Chiral Vanadium-Based Catalysts for Asymmetric Epoxidation of Allylic Alcohols

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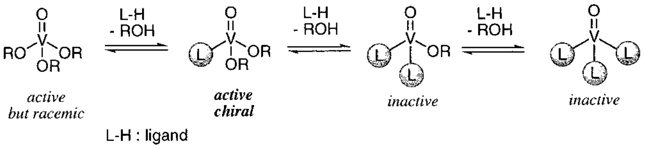
Received November 3, 1998

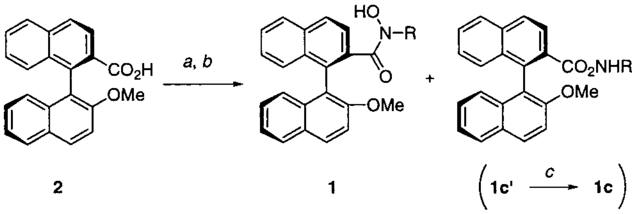
The asymmetric oxidation of unfunctionalized as well as functionalized olefins is a subject of current interest and intensive research in organic synthesis.[1] The sharpless asymmetric epoxidation protocol of allylic alcohols has proven to be an extremely useful means of synthesizing enantiomerically enriched compounds.[2] In comparison with the titanium catalysts, only a few examples of chiral vanadium catalysts for the epoxidation have been reported so far,[3] although VO(acac)$_2$ is the catalyst of choice for stereoselective epoxidation of allylic alcohols.[4] Since during the course of oxidation both vanadium(IV) and -(V) are thought to exist as an oxovanadium(V) complex[5] that has three alkoxy groups for substrates, hydroperoxides, and ligands, ligand design of chiral vanadium catalysts has never been successfully established to control such a complexation mode as proposed by Sharpless (vide infra).[6] We report here new chiral hydroxamic acids derived from 2,2′-binaphthol that serve as monovalent ligands with a vanadium complex for the catalytic asymmetric epoxidation of allylic alcohols.



Our first attempt to modify optically active known **2** derived from binaphthol in several steps involved conversion of the carboxylic acid into a hydroxamic acid group that has high affinity to vanadium complexes as outlined in Scheme 1.[7] Transformation of **2** to **1** was carried out in the usual manner via reaction of the corresponding acid chloride with several hydroxylamines **3** in the presence of NEt$_3$ to furnish hydroxamic acid **1**. Coupling reaction of the acid chloride with **3c** gave **1c** together with a significant amount of the undesired O-acylated byproduct **1c′**, which underwent smooth isomerization to **1c** by treatment with *t*-BuLi under the mild conditions.

Then, we set out to test epoxidation of *trans*-2,3-diphenyl-2-propenol in the presence of a vanadium catalyst (5 mol %) and a small excess of **1** under various reaction conditions (Table 1). The epoxidation rate is highly dependent on the structure of the hydroxylamine moiety and the oxidation state of starting vanadium complexes. Sterical hindrance and/or π-electronic properties of both the *N*-alkyl group of **1** and the alkyl group of peroxides led to a dramatic increase in enantioselectivity (entries 1 and 6). The higher oxidation state (V) might facilitate clean generation of the chiral active species (entries 3 and 4). In place of toluene, CH$_2$Cl$_2$ can also be used as solvent, but the enantioselectivity falls significantly (from 86 to 62%). It should be noted that the ee value of 73% was observed even when 1.2 equiv of **1c** based on vanadium were employed. These results support our hypothesis that a 1:1 complex between vanadium(V) and

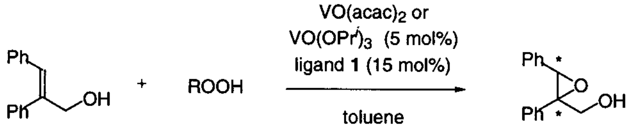
Scheme 1[a]



hyroxamic acid	yield from **2** (%)
1a (R = cyclohexyl)	84
b (R = Bn)	72
c (R = CHPh$_2$)	89

[a] Key: (a) (COCl)$_2$, cat.DMF, CH$_2$Cl$_2$; (b) **3**, NEt$_3$, CH$_2$Cl$_2$; (c) *t*-BuLi, THF, −78 to 0 °C.

