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Enantioselective synthesis of N–C axially chiral indoles through chiral palladium-catalyzed 5-*endo*-hydroaminocyclization

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ABSTRACT

In the presence of (*R*)-SEGPHOS-$PdCl_2$ catalyst, 5-*endo*-hydroaminocyclization of various 2-(*tert*-butyl)-*N*-(2-ethynylphenyl)anilines proceeds enantioselectively to afford optically active N–C axially chiral *N*-(2-*tert*-butylphenyl)indole derivatives in good yields. The enantioselectivity depends strongly on the bulkiness of *ortho*-substituents and the electron density on the arylethynyl group, and it is explained by the dynamic axial chirality generated by the twisting of the aryl substituent.

1. Introduction

Atropisomeric compounds with an N–C chiral axis have received much attention as novel chiral molecules.[1] Recent noteworthy topics in this field include catalytic enantioselective syntheses of N–C axially chiral compounds.[2,3] In 2005, we succeeded in the highly enantioselective synthesis of *N*-arylated *ortho-tert*-butylanilides **I** and *N*-(*ortho-tert*-butylphenyl)-3,4-dihydroquinolin-2-ones **VII** through chiral palladium-catalyzed Buchwald-Hartwig amination (Fig. 1).[2c,d] This reaction was the first practical catalytic asymmetric synthesis of N–C axially chiral compounds. After our publication, highly enantioselective syntheses of various N–C axially chiral compounds **I**–**IX** through catalytic asymmetric reactions have been reported by many other groups.[2,3] These compounds have amide skeletons, and include anilides **I**, **II**, ureas **III**, carbamates **IV**, **V**, imides **VI** and lactams **VII**–**IX**. However, although a considerable number of N–C axially chiral compounds with non-amide structure have also been found,[1a,1q,1s,1t] there has been no report on their catalytic enantioselective synthesis.[4]

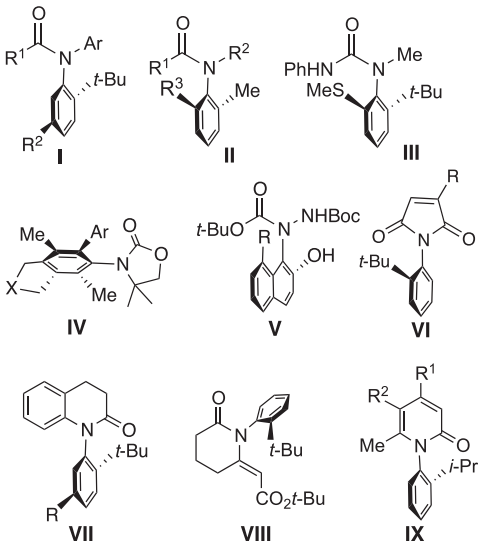

Fig. 1. Various N–C axially chiral compounds prepared with catalytic enantioselective reactions.

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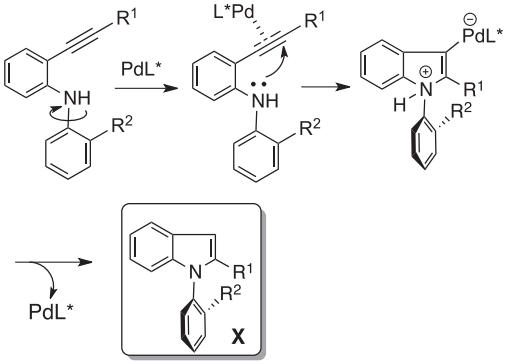
0040-4020/

In 2010, we succeeded in the enantioselective synthesis of various N–C axially chiral indoles via (*R*)-SEGPHOS-$PdCl_2$-catalyzed 5-*endo*-hydroaminocyclization of 2-(*tert*-butyl)-*N*-(2-ethynylphenyl) anilines (Scheme 1, R^2=*t*-Bu).[5] The present reaction is the first catalytic asymmetric synthesis of non-amide type N–C axially chiral compounds. We report here a full article of this reaction. In addition to detailing the scope and limitations of the reaction and the stereochemical assignment of the chiral axis, this paper describes new insights such as the additive effects of protic acid and the relationship between the enantioselectivity and the electron density on arylalkynyl group.



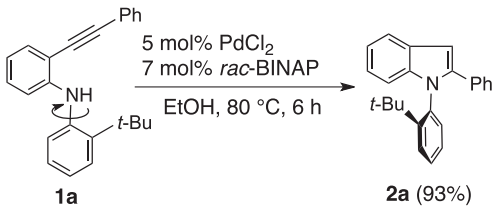
Scheme 1. N–C axially chiral indoles and their catalytic asymmetric synthesis.

2. Results and discussion

In 2006, Kamikawa and Uemura reported that 2-substituted indole derivatives possessing an *ortho*-mono-substituted or *ortho*-di-substituted phenyl group on the nitrogen atom have a high rotational barrier around the N–Ar bond.[6] In these indole substrates, it is significant that even the *N*-(2-methylphenyl)indole derivatives display stable atropisomerism (Scheme 1, **X**: R^2=Me). They also succeeded in the highly enantioselective synthesis of these indole derivatives, although a stoichiometric chiral source was required in their method.[6]

We expected that *N*-(2-*tert*-butylphenyl)indoles (**X**: R^2=*t*-Bu) would have an extremely high rotational barrier, and that their catalytic asymmetric synthesis might be achievable through the chiral transition metal-catalyzed 5-*endo*-hydroaminocyclization of 2-(*tert*-butyl)-*N*-(2-ethynylphenyl)anilines shown in Scheme 1. Although 5-*endo*-hydroaminocyclization of *ortho*-ethynyl anilines, which provides efficient synthesis of indole derivatives, has been broadly investigated by many groups,[7] its application to an asymmetric reaction has not been reported to date.

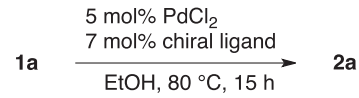
Before investigating enantioselective reactions, we explored the optimization of the reaction conditions by using 2-(*tert*-butyl)-*N*-(2-(phenylethynyl)phenyl)anilines **1a** as a substrate. After a survey of various transition metal catalysts coordinating *rac*-BINAP, solvents and reaction temperatures (room temperature to 80 °C), it was found that when the reaction of **1a** was performed in the presence of $PdCl_2$ (5 mol %) and *rac*-BINAP (7 mol %) in EtOH for 6 h at 80 °C, indole product **2a** was obtained in excellent yield (93%, Scheme 2). The use of other transition metal catalysts (AuCl, $AuCl_3$, $PtCl_2$, $NiCl_2$, AgOTf) instead of $PdCl_2$ gave the significantly lower chemical yields (trace-59%). In the present reaction with *rac*-BINAP-$PdCl_2$ catalyst, the use of protic solvents was required. That is, similar to the reaction in EtOH, those in MeOH, CF_3CH_2OH and $(CF_3)_2CHOH$ gave **2a** in excellent yields (91%–93%), while reaction in aprotic solvent such as THF, toluene, DMF, CH_3CN, gave remarkably lower chemical yields (trace-19%).



Scheme 2. Synthesis of *racemic*-indole **2a** through 5-*endo*-hydroaminocyclization.

Subsequently, under the optimized conditions, a screening of various chiral ligands was performed (Table 1). When (*R*)-C3-Tunephos or (*R*)-SEGPHOS[8] were used as the chiral ligand, relatively good results were obtained (entries 12 and 13). In these cases, indole product **2a** was obtained in excellent yields (99%, 93%) and moderate ee (58%ee, 60% ee). In general, the reaction in the presence of a chiral ligand required a longer reaction time than that of ligand-free reactions (in the presence of only $PdCl_2$).

