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# Application of Tridentate Bis(oxazoline) Ligands in Catalytic Asymmetric Nozaki–Hiyama Allylation and Crotylation: An Example of High Enantioselection with a Non-Symmetric Bis(oxazoline) Ligand

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**Abstract:** A series of both symmetric and non-symmetric bis(oxazoline) ligands was applied in the Nozaki–Hiyama allylation and crotylation of benzaldehyde. It was found that both the magnitude and sense of the asymmetric induction depended strongly on the nature and combination of the oxazoline substituents. For both reactions, the non-symmetric *tert*-butyl/benzyl-substituted ligand proved to be the optimal ligand and was applied successfully in the allylation and crotylation of a range of aryl and aliphatic aldehydes. The enantioselectivities obtained in allylation were up to 91% ee and in crotylation up to 92% with typical *syn:anti* ratios of up to 80:20.

**Keywords:** allylation; asymmetric catalysis; ligand design; N ligands; tridentate ligands

## Introduction

The Nozaki–Hiyama–Kishi reaction, first reported by Nozaki and Hiyama, is an important and versatile carbon-carbon bond forming transformation involving the nucleophilic addition to carbonyl compounds (in particular aldehydes) of intermediate organochromium(III) reagents, which are generated *in situ* from the insertion of chromium(II) species into allyl, alkenyl, alkynyl, propargyl and aryl halides/sulfonates.[1] This methodology was enhanced by independent reports from Nozaki and Kishi that the addition of trace amounts of nickel(II) salts accelerated the formation of organochromium(III) intermediates especially with less reactive substrates such as alkenyl and aryl halides/triflates.[2] Following these reports, extensive research in this transformation revealed a number of unique and important features: (i) applicability of a broad range of substrates to the insertion of chromium(II) under mild conditions; (ii) pronounced chemoselectivity of the organochromium(III) reagents for reactions with aldehydes in the presence of ketones; (iii) a strong driving force for the nucleophilic addition due to the formation of highly stable O–Cr(III) bonds; (iv) an unprecedented compatibility with numerous functional groups such as esters or nitriles in both reaction partners; (v) distinct stereochemical preferences particularly in reactions with crotylchromium reagents; (vi) excellent reliability even when applied to sensitive and polyfunctional compounds; (vii) high preference for the formation of allylchromium reagents in the presence of alkyl and alkenyl halides. As a consequence, this reaction has been utilized effectively in numerous total syntheses of complex natural products.[3]

The synthetic utility of the reaction was significantly increased by the development by Fürstner of a catalytic redox process in which chromium(II) is recycled from chromium(III), thus allowing the use of much reduced quantities of toxic chromium salts and therefore making the reaction more environmentally benign.[4] Chromium(III) chloride is preferred because, in contrast to chromium(II) chloride, it is cheap, relatively insensitive to oxygen and moisture and much easier to manipulate. Other catalytic versions of the Nozaki–Hiyama–Kishi reaction employing an organic reducing agent [tetrakis(dimethylamino)ethylene][5] or electrochemical driving forces have also been reported.[6]

The development of an enantioselective Nozaki–Hiyama–Kishi reaction was highly desirable, but due to difficulties such as ligand coordination and specificity

