# Synthesis of non-symmetric bis(oxazoline)-containing ligands and their application in the catalytic enantioselective Nozaki–Hiyama–Kishi allylation of benzaldehyde†

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We report the good to high-yielding three-step synthesis of non-symmetrical bis(oxazoline)-containing ligands possessing an *N*-thienylaniline unit. The convergent synthesis employed a palladium-catalysed aryl amination of 2-(2′-bromothiophene)nitrile as the key step, with sixteen ligands prepared in total. These ligands were subsequently applied in the chromium-catalysed enantioselective Nozaki–Hiyama–Kishi allylation of benzaldehyde with an optimal enantioselectivity of 73%.

## Introduction

Because of their ready availability, modular nature, and applicability in a wide range of metal-catalysed transformations, compounds containing a chiral oxazoline ring have become one of the most successful, versatile and commonly used classes of ligands for asymmetric catalysis.[1] The majority of these ligands are synthesised from commercially available chiral amino alcohols in a few high-yielding steps. Tridentate bis(oxazoline) ligands have been designed by incorporating a donor atom which links the two chiral oxazoline rings. Of particular interest to us are tridentate [*NNN*] bis(oxazoline) ligands (Fig. 1). Nishiyama's "pybox" ligand **1** has been used in various asymmetric reactions including Ru-catalysed cyclopropanation of olefins, Rh-catalysed hydrosilylation of ketones and Cu-catalysed allylic oxidation of olefins.[2] Zhang's "ambox" ligand **2** has resulted in excellent conversions and enantioselectivities in the Ru-catalysed transfer hydrogenation of aromatic ketones.[3] Nakada's bis(oxazolinyl)carbazole ligand **3b** provided enantioselectivities of up to 93% ee in the asymmetric allylation of benzaldehyde.[4]

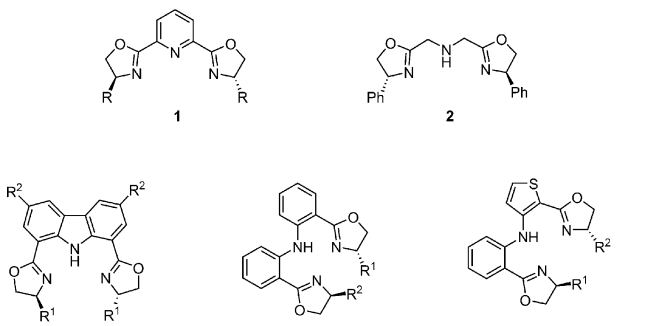


**Fig. 1**

We have previously reported the synthesis of ligand class **4** in which an *N*-phenylaniline unit links the two oxazoline rings, and their application in the enantioselective Nozaki–Hiyama–Kishi (NHK) allylation, crotylation and methallylation of a range of aromatic and aliphatic aldehydes.[5] The highest enantioselectivities in all three NHK processes were obtained utilising the non-$C_2$-symmetric ligand with *t*-Bu/Bn-substituted oxazolines, which, for example, afforded 99.5% ee in the methallylation of benzaldehyde. We wished to investigate further non-$C_2$-symmetric bis(oxazoline) ligands and thus designed ligand class **5** in which one of the arene rings is replaced by a thiophene in order to study the effect of this desymmetrisation of the ligand.

## Results and discussion

### Ligand synthesis

We envisaged using a similar synthetic strategy to that employed in the synthesis of ligand class **4**. Accordingly, we proposed that ligand class **5** could be synthesised by a three-step convergent synthesis with the key step being a palladium-catalysed aryl amination between 2-(2′-aminophenyl)oxazolines **8** and 2-(2′-bromothiophene)oxazolines **10**.

