Tetrahedron: *Asymmetry* 23 (2012) 1218–1225

Contents lists available at SciVerse ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Asymmetric cyanohydrin synthesis using an aluminium(salan) complex

Michael North *, Emma L. Stewart, Carl Young

School of Chemistry and University Research Centre in Catalysis and Intensified Processing, Newcastle University, Bedson Building, Newcastle upon Tyne, NE1 7RU England, UK

ARTICLE INFO

Article history:
Received 26 July 2012
Accepted 27 July 2012

ABSTRACT

The asymmetric addition of trimethylsilyl cyanide to aldehydes catalysed by chiral metal(salan) complexes has been investigated. Salan complexes of titanium and vanadium displayed only low catalytic activity, but a bimetallic aluminium(salan) complex gave high levels of catalytic activity and reasonable asymmetric induction when used with triphenylphosphine oxide as a cocatalyst. Mechanistic studies showed that the reactions were first order in catalyst and aldehyde concentrations, but zero order in trimethylsilyl cyanide and triphenylphosphine oxide concentrations. A Hammett analysis indicated that there was no significant change in the electron density at the aldehyde benzylic position during the rate determining step of the catalytic cycle. On the basis of the kinetic data, a catalytic cycle is proposed which accounts for the differences observed between $[Al(salen)]_2O$ and $[Al(salan)]_2O$ based catalysts.

1. Introduction

Over the last 15 years there have been enormous advances in the development of catalysts for asymmetric cyanohydrin synthesis.[1] Oxynitrilases have been cloned and over-expressed, thus facilitating the enzymatic addition of hydrogen cyanide to aldehydes[2] and numerous purely organic[3] or metal-based catalysts[4] for the asymmetric addition of trimethylsilyl cyanide (and other cyanide sources) to aldehydes and ketones have been developed. Prominent amongst the latter class of catalysts are salen complexes of metals including titanium,[5] vanadium,[6] lithium,[7] manganese[8] and aluminium.[9] Mechanistic studies on the titanium, vanadium and aluminium(salen) based catalysts indicated that they were catalytically active as bimetallic complexes[10] (Fig. 1) and that for vanadium and aluminium based catalysts, Lewis base as well as Lewis acid catalysis was important to the catalytic activity.[11] On the basis of the bimetallic nature of the catalyst, the groups of Ding[12] and Sun[13] prepared titanium(salen) complexes in which the two salen ligands were covalently linked together and Khan et al. prepared a macrocycle containing two vanadium(salen) units.[14] Complex **1** developed by Ding[12] is the most active catalyst yet discovered for the asymmetric addition of trimethylsilyl cyanide to aldehydes, with a catalyst loading as low as 0.0005 mol % being sufficient to catalyse the reaction in some cases. A key feature of the transition state shown in Figure 1 is that to allow intramolecular cyanide transfer, the salen ligand has to adopt a non-planar, chiral, *cis*-β configuration. It is well known that salen ligands are capable of adopting a *cis*-β configuration, though the planar configuration is generally energetically more favourable.[10c,15]

The reduced forms of salen ligands referred to as salan **2** and salalen **3** (Fig. 2) are more flexible than a salen ligand and are more prone to forming complexes with a *cis*-β configuration.[16] The *cis*-β configuration leaves the other two coordination sites *cis*—to one another, which is ideal for reaction between coordinated reactants in either a monometallic complex or within a μ–oxo bridged dimer as shown in Figure 1. As a result, there has recently been significant interest in using metal(salan) and metal(salalen) complexes as asymmetric catalysts. Thus, monometallic iron(salan)[17] and bimetallic titanium(salan),[18] titanium(salalen)[19] and niobium(salan)[20] complexes have all been used as catalysts for asymmetric epoxidations; VO(salan) complexes,[21] monometallic iron(salan)[22] or aluminium(salalen)[23] and bimetallic titanium(salan)[24] and iron(salan)[25] complexes have been used to catalyse asymmetric sulphide oxidation; bimetallic iron(salan) complexes have been used to catalyse asymmetric naphthol couplings;[26] a molybdenum(salan) complex has been used to catalyse asymmetric pinacol couplings;[27] copper(salan) complexes catalyse asymmetric Henry reactions;[28] an aluminium(salalen) complex catalyses the asymmetric hydrophosphonylation of aldehydes[29] and imines;[30] aluminium(salalen) complexes also catalyse asymmetric cyclopropanations[31] and heterobimetallic nickel(salan)–lanthanum complexes[32] have been used to catalyse asymmetric Michael additions. In addition, aluminium(salan)[33] and aluminium(salalen)[34] complexes as well as titanium, zirconium and hafnium(salalen) complexes[35] have been used as initiators for stereocontrolled lactide polymerisation; titanium(salan),[36] zirconium(salan)[36,37] and titanium(salalen)[38] complexes initiate the stereocontrolled polymerisation of alkenes and chromium(salan) complexes initiate the stereocontrolled copolymerisation of epoxides and carbon dioxide.[39]

There has only been limited work on the use of metal(salan) or metal(salalen) complexes in asymmetric cyanohydrin synthesis.

* Corresponding author. Tel.: +44 191 222 7128; fax: +44 191 222 6929.
E-mail address: Michael.north@ncl.ac.uk (M. North).

0957-4166/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetasy.2012.07.011

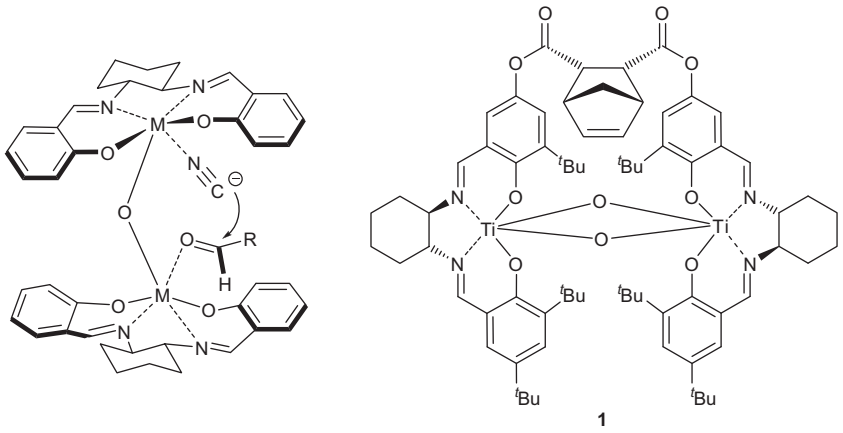


Figure 1. Bimetallic transition state for asymmetric cyanohydrin synthesis and bimetallic complex **1**.

Thus, Katsuki showed that VO(salalen) complexes would catalyse the asymmetric transfer of cyanide from acetone cyanohydrin to aliphatic aldehydes[40] and Sun showed that titanium(salan) complexes would catalyse the asymmetric addition of trimethylsilyl cyanide to aldehydes.[41]

2. Results and discussion

In view of the high levels of catalytic activity and asymmetric induction obtained during our previous work on $[Ti(salen)O]_2$ **4** catalysed asymmetric cyanohydrin synthesis,[10,11,42] we initially aimed to prepare the corresponding $[Ti(salan)O]_2$ complex **5** (Fig. 3). However, all attempts to isolate pure complex **5** using titanium tetraisopropoxide or titanium tetrachloride as the titanium source were unsuccessful. Therefore, salan ligand **6**[43] was treated with titanium tetraisopropoxide followed by water and then the solvent was removed to leave a titanium(salan) complex which was used without purification (Scheme 1). This yellow powder was then used to catalyse the asymmetric addition of trimethyl-

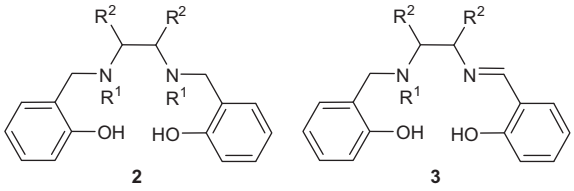
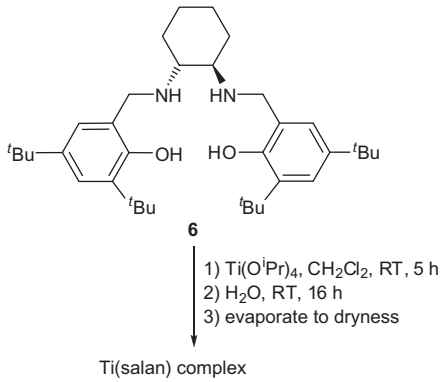
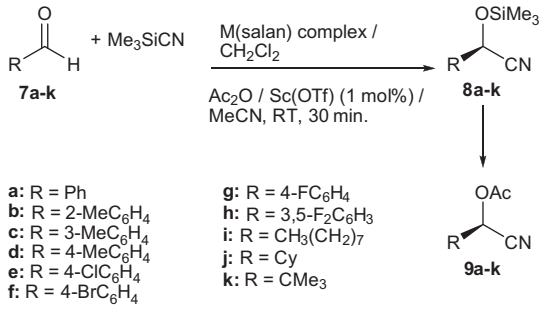


Figure 2. General structures of salan **2** and salalen **3** ligands.



