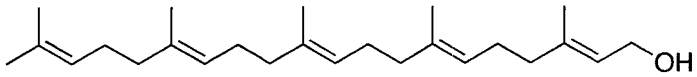
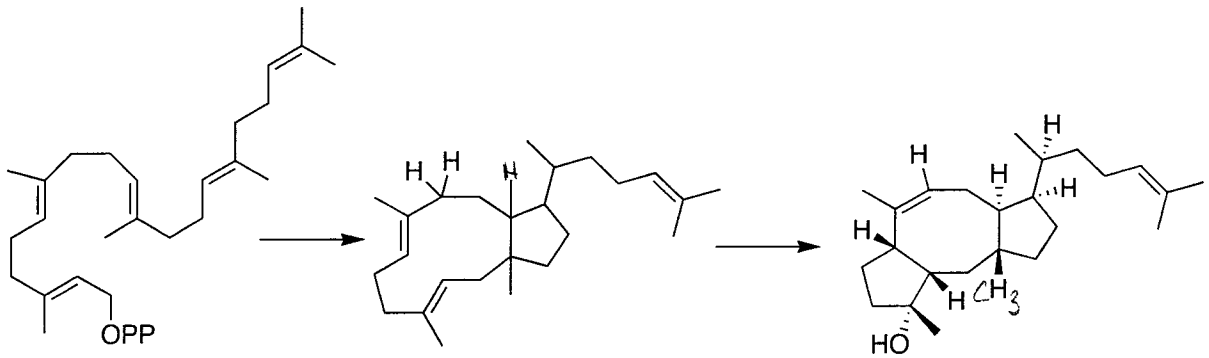
Terpene Biosynthesis:
C25: Sesterterpenes



geranylfaresol



Ophiobolene

Not much reported
Limited to certain fungal/marine species

Squalene Synthase
Enzyme responsible for squalene biosynthesis from 2 units of farnesyl PP, head to head

Cloned from variety of organisms plants, rat, human, yeast
One active site
Form presqualene synthase and then reductive rearrangement (NADPH) to squalene
Cyclopropyl intermediate

