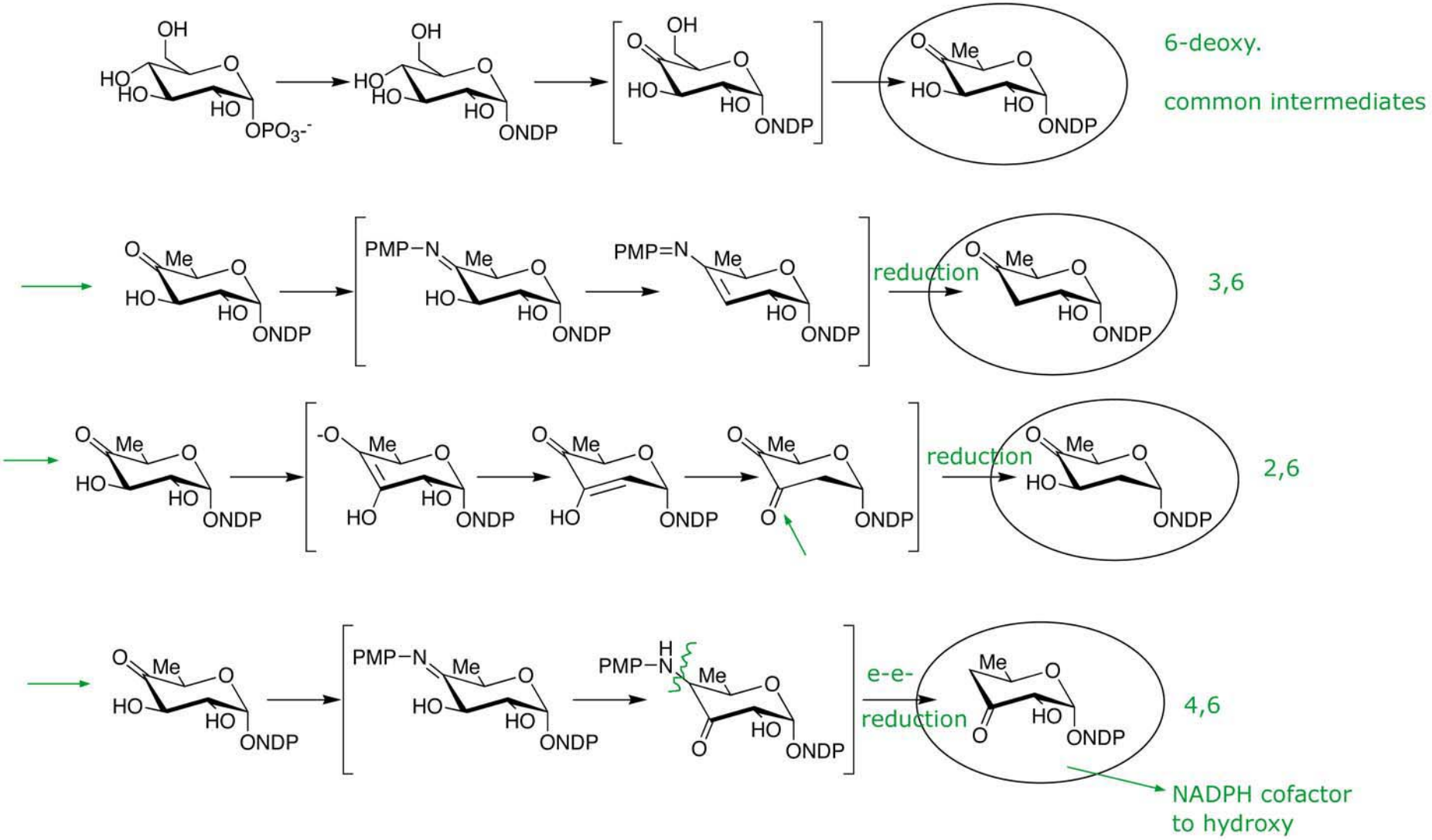
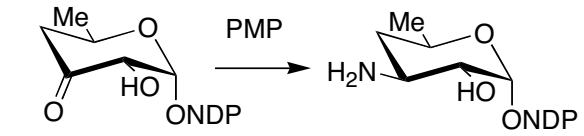
5.451 F2005
Saccharide Biosynthesis
Deoxy sugar biosynthesis review

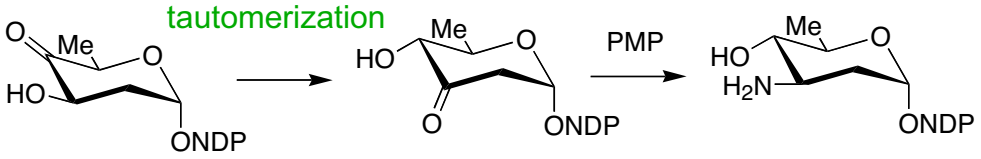


5.451 F2005
Saccharide Biosynthesis
Deoxy sugar biosynthesis review

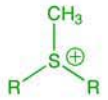
Amination requires the presence of a keto group; otherwise timing not specified