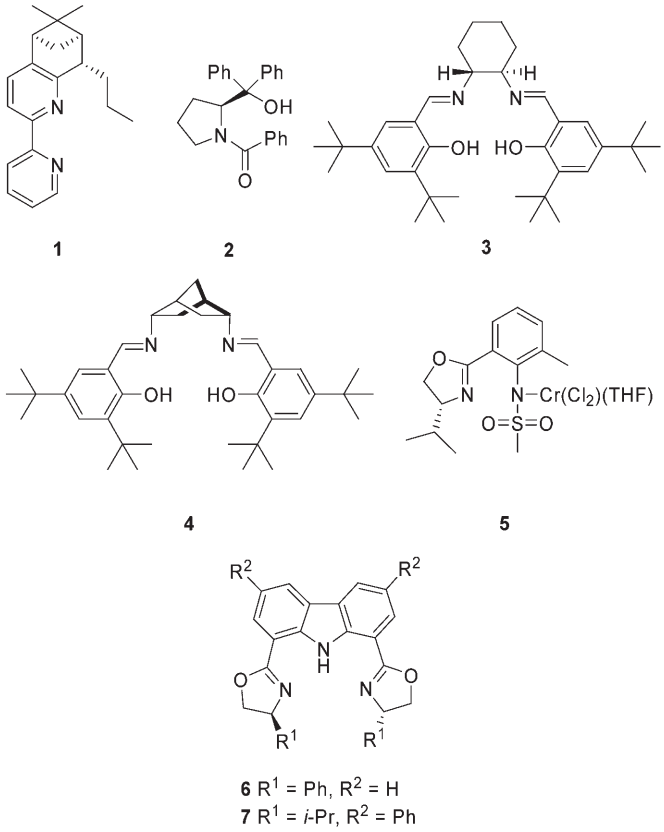
and the tendency of chromium(II) to form dimers or clusters with polydentate ligands, relatively few reports relating to the enantioselective variant have been published. As a consequence, only a selection of ligands has been reported to give good enantiocontrol and high reactivity, mainly in the allylation of aldehydes.

The first somewhat successful reactions relied on over stoichiometric amounts (up to 400%) of specially designed chiral ligands and afforded only moderate yields. The best of these ligands were the chiral bipyridine ligand **1** developed by Kishi,[7] which gave poor to good enantioselectivities (28–74% ee) for the allylation and alkenylation of benzaldehyde and the *N*-benzoylprolinol derivative **2** which gave up to 98% ee for the reaction of allyl bromide with different aldehydes.[8]

Cozzi developed the first catalytic enantioselective Nozaki–Hiyama–Kishi reaction using chromium(II) complexes (10 mol %) of the commercially available chiral salen ligand **3**.[9] High levels of enantiodiscrimination were afforded for both the allylation (77–90% ee) and crotylation (78–90% ee) of a range of aldehydes using allyl chloride and crotyl bromide, respectively.[10] However, only moderate yields of product were obtained (41–67%) due to the formation of a considerable quantity of the corresponding pinacol side product. Berkessel employed the salen derivative [(*S*,*S*)-DIANANE] **4** and obtained higher enantiodiscrimination in the reaction of benzaldehyde with allyl bromide (90% ee) than with allyl chloride (79% ee).[11]

Oxazoline-containing ligands have also been used with some success in the enantioselective Nozaki–Hiyama–Kishi reaction. The chromium(III)/sulfonamide-oxazoline ligand complex **5** gave good enantioselectivities for the Ni/Cr-mediated alkenylation and the Co/Cr-mediated alkylation of aliphatic aldehydes and was thus applied by Kishi in the synthesis of the $C_{14}-C_{26}$ segment of halichondrins.[12] Nakada developed the tridentate bis(oxazolinyl)carbazole ligand **6** and it induced good enantioselectivities (up to 73% ee) in the asymmetric allylation of benzaldehyde.[13] The introduction of phenyl substituents at the 3 and 6 positions of the carbazole backbone provided a highly effective ligand **7**, which afforded very high levels of enantioselection (86–96% ee) for the allylation and methallylation of various aromatic and aliphatic aldehydes.[14] Crotylation of benzaldehyde using this ligand was less successful affording the *anti* product preferentially (*anti*:*syn* = 73:27) in 38% yield and 75% ee. The chromium complex of ligand **6** was water-tolerant and amenable to catalyst recycling with little change in the enantiodiscrimination.

