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Catalytic Enantioselective Synthesis of N-C Axially Chiral Phenanthridin-6-one Derivatives

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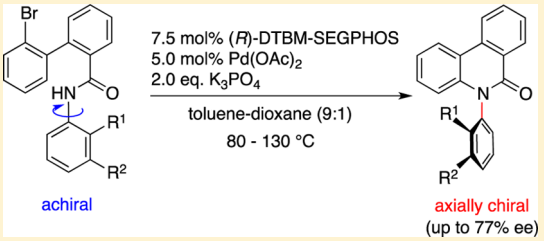
Supporting Information

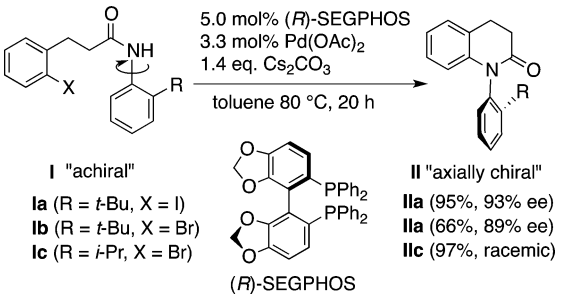
ABSTRACT: N-C axially chiral phenanthridin-6-one derivatives bearing various *ortho*-substituted phenyl groups on the nitrogen atom were enantioselectively prepared through (*R*)-DTBM-SEGPHOS-Pd(OAc)$_2$-catalyzed intramolecular Buchwald–Hartwig amination. The enantioselectivity strongly depended on solvents, bases, and reaction temperature as well as on the bulkiness of *ortho*-substituents.



Recently, catalytic enantioselective syntheses of N-C axially chiral compounds have received considerable attention. Various N-C axially chiral compounds have been prepared with high enantioselectivity through an original catalytic asymmetric reaction developed for an each group.[1,2] These N-C axially chiral compounds usually have *ortho*-*tert*-butyl- or 2,6-disubstituted anilide skeletons,[1,2] while catalytic enantioselective synthesis of anilide derivatives bearing an *ortho*-monosubstituent except for a *tert*-butyl group is far less common.[3]

We succeeded in the highly enantioselective synthesis of *N*-(2-*tert*-butylphenyl)-3,4-dihydroquinolin-2-one derivative **IIa** through chiral palladium-catalyzed intramolecular Buchwald–Hartwig amination of NH-anilides **Ia,b** (Scheme 1).[1a] This

Scheme 1. Catalytic Enantioselective Synthesis of N-C Axially Chiral 3,4-Dihydroquinolin-2-one Derivatives II



reaction is the first practical catalytic asymmetric synthesis of N-C axially chiral compounds. When this reaction was applied to *ortho*-*iso*-propyl derivative **Ic**, the product **IIc** was obtained in racemic form.[4] Since the rotational barrier around a chiral axis in **IIc** is approximately 25 kcal/mol (the rotational barrier of **IIa** = 32.0 kcal/mol), the racemization of **IIc** should easily occur under the present conditions (80 °C, 20 h). Thus, the reaction of Scheme 1 would be difficult to apply to the synthesis of *N*-aryl-3,4-dihydroquinolin-2-one derivatives **II** bearing *ortho*-monosubstituents except for a *tert*-butyl group.

On the other hand, it has been reported that phenanthridin-6-one derivatives **2** (Scheme 2) maintain a stable axially chiral structure even in substrates bearing a small *ortho*-substituent such as a methyl group (R = Me, $\Delta G^{\ddagger}$ = 28.5 kcal/mol);[5,6] however, their enantioselective synthesis has not yet been achieved. We expected that catalytic enantioselective synthesis of phenanthridin-6-one derivatives bearing various *ortho*-substituted phenyl groups could be achieved by applying the

Scheme 2. Synthesis of Biphenyl Amide Substrates 1 and Attempted Catalytic Asymmetric Synthesis of N-C Axially Chiral Phenanthridin-6-one Derivatives 2

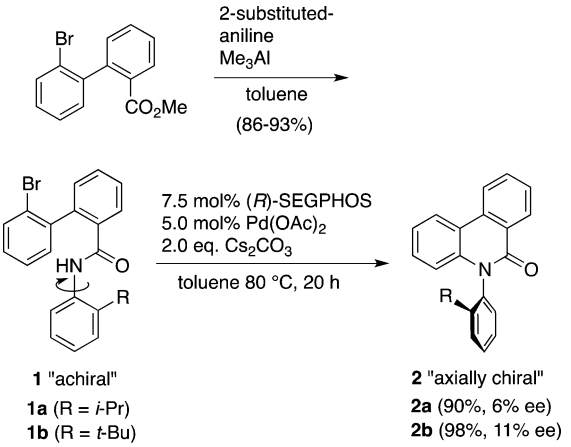


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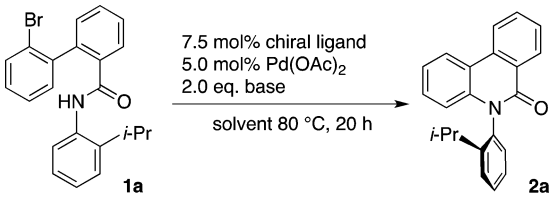
Table 1. Screening of Chiral Ligands, Solvents, and Bases in the Reaction of 1a



