Enantioselective Cyanoformylation of Aldehydes Catalyzed with Solid Base Mediated Chiral V(V) Salen Complexes

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ABSTRACT Polymeric and monomeric V(V) chiral salen complexes-catalyzed enantioselective ethyl cyanoformylation of aldehydes using ethyl cyanoformate as a source of cyanide was accomplished in the presence of several basic cocatalysts viz., NaOH, KOH, basic Al_2O_3 and hydrotalcite. Excellent yield (>95%) of chiral ethyl cyanohydrincarbonate with high enantioselectivity up to 94% was achieved in 24–36 h when hydrotalcite was used as an additive. The polymeric catalyst **1** is more reactive than the monomeric catalyst **2** to produce chiral ethyl cyanohydrincarbonate in high optical purity. The chiral polymeric catalyst **1** and cocatalysts hydrotalcite and basic alumina used in this study were recoverable and recyclable several times with retention of its performance. *Chirality 22:153–158, 2010.* © 2009 Wiley-Liss, Inc.

KEY WORDS: cyanoformylation; V(V) salen complex; solid base; enantioselective; aldehydes

INTRODUCTION

Optically pure cyanohydrins play an important role in organic synthesis for the preparation of various versatile synthetic building blocks for pharmaceuticals, agrochemicals, insecticides,[1–7] and chiral auxiliaries.[8–13] Over the last two decades, attempts were made to achieve chirally pure cyanohydrins of aldehydes through chiral catalytic route[14–35] with different sources of cyanide viz., trimethylsilyl cyanide (TMSCN), hydrogen cyanide, and KCN. Among different catalysts used V(V) salen complex has revealed remarkable results in terms of enantio-induction for *O*-trimethylsilyl cyanohydrins with TMSCN[18–21] as a cyanide source. However, the product *O*-trimethylsilyl cyanohydrins are less stable and can readily undergo hydrolysis to give cyanohydrins that are prone to racemization. As a result, currently, other sources of cyanide such as acetyl cyanide, cyanoformate esters (ROCOCN), diethyl cyanophosphonate, and benzoyl cyanide have been explored to prepare optically pure cyanohydrins with different catalytic systems.[36–57] Belokon et al.,[40] has reported the ethyl cyanoformylation of aldehydes using Ti(IV) salen complex (5 mol %) as catalyst at -40°C giving the product in high yield with excellent enantiomeric excess (ee) in 6–48 h. Later, Moberg and coworkers[48] have significantly reduced the time (4–12 h) for this reaction in the presence of various Lewis bases as co-catalyst best among which was found to be triethylamine. Feng and coworkers[56] undertook cyanoethoxycarbonylation of aldehydes catalyzed by heterobimetallic aluminum lithium bis(binaphthoxide) and cinchonine to give the product in excellent yield (up to 99%) with moderate to high enantioselectivity (up to 95% ee) in short time. Feng et al. also reported the use of salen-Ti(O^iPr)$_4$ complex as catalyst in the enantioselective cyanoformylation of aldehydes in isopropanol:chloroform mixture as solvent at -20°C to give the products in excellent yields (up to 99%) and with high enantioselectivities (up to 91% ee). Recently, we have reported monomeric V(V) salen complex as a catalyst for the enantioselective cyanoformylation of aldehydes in the presence of imidazole as cocatalyst to give products in excellent yield (up to 97%) and enantioselectivity (up to 96% ee).[58] Among all the catalytic systems reported for cyanoformylation of aldehydes hitherto none had reported the recyclablity of the essentially expensive catalyst which is desirable from economic point of view. In view of our on going interest in asymmetric cyanation reaction as well as making the catalyst recyclable,[59–63] we present here the use of V(V) polymeric and monomeric salen complexes **1** and **2** as efficient catalysts for the enantioselective cyanation of aldehydes using ethylcyanoformate as a source of cyanide in combination with hydrotalcite as cocatalyst. Excellent yield (95%) and ee (94%) was achieved for the ethyl cyanocarbonate of 2-benzyloxybenzaldehyde with the added advantage of several times re-cyclablity of polymeric complex **1** with HT and alumina.

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EXPERIMENTAL

Materials and Methods

Vanadyl sulfate hydrate (Loba Chemie, India), Hydrotalcite $\{Mg_6Al_2(CO_3)(OH)_{16}{\cdot}4H_2O\}$, benzaldehyde, 4-methoxybenzaldehyde, 3-methoxybenzaldehyde, 2-methoxybenzaldehyde, 4-chlorobenzaldehyde, 4-bromobenzaldehyde, 4-fluorobenzaldehyde, crotonaldehyde, isovaraldehyde, hexanal, 3-methyle-2-butenal, 2-ethoxybenzaldehyde, 2-benzyloxybenzaldehyde, and ethylcyanoformate were purchased from Aldrich Chemicals and were used as received. 2-Methylbenzaldehyde, 3-methylbenzaldehyde, and 4-methylbenzaldehyde were from Merck chemicals where as basic Al_2O_3, NaOH, and KOH were from s. d. Fine-Chemicals Limited, Mumbai (India). All the solvents were distilled and dried by standard procedures[64] and stored under nitrogen. The synthesis and characterization of poly [(*R,R*)-*N,N′*-bis-{3-(1,1-dimethylethyl)-5-methylene salicylidene} cyclohexane-1,2-diamine] and its precursors was carried out as described in Ref. 65.

