Monophosphine Ligands Promote Mild Pd-Catalyzed C–S Coupling Reactions at Room Temperature and with Soluble Bases

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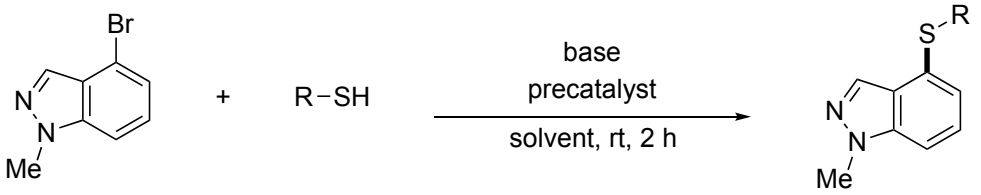
General Information

Anhydrous *tert*-butyl alcohol (tBuOH) and lithium bis(trimethylsilyl)amide solution (LiHMDS, 1 M in THF) were purchased from Sigma-Aldrich in Sure-Seal™ bottles and were used as received. $CDCl_3$ and C_6H_6 were purchased from Cambridge Isotope Laboratories, and $CDCl_3$ was optionally stored over K_2CO_3. All aryl bromides and thiols are available from commercial sources including Sigma Aldrich, Alfa Aesar, Acros Organics, TCI, Enamine, and Combi-Blocks and were used as received. XPhos, BrettPhos, tBuBrettPhos, and tBuXPhos were gifts from Sigma-Aldrich and were used without further purification. The JosiPhos ligand **L7** was a gift from Solvias and was used without further purification. **L5** was prepared according to literature procedure[1] and was stored in a desiccator. The ligand is stable for at least 6 months. tBuBrettPhos-Pd-G3·CH_2Cl_2 was purchased from Strem and used directly. All other chemicals were purchased from commercial sources and used without further purification, unless otherwise indicated. Title compounds were purified by flash chromatography using Silicycle® SiliaFlash P60 (230-400 mesh) silica gel with the aid of a Biotage SP4 or Teledyne Isco CombiFlash R_f instrument. Phase separation when indicated, was performed with an ISOLUTE® Phase separator column (6 mL, Cat. No. 120-1905-C). Organic solutions were concentrated in vacuo using a Buchi or Heidolph rotary evaporator.

General Analytical Information

All new compounds were characterized by NMR spectroscopy, IR spectroscopy, either elemental analysis (EA) or high-resolution mass spectrometry (HRMS), and melting point analysis (if crystalline solids). ^1H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker Avance-600 MHz, Bruker Avance-400 MHz, or Varian 600 spectrometer. ^1H and ^{13}C spectra were referenced to residual protonated solvent as an internal standard ($CDCl_3$: δ 7.26 ppm and δ 77.36 ppm, respectively). ^{31}P NMR spectra were referenced to a standard of H_3PO_4 (δ 0.0 ppm) (diluted in D_2O and sealed in a capillary tube). The following abbreviations were used to denote multiplicities: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA, USA. HRMS was recorded on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS) or Waters Xevo G2 QTof (electrospray). Melting points were obtained using a Stanford Research Systems EZ-Melt melting point apparatus.

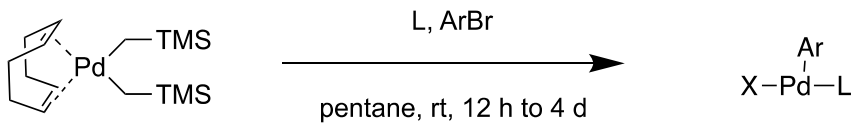
General Procedure for Reaction Screening



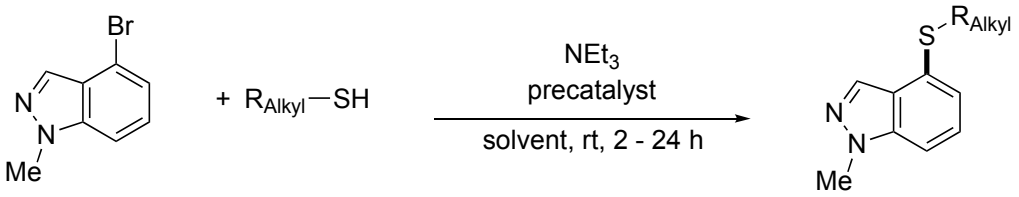
All screening reactions were set up inside a nitrogen-filled glovebox. For all reactions, stock solutions of certain reagents with the indicated concentrations and solvents were made inside the glovebox and dispensed by volume. Alternatively, in cases where reagents were only partially soluble, individual portions of these reagents were weighed and added as a slurry in solvent using a wide-bore needle, washing with additional solvent to ensure complete transfer.

Inside the glovebox, stock solutions of the precatalysts in the reaction solvent (50 μL of 0.2 M solution, 0.010 mmol) were transferred to oven-dried reaction tubes (Fisher, 13 x 100 mm tubes – Cat. No. 1495935C) equipped with oven-dried magnetic stir bars. A stock solution of aryl bromide (0.67 M) in the reaction solvent was prepared in a separate oven-dried reaction tube. All reaction tubes were capped with screw caps containing Teflon septa and removed from the glovebox. Thiol (1.2 equiv relative to aryl bromide) and base (2.0 equiv relative to aryl bromide) were added to the tube containing aryl bromide via syringe. 150 μL of the resulting solution was diluted with 50 μL of THF and retained as a GC standard. The reactions were initiated by injecting the combined aryl bromide, thiol, and base stock solution (150 μL) into each of the reaction tubes containing precatalysts. In all cases, the total volume of THF was 200 μL (0.050 M). The reaction mixtures were allowed to stir for 2 h at rt. At this time, tetradecane (26 μL, 0.10 mmol) was added to each reaction tube as an internal standard. The mixtures were diluted with EtOAc (roughly 5 mL) and filtered through a short plug of silica gel, washing with additional EtOAc (roughly 5 mL). The resulting solution was analyzed by GC to determine the conversion and yield of product.

General Procedure for the Preparation of Oxidative Addition Complexes



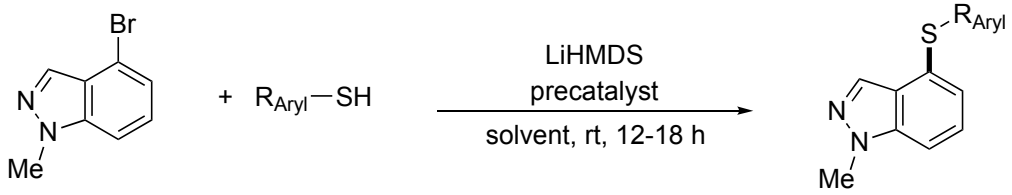
An oven-dried reaction tube (Fisher 20 x 125 mm tube – Cat. No. 1495937A) equipped with an oven-dried stir bar was charged with the desired ligand (1.0 equiv) and aryl bromide (1.2–2.0 equiv). The reaction tube was brought into a nitrogen-filled glovebox and pentane (6.0 mL) was added. The solution was stirred vigorously to dissolve the ligand. If the ligand remained undissolved, additional pentane (up to 6.0 mL) was added. (COD)Pd($CH_2TMS)_2$ (1.0 equiv) was added to the solution (still stirring vigorously) in one portion. Often, this addition resulted in an immediate color change. Pentane (2.0 mL) was used to wash the walls of the reaction tube. The mixture was capped with a screw cap containing a septum insert and the solution was stirred in the glovebox for 12 h to 4 d to give a yellow, orange or white suspension. The solid was filtered in the inert atmosphere glovebox and was washed with pentane (4 x 15 mL) to afford the oxidative addition complex as a solid. These oxidative addition complexes were then used without further purification and were stored in a glovebox freezer. Oxidative addition complexes **P2** and **P4** were stored outside of the glovebox.



General Procedure for the Pd-Catalyzed Coupling of Aryl Bromides with Alkyl Thiols

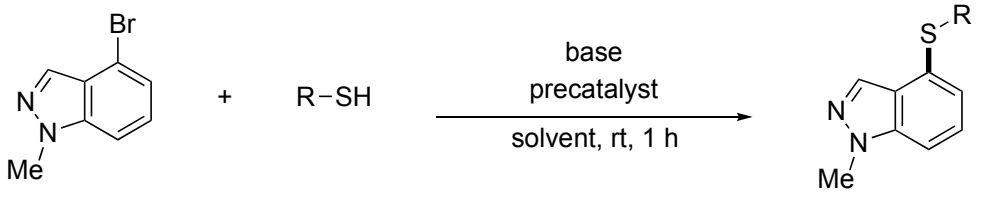
An oven-dried reaction tube (Fisher 20 x 125 mm tube – Cat. No. 1495937A) equipped with an oven-dried stir bar was charged with aryl bromide (if solid, 1.0 mmol, 1.0 equiv). A second oven-dried reaction tube (Fisher 13 x 100 mm tube – Cat. No. 1495935C) was charged with the precatalyst (**P2** or **P4**) indicated in the specific example outside of the glovebox. Both tubes were sealed with a screw cap containing a Teflon septum and were pierced with a needle connected to a vacuum manifold. The reaction tubes were evacuated and backfilled with nitrogen (this process was repeated a total of three times). tBuOH was warmed in a 40 °C water bath to melt the solid. Using a syringe, solvent (tBuOH or THF) was added to the reaction tube containing the precatalyst, to prepare a catalyst stock mixture (5.0 mM). The suspension was sonicated for several minutes until there were no catalysts grains pooling at the bottom of the reaction tube. If necessary, the suspension was melted in a 40 °C water bath. Then, aryl bromide (if liquid, 1.00 mmol, 1.00 equiv), catalyst stock mixture (2.00 mL), triethylamine (279 μL, 2.00 mmol, 2.0 equiv), and thiol (if liquid,

1.20 mmol, 1.20 equiv) or thiol stock solution (if solid, 1.2 mmol, 1.2 equiv in 2.00 mL THF) were added to the first reaction tube successively via syringe. The reaction was stirred at rt for 2–24 h (or until complete consumption of the aryl bromide, as indicated by TLC analysis), after which it was diluted with ethyl acetate and washed with sat. Na_2CO_3 solution (5 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, concentrated *in vacuo*, and purified via automated silica gel column chromatography.



General Procedure for the Pd-catalyzed coupling of Aryl Bromides with Aryl Thiols

A microwave vial (Biotage 0.2–2 mL process vial – Cat. No. 354625) equipped with a stir bar was charged with tBuBrettPhos-Pd-G3·CH_2Cl_2 (7.1 mg, 0.0075 mmol, 3 mol%), aryl halide (0.25 mmol), and aromatic thiol (0.3 mmol, 1.2 equiv). The vial was sealed with a septum cap and was pierced with a needle connected to a vacuum manifold in addition to a vent needle. The reaction tube was purged with a stream of nitrogen to remove air from the headspace. The vent needle was removed, the vial and its contents were cooled to 0 ºC in an ice bath, and a solution of 1 M LiHMDS in THF (0.6 mL, 2.4 equiv), cooled in an ice bath, was added dropwise. The resulting deep-colored solution was stirred at 0 ºC for 5 min, and then warmed to rt in a water bath. The reaction mixture was stirred at rt for 12–18 h, after which it was diluted with ethyl acetate and washed with sat. NH_4Cl (5 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were passed through an ISOLUTE® phase separator column (6 mL, Cat. No. 120-1905-C) to remove residual water, concentrated *in vacuo*, and purified via automated silica gel column chromatography.

