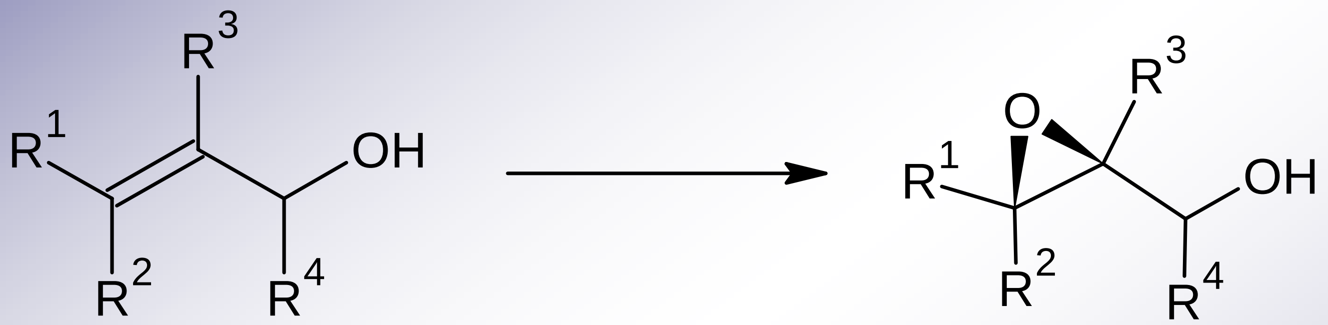
Sharpless Asymmetric Epoxidation (SAE)