Accordingly, both **8** and **10** were prepared from the corresponding commercially available nitriles **6** and **9** by the reaction with the appropriate chiral amino alcohol in the presence of $ZnCl_2$ in yields of 65–80% (Scheme 1).[6]

We then attempted the palladium-catalysed aryl amination using **8a** (R = Bn) and **10** as the test coupling partners. The formation of an aryl–amine bond by the Pd-catalysed reaction of an aryl halide with an aryl/alkyl amine has been extensively studied by the groups of Buchwald and Hartwig and is a rapidly expanding area of research.[7] A range of Pd precursors, ligands, bases and solvents have been used in an attempt to increase yields, decrease reaction times, reduce diarylation and β-hydride elimination products and widen the substrate scope. Although functionalised thiophenes are useful precursors for pharmaceuticals and natural products, there are few reports of halothiophenes being applied as substrates in palladium-catalysed aryl aminations.[8]

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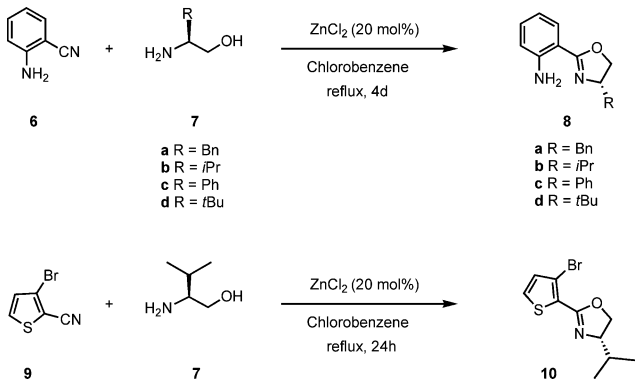
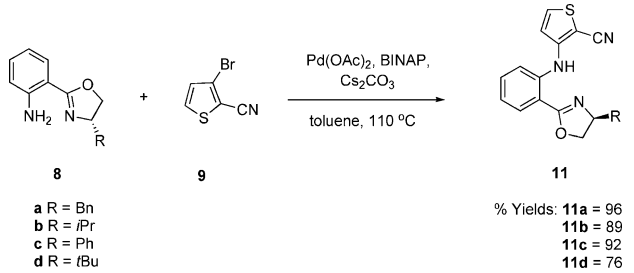


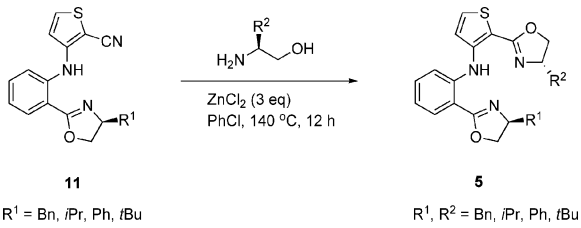

**Scheme 1**

We screened a range of Pd complexes of diphosphines and monophosphines, including the bulky, electron-rich biaryl ligands recently successfully applied in the aryl amination of chlorothiophene by Buchwald *et al*.[9] However, in each case the attempted coupling of **8a** and **10** failed to afford any of the desired product. We then proposed removing the oxazoline from **10** and instead attempting the aryl amination with its nitrile precursor **9** as we were encouraged by the recent report by Luker *et al.* who reported the aryl amination of **9** with $BuNH_2$ using BINAP and $Pd(OAc)_2$ with an isolated yield of 89% after 20 hours.[10] We thus coupled **8** and **9** under similar conditions and were pleased to find the reaction proceeded in high to excellent yields after 36 hours at 110 °C (Scheme 2).




**Scheme 2**

Conversion of the aryl amination products **11a–d** to the required bis(oxazoline)-containing ligands **5a–p** was carried out using $ZnCl_2$ and the appropriate amino alcohol (Scheme 3). These reactions proceeded in good to high yields (Table 1). This approach allows for the synthesis of non-symmetric ligands as with ligand class **4** and, in addition, offers the opportunity for the selective placement of different substituents on both oxazoline rings. This




**Scheme 3**

would allow us to investigate the effect on enantioselectivity of having a particular substituent on the arylamine or thienylamine oxazoline ring (*e.g.* comparing **5e** *versus* **5f**, **5g** *versus* **5h**, *etc.*).

