Corey-Bakshi-Shibata Reduction

Name Reaction

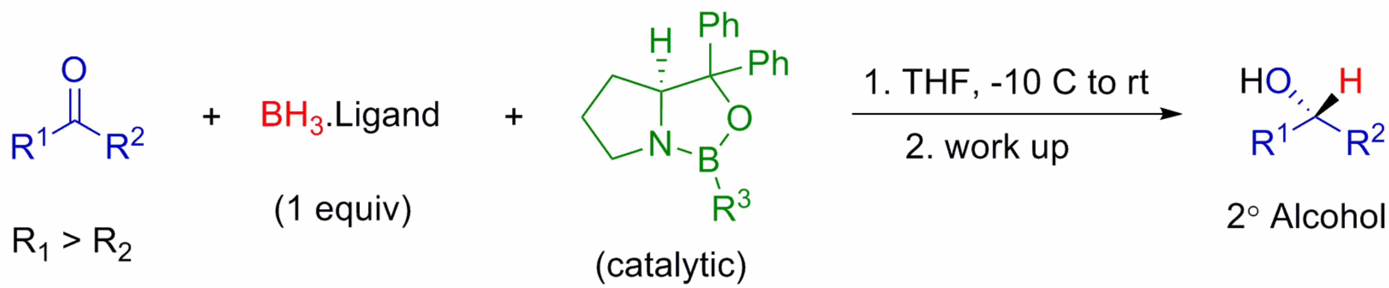
Nilanjana Majumdar

02.27.09

Outline

- Introduction
- Background
- CBS Reaction
- Application to Synthesis

Introduction



R^{1-2} = alkyl, aryl; Ligand: THF, Me_2S, 1,4-thioxane, diethylaniline; R^3 = H, alkyl

- Born: 12th July, 1928 in Methuen, Massachusetts, USA
- Bachelors Degree in 1948 and Ph. D. in 1951 from MIT
- Faculty in University of Illinois at Urbana-Champaign in 1951
- Faculty in Harvard University in 1959
- Wolf Prize in Chemistry in 1986
- Japan Prize in 1989
- Nobel Prize in Chemistry in 1990 *"for his development of the theory and methodology of Organic Synthesis"*, specifically retrosynthetic analysis
- Priestly Medal in 2004

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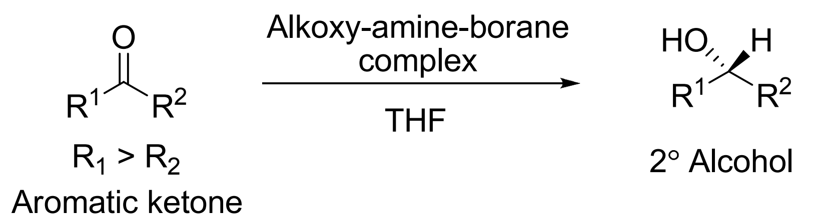
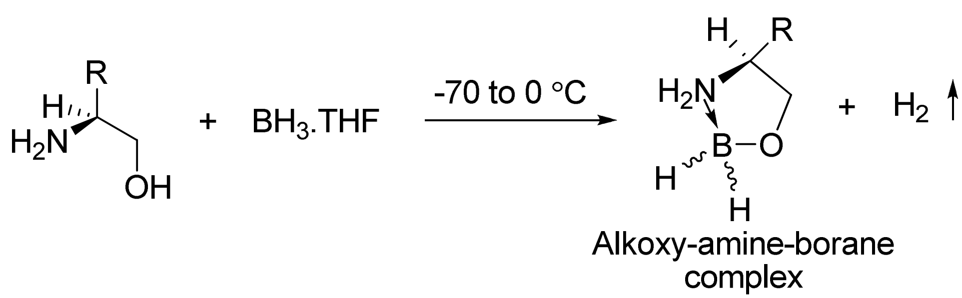
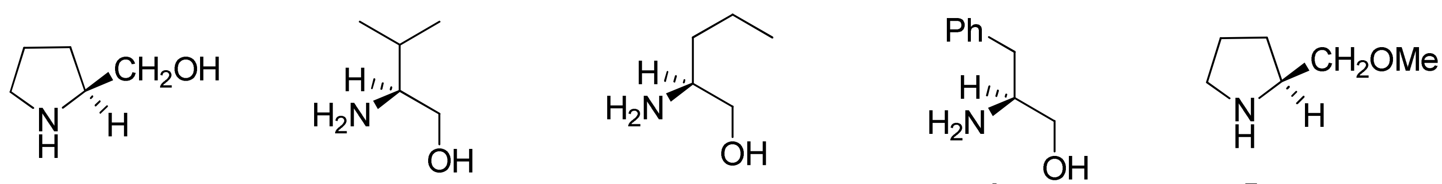
Background

