Highly enantioselective epoxidation of unfunctionalized olefins catalyzed by a novel recyclable chiral poly-salen–Mn(III) complex

Yuming Song, Xiaoquan Yao, Huilin Chen, Guizhi Pan, Xinquan Hu and Zhuo Zheng*

Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, 116023, P. R. China

A new soluble recyclable poly-salen–Mn(III) complex has been synthesized and found to give high enantioselectivities (up to 97% ee) for the asymmetric epoxidation of unfunctionalized olefins.

Introduction

Great progress has been achieved in the area of asymmetric catalysis over the last decade. Salen–Mn(III) complex catalyzed asymmetric epoxidation of unfunctionalized olefins has proved to be a most useful reaction, and the most used Salen–Mn(III) complex (Jacobsen's catalyst, Fig. 1) exhibits excellent activities
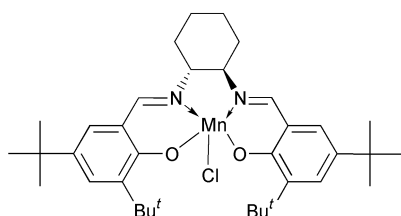

Fig. 1 Jacobsen's catalyst.

and enantioselectivities for libraries of substrates.[1] However, salen–Mn(III) complexes undergo decomposition under the reaction conditions and cannot be recovered and re-used, therefore many groups have directed their research to modifications of typical salen–Mn(III) complexes, such as polymer-supported systems;[2] non-covalent immobilization on zeolites, clays, or siloxane membranes;[3] grafted catalyst systems onto silica or MCM-41,[4] and FBS (fluorous biphase systems).[5] Although these modified catalysts showed very good separation features, their catalytic efficiencies seldom reached that of the original salen–Mn(III) complex. Recent work reported by Seebach's group, however makes a major contribution in this respect.[6]

In our previous work involving the enantioselective epoxidation of unfunctionalized olefins,[7] two soluble poly-salen–Mn(III) complexes derived from two substituted bis-salicyl-aldehydes and (*R,R*)-cyclohexane-1,2-diamine have been reported. Unlike the modified catalysts mentioned above, these two poly-salen–Mn(III) complexes can be regarded as polymers of "monomer" salen–Mn(III) catalyst, which, however, showed somewhat reduce enantioselectivities relative to Jacobsen's catalyst (90% ee for 6-cyano-2,2-dimethylchromene **10c**). However, both catalysts could be easily recovered and reused. Considering that Jacobsen's catalyst has two hindered *tert*-butyl groups at the 5,5′ positions, which are considered very important in introducing high ee during enantioselective epoxidation, while our earlier polymers have only –CH₂– or –CH₂–O–CH₂– groups at the same position, we sought to introduce two geminal methyl groups on the linking carbon atom, with the expectation of achieving the same enantio-selectivities as Jacobsen's catalyst.

