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Preparation and Application of Amino Phosphine Ligands Bearing Spiro[indane-1,2′-pyrrolidine]Backbone

Shasha Li, Jinxia Zhang, Hongjie Li, Lifei Feng, and Peng Jiao*.

Key Laboratory of Radiopharmaceuticals, College of Chemistry, Beijing Normal University, Beijing 100875, P.R. China.

Supporting Information Placeholder

ABSTRACT: P,N$_{sp3}$-Bidentate chiral ligands bearing spiro[indane-1,2′-pyrrolidine] backbone were prepared in gram-scale for the first time. Pd complexes of these air-stable amino phosphine ligands could catalyze asymmetric allylic substitutions of malonate, alcohol and amine type nucleophiles in up to 97% ee and 99% yield. A crystal structure of [Pd(II)(η^3-1,3-diphenylallyl)(ligand)]PF_6 indicated possible transition states of the catalytic reactions. These ligands are characteristic of a very rigid backbone, which is simple but highly effective. They rival C_2-symmetric bisphosphine, P,N$_{sp2}$-bidentate and P,N$_{sp3}$-bidentate ligands in tested allylic substitutions.

Introduction

Chiral ligands play important roles in transition metal catalyzed asymmetric reactions. Effective chiral ligands constitute the basis for development of methodologies for catalytic asymmetric synthesis. Various chiral ligands have been developed to date. Certain chiral ligands are coined as privileged ligands[1,2] due to their excellent performances in certain types of reactions.C_2 symmetry prevails in many privileged chiral ligands, such as BOX, salen, BINAP, SDP,[3] SKP,[4]MonoPhos, SIPhos,[5] and DpenPhos.[6] On the other hand, non-C_2-symmetric chiral ligands often perform better than C_2-symmetric analogues. Notable non-C_2-symmetric ligands include MOP,[7]JosiPhos,[8] PHOX,[9] SpinPHOX,[10] SIPHOX,[11]SpiroPAP,[12]BI-DIME[13] and so on. P,N-Bidentate compounds are well-known as chiral ligands. Though various chiral P,N-bidentate ligands have been reported,[14] successful reports on P,N$_{sp3}$-bidentae ligands[15] are still limited. The heterobidentate character as well as the underdevelopment state of P,N$_{sp3}$-bidentate ligands arouses our interest. We became interested in a type of structurally simple ligands, in which a chiral benzylic center bearing an amino group is incorporated with triarylphosphine (Figure 1a). Such ligands bearing an(*ortho*-diphenylphosphino)benzylamino structure have been reported by Tsuji,[16] Ding,[17] Vasse,[18] and Zheng.[19]P,N-Bidentate compounds bearing an (*o*-diphenylphosphino)benzylamino structure and extra axial or planar chirality, or a ferrocene backbone were reported by Li,[20] Hayashi,[8,21] Alberico and Salzer,[22] and Weissensteiner[23]. Generally, these P,N$_{sp3}$-bidentate compounds did not perform well in transition metal catalyzed asymmetric reactions. Here, we report the preparation of new ligands (Figure 1b) by constructing a spiro[indane-1,2′-pyrrolidine] skeleton and then introducing a diarylphosphino group. Our new ligand is conformationally very rigid and the P,N-atoms tethered by highly constrained bonds are in well-prepared positions awaiting a transition metal. The performance of palladium complexes of our new ligands was evaluated in asymmetric allylic substitutions with various nucleophiles.[14b,24,25]

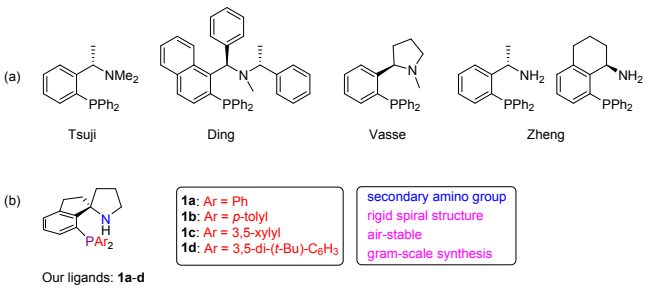


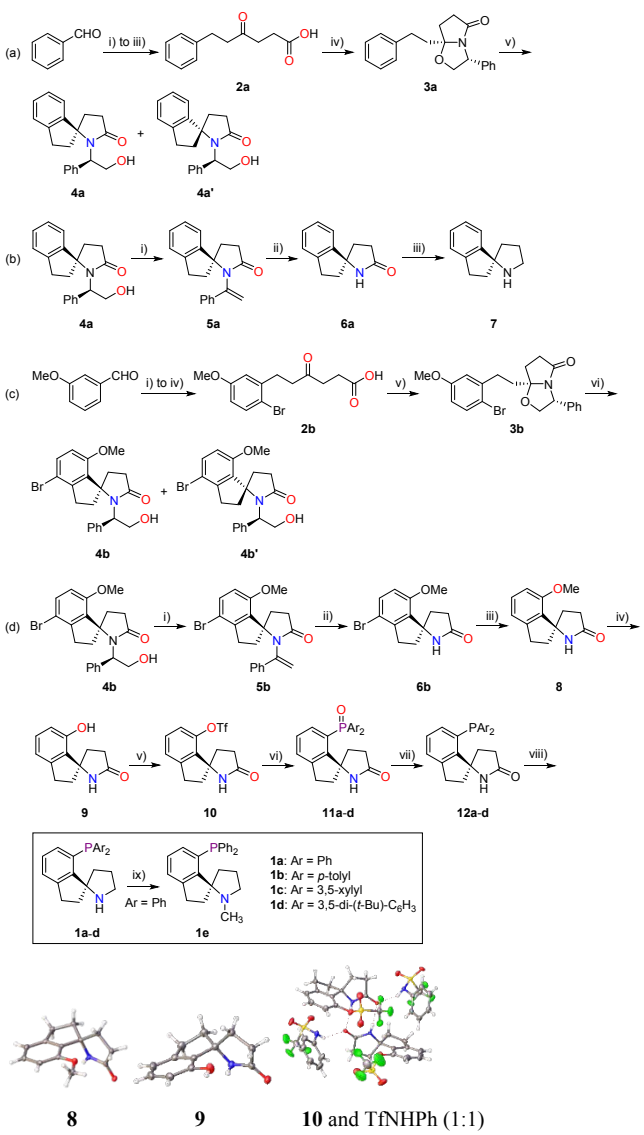
Figure 1. (a) P,N$_{sp3}$-Bidentate ligands with an (o-diphenylphosphino)benzylamino substructure. (b) P,N$_{sp3}$-Bidentate ligands with a rigid spiro[indane-1,2'-pyrrolidine] backbone.

Results and Discussion

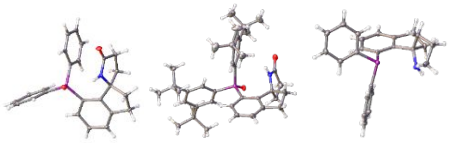
We commenced the synthesis of our chiral ligands with benzaldehyde and ethyl levulinate (Scheme 1a). Piperidine and acetic acid mediated condensation followed by hydrogenation and hydrolysis gave 6-phenyl-4-oxo-hexanoic acid (**2a**) in 80% yield.[26] Condensation of **2a** with *D*-phenylglycinol gave **3a** in >99% yield.[27] The phenyl and the phenethyl groups are believed to be in a *cis*-configuration.[27] The key step of building the spiral center was accomplished through $AlCl_3$ mediated intramolecular Friedel–Crafts type reaction.[28] Two diastereomers **4a** and **4a′**(67:23) were obtained in 90% isolated yield and separated by silica gel chromatography. When **4a** was reacted with $LiOH{\cdot}H_2O$ in DMSO at 170 °C for 12 h,[29] **5a** was obtained in 92% yield (Scheme 1b). Hydrolysis of **5a** with aqueous HCl in THF smoothly gave **6a** in 93% yield. Crystal structures of **4a**,[28] the debromination product of **4b′**, the enantiomer of **5a**, and **6a** were obtained. Reduction of **6a** with $LiAlH_4$ gave **7** in >99% yield. Introduction of a 7-diphenylphosphino group into **7** was attempted but failed.

Alternatively, we started from 3-methoxybenzaldehyde in hope of introducing a PPh_2 group via the potent phenolic hydroxy group (Scheme 1c, d). **4b** and **4b′** (48:42) were obtained in 90% isolated yield. In a typical run, 5 g of **4b** could be obtained after three recrystallizations. Under the conditions established for **6a**, compound **6b** was prepared smoothly, the structure of which was confirmed by single crystal XRD analysis. Debromination of **6b** gave **8**. Demethylation of **8** followed by triflation of the phenolic hydroxy group of **9**,[30] coupling with diphenylphosphine oxide[31] and two subsequent reduction steps gave the ligand **1a**.[32] Crystal structures of **8**, **9**, a 1:1 complex of **10** with *N*-phenyl triflamide, **11a**, **11d**, and **1a** were obtained. Ligands **1b–d** were prepared from **10** and the corresponding diarylphosphine oxide.[31] The ligand **1e** having an *N*-methyl group was prepared from **1a** in 98% yield.

Scheme 1. Preparation of (*R*)-spiro[indane-1,2′-pyrrolidine] (**7**) and the amino phosphine ligands **1a–e**.



8 **9** **10** and TfNHPh (1:1)



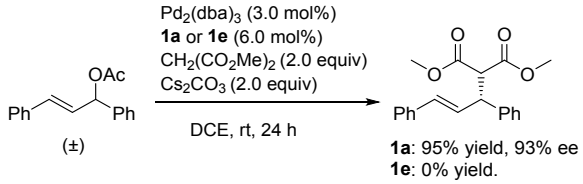
11a **11d** **1a**

Reagents and conditions for the preparation of **7**: (a) i) Ethyl levulinate (2.0 equiv), piperidine, AcOH, benzene, reflux, 80% yield; ii) H_2, Pd/C, EtOH, >99% yield; iii) aq. NaOH, EtOH; aq. HCl, >99% yield; iv) *D*-phenylglycinol (1 equiv), toluene, reflux, >99% yield; v) $AlCl_3$ (5.0 equiv), DCE, −5 °C, 90% total yield; (b) i) $LiOH·H_2O$ (10 equiv), DMSO, 170 °C, 92% yield; ii) 4 N HCl, THF, 70 °C, 93% yield; iii) $LiAlH_4$ (5.0 equiv), Et_2O, reflux, >99% yield.

Reagents and conditions for the preparation of **1a–e**: (c) i) Ethyl levulinate (2.0 equiv), piperidine, AcOH, benzene, reflux, 85% yield; ii) H_2, Pd/C, EtOH, 97% yield; iii) Br_2 (1.7 equiv), CH_2Cl_2, >99% yield; iv) aq. NaOH, EtOH; aq. HCl, 98% yield; v) *D*-phenylglycinol (1 equiv), toluene, reflux, 92% yield; vi) $AlCl_3$ (3.0 equiv), DCE, −10 °C, 90% total yield; (d) i) $LiOH·H_2O$ (10 equiv), DMSO, 170 °C, 90% total yield; ii) 4 N HCl, THF, 70 °C, 93% yield; iii) H_2, Pd/C, MeOH, >99% yield; iv) BBr_3 (5.0 equiv), CH_2Cl_2, −20 °C, >99% yield; v) $PhNTf_2$ (1.5 equiv), DMF, >99% yield; vi) $Ar_2P(O)H$ (2.0 equiv), $Pd(OAc)_2$, dppb, *i*-Pr_2NEt, DMSO, 76–>99% yields; vii) Cl_3SiH (15.0 equiv), toluene, 85 °C; viii) $LiAlH_4$ (5.0 equiv), THF, 60 °C, 82–86% yields for two steps; ix) $ClCO_2Et$ (1.5 equiv), pyridine, toluene; $LiAlH_4$ (5.0 equiv), THF, 60 °C, 98% yield.

With the amino phosphine ligand **1a** in hand, Pd catalyzed asymmetric allylic substitutions of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate were first tested (Scheme 2).[33] Using 3.0 mol% $Pd_2(dba)_3$, 6.0 mol% ligand **1a**, and Cs_2CO_3 as the base, 95% yield and 93% ee were obtained in $ClCH_2CH_2Cl$ (DCE). When ligand **1e** was used instead of **1a** in DCE, no alkylation was observed even after 4 d. This indicated the presence of NH in the ligand was essential for the catalytic reactivity. The *N*-methyl group in **1e** might increase the steric hindrance and blocked the coordination of **1e** to Pd.

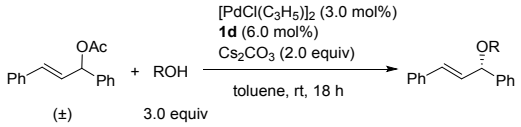
Scheme 2. Allylic alkylation with dimethyl malonate.



The allylic substitution with CH_3OH was used as a benchmark to evaluate both the reactivity and the enantioselectivity of the heterobidentate ligands **1a–d**. Using 3.0 mol% $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and Cs_2CO_3 as the base, the ligands were screened in toluene at rt. While all the ligands delivered the methyl ether in ≥ 93% ee, **1d** gave the highest ee of 97%, and **1a**, **1c**, **1d** gave the same yields (82%).[33] We then used **1d** as a chiral ligand to screen the Pd precursor, the solvent and the reaction temperature.[33]Under the optimized conditions, several alcohols were used as nucleophiles in the allylic substitutions (Table 1). *n*-Butanol gave the highest ee of 97% as methanol (entry 1, 3). Ethanol, 2-furylmethanol, tetrahydrofurfuryl alcohol and 2-indanol gave 91–94% ee (entry 2, 9, 12, 13). Benzyl alcohol and phenethyl alcohol gave 80% ee and 72% ee, respectively (entry 6, 7). Other primary alcohols with an alkene group or a heteroaromatic ring gave ee ranged 64–82% (entry 4, 5, 8, 10, 11). The reactions of

methanol with symmetrically 1,3-disubstituted 2-propenyl acetates were also tested (Table 2). The acetate with an *m*-tolyl or *p*-tolyl group gave ≥93% ee (entry 2, 3). The acetate with an *o*-tolyl or *p*-chlorophenyl group gave 86% ee (entry 1, 4). The acetate with a *p*-methoxyphenyl group gave the product in 90% yield but in only 3% ee (entry 5).