				2a	
entry	ligand	solvent	base	yield (%)[a]	ee (%)[b]
1	(*R*)-SEGPHOS	toluene	Cs_2CO_3	90	6
2	(*R*)-BINAP	toluene	Cs_2CO_3	98	15
3	chiral-NHC	toluene	Cs_2CO_3	91	0
4	(*R*)-MOP	toluene	Cs_2CO_3	97	5
5	(*S*,*R*)-PPFA	toluene	Cs_2CO_3	52−92	51−73
6	(*R*)-DTBM-SEGPHOS	toluene	Cs_2CO_3	94	63
7	(*R*)-DTBM-SEGPHOS	toluene	K_2CO_3	93	59
8	(*R*)-DTBM-SEGPHOS	toluene	*t*-BuOK	98	17
9	(*R*)-DTBM-SEGPHOS	toluene	NaH	39	31
10	(*R*)-DTBM-SEGPHOS	toluene	K_3PO_4	58	75
11	(*R*)-DTBM-SEGPHOS	1,4-dioxane	K_3PO_4	96	49
12	(*R*)-DTBM-SEGPHOS	toluene−1,4-dioxane (1:1)	K_3PO_4	94	65
13	(*R*)-DTBM-SEGPHOS	toluene−1,4-dioxane (9:1)	K_3PO_4	95	77
14	(*R*,*R*)-CHI-RAPHOS	toluene−1,4-dioxane (9:1)	K_3PO_4	96	9
15	(*R*)-SYNPHOS	toluene−1,4-dioxane (9:1)	K_3PO_4	62	36

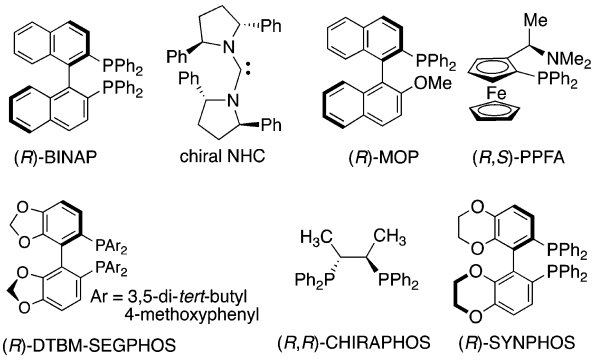
[a]Isolated yields. [b]The ee was determined by HPLC analysis using a chiral column.

reaction of Scheme 1 to biphenyl amide substrates **1**.[7] In this paper, we report catalytic asymmetric synthesis of N-C axially chiral phenanthridin-6-one derivatives bearing various *ortho*-substituted phenyl groups on the nitrogen atom through (*R*)-DTBM-SEGPHOS-Pd(OAc)$_2$-catalyzed intramolecular Buchwald−Hartwig amination.[8] The mechanistic consideration of the present reaction and the stereochemical assignment of a chiral axis are also described.

The biphenylamide substrates **1** were easily prepared through the condensation of methyl 2′-bromo-(1,1′-biphenyl)-2-carboxylate[7,9] (commercially available) with *ortho*-substituted-aniline in the presence of Me_3Al (Scheme 2). Initially, the reaction of biphenylamide **1a** bearing an *ortho-iso*-propyl group was conducted under the conditions shown in Scheme 1 (Scheme 2). Although the reaction proceeded smoothly to give phenanthridin-6-one **2a** in a good yield (90%), little enantioselectivity was observed (6% ee). Moreover, in the reaction with *ortho-tert*-butyl derivative **1b**, the enantioselectivity was unexpectedly poor (96%, 11% ee).

Thus, since the reaction with biphenyl amides **1** was found to be very different from the reaction in Scheme 1, we reexamined the screening of chiral ligands, bases, and solvents in the reaction of **1a**.

The results are shown in Table 1. As a chiral ligand (entries 1−6), the use of (*R*)-DTBM-SEGPHOS[10] gave the best result.[11] In this case, an N-C axially chiral phenanthridinone **2a** was obtained in 94% yield and 63% ee (entry 6). With (*S*,*R*)-PPFA, good reproducibility for both the chemical yield and the enantioselectivity was not obtained (entry 5).



In the presence of (*R*)-DTBM-SEGPHOS-Pd(OAc)$_2$ catalyst, bases and solvents were investigated next. When *t*-BuOK and NaH were used as the base, the enantioselectivity decreased significantly (17% ee and 31% ee, entries 8 and 9). The use of K_3PO_4 gave the best enantioselectivity (75% ee), but a decrease in the chemical yield was also observed (58%, entry 10). To improve the chemical yield, a survey of solvents was conducted. Although the reaction in 1,4-dioxane gave the product **2a** in an excellent yield (96%), the enantioselectivity was significantly lower (49% ee, entry 11). A relatively good result was obtained when a mixed solvent of toluene and 1,4-dioxane was used: in particular, the reaction in toluene:1,4-dioxane = 9:1 gave the best chemical yield and enantioselectivity (95%, 77% ee, entry 13). Under the conditions of entry 13, although the other chiral phosphine ligands such as (*R*,*R*)-CHIRAPHOS and (*R*)-SYNPHOS were further investigated, good results were not obtained (entry 14: 96%, 9% ee; entry 15: 62%, 36% ee).

