Enantioselective construction of C_2-symmetric spiro skeleton through intramolecular copper-catalyzed N-arylation

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Dedicated to Professor Jürgen Martens on the occasion of his outstanding contribution to organic synthetic chemistry

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Abstract
Enantioselective construction of a C_2-symmetric spirobi(1,2,3,4-tetrahydroquinoline) framework has been achieved through an intramolecular Cu-catalyzed C–N bond coupling of 1,3-propanediamide substrates possessing bromophenyl substituents. The use of *N*,*N*'-dimethyl-1,2-diphenylethylenediamine as the chiral ligand was found to be essential in this asymmetric catalysis. Optically pure compound was shortly obtained by a single recrystallization of the enantioenriched product, which was successfully derivatised to a new chiral diphosphine ligand.

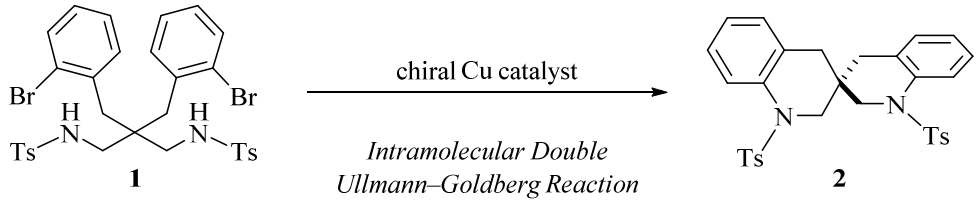
Keywords: Enantioselective catalysis, chiral spiro skeleton, Cu catalysis, N-arylation

Introduction

Considerable attention has recently been paid to C_2-symmetric spiro frameworks in organic synthesis owing to their potent asymmetric surroundings. A variety of functional molecules based on the rigid chiral backbone have therefore been developed for the fine chemical production. Representative examples of such compounds include chiral ligands[1-5] and chiral organocatalysts.[6-8] Since the seminal work of Tamao in which hydrosilylation catalyzed by a chiral Rh complex gave an optically active 5-silaspiro[4.4]nonane derivative,[9] enantioselective catalysis has been expected to be a straightforward method for the construction of C_2-symmetric spiro skeletons. Other Rh-catalyzed intramolecular cyclizations via hydroacylation,[10,11] carbenoid insertion,[12] or [2+2+2] cycloaddition,[13] have likewise been applicable to asymmetric spirane synthesis. Spiroketal has been obtained enantioselectively through Ir-catalyzed asymmetric hydrogenation of α,α'-bis(2-hydroxyarylidene) ketones.[14,15] Very recently, Gong et

al. have established the use of a chiral iodine reagent as an organocatalyst, where oxidative C–H arylation has furnished enantioenriched spirooxindoles.[16] We have also accomplished an enantioselective synthesis of spirobi(3,4-dihydro-2-quinolone) by using Pd-catalyzed *N*-arylation referred to as the Buchwald–Hartwig reaction.[17]

To further explore a practical synthetic route to the C_2-symmetric spirane, we focused on the Cu-catalyzed Ullmann–Goldberg reaction recognized as a powerful C–N bond forming process between aryl halides and nitrogen nucleophiles.[18] However, little interest has been directed to the development of its asymmetric catalysis because no stereogenic center is normally generated in this transformation. In 2012, Yu, Cai, and co-workers reported asymmetric desymmetrization based on the Cu-catalyzed C–N coupling leading to indoline derivatives with excellent enantiopurities.[19] We envisioned that the intramolecular double *N*-arylation of *N*,*N*'-(2,2-bis(2-bromobenzyl)propane-1,3-diyl)bis(4-methylbenzenesulfonamide) (**1**) using a chiral Cu catalyst provided spirobi(1,2,3,4-tetrahydroquinoline) product **2** in an optically active form (Equation 1). Herein we disclose a facile construction of C_2-symmetric spiro framework by way of the enantioselective Ullmann–Goldberg reaction.

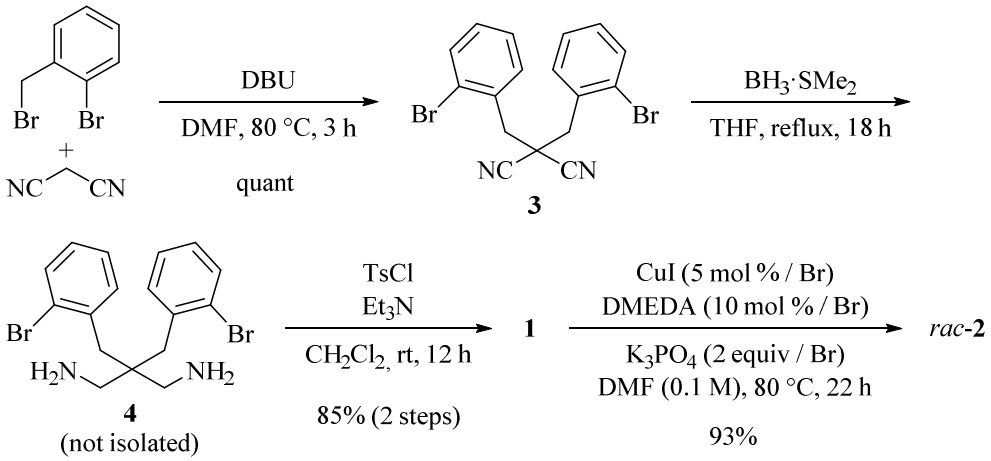


Equation 1. Enantioselective synthesis of C_2-symmetric spirane **2** via intramolecular double Cu-catalyzed *N*-arylation of **1**.

