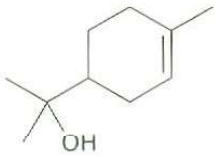
WORKED EXAMPLE 27.1 ***Proposing a Terpenoid Biosynthesis Pathway***

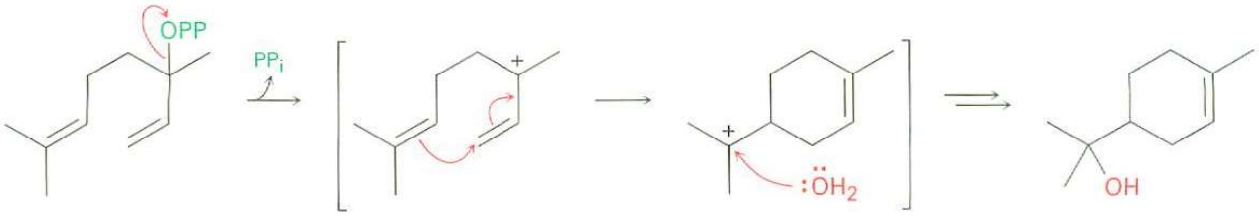
Propose a mechanistic pathway for the biosynthesis of α-terpineol from geranyl diphosphate.



α-Terpineol

Strategy α-Terpineol, a monoterpenoid, must be derived biologically from geranyl diphosphate through its isomer linalyl diphosphate. Draw the precursor in a conformation that approximates the structure of the target molecule, and then carry out a cationic cyclization, using the appropriate double bond to displace the diphosphate leaving group. Since the target is an alcohol, the carbocation resulting from cyclization must react with water.

Solution

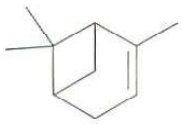


Linalyl diphosphate

α-Terpineol

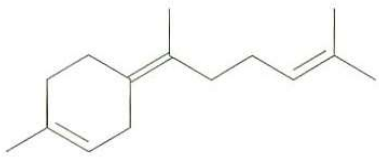
Problem 27.7 Propose mechanistic pathways for the biosynthetic formation of the following terpenes:

(a)



α-Pinene

(b)



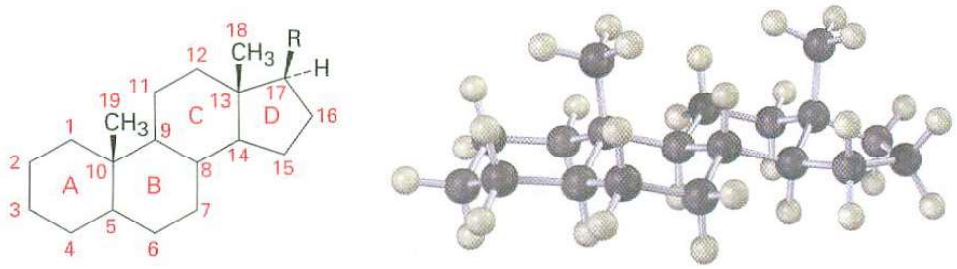
γ-Bisabolene

27.6 Steroids

ThomsonNOW Click *Organic Interactive* to **use a web-based palette to assign *R,S* designations to chiral centers in steroids.**

In addition to fats, phospholipids, eicosanoids, and terpenoids, the lipid extracts of plants and animals also contain **steroids**, molecules that are derived from the triterpene lanosterol (Figure 27.6) and whose structures are based on a tetracyclic ring system. The four rings are designated A, B, C, and D, beginning at the lower left, and the carbon atoms are numbered beginning in the A ring. The three six-membered rings (A, B, and C) adopt chair conformations but are

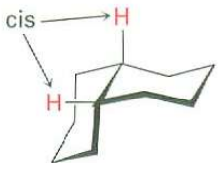
prevented by their rigid geometry from undergoing the usual cyclohexane ring-flips (Section 4.6).

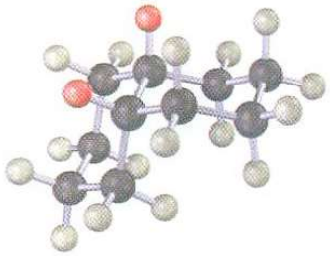


A steroid
(R = various side chains)

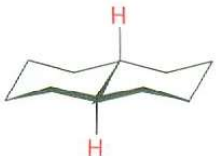
Two cyclohexane rings can be joined in either a cis or a trans manner. With cis fusion to give *cis*-decalin, both groups at the ring-junction positions (the *angular* groups) are on the same side of the two rings. With trans fusion to give *trans*-decalin, the groups at the ring junctions are on opposite sides.

