Supporting Information

A One-Pot Suzuki-Hydrogenolysis Protocol for the Modular Synthesis of 2,5-Diaryl Tetrazoles

Keith Livingstone,¹ Sophie Bertrand² and Craig Jamieson*¹

¹Department of Pure and Applied Chemistry, University of Strathclyde, 295 Cathedral Street, Glasgow, UK
²GlaxoSmithKline Medicines Research Centre, Gunnels Wood Road, Stevenage, Hertfordshire, UK, SG1 2NY.

*Email: Craig.Jamieson craig.jamieson@strath.ac.uk
Contents

General Procedures

S3
Optimization of Reaction
S5

NMR Spectra of Selected Compounds S33

References S72
1 General Procedures

1.1 A: Optimization of Suzuki Reaction Using High-Throughput Screening

In a glovebox, a 24 or 96-well plate containing 1 mL or 250 uL vials was charged with a relevant Pd precatalyst (10 mol%). 1-benzyl-5-bromo-1H-tetrazole (1 equiv.) and an aryl boronic acid (1.5 equiv.) were then added as a solution/slurry in a specified solvent (0.1 M). An inorganic base (2 equiv.) was then added as a solution in water (20 % volume of solvent). The plate was then sealed, removed from the glovebox and stirred at 100 °C for 24 hours. The reaction mixtures were diluted to a concentration of around 4 mM with acetonitrile containing a known concentration of internal standard, and analyzed by HPLC. Conversion values obtained were first normalized using the internal standard peak, and reported as relative values of the most successful reaction mixture.

1.2 B: Targeted Optimization of Suzuki Reaction

1-benzyl-5-bromo-1H-tetrazole (1 equiv.) and an aryl boronic acid were added to either 0.5-2 mL microwave vials or 2 mL HPLC vials. The vessels were then charged with the relevant palladium precatalyst as a solution in the solvent. In the instances where a palladium source and ligand was employed, both catalyst and ligand were added as a solution in the solvent. In the instances where the palladium source was not soluble in the solvent, the catalyst was added as a solid prior to the solvent. Base was added as a solution in water, and the vessel was sealed and purged with nitrogen. In the instances where extremely low equivalents of water were used, the base was added as a solid after the addition of water. Following reaction completion, the reaction mixture was diluted with a solution of caffeine (0.5 equiv.) in acetonitrile. The mixture was further diluted to a concentration of around 4 mM, analyzed by LCMS, and conversion values obtained.

1.3 C: Optimization of Debenzylation Using High-Throughput Screening

To a 24 or 96-well plate containing 1 mL vials was added a palladium on carbon catalyst, which was weighed using a Mettler Toledo QX-96 automated weighing instrument. 1-benzyl-5-phenyl-1H-tetrazole (1 equiv.) was added as a solution in the relevant solvent (0.17 M), and in some specified cases, acetic acid (1 equiv.) was added at this stage. The vials were sealed using caps that had been pierced 5-10 times with a blunt needle, and exposed to a hydrogen atmosphere of known pressure for 24 hours at either 40 °C or room temperature. Following reaction completion, the reaction mixtures were diluted to concentration of around 4 mM with acetonitrile and analyzed by HPLC. Conversion values are reported as a ratio of debenzylated product relative to remaining starting material.
1.4 D: Targeted Optimization of Debenzylation

To eight HEL HP ChemScan reaction vessels was added a palladium on carbon catalyst. 1-benzyl-5-phenyl-1\(H\)-tetrazole (1 equiv.) was added as a solution in ethanol (0.1 M). The vessels are then sealed and exposed to a hydrogen atmosphere of a known pressure at room temperature for 16 hours. Following reaction completion, the reaction mixtures were diluted to concentration of around 4 mM with acetonitrile and analyzed by HPLC. Conversion values are reported as a ratio of debenzylated product relative to remaining starting material.

1.5 E: Optimization of One-Pot Suzuki Hydrogenolysis

To eight Biotage Endeavor reaction vessels was added a solution of 1-benzyl-5-phenyl-1\(H\)-tetrazole (1 equiv.), phenylboronic acid (1.3 equiv.), and XPhos Pd G3 (3 mol%) as a solution in a known volume of solvent. Evonik Noblyst® P1071 20% palladium on carbon was added to each vessel, before cesium carbonate (1.5 equiv.) was added as a solution in water (100 equiv.). The vessels were purged with nitrogen, and heated at 100 °C for 4 hours. The vessels were then cooled to 40 °C, and in some instances ethanol was added to the mixture at this stage. The reaction mixture was then stirred under a hydrogen atmosphere of a specified pressure at 40 °C for between 16 and 24 hours. Following reaction completion, the reaction mixture was diluted with a solution of caffeine (0.5 equiv.) in acetonitrile. The mixture was further diluted to a concentration of around 4 mM, analyzed by LCMS, and conversion values obtained.
2 Optimization of Reaction Conditions

2.1 Optimization of Suzuki Reaction

High-Throughput Screen 1

The screen was conducted as outlined in general procedure A using 24 x 250 μL vials, each containing 1-benzyl-5-bromo-1H-tetrazole (0.60 mg, 2.5 μmol), phenylboronic acid (0.46 mg, 3.75 μmol), XPhos, SPhos, DTnBuP, AmPhos, DTBPF, or tBu3P Pd G3 precatalysts (all 0.25 μmol), potassium carbonate (0.70 mg, 5 μmol) or potassium phosphate (1.06 mg, 5 μmol), toluene or dioxane (both 240 μL), and water (60 μL). The results obtained are detailed in Table S1.

| Entry | Catalyst | Solvent | Base         | Conversion° |
|-------|----------|---------|--------------|-------------|
| 1     | XPhos    | Toluene | K3PO4        | 0.36        |
| 2     | SPhos    | Toluene | K3PO4        | 0.14        |
| 3     | DTnBuP   | Toluene | K3PO4        | 0.03        |
| 4     | AmPhos   | Toluene | K3PO4        | 0.01        |
| 5     | DTBPF    | Toluene | K3PO4        | 0.09        |
| 6     | tBu3P    | Toluene | K3PO4        | 0.02        |
| 7     | XPhos    | Toluene | K2CO3        | 1.00        |
| 8     | SPhos    | Toluene | K2CO3        | 0.17        |
| 9     | DTnBuP   | Toluene | K2CO3        | 0.25        |
| 10    | AmPhos   | Toluene | K2CO3        | 0.37        |
| 11    | DTBPF    | Toluene | K2CO3        | 0.13        |
| No. | Catalyst      | Solvent | Base            | Conversion |
|-----|---------------|---------|-----------------|------------|
| 12  | tBu₃P        | Toluene | K₂CO₃           | 0.06       |
| 13  | XPhos        | Dioxane | K₃PO₄           | 0.17       |
| 14  | SPhos        | Dioxane | K₃PO₄           | 0.24       |
| 15  | DTnBuP       | Dioxane | K₃PO₄           | 0.08       |
| 16  | AmPhos       | Dioxane | K₂CO₃           | 0.05       |
| 17  | DTBPF        | Dioxane | K₃PO₄           | 0.06       |
| 18  | tBu₃P        | Dioxane | K₃PO₄           | 0.03       |
| 19  | XPhos        | Dioxane | K₂CO₃           | 0.18       |
| 20  | SPhos        | Dioxane | K₂CO₃           | 0.16       |
| 21  | DTnBuP       | Dioxane | K₂CO₃           | 0.15       |
| 22  | AmPhos       | Dioxane | K₂CO₃           | 0.10       |
| 23  | DTBPF        | Dioxane | K₂CO₃           | 0.03       |
| 24  | tBu₃P        | Dioxane | K₂CO₃           | 0.04       |

<Conversions determined by HPLC and reported relative to the highest recorded value with reference to an internal standard.

