Electronic Supplementary Material (ESI) for RSC Advances.

Synthesis of 3-aryl-1*H*-indazoles via iridium-catalysed C-H borylation and Suzuki-Miyaura coupling

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Reagents

The following reagents were obtained from commercial suppliers: XPHOS-2nd Generation Precatalyst (XPHOS-Pd-G2) and $[Ir(OMe)COD]_2$ (Strem), di-*tert*-butyl bipyridine (dtbpy), *tert*-butyl methyl ether (TBME) and potassium phosphate (Sigma Aldrich), bis(pinacolato)diboron (B_2Pin_2) (Alfa Aesar). All reagents were used without purification.

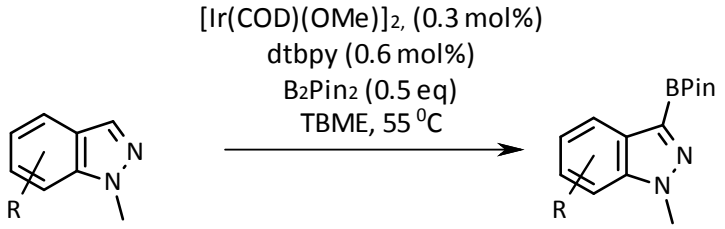
Starting Materials

All aryl halides were purchased from commercial suppliers and used without further purification. The following indazoles were obtained from commercial suppliers: 1-methyl-*1H*-indazole (Combi-Blocks), methyl 1-methyl-1H-indazole-4-carboxylate (Apollo Scientific) and methyl 1-methyl-1H-indazole-5-carboxylate (Apollo Scientific). Other indazoles were synthesised using modified procedures from the literature: 1-methylpyrazolo[3,4-b]pyridine[1] and 1-(methoxymethyl)indazole[2].

1. Lynch, B. M.; Khan, M. A.; Teo, H. C.; Pedrotti, F. *Can. J. Chem*, 1988, 66, 420-428.

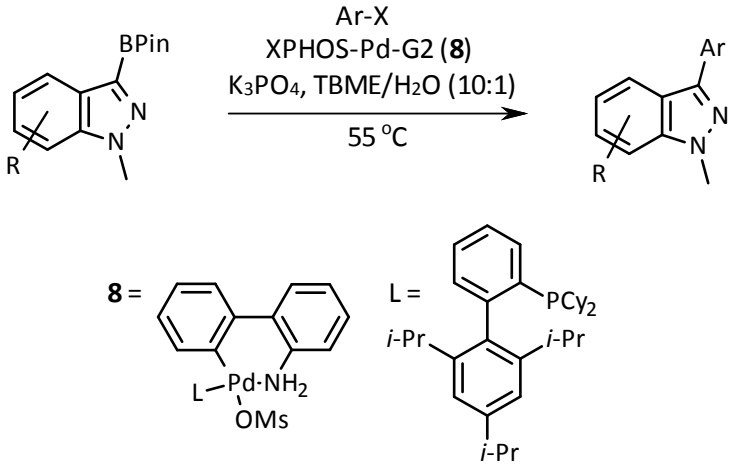
2. Unsinn, A.; Knochel, P. *Chem. Commun*. 2012, 48, 2680-2682.

General Procedure 1: Indazole Borylation



A round-bottomed flask equipped with reflux condenser was charged with indazole (1.0 Eq.), B_2Pin_2 (0.505 Eq.), dtbpy (0.006 Eq.) and $[Ir(OMe)COD]_2$ (0.003 Eq.) in TBME (typically 0.2 M) and the resultant solution was heated at reflux (55 ^oC) under an atmosphere of N_2. The reaction monitored by GC-MS analysis until completion (typical reaction times of 0.5-4 h, with a reaction conversion of approx. 70-95%). The reaction was cooled to RT before being quenched with water and extracted with DCM. The combined organics were collected, dried and concentrated *in vacuo*. Purification via flash column chromatography afforded the product. This could be further purified (to remove any pinacol/boronate residues) by recrystallization from hexane or trituration from hexane at 5 ^oC. The pinacolato-boronate products were typically obtained as colourless crystalline solids, stable at RT, however they were kept in the freezer for long-term storage.

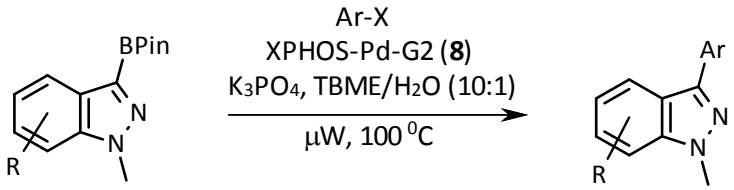
General Procedure 2: Thermal Suzuki



A round-bottomed flask equipped with reflux condenser was charged with boryl-indazole (1.1-1.5 Eq.), tripotassium phosphate (2.1 Eq.), XPHOS-Pd-G2(0.02 Eq.) and aryl halide (1.0 Eq.) in TBME and water (typically in a 10:1 ratio at 0.1 M). The reaction mixture was heated at reflux (55 ^oC) under N_2 for 0-24 h (typically 16 h). The reaction was monitored by a combination of TLC, GC-MS

