Supporting Information

Synthesis of Adducts of *o*-Quinone Metabolites of Carcinogenic Polycyclic Aromatic Hydrocarbons with 2'-Deoxyribonucleosides

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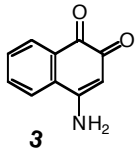
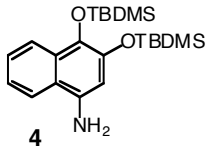


3

4-Aminonaphthalene-1,2-dione (3). To a solution of naphthalene-1,2-dione (5.0 g, 32 mmol) in DMF (10 mL) under argon was added dropwise azidotrimethylsilane (5.3 mL, 38 mmol). Following initial evolution of nitrogen, the mixture was heated at 80 °C for 2 h. Then the solution was cooled to ambient temperature, and EtOAc (50 mL) was added. The orange solid precipitate of **3** was removed by filtration, and additional **3** was obtained by evaporation of the solvent and chromatography of the residue on a column of silica gel. Combined yield of **3**: 85%, mp >298 °C, ^{1}H NMR (DMSO-d_6): 8.25 (br s, 1), 8.09 (br s, 1), 7.92 (d, 1, J = 7.8 Hz), 7.84 (dd, 1, J = 7.6, 1.2 Hz), 7.78 (m, 1), 7.66 (m, 1), 5.61 (s, 1); ^{13}C NMR(DMSO-d_6): 182.6, 175.0, 158.4, 134.6, 132.0, 130.9, 128.2, 124.5, 101.5, 101.4.

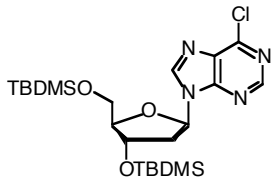


4

4-Amino-1,2-(*tert*-butyldimethylsilyloxy)naphthalene (4). <u>*Method 1*</u>: To a solution of **3** (400 mg, 2.31 mmol) in anhydrous DMF (10 mL) under argon was added $NaBH_4$ (111 mg, 2.92 mmol), and evolution of hydrogen and heating was observed. The solution was stirred at room temperature for 0.5 h, then excess TMDMS-Cl (1.50 g, 10 mmol) and imidazole (13.36 g, 20 mmol) were added. After 4 h, EtOAc and water was added. The organic phase was washed with water and brine, and dried over $MgSO_4$. After filtration,

EtOAc was removed and the residue was passed through a silica gel column eluted with hexane-CH_2Cl_2 (1:1) to furnish **4** (20%) as colorless oil: ^{1}H NMR ($CDCl_3$) 8.06 (d, 1, *J* =8.0 Hz), 7.71 (d, 1, *J* =8.3 Hz), 7.41 (t, 1), 7.31 (t, 1), 6.47 (s, 1), 3.75 (br s, 2), 1.29 (s, 9), 1.04 (s, 9), 0.28 (s, 6), 0.11 (s, 6); ^{13}C NMR ($CDCl_3$): 142.3, 136.2, 133.1, 130.0, 125.1, 123.0, 122.8, 120.8, 120.6, 107.4, 26.3, 26.2, 18.6, 3.6; MS Calcd for $C_{22}H_{37}O_2Si_2$: $[MH]^+$ 403.2. Found: 404.1. Compound **4** obtained via this route became black, even under vacuum and it had to be prepared freshly before use.

Method 2: To a solution of **3** (400 mg, 2.3 mmol) in anhydrous DMF (10 mL) under argon. was added $NaBH_4$ (111 mg, 2.9 mmol). The solution was stirred at rt for 0.5 h, then *N*-(*tert*-butyldimethylsilyl)-*N*-methyltrifluoroacetamide (1 mL) was added. After 0.5 h, EtOAc and water were added, the organic phase was washed with water and brine, and dried over Na_2SO_4. After filtration, the solvent was removed and the residue was purified by rapid chromatography on a silica gel column eluted with hexane-CH_2Cl_2 (1:1) to provide **4** (50%) as a colorless oil.

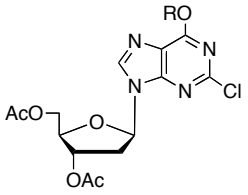


5d

6-Chloro-9-[2'-deoxy-3',5'-bis-O-(*tert*-butyldimethylsilyl)-*β*-D-erythropentofurano-syl]purine (5d). To a flask containing 3',5'-bis-(*tert*-butyldimethylsilyl)-2'-deoxyadeno-sine[1] (1.46 g, 3.0 mmol) and CH_2Cl_2 (30 mL) under argon at 0 ˚C was added dropwise trimethylsilyl chloride (770 mL, 2.0 equiv.) followed by *t*-butyl nitrite (804 mL, 5.0 equiv.). The solution was stirred at 0 ˚C for 4 h, and reaction was quenched by addition of a saturated solution of $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2 , combined with the organic phase, washed with water, and dried over $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by chromatography on a silica gel column eluted with hexane-EtOAc (4:1) to provide **5d** (912 mg, 60%): ^{1}H NMR ($CDCl_3$) 8.73 (s, 1), 8.48 (s, 1), 6.51 (t, 1, *J* =6.4 Hz), 4.62 (m, 1), 4.04 (m, 1),

[1] Watkins, B. E.; Kiely, J. S.; Rapoport, H. *J. Am. Chem. Soc.* **1982**, *104*, 5702-5708.

