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New Thiazoline–Oxazoline Ligands and Their Application in the Asymmetric Friedel–Crafts Reaction

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Six members of a novel non-C_2-symmetric ligand class incorporating an oxazoline and thiazoline unit have been prepared in a four-step, high-yielding and convergent synthesis, in which the key step is a microwave-assisted palladium-catalyzed aryl amination. The new ligands induced enantiomeric excesses of up to 76% in the asymmetric Friedel–Crafts reaction.

Introduction

Compounds containing a chiral oxazoline ring are one of the most successful, versatile, and commonly used classes of ligands for asymmetric catalysis.[1] One of the main reasons for their popularity is that the majority of these ligands are easily synthesised in a few high-yielding steps from commercially available chiral amino alcohols. In contrast to the widely applied oxazoline ligands, the thiazolines have rarely been used in asymmetric catalysis since they were first investigated by Helmchen in 1991.[2] Studies since then have demonstrated that replacing an oxazoline with a thiazoline infers quite different reactivity on the resulting ligand when applied in asymmetric catalysis.[3] Therefore, a ligand containing both of these structural motifs would offer a unique analogue of previous similar bis(oxazoline) or bis(thiazoline) ligands, which have proven successful in asymmetric catalysis. It would also serve as a method of individually tuning the steric and electronic properties of both ring systems in order to maximise the ligand's efficacy and enantiodifferentiating ability.

We have previously synthesised the [*N*,*N*,*N*]-bis(oxazoline) ligands **1** and **2**, and found them to be successful in the chromium-catalyzed Nozaki–Hiyama–Kishi reaction.[4,5] The key step in their synthesis was a palladium-catalyzed aryl amination which allowed us to prepare both C_2- and non-C_2-symmetric analogues. These ligands were synthesised by a Pd-catalyzed aryl amination. Ligand series **3**, synthesised by Du, incorporates a bis(thiazoline) unit and was prepared by a linear synthesis, which can only produce C_2-symmetric examples.[6] Here we disclose a facile, microwave-enhanced, and convergent synthesis of the first example of chiral tridentate ligands **4**, which contain both an oxazoline and a thiazoline moiety. Gaumont has reported the only other ligand possessing an oxazoline and a thiazoline, and this was a bidentate ligand (Figure 1).[7]

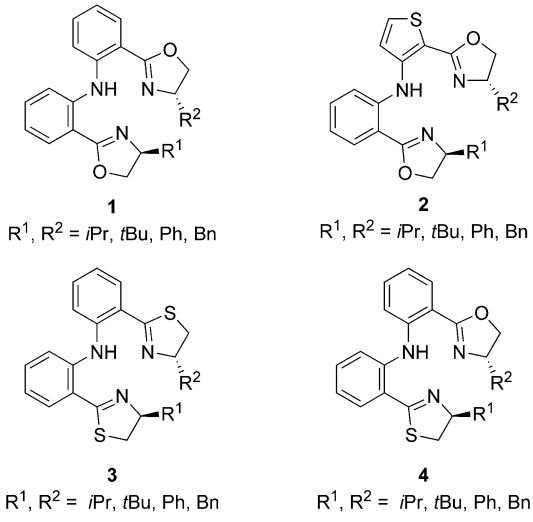

Figure 1. Tridentate oxazoline and thiazoline ligands.

Results and Discussion

Synthesis of New Thiazoline–Oxazoline Ligands 4a–f

The synthesis of these new ligands began with the coupling of the appropriate chiral α-amino alcohol with the acyl chloride derived from 2-bromobenzoic acid, which af-

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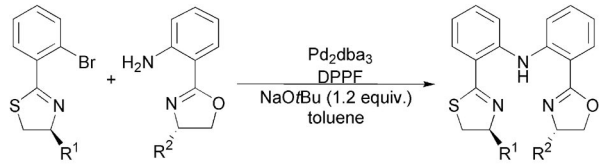
forded the hydroxyamide intermediates **5a**–**d** in excellent yields (Scheme 1). The carbonyl group was sulfinated by using phosphorus pentasulfide[8] and the hydroxythioamide subsequently cyclocondensed under reflux in pyridine to form the thiazoline-containing bromo-coupling partners **6a**–**d** in high overall yield. The amino-coupling partners **7a**–**d** were prepared in good yields in one step from commercially available 2-aminobenzonitrile and the appropriate chiral α-amino alcohol in the presence of $ZnCl_2$.[9]

We then embarked on the investigation of the aryl amination towards the synthesis of ligands **4a**–**f** (Table 1). As in our synthesis of **1**,[4,10] the optimised reaction conditions determined were toluene as solvent, Pd_2dba_3 as the palladium source, sodium *tert*-butoxide as base and DPPF as the ligand.

The yields obtained were considerably lower than those previously achieved in the synthesis of bis(oxazoline) ligand **1**, which itself proved to be a slow reaction requiring 7 d to achieve good yields. In the present study, poor yields were observed even after 7 d of heating at 90 °C (Table 1, Thermal). Yields were improved by the use of microwave assistance, whereby heating the reaction mixture at 180 °C with 300 W for 1 h and by increasing the catalyst loading resulted in the synthesis of ligands **4a**–**f** in 25–85% yields. The low yield of 25% (and 6% using thermal conditions) was obtained for the preparation of the phenylglycinol-derived ligand **4c**. In addition, we noted that this ligand was enantiomerically not pure, as we obtained a *dr* of 5:1 and 9:1, respectively. Initially, we had believed that the second set of peaks in the ^1H NMR spectra were due to differences in hydrogen bonding. However, we independently prepared thiazoline (*R*)-**6c** and coupled it to oxazoline (*S*)-**7c** to yield the diastereomer of ligand **4c**, whose peaks were identical to those of the minor product previously observed. Such epimerisation at (*S*)-4-phenyloxazolines are generally not observed and has not been reported to date for 4-phenylthiazolines. The diastereomeric ratio was increased by way of the microwave method (Table 1, Entry 3).

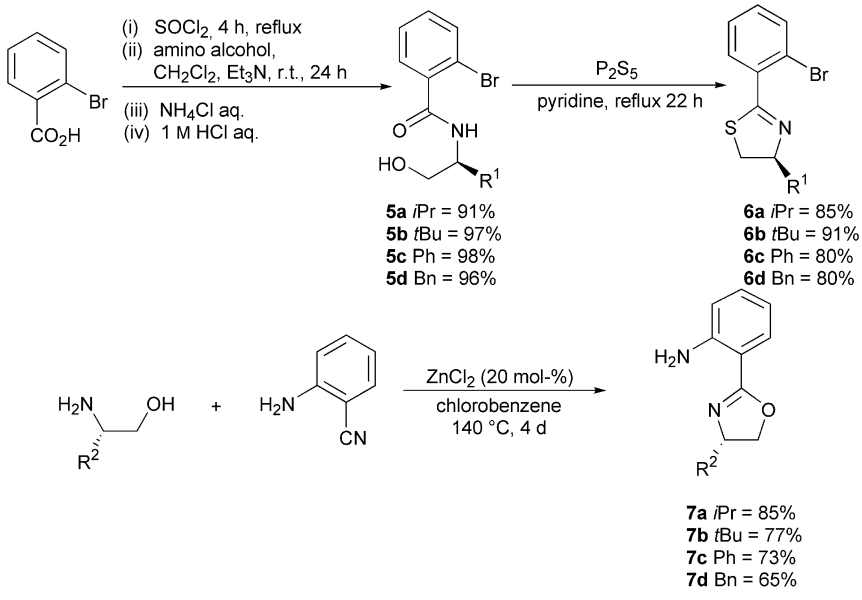
Table 1. Synthesis of ligands **4a**–**f** by Pd-catalyzed aryl amination.



Entry	Ligand	R^1	R^2	Thermal[a] (% yield)	Microwave[b] (% yield)
1	**4a**	*i*Pr	*i*Pr	26 (23)[c]	64 (45)[d]
2	**4b**	*t*Bu	*t*Bu	28	83
3	**4c**	Ph	Ph	6[e]	25[f]
4	**4d**	Bn	Bn	19	64
5	**4e**	*t*Bu	Bn	27	72
6	**4f**	Bn	*t*Bu	17	61

[a] Used 2.5 mol-% Pd_2dba_3, 5 mol-% DPPF at 90 °C for 7 d. [b] Used 5 mol-% Pd_2dba_3, 10 mol-% DPPF at 180 °C, 300 W for 1 h. [c] Used 5 mol-% Pd_2dba_3, 10 mol-% DPPF at 90 °C for 7 d. [d] Used 2.5 mol-% Pd_2dba_3, 5 mol-% DPPF. [e] Diastereomeric ratio 5:1. [f] Diastereomeric ratio 9:1. See Supporting Information for details.

At this point crystals suitable for X-ray analysis were grown by slow concentration at room temperature of a saturated solution of **4f** in a mixture of dichloromethane/*n*-hexane (1:1). From the crystallographic structure we can see that the three nitrogen atoms are in plane with one another forming a concave pocket (Figure 2).



Scheme 1.

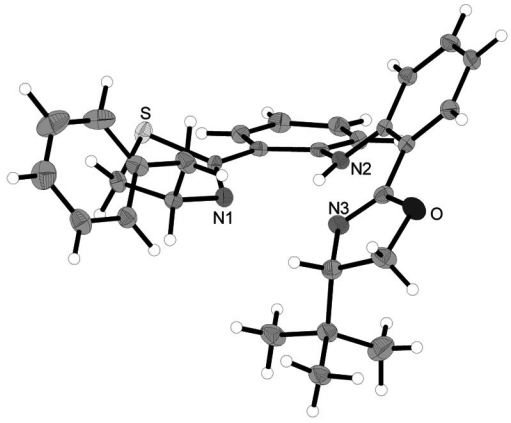


Figure 2. Crystal structure of ligand **4f**, thermal ellipsoids are drawn on the 50% probability level.

