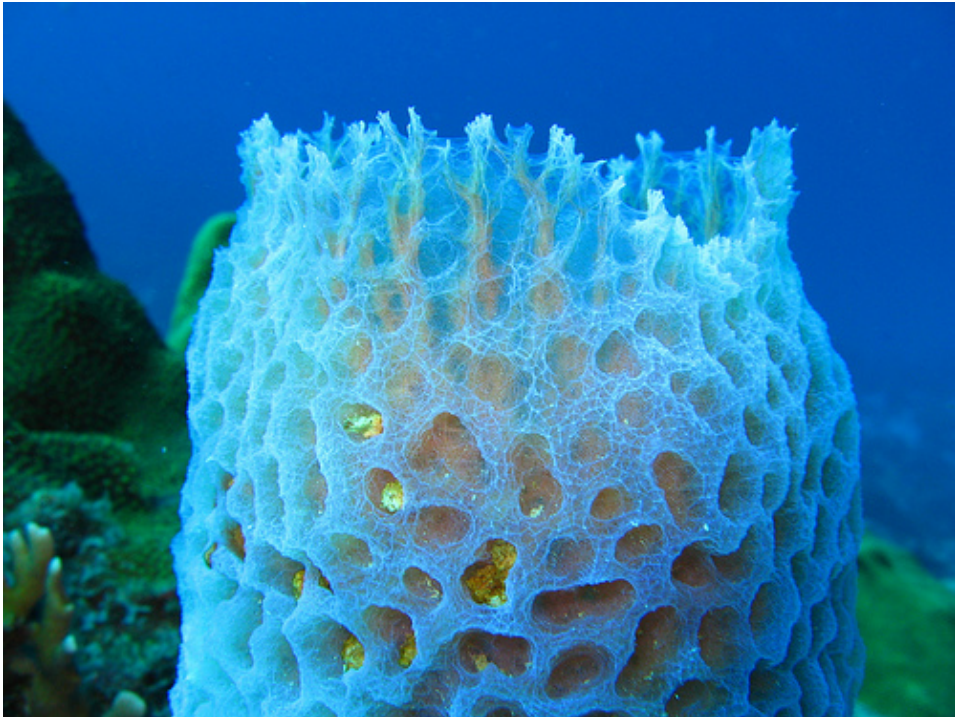


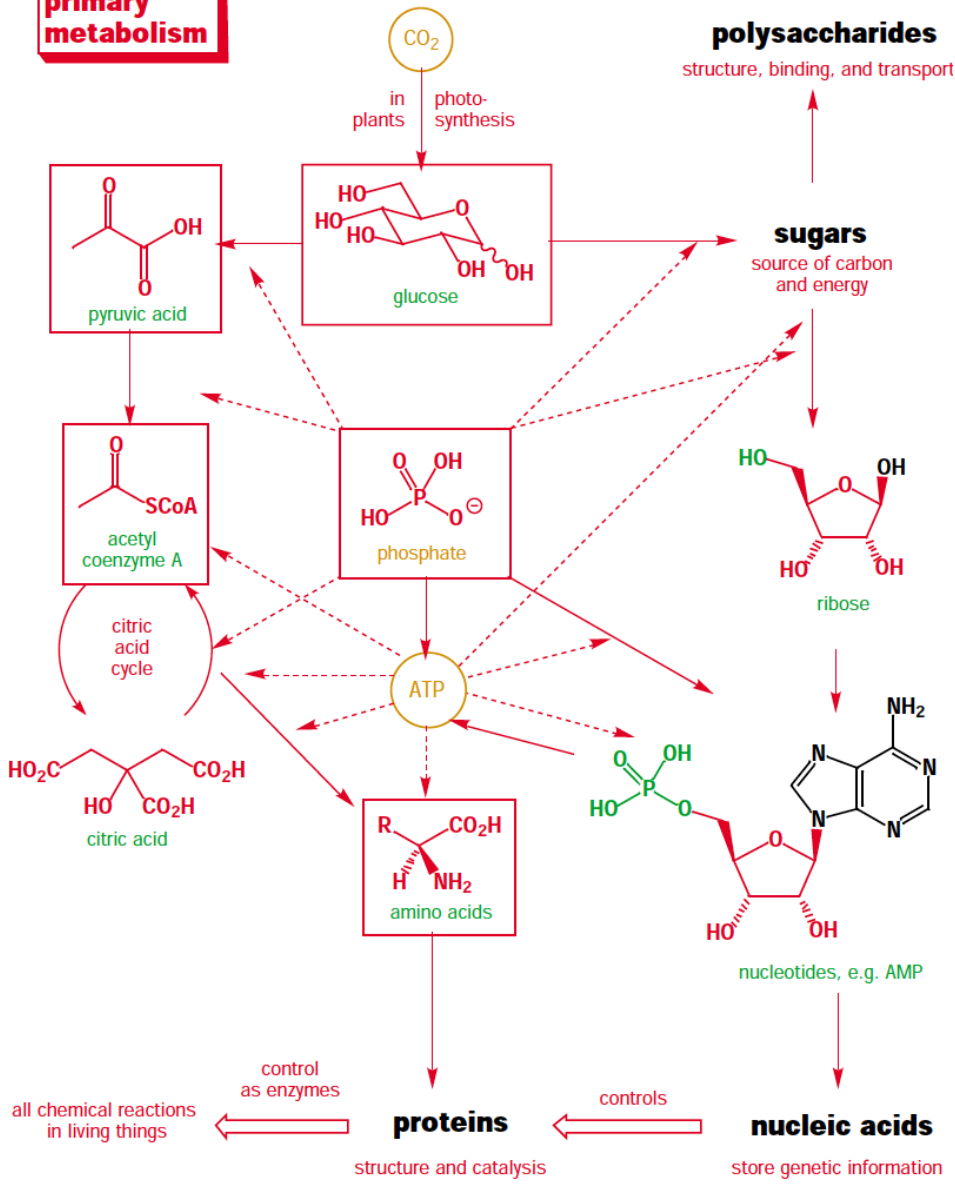
CHIMICA DELLE SOSTANZE ORGANICHE NATURALI