Results and discussion

Synthesis of the polymer catalyst

The bisphenol **3** can be prepared in 50% yield by the condensation of 2-*tert*-butylphenol **2** and acetone catalyzed by H₂S–HCl at ambient temperature.[8] No ether linkage product was found in the condensation. The bis-salicylaldehyde **4** was readily prepared in 40% yield *via* a modified Duff reaction, and the corresponding polymeric ligand **5** with an average molecular weight up to 19893 (GPC, Mn) was synthesised through the condensation of **4** and (*R,R*)-cyclohexane-1,2-diamine *via* a modified procedure for synthesis of salen ligands.[9] The poly-salen–Mn(III) catalyst **1**, which is very soluble in dichloromethane, slightly soluble in ether and insoluble in hexane, was prepared according to the same procedure as our previous polymer catalysts[7] (Scheme 1).
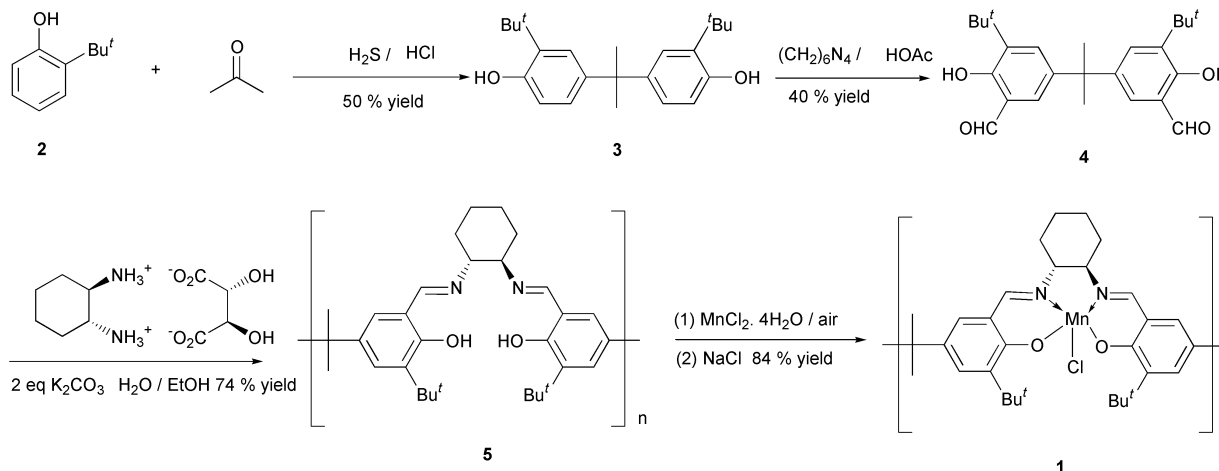
**Scheme 1** Synthetic route for the novel poly-salen–Mn(III) complex.

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Table 1 The poly-salen–Mn(III) complex catalysed enantioselective epoxidation with NaClO–4-PPNO[a] and MCPBA–NMO[b]

Entry	Substrate	Product	$T/°C$	Oxidant	t/h	Yield[c] (%)	Ee[d] (%)	Configuration[e]
1	**6**	**7**	0	NaClO–4-PPNO	2.5	86	37	*R*
2	**6**	**7**	−22	MCPBA–NMO	0.5	83	51	*R*
3	**6**	**7**	−78	MCPBA–NMO	1	ND[g]	36	*R*
4[f]	**8**	**9**	0	NaClO–4-PPNO	3	87	88	1*S*, 2*R*
5[f]	**8**	**9**	0	MCPBA–NMO	0.5	87	89	1*S*, 2*R*
6	**10a**	**11a**	0	NaClO–4-PPNO	2	81	96	3*R*, 4*R*
7	**10a**	**11a**	0	MCPBA–NMO	0.5	73	97	3*R*, 4*R*
8	**10b**	**11b**	0	NaClO–4-PPNO	5.5	90	95	ND[g]
9	**10b**	**11b**	0	MCPBA–NMO	0.5	92	97	ND[g]
10	**10c**	**11c**	0	NaClO–4-PPNO	6	96	96	3*R*, 4*R*
11	**10c**	**11c**	0	MCPBA–NMO	0.5	89	96	3*R*, 4*R*
12	**10d**	**11d**	0	NaClO–4-PPNO	4	86	94	3*R*, 4*R*
13	**10d**	**11d**	0	MCPBA–NMO	0.5	83	95	3*R*, 4*R*

[a] The reactions were carried out in 2 ml of CH_2Cl_2 with 1.0 mmol of olefin substrate. The mole ratio of substrate–NaClO–4-PPNO–catalytic unit was 1 : 2 : 0.2 : 0.04. TLC was used to detect the total conversion. [b] The reaction was carried out in 8 ml of CH_2Cl_2 with 1.0 mmol of olefin substrate. The mole ratio of substrate–MCPBA–NMO–catalytic unit was 1 : 2 : 5 : 0.04. TLC was used to detect the total conversion. [c] Isolated yield. [d] The ee's for the epoxides were determined by GC using a chiral capillary column (cyclodex-β,2,3,6-methylated, 30 m × 0.25 mm id; carrier, H_2 for 2,2-dimethylchromene oxides and N_2 for styrene oxide and (*Z*)-β-methylstyrene oxides). [e] Absolute configurations were compared with the literature.[10] [f] Overall yield of (*Z*)-β-methylstyrene oxides and the ee of *cis* products. [g] ND, not determined.