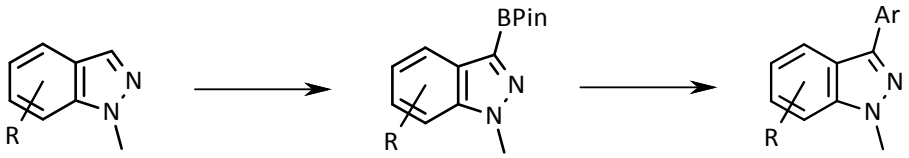
and LC-MS analysis. After cooling to RT, reactions were quenched with water and extracted with organic solvent (typically DCM or EtOAc), washed with sat'd brine solution, dried and concentrated *in vacuo*. Purification by flash column chromatography afforded the product.

General Procedure 3: Microwave Assisted Suzuki



The reaction was performed under analogous conditions to General Procedure 2, except the reaction was heated in a microwave reactor at 100 °C for 20 min. The reaction was monitored by a combination of TLC, GC-MS and LC-MS analysis. After cooling to RT, reactions were diluted with water and extracted with organic solvent (typically DCM or EtOAc), washed with sat'd brine solution, dried and concentrated *in vacuo*. Purification by flash column chromatography afforded the product.

General Procedure 4: One-Pot Thermal Borylation Suzuki

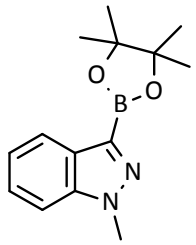


A round-bottomed flask equipped with reflux condenser was charged with indazole (1.0 Eq.), B_2Pin_2 (0.505 Eq.), dtbpy (0.006 Eq.) and $[Ir(OMe)COD]_2$ (0.003 Eq.) in TBME (0.2 M) and the resultant solution was heated at reflux (55 °C) under an atmosphere of nitrogen. The reaction was monitored by GC-MS analysis (typical conversion of 80%). The reaction was cooled to RT and tripotassium phosphate (2.1 Eq.), XPHOS-Pd-G2 (0.02 Eq.), aryl halide (1.0 eq)* and water (1:10 ratio with TBME) were added. The reaction mixture was heated at reflux (55 °C). Alternatively, the reaction mixture could be transferred to a microwave vial and heated in a microwave reactor at 100 °C for 20 min. The reaction was monitored by a combination of TLC, GC-MS and LC-MS analysis. After cooling to RT, reactions were diluted with water and extracted with organic solvent

(typically DCM or EtOAc), washed with sat'd brine solution, dried and concentrated *in vacuo*. Purification by flash column chromatography afforded the product.

*N.B. As the aryl halide is used as the limiting reagent and the boryl-indazole in excess, a relative ratio of indazole:aryl halide of 1.6:1, ensures that the active concentration of boryl-indazole of approx. 1.3 Eq., relative to the aryl halide, based on an 80% conversion in the borylation step.).

1-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole, 7

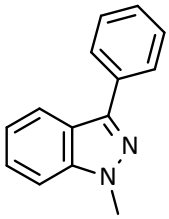


Using General Procedure 1, 1-methyl-*1H*-indazole (4.96 g, 37.5 mmol, 1.0 Eq.), B_2Pin_2 (4.80 g 18.9 mmol, 0.504 Eq.), dtbpy (60 mg, 0.23 mmol, 0.006 Eq.) and $[Ir(OMe)COD]_2$ (75 mg 0.113 mmol, 0.003 Eq.) in TBME (150 mL) were heated at reflux (55 ^oC) under N_2 for 90 min. The reaction was diluted with water (80 mL) and extracted with DCM (3 x 100 mL) and the combined organics were collected and passed through a phase separator cartridge. The organics were concentrated *in vacuo.* Flash column chromatography, elution with 0-50% EtOAc:Hexane, afforded the product. Further purification via trituration from hexane at 5 ^oC provided the desired product, 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (4.84 g, 18.8 mmol, 50%) as a colourless crystalline solid. NMR analysis showed a trace of pinacol present that did not affect future reactions.

^1H NMR (400 MHz, DMSO-d_6) δ ppm 1.34 (12 H, s) 4.11 (3 H, s) 7.21 (1 H, t, *J*=7.2 Hz) 7.40 (1 H, t, *J*=7.3 Hz) 7.68 (1 H, d, *J*=8.4 Hz) 7.90 (1 H, d, *J*=8.1 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 25.2, 36.2, 83.9, 110.4, 121.6, 122.0, 126.2, 129.8, 140.2. MP: 105-107 ^oC. GCMS (EI): m/z = 258, R_t = 2.81 / 5.00 min.

Note: *ipso*-carbon (3 position on indazole) signal not visible in ^{13}C spectrum.