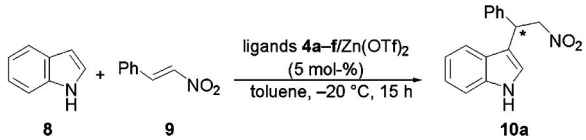
Friedel–Crafts Catalysis

The Friedel–Crafts alkylation of arenes with electron-deficient alkenes is one of the most important organic transformations to employ Lewis acid catalysts.[11,12] Recently, nitroalkenes have been used extensively as substrates in the asymmetric Friedel–Crafts alkylation of indoles.[13,14] The nitro group is one of the strongest electron-withdrawing groups known, so nitroalkenes have proven excellent Michael acceptors.[15] This, coupled with the fact that the nitro group is easily transformed into a range of different functionalities, has resulted in their wide application in organic synthesis.[16] The literature reports employing chiral Lewis acids include the application of symmetrical examples of tridentate ligands **1** and **3** by Du who obtained *ee* values up to 83% (*R*) when ligand **1** (R^1 and R^2 = Ph) was employed.[17] The application of an analogue of ligand **1** which contained *cis*-phenyl substituents at both the 4- and 5-positions of the oxazoline rings was found to increase the *ee* values in this transformation to 94% (*R*).[17] It was therefore of interest to investigate our novel thiazoline–oxazoline-containing ligands in this process, the results of which are given in Table 2.

In the present study we were pleased to find that quantitative yields were observed for all ligands tested. However, poor enantiomeric excesses were obtained when both R^1, R^2 were alkyl substituents (Table 2, Entries 1 and 2). Good enantiomeric excesses were obtained with the use of aromatic R groups (Table 2, Entries 3 and 4). The combination of a bulky *tert*-butyl group with a benzyl group also resulted in good enantiomeric excess (Table 2, Entries 5 and 6). It was also of interest to note that a higher *ee* value was obtained with ligand **4e** compared to **4f** so that it is preferable to have the benzyl substituent on the oxazoline rather than the thiazoline.

On the basis of these results further investigations were warranted to examine the compatibility of the optimal catalyst derived from ligand **4e** with β-nitrostyrene substrates possessing a range of steric and electronic variations (Table 3).

Table 2. The application of ligands **4a**–**f** in the asymmetric Friedel–Crafts alkylation of indole.

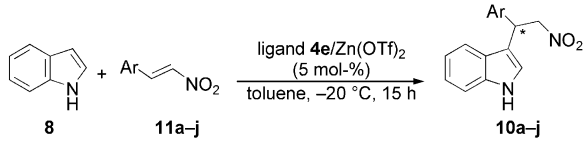


8 **9** **10a**

Entry	Ligand	R^1	R^2	Yield[a] (%)	*ee*[b] (%)
1	**4a**	*i*Pr	*i*Pr	100	14 (*R*)
2	**4b**	*t*Bu	*t*Bu	100	13 (*R*)
3	**4c**	Ph	Ph	100	67 (*R*)
4	**4d**	Bn	Bn	100	51 (*R*)
5	**4e**	*t*Bu	Bn	100	71 (*R*)
6	**4f**	Bn	*t*Bu	100	52 (*R*)

[a] Isolated yields by column chromatography. [b] Determined by chiral HPLC analysis of the products using a Daicel Chiralcel OD column (hexane/2-propanol, 70:30; 0.9 mL/min), the absolute configurations of the products were assigned by comparison of the chiral HPLC retention times with literature values.[13]

Table 3. Asymmetric alkylation of indole with nitroalkenes catalyzed by **4e**/$Zn(OTf)_2$.



8 **11a–j** **10a–j**

Entry	Ar	Product	Yield[a] (%)	*ee*[b] (%)
1	Ph	**10a**	100	71 (*R*)
2	2-furylC_6H_4	**10b**	99	28
3	2-MeOC_6H_4	**10c**	99	17
4	2-ClC_6H_4	**10d**	100	20
5	3-BrC_6H_4	**10e**	100	76
6	3-ClC_6H_4	**10f**	100	64
7	4-MeOC_6H_4	**10g**	88	74
8	4-BrC_6H_4	**10h**	92	60
9	4-ClC_6H_4	**10i**	100	67
10	3,4-$(MeO)_2C_6H_3$	**10j**	94	38

[a] Isolated yields by column chromatography. [b] Determined by chiral HPLC analysis of the products using a Daicel Chiralcel OD column (hexane/2-propanol, 70:30; 1.0 mL/min).

Excellent yields were achieved for all substrates. In terms of enantioselectivity certain trends became evident, particularly in terms of the effect of the position of substitution on the phenyl ring. Poor enantioselectivities were observed for replacement of the phenyl substituent with an electron-rich heterocycle and for substitution of the phenyl ring on the *ortho* position regardless of the electronic nature of the substituent (Table 3, Entries 2–4). Good enantioselectivities were obtained when the ring was monosubstituted at the *meta* or *para* position by either electron-donating or -withdrawing groups (Table 3, Entries 5–9). However, it was found that disubstitution by methoxy groups in the *meta* and *para* positions resulted in a large decrease in *ee* (Table 3, Entry 7).

Conclusions

The first synthesis and application of chiral tridentate ligands containing both a thiazoline and oxazoline is reported. The key step in this convergent synthesis is a palladium-catalyzed aryl amination allowing, in future, for a diverse analogue synthesis. This step was greatly enhanced by the use of microwave conditions in comparison to conventional heating. The six ligands synthesised were subsequently applied in the zinc-catalyzed enantioselective Friedel–Crafts alkylation of indole with a series of *trans*-β-nitrostyrenes, yielding enantioselectivities up to 76%. Our results highlight that, just as in our application of bis(oxazoline) ligands **1** and **2** in the Nozaki–Hiyama–Kishi reaction, where non-C_2-symmetric analogues proved optimal, the thiazoline–oxazoline ligands possessing different R groups induced the highest levels of enantioselectivity. However, they did not lead to an enhancement of enantioselectivity relative to the analogous C_2-symmetric bis(oxazolines). We are currently investigating the application of non-C_2-symmetric examples of ligand series **1** in this reaction and the application of these novel thiazoline–oxazoline ligands to a range of other catalytic asymmetric processes. The results of these investigations will be reported in due course.

Experimental Section

General Experimental: ^{1}H NMR (300, 400, 500 and 600 MHz) and ^{13}C (75, 100, 125 and 150 MHz) spectra were recorded with Varian Oxford 300, 400, 500 or 600 MHz spectrometers by using tetramethylsilane as an internal standard. Chemical shifts (δ) are given in ppm and coupling constants (J) are given as absolute values in Hz. Elemental analysis was performed in the School of Chemistry and Chemical Biology, University College of Dublin. Crystal data was collected with a Bruker SMART APEX CCD area detector diffractometer in the School of Chemistry and Chemical Biology, University College of Dublin. Routine electrospray mass spectrometric analysis was performed with a Waters Micromass Quattro Ultima mass spectrometer. High-resolution mass spectra were obtained by using a Micromass/Waters LCT instrument. Infrared spectra were recorded with a Perkin–Elmer Infrared FT spectrometer. Optical rotation values were measured at room temperature with a Perkin–Elmer 343 polarimeter. Melting points were determined in open capillary tubes with a Gallenkamp melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was carried out on aluminium sheets precoated with silica gel 60 F_{254} (Merck). Column chromatography separations were performed by using Merck Kieselgel 60 (0.040–0.060 mm). Preparative layer chromatography was carried out on glass plates precoated with silica gel 60 $HF_{254+366}$ (Merck). All amination reactions were conducted in a CEM Discover S-Class microwave reactor. HPLC analyses were performed with an LC 2010A machine equipped with a UV/Vis detector by employing a chiral OD column from Daicel Chemical Industries. Solvents were dried immediately before use by distillation from standard drying agents. Anhydrous pyridine and chlorobenzene were purchased from Sigma–Aldrich and used without further purification.

General Procedure for the Synthesis of 2-(*o*-Bromophenyl)hydroxyamides 5a–e: A solution of 2-bromobenzoic acid (1.407 g, 7.0 mmol), and thionyl chloride (5 mL), was refluxed for 4 h. The excess thionyl chloride was then removed in vacuo to leave the acyl chloride as a white precipitate. This was dissolved in dichloromethane (70 mL) and added dropwise to a solution of the amino alcohol (7.0 mmol) in triethylamine (2.45 mL, 17.5 mmol) and dichloromethane (20 mL) at 0 °C. The solution was then stirred at room temperature for 24 h. The reaction mixture was then washed successively with a saturated aqueous solution of ammonium chloride, HCl (1 M), saturated aqueous solution of sodium hydrogen carbonate and brine. The resulting organic layer was then dried with anhydrous sodium sulfate and concentrated in vacuo to yield pure product.

(*S*)-2-Bromo-*N*-(1-hydroxy-3-methylbut-2-yl)benzamide (5a): Yield 91%, white solid. M.p. 109–111 °C (ref.[1] 113–115 °C). TLC: R_f = 0.38 (EtOAc). $[\alpha]_D^{20}$ = –19.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 [d, ^3J = 2.8 Hz, 3 H, CH(CH_3)$_2$], 0.99 [d, ^3J = 2.8 Hz, 3 H, CH(CH_3)$_2$], 1.99–2.07 [m, 1 H, CH(CH$_3$)$_2$], 2.71 (br. s, 1 H, OH), 3.68–3.77 (m, 2 H, CH_2O), 3.87–3.93 (m, 1 H, CHN), 6.26 (br. d, ^3J = 7.9 Hz, 1 H, 1 H, NH), 7.22 (ddd, ^3J = 8.0, ^3J = 7.5, ^4J = 1.8 Hz, 1 H, Ar-HC), 7.29 (ddd, ^3J = 8.8, ^3J = 7.6, ^4J = 1.2 Hz, 1 H, Ar-HC), 7.47 (dd, ^3J = 7.6, ^4J = 1.8 Hz, 1 H, Ar-HC), 7.53 (dd, ^3J = 8.0, ^4J = 1.2 Hz, 1 H, Ar-HC) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.9 [CH(CH_3)$_2$], 19.6 [CH(CH_3)$_2$], 29.1 [CH(CH$_3$)$_2$], 57.7 (CHN), 63.6 (CH_2O), 119.1 [C_{Ar}(CO)], 127.6, 129.5, 131.2, 133.3 [C_{Ar}(H)], 137.9 [C_{Ar}(Br)], 168.4 (CON) ppm. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 3404, 3278, 3067, 2962, 2878, 1642, 1538, 1466, 1321, 1252, 1032, 752 cm^{-1}. HRMS (ES$^+$): calcd. for $C_{12}H_{16}BrNO_2$ [M + H]$^+$ 286.0443; found 286.0456. $C_{12}H_{16}BrNO_2$ (286.16): calcd. C 50.37, H 5.64, Br 27.92, N 4.89; found C 49.98, H 5.48, Br 28.30, N 4.88.

