Pergamon

Tetrahedron: Asymmetry, Vol. 8, No. 17, pp. 2921–2926. 1997

Printed in Great Britain
PII: S0957-4166(97)00352-2
0957-4166/97 $17.00 + 0.00

New C_2-symmetric chiral ketones for catalytic asymmetric epoxidation of unfunctionalized olefins

Choong Eui Song,[a,*] Yang Hee Kim,[a] Kyo Chul Lee,[a] Sang-gi Lee [a] and Byung Woo Jin [b]

[a] Division of Applied Science, Korea Institute of Science and Technology, P.O. Box 131, Cheongryang, Seoul 130–650, Korea

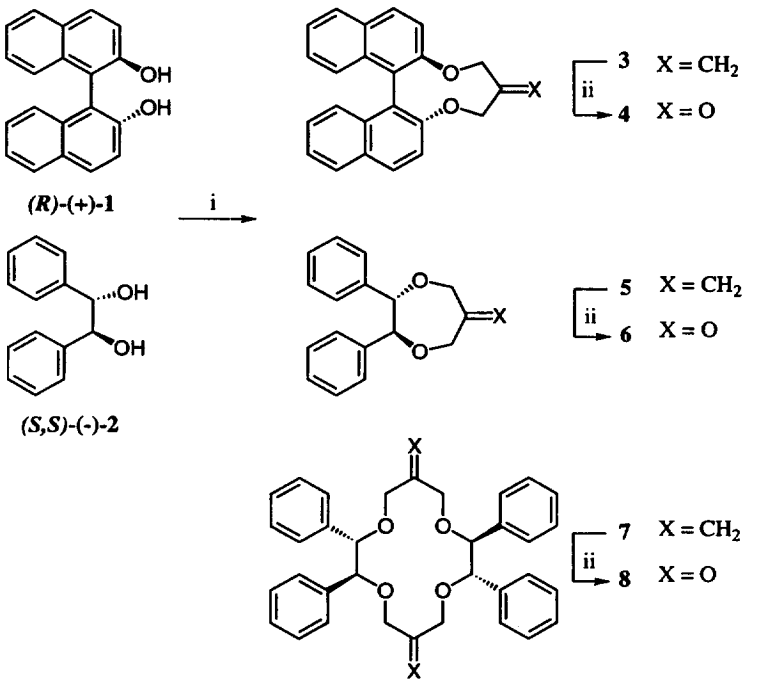
[b] Chong Kun Dang Corp, Shindorim-dong 410, Guro-gu, Seoul, Korea

Abstract: Using new C_2-symmetric chiral ketones **4** and **6** as precursors for chiral dioxiranes generated *in situ*, the asymmetric epoxidation of olefins has been achieved in moderate ee. © 1997 Elsevier Science Ltd

Enantioselective epoxidation of olefins bearing no functionality to precoordinate to the catalyst represents one of the most useful synthetic transformations for the introduction of functionality into organic molecules. In this respect, various metal complex catalysts have been developed and the most spectacular advances were recently achieved by Jacobsen with the introduction of Mn(III)–salen complex catalysts.[1] In contrast with metal complex catalysts, there were no efficient non-metal catalysts for the asymmetric epoxidation of unfunctionalized olefins. Therefore, much effort has been directed towards the development of non-metal catalysts for this purpose.[2] Amongst these, the ketone-Oxone® epoxidation has received a great deal of attention, because it is a catalytic process and in particular asymmetric epoxidation using chiral ketones is potentially very important.[3,4] However, the structure of the reactive intermediate responsible for the epoxidation of olefins using ketone-Oxone® still remains a controversy. Experiments using ^{18}O labelled $KHSO_5$ have provided evidence that a dioxirane intermediate is involved.[5] Whereas, an experiment using ^{18}O labelled ketone suggests that a dioxirane is not responsible for alkene epoxidation using ketone-Oxone® in a biphasic solvent system (e.g. CH_2Cl_2–H_2O).[6] For the development of efficient chiral ketones, understanding of the nature of the reactive oxidizing species in reaction medium may be important. Recently, we discovered that a dioxirane is reactive intermediate for alkene epoxidation using racemic ^{18}O labelled ketone **4** and Oxone in the CH_3CN–H_2O solvent system.[7] Based on this result, we assumed that optically pure ketone **4** could be a promising catalyst for asymmetric epoxidation of unfunctionalized olefins. This ketone is electronically activated by α,α'-oxygen atoms and the carbonyl group is not hindered sterically. Therefore, it is expected that ketone **4** is highly active for epoxidation. Moreover, enantiomerically pure ketone **4** possessing C_2-symmetry and rigid conformation might have potential for asymmetric epoxidation. Here we report our results for asymmetric epoxidation of unfunctionalized olefins using new C_2-symmetric chiral ketone catalysts **4** and **6**.

