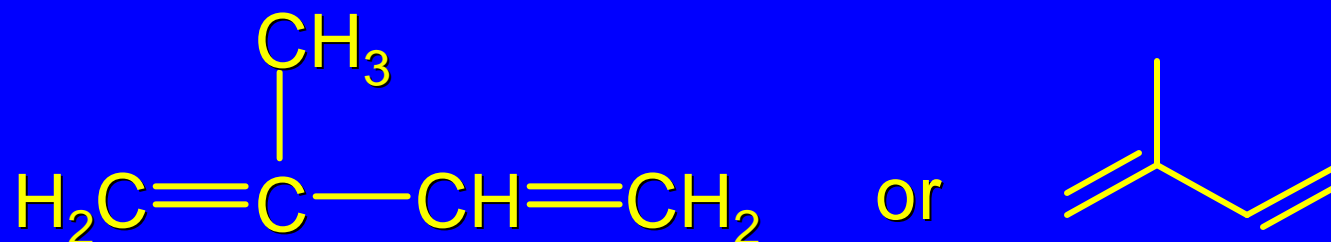


26.7

Terpenes: The Isoprene Rule

Terpenes

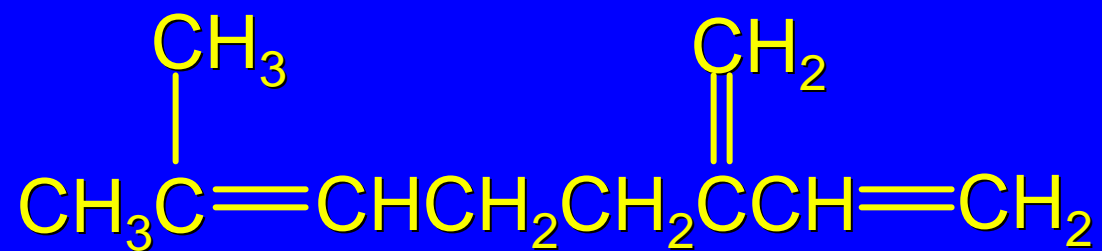
Terpenes are natural products that are structurally related to isoprene.



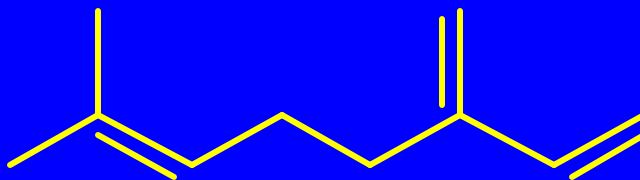
Isoprene
(2-methyl-1,3-butadiene)

Terpenes

Myrcene (isolated from oil of bayberry)
is a typical terpene.

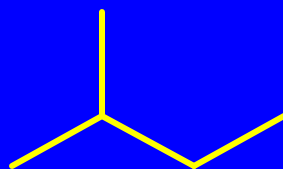


or

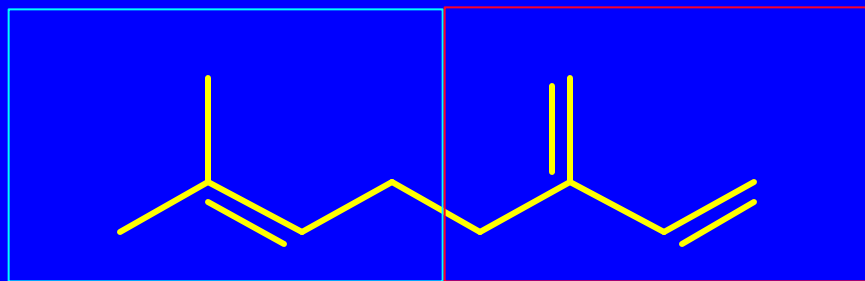


The Isoprene Unit

An isoprene unit is the carbon skeleton of isoprene (ignoring the double bonds)



Myrcene contains two isoprene units.



The Isoprene Unit

The isoprene units of myrcene are joined "head-to-tail."

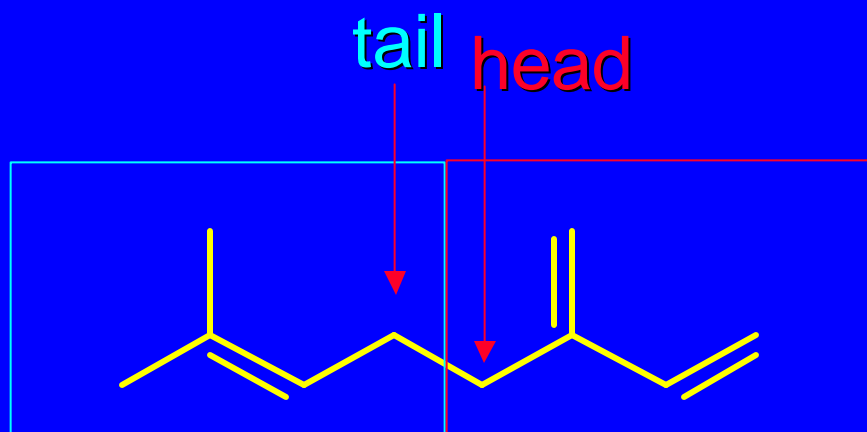
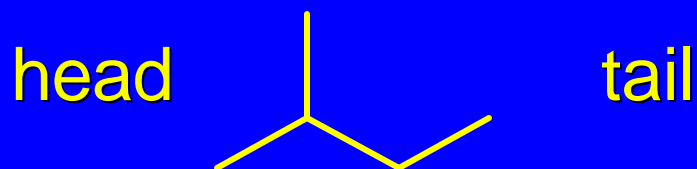


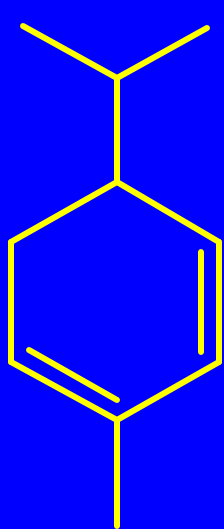
Table 26.2

Classification of Terpenes

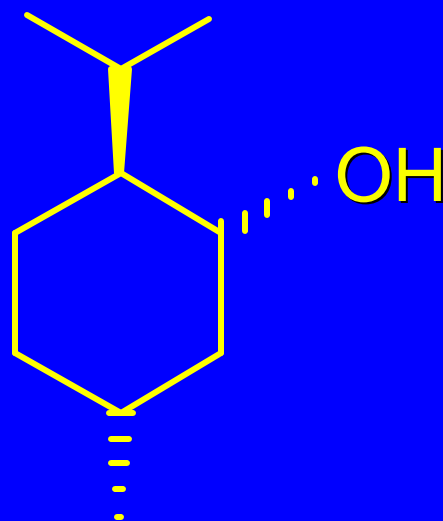
Class	Number of carbon atoms
Monoterpene	10
Sesquiterpene	15
Diterpene	20
Sesterpene	25
Triterpene	30
Tetraterpene	40

Figure 26.6

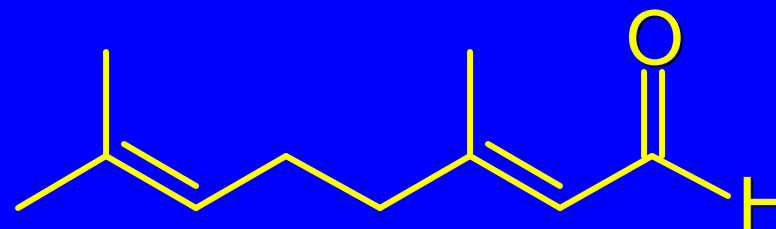
Representative Monoterpenes



α -Phellandrene
(eucalyptus)



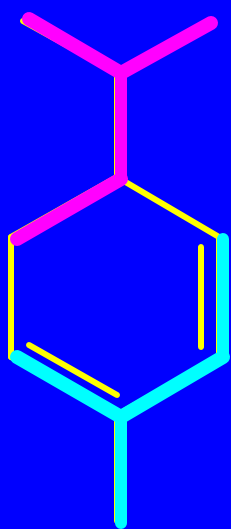
Menthol
(peppermint)



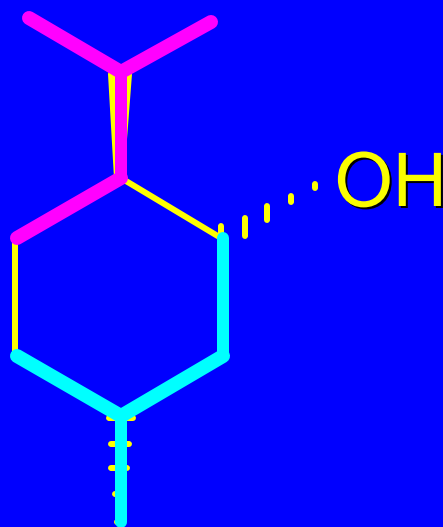
Citral
(lemon grass)