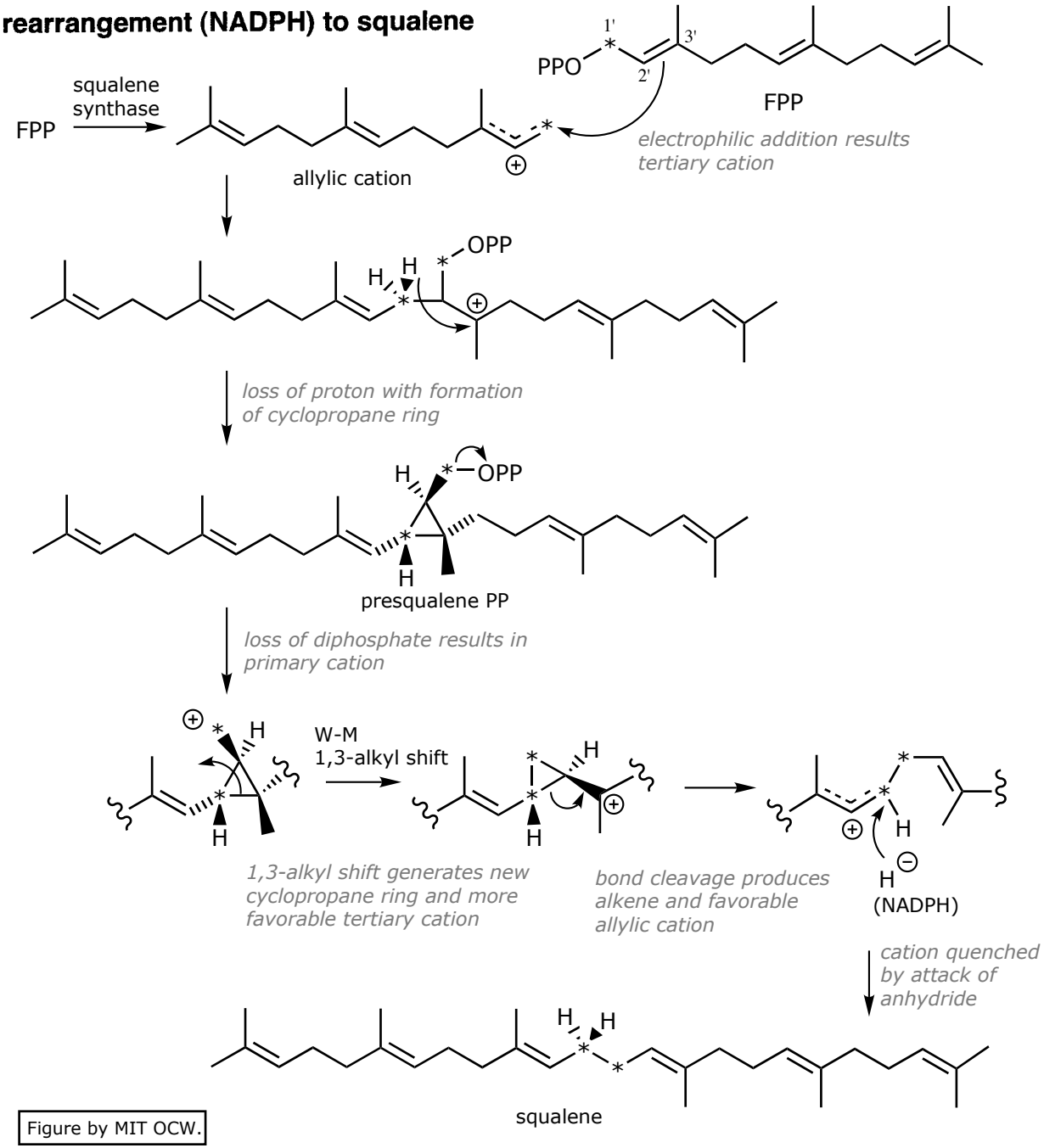
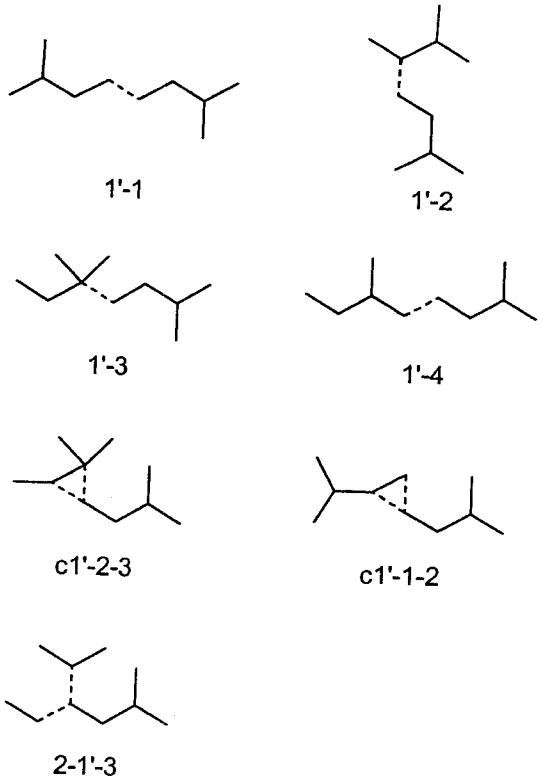
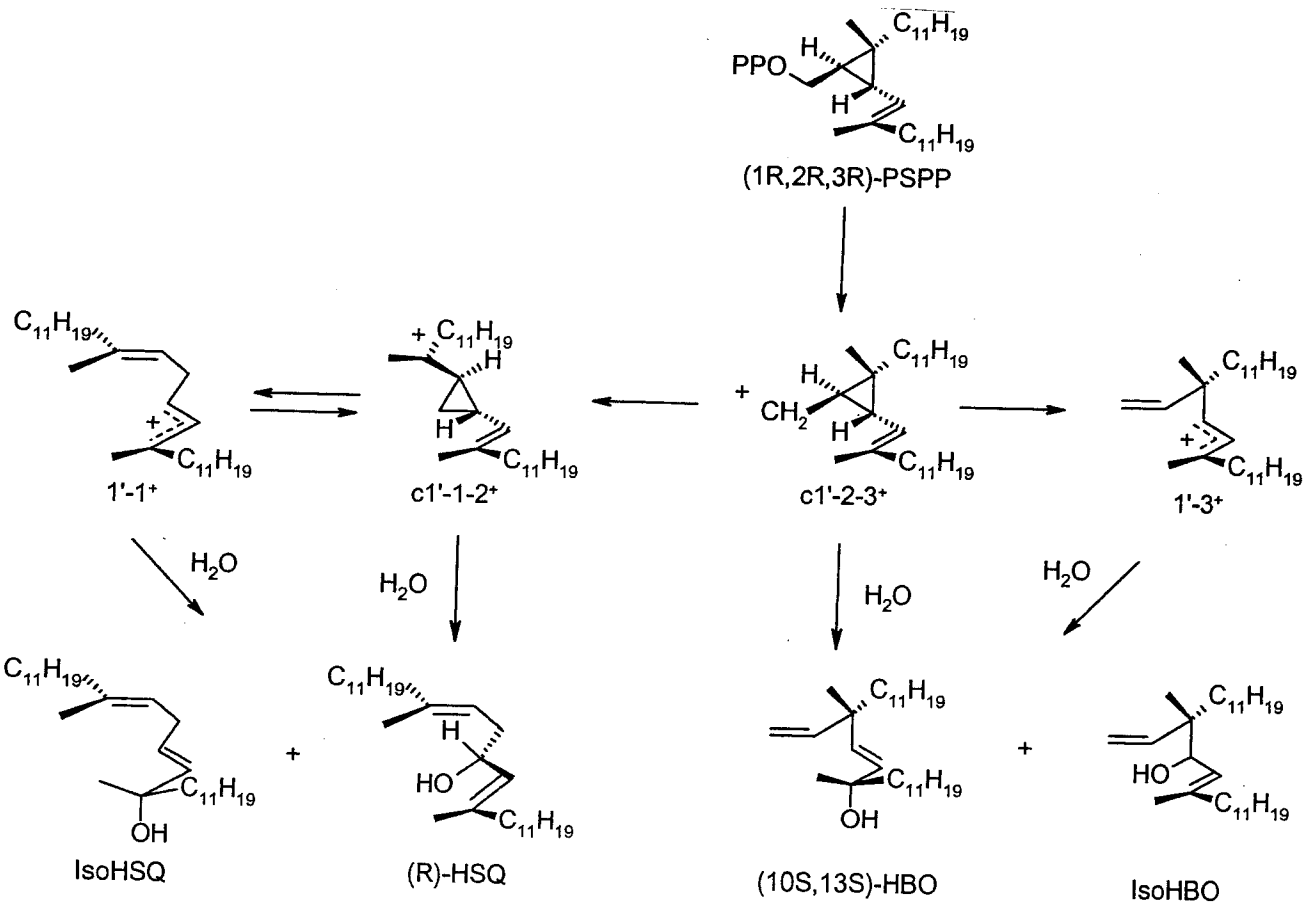


Figure by MIT OCW.