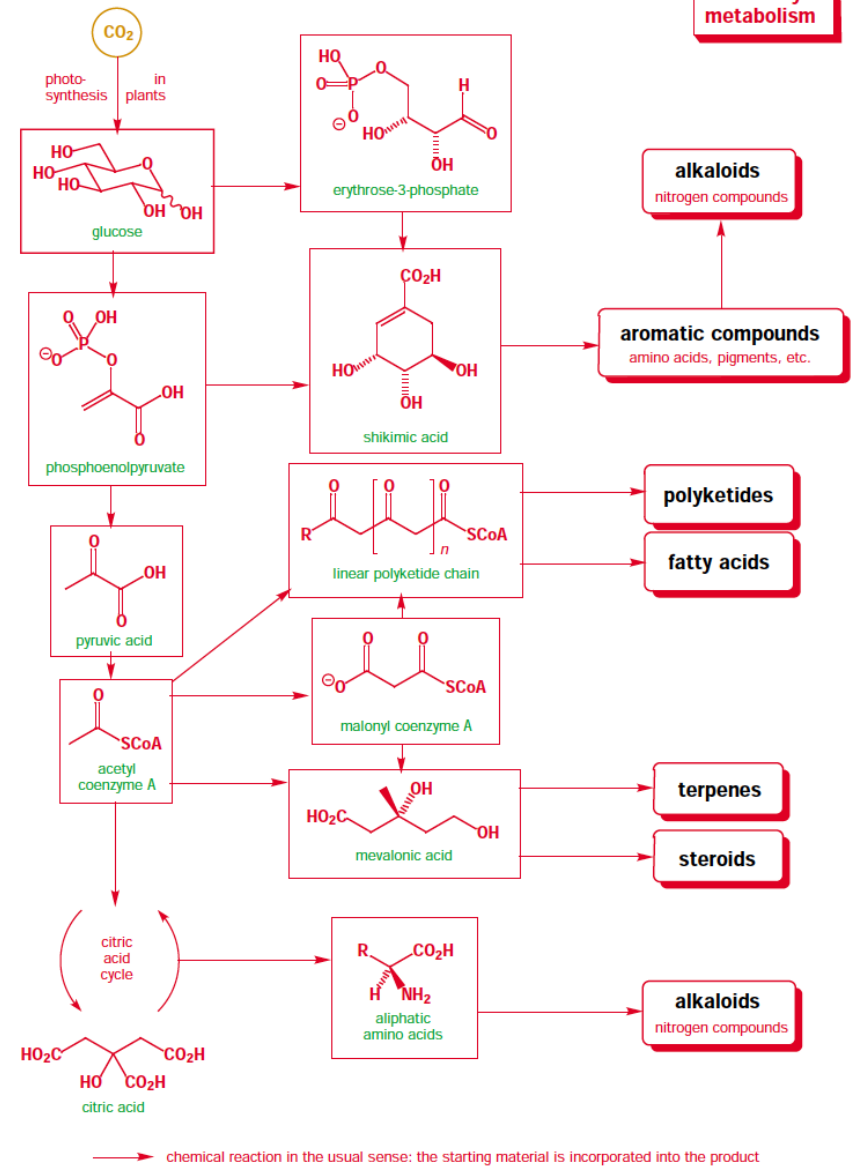
DISCODERMIA DISSOLUTA

LA VIA
DELL'ACETATO:
ACIDI GRASSI E
POLICHETIDI

primary metabolism

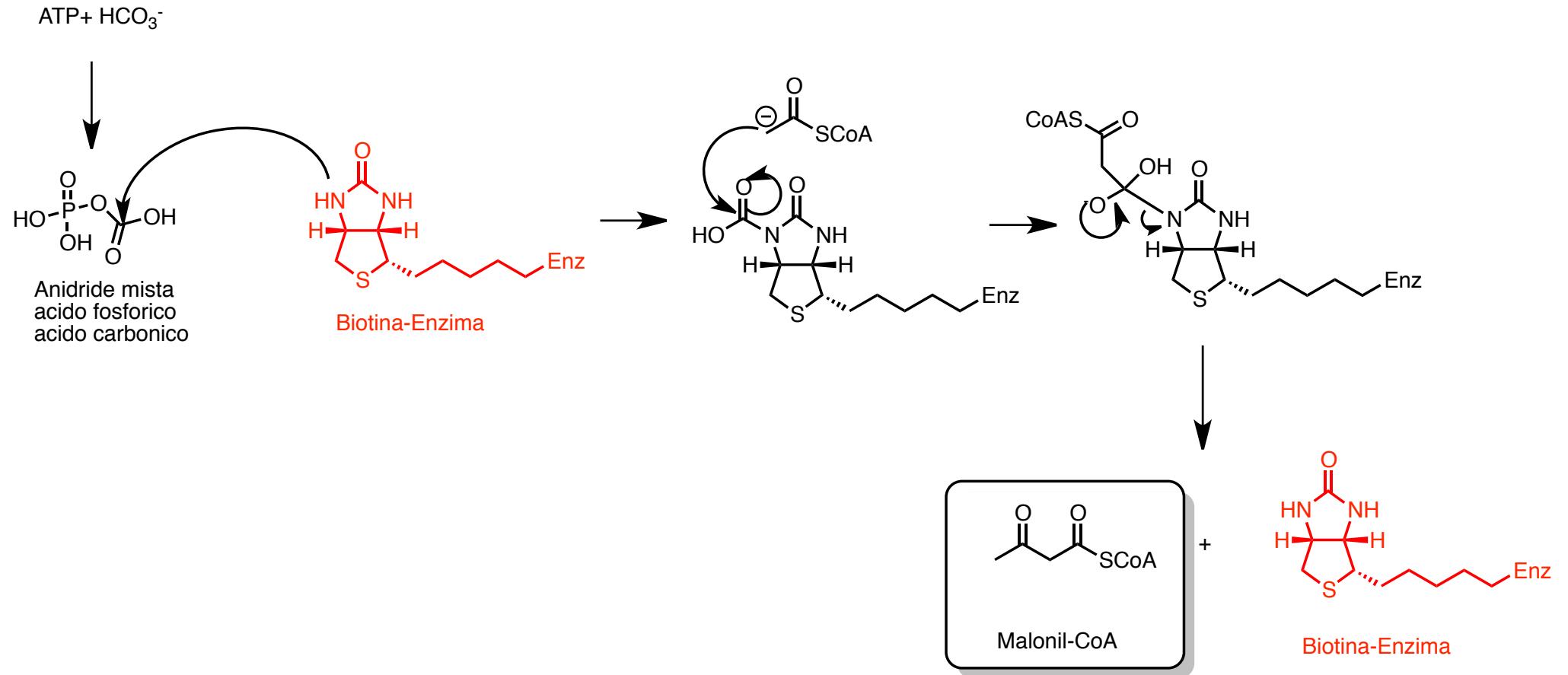


secondary metabolism



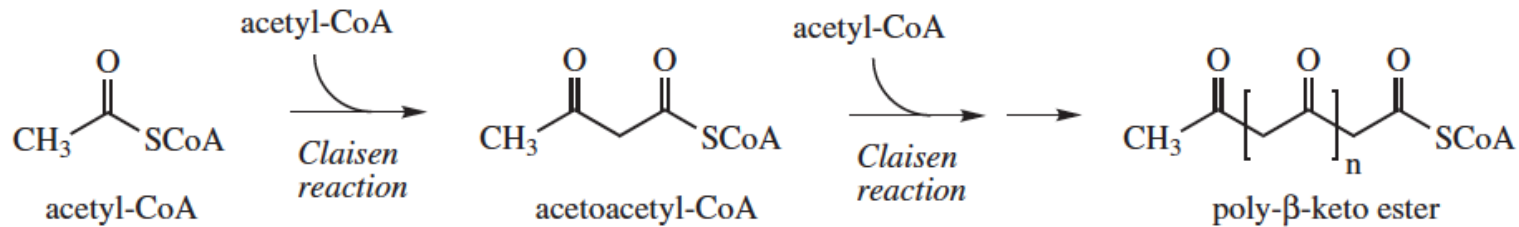
→ chemical reaction in the usual sense: the starting material is incorporated into the product

