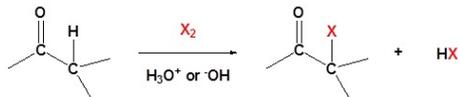


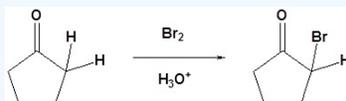
23.4: ALPHA HALOGENATION OF CARBONYLS

Ketones with alpha hydrogens can undergo a substitution reaction with halogens. This reaction occurs because of the tendency of carbonyl compounds to form enolates in basic condition and enols in acidic condition. In these cases even weak bases, such as the hydroxide anion, is sufficient enough to cause the reaction to occur because it is not necessary for a complete conversion to the enolate. For this reaction Cl_2 , Br_2 or I_2 can be used as the halogens.

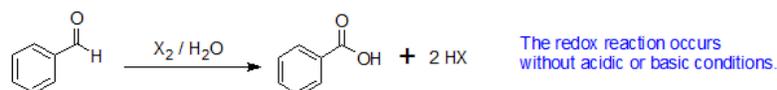
General reaction



Example 1



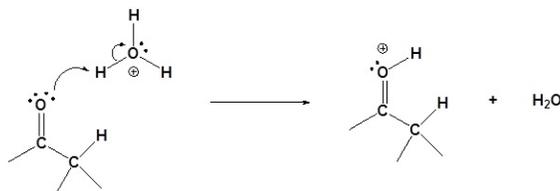
Aldehydes are oxidized by the halogens so this reaction pathway is not synthetically useful. For example, when benzaldehyde is added to either set of reagents described above for ketones, the major product is benzoic acid.



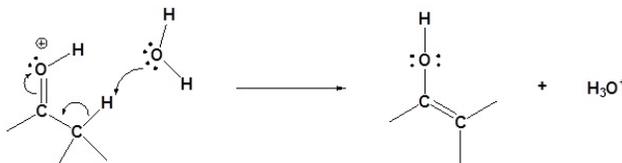
ACID CATALYZED MECHANISM

Under acidic conditions the reaction occurs through the formation of an enol which then reacts with the halogen.

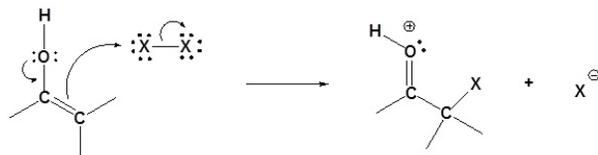
1) Protonation of the carbonyl



2) Enol formation



3) $\text{S}_{\text{N}}2$ reaction



4) Deprotonation



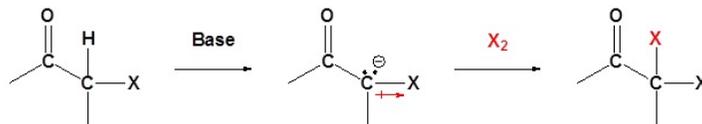
Kinetic studies provide some evidence for the mechanism shown above. The rate law for the alpha-halogenation of a ketone can be given by:

$$\text{rate} = [\text{ketone}][\text{H}^+]$$

The implication is that the rate determining step is dependent on the concentrations of the ketone and acid catalyst and therefore associated with the enol formation part of the mechanism. The halogen does not even appear in the rate law. Indeed, the overall rate is completely independent of the concentration of the halogen and suggests the halogenation step occurs rapidly.

BASE PROMOTED MECHANISM

Under basic conditions the enolate forms and then reacts with the halogen.



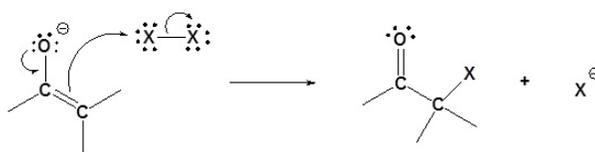
Note! This is base *promoted* and not base *catalyzed* because an entire equivalent of base is required.

It is difficult to stop the base promoted reaction after a single substitution, so acidic conditions are used when a monohalo product is required.

1) Enolate formation

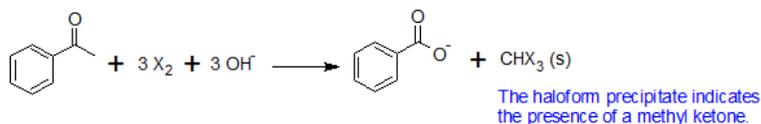


2) S_N2 reaction



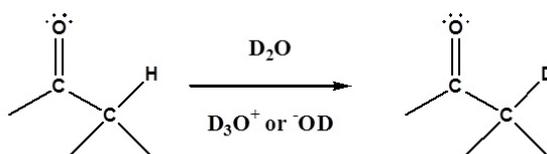
THE HALOFORM QUALITATIVE REACTION TO IDENTIFY METHYL KETONES

The overreaction during base promotion of alpha halogenation is used as a qualitative test called the haloform reaction to identify methyl ketones. Under basic conditions, subsequent halogenation reactions occur because the halogenated product is more reactive than the starting material due to the electron withdrawing effect of the halogen. The halogen inductively stabilizes the conjugate base and increases the relative acidity of the remaining alpha-carbons. Halogenations occur at the alpha-carbon until the haloform becomes a leaving group and is observed as a precipitate as shown in the example below.