Previous work by Itsuno and co-workers:



[complex] : [ketone] = 1 : 0.8

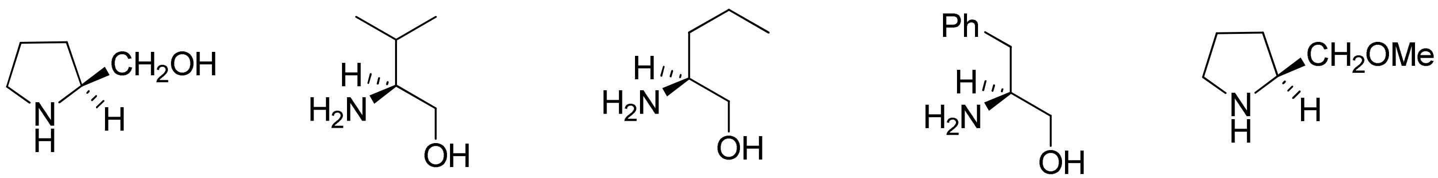




1 **2** **3** **4** **5**

Itsuno, S.; Hirao, A.;Nakahama, S.; Yamazaki, N. *J. Chem Soc., Chem. Commun.* **1981**, 315

Background



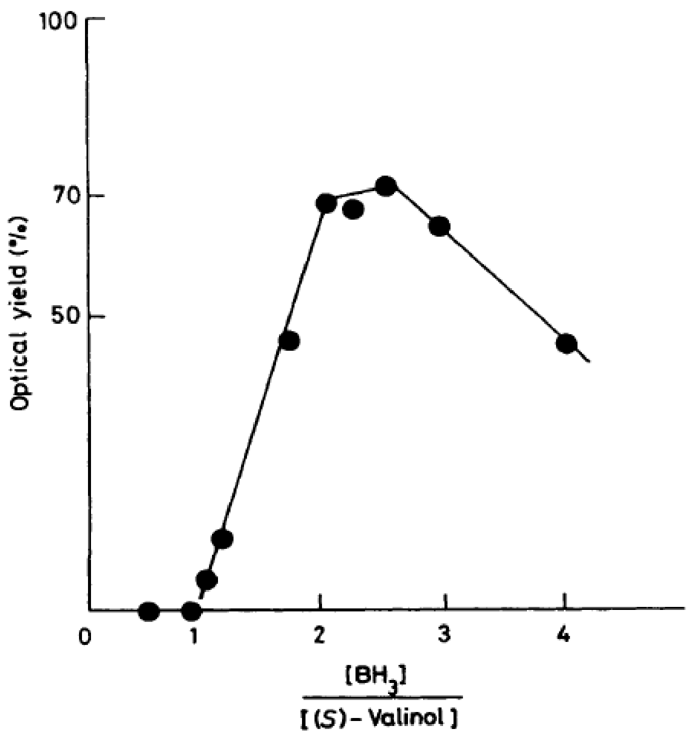
1 2 3 4 5

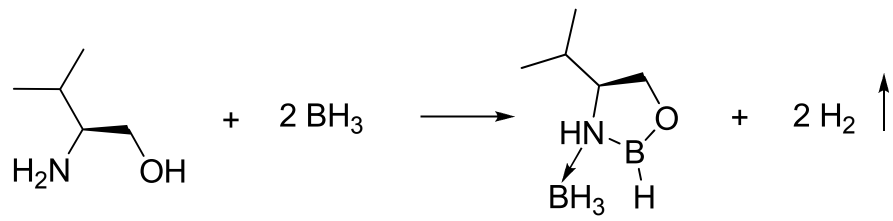
Entry	Amino-alcohol	Ketone	Solvent	Yield (%)	$[\alpha]_D^{20}/°$	Optical yield (%)	Absolute configuration
1	(**1**)	EtCOPh	THF	99	+20.74	44	(*R*)
2	(**1**)	EtCOPh	THF	93	+21.49	46	(*R*)
3	(**1**)	EtCOPh	C_6H_6	100	+3.41	7.3	(*R*)
4	(**1**)	EtCOPh	$MeOH-H_2O$ (2:1)	100	+7.80	17	(*R*)
5	(**1**)	EtCOPh	$CHCl_3$	88	–8.29	18	(*S*)
6	(**1**)	MeCOPh	THF	98	+23.30	44	(*R*)
7	(**2**)	MeCOPh	THF	99	+25.60	49	(*R*)
8	(**2**)	EtCOPh	THF	99	+27.93	60	(*R*)
9	(**2**)	β-Naphthyl methyl ketone	THF	93	+21.49	52	(*R*)
10	(**3**)	EtCOPh	THF	100	+19.08	41	(*R*)
11	(**4**)	EtCOPh	THF	100	+17.59	37	(*R*)
12	(**5**)	EtCOPh	THF	99	+7.43	16	(*R*)