Instrumentation

Microanalysis of the complex was done on CHNS analyzer, Perkin Elmer model 2400. NMR spectra were obtained with a Bruker F113V spectrometer (500 MHz and 125 MHz for ^1H and ^{13}C, respectively) and are referenced internally with TMS. FTIR spectra were recorded on Perkin Elmer Spectrum GX spectrophotometer in KBr window. High-resolution mass spectra were obtained with a LC-MS (Q-TOF) LC (Waters), MS (Micromass) instruments. For the product purification, flash chromatography was performed using silica gel 100–200 mesh purchased from s. d. Fine-Chemicals Limited, Mumbai (India). The product formation and quantification was determined on capillary GC column SPB-5 (60 m) using Shimadzu 2010 with respect to internal standard (*n-tri*decane). Enantiomeric excess were determined by HPLC (Shimadzu SCL-10AVP) using Daicel Chiralpak OD and OD-H chiral columns with 2-propanol/hexane as eluent. HPLC traces were compared with racemic samples and GC analysis CHIRALDEX G-TA (30 m, 0.25 mm) column. Optical rotations were measured with a Digipol 781 Automatic Polarimeter, Rudolph Instrument.

Synthesis of Complex 1

The complex **1** was synthesized by the reported procedure.[59,60] The solution of poly[(*R,R*)-*N,N′*-bis-{3-(1,1-dimethylethyl)-5-methylene salicylidene} cyclohexane 1,2-diamine] (0.799 g, 1.79 mmol) was dissolved in mixed solvent ethanol:CH_2Cl_2 (3:2, 15 ml) to which an aqueous solution of vanadyl sulfate hydrate (0.453 g, 1.79 mmol in 2 ml water) was added drop-wise under an inert atmosphere at room temperature. The resulting solution was refluxed for 4 h and then cooled to room temperature with an extended stirring for 12 h while opening the side arm of the reaction flask for aerial oxidation. Solvent was completely evaporated and the residue was dissolved in CH_2Cl_2 (10 ml), washed with water (3 × 5 ml) and finally with brine. The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated to give dark green polymeric V(V) complex.

Synthesis of Complex 2

The complex **2** was synthesized by the reported procedure.[19] The solution of (1*R, 2R*)-*N,N′*-bis[3, 5-di(*tetr*-butyl)-salicyliden] cyclohexane-1, 2-diamine (2.7 mmol, 1.5 g) in THF (20 ml) and vanadyl sulfate hydrate (2.7 mmol, 0.69 g) in hot ethanol (30 ml) were mixed. The resulting solution were refluxed for 2 h under inert atmosphere and then cooled to room temperature with an extended stirring for 12 h while opening the side arm of the reaction flask. Solvent was completely evaporated and the residue was dissolved in CH_2Cl_2 (15 ml), washed with water (3 × 5 ml) and finally with brine. The organic layer was dried over anhydrous Na_2SO_4, the complex was purified by column chromatography as a dark green solid.

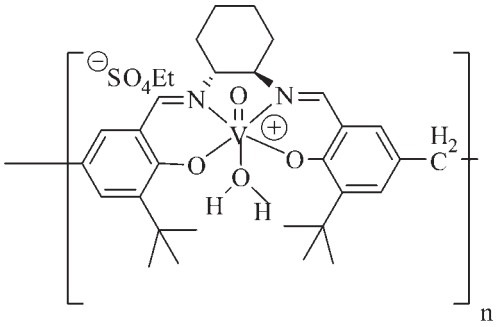
Typical Experimental Procedure for the Enantioselective Cyanoformylation of Aldehydes

A solution of V(V) salen complexes **1/2** (0.015 mmol) and appropriate aldehyde (0.62 mmol) in dry CH_2Cl_2 (0.8 ml) was stirred for 10 min at room temperature under N_2 atmosphere. To this solution, hydrotalcite/basic alumina (25 mg) was added and the solution was cooled to 15°C. To this cooled solution, ethyl cyanoformate (77 μl, 0.78 mmol) was added drop-wise over a period of 5 min. The reaction was monitored on TLC. After completion of the reaction, the product was purified by flash column chromatography on a silica gel column (eluent, hexane/ethyl acetate = 90:10). The purified products were characterized by ^1H and ^{13}C NMR which were in agreement with the reported values (see supporting information).[42–57]

RESULTS AND DISCUSSION

Chiral vanadium salen complexes **1** and **2** were synthesized by the reaction of poly[(*R,R*)-*N,N′*-bis-{3-(1,1-dimethylethyl)-5-methylene salicylidene} cyclohexane 1,2-diamine]/(1*R, 2R*)-*N,N′-bis*[3, 5-di(*tert*-butyl)salicylidene] cyclohexane-1, 2-diamine with vanadyl sulfate hydrate followed by auto-oxidation by the reported method (see Fig. 1).[19,59,60] Earlier, we[58] and others[46,48,49] have reported that the presence of a cocatalyst greatly influence the chiral metal complexes catalyzed enantioselective addition of ethylcyanoformate to aldehydes. The cocatalysts used so far for this reaction are essentially organic bases and are non-recoverable after the catalytic run is over. We explored here the use of solid base like hydrotalcite and alumina as recoverable cocatalysts. Simultaneously we also used polymeric V(V) salen complex as an active and recoverable catalyst for the ethylcyanoformylation of aldehydes.