Table 1
Screening of chiral ligands for the catalytic enantioselective 5-*exo*-aminocyclization of **1a**



Entry	Chiral ligand	Yield (%)[a]	ee (%)[b]
1	(*R*,*R*)-Ph-box	85	4
2	(*S*,*S*)-*t*-Bu-box	85	11
3	(*S*)–P,N-Ligand	Trace	—
4	(*S*,*S*)-Trost ligand	Trace	—
5	(*R*)-(*S*)-BPPFA	14	3
6	(*R*,*R*)-Me-DUPHOS	45	4
7	(*R*)-DTBM-SEGPHOS	8	1
8	(*R*)-BINAP	82	0
9	(*R*)-MOP	69	2
10	(*R*)-DIFLUOROPHOS	89	26
11	(*R*)-SYNPHOS	99	55
12	(*R*)-C3-Tunephos	99	58
13	(*R*)-SEGPHOS	93	60

[a] Isolated yield.
[b] The ee was determined by HPLC analysis using a chiral column.

To evaluate the effect of an *ortho*-substituent on enantioselectivity, the reaction of 2-(phenylethynyl)aniline **3a**–**d** with various *ortho*-substituted phenyl groups on the nitrogen atom was examined in the presence of (*R*)-SEGPHOS-$PdCl_2$ catalyst in EtOH (Table 2). The enantioselectivity decreased with decreasing bulkiness of the *ortho*-substituent, and the reaction with *ortho*-methoxy derivative **3d** gave the racemic product **4d**. The indole products **2a** and **4a**–**c** were confirmed to have a high rotational barrier. That is, when isolated **2a** and **4a**–**c** were heated in EtOH for 15 h at 80 °C, no appreciable change in the ee was detected, providing evidence that the partial racemization of indole products **2a** and **4a**–**c** does not occur under the present reaction conditions.

The enantioselectivity and the rate in the present reaction were also significantly influenced by the substituents on the alkyne (Table 3). Unlike phenylethynyl derivative **1a**, the reaction of ethynyl aniline **1b**,**c** possessing an aliphatic substituent such as *n*-butyl or cyclohexyl groups was negligible under the same conditions. In the reaction of such less reactive substrates as **1b**,**c**, the addition of AgOTf (5 mol %), which leads to the generation of a more reactive cationic Pd species, was effective. In these cases, indole products **2b**,**c** were obtained in good yields (84%, 72%), while a decrease in the enantioselectivity was observed in comparison with that of **2a** (29%ee, Entries 2 and 3). On the other hand,

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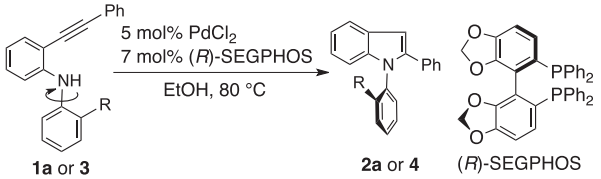
Table 2
The *ortho*-substituent's effect on enantioselectivity

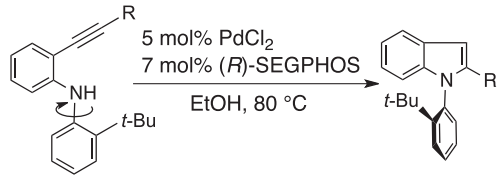


1a or 3 2a or 4 (*R*)-SEGPHOS

Entry	1 or 3	R	2 or 4	Time (h)	Yield (%)[a]	ee (%)[b]
1	**1a**	*t*-Bu	**2a**	4	94	60
2	**3a**	CF_3	**4a**	4	99	56
3	**3b**	*i*-Pr	**4b**	2	97	45
4	**3c**	Ph	**4c**	12	87	29
5	**3d**	OMe	**4d**	4	90	0

[a] Isolated yield.
[b] The ee was determined by HPLC analysis using a chiral column.

Table 3
Catalytic enantioselective 5-*exo*-aminocyclization with various aniline substrates



1 2

Entry	1	R	2	Time (h)	Yield (%)[a]	ee (%)[b]
1	**1a**	C_6H_5	**2a**	4	93	60
2[c]	**1b**	*n*-C_4H_9	**2b**	24	84	29
3[c]	**1c**	Cyclohexyl	**2c**	38	72	29
4	**1d**	2-MeC_6H_4	**2d**	9	95	67
5	**1e**	2-$MMOCH_2C_6H_4$[d]	**2e**	7	71	77
6	**1f**	2-*i*-PrC_6H_4	**2f**	12	90	80
7[c]	**1g**	2-$NO_2C_6H_4$	**2g**	24	67	82
8	**1h**	2-ClC_6H_4	**2h**	13	85	83
9	**1i**	2-BrC_6H_4	**2i**	23	90	83

[a] Isolated yield.
[b] The ee was determined by HPLC analysis using a chiral column.
[c] 5 mol % of AgOTf was added.
[d] MMO=methoxymethoxy.

the reactions of alkynyl anilines **1d**–**i** with *ortho*-substituted phenyl groups increased in enantioselectivity (67%ee to 83% ee, Entries 4–9). In particular, the reactions of **1f**–**i** possessing bulkier *ortho*-substituents such as *iso*-propyl, NO_2, Cl and Br groups gave the indole products **2f**–**i** with relatively good enantioselectivity (80% ee to 83% ee, Entries 6–9). For the less reactive *ortho*-nitro derivative **1g**, the addition of AgOTf was required to get product **2g** (Entry 7).

The increased enantioselectivity with an *ortho*-substituent may be due to chiral relay through the dynamic axial chirality formed around the $C_{alkynyl}$–C_{phenyl} bond (Fig. 2).[9] That is, in the present reaction, the construction of N–C axial chirality should occur in the N–C bond forming step. In this step, direct enantiocontrol by the chiral ligand on the Pd atom should be difficult because the chiral ligand is relatively far way from the newly formed N–C axially chiral structure. In the reaction of substrates having a bulky *ortho*-substituent, chiral information of (*R*)-SEGPHOS may be effectively transferred to the N–C chiral bond via the dynamic axial chirality generated by twisting around the $C_{alkynyl}$–C_{phenyl} bond.

The enantioselectivity was also remarkably dependent on the electron density on the arylethynyl group (Table 4). When reactions of alkynylanilines **1j**–**m** possessing several *para*-substituted phenyl groups (X=NO_2, Cl, Me, OMe) were performed under the same conditions, the ee varied significantly (18%ee to 79% ee) increasing

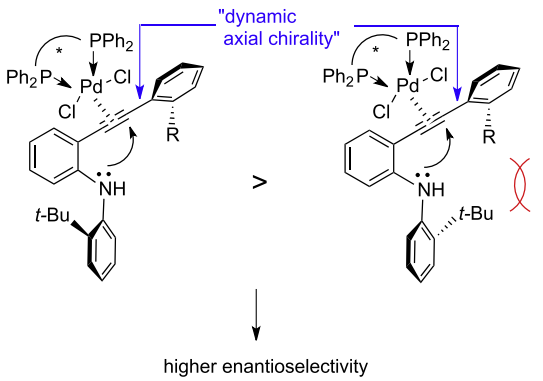
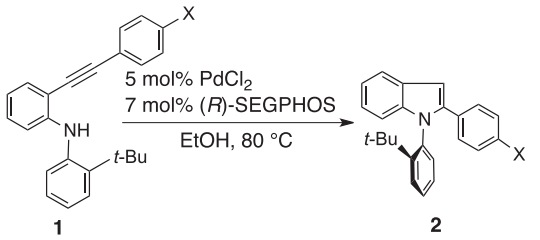


Fig. 2. The origin of increased enantioselectivity due to an *ortho*-substituent.

along the electron-withdrawing character of *para*-substituent. In contrast, the reaction rate decreased as the electron-withdrawing character of *para*-substituent increased (the reaction of **1j** possessing a *para*-nitro group was negligible in the absence of AgOTf).

Table 4
The effect of *para*-substituents X on enantioselectivity



1 2

Entry	1	X	2	Time (h)	Yield (%)[a]	ee (%)[b]
1[c]	**1j**	NO_2	**2j**	17	83	79
2	**1k**	Cl	**2k**	8	97	70
3	**1a**	H	**2a**	4	93	60
4	**1l**	Me	**2l**	4	89	49
5	**1m**	OMe	**2m**	3	89	18

[a] Isolated yield.
[b] The ee was determined by HPLC analysis using a chiral column.
[c] 5 mol % of AgOTf was added.

