CHEM 222 section 01

LECTURE #25 Tues., Nov.27, 2007

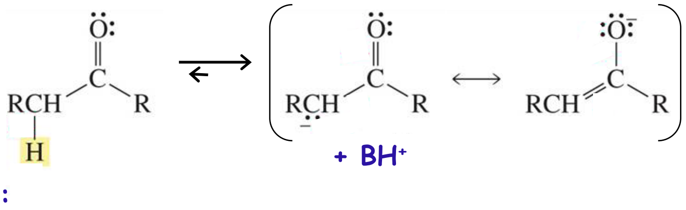
Lecture topics & readings

Today's class
- continue rxns of carbonyl compounds (Ch. 18)

Before next class
- PRACTICE Ch.17-18 problems
- PRACTICE synthesis & using protecting groups
  mechanisms for reactions of enolates

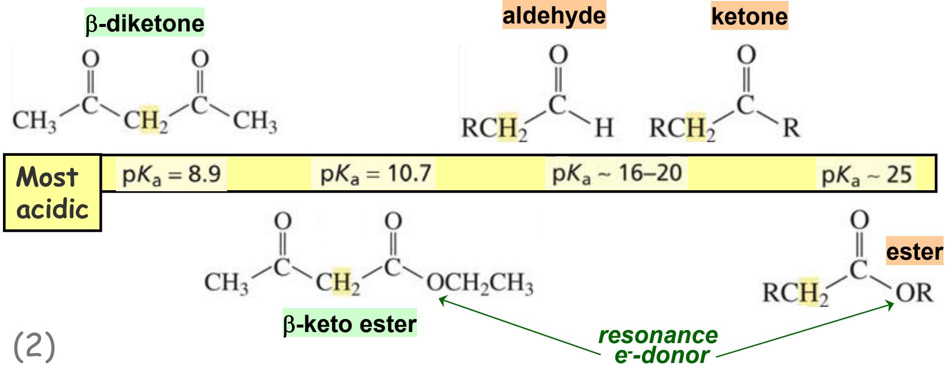
Final class
- our last topic in rxns of carbonyl compounds (Ch. 18)

(18.1) An H α to a carbonyl is relatively acidic: *resonance…*



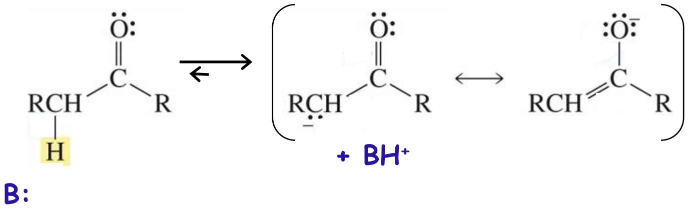
An ENOLATE
- Resonance-stabilized
- Resonance e⁻-withdrawal by carbonyl oxygen

Analyze resonance structures of enolate to learn trends in acidity:



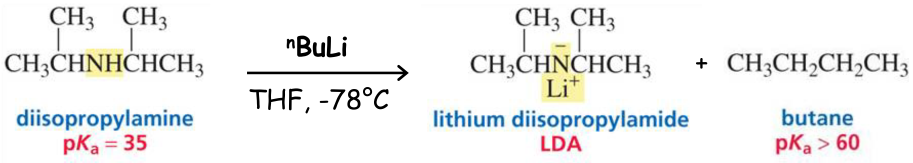
(18.3,4,8) **Deprotonated CO compounds = ENOLATES = good Nu's**

- Making an enolate for synthetic purposes: **very strong base (not OH^-)**
  get 100% yield of enolate



ENOLATE
- Resonance-stabilized
- **Acts as C-Nu**
  (rxns next)

Good strong, bulky base = LDA (lithium diisopropyl amide)



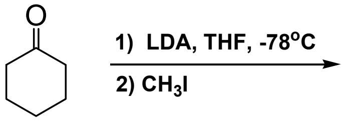
(3)

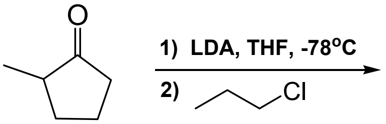
As line structure?

Typical reactions of enolates: α-substitution (enolate + E^+)

- **Alkylation** (18.9):

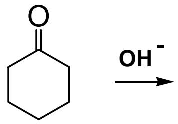
Use polarity as a guide!