Squalene Synthase
Enzyme responsible for squalene biosynthesis from 2 units of farnesyl PP, head to head

Removal of NADPH



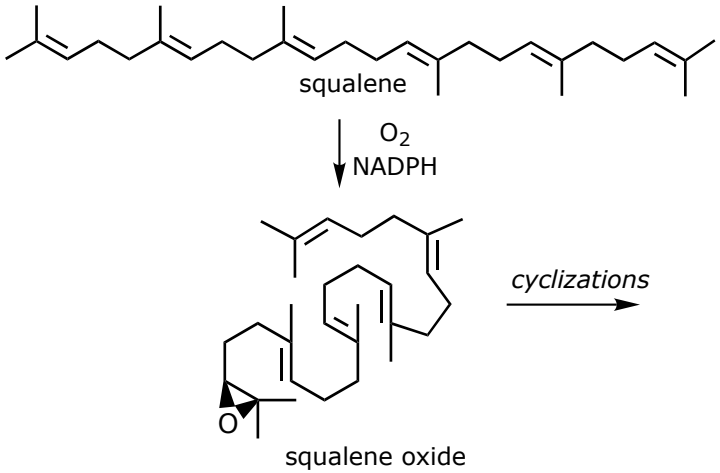


Oxidosqualene Cyclase

In mammals, sterol biosynthesis best studied

cyclization to lanosterol (animals, fungi)
Chair boat chair conformation
Protonate epoxide and open 1,2 hydride/methyl shifts to protosteryl cation
Lanosterol synthase (fungi, animals)
Cycloartenol synthase (plants)
Also diepoxide substate oxysterols