Feasibility of the enantioselective cyanoformylation reaction using benzaldehyde as a model substrate with polymeric V(V) salen complex **1** (2.5 mol %) as catalyst and various inorganic bases as cocatalyst at 0–25°C was systematically studied and the data are presented in Figure 2 and Table 1. Both hydrotalcite and basic alumina were effective cocatalysts; however, former was better (Table 1, Entries 1 and 2). The use of NaOH and KOH (Table 1, Entries 3 and 4) as cocatalyst hasten the reaction (8–9 h) but the reaction took racemic pathway (ee, 3–20%), due to the fact that alkali alone (Entry 5) is an active achiral catalyst for this reaction.



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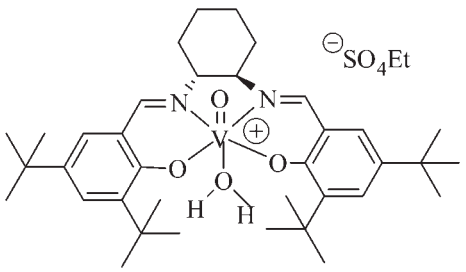

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Fig. 1. Structure of complexes **1** and **2**.

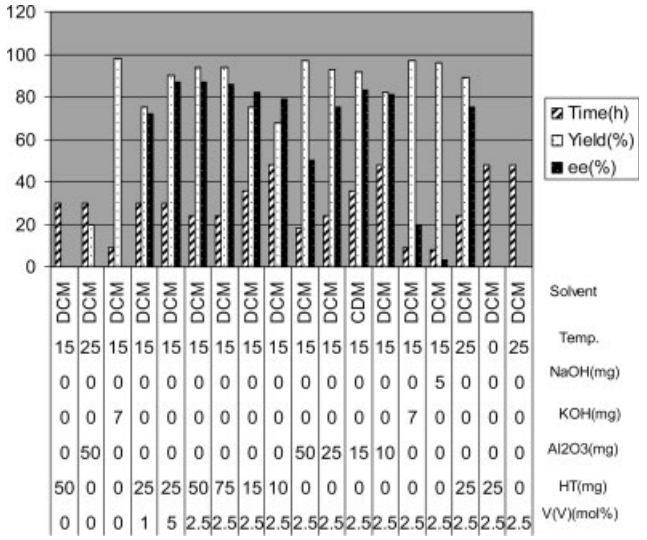


Fig. 2. Optimized reaction condition.

In the absence of any cocatalyst, the catalyst **1** failed to catalyze this reaction (Entry 8). Investigation of reaction parameters viz., catalyst and hydrotalcite loading, and temperature suggest that catalyst **1** loading 2.5 mol % and 25 mg of hydrotalcite at 15°C is optimum for this reaction.

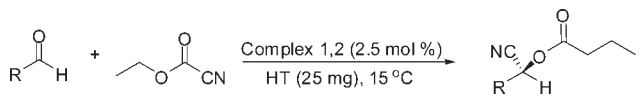
Under the optimized reaction conditions as described earlier (Table 1, Entry 1), we extended this protocol of ethyl cyanoformylation reaction to a variety of aromatic and aliphatic aldehydes using the complex **1** as catalyst. The data in Table 2 is an indicative of applicability of this protocol over a range of substrates where good to excellent isolated yield (88–95%) and ee (75–94%) for the products were achieved in 21–30 h (Entries 1–24). Surprisingly, electronic and steric factors for different substituents on the aromatic

TABLE 1. Optimization of reaction condition for the enantioselective addition of ethyl cyanoformate to benzaldehyde in presence of polymeric V(V) salen complex 1[a]

Entry	Catalyst (mol %)	Cocatalyst	Time (h)	Temp. (°C)	Yield (%)[b]	ee (%)[c]
1	2.5	HT (25 mg)	24	15	94	88
2	2.5	Al_2O_3 (25 mg)	24	15	93	75
3	2.5	NaOH (5 mg)	8	15	96	03
4	2.5	KOH (7 mg)	9	15	97	20
5	–	KOH (7 mg)	9	15	98	Racemic
6	–	Al_2O_3 (50 mg)	30	25	20	–
7	–	HT (50 mg)	30	15	Trace	–
8	2.5	–	48	25	–	–
9	5	HT (25 mg)	30	15	90	87
10	1	HT (25 mg)	30	15	75	72
11	2.5	HT (50 mg)	24	15	94	87
12	2.5	HT (75 mg)	24	15	94	86
13	2.5	HT (15 mg)	36	15	75	82
14	2.5	HT (10 mg)	48	15	68	79
15	2.5	Al_2O_3 (50 mg)	18	15	97	50
16	2.5	Al_2O_3 (15 mg)	36	15	92	83
17	2.5	Al_2O_3 (10 mg)	48	15	82	81
18	2.5	HT (25 mg)	24	25	89	75
19	2.5	HT (25 mg)	48	0	Trace	–

