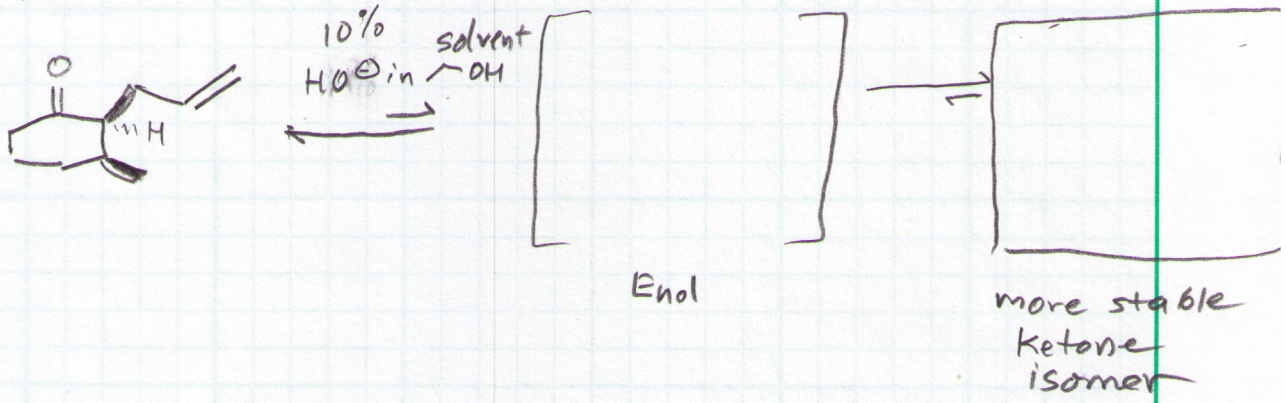
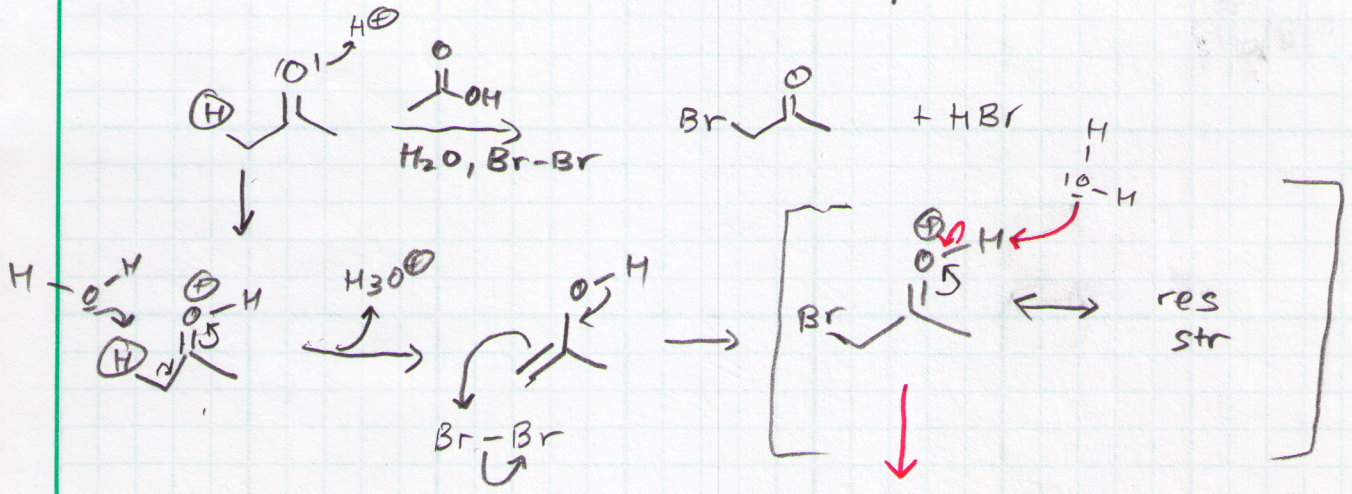
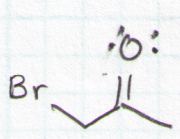
Because of enolizat^{n}, what do you imagine will happen here?



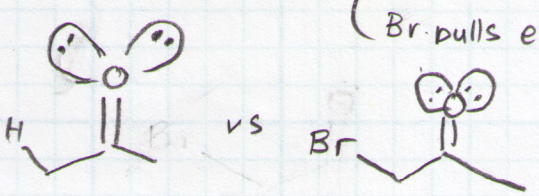
Halogenation of aldeHydes and Ke`y'tones via ENOLS