3.88 (dd, 1, *J* =10.4, 3.8 Hz), 3.77 (dd, 1, *J* =10.4, 2.8 Hz), 2.61 (m, 1), 2.40 (m, 1), 1.01 (s, 9), 0.98 (s, 9), 0.09 (s, 6), -0.02 (s, 6).

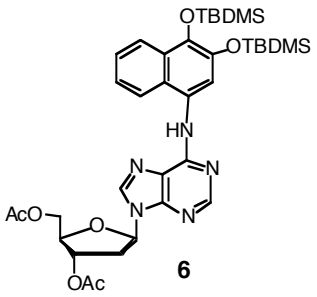


8a: R = Bn
b: R = *p*-nitrophenylethyl

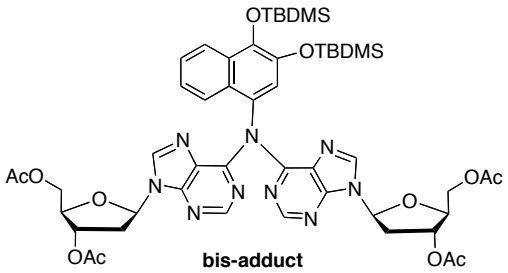
2-Chloro-6-benzyloxy-9-[2'-deoxy-ß-D-erythropentofuranosyl]purine diacetate (8a). Compound **8a** was prepared by the procedure described below for preparation of **8b** (60% yield): ^{1}H NMR ($CDCl_3$) □ 8.08 (s, 1), 7.52 (d, 2), 7.32 (m, 3), 6.41 (t, 1), 5.64 (s, 2), 5.38 (m, 1), 4.35 (m, 3), 2.79 (m, 1), 2.62 (m, 1), 2.12 (s, 3), 2.06 (s, 3); ^{13}C NMR ($CDCl_3$) □ 170.3, 170.2, 160.8, 153.1, 152.7, 140.5, 140.4, 135.2, 128.7, 128.5, 128.4, 121.0, 84.6, 82.6, 74.3, 69.6, 63.6, 37.9, 20.8, 20.7; MS: $[MH]^+$ 461.0 (Mass: 460.1.1).

2-Chloro-6-(*p*-nitrophenylethyloxy)-9-[2'-deoxy-ß-D-erythropentofuranosyl]purine diacetate (8b). To a flask containing 2-amino-6-(*p*-nitrophenylethyloxy)-9-[2'-deoxy -ß-D-erythropentofuranosyl]purine diacetate [2] (189 mg, 0.378 mmol) and CH_2Cl_2 (12 mL) under argon at 0 ˚C was added dropwise trimethylsilyl chloride (118 mL, 3.0 equiv.) followed by *t*-butyl nitrite (206 mL, 5.0 equiv.). The solution was stirred at 0 ˚C for 1 h, and reaction was quenched by addition of a saturated solution of $NaHCO_3$. Workup by the procedure for preparation of **5d** followed by purification on a silica gel column eluted with 3% MeOH in CH_2Cl_2 to provide **8b** (147 mg, 75%): ^{1}H NMR ($CDCl_3$) □ 8.09 (dd, 2, *J* =8.6 Hz) 8.07 (s, 1), 7.44 (d, 2, *J* =8.6 Hz), 6.38 (t, 1), 5.30 (m, 1), 4.78 (t, 2), 4.35 (m, 3), 3.25 (t, 2) 2.85 (m, 1), 2.65 (m, 1), 2.07 (s, 3), 2.04 (s, 3); ^{13}C NMR ($CDCl_3$) □ 170.3, 170.2, 160.6, 153.0, 152.7, 146.8, 145.3, 140.8, 129.9, 123.7, 120.7, 84.6, 82.7, 74.3, 67.5, 63.6, 37.8, 34.9, 20.9, 20.8; MS: $[MH]^+$ 520.0 (Mass: 519.1).

[2] Sigmund, H.; Pfleiderer, W. *Helv. Chim. Acta* **2003**, *86*, 2299-2334.

