Supplementary Material (ESI) for Chemical Communications

The First Direct C-H Arylation of Purine Nucleosides

Igor Čerňa, Radek Pohl and Michal Hocek*

Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Gilead & IOCB Research Center, Flemingovo nam. 2, CZ-16610 Prague 6, Czech Republic. Fax: +420 220183559; Tel: +420 220183324; E-mail: hocek@uochb.cas.cz

Experimental section

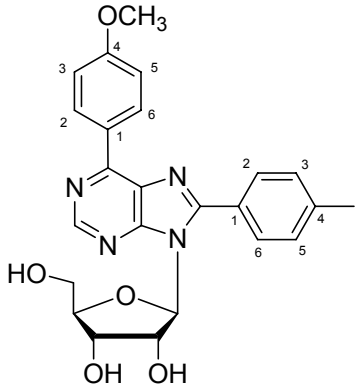
General

$Pd(OAc)_2$, piperidine (99 %), CuI (98 %) were purchased from Aldrich and used without any further treatment. All starting aryl halides were purchased from Aldrich and used as received. Dry DMF was used as received from supplier. All reactions were carried out in flame-dried glassware with magnetic stirring. 9-Benzyl-6-phenyl-9*H*-purine,[1] 6-(4-methoxyphenyl)-9-(β-D-ribofuranosyl)purine[2] were prepared according to published procedures.

General procedure for C-H arylation of 3

DMF (3 mL) and piperidine (247 μL, 2.5 mmol) were added through a septum to an argon purged vial containing a 6-(4-methoxyphenyl)purine ribonucleoside **3** (179.2 mg, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 5 mol %), CuI (285.7 mg, 1.5 mmol) and an aryl halide (2 equiv.). Reaction mixture was heated to 125 °C for 49 h. The solvent was evaporated under reduced pressure. Products were isolated by flash column chromatography (gradient elution chloroform → 4 % methanol in chloroform). Analytical samples were crystallized from $CHCl_3$/heptane. For yields of the particular compounds under particular conditions, see Tables in the main part of the paper.

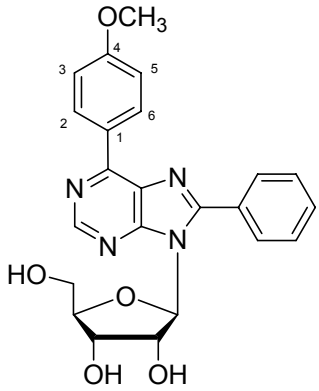
6-(4-Methoxyphenyl)-8-(p-tolyl)-9-(β-D-ribofuranosyl)purine (4a)



Yellow solid, mp 122-125 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 2.45 (s, 3H, CH_3); 3.60 (ddd, 1H, J_{gem} = 11.9, $J_{5'b,OH}$ = 7.5, $J_{5'b,4'}$ = 4.9, H-5′b); 3.76 (ddd, 1H, J_{gem} = 11.9, $J_{5'a,4'}$ = 4.9, $J_{5'a,OH}$ = 4.7, H-5′a); 3.87 (s, 3H, CH_3O); 3.95 (td, 1H, $J_{4',5'}$ = 4.9, $J_{4',3'}$ = 2.7, H-4′); 4.27 (ddd, 1H, $J_{3',2'}$ = 5.1, $J_{3',OH}$ = 4.7, $J_{3',4'}$ = 2.7, H-3′); 5.16 (dd, 1H, $J_{OH,5'}$ = 7.5, 4.7, OH-5′); 5.21 (d, 1H, $J_{OH,3'}$ = 4.7, OH-3′); 5.34 (ddd, 1H, $J_{2',1'}$ = 6.8, $J_{2',OH}$ = 6.2, $J_{2',3'}$ = 5.1, H-2′); 5.47 (d, 1H, $J_{OH,2'}$ = 6.2, OH-2′); 5.86 (d, 1H, $J_{1',2'}$ = 6.8, H-1′); 7.17 (m, 2H, H-3,5-C_6H_4OMe); 7.48 (m,

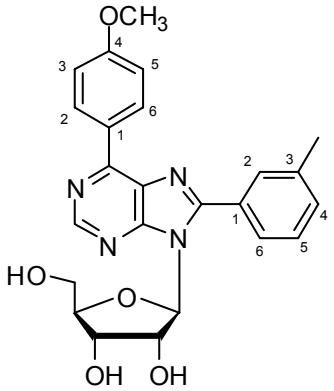
2H, H-3,5-C_6H_4Me); 7.78 (m, 2H, H-2,6-C_6H_4Me); 8.88 (m, 2H, H-2,6-C_6H_4OMe); 8.94 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 21.25 (CH_3); 55.58 (CH_3O); 62.16 (CH_2-5′); 70.78 (CH-2′); 70.89 (CH-3′); 86.46 (CH-4′); 89.57 (CH-1′); 114.40 (CH-3,5-C_6H_4OMe); 126.12 (C-1-C_6H_4Me); 127.91 (C-1-C_6H_4OMe); 129.74 (CH-3,5-C_6H_4Me); 129.95 (CH-2,6-C_6H_4Me); 130.26 (C-5); 131.43 (CH-2,6-C_6H_4OMe); 141.17 (C-4-C_6H_4Me); 151.41 (CH-2); 152.73 (C-6); 153.17 (C-4); 155.96 (C-8); 161.95 (C-4-C_6H_4OMe). MS (FAB), *m/z* (% relative intensity): 317.0(100), 359.0(6), 449.1(12). HRMS (FAB): Calculated for $C_{24}H_{24}N_4O_5$: 449.182495; found: 449.181595. Anal. calculated for $C_{24}H_{24}N_4O_5.1/2\ H_2O$: C 63.01 %, H 5.51 %, N 12.25 %; found: C 63.42 %, H 5.42%, N 12.02 %.

