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BINAM and H^8-BINAM-based chiral imines and Zn(OTf)$_2$-catalyzed enantioselective Friedel–Crafts alkylation of indoles with nitroalkenes

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ABSTRACT

Axially chiral imine ligands derived from (*R*)-BINAM are effective chiral ligands in the Zn(OTf)$_2$-promoted enantioselective Friedel–Crafts alkylation of indoles with nitroalkenes under mild conditions to give the corresponding adducts in good yields and moderate enantioselectivities.

1. Introduction

Friedel–Crafts alkylation is a powerful method for constructing new C–C bonds in synthetic organic chemistry.[1] Aromatic substrates and electron-deficient alkenes, such as β,γ-unsaturated-α-ketoesters,[2] acyl phosphonates,[3] alkylidene malonates,[4] α-hydroxy enones,[5] acyl heterocyclic compounds[6] and nitroalkenes,[7] are generally required for this reaction. Recently, the products derived from asymmetric Friedel–Crafts alkylation of indoles with electron-deficient alkenes have attracted much attention,[8] because most of them can be applied to access many important compounds with a biologically active indole framework, such as *physostigmine*[9] and clinical *anticholinergic drugs*.[10] Therefore, the Friedel–Crafts alkylation of indoles with nitroalkenes could be a more attractive reaction since the nitro functional group is a strongly electron-withdrawing group that can be readily transformed into an amino functional group.[11]

In some pioneering reports, several efficient chiral Lewis acids derived from chiral ligands and metal salts have been successfully applied in asymmetric Friedel–Crafts reaction of heterocycles with electron-deficient olefins. For example, various C_2-bisoxazoline-metal complexes have been used as chiral Lewis acids in the asymmetric Friedel–Crafts reaction of five- or six-membered heterocycles with α,β-unsaturated carbonyl compounds to give the corresponding alkylation products in good yields and high ees.[12] Moreover, the zirconium(IV)-(*R*)-[1,1′]binaphthalenyl-2,2′-diol (BINOL)-type complexes newly developed by Pedro et al. in 2007 were another highly efficient catalytic system in the asymmetric Friedel–Crafts reaction of indole and enones.[13] Although these efficient catalytic asymmetric systems have been developed, the exploration of new chiral ligands in an asymmetric Friedel–Crafts reaction remains a challenging task. Our group has been working on the development of chiral imine ligands derived from axially chiral [1,1′]binaphthalenyl-2,2′-diamine (BINAM) in simple experimental procedures.[14] Herein, we report our results on the enantioselective Friedel–Crafts alkylation of indole **1** with nitroalkene **2**, catalyzed by Zn(OTf)$_2$ and (*R*)-BINAM-based chiral imine ligands.[15]

2. Results and discussion

These chiral imine ligands **L1**–**L9** and **L13**–**L14** derived from (*R*)-BINAM (1.0 mmol) were synthesized from the reactions with aromatic and heteroaromatic aldehydes (2.1 mmol) in dry toluene in the presence of molecular sieves (MS) 4 Å (50 mg) at room temperature for 24 h in 39–88% yields (Scheme 1). Similarly, these chiral imine ligands **L10**–**L12** derived from (*R*)-H^8-BINAM were prepared from (*R*)-H^8-BINAM **LA** and **LB**, as shown in Scheme 2, in 39%, 33% and 73% yields, respectively, according to the literature procedure.[16] In addition, (*R*)-BINAM-based salen-type ligands **L15** and **L16** were easily synthesized from the reactions with salicyl aldehydes at reflux in ethanol for 12 h in 51% and 66% yields, respectively (Scheme 3).

Initially, we utilized chiral bisimine ligand **L1** (0.02 mmol) with Zn(OTf)$_2$ (0.02 mmol) to catalyze the enantioselective Friedel–Crafts alkylation of indole **1a** (0.2 mmol) with nitroalkene **2c** (0.2 mmol) to examine the catalytic ability of this system, and subsequently found that, when using anhydrous toluene as a solvent and MS 4 Å (50 mg) as an additive, the corresponding Friedel–Crafts reaction product **3c** was obtained in 71% yield and 49% ee at room temperature (Table 1, entry 1). Next, chiral bisimine ligands **L2**–**L6** were tested in this reaction under identical conditions. It was found that the corresponding product **3c** was produced in 62–71% yields and 53–63% ee's (Table 1, entries 2–6). In addition, the chiral bisimine ligands **L7**–**L9** prepared from 2-naphthyl aldehyde, 2-quinolinyl aldehyde and 2-pyridyl aldehyde with (*R*)-BINAM did not improve the ee of **3c** under the standard conditions, to afford **3c** in 53% ee, 0% ee and 50% ee,

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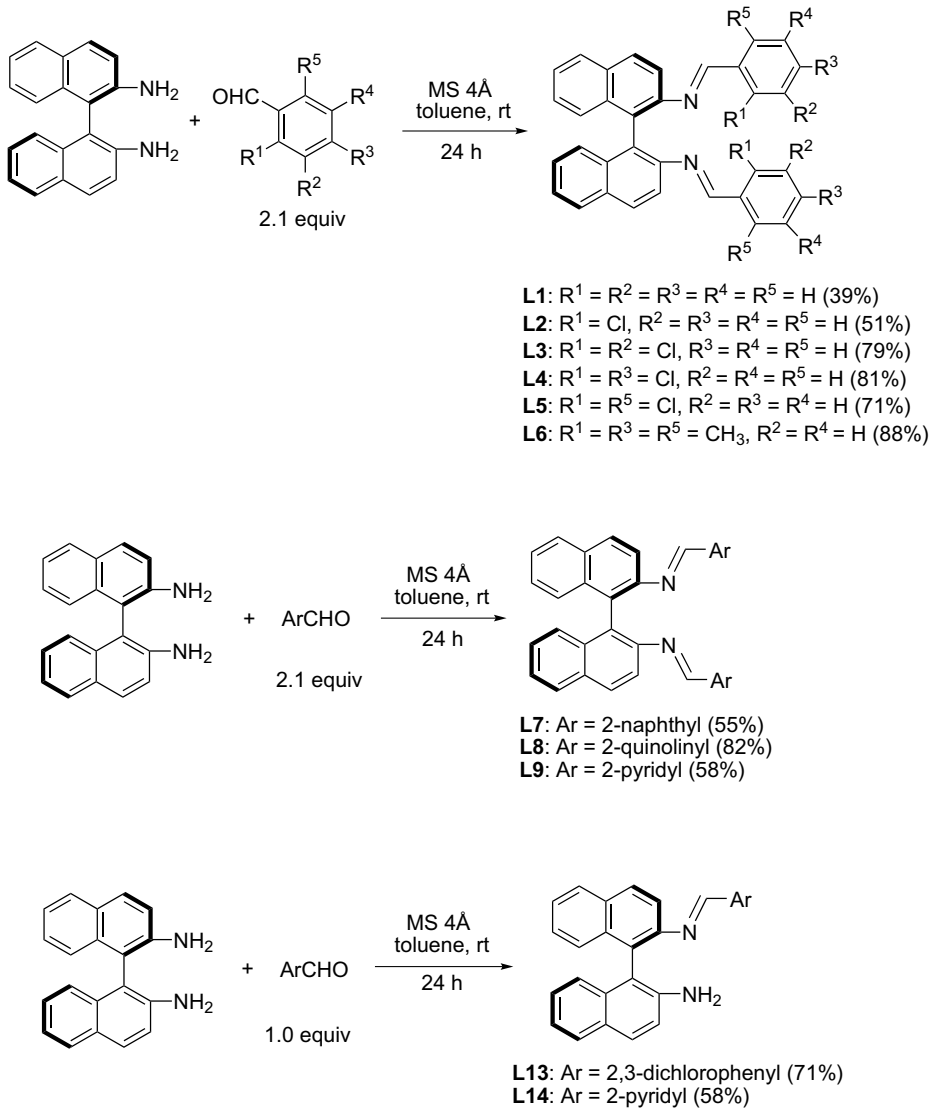