1-Methyl-3-phenyl-indazole, 9



Synthesis from Chlorobenzene

Using General Procedure 2, XPHOS-Pd-G2 (7 mg, 8 µmol, 0.02 Eq., tripotassium phosphate (176 mg, 0.828 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (132 mg, 0.513 mmol, 1.3 Eq.), chlorobenzene (44 mg, 0.39 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated at reflux (55 ^{o}C) under N_2 for 18 h. Standard work up, followed by flash column chromatography, elution with 0-15% DCM:Hexane, provided the desired product 1-methyl-3-phenyl-indazole **9** (58 mg, 0.28 mmol, 71%) as a colourless crystalline solid.

Using General Procedure 3, XPHOS-Pd-G2 (7 mg, 8 µmol, 0.02 Eq.), tripotassium phosphate (177 mg, 0.83 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (131 mg, 0.511 mmol, 1.3 Eq.), chlorobenzene (44 mg, 0.39 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 ^{o}C for 1 h. Standard work up with DCM, followed by flash column chromatography, elution with 0-15% DCM:Hexane, provided the desired product 1-methyl-3-phenyl-indazole **9** (54 mg, 0.26 mmol, 66%) as a colourless crystalline solid.

Using General Procedure 4, 1-methyl-*1H*-indazole (300 mg, 2.27 mmol), B_2Pin_2 (288 mg 1.13 mmol), dtbpy (1.8 mg, 6.8 µmol) and $[Ir(OMe)COD]_2$ (2.3 mg 3.4 µmol) in TBME (5 mL) were heated at reflux (55 ^{o}C) under N_2 for 90 min. The reaction was cooled to RT and tripotassium phosphate (534 mg, 2.52 mmol), XPHOS-Pd-G2(15 mg, 18 µmol), chlorobenzene (135 mg, 1.20 mmol, 1.0 eq) and water (0.5 mL) were added.* The reaction mixture was heated at reflux (55 ^{o}C) for 16 h. Standard work up with DCM, followed by flash column chromatography, elution with 0-15% DCM:Hexane, provided the desired product 1-methyl-3-phenyl-indazole **9** (176 mg, 0.85 mmol, 70%) as a colourless crystalline solid.

*Based on GC-MS for borylation step: 74% conversion to 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** provides approx. 1.68 mmol, 1.4 Eq. of active boronate species.

Synthesis from Bromobenzene

Using General Procedure 2, XPHOS-Pd-G2(9 mg, 10 µmol, 0.02 Eq.), tripotassium phosphate (227 mg, 1.07 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (144 mg, 0.56 mmol, 1.1 Eq.), bromobenzene (80 mg, 0.51 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated at reflux (55 ^{o}C) under N_2 for 16 h. Standard work up with DCM, followed by flash column chromatography, elution with 0-30% DCM:Hexane, provided the desired product 1-methyl-3-phenyl-indazole **9** (91 mg, 0.44 mmol, 86%) as a white solid.

Using General Procedure 3, XPHOS-Pd-G2 (9 mg, 10 µmol, 0.02 Eq.), tripotassium phosphate (227 mg, 1.07 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (170 mg, 0.66 mmol, 1.3 Eq.), bromobenzene (81 mg, 0.51 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 ^{o}C for 1 h. Standard work up, followed by flash column chromatography, elution with 2.5% EtOAc:Hexane, provided the desired product 1-methyl-3-phenyl-indazole **9** (57 mg, 0.35 mmol, 68%) as a white solid.

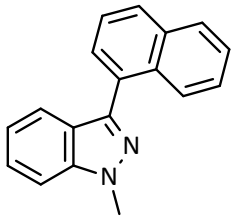
Synthesis from Iodobenzene

Using General Procedure 2, XPHOS-Pd-G2 (6 mg, 7 µmol, 0.02 Eq.), tripotassium phosphate (160 mg, 0.753 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (102 mg, 0.395 mmol, 1.1 Eq.), iodobenzene (73 mg, 0.36 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated at reflux (55 ^{o}C) under N_2 for 16 h. Standard work up with DCM, followed by flash column chromatography, elution with 0-50% DCM:Hexane, provided the desired product 1-methyl-3-phenyl-indazole **9** (54 mg, 0.26 mmol, 72%) as a white solid.

Using General Procedure 3, XPHOS-Pd-G2 (6 mg, 7 µmol, 0.02 Eq.), tripotassium phosphate (160 mg, 0.753 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (102 mg, 0.395 mmol, 1.1 Eq.), iodobenzene (73 mg, 0.36 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 ^{o}C for 45 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-50% DCM:Hexane, provided the desired product 1-methyl-3-phenyl-indazole **9** (55 mg, 0.27 mmol, 74%) as a white solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.12 (3 H, s) 7.24 (1 H, t, *J*=7.6 Hz) 7.38 - 7.43 (1 H, m) 7.46 (1 H, t, *J*=7.6 Hz) 7.52 (2 H, t, *J*=7.6 Hz) 7.70 (1 H, d, *J*=8.3 Hz) 7.98 (2 H, d, *J*=7.3 Hz) 8.07 (1 H, d, *J*=8.3 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 36.0, 110.6, 121.1, 121.3, 121.7, 126.7, 127.2, 128.2, 129.4, 133.8, 141.7, 142.4. m/z [CI$^+$, isobutane] 209 [M+H]$^+$ (100%), HRMS found [M+H]$^+$ 209.1073, $C_{14}H_{13}N_2$ requires 209.1079. MP: 74-76 ^{o}C.

