Supporting information for:

Palladium-Catalyzed Alkylation of Aryl C-H Bonds with sp^3 Organotin Reagents Using Benzoquinone as a Crucial Promoter

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General Information

Solvents were obtained from Aldrich, Acros and Fisher and used directly without further purification. All organotin reagents are commercially available. Organic solutions were concentrated by rotary evaporation (house vacuum, ~25 Torr) at 23-30 °C. Flash column chromatography was performed by employing silica gel (60-Å pore size, 230-400 mesh, standard grade). Analytical thin layer chromatography was performed using aluminum plates pre-coated with silica gel (0.25 mm, 60-Å pore size, 230-400 mesh, Merck KGA) impregnated with a fluorescent indicator (254 mm). TLC plates were visualized by exposure to ultraviolet light (UV) and/or exposure to phosphmolybdic acid (PMA)

followed by brief heating on a hot plate. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) were recorded with Varian Mercury 400 (400 MHz / 100 MHz) NMR spectrometers. Chemical shifts for protons are reported in parts per million scale (δ scale) and internally referenced to tetramethylsilane signal. Chemical shifts for carbon are reported in parts per million (δ scale) and referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.36, the middle peak). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, dt = double triplet, td = triple doublet), coupling constant in Hz, and integration. Infrared (IR) spectra were recorded on a Perkin Elmer FT-IR Spectrometer. High resolution mass spectra were obtained at the Mass Spectrometry Facilities of University of Illinois at Urbana-Champaign. The Microwave reaction was performed using a Discover®LabMate^{TM} in a 20 mL septum-capped vial with stirring, at 100 W. The temperature reported is the maximum temperature the sample reached, and the time reported includes the time required to reach the target temperature. Samples were cooled using 40 psi pressurized air.

List of Abbreviation

BQ	benzoquinone
Calcd	calculated
$Cu(OAc)_2$	copper acetate
CH_3CN	Acetonitrile
CH_2Cl_2	dichloromethane
$ClCH_2CH_2Cl$	dichloroethane

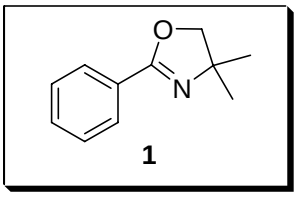
$Cl_2CHCHCl_2$	tetrachloroethane
CCl_4	carbon tetrachloride
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
EI	electron ionization
equiv	equivalent
EtOAc	ethyl acetate
g	gram
HRMS	high resolution mass spectrometry
Hz	hertz
J	coupling constant
mg	milligram
mL	milliliter
μL	microliter
Me_4Sn	tetramethyltin
mmol	millimole
NMP	*N*-methylpyrrolidone
NMR	nuclear magnetic resonance
THF	tetrahhydrofuran
$Pd(OAc)_2$	palladium acetate
ppm	parts per million

Preparation of Substrates

General procedure for the preparation of oxazoline substrates

To the carboxylic acid (20 mmol) solution in 25 mL of CH_2Cl_2, oxalyl chloride (22 mmol, 2 M in CH_2Cl_2) was added dropwise at 0 °C over 10 minutes. After stirring for 2 hours, the solvent was removed under reduced pressure and the residue was dissolved in 20 mL of dry THF. The newly-prepared acid chloride was added dropwise at 0 °C over 10 minutes to the mixture of 2-amino-2-methyl-1-propanol (1.78 g, 20 mmol) and triethylamine (1.42 g, 20mmol) in 30 mL of dry THF. The reaction was continued for 3 hours at room temperature before the solvent was removed under vacuum. To the residue of the reaction mixture, triphenylphosphine (20.96 g, 80 mmol), 48 mL of CCl_4, triethylamine (32.30 g, 320 mmol) and 100 mL of acetonitrile were added separately. The reaction was kept stirring for 16 hours at room temperature under N_2. To the reaction mixture, 100 mL of ethyl acetate was added and then washed with saturated $NaHCO_3$ aqueous solution (100 mL × 2). The separated organic layer was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel with EtOAc / hexane (1: 9) to give the corresponding oxazoline.

Other substrates **1, 8** and **9** were purchased from Aldrich and used as received.



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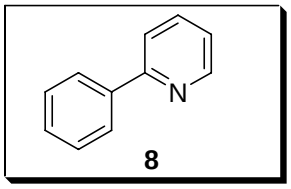

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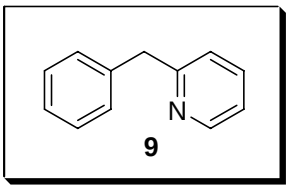

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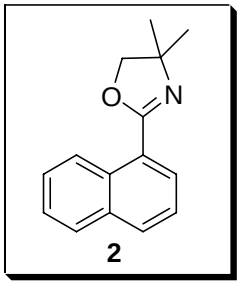
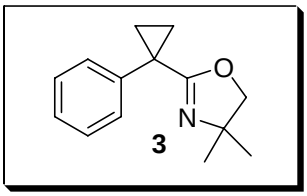


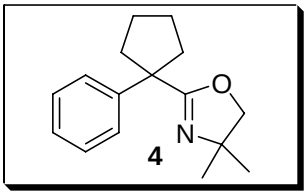
2

4,4-dimethyl-2-(naphthalen-5-yl)oxazoline (2) 3.60 g of substrate **2** was obtained as a brown solid after column chromatography (80% yield over 3 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, *J* = 8.4 Hz, 1H), 8.04 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.59 (td, *J* = 8.4, 1.2 Hz, 1H), 7.52-7.44 (m, 2H), 4.13 (s, 2H), 1.46 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.14, 133.98, 131.91, 131.46, 129.03, 128.66, 127.53, 126.65, 126.32, 125.32, 124.91, 78.57, 68.68, 28.87; IR (neat) ν 2968, 1642, 1512, 1295, 1118, 1005 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{15}NO$ (M^+) 225.1154, found 225.1157.

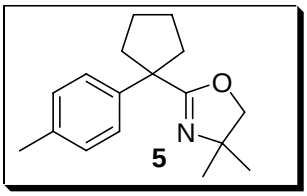


3

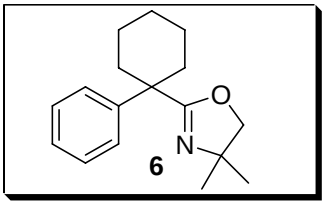
4,4-dimethyl-2-(1-phenylcyclopropyl)oxazoline (3) 2.54 g of substrate **3** was obtained as a white solid after column chromatography (59% yield over 3 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 11.2 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 3.86 (s, 2H), 1.48 (dd, *J* = 11.2, 8.4 Hz, 2H), 1.23 (s, 6H), 1.14 (dd, *J* = 11.2, 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.91, 140.49, 129.61, 128.24, 127.02, 79.39, 66.86, 28.24, 24.17, 15.03; IR (neat) ν 2965, 1655, 1354, 1137 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{17}NO$ (M^+) 215.1310, found 215.1306.



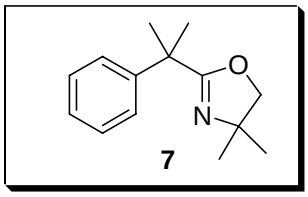
4,4-dimethyl-2-(1-phenylcyclopentyl)oxazoline (4) 2.92 g of substrate **4** was obtained as a white solid after column chromatography (60% yield over 3 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 8.0 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 3.82 (s, 2H), 2.58-2.52 (m, 2H), 1.99-1.92 (m, 2H), 1.79-1.73 (m, 4H), 1.26 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.57, 144.48, 128.50, 126.76, 79.49, 67.12, 52.98, 37.02, 28.39, 23.83; IR (neat) ν 2965, 1654, 1449, 1189 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{21}NO$ (M^+) 243.1623, found 243.1617.