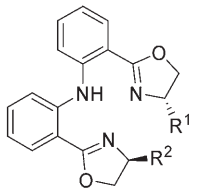
We have recently reported the preparation of a similar class of bis(oxazoline) ligands **8**, in which an *N*-phenylaniline unit links the two chiral oxazoline rings, by employing a palladium-catalyzed Hartwig–Buchwald-type aryl amination as the key synthetic step.[15] This approach, unlike a more recent synthesis by Xu and Du,[16] allowed for the preparation of symmetric ligands in addition to non-symmetric analogues. Here we define 'symmetric' as those with identical substituents at the oxazoline chiral centre and 'non–symmetric' as those with different substituents. The similarity of our tridentate bis(oxazoline) ligands **8** to the bis(oxazolinyl)carbazole ligands **6** and **7** prompted us to probe their enantiodifferentiating ability in the Nozaki–Hiyama–Kishi allylation and crotylation of benzaldehyde. Chiral tridentate bis(oxazoline) ligands of this type are thought to be good candidates for this reaction as stabilisation of the allylchromium(III)/ligand complex by three bonds, a σ-bond with the central nitrogen atom and two coordination bonds with the oxazoline nitrogen atoms, would prevent any significant dissociation. We now report our results on the application of these ligands in the asymmetric Nozaki–Hiyama allylation and crotylation of aldehydes.




## Results and Discussion

Ligands **8a–j** were first investigated in the chromium(II)-mediated reaction of benzaldehyde **9a** with allyl bromide **10a** (Table 1). An optimization of reaction conditions revealed THF/acetonitrile (7:1) and *N*,*N*-diisopropylethylamine (DIPEA) as the best solvent and base in terms of easy reduction of chromium(III), yield and enantioselectivity. In all cases, the reactions pro-



**8**

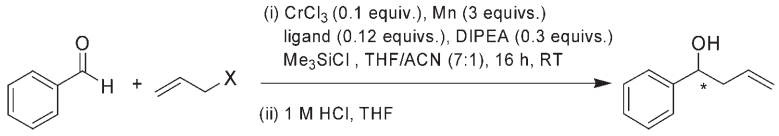
**8a** $R^1$ = Bn, $R^2$ = Bn
**8b** $R^1$ = *i*-Pr, $R^2$ = *i*-Pr
**8c** $R^1$ = Ph, $R^2$ = Ph
**8d** $R^1$ = *t*-Bu, $R^2$ = *t*-Bu
**8e** $R^1$ = Ph, $R^2$ = Bn
**8f** $R^1$ = *t*-Bu, $R^2$ = Bn
**8g** $R^1$ = *t*-Bu, $R^2$ = *i*-Pr
**8h** $R^1$ = *i*-Pr, $R^2$ = Ph
**8i** $R^1$ = *t*-Bu, $R^2$ = Ph
**8j** $R^1$ = Bn, $R^2$ = *i*-Pr

ceeded with excellent conversions after 16 h at room temperature with no evidence of any by-products. Of the four symmetric ligands **8a**–**d**, only the diisopropyl- and diphenyl-substituted ligands **8b** and **8c** afforded 1-phenylbut-3-en-1-ol **11** with significant levels of enantioselectivity [69% ee (*S*) and 44% ee (*S*)], respectively) (Table 1, entries 1–4). Although the majority of the non-symmetric ligands **8e**–**j** gave poor enantioselectivities (up to 18% ee) (Table 1, entries 5–12), notable exceptions include the *tert*-butyl/benzyl-substituted ligand **8f** and the *tert*-butyl/isopropyl-substituted ligand **8g**, which provided (*R*)-**11a** in 87 and 71% ee, respectively (Table 1, entries 6 and 9). Interestingly, the results furnished by both the symmetric and non-symmetric ligands revealed that both the extent and sense of the asymmetric induction were highly dependent on the nature and combination of the substituents on the oxazoline rings and that small changes in the substituents translated into large variation in enantiodiscrimination. This was particularly evident from the similar levels of enantioselection (69 and 71% ee) but opposite absolute configuration of product afforded by the diisopropyl-substituted ligand **8b** and the *tert*-butyl/isopropyl-substituted ligand **8g** (Table 1, entries 2 and 9).

