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A new class of nitrogen based chiral ligands: 2*H*-1,3-benzoxazines. Ligand synthesis, X-ray structural studies and asymmetric catalysis

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Abstract

A new class of chiral ligands, e.g., (−)-**9**, based on the benzoxazine nucleus, has been designed and synthesized in three steps from the commercially available starting materials salicylamide and (−)-menthone. Application of (−)-**9** in the palladium catalyzed-allylic substitution of 1,3-diphenyl-2-propenylacetate with dimethyl malonate gave enantioselectivities of up to 62%ee. Ees of 42% and 20% in asymmetric hydrosilylations and diethylzinc additions, respectively, were also obtained.
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Keywords: 2*H*-1,3-benzoxazines; Ligand; Crystal structures; Enantioselective; Allylation; Diethylzinc addition; Hydrosilylation

1. Introduction

Chiral oxazolines and their derivatives comprise an intensively studied class of chiral nitrogen donor ligands due to the high enantioselectivities they confer in a range of reactions [1,2]. The mechanism of these reactions and the characterization of precursors and intermediate metal species have also been studied in depth. On the other hand, the preparation of analogous *oxazine*-based ligands has only recently been reported (Fig. 1) [3].

Indeed, only one benzoxazine-based chiral ligand – a 4*H*-benzoxazine bearing a phosphine group (**3**) has been reported [3]. Here we introduce a new class of ligands, containing a 2*H*-benzoxazine skeleton and a pyridyl moiety. The general structure of these new ligands is shown below (Fig. 2). Specifically, the C-2 chiral centre in benzoxazine based ligands is closer to metal than the chiral centre in the oxazoline-based ligands [3]. and these new structures have considerable potential as ligands for asymmetric catalysis as: (a) the chiral centre is slightly closer to the coordinated metal [3] than is the case for corresponding oxazoline complexes; (b) the electronics are fine tuneable through the benzene and pyridine rings; (c) the benzene rings offer obvious sites for attachment to solid supports.

In principle, ligand **4** could be synthesized in 3 steps from commercially available salicylamide and a wide range of aldehydes or ketones. Benzoxazinones such as **6** have been prepared before through condensation of salicylamide with a ketone using either acid or base catalysis under Dean–Stark conditions [4]. Chiral 2*H*-1,3-benzoxazinones **6** (R or $R'' \neq H$) should be accessible be from chiral ketones, e.g., (−)-menthone. Negishi-type Pd-catalyzed cross-coupling of the corresponding enol triflate **5** with 2-pyridylzinc chloride and its related derivatives should give the ligands **4** (Scheme 1).

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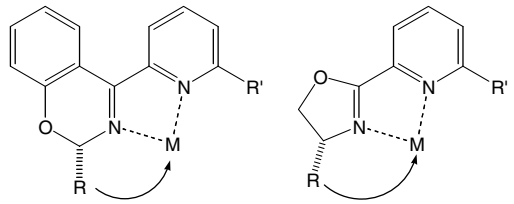
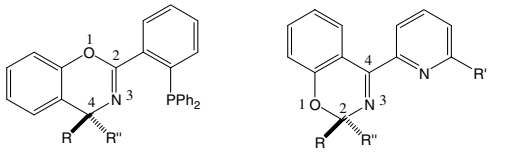


1 **2**

Fig. 1.



4*H*-Benzoxazine, **3** (Kündig) [R=H, R''= *i*-Pr, *t*-Bu]

2*H*-Benzoxazine, **4** (this work) [R=R'≠ H]

Fig. 2.

2. Results and discussion

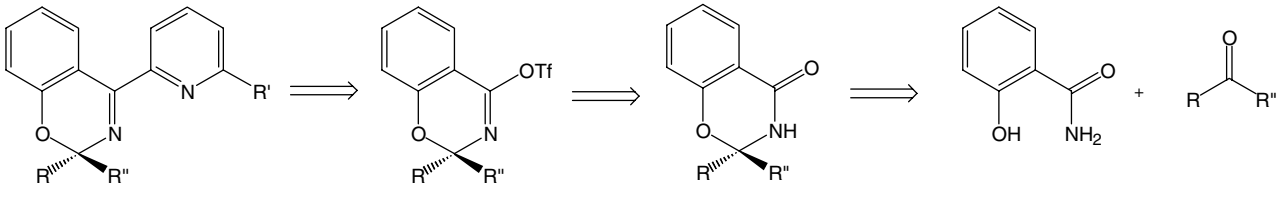
2.1. Preparation of the chiral ligands *9* and *10*

Synthesis of the new ligands is described in Scheme 2. 2*H*-1,3-benzoxazinone (**7**) was obtained by condensation of salicylamide with (−)-menthone. The condensation was carried out at reflux in the presence of Conc. H_2SO_4 using chloroform as solvent. **7** was obtained as a mixture with isomeric **11** in a 3:2 ratio. In contrast, when the reaction was carried out in toluene, isomers **7** and **11** were obtained in a 1:1 ratio. **7** was separated from its isomer **11** by flash chromatography [5]. Triflate **8** was obtained in quantitative yield by reacting compound **7** with triflic anhydride and freshly distilled 2,6-lutidine in dry dichloromethane [6]. The crude triflate **8** was used in the next step without further purification. Palladium catalysed cross-coupling of the triflate **8** with 2-pyridylzinc or 6-methyl-2-pyridylzinc halide (e.g., chloride or bromide) gave the chiral ligands **9** and **10**, respectively, as well as the by-product **12**.

