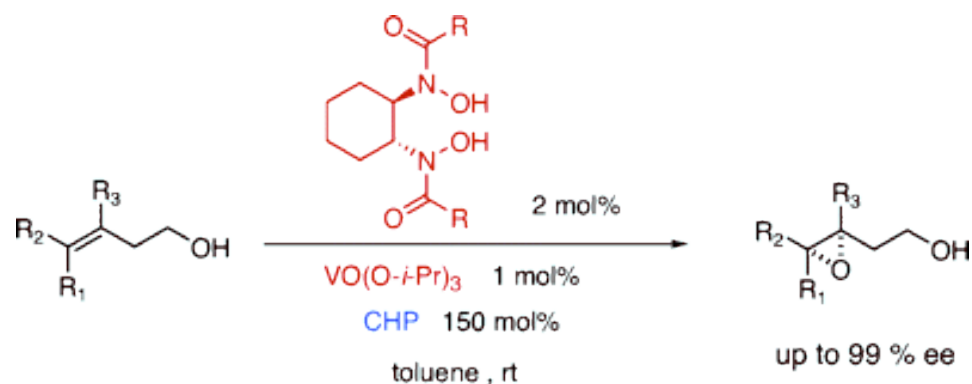


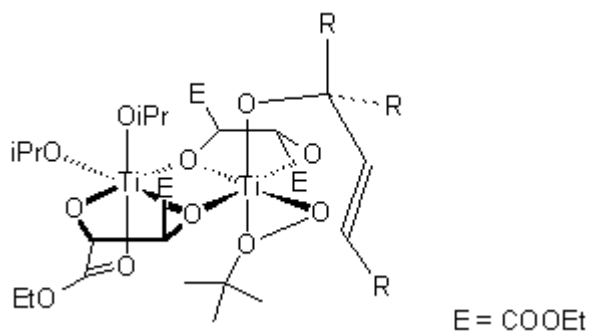
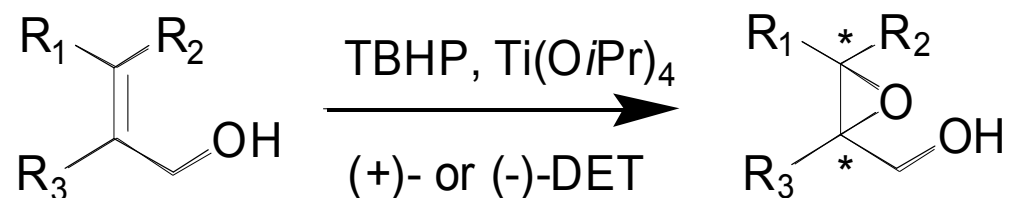
Vanadium-Catalyzed Asymmetric Epoxidation of Homoallylic Alcohols



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

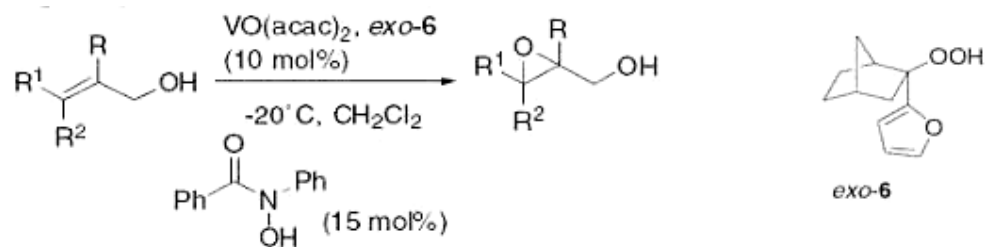
Current Literature
Chenbo Wang @ Wipf Group
Jan 6th, 2007