4,4-dimethyl-2-(1-p-tolylcyclopentyl)oxazoline (5) 3.19 g of substrate **5** was obtained as a yellow solid after column chromatography (62% yield over 3 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 3.79 (s, 2H), 2.55-2.50 (m, 2H), 2.30 (s, 3H), 1.96-1.90 (m, 2H), 1.76-1.69 (m, 4H), 1.24 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.61, 141.33, 136.07, 129.08, 126.50, 79.32, 66.93, 52.48, 36.90, 28.25, 23.68, 21.12; IR (neat) ν 2961, 1656, 1445, 1364, 1142 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{23}NO$ (M^+) 257.1780, found 257.1778.



4,4-dimethyl-2-(1-phenylcyclohexyl)oxazoline (6) 3.45 g of substrate **6** was obtained as a white solid after column chromatography (67% yield over 3 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.32 (td, *J* = 8.0, 2.0 Hz, 2H), 7.23-7.20 (m, 1H), 3.81 (s, 2H), 2.41 (d, *J* = 12.8 Hz, 2H), 1.78-1.56 (m, 8H), 1.30 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.57, 145.54, 128.60, 126.75, 126.04, 78.90, 67.40, 44.80, 35.61, 28.48, 26.07, 23.67; IR (neat) ν 2936, 1656, 1450, 1247, 1115 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{23}NO$ (M^+) 257.1780, found 257.1783.

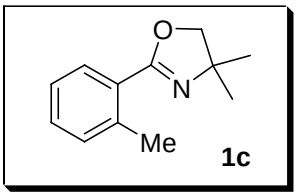


4,4-dimethyl-2-(2-phenylpropan-2-yl)oxazoline (6) 2.26 g of substrate **7** was obtained as a pale yellow oil after column chromatography (52% yield over 3 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.29 (m, 4H), 7.24-7.20 (m, 1H), 3.85 (s, 2H), 1.59 (s, 6H), 1.30 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.89, 145.71, 128.62, 126.77, 125.63, 79.43, 67.06, 40.74, 28.45, 27.62; IR (neat) ν 2973, 1656, 1496, 1365, 1121 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{19}NO$ (M^+) 217.1467, found 217.1457.

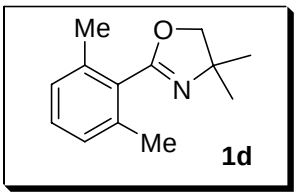
Catalytic Alkylation

General procedure for alkylation

In a 20 mL tube, substrate (0.2 mmol, 1 equiv), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 10 mol%), $Cu(OAc)_2$ (36.4 mg, 0.2 mmol, 1 equiv) and benzoquinone (21.6 mg, 0.2mmol, 1 equiv) were dissolved in 1 mL of CH_3CN under atmospheric air. The tube was sealed with a Teflon lined cap, and the reaction mixture was stirred at 100 °C for 4 hours. Then the first portion of tetraalkyltin (0.015 mmol, in 50 μL CH_3CN, 0.075 equiv) was added to the reaction mixture. The addition of the same amount of organotin reagent was repeated 9 more times every 4 hours. After the introduction of the last portion of the organotin reagent, the reaction was continued for another hour. The reaction mixture was diluted with 20 mL of EtOAc and then treated with 10 mL of saturated Na_2S aqueous solution. The mixture was filtered through a pad of Celite, and the filtrate was washed twice with saturated brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel with a gradient eluent of hexane and ether (from 15:1 to 4:1) to give the alkylated product.



1c

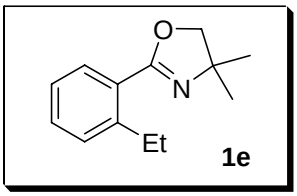


1d

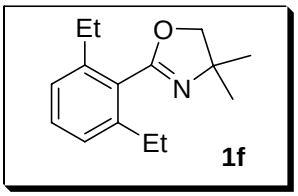
4,4-dimethyl-2-o-tolyloxazoline (1c) and 4,4-dimethyl-2-(2,6-imethylphenyl)oxazoline (1d) Substrate **1** was methylated following the general procedure. After purification by column chromatography, **1c** was obtained as a colorless oil (7.6 mg, 20%), and **1d** was obtained as a colorless oil (26.0 mg, 64%).

1c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.32 (td, *J* = 7.6, 1.2 Hz, 1H) 7.21 (t, *J* = 8.4 Hz, 2H), 4.07 (s, 2H), 2.56 (s, 3H), 1.39 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.18, 138.76, 131.36, 130.68, 130.08, 125.84, 78.95, 68.20, 28.83, 21.69; IR (neat) ν 2966, 2360, 1646, 1458, 1309, 1041 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{15}NO$ (M^+) 189.1154, found 189.1150.

1d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (t, *J* = 7.2 Hz, 1H), 7.02 (d, *J* = 7.2 Hz, 2H), 4.10 (s, 2H), 2.33 (s, 6H), 1.42 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.54, 137.16, 129.56, 127.60, 79.15, 68.31, 28.84, 19.81; IR (neat) ν 2966, 1661, 1464, 1292, 1045 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{17}NO$ (M^+) 203.1310, found 203.1301.



1e



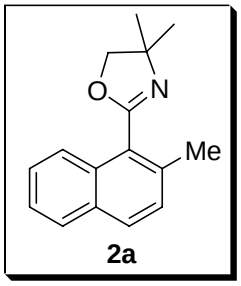
1f

4,4-dimethyl-2-(2-ethylphenyl)oxazoline (1e) and 4,4-dimethyl-2-(2,6-diethylphenyl)oxazoline (1f) Substrate **1** was ethylated following the general procedure. After purification by column chromatography, **1e** was obtained as a colorless oil (6.1 mg, 15%), and **1f** was obtained as a white solid (34.2 mg, 74%).

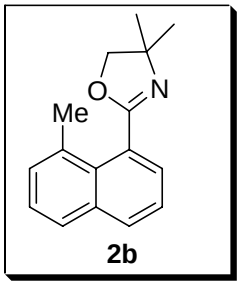
1e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.34 (td, *J* = 7.6, 1.2 Hz, 1H), 7.26-7.18 (m, 2H), 4.07 (s, 2H), 2.96 (q, *J* = 7.6 Hz, 2H), 1.38 (s, 6H), 1.21 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.09, 144.71, 130.80, 130.24, 129.73, 127.65, 125.82, 79.02, 68.04, 28.67, 27.50, 15.94; IR (neat) ν 2968, 1646, 1457, 1349, 1305, 1048 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{17}NO$ (M^+) 203.1310, found 203.1307.

1f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (td, *J* = 8.0, 1.6 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 2H), 4.10 (s, 2H), 2.65 (q, *J* = 7.6 Hz, 4H), 1.42 (s, 6H), 1.22 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 162.44, 143.32, 129.96, 128.36, 126.10, 79.79, 68.31, 28.70, 26.92, 15.99; IR (neat) ν 2967, 1663, 1463, 1297, 1208, 1031 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{21}NO$ (M^+) 231.1623, found 231.1630.



2a



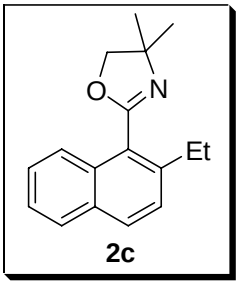
2b

4,4-dimethyl-2-(2-methylnaphthalen-1-yl)oxazoline (2a) and 4,4-dimethyl-2-(1-methylnaphthalen-8-yl)oxazoline (2b) Substrate **2** was methylated following the general procedure to give two products. After purification by column chromatography, **2a** was obtained as a white solid (33.5 mg, 70%), and **2b** was obtained as a white solid (8.1 mg, 17%).

