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Screening of Homogeneous Catalysts by Fluorescence Resonance Energy Transfer. Identification of Catalysts for Room Temperature Heck Reactions.

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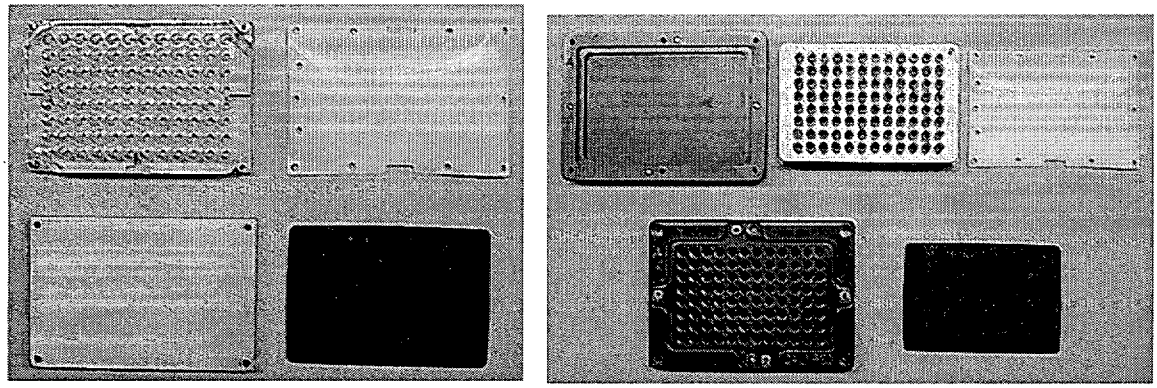
Supporting Information

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 400 MHz Spectrometer, General Electric QE 300 MHz spectrometer, or a General Electric Omega 500 spectrometer with tetramethylsilane or residual protiated solvent used as a reference. Elemental analyses were performed by Robertson Microlabs, Inc., Madison, NJ. Fluorescence measurements were recorded on a Packard Fluorocount Spectrometer. Pictures and dimensions of the aluminum blocks are shown below. The Teflon sheet and glass plate were purchased through Spike International, Wilmington, NC. The rubber gasket is a Viton material purchased from Robbins Scientific Inc., California. The aluminum components of the reaction blocks were constructed by the Gibbs Machine Shop at Yale University. The Calypso aluminum block holder shown on the top and bottom left of the right panel picture below, was purchased from Charybdis Technologies Inc., Carlsbad, California. Chromatographic purifications were performed by flash chromatography[1] using silica gel (200-400 mesh) from Natland International Corporation. Yields for final product in Table 1 refer to isolated yields of compounds of greater than 95% purity, as determined by ^{1}H-NMR and capillary gas chromatography (GC). All ^{31}P and ^{13}C NMR spectra were proton decoupled. GC analyses were performed on a HP-5890 series II instrument equipped with an HP3395 intelligent recorder. GC/MS spectra were recorded on a HP5890 instrument equipped with a HP5971A Mass Spectral Analyzer. Both GC and GC/MS were performed using a HP-1 methyl silicone column. Yields reported in Table 1 are an average of two runs. Methyl acrylate, 2-bromoanisole, 4-bromoanisole, 4-bromotoluene, 1-bromonapthalene, 4-bromobenzotrifluoride, bromobenzene, and 2-(3-bromophenyl)-1,3-dioxolane were purchased from Aldrich and used without further purification. Dioxane and dimethylformamide were purchased as anhydrous grade and stored in a drybox. Propyl methyl ketone and butyronitrile were purchased from Aldrich and degassed before use. Triethylamine was purchased from Aldrich and dried over molecular sieves before use. Ether, toluene,

tetrahydrofuran, benzene, and pentane were distilled from sodium/benzophenone. $CpPd(allyl)^2$ and $Pd(dba)_2$[3] were prepared according to literature procedures.

All phosphines not discussed below were commercially available. The following ligands (according to numbering scheme of the assay) were prepared using literature procedures or slightly modified variations: 19, 23, 28, 30, 31, 32, 78, and 79;[4] 38, 39, 40, 54, 73, and 74,[5] 44, 65, 71 and 75,[6] 41,[7] 42,[8] 50,[9] 57,[10] 58,[11] 61,[12] 69,[13] 70,[14] 72,[15] and 88-90[16]. All other ligand syntheses are described below.

Reaction Blocks used for the First and Second Screens.



Left Panel Right Panel

The left panel depicts the materials used in the first screen of catalysts. The right panel shows the materials used in the second screen of catalysts with different solvents. Both systems are shown unassembled. The aluminum block below the glass plate in the left panel is 127 mm x 85 mm x 3 mm. It has a female screw adapter in each corner that are 14 mm in length. The aluminum block in the bottom left corner of the left panel is 127 mm x 85 mm x 15 mm. After addition of reagents to the block, Teflon sheet was placed over the plate, followed by the rubber gasket and then the top aluminum plate. The bolts were then tightened with 11 in lbs of force using a torque wrench. In the right panel, the aluminum block in the middle of the top row is 127 mm x 85 mm x 33 mm. It has 96 holes that are 7 mm in diameter and 30 mm in depth, into which were placed 96 vials of dimension 7 x 40 mm. The Teflon sheet and rubber gasket were place on top of the vials, and the system was sealed with the top plate of the Calypso apparatus. The bolts were tightened to 11 in lbs with a torque wrench.

General Procedure for Preparation of Biphenyl Ligands 1-5, 7-8, and 12-16. Reactions were typically conducted in parallel using up to four Grignard reagents. In a dry box a 100 mL round bottom flask was charged with 750 mg (2.7 mmol) of chlorophosphine **103**, 51 mg of CuI (0.27 mmol), 47 mg of LiBr (0.54 mmol) and 25-30 mL of THF. The mixture was sealed with a 14/20

septum and placed under N_2 in a fume hood and then cooled to -78 °C using a dry ice/acetone bath. To this mixture was added 1.5 equiv of a solution of a Grignard reagent. Grignard reagents used for ligands **14** - **16** were prepared using known methods from their respective aryl bromides. After 1 h the mixture was warmed to 0 °C and maintained at that temperature for 2 h. The reaction was then allowed to warm to room temperature and, after stirring overnight, the mixture was quenched with degassed H_2O (5 mL) and placed in a separatory funnel with 100 mL of Et_2O. The organic layer was treated with degassed NH_4OH (2-3 x 30mL), degassed brine, and then dried over Na_2SO_4. After evaporation of solvent, the crude solid was recrystallized from degassed hot MeOH to afford a phosphine that was at least 95% pure, as judged by ^1H and ^{31}P NMR spectroscopy.

2-(*tert*-Butylmethylphosphino)biphenyl (1). Prepared from **103** according to the general procedure to afford a white powder (47%): ^1H NMR ($CDCl_3$, 500 MHz) δ 0.93 (d, 9H, J = 11.5), 1.16 (br s, 3H), 7.17 (d, 1H, J = 7.7), 7.29 (d, 1H, J = 6.7), 7.33-7.39 (m, 6H), 7.72 (br t, 1H, J = 10.0); ^{31}P NMR ($CDCl_3$, 202 MHz) δ -8.38; MS *m/z* (relative, %): 256 (M+, 15).

2-(*tert*-Butyl-*n*-butylphosphino)biphenyl (2). Prepared from **103** according to the general procedure to afford (72%): ^1H NMR (C_6D_6, 500 MHz) δ 0.85 (d, 9H, J = 11.7), 0.94 (t, 3H, J = 7.1) 1.47 (m, 2H), 1.64 (br m, 2H), 2.00 (m, 2H), 7.33-7.43 (m, 8H), 7.61 (m, 1H); ^{31}P NMR (C_6D_6, 202 MHz) δ -13.07; MS *m/z* (relative intensity, %): 298 (M+, 75).

2-(*tert*-Butylbenzylphosphino)biphenyl (3). Prepared from **103** according to the general procedure to afford a white solid (78%): ^1H NMR ($CDCl_3$, 500 MHz) δ 0.93 (d, 9H, J = 11.0), 3.10 (unresolved d, 1H), 3.33 (d, 1H, J = 13.1), 7.23 (m, 8H), 7.84 (d, 1H, J = 6.8); ^{31}P NMR ($CDCl_3$, 202 MHz) δ -5.02; MS *m/z* (relative intensity, %): 332 (M+, 28).

