Medicinal Chemistry - Biosynthesis Inspiration for Drug Discovery (2007-2008)

Q1 (Resit)

Answer BOTH part (a) AND part (b).

a) Outline the chemical steps involved in the biosynthesis of chorismate (3) from erythrose-4-phosphate (E4P, 1) and phosphoenolpyruvate (PEP, 2). Include in your answer plausible curley arrow mechanisms for the transformations invoked.

\[
\text{1. E4P} \quad \text{2. PEP} \quad \text{3. chorismate}
\]

(13 marks)

b) Answer TWO of the following:

i) Provide a mechanism by which an FADH\textsubscript{2}/O\textsubscript{2}-dependent enzyme mediates the oxidation of squalene to 2,3-oxidosqualene (\textit{NB}. FADH\textsubscript{2} = 4, below)

\[
\text{squalene} \quad \text{O}_2 + \text{FADH}_2 \quad \text{2,3-oxidosqualene}
\]

ii) Provide a mechanism by which an NADH dependent enzyme mediates the reduction of the iminium ion 5 to homospermidine (\textit{NB}. NADH= 6, below).

\[
\text{H}_2\text{N}\quad \text{H}_3\text{N} \quad \text{NADH} \quad \text{H}_2\text{N} \quad \text{H}_3\text{N} \quad \text{homospermidine}
\]

iii) Provide mechanisms for the sequence of transformations shown below for the biosynthesis of \(\alpha\)-terpene. Indicate any selectivity that may be controlled by the enzyme(s) involved (\textit{NB}. OPP = pyrophosphate)

\[
\text{pyrophosphate} \quad \text{OPP} \quad \text{\(\alpha\)-pinene}
\]

(6 marks each)