Figure 26.6

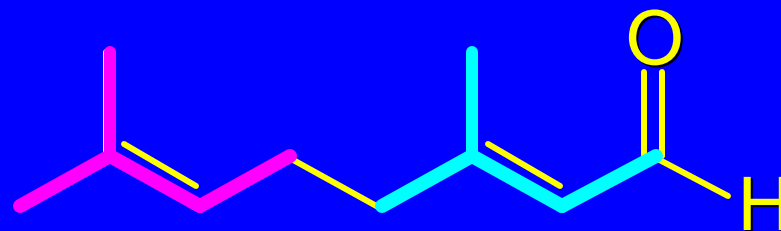
Representative Monoterpenes



α -Phellandrene
(eucalyptus)



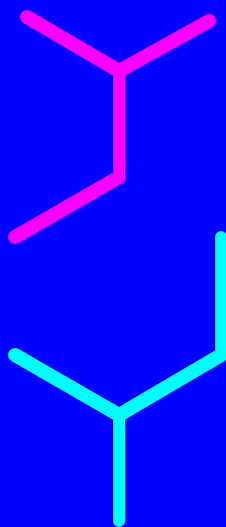
Menthol
(peppermint)



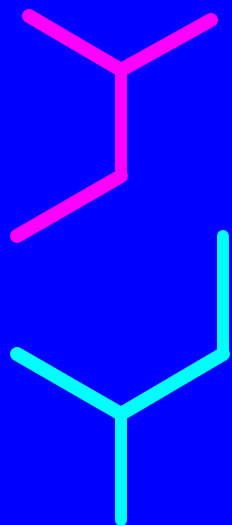
Citral
(lemon grass)

Figure 26.6

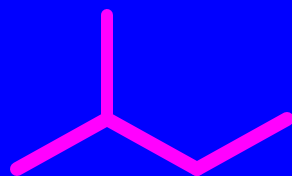
Representative Monoterpenes



α -Phellandrene
(eucalyptus)



Menthol
(peppermint)



Citral
(lemon grass)

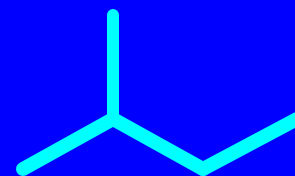
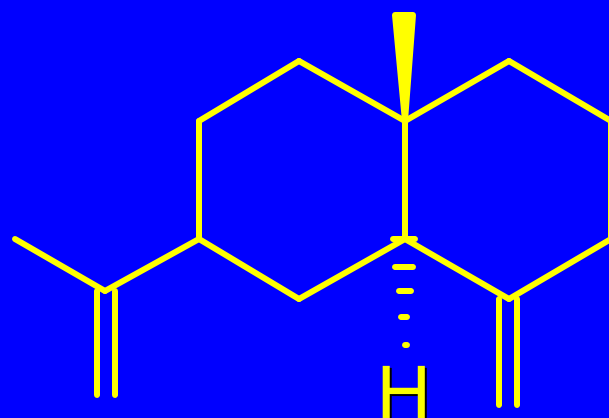


Figure 26.6

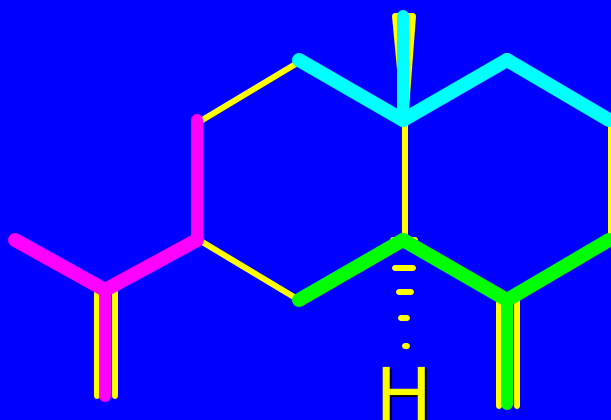
Representative Sesquiterpenes



α -Selinene
(celery)

Figure 26.6

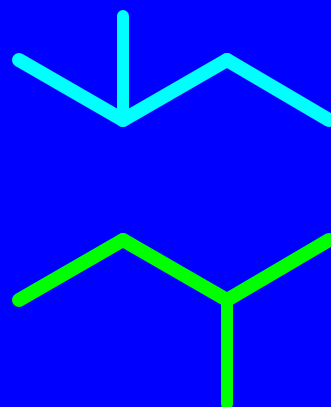
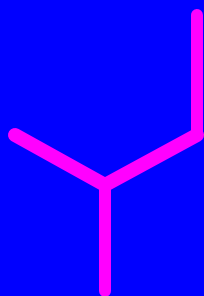
Representative Sesquiterpenes



α -Selinene
(celery)

Figure 26.6

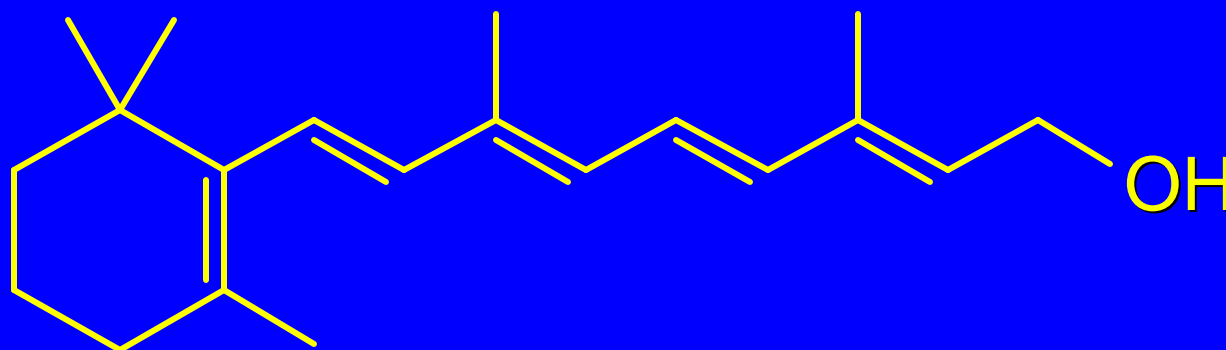
Representative Sesquiterpenes



α -Selinene
(celery)