Need terminal methyl group for correct folding (C10)
chair chair boat



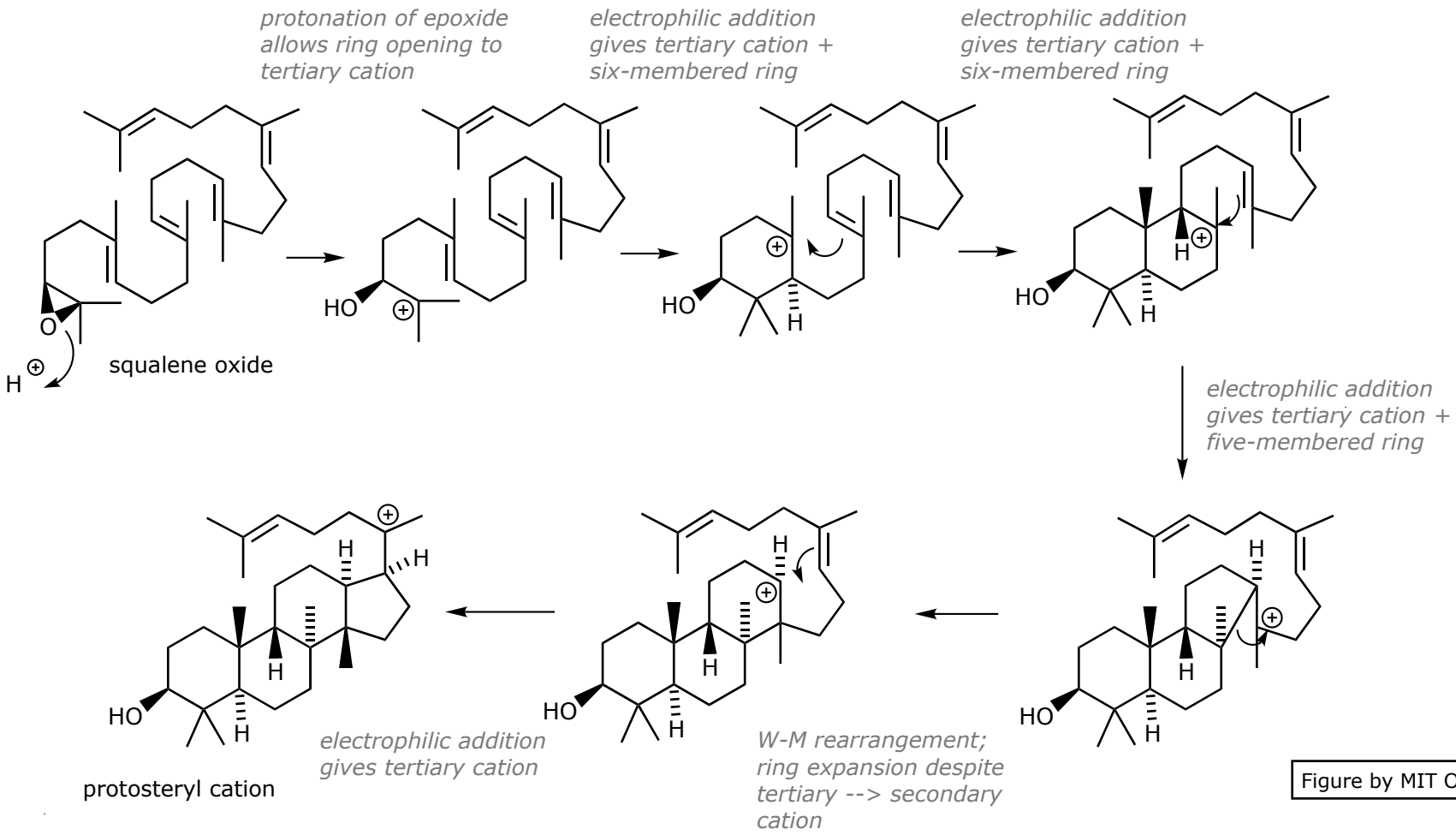


Figure by MIT OCW

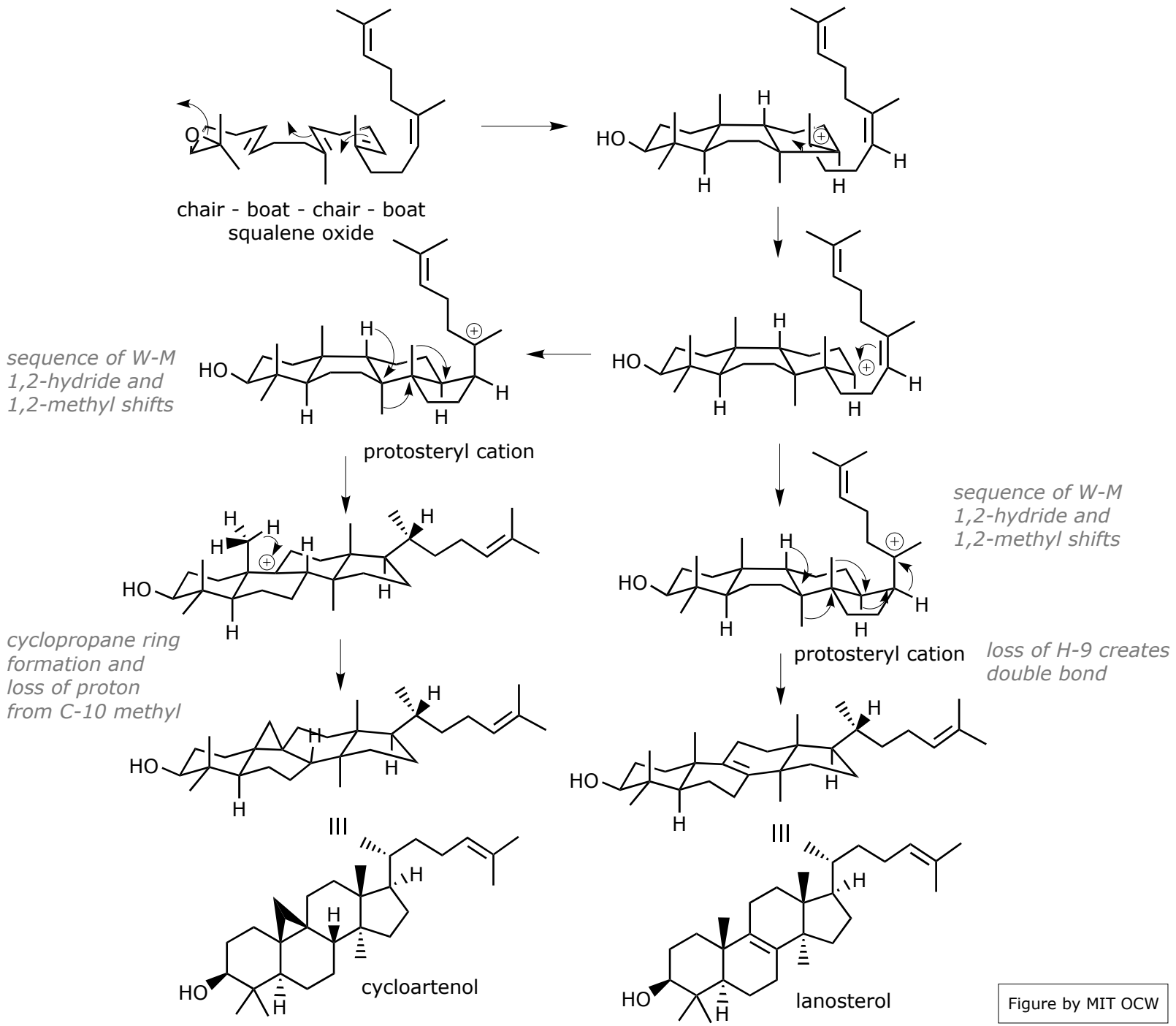
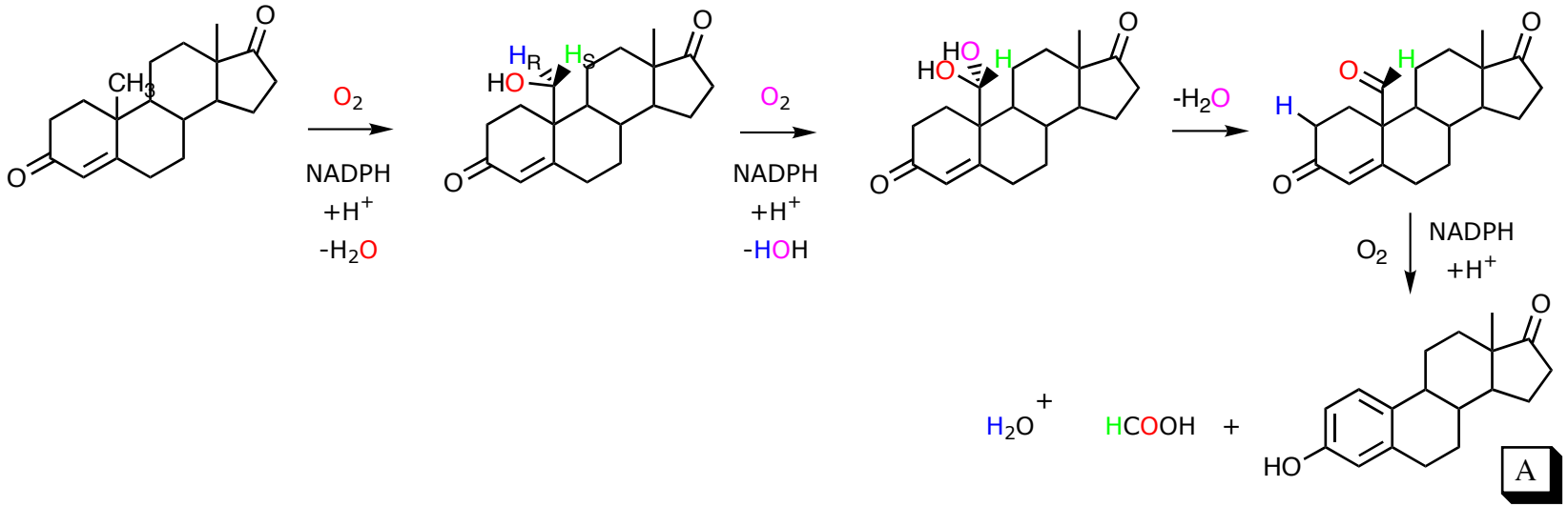


Figure by MIT OCW

Aromatase-catalyzed conversion of androstenedione to estrone



Three possible mechanisms for the last step in the aromatase-catalyzed oxygenation of androstenedione.

