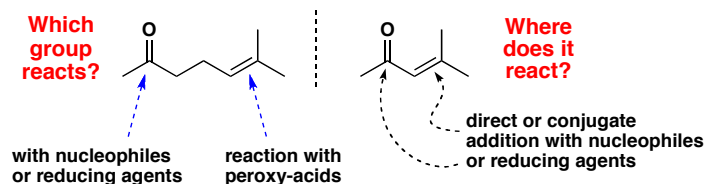


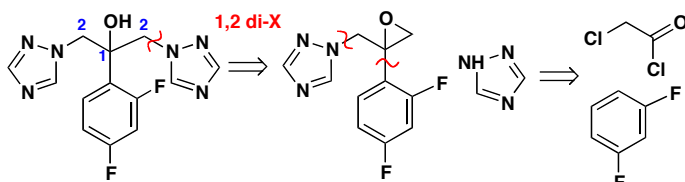
■ Lecture 1 Recap

■ Chemo- and Regio- selectivity



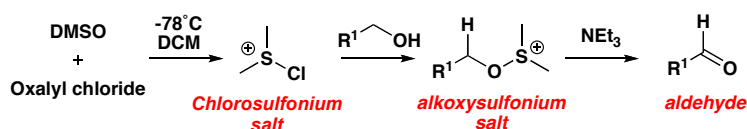
- Selectivity is paramount in synthesis
- Must consider reactivity of starting material and product when designing a reaction sequence
- Some functional groups possess similar reactivity; some possess different

■ The 1,2 difunctional disconnection



- Disconnection defines strategy
- Two-group disconnections are very powerful
- We must consider the order of events when considering bond formation

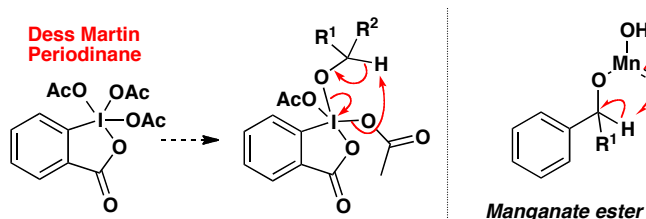
■ The Swern oxidation



- One of several activated DMSO oxidations methods
- Effective oxidant - chlorosulfonium salt - is not stable above approx. -60°C
- Et_3N is added after formation of alkoxy-sulfonium salt

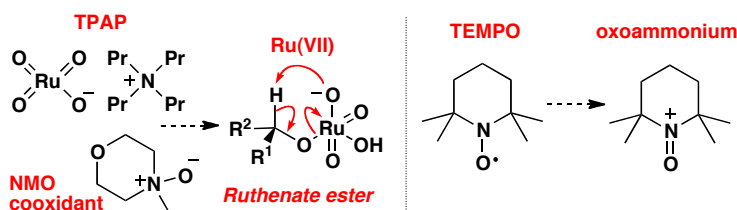
■ Lecture 2 Recap

■ Stoichiometric oxidants (1° alcohol to aldehyde)



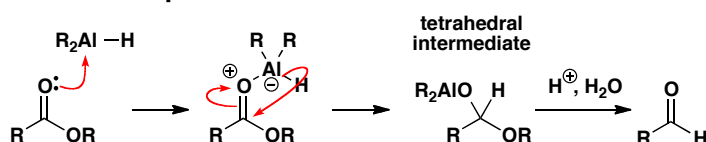
- Selective oxidation to aldehyde in absence of water (no overoxidation)
- DMP: high-valent iodine; good for complex structures
- MnO_2 selective for allylic/benzylic alcohol oxidation (radical mechanism)

■ Catalytic oxidants (1° alcohol to aldehyde)



- Catalytic: all need a co-oxidant
- TPAP: Ru(VII) with NMO reoxidant - probably via ruthenate ester
- TEMPO: Oxoammonium actual oxidizing agent; regenerate catalyst through reoxidation with NaOCl