## Application in catalysis: the asymmetric Nozaki–Hiyama–Kishi reaction

The Nozaki–Hiyama–Kishi reaction was first reported in the late 1970's and has proven to be a highly versatile procedure for the formation of C–C bonds involving the nucleophilic addition to carbonyl compounds of intermediate organochromium(III) reagents. These reagents are typically generated *in situ* from the insertion of chromium(II) species into allyl, alkenyl, alkynyl, propargyl and aryl halides or sulfonates.[11] A number of unique and important features, including pronounced chemoselectivity for reactions with aldehydes in the presence of ketones and an unprecedented compatibility with numerous functional groups in both reaction partners, has led to the reaction being utilised in the synthesis of many complex natural products. Two such examples are the total synthesis of palytoxin and halichondrin B which both involve extensive use of chromium additions.[12]

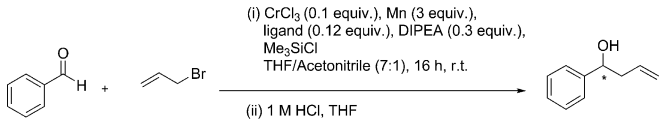
The development of the asymmetric Nozaki–Hiyama-–Kishi reaction has recently been reviewed[13] and to date a limited range of ligand classes have been tested in this reaction, with the most promising examples emerging from the groups of Yamamoto,[14] Sigman,[15] Cozzi and Umani-Ronchi,[16] Nakada,[4] Berkessel,[17] Kishi[18] and ourselves.[5,19] Our new ligand class **5** was applied in the chromium-catalysed reaction of allyl bromide with benzaldehyde (Table 2).

Our previous studies have shown that the optimal reaction conditions for allylation require THF–acetonitrile (7 : 1) as the solvent and *N*,*N*-diisopropylethylamine as the base. The reactions proceeded cleanly under these conditions with high conversions after 16 hours at room temperature. Of the ligands possessing identical oxazoline substituents (**5a–d**), the highest enantioselectivity of 63% (*S*) was obtained with the bis(isopropyl) oxazolines **5b** (entry 2). This substitution also provided the highest enantioselectivities in our original ligand class **4**.[5b] Of the ligands

**Table 1** Conversion of **11a–d** to **5a–p**

| Entry | Ligand | $R^1$ | $R^2$ | Yield (%) | Entry | Ligand | $R^1$ | $R^2$ | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **5a** | Bn | Bn | 70 | 9 | **5i** | *t*-Bu | i-Pr | 68 |
| 2 | **5b** | i-Pr | i-Pr | 74 | 10 | **5j** | i-Pr | *t*-Bu | 69 |
| 3 | **5c** | Ph | Ph | 78 | 11 | **5k** | i-Pr | Ph | 72 |
| 4 | **5d** | *t*-Bu | *t*-Bu | 56 | 12 | **5l** | Ph | i-Pr | 71 |
| 5 | **5e** | Ph | Bn | 71 | 13 | **5m** | *t*-Bu | Ph | 65 |
| 6 | **5f** | Bn | Ph | 70 | 14 | **5n** | Ph | *t*-Bu | 67 |
| 7 | **5g** | *t*-Bu | Bn | 69 | 15 | **5o** | Bn | i-Pr | 73 |
| 8 | **5h** | Bn | *t*-Bu | 75 | 16 | **5p** | i-Pr | Bn | 76 |