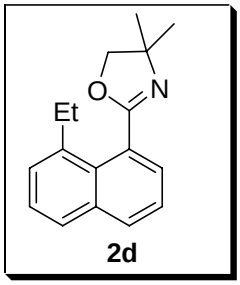
2a: ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.8 Hz, 1H), 7.79 (d, J = 8.8 Hz, 2H), 7.49 (td, J = 6.8, 1.2 Hz, 1H), 7.42 (td, J = 6.8, 1.2 Hz, 1H), 4.23 (s, 2H), 2.54 (s, 3H), 1.53 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.99, 135.81, 132.02, 131.99, 129.97, 128.63, 128.27, 127.12, 125.57, 125.46, 124.93, 79.34, 68.68, 29.05, 20.37; IR (neat) ν 2964, 2360, 1663, 1508, 1201, 1122 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{17}NO$ (M^+) 239.1310, found 239.1303.

2b: ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.46-7.34 (m, 3H), 4.21 (s, 2H), 2.76 (s, 3H), 1.46 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.00, 134.90, 134.60, 132.05, 130.70, 130.09, 130.04, 127.60,

126.86, 126.18, 124.56, 79.80, 68.13, 28.51, 22.13; IR (neat) ν 2968, 2362, 1662, 1462, 1298 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{17}NO$ (M^+) 239.1310, found 239.1308.



2c

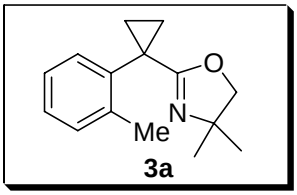


2d

4,4-dimethyl-2-(2-ethylnaphthalen-1-yl)oxazoline (2c) and 4,4-dimethyl 2-(1-ethylnaphthalen-8-yl)oxazoline (2d) Substrate **2** was ethylated following the general procedure. After purification by column chromatography, **2c** was obtained as a white solid (35.0 mg, 69%), and **2d** was obtained as a white solid (8.6 mg, 17%).

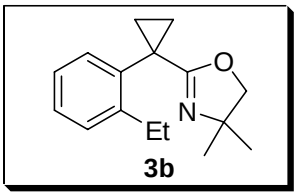
2c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.8 Hz, 1H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.49 (td, *J* = 6.8, 1.2 Hz, 1H), 7.42 (td, *J* = 6.8, 1.2 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 4.23 (s, 2H), 2.85 (q, *J* = 7.6 Hz, 2H), 1.53 (s, 6H), 1.30 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.93, 141.90, 140.32, 132.03, 130.26, 128.24, 127.21, 127.08, 125.64, 125.03, 79.34, 68.67, 28.99, 27.58, 16.25; IR (neat) ν 2967, 1666, 1462, 1200, 1121, 1005 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{19}NO$ (M^+) 253.1467, found 253.1461.

2d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.73 (dd, *J* = 6.8, 2.4 Hz, 1H), 7.63 (dd, *J* = 6.8, 1.2 Hz, 1H), 7.47-7.41 (m, 3H), 4.19 (s, 2H), 3.14 (q, *J* = 7.2 Hz, 2H), 1.47 (s, 6H), 1.31 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.14, 140.68, 135.08, 132.31, 130.40, 129.95, 127.81, 127.61, 126.39, 126.33, 124.46, 79.78, 68.17, 28.53, 27.08, 16.00; IR (neat) ν 2967, 1660, 1461, 1297, 1189 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{19}NO$ (M^+) 253.1467, found 253.1458.



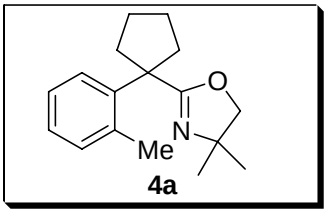
3a

4,4-dimethyl-2-(1-o-tolylcyclopropyl)oxazoline (3a) Substrate **3** was methylated following the general procedure. Column chromatography gave **3a** as a white solid (28.4 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.28 (m, 1H), 7.19-7.15 (m, 3H), 3.85 (s, 2H), 2.38 (s, 3H), 1.58 (dd, *J* = 6.8, 4.4 Hz, 2H), 1.22 (s, 6H), 1.12 (dd, *J* = 6.8, 4.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.97, 139.65, 139.08, 130.45, 130.41, 127.76, 126.04, 79.81, 67.30, 28.59, 23.40, 19.79, 16.25; IR (neat) ν 2964, 1653, 1458, 1364, 1174 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{19}NO$ (M^+) 229.1467, found 229.1460.



3b

4,4-dimethyl-2-(1-(2-ethylphenyl)cyclopropyl)oxazoline (3b) Substrate **3** was ethylated following the general procedure. Column chromatography gave **3b** as a pale yellow liquid (29.2 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.2 Hz, 1H), 7.26-7.22 (m, 2H), 7.17-7.13 (m, 1H), 3.84 (s, 2H), 2.79 (q, *J* = 7.6 Hz, 2H), 1.58 (dd, *J* = 11.2, 8.4 Hz, 2H), 1.25 (t, *J* = 7.6 Hz, 3H), 1.22 (s, 6H), 1.13 (dd, *J* = 11.2, 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.47, 145.16, 138.40, 130.68, 128.30, 127.96, 125.92, 79.82, 67.20, 28.58, 24.97, 23.19, 16.43, 14.84; IR (neat) ν 2967, 1652, 1364, 1144, 1122 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{21}NO$ (M^+) 243.1623, found 243.1620.

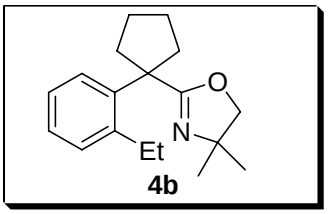


4a

4,4-dimethyl-2-(1-o-tolylcyclopentyl)oxazoline (4a) Substrate **4** was methylated following the general procedure. Column chromatography gave **4a** as a white solid (45.3 mg, 88%).

4,4-dimethyl-2-(1-o-tolylcyclopentyl)oxazoline (4a) Substrate **4** was reacted with tetramethyltin (added in 20 batches, the interval between each addition is 3 hours) in the presence of 5 mol% $Pd(OAc)_2$. The general procedure was followed to give the product **4a** (36.5 mg, 71%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (m, 1H), 7.17-7.11 (m, 3H), 3.83 (s, 2H), 2.63-2.57 (m, 2H), 2.39 (s, 3H), 2.07-2.00 (m, 2H), 1.85-1.77 (m, 2H), 1.74-1.69 (m, 2H), 1.27 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.90, 142.51, 137.65, 132.10, 127.02, 126.71, 125.95, 79.84, 67.32, 52.82, 37.38, 28.55, 24.43, 21.45; IR (neat) ν 2962, 1651, 1452, 1138, 1004 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{23}NO$ (M^+) 257.1780, found 257.1773.

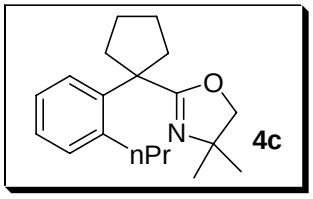


4b

4,4-dimethyl-2-(1-(2-ethylphenyl)cyclopentyl)oxazoline (4b) Substrate **4** was ethylated following the general procedure. Column chromatography gave **4b** as a white solid (45.6 mg, 84%).