To evaluate the effect of the *para*-substituents in Table 4, an analysis was performed using a Hammett plot.[10] As shown in Fig. 3, relatively good linear relationships were observed between Hammett σ-values and enantioselectivities [log(major enantiomer/minor enantiomer)] for substrates **1a**, **1j**–**l** except for *para*-methoxy derivative **1m** (R^2=0.95). In addition, the obtained positive reaction constant (ρ-value=+0.48) may suggest that the enantioselectivity-determining step involves the nucleophilic attack of an aniline nitrogen on an electrophilic Pd-alkyne complex.[10] Only *para*-methoxy derivative **1m** departed significantly from the Hammett straight line, and this may be due to the positive resonance effect of the *para*-methoxy group.

In substrates **1a**, **1j**–**l**, the incomplete twisting of the aryl group on the alkyne may lead to dynamic axial chirality such as that of the *ortho*-substituted phenyl derivatives shown in Fig. 2 (**1J** in Fig. 4). Thus chiral information of (*R*)-SEGPHOS is effectively transferred to the N–C chiral bond via chiral relay of this dynamic axial chirality. As a result, in several substrates possessing a *para*-substituted phenyl group, relatively good enantioselectivity was observed. However, with *para*-methoxy derivative **1m**, dynamic axial chirality could not be generated because of the formation of allenyl intermediate **1M** due to the positive resonance effect of the *para*-

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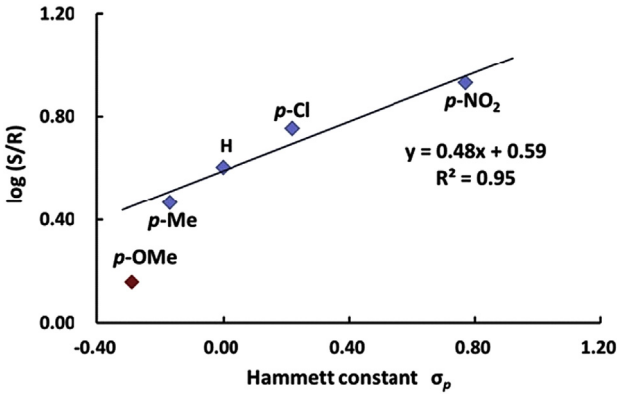


Fig. 3. Hammett plot of enantioselectivity in **1j**, **k**, **a**, **l**, **m**.

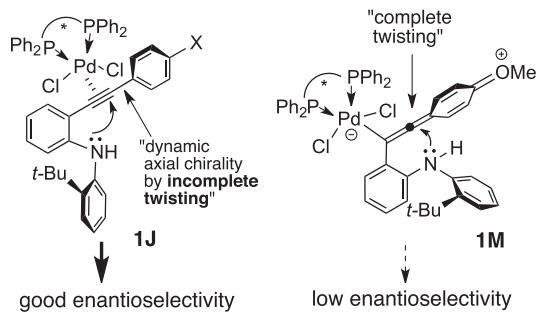


Fig. 4. A possible structure for the enantioselectivity determining step.

methoxy group (Fig. 4). Such an allene-like intermediate that allows complete twisting structure may result in a significant decrease in enantioselectivity.

In the present reaction, we found that the addition of a protic acid increased the reaction rate. When the reaction of **1a** with (*R*)-SEGPHOS-$PdCl_2$ catalyst was performed for 4 h at 40 °C, the chemical yield (34%) of **2a** decreased significantly in comparison with that (93%) at 80 °C, allowing recovery of 60% of starting material **1a** (Table 5, entry 1). However, under the same conditions, the addition of 1 equiv of *p*-toluene sulfonic acid (*p*-TsOH) led to a remarkable increase in the yield (95%, entry 2). In the presence of 0.3 equiv of *p*-TsOH, the product **2a** was also obtained in good yield (86%, entry 3), while neither trifluoroacetic acid nor acetic acid accelerated the reaction (entries 4 and 5).

The acceleration of the reaction rate by *p*-TsOH indicates that the nucleophilic 5-*exo*-cyclization step, which determines the enantioselectivity, is not the rate-limiting step. On this basis, we propose the reaction mechanism in Fig. 5. That is, Pd-aniline complex **1-A** is formed initially, and then **1-A** is converted to alkyne-Pd complex **1-B** to give indole intermediate **1-C** through subsequent 5-*exo*-cyclization. The conversion to **1-B** from **1-A** proceeds slowly in comparison with 5-*exo*-cyclization, and a strong protic acid such as *p*-TsOH may promote the conversion to **1-B** through the protonation of an aniline nitrogen to accelerate the reaction (Fig. 6).

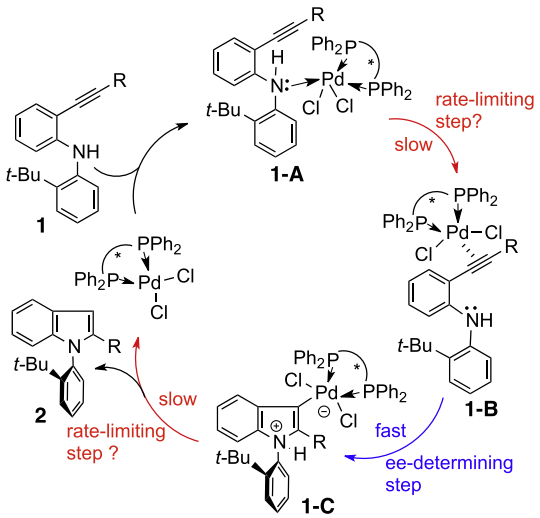


Fig. 5. A possible mechanism for enantioselective 5-*exo*-aminocyclization.

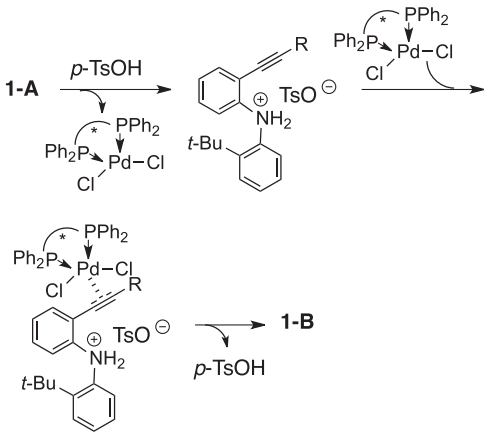
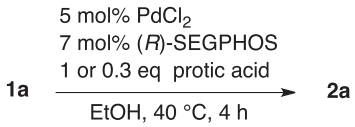


Fig. 6. A possible mechanism for the additive effect of *p*-TsOH.

Table 5
Effect of protic acid on the reaction of **1a**

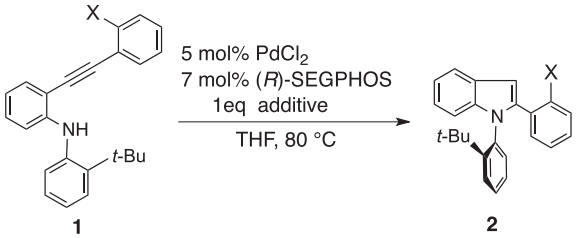


Entry	Protic acid	Yield (%)[a]	ee (%)[b]
1	None	34	56
2	*p*-TsOH (1 equiv)	95	60
3	*p*-TsOH (0.3 equiv)	86	59
4	CF_3COOH (1 equiv)	34	58
5	CH_3COOH (1 equiv)	16	55

[a] Isolated yield.
[b] The ee was determined by HPLC analysis using a chiral column.