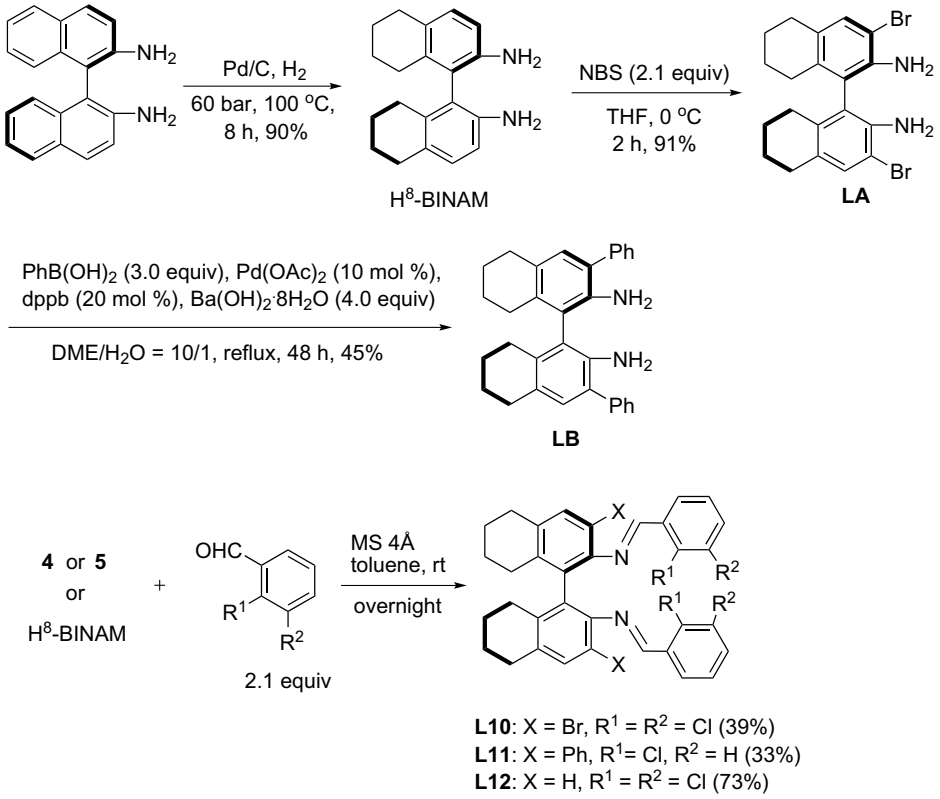
Scheme 1. Preparation of (*R*)-BINAM-based chiral imine ligands **L1**–**L9** and **L13**–**L14**.

respectively (Table 1, entries 7–9). The sterically bulky chiral bisimine ligands **L10**–**L12** with a cyclized alkyl skeleton afforded the corresponding product **3c** in low enantioselectivities (up to 24% ee) under identical conditions (Table 1, entries 10–12). To search for more efficient chiral imine ligands, we found that the chiral imine ligands **L13** and **L14** afforded **3c** in 67% ee and 60% ee, respectively (Table 1, entries 13 and 14). These BINAM-salen type ligands **L15** and **L16** are not as effective as **L13** and **L14** to produce **3c** in lower ee's under otherwise identical conditions (Table 1, entries 15 and 16).

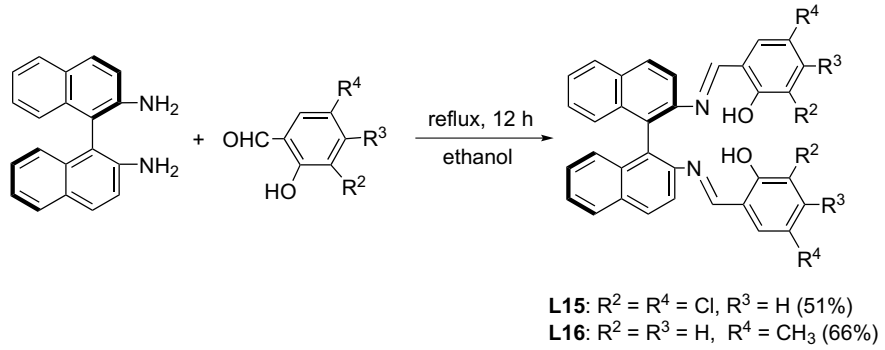
With the best chiral imine ligand being identified, we next examined the solvent and additive effects; the results of these experiments are summarized in Table 2. When the alkylation was carried out in methanol or hexane, no reaction occurred (Table 2, entries 4 and 5). In acetonitrile, **3c** was obtained in 59% yield but no ee (Table 2, entry 3). Using tetrahydrofuran (THF) or dichloromethane as the solvent afforded **3c** in lower ee (Table 2, entries 1 and 2). Therefore, toluene is the solvent of choice. In the asymmetric Friedel–Crafts alkylation, the additives often changed the reactivity and enantioselectivity under identical conditions. We found that the addition of 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) (2 equiv) could accelerate the reaction rate, but did not improve the enantioselectivity (Table 2, entry 7).[4d] Moreover, adding 0.2 equiv of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[7c] decreased both the yield and enantioselectivity of **3c** (Table 2, entry 8).