Figure 26.6

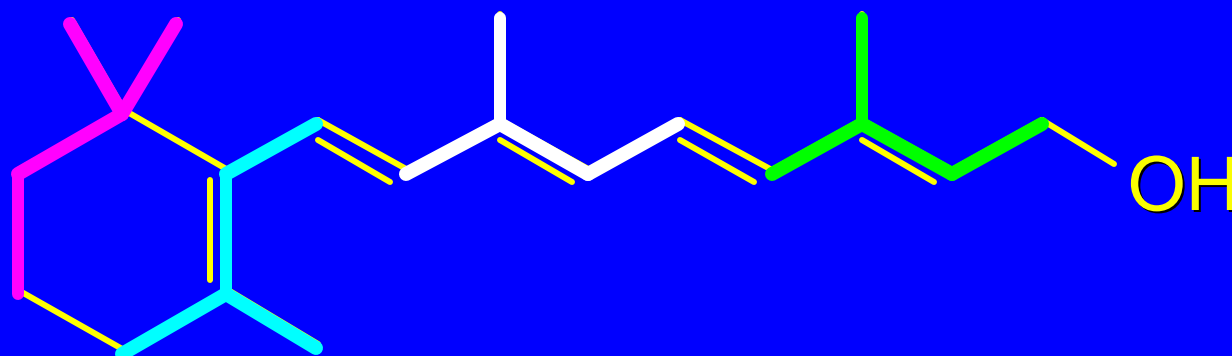
Representative Diterpenes



Vitamin A

Figure 26.6

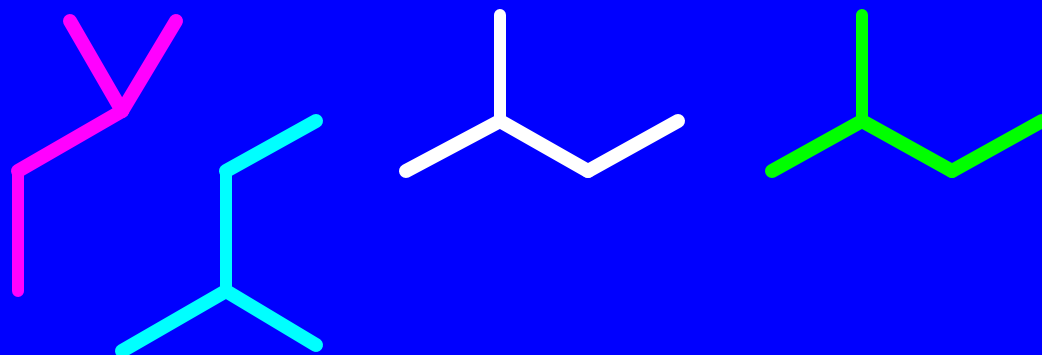
Representative Diterpenes



Vitamin A

Figure 26.6

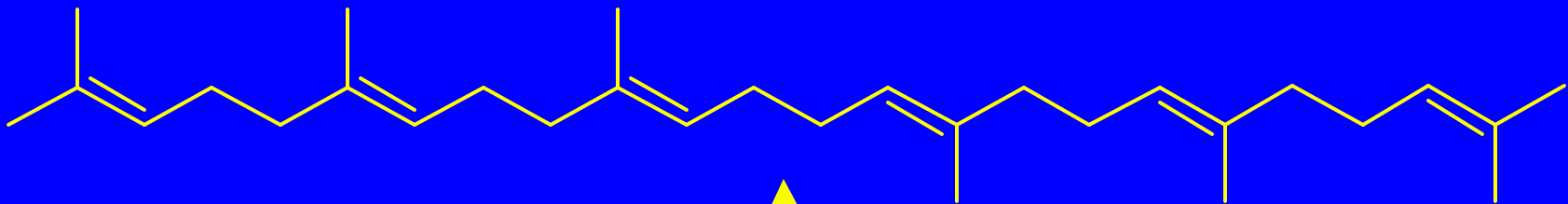
Representative Diterpenes



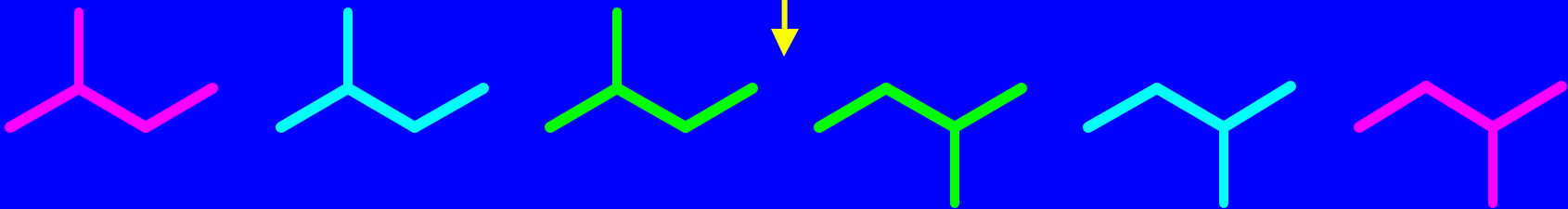
Vitamin A

Figure 26.6

Representative Triterpene



tail-to-tail linkage of isoprene units



Squalene
(shark liver oil)

26.8

Isopentenyl Pyrophosphate:
The Biological Isoprene Unit

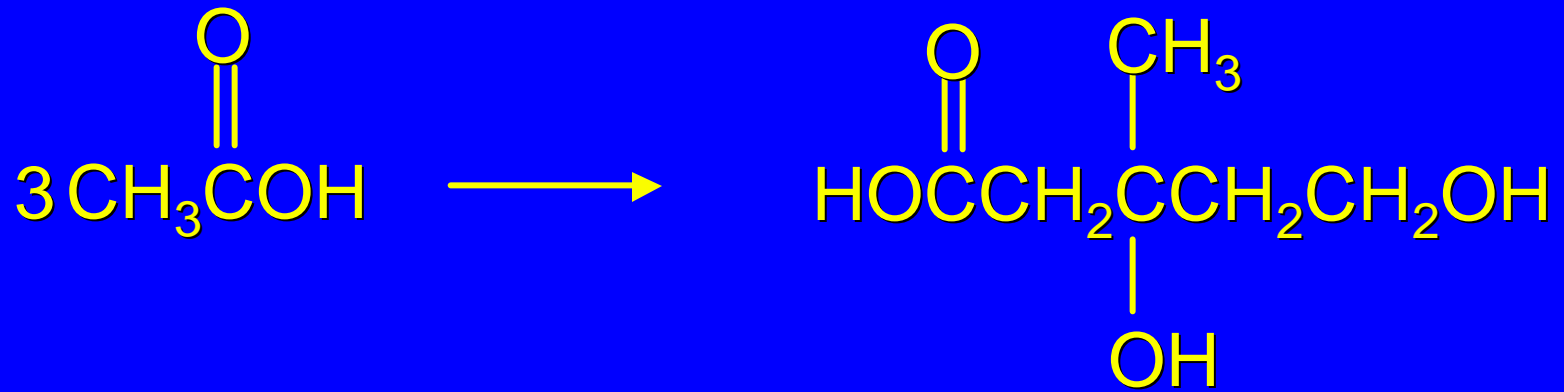
The Biological Isoprene Unit

The isoprene units in terpenes do not come from isoprene.

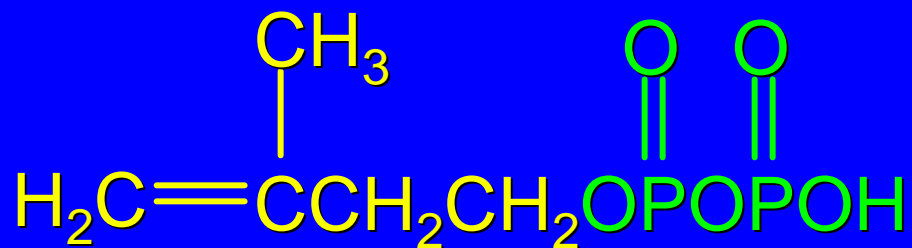
They come from isopentenyl pyrophosphate.

Isopentenyl pyrophosphate (5 carbons) comes from acetate (2 carbons) via mevalonate (6 carbons).

The Biological Isoprene Unit

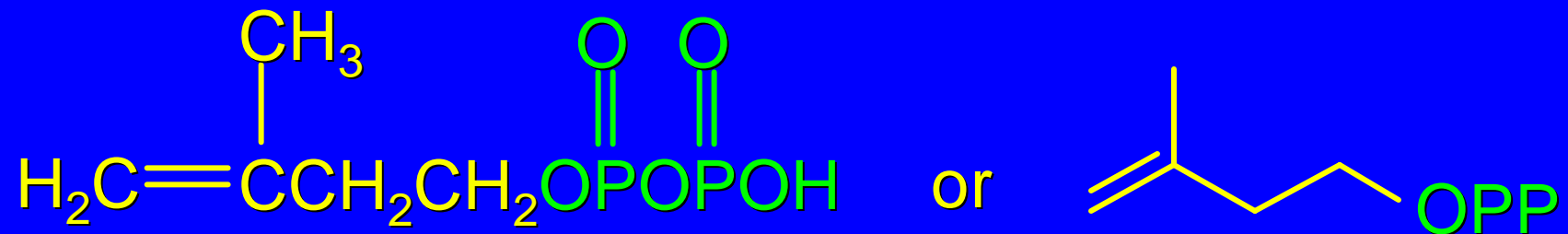


Mevalonic acid



Isopentenyl pyrophosphate

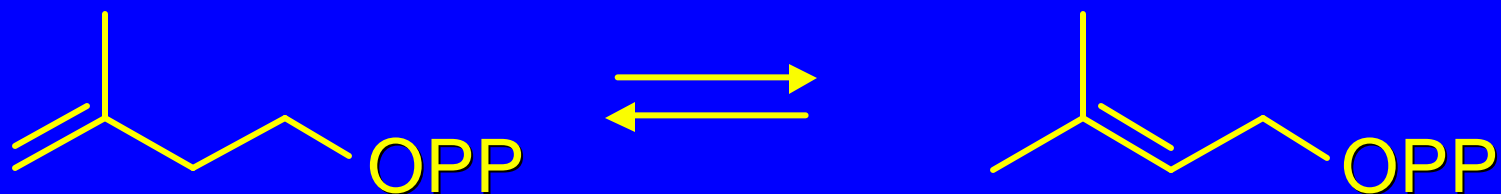
Isopentenyl Pyrophosphate



Isopentenyl pyrophosphate

Isopentenyl and Dimethylallyl Pyrophosphate

Isopentenyl pyrophosphate is interconvertible with 2-methylallyl pyrophosphate.



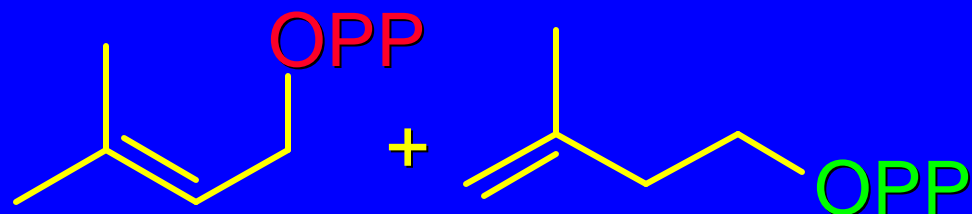
Isopentenyl pyrophosphate

Dimethylallyl pyrophosphate

Dimethylallyl pyrophosphate has a leaving group (pyrophosphate) at an allylic carbon; it is reactive toward nucleophilic substitution at this position.

