

Conjugate Addition

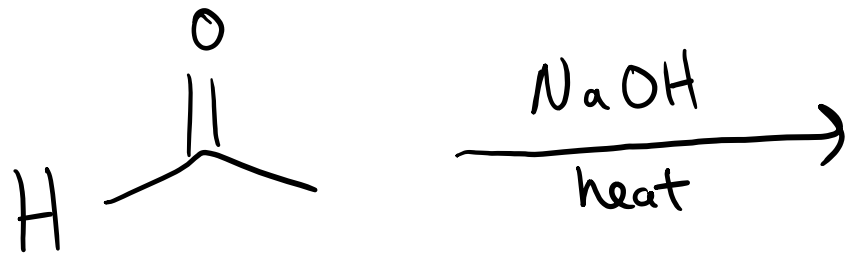
Exam 2 Review

3/29/2023

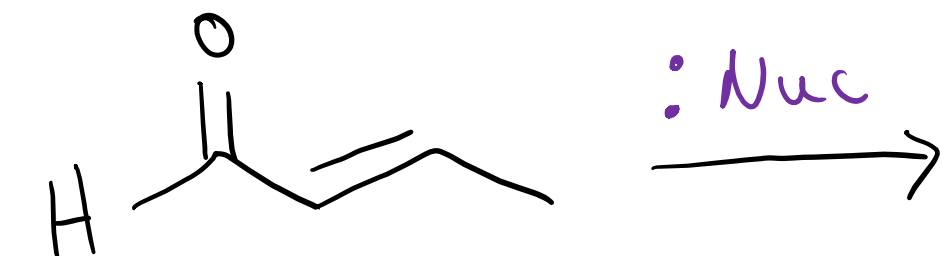
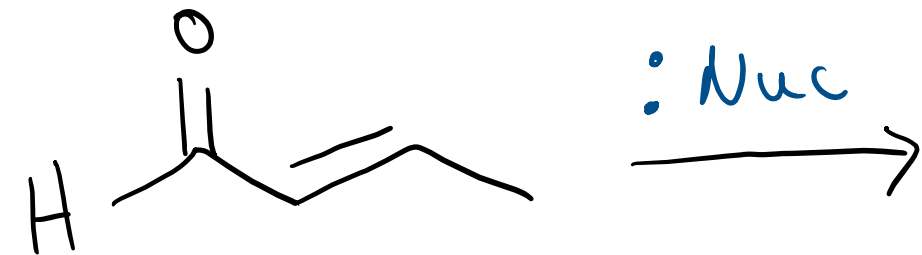
Conjugate Addition

(21.6)

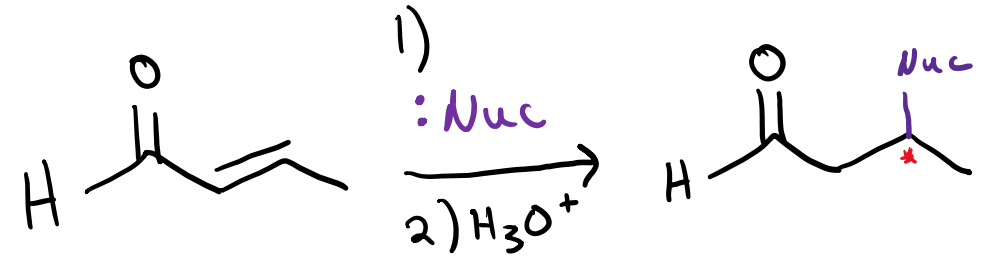
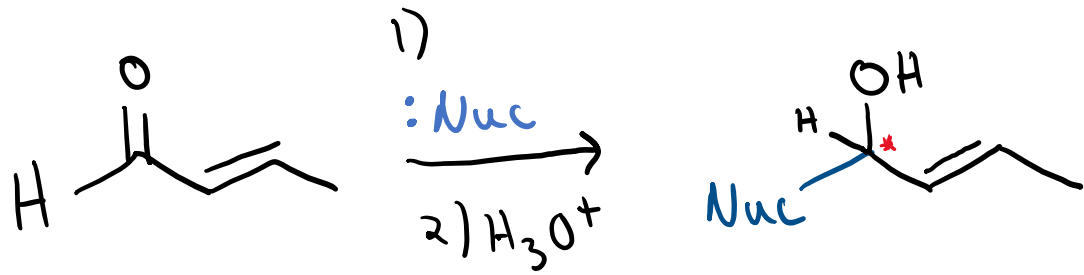
Remember Aldol condensation:



1,2- vs 1,4-addition



1,2- vs 1,4-addition: Strength of Nucleophiles and Regioselectivity



Ch 19: Wittig Reaction

- Overall reaction/recipe
- Stereochemistry (E vs Z) and dependence on ylide structure
- Reduction (Hydride transfer) & reaction of Grignard reagents with aldehydes and ketones may be relevant!