Table 1. Catalytic Enantioselective Epoxidation of *trans*-2,3-Diphenyl-2-propenol[a]



entry	catalyst	ROOH[b]	conditions (°C, h)	ee[c] (%)
1	VO(acac)$_2$/**1a**	CHP	0, 6 days	25
2	**1b**	CHP	0, 8 days	54
3	**1c**	CHP	0, 19	65
4	VO(OPr^i)$_3$/**1c**	CHP	0, 3	68
5		TBHP	−40, 10	40
6		TrOOH	−20, 68	86
7[d]		TrOOH	−20, 24	83
8[e]		TrOOH	−20, 24	73

[a] Unless otherwise noted, the reaction was carried out in toluene in the presence of vanadium complex (5 mol %) and **1** (15 mol %). The isolated yield in each entry was around 80%. [b] CHP = cumenehydroperoxide, TBHP = *tert*-butyl hydroperoxide, TrOOH = triphenylmethyl hydroperoxide. [c] The absolute configuration of the major enantiomer in each run was 2*S*,3*S*, and the ee values were determined by chiral HPLC (column, OD-H) analysis. [d] 7.5 mol % of **1c**. [e] 6.0 mol % of **1c**.

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(1) (a) Sharpless, K. B.; Finn, M. G. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: London, 1985; Vol. 5, pp 247−308. (b) Höft, E. *Top. Curr. Chem.* **1993**, *164*, 63. (c) Pedragosa-Moreau, S.; Archelas, A.; Furstoss, R. *Bull. Soc. Chim. Fr.* **1995**, *132*, 769.

(2) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Rossiter, B. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: London, 1985; Vol. 5, pp 193−246. (c) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765. (d) Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 113

(3) For chiral molybdenum and vanadium catalysts for asymmetric epoxidation of allylic alcohols: (a) Yamada, S.; Mashiko, T.; Terashima, S. *J. Am. Chem. Soc.* **1977**, *99*, 1988. (b) Michaelson, R. C.; Palermo, R. E.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 1990. (c) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* **1979**, *12*, 63 and a reference therein. (d) Bolm, C.; Luong, T. K. K.; Harms, K. *Chem. Ber./Recueil* **1997**, *130*, 887.

(4) For achiral metal-catalyzed regio- and stereoselective epoxidation of allylic alcohols, see: (a) Sharpless, K. B.; Michaelson,, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. (b) Tanaka, S.; Yamamoto, H.; Nozaki, H.; Sharpless, K. B.; Michaelson, R. C.; Cutting, J. D. *J. Am. Chem. Soc.* **1974**, *96*, 5254.

(5) (a) Gould, E. S.; Hiatt, R. R.; Irwin, K. C. *J. Am. Chem. Soc.* **1968**, *90*, 4573. (b) Cenci, S.; Furia, F. D.; Modena, G.; Curci, R.; Edwards, J. O. *J. Chem. Soc., Chem. Commun.* **1978**, 979.

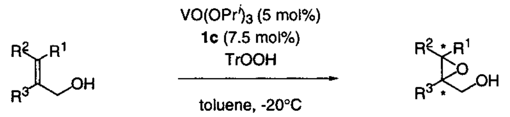
(6) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059.

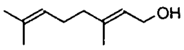
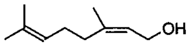
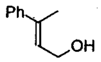
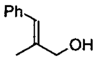
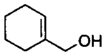
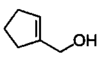
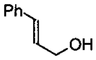
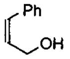
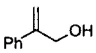
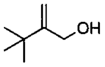
(7) (a) Miyano, S.; Okada, S.; Suzuki, T.; Handa, S.; Hashimoto, H *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2044. (b) Miyano, S.; Hotta, H.; Takeda, M.; Kabuto, C.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1989**, *52*, 1528.

