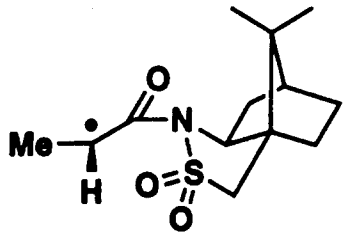
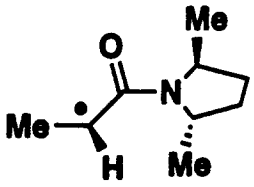
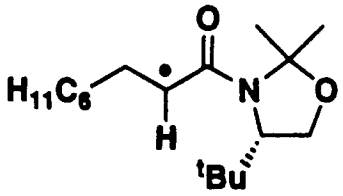
Chiral auxiliaries



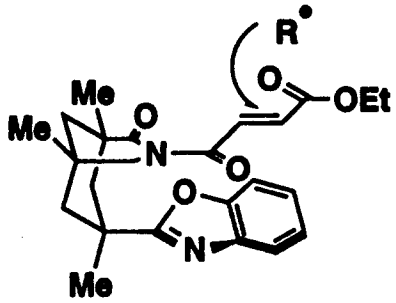
Curran; *J. Am. Chem. Soc.* **1990**, *112*, 6738.





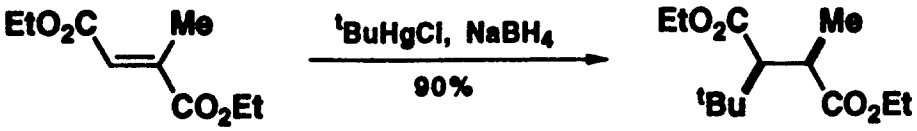
Porter; *J. Am. Chem. Soc.* **1991**, *113*, 7788.

Porter; *J. Am. Chem. Soc.* **1990**, *112*, 6740.



Curran, Rebek; *J. Am. Chem. Soc.* **1991**, *113*, 5918.

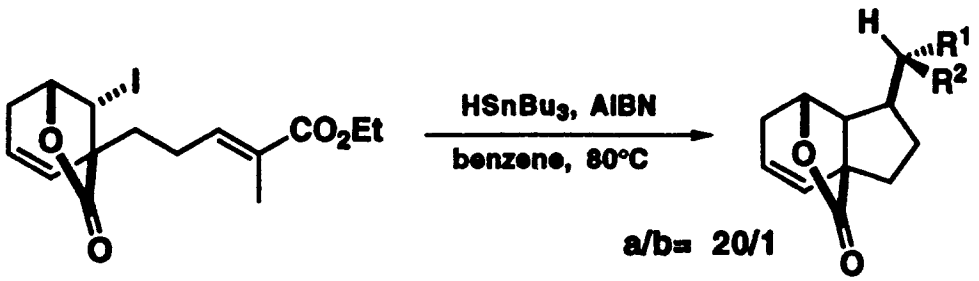
1,2- induction



threo

Giese; *Synlett* **1991**, 423.

(*threo/erythro* = 40/1)

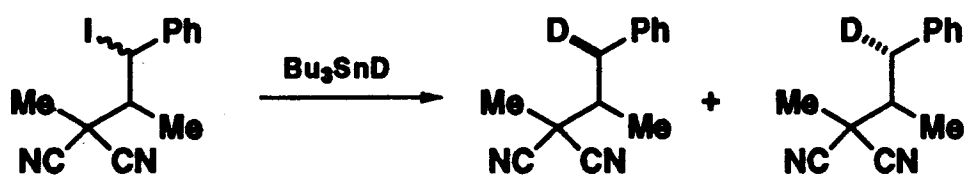


a/b= 20/1

a, R^1= **Me**, R^2= CO_2Et

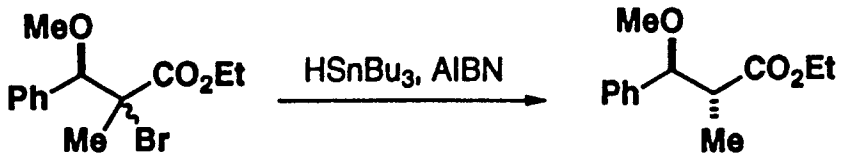
b, R^1= CO_2Et, R^2= **Me**

Hart; *J. Am. Chem. Soc.* **1989**, *111*, 7507.



4 / 1

Curran; *Tetrahedron Lett.* **1991**, *32*, 6307.

