# Azoles as Suzuki Cross-Coupling Leaving Groups: Syntheses of 6-Arylpurine 2'-Deoxynucleosides and Nucleosides from 6-(Imidazol-1-yl)- and 6-(1,2,4-Triazol-4-yl)purine Derivatives

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# Supporting Information

I. Pages S2–S8: Experimental details and characterization data.
II. Pages S9–S23: $^{1}$H NMR spectra of reaction products in the order presented in pages S2–S8.

**General Information:** $^{1}H$ (500 MHz) and $^{13}C$ (125 MHz) spectra were determined with solutions in $CDCl_3$ unless otherwise indicated. High-resolution mass spectra (MS) were determined in the FAB mode (glycerol, NaOAc).

**Method 1.** Under a flushing atmosphere of argon in a glove bag, 6-(imidazol-1-yl)-9-[2,3,5-tri-*O*-(4-methylbenzoyl)-β-D-ribofuranosyl]purine (100 mg, 0.149 mmol), $Ni(COD)_2$ (4.1 mg, 0.015 mmol), SIPr·HCl (6.4 mg, 0.015 mmol), a boronic acid (2 equiv.), and $K_3PO_4$ (95 mg, 0.446 mmol) were added to a Schlenk flask containing a magnetic stir bar. The flask was evacuated and refilled with argon three times and then charged with THF. The mixture was heated with stirring at 60 ˚C for 8 h and allowed to cool to ambient temperature. The mixture was filtered, and the filter cake was washed with EtOAc. Volatiles were removed in vacuo, and the residue was purified by chromatography (silica gel; EtOAc/hexanes, 1:4) to give the isolated coupling products.

**Method 2.** Under a flushing atmosphere of argon in a glove bag, 9-(3,5-di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-6-(1,2,4-triazol-4-yl)purine (50 mg, 0.129 mmol), $Ni(COD)_2$ (4 mg, 0.013 mmol), IPr·HCl (6 mg, 0.013 mmol), a boronic acid (2 equiv.), and CsF (59 mg, 0.39 mmol) were added to a Schlenk flask containing a magnetic stir bar. The flask was evacuated and refilled with argon three times and then charged with THF. The mixture was heated with stirring at 60 ˚C for 8 h and then allowed to cool to ambient temperature. The mixture was filtered, and the filter cake was washed with EtOAc. Volatiles were evaporated in vacuo, and the residue was purified by chromatography (silical gel ; $CH_2Cl_2/Me_2CO$, 15:1) to give the isolated coupling products.

**6-(Imidazol-1-yl)-9-[2,3,5-tri-*O*-(4-methylbenzoyl)-β-D-ribofuranosyl]purine (3).** $^{1}H$ NMR δ 2.39, 2.40, 2.44 (3 × s, 3 × 3H), 4.67 (dd, $J$ = 12.5, 4.4 Hz, 1H), 4.84-4.87 (m, 1H), 4.93 (dd, $J$ =

12.5, 3.5 Hz, 1H), 6.22 (t, *J* = 5.0 Hz, 1H), 6.43 (t, *J* = 5.4 Hz, 1H), 6.49 (d, *J* = 4.9 Hz, 1H), 7.16-7.97 (m, 13H), 8.27, 8.69, 9.14 (3 × s, 3 × 1H), 8.357-8.363 (m, 1H); $^{13}$C NMR δ 21.96, 21.99, 22.02, 63.5, 71.6, 74.0, 81.4, 87.6, 117.6, 123.3, 125.8, 126.2, 126.7, 129.5, 129.6, 130.0, 130.1, 131.0, 137.9, 143.4, 144.6, 144.9, 145.1, 146.1, 152.8, 153.4, 165.5, 165.7, 166.4; HRMS *m/z* 695.2230 [$MNa^+$ ($C_{37}H_{32}N_6O_7Na$) = 695.2230].

