Synthesis of Tridentate Ligands Based on Chiral Diamines and Their Application to Enantioselective Friedel-Crafts Alkylation of Indoles with Nitroalkenes

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A new type of chiral tridentate ligands were prepared and their Zn complexes were examined for the asymmetric Friedel-Crafts alkylation of indoles with nitroalkenes, which gave rise to good yields and moderate enantioselectivities.

Keywords Friedel-Crafts alkylation, N ligands, indoles, nitroalkenes, asymmetric catalysis

Introduction

Asymmetric Friedel-Crafts (F-C) alkylation of indole derivatives with electron-deficient alkenes is an extremely powerful reaction in the organic synthesis for the formation of valuable N-heterocycles derivatives[1] and has attracted considerable attention in the past few years.[2] The substrates which are suitable for the F-C reaction involve alkylidene malonates,[3] β,γ-unsaturated α-ketoesters,[4] acyl phosphonates,[5] acyl heterocyclic compounds[6] and nitroalkenes.[7] Among these kinds of electron-deficient acceptors, nitroalkenes have attracted considerable interest and witnessed significant progress since nitro functional group is a strongly electron-withdrawing group that allows subsequent versatile transformation. Recently, comparative attention is being paid to nitroalkenes which have achieved asymmetric F-C alkylation with indoles, and extensive progress has been accomplished in this direction. After pioneering work which led to the SalenAlCl catalyst,[8] thioureas,[9] phosphoric acids,[10] bis-sulfonamides,[7a] zinc,[7d-7h] and copper[11] catalysts have since been successfully applied to F-C reaction of indoles with nitroalkenes. Among these catalyst systems, various bisoxazoline-metal complexes have been used as chiral Lewis acids in asymmetric F-C reaction of five- or six-membered heterocycles to give the corresponding alkylation products in good yields and high *ee* values. Moreover, bis-sulfonamides have been reported as the catalyst for asymmetric F-C reaction.[7a] Recently, we have successfully synthesized a series of new chiral tetradentate nitrogen ligands together with their manganese complexes, which exhibit rapid, highly enantioselective epoxidation of various α,β-enones.[12] Encouraged by these conceptual strategies, we have designed and prepared a series of new types of tridentate ligands based on chiral diamines, which could be subjected to asymmetric F-C alkylation reaction of indoles with nitroalkenes.

Results and discussion

These chiral tridentate ligands **3a**—**3e** were synthesized with **2a**—**2e** and the corresponding Grignard reagents. The experimental procedure is shown in Scheme 1. Similarly, chiral tridentate ligand **3f** was prepared with **2f** and PhMgBr as shown in Scheme 1.

Initially, we evaluated the enantioselective F-C reaction of indole and nitroalkene **4a** with the catalyst generated *in situ* with ligand **3a** and $Zn(OTf)_2$, and found that the corresponding F-C reaction product was obtained in an 80% yield and a 27% *ee* using CH_2Cl_2 as solvent at room temperature for 24 h. Subsequently, we examined a series of metallic salts with chiral ligand **3a** and the results are shown in Table 1, the combination of ligand **3a** with $Fe(OTf)_2$ or $Cu(OAc)_2$ in CH_2Cl_2 gave no product. $Cu(OTf)_2$ and $(CuOTf)_2$•Ph showed the similar *ee* values and catalytic activity with that of $Zn(OTf)_2$. Employing $Mn(OTf)_2$ as a metal source, lower yield and *ee* value were observed. Nearly racemic product was obtained when AgOTf or $NiCl_2$•$6H_2O$ was used (Table 1, Entries 6 and 8).

With $Zn(OTf)_2$ as the metallic salt and **3a** as ligand, we next studied the effects of solvent. When CH_3OH or Et_2O was applied, no reaction occurred. Using toluene as the solvent gave the product in higher yield but slightly low enantioselectivity. The reactivity and stereoselectivity decreased dramatically when the reac-

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Scheme 1 The synthesis of ligands **3a**—**3f**