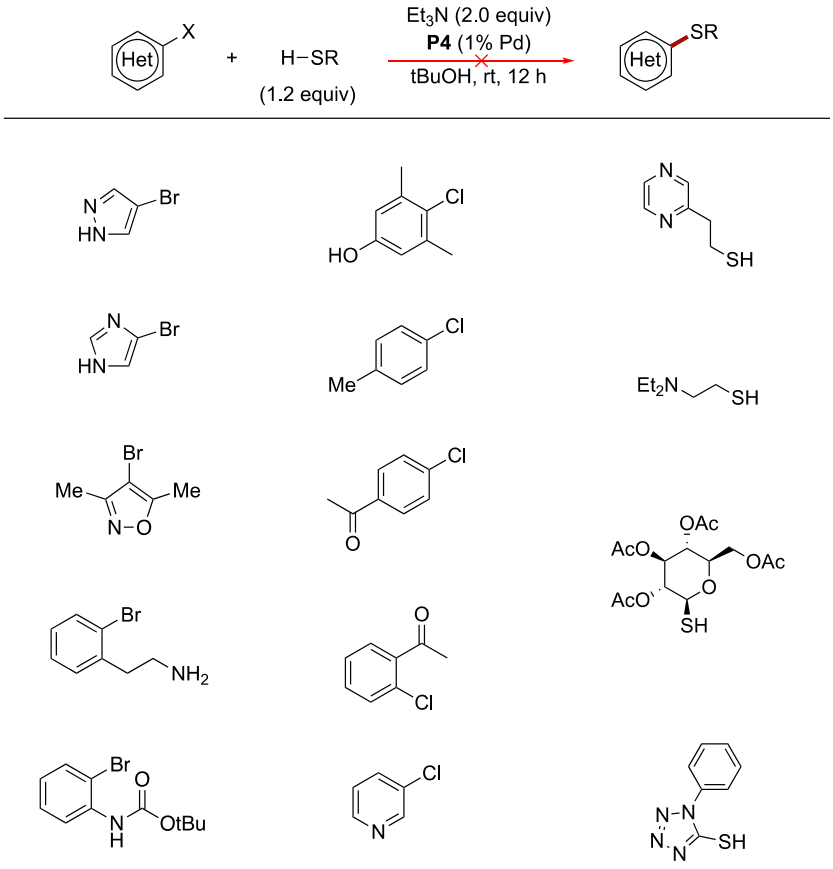


General Procedure for the Spectroscopic Investigation of Catalyst Resting State

An oven-dried NMR tube and NMR septum cap were brought into a nitrogen-filled glovebox. Stock solutions of [Pd] (0.020 mM), aryl bromide (0.50 mM), and LiHMDS (1 M, if relevant) in the reaction solvent were prepared in the glovebox. The [Pd] stock solution (150 μL, 0.0030 mmol) was added to the NMR tube, followed by the aryl bromide stock solution (200 μL, 0.10 mmol). An additional 100 μL of solvent was added to the tube. The NMR tube was capped with the septum cap and removed from the glovebox. For the alkyl thiol NMR experiments, the base (0.20 mmol, 2.0 equiv) was added by piercing the septum with a syringe, followed by the addition of alkyl thiol (0.12 mmol, 1.2 equiv). For the aryl thiol experiments, aryl thiol (0.12 mmol, 1.2 equiv) was added to the NMR tube by piercing the septum with syringe. The tube was cooled to 0 ºC in an ice-water bath, and a solution of base (240 μL, 0.24 mmol, 2.4 equiv) was added slowly by syringe. The tubes were repeatedly inverted to mix the contents. After 1 h, ^{31}P and ^{1}H NMR spectra were collected and analyzed. The resulting solution was analyzed by GC to confirm that aryl bromide was still present in the reaction mixture.

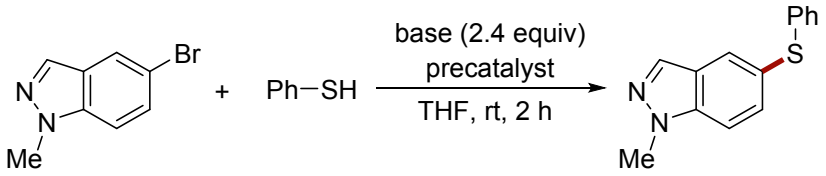
Substrate Scope Limitations

Table S1. Examples of thiol or aryl (pseudo)halide reactants that failed to react (<10% yield) under our reaction conditions.



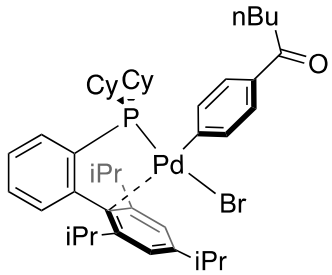
Extended Screening Data

Table S2. Additional catalyst screening data, following General Procedure for Reaction Screening (2 h reaction time).



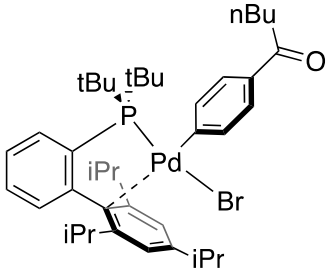
Precatalyst	Yield (%)	
	Using LiHMDS	**Using NEt_3**
AdBrettPhos Pd G3	0	0
APhos Pd G3	0	0
rac-BINAP-Pd-G3	0	0
BrettPhos Pd G4	35	0
cataCXium® A Pd G3	0	0
CPhos-Pd-G3	94	2
CyJohnPhos Pd G3	0	0
DavePhos-Pd-G3	0	0
DPPF Pd G3	0	0
JackiePhos Pd G3	3	0
JosiPhos-SL-J009-1-Pd-G3	61	0
meCgPPh Pd G3	0	0
Me4tBuXPhos Pd G3	9	0
MorDalphos Pd G3	42	0
P(Cy3) Pd G3	0	0
P(t-Bu)3 Pd G2	14	0
Pd-PEPPSI™-IPent	0	0
RuPhos Pd G4	95	0
SPhos Pd G4	53	0
tBuBrettPhos Pd G3	100	4
tBuXPhos Pd G3	95	8
XantPhos Pd G3	14	2
XPhos Pd G4	18	0
$PdCl_2(PPh_3)_2$	0	0

Characterization of Palladium Complexes



XPhos (L1) Supported Oxidative Addition Complex, P*1

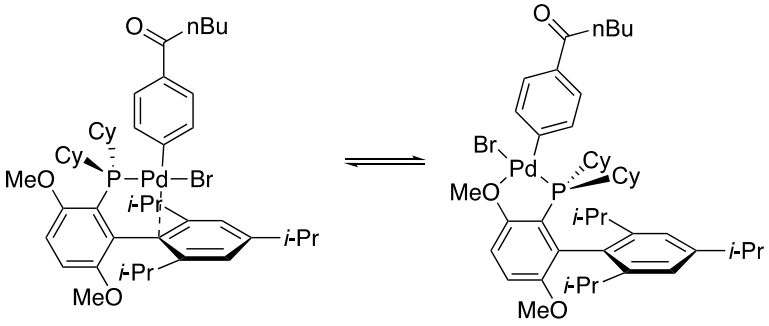
The general procedure was followed on a 0.40 mmol scale using XPhos (191 mg, 0.40 mmol), (COD)Pd($CH_2TMS)_2$ (156 mg, 0.40 mmol), and 1-(4-bromophenyl)pentan-1-one (193 mg, 0.80 mmol), which afforded a white powder. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.68 (td, *J* = 6.5, 3.1 Hz, 1H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.48 – 7.42 (m, 2H), 7.24 (dd, *J* = 8.4, 1.9 Hz, 4H), 7.17 (s, 2H), 6.90 (dq, *J* = 5.8, 3.6 Hz, 1H), 3.14 (hept, *J* = 6.9 Hz, 1H), 2.88 (t, *J* = 7.5 Hz, 2H), 2.46 (hept, *J* = 6.8 Hz, 2H), 2.27 – 2.18 (m, 2H), 1.96 (s, 2H), 1.85 – 1.79 (m, 3H), 1.76 – 1.69 (m, 6H), 1.71 – 1.64 (m, 4H), 1.63 (d, *J* = 6.8 Hz, 7H), 1.43 (s, 1H), 1.40 (dd, *J* = 14.4, 7.2 Hz, 8H), 1.30 – 1.19 (m, 4H), 1.22 – 1.10 (m, 2H), 1.00 – 0.88 (m, 10H), 0.67 (qt, *J* = 12.5, 3.2 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.0, 156.5, 149.7, 147.5, 147.3, 146.1, 137.03, 137.01, 134.2, 134.0, 133.6, 133.5, 132.8, 131.8, 130.6, 126.93, 126.90, 126.0, 125.0, 124.9, 38.0, 35.3, 35.2, 34.2, 31.6, 28.4, 27.7, 27.55, 27.46, 27.2, 27.1, 26.9, 25.8, 25.5, 24.7, 24.5, 24.1, 22.6, 14.00. **^{31}P NMR** (243 MHz, $CDCl_3$) δ 26.6. **IR** (neat, cm^{-1}): 733, 1005, 1054, 1567, 1674, 2852, 2922, 2959. **LC/MS**: m/z calcd. for $C_{44}H_{62}OPPd$ $[M\text{-}Br]^+$: 743.3573. Found: 743.3569.