OH group plays an important role

Itsuno, S.; Hirao, A.;Nakahama, S.; Yamazaki, N. *J. Chem Soc., Chem. Commun.* **1981**, 315

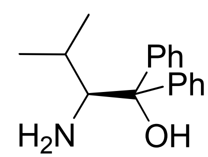
Background





Important observations:

- (S)-Valinol gave best selectivity
- Optimum [BH_3] : [(S)-Valinol] is 2:1 to 3:1
- Structure of active complex responsible for asymmetric reduction
- Amino alcohol can be recovered after reaction and recycled
- (S)-2-amino-3-methyl-1,1-diphenylbutan-1-ol showed better selectivity



Itsuno, S.; Hirao, A.; Nakahama, S.; Yamazaki, N. *J. Chem. Soc. Perkin Trans. 1* **1983**, 1673

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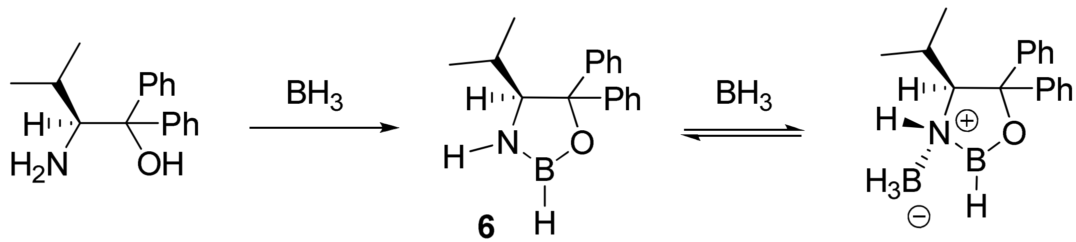
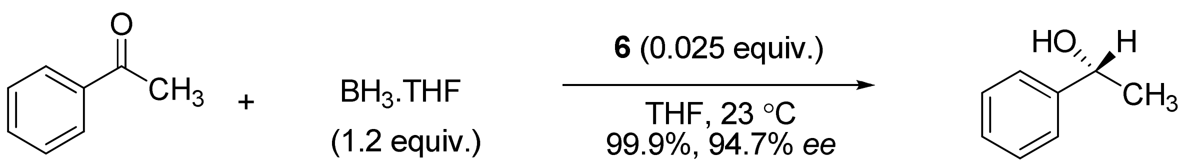
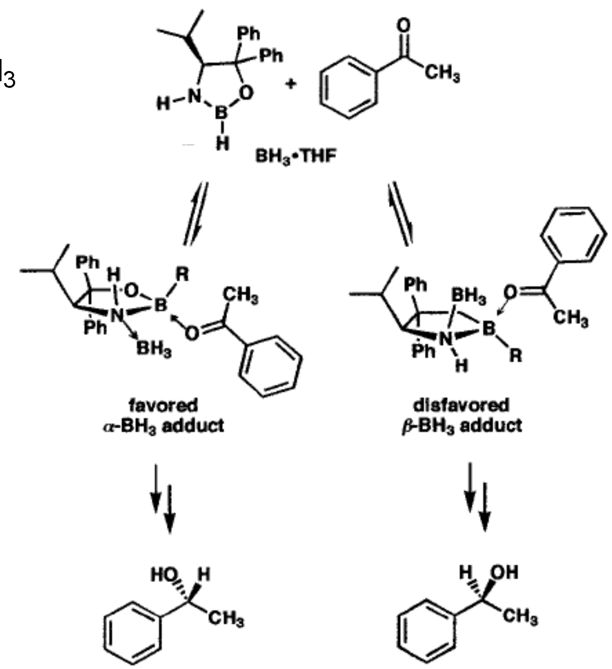
Development of CBS Catalyst