Results and Discussion

Ditosylamide **1** was able to be prepared without any difficulty from cheap and commercially available chemicals as shown in Scheme 1. Alkylation of malononitrile with 2-bromobenzyl bromide in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in DMF afforded 2,2-bis(2-bromobenzyl)malononitrile (**3**) quantitatively.[20] The nitrile functionalities of **3** were then reduced with an excess amount of $BH_3 \cdot SMe_2$ in THF to give 2,2-bis(2-bromobenzyl)propane-1,3-diamine (**4**). Without purification of **4**, the resulting amino groups were tosylated to produce **1** in 85% yield over 2 steps. To check whether the nitrogen-containing C_2-symmetric spiro skeleton was indeed created, we conducted the Ullmann–Goldberg reaction of 1,3-propanediamide **1** in a non-enantioselective manner. After surveying reaction conditions, we were pleased to find the nearly quantitative formation of desired spirobiquinoline **2** by employing a combination of CuI and *N*,*N*'-dimethylethylenediamine (DMEDA) as the catalyst system. Thus, treatment of **1** with CuI (5 mol % / Br) and DMEDA (10 mol % / Br) in the

presence of K_3PO_4 (2 equiv / Br) in DMF at 80 °C for 22 h gave racemic **2** in 93% yield. No special care such as high dilution was required for preventing possible intermolecular *N*-arylation. It is noteworthy that Pd catalysis, the Buchwald–Hartwig reaction, was not effective for the preparation of **2**.

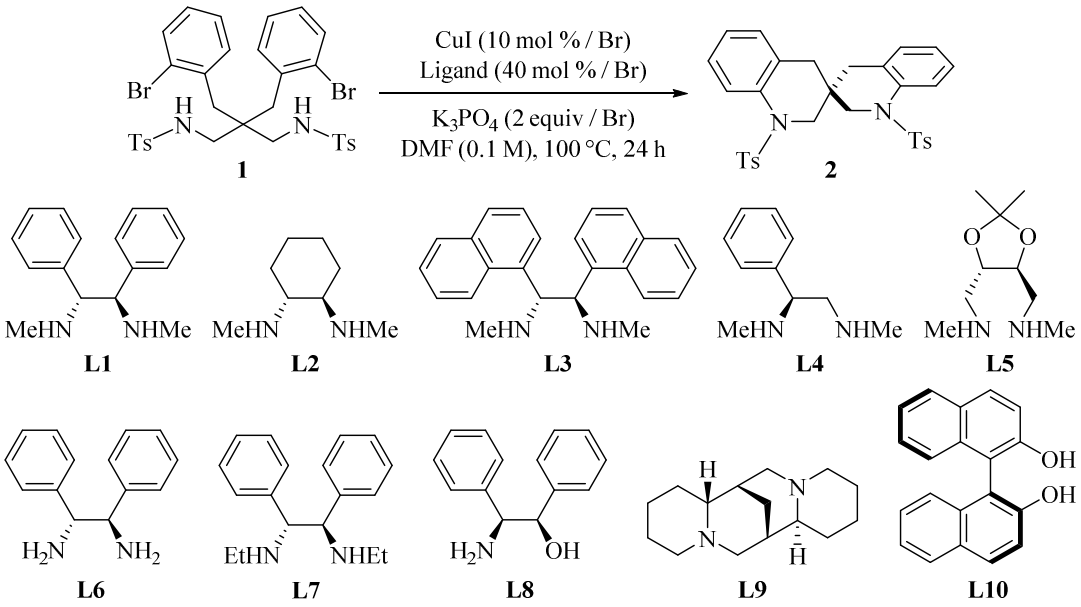


Scheme 1. Preparation of substrate **1** and racemic product **2**.

Various chiral ligands were next screened under slightly modified conditions (10 mol % of CuI and 40 mol % of ligand at 100 °C for 24 h) to achieve the enantioselective Ullmann–Goldberg reaction. Representative results are summarized in Table 1. Firstly, chiral diamine ligands **L1–L4** analogous to DMEDA were applied to the Cu-catalyzed *N*-arylation of **1**. The reaction using **L1** and **L2** led to a quantitative yield of **2**, whose optical purity was determined to be 31% ee and 17% ee, respectively (entries 1 and 2). The chiral backbone was presumably important for the catalyst activity as well as the enantioselectivity. Spirane product **2** was obtained in 45% yield with 29% ee in the reaction with **L3**, whereas the chemical yield and the selectivity were decreased to 10% and 13% ee with **L4** (entries 3 and 4). *N*,*N*'-Dimethyldiamine **L5** derived from L-tartaric acid gave only a trace amount of **2** (entry 5). The nitrogen substituent of ligands also exerted an influence on the catalytic process. The reaction in the presence of primary amine ligand **L6** afforded **2** in 95% yield with 20% ee (entry 6). Introduction of an ethyl group at the nitrogen atom (**L7**), however, significantly retarded the reaction (entry 7). When chiral amino alcohol **L8** was employed as the ligand, the enantiopurity of **2** was as low as 8% ee (entry 8). The intramolecular *N*-arylation of **1** hardly proceeded with (–)-sparteine **L9** bearing tertiary amine units (entry 9). 1,1'-Binaphthalene-2,2'-diol **L10**, an effective ligand scaffold in the Cu-catalyzed asymmetric indoline synthesis,[19] did not exhibit any positive impacts in this 6-membered ring formation (entry 10). From the screening study, **L1** turned out to be a valuable chiral ligand for the enantioselective construction of C_2-symmetric spirane **2**. Unfortunately, no improvements on the enantioselectivity were observed even when other reaction parameters such as the base, solvent, and protecting group on the nitrogen atom were changed. Although the