tBuXPhos (L2) Supported Oxidative Addition Complex, P*2

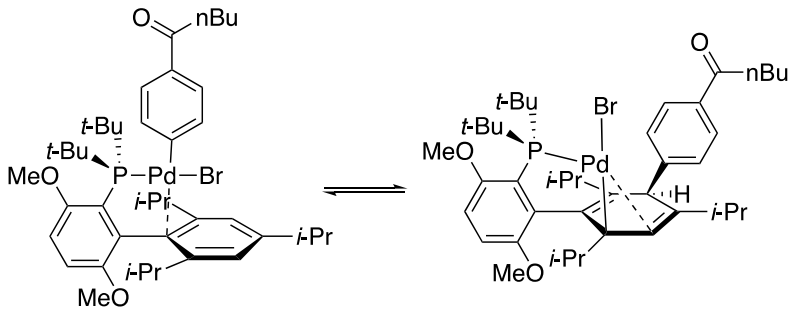
The general procedure was followed on a 0.40 mmol scale using tBuXPhos (170. mg, 0.40 mmol), (COD)Pd($CH_2TMS)_2$ (156 mg, 0.40 mmol), and 1-(4-bromophenyl)pentan-1-one (193 mg, 0.80 mmol), which afforded a yellow powder. **^{1}H NMR** (600 MHz, C_6D_6) δ 7.57 (d, *J* = 8.2 Hz, 3H), 7.52 – 7.48 (m, 2H), 7.32 (s, 2H), 6.86 (td, *J* = 8.6, 7.4, 4.3 Hz, 2H), 6.53 (dt, *J* = 6.6, 3.0 Hz, 1H), 3.23 – 3.10 (m, *J* = 6.9 Hz, 1H), 2.63 (hept, *J* = 6.8 Hz, 2H), 2.53 (t, *J* = 7.4 Hz, 2H), 1.76 (d, *J* = 6.8 Hz, 5H), 1.66 (p, *J* = 7.4 Hz, 2H), 1.51 (d, *J* = 6.9 Hz, 5H), 1.25 (dq, *J* = 11.8, 7.4 Hz, 4H), 1.16 (d, *J* = 13.9 Hz, 18H), 0.93 (d, *J* = 6.6 Hz, 6H), 0.87 (t, *J* = 7.2 Hz, 2H), 0.82 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, C_6D_6) δ 198.6, 157.6, 151.6, 139.5, 139.5, 134.9, 134.6, 134.5, 133.0, 129.6, 125.2, 125.1, 124.8, 39.0, 39.0, 37.5, 34.6, 31.4, 31.1, 31.1, 26.4, 25.3, 24.7, 24.6, 22.5, 22.4, 13.9, 13.8. **^{31}P NMR** (243 MHz, C_6D_6) δ 49.1. **IR** (neat, cm^{-1}): 784, 1005,

1046, 1567, 2862, 2921, 2957. **LC/MS**: m/z calcd. for $C_{40}H_{58}OPPd$ [M-Br]$^+$: 691.3260. Found: 691.3268.



BrettPhos (L3) Supported Oxidative Addition Complex, P*3

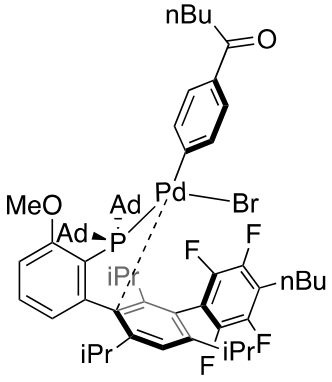
The general procedure was followed on a 0.40 mmol scale using BrettPhos (215 mg, 0.40 mmol), (COD)Pd($CH_2TMS)_2$ (156 mg, 0.40 mmol), and 1-(4-bromophenyl)pentan-1-one (193 mg, 0.80 mmol), which afforded a white powder. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 4H), 7.05 – 7.00 (m, 2H), 6.86 (s, 1H), 6.84 – 6.74 (m, 3H), 4.16 (s, 2H), 3.59 (s, 2H), 3.37 (s, 2H), 3.13 (s, 2H), 2.62 (td, *J* = 7.5, 2.3 Hz, 3H), 2.52 (q, *J* = 12.0 Hz, 2H), 2.26 (hept, *J* = 6.8 Hz, 2H), 2.09 (hept, *J* = 7.6, 6.6 Hz, 2H), 1.68 – 1.61 (m, 2H), 1.57 – 1.52 (m, 2H), 1.52 – 1.38 (m, 10H), 1.38 – 1.31 (m, 7H), 1.27 (s, 1H), 1.24 – 1.18 (m, 3H), 1.14 (dd, *J* = 14.4, 7.2 Hz, 9H), 1.02 (dd, *J* = 6.8, 4.1 Hz, 14H), 0.95 – 0.88 (m, 3H), 0.74 – 0.65 (m, 12H), 0.65 – 0.55 (m, 8H), 0.38 (dtd, *J* = 16.2, 12.6, 10.9, 6.2 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.2, 201.0, 157.4, 154.6, 154.0, 153.9, 152.0, 149.6, 149.1, 146.7, 138.2, 138.1, 137.8, 137.8, 133.5, 132.4, 132.3, 130.1, 125.4, 125.4, 124.6, 121.4, 116.5, 113.3, 113.2, 111.2, 111.1, 110.9, 77.2, 77.0, 76.8, 62.2, 54.9, 54.6, 54.4, 38.0, 36.4, 36.2, 35.3, 35.1, 34.4, 34.3, 31.4, 30.9, 30.8, 29.4, 29.3, 29.3, 27.8, 27.8, 27.7, 27.7, 26.9, 26.9, 26.7, 26.6, 26.4, 26.3, 26.1, 25.8, 25.4, 25.4, 25.2, 24.8, 24.5, 24.0, 23.4, 22.6, 22.6, 14.1, 14.0, 13.9. **^{31}P NMR** (243 MHz, $CDCl_3$) δ 45.7, 36.3. IR (neat, cm^{-1}): 1006, 1052, 1241, 1569, 1669, 2858, 2926, 2959. **LC/MS**: m/z calcd. for $C_{46}H_{66}O_3PPd$ [M-Br]$^+$: 803.3784. Found: 803.3783.



tBuBrettPhos (L4) Supported Oxidative Addition Complex, P*4

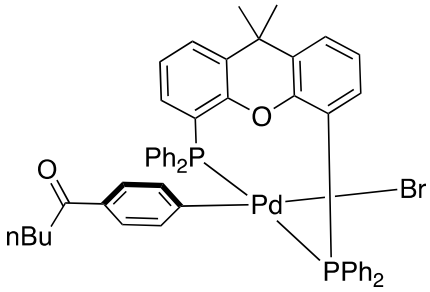
The general procedure was followed on a 0.40 mmol scale using tBuBrettPhos (194. mg, 0.40 mmol), (COD)Pd($CH_2TMS)_2$ (156 mg, 0.40 mmol), and 1-(4-bromophenyl)pentan-1-one

(193 mg, 0.80 mmol), which afforded a yellow powder. **^{1}H NMR** (600 MHz, C_6D_6) δ 7.63 – 7.56 (m, 4H), 7.32 (s, 3H), 6.36 – 6.30 (m, 2H), 6.28 (dd, *J* = 8.9, 2.4 Hz, 1H), 3.26 – 3.18 (m, 3H), 3.09 (s, 1H), 3.05 (s, 3H), 2.86 (s, 3H), 2.74 (h, *J* = 6.7 Hz, 2H), 2.58 (t, *J* = 7.3 Hz, 2H), 1.85 (d, *J* = 6.8 Hz, 6H), 1.69 (hept, *J* = 6.4 Hz, 3H), 1.63 (s, 2H), 1.62 – 1.50 (m, 12H), 1.33 (d, *J* = 14.7 Hz, 20H), 1.26 (dt, *J* = 14.9, 7.0 Hz, 4H), 1.21 – 1.14 (m, 2H), 0.93 (d, *J* = 6.5 Hz, 7H), 0.86 – 0.76 (m, 6H), 0.43 (s, 2H). **^{13}C NMR** (151 MHz, C_6D_6) δ 199.2, 153.6, 140.8, 132.8, 128.3, 125.5, 124.6, 113.0, 110.3, 54.2, 53.2, 41.0, 41.0, 37.9, 34.9, 32.6, 32.6, 31.8, 26.8, 26.1, 25.1, 24.9, 22.9, 14.2. **^{31}P NMR** (243 MHz, C_6D_6) δ 82.2, 68.9. **IR** (neat, cm^{-1}): 821, 1004, 1044, 1267, 1421, 1567, 2863, 2928, 2959. **LC/MS**: m/z calcd. for $C_{42}H_{62}O_3PPd$ $[M\text{-}Br]^+$: 751.3471 Found: 751.3486.



AlPhos (L5) Supported Oxidative Addition Complex, P*5

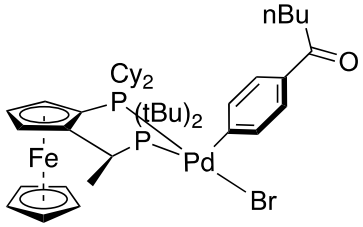
The general procedure was followed on a 0.10 mmol scale using AlPhos (82 mg, 0.10 mmol), (COD)Pd(CH_2TMS)$_2$ (38.9 mg, 0.10 mmol), and 1-(4-bromophenyl)pentan-1-one (48 mg, 0.20 mmol)which afforded a yellow powder. Spectroscopic data for this compound matched previously reported data[1].



XantPhos (L6) Supported Oxidative Addition Complex, P*6

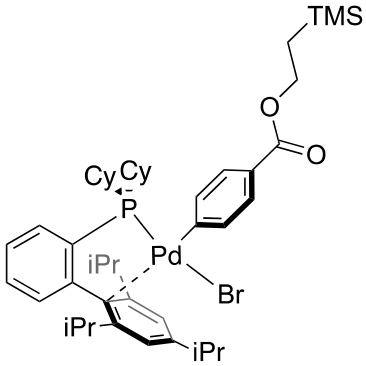
P6 was prepared according to a literature procedure with XantPhos (127. mg, 0.22 mmol, 1.1 equiv), $Pd_2(dba)_3$ (92 mg, 0.10 mmol, 0.20 mmol of Pd), and 1-(4-bromophenyl)pentan-1-one (217 mg, 0.90 mmol, 4.5 equiv). The product resulting from the literature procedure was triturated with pentane, filtered, and placed under vacuum for 8 h, which afforded the title compound as a yellow powder. **^{1}H NMR** (600 MHz, C_6D_6) δ 8.63 (s, 1H), 7.30 (q, *J* = 5.9 Hz, 2H), 7.14 – 6.37 (m, 26H), 2.57 (t, *J* = 7.3 Hz, 2H), 1.71 (p, *J* = 7.4 Hz, 2H), 1.43 (s, 5H), 1.31 (h, *J* = 7.3 Hz, 2H), 0.88 (q, *J* = 7.8 Hz, 4H). **^{13}C NMR** (151 MHz, C_6D_6) δ 199.7, 171.0, 156.9, 156.9, 156.9, 135.7, 132.8, 131.8, 128.9, 128.0, 126.4, 125.0, 125.0, 125.0, 123.8, 123.6, 123.4, 123.3, 38.6, 36.8, 28.0, 23.5, 14.8. **^{31}P NMR** (243 MHz, $CDCl_3$): δ 8.8. **IR**

(neat, cm^{-1}): 695, 744, 753, 1398, 2869, 2956, 298, 3056. **LC/MS**: m/z calcd. for $C_{50}H_{45}O_2P_2Pd$: 845.19296. Found: 845.1892.



