

Supporting Information

for

Enantioselective Pd(II)-Catalyzed Intramolecular Oxidative 6-*endo* Aminoacetoxylation of Unactivated Alkenes

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General Procedures and New Compounds Characterization

Content:

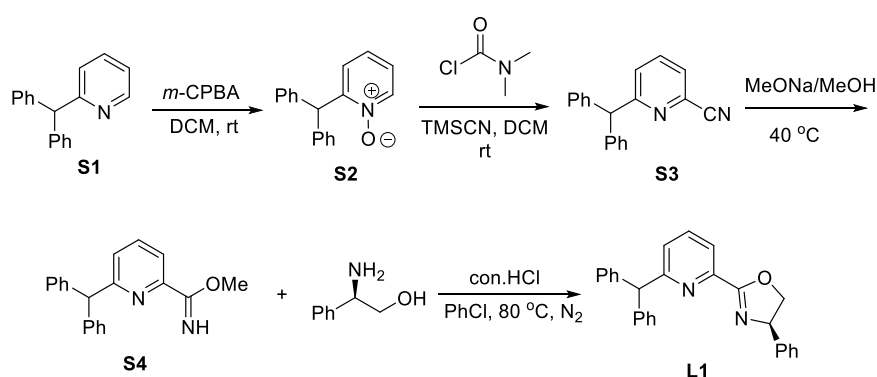
- 1. General Consideration**
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1. General Consideration:

All commercially available compounds were purchased from Aldrich, Alfa TCI, Aesar or Adamas, and used without further purification, unless otherwise noted. NMR spectra were recorded on Varian 400 and Agilent 400 (400 MHz for ^1H ; 376 MHz for ^{19}F ; 100 MHz for ^{13}C) spectrometer. The chemical shifts (δ) are given in parts per million relative to CDCl_3 (7.26 ppm for ^1H) or TMS (0 ppm for ^1H) and CDCl_3 (77.0 ppm for ^{13}C), and ^{19}F NMR chemical shifts were determined relative to CFCl_3 as outside standard and low field is positive. ^1H and ^{19}F multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), quartet (q), multiplet (m), and broad resonance (br). High performance liquid chromatography was performed on Waters 2487-600E, Waters ACQUITY UPC², and Agilent Series HPLC, using IC, IC3, PC1 chiral column eluted with a mixture of hexane and isopropyl alcohol. Optical rotation was measured on a Rudolph-Autopol I. Flash column chromatography was performed on silica gel (particle size 200-300 mesh) and eluted with petroleum ether/ethyl acetate. High Resolution Mass spectral data were obtained on a Waters Micromass GCT spectrometer in EI mode or on Agilent Technologies 6224 TOF LC MS spectrometer in ESI mode. PhCF_3 were purchased from TCI and used without further purification.

2. Experimental Section

2.1 Synthesis of Ligand L1



In a 250 mL round bottom flask, 2-benzhydrylpyridine **S1** (4.9 g, 20 mmol) was dissolved in DCM (100 mL). Then *m*-CPBA (*meta*-chloroperoxybenzoic acid, 7.2 g, 35 mmol) was added, and the mixture was stirred at room temperature. The reaction

was monitored by TLC. After the reaction was completed, K_2CO_3 (5.0 g) was added. The mixture was stirred for 30 min at room temperature and filtered through a celite pad. The filtrate was concentrated under vacuum to give the product **S2**, which can be used in next step without further purification.

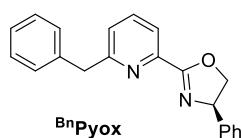
To a solution of the crude **S2** in CH_2Cl_2 (40 mL), TMSCN (2.5 g, 26 mmol) was added at room temperature. The mixture was stirred for 10 min. Then dimethylcarbamic chloride (2.7 g, 26 mmol) was added, and the mixture was stirred at room temperature. The reaction was monitored by TLC. After the reaction was completed, the mixture was quenched with 10% aqueous K_2CO_3 solution (80 mL). The mixture was extracted by CH_2Cl_2 (2× 100 mL). The combined organic phase was washed with brine (50 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under vacuum. The crude residue was purified by column chromatography on silica gel to afford product **S3** (2.1 g, 39% yield in two steps) as a white solid. ^1H NMR (400MHz, CDCl_3) δ 7.74 (t, J = 7.6 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.36-7.23(m, 7H), 7.17-7.14 (m, 4H), 5.73 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 165.1, 141.5, 137.4, 133.4, 129.2, 128.6, 127.2, 126.9, 126.4, 117.3 59.1. HRMS: m/z (EI) calculated $[\text{M}]^+$: 270.1157, measured: 270.1158.

In a 50mL round bottom flask, **S3** (2.10 g, 7.7 mmol) was dissolved in MeOH (10 mL). Then NaOMe (125 mg, 2.3 mmol) was added. The reaction mixture was stirred at 40°C for overnight. After that, the solvent was removed under vacuum, and the residue was redissolved in EtOAc (20 mL). The solution was washed by water and brine, then the organic phase was separated and dried over MgSO_4 . After filtered, the filtrate was concentrated under vacuum to give the product **S4** (2.1 g, 90% yield) as a pale solid, which can be used in next step without further purification. ^1H NMR (400MHz, CDCl_3) δ 9.14 (br, 1H), 7.77-7.69 (m, 2H), 7.31-7.18 (m, 11H), 5.71 (s, 1H), 3.98 (s, 3H).

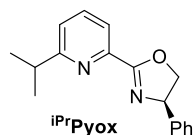
In a 25 mL round bottom flask, the crude **S4** (2.1 g, 7 mmol), (*R*)-2-amino-2-phenylethan-1-ol (586 mg, 5 mmol) were dissolved in PhCl (15 mL). Concentrated HCl (2 drops) was added to the solution and the mixture was heated to 80°C under N_2 atmosphere. After the reaction was completed, the organic solvent was removed under

vacuum. The residue was purified by flash column chromatography on silica gel (PE:EA:Et₃N = 10:1:0.1) to afford ligand **L1** (1.14 g, 42% yield) as a white solid. M.p. 106-108°C. $[\alpha]_D^{27.2} = 61.18$ (*c* 1.06, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 8.0 Hz, 1H), 7.38-7.29 (m, 9H), 7.25-7.20 (m, 3H), 7.17-7.14 (m, 4H), 5.98 (s, 1H), 5.43 (t, *J* = 9.6 Hz, 1H), 4.88 (t, *J* = 9.6 Hz, 1H), 4.38 (t, *J* = 8.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 164.0, 163.4, 146.3, 142.5, 141.8, 136.8, 129.3, 128.7, 128.4, 127.6, 126.8, 126.5, 126.0, 122.3, 75.4, 70.1, 59.2. HRMS: *m/z* (ESI) calculated [M+H]⁺: 391.1805, measured: 391.1798.

Other ligands were synthesized according to the same procedure as above.



$[\alpha]_D^{32.0} = 30.55$ (*c* 1.33, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 8.02 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.39-7.24 (m, 10H), 7.14 (d, *J* = 7.6 Hz, 1H), 5.45 (dd, *J* = 10.0, 8.4 Hz, 1H), 4.91 (dd, *J* = 10.0, 8.4 Hz, 1H), 4.41 (t, *J* = 8.4 Hz, 1H), 4.31 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 164.0, 161.6, 146.0, 141.8, 138.9, 137.0, 129.3, 128.7, 128.6, 127.7, 126.8, 126.5, 125.3, 122.0, 75.4, 70.2, 44.6. HRMS: *m/z* (ESI) calculated [M+H]⁺: 315.1492, measured: 315.1487.



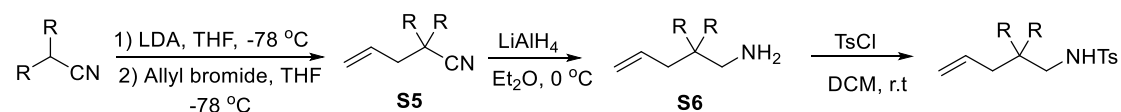
$[\alpha]_D^{32.8} = 64.09$ (*c* 1.12, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 8.01 (d, *J* = 7.6 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.39-7.27 (m, 6H), 5.43 (dd, *J* = 10.0, 8.4 Hz, 1H), 4.90 (dd, *J* = 10.0, 8.4 Hz, 1H), 4.39 (t, *J* = 8.4 Hz, 1H), 3.28-3.21 (m, 1H), 1.35 (s, 3H), 1.33 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 167.9, 164.3, 145.7, 141.9, 136.9, 128.7, 127.6, 126.8, 122.2, 121.9, 75.4, 70.2, 36.6, 22.7. HRMS: *m/z* (ESI) calculated [M+H]⁺: 267.1492, measured: 267.1488.

2.2 Synthesis of Substrate

Substrates **1a**¹, **1b**, **1c**¹, **1d**, **1e**, **1f**², **1h**¹, **1i**, **1j**, **1k-1m**³, **1n**, **1o**², **1p**², **1q**, **1r**, **1t**, **4a** were prepared from the corresponding nitriles according to the same following

procedure. **1s**⁴, **1u**⁵, **1v**⁴, **1w**⁴ were prepared according to the reported procedure.

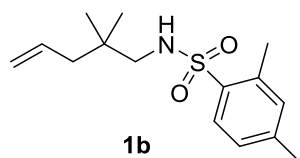
2.2.1 General procedure for the preparation of substrates



A solution of LDA (2.5 equiv) in THF was cooled to -78°C , and nitrile (1.0 equiv) was added dropwise. After stirring 2 h at -78°C , a solution of allyl bromide (1.0 equiv) in THF was added. The mixture was monitored by TLC. After completion, the reaction was quenched by a saturated aqueous solution of NH_4Cl . The mixture was extracted with ether. The combined organic phase was dried over Na_2SO_4 , and filtered. The filtrate was concentrated under vacuum to give the crude residue **S5**, which was used directly for the next step.

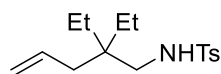
To a suspended solution of LiAlH_4 (2.0 equiv) in Et_2O , a solution of **S5** in Et_2O was added dropwise at 0°C under N_2 atmosphere. The reaction mixture was stirred for 2 h. The reaction was quenched by wet THF, 15% aqueous NaOH and water (v/v/v=1:1:3) sequentially. The reaction mixture was stirred at room temperature for 15 min, and the solid was filtered off. The filtrate was concentrated under vacuum to give the product **S6**.

To a solution of **S6** and triethylamine (2.0 equiv) in CH_2Cl_2 , TsCl (1.5 equiv) was added at 0°C . The reaction was stirred at room temperature for 12 h. The mixture was washed with 10% NaHCO_3 , brine, and dried with Na_2SO_4 . The solvent was evaporated and the residue was purified by flash column chromatography on silica gel to give the desired product.



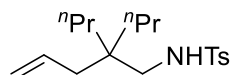
White solid. M.p. $55\text{--}56^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, $J = 8.4$ Hz, 1H), 7.11–7.09 (m, 2H), 5.73–5.65 (m, 1H), 5.03–4.97 (m, 2H), 4.50 (br, 1H), 2.64 (d, $J = 7.2$ Hz, 2H), 2.59 (s, 3H), 2.37 (s, 3H), 1.94 (d, $J = 7.2$ Hz, 2H), 0.84 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.3, 136.6, 134.6, 134.3, 133.2, 129.8, 126.7, 117.8,

52.6, 44.1, 34.0, 24.9, 21.2, 20.2. HRMS: m/z (ESI) calculated $[M+H]^+$: 282.1522, measured: 282.1517.



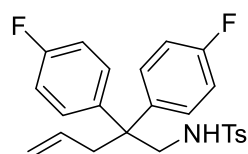
1d

White solid. M.p. 66-69 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.74 (d, $J = 8.4$ Hz, 2H), 7.30 (d, $J = 8.4$ Hz, 2H), 5.70-5.61 (m, 1H), 5.03-4.98 (m, 2H), 4.56 (t, $J = 6.4$ Hz, 1H), 2.65 (d, $J = 7.2$ Hz, 2H), 2.42 (s, 3H), 1.93 (d, $J = 7.6$ Hz, 2H), 1.21 (q, $J = 7.6$ Hz, 4H), 0.72 (t, $J = 7.6$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.3, 136.7, 134.0, 129.7, 127.0, 117.7, 47.3, 38.9, 38.5, 26.0, 21.5, 7.1. HRMS: m/z (ESI) calculated $[M+H]^+$: 296.1679, measured: 296.1673.



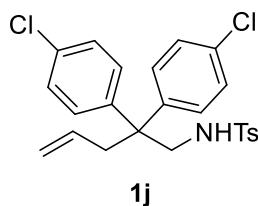
1e

White solid. M.p. 67-69 °C. ^1H NMR (400MHz, CDCl_3) δ 7.74 (d, $J = 8.4$ Hz, 2H), 7.30 (d, $J = 8.4$ Hz, 2H), 5.72-5.61 (m, 1H), 5.01-4.97 (m, 2H), 4.73 (t, $J = 6.4$ Hz, 1H), 2.64 (d, $J = 6.8$ Hz, 2H), 2.42 (s, 3H), 1.93 (d, $J = 7.6$ Hz, 2H), 1.20-1.11 (m, 8H), 0.82-0.79 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.2, 136.7, 134.0, 129.6, 127.1, 117.7, 48.2, 39.4, 38.9, 36.8, 21.5, 15.9, 14.7. HRMS: m/z (ESI) calculated $[M+H]^+$: 324.1992, measured: 324.1983.