**Table 2** Application of ligands **5** in NHK allylation of benzaldehyde

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| Entry | Ligand | $R^1$ | $R^2$ | Conv.[a] (%) | Yield[b] (%) | Ee[c] (%) (Conf.)[d] |
|---|---|---|---|---|---|---|
| 1 | **5a** | Bn | Bn | 80 | 78 | 8 (*S*) |
| 2 | **5b** | i-Pr | i-Pr | 82 | 78 | 63 (*S*) |
| 3 | **5c** | Ph | Ph | 80 | 72 | 38 (*S*) |
| 4 | **5d** | *t*-Bu | *t*-Bu | 83 | 79 | 22 (*R*) |
| 5 | **5e** | Ph | Bn | 75 | 73 | 12 (*R*) |
| 6 | **5f** | Bn | Ph | 88 | 75 | 13 (*S*) |
| 7 | **5g** | *t*-Bu | Bn | 88 | 83 | 73 (*R*) |
| 8 | **5h** | Bn | *t*-Bu | 85 | 82 | 62 (*R*) |
| 9 | **5i** | *t*-Bu | i-Pr | 84 | 76 | 48 (*R*) |
| 10 | **5j** | i-Pr | *t*-Bu | 78 | 70 | 35 (*S*) |
| 11 | **5k** | i-Pr | Ph | 90 | 87 | 43 (*R*) |
| 12 | **5l** | Ph | i-Pr | 82 | 79 | 32 (*R*) |
| 13 | **5m** | *t*-Bu | Ph | 85 | 78 | 49 (*R*) |
| 14 | **5n** | Ph | *t*-Bu | 82 | 78 | 13 (*S*) |
| 15 | **5o** | Bn | i-Pr | 100 | 90 | 33 (*S*) |
| 16 | **5p** | i-Pr | Bn | 91 | 84 | 15 (*R*) |

[a] Determined from the 300 MHz $^1$H NMR spectrum of the crude silylated product. [b] Isolated yields of the allylic alcohol **14**. [c] Determined by chiral HPLC analysis of the alcohol product **14** using a Daicel Chiralcel OD column. [d] Determined by comparison of the chiral HPLC retention times with literature values.[12]

with different oxazoline substituents (**5e-p**) the best enantioselectivities of 73% (*R*) and 62% (*R*) (entries 7,8) were achieved with the ligands containing the benzyl/*tert*-butyl substituted oxazolines (**5g**, **5h**), again following the trend observed in allylation studies employing ligand class **4**. It is clear from the results obtained herein that the magnitude of stereoinduction changes when $R^1$ and $R^2$ are reversed, reflecting both the steric and electronic effects of the aromatic rings. Interestingly, the sense of stereoinduction is maintained only when the oxazoline substituents are *tert*-butyl/benzyl- and isopropyl/phenyl-containing.

Ideally a proposal to explain the asymmetric induction observed would be strengthened by obtaining an X-ray structure of a chromium–ligand **5** complex. However, despite many attempts we have not yet obtained such a structure although we have obtained an X-ray structure of a zinc complex of the related bis{2-[(4*S*)-4-*tert*-butyl-4,5-dihydrooxazol-2-yl]phenyl}methylamine ligand **4** ($R^1$, $R^2$ = *t*-Bu).[20] That complex shows that only the oxazoline nitrogen atoms were coordinated and we propose a similar binding mode of chromium to ligand **5g**. In the absence of coordination through the secondary amine unit, the role of DIPEA is important as results obtained in its absence show lowered levels of enantioselectivities. In addition we believe that only one ligand is coordinated in the active complex as a two-fold excess of ligand was found to lead to a diminution of enantiomeric excesses. However, an accurate picture of the precise coordination sphere around chromium is still unavailable for the ligands reported herein and related bis(oxazoline)-containing ligand systems.

