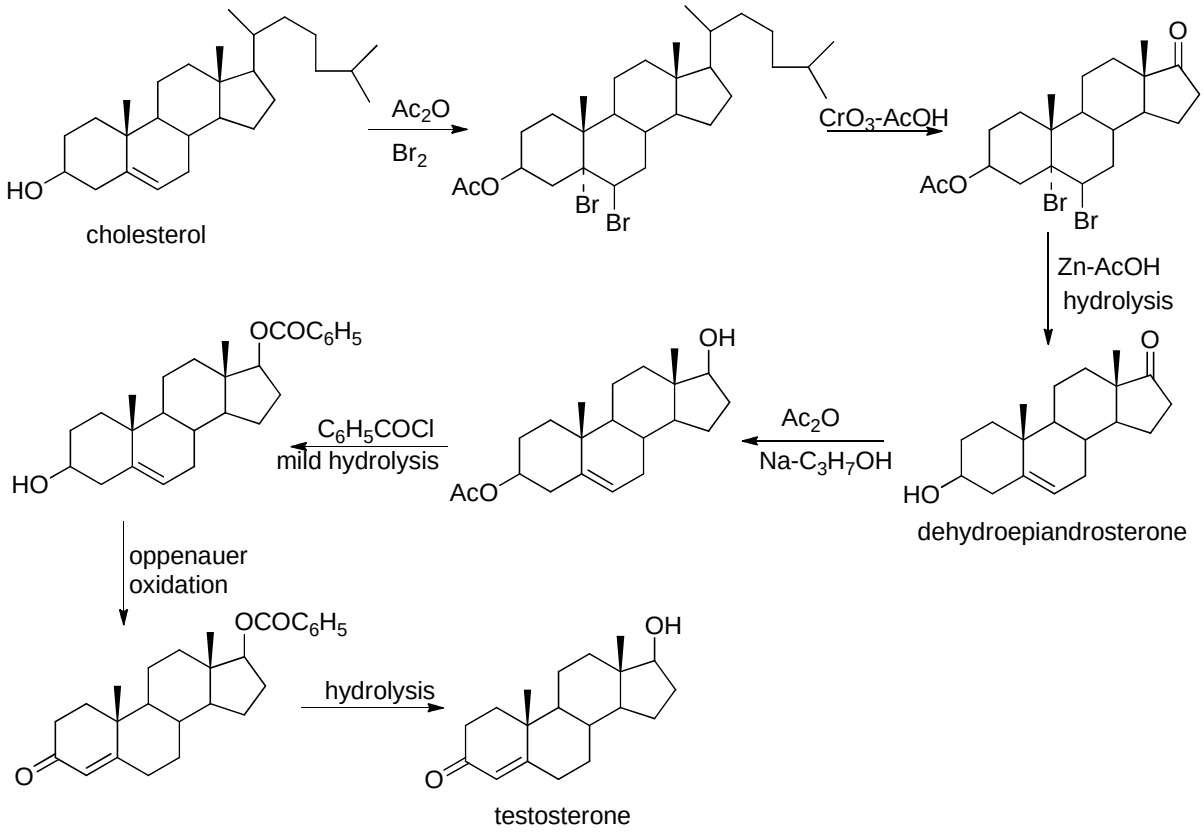
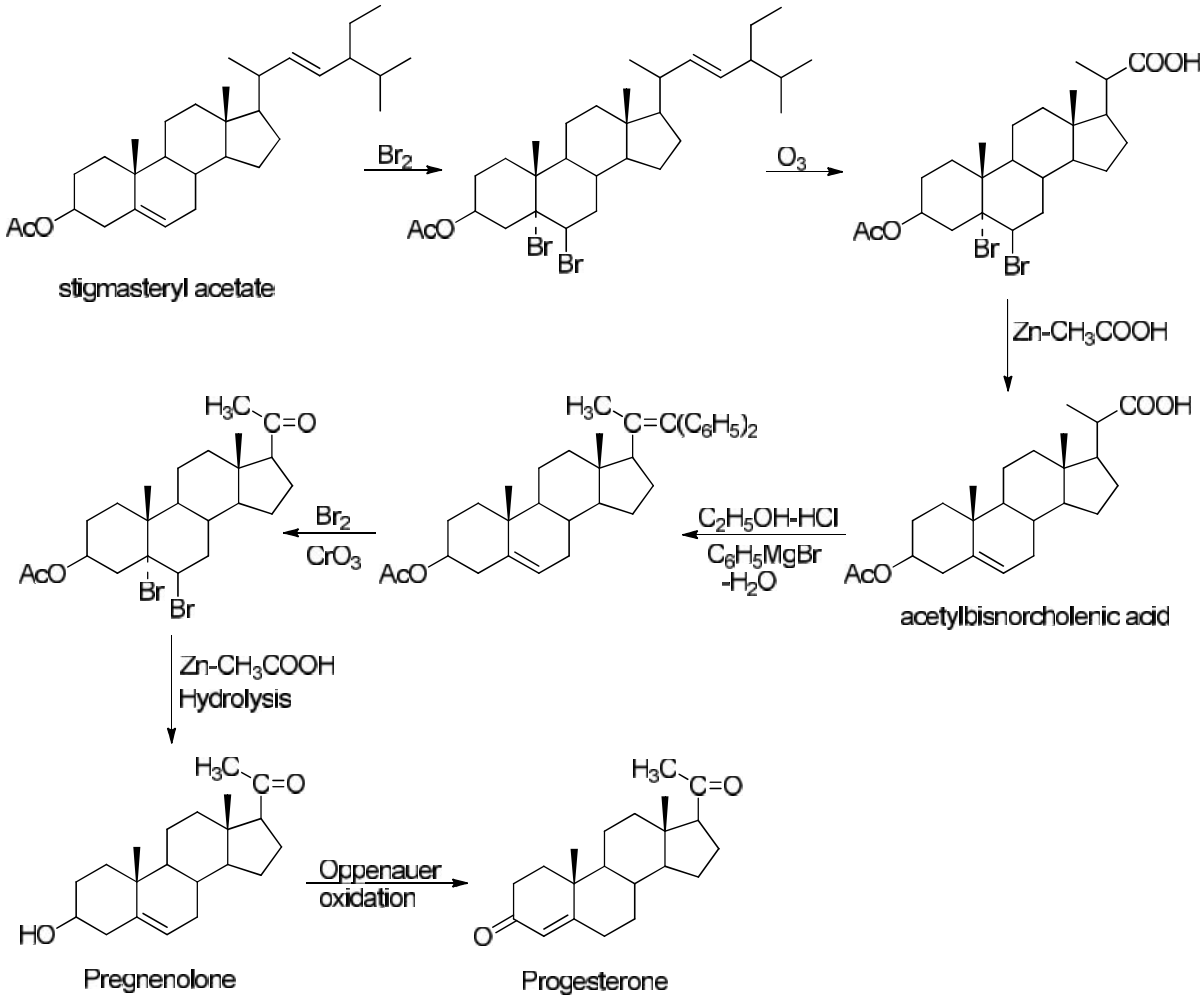
Synthesis of Testosterone from cholesterol