To further optimize the reaction conditions, we attempted to evaluate other metal Lewis acids with chiral imine ligand **L13**. The combination of **L13** with $Cu(OAc)_2$ in toluene afforded **3c** in 50% yield, but with no ee (Table 3, entry 1). Using $Cu(OTf)_2$ or $Ni(ClO_4)_2{\cdot}6H_2O$ instead of $Cu(OAc)_2$ gave **3c** in 47% yield and 71% yield as well as 23% ee and 5% ee, respectively (Table 3, entries 2 and 3). Therefore, $Zn(OTf)_2$ is a better metal Lewis acid in this reaction. With $Zn(OTf)_2$ as a Lewis acid under the best conditions, we also examined the influence of reaction temperatures on the ee of **3c**. However, we found that decreasing the reaction temperature to 0 °C or −20 °C did not improve the ee of **3c** (Table 3, entries 4–6).

Next, the generality of this asymmetric Friedel–Crafts alkylation was investigated. The results of these examinations are shown in Table 4. As can be seen, by using various aromatic nitroalkenes **2a**, **2b**, **2d**, **2e**, **2f**, and **2g**, **2i**, **2j** in this reaction, the corresponding Friedel–Crafts alkylation products **3a**, **3b**, **3d**, **3e**, **3f**, and **3g**, **3i**, **3j**, **3k** were obtained in 60–90% yields and 42–67% ee's under standard conditions (Table 4, entries 1–4 and 6, 8–10). Only in the reaction between indole **1a** and nitroalkene **2h** having an



Scheme 2. Preparation of (*R*)-H^8-BINAM-based chiral imine ligands **L10**–**L12**.



Scheme 3. Preparation of BINAM-salen type ligands **L15**–**L16**.

ortho-nitrobenzene moiety, the corresponding product **3h** was formed in 60% yield and 32% ee (Table 4, entry 7). However, using the N-protected indole **1b** in this asymmetric Friedel–Crafts reaction afforded the corresponding product **3l** in 23% yield and 9% ee, suggesting that N-blocked indole is not an effective substrate in this catalytic system (Table 4, entry 11).

3. Conclusion

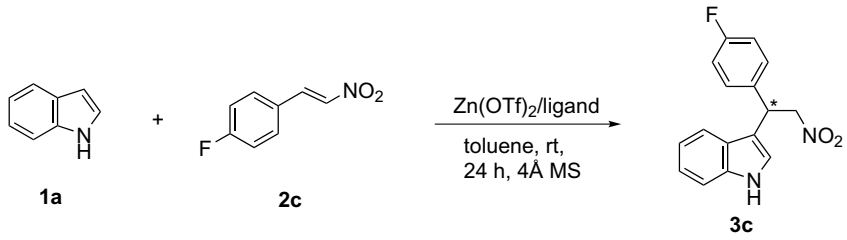
In conclusion, chiral imine ligand **L13**, which can be readily prepared from commercially available (*R*)-BINAM and 2,3-dichlorophenyl aldehyde, was found to be an effective chiral ligand for the Zn(OTf)$_2$-catalyzed enantioselective Friedel–Crafts alkylation of indoles with nitroalkenes to give the corresponding adducts in good yields and moderate enantioselectivities. Although the achieved ees are not yet good enough in synthetic organic chemistry, based on above results, we are currently planning to design and synthesize more effective chiral imine ligands in the asymmetric Friedel–Crafts alkylation. Work along this line is currently in progress.

4. Experimental

4.1. General methods

MP was obtained with a Yanagimoto micro melting point apparatus and is uncorrected. Optical rotations were determined in a solution of $CHCl_3$ or CH_2Cl_2 at 20 °C by using a Perkin–Elmer-241 MC polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. Infrared spectra were measured on a spectrometer. Unless noted, ^{1}H NMR spectra were recorded for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; ^{19}F NMR spectra were

Table 1
Effect of chiral imine ligands on the $Zn(OTf)_2$-catalyzed Friedel–Crafts alkylation of indole **1a** with nitroalkene **2c**

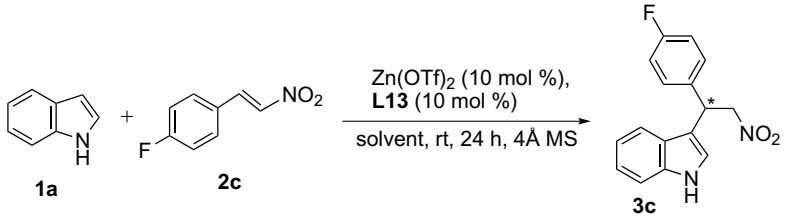


1a **2c** **3c**

Entry[a]	Ligand	Yield[b] (%)	ee[c] (%)
1	**L1**	71	49
2	**L2**	62	55
3	**L3**	71	63
4	**L4**	66	63
5	**L5**	70	60
6	**L6**	67	53
7	**L7**	71	50
8	**L8**	53	0
9	**L9**	76	37
10	**L10**	70	6
11	**L11**	65	24
12	**L12**	62	9
13	**L13**	70	67
14	**L14**	76	60
15	**L15**	80	5
16	**L16**	75	32

[a] All reactions were performed with indole **1a** (0.20 mmol), nitroalkene **2c** (0.20 mmol) and 50 mg of MS 4 Å in 1.0 mL of toluene in the presence of 10 mol % of $Zn(OTf)_2$-ligand complex.
[b] Isolated yield.
[c] Determined by HPLC on OD-H column (hexane/2-propanol = 70/30, 1.0 mL/min).

