J. Org. Chem. 1993, 58, 1991-1993

Asymmetric Dihydroxylation of Olefins with a Simple Chiral Ligand

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Received December 9, 1992 (Revised Manuscript Received February 11, 1993)

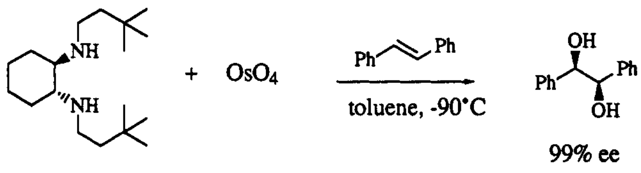
Summary: A C_2 symmetrical chiral ligand derived from (R,R)-*trans*-1,2-diaminocyclohexane is highly effective in the asymmetric cis-dihydroxylation of aromatic and aliphatic di- and trisubstituted olefins under stoichiometric conditions.

The asymmetric dihydroxylation of olefins using osmium tetraoxide in the presence of a chiral ligand or catalyst has received considerable attention since the early seminal contributions by Sharpless and co-workers.[1] Indeed, over the past 12 years, the literature reports several protocols for the conversion of trans and certain cis olefins into the corresponding enantiomerically pure or enriched diols, using stoichiometric[2] conditions in the presence of external chiral amine ligands. Presently, the most recently developed catalytic dihydroxylation reaction conditions by Sharpless and co-workers[3] offer variety in applicability and convenience in execution. Other reports on catalytic processes are also emerging.[4]

We wish to report on the development of an asymmetric dihydroxylation reaction using probably the simplest chiral ligand to date, exemplified by the readily available C_2 symmetrical 1,2-diamine 1 and its enantiomer (Scheme I).[5]

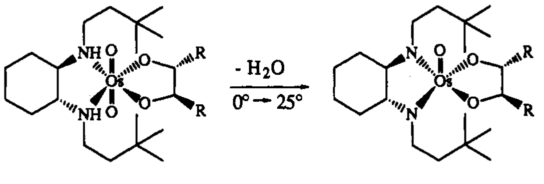
With one exception,[2f] previous ligands have all consisted of *tertiary* diamines, some of which require several steps in their preparation. In this paper, we demonstrate that 1 or its enantiomer effect good to excellent levels of asymmetric cis-dihydroxylations of a variety of aromatic and aliphatic olefins as shown in Table I.[6]

Scheme I



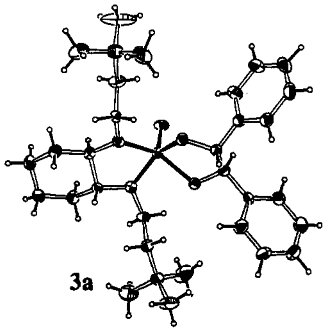
1

Scheme II



2a, R = Ph
2b, R = CO_2Me

3a, R = Ph
3b, R = CO_2Me



3a

In general, the enantiomeric excesses obtained on an average of 2-3 runs per entry are comparable if not exceeding literature values. Noteworthy examples include 1-phenylcyclohexene, indene, and dihydronaphthalene where previous results[2-4] report ee values in the range of 18-99%, 12-67%, and 16-43%, respectively, depending on the method (Table I). Also of interest are the levels achieved with dimethyl fumarate, an apparently unreactive substrate in the Sharpless asymmetric AD reaction.[16] Simple and substituted aliphatic cis olefins, which have resisted to provide good levels of induction in the asymmetric dihydroxylation reaction,[7] remain impregnable under the present conditions for the time being. However, the results obtained in the cases of (*Z*)-methyl cinnamate and (*Z*)-3-phenyl-2-propene (entries 12, 13) are extremely gratifying and compare favorably with two precedents.[2e,8]

The design of the "optimized" ligand structure 1 was arrived at after exploring a number of N-alkyl and N-aralkyl substituents.[9] Indeed, molecular models clearly show the potential for a "shielding cone" at an optimum distance in an activated OsO_4-ligand complex or in an

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[1] (a) Hentges, S. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 4263. (b) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*, Ojima, I., Ed.; VCH: New York, in press.