High-Throughput Screen 2

The screen was conducted as outlined in general procedure A using 96 x 1 mL vials, each containing 1-benzyl-5-bromo-1H-tetrazole (2.40 mg, 10 μmol), 4-methoxyphenylboronic acid, 4-fluorophenylboronic acid, 4-cyanophenylboronic acid, or 4-pyridinylboronic acid (all 15 μmol), XPhos, SPhos, DTnBuP, AmPhos, DTBPF, or tBu₃P Pd G3 precatalysts (all 1 μmol), potassium carbonate (2.80 mg, 20 μmol) or cesium carbonate (2.50 mg, 20 μmol), toluene or acetonitrile (both 960 μL), and water (240 μL). The results obtained are detailed in Table S2.
Table S2: Conversion values obtained from high-throughput screen 2

| Entry | Boronic Acid       | Catalyst | Solvent | Base       | Conversion* |
|-------|--------------------|----------|---------|------------|-------------|
| 1     | 4-methoxyphenyl    | XPhos    | MeCN    | Cs₂CO₃     | 0.27        |
| 2     | 4-methoxyphenyl    | SPhos    | MeCN    | Cs₂CO₃     | 0.19        |
| 3     | 4-methoxyphenyl    | DTnBuP   | MeCN    | Cs₂CO₃     | 0.22        |
| 4     | 4-methoxyphenyl    | AmPhos   | MeCN    | Cs₂CO₃     | 0.03        |
| 5     | 4-methoxyphenyl    | DTBPF    | MeCN    | Cs₂CO₃     | 0.12        |
| 6     | 4-methoxyphenyl    | tBu₃P    | MeCN    | Cs₂CO₃     | 0.01        |
| 7     | 4-methoxyphenyl    | XPhos    | MeCN    | K₂CO₃      | 0.30        |
| 8     | 4-methoxyphenyl    | SPhos    | MeCN    | K₂CO₃      | 0.22        |
| 9     | 4-methoxyphenyl    | DTnBuP   | MeCN    | K₂CO₃      | 0.31        |
| 10    | 4-methoxyphenyl    | AmPhos   | MeCN    | K₂CO₃      | 0.03        |
| 11    | 4-methoxyphenyl    | DTBPF    | MeCN    | K₂CO₃      | 0.02        |
| 12    | 4-methoxyphenyl    | tBu₃P    | MeCN    | K₂CO₃      | 0.04        |
| 13    | 4-methoxyphenyl    | XPhos    | Toluene | Cs₂CO₃     | 0.93        |
| 14    | 4-methoxyphenyl    | SPhos    | Toluene | Cs₂CO₃     | 0.73        |
| 15    | 4-methoxyphenyl    | DTnBuP   | Toluene | Cs₂CO₃     | 1.00        |
| 16    | 4-methoxyphenyl    | AmPhos   | Toluene | Cs₂CO₃     | 0.18        |
| 17    | 4-methoxyphenyl    | DTBPF    | Toluene | Cs₂CO₃     | 0.11        |
| 18    | 4-methoxyphenyl    | tBu₃P    | Toluene | Cs₂CO₃     | 0.15        |
| 19    | 4-methoxyphenyl    | XPhos    | Toluene | K₂CO₃      | 0.67        |
| 20    | 4-methoxyphenyl    | SPhos    | Toluene | K₂CO₃      | 0.79        |
| 21    | 4-methoxyphenyl    | DTnBuP   | Toluene | K₂CO₃      | 0.61        |
| 22    | 4-methoxyphenyl    | AmPhos   | Toluene | K₂CO₃      | 0.18        |
|   | 4-fluorophenyl | Ligand   | Solvent | Base   | Yield  |
|---|----------------|----------|---------|--------|--------|
| 23 | 4-methoxyphenyl | DTBPF    | Toluene | K$_2$CO$_3$ | 0.11 |
| 24 | 4-methoxyphenyl | tBu$_3$P | Toluene | K$_2$CO$_3$ | 0.20 |
| 25 | 4-fluorophenyl  | XPhos    | MeCN    | Cs$_2$CO$_3$ | 0.22 |
| 26 | 4-fluorophenyl  | SPhos    | MeCN    | Cs$_2$CO$_3$ | 0.16 |
| 27 | 4-fluorophenyl  | DTnBuP   | MeCN    | Cs$_2$CO$_3$ | 0.23 |
| 28 | 4-fluorophenyl  | AmPhos   | MeCN    | Cs$_2$CO$_3$ | 0.02 |
| 29 | 4-fluorophenyl  | DTBPF    | MeCN    | Cs$_2$CO$_3$ | 0.02 |
| 30 | 4-fluorophenyl  | tBu$_3$P | MeCN    | Cs$_2$CO$_3$ | 0.01 |
| 31 | 4-fluorophenyl  | XPhos    | MeCN    | K$_2$CO$_3$  | 0.20 |
| 32 | 4-fluorophenyl  | SPhos    | MeCN    | K$_2$CO$_3$  | 0.15 |
| 33 | 4-fluorophenyl  | DTnBuP   | MeCN    | K$_2$CO$_3$  | 0.20 |
| 34 | 4-fluorophenyl  | AmPhos   | MeCN    | K$_2$CO$_3$  | 0.06 |
| 35 | 4-fluorophenyl  | DTBPF    | MeCN    | K$_2$CO$_3$  | 0.06 |
| 36 | 4-fluorophenyl  | tBu$_3$P | MeCN    | K$_2$CO$_3$  | 0.01 |
| 37 | 4-fluorophenyl  | XPhos    | Toluene | Cs$_2$CO$_3$ | 1.00 |
| 38 | 4-fluorophenyl  | SPhos    | Toluene | Cs$_2$CO$_3$ | 0.95 |
| 39 | 4-fluorophenyl  | DTnBuP   | Toluene | Cs$_2$CO$_3$ | 0.38 |
| 40 | 4-fluorophenyl  | AmPhos   | Toluene | Cs$_2$CO$_3$ | 0.16 |
| 41 | 4-fluorophenyl  | DTBPF    | Toluene | Cs$_2$CO$_3$ | 0.08 |
| 42 | 4-fluorophenyl  | tBu$_3$P | Toluene | Cs$_2$CO$_3$ | 0.14 |
| 43 | 4-fluorophenyl  | XPhos    | Toluene | K$_2$CO$_3$  | 0.98 |
| 44 | 4-fluorophenyl  | SPhos    | Toluene | K$_2$CO$_3$  | 0.71 |
| 45 | 4-fluorophenyl  | DTnBuP   | Toluene | K$_2$CO$_3$  | 0.32 |
