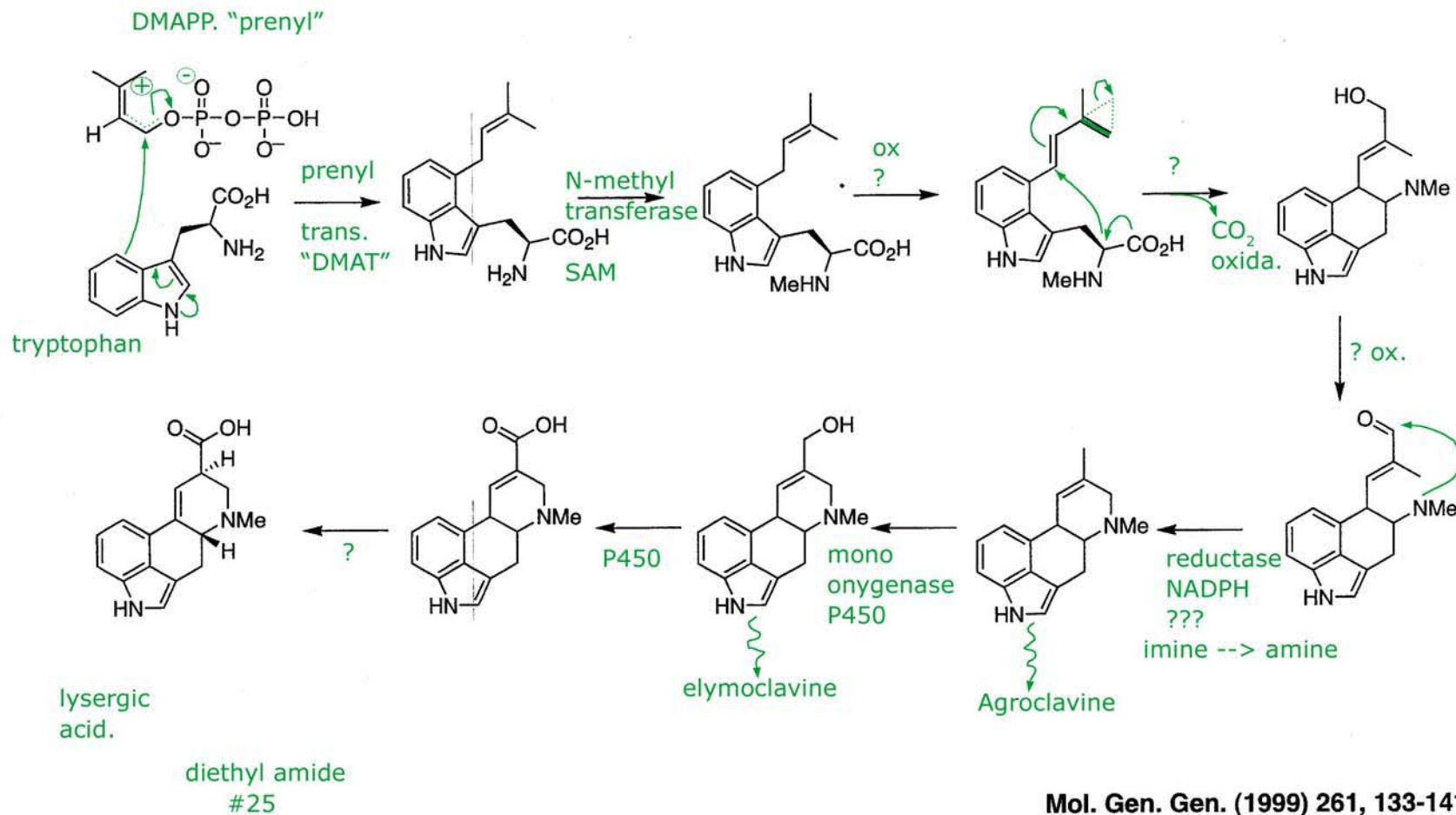


5.451 F2005

### Alkaloid Biosynthesis:

#### Tryptophan

Ergot Alkaloids --> intersection of terpene, alkaloid, peptide

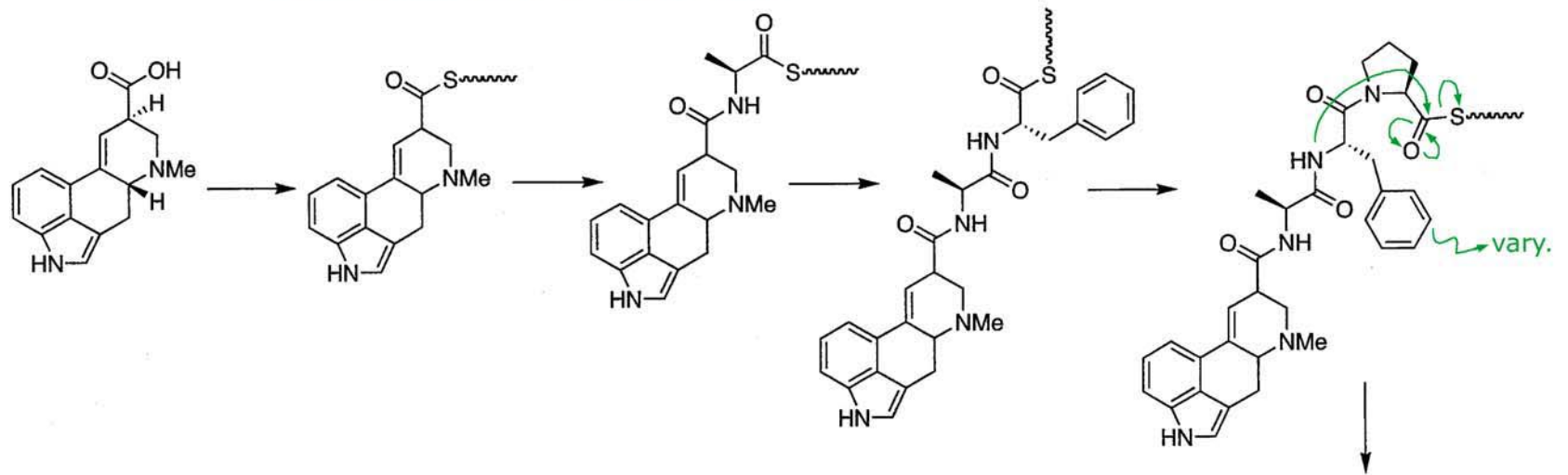


