ELSEVIER

Coordination Chemistry Reviews 140 (1995) 189–214

COORDINATION CHEMISTRY REVIEWS

Catalytic asymmetric oxidations using optically active (salen)manganese(III) complexes as catalysts

Tsutomu Katsuki

Department of Chemistry, Faculty of Science, Kyushu University 33, Hakozaki, Higashi-ku, Fukuoka 812, Japan

Received 8 April 1994

Contents

Abstract

This review deals with enantioselective one oxygen atom transfer reactions (epoxidation, oxidation of enolates, and oxidation of sulphide to sulphoxides) catlaysed by optically active (salen)manganese(III)complexes. Asymmetric aziridination is also discussed briefly.

Keywords: Oxidation; Catalysis; (Salen)manganese(III); Optical activity

1. Introduction

One oxygen atom transfer reactions (hereafter referred to as oxo transfer reactions) defined by:

$$M^zO_nL_m + TO \rightarrow M^{z+2}O_{n+1}L_m \quad (1)$$

SSDI 0010-8545(94)01124-9

$$M^{z+2}O_{n+1}L_m + S \rightarrow M^zO_nL_m + SO \quad (2)$$

M^z, metal ion; L, ligand; TO, terminal oxidant; S, substrate

are mediated by various metal complexes including some metal enzymes that play an important role in oxidative biochemical pathways [1]. Among the oxo transfer enzymes cytochrome P-450 in particular attracted the organic chemist's attention, since it catalyses the mono-oxygenation of various compounds, both biotic and exobiotic, with high stereo- and regioselectivity under mild conditions. Accordingly, a great deal of effort has been devoted to the study of the function of P-450 bearing an iron–porphyrin complex as its active site. The P-450-catalysed oxo transfer reaction was proposed by Groves and Nemo to proceed through an oxohaem catalytic intermediate (Fig. 1) [2].

Furthermore, Groves et al. reported that simple iron(III) porphyrins are good models for the reaction site of cytochrome P-450 and that they are readily oxidized to the active oxo species by their treatment with iodosylbenzene (shunt path, Fig. 1) [3]. Since then, many metalloporphyrin complexes have been synthesized and used for various oxo transfer reactions. Among them, iron(III), manganese(III), and ruthenium(IV) porphyrins have been found to be efficient catalysts for the epoxidation of simple olefins and the oxidation of sulphides [1b]. From these basic results, many optically active iron and manganese porphyrins (**1**–**7**) were synthesized to effect asymmetric oxo transfer reactions [4–10], and moderate to good levels of enantioselectivity (up to 89% entantiomeric excess (ee)) have been achieved in the epoxidation of styrene derivatives as shown in Fig. 2. Although these porphyrin chemistries accelerate the progress of asymmetric epoxidation of simple olefins which could not be effected even with the prominent titanium tartrate catalyst [11], there is still a considerable limitation for their use in organic synthesis.

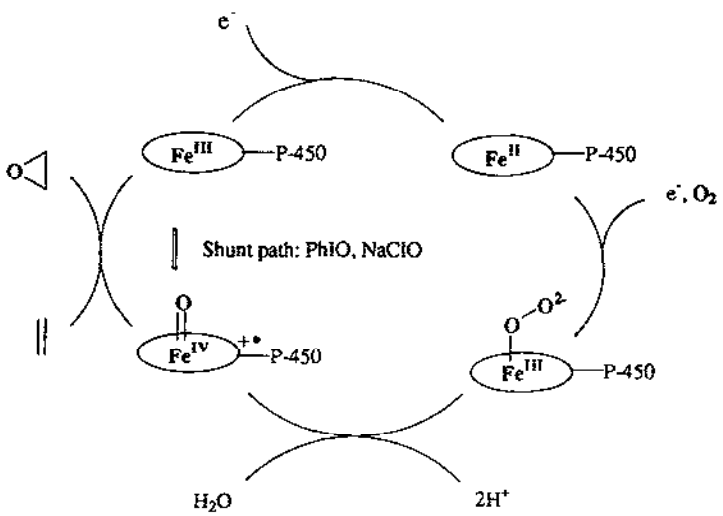


Fig. 1. Catalytic cycle of cytochrome P-450.

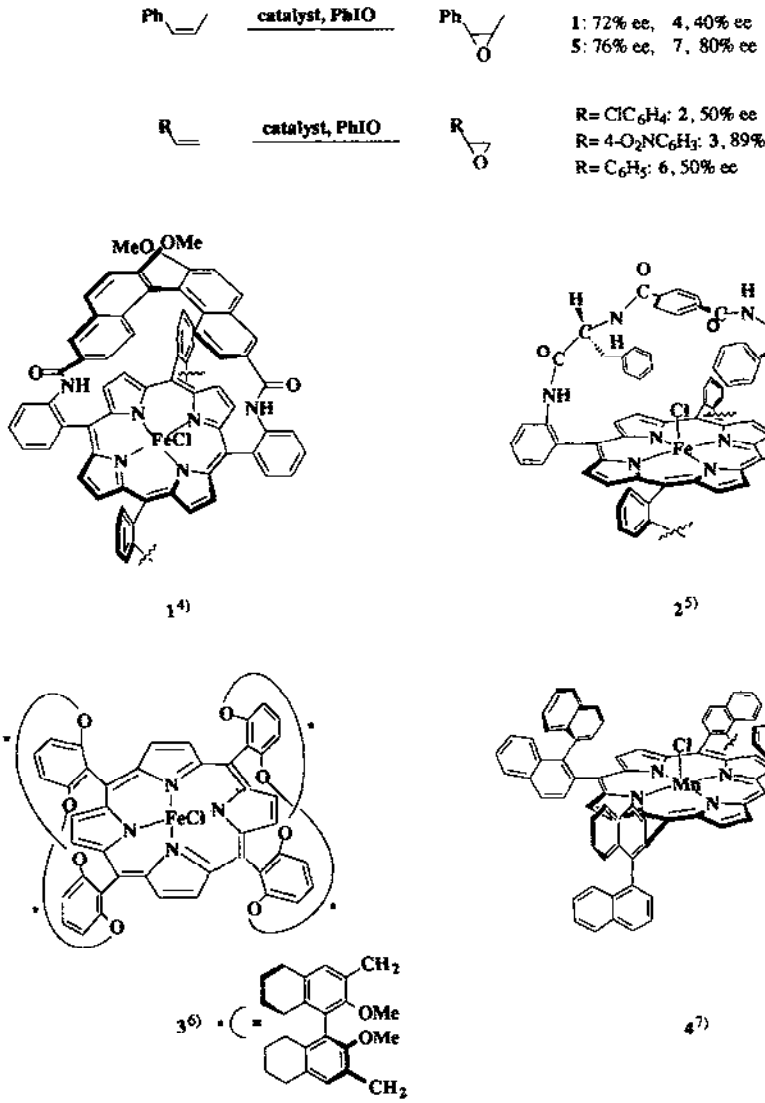
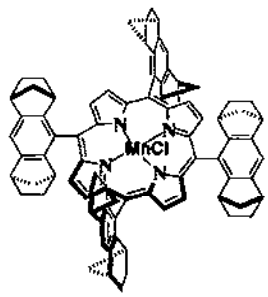
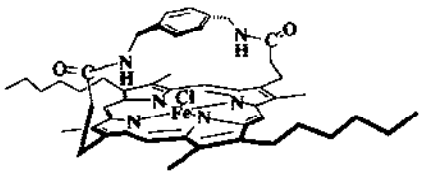


Fig. 2. Examples of porphyrin-catalysed asymmetric epoxidation.