Optimisation of the conditions in the palladium catalysed cross-coupling step by employing diethylether as solvent instead of using THF [6] as well as refluxing overnight provided better yields (from 42% to 75%) and fewer by-products. An X-ray crystal structure analysis of **12** confirmed the proposed structure (Fig. 3). Remarkably the isomerization of **8** proceeds with complete retention of stereochemistry.

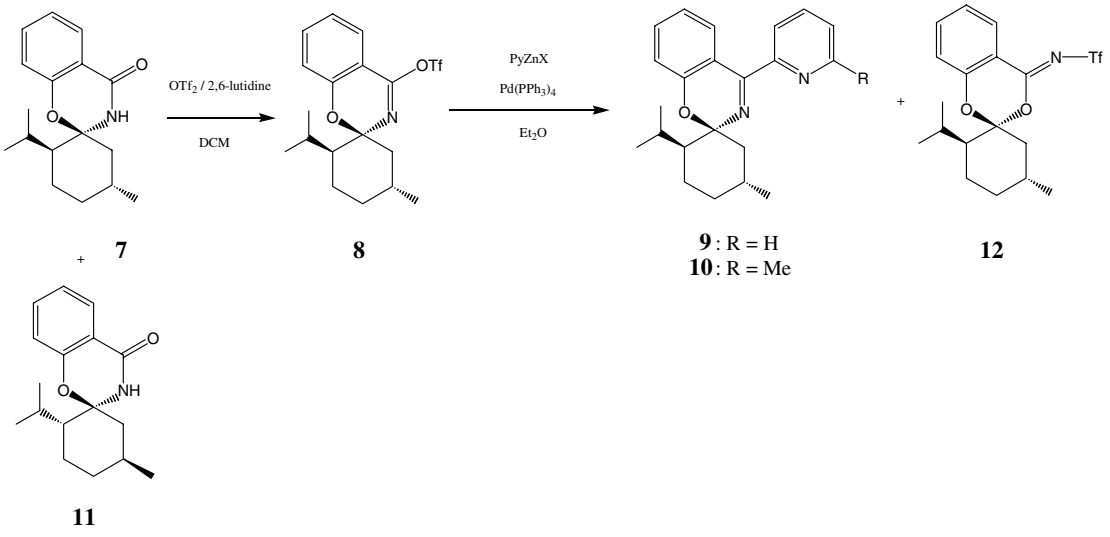
2.2. Preparation of a zinc complex of compound *9*

The potential for compound **9** to act as a ligand was investigated by treating **9** with zinc chloride in dry THF.



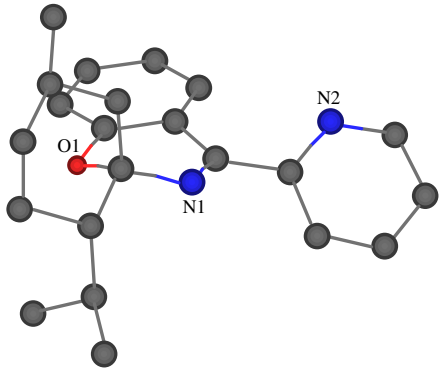
4 **5** **6**

Scheme 1. Retrosynthesis of chiral ligand **4**.

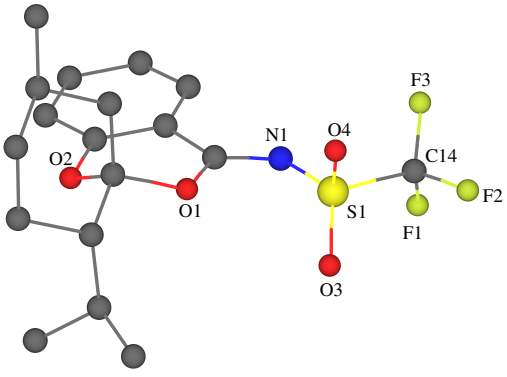


7 **8** **9**: R = H; **10**: R = Me **12** **11**

Scheme 2. Synthesis of the chiral ligands **9** and **10**.

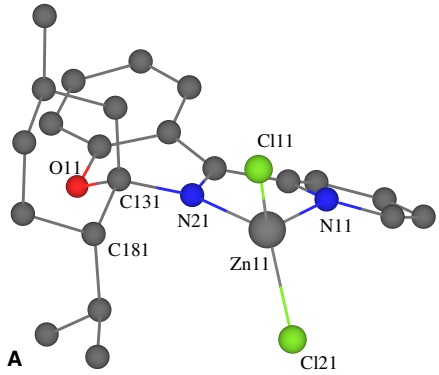


Chiral ligand **9**



By-product **12**

Fig. 3. X-ray crystal structure of chiral ligand **9** and by-product **12**, hydrogen atoms have been omitted for clarity.