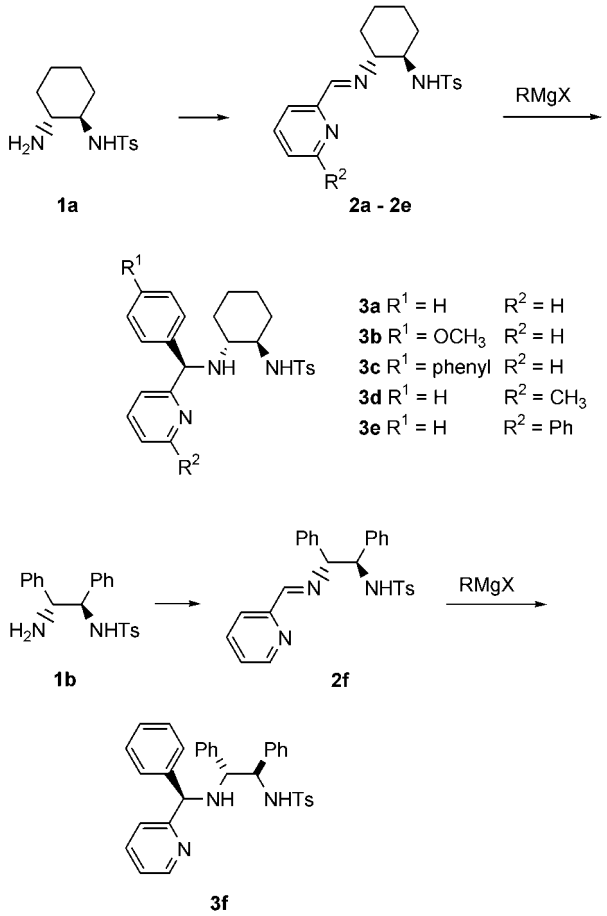
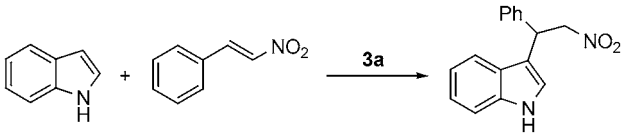


Table 1 Asymmetric F-C reaction catalyzed by ligand **3a** and a variety of metallic salts[a]



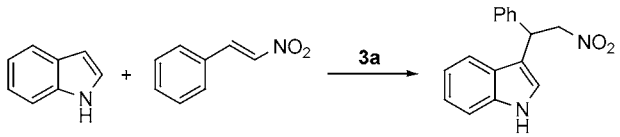
Entry	Metallic salt	Yield[b]/%	*ee*[c]/%
1	$Zn(OTf)_2$	80	27
2	$Cu(OTf)_2$	78	25
3	$Mn(OTf)_2$	54	14
4	$Fe(OTf)_2$	N.R.	
5	$(CuOTf)_2$•Ph	80	24
6	AgOTf	32	7
7	$Cu(OAc)_2$	N.R.	
8	$NiCl_2$•$6H_2O$	63	2

[a] All reactions were performed with nitroalkene (0.2 mmol), indole (0.2 mmol) in 1.0 mL of CH_2Cl_2 in the presence of 6 mol% ligand and 5 mol% metallic salts at room temperature. [b] Isolated yield. [c] Determined by HPLC using a Chiralcel OD-H column.

tion was carried out in acetone (Table 3). Therefore, dichloromethane was optimal in terms of both enantioselectivity and yield.

To further optimize the reaction conditions, we

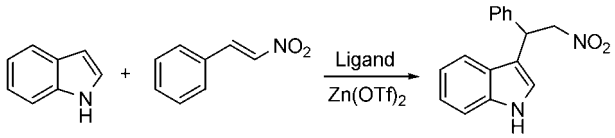
Table 2 Effect of solvents on asymmetric F-C reaction[a]



Entry	Solvent	Yield[b]/%	*ee*[c]/%
1	Dichloromethane	80	27
2	Methanol	N.R.	
3	Acetone	57	13
4	Diethyl ether	N.R.	
5	Toluene	90	23

[a] All reactions were performed with nitroalkene (0.2 mmol), indole (0.2 mmol) in 1.0 mL of CH_2Cl_2 in the presence of 6 mol% ligand **3a** and 5 mol% $Zn(OTf)_2$ at room temperature. [b] Isolated yield. [c] Determined by HPLC using a Chiralcel OD-H column.