Using the optimal ligand, the *tert*-butyl/benzyl-substituted derivative **8f**, the chromium(II)-catalysed reaction of benzaldehyde with other allyl halides was examined (Table 1, entries 7 and 8). Although the reaction with allyl iodide showed a similar reactivity profile (98% conversion after 16 h) to that of allyl bromide, the reaction with allyl chloride was sluggish giving only 19% conversion over the same time period. In terms of enantiodiscrimination, both reactions were less enantioselective than that with allyl bromide, giving the homoallylic alcohol **11a** in 74 and 80% ee with allyl chloride and allyl iodide, respectively.

The enantiodiscriminating ability of ligand **8f** in the chromium(II)-catalysed reaction of allyl bromide with a range of aldehydes was also investigated (Table 2). In all cases, complete consumption of the aldehyde, good to excellent isolated yields and high enantioselectivities (86–91% ee) were obtained. Reactions with 4-methoxybenzaldehyde **9b** and 4-chlorobenzaldehyde **9c** proceeded with a similar level of enantioselectivity

**Table 1.** Catalytic asymmetric Nozaki–Hiyama allylation of benzaldehyde using ligands **1a**–**j**.




**9a** **10a** X = Br, **10b** X = Cl, **10c** X = I → **11a**

| Entry | Ligand | $R^1$ | $R^2$ | X | Yield.[a] (Conv.[c]) [%] | ee[b] [%] (Conf.[d]) |
|---|---|---|---|---|---|---|
| 1 | **8a** | Bn | Bn | Br | 75 (99) | 10 (*R*) |
| 2 | **8b** | *i*-Pr | *i*-Pr | Br | 78 (96) | 69 (*S*) |
| 3 | **8c** | Ph | Ph | Br | 60 (99) | 44 (*S*) |
| 4 | **8d** | *t*-Bu | *t*-Bu | Br | 63 (88) | 11 (*S*) |
| 5 | **8e** | Ph | Bn | Br | 78 (98) | 3 (*S*) |
| 6 | **8f** | *t*-Bu | Bn | Br | 87 (100) | 87 (*R*) |
| 7 | **8f** | *t*-Bu | Bn | Cl | 10 (19) | 74 (*R*) |
| 8 | **8f** | *t*-Bu | Bn | I | 88 (98) | 80 (*R*) |
| 9 | **8g** | *t*-Bu | *i*-Pr | Br | 97 (100) | 71 (*R*) |
| 10 | **8h** | *i*-Pr | Ph | Br | 90 (100) | 18 (*R*) |
| 11 | **8i** | *t*-Bu | Ph | Br | 65 (100) | *Rac* |
| 12 | **8j** | Bn | *i*-Pr | Br | 75 (100) | 8 (*R*) |

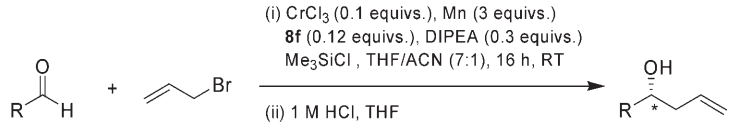
[a] Yields of the isolated homallylic alcohol.
[b] Determined by chiral GC analysis of the alcohol product **11a** on a Supelco β-Dex 120 column [30 m, 0.25 mm (diam.), 0.25 μm].
[c] Determined from the 300 MHz $^1$H NMR spectrum of the crude silylated product.
[d] Determined by comparison of the chiral GC retention times with literature values.[10b]

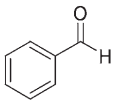
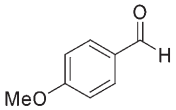
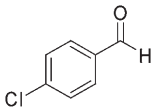
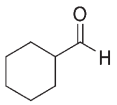
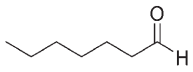
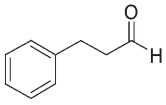
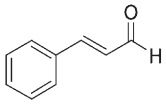
  