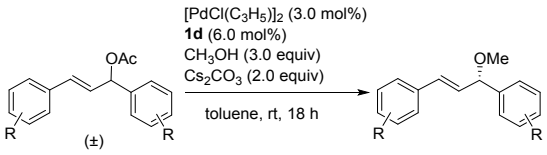
Table 1. Asymmetric substitutions with different alcohols.



Entry	ROH	Yield (%)	Ee (%)[a]
1	CH_3OH	82	97
2	C_2H_5OH	85	94
3	*n*-BuOH	82	97
4	allyl alcohol	81	82
5	3-methyl-2-butenol	60	69
6	$PhCH_2OH$	83	80
7	$PhCH_2CH_2OH$	85	72
8	cinnamyl alcohol	87	78
9	2-furylmethanol	84	92
10	2-thienylmethanol	80	72
11	2-pyridinemethanol	70	64
12	tetrahydrofurfuryl alcohol	60	93
13	2-indanol	60	91

[a] The absolute configuration was deduced by comparison of the retention time of chiral HPLC with literature data.

Table 2. Asymmetric substitutions of different 1,3-diaryl-2-propenyl acetates with CH_3OH.

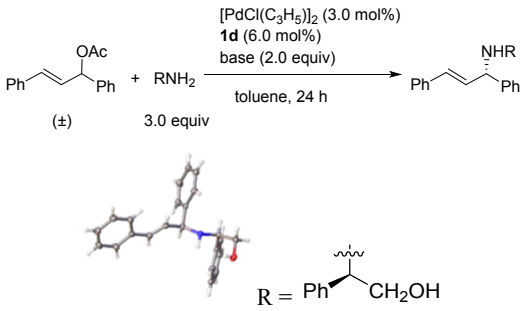


Entry	R	Yield (%)	Ee (%)[a]
1	*o*-CH_3	99	86
2	*m*-CH_3	99	97
3	*p*-CH_3	70	93
4	*p*-Cl	62	86
5	*p*-OCH_3	90	3

[a] The absolute configuration was assigned by analogy.

Allylic substitutions with primary amines were preliminarily studied (Table 3). At rt, aniline did not react with 1,3-diphenyl-2-propenyl acetate. At 60 °C, 93% yield and 70% ee were obtained using Cs_2CO_3 as the base (entry 1). When BSA was used instead of Cs_2CO_3, 92% yield and 61% ee were obtained (entry 2). Benzyl amine reacted at 60 °C to give the product in 72% yield and 81% ee (entry 3). When (*R*)-phenylglycinol was used, the secondary amine products were obtained in 72% yield at rt though a long reaction time (40 h) was needed (entry 4). Both HPLC and ^{1}H NMR indicated a 96% de. The structure of the major diastereomer was confirmed by single crystal XRD analysis. The newly generated chiral center was in an (*S*) configuration. At 40 °C, the yield was improved to 89% but the de decreased to 85% (entry 5). No ether product was obtained. When (*S*)-phenylglycinol was used, 72% yield and 85% de were obtained at rt (entry 6). ^{1}H NMR indicated the major diastereomer had an (*S*,*S*) configuration, indicating the newly generated chiral center was also in an (*S*) configuration. These are the first reports on allylic substitutions using an amino alcohol as the nucleophile.[34] Comparing the molecular structure of phenylglycinol with benzylamine, we believe the reactivity of the primary amino group in phenylglycinol was enhanced due to the presence of adjacent hydroxy group.

Table 3. Asymmetric substitutions with primary amines.

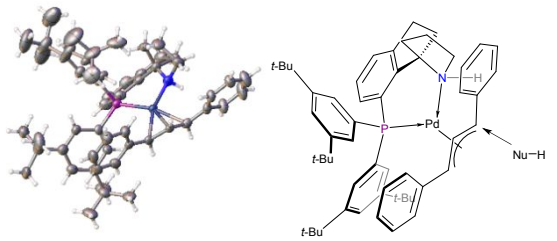


Entry	RNH_2	Base	T (°C)	Yield (%)	Ee (%)
1	$PhNH_2$	Cs_2CO_3	60	93	70
2	$PhNH_2$	BSA	60	92	61
3	$BnNH_2$	Cs_2CO_3	60	72	81
4[a]	(*R*)-phenylglycinol	Cs_2CO_3	rt	72	96[b]
5[a]	(*R*)-phenylglycinol	Cs_2CO_3	40	89	85[b]
6[a]	(*S*)-phenylglycinol	Cs_2CO_3	rt	72	85[b]

[a] The reaction time was 40 h.[b] de for the diastereomeric mixture.

Based on the absolute configurations of the Pd (II) complex with ligand **1d** and η^3-1,3-diphenylallyl paired with a PF_6^- anion (Figure 2a), and the allylic substitution products of malonates, alcohols and amines, we proposed the following transition state for allylic substitutions (Figure 2b). The ligand **1d** complexed with Pd in a P,N-bidentate mode to form the catalyst precursor. 1,3-Diphenyl-2-propenyl acetate reacted with the pre-catalyst to form the cationic allyl complex, in which the 1,3-diphenylallyl moiety adopted a W orientation due to possible π–π stacking between the phenyl rings of the substrate and the ligand.[25,35] Then the nucleophile would approach the allyl terminus *trans* to the coordinating P atom from the *Si* face. ^{1}H, ^{13}C and ^{31}P NMR spectra all indicated the Pd (II) complex in Figure 2a was a single species rather than a mixture of diastereomers in $CDCl_3$ at rt, which strongly

supported the η^3-1,3-diphenylallyl moiety exclusively adopted a W orientation.



a b

Figure 2. (a) Crystal structure of [Pd(II)(η^3-PhCHCHCHPh)(**1d**)]PF_6. PF_6^- was omitted for clarity. (b) Suggested transition state for allylic substitutions catalyzed by **1d** and Pd.

Conclusion

In summary, we reported the preparation of a new class of amino phosphine ligands bearing spiro[indane-1,2′-pyrrolidine] backbone and their performances in Pd-catalyzed asymmetric allylic substitution reactions. Crystal structure of [Pd(η^3-1,3-diphenylallyl)(**1d**)]PF_6 indicated possible transition states of the catalytic reactions. These air stable ligands could be prepared in gram-scale. The key intermediates **4b** and **4b′** for the chiral P,N-ligands could be obtained in 10 g scale and are separable by crystallizations. Our ligands are among those delivering high ee for Pd-catalyzed asymmetric allylic substitutions. We believe these structurally simple and conformationally rigid chiral ligands will find more applications in asymmetric synthesis.

EXPERIMENTAL SECTION

All glassware for reactions using anhydrous solvents were dried under high vacuum (< 0.1 torr) using a heat gun. General Schlenk techniques were applied for addition and transfer operations.

Commercial reagents and solvents were purchased from Acros, Alfa Aesar, J&K Scientific Ltd., Sinopharm Chemical Reagent Co. or Beijing Chemical Works, and used as received unless otherwise noted. THF was distilled over sodium benzophenone ketyl under N_2. CH_2Cl_2 was distilled over CaH_2 under N_2. Silica gel products were purchased from Qingdao Haiyang Chemical Co. Thin-layer chromatography was performed on precoated silica gel (0.2–0.25 mm thick) plates with fluorescent indicator 254 nm. The plate was visualized with 254 nm UV lamp, PMA or $KMnO_4$ stain. Column chromatography was performed on 200–300 mesh silica gel.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400, JEOL ECZ 400R or 600R spectrometer. Chemical shifts of ^{1}H NMR and ^{13}C NMR were referred to TMS (δ = 0) or chloroform (δ = 7.26 for ^{1}H NMR, 77.0 for ^{13}C NMR) respectively. Chemical shifts of ^{31}P NMR and ^{19}F NMR were referred to external 85% H_3PO_4 (δ = 0) and $CFCl_3$ (δ = 0), respectively. The following abbreviations were used to denote the multiplicity of each peak: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), m (multiplet). IR spectra were recorded on a Nicolet AVATAR 360 FT-IR spectrometer. The sample was prepared as a thin-film on a NaCl disc. MS spectra were obtained on a Waters Quattro Micro triple quadrupole mass spectrometer. Specific rotation was measured on a Perkin-Elmer 343 Polarimeter using the 589 nm D-line of sodium lamp and a quartz cell with 10 cm path length. HPLC was performed at room temperature using a Shimazu LC-20AT solvent delivery unit equipped with an SPD-20A UV/VIS detector. A Daicel OJ-H, OD-H, or AD-H column (0.46 cm Φ × 25 cm) without guard column was used. X-ray diffraction experiment was conducted on a Rigaku Oxford Diffraction SuperNova Dual Atlas S2 diffractometer using Cu Kα radiation.

Ethyl (*E*)-4-oxo-6-phenyl-5-hexenoate: To a three-necked flask equipped with a Dean-Stark apparatus, ethyl levulinate (57.0 mL, 400 mmol), piperidine (7.3 mL, 80 mmol), acetic acid (22.9 mL, 400 mmol) and benzene (100 mL) were added. The mixture was heated to gentle reflux. Benzaldehyde (20.3 mL, 200 mmol) in benzene (100 mL) was added dropwise. Then the mixture was stirred at 100 °C (oil bath) for 6 h. Water was removed via a Dean-Stark apparatus. The solution was washed with 2 N HCl, saturated $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated, and excess ethyl levulinate was distilled out under vacuum and recovered. The residue was dissolved in EtOH/hexanes (3:1). Most of the desired product crystallized out. The remaining crude product was purified by column chromatography (5:1 hexanes/AcOEt) to afford a white solid (37.4 g, 80% yield). R_f = 0.34 (5:1 hexanes/AcOEt); m.p. 46.4–47.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 16.3 Hz, 1H), 7.56–7.54 (m, 2H), 7.41–7.39 (m, 3H), 6.77 (d, J = 16.2 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.02 (t, J = 6.7 Hz, 2H), 2.69 (t, J = 6.7 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 198.0, 172.8, 142.8, 134.3, 130.5, 128.9, 128.3, 125.8, 60.0, 35.2, 28.1, 14.2; IR (film): ν_{max} 3447, 2982, 2932, 2909, 2818, 1739, 1666, 1614, 1450, 1410, 1368, 1204, 1163, 1098, 1020, 998, 750, 692 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{17}O_3$ 233.1178; Found 233.1173.

Ethyl 4-oxo-6-phenylhexanoate: To a round-bottom flask, ethyl (*E*)-4-oxo-6-phenyl-5-hexenoate (3.61 g, 15.6 mmol), 10% Pd/C (200 mg), and EtOH (50 mL) were added. The mixture was well stirred under hydrogen atmosphere for 12 h. Pd/C was filtered off. The filtrate was concentrated and the residue dried in vacuo to give the product as colorless oil (3.65 g, >99% yield), which was directly used without further purification. R_f = 0.34 (5:1 hexanes/AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (t, J = 7.9 Hz, 2H), 7.19 (t, J = 6.7 Hz, 3H), 4.13 (q, J = 7.1 Hz, 2H), 2.91 (t, J = 7.3 Hz, 2H), 2.79 (t, J = 7.8 Hz, 2H), 2.70 (t, J = 6.3 Hz, 2H), 2.58 (t, J = 6.7 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 208.0, 172.8, 141.0, 128.5, 128.3, 126.1, 60.6, 44.2, 37.2, 29.6, 27.9, 14.2.

4-Oxo-6-phenylhexanoic acid (2a): To a round-bottom flask, ethyl 4-oxo-6-phenylhexanoate(1.12 g, 4.78 mmol) and EtOH/H_2O (10 mL/10 mL) were added. To this solution, NaOH (400 mg, 10.0 mmol) in 100 mL H_2O was added dropwise. After stirring for 2 h at room temperature, 1 N HCl was added dropwise till the pH was approximately 7. EtOH was evaporated. 1 N HCl was added dropwise with stirring till the pH was about 1. The solvent was removed by rotary evaporation. The residue was dissolved in CH_2Cl_2, washed with saturated brine, and dried over anhydrous Na_2SO_4. CH_2Cl_2 was evaporated to give **2a** as a brown solid (1.03 g, >99% yield). The product was directly used without further purification. m.p. 87.3–88.0 °C; R_f = 0.31 (2:1 hexanes/AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.26 (m, 2H), 7.21–7.17 (m, 3H), 2.94–2.90 (m, 2H), 2.81–2.78 (m,

2H), 2.72–2.69 (m, 2H), 2.65–2.62 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 208.0, 179.1, 140.9, 128.6, 128.3, 126.2, 44.2, 37.0, 30.0, 27.8; IR (film): ν_{max} 2956, 2924, 2851, 1712, 1377, 669 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{12}H_{15}O_3$ 207.1021; Found 207.1017.