| 46 | 4-fluorophenyl  | AmPhos   | Toluene | K$_2$CO$_3$  | 0.15 |
| No. | Ligand            | Additive | Solvent | Base   | Yield |
|-----|------------------|----------|---------|--------|-------|
| 47  | 4-fluorophenyl  | DTBPF    | Toluene | K$_2$CO$_3$ | 0.07  |
| 48  | 4-fluorophenyl  | tBu$_3$P | Toluene | K$_2$CO$_3$ | 0.10  |
| 49  | 4-cyanophenyl   | XPhos    | MeCN    | Cs$_2$CO$_3$ | 0.33  |
| 50  | 4-cyanophenyl   | SPhos    | MeCN    | Cs$_2$CO$_3$ | 0.00  |
| 51  | 4-cyanophenyl   | DTnBuP   | MeCN    | Cs$_2$CO$_3$ | 0.00  |
| 52  | 4-cyanophenyl   | AmPhos   | MeCN    | Cs$_2$CO$_3$ | 0.00  |
| 53  | 4-cyanophenyl   | DTBPF    | MeCN    | Cs$_2$CO$_3$ | 0.19  |
| 54  | 4-cyanophenyl   | tBu$_3$P | MeCN    | Cs$_2$CO$_3$ | 0.00  |
| 55  | 4-cyanophenyl   | XPhos    | MeCN    | K$_2$CO$_3$  | 0.33  |
| 56  | 4-cyanophenyl   | SPhos    | MeCN    | K$_2$CO$_3$  | 0.28  |
| 57  | 4-cyanophenyl   | DTnBuP   | MeCN    | K$_2$CO$_3$  | 0.21  |
| 58  | 4-cyanophenyl   | AmPhos   | MeCN    | K$_2$CO$_3$  | 0.07  |
| 59  | 4-cyanophenyl   | DTBPF    | MeCN    | K$_2$CO$_3$  | 0.00  |
| 60  | 4-cyanophenyl   | tBu$_3$P | MeCN    | K$_2$CO$_3$  | 0.17  |
| 61  | 4-cyanophenyl   | XPhos    | Toluene | Cs$_2$CO$_3$ | 1.00  |
| 62  | 4-cyanophenyl   | SPhos    | Toluene | Cs$_2$CO$_3$ | 0.56  |
| 63  | 4-cyanophenyl   | DTnBuP   | Toluene | Cs$_2$CO$_3$ | 0.73  |
| 64  | 4-cyanophenyl   | AmPhos   | Toluene | Cs$_2$CO$_3$ | 0.14  |
| 65  | 4-cyanophenyl   | DTBPF    | Toluene | Cs$_2$CO$_3$ | 0.58  |
| 66  | 4-cyanophenyl   | tBu$_3$P | Toluene | Cs$_2$CO$_3$ | 0.61  |
| 67  | 4-cyanophenyl   | XPhos    | Toluene | K$_2$CO$_3$  | 0.81  |
| 68  | 4-cyanophenyl   | SPhos    | Toluene | K$_2$CO$_3$  | 0.00  |
| 69  | 4-cyanophenyl   | DTnBuP   | Toluene | K$_2$CO$_3$  | 0.00  |
| 70  | 4-cyanophenyl   | AmPhos   | Toluene | K$_2$CO$_3$  | 0.00  |
|    | Ligand            | Phosphine | Solvent  | Base    | Conversion |
|----|------------------|-----------|----------|---------|------------|
| 71 | 4-cyanophenyl    | DTBPF     | Toluene  | K$_2$CO$_3$ | 0.33       |
| 72 | 4-cyanophenyl    | tBu$_3$P  | Toluene  | K$_2$CO$_3$ | 0.12       |
| 73 | 4-pyridinyl      | XPhos     | MeCN     | Cs$_2$CO$_3$ | 0.00       |
| 74 | 4-pyridinyl      | SPhos     | MeCN     | Cs$_2$CO$_3$ | 0.00       |
| 75 | 4-pyridinyl      | DTnBuP    | MeCN     | Cs$_2$CO$_3$ | 0.00       |
| 76 | 4-pyridinyl      | AmPhos    | MeCN     | Cs$_2$CO$_3$ | 0.00       |
| 77 | 4-pyridinyl      | DTBPF     | MeCN     | Cs$_2$CO$_3$ | 0.00       |
| 78 | 4-pyridinyl      | tBu$_3$P  | MeCN     | Cs$_2$CO$_3$ | 0.00       |
| 79 | 4-pyridinyl      | XPhos     | MeCN     | K$_2$CO$_3$  | 0.00       |
| 80 | 4-pyridinyl      | SPhos     | MeCN     | K$_2$CO$_3$  | 0.00       |
| 81 | 4-pyridinyl      | DTnBuP    | MeCN     | K$_2$CO$_3$  | 0.00       |
| 82 | 4-pyridinyl      | AmPhos    | MeCN     | K$_2$CO$_3$  | 0.00       |
| 83 | 4-pyridinyl      | DTBPF     | MeCN     | K$_2$CO$_3$  | 0.00       |
| 84 | 4-pyridinyl      | tBu$_3$P  | MeCN     | K$_2$CO$_3$  | 0.00       |
| 85 | 4-pyridinyl      | XPhos     | Toluene  | Cs$_2$CO$_3$ | 0.00       |
| 86 | 4-pyridinyl      | SPhos     | Toluene  | Cs$_2$CO$_3$ | 0.00       |
| 87 | 4-pyridinyl      | DTnBuP    | Toluene  | Cs$_2$CO$_3$ | 0.00       |
| 88 | 4-pyridinyl      | AmPhos    | Toluene  | Cs$_2$CO$_3$ | 0.00       |
| 89 | 4-pyridinyl      | DTBPF     | Toluene  | Cs$_2$CO$_3$ | 0.00       |
| 90 | 4-pyridinyl      | tBu$_3$P  | Toluene  | Cs$_2$CO$_3$ | 0.00       |
| 91 | 4-pyridinyl      | XPhos     | Toluene  | K$_2$CO$_3$  | 0.00       |
| 92 | 4-pyridinyl      | SPhos     | Toluene  | K$_2$CO$_3$  | 0.00       |
| 93 | 4-pyridinyl      | DTnBuP    | Toluene  | K$_2$CO$_3$  | 0.00       |
| 94 | 4-pyridinyl      | AmPhos    | Toluene  | K$_2$CO$_3$  | 0.00       |
The screen was conducted as outlined in general procedure B using 5 x microwave vials, each containing 1-benzyl-5-bromo-1H-tetrazole (12.0 mg, 50 μmol), phenylboronic acid (9.1 mg, 75 μmol), XPhos Pd G3 (4.2 mg, 5 μmol), potassium carbonate (14 mg, 100 μmol), toluene (500 μL), and water (1-50 equivalents). The reaction was stirred at 100 °C for 3 hours. The results obtained are detailed in Table S3.