[2] (a) Tokles, M.; Snyder, J. K. *Tetrahedron Lett.* **1986**, *27*, 3951. (b) Yamada, T.; Narasaka, K. *Chem. Lett.* **1986**, 131. (c) Tomioka, K.; Nakajima, M.; Koga, K. *J. Am. Chem. Soc.* **1987**, *109*, 6213. (d) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L.; Stefanelli, S. *Tetrahedron Lett.* **1987**, *28*, 3139. (e) Oishi, T.; Hirama, M. *J. Org. Chem.* **1989**, *54*, 5834. (f) Corey, E. J.; DaSilva Jardine, P.; Virgil, S.; Yuen, P.-W.; Connell, R. D. *J. Am. Chem. Soc.* **1989**, *111*, 9243. (g) Tomioka, K.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1990**, *31*, 1741. (h) Fuji, K.; Tanaka, K.; Miyamoto, H. *Tetrahedron Lett.* **1992**, *33*, 4021.

[3] (a) Sharpless, K. B.; Amberg, W., Bennani, Y. L., Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768. (b) Xu, D.; Crispino, G. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7570. (c) Crispino, G. A.; Sharpless, K. B. *Tetrahedron Lett.* **1992**, *33*, 4273. (d) Hashiyama, T.; Morikawa, K.; Sharpless, K. B. *J. Org. Chem.* **1992**, *57*, 5067. (e) Lohray, B. B.; Kalanta, T. H.; Kim, B. M.; Park, C. Y.; Shibata, T.; Wai, J. S. M.; Sharpless, K. B. *Tetrahedron Lett.* **1989**, *30*, 2041. (f) Jacobsen, E. N.; Marko, I.; France, M. B.; Svendsen, J. S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 737. (g) Wai, J. S. M.; Marko, I.; Svendsen, J. S.; Finn, M. G., Jacobsen, E. N.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 1123. (h) Jacobsen, E. N.; Marko, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968.

[4] (a) Oishi, T.; Hirama, M. *Tetrahedron Lett.* **1992**, *33*, 639. (b) Imada, Y.; Saito, T.; Kawakami, T.; Murahashi, S.-I. *Tetrahedron Lett.* **1992**, *33*, 5081.

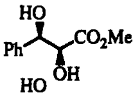
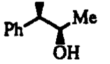
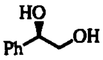
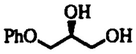
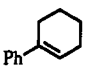
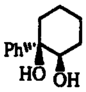
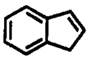
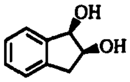
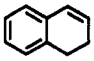
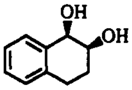
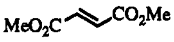
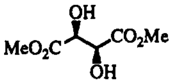
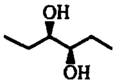
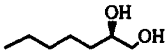
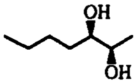
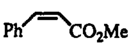
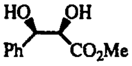
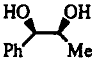
[5] For the preparation of 1, see supplementary material. For related chiral ligands in asymmetric reactions, see: Hanessian, S.; Delorme, D.; Beaudoin, S.; Leblanc, Y. *J. Am. Chem. Soc.* **1984**, *106*, 5754. Hanessian, S.; Bennani, Y. L.; Delorme, D. *Tetrahedron Lett.* **1990**, *31*, 6461. Hanessian, S.; Bennani, Y. L. *Tetrahedron Lett.* **1990**, *31*, 6465, 6468. Hanessian, S.; Beaudoin, S. *Tetrahedron Lett.* **1992**, *33*, 7655, 7659.

[6] Reactions were carried out at -90 °C in the specified solvent using 1.16 equiv of OsO_4 and 1.2 equiv of ligand per 1 equiv of olefin. The preparation of diols in entries 3, 8, 11, and 12 is described in detail in the supplementary material.

[7] Jeong, K.-S.; Sjö, P.; Sharpless, K. B. *Tetrahedron Lett.* **1992**, *33*, 3833.

[8] Wang, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7568.