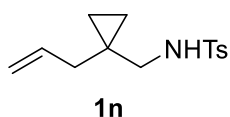


1i

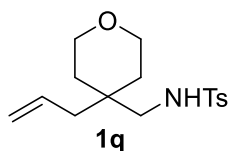
White solid. M.p. 124-126 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.59 (d, $J = 8.0$ Hz, 2H), 7.28 (d, $J = 8.0$ Hz, 2H), 7.02-6.92 (m, 8H), 5.28-5.19 (m, 1H), 4.96-4.91 (m, 2H), 3.86 (t, $J = 6.8$ Hz, 1H), 3.46 (d, $J = 6.4$ Hz, 2H), 2.83 (d, $J = 7.2$ Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 161.4 (d, $J = 245.2$ Hz), 143.6, 140.0 (d, $J = 3.0$ Hz), 136.1, 132.5, 129.7, 129.3 (d, $J = 8.4$ Hz), 127.1, 119.5, 115.3 (d, $J = 21.5$ Hz), 49.4, 48.7, 41.6, 21.5. HRMS: m/z (ESI) calculated $[M+\text{NH}_4]^+$: 445.1756, measured: 445.1749.



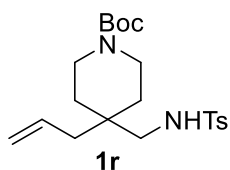
White solid. M.p. 126-128 °C. ^1H NMR (400MHz, CDCl_3) δ 7.58 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 4H), 6.95 (d, J = 8.4 Hz, 4H), 5.29-5.21 (m, 1H), 4.97-4.93 (m, 2H), 3.89 (t, J = 6.8 Hz, 1H), 3.46 (d, J = 6.8 Hz, 2H), 2.82 (d, J = 7.2 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.7, 142.6, 136.0, 132.9, 132.3, 129.7, 129.1, 128.6, 127.0, 119.8, 49.1, 48.9, 41.2, 21.5. HRMS: m/z (ESI) calculated $[\text{M}+\text{NH}_4]^+$: 477.1165, measured: 477.1163.



White solid. M.p. 39-40 °C. ^1H NMR (400MHz, CDCl_3) δ 7.73 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 5.74-5.63 (m, 1H), 4.99-4.94 (m, 2H), 4.62 (br, 1H), 2.79 (d, J = 6.4 Hz, 2H), 2.42 (s, 3H), 2.02 (d, J = 6.8 Hz, 2H), 0.38-0.30 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.3, 136.9, 135.2, 129.6, 127.1, 117.2, 49.6, 38.6, 21.5, 19.3, 10.1. HRMS: m/z (ESI) calculated $[\text{M}+\text{H}]^+$: 266.1209, measured: 266.1204.

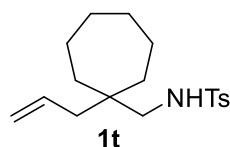


White solid. M.p. 79-81 °C; ^1H NMR (400MHz, CDCl_3) δ 7.74 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 5.75-5.66 (m, 1H), 5.08-5.04 (m, 2H), 4.87-4.83 (m, 1H), 3.65-3.54 (m, 4H), 2.82 (d, J = 7.2 Hz, 2H), 2.43 (s, 3H), 2.13 (d, J = 7.6 Hz, 2H), 1.42 (t, J = 5.6 Hz, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.5, 136.7, 133.1, 129.8, 127.0, 118.7, 63.2, 48.6, 39.9, 34.4, 33.1, 21.5. HRMS: m/z (ESI) calculated $[\text{M}+\text{H}]^+$: 310.1471, measured: 310.1466.

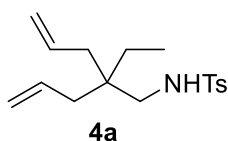


White solid. M.p. 86-87 °C. ^1H NMR (400MHz, CDCl_3) δ 7.74 (d, J = 8.4 Hz, 2H),

7.31 (d, $J = 8.0$ Hz, 2H), 5.75-5.65 (m, 1H), 5.08-4.96 (m, 2H), 4.61 (t, $J = 7.2$ Hz, 1H), 3.33 (t, $J = 7.2$ Hz, 4H), 2.78 (br, 2H), 2.43 (s, 3H), 2.09 (d, $J = 7.2$ Hz, 2H), 1.43 (s, 9H), 1.40-1.30 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 154.8, 143.5, 136.7, 133.1, 129.8, 126.9, 118.7, 79.5, 48.4, 39.6, 38.6, 35.2, 32.3, 28.4, 21.5. HRMS: m/z (ESI) calculated $[\text{M}+\text{NH}_4]^+$: 426.2421, measured: 426.2414.

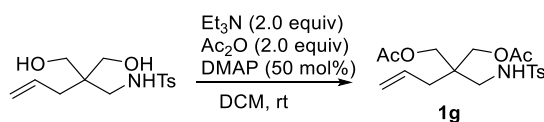


White solid. M.p. 77-79 °C. ^1H NMR (400MHz, CDCl_3) δ 7.72 (d, $J = 8.4$ Hz, 2H), 7.30 (d, $J = 8.0$ Hz, 2H), 5.76-5.65 (m, 1H), 5.03-4.99 (m, 2H), 4.43 (t, $J = 6.8$ Hz, 1H), 2.65 (d, $J = 6.8$ Hz, 2H), 2.42 (s, 3H), 1.97 (d, $J = 7.6$ Hz, 2H), 1.46-1.40 (m, 4H), 1.39-1.27 (m, 8H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.3, 136.8, 134.7, 129.7, 127.1, 117.9, 50.3, 42.5, 39.6, 35.9, 30.8, 22.5, 21.5. HRMS: m/z (ESI) calculated $[\text{M}+\text{H}]^+$: 322.1835, measured: 322.1829.



White solid. M.p. 75-78 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.72 (d, $J = 8.0$ Hz, 2H), 7.31 (d, $J = 7.6$ Hz, 2H), 5.76 - 5.65 (m, 2H), 5.04 – 5.01 (m, 4H), 4.53 (br, 1H), 2.67 (d, $J = 6.8$ Hz, 2H), 2.43 (s, 3H), 1.97 (d, $J = 7.2$ Hz, 4H), 1.26 (q, $J = 7.2$ Hz, 2H), 0.77 (t, $J = 7.6$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.3, 136.6, 133.7, 129.7, 127.0, 118.2, 48.1, 39.3, 38.9, 26.6, 21.5, 7.2. HRMS: m/z (ESI) calculated $[\text{M}+\text{H}]^+$: 308.1679, measured: 308.1673.

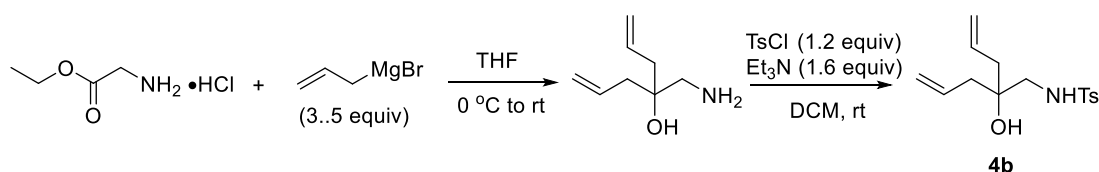
2.2.2 Procedure for the Synthesis of 1g



To a solution of *N*-(2,2-bis(hydroxymethyl)pent-4-en-1-yl)-4-methylbenzene sulfonamide ⁴ (299 mg, 1 mmol) and Et_3N (242 mg, 2 mmol) in CH_2Cl_2 , Ac_2O (2 mmol) and DMAP (61 mg, 0.5 mmol) were added at room temperature. The mixture was stirred overnight. The solution was washed with brine, dried over anhydrous Na_2SO_4 , and the filtrate was concentrated under reduced pressure. The crude residue

was purified by column chromatography on silica gel to give **1g** (298 mg, 78%). White solid. M.p. 83 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.74-5.65 (m, 1H), 5.14-5.07 (m, 3H), 3.96-3.89 (m, 4H), 2.78 (d, *J* = 7.2 Hz, 2H), 2.43 (s, 3H), 2.13 (d, *J* = 7.2 Hz, 2H), 2.02 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 170.9, 143.6, 136.6, 131.5, 129.8, 127.0, 119.9, 64.1, 44.3, 41.1, 34.8, 21.5, 20.7. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 401.1741, measured: 401.1733.

2.2.3 Procedure for the Synthesis of **4b**

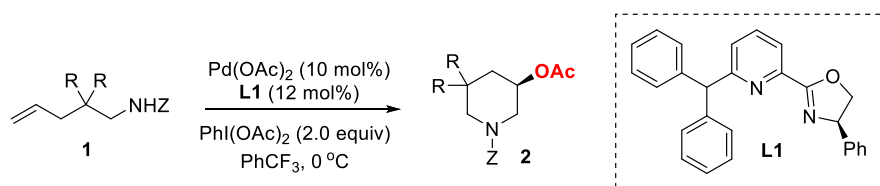


In a dry 500 mL three-necked flask, glycine ethyl ester hydrochloride (13.9 g, 100 mmol) was dissolved in dry THF (200 mL) and cooled to 0 °C under N₂ atmosphere. Then allylmagnesium bromide (350 mL, 350 mmol, 1 M in THF) was added dropwise. The mixture was warmed to ambient temperature and stirred for overnight. The solution was quenched with water and extracted with Et₂O. The organic layer was dried over anhydrous Na₂SO₄, and the filtrate was concentrated under reduced pressure. The crude residue was used directly for the next step.

To a solution of amine and triethylamine (16.1 g, 160 mmol) in CH₂Cl₂, TsCl (22.8 g, 120 mmol) was added at 0 °C. The reaction was stirred at room temperature for 12 h. The mixture was washed with brine, and dried with Na₂SO₄. The solvent was evaporated and the residue was purified by flash column chromatography on silica gel to give the desired product **4b**. White solid. M.p. 60-62 °C. ¹H NMR (400 MHz, CDCl₃) 7.73 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.83 - 5.73 (m, 2H), 5.17 - 5.09 (m, 4H), 4.76 (t, *J* = 6.4 Hz, 1H), 2.89 (d, *J* = 6.8 Hz, 2H), 2.43 (s, 3H), 2.32-2.21 (m, 4H), 2.02 (br, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 143.5, 136.6, 132.4, 129.7, 127.0, 119.9, 72.7, 49.9, 41.7, 21.5. HRMS: *m/z* (ESI) calculated [M+H]⁺: 313.1580, measured: 313.1575.

2.3 General Procedure for Enantioselective Pd(II)-Catalyzed Aminoacetoxo-

lation of Unactivated Alkenes



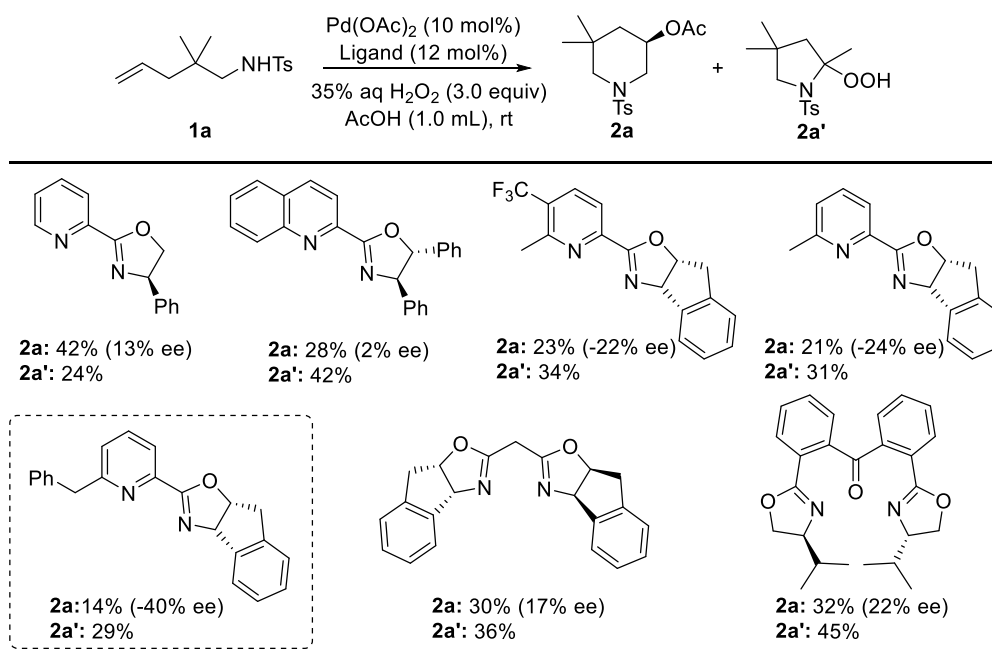
In a dried glass vial, Pd(OAc)₂ (4.4 mg, 0.02 mmol), ligand **L1** (9.4 mg, 0.024 mmol), alkene substrate **1** (0.2 mmol), and PhI(OAc)₂ (128.8 mg, 0.4 mmol) were dissolved in the PhCF₃ (0.6 mL). The reaction mixture was stirred at 0 °C for 18 h and monitored by TLC. After the consumption of alkene substrate **1**, the mixture was diluted with EtOAc (4.0 mL) and filtrated through a short pad of silica gel. The filtrate was concentrated under vacuum, and the crude residue was purified by column chromatography on silica gel with a gradient eluant of petroleum ether and ethyl acetate to give product **2**.