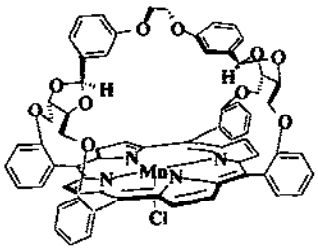
Parallel to these porphyrin chemistries, the use of metal complexes (**8**) of *N,N*-ethylenebis(salicylideneaminato) ligand (salen ligand) as a catalyst for the oxo transfer reaction has also been examined, since they have features in common with metalloporphyrins with respect to their electronic structure and catalytic activity: various salen complexes have indeed been found to be efficient catalysts. However, these two complexes differ from one another in structure. In contrast to the porphyrin ligand where the peripheral carbon atoms are all sp^2, the salen ligand bears two sp^3 carbon atoms at Cl″ and C2″ which might be replaced with



5[8]

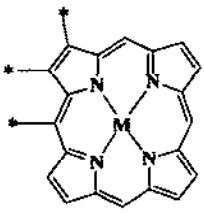


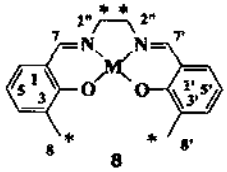
6[9]



7[10]

Fig. 2. (continued)





8

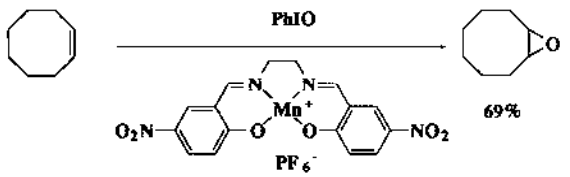
*= stereogenic carbon

stereogenic carbon atoms. Furthermore, it can have chiral substituents at C3 and C3′ (for the sake of convenience, the numbering shown on compound **8** is used for all the salen complexes described in this paper). These stereogenic centres reside proximate to the metal centre and this renders the salen ligand a promising chiral template for the construction of an asymmetric reaction site. Actually, a breakthrough has recently been made with this type of salen complex in the epoxidation of simple olefins. In this review, we briefly describe recent developments in salen-catalysed asymmetric oxo transfer reaction (epoxidation of olefins and oxidation of sulphides), together with aziridination which is mechanistically related to epoxidation (preliminary aspects of salen-catalysed asymmetric epoxidation have been reviewed in Ref. [12]).

2. Salen-catalysed asymmetric epoxidation

2.1. Design of optically active (salen)manganese(III) complex

Although various metal ions form complexes with salen ligands, only some (chromium [13], manganese [14], nickel [15] and ruthenium [16]) have been used as a catalyst for epoxidation. Among them, the cationic (salen)manganese(III) complexes have been reported by Kochi and co-workers to be the most efficient catalysts [14]:



(3)

In contrast to the oxo porphyrin complex, where the active species in porphyrin-catalysed epoxidation (Fig. 1) has only been identified spectroscopically, the oxo(salen)chromium(V) complex **9** was isolated by Kochi and co-workers and its structure determined unambiguously by X-ray diffraction [13]. The oxochromium(V) complex has roughly square pyramidal coordination, and the chromium atom is displaced 0.53 Å above the mean salen plane. This oxochromium(V) species smoothly epoxidizes norbornene. In this study, the oxochromium(V) adduct with pyridine *N*-oxide as the axial ligand was also isolated and its X-ray diffraction showed that the adduct was octahedral with the chromium atom displaced 0.26 Å above the salen plane (Fig. 3). Thus the chromium atom is pulled back by 0.27 Å by coordination with the axial ligand, compared with the chromium atom in the above 5-coordinate complex. This oxochromium(V) adduct also epoxidizes olefins. These results strongly suggest that other salen-catalysed epoxidations also proceed through the corresponding oxo species, although oxo species other than the oxochromium complex have not been isolated. Acutally an oxo species is also postulated as an active species in epoxidation using (salen)manganese(III) [14,17] or (salen)nickel(II) [15] complexes as a catalyst.

Following these results, Jacobsen and the present author independently designed optically active (salen)manganese(III) complexes as catalysts. To achieve high enan-

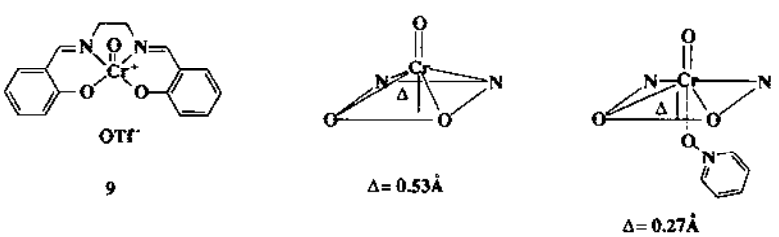


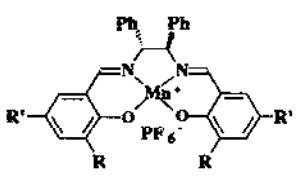
Fig. 3. Effect of axial ligand on the structure of oxo (salen) chromium complex.

tioselectivity in the salen-catalysed epoxidation, two factors, the pathway of the oncoming olefins and its conformational orientation, must be strictly controlled. Accordingly, knowledge about how the olefins approach the active oxo species is indispensable for the construction of an efficient chiral salen catalyst but there was no report on this subject. Fortunately, abundant studies have been reported on porphyrin-catalysed epoxidation wherein olefins have been proposed to approach the metal–oxo bond from the side and parallel to the porphyrin ring (side-on-approach) [2]. This side-on approach is considered also to be applicable to the salen-catalysed epoxidation, because of structural similarity between porphyrin and salen complexes. (For example, Jorgensen explained the stereochemistry observed in the epoxidation using (salen)manganese and manganese porphyrin catalysts, with the same transition state model [2].) Although the problem of how to control the direction of the olefin's approach remains, this is considered to be solved by appropriately introducing substituents onto the salen ligand. That is, the substituent standing on the salen ligand must interact strongly with the incoming olefin parallel to the salen ligand and, therefore, enforce the olefin to approach the metal–oxo bond away from the substituent. On the basis of this consideration, the following (salen)manganese(III) complexes have been synthesized to date and used for the epoxidation of simple olefins.

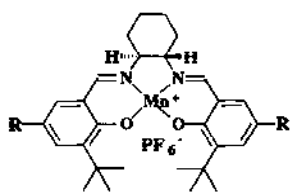
In 1990, Jacobsen and co-workers reported the (salen)manganese(III) complex (**10**) bearing stereogenic carbon atoms at C1″ and C2″ and *t*-butyl groups at C3 and C3′ [18a]. Although the C3 and C3′ substituents are achiral, their presence is essential to achieve high enantioselectivity. The salen complex (**11**) bearing no substituents at C3 and C3′ exhibits only poor asymmetric induction, probably because the olefins approach the metal–oxo bond more easily from the sterically less hindered side which is remote from the stereogenic centres. The size of the C3 and C3′ substituents affects enantioselectivity. Although a small substituent such as a methyl group decreases the enantioselectivity, too large a substituent such as the 9-methyl-9-fluorenyl group also diminishes the enantioselectivity to a small extent [18b].

Jacobsen et al. also synthesized the (salen)manganese(III) complex (**12a**) bearing *t*-butyl groups at C5 and C5′ as well as at C3 and C3′, the presence of which made **12a** an excellent catalyst for the epoxidation of cis-olefins for steric reasons (vide infra) [19].

In the same year, the present author and co-workers also reported



10a: R= *t*-Bu, R'= H
10b : R= *t*-Bu, R'= Me
11 : R,R'= H

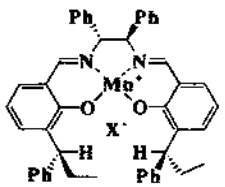


12a : R= *t*-Bu
12b : R= Me

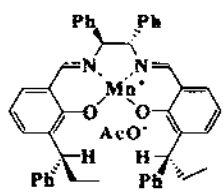
(salen)manganese(III) complexes (**13**–**16**) bearing stereogenic centres at Cl″, C2″, C8, and C8′ [20]. Differing from those of Jacobsen et al., these complexes bear bulky and chiral C3 and C3′ substituents. The conformation of the C3 and C3′ chiral substituents has considerable influence on the asymmetric induction. The salen complex (**15**) with C4 and C4′ methyl groups which confine the conformation of the C3 and C3′ substituents to hydrogen atoms in the aromatic plane is generally a better catalyst than the complex **13** without C4 and C4′ methyl groups. Replacement of C8 and C8′ phenyl groups of **15** with more bulky 4-*t*-butylphenyl group produces more effective catalysts (**17** [21,22], **18** [21]).

To explore the effect of C8 and C8′ stereogenic centres on asymmetric induction in detail, the present author and co-workers further synthesized (salen)managanese(III) complexes (**19** and **20**) [23]. Results with these complexes showed that the C8 (C8′) medium substituent as well as the C8 (C8′) large substituent affected asymmetric induction.

