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Efficient chirality switching in the asymmetric addition of indole to *N*-tosylarylimines in the presence of axially chiral cyclometalated bidentate N-heterocyclic carbene palladium(II) complexes

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ABSTRACT

Efficient dual stereocontrol can be achieved by using axially chiral cyclometalated bidentate N-heterocyclic carbene palladium(II) complexes for the addition of indole to *N*-tosylarylimines simply by the adjustment of the R group on the benzene rings of the NHC–Pd(II) complexes.

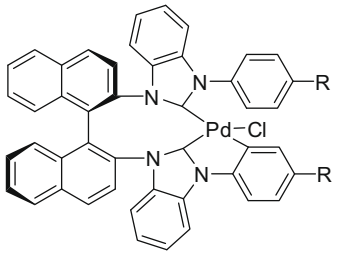
1. Introduction

In recent years, much interest has been attracted to indole derivatives possessing substituents at the 3-position due to their numerous biological activities.[1] A variety of synthetic methods including asymmetric catalysis have been reported for the preparation of 3-substituted indoles.[2] For example, the enantioselective catalytic Friedel–Crafts (F–C) reactions of indoles with imines have been successfully developed to provide enantiopure 3-indolyl methanamine derivatives in good yields.[3] Synthesis of both enantiomers of a chiral compound is a very important task in asymmetric synthesis. Traditionally, this goal can be realized through the preparation of both enantiomers of the ligands employed. A more challenging approach is dual stereocontrol over the outcome of the reaction by modification of the achiral structural components, thereby allowing the preparation of either of the enantiomers from a single configuration of the chiral elements of the catalyst.[4]

Recently, N-heterocyclic carbenes (NHCs) have become a very important class of ligands in organometallic chemistry and catalysis.[5] In addition, palladacycles are one of the most popular class of organopalladium derivatives. However, to the best of our knowledge, there have been only a few examples of spectroscopically characterized cyclometalated NHC–Pd(II) complexes reported.[6] Although palladacycles have shown many advantages in catalysis, they are mainly used in Heck-type reactions and other coupling reactions.[7] To explore the applications of chiral palladacycles as effective catalysts in asymmetric catalysis is still a challenging topic in organometallic chemistry. Herein, we report the preparation of both enantiomers of the addition products from the asymmetric Friedel–Crafts reaction of indole to *N*-tosylarylimines by using novel axially chiral cyclometalated bidentate N-heterocyclic carbene palladium(II) complexes derived from binaphthyl-2,2′-diamine (BINAM), subsequently enriching the chemistry of chiral NHC–metal complexes in asymmetric catalysis.

2. Results and discussion

We had previously reported the preparation of axially chiral cyclometalated bidentate N-heterocyclic carbene palladium(II) complexes **1a–c** derived from binaphthyl-2,2′-diamine (BINAM) and demonstrated their highly catalytic activities in the Suzuki–Miyaura coupling reaction and Friedel–Crafts reaction (Fig. 1).[6e] These results inspired us to apply them in the asymmetric Friedel–Crafts reaction of indole with *N*-tosylarylimines to examine their chiral induction abilities in asymmetric catalysis.



1a: R = H
1b: R = CH_3
1c: R = CF_3

Figure 1. Axially chiral cyclometalated bidentate NHC–Pd(II) complexes.

The initial examination was carried out by the reaction of *N*-(4-bromobenzylidene)-4-methylbenzenesulfonamide **2a** with indole catalyzed by axially chiral cyclometalated bidentate N-heterocyclic carbene palladium(II) complexes to develop the optimal reaction conditions (Scheme 1). As shown in Scheme 1, it is well known that

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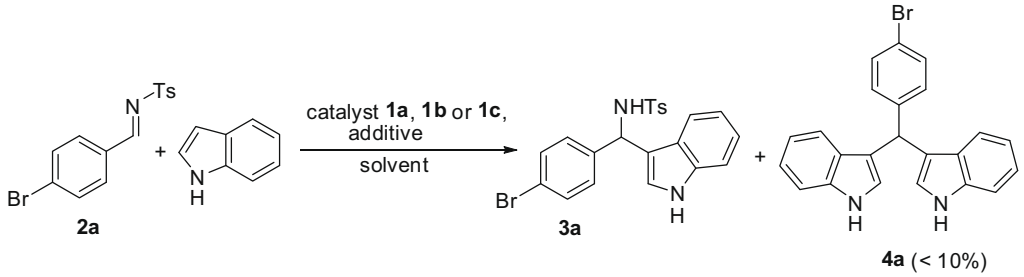