2-(*tert*-Butylcyclohexylphosphino)biphenyl (4). Prepared from **103** according to the general procedure to afford white crystals (79%): ^1H NMR (C_6D_6, 500 MHz) δ 0.94 (d, 9H, J = 8.9), 1.30 (br s, 3H), 1.43 (br m, 2H), 1.60 (br s, 1H), 1.73 (br s, 2H), 1.84 (br s, 1H), 2.02 (br s, 1H), 2.22 (br s, 1H), 7.32 (br s, 3H), 7.40 (br s, 5H), 7.72 (br s, 1H); ^{31}P NMR (C_6D_6, 202 MHz) δ 0.66; MS *m/z* (relative intensity, %): 323 (M+, 40).

2-(*tert*-Butyl-*iso*-propylphosphino)biphenyl (5). Prepared from **103** according to the general procedure to afford small white crystals (49%): ^1H NMR ($CDCl_3$, 500 MHz) δ 1.07 (d, 9H, J = 14.0), 1.23 (dd, 3H, J = 13.0, 7.0), 1.52 (dd, 3H, J = 16.0, 7.0) 2.72 (sept, 1H, J = 7.0), 7.30 -

7.81 (m, 9H); ^{31}P NMR ($CDCl_3$, 202 MHz) δ -0.52; MS *m/z* (relative intensity, %): 284 (M+, 19).

2-(*tert*-Butyl-2-methyl-2-phenylpropylphosphino)biphenyl (7). Prepared from **103** according to the general procedure to afford a fine white powder (40%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.00 (d, 9H, *J* = 14.7), 1.44 (s, 3H), 1.71 (s, 3H), 2.26 (dd, 1H, *J* = 14.8, 5.6), 2.89 (unresolved dd, 1H), 5.64 (br s, 1H), 7.06 (d, 1H, *J* = 7.5), 7.14 (dd, 1H, *J* = 6.8, 5.2), 7.23-7.49 (m, 10H), 7.68 (t, 1H, *J* = 6.9); ^{31}P NMR ($CDCl_3$, 202 MHz) δ -6.70; MS *m/z* (relative intensity, %): 374 (M+, 4).

2-(*tert*-Butyltrimethyl-silanylmethylphosphino)biphenyl (8). Prepared from **103** according to the general procedure to afford large off-white crystals (74%): ^{1}H NMR (C_6D_6, 400 MHz) δ -0.00 (s, 9H), 0.53 (dd, 1H, *J* = 13.6, 2.8), 0.77 (d, 9H, *J* = 12.4), 1.20 (dd, 1H, *J* = 13.6, 1.2), 7.10 (m, 3H), 7.21 (app t, 3H, *J* = 7.6), 7.46 (m, 3H); ^{31}P NMR (C_6D_6, 202 MHz) δ -21.2; MS (EI, 70 eV) *m/z* (relative intensity, %): 328 (M+, 75).

2-(Di-*iso*-propylphosphino)biphenyl (9). 2-Bromobiphenyl (1.5 g, 6.44 mmol) was lithiated with *n*-BuLi (2.83 mL, 2.5 M, 7.08 mmol) as described in the procedure for preparation for chlorophosphine **103**. To the resulting solution containing aryl lithium at -78 °C was added chlorodiisopropylphosphine (1.28 g, 1.30 mL, 8.37 mmol) via syringe in one portion. The mixture was warmed to room temperature and allowed to stir overnight. The solvent was evaporated under vacuum and the crude residue partitioned between Et_2O (150 mL) and degassed H_2O (75 mL). The layers were separated, and the organic layer washed with brine and dried over Na_2SO_4. Evaporation of solvent and subsequent recrystallization of the crude product from hot MeOH afforded 1.71 g of small white crystals (98%): mp 62–3 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.98 (dd, 6H, *J* = 11.6, 6.7), 1.07 (dd, 6H, *J* = 14.5, 6.7), 2.11 (overlapping sept, 2H, *J* = 7.0), 7.41 (m, 8H), 7.65 (m, 1H); ^{31}P NMR ($CDCl_3$, 202 MHz) δ -4.20; MS *m/z* (relative intensity, %): 270 (M+, 30); Anal. calcd. for $C_{18}H_{23}P$: C, 79.97; H, 8.58. Found: C, 79.80; H, 8.55.

2-(*tert*-Butylphenylphosphino)biphenyl (12). Prepared from **103** according to the general procedure to afford the title compound as a pale yellow solid (90%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.14 (d, 9H, *J* = 13.5), 7.17-7.41 (m, 13H), 7.77 (m, 1H); ^{31}P NMR ($CDCl_3$, 202 MHz) δ 6.70; MS *m/z* (relative intensity, %): 318 (M+, 6).

2-(*tert*-Butyl-*ortho*-tolylphosphino)biphenyl (13). Prepared from **103** according to the general procedure to afford an oil which crystallized upon standing (78%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.18 (d, 9H, J = 11.8), 2.11 (s, 3H), 6.97-7.34 (m, 12H), 7.76 (m, 1H); ^{31}P NMR ($CDCl_3$, 202 MHz) δ -5.24; MS *m/z* (relative intensity, %): 332 (M+, 15).

2-(*tert*-Butyl-4-methoxyphenylphosphino)biphenyl (14). Prepared from **103** according to the general procedure to afford small off-white crystals (89%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.10 (d, 9H, J = 12.4), 3.80 (s, 3H), 6.78 (d, 2H, J = 7.8), 7.11-7.40 (m, 10H), 7.80 (d, 1H, J = 7.0); ^{31}P NMR ($CDCl_3$, 202 MHz) δ 5.02; MS *m/z* (relative intensity, %): 348 (M+, 7).

2-(*tert*-Butyl-4-trifluoromethylphenylphosphino)biphenyl (15). Prepared from **103** according to the general procedure to afford light reddish-orange crystals (79%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.35 (d, 9H, J = 14.7), 7.14-7.49 (m, 12H), 7.73 (br s, 1H); ^{31}P NMR ($CDCl_3$, 202 MHz) δ 7.68; MS *m/z* (relative intensity, %): 386 (M+, 5).

Bis-biphenyl-2-yl-tert-butyl-phosphane (16). Prepared from **103** according to the general procedure to afford small white crystals (40%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.93 (d, 9H, J = 12.8), 6.77 (d, 2H, J = 6.1), 7.13-7.36 (m, 14H), 7.59 (d, 2H, J = 7.3); ^{31}P NMR ($CDCl_3$, 202 MHz) δ -4.32; MS *m/z* (relative intensity, %): 394 (M+, 5).

1-Adamantyl-di(*tert*)-butyl phosphane (53). In a drybox, 0.520 g (2.88 mmol) of $ClP(t\text{-}Bu)_2$, 53 mg (0.28 mmol) of copper(I) iodide, 48 mg (0.56 mmol) of lithium bromide and 10 mL of ether were combined in a Schlenk flask, removed from the dry box and put under nitrogen. The flask was stirred and cooled to 0 °C while 12 mL of a 0.48 M solution of 1-adamantyl-magnesium bromide[17] was added dropwise from a cannula. The reaction mixture immediately turned purple. The reaction was removed from the ice bath and stirred for 17 h at room temperature. The solvent was evaporated under vacuum, and the residue was dissolved in benzene and filtered through a pad of Celite. The filtrate was collected, and the benzene was removed under vacuum . Distillation of the solid residue (159-165 °C, 1 Torr) under a nitrogen atmosphere afforded 0.696 g (86.4%) of a a white solid. ^{1}H NMR (400 MHz, C_6D_6): δ 1.32 (d, J = 9.6 Hz, 18H), 1.66 (br, 6H), 1.86 (br, 3H), 2.14 (br, 6H). ^{31}P NMR (202 MHz, C_6D_6): δ 63.0. Anal. Calcd. for $C_{18}H_{33}P$: C: 77.09, H: 11.86. Found: C: 77.09, H: 11.77.