Table S3: Conversion values obtained from targeted screen 1

| Entry | Water Stoichiometry (equivs) | Conversiona |
|-------|-------------------------------|-------------|
| 1     | 1                             | 64          |
| 2     | 5                             | 73          |
| 3     | 10                            | 76          |
| 4     | 20                            | 75          |
| 5     | 50                            | 70          |

*a*Conversions determined by LCMS with reference to caffeine as an internal standard.
Targeted Screen 2

The screen was conducted as outlined in general procedure B using 5 x microwave vials, each containing 1-benzyl-5-bromo-1H-tetrazole (12.0 mg, 50 µmol), phenylboronic acid (9.1 mg, 75 µmol), an XPhos precatalyst (5 µmol), potassium carbonate (14 mg, 100 µmol), toluene (500 µL), and water (9 µL, 500 µmol). In the instance where XPhos (2.7 mg, 5 µmol) was employed, palladium(II) acetate (1.1 mg, 5 µmol) was also added as a palladium source. The reaction was stirred at 100 °C for 3 hours. The results obtained are detailed in Table S4.

Table S4: Conversion values obtained from targeted screen 2

| Entry | (Pre)catalyst | Conversion* |
|-------|---------------|-------------|
| 1     | XPhos + Pd(OAc)$_2$ | 50          |
| 2     | XPhos Pd G1    | 65          |
| 3     | XPhos Pd G2    | 66          |
| 4     | XPhos Pd G3    | 63          |
| 5     | XPhos Pd G4    | 70          |

*Conversions relative to highest recorded value with reference to caffeine as an internal standard.

Targeted Screen 3

The screen was conducted as outlined in general procedure B using 48 x 2 mL HPLC vials, each containing 1-benzyl-5-bromo-1H-tetrazole (12.0 mg, 50 µmol), (4-(trifluoromethyl)phenyl)boronic acid (14.2 mg, 75 µmol), (4-cyanophenyl)boronic acid (11.0 mg, 75 µmol), (4-(trifluoromethyl)phenyl)boronic acid pinacol ester (20.4 mg, 75 µmol), or (4-cyanophenyl)boronic acid pinacol ester (17.2 mg, 75 µmol), XPhos Pd G3 (4.2 mg, 5.0 µmol) or SPhos Pd G3 (3.9 mg, 5.0
µmol), cesium carbonate (32.6 mg, 100 µmol), potassium phosphate (21.2 mg, 100 µmol) or potassium carbonate (13.8 mg, 100 µmol), toluene or n-butanol (both 500 µL), and water (45 µL, 2500 µmol). The reaction was stirred at 100 °C for 16 hours. The results obtained are detailed in Table S5.

Table S5: Conversion values obtained from targeted screen 3

| Entry | Boron Species     | Catalyst | Solvent | Base     | Conversion* |
|-------|-------------------|----------|---------|----------|-------------|
| 1     | (4-CF₃)PhB(OH)₂   | XPhos    | Toluene | K₂CO₃    | 54          |
| 2     | (4-CF₃)PhB(OH)₂   | XPhos    | Toluene | Cs₂CO₃   | 59          |
| 3     | (4-CF₃)PhB(OH)₂   | XPhos    | Toluene | K₃PO₄    | 52          |
| 4     | (4-CF₃)PhB(OH)₂   | SPhos    | Toluene | K₂CO₃    | 32          |
| 5     | (4-CF₃)PhB(OH)₂   | SPhos    | Toluene | Cs₂CO₃   | 30          |
| 6     | (4-CF₃)PhB(OH)₂   | SPhos    | Toluene | K₃PO₄    | 39          |
| 7     | (4-CF₃)PhB(OH)₂   | XPhos    | n-Butanol | K₂CO₃ | 13          |
| 8     | (4-CF₃)PhB(OH)₂   | XPhos    | n-Butanol | Cs₂CO₃ | 10          |
| 9     | (4-CF₃)PhB(OH)₂   | XPhos    | n-Butanol | K₃PO₄ | 9           |
| 10    | (4-CF₃)PhB(OH)₂   | SPhos    | n-Butanol | K₂CO₃ | 9           |
| 11    | (4-CF₃)PhB(OH)₂   | SPhos    | n-Butanol | Cs₂CO₃ | 7           |
| 12    | (4-CF₃)PhB(OH)₂   | SPhos    | n-Butanol | K₃PO₄ | 8           |
| 13    | (4-CF₃)PhBPin     | XPhos    | Toluene | K₂CO₃    | 4           |
| 14    | (4-CF₃)PhBPin     | XPhos    | Toluene | Cs₂CO₃   | 9           |
| 15    | (4-CF₃)PhBPin     | XPhos    | Toluene | K₃PO₄    | 15          |
| 16    | (4-CF₃)PhBPin     | SPhos    | Toluene | K₂CO₃    | 5           |
| 17    | (4-CF₃)PhBPin     | SPhos    | Toluene | Cs₂CO₃   | 5           |
|   | Reaction  | Catalyst | Solvent  | Base       | Yield |
|---|-----------|----------|----------|------------|-------|
| 18| (4-CF<sub>3</sub>)PhBPin | SPhos    | Toluene  | K<sub>3</sub>PO<sub>4</sub> | 8     |
| 19| (4-CF<sub>3</sub>)PhBPin | XPhos    | n-Butanol| K<sub>2</sub>CO<sub>3</sub> | 15    |
| 20| (4-CF<sub>3</sub>)PhBPin | XPhos    | n-Butanol| Cs<sub>2</sub>CO<sub>3</sub> | 11    |
| 21| (4-CF<sub>3</sub>)PhBPin | XPhos    | n-Butanol| K<sub>3</sub>PO<sub>4</sub> | 12    |
| 22| (4-CF<sub>3</sub>)PhBPin | SPhos    | n-Butanol| K<sub>2</sub>CO<sub>3</sub> | 0     |
| 23| (4-CF<sub>3</sub>)PhBPin | SPhos    | n-Butanol| Cs<sub>2</sub>CO<sub>3</sub> | 8     |
| 24| (4-CF<sub>3</sub>)PhBPin | SPhos    | n-Butanol| K<sub>3</sub>PO<sub>4</sub> | 8     |
| 25| (4-CN)PhB(OH)<sub>2</sub> | XPhos    | Toluene  | K<sub>2</sub>CO<sub>3</sub> | 7     |
| 26| (4-CN)PhB(OH)<sub>2</sub> | XPhos    | Toluene  | Cs<sub>2</sub>CO<sub>3</sub> | 6     |
| 27| (4-CN)PhB(OH)<sub>2</sub> | XPhos    | Toluene  | K<sub>3</sub>PO<sub>4</sub> | 3     |
| 28| (4-CN)PhB(OH)<sub>2</sub> | SPhos    | Toluene  | K<sub>2</sub>CO<sub>3</sub> | 13    |
| 29| (4-CN)PhB(OH)<sub>2</sub> | SPhos    | Toluene  | Cs<sub>2</sub>CO<sub>3</sub> | 12    |
| 30| (4-CN)PhB(OH)<sub>2</sub> | SPhos    | Toluene  | K<sub>3</sub>PO<sub>4</sub> | 7     |
| 31| (4-CN)PhB(OH)<sub>2</sub> | XPhos    | n-Butanol| K<sub>2</sub>CO<sub>3</sub> | 11    |
| 32| (4-CN)PhB(OH)<sub>2</sub> | XPhos    | n-Butanol| Cs<sub>2</sub>CO<sub>3</sub> | 9     |
| 33| (4-CN)PhB(OH)<sub>2</sub> | XPhos    | n-Butanol| K<sub>3</sub>PO<sub>4</sub> | 5     |
| 34| (4-CN)PhB(OH)<sub>2</sub> | SPhos    | n-Butanol| K<sub>2</sub>CO<sub>3</sub> | 4     |
| 35| (4-CN)PhB(OH)<sub>2</sub> | SPhos    | n-Butanol| Cs<sub>2</sub>CO<sub>3</sub> | 2     |
| 36| (4-CN)PhB(OH)<sub>2</sub> | SPhos    | n-Butanol| K<sub>3</sub>PO<sub>4</sub> | 2     |
| 37| (4-CN)PhBPin  | XPhos    | Toluene  | K<sub>2</sub>CO<sub>3</sub> | 9     |
| 38| (4-CN)PhBPin  | XPhos    | Toluene  | Cs<sub>2</sub>CO<sub>3</sub> | 27    |
| 39| (4-CN)PhBPin  | XPhos    | Toluene  | K<sub>3</sub>PO<sub>4</sub> | 21    |
| Entry | Catalyst Loading (mol%) | Conversion |
|-------|-------------------------|------------|
| 1     | 10                      | 52         |
| 2     | 5                       | 47         |
| 3     | 2.5                     | 14         |