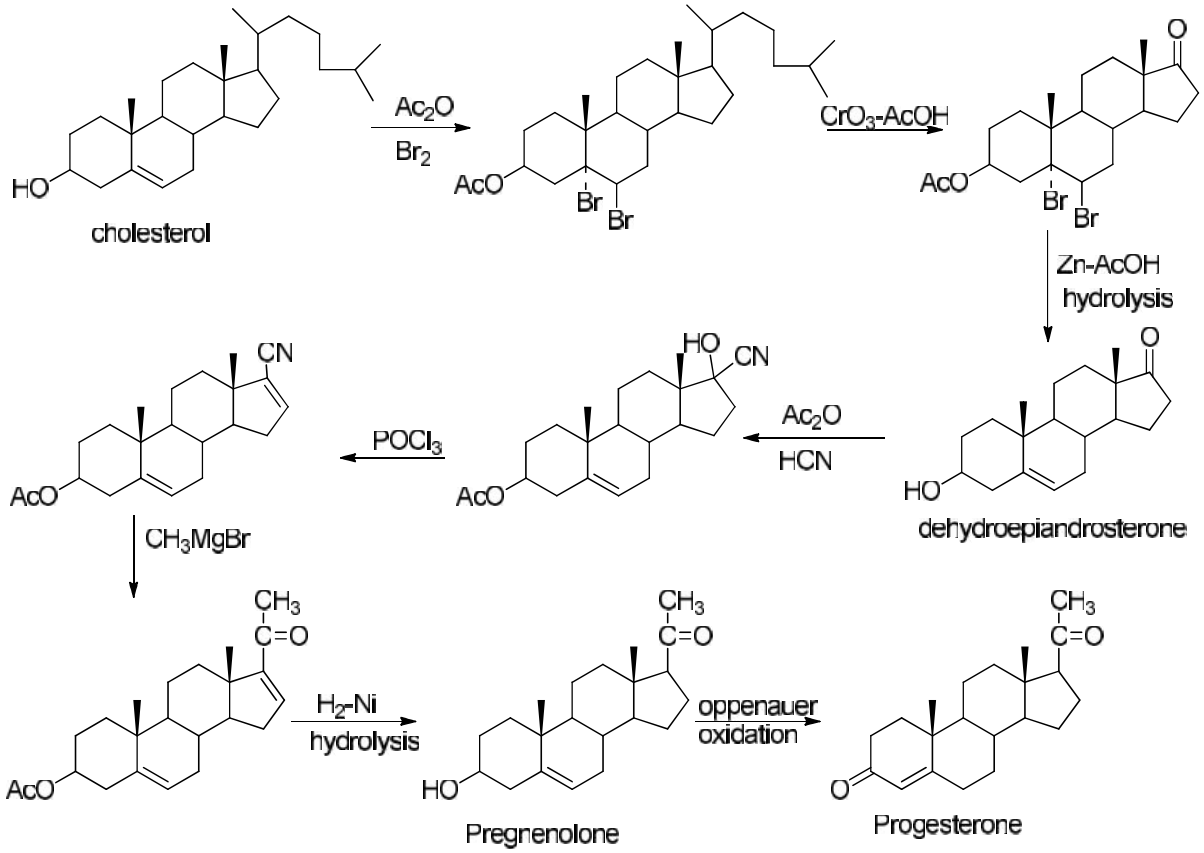


Testosterone from cholesterol: Cholesterol on acetylation, bromination followed by oxidation yields dehydroepiandrosterone. Acetylation followed by selective hydrogenation reduces the C-17 carbonyl group. Benzoylation followed by selective hydrolysis and oppenauer oxidation yields testosterone.

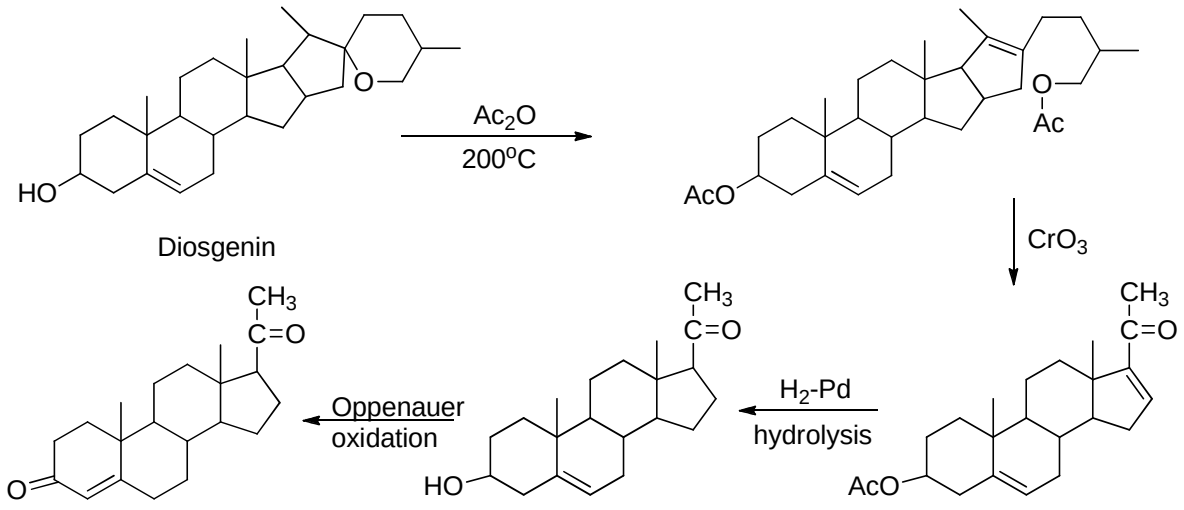
Synthesis of progesterone from stigmasterol acetate: Bromination followed by ozonization and debromination of stigmasterol acetate yields acetylbisnorcholenic acid, which on reaction with Grignard reagent yields diphenylethylene derivative. Bromination followed by oxidation, debromination and hydrolysis yields pregnenolone. Oppeneauer oxidation of pregnenolone yields progesterone