Scheme 1. Synthesis of a Ti(salan) complex.



Scheme 2. Metal(salan) catalysed asymmetric cyanohydrin synthesis.

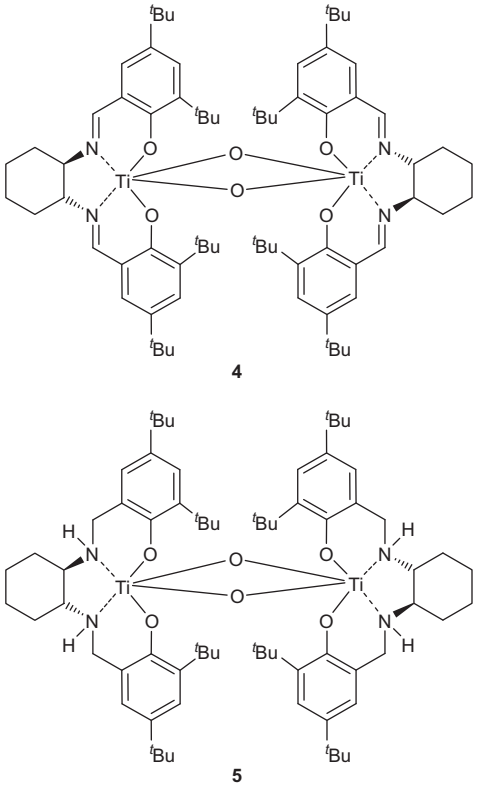


Figure 3. Bimetallic Ti(salen) and Ti(salan) complexes.

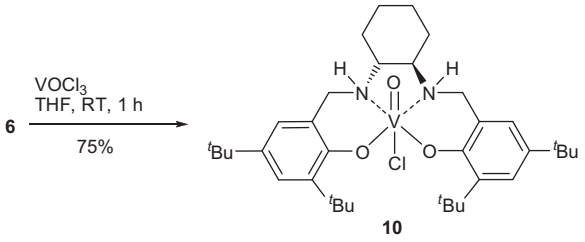
Table 1
Synthesis of cyanohydrin trimethylsilyl ether **8a** using a Ti(salan) complex

Entry	Catalyst (mol %)	T (°C)	t (h)	Conv. (%)	ee
1	0.1	22	24	60	10 (*R*)
2	0.1	22	240	60	9 (*R*)
3	1	22	24	75	23 (*R*)
4	1	0	24	45	31 (*R*)
5	1	−40	24	25	39 (*R*)
6	5	22	24	100	13 (*R*)
7	5	0	24	95	23 (*R*)
8	5	−40	24	43	30 (*R*)

silyl cyanide to benzaldehyde **7a** to give cyanohydrin trimethylsilyl ether **8a** (Scheme 2). To determine the enantiomeric excess of compound **8a** it was converted into the corresponding cyanohydrin acetate[44] **9a** and analysed by chiral GC. The results of this study are presented in Table 1. Under the standard conditions used for asymmetric cyanohydrin synthesis catalysed by titanium(salen) complex **4**, the titanium(salan) complex gave a moderate conversion of benzaldehyde into mandelonitrile trimethylsilyl ether, but with very low asymmetric induction (entry 1). Entry 2 shows that increasing the reaction time to 10 days changed neither the conversion nor the asymmetric induction, suggesting that the catalyst was already deactivated within the first 24 h. Increasing the catalyst loading to 1 mol % increased both the conversion and asymmetric induction (entry 3) and the latter could be further increased to a maximum of 39% by reducing the reaction temperature (entries 4 and 5). Further increasing the catalyst loading to 5 mol % resulted in higher conversions, but reduced asymmetric induction (entries 6–8) suggesting that 1 mol % is the optimal amount of catalyst.

One notable feature of the results in Table 1 is that the Ti(salan) complex derived from (*R,R*)-salan ligand **6** always gave predominantly the (*R*)-enantiomer of cyanohydrin trimethylsilyl ether **8a**, whilst complex **4** (which is derived from the corresponding (*R,R*)-salen ligand) always gave predominantly (*S*)-cyanohydrin trimethylsilyl ethers.[10,11,42]

In view of the low levels of asymmetric induction and the inability to isolate a pure, characterisable titanium(salan) catalyst, it was decided to investigate the use of vanadium(salan) complexes instead since excellent levels of asymmetric induction had previously been obtained in asymmetric cyanohydrin synthesis using VO(salen)X complexes.[6] Therefore, VO(salan)Cl complex **10** was prepared as a dark green solid by treatment of salan ligand **6** with $VOCl_3$ (Scheme 3). Complex **10** was then used to convert benzaldehyde **7a** into cyanohydrin trimethylsilyl ether **8a** as shown in Scheme 2 with the results being shown in Table 2.



Scheme 3. Synthesis of VO(salan)Cl **10**.

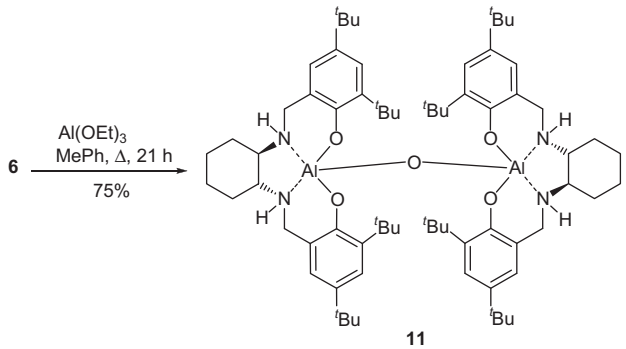
An initial experiment carried out using 0.1 mol % of catalyst **10** at room temperature was not promising, giving cyanohydrin trimethylsilyl ether **8a** with moderate conversion and low enantioselectivity after a reaction time of 24 h (Table 2, entry 1). Increasing the catalyst loading to 1 mol % was beneficial to both the conversion and enantioselectivity (entry 2). Lowering the temperature to 0 °C had no effect on the yield or conversion (entry 3), but further increasing the catalyst loading to 5 mol % did result in good conversion and improved asymmetric induction (entry 4). Further lowering the reaction temperature to −20 °C had a detrimental effect on both conversion and asymmetric induction, even when the catalyst loading was increased to 10 mol % (entries 5 and 6).

