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Chiral ketone-catalyzed asymmetric epoxidation of olefins with Oxone®

Koichiro Matsumoto and Kiyoshi Tomioka*

Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan

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Abstract—Chiral ketones **1** and **2** bearing 1-aza-7-oxabicyclo[3.5.0]decane skeleton and their C_2-symmetric analogue **3** were readily prepared and evaluated as a chiral dioxirane precursor for asymmetric epoxidation of olefins with Oxone®. The ketone **2**, bearing a diphenyl steric wall, was not effective and gave quite poor selectivity. Good selectivity up to 83% ee was obtained using **1** and **3**, which suggested that Coulomb repulsion by carbonyl and ether oxygen atoms are operative as an electronic wall rather than a steric wall. © 2002 Elsevier Science Ltd. All rights reserved.

As part of our studies directed toward the development of external chiral ligands that effectively control a variety type of catalytic asymmetric reactions,[1,2] we designed and evaluated several types of chiral ketones for precursors to chiral dioxiranes that mediate asymmetric epoxidation of olefins with Oxone®.[3] Reported and our own stereochemical control methodology relied on a steric wall concept operative through interference of sterically unfavorable approach of an olefin to a dioxirane.[4] Our chiral ketones were characteristic by 1,2-diphenylethane-1,2-diamine[5] or binaphthyl as a chiral backbone and arylsulfonamide moiety as a steric wall as well as an electron-withdrawing group for electrophilic activation of a ketone for the formation of a dioxirane.[6] However, enantioselectivity was unexpectedly poor, at most 30% ee for epoxidation of stilbene, even though the sense of enantiofacial differentiation was the same as we predicted.[7] The second generation of our asymmetric epoxidation was focused on the use of chiral heterocycles as a backbone of the ketone. New chiral ketone **1** has a 1-aza-7-oxabicyclo[3.5.0]decane skeleton and its dioxirane takes a MM2-calculated conformation **A** (Figs. 1 and 2). Diphenyl version **2** was firstly expected to behave better from the viewpoint of a steric wall because both of left-up and right-bottom sides were blocked by a pyrrolidone and a phenyl rings (**B**), respectively, giving superior stereoselection.

New ketones **1** and **2** were readily prepared in two steps through annelation[8] of the heterocycles **7** and **8**[9] with 3-chloro-2-chloromethylpropene to **4** and **5** and following oxidative degradation of the *exo*-methylene in 99 and 93% overall yields. Epoxidation of *trans*-stilbene **10a** with Oxone® in the presence of a stoichiometric amount of **1** in acetonitrile–dimethoxymethane (DMM)–water (2:1:2) afforded (*S*,*S*)-stilbene oxide **11a** in 60% ee, whereas the reaction with **2** gave (*R*,*R*)-**11a**

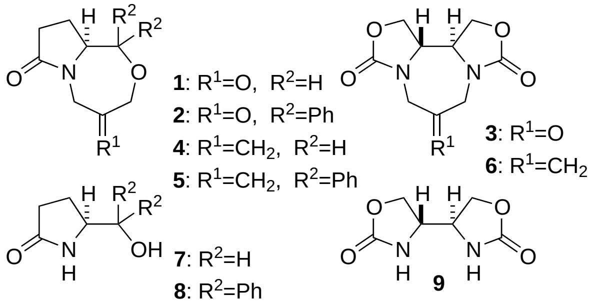

Figure 1. Chiral ketones and precursors.

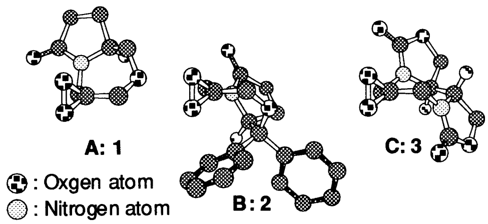

Figure 2. Chiral dioxiranes derived from **1**–**3**. For clarification, protons are omitted except protons at the chiral center and **C** is presented as an antipode.

