

Quadrant II – Transcript and related material

Programme: Bachelor of Science

Subject: Chemistry

Paper Code: CHC 110

Paper Title: Organic Chemistry

Unit: IV

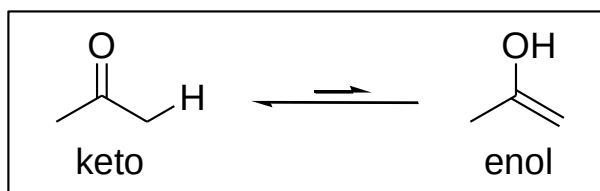
Module Name: Definition of enolate ion, acidity of carbonyl compounds, pK_a values, generation of enolate ion, role of bases in enolate formation

Module No: 14

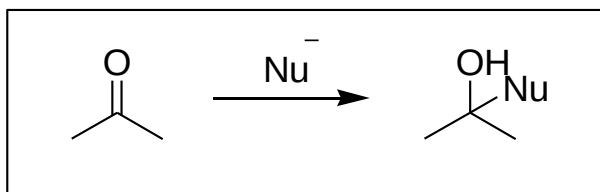
Name of the Presenter: Ms. Padmini Chandan Raiker

Notes:

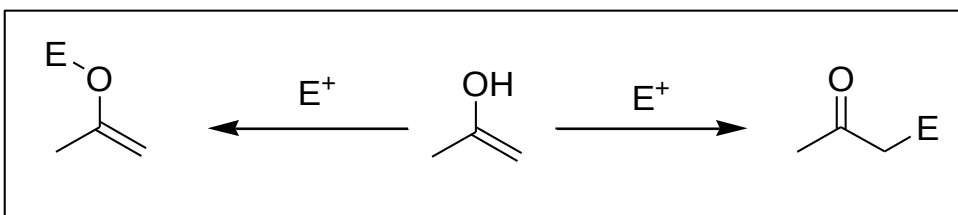
In most cases the equilibrium lies almost completely on the side of the ketone.



The ketone tautomer is electrophilic and reacts with nucleophiles:

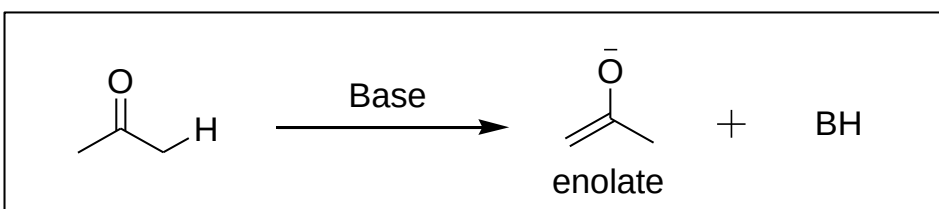


The enol tautomer is nucleophilic and reacts with electrophiles. There are two possible products - enols are ambident nucleophiles:



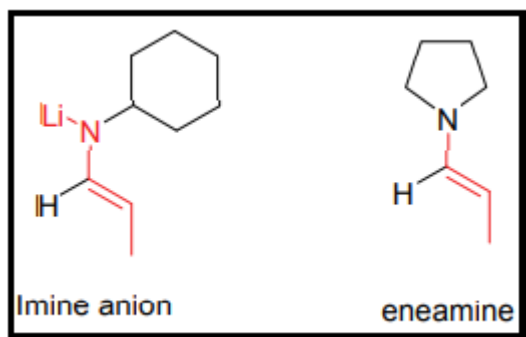
The nucleophilic enol tautomer (and especially the enolate variant) is one of the most important reactive species for C-C bond formation.

Treat a ketone with an appropriate base and can get deprotonation at the α -position to form an enolate:



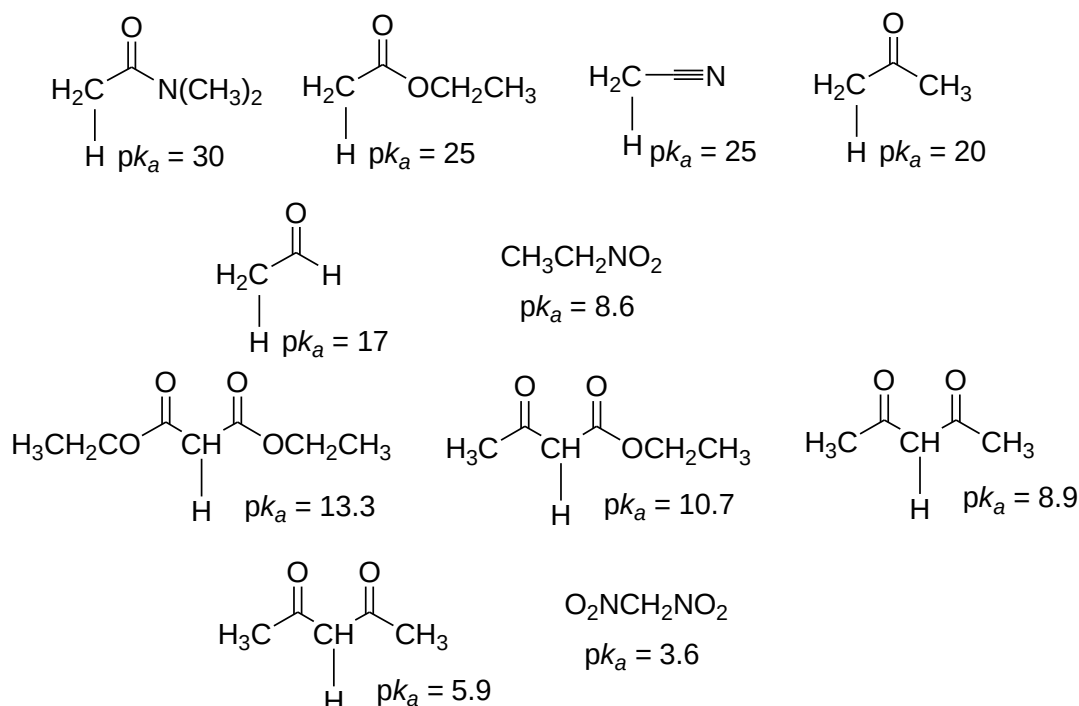
Enolates are synthetically much more useful than enols (although they react analogously).