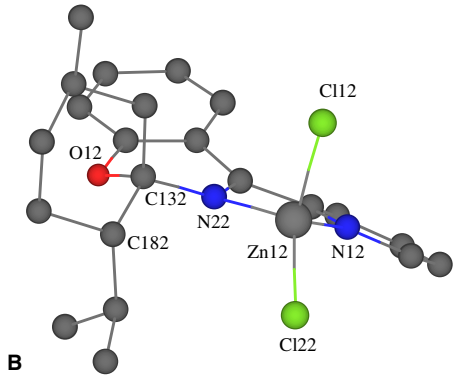


Fig. 4. Two independent molecules **A** and **B** of [$ZnCl_2$-**9**]. Selected bond lengths (Å) and angles (°), hydrogen atoms have been omitted for clarity: Zn(11)–N(11) = 2.051(3), Zn(11)–N(21) = 2.099(3), Zn(11)–Cl(21) = 2.2045(12), Zn(11)–Cl(11) = 2.2181(11), N(21)–C(131) = 1.473(4), N(21)–C(131)–C(181) = 108.9(3), N(11)–Zn(11)–N(21) = 79.41(11), N(11)–Zn(11)–Cl(21) = 115.02(10), N(21)–Zn(11)–Cl(21) = 122.81(8), N(11)–Zn(11)–Cl(11) = 110.50(9), N(21)–Zn(11)–Cl(11) = 108.09(9), Cl(21)–Zn(11)–Cl(11) = 115.58(4), for molecule **A**; Zn(12)–N(22) = 2.065(3), Zn(12)–N(12) = 2.070(3), Zn(12)–Cl(22) = 2.1983(10), Zn(12)–Cl(12) = 2.2092(10), N(22)–C(132) = 1.495(4), N(22)–C(132)–C(182) = 108.5(3), N(22)–Zn(12)–N(22) = 79.85(11), N(22)–Zn(12)–Cl(22) = 106.88(8), N(12)– Zn(12)–Cl(22) = 122.35(9), N(22)–Zn(12)–Cl(12) = 121.41(9), N(12)–Zn(12)–Cl(12) = 101.70(9), Cl(22)–Zn(12)–Cl(12) = 119.20(4) for molecule **B.**

After stirring overnight the solvent was removed in a vacuum leaving a yellow powder. The product was analysed by ^1H and ^{13}C NMR spectroscopy and elemental analysis and was found to be the zinc complex, $ZnCl_2$-**9**. Crystals of $ZnCl_2$-**9** suitable for X-ray diffraction were grown from a solution of the complex in methanol. An X-ray structure was obtained and is displayed in Fig. 4. The geometry at the metal centre was found to be tetrahedral and as anticipated **9** was found to act as a bidentate ligand binding to the metal through the pyridyl and imino nitrogens.

The angles at N(21)–C(131)–C(181) and N(22)–C(132)–C(182) of molecules **A** and **B** are 108.9(3) and 108.5(3) which are significantly smaller than the corresponding angles found in related oxazoline ligands (about 113°) [7]. This confirms that the substituent attached to the stereogenic centre in benzoxazine-based ligands is closer to the metal centre than is the case for oxazoline-based ligands.

2.3. Preliminary evaluation of 2H-1,3-benzoxazines in asymmetric transformations

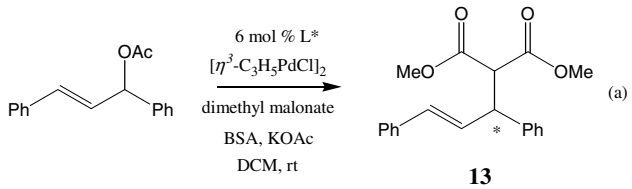
2.3.1. Asymmetric allylic alkylation

The chiral ligands **9** and **10** were first evaluated in asymmetric allylations. Allylic substitution of *rac*-1,3-diphenyl-2-propenyl acetate was performed in dichloromethane at room temperature in the presence of a (π-allyl)palladium-ligand complex generated in situ from 2.5 mol% of bis[(π-allyl)palladium chloride] and 5 mol% of the appropriate ligand. The nucleophile was generated from dimethylmalonate in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and a catalytic amount of KOAc (Eq. (a)). The results showed that the chiral ligand **9** afforded higher enantioselectivity than chiral ligand **10**. To our surprise, ligand **10** led to (*S*) selectivity with 40%ee, whereas ligand **9** gave the (*R*) selectivity with 62%ee (Table 1). Further studies are under way to elucidate the influence of pyridyl substituents on the stereoselectivities of this process.

2.3.2. Asymmetric diethylzinc addition

Table 2 summarised the enantioselectivities obtained from the addition of diethylzinc to benzaldehyde under

Table 1
Enantioselective allylic alkylation of *rac*-1,3-diphenyl-2-propenyl acetate with dimethylmalonate catalyzed by chiral ligands **9** and **10** according to Eq. (a)

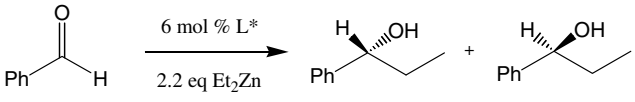


13

Ligand	Yield[a] (%)	Configuration[b]	%ee[c]
9	95	*S*	62
10	80	*R*	40

[a] Conversion determined by ^{1}H NMR spectroscopy.
[b] Major enantiomer of the adduct (absolute configuration from the elution order in HPLC).
[c] Enantiomeric excess determined by chiral chromatography (Diecel Chiracel OD-H column).