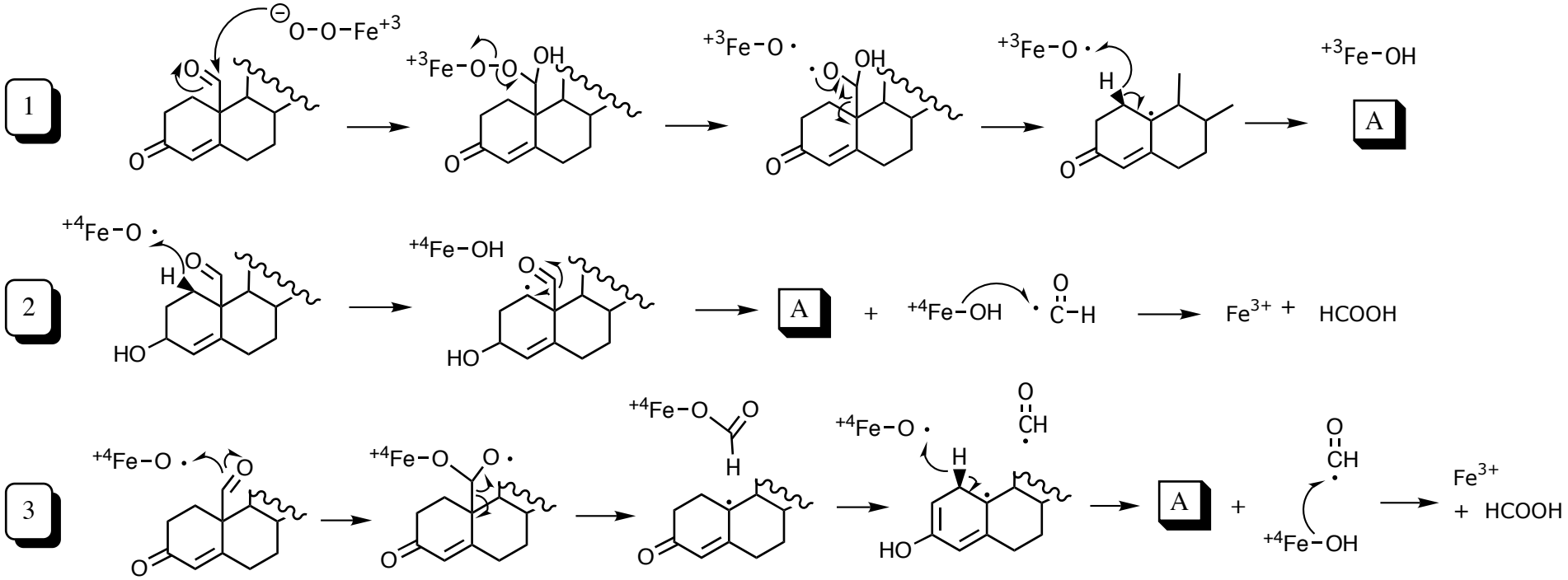
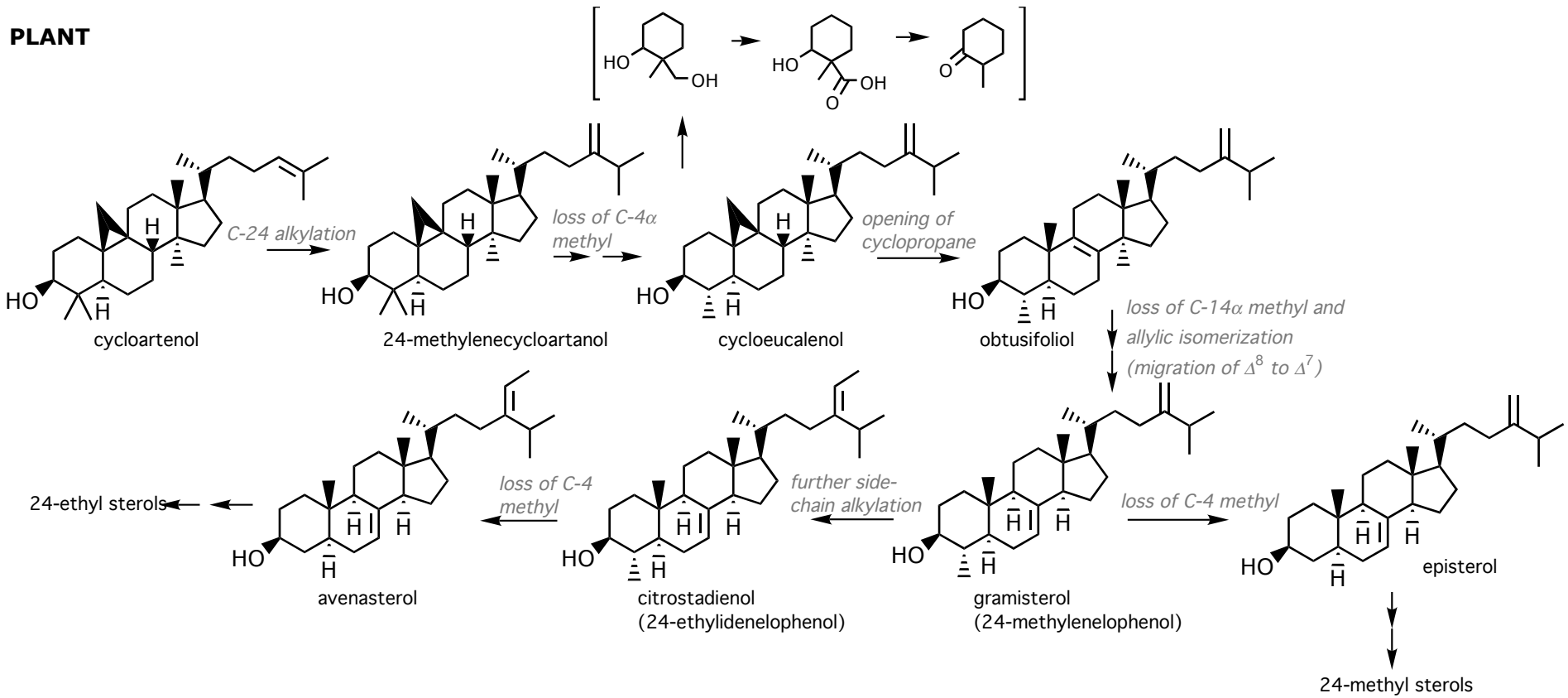


Figure by MIT OCW.



