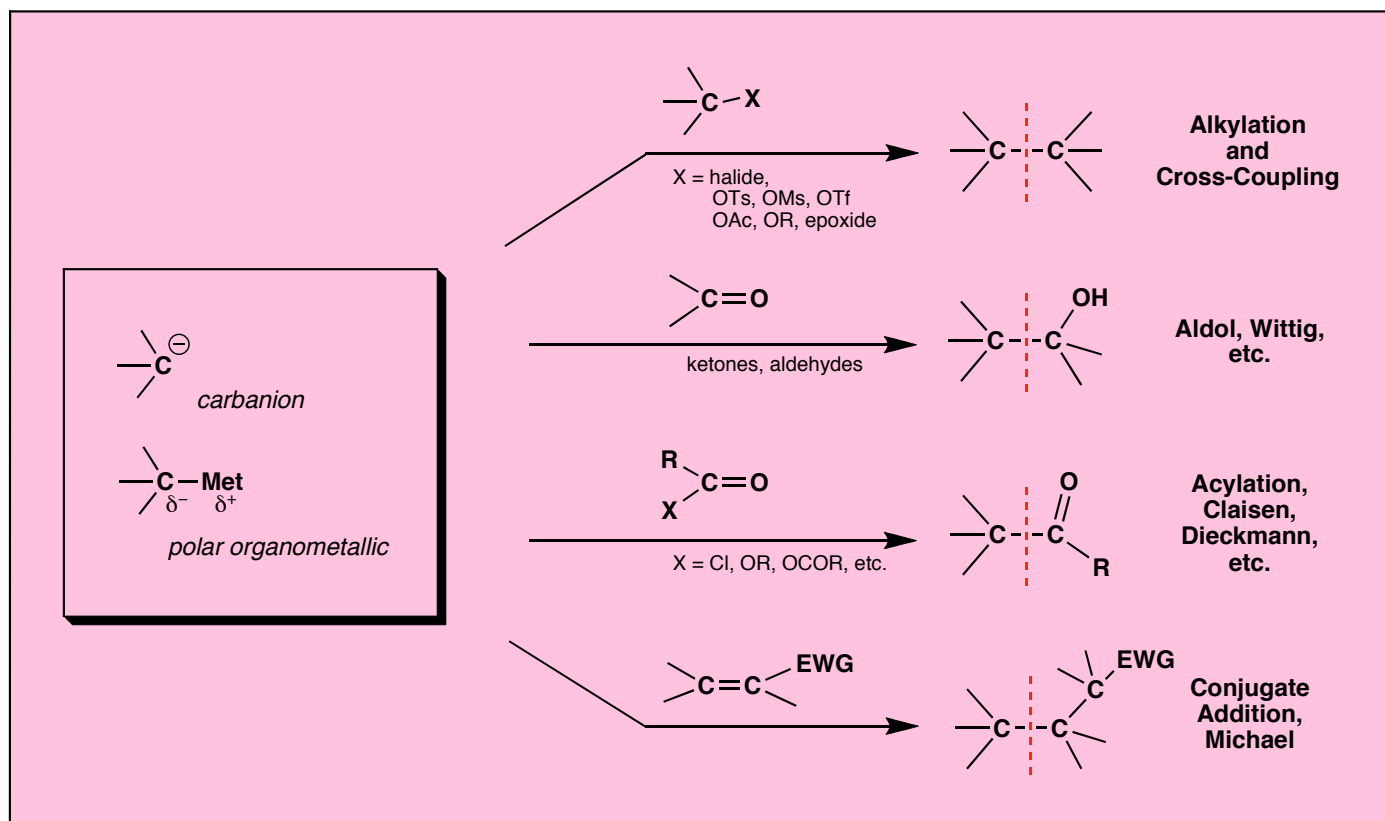


Massachusetts Institute of Technology
Organic Chemistry 5.511

October 17, 2007
Prof. Rick L. Danheiser

Lecture 5
Unit 2: Carbanionic Synthons



Reading Assignment

Background: Clayden et al. Sections of Chapters 9, 21, and 26

Carey and Sundberg Part B, Chapters 1, 7 (Sections 7.1, 7.2, and 7.3.1), and 8 (Section 8.1)

Note: some stereochemical features of this chemistry will not be covered until later units

Unit 2 Outline

Introduction to General Reactivity and Overview of General Methods for the Generation of Carbanionic Synthons

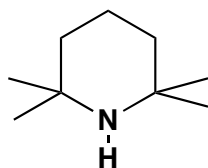
1. Metalation with base (deprotonation)
2. Oxidative addition (reductive metalation)
3. Halogen-metal exchange
4. Transmetalation
5. Addition to π -bonds
6. Fragmentation and cleavage

pKa Values for Some Typical Carbon Acids

Carbon Acid	pKa (H ₂ O)	pKa (DMSO)
Nitro compounds	10	17-18
CH ₃ COCH ₂ CO ₂ Et	11	14
CH ₂ (CO ₂ Et) ₂	13	16
Cyclopentadiene	15	18
Me ₃ S ⁺ -O ⁻		18
Ph ₃ P ⁺ -CH ₃		22
Ketones and aldehydes	19-24	24-27
Acetylenes C $\equiv$ C-H	25	24-29
Esters and lactones	22-25	24-28
Nitriles	22-25	27-30
Sulfones		29-33
Sulfoxides		29-33
Dithiane		39
Alkenes and arenes	C=C-H	37-45
Allylic and benzylic	C=C-C-H	40-45
Alkanes		>50

