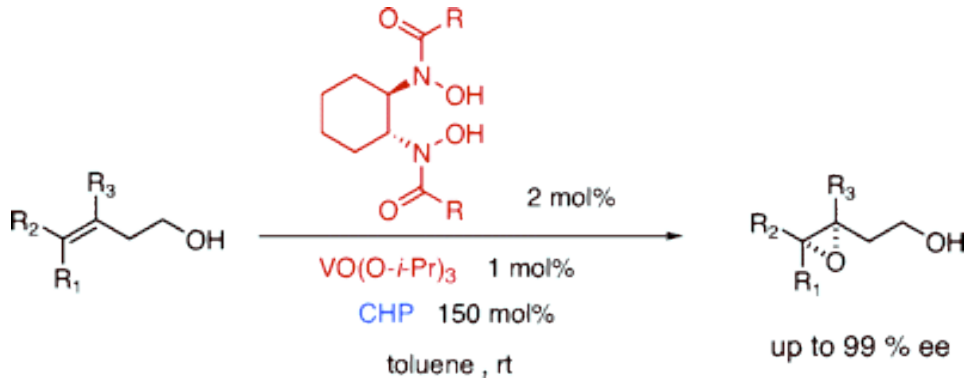
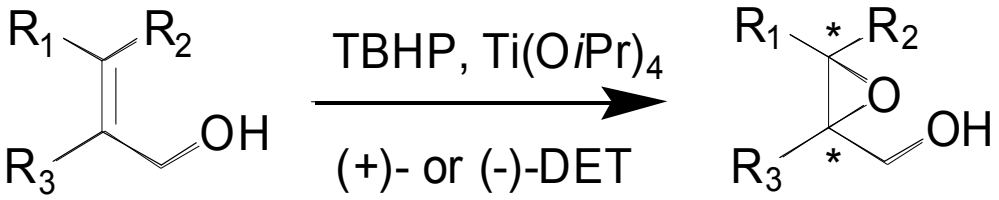
Vanadium-Catalyzed Asymmetric Epoxidation of Homoallylic Alcohols

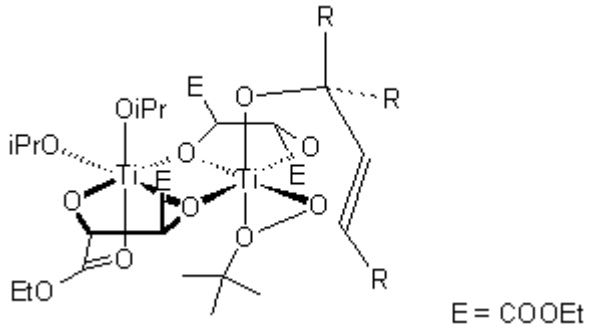


Zhang, W. and Yamamoto, H.
J. Am. Chem. Soc. ASAP

Current Literature
Chenbo Wang @ Wipf Group
Jan 6th, 2007

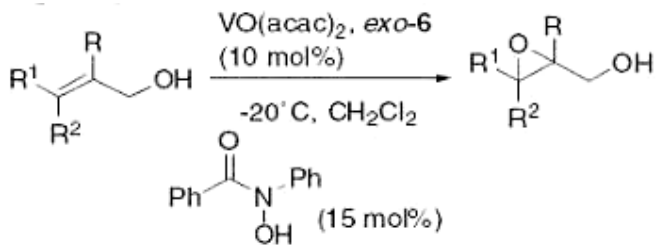
Metal Catalyzed Asymmetric Epoxidation of Allylic Alcohols: Chiral Ligand (Sharpless epoxidation)