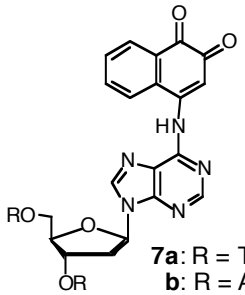


6



bis-adduct

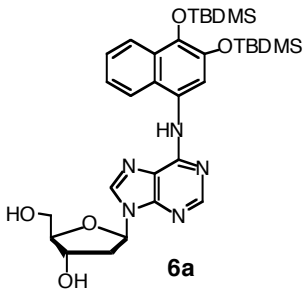
General Procedure for Coupling Halopurines: Synthesis of 6. A 15 mL pressure tube was flushed with argon, $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), racemic BINAP (9.3 mg, 0.015 mmol), and toluene (1 mL) were added and the mixture was stirred for 5 min. Then a solution of **4** (42 mg, 0.113 mmol) in toluene (2 mL), Cs_2CO_3 (37 mg), and a solution of **5b** (43 mg, 0.113 mmol) in toluene (2 mL) were added under of argon. The pressure tube was reflushed with argon, sealed, and heated at 80 °C overnight. The mixture was cooled to rt and chromatographed on a silica gel column eluted with hexane-EtOAc (1:1) to give **6** as yellow oil (36 mg, 47%): ^{1}H NMR ($CDCl_3$) 8.42 (s, 1H), 8.14 (d, 1 J =8.4 Hz) 8.02 (s, 1), 7.96 (s, 1), 7.94 (s, 1), 7.92 (d, 1 J =8.4 Hz) 7.44 (m, 1), 7.36 (m, 1), 6.46 (m, 1), 5.46 (m, 1), 4.44 (m, 1), 4.37 (m, 2), 3.01 (m, 1), 2.66 (m, 1), 2.14 (s, 3), 2.11 (s, 3), 1.13 (s, 9), 1.01 (s, 9), 0.31 (s, 6), 0.18 (s, 6); ^{13}C NMR ($CDCl_3$) 170.4, 170.3, 153.3, 153.1, 149.2, 141.9, 138.6, 137.7, 129.8, 126.6, 125.2, 124.4, 124.1, 123.1, 121.0, 118.0, 84.6, 82.6, 74.5, 63.8, 37.5, 26.2, 21.0, 20.9,20.8, 18.7, 18.6. –0.04, -3.56, -3; HRMS Calcd for $C_{36}H_{51}N_5O_7Si_2$ $[MNa]^+$ 744.3225. Found 744.3231. There was also obtained a small amount of the bis-adduct: ^{1}H NMR ($CDCl_3$) 8.59 (s, 2), 8.13 (d, 1, J =8.5 Hz), 7.12-7.87 (m, 5), 6.45 (m, 2), 5.41 (m, 2), 4.35 (m, 6), 2.93 (m, 2), 2.61 (m, 2), 2.11 (s, 6), 2.04 (m, 6), 1.13 (s, 9), 0.87 (s, 9), 0.17 (s, 6), 0.08 (s, 6); MS Calcd for $C_{50}H_{65}N_9O_{12}Si_2$: $[MH]^+$ 1040.4. Found: 1040.3. When the chloropurine (**5c**) was substituted for **5b**, reaction took place at lower temperature (60 °C), required 1 h for completion, and gave **6** in higher yield **6** (85%).



7a: R = TBDMS
b: R = Ac
c: R = H

Conversion of 6 to the NQ-dA Adduct (7c). (a) *Removal of TBDMS groups*. To a solution of **6** (70 mg, mmol) in CH_3CN (10 mL) under argon was added TBAF (0.2 mL of 1 M solution in THF, 0.2 mmol). The colorless solution was stirred at rt for 0.5 h. It became purple. The solvents were removed under reduced pressure, and the residue was purified by chromatography on a silica gel column to provide **7b** as purple oil (80%): ^{1}H NMR ($CDCl_3$) 8.65 (s, 1H), 8.20 (s, 1), 8.10 (d, 1, *J* =8.4 Hz) 7.85 (br s, 1), 7.58 (m, 1), 6.48 (m, 1), 5.46 (m, 1), 4.72 (m, 1), 4.38 (m, 2), 3.04 (m, 1), 2.13 (s, 3), 2.07 (s, 3). ^{13}C NMR ($CDCl_3$) 170.4, 170.3, 152.5, 141.5, 134.7, 131.4, 85.0, 82.8, 74.4, 63.6, 37.6, 20.9, 20.8. MS Calcd for $C_{24}H_{21}N_5O_7$ $[MH]^+$ 492.1. Found: 492.1.