Table 3 Effect of chiral ligands on the $Zn(OTf)_2$ catalyzed F-C reaction[a]



Entry	Ligand	*T*/℃	Yield[b]/%	*ee*[c]/%
1	**3a**	r.t.	80	27
2	**3b**	r.t.	89	27
3	**3c**	r.t.	88	28
4	**3d**	r.t.	94	43
5	**3d**	0	82	54
6	**3d**	−10	79	51
7	**3d**	−20	57	28
8	**3e**	r.t.	64	8
9	**3f**	r.t.	84	23

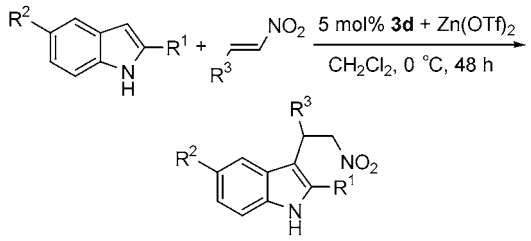
[a] All reactions were performed with nitroalkene (0.2 mmol), indole (0.2 mmol) in 1.0 mL of CH_2Cl_2 in the presence of 6 mol% ligands **3a**—**3f** and 5 mol% $Zn(OTf)_2$. [b] Isolated yield. [c] Determined by HPLC using a Chiralcel OD-H column.

synthesized ligands **3b**—**3f** and examined the influence of the substituted groups R^1 on the yields and *ee* values of the reactions. It can be seen that both the **3b** and **3c** gave the similar *ee* values but slightly high catalytic activity to the catalyst system with ligand **3a** (Table 3, Entries 1—3). Subsequently, the effect of group of pyridine (R^2) on the yields and *ee* values was investigated. Higher yield and *ee* value were obtained when R^2 was larger substituted group methyl (Table 3, Entry 4) at room temperature. Ligand **1e** bearing phenyl group on the R^2 led to low *ee* (Table 3, Entry 8). Ligand **1f** derived from (1*R*,2*R*)-1,2-diphenyl-ethanediamine was also investigated in the F-C alkylation of indole and nitroalkene, only 23% *ee* was observed (Table 3, Entry 9). In light of these results, the ligand **3d** was found to

be the best ligand. With $Zn(OTf)_2$ as metallic salt and **3d** as ligand, we also examined the influence of the reaction temperature on the *ee* value. We were pleased to find that the product was obtained in 54% *ee* when temperature was lowered to 0 ℃ (Table 3, Entry 5). When the reaction was performed at −10 ℃, a slightly decreased *ee* was observed (Table 3, Entry 6). Lowering temperature to −20 ℃, both the chemical reaction activity and enantioselectivity reduced dramatically. Based on the discussion above, we can conclude that the reaction should perform in the presence of $Zn(OTf)_2$ and ligand **3d** in dichloromethane at 0 ℃ for 48 h.

Under the optimized reactions, we explored the limitations and scope by using various nitroalkenes and indoles, and the results are summarized in Table 4. We found that moderate enantioselectivities were achieved when the nitroalkenes with electron-withdrawing and slender electron-donating substituted groups were involved (Table 4, Entries 3—5). However, the nitroalkene with strong electron-donating substitute afforded the product with significantly decreased enantioselectivity (Table 4, Entry 6). When 2-substituted nitroalkene was used, a comparative *ee* was accomplished with that of 4-substituted nitroalkenes (Table 4, Entry 3). When the substituent of indole such as **4b** and **4g** were selected as substrate, lower *ee* values were obtained (Table 4, Entries 2, 7).

Table 4 Asymmetric F-C reaction of various substrates[a]



Entry	Substrate	R^1	R^2	R^3	Yield[b]/%	*ee*[c]/%
1	**4a**	H	H	Ph	82	54
2	**4b**	CH_3	H	Ph	90	47
3	**4c**	H	H	2-Cl-C_6H_4	86	50
4	**4d**	H	H	4-CH_3-C_6H_4	76	54
5	**4e**	H	H	4-F-C_6H_4	60	57
6	**4f**	H	H	4-OCH_3-C_6H_4	67	36
7[d]	**4g**	H	Br	Ph	56	36

[a] All reactions were performed with nitroalkene (0.2 mmol), indole (0.2 mmol) in 1.0 mL of CH_2Cl_2 in the presence of $Zn(OTf)_2$ and ligand **3d** at 0 ℃ for 48 h. [b] Isolated yield. [c] Determined by HPLC using a Chiralcel OD-H, AD-H or AS column. [d] Performed at room temperature.