The chiral ketone **4** was simply synthesized by the reaction of (*R*)-(+)-1,1′-bi-2-naphthol (**1**) with 3-chloro-2-chloromethyl-1-propene, followed by ozonolysis as shown in Scheme 1. The structure of **4** was confirmed by single crystal X-ray structure analysis (Figure 1). X-Ray analysis revealed that ketone **4** indeed has a C_2-symmetric structure: the keto group lies on C_2 axis of the molecule and the dihedral angle of the two naphthalene rings is 71°. However, the reaction of (*S,S*)-(−)-1,2-diphenyl-1,2-diol (**2**) with 3-chloro-2-chloromethyl-1-propene gave a mixture of olefin **5** as a colorless viscous oil and dimeric olefin **7** as a white solid. The ozonolysis of **5** and **7** gave the ketone **6** and **8**,[8] respectively. The structure of ketone **8** was also determined by X-ray single crystal structure analysis.

* Corresponding author.



Scheme 1. Reagents: i) NaH/DMF, $ClCH_2C(=CH_2)CH_2Cl$; ii) O_3/CH_2Cl_2 then PPh_3.

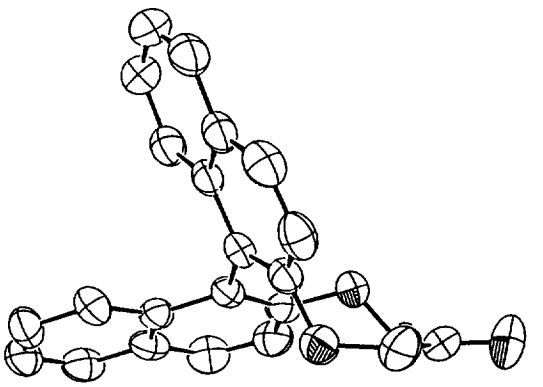
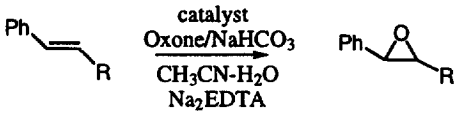


Figure 1. X-Ray structure of ketone **4**.

In order to examine the catalytic efficiency of ketones **4**, **6** and **8**, the epoxidation reactions of *trans*-stilbene and *trans*-β-methyl styrene were carried out in a homogeneous CH_3CN–H_2O solvent system under same conditions reported in the literature[9] and the results are summarized in Table 1.

In a 1:1 ketone:olefin ratio at room temperature, epoxidation catalyzed by ketones **4** and **6** proceeded within 1 h, and afforded *trans*-stilbene oxide with moderate ee in good yields (entries 1 and 3, entries 6 and 7). The enantioselectivities were increased by decreasing the reaction temperature but the reaction rates were decreased. For instance, when the epoxidation was carried out at room temperature, the reaction was completed within 1 h with 30% ee (entry 3). Whereas, the reaction was completed in 5 h at 0°C, but the enantioselectivity was increased to 59% ee (entry 4). However, the temperature dependency of the enantioselectivity in ketone **4** is not as much as in ketone **6** (entries 1 and 2).

Table 1. Asymmetric epoxidation of unfunctionalized olefins catalyzed by ketones **4** and **6**[a]



entry	catalyst	R=	temp.	time	yield (%)[b]	ee (%)[c]	config[d]
1	**4**	Ph	rt	1 h	90	20	*S, S*
2	**4**	Ph	0 °C	5 h	79	26	*S, S*
3	**6**	Ph	rt	1 h	73	30	*S, S*
4	**6**	Ph	0 °C	5 h	72	59	*S, S*
5	**8**	Ph	rt	2 days	n.d.	n.d.	n.d.
6	**4**	CH_3	rt	1 h	95	29	*S, S*
7	**6**	CH_3	rt	1 h	61	20	*S, S*

[a] Unless otherwise indicated, all the epoxidation reactions were carried out with substrate (1 equiv), ketone (1 equiv), Oxone (5 equiv), and $NaHCO_3$ (15.5 equiv) in CH_3CN-aqueous EDTA (4 x 10^{-4} M) (~1.5:1). [b] GC yields. [c] Determined by ^1H NMR using chiral shift reagent Eu(hfc)$_3$. [d] The configuration of predominant enantiomer is given.[10]

Surprisingly, however, the ketone **8** exhibited very low catalytic activity. For example, under the same reaction conditions only trace amounts of *trans*-stilbene oxide were detected after 2 days. It is not clear yet why ketone **8** showed poor catalytic activity.

