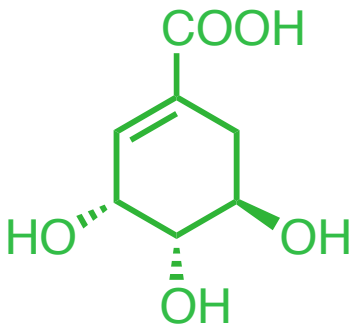
CHIMICA DELLE SOSTANZE ORGANICHE NATURALI

ILLICIUM ANISATUM

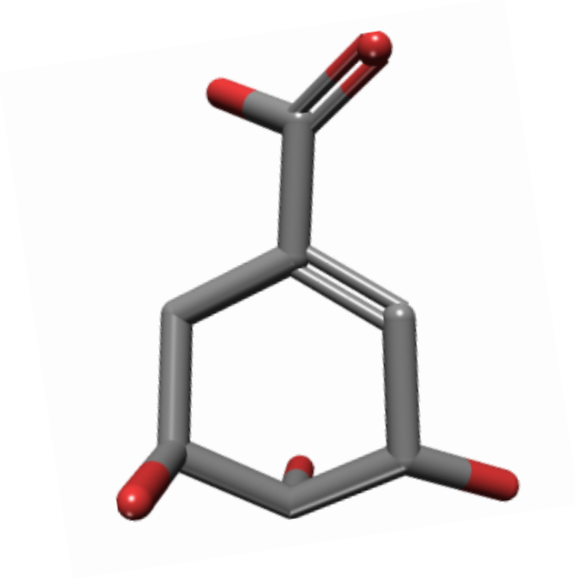
LA VIA DELLO SHIKIMATO: AMMINOACIDI AROMATICI E FENILPROPANOIDI

LA VIA DELL'ACIDO SHIKIMICO

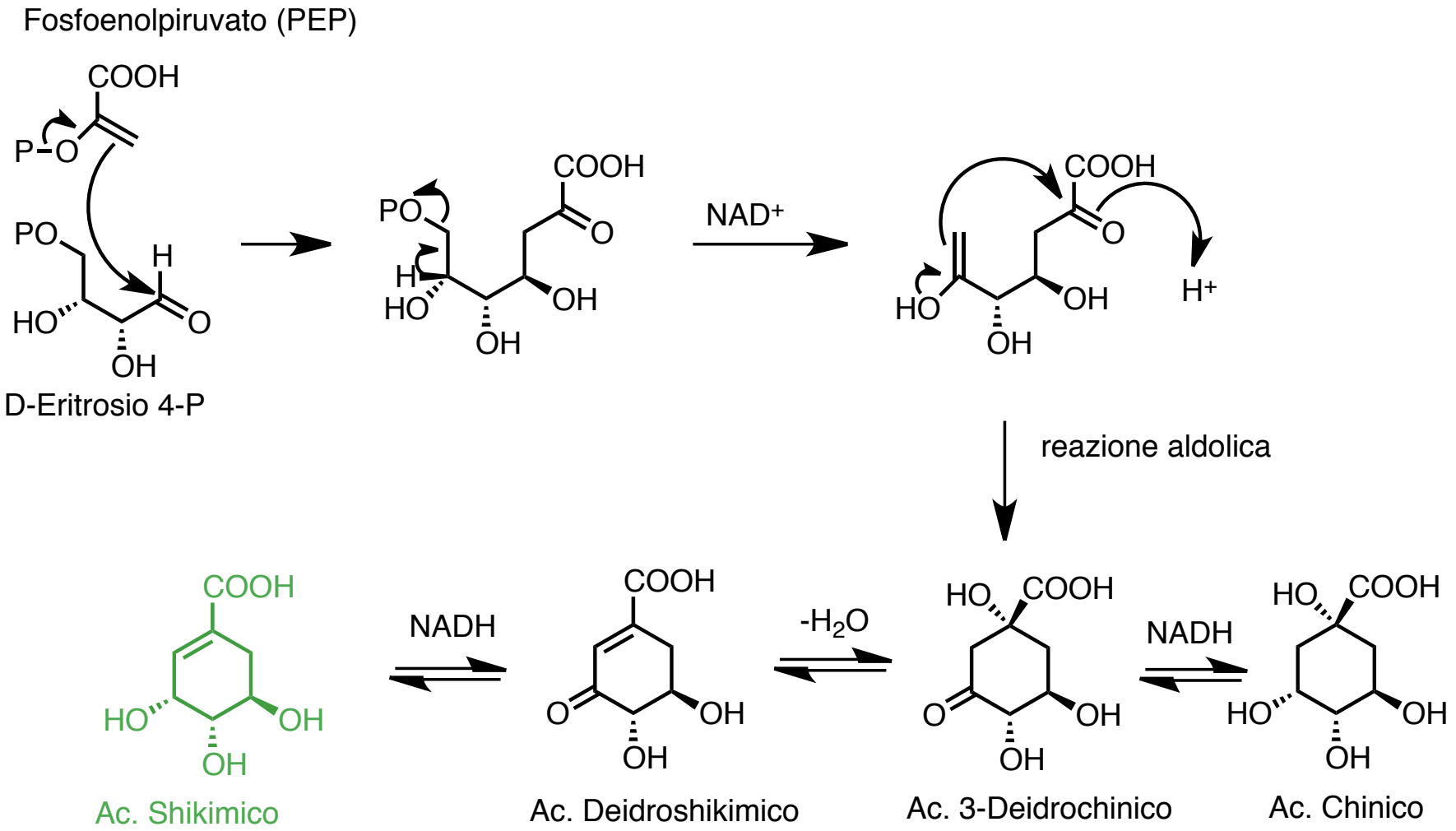
Il nome deriva dalla pianta da cui è stato estratto per la prima volta ***Illicium anisatum*** o Anice giapponese, infatti in giapponese questa pianta si chiama **Shikimi**