1-Methyl-3-(1-naphthyl)indazole, 10

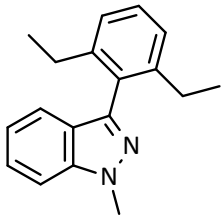


Using General Procedure 2, XPHOS-Pd-G2 (6 mg, 7 µmol, 0.02 Eq.), tripotassium phosphate (163 mg, 0.770 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (104 mg, 0.403 mmol, 1.1 Eq.), 1-chloronaphthalene (60 mg, 0.37 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated at reflux (55 ^{o}C) under N_2 for 10 h. Standard work up with DCM, followed by flash column chromatography, elution with 0-100% DCM:Hexane, provided the desired product 1-Methyl-3-(1-naphthyl)indazole **10** (60 mg, 0.63 mmol, 63%) as a white solid.

Using General Procedure 3, XPHOS-Pd-G2 (7 mg, 9 µmol, 0.02 Eq.), tripotassium phosphate (193 mg, 0.910 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (153 mg, 0.592 mmol, 1.3 Eq.), 1-chloronaphthalene (73 mg, 0.36 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 ^{o}C for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-100% DCM:Hexane, provided the desired product, 1-methyl-3-(1-naphthyl)indazole **10** (114 mg, 0.97 mmol, 97%) as a white solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.20 (3 H, s) 7.20 (1 H, t, *J*=7.5 Hz) 7.46 - 7.69 (5 H, m) 7.76 (2 H, d, *J*=7.7 Hz) 8.04 (2 H, d, *J*=8.1 Hz) 8.29 (1 H, d, *J*=8.3 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 36.1, 110.6, 121.0, 121.5, 123.1, 126.1, 126.3, 126.6, 126.8, 126.9, 128.3, 128.8, 128.9, 130.5, 131.6, 134.2, 141.1, 142.5. m/z [CI$^+$, isobutane] 259 [M+H]$^+$ (100%), HRMS found [M+H]$^+$ 259.1228, $C_{18}H_{15}N_2$ requires 259.1235. MP: 135-138 ^{o}C.

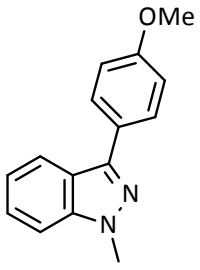
3-(2,6-Diethylphenyl)-1-methyl-indazole, 11



Using General Procedure 3, XPHOS-Pd-G2 (9 mg, 10 µmol, 0.02 Eq.), tripotassium phosphate (230 mg, 1.08 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (173 mg, 0.671 mmol, 1.3 Eq.), 2-bromo-1,3-diethyl-benzene (110 mg, 0.516 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 °C for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-3% EtOAc:Hexane, provided the desired product, 3-(2,6-diethylphenyl)-1-methyl-indazole **11** (123 mg, 0.465 mmol, 90%) as a white solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.90 (6 H, t, *J*=7.5 Hz) 2.15 - 2.24 (2 H, m) 2.24 - 2.34 (2 H, m) 4.10 (3 H, s) 7.10 (1 H, t, *J*=7.1 Hz) 7.20 (2 H, d, *J*=7.7 Hz) 7.26 (1 H, d, *J*=8.2 Hz) 7.36 (1 H, t, *J*=7.7 Hz) 7.40 - 7.44 (1 H, m) 7.68 (1 H, d, *J*=8.6 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 16.2, 26.8, 35.8, 110.3, 120.5, 120.9, 123.7, 126.2, 126.5, 129.2, 131.2, 140.6, 142.4, 144.4. m/z [CI$^+$, isobutane] 265 [M+H]$^+$ (100%), HRMS found [M+H]$^+$ 265.1697, $C_{18}H_{21}N_2$ requires 265.1705. MP: 91-93 °C.

3-(4-Methoxyphenyl)-1-methyl-indazole, 12

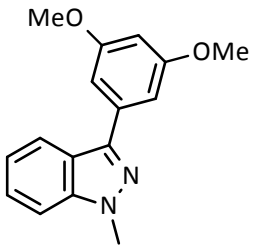


Using General Procedure 3, XPHOS-Pd-G2 (6 mg, 8 µmol, 0.02 Eq.), tripotassium phosphate (169 mg, 0.795 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (127 mg, 0.492 mmol, 1.3 Eq.), 1-chloro-4-methoxy-benzene (54 mg, 0.379 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 °C for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-5% EtOAc:Hexane,

provided the desired product, 3-(4-methoxyphenyl)-1-methyl-indazole **12** (69 mg, 0.290 mmol, 76%) as a colourless oil.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.83 (3 H, s) 4.09 (3 H, s) 7.03 - 7.14 (2 H, m) 7.21 (1 H, t, *J*=7.5 Hz) 7.45 (1 H, t, *J*=7.5 Hz) 7.67 (1 H, d, *J*=8.3 Hz) 7.84 - 7.96 (2 H, m) 8.03 (1 H, d, *J*=7.8 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 35.9, 55.7, 110.5, 114.8, 121.0, 121.3, 121.4, 126.4, 126.6, 128.4, 141.6, 142.4, 159.4. m/z [Cl$^+$, isobutane] 239 [M+H]$^+$ (100%), HRMS found [M+H]$^+$ 239.1176, $C_{15}H_{15}N_2O$ requires 239.1184.

