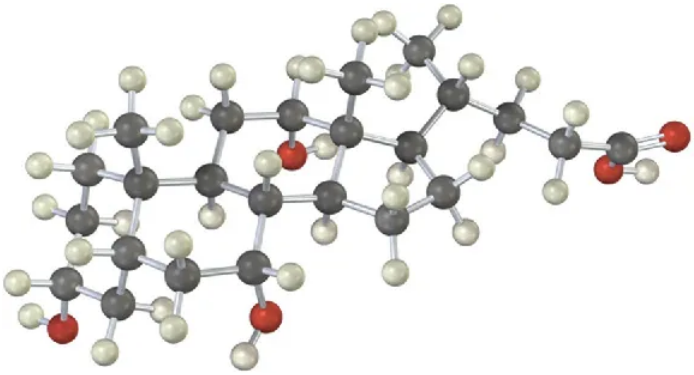
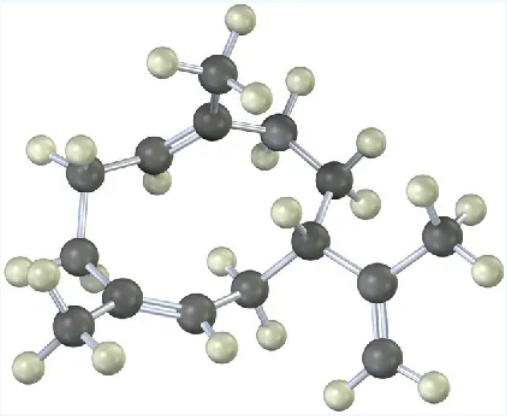
13.9: Additional Problems

Visualizing Chemistry

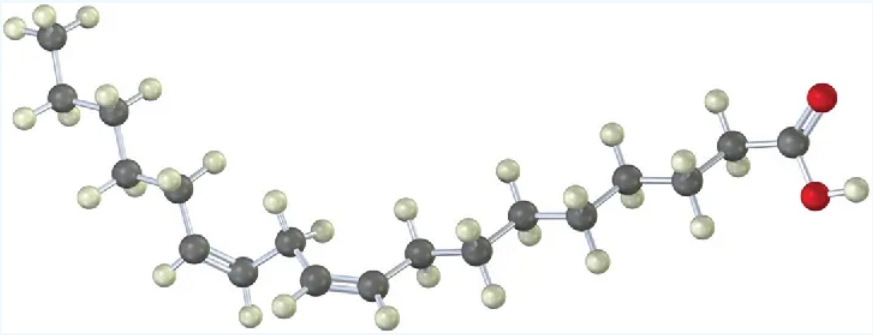
The following model is that of cholic acid, a constituent of human bile. Locate the three hydroxyl groups, and identify each as axial or equatorial. Is cholic acid an A–B trans steroid or an A–B cis steroid?



Propose a biosynthetic pathway for the sesquiterpenoid helminthogermacrene from farnesyl diphosphate.

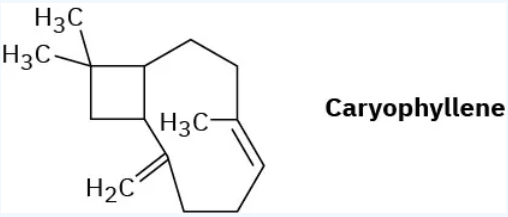


Identify the following fatty acid, and tell whether it is more likely to be found in peanut oil or in red meat:



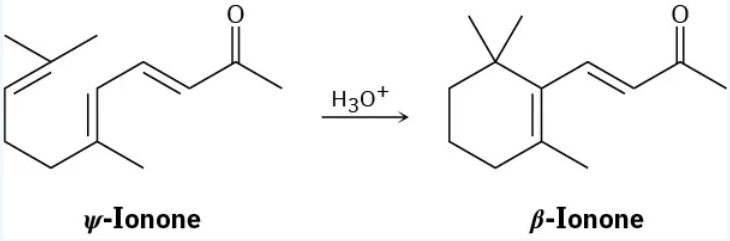
Mechanism Problems

Propose a mechanistic pathway for the biosynthesis of caryophyllene, a substance found in clove oil.