Poly-salen–Mn(III) complex 1 catalyzed epoxidation of unfunctionalized olefins

The epoxidation process was performed following typical Jacobsen's procedures using either NaClO–4-PPNO or MCPBA–NMO (Scheme 2).[10] The results are summarized in
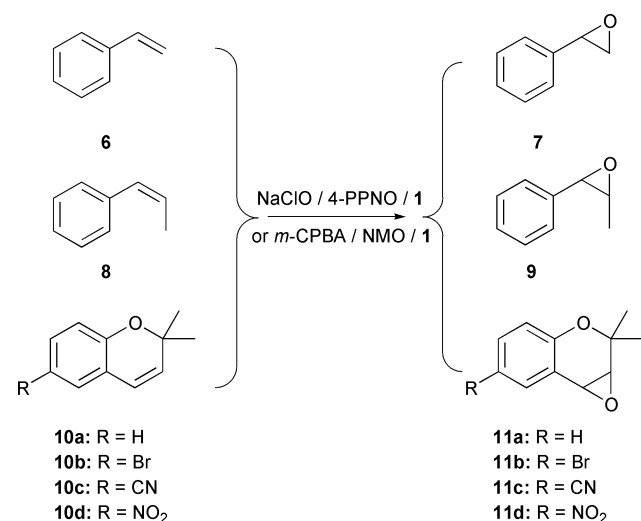
Scheme 2 Enantioselective epoxidation catalyzed by poly-salen–Mn(III) catalyst **1**.

Table 1. In the NaClO–4-PPNO system, the poly-salen–Mn(III) catalyst **1** exhibited excellent catalysis under typical conditions. Almost the same enantioselectivities were obtained as those using Jacobsen's catalyst for (*Z*)-β-methylstyrene **8** and substituted 2,2-dimethylchromenes **10** as epoxidation substrates (88–96% ee; for the typical Jacobsen's catalyst, 88–98% ee could be obtained). The catalyst could be recovered as an oil layer by precipitation from the reaction mixture with hexanes and used for the next reaction without further purification. In the MCPBA–NMO system, excellent ee's could also be obtained at 0 °C for (*Z*)-β-methylstyrene **8** and substituted 2,2-dimethylchromenes **10** as epoxidation substrates (89–97% ee). The best result for styrene oxide was obtained with 51% ee at −22 °C (entry 3, Table 1), which is much better than that from the NaClO–4-PPNO system (37% ee, entry 1, Table 1). However, obvious decomposition of the poly-salen–Mn(III) catalyst **1** in the MCPBA–NMO system was observed, the decomposed species from the catalyst being detected by TLC.[11] Lowering the reaction temperature to −78 °C to slow down the potential decomposition of the catalyst was helpful, but the catalyst

Table 2 Recycling enantioselective epoxidation of 2,2-dimethylchromene **10a** using NaClO–4-PPNO as the oxidant[a]

Entry	Cycle	t/h	Isolated yield (%)	Ee (%)[b]
1	Fresh	1.5	81	96
2	1	1.5	77	95
3	2	1.5	75	94
4	3	2	70	96
5	4	2	63	95

[a] The reactions were carried out in 8 ml of CH_2Cl_2 with 4.0 mmol of **10a**. The mole ratio of **10a**–NaClO–4-PPNO–catalytic unit was 1 : 2 : 0.2 : 0.04. The aqueous NaClO was added dropwise. After the total coversion (as detected with TLC), the aqueous layer and most of the solvent were removed. The catalyst was recovered by precipitation from the mixture using hexanes and drying *in vacuo*. [b] The ee's for the epoxides were determined by GC using a chiral capillary column (cyclodex-β,2,3,6-methylated, 30 m × 0.25 mm id; carrier, H_2).

showed much lower activity and enantioselectivity for styrene oxide under these conditions (entry 3, Table 1). It is possible that the linear polymer catalyst is in a rigid and contracted form at −78 °C. Indeed some direct evidence was that solid catalyst granules could be observed during the reaction. Therefore, it was impossible to re-use the poly-salen–Mn(III) catalyst **1** with the MCPBA–NMO system.