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



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

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

Asymmetric Epoxidation of Allylic Alcohols: Chiral Ketone

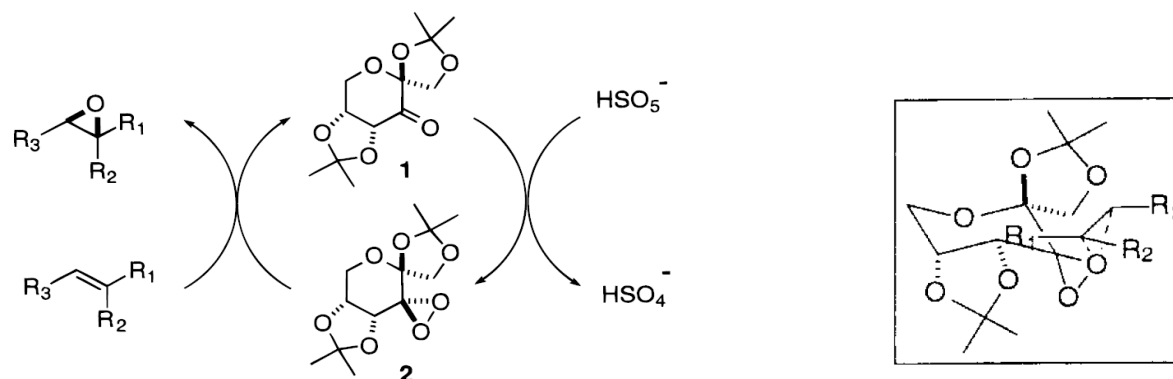






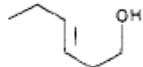









Table 15 Asymmetric Epoxidation of Representative Hydroxyalkenes Catalyzed by Ketone

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 <i>R</i>	+ (CH ₂ Cl ₂)
 2a	 2b	50 ^a 30 ^b	36 50	3 <i>R</i> ,4 <i>S</i> 3 <i>R</i> ,4 <i>S</i>	+ (EtOH _{abs}) + (EtOH _{abs})
 3a	 3b	34-50 ^b	41	3 <i>R</i> ,4 <i>R</i>	+ (EtOH _{abs})
 4a	 4b	41 ^{b,c}	27	3 <i>R</i>	+ (CHCl ₃)
 5a	 5b	60 ^b	23		+ (EtOH _{abs})
 6a	 6b	15 ^b	<i>d</i>		+ (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

Reaction scheme: $\text{Zr}(\text{O}t\text{-Bu})_4$ 20mol%, ligand, CHP, MS 4A, PhCl

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

^a Method A: $\text{Zr}(\text{O}t\text{-Bu})_4$ /(L)-DBTA = 0.20 equiv/0.22 equiv, reaction temp = $-40\text{ }^\circ\text{C}$, reaction time = 1 day. Method B: $\text{Zr}(\text{O}t\text{-Bu})_4$ /(L)-DIPT = 0.20 equiv/0.41 equiv, reaction temp = $0\text{ }^\circ\text{C}$, 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 ^1H NMR using triphenylmethane as an internal standard. ^f Determined by ^1H 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

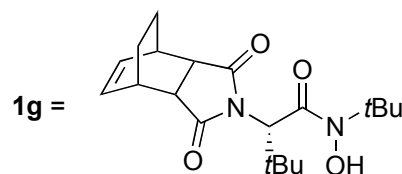
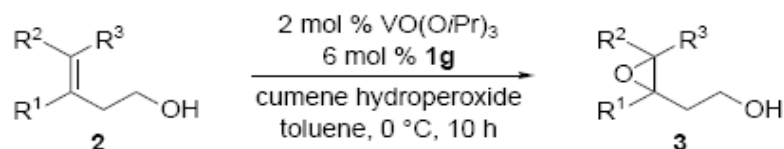
Table I. V⁵⁺/TBHP Epoxidations of Homoallylic Alcohols^{a,j}

entry	homoallylic ^b alcohol	major epoxy alcohol ^c	selectivity ^d	yield, ^e %	entry	homoallylic ^b alcohol	major epoxy alcohol ^c	selectivity ^d	yield, ^e %
1			>400:1	90	9			104:1	92
2			24:1	93 ^f	10			>400:1	97
R = (CH ₂) ₇ CO ₂ CH ₃									
3			1.4:1	99	11			70:1	73 ^g
4			12:1	83	12			85:1	70
5			4.6:1	50	13			2.1:1	91 ^h
6			4.8:1	98	14			15.9:1	81
7			3:1	88	15			211:1	95
8			5:1	88 ⁱ					

^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,

Previous Works on Vanadium Catalyzed Asymmetric Epoxidation of Homoallylic Alcohols

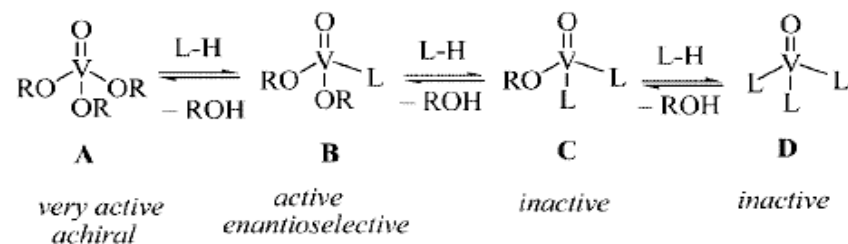
Table 2: Asymmetric epoxidation of homoallylic alcohols **2** using **1g** as ligand.