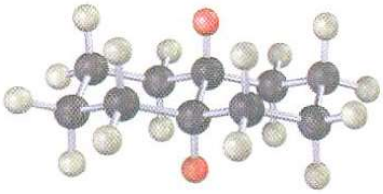
***cis*-Decalin**





***trans*-Decalin**

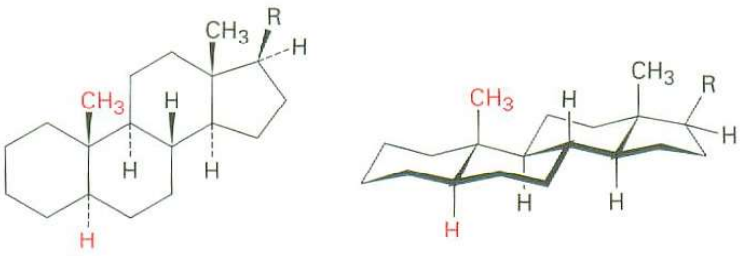




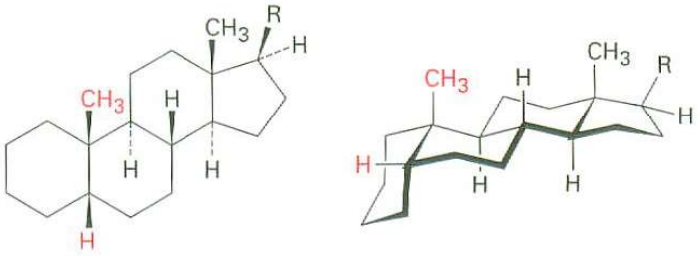
As shown in Figure 27.11, steroids can have either a cis or a trans fusion of the A and B rings, but the other ring fusions (B–C and C–D) are usually trans. An A–B trans steroid has the C19 angular methyl group up, denoted β, and the hydrogen atom at C5 down, denoted α, on opposite sides of the molecule. An A–B cis steroid, by contrast, has both the C19 angular methyl group and the C5 hydrogen atom on the same side (β) of the molecule. Both kinds of steroids are relatively long, flat molecules that have their two methyl groups (C18 and C19) protruding axially above the ring system. The A–B trans steroids are the more common, although A–B cis steroids are found in liver bile.

Figure 27.11 Steroid conformations. The three six-membered rings have chair conformations but are unable to undergo ring-flips. The A and B rings can be either cis-fused or trans-fused.

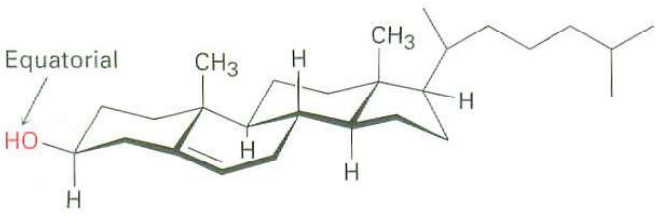
An A–B trans steroid

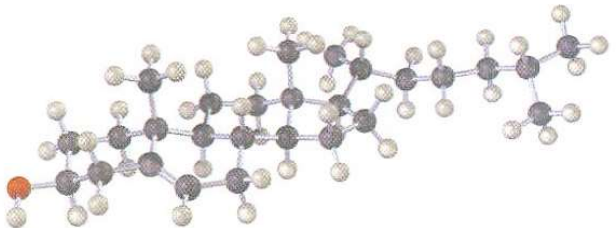


An A–B cis steroid



Substituent groups on the steroid ring system can be either axial or equatorial. As with simple cyclohexanes (Section 4.7), equatorial substitution is generally more favorable than axial substitution for steric reasons. The hydroxyl group at C3 of cholesterol, for example, has the more stable equatorial orientation. Unlike what happens with simple cyclohexanes, however, steroids are rigid molecules whose geometry prevents cyclohexane ring-flips.

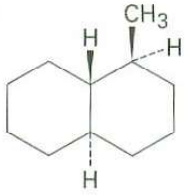




Cholesterol

Problem 27.8 Draw the following molecules in chair conformations, and tell whether the ring substituents are axial or equatorial:

(a)



(b)