Table 2
Optimization of the reaction conditions in the asymmetric Friedel–Crafts alkylation of indole **1a** with nitroalkene **2c**



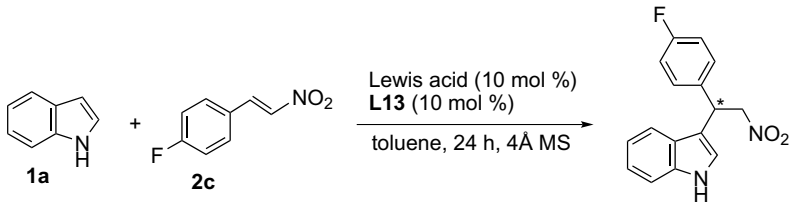
1a **2c** **3c**

Entry[a]	Solvent	Time (h)	Additive	Yield[b] (%)	ee[c] (%)
1	THF	72	–	36	1
2	CH_2Cl_2	24	–	63	10
3	CH_3CN	72	–	59	0
4	CH_3OH	72	–	0	–
5	Hexane	72	–	0	–
6	Toluene	24	–	70	67
7[d]	Toluene	8	HFIP	70	62
8[e]	Toluene	24	DBU	58	52

[a] All reactions were performed with indole **1a** (0.20 mmol), nitroalkene **2c** (0.20 mmol) and 50 mg of MS 4 Å in 1.0 mL of solvent in the presence of 10 mol % of $Zn(OTf)_2$-**L13** complex.
[b] Isolated yield.
[c] Determined by HPLC on OD-H column (hexane/2-propanol = 70/30, 1.0 mL/min).
[d] Treated with 2.0 equiv HFIP.
[e] Treated with 0.20 equiv of DBU.

recorded at 282 MHz for a solution in $CDCl_3$ with $CFCl_3$ as the external reference. *J*-Values are in Hetrz. Mass spectra were recorded with a HP-5989 instrument and HRMS was measured by a Finnigan MA+ mass spectrometer. The organic solvents used were dried by standard methods when necessary. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai $60F_{254}$ silica gel-coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at an increased pressure. All Henry reactions were performed under argon using standard Schlenk techniques. The enantiomeric purities of adducts were determined by HPLC analysis using a chiral stationary phase column (column, Daicel Co. Chiralcel AD and OD) and the absolute configuration of the major enantiomer was assigned according to the sign of the specific rotation.

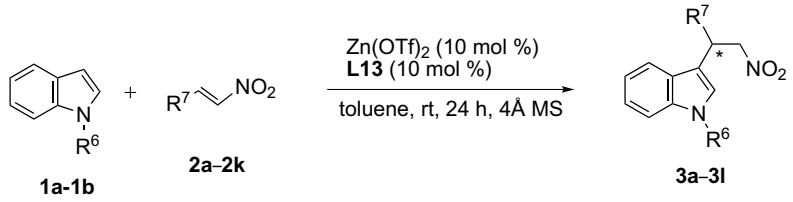
Table 3
Asymmetric Friedel–Crafts alkylation of indole **1a** with nitroalkene **2c** catalyzed by chiral ligand **L13** and a variety of Lewis acids



Entry[a]	Lewis acid	Time (h)	Temp (°C)	Yield[b] (%)	ee[c] (%)
1	$Cu(OAc)_2$	72	rt	50	0
2	$Cu(OTf)_2$	72	rt	47	23
3	$Ni(ClO_4)_2{\cdot}6H_2O$	24	rt	71	5
4	$Zn(OTf)_2$	36	−20	55	26
5	$Zn(OTf)_2$	36	0	56	53
6	$Zn(OTf)_2$	24	rt	70	67

[a] All reactions were performed with indole **1a** (0.20 mmol), nitroalkene **2c** (0.20 mmol) and 50 mg of MS 4 Å in 1.0 mL of toluene in the presence of 10 mol % of Lewis acids-**L13** complex.
[b] Isolated yield.
[c] Determined by HPLC on OD-H column (hexane/2-propanol = 70/30, 1.0 mL/min).

Table 4
Asymmetric Friedel–Crafts alkylation of indoles **1** with nitroalkenes **2** under optimal conditions



Entry[a]	Indole	R^6	Nitroalkene	R^7	Product	Yield[b] (%)	ee[c] (%)
1	**1a**	H	**2a**	C_6H_5	**3a**	68	61
2	**1a**	H	**2b**	4-ClC_6H_4	**3b**	75	60
3	**1a**	H	**2d**	4-MeC_6H_4	**3d**	90	58
4	**1a**	H	**2e**	4-$OMeC_6H_4$	**3e**	69	55
5	**1a**	H	**2f**	4-$NO_2C_6H_4$	**3f**	78	62
6	**1a**	H	**2g**	3-ClC_6H_4	**3g**	72	67
7	**1a**	H	**2h**	2-$NO_2C_6H_4$	**3h**	60	32
8	**1a**	H	**2i**	2-Furyl	**3i**	60	52
9	**1a**	H	**2j**	2-Naphthyl	**3j**	62	42
10	**1a**	H	**2k**	4-BrC_6H_4	**3k**	72	62
11	**1b**	Bn	**2c**	4-FC_6H_4	**3l**	23	9

[a] All reactions were performed with indole **1** (0.20 mmol), nitroalkene **2** (0.20 mmol) and 50 mg of MS 4 Å in 1.0 mL of toluene in the presence of 10 mol % of $Zn(OTf)_2$-**L13** complex.
[b] Isolated yield.
[c] Determined by HPLC on OD-H column (hexane/2-propanol = 70/30, 1.0 mL/min).

4.2. General procedure of the preparation of BINAM-based chiral imine ligands L1–L9 and L13–L14

To a solution of (*R*)-1,1′-binaphthyl-2,2′-diamine (1 mmol) and aromatic aldehyde (2.1 mmol or 1.0 mmol) in dry toluene (5.0 mL), the mixture was stirred at room temperature for 24 h. After removal of the solvent under reduced pressure, the corresponding enantiomerically pure imines were afforded as a yellow solid. Analytically pure samples could be obtained by crystallization, typically in PE/CH_2Cl_2.

4.2.1. (*R*)-(+)-*N*,*N*′-Dibenzylidene-1,1′-binaphthyl-2,2′-diamine L1

This is a known compound.[14] $[\alpha]_D^{20} = +161.8$ (*c* 0.50, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 7.25–7.31 (8H, m, Ar), 7.34–7.42 (10H, m, Ar), 7.90 (2H, d, *J* = 8.1 Hz, Ar), 7.95 (2H, d, *J* = 8.1 Hz, Ar), 8.18 (2H, s, CH).

4.2.2. (*R*)-(+)-*N*,*N*′-Bis(2-chlorobenzylidene)-1,1′-binaphthyl-2,2′-diamine L2

This is a known compound.[14a] $[\alpha]_D^{20} = +105.8$ (*c* 0.50, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 7.06–7.21 (6H, m, Ar), 7.29–7.58 (8H, m, Ar), 7.71–7.81 (3H, m, Ar), 7.88–7.97 (3H, m, Ar), 8.67 (2H, s, CH).