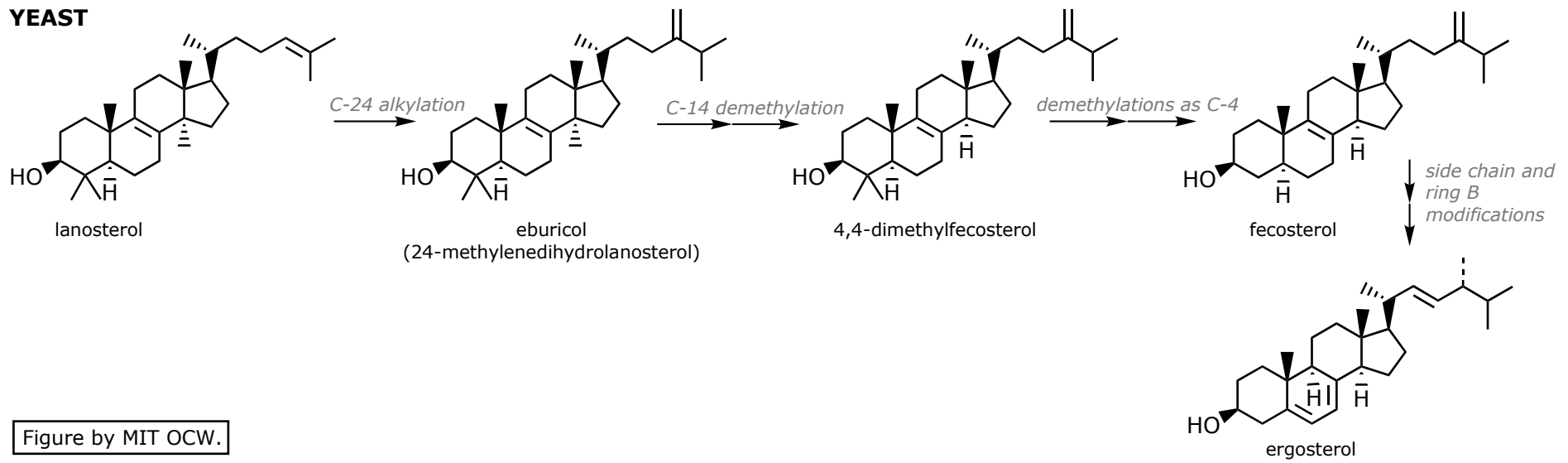


Figure by MIT OCW.

Squalene-Hopene Cyclase

Prokaryote triterpene synthesis
Squalene is the substrate- not squalene epoxide

Chair chair chair substrate conformation

DDTAV
Change to DCTAE: specific for oxosqualene

Crystal structure (Alicyclobacillus acidocaldarius)
Large binding pocket
Can accept larger substrates
C35