Table 2
Synthesis of cyanohydrin trimethylsilyl ethers using VO(salan)Cl complex **10**

Entry	Aldehyde	**10** (mol %)	T (°C)	t (h)	Conv. (%)	ee
1	**7a**	0.1	22	24	44	9 (*R*)
2	**7a**	1	22	24	70	45 (*R*)
3	**7a**	1	0	24	67	43 (*R*)
4	**7a**	5	0	24	92	60 (*R*)
5	**7a**	5	−20	24	38	50 (*R*)
6	**7a**	10	−20	24	10	47 (*R*)
7	**7b**	5	0	24	18	45 (*R*)
8	**7c**	5	0	24	17	55 (*R*)
9	**7d**	5	0	24	15	43 (*R*)
10	**7e**	5	0	24	33	20 (*R*)
11	**7f**	5	0	24	63	35 (*R*)

The conditions of Table 2 entry 4 were then taken as optimal and applied to aromatic aldehydes **7b–f** (Table 2, entries 7–11). Unfortunately, electron rich aromatic aldehydes **7b–d** all gave very low conversions and only moderate asymmetric induction under these conditions and electron deficient aromatic aldehydes **7e–f** gave only low levels of asymmetric induction. Again, it was notable that complex **10** always gave predominantly the (*R*)-enantiomer of cyanohydrin trimethylsilyl ethers **8a–f**, whilst the corresponding VO(salen)Cl complex derived from the (*R,R*)-salen ligand always gave predominantly (*S*)-cyanohydrin trimethylsilyl ethers.[6] Although the results obtained using isolable VO(salen)Cl catalyst **10** were a significant improvement on those of the Ti(salan) catalyst, they still lacked generality and the asymmetric induction was moderate at best. Therefore, our attention turned to an aluminium(salan) derived catalyst system in which the Lewis basicity of a cocatalyst was expected to be able to influence the catalytic activity and asymmetric induction.[9,11]

Bimetallic aluminium(salan) complex **11** was prepared by treating ligand **6** with aluminium triethoxide in refluxing toluene (Scheme 4) and obtained as a pale yellow solid. Table 3 shows the results of optimisation experiments for the synthesis of cyanohydrin trimethylsilyl ether **8a** using catalyst **11**. Entries 1–4 show that when used in the absence of a Lewis base cocatalyst, complex **11** is a competent catalyst, but gives at best 55% asymmetric induction (entry 4), again with the (*R*)-enantiomer of cyanohydrin trimethylsilyl ether predominating in contrast to the results obtained with the corresponding aluminium(salen) complex **12** derived from the (*R,R*)-salen ligand.[9,11]



Scheme 4. Synthesis of $[Al(salan)]_2O$ **11**.

Triphenylphosphine oxide has previously been shown to be an effective Lewis basic cocatalyst when used with $[Al(salen)]_2O$ **12** and is known to activate trimethylsilyl cyanide through the forma-

Table 3
Synthesis of cyanohydrin trimethylsilyl ether **8a** using [Al(salan)]$_2$O complex **11**[a]

Entry	**11** (mol %)	Ph_3PO (mol %)	T (°C)	Solvent	Conv. (%)	ee
1	0.1	0	22	CH_2Cl_2	45	35 (*R*)
2	1	0	22	CH_2Cl_2	90	53 (*R*)
3	1	0	0	CH_2Cl_2	85	47 (*R*)
4	5	0	0	CH_2Cl_2	95	55 (*R*)
5	0.1	1	22	CH_2Cl_2	65	38 (*R*)
6	0.1	5	22	CH_2Cl_2	89	67 (*R*)
7	0.1	10	22	CH_2Cl_2	96	77 (*R*)
8	0.1	20	22	CH_2Cl_2	99	70 (*R*)
9	0.3	1	22	CH_2Cl_2	72	49 (*R*)
10	0.3	5	22	CH_2Cl_2	100	72 (*R*)
11	0.3	10	22	CH_2Cl_2	100	74 (*R*)
12	0.3	20	22	CH_2Cl_2	100	70 (*R*)
13	1	1	22	CH_2Cl_2	89	57 (*R*)
14	1	2	22	CH_2Cl_2	100	61 (*R*)
15	1	4	22	CH_2Cl_2	100	63 (*R*)
16	1	5	22	CH_2Cl_2	100	65 (*R*)
17	1	6	22	CH_2Cl_2	100	65 (*R*)
18	1	8	22	CH_2Cl_2	100	69 (*R*)
19	1	10	22	CH_2Cl_2	100	71 (*R*)
20	1	20	22	CH_2Cl_2	100	78 (*R*)
21	1	30	22	CH_2Cl_2	100	75 (*R*)
22	1	40	22	CH_2Cl_2	100	74 (*R*)
23	1	60	22	CH_2Cl_2	100	75 (*R*)
24	1	10	0	CH_2Cl_2	92	75 (*R*)
25	1	10	−10	CH_2Cl_2	44	71 (*R*)
26	1	10	−20	CH_2Cl_2	25	67 (*R*)
27	1	20	0	CH_2Cl_2	100	72(*R*)
28	1	20	−10	CH_2Cl_2	67	75 (*R*)
29	1	20	−30	CH_2Cl_2	10	25 (*R*)
30	1	20	22	MePh	100	77 (*R*)
31	1	20	0	MePh	100	75 (*R*)
32	1	20	22	MeCN	94	67 (*R*)
33	1	20	22	THF	18	48 (*R*)

[a] All reactions carried out for 24 h.

tion of adduct **13** (Fig. 4).[45] Therefore, the use of triphenylphosphine oxide as a cocatalyst in reactions catalysed by complex **11** was investigated. As shown by entries 5–8 of Table 3, addition of triphenylphosphine oxide to reactions catalysed by just 0.1 mol % of aluminium(salan) complex **11** had a very beneficial effect on both the conversion and asymmetric induction. The optimal results were obtained when 10 mol % of triphenylphosphine oxide was added (entry 7), giving cyanohydrin trimethylsilyl ether **8a** in 96% yield and with 77% enantiomeric excess. When the amount of complex **11** used was increased to 0.3 mol %, a similar influence of triphenylphosphine oxide was seen (Table 3, entries 9–12). In this case, complete conversion of benzaldehyde **7a** into cyanohydrin trimethylsilyl ether **8a** could be obtained (entries 10–12) and the maximum level of asymmetric induction was again obtained using 10 mol % triphenylphosphine oxide (entry 11), though this was slightly reduced compared to the use of 0.1 mol % of complex **11** (compare entries 7 and 11).

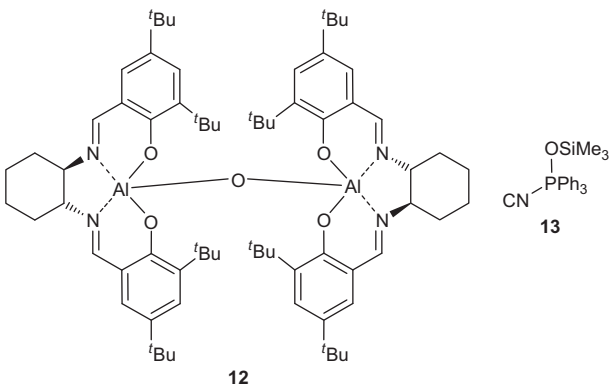


Figure 4. Structure of compounds **12** and **13**.

A more detailed analysis of the effect of triphenylphosphine oxide was carried out using 1 mol % of catalyst **11** (Table 3, entries 13–23). Increasing the concentration of triphenylphosphine oxide steadily increases the asymmetric induction and in this case the maximum asymmetric induction is reached using 20 mol % of triphenylphosphine oxide (entry 20), with higher concentrations of triphenylphosphine oxide resulting in a slight decrease in asymmetric induction. Lowering the reaction temperature from 22 to 0 °C when using 1 mol % of complex **11** and 10 mol % of triphenylphosphine oxide resulted in a slight increase in the enantioselectivity of the reaction, but a decrease in the conversion after 24 h (Table 3, entry 24). However, further lowering of the reaction temperature had a detrimental effect on the level of asymmetric induction and a very detrimental impact on the conversion (entries 25 and 26). A similar effect was seen in reactions using 1 mol % of complex **11** and 20 mol % of triphenylphosphine oxide (entries 27–29).

Finally, the effect of changing the solvent was investigated. Use of toluene (Table 3, entry 30) gave almost identical results to the use of dichloromethane (entry 20), but was less convenient and reducing the reaction temperature again failed to result in an increase in the asymmetric induction (entry 31). Acetonitrile gave slightly lower conversions and enantioselectivity than either dichloromethane or toluene (entry 32) and THF gave a very low conversion and only moderate asymmetric induction (entry 33). Thus, the optimal conditions were determined to be those of Table 3, entry 20 which gave complete conversion of **7a** into **8a** with 78% asymmetric induction.