(3*R*,7a*S*)-3-Phenyl-7a-(2-phenylethyl)-2,3,7,7a-tetrahydropyrrolo[2,1-*b*]oxazol-5-one (3a): To a round-bottom flask, **2a** (1.03 g, 5.00 mmol), *D*-phenylglycinol (686 mg, 5.00 mmol) and toluene (80 mL) were added. The reaction mixture was heated at 130 °C (oil bath) for 36 h. Water was removed by a Dean-Stark apparatus. The solvent was removed by rotary evaporation. The residue was purified by column chromatography (3:1 hexanes/AcOEt) to afford **3a** as a yellow oil (1.54 g, >99% yield). R_f = 0.22 (3:1 hexanes/AcOEt); m.p. 109.4–110.2 °C; $[\alpha]_D^{20}$–109 (*c* 1.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.26 (m, 2H), 7.37–7.33 (m, 2H), 7.29–7.22 (m, 5H), 7.19–7.15 (m, 1H), 7.07–7.05 (d, 2H, *J* = 7.1Hz), 5.23 (t, *J* = 7.7Hz, 1H), 4.67 (t, *J* = 8.5Hz, 1H), 4.13 (dd, *J* = 8.7, 7.3Hz, 1H), 2.88 (dt, J = 17.4, 9.8Hz, 1H), 2.74–2.60 (m, 3H), 2.46–2.40 (m, 1H), 2.28–2.19 (m, 1H), 2.05–1.98 (m, 1H), 1.94–1.86 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 179.5, 144.1, 140.1, 128.9, 128.6, 128.3, 127.6, 126.2, 125.7, 102.5, 72.9, 57.8, 38.3, 33.4, 31.1, 30.6; IR (film): ν_{max} 3027, 2951, 2882, 1713, 1497, 1453, 1355, 1029, 700 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{22}NO_2$ 308.1651; Found 308.1647.

(*R*)-1′-((*R*)-2-Hydroxy-1-phenylethyl)-spiro[indane-1,2′-pyrrolidin]-5′-one (4a) and (*S*)-1′-((*R*)-2-Hydroxy-1-phenylethyl)-spiro[indane-1,2′-pyrrolidin]-5′-one (4a′)[36]: To a three-necked flask equipped with a dropping funnel, $AlCl_3$ (1.0 g, 7.5 mmol) in DCE (15 mL) was added under N_2 atmosphere. The solution was cooled to –5 °C. Compound **3a** (461 mg, 1.5 mmol) in DCE (15 mL) was added dropwise to the flask under N_2 atmosphere through the dropping funnel. The mixture was stirred at –5 °C for 12 h, and then poured onto ice, acidified by with dilute sulfuric acid (1 N) and extracted twice with CH_2Cl_2. The CH_2Cl_2 solution was dried over anhydrous Na_2SO_4. The solvent was removed by rotary evaporation to give a mixture of **4a** and **4a′**. The crude product was purified by column chromatography (AcOEt) to afford **4a** as a white solid (311 mg, 67% yield).

(*R*)-1′-((*R*)-2-Hydroxy-1-phenylethyl)-spiro[indane-1,2′-pyrrolidin]-5′-one (4a): R_f = 0.34 (AcOEt); m.p. 194.0–194.8 °C; $[\alpha]_D^{20}$ +63.8 (*c* 1.05, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.22–7.18 (m, 4H), 7.15–7.09 (m, 3H), 6.79 (t, *J* = 7.4Hz, 1H), 6.46 (d, *J* = 7.6Hz, 1H), 4.32–4.25 (m, 1H), 4.03 (dd, *J* = 9.0, 4.0Hz, 1H), 3.98–3.92 (m, 2H), 3.09–3.02 (m, 1H), 2.96–2.88 (m, 1H), 2.764–2.58 (m, 2H), 2.43–2.3 (m, 2H), 2.29–2.23 (m, 1H), 2.19–2.11 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 177.2, 143.2, 143.0, 139.2, 128.6, 128.2, 128.1, 127.3, 126.6, 124.8, 124.7, 77.6, 77.5, 76.8, 65.3, 61.9, 35.9, 35.2, 31.2, 29.5; IR (film): ν_{max} 3331, 1662, 1420, 1357, 1079, 759 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{22}NO_2$ 308.1651; Found 308.1645.

(*S*)-1′-((*R*)-2-Hydroxy-1-phenylethyl)-spiro[indane-1,2′-pyrrolidin]-5′-one (4a′): Light yellow solid (105 mg, 23% yield), R_f = 0.53 (AcOEt); m.p. 112.7–113.0 °C; $[\alpha]_D^{20}$ +50.3 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.30 (m, 4H), 7.27–7.24 (m, 3H), 7.22–7.20 (m, 2H), 4.94–4.91 (m, 1H), 4.12–4.01 (m, 3H), 2.82–2.66 (m, 4H), 2.34–2.20 (m, 2H), 2.02–1.90 (m, 2H), 2.96–2.88 (m, 1H), 2.764–2.58 (m, 2H), 2.43–2.30 (m, 2H), 2.29–2.23 (m, 1H), 2.19–2.11 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 177.6, 144.6, 143.1, 139.2, 128.9, 128.6, 127.7, 127.5, 127.4, 125.5, 123.0, 77.5, 77.4, 76.8, 66.0, 61.3, 36.8, 35.2, 30.8, 29.4; IR (film): ν_{max} 3383, 1665, 1419, 1352, 1077 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{22}NO_2$ 308.1651; Found 308.1646.

(*R*)-1'-(1-Phenylvinyl)-spiro[indane-1,2′-pyrrolidin]-5'-one (5a): A mixture of **4a** (311 mg, 1.01 mmol) and $LiOH{\cdot}H_2O$ (425 mg, 10.1 mmol) in DMSO (20 mL) was heated at 170 °C for 12 h under N_2 atmosphere. The mixture was cooled to room temperature, diluted with H_2O, and extracted with AcOEt. The organic layers were washed with brine, and the brine washings back-extracted with AcOEt. The organic phase was dried over anhydrous Na_2SO_4. The solvent was removed to give crude **5a**. The crude product was purified by column chromatography (AcOEt) to afford **5a** as a brown oil (269 mg, 92% yield). R_f = 0.65 (AcOEt); $[\alpha]_D^{20}$ +57.1 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.32 (m, 2H), 7.30–7.26 (m, 3H), 7.20–7.16 (m, 3H), 5.49 (s, 1H), 4.73 (s, 1H), 2.91–2.66 (m, 4H), 2.45–2.35 (m, 3H), 2.09–2.03 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.5, 145.0, 142.6, 142.0, 137.3, 128.34, 128.25, 128.2, 126.8, 125.7, 125.0, 122.9, 114.9, 75.9, 37.2, 35.3, 30.4, 29.6; IR (film): ν_{max} 2934, 2850, 1699, 1626, 1364, 773 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{20}NO$ 290.1545; Found 290.1538.

(*R*)-Spiro[indane-1,2′-pyrrolidin]-5'-one (6a): A solution of **5a** (269 mg, 0.93 mmol) and 4 N aqueous HCl (2.3 mL) in THF (20 mL) was heated to reflux for 8 h. After cooling to room temperature, aq. $NaHCO_3$ was added till the bubbling ceased. After concentration in vacuo, the residue was extracted with CH_2Cl_2 and the combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed and the crude product was purified by column chromatography (AcOEt) to afford **6a** as a white solid (162 mg, 93% yield). R_f = 0.31 (AcOEt); m.p. 139.5–139.7 °C; $[\alpha]_D^{20}$ −24.3 (*c* 1.05, $CHCl_3$); HPLC (Daicel AD-H column, *n*-hexane:*i*-PrOH = 95:5, Flow rate = 1 mL/min, λ = 220 nm): t_{minor} = 15.7 min, t_{major} = 20.0 min. ^1H NMR (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 4H), 6.09 (s, 1H), 2.94–2.90 (m, 2H), 2.55–2.51 (m, 2H), 2.39–2.26 (m, 2H), 2.20–2.11 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 177.7, 146.3, 142.2, 128.4, 127.3, 125.0, 122.4, 69.6, 40.3, 35.2, 30.7, 29.2; IR (film): ν_{max} 3174, 2940, 2848, 2847, 1694, 1660, 1653, 1458, 1357, 763 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{12}H_{14}NO$ 187.1075, Found 188.1074.

(*R*)-Spiro[indane-1,2′-pyrrolidine] (7): A Schlenk tube was charged with **6a** (137 mg, 0.73 mmol) and anhydrous Et_2O (10 mL). The solution was cooled to 0 °C. $LiAlH_4$ (139 mg, 3.7 mmol) was added portionwise. The resulting mixture was stirred at 50 °C (oil bath) for 24 h. After cooling to room temperature, the mixture was diluted with AcOEt and quenched with small amount of 1 N NaOH. Then the mixture was stirred for 20 min. The resulting suspension was filtered through Celite and the filter cake washed with AcOEt. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to afford **7** as a brown oil (137 mg, >99% yield). The product was directly used without further purification. R_f = 0.37 (MeOH); $[\alpha]_D^{20}$ −13.4 (*c* 1.30, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.23–7.21 (m, 1H), 7.17–7.16 (s, 1H), 3.20–3.14 (m, 1H), 3.07–3.01 (m, 1H), 2.97–2.90 (m, 1H), 2.83–2.76 (m, 2H), 2.13–1.85 (m, 7H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.4, 143.0, 127.1, 126.5, 124.5, 122.0, 72.4, 45.5, 41.5, 38.1, 29.9, 26.0; IR (film): ν_{max} 2955, 2943, 2850, 1457, 756 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{12}H_{16}N$ 174.1283; Found 174.1280.

Ethyl (*E*)-6-(3-methoxyphenyl)-4-oxo-5-hexenoate: To a three-necked flask equipped with a Dean-Stark apparatus, ethyl levulinate (23.0 mL, 164 mmol), piperidine (3.0 mL, 32.8 mmol), acetic acid (9.4 mL, 164 mmol), 3-methoxybenzaldehyde (10.0 mL, 82.0 mmol) and benzene (100 mL) were added. The mixture was stirred at 100 °C (oil bath) for 12 h. Water was removed via a Dean-Stark apparatus. The solution was washed with 2 N HCl, saturated $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated, and excess ethyl levulinate was distilled out under vacuum and recovered. The crude product was purified by column chromatography (5:1 hexanes/AcOEt) to afford the product as a brown oil (18.28 g, 85% yield). R_f = 0.33 (5:1 hexanes/AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 16.2Hz, 1H), 7.31 (t, J = 7.9 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 7.06 (t, J = 2.0 Hz, 1H), 6.95 (dd, J = 8.2, 2.0 Hz, 1H), 6.74 (d, J= 16.2 Hz, 1H), 4.16 (q, J= 7.2 Hz, 2H), 3.84 (s, 3H), 3.02 (t, J = 6.7 Hz, 2H), 2.69 (t, J = 6.7 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 198.1, 172.9, 160.0, 142.8, 135.8, 130.0, 126.2, 121.1, 116.5, 113.1, 60.7, 55.4, 35.3, 28.2, 14.2; IR (film): ν_{max} 2980, 2938, 1732, 1667, 1613, 1578, 1489, 1260, 1159, 1099, 1042, 858, 783, 689 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{15}H_{18}NaO_4$ 285.1103; Found 285.1094.

Ethyl 6-(3-methoxyphenyl)-4-oxohexanoate: To a round-bottom flask, ethyl (*E*)-6-(3-methoxyphenyl)-4-oxo-5-hexenoate (18.28 g, 70.0 mmol), 10% Pd/C (1.00 g), and EtOH (150 mL) were added. The mixture was well stirred under hydrogen atmosphere for 24 h. Pd/C was filtered off. The filtrate was concentrated and the residue dried in vacuo to give the product as a brown oil (17.90 g, 97% yield), which was directly used without further purification. R_f = 0.33 (5:1 hexanes/AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (dd, J = 8.8, 7.8 Hz, 1H), 6.76–6.71 (m, 3H), 4.11 (q, J = 6.9 Hz, 2H), 3.77 (s, 3H), 2.88 (t, J = 7.5 Hz, 2H), 2.77 (t, J = 7.0 Hz, 2H), 2.69 (t, J= 6.9 Hz, 2H), 2.56 (t, J= 6.1 Hz, 2H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 207.9, 172.7, 159.7, 142.6, 129.4, 120.6, 114.0, 111.4, 60.6, 55.1, 44.1, 37.2, 29.7, 27.9, 14.1; IR (film): ν_{max} 2964, 2913, 1719, 1593, 1260, 1093, 1025, 866, 799, 694 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{15}H_{20}NaO_4$ 287.1259; Found 287.1255.

Ethyl 6-(2-bromo-5-methoxyphenyl)-4-oxohexanoate[37]: To a three-necked flask equipped with a dropping funnel,ethyl 6-(3-methoxyphenyl)-4-oxohexanoate (17.90 g, 67.7 mmol) in anhydrous CH_2Cl_2 (100 mL) was added under N_2 atmosphere. Then pyridine (10.0 mL, 124.7 mmol) was added. The solution was cooled to –10 °C. Anhydrous Br_2 (6.0 mL, 117.8 mmol) in anhydrous CH_2Cl_2 (30 mL) was added dropwise to the flask under N_2 atmosphere through the dropping funnel. The mixture was stirred at room temperature for 12 h. The reaction was quenched with saturated aq. $NaHCO_3$. The organic layers were washed with 1 N aqueous HCl, brine, and dried over anhydrous Na_2SO_4. The solvent was removed by rotary evaporation. The crude product was purified by column chromatography (5:1 hexanes/AcOEt) to afford the productas a colorless oil (23.3 g, >99% yield). R_f = 0.33 (5:1 hexanes/AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 8.8 Hz, 1H), 6.78 (d, J = 3.0 Hz, 1H), 6.63 (dd, J = 8.8 Hz, 3.0 Hz, 1H), 4.12 (q, J = 7.2 Hz, 2H), 3.76 (s, 3H), 2.97 (t, J = 7.3 Hz, 2H), 2.78 (t, J= 8.0 Hz, 2H), 2.72 (t, J= 6.3 Hz, 2H), 2.58 (t, J = 6.7 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 207.6, 172.7, 159.1, 141.3, 133.4, 116.2, 114.7, 113.7, 60.7, 55.5, 42.5, 37.2, 30.5, 28.1, 14.2; IR (film): ν_{max} 2932, 1724, 1586, 1472, 1248, 1175, 1094, 1024, 802, 600 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{15}H_{20}BrO_4$ 343.0545; Found 343.0538.