Conclusion

In summary, a new type of tridentate ligands (**3a**—**3f**) were successfully designed and synthesized. The tridentate ligands and $Zn(OTf)_2$ were applied to the asymmetric F-C alkylation reaction of indoles with nitroalkenes, showing satisfactory yields and moderate enantioselectivity. Further applications of these ligands on other asymmetric reactions are underway in our laboratory.

Experimental

General remarks

Commercially available compounds were used without further purification. Solvents were dried according to standard methods. Column chromatography was carried out using silica gel (200—300 mesh). The ^1H NMR spectra and ^{13}C NMR spectra were recorded on a Bruker Avance III 400MHz spectrometer. The enationmeric excesses were determined by chiral HPLC analysis using Waters 1525 instrument. **1a** and **1b** were prepared according to literature method.[13,14]

General procedure for the preparation of 3a—3f

To the solution of RMgBr (30 mmol) in Et_2O was added **2a**—**2f** and the solution was stirred for 12 h at room temperature. Saturated NH_4Cl was added to quench the reaction and the organic layer was separated and dried over anhydrous Na_2SO_4. The mixture was directly separated by silica gel chromatography with petroleum ether/ethyl acetate (V∶V=3∶1) as eluent. The product was obtained with 58%—71% yield as a colorless solid.

3a: Colorless solid; $[\alpha]_D^{20}$ −64.5 (*c* 0.1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.51 (d, J=4.8 Hz, 1H, ArH), 7.76 (d, J=8.4 Hz, 2H, ArH), 7.56 (t, J=7.6 Hz, 1H, ArH), 7.39—7.24 (m, 7H, ArH), 7.13 (t, J=6.0 Hz, 1H, ArH), 7.04 (d, J=7.6 Hz, 1H, ArH), 5.54 (s, 1H, NH), 4.98 (s, 1H, CH), 2.72 (s, 1H, CH), 2.42 (s, 3H, CH_3), 2.19—2.07 (m, 3H, CH), 1.60 (t, J=12.8 Hz, 2H, CH), 1.13—0.96 (m, 4H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 162.28, 148.67, 143.02, 142.07, 137.27, 136.55, 129.54, 128.87, 128.06, 127.68, 127.32, 121.97, 121.84, 64.35, 58.07, 57.42, 32.72, 31.21, 24.63, 24.31, 21.57; HRMS (ESI-MS) calcd for $C_{25}H_{29}N_3O_2S$ $[M+H]^+$: 436.2053, found 436.2056.

3b: Colorless solid; $[\alpha]_D^{20}$ −64.9 (*c* 0.1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ: 8.50 (d, J=4.0 Hz, 1H, ArH), 7.76 (d, J=8.0 Hz, 2H, ArH), 7.56 (t, J=8.0 Hz, 1H, ArH), 7.27—7.24 (m, 4H, ArH), 7.13—7.11 (m, 1H, ArH), 7.04 (d, J=8.0 Hz, 1H, ArH), 6.90 (d, J=8.8 Hz, 2H, ArH), 5.60 (s, 1H, NH), 4.93 (s, 1H, CH), 3.81 (s, 3H, OCH_3), 2.69 (d, J=7.2 Hz, 1H, CH), 2.41 (s, 3H, CH_3), 2.20—2.07 (m, 4H, CH), 1.60 (t, J_1=14.0 Hz, J_2=16.4 Hz, 2H, CH), 1.16—0.92 (m , 3H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 162.62, 159.03, 148.62, 143.01, 137.25, 136.53, 134.00, 129.53, 129.13, 127.32, 121.89, 121.74, 114.24, 63.64, 58.07, 57.19, 55.25, 32.73, 31.16, 24.66, 24.31, 21.57; HRMS (ESI-MS) calcd for $C_{26}H_{31}N_3O_3S$ $[M+H]^+$: 466.2159, found 466.2157.

