Supporting Information

**sp³ C-H Bond Arylation Directed by Amidine Protecting Group: α-Arylation of Pyrrolidines and Piperidines.**

Stefan J. Pastine, Denis V. Gribkov, Dalibor Sames*

Department of Chemistry, Columbia University, New York, NY 10027

I. General

Argon was purified by passage through Drierite. Nuclear Magnetic Resonance spectra were recorded on Bruker 300 or 400 Fourier Transform NMR spectrometers. Spectra were recorded in CDCl$_3$ or DMSO solutions at 300 K (unless otherwise noted), and were referenced to TMS or the solvent residual peak. Flash chromatography was performed on SILICYCLE silica gel (230-400 mesh). Mass spectra were recorded on a JEOL LCmate (Ionization mode: APCI+). Gas chromatography was performed on an Agilent Technologies 6890N gas chromatograph equipped with a 25 m polydimethylsiloxane capillary column and 5973 Mass Selective Detector. All arylation reactions were carried out in capped glass vials (VWR, 4 mL) equipped with a cap (Teflon septum inside, Kimble Glass), and heated in a 34-well reaction block (Chemglass).

**Ia. Materials.**

Ruthenium carbonyl [$\text{Ru}_3(\text{CO})_{12}$] was purchased from Strem and used as received. Pinacolone (98%) was purchased from Aldrich and stored over 4 Å molecular sieves. 2-Phenylpyrrolidine was purchased from Tyger Scientific, Inc. and distilled under reduced pressure. Boronic esters were purchased from Aldrich and used as received or were prepared from the corresponding boronic acids according to the method of Boyle and Shi.$^1$

**Ib. Ineffective Arylation Catalysts.**

$\text{Ru(H}_2\text{CO(PPh}_3\text{)}_3$ (purchased from Strem), $\text{Ru(COD)(COT)}$, $^2$ $\text{Ru(H}_2\text{(I}^\text{Bu})(\text{PPh}_3)_2$, $^3$ $\text{Ru}_2(\text{CO})(\mu-\text{PPh}_2)(\mu-\text{NC}_3\text{H}_4)(\text{PPh}_3)(\text{CO})_5$. $^4$

II. Synthesis of Starting Materials

**IIa. Synthesis of Amidine Substrates.**

Amidine substrates were prepared by the reaction of 2-methoxy-1-pyrroline (1.05-1.1 equiv) with the appropriate amine (1.0 equiv), neat at 80 °C (reaction monitored via GC-
MS; Reaction time typically <4 h) in the presence of a catalytic amount of acetic acid (2 mol%). 2-Methoxy-1-pyrroline was prepared by reaction of 2-pyrrolidinone (1 equiv.) with dimethyl sulfate (1 equiv.) according to a literature procedure.

In an 8 mL vial was placed 2-phenylpyrrolidine (1.50 g, 10.2 mmol, 1.0 equiv.), 2-methoxy-1-pyrroline (1.06 g, 10.7 mmol, 1.05 equiv) and 12 µL of acetic acid (2 mol%). The reaction was heated at 80 °C for 3 hours, cooled to ambient temperature and then 0.5 mL of 1M NaOH and a few mL of ether were added to the vial. The layers separated and the aqueous layer extracted with ether (2 X 5 mL). The organic layers were combined, dried over K$_2$CO$_3$, and concentrated in vacuo. The resulting crude solid was recrystallized from a pentane/hexanes mixture to give the product (2.04 g, 93% yield) as a white solid: $^1$H NMR (CDCl$_3$, 300 MHz) δ 1.77-1.94 (m, 5H), 2.05-2.16 (m, 1H), 2.27-2.44 (m, 2H), 3.57-3.67 (m, 2H), 3.72-3.79 (m, 1H), 4.84 (d, $J=6.6$ Hz, 1H), 7.15-7.24 (m, 3H), 7.28-7.33 (m, 2H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 22.7, 23.9, 32.5, 36.0, 48.6, 56.6, 62.7, 125.5, 126.7, 128.5, 144.8, 166.8; MS (LR-APCI): calculated for C$_{14}$H$_{18}$N$_2$ 214.15, measured 215.21 (M+H$^+$).

In a 5 mL round bottom flask was placed 2-(tert-butyl-dimethyl-siloxyethyl)-pyrrolidine (539 mg, 2.50 mmol, 1.0 equiv), 2-methoxy-1-pyrroline (273 mg, 2.75 mmol, 1.1 equiv) and 3 µL of acetic acid (2 mol%). The resulting reaction was stirred for 3 hours at 80 °C and then cooled to ambient temperature. Solid Na$_2$CO$_3$ was added to quench the acetic acid and then the product was purified by distillation under reduced pressure (590 mg, 84% yield, bp 92 °C; 0.1 mmHg) as a colorless oil: $^1$H NMR (CDCl$_3$, 400 MHz) δ 0.02 (s, 6H), 0.87 (s, 9H), 1.84-1.98 (m, 6H), 2.48 (pentet, $J_{av}=6.0$ Hz, 1H), 2.60 (pentet, $J_{av}=6.0$ Hz, 1H), 3.35-3.45 (m, 2H), 3.59-3.57 (m, 1H), 3.66 (t, $J=7.1$ Hz, 2H), 3.85 (bs, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ -5.4, 18.2, 23.4, 23.8, 25.9, 27.9, 32.6, 48.4, 56.5, 60.0, 63.9, 166.4; MS (LR-APCI): calculated for C$_{15}$H$_{30}$N$_2$O$_3$ 282.21, measured 283.32 (M+H$^+$).