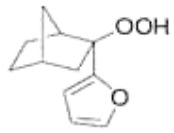




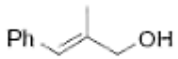
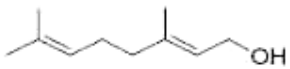
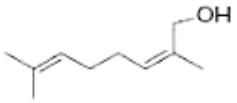
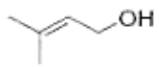
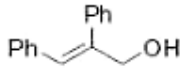
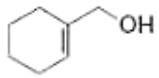
Katsuki, T. and Sharpless, K. B. *J. Am. Chem. Soc.* **1980,** *102,* 5974
Williams, I. D.; Pedersen, S. F.; Sharpless, K. B. and Lippard, S. J. *J. Am. Chem. Soc.* **1984,** *106,* 6430

Metal Catalyzed Asymmetric Epoxidation of Allylic Alcohols: Chiral Peroxide





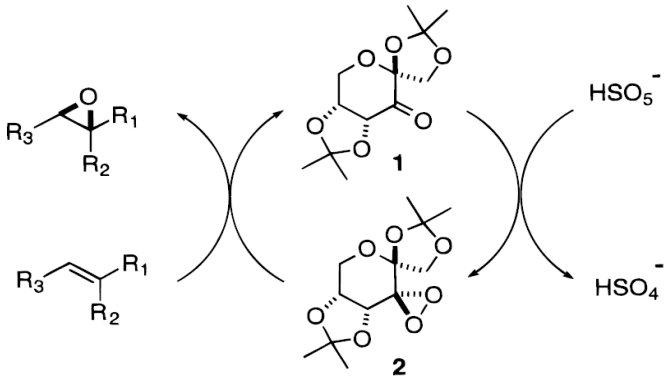
exo-**6**

Entry	Allylic alcohol	t (h)	Yield %	ee %
1		48	70	61 (2*R*,3*R*)
2		45	64	40 (2*R*,3*R*)
3		72	61	41 (2*R*,3*S*)
4		42	98	44 (2*R*)
5[a]		23	88	44 (2*R*,3*R*)
6		23	76	45 (2*R*,3*R*)

[a] The reaction was carried out in toluene using $VO(O\textit{i}\text{-}Pr)_3$.

Lattanzi, A; Piccirillo, S. and Scettri, A. *Eur. J. Org. Chem*. **2005**, 1669.

Asymmetric Epoxidation of Allylic Alcohols: Chiral Ketone



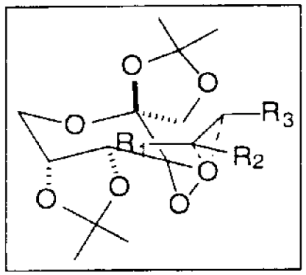
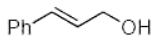
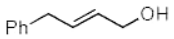
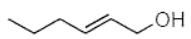
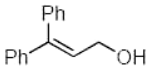
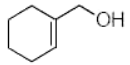
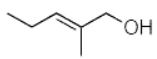
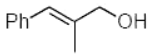
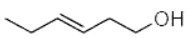
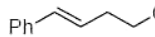
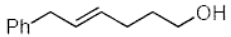


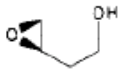
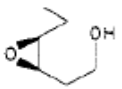
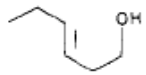
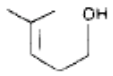
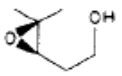
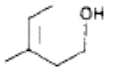
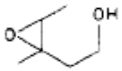
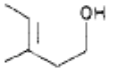
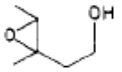
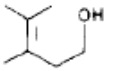
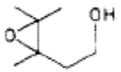
Table 15 Asymmetric Epoxidation of Representative Hydroxyalkenes Catalyzed by Ketone

Entry	Substrate	T (°C)	Yield (%)	ee(%)	Configuration
1		–10	85	94	(+)-(*R*,*R*)
2		–10	45	91	(+)-(*R*,*R*)
3		–10	68	91	(+)-(*R*,*R*)
4		0	87	94	(+)-(*R*)
5		–15	93	94	(+)-(*R*,*R*)
6		–15	85	92	(+)-(*R*,*R*)
7		–15	75	74	(+)-(*R*,*R*)
8		–10	82	90	(+)-(*R*,*R*)
9		0	90	91	(+)-(*R*,*R*)
10		–15	83	91	(+)-(*R*,*R*)
11		0	87	91	(+)-(*R*,*R*)

Wang, Z.-X. and Shi, Y. *J. Org. Chem*. **1998**, *63*, 3099.