3c: Colorless solid; $[\alpha]_D^{20}$ −53.4 (*c* 0.1, $CHCl_3$);

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^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.53 (d, J=4.4 Hz, 1H, ArH), 7.78 (d, J=8.4 Hz, 2H, ArH), 7.61—7.58 (m, 5H, ArH), 7.57—7.41 (m, 4H, ArH), 7.36—7.32 (m, 1H, ArH), 7.26—7.11 (m, 4H, ArH), 5.56 (s, 1H, NH), 5.04 (s, 1H, CH), 2.77 (t, J=9.6 Hz, 1H, CH), 2.41 (s, 3H, CH_3), 2.36—2.10 (m, 3H, CH), 1.64—1.53 (m, 2H, CH), 1.21—0.93 (m, 4H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 162.21, 148.76, 143.05, 140.61, 140.49, 137.33, 136.64, 129.56, 128.77, 128.44, 127.56, 127.31, 127.04, 122.05, 121.84, 64.11, 58.07, 57.49, 32.68, 31.22, 24.61, 24.32, 21.57; HRMS (ESI-MS) calcd for $C_{31}H_{33}N_3O_2S$ $[M+H]^+$: 512.2366, found 512.2360.

3d: Colorless solid; $[\alpha]_D^{20}$ −65.0 (c 0.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.75 (d, J=3.6 Hz, 2H, ArH), 7.44 (t, J=8.0 Hz, 1H, ArH), 7.36—7.26 (m ,7H, ArH), 6.98 (d, J=7.6 Hz, 1H, ArH), 6.83 (d, J=7.6 Hz, 1H, ArH), 5.57 (s, 1H, NH), 4.93 (s, 1H, CH), 2.72—2.68 (m, 1H, CH), 2.53 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.19—2.09 (m, 3H, CH), 1.63—1.55 (m, 2H, CH), 1.16—0.92 (m, 4H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 161.57, 157.36, 142.98, 142.35, 137.38, 136.72, 129.50, 128.77, 128.11, 127.57, 127.32, 121.49, 118.76, 64.28, 58.11, 57.39, 32.61, 31.22, 24.69, 24.46, 24.30, 21.54; HRMS (ESI-MS) calcd for $C_{26}H_{31}N_3O_2S$ $[M+H]^+$: 450.2210, found 450.2215.

3e: Colorless solid; $[\alpha]_D^{20}$ −153.2 (c 0.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.01 (d, J=6.8 Hz, 2H, ArH), 7.73 (d, J=6.4 Hz, 2H, ArH), 7.60—7.26 (m, 10H, ArH), 7.11 (d, J=8.0 Hz, 2H, ArH), 6.91 (d, J=6.8 Hz, 1H, ArH), 5.43 (s, 1H, NH), 5.01 (s, 1H, CH), 2.71—2.68 (m, 1H, CH), 2.26 (s, 3H, CH_3), 2.19—2.09 (m, 3H, CH), 1.61—1.57 (m, 2H, CH), 1.26—1.09 (m, 4H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 161.73, 155.98, 143.01, 142.38, 139.17, 137.24, 137.06, 129.48, 129.02, 128.86, 128.72, 128.19, 127.66, 127.27, 126.91, 120.40, 118.49, 64.36, 58.17, 57.59, 32.59, 31.26, 24.69, 24.31, 21.43; HRMS (ESI-MS) calcd for $C_{31}H_{33}N_3O_2S$ $[M+H]^+$: 512.2366, found 512.2359.

3f: Colorless solid; $[\alpha]_D^{20}$ −60.0 (c 0.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.53 (d, J=4.4 Hz, 1H, ArH), 7.50 (t, J=8.8 Hz, 1H, ArH), 7.39—6.80 (m, 21H, ArH), 6.42 (s, 1H, NH), 4.57 (s, 1H, CH), 4.34 (d, J=8.0 Hz, 1H, CH), 3.56—3.31 (m, 2H, CH), 2.33 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 161.41, 156.01, 148.61, 142.61, 141.13, 138.61, 138.13, 137.05, 136.47, 129.57, 129.05, 128.77, 128.50, 128.30, 127.94, 127.74, 127.70, 127.48, 127.16, 125.38, 121.97, 120.34, 115.43, 64.57, 63.93, 63.37, 21.45; HRMS (ESI-MS) calcd for $C_{33}H_{31}N_3O_2S$ $[M+H]^+$: 534.2210, found 534.2215.

Typical procedure for the asymmetric F-C alkylation reaction

To an oven-dried Schlenk tube were added ligand **3d** (2.4 μmol) and $Zn(OTf)_2$ (2 μmol) under nitrogen, followed by addition of dichloromethane (1 mL). The mixture was stirred at room temperature for 3 h. The mixture was cooled to 0 ℃ and then nitroalkene was added. After 10 min indole was added and the mixture was stirred for 48 h. The mixture was directly separated by silica gel chromatography with petroleum ether/ethyl acetate (V∶V=10∶1) as eluent.