[a]All reaction carried out at 0–25°C using catalyst **1** (indicated amount), benzaldehyde (0.62 mmol), ethyl cyanoformate (1.24 mmol), and cocatalyst (indicted amount) in dry DCM (0.8 ml).
[b]Isolated yield.
[c]ee was determined using chiracel OD column.

TABLE 2. Enantioselective addition of ethyl cyanoformate to various aldehydes using V(V) salen complex 1and 2 with HT as a cocatalyst[a]



Entry	Substrate	Time (h)	Yield (%)[b]	ee (%)[c]
1 (2)[d]	Benzaldehyde	24 (30)	94 (93)	88 (87)
3 (4)	2-Methylbenzaldehyde	30 (36)	91 (90)	81 (80)
5 (6)	3-Methylbenzaldehyde	24 (36)	93 (91)	83 (81)
7 (8)	4-Methylbenzaldehyde	24 (28)	91 (89)	80 (78)
9 (10)	2-Methoxybenzaldehyde	24 (36)	92 (89)	91 (90)
11 (12)	3-Methoxybenzaldehyde	24 (36)	89 (87)	84 (82)
13 (14)	4-Methoxybenzaldehyde	24 (36)	90 (89)	83 (79)
15 (16)	2-Ethoxy benzaldehyde	24 (36)	90 (87)	84 (81)
17 (18)	2-Benzyloxybenzaldehyde	24 (30)	92 (91)	94 (92)
19 (20)	4-Fluorobenzaldehyde	24 (24)	95 (93)	90 (88)
21 (22)	4-Chlorobenzaldehyde	24 (30)	88 (89)	75 (71)
23 (24)	4-Bromobenzaldehyde	24 (30)	89 (90)	85 (86)
25 (26)	Hexanal	21 (30)	93 (91)	81 (80)
27 (28)	3-Methyl-2-butenealdehyde	24 (36)	91 (89)	83 (82)
29 (30)	Crotonaldehyde	24 (36)	88 (87)	77 (75)
31 (32)	Isovaraldehyde	21 (30)	90 (92)	86 (85)

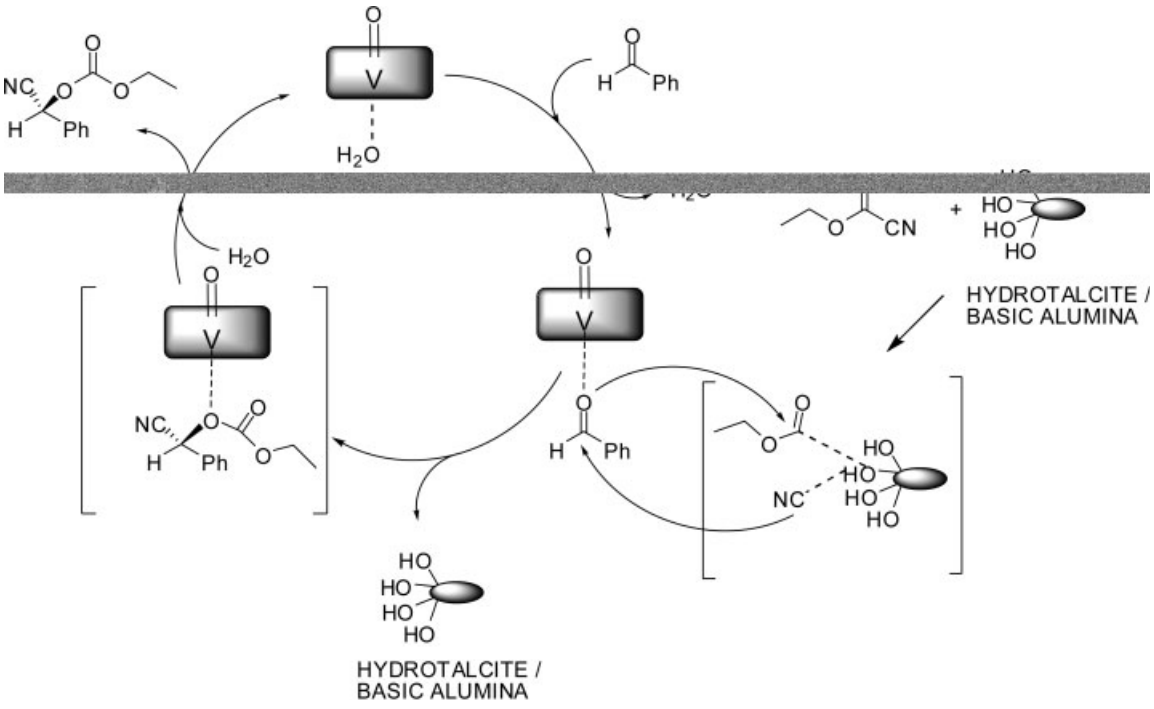
[a]All reaction carried out at 15°C using catalyst 1 and 2 (2.5 mol %), aldehyde (0.62 mmol), ethyl cyanoformate (1.24 mmol), and HT (25 mg) in dry DCM (0.8 ml).
[b]Isolated yield.
[c]ee determined by chiral HPLC and GC.
[d]The data in parentheses given for complex **2.**