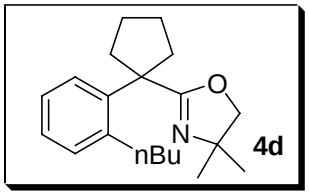
4,4-dimethyl-2-(1-(2-ethylphenyl)cyclopentyl)oxazoline (4b) Substrate **4** was reacted with tetraethyltin (added in 20 batches, the interval between each addition is 3 hours) in the presence of 5 mol% $Pd(OAc)_2$. The general procedure was followed to give the product **4b** (42.9 mg, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.0 Hz, 1H), 7.26-7.19 (m, 2H), 7.15 (t, *J* = 8.0, 2.0 Hz, 1H), 3.81 (s, 2H), 2.79 (q, *J* = 7.6 Hz, 2H), 2.61-2.55 (m, 2H), 2.08-2.01 (m, 2H), 1.84-1.77 (m, 2H), 1.75-1.68 (m, 2H), 1.27 (s, 6H), 1.20 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.44, 143.84, 141.71, 130.11, 127.18, 126.60, 125.76, 79.77, 67.24, 52.68, 37.97, 28.53, 25.50, 24.33, 16.30; IR (neat) ν 2963, 1652, 1456, 1138, 1004 cm^{-1}; HRMS (EI) Calcd for $C_{18}H_{25}NO$ (M^+) 271.1936, found 271.1942.

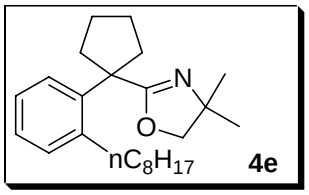


4c

4,4-dimethyl-2-(1-(2-propylphenyl)cyclopentyl)oxazoline (4c) Substrate **4** was reacted with tetrapropyltin (added in 20 batches, the interval between each addition is 3 hours) in the presence of 5 mol% $Pd(OAc)_2$. The general procedure was followed to give the product **4c** as a white solid (46.8 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (d, *J* = 7.6 Hz, 1H), 7.25-7.12 (m, 3H), 3.81 (s, 2H), 2.71 (t, *J* = 8.4 Hz, 2H), 2.61-2.55 (m, 2H), 2.08-2.01 (m, 2H), 1.84-1.77 (m, 2H), 1.74-1.68 (m, 2H), 1.64-1.56 (m, 2H), 1.27 (s, 6H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.51, 142.39, 141.98, 130.36, 127.01, 126.64, 125.75, 79.75, 67.24, 52.65, 38.03, 34.99, 28.46, 25.13, 24.43, 14.90; IR (neat) ν 2960, 2871, 2089, 1651, 1452, 1193, 1004 cm^{-1}; HRMS (EI) Calcd for $C_{19}H_{27}NO$ (M^+) 285.2093, found 285.2089.

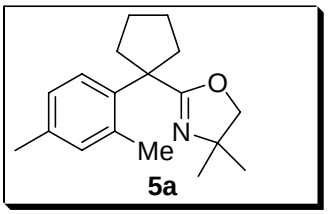


4,4-dimethyl-2-(1-(2-butylphenyl)cyclopentyl)oxazoline (4d) Substrate **4** was reacted with tetrabutyltin (added in 20 batches, the interval between each addition is 3 hours) in the presence of 5 mol% $Pd(OAc)_2$. The general procedure was followed to give the product **4d** as a white solid (44.9 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 7.6 Hz, 1H), 7.26-7.12 (m, 3H), 3.81 (s, 2H), 2.72 (t, J = 8.0 Hz, 2H), 2.60-2.54 (m, 2H), 2.06-2.01 (m, 2H), 1.84-1.77 (m, 2H), 1.72-1.68 (m, 2H), 1.59-1.53 (m, 2H), 1.46-1.40 (m, 2H), 1.26 (s, 6H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.57, 142.55, 142.00, 130.40, 127.00, 126.61, 125.70, 79.77, 67.26, 52.65, 38.06, 34.29, 32.68, 28.45, 24.48, 23.58, 14.44; IR (neat) ν 2956, 2869, 2094, 1650, 1449, 1192, 1138, 1003 cm^{-1}; HRMS (EI) Calcd for $C_{20}H_{29}NO$ (M^+) 299.2249, found 299.2246.



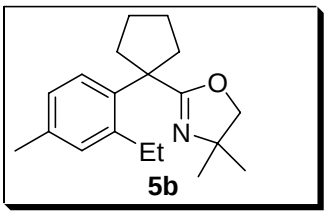
4,4-dimethyl-2-(1-(2-octylphenyl)cyclopentyl)oxazoline (4e) Substrate **4** was reacted with tetraoctyltin (added in 20 batches, the interval between each addition is 3 hours) in the presence of 5 mol% $Pd(OAc)_2$. The general procedure was followed to give the product **4e** as a slurry liquid (59.0 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, J = 8.0, 1.2 Hz, 1H), 7.24-7.11 (m, 3H), 3.81 (s, 2H), 2.71 (t, J = 8.0 Hz, 2H), 2.59-2.54 (m, 2H), 2.06-2.01 (m, 2H), 1.83-1.80 (m, 2H), 1.72-1.70 (m, 2H), 1.60-1.56 (m, 2H), 1.42-1.38 (m, 2H), 1.26 (m, 14H), 0.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.57,

142.58, 141.96, 130.36, 127.01, 126.59, 125.69, 79.75, 67.24, 52.63, 38.04, 32.96, 32.18, 30.52, 29.94, 29.64, 28.44, 24.45, 22.99, 14.44; IR (neat) ν 2926, 2856, 1650, 1462, 1363, 1193, 1138, 1004 cm^{-1}; HRMS (EI) Calcd for $C_{24}H_{37}NO$ (M^+) 355.2875, found 355.2871.



5a

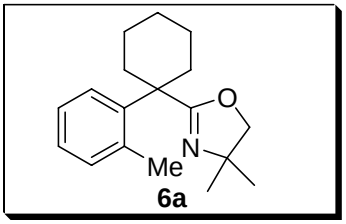
4,4-dimethyl-2-(1-(2,4-dimethylphenyl)cyclopentyl)oxazoline (5a) Substrate **5** was methylated following the general procedure. Column chromatography gave **5a** as a white solid (41.2 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 3.83 (s, 2H), 2.61-2.55 (m, 2H), 2.36 (s, 3H), 2.28 (s, 3H), 2.05-1.98 (m, 2H), 1.83-1.78 (m 2H), 1.74-1.66 (m, 2H), 1.27 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.04, 139.56, 137.41, 136.47, 133.01, 126.67, 126.62, 79.85, 67.27, 52.46, 37.46, 28.56, 24.43, 21.31, 21.10; IR (neat) ν 2961, 2360, 1653, 1457, 1138 cm^{-1}; HRMS (EI) Calcd for $C_{18}H_{25}NO$ (M^+) 271.1936, found 271.1941.



5b

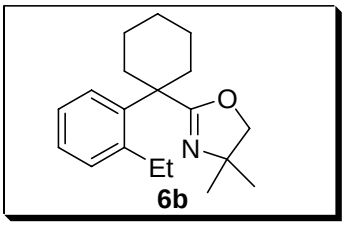
4,4-dimethyl-2-(1-(2-ethyl-4-methylphenyl)cyclopentyl)oxazoline (5b) Substrate **5** was ethylated following the general procedure. Column chromatography gave **5b** as a white solid (51.4 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.0 Hz, 1H), 7.05 (s, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 3.81 (s, 2H), 2.75 (q, *J* = 7.6 Hz, 2H), 2.59-2.53 (m, 2H),

2.30 (s, 3H), 2.05-1.99 (m, 2H), 1.83-1.79 (m, 2H), 1.71-1.69 (m, 2H), 1.26 (s, 6H), 1.20 (t, J = 7.6, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.58, 143.62, 138.79, 136.58, 130.97, 126.58, 126.55, 79.77, 67.20, 52.34, 38.04, 28.53, 25.40, 24.33, 21.25, 16.33; IR (neat) ν 2962, 1652, 1456, 1138, 1004 cm^{-1}; HRMS (EI) Calcd for $C_{19}H_{27}NO$ (M^+) 285.2093, found 285.2085.