selectivity of this asymmetric Ullmann–Goldberg reaction was unsatisfactory, optically pure **2** was readily obtained by recrystallization of the enantioenriched product from $CHCl_3$ and MeOH due to the high crystallization ability of the racemate. X-ray crystallographic analysis of **2** unambiguously demonstrated its spiro structure and absolute configuration, the latter of which was definitely determined to be *M* based on the Flack parameter (Figure 1).

Table 1. Ligand screening[a]



Entry	Ligand	Yield (%)[b]	Ee (%)[c]
1	**L1**	>98	31 (>99)[d]
2	**L2**	>98	17
3	**L3**	45	29[e]
4	**L4**	10	13[e]
5	**L5**	trace	—
6	**L6**	95	20[e]
7	**L7**	trace	—
8	**L8**	49	8[e]
9	**L9**	trace	—
10	**L10**	no reaction	—

[a] All reactions were performed in the presence of 10 mol % / Br of CuI, 40 mol % / Br of chiral ligand, and 2 equiv / Br of K_3PO_4 at 100 °C for 24 h in DMF (0.1 M) under a nitrogen atmosphere. [b] NMR yields using 1,3,5-trimethoxybenzene as an internal standard. [c] Determined by HPLC equipped with a Chiralpak IA column. [d] The number in parentheses is the enantiopurity of the product after recrystallization. [e] The major enantiomer was opposite to that obtained in entry 1.

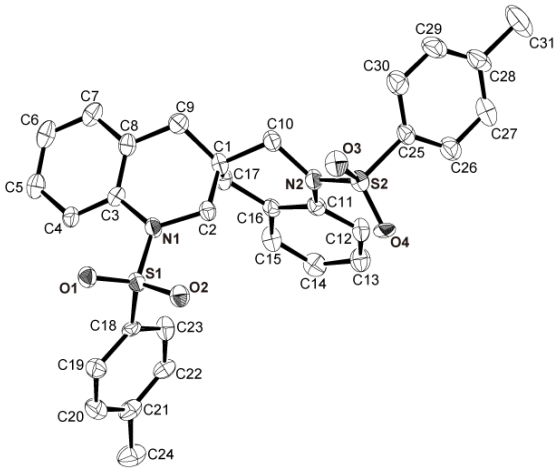
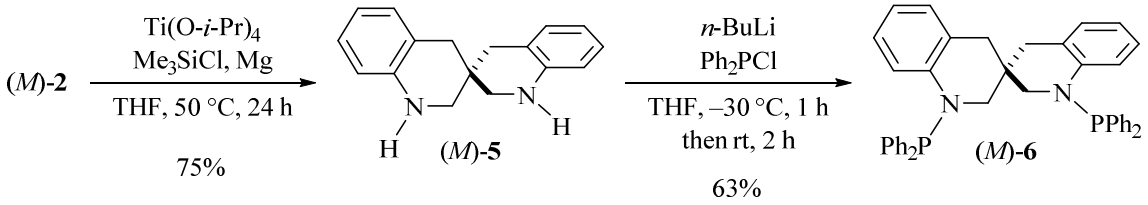


Figure 1. X-ray structure of C_2-symmetric spiro compound **2** with thermal ellipsoids at the 50% probability level. All hydrogen atoms are omitted for clarity. One of the two independent molecules is shown.

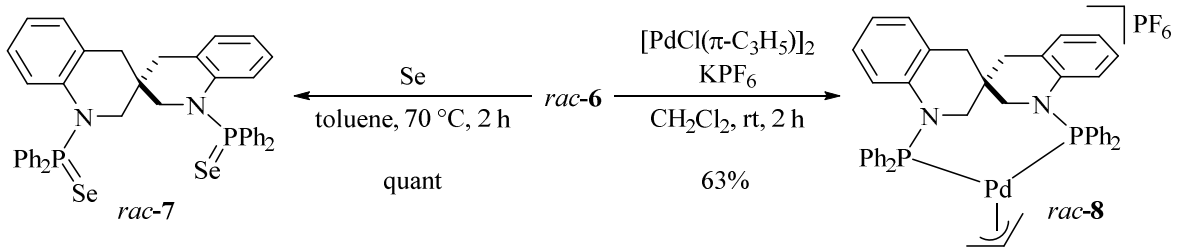
With enantiopure **2** in hand, we carried out the development of a new chiral ligand based on the spirobiquinoline. The tosyl groups of (*M*)-**2** were initially removed according to the reported procedure[21] to give spirobiquinoline (*M*)-**5**[22] (Scheme 2). Diphosphine (*M*)-**6** was successfully synthesized by the treatment of secondary amine **5** with *n*-BuLi followed by the addition of Ph_2PCl. A sharp singlet appeared at δ 49.7 in the ^{31}P NMR spectrum of (*M*)-**6** and a peak at *m*/*z* 619.2423 in the HRMS spectrum indicated the smooth incorporation of two diphenylphosphino groups into the spiro framework. This aminophosphine was obtained as air-stable white solids, which was gradually oxidized in solution upon exposure to air.