4,6 dideoxy



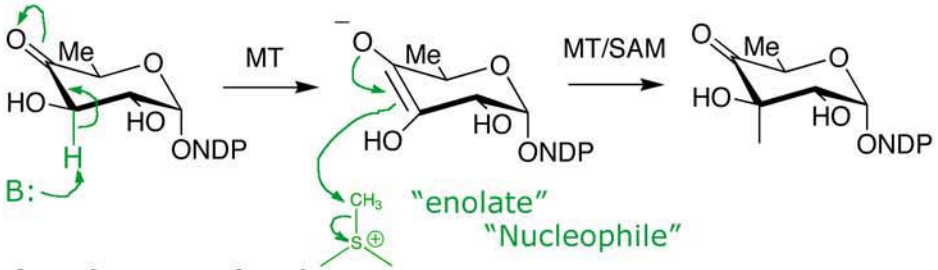
Desosimine --> erythromycin

SAM =  = electrophilic

5.451 F2005
Saccharide Biosynthesis
Deoxy sugar biosynthesis review

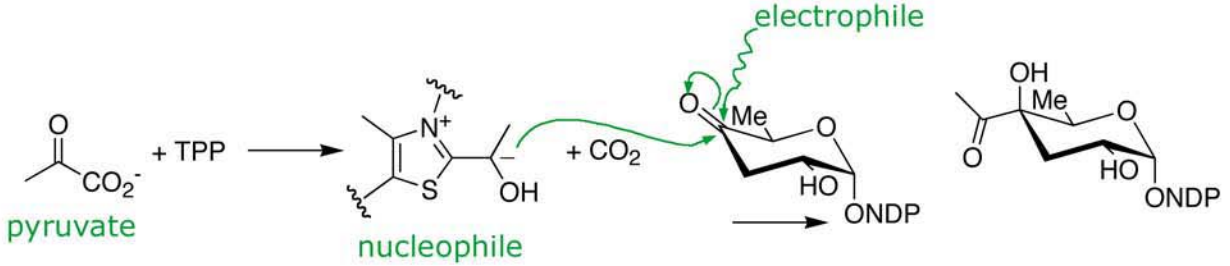
Attachement of carbon

1. If a single methyl group is attached, SAM is cofactor, and a nucleophilic site on the sugar is required enzyme will help generate enolate

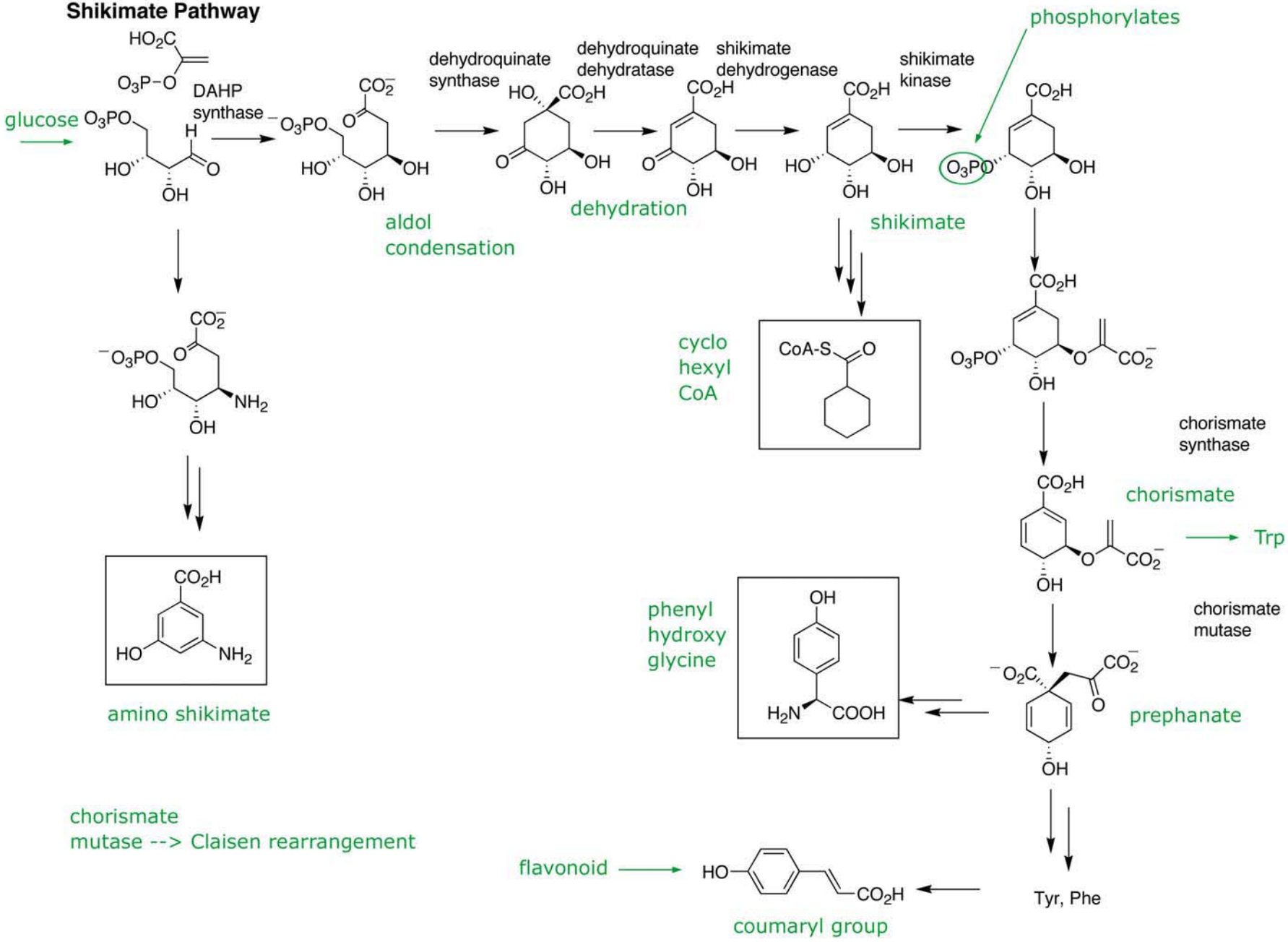


Attachement of carbon

2. If a 2-carbon group is attached, pyruvate is the source. Pruvate acts as a nucleophile (with the help of TPP cofactor) and an electrophilic site on the sugar - i.e. a carbonyl carbon- is required