Table 2
Enantioselective addition of diethylzinc to benzaldehyde



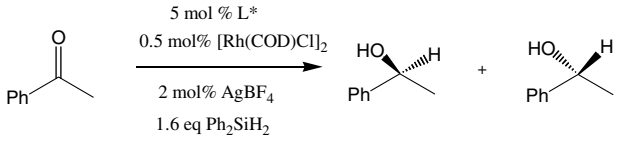
(*R*)-**14** (*S*)-**14**

Ligand[a]	Temperature (°C)	Yield[b] (%)	Configuration[c]	%ee[d]
9	rt	80	*R*	16
9	0	75	*R*	20
10	0	90	*R*	11

[a] In hexane–toluene, 6 mol% chiral ligand.
[b] Conversion determined by ^{1}H NMR spectroscopy.
[c] Major enantiomer of the 1-phenyl-1-propanol product (absolute configuration from the elution order in HPLC).
[d] Enantiomeric excess determined by chiral chromatography (Diecel Chiracel OD-H column).

catalysis with chiral ligands **9** and **10**. Highest enantioselectivity was obtained with chiral ligand **9** (20%ee, entry 2 in Table 2).

2.3.3. Asymmetric hydrosilylation



The hydrosilylation of acetophenone was carried out neat under standard conditions [2] with $[Rh(cod)Cl]_2$ (cod = cyclooctadiene) complex. Diphenylsilane was used as a hydrosilylation agent with 5 mol% of the chiral ligand **9**. Hydrosilylation proceeded slowly (4 days) to give the diphenylsilyl ether of 1-phenylethanol in moderate yield (60% conversion) with 42%ee of the (*S*)-isomer.

In this preliminary report we have disclosed a simple route to a new class of ligands. Initial experiments indicate that these ligands form metal complexes which deliver moderate enantioselectivities in several asymmetric processes. Optimisation of these new ligand structures for asymmetric synthesis is continuing and will be reported on again shortly.

3. Experimental

3.1. General

Elemental analyses were performed by Chemical & Micro analytic Services, Essendon North, Victoria or University of Otago, Dunedin, New Zealand. The ^{1}H and ^{13}C NMR spectra were recorded on either a 400 Mz Bruker Avance DRX 400 or a 300 Mz Varian Mercury spectrometer. The spectra were referenced using residual protonated solvent as an internal standard applying $CDCl_3$ ^{1}H NMR = 7.26 ppm and ^{13}C = 77.36 ppm. High resolution mass spectra (HRMS) for accurate mass determinations were recorded on a Bruker BioApex 47e FTMS fitted with an Analytica electrospray source using NaI for accurate mass calibration.

3.2. Ligand synthesis

3.2.1. Preparation of (1S,4R,2′R)-(−)-4′-(trifluoromethanesulfonyloxy)spiro[menthane-2,2′-benzo[e][1,3]oxazine(2H)], **8** [6]

Trifluoromethanesulfonic anhydride (185 μl, 1.1 mmol) was added dropwise to a solution of compound **7** (200 mg, 0.73 mmol) in dry dichloromethane (8 ml) under a nitrogen atmosphere at −78 °C and the mixture was stirred for 40 min. Then fresh distilled 2,6-lutidine (128 μl, 1.1 mmol) was added dropwise and stirred for 30 min. The reaction was quenched with saturated $NaHCO_3$ solution (10 ml) and extracted with dichloromethane (20 ml), dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure to give the *title compound* **8** as a brown oil. This was used in the next step without further purification. HRMS Calc. (found) for $C_{18}H_{21}F_3NO_4S$ ($M - H^+$): *m/z* 404.1143 (404.1170). ^1H NMR [300 MHz, $CDCl_3$]: δ 0.85 (6H, d, $J = 6.9$ Hz), 0.95 (3H, d, $J = 6.9$ Hz), 1.02 (1H, m), 1.28 (1H, t), 1.60 (3H, m), 1.80 (2H, m), 2.35 (2H, m), 6.85 (1H, d, $J = 8.1$ Hz), 6.95 (1H, t, $J = 7.8$ Hz), 7.36 (1H, d, $J = 7.8$ Hz), 7.43 (1H, dd, $J = 1.5$ and 7.5 Hz). ^{13}C NMR [75 MHz, $CDCl_3$]: δ 18.24, 22.25, 23.38, 23.90, 26.49, 28.72, 35.09, 47.73, 51.70, 98.19, 109.51, 112.37, 136.35, 150.07, 157.30.