Di-(1-adamantyl)-*tert*-butyl phosphane (55). In a drybox, a 250 mL 2-neck round bottom flask was charged with $Cl_2P(t\text{-}Bu)$ (1.831g, 11.52 mmol), CuI (240 mg, 1.26 mmol), LiBr (218 mg, 2.52 mmol) and 25 mL of ether. The flask was sealed with a septum and removed from the

drybox and attached to a nitrogen line. The septum was replaced by a condenser, and the reaction was cooled to 0 °C. Previously prepared 1-AdMgBr,[17] (58 mL of a 0.48 M solution, 28 mmol) was added dropwise through the septum by canula, while stirring the reaction. A white precipitate formed immediately, and the solution changed from clear to yellow. The reaction was heated at 35 °C for 20 h. The ether was evaporated on a vacuum line. The remaining yellow residue was dissolved in THF, stirred, and cooled to 0 °C. BH_3 in THF (12 mL of a 1.5 M solution, 18 mmol) was added slowly to the reaction by syringe. After complete addition of the borane, the reaction was stirred for 1 h at room temperature. Any excess borane was quenched with MeOH. The remaining solvent was evaporated on a vacuum line. The crude residue was adsorbed onto a SiO_2 plug. The product was isolated by first eluting with hexanes (125 mL) to remove nonpolar impurities and then eluting with CH_2Cl_2 (200 mL). Evaporation of CH_2Cl_2 left a white solid, which was dissolved in degassed morpholine (approx. 30 mL/200 mg) and heated at 110 °C for 1 h. All volatile materials were then evaporated on a vacuum line. The crude mixture was brought into the drybox, dissolved in pentane, and filtered through a SiO_2 plug. Evaporation of pentane gave 1.25 g (30.3% yield) of a white solid. ^{1}H NMR (300 MHz, C_6D_6): δ 1.39 (d, J = 10.8 Hz, 9H), 1.69 (br m, 12H), 1.89 (br s, 6H), 2.24 (br s, 12 H) ppm. ^{31}P NMR (202 MHz, C_6D_6): δ 62.4 ppm. MS *m/z* (relative intensity, %): 358 (M^+, 8).

2-Adamantyl-di(*tert*)-butyl phosphane (56). Ligand **56** was prepared in a manner similar to compound **53**. ^{1}H{^{31}P} (400 MHz, C_6D_6): δ 1.19 (s, 18H), 1.53-1.56 (br, 2H), 1.72-1.93 (m, 8H), 2.23-2.25 (br d, 3H), 2.57-2.60 (br d, 2H). ^{31}P NMR (202 MHz, C_6D_6): δ 32.6 ppm. MS *m/z* (relative intensity, %): 280 (M^+, 4).

Di-(*tert*)-butoxy-*tert*-butyl phosphane (62). In a drybox, sodium *tert*-butoxide (0.875 g, 9.10 mmol) was added to 20 mL of THF. While stirring, Cl_2P(*t*-Bu) (0.690 g, 4.34 mmol) was added slowly over a period of 1 min. The reaction was stirred for 1.5 hr. The solvent was evaporated, and the crude residue was dissolve in toluene and filtered through a Celite pad. Evaporation of toluene gave a light yellow oil in 28% yield. ^{1}H NMR (300 MHz, C_6D_6): δ 1.08 (d, J = 12.9 Hz, 9H), 1.28 (s, 18H). ^{31}P NMR (202 MHz, C_6D_6): δ 150.9.

3,3'-Di-*tert*-butyl-5,5'-dimethoxybiphenyl-2,2'-diyl-*tert*-butylphosphoramidite (63). 28% yield of an off-white solid was prepared by modifying the procedure used to make ligand **61**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.16 (d, J = 12.0 Hz, 9H), 1.45 (s, 18H), 3.81 (s, 6H), 6.67 (br s, 2H), 6.96 (br s, 2H). ^{31}P NMR (202 MHz, $CDCl_3$): δ 202.2. MS *m/z* (relative intensity, %): 444 (M^+, 6).

General procedure for the Synthesis of Ligands 66-68. Under inert conditions, 0.859 g (21.4 mmol) of KH was suspended in 25 mL of THF, and the stirred mixture was cooled at 0 °C. Indole (2.44 g, 20.8 mmol) was added to the suspension, and the reaction was stirred for 10 min at 0 °C and 1 h at room temperature. $Cl_2P(t\text{-Bu})$ (0.668 g, 4.20 mmol) was dissolved in 5 mL of THF and added by syringe to the reaction. The reaction was stirred for 12 h. The solvents were evaporated at this time, and the crude residue was dissolved in toluene and filtered through a Celite pad. The toluene was evaporated to give a crude solid, which was recrystallized from pentane at –35 °C.

Bis-diisopropylamido-*tert*-butyl phosphane (66). 48% Yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.04-1.30 (br m, 33H), 3.36 (sept, 4H). ^{31}P NMR (202 MHz, $CDCl_3$): δ 45.1 ppm.

Bis-diindolyl-*tert*-butyl phosphane (67). 27% Yield. ^{1}H NMR (500 MHz, CD_2Cl_2): δ 1.32 (d, J = 16.5 Hz, 9H), 6.72 (d, J = 3.2 Hz, 2H), 7.15 (dd, J = 7.1, 7.6 Hz, 2H), 7.24 (dd, J = 7.0, 7.6 Hz, 2H), 7.58 (d, J = 7.4 Hz, 2H), 7.60 (d, J = 2.5 Hz, 2H), 7.92 (d, J = 7.8 Hz, 2H). ^{31}P NMR (202 MHz, CD_2Cl_2): δ 63.2. MS *m/z* (relative intensity, %): 320 (M^+, 4).

Bis-diphenylamido-*tert*-butyl phopshine(68). 55% Yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.95 (d, J = 14.8 Hz, 9H), 6.96 (d, J = 7.9 Hz, 8H), 7.05 (t, J = 7.2 Hz, 8H), 7.21 (dd, J = 7.8, 8.5 Hz, 4H). ^{31}P NMR: (202 MHz, $CDCl_3$) δ 97.2. MS *m/z* (relative intensity, %): 424 (M^+, 6).

General Procedure for Preparation of Ferrocene Ligands 80-87. In a dry box a 100 mL round bottom flask was charged with 1.00 g (3.24 mmol, corrected for 10% tin by-product) of chlorophosphine **104**, 54 mg of CuI (0.32 mmol), 56 mg of LiBr (0.65 mmol) and 35 mL of THF. The reaction was sealed with a 14/20 septum, placed under N_2, and cooled to -78 °C using a dry ice/acetone bath. To this mixture was added 1.5 equiv of a solution of Grignard reagent. Grignard reagents used to prepare ligands **84-87** were generated using standard methods from the respective aryl bromides. After 1 h the mixture was warmed to 0 °C and maintained at that temperature for 2 h. The reaction was then allowed to warm to room temperature, and after stirring overnight, the mixture was quenched with degassed H_2O (5 mL) and placed into a separatory funnel containing 100 mL of Et_2O. The organic layer was treated with degassed NH_4OH (2-3 x 30 mL), followed by degassed brine, and dried over Na_2SO_4. After solvent evaporation the crude solid was brought into a dry box. Elution over silica gel using pentane removed small amounts of $(n\text{-Bu})_4Sn$ contained in the product from the chlorophoshine preparation. The product was then eluted with 1-2% Et_2O/pentane. In some cases, product purity was inadequate after chromatography, and a subsequent recrystallization at –35 °C from

pentane was performed to provide phosphine that was judged to be >95% pure by both ^{1}H and ^{31}P NMR spectroscopy.

1-(*tert*-Butylcyclohexylphosphino)ferrocene (80). Prepared from **104** according to the general procedure to afford a dark orange powder (42%): ^{1}H NMR (C_6D_6, 400 MHz) δ 1.20 (d, 9H, J = 11.2), 1.32 (sext of t, 3H, J = 12.4, 3.2), 1.62 (sext of t, 2H, J = 12.8, 3.2), 1.76 (br d, 1H, J = 10.0), 1.88 (br s, 2H), 2.04 (br td, 1H, J = 11.9, 2.4), 2.22 (br d, 1H, J = 11.2), 2.45 (br d, 1H, J = 10.4), 4.20-4.22 (m, 7H), 4.39 (br s, 2H); ^{31}P NMR (C_6D_6, 202 MHz) δ 12.92; MS (EI, 70 eV) *m/z* (relative intensity, %): 356 (M+, 20).