Imine anions and enamines are synthetic equivalents of enolate anions.

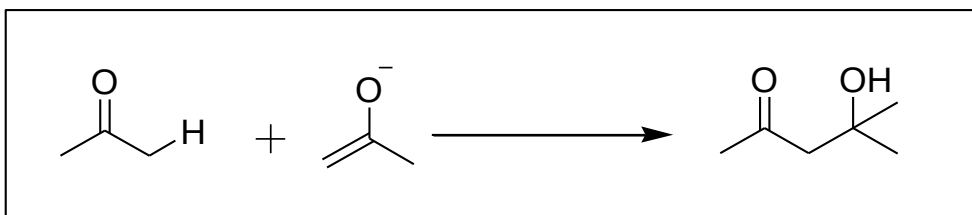


By knowing the pK_a values of the relevant acidic protons it is possible to predict suitable bases for forming the corresponding enolates.

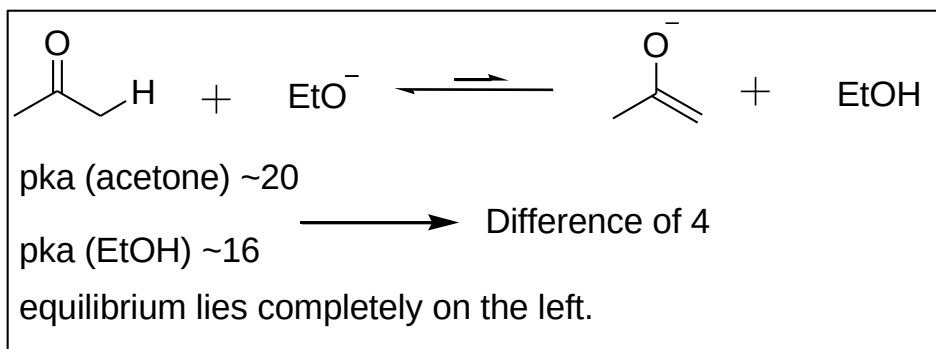
Some Important pK_a Values



Enolates are nucleophiles and ketones are electrophiles - therefore there is always the potential problem for self condensation.



If this is desirable, we need to use a base which does not completely deprotonate the carbonyl compound i.e., set up an equilibrium. This is best achieved when the pK_a of the carbonyl group and conjugate acid (of the base) are similar:



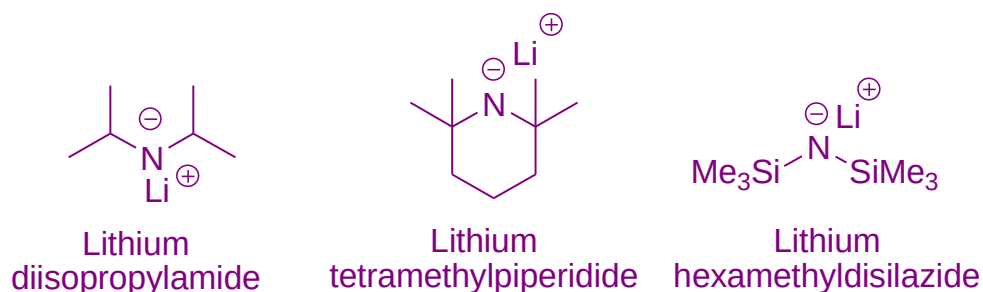
pK_a (tBuOH) ~ 18 . A stronger base. pK_a difference of 2. Ratio of ketone to enolate will be of the order 100:1 i.e. there will be about 1% enolate in solution.

The greater is the difference in pK_a 's the more heavily shifted is the equilibrium (to either left or right). When it is desirable to generate the enolate in small quantities, an alkoxide base is ideal (at least with standard ketones).

NOTE: All bases are potential nucleophiles. Alkoxide addition to the carbonyl group is reversible in the case of ketones and is therefore usually not a problem. Ideally we want to use non-nucleophilic bases to avoid potential chemoselectivity problems. Most non-nucleophilic bases have the nucleophilic centre surrounded by sterically very demanding substituents.

How can we avoid self-condensation? Use a very strong base to shift the equilibrium completely over to the right.

Important 'Strong' Bases for Forming Enolates from Ketones:



So, for LDA the pK_a difference between acetone (20) and diisopropylamine (38) is 18 (very large). Consequently, treatment of a ketone with 1 equivalent of LDA causes essentially complete deprotonation to form the corresponding lithium enolate.

Butyl Lithium (BuLi) is an excellent base and even stronger than any lithium amide, but is only very rarely used to form enolates from ketones. BuLi is a strong nucleophile with little steric hindrance.