6-(4-Methoxyphenyl)-8-phenyl-9-(β-D-ribofuranosyl)purine (4b)



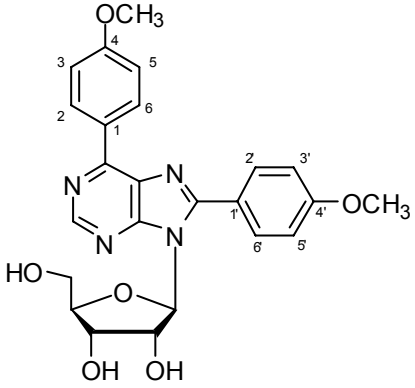
White solid, mp 133-135 °C. ^1H NMR (600 MHz, DMSO-d_6): 3.60 (ddd, 1H, J_{gem} = 11.9, $J_{5'b,OH}$ = 7.5, $J_{5'b,4'}$ = 4.9, H-5′b); 3.76 (ddd, 1H, J_{gem} = 11.9, $J_{5'a,4'}$ = 4.9, $J_{5'a,OH}$ = 4.7, H-5′a); 3.86 (s, 3H, CH_3O); 3.96 (td, 1H, $J_{4',5'}$ = 4.9, $J_{4',3'}$ = 2.7, H-4′); 4.26 (ddd, 1H, $J_{3',2'}$ = 5.2, $J_{3',OH}$ = 4.7, $J_{3',4'}$ = 2.7, H-3′); 5.19 (dd, 1H, $J_{OH,5'}$ = 7.5, 4.7, OH-5′); 5.24 (d, 1H, $J_{OH,3'}$ = 4.7, OH-3′); 5.34 (ddd, 1H, $J_{2',1'}$ = 6.7, $J_{2',OH}$ = 6.2, $J_{2',3'}$ = 5.2, H-2′); 5.52 (d, 1H, $J_{OH,2'}$ = 6.2, OH-2′); 5.87 (d, 1H, $J_{1',2'}$ = 6.7, H-1′); 7.17 (m, 2H, H-3,5-C_6H_4OMe); 7.65-7.71 (m, 3H, H-*m,p*-Ph); 7.89 (m, 2H, H-*o*-Ph); 8.88 (m, 2H, H-2,6-C_6H_4OMe); 8.96 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 55.64 (CH_3O); 62.21 (CH_2-5′); 70.90 (CH-2′); 70.95 (CH-3′); 86.57 (CH-4′); 89.62 (CH-1′); 114.48 (CH-3,5-C_6H_4OMe); 127.90 (C-1-C_6H_4OMe); 129.05 (C-*i*-Ph); 129.27 (CH-*m*-Ph); 130.11 (CH-*o*-Ph); 130.29 (C-5); 131.24 (CH-*p*-Ph); 131.52 (CH-2,6-C_6H_4OMe); 151.61 (CH-2); 152.98 (C-6); 153.17 (C-4); 155.88 (C-8); 162.05 (C-4-C_6H_4OMe). MS (FAB), *m/z* (% relative intensity): 55 (26), 137 (42), 154 (48), 226 (100), 342 (MH^+, 20). HRMS (FAB) calculated for $C_{23}H_{22}N_4O_5$: 435.166845; found: 435.165662.

6-(4-Methoxyphenyl)-8-(m-tolyl)-9-(β-D-ribofuranosyl)purine (4c)



Yellow solid, mp 98-103 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 2.46 (bs, 3H, CH_3); 3.60 (ddd, 1H, J_{gem} = 11.9, $J_{5'b,OH}$ = 7.5, $J_{5'b,4'}$ = 4.9, H-5′b); 3.76 (ddd, 1H, J_{gem} = 11.9, $J_{5'a,4'}$ = 4.8, $J_{5'a,OH}$ = 4.7, H-5′a); 3.86 (s, 3H, CH_3O); 3.96 (dt, 1H, $J_{4',5'b}$ = 4.9, $J_{4',5'a}$ = 4.8, $J_{4',3'}$ = 2.8, H-4′); 4.26 (dt, 1H, $J_{3',2'}$ = 5.2, $J_{3',OH}$ = 4.7, $J_{3',4'}$ = 2.8, H-3′); 5.19 (dd, 1H, $J_{OH,5'b}$ = 7.5, $J_{OH,5'a}$ = 4.7, OH-5′); 5.23 (d, 1H, $J_{OH,3'}$ = 4.7, OH-3′); 5.32 (dt, 1H, $J_{2',1'}$ = 6.7, $J_{2',OH}$ = 6.2, $J_{2',3'}$ = 5.2, H-2′); 5.50 (d, 1H, $J_{OH,2'}$ = 6.2, OH-2′); 5.86 (d, 1H, $J_{1',2'}$ = 6.7, H-1′); 7.17 (m, 2H, H-3,5-C_6H_4OMe); 7.50 (dm, 1H, $J_{4,5}$ = 7.6, H-4-C_6H_4Me); 7.55 (t, 1H, $J_{5,4}$ = 7.6, $J_{5,6}$ = 7.6, H-5-C_6H_4Me); 7.66 (dm, 1H, $J_{6,5}$ = 6.7, H-6-C_6H_4Me); 7.70 (m, 1H, H-2-C_6H_4Me); 8.87 (m, 2H, H-2,6-C_6H_4OMe); 8.95 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 21.24 (CH_3) 55.61 (CH_3O); 62.21 (CH_2-5′); 70.89 (CH-3′); 70.93 (CH-2′); 86.51 (CH-4′); 89.61 (CH-1′); 114.45 (CH-3,5-C_6H_4OMe); 127.14 (CH-6-C_6H_4Me); 127.91 (C-1-C_6H_4OMe); 129.01 (C-1-C_6H_4Me); 129.04 (CH-5-C_6H_4Me); 130.27 (C-5); 130.55 (CH-2-C_6H_4Me); 131.5 (CH-2,6-C_6H_4OMe); 131.83 (CH-4-C_6H_4Me); 138.75 (C-3-C_6H_4Me); 151.54 (CH-2); 152.91 (C-6); 153.15 (C-4); 155.99 (C-8); 162.01 (C-4-C_6H_4OMe). MS (FAB), *m/z* (% relative intensity): 109 (31), 137 (79), 154 (76), 177 (59), 231 (28), 317 (36), 449 (MH^+, 13). HRMS (FAB) calculated for $C_{24}H_{24}N_4O_5$: 449.182495; found: 449.181838.