1-(*tert*-Butyl-*ortho*-tolylphosphino)ferrocene (81). Prepared from **104** according to the general procedure to afford large red crystals (37%): ^{1}H NMR (C_6D_6, 400 MHz) δ 1.22 (d, 9H, J = 12.1), 2.89 (s, 3H), 4.02 (s, 5H), 4.22 (s, 1H), 4.22 (s, 1H), 4.24 (s, 1H), 4.35 (s, 1H), 7.21 (m, 2H), 7.27 (m, 1H), 7.75 (d, 1H, J = 7.1); ^{31}P NMR (C_6D_6, 121 MHz) δ -10.07; MS (EI, 70 eV) *m/z* (relative intensity, %): 365 (M+, 60).

1-(*tert*-Butylbenzylphosphino)ferrocene (82). Prepared from **104** according to the general procedure to afford small yellow crystals (30%): ^{1}H NMR (C_6D_6, 500 MHz) δ 0.83 (d, 9H, J = 11.3), 2.91 (dd, 1H, J = 14.4, 2.5), 3.13 (dd, 1H, J = 14.4, 2.4), 3.80 (s, 5H), 3.92 (s, 1H), 3.98 (d, 2H, J = 6.1), 4.18 (s, 1H), 6.96 (t, 1H, J = 7.3), 7.12 (t, 2H, J = 7.6), 7.42 (d, 2H, J = 7.7); ^{31}P NMR (C_6D_6, 202 MHz) δ 1.18; MS (EI, 70 eV) *m/z* (relative intensity, %): 364 (M+, 51).

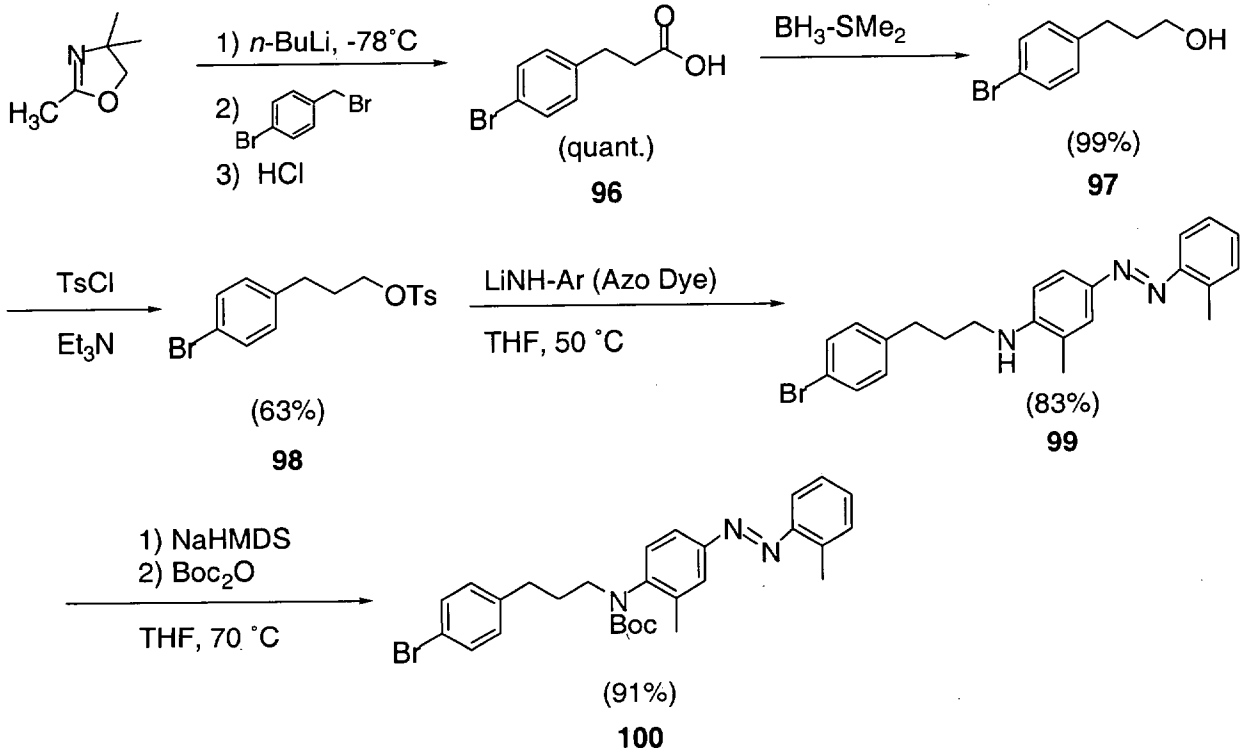
1-(*tert*-Butyl-2-methyl-2-phenyl-propylphosphino)ferrocene (83). Prepared from **104** according to the general procedure to afford the title compound as a pale yellow-orange powder (32%): ^{1}H NMR (C_6D_6, 500 MHz) δ 0.85 (d, 9H, J = 14.9), 1.61 (s, 3H), 1.63 (s, 3H), 2.07 (dd, 1H, J = 14.6, 5.7), 2.24 (dd, 1H, J = 14.7, 5.0), 3.79 (s, 1H), 4.01 (s, 1H), 4.07 (s, 6H), 4.24 (s, 1H) 7.13 (t, 1H, J = 7.3), 7.27 (t, 2H, J = 7.6), 7.51 (d, 2H, J = 7.7); ^{31}P NMR (C_6D_6, 202 MHz) δ -14.79; MS (EI, 70 eV) *m/z* (relative intensity, %): 406 (M+, 45).

1-(*tert*-Butyl-1-naphthylphosphino)ferrocene (84). Prepared from **104** according to the general procedure to afford the title compound as reddish orange crystals (5%): ^{1}H NMR (C_6D_6, 400 MHz) δ 1.13 (d, 9H, J = 12.6), 3.85 (s, 5H), 4.10 (m, 1H), 4.15 (m, 1H), 4.24 (m, 1H), 4.49 (m, 1H), 7.26 (t, 2H, J = 6.7), 7.41 (t, 1H, J = 7.8), 7.65 (d, 2H, J = 7.8), 7.84 (dd, 1H, J = 6.3, 2.0), 9.51 (t, 1H, J = 7.7); ^{31}P NMR (C_6D_6, 121 MHz) δ -13.17; MS (EI, 70 eV) *m/z* (relative intensity, %): 400 (M+, 50).

1-(*tert*-Butyl-2-biphenylphosphino)ferrocene (85). Prepared from **104** according to the general procedure to afford the product as a yellow orange powder (28%): ^{1}H NMR (C_6D_6, 400 MHz) δ 1.13 (d, 9H, J = 12.4), 4.03 (br s, 5H), 4.22 (m, 2H), 4.35 (m, 1H), 4.42 (m, 1H), 7.29 (3H under overlapping C6H6 solvent signal), 7.41 (m, 3H), 7.72 (dd, 2H, J = 10.5, 1.2), 7.91 (m, 1H); ^{31}P NMR (C_6D_6, 202 MHz) δ -8.12; MS (EI, 70 eV) *m/z* (relative intensity, %): 426 (M+, 35).

1-(*tert*-Butyl-4-trifluoromethylphenylphosphino)ferrocene (86). Prepared from **104** according to the general procedure to afford a yellow orange powder (98%): ^{1}H NMR (C_6D_6, 400 MHz) δ 0.99 (d, 9H, J = 12.4), 3.85 (s, 5H), 4.05 (m, 1H), 4.10 (m, 2H), 4.34 (br s, 1H), 7.35 (d, 2H, J = 8.0), 7.63 (t, 2H, J = 7.6); ^{31}P NMR (C_6D_6, 202 MHz) δ 9.09; MS (EI, 70 eV) *m/z* (relative intensity, %): 418 (M+, 25).

1-(*tert*-Butyl-4-methoxy-phenylphosphino)ferrocene (87). Prepared from **104** according to the general procedure to afford a pale yellow orange powder (15%): ^{1}H NMR (C_6D_6, 400 MHz) δ 1.10 (d, 9H, J = 12.4), 3.28 (s, 3H), 3.93 (s, 5H), 4.14 (s, 2H), 4.25 (s, 1H), 4.46 (s, 1H), 6.79 (d, 2H, J = 8.4), 7.76 (t, 2H, J = 8.0, $^3J_{PH}$ and $^2J_{HH}$ *ortho* coupling were equivalent); ^{31}P NMR (C_6D_6, 121 MHz) δ 6.20; MS (EI, 70 eV) *m/z* (relative intensity, %): 380 (M+, 40).



Scheme 1. Synthetic Route used for the Preparation of Bromodye Substrate.