3-(2-Nitro-1-phenylethyl)-1*H*-indole This is a known compound.[7d] $[\alpha]_D^{20}$ +16.3 (c 0.42, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.07 (s, 1H, NH), 7.42 (d, J=6.4 Hz, 1H, ArH), 7.33—7.21 (m, 5H, ArH), 7.20—7.14 (m, 1H, ArH), 7.06 (t, J=8.0 Hz, 1H, ArH), 6.98 (d, J=2.0 Hz, 1H, ArH), 5.17 (t, J=8.0 Hz, 1H, CH), 5.04 (dd, J=12.4, 7.6 Hz, 1H, CH), 4.92 (dd, J=12.4, 8.4 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 139.18, 136.47, 128.90, 127.75, 127.54, 126.08, 122.66, 121.61, 119.92, 118.90, 114.35, 111.39, 79.52, 41.54. The *ee* value was determined by chiral HPLC on a Daicel Chiralcel OD-H column (hexane/2-propanol, V∶V=70∶30, 1.0 mL•min^{-1}, 254 nm, t_{major}=21.18 min, t_{minor}=19.57 min).

2-Methyl-3-(2-nitro-1-phenylethyl)-1*H*-indole This is a known compound.[7d] $[\alpha]_D^{20}$ −8.3 (c 0.48, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.83 (s, 1H, NH), 7.36 (d, J=7.6 Hz, 1H, ArH), 7.31—7.19 (m, 6H, ArH), 7.09 (t, J=7.6 Hz, 1H, ArH), 7.01 (t, J=7.6 Hz, 1H, ArH), 5.23—5.07 (m, 3H, CH), 2.34 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 139.49, 135.38, 132.84, 128.75, 127.28, 127.05, 126.82, 121.30, 119.71, 118.56, 110.69, 108.81, 78.60, 40.43, 11.95. The *ee* value was determined by chiral HPLC on a Daicel Chiralcel AS column (hexane/2-propanol, V∶V=94∶6, 1.0 mL•min^{-1}, 254 nm, t_{major}=27.60 min, t_{minor}=30.78 min).

3-[1-(2-Chlorophenyl)-2-nitroethyl]-1*H*-indole This is a known compound.[7d] $[\alpha]_D^{20}$ +35.8 (c 0.55, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.08 (s, 1H, NH), 7.43—7.41 (m, 2H, ArH), 7.32 (d, J=8.0 Hz, 1H, ArH), 7.23—7.04 (m, 6H, ArH), 5.73 (t, J=8.0 Hz, 1H, CH), 5.01—4.91 (m, 2H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 136.45, 133.82, 130.12, 128.96, 128.83, 127.27, 126.16, 122.76, 121.96, 120.01, 118.90, 113.20, 113.39, 77.70, 37.94. The *ee* value was determined by chiral HPLC on a Daicel Chiralcel OD-H column (hexane/2-propanol, V∶V=70∶30, 1.0 mL•min^{-1}, 254 nm, t_{major}=25.07 min, t_{minor}=16.48 min).

3-[1-(4-Methylphenyl)-2-nitroethyl]-1*H*-indole This is a known compound.[7d] $[\alpha]_D^{20}$ +7.8 (c 0.49, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.99 (s, 1H, NH), 7.43 (d, J=7.6 Hz, 1H, ArH), 7.28 (d, J=8.4 Hz, 1H, ArH), 7.20—7.03 (m, 6H, ArH), 6.93 (d, J=2.4 Hz, 1H, ArH), 5.12 (t, J=8.0 Hz, 1H, CH), 5.00 (dd, J=12.4, 7.6 Hz, 1H, CH), 4.88 (dd, J=12.4, 8.4 Hz, 1H, CH), 2.28 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 137.25, 136.53, 136.22, 129.64, 127.67, 126.16, 122.66, 121.62, 119.93, 118.98, 114.57, 111.45, 79.69, 41.25, 21.09. The *ee* value was determined by chiral HPLC on a Daicel Chiralcel OD-H column (hexane/2-propanol, V∶V=70∶30, 1.0 mL•min^{-1}, 254 nm, t_{major}=16.06 min, t_{minor}=17.95 min).