Scheme 2. Preparation of new chiral spiro phosphine (*M*)-**6**.

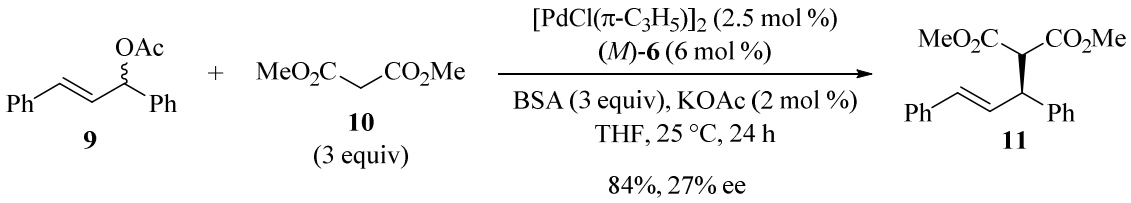
To evaluate the donor property of **6**, we prepared the corresponding phosphine selenide *rac*-**7** by heating *rac*-**6** in toluene with an excess amount of selenium metal (Scheme 3). The ^{31}P NMR spectrum of *rac*-**7** displayed one sharp resonance at δ 62.0 with ^{77}Se satellites. Its coupling constant ($^1J_{P–Se}$ 770 Hz) fell within the range of magnitudes reported for aminophosphines,[23] suggesting that the electron-donating ability of **6** was somewhat weaker than those of triarylphosphines.[24] Coordination behavior of bis(aminophosphine) **6** was then examined through the complexation with Pd: *rac*-**6** was reacted with $[PdCl(\pi\text{-}C_3H_5)]_2$ in the presence of

KPF_6 in CH_2Cl_2 to furnish chelate Pd complex *rac*-**8** (Scheme 3). The ESI-HRMS spectrum showed a solitary peak at *m*/*z* 765.1782 having the expected isotopic profile of the $[M - PF_6]^+$ cation. A pair of doublets ($^2J_{P-P}$ 19.7 Hz) was observed in the ^{31}P NMR spectrum, indicating the non-symmetric nature of *rac*-**8**. The disappearance of C_2-symmetry in phosphine **6** was caused by coordination to the C_s-symmetric Pd(π-C_3H_5) moiety.



Scheme 3. Derivatization and complexation of *rac*-**6**.

We briefly checked the function of chiral phosphine ligand **6** in the Pd-catalyzed asymmetric allylic alkylation of 1,3-diphenylpropenyl acetate (**9**) with dimethyl malonate (**10**). A mixture of **9**, **10** (3 equiv), and *N*,*O*-bis(trimethylsilyl)acetamide (BSA, 3 equiv) was treated with [PdCl(π-C_3H_5)]$_2$ (2.5 mol %), (*M*)-**6** (6 mol %), and KOAc (2 mol %) in THF at 25 °C for 24 h to give desired product **11** in 84% yield with 27% ee (Equation 2).



Equation 2. Pd-catalyzed asymmetric allylic alkylation using (*M*)-**6**.

Conclusions

We have developed an efficient protocol for the construction of a C_2-symmetric spiro framework, where the Cu-catalyzed enantioselective *N*-arylation of 1,3-propanediamide **1** is involved as the key step. The desired optically pure product **2** was obtained from readily accessible chemicals without tedious chromatographic purification and optical resolution. Derivatizaton of spirobiquinoline **2** successfully led to new chiral diphosphine ligand **6**, which proved to coordinate to Pd in a chelating fashion. Further study on the synthetic utility of the C_2-symmetric spiranes is now in progress.

Experimental Section

General. All reactions were carried out with standard Schlenk techniques under a nitrogen atmosphere. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECS400 (400 MHz for ^{1}H and 100 MHz for ^{13}C). All signals in the ^{1}H NMR spectra were expressed as δ down field from Me_4Si used as internal standard. Chemical shifts of the ^{13}C NMR signals are reported in δ referenced to $CDCl_3$ (δ 77.0). ^{31}P NMR spectra were recorded on JEOL JNM-ECS600 (243 MHz) and the data are given relative to external 85% H_3PO_4. Optical rotations were measured with JASCO P-1030 polarimeter. HPLC analyses were performed on JASCO HPLC system (JASCO PU 2080 pump and MD-2010 UV/Vis detector). Mass spectra were recorded on JEOL JMS-T100LC (ESI-HRMS or APCI-HRMS). Melting points were measured with Yanaco micro melting point apparatus model MP-S9 and were uncorrected. Anhydrous THF and toluene were purchased from Kanto Chemicals and further purified by passage through activated alumina using a GlassContour solvent purification system.[25] Column chromatography was performed on Kishida Silica Gel 60 (63–200 μm). Merck silica gel 60 F_{254} plates were used for TLC.

