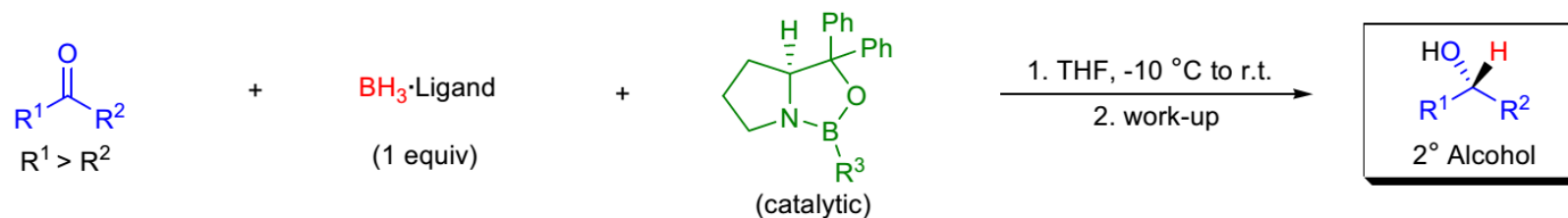


# COREY-BAKSHI- SHIBATA REDUCTION

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(CBS REDUCTION)

# Importance



R<sup>1-2</sup> = alkyl, aryl; Ligand: THF, Me<sub>2</sub>S, 1,4-thioxane, diethylaniline; R<sup>3</sup> = H, alkyl

# Importance

In 1981, S. Itsuno and co-workers were the first to report that stoichiometric mixtures of chiral amino alcohols and borane-tetrahydrofuran complex ( $\text{BH}_3\cdot\text{THF}$ ) reduced achiral ketones to the corresponding chiral secondary alcohols enantioselectively and in high yield.

Several years later, E.J. Corey and co-workers showed that the reaction of borane ( $\text{BH}_3$ ) and chiral amino alcohols leads to the formation of oxazaborolidines, which were found to catalyze the rapid and highly enantioselective reduction of achiral ketones in the presence of  $\text{BH}_3\cdot\text{THF}$ .

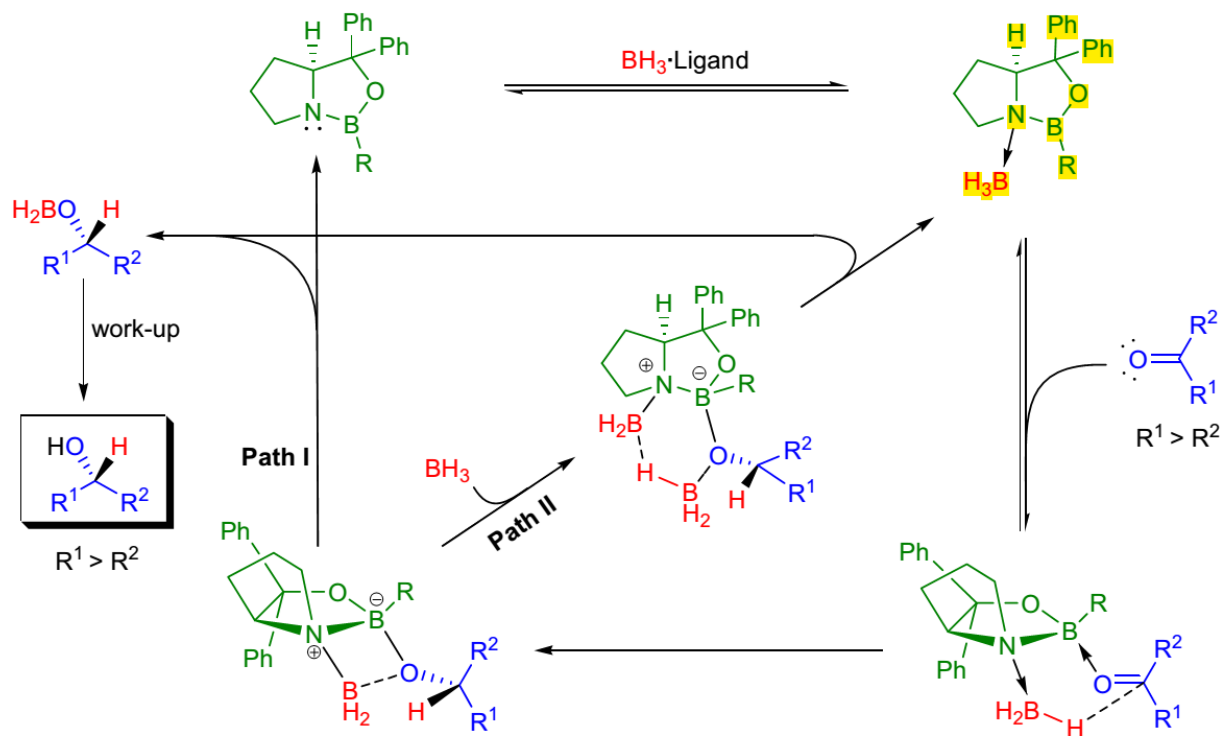
The enantioselective reduction of ketones using catalytic oxazaborolidine is called the Corey-Bakshi-Shibata reduction or CBS reduction.

