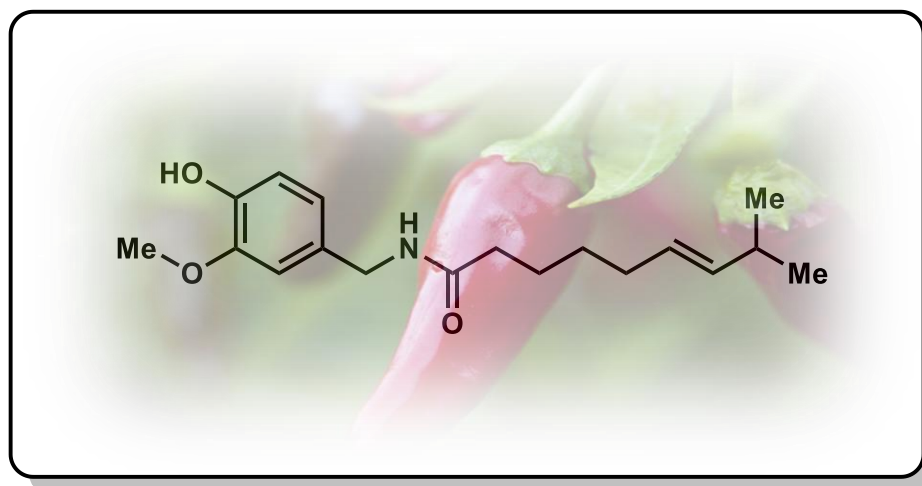


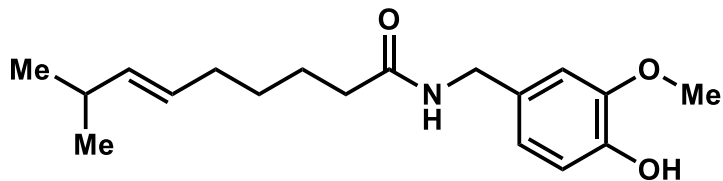


Katerina Duda
10.01.26
The Biegasiewicz Lab



Capsicum annuum

- Subject of 1816 capsaicin isolation
- Native to Americas
- Jalepeño, serrano, cayenne, & bell peppers



capsaicin

Scoville Heat Units (SHU)