ACIDO SHIKIMICO



LA VIA DELL'ACIDO SHIKIMICO



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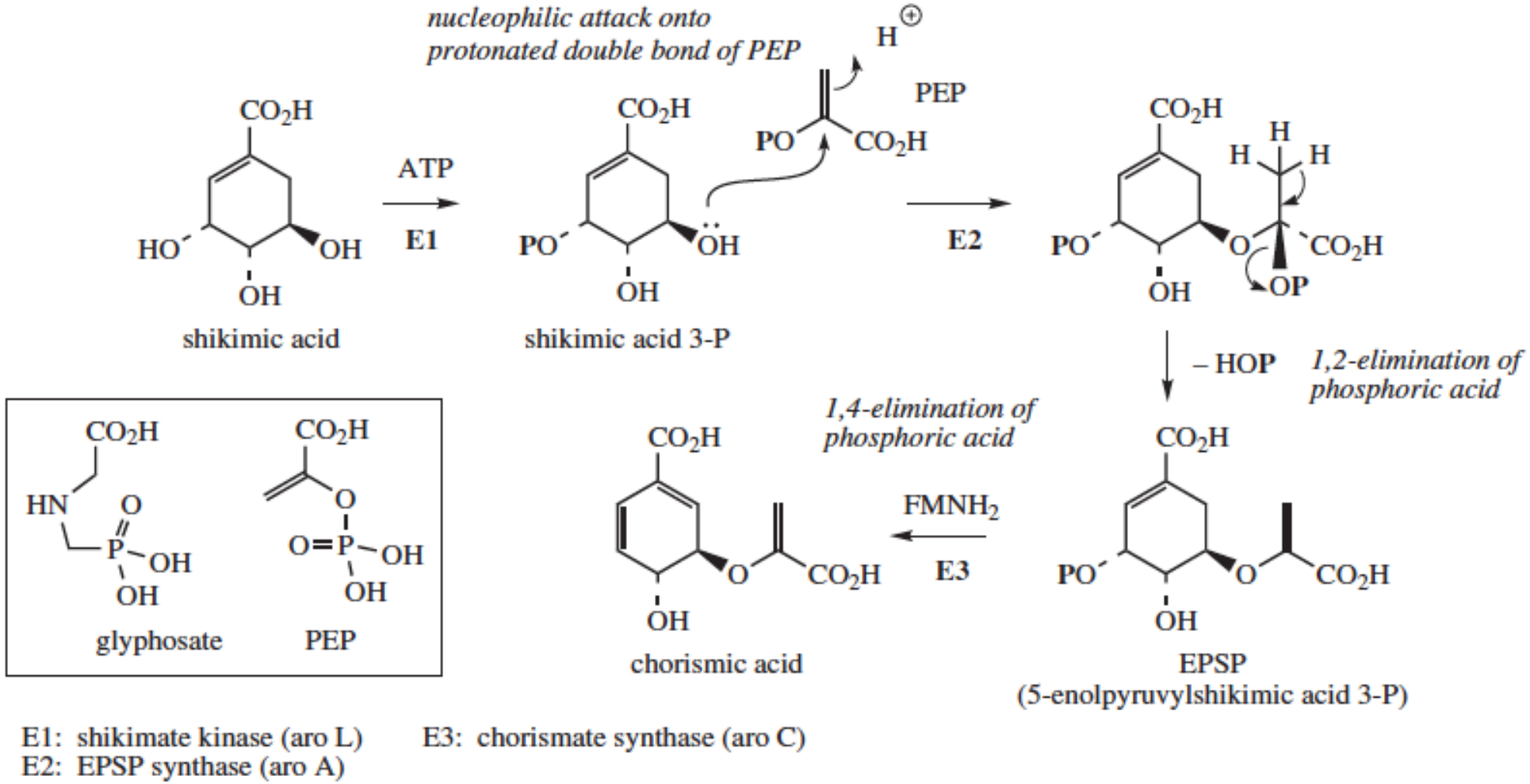
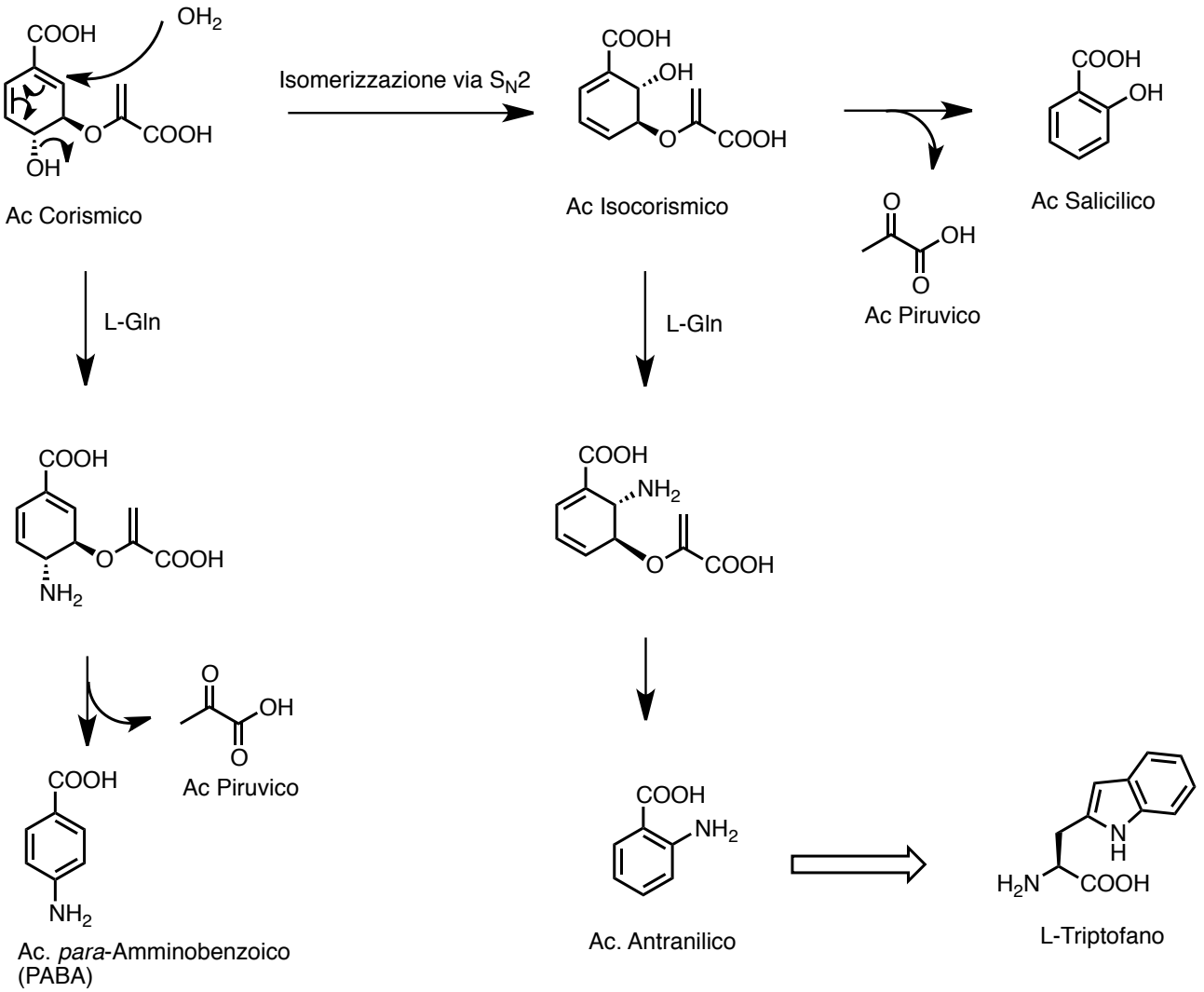
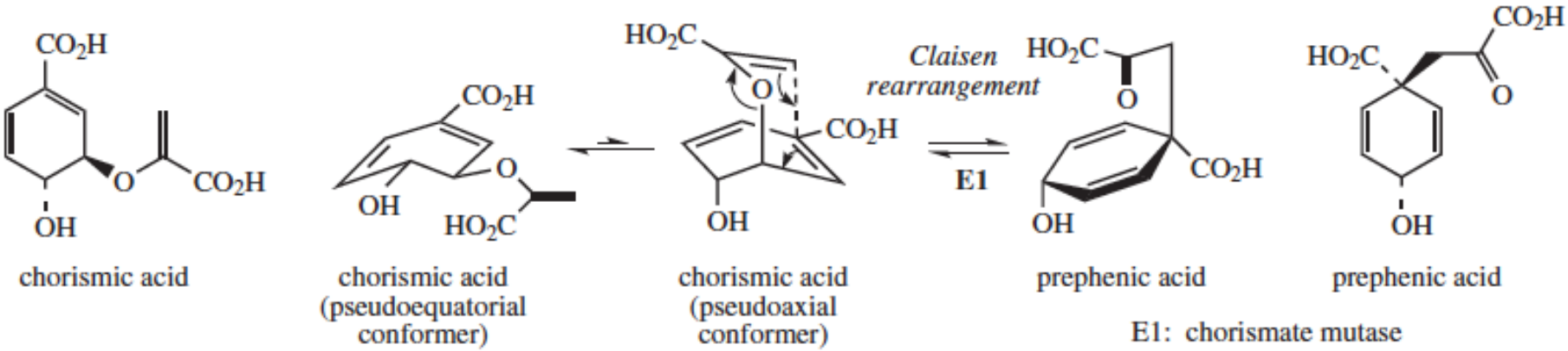


