

Organic Chemistry II CHM 3150, Dr. Laurie S. Starkey, Cal Poly Pomona

Chapter 21 Summary (Klein): Enols and Enolates

- I. Review of the Carbonyl C=O (21.1)
- A) carbonyl: carbonyl carbon is electrophilic (E^+), α -hydrogens are acidic
 - B) enol form is present in small amounts at equilibrium
 - i) keto-enol tautomerization mechanism (2-steps; protonation/deprotonation)
 - ii) enols make α -carbon of a carbonyl nucleophilic (Nu:)
- II. Review of Stabilized Carbanions (Nu:)
- A) organometallics (RLi, RMgX, R_2CuLi , prepared from RX; 12.6)
 - B) alkynyl (9-10), cyanide, Wittig reagent (19.10)
 - C) resonance-stabilized (21.1) **SkillBuilder 21.1**
 - i) enolate (α to a carbonyl electron-withdrawing group)
 - ii) α to nitro (NO_2) or cyano (CN) electron-withdrawing groups (EWG)
 - iii) active methylene (CH_2 α to 2 EWG's)
- III. Formation and Reactions of Enols and Enolates
- A) bases that can be used to deprotonate α hydrogens (LDA, $NaNH_2$, NaH) (21.1)
 - B) halogenation of the α carbon (base- and acid-catalyzed mechanisms) (21.2)
 - C) reactions with RX electrophiles (alkylation) (21.5)
 - D) selective alkylation of active methylenes (21.5)
- IV. Aldol Reaction & Aldol Condensation (21.3) **SkillBuilder 21.2, SkillBuilder 21.3**
- A) forms a new C–C bond between an α -C (Nu:) and a carbonyl C (E^+)
 - B) addition of heat to lose H_2O (β -elimination, $E1cB$)
 - C) acid- and base-catalyzed mechanisms
 - D) mixed/crossed aldol reactions **SkillBuilder 21.4**
 - E) *Aldol skills/LOs: predict the product, draw mechanism (acid or base), retrosynthetic analysis of aldol product (β -hydroxy carbonyl or α,β -unsaturated carbonyl)*
- V. Claisen Condensation (aldol reaction with esters) (21.4)
- A) forms β -keto esters with active methylene groups (the reaction's driving force)
 - B) *Claisen skills/LOs: predict the product, draw mechanism, explain choice of base & need for acidic workup, retrosynthetic analysis of Claisen product (β -ketoester)*
- VI. Enones: α,β -unsaturated carbonyls (21.6)
- A) definition of conjugated π bonds
 - B) resonance stabilized with a δ^+ on carbonyl carbon and β carbon (both are E^+)
 - C) 1,4-(conjugate) addition of Nu: (attack β carbon)
 - i) mechanism is via enolate intermediate
 - ii) possible for electrophilic alkenes ($CH_2=CH-EWG$)
 - D) 1,4-(conjugate) addition of enolates
 - i) Michael reaction (enolate Nu: and enone E^+)
 - ii) enolate and enone equivalents (carbonyl-like EWG's: $-NO_2$ and $-CN$)
 - iii) Robinson annulation
 - a) ketone + MVK gives cyclohexenones
 - b) mechanism: Michael addition followed by aldol condensation
 - E) *FYI: Enamines (synthetic equivalent of enolates) SkillBuilder 21.7*
 - i) *ketone + 2° amine \rightarrow enamine*
 - ii) *enamine + enone, then H_3O^+ \rightarrow Michael reaction*
 - iii) *enamine + RX, then H_3O^+ \rightarrow α -alkylated ketone*
- VII. Synthesis - disconnection approach to retrosynthetic analysis (21.7) **SkillBuilder 21.8**
- A) Synthesis with active methylenes (21.5) **SkillBuilder 21.5, SkillBuilder 21.6**
 - i) decarboxylation ($-CO_2$) of β -carbonyl acids
 - ii) use of malonic ester and acetoacetate ester as synthetic equivalents
 - B) Alkylation of α and β positions **SkillBuilder 21.9**

SKIP: Haloform reaction and HVZ reaction (section 21.2)
SKIP: Stork Enamine Synthesis (SkillBuilder 21.7)