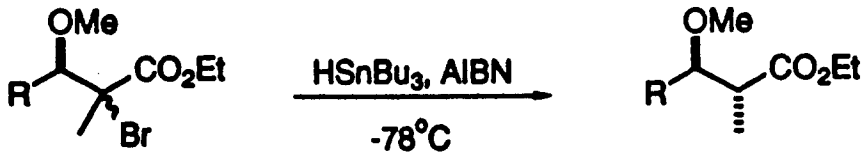


t (°C)	ratio (*threo / erythro*)
50	7/1
-10	11/1
-45	20/1
-78	32/1

Guindon et al; *Tetrahedron Lett.* **1990**, *31*, 2845.

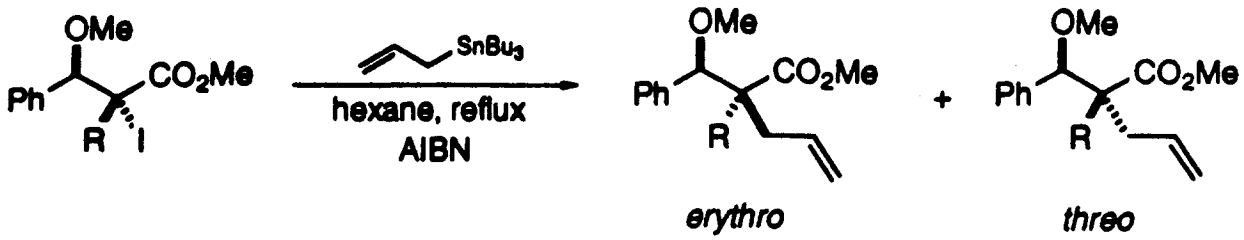
Substituent effects :

Size of the beta-alkyl group



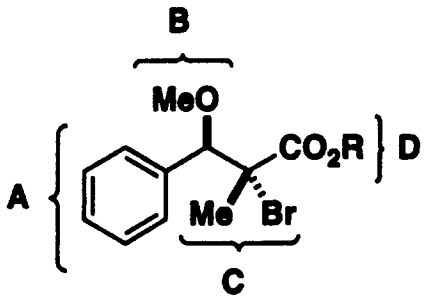
R	ratio (*threo/erythro*)
Me	3/1
^{i}pr	8/1
C_6H_{11}	12/1
Ph	32/1

Secondary *vs* tertiary radicals



erythro *threo*

R	Ratio (*erythro*/*threo*)	Yield (%)
H	5/1 (60°C)	82
	17/1 (-78°C)	75
Me	13/1 (60°C)	62
	—	No reaction



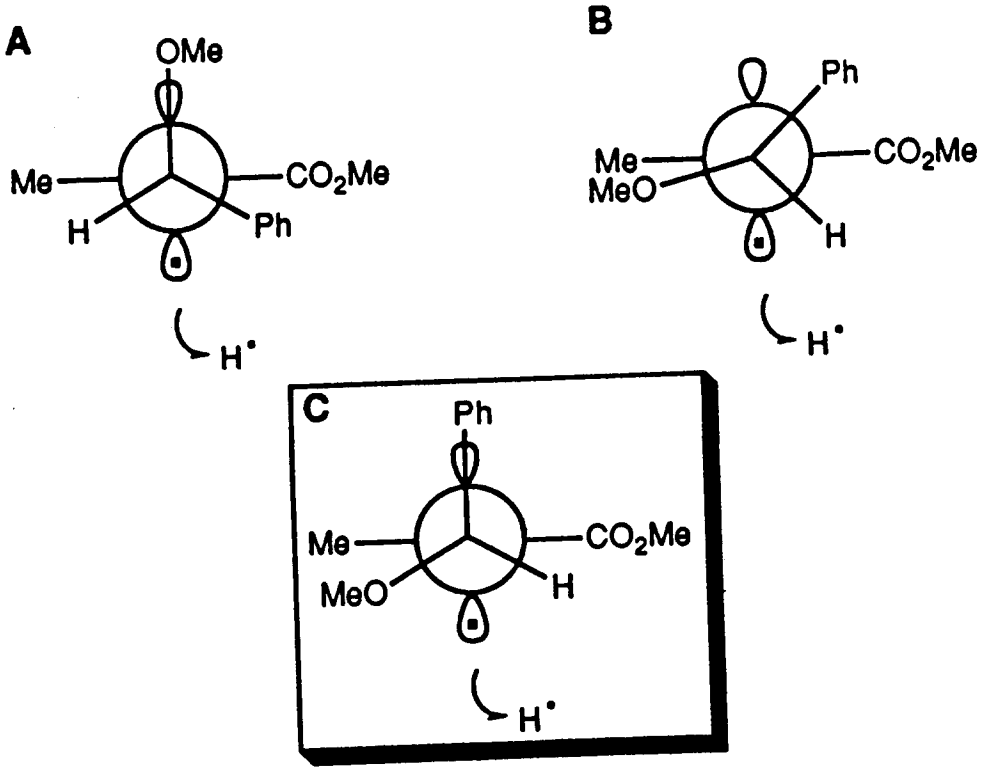
A- Steric factors improve stereoselection;