JosiPhos (L7) Supported Oxidative Addition Complex, P*7

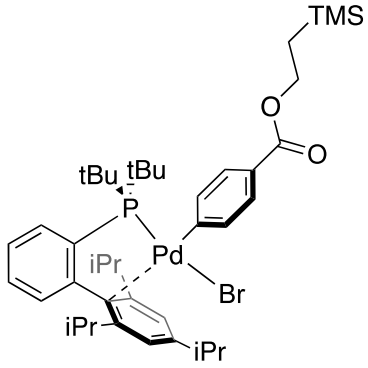
An oven-dried reaction tube (Fisher 20 x 125 mm tube – Cat. No. 1495937A) equipped with a stir bar was charged with **P4** (77.2 mg, 0.10 mmol, 1.0 equiv), and JosiPhos (61 mg, 0.11 mmol, 1.1 equiv). The reaction tube was brought into a nitrogen-filled glovebox and THF (2 mL) was added. The tube was capped, and the solution was removed from the glove box. The reaction mixture was heated to 60 ºC for 3 h. After cooling to room temperature, the solution was concentrated *in vacuo*, and pentane (2 mL) was added to the reaction vial. The crude mixture was then stirred for 1 hour. The solid was filtered outside of the glovebox and was washed with pentane (4 x 15 mL) to afford the oxidative addition complex as an orange solid. This solid was then transferred into the glovebox for storage. **^{1}H NMR** (600 MHz, C_6D_6) δ 7.97 (s, 3H), 7.84 (d, *J* = 8.1 Hz, 1H), 4.62 (s, 1H), 4.04 – 3.99 (m, 2H), 3.96 (s, 4H), 3.08 (d, *J* = 7.8 Hz, 1H), 2.69 (td, *J* = 7.2, 2.5 Hz, 3H), 2.31 – 2.16 (m, 2H), 1.84 (s, 1H), 1.78 – 1.76 (m, 1H), 1.76 – 1.69 (m, 4H), 1.66 (d, *J* = 11.6 Hz, 8H), 1.60 (t, *J* = 7.4 Hz, 5H), 1.48 (s, 1H), 1.37 (s, 1H), 1.29 (t, *J* = 13.4 Hz, 10H), 1.26 – 1.19 (m, 4H), 1.19 – 1.16 (m, 2H), 1.15 (d, *J* = 6.4 Hz, 1H), 1.03 – 0.97 (m, 1H), 0.85 (dt, *J* = 18.2, 7.2 Hz, 6H). **^{13}C NMR** (151 MHz, C_6D_6): δ ^{13}C NMR (151 MHz, C_6D_6) δ 199.1, 135.7, 133.1, 128.0, 127.8, 127.6, 123.1, 123.0, 97.4, 97.4, 97.3, 97.3, 72.2, 69.4, 69.0, 68.3, 68.2, 38.5, 37.6, 36.6, 36.6, 34.1, 32.8, 32.8, 32.3, 32.2, 31.0, 31.0, 27.2, 27.2, 27.1, 27.0, 26.7, 26.7, 26.6, 26.4, 25.9, 22.5, 22.4, 17.3, 17.3, 13.9, 13.9. **^{31}P NMR** (243 MHz, C_6D_6) δ 74.0, 73.9 (d, *J* = 26.7 Hz), 16.5. **IR** (neat, cm^{-1}): 1004, 1041, 1178, 1241, 1563, 1658, 2852, 2926. **LC/MS**: m/z calcd. for $C_{43}H_{65}FeOP_2Pd$ [M-Br]$^+$: 821.28949. Found: 821.2902.



XPhos (L1) Supported Oxidative Addition Precatalyst, P1

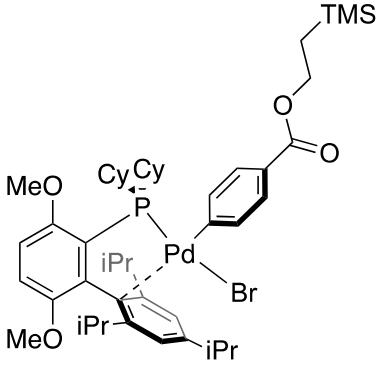
The general procedure was followed on a 0.200 mmol scale using XPhos (105 mg, 0.220 mmol), (COD)Pd(CH_2TMS)$_2$ (77.8 mg, 0.200 mmol), and 2-(trimethylsilyl)ethyl 4-bromobenzoate (72.3 mg, 0.240 mmol), which afforded a white powder (95 g, 54% yield) after 4 days. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.66 (td, J = 6.4, 3.0

Hz, 1H), 7.59 – 7.54 (m, 2H), 7.42 (ddt, J = 7.3, 5.0, 2.5 Hz, 2H), 7.21 – 7.16 (m, 2H), 7.14 (s, 2H), 6.87 (dt, J = 7.6, 3.3 Hz, 1H), 4.38 – 4.32 (m, 2H), 3.12 (hept, J = 6.9 Hz, 1H), 2.44 (hept, J = 6.7 Hz, 2H), 2.20 (td, J = 12.5, 9.9 Hz, 2H), 1.94 (s, 1H), 1.80 (d, J = 12.7 Hz, 2H), 1.69 (d, J = 14.2 Hz, 6H), 1.60 (d, J = 6.8 Hz, 7H), 1.39 (d, J = 6.9 Hz, 5H), 1.28 – 1.14 (m, 5H), 1.14 – 1.10 (m, 2H), 1.10 – 1.05 (m, 2H), 0.90 (d, J = 6.7 Hz, 6H), 0.66 (dtd, J = 12.8, 9.1, 3.7 Hz, 2H), 0.06 (s, 8H). **^{13}C NMR** (151 MHz, CDCl3) δ 167.6, 156.5, 149.6, 147.5, 147.4, 145.1, 136.9, 136.8, 134.3, 133.6, 133.5, 131.8, 130.5, 127.3, 126.9, 125.9, 125.1, 124.9, 77.2, 77.0, 76.8, 62.6, 35.4, 35.2, 34.2, 31.5, 28.4, 27.7, 27.6, 27.5, 27.2, 27.2, 25.9, 25.5, 24.7, 24.5, 17.4, -1.4. **^{31}P NMR** (243 MHz, CDCl3) δ 26.4. **IR** (neat, cm^{-1}): 758, 837, 1009, 1256, 1272, 1572, 1709. **LC/MS:** m/z calcd. for $C_{45}H_{66}O_2PPdSi$ $[M\text{-}Br]^+$: 803.36045. Found: 803.3622.



tBuXPhos (L2) Supported Oxidative Addition Precatalyst, P2

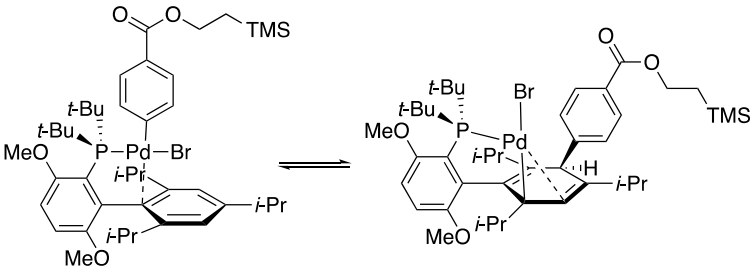
The general procedure was followed on a 1.60 mmol scale using tBuXPhos (747 mg, 1.76 mmol), (COD)Pd($CH_2TMS)_2$ (622 mg, 1.60 mmol), and 2-(trimethylsilyl)ethyl 4-bromobenzoate (502 mg, 1.76 mmol), which afforded a yellow powder (1.04 g, 78% yield). **^{1}H NMR** (600 MHz, C_6D_6) δ 8.04 – 7.99 (m, 2H), 7.69 – 7.58 (m, 3H), 7.41 (s, 2H), 7.25 (p, *J* = 1.1 Hz, 2H), 6.99 – 6.91 (m, 2H), 6.61 (ddd, *J* = 6.8, 3.3, 1.9 Hz, 1H), 4.46 – 4.40 (m, 2H), 3.32 – 3.23 (m, *J* = 6.6 Hz, 1H), 2.70 (hept, *J* = 6.8 Hz, 2H), 1.83 (d, *J* = 6.8 Hz, 6H), 1.61 (d, *J* = 6.9 Hz, 6H), 1.52 – 1.44 (m, 1H), 1.39 – 1.28 (m, 2H), 1.23 (d, *J* = 13.9 Hz, 19H), 1.13 – 1.07 (m, 1H), 1.05 – 0.92 (m, 9H), 0.00 (s, 8H). **^{13}C NMR** (151 MHz, C_6D_6) δ 167.2, 157.9, 152.0, 147.8, 147.7, 142.4, 139.9, 139.9, 136.8, 136.7, 135.3, 134.9, 134.9, 132.3, 132.0, 130.0, 128.3, 126.7, 126.4, 125.7, 125.6, 125.6, 125.6, 125.5, 62.4, 39.4, 39.3, 34.9, 31.8, 31.5, 31.5, 25.7, 25.1, 25.0, 17.6, -1.5. **^{31}P NMR** (243 MHz, C_6D_6) δ 49.07. **IR** (neat, cm^{-1}): 754, 841, 1010, 1573, 1704, 2864, 2899, 2922, 2960. **LC/MS:** m/z calcd. for $C_{41}H_{62}O_2PPdSi$ $[M\text{-}Br]^+$: 751.32915. Found: 751.3298.



BrettPhos (L3) Supported Oxidative Addition Precatalyst, P3

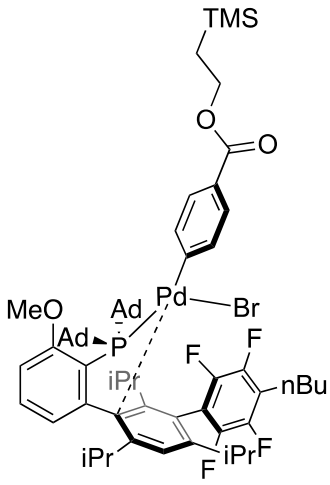
The general procedure was followed on a 0.200 mmol scale using BrettPhos (118 mg, 0.220 mmol), (COD)Pd($CH_2TMS)_2$ (77.8 mg, 0.200 mmol), and 2-(trimethylsilyl)ethyl 4-bromobenzoate (72.3

mg, 0.240 mmol), which afforded an off-white powder (144 mg, 81% yield). **^{1}H NMR** (400 MHz, C_6D_6) δ 8.09 – 7.99 (m, 2H), 7.92 (s, 1H), 7.62 (dd, J = 8.4, 1.4 Hz, 1H), 7.39 (s, 1H), 7.07 (s, 1H), 6.37 – 6.26 (m, 2H), 4.40 – 4.30 (m, 2H), 4.14 (s, 1H), 3.27 (hept, J = 6.9 Hz, 1H), 3.12 (s, 2H), 2.87 (d, J = 1.3 Hz, 4H), 2.74 (d, J = 6.8 Hz, 1H), 2.71 (d, J = 6.2 Hz, 1H), 2.09 (s, 1H), 1.85 (d, J = 6.7 Hz, 4H), 1.77 (s, 1H), 1.65 (d, J = 12.1 Hz, 2H), 1.57 (d, J = 6.9 Hz, 4H), 1.52 (d, J = 8.5 Hz, 1H), 1.38 (s, 1H), 1.21 (d, J = 6.7 Hz, 4H), 1.18 – 1.06 (m, 8H), 1.06 – 1.00 (m, 4H), 0.92 (dd, J = 19.1, 7.4 Hz, 7H), 0.87 (t, J = 6.9 Hz, 1H), 0.75 (s, 1H), -0.09 (d, J = 4.1 Hz, 9H). **^{13}C NMR** (151 MHz, C_6D_6) δ 167.0, 157.4, 151.3, 138.5, 138.5, 128.0, 127.8, 127.7, 127.5, 126.7, 126.2, 124.9, 113.0, 110.7, 62.0, 62.0, 54.1, 53.9, 35.4, 35.2, 34.5, 34.4, 31.6, 29.5, 27.8, 27.7, 27.6, 26.1, 25.4, 24.8, 24.5, 23.8, 17.2, -1.8, -1.9. **^{31}P NMR** (243 MHz, C_6D_6) δ 34.1. **IR** (neat, cm^{-1}): 754, 1009, 1055, 1459, 1575, 1707. **LC/MS:** m/z calcd. for $C_{41}H_{62}O_2PPdSi$ $[M\text{-}Br]^+$: 863.38158. Found: 863.3822.



tBuBrettPhos (L4) Supported Oxidative Addition Precatalyst, P4

The general procedure was followed on a 2.00 mmol scale using tBuBrettPhos (1.07 g, 2.20 mmol), COD(Pd($CH_2TMS)_2$) (778 mg, 2.00 mmol), and 2-(trimethylsilyl)ethyl 4-bromobenzoate (628 mg, 2.20 mmol), which afforded a yellow powder (1.23 g, 69% yield). Spectroscopic data for this compound matched previously reported data[2].