5.451 F2005
Shikimate Pathway



5.451 F2005
Shikimate Pathway

Normally usd in synthesis of aromatic amino acid

Branch points from a primary metabolic pathway to make a variety of natural products

1. **phenyl-glycine amino acids** --> vancomycin --> comparison (incorporated peptide products)
   PKS

2. **amino shikimate** --> rifamycin --> PK product

3. **cyclohexyl CoA** --> avermectins --> incorporated into a PK product

4. **coumaryl CoA derivatives for flavonoid biosynthesis**
   starting materials

5.451 F2005
Shikimate Pathway

transfer plant genes to e. coli
+ express S.A. in e.coli

28g/L

14% yield based glucose
starting material

another technique

culture presence of a solid
ion exchange resin

Figure removed due to copyright reasons.

Please see Scheme 1a in *JACS* 123 (2001): 10173-10172.

based coumpounds accumulate
Knock out transporter = leave shik. acid
in media outside cell --> 52g/L 18% yield

5.451 F2005
Shikimate Pathway

Figure removed due to copyright reasons.

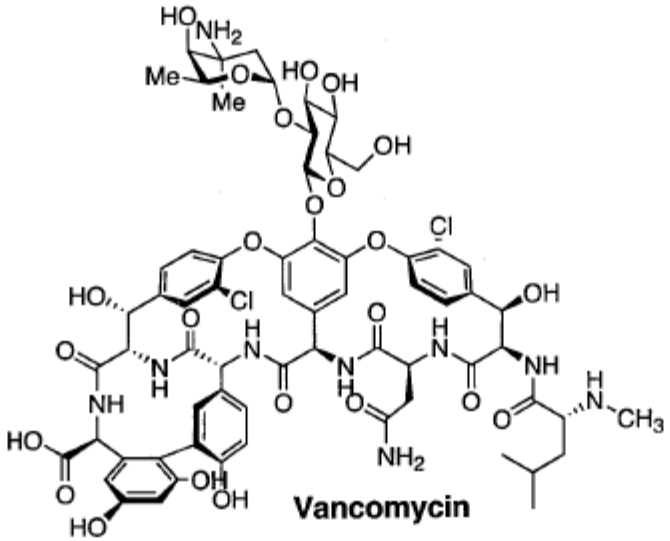
Please see: Hubbard, Brian K., and Christopher T. Walsh.

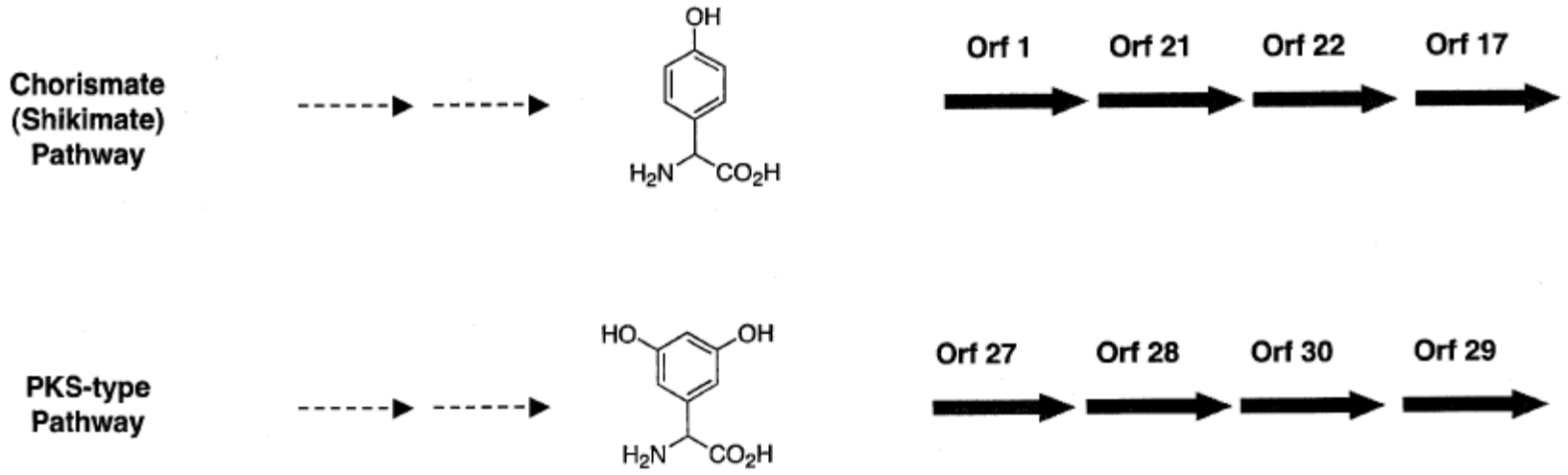
Scheme 2 in “Vancomycin Assembly: Nature's Way.” *Angew Chem Intl Ed* 42 (2004): 730-765.