3-(4-Bromo-phenyl)-propionic acid (96).[18] This compound was prepared using a modified literature procedure of Beak and Selling.[19] To 22.5 mL (0.177 mol) of 2,4,4-trimethyl-2-oxazoline in 600 mL of THF at –78 °C was added 71 mL (0.177 mol) of *n*-BuLi dropwise. After 45 min at this temperature, a 100 mL THF solution containing 4-bromobenzyl bromide (44.0 g, 0.177 mol) was added over 30 min. Upon complete addition, the reaction was allowed to warm to room temperature and stir overnight. The mixture was then quenched with 35 mL of H_2O, and was concentrated on a rotary evaporator to ca. 100-200 mL Et_2O (400 mL) was then added. The organic layer was extracted with 10% HCl (5 x 75 mL), and the resulting aqueous layers combined. The combined aqueous extracts were made more basic with saturated Na_2CO_3 (ca. 15 mL) and 40% NaOH. The product was extracted repeatedly with Et_2O (5 x 100 mL), and the ether layer was washed with brine and then dried over Na_2SO_4. The Et_2O was evaporated under vacuum to give a cloudy oil, which was then refluxed in 10% HCl (500 mL) for 1 h. Upon cooling the mixture to room temperature, the product precipitated and was collected by vacuum filtration. The resulting solid was rinsed with cold H_2O to afford 36.5 g of **96** as a white solid (90%). ^{1}H NMR spectra of **96** were consistent with that reported in the literature and indicated the product was of sufficient purity for synthetic purposes: ^{1}H NMR (DMSO-d_6, 500 MHz) δ 2.52 (t, 2H, J = 7.5), 2.77 (t, 2H, J = 7.5), 7.16 (d, 2H, J = 8.5), 7.43 (d, 2H, J = 9.0).

3-(4-Bromo-phenyl)-propan-1-ol (97).[20] To a 1 L flask containing **96** (30 g, 0.131 mol) in 500 mL of THF at 0 °C was added 64 mL of BH_3-SMe_2 (0.653 mmol) dropwise. After complete addition the mixture was maintained at 0 °C for an additional 0.5 h and then allowed to reach room temperature and stir overnight. The reaction was quenched by careful addition of MeOH (200 mL) at 0 °C. After allowing the mixture to reach room temperature and stir for 1 h, the solvent was concentrated in vacuo to afford a cloudy oil. Et_2O (400 mL) was added to the crude oil, and the organic layer washed consecutively with 10% aq. NaOH and brine. Upon drying over Na_2SO_4 and evaporation of solvent, 27.8 g of the title compound was obtained as a light yellow oil (99%). ^{1}H NMR spectra for **97** were consistent with that reported in the literature and indicated the product of was of sufficient purity for synthetic purposes: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.41 (s, 1H, exchangeable with D_2O), 1.86 (quint, 2H, J = 6.5), 2.67 (t, 2H, J = 7.0), 3.66 (q, 2H, J = 5.0), 7.07 (d, 2H, J = 8.0), 7.40 (d, 2H, J = 8.0).

Toluene-4-sulfonic acid 3-(4-bromo-phenyl)-propyl ester (98). To a 1 L flask containing 22 g of **97** (0.102 mol) in 500 mL of CH_2Cl_2 at 0 °C was added portionwise 19.4 g (0.102 mol) of *para*-toluene sulfonyl chloride. The reaction was allowed to reach room temperature and stir for 24 h. At this time H_2O (200 mL) was added, the layers were separated, and the organic layer

was washed consecutively with 10% aq. NaOH (150 mL) and brine (100 mL). After evaporation of the solvent, 35 g of a crude oil was obtained. Purification by flash chromatography (gradient, 5 to 10% ethyl acetate/hexanes) gave 23.6 g of analytically pure **98** as a white chalky solid (64%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.91 (quint, 2H, J = 8.4), 2.43 (s, 3H), 2.57 (t, 2H, J = 7.6), 3.98 (t, 2H, J = 6.4), 6.92 (d, 2H, J = 8.4), 7.32 (app t due to overlapping d's, 4H, J = 8.0), 7.76 (d, 2H, J = 8.4); ^{13}C NMR APT ($CDCl_3$, 100 MHz) δ 21.7 (CH_3), 30.1 (CH_2), 30.8 (CH_2), 69.3 (CH_2), 119.8 (ArC), 127.9 (ArCH), 129.2 (ArCH), 130.2 (ArCH), 131.4 (ArCH), 132.8 (ArC), 139.3 (ArC), 144.9 (ArC); Anal. calcd. for $C_{16}H_{17}BrO_3S$: C, 52.04; H, 4.64. Found: C, 52.02; H, 4.76.

[3-(4-Bromophenyl)-propyl]-(2-methyl-4-*o*-tolylazophenyl)-amine (99). In a dry box a 1 L flask was charged with 25.7 g (0.114 mol) of GBC fast garnet base (2-Methyl-4-*o*-tolylazo-phenylamine) and 400 mL of THF. To this solution was added portionwise 11.6 g (0.108 mol) of solid lithium diisopropylamide. The dark purple solution was sealed with a 24/40 septum, brought outside the box, and placed in a fume hood in an ice bath. To this solution was added 100 mL of a THF solution containing tosylate **98** (21 g, 0.057 mol). The mixture was then heated at 65 °C for 12 h. At this time the reaction was cooled to room temperature, quenched with H_2O (200 mL), and extracted once with Et_2O (350 mL). The ether layer was washed with brine (100 mL), dried over Na_2SO_4, and evaporated. The resulting solid was purified by flash chromatography (5% ethyl acetate/hexanes) to give 20 g (83%) of the title compound. During some preparations the product was recrystallized from 5% ethyl acetate/hexane instead of isolating by chromatography: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.97 (quint, 2H, J = 6.8), 2.14 (s, 3H), 2.67 (s overlapping q, 3H), 2.69 (q overlapping s, 2H, J = 7.2), 3.23 (q, 2H, J = 5.6), 3.84 (t, 1H, J = 5.2), 6.58 (d, 1H, J = 8.4), 7.06 (AA'XX', 2H, J = 8.8, 2.0), 7.24 (m, 3H), 7.40 (AA'XX', 2H, J = 8.4, 1.6), 7.56 (dd, 1H, J = 7.6, 1.6), 7.70 (dd, 1H, J = 2.4, 0.8), 7.77 (dd, 1H, J = 8.8, 2.4); ^{13}C NMR APT ($CDCl_3$, 100 MHz) δ 17.9 (CH_3), 18.0 (CH_3), 31.1 (CH_2), 33.3 (CH_2), 43.4 (CH_2), 108.9 (ArCH), 115.6 (ArCH), 120.0 (ArC), 121.8 (ArC), 124.2 (ArCH), 125.1 (ArCH), 126.5 (ArCH), 129.5 (ArCH), 130.3 (ArCH), 131.1 (ArCH), 131.7 (ArCH), 136.9 (ArC), 140.4 (ArC), 144.8 (ArC), 151.4 (ArC); MS (EI, 70 eV) *m/z* (relative intensity, %): 422 (M+, 10); Anal. calcd. for $C_{23}H_{24}N_3Br$: C, 65.41; H, 5.73; N, 9.95. Found: C, 65.27; H, 5.69; N, 9.86

[3-(4-Bromophenyl)-propyl]-(2-methyl-4-*o*-tolylazo-phenyl)-*N*-(*tert*-butoxycarbonyl)-amine (100, numbered as 2 in Scheme 1 of the manuscript). In a 1 L flask fitted with a 24/40 septum was placed 16.5 g of **99** (43.7 mmol) and 10.5 g of *tert*-butoxycarbonyl anhydride (48.0 mmol) in 350 mL of THF. After cooling to 0 °C a 50 mL THF solution of sodium hexamethyldisilazide

(9.75 g, 0.053 mol) was added. Upon complete addition, the mixture was placed in a 70 °C oil bath. TLC indicated complete conversion within 6 h. Upon cooling to room temperature, the reaction was quenched with H_2O (100 mL). Et_2O was added (200 mL), and the organic layer was washed with brine and dried over Na_2SO_4. The solvent was removed in vacuo, and the crude reaction mixture was purified by flash chromatography (10% acetone/hexanes) to afford the desired bromo dye substrate **100** as a thick red oil (91%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.36-1.51 (2 br s due to *t*-Boc conformers, 9H), 1.87 (br t, 2H, *J* = 7.0), 2.32 (s, 3H), 2.59 (t, 2H, *J* = 7.0), 2.74 (s, 3H), 3.51 (br m, 1H), 3.72 (br m, 1H), 7.03 (d, 2H, *J* = 8.0), 7.18 (d, 1H, *J* = 7.6), 7.27-7.39 (m, 6H), 7.62 (d, 1H, *J* = 8.0), 7.74 (d, 1H, *J* = 8.2), 7.81 (s, 1H); ^{13}C NMR δ 17.7, 18.2, 28.5, 30.2, 31.1, 32.9, 49.4, 115.6, 119.9, 121.1, 125.6, 126.6, 130.2, 131.1, 131.5, 131.7, 138.3, 140.7, 143.6, 150.9, 151.7; Anal. calcd. for $C_{28}H_{32}N_3BrO_2$-0.5H_2O: C, 63.28; H, 6.26; N, 7.91. Found: C, 63.24; H, 6.05; N, 7.61.