Table I

entry	olefin	solvent, time	product[a]		% yield[b]	% ee[c]	ref[f]
1		toluene, 6h		2S,3R-	80	99	A
2		toluene, 6h		1R,2R-	82	95	B
3		toluene, 4h		R	70	99	C
4		CH_2Cl_2, 4h		S-[d]	56	64	D
5		toluene, 4h		R,R-	84	90	E
6		toluene, 4h		1R,2S-	70	80	F
7		toluene, 4h		1R,2S-	73	70	G
8		CH_2Cl_2, 4h		S,S-	67	96	H
9		CH_2Cl_2, 5h		R,R-	78	90	I
10		CH_2Cl_2, 5h		R-	70	65	J
11		CH_2Cl_2, 5h		2R,3R-[e]	61	90	-
12		toluene, 5h		2R,3R-	60	87	K
13		toluene, 2h		1R,2S-	80	77	B

[a] Absolute configuration was established by comparison with authentic samples and with literature data unless otherwise noted. [b] Isolated yield after flash column chromatography. [c] Determined by ^{19}F NMR of Mosher's esters (see: Mosher, H. S.; Dale, J. A. *J. Am. Chem. Soc.* **1973**, *95*, 512) by HPLC on CHIRALCEL columns, and by optical rotation whenever appropriate; see supplementary material. [d] Tentatively assigned by analogy from optical rotations of closely related diols; see ref D. [e] Tentatively assigned by analogy. [f] (A) Denis, J. N.; Correa, A.; Greene, A. E. *J. Org. Chem.* **1990**, *55*, 1957. (B) Fisher, F. *Chem. Ber.* **1961**, *94*, 893. (C) Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1970**, *35*, 4002. (D) Rama Rao, A. V.; Gurjar, M. K.; Joshi, S. V. *Tetrahedron: Asymmetry* **1990**, *1*, 697. Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino G. A.; Hartung, J.; Jeong, K. S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768. (E) Berti, G.; Macchia, B.; Macchia, F.; Monti, L. *J. Chem. Soc. C* **1971**, 3371. (F) Imuta, M.; Ziffer, H. *J. Org. Chem.* **1978**, *43*, 4540. (G) Boyd, D. R.; Sharma, N. D.; Boyle, R.; McMordie, R. A. S.; Chima, J.; Dalton H. *Tetrahedron Lett.* **1992**, *33*, 1241. (H) Buchanan, C. *J. Chem. Soc.* **1937**, 582. (I) Cope, A. C.; Shen, T. Y. *J. Am. Chem. Soc.* **1956**, *78*, 5916. (J) Levene, P. A.; Walti, A.-J. *Biol. Chem.* **1932**, *98*, 735. (K) Mathews, B. R.; Jackson, W. R.; Jacobs, H. A.; Watson, K. B. *Aust. J. Chem.* **1990**, *43*, 1195.

OsO_4–olefin–ligand complex. While the precise mechanism and order of events in such ligand-accelerated asymmetric osmylation reactions are still under investigation,[10-13] our simple ligand has provided some intriguing insights into the reactivity of intermediate osmate esters.

A crystalline compound isolated from the reaction of stilbene proved to be the osmate ester **3a** where a molecule of water is lost from the initially formed C_2 symmetrical ester **2a** (Scheme II). The structure of **3a** was confirmed by single-crystal X-ray analysis.[14] This phenomenon occurs readily in all cases listed in Table I, and it can be followed by ^1H and ^{13}C NMR in the case of C_2 symmetrical substrates. We have found that the 1,2-diamine ligand

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(9) For example, the asymmetric dihydroxylation values of styrene with N,N′-substituted *trans*-1,2-diaminocyclohexanes were as follows: benzyl, 36% ee; 2-propyl, 26% ee; 2,2-dimethyl-1-ethyl, 0% ee; 3-methyl-1-butyl, 57% ee; No induction was achieved with the *N,N′*-tetramethyl derivative (stilbene, 1-heptene); see, however, ref 2a.

(10) For recent reviews, see: (a) Jorgensen, K. A.; Schiott, B. *Chem. Rev.* **1990**, *90*, 1483. (b) Schröder, M. *Chem. Rev.* **1980**, *80*, 187.