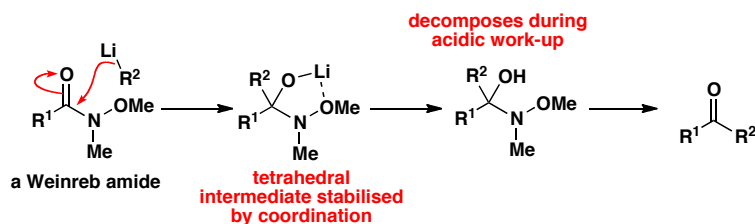
■ DIBALH permits selective reduction



- DIBALH is an electrophilic source of nucleophilic hydride
- Mechanism: precomplexation and internal delivery
- Tetrahedral intermediate stable: can reduce ester to aldehyde (at -78°C)

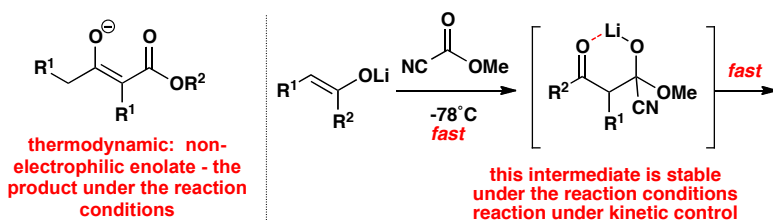
Lecture 3 Recap

- Weinreb amides allow us to stop reactions halfway



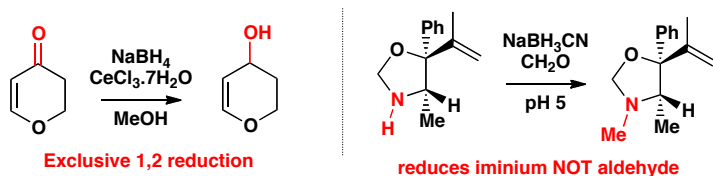
- Weinreb amides allow generation of products that are more reactive than SM
- Intermediate stabilized by coordination so reactive product not unmasked in presence of nucleophilic species
- DIBALH, RLi, RMgBr, LiAlH₄ all OK

- Selective C-acylation: kinetic or thermodynamic control



- The Claisen condensation generates a stable enolate (reversibly!) under the reaction conditions
- Kinetic C-acylation: generate a stable intermediate: use methyl cyanoformate

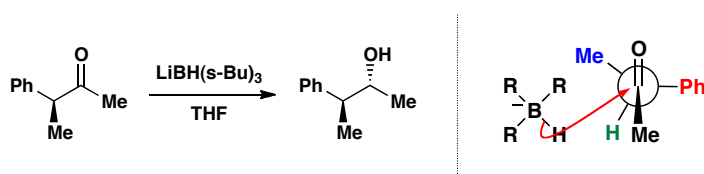
- Different hydrides have different properties



- LiAlH₄ reduces: amides, ketones, esters, nitriles, lactones...
- LiBH₄: esters NOT amides
- NaBH₄: aldehydes, ketones not esters
- CeCl₃ makes NaBH₄ more 1,2 selective
- NaBH₃CN best for reductive amination

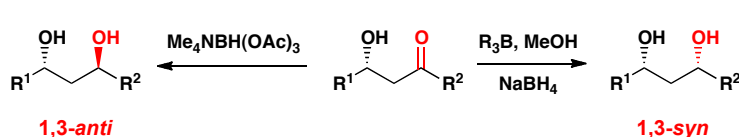
Lecture 4 Recap

- 1,2-stereoselection rationale: Felkin-Anh model



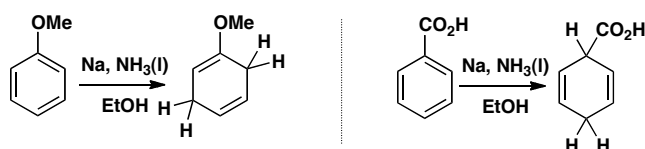
- Based on reactive conformations (NOT most stable!) & SM-like TS
- Attack at Bürgi-Dunitz angle, away from R^L and 'over' R^S
- Felkin polar & chelation models for electronegative atoms & chelating metals respectively

- 1,3-syn & 1,3-anti diols by choice of reducing agent



- 1,3-anti diols through intramolecular delivery of hydride (chair TS)
- 1,3-syn diols through chair-like Lewis acid chelate and intermolecular axial delivery of hydride

- The Birch reduction of arenes



- Non-conjugated dienes through kinetic protonation
- Regiochemistry; EDG: ortho-protonation; EWG: para-protonation (think about anionic intermediates)
- Proton source important for reactivity