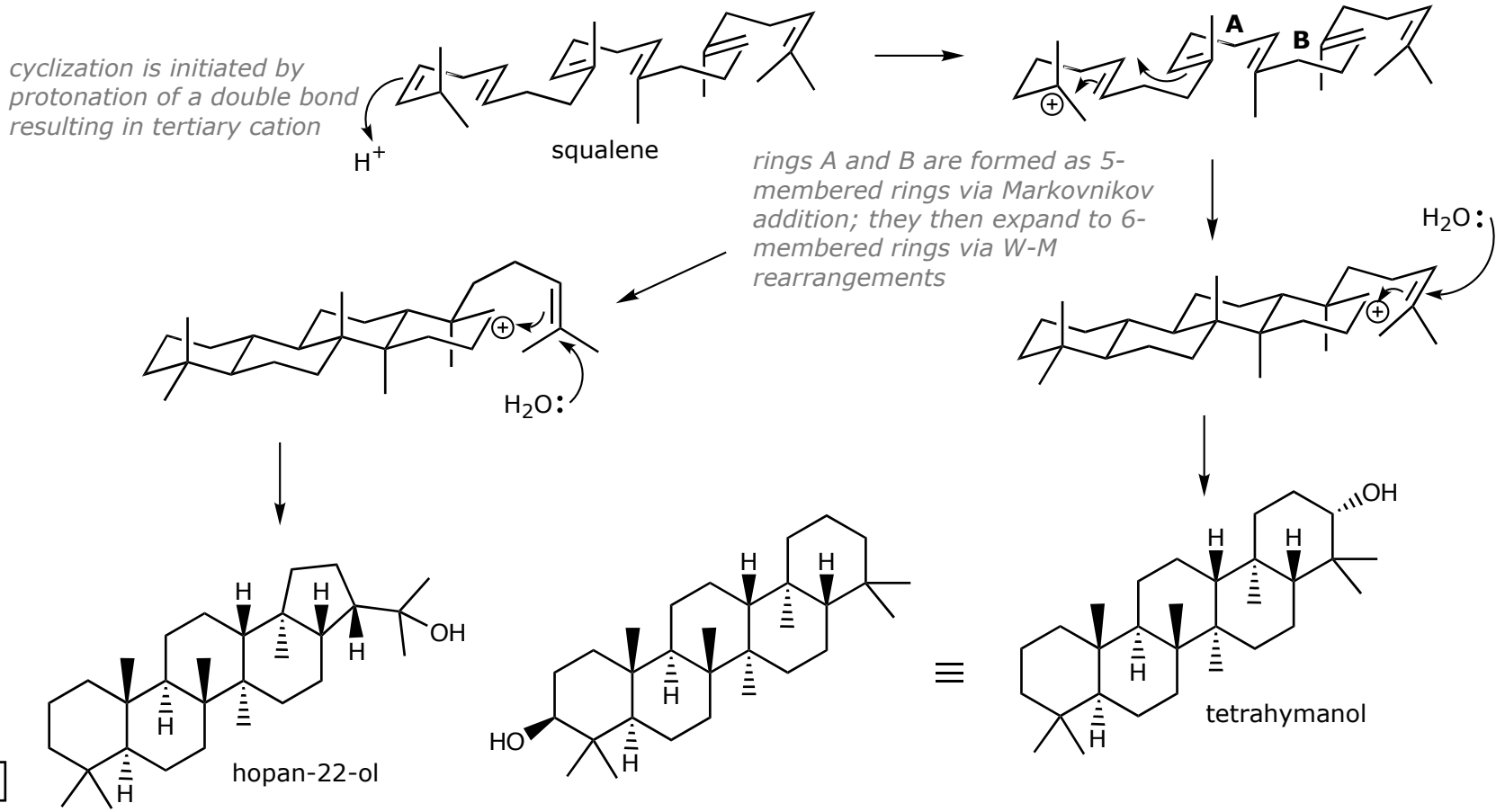


Figure by MIT OCW

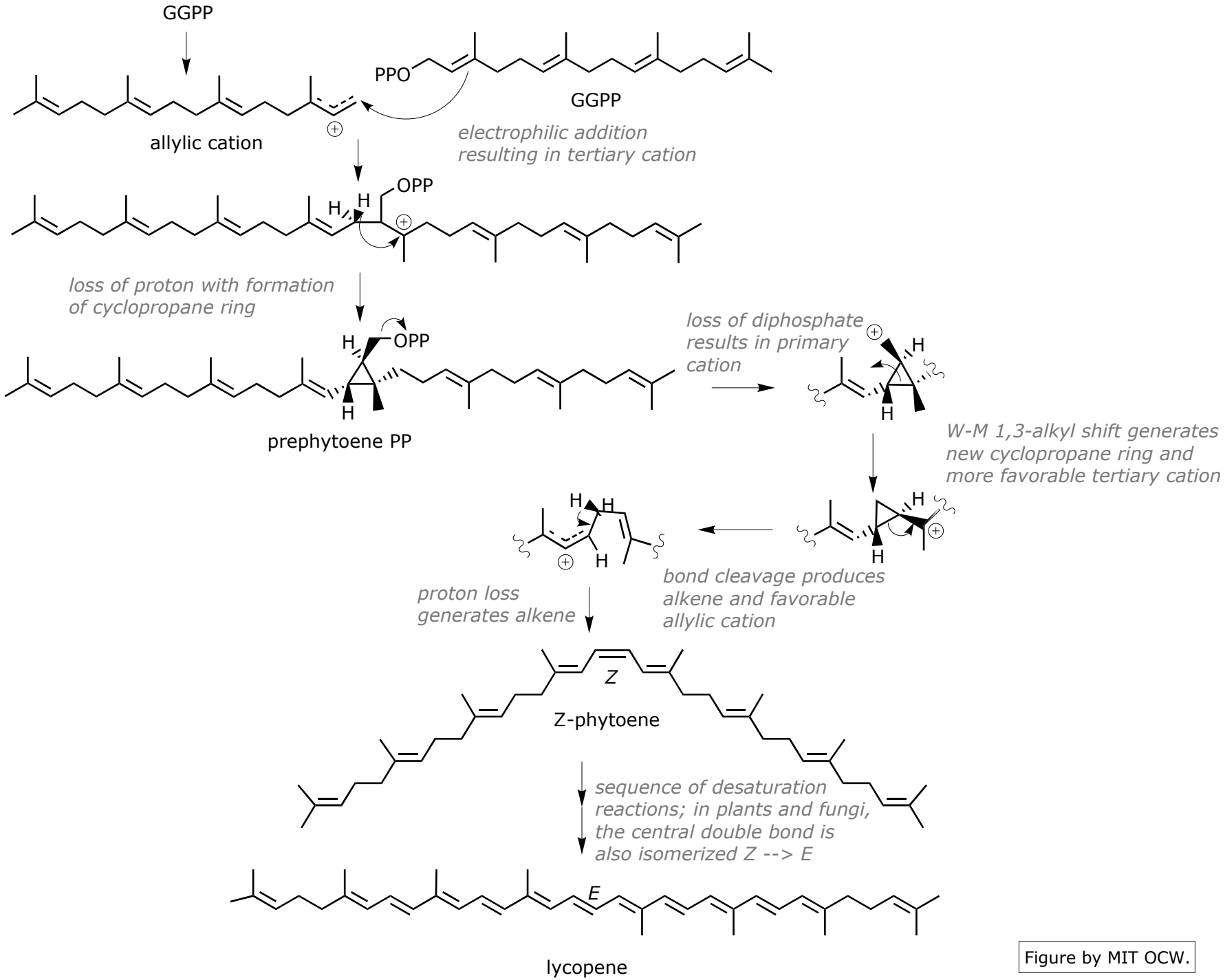
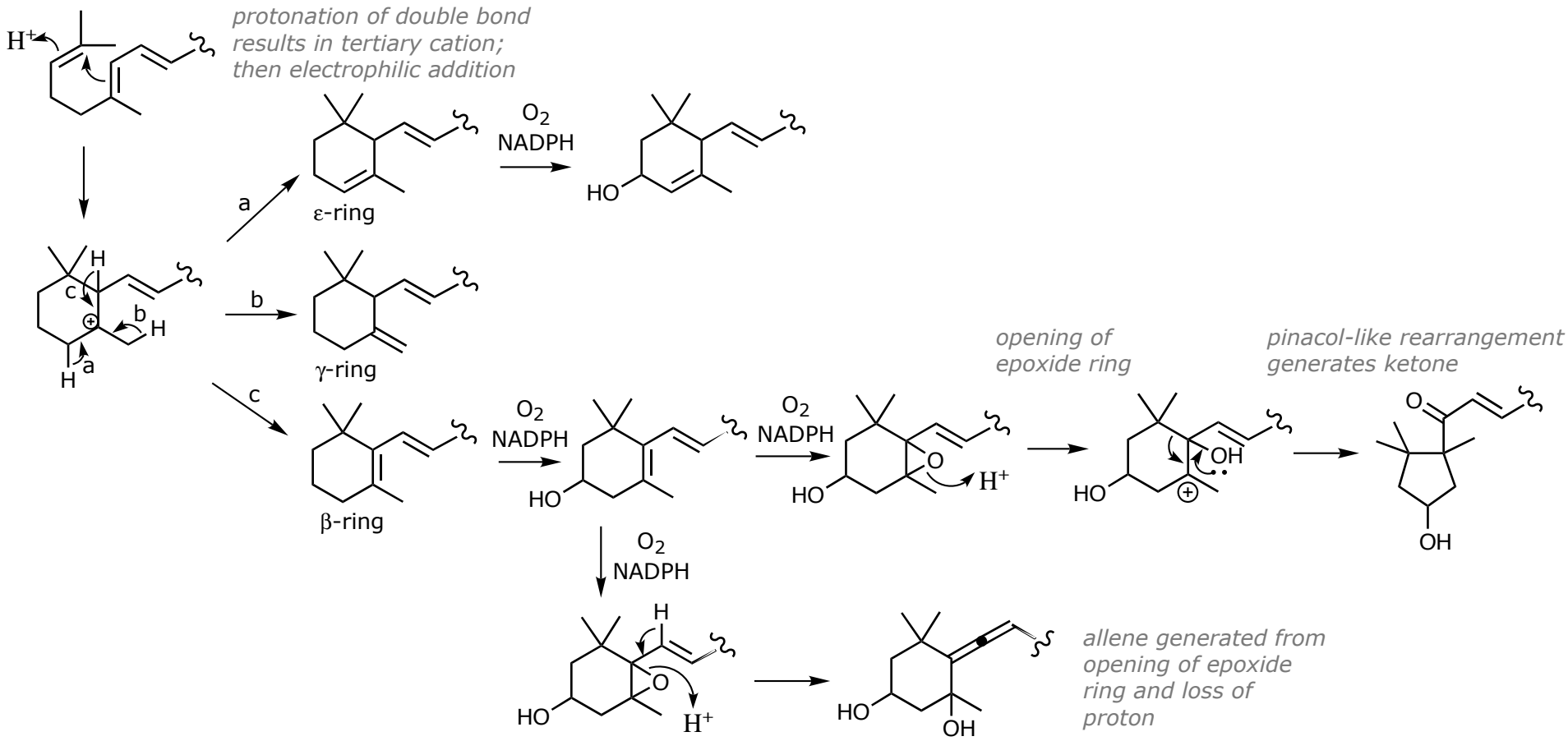