**6-(Benzimidazol-1-yl)-9-[2,3,5-tri-*O*-(4-methylbenzoyl)-β-D-ribofuranosyl]purine (6).** $^1$H NMR δ 2.36, 2.39, 2.44 (3 × s, 3 × 3H), 4.68 (dd, *J* = 12.5, 4.2 Hz, 1H), 4.86-4.88 (m, 1H), 4.95 (dd, *J* = 12.2, 3.4 Hz, 1H), 6.25 (t, *J* = 5.1 Hz, 1H), 6.43 (t, *J* = 5.4 Hz, 1H), 6.47 (t, *J* = 5.4 Hz, 1H), 6.53 (d, *J* = 4.9 Hz, 1H), 7.17-7.25 (m, 6H), 7.41-7.48 (m, 2H), 7.83-7.97 (m, 7H), 8.29, 9.88 (2 × s, 2 × 1H), 8.83-8.84 (m, 2H); $^{13}$C NMR δ 21.9, 22.0, 63.5, 71.6, 74.1, 81.4, 87.5, 116.8, 120.7, 123.5, 124.7, 125.2, 125.8, 126.2, 126.7, 129.5, 129.6, 130.0, 130.1, 132.2, 142.6, 144.3, 144.6, 144.9, 145.0, 148.1, 152.8, 152.9, 165.5, 165.7, 166.4; HRMS *m/z* 745.2402 [$MNa^+$ ($C_{41}H_{34}N_6O_7Na$) = 745.2387].

**9-[2-Deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-D-*erythro*-pentofuranosyl]-6-(imidazol-1-yl)purine.** $^1$H NMR δ 2.36, 2.45 (2 × s, 2 × 3H), 2.90-2.95 (m, 1H), 3.19-3.25 (m, 1H), 4.64-4.70 (m, 2H), 4.82 (dd, *J* = 11.7, 3.4 Hz, 1H), 5.84-5.87 (m, 1H), 6.60-6.62 (m, 1H), 7.16-7.99 (m, 9H), 8.28, 8.35, 8.72, 9.12 (4 × s, 4 × 1H); $^{13}$C NMR δ 21.9, 22.0, 38.2, 64.0, 75.2, 83.6, 85.6, 117.6, 123.2, 126.5, 126.7, 129.4, 129.6, 129.8, 130.1, 131.0, 137.9, 142.9, 144.5, 144.9, 146.0, 152.5, 153.2, 166.2, 166.3; HRMS *m/z* 561.1874 [$MNa^+$ ($C_{29}H_{26}N_6O_5Na$) = 561.1862].

**6-Phenyl-9-[2,3,5-tri-*O*-(4-methylbenzoyl)-β-D-ribofuranosyl]purine.** Treatment of **3** (100 mg, 0.15 mmol) with phenylboronic acid (36 mg, 0.30 mmol) by method 1gave the title compound (74mg, 73%): $^1$H NMR δ 2.39, 2.40, 2.43, (3 × s, 3 × 3H), 4.68 (dd, *J* = 12.2, 3.9 Hz, 1H), 4.84-4.86 (m, 1H), 4.92 (dd, *J* = 12.2, 3.4 Hz, 1H), 6.26 (t, *J* = 5.5 Hz, 1H), 6.47 (t, *J* = 5.3

Hz, 1H), 6.53 (d, *J* =5.4 Hz, 1H), 7.16-8.00 (m, 15H), 8.28, 8.95 (2 × s, 2 × 1H), 8.71-8.73 (m, 2H); $^{13}$C NMR δ 21.98, 22.01, 63.7, 71.7, 73.9, 81.2, 87.1, 125.9, 126.3, 126.8, 128.9, 129.5, 129.6, 130.01, 130.04, 130.1, 131.3, 131.9, 135.7, 143.1, 144.5, 144.8, 144.9, 152.3, 153.0, 155.7, 165.4, 165.7, 166.5; HRMS *m/z* 705.2324 [MNa$^+$ ($C_{40}H_{33}N_4O_7Na$) = 705.2305].