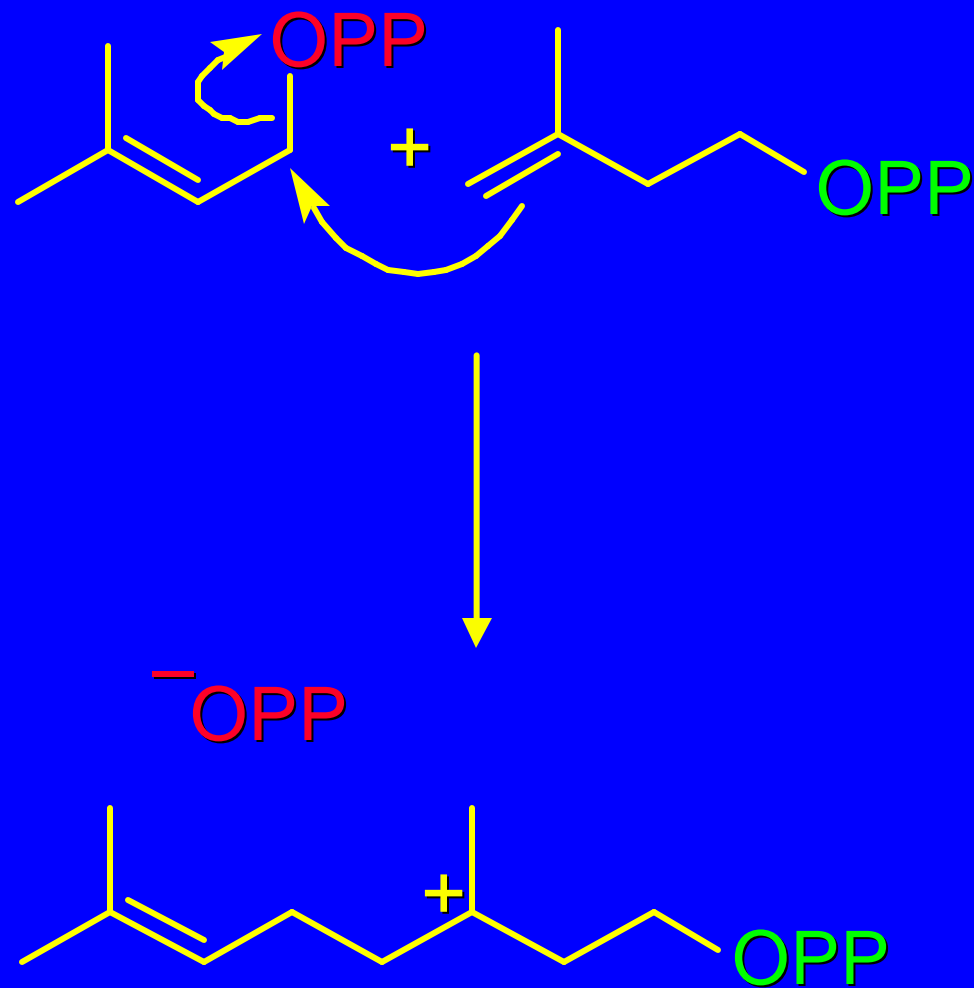
26.9
Carbon-Carbon Bond Formation in
Terpene Biosynthesis

Carbon-Carbon Bond Formation



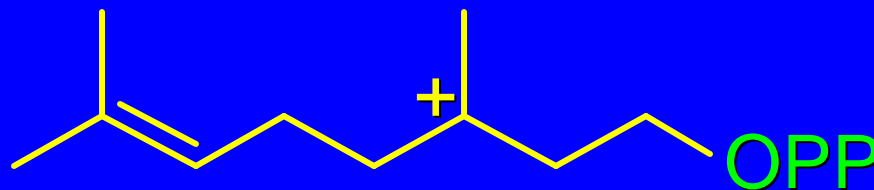
The key process involves the double bond of isopentenyl **pyrophosphate** acting as a nucleophile toward the allylic carbon of dimethylallyl **pyrophosphate**.

Carbon-Carbon Bond Formation

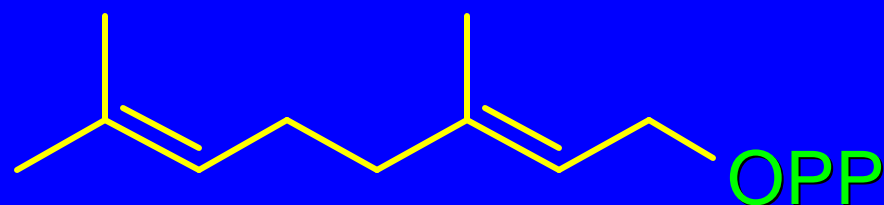


After C—C Bond Formation...

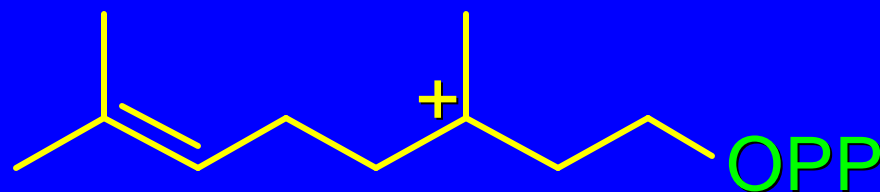
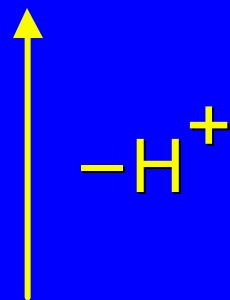
The carbocation can lose a proton to give a double bond.



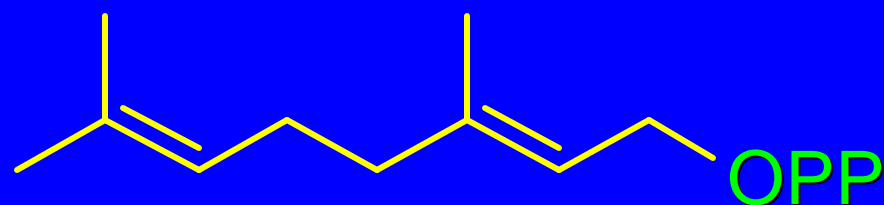
After C—C Bond Formation...



The carbocation
can lose a proton
to give a double
bond.

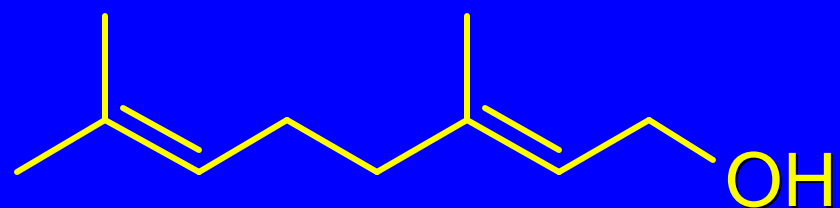
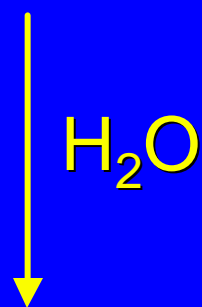
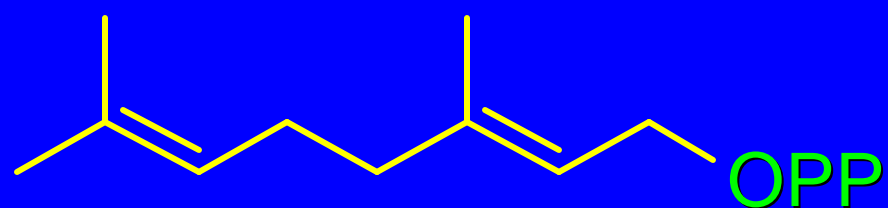


After C—C Bond Formation...



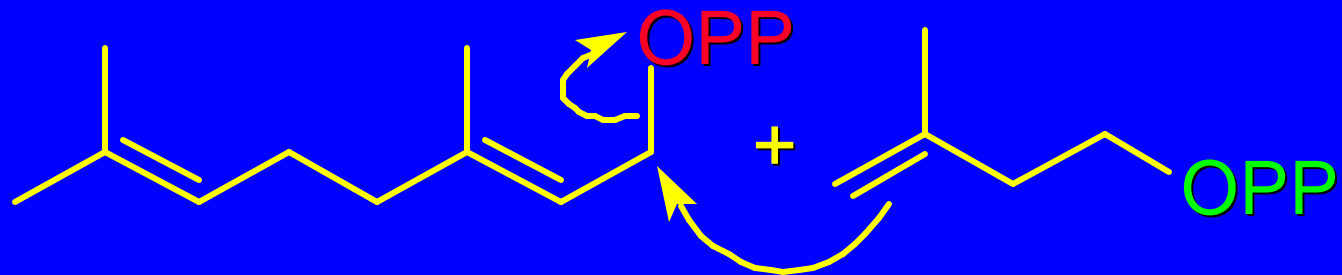
This compound is called geranyl pyrophosphate. It can undergo hydrolysis of its pyrophosphate to give geraniol (rose oil).