Preparation of dimethyl-(5-{[methyl-(4-vinyl-phenyl)-amino]-methyl}-napthalen-1-yl)-amine (101, numbered as 1 in Scheme 1 of the manuscript).

A 100 mL round bottomed flask was charged with a stir bar, 1.21 g (4.48 mmol) of dansyl chloride, 42 mg (0.34 mmol) of dimethylamino pyridine, 0.33 mL (4.10 mmol) of pyridine, and 504 mg (4.23 mmol) of 4-aminostyrene. Forty mL of 1,2-dichloroethane were added and the red reaction mixture was stirred for 6 h at 60-65 °C. All volatile components were evaporated leaving a light brown residue. The residue was dissolved in 25 mL of DMF, and 1.862 g (13.47 mmol) of potassium carbonate was added. The reaction was capped with a septum fit with a ventilation needle and stirred under a stream of nitrogen. After 30 min, the ventilation needle was removed, and 0.80 mL (13.5 mmol) of iodomethane was added by syringe to the flask. The reaction was heated at 35-40 °C for 3 h. The reaction mixture was poured into a saturated solution of LiCl and extracted 3 times with Et_2O. Evaporation of ether followed by flash chromatography afforded 0.908 g (2.48 mmol, 55.3%) of a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): 2.89 (s, 6H), 3.24 (s, 3H), 5.25 (d, *J* = 10.8 Hz, 1H), 5.70 (d, *J* = 17.7 Hz, 1H), 6.66 (dd, *J* = 17.4, 10.8 Hz, 1H), 7.08 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 7.3 Hz, 1H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.35 (vt, *J* = 7.5, 8.6 Hz, 2H), 7.46 (vt, *J* = 7.4, 8.6 Hz, 1H), 8.06 (d, *J* = 8.8 Hz, 1H), 8.10 (d, *J* = 7.3 Hz, 1H), 8.53 (d, *J* = 8.7 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 38.7, 45.8, 114.9, 115.5, 120.4, 123.5, 127.0, 127.5, 128.1, 130.3, 130.8, 131.0, 131.3, 133.8, 136.3, 136.8, 141.3, 151.9 ppm. Anal. Calc'd. for $C_{21}H_{22}N_2S$: C: 68.82, H: 6.05, N: 7.64, S: 8.75 Found: C: 68.98, H: 6.07, N: 7.54, S: 8.74.

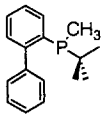
{3-[4-(2-{4-[(5-Dimethylamino-naphthalene-1-sulfonyl)-methyl-amino]-phenyl}-vinyl)-phenyl]-propyl}-(2-methyl-4-*o*-tolylazo-phenyl)-carbamic acid *tert*-butyl ester (102). In a

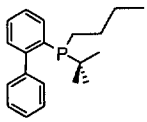
drybox, compound **101** (178 mg, 0.486 mmol), compound **100** (254 mg, 0.487 mmol), $Pd(dba)_2$ (14 mg, 0.024 mmol), P(*t*-Bu)$_3$ (5 mg, 0.03 mmol), and sodium acetate (48 mg, .58 mmol), were dissolved in 2 mL of DMF. The reaction was heated at 100-105 °C for 16 h. The reaction mixture was poured into a saturated solution of lithium chloride and extracted 3 times with ether. Evaporation of ether followed by flash chromatography gave 242 mg (0.300 mmol, 55.3%) of an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) 1.36-1.52 (2 br s due to *t*-Boc conformers, 9H), 1.90 (br t, J = 7.0 Hz, 2H), 2.32 (s, 3H), 2.63 (t, J = 6.8 Hz, 2H), 2.73 (s, 3H), 2.88 (s, 6H), 3.24 (s, 3H), 3.51 (br m, 1H), 3.73 (br m, 1H), 7.03 (br, 2H), 7.08-7.15 (m, 6H), 7.28-7.48 (m, 9H), 7.62 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.80 (br s, 1H), 8.06 (d, J = 9.2 Hz, 1H), 8.11 (d, J = 7.2 Hz, 1H), 8.53 (d, J = 8.4 Hz, 1H) ppm.

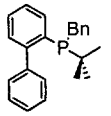
Biphenyl-2-yl-*tert*-butyl-chlorophosphine (103). To a 250 mL flask containing 2-bromobiphenyl (5.00 g, 3.70 mL, 21.5 mmol) in 100 mL of THF at –78 °C was added *n*-BuLi (9.5 mL, 2.5 M, 24 mmol) dropwise. The mixture was stirred for 45 min at –78 °C and then transferred by cannula over the coarse of 1 h to another flask containing a THF solution (100 mL) of *tert*-butyldichlorophosphine (6.84 g, 43 mmol) that had been cooled to –78 °C. After complete transfer the mixture was warmed to room temperature. GC analysis indicated complete conversion within 2 h. Solvent and excess chlorophosphine were evaporated under vacuum. The resulting oil was taken into a dry box, dissolved in pentane (100 mL), and the solution filtered through a pad of Celite. The filtrate was concentrated to precipitate 5.55 g of product as a pasty white solid (93%): ^{1}H NMR (C_6D_6, 300 MHz) δ 0.90 (d, 9H, J = 13.6), 7.35 (m, 8H), 8.0 (m, 1H); ^{31}P NMR (C_6D_6, 202 MHz) δ 103.9.

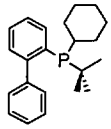
Ferrocenyl-*tert*-butyl-chlorophosphine (104). Into a 500 mL flask containing (tri-*n*-butylstannyl)ferrocene[21] (20.0 g, 42.0 mmol) and THF (200 mL) was added at -78 °C *n*-BuLi dropwise over 10 min. The reaction was allowed to stand at -78 °C for 45 min, after which time it was transferred by cannula to a another flask at -78 °C containing a THF (50 mL) solution of *tert*-butyldichlorophosphine (8.68 g, 54.6 mmol). Upon complete transfer (approx. 1h) the mixture was warmed to room temperature and allowed to stir overnight. The solvent was evaporated under vacuum to afford an orange solid. The solid was recrystallized under N_2 from pentane to furnish 9.4 g of small orange crystals. Despite further recrystallizations, 10-15% of (*n*-Bu)$_4$Sn remained in the product mixture, as indicated by ^{1}H NMR spectroscopy. This material was used in the next step without further purification. After correcting for the remaining tin, a yield of 66% was obtained. ^{1}H NMR (C_6D_6, 500 MHz, resonances listed for product only) δ 1.05 (d, 9H, J = 13.6), 4.11 (s, 1H), 4.18 (s, 1H), 4.21 (s, 5H), 4.26 (s, 1H), 4.45 (s, 1H); ^{31}P NMR (C_6D_6, 202 MHz) δ 111.19.

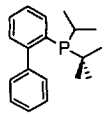
1-(*tert*-Butyl-1-adamantylphosphino)ferrocene (105). Prepared from **104** according to the general procedure to afford the title compound as a fine orange powder (30%): ^{1}H NMR (C_6D_6, 400 MHz) δ 1.40 (d, 9H, J = 10.8), 1.76 (br s, 6H), 1.98-2.06 (m, 6H), 2.19-2.23 (m, 3H), 4.19 (s, 5H), 4.24 (m, 2H), 4.28 (dt, 1H, J = 2.8, 1.4), 4.38 (dt, 1H, J = 2.8, 1.2); ^{31}P NMR (C_6D_6, 121 MHz) δ 27.04; MS (EI, 70 eV) *m/z* (relative intensity, %): 408 (M+, 14).