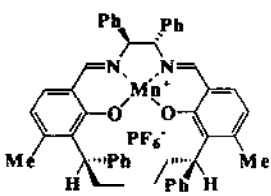
We have also synthesized (salen)manganese(III) complexes (**21**–**24**) possessing axial chirality instead of C8 and C8′ central chirality as in salen complexes **13**–**20**



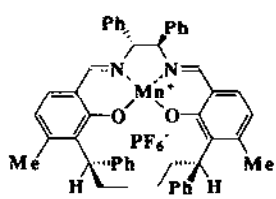
13a: X= AcO⁻, b= PF_6



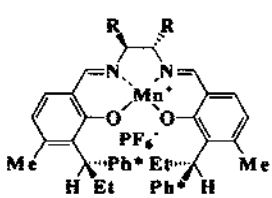
14



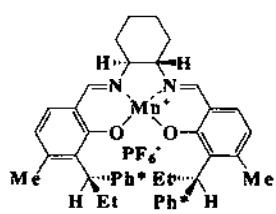
15



16

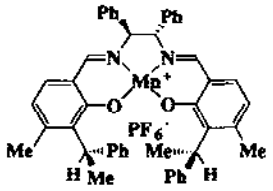


17, a: R= Ph; b: R= Me

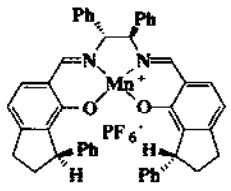


18

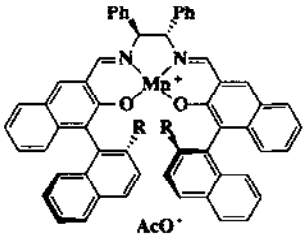
Ph*= 4-*t*-Bu-Ph



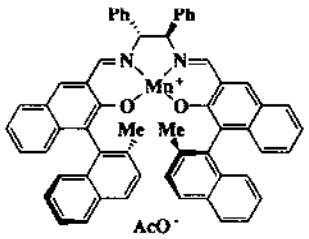
19



20



21: R= H
22: R= Me
24: R= Ph



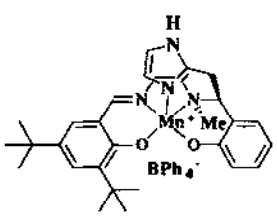
23

[24]. Among them, **24** was shown to be an excellent catalyst for the epoxidation of cis-olefins (vide infra).

Schwenkreis and Berkessel synthesized a chiral pentadentate (dihydrosalen)manganese(III) complex (**25**) as a biomimetic catalyst [25].

2.2. Reaction conditions and results

Epoxidation is usually carried out in the presence of a catalytic amount of the (salen)manganese(III) complex (1–10 mol.%) by using 1–2 equivalents of a terminal oxidant at room temperature, at 0 °C, or at −20 °C in various solvents. Usually acetonitrile, dichloromethane, and dichloroethane are used as solvents but the use of fluorobenzene has been recommended, when molecular oxygen is used as an oxidant [26]. Iodosylbenzene and its derivatives, sodium hypochlorite [18b], hydrogen peroxide [27], and molecular oxygen in combination with aldehyde [26] can be used as terminal oxidants. Iodosylbenzene and sodium hypochlorite are considered to oxidize (salen)manganese(III) complexes directly to the corresponding



25

oxo manganese species [13,14]. When hydrogen peroxide is used as an oxidant, addition of a donor ligand is indispensable probably because the coordination of an axial ligand is crucial to the O—O bond cleavage of the intermediary hydroperoxide species [HO—O—Mn^{III}] [27]. The epoxidation using a combination of molecular oxygen and aldehyde is also accelerated by the addition of donor ligand [26].

To compare the asymmetry-inducing ability of (salen)manganese(III) complexes so far prepared, their catalytic activity towards the epoxidation of dihydronaphthalene and trans-stilbene is summarized in Table 1.

These results show that complexes **12a**, **18**, **24**, and **28** are catalysts of choice. Furthermore, Table 1 reveals some interesting features of salen-catalysed asymmetric epoxidation. (i) Bulky and/or chiral C3 and C3′ substituents in the salen ligand are proven to be essential for the realization of high enantioselectivity as described in the preceding section. However, complex **26** which has bulky trialkylsilyl groups at C3 and C3′ exhibits considerably lower enantioselectivity compared with the corresponding C3(C3′)-*t*-butylated salen complex **10a**, although the epoxidation of dihydronaphthalene with **26** as a catalyst has not been reported [30]. This is attributed to a longer carbon–silicon bond length compared with carbon–carbon bond length (vide infra). (ii) Cis-olefins are generally better substrates than trans-olefins. (iii) Enantiofacial selection of cis-olefins is preferentially controlled by the chirality at C1″ and C2″ and that of trans-olefins by the chirality at C8 and C8′ [20a,b]. This hypothesis is supported by the following observation. Thus, the epoxides obtained from dihydronaphthalene with **13** and **15** are enantiomeric to the epoxides obtained with **14** and **16**, respectively, although the optical purity of the former epoxides is a little better than that of the latter (entries 5, 6, 7, and 9). Since **13** and **15** are diastereomeric to **14** and **16** respectively, with respect to the chirality at C1″ and C2″, this suggests that the enantiofacial selection of dihydronaphthalene is mainly controlled by the chirality at C1″ and C2″. On the contrary, epoxidation of trans-stilbene with **13**–**16** gives 1*R*,2*R*-epoxide (entries 22–25), suggesting that the enantiofacial selection of trans-stilbene is strongly influenced by the chirality at C8 and C8′. This hypothesis is also compatible with the fact that Jacobsen's catalyst **12a** bearing achiral C8 and C8′ substituents is not very effective in the epoxidation of trans-olefins [12]. Furthermore, complexes **27a** [28] and **27b** [21] bearing no chirality at C1″ and C2″ exhibit the same level of asymmetric induction in the epoxidation of trans-stilbene as complexes **15** and **18** respectively (entries 22, 27, 31, and 32), while **27a** displays considerably lower asymmetric induction in the epoxidation of cis-olefins compared with **15** (entries 7 and 19).

Asymmetric induction by an optically active salen catalyst is sometimes dependent on the substrates used, as exemplified by the epoxidation of dihydronaphthalene and 6-acetoamido-2,2-dimethyl-7-nitrochromene:

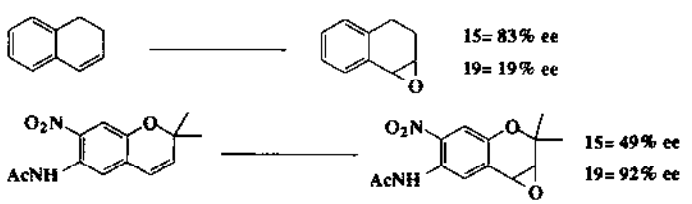
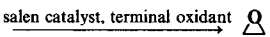


Table 1
Asymmetric epoxidation of dihydronaphthalene and trans-stilbene using (salen)manganese(III) complexes as a catalyst:



Entry	Substrate	Catalyst	Solvent	Oxidant	Temperature	Yield (%)	ee (%)	Configuration	Ref.
1		**10a**	CH_3CN	Me_3PhIO	25 °C	72	78	1*R*,2*S*	[18a]
2		*ent*-**10b**	Fluorobenzene	O_2[a]	RT	62	52	1*S*,2*R*	[26]
3		**12a**	CH_2Cl_2	NaClO	0 °C	67	86	1*S*,2*R*	[12]
4		**12b**	Fluorobenzene	O_2[a]	RT	78	63	1*S*,2*R*	[26]
5		**13**	CH_3CN	PhIO	RT	93	49	1*R*,2*S*	[20a]
6		**14**	CH_3CN	PhIO	RT	25	43	1*S*,2*R*	[20a]
7		**15**	CH_3CN	PhIO	RT	65	72	1*S*,2*R*	[20b]
8		**15**	CH_2Cl_2	PhIO	RT	71	83[b]	1*S*,2*R*	[20c]
9		**16**	CH_3CN	PhIO	RT	24	60	1*R*,2*S*	[20b]
10		**18**	CH_2Cl_2	PhIO	RT	38	91[c]	1*S*,2*R*	[21]
11		**19**	CH_3CN	PhIO	RT	81	49	1*S*,2*R*	[23]
12		**20**	CH_3CN	PhIO	RT	50	45	1*R*,2*S*	[23]
13		**21**	CH_3CN	PhIO	RT	59	32	1*S*,2*R*	[24a]
14		**22**	CH_3CN	PhIO	RT	41	68	1*S*,2*R*	[24a]
15		**22**	CH_3CN	PhIO	RT	77	86[b]	1*S*,2*R*	[24a]
16		**23**	CH_3CN	PhIO	RT	52	38	1*R*,2*S*	[24a]
17		**24**	CH_3CN	PhIO	RT	—	92	1*S*,2*R*	[24b]
18		**25**	CH_2Cl_2	H_2O_2	0°C	72	64	1*R*,2*S*	[25]
19		**27a**	CH_3CN	H_2O_2	RT	87	36	1*S*,2*R*	[28]
20		**28**	CH_3CN	H_2O_2	RT	61	96[b]	1*S*,2*R*	[29]
21	Ph⟋⟍Ph	**11**	CH_3CN	Me_3PhIO	25°C	63	33	1*S*,2*S*	[18a]
22		**15**	CH_3CN	PhIO	RT	95	48	1*R*,2*R*	[20b]
23		**15**	CH_2Cl_2	PhIO	RT	36	36[b]	1*R*,2*R*	[20b]
24		**16**	CH_3CN	PhIO	RT	19	6	1*R*,2*R*	[20b]

