Communications to the Editor

Bull. Korean Chem. Soc. 2009, Vol. 30, No. 3 541

A Green Protocol for Asymmetric Epoxidation of Olefins Catalyzed by Carbon Dioxide Soluble Chiral Salen-Mn(III) Complexes in Supercritical CO_2

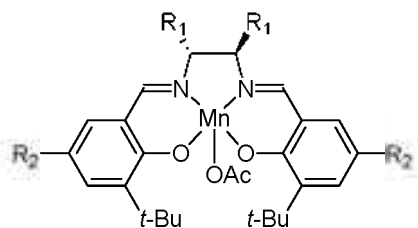**Chunji Gao, Wooseob Shin, Jungmin Han, Donggyun Han, M. Adharvana Chari, Hongdoo Kim, and Kwang-Hyun Ahn***

*Department of Applied Chemistry and MRCID, Kyung Hee University, Yongin 446-701, Korea. *E-mail: khahn@khu.ac.kr
Received November 26, 2008, Accepted February 5, 2009*

Present in industry, one of the major challenges for chemists is to develop processes that fulfill the environmental, economical and social goals of green chemistry.[1] The application of supercritical fluids as a solvent in various areas of chemical processes, such as HPLC analysis and a crystallization process, has received much attention over the last decade because of the potential advantage that this technology offers over traditional organic solvents.[2,3] Especially, supercritical CO_2 ($scCO_2$) has been widely tested because CO_2 is abundant, cheap, non-toxic and neither combustible nor explosive. Further, it has been successfully demonstrated that organic reaction[4] can be performed in $scCO_2$.

We have been interested in using $scCO_2$ as a reaction solvent because it may provide a different reactivity compared with common organic solvents. In particular, we wanted to perform the asymmetric epoxidation of olefins catalyzed by chiral Salen-Mn(III) complex in $scCO_2$ to test the potential of $scCO_2$ as a solvent. Since the Salen-Mn(III) catalyzed epoxidation[5,6] has been recognized as one of the most useful reactions to synthesize chiral epoxides,[7-9] which are versatile synthetic intermediates for the syntheses of biologically and pharmaceutically important molecules, with high levels of enantioselectivity, it will be interesting to see the effect of $scCO_2$ to the enantioselectivity of the reaction.

To study the asymmetric epoxidation in $scCO_2$, a chiral Mn-complex which may be soluble in $scCO_2$ has to be prepared. It is well known that a perfluorinated alkyl group increases the solubility of organic compounds in $scCO_2$.[10] Thus, we decided to prepare perfluorinated Salen-Mn(III) complexes and found that Salen-Mn(III) complexes such as 1 and 2 were already reported by Pozzi's group.[11] The 1 and 2 contain the sterically hindered *t*-butyl group at C3 and C3' positions that is required to obtain the high degree of enantioselectivity in chiral
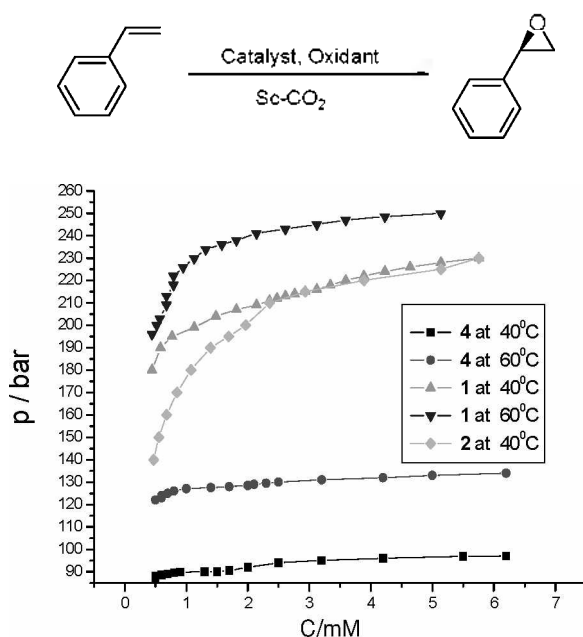
Salen-Mn(III) complex catalyzed epoxidations of alkenes.[12] and the perfluorinated alkyl group at C5 and C5' position.