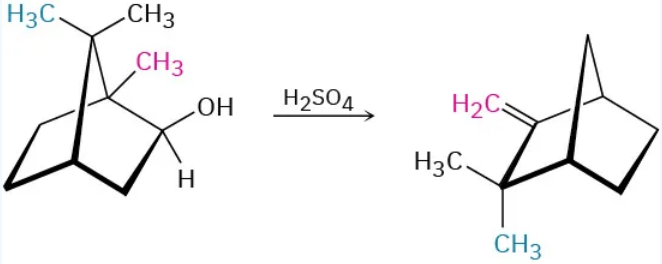
Caryophyllene

Suggest a mechanism by which ψ-ionone is transformed into β-ionone on treatment with acid.



ψ-Ionone **β-Ionone**

Isoborneol is converted into camphene on treatment with dilute sulfuric acid. Propose a mechanism for the reaction, which involves a carbocation rearrangement.



Isoborneol **Camphene**

Fats, Oils, and Related Lipids

Fatty fish like salmon and albacore are rich in *omega-3* fatty acids, which have a double bond three carbons in from the noncarboxyl end of the chain and have been shown to lower blood cholesterol levels. Draw the structure of 5,8,11,14,17-eicosapentaenoic acid, a common example. (Eicosane = $C_{20}H_{42}$.)

Fats can be either optically active or optically inactive, depending on their structure. Draw the structure of an optically active fat that yields 2 equivalents of stearic acid and 1 equivalent of oleic acid on hydrolysis. Draw the structure of an optically inactive fat that yields the same products.

Spermaceti, a fragrant substance from sperm whales, was widely used in cosmetics until it was banned in 1976 to protect whales from extinction. Chemically, spermaceti is cetyl palmitate, the ester of cetyl alcohol (n-$C_{16}H_{33}OH$) with palmitic acid. Draw its structure.

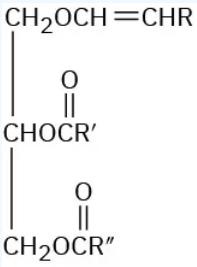
Excess Br_2 in CH_2Cl_2

(b) H_2/Pd (c) NaOH/H_2O (d) O_3, then Zn/CH_3CO_2H (e) $LiAlH_4$, then H_3O^+ (f) CH_3MgBr, then H_3O^+

Methyl oleate

(b) Methyl stearate (c) Nonanal (d) Nonanedioic acid (e) 9-Octadecynoic acid (stearolic acid) (f) 2-Bromostearic acid (g) 18-Pentatriacontanone, $CH_3(CH_2)_{16}CO(CH_2)_{16}CH_3$

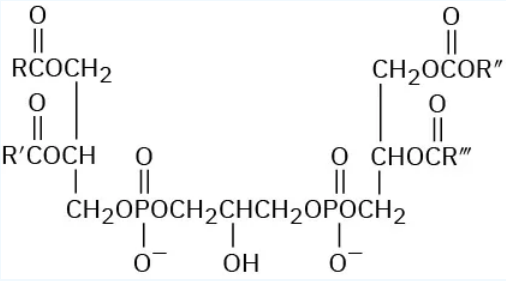
Plasmalogens are a group of lipids found in nerve and muscle cells. How do plasmalogens differ from fats?



A plasmalogen

What products would you obtain from hydrolysis of a plasmalogen (Problem 27-22) with aqueous NaOH? With H_3O^+?

Cardiolipins are a group of lipids found in heart muscles. What products would be formed if all ester bonds, including phosphates, were saponified by treatment with aqueous NaOH?

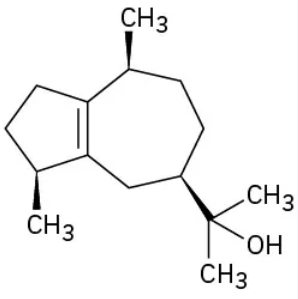


A cardiolipin

Stearolic acid, $C_{18}H_{32}O_2$, yields stearic acid on catalytic hydrogenation and undergoes oxidative cleavage with ozone to yield nonanoic acid and nonanedioic acid. What is the structure of stearolic acid?

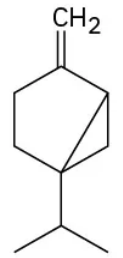
How would you synthesize stearolic acid (Problem 27-25) from 1-decyne and 1-chloro-7-iodoheptane?