(*S*)-2-Bromo-*N*-(1-hydroxy-3,3-dimethylbut-2-yl)benzamide (5b): Yield 97%, white solid. M.p. 110–112 °C (ref.[2] 50.0–51.0 °C from acetone/hexanes). TLC: R_f = 0.40 (EtOAc). $[\alpha]_D^{20}$ = –2.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 [s, 9 H, C(CH_3)$_3$], 2.40 (br. s, 1 H, OH), 3.68 (app. t, ^3J = 8.0 Hz, 1 H, CH_2O), 3.95 (br. d, ^3J = 11.3 Hz, 1 H, CH_2O), 4.06 (m, 1 H, CHN), 6.20 (br. d, ^3J = 8.2 Hz, 1 H, 1 H, NH), 7.28 (ddd, Ar-HC, ^3J = 7.9, ^4J = 1.7 Hz, 1 H, 9.2 Hz), 7.36 (ddd, ^3J = 8.8, ^3J = 7.4, ^4J = 0.8 Hz, 1 H, Ar-HC), 7.56 (dd, ^3J = 7.6, ^4J = 1.6 Hz, 1 H, Ar-HC), 7.59 (br. d, ^3J = 8.0 Hz, 1 H, Ar-HC) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.3 [C(CH_3)$_3$], 34.0 [C(CH$_3$)$_3$], 60.5 (CHN), 63.3 (CH_2O), 119.3 [C_{Ar}(CO)], 127.9, 130.0, 131.5, 133.6 [C_{Ar}(H)], 138.2 [C_{Ar}(Br)], 168.9 (CON) ppm. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 3243, 3067, 2961, 1641, 1555, 1469, 1362, 1314, 1255, 1087, 1049, 750 cm^{-1}. HRMS (ES$^+$): calcd. for $C_{13}H_{18}BrNO_2$ [M + H]$^+$ 300.0599; found 300.0606. $C_{13}H_{18}BrNO_2$ (300.19): calcd. C 52.01, H 6.04, Br 26.62, N 4.67; found C 51.96, H 6.03, Br 26.99, N 4.60.

(*S*)-2-Bromo-*N*-(2-hydroxy-1-phenylethyl)benzamide (5c): Yield 98%, white solid. M.p. 122–124 °C. TLC: R_f = 0.49 (EtOAc). $[\alpha]_D^{20}$ = +10.5 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.55 (br. s, 1 H, OH), 3.97 (br. s, 2 H, CH_2O), 5.24–5.29 (m, 1 H, CHN), 6.81 (br. d, ^3J = 6.4 Hz, 1 H, NH), 7.25–7.39 [m, 7 H, Ar-HC, Ar-HC(Ph)], 7.55 (dd, ^3J = 7.8, ^4J = 1.5 Hz, 1 H, Ar-HC), 7.58 (dd, ^3J = 7.8, ^4J = 1.0 Hz, 1 H, Ar-HC) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 56.4 (CHN), 66.3 (CH_2O), 119.3 [C_{Ar}(CO)], 126.9, 127.6, 128.0, 128.9, 129.8, 131.4, 133.4, 137.4 [C_{Ar}(H)], 138.5 [C_{Ar}(Br)], 167.7 (CON) ppm. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 3297, 3062, 2938, 2874, 1643, 1532, 1462, 1311, 1033, 750, 698 cm^{-1}. HRMS (ES$^+$): calcd. for $C_{15}H_{14}BrNO_2$ [M + H]$^+$ 320.0286; found 320.0300. $C_{15}H_{14}BrNO_2$ (320.18): calcd. C 56.27, H 4.41, Br 24.96, N 4.37; found C 56.06, H 4.40, Br 24.79, N 4.23.

(*S*)-2-Bromo-*N*-(1-hydroxy-3-phenylprop-2-yl)benzamide (5d): Yield 96%, white solid. M.p. 97–98 °C. TLC: R_f = 0.44 (EtOAc). $[\alpha]_D^{20}$ =

–22.2 (c = 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.57 (br. s, 1 H, O*H*), 3.00 (d, ^3J = 7.4 Hz, 2 H, CH_2Ph), 3.69 (dd, ^2J = 11.1, ^3J = 4.7 Hz, 1 H, CH_2O), 3.79 (dd, ^2J = 11.1, ^3J = 3.6 Hz, 1 H, CH_2O), 4.38–4.44 (m, 1 H, C*H*N), 6.29 (br. d, ^3J = 7.4 Hz, 1 H, N*H*), 7.22–7.33 [m, 7 H, Ar-*H*C(Ph), Ar-*H*C], 7.38 (dd, ^3J = 7.6, ^4J = 1.8 Hz, 1 H, Ar-*H*C), 7.54 (dd, ^3J = 7.9, ^4J = 1.0 Hz, 1 H, Ar-*H*C) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.9 (*C*H_2Ph), 53.3 (*C*HN), 63.7 (*C*H_2O), 119.2 [C_{Ar}(CO)], 126.7, 127.5, 128.7, 129.3, 129.4, 131.3, 133.3, 137.5, [C_{Ar}(H)], 137.7 [C_{Ar}(Br)],168.0 (*C*ON) ppm. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 3391, 3276, 3064, 2931, 1641, 1536, 1461, 1333, 1095, 1035, 748, 698 cm^{-1}. HRMS (ES^+): calcd. for $C_{16}H_{16}BrNO_2$ [M + H]$^+$ 334.0443; found 334.0437. $C_{16}H_{16}BrNO_2$ (334.21): calcd. C 57.50, H 4.83, Br 23.91, N 4.19; found C 57.11, H 4.73, Br 23.91, N 4.11.

(*R*)-2-Bromo-*N*-(2-hydroxy-1-phenylethyl)benzamide (5e): Yield 93%, white solid. M.p. 122–124 °C. TLC: R_f = 0.49 (EtOAc). $[\alpha]_D^{20}$ = –12.2 (c = 1.15, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.51 (br. s, 1 H, O*H*), 3.99 (app. t, ^3J = 4.7 Hz, 2 H, CH_2O), 5.25–5.29 (m, 1 H, C*H*N), 6.80 (br. d, ^3J = 6.4 Hz, 1 H, N*H*), 7.25–7.40 [m, 7 H, Ar-*H*C, Ar-*H*C(Ph)], 7.55 (dd, ^3J = 7.8, ^4J = 1.5 Hz, 1 H, Ar-*H*C), 7.58 (dd, ^3J = 7.8, ^4J = 1.0 Hz, 1 H, Ar-*H*C) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 56.4 (*C*HN), 66.3 (*C*H_2O), 119.3 [C_{Ar}(CO)], 126.9, 127.6, 128.0, 128.9, 129.8, 131.4, 133.4, 137.3 [C_{Ar}(H)], 138.5 [C_{Ar}(Br)], 167.7 (*C*ON) ppm. IR (KBr): $\tilde{\nu}$ = 3300, 3074, 2950, 2885, 1635, 1542, 1464, 1318, 1036, 752, 699 cm^{-1}. MS (ESI): m/z = 320.2/322.2 (1:1). $C_{15}H_{14}BrNO_2$ (320.18): calcd. C 56.27, H 4.41, Br 24.96, N 4.37; found C 56.07, H 4.28, Br 24.67, N 4.33.

General Procedure for the Synthesis of 2-(*o*-Bromophenyl)thiazolines 6a–e: To a solution of 2-(*o*-bromophenyl)hydroxyamide (9.0 mmol) in dry pyridine (40 mL), was added phosphorus pentasulfide (8.00 g, 17.9 mmol), and the mixture was refluxed for 22 h. The reaction mixture was cooled, and 20% potassium hydroxide solution (aq.) (35 mL) was added. The resulting aqueous phase was then extracted with dichloromethane (3× 15 mL). The organic phases were combined, washed with 2 N HCl, dried with anhydrous sodium sulfate and concentrated in vacuo to yield the crude product. This was purified by column chromatography on silica gel (pentane/EtOAc, 1:1), to yield pure product.

(*S*)-2-(2-Bromophenyl)-4-isopropyl-4,5-dihydrothiazole (6a): Yield 85% (2.174 g), colourless oil. TLC: R_f = 0.31 (pentane/EtOAc, 3:1). $[\alpha]_D^{20}$ = –71.4 (c = 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.07 [d, ^3J = 6.8 Hz, 3 H, CH(CH_3)$_2$], 1.12 [d, ^3J = 6.8 Hz, 3 H, CH(CH_3)$_2$], 2.17 [oct, ^3J = 6.8 Hz, 1 H, C*H*(CH$_3$)$_2$], 3.23 (dd, ^2J = 10.8, ^3J = 9.6 Hz, 1 H, CH_2S), 3.46 (dd, ^2J = 10.8, ^3J = 9.0 Hz, 1 H, CH_2S), 4.47–4.53 (m, 1 H, C*H*N), 7.23 (ddd, ^3J = 7.9, ^3J = 7.5, ^4J = 1.8 Hz, 1 H, Ar-*H*C), 7.32 (ddd, ^3J = 7.9, ^3J = 7.6 H, 1.2 Hz, Ar-*H*C), 7.49 (dd, ^3J = 7.7, ^4J = 1.8 Hz, 1 H, Ar-*H*C), 7.60 (dd, ^3J = 8.0, ^4J = 1.2 Hz, 1 H, Ar-*H*C) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3 [C(*C*H$_3$)$_2$], 19.9 [C(*C*H$_3$)$_2$], 33.2 [*C*(CH$_3$)$_2$], 36.8 (*C*H_2S), 84.5 (*C*HN), 121.4 [C_{Ar}(C=N)], 127.4, 130.6, 131.1, 133.1 [C_{Ar}(H)], 135.7 [C_{Ar}(Br)], 165.5 (*C*=N) ppm. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 2959, 2873, 1624, 1465, 1228, 1021, 935, 759 cm^{-1}. HRMS (ES^+): calcd. for $C_{12}H_{14}BrNS$ [M + H]$^+$ 284.0109; found 284.0113. $C_{12}H_{14}BrNS$ (284.22): calcd. C 50.71, H 4.96, Br 28.11, N 4.93, S 11.28; found C 50.73, H 4.89, Br 27.67, N 4.82, S 11.50.