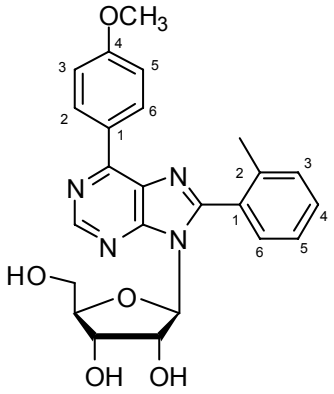
6,8-Bis(4-methoxyphenyl)-9-(β-D-ribofuranosyl)purine (4d)



White solid, mp 110-115 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 3.61 (bdt, 1H, J_{gem} = 12.0, $J_{5'a,4'}$ = 4.8, $J_{5'a,OH}$ = 4.5, H-5′b); 3.77 (bdd, 1H, J_{gem} = 12.0, $J_{5'a,4'}$ = 4.5, $J_{5'a,OH}$ = 4.5, H-5′a); 3.86 (s, 3H, CH_3O); 3.89 (s, 3H, CH_3O); 3.97 (dt, 1H, $J_{4',5'}$ = 4.8, $J_{4',3'}$ = 2.8, H-4′); 4.28 (m, 1H, $J_{3',2'}$ = 4.2, $J_{3',OH}$ = 3.5, $J_{3',4'}$ = 2.8, H-3′); 5.19 (bt, 1H, $J_{OH,5'}$ = 4.5, OH-5′); 5.24 (bd, 1H, $J_{OH,3'}$ = 3.5, OH-3′); 5.35 (q, 1H, $J_{2',1'}$ = 6.7, $J_{2',OH}$ = 5.9, $J_{2',3'}$ = 4.2, H-2′); 5.51 (d, 1H, $J_{OH,2'}$ = 5.9, OH-2′); 5.88 (d, 1H, $J_{1',2'}$ = 6.7, H-1′); 7.17 (m, 2H, H-3,5-C_6H_4OMe); 7.22 (m, 2H, H-3′,5′-C_6H_4OMe); 7.86 (m, 2H, H-2′,6′-C_6H_4OMe); 8.88 (m, 2H, H-2,6-C_6H_4OMe); 8.93 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 55.61 (CH_3O); 55.75 (CH_3O); 62.22 (CH_2-5′);

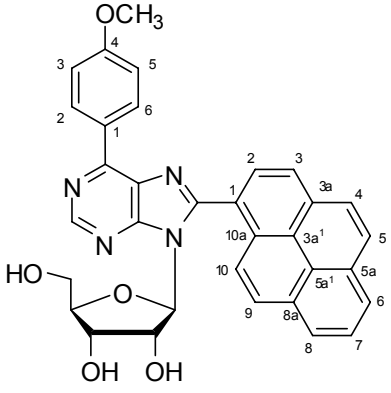
70.82 (CH-2′); 70.95 (CH-3′); 86.5 (CH-4′); 89.65 (CH-1′); 114.43 (CH-3,5-C_6H_4OMe); 114.75 (CH-3′,5′-C_6H_4OMe); 121,08 (C-1′-C_6H_4OMe); 127.99 (C-1-C_6H_4OMe); 130.33 (C-5); 131.45 (CH-2,6-C_6H_4OMe); 131,70 (CH-2′,6′-C_6H_4OMe); 151.30 (CH-2); 152.52 (C-6); 153.27 (C-4); 155.89 (C-8); 161.59 (C-4′-C_6H_4OMe); 161.95 (C-4-C_6H_4OMe). MS (FAB), *m/z* (% relative intensity): 333 (100), 375 (7), 465 (MH^+, 20). HRMS (FAB) calculated for $C_{24}H_{24}N_4O_5$: 465.177410; found: 465.176849. Anal. calculated for $C_{24}H_{24}N_4O_6.H_2O$: C 59.74 %, H 5.43 %, N 11.61 %; found: C 59.25 %, H 4.99 %, N 11.61 %.

6-(4-Methoxyphenyl)-8-(o-tolyl)-9-(β-D-ribofuranosyl)purine (4e)