After C—C Bond Formation...

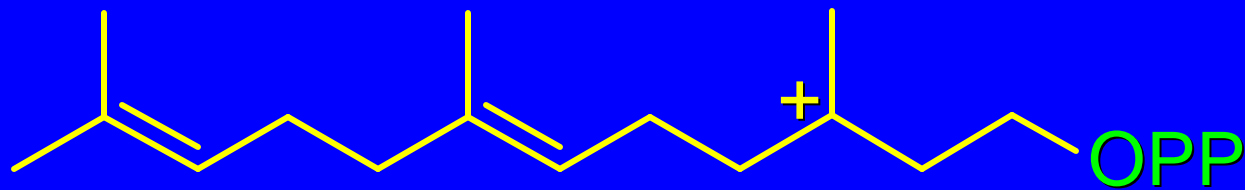


Geraniol

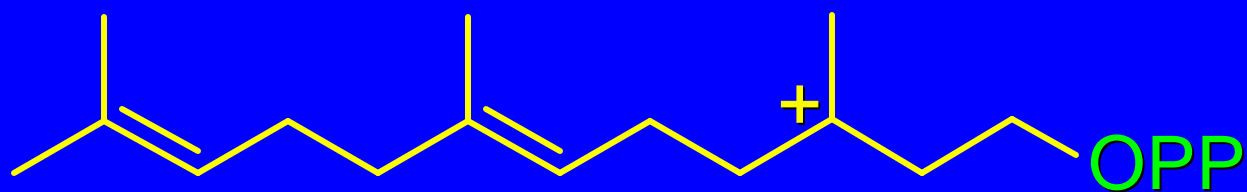
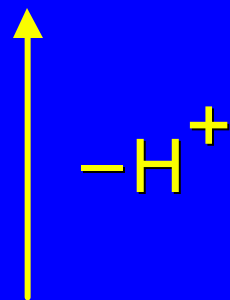
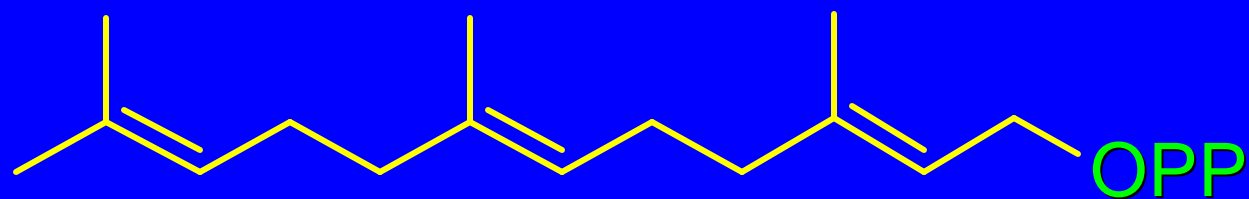
From 10 Carbons to 15



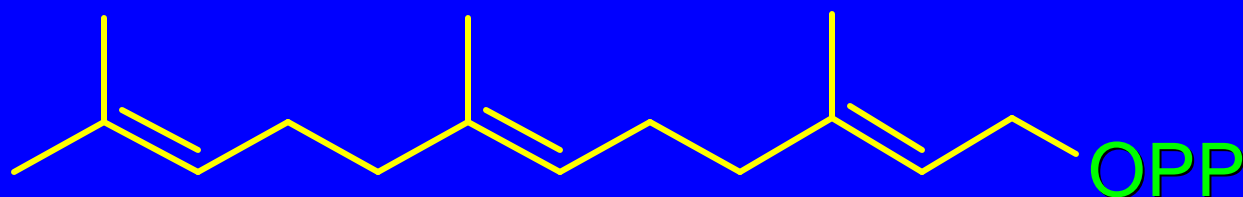
Geranyl pyrophosphate



From 10 Carbons to 15



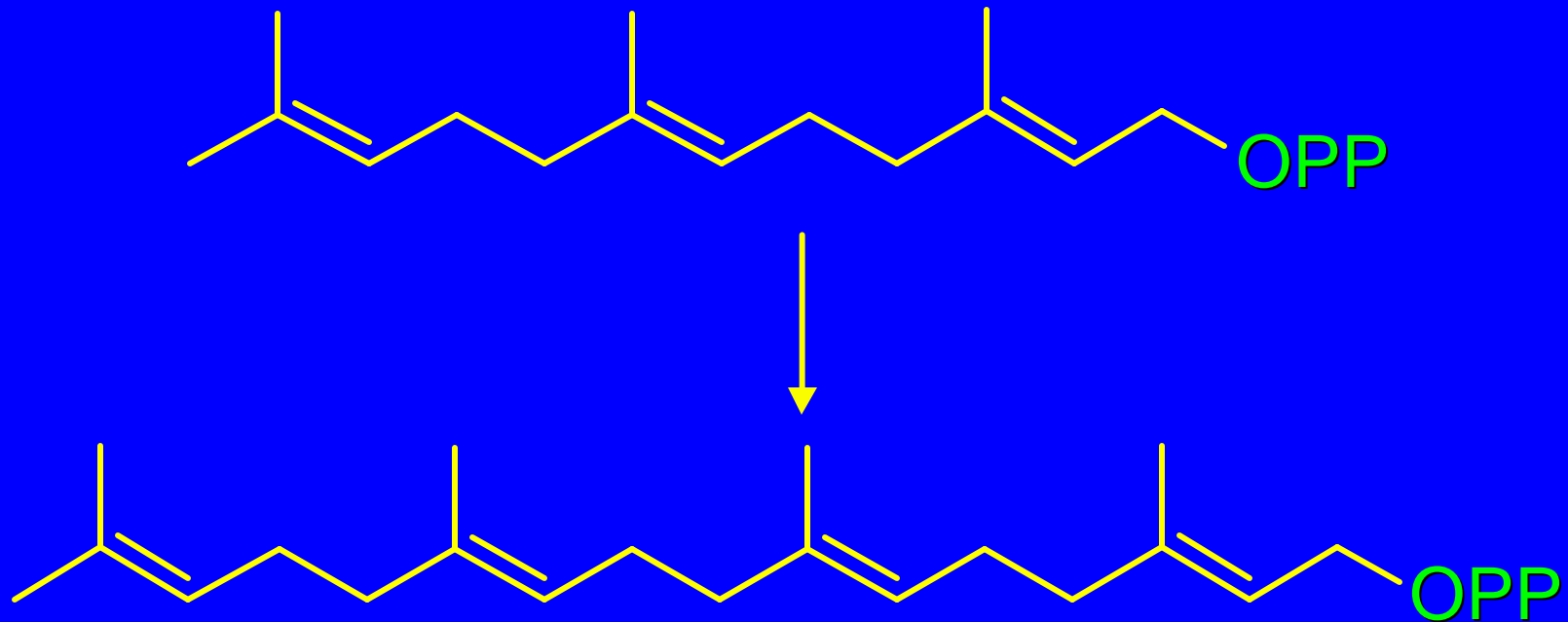
From 10 Carbons to 15



This compound is called farnesyl pyrophosphate.

Hydrolysis of the pyrophosphate ester gives the alcohol farnesol (Figure 26.6).