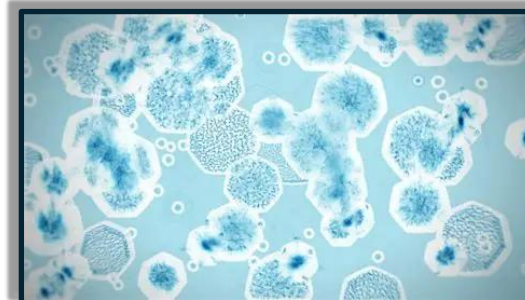
Jalapeño
2-6k SHU

← *n-fold dilution in sugar water** →



Carolina Reaper
1.5 M SHU

Antimicrobial



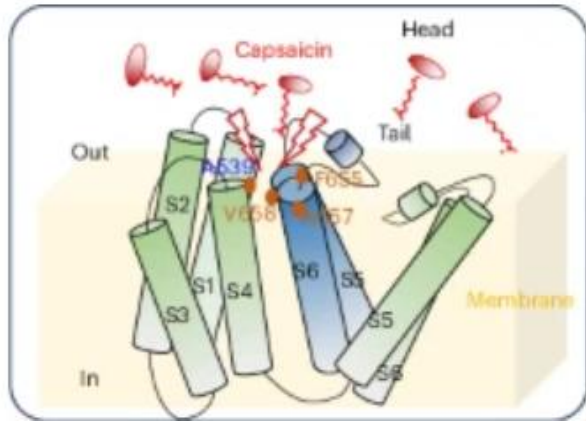
Food additive



Anti-inflammatory



TPRV1 Receptor Binding

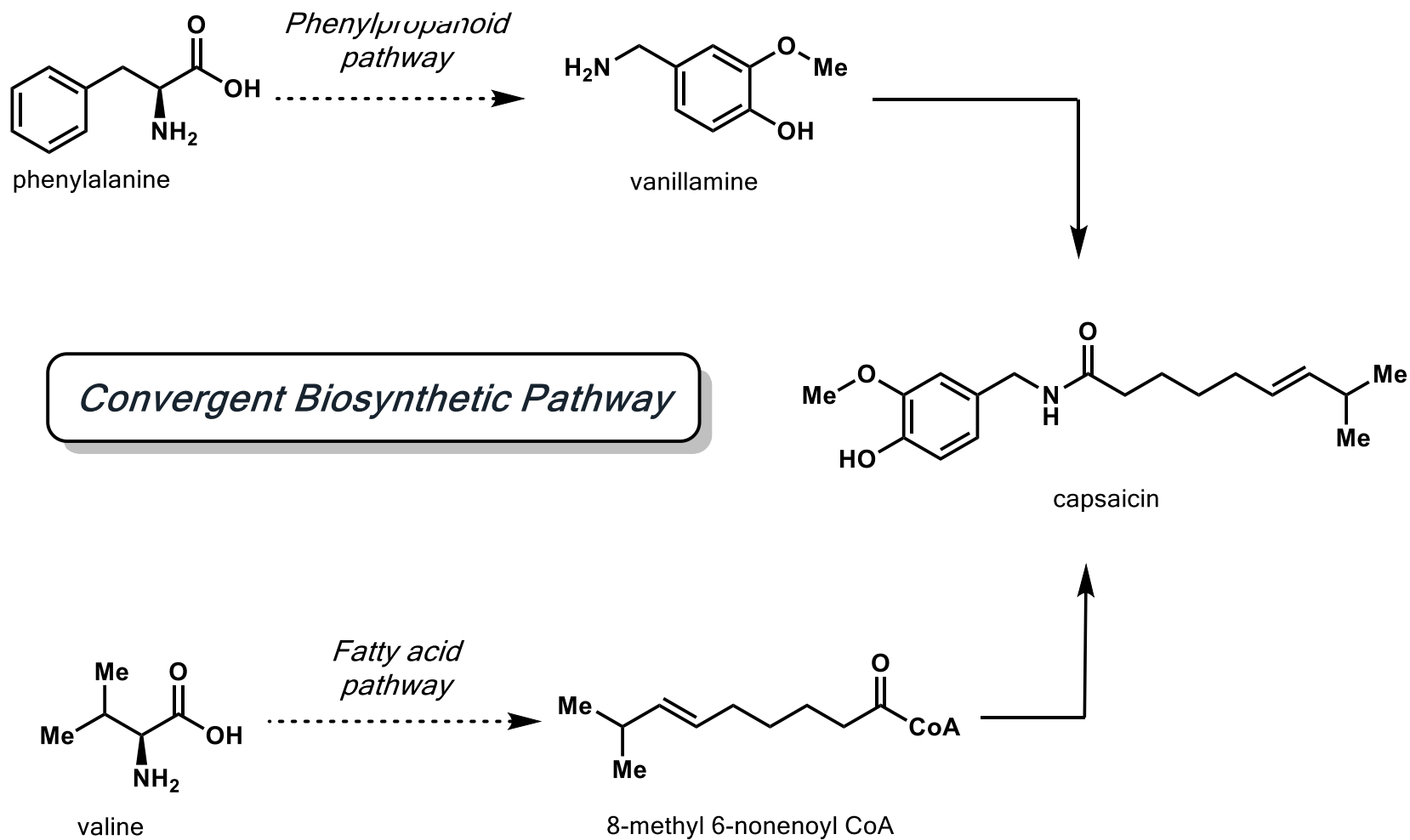


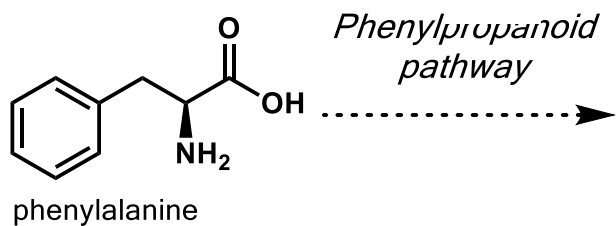
- TRPV1 receptors typically activate at 43°C to detect burning
- Capsaicin binds at buried vanilloid site
- Conformational change opens ion channel
- Pain response is triggered **without tissue damage**

Chemistry-Based Spice Mitigation

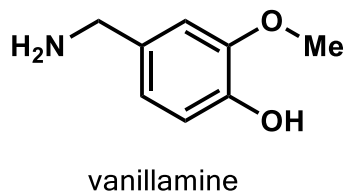


- Fats and oils (soluble)
- Sugar
- Alcohol*
- Cold substances (pain relief; not water).
- Dairy: Casein phosphoproteins will form a micelle around capsaicin molecules.

