Massachusetts Institute of Technology Organic Chemistry 5.512

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Strategies for Stereocontrolled Synthesis

☆ Reagent Control Strategies and Double Asymmetric Synthesis ☆

"What changes may organic synthesis undergo? With appropriate chiral reagents and catalysts at hand, the synthetic design of many natural (and unnatural) products will become straightforward, and as a result some of the aesthetic elements of traditional organic synthesis, as exemplified by the synthesis of erythronolide A in Section 7, may well be lost. However, the power of the new strategy has already made possible what appeared to be almost impossible even a few years ago. In this sense a new era which is characterized by the evolution from substrate-controlled to reagent-controlled organic synthesis is definitely emerging."

S. Masamune et al., "Double Asymmetric Synthesis and a New Strategy for Stereochemical Control in Organic Synthesis", *Angew. Chem. Int. Ed.* **1985**, *24*, 1.

OH Ti(OiPr)₄
TBHP
OH
$$\begin{array}{c}
Ti(OiPr)_4 \\
TBHP
\end{array}$$

$$\begin{array}{c}
Ti(OiPr)_4 \\
TBHP
\end{array}$$

$$\begin{array}{c}
OH \\
Ph \\
OO
\end{array}$$

Comparison of Substrate and Reagent Control Strategies

	Advantages	Disadvantages
Substrate Control	★ Exploits resident chirality	★ Requires strong bias in substrate
		★ Different strategy needed for each epimer
Reagent Control	★ Same strategy sometimes applicable to synthesis of both epimers	★ Not applicable if substrate has strong bias
	★ Applicable to substrates with low bias	★ Requires reagents with very strong bias