The solubility of Salen-Mn(III) complexes 1, 2 and metal free ligand (4) of complex 1 prepared according to the literature procedure[11] in supercritical CO_2 was studied and the results were presented in the Figure 1. As shown in the figure. Salen ligand 4 showed a good solubility in CO_2 at below 100 bar and 40 °C. At 60 °C, a higher CO_2 pressure was required to dissolve the ligand. The solubility of Salen-Mn(III) complexes was found to be low compared with Salen ligand 4. However, both complexes 1 and 2 were soluble in CO_2 at 250 bar and 40 °C. Based on these solubility data, the epoxidation of olefins was performed at 250 bar and 35 °C. Since the enantioselectivity obtained in a catalytic asymmetric reaction is increased, in general, at a low reaction temperature, 35 °C instead of 40 °C was used as the reaction temperature.

Initially, we studied the epoxidation of styrene (1 eq) with PhIO (2 eq) in the presence of 5 mol% of 1 in a 10 mL view cell, at 35 °C and 250 bar pressure in supercritical CO_2 (Table 1). Styrene oxide was obtained in 66% yield with 21% ee. (entry 1).

When the iodosylbenzene was increased up to 4 equivalents

R_1 = -(CH$_2$)$_6$-, R_2 = -(CF$_2$)$_7$CF$_3$: (*R,R*)-**1**
R_1 = Ph, R_2 = -(CF$_2$)$_7$CF$_3$: (*R,R*)-**2**
R_1 = -(CH$_2$)$_6$-, R_2 = -*t*-Bu : (*R,R*)-**3**

Figure 1. Solubility of salen ligand 4, salen metal complexes 1 and 2 in CO_2.

Table 1. Epoxidation of styrene at various amounts of oxidant and chiral salen-Mn(III) catalysts in scCO$_2$.

Entry	Catalyst (mol%)	Oxidant (eq)	Time (hr)	Yield[a] (%)	% ee[b]
1	(R,R)-1 (5)	PhIO (2)	5	66	21(R)[c]
2	(R,R)-1 (5)	PhIO (4)	5	100	21(R)
3	(R,R)-2 (5)	PhIO (2)	5	27	27(R)
4	(R,R)-2 (5)	PhIO (4)	5	31	27(R)
5	(R,R)-2 (10)	PhIO (4)	5	57	27(R)
6	No catalyst	PhIO (4)	5	0	-
7	(S,S)-3 (5)	PhIO (4)	5	29	3(S)

[a]GC yields. [b]Determined by GC with Supelco chiral β-dex 325 column. [c]Absolute configuration of major isomer was assigned according to the literature procedure.

Table 2. Chiral salen-Mn(III) complexes catalyzed PhIO (4 eq.) epoxidations of olefins in supercritical carbon dioxide.

Entry	Substrate	Catalyst (mol%)	Yield[a] (%)	% ee[b] (config)[c]
1	Cis-β-methylstyrene	1 (5)	100(3.2)[d]	47(R,S)
2	Cis-β-methylstyrene	2 (10)	60(3.2)[d]	47(R,S)
3	1,2-Dihydronaphalene	1 (5)	100	38(1R,2S)
4	1,2-Dihydronapthalene	2 (10)	71	45(1R,2S)
5	Indene	1 (5)	100	43(R,S)
6	Indene	2 (10)	68	46(R,S)
7	2,2-Dimethyl-2H-chromene	1 (5)	No[e]	--

[a]GC yields. [b]Determined by GC with Supelco chiral β-dex 325 column. [c]Absolute configuration was assigned according to the literature procedure. [d]cis/trans-epoxide ratio. [e]Epoxide was decomposed.

to styrene, the yield was improved significantly (entry 2), however, without any effect on the enantioselectivity. The enantioselectivity was slightly improved when a sterically hindered catalyst **2** was used as the catalyst (entry 3-5). However, the enantioselectivity was remained even though the catalyst amount was increased to 10 mol% (entry 5). The same result was observed even in the presence of 4-phenyl-pyridine N-oxide as an additive. Low yield and enantioselectivity was obtained with Jacobsen's catalyst **3** (entry 7) which may be due to the insolubility of this catalyst in supercritical CO$_2$. The epoxide was not produced without the catalyst under the same reaction condition (entry 6). The reaction was not proceeded when H$_2$O$_2$ was used as oxidant, even in the presence of additives such as NMO and N-methylimidazole.

