Supporting Information

Facile Pd-catalyzed Cross-Coupling of 2'-Deoxyguanosine O⁶-Arylsulfonates with Arylboronic Acids

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Thin-layer chromatography was performed on 250 μ silica plates (Analtech), while column chromatographic purifications were performed on 200-300 mesh silica gel (Natland). The arylboronic acids were obtained from Frontier Scientific and Aldrich. Components for the catalytic systems; Pd(OAc)₂, 2-(dicyclohexylphosphino)biphenyl, 2-(di-*tert*-butylphosphino)-biphenyl, 1,1'-bis(diphenylphosphino)ferrocene, ($\pm$)-2,2'-(diphenylphosphino)-1,1'-binaphthyl and 2-(dicyclohexylphosphino)-2'-(*N,N*-dimethylamino)-1,1'-biphenyl were purchased from Strem. All other reagents were obtained from commercial sources and used without further purification. 1,4-Dioxane was distilled over NaBH₄ and then stored over Na. Prior to each reaction 1,4-dioxane was freshly distilled. Compound **5** was prepared as described in the literature.²⁰ NMR spectra were recorded at 200 MHz in deacidified CDCl₃ (deacidification was performed by percolating the solvent through a bed of solid NaHCO₃ and basic alumina). Chemical shifts (δ) are in ppm and coupling constants (*J*) are in Hz.

Typical procedure for the cross-coupling of **5 with arylboronic acids.**

In an over-dried screwcap vial, equipped with a stirring bar, were placed Pd(OAc)₂ (1.6 mg, 7.1 μ mol), 2-(dicyclohexylphosphino)biphenyl (5.2 mg, 14.8 μ mol), K₃PO₄ (31.3 mg, 0.15 mmol), the nucleoside sulfonate **5** (50 mg, 73.7 μ mol), and the boronic acid (1.5 molar equiv, see individual compound headings for deviations). Anhydrous 1,4-dioxane (0.87 mL) was added, the vial was flushed with nitrogen, sealed with a Teflon-lined cap, and the mixture was heated at 80-82 °C in a pre-equilibrated sand bath. Upon completion of the reaction, the mixture was filtered through Celite and the residue was washed with acetone. Evaporation of the filtrate provided the crude mixtures that were purified by column chromatography on silica gel using solvents listed under the individual compound headings.

2-Amino-6-phenyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6a**).**

Chromatography: CH₂Cl₂ followed by 3% acetone in CH₂Cl₂. Pale yellow foam, R_f (5% acetone in CH₂Cl₂) = 0.88. ¹H NMR: 8.64-8.59 (m, 2H, Ar-*H*), 8.05 (s, 1H, Purine-*H*), 7.54-7.46 (m, 3H, Ar-*H*), 6.39 (t, 1H, 1', *J* = 6.6), 4.99 (br s, 2H, NH₂), 4.64-4.58 (m, 1H, 3'), 4.00 (app q, 1H, 4', *J* ~ 3.6), 3.86-3.71 (two overlapping dd, 2H, 5'a and 5'b, *J*(5'a) = 4.4; 11.0, *J*(5'b) = 3.4; 11.0), 2.65 (app quint, 1H, 2', *J* ~ 6.5), 2.38 (ddd, 1H, 2', *J* = 3.5; 5.9; 12.9), 0.91, 0.89 (2s, 18H,

$C(CH_3)_3$), 0.10, 0.06 (2s, 12H, Si- CH_3). HRMS calcd for $C_{28}H_{46}N_5O_3Si_2$ ($M^+ + H$) 556.3139, found 556.3118.

2-Amino-6-(3-methoxyphenyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6b).