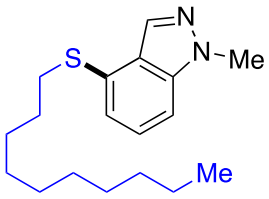


AlPhos (L5) Supported Oxidative Addition Precatalyst, P5

The general procedure was followed on a 0.100 mmol scale using AlPhos (81.5 mg, 0.100 mmol), (COD)Pd($CH_2TMS)_2$ (38.9 mg, 0.100 mmol), and 2-(trimethylsilyl)ethyl 4-bromobenzoate (36.2 mg, 0.120 mmol), which afforded a yellow powder (34.1 mg, 39% yield). **^{1}H NMR** (600 MHz, C_6D_6) δ 7.99 (d, J = 8.3 Hz, 1H), 7.85 (tt, J = 8.5, 4.2 Hz, 1H), 7.76 (s, 1H), 7.75 (s, 1H), 7.60 (s, 1H), 6.83 (td, J =

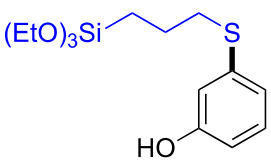
7.9, 1.4 Hz, 1H), 6.30 – 6.25 (m, 1H), 6.22 – 6.18 (m, 1H), 4.34 (dd, J = 8.9, 7.7 Hz, 2H), 3.48 (p, J = 7.1 Hz, 1H), 3.10 (d, J = 3.9 Hz, 3H), 2.79 (p, J = 6.8 Hz, 1H), 2.57 (dt, J = 13.3, 7.2 Hz, 4H), 2.51 (s, 2H), 2.46 (d, J = 11.7 Hz, 3H), 2.22 (d, J = 11.9 Hz, 2H), 2.15 (s, 1H), 1.97 (d, J = 12.6 Hz, 2H), 1.94 – 1.84 (m, 7H), 1.76 (s, 2H), 1.71 (t, J = 13.4 Hz, 4H), 1.68 – 1.56 (m, 11H), 1.53 (s, 1H), 1.51 – 1.44 (m, 3H), 1.43 (s, 2H), 1.27 (d, J = 6.8 Hz, 3H), 1.20 (hept, J = 7.3 Hz, 3H), 1.10 (dd, J = 7.1, 1.9 Hz, 3H), 0.96 – 0.90 (m, 2H), 0.86 (t, J = 7.1 Hz, 3H), 0.82 – 0.74 (m, 3H), -0.09 (s, 6H). **^{13}C NMR** (151 MHz, C_6D_6) δ 166.9, 160.6, 157.0, 152.0, 150.4, 150.2, 141.3, 138.6, 131.2, 128.0, 127.8, 127.7, 127.5, 126.7, 126.4, 126.0, 125.9, 125.5, 123.7, 123.6, 109.0, 61.9, 52.8, 47.2, 47.1, 46.2, 46.2, 42.5, 40.4, 36.4, 36.1, 36.0, 33.4, 31.6, 31.3, 31.3, 29.6, 29.5, 29.4, 29.3, 26.5, 25.3, 24.9, 24.3, 23.9, 22.5, 22.2, 17.3, 13.5, -1.9. **^{31}P NMR** (162 MHz, C_6D_6): δ 65.1. **IR** (neat, cm^{-1}): 755, 1252, 1272, 1476, 1570, 1713. **LC/MS:** m/z calcd. for $C_{64}H_{84}F_4O_3PPdSi$ $[M\text{-}Br]^+$: 1141.4898. Found: 1141.4923

Characterization of Products 2a-2o



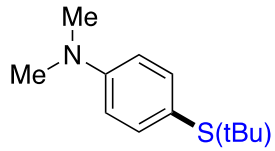
4-(decylthio)-1-methyl-1*H*-indazole (2a)

2a was prepared according to the general procedure for the coupling of alkyl thiols (3 h at rt) using 4-bromo-1-methyl-1*H*-indazole (211 mg, 1.00 mmol), triethylamine (279 µL 2.00 mmol, 2.0 equiv), (249 µL, 1.20 mmol, 1.2 equiv), and **P2** solution in *t*BuOH (1.0 mL, 0.010 mmol, 0.50 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–10% EtOAc in Hexanes, 10 g silica gel) to afford a waxy yellow solid (1st run: 294 mg, 96%, 2nd run: 298 mg, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.31 (d, *J* = 15.6 Hz, 1H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.05 (d, *J* = 7.1 Hz, 1H), 4.06 (s, 3H), 3.05 (t, *J* = 7.4 Hz, 2H), 1.70 (p, *J* = 7.4 Hz, 2H), 1.45 (d, *J* = 7.6 Hz, 2H), 1.36 – 1.25 (m, 12H), 0.90 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.8, 131.8, 130.7, 126.5, 124.1, 119.2, 106.5, 35.7, 33.0, 31.9, 29.6, 29.5, 29.3, 29.2, 28.9, 22.7, 14.2. **IR** (neat, cm^{-1}): 820, 934, 1193, 1200, 1468, 2847, 2913, 2950. **MP:** 31–32°C. **HRMS:** Calculated m/z: 305.205145. Found: 305.2043.



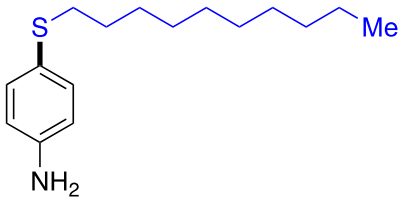
3-((3-(triethoxysilyl)propyl)thio)phenol (2b)

2b was prepared according to the general procedure for the coupling of alkyl thiols (24 h at rt) using 3-bromophenol (173 mg, 1.00 mmol), triethylamine (279 µL 2.00 mmol, 2.00 equiv), 3-(triethoxysilyl)propane-1-thiol (290. µL, 1.20 mmol, 1.20 equiv), and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–10% EtOAc in Hexanes, 10 g silica gel) to afford an off-white oil (1st run: 328 mg, 99%, 2nd run: 318 mg, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.12 (t, *J* = 7.9 Hz, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.80 (t, *J* = 2.0 Hz, 1H), 6.62 (dd, *J* = 8.1, 2.4 Hz, 1H), 5.46 (d, *J* = 2.3 Hz, 1H), 3.81 (q, *J* = 7.0 Hz, 6H), 2.93 (t, *J* = 7.4 Hz, 2H), 1.77 (p, *J* = 7.6 Hz, 2H), 1.21 (t, *J* = 7.0 Hz, 9H), 0.79 (dd, *J* = 9.4, 6.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.0, 138.3, 129.8, 120.8, 115.2, 112.7, 58.5, 35.9, 22.6, 18.2, 9.7. **IR** (neat, cm^{-1}): 685, 770, 955, 2887, 2926, 2974, 3344 (broad). **Elemental Analysis:** C, 54.51; H, 7.93 found: C, 54.65; H, 8.09.



4-(*tert*-butylthio)-*N*,*N*-dimethylaniline (2c)

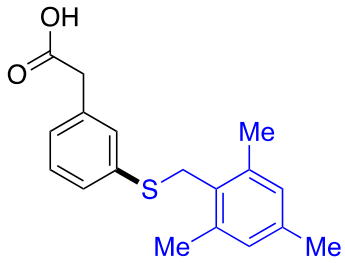
2c was prepared according to the general procedure for the coupling of alkyl thiols (24 h at rt) using 4-bromo-*N*,*N*-dimethylaniline (200. mg, 1.00 mmol), 2-methylpropane-2-thiol (137 µL, 1.20 mmol, 1.2 equiv), triethylamine (279 µL 2.00 mmol, 2.0 equiv), and **P2** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–10% EtOAc in Hexanes, 10 g silica gel) to afford an orange solid (1st run: 206 mg, 98%, 2nd run: 212 mg, 100%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.6 Hz, 2H), 6.56 (d, *J* = 8.4 Hz, 2H), 2.89 (s, 6H), 1.16 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.7, 138.6, 118.0, 112.0, 45.4, 40.3, 30.7. **IR** (neat, cm^{-1}): 817, 1357, 1504, 1589, 2808, 2859, 2894, 2920, 2962. **M.P.**: 78–80°C. **Elemental Analysis:** C, 68.85; H, 9.15 found: C, 69.01; H, 9.22.



4-(decylthio)aniline (2d)

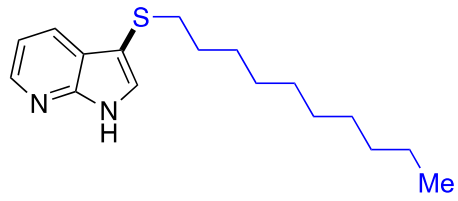
2d was prepared according to the general procedure for the coupling of alkyl thiols (2 h at rt) using 4-bromoaniline (172 mg, 1.00 mmol), triethylamine (279 µL 2.00 mmol, 2.0 equiv), decane-1-thiol (249 µL, 1.20 mmol, 1.2 equiv), and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–10% EtOAc in Hexanes, 10 g silica gel) to afford an orange solid (1st

run: 255 mg, 96%, 2nd run: 259 mg, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 2H), 6.65 – 6.58 (m, 2H), 3.68 (s, 2H), 2.76 (t, *J* = 7.4 Hz, 2H), 1.56 (p, *J* = 7.2 Hz, 2H), 1.38 (q, *J* = 7.1 Hz, 2H), 1.29 (d, *J* = 8.3 Hz, 2H), 1.25 (s, 10H), 0.88 (t, *J* = 6.8 Hz, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.7, 133.7, 123.9, 115.6, 36.4, 31.9, 29.6, 29.6, 29.4, 29.3, 29.2, 28.7, 22.7, 14.2. **IR** (neat, cm^{-1}): 1495, 2848, 2915, 2937, 3347, 3444. **MP:** 38–41°C. **HRMS:** calculated m/z: 266.194247. found: 266.1947



2-(3-((2,4,6-trimethylbenzyl)thio)phenyl)acetic acid (2e)

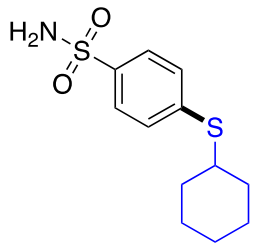
2e was prepared according to the general procedure for the coupling of alkyl thiols (3 h at rt) using 2-(3-bromophenyl)acetic acid compound, triethylamine (446 µL 3.20 mmol, 3.2 equiv), mesitylmethanethiol (200 mg, 1.20 mmol, 1.2 equiv) solubilized in 2 mL THF, and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–15% EtOAc in Hexanes, 10 g silica gel) to afford a white solid (1st run: 274 mg, 91%, 2nd run: 265 mg, 88%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.25 (m, 4H), 7.16 (dt, *J* = 6.8, 1.9 Hz, 1H), 6.87 (s, 2H), 4.16 (s, 2H), 3.66 (s, 2H), 2.37 (s, 6H), 2.28 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.5, 138.2, 137.3, 137.0, 133.9, 130.3, 129.6, 129.1, 129.1, 128.4, 127.2, 40.9, 33.4, 21.0, 19.6. **IR** (neat, cm^{-1}): 1236, 1404, 1692, 2913, 2944, 2996. **MP:** 93–95°C. **Elemental Analysis:** C, 71.30; H, 6.34 found: C, 72.02; H, 6.72.