(*S*)-2-(2-Bromophenyl)-4-*tert*-butyl-4,5-dihydrothiazole (6b): Yield 91% (2.443 g), cream crystals. M.p. 97–98 °C. TLC: R_f = 0.48 (pentane/EtOAc, 3:1). $[\alpha]_D^{20}$ = –87.5 (c = 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.10 [s, 9 H, C(CH_3)$_3$], 3.30 (app. t, ^3J = 10.8 Hz, 1 H, CH_2S), 3.40 (app. t, ^3J = 10.0 Hz, 1 H, CH_2S), 4.41 (app. t, ^3J = 10.0 Hz, 1 H, C*H*N), 7.23 (app. t, ^3J = 7.9 Hz, 1 H, Ar-*H*C), 7.32 (app. t, ^3J = 7.5 Hz, 1 H, Ar-*H*C), 7.50 (br. d, ^3J = 7.6 Hz, 1 H, Ar-*H*C), 7.61 (br. d, ^3J = 8.0 Hz, 1 H, Ar-*H*C) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.0 [C(*C*H$_3$)$_3$], 35.4 [*C*(CH$_3$)$_3$, *C*H$_2$S], 88.3 (*C*HN), 121.1 [C_{Ar}(C=N)], 127.2, 130.4, 130.8, 133.7 [C_{Ar}(H)], 135.5 [C_{Ar}(Br)], 165.0 (*C*=N) ppm. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 2956, 2838, 1618, 1466, 1366, 1272, 1221, 1118, 1055, 1028, 932, 761 cm^{-1}. HRMS (ES^+): calcd. for $C_{13}H_{16}BrNS$ [M + H]$^+$ 298.0265; found 298.0269. $C_{13}H_{16}BrNS$ (298.24): calcd. C 52.35, H 5.41, Br 26.79, N 4.70, S 10.75; found C 52.55, H 5.39, Br 26.85, N 4.59, S 10.55.

(*S*)-2-(2-Bromophenyl)-4-phenyl-4,5-dihydrothiazole (6c): Yield 80% (2.291 g), colourless oil. TLC: R_f = 0.57 (pentane/EtOAc, 3:1). $[\alpha]_D^{20}$ = +50.3 (c = 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.43 (dd, ^2J = 10.9, ^3J = 10.1 Hz, 1 H, CH_2S), 3.89 (dd, ^2J = 10.9, ^3J = 8.9 Hz, 1 H, CH_2S), 5.75 (app. t, ^3J = 9.5 Hz, 1 H, C*H*N), 7.26–7.42 [m, 5 H, Ar-*H*C(Ph)], 7.46–7.49 (m, 2 H, Ar-*H*C), 7.61 (dd, ^3J = 7.7, ^4J = 1.7 Hz, 1 H, Ar-*H*C), 7.66 (dd, ^3J = 8.0, ^4J = 1.2 Hz, 1 H, Ar-*H*C) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.6 (*C*H_2S), 81.2 (*C*HN), 121.5 [C_{Ar}(C=N)], 127.0, 127.5, 128.0, 129.0, 130.7, 131.4, 133.9 [C_{Ar}(H)], 135.5 [C_{Ar}(4°)], 142.0 [C_{Ar}(4°)], 167.9 (*C*=N) ppm. IR (KBr): $\tilde{\nu}$ = 3061, 3028, 2927, 2851, 1617, 1467, 1434, 1028, 940, 759, 698 cm^{-1}. HRMS (ES^+): calcd. for $C_{15}H_{12}BrNS$ [M + H]$^+$ 317.9952; found 317.9959. $C_{15}H_{12}BrNS$ (318.23): calcd. C 56.61, H 3.80, Br 25.11, N 4.40, S 10.08; found C 56.64, H 3.79, Br 24.68, N 4.34, S 9.80.

(*S*)-4-Benzyl-2-(2-bromophenyl)-4,5-dihydrothiazole (6d): Yield 80% (2.392 g), colourless oil. TLC: R_f = 0.55 (pentane/EtOAc, 3:1). $[\alpha]_D^{20}$ = –34.0 (c = 1.05, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.91 (dd, ^2J = 13.7, ^3J = 9.1 Hz, 1 H, CH_2Ph), 3.20 (dd, ^2J = 11.1, ^3J = 6.8 Hz, 1 H, CH_2S), 3.34 (dd, ^2J = 13.7, ^3J = 5.1 Hz, 1 H, CH_2Ph), 3.41 (dd, ^2J = 11.1, ^3J = 8.4 Hz, 1 H, 1 H, CH_2S), 4.93–5.03 (m, 1 H, C*H*N), 7.22–7.36 [m, 7 H, Ar-*H*C(Ph), Ar-*H*C], 7.51 (dd, ^3J = 7.6, ^4J = 1.7 Hz, 1 H, Ar-*H*C), 7.63 (dd, ^3J = 7.9, ^4J = 1.0 Hz, 1 H, Ar-*H*C) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.7 (*C*H_2Ph), 40.1 (*C*H_2S), 79.1 (*C*HN), 121.4 [C_{Ar}(C=N)], 126.8, 127.5, 128.8, 129.6, 130.6, 131.2, 133.8 [C_{Ar}(H)], 135.5 [C_{Ar}(4°)], 138.6 [C_{Ar}(4°)], 166.6 (*C*=N) ppm. IR (KBr): $\tilde{\nu}$ = 3060, 2926, 1617, 1464, 1268, 1049, 937, 756 cm^{-1}. HRMS (ES^+): calcd. for $C_{16}H_{14}BrNS$ [M + H]$^+$ 332.0109; found 332.0100. $C_{16}H_{14}BrNS$ (332.26): calcd. C 57.84, H 4.25, Br 24.05, N 4.22, S 9.65; found C 57.60, H 4.21, Br 23.69, N 4.12, S 9.71.

(*R*)-2-(2-Bromophenyl)-4-phenyl-4,5-dihydrothiazole (6e): Yield 75% (2.148 g), colourless oil. TLC: R_f = 0.57 (pentane/EtOAc, 3:1). $[\alpha]_D^{20}$ = –47.2 (c = 1.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.40 (dd, ^2J = 11.0, ^3J = 10.1 Hz, 1 H, CH_2S), 3.87 (dd, ^2J = 11.0, ^3J = 8.9 Hz, 1 H, CH_2S), 5.73 (app. t, ^3J = 9.5 Hz, 1 H, C*H*N), 7.24–7.39 [m, 5 H, Ar-*H*C(Ph)], 7.44–7.47 (m, 2 H, Ar-*H*C), 7.60 (dd, ^3J = 7.6, ^4J = 1.7 Hz, 1 H, Ar-*H*C), 7.64 (dd, ^3J = 8.0, ^4J = 1.1 Hz, 1 H, Ar-*H*C) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.4 (*C*H_2S), 80.9 (*C*HN), 121.4 [C_{Ar}(C=N)], 126.8, 127.3, 127.7, 128.7, 130.5, 131.1, 133.7 [C_{Ar}(H)], 135.2 [C_{Ar}(4°)], 141.8 [C_{Ar}(4°)], 167.6 (*C*=N) ppm. IR (KBr, $CHCl_3$ film): $\tilde{\nu}$ = 3053, 2927, 2859, 1614, 1451, 1281, 1229, 1021, 939, 753, 701 cm^{-1}. MS (ESI): m/z = 318.2/320.2 (1:1). $C_{15}H_{12}BrNS$ (318.23): calcd. C 56.61, H 3.80, Br 25.11, N 4.40, S 10.08; found C 56.63, H 3.78, Br 24.95, N 4.35, S 9.99.

General Procedure for the Screening of Conditions for Palladium-Catalysed Aryl Aminations: To an oven-dried Radleys® tube was added the amino- (0.60 mmol) and bromo-coupling partners (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 via syringe and the reaction mixture stirred under nitrogen at the required temperature for 7 d. The reaction mixture was co-

oled to room temperature. The solvent was removed in vacuo, and a ^{1}H NMR spectrum was obtained to determine if any of the arylamine product had formed.

Thermal Procedure for the Synthesis of Ligands 4a–g (Method A): An oven-dried Schlenk tube was charged with 2-(2-bromophenyl)-thiazoline (1.00 mmol), sodium *tert*-butoxide (0.115 g, 1.2 mmol), 1,1′-bis(diphenylphosphanyl)ferrocene (DPPF) (0.055 g, 0.10 mmol), Pd_2dba_3 (0.023 g, 0.025 mmol), and 2-(*o*-aminophenyl)-oxazoline (1.2 mmol). After the addition of dry, degassed toluene (8 mL) via syringe, the Schlenk tube was capped under nitrogen and the reaction mixture (brown suspension) was heated at 90 °C for 7 d. The reaction mixture was then cooled to room temperature and concentrated in vacuo to give a brown oil. This was purified by preparative layer chromatography on silica gel (cyclohexane/EtOAc, 8:1) to yield pure product.

Microwave Procedure for the Synthesis of Ligands 4a–g (Method B): An oven-dried tube was charged under nitrogen with 2-(2-bromophenyl)thiazoline (0.500 mmol), sodium *tert*-butoxide (0.0577 g, 0.6 mmol), 1,1′-bis(diphenylphosphanyl)ferrocene (DPPF) (0.0225 g, 0.05 mmol), Pd_2dba_3 (0.0115 g, 0.0125 mmol), and 2-(*o*-aminophenyl)oxazoline (0.6 mmol). After the addition of dry, degassed toluene (2 mL) via syringe, the tube was sealed under nitrogen, and the reaction mixture was placed in a microwave oven and heated at 180 °C for 1 h. The reaction mixture was then cooled to room temperature before removing the seal and concentrated in vacuo to yield a brown oil. This was purified by preparative layer chromatography on silica gel (cyclohexane/EtOAc, 8:1) to yield pure product.

