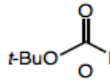
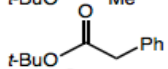
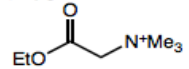
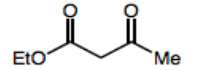
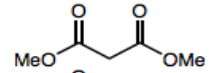
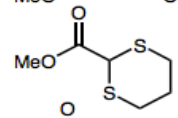
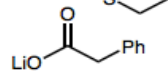
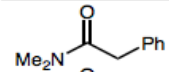
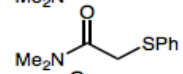
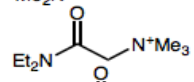
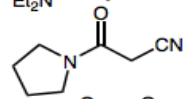
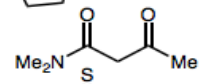
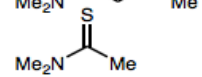
CHM 2120
Module 4, Part Ci:
α-carbon nucleophiles

Class notes

Enol and enolate videos

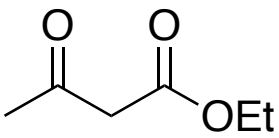
Acidity of α protons (thermodynamic)

Substrate	pKa	H_2O (DMSO)
ESTERS		
	24.5	(30.3)
		(23.6)
		(20.0)
	11	(14.2)
	13	(15.7)
		(20.9)
		[30.2 (THF)]
AMIDES		
		(26.6)
		(25.9)
		(24.9)
		(17.2)
		(18.2)
		(25.7)

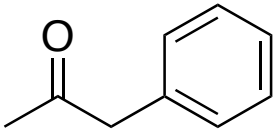
Substrate	pKa	H_2O (DMSO)
KETONES		
 X= H		(26.5)
Ph		(19.8)
SPh		(18.7)
$COCH_3$	9	(13.3)
SO_2Ph		(12.5)
	19-20	(27.1)
		(28.3)
		(27.7)
		(26.3)
X= H		(24.7)
CH_3		(24.4)
Ph		(17.7)
$COCH_3$		(14.2)
COPh		(13.3)
CN		(10.2)
F		(21.6)
OMe		(22.85)
OPh		(21.1)
SPh		(16.9)
SePh		(18.6)
NPh_2		(20.3)
N^+Me_3		(14.6)
NO_2		(7.7)
SO_2Ph		(11.4)

