Nagata Hydrocyanation

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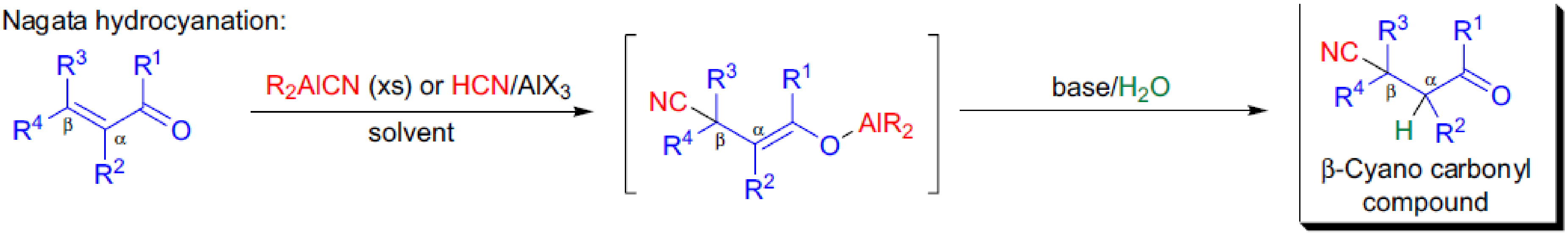
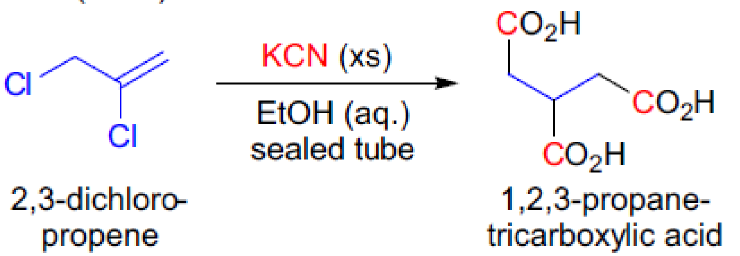
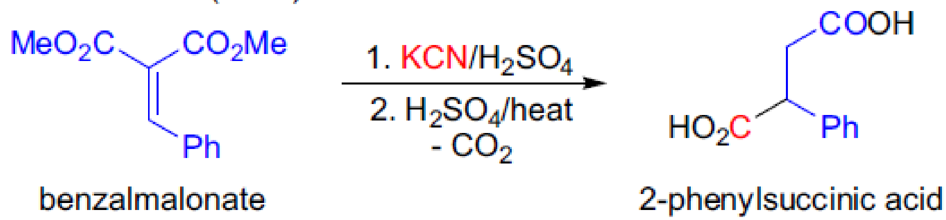


R^1 = alkyl, aryl, *O*-alkyl, *O*-aryl, (NR_2); R^{2-4} = H, alkyl, aryl; R = Me, Et, *i*-Bu; AlX_3 = $EtAlCl_2$, Me_3Al, Et_3Al, Et_2AlCl

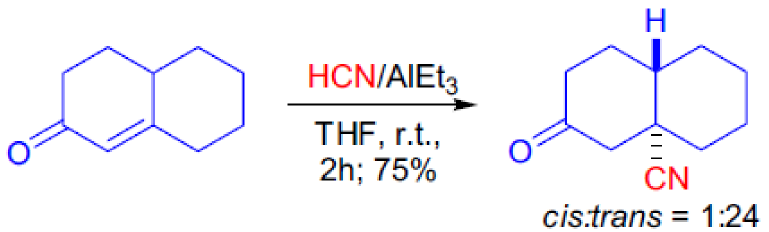
Claus (1873):