(88 and 86% ee, respectively) compared to benzaldehyde **9a** (87% ee) indicating that the presence of electron-donating and electron-withdrawing substituents did not have a profound effect on the asymmetric induction (Table 2, entries 1–3). Aliphatic compounds were also found to be good substrates for this reaction with both cyclic **9d** and linear (**9e** and **9f**) aldehydes providing enantioselectivities (=90% ee) slightly higher than the aromatic substrates (Table 2, entries 4–6). The allylation of an α,β-unsaturated aldehyde, *trans*-cinnamaldehyde **9g**, was also successful furnishing the corresponding homoallylic alcohol **11g** in 89% ee (Table 2, entry 7).

The chiral bis(oxazoline) ligands **8** were also investigated in asymmetric Nozaki–Hiyama crotylation. All ten ligands were examined for their stereocontrolling ability in the reaction of benzaldehyde **9a** with crotyl bromide **12** and some interesting results were obtained (Table 3).[18] All reactions again proceeded with high

**Table 2.** Catalytic asymmetric Nozaki–Hiyama allylation of aldehydes **9a–g** using ligand **8f**.

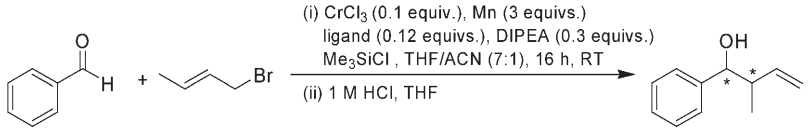



| Entry | Aldehyde | Yield[a] (Conv.[c]) [%] | ee[b] [%] (Conf.[d]) |
|---|---|---|---|
| 1 |  **9a** | 87 (100) | 87 (*R*) |
| 2 |  **9b** | 93 (100) | 88 (*R*) |
| 3 |  **9c** | 98 (100) | 86 (*R*) |
| 4[e] |  **9d** | 64 (100) | 90 (*R*) |
| 5[f] |  **9e** | 69 (100) | 91 (*S*) |
| 6 |  **9f** | 82 (100) | 90 (*S*) |
| 7 |  **9g** | 84 (100) | 89 (*R*) |

[a] Isolated yields of the homallylic alcohol.
[b] Determined by chiral GC analysis on a Supelco β-Dex 120 column or chiral HPLC analysis on a Daicel Chiralcel OD or OD-H column.
[c] Determined from the 300 MHz $^1$H NMR spectrum of the crude silylated product.
[d] Determined by comparison of the chiral GC/HPLC retention times with literature values.[10b,12d,14b,17]
[e] ee determined by HPLC analysis of the 3,5-dinitrobenzoate ester.
[f] Configuration determined by analogy with alcohol **11f**.

**Table 3.** Catalytic asymmetric Nozaki–Hiyama crotylation of benzaldehyde using ligands **8a**–**j**.




| Entry | Ligand | Yield.[a] (Conv.[d]) [%] | *anti*:*syn*[b] | ee[b] [%] (Conf.)[c] | |
|---|---|---|---|---|---|
| | | | | *anti* | *syn* |
| 1 | **8a** | 70 (92) | 77:23 | 10 (1*S*,2*S*) | 31 (1*R*,2*S*) |
| 2 | **8b** | 86 (100) | 77:23 | 65 (1*S*,2*S*) | 56 (1*S*,2*R*) |
| 3 | **8c** | 74 (98) | 87:13 | 64 (1*S*,2*S*) | 7 (1*S*,2*R*) |
| 4 | **8d** | 50 (78) | 87:13 | Rac. | 5 (1*S*,2*R*). |
| 5 | **8e** | 62 (84) | 78:22 | 11 (1*S*,2*S*) | 10 (1*R*,2*S*) |
| 6 | **8f** | 77 (94) | 77:23 | 82 (1*R*,2*R*) | 90 (1*R*,2*S*) |
| 7 | **8g** | 79 (100) | 77:23 | 56 (1*R*,2*R*) | 66 (1*R*,2*S*) |
| 8 | **8h** | 68 (96) | 81:19 | 2 (1*S*,2*S*) | 43 (1*R*,2*S*) |
| 9 | **8i** | 80 (88) | 88:12 | 4 (1*R*,2*R*) | 48 (1*R*,2*S*) |
| 10 | **8j** | 68 (87) | 77:23 | 5 (1*S*,2*S*) | 27 (1*R*,2*S*) |