TABLE 3. Data for the enantioselective addition of ethyl cyanoformate to benzaldehyde using recycle polymeric V(V) salen complex 1 with recycle HT and basic Al_2O_3 as a cocatalyst

Run	1	2	3	4
Time (h)	24	28	30	30
Yield (%)[a]	94 (93)[b]	92 (90)	92 (91)	89 (88)
ee (%)[c]	88 (75)	88 (72)	87 (74)	86 (71)

[a]Isolated Yield.
[b]The data in the parenthesis given for basic Al_2O_3 as a cocatalyst.
[c]The ee was determined by using chiralpak HPLC OD column.

substrate did not have noticeable effect on the yield and selectivity of the products. Similarly, aliphatic substrates were also ethyl cyanoformylated with similar yield and enantioselectivity (Table 2, Entries 25–31). We also extended this cyanoformylation protocol to these substrates using monomeric V(V) salen complex **2** as catalyst which showed comparable yields and enantioselectivities. However, the reaction took longer time when compared with the use of polymeric V(V) salen complex **1** as catalyst (Table 2, Entries 2, 4, 6, 8, 10, 12, 14, 16, 18, 22, 24, 26, 28, 30, 32). Moreover, in the case of monomeric complex **2**, the catalyst was not recoverable though the hydrotalcite was recovered and recycled at the end of the catalytic run, whereas in the case of polymeric catalyst both catalyst and hydrotalcite were recoverable and recyclable. The enhanced reactivity in the case of polymeric complex as against monomeric complex may be attributed to the



Scheme 1. Probable mechanism of cyanoethylation of aldehydes.

increase reactive sites which may be working in co-operation.[59,60,63] In all the catalytic runs, the (*R*)- form of V(V) salen complexes **1** and **2** as catalysts resulted in to (*S*) enantiomer of the product ethyl cyanohydrincarbonates.

To assess the recyclability of the polymeric complex **1**, the catalytic runs for the ethyl cyanoformylation of benzaldehyde was taken as representative test run using hydrotalcite/basic alumina as cocatalysts under the reaction condition mentioned in Entries 1 and 2 (Table 1). Consequently, after the first catalytic runs excess amount of hexane was added to each reaction mixture and the resulting solids were collected by filtration. The recovered solids were thoroughly washed with hexane and vacuum dried before reuse. The recovered solids containing both the catalyst **1** and the cocatalysts hydrotalcite/basic alumina were used as such in the manner same as fresh catalyst in the ethyl cyanoformylation of benzaldehyde which showed similar activity and enantioselectivity in the recycle experiments (Table 3, Runs 2–4) though there was some increase in reaction time. The recyclability of this catalytic system has clear edge over previously reported polymeric V(V) salen complexes.[17,59,60]

Mechanism

On the basis of the product distribution, a probable mechanism of cyanoformylation of aldehydes is proposed (Scheme 1). In view of high chiral induction in the product, it would be appropriate to consider that the substrate is activated by the way of its interaction with the acidic metal site of the chiral complex. Concomitantly, the solid base activates the source of cyanide. In a concerted manner, then nucleophilic attack of CN took place while the ethylformyl group moves to the aldehydic oxygen to produce the desired product in high chiral purity.[58]

CONCLUSION

In conclusion, a highly efficient enantioselective ethyl cyanoformylation of various aromatic and aliphatic aldehydes was carried out by using V(V) chiral polymeric and monomeric salen complexes **1** and **2**, respectively, as catalysts with ethyl cyanoformate as a source of cyanide in the presence of several cocatalysts. Excellent yield (95%) and enantioselectivity up to 94% for the product ethyl cyanohydrincarbonate was achieved when hydrotalcite was used as cocatalyst. The chiral polymeric catalyst **1** and solid base used as cocatalysts were recyclable several times with retention of their performances.