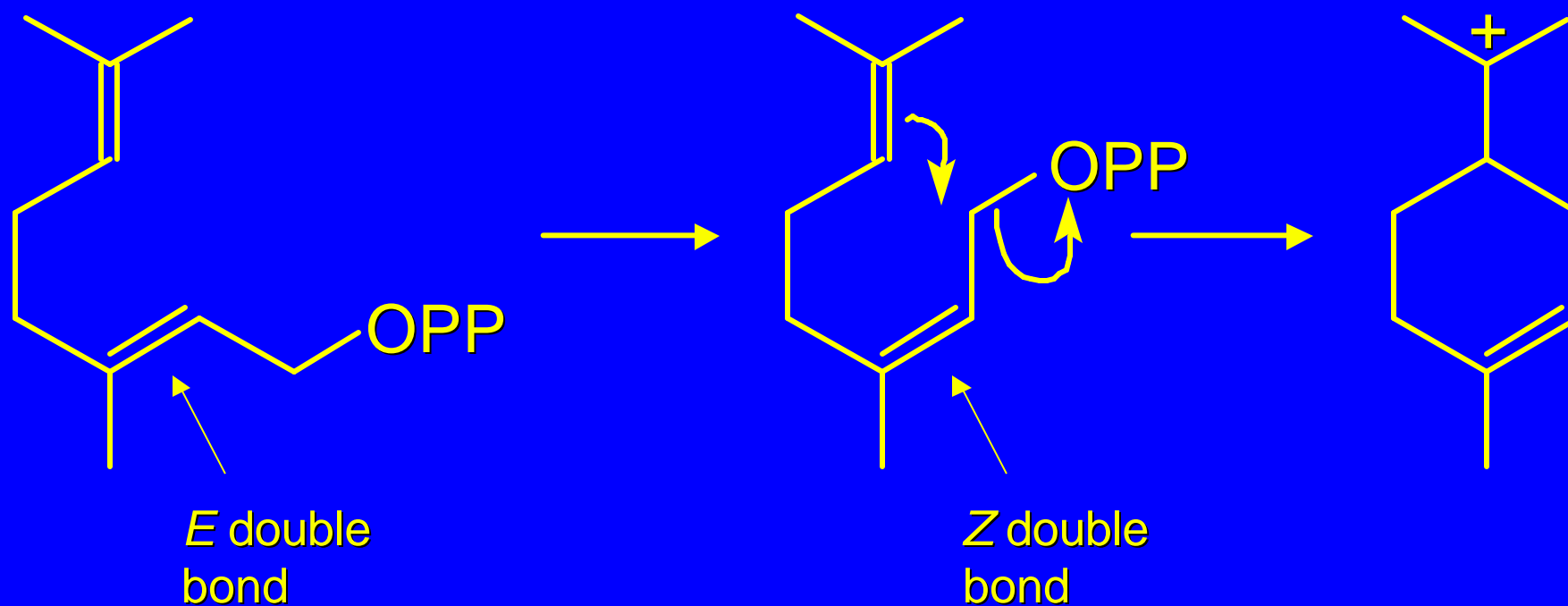
From 15 Carbons to 20



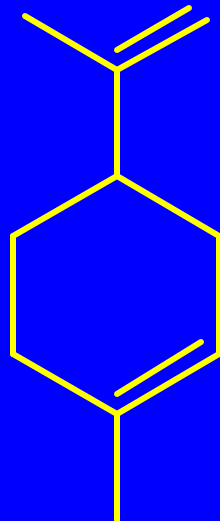
Farnesyl pyrophosphate is extended by another isoprene unit by reaction with isopentenyl pyrophosphate.

Cyclization

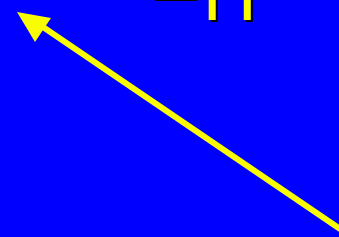
Rings form by intramolecular carbon-carbon bond formation.



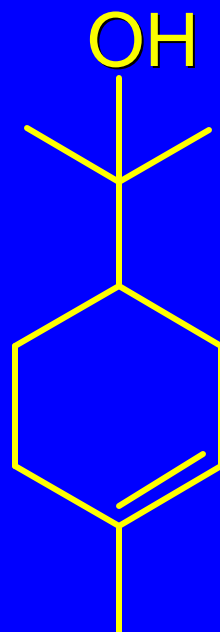
Limonene



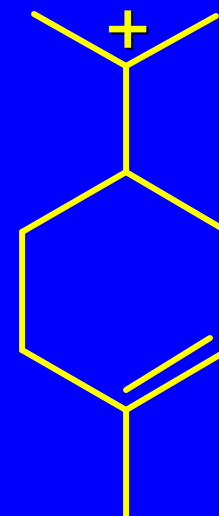
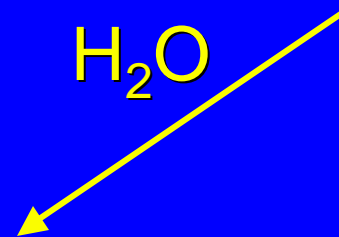
$-H^+$



