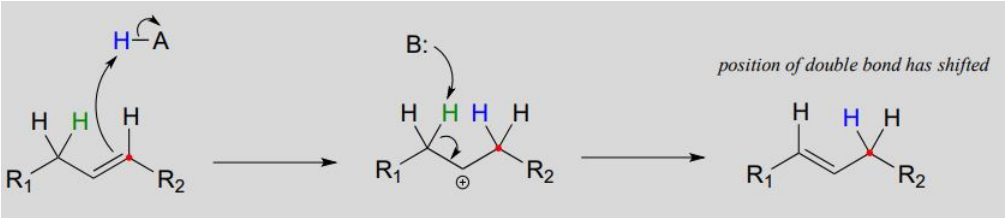
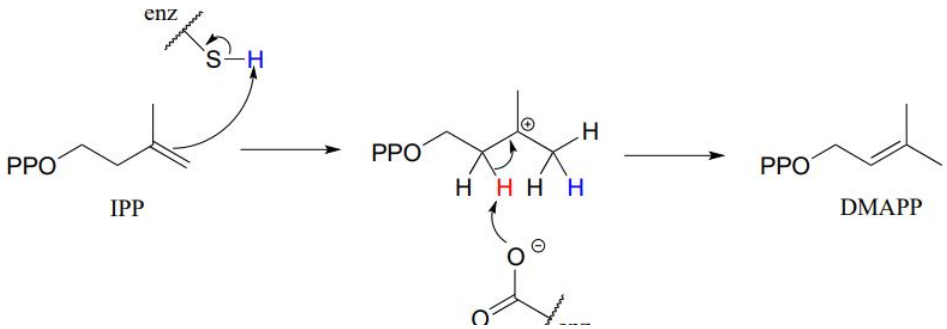
14.4: Electrophilic Isomerization

Electrophilic reactions in biochemistry are not limited to addition to alkene double bonds. The position of a double bond in an alkene can also be shifted through an electrophilic, carbocation-intermediate reaction. An electrophilic alkene isomerization occurs when an initial π bond protonation event (step 1 below) is followed by deprotonation of an adjacent carbon to re-form the π bond in a different location.

Electrophilic isomerization mechanism:



In a key early step in the biosynthesis of isoprenoid compounds, isopentenyl diphosphate (IPP), the isoprenoid 'building block' molecule, is isomerized to dimethylallyl diphosphate (DMAPP) (EC 5.3.3.2).



In the first step, the p bond between carbon #3 and carbon #4 is protonated by a cysteine residue in the active site. X-ray crystallography studies on the isomerase enzyme (EMBO J. 2001, 20, 1530) show that the carbocation intermediate is bound in a very deep, hydrophobic active site cavity that seals out any water molecules that could potentially attack the carbocation to form an undesired alcohol product. stead, a basic glutamate residue is positioned in the active site to abstract a proton from carbon #2 (step 2), serving to reestablish the double bond in a new position between carbons #2 and #3.

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