10.1021/jo9821933 CCC: $18.00

the sterically congested hydroxamic acid forms predominantly. Unlike the titanium tartrate system, molecular sieves to sequester water, which has a deleterious effect on both the rate and selectivity, are not required in our case.[8]

Table 2. Catalytic Epoxidation of Various Substituted Allyl Alcohols in the Presence of VO(OPr^i)$_3$/1c[a]



entry	allylic alcohol	yield (%)[b]	ee (%)[c]	config.(2,3)[d]
1		80	66	(*S*,*S*)
2		87	41	(*S*,*R*)
3		70	78	(*S*,*S*)
4		96	91	(*S*,*S*)
5		61	87[e]	(*S*,*S*)
6		59	94[e]	(*S*,*S*)
7		14	71	(*S*,*S*)
8		19	38	(*S*,*R*)
9		53	39	(2*S*)
10		16	40	(2*S*)

[a] The epoxidation was conducted at −20 °C for 2−3 days in toluene in the presence of VO(OPr^i)$_3$ (5 mol %) and **1c** (7.5 mol %), but the reaction time (entries 7−10) was 1 week. [b] Isolated yield. [c] Determined by chiral HPLC (column, OD-H) analysis. [d] Determined by comparison of reported optical rotation. [e] Determined by chiral GLC (column, β-TA) analysis.

To explore further the potential of these new catalysts, we examined epoxidation of various substituted allyl alcohols under the optimized conditions in Table 1, and these results are summarized in Table 2. Epoxidation of 3,3-disubstituted allyl alcohols using catalytic VO(OPr^i)$_3$ with **1c** proceeded smoothly to yield the corresponding epoxides in moderate to good yields with mediocre selectivities (entries 1−3). On the other hand, in the case of 2,3-disubstituted allyl alcohols, irrespective of bearing aromatic groups, a uniformly high degree of enantioselectivities around 90% was obtained (entries 4−6). Notably, the productivity of our catalyst for 1-cyclopentenylmethanol is superior to the stoichiometric epoxidation with the titanium tartrate (entry 6).[9] Monosubstituted allyl alcohols gave unsatisfactory results. A typical procedure is as follows (entry 4 in Table 2): To a solution of the chiral vanadium catalyst (9.8 mM, 12.7 μmol) readily prepared from **1c** and VO(OPr^i)$_3$ in dry toluene (25 °C, 1 h) were added *trans*-2-methylcinnamyl alcohol (0.254 mmol) and trityl hydroperoxide (0.381 mmol) at −20 °C under argon atmosphere. After the solution was stirred for 48 h at this temperature, the reaction was quenched by addition of saturated Na_2SO_3 (aq) (2 mL). Extraction of the product with ether, evaporation of solvents, and chromatographic purification on silica gel afforded the corresponding 2,3-epoxy alcohol in a yield of 96%.

In conclusion, we have developed new chiral vanadium catalysts for the asymmetric epoxidation of allylic alcohols, and careful ligand modification was found to yield the desired complexation mode of vanadium. To the best of our knowledge, our catalysis, particularly the VO(OPr^i)$_3$−**1c** system, is the best among previously known examples of chiral vanadium complexes with respect to selectivity. Extension of the scope and elucidation of structure-selectivity correlations for the present catalysts will be reported in due course.

Acknowledgment. We are grateful to Dr. S. Saito (Nagoya University) for helpful discussions on X-ray analysis.

Supporting Information Available: Experimental procedures, characterization data for all new compounds, and X-ray data for **1c** (28 pages).

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[8] (a) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922. (b) Reference 2c.

[9] Sandararaman, P.; Barth, G.; Djerassi, C. *J. Am. Chem. Soc.* **1981**, *103*, 5004.