Recycling of the polymer catalyst 1

Re-use of the recovered poly-salen–Mn(III) catalyst **1** was performed with the NaClO–4-PPNO system employing 2,2-dimethylchromene (**10a**) as the substrate and the results of five cycling experiments are listed in Table 2. Despite the possible loss of catalyst during the recovery and re-use process, the cycling experiments were successfully carried out up to four times. It proved very important to add the pre-cooled aqueous NaClO dropwise, otherwise there was 2–4% drop in ee if aqueous NaClO was added in one portion. All reactions were complete within 2 hours. The data in Table 2 show that the recovered catalyst maintains its enantioselectivity but there is a small loss in the yield of the epoxide in each cycle, suggesting that some catalyst decomposed.

Conclusions

In conclusion, we have prepared a novel tertiary carbon-linked poly-salen–Mn(III) catalyst, which exhibits activities and enantioselectivities as good as the Jacobsen's homogeneous catalyst, and this catalyst can be easily recovered and reused several times without loss of enantioselectivity.

Experimental

General

Melting points were measured on a Yazawa micro melting point apparatus (uncorrected). Optical rotations were measured on a Horiba SEPA-200 highly sensitive polarimeter. $[a]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. The ^{1}H NMR spectra were recorded on a Bruker DRX 400 system with TMS as an internal standard. M_n and M_w/M_n were measured on a PL-GPC210 instrument. Enantiomeric excesses (%ee) were determined by GC (HP 4890 series) analysis.

Materials

2-*tert*-Butylphenol, MCPBA and 4-PPNO (4-phenylpyridine *N*-oxide) were obtained from Acros and (*Z*)-β-methylstyrene was obtained from TCI. Substituted 2,2-dimethylchromenes and (*R*,*R*)-cyclohexane-1,2-diyldiammonium mono-(+)-tartrate salt were prepared according to the reported method.[12] Other materials were laboratory grade species from local suppliers. All solvents were purified by standard procedures.

2,2′-Di-*tert*-butyl-4,4′-(propane-2,2-diyl)diphenol 3

Dry gaseous H$_2$S was bubbled through 77.4 g of **2** (0.52 mol) and 10.9 g of acetone (0.19 mol) in 100 ml petroleum ether at 20 °C until the mixture was saturated, after which gaseous HCl was continuously bubbled through for three days at 22–23 °C. The mixture was filtered, the isolated solid was washed with water (50 ml × 4) and petroleum ether (50 ml × 4) and dried *in vacuo* as a first portion of the product. The filtrate was washed with saturated aqueous NaHCO$_3$ (100 ml × 3) and brine (100 ml × 3), and dried over Na$_2$SO$_4$. After removal of the solvent from the filtrate, 2-*tert*-butylphenol was collected by vacuum distillation. The residue was recrystallized to afford a second portion of the product powder. A combined yield of 32 g of pure **3** was obtained. The yield was 50% based on acetone. Mp 114–116 °C; ^{1}H NMR (CDCl$_3$): δ 1.35 (s, 18H), 1.62 (s, 6H), 6.52 (d, *J* = 4.2 Hz, 2H), 6.91 (dd, J_1 = 2.7 Hz, J_2 = 8.2 Hz, 2H), 7.12 (d, *J* = 2.3 Hz, 2H); ^{13}C NMR δ 29.64, 31.19, 34.62, 42.09, 115.84, 125.02, 125.67, 134.97, 142.84, 151.70.