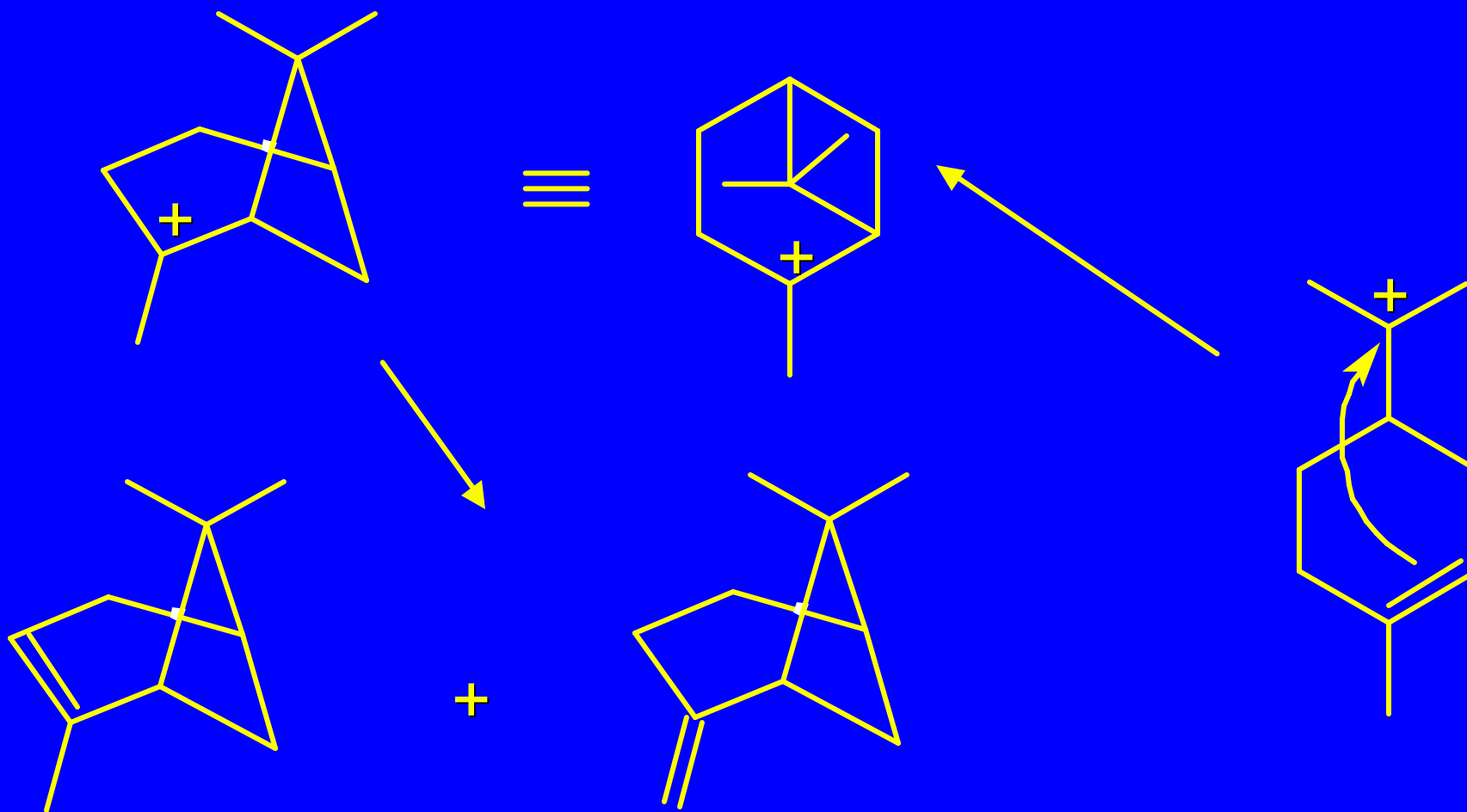
α -Terpineol



H_2O



Bicyclic Terpenes



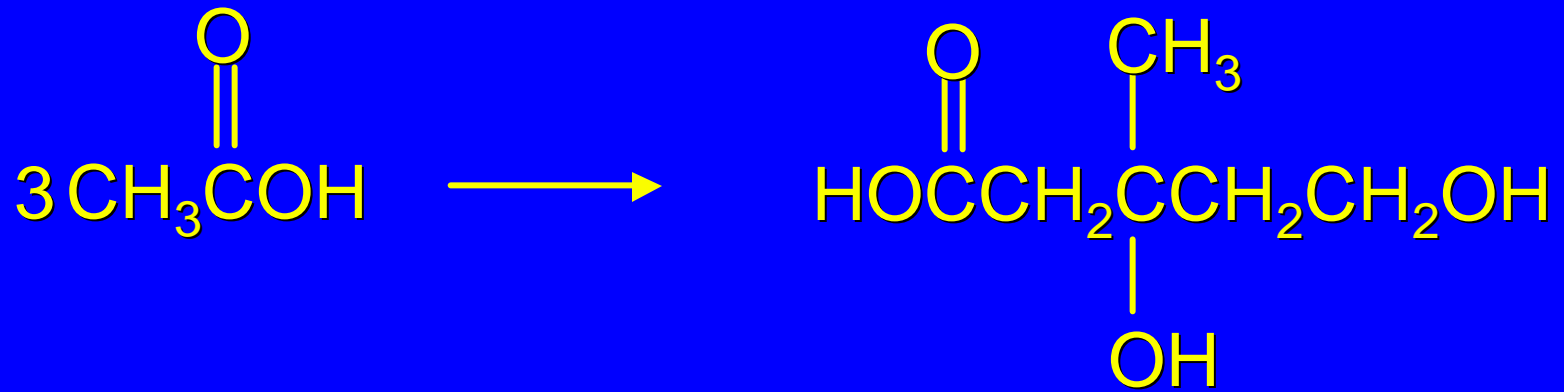
α -Pinene

β -Pinene

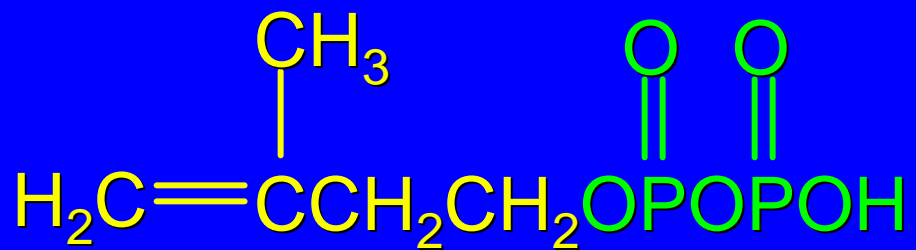
26.10

The Pathway from Acetate to
Isopentenyl Pyrophosphate

Recall



Mevalonic acid

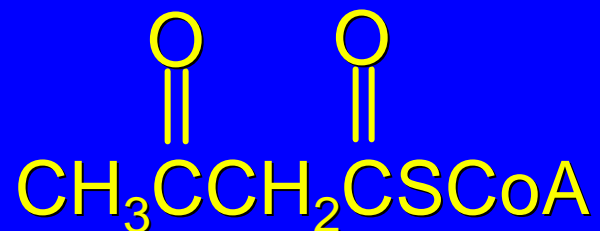


Isopentenyl pyrophosphate



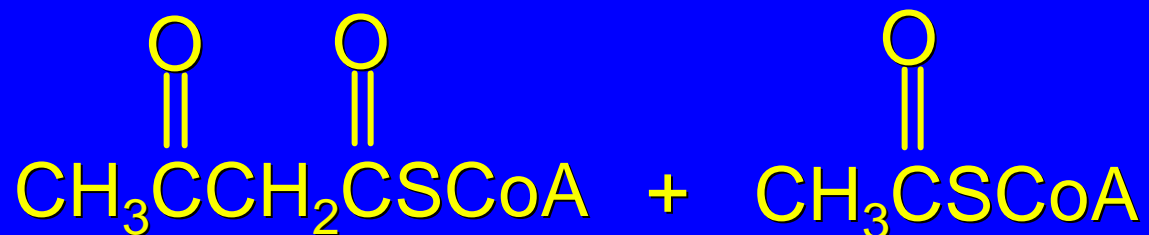
Biosynthesis of Mevalonic Acid

In a sequence analogous to the early steps of fatty acid biosynthesis, acetyl coenzyme A is converted to *S*-acetoacetyl coenzyme A.



S-Acetoacetyl
coenzyme A

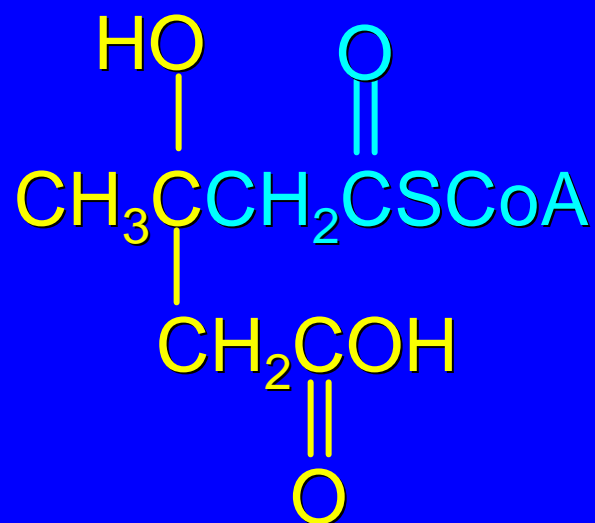
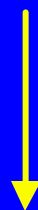
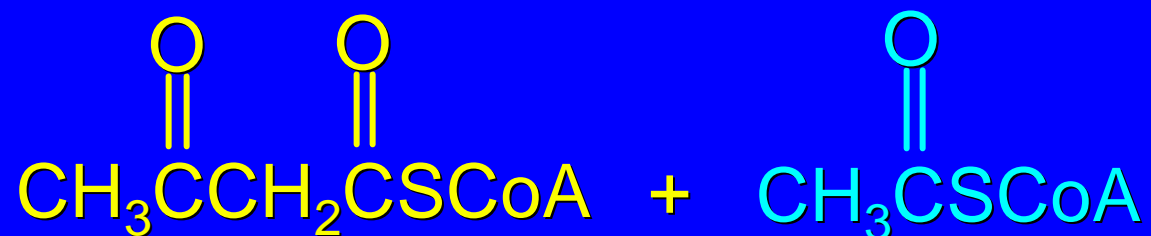
Biosynthesis of Mevalonic Acid



In the next step, S-acetoacetyl coenzyme A reacts with acetyl coenzyme A.

Nucleophilic addition of acetyl coenzyme A (probably via its enol) to the ketone carbonyl of S-acetoacetyl coenzyme A occurs.

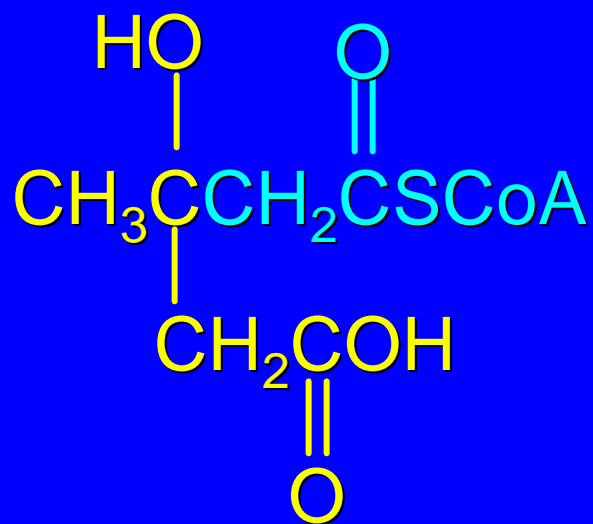
Biosynthesis of Mevalonic Acid

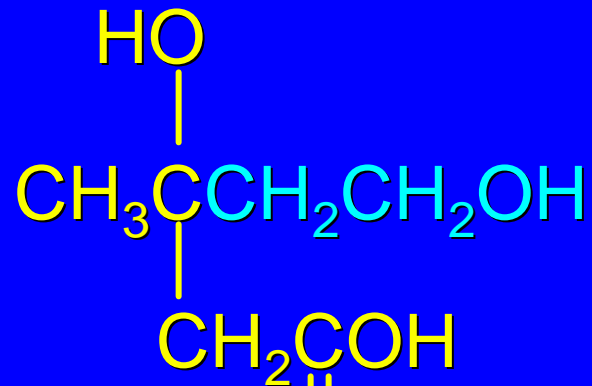


Biosynthesis of Mevalonic Acid

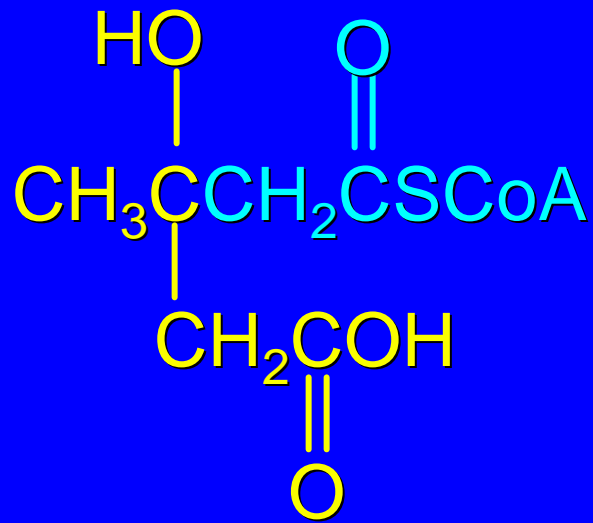
Next, the acyl coenzyme A function is reduced.