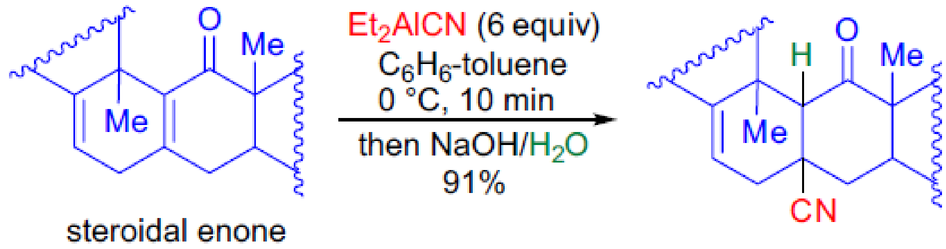
Bredt & Kallen (1896):

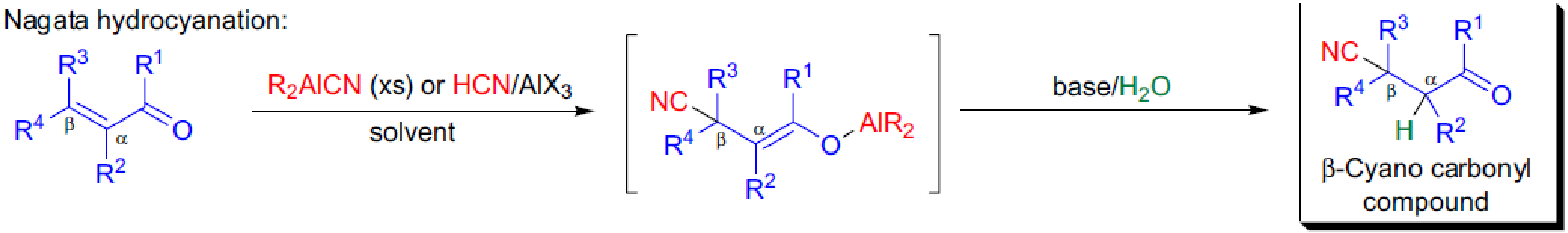


Nagata (1962):



Nagata (1966):





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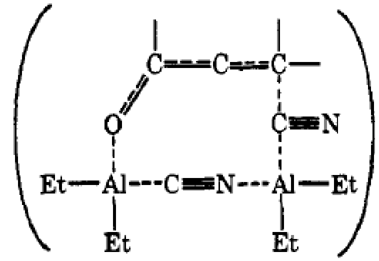
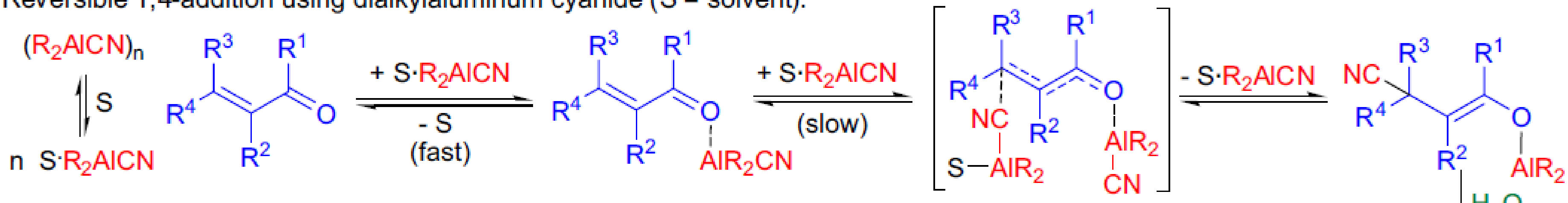
1)In the overwhelming majority of cases the carbonyl compound is a ketone and rarely the aldehyde (since it undergoes 1,2-addition)
2)HCN is used in conjunction with aluminum trialkyls or with alkylaluminum halides, the order of reactivity is as follows: EtAlCl2>Me3Al>Et3Al>Et2AlC
3)The reaction is almost exclusively conducted in a dipolar aprotic solvent such as THF, hydrocarbon solvents are not suitable, since the HCN reacts with AlX3 immediately in nonpolar media
4)A small amount of water in the reaction medium accelerates the hydrocyanation when HCN/AlMe3 is used (substrates with free hydroxyl groups have the same effect)
5)The reactivity of the dialkylaluminum cyanide reagent is strongly dependent on the basicity of the solvent and increases with decreasing solvent basicity: THF>dioxane>*i*-Pr2O>benzene>toluene;