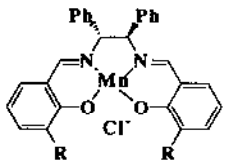
25	**17a**	CH_3CN	PhIO	RT	70	56	1*R*,2*R*	[21]
26	**17b**	CH_3CN	PhIO	RT	70	66	1*R*,2*R*	[22]
27	**18**	CH_3CN	PhIO	RT	65	62	1*R*,2*R*	[21]
28	**19**	CH_3CN	PhIO	RT	83	34	1*R*,2*R*	[23]
29	**20**	CH_3CN	PhIO	RT	40	4	1*R*,2*R*	[23]
30	**22**	CH_3CN	PhIO	RT	52	0	—	[24]
31	**27a**	CH_3CN	PhIO	RT	37	49	1*R*,2*R*	[28]
32	**27b**	CH_3CN	PhIO	RT	64	61	1*R*,2*R*	[28]

RT, room temperature.

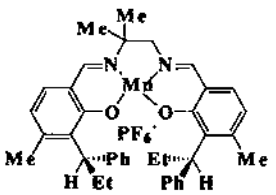
[a] The reaction was carried out in the presence of pivalaldehyde and *N*-methylimidazole.

[b] The reaction was carried out in the presence of pyridine *N*-oxide.

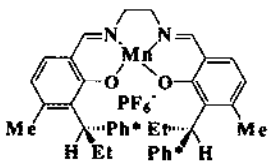
[c] The reaction was carried out in the presence of 4-*N*,*N*-dimethylaminopyridine *N*-oxide.



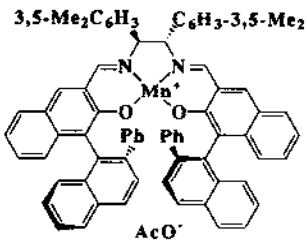
26a: R= Me_3Si
26b: R= t-$BuMe_2Si$



27a



27b Ph*= 4-t-Bu-Ph



28

Complex **15** exhibits better asymmetric induction in the epoxidation of dihydronaphthalene than **19**, while complex **19** causes better asymmetric induction in the epoxidation of 6-acetoamido-2,2-dimethyl-7-nitrochromene than **15**. Despite this description, complexes **12a**, **18**, **24**, and **28** [29] mentioned above have wider applicability and higher asymmetry-inducing ability for asymmetric epoxidation of simple olefins compared with other salen catalysts, especially for cis-olefins.

Table 2 shows the epoxidation of other olefins with salen catalysts. These results suggested that cis-olefins conjugated with aryl, acetylenic and olefinic groups are the best substrates for salen-catalysed epoxidation. Conjugated trisubstituted olefins bearing a methyl group cis to the hydrogen atom are also good substrates (entries 38 and 39). Epoxidation of these classes of olefins exhibits high enantioselectivity (more than 90% ee) when an appropriate catalyst such as **12a**, **18**, **24**, and **28**, is used. However, cis-olefins bearing only alkyl substituents exhibit considerably diminished enantioselectivity (entry 3). Cis-olefin conjugated with π bonds at both terminal carbon atoms is also a poor substrate (entry 36). Trans-olefins also display only moderate enantioselectivity (entries 40–44). These stereochemical features of salen-catalysed epoxidation are well understood by consideration of the mechanism of salen-catalysed epoxidation (vide infra).

Table 2
Asymmetric epoxidation of various olefins

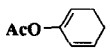
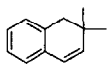
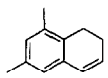
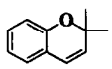
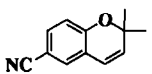
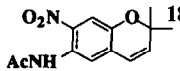
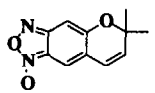
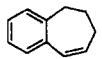
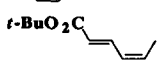
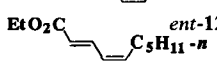
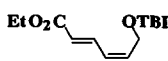
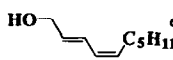
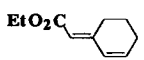
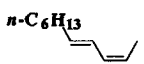
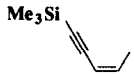
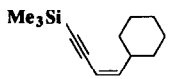
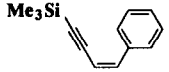
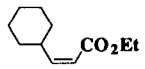
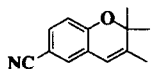
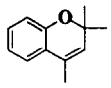
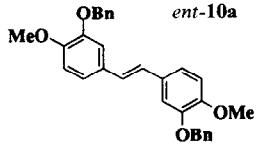
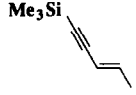
Entry	Substrate	Catalyst	Solvent	Oxidant	Yield (%)	ee (%)	Configuration	Ref.
1	Ph, Me	**12a**	CH_2Cl_2	NaClO	81	92	1*S*,2*R*	[19]
2		**18**	CH_2Cl_2	NaClO	36	86	1*S*,2*R*	[21]
3		**18**	CH_3CN	PhIO		50	—	[31]
4		**12a**	CH_2Cl_2	NaClO	63	94	—	[19]
5		**18**	CH_3CN	PhIO		87	—	[31]
6		**28**	CH_3CN	PhIO	50	92	—	[29]
7		**12a**	CH_2Cl_2	NaClO	80	88	—	[12]
8		*ent*-**12a**	Et_2O	NaClO[a]	33	61	—	[32]
9		**32**	Et_2O	NaClO[a]	30	65	—	[32]
10	AcO 	*ent*-**12a**	Et_2O	NaClO[a]	30	85	—	[32]
11		**32**	Et_2O	NaClO[a]	32	90	—	[32]
12		*ent*-**12a**	EtOAc	NaClO[a]	64	73	—	[32]
13		**32**	EtOAc	NaClO[a]	49	70	—	[32]
14		**12a**	CH_2Cl_2	NaClO	51	45	—	[33a]
15		**28**	CH_3CN	PhIO	75	62	—	[29]
16		**32**	Et_2O	NaClO[a]	55	57	—	[32]
17		**12b**	Fluorobenzene	O_2[b]	80	72	—	[26]
18		**12b**	Fluorobenzene	O_2[b]	73	52	—	[26]

Table 2 (continued)

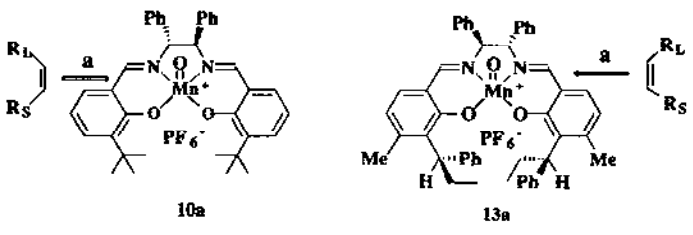
Entry	Substrate	Catalyst	Solvent	Oxidant	Yield (%)	ee (%)	Configuration	Ref.
19		*ent*-**12a**	CH_2Cl_2	NaClO	87	98	3*R*,4*R*	[34]
20		*ent*-**12a**	CH_2Cl_2	NaClO	96	97	3*R*,4*R*	[34]
21		**18**	CH_3CN	PhIO	78	96	—	[21]
22		**28**	CH_3CN	PhIO	72	98	—	[29]
23		**18**	CH_3CN	PhIO	63	94	3*S*,4*S*	[21]
24		**28**	CH_3CN	PhIO	72	97	3*S*,4*S*	[29]
25		**12b**	Fluorobenzene	O_2[b]	52	77	—	[26]
26		*ent*-**12a**	CH_2Cl_2	NaClO	56	95–97	2*R*,3*R*	[35]
27		**12a**	CH_2Cl_2	NaClO	67 (7:1)[c]	66[d]	—	[33a]
28		*ent*-**12a**	CH_2Cl_2	NaClO[a]	81 (9:1)[c]	87[d]	4*R*,5*R*	[36]
29		*ent*-**12a**	CH_2Cl_2	NaClO[a]	58 (7.3:1)[c]	83[d]	4*R*,5*R*	[36]
30		*ent*-**12a**	CH_2Cl_2	NaClO[a]	16 (2.3:1)[c,e]	83[d]	4*R*,5*R*	[36]
31		*ent*-**12a**	CH_2Cl_2	NaClO[a]	58	77	—	[36]
32		*ent*-**12a**	CH_2Cl_2	NaClO[a]	50 (1:1)[c]	92[d]	—	[36]