Scheme 1. Asymmetric Friedel–Crafts reaction of indole with N-sulfonated imine **2a** catalyzed by axially chiral cyclometalated bidentate N-heterocyclic carbene palladium(II) complexes.

besides the F–C reaction of indole with aldimine **2a**, the formation of a double-alkylation product, such as **4a**, is the main side-reaction in this kind of F–C reaction to reduce the yield of *N*-((4-bromophenyl)(1*H*-indol-3-yl)methyl)-4-methylbenzenesulfonamide **3a**. Moreover, the hydrolysis of the aldimine **2a** by ambient moisture can also reduce the yield of **3a**. It was pleasing to find that only a small amount of achiral double-alkylation product **4a** (<10%) was detected in the F–C reaction of indole with aldimine **2a** using cyclometalated bidentate N-heterocyclic carbene palladium(II) as the catalysts. In addition, the hydrolysis of aryl aldimines can be reduced by increasing the amount of indole employed and by adding 4 Å molecular sieves (30 mg for 0.15 mmol of **2a**) into the reaction system. The results of these experiments are summarized in Table 1.

Table 1
Catalyst and additive effect on the reaction of *N*-tosylimine **2a** with indole[a]

Entry	Catalyst	Additive	Yield[d] (%) **3a**	ee[e] (%) **3a**
1	**1a**	None	70	3
2	**1a**	Et_3N	57	17
3	**1a**	Et_2NH	63	23
4	**1a**	$C_6H_5NH_2$	74	3
5	**1a**	KOH	76	15
6	**1a**	$C_6H_5CO_2H$	73	50
7	**1a**	4-$MeOC_6H_4CO_2H$	73	46
8	**1a**	4-$NO_2C_6H_4CO_2H$	66	54
9[b]	**1a**	4-$NO_2C_6H_4CO_2H$	76	54 (*R*)[f]
10	**1a**	4-$ClC_6H_4CO_2H$	71	52
11[b]	**1b**	4-$NO_2C_6H_4CO_2H$	64	48 (*R*)[f]
12	**1c**	None	36	−60
13[c]	**1c**	Et_2NH	37	−4
14[b]	**1c**	4-$NO_2C_6H_4CO_2H$	84	−74 (*S*)[f]

[a] Unless stated otherwise, the reaction was carried out with 1 equiv of imine and 5 equiv of indole in the presence of 5 mol % of catalyst and additive (10 mol %) in 0.5 mL of CH_2Cl_2 at rt for 48 h.
[b] 4 Å MS (30 mg) and 5 mol % of additive were added.
[c] 5 mol % of additive was used.
[d] Isolated yield.
[e] Ee was determined by chiral HPLC.
[f] Determined by comparison of the sign of the specific rotation to the literature values.[3b]

Using axially chiral cyclometalated bidentate N-heterocyclic carbene palladium(II) **1a** (5 mol %) as the catalyst afforded the corresponding addition product **3a** in 70% yield with only 3% ee without any additive (Table 1, entry 1). It was found that with the addition of various amines or potassium hydroxide as the additives, the ee of **3a** can be slightly improved under identical conditions (Table 1, entries 2–5). Furthermore, we found that adding various benzoic acids into the reaction system provided the adduct **3a** in higher ees, presumably due to the fact that benzoic acids might be able to decompose the palladacycle to give the catalytically active Pd(II) species (Table 1, entries 6–10 and Scheme 2). The best result was obtained when 4-nitrobenzoic acid was used as the additive to produce **3a** in 66% yield and 54% ee (Table 1, entry 8). With the addition of 4 Å molecular sieves (30 mg), the yield of F–C product **3a** could be improved to 76% along with 54% ee using **1a** as the catalyst in the presence of 5 mol % of 4-nitrobenzoic acid (Table 1, entry 9). Using **1b** as the catalyst, the product **3a** was obtained in 64% yield and 48% ee (Table 1, entry 11). Nevertheless, the most significant observation is that the axially chiral catalysts **1a** and **1b** with an (*R*)-configuration afforded product **3a** with an (*R*)-configuration as the major enantiomer, whilst the axially chiral catalyst **1c** with an (*R*)-configuration produced product **3a** in moderate to good yields with an (*S*)-configuration as the predominant enantiomer (Table 1, entries 12–14). The examination of the additives using catalyst **1c** revealed that 4-nitrobenzoic acid was still the best choice under identical conditions, providing the adduct **3a** in 84% yield and −74% ee (Table 1, entry 14).