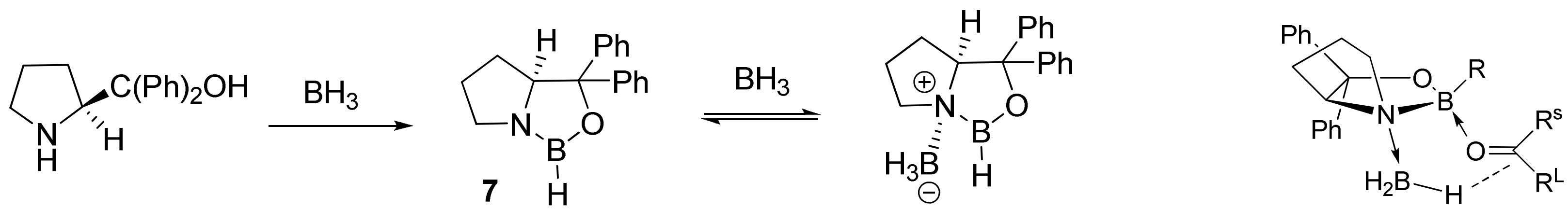


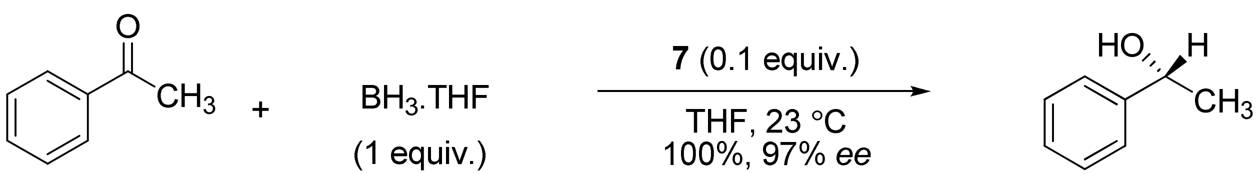
From possible mechanistic pathway :

Competition between *α*-BH_3 adduct and *β*-BH_3 adduct decreases selectivity

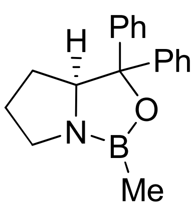
Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551