B- Electronegativity improves stereoselection;

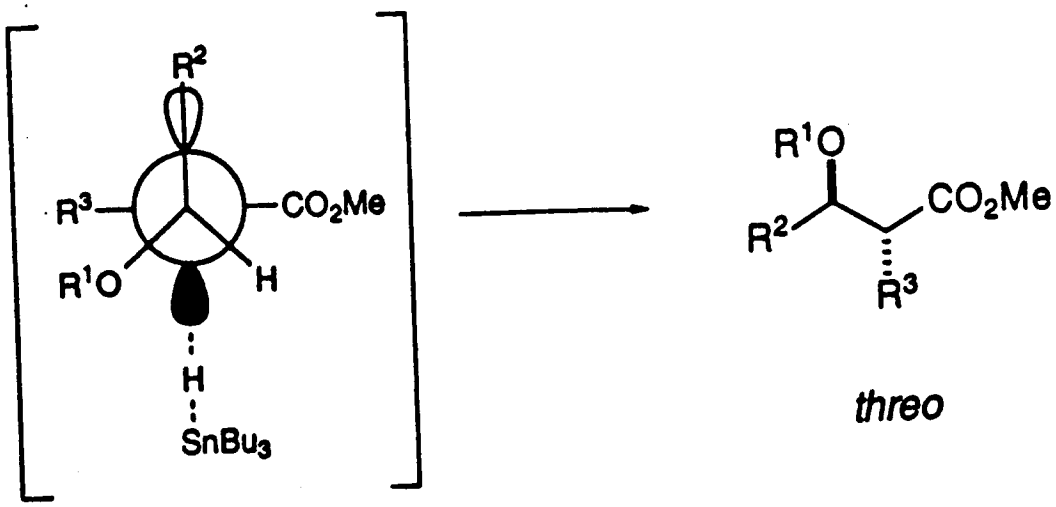
C- Stereochemistry of the carbon-halide is not important for stereoselection;

D- Carbonyl is necessary for stereoselection.