The product of this reduction is mevalonic acid.

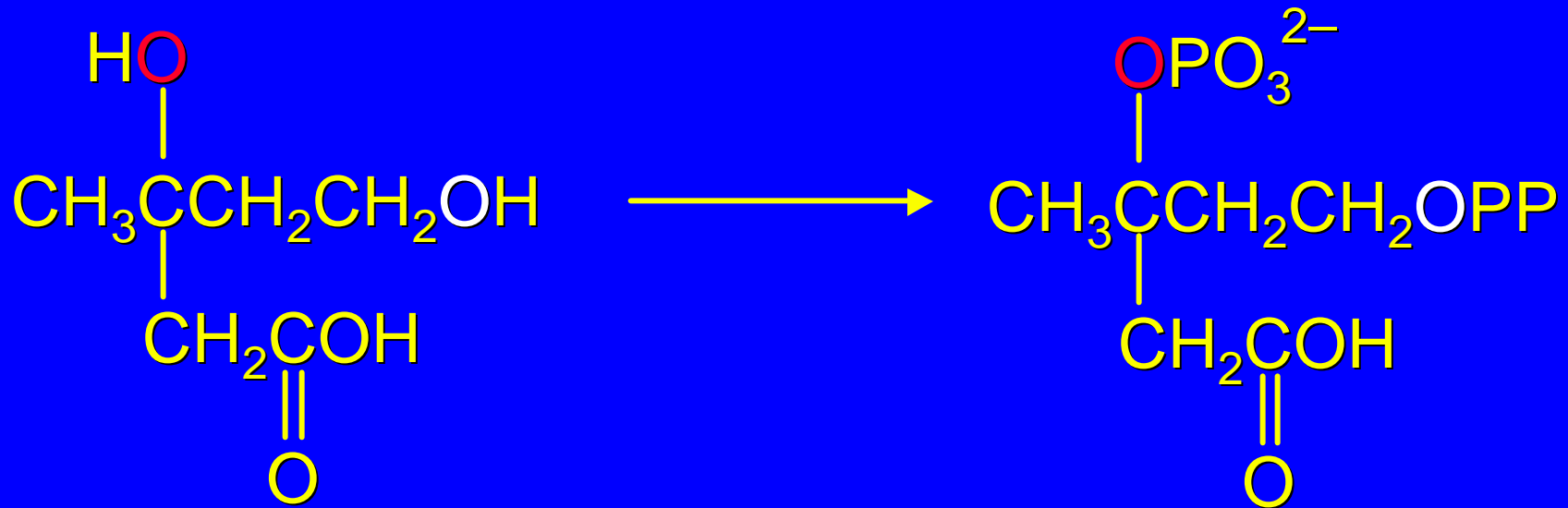




Mevalonic
acid

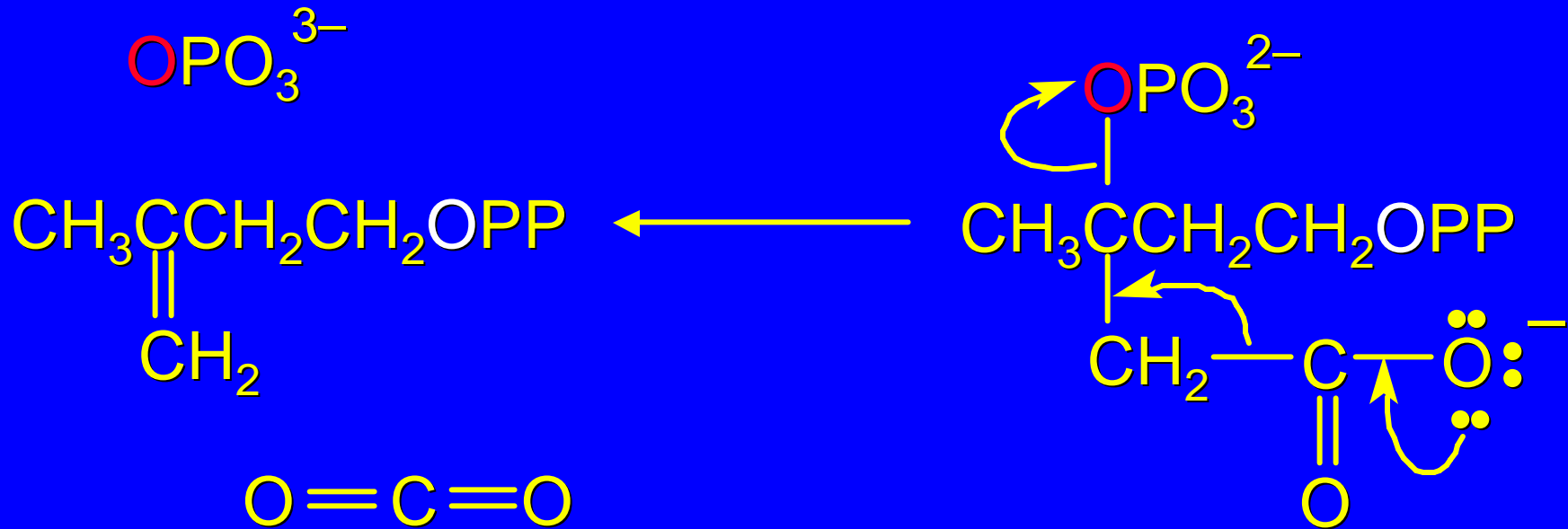


*Conversion of Mevalonic Acid to
Isopentenyl Pyrophosphate*



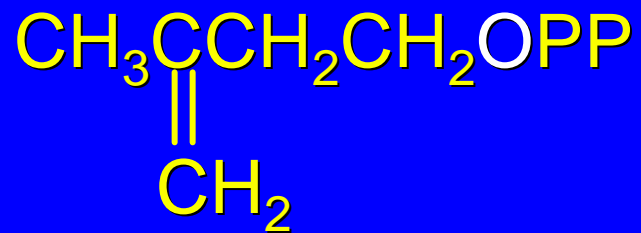
The two hydroxyl groups of mevalonic acid undergo phosphorylation.

Conversion of Mevalonic Acid to Isopentenyl Pyrophosphate



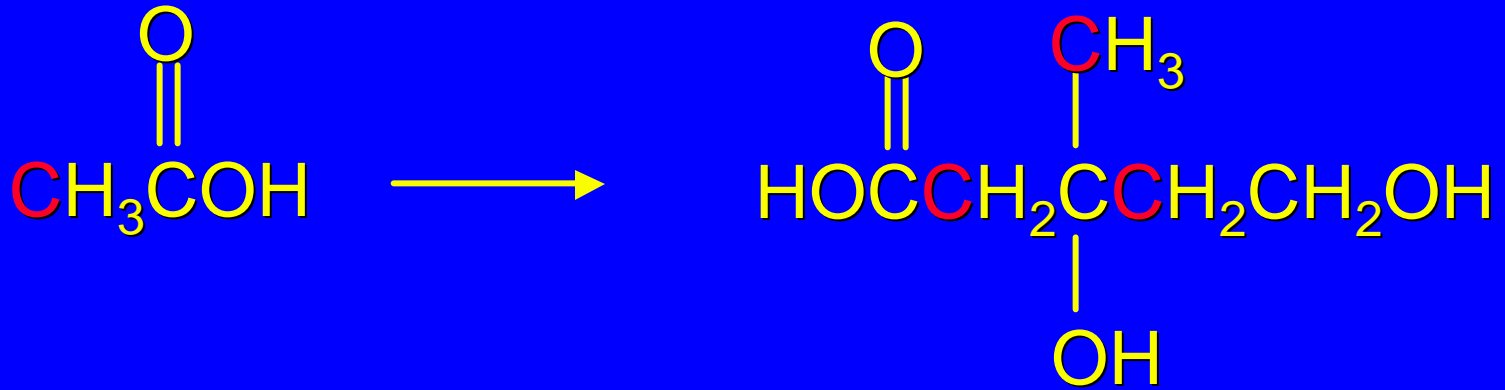
Phosphorylation is followed by a novel elimination involving loss of CO_2 and PO_4^{3-} .

*Conversion of Mevalonic Acid to
Isopentenyl Pyrophosphate*



The product of this elimination is isopentenyl pyrophosphate.

Biosynthetic pathway is based on experiments with ^{14}C -labeled acetate



Mevalonic acid



Isopentenyl pyrophosphate

Biosynthetic pathway is based on experiments with ^{14}C -labeled acetate

Citronellal biosynthesized using ^{14}C -labeled acetate as the carbon source had the labeled carbons in the positions indicated.