http://evans.harvard.edu/pdf/evans_pka_table.pdf

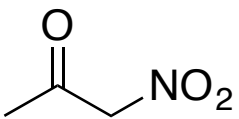
Rank in order of increasing pK_a



1

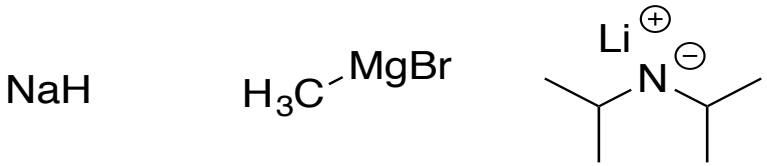


2



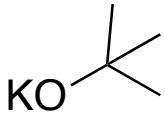
3

Choice of base to generate an enolate



A **B** **C**

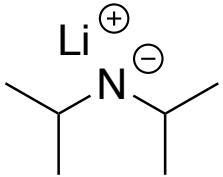
Choice of base to generate an enolate



A

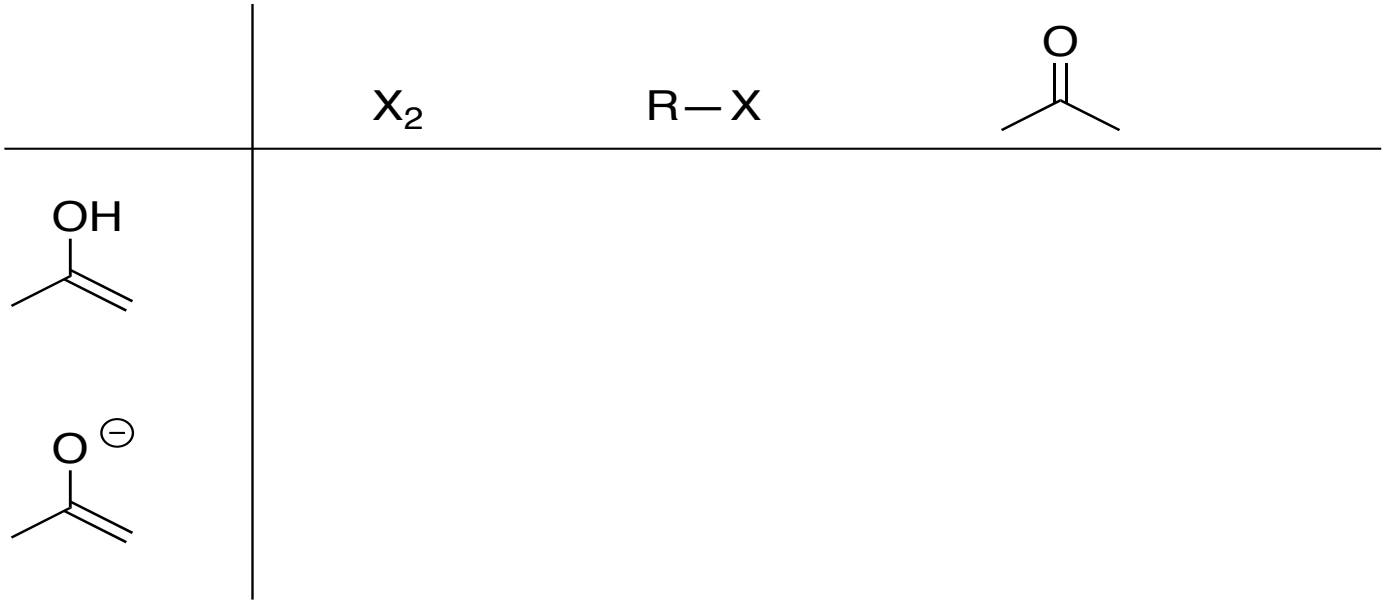
NaOH

B



C

Enols and enolates are nucleophiles



Enol Halogenation

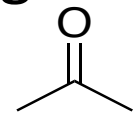
Nucleophile: enol

Electrophile: X_2

Enol Halogenation: *Monohalogenation* only—WHY?

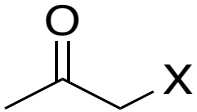
Nucleophile: enol
Electrophile: X_2

- Which oxygen is most basic?



A

starting material



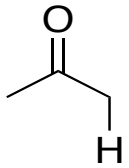
B

product

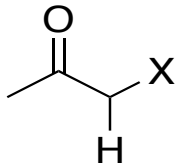
Polyhalogenation occurs under basic conditions: “Haloform reaction”

Nucleophile: enol
Electrophile: X_2

- Which proton is most acidic?



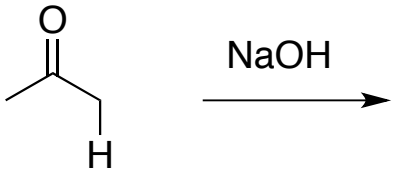
A
starting material



B
product

Polyhalogenation occurs under basic conditions: “Haloform reaction”