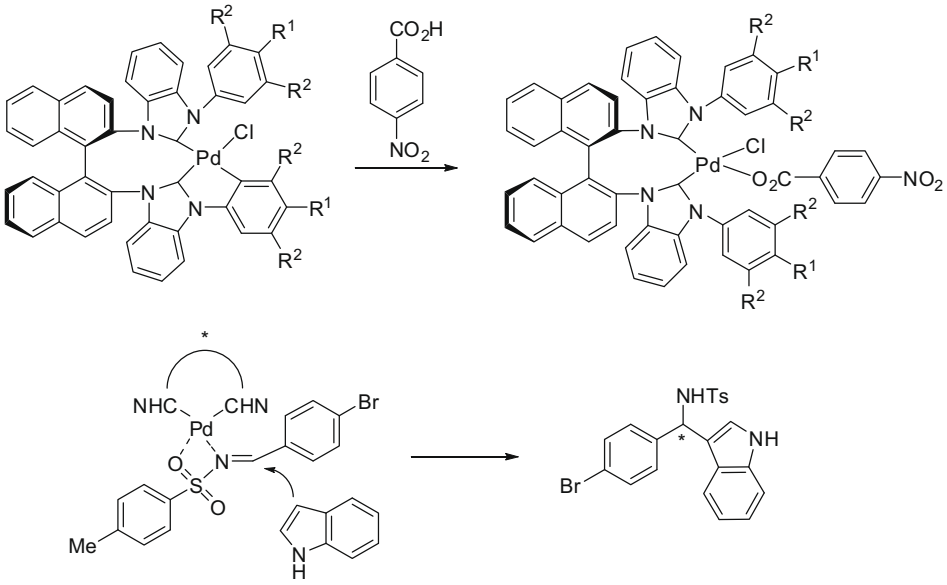
Next, we used **1a** as the catalyst to investigate the solvent and temperature effects of this reaction under the same reaction conditions, and the results of these experiments are summarized in Table 2. As can be seen, it was found that CH_2Cl_2 was the best solvent (Table 2, entries 1–7), and lowering or elevating the reaction temperature resulted in a decrease of the yield as well as the ee of **3a** (Table 2, entries 8–10).

Therefore, the best reaction conditions is to carry out the reaction in CH_2Cl_2 at room temperature using the cyclometalated bidentate N-heterocyclic carbene palladium(II) **1a** or **1c** as the catalyst in the presence of molecular sieves 4 Å and 4-nitrobenzoic acid.

A wide range of substituted imines have been tested under the optimized reaction conditions using catalysts **1a** and **1c**, and the results of these experiments are summarized in Table 3. This dual stereocontrol seems to be quite general because most of the reactions proceeded smoothly to afford the corresponding adducts **3** in moderate to good yields and moderate to good ees for various aldimines **2** with reversed enantioselectivities (Table 3, entries 1–4 and 7–12). As for the *ortho*-substituted imines, it should be noted that the corresponding products **3d** and **3h** were obtained in the same enantioselectivities using either catalyst **1a** or **1c** under identical conditions, presumably due to the steric bulkiness of the *ortho*-substituted substrate (Table 3, entries 5, 6, 13, and 14). Judging from the results, the electronic character of the R group on the benzene rings of the Pd(II) complexes might play an important role in controlling the asymmetric induction, although the assumption lacks supporting information from the calculation of relative energies of all reasonable transition states. Further efforts are underway to elucidate the mechanistic details of this dual stereocontrolled F–C reaction of indole with *N*-tosylarylimines.

3. Conclusion

In conclusion, the results presented in this paper revealed that efficient dual stereocontrol can be achieved by using cyclometalated bidentate N-heterocyclic carbene palladium(II) complexes **1a**



Scheme 2. The role of acid in this asymmetric catalysis.