# advantage

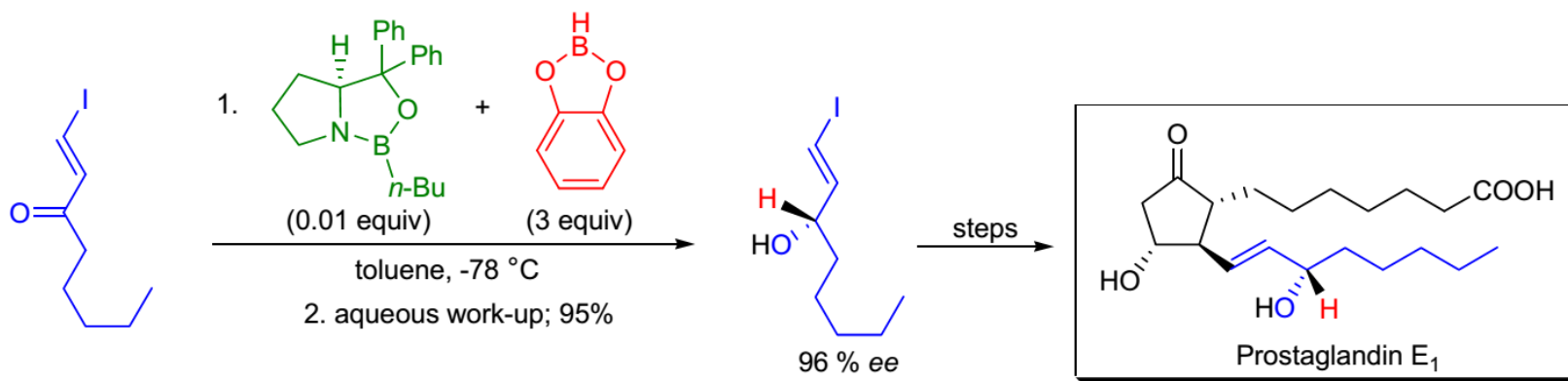
- ease of preparation
- air and moisture stability
- short reaction times (high catalyst turnover)
- high enantioselectivity
- typically high yields
- recovery of catalyst precursor by precipitation as the HCl salt
- prediction of the absolute configuration from the relative steric bulk of the two substituents attached to the carbonyl group

# Mechanism

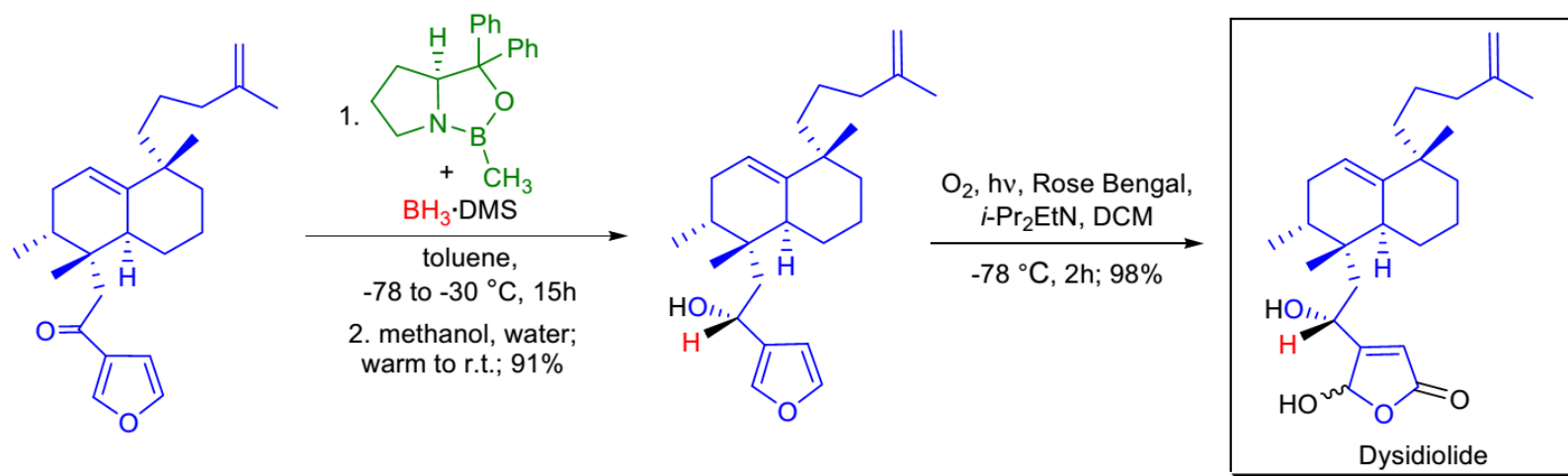
The first step of the mechanism is the coordination of  $\text{BH}_3$  (Lewis acid) to the tertiary nitrogen atom (Lewis base) of the CBS catalyst from the  $\alpha$ -face.<sup>27</sup> This coordination enhances the Lewis acidity of the endocyclic boron atom and activates the  $\text{BH}_3$  to become a strong hydride donor. The CBS catalyst-borane complex then binds to the ketone at the sterically more accessible lone pair (**the lone pair closer to the smaller substituent**) *via* the endocyclic boron atom. At this point the ketone and the coordinated borane in the vicinal position are *cis* to each other and the unfavorable steric interactions between the ketone and the CBS catalyst are minimal. The face-selective hydride transfer takes place *via* a six-membered transition state.<sup>24,26</sup> The last step (regeneration of the catalyst) may take place by two different pathways (**Path I or II**).<sup>25,19,21</sup>