Another possibility is that the generation of an indole product **2** from an indole-Pd intermediate **1-C** may be the rate-limiting step, in which case *p*-TsOH would lead to an increase in the reaction rate by promoting the protonation of **1-C** (Fig. 5).[11,12]

As mentioned above, the present reaction did not efficiently proceed in an aprotic solvent. For example, the reaction of **1a** in THF gave **2a** in a poor yield (12%, Scheme 3). On the other hand, when the reaction in THF was performed in the presence of 1 equiv of *p*-TsOH, the indole product **2a** was obtained in a quantitative yield (99%).[12] Furthermore, in comparison with the reaction in EtOH (Table 3, Entry 1, 60% ee), slight increase in the enantioselectivity was observed (73% ee). In the reaction with **1i** bearing *ortho*-bromophenyl



	Additive	Time (h)		Yield (%)	ee (%)
1a (R=H)	none	9	**2a**	12	-
1a (R=H)	*p*-TsOH	9	**2a**	99	73
1i (R=Br)	*p*-TsOH	23	**2i**	92	86

Scheme 3. The effect of *p*-TsOH and solvent on the reaction of **1**.

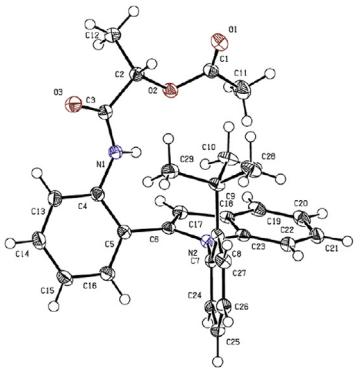
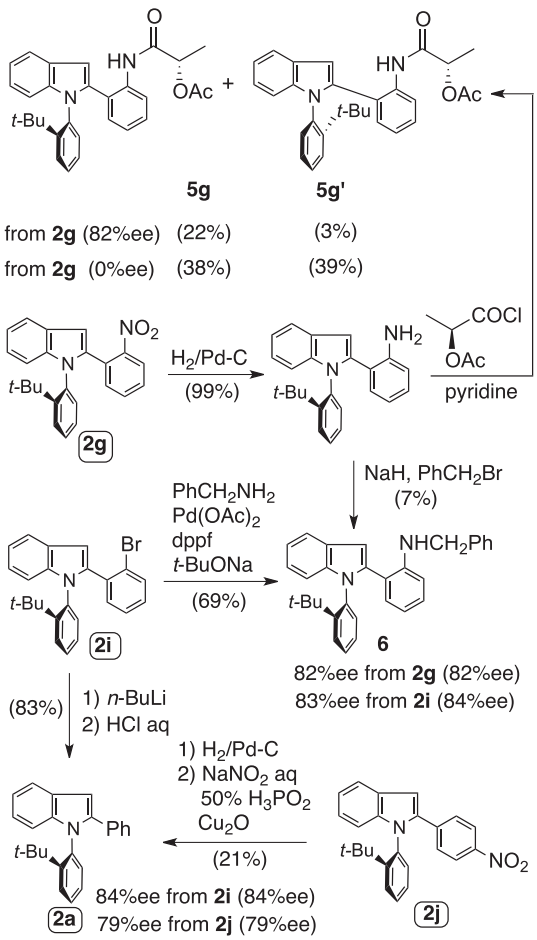


Fig. 7. X-ray crystal structure of **5g′**.

group, the enantioselectivity (86% ee) also slightly increased in comparison with that in EtOH (Table 3, Entry 9, 83% ee).

The absolute stereochemistries of major enantiomers in several indole products **2a**, **2g**, **2i**, **2j** were determined in accordance with Scheme 4. The reduction of the nitro group in **2g** (82%ee) and subsequent condensation with (*S*)-acetoxypropionyl chloride gave diasteromeric amides **5g** and **5g′**. By MPLC separation of **5g** and **5g′** followed by X-ray crystal analysis of the minor diastereomer **5g′** (Fig. 7),[13] the major enantiomer in **2g** obtained by the use of (*R*)-SEGPHOS was determined to be (*S*)-configuration bearing a β-facial *t*-Bu group. The major enantiomers in three other indole products **2a**, **2i**, **2j** were also confirmed to have the same configurations through the conversion shown in Scheme 4.



Scheme 4. Stereochemical assignment of several indole products **2a**, **2g**, **2i**, **2j**.

3. Conclusion

We performed the enantioselective synthesis of N–C axially chiral indole derivatives through (*R*)-SEGPHOS-$PdCl_2$-catalyzed 5-*endo*-hydroaminocyclization of achiral *ortho*-alkynyl anilines possessing an *N*-(*ortho*-*tert*-butyl)phenyl group (up to 83% ee). The enantioselectivity depended remarkably on the bulkiness of *ortho*-substituents and the electron density on an arylethynyl group, which can be explained as chiral relay due to the dynamic axial chirality generated by the twisting of an aryl substituent. The present reaction is the first asymmetric application in indole synthesis of the 5-*endo*-hydroaminocyclization of *ortho*-alkynylaniline as well as the first example of a catalytic enantioselective synthesis of non-amide N–C axially chiral compounds.

4. Experimental section

4.1. General techniques

Melting points were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. In ^1H and ^{13}C NMR spectra, chemical shifts were expressed in δ (ppm) downfield from $CHCl_3$ (7.26 ppm) and $CDCl_3$ (77.0 ppm), respectively. Mass spectra were recorded by electrospray ionization (TOF). Column chromatography was performed on silica gel (75–150 mm). Medium-pressure liquid chromatography (MPLC) was performed on a 25×4 cm i.d. prepacked column (silica gel, 10 μm) with a UV detector. High-performance liquid chromatography (HPLC) was performed on a 25×0.4 cm i.d. chiral column with a UV detector.

4.2. Synthesis of hydroaminocyclization precursors

Precursors **1a**, **1b**, **1d**, **1e**, **1f**, **1g**, **1h**, **1i**, **1l** were prepared in accordance with the procedure described in preliminary communication.[5] Other precursors **1c**, **1j**, **1k**, **1m**, **3a**–**3d** were prepared as follows.

*4.2.1. 2-tert-Butyl-N-(2-(cyclohexylethynyl)phenyl)aniline (**1c**).* To a solution of $(Ph_3P)_2PdCl_2$ (42 mg, 0.06 mmol) and CuI (24 mg, 0.1 mmol) in Et_3N (4 mL) were added 2-bromo-iodobenzene (0.38 mL, 3.0 mmol) and ethynylcyclohexane (0.39 mL, 3.0 mmol) at rt. After being stirred for 23 h at rt, the mixture was poured into saturated NH_4Cl aq and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane only) gave 1-bromo-2-(cyclohexylethynyl)benzene (777 mg, 98%). To a solution of $Pd(OAc)_2$ (27 mg, 0.12 mmol) and (*o*-tol)$_3$P (71 mg, 0.23 mmol), *t*-BuONa (421 mg, 4.4 mmol) in toluene (10 mL) were added 1-bromo-2-(cyclohexylethynyl)benzene

(769 mg, 2.9 mmol) and 2-*tert*-butylaniline (0.46 mL, 2.9 mmol) at rt. After being stirred for 13 h at 100 °C, the mixture was poured into saturated $NaHCO_3$ aq and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over Na_2SO_4, and evaporated to dryness. Purification of the residue by column chromatography (hexane only) gave **1c** (534 mg, 55%). **1c**: yellow oil; IR (neat) 3420 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.45 (1H, dd, J=1.4 and 7.8 Hz), 7.32–7.36 (2H, m), 7.20 (1H, dt, J=1.4, 7.3 Hz), 7.11 (1H, dt, J=1.4, 7.3 Hz), 7.05 (1H, dt, J=1.4, 8.2 Hz), 6.75 (1H, d, J=8.2 Hz), 6.66 (1H, dt, J=0.9, 7.3 Hz), 6.36 (1H, br s), 2.64 (1H, m), 1.89–1.92 (2H, m), 1.72–1.79 (2H, m), 1.26–1.59 (6H, m), 1.43 (9H, s); ^{13}C NMR ($CDCl_3$) δ: 146.8, 144.5, 140.0, 132.1, 128.7, 127.14, 127.11, 126.8, 124.6, 117.5, 111.7, 109.5, 100.3, 77.1, 34.9, 33.0, 30.7, 30.0, 25.9, 25.0; MS (m/z) 331 (M^+); Anal. Calcd for $C_{24}H_{29}N$: C, 86.96; H, 8.82; N, 4.23. Found: C, 86.83; H, 8.60; N, 4.19.