Sharpless Asymmetric Epoxidation on Homoallylic Alcohols

Table I. Asymmetric Epoxidation of Homoallylic Alcohols

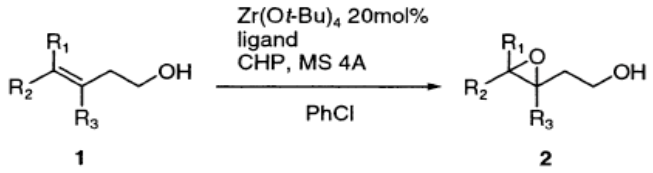
homoallylic alcohol	epoxy alcohol	yield, %	ee, %	confign	rotation (solvent)
 1a	 1b	11–25[a]	55	3*R*	+ (CH_2Cl_2)
 2a	 2b	50[a] 30[b]	36 50	3*R*,4*S* 3*R*,4*S*	+ ($EtOH_{abs}$) + ($EtOH_{abs}$)
 3a	 3b	34–50[b]	41	3*R*,4*R*	+ ($EtOH_{abs}$)
 4a	 4b	41[b,c]	27	3*R*	+ ($CHCl_3$)
 5a	 5b	60[b]	23		+ ($EtOH_{abs}$)
 6a	 6b	15[b]	*d*		+ ($EtOH_{abs}$)
 7a	 7b	62[b]	48		+ ($EtOH_{abs}$)

[a] Performed at 0 °C. [b] Performed at −20 °C. [c] Isolated as the acetate. [d] Percent ee was not determined for this product.

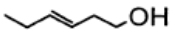
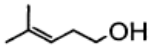
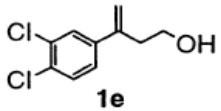
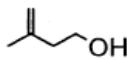
Rossiter, B. E. and Sharpless, K. B. *J. Org. Chem.* **1984**, *49*, 3707

Zr Catalyzed Asymmetric Epoxidation of Homoallylic Alcohols

Table 2. Catalytic Asymmetric Epoxidation of Homoallylic Alcohols



1 **2**

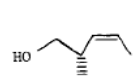
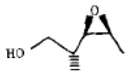
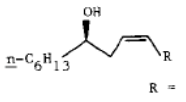
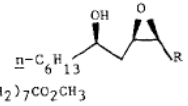
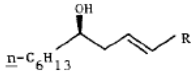
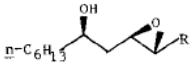
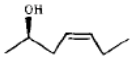
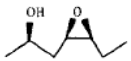
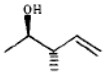
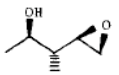
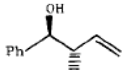
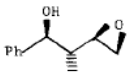
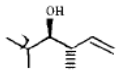
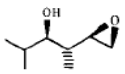
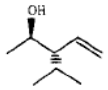
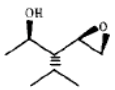
substrate	method[a]	yield (%)[b]	ee (%)[c]	abs. config.[d]
 **1a**	A	92	87	3*S*, 4*S*
	B	86	71	3*R*, 4*R*
 **1b**	A	93	72	3*S*, 4*R*
	B	45	49	3*R*, 4*S*
 **1c**	A	95	47	3*S*
	B	93	59	3*R*
 **1d**	A	55 (94)[e]	78	3*S*
	B	15 (25)[e]	82	3*R*
 **1e**	A	98	73	3*R*
	B	93	89	3*S*
 **1f**	A	83 (98)[f]	74	3*S*
	B	78 (96)[f]	86	3*R*