Biosintesi MALONIL-CoA

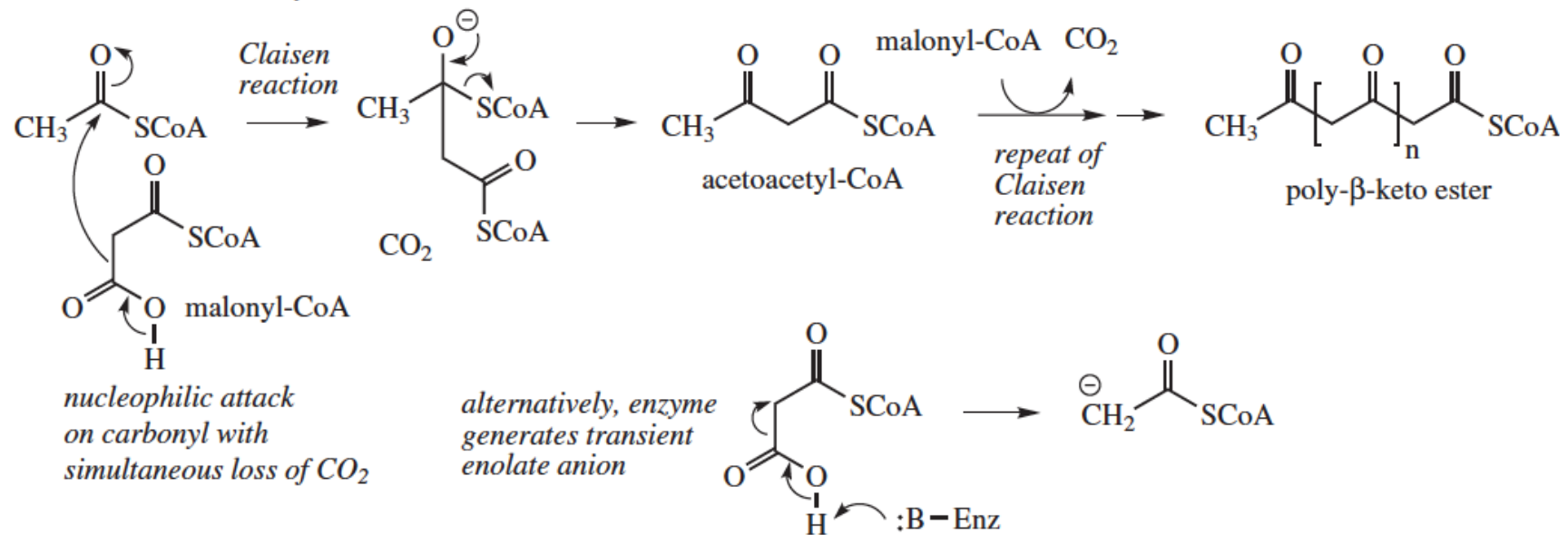


Biosintesi degli acidi grassi

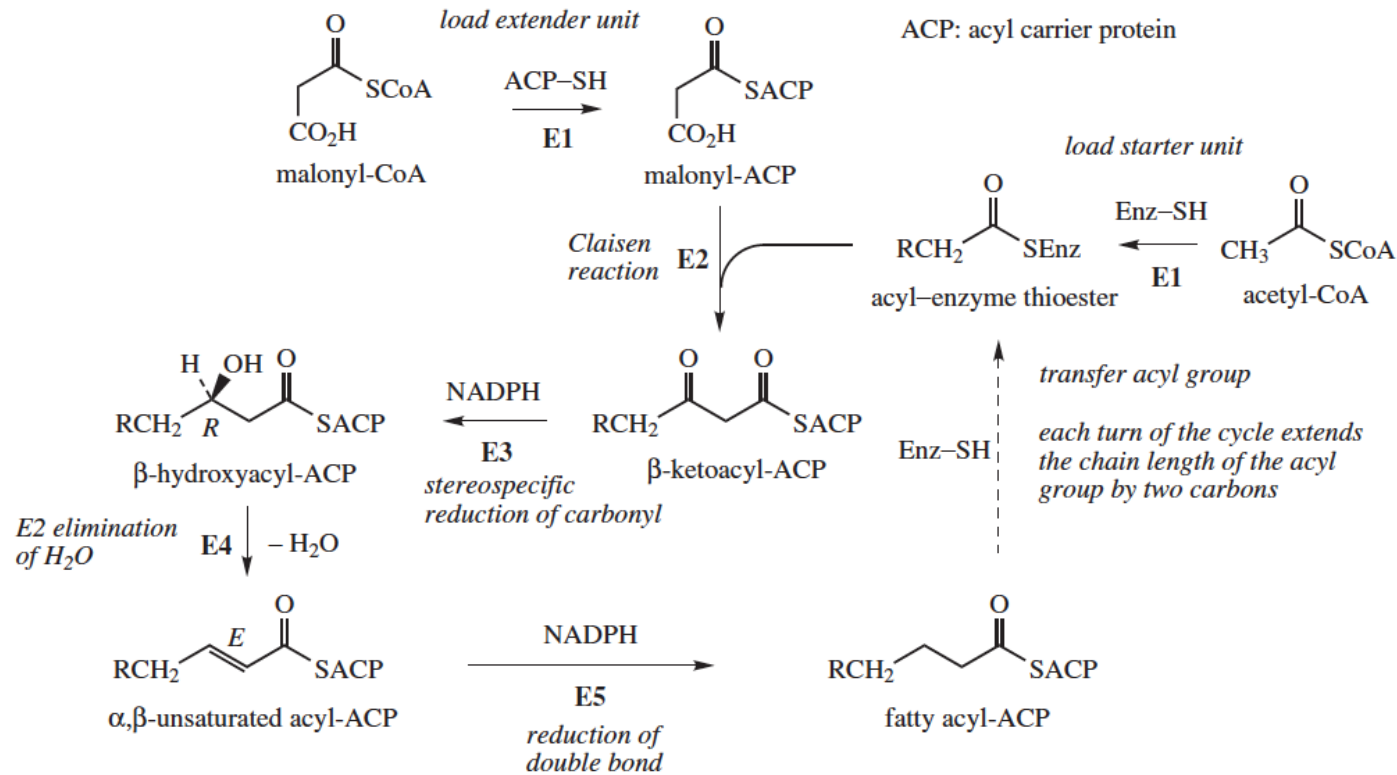
Claisen reaction: acetyl-CoA



Claisen reaction: malonyl-CoA

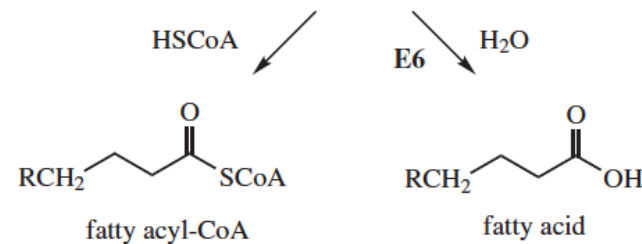


Biosintesi degli acidi grassi

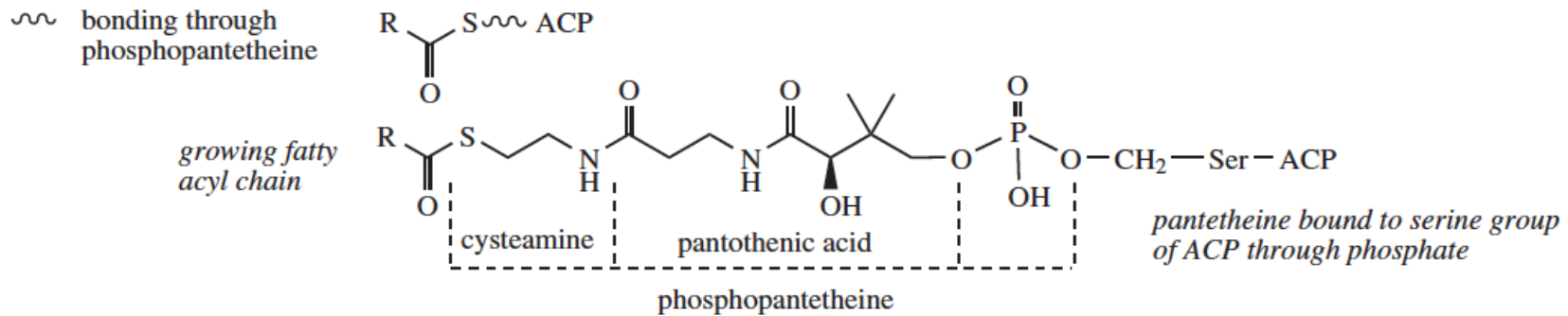
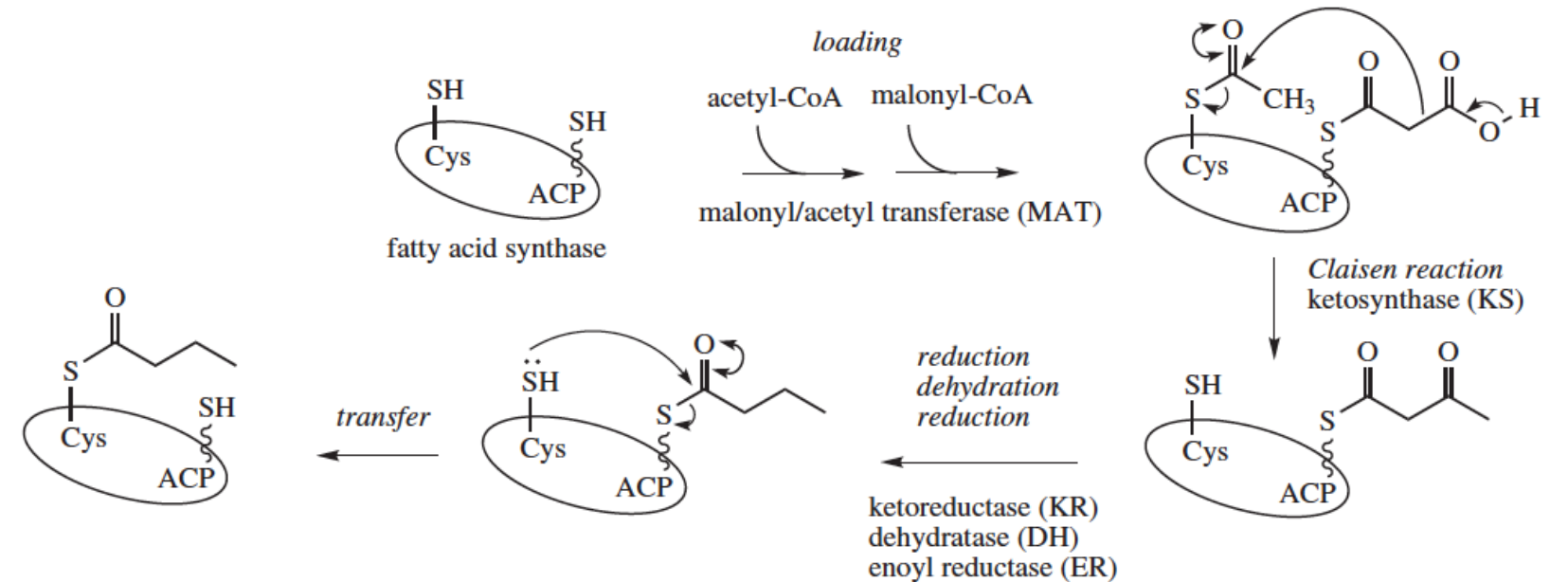