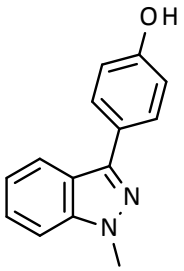
3-(3,5-Dimethoxyphenyl)-1-methyl-indazole, 13



Using General Procedure 3, XPHOS-Pd-G2 (6 mg, 7 µmol, 0.02 Eq.), tripotassium phosphate (147 mg, 0.694 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (111 mg, 0.429 mmol, 1.3 Eq.), 1-chloro-3,5-dimethoxy-benzene (57 mg, 0.330 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 ^{o}C for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-7.5% EtOAc:Hexane, provided the desired product, 3-(3,5-Dimethoxyphenyl)-1-methyl-indazole **13** (81 mg, 0.302 mmol, 91%) as a colourless oil.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.84 (6 H, s) 4.11 (3 H, s) 6.55 (1 H, t, *J*=2.2 Hz) 7.06 (2 H, d, *J*=2.4 Hz) 7.24 (1 H, t, *J*=7.6 Hz) 7.42 - 7.50 (1 H, m) 7.70 (1 H, d, *J*=8.3 Hz) 8.04 (1 H, d, *J*=7.8 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 36.0, 55.8, 100.4, 105.1, 110.6, 121.1, 121.2, 121.8, 126.7, 135.7, 141.7, 142.3, 161.3. m/z [Cl$^+$, isobutane] 269 [M+H]$^+$ (100%), HRMS found [M+H]$^+$ 269.1282, $C_{16}H_{17}N_2O_2$ requires 269.1290. MP: 47-50 ^{o}C.

4-(1-Methylindazol-3-yl)phenol, 14



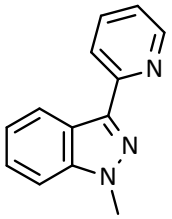
Using General Procedure 3, XPHOS-Pd-G2 (7 mg, 8 µmol, 0.02 Eq.), tripotassium phosphate (173 mg, 0.817 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (131 mg, 0.506 mmol, 1.3 Eq.), 4-chlorophenol (50 mg, 0.326 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 °C for 20 min. Standard work up with EtOAc, followed by flash column chromatography, elution with 0-40% EtOAc:Hexane, provided the desired product, 4-(1-Methylindazol-3-yl)phenol **14** (73 mg, 0.326 mmol, 84%) as a white solid.

Using General Procedure 4, 1-methyl-*1H*-indazole (300 mg, 2.27 mmol), B_2Pin_2 (288 mg 1.13 mmol), dtbpy (1.8 mg, 6.8 µmol, 0.003 Eq.) and $[Ir(OMe)COD]_2$ (2.3 mg 3.4 µmol) in TBME (5 mL) were heated at reflux (55 °C) under N_2 for 90 min. The reaction was cooled to RT and the contents were transferred to a microwave vial. Tripotassium phosphate (534 mg, 2.52 mmol), XPHOS-Pd-G2(15 mg, 18 µmol), 4-chlorophenol (154 mg, 1.20 mmol) and water (0.5 mL) were added.* The reaction mixture was heated in a microwave reactor at 100 °C for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-40% EtOAc:Hexane, provided the desired product, 4-(1-methylindazol-3-yl)phenol **14** (71 mg, 0.318 mmol, 82%) as a white solid.

*Based on GC-MS for borylation step: 74% conversion to 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** provides approx. 1.68 mmol, 1.4 Eq. of active boronate species.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.06 (3 H, s) 6.93 (2 H, d, *J*=8.6 Hz) 7.18 (1 H, t, *J*=7.5 Hz) 7.42 (1 H, t, *J*=7.6 Hz) 7.62 (1 H, d, *J*=8.6 Hz) 7.80 (2 H, d, *J*=8.6 Hz) 8.00 (1 H, d, *J*=8.2 Hz) 9.65 (1 H, s). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 35.8. 110.3, 116.2, 120.9, 121.2, 121.4, 124.8, 126.5, 128.5, 141.6, 142.8, 157.7. m/z [Cl^+, isobutane] 225 $[M+H]^+$ (100%), HRMS found $[M+H]^+$ 225.1019, $C_{14}H_{12}N_2O$ requires 225.1028. MP: 242-145 °C.