[a] Isolated yields of alcohols **13a**.
[b] Determined by chiral GC analysis of the corresponding methyl ether derivative on a Supelco β-Dex 120 column.
[c] Determined by comparison of the chiral GC retention times with literature values.[12d]
[d] Determined from the 300 MHz $^1$H NMR spectrum of the crude silylated product.

conversions with no evidence of any by-products and were *anti*-selective with the *tert*-butyl/phenyl-substituted ligand **8i** affording the highest *anti*:*syn* selectivity of 88:12 (Table 3, entry 9). As for the reactions with allyl bromide, both the magnitude and sense of asymmetric induction depended strongly on the combination of oxazoline substituents. The highest level of enantiodiscrimination was again achieved using the non-symmetric *tert*-butyl/benzyl-substituted ligand **8f**, which afforded 82% ee (1*R*,2*R*) for *anti*-2-methyl-1-phenylbut-3-en-1-ol **13a** and 90% ee (1*R*,2*S*) for the *syn*-diastereomer (Table 3, entry 6). The *tert*-butyl/isopropyl-substituted ligand **8g** and the *tert*-butyl/phenyl-substituted ligand **8i** also afforded the same *anti*- and *syn*-diastereomers but with lower enantioselectivities (Table 3, entries 7 and 9). All three ligands induced a higher level of asymmetric induction in the formation of the minor *syn*-product than that of the major *anti*-product. As in the allylation reactions, ligands **8f** and **8g** favoured a different enantiomeric product (for both the *anti*- and *syn*-diastereomers) compared to the symmetric ligands **8b** and **8c** (Table 2, entries 2 and 3). Ligands **8b**, **8c**, **8f**, **8g** and **8i** induced the same enantiofacial selectivity of benzaldehyde for both the *anti*- and *syn*-products which was the same as that observed in Nozaki–Hiyama allylation. In contrast to this finding, ligands **8a**, **8e**, **8h** and **8j** promoted different enantiofacial selectivity of benzaldehyde on reaction with crotyl bromide (for both the *anti*- and *syn*-products), albeit with low to moderate enantioselectivity (Table 3, entries 1, 5, 8 and 10). In addition, the facial selectivity of the major *anti*-product was opposite to that obtained in allylation.

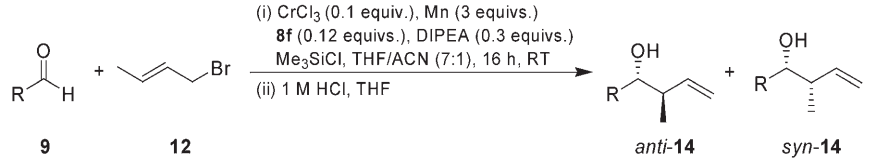
The ligand of choice **8f** was then applied in the asymmetric crotylation of a range of aldehydes (Table 4). In all cases, excellent conversions (94–100%), good isolated yields (60–87%) and moderate diastereoselectivity (up to 80:20 *anti*:*syn*) were obtained. In addition, the enantioselectivity of the *syn*-diastereomer was greater than that of the *anti*-diastereomer for the majority of substrates. 4-Methoxybenzaldehyde **9b**, 4-chlorobenzaldehyde **9c** and the aliphatic aldehydes **9e** and **9f** all provided good levels of enantiodiscrimination for both the *anti*- and *syn*-products (71–92% and 80–91% ee, respectively) (Table 4, entries 2–5). However, the reaction with the α,β-substituted benzaldehyde, *trans*-cinnamaldehyde **9g**, was considerably less enantioselective affording *anti*-and *syn*-**14g** in 38 and 52% ee, respectively (Table 4, entry 6).