On the bases of the present and reported results,[4] symmetricity and the rigid ring conformation of the chiral dioxirane generated *in situ* and the distances between the chiral center and one of the diastereotopic oxygen atoms of the dioxirane may be important to achieve high enantioseletivities. Therefore, it seems the structure of chiral dioxirane and of the prochiral alkene have influence on the enantioselectivity. Our efforts are continuing into the design of chiral ketones having suitable structural features to increase enantioselectivities.

Experimental

(R)-3-Methylene-3,4-dihydro-2H-dinaphtho[2,1-f:1,2-h][1,5]dioxonine (3)

To a solution of (*R*)-(+)-1,1′-bis-2-naphthol (5.0 g, 17.46 mmol) in dried DMF (150 mL), 60% NaH in mineral oil (1.75 g, 43.65 mmol) was added at 0°C under N_2. After stirring for 1 h at room temperature, 3-chloro-2-chloromethyl-1-propene (2.18 g, 17.46 mmol) was added, and the mixture was stirred for 1 h at 60°C. The reaction mixture was allowed to cool to room temperature, poured into saturated NH_4Cl aqueous solution, and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4. After evaporation of the solvent, the residue was crystallized with ethyl ether to give olefin **3** (4.32 g, 73.1%). mp 188–190°C; $[\alpha]^{25}_D$ −384.7 (*c* 1.04, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.76 (s, 4 H, OCH_2–), 5.21 (s, 2 H, C=CH_2), 7.1–8.0 (m, 12 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 154.99, 142.02, 133.49, 130.57, 129.69, 128.18, 126.40, 126.38, 124.42, 123.85, 121.63, 119.37, 76.08; EIHRMS *m/e* calcd for $C_{24}H_{18}O_2$: 338.1307. Found: 338.1305. Anal. Calcd for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 84.8; H, 5.42.

(R)-3,4-Dihydro-2H-dinaphtho[2,1-f:1,2-h][1,5]dioxonin-3-one (4)

A solution of olefin **3** (4.17 g, 12.32 mmol) in CH_2Cl_2 (150 mL) was ozonized at −78°C by passing the O_3/O_2 stream until the solution was saturated with O_3. Excess O_3 was removed by O_2 stream, and triphenyl phosphine (5.46 g, 20.81 mmol) was added portionwise to the reaction mixture. After stirring for 30–40 min at −78°C, the mixture was allowed to warm to room temperature. The solvent was evaporated, and the residue was purified chromatographically on silica gel (ethyl acetate/hexane=1:2 as eluent) to give (*R*)-(+)-1,1′-bi-2-naphthol ketone **4** (2.39 g, 56.9%). If necessary, this material can be recrystallized from ethyl acetate to furnish single crystals. mp 196–198°C; $[\alpha]^{25}_D$ −545.9 (*c* 1.03, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.95 (AB q, *J*=16.8 Hz, 4 H, OCH_2–), 7.2–8.0 (m, 12 H, ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 208.72, 156.32, 133.73, 131.07, 128.81, 127.27, 127.11, 125.33, 121.76, 118.77, 79.87; IR (KBr) 1718.0 cm^{-1}; EIHRMS *m/e* calcd for $C_{23}H_{16}O_3$: 340.1099. Found: 340.1094. Anal. Calcd for $C_{23}H_{16}O_3$: C, 81.16; H, 4.74. Found: C, 80.7; H, 4.78.

Crystal data: $C_{23}H_{16}O_3$, orthorhombic, $P2_12_12_1$, *a*=8.976(4), *b*=12.150(3), *c*=15.566(3) Å, V=1697.5(8) $Å^3$, Z=4, D_c=1.332 g/cm^3, F(000)=712, λ(MoKα)=0.71073 Å, 1131 Independent reflections with I/σ (I)≥2.0 were used on the analysis. R=0.059. Data for crystallographic analysis were measured on an Enraf–Nonius CAD-4 diffractometer using Mo radition and ϖ-2 scans in the range of θ; 1.79<θ<24.96. Structure was solved by direct methods and refined by least squares using the SHEL-X.