For the reactions of **1h- 1m**, AcOH (5.0 equiv) was added as additive, and the solvent was replaced by EtOAc (0.6 mL). All the results were listed in Table 2

2.4 Optimization of the Reaction Conditions

2.4.1 Ligand Screening with H₂O₂ as the oxidant in HOAc

In a dried glass vial, Pd(OAc)₂ (0.01 mmol, 2.2 mg), ligand **L** (0.012 mmol), and alkene substrate **1a** (0.1 mmol, 26.8 mg) were dissolved in AcOH (1.0 mL) at room temperature. Then H₂O₂ (3.0 equiv, 35% wt in aqueous) was added, and the reaction mixture was stirred at room temperature for 24 h and monitored by TLC. After alkene substrate **1a** was consumed, the mixture was diluted by EtOAc (4.0 mL) and filtrated through a short pad of silica gel. The filtrate was concentrated under vacuum, and the crude residue was analyzed by ¹H NMR with CH₃NO₂ as an internal standard and purified by column chromatography on silica gel with a gradient eluant of petroleum ether and ethyl acetate to give product **2a**. Then the ee was determined by HPLC on chiral stationary phase. The results were listed in Table S1.

Table S1. Initial studies on the asymmetric aminoacetoxylation with H₂O₂/HOAc.

^aReaction conditions: substrate (0.1 mmol), Pd(OAc)₂ (10 mol %), ligand (12 mol %), 35% aq H₂O₂ (3.0 equiv), AcOH (1.0 mL), rt. ^bYield was determined by ¹H NMR with CH₃NO₂ as an internal standard and ee determined by HPLC on chiral stationary phase.

Table S2. Oxidant Screening.^{a,b}

Reaction scheme showing the conversion of substrate **1a** to product **2a** using $\text{Pd}(\text{OAc})_2$ (10 mol%), L (15 mol%), and an Oxidant in AcOH (1 mL) at room temperature (rt).

entry	Oxidant	Yield (%) ^b	ee(%)	
1	H_2O_2 (35% aq)	14	-40	
2	Selectflor	trace	nd	← 15% Wacker product
3	NFSI	trace	nd	← 18% Wacker product
4	PhI(OAc)₂	71	-44	
5	Oxone	0	---	} substrate 1a decomposed
6	$\text{Na}_2\text{S}_2\text{O}_8$	0	---	
7	$\text{K}_2\text{S}_2\text{O}_8$	0	---	← 14% Wacker product
8	$\text{O}_2 + \text{NaNO}_2$	0	---	← 50% 1a recovered

^aAll reactions were run at 0.1 mmol scale. ^bYield was determined by ¹H NMR with CH₃NO₂ as an internal standard and ee determined by HPLC on chiral stationary phase.

Table S3. Solvent Screening in the Presence of AcOH.^{a,b}

Entry	Solvent	Yield(%) ^b	ee (%)
1	MeCN	trace	nd
2	Toluene	32	-64
3	DCM	28	-55
4	THF	30	-61
5	Acetone	trace	nd
6	EtOAc	33	-65

^aAll reactions were run at 0.1 mmol scale. ^bYield was determined by ¹H NMR with CH₃NO₂ as an internal standard and ee determined by HPLC on chiral stationary phase.

Table S4. Further Optimization of the Reaction Conditions.^{a,b}

Entry	Pd catalyst	Ligand	Yield(%) ^b	ee (%)
1	Pd(OAc) ₂	LS1	33	-65
2 ^c	Pd(OAc) ₂	LS1	59	-66
3 ^c	Pd(OAc) ₂	LS2	43	-22
4 ^c	Pd(OAc) ₂	LS3	53	-37
5 ^c	Pd(OAc) ₂	LS4	37	40
6 ^c	Pd(OAc) ₂	BnPyox	66	75
7 ^c	PdCl ₂	BnPyox	51	64
8 ^c	Pd(TFA) ₂	BnPyox	59	74
9 ^{c,d}	Pd(OAc) ₂	BnPyox	74	78
10 ^{c,d,e}	Pd(OAc) ₂	BnPyox	75	81
11 ^{d,e,f}	Pd(OAc) ₂	BnPyox	69	84
12 ^{e,f,g}	Pd(OAc)₂	BnPyox	52	91

LS1

LS2

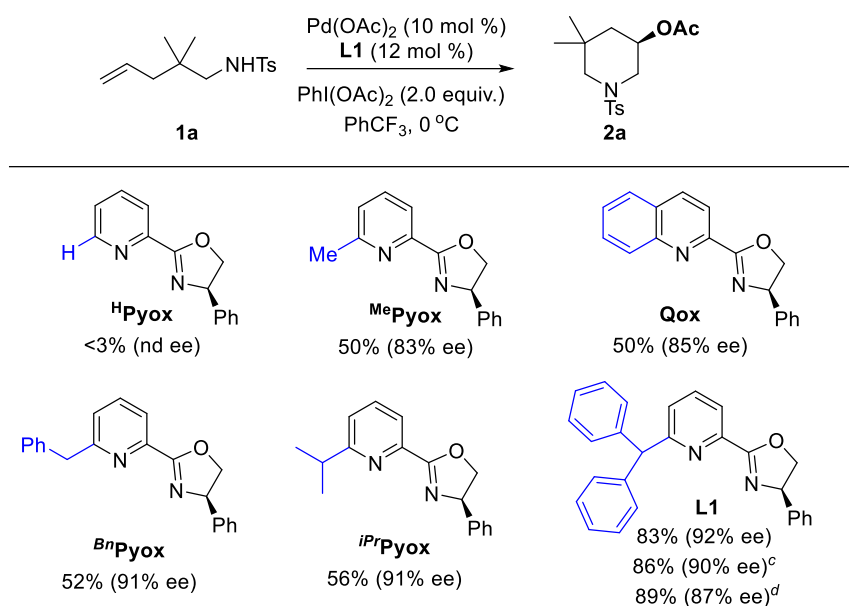
LS3

LS4

^aAll reactions were run at 0.1 mmol scale. ^bYield obtained by ¹H NMR with MeNO₂ as internal standard and ee determined by HPLC on chiral stationary phase. (12 mol%). ^cEtOAc (0.3 mL). ^dAcOH (5.0 equiv.). ^e0 °C. ^fPhCF₃ (0.3 mL). ^gNo AcOH.

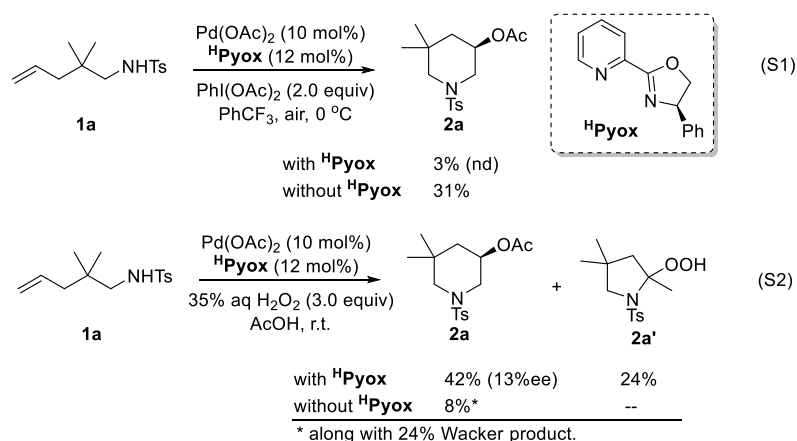
Above systematic optimization of the reaction conditions revealed that the novel ligand **BnPyox** bearing a benzylic group at C6 of pyridine ring exhibits moderate reactivity (52% yield) but excellent enantioselectivity (91% ee, yellow highlighted in Table S4), which prompted us to survey more ligands with different substituents at the C6 position. The data were listed in Table S5; the new ligand **L1** bearing a more bulky group at C6 exhibited excellent reactivity (83% yield) and enantioselectivity (92% ee).

Table S5. Steric Effect of Ligand on the reaction of **1a**.^{a,b}



^aThe reaction of **1a** was conducted on a 0.1 mmol scale. ^b Yields determined by ¹H NMR spectroscopy of the crude mixture with MeNO₂ as an internal standard, and the ee value in parenthesis was determined by HPLC on a chiral stationary phase. ^cAcOH (1.0 equiv). ^dAcOH (5.0 equiv).

For the comparison experiments, the results were provided in the eq S1-2 (see below): The reaction with the PhI(OAc)₂ conditions in the absence of ligand gave product **2a** in 31% yield; however, yield of the desired product **2a** was diminished to trace amount by the addition of **HPyox** ligand. Under our previous HOAc/H₂O₂ conditions, addition of **HPyox** gave a reasonable yield but very low ee. For other ligands, please see the results in Table S1. However, the reaction without the **HPyox** ligand was not selective for cyclization and only a small amount of **2a** was detected.



2.4.2 Comparison of reactions with $\text{PhI}(\text{OAc})_2$ and H_2O_2 .

For the alternative I(III)-mediated cyclization pathway, the alkyl C-Pd bond forming and oxidative cleavage should not be involved in the enantioselective cyclization. Thus, if other oxidants, such as H_2O_2 was used, the enantioselectivity should be distinctly different from the reaction with $\text{PhI}(\text{OAc})_2$. On the other hand, if other Lewis acid was used to replace the palladium catalyst, the similar reaction should be observed. Based on this hypothesis, the parallel reactions were conducted with the same reaction conditions except oxidants. As shown in Table S6, the identical enantioselectivities were obtained in the different solvent system (entries 1 vs 2, 3 vs 4), but with different reaction yields. We reasoned that the poor yield is possibly derived from the slow generation of Pd(IV) species by oxidation of alkyl C-Pd(II) species with H_2O_2 , which was reported in our previous study. While, the same enantioselectivities obtained in both $\text{PhI}(\text{OAc})_2$ and H_2O_2 possibly stem from the aminopalladation pathway.

Table S6. Controlling experiments with $\text{PhI}(\text{OAc})_2$ or H_2O_2 as oxidants.

$\text{Pd}(\text{OAc})_2$ (10 mol%) L1 (12 mol%) [O] (x equiv) HOAc (y equiv) temp					
Entry	[O]	HOAc	Solvent	Temp	Product
1	$\text{PhI}(\text{OAc})_2$ (2 eq)	10 eq	PhCF_3 (0.6 mL)	0 °C	73% (86% ee)
2	H_2O_2 (4 eq)	10 eq	PhCF_3 (0.6 mL)	0 °C	13% (86% ee)
3	$\text{PhI}(\text{OAc})_2$ (2 eq)	10 eq	EA (0.6 mL)	0 °C	70% (81% ee)
4	H_2O_2 (2 eq)	10 eq	EA (0.6 mL)	0 °C	9% (81% ee)

Secondly, a series of metal catalysts, such as Cu, Ni, Zn, Fe, Au, Ag, and Sc, were employed as Lewis acid to replace palladium catalyst, however, no desired product was detected in these reactions (Table S7). These results also support the more likely mechanism involving aminopalladation pathway.

Table S7. Oxidative aminoacetoxylation catalyzed by other metal catalysts.

Entry	M	2a/3a	Entry	M	2a/3a
1	CuOAc	0%/0%	6	AuCl ₃	0%/0%
2	Cu(OAc) ₂	0%/0%	7	AgOAc	0%/0%
3	Fe(OAc) ₂	0%/0%	8	Zn(OTf) ₂	0%/0%
4	PtCl ₂	0%/0%	9	Sc(OTf) ₃	0%/0%
5	NiCl ₂	0%/0%			

2.4.3 Screening of substrates with different protecting groups on nitrogen.

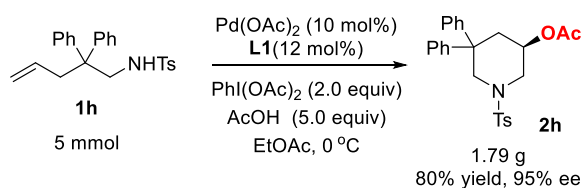
Typical procedure for optimization reaction condition with PhI(OAc)₂: more substrates with various sulfonyl protecting groups were examined, the results were listed in Table S8.

Table S8. Substrates with various sulfonyl protecting groups.

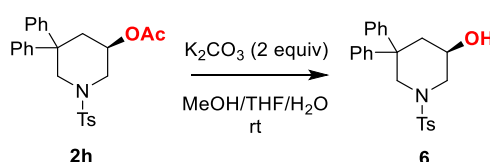
Entry	Alkene	Product	yield	ee
1		Z= Ps	73%	90%
2		PMPs	73%	93%
3		2,4-DMPs	75%	95%
4		<i>p</i> - ^t BuPs	69%	92%
5		<i>p</i> -Ns	45%	81%
6		<i>o</i> -Ns	9%	81%
7		Tces	24% ^c	nd

^a Reaction conditions: substrate (0.2 mmol), Pd(OAc)₂ (10 mol %), ligand **L1** (12 mol %), PhI(OAc)₂ (2 equiv), PhCF₃ (0.6 mL), 0 °C, 18 h. ^b Isolated yield. and ee determined by HPLC on chiral stationary phase. ^c The product contains some unidentified impurities, which is unable to detecting ee values. Ps = phenylsulfonyl, PMPs = *para*-MeO-phenylsulfonyl, 2,4-DMPs = 2,4-dimethyl-phenylsulfonyl, *p*-^tBuPs = *para*-*tert*-butyl-phenylsulfonyl, Ns = Nitrophenylsulfonyl, *p*-Ns = *para*-nitrophenylsulfonyl, *o*-Ns = *ortho*-nitrophenylsulfonyl, Tces = Trichloroethoxysulfonyl.

2.5 Procedure for Large-scale Reaction and Deprotection

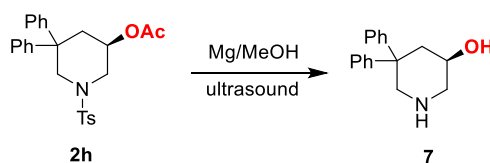


In a 50 mL round bottom flask, $\text{Pd}(\text{OAc})_2$ (110 mg, 0.5 mmol), ligand **L1** (235 mg, 0.6 mmol), alkene substrate **1h** (195.5 mg, 5.0 mmol), $\text{PhI}(\text{OAc})_2$ (3.2 g, 10.0 mmol) were dissolved in the EtOAc (15 mL). Then AcOH (1.5 g, 25 mmol) was added and the reaction mixture was stirred at 0°C for 18 h and monitored by TLC. After alkene substrate **1h** was consumed, the mixture was diluted with EtOAc and filtrated through a short pad of silica gel. The filtrate was concentrated under vacuum, and the crude residue was purified by column chromatography on silica gel with a gradient eluant of petroleum ether and ethyl acetate to give product **2h** (1.79 g, 80% yield, 95% ee).