The results in Table 3 can be explained by the interplay of three effects:

- Catalyst **11** will catalyse the addition of trimethylsilyl cyanide to aldehyde **7a** in the absence of triphenylphosphine oxide (entries 1–4).
- Addition of triphenylphosphine oxide results in only a modest rate enhancement (compare entries 1 and 6), but a significant increase in enantioselectivity.
- Triphenylphosphine oxide is known to be a poor catalyst on its own for the racemic addition of trimethylsilyl cyanide to aldehydes,[46] but will show some activity at higher concentrations.

Thus, a high concentration of triphenylphosphine oxide relative to complex **11** is needed to ensure that the catalysis occurs through the more enantioselective combined Lewis acid/Lewis base catalysed route, but if the concentration of triphenylphosphine oxide is too high then it will start to act as a racemic Lewis base catalyst. The lack of increase of asymmetric induction on lowering the reaction temperature (entries 24–29) could be due to a decrease in the rate of formation of adduct **13**, thus decreasing the relative importance of the more enantioselective Lewis acid/Lewis base catalysed reaction.

The optimal conditions were then applied to ten other aldehydes (**7b–k**), giving the results shown in Table 4. In every case, complete conversion of aldehyde into cyanohydrin trimethylsilyl ether was observed under these reaction conditions. Electron rich aromatic aldehydes **7b–d** all gave enantioselectivities of 62–68% (entries 2–4), as did 4-fluorobenzaldehyde **7g** (entry 7). Mildly electron deficient aromatic aldehydes **7e**,**f** gave just slightly lower enantioselectivities (57–60%, entries 5 and 6), but very electron deficient 3,5-difluorobenzaldehyde gave a much lower enantioselectivity (entry 8). Primary and secondary aliphatic aldehydes gave enantioselectivities of 61–62% (entries 9 and 10), but pivaldehyde gave a lower enantioselectivity (52%, entry 11).

Table 4
Synthesis of cyanohydrin trimethylsilyl ethers using $[Al(salan)]_2O$ complex **11** and Ph_3PO[a]

Entry	Aldehyde (RCHO)	Conv. (%)	ee
1	**7a** (R = Ph)	100	78 (*R*)
2	**7b** (R = 2-MeC_6H_4)	100	62 (*R*)
3	**7c** (R = 3-MeC_6H_4)	100	65 (*R*)
4	**7d** (R = 4-MeC_6H_4)	100	68 (*R*)
5	**7e** (R = 4-ClC_6H_4)	100	60 (*R*)
6	**7f** (R = 4-BrC_6H_4)	100	57 (*R*)
7	**7g** (R = 4-FC_6H_4)	100	66 (*R*)
8	**7h** (R = 3,5$F_2C_6H_3$)	100	32 (*R*)
9	**7i** (R = $Me(CH_2)_8$)	100	61 (*R*)
10	**7j** (R = cyclohexyl)	100	62 (*R*)
11	**7k** (R = CMe_3)	100	52 (*R*)

[a] All reactions carried out at 22 °C for 24 h using 1 mol % of complex **11** and 20 mol % of Ph_3PO.

To further investigate the reaction mechanism, a kinetic study of the asymmetric addition of trimethylsilyl cyanide to benzaldehyde **7a** was undertaken. These reactions were all carried out at 0 °C using concentrations of all reagents comparable to those used for the synthetic work (Table 3, entry 27) and the reactions were monitored by spectrophotometric analysis of samples removed from the reaction mixture as we have previously reported.[10] An initial kinetic experiment under the conditions of Table 3, entry 27 showed that the reaction obeyed overall first order kinetics (Fig. 5). By varying the initial concentrations of benzaldehyde or trimethylsilyl cyanide whilst keeping the concentration of all other reaction components constant, it was then possible to show that the reactions were first order in benzaldehyde concentration and zero order in trimethylsilyl cyanide concentration (Fig. 6). Thus, the reaction was found to obey the rate equation:

$$\text{Rate} = k_{obs}[\text{PhCHO}] \text{ where } k_{obs} = k[11]^a[Ph_3PO]^b$$

This contrasts markedly with the kinetics previously determined for reactions catalysed by aluminium(salen) complex **12**,[9f,10f] which also obeyed first order kinetics, but for which the rate equation was found to be:

$$\text{Rate} = k_{obs}[Me_3SiCN]$$

To determine the orders with respect to complex **11** and triphenylphosphine oxide concentrations, reactions were carried out at different concentrations of these catalysts whilst keeping the initial concentrations of all other reaction components constant. The results shown in Figure 7 show that the reaction is first order in complex **11** concentration and zero order in triphenylphosphine concentration. Thus, the full rate equation is:

$$\text{Rate} = k[\mathbf{11}].[\text{PhCHO}]$$

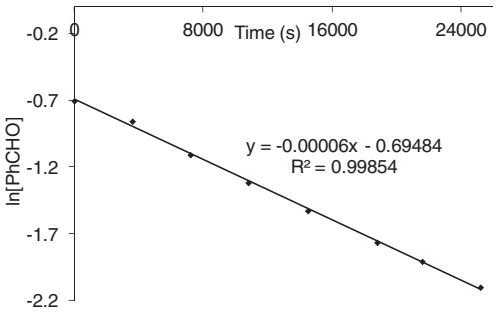


Figure 5. First order kinetics plot for the addition of Me_3SiCN to PhCHO at 0 °C catalysed by complex **11** and Ph_3PO in CH_2Cl_2. $[PhCHO]_0$ = 0.49 M, $[Me_3SiCN]_0$ = 0.56 M, [**11**] = 9.8 mM, $[Ph_3PO]$ = 0.1 M.

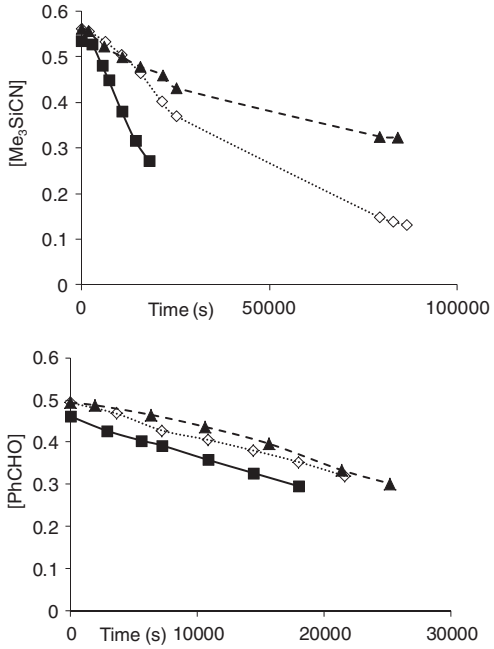


Figure 6. Kinetic plots for the addition of Me_3SiCN to PhCHO at 0 °C catalysed by complex **11** in CH_2Cl_2. Unless specified otherwise, the initial concentrations used were $[PhCHO]_0$ = 0.49 M, $[Me_3SiCN]_0$ = 0.56 M, [**11**] = 4.9 mM and $[Ph_3PO]$ = 0.1 M. Top: variation of $[PhCHO]_0$; filled squares with solid line $[PhCHO]_0$ = 0.98 M, empty diamonds with dotted line $[PhCHO]_0$ = 0.49 M, filled triangles with dashed line $[PhCHO]_0$ = 0.25 M. Bottom: variation of $[Me_3SiCN]_0$; filled squares with solid line $[Me_3SiCN]_0$ = 1.12 M, empty diamonds with dotted line $[Me_3SiCN]_0$ = 0.56 M, filled triangles with dashed line $[Me_3SiCN]_0$ = 0.28 M.