3-[1-(4-Fluorophenyl)-2-nitroethyl]-1*H*-indole This is a known compound.[7d] $[\alpha]_D^{20}$ +20.7 (*c* 0.35, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.08 (s, 1H, NH), 7.39 (d, J=8.0 Hz, 1H, ArH), 7.33 (d, J=8.4 Hz, 1H, ArH), 7.30—7.23 (m, 2H, ArH), 7.19 (t, J=7.2 Hz, 1H, ArH), 7.07 (t, J=7.6 Hz, 1H, ArH), 7.01—6.95 (m, 3H, ArH), 5.15 (t, J=8.0 Hz, 1H, CH), 5.03 (dd, J=12.4, 7.2 Hz, 1H, CH), 4.88 (dd, J=12.4, 8.4 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 163.29, 160.84, 136.50, 134.96, 134.92, 129.40, 129.32, 125.93, 122.81, 121.45, 120.04, 118.83, 115.92, 115.70, 114.21, 111.46, 79.53, 40.86. The *ee* value was determined by chiral HPLC on a Daicel Chiralcel OD-H column (hexane/2-propanol, V∶V=70∶30, 1.0 mL•min^{-1}, 254 nm, t_{major}=22.44 min, t_{minor}=27.32 min).

3-[1-(4-Methoxyphenyl)-2-nitroethyl]-1*H*-indole This is a known compound.[7d] $[\alpha]_D^{20}$ +11.6 (*c* 0.57, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.07 (s, 1H, NH), 7.43 (d, J=8.0 Hz, 1H, ArH), 7.35 (d, J=8.4 Hz, 1H, ArH), 7.25—7.23 (m, 2H, ArH), 7.19 (t, J=8.0 Hz, 1H, ArH), 7.07 (t, J=7.6 Hz, 1H, ArH), 7.02 (d, J=2.0 Hz, 1H, ArH), 6.85 (d, J=6.8 Hz, 2H, ArH), 5.14 (t, J=8.0 Hz, 1H, CH), 5.05 (dd, J=12.4, 7.6 Hz, 1H, CH), 4.90 (dd, J=12.4, 8.4 Hz, 1H, CH), 3.77 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 158.91, 136.52, 131.17, 128.81, 126.11, 122.70, 121.43, 119.94, 119.01, 114.83, 114.28, 111.34, 79.75, 55.25, 40.86. The *ee* value was determined by chiral HPLC on a Daicel Chiralcel OD-H column (hexane/2-propanol, V∶V=70∶30, 1.0 mL•min^{-1}, 254 nm, t_{major}=20.72 min, t_{minor}=22.83 min).

5-Bromo-3-(2-nitro-1-phenylethyl)-1*H*-indole This is a known compound.[7d] $[\alpha]_D^{20}$ −19.7 (*c* 0.54, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.17 (s, 1H, NH), 7.54 (s, 1H, ArH), 7.35—7.19 (m, 7H, ArH), 7.05 (d, J=2.0 Hz, 1H, ArH), 5.11 (t, J=8.0 Hz, 1H, CH), 5.01 (dd, J=12.4, 8.0 Hz, 1H, CH), 4.91 (dd, J=12.4, 8.0 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 138.65, 135.05, 129.04, 127.82, 127.76, 127.64, 125.63, 122.72, 121.43, 113.98, 113.22, 112.85, 79.38, 41.27. The *ee* value was determined by chiral HPLC on a Daicel Chiralcel AD-H column (hexane/2-propanol, V∶V=90∶10, 1.0 mL•min^{-1}, 254 nm, t_{major}=16.04 min, t_{minor}=14.71 min).

References

1 (a) Olah, G. A.; Khrisnamurti, R.; Prakash, G. K. S. In *Comprehensive Organic Synthesis*, Vol. III, 1st ed., Eds.: Trost, B. M.; Fleming, I., Pergamon, Oxford, **1991**, p. 293.
(b) Roberts, R. M.; Khalaf, A. A. *Friedel-Crafts Alkylation Chemistry*. *A Century of Discovery*, Marcel Dekker, New York, **1984**.