3-(decylthio)-1*H*-pyrrolo[2,3-*b*]pyridine (2f)

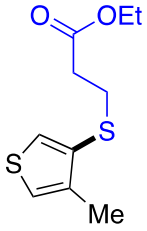
2f was prepared according to the general procedure for the coupling of alkyl thiols (24 h at rt) using 3-bromo-1*H*-pyrrolo[2,3-*b*]pyridine (197 mg, 1.0 mmol), triethylamine (279 µL 2.00 mmol, 2.0 equiv), decane-1-thiol (249 µL, 1.20 mmol, 1.2 equiv), and **P4** stock solution in THF (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–10% EtOAc in Hexanes, 10 g silica gel) to afford an off-white solid (1st run: 267 mg, 92%, 2nd run: 277 mg, 95%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 10.68 (s, 1H), 8.39 (dd, *J* = 4.9, 1.5 Hz, 1H), 8.11 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.51 (d, *J* = 1.9 Hz, 1H), 7.20 (dd, *J* = 7.9, 4.8 Hz, 1H), 2.71 (t, *J* = 7.4 Hz, 2H), 1.57 (q, *J* = 7.3

Hz, 2H), 1.40 (q, J = 7.0 Hz, 2H), 1.30 (q, J = 6.4, 5.7 Hz, 2H), 1.25 (s, 9H), 0.89 (t, J = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.9, 143.3, 130.1, 128.0, 122.4, 116.4, 104.8, 36.7, 31.9, 29.9, 29.6 (2C), 29.3, 29.2, 28.5, 22.7, 14.1. **IR** (neat, cm^{-1}): 720, 815, 1283, 1410, 2846, 2912. **M.P.:** 82–84°C. **Elemental Analysis:** C, 70.30; H, 9.02 found: C, 70.58; H, 9.07.



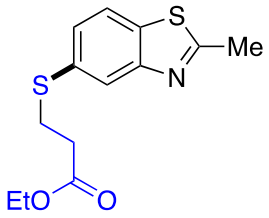
4-(cyclohexylthio)benzenesulfonamide (2g)

2g was prepared according to the general procedure for the coupling of alkyl thiols (24 h at rt) using 4-bromobenzenesulfonamide (236 mg, 1.00 mmol), triethylamine (279 µL 2.00 mmol, 2.0 equiv), cyclohexanethiol (147 µL, 1.20 mmol, 1.2 equiv), and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–20% EtOAc in Hexanes, 10 g silica gel) to afford a yellow solid (1st run: 261 mg, 96%, 2nd run: 252 mg, 93%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 2H), 7.40 (d, J = 8.3 Hz, 2H), 4.88 (d, J = 4.7 Hz, 2H), 3.30 (tt, J = 10.2, 3.7 Hz, 1H), 2.08 – 1.96 (m, 2H), 1.85 – 1.76 (m, 2H), 1.65 (dd, J = 11.2, 4.9 Hz, 1H), 1.50 – 1.17 (m, 5H) **^{13}C NMR** (101 MHz, $CDCl_3$): δ 143.5, 138.5, 128.9, 126.8, 45.2, 33.0, 25.9, 25.6. **IR** (neat, cm^{-1}): 814, 1158, 2852, 2928, 2946, 3262, 3383 **M.P.:** 117–119°C. **Elemental Analysis:** C, 53.11; H, 6.31 found: C, 53.35; H, 6.48.



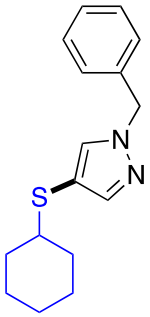
ethyl 3-((4-methylthiophen-3-yl)thio)propanoate (2h)

2h was prepared according to the general procedure for the coupling of alkyl thiols (24 h at rt) using 3-bromo-4-methylthiophene (112 µL, 1.00 mmol), triethylamine (279 µL 2.00 mmol, 2.0 equiv), ethyl 3-mercaptopropanoate (152 µL, 1.20 mmol, 1.2 equiv), and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–10% EtOAc in Hexanes, 10 g silica gel) to afford a colorless oil (1st run: 208 mg, 90%, 2nd run: 199 mg, 86%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.12 (d, J = 3.2 Hz, 1H), 6.91 (dd, J = 3.3, 1.4 Hz, 1H), 4.05 (q, J = 7.2 Hz, 2H), 2.93 (t, J = 7.3 Hz, 2H), 2.51 (t, J = 7.4 Hz, 2H), 2.17 (d, J = 1.1 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.8, 138.8, 130.8, 126.0, 121.7, 60.7, 34.5, 29.7, 14.8, 14.2. **IR** (neat, cm^{-1}): 785, 858, 1177, 1240, 1729, 2935, 2979, 3099. **Elemental Analysis:** C, 52.14; H, 6.13 found: C, 52.41; H, 6.05.



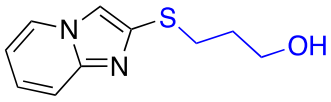
ethyl 3-((2-methylbenzo[*d*]thiazol-5-yl)thio)propanoate (2i)

2i was prepared according to the general procedure for the coupling of alkyl thiols (24 h at rt) using 5-bromo-2-methylbenzo[*d*]thiazole (228 mg, 1.00 mmol), triethylamine (279 µL 2.00 mmol, 2.0 equiv), ethyl 3-mercaptopropanoate (152 µL, 1.20 mmol, 1.2 equiv), and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–15% EtOAc in Hexanes, 25 g silica gel) to afford an off-white oil (1st run: 246 mg, 88%, 2nd run: 259 mg, 92%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, J = 1.7 Hz, 1H), 7.67 (d, J = 8.3 Hz, 1H), 7.30 (dt, J = 8.3, 1.4 Hz, 1H), 4.07 (q, J = 7.1 Hz, 2H), 3.15 (t, J = 7.4 Hz, 2H), 2.77 (d, J = 1.1 Hz, 3H), 2.57 (t, J = 7.4 Hz, 2H), 1.18 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.7, 168.1, 154.0, 134.2, 133.1, 127.3, 123.8, 121.7, 60.8, 34.4, 29.6, 20.2, 14.2. **IR** (neat, cm^{-1}): 1173, 1241, 1370, 1437, 1728, 2928, 2979. **Elemental Analysis:** C, 55.49; H, 5.37 found: C, 55.42; H, 5.55.



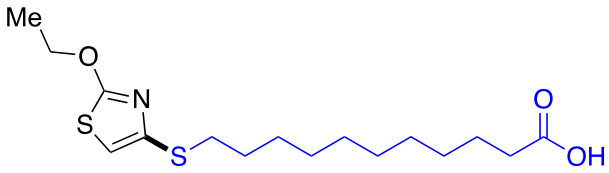
benzyl-4-(cyclohexylthio)-1*H*-pyrazole (2j)

2j was prepared according to the general procedure for the coupling of alkyl thiols (24 h at rt) using 1-benzyl-4-bromo-1*H*-pyrazole (237 mg, 1.00 mmol, triethylamine (279 µL 2.00 mmol, 2.0 equiv), cyclohexanethiol (1.47 µL, 1.20 mmol, 1.2 equiv), and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–10% EtOAc in Hexanes, 10 g silica gel) to afford a yellow, waxy solid (1st run: 267 mg, 98%, 2nd run: 255 mg, 94%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.43 – 7.28 (m, 4H), 7.27 – 7.20 (m, 2H), 5.30 (s, 2H), 2.65 (ddq, J = 11.1, 7.3, 3.7 Hz, 1H), 1.93 (dd, J = 8.5, 4.8 Hz, 2H), 1.77 (hept, J = 6.3 Hz, 2H), 1.60 (dd, J = 10.5, 5.1 Hz, 1H), 1.25 (h, J = 12.2, 11.8 Hz, 5H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.9, 136.1, 134.2, 128.9, 128.2, 127.8, 109.1, 56.3, 47.7, 33.4, 26.1, 25.6. **IR** (neat, cm^{-1}): 634, 694, 716, 981, 1447, 2850, 2926. **MP**: 42–44°C. **Elemental Analysis:** C, 70.55; H, 7.40 found: C, 70.77; H, 7.29.