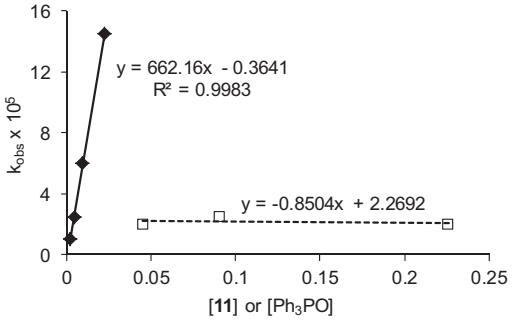
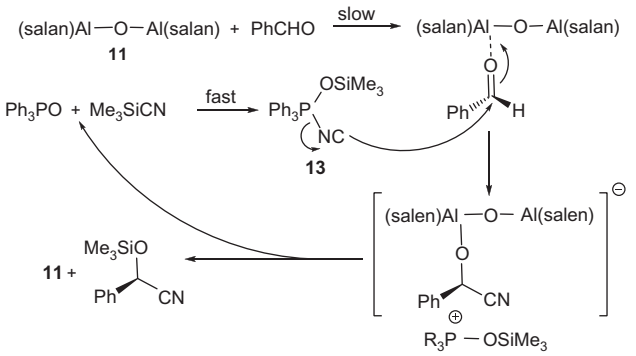


Figure 7. Plot of [**11**] or $[Ph_3PO]$ against k_{obs} for the addition of Me_3SiCN to PhCHO at 0 °C in CH_2Cl_2. $[PhCHO]_0$ = 0.49 M, $[Me_3SiCN]_0$ = 0.52 M. Solid line and filled diamonds: $[Ph_3PO]$ = 0.1 M, [**11**] = 0.9–23 mM. Broken line and empty squares: [**11**] = 4.9 mM, $[Ph_3PO]$ = 0.045–0.226 M.

This also contrasts with the rate equation for aluminium(salen) complex **12** as in that case the reaction was found to be first order in both catalyst and triphenylphosphine oxide concentrations.

The kinetic data suggest that for reactions catalysed by complex **11**, coordination of the aldehyde to complex **11** is the rate determining step. Since triphenylphosphine oxide and trimethylsilyl cyanide are present in much higher concentrations than complex **11**, then provided the formation of adduct **13** is fast compared to the coordination of aldehyde to **11**, it will be present at constant concentration and the mechanism shown in Scheme 5 is consistent with the kinetic data. This is very similar to the mechanism previously deduced for reactions catalysed by $[Al(salen)]_2O$ **12**, but with a different rate determining step which indicates that $[Al(salan)]_2O$ is less Lewis acidic than $[Al(salen)]_2O$.[9f,10f] The decrease in Lewis acidity of the aluminium ions in complex **11** compared to $[Al(salen)]_2O$ **12** may also explain the reversal in enantioselectivity be-



Scheme 5. Possible mechanism for asymmetric cyanohydrin synthesis catalysed by complex **11**.

tween the two complexes. Thus, $[Al(salen)]_2O$ **12** was previously proposed to coordinate to both the aldehyde and adduct **13**, with cyanide transfer then occurring intramolecularly (Fig. 8). In contrast, the mechanism shown in Scheme 5 lacks this interaction between adduct **13** and an aluminium ion of the $[Al(salan)]_2O$/aldehyde complex, so cyanide transfer occurs intermolecularly to the less hindered face of the aldehyde.

To probe the Lewis acidity of complex **11** and investigate the nature of any electron transfer in or before the rate determining transition state, a Hammett analysis of asymmetric cyanohydrin synthesis catalysed by complex **11** (1 mol %) and triphenylphosphine oxide (20 mol %) at 0 °C was carried out using eleven *meta*- or *para*-substituted aldehydes. The resulting rate data are shown in Table 5 and the Hammett plot is shown in Figure 9. The absence of any correlation suggests that there is little change in the electron density around the benzylic carbon atom of the aldehyde and is consistent with complex **11** being only a very weak Lewis acid and cyanide transfer to the aldehyde occurring only after the rate determining step of the mechanism.

3. Conclusions

Metal(salan) complexes derived from titanium, vanadium or aluminium have been shown to catalyse the asymmetric addition of trimethylsilyl cyanide to aldehydes. In each case, the absolute configuration of the cyanohydrin trimethylsilyl ether was the opposite of that obtained with the corresponding metal(salen) complex. The best results were obtained with $[Al(salan)]_2O$ **11** in the presence of triphenylphosphine oxide as cocatalyst and a kinetic study provided evidence for a reaction mechanism and an explanation of the inverted sense of asymmetric induction.

4. Experimental

4.1. Chemicals and instrumentation

Chromatographic separations were performed using silica gel 60 (230–400 mesh, Davisil). Infrared spectra were recorded at room temperature on a Varian 800 FT-IR Scimitar series spectrometer.

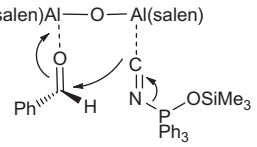


Figure 8. Intramolecular cyanide transfer in asymmetric cyanohydrin synthesis catalysed by aluminium(salen) complex **12** and Ph_3PO.

Table 5
Rate data for the construction of a Hammett plot for asymmetric cyanohydrin synthesis catalysed by $[Al(salan)]_2O$ complex **11** and Ph_3PO[a]

Entry	Aldehyde (RCHO)	σ	k_1 ($\times10^5$)	k_2 ($\times10^5$)	k_{avg} ($\times10^5$)
1	R = Ph	0	2.0	3.0	2.5
2	R = 4-$MeOC_6H_4$	−0.27	1.0	2.0	1.5
3	R = 3,4-$Me_2C_6H_3$	−0.24	2.0	2.0	2.0
4	R = 4-MeC_6H_4	−0.14	3.0	4.0	3.5
5	R = 3-MeC_6H_4	−0.06	3.0	3.0	3.0
6	R = 4-$MeSC_6H_4$	0	2.0	2.0	2.0
7	R = 4-FC_6H_4	0.06	3.0	3.0	3.0
8	R = 4-ClC_6H_4	0.23	3.0	3.0	3.0
9	R = 3-FC_6H_4	0.34	5.0	4.0	4.5
10	R = 3-ClC_6H_4	0.37	4.0	4.0	4.0
11	R = 3,5-$F_2C_6H_3$	0.68	3.0	3.0	3.0

[a] All reactions carried out at 0 °C in CH_2Cl_2 with $[ArCHO]_0$ = 0.49 M; $[Me_3SiCN]_0$ = 0.56 M; [**11**] = 4.9 mM; $[Ph_3PO]$ = 0.1 M. k_1 and k_2 refer to the rate constants measured in two separate experiments and k_{avg} is the average of these measurements and was used to construct the Hammett plot.

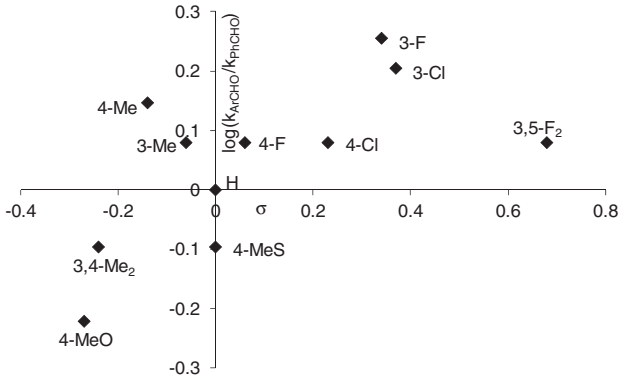


Figure 9. Hammett plot for asymmetric cyanohydrin trimethylsilyl ether synthesis catalysed by complex **11** (1 mol %) and Ph_3PO (20 mol %) at 0 °C in CH_2Cl_2.

Melting points were determined on a Stuart SMP3 system. Optical rotation measurements were conducted on a Polaar 2001 Optical Activity automatic polarimeter at the sodium D-line using 0.25 and 0.5 dm thermostated cuvettes and a suitable solvent that is reported along with the concentration (g/100 ml). High- and low-resolution electrospray ionisation (ES) mass spectra were recorded on a Waters LCT Premier LCMS spectrometer using direct injection of the sample dissolved in MeOH. Chiral gas chromatography was performed on a Varian450-GC instrument with a TCD detector using a Supelco Gamma DEX 120 fused silica capillary column (30 m × 0.25 mm × 0.25 μm film thickness) with hydrogen as a carrier gas. Aldehyde concentrations during kinetic studies were calculated by measuring UV absorbance maxima at the appropriate wavelength using a Biochrom Libra S12 UV–visible spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Jeol ECS400 spectrometer at resonance frequencies of 400 and 100 MHz, respectively. All spectra were recorded at room temperature in $CDCl_3$. Chemical shifts are reported in ppm and are relative to TMS internally referenced to the residual solvent peak. The multiplicity of signals is reported as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (br) or a combination of any of these. Spectra were assigned with the aid of DEPT, ^1H–^1H COSY and ^1H–^{13}C COSY spectra. Superscripts a and b are used to refer to the two diastereotopic spin systems within a salan ligand in complex **11**.