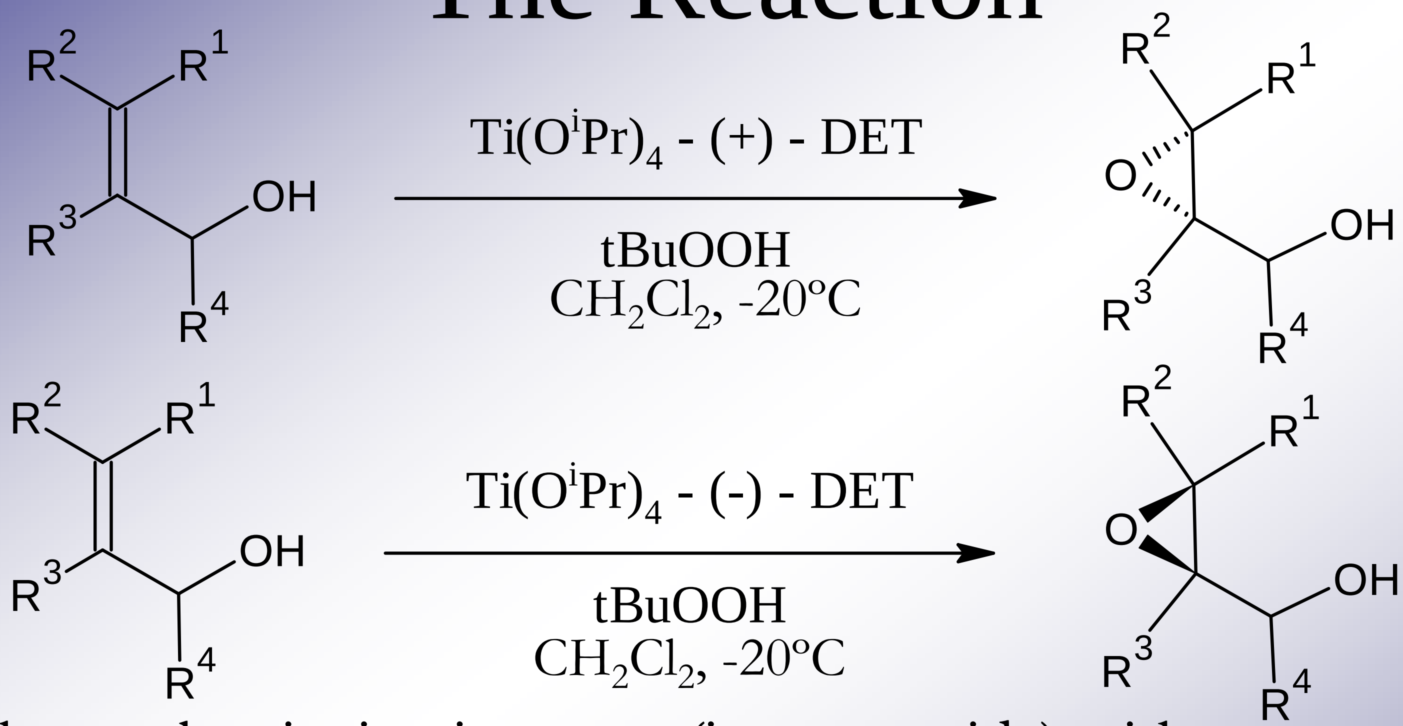


- Converts primary and secondary allylic alcohols into 2,3 epoxyalcohols

-The reaction is enantioselective (only one enantiomer produced)

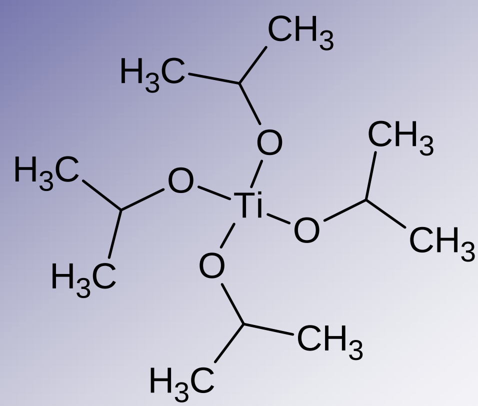
-Enantiomer formed depends on stereochemistry of catalyst

The Reaction

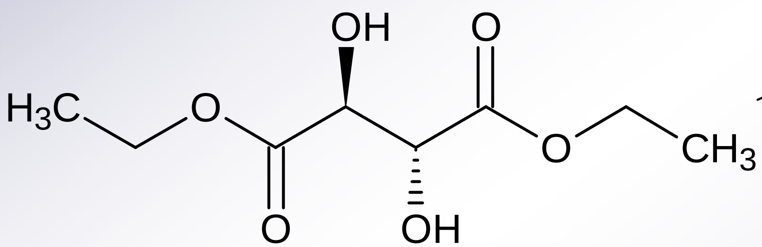


- The catalyst is titanium tetra(isopropoxide) with diethyltartrate.
- The use of + or – tartrate will yield different enantiomers
- Tertbutylperoxide is used as the oxidizing agent
- Dichloromethane solvent and -20ºC temperature