Mol. Gen. Gen. (1999) 261, 133-141  
The Alkaloids, G. Cordell pp. 170-218

produced by fungi --> endophyte of grains

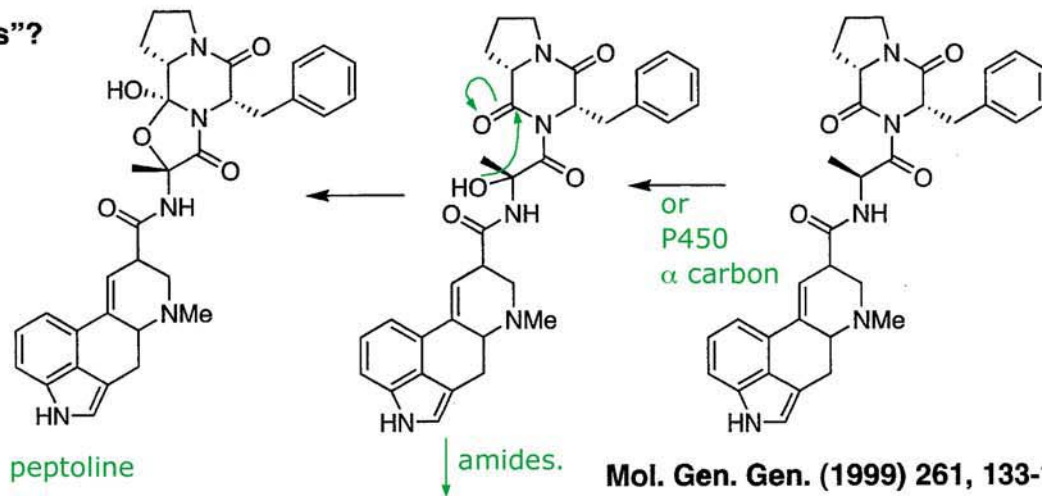
5.451 F2005  
**Alkaloid Biosynthesis:**  
**tryptophan**  
**Ergot Alkaloids**