(b) *Deacetylation.* To a solution of **7b** (25 mg, mmol) in CH_2Cl_2 (2 mL) and methanol (2 mL) was added a solution of guanidine hydrochloride (9.8 mg) and MeONa (3.8 mg) in MeOH (1 mL). TLC showed reaction was complete within an hour. The solvents were removed and the residue was purified on a column of silica gel to give **7c** (75%) as a purple solid: ^{1}H NMR (DMSO-d_6) 8.70 (s, 1H), 8.67 (s, 1), 8.25 (d, 1, *J* =7.5 Hz) 8.04 (d, 1, *J* =7.5 Hz), 7.84 (m, 1), 7.74 (m, 1), 6.46 (t, 1), 5.40 (br s, 1), 5.05 (br s, 1), 4.43 (m, 1), 3.89 (m, 1), 3.62 (m, 1), 3.35 (m, 1), 2.78 (m, 1), 2.36 (m, 1); ^{1}H NMR (CD_3OD) 8.68 (s, 1H), 8.62 (s, 1), 8.34 (d, 1, *J* =7.5 Hz), 8.12 (d, 1, *J* =7.5 Hz), 7.80 (m, 1), 7.69 (m, 1), 6.90 (br s, 1), 6.55 (t, 1), 4.61 (m, 1), 4.07 (m, 1), 3.86 (m, 1), 3.75 (m, 1), 2.85 (m, 1), 2.51 (m, 1); ^{13}C NMR (DMSO-d_6), 180.7, 152.2, 151.5, 143.6, 134.6, 133.1, 132.0, 131.4, 127.5, 125.8, 124.3, 88.4, 84.2, 71.0, 61.9; MS: Calcd for $C_{20}H_{17}N_5O_5$ $[M-H]^+$ 406.1. Found: 406.0; HRMS: Calcd for $C_{20}H_{17}N_5O_5$ $[M+Na]^+$ 430.1127. Found: 430.1140.

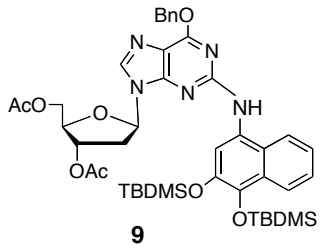


6a

Alternative Method of Deprotection of 6 and Conversion to the NQ-dA Adduct (7c).

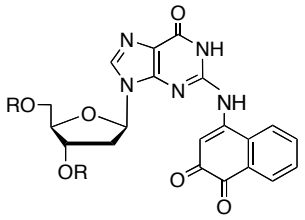
(a) *Deacetylation*. To a solution of **6a** (52 mg, 0.072 mmol) in CH_2Cl_2 (2 mL) and MeOH (2 mL) was added *N,N,N′,N′*-tetramethylguanidine (10 μL, 0.08 mmol). TLC showed reaction was complete in 1 h. Following removal of the solvents under vacuum, the residue was chromatographed on a column of silica gel to give deacetylated **6a** as a colorless oil (96%): ^{1}H NMR ($CDCl_3$) δ 8.39 (s, 1H), 8.35 (s, 1), 8.14 (d, 1 *J* =8.5 Hz), 7.93 (d, 1, *J* =8.5 Hz), 7.86 (s, 1), 7.72 (s, 1), 7.44 (m, 1), 7.34 (m, 1), 6.24 (m, 1), 4.75 (m, 1), 4.20 (m, 1), 3.94 (d, 1, *J* =13.0 Hz), 3.75 (d, 1, *J* =13.0 Hz), 3.04 (m, 1), 2.27 (m, 1), 1.13 (s, 9), 1.00 (s, 9), 0.28 (s, 6), 0.17 (s, 6); ^{13}C NMR ($CDCl_3$) δ 153.7, 152.3, 148.1, 141.8, 140.1, 138.0, 129.7, 126.2, 125.2, 124.6, 124.1, 123.0, 121.8, 121.2, 118.6, 89.7. 87.8, 73.2, 63.4, 40.8, 26.2, 26.1, 18.7, 18.6, -3.6, -3.7; MS: Calcd for $C_{32}H_{47}N_5O_5Si_2$ $[MH]^+$ 638.3. Found: 638.2.

(b) *Removal of TBDMS groups*. To a solution of **6a** (25 mg, 0.039 mmol) in DMF (2 mL) KF (2.3 mg, 0.039 mmol) and water (2 drops) were added. TLC showed that reaction was complete in 1 h. The solvents were removed under vacuum, and the residue was purified by chromatography on a column of silica gel to provide **7c** (4.4 mg, 90%) identical by NMR with **7c** prepared by the previous method.



9

Coupling Reaction of 4 with 8a: Synthesis of 9. The general coupling procedure described above was employed in the coupling of **4** with **8a**, and reaction was conducted at 60 °C overnight. The adduct **9** was obtained in 88% yield: ^{1}H NMR ($CDCl_3$) □ 8.05 (d, 1 *J* =8.5 Hz) 7.78 (d, 1 *J* =8.5 Hz), 7.69 (s, 1), 7.39 (s, 1), 7.35 (m, 1), 7.22 (m, 1), 7.13-7.18 (m, 5), 6.94 (s, 1), 6.21 (m, 1), 5.30 (s, 2), 5.19 (m, 1), 4.13 (m, 3), 2.78 (m, 1), 2.38 (m, 1), 2.01 (s, 3), 1.98 (s, 3), 1.03 (s, 9), 0.91 (s, 9), 0.15 (s, 6), 0.05 (s, 6); ^{13}C NMR ($CDCl_3$) □ 170.4, 170.2, 160.8, 157.9, 153.5, 141.9, 138.0, 137.5, 136.1, 129.8, 128.6, 128.3, 127.9, 125.9, 125.1, 124.0, 122.9, 122.3, 119.1, 116.5, 84.1, 82.2, 74.7, 68.0, 63.6, 36.9, 26.3, 26.1, 20.9, 20.8, 18.6, 18.5, 0.0, -3.5. HRMS: Calcd for $C_{43}H_{57}N_5O_8Si_2$ $[MH]^+$ 828.3824. Found: 828.3796.

