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Catalytic and Highly Enantioselective Aziridination of Styrene Derivatives

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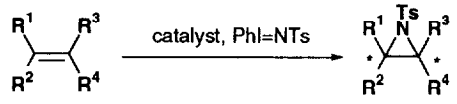
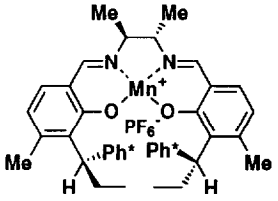
Abstract: Highly enantioselective catalytic aziridination of styrene derivatives was realized by using the newly designed (salen)manganese(III) complex as a catalyst. Copyright © 1996 Elsevier Science Ltd

Aziridines are contained in some natural products as subunits and their biological activities are influenced by the stereochemistry of the aziridine moiety. Furthermore, aziridines are useful building blocks for the construction of compounds containing nitrogen functionalities.[1] Accordingly, asymmetric aziridination of olefins is an important objective in organic synthesis (Scheme 1). In recent years, several metal-catalyzed asymmetric aziridination reactions using Cu(I)-dinitrogen ligand complexes,[2,3,4] or a (salen)manganese(III) complex[5] as a catalyst and [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane as an aziridinating reagent have been reported. The optically active copper complexes such as Cu(I)-bis(oxazolines) complex[2] and Cu(I)-diimine complex[3] catalyzed the desired reaction smoothly, showing moderate to excellent enantioselectivity. For example, aziridination of 2,2-dimethyl-6-cyanochromene using Cu(I)-diimine complex as a catalyst proceeded with the high enantioselectivity of 98% ee.[3] In contrast to this, aziridination of simple olefins such as styrene with Cu(I)-bis(oxazolines) or Cu(I)-diimine complex showed only moderate enantioselectivity (63 and 66% ee), though the chemical yields of the aziridines are good.[2,3,6] Aziridination of styrene with our early (salen)manganese(III) complex **1** also showed moderate enantioselectivity of 61% ee, but the chemical yield was low.[5]

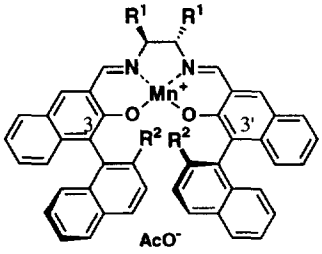


Scheme 1

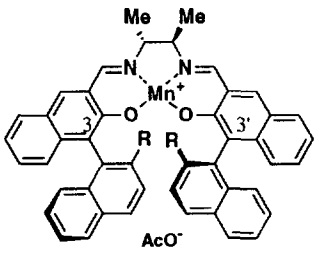


1 Ph*= 4-*t*-BuC_6H_4

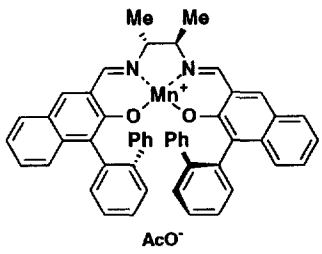
On the other hand, we recently found that the modified (salen)manganese(III) complex **2** bearing optically active binaphthyl groups as chiral elements showed much higher asymmetric induction than the earlier complex **1** in epoxidation of conjugated olefins.[7] Furthermore, the rate of epoxidation using **2** was found to be generally two or three times faster than that using simple (salen)manganese(III) complexes, suggesting that ligand acceleration occurred in the former reaction.[8] This result prompted us to reinvestigate aziridination using the (salen)manganese(III) complex as a catalyst, because the ligand acceleration might occur also in aziridination using complex **2** or its derivatives as a catalyst and improve the chemical yield of the aziridines. In this paper,



2: R^1= C_6H_3-3,5-Me_2, R^2= Ph
3: R^1= Me, R^2= Ph
4: R^1= Me, R^2= Me



5: R= Me
6: R= H



7

we describe the highly enantioselective aziridination of styrene derivatives with a newly modified (salen)manganese(III) complex as a catalyst.