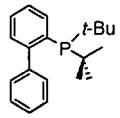
1 

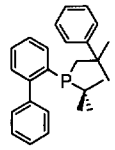
2 

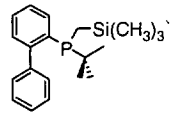
3 

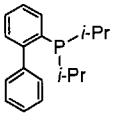
4 

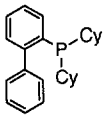
5 

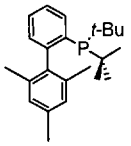
6 

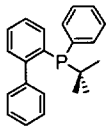
7 

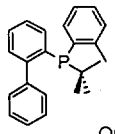
8 

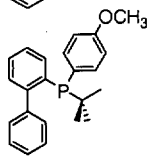
9 

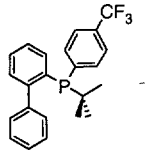
10 

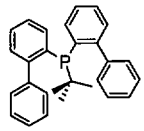
11 

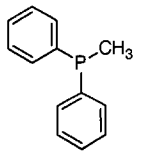
12 

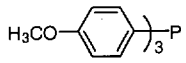
13 

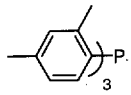
14 

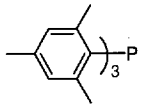
15 

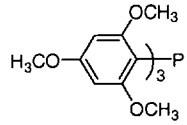
16 

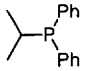
17 

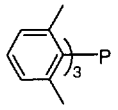
18 

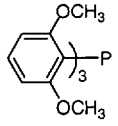
19 

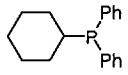
20 

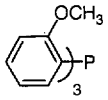
21 

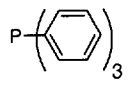
22 

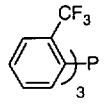
23 

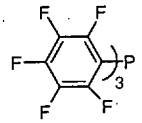
24 

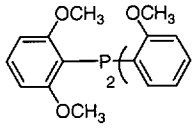
25 

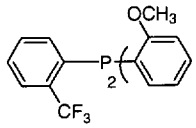
26 

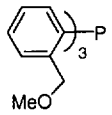
27 

28 

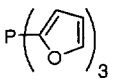
29 

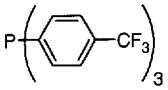
30 

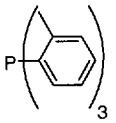
31 

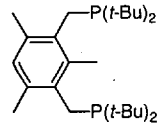
32 

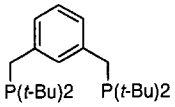
33 AsPh3

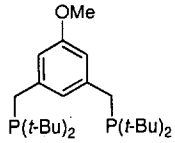
34 

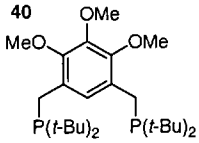
35 

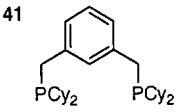
36 

37 

38 

39 

40 

41 

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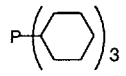
46 

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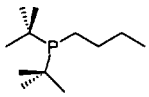
50 

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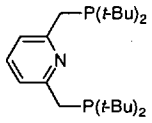
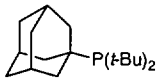
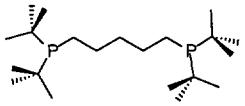
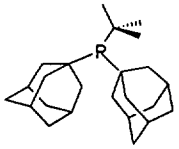
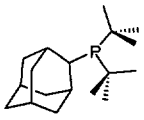
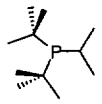
52 

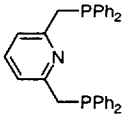
53 

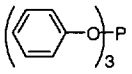
54 

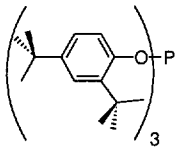
55 

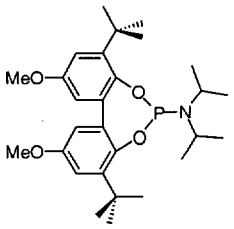
56 

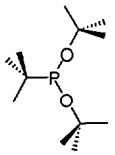
57 

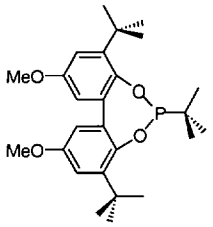
58 

59 

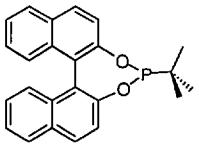
60 

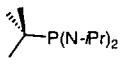
61 

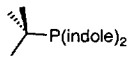
62 

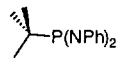
63 

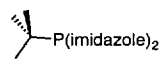
64 $P(NMe_2)_3$

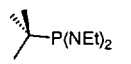
65 

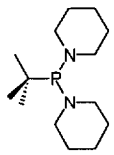
66 

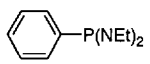
67 

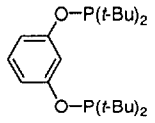
68 

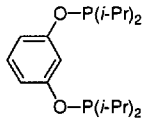
69 

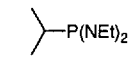
70 

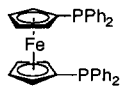
71 

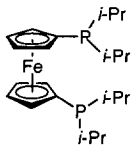
72 

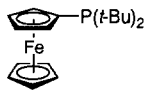
73 

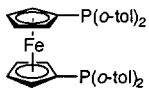
74 

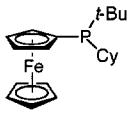
75 

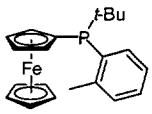
76 

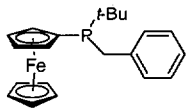
77 

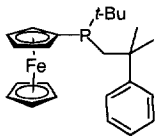
78 

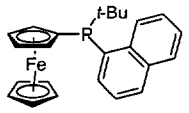
79 

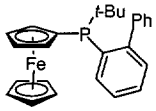
80 

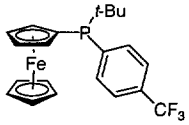
81 

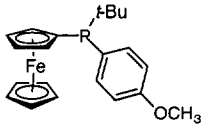
82 

83 

84 

85 

86 

87 

88

89

(Ar = p-$MeOC_6H_4$)

90

(Ar = p-$CF_3C_6H_4$)

91

92 DPPE

93 DPPB

94

95 (R)-tol-BINAP

General Procedure for Room Temperature Palladium Catalyzed Heck Reactions: The reaction conditions and results are shown in Table 1. A typical procedure is given for the reaction of Entry 1 in Table 1.

A 4 mL vial was charged with 4-bromoanisole (187 mg, 1.00 mmol), $Pd(dba)_2$ (14.4 mg, 0.0250 mmol), $Ph_5FcP(t\text{-}Bu)_2$ (35.5 mg, 0.0500 mmol), and 1 mL of anhydrous DMF. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. NEt_3 (167 μL, 1.20 mmol) was added by syringe. The reaction was stirred at room temperature for 20 h. The reaction mixture was then poured into a saturated lithium chloride solution and extracted (3 x 10 mL) with ether. The ether was evaporated under vacuum, and the product was isolated by flash chromatography, eluting with 15% ethyl acetate/hexanes, to give 176 mg (92%) of 3-(4-methoxy-phenyl)acrylic acid methyl ester.

Spectroscopic Data of Products in Table 1:

Table 1, Entry 1. The ^{1}H NMR spectroscopic data of 3-(4-methoxy-phenyl)acrylic acid methyl ester were identical to that published previously.[22]

Table 1, Entry 2. The ^{1}H NMR spectroscopic data of 3-*p*-tolyl-acrylic acid methyl ester was identical to that published previously.[23]

Table 1, Entry 3. The ^{1}H NMR spectroscopic data of 3-napthalen-1-yl-acrylic acid methyl ester was identical to that published previously.[24]

Table 1, Entry 4. The ^{1}H NMR spectroscopic data of 3-(4-trifluoromethyl-phenyl)-acrylic acid methyl ester was identical to that published previously.[23]

Table 1, Entry 5. 3-(3-[1,3]dioxolan-2-yl-phenyl)-acrylic acid methyl ester. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 3H), 4.03-4.16 (m, 4H), 5.82 (s, 1H), 6.47 (d, J = 15.8 Hz, 1H), 7.40 (dd, J = 7.7, 7.8 Hz, 1H), 7.49-7.53 (m, 2H), 7.65 (s, 1H), 7.70 (d, J = 16.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.67, 65.29, 103.1, 118.2, 125.9, 128.3, 128.8, 128.9, 134.5, 138.7, 144.4, 167.2. MS: m/z, 233 (M^+-1).