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LITERATURE CITED

1. Kusumoto T, Hanamoto T, Hiyama T, Takehera S, Shoji T, Osawa M, Kuriyama T, Nakamura K, Fujisawa T. Optically active *O*-acyl cyanohydrines chiral dopants for ferroelectric liquid crystals. Chem Lett 1990;19:1615–1618.
2. Thierry RJA, Lisa AC, Michael N. Asymmetric catalysis of carbon-carbon bond-forming reactions using metal(salen) complexes. Synlett 2005;12:1828–1847.
3. Kanai M, Kato N, Ichikawa E, Shibasaki M. Power of cooperativity: Lewis acid-Lewis base bifunctional asymmetric catalysis. Synlett 2005;125:1491–1508.
4. Chen FX, Feng XM. Synthesis of racemic tertiary cyanohydrins. Synlett 2005;125:892–899.
5. Brunel JM, Holmes IP. Chemically catalyzed asymmetric cyanohydrin syntheses. Angew Chem Int Ed 2004;43:2752–2778.
6. North M. Synthesis and applications of non-racemic cyanohydrins. Tetrahedron: Asymmetry 2003;14:147–176.
7. Gregory RJH. Cyanohydrins in nature and the laboratory: biology, preparations, and synthetic applications. Chem Rev 1999;99:3649–3682.
8. North M. In: Murahashi SI, editor. Science of synthesis introduction of the cyano group by addition to a carbonyl group, Vol. 19. Stuttgart: Thieme; 2004. p 235–284.
9. Shibasaki M, Kanai M, Funabashi K. Recent progress in asymmetric two-center catalysis. J Chem Soc Chem Commun 2002;1989–1999.
10. Smith MB, March J. March's advanced organic chemistry, 5th ed. New York: Wiley; 2001. p 1239–1240.
11. Ojima I. Catalytic asymmetric synthesis. New York: Wiley; 2000. p 235–284.
12. Mori A, Inoue S. Cyanation of carbonyl and amino groups. In: Jacobsen EN, Pfaltz A, Yamamoto H, editors. Comprehensive asymmetric synthesis. Heidelberg: Springer-Verlag; 1999. p 983–992.
13. Effenberger F. Synthesis and reactions of optically active cyanohydrins. Angew Chem 1994;106:1609–1619; Angew Chem Int Ed Engl 1994;33:1555–1564.
14. Belokon YN, Gutnov AV, Moskalenko MA, Yashkina LV, Lesovoy DE, Ikonnikov NS, Larichev VS, North M. Catalytic asymmetric synthesis of *O*-acetyl cyanohydrins from KCN, Ac_2O and aldehydes. Chem Commun 2002;244–245.
15. Belokon YN, Cepas SC, Green B, Ikonnikov NS, Khrustalev VN, Larichev VS, Moscalenko MA, North M, Orizu C, Tararov VI, Tasinazzo M, Timofeeva GI, Yashkina LV. The asymmetric addition of trimethylsilyl cyanide to aldehydes catalyzed by chiral (salen)titanium complexes. J Am Chem Soc 1999;121:3968–3973.
16. Belokon YN, Maleev VI, North M, Usanov DL. VO(salen)(X) catalysed asymmetric cyanohydrin synthesis: an unexpected influence of the nature of anion X on the catalytic activity. Chem Commun 2006;4614–4616.
17. Huang W, Song Y, Wang J, Cao G, Zheng Z. Polymeric salen-Ti(IV) or V(V) complex catalyzed asymmetric synthesis of *O*-acetylcyanohydrins from KCN, Ac_2O and Aldehydes. Tetrahedron 2004;60:10469–10477.
18. Belokon YN, North M, Maleev VI, Voskoboev NV, Moskalenko MA, Peregudov AS, Dmitriev AV, Ikonnikov NS, Kagan HB. In situ formation of a heterobimetallic chiral [(salen)TiIV]/[(salen)VV] catalyst for the asymmetric addition of TMSCN to benzaldehyde. Angew Chem Int Ed 2004;43:4085–4089.
19. Belokon YN, Carta P, Gutnov AV, Maleeev V, Moskalenko MA, Yashkina LV, Ikonnikov NS, Voskoboev NV, Khrustalev VN, North M. Catalytic asymmetric synthesis of *O*-acetylcyanohydrins from potassium cyanide, acetic anhydride, and aldehydes, promoted by chiral salen complexes of titanium(IV) and vanadium(V). Helevetica Chim Acta 2002;85:3301–3312.
20. Belokon YN, North M, Parsons T. Vanadium-catalyzed asymmetric cyanohydrin synthesis. Org Lett 2000;2:1617–1619.
21. Belokon YN, Green B, Ikonnikov NS, North M, Parsons T, Taravov VI. Optimized catalysts for the asymmetric addition of trimethylsilyl cyanide to aldehydes and ketones. Tetrahedron 2001;57:771–779.
22. Xiong Y, Huang X, Gou SH, Huang JL, Wen YH, Feng XM. Enantioselective cyanosilylation of ketones catalyzed by a nitrogen-containing bifunctional catalyst. Adv Synth Catal 2006;348:538–544.
23. Liu XH, Qin B, Zhou X, He B, Feng XM. Catalytic asymmetric cyanosilylation of ketones by a chiral amino acid salt. J Am Chem Soc 2005;127:12224–12225.