Development of CBS Catalyst





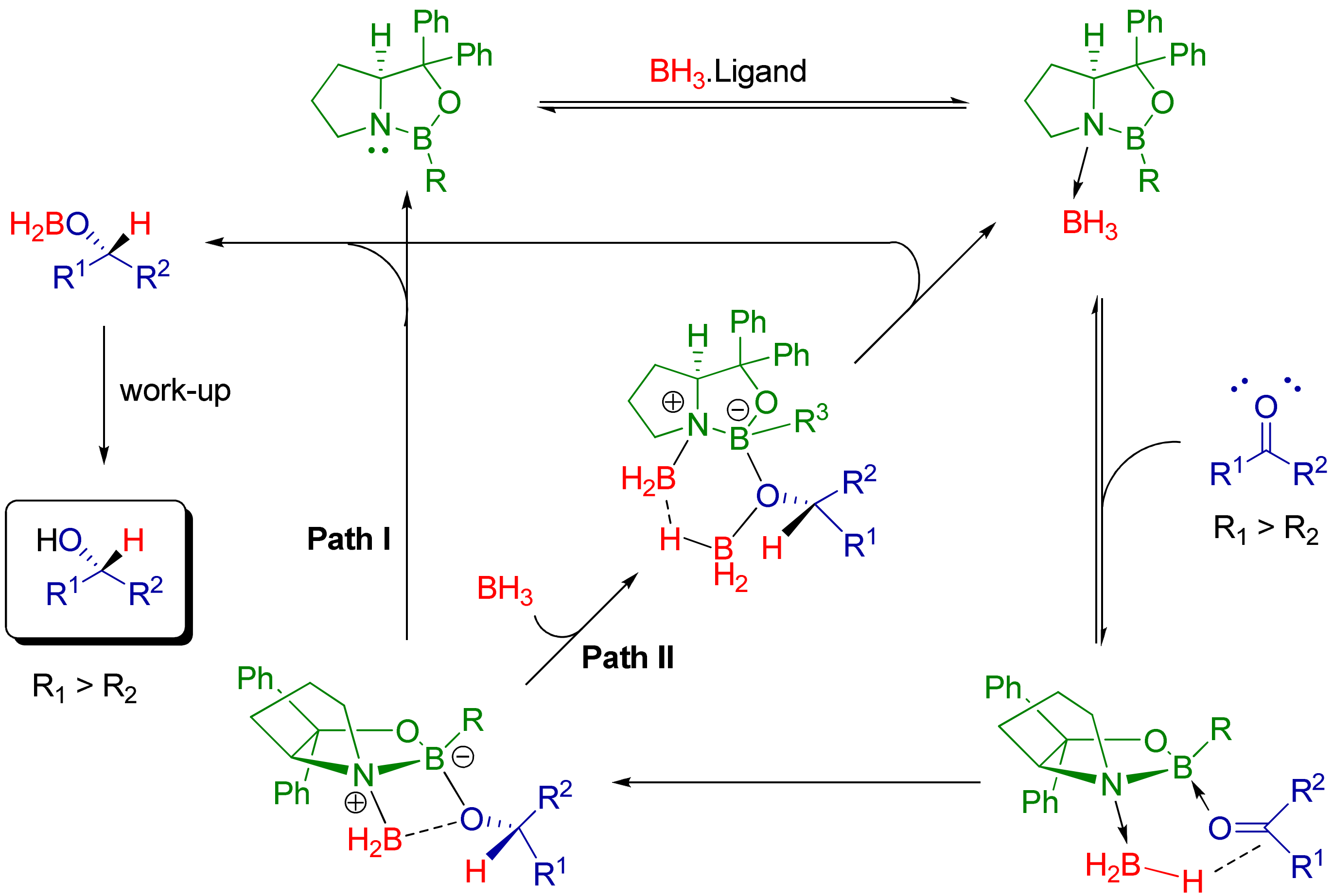
Better selectivity



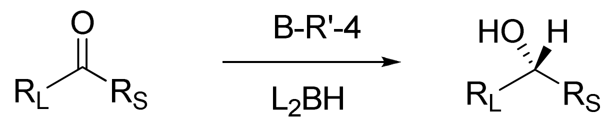
Further improvement in catalyst:

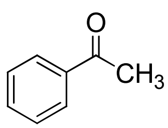
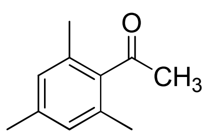
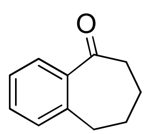
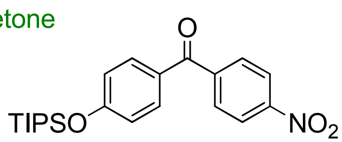
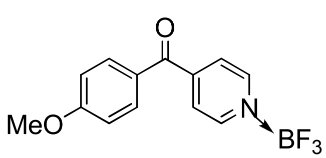
1. B-H catalyst is extremely air and moisture sensitive
2. B-Me catalyst is less sensitive
3. Preparation is easier
4. Same or higher enantioselectivity

Mechanism

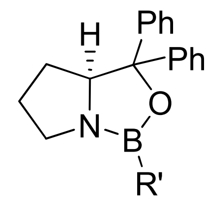


Scope of CBS Reaction



Ketone	ee [%]	Catalyst	L_2BH	T [°C]
R_L R_S				
Aryl-alkyl ketone 	99	*B*-Me-**4**	BDEA	30
	99.7	*B*-*n*Bu-**4**	CB	-78
	99	*B*-Me-**4**.BH_3	BMS	30
Diaryl ketone 	95	*B*-*n*Bu-**4**	CB	-78
	93	*B*-*n*Bu-**4**	CB	-78

Electronic Effect



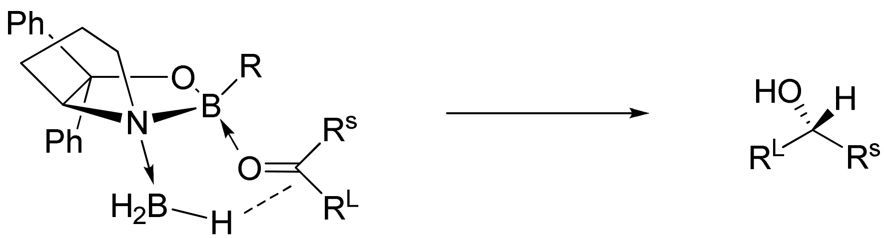
(B-R'-4)