Transition state models

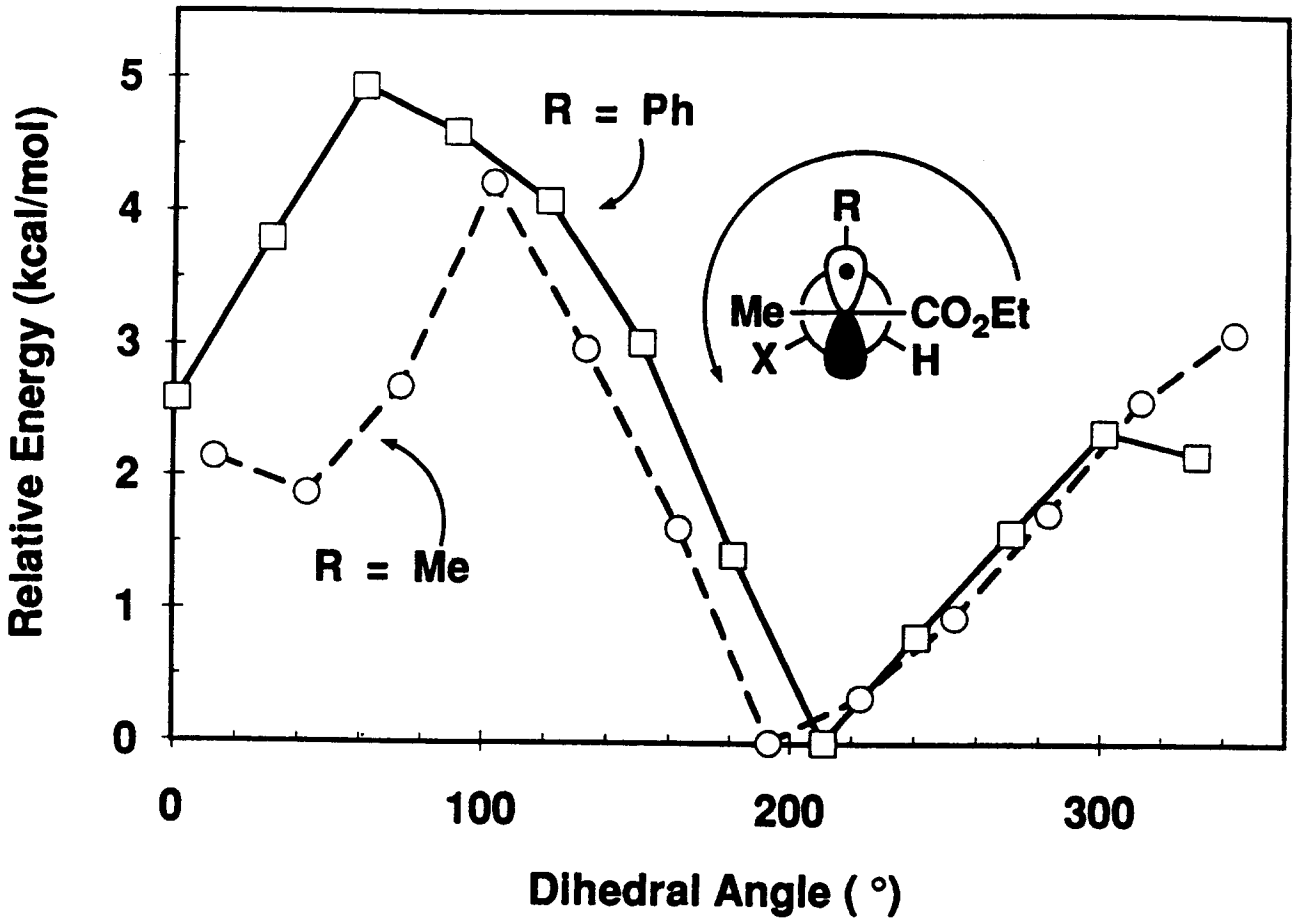


Proposed transition state :



threo

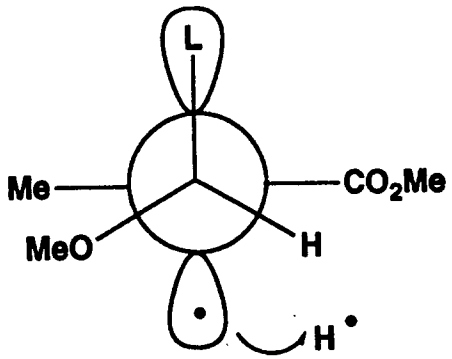
- Minimization of $A^{1,3}$ strain;
-Stabilization of the emerging σ^* orbital by hyperconjugation with the $\sigma_{C\text{-}R}2$ bond (best σ donnor);
-Minimization of dipole-dipole interactions.

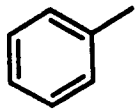
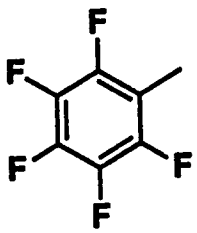
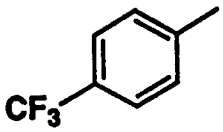
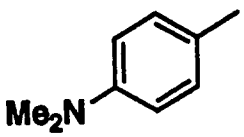


*Calculations utilized a dihedral driver approach with MOPAC 5.0 using the AM1 Hamiltonian (RHF/DOUBLET)

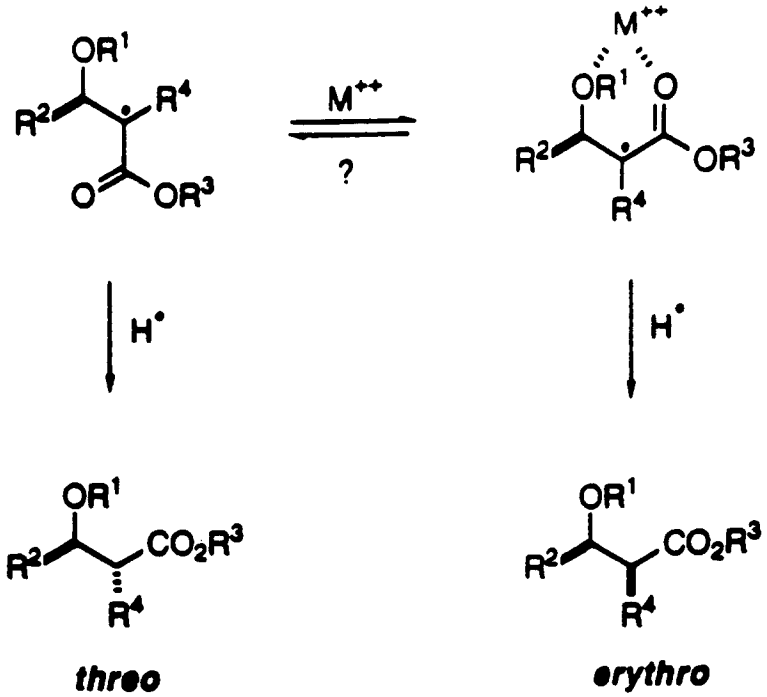
Dewar, M.J.S.; Zoebisch, E.G.; Healy, E.F.; Stewart, J.J.P. *J. Am. Chem. Soc.* **1985**, *107*, 3902