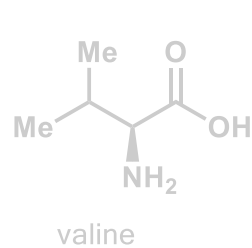




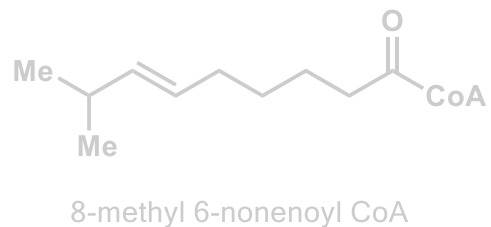
Phenylpropanoid pathway



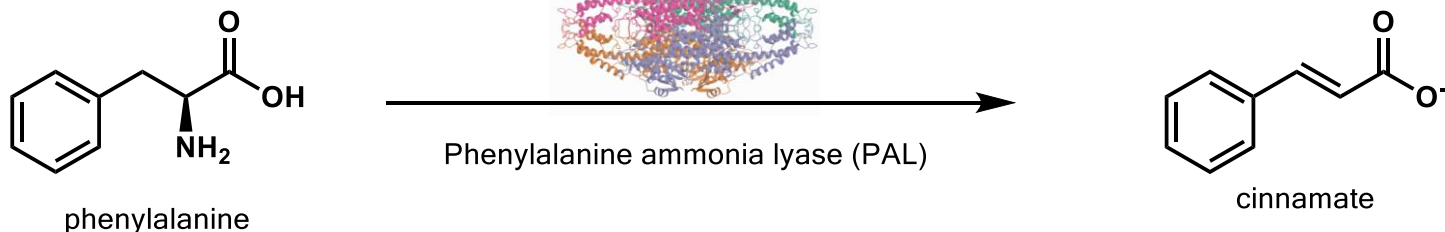
Convergent Biosynthetic Pathway



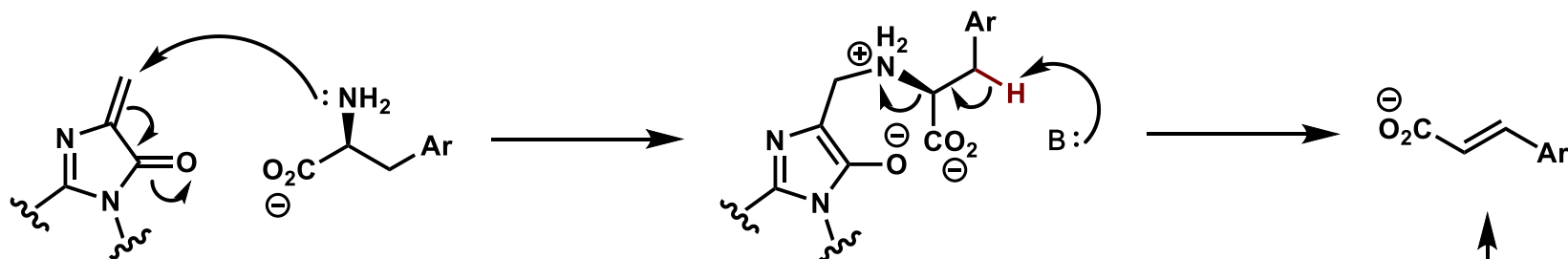
Fatty acid pathway



Deamination of Phenylalanine

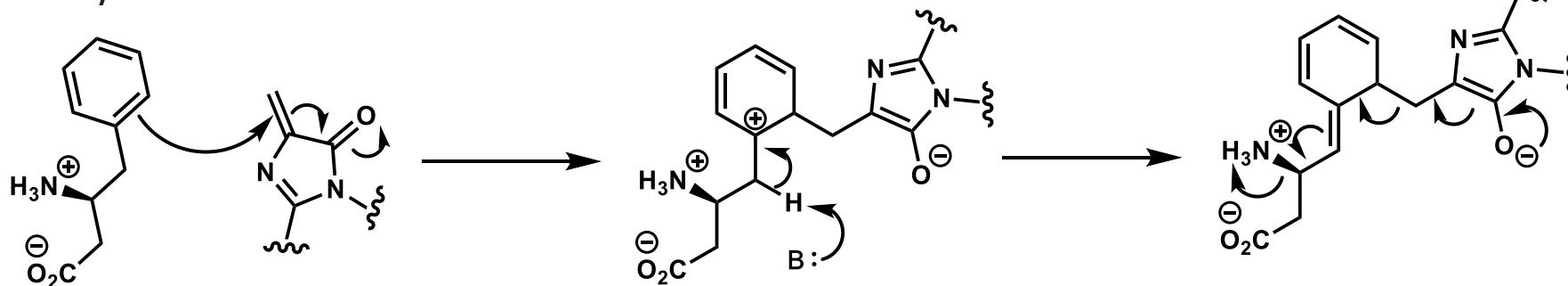


Proposed Mechanism 1

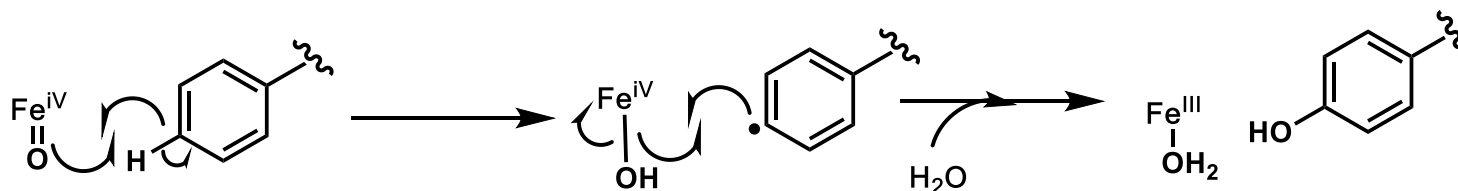
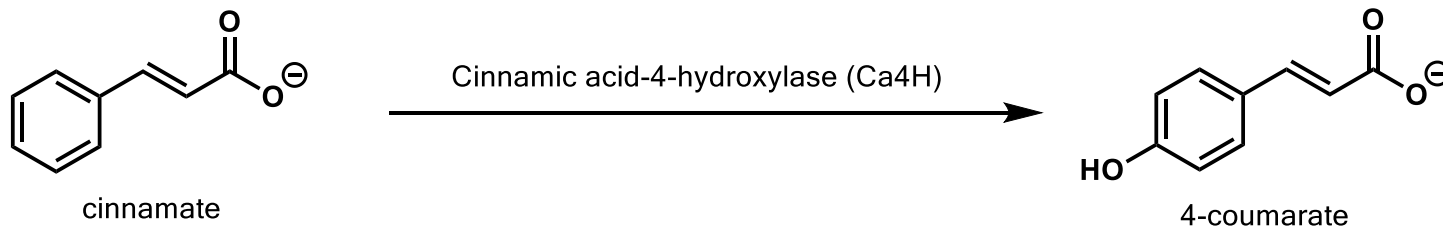