2,2-Bis(2-bromobenzyl)malononitrile (3).[20] To a solution of malononitrile (2.64 g, 40.0 mmol) and 2-bromobenzyl bromide (22.1 g, 88.4 mmol) in DMF (20 mL) was added DBU (13.4 g, 88.0 mmol) dropwise at 0 °C. The reaction mixture was allowed to stir at 80 °C for 3 h. After being cooled to room temperature, water was added to the reaction mixture, which was extracted with EtOAc. The organic phase was washed with water, 1 M aq. HCl and brine, and then dried over Na_2SO_4. The volatiles were removed by evaporation under reduced pressure. The resulting solid was triturated with a mixture of EtOH and hexane to give the titled compound (16.2 g, quant). White solid, mp 129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.60 (s, 4H, CH_2Ar), 7.25 (dt, *J* 7.8 Hz, 1.5 Hz, 2H, ArH), 7.38 (dt, *J* 7.8 Hz, 1.1 Hz, 2H, ArH), 7.59 (dd, *J* 7.8 Hz, 1.5 Hz, 2H, ArH), 7.66 (dd, *J* 7.8 Hz, 1.1 Hz, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 39.4 (C), 41.4 (CH_2), 114.6 (CN), 126.0 (C, Ar), 128.1 (CH, Ar), 130.4 (CH, Ar), 131.8 (C, Ar), 131.9 (CH, Ar), 133.6 (CH, Ar). HRMS (ESI): calcd for $C_{17}H_{12}Br_2N_2Na$: *m/z* 424.9265 $[M + Na]^+$, found 424.9251.

***N,N'*-(2,2-Bis(2-bromobenzyl)propane-1,3-diyl)bis(4-methylbenzenesulfonamide) (1).** To a flask containing **3** (808 mg, 2.00 mmol) was added a 2 M solution of $BH_3 \cdot SMe_2$ in THF (6 mL, 12.0 mmol). The reaction mixture was refluxed for 18 h. To this solution was carefully added 6 M aq. HCl (3 mL) at 0 °C, which was again refluxed for 2 h. After being cooled to room temperature, the mixture was basified with 6 M aq. NaOH. The crude product was extracted with CH_2Cl_2 and dried over Na_2SO_4. Evaporation of the volatiles under reduced pressure afforded diamine **4**. Crude **4** was redissolved in CH_2Cl_2 (10 mL), to which Et_3N (607 mg, 6.00 mmol) and subsequently TsCl (915 mg, 4.80 mmol) were added at 0 °C. The reaction mixture was stirred at room temperature for 12 h. The reaction was then quenched by the addition of 1 M aq. HCl and extracted with CH_2Cl_2. The organic layer was washed with sat. aq. $NaHCO_3$, dried over Na_2SO_4, and evaporated to dryness. The resulting solid was recrystallized from $CHCl_3$/hexane to give the titled compound (1.22 g, 85% over 2 steps). White solid, mp 177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (s, 6H, CH_3), 2.95 (s, 4H, CH_2Ar), 3.03 (d, *J* 7.3 Hz, 4H, CH_2N), 4.65 (t, *J* 7.3 Hz, 2H, NH), 7.09 (dt, *J* 7.8 Hz, 1.8 Hz, 2H, ArH), 7.22 (dt, *J* 7.8 Hz, 1.4 Hz, 2H, ArH), 7.27 (dd, *J* 7.8 Hz, 1.8 Hz, 2H, ArH), 7.32 (d, *J* 8.2 Hz, 4H, ArH), 7.51 (dd, *J* 7.8 Hz, 1.4 Hz, 2H, ArH), 7.69 (d, *J* 8.2 Hz, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6 (CH_3), 40.0 (CH_2), 44.5 (C), 47.0 (CH_2), 125.5 (C, Ar), 127.0 (CH, Ar), 127.7 (CH, Ar), 128.8 (CH, Ar), 129.8 (CH, Ar), 132.6 (CH, Ar), 133.4 (CH, Ar), 136.0 (C, Ar), 136.7 (C, Ar), 143.7 (C, Ar). HRMS (ESI): calcd for $C_{31}H_{32}Br_2N_2NaO_4S_2$: *m/z* 741.0068 $[M + Na]^+$, found 741.0060.