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* Corresponding author. Tel.: +81-75-753-4553; fax: +81-75-753-4604; e-mail: tomioka@pharm.kyoto-u.ac.jp

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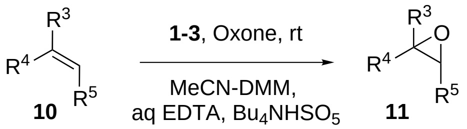
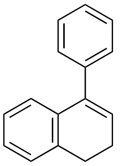
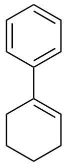
Table 1. Asymmetric epoxidation of olefins with ketone–Oxone®



Run	10	R^3	R^4	R^5	1-3	Time h	Yield %	Ee %	Confgn
1	**a**	Ph	H	Ph	**1**	2	99	57	*S,S*
2					**2**	2	40	6	*R,R*
3					**3**	2	93	64	*R,R*
4	**b**	C_6H_{13}	H	C_6H_{13}	**1**	3	41	18	*S,S*
5					**3**	2	24	27	*R,R*
6	**c**	Ph	H	CH_3	**1**	2	52	57	*S,S*
7					**3**	2	78	62	*R,R*
8	**d**	Ph	Ph	Ph	**1**	5	63	70	*S*
9					**3**	6	48	73	*R*
10	**e**				**1**	2	99	75	1*R*,2*S*
11					**3**	2	99	61	1*S*,2*R*
12	**f**				**1**	2	99	71	*S,S*
13					**3**	2	99	75	*R,R*
14					**1**	2	99	78	*S,S*
15					**3**	2	99	82	*R,R*


10e


10f

Run 14,15; A mixture of 1,4–dioxane and water was used as a solvent at –8°C.

in only 6% ee (Table 1, runs 1 and 2). It was surprising to know that the diphenyl steric wall of **2** was not effective and **1** behaved favorably more than **2**. Since the more vacant space seems to be available in the bottom side of **A** rather than the top side, there should be some factors other than steric, which control the stereoselection in the bottom side. The conformational difference between **A** and **B** was assumed to be responsible for the selectivity, if ether and carbonyl oxygen atoms of **A** produce Coulomb repulsion with the phenyl ring of stilbene more effectively than those of **B**. Poorer selectivity, 18% ee, in the reaction of *trans*-olefin **10b** bearing alkyl substituents at the both olefin terminal agreed with the assumption (run 4). Based on both the electronic wall hypothesis above and an advantageous motif C_2 symmetry, we designed and prepared a ketone **3** starting from **9**[10] via **6** (Figs. 1 and 2). Epoxidation of **10a** with **3** provided **11a**[11] in 66% ee (run 3).

The alkyl substituent at one end was not an obstacle allowing epoxidation of **10c** in 57% ee (run 6). Epoxidation of linear *trans*-di **10a–c** (runs 1–7), tri-substituted **10d** (runs 8 and 9), and cyclic **10e** and **10f** (runs 10–13) olefins was examined with 2 equiv. of **1** or **3** in acetonitrile–DMM at room temperature. The sense of enantiofacial selection was the same, top face attack to **10** for **1**, and bottom face attack for **3** of the reversed-type of absolute configuration to **1**. Generally, C_2 symmetric ketone **3** behaved in a better way than **2**. The best ee value was obtained by the reaction of 1-phenylcyclohexene **10f** using **3** in a mixture of 1,4-dioxane and water (3:2) at −8°C to give **11f** in 82% ee (run 15).

It is noteworthy that the catalytic epoxidation of **10f** with substoichiometric amount of **1** and **3** in MeCN–DMM–water gave **11f** in a reasonably high enantioselectivity. The reaction with 40 mol% of **1** and **3** at rt for 2 h gave quantitatively **11f** in 71 and 76% ee, respectively. It was remarkable to find that the reaction with 20 mol% of **3** at −12°C for 4 h gave **11f** in 83% ee and quantitative yield.

Acknowledgements

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