In an 8 mL vial was placed piperidine (426 mg, 5.0 mmol, 1.0 equiv.), 2-methoxy-1-pyrroline (545 g, 5.5 mmol, 1.1 equiv) and 6 µL of acetic acid (2 mol%). The reaction was heated at 80 °C for 1.5 hours, cooled to ambient temperature and then 0.5 mL of 1M NaOH and a few mL of ether were added to the vial. The layers separated and the aqueous layer extracted with ether (2 X 5 mL). The organic layers were combined, dried over K$_2$CO$_3$, and concentrated in vacuo. The product was used with out further purification (723 mg, 95% yield): $^1$H NMR (CDCl$_3$, 300 MHz) δ 1.42 (bs, 6H), 1.78-1.83 (bm, 2H), 2.34 (bt, $J_{av}=7.7$ Hz, 2H), 3.19 (bs, 4H), 3.52-3.54 (bm, 2H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 23.3, 24.2, 25.3, 31.0, 46.8, 56.1, 168.1; MS (LR-APCI): calculated for C$_9$H$_{16}$N$_2$ 152.13, measured 153.12 (M+H$^+$).

IIb. Synthesis of N-(2-Pyridyl)-Substituted Substrates.

These substrates were obtained from the reaction of 2-bromopyridine and the appropriate amines using the palladium-catalyzed amination procedure of Buchwald.6

A white solid (67% yield, SiO₂; Hex:EtOAc = 8:1 then 5:1 then recrystallized from hexanes/pentane): 1H NMR (CDCl₃, 300 MHz) δ 1.94-2.03 (m, 3H), 2.39-2.46 (m, 1H), 3.67-3.76 (m, 1H), 3.86-3.92 (m, 1H), 4.90 (dd, J = 8.4, 2.4 Hz, 1H), 6.15 (dm, J = 8.7 Hz, 1H), 6.49 (ddd, J = 7.2, 5.1, 0.9 Hz, 1H), 7.18-7.32 (m, 6H), 8.15 (ddd, J = 5.1, 1.8, 0.9 Hz, 1H); 13C NMR (75 MHz) δ 22.8, 36.1, 48.1, 61.7, 107.4, 111.6, 125.8, 126.7, 128.5, 136.7, 144.0, 148.2, 157.1; MS (LR-APCI): calculated for C₁₅H₁₅N₂ 224.13, measured 225.19 (M+H⁺).

Pale yellow oil (90% yield, bp 115-120 °C; 0.1 mmHg): The spectral data is in agreement with literature values.7

IIc. Synthesis of N-(2-Pyrimidinyl)-Substituted Substrate.

The substrate was obtained from the reaction of 2-chloropyrimidine (1.0 equiv) and 2-pyrrolidine-methanol (1.0 equiv) in the presence of Na₂CO₃ (1.1 equiv) in acetonitrile at 80 °C, and subsequent protection of the resulting alcohol (TBSCl, imidazole, DMF).

Colorless oil (47% yield, SiO₂; 100% Hex then Hex:EtOAc = 3:1): 1H NMR (CDCl₃, 300 MHz) δ -0.04 (s, 3H), 0.00 (s, 3H), 0.86 (s, 9H), 1.88-2.15 (m, 4H), 3.45-3.66 (m, 3H), 3.81 (dd, J = 9.9, 3.3 Hz, 1H), 4.18-4.22 (m, 1H), 6.41 (t, J = 4.8 Hz, 1H), 8.27 (d, J = 4.8 Hz, 2H); 13C NMR (CDCl₃, 75 MHz,) δ -5.4, 18.2, 23.4, 25.9, 28.0, 47.5, 58.9, 62.7, 109.1, 157.6, 160.4; MS (LR-APCI): calculated for C₁₅H₁₅N₂OSi 293.19, measured 294.27 (M+H⁺).

III. General Procedure for Arylation

Ruthenium carbonyl was purchased from Strem and used as received. Throughout the course of this work several 1 gram bottles were consumed with no noticeable difference in activity between batches. Pinacolone (98%) was purchased from Aldrich and stored over 4 Å molecular sieves. All reactions were carried out in glass vials (VWR, 4 mL)

equipped with a cap (Teflon septum inside, Kimble Glass), heated in a 34-well reaction block (Chemglass) **without stirring**. The vials were almost completely encapsulated by the reaction block to help insure that the internal temperature of the reactions approaches the temperature of the reaction block. The Teflon screw caps must be on tight to prevent evaporation of pinacolone. Vials were **not** dried prior to use. All yields and reaction times correspond to reactions carried out with 0.5 mmol of substrate. Select reactions have been performed on scales up to 2.0 mmol with the same experimental setup; yields on this scale were essentially the same as reactions run on 0.5 mmol scale, but longer reaction times were required for the larger scale reactions. All reagents were weighed in air on the benchtop. Reactions were monitored by GC-MS. Visualization of reaction products on TLC was achieved by UV and/or permanganate stain (bright purple spots that fade relatively quickly).

**Amidine substrates:**

The *trans*-diastereomers have larger Rs than the *cis*-diastereomers; starting materials have low or negligible mobility under the purification conditions. 10-20 mL of SiO₂ was used for product isolation. After loading the crude reactions onto SiO₂, it is important to elute with EtOAc (1-2 column lengths) before elution with EtOAc/Triethylamine mixtures, or otherwise the products can be contaminated with unreacted arylboronic esters. Visualization of the *cis*-diastereomer after flash chromatography is difficult. After chromatography, the *cis*-diastereomer may be contaminated with small amounts of diol (pinacol or neopentyl glycol) from the arylboronic ester. Diols can be removed from products by dissolving in methylene chloride and washing the organic layer with water.

