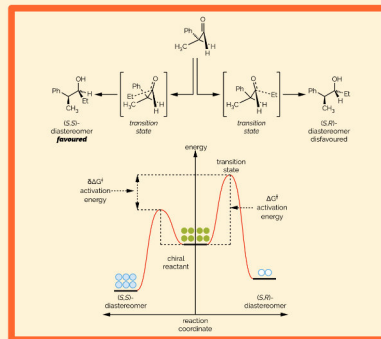


# HIGHLIGHTS

- The Bürgi-Dunitz trajectory
- The Felkin-Anh model
- The polar Felkin-Anh model
- The modified Cornforth model
- Cram chelation control



Nucleophilic addition to an aldehyde or ketone can create a new stereocenter, with a flat,  $sp^2$  hybridized carbon, transformed into a tetrahedral  $sp^3$  carbon atom. If the aldehyde or ketone already contains a stereocenter, diastereoisomers are formed, and there is the opportunity for **substrate control**. The existing stereocenter can influence which diastereotopic face of the carbonyl the nucleophile attacks.

This summary introduces the most common models for predicting or rationalizing the stereochemical outcome of addition of an achiral nucleophile to an electrophile with an  $\alpha$ -stereocenter.

## CHEMISTRY CLASSICS

### ADDITION TO THE CARBONYL GROUP

#### DIASTEREOSELECTIVE ADDITION TO ALDEHYDES & KETONES

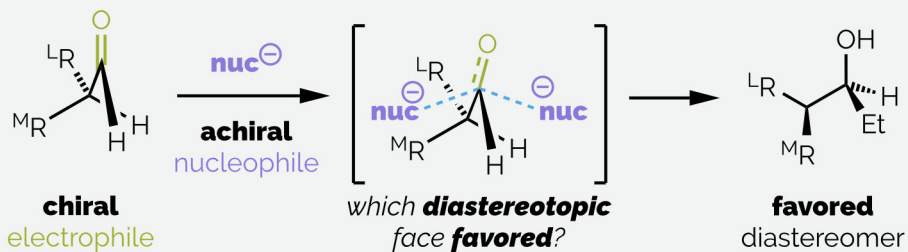


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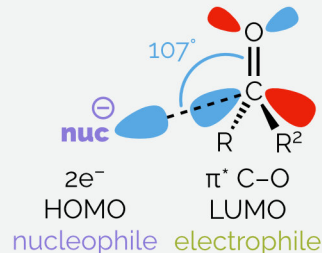
# Diastereoselective Addition to C=O

## 1. Diastereoselective addition



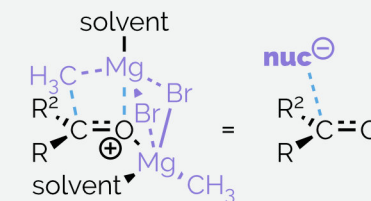
Chiral aldehyde/ketone with  $\alpha$ -stereocenter, the faces of carbonyl are **diastereotopic**. **Substrate control**, attack on one face favored preferentially giving one diastereomer.

## 2. Trajectory of attack



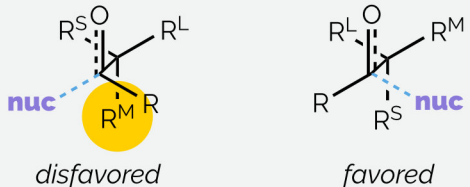
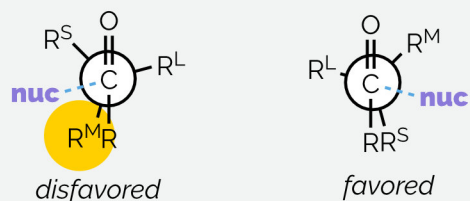
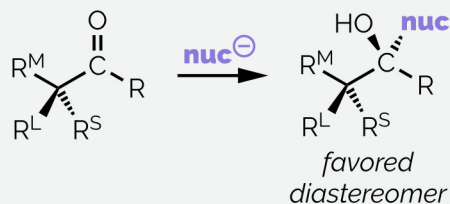
Bürgi-Dunitz angle of attack important. Causes interaction with the stereocenter.

## 3. The nucleophile



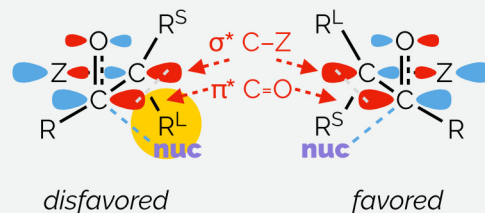
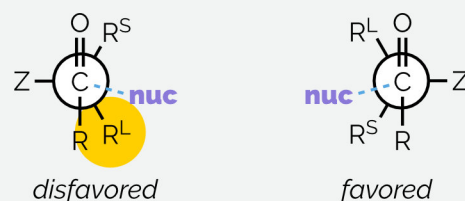
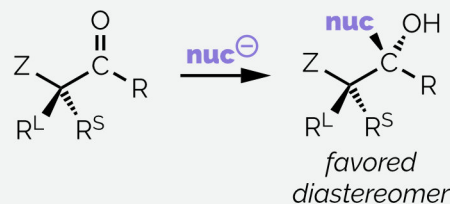
Structure of nucleophile ignored & simplified to spherical anionic group.

## 4. Felkin-Anh



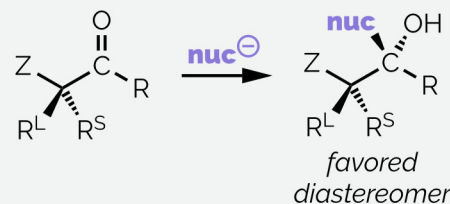
**Sterics** - Largest group ( $R^L$ ) *anti*-nucleophile to stabilize transition state.  
**Favored** - nucleophile passes smaller substituent.

## 5. Polar Felkin-Anh



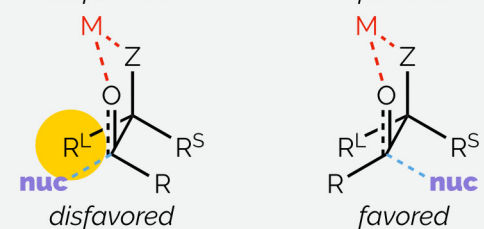
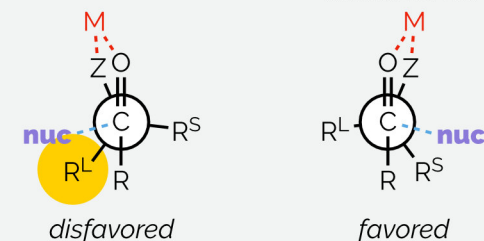
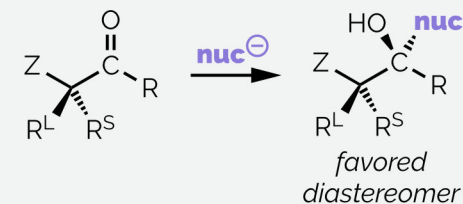
**Hyperconjugation** - electronegative Z perpendicular to C=O for delocalization.  
**Favored** - nucleophile passes smaller substituent.

## 6. Modified Cornforth



**Electrostatics** - minimization of dipole within transition state.  
**Favored** - electronegative Z opposes C=O & nucleophile *anti* largest group  $R^L$ .

## 7. Cram chelation



**Sterics** - Lewis acid M coordinates C=O and Z, locking conformation of substrate.  
**Favored** - nucleophile approaches passed smallest substituent  $R^S$ .