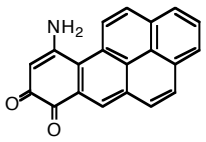


10a: R = Ac
b: R = H

Conversion of 9 to the NQ-dG Adduct (10). (a) ***Debenzylation*.** To a solution of **9** (50 mg, mmol) in MeOH (2 mL) and THF (2 mL) was added 5% Pd-C (20 mg). H_2 was bubbled through the solution for 2 h. then the mixture was allowed to stand under a hydrogen atmosphere overnight. TLC indicated that **9** was completely consumed and a single major product was formed. Removal of the catalyst by filtration and evaporation of the solvents afforded a residue that was purified by chromatography on a column of silica gel. Elution with 7% MeOH in CH_2Cl_2 afforded **10a** (80%) as oil: ^{1}H NMR ($CDCl_3$) □ 9.40 (br s, 1), 8.11 (d, 1 *J* =8.5 Hz) 7.92 (d, 1 *J*=8.5 Hz), 7.43 (t, 1), 7.32 (t, 1), 7.26 (s, 2), 5.98 (m, 1), 5.24 (m, 1), 4.09 (m, 1), 3.98 (m, 1), 3.87 (m, 1), 2.63 (m, 1), 2.17 (m, 1), 2.03 (s, 3), 1.81 (s, 3), 1.13 (s, 9), 0.98 (s, 9), 0.26 (s, 3), 0.25 (s, 3), 0.15 (s, 3), 0.12 (s, 3); ^{13}C NMR ($CDCl_3$) □ 170.2, 169.9, 159.2, 152.6, 150.7, 141.8, 139.1, 135.6, 131.8, 129.7, 127.9, 127.0, 126.9, 125.4, 123.2, 122.5, 121.8, 118.1, 84.2, 82.0, 74.6. 63.1, 36.4, 26.2, 26.1, 20.8, 20.5, 18.6, 18.5, -0.1, -3.5, -3.6; MS Calcd for $C_{36}H_{51}N_5O_8Si_2$ $[MH]^+$ 738.3. Found: 738.3.

(b) *Deacetylation*. To a solution of **10a** (50 mg, mmol) in MeOH (2 mL) and CH_2Cl_2 (2 mL) was added TMG (10 μL, mmol). TLC showed reaction was complete after 0.5 h. Chromatography on a silica gel column eluted with 12% MeOH in CH_2Cl_2 gave **10b** as colorless oil (88%): ^{1}H NMR ($CDCl_3$) δ 8.60 (br s, 1), 8.07 (d, 1 *J* =8.8 Hz) 7.78 (d, 1 *J* =8.5 Hz), 7.39 (m, 1), 7.26 (m, 2), 7.19 (s, 1), 6.07 (m, 1), 4.48 (m, 1), 4.11 (m, 1), 3.85 (m, 2), 2.61 (m, 1), 2.13 (m, 1), 1.10 (s, 9), 0.92 (s, 9), 0.19 (s, 6), 0.06 (s, 6); ^{13}C NMR ($CDCl_3$) δ 152.0, 150.3, 141.9, 138.0, 130.0, 126.8, 125.6, 124.7, 122.8, 122.5, 122.0, 118.2, 87.4, 85.0, 71.0, 61.9, 40.0, 26.1, 26.0, 18.6, 18.5, -0.1, -3.5, -3.6; MS: Calcd for $C_{32}H_{47}N_5O_6Si_2$ $[MH]^+$ 654.3. Found: 654.2.

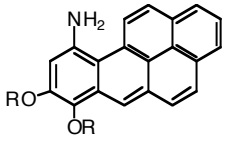
(c) *Removal of TBDMS*. To a solution of **12** (25 mg, 0.04 mmol) in DMF (2 mL) was added KF (2.3 mg, 0.04 mmol) and water (2 drops). TLC showed reaction was complete within 1 h. The solvents were evaporated and the residue was chromatographed on a silica gel column to provide the NQ-dG adduct (**10**) as a purple solid (85%): ^{1}H NMR (DMSO-d_6) δ 11.2 (br s, 1), 8.23 (d, 1, *J* =7.1 Hz), 7.96 (s, 1), 7.76 (d, 1, *J* =7.5 Hz), 7.55 (t, 1), 7.44 (t, 1), 6.30 (s, 1), 6.12 (m, 1), 5.20 (s., 1), 4.98 (br s, 1), 4.25 (m, 1), 3.72 (m, 1), 3.42 (m, 2), 2.56 (m, 1), 2.13 (m, 1); ^{13}C NMR (DMSO-d_6) δ 186.1, 172.0, 160.7, 158.3, 157.8, 150.2, 137.8, 137.6, 133.2, 132.4, 130.1, 126.0, 120.0, 103.9, 88.1, 83.6, 71.2, 62.2, 39.8; MS: Calcd for $C_{20}H_{17}N_5O_6$ $[M-H]^+$ 422.1. Found: 422.1. HRMS: Calcd for $C_{20}H_{17}N_5O_6$ $[M+Na]^+$ 446.1077. Found: 446.1088.