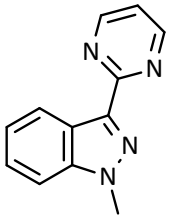
1-Methyl-3-(2-pyridyl)indazole, 15



Using General Procedure 3, XPHOS-Pd-G2 (7 mg, 9 µmol, 0.02 Eq.), tripotassium phosphate (196 mg, 0.925 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (148 mg, 0.573 mmol, 1.3 Eq.), 2-chloropyridine (50 mg, 0.440 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 °C for 20 min. Standard work up with EtOAc, followed by flash column chromatography, elution with 0-2% MeOH:DCM, provided the desired product, 1-methyl-3-(2-pyridyl)indazole **15** (80 mg, 0.382 mmol, 87%) as a colourless oil.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.14 (3 H, s) 7.26 (1 H, t, *J*=7.5 Hz) 7.35 (1 H, t, *J*=6.2 Hz) 7.46 (1 H, t, *J*=7.6 Hz) 7.69 (1 H, d, *J*=8.6 Hz) 7.88 (1 H, td, *J*=7.8, 1.7 Hz) 8.13 (1 H, d, *J*=7.9 Hz) 8.59 (1 H, d, *J*=8.2 Hz) 8.72 (1 H, d, *J*=4.8 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm 36.2, 110.4, 120.5, 122.0, 122.0, 122.9, 123.7, 126.9, 137.3, 141.8, 141.9, 149.8, 153.6. m/z [Cl$^+$, isobutane] 210 [M+H]$^+$ (100%), HRMS found [M+H]$^+$ 210.1022, $C_{13}H_{12}N_3$ requires 210.1031.

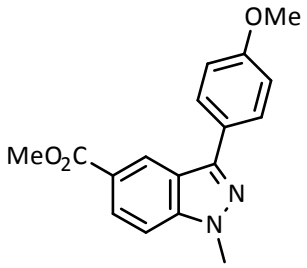
1-Methyl-3-pyrimidin-2-yl-indazole, 16



Using General Procedure 3, XPHOS-Pd-G2 (9 mg, 10 µmol, 0.02 Eq.), tripotassium phosphate (224 mg, 1.06 mmol, 2.10 Eq.), 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole **7** (156 mg, 0.604 mmol, 1.3 Eq.), 2-bromopyrimidine (80 mg, 0.503 mmol, 1.00 Eq.) in TBME (5 mL) and water (0.5 mL) was heated in a microwave reactor at 100 °C for 20 min. Standard work up with EtOAc, followed by flash column chromatography, elution with 0-100% EtOAc:Hexane, provided the desired product, 1-methyl-3-pyrimidin-2-yl-indazole **16** (103 mg, 0.490 mmol, 97%) as a beige solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.23 (3 H, s) 7.22 (1 H, t, *J*=4.8 Hz) 7.32 (1 H, ddd, *J*=8.1, 4.7, 3.2 Hz) 7.45 - 7.48 (2 H, m) 8.68 (1 H, d, *J*=8.2 Hz) 8.89 (2 H, d, *J*=4.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 36.2, 109.2, 119.0, 122.2, 123.2, 123.6, 126.6, 141.4, 141.6, 157.4, 161.7. m/z [CI^+, isobutane] 211 $[M+H]^+$ (100%), HRMS found $[M+H]^+$ 211.0976, $C_{12}H_{11}N_4$ requires 211.0984. MP: 76-78 °C.

Methyl 3-(4-methoxyphenyl)-1-methyl-indazole-5-carboxylate, 17

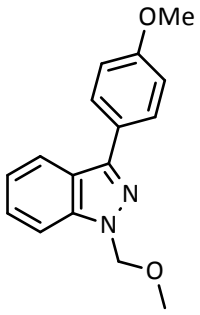


Using General Procedure 4, methyl 1-methyl-*1H*-indazole-5-carboxylate (225 mg, 1.18 mmol), B_2Pin_2 (300 mg 1.18 mmol), dtbpy (1.9 mg, 7.1 µmol) and $[Ir(OMe)COD]_2$ (2.3 mg, 3.5 µmol) in TBME (5 mL) were heated at reflux (55 °C) under N_2 for 2.5 h. The reaction was cooled to RT and the contents were transferred to a microwave vial. Tripotassium phosphate (309 mg, 1.46 mmol), XPHOS-Pd-G2 (12 mg, 15 µmol), 1-chloro-4-methoxy-benzene (104 mg, 0.728 mmol) and water (0.5 mL) were added.* The reaction mixture was heated in a microwave reactor at 100 °C for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-10% EtOAc:Hexane, provided the desired product, methyl 3-(4-hydroxyphenyl)-1-methyl-indazole-5-carboxylate **17** (140 mg, 0.473 mmol, 65%) as a white solid.

*Based on GC-MS for borylation step: 80% conversion to methyl 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole-5-carboxylate provides approx. 0.946 mmol, 1.3 Eq. of active boronate species.