*4.2.2. 2-tert-Butyl-N-(2-(4-chlorophenyl)ethynyl)phenyl)aniline (**1k**).* To a solution of $Pd(OAc)_2$ (26.9 mg, 0.12 mmol) and (o-tol)$_3$P (73.0 mg, 0.24 mmol), *t*-BuONa (0.43 g, 4.50 mmol) in toluene (10 mL) were added 1-bromo-2-trimethylsilylethynylbenzene[5] (0.76 g, 3.0 mmol) and 2-*tert*-butylaniline (0.47 mL, 3.0 mmol) at rt. After being stirred for 4 h at 100 °C, the mixture was poured into saturated $NaHCO_3$ aq and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over Na_2SO_4, and evaporated to dryness. Purification of the residue by column chromatography (hexane only) gave 2-*tert*-butyl-*N*-(2-(trimethylsilylethynyl)phenyl)aniline (510 mg, 53%). To a solution of 2-*tert*-butyl-*N*-(2-(trimethylsilylethynyl)phenyl)aniline (940 mg, 2.92 mmol) in CH_2Cl_2 (1 mL) and CH_3OH (2 mL) was added K_2CO_3 (525 mg, 3.80 mmol). After being stirred for 3 h at rt, the mixture was poured into water and extracted with haxane. The hexane extracts were washed with brine, dried over Na_2SO_4, and evaporated to dryness. Purification of the residue by column chromatography (hexane only) gave 2-*tert*-butyl-*N*-(2-(ethynyl)phenyl)aniline (649 mg, 89%). To a solution of $(Ph_3P)_2PdCl_2$ (32 mg, 0.04 mmol) and CuI (17 mg, 0.09 mmol) in Et_3N (2.0 mL) were added 1-chloro-4-iodobenzene (542 mg, 2.27 mmol) and 2-*tert*-butyl-*N*-(2-(ethynyl)phenyl)aniline (567 mg, 2.27 mmol) in Et_3N (2.0 mL) at rt. After being stirred for 6 h at rt, the mixture was poured into saturated NH_4Cl aq and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over Na_2SO_4, and evaporated to dryness. Purification of the residue by column chromatography (hexane only) gave **1k** (761 mg, 93%). **1k**: yellow oil; IR (neat) 3425, 2206 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.40–7.47 (4H, m), 7.36 (1H, dd, J=1.4, 7.8 Hz), 7.30–7.33 (2H, m), 7.22 (1H, dt, J=1.4, 7.3 Hz), 7.11–7.16 (2H, m), 6.82 (1H, d, J=8.7 Hz), 6.73 (1H, dt, J=0.9, 7.6 Hz), 6.45 (1H, br s), 1.44 (9H, s); ^{13}C NMR ($CDCl_3$) δ: 147.1, 144.4, 139.6, 134.3, 132.5, 132.3, 129.9, 128.8, 127.2, 126.93, 126.88, 124.9, 121.6, 117.8, 112.1, 108.2, 94.0, 87.3, 34.9, 30.6; MS (m/z) 359 (M^+, ^{35}Cl); Anal. Calcd for $C_{24}H_{22}ClN$: C, 80.10; H, 6.16; N, 3.89. Found: C, 80.24; H, 6.26; N, 3.86.

*4.2.3. 2-tert-Butyl-N-(2-(4-nitrophenyl)ethynyl)phenyl)aniline (**1j**).* **1j** was prepared from 1-iodo-4-nitrobenzene (499 mg, 2.0 mmol) and 2-*tert*-butyl-*N*-(2-(ethynyl)phenyl)aniline (500 mg, 2.0 mmol) in accordance with the procedure for the synthesis of **1k** (622 mg, 84%). **1j**: yellow solid; mp 143–144 °C; IR (neat) 3377, 2177 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 8.21 (2H, d, J=8.7 Hz), 7.61 (2H, d, J=8.7 Hz), 7.46–7.49 (2H, m), 7.35 (1H, dd, J=0.9, 7.8 Hz), 7.14–7.26 (3H, m), 6.82 (1H, d, J=8.2 Hz), 6.75 (1H, dt, J=0.9, 7.3 Hz), 6.42 (1H, br s), 1.45 (9H, s); ^{13}C NMR ($CDCl_3$) δ: 147.5, 146.9, 144.5, 139.3, 132.7, 131.8, 130.8, 130.1, 127.3, 127.1, 127.0, 125.2, 123.8, 118.0, 112.3, 107.2, 93.5, 92.0, 34.9, 30.6; MS (m/z) 370 (M^+); Anal. Calcd for $C_{24}H_{22}N_2O_2$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.53; H, 5.98; N, 7.53.

*4.2.4. 2-tert-Butyl-N-(2-(4-methoxyphenyl)ethynyl)phenyl)aniline (**1m**).* **1m** was prepared from 1-ethynyl-4-methoxybenzene (0.65 mL, 5.0 mmol) in accordance with the procedure for the synthesis of **1c** (296 mg, 17%). **1m**: colorless oil; IR (neat) 3421, 2361 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.42–7.47 (4H, m), 7.37 (1H, dd, J=1.4, 7.8 Hz), 7.22 (1H, dt, J=1.4, 7.3 Hz), 7.09–7.14 (2H, m), 6.87 (2H, d, J=8.7 Hz), 6.83 (1H, d, J=8.2 Hz), 6.72 (1H, dt, J=0.9, 7.3 Hz), 6.51 (1H, br s), 3.83 (3H, s), 1.45 (9H, s); ^{13}C NMR ($CDCl_3$) δ: 159.6, 146.8, 144.3, 139.8, 132.8, 132.1, 129.3, 127.2, 126.8, 124.6, 117.7, 115.2, 114.1, 111.9, 109.0, 95.2, 84.8, 55.3, 34.9, 30.6; MS (m/z) 355 (M^+); Anal. Calcd for $C_{25}H_{25}NO$: C, 84.47; H, 7.09; N, 3.94. Found: C, 84.61; H, 6.99; N, 3.91.

*4.2.5. 2-Trifluoromethyl-N-(2-(phenylethynyl)phenyl)aniline (**3a**).* To a solution of $Pd(OAc)_2$ (11 mg, 0.05 mmol) and *rac*-BINAP (50 mg, 0.08 mmol), Cs_2CO_3 (456 mg, 1.4 mmol) in toluene (6 mL) were added 1-bromo-2-(phenylethynyl)benzene[5] (257 mg, 1.0 mmol) and 2-trifluoromethylaniline (193 mg, 1.2 mmol) at rt. After being stirred for 2 h at 100 °C, the mixture was poured into saturated $NaHCO_3$ aq and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over Na_2SO_4, and evaporated to dryness. Purification of the residue by column chromatography (hexane only) gave **3a** (297 mg, 88%). **3a**: colorless oil; IR (ATR) 3410, 2210 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.67 (1H, d, J=7.8 Hz), 7.56–7.61 (4H, m), 7.48 (1H, t, J=7.8 Hz), 7.34–7.41 (4H, m), 7.29 (1H, dt, J=2.3, 6.9 Hz), 7.06–7.10 (2H, m), 6.97 (1H, t, J=7.8 Hz); ^{13}C NMR ($CDCl_3$) δ: 143.2, 140.4, 132.63, 132.59, 131.4, 129.3, 128.5, 128.4, 127.0 (q, J_{C-F}=5.8 Hz), 124.6, (q, J_{C-F}=273.2 Hz), 122.7, 121.2, 120.7, 119.4, 119.3 (q, J_{C-F}=28.8 Hz), 115.1, 112.2, 96.2, 84.9; ^{19}F NMR ($CDCl_3$) δ: −62.1; MS (m/z) 360 (MNa^+); Anal. Calcd for $C_{21}H_{14}F_3N$: C, 74.77; H, 4.18; N, 4.15. Found: C, 74.84; H, 4.40; N, 4.34.