10-Amino-BPQ

10-Aminobenzo[*a*]pyrene-7,8-dione (10-Amino-BPQ). To a solution of BPQ (1.0g, 3.50 mmol) in DMF (10 mL) under argon was added dropwise trimethylsilyl azide (0.86 mL, 4.20 mmol). The reaction took place with evolution of heat and nitrogen gas, and the color changed from purple to brown. The mixture was stirred at rt overnight, then EtOAc (50 mL) and H_2O were added. The orange solid precipate of 10-amino-BPQ was filtered off. Additional 10-amino-BPQ was obtained by concentration of the filtrate under vacuum and chromatography of the residue on a silica gel column (combined yield 65%),

Mp. >290 °C: ^{1}H NMR ($CDCl_3$) δ: 8.72 (d, 1, *J* =11.5 Hz), 8.44 (s, 1), 7.99-8.23 (m, 7), 5.72 (m, 2); ^{13}C NMR (DMSO-d_6) δ 183.5, 175.0, 162.7, 162.3, 132.4, 131.9, 130.7, 130.2, 130.0, 129.4, 128.5, 128.4, 127.7, 127.5, 127.3, 126.9, 125.4, 124.8, 124.4, 123.6, 101.8; MS Calcd for $C_{20}H_{11}NO_2$, 297.1. Found: 298.0.



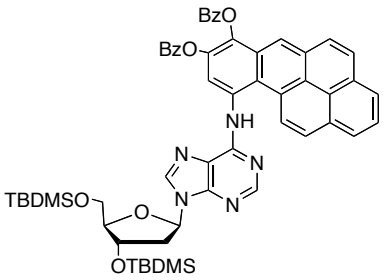
11a: R = TBDMS
b: R = Bz

10-Amino-7,8-*bis*(*tert*-butyldimethoxysilyoxy)benzo[*a*]pyrene (11a). *Method A: Reduction with* $NaBH_4$. To a solution of 10-**amino**-BPQ (50.8 mg, 0.169 mmol) in anhydrous DMF (5 mL) under argon was added $NaBH_4$ (100 mg, mmol). Reaction took place with evolution of heat and H_2. Stirring was continued at rt for 0.5 h, then TMDMS-Cl (500 mg) and imidazole (500 mg) were added. After an additional 4 h, EtOAc and water were added and the organic phase was washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated, and the residue was chromatographed on a silica gel column eluted with 5-7.5% EtOAc in hexane to give **11a** (20%) as yellow oil: ^{1}H NMR ($CDCl_3$) δ 9.72 (d, 1 *J* = 9.0 Hz). 8.78 (s, 1), 8.22 (d, 1, *J* =11.0 Hz), 8.15 (d, 1, *J* =7.5 Hz), 8.01 (d, 1, *J* =7.0 Hz), 7.89 (m, 3), 6.78 (s, 1), 4.32 (s, 2), 1.21 (s, 9), 1.04 (s, 9), 0.30 (s, 6), 0.15 (s, 6); ^{13}C NMR ($CDCl_3$) δ 142.2, 139.0, 133.6, 131.6, 130.2, 129.0, 128.8, 128.4, 128.0, 127.5, 126.3, 125.5, 125.4, 125.1, 124.9, 124.4, 123.1, 120.6, 115.7, 110.4, 26.4, 26.1, 18.7, 18.6, -0.1, -3.6; HRMS: Calcd for $C_{36}H_{51}N_5O_8Si_2$ $[MH]^+$ 528.2771. Found: 528.2763.