Enzyme activities of mammalian fatty acid synthase

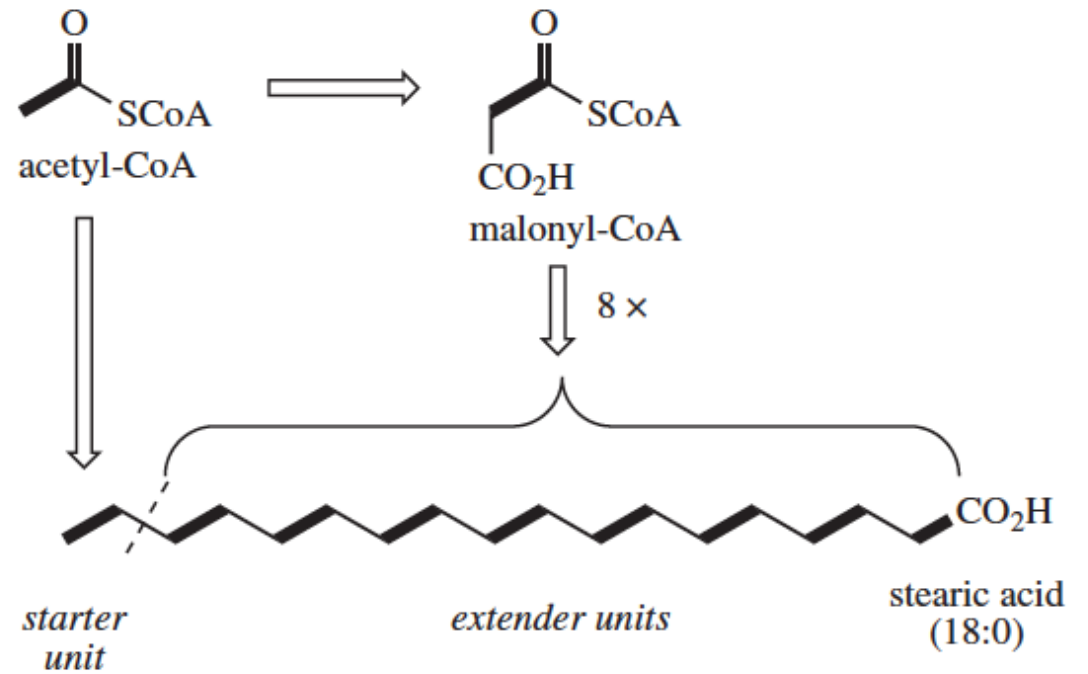
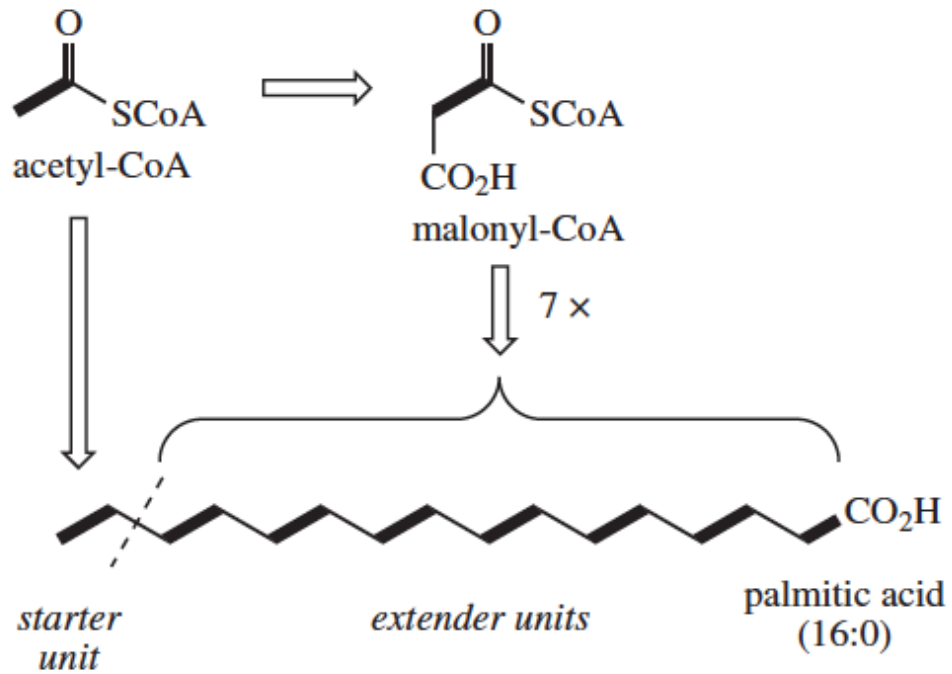
- E1: malonyl/acetyl transferase (MAT; malonyl-CoA/acetyl-CoA-ACP-transacylase)
- E2: ketosynthase (KS; β -ketoacyl synthase)
- E3: ketoreductase (KR; β -ketoacyl reductase)
- E4: dehydratase (DH)
- E5: enoyl reductase (ER; β -enoyl reductase)
- E6: thioesterase (TE)



Biosintesi degli acidi grassi



Biosintesi degli acidi grassi



Biosintesi degli acidi grassi

Common naturally occurring fatty acids

Saturated

butyric	4:0	
caproic *	6:0	
caprylic *	8:0	
capric *	10:0	
lauric	12:0	
myristic	14:0	
palmitic	16:0	
stearic	18:0	
arachidic	20:0	
behenic	22:0	
lignoceric	24:0	
cerotic	26:0	
montanic	28:0	
melissic	30:0	

Abbreviations:

Number of carbon atoms

Position of double bonds

18:2 (9c,12c)












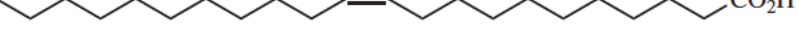



Stereochemistry of double bonds
(c = cis/Z; t = trans/E)

Number of double bonds

* To avoid confusion, systematic nomenclature (hexanoic, octanoic, decanoic) is recommended

Biosintesi degli acidi grassi

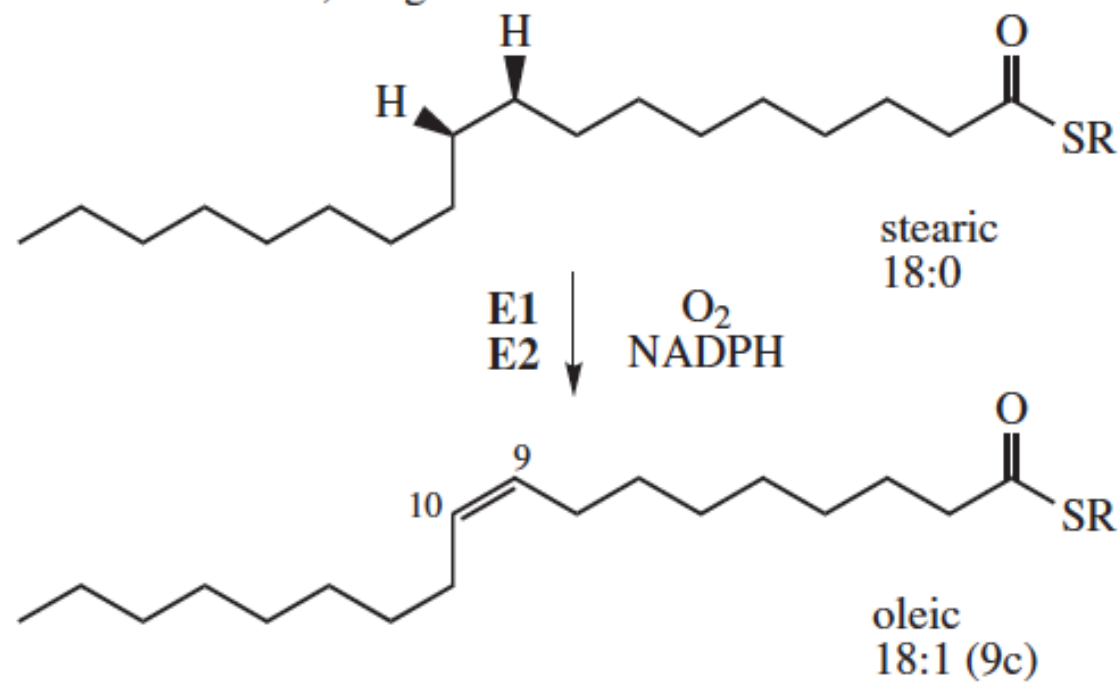
Unsaturated

palmitoleic		16:1 (9c)
oleic		18:1 (9c)
<i>cis</i> -vaccenic		18:1 (11c)
linoleic		18:2 (9c,12c)
α -linolenic		18:3 (9c,12c,15c)
γ -linolenic		18:3 (6c,9c,12c)
gadoleic		20:1 (9c)
gondoic		20:1 (11c)
arachidonic		20:4 (5c,8c,11c,14c)
eicosapentaenoic (EPA)		20:5 (5c,8c,11c,14c,17c)
cetoleic		22:1 (11c)
erucic		22:1 (13c)
docosapentaenoic (DPA)		22:5 (7c,10c,13c,16c,19c)
docosahexaenoic (DHA)		22:6 (4c,7c,10c,13c,16c,19c)
nervonic		24:1 (15c)