1,1'-Bis(4-methylbenzenesulfonyl)-1,1',4,4'-tetrahydro-2*H*,2'*H*-3,3'-spirobi[quinoline] (2). A mixture of **1** (36.0 mg, 0.05 mmol), CuI (1.91 mg, 0.01 mmol), (1*R*,2*R*)-*N*,*N*'-dimethyl-1,2-diphenyl-1,2-ethylenediamine **L1** (9.61 mg, 0.04 mmol) and K_3PO_4 (42.5 mg, 0.20 mmol) in *N*,*N*-dimethylformamide (0.5 mL) was stirred at room temperature for 30 min, then at 100 °C for 24 h. The reaction mixture was quenched with 1 M aq. HCl, extracted with EtOAc, washed with water, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was filtered through a short pad of silica gel, which was rinsed with $CHCl_3$. The filtrate was evaporated to dryness to give **2** (27.7 mg, 99%). The enantiomeric excess was determined by HPLC analysis using a chiral stationary phase column (Daicel Chiralpak IA, hexane:$CHCl_3$ 2:1, Flow rate 0.5 mL/min: t_R (minor) 19.6 min, t_R (major) 28.6 min) to be 31% ee. Optically pure **2** was obtained by a single recrystallization from $CHCl_3$/MeOH. White solid, mp 215 °C. $[\alpha]_D^{24}$ –7.7 (*c* 1.14, $CHCl_3$) for *M* isomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (d, *J* 16.0 Hz, 2H, CH_2Ar), 2.41 (s, 6H, CH_3), 2.47 (d, *J* 16.0 Hz, 2H, CH_2Ar), 3.54 (d, *J* 12.5 Hz, 2H, CH_2N), 3.77 (d, *J* 12.5 Hz, 2H, CH_2N), 6.94 (d, *J* 7.3 Hz, 2H, ArH), 7.00 (t, *J* 7.3 Hz, 2H, ArH), 7.15 (t, *J* 7.3 Hz, 2H, ArH), 7.27 (d, *J* 8.3 Hz, 4H, ArH), 7.62 (d, *J* 7.3 Hz, 2H, ArH), 7.65 (d, *J* 8.3 Hz, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6 (CH_3), 35.4 (C), 36.9 (CH_2), 54.3 (CH_2), 121.1 (CH, Ar), 124.2 (CH, Ar), 126.5 (C, Ar), 126.9 (CH, Ar), 127.1 (CH, Ar), 129.8 (CH, Ar), 130.1 (CH, Ar), 136.4 (C, Ar), 136.8 (C, Ar), 143.9 (C, Ar). HRMS (ESI): calcd for $C_{31}H_{30}N_2NaO_4S_2$: *m/z* 581.1545 $[M + Na]^+$, found 581.1534. X-ray measurements were made on a Rigaku R-AXIS RAPID 191R diffractometer using filtered Cu-Kα radiation: Empirical formula, $C_{31}H_{30}N_2O_4S_2$; Crystal system, monoclinic; Lattice type, primitive; Space group, $P2_1$ (No. 4); *a* = 9.3335(2) Å; *b* = 31.9577(6) Å; *c* = 9.7493(7) Å; β = 112.206(8)°; *V* = 2692.3(3) Å^3; *Z* = 4; D_{calc} = 1.378 g/cm^3; μ(CuKα) = 21.259 cm^{-1}; Reflection/Parameter Ratio = 12.76; *R* (All reflections) = 0.0765; w*R*2 (All reflections) = 0.1447; Goodness of Fit Indicator = 1.004; Flack Parameter (Friedel pairs = 4744) = –0.010(14). CCDC 1005112 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif.

(*M*)-1,1',4,4'-Tetrahydro-2*H*,2'*H*-3,3'-spirobi[quinoline] ((*M*)-5).[21] To a mixture of (*M*)-**2** (55.9 mg, 0.100 mmol) and Mg powder (24.3 mg, 1.00 mmol) in THF (0.5 mL) were added Ti(O-*i*-Pr)$_4$ (56.8 mg, 0.200 mmol) and Me_3SiCl (32.8 mg, 0.302 mmol). The reaction mixture was allowed to stir at 50 °C for 24 h. After being cooled to room temperature, to the mixture were added sat. aq. $NaHCO_3$, THF, and anhydrous NaF sequentially, which was stirred for 30 min. The mixture was filtered through a pad of Celite and the filtrate was concentrated under

reduced pressure. The residue was passed quickly through a short pad of silica gel using hexane/EtOAc (5:1). The filtrate was evaporated to dryness, affording the titled compound (18.7 mg, 75%). An analytically pure product was obtained by recrystallization from $CHCl_3$/hexane. White solid, mp 215 °C. $[\alpha]_D^{20}$ –28.7 (*c* 0.99, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.59 (d, *J* 16.2 Hz, 2H, CH_2Ar), 2.68 (d, *J* 16.2 Hz, 2H, CH_2Ar), 3.05 (d, *J* 11.2 Hz, 2H, CH_2N), 3.14 (d, *J* 11.2 Hz, 2H, CH_2N), 3.91 (s, 2H, NH), 6.52 (d, *J* 7.4 Hz, 2H, ArH), 6.63 (t, *J* 7.4 Hz, 2H, ArH), 6.96 (t, *J* 7.4 Hz, 2H, ArH), 7.00 (d, *J* 7.4 Hz, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.5 (C), 37.0 (CH_2), 48.2 (CH_2), 113.7 (CH, Ar), 117.2 (CH, Ar), 119.3 (C, Ar), 126.9 (CH, Ar), 130.1 (CH, Ar), 143.7 (C, Ar). HRMS (ESI): calcd for $C_{17}H_{19}N_2$: *m/z* 251.1548 $[M + H]^+$, found 251.1536.