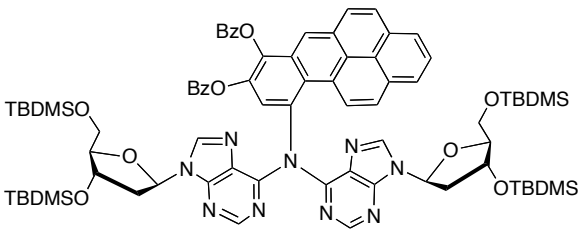
Method B: Pd-Catalyzed Reduction with H_2. To a solution of 10-**amino**-BPQ (50.8 mg, 0.169 mmol) in anhydrous DMF (5 mL) under argon was added 5% Pd-C (25 mg), and H_2 was bubbled through the mixture for 0.5 h. The dark red suspension became yellow, indicating that reduction of the quinone to the catechol was complete. The catalyst was removed by filtration under argon, and *N*-methyl TBDMS trifluoroacetamide (0.5 mL, 2.12 mmoL) was added to the filtrate. The mixture was stirred for 0.5 h, then EtOAc (50 mL) and water (50 mL) were added. The organic phase was washed with water and brine, and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was

purified on a silica gel column eluted with (5-7.5% EtOAc in hexane) to furnish **11a** (40%) as yellow oil. A tri-TBDMS by-product was also isolated. It was converted to **11a** by treatment with MeOH (combined yield of **11a** 60%).

10-Amino-7,8-*bis*(benzoyloxy)benzo[*a*]pyrene (11b). To a solution of 10-amino-BPQ (52.8 mg, 0.178 mmol) in anhydrous DMF (5 mL) under argon was added 5% Pd-C (20 mg), and H_2 was bubbled through the mixture for 0.5 h. The dark red solution turned dark yellow. The catalyst was removed by filtration under argon, and benzoic anhydride (116 mg, 2.5 equiv.) and potassium carbonate (138 mg, 2.5 equivalent) were added to the filtrate. The mixture was stirred at room temperature for 4 h, then MeOH was added to quench the reaction. After removal of the solvents under reduced pressure, water and EtOAc were added. The organic phase was washed with water and brine and then dried over Na_2SO_4. After removal of the solvent under vacuum, the furnish **11b** (65%) as yellow oil: ^{1}H NMR (DMSO-d_6) : 9.83 (d, 1 J = 9.4 Hz). 8.46 (s, 1), 8.34 (d, 1, J = 9.5 Hz), 8.27 (d, 1, J =7.7 Hz), 8.10 (m, 3), 7.93 (m, 5), 7.64 (t, 1, J = 7.5 Hz), 7.58 (t, 1, J = 7.5 Hz), 7.49 (t, 2, J =7.9 Hz), 7.40 (t, 2, J =7.8 Hz), 7.24 (s, 1), 6.14 (s, 2); ^{13}C NMR (DMSO-d_6) 165.1, 164.1, 147.1, 139.9, 134.6, 131.3, 130.5, 130.4, 130.3, 130.0, 129.4, 129.3, 128.9, 128.7, 128.6, 128.4, 128.3, 127.4, 127.2, 126.8, 126.1, 125.7, 125.4, 124.5, 123.1, 118.1, 117.0, 107.5; HRMS: Calcd for $C_{34}H_{21}NO_4$ $[MNa]^+$ 530.1368. Found: 530.1385.



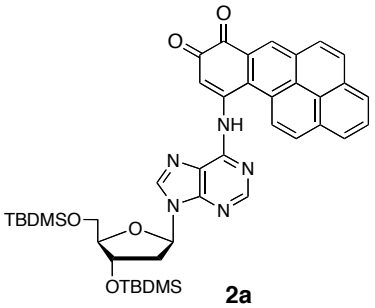
12 b



Bis-adduct

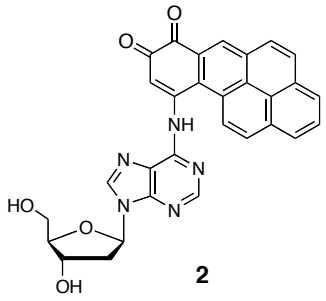
Synthesis of 12b via Coupling 5d with 11b. The coupling of **11b** (50 mg, mmol) with **5d** was carried out by the general procedure at 60 °C overnight. Chromatography of the product on a silica gel column eluted with 10% EtOAc in CH_2Cl_2 afforded the coupled adduct **12b** (50%) and the corresponidng bis-adduct in ~ 2:1 ratio. For **12b**: ^{1}H NMR

(DMSO-d_6) □ 10.79 (s, 1H), 9.76 (d, 1, *J* =9.5 Hz) 8.81 (s, 1), 8.49 (s, 1), 7.98-8.24 (m, 9), 7.76 (t, 1, *J* =8.0 Hz) 7.63 (t, 1, *J* =7.2 Hz), 7.60 (t, 2, *J* =7.7 Hz), 7.46 (t, 2, *J* =7.7 Hz), 6.39 (t, 1, *J* =6.5 Hz), 4.65 (m, 1), 3.86 (m, 1), 3.67-3.79 (m, 2), 2.98 (m, 1), 2.34 (m, 1), 0.87 (s, 9), 0.81 (s, 9), 0.10 (s, 6), -0.01 (s, 3), -0.03 (s, 3); ^{13}C NMR (DMSO-d_6) □: 164.6, 163.9, 153.0, 154.1, 152.7, 150.1, 141.8, 140.0, 138.5, 136.3, 135.4, 134.9, 134.7, 131.5, 130.8, 130.7, 130.5, 130.0, 129.5, 129.4, 129.3, 128.4, 128.3, 128.0, 127.8, 127.3, 127.0, 126.1, 126.0, 125.0, 124.4, 124.3, 124..0, 123.5, 122.2, 121.6, 119.9, 118.6, 87.5, 83.8, 72.3, 62.9, 38.8, 26.1, 18.3, 18.1, -4.4, -4.6, -5.1; HRMS: Calcd for $C_{56}H_{59}N_5O_7Si_2$ $[MH]^+$ 970.4031. Found: 970.4034.