## Conclusion

A new class of bis(oxazoline)-containing ligands **5** has been prepared in good yield. Although Pd-catalysed aryl amination between 2-(2′-aminophenyl)oxazolines **8a–d** and 2-(2′-bromothiophene)oxazoline **10** was unsuccessful, the ligand class was accessed in an alternative synthetic strategy by coupling 2-(2′-aminophenyl)oxazolines **8a–d** and 2-(2′-bromothiophene)nitrile **9**. This is one of the few examples reported to date where a substituted thiophene has been successfully employed as a substrate in aryl aminations. Subsequent $ZnCl_2$-mediated reaction of intermediates **11a–d** furnished ligand class **5** in good to high yields. The synthetic route allowed for the synthesis of non-symmetric bis(oxazoline)-containing ligands possessing either identical or different oxazoline substituents and the option for selective placement of substituents on each oxazoline ring. The ligands were applied in the chromium-catalysed enantioselective allylation of benzaldehyde with excellent conversions and good enantioselectivities of up to 73% being observed. Our results again highlight the significant effect that the substituents on the oxazoline rings have on both the magnitude and sense of asymmetric induction. The application of these ligands in other chromium-catalysed processes will be reported in due course from these laboratories.

## Experimental

### General experimental

$^1$H NMR (300 and 400 MHz) and $^{13}$C (75 and 100 MHz) spectra were recorded on Varian Oxford 300 or 400 spectrometers at room temperature in $CDCl_3$ using tetramethylsilane as an internal standard. Chemical shifts ($\delta$) are given in parts per million and coupling constants are given as absolute values expressed in Hertz. HRMS were obtained using a Micromass/Waters LCT instrument. Infra-red spectra were recorded on a Perkin-Elmer infra-red FT spectrometer. Optical rotation values were measured on a Perkin-Elmer 343 polarimeter at room temperature.

 

Melting points were determined in open capillary tubes in a Gallenkamp melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was carried out on plastic sheets pre-coated with silica gel 60 F254 (Merck). Column chromatography separations were performed using Merck Kieselgel 60 (0.040–0.063 mm). HPLC analysis was performed on an LC 2010A machine equipped with a UV–vis detector employing a Chiracel® OD column from Daicel Chemical Industries. All reagents were purchased from Sigma-Aldrich and used as received. Solvents were dried before use by distillation from standard drying agents. Anhydrous chlorobenzene was purchased from Sigma-Aldrich and used without further purification. $ZnCl_2$ (Sigma-Aldrich) and $CrCl_3$ were flame-dried under vacuum immediately prior to use.

General procedures for the two key steps of ligand syntheses will be described and physical data of a typical product per step (**11a** and **5a**) are given. Physical data for all other products (**11a–d** and **5b–p**) are available in the electronic supplementary information†. The general procedure employed for the Nozaki–Hiyama–Kishi allylation of benzaldehyde is described below.

### General procedure for the screening of conditions for palladium-catalysed aryl aminations

To an oven-dried Radleys® tube was added 2-(*o*-aminophenyl)-oxazoline **8a** (0.60 mmol), 3-(bromo-thiophene)oxazoline **10** (0.50 mmol), base (0.60 mmol), ligand (0.05 mmol) and palladium precursor (0.025 mmol Pd). Dry degassed solvent (1.5 mL) was added and the reaction was stirred under an atmosphere of nitrogen at the required temperature for 7 days. The reaction mixture was cooled to room temperature, solvent was removed *in vacuo* and the resulting brown oil was passed through a short pad of silica using pentane–ethyl acetate as eluent. The solvent was removed *in vacuo* and a $^1$H NMR spectrum obtained to determine if any aryl–amine product had formed.

### General procedure for the palladium-catalysed aryl amination of 2-(2-aminophenyl)oxazoline 8a–d and 3-bromothiophene-2-carbonitrile 9

An oven-dried Radleys® tube was charged with 3-bromothiophene-2-carbonitrile **9** (188 mg, 1.00 mmol), 2-(*o*-aminophenyl)-oxazoline **8a–d** (1.20 mmol), 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) (62.3 mg 0.10 mmol), $Pd(OAc)_2$ (22.4 mg, 0.10 mmol) and cesium carbonate (456 mg, 1.4 mmol). After the addition of dry, degassed toluene (10 mL) *via* syringe, the tube was capped under an atmosphere of nitrogen and the reaction mixture was heated at 120 °C for 36–48 hours, with monitoring by TLC. On completion, the dark orange–brown reaction mixture was cooled to room temperature and concentrated *in vacuo* to give a brown oil which was purified by column chromatography on silica gel.