4.2.3. (*R*)-(+)-*N*,*N*′-Bis(2,3-dichlorobenzylidene)-1,1′-binaphthyl-2,2′-diamine L3

This is a known compound.[14a] $[\alpha]_D^{20} = +217.5$ (*c* 0.50, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 7.02 (2H, t, *J* = 7.8 Hz, Ar), 7.26–7.48 (12H, m, Ar), 7.92 (2H, d, *J* = 7.8 Hz, Ar), 7.98 (2H, d, *J* = 7.8 Hz, Ar), 8.63 (2H, s, CH).

4.2.4. (*R*)-(+)-*N*,*N*′-Bis(2,4-dichlorobenzylidene)-1,1′-binaphthyl-2,2′-diamine LA

This is a known compound.[14a] $[\alpha]_D^{20} = +140.5$ (*c* 0.50, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 7.03–7.21 (3H, m, Ar), 7.26–7.55 (11H, m, Ar), 7.78 (2H, d, *J* = 12.6 Hz, Ar), 7.88 (2H, d, *J* = 12.6 Hz, Ar), 8.57 (2H, s, CH).

4.2.5. (*R*)-(+)-*N*,*N*′-Bis(2,6-dichlorobenzylidene)-1,1′-binaphthyl-2,2′-diamine LB

This is a known compound.[14a] $[\alpha]_D^{20} = -109.5$ (*c* 0.50, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 6.99–7.04 (2H, m, Ar), 7.09–7.12 (4H, m, Ar), 7.24–7.42 (8H, m, Ar), 7.90 (2H, d, *J* = 7.8 Hz, Ar), 7.99 (2H, d, *J* = 7.8 Hz, Ar), 8.63 (2H, s, CH).

4.2.6. (*R*)-(+)-*N*,*N*′-Bis(2,4,6-trimethylbenzylidene)-1,1′-binaphthyl-2,2′-diamine L6

This is a known compound.[17] $[\alpha]_D^{20} = -62.5$ (c 0.50, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.89 (12H, s, CH_3), 2.16 (6H, s, CH_3), 6.67 (4H, s, Ar), 7.12–7.35 (8H, m, Ar), 7.86 (2H, d, *J* = 8.1 Hz, Ar), 7.93 (2H, d, *J* = 8.1 Hz, Ar), 8.68 (2H, s, CH).

4.2.7. (*R*)-(+)-*N*,*N*′-Bis(2-naphthyl)-1,1′-binaphthyl-2,2′-diamine L7

This is a known compound.[17d] $[\alpha]_D^{20} = +104.6$ (*c* 0.50, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 7.07–7.26 (6H, m, Ar), 7.34–7.53 (10H, m, Ar), 7.72–7.83 (6H, m, Ar), 7.98–8.08 (4H, m, Ar), 8.79 (1H, s, CH), 8.87 (1H, s, CH).

4.2.8. (*R*)-(+)-*N*,*N*′-Bis(2-quinolyl)-1,1′-binaphthyl-2,2′-diamine L8

This is a known compound.[17e] $[\alpha]_D^{20} = +16.1$ (*c* 0.35, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 7.29–7.43 (6H, m, Ar), 7.51–7.64 (8H, m, Ar), 7.75 (2H, d, *J* = 8.1 Hz, Ar), 7.89 (2H, d, *J* = 8.7 Hz, Ar), 7.95 (4H, d, *J* = 8.7 Hz, Ar), 8.05 (2H, d, *J* = 9.0 Hz, Ar), 8.63 (2H, s, CH).

4.2.9. (*R*)-(+)-*N*,*N*′-Bis(pyridin-2-ylmethylene)-1,1′-binaphthyl-2,2′-diamine L9

This is a known compound.[17] $[\alpha]_D^{20} = +102$ (*c* 0.25, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 7.15–7.20 (3H, m, Ar), 7.24–7.33 (3H, m, Ar), 7.38–7.43 (4H, m, Ar), 7.45–7.52 (4H, m, Ar), 7.92 (2H, d, *J* = 8.1 Hz, Ar), 7.99 (2H, d, *J* = 8.1 Hz, Ar), 8.45 (2H, s, CH), 8.48–7.51 (2H, m, Ar).

4.2.10. (*R*)-(+)-*N*-(2,3-Dichlorobenzylidene)-1,1′-binaphthyl-2,2′-diamine L13

This is a known compound.[14a] $[\alpha]_D^{20} = +117.7$ (*c* 0.50, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 3.45 (2H, s, NH), 6.99–7.30 (6H, m, Ar), 7.33–7.48 (4H, m, Ar), 7.51–7.81 (2H, m, Ar), 7.90–8.03 (2H, m, Ar), 8.63 (0.6H, s, CH), 8.63 (0.4H, s, CH).

4.2.11. (*R*)-(+)-*N*-(Pyridin-2-ylmethylene)-1,1′-binaphthyl-2,2′-diamine L14

This is a known compound.[17] $[\alpha]_D^{20} = +85.3$ (*c*9 0.50, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 3.64 (1H, s, NH), 3.69 (1H, s, NH), 6.99–7.34 (7H, m, Ar), 7.42–7.53 (3H, m, Ar), 7.73–7.82 (2H, m, Ar), 7.93 (1H, t, *J* = 8.1 Hz, Ar), 8.01 (1H, t, *J* = 8.1 Hz, Ar), 8.45 (0.5H, s, CH), 8.48 (0.5H, s, CH), 8.50 (0.5H, d, *J* = 4.8 Hz, Ar), 8.55 (0.5H, d, *J* = 4.8 Hz, Ar).

4.3. General procedure for the preparation of H^8-BINAM-based chiral imine ligands L10–L12

4.3.1. (*R*)-5,6,7,8,5′,6′,7′,8′-Octahydro-[1,1′]binaphthalenyl-2,2′-diamine

(*R*)-BINAM (284 mg, 1.0 mmol), 5% Pd/C (142 mg) and 50 mL of EtOAc were placed into a 100 mL autoclave and the reaction mixture was stirred under 60 bar H_2 at 100 °C for 8 h. After no more hydrogen consumption was detected, the reaction mixtures were cooled to room temperature and the Pd/C metal catalyst was filtered off, and then washed with CH_2Cl_2 (3 × 25 mL). The combined filtrates were concentrated in vacuum, then the residue was purified by flash column chromatography on silica gel (PE/EA = 4/1) to afford H^8-BINAM, which was a pure product on the basis of ^1H NMR spectroscopic data (262 mg, 0.90 mmol, 90% yield). This is a known compound.[17] ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.65–1.75 (8H, m, CH_2), 2.11–2.32 (4H, m, CH_2), 2.69–2.73 (4H, m, CH_2), 3.23 (4H, s, NH_2), 6.60 (2H, d, *J* = 8.1 Hz, Ar), 6.91 (4H, d, *J* = 8.1 Hz, Ar).