6-(2-Bromo-5-methoxyphenyl)-4-oxohexanoic acid (2b): To a round-bottom flask, ethyl 6-(2-bromo-5-methoxyphenyl)-4-oxohexanoate (23.3 g, 67.9 mmol) and EtOH/H_2O (100 mL/100 mL) were added. To this solution, NaOH (5.59 g, 140 mmol) in 100 mL H_2O was added dropwise. After stirring for 2 h at room temperature, 1 N HCl was added dropwise till the pH was approximately 7. EtOH was evaporated. 1 N HCl was added dropwise with stirring till the pH was about 1. The solvent was removed by rotary evaporation. The residue was dissolved in CH_2Cl_2, washed with saturated brine, and dried over anhydrous Na_2SO_4. CH_2Cl_2 was evaporated to afford **2b** as a brown solid (20.98 g, 98% yield). The product was directly used without further purification. R_f = 0.31 (2:1 hexanes/AcOEt); m.p. 83.0–84.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, J = 8.8 Hz, 1H), 6.78 (d, J = 3.0 Hz, 1H), 6.63 (m, 1H), 3.78 (s, 1H), 3.76 (s, 3H), 2.97 (t, J= 8.0 Hz, 2H), 2.78 (t, J= 7.4 Hz, 2H), 2.72 (t, J= 5.6 Hz, 2H), 2.64 (t, J = 6.2 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 207.4, 178.6, 159.0, 141.1, 133.3, 116.1, 114.6, 113.7, 55.4, 42.3, 36.8, 30.4, 27.8; IR (film): ν_{max} 2939, 1712, 1580, 1473, 1244, 1167 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{13}H_{15}BrNaO_4$ 337.0051; Found 337.0047.

(3*R*,7a*S*)-7a-(2-Bromo-5-methoxyphenethyl)-3-phenyltetrahydropyrrolo[2,1-*b*]oxazol-5-one (3b): To a round-bottom flask, **2b** (9.98 g, 31.7 mmol), *D*-phenylglycinol (4.35 g, 31.7 mmol) and toluene (80 mL) were added. The mixture was heated at 130 °C (oil bath) for 36 h. Water was removed by a Dean-Stark apparatus. After cooling, the solvent was removed by rotary evaporation. The residue was purified by column chromatography (2:1 hexanes/AcOEt) to afford **3b** as a yellow oil (12.11 g, 92% yield). R_f = 0.31 (2:1 hexanes/AcOEt); $[\alpha]_D^{20}$ −81.9 (*c* 1.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.32 (m, 3H), 7.28–7.26 (m, 3H), 6.62–6.56 (m, 2H), 5.2 (t, 1H), 4.67 (t, J = 8.5 Hz, 1H), 4.18 (dd, J= 8.7, 7.3 Hz, 1H), 3.71 (s, 3H), 2.95–2.86 (m, 1H), 2.84–2.76 (m, 1H), 2.75–2.70 (m, 1H), 2.68–2.61 (m, 1H), 2.58–2.51 (m, 1H), 2.29–2.21 (m, 1H), 2.03–1.96 (m, 1H), 1.88–1.81 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 179.2, 158.9, 141.0, 139.8, 133.2, 128.6, 127.3, 125.5, 115.8, 114.4, 113.3, 102, 72.6, 57.4, 55.2, 36.3, 33.1, 31.2, 30.7; IR (film): ν_{max} 2958, 2938, 1714, 1572, 1475, 1364, 1241, 1027, 699 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{23}BrNO_3$ 416.0861; Found 416.0855.

(*R*)-4-Bromo-1'-((*R*)-2-hydroxy-1-phenylethyl)-7-methoxy-spiro[indane-1,2′-pyrrolidin]-5'-one (4b) and (*S*)-4-bromo-1'-((*R*)-2-hydroxy-1-phenylethyl)-7-methoxy-2,3-dihydrospiro[1*H*-indene-1,2'-pyrrolidin]-5'-one (4b′)[36]: To a three-necked flask equipped with a dropping funnel, $AlCl_3$ (11.64 g, 87.3 mmol) in DCE (100 mL) was added under N_2 atmosphere. The solution was cooled to –10 °C. Compound **3b** (12.11 g, 29.09 mmol) in DCE (50 mL) was added dropwise to the flask under N_2 atmosphere through the dropping funnel. The mixture was stirred at –10 °C for 48 h. It was poured onto ice, acidified by addition of dilute sulfuric acid (1 N) and extracted twice with CH_2Cl_2. The CH_2Cl_2 solution was dried over anhydrous Na_2SO_4. The solvent was removed by rotary evaporation to give a mixture of **4b** and **4b′**. **4b** crystallized out from a solution of **4b** and **4b′** in acetone and hexanes. Most **4b** could be obtained after three crystallizations. The

remaining **4b** and **4b′** was subjected to column chromatography (AcOEt) to afford **4b′** as a white solid.

(*R*)-4-Bromo-1'-((*R*)-2-hydroxy-1-phenylethyl)-7-methoxy-spiro[indane-1,2′-pyrrolidin]-5'-one (4b): White solid (5.80 g, 48% yield). R_f = 0.48 (AcOEt); m.p. 169.0–170.2 °C; $[\alpha]_D^{20}$ −12.1 (*c* 1.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (d, *J* = 8.6 Hz, 1H), 7.05–7.02 (m, 3H), 6.96–6.94 (m, 2H), 6.06 (d, *J* = 8.6 Hz, 1H), 4.34–4.27 (m, 1H), 4.08–4.05 (m, 1H), 3.93–3.88 (m, 1H), 3.84–3.82 (m, 1H), 3.19 (s, 3H), 3.12–3.04 (m, 1H), 2.97–2.90 (m, 1H), 2.76–2.68 (m, 1H), 2.66–2.55 (m, 3H), 2.39–2.31 (m, 1H), 2.17–2.09 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 176.6, 155.6, 144.9, 138.7, 133.0, 131.8, 128.0, 127.5, 126.9, 110.2, 110.1, 77.3, 65.0, 62.1, 54.4, 38.4, 32.8, 32.4, 31.3; IR (film): ν_{max} 3360, 2940, 1659, 1473, 1438, 1359, 1267, 1074, 1049, 757, 702 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{23}BrNO_3$ 416.0861; Found 416.0852.

(*S*)-4-Bromo-1'-((*R*)-2-hydroxy-1-phenylethyl)-7-methoxy-2,3-dihydrospiro[1H-indene-1,2'-pyrrolidin]-5'-one (4b′): White solid (5.07 g, 42% yield), R_f = 0.53 (AcOEt); m.p. 85.5–86.6 °C; $[\alpha]_D^{20}$ +59.0 (*c* 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 8.6 Hz, 1H), 7.34–7.30 (m, 2H), 7.27–7.23 (m, 3H), 6.70 (d, *J* = 8.6 Hz, 1H), 5.03 (dd, *J* = 6.6, 4.9 Hz, 1H), 3.97–3.94 (m, 2H), 3.92–3.90 (m, 1H), 3.86 (s, 3H), 3.81–2.63 (m, 4H), 2.51–2.44 (m, 1H), 2.24–2.17 (m, 1H), 2.10–2.03 (m, 1H), 1.98–1.91 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 177.2, 155.5, 145.2, 139.1, 133.2, 132.4, 128.5, 127.3, 127.2, 111.2, 111.1, 78.2, 65.0, 61.5, 55.4, 36.9, 33.2, 31.2, 31.1; IR (film): ν_{max} 3337, 2943, 1663, 1581, 1474, 1437, 1417, 1351, 1266, 1181, 1081, 756 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{23}BrNO_3$ 416.0861; Found 416.0857.

Note: When **3b** was reacted with 5 equiv $AlCl_3$ in DCE at −5 °C, (±)-**6b** was always isolated in ca. 9% yield except for **4b** and **4b′**.

(*S*)-1'-((*R*)-2-Hydroxy-1-phenylethyl)-7-methoxy-spiro[indane-1,2′-pyrrolidin]-5'-one (debrominated 4b'): To a round-bottom flask, **4b′** (621 mg, 1.5 mmol), 10% Pd/C (10 mg) and MeOH (40 mL) were added. The mixture was well stirred under hydrogen atmosphere for 12 h. Pd/C was filtered off. The solvent was removed by rotary evaporation. The residue was dissolved in CH_2Cl_2, washed with saturated aq. $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. The filtrate was concentrated and the residue dried in vacuo to give a white solid (478 mg, 95% yield). R_f = 0.39 (AcOEt); m.p. 139.8–140.5 °C; $[\alpha]_D^{20}$ +69.4 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.23 (m, 6H), 6.84 (d, *J* = 7.6 Hz,1H), 6.78 (d, *J* = 8.1 Hz, 1H), 5.14 (br, 1H), 3.96 (m, 3H), 3.89 (s, 3H), 2.78–2.68 (m, 4H), 2.52 (m, 1H), 2.21 (m, 1H), 2.04 (m, 1H), 1.95 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 176.9, 155.9, 145.2, 139.2, 130.4, 130.1, 128.0, 127.0, 126.7, 117.2, 108.5, 76.9, 64.7, 60.9, 54.7, 37.3, 32.6, 30.8, 29.3; IR (film): ν_{max} 3321, 2941, 2241, 1660, 1435, 1352, 1265, 1082, 1064, 731, 700 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{24}NO_3$ 338.1756; Found 338.1754.

(*R*)-4-Bromo-7-methoxy-1'-(1-phenylvinyl)-spiro[indane-1,2′-pyrrolidin]-5'-one (5b): A solution of **4b** (5.80 g, 14.0 mmol) and $LiOH{\cdot}H_2O$ (5.87 g, 140 mmol) in DMSO (50 mL) was heated at 170 °C for 12 h under N_2 atmosphere. The mixture was cooled to room temperature, diluted with H_2O, and extracted with AcOEt. The organic layers were washed with brine, and the brine washings back-extracted with AcOEt. The organic phase was dried over anhydrous Na_2SO_4. The solvent was removed by rotary evaporation to give a mixture of **5b** and debrominated **5b**. The crude product was purified by column chromatography (1:2 hexanes/AcOEt) to afford **5b** as a brown oil (4.46 g, 80% yield). R_f = 0.32 (1:2 hexanes/AcOEt). $[\alpha]_D^{20}$ +75.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 3H), 7.21–7.19 (m, 3H), 6.52 (d, *J* = 8.6 Hz, 1H), 5.50 (s, 1H), 4.78 (s, 1H), 3.82 (s, 3H), 2.98–2.87 (m, 1H), 2.77–2.60 (m, 4H), 2.45–2.38 (m, 1H), 2.34–2.24 (m, 1H), 2.12–2.05 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.1, 155.6, 145.4, 142.6, 137.5, 133.4, 132.7, 128.3, 128.1, 125.9, 115.8, 110.8, 110.6, 76.5, 55.4, 38.8, 33.6, 31.8, 31.1; IR (film): ν_{max} 3225, 2930, 1698, 1644, 1577, 1472, 1435, 1416, 1353, 1286, 1265, 1253, 1068, 813, 745, 730, 648 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{21}BrNO_2$ 398.0756; Found 398.0754.

(*R*)-7-Methoxy-1'-(1-phenylvinyl)-spiro[indane-1,2′-pyrrolidin]-5'-one (debrominated 5b): Brown oil (450 mg, 10% yield), R_f = 0.27 (1:2 hexanes/AcOEt). $[\alpha]_D^{20}$ +62.1 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.25 (m, 5H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.67 (s, 1H), 5.48 (s, 1H), 4.73 (s, 1H), 3.77 (s, 3H), 2.88–2.79 (m, 1H), 2.75–2.65 (m, 3H), 2.46–2.35 (m, 3H), 2.11–2.04 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.4, 160.1, 144.7, 142.2, 137.5, 137.0, 128.2, 125.8, 123.9, 115.1, 113.3, 109.7, 77.2, 75.6, 55.3, 37.7, 35.5, 30.5, 29.9; IR (film): ν_{max} 3001, 2922, 2851, 1694, 1609, 1491, 1454, 1368, 1256, 1026, 909, 754 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{22}NO_2$ 320.1651; Found 320.1651.

(*R*)-4-Bromo-7-methoxy-spiro[indane-1,2′-pyrrolidin]-5'-one (6b): A solution of **5b** (4.46 g, 11.1 mmol) and 4 N aqueous HCl (27.8 mL) in THF (100 mL) was heated to reflux for 12 h. After cooling to room temperature, aq. $NaHCO_3$ was added till the bubbling ceased. After concentration in vacuo, the residue was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by column chromatography (AcOEt) to afford **6b** as a white solid (3.06 g, 93% yield). R_f = 0.34 (AcOEt); m.p. 215.6–216.0 °C; $[\alpha]_D^{20}$ −62 (*c* 0.90, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 8.6 Hz, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 5.67 (br s, 1H), 3.80 (s, 3H), 2.89 (m, 2H), 2.64 (m, 1H), 2.50 (m, 2H), 2.67 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 176.6, 154.8, 143.4, 133.4, 131.4, 110.2, 109.7, 69.4, 54.5, 40.0, 32.5, 30.0, 29.9; IR (film): ν_{max} 3219, 2932, 1697, 1644, 1577, 1472, 1262, 1073 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{13}H_{15}BrNO_2$ 296.0286; Found 296.0280.