33		**12a**	CH_2Cl_2	NaClO	84 (2.5:1)[c]	90[d]	3*R*,4*R*	[33a]
34		**12a**	CH_2Cl_2	NaClO	85 (2:1)[c]	93[d]	3*R*,4*R*	[33a]
35		**12a**	CH_2Cl_2	NaClO	65 (5.2:1)[c]	98[d]	3*R*,4*R*	[33a]
36		**12a**	CH_2Cl_2	NaClO	34 (1:1)[c]	35[d]	—	[33a]
37		**25**	CH_3CN	PhIO	—	50	—	[29]
38		*ent*-**12a**	CH_2Cl_2	NaClO	82	>98	3*R*,4*R*	[34]
39		*ent*-**12a**	CH_2Cl_2	NaClO	51	97	3*R*,4*R*	[34]
40		*ent*-**10a**	CH_2Cl_2	2,4,6-$Me_3C_6H_2IO$	—	30	1*R*,2*R*	[37]
41		**12a**	CH_2Cl_2	NaClO	23 (2:1)	46[d]	—	[34]
42		**18**	CH_3CN	PhIO	61	9	1*R*,2*R*	[21]
43		*ent*-**12a**	CH_2Cl_2–MeOH[b]	H_2O_2	34	47	1*R*,2*R*	[27]
44		**13a**	CH_2Cl_2	PhIO	32	56	1*R*,2*R*	[21]

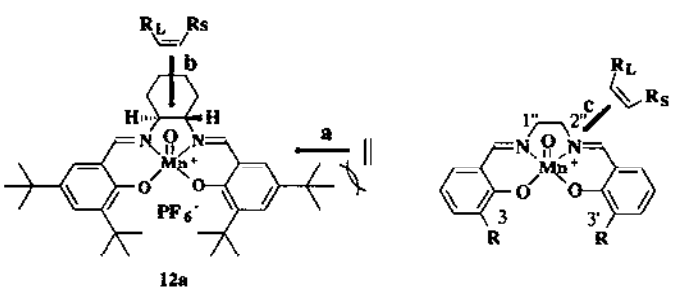
[a] Reaction was carried out in the presence of 4-phenylpyridine. [b] Reaction was carried out in the presence of *N*-methylimidazole.
[c] Product is a mixture of trans- and cis-epoxides. Numbers in parentheses are the ratio of trans- and cis-epoxides.
[d] The number stands for the ee of trans-epoxide. [e] The allylic alcohol was oxidized to the corresponding aldehyde.

2.3. Mechanistic considerations

As described in Section 2.1, olefins are considered to approach the metal–oxo bond from the side and parallel to the salen ring (side-on approach), avoiding steric repulsion with substituents on the salen ligand. Thus olefins had been assumed to approach the metal–oxo bond along pathway **a** in the epoxidation reaction using the first-reported (salen)manganese(III) complexes (**10a**) [18a] and **13a** [20a,27]. Later, Jacobsen et al. proposed pathway **b** as the more favoured in the epoxidation using **12a** owing to the presence of the C5- and C5′-*t*-butyl groups [19]. These proposed pathways (**a** and **b**) can approximately explain the stereochemistry observed in the epoxidation using complexes (**10**, **12**, and **13**) by repulsive steric interaction between the substituents on the salen ligands and the olefinic substituents. In the epoxidation catalysed by **10a** and **13a**, for example, olefins approach the metal–oxo bond orienting their larger substituents away from the bulky C3 or C3′ substituent. In the epoxidation with **12a**, olefins are considered to approach directing their larger substituents away from the C2″ axial hydrogen atom [19]. However, some results are difficult to explain by steric interaction only. Although cis-β-methylstyrene exhibits good enantioselectivity (Table 2, entries 1 and 2), (Z)-1-cyclohexyl-1-propene exhibits only moderate selectivity (entry 3) even though the cyclohexyl group is sterically more bulky than the phenyl group. 4-Cyclohexyl-1-trimethylsilyl-3-buten-1-yne is also a better substrate than 4-phenyl-1-trimethylsilyl-3-buten-1-yne (entries 35 and 36). These stereochemistries seem strange on the surface, but they can be rationalized by pathway **c** which we proposed [22,31]. Olefins approaching along the nitrogen–manganese bond axis (pathway **c**) feel a different electronic atmosphere at either side of the bond axis, because the salicylaldehyde side is rich in π electrons



R_L = larger substituent R_S = smaller substituent

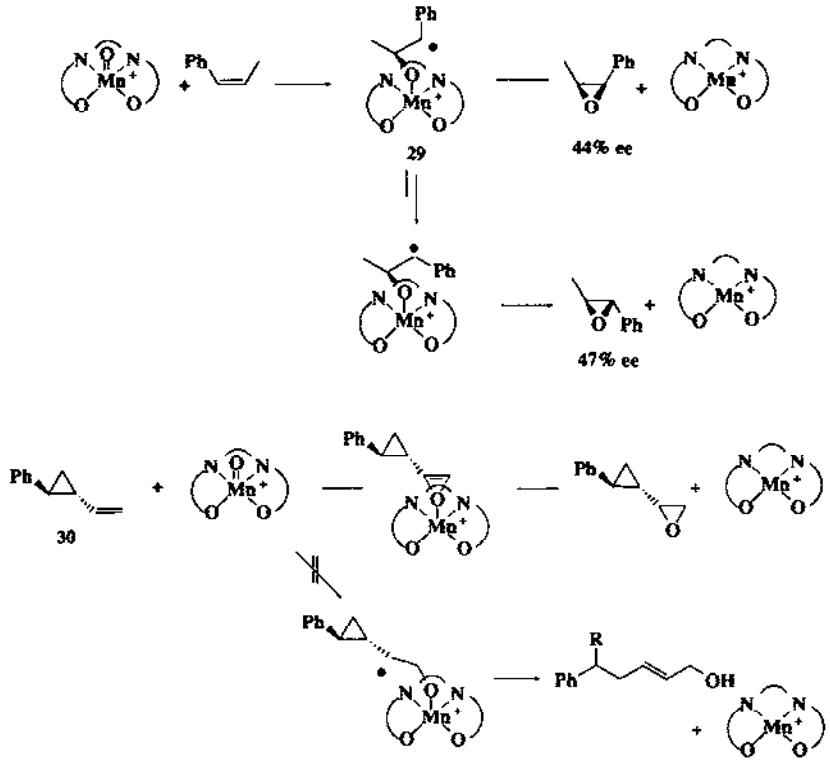


and the ethylenediamine side has no π electrons. We consider that a repulsive π–π electron interaction between the benzene ring of the salen ligand and the substituent on the olefin plays an important role in inducing asymmetry together with steric interaction. If one substituent on the olefin is sterically bulky and rich in π electrons, high enantioselectivity can be expected. Both the stereochemistry and the sense of asymmetric induction observed in the epoxidation of enynes can first be rationalized by considering the electronic repulsion. All results so far obtained are compatible with pathway **c**. C5(C5′)-*t*-butyl groups in **12a** which reside near pathway **c** cause strong steric repulsion with the substituent of the incoming olefin. This makes complex **12a** an excellent catalyst. The phenyl group on the binaphthyl moiety that projects toward the space above the C2′ carbon atom makes **24** and **28** among the best catalysts for the epoxidation of cis-olefins for the same reason. In contrast to this, complex **26** is a less efficient catalyst because the bulky silyl group is located away from pathway **c** owing to the long carbon–silicon bond.

Although there is still controversy on the mechanism of the reaction between the olefinic π bond and the metal–oxo bond, stepwise radical and concerted mechanisms at least seem compatible with the results of the present salen-catalysed epoxidation, depending on the substrates used. Kochi and co-workers have suggested that the epoxidation catalysed by (salen)manganese(III) complex proceeds by way of a radical intermediate [14]. This hypothesis was supported by the present author's result: the epoxidation of cis-β-methylstyrene with **13a** gives a mixture of the corresponding cis- and trans-epoxides of almost the same optical purity (44% ee and 47% ee, respectively), which should be derived from a common radical species (**29**) [20a]. In the case of enynes, however, the optical purity of trans-epoxides is generally higher than that of cis-epoxides [33]. This interesting phenomenon has been explained by assuming that isomerization of the radical intermediate leading to the major enantiomer of the epoxide is faster than that of the radical intermediate leading to the minor enantiomer [33b]. On the contrary, alkyl-substituted olefins were suggested by Jacobsen and co-workers to be epoxidized in a concerted process [38]. Epoxidation of trans-2-phenyl-1-vinylcyclopropane (**30**) gives the corresponding epoxide and no product of cyclopropane cleavage is detected. If a radical intermediate intervenes, a product of cyclopropane cleavage should be detected, since the rate of rearrangement of a secondary phenylcyclopropyl radical is very fast (above 10^{10} s^{-1}).