Ch 20: Carboxylic Acid Derivatives

- Synthesis of carboxylic acids (including oxidation of alcohols, hydrolysis of nitriles, & haloform reaction)
- Acyl transfer reaction mechanisms (general)
 - Neutral nucleophile + weak acid
 - Neutral nucleophile + weak base
 - Anionic nucleophile
 - I will *not* ask about any of the “weird” mechanisms with carboxylic acids – ($\text{BH}_3\text{-THF}$, LiAlH_4 , and SOCl_2)
- Synthesis of Esters (via $\text{S}_\text{N}2$, Fischer Esterification, alcoholysis)
- Synthesis of Acid Chlorides
- Synthesis of Anhydrides
- Reactions of Acid Chlorides/Acid Chlorides (react in the same way)
 - Hydrolysis, alcoholysis, aminolysis

Ch 20: Carboxylic Acid Derivatives

- Hydrolysis of Esters (acidic and basic conditions)
- LeChatelier's principle
- Synthesis (ammonolysis of Acid Chloride/Anhydride) and hydrolysis of Amides
- Weinreb Amides – reactions with hydride and carbon nucleophiles and difference vs regular Amide
- Hydride transfer reagents with: Aldehyde/ketone, Amide, Weinreb Amide, Acid chloride/Anhydride, Ester, and Carboxylic Acid
 - Know which F.G.'s use which reducing reagents
 - Know the difference in outcomes for each F.G.! They don't all have C=O become C-OH....
 - Final slide of 3/1 handout (Friday before spring break)
- Grignard and Gilman reagents with all of the above F.G.'s
 - Except Carboxylic Acids (why not?) and **regular** Amides
 - Know the difference in outcomes! The F.G.'s don't all react the same way!
- I will not count off for leaving out the quenching step " 2)H₃O⁺ " *only if* it doesn't actually show up in the mechanism (i.e. with a Gilman reagent)

Ch 21: Alpha-carbon reactions (*all* mechanisms are fair game)

- Using pKa table to compare acidity of various functional groups
- Using pKa table to predict K_{eq} of an acid-base reaction
- Comparing acidity: qualitatively
- Keto-enol tautomerism (acidic and basic conditions)
- Alpha-halogenation (acidic and basic conditions)
 - Regioselectivity under acidic conditions
 - E2 reaction of mono-halogenated product from acidic conditions
 - Difference in outcomes acidic vs basic mechanism (and why)
 - Haloform reaction & mechanism
- Acidity of alpha-carbons (and “double-alpha” protons between two C=O groups)

Ch 21: Alpha-carbon reactions (*all* mechanisms are fair game)

- (“self”)-Aldol and retro-Aldol reactions
 - Choice of base and why
- Cross-Aldol reactions and mechanism
 - Backtracking steps from product (who was enolate, who was electrophile etc)
 - Choice of base and why
- Aldol condensation reaction and stereochem
- Intramolecular Aldol
 - Ring strain! 5- or 6- member rings are the least strained
- Claisen Condensation – all the same things as Aldol
 - Reaction, mechanism, backtracking from product
 - Choice of base and why
 - Crossed-Claisen and Intramolecular Claisen
- Alpha-alkylation
 - Choice of base – regioselectivity and why
 - Malonic Ester Synthesis and why we care about it (alpha-alkylated carboxylic acid)
 - Acetoacetic ester synthesis and why we care about it (alpha-alkylated acetone but with 2° R-X)

Exam Format

- A *bunch* of fill-in-the-blank reaction schemes
- 1-2 Flawed Synthesis
- 2-3 Mechanisms* (see previous slides)
- Guided and less-guided synthesis
 - No fully “open ended” synthesis – closest I would give to that is like the practice exam question
- Random assorted conceptual things
- Approx 5-6 pages, designed to be completed in about 1 hr 20 minutes total.