(*M*)-1,1'-Bis(diphenylphosphino)-1,1',4,4'-tetrahydro-2*H*,2'*H*-3,3'-spirobi[quinoline] ((*M*)-6). To a solution of (*M*)-**5** (50.0 mg, 0.20 mmol) in THF (1.8 mL), *n*-BuLi (2.65 M in hexane; 0.16 mL, 0.42 mmol) was added dropwise at –30 °C, which was stirred at this temperature for 20 min. To this mixture was added dropwise a solution of $ClPPh_2$ (92.7 mg, 0.42 mmol) in THF (0.37 mL). The mixture was stirred at –30 °C for 1 h and then at room temperature for further 2 h. After removal of the volatiles by evaporation, the residue was filtered through a short pad of silica gel, which was rinsed with a 5:1 mixture of CH_2Cl_2 and hexane. The filtrate was evaporated to dryness and the crude product was purified by silica gel column chromatography using CH_2Cl_2 and hexane (2:1, v/v) as an eluent to give **6** (77.9 mg, 63%). White solid, mp 95 °C. $[\alpha]_D^{22}$ +20.2 (*c* 1.1, $CHCl_3$) (*M* isomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.19 (d, *J* 16.2 Hz, 2H, CH_2Ar), 2.28 (d, *J* 16.2 Hz, 2H, CH_2Ar), 2.55 (d, *J* 12.4 Hz, 2H, CH_2N), 2.99 (d, *J* 12.4 Hz, 2H, CH_2N), 6.71 (dt, *J* 7.4 Hz, 1.0 Hz, 2H, ArH), 6.79 (d, *J* 7.4 Hz, 2H, ArH), 7.02 (dt, *J* 7.4 Hz, 1.8 Hz, 2H, ArH), 7.20–7.35 (m, 20H, PhH), 7.55 (t, *J* 7.4 Hz, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.8 (C), 36.8 (CH_2), 52.0 (d, $^2J_{C-P}$ 7.7 Hz, CH_2), 116.5 (d, $^3J_{C-P}$ 34.5 Hz, CH, Ar), 119.2 (CH, Ar), 122.6 (d, $^3J_{C-P}$ 4.8 Hz, C, Ar), 126.5 (CH, Ar), 128.3 (d, $^3J_{C-P}$ 6.2 Hz, CH, Ph), 128.4 (d, $^3J_{C-P}$ 6.2 Hz, CH, Ph), 128.8 (CH, Ph), 129.3 (CH, Ph), 130.2 (CH, Ar), 132.2 (d, $^2J_{C-P}$ 20.6 Hz, CH, Ph), 132.7 (d, $^2J_{C-P}$ 20.6 Hz, CH, Ph), 136.2 (d, $^1J_{C-P}$ 14.4 Hz, C, Ph), 136.8 (d, $^1J_{C-P}$ 14.4 Hz, C, Ph), 145.1 (d, $^2J_{C-P}$ 22.0 Hz, C, Ar). ^{31}P NMR (243 MHz, $CDCl_3$): δ 49.7. HRMS (APCI): calcd for $C_{41}H_{37}N_2P_2$: *m/z* 619.2432 $[M + H]^+$, found 619.2423.

1,1'-Bis(diphenylphosphinoselenoyl)-2,2',4,4'-tetrahydro-1*H*,1'*H*-3,3'-spirobi[quinoline] (*rac*-7). A mixture of *rac*-**6** (15.0 mg, 0.024 mmol) and selenium (9.57 mg, 0.12 mmol) in degassed toluene (0.9 mL) was stirred at 70 °C for 1 h. After being cooled to room temperature, the solution was filtered and concentrated *in vacuo* to give the titled compound (18.5 mg, quant). White solid, mp 150 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.67 (d, *J* 15.8 Hz, 2H, CH_2Ar), 2.79 (d, *J* 15.8 Hz, 2H, CH_2Ar), 2.88 (dd, *J* 12.3 Hz, 6.5 Hz, 2H, CH_2N), 3.29 (d, *J* 12.3 Hz, 6.5 Hz, 2H, CH_2N), 6.80–6.87 (m, 4H, ArH), 7.02 (d, *J* 7.4 Hz, 2H, ArH), 7.09 (d, *J* 7.4 Hz, 2H, ArH), 7.37–7.47 (m, 12H, PhH), 7.84–7.90 (m, 8H, PhH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.5 (t, $^3J_{C-P}$ 5.8 Hz, C), 38.0 (CH_2), 53.9 (CH_2), 121.8 (d, $^3J_{C-P}$ 6.7 Hz, CH, Ar), 122.2 (CH, Ar), 125.7 (CH, Ar), 127.0 (d, $^3J_{C-P}$ 5.8 Hz, C, Ar), 128.6 (d, $^3J_{C-P}$ 12.9 Hz, CH, Ph), 128.7 (d, $^3J_{C-P}$ 12.9 Hz, CH, Ph), 129.9 (CH, Ar), 131.8 (d, $^4J_{C-P}$ 2.9 Hz, CH, Ph), 131.9 (d, $^4J_{C-P}$ 2.9 Hz, CH, Ph), 132.3 (d,

$^{2}J_{C–P}$ 11.0 Hz, CH, Ph), 132.3 (d, $^{1}J_{C–P}$ 92.0 Hz, C, Ph), 132.4 (d, $^{2}J_{C–P}$ 11.0 Hz, CH, Ph), 132.5 (d, $^{1}J_{C–P}$ 92.0 Hz, C, Ph), 140.2 (C, Ar). ^{31}P NMR (243 MHz, $CDCl_3$): δ 62.0 (s with satellites, $^{1}J_{P–Se}$ 770 Hz). HRMS (ESI): calcd for $C_{41}H_{36}N_2NaP_2Se_2$: *m/z* 801.0582 $[M + Na]^+$, found 801.0571.