2.4. *Axial ligand effects on enantioselectivity*

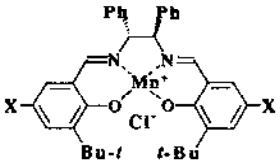
As described in the beginning of Section 2.1, the oxo functionality on the metal centre is displaced closer to the salen plane when an axial ligand coordinates. Since olefins approach the metal–oxo bond from the side, interaction between the incoming olefin and substituents on the salen ligand is considered to become stronger as the oxo bond becomes closer to the salen plane. Coordination of an axial ligand is also expected to decrease the reactivity of the oxo species and to enhance the enantioselectivity (see also the next section). Based on these assumptions, the present author and co-workers examined the effect of an axial ligand on enantioselectivity and found that the addition of a donor ligand usually gives a favourable influence on the



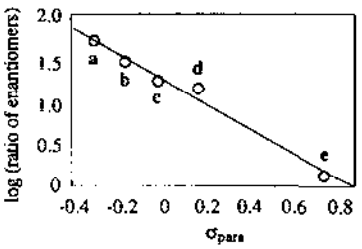
asymmetric induction by salen complexes (Table 1, entries 8, 10, and 15) [20c,39]. However, this is not always the case. Enantioselectivity in the epoxidation of trans-stilbene is diminished when pyridine *N*-oxide is added to the reaction medium (entry 23). The reason for this unexpected negative effect is unclear at present.

2.5. *Electronic effects on enantioselectivity*

Jacobsen et al. observed that the electronic nature of the aromatic substituent in the salen ligand strongly influences enantioselectivity: complexes with an electron-donating group exhibit a higher asymmetric induction than that with an electron-withdrawing group [40]. The electronic effect of substituents corresponds well to the σ values. For example, enantioselectivity in the epoxidation of 2,2-dimethylchromene ranges from 96% ee with **31a** to 22% ee with **31e**. The linear correlation between ee and the substituent's σ value indicates that this substituent effect is not steric but electronic [12]. An electronic effect has been attributed to the change in the reactivity of oxo species. As first reported by Kochi and co-workers, electron-donating substituents decrease the reactivity of the oxo species [14] and the reaction with a less reactive oxo species proceeds via a more product-like transition state, resulting in more specific non-bonded interactions [40].



31 a: X= OMe
b: X= Me
c: X= H
d: X= Cl
e: X= NO_2

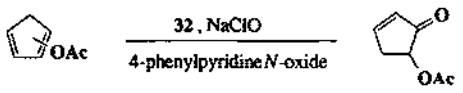


By the same token, complex **32** bearing a triisopropopylsiloxy group at C5 and C5′ carbon atoms exhibits higher asymmetric induction than **12a** (Table 2, entries 8–13).

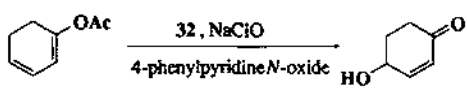
3. Asymmetric oxidation of silyl enol ethers and enol acetates

Reddeppa Reddy and Thornton have reported asymmetric oxidation of silyl enol ethers using complex **33** as a catalyst, giving a mixture of α-hydroxy ketones and their trimethyl silyl ethers [41]. The enantioselectivity of the reaction varies with substrate from 15% to 62% ee (Table 3).

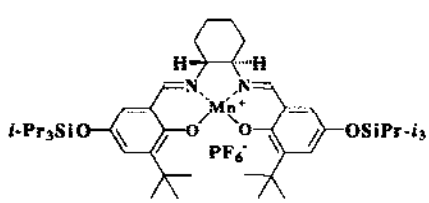
Oxidation of enol acetates using **32** as a catalyst proceeds with moderate to good enantioselectivity:



35%, 71% ee (6)

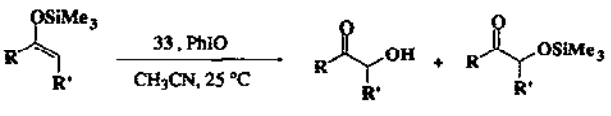


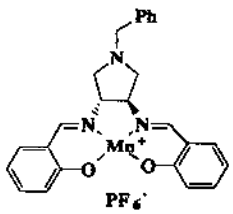
47%, 68% ee (7)



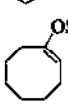
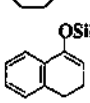
32

Table 3
Asymmetric oxidation of silyl enol ethers:





33

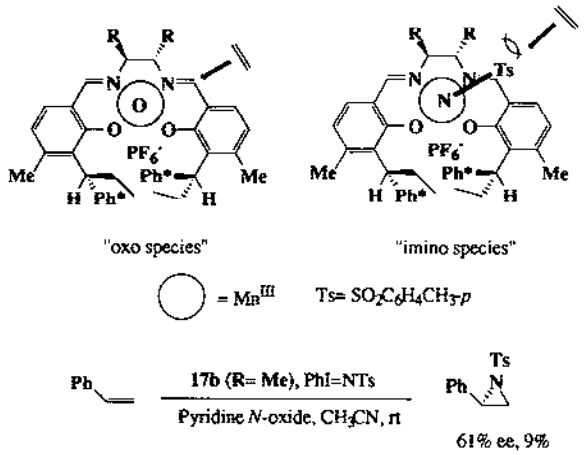
Entry	Substrate	Yield (%)[a]	Ratio (34:35)	ee (%)[b]
1		70	2.6:1	30
2		78	1.4:1	51
3		68	0.8:1	15
4		72	0.8:1	62

[a] Total yield of **34** and **35**.
[b] The ee of **34**.

4. Salen-catalysed asymmetric aziridination

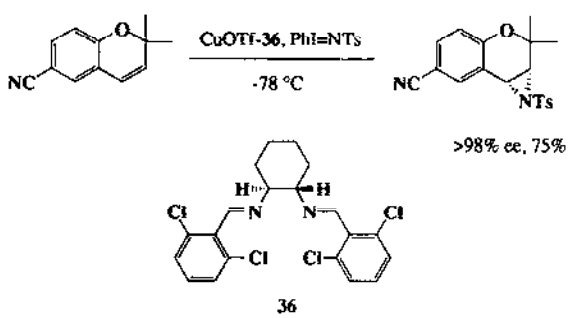
Metalloporphyrin complexes have been known to catalyse aziridination [42]. Although salen-catalysed aziridination has been examined by analogy with porphyrin-catalysed reactions, results are not yet promising. Burrows et al. reported that aziridination with **26a** or **26b** did not display any asymmetric induction [30]. We have also examined aziridination with **13** and **15** but the reactions exhibit much poorer enantioselectivity (4%–26% ee) and chemical yield compared with those in the corresponding epoxidation [43]. This difference in chemical yield and enantioselectivity between asymmetric epoxidation and aziridination has been attributed to the structural difference in the active intermediates between epoxidation and aziridination. Differing from the oxo species, the imino species has a substituent on the nitrogen atom which directs toward the incoming olefin to retard aziridination. Therefore, it is expected that enantioselectivity and reaction rate would be enhanced if the imino substituent could rotate away from the approach path of the olefin. Based on this assumption, complex **17b** bearing a small methyl group as C1″ and

C2″ substituents has been used and a moderate enantioselectivity of 61% ee has been achieved although the chemical yield is still poor [44]:



(8)

Although (salen)manganese(III) complexes do not exhibit sufficient catalytic activity for aziridination, Jacobsen and co-workers have reported that a copper complex bearing a modified Schiff base ligand **36** displayed high enantioselectivity [44]:



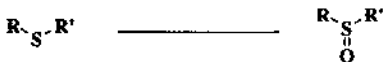
(9)

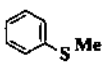
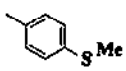
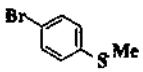
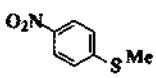
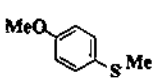
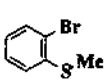
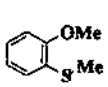
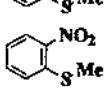
36

