CHEM – 750

Advanced Organic synthesis

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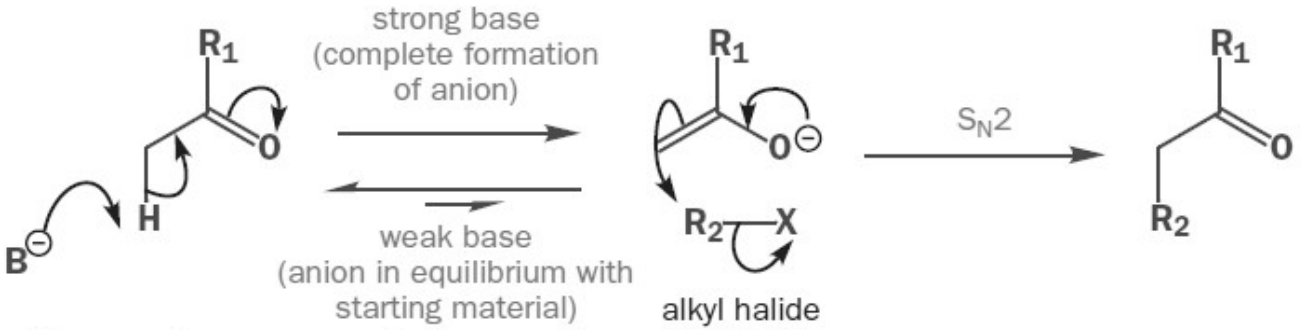
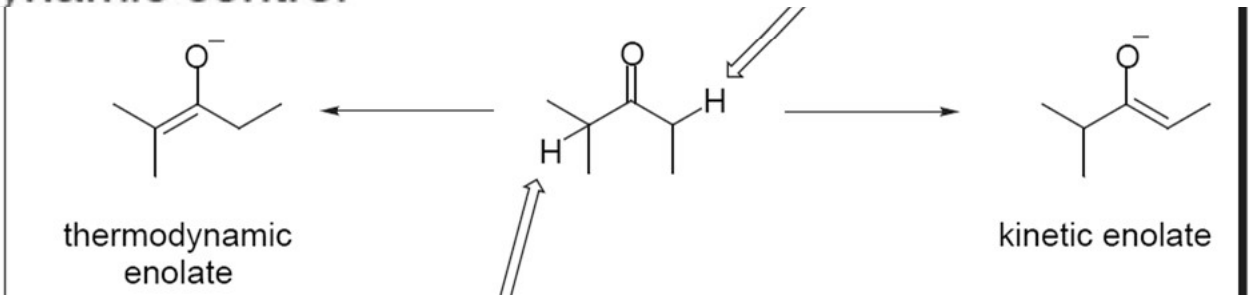
C-C BOND FORMATION