--> incorporated NRPS --> 3 amino acids



Potential for “combinatorial biosynthesis”?  
 Central amino acid varies

Ergovaline eliminated from a strain  
 of symbiant  
 “ryegrass staggers”  
 (PNAS (2001) 98 12820)

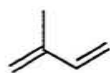


Mol. Gen. Gen. (1999) 261, 133-141  
 The Alkaloids, G. Cordell pp. 170-218

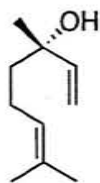
Journal of Biological Chemistry (1995), 270(41), 24475-81.

5.451 F2005

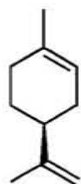
**Terpene Biosynthesis:  
Examples**



**Isoprene**



**+ Linalool**

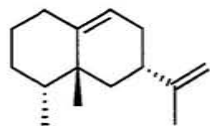


**- Limonene**



**+ β pinene**

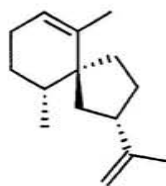
monoterpenes  
C 10



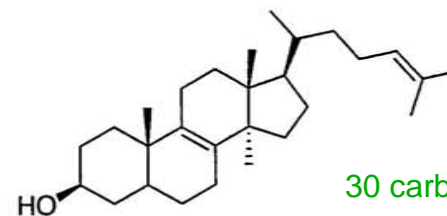
**aristolochene**

sesquiterpenes

C 15

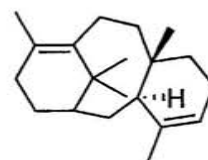


**vetispiradiene**

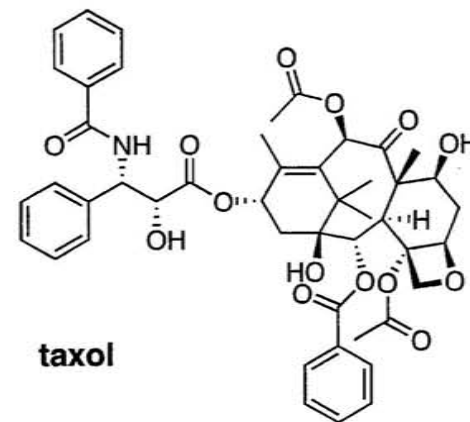


30 carbons

**lanosterol**



diterpene  
C 20



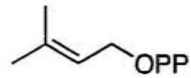
**taxol**

**General References: Chapter 5 Dewick, Top. Curr. Chem. (2000) 209, 53-95**

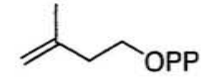
5.451 F2005

Terpene Biosynthesis:

Classifications of Terpenes



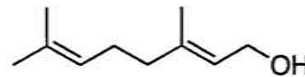
DMAPP



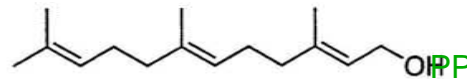
IPP

(diphosphate)