4.3.2. (*R*)-3,3′-Dibromo-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]-binaphthalenyl-2, 2′-diamine LA

To a stirred solution of (*R*)-H^8-BINAM (292 mg, 1.0 mmol) in anhydrous THF (3.0 mL) was added NBS (374 mg, 2.1 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 3 h. Then, the reaction was quenched with saturated $NaHCO_3$ aqueous solution and saturated Na_2SO_3 aqueous solution at 0 °C, and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: PE/EA = 20/1) to afford the pure product (*R*)-**4** detected by ^1H NMR spectroscopic data (409 mg, 0.91 mmol, 91% yield). This is a known compound.[17] $[\alpha]_D^{20} = +40.0$ (*c* 0.95, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.64–1.71 (8H, m, CH_2), 2.03–2.26 (4H, m, CH_2), 2.67–2.71 (4H, m, CH_2), 3.52 (4H, s, NH_2), 7.21 (2H, s, Ar).

4.3.3. (*R*)-3,3′-Diphenyl-5,6,7,8,5′,6′,7′,8′-octahydro[1,1′]-binaphthalenyl-2,2′-diamine LB

A mixture of (*R*)-**4** (450 mg, 1.0 mmol), $Pd(OAc)_2$ (22 mg, 0.1 mmol), dppb (85 mg, 0.2 mmol), $Ba(OH)_2{\cdot}8H_2O$ (1.26 g, 4.0 mmol) and phenylboronic acid (366 mg, 3.0 mmol) in degassed DME (4.0 mL) and H_2O (400 μL) was refluxed for 48 h. After cooling to room temperature, the resulting mixture was poured into water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: PE/EA = 55/1) to afford pure (*R*)-**5**, which is detected on the basis of ^1H NMR spectroscopic data (198 mg, 0.45 mmol, 45% yield). This is a known compound.[17] $[\alpha]_D^{20} = -27.4$ (*c* 1.13, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.66–1.74 (8H, m, CH_2), 2.23–2.41 (4H, m, CH_2), 2.74–2.76 (4H, m, CH_2), 3.53 (4H, s, NH_2), 6.92 (2H, s, Ar), 7.31 (2H, t, *J* = 6.9 Hz, Ar), 7.42 (4H, t, *J* = 7.5 Hz, Ar), 7.50 (4H, d, *J* = 6.9 Hz, Ar).

To a solution of (*R*)-1,1′-binaphthyl-2,2′-diamine (1.0 equiv) or the derivatives **4** or **5** in dry toluene (5.0 mL), was added the aromatic aldehyde (2.1 equiv or 1.0 equiv), after which the reaction mixture was stirred at room temperature for 24 h. After removal of the solvent under reduced pressure, the corresponding enantiomerically pure imine was produced as a yellow solid. Analytically pure samples could be obtained by recrystallization from solvent, typically from PE/CH_2Cl_2.

4.3.4. (*R*)-(+)-3,3′-Dibromo-*N*,*N*′-bis(2,3-dichlorobenzylidene)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine L10

$[\alpha]_D^{20} = +9.3$ (*c* 1.25, CH_2Cl_2). IR (CH_2Cl_2) *ν* 3473, 3378, 3045, 2932, 2857, 2836, 1697, 1691, 1630, 1604, 1585, 1556, 1471, 1459, 1421, 1383, 1354, 1309, 1263, 1198, 1136, 1099, 1051, 869, 824, 739 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.66–1.76 (8H, m, CH_2), 1.95–2.33 (4H, m, CH_2), 2.53–2.70 (4H, m, CH_2), 7.07 (2H, s, Ar), 7.21–7.23 (2H, m, Ar), 7.32–7.41 (2H, m, Ar), 7.87–7.91 (2H, m, Ar), 8.34 (2H, s, CH). MS (ESI) *m*/*z* 760.9

(M+H$^+$, 100). HRMS (ESI) Calcd for $C_{34}H_{26}Br_2N_2Cl_4$ requires (M$^+$+H) 759.9217, Found: 760.9290.

4.3.5. (*R*)-(+)-*N*,*N*′-Bis(2-chlorobenzylidene)-3,3′-diphenyl-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine L11

$[\alpha]_D^{20} = +3.8$ (*c* 0.35, CH_2Cl_2). IR (CH_2Cl_2) *ν* 3473, 3379, 3057, 3029, 2929, 2856, 2835, 1698, 1628, 1592, 1567, 1495, 1437, 1267, 1051, 1032, 779, 755, 739, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.65–1.78 (8H, m, CH_2), 2.27–2.51 (4H, m, CH_2), 2.73–2.88 (4H, m, CH_2), 7.08 (2H, s, Ar), 7.09–7.12 (4H, m, Ar), 7.18–7.26 (6H, m, Ar), 7.30–7.33 (4H, m, Ar), 7.39–7.47 (2H, m, Ar), 7.55–7.59 (2H, m, Ar), 8.33 (2H, s, CH). MS (ESI) *m*/*z* 689.3 (M+H$^+$, 100). HRMS (ESI) Calcd for $C_{46}H_{38}N_2Cl_2$ requires (M$^+$+H) 689.2412. Found: 689.2485.

4.3.6. (*R*)-(+)-*N*,*N*′-Bis(2,3-dichlorobenzylidene)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine L12

This is a known compound.[14b] $[\alpha]_D^{20} = +177.7$ (*c* 2.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 1.68–1.69 (8H, m, CH_2), 2.24–2.34 (4H, m, CH_2), 2.69–2.80 (4H, m, CH_2), 6.84 (2H, d, *J* = 8.4 Hz, Ar), 7.05–7.09 (4H, m, Ar), 7.38 (2H, d, *J* = 7.8 Hz, Ar), 7.59 (2H, d, *J* = 7.8 Hz, Ar), 8.61 (2H, s, CH).

4.4. General procedure for the preparation of chiral BINAM-Salen type ligands L15–L16

To a solution of (*R*)-1,1′-binaphthyl-2,2′-diamine (1 mmol) and salicylaldehyde (2.1 mmol) in absolute ethanol (8.0 mL), the reaction mixture was stirred at reflux for 12 h. After cooling to room temperature, yellow precipitates settled out, which were filtered to give the corresponding BINAM-salen type ligand **L15** and **L16** as a yellow solid.