### {2[(4*S*)-4-Benzyl-4,5-dihydrooxazol-2-yl]phenyl}(thiophene-2-carbonitrile)amine 11a

Yield: 96% (0.35 g), pale orange oil; TLC: $R_f$ = 0.60 ($CH_2Cl_2$); $[a]_D$ = +55.2 ($c$ = 0.90 in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.72 (dd, $J$ = 13.8, 8.1 Hz, 1H, C$H_2$Ph), 3.14 (dd, $J$ = 13.8, 5.6 Hz, 1H, C$H_2$Ph), 3.99 (m, 1H, C$H_2$O), 4.22 (m, 1H, C$H_2$O), 4.59 (m, 1H, C$H$N), 6.80 (m, 1H, Ar-$H$C(2)), 7.09–7.36 (2 × m, 9H, Ar-$H$C(3), Ar-$H$C(4), Ar-$H$C(4′), Ar-$H$C(5′), Ar-$H$C(phenyl)), 7.70 (dd, $J$ = 7.9, 1.5 Hz, 1H, Ar-$H$C(1)), 11.43 (br s, 1H, NH); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 41.9 ($CH_2$Ph), 68.0 ($C$HN), 70.7 ($CH_2$O), 91.6 (Ar-$C$(2′)), 112.0 ($C$≡N), 114.5 (Ar-$C$(5)), 114.8 (Ar-H$C$(3), Ar-H$C$(4), Ar-H$C$(4′), Ar-H$C$(5′), Ar-H$C$(phenyl), 119.6 (Ar-H$C$(2)), 121.0, 126.7, 128.8, 129.5 (Ar-H$C$(3), Ar-H$C$(4), Ar-H$C$(4′), Ar-H$C$(5′), Ar-H$C$(phenyl), 130.2 (Ar-H$C$(1)), 132.0, 132.4 (Ar-H$C$(3), Ar-H$C$(4), Ar-H$C$(4′), Ar-H$C$(5′), Ar-H$C$(phenyl), 138.0 (*ipso*-Ph), 143.6 (Ar-$C$(6)), 150.6 (Ar-$C$(3′), 163.9 ($C$=N); IR ($CHCl_3$ film): $\nu$ = 1420, 1466, 1554, 1633, 2105, 2204, 3027, 3115 cm$^{-1}$; HRMS (ES$^+$) calculated for $C_{21}H_{18}N_3OS$ [M + H]$^+$: 360.1171, found: 360.1161.

### General procedure for the synthesis of ligands 5a–p

To a flame-dried Schlenk tube was added **11a–d** (0.40 mmol), the required amino alcohol (0.80 mmol, 2 equiv.) and flame-dried $ZnCl_2$ (163 mg, 1.20 mmol, 3 equiv.) under an atmosphere of nitrogen. Anhydrous chlorobenzene (5 mL) was added *via* syringe and the resulting mixture was stirred at 145 °C for 12 hours. The reaction was cooled to room temperature and solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel to yield pure product.

### {2-[(4*S*)-4-Benzyl-4,5-dihydrooxazol-2-yl]-phenyl}{2-[(4*S*)-4-benzyl-4,5-dihydrooxazol-2-yl]-thiophene-3-yl}amine 5a