6a

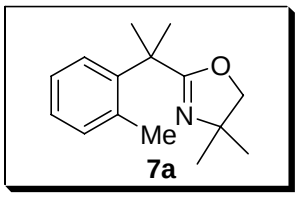
4,4-dimethyl-2-(1-o-tolylcyclohexyl)oxazoline (6a) Substrate **6** was methylated following the general procedure. Column chromatography gave **6a** as a white solid (42.4 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.2 Hz, 1H), 7.18 (td, J = 7.2, 1.6 Hz, 1H), 7.16-7.09 (m, 2H), 3.81 (s, 2H), 2.47 (s, 3H), 2.42-2.37 (m, 2H), 1.99-1.92 (m, 2H), 1.82-1.73 (m, 2H), 1.64-1.57 (m, 4H), 1.31 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.23, 142.47, 137.45, 132.92, 127.12, 126.87, 126.17, 78.98, 67.59, 45.08, 35.30, 28.73, 26.42, 23.01, 21.65; IR (neat) ν 2928, 2361, 1654, 1456, 1109 cm^{-1}; HRMS (EI) Calcd for $C_{18}H_{25}NO$ (M^+) 271.1936, found 271.1943.



6b

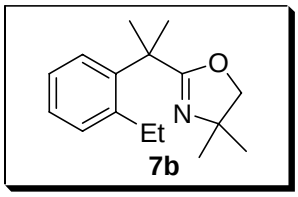
4,4-dimethyl-2-(1-(2-ethylphenyl)cyclohexyl)oxazoline (6b) Substrate **6** was ethylated following the general procedure. Column chromatography gave **6b** as a white solid (48.5 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, J = 8.4, 1.2 Hz, 1H), 7.24-7.15 (m,

3H), 3.79 (s, 2H), 2.86 (q, J = 7.6 Hz, 2H), 2.38-2.35 (m, 2H), 2.00-1.93 (m, 2H), 1.82-1.74 (m, 2H), 1.64-1.55 (m, 4H), 1.30 (s, 6H), 1.20 (t, J = 7.6, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.53, 143.65, 141.17, 130.71, 126.75, 126.68, 125.54, 78.55, 67.12, 44.48, 35.67, 28.32, 26.05, 25.04, 22.76, 16.67; IR (neat) ν 2929, 1651, 1454, 1109 cm^{-1}; HRMS (EI) Calcd for $C_{19}H_{27}NO$ (M^+) 285.2093, found 285.2084.



7a

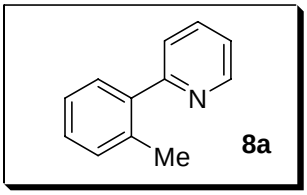
4,4-dimethyl-2-(2-o-tolylpropan-2-yl)oxazoline (7a) Substrate **7** was methylated by a general procedure. Column chromatography gave **7a** as a pale yellow liquid (39.8 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.36 (m, 1H), 7.21-7.12 (m, 3H), 3.90 (s, 2H), 2.36 (s, 3H), 1.64 (s, 6H), 1.32 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.13, 142.90, 136.81, 132.20, 127.15, 126.36, 125.67, 79.93, 67.22, 41.10, 28.54, 28.14, 20.90; IR (neat) ν 2972, 1657, 1464, 1301, 1115 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{21}NO$ (M^+) 231.1623, found 231.1620.



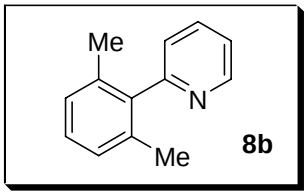
7b

4,4-dimethyl-2-(2-(2-ethylphenyl)propan-2-yl)oxazoline (7b) Substrate **7** was ethylated by a general procedure. Column chromatography gave **7b** as a pale yellow liquid (38.2 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 7.2 Hz, 1H), 7.25-7.15 (m, 3H), 3.87 (s, 2H), 2.72 (q, J = 7.6 Hz, 2H), 1.64 (s, 6H), 1.31 (s, 6H), 1.22 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.53, 143.18, 142.12, 130.11, 127.33, 126.13, 125.60,

79.82, 67.20, 40.99, 28.85, 28.58, 25.03, 16.25; IR (neat) ν 2969, 1655, 1464, 1116 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{23}NO$ (M^+) 245.1780, found 245.1771.



8a

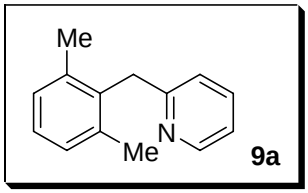


8b

2-o-tolylpyridine (8a) and 2-(2,6-dimethylphenyl)pyridine (8b) Substrate **8** was methylated following the general procedure. After purification by column chromatography, **8a** was obtained as a colorless oil (5.1 mg, 15%), and **8b** was obtained as a colorless oil (24.5 mg, 67%).

8a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.4 Hz, 1H), 7.75 (tt, *J* = 8.0, 2.0 Hz, 1H), 7.42-7.39 (m, 2H), 7.33-7.23 (m, 4H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.33, 149.49, 140.70, 136.50, 136.07, 131.06, 129.95, 128.62, 126.20, 124.47, 121.98, 20.60; IR (neat) ν 2893, 2089, 1643, 1300, 1123 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{11}N$ (M^+) 169.0891, found 169.0889.

8b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (dt, *J* = 4.4, 1.6 Hz, 1H), 7.76 (td, *J* = 8.0, 1.6 Hz, 1H), 7.29-7.19 (m, 3H), 7.12-7.09 (m, 2H), 2.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.27, 150.01, 136.64, 136.12, 128.21, 127.86, 124.82, 122.77, 122.00, 20.53; IR (neat) ν 2308, 1610, 1429, 1245 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{13}N$ (M^+) 183.1048, found 183.1045.

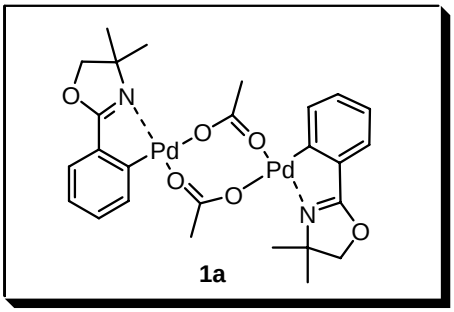


9a

2-(2,6-dimethylbenzyl)pyridine (9a) Substrate **9** was methylated following the general procedure. Column chromatography gave **9a** as a purple liquid (25.6 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 4.4 Hz, 1H), 7.49 (td, *J* = 7.6, 2.0 Hz, 1H), 7.13-7.06 (m, 4H), 6.72 (d, *J* = 7.6 Hz, 1H), 4.25 (s, 2H), 2.25 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.43, 149.67, 137.66, 136.94, 136.03, 128.56, 126.99, 121.67, 121.37, 38.60, 20.67; IR (neat) ν 2089, 1640, 1307, 1239 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{15}N$ (M^+) 197.1204, found 197.1207.