Biosintesi degli acidi grassi

R = ACP in plants

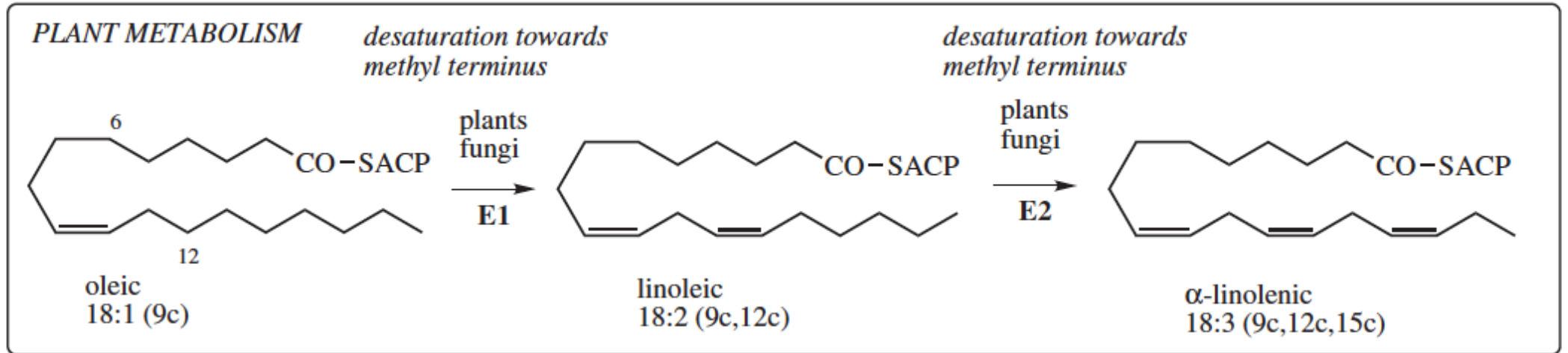
R = CoA in animals, fungi



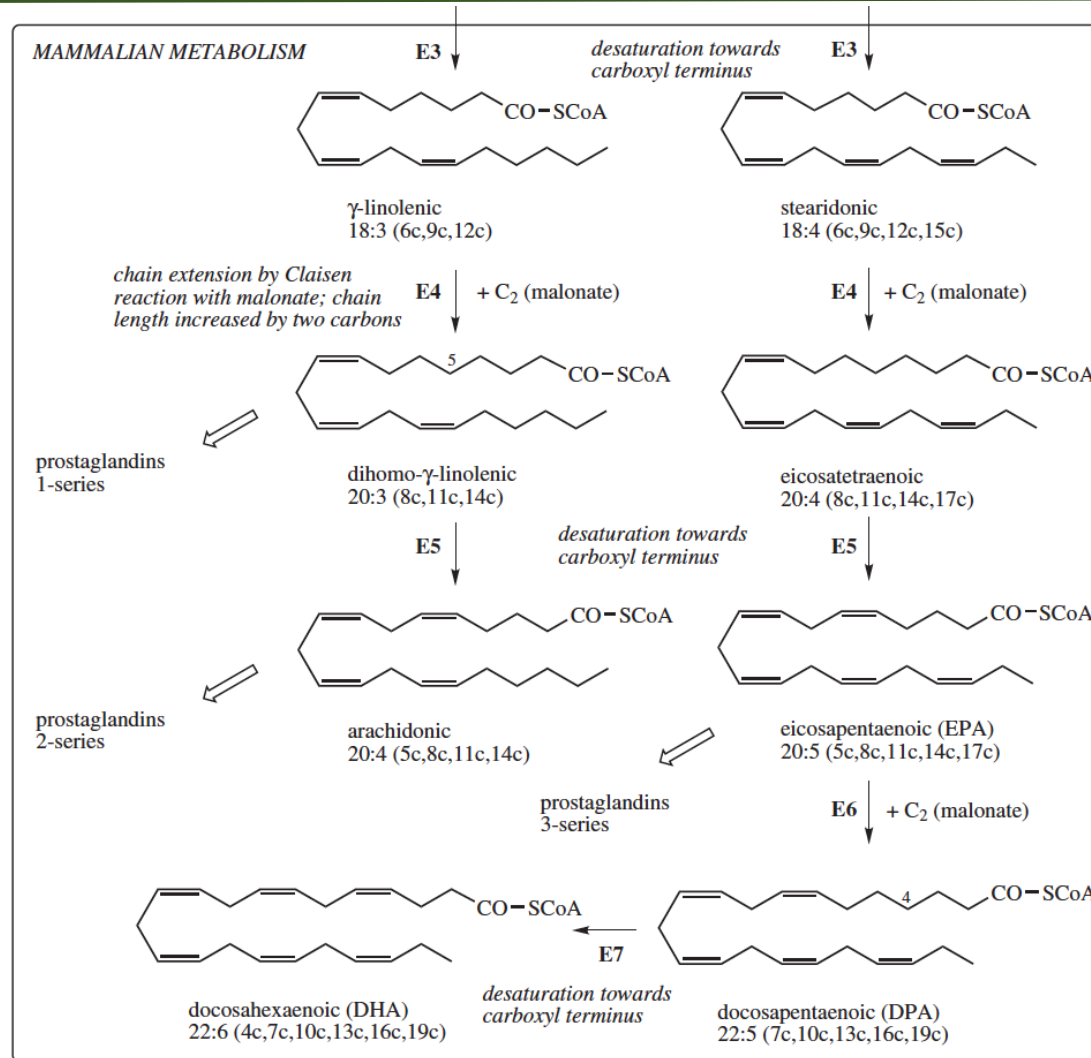
E1: stearoyl-ACP Δ^9 -desaturase

E2: stearoyl-CoA Δ^9 -desaturase

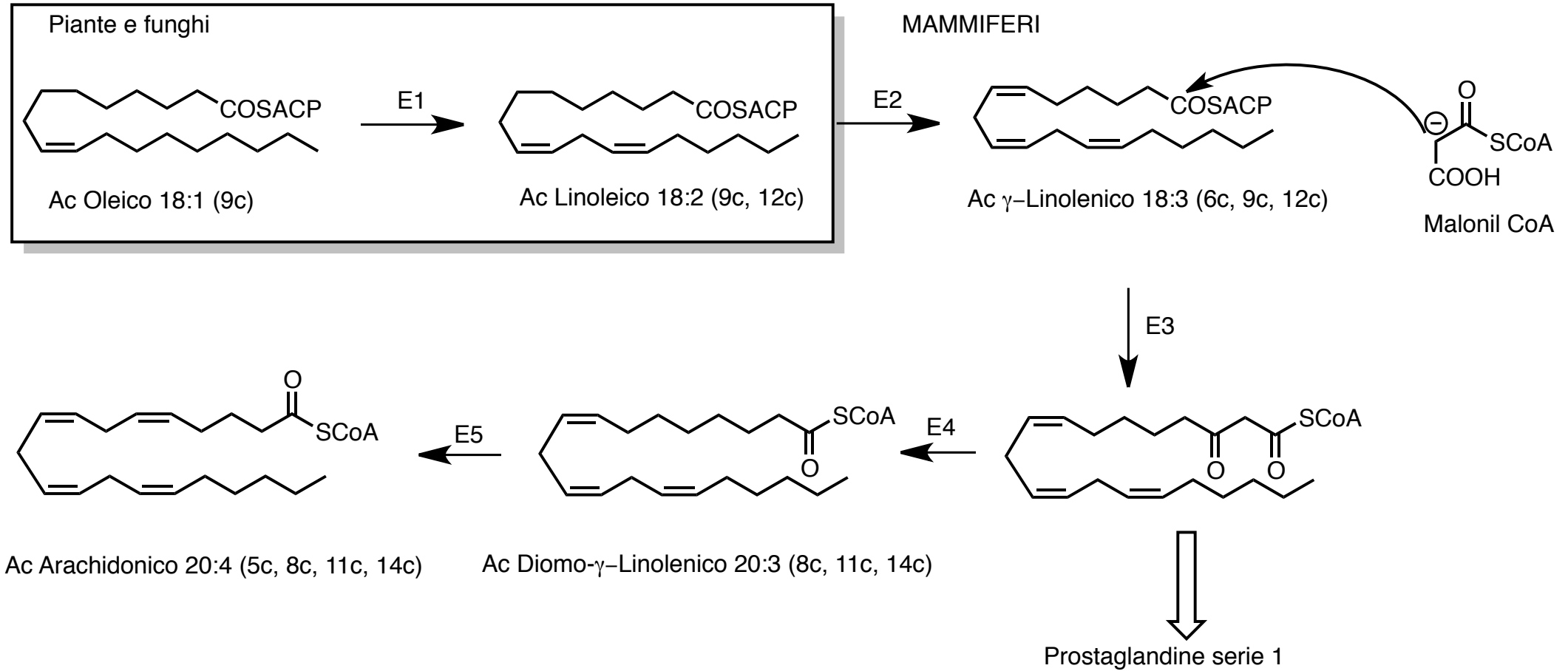
Biosintesi degli acidi grassi



Biosintesi degli acidi grassi

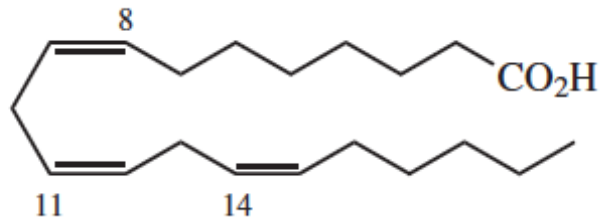


Biosintesi degli acidi grassi

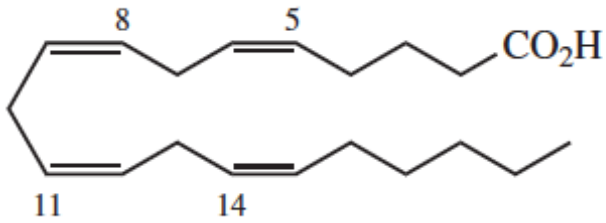


ENZIMI: E1 Δ^{12} Desaturasi; E2 Δ^6 Desaturasi; E3 C_{18} Elongasi; E4 NADPH, Deidratasi, Reduttasi; E5 Δ^5 Desaturasi.

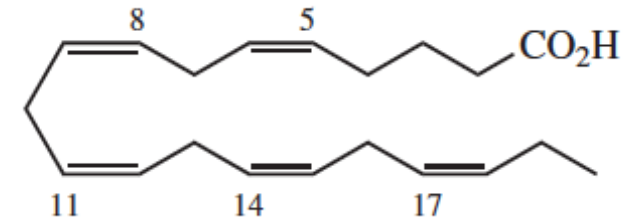
Biosintesi PROSTAGLANDINE SERIE 2



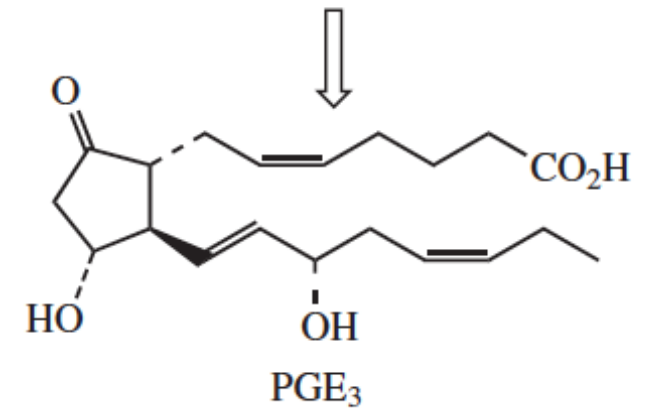
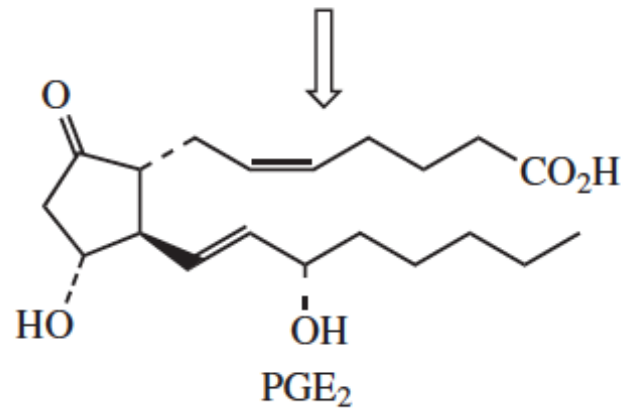
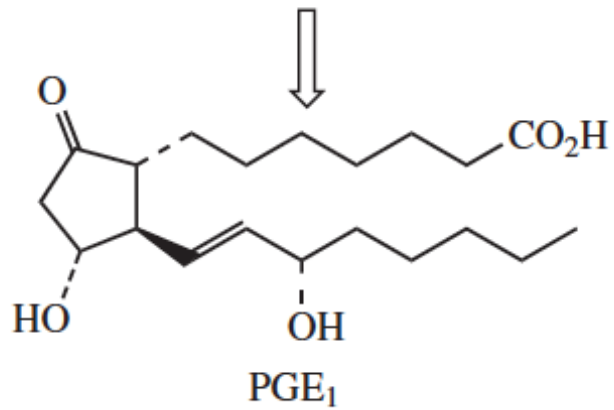
dihomo- γ -linolenic ($\Delta^{8,11,14}$)