3.2.2. Preparation of (1S,4R,2′R)-(−)-4′-(2-pyridyl)spiro[menthane-2,2′-benzo[e][1,3]oxazine(2H)], **9** [6]

A 1.6 M *n*-BuLi hexane solution (5.62 ml, 8.99 mmol) was added dropwise to a solution of 2-bromopyridine (703 μl, 7.37 mmol) in dry Et_2O (40 ml) under a nitrogen atmosphere at −78 °C. The reaction mixture was stirred at this temperature for 2 h. To this mixture was added a solution of $ZnCl_2$ (2 g, 14.97 mmol) in dry Et_2O (20 ml) at −78 °C then the reaction mixture was warmed up to 0 °C and stirred at this temperature for 1 h. A solution of $Pd(PPh_3)_4$ (207 mg, 0.18 mmol) in dry Et_2O was added dropwise to the mixture, follow by a solution compound **8** (from previous step) in dry Et_2O and the reaction mixture was refluxed overnight. The reaction was quenched with saturated $NaHCO_3$ (20 ml) and extracted with dichloromethane (3×50 ml). The combined extract was washed with brine (10 ml), dried over anhydrous $MgSO_4$ and concentrated in a vacuum to give a brown oil as a crude product. The crude product was purified by flash chromatography (EtOAc/hexane 1:8) to give the *title compound* (−)-**9**. Yield: 1.54 g, 75%; m.p., 105–107 °C. $[\alpha]_D^{25}$ (C = 1, $CHCl_3$): −341 Anal. Calc. (found) for $C_{22}H_{26}N_2O$: C, 79.00 (79.21); H, 7.84 (8.02); N, 8.38 (8.58). HRMS Calc. (found) for $C_{22}H_{27}N_2O$ ($M + H^+$): *m/z* 335.2045 (335.2118). ^1H NMR [400 MHz, $CDCl_3$]: δ 0.84 (3H, d, $J = 6.4$ Hz,), 0.89 (3H, d, $J = 6.9$ Hz), 0.96 (3H, d, $J = 7.0$ Hz), 1.03 (1H, q, $J = 4.0$ Hz), 1.25 (1H, dd, $J = 12.2$ and 13.7 Hz), 1.76 (5H, m), 2.18 (1H, dd, $J = 2.2$ and 13.8 Hz), 2.23 (1H, q, $J = 2.0$ and 6.9 Hz), 6.86 (2H, m), 7.31 (1H, dd, $J = 1.6$ and 7.4 Hz), 7.35 (1H, t, $J = 1.6$ and 7.1 Hz), 7.68 (1H, dd, $J = 1.6$ and 7.7 Hz), 7.78 (2H, m), 8.69 (1H, dd, $J = 1.6$ and 4.8 Hz). ^{13}C NMR [100 MHz, $CDCl_3$]: δ 18.41, 21.43, 21.95, 23.66, 26.76, 27.76, 34.82, 42.00, 51.28, 94.17, 116.14, 116.84, 120.30, 123.49, 123.84, 128.16, 133.28, 136.87, 148.42, 154.45, 156.33, 159.38.

By-product **12** was obtained as a white solid. Yield: 590 mg, 23%; m.p., 146–147 °C. $[\alpha]_D^{25}$ (C = 1, $CHCl_3$): +170 Anal. Calc. (found) for $C_{18}H_{22}F_3NO_4S$: C, 53.32 (53.37); H, 5.47 (5.61); N, 3.45 (3.42). HRMS Calc. (found) for $C_{18}H_{22}F_3NO_4SNa$ ($M + Na^+$): *m/z* 428.1119 (428.1122). ^1H NMR [400 MHz, $CDCl_3$]: δ 0.83 (3H, d, $J = 6.6$ Hz), 0.95 (3H, d, $J = 6.9$ Hz), 1.03 (3H, d, $J = 7.0$ Hz), 1.08 (1H, m), 1.39 (1H, t, $J = 12.7$ and 13.5 Hz), 1.63 (m, 3H), 1.85 (3H, m), 2.35 (1H, m), 7.02 (1H, d, $J = 8.0$ Hz), 7.16 (1H, t, $J = 1.0$ and 7.6 Hz), 7.64 (1H, t, $J = 1.7$ and 7.8 Hz), 7.96 (1H, d, $J = 1.7$ and 7.9 Hz). ^{13}C NMR [100 MHz, $CDCl_3$]: δ 18.64, 21.28, 22.80, 23.08, 25.80, 29.60, 33.64, 40.98, 49.11, 112.29, 112.56, 114.18, 117.36, 117.76, 120.54, 123.39, 123.72, 129.40, 138.30, 154.72, 163.33.

