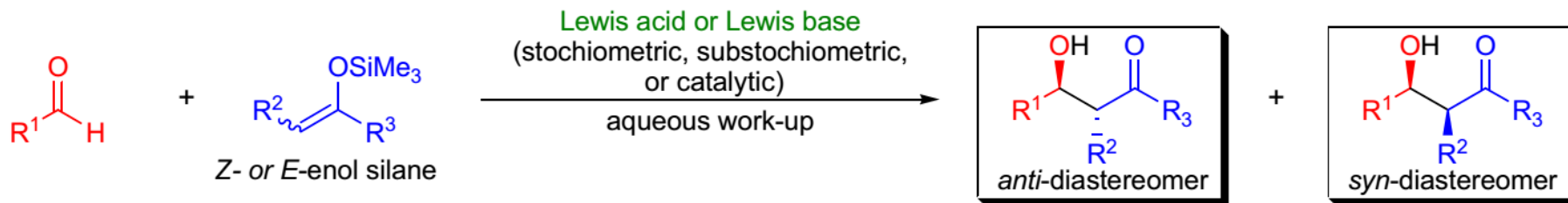




# Mukaiyama Aldol Reaction

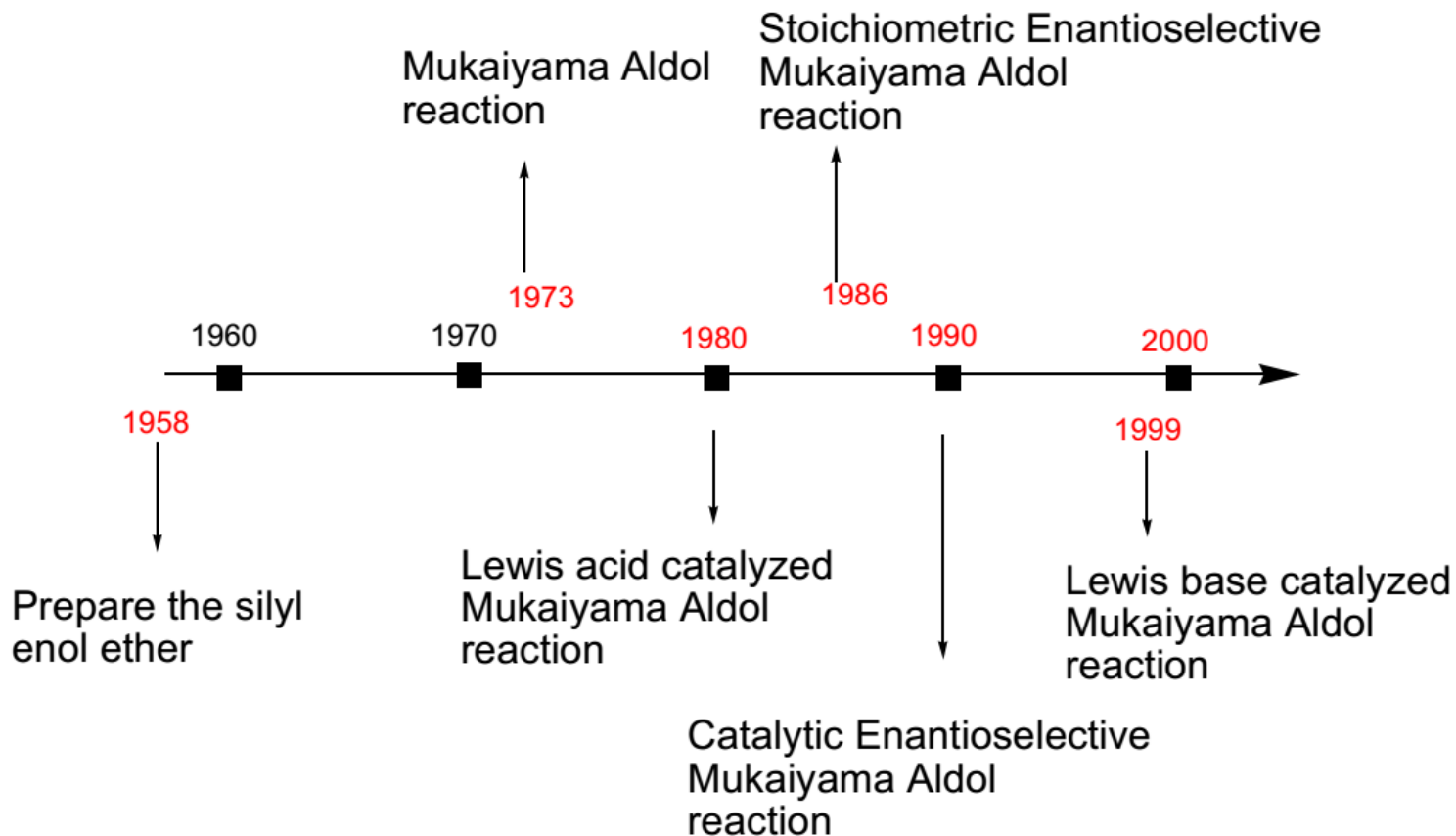
Chem. Lett. 1973, 1011-1014

- Powerful reaction in carbon-carbon formation.
- Widely used in asymmetric synthesis.
- Widely used in total synthesis.

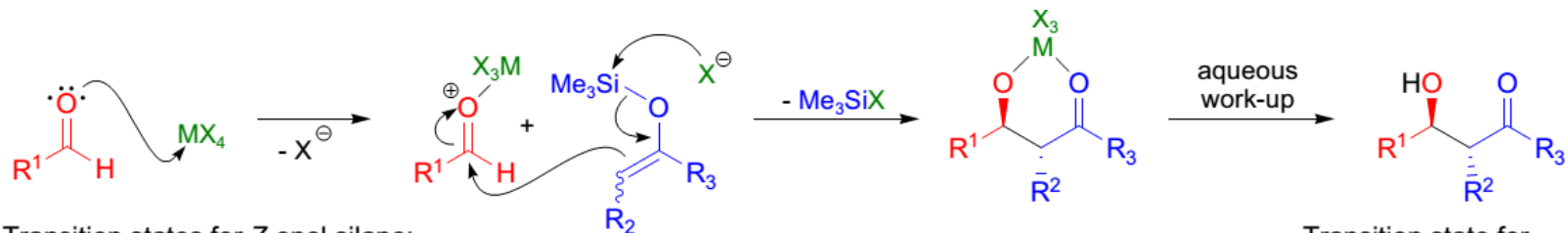


$R^1$  = alkyl, aryl, -OR;  $R^2$  = H, alkyl, aryl;  $R^3$  = alkyl, aryl, -OR, -SR, H; **Lewis acid** = Sn<sup>(IV)</sup>, Sn<sup>(II)</sup>, Mg<sup>(II)</sup>, Zn<sup>(II)</sup>, Li<sup>(I)</sup>, Bi<sup>(III)</sup>, In<sup>(III)</sup>, Ln<sup>(III)</sup>, Pd<sup>(II)</sup>, Ti<sup>(IV)</sup>, Zr<sup>(IV)</sup>, Ru<sup>(II)</sup>, Rh<sup>(III)</sup>, Fe<sup>(II)</sup>, Al<sup>(III)</sup>, Cu<sup>(II)</sup>, Au<sup>(I)</sup>, R<sub>3</sub>SiX, Ar<sub>3</sub>C<sup>+</sup>, clay; **Lewis base** = F<sup>-</sup>, (R<sub>2</sub>N)<sub>3</sub>PO;