Chromatography: CH_2Cl_2 followed by 3% acetone in CH_2Cl_2 . Pale yellow thick oil, R_f (5% acetone in CH_2Cl_2) = 0.63. 1H NMR: 8.27 (br d, 1H, Ar- H , J = 8.1), 8.16 (narrow m, 1H, Ar- H), 8.06 (s, 1H, Purine- H), 7.42 (t, 1H, Ar- H , J = 8.1), 7.03 (br dd, 1H, Ar- H , J = 1.7; 8.0), 6.39 (t, 1H, 1', J = 6.7), 5.05 (br s, 2H, NH_2), 4.63-4.57 (m, 1H, 3'), 3.99 (app q, 1H, 4', J ~ 3.5), 3.90 (s, 3H, OCH_3), 3.85-3.71 (two overlapping dd, 2H, 5'a and 5'b, $J(5'a)$ = 4.1; 10.6, $J(5'b)$ = 3.2; 10.6), 2.63 (app quint, 1H, 2', J ~ 6.4), 2.38 (ddd, 1H, 2', J = 3.6; 5.9; 12.9), 0.91, 0.89 (2s, 18H, $C(CH_3)_3$), 0.10, 0.06 (2s, 12H, Si- CH_3). HRMS calcd for $C_{29}H_{48}N_5O_4Si_2$ ($M^+ + H$) 586.3245, found 586.3246.

2-Amino-6-(4-methoxyphenyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6c).

Chromatography: CH_2Cl_2 followed by 3% acetone in CH_2Cl_2 . Yellow thick oil, R_f (5% acetone in CH_2Cl_2) = 0.62. 1H NMR: 8.65 (d, 2H, Ar- H , J = 8.8), 8.04 (s, 1H, Purine- H), 7.02 (d, 2H, Ar- H , J = 8.8), 6.37 (t, 1H, 1', J = 6.6), 5.00 (br s, 2H, NH_2), 4.63-4.57 (m, 1H, 3'), 3.99 (app q, 1H, 4', J ~ 3.4), 3.86 (s, 3H, OCH_3), 3.83-3.70 (two overlapping dd, 2H, 5'a and 5'b, $J(5'a)$ = 3.8; 11.0, $J(5'b)$ = 3.4; 11.0), 2.63 (app quint, 1H, 2', J ~ 6.5), 2.37 (ddd, 1H, 2', J = 3.5; 5.9; 12.9), 0.91, 0.89 (2s, 18H, $C(CH_3)_3$), 0.10, 0.06 (2s, 12H, Si- CH_3). HRMS calcd for $C_{29}H_{48}N_5O_4Si_2$ ($M^+ + H$) 586.3245, found 586.3244.

2-Amino-6-(3,4-methylenedioxyphenyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6d).

Chromatography: CH_2Cl_2 followed by 3% acetone in CH_2Cl_2 . Dark yellow thick oil, R_f (5% acetone in CH_2Cl_2) = 0.57. 1H NMR: 8.35 (dd, 1H, Ar- H , J = 1.7; 8.4), 8.16 (d, 1H, Ar- H , J = 1.4), 8.03 (s, 1H, Purine- H), 6.94 (d, 1H, Ar- H , J = 8.3), 6.37 (t, 1H, 1', J = 6.4), 6.01 (s, 2H, OCH_2O), 5.00 (br s, 2H, NH_2), 4.63-4.57 (m, 1H, 3'), 3.99 (app q, 1H, 4', J ~ 3.5), 3.85-3.70 (two overlapping dd, 2H, 5'a and 5'b, $J(5'a)$ = 4.1; 11.3, $J(5'b)$ = 3.3; 11.3), 2.62 (app quint, 1H, 2', J ~ 6.6), 2.37 (ddd, 1H, 2', J = 3.5; 6.1; 13.0), 0.91, 0.89 (2s, 18H, $C(CH_3)_3$), 0.09, 0.06 (2s, 12H, Si- CH_3). HRMS calcd for $C_{29}H_{46}N_5O_5Si_2$ ($M^+ + H$) 600.3037, found 600.3060.

2-Amino-6-(4-acetylphenyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6e).