White solid, mp 105-110 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 2.28 (bs, 3H, CH_3); 3.55 (ddd, 1H, J_{gem} = 11.8, $J_{5'b,OH}$ = 7.5, $J_{5'b,4'}$ = 4.8, H-5′b); 3.70 (ddd, 1H, J_{gem} = 11.8, $J_{5'a,4'}$ = 4.8, $J_{5'a,OH}$ = 4.2, H-5′a); 3.85 (s, 3H, CH_3O); 3.89 (td, 1H, $J_{4',5'}$ = 4.8, $J_{4',3'}$ = 2.5, H-4′); 4.17 (ddd, 1H, $J_{3',2'}$ = 4.5, $J_{3',OH}$ = 4.3, $J_{3',4'}$ = 2.5, H-3′); 5.17 (d, 1H, $J_{OH,3'}$ = 4.3, OH-3′); 5.17 (bdd, 1H, $J_{5'b,OH}$ = 7.5, $J_{5'a,OH}$ = 4.2, OH-5′); 5.21 (bq, 1H, $J_{2',1'}$= 6.8, $J_{2',OH}$ = 5.8, H-2′); 5.44 (d, 1H, $J_{OH,2'}$ = 5.8, OH-2′); 5.48 (d, 1H, $J_{1',2'}$ = 6.8, H-1′); 7.15 (m, 2H, H-3,5-C_6H_4OMe); 7.43 (tm, 1H, $J_{5,4}$=7.6, $J_{5,6}$=7.6, H-5-C_6H_4Me); 7.48 (dm, 1H, $J_{3,4}$=7.6, H-3-C_6H_4Me); 7.49 (dd, 1H, $J_{6,5}$=7.6, H-6-C_6H_4Me); 7.56 (td, 1H, $J_{4,3}$=7.6, $J_{4,5}$=7.6, H-4-C_6H_4Me); 8.84 (m, 2H, H-2,6-C_6H_4OMe); 8.97 (s, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 19.70 (CH_3); 55.60 (CH_3O); 62.22 (CH_2-5′); 71.02 (CH-2′); 71.02 (CH-3′); 86.57 (CH-4′); 89.54 (CH-1′); 114.46 (CH-3,5-C_6H_4OMe); 126.17 (CH-4-C_6H_4Me); 127.85 (C-1-C_6H_4OMe); 128.99 (C-1-C_6H_4Me); 130.26 (C-5); 130.79 (CH-6-C_6H_4Me); 130.88 (CH-5-C_6H_4Me); 131.52 (CH-2,6-C_6H_4OMe); 138.21 (C-2-C_6H_4Me); 151.62 (CH-2); 152.48 (C-4); 152.91 (C-6); 155.42 (C-8); 162.02 (C-4-C_6H_4OMe). MS (FAB), *m/z* (% relative intensity): 57 (59), 69 (30), 91 (28), 149 (22), 227 (32), 317 (100), 359 (6), 449 (MH^+, 20). HRMS (FAB) calculated for $C_{24}H_{24}N_4O_5$: 449.182495; found: 449.182699.

6-(4-Methoxyphenyl)-8-(pyren-1-yl)-9-(β-D-ribofuranosyl)purine (4f)

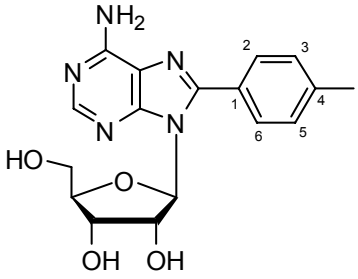


Brown solid, mp >300 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 3.54 (bm, 1H, H-5′b); 3.68 (bm, 1H, H-5′a); 3.82 (bm, 1H, H-4′); 3.83 (s, 3H, CH_3O); 4.13 (bs, 1H, H-3′); 5.02 (d, 1H, $J_{OH,3'}$ = 4.5, OH-3′); 5.10-5.50 (bm, 3H, H-2′ and OH-2′,5′); 5.58 (bm, 1H, H-1′); 7.14 (m, 2H, H-3,5-C_6H_4OMe); 8.12 (bm, 1H, H-10-pyrene); 8.19 (t, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.6, H-7-pyrene); 8.29 (d, 1H, $J_{9,10}$ = 9.3, H-9-pyrene); 8.30 (d, 1H, $J_{2,3}$ = 7.6, H-2-pyrene); 8.36 (d, 1H, $J_{4,5}$ = 9.1, H-4-pyrene); 8.40 (d, 1H, $J_{5,4}$ = 9.1, H-5-pyrene); 8.41 (dd, 1H, $J_{6,7}$ = 7.6, $J_{6,8}$ = 0.9, H-6-pyrene); 8.46 (dd, 1H, $J_{8,7}$ = 7.6, $J_{8,6}$ = 0.9, H-8-pyrene); 8.53 (d, 1H, $J_{3,2}$ = 7.6, H-3-pyrene); 8.90 (m, 2H, H-2,6-C_6H_4OMe); 9.06 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 55.60 (CH_3O); 62.17 (CH_2-5′); 70.94 (CH-3′); 71.16 (CH-2′); 86.58 (CH-4′); 89.83 (CH-1′); 114.49 (CH-3,5-C_6H_4OMe); 123.21 (C-1-pyrene); 123.58 (C-3a^1-pyrene); 123.91 (C-5a^1-pyrene); 124.63 (CH-10-pyrene); 124.79 (CH-3-pyrene); 126.36 (CH-6-pyrene); 126.62 (CH-8-pyrene); 127.19 (CH-7-pyrene); 127.46 (CH-4-pyrene); 127.92 (C-1-C_6H_4OMe); 128.23 (CH-2-pyrene); 129.37 (CH-9-pyrene); 129.42 (CH-5-pyrene); 130.29 (C-10a-pyrene); 130.42 (C-8a-pyrene); 130.61 (C-5); 130.96 (C-5a-pyrene); 131.55 (CH-2,6-C_6H_4OMe); 132.57 (C-3a-pyrene); 151.80 (CH-2); 152.85 (C-6); 153.14 (C-4); 154.92 (C-8); 162.06 (C-4-C_6H_4OMe). MS (EI), *m/z* (% relative intensity): 41 (92), 55 (70), 69 (40), 227 (100), 426 (90), 558 (MH^+, 5). HRMS (EI) calculated for $C_{33}H_{28}N_4O_5$: 558.190320; found: 558.189346.

General procedure for C-H arylation of 5

DMF (3 mL) and piperidine (247 μL, 2.5 mmol) were added through a septum to an argon purged vial containing adenosine (133.6 mg, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 5 mol %), CuI (285.7 mg, 1.5 mmol) and an aryl halide (2 equiv.). Reaction mixture was heated to 150 °C for 5 h. The solvent was evaporated under reduced pressure. Products were isolated by flash column chromatography (gradient elution chloroform → 8 % methanol in chloroform). Analytical samples were crystallized from $CHCl_3$/heptane/methalol. For yields of the particular compounds under particular conditions, see Tables in the main part of the paper.