Pd-bis(aminophosphine) complex *rac*-8. A mixture of $[PdCl(\pi\text{-}C_3H_5)]_2$ (3.0 mg. 8.1 μmol), *rac*-**6** (10.0 mg, 16 μmol) and KPF_6 (4.5 mg, 24 μmol) in CH_2Cl_2 (0.33 mL) was stirred at room temperature for 4 h. The mixture was filtered through a pad of Celite. The filtrate was concentrated to afford the desired product **8** in 63% yield. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.77–3.12 (m, 6H, CH_2Ar and CH_2N), 3.24 (t, *J* 6.4 Hz, 1H, CH_2, π-allyl), 3.63 (t, *J* 6.4 Hz, 1H, CH_2, π-allyl), 3.67–3.75 (m, 2H, CH_2N), 4.21 (t, *J* 13.7 Hz, 1H, CH_2, π-allyl), 4.83 (t, *J* 13.7 Hz, 1H, CH_2, π-allyl), 5.66 (tt, *J* 13.6 Hz, 6.8 Hz, 1H, CH, π-allyl), 6.28 (d, *J* 7.8 Hz, 1H, ArH), 6.50 (d, *J* 7.8 Hz, 1H, ArH), 6.62 (t, *J* 7.8 Hz, 1H, ArH), 6.70 (t, *J* 7.8 Hz, 1H, ArH), 6.82 (d, *J* 7.8 Hz, 1H, ArH), 6.87 (d, *J* 7.8 Hz, 1H, ArH), 6.99 (dd, *J* 7.8 Hz, 2.1 Hz, 2H, ArH), 7.03–7.08 (m, 4H, ArH), 7.15–7.18 (m, 4H, ArH), 7.35–7.40 (m, 3H, ArH), 7.45–7.55 (m, 7H, ArH), 7.59–7.63 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.4 (CH_2Ar), 40.6 (C), 41.4 (CH_2Ar), 56.8 (d, $^{2}J_{C–P}$ 14.4 Hz, CH_2N), 60.1 (d, $^{2}J_{C–P}$ 16.3 Hz, CH_2N), 78.1 (d, $^{2}J_{C–P}$ 30.7 Hz, CH_2, π-allyl), 80.7 (d, $^{2}J_{C–P}$ 29.7 Hz, CH_2, π-allyl), 121.3 (CH, Ar), 122.3 (CH, Ar), 123.4–123.5 (overlapped, CH, Ar and π-allyl), 125.2 (CH, Ar), 125.8 (CH, Ar), 128.6 (d, $^{3}J_{C–P}$ 11.5 Hz, CH, Ph), 128.7 (d, $^{3}J_{C–P}$ 10.5 Hz, CH, Ph), 128.8 (br s, C, Ar), 129.3 (CH, Ar), 129.5 (d, $^{3}J_{C–P}$ 10.5 Hz, CH, Ph), 129.5 (d, $^{3}J_{C–P}$ 10.5 Hz, CH, Ph), 129.7 (CH, Ar), 130.1 (d, $^{2}J_{C–P}$ 13.4 Hz, CH, Ph), 130.8–131.1 (overlapped, CH, Ph), 131.2 (d, $^{3}J_{C–P}$ 1.9 Hz, C, Ar), 131.5 (d, $^{1}J_{C–P}$ 45.0 Hz, C, Ph), 131.6 (d, $^{2}J_{C–P}$ 13.4 Hz, CH, Ph), 132.3 (d, $^{2}J_{C–P}$ 15.3 Hz, CH, Ph), 133.4 (d, $^{1}J_{C–P}$ 49.8 Hz, C, Ph), 134.9 (d, $^{1}J_{C–P}$ 37.4 Hz, C, Ph), 137.8 (d, $^{1}J_{C–P}$ 44.1 Hz, C, Ph), 142.4 (d, $^{2}J_{C–P}$ 7.7 Hz, C, Ar), 143.3 (d, $^{2}J_{C–P}$ 5.8 Hz, C, Ar). ^{31}P NMR (243 MHz, $CDCl_3$): δ 75.9 (d, $^{2}J_{P–P}$ 19.7 Hz), 79.9 (d, $^{2}J_{P–P}$ 19.7 Hz). HRMS (ESI): calcd for $C_{44}H_{41}N_2P_2Pd$: *m/z* 765.1780 $[M – PF_6]^+$, found 765.1782.

Pd-catalyzed asymmetric allylic alkylation of 1,3-diphenylpropenyl acetate. To a test tube placed with ligand (*M*)-**6** (3.71 mg, 6.0 μmol), $[PdCl(\pi\text{-}C_3H_5)]_2$ (0.91 mg, 2.5 μmol) was added degassed THF (0.2 mL) under a nitrogen atmosphere and the mixture was stirred for 1 h at room temperature. Then, a solution of 1,3-diphenylpropenyl acetate (**9**) (25.2 mg, 0.10 mmol) and KOAc (0.20 mg, 2.0 μmol) in THF was added into a catalyst solution. After addition of dimethyl malonate (**10**) (39.63 mg, 0.30 mmol) and BSA (63.03 mg, 0.30 mmol), the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was filtered through a short pad of silica gel using EtOAc as an eluent and the resulting filtrate was concentrated. The product yield was determined by NMR analysis (1,3,5-trimethoxybenzene was used as an internal standard) to be 84% yield. The enantiomeric excess was determined by HPLC analysis using a chiral stationary phase column (Daicel Chiralcel OD-H, hexane:*i*-PrOH 99:1, Flow rate 0.2 mL/min: t_R (major) 62.7 min, t_R (minor) 67.4 min) to be 27% ee.

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