Since a detectable change in the ee for the product **2a** was not observed under the present reaction conditions (for 20 h at

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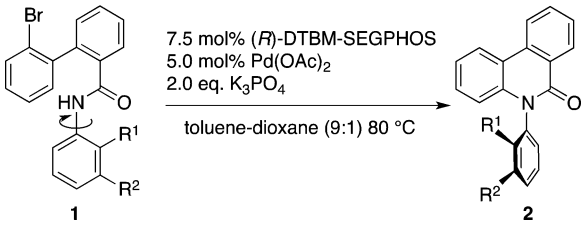
Table 2. Reaction of Substrates Bearing Various *ortho*-Substituted Phenyl Groups



					2	
entry	1	R^1, R^2	heating time (h)	2	yield (%)[a]	ee (%)[b]
1	**1a**	R^1 = *i*-Pr, R^2 = H	17	**2a**	95	77
2	**1c**	R^1 = R^2 = CH=CH-CH=CH	17	**2c**	94	70
3	**1d**	R^1 = Et, R^2 = H	9	**2d**	68	68
4	**1e**	R^1 = Me, R^2 = H	9	**2e**	71−92	25−42
5	**1b**	R^1 = *t*-Bu, R^2 = H	17	**2b**	26	44
6[c]	**1b**	R^1 = *t*-Bu, R^2 = H	7	**2b**	90	69

[a]Isolated yields. [b]The ee was determined by HPLC analysis using a chiral column. [c]The reaction was performed at 130 °C.

80 °C in toluene), the ee in Table 1 reflects the actual enantioselectivity of the reaction.

Under optimized conditions [7.5 mol % (*R*)-DTBM-SEGPHOS, 5 mol % $Pd(OAc)_2$, 2 equiv of K_3PO_4 in toluene-1,4-dioxane (9:1) at 80 °C], the reactions of biphenyl amides **2** bearing various *ortho*-substituted phenyl groups were further examined (Table 2). The reaction of **1c** bearing the naphthyl-1-yl group gave the product **2c** in an excellent yield (94%) and in 70% ee (entry 2). Under the same conditions (for 17 h at 80 °C), the reaction of *ortho*-ethyl derivative **1d** resulted in a significant decrease in the ee of **2d** (98%, 40% ee). Meanwhile when the reaction of **1d** was finished in a shorter time (for 9 h at 80 °C), the ee of **2d** increased to 68%, while the chemical yield was lower at 68% (entry 3). This result indicates that partial racemization of the *N*-(*ortho*-ethylphenyl)-phenanthridinone **2d** occurs under the present reaction conditions. In the reaction of amide **1e** bearing the *ortho*-methyl group, not only was there a further decrease in the ee but also the dispersion of the ee was also observed (25−42% ee, entry 4). With substrates bearing a small *ortho*-substituent, the products **2** with high ee may be difficult to obtain because of the racemization of the product as well as the decrease in the enantioselectivity of the reaction.

On the basis of these results, we expected that the reaction of *ortho*-*tert*-butyl substrate **1b** would give the product **2b** with high ee. However, the reaction with **1b** gave **2b** in a poor chemical yield (26%) and lower ee (44% ee) than those of **2a**, **2c**, **2d** (entry 5). Interestingly, when the reaction temperature was increased from 80 to 130 °C (oil bath), an increase in the enantioselectivity as well as the chemical yield was observed (90%, 69% ee, entry 6).

These results may be explained as follows (Figure 1). The present reaction proceeds via the pathway shown in Figure 1, and the enantioselectivity may be determined by diastereomeric Pd-amide intermediates **1C** and **1C′** formed from **1B** by ligand exchange. When the interconversion between **1C** and **1C′** proceeds smoothly and their thermodynamic stability (or the rate of reductive elimination) is very different, the reaction may proceed with high enantioselectivity. In the reaction of **1b** bearing a bulky *ortho*-*tert*-butyl group, since the interconversion between **1C** and **1C′** does not occur efficiently because of the high rotational barrier around the chiral axis, the enantioselectivity may be lower in comparison with those of **1a** and **1c**

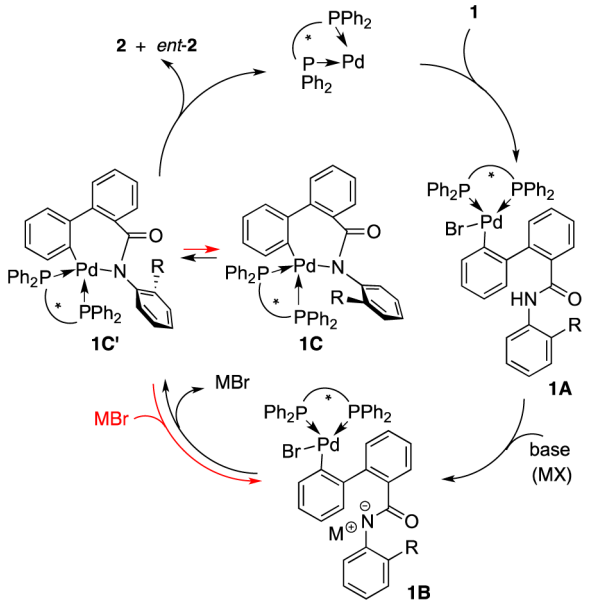


Figure 1. Possible mechanism for the present reaction.

that bear less bulky *iso*-propyl and naphthyl-1-yl groups (Table 2, entry 5).