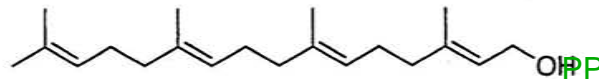
C10 geranyl



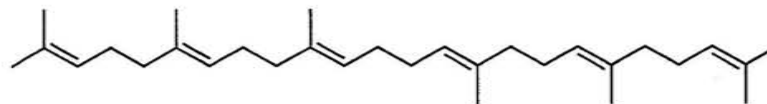
C15 farnesyl



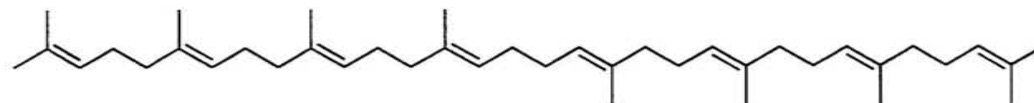
C20 geranylgeranyl



diterpene



C30 squalene



C40 carotenoid

C5, C10, C15, C20, C25, C30

**Terpene Biosynthesis:  
Synthesis of Monomers DMAPP and IPP**

**mevalonic acid pathway**

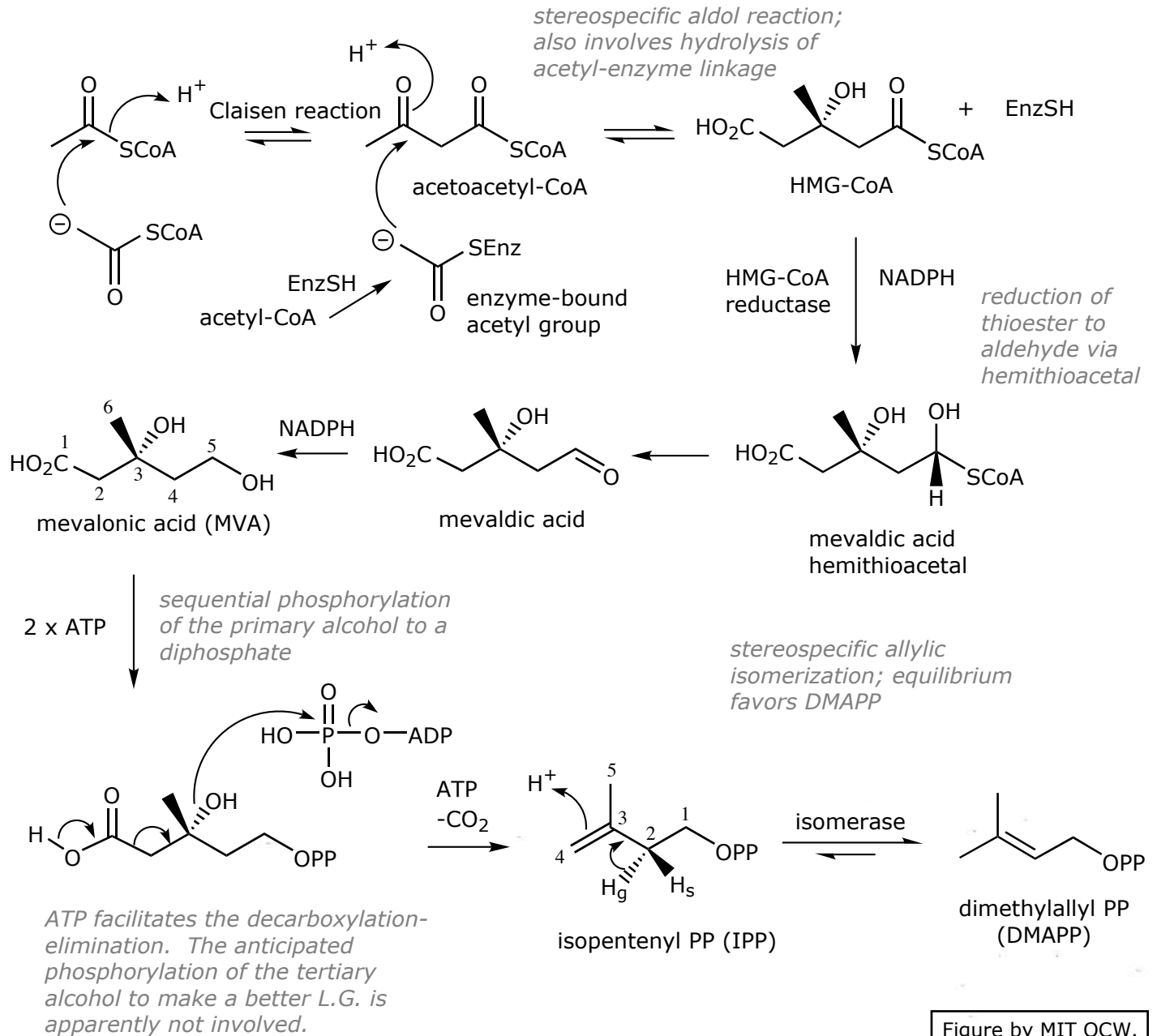
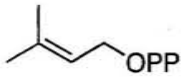


