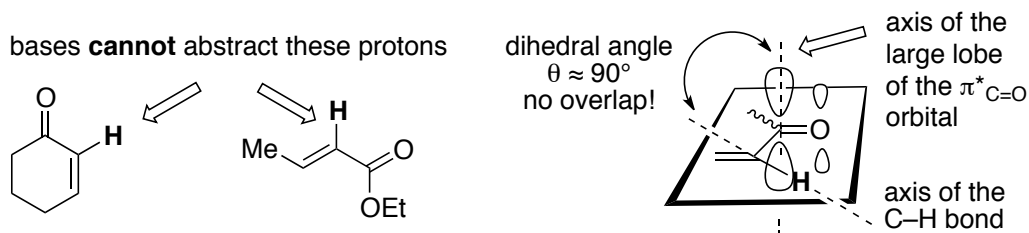


# CHEM 330

## Topics Discussed on Oct 16

### Deprotonation of $\alpha,\beta$ -unsaturated (= conjugated) carbonyl compounds

**Important:** bases cannot abstract protons connected to the olefinic  $\alpha$ -position of a conjugated carbonyl compound, because resonance interactions force the C=O and C=C  $\pi$ -systems to be coplanar. As a result, the dihedral angle  $\theta$  between the axis of the olefinic  $\alpha$ -C-H s bond and the axis of the lobes of the  $\pi^*_{C=O}$  orbital is ca.  $90^\circ$ . There is no overlap between  $\sigma_{C-H}$  and  $\pi^*_{C=O}$  orbitals  $\rightarrow$  no deprotonation is possible



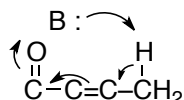
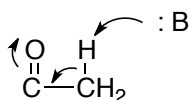
### Definition of $\alpha$ , $\beta$ , $\gamma$ , ... carbons of an $\alpha,\beta$ -unsaturated carbonyl compound



Principle of vinylogy (= "vinyl analogy"): the interposition of a C=C unit between the components of a functional group generates a new chemical entity, which retains the chemical characteristics of the original

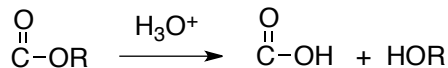
#### Examples:

an enolizable carbonyl compound: deprotonation is possible because of resonance delocalization of (-) charge on the electronegative O atom

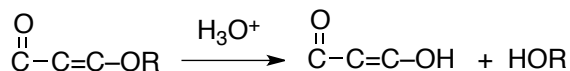


a vinylog of the original: resonance delocalization of (-) charge on the O atom still possible through the C=C bond: can undergo deprotonation

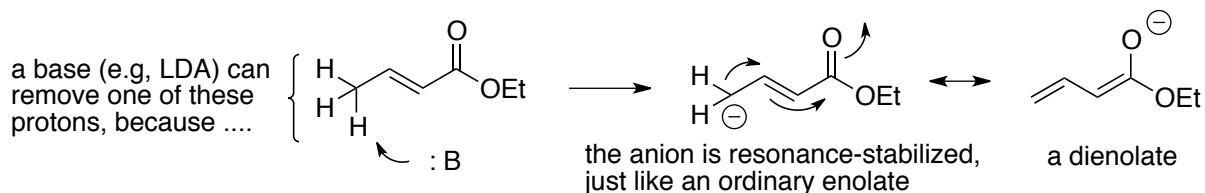
an ester: it undergoes hydrolysis to an acid and an alcohol when treated with, e.g. aqueous HCl



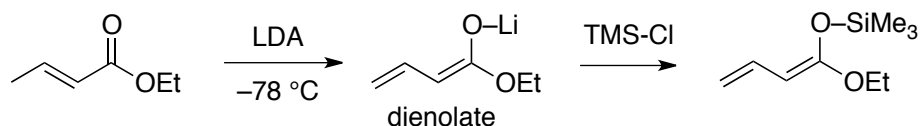
a vinylogous ester: reacts with aq. HCl like the original



