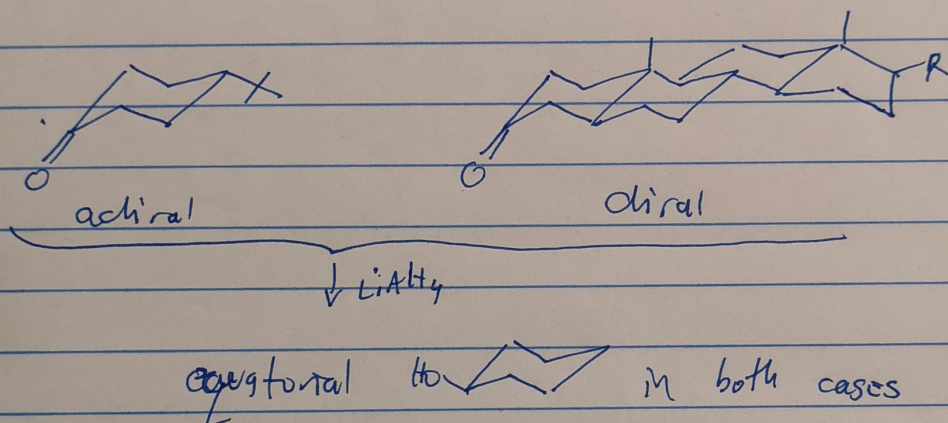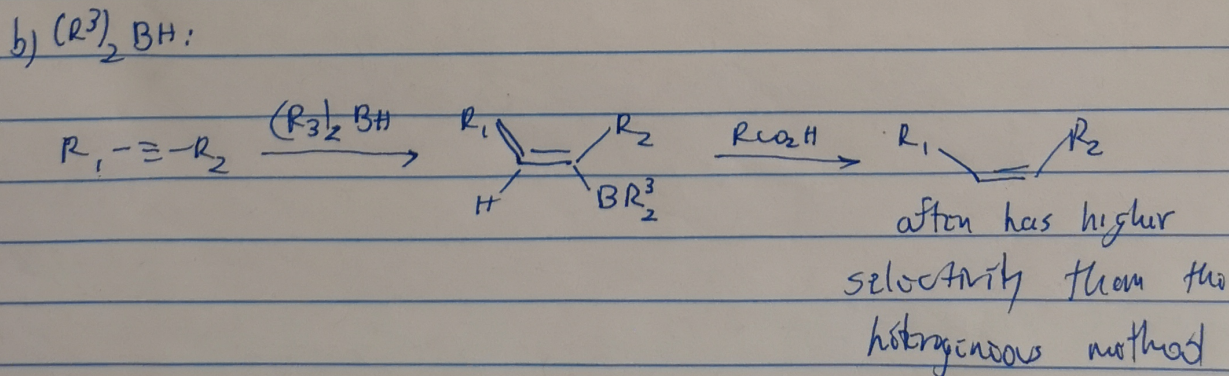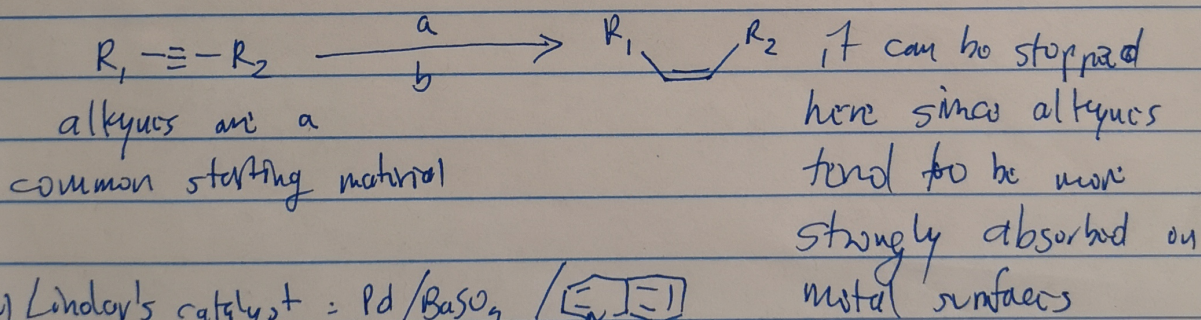## Lecture XXVI: Diastereoselective Synthesis of E Alkenes   04-06-2020
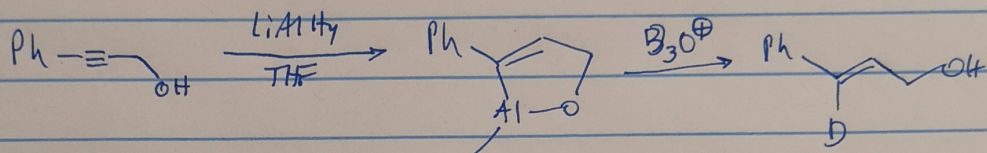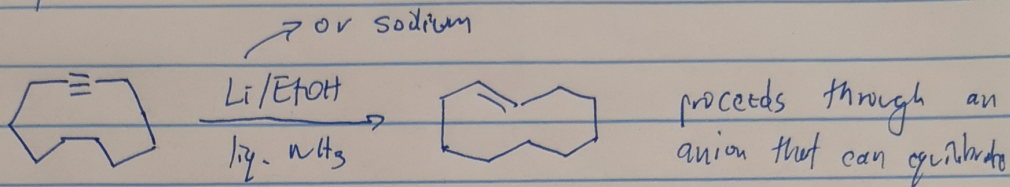
We'll talk first about diastereoselective synthesis of **achiral** compounds, and then move on to chiral compounds with multiple chiral centers. Some of these concepts are shared with chiral compounds too.
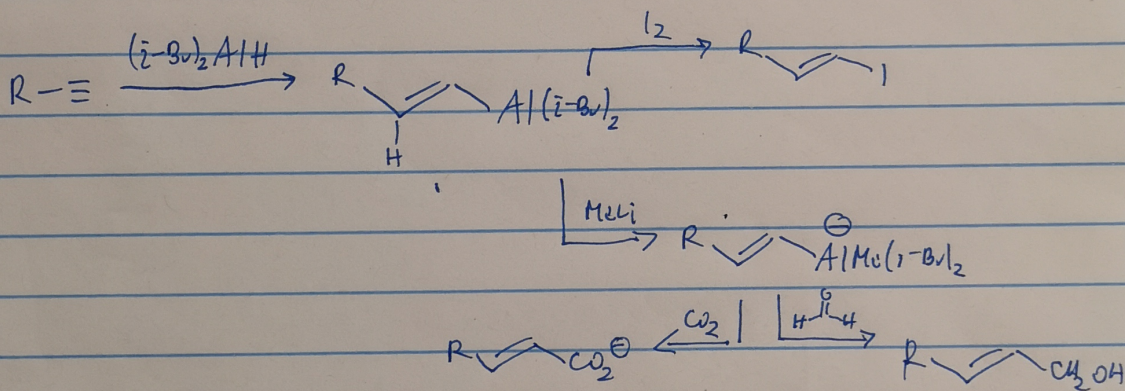