Yield: 61% (0.21 g), pale yellow solid; mp: 50–54 °C; TLC: $R_f$ = 0.50 (pentane–ethyl acetate 5 : 1); $[a]_D$ = +87.7 ($c$ = 0.80 in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.60–2.73 (m, 2H, C$H_2$Ph), 3.08–3.19 (m, 2H, C$H_2$Ph), 3.88–3.98 (m, 2H, C$H_2$O), 4.16 (dd, $J$ = 18.3, 9.2 Hz, 2H, C$H_2$O), 4.38 (t, $J$ = 6.3 Hz, 1H, C$H$N), 4.47 (t, $J$ = 7.1 Hz, 1H, C$H$N), 6.79 (t, $J$ = 6.7 Hz, 1H, Ar-$H$C(2)), 7.14–7.32 (m, 14H, Ar-$H$C(3), Ar-$H$C(4), Ar-$H$C(4′), Ar-$H$C(5′), Ar-$H$C(phenyl)), 7.72 (d, $J$ = 7.6 Hz, 1H, Ar-$H$C(1)), 10.87 (br s, 1H, N$H$); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 40.8 ($CH_2$Ph), 40.9 ($CH_2$Ph), 66.8 ($C$HN), 67.0 ($C$HN), 69.3 ($CH_2$O), 70.5 ($CH_2$O), 107.4 (Ar-$C$(2′)), 112.0 (Ar-$C$(5)), 115.2 (Ar-H$C$(3), Ar-H$C$(4), Ar-H$C$(4′), Ar-H$C$(5′), Ar-H$C$(phenyl)), 118.0 (Ar-H$C$(3), Ar-H$C$(4), Ar-H$C$(4′), Ar-H$C$(5′), Ar-H$C$(phenyl)), 120.1 (Ar-H$C$(2)), 124.2, 125.3, 125.4, 127.0, 127.2, 127.4, 128.0, 128.2, 128.3, 129.0 (Ar-H$C$(3), Ar-H$C$(4), Ar-H$C$(4′), Ar-H$C$(5′)), 130.7 (Ar-H$C$(1)), 136.9 (*ipso*-Ph), 137.2 (*ipso*-Ph), 142.7 (Ar-$C$(6), Ar-$C$(3′)), 142.9 (Ar-$C$(6), Ar-$C$(3′)), 158.7 ($C$=N), 162.0 ($C$=N); IR ($CHCl_3$ film): $\nu$ = 1412, 1557, 1584, 1633, 2360, 2924, 3026 cm$^{-1}$; HRMS (ES$^+$) calculated for $C_{30}H_{27}N_3O_2S$ [M + H]$^+$: 494.1884, found: 494.1878.

### General procedure for the Nozaki–Hiyama–Kishi allylation of benzaldehyde

A flame-dried Schlenk tube was charged with dry THF (1 mL) and dry acetonitrile (150 μL). Anhydrous chromium(III) chloride (4.0 mg, 25.3 μmol) and manganese (41.7 mg, 0.76 mmol) were added simultaneously to the solvent mixture. The resulting suspension was allowed to stand at room temperature for approximately 30 minutes until the characteristic purple colour of the chromium(III) salt disappeared. The mixture was stirred vigorously under an atmosphere of nitrogen for 1 h resulting in a green reaction mixture. DIPEA (13 μL, 75.9 μmol) was added followed by the ligand **5** (30.4 μmol) resulting in an immediate green catalyst

mixture. This was stirred at room temperature for 1 hour prior to the addition of the allyl bromide (0.51 mmol) with the resulting chromium(III) allyl solution being stirred for a further 1 hour. The reaction was 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 hours. 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 concentrated *in vacuo* 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 $^1H$ 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. Peaks consistent with the product of pinacol coupling were not observed in any of the catalytic studies employing ligands **5**. The yellow oil was dissolved in THF (1 mL), a few drops of aqueous 1 M HCl were added, and the resulting solution was stirred for 10 min when TLC (pentane–AcOEt 9 : 1) showed complete desilylation. The solvent was removed *in vacuo* 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 *in vacuo* to give a yellow oil. This was purified by flash column chromatography on silica gel (1 × 15 cm) using cyclohexane–AcOEt 5 : 1 as the eluent to give the required product as a pale yellow oil. Enantioselectivity was determined by HPLC: Chiralcel OD, hexane–isopropanol 98 : 2, flow rate 0.3 mL $min^{-1}$: (*R*) 35.1 min, (*S*) 41.7 min.

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