On the other hand, the increase in the reaction temperature leads to relatively efficient interconversion between **1C** and **1C′**, which leads to an increase in the enantioselectivity (entry 6). As mentioned above, the enantioselectivity was also significantly influenced by which bases and solvents were used (Table 1, entries 6−13). This result may indicate that the interconversion between **1C** and **1C′** occurs not only by the rotation about the chiral axis but also by reversible conversion between **1C** (or **1C′**) and **1B**.

The optical purification and the determination of absolute stereochemistry in axially chiral phenanthridinone derivative **2** were achieved in accordance with Schemes 3 and 4, respectively. **2a** (82% ee) and **2b** (72% ee) were converted into an almost enantiomerically pure form (>99% ee) through self-disproportionation of enantiomers (SDE) by medium-pressure liquid chromatography (MPLC) using an achiral silica gel column (Scheme 3).[12] That is, the MPLC chart of **2a** (82% ee, 42 mg) and **2b** (72% ee, 90 mg) gave two distinct peaks and

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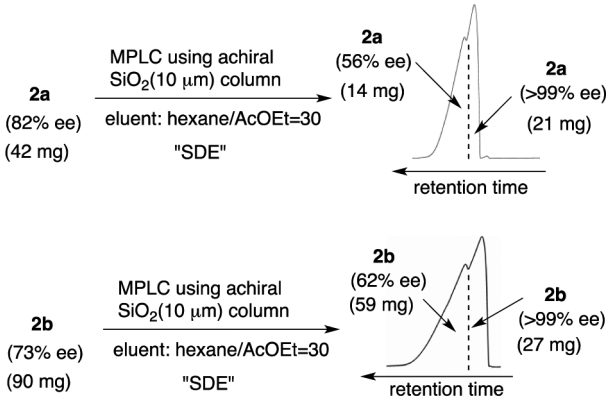
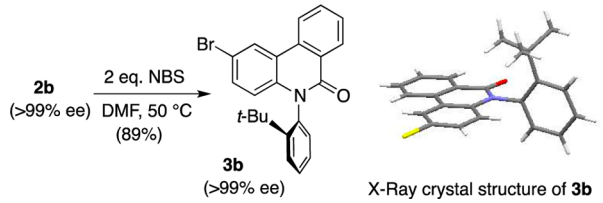
Scheme 3. Optical Purification through SDE of 2a and 2b Using MPLC



Scheme 4. Regioselective Bromination of 2b and X-ray Crystal Structure of 3b



looked like the usual chart that is seen for a mixture of two different compounds. The ee of **2a** and **2b** obtained from the less polar fraction was >99% ee.[13]

Subsequently, optically pure **2b** was treated with NBS in DMF to be converted to mono-bromo derivative **3b** with complete regioselectivity and a high yield (89%, Scheme 4). The X-ray crystal structure of **3b** indicates that the absolute stereochemistry of the major enantiomer in **2b** has an (*S*)-configuration[14] and bromination of **2b** occurs selectively at the C2-position (Scheme 4).[15] The absolute stereochemistries of other phenanthridinones **2a,c,d,e**, which have large positive $[\alpha]_D$ values as in **2b**, also had the (*S*)-configuration tentatively assigned to them.

In conclusion, we succeeded in the catalytic enantioselective synthesis of N-C axially chiral phenanthridin-6-one derivatives bearing various *ortho*-substituted phenyl groups on the nitrogen atom through (*R*)-DTBM-SEGPHOS-Pd(OAc)$_2$-catalyzed intramolecular Buchwald−Hartwig amination. The enantioselectivity was found to strongly depend on solvents, bases, and reaction temperature as well as on the bulkiness of *ortho*-substituents.

EXPERIMENTAL SECTION

Melting points were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 400 and 100 MHz spectrometer, respectively. In ^{1}H 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. High-resolution mass spectra (HRMS) were obtained using the electron spray ionization technique (ESI) and TOF mass analyzer. 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.

2′-Bromo-*N*-(2-*iso*-propylphenyl)-[1,1′-biphenyl]-2-carboxamide (1a). Under an Ar atmosphere, to 2-*iso*-propylaniline (0.481 g, 3.56 mmol) in toluene (10.0 mL) was added a 1.1 M hexane solution of Me_3Al (4.9 mL, 5.4 mmol) at 0 °C. After being stirred for 10 min at 0 °C, methyl 2′-bromo-[1,1′-biphenyl]-2-carboxylate[7] (commercially available, 1.036 g, 3.6 mmol) was added to the mixture, and then the reaction mixture was stirred for 16 h at 70 °C. The mixture was poured into 2% HCl 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 = 15−5) gave **1a** (1.30 g, 93%). **1a**: white solid; mp 87−89 °C; IR (neat) 3275, 1651 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.85−7.90 (1H, m), 7.67 (1H, d, J = 8.4 Hz), 7.48−7.56 (3H, m), 7.29−7.42 (3H, m), 7.23 (1H, dt, J = 2.0, 7.6 Hz), 7.17−7.20 (1H, m), 7.10−7.15 (2H, m), 7.02 (1H, brs), 2.39 (1H, sept, J = 6.8 Hz), 1.05 (3H, d, J = 6.8 Hz), 1.03 (3H, d, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ: 167.2, 141.0, 140.9, 138.2, 136.0, 133.6, 133.0, 131.2, 131.0, 130.1, 129.7, 128.8, 128.4, 127.7, 126.2, 125.5, 124.7, 123.1, 27.3, 23.4, 23.1; MS (m/z) 416 (MNa^+, ^{79}Br), 418 (MNa^+, ^{81}Br); HRMS. Calcd for $C_{22}H_{20}{}^{79}BrNONa$ (MNa^+) 416.06260. Found: 416.06280. Anal. Calcd for $C_{22}H_{20}BrNO$: C, 67.01; H, 5.11; N, 3.55. Found: C, 67.04; H, 4.90; N, 3.66.