At first, we examined aziridination of styrene at room temperature with complex **2** as a catalyst. Enantioselectivity was low (8.1% ee)[9] but the chemical yield of the corresponding aziridine was moderate (60%) as expected. Encouraged by this high catalytic activity of **2** and also by our previous result,[10] we synthesized complex **3** bearing (2*S*,3*S*)-2,3-diaminobutane as an ethylenediamine moiety and examined the aziridination. However, only modest improvement in enantioselectivity (34% ee) was observed. Since the binaphthyl moiety of the salen ligand was considered to play an important role in promoting ligand acceleration,[11] we decided to modify the binaphthyl moiety of **3**. Thus, we synthesized the modified complexes (**4** and its diastereomer **5**) bearing a methyl group at the binaphthyl moiety instead of a phenyl group. Although the reaction with **4** showed low enantioselectivity (7% ee), complex **5** exhibited further improved enantioselectivity of 47% ee. We further synthesized complex **6** which had no substituent at the naphthyl moiety. This complex **6** showed low enantioselectivity (10% ee) as well as poor catalytic activity. With these results, we synthesized another complex **7** which had the phenyl substituent but lacked one benzene ring of the naphthyl group in **3** (Scheme 2). Aziridination of styrene using catalyst **7** was found to proceed with remarkably improved enantioselectivity of 94% ee as well as high chemical yield (Table 1, entry 1). Reaction of other styrene derivatives also showed high enantioselectivity (entries 2 and 3). Aziridination of indene was also examined but enantioselectivity was

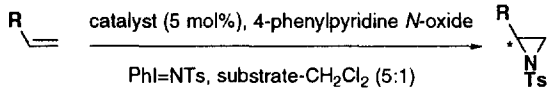


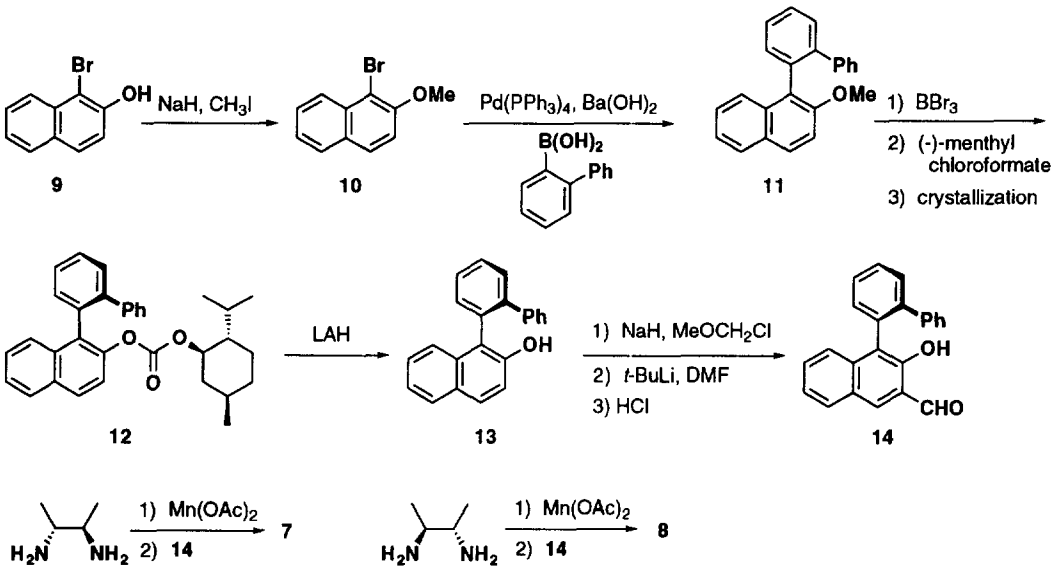
Table 1. Catalytic aziridination of styrene derivatives using (salen)manganese(III) complex as a catalyst.