Mechanistic Investigations and optimizations

1. Benzoquinone effect on the C-H activation and coupling steps



1a

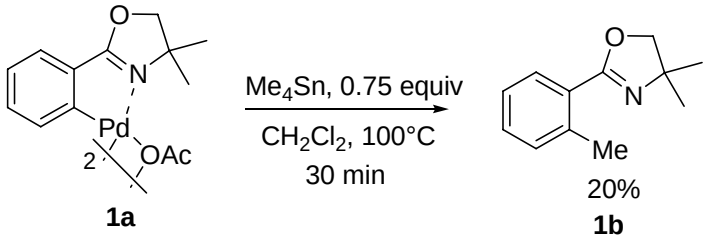
Synthesis of palladacycle 1a

Method 1: A mixture of substrate **1** (0.35 g, 2 mmol, 1 equiv) and palladium acetate (0.45 g, 2 mmol, 1 equiv) in 2 mL of acetic acid was stirred for 30 min at 95°C. Then the mixture was continually stirred at room temperature for 12 hours. The precipitate was filtered off, washed with acetic acid then water, and then dried and dissolved in chloroform. The solution was filtered through Celite then evaporated, and the residue crystallized from heptane to give 0.46 g of **1a** as a yellow solid (yield in 68%)[2]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10-7.08 (d, *J* = 7.2 Hz, 2H), 7.02-6.95 (m, 6H), 4.25 (d, AB, *J* = 8.4 Hz, 2H), 4.06 (d, AB, *J* = 8.4 Hz, 2H), 2.16 (s, 6H), 1.41 (s, 6 H), 0.78 (s, 6 H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 181.73, 172.92, 146.79, 132.78, 131.69, 130.38, 125.29, 123.93, 81.72, 65.39, 27.64, 24.94; IR (neat) ν 2972, 2360, 1629, 1587, 1408 cm^{-1}.

Method 2: The palladacycle was also prepared by the procedure under the condition of the catalytic reaction. A mixture of substrate **1** (35 mg, 0.2 mmol, 1 equiv) and palladium acetate (44.8 g, 0.2 mmol, 1 equiv) in 1 mL of dichloromethane was stirred for 4 hours at 100°C. The reaction mixture was filtered through Celite then evaporated. The ^1H NMR spectrum of the residue was identical to the standard spectrum of **1a**.

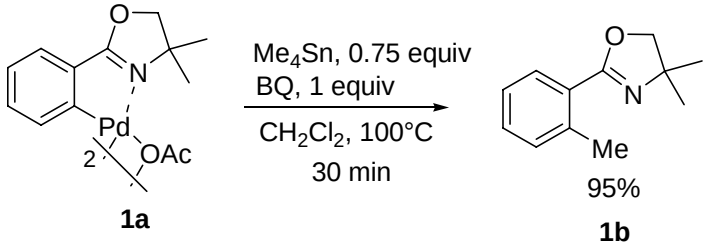
Stoichiometric reaction of palladacycle with tetramethyltin



1a **1b**

In a 20 mL tube, oxazoline palladacycle **1a** (13.6 mg, 0.02 mmol, 1 equiv) and tetramethyltin (0.03 mmol, in 50 μL CH_2Cl_2, 0.75 equiv according to Pd) were dissolved in 1 mL of CH_2Cl_2 under atmospheric air. The tube was sealed with a Teflon lined cap, and the reaction mixture was heated at 100 °C for 30 min. The mixture was filtered through a pad of Celite and the filtrate was concentrated under vacuum. The yield of **1b** determined by ^1H NMR analysis was 20%.

Stoichiometric reaction of palladacycle with tetramethyltin in the presence of benzoquinone



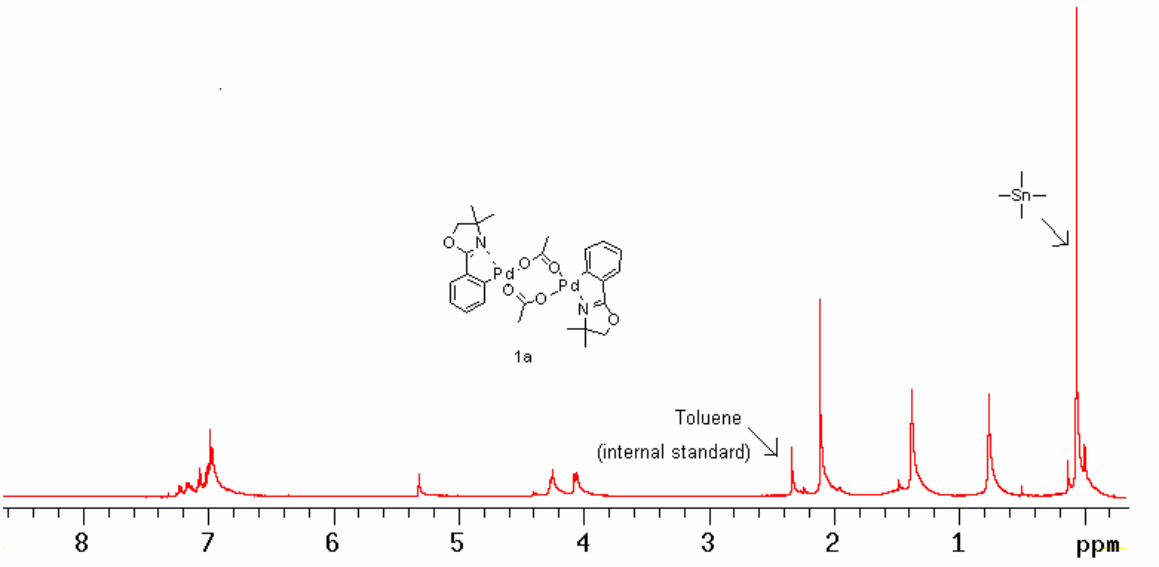
1a **1b**

In a 20 mL tube, oxazoline palladacycle **1a** (13.6 mg, 0.02 mmol, 1 equiv), tetramethyltin (0.03 mmol, in 50 μL CH_2Cl_2, 0.75 equiv according to Pd) and benzoquinone (2.2 mg, 0.02 mmol, 1 equiv) were dissolved in 1 mL of CH_2Cl_2 under atmospheric air. The tube was sealed with a Teflon lined cap, and the reaction mixture was heated at 100 °C for 30 min. The mixture was filtered through a pad of Celite and the filtrate was concentrated under vacuum. The yield of **1b** determined by ^{1}H NMR analysis was 95%.

Monitoring the stoichiometric reaction of palladacycle with tetramethyltin in the presence of benzoquinone by ^{1}H NMR.

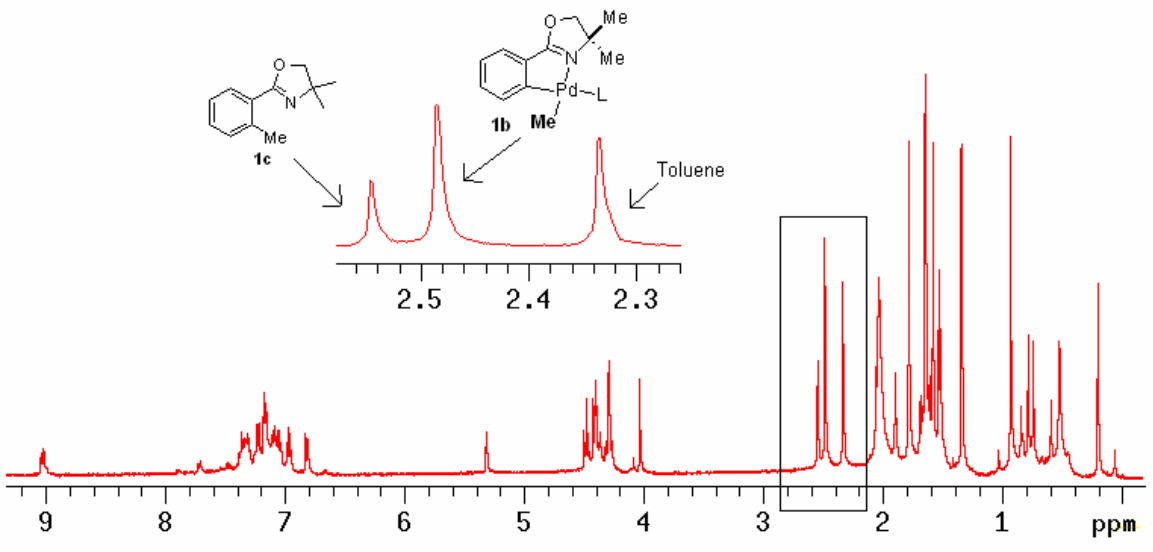
In a capped NMR tube, oxazoline palladacycle **1a** (13.6 mg, 0.02 mmol, 1 equiv) and tetramethyltin (0.03 mmol, 0.75 equiv according to Pd) were dissolved in 1 mL of CD_2Cl_2. Dry toluene (0.02 mmol, 2.1 μL, 1 equiv) was added as the internal standard. The tube was sealed with a Teflon lined cap, and the reaction mixture was heated at 50 °C for 10 min. The ^{1}H NMR spectrum showed that the palladacycle **1a** was stable under these conditions (Scheme 1).