*Conversion values determined by LCMS with reference to caffeine as an internal standard.

**Targeted Screen 4**

The screen was conducted as outlined in general procedure B using 5 x microwave vials, each containing 1-benzyl-5-bromo-1H-tetrazole (12.0 mg, 50 μmol), 4-fluorophenylboronic acid (10.5 mg, 75 μmol), XPhos Pd G3 (0.5-10 mol%), cesium carbonate (32.6 mg, 100 μmol), toluene (500 μL), and water (9 μL, 500 μmol). The reaction was stirred at 100 °C for 16 hours. The results obtained are detailed in Table S6.

**Table S6: Conversion values obtained from targeted screen 4**
Conversion values determined by LCMS with reference to caffeine as an internal standard.

**Targeted Screen 5**

The screen was conducted as outlined in general procedure B using 8 x 2 mL HPLC vials, each containing 1-benzyl-5-bromo-1H-tetrazole (12.0 mg, 50 μmol), (4-(trifluoromethyl)phenyl)boronic acid (14.2 mg, 75 μmol), (4-cyanophenyl)boronic acid (11.0 mg, 75 μmol), (4-(trifluoromethyl)phenyl)boronic acid pinacol ester (20.4 mg, 75 μmol), or (4-cyanophenyl)boronic acid pinacol ester (17.2 mg, 75 μmol), XPhos Pd G3 (2.1 mg, 2.5 µmol) or tetrakis(triphenylphosphine)palladium(0) (2.9 mg, 2.5 µmol), cesium carbonate (32.6 mg, 100 μmol), toluene (400 μL), and water (90 μL, 5000 μmol). The reaction was stirred at 100 °C for 16 hours. The results obtained are detailed in Table S7.

**Table S7: Conversion values obtained from targeted screen 5**

| Entry | Catalyst           | Boron Species          | Conversion\(^a\) |
|-------|--------------------|------------------------|------------------|
| 1     | XPhos Pd G3        | (4-CF\(_3\))PhB(OH)_2 | 60               |
| 2     | XPhos Pd G3        | (4-CF\(_3\))PhBPin    | 20               |
| 3     | XPhos Pd G3        | (4-CN)PhB(OH)_2       | 13               |
| 4     | XPhos Pd G3        | (4-CN)PhBPin          | 8                |
| 5     | Pd(PPh\(_3\))\(_4\) | (4-CF\(_3\))PhB(OH)_2 | 16               |
| 6     | Pd(PPh\(_3\))\(_4\) | (4-CF\(_3\))PhBPin    | 4                |
| 7     | Pd(PPh\(_3\))\(_4\) | (4-CN)PhB(OH)_2       | 22               |
| 8     | Pd(PPh\(_3\))\(_4\) | (4-CN)PhBPin          | 36               |

\(^a\)Conversion values determined by LCMS with reference to caffeine as an internal standard.
Targeted Screen 6

![Chemical Structures]

The screen was conducted as outlined in general procedure B using 24 x 2 mL HPLC vials, each containing 1-benzyl-5-bromo-1H-tetrazole (12.0 mg, 50 µmol), (4-(trifluoromethyl)phenyl)boronic acid (14.2 mg, 75 µmol), (4-cyanophenyl)boronic acid (11.0 mg, 75 µmol), (4-(trifluoromethyl)phenyl)boronic acid pinacol ester (20.4 mg, 75 µmol), or (4-cyanophenyl)boronic acid pinacol ester (17.2 mg, 75 µmol), 3BuXPhos Pd G1 (1.7 mg, 2.5 µmol), RockPhos Pd G3 (2.1 mg, 2.5 µmol), BrettPhos Pd G3 (2.3 mg, 2.5 µmol), RuPhos Pd G3 (2.1 mg, 2.5 µmol), XPhos Pd G3 (2.1 mg, 2.5 µmol) or tetrakis(triphenylphosphine)palladium(0) (2.9 mg, 2.5 µmol), cesium carbonate (32.6 mg, 100 µmol), toluene (400 µL), and water (90 µL, 5000 µmol). The reaction was stirred at 100 °C for 16 hours. The results obtained are detailed in Table S8.

Table S8: Conversion values obtained from targeted screen 6

| Entry | Catalyst       | Boron Species     | Conversion* |
|-------|----------------|------------------|-------------|
| 1     | Pd(PPh₃)₄     | (4-CF₃)PhB(OH)₂  | 17          |
| 2     | Pd(PPh₃)₄     | (4-CF₃)PhBPin    | 4           |
| 3     | Pd(PPh₃)₄     | (4-CN)PhB(OH)₂   | 18          |
| 4     | Pd(PPh₃)₄     | (4-CN)PhBPin     | 22          |
| 5     | XPhos Pd G3    | (4-CF₃)PhB(OH)₂  | 31          |
| 6     | XPhos Pd G3    | (4-CF₃)PhBPin    | 25          |
| 7     | XPhos Pd G3    | (4-CN)PhB(OH)₂   | 2           |
| 8     | XPhos Pd G3    | (4-CN)PhBPin     | 29          |
| 9     | 3BuXPhos Pd G1 | (4-CF₃)PhB(OH)₂  | 2           |
| 10    | 3BuXPhos Pd G1 | (4-CF₃)PhBPin    | 1           |
| 11    | 3BuXPhos Pd G1 | (4-CN)PhB(OH)₂   | 0           |
| #  | Pd Source                  | Boronic Acid          | Conversion Value |
|----|---------------------------|-----------------------|------------------|
| 12 | 'BuXPhos Pd G1            | (4-CN)PhBPin          | 1                |
| 13 | BrettPhos Pd G3           | (4-CF$_3$)PhB(OH)$_2$ | 20               |
| 14 | BrettPhos Pd G3           | (4-CF$_3$)PhBPin      | 15               |
| 15 | BrettPhos Pd G3           | (4-CN)PhB(OH)$_2$     | 9                |
| 16 | BrettPhos Pd G3           | (4-CN)PhBPin          | 17               |
| 17 | RockPhos Pd G3            | (4-CF$_3$)PhB(OH)$_2$ | 3                |
| 18 | RockPhos Pd G3            | (4-CF$_3$)PhBPin      | 0                |
| 19 | RockPhos Pd G3            | (4-CN)PhB(OH)$_2$     | 0                |
| 20 | RockPhos Pd G3            | (4-CN)PhBPin          | 0                |
| 21 | RuPhos Pd G3              | (4-CF$_3$)PhB(OH)$_2$ | 9                |
| 22 | RuPhos Pd G3              | (4-CF$_3$)PhBPin      | 6                |
| 23 | RuPhos Pd G3              | (4-CN)PhB(OH)$_2$     | 9                |
| 24 | RuPhos Pd G3              | (4-CN)PhBPin          | 14               |