On the importance of electron donating effect



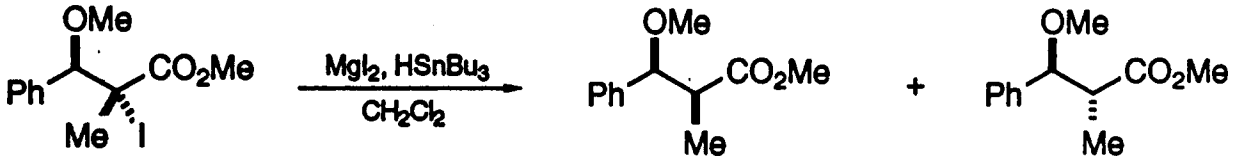
L	ratio (*threo/erythro*)
	> 25/1
	12/1
	> 25/1
	> 25/1

Access to the *erythro* diastereomer



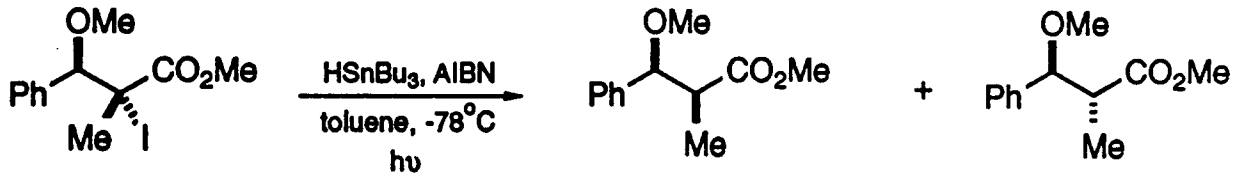
threo ***erythro***

Results



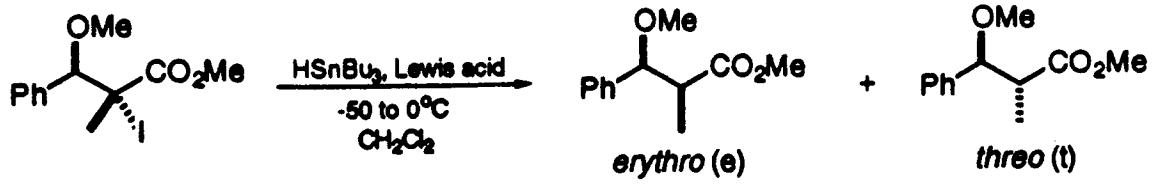
Temperature (°C)		
-78	—	—
-50	>25 (78%)	1

Recall :



1 >25

Effect of the amount of the Lewis acid upon the selectivity of the reduction

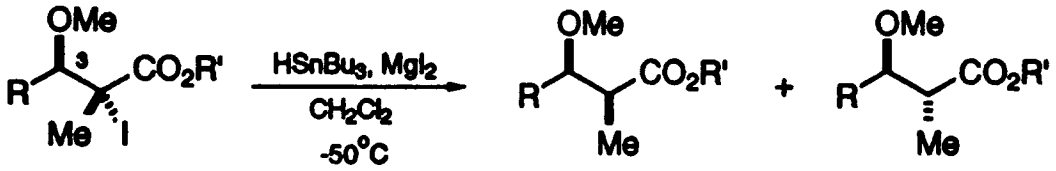


entry	eq.	Lewis acid	ratio (*e*/*t*)[a]	*e* formed(%)
1	1.0	MgI_2	>25/1	78
2	0.25	MgI_2	25/1	71
3	1.0	$MgBr_2{\cdot}OEt_2$	>25/1	84
4	0.25	$MgBr_2{\cdot}OEt_2$	>25/1	81
5	1.0	$AlCl_3$	>25/1[b]	75
6	0.24	$AlCl_3$	1/1.8	--

[a] Ratios were determined by ^1H NMR spectroscopy . [b] *threo* diastereomer could not be detected in the crude ^1H NMR .