achiral   chiral

$\downarrow$ LiAlH$_4$

equatorial HO $\diagdown\diagup\diagdown$ in both cases

E/Z Selectivity in Syntheses of Alkenes

$$R_1 -\!\!\equiv\!\!- R_2 \xrightarrow[b]{a} R_1 \diagdown\diagup R_2$$ it can be stopped here since alkynes tend to be more strongly absorbed on metal surfaces

alkynes are a common starting material

a) Lindlar's catalyst : Pd/BaSO$_4$ / $\boxed{E}$ $\boxed{=}$

b) (R^3)$_2$ BH:

$$R_1 -\!\!\equiv\!\!- R_2 \xrightarrow{(R_3)_2 BH} R_1 \diagup\!\!=\!\!\diagdown \begin{smallmatrix} R_2 \\ \\ BR_2^3 \end{smallmatrix} \xrightarrow{RCO_2H} R_1 \diagdown\diagup R_2$$

(with H below R$_1$)

often has higher selectivity than the heterogeneous method

E-selectivity:

↗ or sodium

Li/EtOH / liq. NH₃ → proceeds through an anion that can equilibrate

Ph—≡—OH $\xrightarrow[\text{THF}]{\text{LiAlH}_4}$ Ph (cyclic, Al—O) $\xrightarrow{B_3O^\oplus}$ Ph ~ OH / D

Conversions of C≡C into C=C don't have to be reductive:

R—≡ $\xrightarrow{(i\text{-}Bu)_2AlH}$ R (=) H / Al(i-Bu)₂ $\xrightarrow{I_2}$ R ~ I

$\downarrow$ MeLi

R (=) AlMe(i-Bu)₂⁻

$\xrightarrow{CO_2}$ ← ... R ~ CO₂⁻ / CO₂⁻ ← $\xrightarrow{H_4}$ R ~ CH₂OH
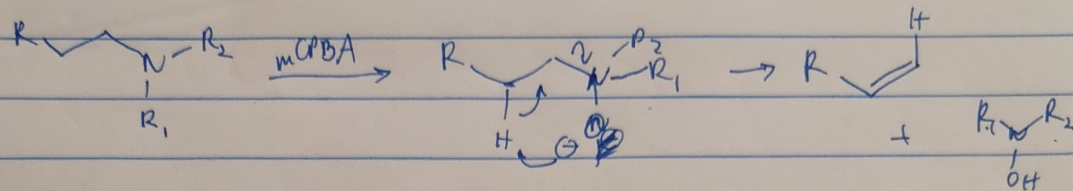

Elimination reactions are a broad group of methods for producing alkenes. If they are bimolecular, they will generally be requiring an antiperiplanar geometry. E2 rxn is a prime example:
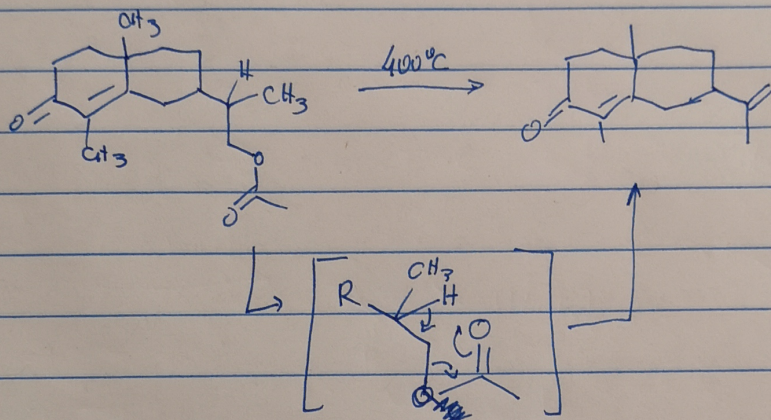
Ph Br Ph (structure) AlH₃ → Br Ph CH₃ / Ph H base⁻ → Ph Ph / H CH₃

other examples of similar reactions are eliminations of X₂, or eliminations of 1,2-halohydrins.
On the other hand, if a reaction is unimolecular, it will likely require a syn-antiperiplanar geometry.
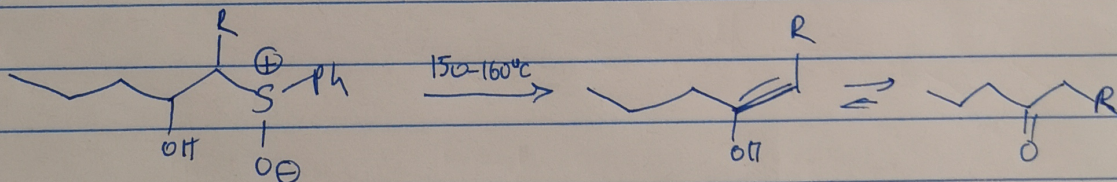
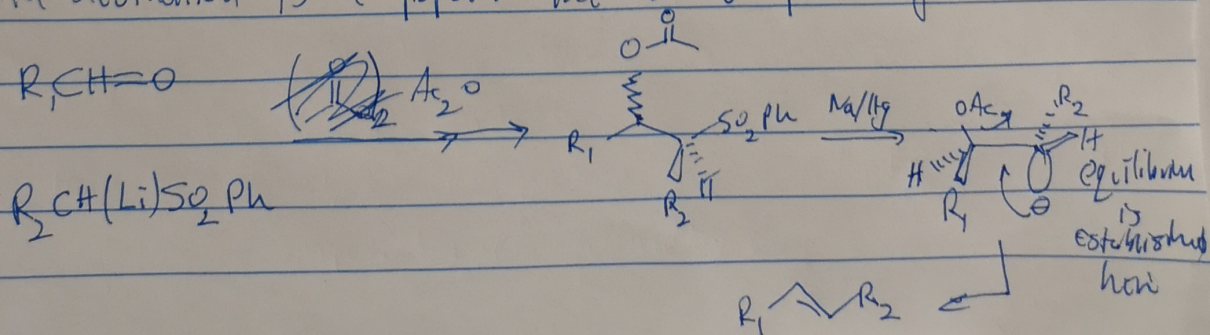Eliminations of amino oxides under pyrolytic conditions:
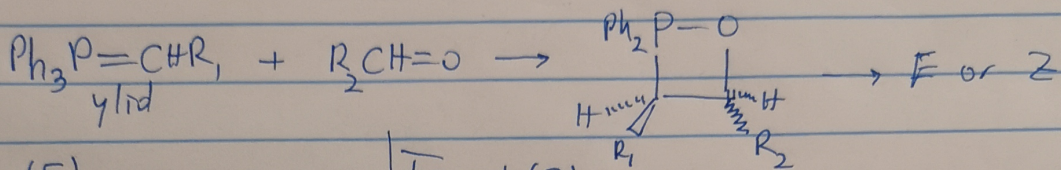