**6-(4-Methylphenyl)-9-[2,3,5-tri-*O*-(4-methylbenzoyl)-β-D-ribofuranosyl]purine.** Treatment of **3** (100 mg, 0.15 mmol) with 4-methylphenylboronic acid (40 mg, 0.30 mmol) by method 1 gave the title compound (84 mg, 81%). $^1$H NMR δ 2.38, 2.40, 2.43, 2.45 (4 × s, 4 × 3H), 4.68 (dd, *J* = 12.2, 3.9 Hz, 1H), 4.83-4.85 (m, 1H), 4.91(dd, *J* = 12.2, 3.0 Hz, 1H), 6.26 (t, *J* = 5.2 Hz, 1H), 6.46 (t, *J* = 5.3 Hz, 1H), 6.53 (t, *J* = 5.4 Hz, 1H), 7.16-8.00 (m, 14H), 8.27, 8.93 (2 × s, 2 × 1H), 8.64 (d, *J* = 8.0 Hz, 2H); $^{13}$C NMR δ 21.87, 21.95, 22.01, 63.7, 71.7, 73.9, 81.2, 87.0, 125.9, 126.3, 126.8, 129.47, 129.52, 129.6, 129.7, 130.0, 130.1, 131.7, 132.9, 141.8, 142.8, 144.4, 144.8, 144.9, 152.2, 152.9, 155.7, 165.4, 165.7, 166.5 HRMS *m/z* 719.2483 [Mna$^+$ ($C_{41}H_{36}N_4O_7Na$) = 719.2482].

**6-(4-Methoxyphenyl)-9-[2,3,5-tri-*O*-(4-methylbenzoyl)-β-D-ribofuranosyl]purine (5).** Treatment of **3** (100 mg, 0.15 mmol) with 4-methoxyphenylboronic acid (**4**) (45 mg, 0.30 mmol) by method 1 gave **5** (88mg, 83%): $^1$H NMR δ 2.38, 2.40, 2.43 (3 × s, 3 × 3H), 3.90 (s, 3H), 4.69 (dd, *J* = 12.2, 3.9 Hz, 1H), 4.85 (dd, *J* = 7.8, 4.4 Hz, 1H), 4.92 (dd, *J* = 12.2, 3.4 Hz, 1H), 6.27 (t, *J* = 5.3 Hz, 1H), 6.47 (t, *J* = 5.3 Hz, 1H), 6.54 (d, *J* = 5.4 Hz 1H), 7.06–8.01 (m, 14H), 8.27 (s, 1H), 8.77 (d, *J* = 8.8 Hz, 2H), 8.91 (s, 1H); $^{13}$C NMR δ 21.9, 21.97, 22.00, 55.6, 63.7, 71.7, 74.0, 81.2, 87.1, 114.3, 126.0, 126.3, 126.8, 128.4, 129.48, 129.52, 129.6, 130.0, 130.1, 130.2, 131.3, 131.8, 142.6, 144.4, 144.8, 144.9, 152.2, 152.9, 155.3, 162.3, 165.5, 165.7, 166.5; HRMS *m/z* 735.2416 [MNa$^+$ ($C_{41}H_{36}N_4O_8Na$) = 735.2431].