Chromatography: CH₂Cl₂ followed by 3% EtOAc in CH₂Cl₂. Yellow foam, R_f (5% acetone in CH₂Cl₂) = 0.45. ¹H NMR: 8.74 (d, 2H, Ar-*H*, *J* = 8.2), 8.10 (s, 1H, Purine-*H*), 8.08 (d, 2H, Ar-*H*, *J* = 8.2), 6.40 (t, 1H, 1', *J* = 6.5), 5.06 (br s, 2H, NH₂), 4.64-4.58 (m, 1H, 3'), 4.00 (app q, 1H, 4', *J* ~ 3.4), 3.86-3.71 (two overlapping dd, 2H, 5'a and 5'b, *J*(5'a) = 4.1; 11.0, *J*(5'b) = 3.6; 11.0), 2.65 (s, 3H, COCH₃), 2.63 (app quint, 1H, 2', *J* ~ 6.6), 2.39 (ddd, 1H, 2', *J* = 3.5; 6.1; 12.9), 0.91, 0.90 (2s, 18H, C(CH₃)₃), 0.10, 0.07 (2s, 12H, Si-CH₃). HRMS calcd for C₃₀H₄₈N₅O₄Si₂ (M⁺ + H) 598.3245, found 598.3249.

2-Amino-6-(3-nitrophenyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6f).

Chromatography: CH₂Cl₂ followed by 3% acetone in CH₂Cl₂. Yellow-orange thick oil, R_f (5% acetone in CH₂Cl₂) = 0.57. ¹H NMR: 9.53 (s, 1H, Ar-*H*), 9.13 (d, 1H, Ar-*H*, *J* = 8.1), 8.32 (d, 1H, Ar-*H*, *J* = 8.1), 8.12 (s, 1H, Purine-*H*), 7.68 (t, 1H, Ar-*H*, *J* = 8.1), 6.39 (t, 1H, 1', *J* = 6.3), 5.06 (br s, 2H, NH₂), 4.62-4.58 (m, 1H, 3'), 4.00 (app q, 1H, 4', *J* ~ 3.4), 3.86-3.71 (two overlapping dd, 2H, 5'a and 5'b, *J*(5'a) = 4.1; 11.1, *J*(5'b) = 4.0; 11.1), 2.63 (app quint, 1H, 2', *J* ~ 6.4), 2.39 (ddd, 1H, 2', *J* = 3.8; 6.2; 13.0), 0.91, 0.90 (2s, 18H, C(CH₃)₃), 0.10, 0.07 (2s, 12H, Si-CH₃). HRMS calcd for C₂₈H₄₅N₆O₅Si₂ (M⁺ + H) 601.2990, found 601.2993.

2-Amino-6-(3-formylphenyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6g).

Chromatography: CH₂Cl₂ followed by 5% EtOAc in CH₂Cl₂. Yellowish-brown solid, R_f (5% acetone in CH₂Cl₂) = 0.39. ¹H NMR: 10.14 (s, 1H, CHO), 9.14 (s, 1H, Ar-*H*), 8.98 (d, 1H, Ar-*H*, *J* = 8.3), 8.10 (s, 1H, Purine-*H*), 8.01 (d, 1H, Ar-*H*, *J* = 7.2), 7.67 (t, 1H, Ar-*H*, *J* = 7.7), 6.40 (t, 1H, 1', *J* = 6.6), 5.04 (br s, 2H, NH₂), 4.62-4.59 (m, 1H, 3'), 4.00 (app q, 1H, 4', *J* ~ 3.3), 3.86-3.71 (two overlapping dd, 2H, 5'a and 5'b, *J*(5'a) = 4.1; 11.0, *J*(5'b) = 3.9; 11.0), 2.62 (app quint, 1H, 2', *J* ~ 6.5), 2.38 (ddd, 1H, 2', *J* = 3.8; 5.4; 13.2), 0.91, 0.89 (2s, 18H, C(CH₃)₃), 0.10, 0.07 (2s, 12H, Si-CH₃). HRMS calcd for C₂₉H₄₆N₅O₄Si₂ (M⁺ + H) 584.3088, found 584.3056.