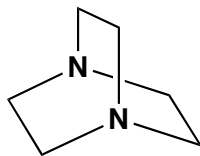
pKa Values for Some Common Bases

Base	Conjugate Acid	pKa (H ₂ O)	pKa (DMSO)
NaOAc	AcOH	4.8	12.3
pyridine	C ₅ H ₅ NH ⁺	5.2	
NaHCO ₃	H ₂ CO ₃	6.4	
imidazole	C ₃ H ₄ N ₂ H ⁺	7	
DABCO	C ₆ H ₁₂ N ₂ H ⁺	8.8	
DMAP	C ₆ H ₁₁ N ₂ H ⁺	9.2	
NaOPh	PhOH	10	18.0
Na ₂ CO ₃	NaHCO ₃	10.3	
Et ₃ N	Et ₃ NH ⁺	10.8	
DBU	C ₉ H ₁₆ N ₂ H ⁺	12	
NaOH	HOH	15.7	31.2
NaOMe	MeOH	16	29.0
NaOEt	EtOH	16	
KOt-Bu	<i>t</i> -BuOH	19	29.4
LiHMDS	(Me ₃ Si) ₂ NH		30
NaCPh ₃	Ph ₃ CH	31.5	30.6
NaNH ₂	NH ₃		41
NaCH ₂ SOCH ₃	DMSO		35
LDA (Li <i>n</i> -iPr ₂)	<i>i</i> -Pr ₂ NH		36
LiTMP	C ₉ H ₁₈ NH ⁺		37
EtMgBr	CH ₃ CH ₃		ca. 50
<i>n</i> -BuLi	CH ₃ CH ₂ CH ₂ CH ₃		ca. 50
<i>t</i> -BuLi	(CH ₃) ₃ CH		>50



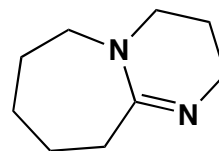
TMP

2,2,6,6,-tetramethylpiperidine



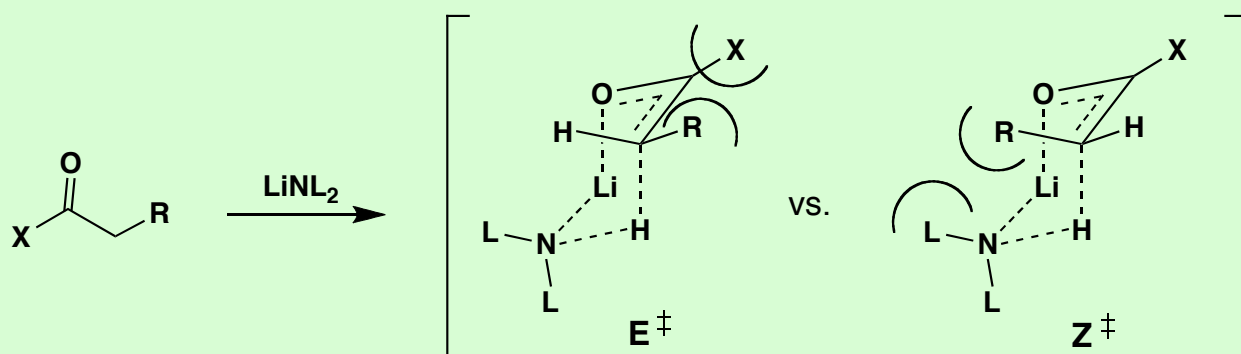
DABCO

1,4- Diazabicyclo[2.2.2]octane

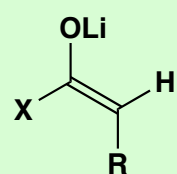


DBU

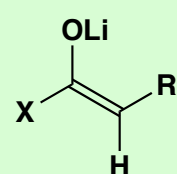
1,8-Diazabicyclo[5.4.0]undec-7-ene



Transition State
 Models for
 Kinetic Deprotonation



E(O) Enolate



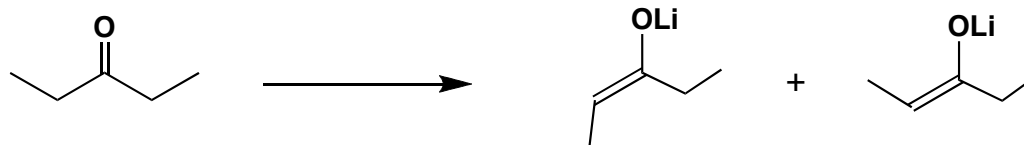
Z(O) Enolate



LDA, THF
 LDA, THF-HMPA

95
 10-15

5
 85-90



LDA, THF
 LiTMP, THF
 LiHMDS, THF
 LiN(SiMe₂Ph)₂

77
 86
 34
 0

23
 14
 66
 100