2′-Bromo-*N*-(2-*tert*-butylphenyl)-[1,1′-biphenyl]-2-carboxamide (1b). **1b** was prepared from 2-*tert*-butylaniline (0.298 g, 2.0 mmol) in accordance with the procedure described in the preparation of **1a**. Purification of the residue by column chromatography (hexane/AcOEt = 10) gave **1b** (0.72 g, 86%). **1b**: pale yellow liquid; IR (neat) 3291, 1667 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.82 (1H, d, J = 6.8 Hz), 7.62 (1H, d, J = 8.4 Hz), 7.49−7.55 (2H, m), 7.44 (1H, dd, J = 1.6, 7.6 Hz), 7.38 (1H, t, J = 7.2 Hz), 7.31−7.35 (2H, m), 7.20 (1H, dt, J = 1.6, 7.6 Hz), 7.07−7.15 (4H, m), 1.27 (9H, s); ^{13}C NMR ($CDCl_3$) δ: 167.3, 143.8, 140.9, 138.7, 136.2, 134.8, 132.9, 131.3, 130.9, 130.1, 129.7, 128.5, 128.4, 128.1, 127.5, 126.7, 126.6, 126.4, 123.1, 34.5, 30.6; MS (m/z) 430 (MNa^+, ^{79}Br), 432 (MNa^+, ^{81}Br); HRMS. Calcd for $C_{23}H_{22}{}^{79}BrNONa$ (MNa^+) 430.07825. Found: 430.08011.

2′-Bromo-*N*-(naphthalen-1-yl)-[1,1′-biphenyl]-2-carboxamide (1c). **1c** was prepared from 1-naphthylamine (0.73 g, 5.11 mmol) in accordance with the procedure described in the preparation of **1a**. Purification of the residue by column chromatography (hexane/AcOEt = 5) gave **1c** (1.82 g, 90%). **1c**: white solid; mp 134−136 °C; IR (neat) 3256, 1645 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.97 (1H, d, J = 7.6 Hz), 7.82 (1H, d, J = 7.2 Hz), 7.79 (1H, d, J = 8.8 Hz), 7.68 (1H, d, J = 8.4 Hz), 7.64 (1H, d, J = 8.4 Hz), 7.53−7.60 (3H, m), 7.31−7.47 (6H, m), 7.24 (1H, t, J = 7.6 Hz), 7.13 (1H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ: 167.2, 141.0, 138.4, 135.8, 133.8, 133.1, 132.1, 131.3, 131.0, 130.3, 129.8, 129.0, 128.5, 128.5, 127.9, 127.0, 126.0, 125.8, 125.6, 123.2, 120.5, 120.5; MS (m/z) 424 (MNa^+, ^{79}Br), 426 (MNa^+, ^{81}Br); HRMS. Calcd for $C_{23}H_{16}{}^{79}BrNONa$ (MNa^+) 424.03130. Found: 424.02954. Anal. Calcd for $C_{23}H_{16}BrNO$: C, 68.67; H, 4.01; N, 3.48. Found: C, 68.50; H, 3.91; N, 3.73.

2′-Bromo-*N*-(2-ethylphenyl)-[1,1′-biphenyl]-2-carboxamide (1d). **1d** was prepared from 2-ethylaniline (0.30 g, 2.5 mmol) in accordance with the procedure described in the preparation of **1a**. Purification of the residue by column chromatography (hexane/AcOEt = 10) gave **1d** (0.89 mg, 94%). **1d**: white solid; mp 102−104 °C; IR (neat) 3250, 1653 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.88 (1H, dd, J = 2.8, 6.4 Hz), 7.66 (1H, d, J = 8.4 Hz), 7.63 (1H, d, J = 8.0 Hz), 7.50−7.56 (2H, m), 7.29−7.41 (3H, m), 7.23 (1H, m), 7.05−7.17 (3H, m), 7.03 (1H, brs), 2.16 (2H, q, J = 7.6 Hz), 1.04 (3H, d, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ: 166.9, 140.9, 138.3, 135.9, 135.3, 134.6, 133.0, 131.2, 131.0, 130.1, 129.7, 128.8, 128.4, 128.2, 127.8, 126.4, 125.6, 123.6, 123.1, 23.5, 14.0; MS (m/z) 402 (MNa^+, ^{79}Br), 404 (MNa^+, ^{81}Br); HRMS. Calcd for $C_{21}H_{18}{}^{79}BrNONa$ (MNa^+) 402.04695. Found: 402.04844. Anal. Calcd for $C_{21}H_{18}BrNO$: C, 66.33; H, 4.77; N, 3.68. Found: C, 66.30; H, 4.69; N, 3.75.

