Robinson Annulation

1886.09.13~1975.02.08
Nobel Prize for Chemistry (1947)

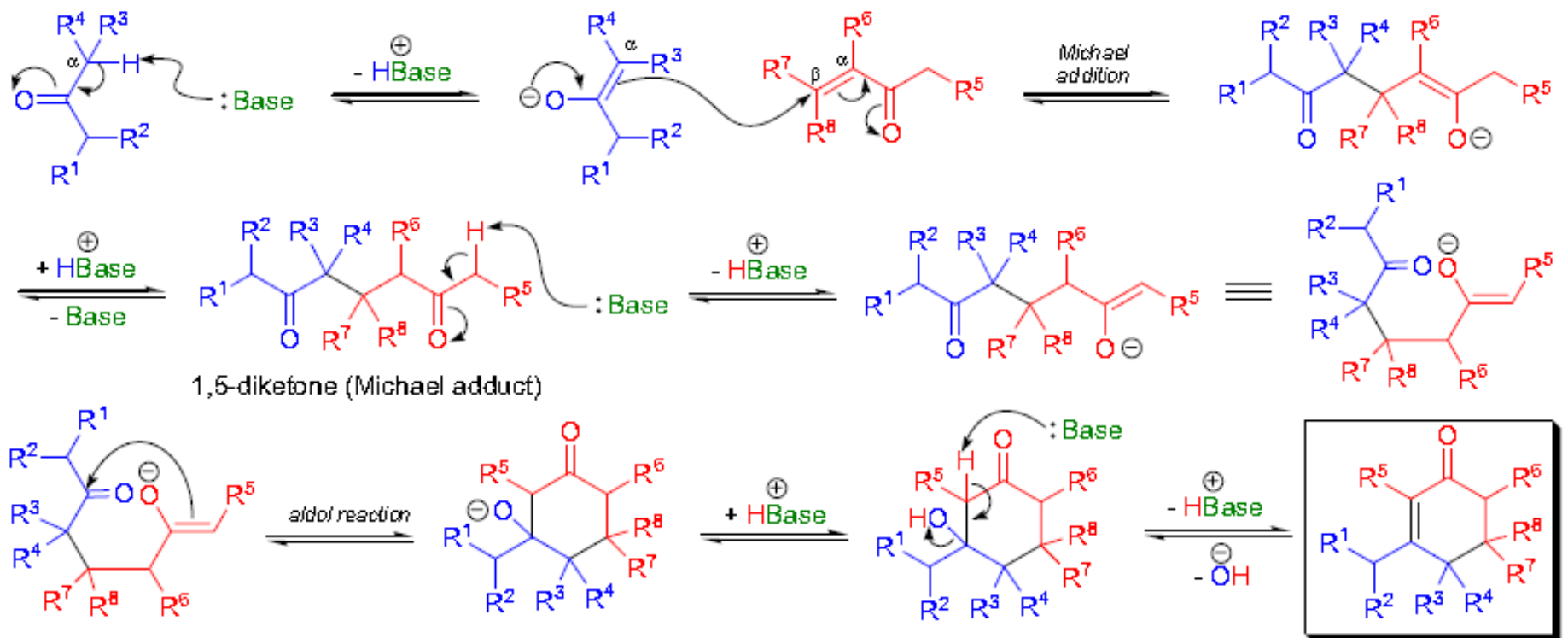Robinson annulation:

ketone + α,β-unsaturated ketone → [ ] → β-hydroxy ketone → Substituted 2-cyclohexenone

