Application of new unsymmetrical chiral Mn(III), Co(II,III) and Ti(IV) salen complexes in enantioselective catalytic reactions

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New unsymmetrical chiral salen complexes were synthesized and the efficiency of Mn(III), Ti(IV), Co(II) and Co(III) type catalysts was examined in the enantioselective epoxidation of styrene and α-methylstyrene, the trimethylsilylcyanation of benzaldehyde, the borohydride reduction of aromatic ketones and asymmetric hydrolysis of epoxides to diols, respectively. A very high level of enantioselectivity was attainable over the unsymmetrical chiral salen complexes prepared mainly from salicylaldehyde and 2-formyl-4,6-di-*tert*-butylphenol derivatives. Enantiomeric excess of the corresponding reaction product obtained using unsymmetrical chiral salen catalysts was generally higher than that over conventional symmetric chiral salen catalysts.

Keywords: unsymmetrical chiral salen, epoxidation, reduction, hydrolysis, trimethylsilylcyanation, enantioselectivity

1. Introduction

Chiral salen Mn(III) complexes have been found to be highly enantioselective for the asymmetric epoxidation of conjugated *cis*-disubstituted and trisubstituted olefins [1–3]. As an application, Janssen et al. have synthesized a dimeric form of Mn(III) salen ligand and retained this complex in the cross-linked polymer membrane to use as a catalyst for epoxidation [4]. Chiral salen complexes of Cr(III) were shown by Martinez et al. to be efficient catalysts for the enantioselective ring opening of epoxides with Me_3SiN_3 [5]. Belokon et al. have reported a set of aromatic and α,β-unsaturated aldehydes were asymmetically trimethylsilylcyanated over chiral salen Ti(IV) complexes of similar type with high e.e.% [6]. It is well known that cyanohydrin derivatives are important and attractive intermediates from the synthetic point of view. The enantioselective synthesis of cyanohydrine was performed successfully by the addition of Me_3SiCN (TMSCN) to aldehydes using catalysts prepared *in situ* from titanium isopropoxide and optically active ligands such as Ti(IV)-tridentate Schiff's base complexes of N-(2-hydroxy-3-*tert*-butylbenzylidene)-(S or R)-valinol and Ti(IV)-tetradentate Schiff's bases [7]. These catalysts showed very high e.e. values up to 96%. In addition, chiral salen complexes of Co(III) were also shown by Tokunaga et al. to be efficient catalysts for the enantioselective ring opening of epoxides with water [8]. Recently, Nagata et al. have reported a set of ketones were asymmetrically reduced over conventional symmetrical chiral salen Co(II) complexes with high e.e.'s [9].

In most salen complexes studied to date, the two identical salicylaldehyde derivative moieties are connected to both sides of one diamine on the ligand [1–6]. A new class of unsymmetrical chiral salen Schiff base ligands can be synthesized efficiently by a stepwise condensation method, possessing two different salicylaldehyde derivatives, each with different substituent groups, as reported by Lopez et al. [10]. The synthesis of one chiral half unit of **3a**–**3d**, as shown in scheme 1, is needed first[1] and then this intermediate allows the construction of the desired compounds by reacting the remaining free amine with other salicylaldehyde derivatives.[2]

[1] 10 mmol salicylaldehyde (or *o*-vanillin) in 50 ml chloroform was added dropwise to a stirred solution of 30 mmol (1S,2S)-(+)-1,2-diaminocyclohexane (or (1S,2S)-(−)-1,2-diphenylethylenediamine) in 100 ml chloroform containing molecular sieve 4A at 0 °C. The addition of salicylaldehyde (or *o*-vanillin) took 5 h. A pale-yellow creamy solid was obtained after evaporation of solvent under vacuum and washing with water to remove the unreacted diamines.
Sample **3b**: IR (CCl_4): 3400, 3091, 2930, 2870, 1630, 1580, 1497, 1461, 1448, 1414, 1281, 1211, 1150, 1118, 1091, 1064, 1045, 942. ^{1}H-NMR ($CDCl_3$/TMS): 1.18–1.49 (m, 4H), 1.62–1.78 (m, 4H), 1.78–1.90 (m, 2H), 2.84 (q, 1H), 3.27–3.29 (m, 1H), 6.73 (t, 1H), 7.10 (d, 1H), 7.11–7.26 (m, 1H), 8.17 (s, 0.7H), 8.41 (s, 0.3H), 13.31 (s, 1H).
Sample **3d**: IR (CCl_4): 3404, 3060, 2931, 2868, 1631, 1582, 1464, 1417, 1345, 1275, 1256, 1092, 1082, 1042, 973, 907. ^{1}H-NMR ($CDCl_3$/TMS): 1.19–1.44 (m, 4H), 61–1.79 (m, 4H), 1.79–1.88 (m, 2H), 2.15 (d, 0.5H), 2.77 (d, 1H), 3.23 (d, 0.5H), 3.79 (d, 3H), 6.64–6.88 (m, 3H), 8.18 (s, 0.5H), 8.35 (s, 0.5H), 13.33 (s, 1H).