In a 50 mL round bottom flask, **2h** (449 mg, 1.0 mmol) was dissolved in the $\text{THF}/\text{H}_2\text{O}/\text{MeOH}$ (v/v/v = 1:1:1, 30 mL). Then K_2CO_3 (276 mg, 2 mmol) was added and the reaction mixture was stirred at room temperature and monitored by TLC. After **2h** was consumed, the mixture was diluted with EtOAc , washed with brine, the phases were separated, and then dried over sodium sulfate. After concentration, the obtained crude residue was purified by column chromatography on silica gel with a gradient eluant of petroleum ether and ethyl acetate to give product **6** (366.3 mg, 90% yield, 93% ee). $[\alpha]_{\text{D}}^{33.1} = -119.09$ (c 1.03, CHCl_3). Known compound **6**: ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, $J = 8.0$ Hz, 2H), 7.43 (d, $J = 7.6$ Hz, 2H), 7.35-7.15 (m, 10H), 4.26 (d, $J = 12.4$ Hz, 1H), 3.83-3.71 (m, 2H), 2.70 (d, $J = 12.0$ Hz, 1H), 2.60 (d, $J = 12.0$ Hz, 1H), 2.41 (s, 3H), 2.29 (dd, $J = 9.6, 9.2$ Hz, 1H), 2.08 (dd, $J = 12.4, 10.0$ Hz, 1H), 1.74 (brs, 1H, OH). ^{13}C NMR (100 MHz, CDCl_3) δ 145.8, 144.2, 143.9, 132.3, 129.8, 128.6, 128.5, 127.8, 127.7, 126.8, 126.7, 126.3, 64.6, 53.9, 52.6, 46.2, 43.2, 21.5.

HPLC (IC, 0.46×25 cm, $5\ \mu\text{m}$, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 20.73 min (major) and 76.51 min (minor).



Compound **2h** (89.8 mg, 0.2 mmol) and fresh Mg turnings (96 mg, 4 mmol) were placed into an oven-dried sealed tube (10 mL). Then fresh dried MeOH (2 mL) was added under N₂ atmosphere. The reaction mixture was sonicated (ultrasonic cleaning bath) over 5 h. After that, the solvent was removed under vacuum. The crude residue was purified by column chromatography on silica gel with a gradient eluant of DCM/MeOH (10:1) to give product **7** as a yellow solid (35.6 mg, 70% yield, 95% ee). M.p. 110-112 °C. $[\alpha]_D^{20.7} = -18.33$ (c 0.91, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.31 (m, 4H), 7.28-7.13 (m, 6H), 3.74-3.66 (m, 2H), 3.16 (dd, *J* = 11.2, 2.8 Hz, 1H), 3.05 (d, *J* = 14.0 Hz, 1H), 2.91 (d, *J* = 12.8 Hz, 1H), 2.59 (dd, *J* = 11.6, 9.6 Hz, 1H), 2.19 (dd, *J* = 12.0, 10.8 Hz, 1H), 1.89 (brs, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 147.2, 144.8, 128.8, 128.4, 127.4, 126.4, 126.14, 126.12, 65.7, 54.9, 53.6, 47.4, 43.9. HRMS: *m/z* (ESI) calculated [M+H]⁺: 254.1539, measured: 254.1537. HPLC (PC1, 0.46*25 cm, 5 μm, acetonitrile/water = 95/5, flow 0.7 mL/min, detection at 254 nm) retention time = 9.68 min (major) and 11.65 min (minor).

3. Mechanism Studies

3.1 The Ligands Effect on the reaction rate.

According to the general procedure 2.3, the reaction of **1a** (0.1 mmol) was conducted with different ligand (**^HPyox**, **^{Me}Pyox**, **^{iPr}Pyox** and **L1**) or without ligand independently. The reactions were conducted for the specified time (such as 1 h, 2 h, 3 h, 5 h, 7 h), then the mixture was immediately diluted by CH₂Cl₂ and filtrated through a short pad of silica gel. The filtrate was concentrated under vacuum, and the crude residue was analyzed by ¹H NMR with CH₃NO₂ as internal standard. The results were listed in Figure S1.

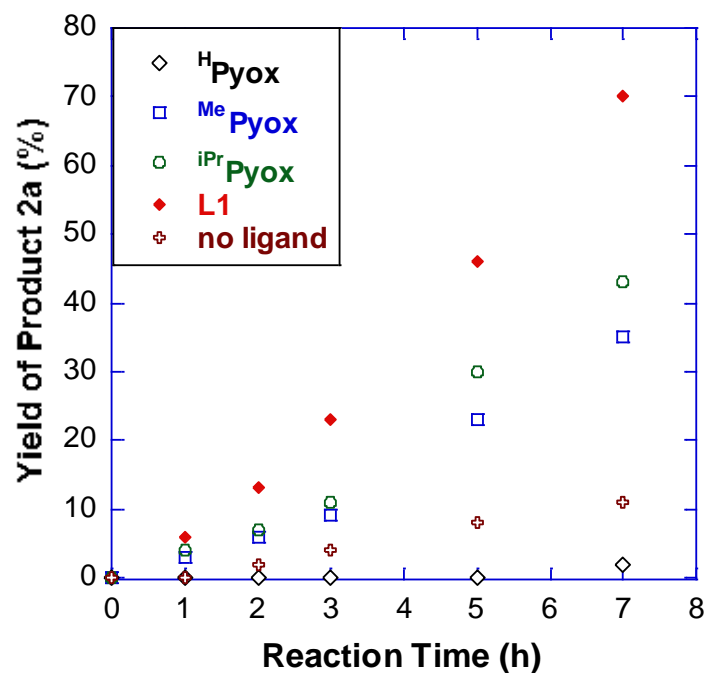
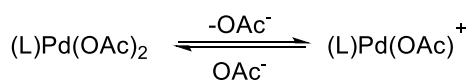
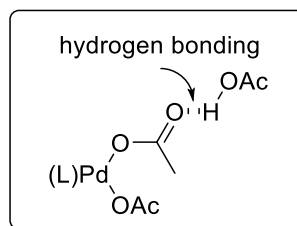


Figure S1. The Ligands Effect on the reaction rate.

3.2 The Effect of Additives.



- * adding acid could accelerate dissociation due to the hydrogen bonding (see right)
- * adding acetate anion could shift equilibrium to left.



In order to survey the possible of acetate association from $LPd(OAc)_2$ center, Stahl and coworkers reported that adding catalytic amount of acid could accelerate benzoate to associate from $Pd(II)$ complex. In contrast, adding acetate anion could also retard this dissociation. In order to get more insight on this process, the individual reaction rates with/without additives (e.g. $HOAc$ and Bu_4NOAc) were measured according to the general procedures 2.3: the reaction of **1a** (0.1 mmol) was conducted with $HOAc$ (20 mol% and 50 mol%), Bu_4NOAc (20 mol% and 50 mol%) or without additives independently. The reactions were conducted for the specified time (such as 1 h, 2 h, 3 h, 5 h, 7 h). Then the mixture was immediately diluted by CH_2Cl_2 and filtrated through a short pad of silica gel. The filtrate was concentrated under vacuum, and the crude residue was analyzed by 1H NMR with CH_3NO_2 as internal standard. The results were listed in Figure S2.

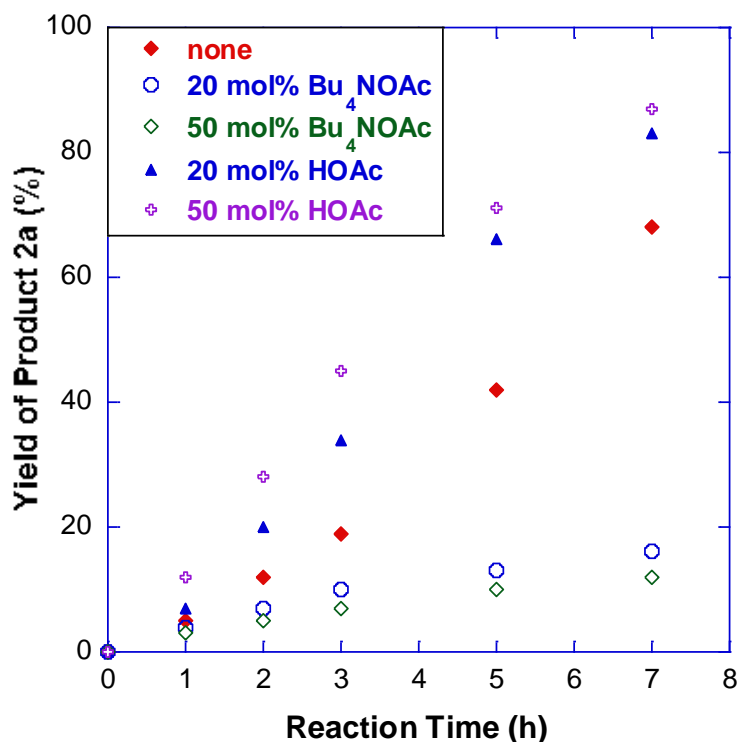
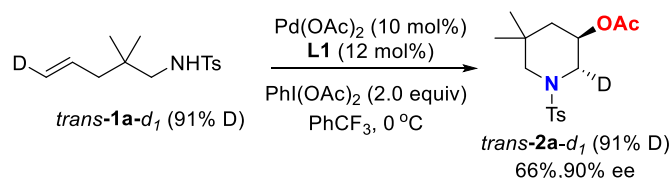


Figure S2. The Additive Effect on the reaction rate.

3.3 Stereochemistry



In a dried glass vial, Pd(OAc)_2 (4.4 mg, 0.02 mmol), ligand **L1** (9.4 mg, 0.024 mmol), alkene substrate *trans*-**1a-d**₁ (53.6 mg, 0.2 mmol), PhI(OAc)_2 (128.8 mg, 0.4 mmol) were dissolved in the PhCF_3 (0.6 mL). The reaction mixture was stirred at 0 °C for 18 h and monitored by TLC. After *trans*-**1a-d**₁ was consumed, the mixture was diluted with EtOAc (4.0 mL) and filtrated through a short pad of silica gel. The filtrate was concentrated under vacuum, and the crude residue was purified by column chromatography on silica gel with a gradient eluant of petroleum ether and ethyl acetate to give a single isomer, and its structure was determined as *trans*-**2a-d**₁. The ^1H NMR spectrum of *trans*-**2a-d**₁ was listed Figure S3. For the detailed configuration analysis of *trans*-**2a-d**₁, please see the supporting information of the reference 1c.

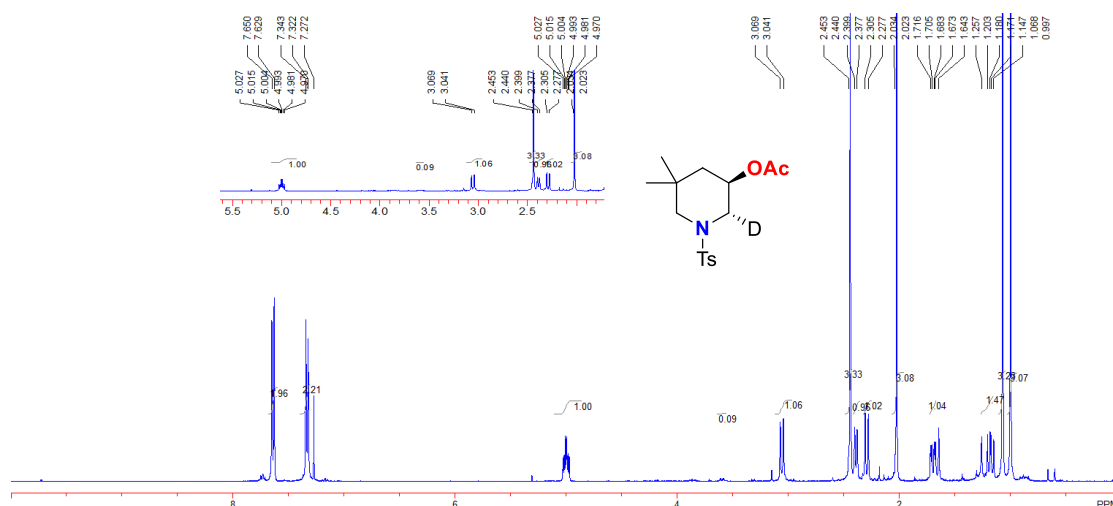
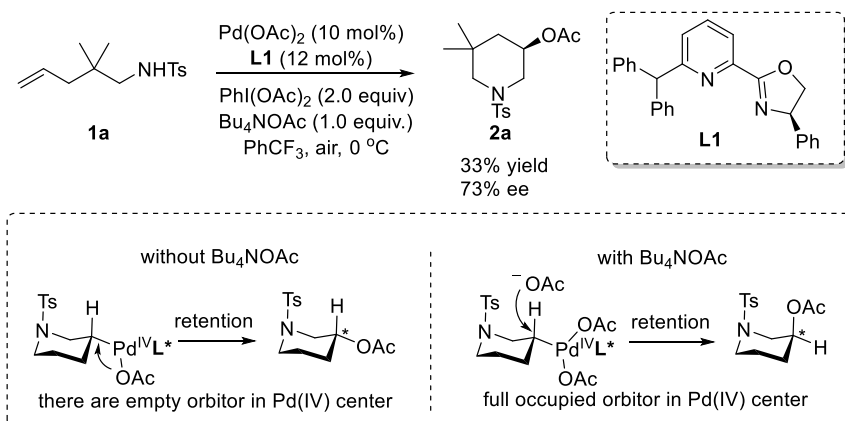


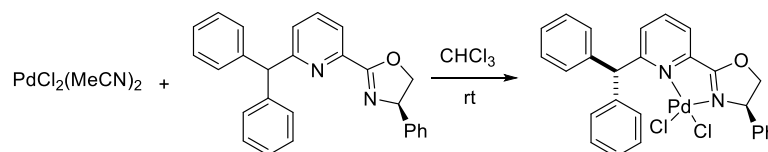
Figure S3. The ^1H NMR spectrum of *trans*-**2a**- d_1 .