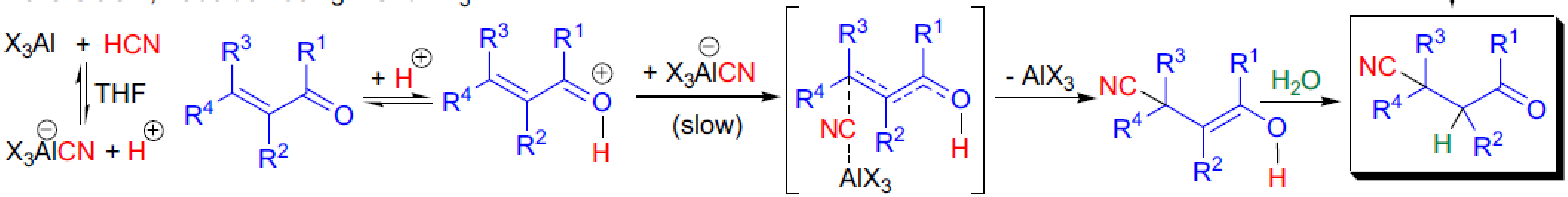
Mechanism



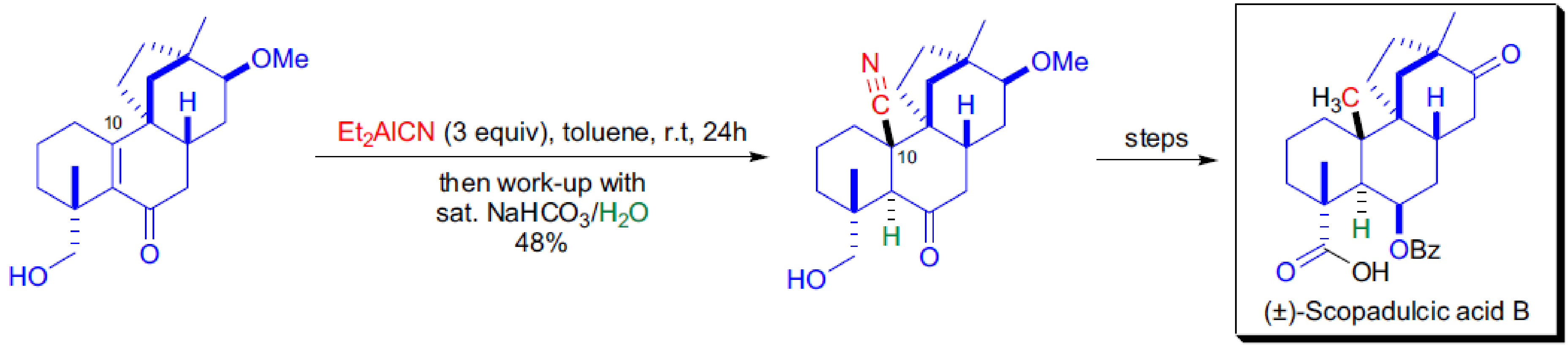
Reversible 1,4-addition using dialkylaluminum cyanide (S = solvent):