Table 2
Solvent and temperature effects on the reaction of *N*-tosylimine 2a with indole[a]

Entry	Solvent	*T* (°C)	Time (h)	Yield[b] (%) **3a**	ee[c] (%) **3a**
1	CH_2Cl_2	rt	48	76	54
2	$CHCl_3$	rt	48	70	44
3	DCE	rt	48	67	44
4	Toluene	rt	48	54	28
5	THF	rt	48	51	−6
6	CH_3CN	rt	48	46	−8
7	^{i}PrOH	rt	48	Trace	–
8	CH_2Cl_2	35	40	51	36
9	CH_2Cl_2	0	60	48	38
10	CH_2Cl_2	−10	72	53	50

[a] Unless stated otherwise, the reaction was carried out with 1 equiv of imine and 5 equiv of indole in the presence of 5 mol % of catalyst **1a**, 5 mol % of 4-$NO_2C_6H_4$-CO_2H and 30 mg of 4 Å MS in 0.5 mL of solvent for 40–72 h.
[b] Isolated yield.
[c] Determined by chiral HPLC.

and **1c** for the addition of indole to *N*-tosylarylimines in most cases just by an adjustment of the R group on the benzene rings of the NHC–Pd(II) complexes. Further efforts to apply the catalytic systems to other processes as well as to optimize the structure of the catalysts are undergoing.

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 recorded at 282 MHz for a solution in $CDCl_3$ with $CFCl_3$ as the external reference. *J*-values are in Hz. Mass spectra were recorded with a HP-5989 instrument, and HRMS was measured by a Finnigan MA+ mass spectrometer. 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 increased pressure. All 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.

Axially chiral cyclometalated NHC–Pd(II) complexes **1a**–**c** were prepared according to our previously reported procedure.[6e]

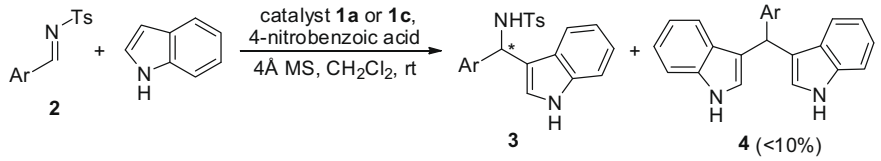
4.2. General procedure for the catalytic asymmetric Friedel–Crafts reaction and analytical data of the products

In a dried Schlenk tube, catalyst (0.0075 mmol), 4 Å molecular sieves (30 mg), 4-nitrobenzoic acid (0.0075 mmol), aldimines (0.15 mmol)and indole (0.75 mmol) were dissolved in CH_2Cl_2 (0.5 mL) under argon atmosphere. The solution was stirred at room temperature. After the reaction completed (monitored by TLC), the solvent was removed under vacuum and the residue was purified by flash column chromatography on silica gel eluted with ethyl acetate/petroleum ether (1:4, v/v) to afford the products.

N-[(4-Bromophenyl)-(1*H*-indol-3-yl)-methyl]-4-methylbenzenesulfonamide **3a**: This is a known compound.[3b] ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ 2.41 (3H, s, CH_3), 5.04 (1H, d, J = 6.3 Hz, NH), 5.80 (1H, d, J = 6.6 Hz, CH), 6.64 (1H, d, J = 2.7 Hz, =CH), 7.02 (1H, t, J = 7.5 Hz, Ar), 7.12–7.21 (6H, m, Ar), 7.30–7.35 (3H, m, Ar), 7.57 (2H, d, J = 8.4 Hz, Ar), 8.04 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/^{i}PrOH = 76/24, 1.0 mL/min, 254 nm, t_R = 14.30 and 26.27 min); **3a** (catalyzed by **1a**): 54% ee, $[\alpha]_D^{20} = +5.1$ (*c* 0.91, $CHCl_3$), 76% yield. Compound **3a** (catalyzed by **1c**): −74% ee, $[\alpha]_D^{20} = -10.5$ (*c* 0.82, $CHCl_3$), 84% yield.