4.2. Synthesis of a Ti(salan) complex

Salan ligand **6** (0.68 g, 1.2 mmol) was dissolved in CH_2Cl_2 (3.5 ml) and $Ti(O^iPr)_4$ (0.37 g, 1.3 mmol) was added with stirring

resulting in the formation of a pale yellow solution. The solution was stirred at room temperature for 5 h, followed by the addition of water (10 drops). The resulting solution was sealed and stirred vigorously for 16 h, resulting in the formation of an orange solution. The solvent was evaporated in vacuo and the residue dried on a vacuum line to remove any remaining water, leaving a yellow residue which was used without purification.

4.3. Synthesis of VO(salan)Cl complex 10

Salan ligand **6** (0.22 g, 0.4 mmol) was dissolved in THF (3 ml) and $VOCl_3$ (0.09 g, 0.54 mmol) added with vigorous stirring. The flask was sealed and stirred for 1 h, resulting in the formation of a deep green solution. The solvent was evaporated in vacuo and the residue was dissolved in CH_2Cl_2 (2 ml) and purified by flash chromatography on silica eluting first with CH_2Cl_2 to remove V(IV) species and then with methanol to give complex **10** (0.85 g, 75%) as a dark green solid. Mp >280 °C (decomp.); $[\alpha]_D^{23} = +1680$ (*c* 0.01, $CHCl_3$); ν_{max} 2953 and 1628 cm^{-1}; *m*/*z*(ESI) 1262 (2M-2Cl+MeO)$^+$, 615 (M-Cl)$^+$, 376, 340; Found (ESI) 615.3740; $C_{36}H_{56}N_2O_3V$ (M-Cl)$^+$ requires 615.3730. Traces of paramagnetic V(IV) species were always present which prevented ^1H or ^{13}C NMR spectra from being recorded.

4.4. Synthesis of [Al(salan)]$_2$O complex 11

Salan ligand **6** (0.38 g, 0.68 mmol, 1 eq) was dissolved in dry toluene (20 ml) and $Al(OEt)_3$ (0.19 g, 1.15 mmol) added. The solution was stirred under an argon atmosphere and heated at reflux for 5 h, then at 80 °C for a further 16 h. The solution was then cooled to room temperature and solvent evaporated in vacuo to leave a yellow solid which was dissolved in CH_2Cl_2 (25 ml) and washed with water (2 × 25 ml), brine (2 × 25 ml) and dried (Na_2SO_4) to leave complex **11** (0.58 g, 75%) as a pale yellow solid. Mp 276–280° C; $[\alpha]_D^{23} = +14.8$ (*c* 1.0, $CHCl_3$); ν_{max} 3190, 2960, 2903, 2866 and 1478 cm^{-1}; $\delta_H(CDCl_3)$ 0.89–1.85 (6H, m, $(CH_2)_4$), 0.94 (9H, s, $(CH_3)_3$), 1.09–1.15 (1H, m, NH^a), 1.27 (9H, s, $(CH_3)_3$), 1.30 (9H, s, $(CH_3)_3$), 1.61 (9H, s, $(CH_3)_3$), 2.15–2.27 (2H, m, $NC^bH + C^bH_2CHN$), 2.40–2.45 (1H, m, C^aH_2CHN), 2.65 (1H, qd *J* 11.7 and 3.1 Hz, NC^aH), 3.62 (1H, d *J* 9.7 Hz, NC^aH_2), 3.68–3.73 (1H, m, NC^bH_2), 3.78–3.74 (1H, m, NC^aH_2), 4.69 (1H, d *J* 10.9 Hz, NH^b), 4.77 (1H, d *J* 13.1 Hz, NC^bH_2), 6.75 (2H, d *J* 2.4 Hz, 2 × ArH), 7.13 (1H, d *J* 2.6 Hz, ArH), 7.34 (1H, d *J* 2.5 Hz, ArH); $\delta_C(CDCl_3)$ 24.46 (CH_2), 24.66 (CH_2), 29.11 (C^aH_2), 29.76 (CH_3), 30.02 (C^bH_2), 31.20 (CH_3), 31.72 (CH_3), 31.75 (CH_3), 33.77 (*C*Me_3), 33.89 (*C*Me_3), 34.73 (*C*Me_3), 35.34 (*C*Me_3), 49.09 (NC^aH_2), 50.93 (NC^bH_2), 56.63 (NC^bH), 58.95 (N^aCH), 121.83 (ArC), 123.03 (ArCH), 123.33 (ArCH), 124.68 (ArCH), 124.79 (ArCH), 125.28 (ArC), 136.36 (ArC), 137.24 (ArC), 138.10 (ArC), 138.16 (ArC), 158.00 (ArC), 160.40 (ArC); *m*/*z*(ESI) 1189.8 (M+Na)$^+$, 1167.8 (MH$^+$), 607.4, 575.4. Found (ESI): 1167.8297; $C_{72}H_{113}Al_2N_4O_5$ (MH$^+$) requires 1167.8342.

4.5. General procedure for the synthesis of cyanohydrin trimethylsilyl ethers 8a–k

A metal(salan) catalyst (0.1–10 mol %) and Ph_3PO (0–60 mol %) were dissolved in CH_2Cl_2 or an alternative solvent (3 ml). An aldehyde (1.0 mmol) and Me_3SiCN (0.12 ml, 1.2 mmol) were added to the stirred solution and the reaction was stirred at −40 to 22 °C for 24–240 h. The solution was then filtered through a short path of silica and evaporated in vacuo to leave cyanohydrin trimethylsilyl ethers **8a–k** as yellow oils. The cyanohydrin trimethylsilyl ethers had spectroscopic data consistent with those reported previously[11] and the conversion was determined by integration of the ^1H NMR CHO signals of the cyanohydrin and unreacted aldehyde.

4.6. General procedure for determining the enantiomeric excess of cyanohydrin trimethylsilyl ethers 8a–k

A cyanohydrin trimethylsilyl ether (1.0 mmol) was dissolved in MeCN (1 ml), then $Sc(OSO_2CF_3)_3$ (5 mg, 0.01 mmol) and Ac_2O (0.22 g, 2.1 mmol) were added and the reaction stirred at rt for 1 h. The solution was passed through a short path of silica and evaporated in vacuo to leave cyanohydrin acetates **9a–k** as yellow oils. Compounds **9a–k** were analysed by chiral GC under the conditions previously reported[11] to determine their enantiomeric excesses.

4.7. General procedure for kinetic experiments

Solutions of catalyst **11** and Ph_3PO in CH_2Cl_2 were added to a 5 ml round bottomed flask fitted with a Suba Seal stopper. CH_2Cl_2 was added to dilute the reactants to the required concentrations. An aliquot (0.5 μL) was taken via a microsyringe and diluted into CH_2Cl_2 (3 ml); this sample provided the reference for UV measurements. Aldehyde (0.94 mmol) was then added and another aliquot (0.5 μL) taken to calculate the concentration at time = 0. Me_3SiCN (0.14 ml, 1.03 mmol) was added and simultaneously a timer was started. Samples (0.5 μL) were taken and diluted into CH_2Cl_2 (3 ml) at appropriate intervals and the UV absorbance measured to determine the concentration of the remaining aldehyde. The amount of CH_2Cl_2 used to dissolve the catalyst and Ph_3PO in a particular reaction was varied to ensure that the total initial reaction volume (CH_2Cl_2 + aldehyde + Me_3SiCN) was kept constant at 2.0 ml.

Acknowledgement

The authors thank the Newcastle University for financial support.