(*R*)-7-Methoxy-spiro[indane-1,2′-pyrrolidin]-5'-one (8): To a round-bottom flask, **6b** (3.06 g, 10.3 mmol), 10% Pd/C (200 mg) and MeOH (100 mL) were added. The mixture was well stirred under hydrogen atmosphere for 24 h. Pd/C was filtered off. The solvent was removed by rotary evaporation. The residue was dissolved in CH_2Cl_2, washed with saturated aq. $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. The filtrate was concentrated and the residue dried in vacuo to give **8** as a white solid (2.24 g, 99% yield). R_f = 0.34 (AcOEt); m.p. 218.7–220.0 °C; $[\alpha]_D^{20}$ −49.2 (*c* 1.00, $CHCl_3$); HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 90:10, Flow rate = 1 mL/min, λ = 220 nm): t_{minor} = 9.1 min, t_{major} = 14.5 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (t, *J* = 8.0 Hz, 1H), 6.81 (d, *J* = 7.2 Hz, 1H), 6.72 (d, *J* = 7.6 Hz, 1H), 5.73 (br s, 1H), 3.81 (s, 3H), 2.97–2.82 (m, 2H), 2.71–2.57 (m, 1H), 2.57–2.43 (m, 2H), 2.34–2.17 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 177.7, 156.7, 144.9, 132.5, 130.2, 117.3, 109.1, 69.4, 55.3,

42.0, 33.5, 31.1, 29.8, 29.7; IR (film): ν_{max} 2926, 1654, 1635, 1592, 1480, 1266, 1064 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{13}H_{16}NO_2$ 218.1181; Found 218.1178.

Note: After filtering off Pd/C, the filtrate was concentrated to give the crude product as a white crystalline solid, which was a mixture of **8** with HBr and CH_3OH. The crystal structure and ^{1}H NMR data of the mixture are as following. The ^{1}H NMR chemical shifts changed as the mixture was placed at rt for some time. After silica gel chromatography or aq. $NaHCO_3$ treatment, HBr and CH_3OH were completely removed from the mixture. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (br s, 1H), 8.35 (br s, 1H), 7.25 (t, J = 7.2 Hz, 1H), 6.83 (d, J = 7.6 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 3.83 (s, 3H), 3.02–2.98 (m, 2H), 2.92–2.75(m, 2H), 2.62–2.54 (m, 1H), 2.50-2.41 (m, 1H), 2.33–2.24 (m, 2H).

(*R*)-7-Hydroxy-spiro[indane-1,2′-pyrrolidin]-5'-one (9): A Schlenk tube was charged with **8** (2.24 g, 10.3 mmol) and anhydrous CH_2Cl_2 (40 mL). The solution was cooled to –78 °C. Then BBr_3 (4.85 mL, 51.5 mmol) was added dropwise under N_2 atmosphere. After that, the mixture was stirred at –20 °C for 24 h, and then quenched by adding water dropwise. Brine was added followed by $NaHCO_3$ till the pH was approximately 7. After concentration in vacuo, the residue was extracted with THF. The combined organic layers were dried over anhydrous Na_2SO_4. The filtrate was concentrated and the residue was dried in vacuo to give **9** as a white solid (2.09 g, 99% yield). R_f = 0.27 (AcOEt); m.p. 229.0–230.1 °C; $[\alpha]_D^{20}$ −59.9 (*c* 1.00, MeOH); HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 90:10, Flow rate = 1 mL/min, λ = 220 nm): t_{minor} = 10.1 min, t_{major} = 19.5 min. ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.43 (s, 1H), 7.88 (s, 1H), 7.01 (t, J = 7.8 Hz, 1H), 6.62 (t, J = 6.6 Hz, 2H), 2.87–2.83 (m, 1H), 2.73–2.69 (m, 1H), 2.49–2.43 (m, 1H), 2.38–2.33 (m, 1H), 2.25–2.19 (m, 1H), 2.18–2.07 (m, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 176.6, 155.1, 145.7, 132.5, 129.9, 116.1, 114.5, 69.2, 42.2, 33.4, 31.8, 30.1; IR (film): ν_{max} 3194, 2941, 1705, 1592, 1281, 1004, 777, 744 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{12}H_{14}NO_2$ 204.1025; Found 204.1016.

(*R*)-7-Trifluoromethanesulfoxy-spiro[indane-1,2′-pyrrolidin]-5′-one (10): A Schlenk tube was charged with **9** (2.09 g, 10.3 mmol), $PhNTf_2$ (5.5 g, 15.5 mmol), Cs_2CO_3 (5.1 g, 15.5 mmol) and anhydrous DMF (40 mL) under N_2 atmosphere. The mixture was stirred at room temperature for 36 h, and then diluted with H_2O, extracted with CH_2Cl_2. The organic layers were washed with saturated aqueous NH_4Cl and brine. The aqueous layers were back-extracted with CH_2Cl_2. The combined organic phases were dried over Na_2SO_4. The solvent was removed and the crude product purified by column chromatography (AcOEt) to afford **10** as a white solid (3.45 g, 99% yield). R_f = 0.41 (AcOEt); m.p. 62.0–63.7 °C; $[\alpha]_D^{20}$ −4.70 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.28 (m, 1H), 7.21–7.19 (m, 1H), 7.15–7.00 (m, 1H), 3.00–2.88 (m, 2H), 2.56–2.52 (m, 2H), 2.36–2.23 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 177.9, 146.9, 136.8, 130.6, 128.9, 125.2, 119.6, 118.2 (q, J = 318 Hz, CF_3), 69.6, 41.3, 33.0, 30.1, 29.3; IR (film): ν_{max} 3242, 2922, 1697, 1666, 1462, 1419, 1356, 1305, 1207, 1141, 979, 929, 856, 605 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{13}H_{13}F_3NO_4S$ 336.0517; Found 336.0511.

Note: PhNHTf was eluted out following **10**. ^{13}C NMR indicated **10** was contaminated with small amount of PhNHTf (δ 145.9, 139.2, 124.2, 123.1). Small amount of crystals of a 1:1 complex of **10** with PhNHTf was obtained from the elution.

(*R*)-7-(Diphenylphosphinoyl)-spiro[indane-1,2′-pyrrolidin]-5'-one (11a): A Schlenk tube was charged with **10** (1.23 g, 3.67 mmol), *i*-Pr_2NEt (2.5 mL, 14.7 mmol), dppb (76.8 mg, 0.18 mmol), $Pd(OAc)_2$ (40 mg, 0.18 mmol) and anhydrous DMSO (40 mL) under N_2 atmosphere. Diphenyphosphine oxide (1.48 g, 7.3 mmol) was added. The resulting solution was stirred at 100 °C for 24 h. After cooling to room temperature, the mixture was diluted with H_2O, and extracted with AcOEt. The organic layers were washed with 1 N aqueous HCl, saturated $NaHCO_3$,brine, and dried over anhydrous Na_2SO_4. The solvent was removed by rotary evaporation. The crude product was purified by column chromatography (10:1 AcOEt/MeOH) to afford **11a** as a white solid (1.36 g, 96% yield, 100% ee). R_f = 0.22 (10:1 AcOEt/MeOH). m.p. 184.4–184.7 °C; $[\alpha]_D^{20}$ +87.4 (*c* 0.95, $CHCl_3$); HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 90:10, Flow rate = 1.0 mL/min, λ = 210 nm): t_{major} = 22.1 min, t_{minor} = 31.3 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68–7.60 (m, 4H), 7.57–7.45 (m, 6H), 7.39 (d, J = 7.5 Hz, 1H), 7.18(td, J = 7.6, 2.1 Hz, 1H), 6.90(dd, J = 14.2, 7.6 Hz, 1H), 5.43 (br s, 1H), 2.98–2.85 (m, 2H), 2.46 (q, J = 10.4 Hz, 1H), 2.36–2.17 (m, 3H), 2.11 (t, J = 9.9 Hz, 1H), 1.96 (q, J = 11.5 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 177.6, 150.6, 144.6, 132.9, 132.2, 131.8, 131.4, 129.2, 128.7, 128.8, 128.7, 128.6, 128.6, 127.3, 70.7, 41.7, 33.1, 29.9, 29.3; ^{31}P NMR (243 MHz, $CDCl_3$): δ 30.73 (1P); IR (film): ν_{max} 2920, 2850, 2359, 2341, 1697, 1437, 1180, 1116, 721, 694, 545 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{24}H_{23}NO_2P$ 388.1466; Found 388.1483.

(*R*)-7-(Di(*p*-tolyl)phosphinoyl)-spiro[indane-1,2′-pyrrolidin]-5'-one (11b): White solid (>99% yield), R_f = 0.17 (10:1 AcOEt/MeOH); m.p. 108.8–109.4 °C; $[\alpha]_D^{20}$ +57.8 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.48 (m, 4H), 7.36 (d, J = 7.4 Hz, 1H), 7.31–7.26 (m, 4H), 7.17–7.14 (m, 1H), 6.91 (dd, J = 14.0, 7.84 Hz, 1H), 5.38 (br s, 1H), 2.97–2.83 (m, 2H), 2.54–2.46 (m, 1H), 2.41 (s, 3H), 2.40 (s, 3H), 2.36–2.21 (m, 4H), 2.12–2.07 (m, 1H), 1.98–1.90 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 177.2, 150.4, 144.4, 144.3, 142.3, 142.2, 133.0, 132.9, 132.4, 132.3, 131.5, 131.4, 130.8, 130.6, 130.1, 129.7, 129.6, 129.54, 129.49, 129.3, 129.2, 129.1, 127.4, 127.3, 77.4, 70.6, 14.8, 41.2, 33.2, 29.8, 29.0, 21.74, 21.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ 30.7; IR (film): ν_{max} 3430, 2950, 2364, 1700, 1602, 1405, 1181, 1115, 925, 730, 660, 623, 541 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{26}H_{27}NO_2P$ 416.1779; Found 416.1771.

(*R*)-7-(Bis(3,5-dimethylphenyl)phosphinoyl)-spiro[indane-1,2′-pyrrolidin]-5'-one (11c): White solid (76% yield), R_f = 0.29 (5:1 AcOEt /MeOH); m.p. 124.1–124.6 °C; $[\alpha]_D^{20}$ +20.0 (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, J = 7.4 Hz, 1H), 7.28–7.23 (m, 4H), 7.20–7.15 (m, 3H), 6.94 (dd, J = 14.1, 7.6 Hz, 1H), 5.63 (br s, 1H), 2.93–2.84 (m, 2H), 2.50–2.45 (m, 1H), 2.37–2.17 (m, 14H), 2.11–2.07 (m, 1H), 1.97–1.89 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 177.4, 150.34, 150.27, 144.4, 144.3, 138.5, 138.4, 138.3, 138.1, 133.7, 133.5, 133.2, 133.0, 132.9, 132.4, 132.1, 130.0, 129.9, 129.8, 129.04, 128.94, 127.4, 127.3, 70.4, 41.7, 32.9, 29.9, 29.0, 21.5, 21.4; ^{31}P NMR (162 MHz, $CDCl_3$): δ 31.0; IR (film): ν_{max} 2951, 2922, 1705, 1456, 1418, 1182, 1126, 872, 849, 731, 694, 581 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{28}H_{30}NNaO_2P$ 466.1912; Found 466.1903.

(*R*)-7-(Bis(3,5-di-*tert*-butylphenyl)phosphinoyl)-spiro[indane-1,2′-pyrrolidin]-5'-one (11d): White solid (83% yield); R_f = 0.51 (10:1 EtOAc/MeOH); m.p. 104.9–105.1 °C; $[\alpha]_D^{20}$ +18.0 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 4.6 Hz, 2H), 7.44 (t, *J* = 12.8 Hz, 4H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.16 (td, *J* =7.6, 2.0 Hz, 1H), 6.88 (dd, *J* =14.4, 7.6 Hz, 1H), 5.83 (br s, 1H), 2.90–2.86 (m, 2H), 2.26–2.16 (m, 3H), 2.05–1.90 (m, 3H), 1.27 (d, 36H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 176.7, 151.1, 150.8, 149.9, 144.3, 132.8, 132.3, 131.2, 130.1, 129.1, 127.3, 126.3, 125.9, 125.7, 118.7, 115.7, 70.6, 41.6, 35.0, 32.6, 31.3, 29.5, 28.9; ^{31}P NMR (162 MHz, $CDCl_3$): δ 33.2; IR (film): ν_{max} 3430, 2964, 2868, 2228, 1705, 1696, 1592 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{40}H_{55}NO_2P$ 612.3970; Found 612.3969.

(*R*)-7-(Diphenylphosphanyl)-2,3-dihydrospiro[indene-1,2'-pyrrolidin]-5'-one (12a) and (*R*)-7-(Diphenylphosphino)-spiro[indane-1,2′-pyrrolidine] (1a): A Schlenk tube was charged with **11a** (1.36 g, 3.51 mmol) and anhydrous toluene (10 mL). Cl_3SiH (5.78 mL, 55.1 mmol) was added at 0 °C under N_2 atmosphere. The mixture was degassed and covered with N_2. The resulting solution was stirred at 85 °C for 24 h. After cooling to room temperature, the solvent was removed under vacuum and anhydrous THF (5 mL) was added. The solution was cooled to 0 °C, a mixture of $LiAlH_4$ (694 mg, 18.3 mmol) and THF (5 mL) was added dropwise. The mixture was degassed and covered with N_2. The resulting mixture was stirred at 60 °C for 24 h. After cooling to room temperature, the mixture was diluted with AcOEt and quenched with small amount of 1 N NaOH. Then 1 N NaOH (10 mL) was added and the mixture was stirred for 20 min. The aqueous layer was extracted with AcOEt. The combined organic layers were washed with brine and dried over Na_2SO_4. After filtration, the filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (AcOEt) under N_2 to afford **1a** as white solid (1.08 g, 86% yield).

