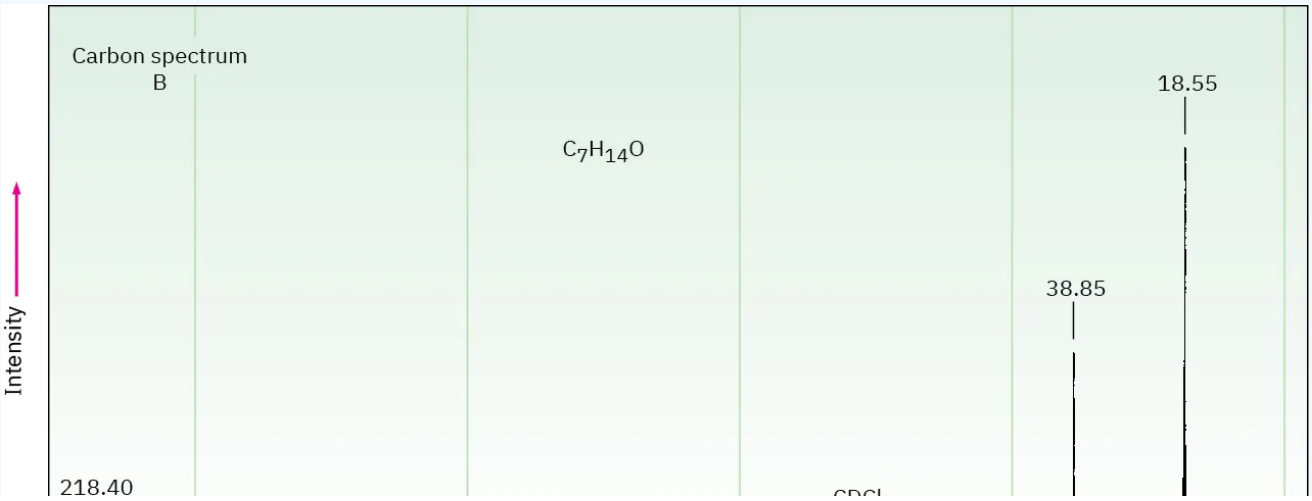


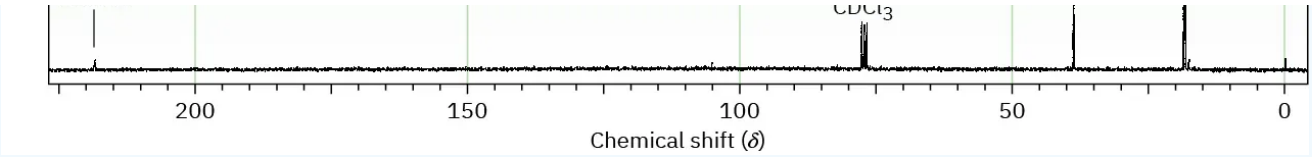
Glucose **Sorbitol**

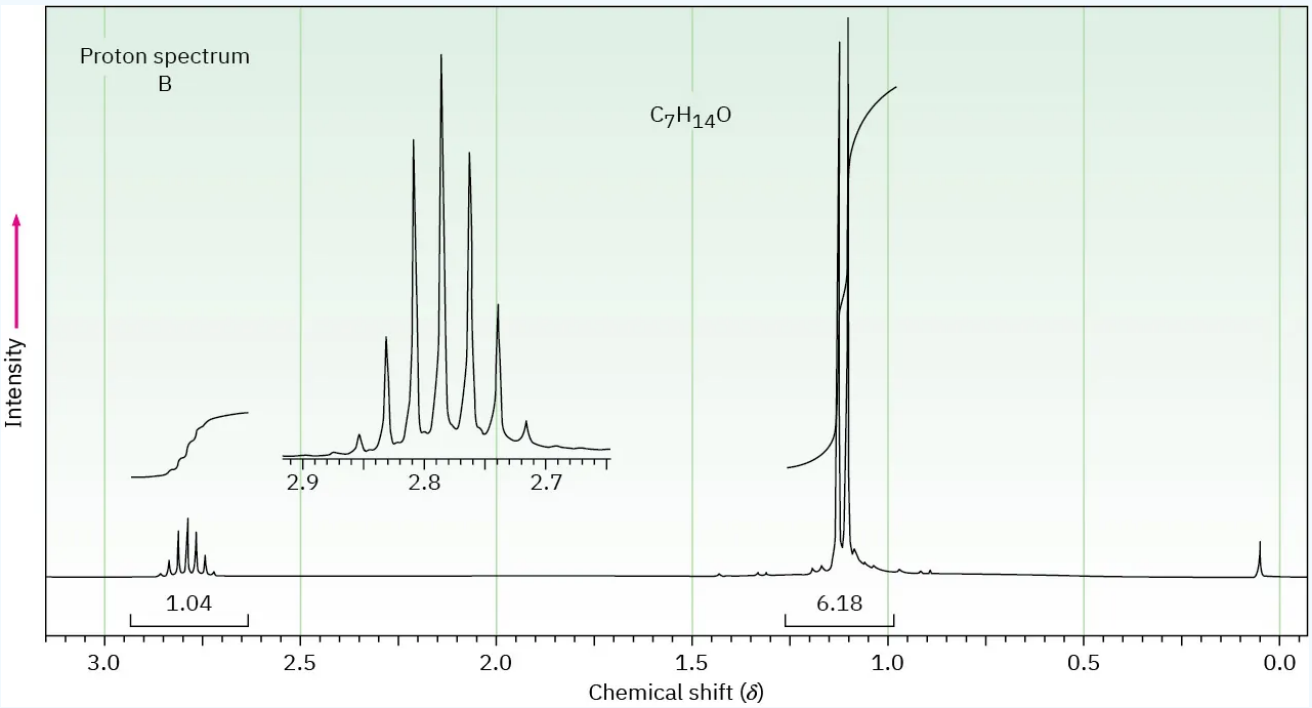
The proton and carbon NMR spectra for each of three isomeric ketones with the formula $C_7H_{14}O$ are shown. Assign a structure to each pair of spectra.