4.4.1. (*R*)-(+)-1,1′-Binaphthyl-2,2′-diylbis(azan-1-yl-1-ylidene)-bis(methan-1-yl-1-ylidene)bis(2,4-dichlorophenol) L15

This is a known compound.[17d] $[\alpha]_D^{20} = -549.6$ (*c* 0.50, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 7.10 (2H, d, *J* = 2.4 Hz, Ar), 7.17 (2H, d, *J* = 8.4 Hz, Ar), 7.19–7.28 (4H, m, Ar), 7.49 (2H, t, *J* = 5.4 Hz, Ar), 7.61 (2H, d, *J* = 8.1 Hz, Ar), 7.98 (2H, d, *J* = 8.1 Hz, Ar), 8.11 (2H, d, *J* = 8.1 Hz, Ar), 8.56 (2H, s, CH), 12.76 (2H, s, OH).

4.4.2. (*R*)-(+)-1,1′-Binaphthyl-2,2′-diylbis(azan-1-yl-1-ylidene)-bis(methan-1-yl-1-ylidene)bis(4-methylphenol) L16

This is a known compound.[17d] $[\alpha]_D^{20} = -375.3$ (*c* 0.50, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 2.20 (6H, s, CH_3), 6.62 (2H, d, *J* = 8.1 Hz, Ar), 6.98 (4H, d, *J* = 10.8 Hz, Ar), 7.22–7.30 (4H, m, Ar), 7.44 (2H, t, *J* = 7.5 Hz, Ar), 7.61 (2H, d, *J* = 8.1 Hz, Ar), 7.96 (2H, d, *J* = 8.4 Hz, Ar), 8.10 (2H, d, *J* = 8.4 Hz, Ar), 8.59 (2H, s, CH), 11.85 (2H, s, OH).

4.5. Typical reaction procedure

$Zn(OTf)_2$ (7.4 mg, 0.02 mmol) and chiral imine ligand **L13** (8.4 mg, 0.02 mmol) were added into a dried Schlenk tube under an Ar atmosphere, and then dry toluene (1.0 mL) was added into the reaction vessel. The reaction solution was stirred at room temperature for 1 h under an Ar atmosphere and 1-fluoro-4-(2-nitrovinyl)benzene **2c** (31.6 mg, 0.2 mmol) was added into the reaction vessel. After stirring for 20 min at room temperature, indole **1a** (22.8 mg, 0.2 mmol) was added into the reaction mixtures. The resulting solution was stirred for 24 h. Then, the solvent was removed under vacuum and the residue was chromatographed on silica gel column with ethyl acetate/petroleum ether (1/9, v/v) as eluent to afford the corresponding product pure **3c** as a yellow oil.

4.5.1. 3-(2-Nitro-1-phenylethyl)-1*H*-indole 3a

This is a known compound.[7a,d] $[\alpha]_D^{20} = +24.7$ (*c* 1.05, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 4.93 (1H, dd, *J* = 12.6, 8.7 Hz, CH_2), 5.05 (1H, dd, *J* = 12.6, 7.8 Hz, CH_2), 5.17 (1H, t, *J* = 7.8 Hz, CH), 6.97 (1H, d, *J* = 2.1 Hz, Ar), 7.06 (1H, t, *J* = 7.2 Hz, Ar), 7.21–7.34 (6H, m, Ar), 7.43 (1H, d, *J* = 7.8 Hz, Ar), 8.05 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 25.13 min, t_{major} = 32.73 min; 61% ee).

4.5.2. 3-[1-(4-Chlorophenyl)-2-nitroethyl]-1*H*-indole 3b

This is a known compound.[7c,d] $[\alpha]_D^{20} = +10.2$ (*c* 0.95, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 4.88 (1H, dd, *J* = 12.3, 8.4 Hz, CH_2), 5.03 (1H, dd, *J* = 12.3, 7.5 Hz, CH_2), 5.15 (1H, t, *J* = 7.8 Hz, CH), 6.98 (2H, d, *J* = 2.1 Hz, Ar), 7.08 (1H, t, *J* = 7.2 Hz, Ar), 7.20–7.27 (4H, m, Ar), 7.36 (2H, dd, *J* = 13.8, 8.1 Hz, Ar), 8.10 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 30.52 min, t_{major} = 40.26 min; 60% ee).

4.5.3. 3-[1-(4-Fluorophenyl)-2-nitroethyl]-1*H*-indole 3c

This is a known compound.[7c,d] $[\alpha]_D^{20} = +26.3$ (*c* 1.80, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 4.90 (1H, dd, *J* = 12.0, 8.7 Hz, CH_2), 5.04 (1H, dd, *J* = 12.0, 7.5 Hz, CH_2), 5.18 (1H, t, *J* = 7.8 Hz, CH), 6.98–7.11 (4H, m, Ar), 7.19–7.33 (3H, m, Ar), 7.39 (2H, t, *J* = 8.4 Hz, CH), 8.14 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 24.08 min, t_{major} = 31.65 min; 67% ee).

4.5.4. 3-[1-(4-Methylphenyl)-2-nitroethyl]-1*H*-indole 3d

This is a known compound.[7c] $[\alpha]_D^{20} = +9.2$ (*c* 1.95, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 2.29 (3H, s, CH_3), 4.83 (1H, dd, *J* = 12.3, 8.7 Hz, CH_2), 5.01 (1H, dd, *J* = 12.3, 7.5 Hz, CH_2), 5.13 (1H, t, *J* = 7.8 Hz, CH), 6.95 (1H, d, *J* = 1.8 Hz, Ar), 6.96–7.45 (6H, m, Ar), 7.30 (1H, d, *J* = 7.8 Hz, Ar), 7.43 (1H, d, *J* = 7.8 Hz, Ar), 8.02 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 21.29 min, t_{major} = 25.89 min; 58% ee).

4.5.5. 3-[1-(4-Methoxyphenyl)-2-nitroethyl]-1*H*-indole 3e

This is a known compound.[7c,d] $[\alpha]_D^{20} = +15.1$ (*c* 1.15, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 3.76 (3H, s, OCH_3), 4.82 (1H, dd, *J* = 12.3, 8.4 Hz, CH_2), 5.03 (1H, dd, *J* = 12.3, 7.2 Hz, CH_2), 5.13 (1H, t, *J* = 7.8 Hz, CH), 6.83 (2H, d, *J* = 8.4 Hz, Ar), 6.99 (1H, d, *J* = 2.1 Hz, Ar), 7.07 (1H, t, *J* = 8.1 Hz, Ar), 7.16–7.44 (3H, m, Ar), 7.48 (1H, d, *J* = 7.8 Hz, Ar), 7.56 (1H, d, *J* = 7.8 Hz, Ar), 8.08 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 29.35 min, t_{major} = 34.86 min; 55% ee).