2-Amino-6-(2-ethoxyphenyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6h).

Reaction was conducted with 3.0 molar equiv of the boronic acid. Chromatography: CH₂Cl₂ followed by 3% acetone in CH₂Cl₂. Clear thick oil, R_f (5% acetone in CH₂Cl₂) = 0.36. ¹H

NMR: 7.96 (s, 1H, Purine-*H*), 7.50 (dd, 1H, Ar-*H*, $J = 1.8$; 7.4), 7.38 (dt, 1H, Ar-*H*, $J = 1.5$; 7.7), 7.03 (t, 2H, Ar-*H*, $J = 8.5$), 6.37 (dd, 1H, 1', $J = 6.1$; 7.1), 5.18 (br s, 2H, NH₂), 4.62-4.56 (m, 1H, 3'), 4.06 (q, 2H, OCH₂, $J = 6.8$), 3.99 (app q, 1H, 4', $J \sim 3.6$), 3.85-3.71 (two overlapping dd, 2H, 5'a and 5'b, $J(5'a) = 4.2$; 11.2, $J(5'b) = 3.6$; 11.2), 2.65 (app quint, 1H, 2', $J \sim 6.5$), 2.35 (ddd, 1H, 2', $J = 3.2$; 6.0; 12.8), 1.22 (t, 3H, CH₃, $J = 6.8$), 0.91, 0.88 (2s, 18H, C(CH₃)₃), 0.10, 0.05, 0.04 (3s, 12H, Si-CH₃). HRMS calcd for C₃₀H₅₀N₅O₄Si₂ (M⁺ + H) 600.3401, found 600.3376.

2-Amino-6-(4-*tert*-butylphenyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6i).

Reaction was conducted with 3.0 molar equiv of the boronic acid. Chromatography: CH₂Cl₂ followed by 3% acetone in CH₂Cl₂. Clear thick oil, R_f (5% acetone in CH₂Cl₂) = 0.60. ¹H NMR: 8.50 (d, 2H, Ar-*H*, $J = 8.5$), 8.03 (s, 1H, Purine-*H*), 7.53 (d, 2H, Ar-*H*, $J = 8.5$), 6.38 (t, 1H, 1', $J = 6.6$), 4.99 (br s, 2H, NH₂), 4.62-4.59 (m, 1H, 3'), 3.99 (app q, 1H, 4', $J \sim 3.5$), 3.85-3.68 (two overlapping dd, 2H, 5'a and 5'b, $J(5'a) = 4.0$; 11.1, $J(5'b) = 3.4$; 11.1), 2.65 (app quint, 1H, 2', $J \sim 6.5$), 2.36 (ddd, 1H, 2', $J = 3.5$; 5.9; 13.0), 1.34 (s, 9H, C(CH₃)₃), 0.91, 0.89 (2s, 18H, C(CH₃)₃), 0.10, 0.06 (2s, 12H, Si-CH₃). HRMS calcd for C₃₂H₅₄N₅O₃Si₂ (M⁺ + H) 612.3765, found 612.3752.

2-Amino-6-(3-thienyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6j).

Reaction was conducted with 2.5 molar equiv of the boronic acid. Chromatography: CH₂Cl₂ followed by 3% acetone in CH₂Cl₂. Yellow foam, R_f (5% acetone in CH₂Cl₂) = 0.65. ¹H NMR: 8.77 (d, 1H, Ar-*H*, $J = 2.6$), 8.16 (d, 1H, Ar-*H*, $J = 5.1$), 8.04 (s, 1H, Purine-*H*), 7.39 (dd, 1H, Ar-*H*, $J = 3.0$; 5.1), 6.37 (t, 1H, 1', $J = 6.7$), 4.95 (br s, 2H, NH₂), 4.63-4.57 (m, 1H, 3'), 3.99 (app q, 1H, 4', $J \sim 3.5$), 3.85-3.70 (two overlapping dd, 2H, 5'a and 5'b, $J(5'a) = 4.1$; 11.1, $J(5'b) = 3.6$; 11.1), 2.63 (app quint, 1H, 2', $J \sim 6.4$), 2.37 (ddd, 1H, 2', $J = 3.5$; 6.0; 12.9), 0.91, 0.89 (2s, 18H, C(CH₃)₃), 0.09, 0.06 (2s, 12H, Si-CH₃). HRMS calcd for C₂₆H₄₄N₅O₃SSi₂ (M⁺ + H) 562.2703, found 562.2719.