Scheme 1



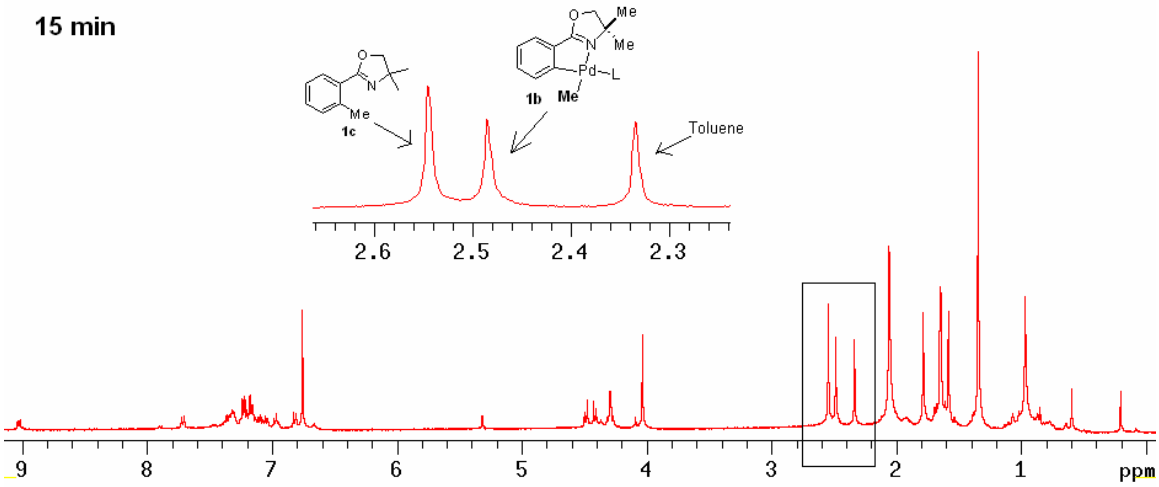
Then the reaction temperature was increased to 100 °C. Two peaks appeared at 2.48 ppm and 2.55 ppm corresponding to a LPd(Aryl)(Me) complex **1b** and the methylated product **1c.** Only 30% of **1c** was formed after 2 h (Scheme 2).

Scheme 2

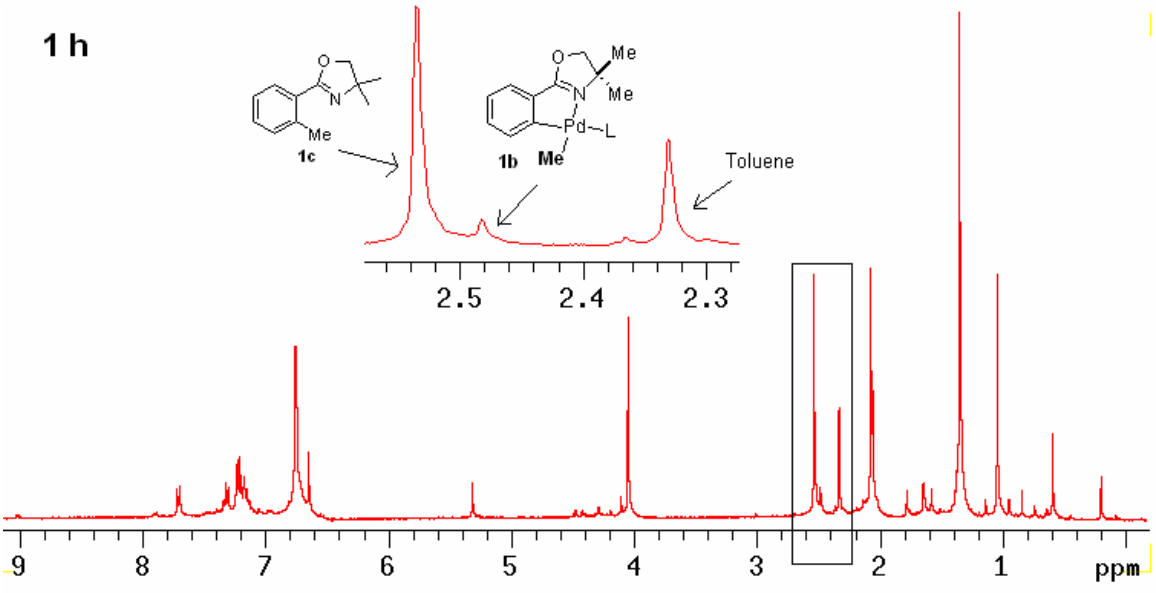


Then benzoquinone (2.2 mg, 0.02 mmol, 1 equiv) was added to the reaction mixture at the same temperature. It was shown that **1b** was converted to the methylated product **1c** within 1 h (Scheme 3 and 4).

Scheme 3



Scheme 4



Benzoquinone effect on the C-H activation of substrate 1

C-H activation step without benzoquinone: In a 20 mL tube, substrate **1** (35 mg, 0.2 mmol, 1 equiv), $Pd(OAc)_2$ (9 mg, 0.04 mmol, 20 mol%), and $Cu(OAc)_2$ (36.4 mg, 0.2 mmol, 1 equiv) were dissolved in 1 mL of CH_2Cl_2 under atmospheric air. The tube was sealed with a Teflon lined cap, and the reaction mixture was heated at 100 °C for 4 hours. Then benzoquinone (21.6 mg, 0.2 mmol, 1 equiv) and tetramethyltin (0.03 mmol, in 50 μL CH_2Cl_2, 0.75 equiv according to Pd) were added to the reaction mixture. The reaction was continued for another 30 min. The reaction mixture was diluted with 20 mL of CH_2Cl_2 and then treated with 10 mL of saturated Na_2S aqueous solution. The mixture was filtered through a pad of Celite, and the filtrate was washed twice with saturated brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The yield of **1b** determined by ^1H NMR analysis was 17%.

C-H activation step with benzoquinone: In a 20 mL tube, substrate **1** (35 mg, 0.2 mmol, 1 equiv), $Pd(OAc)_2$ (9 mg, 0.04 mmol, 20 mol%), $Cu(OAc)_2$ (36.4 mg, 0.2 mmol,

1 equiv) and benzoquinone (21.6 mg, 0.2 mmol, 1 equiv) were dissolved in 1 mL of CH_2Cl_2 under atmospheric air. The tube was sealed with a Teflon lined cap, and the reaction mixture was heated at 100 °C for 4 hours. Then tetramethyltin (0.03 mmol, in 50 μL CH_2Cl_2, 0.75 equiv according to Pd) was added to the reaction mixture. The reaction was continued for another 30 min. The reaction mixture was diluted with 20 mL of CH_2Cl_2 and then treated with 10 mL of saturated Na_2S aqueous solution. The mixture was filtered through a pad of Celite, and the filtrate was washed twice with saturated brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The yield of **1b** determined by ^1H NMR analysis was 18%.