MIO cofactor

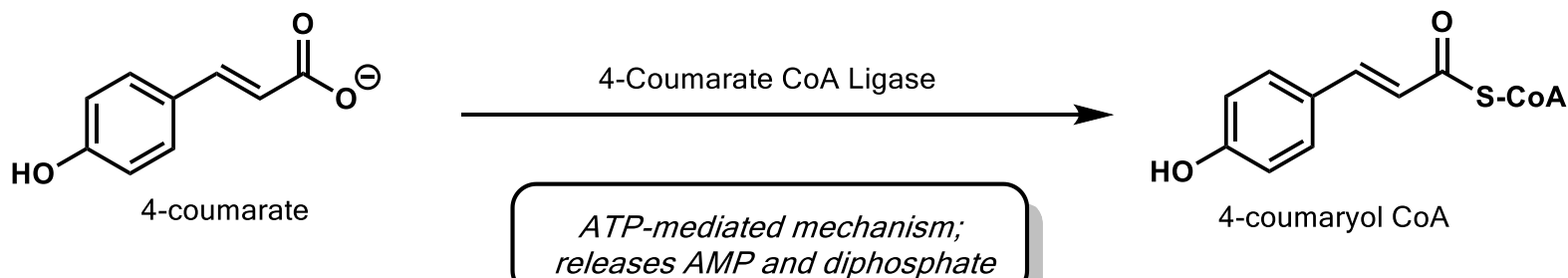
Proposed Mechanism 2

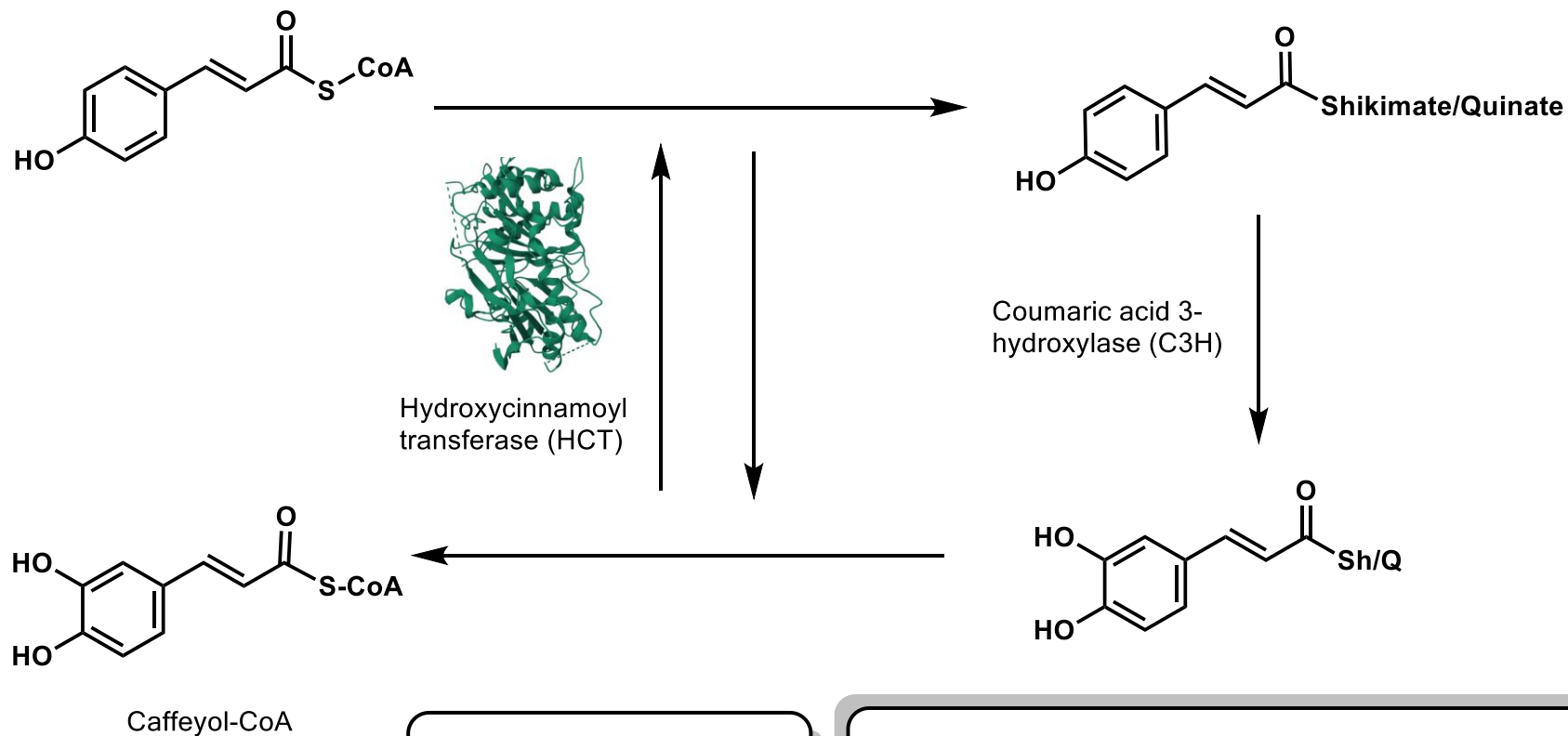


Hydroxylation (Cytochrome P450)

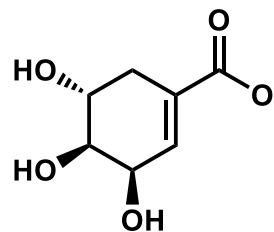


Activation of Coumarate

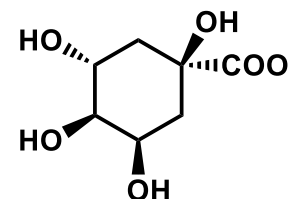




-C3H functions through same cytochrome P450 mechanism
-HCT transfers on/off shikimate or quinate groups to facilitate

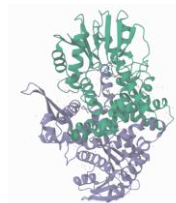
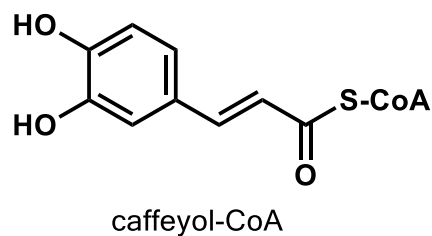


shikimate

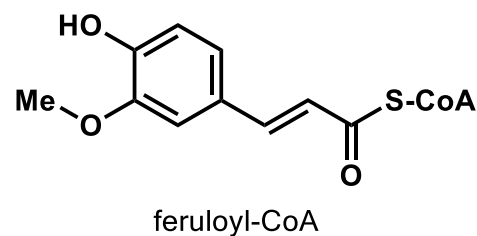


quinate

Methylation of Caffeyol-CoA

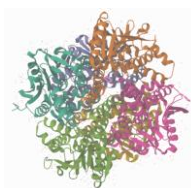
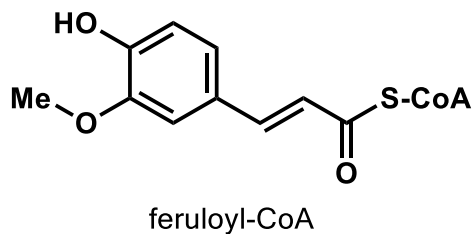


Caffeic Acid O-methyl transferase
(CoMT)

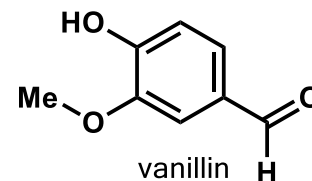


-S_N2 style mechanism with SAM

Cleavage of Feruloyl-CoA

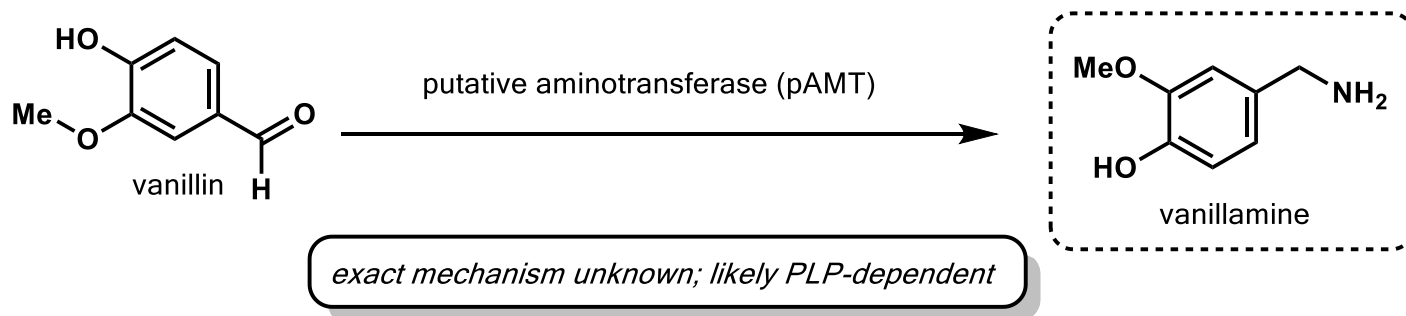


4-Hydroxycinnamoyl-CoA
Hydratase/Lyase (HCHL)