*4.2.6. 2-iso-Propyl-N-(2-(phenylethynyl)phenyl)aniline (**3b**).* **3b** was prepared from 1-bromo-2-(phenylethynyl)benzene[5] (722 mg, 2.8 mmol) and 2-*iso*-propylaniline (380 mg, 2.8 mmol) in accordance with the procedure for the synthesis of **1c** (529 mg, 61%). **3b**: white solid; mp 70–72 °C, IR (ATR) 3398, 2208 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.58–7.61 (2H, m), 7.55 (1H, dd, J=1.4, 7.3 Hz), 7.39–7.46 (5H, m), 7.27 (1H, dt, J=1.8, 7.3 Hz), 7.22 (2H, dt, J=1.4, 7.3 Hz), 6.98 (1H, d, J=8.2 Hz), 6.84 (1H, dt, J=0.9, 7.3 Hz), 6.47 (1H, br s), 3.32 (1H, sep, J=6.9 Hz), 1.33 (6H, d, J=6.9 Hz); ^{13}C NMR ($CDCl_3$) δ: 146.5, 142.1, 138.3, 132.3, 131.4, 129.6, 128.4, 128.3, 126.4, 126.3, 124.6, 123.6, 123.0, 118.2, 112.4, 108.9, 95.4, 85.8, 27.9, 23.1; MS (m/z) 334 (MNa^+); Anal. Calcd for $C_{23}H_{21}N$: C, 88.71; H, 6.80; N, 4.50. Found: C, 88.45; H, 6.73; N, 4.53.

*4.2.7. 2-Phenyl-N-(2-(phenylethynyl)phenyl)aniline (**3c**).* **3c** was prepared from 1-bromo-2-(phenylethynyl)benzene[5] (257 mg, 1.0 mmol) and 2-phenylaniline (169 mg, 1.0 mmol) in accordance with the procedure for the synthesis of **1c** (264 mg, 76%). **3c**: white solid; mp 113–115 °C, IR (ATR) 3379, 2203 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.58 (1H, dd, J=0.9, 8.7 Hz), 7.43–7.50 (4H, m), 7.23–7.38 (9H, m), 7.13 (2H, dd, J=1.4, 7.8 Hz), 7.09 (1H, dt, J=0.9, 7.3 Hz), 6.84 (1H, dt, J=1.4, 7.3 Hz), 6.69 (1H, s); ^{13}C NMR ($CDCl_3$) δ: 144.3, 138.7, 138.6, 132.6, 132.3, 131.3, 131.0, 129.35, 129.32, 128.8, 128.2, 128.1, 127.5, 122.8, 122.0, 119.3, 118.4, 113.5, 110.7, 95.7, 85.3; MS (m/z) 368 (MNa^+); Anal. Calcd for $C_{26}H_{19}N$: C, 90.40; H, 5.54; N, 4.05. Found: C, 90.32; H, 5.61; N, 4.10.

*4.2.8. 2-Methoxy-N-(2-(phenylethynyl)phenyl)aniline (**3d**).* **3d** was prepared from 1-bromo-2-(phenylethynyl)benzene[5] (771 mg, 3.0 mmol) and 2-methoxyaniline (369 mg, 3.0 mmol) in accordance with the procedure for the synthesis of **3a** (165 mg, 28%). **3d**: yellow oil; IR (ATR) 3386, 2204 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.53–7.58 (2H, m), 7.49 (1H, dd, J=1.8, 7.8 Hz), 7.44–7.47 (1H, m), 7.41 (1H, d, J=7.3 Hz), 7.34–7.40 (3H, m), 7.25 (1H, dt, J=1.4, 8.2 Hz), 7.08 (1H, br s), 6.92–6.96 (3H, m), 6.85 (1H, dt, J=0.9, 7.3 Hz), 3.91 (3H, s); ^{13}C NMR ($CDCl_3$) δ: 149.2, 144.1, 132.4, 131.5, 131.4, 129.4, 128.4, 128.2,

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123.3, 121.1, 120.7, 119.3, 116.3, 114.0, 111.1, 110.8, 95.7, 85.9, 55.7; MS (*m*/*z*) 322 (MNa^+); HRMS. Calcd for $C_{21}H_{17}NONa$ (MNa^+) 322.1208. Found: 322.1214.

4.3. Synthesis of axially chiral indoles

Indoles **2a**, **2b**, **2d**, **2e**, **2f**, **2g**, **2h**, **2i**, **2l** were prepared in accordance with the procedure described in preliminary communication.[5] Other indoles **2c**, **2j**, **2k**, **2m**, **4a**–**4d** were prepared as follows.

*4.3.1. 1-(2-tert-Butylphenyl)-2-cyclohexyl-1H-indole (**2c**).* A solution of $PdCl_2$ (2.6 mg, 0.015 mmol) and (*R*)-SEGPHOS (12.4 mg, 0.020 mmol) in EtOH (1 mL) was stirred for 10 min at rt, and then AgOTf (3.7 mg, 0.014 mmol) was added to the reaction mixture. After being stirred for 20 min at 80 °C, **1c** (96.2 mg, 0.29 mmol) in EtOH (2 mL) was added, and the mixture was stirred for 38 h at 80 °C. EtOH solvent was evaporated to dryness. Purification of the residue by column chromatography (hexane only) and subsequently MPLC (hexane only) gave **2c** (70.4 mg, 73%). The ee (29% ee) of **2c** was determined by HPLC analysis using a CHIRALCEL OD-3 column [25 cm×0.46 cm i.d.; 1.0% *i*-PrOH in hexane; flow rate, 0.4 mL/min; (+)-**2c** (major); t_R=8.9 min, (−)-**2c** (minor); t_R=9.8 min]. **2c** (29%ee): pale yellow solid; mp 113–114 °C, $[\alpha]_D$ +2.7 (*c* 0.51, $CHCl_3$); IR (KBr) 2930 cm^{-1}; ^1H NMR ($CDCl_3$) *δ*: 7.68 (1H, dd, *J*=1.4, 8.2 Hz), 7.57 (1H, dd, *J*=1.4, 6.8 Hz), 7.45 (1H, dt, *J*=1.4, 7.6 Hz), 7.27 (1H, dt, *J*=1.4, 7.8 Hz), 6.99–7.08 (3H, m), 6.74 (1H, dd, *J*=1.4, 8.0 Hz), 6.39 (1H, s), 2.24 (1H, tt, *J*=3.2, 11.9 Hz), 1.99 (1H, d, *J*=13.3 Hz), 1.83 (2H, dd, *J*=1.4, 11.0 Hz), 1.61–1.73 (3H, m), 1.15–1.29 (3H, m), 1.08 (9H, s), 0.97–1.05 (1H, m); ^{13}C NMR ($CDCl_3$) *δ*: 149.0, 148.8, 139.1, 135.0, 132.5, 129.3, 128.9, 128.1, 126.7, 120.7, 119.6, 119.4, 111.2, 97.6, 36.4, 36.1, 35.8, 32.0, 31.6, 26.7, 26.4, 26.0; MS (*m*/*z*) 331 (M^+); Anal. Calcd for $C_{24}H_{29}N$: C, 86.96; H, 8.82; N, 4.23. Found: C, 86.66; H, 8.62; N, 4.18.

