Tetrahedron Letters, Vol. 33, No 27, pp. 3833-3836, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

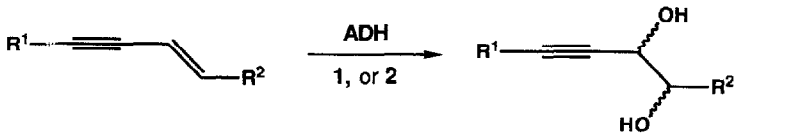
ASYMMETRIC DIHYDROXYLATION OF ENYNES

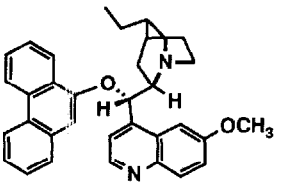
Kyu-Sung Jeong, Peter Sjö, and K. Barry Sharpless*

Department of Chemistry, Massachusetts Institute of Technology,
Cambridge, Massachusetts 02139, USA
Department of Chemistry, The Scripps Research Institute,
La Jolla, California 92037, USA

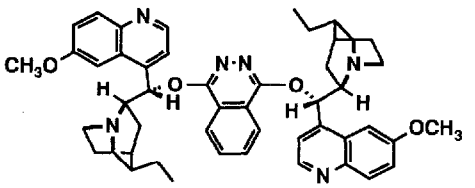
Summary: Catalytic asymmetric dihydroxylations of 1,3-enynes were studied using 9-*O*-(9'-phenanthryl) dihydroquinidine (PHN-DHQD) **1** and 1,4-bis-(9-*O*-dihydroquinidine) phthalazine ($DHQD_2$-PHAL) **2**. Terminal olefins showed moderate (38-79% ee) and *trans*-disubstituted olefins high enantioselectivities (73 - 97% ee).

Several years ago we developed the osmium-catalyzed asymmetric dihydroxylation (AD) of olefins using cinchona alkaloid derivatives as the chiral ligand.[1] Continuing efforts in this laboratory provided a much improved AD process in terms of enantioselectivity and convenience.[2] Since enynes can be easily prepared by various methods, and are useful intermediates in organic synthesis,[3] we report here the osmium-catalyed AD of various enynes using 9-*O*-(9'-phenanthryl)dihydroquinidine (PHN-DHQD) **1** and 1,4-bis-(9-*O*-dihydroquinidine) phthalazine ($DHQD_2$-PHAL) **2**.[4]





1



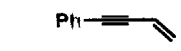
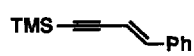
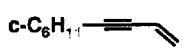
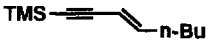
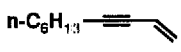
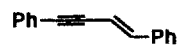
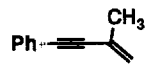
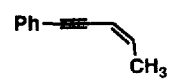
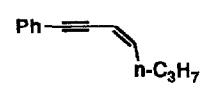
2

Initial studies were performed by using PHN-DHQD **1** which has shown high enantioselectivity in the AD for several classes of olefin.[2d] Although it is known that triple bonds can be oxidized to the corresponding α-diketones by OsO_4,[5] all reactions showed excellent chemoselectivity, i. e. yne-diol was observed as the sole product under the reaction conditions.[6]

Over 30 enynes were employed in the catalytic AD and the representative results are summarized in Table 1. Enynes generally showed poorer enantioselectivity than the corresponding saturated olefins since the triple bond is one of the least sterically demanding functional groups. For example, dihydroxylation of

1-decen-3-yne (entry 3) afforded only 38% ee of (*R*)-3-decyne-1,2-diol[7] using PHN-DHQD **1**, while the AD of 1-decene provided 74% ee of (*R*)-1,2-decanediol under the same conditions.[2d]

Table 1. The Results of the Catalytic AD of Enynes Using PHN-DHQD 1[a]

entry	enyne[b]	yield[c]	% ee[d]	entry	enyne[b]	yield[c]	% ee[d]
1		91	53	7		66	94
2		67	44	8		56	93
3		76	38	9		67	97
4		91	48	10		82	29
5		98	73	11		94[e]	54
6		94[e]	90	12		61	62