Terpenoids and Steroids



Guaiol

(b)



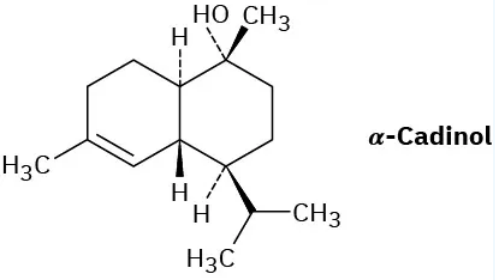
Sabinene

Problem 27-28
Indicate by asterisks the chirality centers present in each of the terpenoids shown in Problem 27-27. What is the maximum possible number of stereoisomers for each?

Assume that the three terpenoids in Problem 27-27 are derived biosynthetically from isopentenyl diphosphate and dimethylallyl diphosphate, each of which was isotopically labeled at the diphosphate-bearing carbon atom (C1). At what positions would the terpenoids be isotopically labeled?

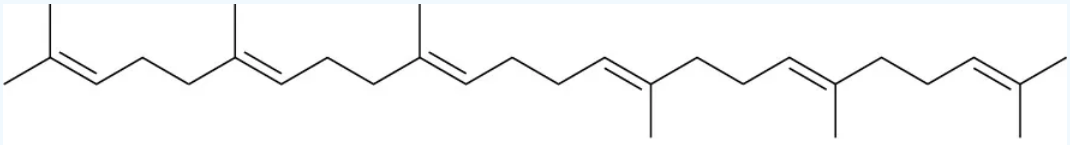
Assume that acetyl CoA containing a ^{14}C isotopic label in the carboxyl carbon atom is used as starting material for the biosynthesis of mevalonate, as shown in Figure 27.8. At what positions in mevalonate would the isotopic label appear?

Assume that acetyl CoA containing a ^{14}C isotopic label in the carboxyl carbon atom is used as starting material and that the mevalonate pathway is followed. Identify the positions in α-cadinol where the label would appear.



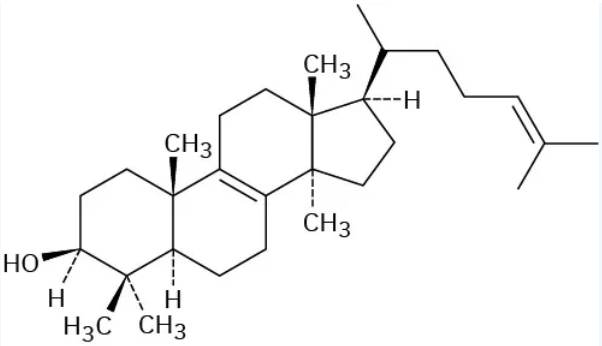
α-Cadinol

Assume that acetyl CoA containing a ^{14}C isotopic label in the carboxyl carbon atom is used as starting material and that the mevalonate pathway is followed. Identify the positions in squalene where the label would appear.



Squalene

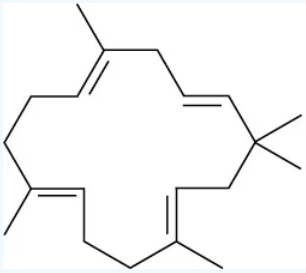
Assume that acetyl CoA containing a ^{14}C isotopic label in the carboxyl carbon atom is used as starting material and that the mevalonate pathway is followed. Identify the positions in lanosterol where the label would appear.



Lanosterol

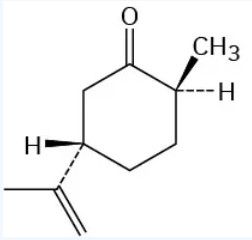
General Problems

Flexibilene, a compound isolated from marine coral, is the first known terpenoid to contain a 15-membered ring. What is the structure of the acyclic biosynthetic precursor of flexibilene? Show the mechanistic pathway for the biosynthesis.



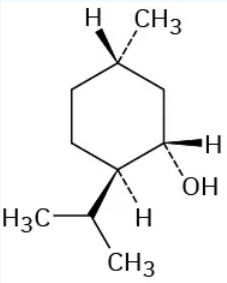
Flexibilene

Draw the most stable chair conformation of dihydrocarvone.