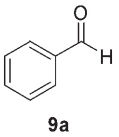
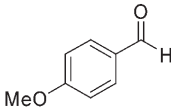
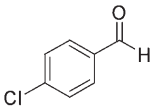
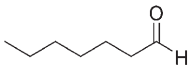
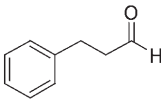
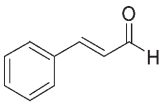
## Conclusion

In conclusion, both symmetric (**8a**–**d**) and non-symmetric (**8e**–**j**) bis(oxazoline) ligands were applied in the Nozaki–Hiyama allylation and crotylation of benzaldehyde. It was found that both the magnitude and sense of the asymmetric induction depended strongly on the nature and combination of the oxazoline substituents. A similar trend but to a lesser extent was also noticed by Nakada on the application of his bis(oxazolinyl)car-

**Table 4.** Catalytic asymmetric Nozaki–Hiyama crotylation of aldehydes **2** using ligand **1f**.




| Entry | Aldehyde | Yield [a] (Conv.[d]) [%] | *anti*/*syn*[b] | ee[b] [%] (Conf.[c]) | |
|---|---|---|---|---|---|
| | | | | *anti* | *syn* |
| 1 |  **9a** | 77 (94) | 77:23 | 82 (1*R*,2*R*) | 90 (1*R*,2*S*) |
| 2[e] |  **9b** | 87 (97) | 79:21 | 92 (1*R*,2*R*) | 91 (1*R*,2*S*) |
| 3[e] |  **9c** | 76 (100) | 78:22 | 71 (1*R*,2*R*) | 80 (1*R*,2*S*) |
| 4 |  **9e** | 60 (95) | 74:26 | 83 (3*R*,4*S*) | 90 (3*S*,4*S*) |
| 5 |  **9f** | 65 (96) | 77:23 | 84 (3*S*,4*R*) | 90 (3*S*,4*S*) |
| 6 |  **9g** | 64 (100) | 80:20 | 38 (3*R*,4*R*) | 52 (3*R*,4*S*) |

[a] Isolated yields of alcohols **14**.
[b] Determined by chiral GC analysis on a Supelco β-Dex 120 column or chiral HPLC analysis on a Daicel Chiralcel OD column.
[c] Determined by comparison of the chiral GC/HPLC retention times with literature values.[12d,19]
[d] Determined from the 300 MHz $^1$H NMR spectrum of the crude silylated product.
[e] Configuration determined by analogy with alcohols **14a**.

bazole ligands in asymmetric Nozaki–Hiyama propargylation.[14b] For both reactions, the non-symmetric *tert*-butyl/benzyl-substituted ligand **8f** proved to be the optimal ligand and was applied successfully in the allylation and crotylation of a range of aryl and aliphatic aldehydes. The enantioselectivities obtained in allylation were up to 91% ee and in crotylation up to 92% with typical *syn:anti* ratios of up to 80:20. The results obtained compare favourably and in some cases improve upon the best results reported to date. These results also represent one of the few examples in the literature[20] where non-symmetric bis(oxazoline) ligands are utilized to induce high enantioselectivity in asymmetric catalysis. Studies are currently underway to elucidate the structures of the chromium-ligand complexes in an effort to determine the mechanism of the reaction and to fully explain the effect of the oxazoline substituents on the asymmetric induction.