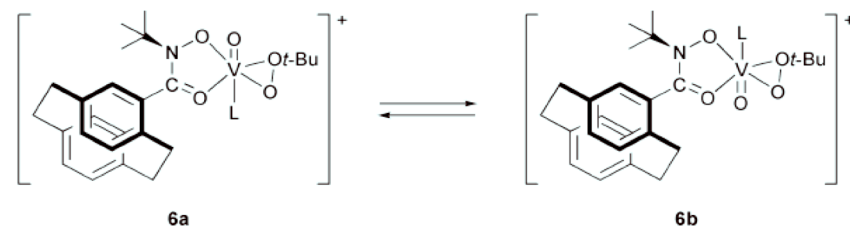
Entry	Homoallylic alcohol 2	ee [%]	Yield [%]
1	2b	40 ^[a]	25
2	2c	46 ^[c]	24
3	2d	36 ^[a]	67
4	2e	74 ^[b]	61
5	2f	84 ^[a]	58
6	2g	90 ^[a]	77
7	2h	90 ^[b]	89
8	2i	89 ^[c]	70
9	2j	91 ^[d]	42

[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).

Possible cause of the low yield and ee:



L = bidentate ligand



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

Vanadium Catalyzed Asymmetric Epoxidation of Homoallylic Alcohols: Screening of Ligands

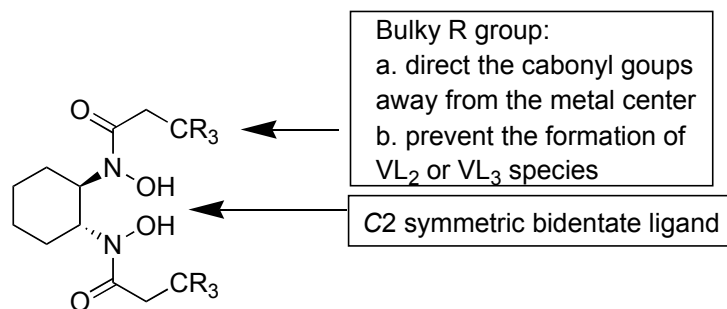


Table 1. Screening of Ligands

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.

Vanadium Catalyzed Asymmetric Epoxidation of Homoallylic Alcohols: Screening of Ligands

Table 2. Scope of Substrates

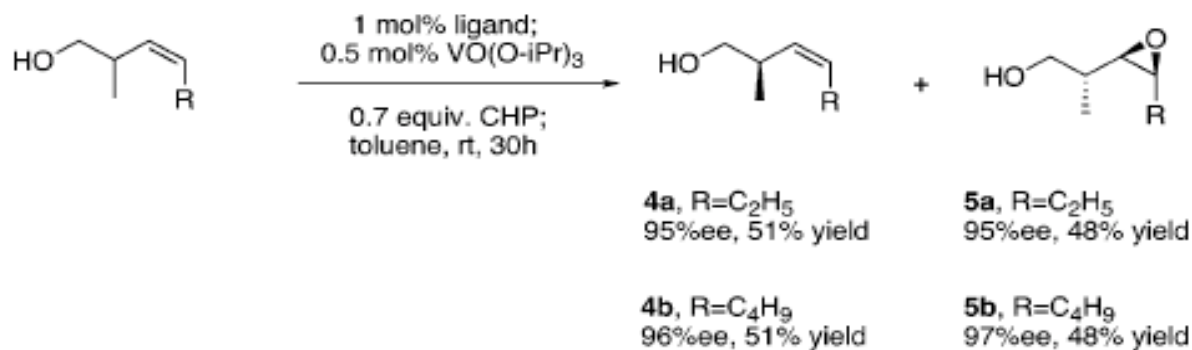
$\text{VO}(\text{O-}i\text{Pr})_3$ (1 mol%)
 ligand **1d** (2 mol%)
 CHP, toluene
 rt, 24h

entry ^a	HAA	epoxy alcohol		%yield ^b , %ee ^c , config.
1			3a	90, 96
2			3b	85, 99
3			3c, R=C₂H₅	85, 93 (<i>3R, 4R</i>)
4			3d, R=C₅H₁₁	89, 96
5			3e, R=C₆H₁₃	92, 98
6			3f, R=C₂H₅	92, 95 (<i>3R, 4S</i>)
7			3g, R=C₃H₇	90, 97
8			3h, R=C₄H₉	91, 99
9			3i, R=C₅H₁₁	90, 99

10

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

Scheme 2. Kinetic Resolution of Homoallylic Alcohols



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?