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Enantioselective Epoxidation of Terminal Olefins by Chiral Dioxirane

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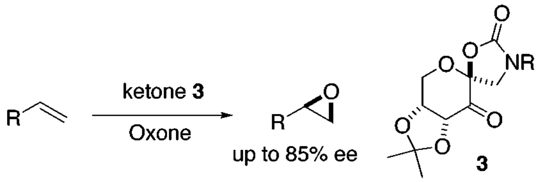
ABSTRACT

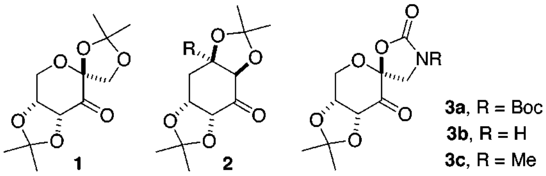


This paper describes an enantioselective epoxidation of terminal olefins using chiral ketone 3 as catalyst and Oxone as oxidant. Up to 85% ee has been obtained.

Asymmetric epoxidation of olefins presents a powerful strategy for the synthesis of enantiomerically enriched epoxides.[1−3] Such epoxides derived from terminal olefins are extremely useful. Asymmetric epoxidation of unfunctionalized terminal olefins has received intensive interest.[4−7] Metal catalysts such as chiral porphyrin and salen complexes have been extensively studied for the epoxidation of terminal olefins. The enantioselectivities have reached the 80% range in a number of cases,[4f,m,o,5c,d,f,g] with >90% ee obtained in a certain case.[4m]

Dioxiranes generated in situ from chiral ketones have been shown to be highly enantioselective for the asymmetric epoxidation of *trans*- and trisubstituted olefins.[8−10] However, highly enantioselective epoxidation of terminal olefins using chiral dioxiranes still remains a challenging problem. During our studies, we found that enantioselectivity for the epoxidation of terminal olefins is highly dependent on ketone structure. The fructose-derived ketone **1**, a very effective catalyst for *trans*- and trisubstituted olefins, gave only 24% ee for styrene (Scheme 1).[10c] On the other hand, up to 70% ee for styrene was obtained when the pseudo C_2 symmetric ketone **2** derived from quinic acid was used.[9p] Recently, we reported ketone **3a**, a nitrogen analogue of **1**, which provided high ee's for the epoxidation of *cis*-olefins.[11] As part of our efforts to gain further understanding of the structural requirements and factors in ketone-catalyzed asymmetric epoxidation, we have investigated the asymmetric epoxidation of some terminal olefins with ketone **3**. Herein we wish to report our preliminary efforts on this subject.

Scheme 1



Initial studies utilized styrene as a test substrate for asymmetric epoxidation. When the reaction was carried out with 15 mol % ketone **3a** at −10 °C, (*R*)-styrene oxide was obtained in 92% yield with 81% ee (Table 1, entry 1).[12] The substituents on the nitrogen of the ketone showed some effect on enantioselectivity, with ketone **3a** giving the best result

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(1) For recent reviews on highly enantioselective epoxidation of allylic alcohols, see: (a) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 4.1. (b) Katsuki, T.; Martin, V. S. *Org. React.* **1996**, *48*, 1.

(2) For recent reviews on metal-catalyzed highly enantioselective epoxidation of unfunctionalized olefins, see: (a) Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I. Ed.; VCH: New York, 1993; Chapter 4.2. (b) Collman, J. P.; Zhang, X.; Lee, V. J.; Uffelman, E. S.; Brauman, J. I. *Science* **1993**, *261*, 1404. (c) Katsuki, T. *Coord. Chem. Rev.* **1995**, *140*, 189. (d) Mukaiyama T. *Aldrichimica Acta* **1996**, *29*, 59.

(3) For a recent review on asymmetric epoxidation of electron-deficient olefins, see: Porter, M. J.; Skidmore, J. *Chem. Commun.* **2000**, 1215.

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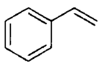
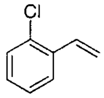
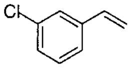
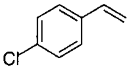
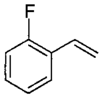
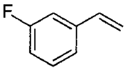
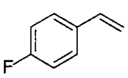
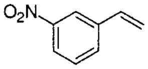
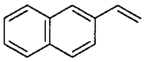
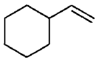
Table 1. Asymmetric Epoxidation of Terminal Olefins Catalyzed by Ketone **3**[a]

entry	substrate	ketone	yield (%)[b]	ee (%)	config.[k]
1[c]		**3a**	100[f]	81[g]	(-)-(R)[13]
2[c]		**3b**	100[f]	68[g]	(-)-(R)
3[c]		**3c**	100[f]	78[g]	(-)-(R)
4[d]		**3a**	61	81[g]	(-)-(R)[13]
5[d]		**3a**	74	83[g]	(-)-(R)[13]
6[d]		**3a**	90	85[g]	(-)-(R)[13]
7[d]		**3a**	87	82[g]	(-)[14]
8[d]		**3a**	93	81[g]	(-)[15]
9[d]		**3a**	94	81[g]	(-)-(R)[16]
10[e]		**3a**	88	74[g]	(-)[4m]
11[c]		**3a**	86	84[h]	(-)-(R)[17]
12[d]		**3a**	93	71[g]	(-)[18]