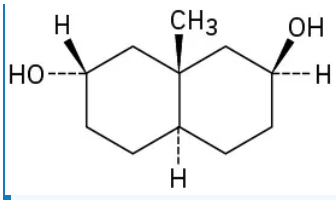


Dihydrocarvone

Draw the most stable chair conformation of menthol, and label each substituent as axial or equatorial.



Menthol (from peppermint oil)



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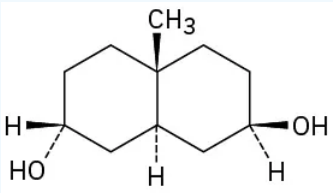
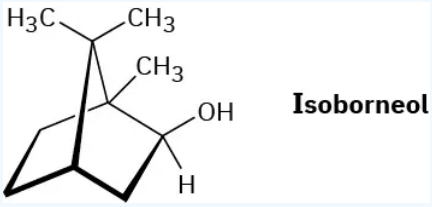


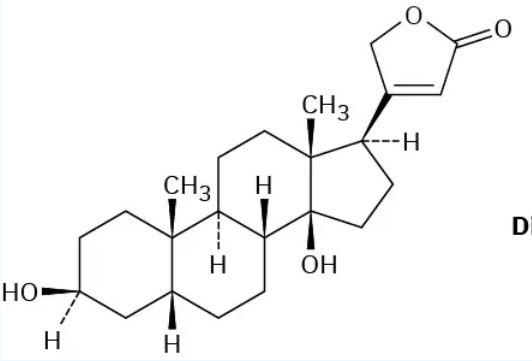
Problem 27-38

Propose a mechanistic pathway for the biosynthesis of isoborneol. A carbocation rearrangement is needed at one point in the scheme.



Isoborneol

Digitoxigenin is a heart stimulant obtained from the purple foxglove *Digitalis purpurea* and used in the treatment of heart disease. Draw the three-dimensional conformation of digitoxigenin, and identify the two –OH groups as axial or equatorial.



Digitoxigenin

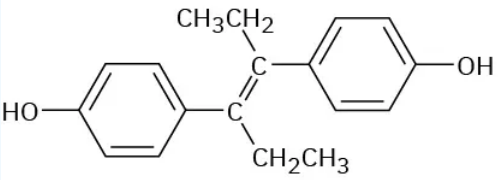
What product would you obtain by reduction of digitoxigenin (Problem 27-39) with $LiAlH_4$? By oxidation with the Dess–Martin periodinane?

Vaccenic acid, $C_{18}H_{34}O_2$, is a rare fatty acid that gives heptanal and 11-oxoundecanoic acid $[OHC(CH_2)_9CO_2H]$ on ozonolysis followed by zinc treatment. When allowed to react with $CH_2I_2/Zn(Cu)$, vaccenic acid is converted into lactobacillic acid. What are the structures of vaccenic and lactobacillic acids?

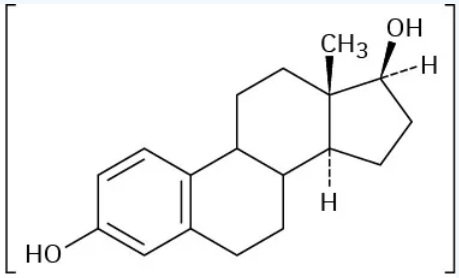
Eleostearic acid, $C_{18}H_{30}O_2$, is a rare fatty acid found in the tung oil used for finishing furniture. On ozonolysis followed by treatment with zinc, eleostearic acid furnishes one part pentanal, two parts glyoxal (OHC–CHO), and one part 9-oxononanoic acid $[OHC(CH_2)_7CO_2H]$. What is the structure of eleostearic acid?

Diterpenoids are derived biosynthetically from geranylgeranyl diphosphate (GGPP), which is itself biosynthesized by reaction of farnesyl diphosphate with isopentenyl diphosphate. Show the structure of GGPP, and propose a mechanism for its biosynthesis from FPP and IPP.

Diethylstilbestrol (DES) has estrogenic activity even though it is structurally unrelated to steroids. Once used as an additive in animal feed, DES has been implicated as a causative agent in several types of cancer. Show how DES can be drawn so that it is sterically similar to estradiol.