[2] The following procedure for the preparation of unsymmetrical chiral salen complexes is general: 1 mmol of the chiral half unit (**3a**–**3d**) in 20 ml ethanol was added dropwise to corresponding salicylaldehyde derivative (1 mmol) in 20 ml of ethanol at room temperature. The mixture was heated to 60 °C and stirred for 8 h. The resulting yellow solid was collected by filtration and recrystallized from cold ethanol.
Sample **A**: $[a]_D^{20}$ +162.8 (c = 1.0, $CHCl_3$). IR (CCl_4): 2942, 2861, 1632, 1581, 1498, 1479, 1461, 1407, 1389, 1361, 1279, 1263, 1251, 1201, 1173, 1150, 1117, 1093, 1043, 1030, 974. ^{1}H-NMR ($CDCl_3$/TMS): 1.31–1.45 (m, 18H), 1.62–2.01 (m, 8H), 2.44 (s, 2H), 2.97 (m, 1H), 3.43 (m, 1H), 3.75 (q, 1H), 4.08 (d, 1H), 6.87 (t, 1H),

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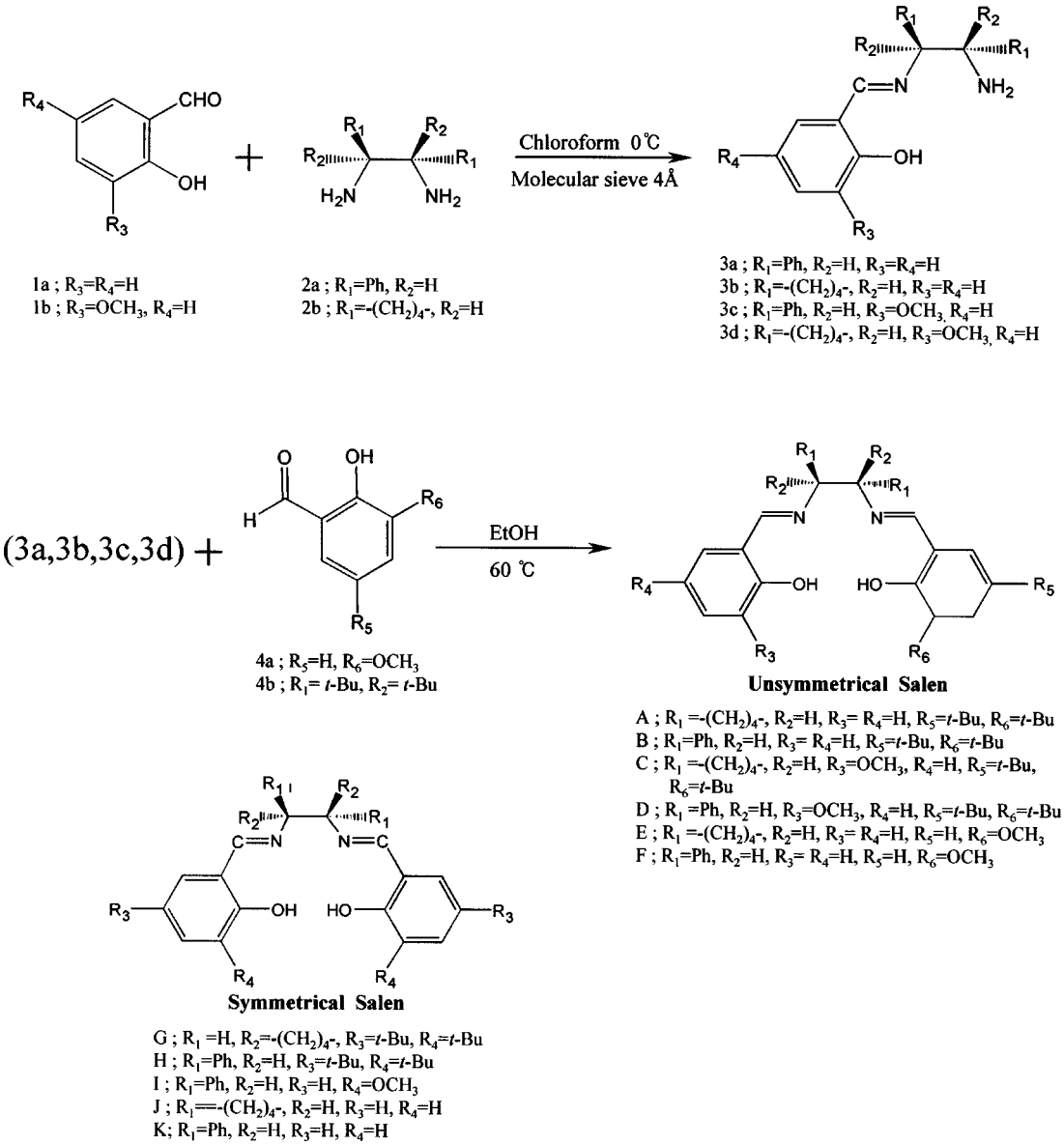


Scheme 1.

In this paper, we report the synthesis and the application of these new unsymmetrical chiral Schiff bases (**A**–**F**) as asymmetric catalysts in the trimethylsilylcyanation of benzaldehyde, the borohydride reduction of aromatic ketones, the epoxidation of unfunctionalized olefins and in the hydrolysis of racemic epoxides into diols. The conventional chiral salen ligands (**G**–**K**) were also used as catalysts to compare the enantioselective catalytic activities. The relation between the structural features of the new unsymmetric salen ligands and enantioselectivity was evaluated.

2. Experimental

The chiral half unit was easily obtained in about 90% yield by the reaction of salicylaldehyde **1a** (or *o*-vanillin, **1b**) with (1S,2S)-(+)-1,2-diaminocyclohexane (or (1S,2S)-(−)-1,2-diphenylethylenediamine) in a chloroform solution at 0 °C. The solvent and unreacted starting compounds were removed under vacuum at 60 °C and a slightly yel-

7.03 (d, 1H), 7.12–7.28 (m, 2H), 7.35 (t, 1H), 7.46 (d, 1H), 8.40 (s, 2H). ^{13}C-NMR ($CDCl_3$/TMS): 24.4, 29.8, 31.3, 33.1, 37.2, 72.4, 116.8, 118.4, 122.2, 124.8, 125.5, 126.7, 128.2, 131.3, 132.0, 132.2, 136.2, 160.8, 164.6 and 165.7 ppm.