2-[(*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl]-*N*-{2-[(*S*)-4-isopropyl-4,5-dihydrothiazol-2-yl]phenyl}benzenamine (4a): Yield 26% (106 mg; Method A), 64% (130 mg; Method B), clear oil. TLC: R_f = 0.28 (cyclohexane/EtOAc, 8:1). $[a]_D^{20}$ = +20.0 (c = 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 [d, ^3J = 6.7 Hz, 3 H, CH(CH_3)$_2$], 0.97 [d, ^3J = 6.7 Hz, 3 H, CH(CH_3)$_2$], 0.98 [d, ^3J = 6.7 Hz, 3 H, CH(CH_3)$_2$], 1.06 [d, ^3J = 6.7 Hz, 3 H, CH(CH_3)$_2$], 1.77 [oct, ^3J = 6.7 Hz, 1 H, CH(CH$_3$)$_2$], 2.07 [oct, ^3J = 6.7 Hz, 1 H, CH(CH$_3$)$_2$], 3.00 (dd, ^2J = 10.7, ^3J = 9.8 Hz, 1 H, CH_2S), 3.27 (dd, ^2J = 10.7, ^3J = 8.7 Hz, 1 H, CH_2S), 3.99–4.11 (m, 2 H, CH_2O, CHN), 4.31 (dd, ^2J = 9.1, ^3J = 7.8 Hz, 1 H, CH_2O), 4.40–4.46 (m, 1 H, CHN), 6.86 (ddd, ^3J = 8.1, ^3J = 6.7, ^4J = 1.6 Hz, 1 H, Ar-HC), 6.94–6.98 (m, 1 H, Ar-HC), 7.23–7.30 (m, 3 H, Ar-HC), 7.39 (d, ^3J = 8.2 Hz, 1 H, Ar-HC), 7.66 (dd, ^3J = 7.8, ^4J = 1.4 Hz, 1 H, Ar-HC), 7.80 (dd, ^3J = 7.6, ^4J = 1.1 Hz, 1 H, Ar-HC), 10.73 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.4 [CH(CH_3)$_2$], 18.8 [CH(CH_3)$_2$], 19.0 [CH(CH_3)$_2$], 19.9 [CH(CH_3)$_2$], 33.1 [CH(CH$_3$)$_2$], 33.2 [CH(CH$_3$)$_2$], 34.6 (CH_2S), 69.1 (CH_2O), 72.9 (CHN), 84.2 (CHN), 115.1 [C_{Ar}(C=N)], 117.8, 119.2, 120.2, 120.9 [C_{Ar}(H)], 123.7 [C_{Ar}(C=N)], 130.2, 130.7, 131.3, 131.5 [C_{Ar}(H)], 141.8 [C_{Ar}(NH)], 144.0 [C_{Ar}(NH)], 162.7 (C=N), 165.1 (C=N) ppm. IR (NaCl): $\tilde{\nu}$ = 3204, 3081, 2958, 1583, 1453, 1314, 1049, 974, 749 cm^{-1}. HRMS (ES$^+$): calcd. for $C_{24}H_{29}N_3OS$ [M + H]$^+$ 408.2110; found 408.2098. $C_{24}H_{29}N_3OS$ (407.57): calcd. C 70.73, H 7.17, N 10.31; found C 70.45, H 7.04, N 10.63.

2-[(*S*)-4-*tert*-Butyl-4,5-dihydrooxazol-2-yl]-*N*-{2-[(*S*)-4-*tert*-butyl-4,5-dihydrothiazol-2-yl]phenyl}benzenamine (4b): Yield 28% (61 mg; Method A), 83% (180 mg; Method B), white solid. M.p. 130–132 °C. TLC: R_f = 0.35 (cyclohexane/EtOAc, 8:1). $[a]_D^{20}$ = +13.3 (c = 0.75, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 [s, 9 H, C(CH_3)$_3$], 1.01 [s, 9 H, C(CH_3)$_3$], 3.05 (app. t, J = 10.8 Hz, 1 H, CH_2S), 3.18 (dd, ^2J = 10.8, ^3J = 8.8 Hz, 1 H, CH_2S), 4.03 (dd, ^3J = 9.8, ^3J = 7.3 Hz, 1 H, CHN), 4.11 (app. t, J = 8.3 Hz, 1 H, CH_2O), 4.28 (dd, ^3J = 9.8, ^2J = 8.3 Hz, 1 H, CH_2O), 4.33 (dd, ^3J = 10.3, ^3J = 8.8 Hz, 1 H, CHN), 6.86 (ddd, ^3J = 8.2, ^3J = 6.5, ^4J = 1.8 Hz, 1 H, Ar-HC), 6.95–6.99 (m, 1 H, Ar-HC), 7.22–7.28 (m, 3 H, Ar-HC), 7.34 (d, ^3J = 8.3 Hz, 1 H, Ar-HC), 7.70 (dd, ^3J = 7.8, ^4J = 1.5 Hz, Ar-HC), 7.82 (dd, ^3J = 8.3, ^4J = 1.5 Hz, Ar-HC), 10.66 (br. s, NH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.9 [C(CH_3)$_3$], 26.9 [C(CH_3)$_3$], 33.3 (CH_2S), 34.0 [C(CH$_3$)$_3$], 35.2 [C(CH$_3$)$_3$], 67.4 (CH_2O), 76.3 (CHN), 87.7 (CHN), 114.9 [C_{Ar}(C=N)], 117.9, 119.2, 120.5, 121.2 [C_{Ar}(H)], 124.3 [C_{Ar}(C=N)], 130.3, 130.8, 131.4, 131.5 [C_{Ar}(H)], 141.9 [C_{Ar}(NH)], 144.3 [C_{Ar}(NH)], 162.7 (C=N), 165.0 (C=N) ppm. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 3220, 3083, 2955, 1641, 1582, 1516, 1453, 1317, 1213, 1051, 750 cm^{-1}. HRMS (ES$^+$): calcd. for $C_{26}H_{33}N_3OS$ [M + H]$^+$ 436.2423; found 436.2402. $C_{26}H_{33}N_3OS$ (435.62): calcd. C 71.69, H 7.64, N 9.65; found C 71.60, H 7.51, N 9.35.

2-[(*S*)-4-Phenyl-4,5-dihydrooxazol-2-yl]-*N*-{2-[(*S*)-4-phenyl-4,5-dihydrothiazol-2-yl]phenyl}benzenamine (4c): Yield 6% (28 mg; Method A), 25% (60 mg; Method B), white semi-solid. TLC: R_f = 0.32 (cyclohexane/EtOAc, 8:1). $[a]_D^{20}$ = +307.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (600 MHz, [D$_6$]benzene): δ = [2.70* (dd, ^2J = 10.8, ^3J = 9.1) and 2.71 (dd, ^2J = 10.8, ^3J = 9.1 Hz)] (1:7, 1 H, CH_2S), [3.03* (dd, ^2J = 10.8, ^3J = 9.1 Hz) and 3.03 (dd, ^2J = 10.8 Hz, ^3J = 9.0 Hz)] (1:7, 1 H, CH_2S), [3.58* (app. t, ^3J = 8.2 Hz) and 3.59 (app. t, ^3J = 8.2 Hz)] (1:7, 1 H, CH_2O), [3.92 (dd, ^3J = 10.1 Hz, ^2J = 8.2 Hz) and 3.95* (dd, ^3J = 10.1 Hz, ^2J = 8.2 Hz)] (7:1, 1 H, CH_2O), [4.70 (dd, ^3J = 10.0 Hz, ^3J = 8.2 Hz) and 4.90* (dd, ^3J = 10.1 Hz, ^3J = 8.2 Hz)] (9:1, 1 H, CHN), [5.25 (app. t, ^3J = 9.0 Hz) and 5.33* (app. t, ^3J = 9.1 Hz)] (13:1, 1 H, CHN), 6.69–6.72 (m, 2 H, Ar-HC), 6.92–6.95 (m, 1 H, Ar-HC), 6.96–7.02 (m, 9 H, Ar-HC), 7.06–7.08 (m, 1 H, Ar-HC), 7.13–7.14 (m, 1 H, Ar-HC), [7.34* (dd, ^3J = 7.8 Hz, ^4J = 0.7 Hz) and 7.41 (dd, ^3J = 7.8 Hz, ^4J = 0.5 Hz)] (1:9, 1 H, Ar-HC), [7.42* (dd, ^3J = 7.3 Hz, ^4J = 0.7 Hz) and 7.46 (dd, ^3J = 8.3 Hz, ^4J = 0.7 Hz)] (1:9, 1 H, Ar-HC), [7.83 (dd, ^3J = 7.7 Hz, ^4J = 1.5 Hz) and 7.91* (dd, ^3J = 7.8 Hz, ^4J = 1.4 Hz)] (9:1, 1 H, Ar-HC), [8.07 (dd, ^3J = 7.8 Hz, ^4J = 1.6 Hz) and 8.08* (dd, ^3J = 7.8 Hz, ^4J = 1.6 Hz)] (9:1, 1 H, Ar-HC), [11.64* (br. s) and 11.80 (br. s)] (1:9, 1 H, NH) ppm. ^{13}C NMR (150 MHz, [D$_6$]benzene): δ [39.8*, 40.2] (CH_2S), [70.0, 70.1*] (CHN), [72.8*, 73.0] (CH_2O), [80.9, 81.0*] (CHN), [114.6, 114.7*] [C_{Ar}(C=N)], [{117.0, 117.5*}, {119.0, 119.2*},{120.0, 120.2*},{120.7, 120.8*}] (C_{Ar}(H)), [123.2*, 123.6] [C_{Ar}(C=N)], [{126.5*, 126.5}, {126.6*, 126.6}] (*o*-Ph, *m*-Ph), [{126.8*, 126.9}] (*p*-Ph), 126.9 (*p*-Ph), [{128.1, 128.2*}, {128.3, 128.3*}] (*o*-Ph, *m*-Ph), [{130.4, 130.6*}, {130.8, 130.9*}, 131.5, {131.6, 132.2*}] [C_{Ar}(H)], [141.7, 142.1*] [C_{Ar}(NH)], [142.6*, 142.6] (*i*-Ph), [142.9, 142.9*] (*i*-Ph), [144.3, 144.4*] [C_{Ar}(NH)], [163.6, 163.7*] (C=N), [166.8*, 166.8] (C=N). HRMS (ES$^+$): calcd. for $C_{30}H_{25}N_3OS$ [M + H]$^+$ 476.1797; found 476.1789. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 3198, 3063, 3027, 2964, 2922, 2851, 1636, 1579, 1515, 1451, 1271, 751, 699 cm^{-1}. $C_{30}H_{25}N_3OS$ (475.60): calcd. C 75.76, H 5.30, N 8.84; found C 75.17, H 5.44, N 8.49.