*4.3.2. 1-(2-tert-Butylphenyl)-2-(4-nitrophenyl)-1H-indole (**2j**).* **2j** was prepared from **1j** (110 mg, 0.3 mmol) in accordance with the procedure for the synthesis of **2c** (80 °C, 4 h, heating). Purification of the residue by column chromatography (hexane/AcOEt=50) and subsequently MPLC (hexane/AcOEt=150) gave **2j** (91 mg, 83%). The ee (79% ee) of **2j** was determined by HPLC analysis using a CHIRALCEL OD-3 column [25 cm×0.46 cm i.d.; 1.0% *i*-PrOH in hexane; flow rate, 1.0 mL/min; (−)-**2j** (major); t_R=7.8 min, (+)-**2j** (minor); t_R=15.8 min]. **2j** (79% ee): yellow solid; mp 97–98 °C, $[\alpha]_D$ −130.3 (*c* 0.59, $CHCl_3$); IR (KBr) 2966 cm^{-1}; ^1H NMR ($CDCl_3$) *δ*: 8.05 (2H, d, *J*=9.2 Hz), 7.70 (1H, dd, *J*=1.4, 8.0 Hz), 7.67 (1H, dd, *J*=1.4, 8.2 Hz), 7.50 (1H, dt, *J*=1.4, 7.3 Hz), 7.42 (2H, d, *J*=9.2 Hz), 7.34 (1H, dt, *J*=1.4, 7.3 Hz), 7.15–7.22 (3H, m), 7.06 (1H, d, *J*=0.9 Hz), 6.88 (1H, dd, *J*=1.4, 7.3 Hz), 0.93 (9H, s); ^{13}C NMR ($CDCl_3$) *δ*: 148.5, 146.2, 141.7, 139.4, 138.5, 135.2, 132.3, 130.3, 129.5, 127.9, 127.3, 123.7, 123.5, 120.9, 120.8, 111.8, 105.1, 36.0, 31.4; MS (*m*/*z*) 370 (M^+); Anal. Calcd for $C_{24}H_{22}N_2O_2$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.68; H, 6.05; N, 7.31.

*4.3.3. 1-(2-tert-Butylphenyl)-2-(4-chlorophenyl)-1H-indole (**2k**).* A solution of $PdCl_2$ (2.6 mg, 0.015 mmol) and (*R*)-SEGPHOS (12.4 mg, 0.020 mmol) in EtOH (1 mL) was stirred for 10 min at rt. **1k** (104 mg, 0.29 mmol) in EtOH (2 mL) was added to the mixture, and the mixture was stirred for 8 h at 80 °C. EtOH solvent was evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt=100) gave **2k** (102 mg, 97%). The ee (70% ee) of **2k** was determined by HPLC analysis using a CHIRALCEL OD-3 column [25 cm×0.46 cm i.d.; hexane only; flow rate, 1.0 mL/min; (−)-**2k** (major); t_R=13.3 min, (+)-**2k** (minor); t_R=16.3 min]. **2k** (70%ee): yellow solid; mp 36–37 °C, $[\alpha]_D$ −53.9 (*c* 0.54, $CHCl_3$); IR (KBr) 2970 cm^{-1}; ^1H NMR ($CDCl_3$) *δ*: 7.65–7.68 (1H, m), 7.63 (1H, dd, *J*=1.4, 8.2 Hz), 7.46 (1H, dt, *J*=0.9, 7.1 Hz), 7.30 (1H, dt, *J*=1.4, 7.3 Hz), 7.13–7.23 (7H, m), 6.83–6.87 (1H, m), 6.85 (1H, s), 0.92 (9H, s); ^{13}C NMR ($CDCl_3$) *δ*: 148.6, 141.1, 140.1, 135.5, 133.2, 132.5, 131.6, 130.1, 129.3, 129.1, 128.5, 127.5, 126.9, 122.3, 120.34, 120.28, 111.6, 102.7, 36.0, 31.4; MS (*m*/*z*) 359 (M^+, ^{35}Cl); Anal. Calcd for $C_{24}H_{22}ClN$: C, 80.10; H, 6.16; N, 3.89. Found: C, 80.00; H, 6.17; N, 3.88.

*4.3.4. 1-(2-tert-Butylphenyl)-2-(4-methoxyphenyl)-1H-indole (**2m**).* **2m** was prepared from **1j** (118 mg, 0.3 mmol) in accordance with the procedure for the synthesis of **2k** (80 °C, 3 h). Purification of the residue by column chromatography (hexane only) gave **2m** (106 mg, 89%). The ee (18%ee) of **2j** was determined by HPLC analysis using a CHIRALCEL OD-H column [25 cm×0.46 cm i.d.; 7.0% *i*-PrOH in hexane; flow rate, 0.8 mL/min; (−)-**2m** (major); t_R=10.9 min, (+)-**2m** (minor); t_R=11.9 min]. **2m** (18%ee): pale yellow solid; mp 114–115 °C, $[\alpha]_D$ −12.4 (*c* 0.52, $CHCl_3$); IR (KBr) 2966 cm^{-1}; H NMR ($CDCl_3$) *δ*: 7.61–7.66 (2H, m), 7.45 (1H, dt, *J*=0.9, 7.3 Hz), 7.30 (1H, dt, *J*=0.9, 7.6 Hz), 7.22 (2H, d, *J*=8.5 Hz), 7.19 (1H, dd, *J*=1.4, 7.8 Hz), 7.10–7.15 (2H, m), 6.76–6.85 (2H, m), 6.75 (2H, d, *J*=8.5 Hz), 3.76 (3H, s), 0.94 (9H, s); ^{13}C NMR ($CDCl_3$) *δ*: 158.9, 148.6, 141.4, 140.8, 135.8, 132.7, 130.0, 129.5, 128.9, 127.8, 126.7, 125.7, 121.7, 120.01, 119.97, 113.7, 111.4, 101.4, 55.2, 36.0, 31.4; MS (*m*/*z*) 355 (M^+); Anal. Calcd for $C_{25}H_{25}NO$: C, 84.47; H, 7.09; N, 3.94. Found: C, 84.73; H, 6.95; N, 3.93.

*4.3.5. 1-(2-Trifluoromethylphenyl)-2-phenyl-1H-indole (**4a**).* **4a** was prepared from **3a** (97 mg, 0.29 mmol) in accordance with the procedure for the synthesis of **2k** (80 °C, 4 h, heating). Purification of the residue by column chromatography (hexane only) gave **4a** (96 mg, 99%). The ee (56% ee) of **4a** was determined by HPLC analysis using a CHIRALCEL OD-3 column [25 cm×0.46 cm i.d.; 0.5% *i*-PrOH in hexane; flow rate, 1.0 mL/min; (−)-**4a** (major); t_R=8.9 min, (+)-**4a** (minor); t_R=13.1 min]. **4a** (56% ee): white solid; mp 111–113 °C, $[\alpha]_D$ −32.6 (*c* 0.40, $CHCl_3$); IR (ATR) 3059 cm^{-1}; ^1H NMR ($CDCl_3$) *δ*: 7.83 (1H, dd, *J*=1.4, 7.8 Hz), 7.69 (1H, dd, *J*=1.4, 6.8 Hz), 7.65 (1H, dt, *J*=1.4, 7.3 Hz), 7.59 (1H, t, *J*=7.3 Hz), 7.37 (1H, d, *J*=7.8 Hz), 7.27–7.30 (2H, m), 7.20–7.25 (3H, m), 7.13–7.19 (2H, m), 6.89 (1H, d, *J*=7.8 Hz), 6.87 (1H, s); ^{13}C NMR ($CDCl_3$) *δ*: 141.8, 140.6, 136.8, 132.9, 132.5, 132.3, 129.5 (q, J_{C-F}=30.7 Hz), 129.0, 128.4, 128.2, 128.1, 127.7 (q, J_{C-F}=5.8 Hz), 127.4, 122.9 (q, J_{C-F}=274.1 Hz), 122.3, 120.7, 120.4, 110.9, 103.7; ^{19}F NMR ($CDCl_3$) *δ*: −61.1; MS (*m*/*z*) 360 (MNa^+); Anal. Calcd for $C_{21}H_{14}F_3N$: C, 74.77; H, 4.18; N, 4.15. Found: C, 74.69; H, 4.45; N, 4.20.