Sample **C**: $[a]_D^{20}$ +423.6 (c = 1.0, $CHCl_3$). IR (CCl_4): 2931, 2859, 1600, 1468, 1439, 1391, 1364, 1278, 1256, 1203, 1172, 1120, 1092, 1042, 1030, 973, 907. ^{1}H-NMR ($CDCl_3$/TMS): 1.19–1.40 (m, 21H), 1.47–2.01 (m, 8H), 3.29 (m, 2H), 3.67 (q, 2H), 3.85 (s, 2H), 6.75 (m, 1H), 6.98 (s, 1H), 7.15–7.25 (m, 1H), 7.30 (s, 1H), 7.46 (d, 1H), 8.30 (s, 2H). ^{13}C-NMR ($CDCl_3$/TMS): 24.0, 29.4, 31.3, 33.9, 34.9, 55.7, 72.3, 113.7, 117.8, 123.0, 125.9, 136.2, 139.8, 157.9, 164.7 and 165.7 ppm.

Sample **E**: IR (CCl_4): 2936, 2860, 1629, 1601, 1581, 1551, 1493, 1465, 1412, 1339, 1278, 1257, 1218, 1171, 1151, 1085, 1061, 1045, 1029, 1008, 975. ^{1}H-NMR ($CDCl_3$/TMS): 1.18–1.23 (m, 3H), 1.40–1.93 (m, 10H), 3.26–3.30 (m, 1H), 3.67 (q, 1H), 3.83 (d, 2H), 6.66–7.24 (m, 7H), 8.22 (s, 2H). ^{13}C-NMR ($CDCl_3$/TMS): 24.0, 32.9, 55.8, 72.5, 113.6, 116.6, 117.8, 118.4, 122.9, 131.4, 132.1, 148.1, 151.2, 160.8 and 164.6 ppm.

low creamy solid (**3a**–**3d**) was obtained. The condensation of this chiral half unit with corresponding salicylaldehyde derivatives in 1 : 1 molar ratio was performed at 60 °C in ethanol solution. The resulting yellow crystals of unsymmetrical salen (**A**–**F**) were collected by filtration. The compound of **A**–**K** in MeOH solution was heated with excess $Mn^{II}(OAc)_2{\cdot}4H_2O$ to reflux for 5 h. 3.0 equiv. of LiCl was added and the mixture was heated to reflux for an additional hour in order to synthesize Mn(III)-**A**–**K** catalysts. Furthermore, the cationic $(Mn(III))^+$ type salen complex was prepared to be immobilized onto the MCM-41 mesoporous material. The compounds **A**–**K** were also heated to reflux with $Mn^{II}(OAc)_2{\cdot}4H_2O$ for insertion of the Mn(II) center. A solution of ferricenium hexafluorophosphate (Cp_2FePF_6) was added to this mixture to obtain the cationic $(Mn\text{-salen})^+PF_6^-$ complex. The mixture was concentrated to dryness and washed with hexane to remove the side product, ferrocene.

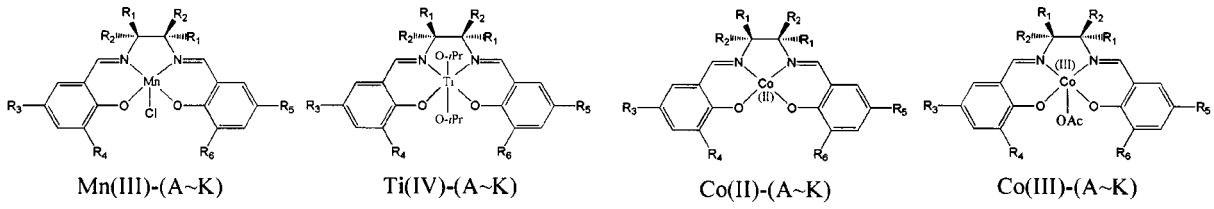
In addition, ion exchangeable Al-containing MCM-41 and purely silicious MCM-41 were synthesized hydrothermally. The following MCM-41 synthesis procedure was applied in this work: MCM-41 of very high crystallinity could be synthesized within 5 h using this modified method. Tetraethylorthosilicate (TEOS, 50 g) and ethanol (33 g) were added to pure water (35 g) and this mixture was heated to reflux (60 °C) for 10 min. 1.25 g HCl was added dropwise and the mixture was vigorously stirred for 90 min. The mole ratio of $TEOS : EtOH : H_2O : HCl$ was $1 : 3 : 8 : 5 \times 10^{-2}$. The reactant mixture was cooled to 25 °C and then stirred again for 30 min. The sample was aged at 50 °C for 30 min without agitation. The mixture was diluted with pure ethanol (360 g) and hexadecyltrimethylammonium bromide (C_{16}TMABr, 8.747 g) was dissolved in the resulting solution. After stirring for 30 min, the solvent was evaporated at 60 °C. The resultant dried solid was heated to 550 °C at the heating rate of 1 °C/min and then calcined at 550 °C in air for 6 h. Aluminum isopropoxide was used as an Al source and added to the TEOS solution as the first step in preparing the Al-containing MCM-41. To immobilize the Mn(salen) complexes onto MCM-41, $(Mn\text{-salen})^+$ complexes were ion exchanged with Na^+ on Al-MCM-41 at 60 °C in ethanol solvent, followed by washing with hexane and drying. Mn(III)-**A**/MCM-41 denotes the cationic Mn(III) salen complex of **A** immobilized on MCM-41. The chiral salen Ti(IV) catalysts were prepared *in situ* by reacting titanium isopropoxide with salen ligands (Ti(IV)-**A**–**K**). These Ti complexes were anchored over mesoporous MCM-41 by reflux in MeOH solution, as shown in scheme 2 (Ti(IV)-**A**–**K**/MCM-41). The unsymmetrical salen Co(II) catalysts were obtained by the reaction of $Co^{II}(OAc){\cdot}4H_2O$ with the corresponding chiral salen ligands in refluxed EtOH solution. The salen Co(III) catalysts were prepared by oxidizing Co(II) complexes with acetic acid in toluene under air.