[a] All reactions were carried out with olefin (0.5 mmol), ketone (0.075−0.15 mmol), Oxone (0.89 mmol), and K_2CO_3 (2.01 mmol) in DME−DMM (3:1, v/v) (7.5 mL) and buffer (0.2 M K_2CO_3−AcOH, pH 8.0) (5 mL) at −10 or 0 °C unless otherwise stated. The reactions were stopped after 3.5 h. For entries 2 and 3, DME was used as solvent instead of DME−DMM. [b] The epoxides were purified by flash chromatography and gave satisfactory spectroscopic characterization. [c] With 0.075 mmol ketone at −10 °C. [d] With 0.15 mmol ketone at −10 °C. [e] With 0.15 mmol ketone at 0 °C. [f] The number is the conversion, which is determined by GC. [g] Enantioselectivity was determined by chiral GC (Chiraldex G-TA). [h] Enantioselectivity was determined by chiral HPLC (Chiralcel OJ). [k] The absolute configurations were determined by comparing the measured optical rotations with the reported ones.

(Table 1, entries 1−3). The good selectivity obtained for styrene encouraged us to extend the epoxidation to other styrenes. The ee's obtained are somewhat dependent on the substituents on the phenyl groups of the olefins (Table 1, entries 4−11). Up to 85% ee was obtained for the substituted styrene substrate (Table 1, entry 6). Certain aliphatic terminal olefins can also be epoxidized selectively. A 71% ee was obtained when a phenyl group on the olefin was replaced

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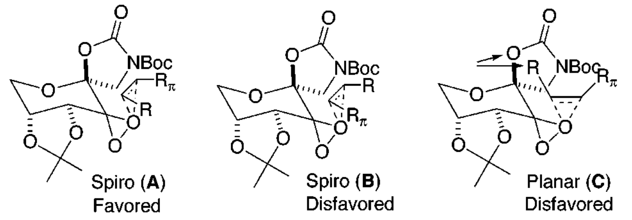
(4) For examples of asymmetric epoxidation of terminal olefins catalyzed by porphyrin complexes, see: (a) Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791. (b) Mansuy, D.; Battioni, P.; Renaud, J.-P.; Guerin, P. *J. Chem. Soc., Chem. Commun.* **1985**, 155. (c) O'Malley, S.; Kodadek, T. *J. Am. Chem. Soc.* **1989**, *111*, 9116. (d) Groves, J. T.; Viski, P. *J. Org. Chem.* **1990**, *55*, 3628. (e) Halterman, R. L.; Jan, S.-T.; *J. Org. Chem.* **1991**, *56*, 5253. (f) Naruta, Y.; Tani, F.; Ishihara, N.; Maruyama, K. *J. Am. Chem. Soc.* **1991**, *113*, 6865. (g) Konishi, K.; Oda, K−i.; Nishida, K.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1992**, *114*, 1313. (h) Collman, J. P.; Lee, V. J.; Zhang, X.; Ibers, J. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1993**, *115*, 3834. (i) Collman, J. P.; Lee, V. J.; Kellen-Yuen, C. J.; Zhang, X.; Ibers, J. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1995**, *117*, 692. (j) Berkessel, A.; Frauenkron, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2265. (k) Gross, Z.; Ini, S. *J. Org. Chem.* **1997**, *62*, 5514. (l) Lai, T.-S.; Zhang, R.; Cheung, K.-K.; Kwong, H.-L.; Che, C.-M. *Chem. Commun.* **1998**, 1583. (m) Collman, J. P.; Wang, Z.; Straumanis, A.; Quelquejeu, M.; Rose, E. *J. Am. Chem. Soc.* **1999**, *121*, 460. (n) Zhang, R.; Yu, W.-Y.; Lai, T.-S.; Che, C.-M. *Chem. Commun.* **1999**, 409. (o) Gross, Z.; Ini, S. *Org. Lett.* **1999**, 2077. (p) Reginato, G.; Bari, L. D.; Salvadori, P.; Guilard, R. *Eur. J. Org. Chem.* **2000**, 1165.