Figure by MIT OCW.



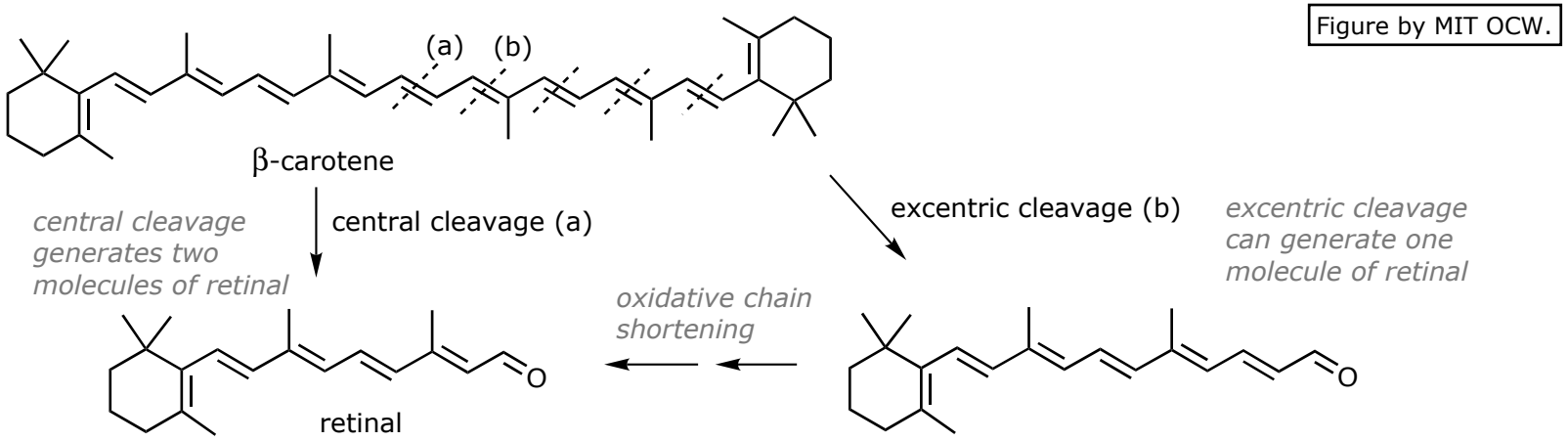


Figure by MIT OCW.

Abietadiene Synthase
bifunctional diterpene cyclase
from fir

cannot separate functional domains

cloned
(a.a. sequence is)

don't know structure

"homology modeling'

ep.-aristolochene
synthase enzyme as a model
(sequiterpene synthase)

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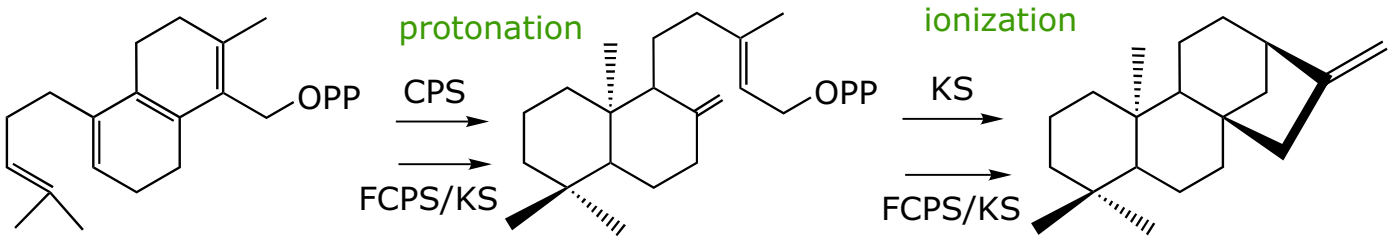
Gibberellin
phytohormone
bifunctional enzyme in fungi
two enzymes in plant

2 individual enzymes

Higher plants



***Phaeosphaeria* sp. L487**

Figure by MIT OCW.

yeast

1 bifunctional enzyme

Figure by MIT OCW.

Index of figures removed due to copyright reasons

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