N-[(4-Chlorophenyl)-(1*H*-indol-3-yl)-methyl]-4-methylbenzenesulfonamide **3b**: This is a known compound.[3b] ^{1}H NMR ($CDCl_3$ 300 MHz, TMS): δ 2.40 (3H, s, CH_3), 5.03 (1H, d, J = 6.6 Hz, NH), 5.82 (1H, d, J = 6.6 Hz, CH), 6.64 (1H, d, J = 2.4 Hz, =CH), 7.01 (1H, t, J = 7.5 Hz, Ar), 7.14–7.21 (8H, m, Ar), 7.30–7.33 (1H, m, Ar), 7.57 (2H, d, J = 8.1 Hz, Ar), 8.02 (1H, s, NH). Enantiomeric excess was

Table 3
Asymmetric Friedel–Crafts reaction of *N*-sulfonyl aldimines with indole using cyclometalated NHC–Pd(II) catalyst **1a** or **1c**[a]



Entry	Ar	Catalyst	Yield[b] (%)	ee[c] (%)
			3	**3**
1	4-ClC_6H_4	**1a**	**3b**, 87	**3b**, 54
2	4-ClC_6H_4	**1c**	**3b**, 89	**3b**, -74
3	3-ClC_6H_4	**1a**	**3c**, 80	**3c**, 64
4	3-ClC_6H_4	**1c**	**3c**, 82	**3c**, −66
5	2-ClC_6H_4	**1a**	**3d**, 74	**3d**, 24
6	2-ClC_6H_4	**1c**	**3d**, 80	**3d**, 66
7	4-FC_6H_4	**1a**	**3e**, 77	**3e**, 56
8	4-FC_6H_4	**1c**	**3e**, 81	**3e**, −48
9	3-FC_6H_4	**1a**	**3f**, 73	**3f**, 58
10	3-FC_6H_4	**1c**	**3f**, 72	**3f**, −62
11	4-$NO_2C_6H_4$	**1a**	**3g**, 71	**3g**, 48
12	4-$NO_2C_6H_4$	**1c**	**3g**, 74	**3g**, −66
13	2,3-$Cl_2C_6H_3$	**1a**	**3h**, 71	**3h**, 30
14	2,3-$Cl_2C_6H_3$	**1c**	**3h**, 78	**3h**, 60

[a] Unless stated otherwise, the reaction was carried out with 1 equiv of imine and 5 equiv of indole in the presence of 5 mol % of catalyst and 4-nitrobenzoic acid (5 mol %) in CH_2Cl_2 0.5 mL at rt for 48 h.
[b] Isolated yield.
[c] Determined by chiral HPLC.

determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 76/24, 1.0 mL/min, 254 nm, t_R = 15.43 and 28.76 min); **3b** (catalyzed by **1a**): 54% ee, $[\alpha]_D^{20} = +2.9$ (*c* 0.96, $CHCl_3$), 87% yield. Compound **3b** (catalyzed by **1c**): −74% ee, $[\alpha]_D^{20} = -13.6$ (*c* 1.0, $CHCl_3$), 89% yield.

N-[(3-Chlorophenyl)-(1*H*-indol-3-yl)-methyl]-4-methylbenzenesulfonamide **3c**: This is a known compound.[3b] ^{1}H NMR ($CDCl_3$ 300 MHz, TMS): δ 2.38 (3H, s, CH_3), 5.18 (1H, d, *J* = 6.9 Hz, NH), 5.80 (1H, d, *J* = 6.6 Hz, CH), 6.61 (1H, d, *J* = 2.7 Hz, =CH), 7.01 (1H, t, *J* = 7.5 Hz, Ar), 7.10–7.20 (7H, m, Ar), 7.23–7.31 (2H, m, Ar), 7.54 (2H, d, *J* = 8.4 Hz, Ar), 8.07 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/*i*PrOH = 85/15, 0.8 mL/min, 230 nm, t_R = 27.58 and 37.83 min); **3c** (catalyzed by **1a**): 64% ee, $[\alpha]_D^{20} = +12.6$ (*c* 0.64, $CHCl_3$), 80% yield. Compound **3c** (catalyzed by **1c**): −66% ee, $[\alpha]_D^{20} = -19.8$ (*c* 0.56, $CHCl_3$), 82% yield.