2-[(*S*)-4-Benzyl-4,5-dihydrooxazol-2-yl]-*N*-{2-[(*S*)-4-benzyl-4,5-dihydrothiazol-2-yl]phenyl}benzenamine (4d): Yield 19% (96 mg; Method A), 64% (160 mg; Method B), white oil. TLC: R_f = 0.28 (cyclohexane/EtOAc, 8:1). $[a]_D^{20}$ = +74.9 (c = 1.03, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.73 (dd, ^2J = 13.8, ^3J = 8.2 Hz, 1 H, CH_2Ph), 2.80 (dd, ^2J = 13.8, ^3J = 8.8 Hz, 1 H, CH_2S), 3.00 (dd, ^2J = 10.9, ^3J = 7.1 Hz, 1 H, CH_2Ph), 3.15 (dd, ^2J = 13.8, ^3J = 5.9 Hz, 1 H, CH_2Ph), 3.19 (dd, ^2J = 10.9, ^3J = 8.2 Hz, 1 H, CH_2Ph), 3.24 (dd, ^2J = 13.8, ^3J = 5.3 Hz, 1 H, CH_2S), 4.00 (app. t, ^3J = 7.9 Hz, 1 H, CH_2O), 4.24 (dd, ^2J = 8.2, ^3J = 9.1 Hz, 1 H, CH_2O), 4.49–4.54 (m, 1 H, CHN), 4.78–4.83 (m, 1 H, CHN), 6.86–6.89 (m, 1 H, Ar-HC), 6.95–6.98 (m, 1 H, Ar-HC), 7.15–7.21 (m, 10 H, Ar-HC), 7.26–7.31 (m, 2 H, Ar-HC), 7.37 (dd, ^3J = 8.5, ^4J

= 0.9 Hz, 1 H, Ar-*H*C), 7.46 (dd, ^3J = 8.2, ^4J = 0.9 Hz, 1 H, Ar-*H*C), 7.65 (dd, ^3J = 7.6, ^4J = 1.5 Hz, 1 H, Ar-*H*C), 7.79 (dd, ^3J = 7.6, ^4J = 1.5 Hz, 1 H, Ar-*H*C), 10.97 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 36.6 (*C*H_2Ph), 40.5 (*C*H_2S), 42.0 (*C*H_2Ph), 68.3 (*C*HN), 70.6 (*C*H_2O), 79.0 (*C*HN), 115.1 [C_{Ar}(C=N)], 117.7, 119.4, 119.7, 120.7 [C_{Ar}(H)], 122.9 [C_{Ar}(C=N)], 126.3, 126.4, 128.4, 129.3, 130.3, 130.9, 131.4, 131.6 [C_{Ar}(H)], 138.1 (*i*-Ph), 138.6 (*i*-Ph), 141.8 [C_{Ar}(NH)], 143.8 [C_{Ar}(NH)], 163.1 (*C*=N), 166.0 (*C*=N) ppm. IR (KBr): $\tilde{\nu}$ = 3166, 3025, 2918, 2850, 1638, 1578, 1515, 1452, 1052, 1031, 739, 699 cm^{-1}. HRMS (ES$^+$): calcd. for $C_{32}H_{29}N_3OS$ [M + H]$^+$ 504.2110; found 504.2101. $C_{32}H_{29}N_3OS$ (503.66): calcd. C 76.31, H 5.80, N 8.34; found C 76.11, H 5.80, N 8.16.

2-[(*S*)-4-Benzyl-4,5-dihydrooxazol-2-yl]-*N*-{2-[(*S*)-4-*tert*-butyl-4,5-dihydrothiazol-2-yl]phenyl}benzenamine (4e): Yield 27% (63 mg; Method A), 72% (170 mg; Method B), white solid. M.p. 124–126 °C. TLC: R_f = 0.28 (cyclohexane/EtOAc, 8:1). $[\alpha]_D^{20}$ = +56.3 (*c* = 1.10, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00 [s, 9 H, C(CH_3)$_3$], 2.70 (dd, ^2J = 13.9, ^3J = 7.8 Hz, 1 H, CH_2Ph), 3.03–3.10 (m, 2 H, CH_2Ph, CH_2S), 3.17 (dd, ^2J = 11.0, ^3J = 9.0 Hz, 1 H, CH_2S), 4.00 (t, ^2J = 7.8, ^3J = 7.8 Hz, 1 H, CH_2O), 4.21–4.27 (m, 2 H, C*H*N, CH_2O), 4.51–4.57 (m, 1 H, C*H*N), 6.88 (ddd, ^3J = 8.2, ^3J = 6.5, ^4J = 1.9 Hz, 1 H, Ar-*H*C), 6.95 (app. t, ^3J = 7.8 Hz, 1 H, Ar-*H*C), 7.15–7.22 (m, 5 H, Ar-*H*C), 7.24–7.30 (m, 3 H, Ar-*H*C), 7.34 (br. d, ^3J = 7.8 Hz, 1 H, Ar-*H*C), 7.67 (dd, ^3J = 7.8, ^4J = 1.2 Hz, 1 H, Ar-*H*C), 7.79 (dd, ^3J = 7.8, ^4J = 1.2 Hz, 1 H, Ar-*H*C), 10.61 (br. s, N*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.9 [C(*C*H$_3$)$_3$], 33.2 (*C*H$_2$S), 35.1 [*C*(CH$_3$)$_3$], 41.9 (*C*H$_2$Ph), 68.1 (*C*HN), 70.7 (*C*H$_2$O), 88.2 (*C*HN), 115.7 [C_{Ar}(C=N)], 119.0, 119.7, 120.6 [C_{Ar}(H)], 123.1 [C_{Ar}(C=N)], 126.4, 128.4, 129.4, 130.4, 130.8, 131.4, 131.7 [C_{Ar}(H)], 138.1 [C_{Ar}(4°)], 142.3 [C_{Ar}(4°)], 143.9 [C_{Ar}(4°)], 163.1 (*C*=N), 165.2 (*C*=N) ppm. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 3219, 3068, 3030, 2950, 1593, 1510, 1455, 1308, 1273, 1219, 1048, 988, 942, 745, 698 cm^{-1}. HRMS (ES$^+$): calcd. for $C_{29}H_{31}N_3OS$ [M + H]$^+$ 470.2266; found 470.2268. $C_{29}H_{31}N_3OS$ (469.64): calcd. C 74.17, H 6.65, N 8.95; found C 73.98, H 6.66, N 8.61.

2-[(*S*)-4-Benzyl-4,5-dihydrothiazol-2-yl]-*N*-{2-[(*S*)-4-*tert*-butyl-4,5-dihydrooxazol-2-yl]phenyl}benzenamine (4f): Yield 17% (80 mg; Method A), 60% (142 mg; Method B), white semi-solid. TLC: R_f = 0.37 (cyclohexane/EtOAc, 8:1). $[\alpha]_D^{20}$ = +35.0 (*c* = 1.25, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.93 [s, 9 H, C(CH_3)$_3$], 2.80 (dd, ^2J = 13.6, ^3J = 8.8 Hz, 1 H, CH_2S), 3.00 (dd, ^2J = 10.9, ^3J = 6.9 Hz, 1 H, CH_2Ph), 3.20–3.24 (m, 2 H, CH_2Ph, CH_2S), 4.02 (dd, ^3J = 9.9, ^3J = 8.1 Hz, 1 H, CH_2O), 4.10 (app. t, ^3J = 9.1 Hz, 1 H, CH_2O), 4.22 (dd, ^3J = 9.9, ^2J = 8.4 Hz, 1 H, CH_2O), 4.89–4.94 (m, 1 H, C*H*N), 6.84–6.87 (m, 1 H, Ar-*H*C), 6.98 (app. t, ^3J = 7.5 Hz, 1 H, Ar-*H*C), 7.17–7.31 (m, 8 H, Ar-*H*C), 7.43 (d, ^3J = 8.2 Hz, 1 H, Ar-*H*C), 7.66 (dd, ^3J = 7.8, ^4J = 1.4 Hz, 1 H, Ar-*H*C), 7.80 (dd, ^3J = 7.8, ^4J = 1.3 Hz, 1 H, Ar-*H*C), 10.86 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 26.0 [C(*C*H$_3$)$_3$], 30.9 [*C*(CH$_3$)$_3$], 36.7 (*C*H$_2$Ph), 40.3 (*C*H$_2$S), 67.3 (*C*H$_2$O), 76.7 (*C*HN), 78.7 (*C*HN), 114.5 [C_{Ar}(C=N)], 116.9, 118.9, 121.0, 121.2 [C_{Ar}(H)], 124.2 [C_{Ar}(C=N)], 126.3, 128.4, 129.4, 130.2, 130.8, 131.3, 131.4 [C_{Ar}(H)], 138.7 (*ipso*-Ph), 141.5 [C_{Ar}(NH)], 144.3 [C_{Ar}(NH)], 162.6 (*C*=N), 165.8 (*C*=N) ppm. IR (KBr): $\tilde{\nu}$ = 3196, 2953, 2903, 2867, 1643, 1578, 1515, 1452, 1315, 1213, 1050, 1027, 749 cm^{-1}. HRMS (ES$^+$): calcd. for $C_{29}H_{31}N_3OS$ [M + H]$^+$ 470.2266; found 470.2255. $C_{29}H_{31}N_3OS$ (469.64): calcd. C 74.17, H 6.65, N 8.95; found C 73.80, H 6.69, N 8.88.