**General procedure:**

The substrate (0.5 mmol), boronic ester (0.6 mmol, 1.2 equiv., unless noted otherwise below) and Ru₃(CO)₁₂ (10.5 mg, 0.0165 mmol, 3.3 mol%, unless noted otherwise below, were weighed into a 4 mL glass vial. The vial was capped (a Teflon septum cap), evacuated and refilled with argon via a needle through the septum two or three times. Pinacolone (2.5 mmol, 310 µL, 5 equiv.) was then added via syringe. The septum cap was quickly replaced with a fully covered solid Teflon lined cap. The reaction vial was then placed in a reaction block at 150 °C. After heating for the appropriate time (*vida infra*), the reaction mixture was loaded onto a SiO₂ column and purified via flash chromatography.

**Determination of Stereochemistry:**

The major products of all reactions exhibit broad resonances in ¹H NMR spectra (most notably the benzylic resonances *(alpha* to nitrogen) at 300 K, with the exception of 15 (both isomers sharp at 300 K). Alternatively, the minor reaction products exhibit relatively sharp resonances at 300 K. An X-ray crystallographic structure of the major isomer of 2 revealed that it was the *trans*-diastereomer. The major products of all reactions were assigned as the *trans*-diastereomer by analogy.
Reaction time = 6 h. The diastereomers were separated via flash chromatography (EtOAc then 70:1 then 15:1 (EtOAc:TEA)).

**Trans-diastereomer:**

$^1$H NMR (CDCl$_3$, 300 MHz, 333K) $\delta$ 1.60-1.85 (m, 4H), 2.05-2.16 (m, 1H), 2.35-2.54 (m, 3H), 3.43-3.63 (m, 2H), 5.29 (bs, 2H), 7.18-7.35 (m, 10H); $^{13}$C NMR (CDCl$_3$, 75 MHz, 333K) $\delta$ 23.9, 33.1, 57.1, 63.4, 125.6, 126.6, 128.4, 144.9, 165.2; MS (LR-APCI): calculated for C$_{20}$H$_{22}$N$_2$ 290.18, measured 291.78 (M+H$^+$).

**Cis-diastereomer:**

$^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.80 (pentet, $J_{av}$ = 7.5 Hz, 2H), 1.97-2.07 (m, 2H), 2.21 (t, $J = 8.1$ Hz, 2H), 2.31-2.41 (m, 2H), 2.35-2.54 (m, 3H), 3.43-3.63 (m, 2H), 5.07 (t, $J_{av} = 5.3$ Hz, 2H), 7.21-7.25 (m, 2H), 7.34 (t, $J_{av} = 7.5$ Hz, 4H), 7.42 (d, $J = 7.4$ Hz, 4H); $^{13}$C NMR (CDCl$_3$, 75 MHz, 300K) $\delta$ 23.9, 33.3, 34.5, 56.7, 65.0, 126.5, 126.7, 128.4, 144.0, 168.4; MS (LR-APCI): calculated for C$_{20}$H$_{22}$N$_2$ 290.18, measured 291.05 (M+H$^+$).

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Reaction time = 6 h. The diastereomers were separated via flash chromatography (EtOAc then 70:1 then 30:1 then 15:1 (EtOAc:TEA)).

**Trans-diastereomer:**

$^1$H NMR (CDCl$_3$, 300 MHz, 333K) $\delta$ 1.60-1.86 (m, 4H), 2.06-2.17 (m, 1H), 2.36-2.51 (m, 3H), 3.43-3.62 (m, 2H), 3.80 (s, 3H), 5.28 (bs, 2H), 6.85-6.89 (m, 2H), 7.11-7.15 (m, 2H), 7.19-7.23 (m, 3H), 7.29-7.34 (m, 2H); $^{13}$C NMR (CDCl$_3$, 75 MHz, 333K) $\delta$ 23.8, 32.2(b), 33.1, 55.3, 56.7, 62.9(b), 63.3(b), 83.6, 114.0, 125.6, 126.6, 128.3, 137.1(b), 144.9(b), 158.6, 165.2 (15 of 17 carbons identified); MS (LR-APCI): calculated for C$_{21}$H$_{24}$N$_2$O 320.19, measured 321.85 (M+H$^+$).

**Cis-diastereomer:**

$^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.82 (pentet, $J_{av}$ = 7.5 Hz, 2H), 1.95-2.10 (m, 2H), 2.23 (t, $J = 8.1$ Hz, 1H), 2.28-2.40 (m, 2H), 3.61 (t, $J_{av} = 7.1$ Hz, 2H), 3.83 (s, 3H), 5.02-5.11 (m, 2H), 6.90 (d, $J = 8.7$ Hz, 2H), 7.23-7.44 (m, 7H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 23.9, 34.5, 56.7, 64.4, 64.8, 113.8, 126.5, 126.6, 127.6, 128.3, 136.2, 144.1, 158.4, 168.3 (16 of 17 carbons identified); MS (LR-APCI): calculated for C$_{21}$H$_{24}$N$_2$O 320.19, measured 321.79 (M+H$^+$).

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Reaction time = 6 h. The diastereomers were separated via flash chromatography (EtOAc then 70:1 then 30:1 then 15:1 (EtOAc:TEA)).