References

1. (a) Wang, W.; Liu, X.; Lin, L.; Feng, X. *Eur. J. Org. Chem.* **2010**, 4751–4769; (b) Wang, W. T.; Lin, L. L.; Liu, X. H.; Feng, X. M. Asymmetric Synthesis of Nitriles. In *Science of Synthesis Knowledge Updates 2011/4*; North, M., Ed.; Georg Thieme Verlag KG: Stuttgart, 2012.
2. Dadashipour, M.; Asano, Y. *ACS Catal.* **2011**, *1*, 1121–1149.
3. (a) Davie, E. A. C.; Mennen, S. M.; Xu, Y.; Miller, S. J. *Chem. Rev.* **2007**, *107*, 5759–5812; (b) Malkov, A. V.; Kočovsky, P. *Eur. J. Org. Chem* **2007**, 29–36.
4. (a) North, M.; Usanov, D. L.; Young, C. *Chem. Rev.* **2008**, *108*, 5146–5226; (b) Khan, N. H.; Kureshy, R. I.; Abdi, S. H. R.; Agrawal, S.; Jasra, R. V. *Coord. Chem. Rev* **2008**, *252*, 593–623.
5. For recent examples see: (a) Zeng, Z.; Zhao, G.; Gao, P.; Tang, H.; Chen, B.; Zhou, Z.; Tang, C. *Catal. Commun.* **2007**, *8*, 1443–1446; (b) Serra, M. E. S.; Murtinho, D.; Goth, A. *Arkivoc* **2010**, 64–69; (c) Serra, M. E. S.; Murtinho, D.; Goth, A.; Gonsalves, A. M. D. R.; Abreu, P. E.; Pais, A. A. C. C. *Chirality* **2010**, *22*, 425–431; (d) Paravidino, M.; Holt, J.; Romano, D.; Singh, N.; Arends, I. W. C. E.; Minnaard, A. J.; Orru, R. V. A.; Molinari, F.; Hanefeld, U. *J. Mol. Catal. B* **2010**, *63*, 87–92; (e) Lv, C.; Cheng, Q.; Xu, D.; Wang, S.; Xia, C.; Sun, W. *Eur. J. Org. Chem.* **2011**, 3407–3411; (f) Wen, Y. Q.; Ren, W. M.; Lu, X. B. *Chinese Chem. Lett.* **2011**, *22*, 1285–1288; (g) Wen, Y.-Q.; Ren, W. M.; Lu, X.-B. *Org. Biomol. Chem.* **2011**, *9*, 6323–6330.
6. (a) Belokon, Y. N.; Maleev, V. I.; North, M.; Usanov, D. L. *Chem. Commun.* **2006**, 4614–4616; (b) Khan, N. H.; Agrawal, S.; Kureshy, R. I.; Abdi, S. H. R.; Mayani, V. J.; Jasra, R. V. *J. Mol. Catal. A* **2007**, *264*, 140–145; (c) Belokon', Y. N.; Hunt, J.; North, M. *Synlett* **2008**, 2150–2154; (d) Belokon', Y. N.; Hunt, J.; North, M. *Tetrahedron: Asymmetry* **2008**(19), 2804–2815; (e) Belokon, Y. N.; Clegg, W.; Harrington, R. W.; Maleev, V. I.; North, M.; Omedes–Pujol, M.; Usanov, D. L.; Young, C. *Chem. Eur. J.* **2009**, *15*, 2148–2165; (f) Yang, H.; Zhang, L.; Wang, P.; Yang, Q.; Li, C. *Green Chem.* **2009**, *11*, 257–264.
7. Holmes, I. P.; Kagan, H. B. *Tetrahedron Lett.* **2000**, *41*, 7457–7460.
8. (a) Kim, S. S.; Lee, S. H. *Synth. Commun.* **2005**, *35*, 751–759; (b) Kim, S. S.; Lee, S. H.; Kwak, J. M. *Tetrahedron: Asymmetry* **2006**, *17*, 1165–1169; (c) Kim, S. S.; Kwak, J. M.; George, S. C. *Appl. Organometal. Chem.* **2007**, *21*, 809–813; (d) Khan, N. H.; Agrawal, S.; Kureshy, R. I.; Abdi, S. H. R.; Prathap, K. J.; Jasra, R. V. *Chirality* **2009**, *21*, 262–270; (e) Qu, Y.; Jing, L.; Wu, Z.; Wu, D.; Zhou, X. *Tetrahedron: Asymmetry* **2010**, *21*, 187–190.
9. (a) Chen, F.-X.; Zhou, H.; Liu, X.; Qin, B.; Feng, X.; Zhang, G.; Jiang, Y. *Chem. Eur. J.* **2004**, *10*, 4790–4797; (b) Kim, S. S.; Song, D. H. *Eur. J. Org. Chem.* **2005**, 1777–1780; (c) Kim, S. S.; Kwak, J. M. *Tetrahedron* **2006**, *62*, 49–53; (d) Alaaeddine, A.;