2-[(*S*)-4-Phenyl-4,5-dihydrooxazol-2-yl]-*N*-{2-[(*R*)-4-phenyl-4,5-dihydrothiazol-2-yl]phenyl}benzenamine (4g): Yield 22% (53 mg; Method B), colourless oil. M.p. 54–57 °C (turned into an oil). TLC: R_f = 0.27 (8:1, cyclohexane/EtOAc). $[\alpha]_D^{20}$ = +7.0 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (600 MHz, [D$_6$]benzene): δ = [2.70 (dd, ^2J = 10.7, ^3J = 9.6 Hz) and 2.71* (dd, ^2J = 10.7 Hz, ^3J = 9.2 Hz)] (3:1, 1 H, CH_2S), [3.02 (dd, ^2J = 10.7, ^3J = 8.7 Hz) and 3.03* (dd, ^2J = 10.8 Hz, ^3J = 8.8 Hz)] (3:1, 1 H, CH_2S), [3.58 (app. t, ^3J = 8.2 Hz) and 3.59* (app. t, ^3J = 8.2 Hz)] (3:1, 1 H, CH_2O), [3.92* (dd, ^3J = 10.1, ^2J = 8.1 Hz) and 3.95 (dd, ^3J = 10.1 Hz, ^2J = 8.1 Hz)] (1:3, 1 H, CH_2O), [4.70* (dd, ^3J = 9.8, ^3J = 8.5 Hz) and 4.90 (dd, ^3J = 10.0 Hz, ^3J = 8.4 Hz)] (1:3, 1 H, C*H*N), [5.25* (app. t, ^3J = 9.0 Hz) and 5.33 (app. t, ^3J = 9.1 Hz)] (1:3, 1 H, C*H*N), 6.69–6.73 (m, 2 H, Ar-*H*C), 6.92–6.95 (m, 1 H, Ar-*H*C), 6.96–7.02 (m, 9 H, Ar-*H*C), 7.06–7.08 (m, 1 H, Ar-*H*C), 7.12–7.14 (m, 1 H, Ar-*H*C), [7.35 (dd, ^3J = 8.4, ^4J = 0.6 Hz) and 7.41* (dd, ^3J = 8.4 Hz, ^4J = 0.6 Hz)] (3:1, 1 H, Ar-*H*C), [7.43 (dd, ^3J = 8.1, ^4J = 0.7 Hz) and 7.47* (dd, ^3J = 8.3 Hz, ^4J = 0.6 Hz)] (3:1, 1 H, Ar-*H*C), [7.83* (dd, ^3J = 7.8, ^4J = 1.5 Hz) and 7.91 (dd, ^3J = 7.9 Hz, ^4J = 1.5 Hz)] (1:3, 1 H, Ar-*H*C), [8.07* (dd, ^3J = 7.8, ^4J = 1.6 Hz) and 8.08 (dd, ^3J = 7.8 Hz, ^4J = 1.6 Hz)] (1:3, 1 H, Ar-*H*C), [11.64 (br. s) and 11.80* (br. s)] (3:1, 1 H, N*H*) ppm. ^{13}C NMR (150 MHz, [D$_6$]benzene): δ = [39.8, 40.2*] (*C*H$_2$S), [70.0*, 70.1] (*C*HN), [72.8, 73.0*] (*C*H$_2$O), [80.8*, 81.0] (*C*HN), [114.6*, 114.7] [C_{Ar}(C=N)], [{117.0*, 117.5}, {119.0*, 119.1},{120.0*, 120.2},{120.7*, 120.8}] (C_{Ar}(H)), [123.2, 123.6*] [C_{Ar}(C=N)], [{126.5, 126.5*}, {126.6, 126.6*}] (*o*-Ph, *m*-Ph), [{126.8*, 126.9}] (*p*-Ph), [{128.1*, 128.2}, {128.3*, 128.3}] (*o*-Ph, *m*-Ph), [{130.4*, 130.6}, {130.7*, 131.0}, {131.5*, 131.6}, 132.2] [C_{Ar}(H)], [141.7*, 142.1] [C_{Ar}(NH)], [142.6, 142.6*] (*i*-Ph), [142.9*, 143.0] (*i*-Ph), [144.3*, 144.4] [C_{Ar}(NH)], [163.6*, 163.7] (*C*=N), [166.7, 166.8*] (*C*=N) ppm. IR (NaCl, $CHCl_3$ film): $\tilde{\nu}$ = 3206, 3066, 3030, 2922, 1629, 1585, 1513, 1451, 1307, 1276, 1307, 750, 694 cm^{-1}. HRMS (ES$^+$): calcd. for $C_{30}H_{25}N_3OS$ [M + H]$^+$ 476.1797; found 476.1811.

General Procedure for the Catalytic Enantioselective Friedel–Crafts Reaction: $Zn(OTf)_2$ (9.3 mg, 0.025 mmol) and ligand **4** (0.025 mmol) were placed in a dried Schlenk tube under nitrogen followed by the addition of dry degassed toluene (2 mL). This solution was stirred at room temperature for 30 min before the nitroalkene **11** (0.5 mmol) was added. The resulting mixture was stirred at room temperature for 10 min and then cooled to –20 °C before adding indole **8** (57 mg, 0.5 mmol). After stirring at –20 °C for 15 h, the solvent was removed in vacuo, and the crude mixture was purified by column chromatography on silica gel (pentane/EtOAc, 5:1) to yield the desired pure product. The enantioselectivity was determined by HPLC using a Chiralcel® OD column.

3-(2-Nitro-1-phenylethyl)-1*H*-indole (10a): TLC: R_f = 0.20 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = –17.2 [*c* = 1.0, CH_2Cl_2, 71% *ee* (*R*)]. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.93 (dd, ^2J = 12.5, ^3J = 8.3 Hz, 1 H, CH_2NO$_2$), 5.05 (dd, ^2J = 12.5, ^3J = 7.6 Hz, 1 H, CH_2NO$_2$), 5.18 (app. t, ^3J = 8.0 Hz, 1 H, C*H*CH$_2$NO$_2$), 7.02 (d, ^3J = 2.2 Hz, 1 H, Ar-*H*C), 7.07 (app. t, ^3J = 7.8 Hz, 1 H, Ar-*H*C), 7.19 (app. t, ^3J = 7.8 Hz, 1 H, Ar-*H*C), 7.23–7.26 (m, 1 H, Ar-*H*C), 7.30–7.35 (m, 5 H, Ar-*H*C), 7.44 (d, ^3J = 7.8 Hz, 1 H, Ar-*H*C), 8.06 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.6 (*C*HCH$_2$NO$_2$), 79.5 (*C*H$_2$NO$_2$), 111.4 [C_{Ar}(H)], 114.5 [C_{Ar}(4°)], 118.9, 120.0, 121.6, 122.7 [C_{Ar}(H)], 126.1 [C_{Ar}(4°)], 127.6 (*p*-Ph), 127.8 (*m*-Ph), 128.9 (*o*-Ph), 136.5, 139.2 [C_{Ar}(4°)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{minor} = 22.8 min, t_{major} = 26.5 min.

3-[1-(Furan-2-yl)-2-nitroethyl]-1*H*-indole (10b): TLC: R_f = 0.11 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = +14.0 (*c* = 1.12, $CHCl_3$, 28% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.90 (dd, ^2J = 12.5, ^3J = 7.4 Hz, 1 H, CH_2NO$_2$), 5.05 (dd, ^2J = 12.5, ^3J = 8.1 Hz, 1 H, CH_2NO$_2$), 5.25

(app. t, ^3J = 7.8 Hz, 1 H, C*H*CH_2NO_2), 6.15–6.16 (m, 1 H, Ar-*H*C), 6.30 (dd, ^3J = 3.3, ^3J = 1.9 Hz, 1 H, Ar-*H*C), 7.10 (d, ^3J = 2.5 Hz, 1 H, Ar-*H*C), 7.13 (ddd, ^3J = 8.0, ^3J = 7.1, ^4J = 1.0 Hz, 1 H, Ar-*H*C), 7.21 (ddd, ^3J = 8.1, ^3J = 7.1, ^4J = 1.0 Hz, 1 H, Ar-*H*C), 7.34–7.38 (m, 2 H, Ar-*H*C), 7.55 (dd, ^3J = 7.9, ^4J = 0.8 Hz, 1 H, Ar-*H*C), 8.10 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.8 (*C*HCH_2NO_2), 77.9 (*C*H_2NO_2), 107.4, 110.5, 111.5 [C_{Ar}(H)], 111.7 [C_{Ar}(4°)], 118.7, 120.0, 122.7, 122.7 [C_{Ar}(H)], 125.7, 136.3 [C_{Ar}(4°)], 142.3 [C_{Ar}(H)], 152.2 [C_{Ar}(4°)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{major} = 14.3 min, t_{minor} = 20.3 min.

3-[1-(2-Methoxyphenyl)-2-nitroethyl]-1*H*-indole (10c): TLC: R_f = 0.12 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = –6.3 (*c* = 1.12, $CHCl_3$, 17% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OC*H*$_3$) 4.96 (dd, ^2J = 12.5, ^3J = 9.0 Hz, 1 H, C*H*$_2NO_2$), 5.02 (dd, ^2J = 12.5, ^3J = 6.8 Hz, 1 H, C*H*$_2NO_2$), 5.59 (dd, ^3J = 9.0, ^3J = 6.8 Hz, 1 H, C*H*CH_2NO_2), 6.81 (ddd, ^3J = 8.5, ^3J = 7.5, ^4J = 1.0 Hz, 1 H, Ar-*H*C), 6.90 (dd, ^3J = 8.2, ^4J = 0.7 Hz, 1 H, Ar-*H*C), 7.03–7.09 (m, 3 H, Ar-*H*C), 7.16 (ddd, ^3J = 8.1, ^3J = 7.0, ^4J = 1.1 Hz, 1 H, Ar-*H*C), 7.21 (ddd, ^3J = 9.1, ^3J = 8.2, ^4J = 1.7 Hz, 1 H, Ar-*H*C), 7.30 (br. d, ^3J = 8.2 Hz, 1 H, Ar-*H*C), 7.46 (dd, ^3J = 7.9, ^4J = 0.5 Hz, 1 H, Ar-*H*C), 8.02 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.5 (*C*HCH_2NO_2), 54.5 (O*C*H$_3$), 77.1 (*C*H_2NO_2), 109.8, 110.2 [C_{Ar}(H)], 112.9 [C_{Ar}(4°)], 118.0, 118.7, 119.7, 120.9, 121.4 [C_{Ar}(H)], 125.5, 126.2 [C_{Ar}(4°)], 127.6, 127.9 [C_{Ar}(H)], 135.3, 155.8 [C_{Ar}(4°)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{minor} = 12.2 min, t_{major} = 14.2 min.

3-[1-(2-Chlorophenyl)-2-nitroethyl]-1*H*-indole (10d): TLC: R_f = 0.12 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = +20.8 (*c* = 1.10, $CHCl_3$, 20% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.91–5.01 (m, 2 H, C*H*$_2NO_2$), 5.73 (app. t, ^3J = 8.0 Hz, 1 H, C*H*CH_2NO_2), 7.04–7.20 (m, 6 H, Ar-*H*C), 7.31 (d, 1 H, Ar-*H*C), 7.40–7.43 (m, 2 H, Ar-*H*C), 8.11 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.0 (*C*HCH_2NO_2), 77.7 (*C*H_2NO_2), 111.4 [C_{Ar}(H)], 113.2 [C_{Ar}(4°)], 118.9, 120.0, 122.0, 122.8, [C_{Ar} (H)], 126.2 [C_{Ar}(4°)], 127.3, 128.9, 129.0, 130.1 [C_{Ar}(H)], 133.8, 136.4, 136.5 [C_{Ar}(4°)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{minor} = 16.5 min, t_{major} = 25.2 min.