## Experimental Section

### General

$^1$H NMR (300 MHz) spectra were recorded on a Varian Oxford 300 spectrometer at room temperature in $CDCl_3$ using tetra-

methylsilane (TMS) as an internal standard. Chemical shifts (δ) are given in parts per million and coupling constants are given as absolute values expressed in Hertz. All reactions were carried out under a nitrogen atmosphere in flame-dried Schlenk tubes. Thin layer chromatography (TLC) was carried out on plastic sheets pre-coated with silica gel 60 $F_{254}$ (Merck). Column chromatography separations were performed using Merck Kieselgel 60 (0.040–0.063 mm). GC analysis was performed using a Shimadzu GC-17A gas chromatograph equipped with a Shimadzu C-R3A chromatopac integrator and a Supelco β-Dex 120 chiral capillary column [30 m, 0.25 mm (diam.) × 0.25 μm] with helium as a carrier gas at 1.0 mL/min and a flame-ionizing detector. HPLC analysis was performed using a Shimadzu LC-2010A liquid chromatograph equipped with a Daicel Chiralcel OD or OD-H column (0.46 cm I. D. × 25 cm). HPLC grade hexane and isopropyl alcohol were used as the eluting solvents. THF was distilled from sodium/benzophenone ketyl. Acetonitrile was distilled from calcium hydride. DIPEA was distilled and stored over KOH under nitrogen. All aldehydes were distilled prior to use. Allyl bromide and crotyl bromide were purchased from Aldrich and distilled before use. Chlorotrimethylsilane was purchased from Aldrich and flushed through a small column of basic alumina (Brockmann, grade 1) immediately prior to use. All other reagents were purchased from Aldrich and were used as received.

### General Procedure for Catalytic Asymmetric Nozaki–Hiyama Allylation and Crotylation

A flame-dried Schlenk tube was charged with dry THF (1 mL) and dry ACN (150 μL). Anhydrous chromium(III) chloride (4.0 mg, 25.3 μmol) and manganese (41.7 mg, 0.76 mmol) were added together to the solvent mixture. The resulting suspension was allowed to stand at room temperature for approx. 10 min and was then stirred vigorously under an atmosphere of nitrogen for 1 h. This resulted in the disappearance of the characteristic purple colour of the chromium(III) salt and the formation of a white/grey suspension with a pale green supernatant. DIPEA (13 μL, 75.9 μmol) was then added followed by the bis(oxazoline) ligand **8** (30.4 μmol) resulting in an immediate deep green catalyst mixture. This was then stirred at room temperature for 1 h prior to the addition of the halide (0.51 mmol) with the resulting chromium(III)-allyl solution being stirred for a further 1 h. The reaction was then initiated by the addition of aldehyde (0.25 mmol) and chlorotrimethylsilane (64 μL, 0.51 mmol) and stirred under an atmosphere of nitrogen at room temperature for 16 h. The resulting green/brown suspension was quenched with saturated aqueous $NaHCO_3$ (1 mL) and extracted with $Et_2O$ (3 × 1 mL). The combined organic layers were then concentrated under vacuum to give a green residue. This was flushed through a small silica gel column (1.5 × 5 cm, pentane/AcOEt, 9:1) to remove the catalyst and after evaporation of the solvent, the reaction products were isolated as a yellow oil. The % conversion of the reaction was determined at this stage from the $^1$H NMR spectrum of the crude product (generally a mixture of silylated and free alcohol) by measuring the ratio of aldehyde to product and assuming that all aldehyde consumed went to product. The yellow oil was then dissolved in THF (1 mL), a few drops of aqueous 1 M HCl were added, and the resulting solution was stirred for 5 min when TLC (pentane/AcOEt, 9:1) showed complete desilylation. The solvent was removed under vacuum and the resulting aqueous phase was extracted with $Et_2O$ (3 × 2 mL). The organic layers were combined, dried over anhydrous $Na_2SO_4$ and concentrated under vacuum to give a yellow oil. This was then purified by flash column chromatography on silica gel (1 × 15 cm) using pentane/AcOEt (9:1) as the eluent to give the required product as a pale yellow oil.

Further experimental information and chromatographic data can be obtained in the Supporting Information.

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