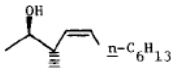
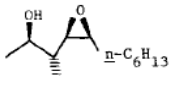
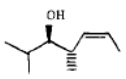
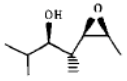
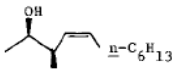
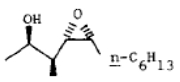
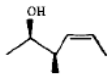
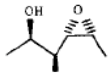
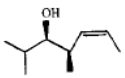
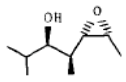
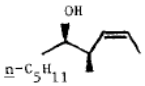
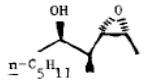
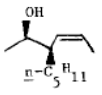
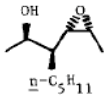
[a] Method A: Zr(O*t*-Bu)$_4$/(L)-DBTA = 0.20 equiv/0.22 equiv, reaction temp = −40 °C, reaction time = 1 day. Method B: Zr(O*t*-Bu)$_4$/(L)-DIPT = 0.20 equiv/0.41 equiv, reaction temp = 0 °C, reaction time = 3−5 days. [b] Isolated yield. [c] Determined by chiral HPLC after transformation to triphenylmethyl ether. [d] Determined by comparison of optical rotation and chiral HPLC (refs 7, 10, and 18). [e] Determined by ^{1}H NMR using triphenylmethane as an internal standard. [f] Determined by ^{1}H NMR using diphenylmethane as an internal standard.

Okachi, T.; Murai, N. and Onaka, M. *Org. Lett.* **2003**, *5*, 85

Vanadium Catalyzed Stereospecific Epoxidation of Homoallylic Alcohols

Table I. V^{5+}/TBHP Epoxidations of Homoallylic Alcohols[a,j]

entry	homoallylic[b] alcohol	major epoxy alcohol[c]	selectivity[d]	yield,[e] %
1			>400:1	90
2			24:1	93[f]
3			1.4:1	99
4			12:1	83
5			4.6:1	50
6			4.8:1	98
7			3:1	88
8			5:1	88[i]

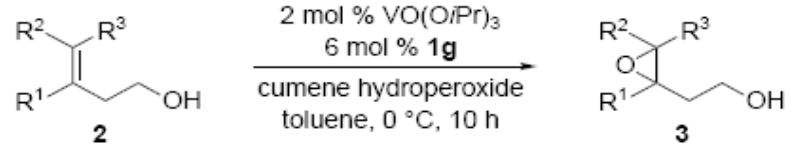
entry	homoallylic[b] alcohol	major epoxy alcohol[c]	selectivity[d]	yield,[e] %
9			104:1	92
10			>400:1	97
11			70:1	73[g]
12			85:1	70
13			2.1:1	91[h]
14			15.9:1	81
15			211:1	95

[a] Epoxidations were carried out by adding the olefin (1–16 mmol), vanadium(IV) oxide bis(2,4-pentanedionate) (1–2 mol%), and anhydrous 1 M *tert*-butyl hydroperoxide (1.5 equiv) to anhydrous methylene chloride (~0.1 M in olefin) at ice bath temperature followed by stirring at room temperature overnight (16 h). The less reactive substrates required longer times: entry 11 (24 h), entry 12 (96 h), entry 13 (41 h). [b] Noncommercial substrates were prepared as follows: entry 1, deconjugative alkylation of 2-pentenoic acid (LDA, MeI,

Mihelich, E. D.; Daniels, K. and Eickhoff, D. J. *J. Am. Chem Soc.* **1981,** *103,* 7690

Previous Works on Vanadium Catalyzed Asymmetric Epoxidation of Homoallylic Alcohols

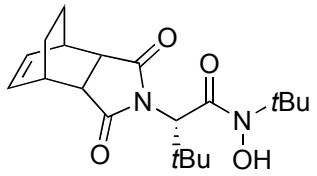
Table 2: Asymmetric epoxidation of homoallylic alcohols **2** using **1g** as ligand.