2 (a) Poilsen, T. B.; Jørgensen, K. A. *Chem*. *Rev*. **2008**, *108*, 2903.
(b) Sheng, Y. F.; Zhang, A. J.; Zheng, S. L.; You, S. L. *Chin*. *J*. *Org*. *Chem*. **2008**, *28*, 605 (in Chinese).
(c) You, S. L.; Cai, Q.; Zeng, M. *Chem*. *Soc*. *Rev*. **2009**, *38*, 2190.

3 (a) Zhuang, W.; Hausen, T.; Jrgensen, K. A. *Chem*. *Commun*. **2001**, 347.
(b) Zhou, J.; Tang, Y. *J*. *Am*. *Chem*. *Soc*. **2002**, *124*, 9030.
(c) Zhou, J.; Tang, Y. *Chem*. *Commun*. **2004**, 432.
(d) Zhou, J.; Ye, M. C.; Huang, Z. Z.; Tang, Y. *J*. *Org*. *Chem*. **2004**, *69*, 1309.
(e) Liu, Y. L.; Shang, D. J.; Zhou, X.; Liu, X. H.; Feng, X. M. *Chem*. *Eur*. *J*. **2009**, *15*, 2055.

4 Jensen, K. B.; Thorhauge, J.; Hazell, R. G.; Jrgensen, K. A. *Angew*. *Chem*., *Int*. *Ed*. **2001**, *40*, 160.

5 Evans, D. A.; Scheidt, K. A.; Frandrick, K. R.; Lam, H. W.; Wu, J. *J*. *Am*. *Chem*. *Soc*. **2003**, *125*, 10780.

6 Bandini, M.; Melloni, A.; Tommasi, S.; Umani-Ronchi, A. *Helv*. *Chim*. *Acta* **2003**, *86*, 3753.

7 (a) Zhuang, W.; Hazell, R. G.; Jørgensen, K. A. *Org*. *Biomol*. *Chem*. **2005**, *3*, 2566.
(b) Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Ricci, A. *Angew*. *Chem*., *Int*. *Ed*, **2005**, *44*, 6576.
(c) Singh, P. K.; Bisai, A.; Singh, V. K. *Tetrahedron Lett*. **2007**, *48*, 1127.
(d) Jia, Y. X.; Zhu, S. F.; Yang, Y.; Zhou, Q. L. *J*. *Org*. *Chem*. **2006**, *71*, 75.
(e) Lu, S. F.; Du, D. M.; Xu, J. X. *Org*. *Lett*. **2006**, *8*, 2115.
(f) Han, L.; Lu, S. F.; Xu, J. X.; Du, D. M. *Chem*. *Asian J*. **2008**, *3*, 1111.
(g) Yuan, Z. L.; Lei, Z. Y.; Shi, M. *Tetrahedron*: *Asymmetry* **2008**, *19*, 1339.
(h) Lin, S. Z.; You, T. P. *Tetrahedron* **2009**, *65*, 1010.

8 Bandini, M.; Garelli, A.; Rovinetti, M.; Tommasi, S.; Umani-Ronchi, A. *Chirality* **2005**, *17*, 522.

9 (a) Fleming, E. M.; McCabe, T.; Connon, S. J. *Tetrahedron Lett*. **2006**, *47*, 7037.
(b) Ganesh, M.; Seidel, D. *J*. *Am*. *Chem*. *Soc*. **2008**, *130*, 16464.

10 (a) Itoh, J.; Fuchibe, K.; Akiyama, T. *Angew*. *Chem*., *Int*. *Ed*. **2008**, *47*, 4016.
(b) Sheng, Y. F.; Li, G. Q.; Kang, Q.; Zhang, A. J.; You, S. L. *Chem*. *Eur*. *J*. **2009**, *15*, 3351.

11 (a) Singh, P. K.; Bisai, A.; Singh, V. K. *Tetrahedron Lett*. **2007**, *48*, 1127.
(b) Yokoyama, N.; Arai, T. *Chem*. *Commun*. **2009**, 3285.

12 Wu, M.; Wang, B.; Wang, S. F.; Xia, C. G.; Sun, W. *Org*. *Lett*. **2009**, *11*, 3622.

13 Ng, K.; Somanathan, R.; Walsh, P. J. *Tetrahedron*: *Asymmetry* **2001**, *12*, 1719.

14 Liu, P. N.; Gu, P. M.; Wang, F.; Tu, Y. Q. *Org*. *Lett*. **2004**, *6*, 169.

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