24. Ryu HD, Corey EJ. Enantioselective cyanosilylation of ketones catalyzed by a chiral oxazaborolidinium ion. J Am Chem Soc 2005;127:5384–5387.
25. Fuerst DE, Jacobsen EN. Thiourea-catalyzed enantioselective cyanosilylation of ketones. J Am Chem Soc 2005;127:8964–8965.
26. Wen YH, Huang X, Hang JL, Xiong Y, Qin B, Feng XM. Asymmetric cyanosilylation of aldehydes catalyzed by novel organocatalysts. Synlett 2005;125:2445–2447.
27. Qin YC, Liu L, Pu L. On-step synthesis of a bifunctional BINOL ligand for the highly enantioselective cyanation of aliphatic aldehydes. Org Lett 2005;7:2381–2383.
28. Li Y, He B, Qin B, Feng XM, Zhang GL. Highly enantioselective cyanosilylation of aldehydes catalyzed by novel β-amino alcohol-titanium complexes. J Org Chem 2004;69:7910–7913.
29. Tian SK, Hong R, Deng L. Catalytic asymmetric cyanosilylation of ketones with chiral Lewis base. J Am Chem Soc 2003;125:9900–9901.
30. Griengl H, Hickel A, Johnson DV, Kratky C, Schmidt M, Schwab H. Enzymatic cleavage and formation of cyanohydrins: a reaction of biological and synthetic relevance. J Chem Soc Chem Commun 1997; 1933–1940.
31. Schmidt M, Griengl H. Oxynitrilases: from cyanogenesis to asymmetric synthesis. Top Curr Chem 1999;200:193–226.
32. Seoane G. Enzymatic C-C bond-forming reactions in organic synthesis. Curr Org Chem 2000;4:283–304.
33. Kim SS, Lee SH, Kwak JM. Enantioselective cyanosilylation of ketones catalyzed by Mn(salen)/Ph_3PO. Tetrahedron: Asymmetry 2006;17:1165–1169.
34. Kim SS, Kwak JM. Asymmetric addition of trimethylsilyl cyanide to ketones catalyzed by Al(salen)/triphenylphosphine oxide. 2006;62:49–53.
35. Kim SS, Song DH. Asymmetric cyanohydrin synthesis catalyzed by Al(salen)/triphenylphosphane oxide. Eur J Org Chem 2005;1777–1780.
36. Yamagiwa N, Tian J, Matsunaga S, Shibasaki M. Catalytic asymmetric cyano-ethoxycarbonylation reaction of aldehydes using a YLi_3Tris(binaphthoxide) (YLB) complex: mechanism and roles of achiral additives. J Am Chem Soc 2005;127:3413–3422.
37. Tian J, Yamagiwa N, Matsunaga S, Shibasaki M. Efficient two-step conversion of α,β-unsaturated aldehydes to optically active γ-Oxy-α,β-unsaturated nitriles and its application to the total synthesis of (+)-patulolide C. Org Lett 2003;5:3021–3024.
38. Tian J, Yamagiwa N, Matsunaga S, Shibasaki M. An asymmetric cyanation reaction and sequential asymmetric cyanation-nitroaldol reaction using a [YLi3{tris(binaphthoxide)}] single catalyst component: catalyst tuning with achiral additives. Angew Chem Int Ed 2002;41:3636–3638.
39. Belokon YN, Blacker AJ, Clutterbuck LA, North M. Synthetic and mechanistic studies on asymmetric cyanohydrin synthesis using a titanium(salen) bimetallic catalyst. Tetrahedron 2004;60:10433–10447.
40. Belokon YN, Blacker AJ, Clutterbuck LA, North M. Catalytic, asymmetric synthesis of cyanohydrin ethyl carbonates. Org Lett 2003;5: 4505–4508.
41. Belokon YN, Ishibashi E, Nomura H, North M. Cyanide ion cocatalysis in Ti(salen) catalysed asymmetric cyanohydrin carbonate synthesis. Chem Commun 2006;1775–1777.
42. Belokon YN, Clegg W, Harrington RW, Young C, North M, Asymmetric cyanohydrin synthesis using heterobimetallic catalysts obtained from titanium and vanadium complexes of chiral and achiral salen ligands. Tetrahedron 2007;63:5287–5299.
43. Belokon YN, Clegg W, Harrington RW, Ishibashi E, Nomura H, North M. Enantioselective and diastereoselective syntheses of cyanohydrin carbonates. Tetrahedron 2007;63:9724–9740.
44. Tian SK, Deng L. A highly enantioselective chiral Lewis base-catalyzed asymmetric cyanation of ketones. J Am Chem Soc 2001; 123:6195–6196.
45. Li H, Song J, Liu X, Deng L. Catalytic enantioselective C-C bond forming conjugate additions with vinyl sulfones. J Am Chem Soc 2005;127:8948–8949.
46. Tian SK, Deng L. Enantioselective cyanocarbonation of ketones with chiral base. Tetrahedron 2006;62:11320–11330.