Substituent effects

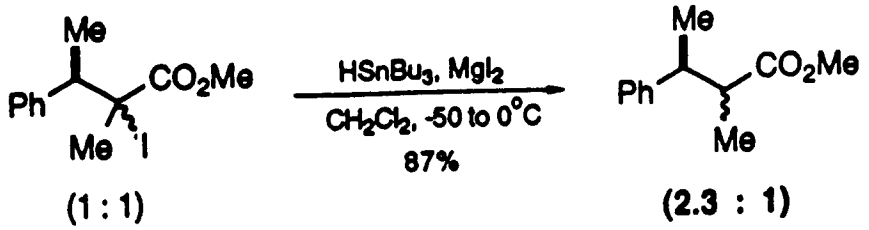
Group at the 3 position



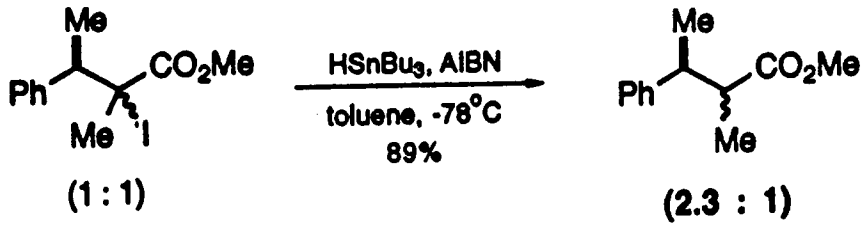
erythro (*e*) *threo* (*t*)

R	R'	Yield (%)	Ratio (*e*/*t*)	(no Lewis acid)
Me	Bn	82	5/1	(1/4; 80%)
^{i}Pr	Me	—	9/1	(1/8)
Ph	Me	78	>25/1	(1/>25)

Evidence for chelation

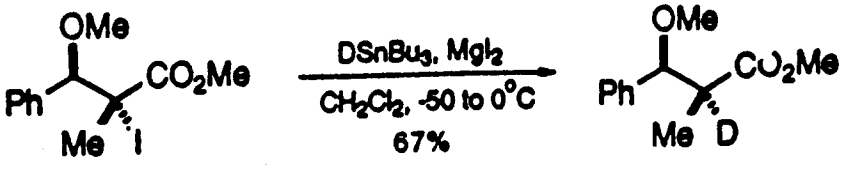


(1 : 1) (2.3 : 1)



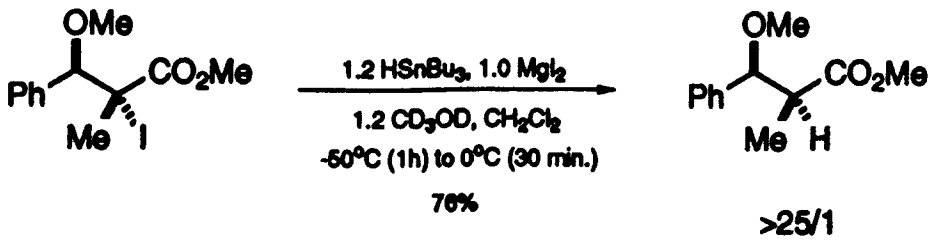
(1 : 1) (2.3 : 1)

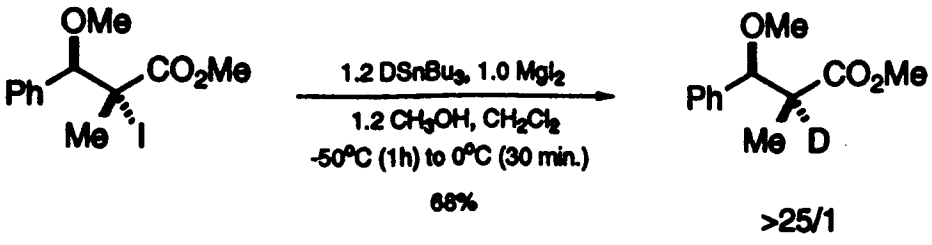
Deuteration experiment



(>25/1)