Table 1, Entry 6. The ^{1}H NMR spectroscopic data of 3-phenyl-acrylic acid methyl ester was identical to that of authentic material (Aldrich).

Table 1, Entry 7. The ^{1}H NMR spectroscopic data of trans-stilbene was identical to that of authentic material (Aldrich).

Table 1, Entry 8. The ^{1}H NMR spectroscopic data of 2-methoxystilbene was identical that published previously.[25]

Table 1, Entry 9. 4-Methoxystilbene was identical to authentic material (Alfa Aesar) by ^{1}H NMR.

Table S1. Yields for Heck Reactions run in a 96-well plate. [a]

	1	2	3	4	5	6	7	8	9	10	11	12
A	3	38	48	86	6	70	0	54	34	14	56	64
B	60	65	55	37	0	1	71	0	0	8	0	1
C	28	24	13	17	0	0	5	0	0	6	0	71
D	5	0	0	1	0	0	25	5	25	0	3	0
E	83	39	0	2	90	59	85	87	69	0	0	15
F	75	0	22	0	4	3	2	6	7	7	3	14
G	0	9	1	33	0	94	54	2	48	35	78	23
H	73	58	13	86	88	91	8	3	0	13	17	9

[a]Percent yields shown are an average of 2 runs. Ligands **1-95** were used and were arranged by increasing ligand number across a column (A1 = **1**, B1 = **13**; Well H12 contained no ligand).

Procedure for Results Obtained in Figure S1. Heck reactions run in a 96-well plate: In a drybox, 293 mg (0.800 mmol) of compound **101** was dissolved in 2.0 mL of DMF. Compound **100** (444 mg, 0.852 mmol) was dissolved in 1.7 mL of DMF. CpPd(allyl) (10 mg, 0.047 mmol) was dissolved in 0.47 mL of *m*-xylene. Stock solutions that were 0.1 M concentration in ligands **1-95** were prepared in *m*-xylene or tetrahydrofuran. All 96 wells of a glass plate were charged with one 3.8 μL aliquot of ligands **1-95** going from left (A1) to right (H12) down the plate (Table S1). Well 96 contained no ligand. To each well was added 3.8 μL of solution containing CpPd(allyl) by multichannel pipet, followed by 3.5 μL of DMF, 18.7 μL of the stock solution of compound **101**, 15.0 μL of the stock solution of compound **100**, and 5.2 μL of neat NEt_3. The plate was sealed with a PTFE sheet followed by a rubber gasket. The plate was placed into an aluminum holder with 4 female posts at each corner. An aluminum block was placed on top of the rubber gasket, and a washer and screw were used to connect the top block to the bottom plate. A torque wrench set at 11 in lbs of force, was used to tighten the screws. The assembly was then removed from the drybox and heated in an agitating aluminum block at 70 °C for 15 h. After this time, 3.3 μL of the reaction solution in each well was removed and diluted to 1 x 10^{-5} M in *m*-xylene and transferred to a 96-well polypropylene plate. The resulting plate was analyzed on a Packard Fluorocount plate reader using a 360 nm excitation filter with a 485 nm emission filter. The entire process was repeated to obtain duplicate data.

Determination of Reaction Yields From a Standard Curve: Fifteen μL of the stock solution containing compound **100**, 18.7 μL of the stock solution of compound **101**, and 16.3 μL of DMF

were added to a vial. An aliquot (6.67 μL) of this solution was dissolved in 1.0 mL of *m*-xylene to make stock solution A. Compound **102**, (1.6 mg, 2.0×10^{-3} mmol) was dissolved in 2.0 mL of *m*-xylene to make stock solution B. 1.98 μL of *m*-xylene was added to six vials. The following amounts of the two stock solutions A and B were then added to the six vials (Table S2).

Table S2. Preparation of a Calibration Curve for Fluorescence Measurements.

Vials	Stock A (μL)	Stock B (μL)	Emission Intensity	Mole Fraction of Coupled Product
1	20	0	55199	0.0
2	16	4	48611	0.2
3	12	8	41410	0.4
4	8	12	31017	0.6
5	4	16	20994	0.8
6	0	20	11367	1.0

From these data, a linear plot of the emission intensity versus mole fraction was generated. For each set of determinations of reaction yields, the instrument gain was set so that the well which contains no ligand in the reactions was within 10% of the maximum intensity listed in Table S2. The intensity values obtained from the reaction were converted to reaction yield using the linear calibration curve.

Table S3. Results from reactions using the ligands in Figure 2 in six solvents (ligand, yield **(%)).**[a]

Toluene		**Dioxane**		**1,2-DCE**		**^{n}PrCN**		**PMK**		**^{n}PrCN:PMK**	
1	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***11***	***12***
49, 80	**36**, 28	**49**, 84	**36**, 32	**49**, 73	**36**, 16	**49**, 81	**36**, 63	**49**, 84	**36**, 29	**49**, 82	**36**, 25
53, 80	**19**, 18	**53**, 70	**19**, 17	**53**, 80	**19**, 13	**53**, 78	**19**, 64	**53**, 73	**19**, 24	**53**, 78	**19**, 40
56, 30	**55**, 68	**56**, 11	**55**, 78	**56**, 18	**55**, 73	**56**, 65	**55**, 74	**56**, 12	**55**, 69	**56**, 39	**55**, 52
78, 62	**88**, 68	**78**, 55	**12**, 79	**78**, 59	**12**, 76	**78**, 83	**12**, 84	**78**, 68	**12**, 76	**78**, 78	**12**, 77
85, 87	**90**, 76	**85**, 81	**90**, 78	**85**, 67	**90**, 77	**85**, 77	**90**, 70	**85**, 72	**90**, 76	**85**, 84	**90**, 38, 90
83, 76	**87**, 75	**83**, 28, 72	**87**, 88	**83**, 39	**87**, 82	**83**, 65	**87**, 71	**83**, 59	**87**, 76	**83**, 70	**87**, 81
6, 81	**105**, 37	**6**, 67	**105**, 20	**6**, 65	**105**, 25	**6**, 77	**105**, 75	**6**, 57	**105**, 45	**6**, 80	**105**, 69
4, 69	**61**, 14	**4**, 75	**61**, 24	**4**, 68	**61**, 9	**4**, 66	**61**, 42	**4**, 66	**61**, 6	**4**, 65	no L, 0

[a]Percent yields are an average of two runs except for E12 and F3 which showed large differences in yields in the two runs. Data is shown in the format Ligand # (see Figure 2), % Yield.

General Procedure for the screening of solvent effects for the Heck reaction using sixteen ligands: Compound **101** (55 mg, 0.15 mmol) was placed into each of six vials, and 375 μL of solvent (toluene, dioxane, 1,2-dichloroethane, butyronitrile, propyl methyl ketone, or a 1:1 mixture of butyronitrile:propyl methyl ketone) were added. Six 78 mg (0.15 mmol) samples of compound **100** were dissolved in 300 μL of the above six solvents. Into an aluminum block with 96 holes were placed 0.7x40 mm glass vials. Each vial in two columns was charged with 3.8 μL of a stock solution containing CpPd(allyl), 3.5 μL of the corresponding solvent, and 5.2 μL of neat NEt_3. This process was repeated with the six solvents to create the array in Table S3. No ligand was added to vial H12. The vials were sealed with a PTFE sheet followed by a rubber gasket. The aluminum block was placed into an aluminum holder and fastened with screws using a torque wrench set at 11 in lbs of force. The assembly stood at room temperature for 8 h. At this time, the block was removed from the drybox and heated in an agitating aluminum block at 70 °C for 8 h. An aliquot from each well (3.3 μL) was removed, diluted to 1 x 10^{-5} M in *m*-xylene, and transferred to a 96-well polypropylene plate. The plate was analyzed on a Packard Fluorocount plate reader using a 360 nm excitation filter with a 485 nm emission filter. The emission intensities were converted to percent yields using the standard curve generated in the first screen. The entire process was repeated to obtain duplicate data.

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