5.451 F2005
Shikimate Pathway

Figure removed due to copyright reasons.
Please see: Hubbard, Brian K., and Christopher T. Walsh.
Figure 6 in “Vancomycin Assembly: Nature's Way.” *Angew Chem Intl Ed* 42 (2004): 730-765.

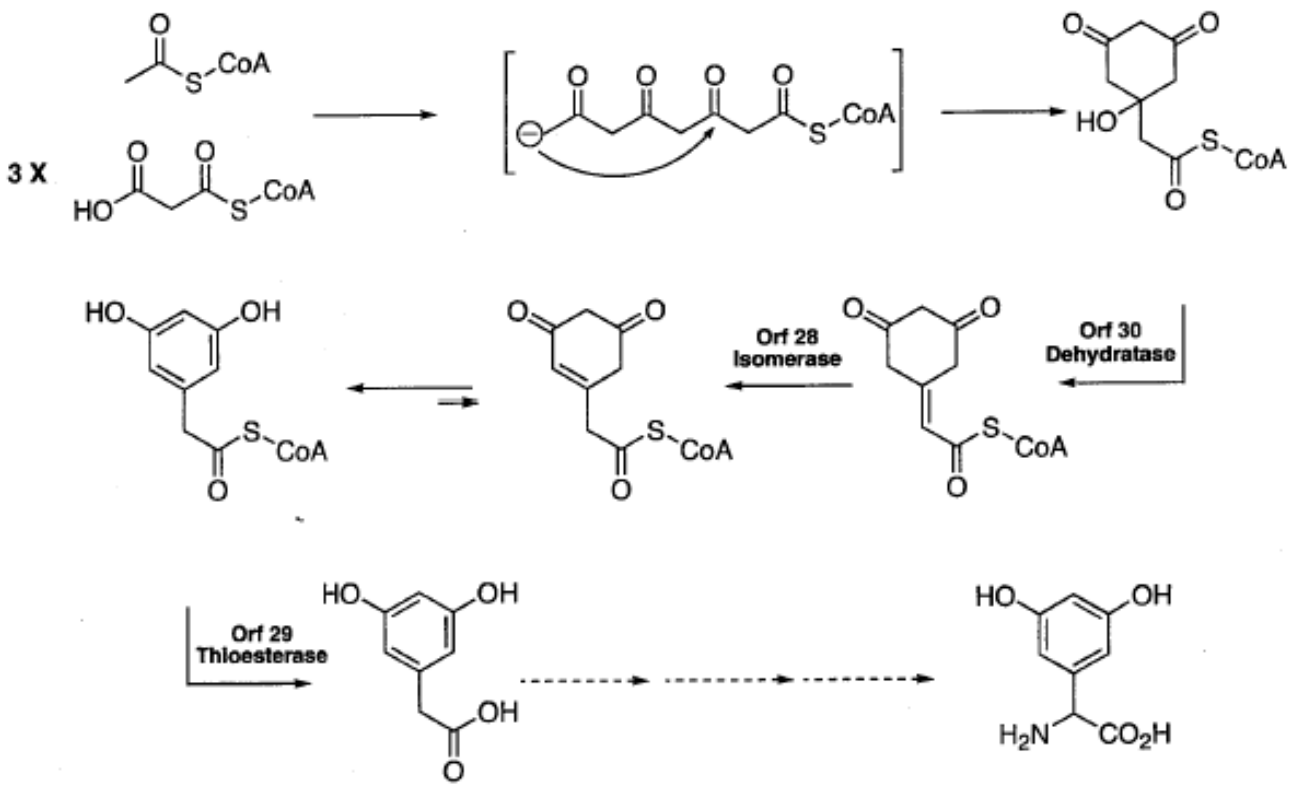
5.451 F2005
Shikimate Pathway





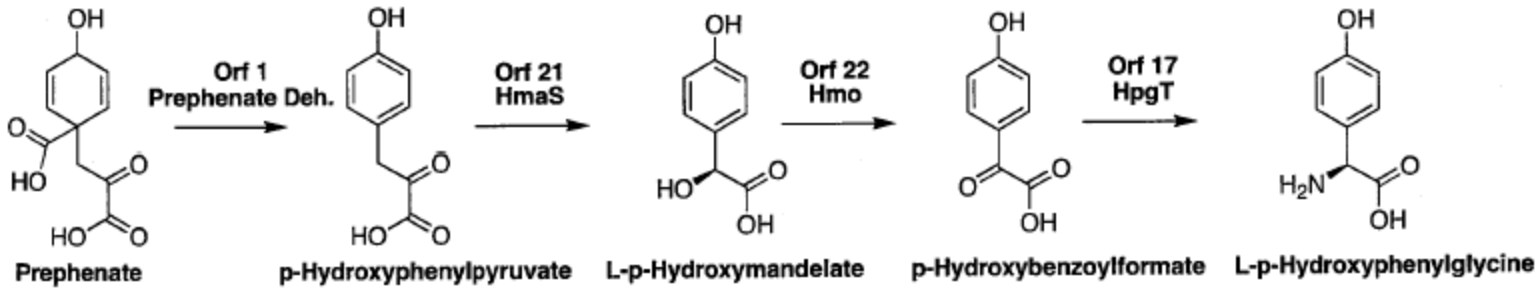
Angew Chem Intl Ed 42 (2003): 730-765.