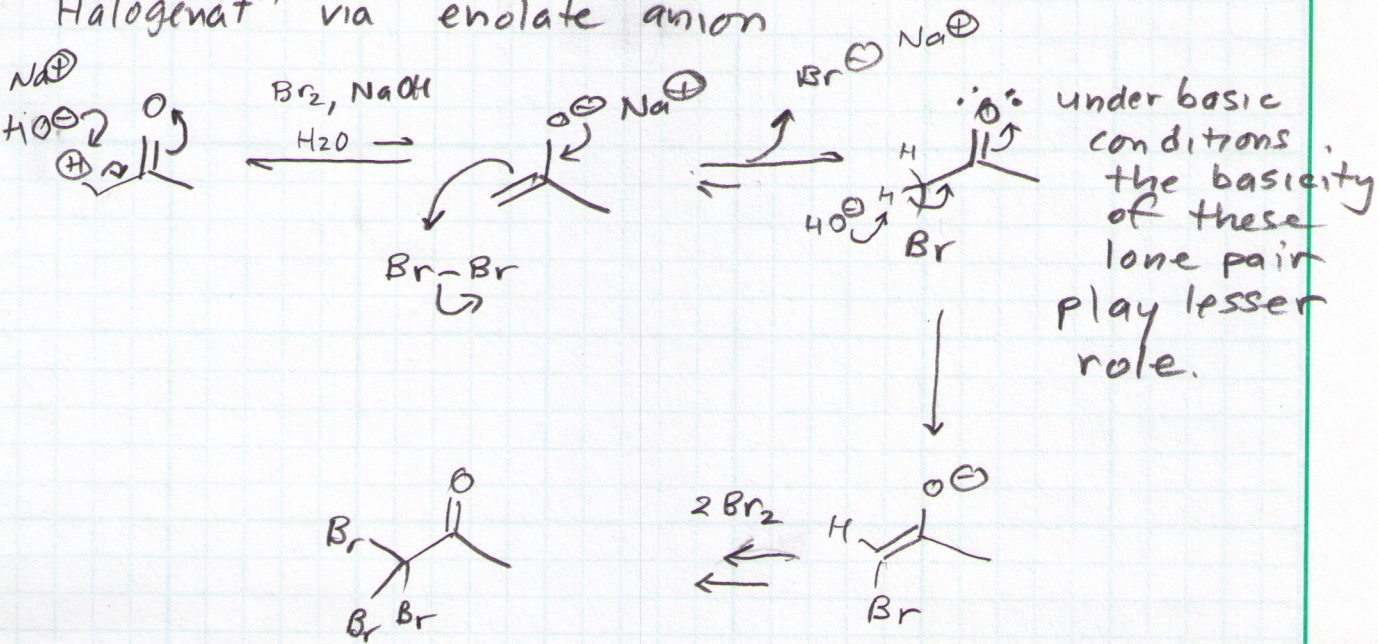
mono bromo under acidic conditions. Br e⁻(–) makes C=O lone pair e⁻ less basic

(Br pulls e⁻ closer to O)

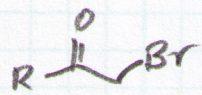


making 1st protonat^{n} step harder

Halogenat^{n} via enolate anion



under basic conditions, the basicity of these lone pair play lesser role.

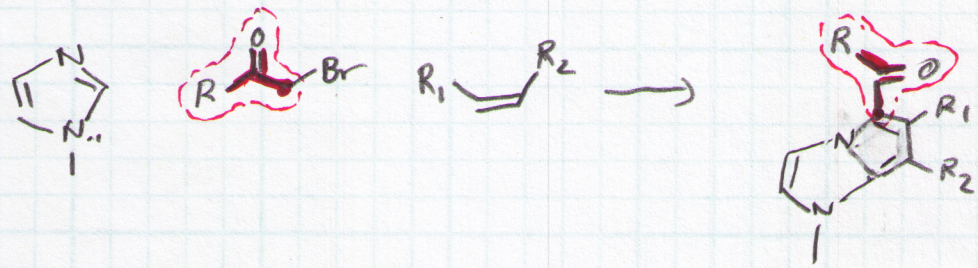
Application of  in a rxn

NOT Exam material but shown as an example

2004

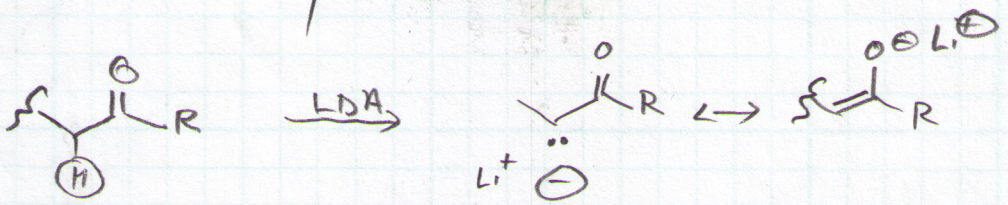
Strategies and Tactics in Organic Synthesis