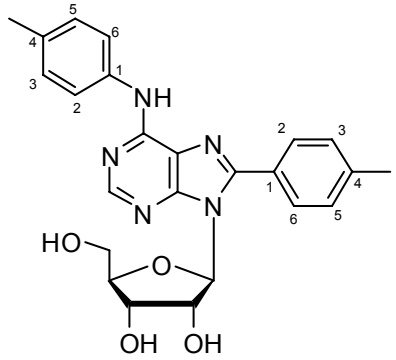
8-(p-tolyl)-adenosine (7a)[3]



Yellow crystals, m.p. 172-180 °C. ^{1}H NMR (500 MHz, DMSO-d_6): 2.41 (s, 3H, CH_3); 3.55 (bddd, 1H, J_{gem} = 12.1, $J_{5'b,OH}$ = 8.8, $J_{5'b,4'}$ = 3.6, H-5′b); 3.70 (bdd, 1H, J_{gem} = 12.1, $J_{5'a,4'}$ = 3.6, H-5′a); 3.94 (td, 1H, $J_{4',5'}$ = 3.6, $J_{4',3'}$ = 1.9, H-4′); 4.17 (bm, 1H, H-3′); 5.13 (d, 1H, $J_{OH,3'}$ = 4.1, OH-3′); 5.18 (ddd, 1H, $J_{2',1'}$ = 7.3, $J_{2',OH}$ = 6.4, $J_{2',3'}$ = 4.9, H-2′); 5.45 (d, 1H, $J_{OH,2'}$ = 6.4, OH-2′); 5.75 (d, 1H, $J_{1',2'}$ = 7.3, H-1′); 5.82 (bd, 1H, $J_{OH,5'b}$ = 8.5, OH-5′); 7.40 (m, 2H, H-3,5-C_6H_4Me); 7.49 (bs, 2H, NH_2); 7.64 (m, 2H, H-2,6-C_6H_4Me); 8.16 (bs, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 21.17 (CH_3); 62.53 (CH_2-5′); 71.32 (CH-3′); 71.39 (CH-2′); 86.88 (CH-4′); 89.27 (CH-1′); 119.36 (C-5); 126.74 (C-1-C_6H_4Me); 129.50 (CH-3,5-C_6H_4Me); 129.77 (CH-2,6-C_6H_4Me); 140.09 (C-4-C_6H_4Me); 149.99 (C-4); 151.29 (C-8); 152.05 (CH-2); 156.35 (C-6). MS (FAB), *m/z* (% relative intensity): 93 (100), 185 (48), 201 (24), 226 (21), 358 (MH^+, 23). HRMS (FAB) calculated for $C_{17}H_{19}N_5O_4$: 358.151529; found:

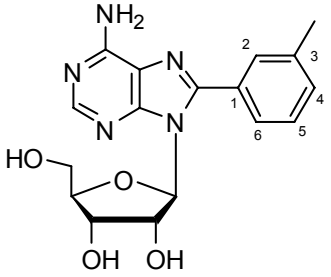
358.151870. Anal. calculated for $C_{17}H_{19}N_5O_4.H_2O$: C 54.39%, H 5.64 %, N 18.66 %; found: C 54.26%, H 5.35 %, N 18.15 %.

N^6,8-Bis(p-tolyl)-adenosine (8a)



Brown crystals, mp >300 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 2.28 (s, 3H, CH_3-NC_6H_4Me); 2.43 (s, 3H, CH_3-C_6H_4Me); 3.57 (ddd, 1H, J_{gem} = 12.2, $J_{5'b,OH}$ = 8.8, $J_{5'b,4'}$ = 4.1, H-5′b); 3.72 (ddd, 1H, J_{gem} = 12.2, $J_{5'a,4'}$ = 4.1, $J_{5'a,OH}$ = 3.8, H-5′a); 3.95 (td, 1H, $J_{4',5'}$ = 4.1, $J_{4',3'}$ = 2.1, H-4′); 4.20 (ddd, 1H, $J_{3',2'}$ = 5.2, $J_{3',OH}$ = 4.3, $J_{3',4'}$ = 2.1, H-3′); 5.18 (d, 1H, $J_{OH,3'}$ = 4.3, OH-3′); 5.23 (ddd, 1H, $J_{2',1'}$ = 7.1, $J_{2',OH}$ = 6.4, $J_{2',3'}$ = 5.2, H-2′); 5.48 (d, 1H, $J_{OH,2'}$ = 6.4, OH-2′); 5.59 (dd, 1H, $J_{OH,5'}$ = 8.8, 3.8, OH-5′); 5.77 (d, 1H, $J_{1',2'}$ = 7.1, H-1′); 7.14 (m, 2H, H-3,5-NC_6H_4Me); 7.43 (m, 2H, H-3,5-C_6H_4Me); 7.70 (m, 2H, H-2,6-C_6H_4Me); 7.81 (m, 2H, H-2,6-NC_6H_4Me); 8.38 (s, 1H, H-2); 9.98 (s, 1H, NH). ^{13}C NMR (151 MHz, DMSO-d_6): 20.72 (CH_3-NC_6H_4Me); 21.24 (CH_3-C_6H_4Me); 62.44 (CH_2-5′); 71.21 (CH-3′); 71.34 (CH-2′); 86.78 (CH-4′); 89.39 (CH-1′); 120.32 (C-5); 121.36 (CH-2,6-NC_6H_4Me); 126.49 (C-1-C_6H_4Me); 129.02 (CH-3,5-NC_6H_4Me); 129.58 (CH-3,5-C_6H_4Me); 129.90 (CH-2,6-C_6H_4Me); 132.05 (C-4-NC_6H_4Me); 137.05 (C-1-NC_6H_4Me); 140.37 (C-4-C_6H_4Me); 150.13 (C-4); 151.64 (CH-2); 152.12 (C-8); 152.34 (C-6). MS (FAB), *m/z* (% relative intensity): 91.0 (7), 118.0 (7), 181.0(5), 226.0(7), 316.1(100), 358.1(9), 448 (MH^+, 32). HRMS (FAB) calculated for $C_{17}H_{19}N_5O_4$: 448.198480; found: 448.198777.

