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

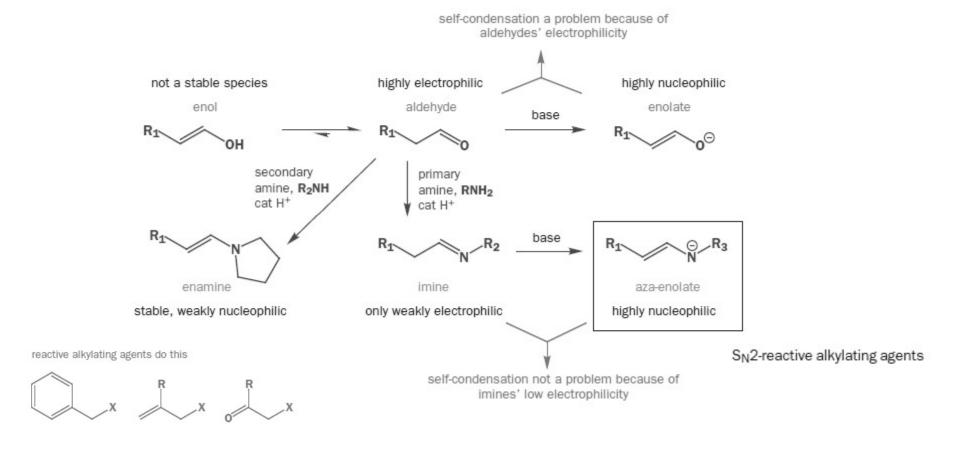
Solution

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 Silylenol ethers

The best alkylating agents for silyl enol ethers are tertiary alkyl halides: they form stable carbocations in the presence of Lewis acids greater stabilization of cationic transition state by methyl group



specific enol equivalents

SUMMARY

self condensation

self-condensation a problem because of aldehydes' electrophilicity not a stable species highly electrophilic highly nucleophilic enol aldehyde enolate base Enamines secondary primary amine, R2NH amine, RNH₂ cat H+ cat H+ Aza-enolates base Silyl enol ethers enamine imine aza-enolate stable, weakly nucleophilic only weakly electrophilic highly nucleophilic OSIMe₃ Me₃SICI, Et₃N DMF, reflux self-condensation not a problem because of imines' low electrophilicity 62% yield CH2Cl2, 50 °C, 2.5 h