Compound (−)-**10**. Yield: 45%; m.p., 89–90 °C. $[\alpha]_D^{25}$ (C = 1, $CHCl_3$): −316 Anal. Calc. (found) for $C_{23}H_{28}N_2O$: C, 79.27 (79.31); H, 8.10 (8.19); N, 8.04 (7.94); HRMS Calc. (found) for $C_{23}H_{28}N_2O^+$ ($M + H^+$): *m/z* 349.2280 (349.2275). ^1H NMR [400 MHz, $CDCl_3$]: δ 0.84 (3H, d, $J = 6.4$ Hz), 0.90 (3H, d, $J = 6.9$ Hz), 0.98 (3H, d, $J = 7.0$ Hz), 1.05 (1H, m), 1.24 (1H, m), 1.78 (4H, m), 2.21 (2H, m), 2.64 (3H, s), 6.84 (2H, m), 7.21 (1H, d, $J = 7.7$ Hz), 7.30 (1H, dd, $J = 1.7$ and 7.4 Hz), 7.55 (1H, d, $J = 7.7$ Hz), 7.68 (2H, t, $J = 7.7$ Hz), 7.73 (1H, dd, $J = 7.8$ Hz). ^{13}C NMR [100 MHz, $CDCl_3$]: δ 18.80, 21.79, 22.30, 24.05, 24.90, 27.08, 28.12, 35.18, 42.51, 51.63, 94.46, 116.62, 117.13, 120.59, 120.83, 123.74, 128.73, 133.55, 137.45, 154.83, 156.26, 157.52, 159.84.

3.3. Preparation of Zn-complex of (1S,4R,2′R)-(−)-4′-(2-pyridyl)spiro[menthane-2,2′-benzo[e][1,3]oxazine(2H)], $ZnCl_2$-**9** [8]

A solution of chiral ligand **9** in dry THF (2 ml) was added to a solution of dry $ZnCl_2$ (0.06 g, 0.45 mmol) in dry THF (5 ml). The reaction mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure and the pale yellow solid was recrystallised in ethanol to give colourless crystal of the *title compound*. Yield: 0.16 g, 75%; m.p., 254 °C.

Anal. Calc. (found) for $C_{22}H_{26}Cl_2N_2OZn$: C, 56.13 (56.07); H, 5.57 (5.58); N, 5.95 (5.94). HRMS Calc. (found) for $C_{22}H_{26}Cl_2N_2OZn$ ($M - Cl^-$): *m/z* 433.1025 (433.1042) ^1H NMR [400 MHz, $CDCl_3$]: δ 0.80 (3H, d, $J = 6.6$ Hz), 0.90 (3H, d, $J = 6.8$ Hz), 1.10 (3H, d, $J = 6.8$ Hz), 1.17 (1H, dd, $J = 3.8$ and 6.8 Hz), 1.63 (1H, m), 1.81 (3H, m), 2.07 (3H, m), 2.32 (1H, m), 7.13 (1H, d, $J = 8.7$ Hz), 7.19 (1H, t, $J = 1.0$ and 7.6 Hz), 7.64 (1H, t, $J = 1.5$ and 6.5 Hz), 7.65 (1H, d, $J = 7.6$ Hz), 7.88 (1H, dd, $J = 5.0$ and 7.6 Hz), 8.16 (1H, d, $J = 7.9$ Hz), 8.23 (1H, t, $J = 1.6$ and 7.9 Hz), 8.93 (1H, d, $J = 0.8$ and 5.0 Hz). ^{13}C NMR [100 MHz, $CDCl_3$]: δ 17.82, 21.58, 21.15, 23.51, 27.14, 28.15, 33.79, 38.68, 50.67, 95.71, 115.29, 118.97, 122.43, 127.83, 127.17, 128.97, 136.91, 140.77, 150.75, 146.74, 155.49, 161.37.

3.4. X-ray crystallographic study

Intensity data of **9**, **12** and $ZnCl_2$-**9** were collected at 123 K on a Nonius Kappa CCD diffractometer with graphite-monochromated Mo Kα radiated ($\lambda = 0.71073$ Å). Crystal data and experimental parameters are presented in Table 3.

Crystal data for **9**: crystals of **9** suitable for X-ray crystallography were grown by slow crystallisation from a mixture of ethyl acetate/hexane: the colourless crystal belongs to the space group $P4_12_12$ with $Z = 8$. Lattice constants were $a = 8.2101(1)$ Å, $b = 8.2101(1)$ Å, $c = 55.9932(1)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$. The crystal selected for intensity measurement was tetragonal with dimensions $0.23 \times 0.18 \times 0.15$ mm^3. The absolute structure model was refined. The Flanck parameter of chiral ligand **9** is indeterminate but the absolute structure can be confirmed by the absolute structure of $ZnCl_2$-**9**.

Crystal data for **12**: crystals of **12** suitable for X-ray crystallography were grown by slow crystallisation from hexane: the colourless crystal belongs to the space group $P2_12_12_1$ with $Z = 4$. Lattice constants were $a = 8.6332(1)$ Å, $b = 13.2793(2)$ Å, $c = 17.2865(2)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$. The crystal selected for intensity measurement was orthorhombic with dimensions $0.25 \times 0.20 \times 0.18$ mm^3. The absolute structure model was refined and the low Flanck parameter = −0.06(9) indicates the absolute structure is correct.