Note: Under the above conditions, **11a** was reduced by Cl_3SiH to a mixture of **12a** and **1a**, which resulted in a low isolated yield of **12a**. In both steps, degassing was necessary for a high yield. In the air, **1a** was stable but prone to deteriorate during silica gel chromatography. N_2 flow as well as deoxygenated eluent should be used for chromatography.

(*R*)-7-(Diphenylphosphanyl)-2,3-dihydrospiro[indene-1,2'-pyrrolidin]-5'-one (12a): Colorless oil (442 mg, 66% yield), R_f = 0.20 (AcOEt); $[\alpha]_D^{20}$ +13.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.18 (m, 12H), 6.88–6.85 (m, 1H), 5.32 (s, 1H), 2.90–2.87 (m, 2H), 2.59–2.46 (m, 3H), 2.32–2.23 (m, 2H), 2.03–1.97 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 177.3, 150.6, 144.5, 144.4, 132.3, 132.2, 131.5, 131.4, 129.3, 128.8, 128.7, 128.6, 128.5, 70.6, 41.7, 33.2, 29.8, 29.0; ^{31}P NMR (162 MHz, $CDCl_3$): δ −18.77; IR (film): ν_{max} 3051, 2955, 2936, 2851, 798, 742, 696, 494 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{24}H_{23}NOP$ 372.1517; Found 372.1511.

(*R*)-7-(Diphenylphosphino)-spiro[indane-1,2′-pyrrolidine] (1a): White solid (1.08 g, 86% yield, 100% ee), R_f = 0.22 (AcOEt); m.p. 163.2–163.6 °C; $[\alpha]_D^{20}$ −13.2 (*c* 1.00, $CHCl_3$); HPLC (Daicel AD-H column, *n*-hexane:*i*-PrOH = 70:30, Flow rate = 0.3 mL/min, λ = 254 nm): t_{minor} = 13.2 min, t_{major} = 14.3 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.14 (m, 11H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.84–6.81 (m, 1H), 3.35–3.32 (m, 1H), 2.96–2.76 (m, 4H), 2.09–1.81 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 152.9, 152.7, 133.9, 133.8, 133.5, 128.6, 128.5, 127.6, 125.8, 75.1, 46.2, 46.1, 43.1, 43.1, 38.0, 29.9, 26.5, 1.15; ^{31}P NMR (162 MHz, $CDCl_3$): δ −19.85; IR (film): ν_{max} 3051, 2955, 2936, 2851, 798, 742, 696, 494 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{24}H_{25}NP$ 358.1725; Found 358.1719.

(*R*)-7-(Di(*p*-tolyl)phosphino)-spiro[indane-1,2′-pyrrolidine] (1b): Yellow oil (82% yield), R_f = 0.38 (10:1 AcOEt/MeOH); $[\alpha]_D^{20}$ +7.5 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11–7.00 (m, 10H), 6.80–6.77 (m, 1H), 3.32–3.27 (m, 1H), 2.90–2.67 (m, 4H), 2.27–2.26 (m, 6H), 2.01–1.75 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.0, 142.9, 137.3, 132.8, 132.6, 132.4, 132.2, 128.3, 128.2, 128.1,126.4, 124.6, 74.1, 45.3, 45.2, 41.9, 36.9, 36.8, 28.8, 25.3, 20.3; ^{31}P NMR (162 MHz, $CDCl_3$): δ −22.2; IR (film): ν_{max} 2958, 2858, 1261,1184, 1091,802, 505 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{26}H_{29}NP$ 386.2038; Found 386.2034.

(*R*)-7-(Bis(3,5-dimethylphenyl)phosphino)-spiro[indane-1,2′-pyrrolidine] (1c): Yellow oil (83% yield), R_f = 0.18 (AcOEt); $[\alpha]_D^{20}$ −3.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, *J* =7.2 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.93–6.84 (m, 7H), 3.39–3.64 (m, 1H), 2.93–2.75 (m, 3H), 2.24 (s, 12H), 2.07–1.94 (m, 5H), 1.85–1.83 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 137.7, 137.7, 133.70, 131.5, 131.3, 131.1, 130.9, 130.2, 130.1, 127.3, 125.5, 75.0, 46.4, 46.3, 43.2, 38.1, 38.0, 29.8, 26.5, 21.3; ^{31}P NMR (162 MHz, $CDCl_3$): δ −21.10; IR (film) ν_{max} 2924, 2854, 845, 779, 694 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{28}H_{33}NP$ 414.2351; Found 414.2342.

(*R*)-7-(Bis(3,5-di-*tert*-butylphenyl)phosphino)-spiro[indane-1,2′-pyrrolidine] (1d): White solid (84% yield), R_f = 0.22 (AcOEt), m.p. 184.8–185.1 °C; $[\alpha]_D^{20}$ −6.1 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–6.84 (m, 9H), 3.40–3.36 (m, 1H), 2.96–2.73 (m, 4H), 2.16–1.82 (m, 6H), 1.22 (s, 36H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 152.1, 151.9, 150.6, 150.5, 150.4, 150.3, 144.0, 143.9, 136.6, 136.5, 136.2, 133.3, 133.1, 133.0, 128.4, 128.2, 128.0, 127.7, 127.0, 125.3, 122.3, 122.1, 75.0, 46.5, 46.4, 43.6, 37.4, 37.3, 34.8, 31.3, 29.8, 26.5; ^{31}P NMR (162 MHz, $CDCl_3$): δ −19.85; IR (film): ν_{max} 2958, 2928, 2866, 1216, 1091, 1018, 802 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{40}H_{57}NP$ 582.4229; Found 582.4225.

Note: Chromatography of **1d** was conducted on silica gel in the air. N_2 flow or deoxygenated eluent was not necessary.

(*R*)-7-(Diphenylphosphino)-1'-methyl-spiro[indane-1,2′-pyrrolidine] (1e): A Schlenk tube was charged with **1a** (50 mg, 0.14 mmol), pyridine (36 μL, 0.44 mmol) and anhydrous toluene (5 mL). Then $ClCO_2Et$ (16 μL, 0.16 mmol) was added at 0 °C under N_2 atmosphere. The whole mixture was degassed and covered with N_2, and stirred at room temperature for 21 h. The mixture was diluted with AcOEt, washed with 1 N HCl and brine, and the aq. washings back-extracted with AcOEt. The combined organic phases were dried over Na_2SO_4. The solvent was removed by rotary evaporation to give the crude *N*-ethoxycarbonyl product.

To a Schlenk tube, the crude product and anhydrous THF (5 mL) were added. The solution was cooled to 0 °C, a mixture of $LiAlH_4$ (27 mg, 0.7 mmol) in THF (3 mL) was added dropwise. The whole mixture was degassed and covered with N_2, and stirred at 60 °C for 24 h. After cooling to room temperature, the mixture was diluted with AcOEt and quenched with small amount of H_2O. Then it was washed with 1 N NaOH and brine, and the aq. washings back-extracted

with AcOEt. The combined organic phases were dried over Na_2SO_4. The crude product was purified by column chromatography (AcOEt) to afford **1e** as a white solid (51 mg, 98% yield). R_f = 0.54 (AcOEt); m.p. 98.5–98.8 °C; $[\alpha]_D^{20}$ +32.2 (*c* 1.00, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30–7.28 (m, 2H), 7.23–7.22 (m, 3H), 7.17–7.15 (m, 3H), 7.06–7.05 (m, 3H), 7.01–6.99 (m, 1H), 6.77–6.76 (m, 1H), 3.08–3.04 (m, 1H), 2.79–2.77 (m, 2H), 2.61–2.59 (m, 1H), 2.27–2.23 (m, 1H), 2.07–1.99 (m, 2H), 1.87–1.84 (m, 1H), 1.77–1.75 (m, 1H), 1.49–1.47 (m, 1H), 1.23 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$): δ 134.2, 133.9, 133.4, 133.3, 133.2, 128.1, 128.0, 127.9, 127.3, 127.2, 124.8, 53.3, 38.2, 34.7, 29.7, 29.6, 28.3, 22.7; ^{31}P NMR (243 MHz, $CDCl_3$): δ −18.59; IR (film): ν_{max} 3051, 2961, 2934, 2853, 2778, 1433, 1306, 1261, 1092, 1069, 1040, 1026, 802, 742, 696 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{25}H_{27}NP$ 372.1881; Found 372.1875.

Preparation of Allyl Alcohols: To a mixture of the aldehyde (10 mmol) and the methyl ketone (10 mmol) in EtOH (30 mL), an aqueous solution of 10% NaOH (12 mL) was added at 0 °C. After the addition was complete, the mixture was stirred at room temperature until the conversion was complete (monitored by TLC). The precipitate was collected by filtration and washed with water to afford the *α*,*β*-unsaturated ketone. To a solution of the *α*,*β*-unsaturated ketone (6 mmol) in MeOH, $NaBH_4$ (0.48 g, 12 mmol) was added portionwise at 0 °C and the reaction mixture was further stirred for 5 h at room temperature. The reaction mixture was adjusted to pH = 7 using 1 N HCl solution and the solvent was removed by evaporation. The mixture was extracted with AcOEt and the organic layers were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (5:1 hexanes/AcOEt) to give the allyl alcohol.

Preparation of Allyl Acetates: To a solution of the 1,3-diaryl-2-propenyl alcohol (5.0 mmol) in DCM, acetic anhydride (10.4 mL, 12.5 mmol), triethylamine (10.4 mL, 12.5 mmol), and DMAP (61 mg, 0.5 mmol) were added. The mixture was stirred at room temperature for 24 h followed by addition of H_2O and DCM. The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (20:1 hexanes/AcOEt) to give the allyl acetate.

(*E*)-1,3-Diphenylallyl acetate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.25 (m, 10H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.44 (d, *J* = 6.8 Hz, 1H), 6.21 (dd, *J* = 16.0, 6.8Hz, 1H), 2.14 (s, 3H).

(*E*)-1,3-Di(*o*-tolyl)allyl acetate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.45 (m, 1H, ArH), 7.41–7.39 (m, 1H), 7.24–7.09 (m, 6H), 6.78 (d, *J* = 15.8 Hz, 1H), 6.61 (d, *J* = 6.8 Hz, 1H), 6.19 (dd, *J* = 16.0, 6.8 Hz, 1H), 2.42 (s, 3H), 2.29 (s, 3H), 2.13 (s, 3H).

(*E*)-1,3-Di(*m*-tolyl)allyl acetate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.05 (m, 8H), 6.60 (d, *J* = 16.0 Hz, 1H), 6.40 (d, *J* = 7.2 Hz, 1H), 6.32 (dd, *J* = 16.0, 7.2Hz, 1H), 2.36 (s, 3H), 2.32 (s, 3H), 2.11 (s, 3H).

(*E*)-1,3-Di(*p*-tolyl)allyl acetate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.24 (m, 4H), 7.40–7.33 (m, 8H), 7.18–7.16 (m, 2H), 7.11–7.09 (m, 2H), 6.58 (d, *J* = 16.0 Hz, 1H), 6.40 (d, *J* = 7.2 Hz, 1H), 6.29 (dd, *J* = 15.6, 7.2 Hz, 1H), 2.34 (s, 3H), 2.32 (s, 3H), 2.11 (s, 3H).

(*E*)-1,3-Di(4-chlorophenyl)allyl acetate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.33 (m, 4H), 7.29–7.28 (m, 4H), 6.56 (d, *J* = 16.0 Hz, 1H), 6.38 (d, *J* = 6.8 Hz, 1H), 6.27 (dd, *J* = 16.0, 6.8 Hz, 1H), 2.13 (s, 3H).

(*E*)-1,3-Di(4-methoxyphenyl)allyl acetate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.30 (m, 4H), 6.91–6.89 (m, 2H), 6.85–6.83 (m, 2H), 6.54 (d, *J* = 16.0 Hz, 1H), 6.38 (d, *J* = 6.8 Hz, 1H), 6.21 (dd, *J* = 16.0, 6.8 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 2.11 (s, 3H).

General Procedure for Pd-Catalyzed Enantioselective Allylic Alkylations[38–40]: Ligand **1a** (10.0 mg, 0.028 mmol, 6 mol%) and $Pd_2(dba)_3$ (8.0 mg, 0.014 mmol, 3 mol%) were dissolved in the solvent (2 mL) in a Schlenk tube under N_2. After stirring at room temperature for 1 h, 1,3-diphenyl-2-propenyl acetate (0.46 mmol) in the same solvent (2 mL) was added, followed by dimethyl malonate (0.92 mmol) and Cs_2CO_3 (300 mg, 0.92 mmol). The reaction mixture was stirred at room temperature until the acetate was consumed, and then was diluted with AcOEt and washed with saturated aq. NH_4Cl. The organic layer was dried over Na_2SO_4 and filtered, and the solvents were evaporated in vacuo. The residue was purified by flash column chromatography, eluting with petroleum ether and AcOEt to afford the alkylation product.

Dimethyl 2-((*S*,*E*)-1,3-diphenylallyl)malonate: Colorless oil; R_f = 0.6 (8:1 hexanes/AcOEt). HPLC (Daicel AD-H column, *n*-hexane:*i*-PrOH = 95:5, Flow rate = 1.0 mL/min, λ = 225 nm): t_{major} = 15.5 min, t_{minor} = 22.2 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.21 (m, 10H), 6.45 (d, *J* = 15.6 Hz, 1H), 6.26 (dd, *J* = 15.6, 8.6 Hz, 1H), 4.22 (dd, *J* = 11.4, 8.6 Hz, 1H), 3.95 (d, *J* = 11.4 Hz, 1H), 3.69 (s, 3H), 3.50 (s, 3H).