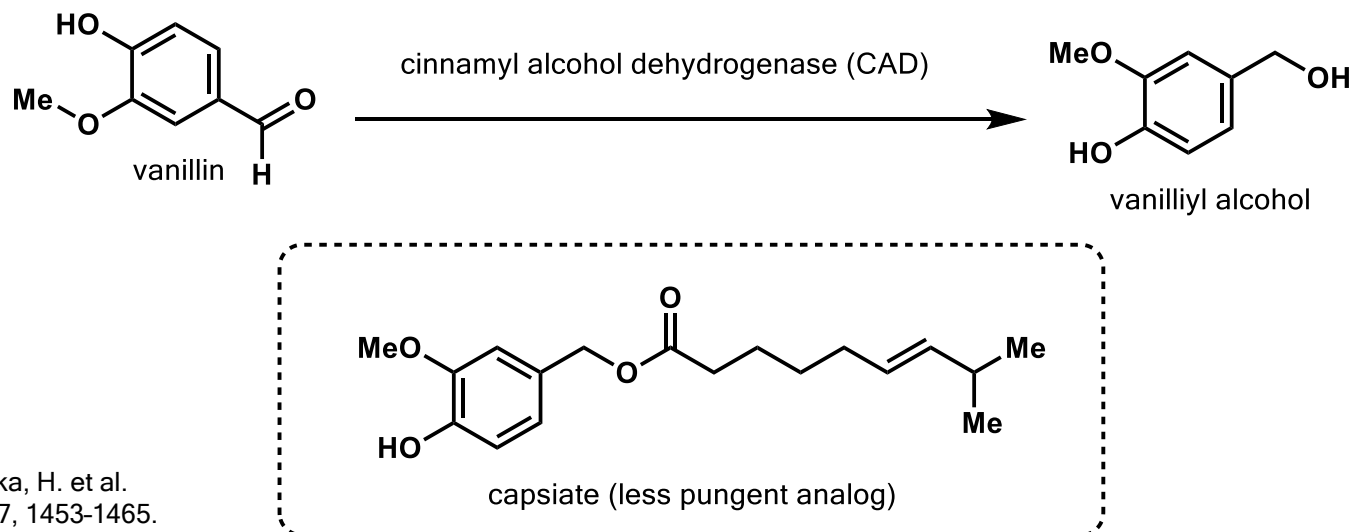


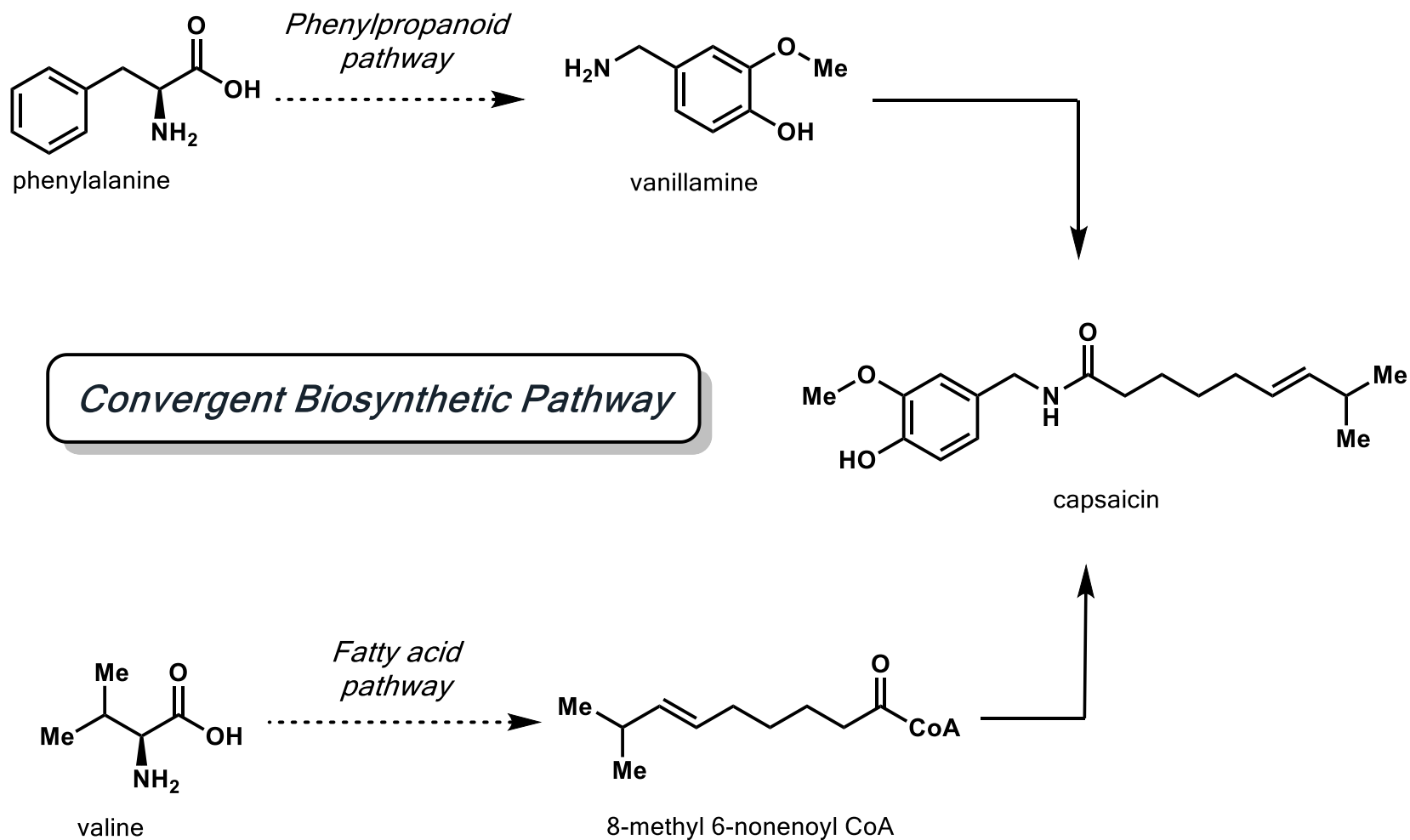
retro-aldol cleavage

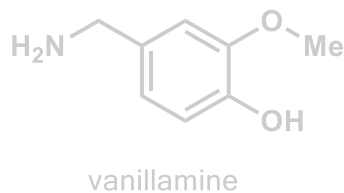
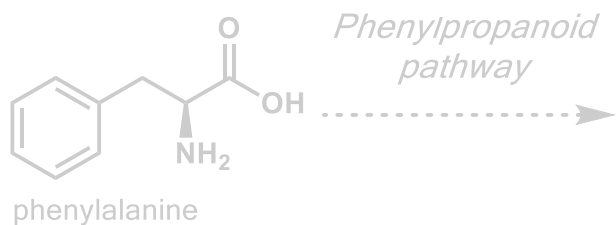
Amino Group Transfer



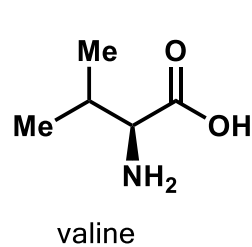