Table 3
X-ray crystal structure and data refinement

Compound	**9**	**12**	$ZnCl_2$-**9**
Colour	Colourless	Colourless	Yellow
Crystal size (mm^3)	$0.23 \times 0.18 \times 0.15$	$0.25 \times 0.20 \times 0.18$	$0.28 \times 0.17 \times 0.17$
Empirical formula	$C_{22}H_{26}N_2O$	$C_{18}H_{22}F_3NO_4S$	$C_{22}H_{26}C_{12}N_2O_1Zn_1$
Temperature (K)	123(2)	123(2)	123(2)
Wavelength (Å)	0.71073	0.71073	0.71073
Crystal system	Tetragonal	Orthorhombic	Monoclinic
Space group	$P4_12_12$	$P2_12_12_1$	C_2
Unit cell dimensions			
a (Å)	8.2101(1)	8.6332(1)	29.5259(8)
b (Å)	8.2101(1)	13.2793(2)	10.2300(3)
c (Å)	55.9932(1)	17.2865(2)	16.1665(5)
α (°)	90	90	90
β (°)	90	90	112.929(1)
γ (°)	90	90	90
Volume (Å^3)	3774.26(7)	1981.77(4)	4497.3(2)
Z	8	4	8
$D_{calculated}$ (Mg/m^3)	1.177	1.359	1.390
Absorption coefficient (mm^{-1})	0.072	0.213	1.344
F(0 0 0)	1440	848	1952
θ Range for data collection (°)	3.83–24.96	3.34–28.29	3.17–27.85
Index ranges	$0 \leqslant h \leqslant 9$, $-6 \leqslant k \leqslant 6$, $0 \leqslant l \leqslant 66$	$-11 \leqslant h \leqslant 11$, $-17 \leqslant k \leqslant 17$, $-22 \leqslant 1 \leqslant 20$	$-38 \leqslant h \leqslant 38$, $-11 \leqslant k \leqslant 13$, $-21 \leqslant l \leqslant 21$
Reflections collected	16,014	24,166	20,580
Independent reflections (R_{int})	2052 (0.064)	4908 (0.1149)	10,238 (0.0613)
Completeness to theta = 24.96°	98.7%	99.7%	99.6%
Absorption correction	None	None	0.826 and 0.738
Refinement method	Full-matrix least-squares on F^2	Full-matrix least- squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	2052/0/229	4908/0/247	10,238/1/511
Goodness-of-fit on F^2	1.053	1.070	1.023
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0435$, $wR_2 = 0.0988$	$R_1 = 0.0519$, $wR_2 = 0.1072$	$R_1 = 0.0436$, $wR_2 = 0.0731$
R indices (all data)	$R_1 = 0.0660$, $wR_2 = 0.1109$	$R_1 = 0.0962$, $wR_2 = 0.1247$	$R_1 = 0.0774$, $wR_2 = 0.0832$
Flanck parameter	Indeterminate	−0.06(9)	−0.01(1)

Crystal data for $ZnCl_2$-**9**: crystals of $ZnCl_2$-**9** suitable for X-ray crystallography were grown by slow crystallisation from methanol: the yellow crystal belongs to the space group C_2 with $Z = 8$. Lattice constants were $a = 29.5259(8)$ Å, $b = 10.2300(3)$ Å, $c = 16.1665(5)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$. The crystal selected for intensity measurement was monoclinic with dimensions $0.28 \times 0.17 \times 0.17$ mm^3. The absolute structure model was refined and the low Flanck parameter = −0.01(1) indicates the absolute structure is correct.

3.5. Asymmetric catalysis

3.5.1. Asymmetric allylic alkylation

A mixture of chiral ligand **9**, (0.02 g, 0.06 mmol) and $[\eta^3$-$C_3H_5)PdCl]_2$ (0.007 g, 0.02 mmol) in dry CH_2Cl_2 (2 ml) was degassed at −78 °C under argon atmosphere for 20 min. The reaction was sealed and refluxed for 2 h. At −78 °C, a solution 1,3-diphenyl-2-propenylacetate (0.25 g, 1 mmol) in dry CH_2Cl_2 (2 ml) was added, followed by dimethyl malonate (0.29 g, 2.25 mmol), BSA (0.61 g, 3.00 mmol) and a few crystals of KOAc. The reaction was stirred at room temperature for 72h. The reaction was diluted with diethyl ether (20 ml) and washed with cold saturated aqueous NH_4Cl (10 ml). The organic extract was dried over anhydrous magnesium sulfate and concentrate to give a crude product. For an analytically pure product the crude product was purified by chromatography on silica gel using ethyl acetate/hexane (1:6) to afford (*R*)-isomer. The enantiomeric excess was determined by chiral HPLC (62%ee): Daicel Chiracel ODH, *i*-PrOH/hexane 2/98, flow rate 0.2 ml/min, t_R 59.30 (*R*)-isomer and 64.46 (*S*)-isomer, 254 nm. HRMS Calc. (found) $C_{20}H_{20}O_4Na^+$ ($M + Na^+$): *m*/*z*347.1236 (347.1251). ^{1}H NMR [400 MHz, $CDCl_3$]: δ 3.52 (3H, s), 3.70 (3H, s), 3.95 (1H, d, $J = 13.8$ Hz), 4.26 (1H, dd, $J = 8.4$ Hz), 6.32 (1H, dd, $J = 8.4$ Hz), 6.47 (1H, d, $J = 15.3$ Hz), 7.30 (10H, m).