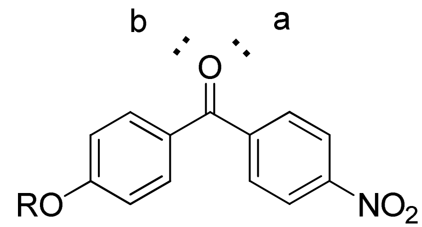
Abbreviations

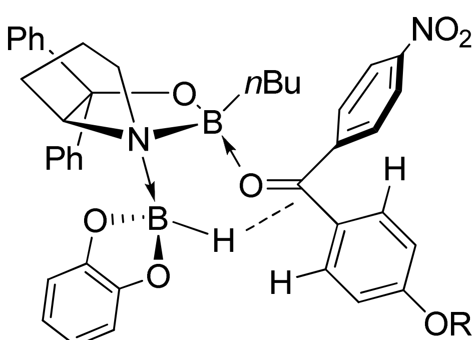
BDEA = BH_3.diethylaniline
CB = Catechol borane
BMS = $BH_3.Me_2S$

Corey, E. J.; Helal, C. J. *Angew. Chem.,Int. Ed. Engl.* **1998**, *37*, 1986

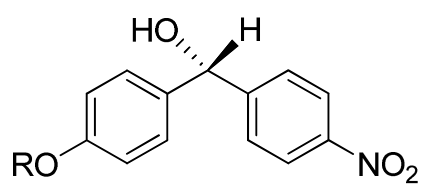
Explanation for Electronic Effect

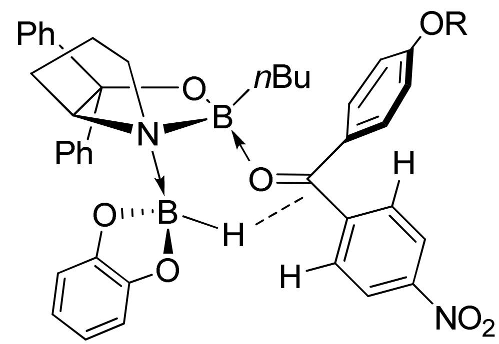






Favored





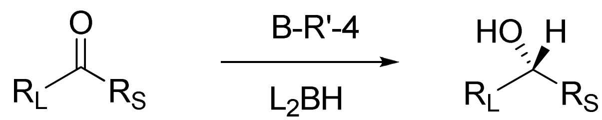
Disfavored

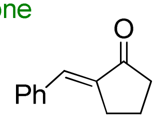
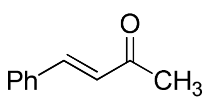
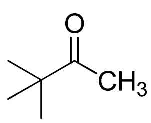
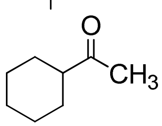
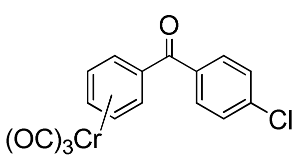
Reasons for the favored intermediate:

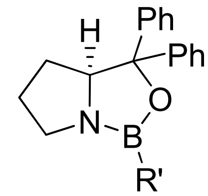
- +R effect makes ketone-boron coordination stronger
- -I effect makes carbonyl carbon more nucleophilic

E. J. Corey, C. J. Helal, *Tetrahedron Lett*. **1995**, *36*, 9153

Scope of CBS Reaction



Ketone	*ee* [%]	Catalyst	L_2BH	*T* [°C]
R_L R_S				
Cyclic α,β-enone				
	96	*B*-Me-**4.**BH_3	BMS	-20
Acyclic α,β-enone				
	97	*B*-*n*Bu-**4**	CB	-78
Dialkyl ketone				
	97.4	*B*-Me-**4**	BDEA	20
	≥99	*B*-Me-**4**	BDEA	20
Ketones in ligands of metal complexes				
	98	*B*-*n*Bu-**4**	CB	-40



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BMS = $BH_3.Me_2S$

Corey, E. J.; Helal, C. J. *Angew. Chem.,Int. Ed. Engl.* **1998**, *37*, 1986

Advantages of CBS Catalyst

- Ease of preparation
- Air and moisture stability
- Short reaction time
- 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