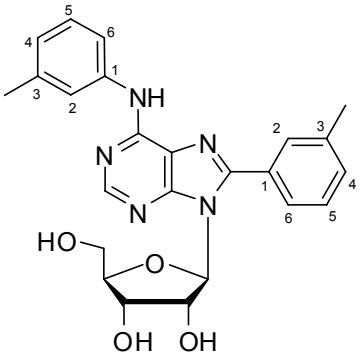
8-(m-Tolyl)-adenosine (7b)



Yellow solid, mp 98-102 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 2.41 (s, 3H, CH_3); 3.55 (bddd, 1H, J_{gem} = 12.2, $J_{5'b,OH}$ = 9.3, $J_{5'b,4'}$ = 3.7, H-5′b); 3.70 (ddd, 1H, J_{gem} = 12.2, $J_{5'a,4'}$ = 3.7, $J_{5'a,4'}$ = 3.4, H-5′a); 3.94 (td, 1H, $J_{4',5'}$ = 3.7, $J_{4',3'}$ = 1.9, H-4′); 4.16 (ddd, $J_{3',2'}$ = 5.1, $J_{3',OH}$ = 4.2, $J_{3',4'}$ = 1.9, 1H, H-3′); 5.15 (d, 1H, $J_{OH,3'}$ = 4.2, OH-3′); 5.16 (ddd, 1H, $J_{2',1'}$ = 7.2, $J_{2',OH}$ = 6.4, $J_{2',3'}$ = 5.1, H-2′); 5.48 (d, 1H, $J_{OH,2'}$ = 6.4, OH-2′); 5.76 (d, 1H, $J_{1',2'}$ = 7.2, H-1′); 5.84 (dd, 1H, $J_{OH,5'}$ = 9.3, 3.4, OH-5′); 7.41 (m, 1H, $J_{4,5}$ = 7.6, $J_{4,2}$ = 2.6, $J_{4,6}$ = 1.2, $J_{4,CH3}$ = 0.7, H-4-C_6H_4Me); 7.47 (t, 1H, $J_{5,4}$ = $J_{5,6}$ = 7.6, H-5-C_6H_4Me); 7.50 (bs, 2H, NH_2); 7.53 (m, 1H, $J_{6,5}$ = 7.6, $J_{6,2}$ = 1.8, $J_{6,4}$ = 1.2, $J_{6,CH3}$ = 0.7, H-6-C_6H_4Me); 7.57 (ddq, 1H, $J_{2,4}$ = 2.6, $J_{2,6}$ = 1.8, $J_{2,CH3}$ = 0.7, H-2-C_6H_4Me); 8.15 (bs, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 21.22 (CH_3); 62.56 (CH_2-5′); 71.34 (CH-3′); 71.46 (CH-2′); 86.93 (CH-4′); 89.32 (CH-1′); 119.32 (C-5); 126.95 (CH-6-C_6H_4Me); 128.83 (CH-5-C_6H_4Me); 129.59 (C-1-C_6H_4Me); 130.47 (CH-2-

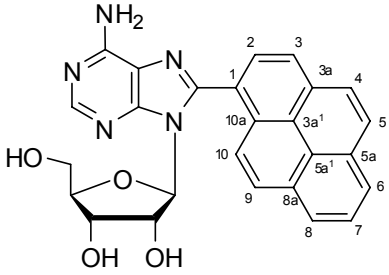
C_6H_4Me); 130.99 (CH-4-C_6H_4Me); 138.41 (C-3-C_6H_4Me); 150.02 (C-4); 151.30 (C-8); 152.21 (CH-2); 156.44 (C-6). MS (FAB), *m/z* (% relative intensity): 57 (100), 77 (60), 91 (52), 149 (60), 226 (92), 358 (MH^+, 21). HRMS (FAB) calculated for $C_{17}H_{19}N_5O_4$: 358.151529; found: 358.151943.

N^6,8-Bis(m-tolyl)-adenosine (8b)



Yelow solid, mp >300 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 2.32 (s, 3H, CH_3-NC_6H_4Me); 2.43 (s, 3H, CH_3-C_6H_4Me); 3.58 (ddd, 1H, J_{gem} = 12.1, $J_{5'b,OH}$ = 8.6, $J_{5'b,4'}$ = 4.1, H-5′b); 3.74 (ddd, 1H, J_{gem} = 12.1, $J_{5'a,4'}$ = 4.1, $J_{5'a,OH}$ = 3.6, H-5′a); 3.96 (dt, 1H, $J_{4',5'}$ = 4.1, $J_{4',3'}$ = 2.2, H-4′); 4.21 (dt, 1H, $J_{3',2'}$ = 5.2, $J_{3',OH}$ = 4.4, $J_{3',4'}$ = 2.2, H-3′); 5.20 (d, 1H, $J_{OH,3'}$ = 4.4, OH-3′); 5.23 (dt, 1H, $J_{2',1'}$ = 7.0, $J_{2',OH}$ = 6.3, $J_{2',3'}$ = 5.2, H-2′); 5.50 (d, 1H, $J_{OH,2'}$ = 6.3, OH-2′); 5.56 (dd, 1H, $J_{OH,5'b}$ = 8.6, $J_{OH,5'a}$ = 3.6, OH-5′); 5.81 (d, 1H, $J_{1',2'}$ = 7.0, H-1′); 6.89 (dm, 1H, $J_{6,5}$ = 7.8, H-6-NC_6H_4Me); 7.22 (dm, 1H, $J_{5.6}$= 7.8, $J_{5,4}$ = 7.8, H-5-NC_6H_4Me); 7.44 (dm, 1H, $J_{4,5}$= 7.6, H-4-C_6H_4Me); 7.50 (t, 1H, $J_{5.6}$= 7.6, $J_{5,4}$ = 7.6, H-5-C_6H_4Me); 7.59 (dm, 1H, $J_{6,5}$ = 7.6, H-6-C_6H_4Me); 7.64 (m, 1H, H-2-C_6H_4Me); 7.73 (dm, 1H, $J_{4,5}$ = 7.8, H-4-NC_6H_4Me); 7.79 (t, 1H, H-2-NC_6H_4Me); 8.42 (s, 1H, H-2); 9.96 (s, 1H, NH). ^{13}C NMR (151 MHz, DMSO-d_6): 21.23 (CH_3-C_6H_4Me); 21.58 (CH_3-NC_6H_4Me); 62.45 (CH_2-5′); 71.20 (CH-3′); 71.39 (CH-2′); 86.80 (CH-4′); 89.46 (CH-1′); 118.58 (CH-4-NC_6H_4Me); 120.44 (C-5); 121.80 (CH-2-NC_6H_4Me); 123.89 (CH-6-NC_6H_4Me); 127.04 (CH-6-C_6H_4Me); 128.49 (CH-5-NC_6H_4Me); 128.88 (CH-5-C_6H_4Me); 129.32 (C-1-C_6H_4Me); 130.59 (CH-2-C_6H_4Me); 131.22 (CH-4-C_6H_4Me); 137.75 (C-3-NC_6H_4Me); 138.44 (C-3-C_6H_4Me); 139.54 (C-1-NC_6H_4Me); 150.25 (C-4); 151.74 (CH-2); 152.21 (C-8); 152.41 (C-6). MS (FAB), *m/z* (% relative intensity): 57 (100), 137 (94), 154 (100), 177 (60), 316 (74), 413 (25), 448 (MH^+, 24). HRMS (FAB) calculated for $C_{24}H_{25}N_5O_4$: 448.198480; found: 448.198629.