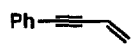
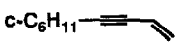
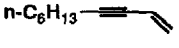
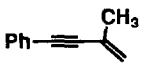
[a] All reactions were performed at 0 °C for 15-30 h. [b] All enynes were prepared using literature procedures[3] except the following: *Cis*-, or *trans*-1-phenyl-3-penten-1-yne (entry 5, 10) was prepared from *cis*-, or *trans*-4-chloro-1-phenyl-3-buten-1-yne, and enynes (entries 7 and 8) from *trans*-4-chloro-1-(trimethylsilyl)-3-buten-1-yne by refluxing for 30 min in THF with the corresponding (methyl, n-butyl, or phenyl) magnesium chloride in the presence of catalytic amounts of $(Ph_3P)_4Pd$ (1-2 mol %). [c] In all cases isolated yields are reported and were not optimized. [d] Enantiomeric excesses (ee's) were determined by HPLC (Pirkle 1-A Ionic column, 25 cm x 10 mm I. D.) analysis of the bis-MTPA esters of the diols (Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512). [e] Reaction was performed using a mixture (*cis/trans* 25:75) of *cis*- and *trans*-1-phenyl-3-hexen-1-ynes.

As shown in Table 1, terminal (entry 1-4) and *cis*-disubstituted olefins (entry 10-12) showed poor enantioselectivities, but *trans*-disubstituted olefins (entry 5-9) provided diols in high enantiomeric excess.

Absolute configurations of all the diols have not been determined. However, it appears that the absolute configurations of the major isomers may be predicted by applying the mnemonic devices which were presented in reference 2d. For example, the AD of 1-phenyl-3-buten-1-yne (entry 1) gave (*R*)-4-phenyl-3-butyne-1,2-diol[8] as the major enantiomer.

Recently, we discovered a new ligand, $DHQD_2$-PHAL, **2** in which two dihydroquinidines are connected to the 1,4- positions of a phthalazine spacer group. Ligand *$DHQD_2$-PHAL* **2** showed much improved enantioselectivities compared to PHN-DHQD **1** in the AD of most classes of olefins.[9] As shown in Table 2, enantioselectivities in the AD of enynes are also increased by up to 30% ee. The catalytic AD of *trans*-disubstitued enynes (entry 5-9, Table 1) using ligand **2** was not studied, but is expected to give higher enantiomeric excesses of diols than those in Table 1.

Table 2. Comparison of Enantiomeric Excesses (ee, %) of Diols Resulting from the ADH of Enynes Using PHN-DHQD 1 and $DHQD_2$-PHAL 2

entry	enyne	% ee PHN-DHQD	% ee $DHQD_2$-PHAL
1		53	73
2		44	72
3		38	54
4		48	79

In conclusion, excellent chemoselectivity and high enantioselectivity were observed in the catalytic AD of various enynes. We recommend the use of the new ligand $DHQD_2$-PHAL **2** for the AD of olefins, especially terminal olefins, to obtain high enantioselectivity.

Acknowledgment: Financial support was provided by the National Science Foundation. We are grateful to Dr. Jens Hartung for providing cinchona alkaloid ligands.

References and Notes:

1. Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968.
2. a) Wai, J. S. M.; Markó, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 1123. b) Shibata, T.; Gilheany, D. G.; Blackburn, B. K.; Sharpless, K. B. *Tetrahedron Lett.* **1990**, *31*, 3817. c) Ogino, Y.; Chen, H.; Kwong, H. -L.; Sharpless, K. B. *Tetrahedron Lett.* **1991**, *32*, 3965. d) Sharpless, K. B.; Amberg, W.; Beller, M.; Chen, H.; Hartung, Y.; Kawanami, Y.; Lübben, D.; Manoury, E.; Ogino, Y.; Shibata, T.; Ukita, T. *J. Org, Chem.* **1991**, *56*, 4585.
3. a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. b) Ratovelomanana, V.; Linstrumelle, G. *Tetrahedron Lett.* **1981**, *22*, 315. c) Rossi, R.; Carpita, A.; Quirici, M. G.; Gaudenzi, M. L. *Tetrahedron* **1982**, *38*, 631. c) Negishi, E. -I.; Okukado, N.; Lovich, S. F.; Luo, F. -T. *J. Org. Chem.* **1984**, *49*, 2629. d) Ratovelomanana, V.; Linstrumelle, G. *Tetrahedron Lett.* **1984**, *25*, 6001. e) Alami, M.; Linstrumelle, G. *Tetrahedron Lett.* **1991**, *32*, 6109.
4. Few studies of the dihydroxylation of enynes have been reported, and none are both a catalytic and an asymmetric process. a) Corey, E. J.; Hopkins, P. B.; Kim, S.; Yoo, S. -E.; Nambiar, K. P.; Falck, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 7131. b) Kende, A. S.; Smith, C. A. *Tetrahedron Lett.* **1989**, *29*, 4217. c) Gigou, A.; Beaucourt, J. -P.; Lellouche, J. -P.; Gree, R. *Tetrahedron Lett.* **1991**, *32*, 635.

5. Bassignani, L.; Brandt, A.; Caciagli, V.; Re, L. *J. Org. Chem.* **1978**, *43*, 4245. For a review, see: Schröder, M. *Chem. Rev.* **1980**, *80*, 187 and references therein.
6. A typical procedure for catalytic asymmetric dihydroxylation using $DHQD_2$-PHAL **2**: To a well-stirred solution of bis-1,4-(9-*O*-dihydroquinidine)phthalazine, $DHQD_2$-PHAL, (7.8 mg, 0.01 mmol, 1 mol %), potassium ferricyanide (0.99 g, 3 mmol), potassium carbonate (0.42 g, 3 mmol), and osmium tetroxide (20 μL of a 0.1 M toluene solution, 0.002 mmol, 0.2 mol %) in 10 mL of a *tert*-butyl alcohol-water (1:1, v/v) at 0 °C, 1-phenyl-3-buten-1-yne (0.128 g, 1 mmol) was added in one portion. The mixture was stirred for 20 h at 0 °C. Solid sodium metabisulfite (1.50 g) was slowly added and the mixture was stirred for 30 min, and then warmed to room temperature. Ethyl acetate (10 mL) was added to the reaction mixture, and the aqueous layer was extracted with ethyl acetate (3 x 5 mL). The combined organic layer was dried over anhydrous magnesium sulfate, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, 80% EtOAc in hexanes) to afford 4-phenyl-3-butyne-1,2-diol as a white solid (0.147 g, 91%).
7. Configuration of 3-decyne-1,2-diol resulting from the ADH of the 1-decen-3-yne was determined as follows: Hydrogenation of 3-decyne-1,2-diol with 5% Pd/C in EtOAc at room temperature under hydrogen atmosphere (hydrogen balloon) afforded 1,2-decanediol, which was converted to the bis MTPA ester derivative. Comparison of retention time with an authentic sample (see ref. 2d) in HPLC analysis indicated that the major isomer was (*R*)-1,2-decanediol.
8. 4-Phenyl-3-butyne-1,2-diol resulting from the ADH of the 1-phenyl-3-buten-yne was hydrogenated to give 4-phenyl 1,2-butanediol; $[\alpha]_D^{23} = +17°$ (c = 1, EtOH). For (*S*)-4-phenyl-1,2-butanediol $[\alpha]_D^{23} = -34.1°$ c = 1, EtOH), see: Hasegawa, J.; Ogura, M.; Tsuda, S.; Maemoto, S. -I; Kutsuki, H; Ohashi, T. *Agric. Biol. Chem.* **1990**, *57*, 1819.
9. The preparation of ligand $DHQD_2$-PHAL **2** and the results of the catalytic ADH of other classes of olefins will be published elsewhere.

(Received in USA 17 March 1992)