E1: shikimate kinase (aro L)
E2: EPSP synthase (aro A)
E3: chorismate synthase (aro C)

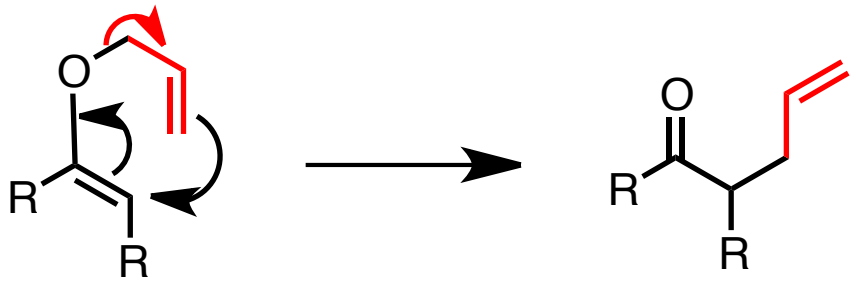
LA VIA DELL'ACIDO SHIKIMICO



LA VIA DELL'ACIDO SHIKIMICO Biosintesi fenilalanina e tirosina



Riarrangiamento di Claisen, formalmente una reazione periciclica [3+3]



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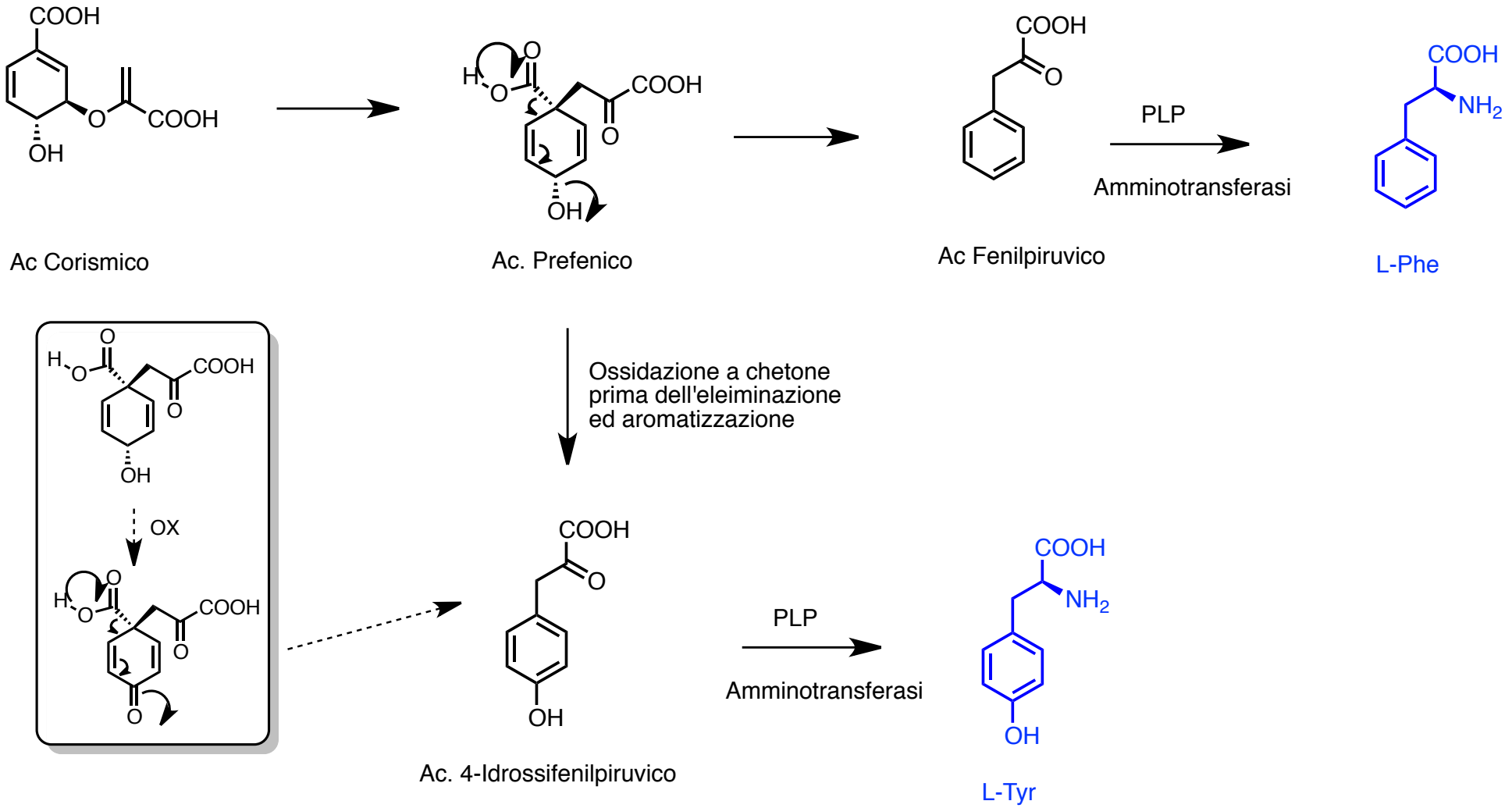
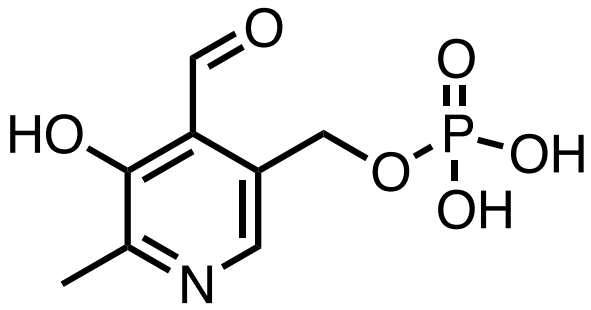
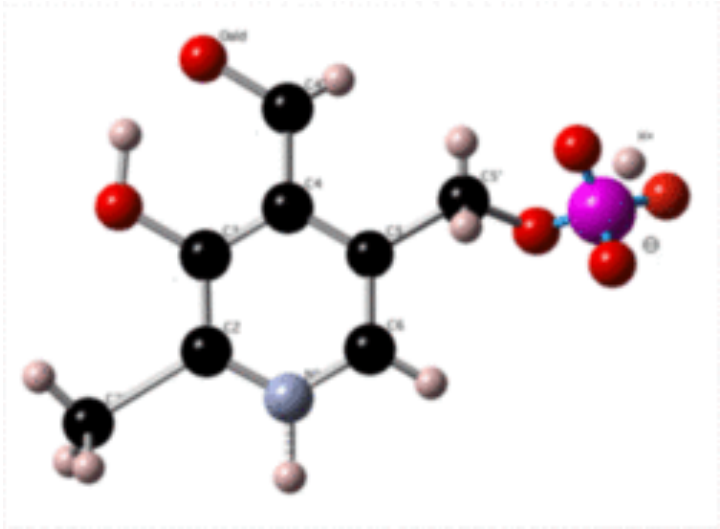