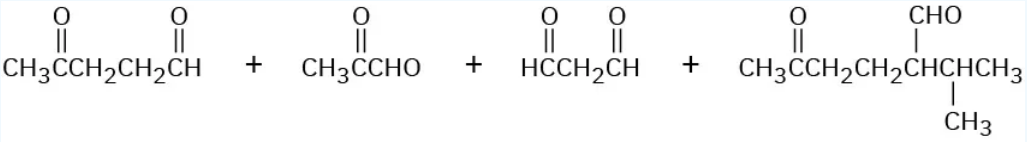


Diethylstilbestrol



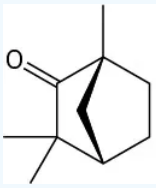
Estradiol

Cembrene, $C_{20}H_{32}$, a diterpenoid hydrocarbon isolated from pine resin, has a UV absorption at 245 nm, but dihydrocembrene ($C_{20}H_{34}$), the product of hydrogenation with 1 equivalent of H_2, has no UV absorption. On exhaustive hydrogenation, 4 equivalents of H_2 react, and octahydrocembrene, $C_{20}H_{40}$, is produced. On ozonolysis of cembrene, followed by treatment of the ozonide with zinc, four carbonyl-containing products are obtained:



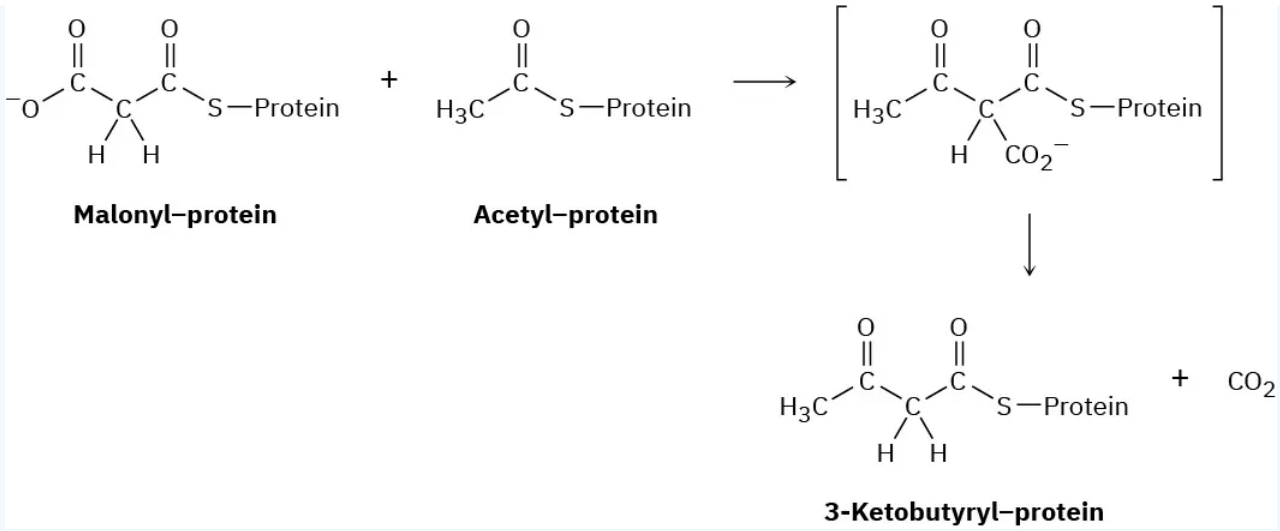
Propose a structure for cembrene that is consistent with its formation from geranylgeranyl diphosphate.

α-Fenchone is a pleasant-smelling terpenoid isolated from oil of lavender. Propose a pathway for the formation of α-fenchone from geranyl diphosphate. A carbocation rearrangement is required.



α-Fenchone

Fatty acids are synthesized by a multistep route that starts with acetate. The first step is a reaction between protein-bound acetyl and malonyl units to give a protein-bound 3-ketobutyryl unit. Show the mechanism, and tell what kind of reaction is occurring.



Propose a mechanism for the biosynthesis of the sesquiterpenoid trichodiene from farnesyl diphosphate. The process involves cyclization to give an intermediate secondary carbocation, followed by several carbocation rearrangements.