3.5.2. Asymmetric diethylzinc addition

To a chilled (0 °C) solution of chiral ligand **9** (0.05 g, 0.15 mmol) in toluene (0.75 ml), 1 M (solution in hexanes) diethylzinc (1.30 ml, 1.30 mmol) was added dropwise and stirred at room temperature for 0.5 h. At 0 °C, fresh distilled benzaldehyde (0.06 ml, 0.65 mmol) was added and stirred at 0 °C for 2 days. The reaction mixture was quenched with cold saturated NH_4Cl (10 ml) and extracted with cold dichloromethane (20 and 10 ml). The extracts were combined, dried over anhydrous $MgSO_4$ and concentrated to give crude product (75% conversion). The crude product was purified by flash chromatography using EtOAc/hexanes (1:9) to afford a pure adduct. The enantiomeric excess was determined by chiral HPLC (20%ee): Daicel Chiracel OD-H, *i*-PrOH/hexane 2/98, flow rate 1.0 ml/min, t_R 15.1 (*S*)-isomer and 18.3 (*R*)-isomer, 254 nm [9]. ^{1}H NMR [400 MHz, $CDCl_3$]: δ 0.90 (3H, t), 1.80 (2H, m), 4.60 (1H, m), 7.35 (5H, m).

3.5.3. Asymmetric hydrosilylation

To a mixture of chiral ligand **9** (0.13 g, 0.4 mmol), $[Rh(COD)Cl]_2$ (0.01 g, 0.04 mmol) and $AgBF_4$ (0.03 g, 0.16 mmol) under argon atmosphere, dry acetophenone (0.93 ml, 8.00 mmol) was added at room temperature and stirred for 20 min. The reaction mixture was cooled down to 0 °C and diphenylsilane (2.3 ml, 12.8 mmol) was added and stirred at 0 °C for 5 days. The reaction was quenched with cold methanol (5 ml) and cold 1 M HCl (10 ml) and stirred at 0 °C for 1 h. The reaction mixture was extracted with diethylether (2×10 ml). The extracts were combined, dried over anhydrous MgSO4 and concentrated to give crude alcohol product with 60% conversion. The crude product was purified by flash chromatography using ethyl acetate/hexane (1:9) to afford (*R*)-1-phenyl-1-ethanol. The enantiomeric excess was determined by chiral HPLC (42%ee): Daicel Chiracel OD-H, *i*-PrOH/hexane 5/95, flow rate 0.5 ml/min, t_R 17.9 (*R*)-isomer and 20.9 (*S*)-isomer, 254 nm. ^{1}H NMR [400 MHz, $CDCl_3$]: δ 1.49 (3H, d, $J = 6.6$ Hz), 1.85 (1H, s), 4.90 (1H, q, $J = 6.6$ Hz), 7.38 (5H, m).

4. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 249387, 249384 and 249.386 for compound **9**, **12** and $ZnCl_2$-**9**, respectively. Copies of this information may be obtained free of charge from the Director CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ddcd.cam.ac.uk or http://www.ccdc.cam.ac.uk).

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References

[1] C. Moberg, U. Bremberg, K. Hallaman, M. Svensson, P.-O. Norrby, A. Hallberg, M. Larhed, I. Csoregh, Pure Appl. Chem. 71 (1999) 1477;
K. Nordstrom, E. Macedo, C. Moberg, J. Org. Chem. 62 (1997) 1604;
C.J. Martin, J.M.J. Williams, Tetrahedron Lett. 34 (1993) 7793;
G.J. Dawson, C.G. Frost, J.M.J. Williams, Tetrahedron Lett. 34 (1993) 3149;

G.C.L.-J.a.A. Pfaltz, Angew. Chem. Int., Ed. Engl. 34 (1995) 462; J.V. Allen, J.M.J. Williams, Tetrahedron Asymm. 5 (1994) 277; H. Nishiyama, S. Yamaguchi, S.-B. Park, K. Itoh, Tetrahedron Asymm. 4 (1993) 143.
[2] H. Brunner, P. Brandl, J. Organomet. Chem. 390 (1990) C81.
[3] E.P. Kündig, P. Meier, Helv. Chim. Acta 82 (1999) 1360.
[4] T. Miyake, M. Seki, Y. Nakamura, H. Ohmizu, Tetrahedron Lett. 37 (1996) 3129.
[5] Compound **7**: colourless oil with $R_f = 0.4$ and compound **11**: white solid (m.p. 163–165 °C) with $R_f = 0.2$ (8:1, hexanes:ethylacetate as eluent). X-ray crystal structure of compound **11** has been deposited at the Cambridge Crystallographic Data Centre, CCDC No. 249388.
[6] S. Yamamoto, S. Hashiguchi, S. Miki, Y. Igata, T. Watanabe, M. Shiraishi, Chem. Pharm. Bull. 44 (1996) 734.
[7] Mats Svensson, Ulf Bremberg, K. Hallman, I. CsÖregh, C. Moberg, Organometallics 18 (1999) 4900.
[8] C. Bolm, K. Weickhardt, M. Zehnder, T. Ranff, Chem. Ber. 124 (1991) 1173.
[9] O.G. Mancheno, S.C.J. Prego, R.G. Arrayas, T. Llamas, J.C. Carretero, J. Org. Chem. 68 (2003) 3679.