- Total Synthesis of Cylindrospermopsin

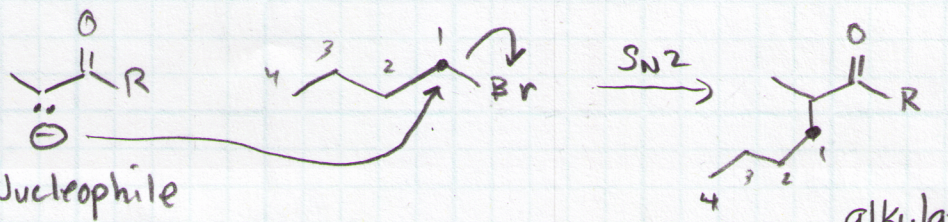


Alkylation at α-C of aldehydes / ketones

We know the C_α-H is rel. acidic and can be removed with a sufficiently strong base

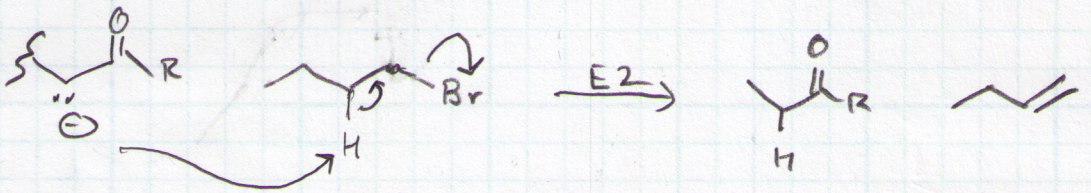


Let's look at what we want to do

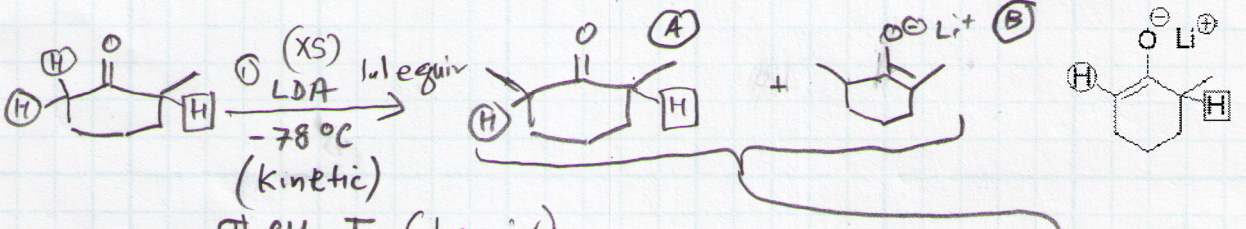


alkylation is desired

NOTE: SN2 nucleophiles (neg charge) can also be good bases.



MORE COMPLICATIONS INVOLVED W/ ALKYLATING C=O COMPOUNDS



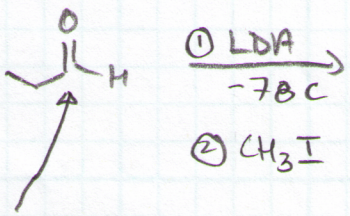
[All in a single rxn vessel]

A mixture of these three ~~two~~ are in the rxn when, e.g. 10% CH_3I is added.

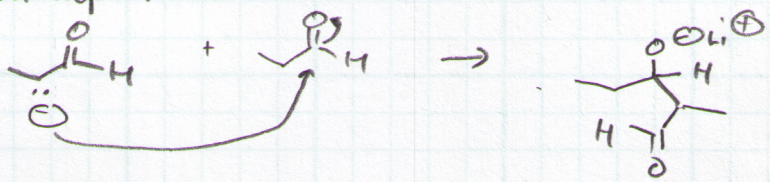
Enolate (B) acts as a base and removes (H) or [H] from (A), so the next CH_3I added can alkylate the enolate of (A)

ALKYLATING ALDEHYDES UNDER LDA CONDITIONS ARE DIFFICULT

Aldehydes react w/ themselves

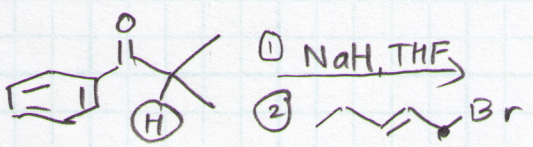


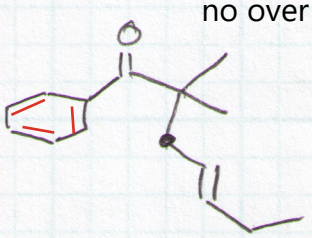
reactive center for nucleophiles such as



RARE ALKYLATION OF A KETONE

Only 1 acidic α-proton; therefore no over alkylation

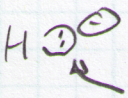




$H_2(g)$

NaBr
salt ppt from solution

$H:^{\ominus}$ is basic but not nucleophic



1s orbital is tiny, whereas nucleophilic e⁻ prefer to be in larger s-orbitals, p-orbitals, sp^3- or d-orbital hybrids

Also, H–H gas is very stable product

Why is hydride of borohydride nucleophilic, but hydride of sodium hydride basic?