PIRIDOSSALFOSFATO

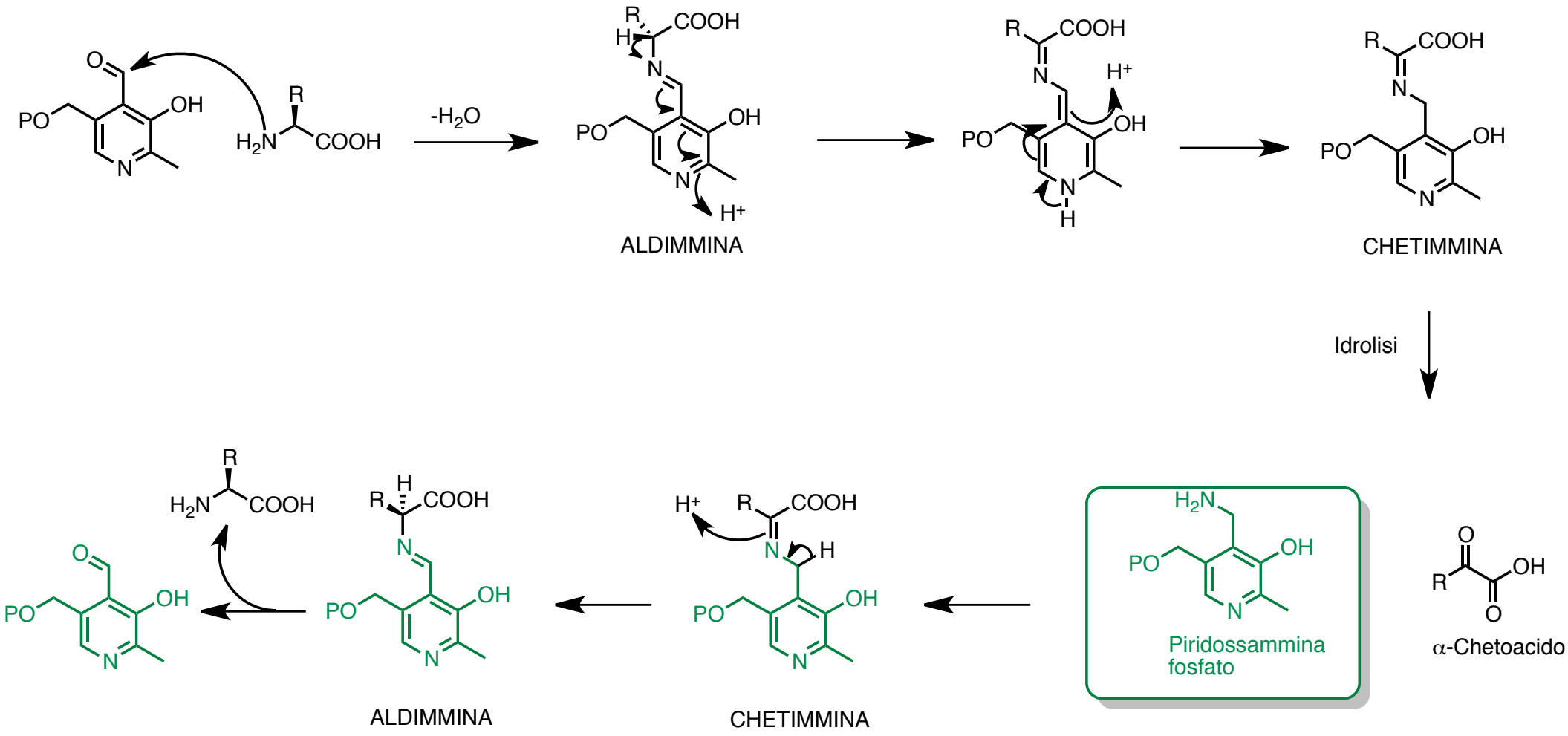


Piridossal fosfato



VITAMINA B6

LA VIA DELL'ACIDO SHIKIMICO

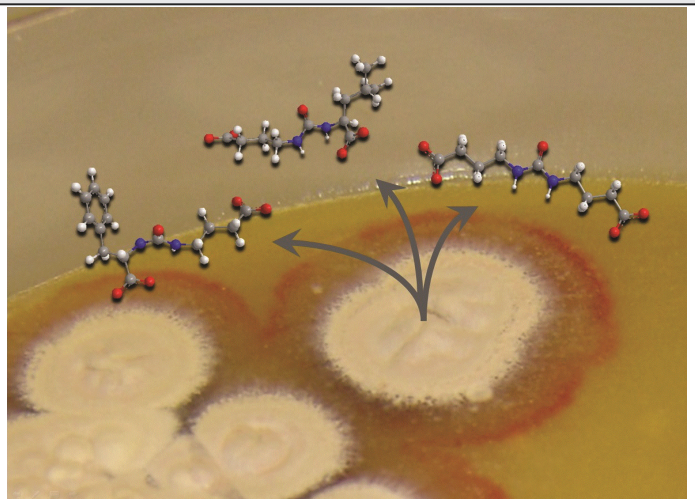


Biosintesi del CLORAMFENICOLO

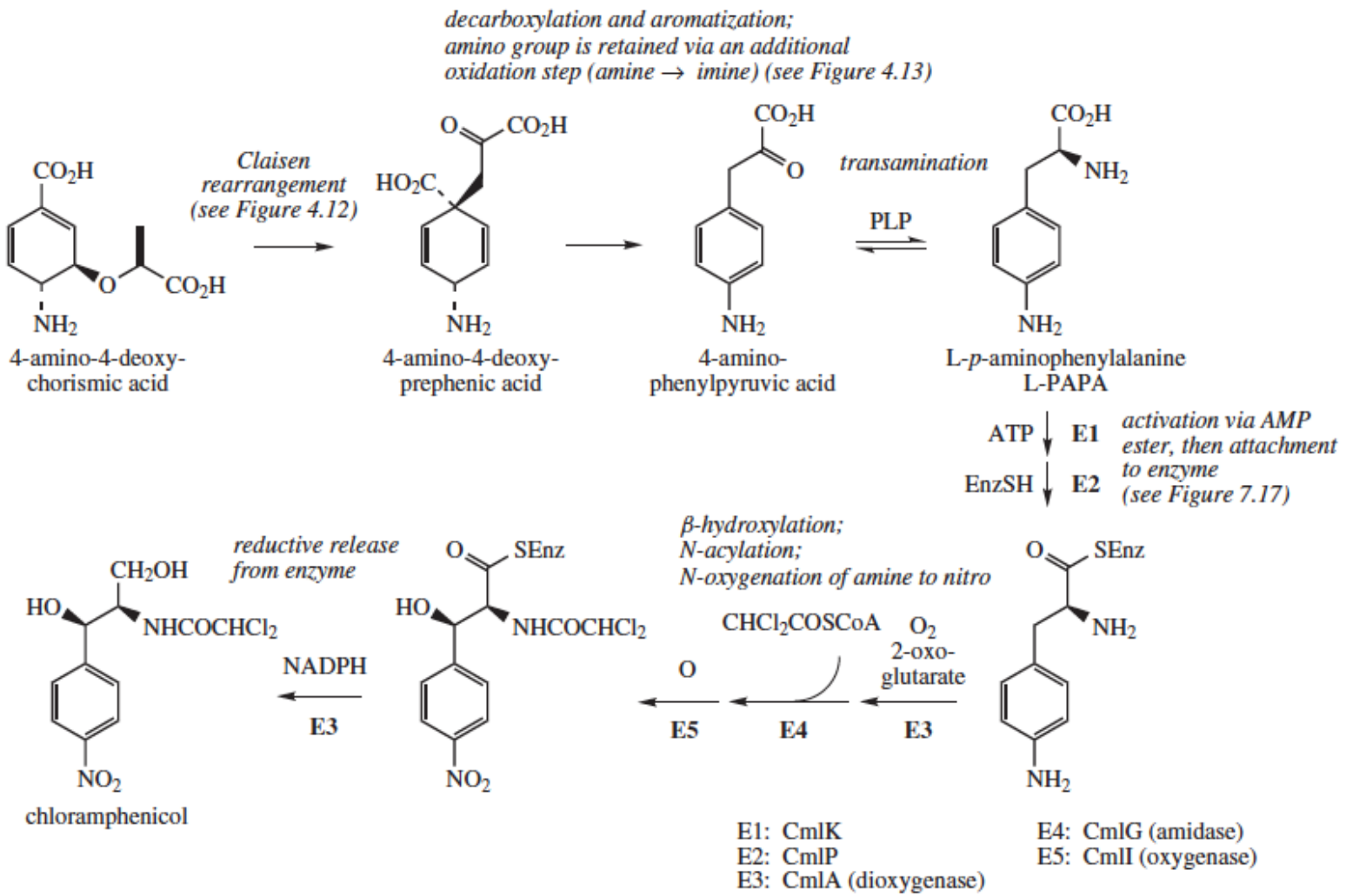
Box 4.2

Chloramphenicol

Chloramphenicol (chloromycetin; Figure 4.15) was initially isolated from cultures of *Streptomyces venezuelae*, but is now obtained for drug use by chemical synthesis. It was one of the first broad-spectrum antibiotics to be developed, and exerts its antibacterial action by inhibiting protein biosynthesis. It binds reversibly to the 50S subunit of the bacterial ribosome, and in so doing it disrupts peptidyl transferase, the enzyme that catalyses peptide bond formation (see page 422). This reversible binding means that bacterial cells not destroyed may resume protein biosynthesis when no longer exposed to the antibiotic. Some microorganisms have developed resistance to chloramphenicol by an inactivation process involving enzymic acetylation of the primary alcohol group in the antibiotic. The acetate binds only very weakly to the ribosomes, so has little antibiotic activity. The value of chloramphenicol as an antibacterial agent has been severely limited by some serious side-effects. It can cause blood disorders, including irreversible aplastic anaemia in certain individuals, and these can lead to leukaemia and perhaps prove fatal. Nevertheless, it is still the drug of choice for some life-threatening infections, such as typhoid fever and bacterial meningitis. The blood constitution must be monitored regularly during treatment to detect any abnormalities or adverse changes. The drug is orally active, but may also be injected. Eye-drops are useful for the treatment of bacterial conjunctivitis.