Corey, E. J.; Helal, C. J. *Angew. Chem.,Int. Ed. Engl.* **1998**, *37*, 1986

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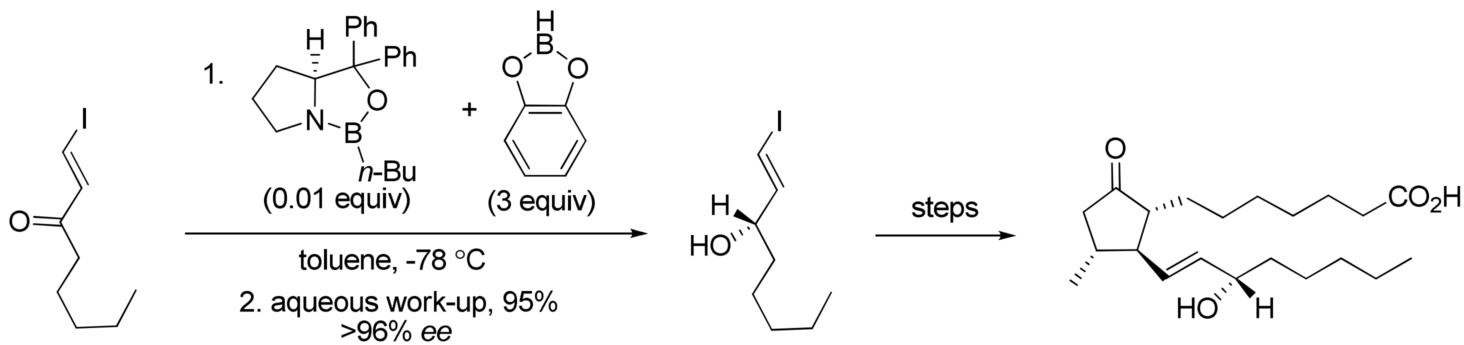
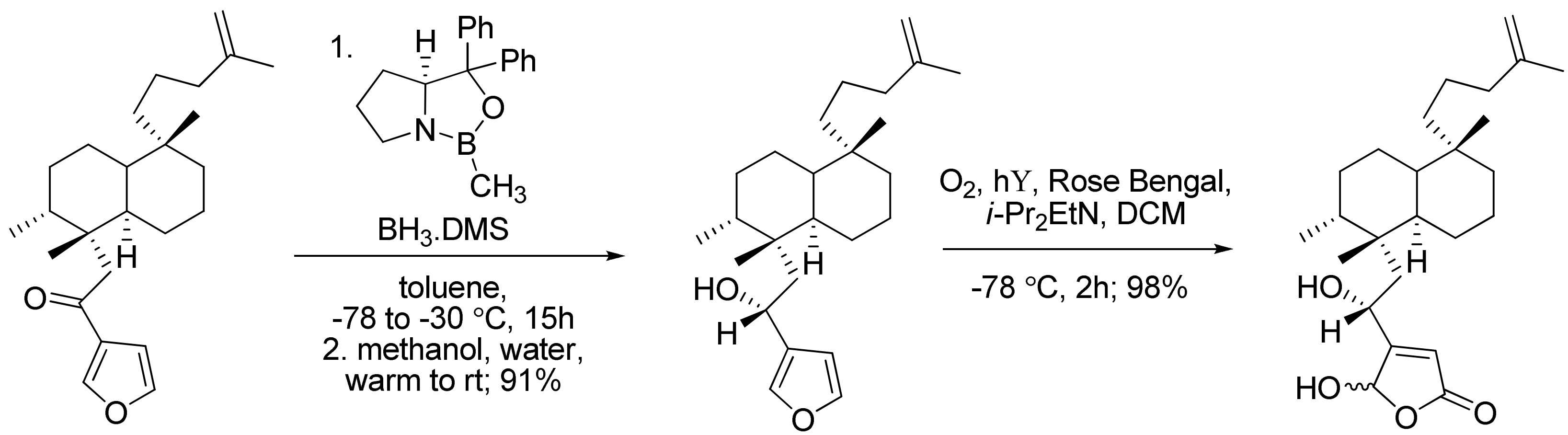
Application to Synthesis