5. Asymmetric oxidation of sulphides

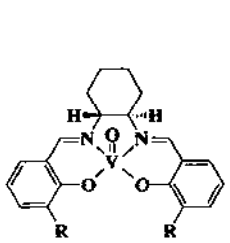
Most of reagents or catalysts used for asymmetric epoxidation have been successfully applied to asymmetric oxidation of sulphides. This is also the case for salen-catalysed oxidation (Table 4). Fujita and co-workers first reported asymmetric oxidation of sulphides by using (salen)vanadium(IV) complexes (**37**–**39**) [45]. Although the enantioselectivity of the reactions is moderate, catalyst **37** bearing electron-donating methoxyl groups has higher asymmetric induction than catalyst **39** bearing sterically bulky *t*-butyl groups at the same position (cf. entries 1 and 4). Fujita and co-workers also reported asymmetric oxidation of sulphide using *t*-butyl hydroperoxide (TBHP) as an oxidant [47] with the μ-oxo titanium complex **40** which dissociates

Table 4
Asymmetric oxidation of sulphides:

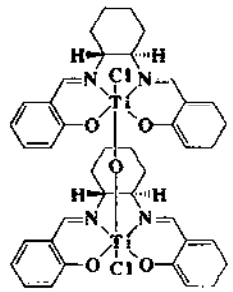


Entry	Substrate	Catalyst	Solvent	Oxidant	Yield (%)	ee (%)	Configuration	Ref.
1		37	CH_2Cl_2	CHP	96	40	*S*	[43]
2		37	CH_2Cl_2	TBHP	90	16	*S*	[43]
3		38	CH_2Cl_2	CHP	81	40	*S*	[43]
4		39	CH_2Cl_2	CHP	70	10	*S*	[43]
5		40	MeOH	TBHP	89	63	*R*	[44]
6		12a	CH_3CN	H_2O_2	72	24	*S*	[45]
7		42	CH_3CN	H_2O_2	90	47	*S*	[45]
8		18	CH_3CN	PhIO	67	3	*R*	[48]
9		43	CH_3CN	PhIO	75	29	*S*	[48]
10		44	CH_3CN	PhIO	76	63	*R*	[48]
11		18	CH_2Cl_2	CHP	71	35	*S*	[43]
12		42	CH_3CN	H_2O_2	95	47	*S*	[45]
13		42	CH_3CN	H_2O_2	93	56	*S*	[45]
14		44	CH_3CN	PhIO	63	75	—	[48]
15		42	CH_3CN	H_2O_2	84	63	*S*	[45]
16		44	CH_3CN	PhIO	67	86	—	[48]
17		44	CH_3CN	PhIO	45	40	—	[48]
18		42	CH_3CN	H_2O_2	80	68	*S*	[45]
19		44	CH_3CN	PhIO	74	88	—	[48]
20		*ent*-42	CH_3CN	H_2O_2	94	34	*R*	[45]
21		44	CH_3CN	PhIO	51	90	—	[48]

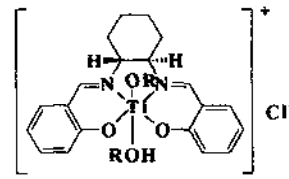
into monomeric species **41** in an alcoholic solvent. However, as TBHP oxidizes phenyl methyl sulphide without catalyst, a high catalyst : substrate ratio (0.2 : 1) is required to achieve the optimal enantioselectivity (63% ee, entry 5). The reaction in dichloromethane which is presumably catalysed by **40** itself exhibits very low enantioselectivity (26% ee). Since the rate law of this reaction is first order in the concentration of sulphides, hydroperoxide, and catalyst, sulphides are considered to coordinate to titanium ion prior to oxidization [46].



37: R= MeO
38: R= EtO
39: R= *t*-Bu



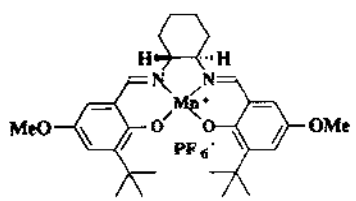
40



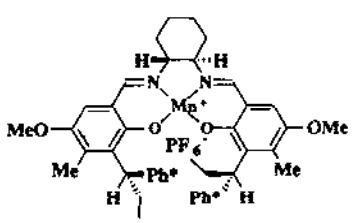
41

Jacobsen's complex **12a** which exhibits a high asymmetric induction in the epoxidation has also been applied to oxidation of sulphides but the enantioselectivity is poor (entry 6) [47]. Similarly to Fujita and co-workers' result, however, complex **42** having a methoxy group instead of a *t*-butyl group displays moderate enantioselectivity ranging from 34% to 68% ee. Sulphides bearing electron-withdrawing groups such as bromo or nitro groups in their aryl moiety exhibit higher enantioselectivity (entries 13, 15, and 18) than sulphides bearing electron-donating groups (entry 20). In this reaction, use of hydrogen peroxide as the terminal oxidant has been recommended to prevent overoxidation of the resulting sulphoxide.

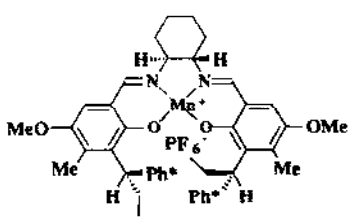
Complex **18** is also a poor catalyst for asymmetric oxidation of sulphides (entry 8), in contrast to epoxidation [48]. Its methoxylated derivative **43** has slightly improved asymmetric induction (entry 9). Surprisingly, however, the use of **44** which is the diastereomer of **43** enhances the enantioselectivity remarkably (entry 10) and oxidation of methyl *o*-nitrophenyl sulphide with **44** gives the corresponding sulphoxide of



42



43



44

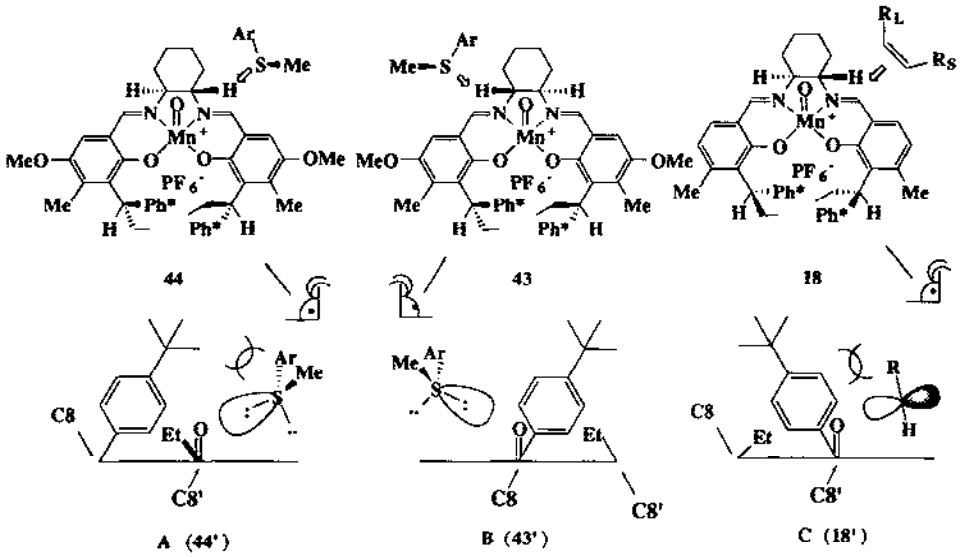


Fig. 4. The views of oxo species (**44'**, **43'** and **18'** derived from **44**, **43**, and **18** respectively) and the incoming substrate, from C3' or C3 substituent side.

90% ee which is the highest achieved in the catalytic asymmetric oxidation of sulphide to date.

The difference in asymmetric induction by the salen catalyst in epoxidation and sulphide oxidation seems to be attributed to the difference in the configuration of the olefinic carbon atom and sulphur atom. That is, the olefinic carbon atom has an sp^2 configuration, while the sulphur atom in the sulphides has an sp^3 configuration. As shown in Fig. 4, the incoming olefins sterically interact with the bulky C8' (or C8) substituent when the complex has an 8*R*, 8'*R*, 1''*S*, 2''*S* (or 8*S*, 8''*S*, 1''*R*, 2''*R*) configuration such as **18** and **43**, but sulphides do not, because substituents on the sulphides stay behind the sulphur atom owing to its sp^3 configuration. On the contrary, the sulphide's substituent is considered to interact with the projected *t*-butylphenyl group from the C8 carbon, when **44** is used as a catalyst [48]. This model correctly predicts the configuration of the sulphoxide obtained with **44**.