*4.3.6. 1-(2-iso-Propylphenyl)-2-phenyl-1H-indole (**4b**).* **4b** was prepared from **3b** (93 mg, 0.3 mmol) in accordance with the procedure for the synthesis of **2k** (80 °C, 2 h, heating). Purification of the residue by column chromatography (hexane only) gave **4b** (91 mg, 97%). The ee (45% ee) of **4b** was determined by HPLC analysis using a CHIRALCEL OD-3 column [25 cm×0.46 cm i.d.; hexane only; flow rate, 2.0 mL/min; (+)-**4b** (minor); t_R=10.2 min, (−)-**4b** (major); t_R=12.0 min]. **4b** (45% ee): yellow oil; $[\alpha]_D$ −29.7 (*c* 1.46, $CHCl_3$); IR (ATR) 3058 cm^{-1}; ^1H NMR ($CDCl_3$) *δ*: 7.73 (1H, dd, *J*=1.8, 7.3 Hz), 7.46 (1H, dt, *J*=1.4, 7.8 Hz), 7.39 (2H, dt, *J*=1.4, 7.3 Hz), 7.31–7.36 (3H, m), 7.21–7.25 (3H, m), 7.15–7.20 (2H, m), 6.99 (1H, dd, *J*=1.8, 6.9 Hz), 6.88 (1H, s), 2.41 (1H, sep, *J*=6.9 Hz), 0.92 (3H, d, *J*=6.9 Hz), 0.69 (3H, d, *J*=6.9 Hz); ^{13}C NMR ($CDCl_3$) *δ*: 147.5, 141.4, 139.8, 135.8, 132.5, 129.8, 129.0, 128.5, 128.1, 127.9, 127.3, 127.0, 126.5, 122.1, 120.31, 120.25, 110.8, 102.2, 27.6, 24.8, 22.4; MS (*m*/*z*) 334 (MNa^+); HRMS. Calcd for $C_{23}H_{21}NNa$ (MNa^+) 334.1572. Found: 334.1574.

*4.3.7. 1-(2-Phenylphenyl)-2-phenyl-1H-indole (**4c**).* **4c** was prepared from **3c** (104 mg, 0.3 mmol) in accordance with the procedure for the synthesis of **2k** (80 °C, 13 h, heating). Purification of the residue by column chromatography (hexane only) gave **4c**

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(89 mg, 86%). The ee (29% ee) of **4c** was determined by HPLC analysis using a CHIRALCEL OD-3 column [25 cm×0.46 cm i.d.; 0.5% *i*-PrOH in hexane; flow rate, 1.0 mL/min; (−)-**4c** (major); t_R=6.6 min, (+)-**4c** (minor); t_R=8.3 min]. **4c** (29% ee): yellow solid; mp 106–108 °C; $[\alpha]_D$ −44.4 (*c* 0.40, $CHCl_3$); IR (ATR) 3059 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.70–7.74 (2H, m), 7.59 (1H, dt, *J*=1.8, 7.8 Hz), 7.52 (1H, dt, *J*=1.4, 7.3 Hz), 7.42 (1H, dd, *J*=1.8, 7.8 Hz), 7.38 (1H, m), 7.23–7.28 (2H, m), 7.06–7.18 (4H, m), 6.97 (2H, t, *J*=7.8 Hz), 6.81 (2H, d, *J*=6.9 Hz), 6.60 (1H, s), 6.42 (2H, d, *J*=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ: 141.1, 140.5, 139.1, 138.2, 135.8, 132.4, 131.3, 129.5, 128.3, 128.20, 128.17, 128.0, 127.8, 127.7, 127.6, 126.8, 122.1, 120.43, 120.39, 110.7, 102.6; MS (*m*/*z*) 368 (MNa^+); HRMS. Calcd for $C_{26}H_{19}NNa$ (MNa^+): 368.1415. Found: 368.1407.

*4.3.8. 1-(2-Mehtoxyphenyl)-2-phenyl-1H-indole (**4d**).* **4d** was prepared from **3d** (90 mg, 0.3 mmol) in accordance with the procedure for the synthesis of **2k** (80 °C, 3 h, heating). Purification of the residue by column chromatography (hexane/AcOEt=300) gave **4d** (89 mg, 99%). The ee (0% ee) of **4d** was determined by HPLC analysis using a CHIRALPAK AD-H column [25 cm×0.46 cm i.d.; 1.0% *i*-PrOH in hexane; flow rate, 1.0 mL/min; **4d**; t_R=9.2 min, *ent*-**4d**; t_R=11.4 min]. **4d**: orange oil; IR (ATR) 3060 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.75 (1H, m), 7.40 (1H, dt, *J*=1.4, 8.2 Hz), 7.20–7.37 (8H, m), 7.15 (1H, m), 7.06 (1H, dt, *J*=1.4, 7.8 Hz), 7.00 (1H, dd, *J*=0.9, 8.2 Hz), 6.87 (1H, s), 3.55 (3H, s); ^{13}C NMR ($CDCl_3$) δ: 155.4, 141.6, 138.9, 133.1, 130.0, 129.2, 128.2, 128.1, 127.9, 127.2, 127.1, 122.0, 120.8, 120.4, 120.3, 112.3, 110.7, 102.5, 55.3; MS (*m*/*z*) 322 (MNa^+); HRMS. Calcd for $C_{21}H_{17}NONa$ (MNa^+) 322.1208. Found: 322.1207.

4.4. Stereochemical assignment of indole products

2a, **2g**, **2i**, **2j**. **2g** and **2i** were converted to **5g** and **5g′** or **6** in accordance with the procedure described in preliminary communication.[5] The conversion of **2i** and **2j** to **2a** is as follows.

*4.4.1. Conversion of **2i** to **2a**.* To a solution of **2i** (105 mg, 0.26 mmol, 84% ee) in THF (2 mL) was added 1.6 M hexane solution of *n*-BuLi (0.20 mL) at −20 °C. After being stirred for 10 minmin at −20 °C, the mixture was poured into 2N HCl aq and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt=100) gave **2a** (71 mg, 83%). The ^1H NMR of **2a** coincided with that described in preliminary communication.[5] The reaction proceeded without any decrease in the ee. The ee (84% ee) of **2a** was determined by HPLC analysis using a CHIRALPACK IA column [25 cm×0.46 cm i.d.; 0.5% *i*-PrOH in hexane; flow rate, 0.5 mL/min; (−)-**1a** (major); t_R=9.2 min, (+)-**1a** (minor); t_R=10.2 min].[5]

*4.4.2. Conversion of **2j** to **2a**.* To a solution of **2j** (91 mg, 0.28 mmol, 79% ee) in MeOH and THF (2.5 and 1.5 mL) was added 5% Pd–C. The reaction mixture was stirred for 20 h under H_2 atmosphere. After removal of Pd–C by filtration, evaporation of solvent gave amine (77 mg, 96%). To a solution of amine (77 mg, 0.23 mmol) in THF (2 mL) were added 0.7 M $NaNO_2$ aq (0.79 mL), H_3PO_2 (0.12 mL, 2.3 mmo) and Cu_2O (2.6 mg, 0.018 mmol) at 0 °C. After being stirred for 23 h at rt, the mixture was poured into Na_2CO_3 aq and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt=100) gave **2a** (17 mg, 22%). The ^1H NMR of **2a** coincided with that described in preliminary communication.[5] The reaction proceeded without any decrease in the ee. The ee (79% ee) of **2a** was determined by HPLC analysis using a CHIRALPACK IA column [25 cm×0.46 cm i.d.; 0.5% *i*-PrOH in hexane; flow rate, 0.5 mL/min; (−)-**1a** (major); t_R=9.2 min, (+)-**1a** (minor); t_R=10.2 min].[5]

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Supplementary data

Supplementary data (Copies of ^1H NMR and ^{13}C NMR spectra of all compounds and crystallographic data for compounds **5g′**.) related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.05.001.

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13. The crystal structure of **5g′** was deposited at the Cambridge Crystallographic Data Center (the deposition number: CCDC 763524). See also Supplementary data.

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