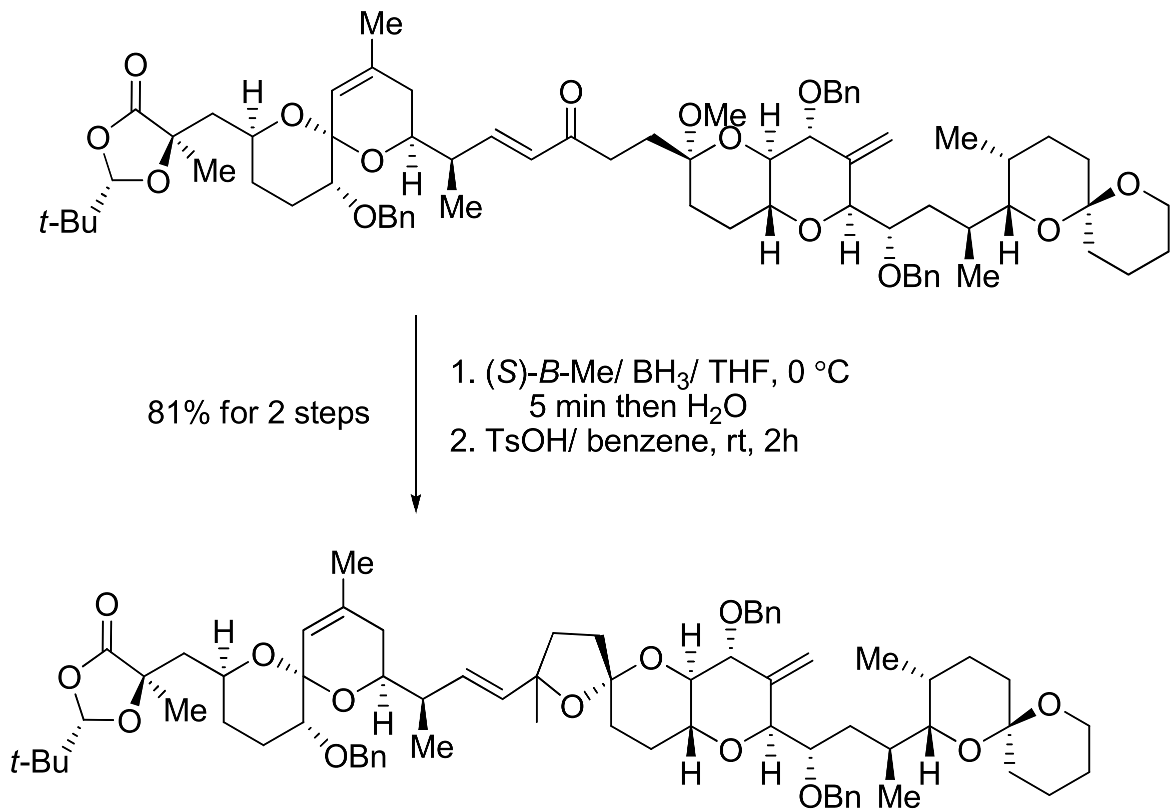
Prostaglandin E_1



Dysidiolide

Rodriguez, A.; Nomen, M.; Spur, B. W. Godfroid, J.-J. *Eur. J. Org. Chem.* **1999**, 2655
Corey, E. J.; Roberts, B. E. *J. Am. Chem. Soc.* **1997**, *119*, 12425

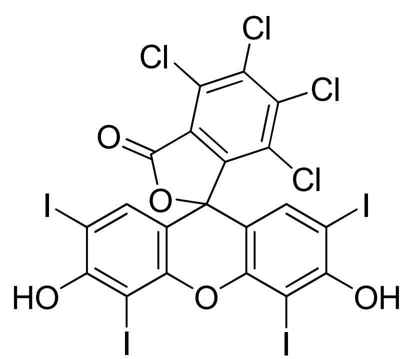
Application to Synthesis



Okadaic acid

Sabes, S. F.; Urbanek, R. A.; Forsyth, C. J. *J. Am. Chem. Soc.* **1998**, *120*, 2534

Rose Bengal



Rose Bengal is also used in synthetic chemistry to generate singlet oxygen from triplet oxygen. The singlet oxygen can then undergo a variety of useful reactions, particularly [2 + 2] cycloaddtion with alkenes and similar systems.

Optical Yield

- In a chemical reaction, the ratio of the enantiomer excess (ee) of the product over the enantiomer excess (ee) of the starting material is called the optical yield.

$$\% \text{ Optical yield} = (ee_{\text{product}} \,/\, ee_{\text{starting material}}) \times 100\%$$

- If the reaction is stereospecific and no racemization occurs, the optical yield is 100%.

Eliel, E. L.; Wilen, S. H.; Mander, L. N. In *Stereochemistry of Organic Compounds*