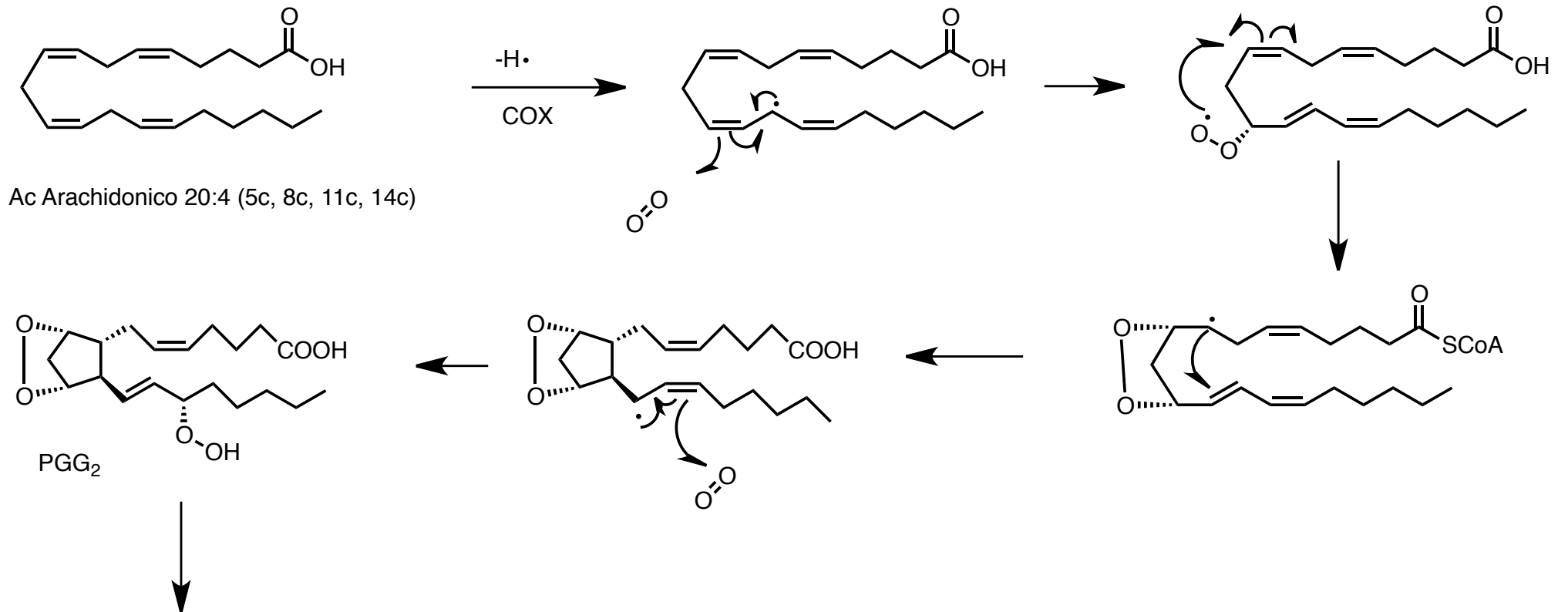
arachidonic ($\Delta^{5,8,11,14}$)



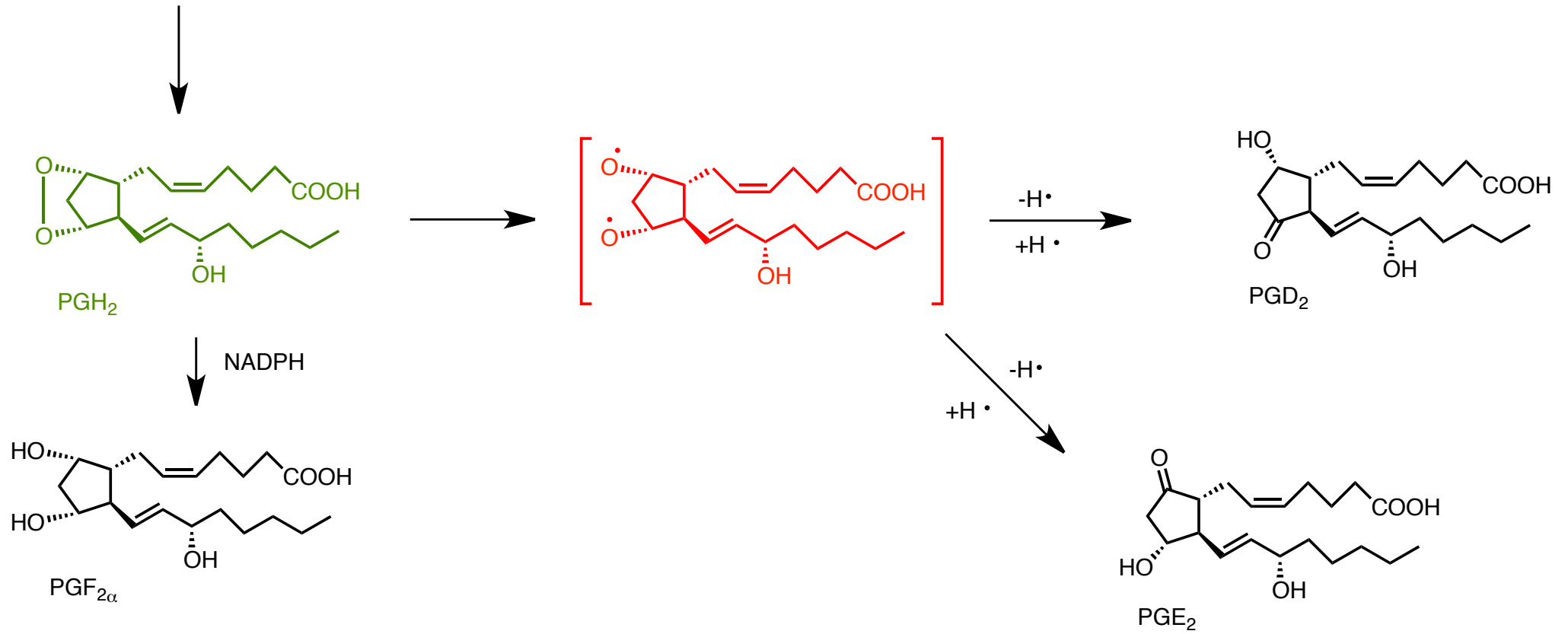
eicosapentaenoic ($\Delta^{5,8,11,14,17}$)



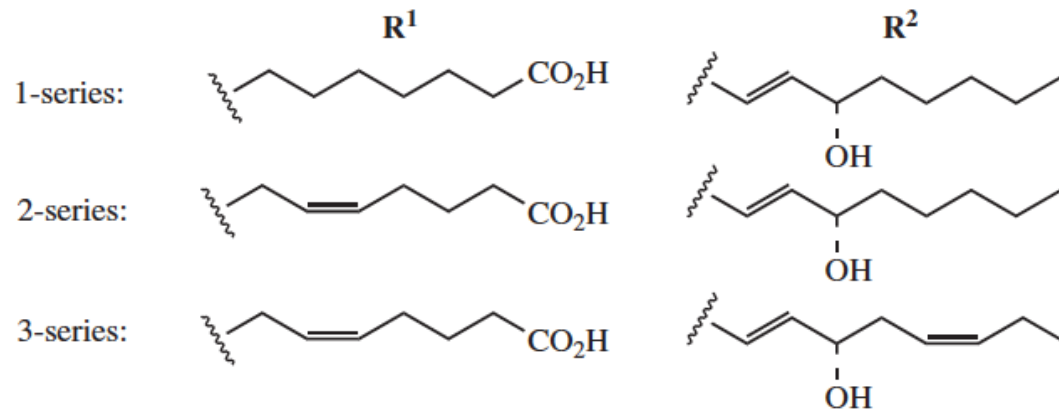
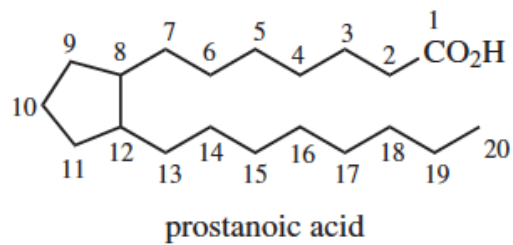
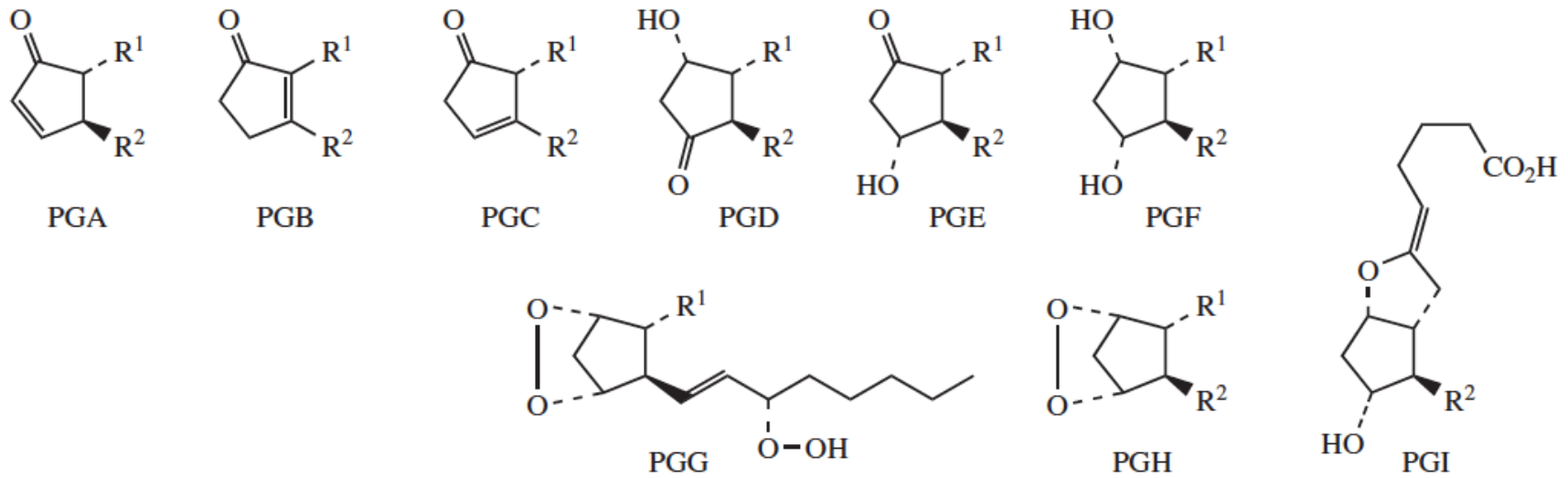
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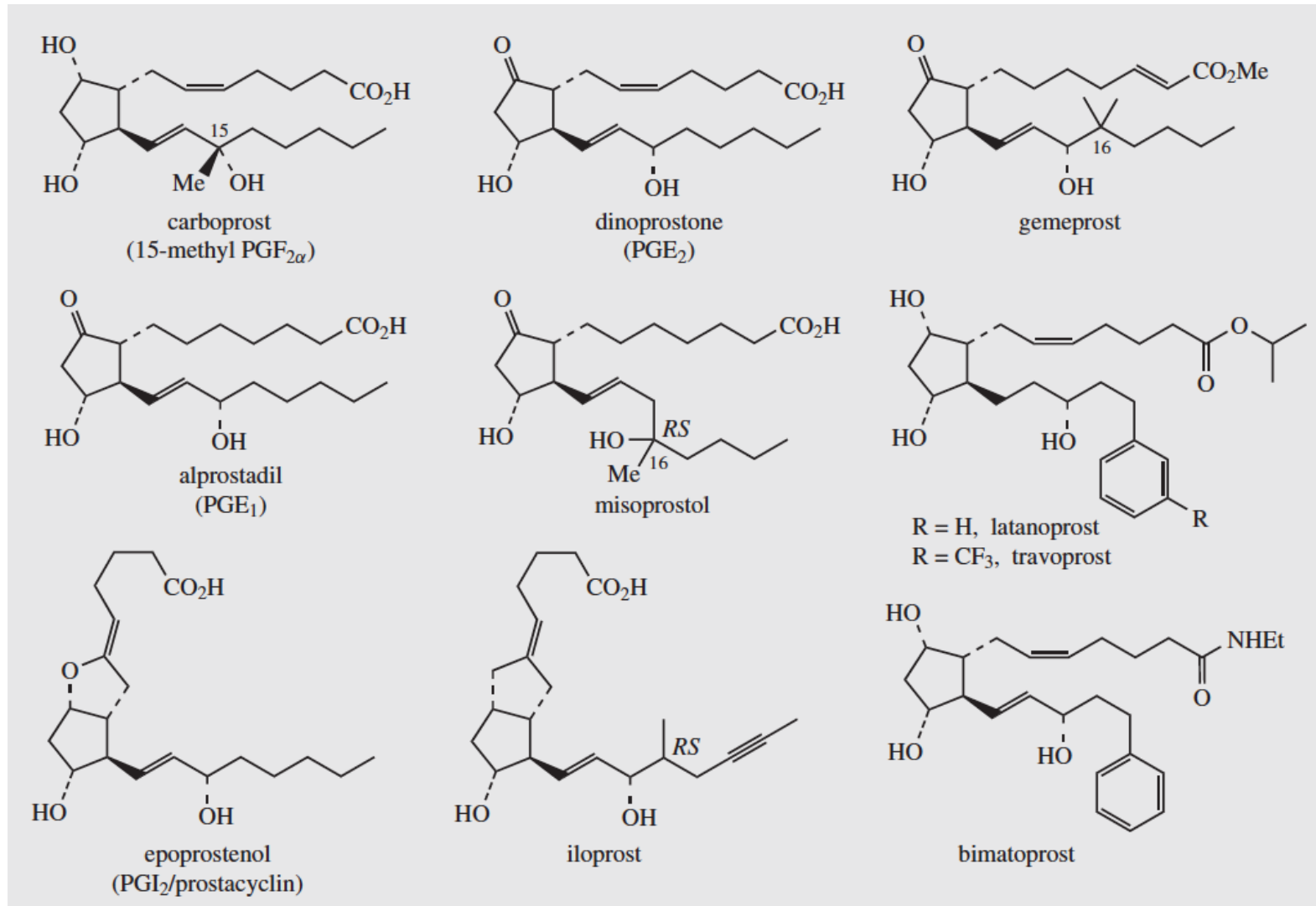
Biosintesi PROSTAGLANDINE SERIE 2