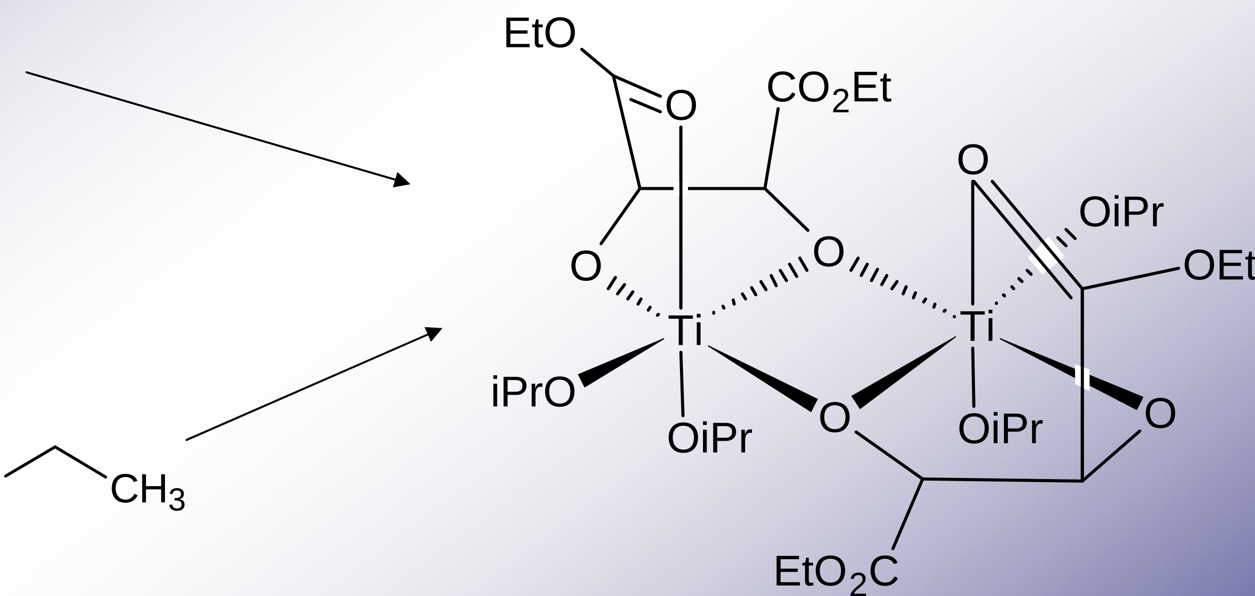
The Catalyst



Ti(O^{i}Pr)$_4$ catalyst

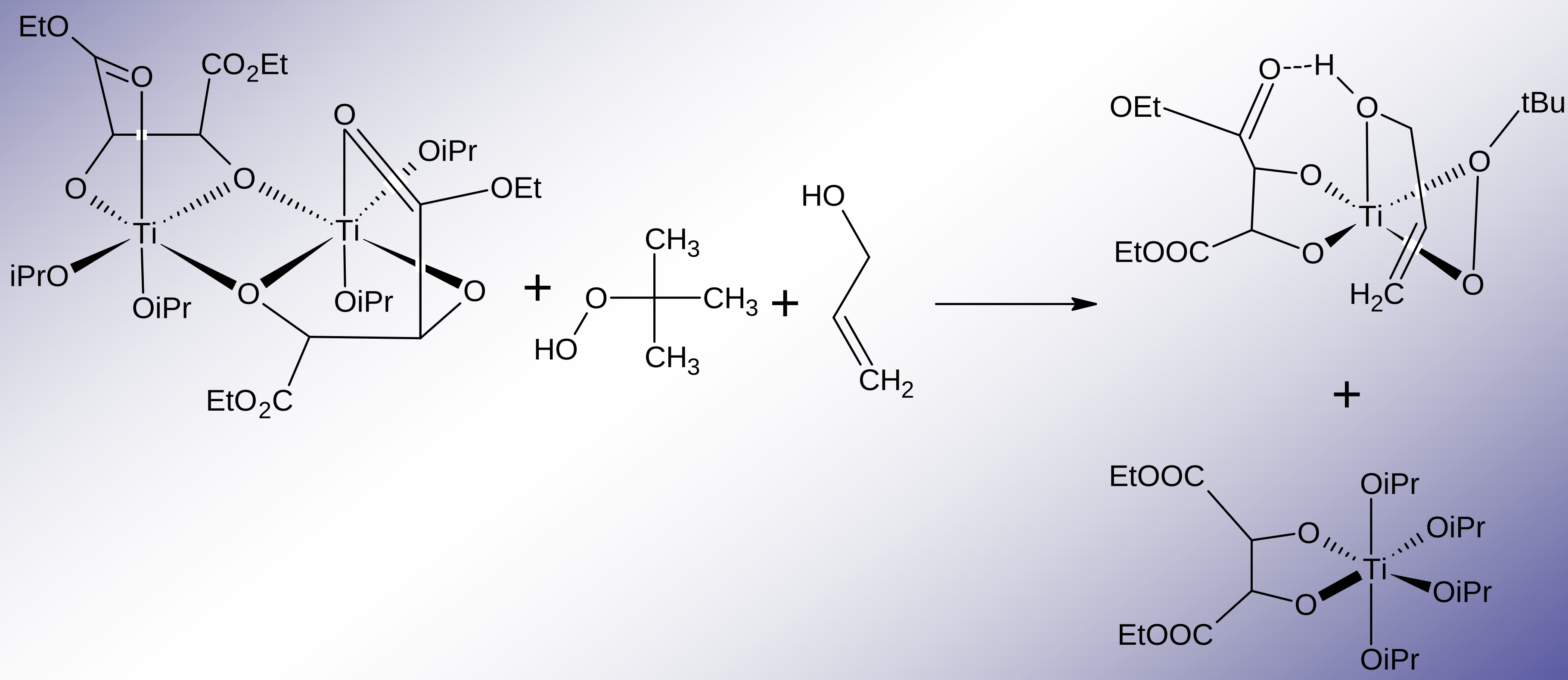


Diethyl Tartrate (DET)
Chirally controls reaction

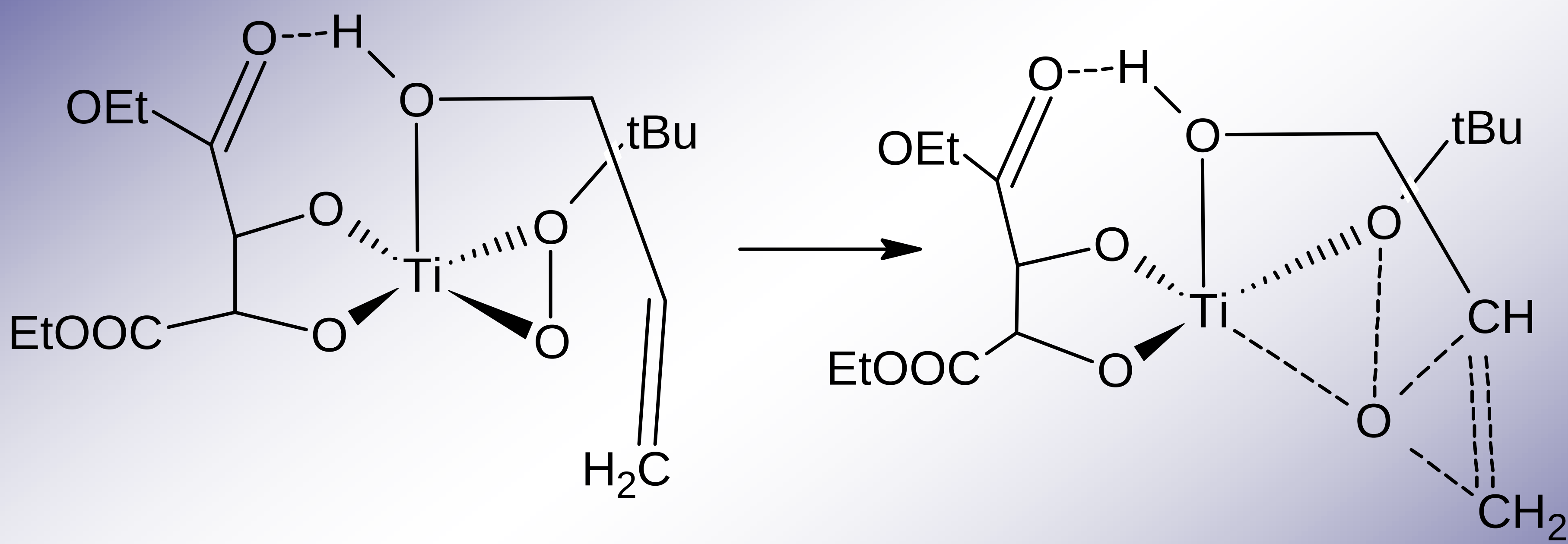


- Via rapid ligand exchange of O^{i}Pr and diethyl tartrate

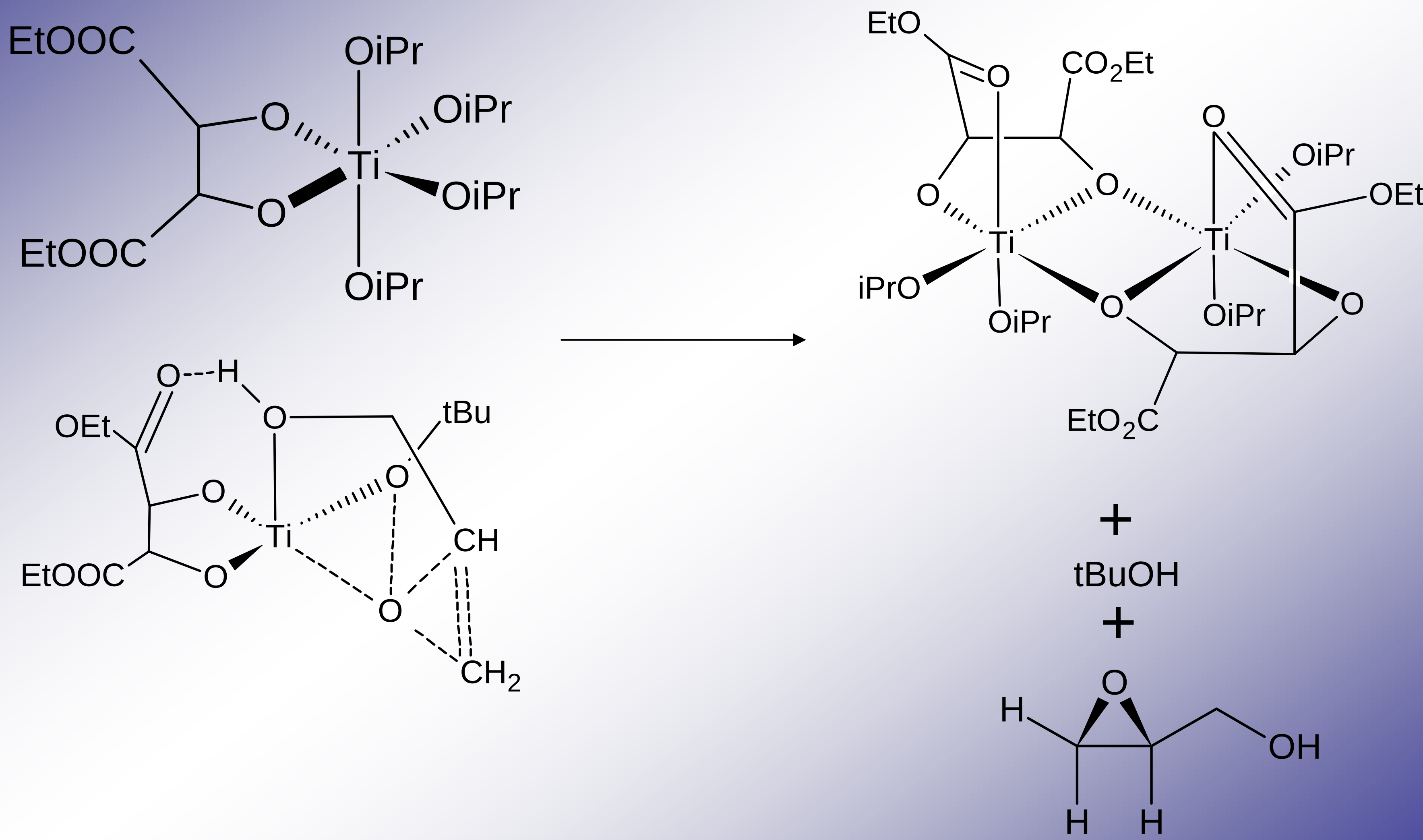
The Mechanism

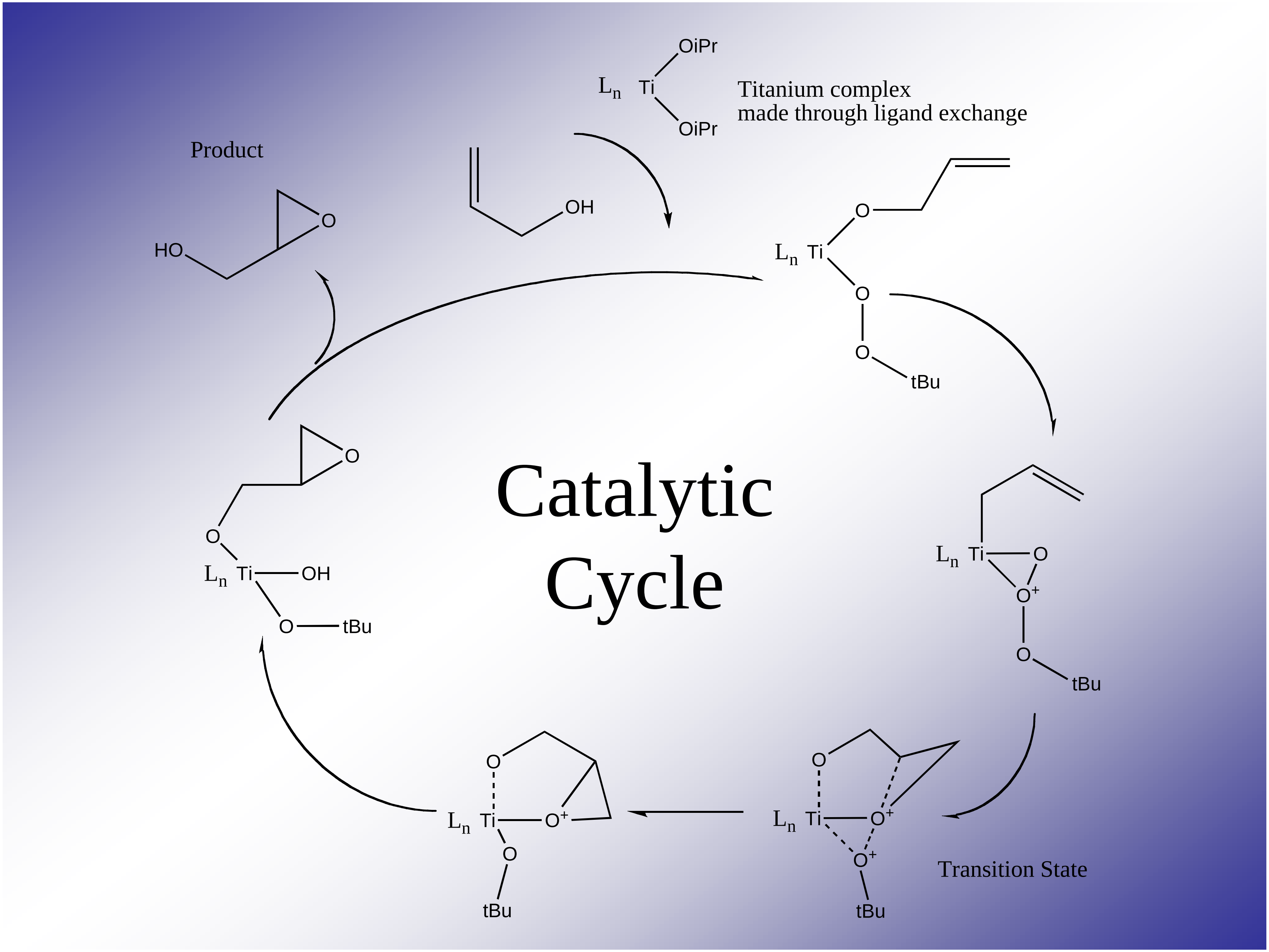


Transition State



Products





Catalytic Cycle
Titanium complex
made through ligand exchange
Product
Transition State

Uses of the Reaction

- The Sharpless Asymmetric Epoxidation converts alkenes into chirally active epoxides
- Innumerable syntheses published that use the SAE
- Chiral epoxides easily converted into:
  - 1,2 Diols
  - Make carbon-carbon bonds (stereospecifically)
  - Aminoalcohols
- Two examples considered:
  - A complex synthesis of **Venustatriol** by EJ Corey
  - Simpler synthesis of **Untenone** by Mizutani *et al.*

Venustatriol

- Marine-derived natural product discovered initially in 1986
- Found in red alga Laurencia venusta
- Derived *in vivo* from squalene, made as a triterpene
- Shown to have antiviral and anti-inflammatory properties
- Structure contains repeated polyether moieties
- Key problems: multiple stereocenters and polyether moieties.
- Corey proposed a "simple and straightforward" disconnection

Untenone

- Isolated from a marine sponge in 1993
- Exhibits inhibitory activity against mammalian DNA polymerases
- These enzymes are important for DNA replication, repair and cell divisions (cancer implications)
- Biosynthetic pathway not investigated
- The critical part of the synthesis is the introduction of a quaternary carbon center (done via **SAE**)
- The total synthesis is 15 steps