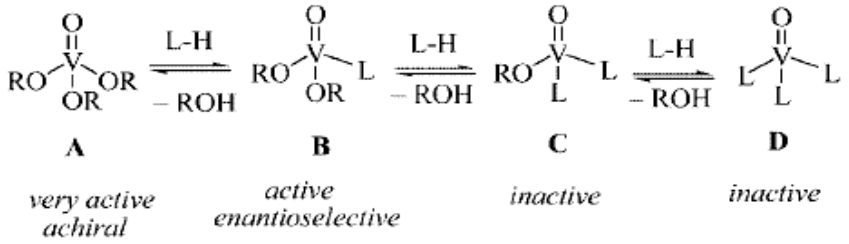
Entry	Homoallylic alcohol **2**	*ee* [%]	Yield [%]
1	Et, OH **2b**	40[a]	25
2	Ph, OH **2c**	46[c]	24
3	OH **2d**	36[a]	67
4	OH **2e**	74[b]	61
5	OH **2f**	84[a]	58
6	*i*Pr, OH **2g**	90[a]	77
7	*t*Bu, OH **2h**	90[b]	89
8	Ph, OH **2i**	89[c]	70
9	1-naphthyl, OH **2j**	91[d]	42

[a] Determined by chiral GLC (column, γ-TA). [b] Determined by chiral GLC (column, β-DM). [c] Determined by chiral HPLC (column, AD-H). [d] Determined by chiral HPLC (column, OD-H).

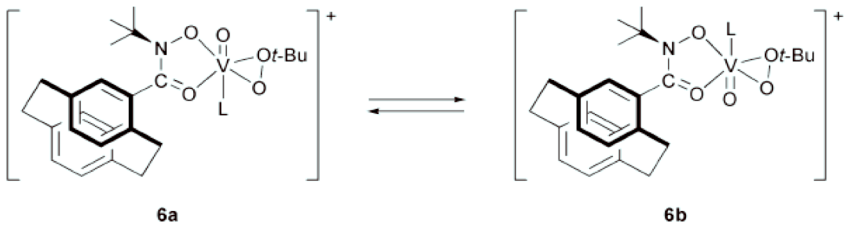
1g =



Possible cause of the low yield and ee:



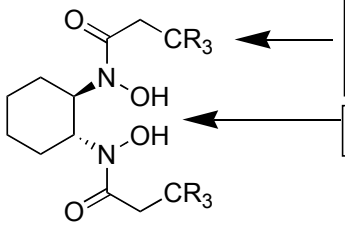
L = bidentate ligand



Scheme 4 Formation of diastereomeric vanadium complexes **6** (with L = *n*-BuOH).

Makita, N.; Hoshino, Y.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2003**, *42*, 941

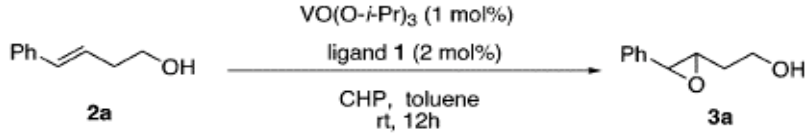
Vanadium Catalyzed Asymmetric Epoxidation of Homoallylic Alcohols: Screening of Ligands

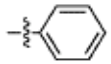
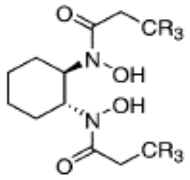
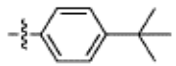
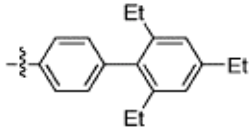


Bulky R group:
a. direct the cabonyl goups away from the metal center
b. prevent the formation of VL_2 or VL_3 species