5,5′-Di-*tert*-butyl-6,6′-dihydroxy-3,3′-(propane-2,2-diyl)-dibenzaldehyde 4

34.0 g of **3** (0.10 mol), 56.0 g of hexamethylenetetramine (0.40 mol) and 100 ml of glacial acetic acid were placed in a 500 ml three-necked round-bottomed flask equipped with a mechanical stirrer. The mixture was heated slowly to 130 °C under Ar, during which it became turbid then viscous, with the subsequent formation of a large quantity of solid material. When **3** was completely consumed (as monitored by TLC), the mixture was cooled to 75 °C. 33% H$_2$SO$_4$ (100 ml) was then added; and the stirred mixture was heated to reflux for an hour and cooled to room temperature. EtOAc (100 ml) was added to dissolve the solid, the organic layer was separated and the aqueous layer was extracted with EtOAc (50 ml × 3). The organic layers were combined and washed with saturated aqueous NaHCO$_3$ until neutral. The organic layer was dried over anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure, and the residue was purified on a 100 g silica gel column, eluent ethyl acetate–petroleum ether (1 : 60). The crude product was recrystallized from EtOH to afford 16.0 g of the bis-salicylaldehyde **4** as yellow powder. The yield was 40%. Mp 120–122 °C. ^{1}H NMR (CDCl$_3$): δ 1.34 (s, 18H), 1.70 (s, 6H), 7.31 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 4H), 9.85 (s, 2H), 11.72 (s, 2H); ^{13}C NMR δ 29.17, 30.79, 34.91, 42.09, 119.90, 128.83, 133.43, 137.90, 140.57, 159.42, 197.16.

Polymer ligand

(*R*,*R*)-Cyclohexane-1,2-diammonium mono-(+)-tartrate salt (3.4 g, 12.9 mmol), 3.6 g of K$_2$CO$_3$ (26.0 mmol) and 200 ml

of EtOH–H$_2$O (5 : 1) were placed in a 500 ml three-necked round-bottomed flask equipped with a reflux condenser and an addition funnel. The mixture was stirred and heated to 80 °C under Ar, after which a solution of 5.0 g of **4** (12.6 mmol) in 100 ml of ethanol and 10 ml of CH$_2$Cl$_2$ was added dropwise over 45 min through the funnel, and the funnel was washed with 50 ml of ethanol. The resulting yellow suspension was refluxed for 6 h. Water (100 ml) was added to dilute the mixture, which was then cooled to room temperature. The solid was collected by suction filtration, the wet cake was carefully washed with 20 ml portions of ethanol until the filtrate was colorless. The solid was dissolved in 50 ml of CH$_2$Cl$_2$ and washed with brine (50 ml × 3). The organic layer was dried over anhydrous Na$_2$SO$_4$ and the solvent was removed under reduced pressure. The resulting yellow powder was washed with 50 ml portions of *n*-hexane until the hexane washings were colorless. The solid was dried *in vacuo* to afford 4.4 g of polymer ligand **4**. The yield was 74%. ^{1}H NMR (CDCl$_3$): δ 1.33 (s, 18H), 1.45 (s, 6H), 1.32–2.00 (m, 8H), 3.31 (m, 2H), 6.90 (d, *J* = 2.0 Hz, 2H), 7.60 (d, *J* = 2.0 Hz, 2H), 8.25 (s, 2H), 13.75 (s, 2H); ^{13}C NMR: δ 24.26, 29.55, 30.97, 33.28, 34.83, 41.63, 72.23, 117.80, 127.26, 128.43, 136.23, 139.41, 158.10, 165.66; $[a]_D^{25} = 156.34$ (*c* 1.014, CH$_2$Cl$_2$); GPC: $M_p = 134640$, $M_w = 122711$, $M_n = 19893$, $M_z = 429682$, $M_w/M_n = 6.169$.

Poly-salen–Mn(III) catalyst 1

MnCl$_2$·4H$_2$O (1.50 g, 7.58 mmol) and 20 ml of methanol were placed in a 100 ml three-necked round-bottomed flask equipped with a reflux condenser and an addition funnel. The mixture was heated to reflux until the solid was completely dissolved, after which a solution of 1.20 g of **5** (2.53 mmol) in 25 ml of toluene was added dropwise. When the addition was complete, air was bubbled through for 2 h, and the resulting black mixture was refluxed for further 4 h then cooled to room temperature. The solution was washed with 50 ml of brine and the organic layer was dried over anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure. The solid obtained was dissolved in 30 ml of CH$_2$Cl$_2$ and washed with brine (30 ml × 3), the organic layer was dried over anhydrous Na$_2$SO$_4$, the solvent was removed under reduced pressure, and the solid was dried *in vacuo* to afford 1.49 g of the polymer catalyst **1** as a black powder. The yield was 84%.