**6-(4-Fluorophenyl)-9-[2,3,5-tri-*O*-(4-methylbenzoyl)-β-D-ribofuranosyl]purine.**

Treatment of **3** (100 mg, 0.15 mmol) with 4-fluorophenylboronic acid (42 mg, 0.30 mmol) by method 1 gave the title compound (81mg, 78%): $^1$H NMR δ 2.38, 2.40, 2.43 (3 × s, 3 × 3H), 4.68 (dd, $J$ = 12.2, 3.9 Hz, 1H), 4.84-4.86 (m, 1H), 4.92 (dd, $J$ = 12.2, 3.0 Hz, 1H), 6.25 (t, $J$ = 5.0 Hz, 1H), 6.46 (t, $J$ = 5.5 Hz, 1H), 6.52 (d, $J$ =5.4 Hz, 1H), 7.16-8.00 (m, 14H), 8.28, 8.92 (2 × s, 2 × 1H), 8.78-8.81 (m, 2H); $^{13}$C NMR δ 21.97, 22.01, 63.7, 71.6, 73.9, 81.2, 87.2, 116.0 (d, $J_{C\text{-}F}$ = 21 Hz), 125.9, 126.2, 126.8, 129.5, 129.6, 130.0, 130.1, 131.6, 131.9, 132.3 (d, $J_{C\text{-}F}$ = 8 Hz), 143.1, 144.5, 144.8, 144.9, 152.4, 152.9, 154.4, 164.9 (d, $J_{C\text{-}F}$ = 251 Hz), 165.5, 165.7, 166.5; HRMS *m/z* 723.2225 [$MNa^+$ ($C_{40}H_{33}N_4O_7Na$) = 723.2231].

**9-[2-Deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-D-*erythro*-pentofuranosyl]-6-phenylpurine.**[1] Treatment of 9-[2-deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-D-*erythro*-pentofuranosyl]-6-(imidazol-1-yl)purine (50 mg, 0.093 mmol) with phenylboronic acid (23 mg, 0.186 mmol) by method 1 gave the title compound (35 mg, 68%): $^1$H NMR δ 2.37, 2.46 (2 × s, 2 × 3H), 2.89-2.94 (m, 1H), 3.20-3.26 (m, 1H), 4.67-4.71 (m, 2H), 4.79-4.82 (m, 1H), 5.85-5.87 (m, 1H), 6.64-6.67 (m, 1H), 7.19-8.00 (m, 11H), 8.31, 8.99 (2 × s, 2 × 1H), 8.74-8.75 (m, 2H); $^{13}$C NMR δ 21.9, 22.0, 38.2, 64.2, 75.4, 83.4, 85.2, 126.6, 126.9, 128.9, 129.5, 129.6, 129.8, 130.0, 130.1, 131.3, 131.9, 135.7, 142.6, 144.4, 144.8, 152.2, 152.7, 155.5, 166.2, 166.4; HRMS *m/z* 571.1949 [$MNa^+$ ($C_{32}H_{28}N_4O_5Na$) = 571.1957].

**9-[2-Deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-D-*erythro*-pentofuranosyl]-6-(4-methylphenyl)purine.** Treatment of 9-[2-deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-D-*erythro*-pentofuranosyl]-6-(imidazol-1-yl)purine (50 mg, 0.093 mmol) with 4-methylphenylboronic acid (25 mg, 0.186 mmol) by method 1 gave the title compound (32mg, 61%): $^1$H NMR δ 2.38, 2.46 (2 × s, 2 × 3H), 2.89-2.93 (m, 1H), 3.20-3.25 (m, 1H), 4.67-4.71 (m, 2H), 4.79-4.82 (m, 1H), 5.85-5.86 (m, 1H), 6.64-6.67 (m, 1H), 7.20-8.00 (m, 10H), 8.23, 8.96 (2 × s, 2 × 1H), 8.65 (d, $J$ =

8.5 Hz, 2H); $^{13}$C NMR δ 21.88, 21.92, 22.0, 38.2, 64.2, 75.4, 83.4, 85.2, 126.6, 126.8, 129.5, 129.6, 129.7, 129.9, 130.0, 130.1, 131.7, 133.0, 141.8, 142.4, 144.4, 144.8, 152.1, 152.7, 155.5, 166.2, 166.4; HRMS *m/z* 585.2122 [$MNa^+$ ($C_{33}H_{30}N_4O_5Na$) = 585.2114].