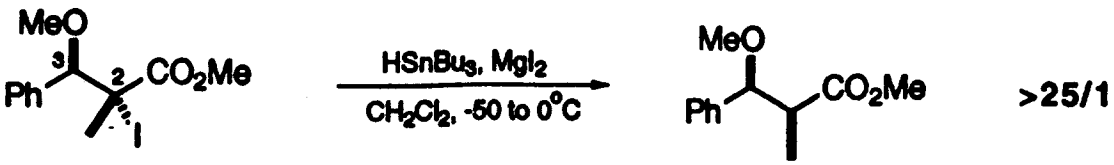
Competition experiments

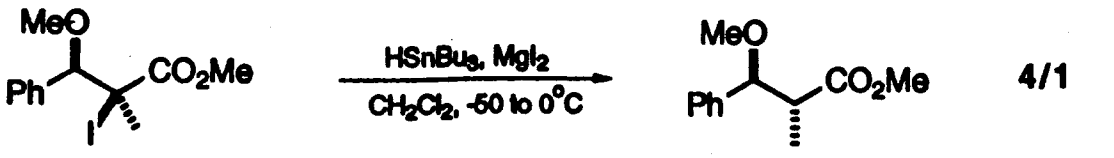




Importance of the relative stereochemistry at the 2 and 3 position

In presence of MgI_2 :