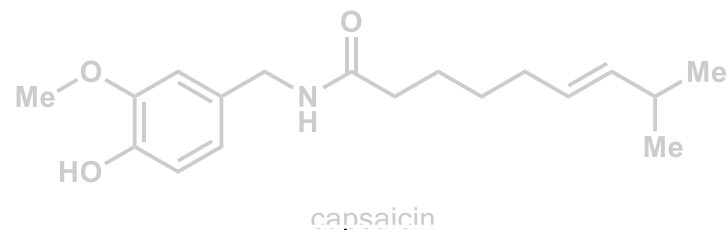
Divergent Pathway in Sweet Chili Peppers



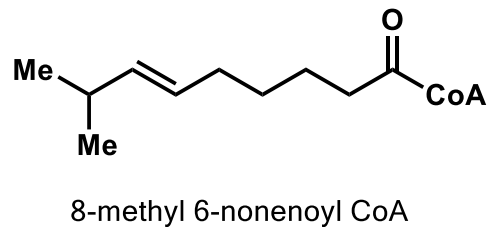


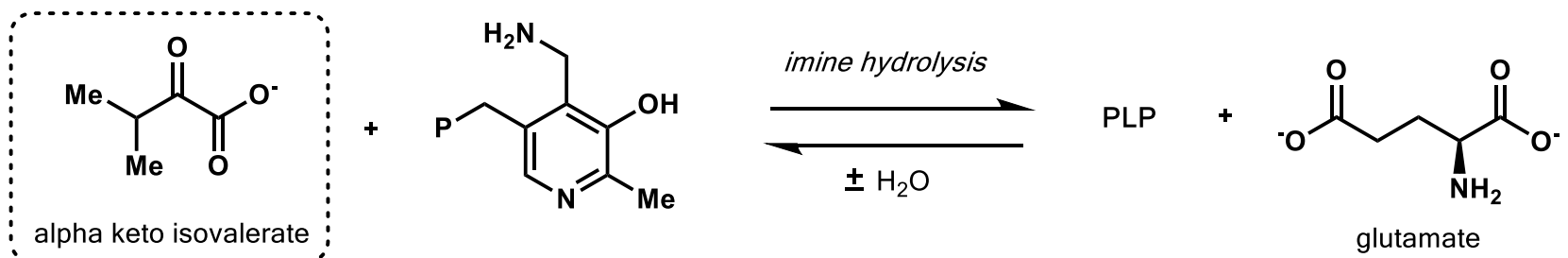
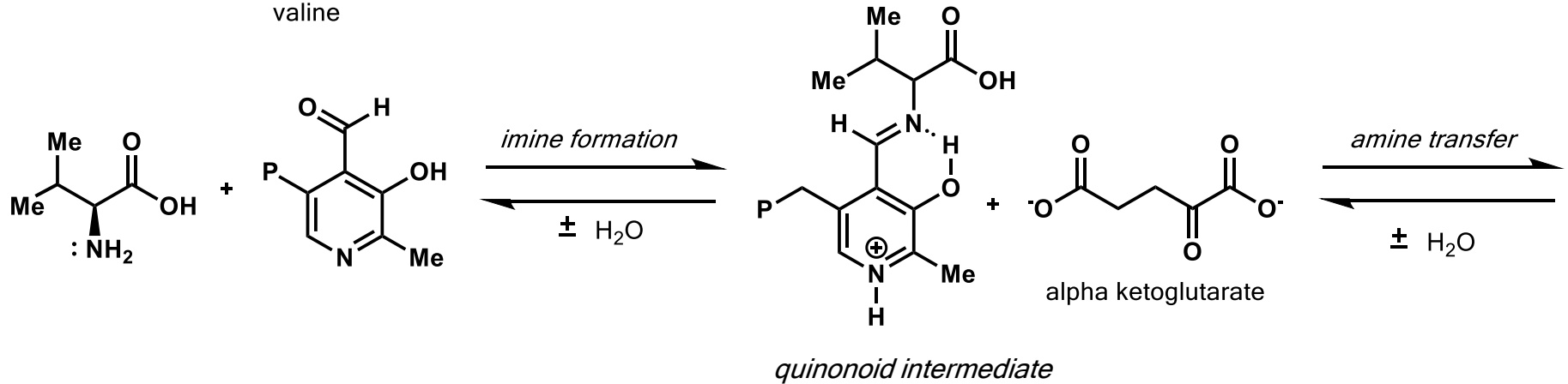
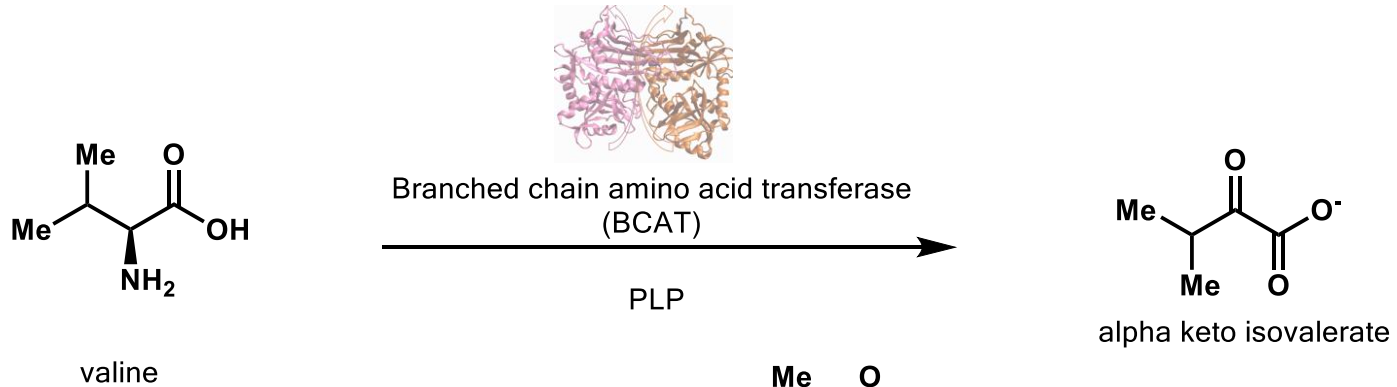