(5) For examples of asymmetric epoxidation of terminal olefins catalyzed by salen complexes, see: (a) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801. (b) O'Connor, K. J.; Wey, S.-J.; Burrows, C. J. *Tetrahedron Lett.* **1992**, *33*, 1001. (c) Palucki, M.; Pospisil, P. J.; Zhang, W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 9333. (d) Palucki, M.; McCormick, G. J.; Jacobsen, E. N. *Tetrahedron Lett.* **1995**, *36*, 5457. (e) Hashihayata, T.; Ito, Y.; Katsuki, T. *Tetrahedron* **1997**, *53*, 9541. (f) Takeda, T.; Irie, R.; Shinoda, Y.; Katsuki, T. *Synlett* **1999**, 1157. (g) Kim, G.-J.; Shin, J.-H. *Tetrahedron Lett.* **1999**, *40*, 6827.

with a cyclohexyl group (Table 1, entry 12). The scope and limitation of this epoxidation are currently being investigated.

A precise understanding of the transition states for the epoxidation of terminal olefins is difficult at this moment. Overall, ketone **3a** gave lower ee's for terminal olefins than *cis*-olefins. For *cis*-olefins, spiro **A** and **B** were the two most plausible transition states (Scheme 2) and groups with a π system preferred to be proximal to the spiro oxazolidinone, with **A** being favored over **B** for substrates containing a π system.[11] A similar analysis could also applied to the terminal olefins. For terminal olefins, planar transition state **C** could also be operating ($R = H$). On the other hand, planar **C** would be less feasible for *cis*-olefins as a result of the steric effect, which could explain that higher ee's were obtained for *cis*-olefins than for terminal olefins with ketone **3a**.

Scheme 2



In summary, the asymmetric epoxidation of terminal olefins using chiral ketone **3** as catalyst has been investigated. Encouragingly high ee's have been obtained for a number of olefins. The results described show that chiral dioxiranes have the potential to epoxidize terminal olefins in a high degree of enantioselectivity in addition to *cis*-, *trans*-, and trisubstituted olefins. Ketone **3** provides a promising lead for further optimization of the ketone structure to enhance the enantioselectivity for terminal olefins.

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Supporting Information Available: GC and HPLC data for the determination of the enantiomeric excess of the epoxides. This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) For examples of asymmetric epoxidation of terminal olefins using chiral oxaziridines and oxaziridinium salts, see: (a) Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3123. (b) Davis, F. A.; Chattopadhyay, S. *Tetrahedron Lett*. **1986**, *27*, 5079. (c) Aggarwal, V. K.; Wang, M. F. *Chem. Commun*. **1996**, 191. (d) Bohe, L.; Lusinchi, M.; Lusinchi, X. *Tetrahedron* **1999**, *55*, 141.

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(8) For general leading references on dioxiranes, see: (a) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187. (b) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res*. **1989**, *22*, 205. (c) Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem*. **1995**, *67*, 811. (d) Clennan, E. L. *Trends Org, Chem*, **1995**, *5*, 231. (e) Adam, W.; Smerz, A. K. *Bull. Soc. Chim. Belg*. **1996**, *105*, 581. (f) Denmark, S. E.; Wu, Z. *Synlett* **1999**, 847. (g) Frohn, M.; Shi, Y. *Synthesis* **2000**, 1979.