Nucleophile: enol
Electrophile: X_2



A

Enolate alkylation

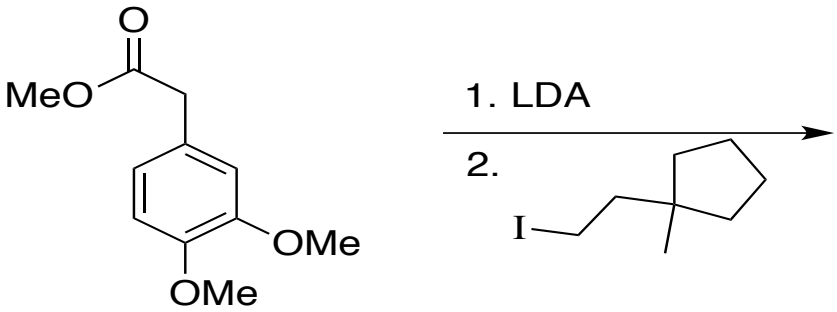
Nucleophile: enolate

Electrophile: RX

Enolate alkylation

Nucleophile: enolate

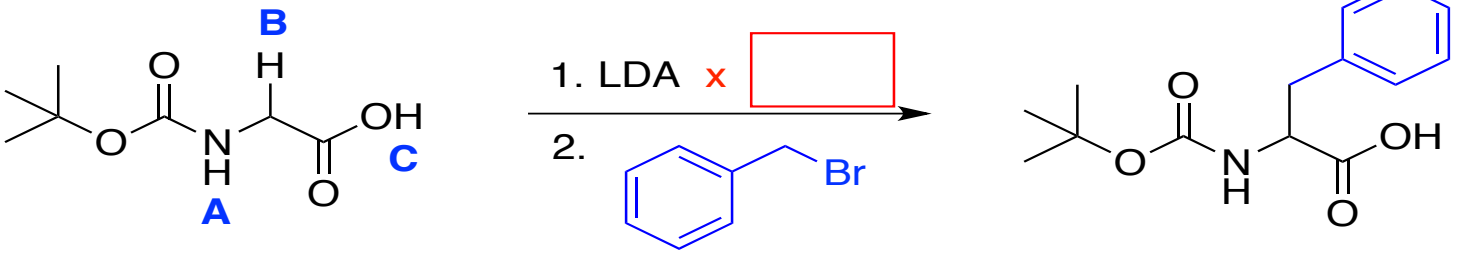
Electrophile: RX



Enolate alkylation

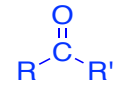
Nucleophile: enolate
Electrophile: RX

Rank the protons from most to least acidic



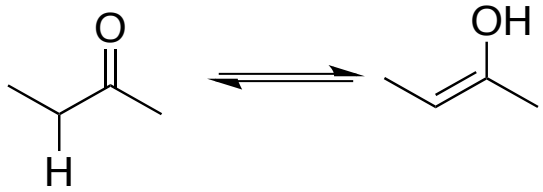
Aldol reaction

Nucleophile: enol(ate)

Electrophile: 

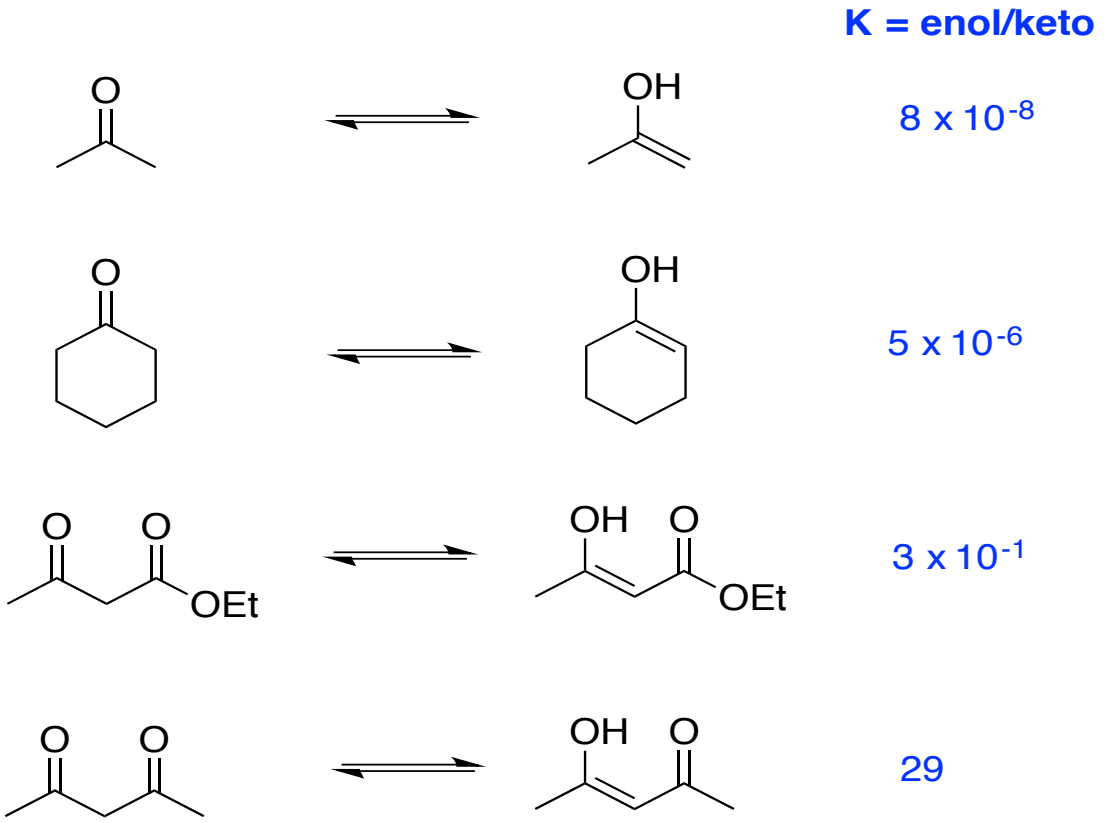
Tautomers: see videos

- Easily interconverted constitutional isomers
- Example: Keto – enol equilibrium

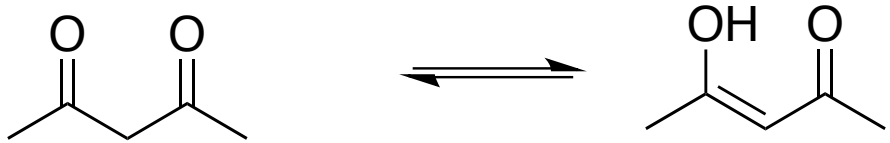


keto enol

Keto form usually more stable



Dicarbonyl compounds



Dicarbonyl compounds