*Conversion values determined by LCMS with reference to caffeine as an internal standard

**Targeted Screen 7**

The screen was conducted as outlined in general procedure B using 6 x microwave vials, each containing 1-benzyl-5-bromo-1H-tetrazole (12.0 mg, 50 µmol), 4-(trifluoromethyl)phenylboronic acid (14.2 mg, 75 µmol), (Pd(dppf)Cl)$_2$ (1.8 mg, 2.5 µmol), palladium(II) chloride (0.4 mg, 2.5 µmol), palladium(II) acetate (0.6 mg, 2.5 µmol), Pd(PPh$_3$)$_2$Cl$_2$ (1.8 mg, 2.5 µmol), Pd$_2$(dba)$_3$ (1.1 mg, 1.25 µmol) or XPhos Pd G3 (2.1 mg, 2.5 µmol), XPhos (2.4 mg, 5.0 µmol), cesium carbonate (32.6 mg, 100 µmol), toluene (500 µL), and water (90 µL, 5000 µmol). The reaction was stirred at 100 °C for 16
hours. The results obtained are detailed in Table S9. Note that no XPhos was added to the reaction vessel where XPhos Pd G3 was used.

Table S9: Conversion values obtained from targeted screen 7

| Entry | Palladium Source   | Conversion |
|-------|--------------------|------------|
| 1     | XPhos Pd G3        | 48         |
| 2     | PdCl₂              | 3          |
| 3     | Pd(OAc)₂           | 7          |
| 4     | Pd[PPh₃]₂Cl₂       | 0          |
| 5     | Pd(dpdpf)Cl₂       | 20         |
| 6     | Pd₂dba₃            | 4          |

*aConversion values determined by LCMS with reference to caffeine as an internal standard.

Targeted Screen 8

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The screen was conducted as outlined in general procedure B using 35 microwave vials, each containing 1-benzyl-5-bromo-1H-tetrazole (12.0 mg, 50 μmol), 4-fluorophenylboronic acid (55 μmol – 125 μmol), XPhos Pd G3 (0.5 μmol – 5 μmol), cesium carbonate (55 μmol – 125 μmol), toluene (50 – 500 μL), and water (250 μmol - 5000 μmol). The reaction was stirred at 100 °C for 3 hours. The results obtained are detailed in Table S10. Design of experiment analysis was conducted on the results of this screen (Figure S1) using Design Expert® software by StatEase."
| Entry | Catalyst Loading (mol%) | Boronic Acid Stoichiometry (eq.) | Base Stoichiometry (eq.) | Water Stoichiometry (eq.) | Concentration (M) | Conversion<sup>a,b</sup> |
|-------|-------------------------|---------------------------------|--------------------------|---------------------------|------------------|------------------|
| 1     | 10                      | 2.5                             | 1.1                      | 100                       | 0.1              | 49               |
| 2     | 1                       | 1.1                             | 1.1                      | 100                       | 0.1              | 21               |
| 3     | 10                      | 2.5                             | 1.1                      | 5                         | 1                | 32               |
| 4     | 1                       | 1.1                             | 2.5                      | 5                         | 0.1              | 2                |
| 5     | 10                      | 1.1                             | 1.1                      | 100                       | 1                | 13               |
| 6     | 10                      | 1.1                             | 1.1                      | 5                         | 0.1              | 50               |
| 7     | 10                      | 1.1                             | 2.5                      | 100                       | 0.1              | 52               |
| 8     | 1                       | 2.5                             | 1.1                      | 5                         | 0.1              | 5                |
| 9     | 10                      | 2.5                             | 2.5                      | 5                         | 0.1              | 54               |
| 10    | 1                       | 1.1                             | 1.1                      | 5                         | 1                | 2                |
| 11    | 10                      | 1.1                             | 2.5                      | 5                         | 1                | 21               |
| 12    | 1                       | 1.1                             | 2.5                      | 100                       | 1                | 1                |
| 13    | 1                       | 2.5                             | 2.5                      | 5                         | 1                | 2                |
| 14    | 10                      | 2.5                             | 2.5                      | 100                       | 1                | 12               |
| 15    | 1                       | 2.5                             | 1.1                      | 100                       | 1                | 1                |
| 16    | 1                       | 2.5                             | 2.5                      | 100                       | 0.1              | 10               |
| 17    | 5.5                     | 1.8                             | 1.8                      | 52.5                      | 0.55             | 10<sup>c</sup>   |

*Conversions values determined by LCMS with reference to caffeine as an internal standard.

<sup>a</sup>Reported values are averages of two runs.

<sup>b</sup>Average of three runs.
Figure S1: A. A half-normal plot of the factors investigated during targeted screen 8, demonstrating that catalyst and concentration have the greatest impact on conversion. B. A graphical representation of this effect.
Targeted Screen 9

The screen was conducted as outlined in general procedure B using 32 microwave HPLC vials, each containing 1-benzyl-5-bromo-1H-tetrazole (12.0 mg, 50 µmol), (4-fluorophenyl)boronic acid (9.1 mg, 65 µmol), XPhos Pd G3 (0.5 µmol – 5 µmol), cesium carbonate (24.4 mg, 75 µmol), toluene (500 µL - 2500 µL), and water (90 µL, 5000 µmol). The reaction was stirred at 100 °C for a defined time period. The results obtained are detailed in Table S11.

Table S11: Conversion values obtained from targeted screen 9

| Entry | Catalyst Loading (mol%) | Time (h) | Concentration (M) | Conversiona |
|-------|-------------------------|----------|-------------------|-------------|
| 1     | 1                       | 4        | 0.1               | 38          |
| 2     | 2                       | 4        | 0.1               | 66          |
| 3     | 3                       | 4        | 0.1               | 71          |
| 4     | 4                       | 4        | 0.1               | 70          |
| 5     | 5                       | 4        | 0.1               | 71          |
| 6     | 6                       | 4        | 0.1               | 71          |
| 7     | 7                       | 4        | 0.1               | 69          |
| 8     | 10                      | 4        | 0.1               | 70          |
| 9     | 1                       | 4        | 0.02              | 37          |
| 10    | 2                       | 4        | 0.02              | 58          |
| 11    | 3                       | 4        | 0.02              | 67          |
| 12    | 4                       | 4        | 0.02              | 68          |
|   |   |   |   |   |
|---|---|---|---|---|
| 13 | 5 | 4 | 0.02 | 66 |
| 14 | 6 | 4 | 0.02 | 73 |
| 15 | 7 | 4 | 0.02 | 73 |
| 16 | 10 | 4 | 0.02 | 58 |
| 17 | 1 | 16 | 0.1 | 38 |
| 18 | 2 | 16 | 0.1 | 74 |
| 19 | 3 | 16 | 0.1 | 69 |
| 20 | 4 | 16 | 0.1 | 72 |
| 21 | 5 | 16 | 0.1 | 71 |
| 22 | 6 | 16 | 0.1 | 72 |
| 23 | 7 | 16 | 0.1 | 72 |
| 24 | 10 | 16 | 0.1 | 72 |
| 25 | 1 | 16 | 0.02 | 34 |
| 26 | 2 | 16 | 0.02 | 57 |
| 27 | 3 | 16 | 0.02 | 69 |
| 28 | 4 | 16 | 0.02 | 81 |
| 29 | 5 | 16 | 0.02 | 74 |
| 30 | 6 | 16 | 0.02 | 71 |
| 31 | 7 | 16 | 0.02 | 66 |
| 32 | 10 | 16 | 0.02 | 58 |