2′-Bromo-*N*-(2-methylphenyl)-[1,1′-biphenyl]-2-carboxamide (1e). **1e** was prepared from 2-methylaniline (0.268 g, 2.5 mmol) in accordance with the procedure described in the preparation of **1a**. Purification of the residue by column chromatography (hexane/AcOEt = 10−4) gave **1e** (0.732 g, 80%). **1e**: white solid; mp 112−114 °C; IR (neat) 3237, 1651 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.89−7.92 (1H, m),

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7.72 (1H, d, J = 7.6 Hz), 7.68 (1H, d, J = 7.6 Hz), 7.50−7.57 (2H, m), 7.32−7.42 (3H, m), 7.24 (1H, dt, J = 2.4, 7.8 Hz), 7.16 (1H, t, J = 7.6 Hz), 7.09 (1H, d, J = 6.8 Hz), 7.00−7.05 (2H, m), 1.90 (3H, s); ^{13}C NMR ($CDCl_3$) δ: 166.6, 141.0, 138.3, 135.9, 135.5, 133.0, 131.3, 131.0, 130.3, 130.2, 129.7, 129.0, 128.9, 128.4, 127.8, 126.6, 125.1, 123.1, 122.6, 17.3; MS (m/z) 366 (MH^+, ^{79}Br), 368 (MH^+, ^{81}Br); HRMS. Calcd for $C_{20}H_{17}{}^{79}BrNO$ (MH^+) 366.04935. Found: 366.04628. Anal. Calcd for $C_{20}H_{16}BrNO$: C, 65.59; H, 4.40; N, 3.82. Found: C, 65.33; H, 4.37; N, 3.78.

5-(2-*iso*-Propylphenyl)phenanthridin-6(5*H*)-one (2a). Under an Ar atmosphere, to the suspension of $Pd(OAc)_2$ (3.4 mg, 0.015 mmol) and (*R*)-DTBM-SEGPHOS (26.5 mg, 0.0225 mmol) in toluene-1,4-dioxane (1.35−0.15 mL) were added **1a** (118 mg, 0.30 mmol) in toluene-1,4-dioxane (1.35 mL-0.15 mL) and subsequently K_3PO_4 (127 mg, 0.6 mmol). After being stirred for 10 min at rt, the reaction mixture was stirred for 17 h at 80 °C. The mixture was poured into 2% HCl solution 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 = 10) gave **2a** (91 mg, 96%, 77% ee). The enantiomers of **2a** were separated by HPLC using a CHIRALCEL OD-3 column [25 cm × 0.46 cm i.d.; 17% *i*-PrOH in hexane; flow rate, 1.5 mL/min; (+)-**2a** (major); t_R = 4.6 min, (−)-**2a** (minor); t_R = 17.1 min]. **2a**: white solid; mp 57−59 °C (77% ee); $[\alpha]_D$ = +49.8 (c = 0.40, $CHCl_3$, 80% ee); IR (neat) 1657 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 8.56 (1H, dd, J = 0.8, 7.6 Hz), 8.34 (1H, d, J = 8.0 Hz), 8.30 (1H, m), 7.81 (1H, ddd, J = 2.0, 7.6, 8.8 Hz), 7.61 (1H, ddd, J = 1.2, 7.6, 8.8 Hz), 7.55 (1H, dd, J = 1.6, 8.0 Hz), 7.50 (1H, dt, J = 1.2, 7.6 Hz), 7.38 (1H, dt, J = 1.6, 7.6 Hz), 7.24−7.31 (2H, m), 7.15 (1H, dd, J = 1.2, 7.8 Hz), 6.57−6.62 (1H, m), 2.64 (1H, sept, J = 6.8 Hz), 1.16 (3H, d, J = 6.8 Hz), 1.01 (3H, d, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ: 161.4, 146.7, 139.0, 135.6, 134.0, 132.7, 129.4, 129.1 129.0, 128.8, 128.0, 127.5, 127.2, 125.8, 122.9, 122.6, 121.7, 118.8, 116.8, 28.0, 23.8, 23.4; MS (m/z) 336 (MNa^+); HRMS. Calcd for $C_{22}H_{19}NONa$ (MNa^+) 336.13643. Found: 336.13928.