Above stereochemistry reveals that the reaction is more likely to undergoes a *trans*-aminopalladation and direct reductive elimination on the Pd(IV) center with stereo-retention pathway. More interesting, when extraneous Bu_4NOAc (1.0 equiv) was added to the standard condition, the enantioselectivity was remarkably decreased to 73% ee (Scheme S1). We reasoned that, in the presence of extraneous Bu_4NOAc , the reductive C-OAc elimination via $\text{S}_{\text{N}}2$ pathway occurred as competitive pathway to generate another enantiomer of **2a**, resulting in the decreased ee values. The similar observation have been reported by Gagne in the C-X reductive elimination on the Pt(IV) center.⁷ This result is also consistent with our above proposed mechanism with *trans*-aminopalladation/ direct reductive elimination (retention). If the reaction undergoes *cis*-aminopalladation/ $\text{S}_{\text{N}}2$ -reductive elimination (inversion) pathway, the higher or similar ee value of product should be observed in the presence of extra Bu_4NOAc , which is opposite to our results in below.



Scheme S1. Effect of extraneous Bu_4NOAc .

3.4 The Synthesis of complex (L1)PdCl₂



PdCl₂(MeCN)₂ (130 mg, 0.5 mmol) and ligand **L1** (130 mg, 0.5 mmol) was dissolved in CHCl₃ (10 mL) at room temperature. The reaction mixture was stirred overnight. The solid was filtered, washed with Et₂O and dried under vacuum. An orange-yellow solid (268mg) was obtained. Crystallization via diffusion of *n*-hexane and chloroform gave yellow needles suitable for X-ray analysis. ¹H NMR (400 MHz, CDCl₃) δ 8.10 (s, 1H), 7.94 (t, *J* = 7.2 Hz, 1H), 7.78 (d, *J* = 6.8 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.36-7.29 (m, 5H), 7.27-7.21 (m, 6H), 7.13 (d, *J* = 7.2 Hz, 2H), 7.09-7.07 (m, 2H), 5.72 (dd, *J* = 10.0, 5.2 Hz, 1H), 5.22 (t, *J* = 9.2 Hz, 1H), 4.69 (dd, *J* = 8.4, 5.6 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 171.5, 169.5, 144.7, 141.5, 140.8, 139.5, 138.6, 131.9, 129.6, 129.3, 128.9, 128.8, 128.6, 128.5, 127.0, 126.9, 126.8, 124.2, 78.9, 65.3, 54.9.

3.5 Chiral model of the aminopalladation.

Deterium-labeling experiment demonstrated that the reaction involves a trans-aminopalladation, which reveals a initial olefin coordination to (L)Pd(II) complex. There are two coordination models A and B, which listed in below. Compared to **model A**, the repulsion between phenyl (in oxazoline ring) and NTs (in substrate **1a**) group in **model B** resulted in an unfavorable *6-endo trans*-aminopalladation. In this scenario, (R)-**int-I** was generated from **model A**, which undergoes a sequential oxidation and direct reductive elimination to give final (R)-**trans-2a-d₁**.

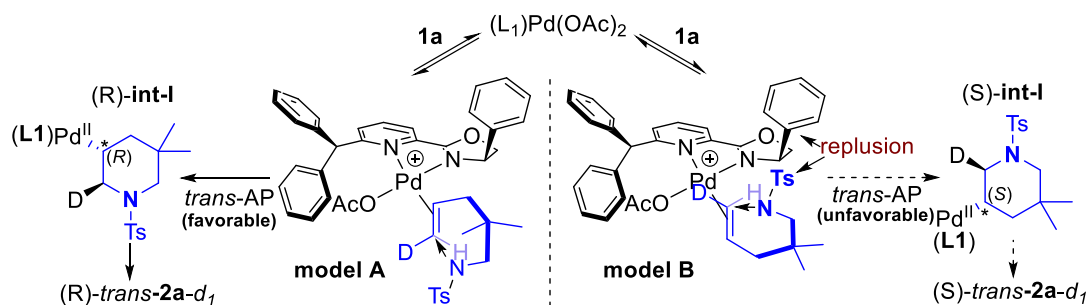
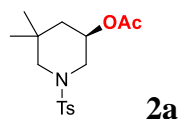


Figure S4. Coordination models of the olefin to Pd species.

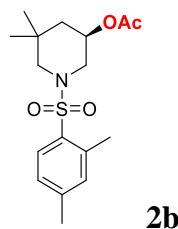
4. New Compounds Characterization



The reaction provided crude products with >20:1 regioselectivity.

Known compound **1c**. White solid (53.1 mg, 82% yield, rr > 20:1; 92% ee). $[\alpha]_D^{26.9} = 41.17$ (*c* 1.00, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.64 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 5.01-4.97 (m, 1H), 3.60 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.04 (d, *J* = 11.2 Hz, 1H), 2.43 (s, 3H), 2.42 (dd, *J* = 10.8, 8.4 Hz, 1H), 2.31 (d, *J* = 11.2 Hz, 1H), 2.02 (s, 3H), 1.68-1.65 (m, 1H), 1.19-1.15 (m, 1H), 1.06 (s, 3H), 1.00 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 143.4, 133.2, 129.5, 127.3, 66.7, 56.6, 49.0, 41.7, 31.5, 27.8, 25.3, 21.3, 20.9.

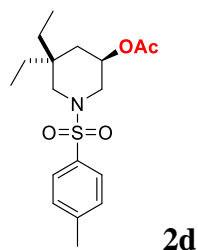
HPLC (IC, 0.46*25 cm, 5 μm, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 15.18 min (minor) and 26.36 min (major).



The reaction provided crude products with >20:1 regioselectivity.

White solid (50.7 mg, 75% yield, 95% ee). M.p. 80 -82 °C. $[\alpha]_D^{33.0} = 29.49$ (*c* 1.00, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.13-7.09 (m, 2H), 4.98-4.93 (m, 1H), 3.59 (dd, *J* = 11.2, 4.0 Hz, 1H), 3.05 (d, *J* = 12.0 Hz, 1H), 2.73 (dd, *J* = 11.6, 8.8 Hz, 1H), 2.65-2.59 (m, 4H), 2.36 (s, 3H), 2.00 (s, 3H), 1.71 (dd, *J* = 13.2, 4.4 Hz, 1H), 1.29 (dd, *J* = 13.2, 9.6 Hz, 1H), 0.97 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 170.0, 143.6, 137.7, 133.4, 132.9, 130.4, 126.7, 66.9, 56.1, 48.2, 41.9, 31.8, 27.9, 25.6, 21.3, 21.1, 20.6. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 357.1843, measured: 357.1836. IR (neat): 2959, 1732, 1596, 1467, 1340, 1236, 1160, 1087, 911, 805, 627 cm⁻¹.

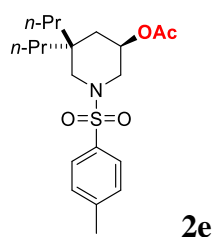
HPLC (IC, 0.46*25 cm, 5 μm, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 14.10 min (minor) and 30.03 min (major).



The reaction provided crude products with 14:1 regioselectivity.

Yellow oil (56.5 mg, 80% yield, 92% ee). $[\alpha]_D^{33.4} = 15.54$ (*c* 0.94, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.02-4.96 (m, 1H), 3.64 (dd, *J* = 10.8, 4.4 Hz, 1H), 3.17 (d, *J* = 11.6 Hz, 1H), 2.43 (s, 3H), 2.36 (t, *J* = 9.6 Hz, 1H), 2.21 (d, *J* = 11.6 Hz, 1H), 2.00 (s, 3H), 1.77 (dd, *J* = 13.2, 4.4 Hz, 1H), 1.50-1.40 (m, 2H), 1.37-1.23 (m, 2H), 1.08 (dd, *J* = 13.2, 10.0 Hz, 1H), 0.83-0.76 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.9, 143.5, 133.5, 129.7, 127.5, 66.7, 53.8, 49.4, 37.9, 36.9, 28.6, 25.3, 21.5, 21.1, 7.2, 7.1. HRMS: *m/z* (ESI) calculated $[\text{M}+\text{NH}_4]^+$: 371.1999, measured: 371.1995.

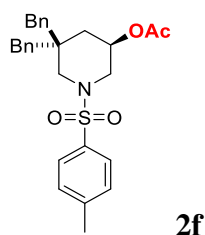
HPLC (IC, 0.46*25 cm, 5 μm , hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 13.90 min (minor) and 21.49 min (major).



The reaction provided crude products with 15:1 regioselectivity.

White solid (62.5 mg, 82% yield, 93% ee). M.p. 92-93 °C. $[\alpha]_D^{23.3} = 18.66$ (*c* 1.07, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 5.02-4.97 (m, 1H), 3.67 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.19 (d, *J* = 11.6 Hz, 1H), 2.44 (s, 3H), 2.36 (t, *J* = 10.0 Hz, 1H), 2.21 (d, *J* = 11.6 Hz, 1H), 2.01 (s, 3H), 1.79 (dd, *J* = 13.6, 4.0 Hz, 1H), 1.41-1.37 (m, 2H), 1.26-1.17 (m, 6H), 1.09 (dd, *J* = 13.2, 10.0 Hz, 1H), 0.92-0.85 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.9, 143.5, 133.4, 129.7, 127.5, 66.7, 54.4, 49.4, 39.5, 38.7, 36.9, 35.9, 21.5, 21.1, 16.0, 14.74, 14.70. HRMS: *m/z* (ESI) calculated $[\text{M}+\text{H}]^+$: 382.2047, measured: 382.2039.

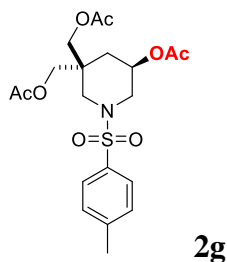
HPLC (IC3, 0.46*25 cm, 5 μm , hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 8.32 min (minor) and 10.94 min (major).



The reaction provided crude products with >20:1 regioselectivity.

Known compound **1c**. White solid (58.0 mg, 68% yield, 87% ee). $[\alpha]_D^{33.6} = -18.05$ (c1.10, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.33-7.17 (m, 10H), 6.97 (d, *J* = 8.0 Hz, 2H), 5.30-5.22 (m, 1H), 3.59 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.31 (d, *J* = 11.2 Hz, 1H), 2.89 (s, 2H), 2.67 (d, *J* = 14.0 Hz, 1H), 2.57 (d, *J* = 14.0 Hz, 1H), 2.40 (s, 3H), 2.30 (d, *J* = 11.6 Hz, 1H), 2.06 (t, *J* = 9.6 Hz, 1H), 2.00 (s, 3H), 1.77 (dd, *J* = 12.8, 4.4 Hz, 1H), 1.15 (dd, *J* = 12.8, 10.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 143.8, 136.9, 136.5, 132.5, 131.0, 130.9, 129.6, 128.1, 127.9, 127.6, 126.5, 126.3, 66.6, 52.3, 49.1, 43.9, 42.5, 38.5, 35.9, 21.5, 21.0.

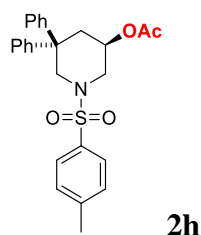
HPLC (IC, 0.46*25 cm, 5 μm, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 17.69 min (minor) and 35.08 min (major).



The reaction provided crude products with 10:1 regioselectivity.

White solid (66.2 mg, 75% yield, 80% ee). M.p. 142-144 °C. $[\alpha]_D^{27.5} = 9.96$ (c 1.00, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 4.98 (m, 1H), 4.15-3.96 (m, 4H), 3.20-2.90 (m, 4H), 2.43 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 2.01 (s, 3H), 1.72-1.68 (m, 1H), 1.58-1.53 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 170.5, 170.4, 169.9, 143.9, 133.3, 129.8, 127.5, 65.7, 65.0, 64.7, 49.1, 48.9, 37.9, 31.8, 21.5, 21.0, 20.7, 20.6. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 459.1796, measured: 459.1790.

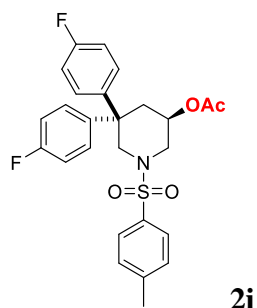
HPLC (IC, 0.46*25 cm, 5 μm, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 35.97 min (minor) and 50.80 min (major).



The reaction provided crude products with >20:1 regioselectivity.

Known compound **1c**. White solid (77.2 mg, 86% yield, 93% ee). $[\alpha]_D^{22.0} = -51.06$ (*c* 1.00, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.35-7.15 (m, 10 H), 4.84-4.77 (m, 1H), 4.23 (d, *J* = 12.4 Hz, 1H), 3.70 (dd, *J* = 10.4, 4.0 Hz, 1H), 2.82-2.80 (m, 2H), 2.47 (t, *J* = 10.0 Hz, 1H), 2.40 (s, 3H), 2.16 (dd, *J* = 12.4, 10.0 Hz, 1H), 1.87 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.7, 145.6, 143.8, 143.3, 132.2, 129.7, 128.5, 128.3, 127.6, 127.4, 126.5, 126.4, 126.3, 66.8, 53.9, 49.1, 45.9, 39.3, 21.4, 20.8.