Convergent Biosynthetic Pathway

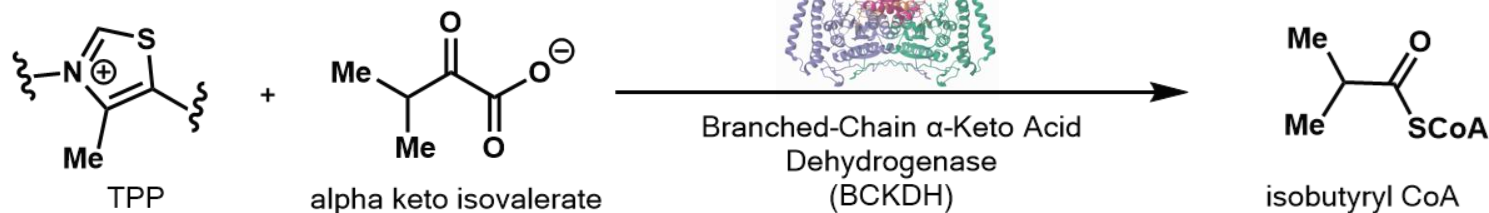


Fatty acid pathway

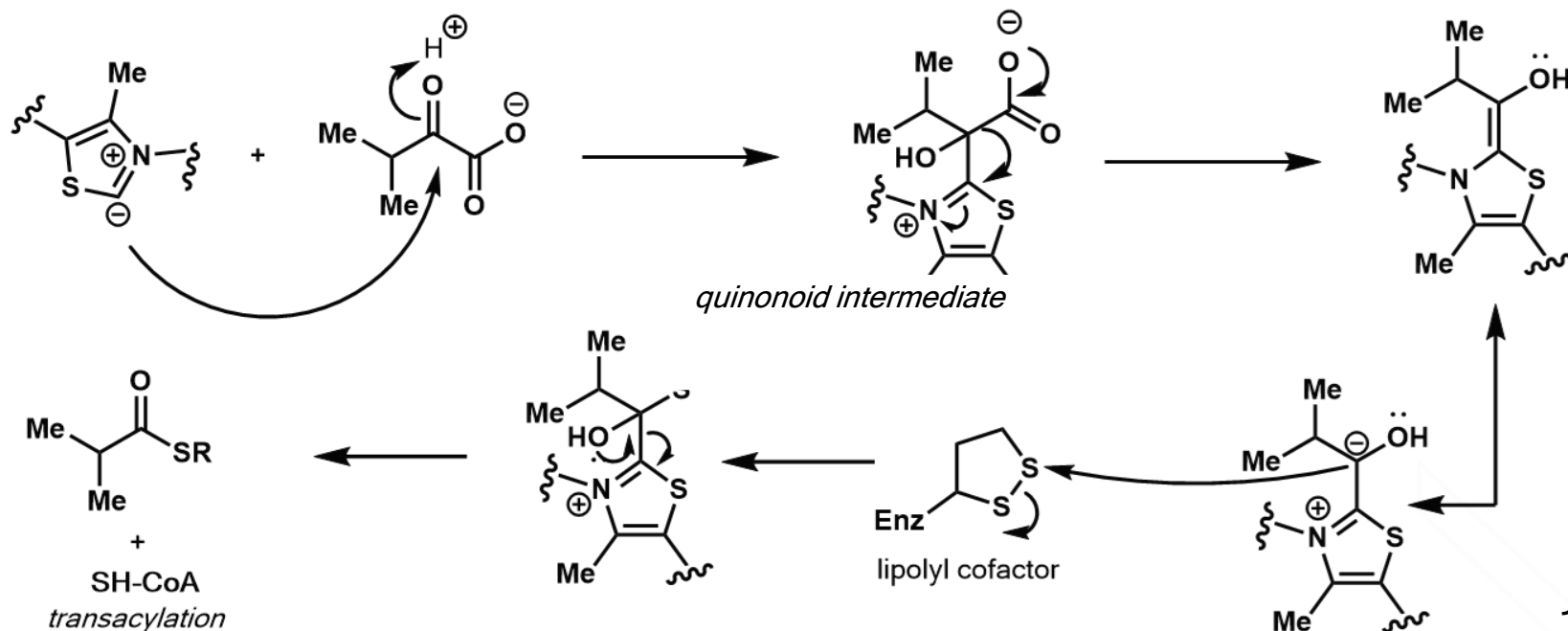




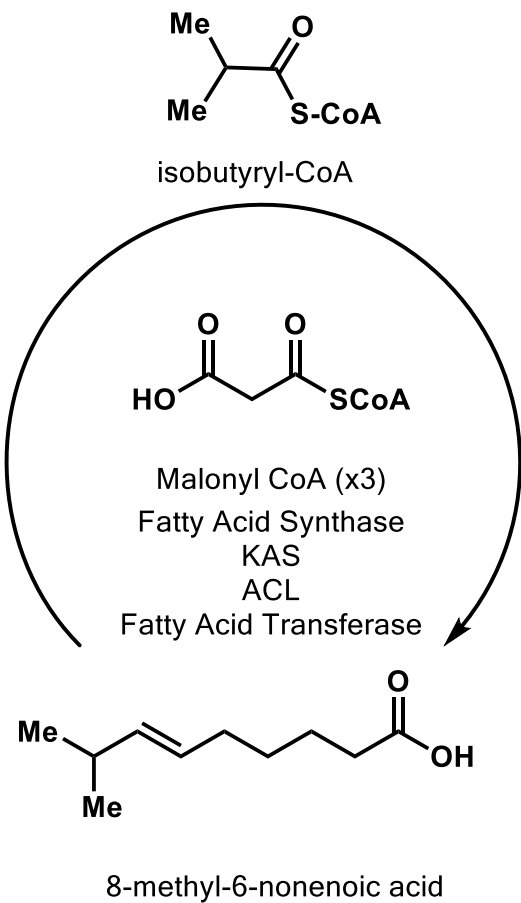
Decarboxylation of Isolevalerate



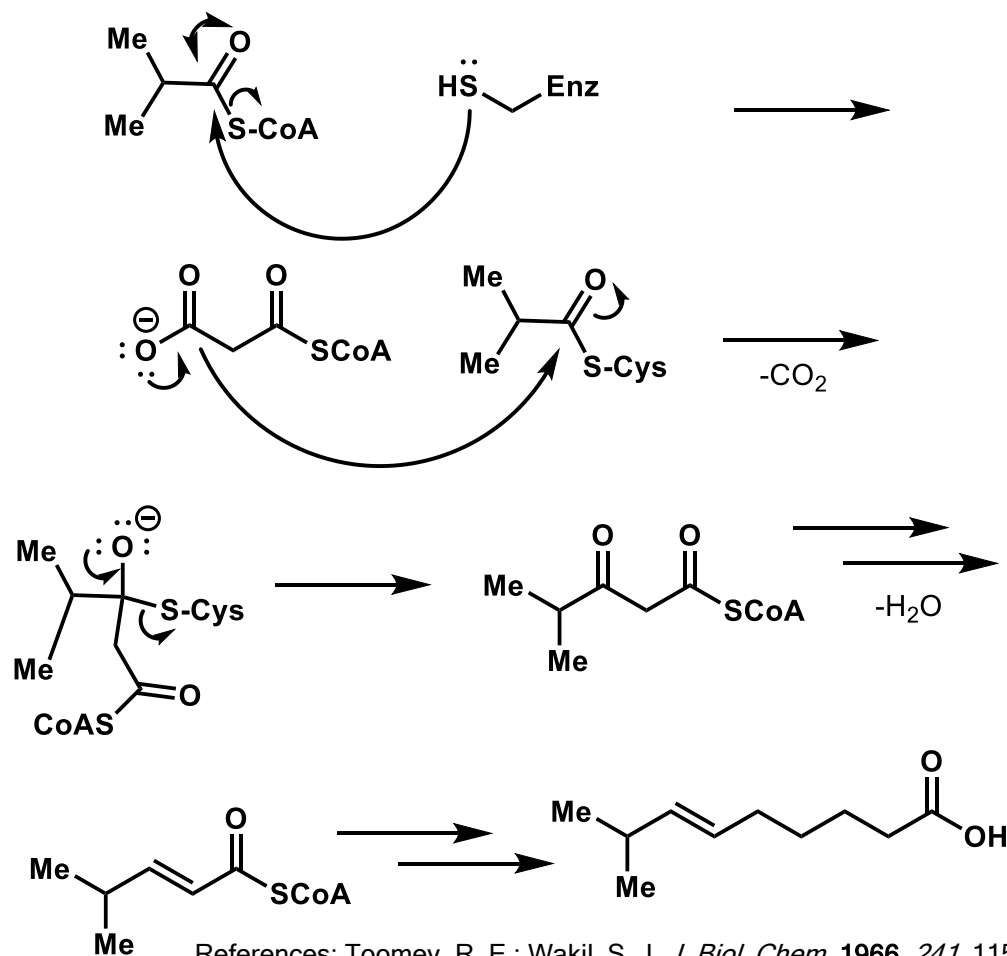
Proposed Mechanism



Malonyl-CoA Condensation

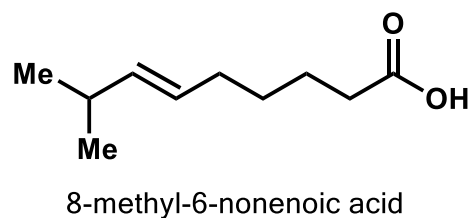