N-[(2-Chlorophenyl)-(1*H*-indol-3-yl)-methyl]-4-methylbenzenesulfonamide **3d**: This is a known compound.[3b] ^{1}H NMR ($CDCl_3$ 300 MHz, TMS): δ 2.40 (3H, s, CH_3), 5.13 (1H, d, *J* = 6.3 Hz, NH), 6.21 (1H, d, *J* = 6.6 Hz, CH), 6.58 (1H, d, *J* = 2.1 Hz, =CH), 7.01 (1H, t, *J* = 7.5 Hz, Ar), 7.15–7.25 (7H, m, Ar), 7.29–7.33 (1H, m, Ar), 7.50–7.53 (1H, m, Ar), 7.67 (2H, d, *J* = 8.7 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_R = 6.52 and 16.36 min); **3d** (catalyzed by **1a**): 24% ee, $[\alpha]_D^{20} = -11.8$ (*c* 0.75, $CHCl_3$), 74% yield. Compound **3d** (catalyzed by **1c**): 66% ee, $[\alpha]_D^{20} = -16.4$ (*c* 0.80, $CHCl_3$), 80% yield.

N-[(4-Fluorophenyl)-(1*H*-indol-3-yl)-methyl]-4-methylbenzenesulfonamide **3e**: Mp 150–151 °C; IR (KBr) ν 3400, 3281, 2925, 1602, 1508, 1418, 1325, 1223, 1157, 1092, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$ 300 MHz, TMS): δ 2.38 (3H, s, CH_3), 5.15 (1H, d, *J* = 6.6 Hz, NH), 5.82 (1H, d, *J* = 6.6 Hz, CH), 6.63 (1H, d, *J* = 2.4 Hz, =CH), 6.85–6.91 (2H, m, Ar), 7.00 (1H, t, *J* = 7.5 Hz, Ar), 7.10–7.15 (2H, m, Ar), 7.18–7.22 (4H, m, Ar), 7.29–7.31 (1H, m, Ar), 7.55 (2H, d, *J* = 8.1 Hz, Ar), 8.03 (1H, s, NH). ^{13}C NMR ($CDCl_3$ 75 MHz, TMS): δ 21.5, 54.3, 111.3, 114.9, 115.2, 116.1, 119.1, 120.0, 122.6, 123.7, 125.1, 127.1, 128.8, 128.9, 129.3, 136.0, 136.5, 137.2, 143.2, 162.0 (d, *J* = 244.6 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ −115.59; MS (EI) *m/e* 394.1 (M^+), 222.1 (M^+−172, 100); HRMS (EI) calcd for $C_{22}H_{19}N_2O_2FS$ requires 394.1151, found 394.1151. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/^{i}PrOH = 80/20, 1.0 mL/min, 254 nm, t_R = 17.10 and 31.30 min); **3e** (catalyzed by **1a**): 56% ee, $[\alpha]_D^{20} = +10.5$ (*c* 0.85, $CHCl_3$), 77% yield. Compound **3e** (catalyzed by **1c**): -48% ee, $[\alpha]_D^{20} = -12.0$ (*c* 0.295, $CHCl_3$), 81% yield.

N-[(3-Fluorophenyl)-(1*H*-indol-3-yl)-methyl]-4-methylbenzenesulfonamide **3f**: Mp 129–130 °C; IR (KBr) ν 3393, 3281, 3059, 1586, 1324, 1154, 1091, 932, 744, 670 cm^{-1}; ^{1}H NMR ($CDCl_3$ 300 MHz, TMS): δ 2.38 (3H, s, CH_3), 5.13 (1H, d, *J* = 6.6 Hz, NH), 5.82 (1H, d, *J* = 6.9 Hz, CH), 6.63 (1H, d, *J* = 2.4 Hz, =CH), 6.85–6.94 (2H, m, Ar), 6.98–7.06 (2H, m, Ar), 7.12–7.22 (5H, m, Ar), 7.29–7.32 (1H, m, Ar), 7.57 (2H, d, *J* = 8.4 Hz, Ar), 8.04 (1H, s, NH). ^{13}C NMR ($CDCl_3$ 75 MHz, TMS): δ 21.5, 54.4, 111.3, 114.1 (d, *J* = 4.9 Hz), 114.4 (d, *J* = 3.4 Hz), 115.7, 119.0, 120.1, 122.7, 112.8 (d, *J* = 2.8 Hz), 123.7, 125.0, 127.1, 129.3, 129.8 (d, *J* = 8.1 Hz), 136.4, 137.1, 142.9 (d, *J* = 5.9 Hz), 143.3, 162.7 (d, *J* = 244.7 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ −113.46; MS (EI) *m/e* 394.1 (M^+), 222.1 (M^+−172, 100); HRMS (EI) calcd for $C_{22}H_{19}N_2O_2FS$ requires 394.1151, found 394.1131. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (hexane/*i*PrOH = 80/20, 0.7 mL/min, 230 nm, t_R = 32.18 and 35.63 min); **3f** (catalyzed by **1a**): 58% ee, $[\alpha]_D^{20} = +6.0$ (*c* 0.87, $CHCl_3$), 73% yield. Compound **3f** (catalyzed by **1c**): −62% ee, $[\alpha]_D^{20} = -6.2$ (*c* 1.025, $CHCl_3$), 72% yield.