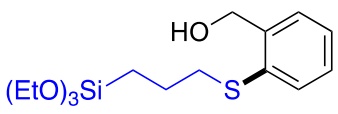
3-(imidazo[1,2-*a*]pyridin-2-ylthio)propan-1-ol (2k)

2k was prepared according to the general procedure for the coupling of alkyl thiols (3 h at rt) using 2-bromoimidazo[1,2-*a*]pyridine (197 mg, 1.00 mmol), triethylamine (279 µL 2.00 mmol, 2.0 equiv), 3-mercaptopropan-1-ol (104 µL, 1.20 mmol, 1.2 equiv), and **P4** stock solution in THF (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The reaction was terminated with 3 mL of water. 100 mg of TCEP was added to the reaction mixture and it was stirred for 15 minutes. The workup was then continued as normal. The product was purified by automated flash column chromatography (50–75% EtOAc in Hexanes, 10 g silica gel) to afford a viscous yellow oil (1st run: 203 mg, 98%, 2nd run: 201 mg, 97%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, J = 6.8 Hz, 1H), 7.47 (d, J = 6.3 Hz, 2H), 7.15 (t, J = 8.0 Hz, 1H), 6.76 (t, J = 6.8 Hz, 1H), 5.42 (s, 1H), 3.83 (t, J = 5.5 Hz, 2H), 3.28 (t, J = 6.4 Hz, 2H), 1.92 (p, J = 5.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.4, 141.7, 124.9, 116.2, 112.6, 110.3, 58.7, 33.5, 29.4. **IR** (neat, cm^{-1}): 700, 1290, 2855, 2927, 2995, 3047, 3137, 3224. **HRMS:** calculated m/z: 209.074859. found: 209.0743



11-((2-ethoxythiazol-4-yl)thio)undecanoic acid (2l)

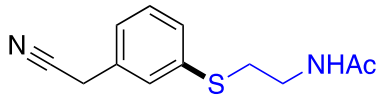
2l was prepared according to the general procedure for the coupling of alkyl thiols (3 h at rt) using 4-bromo-2-ethoxythiazole (208 mg, 1.0 mmol), triethylamine (446 µL 3.20 mmol, 3.2 equiv), 11-mercaptoundecanoic acid (262 mg, 1.20 mmol, 1.2 equiv) solubilized in 2 mL of THF, and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–15% EtOAc in Hexanes, 10 g silica gel) to afford a white solid (1st run: 305.1 mg, 88.3, 2nd run: 300. mg, 87%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.47 (s, 1H), 6.42 – 6.37 (m, 1H), 4.50 – 4.40 (m, 2H), 2.90 (t, J = 7.5 Hz, 2H), 2.33 (t, J = 7.6 Hz, 2H), 1.61 (d, J = 8.5 Hz, 4H), 1.45 – 1.24 (m, 16H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 180.3, 174.0, 142.4, 106.8, 77.4, 77.1, 76.7, 67.9, 34.1, 33.6, 29.4(2C), 29.3, 29.2, 29.1, 29.0, 28.7, 24.7, 14.4. **IR** (neat, cm^{-1}): 1241, 1515, 1697, 2849, 2919, 2941, 2988, 3103. **M.P.:** 56–57°C. **HRMS:** calculated m/z: 346.151062. found: 346.1513.



(2-((3-(triethoxysilyl)propyl)thio)phenyl)methanol (2m)

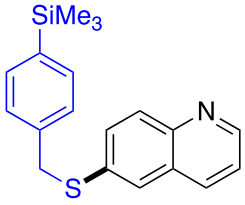
2m was prepared according to the general procedure for the coupling of alkyl thiols (2 h at rt) using (2-bromophenyl)methanol compound

(187 mg, 1.00 mmol), triethylamine (279 µL 2.00 mmol, 2.0 equiv), 3-(triethoxysilyl)propane-1-thiol (290 µL, 1.20 mmol, 1.2 equiv), and **P2** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–10% EtOAc in Hexanes, 10 g silica gel) to afford a yellow oil (1st run: 283 mg, 82%, 2nd run: 268 mg, 78%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 9.6, 7.6 Hz, 2H), 7.31 – 7.17 (m, 2H), 4.78 (s, 2H), 3.81 (q, *J* = 7.0 Hz, 6H), 2.96 (t, *J* = 7.3 Hz, 2H), 1.77 (p, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.0 Hz, 9H), 0.79 (dd, *J* = 9.7, 6.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.7, 134.8, 129.6, 128.2, 128.1, 126.3, 63.6, 58.5, 36.8, 22.8, 18.3, 9.9. **IR** (neat, cm^{-1}): 745, 1070, 1770, 2885, 2925, 2973, 3414. **HRMS:** calculated m/z: 299.113719 (–OEt). found: 299.1125 calculated m/z: 327.145019 (–OH). found: 327.1448



***N*-(2-((3-(cyanomethyl)phenyl)thio)ethyl)acetamide (2n)**

2n was prepared according to the general procedure for the coupling of alkyl thiols (3 h at rt) using 2-(3-bromophenyl)acetonitrile (196 mg, 1.00 equiv), triethylamine (279 µL 2.00 mmol, 2.0 equiv), *N*-(2-mercaptoethyl)acetamide (128 µL, 1.20 mmol, 1.2 equiv) and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (50–75% EtOAc in Hexanes, 10 g silica gel) to afford an orange solid (1st run: 220 mg, 94%, 2nd run: 217 mg, 93%) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (ddt, *J* = 6.4, 4.6, 2.3 Hz, 3H), 7.18 – 7.10 (m, 1H), 6.06 (s, 1H), 3.72 (s, 2H), 3.44 (qd, *J* = 6.4, 2.7 Hz, 2H), 3.07 (td, *J* = 6.6, 2.4 Hz, 2H), 1.94 (d, *J* = 2.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.4, 136.8, 130.9, 129.8, 128.5, 128.5, 128.3, 125.8, 117.6, 38.6, 32.9, 23.5, 23.2. **IR** (neat, cm^{-1}): 1235, 1650, 2917, 2950, 2994, 3307. **M.P.:** 46–47°C. **Elemental Analysis:** C, 61.51; H, 6.02 found: C, 61.66; H, 6.07.

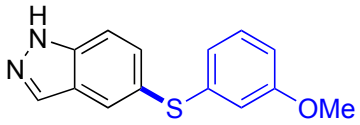


6-((4-(trimethylsilyl)benzyl)thio)quinolone (2o)

2o was prepared according to the general procedure for the coupling of alkyl thiols (2 h at rt) using 6-bromoquinoline (135 µL, 1.00 mmol), triethylamine (279 µL 2.00 mmol, 2.0 equiv), 4-(trimethylsilyl)phenyl)methanethiol (235 µL, 1.20 mmol, 1.2 equiv), and **P4** stock solution in *t*BuOH (2.0 mL, 0.010 mmol, 1.0 mol%, see general procedure for details). The product was purified by automated flash column chromatography (0–10% EtOAc in Hexanes, 25 g silica gel) to afford a yellow solid (1st run: 272

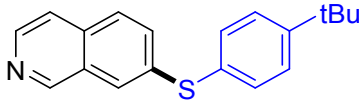
mg, 84%, 2nd run: 267 mg, 83%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.46 (dd, *J* = 4.3, 1.7 Hz, 1H), 7.61 (tt, *J* = 7.3, 1.2 Hz, 2H), 7.28 – 7.21 (m, 2H), 7.07 (d, *J* = 6.3 Hz, 2H), 7.02 – 6.91 (m, 3H), 3.85 (s, 2H), -0.14 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.2, 147.1, 139.8, 137.4, 135.7, 135.2, 133.8, 130.9, 129.9, 128.7, 128.3, 126.4, 121.8, 38.6, -1.0. **IR** (neat, cm^{-1}): 1105, 1239, 1490, 2894, 2951, 3012, 3023. **M.P.:** 91–93°C. **Elemental Analysis:** C, 70.54; H, 6.54 found: C, 70.83; H, 6.65.

Characterization of Products 3a-3l



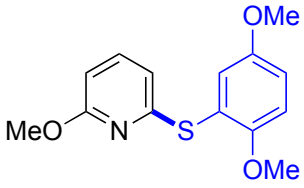
5-((3-methoxyphenyl)thio)-1*H*-indazole (3a)

3a was prepared according to the general procedure for the coupling of aryl thiols using 5-bromo-1*H*-indazole (49.3 mg, 0.25 mmol) and 3-methoxybenzenethiol (37 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash column chromatography (5–15% 3:1 EtOAc/EtOH in Hexanes, 24 g silica gel) to afford a pale orange solid (1st run: 61.4 mg, 96%, 2nd run: 58.4 mg, 91%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.93 (s, 1H), 7.53 – 7.46 (m, 2H), 7.17 (t, *J* = 8.0 Hz, 1H), 6.82 – 6.77 (m, 1H), 6.78 – 6.73 (m, 1H), 6.72 (dd, *J* = 8.2, 2.4 Hz, 1H), 3.73 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.0, 139.6, 139.3, 134.5, 132.5, 129.8, 126.4, 125.8, 124.0, 121.0, 114.2, 111.8, 110.8, 55.2. **HRMS (ESI):** m/z calc'd for $C_{14}H_{13}N_2OS$ $[M+H]^+$: 257.0748, found: 257.0756.



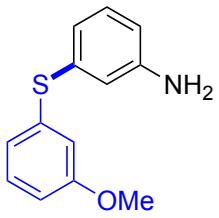
7-((4-(*tert*-butyl)phenyl)thio)isoquinoline (3b)

3b was prepared according to the general procedure for the coupling of aryl thiols using 7-bromoisoquinoline (52.0 mg, 0.25 mmol) and 4-(*tert*-butyl)benzenethiol (52 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash column chromatography (0–15% EtOAc in CH_2Cl_2, 24 g silica gel) to afford an orange oil (1st run: 69.5 mg, 95%, 2nd run: 73.3 mg, 99%). **^{1}H NMR** (600 MHz, $CDCl_3$ δ 9.10 (s, 1H), 8.47 (d, *J* = 5.7 Hz, 1H), 7.77 (s, 1H), 7.72 (d, *J* = 8.6 Hz, 1H), 7.60 (d, *J* = 5.7 Hz, 1H), 7.56 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.41 (s, 4H), 1.34 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 151.7, 151.4, 142.5, 137.3, 134.3, 132.6, 131.9, 129.7, 128.9, 127.1, 126.7, 126.5, 120.4, 34.7, 31.2. **HRMS (ESI):** m/z calc'd for $C_{19}H_{20}NS$ $[M+H]^+$: 294.1316, found: 294.1326.



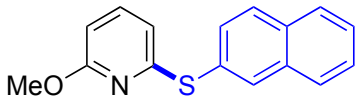
2-((2,5-dimethoxyphenyl)thio)-6-methoxypyridine (3c)

3c was prepared according to the general procedure of aryl thiols using 2-bromo-6-methoxypyridine (47.0 mg, 0.25 mmol) and 2,5-dimethoxybenzenethiol (45 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash chromatogrpahy (60–100% CH_2Cl_2 in Hexanes, 24 g silica gel) to afford a pale yellow oil that solidifies close to ambient temperature (1st run: 65.6 mg, 95%, 2nd run: 64.6 mg, 93%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.8 Hz, 1H), 6.95 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.92 (d, *J* = 9.0 Hz, 1H), 6.45 (d, *J* = 7.5 Hz, 1H), 6.42 (d, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.4, 157.4, 154.1, 153.6, 138.8, 121.8, 119.7, 116.3, 113.3, 112.5, 106.5, 56.6, 55.9, 53.4. **HRMS (ESI):** m/z calc'd for $C_{14}H_{16}NO_3S$ $[M+H]^+$: 278.0851, found: 278.0853.



3-((3-methoxyphenyl)thio)aniline (3d)

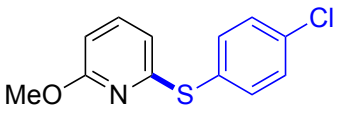
3d was prepared according to the general proceudre for the coupling of aryl thiols using 3-bromoaniline (43.0 mg, 0.25 mmol) and 3-methoxybenzenethiol (37 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash column chromatography (10–100% CH_2Cl_2 in Hexanes, 24 g silica gel) to afford a deep dark green oil (1st run: 48.6 mg, 84%, 2nd run: 49.3 mg, 85%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.21 (t, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 7.9 Hz, 1H), 6.93 (d, *J* = 7.7 Hz, 1H), 6.92 – 6.88 (m, 1H), 6.81 – 6.76 (m, 2H), 6.73 (t, *J* = 1.9 Hz, 1H), 6.64 – 6.60 (m, 1H), 4.02 (br s, 2H), 3.77 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.0, 146.0, 136.9, 136.3, 130.0, 129.9, 123.2, 121.9, 117.8, 116.1, 114.5, 112.9, 55.3. **HRMS (ESI):** m/z calc'd for $C_{13}H_{14}NOS$ $[M+H]^+$: 232.0796, found: 232.0808.