Encouraged by the styrene results, we examined the reaction with several olefins under the optimized conditions[13] (Table 2). In the epoxidation of cis-β-methylstyrene, cis-β-methyl-styrene oxide of 47% ee was obtained (entry 1). However, a large amount of trans-epoxide was also produced (cis/trans-epoxide = 3.2) in the reaction. The result was not improved even with catalyst **2** (entry 2). The epoxidations of 1,2-dihydronaphthalene and indene also produced their epoxides with 38-46% ee. The enatioselectivities are slightly improved when a sterically hindered catalyst **2** was used as the catalyst compared with catalyst **1**.

Overall, the moderate enantioselectivity values were obtained in scCO$_2$, and these values are slightly lower than the result with organic solvent.[12,14] However, our attempts made us to proceed to a clean and green method. Another important feature of this procedure is the stability of a variety of epoxides under these reaction conditions. Epoxides did not react with CO$_2$ and were isolated after completion of the reaction. This procedure not only preserves the simplicity of this reaction but also produces chiral epoxides in good yields with moderate % ee values.

In summary, we demonstrated that the perfluorinated chiral Salen-Mn(III) complexes were soluble in scCO$_2$ and served as efficient catalysts in the asymmetric epoxidation of olefins with PhIO in scCO$_2$. This result revealed the great potential of supercritical CO$_2$ as a green solvent and was, to our knowledge, the first report regarding the catalytic enantioselective epoxidation of olefins in scCO$_2$.

References and Notes

1. Poliakoff, M.; Fitzpatrick, J. M.; Farren, T. R.; Anastas, P. T. *Science* **2002**, *297*, 807.
2. Beckman, E. J. *J. Supercrit. Fluids* **2004**, *28*, 121.
3. Darr, J. A.; Poliakoff, M. *Chem. Rev.* **1999**, *99*, 495.
4. (a) Licence, P.; Ke, J.; Sokolova, M.; Ross, S. K.; Poliakoff, M. *Green Chem.* **2003**, *2*, 99; (b) Hass, G. R.; Kolis, J. W. *Tetrahedron Lett.* **1998**, *39*, 5923; (c) Philip, G. J.; Ikariya, T.; Noyori, R. *Science* **1995**, *269*, 1065; (d) Liu, S.; Xiao, J. *J. Mol. Cat. A: Chem.* **2007**, *270*, 1.
5. McGarrigle, E. M.; Gilheany, D. G. *Chem. Rev.* **2005**, *105*, 1563.
6. Xia, Q.-H.; Ge, H.-Q.; Ye, C.-P.; Liu, Z.-M.; Su, K.-X. *Chem. Rev.* **2005**, *105*, 1603.
7. (a) Sheldon, R. A. *Chirotechnology*; Marcel Dekker: New York, 1993: Chapter 9; (b) Shum, W. P.; Cannarsa, M. J. In *Chirality in Industry II*; Collins, A. N.; Sheldrake, G. N.; Crosby, J., Eds.; John Wiley & Sons: New York, 1997; Chapter 18.
8. Jacobsen, E. N.; Wu, M. H. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer-Verlag: Berlin, 1999: Vol II, p 649.
9. (a) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801; (b) Irie, R.; Noda, K.; Ito, Y.; Matsumoto, N.; Katsuki, T. *Tetrahedron Lett.* **1990**, *31*, 7345.
10. Beckman, E. J. *Chem. Commun.* **2004**, 1885.
11. Cavazzini, M.; Manfredi, A.; Montanari, F.; Quici, S.; Pozzi, G. *Eur. J. Org. Chem.* **2001**, 4639.
12. Katsuki, T. *Coord. Chem. Rev.* **1995**, *140*, 189.
13. The general procedure used for the epoxidation reactions is as follows: To a 10 mL high pressure view cell, olefin (0.5 mmol), internal reference (mesitylene), PhIO (4 eq) and 5 - 10 mol % of catalyst were added. Then, CO$_2$ was injected to the view cell. The mixture was stirred at 35 °C and 250 bar pressure for 5 hr (entries 1-10). After completion of reaction, the high pressure was released. The product was extracted with methylene chloride, washed by aqueous sodium bisulfite and the organic phase was dried over MgSO$_4$ and concentrated in vacuo giving a residue which was subjected to analysis using GC.
14. (a) Ahn, K.-H.; Park, S. W.; Choi, S.; Kim, H. J.; Moon, C. J. *Tetrahedron Lett.* **2001**, *42*, 2485; (b) Jeong, Y.-C.; Choi, S.; Yu, K.; Ahn, K.-H. *Bull. Korean Chem. Soc.* **2003**, *24*, 1.