3-[1-(3-Bromophenyl)-2-nitroethyl]-1*H*-indole (10e): TLC: R_f = 0.14 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = –2.0 (*c* = 1.00, $CHCl_3$, 76% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.89 (dd, ^2J = 12.6, ^3J = 8.4 Hz, 1 H, C*H*$_2NO_2$), 5.02 (dd, ^2J = 12.6, ^3J = 7.5 Hz, 1 H, C*H*$_2NO_2$), 5.14 (app. t, ^3J = 8.0 Hz, 1 H, C*H*CH_2NO_2), 7.00 (dd, ^3J = 2.5, ^4J = 2.0 Hz, 1 H, Ar-*H*C), 7.08 (ddd, ^3J = 8.0, ^3J = 7.2, ^4J = 0.9 Hz, 1 H, Ar-*H*C), 7.17 (t, ^3J = 7.8 Hz, 1 H, Ar-*H*C), 7.20 (ddd, ^3J = 8.1, ^3J = 7.1, ^4J = 1.0 Hz, 1 H, Ar-*H*C), 7.26 (br. d, ^3J = 7.8 Hz, 1 H, Ar-*H*C), 7.34 (br. d, ^3J = 8.2 Hz, 1 H, Ar-*H*C), 7.36–7.39 (m, 1 H, Ar-*H*C), 7.41 (br. d, ^3J = 8.0 Hz, 1 H, Ar-*H*C), 7.45 (app. t, ^4J = 1.8 Hz, 1 H, Ar-*H*C), 8.12 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.1 (*C*HCH_2NO_2), 79.2 (*C*H_2NO_2), 111.5 [C_{Ar}(H)], 113.6 [C_{Ar}(4°)], 118.7, 120.1, 121.6, 122.9 [C_{Ar}(H)], 123.0, 125.9 [C_{Ar}(4°)], 126.5, 130.5, 130.8, 130.9 [C_{Ar}(H)], 136.5, 141.6 [C_{Ar}(4°)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{minor} = 25.0 min, t_{major} = 33.8 min.

3-[1-(3-Chlorophenyl)-2-nitroethyl]-1*H*-indole (10f): TLC: R_f = 0.20 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = –3.0 (*c* = 1.2, $CHCl_3$, 64% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.90 (dd, ^2J = 12.6, ^3J = 8.4 Hz, 1 H, C*H*$_2NO_2$), 5.03 (dd, ^2J = 12.6, ^3J = 7.5 Hz, 1 H, C*H*$_2NO_2$), 5.15 (app. t, ^3J = 8.0 Hz, 1 H, C*H*CH_2NO_2), 7.01 (br. d, ^3J = 2.4 Hz, 1 H, Ar-*H*C), 7.08 (ddd, ^3J = 7.9, ^3J = 7.3, ^4J = 0.8 Hz, 1 H, Ar-*H*C), 7.18–7.24 (m, 4 H, Ar-*H*C), 7.30 (br. s, 1 H, Ar-*H*C), 7.35 (br. d, ^3J = 8.2 Hz, 1 H, Ar-*H*C), 7.41 (br. d, ^3J = 8.0 Hz, 1 H, Ar-*H*C), 8.15 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.2 (*C*HCH_2NO_2), 79.2 (*C*H_2NO_2), 111.5 [C_{Ar}(H)], 113.6 [C_{Ar}(4°)], 118.7, 120.1, 121.6, 122.9 [C_{Ar}(H)], 125.9 [C_{Ar}(4°)] 126.0, 127.9, 128.0, 130.2 [C_{Ar}(H)], 134.8, 136.5, 141.3 [C_{Ar}(4°)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{minor} = 24.4 min, t_{major} = 32.7 min.

3-[1-(4-Methoxyphenyl)-2-nitroethyl]-1*H*-indole (10g): TLC: R_f = 0.10 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = –4.0 (*c* = 1.15, $CHCl_3$, 74% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OC*H*$_3$) 4.89 (dd, ^2J = 12.3, ^3J = 8.4 Hz, 1 H, C*H*$_2NO_2$), 5.04 (dd, ^2J = 12.3, ^3J = 7.5 Hz, 1 H, C*H*$_2NO_2$), 5.13 (app. t, ^3J = 8.0 Hz, 1 H, C*H*CH_2NO_2), 6.82–6.86 (m, 2 H, Ar-*H*C), 7.00 (br. d, ^3J = 1.9 Hz, 1 H, Ar-*H*C), 7.07 (ddd, ^3J = 8.0, ^3J = 7.2, ^4J = 0.9 Hz, 1 H, Ar-*H*C), 7.19 (ddd, ^3J = 8.1, ^3J = 7.1, ^4J = 1.0 Hz, 1 H, Ar-*H*C), 7.22–7.25 (m, 2 H, Ar-*H*C), 7.34 (br. d, ^3J = 8.2 Hz, 1 H, Ar-*H*C), 7.43 (br. d, ^3J = 8.0 Hz, 1 H, Ar-*H*C), 8.07 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.9 (*C*HCH_2NO_2), 55.2 (O*C*H$_3$), 79.8 (*C*H_2NO_2), 111.3 [C_{Ar}(H)], 114.3 [2× C_{Ar}(H)], 114.8 [C_{Ar}(4°)], 119.0, 119.9, 121.4, 122.7 [C_{Ar}(H)], 126.1 [C_{Ar}(4°)], 128.8 [2× C_{Ar}(H)], 131.2, 136.5, 158.9 [C_{Ar}(4°)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{minor} = 23.0 min, t_{major} = 26.4 min.

3-[1-(4-Bromophenyl)-2-nitroethyl]-1*H*-indole (10h): TLC: R_f = 0.1 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = +7.5 (*c* = 1.1, $CHCl_3$, 60% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.90 (dd, ^2J = 12.5, ^3J = 8.6 Hz, 1 H, C*H*$_2NO_2$), 5.04 (dd, ^2J = 12.5, ^3J = 7.3 Hz, 1 H, C*H*$_2NO_2$), 5.14 (t, ^3J = 7.9 Hz, 1 H, C*H*CH_2NO_2), 7.00 (dd, ^3J = 2.5, ^4J = 0.6 Hz, 1 H, Ar-*H*C), 7.08 (ddd, ^3J = 8.0, ^3J = 7.2, ^4J = 1.0 Hz, 1 H, Ar-*H*C), 7.18–7.22 (m, 2 H, Ar-*H*C), 7.35–7.45 (m, 4 H, Ar-*H*C), 8.11 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.0 (*C*HCH_2NO_2), 79.2 (*C*H_2NO_2), 111.5 [C_{Ar}(H)], 113.9 [C_{Ar}(4°)], 118.8, 120.1, 121.5 [C_{Ar}(H)], 122.9 [C_{Ar}(4°)], 125.9, 129.5, 132.1 [C_{Ar}(H)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{minor} = 27.5 min, t_{major} = 34.5 min.

3-[1-(4-Chlorophenyl)-2-nitroethyl]-1*H*-indole (10i): TLC: R_f = 0.07 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = +3.3 (*c* = 1.05, $CHCl_3$, 67% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.89 (dd, ^2J = 12.5, ^3J = 8.6 Hz, 1 H, C*H*$_2NO_2$), 5.04 (dd, ^2J = 12.5, ^3J = 7.3 Hz, 1 H, C*H*$_2NO_2$), 5.15 (app. t, ^3J = 8.0 Hz, 1 H, C*H*CH_2NO_2), 6.99 (dd, ^3J = 2.5, ^4J = 0.4 Hz, 1 H, Ar-*H*C), 7.07 (ddd, ^3J = 8.0, ^3J = 7.2, ^4J = 1.0 Hz, 1 H, Ar-*H*C), 7.20 (ddd, ^3J = 8.1, ^3J = 7.1, ^4J = 1.0 Hz, 1 H, Ar-*H*C), 7.24–7.29 (m, 4 H, Ar-*H*C), 7.34 (d, ^3J = 8.2 Hz, 1 H, Ar-*H*C), 7.39 (d, ^3J = 7.9 Hz, 1 H, Ar-*H*C), 8.11 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.9 (*C*HCH_2NO_2), 79.3 (*C*H_2NO_2), 111.5 [C_{Ar}(H)], 113.9 [C_{Ar}(4°)], 118.9, 120.1, 121.5, 122.9 [C_{Ar}(H)], 125.9 [C_{Ar}(4°)], 129.1, 129.1 (*m*-Ph, *o*-Ph), 133.4, 136.5, 137.7 [C_{Ar}(4°)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{minor} = 25.9 min, t_{major} = 31.9 min.

3-[1-(3,4-Dimethoxyphenyl)-2-nitroethyl]-1*H*-indole (10j): TLC: R_f = 0.05 (pentane/EtOAc, 5:1). $[\alpha]_D^{20}$ = –6.2 (*c* = 1.02, $CHCl_3$, 38% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OC*H*$_3$) 3.83 (s, 3 H, OC*H*$_3$) 4.91 (dd, ^2J = 12.3, ^3J = 8.5 Hz, 1 H, C*H*$_2NO_2$), 5.04 (dd, ^2J = 12.3, ^3J = 7.4 Hz, 1 H, C*H*$_2NO_2$), 5.13 (app. t, ^3J = 8.0 Hz, 1 H, C*H*CH_2NO_2), 6.79–6.83 (m, 2 H, Ar-*H*C), 6.89 (dd, ^3J = 8.2, ^4J = 2.0 Hz, 1 H, Ar-*H*C), 6.99 (d, ^3J = 2.0 Hz, 1 H, Ar-

*H*C), 7.07 (ddd, ^3J = 8.0, ^3J = 7.3, ^4J = 0.9 Hz, 1 H, Ar-*H*C), 7.19 (ddd, ^3J = 8.0, ^3J = 7.2, ^4J = 1.0 Hz, 1 H, Ar-*H*C), 7.34 (d, ^3J = 8.2 Hz, 1 H, Ar-*H*C), 7.45 (d, ^3J = 8.0 Hz, 1 H, Ar-*H*C), 8.19 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.3 (*C*HCH$_2$NO$_2$), 55.8 (O*C*H$_3$), 55.9 (O*C*H$_3$), 79.7 (*C*H$_2$NO$_2$), 111.2, 111.4, 111.4 [C_{Ar}(H)], 114.6 [C_{Ar}(4°)], 118.9, 119.7, 119.9, 121.6, 122.7 [C_{Ar}(H)], 126.1, 131.7, 136.5, 148.4, 149.2 [C_{Ar}(4°)] ppm. Enantiomeric excess determined by HPLC: Chiracel® OD, hexane/2-propanol (70:30), 0.9 mL/min, retention times: t_{minor} = 25.0 min, t_{major} = 30.7 min.

Single-Crystal Structure of 4f: Crystals suitable for X-ray analysis were grown by slow concentration of a saturated solution of **4f** in a mixture of dichloromethane/*n*-hexane (1:1) at room temperature. $C_{29}H_{31}N_3OS$, M = 469.64, orthorhombic, a = 10.3089(8) Å, b = 11.8517(9) Å, c = 20.4721(16) Å, U = 2501.2(3) Å^3, T = 100 K, space group $P2_12_12_1$ (no.19), Z = 4, 15960 reflections measured, 5442 unique (R_{int} = 0.0534), which were used in all calculations. The final $wR(F^2)$ was 0.1010 (all data).

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra for intermediates **5a**–**e**, **6a**–**e** and ligands **4a**–**g**; HPLC chromatograms for the catalysis products **10a**–**j** and crystal data for ligand **4f**.

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