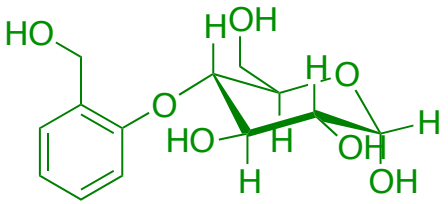
Biosintesi del CLORAMFENICOLO



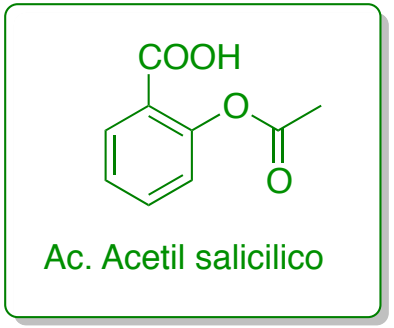
Biosintesi della SALICINA

Salix alba

Come per le altre specie del genere *Salix* , la corteccia fornisce, oltre a tannino, anche la salicina, da cui si ricava acido salicilico, ad azione tonica, antireumatica, febbrifuga, antifermentativa ed astringente.

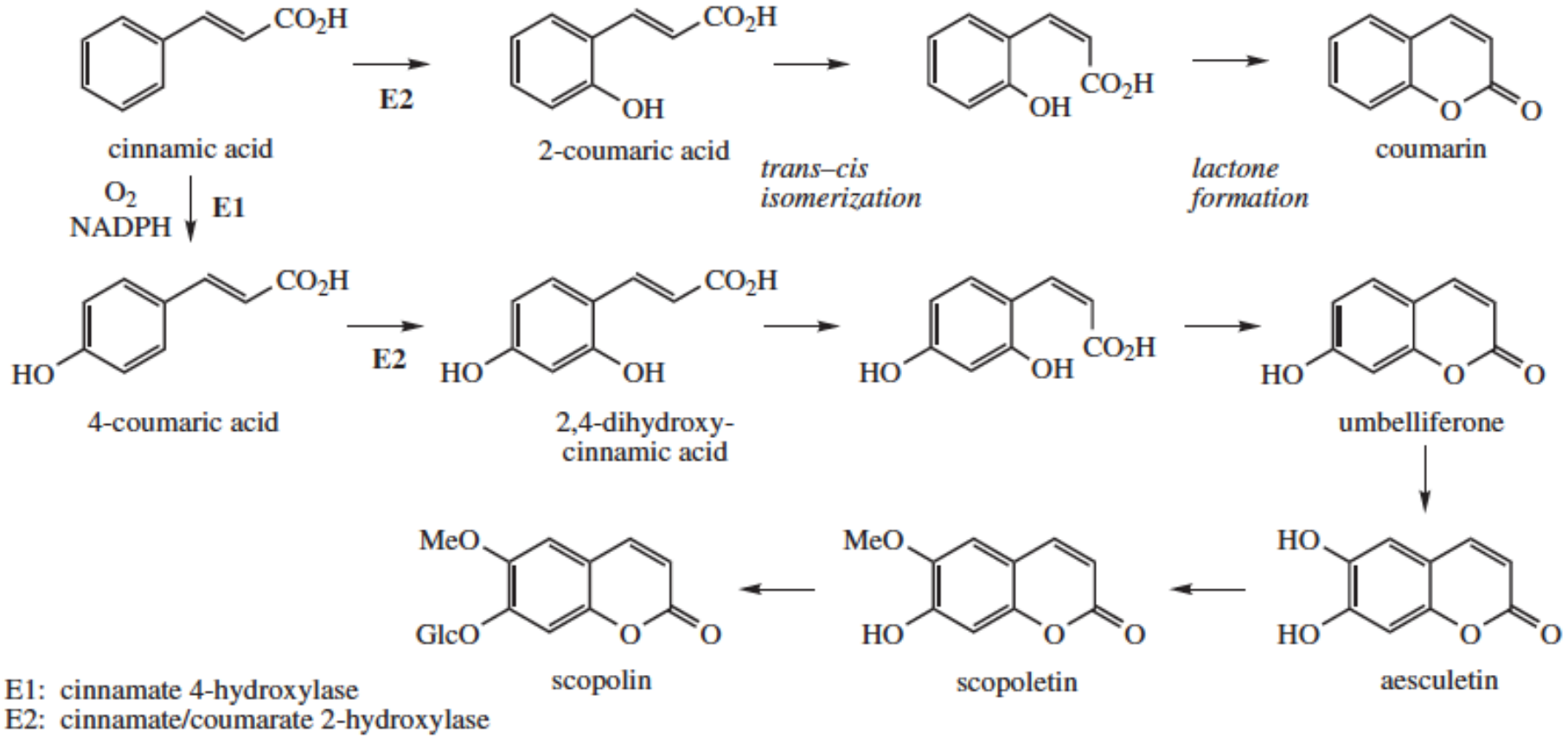


Salicina

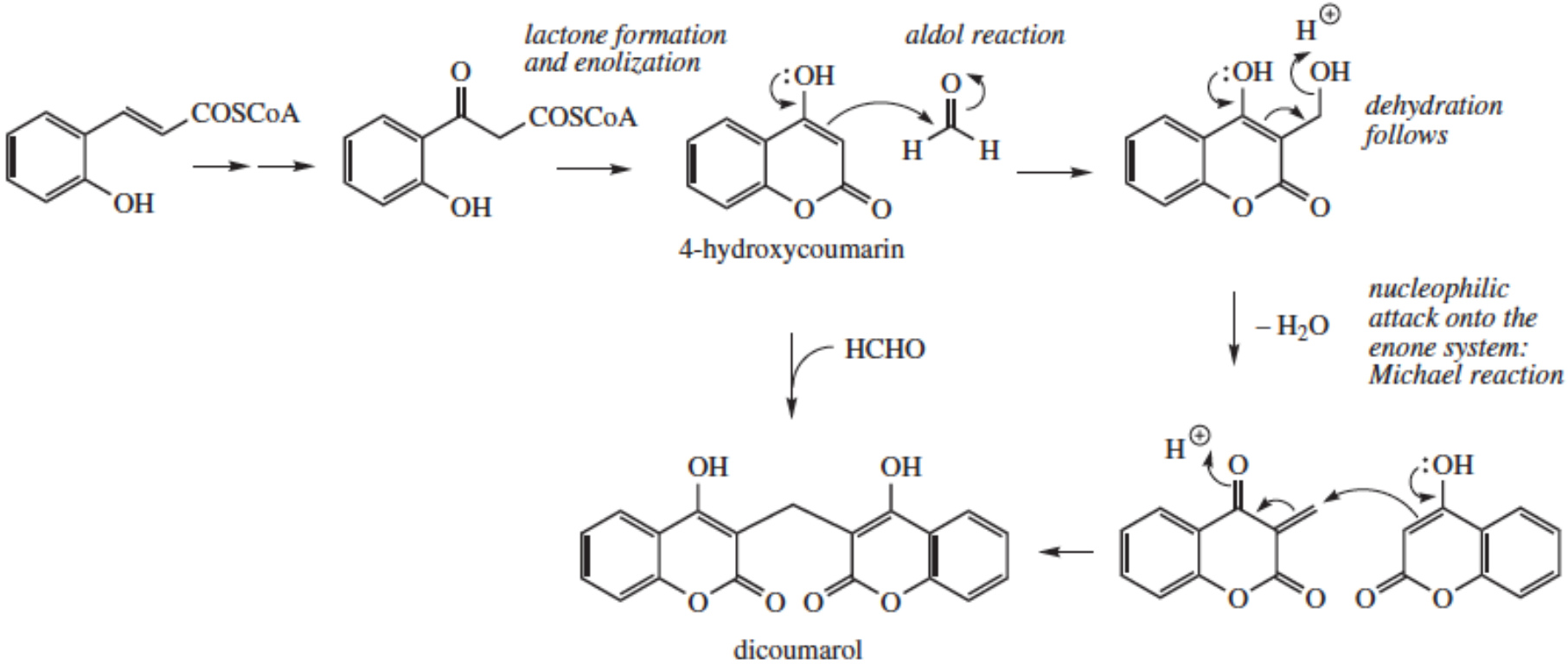


Ac. Acetil salicilico

LA VIA DELL'ACIDO SHIKIMICO: CUMARINE



LA VIA DELL'ACIDO SHIKIMICO



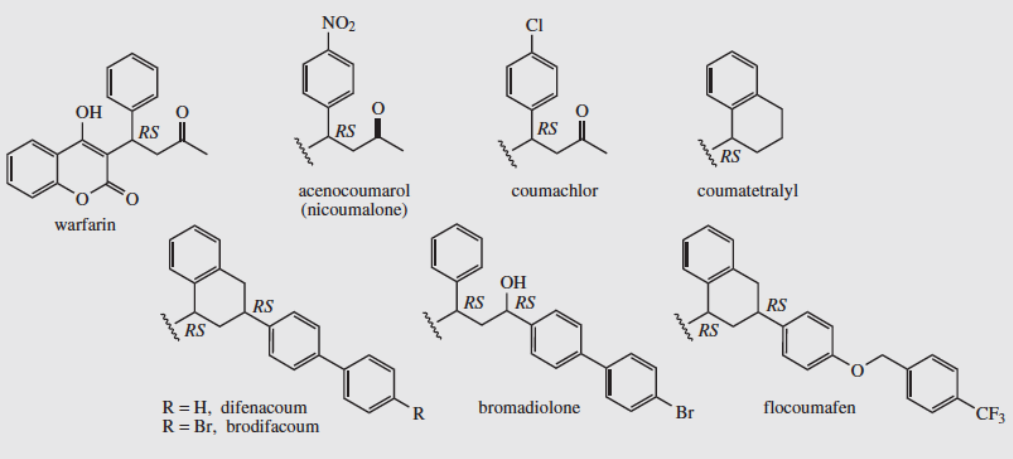
DICUMAROLO E WARFARIN

Melilotus officinalis

Dicoumarol and Warfarin

The cause of fatal haemorrhages in animals fed spoiled sweet clover (*Melilotus officinalis*; Leguminosae/Fabaceae) was traced to dicoumarol (bishydroxycoumarin; Figure 4.31). This agent interferes with the effects of vitamin K in blood coagulation (see page 183), the blood loses its ability to clot, and thus minor injuries can lead to severe internal bleeding. Synthetic dicoumarol has been used as an oral blood anticoagulant in the treatment of thrombosis, where the risk of blood clots becomes life threatening. It has been superseded by salts of **warfarin** and in some cases the nitro analogue **acenocoumarol** (**nicoumalone**; Figure 4.32), which are synthetic developments from the natural product. An overdose of warfarin may be countered by injection of vitamin K_1.

Warfarin was initially developed as a rodenticide and has been widely employed for many years as the first-choice agent, particularly for destruction of rats. After consumption of warfarin-treated bait, rats die from internal haemorrhage. Other coumarin derivatives employed as rodenticides include **coumachlor** and **coumatetralyl** (Figure 4.32). In an increasing number of cases, rodents are developing resistance towards warfarin, an ability which has been traced to elevated production of vitamin K by their intestinal microflora. Modified structures **difenacoum, brodifacoum, bromadiolone**, and **flocoumafen** have been found to be more potent than warfarin, and are also effective against rodents that have become resistant to warfarin.



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