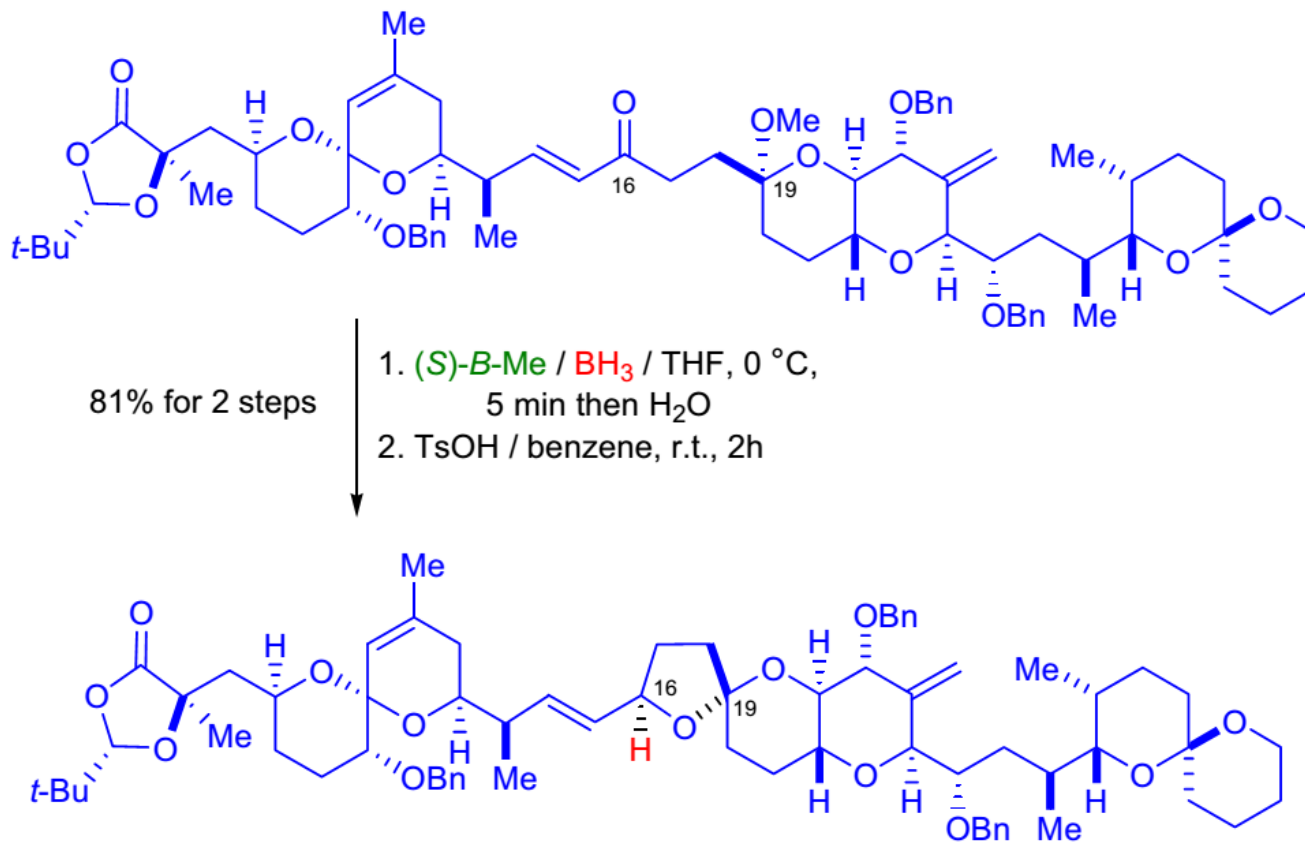
# Synthetic Applications



# Synthetic Applications



# Synthetic Applications





Thanks