4.5.6. 3-[1-(4-Nitrophenyl)-2-nitroethyl]-1*H*-indole 3f

This is a known compound.[7c] $[\alpha]_D^{20} = +3.4$ (*c* 0.35, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 4.92 (1H, dd, *J* = 12.6, 9.0 Hz, CH_2), 5.11 (1H, dd, *J* = 12.6, 9.0 Hz, CH_2), 5.31 (1H, t, *J* = 7.5 Hz, CH), 7.05 (2H, d, *J* = 3.0 Hz, Ar), 7.11 (2H, d, *J* = 8.1 Hz, Ar), 7.24 (2H, t, *J* = 7.5 Hz, Ar), 7.39 (2H, t, *J* = 7.8 Hz, Ar), 7.52 (2H, d, *J* = 9.0 Hz, Ar), 8.18 (1H, s, Ar), 8.21 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 68.56 min, t_{major} = 89.28 min; 62% ee).

4.5.7. 3-[1-(3-Chlorophenyl)-2-nitroethyl]-1*H*-indole 3g

This is a known compound.[7c] $[\alpha]_D^{20} = +9.1$ (*c* 1.25, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 4.90 (1H, dd, *J* = 12.6, 5.4 Hz, CH_2), 5.03 (1H, dd, *J* = 12.6, 5.4 Hz, CH_2), 5.16 (1H, t, *J* = 8.1 Hz, CH), 7.02 (1H, d, *J* = 2.1 Hz, Ar), 7.09 (1H, t, *J* = 6.9 Hz, Ar), 7.18–

7.24 (4H, m, Ar), 7.30 (1H, s, Ar), 7.36 (1H, d, J = 7.5 Hz, Ar), 7.42 (1H, d, J = 7.5 Hz, Ar), 8.12 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 32.33 min, t_{major} = 47.92 min; 67% ee).

4.5.8. 3-[1-(2-Nitrophenyl)-2-nitroethyl]-1*H*-indole 3h

This is a known compound.[7c] $[\alpha]_D^{20} = +55.3$ (c 0.70, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 5.05–5.10 (2H, m, CH_2), 5.86 (1H, t, J = 7.8 Hz, CH), 7.03 (1H, t, J = 8.4 Hz, Ar), 7.10 (1H, d, J = 2.1 Hz, Ar), 7.14 (1H, t, J = 7.5 Hz, Ar), 7.28–7.46 (5H, m, Ar), 7.80 (1H, d, J = 7.8 Hz, Ar), 8.20 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 41.53 min, t_{major} = 78.27 min; 32% ee).

4.5.9. 3-[1-Furan-2-yl-2-nitroethyl]-1*H*-indole 3i

This is a known compound.[7c,d] $[\alpha]_D^{20} = -28.5$ (c 1.00, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 4.89 (1H, dd, J = 12.6, 7.5 Hz, CH_2), 5.04 (1H, dd, J = 12.6, 8.1 Hz, CH_2), 5.23 (1H, t, J = 7.5 Hz, CH), 6.15 (1H, d, J = 3.3 Hz, Ar), 6.29 (1H, dd, J = 2.7, 1.8 Hz, Ar), 7.07 (1H, d, J = 2.7 Hz, Ar), 7.12 (1H, t, J = 6.9 Hz, CH), 7.19 (1H, t, J = 6.9 Hz, CH), 7.33–7.37 (2H, m, Ar), 7.54 (1H, d, J = 7.5 Hz, Ar), 8.11 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 18.17 min, t_{major} = 26.30 min; 52% ee).

4.5.10. 3-[1-Naphth-2-yl-2-nitroethyl]-1*H*-indole 3j

This is a known compound.[7e] $[\alpha]_D^{20} = +9.8$ (c 1.80, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 5.06–5.09 (2H, m, CH_2), 6.06 (1H, t, J = 7.5 Hz, CH), 6.95 (1H, s, Ar), 7.04 (1H, t, J = 7.2 Hz, Ar), 7.18 (1H, t, J = 7.2 Hz, Ar), 7.33–7.41 (3H, m, Ar), 7.43 (1H, d, J = 7.8 Hz, Ar), 7.52 (2H, q, J = 6.6 Hz, Ar), 7.77 (1H, t, J = 5.1 Hz, Ar), 7.88 (1H, dd, J = 12.6, 2.1 Hz, Ar), 8.08 (1H, s, NH), 8.26 (1H, d, J = 7.5 Hz, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 31.91 min, t_{major} = 38.21 min; 42% ee).

4.5.11. 3-[1-(4-Bromophenyl)-2-nitroethyl]-1*H*-indole 3k

This is a known compound.[7c,d] $[\alpha]_D^{20} = -4.6$ (c 0.35, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 4.85 (1H, dd, J = 12.3, 8.4 Hz, CH_2), 5.03 (1H, dd, J = 12.3, 8.4 Hz, CH_2), 5.14 (1H, t, J = 8.1 Hz, CH), 6.99 (1H, d, J = 2.4 Hz, Ar), 7.08 (1H, t, J = 7.2 Hz, Ar), 7.18–7.24 (3H, m, Ar), 7.37 (2H, dd, J = 12.9, 8.4 Hz, Ar), 7.43 (2H, d, J = 8.1 Hz, Ar), 8.12 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 31.26 min, t_{major} = 40.83 min; 62% ee).

4.5.12. 1-Benzyl-3-[1-(4-fluorophenyl)-2-nitroethyl]-1*H*-indole 3l

This is a known compound.[7a] $[\alpha]_D^{20} = +8.8$ (c 0.5, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz, TMS): δ 4.90 (1H, dd, J = 12.6, 8.7 Hz, CH_2), 5.03 (1H, dd, J = 12.6, 7.5 Hz, CH_2), 5.15 (1H, t, J = 8.4 Hz, CH), 5.28 (2H, s, CH_2), 6.95–7.09 (6H, m, Ar), 7.18 (1H, t, J = 8.1 Hz, Ar), 7.25–7.31 (6H, m, Ar), 7.41 (1H, d, J = 8.1 Hz, Ar). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 70/30, 1.0 mL/min, 254 nm, t_{minor} = 26.81 min, t_{major} = 48.21 min; 9% ee).

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