(9) For leading references on asymmetric epoxidation mediated in situ by chiral ketones, see: (a) Curci, R.; Fiorentino, M.; Serio, M. R. *J. Chem. Soc., Chem. Commun*. **1984**, 155. (b) Curci, R.; D'Accolti, L.; Fiorentino, M.; Rosa, A. *Tetrahedron Lett*. **1995**, *36*, 5831. (c) Denmark, S. E.; Forbes, D. C.; Hays, D. S.; DePue, J. S.; Wilde, R. G. *J. Org. Chem*. **1995**, *60*, 1391. (d) Brown, D. S.; Marples, B. A.; Smith, P.; Walton, L *Tetrahedron* **1995**, *51*, 3587. (e) Yang, D.; Yip, Y. C.; Tang, M. W.; Wong, M. K.; Zheng, J. H.; Cheung, K. K. *J. Am. Chem. Soc*. **1996**, *118*, 491. (f) Yang, D.; Wang, X.-C.; Wong, M.-K.; Yip, Y.-C.; Tang, M.-W. *J. Am. Chem. Soc*. **1996**, *118*, 11311. (g) Song, C. E.; Kim, Y. H.; Lee, K. C.; Lee, S. G.; Jin, B. W. *Tetrahedron: Asymm*etry **1997**, *8*, 2921. (h) Adam, W.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1997**, *8*, 3995. (i) Denmark, S. E.; Wu, Z.; Crudden, C. M.; Matsuhashi, H. *J. Org. Chem*. **1997**, *62*, 8288. (j) Wang, Z.-X.; Shi, Y. *J. Org. Chem.* **1997**, *62*, 8622. (k) Adam, W.; Fell, R. T.; Saha-Moller, C. R.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1998**, *9*, 397. (l) Armstrong, A.; Hayter, B. R. *Chem. Commun*. **1998**, 621. (m) Yang, D.; Wong, M.-K.; Yip, Y−C.; Wang, X.-C.; Tang, M.-W.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc.* **1998**, *120*, 5943. (n) Yang, D.; Yip, Y.-C.; Chen, J.; Cheung, K.-K. *J. Am. Chem. Soc*. **1998**, *120*, 7659. (o) Adam, W.; Saha-Moller, C. R.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1999**, *10*, 2749. (p) Wang, Z.-X.; Miller, S. M.; Anderson, O. P.; Shi, Y. *J. Org. Chem*. **1999**, *64*, 6443. (q) Carnell, A. J.; Johnstone, R. A. W.; Parsy, C. C.; Sanderson, W. R. *Tetrahedron Lett.* **1999**, *40*, 8029. (r) Armstrong, A.; Hayter, B. R. *Tetrahedron* **1999**, *55*, 11119. (s) Armstrong, A.; Hayter, B. R.; Moss, W. O.; Reeves, J. R.; Wailes, J. S. *Tetrahedron: Asymmetry* **2000**, *11*, 2057. (t) Solladie-Cavallo, A.; Bouerat, L. *Org. Lett.* **2000**, *2*, 3531.

(10) For examples of asymmetric epoxidation mediated in situ by fructose-derived ketones, see: (a) Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9806. (b) Wang, Z.-X.; Tu, Y.; Frohn, M.; Shi, Y. *J. Org. Chem*. **1997**, *62*, 2328. (c) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224. (d) Frohn, M.; Dalkiewicz, M.; Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Org. Chem*. **1998**, *63*, 2948. (e) Wang, Z.-X.; Shi, Y. *J. Org. Chem*. **1998**, *63*, 3099. (f) Cao, G.-A.; Wang, Z.-X.; Tu, Y.; Shi, Y. *Tetrahedron Lett*. **1998**, *39*, 4425. (g) Zhu, Y.; Tu, Y.; Yu, H.; Shi, Y. *Tetrahedron Lett*. **1998**, *39*, 7819. (h) Tu, Y.; Wang, Z.-X.; Frohn, M.; He, M.; Yu, H.; Tang, Y.; Shi, Y. *J. Org. Chem*. **1998**, *63*, 8475. (i) Wang, Z.-X.; Cao, G.-A.; Shi, Y. *J. Org. Chem*. **1999**, *64*, 7646. (j) Warren, J. D.; Shi, Y. *J. Org. Chem.* **1999**, *64*, 7675. (k) Frohn, M.; Zhou, X.; Zhang, J.-R.; Tang, Y.; Shi, Y. *J. Am. Chem. Soc.* **1999**, *121*, 7718. (l) Shu, L.; Shi. Y. *Tetrahedron Lett.* **1999**, *40*, 8721.

(11) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc*. **2000**, *122*, 11551.

(12) **Representative Asymmetric Epoxidation Procedure.** To a solution of styrene (0.052 g, 0.5 mmol) and ketone **3a** (0.026 g, 0.075 mmol) in DME−DMM (3:1, v/v) (7.5 mL) were added buffer (0.2 M K_2CO_3−AcOH in 4×10^{-4} M aqueous EDTA, buffer pH = 8.0) (5 mL) and Bu_4NHSO_4 (0.0075 g, 0.02 mmol) with stirring. After the mixture was cooled to about −10 °C (bath temperature) via a NaCl−ice bath, a solution of Oxone (0.548 g, 0.89 mmol) in 4×10^{-4} M aqueous EDTA (4.2 mL), and a solution of K_2CO_3 (0.278 g, 2.01 mmol) in 4×10^{-4} M aqueous EDTA (4.2 mL) were added dropwise separately over a period of 3.5 h via a syringe pump. The reaction was then extracted with pentane. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography [the silica gel was buffered with 1% Et_3N in pentane; pentane−ether (1:0 to 10:1) was used as eluent] to give styrene oxide as a colorless liquid (0.055 g, 92% yield, 81% ee).

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(18) (a) Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1994**, *116*, 6142. (b) Nelson, A.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1963.