**Trans-diastereomer:**

$^1$H NMR (CDCl$_3$, 300 MHz, 333K) $\delta$ 1.65-1.83 (m, 4H), 2.03-2.13 (m, 1H), 2.36-2.53 (m, 3H), 3.43-3.61 (m, 2H), 5.24 (bs, 1H), 5.39 (bd, $J = 5.7$ Hz, 1H), 7.19-7.25 (m, 3H), 7.30-7.35 (m, 4H), 7.57 (d, $J = 8.1$ Hz, 2H); MS (LR-APCI): calculated for C$_{21}$H$_{21}$F$_3$N$_2$ 358.17, measured 359.62 (M+H$^+$).
Cis-diastereomer: \( ^1\text{H NMR (CDCl}_3, 300 \text{ MHz)} \delta 1.82 (\text{pentet}, J_{\text{av}} = 7.7 \text{ Hz}, 2\text{H}), 1.96-2.45 (\text{m}, 6\text{H}), 3.58 (t, J = 6.8 \text{ Hz}, 2\text{H}), 4.99 (t, J = 6.6 \text{ Hz}, 1\text{H}), 5.17-5.20 (\text{m}, 1\text{H}), 7.25-7.42 (\text{m}, 5\text{H}), 7.54 (d, J = 8.4 \text{ Hz}, 2\text{H}), 7.60 (d, J = 8.4 \text{ Hz}, 2\text{H}); \text{MS (LR-APCI)}: \text{calculated for C}_{21}\text{H}_{21}\text{F}_3\text{N}_2 358.17, measured 359.61 (M+H\text{)}^+\).

Reaction time = 6 h. The trans-diastereomer was obtained via flash chromatography (EtOAc then 70:1 then 30:1 (EtOAc:TEA)). The cis-diastereomer was contaminated with unidentified side products and was not obtained in satisfactory purity.

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\text{Trans-diastereomer: } ^1\text{H NMR (CDCl}_3, 300 \text{ MHz)} \delta 1.59-1.86 (\text{m}, 4\text{H}), 2.03-2.13 (\text{m}, 1\text{H}), 2.34-2.59 (\text{m}, 6\text{H}), 5.27 (bs, 1\text{H}), 5.38 (bs, 1\text{H}), 7.19-7.24 (\text{m}, 2\text{H}), 7.29-7.34 (\text{m}, 4\text{H}), 7.91 (d, J = 8.2 \text{ Hz}, 2\text{H}); ^{13}\text{C NMR (CDCl}_3, 75 \text{ MHz)} \delta 23.7, 26.3, 31.7, 32.2, 33.0, 56.9, 63.0, 63.7, 125.4, 125.8, 126.8, 128.5, 136.0, 144.6, 150.2, 165.0, 197.3 (17 of 18 carbons identified); \text{MS (LR-APCI)}: \text{calculated for C}_{22}\text{H}_{24}\text{N}_2\text{O} 332.19, measured 333.04 (M+H\text{)}^+\).
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Reaction time = 19 h. The diastereomers were separated via flash chromatography (EtOAc then 60:1 then 30:1 (EtOAc:TEA)).

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\text{Trans-diastereomer: } ^1\text{H NMR (DMSO-D}_6, 300 \text{ MHz, 333K)} \delta 1.50-1.73 (\text{m}, 4\text{H}), 1.83-1.94 (\text{m}, 1\text{H}), 2.33-2.52 (\text{m}, 6\text{H}), 3.21-3.41 (\text{m}, 2\text{H}), 5.31 (d, J = 7.2 \text{ Hz}, 1\text{H}), 5.43 (d, J = 7.2 \text{ Hz}, 1\text{H}), 7.06-7.20 (\text{m}, 4\text{H}), 7.22-7.26 (\text{m}, 3\text{H}), 7.31-7.36 (\text{m}, 2\text{H}); ^{13}\text{C NMR (DMSO-D}_6, 300 \text{ MHz, 350K)} \delta 18.3, 23.0, 29.4, 31.3, 31.9, 55.9, 59.5, 62.4, 123.9, 125.1, 125.7, 125.9, 127.7, 129.9, 133.4, 142.5, 145.0, 163.7 (18 of 19 carbons identified); \text{MS (LR-APCI)}: \text{calculated for C}_{21}\text{H}_{24}\text{N}_2\text{O} 304.19, measured 305.21 (M+H\text{)}^+\).
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\text{Cis-diastereomer: } ^1\text{H NMR (CDCl}_3, 300 \text{ MHz)} \delta 1.76-1.84 (\text{m}, 3\text{H}), 2.04-2.19 (\text{m}, 3\text{H}), 2.31-2.45 (\text{m}, 5\text{H}), 3.57 (t, J = 6.6 \text{ Hz}, 2\text{H}), 5.09-5.17 (\text{m}, 2\text{H}), 7.12-7.27 (\text{m}, 4\text{H}), 7.37 (t, J_{\text{av}} = 7.5 \text{ Hz}, 2\text{H}), 7.51 (d, J = 7.5 \text{ Hz}, 2\text{H}), 7.59 (d, J = 7.2 \text{ Hz}, 1\text{H}); ^{13}\text{C NMR (CDCl}_3, 75 \text{ MHz)} \delta 19.5, 23.9, 33.2, 33.6, 33.8, 56.9, 62.4, 64.6, 125.4, 126.1, 126.5, 126.7, 128.4, 130.6, 134.1, 142.5, 143.9, 168.4 (18 of 19 carbons identified); \text{MS (LR-APCI)}: \text{calculated for C}_{21}\text{H}_{24}\text{N}_2\text{O} 304.19, measured 305.61 (M+H\text{)}^+\).
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Reaction time = 18 h. The diastereomers were separated via flash chromatography (EtOAc then EtOAc:MeOH (13:1) then 15:1 EtOAc:MeOH:TEA (13:1:1)).