8-(Pyren-1-yl)-adenosine (7c)



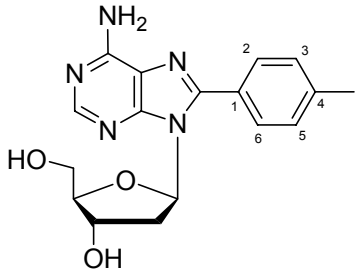
White solid, mp 193-199 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 3.51 (ddd, 1H, J_{gem} = 12.1, $J_{5'b,OH}$ = 9.8, $J_{5'b,4'}$ = 3.4, H-5′b); 3.68 (dt, 1H, J_{gem} = 12.1, $J_{5'a,4'}$ = $J_{5'a,OH}$ = 3.4, H-5′a); 3.82 (bm, 1H, H-4′); 4.04 (bs, 1H, H-3′); 4.92 (bs, 1H, OH-3′); 5.00-5.20 (bm, 2H, H-2′ and OH-5′); 5.41 (bd, 1H, $J_{1',2'}$ = 7.2, H-1′); 6.08 (bs, 1H, OH-2′); 7.62 (bs, 2h, NH_2); 8.04 (bm, 1H, H-10-pyrene); 8.16 (t, 1H, $J_{7,6}$ = $J_{7,8}$ = 7.6, H-7-pyrene); 8.21 (bm, 1H, H-2-pyrene); 8.25 (s, 1H, H-2); 8.26 (d, 1H, $J_{9,10}$ = 9.6, H-9-pyrene); 8.32 (d, 1H, $J_{4,5}$ = 9.1, H-4-pyrene); 8.36 (d,

1H, $J_{5,4}$ = 9.1, H-5-pyrene); 8.39 (dd, 1H, $J_{6,7}$ = 7.6, $J_{6,8}$ = 1.1, H-6-pyrene); 8.42 (dd, 1H, $J_{8,7}$ = 7.6, $J_{8,6}$ = 1.1, H-8-pyrene); 8.47 (d, 1H, $J_{3,2}$ = 7.9, H-3-pyrene). ^{13}C NMR (151 MHz, DMSO-d_6): 62.57 (CH_2-5′); 71.37 (CH-3′); 71.72 (CH-2′); 87.09 (CH-4′); 89.66 (CH-1′); 119.72 (C-5); 123.67 (C-1-pyrene); 123.90 (C-3a^1-pyrene); 124.01 (C-5a^1-pyrene); 124.62 (CH-10-pyrene); 124.75 (CH-3-pyrene); 126.22 (CH-6-pyrene); 126.42 (CH-8-pyrene); 127.10 (CH-7-pyrene); 127.49 (CH-4-pyrene); 128.31 (CH-2-pyrene); 128.92 (CH-9-pyrene); 129.12 (CH-5-pyrene); 130.29 (C-10a-pyrene); 130.49 (C-8a-pyrene); 130.98 (C-5a-pyrene); 132.17 (C-3a-pyrene); 149.71 (C-8); 149.91 (C-4); 152.46 (CH-2); 156.57 (C-6). MS (FAB), *m/z* (% relative intensity): 57 (26), 109 (34), 137 (91), 154 (100), 177 (84), 231 (32), 336 (32), 468 (MH^+, 18). HRMS (FAB) calculated for $C_{26}H_{21}N_5O_4$: 468.167179; found: 468.167598.

General procedure for C-H arylation of 6

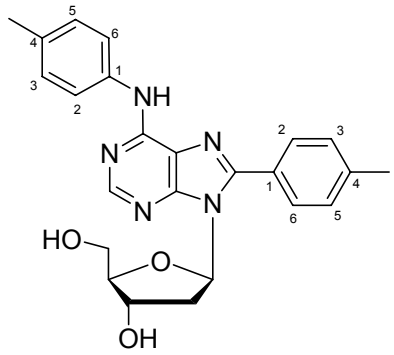
DMF (3 mL) and piperidine (247 μL, 2.5 mmol) were added through a septum to an argon purged vial containing a adenosine (133.6 mg, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 5 mol %), CuI (285.7 mg, 1.5 mmol), Aryl halide (2 equiv.). Reaction mixture was heated to 125 °C for 5 h. The solvent was evaporated under reduced pressure. Products were isolated by flash column chromatography (gradient elution chloroform → 4 % methanol in chloroform). Analytical samples were crystalized from $CHCl_3$/heptane/methalol. For yields of the particular compounds under particular conditions, see Tables in the main part of the paper.