Synthesis of progesterone from cholesterol: The process involves treating chlolesterol with acetic anhydride and bromine yielding dibromo derivative, which on oxidation followed by debromination yields dehydroepiandrosterone. One carbon of chain was introduced by treatment with HCN. Grignard reaction and selective hydrogenation of the conjugated double bond affords pregnenolone

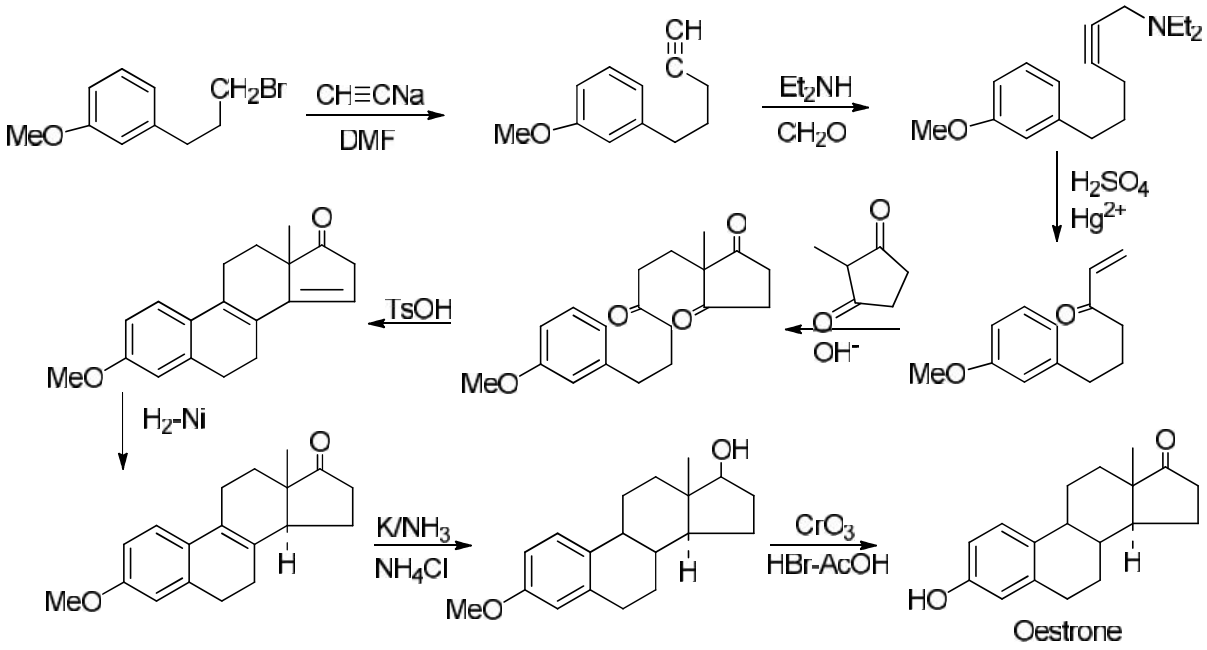


Synthesis of progesterone from diosgenin: Heating diosgenin in a sealed tube at 200oC with acetic anhydride leads to opening of spiro ketal ring, followed by oxidation with chromium trioxide introduces two carbon chain at C-17. Selective reduction, hydrolysis followed by oppenauer oxidation yields progesterone.