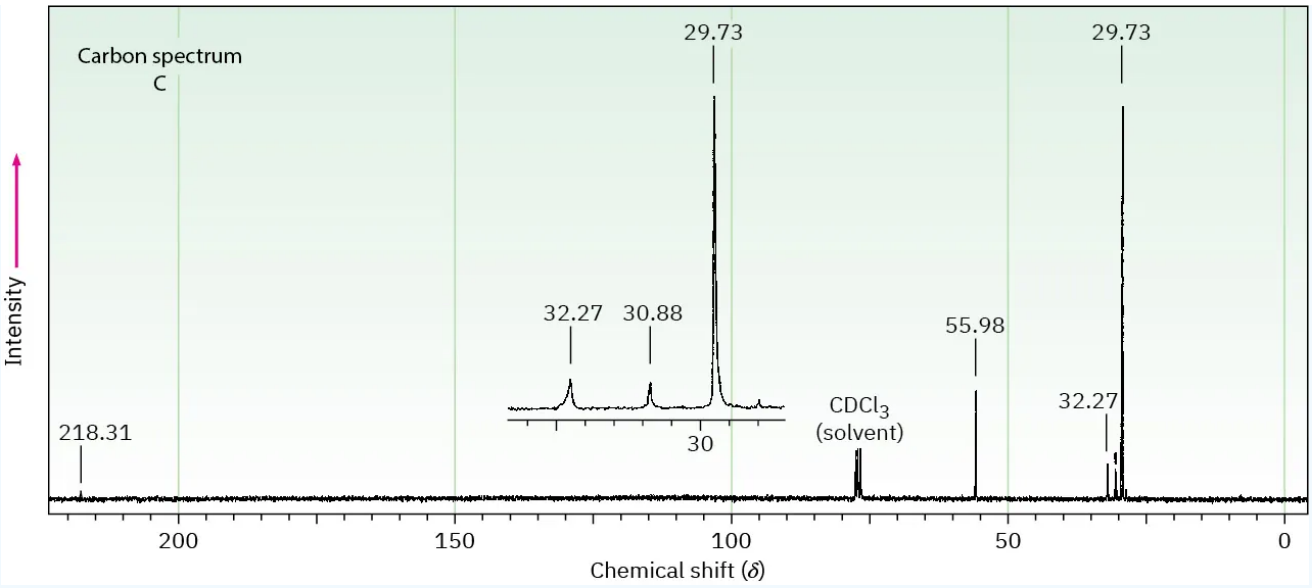


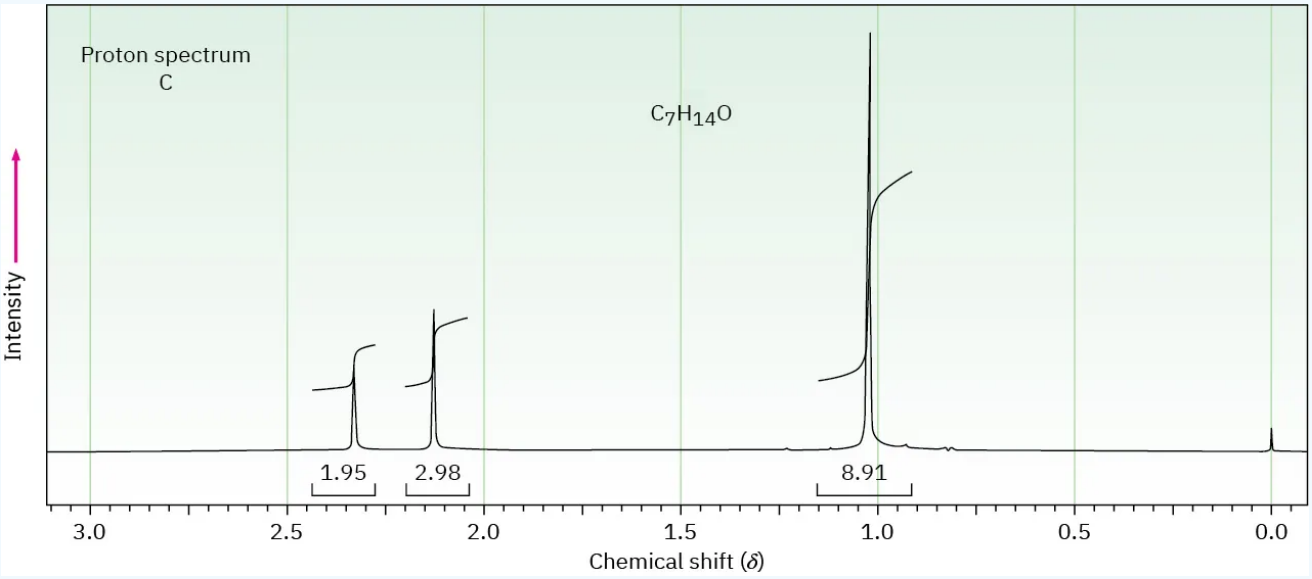




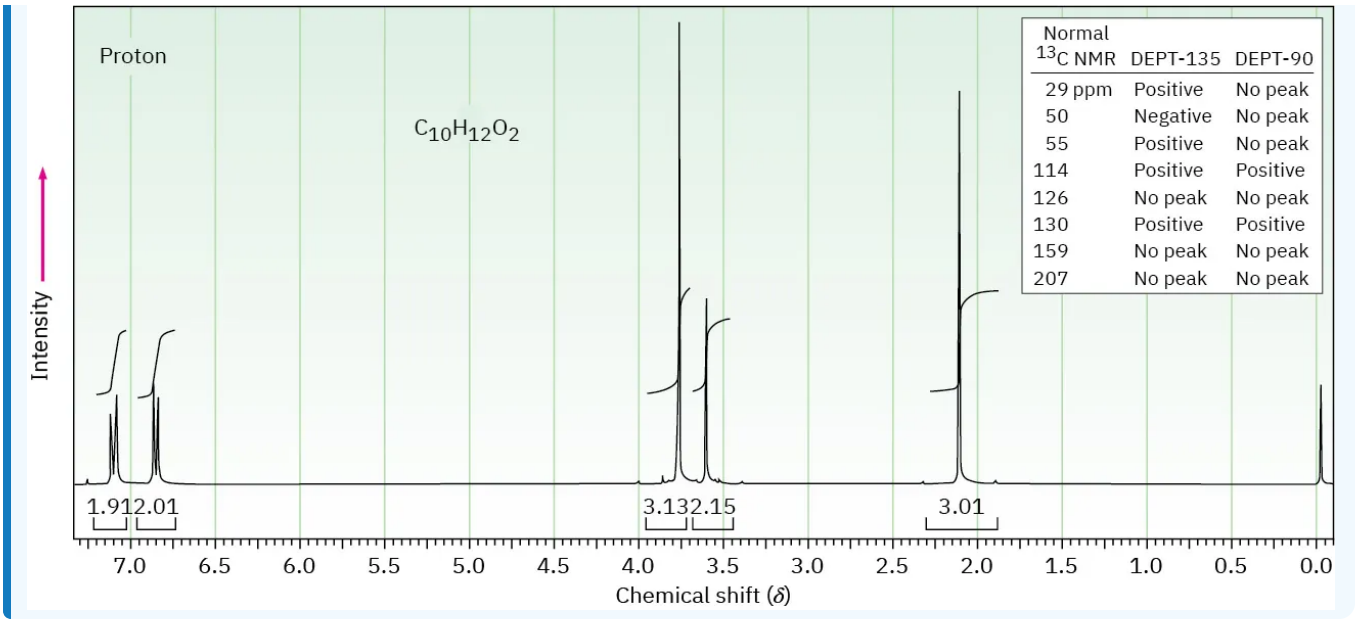

$CDCl_3$
200
150
100
50
0
Chemical shift (δ)


Proton spectrum
B
$C_7H_{14}O$
Intensity
2.9
2.8
2.7
1.04
6.18
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Chemical shift (δ)





The proton NMR spectrum for a compound with formula $C_{10}H_{12}O_2$ is shown below. The infrared spectrum has a strong band at 1711 cm^{-1}. The broadband-decoupled 13C NMR spectral results are tabulated along with the DEPT-135 and DEPT-90 information. Draw the structure of this compound.



Normal ^{13}C NMR	DEPT-135	DEPT-90
29 ppm	Positive	No peak
50	Negative	No peak
55	Positive	No peak
114	Positive	Positive
126	No peak	No peak
130	Positive	Positive
159	No peak	No peak
207	No peak	No peak