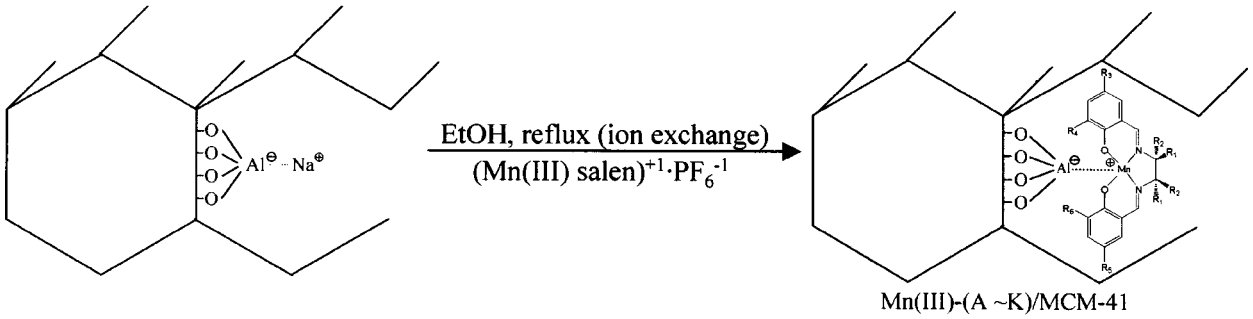
In the asymmetric epoxidation of olefins, m-chloroperoxobenzoic acid (m-CPBA) was used as a terminal oxidant in the presence of N-methylmorpholine N-oxide to prevent the possibility of ion exchange of immobilized Mn(III) salen with Na^+ cations which existed in the NaOCl buffer solution. Epoxidation reactions were run at 0 °C. The solution of styrene or α-methylstyrene (0.96 mmol), N-methylmorpholine N-oxide (NMO,4.80 mmol) and salen Mn complex (0.058 mmol) in 10 ml of CH_2Cl_2 was cooled to 0 °C. m-CPBA (1.92 mmol) was added as a solid in five roughly equal portions over a 5 min period. The reaction mixture was stirred for 6 h. After finishing the reaction, 10 ml of 1 N NaOH was added and the organic phase was separated and washed with brine. The organic phases were dried over $MgSO_4$. The asymmetric trimethylsilylcyanation of benzaldehyde was carried out mainly at −80 °C over chiral Schiff base–Ti complex catalysts to evaluate the relation between the structural features of the new unsymmetric salen ligands and their enantioselectivity. The borohydride reduction of acetophenone and α-tetralone was carried out at −20 °C over chiral Co(II) salen catalysts and the asymmetric hydrolysis of epoxides with water was performed over unsymmetrical Co(III) salen catalysts at room temperature without addition of solvent. The e.e.% values of corresponding products were determined by capillary GC using a chiral column (Astec Gamma-cyclodextrin trifluoroacetyl, 40 m × 0.25 mm i.d.) and by Chiral-iR^{TM} (Bomem Co.) based on vibrational circular dichroism (VCD) spectroscopy.

3. Results and discussion

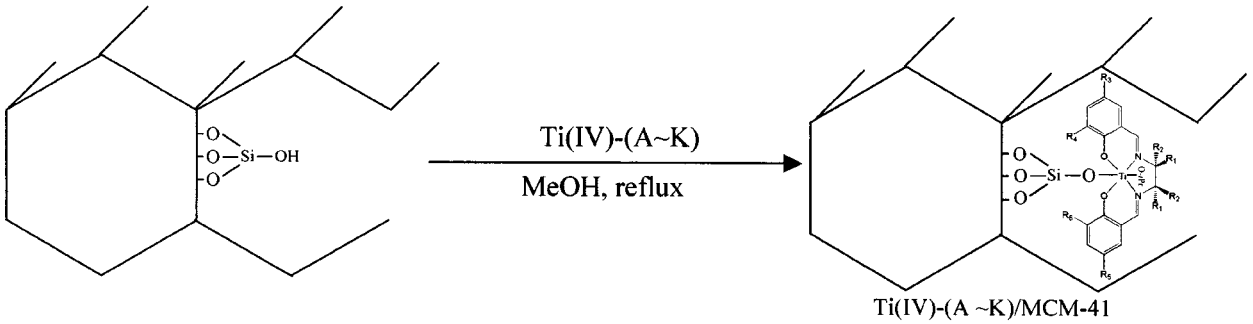
MCM-41 exhibited a very intense (100) peak in the X-ray diffractogram and the calculated d_{100}-spacing was 4.0 nm. Figure 1 shows the TEM image of purely siliceous MCM-41 synthesized by the rapid modification method. Al-containing MCM-41 could also be synthesized with a high crystallinity by this evaporation method. The Si/Al ratio of the obtained sample was 35. These MCM-41 samples were used to immobilize the chiral salen complexes.

The characterization of the samples was carried out using ^{1}H-NMR and ^{13}C-NMR. The NMR spectra showed the synthesis of the chiral half unit and unsymmetrical salen was achieved successfully. The chiral half unit, homogeneous unsymmetrical salen sample and immobilized complexes on MCM-41 were also characterized using FT-IR spectroscopy after the condensation and anchoring reactions shown in scheme 2. Figure 2 shows the FT-IR spectra of salicylaldehyde (**1a**), o-vanillin (**1b**), the chiral half unit of **3b** and the chiral salen complexes of **A**, **E** and **G**. In the IR spectra, salicylaldehyde and o-vanillin show the characteristic C=O (aromatic aldehyde) band near 1680 cm^{-1} and this peak disappeared after condensation with optically pure diamines to synthesize the chiral half unit and the chiral salen complexes. Then, all the unsymmetrical salen complexes as well as the conventional symmetrical chiral salen ligand exhibited the characteristic band at 1640 cm^{-1} after condensation. This peak can be assigned to the stretching vibration of the





Mn salen complex immobilized over Al-MCM-41



Ti salen complex immobilized over MCM-41

Scheme 2.