(2S,3S)-6-Methylene-2,3-diphenyl-1,4-dioxepane (5) and (2S,3S,9S,10S)-6,13-dimethylene-2,3,9,10-tetraphenyl-1,4,8,11-tetraoxacyclotetradecane (7)

To a solution of (*S,S*)-(−)-stilbenediol (5.0 g, 23.33 mmol) in dried DMF (150 mL), 60% NaH in mineral oil (2.33 g, 58.34 mmol) was added at 0°C under N_2. After stirring for 1 h at room temperature, 3-chloro-2-chloromethyl-1-propene (2.92 g, 23.33 mmol) was added, and the mixture was stirred for 1 h at 60°C. The reaction mixture was poured into saturated NH_4Cl aqueous solution and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4. After evaporation of the solvent, the olefin **5** (R_f=0.65) and **7** (R_f=0.58) were separated by column chromatography on silica gel (ethyl acetate/hexane=1:4).

Olefin **5** (2.02 g, 32.5%) as a viscous oil: $[\alpha]^{25}_D$ −78.1 (*c* 3.17, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.54 (s, 2 H), 4.71 (AB q, *J*=14.4 Hz, OCH_2–, 4 H), 5.07 (s, 2 H), 7.0–7.3 (m, ArH, 10 H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 148.00, 137.44, 126.39, 126.13, 125.80, 107.30, 90.55, 72.65; EIHRMS *m/e* calcd for $C_{18}H_{18}O_2$: 266.1306. Found: 266.1306.

Olefin **7** (1.71 g, 27.5%) as a white solid: mp 120–124°C; $[\alpha]^{25}_D$ −18.57 (*c* 1.02, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.26 (q, *J*=11.4 Hz, 4 H, OCH_2–), 4.70 (s, PhCH, 2 H), 5.07 (s, CH_2–, 2 H), 7.0–7.3 (m, ArH, 10 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 142.35, 137.41, 126.14, 114.15, 84.19, 69.10; Anal. Calcd for $(C_{18}H_{18}O_2)_2$: C, 81.17; H, 6.81. Found: C, 81.0; H, 6.81.

(2S,3S)-2,3-Diphenyl-1,4-dioxepan-6-one (6)

Olefin **5** (2.0 g, 7.51 mmol) was ozonized as above described to give chiral ketone **6** (1.45 g, 71.9%) as a colorless oil after purification by column chromatography (ethyl acetate/hexane=2:1): $[\alpha]^{25}_D$ −136.2 (*c* 0.22, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.56 (ABq, *J*=16.5 Hz, OCH_2–, 4 H), 4.64 (s, 2 H, PhCH), 6.9–7.3 (m, Ar H, 10 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 211.93, 138.45, 130.07, 128.66, 127.71, 93.65, 77.99; IR (neat) 1728 cm^{-1}; CI-MS (m/z) 269 (M^++1).

(2S,3S,9S,10S)-2,3,9,10-Tetraphenyl-1,4,8,11-tetraoxacyclotetradecane-6,13-dione (8)

Olefin **7** (1.51 g, 1.89 mmol) was ozonized as above described to give chiral ketone **8** (1.04 g, 68.4%) as a white solid after purification by column chromatography (ethyl acetate/hexane=2:1): mp 178–183°C; $[\alpha]^{25}_D$ −0.65 (*c* 1.23, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.38 (ABq, *J*=15.8 Hz, OCH_2–, 4 H), 4.69 (s, 2 H, PhCH), 7.0–7.2 (m, Ar H, 10 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 203.72,

135.68, 126.49, 126.30, 125.99, 86.74, 72.01; IR (neat) 1732 cm^{-1}; Anal. Calcd for $(C_{17}H_{16}O_3)_2$: C, 76.09; H, 6.01. Found: C, 76.1; H, 6.01.

Acknowledgements

This research was supported by a grant (1-2E14003-24-0) from the Ministry of Science and Technology in Korea. We also thank Dr Kwan Mook Kim for X-ray crystallographic structure determination.

References

1. (a) Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, **1993** and references therein. (b) Chang, S.; Lee, N. H.; Jacobsen, E. N. *J. Org. Chem.* **1993**, *58*, 6939.

2. (a) Rebek, J. *Heterocycles* **1981**, *15*, 517 and references therein. (b) Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3123. (c) Davis, F. A.; Chattopadhyay, S. *Tetrahedron Lett.* **1986**, *27*, 5079. (d) Davis, F. A.; ThimmaReddy, R.; McCauley, J. P.; Przeslawski, R. M.; Harakal, M. E. *J. Org. Chem.* **1991**, *56*, 809.