2-methoxy-6-(naphthalen-2-ylthio)pyridine (3e)

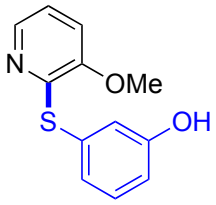
3e was prepared according to the general procedure for the coupling of aryl thiols using 2-bromo-6-methoxypyridine (47.0 mg, 0.25 mmol) and naphthalene-2-thiol (48.0 mg, 0.30 mmol, 1.2 equiv). The product was purified by automated flash chromatography (10–40% CH_2Cl_2 in Hexanes, 24 g silica gel) to afford a pale yellow oil (1st run: 64.4 mg, 96%, 2nd run: 62.7 mg, 93%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.89 – 7.81 (m, 3H), 7.63 (dd,

J = 8.5, 1.7 Hz, 1H), 7.57 – 7.50 (m, 2H), 7.33 (t, J = 7.9 Hz, 1H), 6.51 (d, J = 7.6 Hz, 1H), 6.45 (d, J = 8.1 Hz, 1H), 3.82 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.6, 158.2, 139.0, 134.5, 133.8, 133.1, 131.8, 128.8, 128.4, 127.8, 127.7, 126.9, 126.6, 113.8, 106.8, 53.5. **HRMS (ESI):** m/z calc'd for $C_{16}H_{14}NOS$ $[M+H]^+$: 268.0796, found: 268.0802.



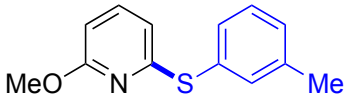
2-((4-chlorophenyl)thio)-6-methoxypyridine (3f)

3f was prepared according to the general procedure for the coupling of aryl thiols using 2-bromo-6-methoxypyridine (47.0 mg, 0.25 mmol) and 4-chlorobenzenethiol (43.4 mg, 0.30 mmol, 1.2 equiv). The product was purified by automated flash chromatography (10–40% CH_2Cl_2 in Hexanes, 24 g silica gel) to afford a pale orange oil (1st run: 58.5 mg, 93%, 2nd run: 60.6 mg, 96%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.55 – 7.51 (m, 2H), 7.40 – 7.35 (m, 3H), 6.53 (d, J = 7.5 Hz, 1H), 6.46 (d, J = 8.1 Hz, 1H), 3.80 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.6, 157.2, 139.0, 136.3, 135.1, 129.7, 129.4, 113.8, 107.0, 53.5. **HRMS (ESI):** m/z calc'd for $C_{12}H_{11}ClNOS$ $[M+H]^+$: 252.0250, found: 252.0262.



3-((3-methoxypyridin-2-yl)thio)phenol (3g)

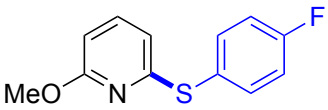
3g was prepared according to the general procedure for the coupling of aryl thiols using 2-bromo-3-methoxypyridine (47.0 mg, 0.25 mmol) and 3-mercaptophenol (31 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash column chromatography (0–10% EtOAc in CH_2Cl_2, 24 g silica gel) to afford an off-white solid (1st run: 46.1 mg, 79%, 2nd run: 48.2 mg, 82%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.42 (br s, 1H), 7.96 (dd, J = 4.5, 1.5 Hz, 1H), 7.25 (t, J = 7.9 Hz, 1H), 7.11 – 6.99 (m, 3H), 6.83 (s, 1H), 6.72 (dd, J = 8.2, 1.9 Hz, 1H), 3.95 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.3, 151.8, 150.2, 140.7, 130.5, 128.2, 126.8, 123.4, 120.7, 117.6, 116.2, 55.9. **HRMS (ESI):** m/z calc'd for $C_{12}H_{12}NO_2S$ $[M+H]^+$: 234.0588, found: 234.0600.



2-methoxy-6-(*m*-tolylthio)pyridine (3h)

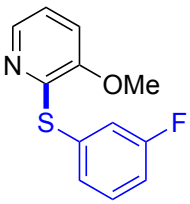
3h was prepared according to the general procedure of aryl thiols using 2-bromo-6-methoxypyridine (47.0 mg, 0.25 mmol) and 3-methylbenzenethiol (36 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash chromatography (10–30% CH_2Cl_2

in Hexanes, 24 g silica gel) to afford a pale orange oil (1st run: 50.3 mg, 87%, 2nd run: 50.1 mg, 87%). **^{1}H NMR** (600 MHz, $CDCl_3$ δ 7.45 (s, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 6.46 (d, *J* = 7.5 Hz, 1H), 6.43 (d, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 2.37 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.5, 158.6, 139.2, 138.9, 135.7, 132.2, 130.6, 129.8, 129.1, 113.4, 106.5, 53.5, 21.2. **HRMS (ESI):** m/z calc'd $C_{13}H_{14}NOS$ $[M+H]^+$: 232.0796, found: 232.0802.



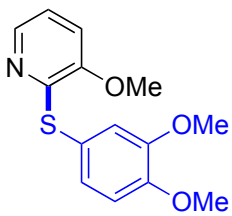
2-((4-fluorophenyl)thio)-6-methoxypyridine (3i)

3i was prepared according to the general procedure of aryl thiols using 2-bromo-6-methoxypyridine (47.0 mg, 0.25 mmol) and 4-fluorobenzenethiol (32 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash chromatography (10–40% CH_2Cl_2 in Hexanes, 24 g silica gel) to afford an pale yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.63 – 7.56 (m, 2H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.15 – 7.08 (m, 2H), 6.46 (d, *J* = 7.5 Hz, 1H), 6.43 (d, *J* = 8.2 Hz, 1H), 3.79 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.5, 163.3 (d, *J* = 249.6 Hz), 158.0, 139.0, 137.5 (d, *J* = 8.4 Hz), 126.1 (d, *J* = 3.4 Hz), 116.4 (d, *J* = 21.9 Hz), 113.2, 106.7, 53.4. **HRMS (ESI):** m/z calc'd for $C_{12}H_{11}FNOS$ $[M+H]^+$: 236.0545, found: 236.0555.



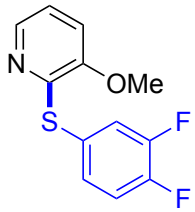
2-((3-fluorophenyl)thio)-3-methoxypyridine (3j)

3j was prepared according to the general procedure of aryl thiols using 2-bromo-3-methoxypyridine (47.0 mg, 0.25 mmol) and 3-fluorobenzenethiol (25 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash chromatography (40–70% CH_2Cl_2 in Hexanes, 24 g silica gel) to afford an off-white solid (1st run: 52.4 mg, 88%, 2nd run: 50.6 mg, 86%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 4.1, 1.9 Hz, 1H), 7.38 – 7.29 (m, 2H), 7.30 – 7.25 (m, 1H), 7.10 – 7.01 (m, 3H), 3.92 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.6 (d, *J* = 248.1 Hz), 152.3, 147.4, 141.4, 132.7 (d, *J* = 8.3 Hz), 130.0 (d, *J* = 8.4 Hz), 129.9 (d, *J* = 2.7 Hz), 121.17, 121.15 (d, *J* = 22.2 Hz), 116.3, 115.4 (d, *J* = 21.0 Hz), 55.8. **HRMS (ESI):** m/z calc'd for $C_{12}H_{11}FNOS$ $[M+H]^+$: 236.0545, found: 236.0546.



2-((3,4-dimethoxyphenyl)thio)-3-methoxypyridine (3k)

3k was prepared according to the general procedure for the coupling of aryl thiols using 2-bromo-3-methoxypyridine (47.0 mg, 0.25 mmol) and 3,4-dimethoxybenzenethiol (43 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash chromatography (0–5% EtOAc in CH_2Cl_2, 24 g silica gel) to afford an off-white solid (1st run: 65.2 mg, 94%, 2nd run: 65.5 mg, 94%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 4.6, 1.4 Hz, 1H), 7.17 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.08 (d, *J* = 2.0 Hz, 1H), 7.02 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.99 (dd, *J* = 8.1, 4.6 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.86 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 151.7, 149.7, 149.4, 149.0, 141.4, 128.5, 120.3, 120.2, 118.5, 115.6, 111.5, 55.9, 55.8, 55.7. **HRMS (ESI):** m/z calc'd for $C_{14}H_{16}NO_3S$ $[M+H]^+$: 278.0851, found: 278.0864.



2-((3,4-difluorophenyl)thio)-3-methoxypyridine (3l)

3l was prepared according to the general procedure of aryl thiols using 2-bromo-3-methoxypyridine (47.0 mg, 0.25 mmol) and 3,4-difluorobenzenethiol (33 µL, 0.30 mmol, 1.2 equiv). The product was purified by automated flash chromatography (40–70% CH_2Cl_2 in Hexanes, 24 g silica gel) to afford an off-white solid (1st run: 59.2 mg, 93%, 2nd run: 58.9 mg, 93%, 3rd run: 61.7 mg, 97%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 4.2, 1.9 Hz, 1H), 7.40 (ddd, *J* = 10.0, 7.5, 2.1 Hz, 1H), 7.29 (ddt, *J* = 8.0, 3.9, 1.8 Hz, 1H), 7.18 (dt, *J* = 10.2, 8.4 Hz, 1H), 7.08 – 7.03 (m, 2H), 3.93 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 152.0, 150.8 (dd, *J* = 250.2, 12.5 Hz), 150.2 (dd, *J* = 250.3, 12.8 Hz), 147.7, 141.3, 131.4 (dd, *J* = 6.5, 3.4 Hz), 126.3 (dd, *J* = 6.2, 4.3 Hz), 124.1 (d, *J* = 17.7 Hz), 121.0, 117.6 (d, *J* = 17.7 Hz), 116.1, 55.8. **HRMS (ESI):** m/z calc'd for $C_{12}H_{10}F_2NOS$ $[M+H]^+$: 254.0451, found: 254.0458.

Supporting Information References

1. Sather, A. C.; Lee, H. G.; De La Rosa, V. Y.; Yang, Y.; Müller, P.; Buchwald, S. L. A Fluorinated Ligand Enables Room-Temperature and Regioselective Pd-Catalyzed Fluorination of Aryl Triflates and Bromides. *J. Am. Chem. Soc.* **2015**, *137*, 13433–13438.
2. Ingoglia, B. T.; Buchwald, S. L. Oxidative Addition Complexes as Precatalysts for Cross-Coupling Reactions Requiring Extremely Bulky Biarylphosphine Ligands. *Org. Lett.* **2017**, *19*, 2853–2856.