C=N bond in the salen ligands. The salen complexes immobilized over MCM-41 also exhibited this band in the IR spectra. The appearance of the spectrum of the complex embedded on MCM-41 is relatively similar to that of the homogeneous complex. The ion exchange ability of MCM-41 mesoporous material allows it to immobilize the chiral salen ligands of cationic types as heterogeneous catalysts.

The trends in reactivity and enantioselectivity of the immobilized chiral Mn(salen)/MCM-41 and the same homogeneous complexes in solution were examined for the epoxidation of styrene and α-methylstyrene. As shown in table 1, high enantioselectivity was obtained particularly with more hindered catalysts such as **B**, **F** and **H**. As expected, the catalyst of unsymmetrical salen **A** (or **C**) which has less steric hindrance showed lower e.e.% value than the conventional symmetrical salen **H** having two *tert*-butyl groups at the *para* and *ortho* position to the salen oxygens. The catalyst **A**, which is less hindered than Mn(III)-**B** in the vicinity of the diimine bridge, showed a decreased enantioselectivity. Furthermore, the unsymmetrical salen catalyst **C** showed very similar catalytic activity, as compared with the common symmetrical bulky catalyst of Mn(III)-**G**. In the case of styrene epoxidation, the salen complexes synthesized from diphenylethylenediamine derivatives such as Mn(III)-**B**, -**F** and -**H** were more efficient catalysts. But in the epoxidation of α-methylstyrene, the Mn(III) salen complexes synthesized from (+)-1,2-diaminocyclohexane derivative exhibited higher enantioselectivity than those obtained from (−)-1,2-diphenylethylenediamine. The sense and degree of enantioselection in the epoxidation using salen catalysts is well explained by the side-on perpendicular approach of olefin to the Mn-oxo bond of salen. Jacobson et al. have emphasized that the use of an unhindered precursor opens a quadrant to olefin approach (side-on approach) in which stereochemical communication between ligand and incoming substrate is maximized [11]. This model predicts that styrene should give the higher selectivity with the catalyst of Mn(III)-**H**. As illustrated in table 1, the catalyst Mn(III)-**H** in fact showed higher enantioselectivity than Mn(III)-**G** in the epoxidation of styrene. The same trend was given by Palucki et al. [2]

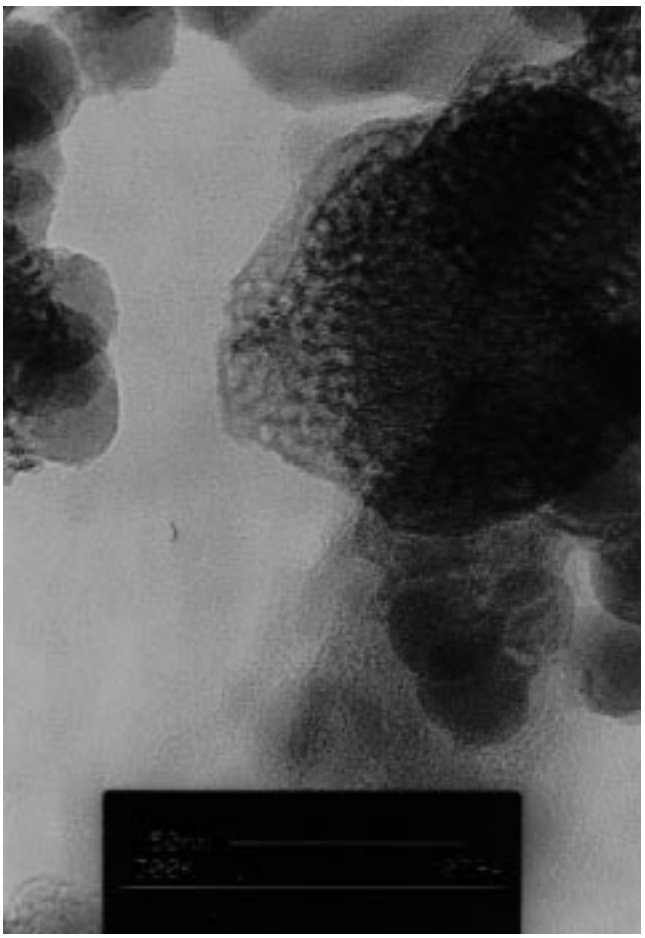


Figure 1. TEM image of MCM-41 obtained by evaporation method.

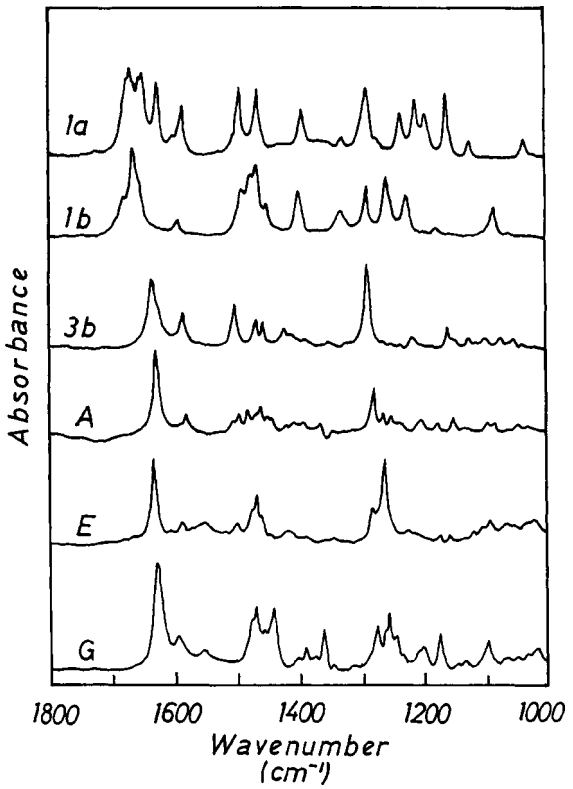


Figure 2. FT-IR spectra of salicylaldehyde (**1a**), *o*-vanilin (**1b**), the chiral half unit of **3b** and salen complexes of **A**, **E** and **G**.

and this result suggested that the catalyst derived from unhindered 1,2-diamines might undergo competitive side-on olefin approach from over the diimine bridge [11]. Although higher enantioselectivity was obtained in the epoxidation of styrene over Mn(III)-**H**, it was decreased for the same catalyst in the methylstyrene epoxidation. This variation in the selectivity also suggests the more hindered terminus of olefins is directed away from the bulky groups in salen catalysts to avoid the unfavorable steric repulsions. However, the improvement in the selectivity for the unsymmetrical salen catalysts may be attributed to the enantiofacial selection of olefins by the favorable perpendicular approach in which the repulsive steric interaction between the substituent on salen catalysts and incoming olefin is minimized. The increase in the enantioselectivity over catalyst **F** may be attributed to the presence of electrodonating methoxy groups.