HPLC (IC, 0.46*25 cm, 5 μm, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 14.02 min (major) and 24.55 min (minor).

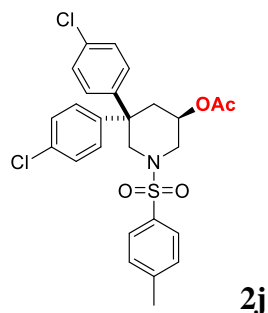


The reaction provided crude products with 17:1 regioselectivity.

White solid (79.6 mg, 82% yield, 92% ee). M.p. 160-162 °C. $[\alpha]_D^{26.1} = -72.35$ (*c* 1.01, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, *J* = 8.4 Hz, 2H), 7.40-7.27 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.14-7.11 (m, 2H), 7.02 (t, *J* = 8.4 Hz, 2H), 6.94 (t, *J* = 8.4 Hz, 2H), 4.79-4.75 (m, 1H), 4.13 (d, *J* = 12.4 Hz, 1H), 3.71 (dd, *J* = 10.4, 4.0 Hz, 1H), 2.76-2.72 (m, 2H), 2.47 (t, *J* = 9.6 Hz, 1H), 2.42 (s, 3H), 2.11 (dd, *J* = 12.4, 10.4 Hz, 1H), 1.90 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 161.3 (d, *J* = 245.2 Hz), 161.2 (d, *J* = 245.2 Hz), 144.0, 141.3 (d, *J* = 2.3 Hz), 138.9 (d, *J* = 3.8 Hz), 132.1, 129.9, 129.2 (d, *J* = 8.4 Hz), 128.1 (d, *J* = 7.6 Hz), 127.7, 115.5 (d, *J* = 21.2 Hz), 115.3 (d, *J* = 21.3 Hz), 66.6, 54.2, 49.1, 45.2, 39.7, 21.5, 20.8. ¹⁹F NMR (376 MHz, CDCl₃) δ -115.8 (m), -115.9 (m). HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 503.1811, measured: 503.1807.

HPLC (IC3, 0.46*25 cm, 5 μm, hexane/isopropanol = 70/30, flow 0.7 mL/min,

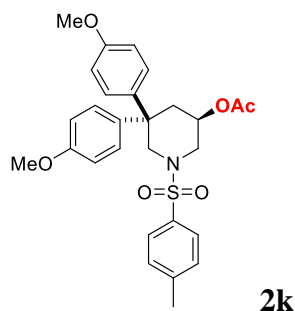
detection at 214 nm) retention time = 12.58 min (minor) and 21.55 min (major).



The reaction provided crude products with >20:1 regioselectivity.

White solid (89.1 mg, 86% yield, 95% ee). M.p. 166-168 °C. $[\alpha]_D^{24.0} = -63.84$ (*c* 1.05, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.36-7.27 (m, 6H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.8 Hz, 2H), 4.79-4.75 (m, 1H), 4.10 (d, *J* = 12.4 Hz, 1H), 3.70 (dd, *J* = 10.4, 3.2 Hz, 1H), 2.77-2.73 (m, 2H), 2.48 (t, *J* = 9.6 Hz, 1H), 2.42 (s, 3H), 2.11 (dd, *J* = 12.4, 10.0 Hz, 1H), 1.90 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.7, 144.1, 143.7, 141.6, 132.7, 132.1, 129.9, 128.9, 128.8, 128.7, 127.9, 127.6, 66.5, 53.8, 49.1, 45.4, 39.3, 21.5, 20.8. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 535.1220, measured: 535.1219.

HPLC (IC3, 0.46*25 cm, 5 μm, hexane/isopropanol = 70/30, flow 0.7 mL/min, detection at 214 nm) retention time = 11.24 min (minor) and 21.44 min (major).

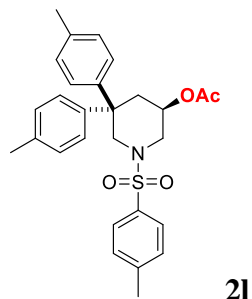


The reaction provided crude products with >20:1 regioselectivity.

White solid (72.5 mg, 71% yield, 92% ee). M.p. 94-96 °C. $[\alpha]_D^{22.4} = -74.13$ (*c* 0.98, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.36-7.29 (m, 4H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 8.8 Hz, 2H), 4.82-4.77 (m, 1H), 4.22 (d, *J* = 12.0 Hz, 1H), 3.79 (s, 3H), 3.78-3.74 (m, 1H), 3.74 (s, 3H), 2.76 (d, *J* = 12.8 Hz, 1H), 2.64 (d, *J* = 12.0 Hz, 1H), 2.41 (s, 3H), 2.38 (t, *J* = 10.0 Hz, 1H), 2.06 (dd, *J* = 12.4, 10.8 Hz, 1H), 1.92 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 157.9, 157.8, 143.8, 138.2, 135.5, 132.3, 129.8, 128.6, 127.7, 127.5, 113.9, 113.7, 66.9, 55.2, 55.1, 54.3, 49.2, 44.9, 39.8, 21.5, 20.9. HRMS: *m/z* (ESI)

calculated $[M+NH_4]^+$: 527.2210, measured: 527.2207.

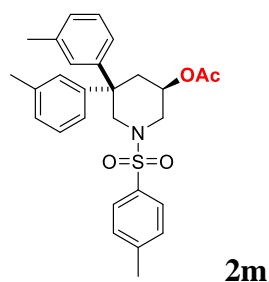
HPLC (IC-3, 0.46*15 cm, 3 μ m, hexane/isopropanol = 70/30, flow 0.7 mL/min, detection at 214 nm) retention time = 27.91 min (major) and 36.12 min (minor).



The reaction provided crude products with >20:1 regioselectivity.

White solid (64.2 mg, 67% yield, 89% ee). M.p. 162 °C. $[\alpha]_D^{26.6} = -45.85$ (c 1.02, $CHCl_3$). 1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, $J = 8.0$ Hz, 2H), 7.32-7.28 (m, 4H), 7.12 (d, $J = 8.0$ Hz, 2H), 7.07-7.03 (m, 4H), 4.82-4.75 (m, 1H), 4.27 (d, $J = 12.0$ Hz, 1H), 3.74 (dd, $J = 10.4, 4.4$ Hz, 1H), 2.80 (d, $J = 12.8$ Hz, 1H), 2.67 (d, $J = 12.0$ Hz, 1H), 2.42 (s, 3H), 2.38 (t, $J = 10.0$ Hz, 1H), 2.30 (s, 3H), 2.27 (s, 3H), 2.07 (dd, $J = 12.4, 10.8$ Hz, 1H), 1.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 143.8, 143.1, 140.4, 136.1, 135.9, 132.4, 129.8, 129.3, 129.1, 127.8, 127.3, 126.3, 67.0, 54.1, 49.2, 45.5, 39.6, 21.5, 20.9, 20.88, 20.83. HRMS: m/z (ESI) calculated $[M+NH_4]^+$: 495.2312, measured: 495.2308.

HPLC (IC-3, 0.46*15 cm, 3 μ m, hexane/isopropanol = 85/15, flow 0.7 mL/min, detection at 214 nm) retention time = 25.32 min (major) and 27.42 min (minor).

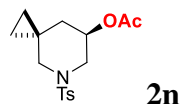


The reaction provided crude products with >20:1 regioselectivity.

White solid (61.6 mg, 65% yield, 94% ee). M.p. 85 °C. $[\alpha]_D^{24.6} = -65.38$ (c 1.12, $CHCl_3$). 1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, $J = 8.0$ Hz, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 7.25-7.19 (m, 3H), 7.14 (t, $J = 8.0$ Hz, 1H), 7.02-6.97 (m, 4H), 4.81-4.76 (m, 1H), 4.27 (d, $J = 12.0$ Hz, 1H), 3.73 (dd, $J = 10.4, 4.0$ Hz, 1H), 2.83 (d, $J = 12.0$ Hz, 1H), 2.73 (d, $J = 12.0$ Hz, 1H), 2.44-2.39 (m, 4H), 2.33 (s, 3H), 2.27 (s, 3H), 2.17-2.04 (m, 1H), 1.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 145.7, 143.8, 143.2, 137.99, 1.90 (s, 3H).

137.95, 132.5, 129.8, 128.4, 128.3, 128.2, 127.7, 127.2, 127.1, 127.0, 124.5, 123.5, 66.9, 53.9, 49.1, 45.7, 39.5, 21.7, 21.6, 21.5, 20.9. HRMS: m/z (ESI) calculated $[M+NH_4]^+$: 495.2312, measured: 495.2308.

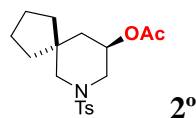
HPLC (IC-3, 0.46*15 cm, 3 μ m, hexane/isopropanol = 85/15, flow 0.7 mL/min, detection at 214 nm) retention time = 19.32 min (major) and 28.11 min (minor).



The reaction provided crude products with >20:1 regioselectivity.

White solid (42.3 mg, 65% yield, 83% ee). M.p. 162-165°C. $[\alpha]_D^{33.5} = 18.14$ (c 1.07, $CHCl_3$). 1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, $J = 8.4$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 4.99-4.93 (m, 1H), 3.48 (dd, $J = 11.6, 4.0$ Hz, 1H), 2.83-2.74 (m, 3H), 2.43 (s, 3H), 2.03 (s, 3H), 1.54-1.47 (m, 2H), 0.55-0.48 (m, 2H), 0.44-0.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 143.6, 133.7, 129.7, 127.6, 67.9, 53.9, 48.8, 37.7, 21.5, 21.1, 15.7, 11.0, 10.8. HRMS: m/z (ESI) calculated $[M+H]^+$: 324.1264, measured: 324.1257.

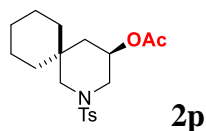
HPLC (IC, 0.46*25 cm, 5 μ m, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 18.60 min (minor) and 43.20 min (major).



The reaction provided crude products with >20:1 regioselectivity.

White solid (59.7 mg, 85% yield, 90% ee). M.p. 84-86 °C. $[\alpha]_D^{32.9} = 23.02$ (c 1.00, $CHCl_3$). 1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 4.94-4.89 (m, 1H), 3.56 (dd, $J = 11.2, 4.0$ Hz, 1H), 3.03 (d, $J = 11.6$ Hz, 1H), 2.48 (dd, $J = 10.4, 8.8$ Hz, 1H), 2.43 (s, 3H), 2.35 (d, $J = 11.6$ Hz, 1H), 2.02 (s, 3H), 1.79-1.50 (m, 7H), 1.43-1.30 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 143.5, 133.4, 129.7, 127.5, 67.5, 54.7, 49.1, 42.7, 41.1, 37.6, 35.7, 24.5, 24.2, 21.5, 21.1. HRMS: m/z (ESI) calculated $[M+NH_4]^+$: 369.1843, measured: 369.1836.

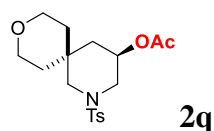
HPLC (IC, 0.46*25 cm, 5 μ m, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 15.23 min (minor) and 23.01 min (major).



The reaction provided crude products with >20:1 regioselectivity.

Known compound **1c**. White solid (52.7 mg, 72% yield, 90% ee). $[\alpha]_D^{34.6} = 14.15$ (*c* 1.01, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 5.00-4.96 (m, 1H), 3.62 (dd, *J* = 10.8, 4.4 Hz, 1H), 3.28 (d, *J* = 11.6 Hz, 1H), 2.45 (dd, *J* = 10.8, 8.8 Hz, 1H), 2.43 (s, 3H), 2.31 (d, *J* = 11.6 Hz, 1H), 2.01 (s, 3H), 1.80 (dd, *J* = 13.2, 4.4 Hz, 1H), 1.50-1.30 (m, 10H), 1.13 (dd, *J* = 13.2, 9.6 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 170.0, 143.5, 133.5, 129.7, 127.4, 66.5, 49.6, 36.5, 34.3, 33.4, 26.2, 21.5, 21.4, 21.2, 21.1.

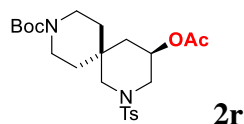
HPLC (IC, 0.46*25 cm, 5 μm, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 15.69 min (minor) and 26.20 min (major).



The reaction provided crude products with 13:1 regioselectivity.

White solid (60.4 mg, 83% yield, 91% ee). M.p. 142-145 °C. $[\alpha]_D^{33.3} = 16.79$ (*c* 0.99, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 4.99-4.89 (m, 1H), 3.70-3.61 (m, 4H), 3.51 (d, *J* = 10.8 Hz, 1H), 3.27 (d, *J* = 11.2 Hz, 1H), 2.63-2.54 (m, 2H), 2.42 (s, 3H), 2.01 (s, 3H), 1.83-1.79 (m, 1H), 1.60-1.52 (m, 4H), 1.30-1.23 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 169.9, 143.7, 133.4, 129.7, 127.4, 66.0, 63.2, 63.1, 53.3, 49.4, 39.9, 35.8, 33.7, 32.1, 21.5, 21.0. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 385.1792, measured: 385.1785.

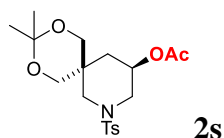
HPLC (IC, 0.46*25 cm, 5 μm, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 31.87 min (minor) and 60.55 min (major).