(11) For theoretical studies, see: (a) Jorgensen, K. A.; Hoffman, R. *J. Am. Chem. Soc.* **1986**, *108*, 1867. (b) Jorgensen, K. A. *Tetrahedron Lett.* **1990**, *31*, 6417. (c) Wu, Y.-D.; Wang, Y.; Houk, K. N. *J. Org. Chem.* **1992**, *57*, 1362.

(12) For spectroscopic studies see: (a) Casey, C. P. *J. Chem. Soc., Chem. Commun.* **1983**, 126. (b) Schröder, M.; Constable, E. C. *J. Chem. Soc., Chem. Commun.*, **1982**, 734.

(13) (a) Lohray, B. B.; Bhushan, V. *Tetrahedron Lett.* **1992**, *33*, 5113. (b) Corey, E. J.; Lotto, G. I. *Tetrahedron Lett.* **1990**, *31*, 2665. (c) Tomioka, K.; Nakajima, M.; Iitaka, Y.; Koga, K. *Tetrahedron Lett.* **1988**, *29*, 573.

(14) See supplementary material for spectroscopic data, X-ray parameters, and procedures.

reported by Corey and co-workers[2f] also loses water once the osmate ester is formed albeit at 50–60 °C in refluxing benzene (^{1}H, ^{13}C NMR). The observation and isolation of such five-coordinate square-based pyramidal Os^{VI} complexes[15] as discreet intermediates for the first time in the context of asymmetric dihydroxylations is noteworthy, even if they do not provide direct mechanistic insights into the early stages of the reaction, which remain as yet unresolved. Regardless of whether these reactions proceed via a 2 + 2[16] or a 3 + 2 cycloaddition,[11] or via a stepwise interaction with equatorial electrophilic and apical nucleophilic oxygen atoms surrounding the osmium atom,[2f] ligand reorganization must occur en route to the C_2 symmetrical and dehydro nonsymmetrical osmate esters **2** and **3**, respectively (Scheme II).[17]

Refinements are in progress to further optimize the structure of ligand **1** for asymmetric dihydroxylation, and to extend its scope to other olefins.[18]

Acknowledgment. We thank NSERCC and FCAR for generous financial assistance. We thank the Fondation pour la Recherche Thérapeutique for a fellowship to P.M.

Supplementary Material Available: Procedures, characterization data, and copies of spectra (31 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(15) See, for example: Lin, J.-H.; Che, C.-M.; Lai, T.-F.; Poon, C.-K.; Cui, Y. X. *J. Chem. Soc., Chem. Commun.* **1991**, 468. Che, C.-M.; Lam, M. H.; Wang, R.-J.; Mak, T. C. W. *J. Chem. Soc., Chem. Commun.* **1990**, 820. Phillips, F. L.; Skapsk, A. C. *Acta Crystallogr.* **1975**, *B31*, 1814.

(16) Sharpless, K. B.; Teranishi, A. Y.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1977**, *99*, 3120.

(17) Inspection of molecular models suggests that a direct attack on the equatorial oxygen atoms of the OsO_4–ligand complex formed from **1** by stilbene, for example, would lead to the enantiomeric (*S*,*S*)-diol; see also ref 2f.

(18) For example, asymmetric dihydroxylation of 3-phenyl-1-propene with reagent **1** gave (2*R*)-3-phenyl-propane-1,2-diol (55% yield; 89% ee, ^{19}F Mosher ester); $[\alpha]^{25}_{D}$ +22.4° (*c* 1, EtOH) (Bergstein, W.; Kleemann, A.; Martens, J. *Synthesis* **1981**, 76); see also ref 2g (86% yield; 47% ee) for the (*S*)-isomer; ref 1h (63% yield; 18% ee) for the (*R*)-isomer. The same reaction with vinylcyclohexane gave (2*R*)-2-cyclohexylethane-1,2-diol (92% yield; 89% ee, ^{19}F Mosher ester); $[\alpha]^{25}_{D}$ −3.7° (*c* 2, $CHCl_3$) (Hirano, T.; Inoue, S.; Tsurata, T. *Makromol. Chem.* **1976**, *177*, 3237); see also ref 3h, 46% ee (*R*)-isomer; using the PHN ligand in the catalytic system gives 80% ee (Prof. K. B. Sharpless, personal communication); see also ref 1b.