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\text{Trans-diastereomer: } ^1\text{H NMR (DMSO-D}_6, 300 \text{ MHz, 350K)} \delta 1.54-1.79 (\text{m}, 4\text{H}), 1.84-1.95 (\text{m}, 1\text{H}), 2.35-2.54 (\text{m}, 3\text{H}), 3.22-3.42 (\text{m}, 2\text{H}), 5.28 (d, J = 7.2 \text{ Hz}, 1\text{H}), 5.34 (d, J = 7.5 \text{ Hz}, 1\text{H}), 7.22-7.38 (\text{m}, 6\text{H}), 7.59-7.62 (\text{m}, 1\text{H}), 8.42-8.48 (\text{m}, 2\text{H}); ^{13}\text{C NMR (DMSO-D}_6, 300 \text{ MHz, 350K)} \delta 23.0, 30.9, 31.6, 32.0, 55.8, 60.1, 62.4, 122.8, 125.0, 126.1, 127.9, 132.8, 139.7, 144.8, 147.1, 163.8 (16 of 17 carbons identified); \text{MS (LR-APCI)}: \text{calculated for C}_{19}\text{H}_{21}\text{N}_3 291.17, measured}
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Cis-diastereomer: $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.78-2.48 (m, 8H), 3.58 (t, $J_{av} = 6.8$ Hz, 2H), 4.98 (t, $J_{av} = 6.6$ Hz, 1H), 5.20 (t, $J_{av} = 6.2$ Hz, 1H), 7.22-7.40 (m, 6H), 7.74 (d, $J = 8.1$ Hz, 1H), 8.49-8.51 (m, 1H), 8.71 (d, $J = 2.1$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 23.9, 33.2, 33.5, 35.0, 56.7, 62.3, 65.3, 123.2, 126.3, 127.1, 128.6, 134.3, 139.0, 143.8, 148.0, 148.4, 168.1; MS (LR-APCI): calculated for C$_{19}$H$_{21}$N$_3$ 291.17, measured 292.56 (M+H$^+$).

Reaction time = 18 h. The diastereomers were separated via flash chromatography (EtOAc then 70:1 then 30:1 then 15:1 (EtOAc:TEA)).

$^1$H NMR (CDCl$_3$, 400 MHz, 333 K) $\delta$ 1.66-1.74 (m, 2H), 1.77-1.82 (m, 2H), 2.04-2.12 (m, 1H), 2.36-2.52 (m, 3H), 3.46 (pentet, $J_{av} = 7.2$ Hz, 1H), 3.53-3.58 (m, 1H), 5.18 (bd, $J = 6.8$ Hz, 1H), 5.40 (bd, $J = 8.0$ Hz, 1H), 6.85 (dd, $J = 8.4$, 2.8 Hz, 1H), 7.18 (d, $J = 7.6$ Hz, 2H), 7.24-7.26 (m, 1H), 7.31-7.35 (m, 2H), 7.62 (td, $J = 8.0$ Hz, 2.4 Hz, 1H), 8.07 (s, 1H); $^{13}$C NMR (DMSO-D$_6$, 300 MHz, 350K) $\delta$ 23.0, 30.8, 31.7, 32.0, 55.9, 59.4, 62.4, 108.3 (d, $J = 37.3$ Hz), 124.9, 126.1, 127.9, 138.0, 139.0 (d, $J = 7.7$ Hz), 144.5 (d, $J = 15.2$ Hz), 144.8, 161.6 (d, $J = 232.6$ Hz), 163.8; MS (LR-APCI): calculated for C$_{19}$H$_{20}$FN$_3$ 309.16, measured 310.61 (M+H$^+$).

Cis-diastereomer: $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.79-2.17 (m, 5H), 2.27-2.49 (m, 3H), 3.56-3.62 (m, 2H), 4.94 (t, $J_{av} = 6.8$ Hz, 1H), 5.24 (t, $J_{av} = 6.2$ Hz, 1H), 6.91 (dd, $J = 8.4$, 3.0 Hz, 1H), 7.24-7.37 (m, 5H), 7.85 (td, $J_{av} = 8.0$ and $J_{av} = 2.5$ Hz, 1H), 8.29 (d, $J = 1.5$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 23.8, 33.1, 33.2, 35.1, 56.5, 61.6, 65.5, 109.0 (d, $J = 37.3$ Hz), 126.2, 127.2, 128.7, 136.5, 139.9 (d, $J = 7.6$ Hz), 143.6, 145.8 (d, $J = 14.7$), 162.6 (d, $J = 234.0$ Hz), 168.0; MS (LR-APCI): calculated for C$_{19}$H$_{20}$FN$_3$ 309.16, measured 310.60 (M+H$^+$).

Reaction time = 9 h; Ru$_3$(CO)$_{12}$ (6.6 mol%). The diastereomers were separated via flash chromatography (EtOAc then 70:1 then 30:1 then 15:1 (EtOAc:TEA)).

$^1$H NMR (DMSO-D$_6$, 300 MHz, 350K) $\delta$ 1.45-1.75 (m, 4H), 1.90-2.00 (m, 1H), 2.35-2.56 (m, 3H), 3.23-3.43 (m, 2H), 3.78 (s, 3H), 5.36 (d, $J = 7.2$ Hz, 2H), 6.40 (d, $J = 2.7$ Hz, 1H), 7.06 (d, $J = 8.7$ Hz, 1H), 7.19-7.39 (m, 8H); $^{13}$C NMR (DMSO-D$_6$, 300 MHz, 350K) $\delta$ 23.0, 31.3, 32.0 (isochronous), 55.8, 62.3, 62.9, 100.0, 109.0, 116.3, 118.8, 125.1, 125.7, 127.6, 127.8, 129.3, 135.3, 145.1, 164.0; MS (LR-APCI): calculated for C$_{23}$H$_{25}$N$_3$ 343.20, measured 344.91 (M+H$^+$).