acid (cat.) or base (cat.) — *Michael addition* — *aldol reaction* — $- H_2O$
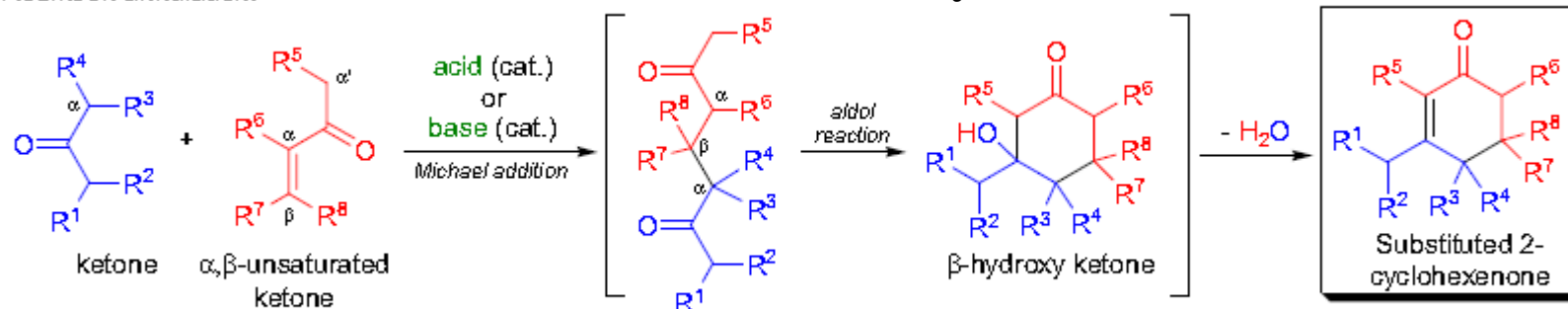
R^{1-4} = H, alkyl, aryl; R^5 = H, alkyl, aryl; R^6 = H, alkyl, aryl, SiR_3; R^{7-8} = H, alkyl, aryl
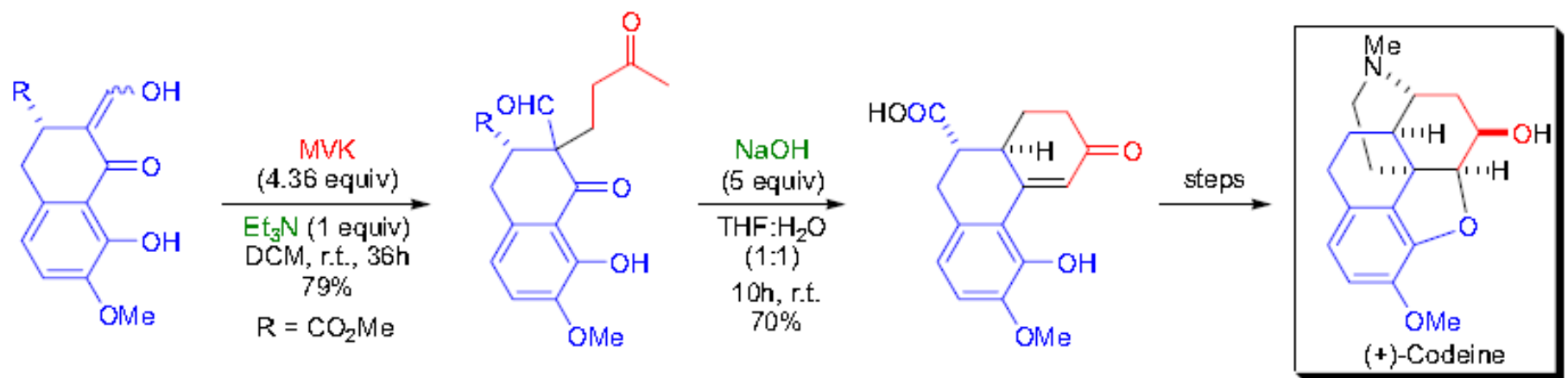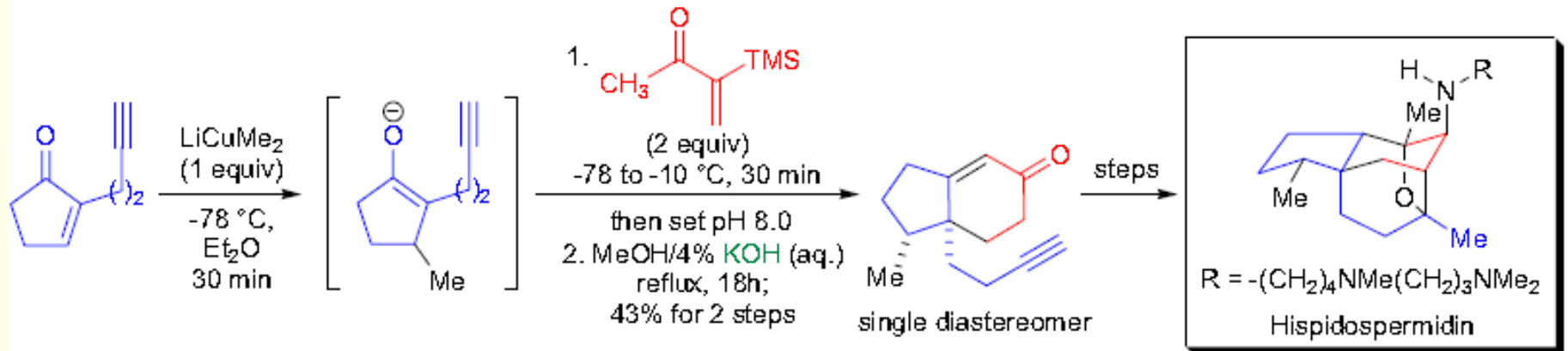
Features