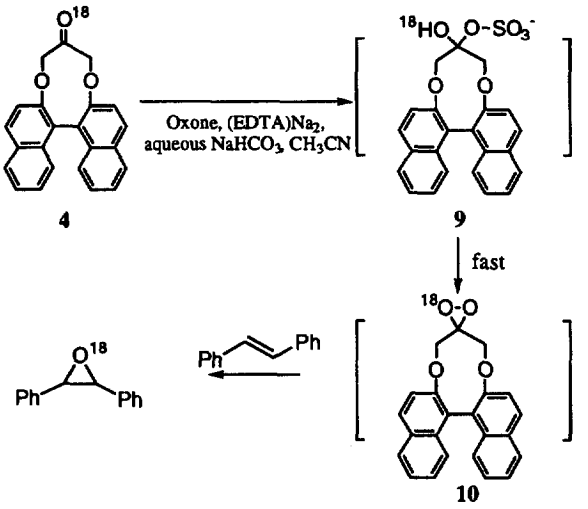
3. For recent reviews on dioxirane chemisty, see: (a) Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem.*, **1995**, *67*, 811. (b) Curci, R. In *Advances in Oxygenated Process*; Baumstark, A. L., Ed.; JAI: Greenwich CT, **1990**; Vol 2, Chapter I, pp 1–59. (c) Adam, W.; Hadjiarapoglou, L. P.; Curci, R.; Mello, R. In *Organic Peroxides*; W. Ando, Ed.; Wiley, New York, **1992**, Chapter 4, pp. 195–219.

4. (a) Curci, R.; Fiorentino, M.; Serio, M. R. *Chem. Commun.* **1984**, 155. (b) Curci, R.; D'Accolti, L.; Fiorentino, M.; Rosa, A. *Tetrahedron Lett.* **1995**, *36*, 5831. (c) Brown, D. S.; Marples, B. A.; Smith, P.; Walton, L. *Tetrahedron* **1995**, *51*, 3587. (d) Yang, D.; Yip, Y.-C.; Tang, M.-W.; Wong, M.-K.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc.* **1996**, *118*, 491. (e) Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9806.

5. Edwards, J. O.; Pater, R. H.; Curci, R.; Di Furia, F. *Photochem. Photobiol.* **1979**, *30*, 63.

6. Armstrong, A.; Clarke, P. A.; and Wood, A. *Chem. Commun.* **1996**, 849.

7. **^{18}O Labelling experiment**: *ca* 55% ^{18}O labelled (by MS analysis) racemic ketone **4** was prepared by stirring in $H_2{}^{18}O$/1,4-dioxane in the presence of catalytic amount of *p*-TsOH for 24 h at room temperature, followed by drying with $MgSO_4$ and evaporation of the solvent. Initially, epoxidation of *trans*-stilbene was performed by reported method where Oxone® was added to a 1:1 ketone **4**: *trans*-stilbene mixture in CH_3CN–H_2O during 1 h at room temperature.[9] However, in GC-MS analysis, it has been showed only less than 2% transfer of the ^{18}O label to stilbene oxide. The lack of label transfer may be due to formation of hydrate causing delabeling of the ketone **4** in aqueous medium. The ^{18}O labeled ketone **4** was delabelled about 65% and up to 98% in 5 min and 1.5 h, respectively, by stirring in CH_3CN–H_2O at room temperature. In order to minimize the delabelling, we modified the reaction conditions. Thus, the ^{18}O labelled ketone **4** was added to a solution of *trans*-stilbene and Oxone® in CH_3CN–H_2O at room temperature resulting incorporation of 15.7% of ^{18}O in stilbene oxide and the reaction was completed within 45 min. Incorporation of ^{18}O in stilbene oxide clearly indicates that dioxirane is responsible for the epoxidation of olefins using ketone-Oxone® which implies that the formation of the dioxirane **10** by ring closure of **9** is faster than that of the epoxidation by **9** in CH_3CN–H_2O solvent system.



4 9 10

8. The X-ray data of **8** will be published later.
9. Yang, D.; Wong, M.-K.; Yip, Y.-C. *J. Org. Chem.* **1995**, *60*, 3887.
10. (a) *trans*-Stilbene oxide: Berti, G.; Bottari, F.; Ferrani, P. L.; Machia, B. *J. Org. Chem.* **1965**, *30*, 4091. (b) *trans*-β-Methyl styrene oxide: Audier, H. E.; Dupin, J. F.; Tullien, *J. Bull. Soc. Chim. Fr.* **1996**, 2811.

(Received in Japan 18 June 1997; accepted 4 August 1997)