The reaction provided crude products with >20:1 regioselectivity.

Semi-solid (65.6 mg, 70% yield, 91% ee). $[\alpha]_D^{26.8} = 9.24$ (*c* 0.97, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 4.99-4.94 (m, 1H), 3.69-3.10 (m, 6H), 3.05-2.69 (m, 1H), 2.55-2.30 (m, 4H), 2.02 (s, 3H), 1.85-1.36 (m, 15H). ¹³C NMR (100 MHz, CDCl₃) δ 169.9, 154.8, 143.7, 133.5, 129.8, 127.4, 79.5, 66.1, 53.1, 49.5, 39.3, 38.5, 34.9, 32.9, 28.4, 25.3, 21.5, 21.0. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 484.2476, measured: 484.2471.

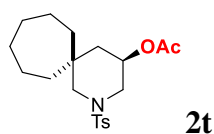
HPLC (IC3, 0.46*25 cm, 5 μ m, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 230 nm) retention time = 24.14 min (minor) and 78.37 min (major).



The reaction provided crude products with 11:1 regioselectivity.

White solid (57.1 mg, 72% yield, 82% ee). M.p. 123-125 °C. $[\alpha]_D^{33.6} = 3.44$ (c 0.20, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 4.95-4.89 (m, 1H), 3.81 (d, *J* = 11.6 Hz, 1H), 3.68-3.58 (m, 3H), 3.27 -2.99 (m, 4H), 2.43 (s, 3H), 2.03 (s, 3H), 1.54-1.50 (m, 1H), 1.41 (s, 6H), 1.38-1.32 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 169.9, 143.7, 133.4, 129.7, 127.6, 98.4, 66.3, 66.2, 65.9, 50.2, 49.4, 33.8, 33.7, 26.8, 21.5, 21.1, 20.3. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 415.1897, measured: 415.1890.

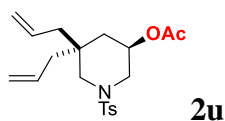
HPLC (IC, 0.46*25 cm, 5 μ m, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 18.81 min (minor) and 23.50 min (major).



The reaction provided crude products with >20:1 regioselectivity.

Semi-solid (56.8 mg, 75% yield, 92% ee). $[\alpha]_D^{26.4} = 15.71$ (c 0.95, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 4.99-4.92 (m, 1H), 3.68 (dd, *J* = 10.8, 4.4 Hz, 1H), 3.17 (d, *J* = 11.6 Hz, 1H), 2.43 (s, 3H), 2.32 (t, *J* = 10.0 Hz, 1H), 2.13 (d, *J* = 11.2 Hz, 1H), 2.01 (s, 3H), 1.87 (dd, *J* = 13.2, 4.4 Hz, 1H), 1.76-1.69 (m, 1H), 1.63-1.35 (m, 11H), 1.06 (dd, *J* = 12.8, 10.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 169.9, 143.5, 133.5, 129.7, 127.4, 66.8, 55.5, 49.3, 41.3, 39.6, 37.6, 35.3, 30.3, 30.2, 22.6, 22.4, 21.5, 21.1. HRMS: *m/z* (ESI) calculated [M+H]⁺: 380.1890, measured: 380.1885.

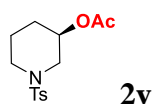
HPLC (IC, 0.46*25 cm, 5 μ m, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 15.53 min (minor) and 22.95 min (major).



The reaction provided crude products with >20:1 regioselectivity.

Semi-solid (36.2 mg, 48% yield, 95% ee). $[\alpha]_{\text{D}}^{33.7} = 3.94$ (c 0.89, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.0$ Hz, 2H), 5.82-5.70 (m, 2H), 5.13-5.00 (m, 5H), 3.58 (dd, $J = 10.8, 4.0$ Hz, 1H), 3.13 (d, $J = 11.2$ Hz, 1H), 2.47-2.42 (m, 4H), 2.35 (d, $J = 11.2$ Hz, 1H), 2.20-2.18 (m, 2H), 2.10-2.06 (m, 2H), 2.02 (s, 3H), 1.75 (dd, $J = 13.6, 4.8$ Hz, 1H), 1.18 (dd, $J = 13.6, 9.6$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.9, 143.6, 133.3, 132.8, 132.7, 129.7, 127.5, 119.1, 118.9, 66.4, 53.7, 49.4, 41.2, 38.6, 37.7, 37.4, 21.5, 21.1. HRMS: m/z (ESI) calculated $[\text{M}+\text{NH}_4]^+$: 395.1999, measured: 395.1991.

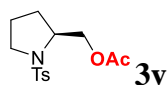
HPLC (IC, 0.46*25 cm, 5 μm , hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 12.91 min (minor) and 16.69 min (major).



The reaction provided crude products **2v** and **3v** with 1.5:1 regioselectivity.

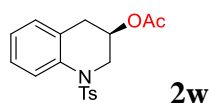
Known compound⁸. Yellow oil (29.7 mg, 50% yield, 90% ee). $[\alpha]_{\text{D}}^{33.5} = 25.31$ (c 0.81, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 4.87-4.83 (m, 1H), 3.25 (dd, $J = 11.6, 2.8$ Hz, 1H), 3.10-3.05 (m, 1H), 2.99-2.91 (m, 1H), 2.43 (s, 3H), 2.04 (s, 3H), 1.88-1.82 (m, 1H), 1.78-1.72 (m, 1H), 1.65-1.59 (m, 1H), 1.53-1.47 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 143.7, 133.8, 129.8, 127.8, 67.6, 49.3, 46.1, 28.7, 21.9, 21.7, 21.3.

HPLC (IC, 0.46*25 cm, 5 μm , hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 25.79 min (minor) and 48.41 min (major).



Yellow oil (20.2 mg, 34% yield, 90% ee). $[\alpha]_{\text{D}}^{34.0} = -40.03$ (c 1.17, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 7.72 (d, $J = 8.0$ Hz, 2H), 7.31 (d, $J = 8.0$ Hz, 2H), 4.19 (dd, $J = 10.8, 4.8$ Hz, 1H), 4.11 (dd, $J = 10.8, 7.2$ Hz, 1H), 3.90-3.86 (m, 1H), 3.46-3.41 (m, 1H), 3.18-3.12 (m, 1H), 2.43 (s, 3H), 2.06 (s, 3H), 1.87-1.81 (m, 1H), 1.73-1.67 (m, 1H), 1.61-1.55 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.8, 143.6, 134.3, 129.7, 127.5, 66.1, 57.8, 49.1, 28.5, 23.9, 21.5, 20.9. HRMS: m/z (ESI) calculated $[\text{M}+\text{H}]^+$: 298.1108, measured: 298.1102.

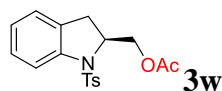
HPLC (IC, 0.46*25 cm, 5 μ m, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 42.92 min (major) and 58.48 min (minor).



The reaction provided crude products with 1.1:1 regioselectivity.

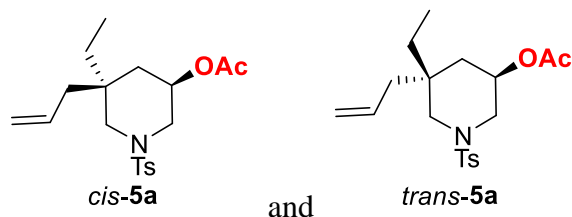
Semi-solid (41% yield, 81% ee). $[\alpha]_D^{33.3} = 44.76$ (*c* 0.62, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.23-7.19 (m, 3H), 7.10 (t, *J* = 7.2 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 4.98-4.95 (m, 1H), 4.11 (dd, *J* = 14.0, 4.4 Hz, 1H), 3.73 (dd, *J* = 14.0, 6.8 Hz, 1H), 2.74 (dd, *J* = 16.0, 5.6 Hz, 1H), 2.54 (dd, *J* = 17.2, 6.4 Hz, 1H), 2.38 (s, 3H), 2.01 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.3, 143.8, 136.8, 136.3, 129.7, 129.4, 127.5, 127.1, 127.0, 125.5, 124.1, 66.6, 49.1, 32.3, 21.5, 21.0. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 363.1373, measured: 373.1365.

HPLC (IC, 0.46*25 cm, 5 μ m, hexane/isopropanol = 70/30, flow 0.7 mL/min, detection at 214 nm) retention time = 26.82 min (minor) and 29.03 min (major).



White solid (38% yield, 86% ee). M.p. 110-112 °C. $[\alpha]_D^{33.7} = 65.62$ (*c* 1.03, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.66 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.24-7.20 (m, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 4.4 Hz, 2H), 4.54-4.48 (m, 1H), 4.21- 4.12 (m, 2H), 2.76 (dd, *J* = 16.4, 9.2Hz, 1H), 2.57 (dd, *J* = 16.8, 2.4Hz, 1H), 2.34 (s, 3H), 2.06 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.9, 144.0, 141.2, 134.8, 131.5, 129.6, 127.9, 127.0, 125.0, 117.8, 65.7, 59.9, 31.4, 21.5, 20.8. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 363.1373, measured: 363.1365.

HPLC (IC, 0.46*25 cm, 5 μ m, hexane/isopropanol = 70/30, flow 0.7 mL/min, detection at 214 nm) retention time = 31.72 min (minor) and 33.43 min (major).

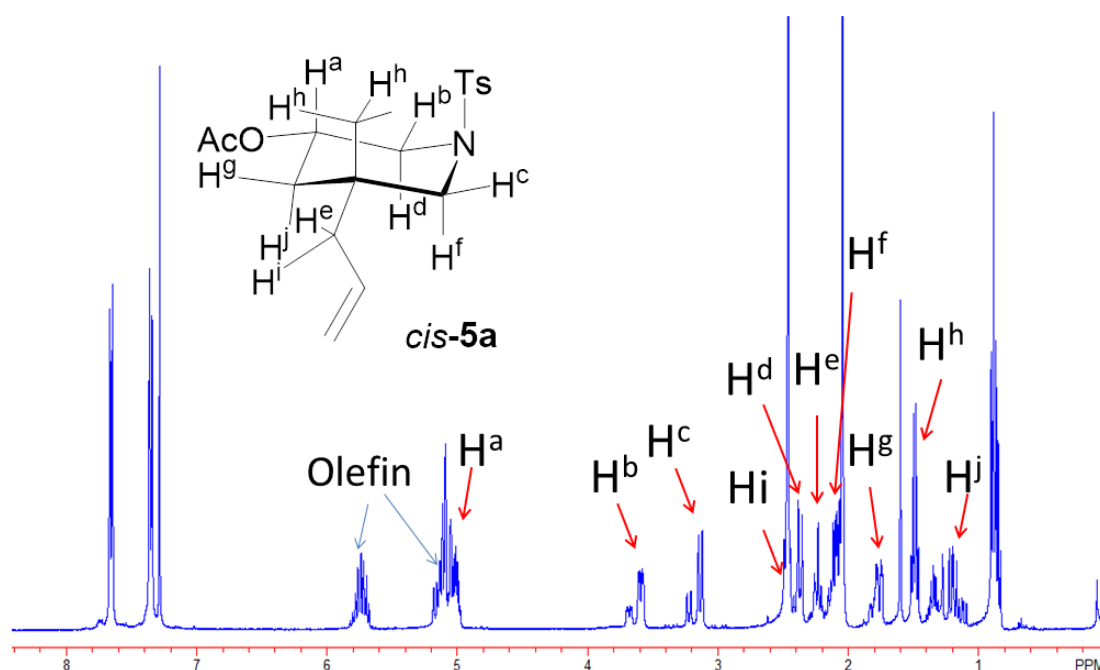


The reaction provided crude products with >20:1 regioselectivity and 2.5:1 diastereoselectivity. However, two isomers can't be separated.

^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.0$ Hz, 2H), 5.76-5.65 (m, 1H), 5.16-4.96 (m, 3H), 3.56 (dd, $J = 11.2, 4.4$ Hz, 1H), 3.11 (d, $J = 11.6$ Hz, 1H), 2.47-2.40 (m, 4H), 2.35 (d, $J = 11.6$ Hz, 1H), 2.24-2.17 (m, 1H), 2.10-2.02 (m, 4H), 1.74 (dd, $J = 13.2, 4.4$ Hz, 1H), 1.48 (q, $J = 7.2$ Hz, 2H), 1.17 (dd, $J = 13.2, 9.2$ Hz, 1H), 0.87 (t, $J = 7.6$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.9, 143.6, 133.4, 132.9, 129.7, 127.5, 118.5, 66.6, 53.7, 49.4, 40.4, 37.8, 37.1, 26.5, 21.5, 21.1, 7.1. HRMS: m/z (ESI) calculated $[\text{M}+\text{H}]^+$: 366.1734, measured: 366.1733.

HPLC (ID-3, 0.46*15 cm, 3 μm , hexane/isopropanol/acetonitrile = 84/15/1, flow 0.7 mL/min, detection at 214 nm) retention time = 11.80 min (minor) and 12.71 min (major); 13.59 min (minor) and 14.76 min (major).

The characterization of major compound **cis-5a**.