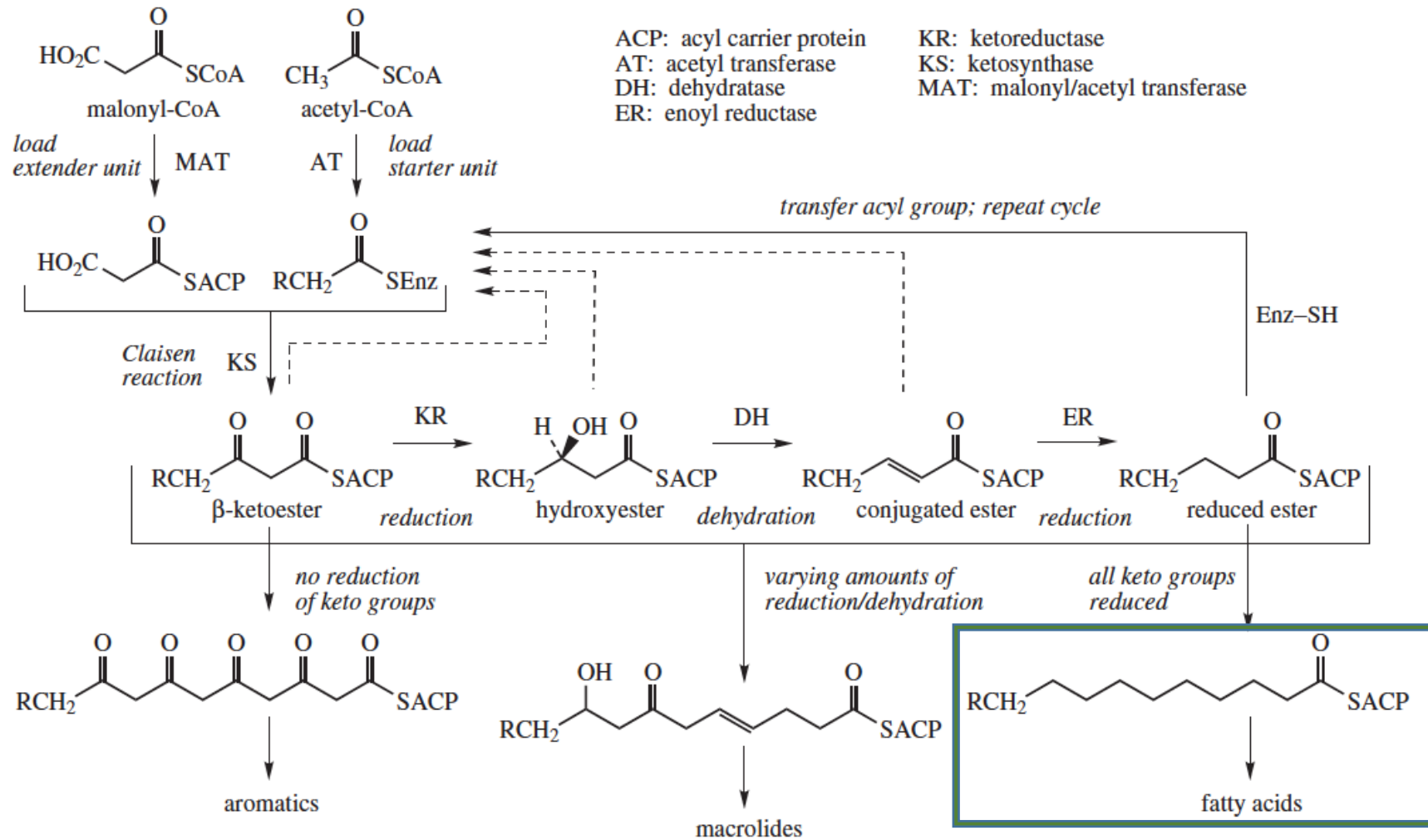
Biosintesi PROSTAGLANDINE SERIE 2



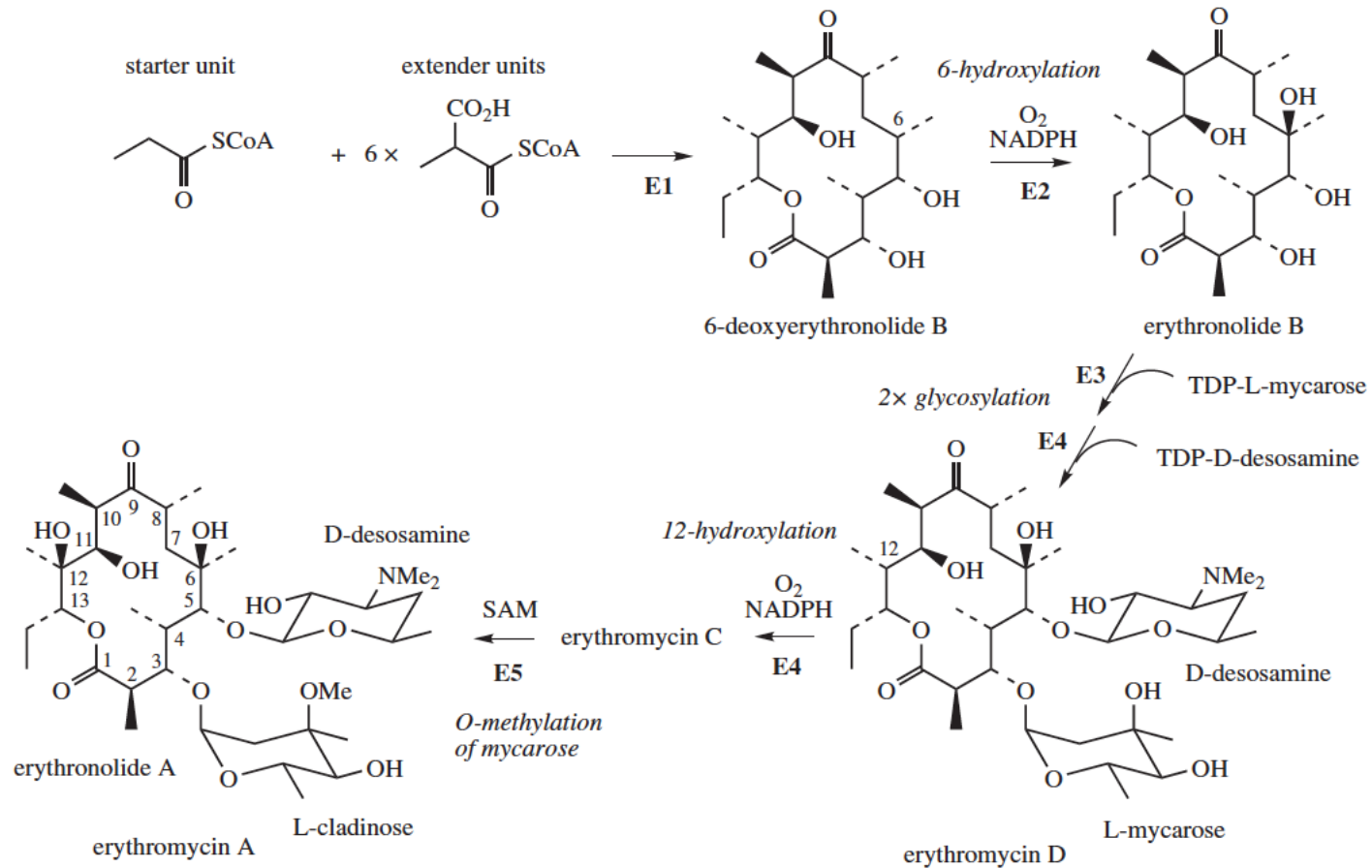
PROSTAGLANDINE in terapia



POLICHETIDI, MACROLIDI, ACIDI GRASSI



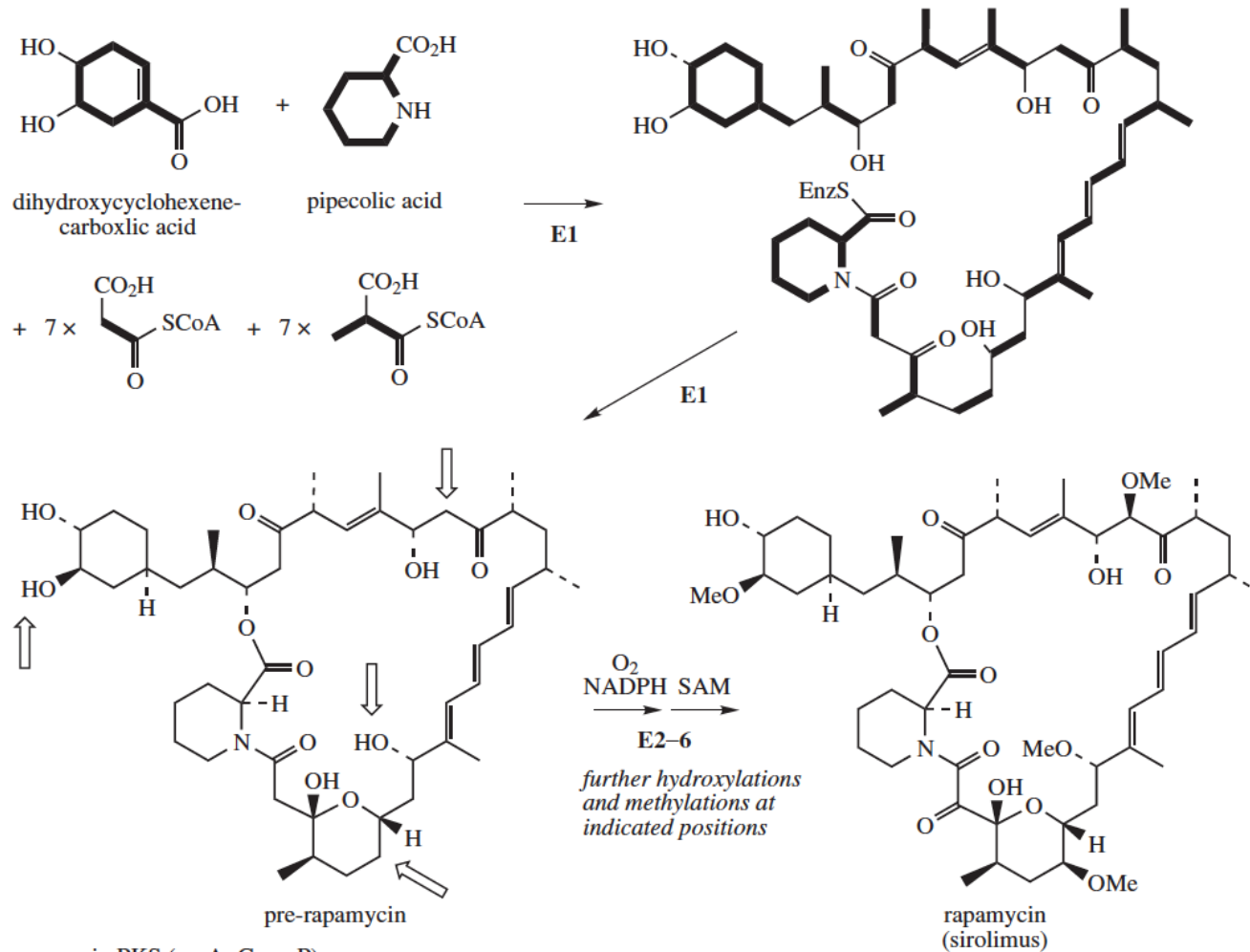
Biosintesi ERITROMICINA A



E1: EryA (6-deoxyerythronolide B synthase; DEBS)
 E2: EryF (6-deoxyerythronolide B hydroxylase)
 E3: EryBV (mycarosyl transferase)

E4: EryCIII (desosaminyl transferase)
 E5: EryK (erythromycin 12-hydroxylase)
 E6: EryG (methyltransferase)

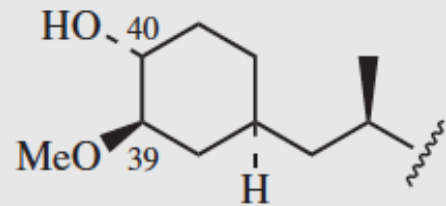
Biosintesi RAPAMICINA



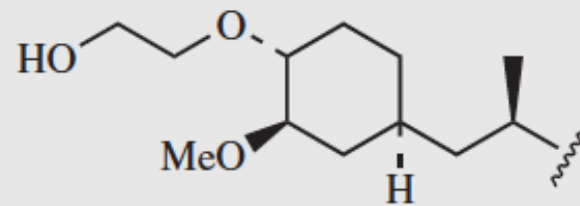
E1: rapamycin PKS (rapA–C, rapP)
 E2, E3: rapJ, rapN (hydroxylases)
 E4–6: rapI, rapM, rapQ (methyltransferases)

DERIVATI IN TERAPIA

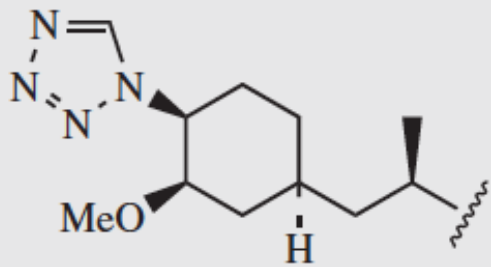
rapamycin derivatives



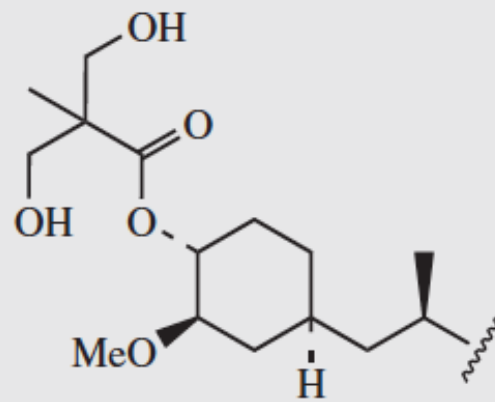
rapamycin
(sirolimus)