Figure by MIT OCV.

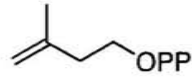
5.451 F2005

Terpene Biosynthesis:

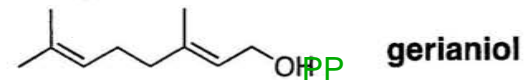
Assembling the Isoprenes: Prenyl Transferase



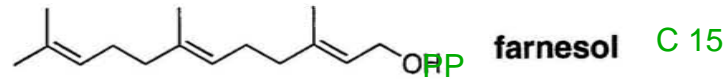
DMAPP



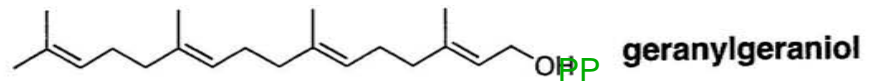
IPP



geraniol



farnesol C 15



geranylgeraniol

**Prenyl transferases: most work done with farnesyl diphosphate synthase**

**Selective for length of chain and stereochemistry of double bonds (terpene biosynthesis all trans)**

**DDXXD or DDXXXXD binds to diphosphate of allylic substrate**

**DDXXD binds IPP**

**Mg<sup>2+</sup>/Mn<sup>2+</sup> dependent**

(1) chemical mechanism

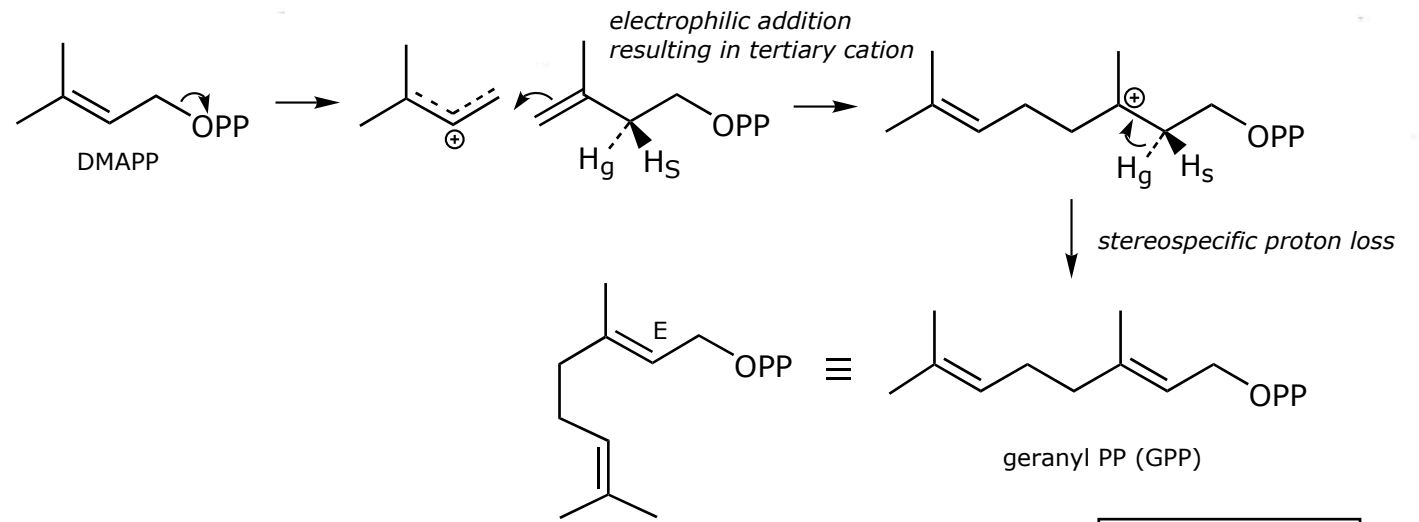
(2) control chain length

Mg<sup>2+</sup> --> anchor for diphosphate of building blocks

**Terpene Biosynthesis:**  
**Assembling the Isoprenes: Prenyl Transferase**

DMAPP electrophile  
IPP nucleophile

ionization - condensation - elimination



farnesyl transferase

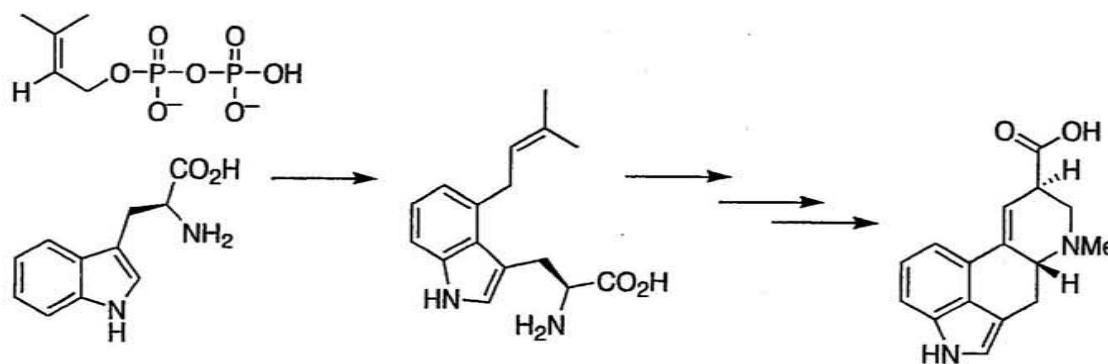
DMAPP + IPP

geranyl PP.

farnesyl PP



Figure by MIT OCW.