General procedures for enantioselective epoxidation [10]

Method A. A solution of 1.0 mmol of olefin in 2.0 ml of CH$_2$Cl$_2$, 0.0225 g of catalyst (0.04 mmol, based on single catalytic unit) and 0.0342 g of 4-PPNO (0.20 mmol) was cooled to 0 °C and stirred for 30 min. Pre-cooled buffered bleach (3.7 ml, 2.0 mmol, 0.55 M, pH = 11.3, 0 °C) was added to the solution and the mixture was stirred at 0 °C until total conversion of the substrate olefin was achieved, as monitored by TLC. The phases were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (2.0 ml × 3). The combined organic layers were washed with brine (2.0 ml × 3) and dried over anhydrous Na$_2$SO$_4$. The epoxide was separated by flash column chromatography.

Method B. A solution of 1.0 mmol of olefin, 0.0225 g of catalyst (0.04 mmol, based on single catalytic unit) and 0.675 g of NMO (*N*-methylmorpholine *N*-oxide) (5.0 mmol) in 8 ml CH$_2$Cl$_2$, was cooled to the appropriate temperature for 30 min, after which pre-cooled solid MCPBA (0.345 g, 2.0 mmol) was added in portions over 5 minutes. When the reaction was complete (as monitored by TLC), NaOH (10 ml, 1.0 M) was added, the phases were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (5.0 ml × 3). The combined organic layers were washed with brine (10 ml × 2) and dried over anhydrous Na$_2$SO$_4$. The pure product was obtained by flash column chromatography.

Modified Jacobsen's procedure for the recycling of 2,2-dimethylchromene

The procedure is similar to that described above except that **10a** (0.64 g, 4.0 mmol) is employed and pre-cooled buffered bleach (14.6 ml, 8.0 mmol, 0.55 M, pH = 11.3, 0 °C) was added dropwise. After removal of most of the solvent, hexane (25 ml) was added to the stirred mixture, and the hexane layer was decanted off. The residue was washed with hexane (5 ml × 3), and dried *in vacuo* to recover the catalyst. Further purification of the hexane layers afforded the olefin oxide.

Determination of enantiomeric excesses

The following are the retention times for racemic products. (a) Chiral capillary GC column: (Cyclodex-β,2,3,6-methylated, 15 m × 0.25 mm id), carrier = N_2, β-methylstyrene oxides, T = 110 °C, t_1 = 5.04 min, t_2 = 5.23 min, t_3 = 5.78 min, t_4 = 6.48 min. (b) Chiral capillary column (Cyclodex-β,2,3,6-methylated, 30 m × 0.25 mm id), carrier = N_2, styrene oxides, T = 100 °C, t_R = 16.25 min, t_S = 16.83 min. (c) Chiral capillary column (Cyclodex-β,2,3,6-methylated, 30 m × 0.25 mm id): carrier = H_2, 2,2-dimethylchromene oxides, T = 120 °C, t_{SS} = 13.63 min, t_{RR} = 14.61 min; 6-bromo-2,2-dimethylchromene oxides, T = 165 °C, t_1 = 9.87 min, t_2 = 10.28 min; 6-cyano-2,2-dimethylchromene oxides, T = 175 °C, t_{SS} = 13.39 min, t_{RR} = 13.99 min; 6-nitro-2,2-dimethylchromene oxides, T = 175 °C, t_{SS} = 21.16 min, t_{RR} = 22.18 min.