5-(2-*tert*-Butylphenyl)phenanthridin-6(5*H*)-one (2b). **2b** was prepared from **1b** (119 mg, 0.3 mmol) in accordance with the procedure described in the preparation of **2a**. Purification of the residue by column chromatography (hexane/AcOEt = 10) gave **2b** (92.6 mg, 97%, 73% ee). The enantiomers of **2b** were separated by HPLC using a CHIRALCEL OD-3 column [25 cm × 0.46 cm i.d.; 9% *i*-PrOH in hexane; flow rate, 1.5 mL/min; (+)-**2b** (major); t_R = 6.9 min, (−)-**2b** (minor); t_R = 11.3 min]. **2b**: white solid; mp 61−63 °C (>99% ee); $[\alpha]_D$ = +97.7 (c = 0.40, $CHCl_3$, 70% ee); IR (neat) 1655 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 8.57 (1H, dd, J = 0.8, 7.6 Hz), 8.33 (1H, d, J = 8.0 Hz), 8.29 (1H, dd, J = 1.6, 7.6 Hz), 7.80 (1H, t, J = 7.2 Hz), 7.72 (1H, dd, J = 1.4, 8.0 Hz), 7.60 (1H, t, J = 7.6 Hz), 7.47 (1H, dt, J = 1.2, 8.0 Hz), 7.37 (1H, dt, J = 1.2, 7.4 Hz), 7.24−7.32 (2H, m), 7.02 (1H, dd, J = 1.4, 7.8 Hz), 6.57 (1H, dd, J = 1.2, 8.0 Hz), 1.16 (9H, s); ^{13}C NMR ($CDCl_3$) δ: 162.4, 147.5, 140.0, 135.7, 134.0, 132.8, 131.3, 130.0, 129.1, 129.0, 128.9, 128.0, 128.0, 126.0, 123.0, 122.5, 121.8, 119.0, 118.0, 36.1, 31.6; MS (m/z) 350 (MNa^+); HRMS. Calcd for $C_{23}H_{21}NONa$ (MNa^+) 350.15208. Found: 350.15242.

5-(Naphthalen-1-yl)phenanthridin-6(5*H*)-one (2c). **2c** was prepared from **1c** (80 mg, 0.2 mmol) in accordance with the procedure described in the preparation of **2a**. Purification of the residue by column chromatography (hexane/AcOEt = 5) gave **2c** (60 mg, 94%, 70% ee). The enantiomers of **2c** were separated by HPLC using a CHIRALCEL OD-3 column [25 cm × 0.46 cm i.d.; 33% *i*-PrOH in hexane; flow rate, 1.0 mL/min; (+)-**2c** (major); t_R = 8.0 min, (−)-**2c** (minor); t_R = 14.9 min]. **2c**: white solid; mp 229−231 °C (70% ee); $[\alpha]_D$ = +131.1 (c = 0.40, $CHCl_3$, 70% ee); IR (neat) 1653 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 8.63 (1H, dd, J = 1.2, 8.0 Hz), 8.42 (1H, d, J = 8.4 Hz), 8.37 (1H, dd, J = 1.2, 8.0 Hz), 8.07 (1H, d, J = 8.4 Hz), 8.01 (1H, d, J = 8.0 Hz), 7.87 (1H, dt, J = 1.2, 7.8 Hz), 7.64−7.72 (2H, m), 7.50−7.55 (2H, m), 7.46 (1H, d, J = 8.4 Hz), 7.38 (1H, t, J = 7.6 Hz), 7.29 (1H, t, J = 7.2 Hz), 7.21 (1H, dt, J = 1.2, 8.0 Hz), 6.54 (1H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ: 161.7, 139.1, 134.9, 134.8, 134.2, 133.0, 130.2, 129.4, 129.3, 129.2, 128.6, 128.1, 127.4, 127.1, 126.6, 126.1, 125.8, 123.0, 122.7, 122.4, 121.8, 119.0, 117.2; MS (m/z) 344 (MNa^+); HRMS. Calcd for $C_{23}H_{15}NONa$ (MNa^+) 344.10513. Found: 344.10539.

5-(2-Ethylphenyl)phenanthridin-6(5*H*)-one (2d). **2d** was prepared from **1d** (74 mg, 0.2 mmol) in accordance with the procedure described in the preparation of **2a**. Purification of the residue by column chromatography (hexane/AcOEt = 5) gave **2d** (40 mg, 68%, 68% ee). The enantiomers of **2d** were separated by HPLC using a CHIRALCEL OD-3 column [25 cm × 0.46 cm i.d.; 17% *i*-PrOH in hexane; flow rate, 1.5 mL/min; (+)-**2d** (major); t_R = 8.7 min, (−)-**2d** (minor); t_R = 12.5 min]. **2d**: colorless liquid; $[\alpha]_D$ = +55.1 (c = 0.38, $CHCl_3$, 70% ee); IR (neat) 1653 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 8.57 (1H, d, J = 8.4 Hz), 8.34 (1H, d, J = 8.4 Hz), 8.29−8.32 (1H, m), 7.81 (1H, dt, J = 1.2, 7.2, Hz), 7.61 (1H, t, J = 7.6 Hz), 7.46−7.52 (2H, m), 7.41 (1H, dt, J = 2.0, 7.2 Hz), 7.26−7.30 (2H, m), 7.19 (1H, d, J = 7.2 Hz), 6.59−6.63 (1H, m), 2.42 (1H, qd, J = 7.6, 15.2 Hz), 2.32 (1H, qd, J = 7.6, 15.2 Hz), 1.07 (3H, t, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ: 161.3, 141.9, 138.9, 136.6, 134.1, 132.8, 129.5, 129.2, 129.1, 128.0, 127.7, 125.9, 123.0, 122.6, 121.8, 119.0, 116.7, 23.6, 13.6; MS (m/z) 322 (MNa^+); HRMS. Calcd for $C_{21}H_{17}NONa$ (MNa^+) 322.12078. Found: 322.12061.

