

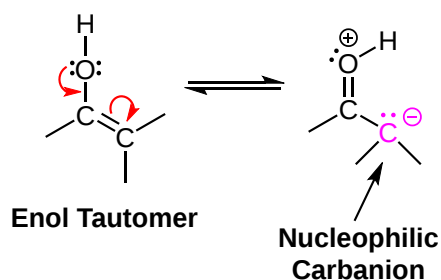
22.2: REACTIVITY OF ENOLS- THE MECHANISM OF ALPHA-SUBSTITUTION REACTIONS

OBJECTIVES

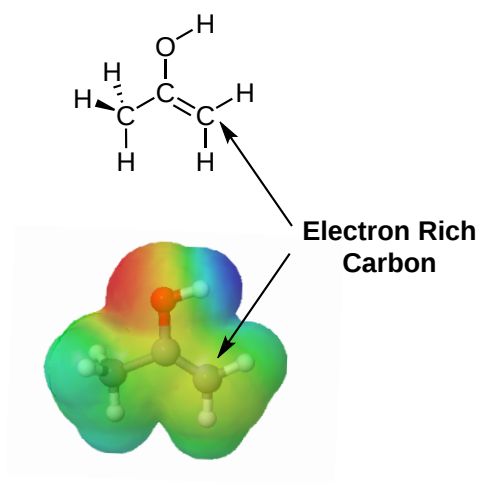
After completing this section, you should be able to write a detailed mechanism for an acid-catalyzed, alpha-substitution reaction of a carbonyl compound.

HOW ENOLS REACT

The oxygen of an enol can donate electron density into its double bond making it electron-rich and more reactive than typical alkenes.



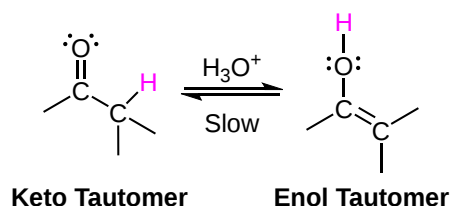
As seen in the electrostatic potential map for propen-2-ol ($\text{CH}_3\text{COH}=\text{CH}_2$), the enol tautomer of acetone, shows an increased electron density on the α -carbon (yellow) especially when compared to the $-\text{CH}_3$ carbon (blue/green). One of the resonance forms of an enol places a lone pair of electrons and a negative charge on the α -carbon forming a carbanion nucleophile. Enols react with electrophiles in a similar fashion as other carbanion nucleophiles, such as Grignard reagents.



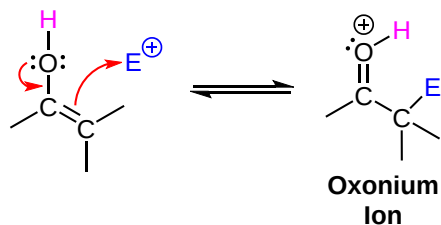
MECHANISM OF ALPHA SUBSTITUTION REACTIONS USING AN ENOL

The mechanism begins with the acid-catalyzed tautomerization to form an enol via the mechanism discussed in **Section 22.1**. Lone pair electrons on the enol oxygen move to become a $\text{C}=\text{O}$ pi bond thus creating a positively charged oxonium ion. This also causes electrons from the $\text{C}=\text{C}$ enol pi bond to attack an electrophile forming a $\text{C}-\text{E}$ sigma bond. These two electron movements in concert represent the enol acting as a nucleophile. In the last step, an H^+ is removed from the carbonyl oxygen, regenerating the acid catalyst, and forming an α -substituted carbonyl.

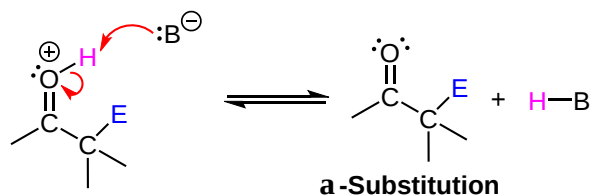
1) Acid catalyzed tautomerization to form an enol



