C=C Bond Formation

C&S Chapt. 2 # 5,6,8,9,12

1. Aldol Condensation
2. Wittig Reaction (Smith, Ch. 8.8.A)
3. Peterson Olefination
4. Julia-Lythgoe Olefination
5. Carbonyl Coupling Reactions (McMurry Reaction) (Smith Ch. 13.7.F)
6. Tebbe Reagent
7. Shapiro and Related Reaction
8. β-Elimination and Dehydration
9. From Diols and Epoxides
10. From Acetylenes
11. From Other Alkenes-Transition Metal Catalyzed Cross-Coupling and Olefin Metathesis

Aldol Condensation - Aldol condensation initially give β-hydroxy ketones which under certain conditions readily eliminated to give α,β-unsaturated carbonyls.

\[
\begin{array}{c}
\text{OMe} \\
\text{OMe} \\
\text{LDA, THF, -78°C} \\
\text{-78°C → RT} \\
\end{array}
\]

Robinson Annulation: Sequential Michael addition/aldol condensation between a ketone enolate and an alkyl vinyl ketone (i.e. MVK) to give a cyclohex-2-en-1-one

\[\text{JOC 1984, 49, 3685} \qquad \text{Synthesis 1976, 777.}\]

Mannich Reaction - α,β-unsaturated carbonyls (α-methylene carbonyls)

mechanism and stereochemistry: *Topic in Stereochemistry* **1994**, *21*, 1

- reaction of phosphonium ylide with aldehydes, ketones and lactols to give olefins

\[
\text{R}^1\text{R}_2\xrightarrow{\text{Ph}_3\text{P}} \text{R}^+\text{PPh}_3 \xrightarrow{\text{strong base}} \left[ -\text{R}^+\text{PPh}_3 \right. \\
\left. \xrightarrow{\text{ylide}} \text{R}^\text{Ph}_3 \xrightarrow{\text{phosphorane}} \right]
\]

- Olefin Geometry

- With "non-stabilized" ylides the Wittig Reaction gives predominantly Z-olefins.
  Seebach et al *JACS*

- "Stabilized ylides" give predominantly E-olefins
- Betaine formation is reversible and the reaction becomes under thermodynamic control to give the most stable product.
- There is NO evidence for a betaine intermediate.
- Vedejs Model:

![Diagram of Vedejs Model]

- Phosphonate Modification (Horner-Wadsworth-Emmons)

![Phosphonate Modification Diagram]

- R is usually restricted to EWG such as CO$_2$H, CO$_2$Me, CN, SO$_2$Ph etc. and the olefin geometry is usually E.
- Still Modification

![Still Modification Diagram]

- CF$_3$CH$_2$O- groups make the betaine less stable, giving more Z-olefin.

![Still Modification with CF$_3$CH$_2$O- Diagram]

- Peterson Olefination

![Peterson Olefination Diagram]

- Silicon can stabilize an $\alpha$-negative charge

- Usually a mixture of E and Z olefins
DCC Bond Formation

**Julia-Lythgoe Olefination**  
*TL 1973, 4833  Tetrahedron 1987, 43, 1027*

\[
\text{SO}_2\text{Ph} \quad \text{LDA, THF, -78°C} \quad \text{PhO}_2\text{CHO} \quad \text{TBSO} \quad \text{CHO} \\
\text{PhO}_2\text{S} \quad \text{OTBS} \quad \text{1) MsCl, Et}_3\text{N} \quad \text{2) Na[Hg], MeOH} \quad \text{mixture of olefins} \quad \text{TL 1991, 32, 495}
\]

**Ramberg-Backlund Rearrangement**

\[
\text{Br} \quad \text{OSiPh}_2\text{tBu} \quad \text{1) NaS•Al}_2\text{O}_3 \quad \text{2) mCPBA} \quad \text{OSiPh}_2\text{tBu} \quad \text{SOCI}_2 \\
\text{Br} \quad \text{OSiPh}_2\text{tBu} \quad \text{MeLi, THF} \quad \text{thiirane dioxide} \quad \text{JACS 1992, 114, 7360}
\]

**Carbonyl Coupling Reactions (McMurry Reaction)**


- reductive coupling of carbonyls with low valent transition metals, Ti(0) or Ti(II), to give olefins

\[
\begin{array}{c}
\text{O} \\
\text{R}_1 \quad \text{R}_2 \\
\end{array} \quad \text{“low-valent Ti”} \quad \begin{array}{c}
\text{R}_1 \quad \text{R}_2 \\
\end{array} + \begin{array}{c}
\text{R}_1 \quad \text{R}_2 \\
\end{array} \quad \text{usually a mixture of E and Z olefins}
\]

excellent method for the preparation of strained (highly substituted) olefins

- Intramolecular coupling gives cyclic olefins
C=C BOND FORMATION

“low-valent Ti”

Tebbe Reagent $Cp_2Ti(CH_2)ClAlMe_2$
- methylenation of ketones and lactones. The later gives cyclic enol ethers.