Cis-diastereomer: $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 1.72-1.82 (m, 2H), 2.02-2.19 (m, 3H), 2.25-2.42 (m, 3H), 3.57 (t, $J_{av} = 7.2$ Hz, 2H), 3.78 (s, 3H), 5.08 (t, $J_{av} = 6.8$ Hz, 1H), 5.17-5.21 (m, 1H), 6.45 (d, $J = 3.0$ Hz, 1H), 7.04 (d, $J = 3.0$ Hz, 1H), 7.21-7.37 (m, 5H), 9.02 (s, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 23.8, 33.1, 33.2, 35.0, 56.7, 62.3, 65.3, 109.0 (d, $J = 37.3$ Hz), 126.2, 127.2, 128.7, 136.5, 139.9 (d, $J = 7.6$ Hz), 143.6, 145.8 (d, $J = 14.7$), 162.6 (d, $J = 234.0$ Hz), 168.0; MS (LR-APCI): calculated for C$_{19}$H$_{20}$FN$_3$ 309.16, measured 310.60 (M+H$^+$).
7.49 (d, J = 7.8 Hz, 2H), 7.66 (s, 1H); \(^{13}\text{C}\) NMR (CDCl\(_3\), 75 MHz) \(\delta\) 23.9, 32.8, 33.3, 34.1, 35.5, 56.6, 64.5, 65.9, 100.9, 109.2, 118.7, 120.6, 126.5, 126.6, 128.3, 128.4, 129.1, 135.2, 144.1, 168.7; MS (LR-APCI): calculated for C\(_{23}\)H\(_{25}\)N\(_3\) 343.20, measured 344.84 (M+H\(^{+}\)).

Reaction time = 6 h. The \(\text{trans}\)-diastereomer was obtained via flash chromatography (EtOAc then 70:1 then 30:1 then (EtOAc:TEA)). The \(\text{cis}\)-diastereomer was contaminated with unidentified byproducts and was not obtained in satisfactory purity. \(^1\text{H}\) NMR (CDCl\(_3\), 300 MHz) \(\delta\) 0.04 (s, 3H), 0.05 (s, 3H), 0.91 (s, 9H), 1.62-1.83 (m, 3H), 1.89-2.12 (m, 3H), 2.25-2.36 (m, 1H), 2.50-2.64 (m, 1H), 3.60 (t, J = 6.7 Hz, 2H), 3.74 (dd, J = 10.0, 2.8 Hz, 1H), 4.03 (dd, J = 10.0, 5.1 Hz, 1H), 4.31 (m, 1H), 4.85 (d, J = 8.2 Hz, 1H), 7.09-7.30 (m, 5H); \(^{13}\text{C}\) NMR (CDCl\(_3\), 75 MHz) \(\delta\) -5.4, 18.3, 23.8, 25.4, 26.0, 33.2, 34.0, 56.9, 60.9, 62.9, 64.1, 125.4, 126.6, 128.5, 146.0, 165.6; MS (LR-APCI): calculated for C\(_{21}\)H\(_{34}\)N\(_2\)O\(_2\)Si 358.24, measured 359.03 (M+H\(^{+}\)).

Reaction time = 12 h. Purification via flash chromatography (toluene/iPrOH = 3:1) then toluene/iPrOH:TEA = 30:10:1 yielded the product: \(^1\text{H}\) NMR (CDCl\(_3\), 300 MHz) \(\delta\) 1.32-1.61 (m, 4H), 1.86-2.04 (m, 3H), 2.25 (m, 1H), 2.38-2.49 (m, 1H), 2.52-2.63 (m, 1H), 3.00 (m, 1H), 3.71 (m, 2H), 3.79 (s, 3H), 3.99 (bd, J = 12.9 Hz, 1H), 5.13 (bm, 1H), 6.86 (m, 2H), 7.12 (m, 2H); \(^{13}\text{C}\) NMR (CDCl\(_3\), 75 MHz) \(\delta\) 19.3, 23.7, 25.5, 28.9, 31.3, 42.3, 55.2, 55.3, 56.4, 113.9, 127.6, 132.7, 158.1, 168.9. MS (LR-APCI): calculated for C\(_{16}\)H\(_{22}\)N\(_2\)O 258.17, measured 259.05 (M+H\(^{+}\)).

Reaction time = 24 h; Ru\(_3\)(CO)\(_{12}\) (10 mol%), arylboronic ester (1.3 equiv.). A diastereomeric mixture (1.3:1) was obtained via flash chromatography (SiO\(_2\), 100% Hex then Hex:EtOAc = 10:1) then 5:1). The \(\text{trans}\)-diastereomer can be obtained in good diastereomeric purity by washing the purified mixture with pentane, or can be obtained as a single diastereomer by recrystallization from hexanes. The \(\text{cis}\)-diastereomer was obtained with good diastereomeric purity by chromatographing the pentane filtrate (SiO\(_2\), 100% Hex then Hex:EtOAc = 20:1).

**Trans-diastereomer (lower R\(f\)):** \(^1\text{H}\) NMR (CDCl\(_3\), 400 MHz, 315K) \(\delta\) 1.78-1.86 (m, 2H), 2.51-2.56 (m, 2H), 5.48 (bs, 2H), 6.15 (d, J = 8.4 Hz, 1H), 6.37-6.40 (m, 1H), 7.16-7.32 (m, 11H), 7.98 (dm, 1H); \(^{13}\text{C}\) NMR (CDCl\(_3\), 100 MHz, 315K) \(\delta\) 32.2, 62.1, 108.3, 111.7, 126.0, 126.4, 128.3, 136.4, 144.2, 148.3, 155.9; MS (LR-APCI): calculated for C\(_{21}\)H\(_{20}\)N\(_2\)O\(_2\)Si 300.16, measured 301.48 (M+H\(^{+}\)).