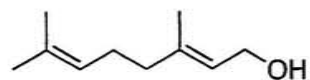


**ergot alkaloids**

5.451 F2005

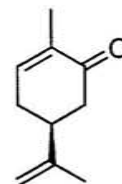
**Terpene Biosynthesis:**

**Rearrangement of the linear chain by terpene cyclases or terpene synthases**

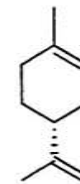


**geraniol**

geraniol-OPP-  
real building block



**+ carvone (caraway)**  
**[- carvone spearmint]**



**+ limonene (oranges)**  
**- limonene (lemons)**

monoterpenes



**Terpene Biosynthesis:**  
**Rearrangement of the C10 geranyl chain:**

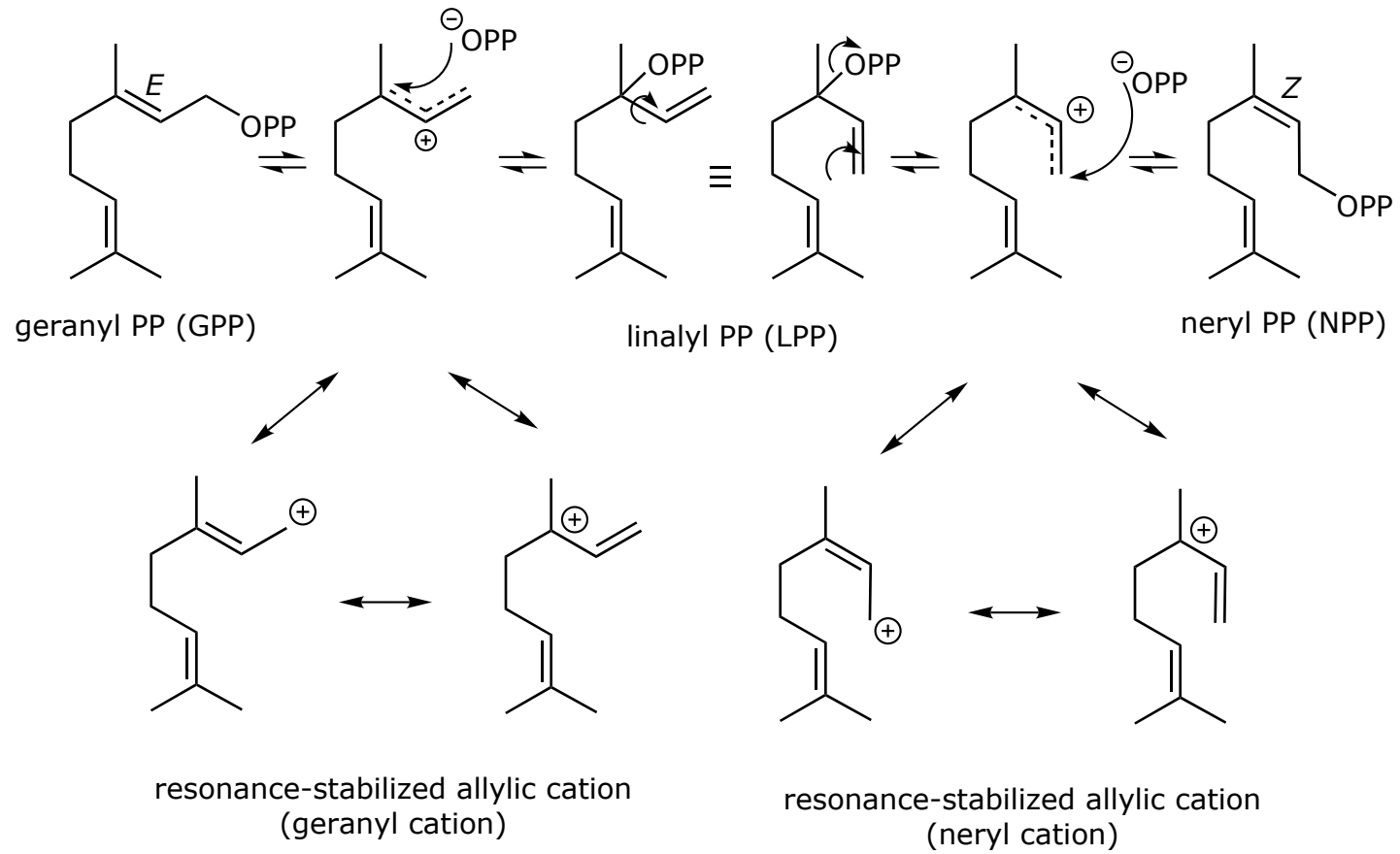
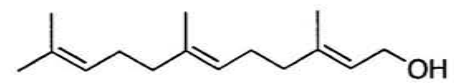
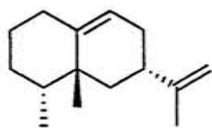


Figure by MIT OCW.