5.451 F2005
Shikimate Pathway



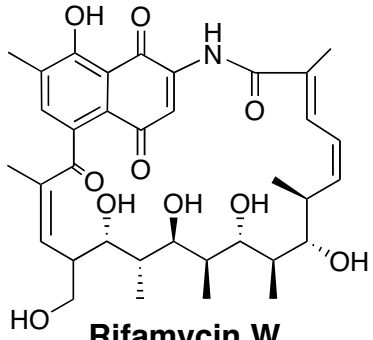
Angew Chem Intl Ed 42 (2003): 730-765.

5.451 F2005
Shikimate Pathway

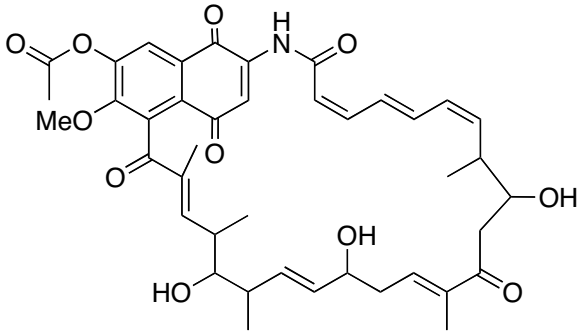


Angew Chem Intl Ed 42 (2003): 730-765.

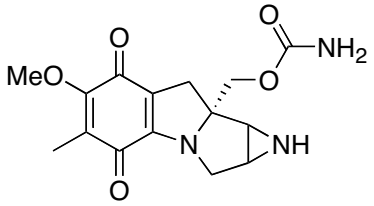
5.451 F2005
Shikimate Pathway
Ansa macrolides: incorporation of amino shikimate