**9-[2-Deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-D-*erythro*-pentofuranosyl]-6-(4-methoxyphenyl)purine.**[1] Treatment of 9-[2-deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-D-*erythro*-pentofuranosyl]-6-(imidazol-1-yl)purine (100 mg, 0.186 mmol) with 4-methoxyphenylboronic acid (**4**) (56 mg, 0.37 mmol) by method 1 gave the title compound (80mg, 75%): $^1$H NMR δ 2.38, 2.46 (2 × s, 2 × 3H), 2.88-2.92 (m, 1H), 3.18-3.23 (m, 1H), 3.91 (s, 3H), 4.68-4.71 (m, 2H), 4.78-4.82 (m, 1H), 5.58-5.86 (m, 1H), 6.64-6.66 (m, 1H), 7.07-8.00 (m, 10H), 8.27, 8.93 (2 × s, 2 × 1H), 8.77 (d, *J* = 8.5 Hz, 2H), $^{13}$C NMR δ 21.9, 22.0, 38.2, 55.6, 64.2, 75.4, 83.4, 85.2, 114.3, 126.7, 126.9, 128.4, 129.5, 129.9, 130.1, 131.3, 131.8, 142.1, 144.4, 144.8, 152.0, 152.6, 155.1, 162.3, 166.2, 166.4; HRMS *m/z* 601.2061 [$MNa^+$ ($C_{33}H_{30}N_4O_6Na$) = 601.2063].

**9-[2-Deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-D-*erythro*-pentofuranosyl]-6-(4-fluorophenyl)purine.**[1] Treatment of 9-[2-deoxy-3,5-di-*O*-(4-methylbenzoyl)-β-D-*erythro*-pentofuranosyl]-6-(imidazol-1-yl)purine (50 mg, 0.093 mmol) with 4-fluorophenylboronic acid (26 mg, 0.186 mmol) by method 1 gave the title compound (34mg, 65%): $^1$H NMR δ 2.37, 2.46 (2 × s, 2 × 3H), 2.89-2.94 (m, 1H), 3.20-3.25 (m, 1H), 4.67-4.71 (m, 2H), 4.79-4.82 (m, 1H), 5.85-5.87 (m, 1H), 6.63-6.66 (m, 1H), 7.20-8.00 (m, 10H), 8.30, 8.95 (2 × s, 2 × 1H), 8.81-8.84(m, 2H); $^{13}$C NMR δ 21.9, 22.0, 38.2, 64.2, 75.4, 83.4, 85.3, 116.0 (d, $J_{C\text{-}F}$ = 22 Hz ), 126.6, 126.8, 129.5, 129.6, 129.8, 130.1, 131.6, 131.9, 132.3 (d, $J_{C\text{-}F}$ = 8 Hz ), 142.6, 144.4, 144.8, 152.2, 152.6, 154.2, 164.9 (d, $J_{C\text{-}F}$ = 252 Hz ), 166.2, 166.4; HRMS *m/z* 589.1865 [$MNa^+$ ($C_{32}H_{27}N_4O_5FNa$) = 589.1863].

**9-[3,5-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl]-6-phenylpurine (8a).** Treatment of **7** (50 mg, 0.13 mmol) with phenylboronic acid (32 mg, 0.26 mmol) by method 2 gave **8a** (41 mg, 80%): $^{1}$H NMR δ 2.11, 2.16 (2 × s, 2 × 3H), 2.68-2.73 (m, 1H), 3.00-3.06 (m, 1H), 4.38-4.47 (m, 3H), 5.47-5.49 (m, 1H), 6.56-6.59 (m, 1H), 7.54-7.60 (m, 3H), 8.32, 9.03 (2 × s, 2 × 1H), 8.76-8.78 (m, 2H); $^{13}$C NMR δ 21.0, 21.2, 37.8, 64.0, 74.8, 82.9, 84.9, 128.9, 130.0, 131.4, 131.9, 135.7, 142.5, 152.2, 152.7, 155.6, 170.5, 170.6; HRMS *m/z* 419.1337 [$MNa^+$ ($C_{20}H_{20}N_4O_5Na$) = 419.1331].