**Cis-diastereomer (higher R\(f\)):** \(^1\text{H}\) NMR (CDCl\(_3\), 400 MHz) \(\delta\) 2.07-2.13 (m, 2H), 2.38-2.43 (m, 2H), 5.16 (m, 2H), 6.29 (d, J = 8.4 Hz, 1H), 6.54 (dd, J = 6.8, 5.2 Hz, 1H), 7.21-7.29 (m, 4H), 7.31-7.35 (m, 4H), 7.48 (d, J = 7.6 Hz, 4H), 8.08-8.10 (m, 1H); \(^{13}\text{C}\) NMR
Reaction time = 48 h; Ru$_3$(CO)$_{12}$ (10 mol%), arylboronic ester (1.4 equiv.). Purification via flash chromatography (Hex:EtOAc = 100% hexanes then 9:1) yielded the product as a mixture of diastereomers (2.4 : 1). The trans-diastereomer was obtained as a single diastereomer via recrystallization by dissolving in a minimal amount of pentane and storing at -20 °C overnight. 

Trans-diastereomer: $^1$H NMR (CDCl$_3$, 300 MHz) δ 0.04 (s, 3H), 0.93 (s, 9H), 1.82 (dd, $J = 12.3$, 6.3 Hz, 1H), 2.06-2.17 (m, 2H), 2.57-2.67 (m, 1H), 3.79 (dd, $J = 9.9$, 6.9, 1H), 4.01 (dd, $J = 9.9$, 3.0 Hz, 1H), 4.50-4.55 (m, 1H), 5.36 (d, $J = 8.4$ Hz, 1H), 6.40 (t, $J = 4.8$ Hz, 1H), 7.11-7.23 (m, 5H), 8.13 (bs, 1H), 8.32 (bs, 1H); $^{13}$C NMR (CDCl$_3$, 75 MHz), δ -5.4, 18.3, 25.2, 25.9, 32.9, 59.8, 61.7, 62.3, 109.4, 125.6, 126.1, 128.1, 144.6, 157.3, 157.6, 160.0; MS (LR-APCI): calculated for C$_{21}$H$_{31}$N$_3$OSi 369.22, measured 370.55 (M+H$^+$).

Reaction time = 36 h; Purification via flash chromatography (Hex:CH$_2$Cl$_2$ = 1:1) yielded the product: $^1$H NMR (CDCl$_3$, 300 MHz) δ 2.10-2.20 (m, 1H), 2.34-2.46 (m, 1H), 2.53-2.74 (m, 2H), 5.70 (t, $J_{av} = 5.3$ Hz, 1H), 6.74 (ddd, $J = 0.9$, 5.1, 7.1, Hz, 1H), 6.87-6.95 (m, 3H), 7.06-7.14 (m, 3H), 7.25-7.29 (m, 2H), 7.37-7.45 (m, 2H), 8.23-8.25 (m, 2H); $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 24.3, 30.1, 58.1, 112.8, 115.1 (d, $J = 21.1$ Hz), 116.1, 120.7, 121.7, 126.3, 127.9 (d, $J = 8.0$ Hz), 129.1, 129.2, 136.9, 139.0, 140.4, 148.5, 158.4, 161.5 (d, $J = 244.1$ Hz); MS (LR-APCI): calculated for C$_{20}$H$_{17}$FN$_2$ 304.14, measured 304.99 (M+H$^+$).

**IV. Cleavage of Amidines**

**IVA. Cleavage of Mono-Aryl Amidines.**

The mono-arylated amine (0.5 mmol) was dissolved in a solution of hydrazine/AcOH (2.5 M / 0.7 M respectively in 95% ethanol, 2 mL) in a 4 mL vial. The vial was filled with argon and tightly closed with a fully covered solid Teflon lined cap. The reaction vial was then heated in a reaction block at 120 °C for 1 h. After cooling to room temperature all the volatiles were removed by rotary evaporation. The residue was treated with 10% NaOH (1-2 mL) and ether (5-7 mL), the organic layer was separated, washed with water (2 mL) and dried by passing through a layer of K$_2$CO$_3$ (pipet). After removal of the solvent, the residue was dried in high vacuum to give pure amine.
97% Yield. The spectral data is in agreement with literature values\(^8\): 

\(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 1.43-1.89 (m, 7H), 2.79 (m, 1H), 3.18 (m, 1H), 3.53 (m, 1H), 3.78 (s, 3H), 6.85 (m, 2H), 7.28 (m, 2H). \(^13\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 25.5, 25.9, 35.0, 47.9, 55.2, 61.7, 113.6, 127.6, 137.9, 158.5.

70% Yield. The spectral data is in agreement with an authentic sample.

**IVb. Cleavage of Bis-Aryl Amidines.**

Method A:

**Trans-2** (102.4 mg, 0.353 mmol) was dissolved in a solution of hydrazine/AcOH (2.5 M/0.7 M respectively in 95% ethanol, 1.5 mL) in a 4 mL vial. The vial was filled with argon and tightly closed with a fully covered solid Teflon lined cap. The reaction vial was then heated in a reaction block at 140 °C for 24 h. After cooling to room temperature all the volatiles were removed by rotary evaporation. The residue was treated with 10% NaOH (1-2 mL) and ether (5-7 mL), the organic layer was separated and dried by passing through a layer of K\(_2\)CO\(_3\) (pipet). After removal of the solvent, the crude material was purified by column chromatography (SiO\(_2\); hexanes/EtOAc = 2:1) to give the product (26.2 mg, 33% yield).