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 3.89 (3 H, s) 3.95 (3 H, s) 4.13 (3 H, s) 7.02 - 7.11 (2 H, m) 7.40 (1 H, d, *J*=8.8 Hz) 7.87 - 7.93 (2 H, m) 8.09 (1 H, dd, *J*=8.8, 1.5 Hz) 8.74 (1 H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 35.7, 52.1, 55.4, 108.8, 114.4, 121.3, 122.9, 125.0, 125.5, 127.2, 128.8, 143.1, 145.5, 159.9, 167.4. m/z [CI^+, isobutane] 297 $[M+H]^+$ (100%), HRMS found $[M+H]^+$ 297.1229, $C_{17}H_{17}N_2O_3$ requires 297.1239. MP: 122-124 °C.

1-(Methoxymethyl)-3-(4-methoxyphenyl)indazole, 18

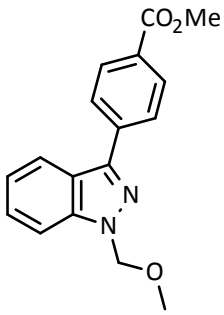


Using General Procedure 4, 1-(methoxymethyl)indazole (471 mg, 2.89 mmol), B_2Pin_2 (738 mg 2.89 mmol), dtbpy (4.6 mg, 17 µmol) and $[Ir(OMe)COD]_2$ (5.8 mg, 8.6 µmol) in TBME (10 mL) were heated at reflux (55 ^oC) under N_2 for 70 min. The reaction was cooled to RT and the contents were transferred to a microwave vial. Tripotassium phosphate (790 mg, 3.72 mmol, 2.0 Eq.), XPHOS-Pd-G2(23 mg, 28 µmol), 1-chloro-4-methoxy-benzene (274 mg, 1.86 mmol) and water (1 mL) were added.* The reaction mixture was heated in a microwave reactor at 100 ^oC for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-4% EtOAc:Hexane, provided the desired product, 1-(methoxymethyl)-3-(4-methoxyphenyl)indazole **18** (349 mg, 1.30 mmol, 70%) as a white solid.

*Based on GC-MS for borylation step: 90% conversion to 1-(methoxymethyl)-3-[4-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)phenyl]indazole provides approx. 2.60 mmol, 1.4 Eq. of active boronate species.

^1H NMR (500 MHz, $CDCl_3$) δ ppm 3.36 (3 H, s) 3.88 (3 H, s), 5.74 (2 H, s) 7.05 (2 H, d, *J*=8.4 Hz) 7.25 (1 H, t, *J*=7.7 Hz) 7.44 (1 H, t, *J*=7.6 Hz) 7.58 (1 H, d, *J*=8.4 Hz) 7.89 - 7.93 (1 H, m) 7.91 (2 H, d, *J*=8.3 Hz) 7.99 (1 H, d, *J*=8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 55.4, 56.6, 79.4, 109.8, 114.3, 121.5, 121.6, 122.6, 125.9, 126.8, 128.9, 141.3, 145.0, 159.7. m/z [CI^+, isobutane] 269 $[M+H]^+$ (100%), HRMS found $[M+H]^+$ 269.1274, $C_{16}H_{17}N_2O_2$ requires 269.1285. MP: 52-53 ^oC.

Methyl 4-[1-(methoxymethyl)indazol-3-yl]benzoate, 19

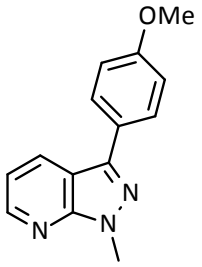


Using General Procedure 4, 1-(methoxymethyl)indazole (471 mg, 2.89 mmol), B_2Pin_2 (738 mg 2.89 mmol), dtbpy (4.6 mg, 17 µmol) and $[Ir(OMe)COD]_2$ (5.8 mg, 8.6 µmol) in TBME (10 mL) were heated at reflux (55 ^oC) under N_2 for 70 min. The reaction was cooled to RT and the contents were transferred to a microwave vial. Tripotassium phosphate (790 mg, 3.72 mmol), XPHOS-Pd-G2(23 mg, 28 µmol), methyl 4-bromobenzoate (400 mg, 1.86 mmol) and water (1 mL) were added.* The reaction mixture was heated in a microwave reactor at 100 ^oC for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-100% DCM:Hexane, provided the desired product, methyl 4-[1-(methoxymethyl)indazol-3-yl]benzoate **19** (430 mg, 1.45 mmol, 78%) as a white solid.

*Based on GC-MS for borylation step: 90% conversion to 1-(methoxymethyl)-3-[4-(4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)phenyl]indazole provides approx. 2.60 mmol, 1.4 Eq. of active boronate species.

^1H NMR (500 MHz, $CDCl_3$) δ ppm 3.38 (3 H, s) 3.96 (3 H, s) 5.78 (2 H, s) 7.28 - 7.33 (1 H, m) 7.46 - 7.51 (1 H, m) 7.63 (1 H, d, *J*=8.5 Hz) 8.05 (1 H, d, *J*=8.2 Hz) 8.07 - 8.10 (2 H, m) 8.17 - 8.20 (2 H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 52.2, 56.7, 79.7, 110.1, 121.2, 122.3, 122.6, 127.1, 127.3, 129.6, 130.1, 137.8, 141.4, 143.9, 166.9. m/z [CI^+, isobutane] 297 $[M+H]^+$ (100%), HRMS found $[M+H]^+$ 297.1223, $C_{17}H_{17}N_2O_3$ requires 297.1234. MP: 110-112 ^oC.