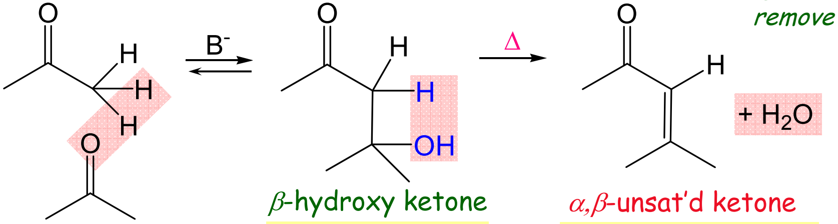
More stable enolate = thermodynamic product
Less hindered enolate = kinetic product ← **LDA used at low T!**

If don't add an electrophile, and have excess ketone…



- **Enol/enolate can attack another C=O ⇨ couples 2 molecules (18.12-13)**

Drive rxn fwd: remove product



β-hydroxy ketone

Aldol addition

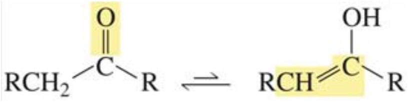
α,β-unsat'd ketone

Aldol condensation

(18.2) Ketones exist in eqm with their "enol tautomer"

- **Tautomers** = isomers in rapid equilibrium (NOT resonance forms)

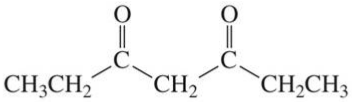
keto tautomer
- *normally much more stable*



enol tautomer
- *normally < 1% present*

Keto-enol tautomerization: H^+ transferred from α-C to C=O oxygen
via solvent in 2 steps -- O is too far from H…

- **Can drive eqm towards enol:** base catalysis (via enolate)
  OR acid catalysis

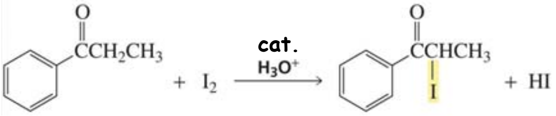


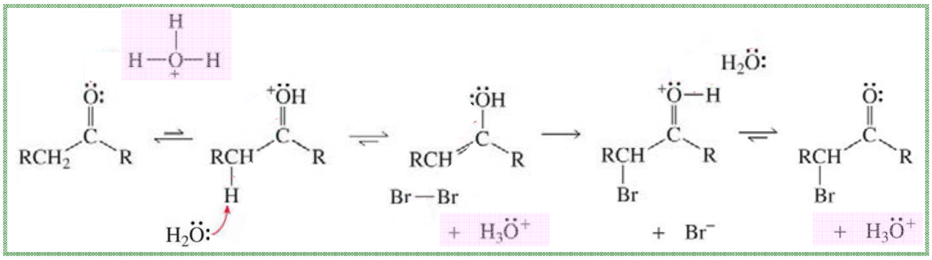
$CH_3CH_2C(=O)CH_2C(=O)CH_2CH_3$

(6) *More than 1 enol possible here. Which is more stable?*

(18.5) α-Halogenation of carbonyl cmpds: enol *OR* enolate + X_2

1. To replace ONE α-H with halide X: acid-cat. α-halogenation **(via enol)**



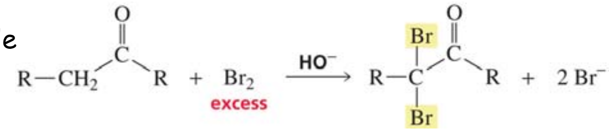


2. To replace ALL α-Hs with X: base-promoted α-halogen'n **(via enolate)**

- 1^{st} halide ↑ α-H acidicity
- enolate forms again…
- attacks 2^{nd} X_2 molecule

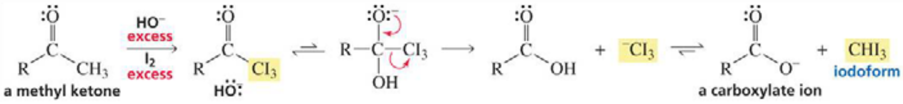
…until no α-Hs remain

Base consumed (not catalyst)…



3. To oxidize methyl ketone to carboxylate: haloform rxn *…seen in lab!*

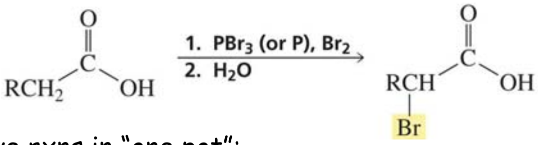
(1) basic α-halogenation ⇨ $CH_3 \rightarrow CX_3$
(2) excess OH^- attacks C=O ⇨ eliminates CX_3^-
(3) new RCOOH group deprotonated by CX_3^- ⇨ haloform + $RCOO^-$



(18.6) α-Halogenation of carboxylic acids: HVZ reaction

If used X_2 / OH^- conditions: OH^- would de-H^+ COOH group, not α-H.

Hell-Volhard-Zelinski (HVZ) reaction:

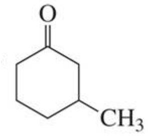


Two successive rxns in "one pot":

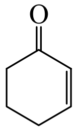
- In situ preparation of acid halide
- base-promated halogenation of acid halide's enol

Using enol / enolate chemistry in synthesis…

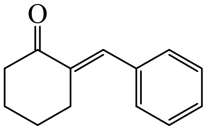
How could we make these from cyclohexanone?



PROBLEM 14



See 18.7



See 18.12-13

More examples…