2-Amino-6-(4-dibenzofuranyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine (6k).

Reaction was conducted with 2.5 molar equiv of the boronic acid. Chromatography: CH₂Cl₂ followed by 1% acetone in CH₂Cl₂. White foam, R_f (5% acetone in CH₂Cl₂) = 0.40. ¹H NMR: 8.25 (d, 1H, Ar-*H*, $J = 7.8$), 8.07 (d, 1H, Ar-*H*, $J = 8.1$), 8.05 (s, 1H, Purine-*H*), 7.97 (d, 1H, Ar-

H , $J = 7.0$), 7.61-7.30 (m, 4H, Ar- H), 6.41 (t, 1H, 1', $J = 6.6$), 5.16 (br s, 2H, NH_2), 4.65-4.59 (m, 1H, 3'), 4.01 (app q, 1H, 4', $J \sim 3.5$), 3.87-3.71 (two overlapping dd, 2H, 5'a and 5'b, $J(5'a) = 4.2$; 11.1, $J(5'b) = 3.6$; 11.1), 2.69 (app quint, 1H, 2', $J \sim 6.5$), 2.39 (ddd, 1H, 2', $J = 3.4$; 6.1; 13.0), 0.92, 0.89 (2s, 18H, $C(CH_3)_3$), 0.11, 0.063, 0.058 (3s, 12H, Si- CH_3). HRMS calcd for $C_{34}H_{48}N_5O_4Si_2$ ($M^+ + H$) 646.3245, found 646.3270.

6-Phenyl-2'-deoxynebularine^{6b} by desilylation of the bis-TBDMS ether.

6-Phenyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxynebularine¹¹ (42.1 mg, 77.8 μ mol) was dissolved in anhydrous THF (0.61 mL) and cooled to 0 °C. A 1 M solution of $n\text{-Bu}_4\text{N}^+\text{F}^-$ (0.171 mL, 0.171 mmol, 2.2 molar equiv) was added and the mixture was stirred at 0 °C for 0.5 h. The mixture was evaporated to dryness and chromatographed on a silica gel column using 3% MeOH in CH_2Cl_2 . The product was isolated as a beige solid (21.4 mg, 88%). R_f (5% acetone in CH_2Cl_2) = 0.17. ^1H NMR: 8.97 (s, 1H, Pur- H), 8.75-8.701 (m, 2H, Ar- H), 8.18 (s, 1H, Pur- H), 7.56-7.54 (m, 3H, Ar- H), 6.43 (dd, 1H, 1', $J = 5.5$; 9.3), 5.88 (br d, 1H, OH, $J = 10.7$), 4.82 (d, 1H, 3', $J = 4.7$), 4.24 (app s, 1H, 4'), 4.00 (d, 1H, 5', $J = 12.6$), 3.81 (app t, 1H, 5', $J \sim 11.5$), 3.15 (ddd, 1H, 2', $J = 5.1$; 9.5; 13.4), 2.36 (dd, 1H, 2', $J = 5.4$; 13.4), 2.21 (br s, 1H, OH). We have also observed the resonances at 5.88 and 2.21 ppm as broad signals, in this event the H5' resonance at 3.81 ppm appears as a doublet. The spectral pattern observed in CDCl_3 was comparable to others described in Lakshman, M. K.; Lehr, R. E. *Nucleosides & Nucleotides* **1992**, *11*, 1039-1046.