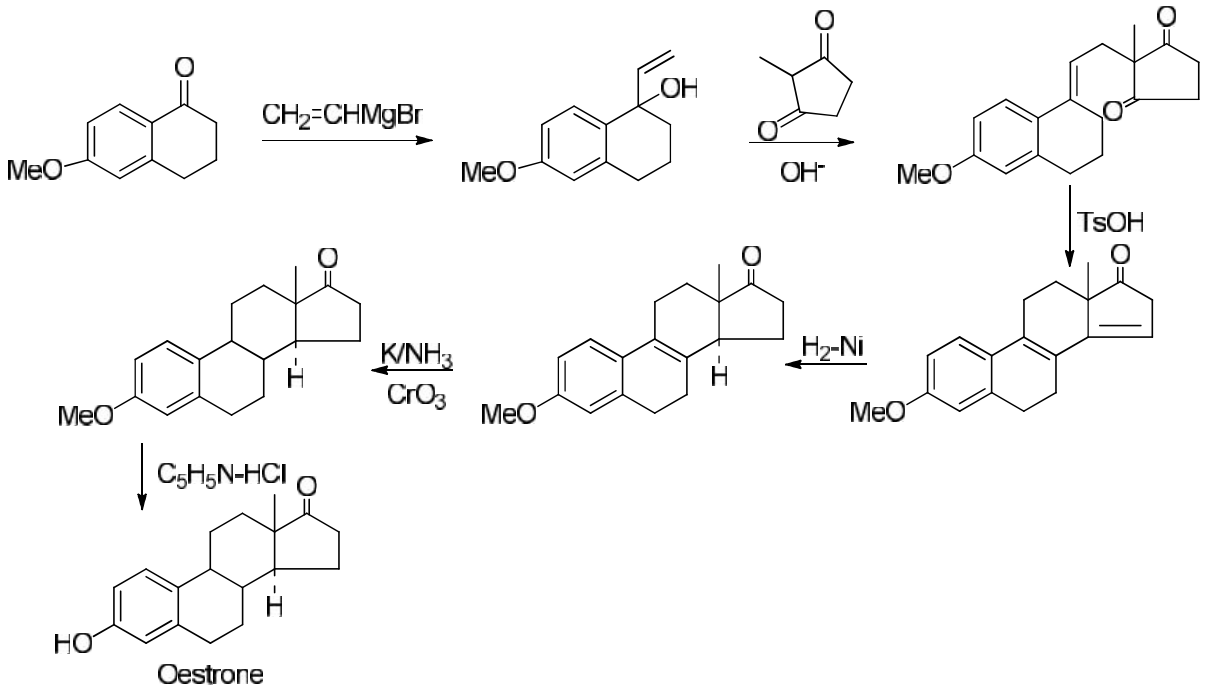


Synthesis of Oestrone

1: Johnson synthesis

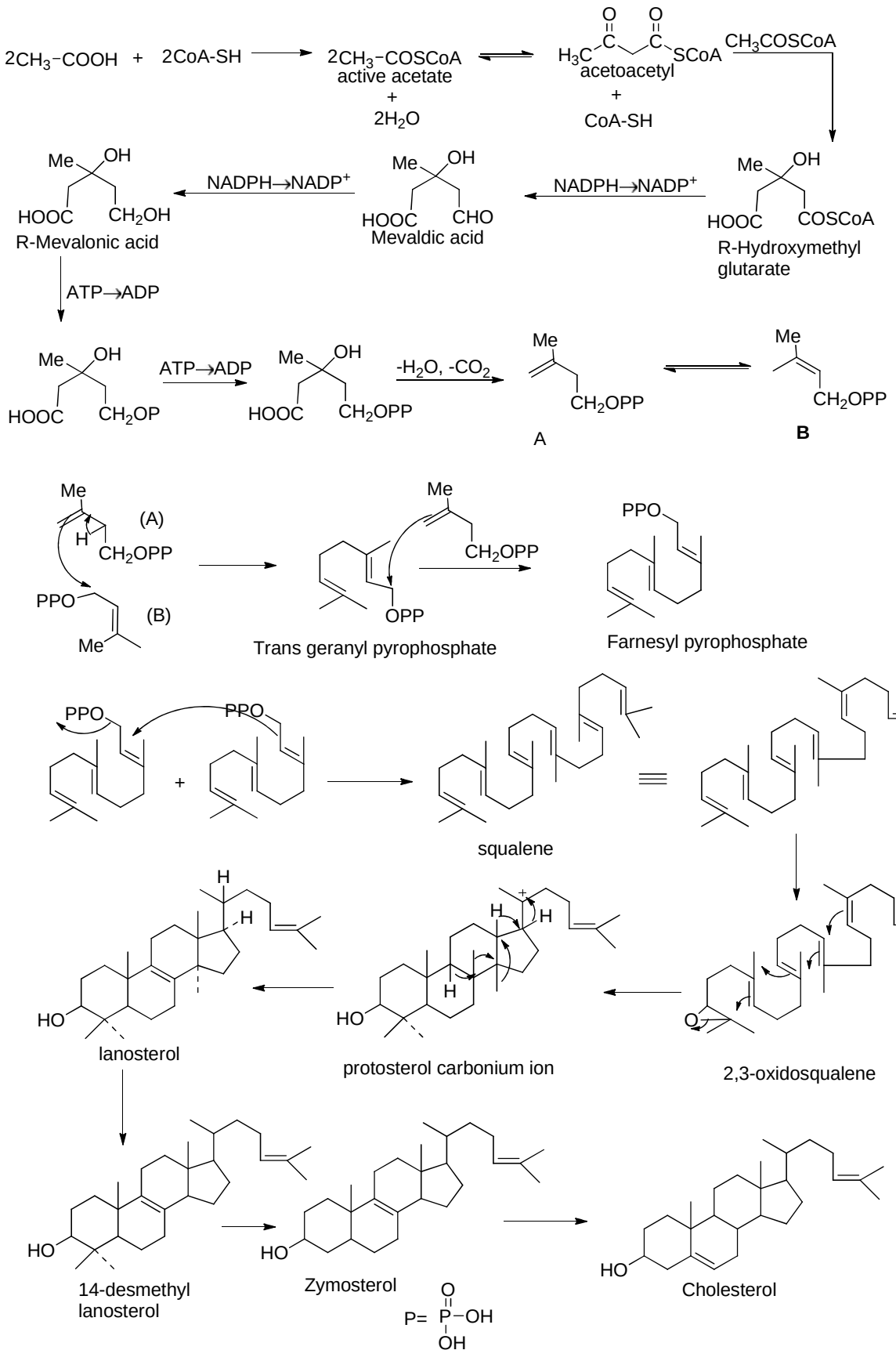


2: Hughes synthesis



Biosynthesis of Cholesterol; Biosynthesis of cholesterol is believed to start with labelled acetic acid. Acetic acid which acts as active acetate combines with coenzyme A to form active acetate, which rearranges to aceto acetyl CoA. This combines with one molecule of active acetate to form hyroxymethylglutarate having R configuration. It is then reduced by NADPH to mevaldic acid, which is further reduced to mevalonic acid. Since mevalonic acid contains six carbon atoms, one carbon is lost by phosphorylation process to yield isoprene unit. Two phosphorylation of mevalonic acid followed by loss of molecule of carbon dioxide and water to form 3-methylbutyl-3-enyl(isopentyl) pyrophosphate (A) which isomerises to 3-methylbut-2-enyl(β,β dimethylallyl) pyrophosphate (B). (A) and (B) combine to give geranyl pryrophosphate with A acting as nucleophile and B acting as electrophile (head to tail union). Geranyl pyrophosphate again combines with (A) to form