Esters:

Sulfoxides:

Selenium–based versions exist too. These are collectively sometimes called **Ei** reactions: thermal syn eliminations or pericyclic syn eliminations. Generally, reagents are not required: these are pyrolytic processes.

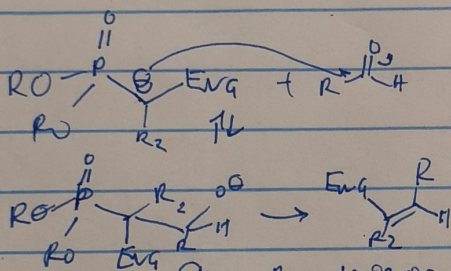Julia olefination is a popular method of producing E-alkenes:

$R_1CH=O$

$R_2CH(Li)SO_2Ph$

Witty reaction is a very general way of making alkenes, but has traditionally suffered from poor E/Z selectivity:

$$Ph_3P=CHR_1 + R_2CH=O \longrightarrow \underset{\text{ylid}}{} \quad Ph_2P=O \longrightarrow E \text{ or } Z$$

To get (E):
- stabilized ylides

To get (Z):
- use unstabilized ylides, (Li) or salt-
    free
    conditions

Org. Lett. 2017, 19, 1414

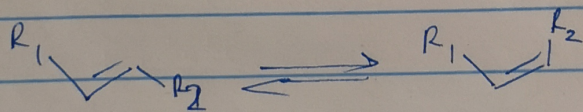Chem. Rev. 1989, 89, 863

There is a number of pericyclic reactions that can produce alkenes with very high E/Z selectivity. We will talk about those when we talk about other pericyclic rxns.

Changing alkene geometry

$$R_1 \diagdown\diagup R_2 \rightleftharpoons R_1 \diagdown\diagup R_2$$

under high temperature
UV irradiation
radical sources

(present)
(last)

This is generally a problem that has to be dealt with, but can occasionally be useful if the two isomers absorb light at different λ_{max}. However, a more general method for the switching of alkene geometry involves using anti addition, followed by syn-elimination.
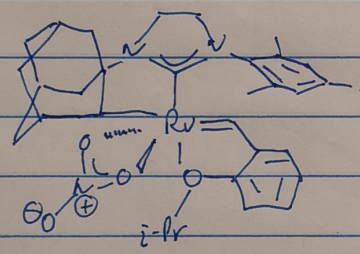
Alkene metathesis is one of the most versatile modern methods for making alkenes. It has historically suffered from poor E/Z selectivity, but that problem seems to have been solved now. For reviews, see:

Catal. Sci. Technol. 2012, 2, 1027

JACS, 2003, 125, 11360

Science, 2016, 352, 569

Chelating catalysts typically favor (Z):

JACS, 2013, 135, 94

otherwise, E tends to dominate because of its higher stability, which is affecting the metallacyclobutadiene equilibrium

However, in the cases of chloro- and fluoro-substituted olefins, the Z isomer is more stable. Hoveyda has solved that problem using Mo-based catalysts that kinetically give E-alkenes:

A

98% E