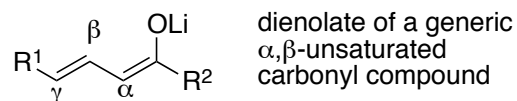
### Deprotonation of $\alpha,\beta$ -unsaturated esters: conversion of, e.g., ethyl crotonate into a dienolate



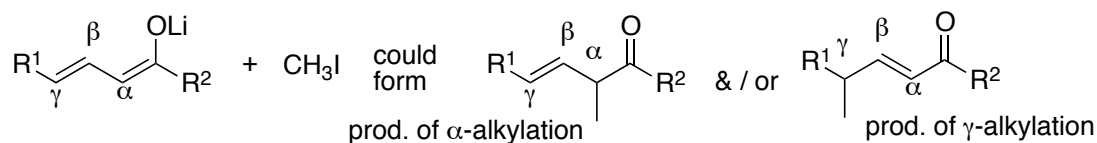
Normal O-reactivity of dienolates of conjugated esters with, e.g., TMS-Cl:



Definition of  $\alpha$ ,  $\beta$ ,  $\gamma$ , etc., positions of a dienolate:

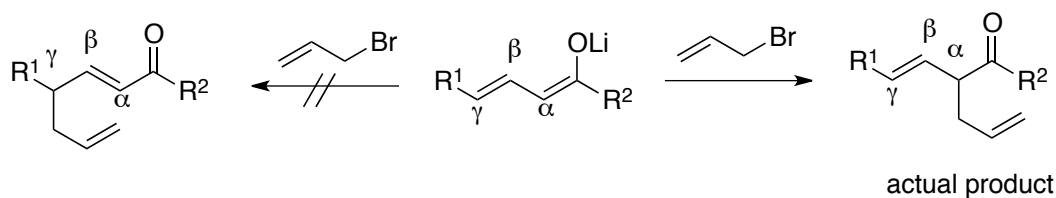


Potential C-reactivity of a dienolate at the  $\alpha$ -carbon or at the  $\gamma$ -carbon, e.g.:

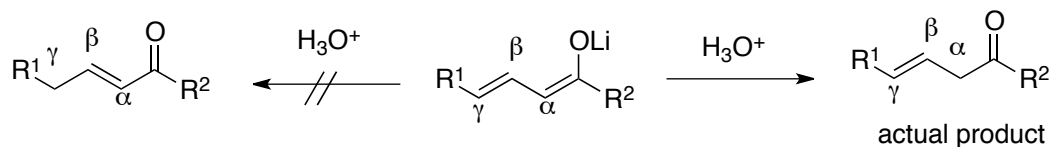


Principle: the nucleophilic C-reactivity of dienolates is expressed selectively at the  $\alpha$ -carbon. This is true both for alkylation and for protonation. E.g.:

- $\alpha$ -alkylation of dienolates:



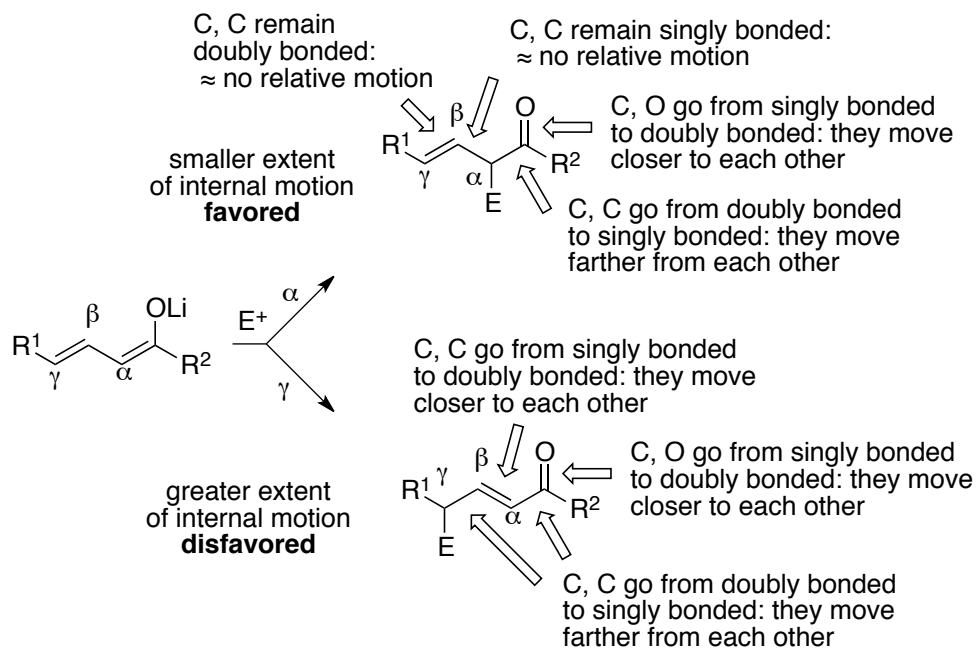
- $\alpha$ -protonation of dienolates: formation of deconjugated carbonyl compounds:



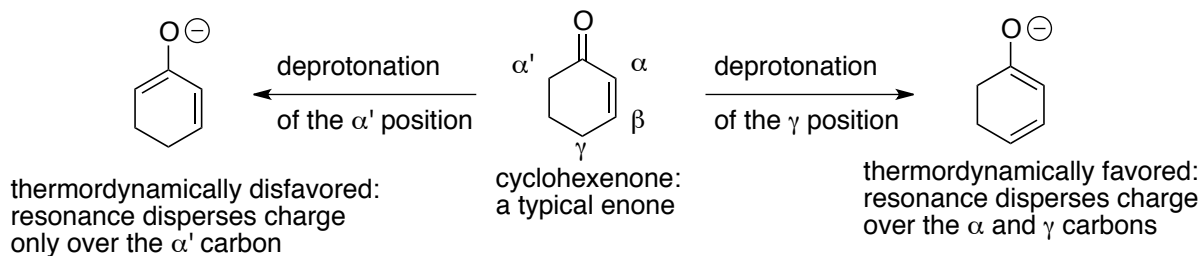
Molecular orbital based rationale for selective  $\alpha$ -carbon reactivity of dienolates: greater electronic density at the  $\alpha$ -carbon relative to the  $\gamma$ -carbon, and consequent greater  $\alpha$ -nucleophilicity relative to  $\gamma$ -nucleophilicity

**Principle of least motion:** a reaction that could theoretically lead to multiple products tends to form preferentially the product that requires the least amount of internal motion due to the repositioning / displacement of atoms during rehybridization.

Invoking the principle of least motion to rationalize the selective  $\alpha$ -carbon reactivity of dienolates:

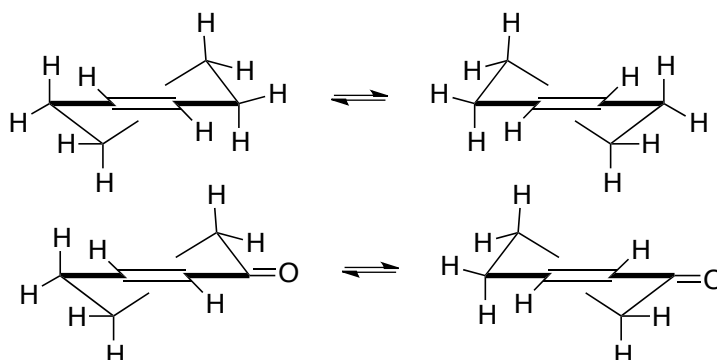


Deprotonation of  $\alpha,\beta$ -unsaturated ketones (= enones), e.g., cyclohexenone: potential formation of two regioisomeric dienolates:

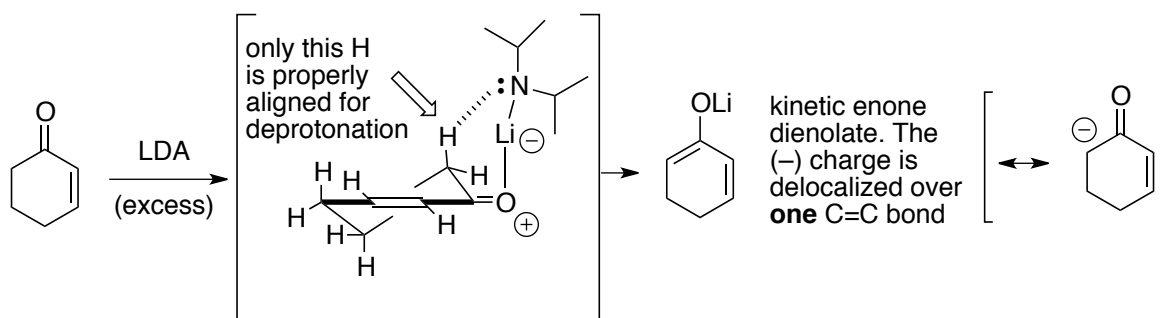


Deprotonation of, e.g., cyclohexenone under kinetic (non-equilibrating) conditions (slight excess of LDA, THF,  $-78^\circ\text{C}$ ): deprotonation occurs selectively at the  $\alpha'$  position:

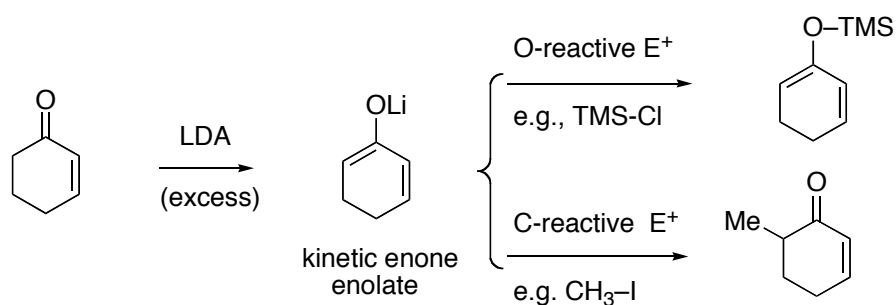
- proper representation of the half-chair conformation of cyclohexene and of cyclohexenone:



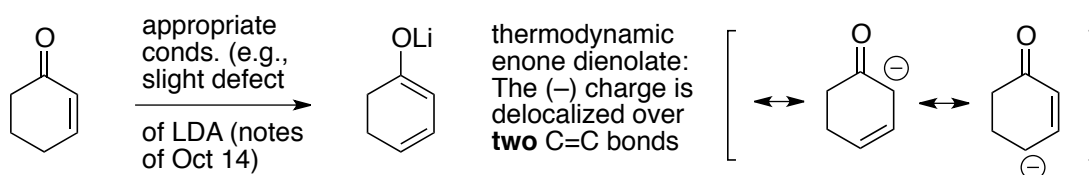
- formation and fate of the enone-LDA complex:



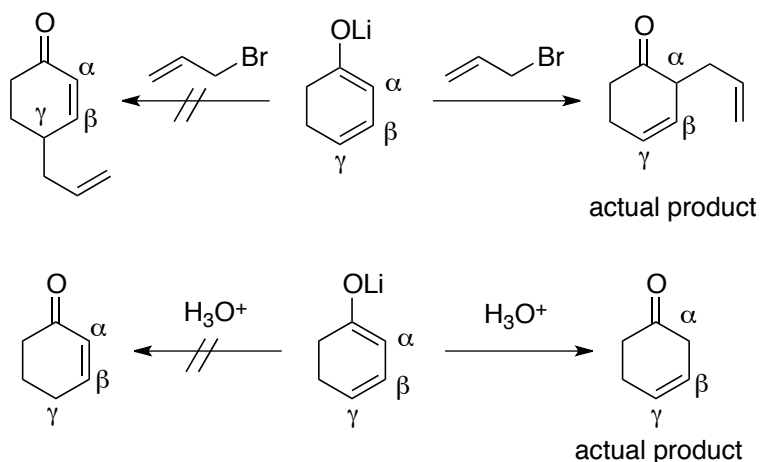
Normal O- and C-reactivity of kinetic dienolates of enones



Deprotonation of enones under thermodynamic (equilibrating) conditions: deprotonation occurs selectively at the  $\gamma$  position:



Selective  $\alpha$ -alkylation and protonation of thermodynamic enone dienolates:



Soft enolization of enones such as cyclohexenone leading directly to regiochemically defined silyl enol ethers

