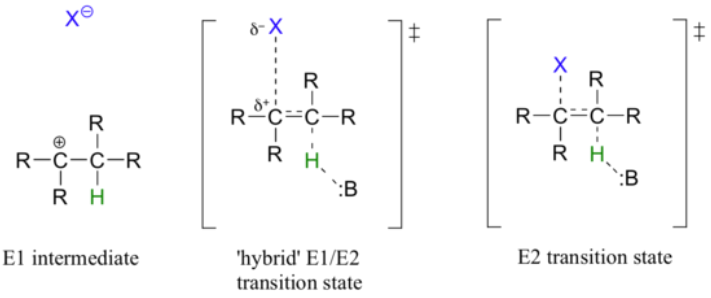
11.11: BIOLOGICAL ELIMINATION REACTIONS

OBJECTIVE

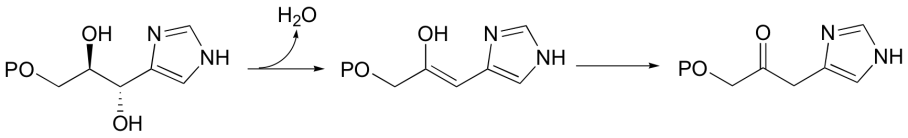
After completing this section, you should have an appreciation that E1, E2 and E1cB mechanisms exist and are well-known in biological chemistry.

ENZYMATIC E1 AND E2 REACTIONS

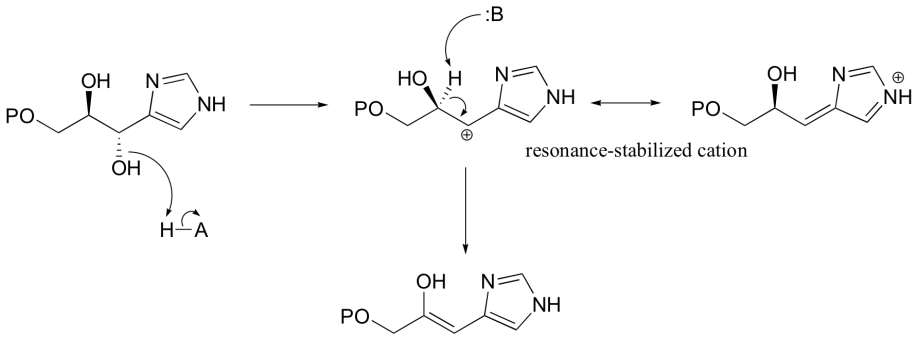
While most biochemical b-elimination reactions are of the E1cb type, some enzymatic E2 and E1 reactions are known. Like the enzymatic S_N2 and S_N1 substitution mechanisms discussed in chapters 8 and 9, the E2 and E1 models represent two possible mechanistic extremes, and actual enzymatic elimination reactions may fall somewhere in between. In an E1/E2 hybrid elimination, for example, C_β-X bond cleavage may be quite advanced (but not complete) before proton abstraction takes place - this would lead to the build-up of transient *partial* positive charge on C_β, but a discreet carbocation intermediate would not form. The extent to which partial positive charge builds up determines whether we refer to the mechanism as 'E1-like' or 'E2-like'.



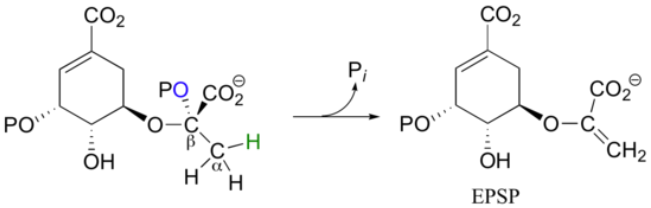
A reaction in the histidine biosynthetic pathway provides a good example of a biological E1-like elimination step (we're looking specifically here at the first, enol-forming step in the reaction below - the second step is simply a tautomerization from the enol to the ketone product (section 13.1A)).



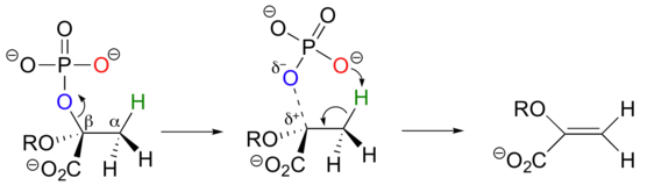
Notice in this mechanism that an E1cb elimination is not possible - there is no electron-withdrawing group (like a carbonyl) to stabilize the carbanion intermediate that would form if the proton were abstracted first. There is, however, an electron-*donating* group (the lone pair on a nitrogen) that can stabilize a positively-charged intermediate that forms when the water leaves.



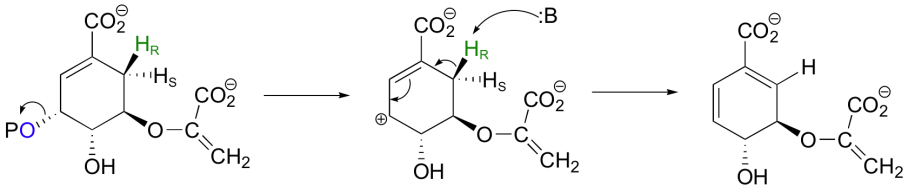
Another good example of a biological E1-like reaction is the elimination of phosphate in the formation of 5-enolpyruvylshikimate-3-phosphate (EPSP), an intermediate in the synthesis of aromatic amino acids.



Experimental evidence indicates that significant positive charge probably builds up on C_β of the starting compound, implying that C-O bond cleavage is advanced before proton abstraction occurs (notice the parallels to the Cope elimination in the previous section):

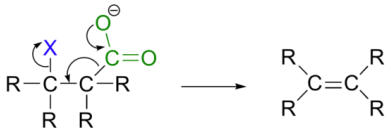


The very next step in the aromatic acid biosynthesis pathway is also an elimination, this time a 1,6-conjugated elimination rather than a simple beta-elimination.

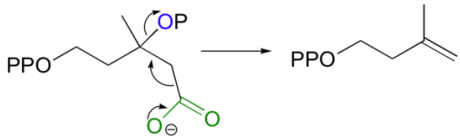


An E1-like mechanism (as illustrated above) has been proposed for this step, but other evidence suggests that a free-radical mechanism may be involved.

While most E1 and E2 reactions involve proton abstraction, eliminations can also incorporate a decarboxylation step.



Isopentenyl diphosphate, the 'building block' for all isoprenoid compounds, is formed from a decarboxylation-elimination reaction.



Phenylpyruvate, a precursor in the biosynthesis of phenylalanine, results from a conjugated 1,6 decarboxylation-elimination.