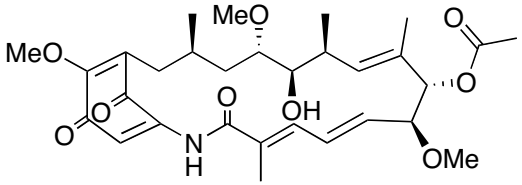
Rifamycin W



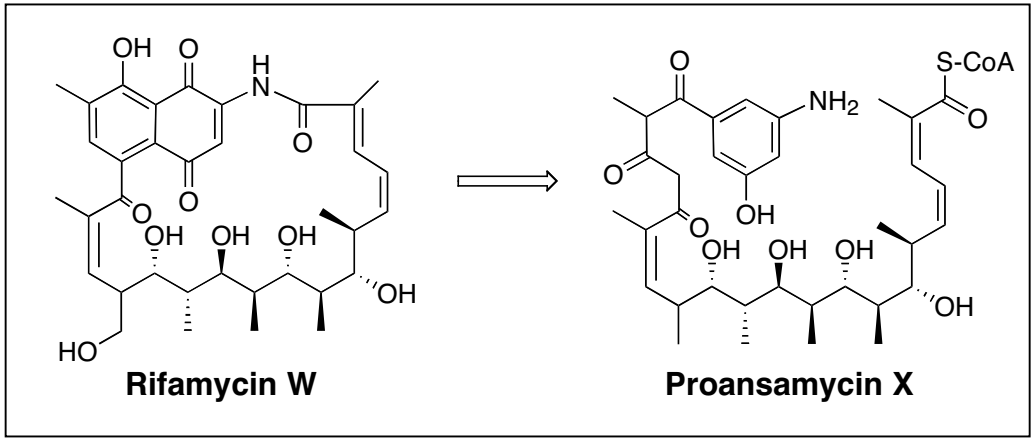
Napthomycin



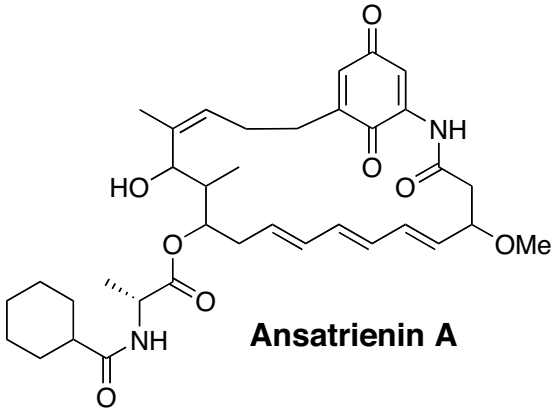
Mitomycin



Geldanamycin

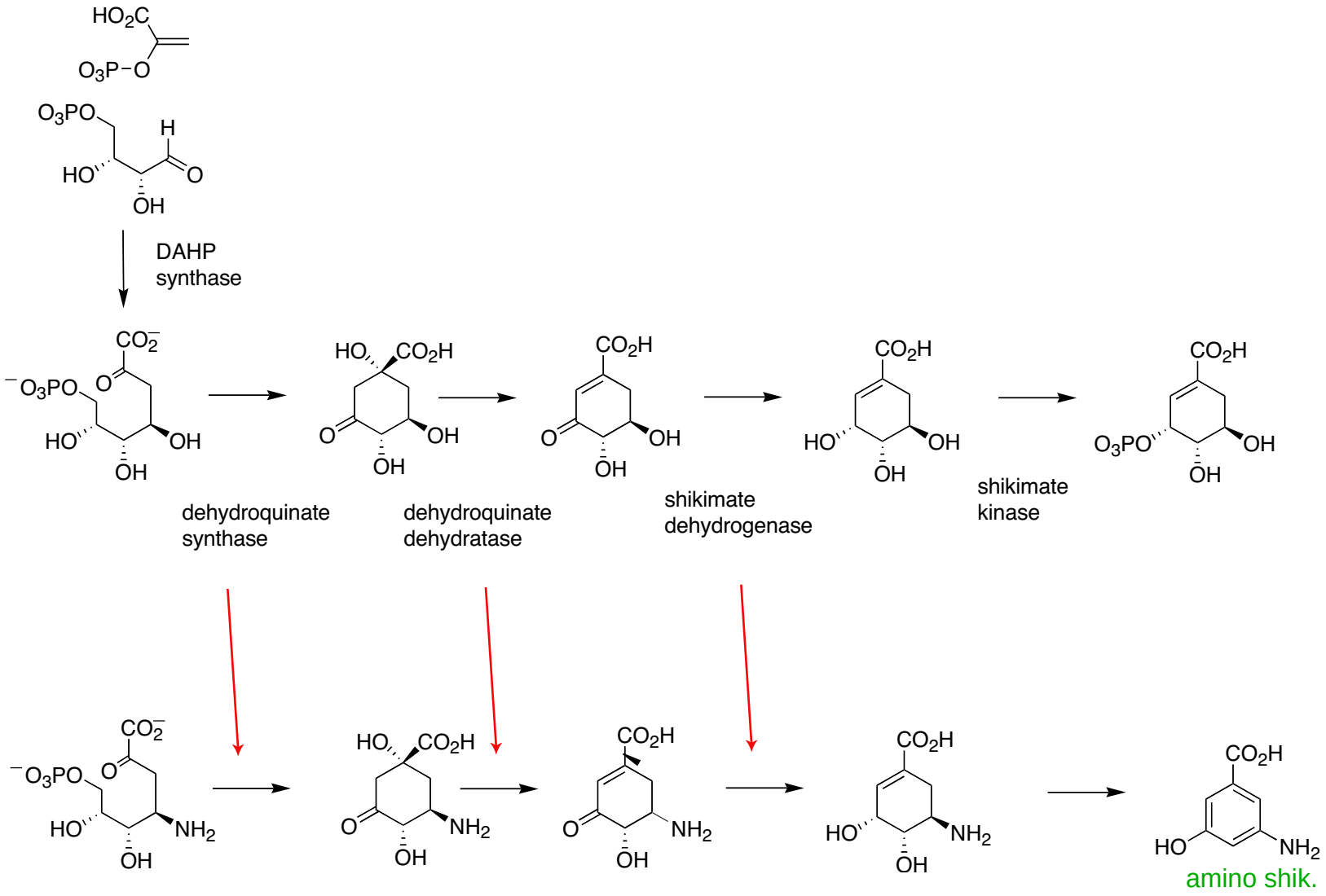


Rifamycin W **Proansamycin X**



Ansatrienin A

5.451 F2005
Shikimate Pathway
Amino Derivatives



enzymes of amino shik. require amine moiety for recognition

5.451 F2005
Shikimate Pathway
Amino Derivatives

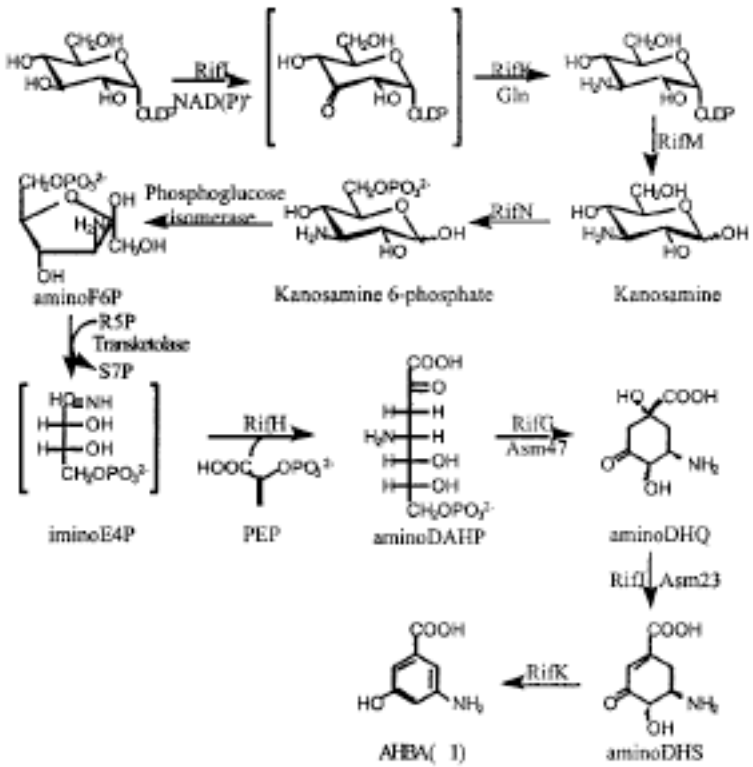
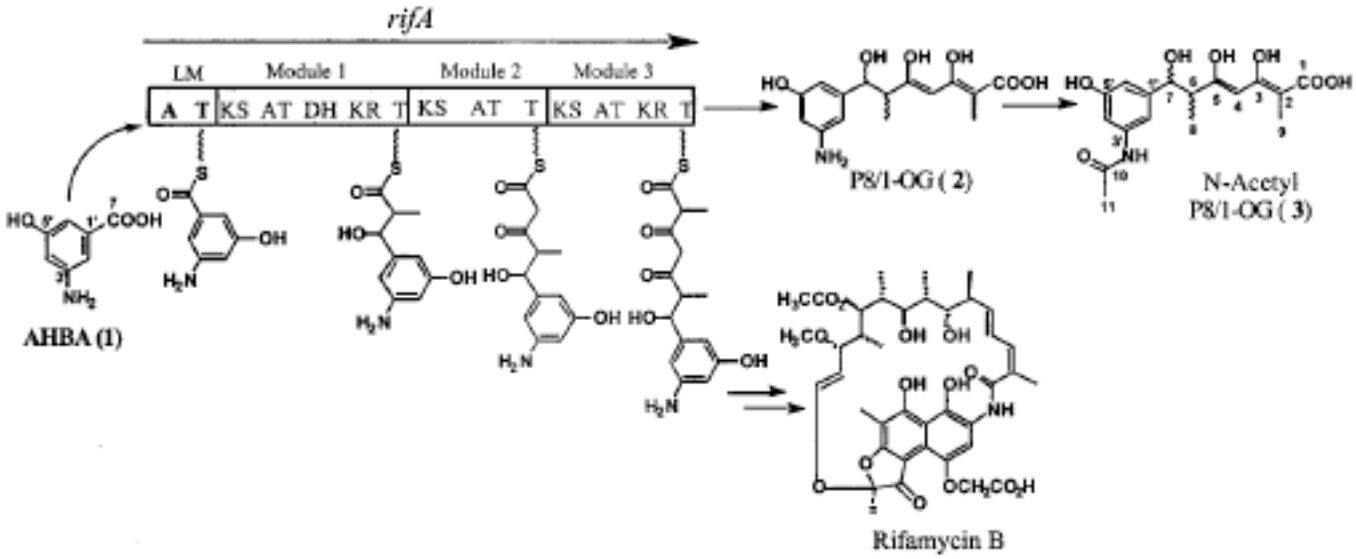