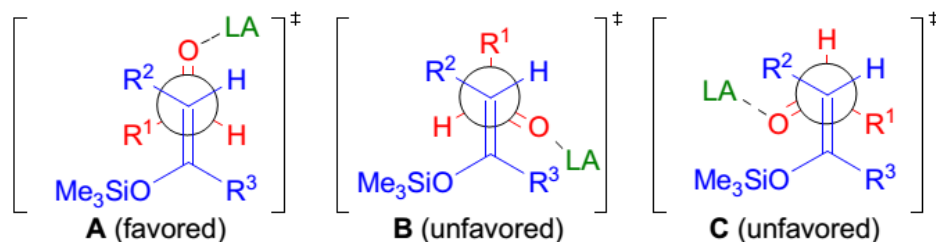
# History of Mukaiyama aldol



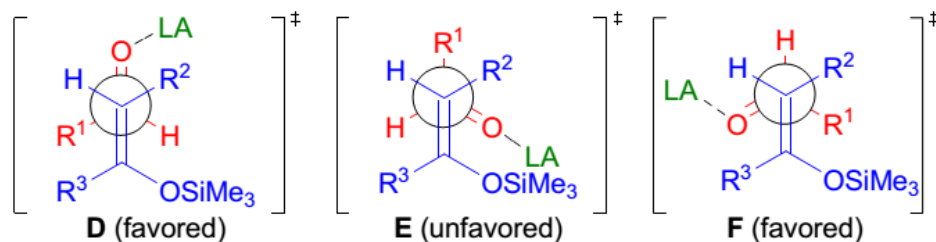
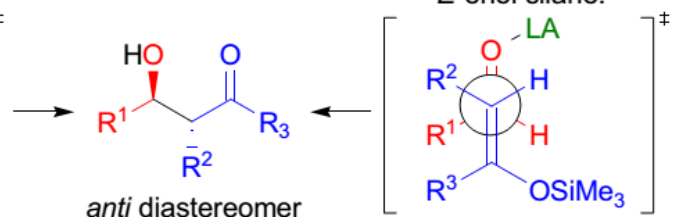
# Mechanism:



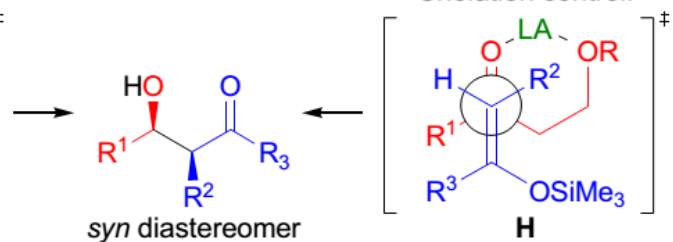
Transition states for Z-enol silane:



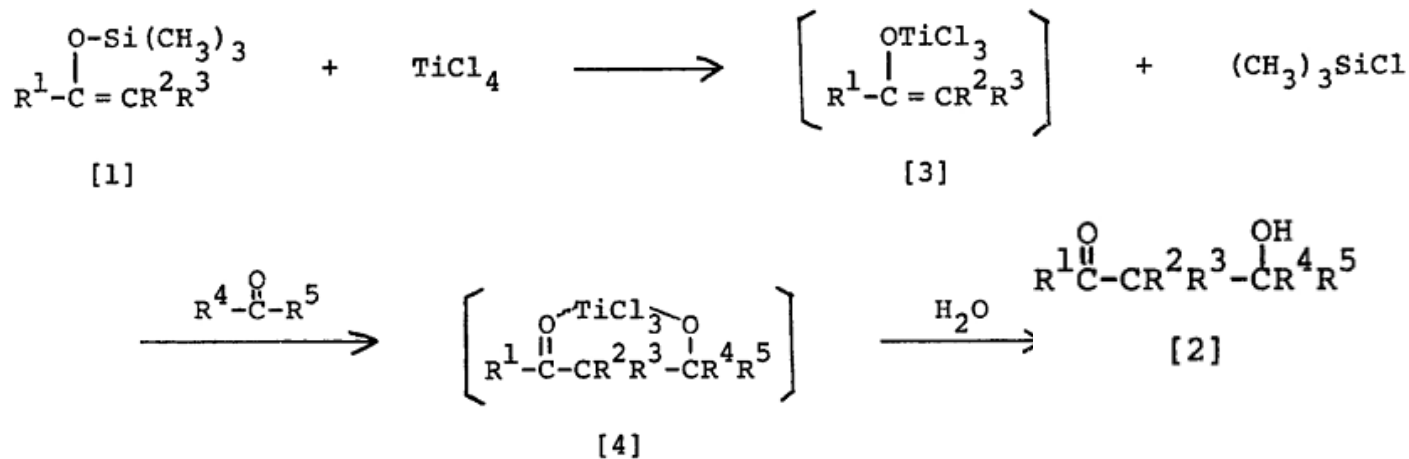
Transition state for E-enol silane:



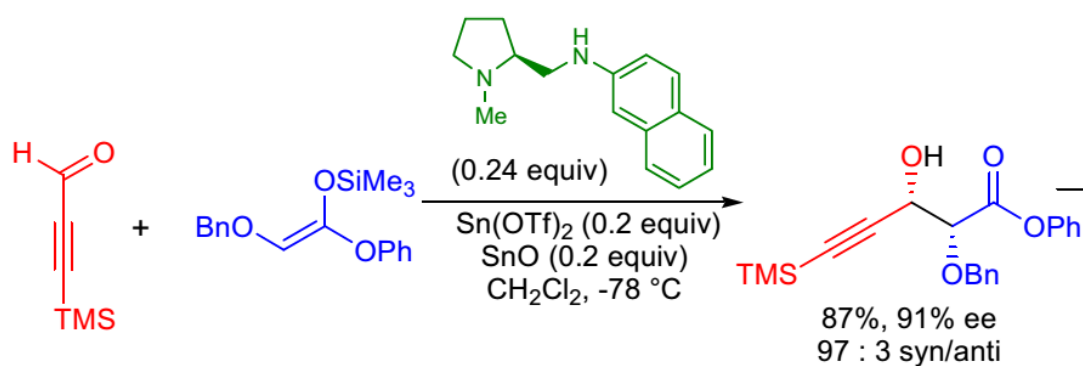
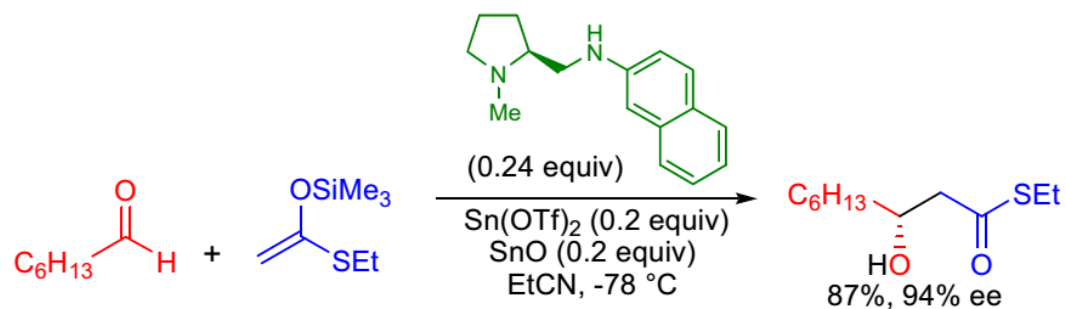
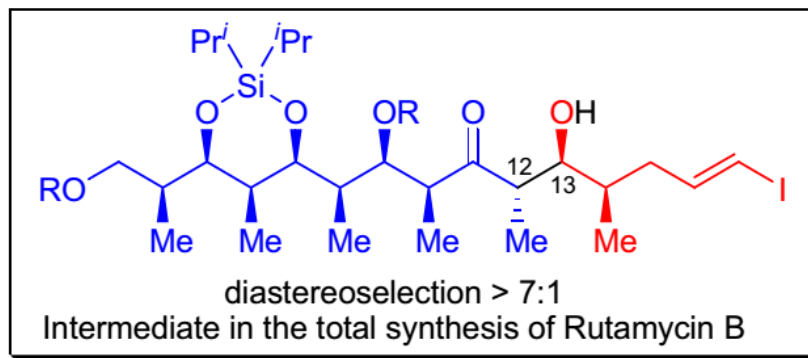
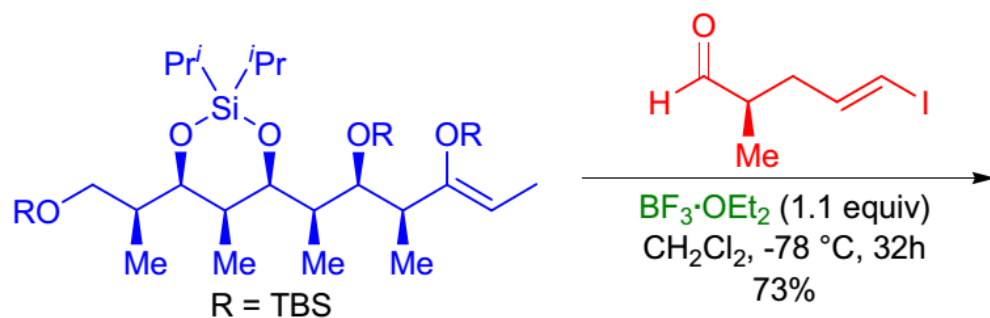
Chelation control:



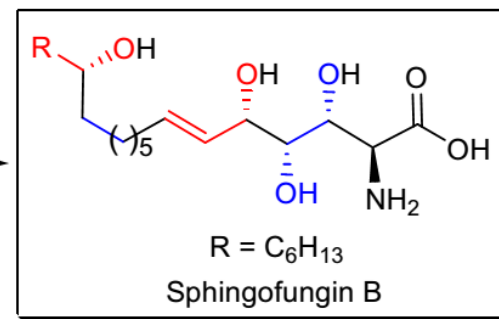
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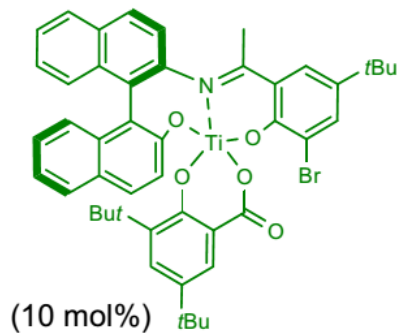
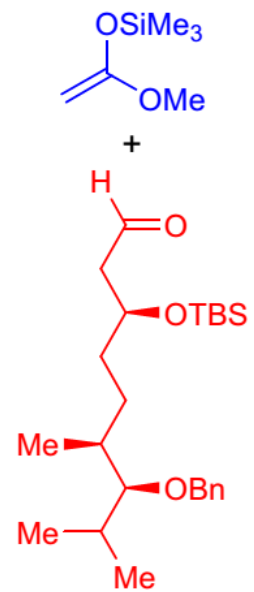


1. stoichiometric quantities of the Lewis acid such as  $\text{TiCl}_4$ ,  $\text{SnCl}_4$ ,  $\text{AlCl}_3$ ,  $\text{BCl}_3 \cdot \text{OEt}_2$ , and  $\text{ZnCl}_2$  were required to effect the transformation.
2. Lewis base:  $\text{F}^-$ ,  $(\text{R}_2\text{N})_3\text{PO}$
3. when  $\text{R}_2$  is small and  $\text{R}_3$  is bulky, the reaction leads to the anti product independent of the double bond geometry.
4. when  $\text{R}_2$  is large, syn diastereoselection predominates independent of the enol silane geometry.
5. Control of the absolute stereochemical: reagent control, chiral Lewis acid complexes and Lewis bases
6. when the aldehyde is capable of chelation, the formation of the syn-diastereomer is preferred.

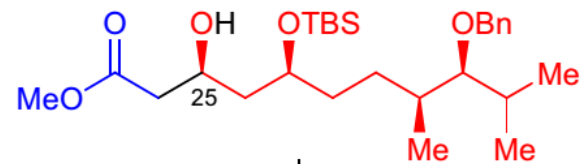


steps





2,6-lutidine (0.2 equiv)  
diethyl ether, -78 °C  
84%



steps