5-(2-Methylphenyl)phenanthridin-6(5*H*)-one (2e). **2e** was prepared from **1e** (72 mg, 0.2 mmol) in accordance with the procedure described in the preparation of **2a**. Purification of the residue by column chromatography (hexane/AcOEt = 5) gave **2e** (42 mg, 74%, 42% ee). The enantiomers of **2e** were separated by HPLC using a CHIRALCEL OD-3 column [25 cm × 0.46 cm i.d.; 9% *i*-PrOH in hexane; flow rate, 1.0 mL/min; (+)-**2e** (major enantiomer); t_R = 25.7 min, (−)-**2e** (minor enantiomer); t_R = 30.4 min]. **2e**: white solid; mp 102−104 °C (42% ee); $[\alpha]_D$ = +26.3 (c = 0.26, $CHCl_3$, 42% ee); IR (neat) 1651 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 8.58 (1H, dd, J = 1.2, 7.6 Hz), 8.34 (1H, d, J = 8.4 Hz), 8.29−8.32 (1H, m), 7.81 (1H, dt, J = 1.2, 7.8 Hz), 7.61 (1H, dt, J = 1.0, 7.8 Hz), 7.38−7.47 (3H, m), 7.26−7.31 (2H, m), 7.21 (1H, dd, J = 2.4, 6.4 Hz), 6.60 (1H, m), 2.05 (3H, s); ^{13}C NMR ($CDCl_3$) δ: 161.0, 138.4, 137.1, 136.5, 134.1, 132.8, 131.5, 129.3, 129.0, 128.9, 128.0, 127.7, 125.9, 123.1, 122.7, 121.8, 119.0, 116.3, 17.4; MS (m/z) 308 (MNa^+); HRMS. Calcd for $C_{20}H_{15}NONa$ (MNa^+) 308.10513. Found: 308.10504.

Optical Purification through SDE by MPLC of 2a. Medium-pressure liquid chromatography (MPLC, eluent: hexane/AcOEt = 30) of **2a** (82% ee, 42 mg) was performed on a 25 × 4 cm i.d. prepacked column (silica gel, 10 μm) with a UV detector. The eluted substrate **2a** was collected in two fractions across the boundary point, and >99% ee (21 mg) and 56% ee (14 mg) of **2a** were obtained from less polar and more polar fractions, respectively.

Optical Purification through SDE by MPLC of 2b. Medium-pressure liquid chromatography (MPLC, eluent: hexane/AcOEt = 30) of **2b** (73% ee, 90 mg) was performed on a 25 × 4 cm i.d. prepacked column (silica gel, 10 μm) with a UV detector. The eluted substrate **2b** was collected in two fractions across the boundary point, and >99% ee (27 mg) and 62% ee (59 mg) of **2b** were obtained from less polar and more polar fractions, respectively.

2-Bromo-5-(2-(*tert*-butyl)phenyl)phenanthridin-6(5*H*)-one (3b). To the solution of **2b** (>99% ee, 44 mg, 0.134 mmol) in DMF (2.0 mL) was added *N*-bromosuccinimide (48 mg, 0.272 mmol). After being stirred for 24 h at 50 °C, the mixture was poured into 2% HCl solution 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 = 15) gave **3b** (50.4 mg, 89%). **3b**: white solid; mp 159−161 °C; $[\alpha]_D$ = +108.7 (c = 0.40, $CHCl_3$); IR (neat) 1659 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 8.56 (1H, d, J = 8.0 Hz), 8.38 (1H, d, J = 2.0 Hz), 8.24 (1H, d, J = 8.0 Hz), 7.81 (1H, dt, J = 1.2, 7.8 Hz), 7.71 (1H, dd, J = 1.4, 8.2 Hz), 7.63 (1H, t, J = 7.6 Hz), 7.47 (1H, dt, J = 1.2, 8.0 Hz), 7.34−7.39 (2H, m), 6.99 (1H, dd, J = 1.2, 7.6 Hz), 6.45 (1H, d, J = 8.4 Hz), 1.16 (9H, s); ^{13}C NMR ($CDCl_3$) δ: 162.1, 147.6, 139.0, 135.3, 133.0, 132.7, 131.7, 131.2, 130.1, 129.2, 129.2, 128.8, 128.1, 126.1, 125.7, 121.9, 120.7, 119.6, 115.7, 36.1, 31.6; MS (m/z) 428 (MNa^+, ^{79}Br), 430 (MNa^+, ^{81}Br); HRMS. Calcd for $C_{23}H_{20}{}^{79}BrNONa$ (MNa^+) 428.06260. Found: 428.05948.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02387.

Copies of ^{1}H NMR and ^{13}C NMR spectra of compounds **1a**−**e**, **2a**−**e**, **3b**, and chiral HPLC data of **2a**−**e** (PDF)

Crystallographic data for compound **3b** (CIF)

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Notes

The authors declare no competing financial interest.

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(13) Although MPLC of *N*-naphthyl-1-yl derivative **2c** (70% ee) was also investigated, the effective SDE was not observed.

(14) Interestingly, the major enantiomer in the present reaction with (*R*)-DTBM-SEGPHOS had the opposite absolute configuration to that in Scheme 1 with (*R*)-SEGPHOS.

(15) The crystal structure of **3b** was deposited at the Cambridge Crystallographic Data Center (the deposition number: CCDC1429036). See also the Supporting Information.

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