Fig. 2. Proposed pathway for AHBA biosynthesis. AminoDHS, 5-amino analog of 3-dehydroshikimic acid; aminoDAHP, 3,4-dideoxy-4-amino-D-*arabino*-heptulosonic acid 7-phosphate; PEP, phosphoenolpyruvic acid; aminoDHQ, 5-deoxy-5-amino-3-dehydroquinic acid.

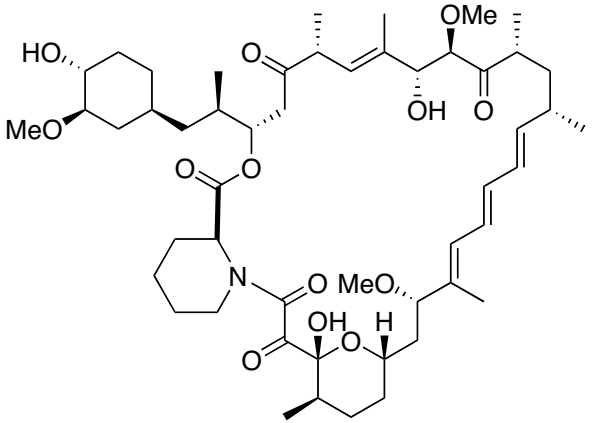
from PNAS(2003) 100, 9774-9778

5.451 F2005
Shikimate Pathway
Amino Derivatives

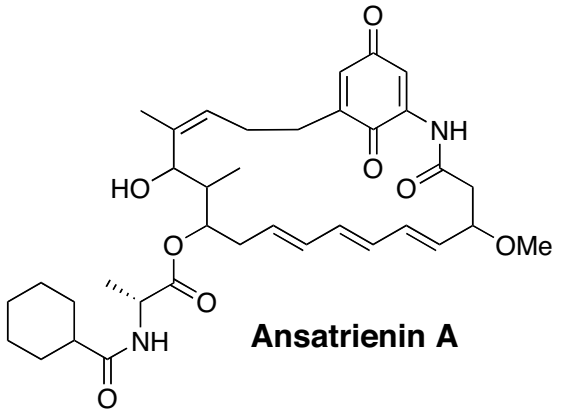


from PNAS(2003) 100, 9774-9778

5.451 F2005
Shikimate Pathway
Cyclohexyl-CoA



Rapamycin
(Ascomycin, FK506)



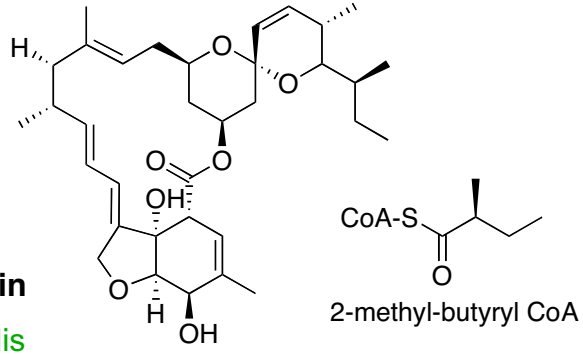
Ansatrienin A

5.451 F2005
Shikimate Pathway
Cyclohexyl-CoA

Figure removed due to copyright reasons.
Please see Figure 2 in *J Indus Microbiol Biotech* 20 (1998): 299-303.