6. Conclusion

The introduction of optically active (salen)manganese(III) complexes has allowed great advances to be made in the fields of the asymmetric epoxidation of simple olefins and the asymmetric oxidation of sulphides as described in this short review, although their scope is currently limited to certain classes of substrates. However, salen complexes have great potential as catalysts for oxo transfer reactions. They even catalyse the stereoselective oxidation of unactivated C—H bonds [49]. Therefore, the further development of these salen catalysts will further the study of

asymmetric oxo transfer reactions and someday we will reach the level of selectivity (chemo-, regio- and stereoselectivities) achieved by cytochrome P-450 in oxidative metabolism.

References

[1] (a) R.H. Holm, Chem. Rev., 87 (1987) 1401. (b) K.A. Jorgensen, Chem. Rev., 89 (1989) 431.
[2] J.T. Groves and T.E. Nemo, J. Am. Chem. Soc., 105 (1983) 5786.
[3] J.T. Groves, T.E. Nemo and R.S. Myers, J. Am. Chem. Soc., 101 (1979) 1032.
[4] (a) J.T. Groves and R.S. Myers, J. Am. Chem. Soc., 105 (1983) 5791. (b) J.T. Groves and P. Viski, J. Org. Chem., 55 (1990) 3628.
[5] D. Mansuy, P. Battioni, J.-P. Renaud and P. Guerin, J. Chem. Soc., Chem. Commun., (1985) 155.
[6] (a) Y. Naruta, F. Tani and K. Maruyama, Chem. Lett., (1989) 1269. (b) Y. Naruta, F. Tani, N. Ishihara and K. Maruyama, J. Am. Chem. Soc., 113 (1991) 6865.
[7] S. O'Malley and T. Kodadek, J. Am. Chem. Soc., 111 (1989) 9116.
[8] R.L. Halterman and S.-T. Jan, J. Org. Chem. Soc., 56 (1991) 5253.
[9] K. Konishi, K. Oda, K. Nishida, T. Aida and S. Inoue, J. Am. Chem. Soc., 114 (1992) 1313.
[10] J.P. Collman, V.J. Lee, X. Zhang, J.A. Ibers and J.I. Braumann, J. Am. Chem. Soc., 15 (1993) 3834.
[11] (a) T. Katsuki and K.B. Sharpless, J. Am. Chem. Soc., 102 (1980) 5974. (b) R. Johnson and K.B. Sharpless, in B.M. Trost (ed.), Comprehensive Organic Synthesis, Vol. 7, Pergamon, Oxford, 1991, pp. 389–436.
[12] E.N. Jacobsen, in I. Ojima (ed.), Catalytic Asymmetric Synthesis, VCH, New York, 1993, pp. 159–202.
[13] E.G. Samsel, K. Srinivasan and J.K. Kochi, J. Am. Chem. Soc., 107 (1985) 7606.
[14] K. Srinivasan, P. Michaud and J.K. Kochi, J. Am. Chem. Soc., 108 (1986) 2309.
[15] H. Yoon and C.J. Burrows, J. Am. Chem. Soc., 110 (1988) 4087.
[16] M.M. Taqui Khan, S.A. Mirza, C. Sreelatha, S.H.R. Abdi and Z.A. Shaikh, Stud. Org. Chem. (Amsterdam), 33 (1988) 211 (Chem. Abstr., 109 (1988) no. 47311m).
[17] C.P. Horwitz, S.E. Creager and R.W. Murray, Inorg. Chem., 29 (1990) 1006.
[18] (a) W. Zhang, J.L. Loebach, S.R. Wilson and E.N. Jacobsen, J. Am. Chem. Soc., 112 (1990) 2801. (b) W. Zhang and E.N. Jacobsen, J. Org. Chem., 56 (1991) 2296.
[19] E.N. Jacobsen, W. Zhang, L.C. Muci, J.R. Ecker and L. Deng, J. Am. Chem. Soc., 113 (1991) 7063.
[20] (a) R. Irie, K. Noda, Y. Ito, N. Matsumoto and T. Katsuki, Tetrahedron Lett., 31 (1990) 7345. (b) R. Irie, K. Noda, Y. Ito and T. Katsuki, Tetrahedron Lett., 32 (1991) 1055. (c) R. Irie, K. Noda, Y. Ito, N. Matsumoto and T. Katsuki, Tetrahedron: Asymmetry, 2 (1991) 481.
[21] N. Hosoya, R. Irie and T. Katsuki, Synlett, (1993) 261.
[22] N. Hosoya, A. Hatakeyama, K. Yanai, H. Fujii, R. Irie and T. Katsuki, Synlett, (1993) 641.
[23] A. Hatayama, N. Hosoya, R. Irie and T. Katsuki, Synlett, (1992) 407.
[24] (a) H. Sasaki, R. Irie and T. Katsuki, Synlett, (1993) 300. (b) H. Naoki, A. Hatayama, R. Irie, H. Sasaki and T. Katsuki, Tetrahedron, 50 (1994) 4311.
[25] T. Schwenkreis and A. Berkessel, Tetrahedron Lett., 34 (1993) 4785.
[26] T. Yamada, K. Imagawa, T. Nagata and T. Mukaiyama, Chem. Lett., (1992) 2231.
[27] (a) P. Pietikäinen, Tetrahedron Lett., 35 (1994) 941. (b) R. Irie, N. Hosoya and T. Katsuki, Synlett, (1994) a55.
[28] N. Hosoya, R. Irie, Y. Ito and T. Katsuki, Synlett, (1991) 691.
[29] H. Sasaki, R. Irie and T. Katsuki, Synlett, (1994) 356.
[30] K.J. O'Connor, S.J. Wey and C.J. Burrows, Tetrahedron Lett., 33 (1992) 1001.
[31] T. Hamada, R. Irie and T. Katsuki, Synlett., (1994) 479.
[32] S. Chang, R.M. Heid and E.N. Jacobson, Tetrahedron Lett., 35 (1994) 669.
[33] (a) N.H. Lee and E.N. Jacobsen, Tetrahedron Lett., 32 (1991) 6533. (b) W. Zhang, N.H. Lee and E.N. Jacobsen, J. Am. Chem. Soc., 116 (1994) 425.

[34] N.H. Lee, A.R. Muci and E.N. Jacobsen, Tetrahedron Lett., 32 (1991) 5065.
[35] L. Deng and E.N. Jacobsen, J. Org. Chem., 57 (1992) 4320.
[36] S. Chang, N.H. Lee and E.N. Jacobsen, J. Org. Chem., 58 (1993) 6940.
[37] R. Hirsenkorn, Tetrahedron Lett., 31 (1990) 7591.
[38] H. Fu, G.C. Look, W. Zhang, E.N. Jacobsen and C.-H. Wong, J. Org. Chem., 56 (1991) 6497.
[39] R. Irie, Y. Ito and T. Katsuki, Synlett, (1991) 265.
[40] E.N. Jacobsen, W. Zhang and M.L. Guller, J. Am. Chem. Soc., 113 (1991) 6703.
[41] D. Reddeppa Reddy and E.R. Thornton, J. Chem. Soc., Chem. Commun., (1992) 172.
[42] (a) J.T. Groves and T. Takahashi, J. Am. Chem. Soc., 105 (1983) 2073. (b) D. Mansuy, P. Battioni and J.-P. Mahy, J. Am. Chem. Soc., 104 (1982) 4487. (c) J.-P. Mahy, P. Battioni and D. Mansuy, J. Am. Chem. Soc., 108 (1986) 1079.
[43] K. Noda, N. Hosoya, R. Irie, Y. Ito and T. Katsuki, Synlett, (1993) 469.
[44] Z. Li, K.R. Conster and E.N. Jacobsen, J. Am. Chem. Soc., 115 (1993) 5326.
[45] K. Nagajima, M. Kojima and J. Fujita, Chem. Lett., (1986) 1483.
[46] C. Sasaki, K. Nakajima, M. Kojima and J. Fujita, Bull. Chem. Soc. Jpn., 64 (1991) 1318.
[47] M. Palucki, P. Hanson and E.N. Jacobsen, Tetrahedron Lett., 33 (1992) 7111.
[48] K. Noda, N. Hosoya, K. Yanai, R. Irie and T. Katsuki, Tetrahedron Lett., 35 (1994) 1887.
[49] M.D. Kaufman, P.A. Grieco and D.W. Bougie, J. Am. Chem. Soc., 115 (1993) 11648.