47. Tian SK, Chen Y, Hang J, Tang L, MaDaid P, Deng L. Asymmetric organic catalysis with modified cinchona alkaloids. Acc Chem Res 2004;37:621–631.
48. Lundgren S, Wingstrand E, Penhoat M, Moberg C. Dual Lewis acid-Lewis base activation in enantioselective cyanation of aldehydes using acetyl cyanide and cyanoformate as cyanide sources. J Am Chem Soc 2005;127:11592–11593.
49. Lundgren S, Wingstrand E, Moberg C. Lewis acid-Lewis base-catalysed enantioselective addition of α-ketonitriles to aldehydes. Adv Synth Catal 2007;349:364–372.
50. Baeza A, Casas J, Nájera C, Sansano J, Saá JM. Enantioselective synthesis of *O*-methoxycarbonyl cyanohydrins: chiral building blocks generated by bifunctional catalysis with BINOLAM-AlCl. Eur J Org Chem 2006;8:1949–1958.
51. Baeza A, Nájera C, Sansano J, Saá JM. Asymmetric synthesis of *O*-benzoyl cyanohydrins by reaction of aldehydes with benzoyl cyanide catalysed by BINOLAM-Ti(IV) complexes. Tetrahedron: Asymmetry 2005;16:2385–2389.
52. Casas J, Baeza A, Sansano JM, Nájera C, Saa JM. Enantioselective cyanoformylation of aldehydes mediated by BINOLAM-AlCl as a monometallic bifunctional catalyst. Tetrahedron: Asymmetry 2003;14:197–200.
53. Baeza A, Casas J, Nájera C, Sansano J, Saa JM. Enantioselective synthesis of cyanohydrin *O*-phosphates mediated by the bifunctional catalyst binolam-AlCl. Angew Chem Int Ed 2003;42:3143–3146.
54. Li Q, Chang L, Liu X, Feng X. Catalytic asymmetric cyano-ethoxycarbonylation reaction of aldehydes using a novel C_2-symmetric chiral *N*,*N*′-dioxide. Synlett 2006;11:1675–1678.
55. Gou S, Chen XH, Xiong Y, Feng X. Highly enantioselective cyanation of aldehydes catalyzed by a multicomponent titanium complex. J Org Chem 2006;71:5732–5736.
56. Chen SK, Peng D, Zhou H, Wang LW, Chen FX, Feng X. Highly enantioselective cyanoformylation of aldehydes catalyzed by a mononuclear salen-Ti(OiPr)4 complex produced in situ. Eur J Org Chem 2007;4:639–644.
57. Gou S, Wang J, Liu X, Wang W, Fu-Xue C, Feng X. Asymmetric cyanoethoxycarbonylation of aldehydes catalyzed by heterobimetallic aluminum lithium bis(binaphthoxide) and cinchonine. Adv Synth Catal 2007;349:343–349.
58. Khan NH, Agrawal S, Kureshy RI, Abdi SHR, Prathap KJ, Jasra RV. Vanadium(V) salen complex catalyzed highly enantioselective cyanoformylation of aldehydes in the presence of imidazole as a cocatalyst. Eur J Org Chem 2008;26:4511–4515.
59. Khan NH, Agrawal S, Kureshy RI, Abdi SHR, Mayani VJ, Jasra RV. Asymmetric addition of trimethylsilyl cyanide to aldehydes promoted by chiral polymeric vanadium (V) salen complex as an efficient and recyclable catalyst. Tetrahedron: Asymmetry 2006;17:2659–2666.
60. Khan NH, Agrawal S, Kureshy RI, Abdi SHR, Mayani VJ, Jasra RV. Easily recyclable polymeric V(V) salen complex for the enantioselective *O*-acetyl cyanation of aldehydes. J Mol Catal A: Chem 2007;264:140–145.
61. Khan NH, Agrawal S, Kureshy RI, Abdi SHR, Mayani VJ, Jasra RV. Asymmetric synthesis of *O*-acetylcyanohydrins by reaction of aldehydes with NaCN/KCN catalyzed by recyclable chiral dimerictitanium(IV)/vanadium(V) salen complexes. Eur J Org Chem 2006;14:3175–3180.
62. Khan NH, Kureshy RI, Abdi SHR, Agrawal S, Jasra RV. Metal catalyzed asymmetric cyanation reactions. Coord Chem Rev 2008;252: 593–623.
63. Khan NH, Agrawal S, Kureshy RI, Abdi SHR, Prathap KJ, Jasra RV. Enantioselective cyanosilylation of ketones catalyzed by recyclable polymeric and dimeric Mn(III) salen complexes at room temperature. Chirality 2009;21:262–270.
64. Perrin DD, Armarego WLF, Perrin DR. Purification of laboratory chemicals, 2nd ed. New York: Pergamon Press; 1981.
65. Kureshy RI, Khan NH, Abdi SHR, Singh S, Ahmad I, Jasra RV. Catalytic asymmetric epoxidation of non-functionalised alkenes using polymeric Mn(III) salen as catalysts and NaOCl as oxidant. J Mol Catal 2004;218:141–146.