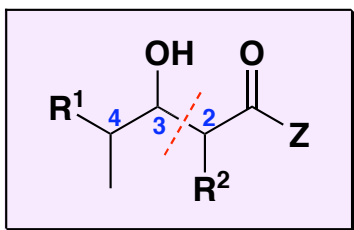


Massachusetts Institute of Technology
Organic Chemistry 5.512

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Unit 6
Stereocontrolled Aldol Reactions

- ★ Overview of the Stereochemistry of the Aldol Reaction and Substrate Control
- ★ Reagent Control: Chiral Auxiliary Strategies
- ★ Reagent Control: Chiral Controller Strategies
- ★ Reagent Control: Chiral Lewis Acid Catalyzed Aldol Reactions



The Aldol Retron

General Review on Recent Advances

"Current Progress in the Asymmetric Aldol Addition Reaction"
Palomo, C.; Oiarbide, M.; Garcia, J. M.
Chem. Soc. Rev. **2004**, 33, 65

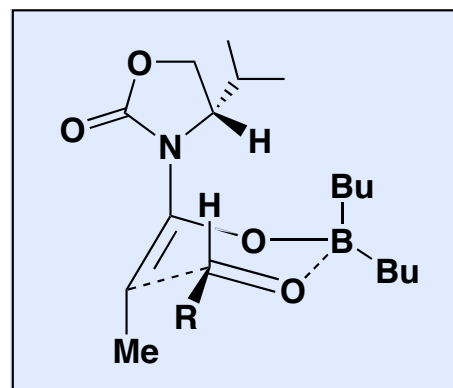
II. Chiral Auxiliary Strategies

★ 2,3-Syn Aldols



Evans Oxazolidinone
Boron Enolates

Gage, J. R.; Evans, D. A.
Org. Synth. Coll. Vol. **8**, 339



Review

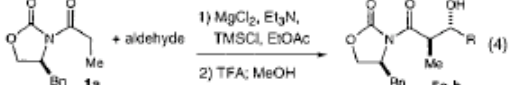
"Asymmetric Aldol Reactions Using Boron Enolates"
Cowden, C. J.; Paterson, I. *Organic Reactions* **1997**, 51, 1

★ 2,3-Anti Aldols

(1) Evans Dones

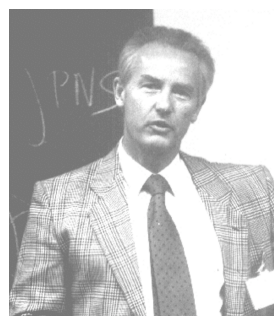
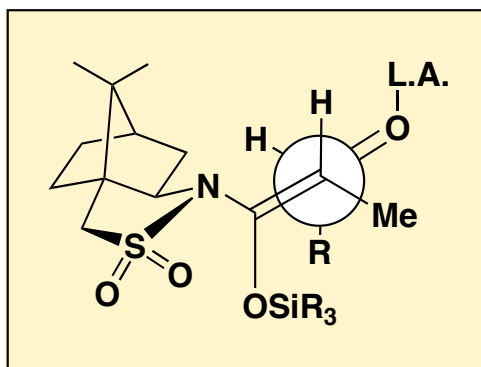
D. A. Evans et al.
J. Am. Chem. Soc. **2002** 124, 392
 and *Org. Lett.* **2002**, 4, 1127

Table 2. Mg-Catalyzed *anti*-Aldol Reactions of **1a** with Representative Aldehydes (Eq 4)^a

				
aldehyde	product	procedure ^{a,b}	dr ^c	yield (%) ^d
	X = Me 5a	A	24:1	-
	X = OMe 5b	A	32:1	91
	X = NO ₂ 5c	B	7:1	71
	X = Ph, Y = H 5d	B	21:1	92
	X = Ph, Y = Me 5e	A	28:1	92
	X = H, Y = Me ^e 5f	B	16:1	77
α-naphthaldehyde	5g	A	14:1	91
furfural	5h	B	6:1	80

^a Procedure A: reactions were conducted with 1.0 equiv **1**, 0.2 equiv MgCl₂, 2.0 equiv of triethylamine, 1.5 equiv of TMSCl, 1.2 equiv of RCHO at 0.5 M in EtOAc for 24 h. ^b Procedure B: reaction conducted as in Procedure A but with 0.1 equiv MgCl₂ and the addition of 0.3 equiv of NaSbF₆ at 0.2 M in ethyl acetate. ^c Table 1 footnote b. ^d Isolated yield of a single diastereomer.

(2) Oppolzer Sultams



(3) Masamune Esters



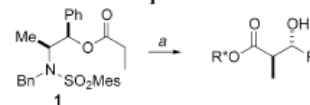
Review

"Boron-Mediated Aldol Reaction of Carboxylic Esters"

Abiko, A. *Acc. Chem. Res.* **2004**, 37, 387

see also *Org. Synth. Coll. Vol.* **10**, 55 and 343

Table 4. anti-Selective Asymmetric Aldol Reaction of Compound **1**



RCHO	yield (%)	ds for anti ^b
MeCHO	92	97:3
EtCHO	90	96:4
<i>n</i> -PrCHO	95	95:5
<i>i</i> -PrCHO	95	98:2
<i>c</i> -HexCHO	91	95:5
<i>t</i> -BuCHO	96	> 99:1
PhCHO	93	95:5
(<i>E</i>)-CH ₃ CH=CHCHO	96	98:2
CH ₂ =C(CH ₃)CHO	97	96:4
BnOCH ₂ CH ₂ CHO	94	95:5
BnOCH ₂ C(CH ₃) ₂ CHO	98	96:4

^a *c*-Hex₂BOTf (2.0 equiv), Et₃N (2.4 equiv), -78 °C for 2 h; then RCHO, -78 °C for 1 h, 0 °C for 1 h. ^b anti/syn = > 98:2; ds = diastereoselectivity.