*Conversion values determined by LCMS with reference to caffeine as an internal standard.*
Targeted Screen 10

\[ \text{Br} \quad \text{N} \quad \text{N} \quad \text{N} \quad \text{N} \quad \text{Ph} \quad \text{N} \quad \text{N} \quad \text{N} \quad \text{N} \]

\[ \text{1} \xrightarrow{\text{Ph\text{B}(OH)\text{H}_2 (x \text{ equiv.})}} \text{2a} \]

XPhos Pd G3 (3 mol %)
Cs\textsubscript{2}CO\textsubscript{3} (x \text{ equiv.}), H\textsubscript{2}O, solvent
100 °C, 3 h
+ additive

The screen was conducted as outlined in general procedure B using 6 x microwave vials, each containing 1-benzyl-5-bromo-1\textsubscript{H}-tetrazole (12.0 mg, 50 µmol), phenylboronic acid (65 µmol or 75 µmol), XPhos Pd G3 (1.3 mg, 1.5 µmol), cesium carbonate (75 µmol or 100 µmol), toluene or n-butanol (both 500 µL), and water (90 µL, 5000 µmol). The reaction was stirred at 100 °C for 3 hours. The results obtained are detailed in Table S12. Evonik Noblyst\textsuperscript{®} P1071 20% palladium on carbon (5.3 mg, 5 µmol) was also added to two of the vessels.

Table S12: Conversion values obtained from targeted screen 10

| Entry | Solvent   | Boronic Acid (eq.) | Base (eq.) | Additive | Conversion\textsuperscript{a} |
|-------|-----------|--------------------|------------|----------|-----------------------------|
| 1     | Toluene   | 1.3                | 1.5        | -        | 77                          |
| 2     | Toluene   | 1.3                | 1.5        | + Pd/C   | 72                          |
| 3     | Toluene   | 1.5                | 2          | -        | 76                          |
| 4     | n-Butanol | 1.3                | 1.5        | -        | 16                          |
| 5     | n-Butanol | 1.3                | 1.5        | + Pd/C   | 22                          |
| 6     | n-Butanol | 1.5                | 2          | -        | 18                          |

\textsuperscript{a}Conversions values determined by LCMS with reference to caffeine as an internal standard.
2.2 Optimization of Debenzylation Reaction

High-Throughput Screen 1

The screen was conducted as outlined in general procedure C using 48 x 1 mL vials, each containing 1-benzyl-5-phenyl-1H-tetrazole (15.0 mg, 63 μmol), a palladium on carbon catalyst (30% wt.), and ethanol, ethyl acetate, or tetrahydrofuran (all 375 μL). Acetic acid (13 μL, 63 μmol) was added to half of the vessels. The reaction was stirred at 40 °C for 16 hours. The results obtained are detailed in Table S13.

Table S13: Conversion values obtained from high-throughput screen 1

| Entry | Pd/C Catalyst | Solvent     | Additive | Conversiona |
|-------|---------------|-------------|----------|-------------|
| 1     | JM A405-028-5 | Ethanol     | -        | 97          |
| 2     | JM A405-032-5 | Ethanol     | -        | 98          |
| 3     | JM A503-032-5 | Ethanol     | -        | 29          |
| 4     | Evonik P1070  | Ethanol     | -        | 96          |
| 5     | Evonik P1071  | Ethanol     | -        | 97          |
| 6     | Evonik P1090  | Ethanol     | -        | 90          |
| 7     | BASF 10318    | Ethanol     | -        | 97          |
| 8     | BASF 10321    | Ethanol     | -        | 96          |
| 9     | JM A405-028-5 | Ethyl Acetate| -        | 67          |
| 10    | JM A405-032-5 | Ethyl Acetate| -        | 71          |
| 11    | JM A503-032-5 | Ethyl Acetate| -        | 12          |
| 12    | Evonik P1070  | Ethyl Acetate| -        | 71          |
|   | Product Code | Solvent   |   |  |
|---|--------------|-----------|---|---|
| 13 | Evonik P1071 | Ethyl Acetate | - | 76 |
| 14 | Evonik P1090 | Ethyl Acetate | - | 66 |
| 15 | BASF 10318 | Ethyl Acetate | - | 76 |
| 16 | BASF 10321 | Ethyl Acetate | - | 10 |
| 17 | JM A405-028-5 | THF | - | 84 |
| 18 | JM A405-032-5 | THF | - | 94 |
| 19 | JM A503-032-5 | THF | - | 14 |
| 20 | Evonik P1070 | THF | - | 97 |
| 21 | Evonik P1071 | THF | - | 97 |
| 22 | Evonik P1090 | THF | - | 91 |
| 23 | BASF 10318 | THF | - | 97 |
| 24 | BASF 10321 | THF | - | 2 |
| 25 | JM A405-028-5 | Ethanol | AcOH | 57 |
| 26 | JM A405-032-5 | Ethanol | AcOH | 98 |
| 27 | JM A503-032-5 | Ethanol | AcOH | 33 |
| 28 | Evonik P1070 | Ethanol | AcOH | 97 |
| 29 | Evonik P1071 | Ethanol | AcOH | 97 |
| 30 | Evonik P1090 | Ethanol | AcOH | 61 |
| 31 | BASF 10318 | Ethanol | AcOH | 98 |
| 32 | BASF 10321 | Ethanol | AcOH | 9 |
| 33 | JM A405-028-5 | Ethyl Acetate | AcOH | 82 |
| 34 | JM A405-032-5 | Ethyl Acetate | AcOH | 81 |
The screen was conducted as outlined in general procedure C using 10 x 1 mL vials, each containing 1-benzyl-5-phenyl-1H-tetrazole (30.0 mg, 127 μmol), a palladium on carbon catalyst (10 % wt. or 20 % wt.), and ethanol (750 μL). The reaction was stirred at 40 °C for 16 hours. The results obtained are detailed in Table S14.
### Table S14: Conversion values obtained from high-throughput screen 2

| Entry | Pd/C Catalyst   | Catalyst Loading (wt. %) | Conversion<sup>a</sup> |
|-------|-----------------|--------------------------|------------------------|
| 1     | JM A405-028-5   | 10                       | 24                     |
| 2     | JM A503-032-5   | 10                       | 20                     |
| 3     | Evonik P1070    | 10                       | 67                     |
| 4     | Evonik P1071    | 10                       | 99                     |
| 5     | BASF 10318      | 10                       | 97                     |
| 6     | JM A405-028-5   | 20                       | 38                     |
| 7     | JM A503-032-5   | 20                       | 33                     |
| 8     | Evonik P1070    | 20                       | 99                     |
| 9     | Evonik P1071    | 20                       | 98                     |
| 10    | BASF 10318      | 20                       | 99                     |

<sup>a</sup>Conversions reported as a percentage of total peak area of product and starting material.