Benzoquinone effect on the C-H activation of substrate 6

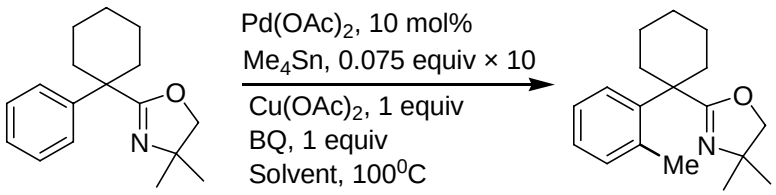
C-H activation step without benzoquinone: In a 20 mL tube, substrate **6** (51.4 mg, 0.2 mmol, 1 equiv), $Pd(OAc)_2$ (9 mg, 0.04 mmol, 20 mol%), and $Cu(OAc)_2$ (0.2 mmol, 36.4 mg) were dissolved in 1 mL of CH_2Cl_2 under atmospheric air. The tube was sealed with a Teflon lined cap, and the reaction mixture was heated at 100 °C for 4 hours. Then benzoquinone (21.6 mg, 0.2 mmol, 1 equiv) and tetramethyltin (0.03 mmol, in 50 μL CH_2Cl_2, 0.75 equiv according to Pd) were added to the reaction mixture. The reaction was continued for another 30 min. The reaction mixture was diluted with 20 mL of CH_2Cl_2 and then treated with 10 mL of saturated Na_2S aqueous solution. The mixture was filtered through a pad of Celite, and the filtrate was washed twice with saturated

brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. No desired compound was detected by ^1H NMR.

C-H activation with benzoquinone: In a 20 mL tube, substrate **6** (35 mg, 0.2 mmol, 1 equiv), $Pd(OAc)_2$ (9 mg, 0.04 mmol, 20 mol%), $Cu(OAc)_2$ (36.4 mg, 0.2 mmol, 1 equiv) and benzoquinone (21.6 mg, 0.2 mmol, 1 equiv) were dissolved in 1 mL of CH_2Cl_2 under atmospheric air. The tube was sealed with a Teflon lined cap, and the reaction mixture was heated at 100 °C for 4 hours. Then tetramethyltin (0.03 mmol, in 50 μL CH_2Cl_2, 0.75 equiv according to Pd) was added to the reaction mixture. The reaction was continued for another 30 min. The reaction mixture was diluted with 20 mL of CH_2Cl_2 and then treated with 10 mL of saturated Na_2S aqueous solution. The mixture was filtered through a pad of Celite, and the filtrate was washed twice with saturated brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The yield of **6a** was determined by ^1H NMR analysis to be 16%.

2. Optimization of reaction conditions

***Table 1*. Screening of solvents using substrate 6**

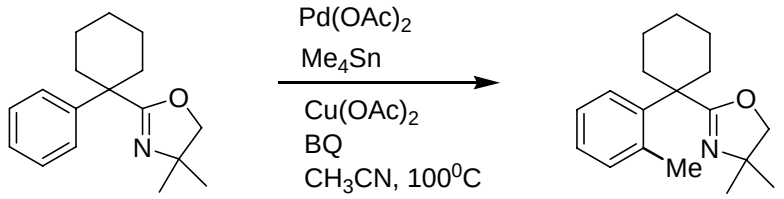


6 **6a**

Entry	Solvent	Yield%*
1	CH_3CN	78
2	CH_2Cl_2	65
3	$ClCH_2CH_2Cl$	23
4	$Cl_2CHCHCl_2$	58
5	DMF	49
6	DMSO	22
7	NMP	35
8	Toluene	17

*Yield was determined by ^{1}H NMR.

***Table 2*. Optimization of various reaction parameters using substrate 6**

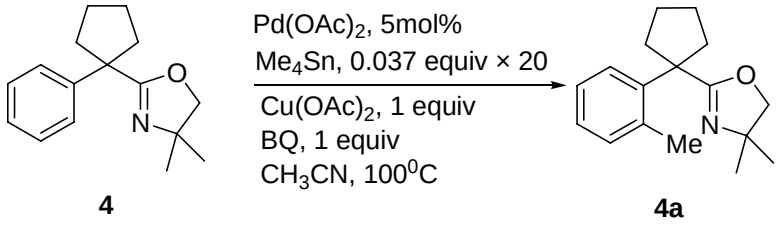


6 **6a**

Entry	$Pd(OAc)_2$	$Cu(OAc)_2$	BQ	Temperature	Me_4Sn addition	Yield %*
1	0	1 equiv	1 equiv	100°C	**One pot**	0
2	10 mol%	1 equiv	1 equiv	100°C	**One pot**	10
3	**20 mol%**	1 equiv	1 equiv	100°C	Batch-wise	83
4	**10 mol%**	**1 equiv**	**1 equiv**	**100°C**	**Batch-wise**	**78**
5	10 mol%	**2 equiv**	1 equiv	100°C	Batch-wise	62
6	10 mol%	1 equiv	**0.2 equiv**	100°C	Batch-wise	26
7	10 mol%	1 equiv	**2 equiv**	100°C	Batch-wise	77
8	10 mol%	1 equiv	1 equiv	**130°C**	Batch-wise	5
9	10 mol%	1 equiv	1 equiv	**75°C**	Batch-wise	38

***** Yield was determined by ^1H NMR.

***Table 3*. Optimization of reaction time using 5mol% $Pd(OAc)_2$**



4 **4a**

Entry	$Cu(OAc)_2$	BQ	Time	Me_4Sn addition	Yield%*
1	1 equiv	1 equiv	40 h	20 batches (batch / 2h)	54
2	1 equiv	1 equiv	60 h	20 batches (batch / 3h)	71

*Yield was determined by ^1H NMR.

Methylation of substrate 4 assisted by microwave radiation

In a 20 mL septum-capped Microwave vial (Microwave model: Discover®LabMate™), substrate **4** (48.6 mg, 0.2 mmol, 1 equiv), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 5 mol%), $Cu(OAc)_2$ (36.4 mg, 0.2 mmol, 1 equiv) and benzoquinone (21.6 mg, 0.2 mmol, 1 equiv) were dissolved in 1 mL of CH_3CN under atmospheric air. The vial was stirred at 90 °C for 0.5 hours at 100 W. Then the first portion of tetramethyltin (0.015 mmol, in 20 μL CH_3CN, 0.037 equiv) was added to the reaction mixture. The addition of the same amount of organotin reagent was repeated 19 more times every 0.5 hour. After the introduction of the last portion of the organotin reagent, the reaction was continued for another 0.5 hour. The reaction mixture was diluted with 20 mL of EtOAc and then treated with 10 mL of saturated Na_2S aqueous solution. The mixture was filtered through a pad of Celite, and the filtrate was washed twice with saturated brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column

chromatography on silica gel with a gradient eluent of hexane and ether (from 15:1 to 4:1) to give the product **4a** (41.7 mg, 81%).

Reference

1. H. Vorbriiggen, K. Krolikiewicz, *Tetrahedron Lett.* **1981**, 22, 4471

2. G. Balavoine, J.C. Clinet, P. Zerbib, *J. Organometallic Chem.* **1990**, 389, 259