Method B:

**Trans-2** (58.3 mg, 0.2 mmol) and benzyl bromide (29 \(\mu\)L, 41 mg, 0.24 mmol) were heated in acetonitrile (0.5 mL) in a 4 mL vial at 80 °C for 2.5 h. The solvent was removed by rotary evaporation and the residue was dissolved in a solution of hydrazine/AcOH (2.5 M/0.7 M respectively in 95% ethanol, 1 mL). The vial was filled with argon and tightly closed with a fully covered solid Teflon lined cap. The reaction vial was then heated in a reaction block at 140 °C for 3 h. After cooling to room temperature, the solvent was removed by rotary evaporation. The residue was treated with 10% NaOH (1 mL) and ether (5 mL). The organic layer was separated, and then dried by passing through a layer of K\(_2\)CO\(_3\) (pipet). After removal of the solvent, the residue was purified by column chromatography (SiO\(_2\); hexanes/EtOAc = 5:1) to give the product (20.5 mg, 46% yield).

The analogous procedure utilizing methyl iodide instead of benzyl bromide gave 68% isolated yield.

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Method C:

*Trans*-2 (58.3 mg, 0.2 mmol) was dissolved in a solution of hydrazine/TFA (2.5 M/0.8 M respectively in 95% ethanol, 0.8 mL) in a 4 mL vial. The vial was filled with argon and tightly closed with a fully covered solid Teflon lined cap. The reaction vial was then heated in a reaction block at 140 °C for 18 h. After cooling to room temperature all the volatiles were removed by rotary evaporation. The residue was treated with 10% NaOH (1 mL) and ether (5-7 mL), the organic layer was separated and passed through a pipet filled with K₂CO₃ (upper layer) and silica (1.5 mL, lower layer) eluating with Et₂O. The solvent was removed to give the product (35.9 mg, 80% yield).

The spectral data is in agreement with literature values:¹¹H NMR (CDCl₃, 400 MHz) δ 1.85-1.95 (m, 2H), 2.05 (bs, 1H), 2.35-2.43 (m, 2H), 4.54 (m, 2H), 7.23 (dt, J = 7.2, 1.2 Hz, 2H), 7.33 (m, 4H), 7.41 (m, 4H). ¹³C NMR (CDCl₃, 100 MHz) δ 35.6, 62.2, 126.3, 126.8, 128.4, 145.9.

Obtained via Method C (66% yield): ¹¹H NMR (CDCl₃, 400 MHz) δ 1.82-1.98 (m, 2H), 2.15 (bs, 1H), 2.36-2.48 (m, 2H), 4.52 (t, Jav = 7.0 Hz, 1H), 4.58 (t, Jav = 7.0 Hz, 1H), 7.24-7.28 (m, 2H), 7.33-7.41 (m, 4H), 7.76 (dt, J = 8.0, 1.6 Hz, 1H), 8.49 (dd, J = 4.8, 1.6 Hz, 1H), 8.64 (d, J = 2.4 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 35.3, 35.4, 59.7, 62.3, 123.4, 126.2, 126.9, 128.5, 133.9, 141.0, 145.3, 148.2, 148.4; MS (LR-APCI): calculated for C₁₅H₁₆N₂ 224.13, measured 225.19 (M+H⁺).

Obtained via Method C (75% yield): ¹¹H NMR (CDCl₃, 400 MHz) δ 1.81-1.97 (m, 2H), 2.06 (bs, 1H), 2.34-2.49 (m, 2H), 4.53 (t, Jav = 7.0 Hz, 1H), 4.62 (t, Jav = 7.0 Hz, 1H), 7.23-7.28 (m, 1H), 7.33-7.41 (m, 4H), 7.52-7.60 (m, 4H); MS (LR-APCI): calculated for C₁₇H₁₆F₃N 291.12, measured 292.18 (M+H⁺).

V. Isomerization Studies

Va. Conversion of Substrate S1: Kinetic Reaction Profile.

A reaction profile was obtained using the general arylation procedure on 0.5 mmol scale; however, dodecane (100 µL) was added as an internal standard. The reaction vial was taken out of the reaction block at time points, and into an argon filled glove box where an aliquot was taken out of the reaction for GC-MS analysis. The reaction vial was then replaced in the reaction block until the next time point. It was noticed that the repetitive stopping and starting of the reaction curtails catalyst activity. The isolated yields herein were obtained from >95% conversion of starting materials.

\[
\text{S1} \quad + \quad \text{O-B-Ph} \quad \xrightarrow{10 \text{ mol}\% \, \text{Ru}_3(\text{CO})_{12} \, 5 \text{ equiv. pinacolone}} \quad \text{dodecane} \quad 150^\circ C \quad \text{15}
\]


Isomerization studies were carried out according to the general arylation procedure; however, the concentration was adjusted to 0.2 M in substrate (ignoring volume of catalyst and boronate ester) with toluene and dodecane (internal standard). The reaction vial was taken out of the reaction block at given time points, and placed into an argon filled glove box where an aliquot was taken out of the reaction for GC-MS analysis. The reaction vial was then put back in the reaction block until the next time point. Studies
were carried out with diasteromerically enriched trans-15 (18.5 : 1) and diasteromerically pure trans-15 (>50 : 1). Under indental conditions diasteromerically enriched cis-15 (>30 : 1) also underwent extensive isomerization (trans / cis = 1 : 3) after 24 hours. Isomerization of trans-15 did not occur thermally (150 °C) in the absence of Ru₃(CO)₁₂ and boronate ester.
VI. $^1$H NMR Spectra of Starting Materials and Products