2) The nucleophilic enol attacks the electrophile



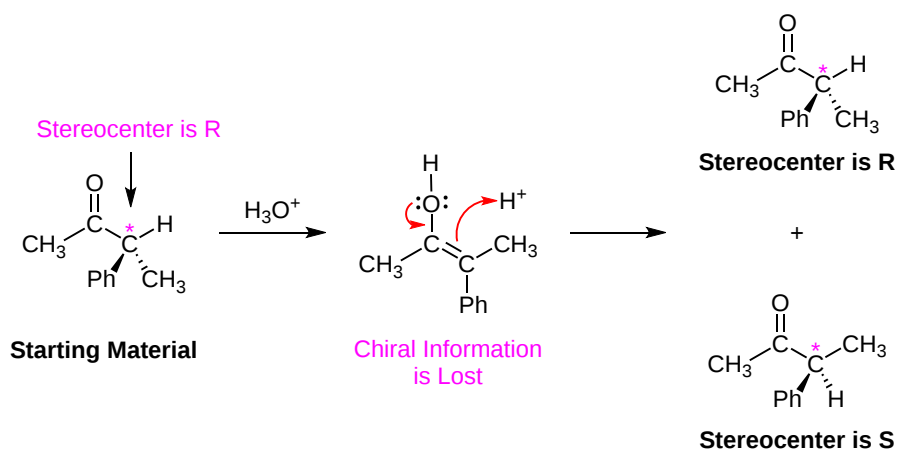
3) Deprotonation of the carbonyl to produce an α -substituted product



STEREOCHEMICAL IMPLICATION OF ENOL FORMATION

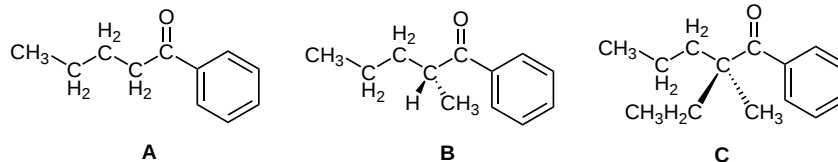
During an acid-catalyzed enol formation, an α -hydrogen is removed to form a sp^2 -hybridized, trigonal planar C=C bond which removes any chiral information from the original alpha carbon. Because the enol alkene is planar the incoming electrophile can attack from either the top or the bottom of the molecule. If the α -carbon of the starting material has a defined stereochemistry or if a new stereocenter is formed during the reaction, the product will typically be a racemic mixture of enantiomers at the site of substitution.

One of the easiest ways of displaying this process is through acid-catalyzed racemization. If a carbonyl compound has an α -carbon with a defined stereochemistry and an α -hydrogen, a racemic mixture can be formed simply through tautomerization. The addition of acid promotes the formation of the enol tautomer which removes the chiral information of the α -carbon. The enol then attacks an H^+ electrophile to reform the keto tautomer which then contains a racemic mixture of enantiomers.

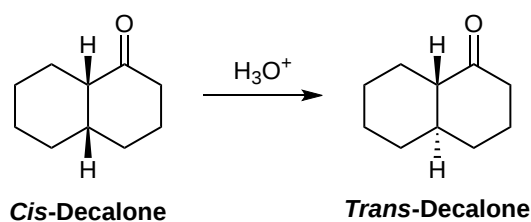


EXERCISES

1) Which of the following optically active ketones would undergo acid-catalyzed racemization? Explain.



2) When *cis*-Decalone is treated with an acid it becomes *trans*-Decalone almost exclusively becomes *trans*-Decalone. Explain.



SOLUTIONS

1) Molecule A would not because the alpha carbon is not a stereocenter. Molecule B would because the alpha carbon is a stereocenter and contains a hydrogen. Molecule C would not because it does not contain an alpha hydrogen.

2) This change involves a process called epimerization. Epimers are diastereomers which differ at only one chiral carbon. Epimerization is a process where only one of multiple chiral carbons is changed. In this example, the stereocenter in question is a chiral carbon. The addition of an acid promotes this carbon becoming part of an enol thereby losing its chiral information. When the enol tautomer converts back to the ketone tautomer, a mixture of both *cis* and *trans* epimers should form. However, as discussed in a previous section, we know that the *trans* isomer of the decalin ring system is more stable than the *cis*. Because there is a defined difference in stability, the *trans* isomer of decalone is preferred.

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