3-(4-Methoxyphenyl)-1-methyl-pyrazolo[3,4-b]pyridine, 20

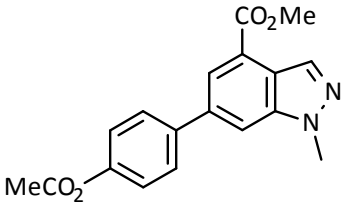


Using General Procedure 4, 1-methylpyrazolo[3,4-*b*]pyridine (245 mg, 1.35 mmol), B_2Pin_2 (173 mg, 0.681 mmol), dtbpy (2.2 mg, 8.1 µmol, 0.006 Eq.) and $[Ir(OMe)COD]_2$ (2.7 mg, 4.1 µmol) in TBME (5 mL) were heated at reflux (55 ^oC) under N_2 for 4 h. The reaction was cooled to RT and the contents were transferred to a microwave vial. Tripotassium phosphate (287 mg, 1.35 mmol), XPHOS-Pd-G2(9 mg, 11 µmol), 1-chloro-4-methoxy-benzene (96 mg, 0.68 mmol) and water (0.5 mL) were added.* The reaction mixture was heated in a microwave reactor at 100 ^oC for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-15% EtOAc:Hexane, provided the desired product, 3-(4-methoxyphenyl)-1-methyl-pyrazolo[3,4-*b*]pyridine **20** (114 mg, 0.476 mmol, 71%) as an off-white solid.

*Based on GC-MS for borylation step: 70% conversion to 1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazolo[3,4-b]pyridine provides approx. 1.95 mmol, 1.4 Eq. of active boronate species.

^1H NMR (400 MHz, $CDCl_3$) δ ppm 3.89 (3 H, s) 4.20 (3 H, s) 7.05 (2 H, d, *J*=8.7 Hz) 7.16 (1 H, dd, *J*=8.1, 4.5 Hz) 7.89 (2 H, d, *J*=8.7 Hz) 8.31 (1 H, d, *J*=8.1 Hz) 8.53 - 8.61 (1 H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 33.9, 55.4, 113.4, 114.4, 116.6, 125.9, 128.2, 130.5, 142.5, 148.6, 151.4, 159.8. m/z [Cl^+, isobutane] 240 $[M+H]^+$ (100%), HRMS found $[M+H]^+$ 240.1130, $C_{14}H_{14}N_3O$ requires 240.1137. MP: 67-69 ^oC.

Methyl 6-(4-methoxycarbonylphenyl)-1-methyl-indazole-4-carboxylate, 21



Using General Procedure 4, methyl 1-methyl-*1H*-indazole-4-carboxylate (232 mg, 1.22 mmol), B_2Pin_2 (310 mg 1.22 mmol), dtbpy (2.0 mg, 7.3 µmol) and $[Ir(OMe)COD]_2$ (2.5 mg, 3.7 µmol) in TBME (5 mL) were heated at reflux (55 ^oC) under N_2 for 6 h. The reaction was cooled to RT and the contents were transferred to a microwave vial. Tripotassium phosphate (259 mg, 1.22 mmol), XPHOS-Pd-G2(8 mg, 9 µmol), methyl 4-bromobenzoate (131 mg, 0.610 mmol) and water (0.5 mL) were added.* The reaction mixture was heated in a microwave reactor at 100 ^oC for 20 min. Standard work up with DCM, followed by flash column chromatography, elution with 0-10% EtOAc:Hexane, provided the undesired product, methyl 6-(4-methoxycarbonylphenyl)-1-methyl-indazole-4-carboxylate **21** (175 mg, 0.540 mmol, 89%) as a white solid.

*Based on GC-MS for borylation step: 85% conversion to methyl 1-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole-4-carboxylate provides approx. 0.854 mmol, 1.4 Eq. of active boronate species.

^1H NMR (400 MHz, $CDCl_3$) δ ppm 3.97 (3 H, s) 4.06 (3 H, s) 4.18 (3 H, s) 7.75 - 7.80 (2 H, m) 7.81 (1 H, t, *J*=1.1 Hz) 8.14 - 8.19 (2 H, m) 8.21 (1 H, d, *J*=1.3 Hz) 8.49 (1 H, d, *J*=0.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 35.9, 52.3, 52.3, 112.0, 122.1, 123.5, 124.1, 127.6, 129.5, 130.3, 133.7, 138.1, 141.0, 144.8, 166.6, 166.8. m/z [Cl^+, isobutane] 325 $[M+H]^+$ (100%), HRMS found $[M+H]^+$ 325.1181, $C_{18}H_{17}N_2O_4$ requires 325.1189. MP: 177-179 ^oC.