5.451 F2005
Shikimate Pathway
Adding on a cyclohexyl starter unit

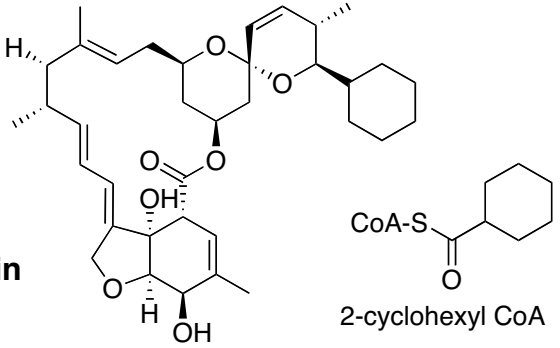
antiparasitic agents



Avermectin

S avermitilis

2-methyl-butyryl CoA



Doramectin

S. collinus

2-cyclohexyl CoA

Figures removed due to copyright reasons.
Please see Figure 3 in *Nature Biotech* 18 (2000): 980-983.

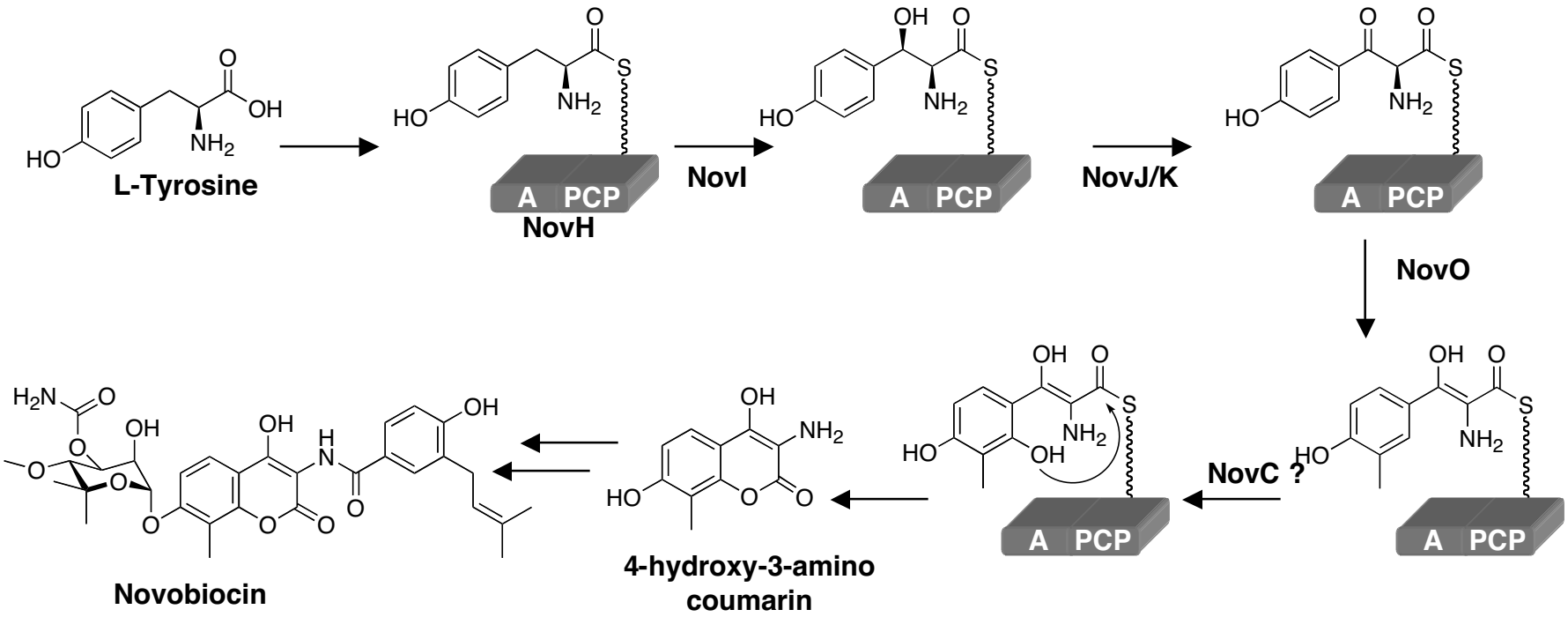
vector or a plasmid containg all cyclo hexyl biosyn genes

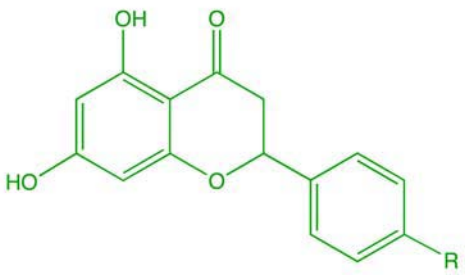
5.451 F2005
Shikimate Pathway
Coumarin

Figure removed due to copyright reasons.

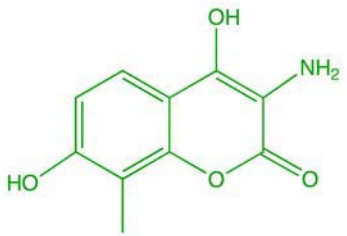
Please see Figure 1 in *J Indus Microbiol Biotech* 30 (2003): 456-461.

5.451 F2005
Shikimate Pathway
Coumarin





coumarin --> PKS | shik.



amino coumarin

5.451 F2005
Shikimate Pathway
Deoxy sugar biosynthesis