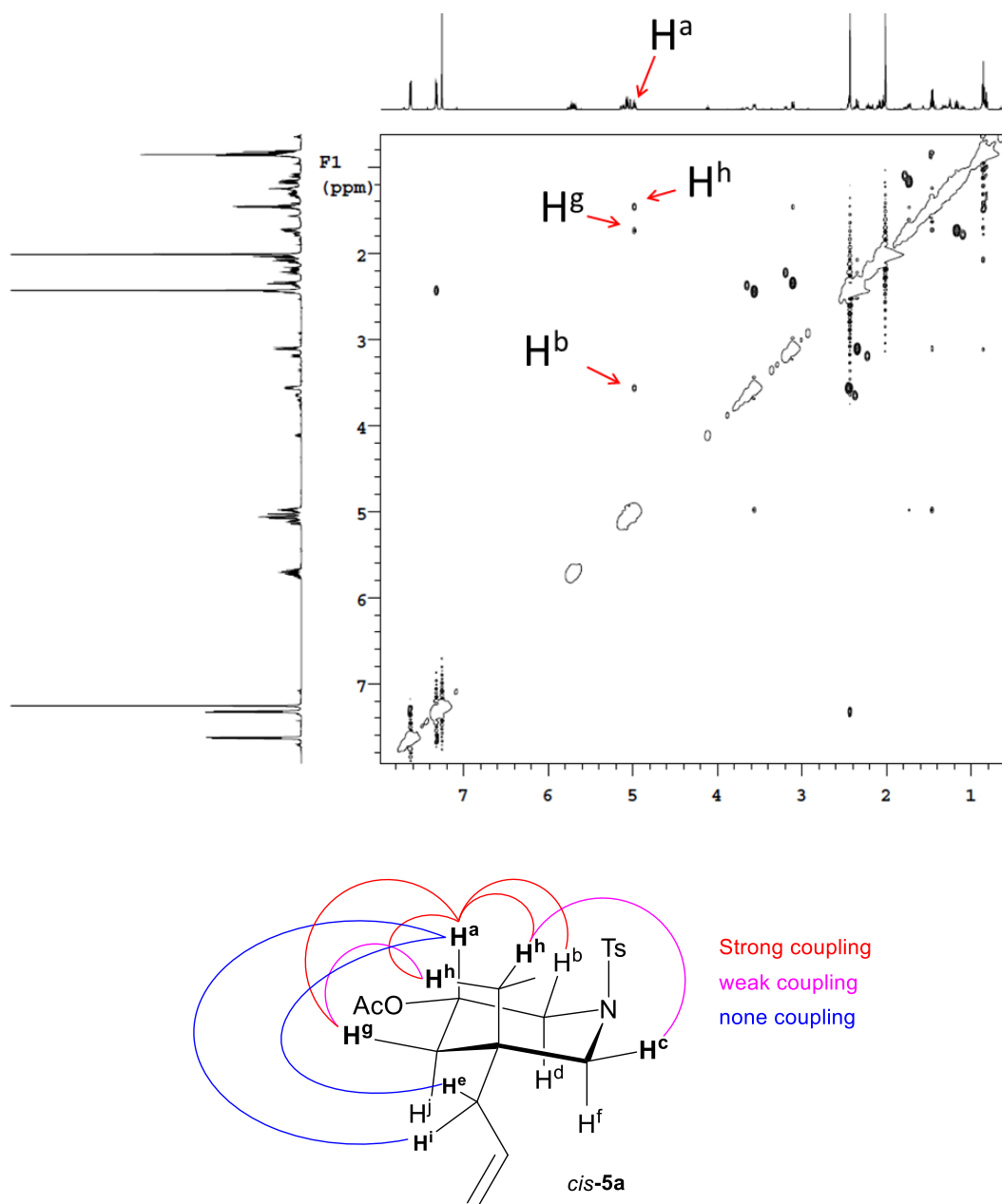
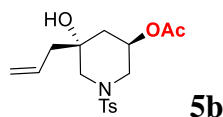


Figure S5. The ^1H NMR spectrum (top) and NOESY spectrum (bottom) of **5a**: *cis*-**5a** (major) and *trans*-**5a** (minor).

The assignment of structure of *cis*-**5a** was shown in Figure S5 (top). The relative configuration of **5a** (major) was analyzed by NOESY spectrum (Figure S5, bottom). The NOESY spectroscopy shows that there are stronger NOE between H^{a} and H^{h} , which means H^{a} and H^{h} in one side of ring, -Et and -OAc in cross sides of ring. Therefore, the relative configuration of major product is the *cis*-**5a**.



The reaction provided crude products with 6:1 regioselectivity, but the 5-*exo* cyclization product can't be separated from some unidentified side products.

White solid (43.9 mg, 62% yield, 98% ee). M.p. 94-96 °C. $[\alpha]_D^{27.8} = 37.04$ (*c* 1.00, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 5.89-5.83 (m, 1H), 5.20-5.12 (m, 3H), 3.71 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.30 (d, *J* = 12.0 Hz, 1H), 2.55 (d, *J* = 12.0 Hz, 1H), 2.48-2.42 (m, 4H), 2.34-2.31 (m, 2H), 2.03 (s, 3H), 1.99 (dd, *J* = 13.6, 4.4 Hz, 1H), 1.38 (dd, *J* = 13.2, 9.6 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 169.9, 143.6, 133.3, 131.9, 129.8, 127.5, 119.9, 69.9, 66.5, 54.8, 48.9, 44.0, 39.8, 21.5, 21.0. HRMS: *m/z* (ESI) calculated [M+NH₄]⁺: 371.1635, measured: 371.1630.

HPLC (IC, 0.46*25 cm, 5 μm, hexane/isopropanol = 50/50, flow 0.7 mL/min, detection at 214 nm) retention time = 30.48 min (minor) and 70.64 min (major).

5. X-Ray Structure of Compound (*R*)-2a, (*R*)-2f, (3*R*, 5*S*)-5b and complex (L1)PdCl₂

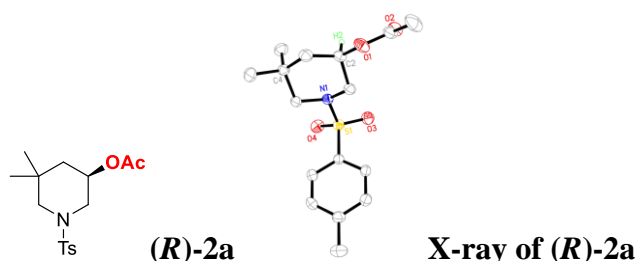
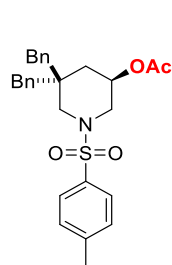


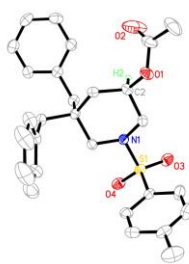
Table S9. Crystal data and structure refinement for **2a**

Identification code	mo_dm17417_0m	
Empirical formula	C ₁₆ H ₂₁ N O ₄ S	
Formula weight	323.40	
Temperature	296 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2 ₁ 2 ₁ 2 ₁	
Unit cell dimensions	<i>a</i> = 8.385(2) Å	<i>a</i> = 90°.
	<i>b</i> = 12.444(3) Å	<i>b</i> = 90°.

	$c = 16.636(4) \text{ \AA}$	$g = 90^\circ$.
Volume	$1735.9(7) \text{ \AA}^3$	
Z	4	
Density (calculated)	1.237 Mg/m^3	
Absorption coefficient	0.202 mm^{-1}	
F(000)	688	
Crystal size	$0.25 \times 0.2 \times 0.15 \text{ mm}^3$	
Theta range for data collection	2.044 to 30.487° .	
Index ranges	$-10 \leq h \leq 11$, $-17 \leq k \leq 17$, $-23 \leq l \leq 23$	
Reflections collected	17459	
Independent reflections	5269 [R(int) = 0.0195]	
Completeness to $\theta = 25.242^\circ$	99.6 %	
Absorption correction	None	
Max. and min. transmission	0.9610 and 0.9361	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5269 / 0 / 203	
Goodness-of-fit on F^2	1.086	
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0427$, $wR2 = 0.1151$	
R indices (all data)	$R1 = 0.0509$, $wR2 = 0.1234$	
Absolute structure parameter	0.015(14)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.412 and $-0.379 \text{ e.\AA}^{-3}$	



(R)-2f



X-ray of (R)-2f

Table S10. Crystal data and structure refinement for **2f**

Identification code	mo_d8v17241_0m
Empirical formula	$\text{C}_{28} \text{H}_{31} \text{N} \text{O}_4 \text{S}$
Formula weight	477.60
Temperature	302.26 K
Wavelength	0.71073 \AA

Crystal system	Monoclinic
Space group	P 1 21 1
Unit cell dimensions	$a = 10.3008(4) \text{ \AA}$ $a = 90^\circ$. $b = 11.0103(4) \text{ \AA}$ $b = 91.5950(10)^\circ$. $c = 11.3288(4) \text{ \AA}$ $g = 90^\circ$.
Volume	$1284.36(8) \text{ \AA}^3$
Z	2
Density (calculated)	1.235 Mg/m^3
Absorption coefficient	0.159 mm^{-1}
F(000)	508
Crystal size	$0.2 \times 0.12 \times 0.05 \text{ mm}^3$
Theta range for data collection	2.708 to 25.992° .
Index ranges	$-12 \leq h \leq 12$, $-13 \leq k \leq 13$, $-13 \leq l \leq 13$
Reflections collected	10869
Independent reflections	4936 [$R(\text{int}) = 0.0655$]
Completeness to $\theta = 25.242^\circ$	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7461 and 0.4189
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4936 / 1 / 309
Goodness-of-fit on F^2	1.052
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0501$, $wR2 = 0.1052$
R indices (all data)	$R1 = 0.0696$, $wR2 = 0.1134$
Absolute structure parameter	0.07(5)
Extinction coefficient	n/a
Largest diff. peak and hole	0.265 and $-0.269 \text{ e.\AA}^{-3}$

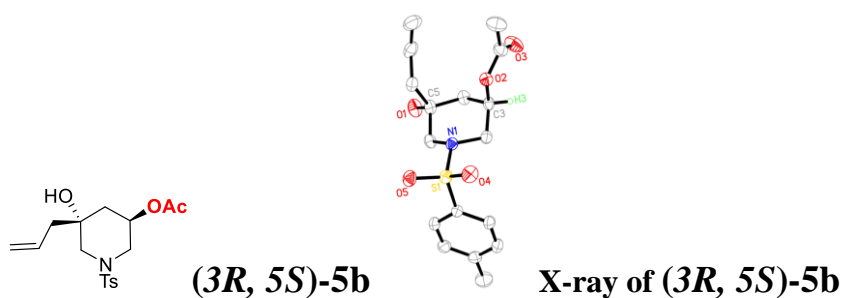
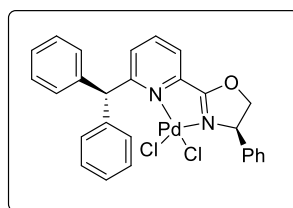


Table S11. Crystal data and structure refinement for **5b**

Identification code	mo_d8v17424_0m
Empirical formula	C17 H23 N O5 S
Formula weight	353.42
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 5.65860(10) Å a = 90°. b = 12.5761(3) Å b = 90°. c = 25.2200(5) Å g = 90°.
Volume	1794.73(6) Å ³
Z	4
Density (calculated)	1.308 Mg/m ³
Absorption coefficient	0.206 mm ⁻¹
F(000)	752
Crystal size	0.180 x 0.150 x 0.120 mm ³
Theta range for data collection	2.287 to 25.997°.
Index ranges	-6<=h<=6, -15<=k<=15, -31<=l<=31
Reflections collected	18463
Independent reflections	3489 [R(int) = 0.0345]
Completeness to theta = 25.242°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6724
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3489 / 0 / 220
Goodness-of-fit on F ²	1.058
Final R indices [I>2sigma(I)]	R1 = 0.0371, wR2 = 0.0921
R indices (all data)	R1 = 0.0426, wR2 = 0.0958
Absolute structure parameter	-0.01(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.207 and -0.195 e.Å ⁻³



(L1)PdCl₂

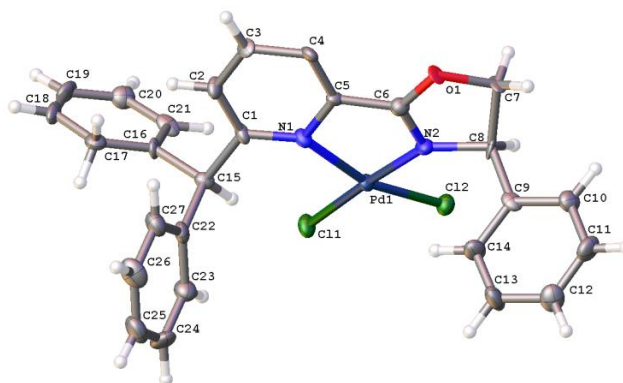


Table S12. Crystal data and structure refinement for (L1)PdCl₂

Identification code	mo_D8V17272_0m
Empirical formula	C ₂₇ H ₂₂ Cl ₂ N ₂ OPd
Formula weight	567.76
Temperature/K	273.15
Crystal system	hexagonal
Space group	P6 ₅
a/Å	20.913(6)
b/Å	20.913(6)
c/Å	10.050(3)
α/°	90
β/°	90
γ/°	120
Volume/Å ³	3807(2)
Z	6
ρ _{calc} /cm ³	1.486
μ/mm ⁻¹	0.963
F(000)	1716.0
Crystal size/mm ³	0.2 × 0.12 × 0.11
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	5.622 to 55.13
Index ranges	-23 ≤ h ≤ 24, -26 ≤ k ≤ 27, -11 ≤ l ≤ 11
Reflections collected	16966
Independent reflections	4920 [R _{int} = 0.1111, R _{sigma} = 0.1355]
Data/restraints/parameters	4920/19/298
Goodness-of-fit on F ²	1.054

Final R indexes [$I \geq 2\sigma(I)$] $R_1 = 0.0599$, $wR_2 = 0.1048$
Final R indexes [all data] $R_1 = 0.1087$, $wR_2 = 0.1236$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$ 0.61/-0.68
Flack parameter -0.04(4)

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