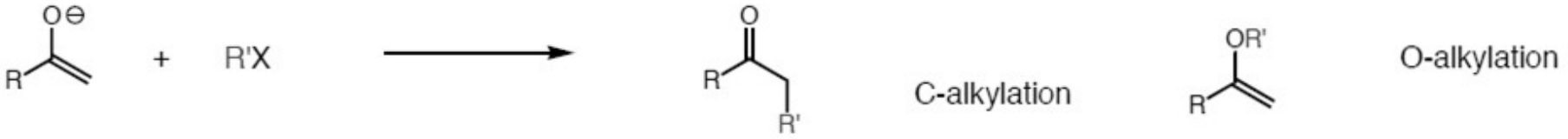
C-alkylation



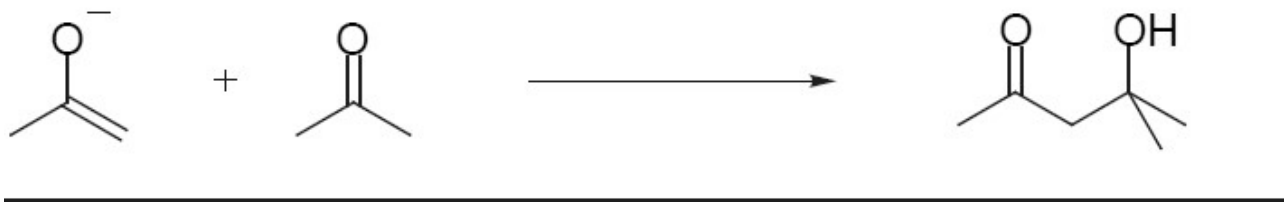
- Kinetic vs. thermodynamic control



Enolates: Ambident Nucleophiles



self condensation: A Potential Problem



10000 1

pK_a(acetone) ~20

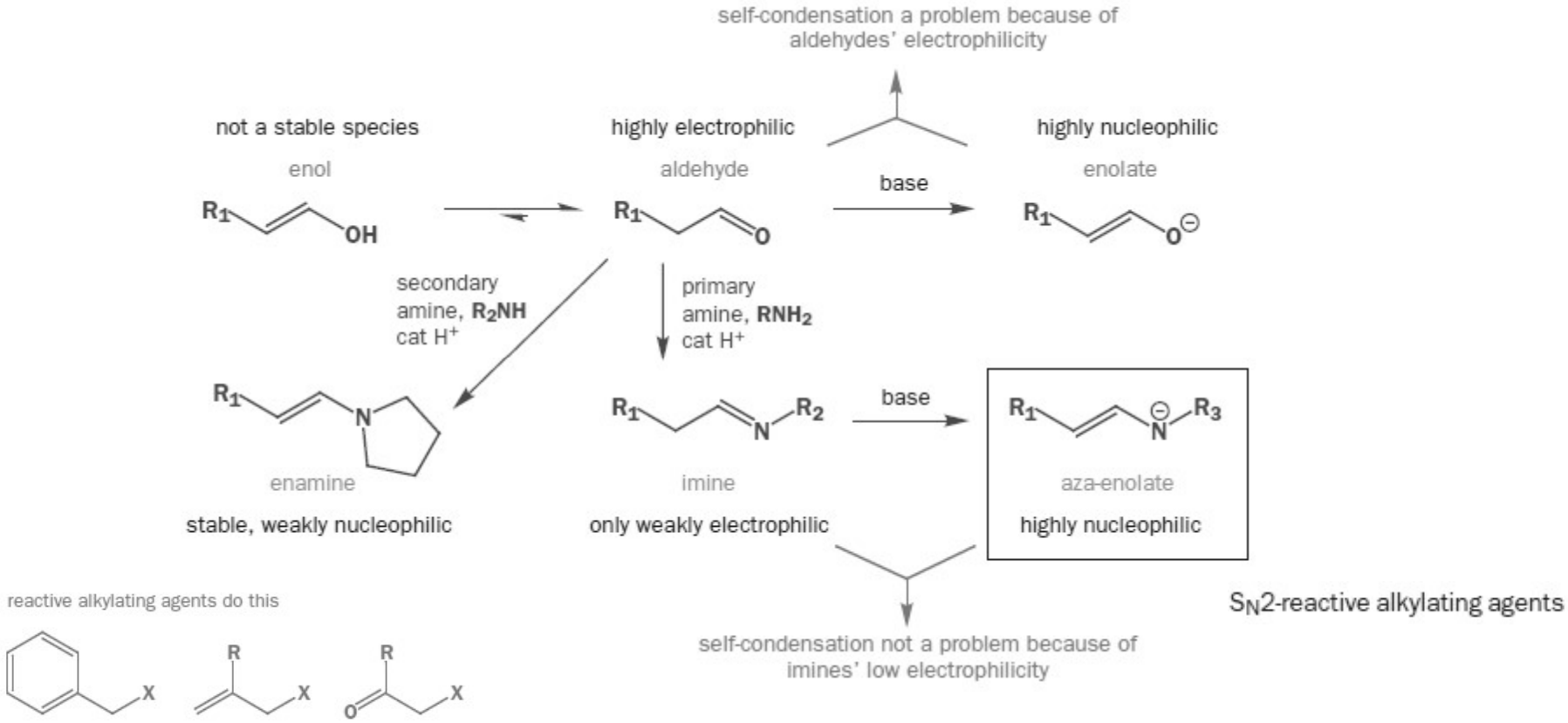
pK_a(EtOH) ~16 ⟹ pK_a difference of 4

Solution

Use a very strong base to shift the ketone-enolate equilibrium completely over to the right *i.e.* completely consume the ketone electrophile before it can react with the enolate nucleophile.

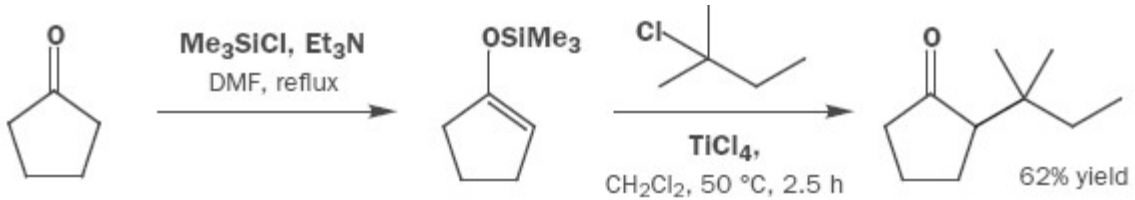
specific enol equivalents

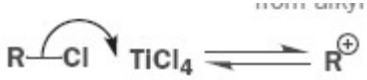
Enamines
Aza-enolates



Kinetically controlled product

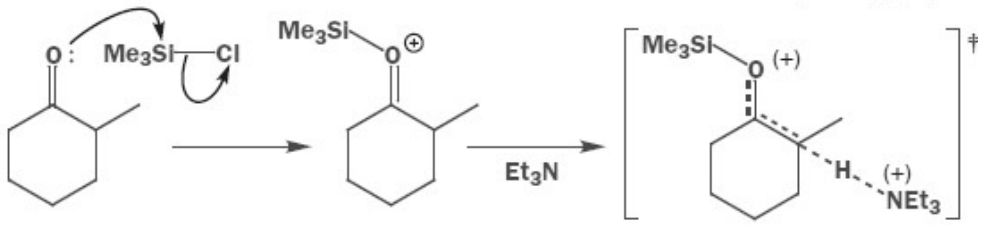
specific enol equivalents Silyl enol ethers

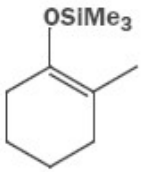




The best alkylating agents for silyl enol ethers are tertiary alkyl halides: they form stable carboca- tions in the presence of Lewis acids

greater stabilization of cationic transition state by methyl group





thermodynamic regioselectivity

more substituted silyl enol ether

specific enol equivalents

SUMMARY

self condensation