Diethyl 2-((*S*,*E*)-1,3-diphenylallyl)malonate: Colorless oil; R_f = 0.41 (8:1 hexanes/AcOEt). HPLC (Daicel AD-H column, *n*-hexane:*i*-PrOH = 90:10, Flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 9.3 min, t_{minor} = 12.2 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.15 (m, 10H), 6.44 (d, *J* = 15.6 Hz, 1H), 6.30 (dd, *J* = 15.6, 8.4 Hz, 1H), 4.22 (dd, *J* = 10.8, 8.4 Hz, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.93 (q, *J* = 7.2 Hz, 2H), 3.88 (m, 1H), 1.17 (t, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H).

General Procedure for Pd-Catalyzed Enantioselective Allylic Etherification Reactions[41–44]: Ligand **1d** (16 mg, 0.028 mmol, 6 mol%) and $[Pd(C_3H_5)Cl]_2$ (5.0 mg, 0.014 mmol, 3 mol%) were dissolved in the solvent (2 mL) in a Schlenk tube under N_2. After stirring at room temperature for 1 h, the allyl acetate (0.46 mmol) in the solvent (2 mL) was added, followed by the alcohol (1.38 mmol) and the base (0.92 mmol). The reaction mixture was stirred at room temperature until the acetate was consumed, and then was diluted with AcOEt and washed with saturated aq. NH_4Cl. The organic layer was dried over Na_2SO_4 and filtered, and the solvents were evaporated in vacuo. The residue was purified by flash column chromatography, eluting with petroleum ether and AcOEt to afford the corresponding ether product.

(*S*,*E*)-1,3-Diphenylallyl methyl ether (Table 1, entry 1): Colorless oil (82% yield, 97% ee), R_f = 0.41 (50:1 hexanes/AcOEt). HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 98:2, Flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 6.3 min, t_{minor} =7.4 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39–6.26 (m, 10H), 6.63 (d, *J* = 16.2 Hz, 1H), 6.28 (dd, *J* = 16.2, 7.8 Hz, 1H), 4.80 (d, *J* = 7.8 Hz, 1H), 3.38 (s, 3H).

(*S*,*E*)-1,3-Diphenylallyl ethyl ether (Table 1, entry 2): Colorless oil (85% yield, 92% ee), R_f = 0.42 (50:1 hexanes/AcOEt). HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 98.5:1.5, Flow rate = 0.5 mL/min, λ = 254 nm): t_{major} = 9.0 min, t_{minor} = 10.1 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ

7.33–6.27 (m, 10H), 6.60 (d, J = 15.6 Hz, 1H), 6.31 (dd, J = 16.0, 8.0 Hz, 1H), 4.91 (d, J = 8.0 Hz, 1H), 3.62–3.55 (m, 1H), 3.52–3.44 (m, 1H), 1.26 (t, J = 7.2 Hz, 3H).

Butyl (*S*,*E*)-1,3-diphenylallyl ether (Table 1, entry 3): Colorless oil (82% yield, 97% ee), R_f = 0.21 (50:1 hexanes/AcOEt). HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 99.5:0.5, Flow rate = 1.0 mL/min, λ = 254 nm): t_{minor} = 10.2 min, t_{major} = 11.4 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.33 (m, 6H), 7.40–7.33 (m, 8H), 7.30–7.25 (m, 3H), 7.23–7.19 (m, 1H), 6.60 (d, J = 16.0 Hz, 1H), 6.29 (dd, J = 16.0, 6.8 Hz, 1H), 4.89 (d, J = 6.8 Hz, 1H), 3.55–3.50 (m, 1H), 3.44–3.39 (m, 1H), 1.66–1.59 (m, 2H), 1.46–1.36 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H).

Allyl (*S*,*E*)-1,3-diphenylallyl ether (Table 1, entry 4): Colorless oil (81% yield, 82% ee), R_f = 0.5 (10:1 hexanes/AcOEt). HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 97.5:2.5, Flow rate = 0.25 mL/min, λ = 254 nm): t_{major} = 36.8 min, t_{minor} = 39.5 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53–7.23 (m, 10H), 6.61 (d, J = 15.6 Hz, 1H), 6.30 (dd, J = 15.6, 6.8 Hz, 1H), 5.99–5.95 (m, 1H), 5.31 (d, J = 17.4 Hz, 1H), 5.21 (d, J = 11.4 Hz, 1H), 4.98 (d, J = 6.8 Hz, 1H), 4.07–4.03 (m, 2H).

(*S*,*E*)-1,3-Diphenylallyl 3-methyl-2-butenyl ether (Table 1, entry 5): Colorless oil (60% yield, 69% ee), R_f = 0.29 (50:1 hexanes/AcOEt). HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 99:1, Flow rate = 0.2 mL/min, λ = 254 nm): t_{major} = 9.2 min, t_{minor} = 10.2 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–6.29 (m, 10H), 6.58 (d, J = 16.0 Hz, 1H), 6.32 (dd, J = 16.0, 7.2 Hz, 1H), 5.41 (t, J = 6.8 Hz, 1H), 4.95 (d, J = 7.2 Hz, 1H), 1.75 (s, 3H), 1.61 (s, 3H).

Benzyl (*S*,*E*)-1,3-diphenylallyl ether (Table 1, entry 6): Colorless oil (83% yield, 80% ee), R_f = 0.26 (50:1 hexanes/AcOEt). HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 98.5:1.5, Flow rate = 0.3 mL/min, λ = 254 nm): t_{major} = 18.7 min, t_{minor} = 20.9 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.20 (m, 15H), 6.62 (d, J = 16.0 Hz, 1H), 6.33 (dd, J = 16.0, 7.2 Hz, 1H), 5.00 (d, J = 7.2 Hz, 1H), 4.57 (s, 2H).

(*S*,*E*)-1,3-Diphenylallyl 2-phenethyl ether (Table 1, entry 7): Colorless oil (85% yield, 72% ee), R_f = 0.16 (20:1 hexanes/AcOEt). HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 99:1, Flow rate = 1.0 mL/min, λ = 254 nm): t_{minor} = 28.3 min, t_{major} = 31.6 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.21 (m, 15H), 6.57 (d, J = 16.0 Hz, 1H), 6.25 (dd, J = 16.0, 7.2 Hz, 1H), 4.91 (d, J = 7.2 Hz, 1H), 3.78–3.72 (m, 1H), 3.67–3.61 (m, 1H), 2.96 (t, J = 6.8 Hz, 2H).

Cinnamyl (*S*,*E*)-1,3-diphenylallyl ether (Table 1, entry 8): Colorless oil (87% yield, 78% ee), R_f = 0.18 (10:1 hexanes/AcOEt). HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 70:30, Flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 14.3 min, t_{minor} = 16.9 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.26 (m, 15H), 6.66–6.31 (m, 2H), 6.37–6.31 (m, 2H), 5.05 (d, J = 6.8 Hz, 1H), 4.22–4.20 (m, 2H).

2-(((*S*,*E*)-1,3-Diphenylallyloxy)methyl)furan (Table 1, entry 9): Colorless oil (84% yield, 92% ee), R_f = 0.32 (50:1 hexanes/AcOEt). HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 90:10, Flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 11.1 min, t_{minor} = 15.1 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41–7.24 (m, 11H), 6.60 (d, J = 16.0 Hz, 1H), 6.33–6.29 (m, 3H), 5.02 (d, J = 6.8 Hz, 1H), 4.51 (s, 1H), 4.49 (s, 1H).

2-(((*S*,*E*)-1,3-Diphenylallyloxy)methyl)thiophene (Table 1, entry 10): Colorless oil (80% yield, 72% ee), R_f = 0.15 (20:1 hexanes/AcOEt). HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 95:5, Flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 16.1 min, t_{minor} = 22.6 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.21 (m, 11H), 6.99–6.64 (m, 2H), 6.62 (d, J = 16.0 Hz, 1H), 6.33 (dd, J = 16.0, 7.2 Hz, 1H), 5.05 (d, J = 7.2 Hz, 1H), 4.70 (s, 2H).

2-(((*S*,*E*)-1,3-Diphenylallyloxy)methyl)pyridine (Table 1, entry 11): Colorless oil (70% yield, 64% ee), R_f = 0.16 (5:1 hexanes/AcOEt). HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 85:15, Flow rate = 0.5 mL/min, λ = 254 nm): t_{major} = 11.5 min, t_{minor} = 14.1 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.53 (d, J = 4.8 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.45 (d, J = 7.8 Hz, 2H), 7.37 (t, J = 8.4 Hz, 4H), 7.31–7.28 (m, 3H), 7.22 (t, J = 6.6 Hz, 1H), 7.17 (t, J = 4.8 Hz, 1H), 6.68 (d, J = 16.0 Hz, 1H), 6.35 (dd, J = 16.0, 6.6 Hz, 1H), 5.09 (d, J = 6.6 Hz, 1H), 4.74 (d, J = 13.8 Hz, 1H), 4.67 (d, J = 13.8 Hz, 1H).

2-(((*S*,*E*)-1,3-Diphenylallyloxy)methyl)tetrahydrofuran (Table 1, entry 12): Colorless oil (60% yield, 93% ee), R_f = 0.39 (5:1 hexanes/AcOEt). HPLC (Daicel AD-H column, *n*-hexane:*i*-PrOH = 99:1, Flow rate = 0.5 mL/min, λ = 254 nm): t_{major} = 14.0, 16.8 min (two (*S*,*E*)-isomers), t_{minor} = 15.2, 16.1 min (two (*R*,*E*)-isomers). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.26 (m, 20H), 6.63 (d, J = 16.0 Hz, 1H), 6.59 (d, J = 16.0 Hz, 1H), 6.33 (dd, J = 16.0, 7.2 Hz, 1H), 6.29 (dd, J =16.0, 7.2 Hz, 1H), 4.98 (d, J = 7.2 Hz, 2H), 4.15–4.10 (m, 2H), 3.92–3.86 (m, 2H), 3.78 (q, J = 8 Hz, 2H), 3.58–3.52 (m, 2H), 3.49–3.42 (m, 2H), 2.00–1.85 (m, 6H), 1.71–1.62 (m, 2H).

2-((*S*,*E*)-1,3-Diphenylallyloxy)-2,3-dihydro-1*H*-indene (Table 1, entry 13): Colorless oil (60% yield, 91% ee), R_f = 0.16 (5:1 hexanes/AcOEt). HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 98.5:1.5, Flow rate = 0.5 mL/min, λ = 254 nm): t_{major} = 38.6 min, t_{minor} = 41.3 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41–7.24 (m, 14H), 6.61 (d, J = 15.6 Hz, 1H), 6.32 (dd, J = 15.6, 7.2 Hz, 1H), 5.08 (d, J = 7.2 Hz, 1H), 4.51 (m, 1H), 3.22–3.02 (m, 4H).

(*S*,*E*)-1,3-Di(*o*-tolyl)allyl methyl ether (Table 2, entry 1): Colorless oil (99% yield, 85% ee), R_f = 0.29 (50:1 hexanes/AcOEt); $[\alpha]_D^{20}$ −3.0 (*c* 1.00, $CHCl_3$). HPLC (Daicel AD-H column, *n*-hexane:*i*-PrOH = 99.7:0.3, Flow rate = 0.3 mL/min, λ = 254 nm): t_{major} = 23.7 min, t_{minor} = 26.6 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.46 (m, 1H), 7.42–7.40 (m, 1H), 7.25–7.12 (m, 6H), 6.80 (d, J = 16.0 Hz, 1H), 6.11 (dd, J = 16.0, 6.8 Hz, 1H), 4.99 (d, J = 6.8 Hz, 1H), 3.39 (s, 3H), 2.38 (s, 3H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 139.0, 135.8, 135.6, 135.5, 130.5, 130.4, 130.2, 129.5, 127.6, 127.5, 126.4, 126.3, 126.1, 125.9, 81.5, 56.4, 19.8, 19.3; IR (film): ν_{max} 3065, 3020, 2953, 2926, 2853, 2818, 1489, 1458, 1188, 1091, 1049, 966, 750, 727, 575 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M - (OCH_3)]^+$ Calcd for $C_{17}H_{17}$ 221.1330; Found 221.1323.

(*S*,*E*)-1,3-Di(*m*-tolyl)allyl methyl ether (Table 2, entry 2): Colorless oil (99% yield, 97% ee), R_f = 0.29 (50:1 hexanes/AcOEt); $[\alpha]_D^{20}$ −6.7 (*c* 0.99, $CHCl_3$); HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 99.5:0.5, Flow rate = 1.0 mL/min, λ = 254 nm): t_{minor} = 23.4 min, t_{major} = 26.6 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.17 (m, 6H), 7.10–7.08 (m, 1H), 7.04–7.03 (m, 1H), 6.59 (d, J = 16.0 Hz, 1H), 6.25 (dd, J = 16.0, 6.8 Hz, 1H), 4.74 (d, J = 6.8 Hz, 1H), 3.37 (s, 3H), 2.35 (s, 3H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 141.0, 138.2, 138.0, 136.6, 131.5, 130.0, 128.5, 128.4, 127.4, 127.3, 123.9, 123.8, 84.4, 56.4, 21.5, 21.3; IR (film): ν_{max} 3026, 2922, 2818, 1604, 1489, 1089, 964, 781, 704, 692 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M - (OCH_3)]^+$ Calcd for $C_{17}H_{17}$ 221.1330; Found 221.1325.