References

1 (a) E. N. Jacobsen, A. Pfaltz and H. Yamamoto, *Comprehensive Asymmetric Catalysis*, 2nd edn., Springer-Verlag, Berlin, Heidelberg, New York, 1999, pp. 649, 1367 and 1378; (b) T. Katsuki, in *Catalytic Asymmetric Synthesis*, ed. I. Ojima, VCH Publishers, New York, 2000, 2nd edn., p. 287.

2 (a) L. Canali, E. Cowan, H. Deleuze, C. L. Gibson and D. C. Sherrington, *Chem. Commun.*, 1998, 2561; (b) T. S. Reger and K. D. Janda, *J. Am. Chem. Soc.*, 2000, **122**, 6929; (c) C. E. Song, E. J. Roh, B. M. Yu, D. Y. Chi, S. C. Kim and K. J. Lee, *Chem. Commun.*, 2000, 615; (d) L. Canali, E. Cowan, H. Deleuze, G. L. Gibson and D. C. Sherrington, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2055.

3 (a) S. Ogunwumi and T. Bein, *Chem. Commun.*, 1997, 901; (b) K. B. M. Jannsen, I. Laquiere, W. Dehaen, R. F. Parton, I. F. J. Vankelecom and P. A. Jacobs, *Tetrahedron: Asymmetry*, 1997, **8**, 3481.

4 (a) M. J. Sabater, A. Corma, A. Domenech, V. Fornes and H. Garcia, *Chem. Commun.*, 1997, 1285; (b) D. Pini, A. Mandoli, S. Orlandi and P. Salvadori, *Tetrahedron: Asymmetry*, 1999, **10**, 3883; (c) G.-J. Kim and J.-H. Shin, *Tetrahedron Lett.*, 1999, **40**, 6827; (d) X.-G. Zhou, X.-Q. Yu, J.-S. Huang, S.-G. Li, I.-S. Li and C.-M. Che, *Chem. Commun.*, 1999, 1789; (e) P. Piaggo, C. Langham, P. McMorn, D. Bethell, P. C. Bulman-Page, F. E. Hancock, C. Sly and G. Hutchings, *J. Chem. Soc., Perkin Trans. 2*, 2000, 143; (f) P. Piaggo, P. McMorn, D. Murphy, D. Bethell, P. C. B. Page, F. I. Hancock, K. O. J. Sly and G. J. Hutchings, *J. Chem. Soc., Perkin Trans. 2*, 2000, 2008.

5 (a) G. Pozzi, F. Cinato, F. Montanari and S. Quici, *Chem. Commun.*, 1998, 877; (b) G. Pozzi, M. Cavazzini, F. Cinato, F. Montanari and S. Quici, *Eur. J. Org. Chem.*, 1999, 1947; (c) M. Cavazzini, A. Manfredi, F. Montanari, S. Quici and G. Pozzi, *Chem. Commun.*, 2000, 2171.

6 H. Sellner, J. K. Karjalainen and D. Seebach, *Chem. Eur. J.*, 2001, **7**, 2873.

7 X. Yao, H. Chen, W. Lü, G. Pan, X. Hu and Z. Zheng, *Tetrahadron Lett.*, 2000, **41**, 10267.

8 A. J. Dietzler, US Pat. 2917550/1959.

9 J. F. Larrow and E. N. Jacobsen, *J. Org. Chem.*, 1994, **59**, 1939.

10 (a) E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker and L. Deng, *J. Am. Chem. Soc.*, 1991, **113**, 7063; (b) M. Palucki, P. J. Pospisil, W. Zhang and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1994, **116**, 9333.

11 D. L. Hughes, G. B. Smith, J. Liu, G. C. Dezeny, C. H. Senanayake, R. D. Larsen, T. R. Verhoeven and P. J. Reider, *J. Org. Chem.*, 1997, **62**, 2222.

12 (a) G. Sartori, G. Casiraghi and L. Bolzoni, *J. Org. Chem.*, 1979, **44**, 803; (b) D. Bell, M. R. Davies, G. R. Geen and I. S. Mann, *Synthesis*, 1995, 707; (c) J. F. Larrow and E. N. Jacobsen, *Org. Synth.*, 1998, **75**, 1.