- Reaction of a tosylhydrazone with a strong base to give an olefin.

Bamford-Stevens Reaction - initial conversion of a tosylhydrazone to a diazo intermediate
a: aprotic- decomposition of the diazo intermediate under aprotic conditions gives and olefin through a carbene intermediate.

b. protic- decomposition of the diazo intermediate under protic conditions an olefin through a carbonium ion intermediate.
β- Eliminations

Anti Eliminations
- elimination of HX from vicinal saturated carbon centers to give an olefin, usually base promoted.
- base promoted E2- type elimination proceeds through an anti-periplanar transition state.

- typical bases: NaOMe, tBuOK, DBU, DBN, DABCO, etc.

- X: -Br, -I, -Cl, -OR, epoxides

Syn Elimination
- often an intramolecular process

Cope Elimination - elimination of R2NOH from an amine oxide

JACS 1979, 101, 2738
Tetrahedron 1977, 35, 613
Selenoxide Elimination


Dehydration of Alcohols
- Alcohols can be dehydrated with protic acid to give olefins via an E₁ mechanism.
- Other reactions dehydrate alcohols under milder conditions by first converting them into a better leaving group, i.e. POCl₃/ pyridine, P₂O₅
  Martin sulfurane; Ph₂S[OCPh(CF₃)₂]₂ JACS, 1972, 94, 4997 dehydration occurs under very mild, neutral conditions, usually gives the most stable olefin

Burgess Reagent (inner salt) JOC, 1973, 38, 26 occurs via a syn elimination

Olefins from Vicinal Diols
- vic-diols can be converted to olefins with K₂WCl₆. *JCCSC 1972*, 370; *JACS 1972*, 94, 6538
- This reaction worked best with more highly substituted diols and give predominantly syn elimination.
- Low valent titanium; McMurry carbonyl coupling is believed to go through the vic-diol. vic-diols are smoothly converted to the corresponding olefins under these conditions. *JOC 1976*, 41, 896

**Olefins from Epoxides**

- *inversion* of R groups

**From Acetylenes**

- Hydrogenation with Lindlar's catalyst gives cis-olefins

**From Other Olefins**

**Sigmatropic Rearrangements**

- transposition of double bonds

**Birch Reduction**

*JChemComm 1989*, 45, 1579
**Olefin Isomerization**

A variety of transition metal (RhCl₃•H₂O) catalyst will isomerize double bonds to more thermodynamically favorable configurations (i.e. more substituted, trans, conjugated).

\[
\begin{align*}
\text{RhCl}_3\cdot3\text{H}_2\text{O} & \rightarrow \text{cis-Olefin} \\
& \rightarrow \text{trans-Olefin}
\end{align*}
\]

**Olefin Inversion** *Tetrahedron* 1980, 557

- Conversion of cis to trans olefins
- Conversion of trans to cis- olefins

**Transition Metal Catalyzed Cross-Coupling Reactions**

Coupling of Vinyl Phosphonates and Triflates to Organometallic Reagents

- reaction with cuprates. 

\[
\text{Acc. Chem. Res. 1988, 25, 47}
\]

- palladium (0) catalyzed cross-coupling of vinyl or aryl halides or triflates with organostannanes (Stille Reaction)

\[
\]

\[
\text{(-)-Macrolactin A}
\]

\[
\text{J. Am. Chem. Soc. 1998, 120, 3935}
\]

\[
\text{CHO 1) BOMe 2) TESOTI, 2,6-lutidine (52%)}
\]

\[
\text{TESO TESO O}_{3}, \text{NaBH}_4 (77%) \quad \text{TESO OTES} \quad \text{a) nBu}_3\text{SnH, (Ph}_3\text{P)}_2\text{PdCl}_2 \\
\text{OH} \quad \text{b) I}_2 (83%) 
\]

\[
\text{Bu}_3\text{SnH, AIBN (38%)} 
\]

\[
\text{TesO CHO Bu}_3\text{SnCHBr}_3, \text{CrCl}_2 (42%) \quad \text{TesO SnBu}_3 \quad \text{CO}_2\text{H} \quad \text{TesO CO}_2\text{H} 
\]

\[
\text{TesO CO}_2\text{H}
\]
palladium (0) catalyzed carbonylations- coupling of a vinyl triflate with an organostanane to give α,β-unsaturated ketones.


Olefin Metathesis  
Metathesis Catalysts:

Schrock’ s Catalyst

Grubbs’ Catalyst

Mechanism:

\[ \text{R}_1 + [\text{M}] \rightleftharpoons \text{R}_1[\text{M}] \rightleftharpoons \text{R}_2 + [\text{M}] \]