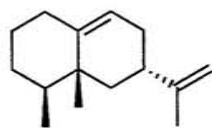
5.451 F2005  
Terpene Biosynthesis:  
C15: Sesquiterpenes



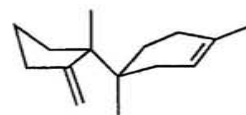
farnesol



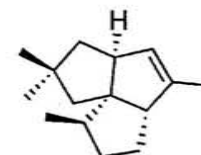
epi-aristolochene



aristolochene

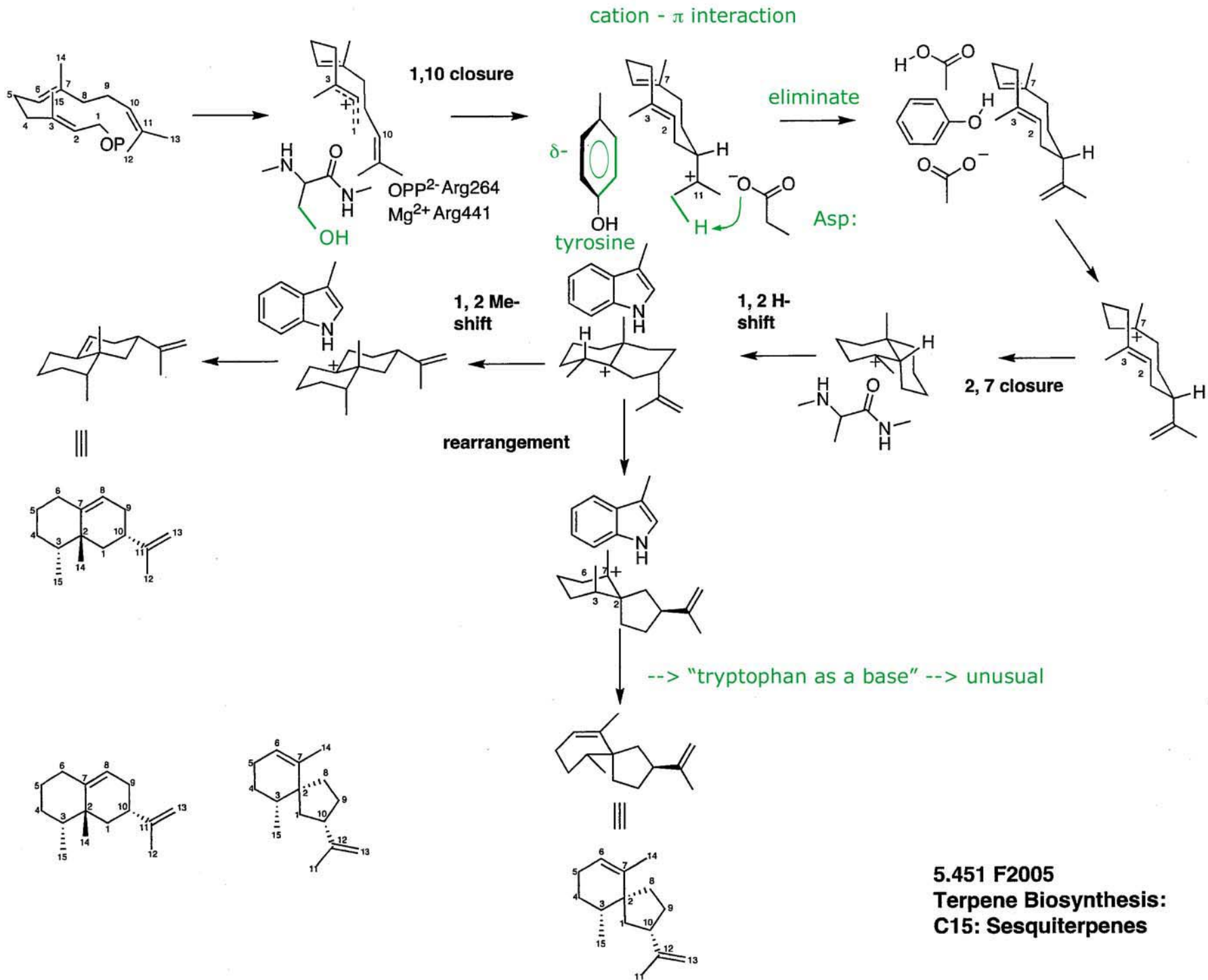


trichodiene



pentalenene

Crystal structures have been solved



## **Index of figures removed due to copyright reasons**

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