Roisnel, T.; Thomas, C. M.; Carpentier, J.-F. *Adv. Syn. Catal.* **2008**, *350*, 731–740; (e) Zeng, Z.; Zhao, G.; Zhou, Z.; Tang, C. *Eur. J. Org. Chem.* **2008**, 1615–1618; (f) North, M.; Williamson, C. *Tetrahedron Lett.* **2009**, *50*, 3249–3252; (g) Cao, J.-J.; Zhou, F.; Zhou, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 4976–4980.
10. (a) Belokon', Y. N.; Green, B.; Ikonnikov, N. S.; Larichev, V. S.; Lokshin, B. V.; Moscalenko, M. A.; North, M.; Orizu, C.; Peregudov, A. S.; Timofeeva, G. I. *Eur. J. Org. Chem.* **2000**, 2655–2661; (b) Belokon, Y. N.; North, M.; Maleev, V. I.; Voskoboev, N. V.; Moskalenko, M. A.; Peregudov, A. S.; Dmitriev, A. V.; Ikonnikov, N. S.; Kagan, H. B. *Angew. Chem., Int. Ed.* **2004**, *43*, 4085–4089; (c) Belokon, Y. N.; Clegg, W.; Harrington, R. W.; Young, C.; North, M. *Tetrahedron* **2007**, *63*, 5287–5299; (d) Belokon', Y. N.; Clegg, W.; Harrington, R. W.; North, M.; Young, C. *Inorg. Chem.* **2008**, *47*, 3801–3814; (e) Chechik, V.; Conte, M.; Dransfield, T.; North, M.; Omedes–Pujol, M. *Chem. Commun.* **2010**, *46*, 3372–3374; (f) North, M.; Villuendas, P.; Williamson, C. *Tetrahedron* **2010**, *66*, 1915–1924.
11. (a) North, M.; Omedes–Pujol, M.; Williamson, C. *Chem. Eur. J.* **2010**, *16*, 11367–11375; (b) North, M.; Omedes–Pujol, M. *Beilstein J. Org. Chem.* **2010**, *6*, 1043–1055.
12. Zhang, Z.; Wang, Z.; Zhang, R.; Ding, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 6746–6750.
13. Lv, C.; Xu, D.; Wang, S.; Miao, C.-X.; Xia, C.; Sun, W. *Catal. Commun.* **2011**, *12*, 1242–1245.
14. Khan, N. H.; Sadhukhan, A.; Maity, N. C.; Kureshy, R. I.; Abdi, S. H. R.; Saravanan, A. S.; Bajaj, H. C. *Tetrahedron* **2011**, *67*, 7073–7080.
15. Matsumoto, K.; Saito, B.; Katsuki, T. *Chem. Commun.* **2007**, 3619–3627.
16. (a) Atwood, D. A. *Coord. Chem. Rev.* **1997**, *165*, 267–296; (b) Arends, I. W. C. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 6250–6252; (c) Tshuva, E. Y.; Ashenhurst, J. A. *Eur. J. Inorg. Chem.* **2009**, 2203–2218.
17. Wu, M.; Miao, C.-X.; Wang, S.; Hu, X.; Xia, C.; Kühn, F. E.; Sun, W. *Adv. Synth. Catal.* **2011**, *353*, 3014–3022.
18. (a) Sawada, Y.; Matsumoto, K.; Kondo, S.; Watanabe, H.; Ozawa, T.; Suzuki, K.; Saito, B.; Katsuki, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 3478–3480; (b) Matsumoto, K.; Sawada, Y.; Katsuki, T. *Synlett* **2006**, 3545–3547; (c) Shimada, Y.; Kondo, S.; Ohara, Y.; Matsumoto, K.; Katsuki, T. *Synlett* **2007**, 2445–2447; (d) Kondo, S.; Saruhashi, K.; Seki, K.; Matsubara, K.; Miyaji, K.; Kubo, T.; Matsumoto, K.; Katsuki, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 10195–10198; (e) Matsumoto, K.; Oguma, T.; Katsuki, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 7432–7436.
19. (a) Sawada, Y.; Matsumoto, K.; Katsuki, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 4559–4561; (b) Berkessel, A.; Brandenburg, M.; Leitterstorf, E.; Frey, J.; Lex, J.; Schäfer, M. *Adv. Synth. Catal.* **2007**, *349*, 2385–2391; (c) Matsumoto, K.; Kubo, T.; Katsuki, T. *Chem. Eur. J.* **2009**, *15*, 6573–6575; (d) Xiong, D.; Hu, X.; Wang, S.; Miao, C.-X.; Xia, C.; Sun, W. *Eur. J. Org. Chem.* **2011**, 4289–4292; (e) Matumoto, K.; Feng, C.; Handa, S.; Oguma, T.; Katsuki, T. *Tetrahedron* **2011**, *67*, 6474–6478.
20. (a) Egami, H.; Katsuki, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 5171–5174; (b) Egami, H.; Oguma, T.; Katsuki, T. *J. Am. Chem. Soc.* **2010**, *132*, 5886–5895.
21. Sun, J.; Zhu, C.; Dai, Z.; Yang, M.; Pan, Y.; Hu, H. *J. Org. Chem.* **2004**, *69*, 8500–8503.
22. Egami, H.; Katsuki, T. *Synlett* **2008**, 1543–1546.
23. (a) Tamaguchi, T.; Matsumoto, K.; Saito, B.; Katsuki, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 4729–4731; (b) Matsumoto, K.; Yamaguchi, T.; Katsuki, T. *Chem. Commun.* **2008**, 1704–1706; (c) Matsumoto, K.; Yamaguchi, T.; Fujisaki, J.; Saito, B.; Katsuki, T. *Chem. Asian J.* **2008**, *3*, 351–358; (d) Fujisaki, J.; Matsumoto, K.; Matsumoto, K.; Katsuki, T. *J. Am. Chem. Soc.* **2011**, *133*, 56–61.
24. (a) Bryliakov, K. P.; Talsi, E. P. *Eur. J. Org. Chem.* **2008**, 3369–3376;; (b) Adão, P.; Avecilla, F.; Bonchio, M.; Carraro, M.; Pessoa, J. C.; Correia, I. *Eur. J. Inorg. Chem.* **2010**, 5568–5578; (c) Bryliakov, K. P.; Talsi, E. P. *Eur. J. Org. Chem.* **2011**, 4693–4698.
25. Egami, H.; Katsuki, T. *J. Am. Chem. Soc.* **2007**, *129*, 8940–8941.
26. (a) Egami, H.; Katsuki, T. *J. Am. Chem. Soc.* **2009**, *131*, 6082–6083; (b) Egami, H.; Matsumoto, K.; Oguma, T.; Kunisu, T.; Katsuki, T. *J. Am. Chem. Soc.* **2010**, *132*, 13633–13635.
27. Yang, H.; Wang, H.; Zhu, C. *J. Org. Chem.* **2007**, *72*, 10029–10034.
28. (a) Bandini, M.; Benaglia, M.; Sinisi, R.; Tommasi, S.; Umani–Ronchi, A. *Org. Lett.* **2007**, *9*, 2151–2153; (b) Constable, E. C.; Zhang, G.; Housecroft, C. E.; Neuburger, M.; Schaffner, S.; Woggon, W.-D.; Zampese, J. A. *New J. Chem.* **2009**, *33*, 2166–2173.
29. (a) Saito, B.; Katsuki, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 4600–4602; (b) Suyama, K.; Sakai, Y.; Matsumoto, K.; Saito, B.; Katsuki, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 797–799.
30. Saito, B.; Egami, H.; Katsuki, T. *J. Am. Chem. Soc.* **2007**, *129*, 1978–1986.
31. Shitama, H.; Katsuki, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 2450–2453.
32. Furutachi, M.; Mouri, S.; Matsunaga, S.; Shibasaki, M. *Chem. Asian J.* **2010**, *5*, 2351–2354.
33. Du, H.; Velders, A. H.; Dijkstra, P. J.; Sun, J.; Zhong, Z.; Chen, X.; Feijen, J. *Chem. Eur. J.* **2009**, *15*, 9836–9845.
34. Hormnirun, P.; Marshall, E. L.; Gibson, V. C.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **2004**, *126*, 2688–2689.
35. Whitelaw, E. L.; Jones, M. D.; Mahon, M. F. *Inorg. Chem.* **2010**, *49*, 7176–7181.
36. Segal, S.; Goldberg, I.; Kol, M. *Organomet.* **2005**, *24*, 200–202.
37. (a) Tshuva, E. Y.; Goldberg, I.; Kol, M. *J. Am. Chem. Soc.* **2000**, *122*, 10706–10707; (b) Segal, S.; Yeori, A.; Shuster, M.; Rosenberg, Y.; Kol, M. *Macromolecules* **2008**, *41*, 1612–1617; (c) Ciancaleoni, G.; Fraldi, N.; Budzelaar, P. H. M.; Busico, V.; Cipullo, R.; Macchioni, A. *J. Am. Chem. Soc.* **2010**, *132*, 13651–13653.
38. Press, K.; Cohen, A.; Goldberg, I.; Venditto, V.; Mazzeo, M.; Kol, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 3529–3532.
39. (a) Li, B.; Wu, C.-P.; Ren, W.-M.; Wang, Y.-M.; Rao, D.-Y.; Lu, X.-B. *J. Polym. Sci. A.* **2008**, *46*, 6102–6113; (b) Darensbourg, D. J.; Ulusoy, M.; Karroonnirum, O.; Poland, R. R.; Reibenspies, J. H.; Çetinkaya, B. *Macromolecules* **2009**, *42*, 6992–6998.
40. (a) Takaki, J.; Egami, H.; Matsumoto, K.; Saito, B.; Katsuki, T. *Chem. Lett.* **2008**, *37*, 502–503; (b) Sakai, Y.; Mitote, J.; Matsumoto, K.; Saito, B.; Katsuki, T. *Chem. Commun.* **2010**, *46*, 5787–5789.
41. Lv, C.; Wu, M.; Wang, S.; Xia, C.; Sun, W. *Tetrahedron: Asymmetry* **2010**, *21*, 1869–1873.
42. (a) Belokon', Y. N.; Caveda-Cepas, S.; Green, B.; Ikonnikov, N. S.; Khrustalev, V. N.; Larichev, V. S.; Moscalenko, M. A.; North, M.; Orizu, C.; Tararov, V. I.; Tasinazzo, M.; Timofeeva, G. I.; Yashkina, L. V. *J. Am. Chem. Soc.* **1999**, *121*, 3968–3973; (b) Belokon', Y. N.; Green, B.; Ikonnikov, N. S.; North, M.; Parsons, T.; Tararov, V. I. *Tetrahedron* **2001**, *57*, 771–779.
43. (a) Tshuva, E. Y.; Gendeziuk, N.; Kol, M. *Tetrahedron Lett.* **2001**, *42*, 6405–6407; (b) García–Zarracino, R.; Ramos–Quiñones, J.; Höpfl, H. *J. Organomet. Chem.* **2002**, *64*, 188–200.
44. Norsikan, S.; Holmes, I.; Lagasse, F.; Kagan, H. B. *Tetrahedron Lett.* **2002**, *43*, 5715–5717.
45. (a) Ryu, D. H.; Corey, E. J. *J. Am. Chem. Soc.* **2004**, *126*, 8106–8107; (b) Ryu, D. H.; Corey, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 5384–5387.
46. Denmark, S. E.; Chung, W.-J. *J. Org. Chem.* **2006**, *71*, 4002–4005.