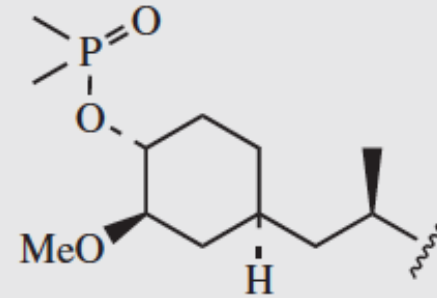
everolimus



zotarolimus

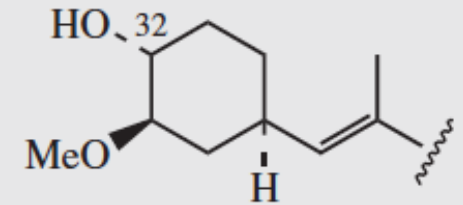


temsirolimus

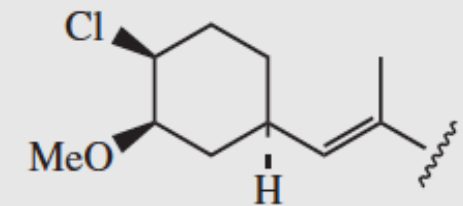


deforolimus

ascomycin derivatives

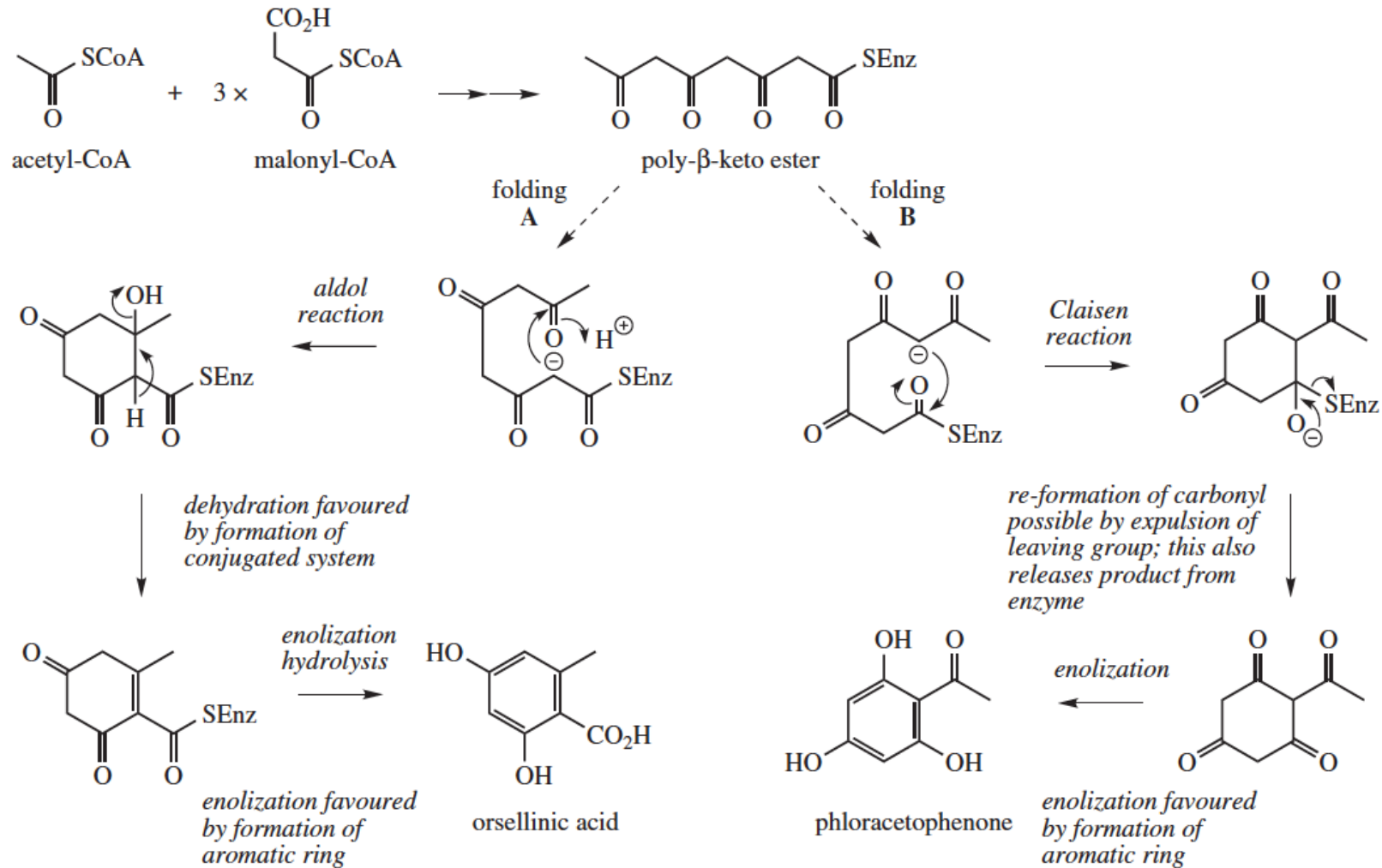


ascomycin

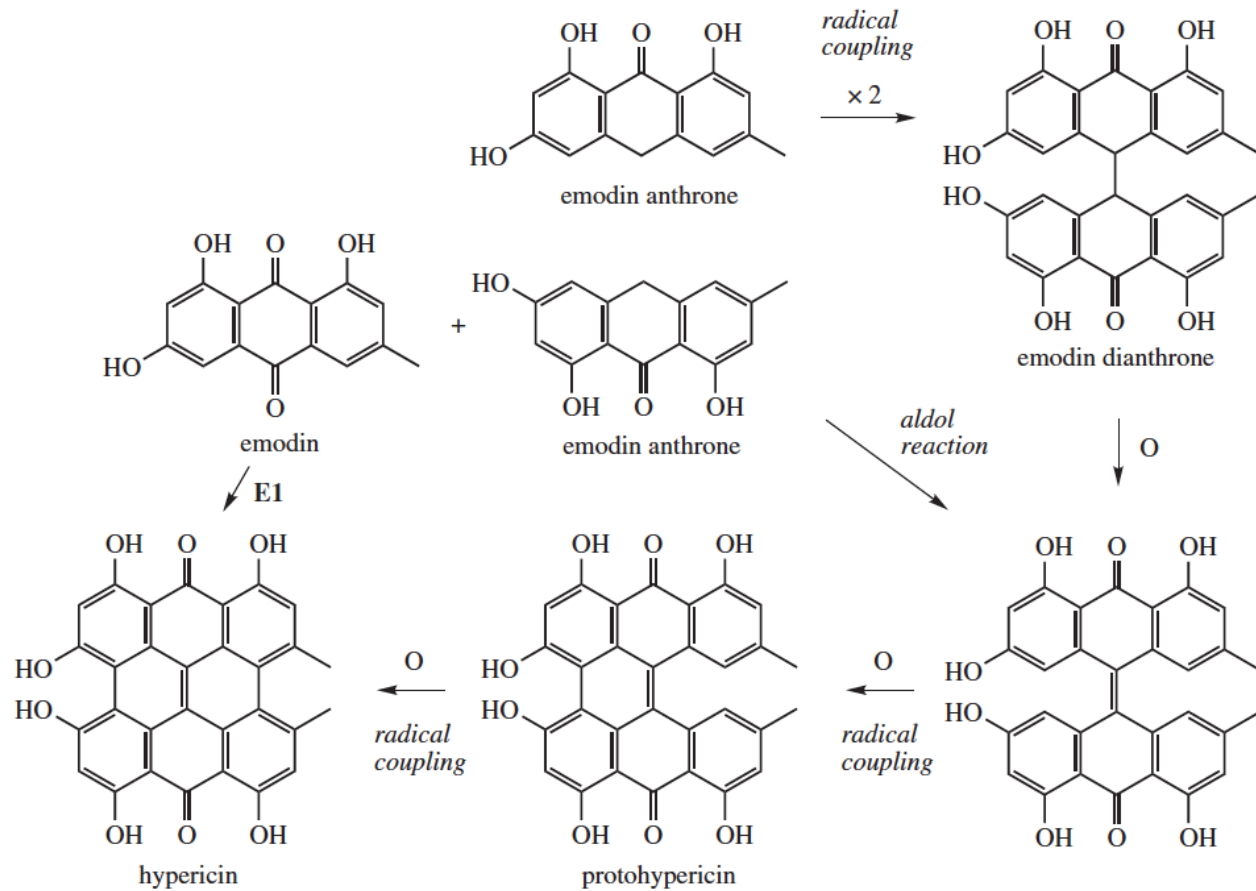


pimecrolimus

Biosintesi ACIDO ORSELLINICO E FLORACETOFENONE



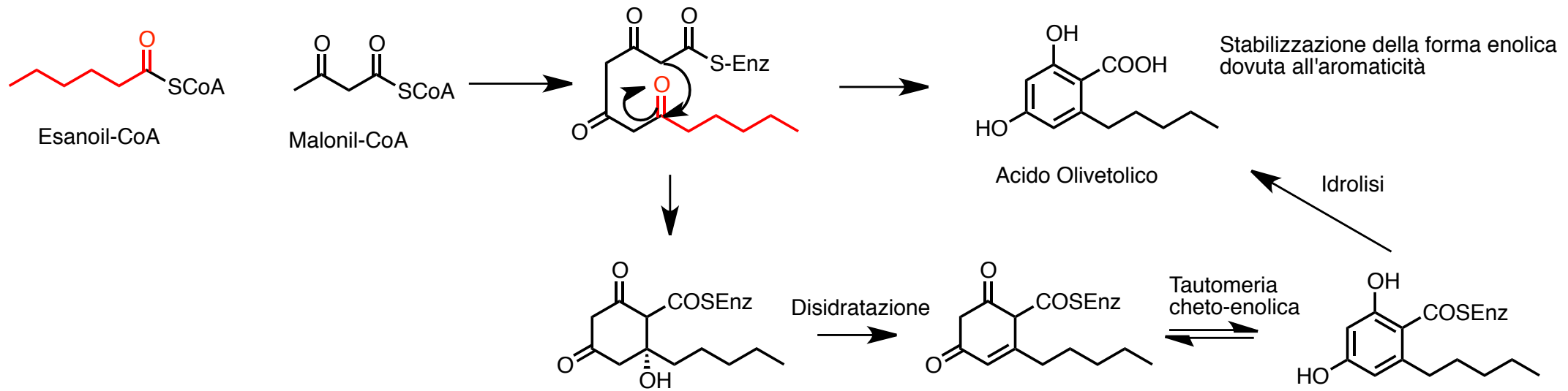
Biosintesi IPERICINA Erba di S. Giovanni (Iperico *Hipericum perforatum*)



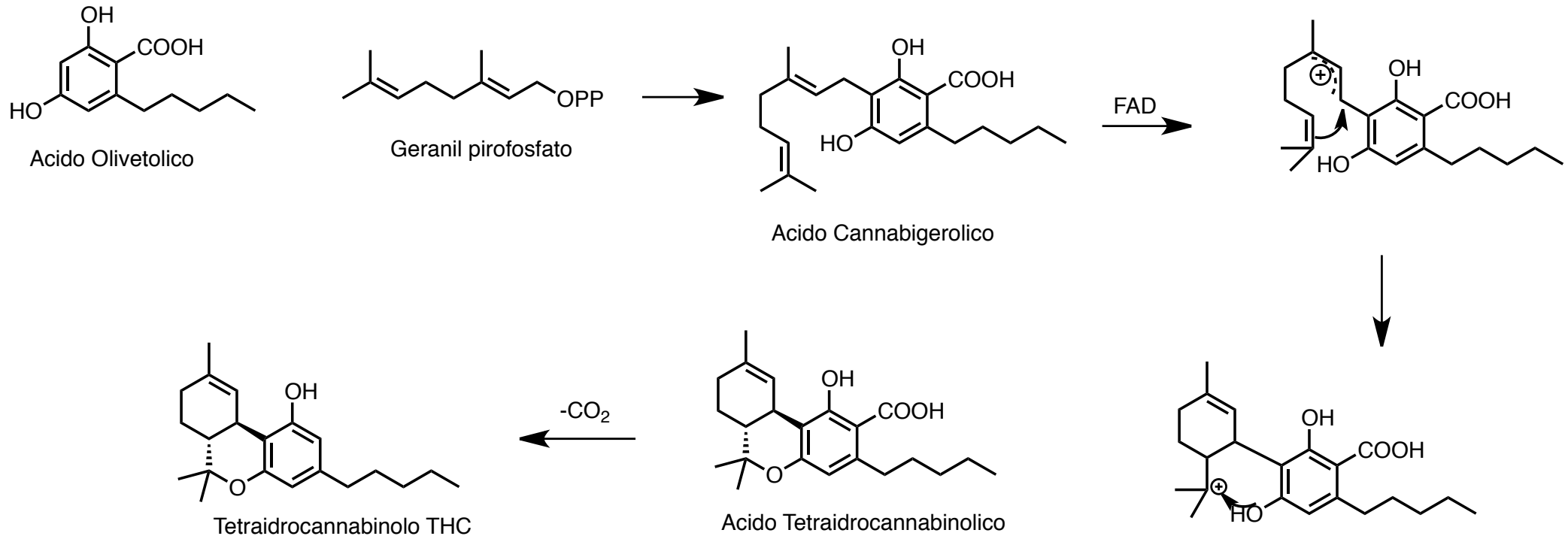
E1: Hyp-1
(emodin is substrate)



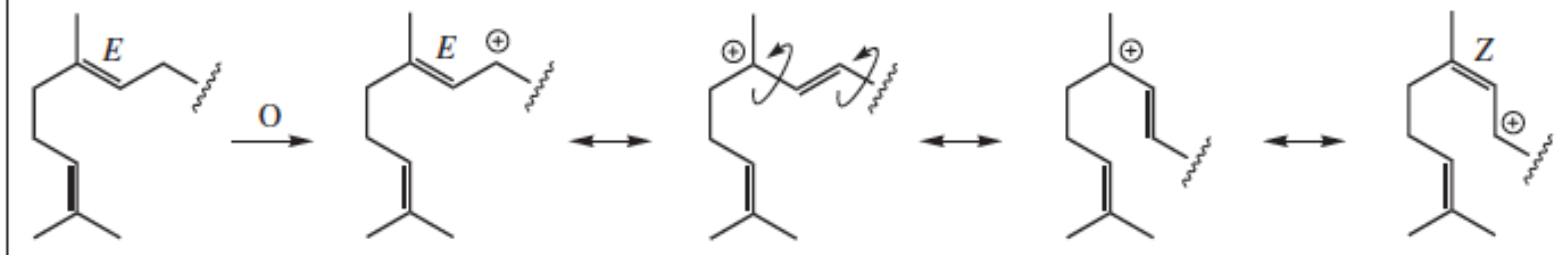
Biosintesi TETRAIDROCANNABINOLO



Biosintesi TETRAIDROCANNABINOLO



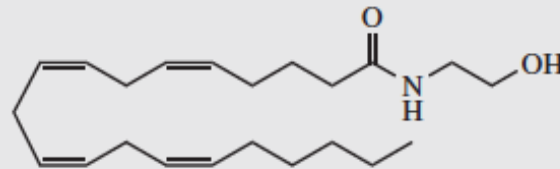
E/Z isomerization in geranyl substituent:



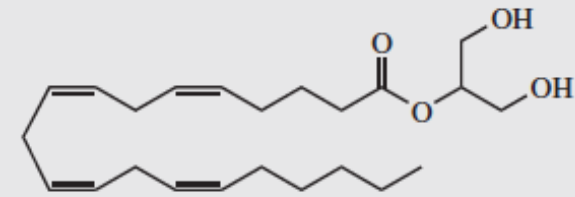
Biosintesi TETRAIDROCANNABINOLO



Two main cannabinoid receptors have been identified: CB₁, predominantly in the central nervous system, and CB₂, expressed mainly in the immune system. This was followed by discovery in animal brain tissue of a natural ligand for CB₁, namely anandamide (Figure 3.95), which is arachidonoyl ethanolamide; ananda is the Sanskrit word for bliss. Anandamide mimics several of the pharmacological properties of THC. The natural ligand of CB₂ is 2-arachidonoylglycerol (Figure 3.95); this also interacts with CB₁, and since levels of 2-arachidonoylglycerol in the brain are some 800 times higher than those of anandamide, it is now thought to be the physiological ligand for both receptors, rather than anandamide. These two compounds are the main ligands, but other related natural compounds from mammalian brain also function in the same way. These include polyunsaturated fatty acid ethanolamides, namely dihomono- γ -linolenoyl- (20:3) and adrenoyl- (22:4) ethanolamides, *O*-arachidonoyl ethanolamine (virodhamine) and 2-arachidonoylglycerol ether (noladin ether). The identification of these endogenous materials may open up other ways of exploiting some of the desirable pharmacological features of cannabis.



anandamide
(arachidonoyl ethanolamide)



2-arachidonoylglycerol