Entry	Substrate	Catalyst	Temp.	Yield (%)	%ee	Config.[a]
1	styrene	**7**	rt	76	94[b]	*S*
2	*p*-chlorostyrene	**7**	rt	70	86[c]	-
3	*p*-methylstyrene	**7**	rt	75	81[b]	-
4	indene	**7**	rt	10	50[d]	-
5	styrene	**8**	rt	25	13	*S*

a) Determined by the comparison of specific rotation with authentic sample (reference 5).
b) Determined by HPLC analysis (Dicel Chiralcel OJ, hexane:*i*-PrOH=1:1).
c) Determined by HPLC analysis (Dicel Chiralcel OF, hexane:*i*-PrOH=4:1).
d) Determined by HPLC analysis (Dicel Chiralpak AD, hexane:*i*-PrOH=15:1).

moderate (entry 4). Although we also synthesized complex **8** (Scheme 2) which was the diastereomer of **7**, it showed only modest enantioselectivity in the aziridination of styrene (entry 5).

Complexes **7** and **8** were synthesized from 1-bromo-2-hydroxynaphthalene (**9**) (Scheme 2). Compound **9** was protected as methyl ether **10** and subjected to Suzuki-Miyaura coupling to give racemic **11**. After deprotection, compound **11** was converted into (1*R*,2*S*,5*R*)-menthyl carbonate **12**[12] which crystallized out from the reaction medium on concentration. Compound **12** was reduced with lithium aluminum hydride (LAH) to give naphthol **13** [$[\alpha]_D^{29}$ +25.1° (*c* 0.48, THF)], enantiomeric excess of which was determined to be >99% by HPLC analysis using Daicel Chiralpak AD (hexane:*i*-PrOH = 30:1). Compound **13** was converted into hydroxy aldehyde **14** [$[\alpha]_D^{29}$ -258.6° (*c* 1.01, THF)], according to the reported procedure.[7a] Compound **14** was treated with a mixture of (2*R*,3*R*)-2,3-diaminobutane and manganese(II) acetate at 50 °C to give complex **7**. Treatment of **14** with a mixture of (2*S*,3*S*)-2,3-diaminobutane and manganese(II) acetate gave complex **8**.



Scheme 2

Typical experimental procedure is exemplified by aziridination of styrene: Complex **7** (2.8 μmol, 2.3 mg) and 4-phenypyridine *N*-oxide (28 μmol, 4.8 mg) was dissolved in dry toluene (1 ml), concentrated *in vacuo*, and again dissolved in dry dichloromethane (0.05 ml). To this solution were added styrene (0.25 ml) and [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane (56 μmol, 21.1 mg), and the reaction mixture was stirred for 3 h at room temperature. The reaction mixture was directly subjected to silica-gel column chromatography (hexane:ethyl acetate=1:0 to 19:1) to give *N*-(*p*-toluenesulfonyl)-2-phenylaziridine (11.6 mg, 76%).

In conclusion, we were able to demonstrate that the well-designed (salen)manganese(III) complex could be an efficient catalyst for asymmetric aziridination, though the mechanism of ligand acceleration is unclear at present. We also demonstrated that the aziridination using Cu(I)-bis(oxazolines) or Cu(I)-diimine complex and the present reaction are complimentary to each other.

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6. Although Masamune and coworker reported that Cu(I)-bisoxazoline complex catalyzed aziridination of styrene with high enantioselectivity of 88% ee (reference 2c), Evans and coworkers have insisted that such a high enantioselectivity was not reproduced in the reaction using the same Cu(I)-bisoxazoline complex as a catalyst (reference 2b).
7. a) Sasaki, H.; Irie, R.; Hamada, T.; Suzuki, K.; Katsuki, T. *Tetrahedron* **1994**, *50*, 11827-11838. b) Katsuki, T. *J. Synth. Org. Chem. Jpn.* **1995**, *53*, 940-951.
8. For the review on ligand acceleration, see: Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059-1070.
9. Enantiomeric excess of the product was determined by HPLC analysis using Daicel Chiralcel OJ (hexane:*i*-PrOH = 1:1).
10. Complex **1** bearing (2*S*,3*S*)-2,3-diaminobutane as its ethylenediamine moiety showed higher asymmetric induction than the corresponding complex bearing (1*S*,2*S*)-1,2-diphenylethylenediamine instead (reference 3).
11. Modification of the ethylenediamine moiety of the early (salen)manganese complexes affected their catalytic activity to a small extent (reference 5).
12. The stereochemistry of **12** was determined by X-ray analysis.

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