(*S*,*E*)-1,3-Di(*p*-tolyl)allyl methyl ether (Table 2, entry 3): Colorless oil (70% yield, 93% ee), R_f = 0.53 (10:1 hexanes/AcOEt); $[\alpha]_D^{20}$ −35.0 (*c* 0.91, $CHCl_3$); HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 99.7:0.3, Flow rate = 2.0 mL/min, λ = 254 nm): t_{major} = 17.4 min, t_{minor} = 19.6 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.26 (m, 4H), 7.17–7.15 (m, 2H), 7.10–7.08 (m, 2H), 6.57 (d, *J* = 16.0 Hz, 1H), 6.22 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.74 (d, *J* = 6.8 Hz, 1H), 3.35 (s, 3H), 2.34 (s, 3H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 138.3, 137.6, 137.4, 134.0, 131.3, 129.4, 129.3, 128.3, 126.9, 126.6, 84.3, 56.4, 21.3, 21.2; IR (film): ν_{max} 3026, 2922, 2818, 1604, 1489, 1236, 1080, 1093, 966, 815, 798, 669 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M - (OCH_3)]^+$ Calcd for $C_{17}H_{17}$ 221.1330; Found 221.1322.

(*S*,*E*)-1,3-Di(*p*-chlorophenyl)allyl methyl ether (Table 2, entry 4): White solid (62% yield, 86% ee), R_f = 0.27 (50:1 hexanes/AcOEt); m.p. 89.0–89.3 °C; $[\alpha]_D^{20}$ −6.5 (*c* 0.55, $CHCl_3$). HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 98:2, Flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 11.1 min, t_{minor} = 12.1 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.35–7.26 (m, 8H), 6.56 (d, *J* = 16.2 Hz, 1H), 6.20 (dd, *J* = 16.2, 6.0 Hz, 1H), 4.76 (d, *J* = 6.0 Hz, 1H), 3.36 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 139.4, 134.9, 133.7, 133.6, 130.6, 130.4, 128.8, 128.3, 127.9, 83.5, 56.6; IR (film): ν_{max} 2931, 2820, 2369, 1593, 1500, 1404, 1091, 1014, 829 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M - (OCH_3)]^+$ Calcd for $C_{15}H_{11}Cl_2$ 261.0238; Found 261.0253.

(*S*,*E*)-1,3-Di(*p*-methoxyphenyl)allyl methyl ether (Table 2, entry 5): Colorless oil (90% yield, 3% ee), R_f = 0.33 (50:1 hexanes/AcOEt). HPLC (Daicel OD-H column, *n*-hexane:*i*-PrOH = 98:2, Flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 11.2 min, t_{minor} = 12.3 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32–7.29 (m, 4H), 7.90–7.89 (m, 2H), 6.84–6.82 (m, 2H), 6.53 (d, *J* = 15.6 Hz, 1H), 6.14 (dd, *J* = 15.6, 4.8 Hz, 1H), 4.73 (d, *J* = 4.8 Hz, 1H), 3.78 (m, 6H), 3.34 (s, 3H).

General Procedure for Pd-Catalyzed Enantioselective Allylic Amination Reactions[41–44]: Ligand **1d** (16 mg, 0.028 mmol, 6 mol%) and $[Pd(C_3H_5)Cl]_2$ (5.0 mg, 0.014 mmol, 3 mol%) were dissolved in the solvent (2 mL) in a Schlenk tube under N_2. After stirring at room temperature for 1 h, 1,3-diphenyl-2-propenyl acetate (0.46 mmol) in the same solvent (2 mL) was added, followed by the primary amine (1.38 mmol) and the base (0.92 mmol). The reaction mixture was stirred at room temperature until the acetate was consumed, and then was diluted with AcOEt and washed with saturated aq. NH_4Cl. The organic layer was dried over Na_2SO_4 and filtered, and the solvents were evaporated in vacuo. The residue was purified by flash column chromatography, eluting with petroleum ether and AcOEt to afford the corresponding amine product.

***N*-[(*S*,*E*)-1,3-Diphenylallyl]aniline (Table 3, entry 1):** Colorless oil (93% yield, 70% ee), R_f = 0.29 (50:1 hexanes/AcOEt). HPLC (Daicel AD-H column, *n*-hexane:*i*-PrOH = 95:5, Flow rate = 1.0 mL/min, λ = 254 nm): t_{minor} = 9.6 min, t_{major} = 11.9 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.42 (m, 2H), 7.37–7.35 (m, 4H), 7.30–7.27 (m, 3H), 7.23–7.19 (m, 1H), 7.15–7.11 (m, 2H), 6.70 (m, 1H), 6.62 (m, 3H), 6.39 (dd, *J* = 15.6, 7.6 Hz, 1H), 5.08 (d, *J* = 7.6 Hz, 1H), 4.01 (s, 1H).

***N*-[(*S*,*E*)-1,3-Diphenylallyl]benzylamine (Table 3, entry 3):** Colorless oil (72% yield, 81% ee), R_f = 0.47 (10:1 hexanes/AcOEt). HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 87:13, Flow rate = 0.5 mL/min, λ = 254 nm): t_{major} = 18.8 min, t_{minor} = 23.1 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.42 (m, 2H), 7.40–7.33 (m, 8H), 7.31–7.25 (m, 4H), 7.22–7.18 (m, 1H), 6.58 (d, *J* = 16.0 Hz, 1H), 6.31 (dd, *J* = 16.0, 7.6 Hz, 1H), 4.39 (d, *J* = 7.6 Hz, 1H), 3.79 (s, 1H), 3.78 (s, 1H), 1.68 (s, 1H).

***N*-[(*S*,*E*)-1,3-Diphenylallyl]-(*R*)-phenylglycinol (Table 3, entry 4):** White solid (72% yield, 96% de), R_f = 0.50 (2:1 hexanes/AcOEt); m.p. 78.3–78.6 °C. HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 98:2, Flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 26.1 min, t_{minor} = 37.0 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.21 (m, 15H), 6.48 (d, *J* = 16.0 Hz, 1H), 6.33 (dd, *J* = 16.0, 7.2 Hz, 1H), 4.28 (d, *J* = 7.2 Hz, 1H), 3.67–3.57 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 141.6, 140.0, 136.5, 132.3, 129.5, 128.4, 128.2, 127.3, 127.2, 127.1, 127.0, 126.1, 66.5, 61.7, 60.8; IR (film): ν_{max} 3385, 3082, 3059, 3026, 2924, 2854, 1599, 1490, 1452, 1069, 1045, 1026, 966, 910, 746, 700, 532 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{24}NO$ 330.1858; Found 330.1852.

***N*-[(*S*,*E*)-1,3-Diphenylallyl]-(*S*)-phenylglycinol (Table 3, entry 6):** Colorless oil (71% yield, 85% de), R_f = 0.38 (2:1 hexanes/AcOEt). HPLC (Daicel OJ-H column, *n*-hexane:*i*-PrOH = 98:2, Flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 24.6 min, t_{minor} = 34.8 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.20 (m, 15H), 6.45 (d, *J* = 16.0 Hz, 1H), 6.22 (dd, *J* = 16.0, 8.0 Hz, 1H), 4.25(d, *J* = 8.0 Hz, 1H), 4.04 (dd, *J* = 8.8, 4.4 Hz, 1H), 3.73 (dd, *J* = 10.4, 4.4 Hz, 1H), 3.58 (dd, *J* = 10.4, 8.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.2, 140.5, 136.8, 131.6, 131.5, 128.8, 128.7, 128.6, 127.7, 127.6, 127.4, 127.3, 127.1, 126.5, 66.9, 61.9, 61.5; IR (film): ν_{max} 3059, 3026, 2926, 2855, 1491, 1449, 1063, 1028, 966, 746, 698 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{24}NO$ 330.1858; Found 330.1852.

Preparation of [Pd(II)(η^3-PhCHCHCHPh)(1d)]PF_6[45]: Bis[(μ-chloro)(η^3-1,3-diphenylallyl)palladium(II)] was prepared according to literature procedures:[46] $PdCl_2$ (350 mg, 1.95 mmol) was added to a Schlenk tube under N_2. LiCl (350 mg, 8.3 mmol) was dissolved in H_2O (2.3 mL) and the solution deoxygenated before it was added to the Schlenk tube. The mixture was stirred for 30 min. Deoxygenated EtOH (3.9 mL) and a deoxygenated solution of (*rac*)-(*E*)-3-acetoxy-l,3-diphenyl-l-propene (1 g, 3.97 mmol) in THF (11 mL) were then added, and the brown solution was cooled to 0 °C. After the addition of 1.2 mL of deoxygenated concentrated HCl, CO was slowly bubbled through the solution for 15 min. Another 0.8 mL of deoxygenated concentrated HCl was added and CO bubbled for 1.5 h. The stream of CO was then stopped and the solution stirred overnight under CO atmosphere at room temperature. The yellow-orange suspension obtained was filtered through paper on a Hirsch funnel, washed with MeOH (100 mL) and Et_2O (30 mL), and then dried under high vacuum. Yield: 643 mg (98%).

Ligand **1d** (38 mg, 0.06 mmol) and bis[(μ-chloro)(η^3-1,3-diphenylallyl)palladium(II)] (20 mg, 0.03 mmol) were stirred in anhydrous CH_2Cl_2 (4 mL) under N_2 for 10 min before $AgPF_6$ (14 mg, 0.06 mmol) was added. The mixture was stirred in the dark under N_2 for 1 h. The AgCl formed was filtered off through a pad of Celite and washed with small amount of CH_2Cl_2 in the glove box. The clear light yellow filtrate was layered with *n*-hexane (1 mL). Pale yellow prismatic single crystals of [Pd(II)(η^3-PhCHCHCHPh)(**1d**)]PF_6 were obtained after slow evaporation of the solvents in the air at rt. Yield: 50 mg, 80%. R_f = 0.59 (1:1 hexanes/AcOEt); m.p. 125.5–126.3 °C; $[\alpha]_D^{20}$ −244 (*c*

1.00, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, J =7.8 Hz, 2H), 7.48–7.41 (m, 6H), 7.31 (d, J =7.8 Hz, 1H), 7.19 (t, J = 7.2 Hz, 1H), 7.08 (d, J = 12.6 Hz, 2H), 6.96 (m, 1H), 6.86–6.84 (m, 5H), 6.71–6.66 (m, 2H), 6.24 (m, 1H), 4.82 (s, 1H), 4.21 (d, J = 12 Hz, 1H), 3.02–2.98 (m, 1H), 2.71–2.65 (m, 1H), 2.5 (s, 2H), 2.25–2.17 (m, 2H), 1.52–1.43 (m, 2H), 1.25–1.17 (m, 36H), 0.89–0.75 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.8, 151.7, 151.0, 150.9, 148.7, 148.6, 144.7, 144.6, 138.3, 135.8, 131.8, 130.0, 129.1, 128.8, 128.7, 128.4, 128.2, 127.9, 127.5, 127.4, 126.8, 125.3, 124.7, 124.3, 124.0, 110.7, 98.3, 98.1, 75.31, 75.26, 72.7, 49.4, 41.3, 35.1, 35.0, 34.3, 31.5, 31.3, 28.7, 23.0, 22.8; ^{31}P NMR (162 MHz, $CDCl_3$): δ 22.7 (PAr), −143.6 (sept, J = 715 Hz, PF_6); ^{19}F NMR (376 MHz, $CDCl_3$): δ −71.7 (d, J = 715 Hz, PF_6); IR (film): ν_{max} 2960, 2926, 2870, 1589, 1364, 1136, 1136, 1018, 912, 841, 731, 694, 557 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - (PF_6)]^+$ Calcd for $C_{55}H_{69}NPPd$ 880.4202; Found 880.4218.

Note: $HOP(O)F_2$ generated by hydrolysis of PF_6^- gave the following NMR signals: ^{31}P NMR (162 MHz, $CDCl_3$): δ −14.4 (t, J = 963 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ −80.5 (d, J = 965 Hz).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website. ^1H, ^{13}C, ^{31}P and ^{19}F NMR spectra, HPLC charts, and X-ray crystallographic data.

Accession Codes

The X-ray crystallographic data for all the reported crystals have been deposited at the Cambridge Crystallographic Data Centre (CCDC). **1a**: CCDC 1881334; **2b**: CCDC 1881360; **4a**: CCDC 1881361; the debromination product of **4b′**: CCDC 1881366; *ent*-**5a**: CCDC 1881367; **6a**: CCDC 1881356; **6b**: CCDC 1881368; (±)-**6b**: CCDC 1881362; **8**: CCDC 1881371; mixture of **8**and HBr: CCDC 1881993; **9**: CCDC 1881372; **10** and PhNHTf (1:1): CCDC 1881373; **11a**: CCDC 1881374; **11d**: CCDC 1881376; the amination product from (*R*)-phenylglycinol: CCDC 1881377; [Pd(II)(η^3-PhCHCHCHPh)(**1d**)]PF_6: 1888454. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

AUTHOR INFORMATION

Corresponding Author

E-mail: pjiao@bnu.edu.cn

ORCID

Peng Jiao: 0000-0003-4039-8300

Notes

The authors declare no competing financial interests.

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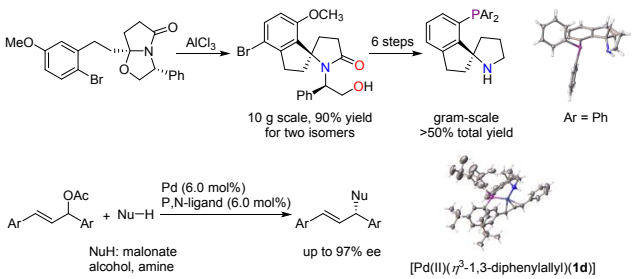
TOC figure:


MeO
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10 g scale, 90% yield
for two isomers
6 steps
PAr2
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H
gram-scale
>50% total yield
Ar = Ph
OAc
Ar
Ar
+ Nu–H
Pd (6.0 mol%)
P,N-ligand (6.0 mol%)
Nu
Ar
Ar
NuH: malonate
alcohol, amine
up to 97% ee
[Pd(II)(η3-1,3-diphenylallyl)(1d)]