The enantioselective epoxidation of styrene and α-methylstyrene was investigated using a new unsymmetrical salen catalyst of Mn(III)-**A** at different substrate/catalyst mole ratios (figure 3). The conversion of olefin and the e.e.% of epoxide increased as the substrate/catalyst ratio decreased. The racemic product was obtained only when the reaction, was performed without addition of salen catalyst. This result indicates that the catalysed reaction over chiral complexes is competing with the achiral reaction, as reported by Janssen et al. [12].

The catalytic activity and selectivity of Ti(IV)-**A**–**K** salen complexes and Ti(IV)-**A**–**K**/MCM-41 were examined in the trimethylsilylcyanation of benzaldehyde. The obtained result is given in table 2. As can be seen in the result, the enantioselectivity was strongly dependent on the structure of the Schiff base ligand. The conventional symmetrical salen Ti(IV) complexes of **I** and **K** were efficient catalysts for this reaction, even though they have no bulky group at *para* or *ortho* position to the salen oxygens. Introduction of *tert*-butyl groups *para* and *ortho* to the salen oxygens as in **G** and **H** resulted in a further improvement of optical yield. The new unsymmetrical Ti(IV) salen catalyst of **A** (or **B**) has afforded a very high level of enantioselectivity in the trimethylsilylcyanation of benzaldehyde. A comparatively higher optical yield was obtained over the catalysts prepared by the condensation of **3a** (or **3b**) with **4b**. In the salen structure, the phenyl group connected to the diimine bridge provides more hindered steric effect than the cyclohexane group. As a result, the increased selectivity on the asymmetrical chiral salen catalyst of unsymmetrical salen **A** may be attributed to the effective approach of substrates by a less hindered group in the vicinity of the different substituent groups of salicylaldehyde derivatives. As well, the chiral Ti(IV) salen complex immobilized onto mesoporous MCM-41 exhibited a similar enantioselectivity for trimethylsilylcyanation of benzaldehyde as compared with homogeneous complexes, respectively. The appear-

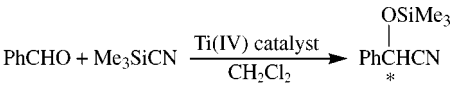
Table 1
Asymmetric epoxidation of styrene and α-methylstyrene:[a]

Entry	Olefin	Catalyst	Reaction temp. (°C)	Conv. (%)	e.e.[b] (%)	Config.
1	Styrene	Mn(III)-**A**	0	97	32	S-(−)
2	Styrene	Mn(III)-**A**/MCM	0	91	37	S-(−)
3	Styrene	Mn(III)-**B**	0	98	63	S-(−)
4	Styrene	Mn(III)-**C**	0	98	45	S-(−)
5	Styrene	Mn(III)-**F**	0	94	68	S-(−)
6	Styrene	Mn(III)-**G**	0	97	48	R-(+)
7	Styrene	Mn(III)-**H**	0	98	66	S-(−)
8	Styrene	Mn(III)-**H**/MCM	0	88	68	S-(−)
9	α-methylstyrene	Mn(III)-**A**	0	98	52	S-(−)
10	α-methylstyrene	Mn(III)-**A**/MCM	0	83	55	S-(−)
11	α-methylstyrene	Mn(III)-**B**	0	93	29	S-(−)
12	α-methylstyrene	Mn(III)-**C**	0	97	53	S-(−)
13	α-methylstyrene	Mn(III)-**D**	0	97	25	S-(−)
14	α-methylstyrene	Mn(III)-**G**	0	97	54	R-(+)
15	α-methylstyrene	Mn(III)-**H**	0	95	30	S-(−)
16	α-methylstyrene	Mn(III)-**H**/MCM	0	81	32	S-(−)

[a] Catalyst, 6 mol% of olefins. Reactions were carried out in CH_2Cl_2 solution, reaction time 6 h. m-chloroperoxobenzoic acid (m-CPBA) was used as a terminal oxidant in the presence of N-methylmorpholine N-oxide additive.

[b] The e.e.% values for styrene oxide were determined by capillary GC using chiral columns (CHIRALDEX™, Gamma-cyclodextrin trifluoroacetyl). The configuration was determined by comparing the retention time with standard samples.