8-(p-Tolyl)-2'-deoxyadenosine (9)[4]



Yellow solid, mp 126-130 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 2.13 (ddd, 1H, J_{gem} = 13.2, $J_{2'b,1'}$ = 6.2, $J_{2'b,3'}$ = 2.1, H-2′b); 2.41 (s, 3H, CH_3); 3.29 (ddd, 1H, J_{gem} = 13.2, $J_{2'a,1'}$ = 8.8, $J_{2'a,3'}$ = 6.0, H-2′a); 3.53 (ddd, 1H, J_{gem} = 12.0, $J_{5'b,OH}$ = 8.4, $J_{5'b,4'}$ = 4.3, H-5′b); 3.69 (dt, 1H, J_{gem} = 12.0, $J_{5'a,4'}$ = $J_{5'a,OH}$ = 3.8, H-5′a); 3.87 (ddd, 1H, $J_{4',5'}$ = 4.3, 3.8, $J_{4',3'}$ = 2.0, H-4′); 4.45 (dddd, 1H, $J_{3',2'}$ = 6.0, 2.1, $J_{3',OH}$ = 4.0, $J_{3',4'}$ = 2.0, H-3′); 5.24 (d, 1H, $J_{OH,3'}$ = 4.0, OH-3′); 5.60 (dd, 1H, $J_{OH,5'}$ = 8.4, 3.8, OH-5′); 6.14 (dd, 1H, $J_{1',2'}$ = 8.8, 6.2, H-1′); 7.41 (m, 2H, H-3,5-C_6H_4Me); 7.44 (bs, 2H, NH_2); 7.60 (m, 2H, H-2,6-C_6H_4Me); 8.14 (bs, 1H, H-2). ^{13}C NMR (151 MHz, DMSO-d_6): 21.22 (CH_3); 37.44 (CH_2-2′); 62.58 (CH_2-5′); 71.72 (CH-3′); 85.93 (CH-1′); 88.61 (CH-4′); 119.40 (C-5); 126.99 (C-1-C_6H_4Me); 129.59 (CH-2,3,5,6-C_6H_4Me); 140.15 (C-4-C_6H_4Me); 150.09 (C-4); 150.81 (C-8); 152.08 (CH-2); 156.34 (C-6). MS (FAB), *m/z* (% relative intensity): 55 (26), 137 (42), 154 (48), 226 (100), 342 (MH^+, 20). HRMS (FAB) calculated for $C_{17}H_{19}N_5O_3$: 342.156615; found: 342.156147.

N^6,8-Bis(p-tolyl)-2'-deoxyadenosine (9)



Yellow solid, mp >300 °C. ^{1}H NMR (600 MHz, DMSO-d_6): 2.17 (ddd, 1H, J_{gem} = 13.2, $J_{2'b,1'}$ = 6.3, $J_{2'b,3'}$ = 2.4, H-2′b); 2.28 (s, 3H, CH_3-NC_6H_4Me); 2.42 (s, 3H, CH_3-C_6H_4Me); 3.34 (ddd, 1H, J_{gem} = 13.2, $J_{2'a,1'}$ = 8.4, $J_{2'a,3'}$ = 5.6, H-2′a); 3.54 (ddd, 1H, J_{gem} = 11.8, $J_{5'b,OH}$ = 7.9, $J_{5'b,4'}$ = 4.8, H-5′b); 3.72 (ddd, 1H, J_{gem} = 11.8, $J_{5'a,4'}$ = 4.6, $J_{5'a,OH}$ = 4.3, H-5′a); 3.87 (ddd, 1H, $J_{4',5'}$ = 4.8, 4.6, $J_{4',3'}$ = 2.3, H-4′); 4.45 (dddd, 1H, $J_{3',2'}$ = 5.6, 2.4, $J_{3',OH}$ = 4.1, $J_{3',4'}$ = 2.3, H-3′); 5.27 (d, 1H, $J_{OH,3'}$ = 4.1, OH-3′); 5.38 (dd, 1H, $J_{OH,5'}$ = 7.9, 4.3, OH-5′); 6.17 (dd, 1H, $J_{1',2'}$ = 8.4, 6.3, H-1′); 7.14 (m, 2H, H-3,5-NC_6H_4Me); 7.43 (m, 2H, H-3,5-C_6H_4Me); 7.66 (m, 2H, H-2,6-C_6H_4Me); 7.81 (m, 2H, H-2,6-NC_6H_4Me); 8.37 (s, 1H, H-2); 9.92 (s, 1H, NH). ^{13}C NMR (151 MHz, DMSO-d_6): 20.72 (CH_3-NC_6H_4Me); 21.26 (CH_3-C_6H_4Me); 37.28 (CH_2-2′); 62.47 (CH_2-5′); 71.61 (CH-3′); 85.88 (CH-1′); 88.53 (CH-4′); 120.38 (C-5); 121.29 (CH-2,6-NC_6H_4Me); 126.75 (C-1-C_6H_4Me); 129.03 (CH-3,5-NC_6H_4Me); 129.61 (CH-3,5-C_6H_4Me); 129.74 (CH-2,6-C_6H_4Me); 131.97 (C-4-NC_6H_4Me); 137.12 (C-1-NC_6H_4Me); 140.37 (C-4-C_6H_4Me); 150.20 (C-4); 151.59 (CH-2); 151.69 (C-8); 152.30 (C-6). MS (FAB), *m/z* (% relative intensity): 57 (100), 69 (49), 137 (64), 149 (95), 177 (50), 231 (23), 316 (62), 413 (40), 432 (MH^+, 27). HRMS (FAB) calculated for $C_{24}H_{25}N_5O_3$: 432.203565; found: 432.202422.

References:

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