*C*2 symmetric bidentate ligand

Table 1. Screening of Ligands



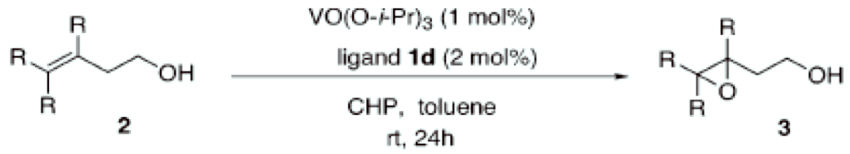
entry[a]	ligand	%yield[b], %ee[c]
1	**1b** R = 	52, 71
2	 **1c** R = 	56, 90
3	**1d** R = 	61, 96

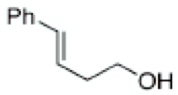
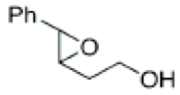
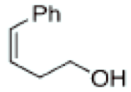
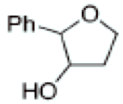
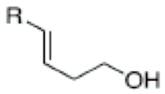
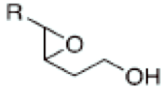
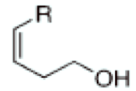
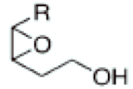
[a] All reactions were carried out in toluene in the presence of 1.5 equiv of cumene hydroperoxide (CHP) (88%) unless otherwise indicated. [b] Isolated yield after chromatographic purification. [c] Enantiomeric excess values were determined by chiral HPLC (AD-H), and the detailed information is provided in the Supporting Information.

Zhang, W. and Yamamoto, H. *J. Am. Chem. Soc.* ASAP

Vanadium Catalyzed Asymmetric Epoxidation of Homoallylic Alcohols: Screening of Ligands

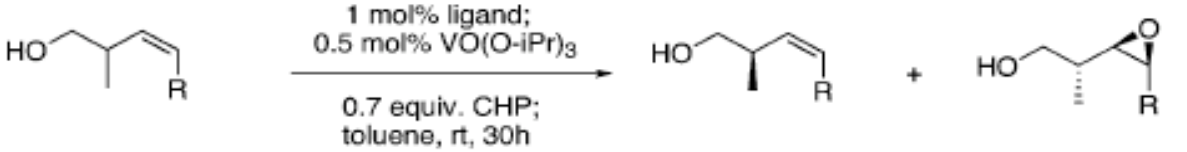
Table 2. Scope of Substrates



entry[a]	HAA	epoxy alcohol		%yield[b], %ee[c], config.
1	 2a		3a	90, 96
2	 2b		3b	85, 99
3			3c, R=C_2H_5	85, 93 *(3R, 4R)*
4	2c-e		3d, R=C_5H_{11}	89, 96
5			3e, R=C_6H_{13}	92, 98
6			3f, R=C_2H_5	92, 95 *(3R, 4S)*
7			3g, R=C_3H_7	90, 97
8	2f-i		3h, R=C_4H_9	91, 99
9			3i, R=C_5H_{11}	90, 99

Vanadium Catalyzed Asymmetric Epoxidation of Homoallylic Acohols: Kinetic Resolution of Homoallylic Alcohols

Scheme 2. Kinetic Resolution of Homoallylic Alcohols



4a, R=C_2H_5
95%ee, 51% yield

5a, R=C_2H_5
95%ee, 48% yield

4b, R=C_4H_9
96%ee, 51% yield

5b, R=C_4H_9
97%ee, 48% yield

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Summary

- Asymmetric epoxidation of homoallylic alcohols was realized:
  - High yield and ee
  - Good substrate Scope
- Future Work:
  - Tri- and tetrasubstituted alkene?
  - Functional group compatibility
  - Suppression of tetrahydrofuran formation
  - Application in total synthesis
  - Where is the experimental procedures?