Abbreviated Mechanism

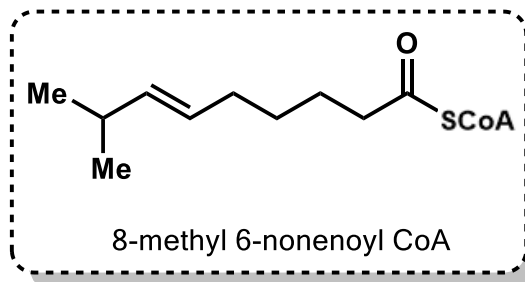


End of Fatty Acid Pathway and Capsaicin Condensation

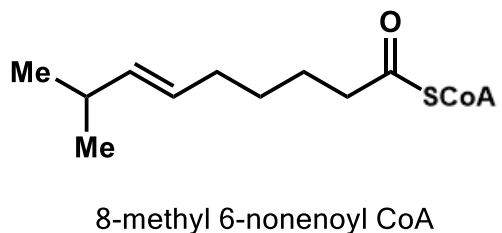
CoA Substitution



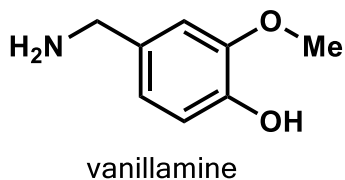
Acetyl-CoA Synthetase (ACS)



Pathway Convergence and Final Condensation



+



Capsaicin Synthase
(*Pun1*)