**9-[3,5-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl]-6-(4-methylphenyl)purine (8b).** Treatment of **7** (50 mg, 0.13 mmol) with 4-methylphenylboronic acid (35 mg, 0.26 mmol) by method 2 gave **8b** (41mg, 78%): $^{1}$H NMR δ 2.11, 2.16, 2.46 (3 × s, 3 × 3H), 2.67-2.72 (m, 1H), 3.00-3.05 (m, 1H), 4.37-4.47 (m, 3H), 5.47-5.49 (m, 1H), 6.55-6.58 (m, 1H), 7.38, 8.69 (2 × d, 2 × 2H), 8.30, 9.00 (2 × s, 2 × 1H); $^{13}$C NMR δ 21.0, 21.2, 21.8, 37.8, 64.0, 74.8, 82.9, 84.9, 129.7, 130.0, 131.7, 133.0, 141.9, 142.2, 152.0, 152.7, 155.6, 170.5, 170.6; HRMS *m/z* 433.1489 [$MNa^+$ ($C_{21}H_{22}N_4O_5Na$) = 443.1488].

**9-[3,5-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl]-6-(4-methoxyphenyl)purine (8c).** Treatment of 9-(3,5-di-*O*-acetyl-2-deoxy-β-D-erythro-pentofuranosyl)-6-(1,2,4-triazol-4-yl)purine (**7**) (50 mg, 0.13 mmol) with 4-methoxyphenylboronic acid (**4**) (39 mg, 0.26 mmol) by method 2 gave **8c** (47mg, 85%): $^{1}$H NMR δ 2.10, 2.16 (2 × s, 2 × 3H), 3.91 (s, 3H), 2.66-2.71 (m, 1H), 2.98-3.04 (m, 1H), 4.37-4.46 (m, 3H), 5.46-5.48 (m, 1H), 6.54-6.57 (m, 1H), 7.08, 8.80 (2 × d, 2 × 2H), 8.28, 8.96 (2 × s, 2 × 1H); $^{13}$C NMR δ 21.0, 21.2, 37.8, 55.6, 64.0, 74.8, 82.9, 84.9, 114.4, 128.4, 131.3, 131.8, 142.0, 151.9, 152.7, 155.2, 162.4, 170.5, 170.6; HRMS *m/z* 427.1621 [$MH^+$ ($C_{21}H_{23}N_4O_6$) = 427.1618].

**9-[3,5-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-pentofuranosyl]-6-(4-fluorophenyl)purine (8d).** Treatment of **7** (50 mg, 0.13 mmol) with 4-fluorophenylboronic acid (39 mg, 0.26 mmol) by method 2 gave **8d** (40mg, 75%): $^{1}$H NMR δ 2.11, 2.16 (2 × s, 2 × 3H), 2.68-2.72 (m, 1H), 3.00-3.05 (m, 1H), 4.36-4.46 (m, 1H), 5.47-5.49 (m, 1H), 6.55-6.58 (m, 1H), 7.23-7.26 (m, 2H), 8.31, 9.00 (2 × s, 2 × 1H), 8.83-8.86 (m, 2H); $^{13}$C NMR δ 21.0, 21.2, 37.8, 64.0, 74.7, 83.0, 85.0, 116.0 (d, $J_{C\text{-}F}$ = 21 Hz ), 131.6, 131.9, 132.2 (d, $J_{C\text{-}F}$ = 8 Hz ), 142.5, 152.1, 152.7, 154.3, 165.0 (d, $J_{C\text{-}F}$ = 252 Hz ), 170.5, 170.6; HRMS *m/z* 415.1421 [$MH^+$ ($C_{20}H_{20}N_4O_5F$) = 415.1418].

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[1] Hocek, M.; Holy, A.; Votruba, I.; Dvorakova, H. *Collect. Czech. Chem. Commun.* **2000**, *65*, 1683–1697.