N-[(1*H*-Indol-3-yl)-(4-nitrophenyl)methyl]-4-methylbenzenesulfonamide **3g**: This is a known compound.[3b] ^{1}H NMR ($CDCl_3$ 300 MHz, TMS): δ 2.42 (3H, s, CH_3), 5.07 (1H, d, *J* = 4.8 Hz, NH), 5.91 (1H, d, *J* = 6.6 Hz, CH), 6.59 (1H, d, *J* = 2.1 Hz, =CH), 7.02 (1H, t, *J* = 7.5 Hz, Ar), 7.07–7.09 (1H, m, Ar), 7.20–7.22 (3H, m, Ar), 7.33–7.36 (1H, m, Ar), 7.53 (2H, d, *J* = 8.7 Hz, Ar), 7.63 (2H, d, *J* = 8.1 Hz, Ar), 8.10 (2H, s, Ar), 8.13 (1H, s, NH). Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/^{i}PrOH = 80/20, 1.0 mL/min, 254 nm, t_R = 32.62 and 62.44 min); **3g** (catalyzed by **1a**): 48% ee, $[\alpha]_D^{20} = +7.0$ (*c* 0.205,

$CHCl_3$), 71% yield. Compound **3g** (catalyzed by **1c**): −66% ee, $[\alpha]_D^{20} = -14.0$ (*c* 0.212, $CHCl_3$), 74% yield.

N-[(2,3-Dichlorophenyl)-(1*H*-indol-3-yl)-methyl]-4-methylbenzenesulfonamide **3h**: Mp 103–105 °C; IR (KBr) *v* 3385, 3281, 2919, 2837, 1594, 1461, 1342, 1158, 1091, 810, 740, 662 cm^{-1}; ^1H NMR (acetone-d_6, 300 MHz): δ 2.39 (3H, s, CH_3), 6.33 (1H, d, J = 7.8 Hz, NH), 6.66 (1H, d, J = 1.8 Hz, CH), 6.96 (1H, t, J = 7.5 Hz, Ar), 7.12 (1H, t, J = 7.6 Hz, Ar), 7.23–7.30 (5H, m, Ar), 7.37 (1H, d, J = 8.1 Hz, Ar), 7.43 (1H, d, J = 8.1 Hz, Ar), 7.65–7.71 (3H, m, Ar), 10.19 (1H, s, NH). ^{13}C NMR (acetone-d_6, 75 MHz): δ 21.2, 52.7, 112.2, 114.6, 119.5, 119.9, 122.6, 125.1, 126.8, 127.7, 128.1, 128.3, 129.5, 130.0, 131.1, 132.9, 137.6, 139.1, 142.6, 143.6; MS (EI) *m/e* 444.0 (M^+), 238.0 (M^+-206, 100); HRMS (EI) calcd for $C_{22}H_{18}N_2O_2SCl_2$ requires 444.0466, found 444.0466. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (hexane/^{i}PrOH = 70/30, 0.7 mL/min, 254 nm, t_R = 6.68 and 15.73 min); **3h** (catalyzed by **1a**): 30% ee, $[\alpha]_D^{20} = -16.4$ (*c* 0.5, $CHCl_3$), 71% yield. Compound **3h** (catalyzed by **1c**): 60% ee, $[\alpha]_D^{20} = -25.3$ (*c* 0.35, $CHCl_3$), 78% yield.

Compound **4**: This is a known compound.[8] ^1H NMR ($CDCl_3$ 300 MHz, TMS): δ 5.84 (1H, s, CH), 6.64 (2H, d, J = 2.1 Hz, =CH), 7.01 (2H, t, J = 7.8 Hz, Ar), 7.15–7.22 (4H, m, Ar), 7.35–7.40 (6H, m, Ar), 7.93 (2H, s, NH).

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