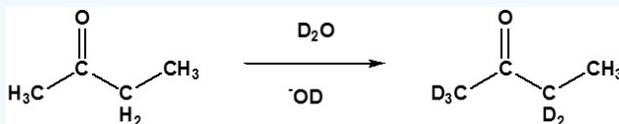


DEUTERIUM EXCHANGE

Due to the acidic nature of α hydrogens they can be exchanged with deuterium by reaction with D₂O (heavy water). The process is accelerated by the addition of an acid or base; an excess of D₂O is required. The end result is the complete exchange of all α hydrogens with deuteriums.

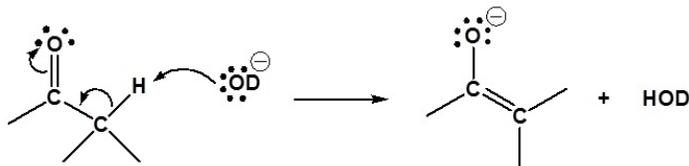


Example 2

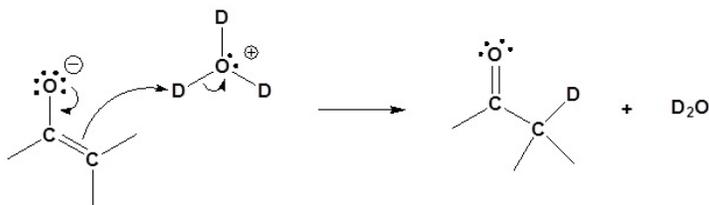


MECHANISM IN BASIC CONDITIONS

1) Enolate Formation

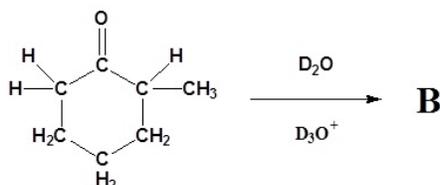
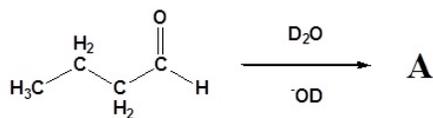


2) Deuteration

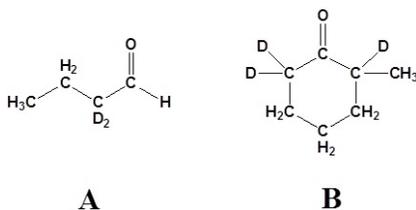


EXAMPLE QUESTION

Draw the product for the following reactions.

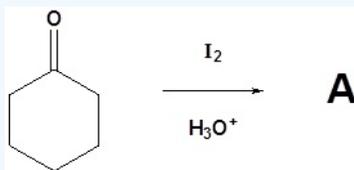


SOLUTIONS TO EXAMPLE QUESTION

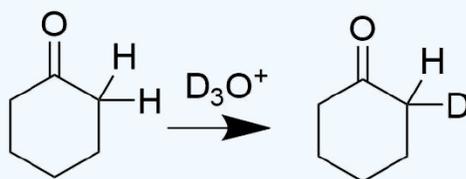


Exercises

5. Draw the products of the following reactions



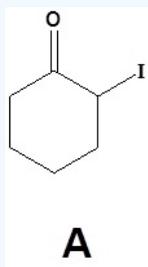
6. Draw out the mechanism for the following reaction.



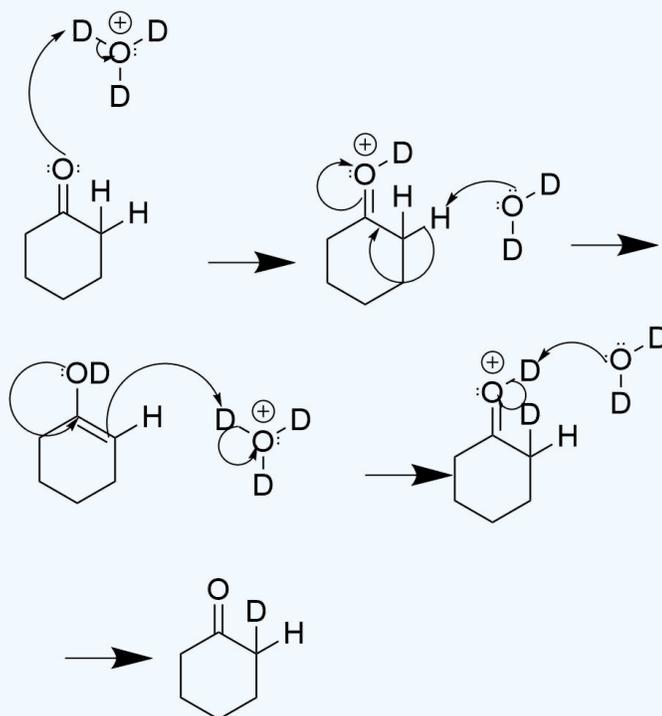
7. How might you form 2-hepten-4-one from 4-heptanone?

Answer

5.



6.



7. 1) Br_2, H_3O^+ ; 2) Pyridine, Heat

CONTRIBUTORS AND ATTRIBUTIONS

- Dr. Dietmar Kennepohl FCIC (Professor of Chemistry, Athabasca University)
- Prof. Steven Farmer (Sonoma State University)

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