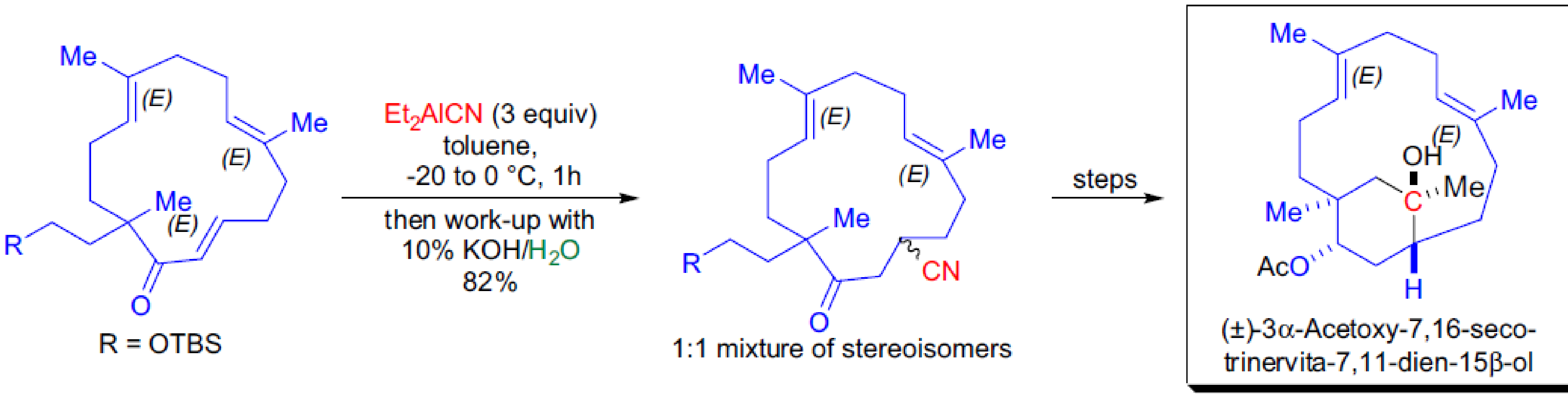


Irreversible 1,4-addition using HCN/AlX$_3$:

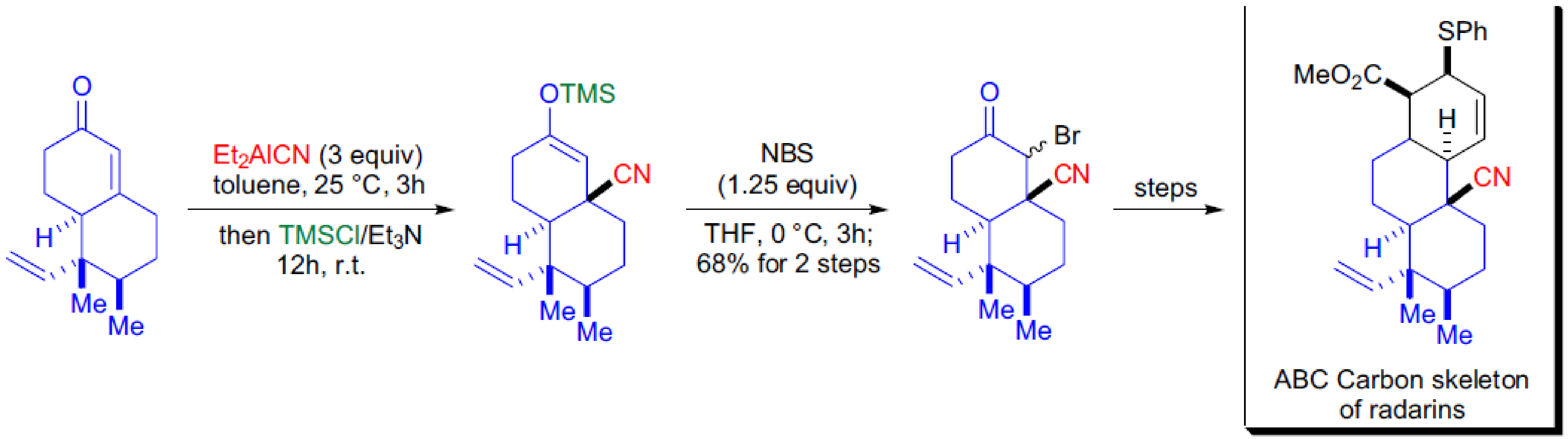


Synthetic Applications





Synthetic Applications



Thanks