farnesyl pyrophosphate. Two farnesyl pyrophosphate molecules undergo tail to tail union to give squalene via NADPH. Oxidosqualene undergo multicyclization intiated by epoxide cleavage to give protosterol carbonium ion two undergo two methyl shifts to give lanosterol .

The methyl group at C-14 is first oxidized t hydroxymethyl and then to carboxyl group followed by decarboxylation to give 14-desmethyl lanosterol. Removal of 4,4-gem dimethyl group proceed through oxidation to hydroxymethyl and then to carboxyl group which decarboxylate to give zymosterol. Isomerization of double bond from 8,9 to 7,8 and then to 5,6 followed by reduction of double bond at C-24 and C-25 gives cholesterol.


2CH3−COOH + 2CoA-SH
2CH3−COSCoA
active acetate
+
2H2O
acetoacetyl
+
CoA-SH
CH3COSCoA
R-Mevalonic acid
NADPH→NADP+
Mevaldic acid
NADPH→NADP+
R-Hydroxymethyl
glutarate
ATP→ADP
ATP→ADP
-H2O, -CO2
A
B
(A)
(B)
Trans geranyl pyrophosphate
Farnesyl pyrophosphate
squalene
lanosterol
protosterol carbonium ion
2,3-oxidosqualene
14-desmethyl
lanosterol
Zymosterol
Cholesterol
P= P−OH

Biosynthesis of cholesterol to other steroids