1.combination of *Michael addition*, *intramolecular aldol reaction*, and dehydration;
2. It can be both acid- and base-catalyzed
3. Acyclic enones and cyclic ketones afford bicyclic enones, whereas cyclic enones and cyclic ketones give rise to polycyclic fused enones;
4. Methyl vinyl ketone (MVK) and its various derivatives and surrogates are used most often as the enone component;
5. yields tend to be higher when the Michael adduct is isolated and then subjected to the *aldol reaction;*
6. the alkylation of an unsymmetrical ketone occurs regioselectively at the most substituted α-position unless severe steric interference dictates otherwise;
7. regioselective cyclization can also be achieved by using preformed enolates or enamines under non-equilibrium conditions;
8. the annulation can generate as many as five stereocenters, but in the dehydration step two of these chiral centers are lost;
9. the relative stereochemistry between R3 and R7 (*cis* or *trans*) is dependent on the reaction conditions (e.g., solvent)
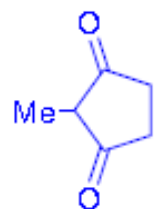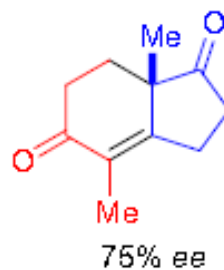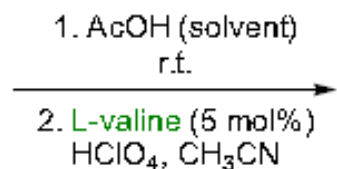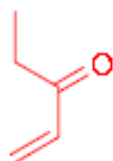10. the enantioselective version is known as the *Hajos-Parrish reaction*

Mechanism

Applications

Applications

(-)-Austalide B
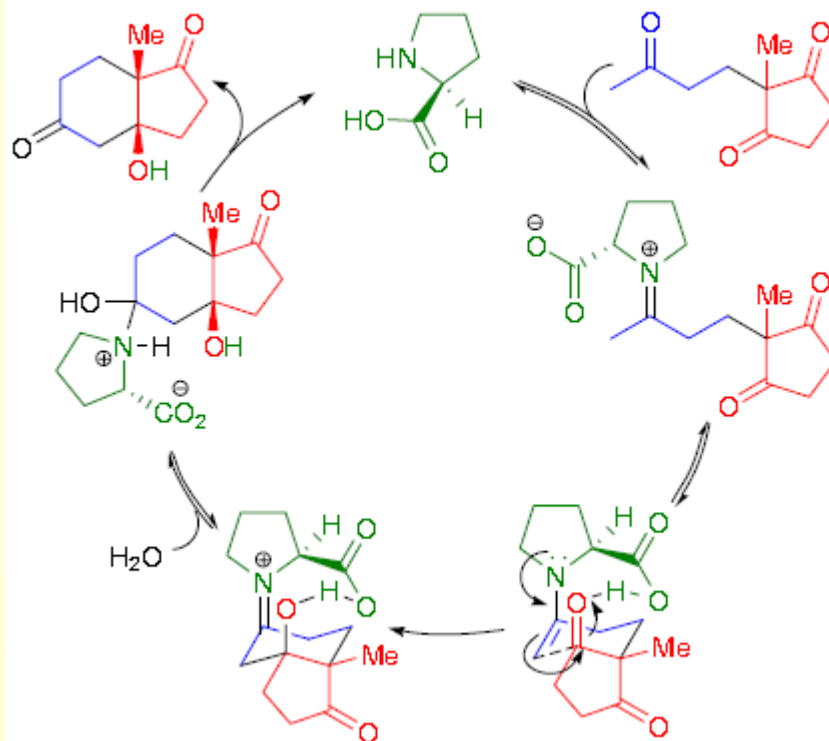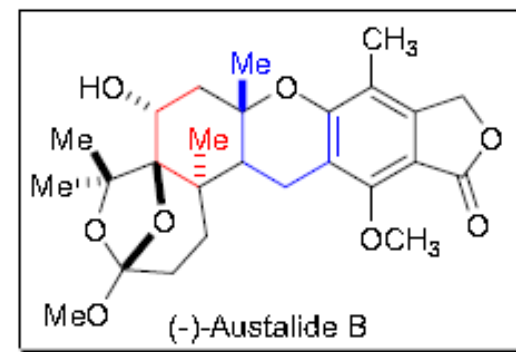
Mechanism of Hajos-Parrish reaction

Applications

R = SiMe₂Ph; R' = TBS

1. mCPBA
(1.2 equiv)
DCM, 0 °C

2. pyr(HF)ₓ
(xs.)
71%

NaOMe
(10 equiv)

PhH:MeOH
(4:1)
r.t., 2h;
85%

steps

R = OAc
(±)-Guanacastepene A