Table 2
Enantioselective trimethylsilylcyanation of benzaldehyde catalyzed by chiral Schiff base titanium complexes:[a]



Entry	Substrate	Catalyst	Temp. (°C)	Conv. (%)	e.e.[b] (%)
1	Benzaldehyde	Ti(IV)-**A**	−80	65	90 (R)
2	Benzaldehyde	Ti(IV)-**A**/MCM	−80	59	94 (R)
3	Benzaldehyde	Ti(IV)-**A**[c]	−80	72	87 (R)
4	p-methoxybenzaldehyde	Ti(IV)-**A**	−80	63	73 (R)
5	2-chlorobenzaldehyde	Ti(IV)-**A**	−80	80	87
6	Benzaldehyde	Ti(IV)-**B**	−80	63	80 (R)
7	Benzaldehyde	Ti(IV)-**C**	−80	63	68 (R)
8	Benzaldehyde	Ti(IV)-**E**	−80	50	66 (R)
9	Benzaldehyde	Ti(IV)-**E**/MCM	−80	44	67 (R)
10	Benzaldehyde	Ti(IV)-**F**	−80	51	72 (R)
11	Benzaldehyde	Ti(IV)-**F**	−25	73	51 (R)
12	Benzaldehyde	Ti(IV)-**F**	−5	89	30 (R)
13	Benzaldehyde	Ti(IV)-**G**	−80	50	77 (S)
14	Benzaldehyde	Ti(IV)-**G**/MCM	−80	50	83 (S)
15	p-methoxybenzaldehyde	Ti(IV)-**G**	−80	48	61 (S)
16	2-chlorobenzaldehyde	Ti(IV)-**G**	−80	78	72
17	Benzaldehyde	Ti(IV)-**H**	−80	53	72 (R)
18	Benzaldehyde	Ti(IV)-**I**	−80	66	65 (R)
19	Benzaldehyde	Ti(IV)-**K**	−80	67	63 (R)

[a] Reaction was carried out using 10 mol% of catalyst; concentration of catalyst was 0.1 mol/l; time 24 h. The catalysts were prepared *in situ* by mixing the corresponding chiral Schiff base (1.1 eq.) and titanium isopropoxide (1.0 eq.) in dichloromethane before reaction.

[b] Determined by GC (CHIRALDEX™, Gamma-cyclodextrin trifluoroacetyl column).

[c] 20 mol% of catalyst, time 24 h.

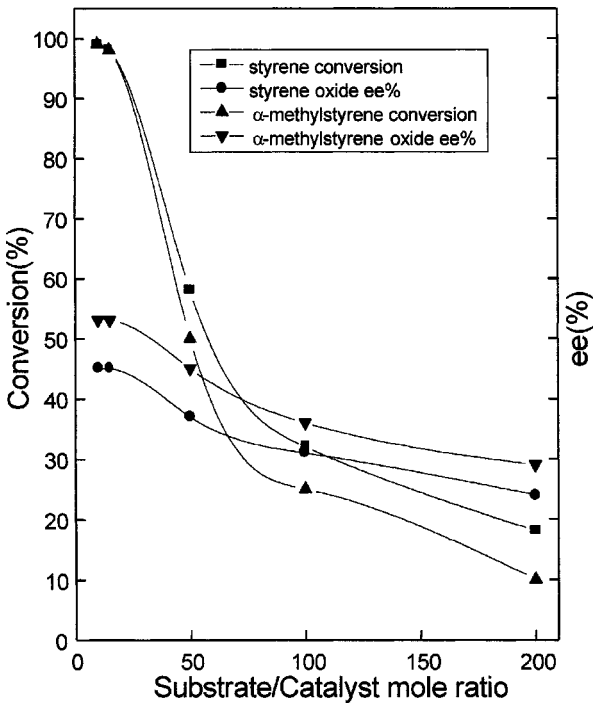


Figure 3. The effect of substrate/catalyst mole ratio on the conversion and enantioselectivity of styrene and α-methylstyrene. The same reaction conditions as shown in table 1.

ance of IR and UV spectra of the anchoring complex on MCM-41 was almost similar to that of the homogeneous complex in solution, indicating that the chiral (salen) Ti complex maintained its structure on the MCM-41. The immobilized Ti salen complex is probably parallel aligned to the surface of the mesopores of MCM-41.

As can be seen in table 3, the optically active Co(II) complexes of unsymmetrical salen also catalyzed the reduction of aromatic ketones with sodium borohydride. The unsymmetrical salen Co(II) catalyst of **A**–**F** afforded a more improved level of enantioselectivity in the enantioselective borohydride reduction of aromatic ketones than the conventional symmetrical salen catalysts of **G** and **H**. The higher optical yield was obtained over the salen ligands synthesized from 1,2-diaminocyclohexane derivative. Introduction of a methoxy group into the unsymmetrical salen ligands resulted in a decrease in enantioselectivity. The Co(II) complexes of conventional salen ligand **I**, containing no bulky groups at the position *para* to the salen oxygens, showed a selective catalytic activity for the reduction of α-tetralone. The catalysts **G** and **H** having two *tert*-butyl groups resulted in a very low enantioselectivity. The presence of bulky groups to prevent substrate approach is also crucial to the enantioselectivity in the borohydride reduction of ketone. The catalysts having bulky groups near both salen oxygens resulted in a lower enantioselectivity. For this reaction, the modification of $NaBH_4$ with tetrahydrofurfuryl alcohol (THFA)–ethanol or THFA–methanol was applied to the reduction of acetophenones and tetralone, as reported by Nagata et al. [9]. It is noted that the proper selection of alcohol in the combination of THFA influenced the enantioselectivity (table 4). Higher optical purity of 66% e.e. was obtained when the mixed solution of THFA and ethanol was used in the reduction of α-tetralone. The conversion and the enantioselectivity were very low without

Table 3
Enantioselective borohydride reduction of ketones catalyzed by chiral salen Co(II) complexes:

aromatic ketone $\xrightarrow[\text{THFA+EtOH+NaBH}_4,\ \text{CHCl}_3]{\text{(S.S)-Co(II) catalyst}}$ (S)-alcohol