### Targeted Screen 1

The screen was conducted as outlined in general procedure D using 8 x 10 mL reaction vessels, each containing 1-benzyl-5-phenyl-1H-tetrazole (70.9 mg, 300 μmol), a palladium on carbon catalyst (7.5 μmol) and ethanol (3 mL). The reaction was stirred at room temperature for 16 hours. The results obtained are detailed in Table S15.

### Table S15: Conversion values obtained from targeted screen 1

| Entry | Pd/C Catalyst   | H<sub>2</sub> pressure (bar) | Conversion<sup>a</sup> |
|-------|-----------------|-----------------------------|------------------------|
| 1     | Evonik P1071    | 4                           | 59                     |

<sup>a</sup>Conversions reported as a percentage of total peak area of product and starting material.
|   | Products  | Conversion (%) |
|---|-----------|----------------|
| 2 | Evonik P1071 | 3 56           |
| 3 | Evonik P1071 | 2 50           |
| 4 | Evonik P1071 | 1 47           |
| 5 | BASF 10318  | 4 48           |
| 6 | BASF 10318  | 3 44           |
| 7 | BASF 10318  | 2 40           |
| 8 | BASF 10318  | 1 40           |

*Conversions reported as a percentage of total peak area of product and starting material.*
2.3 Optimization of One-Pot Suzuki-Hydrogenolysis Reaction

Screen 1

The screen was conducted as outlined in general procedure E using 8 x 10 mL reaction vessels, each containing 1-benzyl-5-phenyl-1H-tetrazole (120 mg, 500 μmol), phenylboronic acid (79 mg, 650 μmol), XPhos Pd G3 (12.7 mg, 15 μmol), Noblyst® P1071 20% Pd/C (13 μmol - 50 μmol), cesium carbonate (244 mg, 750 μmol), water (901 μL, 50 mmol), toluene (5 mL) and ethanol (2.5 mL). The reaction was stirred at 100 °C under a nitrogen atmosphere for 4 hours, and at 40 °C under a hydrogen atmosphere of either 4 or 2 bar for 20 hours. The results obtained are detailed in Table S16.

| Entry | Pd/C loading (mol%) | H₂ pressure (bar) | Conversiona |
|-------|----------------------|-------------------|-------------|
| 1     | 10                   | 4                 | 43          |
| 2     | 7.5                  | 4                 | 48          |
| 3     | 5                    | 4                 | 29          |
| 4     | 2.5                  | 4                 | 17          |
| 5     | 10                   | 2                 | 65          |
| 6     | 7.5                  | 2                 | 52          |
| 7     | 5                    | 2                 | 34          |
| 8     | 2.5                  | 2                 | 35          |

aConversions values determined by LCMS with reference to caffeine as an internal standard.
Screen 2

The screen was conducted as outlined in general procedure E using 7 x 10 mL reaction vessels, each containing 1-benzyl-5-phenyl-1H-tetrazole (120 mg, 500 μmol), phenylboronic acid (79 mg, 650 μmol), XPhos Pd G3 (12.7 mg, 15 μmol), Noblyst® P1071 20% Pd/C (53.2 mg, 50 μmol), cesium carbonate (244 mg, 750 μmol), water (901 μL, 50 mmol), toluene (2.5 mL - 5 mL) and ethanol or n-butanol (both 1 - 2.5 mL). The reaction was stirred at a specified temperature under a nitrogen atmosphere for 4 hours, and at 40 °C under a hydrogen atmosphere of 2 bar for 24 hours. The results obtained are detailed in Table S17.

Table S17: Conversion values obtained from screen 2

| Entry | Solvent          | Suzuki Temperature (°C) | Conversion\(^a\) |
|-------|------------------|-------------------------|------------------|
| 1     | PhMe             | 100                     | 24               |
| 2     | 4:1 (PhMe:nBuOH) | 100                     | 24               |
| 3     | 3:2 (PhMe:nBuOH) | 100                     | 4                |
| 4     | 1:1 (PhMe:nBuOH) | 100                     | 34               |
| 5     | 4:1 (PhMe:EtOH)  | 70                      | 37               |
| 6     | 3:2 (PhMe:EtOH)  | 70                      | 22               |
| 7     | 1:1 (PhMe:EtOH)  | 70                      | 15               |

\(^a\)Conversions values determined by LCMS with reference to caffeine as an internal standard.
3  NMR Spectra of Selected Compounds

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{19}F$ NMR (376 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

$^1$H NMR (400 MHz, CDCl$_3$)
$^{19}$F NMR (376 MHz, CDCl$_3$)

$^{13}$C NMR (121 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, DMSO)

$^{13}$C NMR (101 MHz, DMSO)
$^1$H NMR (400 MHz, DMSO)

$^{19}$F NMR (376 MHz, DMSO)
$^{13}$C NMR (101 MHz, DMSO)

$^1$H NMR (400 MHz, DMSO)
$^{19}$F NMR (376 MHz, DMSO)

$^{13}$C NMR (101 MHz, DMSO)
$^1$H NMR (400 MHz, DMSO)

$^{13}$C NMR (101 MHz, DMSO)
$^1$H NMR (400 MHz, DMSO)

$^{13}$C NMR (101 MHz, DMSO)
$^1$H NMR (400 MHz, DMSO)

$^{13}$C NMR (101 MHz, DMSO)
$^1$H NMR (400 MHz, DMSO)

$^{13}$C NMR (101 MHz, DMSO)
$^1$H NMR (400 MHz, DMSO)

$^{13}$C NMR (101 MHz, DMSO)
$^1$H NMR (500 MHz, DMSO)

$^{13}$C NMR (126 MHz, DMSO)
$^1$H NMR (400 MHz, DMSO)

$^{13}$C NMR (101 MHz, DMSO)
\(^1\)H NMR (500 MHz, DMSO)

\(^{13}\)C NMR (126 MHz, DMSO)
$^1$H NMR (400 MHz, DMSO)

$^{13}$C NMR (101 MHz, DMSO)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, DMSO)

C NMR (101 MHz, DMSO)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{19}$F NMR (471 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical Structure](image)
$^1$H NMR (400 MHz, DMSO)

$^{19}$F NMR (471 MHz, DMSO)
$^{13}$C NMR (101 MHz, DMSO)

![NMR Spectrum]

S61
$^1$H NMR (400 MHz, CDCl$_3$)

$^{19}$F NMR (471 MHz, CDCl$_3$)
\[ { }^{13}\text{C} \text{ NMR (101 MHz, CDCl}_3 \]
$^1$H NMR (400 MHz, CDCl$_3$)

$^{19}$F NMR (471 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical structure](image)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, DMSO)

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$^1$H NMR (400 MHz, CDCl$_3$)

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$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (126 MHz, CDCl$_3$)
4 References

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