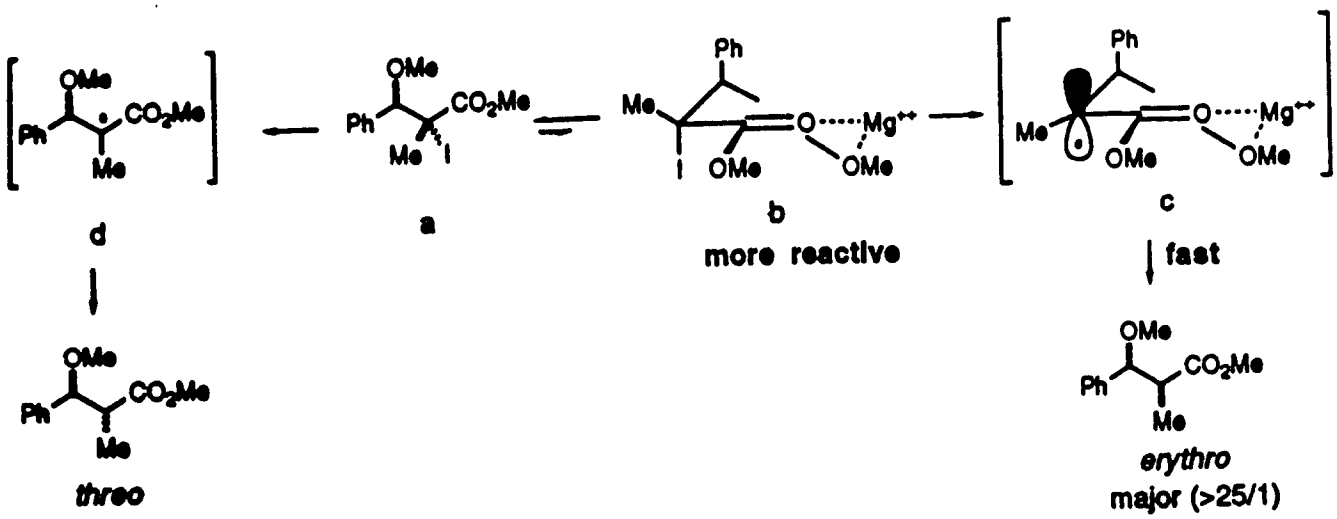




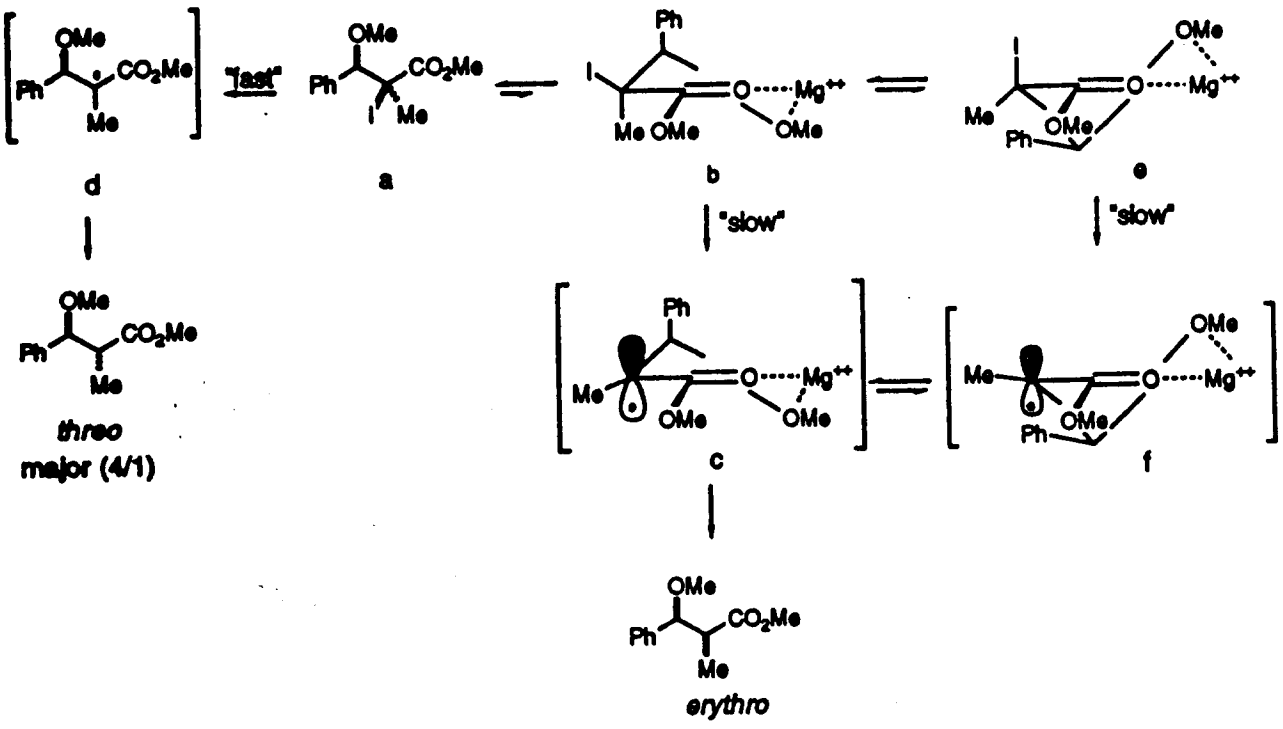
12

Proposed mechanism

Case of the α-Iodo ester giving a high selectivity

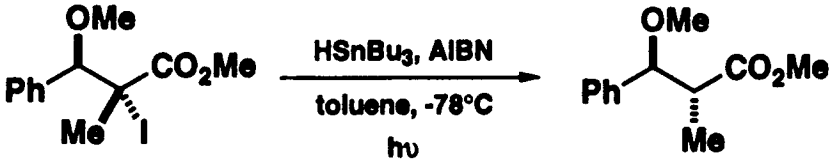


Case of the α-Iodo ester giving a low selectivity

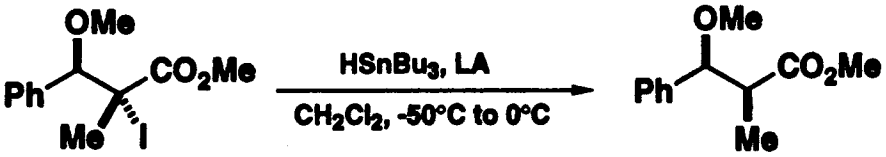


Summary

- Acyclic radicals can react with high selectivity :

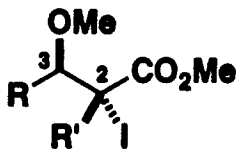


- The addition of a Lewis acid has a dramatic effect on the selectivity: in the cases we studied, MgI_2, $MgBr_2.OEt_2$ and $AlCl_3$ proved to be the most efficient;

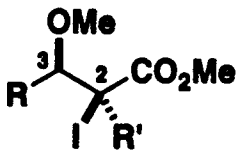


Summary

- The relative stereochemistry at the 2 and 3 position has a profound effect on the reduction diastereoselectivity when a Lewis acid is used:

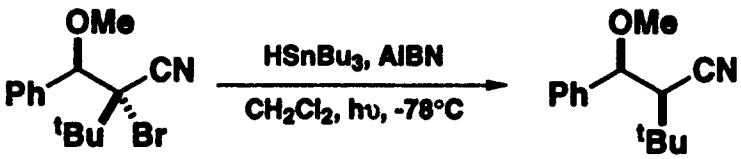


reacts selectively



wrong relative stereochemistry to get high selectivity

- $A^{1,2}$ strain can be used to induce stereoselection in the cyano series:



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