Entry[a]	Schiff base	Substrate	Conv. (%)	e.e.[b] (%)
1	**A**	Acetophenone	96	30 (S)
2	**A**	α-tetralone	95	65 (S)
3	**A**[c]	α-tetralone	97	67 (S)
4	**A**	2-methylacetophenone	50	48 (S)
5	**A**	4-methylacetophenone	53	37 (S)
6	**A**	Isobutylophenone	63	11
7	**B**	Acetophenone	95	15 (S)
8	**B**	α-tetralone	96	22 (S)
9	**C**	α-tetralone	95	46 (S)
10	**D**	α-tetralone	94	20 (S)
11	**E**	α-tetralone	97	58 (S)
12	**G**	Acetophenone	97	12 (R)
13	**G**	α-tetralone	96	16 (R)
14	**G**	2-methylacetophenone	41	12 (R)
15	**G**	4-methylacetophenone	44	10 (R)
16	**H**	Acetophenone	95	12 (S)
17	**H**	α-tetralone	93	17 (S)
18	**I**	Acetophenone	96	31 (S)
19	**I**	α-tetralone	94	60 (S)
20	**J**	Acetophenone	97	32 (S)
21	**J**	α-tetralone	98	46 (S)
22	**J**	4-methylacetophenone	66	30 (S)
23	**K**	Acetophenone	98	30 (S)
24	**K**	α-tetralone	97	42 (S)
25	**K**	2-methylacetophenone	68	26 (S)
26	**K**	4-methylacetophenone	74	24 (S)

[a] Reaction conditions: substrate 0.25 mmol, Co(II) catalyst 0.0375 mmol, $NaBH_4$ 0.75 mmol, EtOH 0.75 mol, THFA 5.15 mmol; $NaBH_4$, tetrahydrofurfuryl alcohol (THFA) and ethanol were stirred for 3 h at 0 °C in 5.0 ml $CHCl_3$ solvent before reaction. H_2 was released during the mixing. The catalyst and the substrate were added to this pre-modified borodydride solution at −20 °C, reaction time 3 h.

[b] The e.e.% values for respective reactions were determined by capillary GC using chiral columns (CHIRALDEX™, Gamma-cyclodextrin trifluoroacetyl, 40 m × 0.25 mm i.d. (Astec)).

[c] 20 mol% of catalyst, reaction time 3 h.

Table 4
The effect of alcohol addition in the enantioselective borohydride reduction of ketones catalyzed by chiral salen Co(II) complexes:

α-tetralone $\xrightarrow[\text{NaBH}_4,\ \text{alcohol},\ \text{CHCl}_3]{\text{(S.S)-Co(II) catalyst}}$ alcohol

Entry[a]	Schiff base	Alcohol	Conv. (%)	e.e. (%)
1	**A**	None	<10	5 (S)
2	**A**	EtOH	60	55 (S)
3	**A**	THFA	85	58 (S)
4	**A**	THFA + MeOH	99	66 (S)
5	**A**	THFA + EtOH	99	65 (S)

[a] Reaction conditions were the same as shown in table 3.

Table 5
Enantioselective hydrolysis of epoxides catalyzed by unsymmetrical chiral salen Co(III) complexes:

$$(\pm)\ \text{epoxide} + H_2O \xrightarrow{\text{(S,S)-Co(III) catalyst}} \text{(S)-epoxide} + \text{(R)-diol}$$

Entry[a]	Schiff base	Substrate	Product yield (%)	e.e. of oxide[b] (%)	e.e. of diol[c] (%)
1	**A**	Epichlorohydrin[d]	84	98 (S)	94 (R)
2	**C**	Epichlorohydrin	78	98 (S)	87 (R)
3	**G**	Epichlorohydrin	83	97 (R)	85 (S)
4	**J**	Epichlorohydrin	80	96 (S)	77 (R)
5	**A**	Styrene oxide[e]	75	98 (S)	98 (R)
6	**C**	Styrene oxide	72	98 (S)	97 (R)
7	**G**	Styrene oxide	76	97 (R)	95 (S)
8	**J**	Styrene oxide	78	95 (S)	83 (R)

[a] Reaction was carried out using 0.3 mol% of catalyst, H_2O/epoxide mole ratio of reactant = 0.55, reaction temperature 20 °C.
[b] The e.e.% values were determined by capillary GC using chiral columns (CHIRALDEX™, Gamma-cyclodextrin trifluoroacetyl, 40 m × 0.25 mm i.d. (Astec)).
[c] The e.e.% values were determined by both capillary GC and VCD analysis (BOMEM Chiral-iR).
[d] Reaction time 12 h.
[e] Reaction time 36 h.

addition of alcohol. The use of the ethanol–THFA combination resulted in an improvement of e.e.%.

Epichlorohydrine and styrene oxide of racemic form were hydrolysed over Co(III)-OAc type chiral salen catalysts at 20 °C without using a solvent. The results are summarized in table 5. By using (S,S)-form catalysts, R-epoxide in racemates was selectively catalysed to R-diol and as a result S-epoxide remained in the final product mixture. Epichlorohydrine and styrene oxide gave very high diol yields and e.e.% over the chiral Co(III) salen complex of **A**. Tokunaga et al. [8] have reported that a Co(III) salen complex of **G** type exhibited 85% e.e. in the hydrolysis of epichlorohydrine. Particularly higher enantioselectivity was obtained over the new unsymmetrical Co(III) salen catalyst of **A** type with 94 and 98% e.e. in the hydrolysis of epichlorohydrine and styrene oxide, respectively. The Co(III) salen complexes prepared from (+)-1,2-diaminocyclohexane were more efficient catalysts than those obtained from the (−)-1,2-diphenylethylenediamine derivative for the asymmetric hydrolysis reaction of epoxides.

In summary, new unsymmetrical chiral salen complexes could be synthesized and they could be applied as catalysts in the epoxidation of styrene, the asymmetric trimethylsilylcyanation of benzaldehyde, the asymmetric reduction of ketones and the hydrolysis of epoxides to diols as Mn(III), Ti(IV), Co(II) and Co(III) forms, respectively. For these reactions, new (salen) complexes showed characteristic activity and enantioselectivity. The unsymmetrical (salen) complexes showed comparatively high enantioselectivity as compared with conventional symmetrical salen complexes, which were prepared mainly from salicylaldehyde and 2-formyl-4,6-di-*tert*-butylphenol derivatives. The enantioselectivity was strongly dependent on the structure of the salen ligand. This work may broaden the application of salen complexes as new asymmetric catalysts.

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