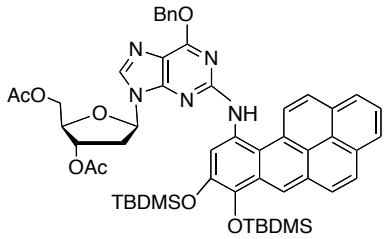
2a

Conversion of 12b to the BPQ-dA adduct (2). *(a) Debenzoylation.* To a solution of **12b** (10 mg, mmol) in CH_2Cl_2 (2 mL) and MeOH (2 mL) was added TMG (10 □L), and the solution was stirred at rt for 1 h. The color turned red, indicative of quinone formation. The solvents were removed under reduced pressure, and the residue was purified by chromatography on a silica gel column eluted with 3-6% MeOH in CH_2Cl_2 to provide **2a** (80%): ^{1}H NMR (DMSO-d_6) □ 10.10 (br s, 1H), 8.97 (s, 1), 8.74 (s, 1), 8.57 (s, 1), 8.31-8.42 (m, 4), 8.15 (t, 1, *J* =7.5 Hz) 7.89 (m, *2*), 7.57 (t, 1, *J* =7.4 Hz), 7.45 (t, 2, *J* =7.7 Hz), 6.45 (t, 1, *J* =6.6 Hz), 4.65 (m, 1), 3.86 (m, 1), 3.67-3.79 (m, 2), 2.98 (m, 1), 2.36 (m, 1), 0.87 (s, 9), 0.79 (s, 9), 0.09 (s, 6), -0.02 (s, 3), -0.04 (s, 3); HRMS: Calcd for $C_{56}H_{59}N_5O_7Si_2$ $[MH]^+$ 760.3351. Found: 760.3331.



2

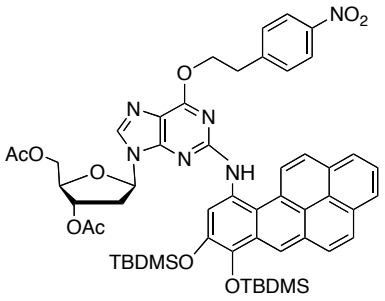
To a solution of **2a** (6 mg, mmol) in acetonitrile (2 mL) was added TBAF (50 μL, 1M), and the mixture was stirred at rt overnight. The solvent was removed under reduced pressure, and the residue was purified by chromatography on a silica gel column elutied with 5-30% MeOH in CH_2Cl_2 to give the BPQ-dA adduct **2** (75%) yield: ^{1}H NMR (DMSO-d_6) δ 10.35 (d, 1, *J* =9.4 Hz), 8.89 (s, 1), 8.65 (s, 1), 8.52 (s, 1), 8.37 (d, 1, *J* =9.0 Hz), 8.34 (d, 1, *J*=7.9 Hz), 8.28-8.31 (m, 2), 8.22 (d, 1, *J* =9.8 Hz), 8.13 (t, 1, *J* =7.6 Hz), 6.46 (t, 1, *J* =6.6 Hz), 5.57 (br s, 1), 5.36 (br, 1), 5.12 (br, 1), 4.44 (m, 1), 3.90 (m, 1), 3.52-3.71 (m, 2), 2.83 (m, 1), 2.34 (m, 1).); ^{13}C NMR (DMSO-d_6) δ: 162.1, 152.7, 151.2, 144.0, 142.5, 131.9, 131.8, 131.4, 130.8, 129.6, 129.5, 128.9, 128.6, 128.5, 128.0, 127.3, 126.7, 126.2, 125.5, 123.9, 123.6, 105.0, 88.4, 84.2, 71.2, 62.1, 39.8. HRMS: Calcd for $C_{30}H_{21}N_5O_5$ $[MNa]^+$ 554.1440. Found: 554.1435.



13a

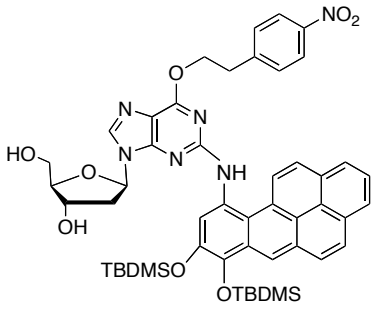
Synthesis of 13a via Coupling 8a with 11b. The general coupling procedure was employed, and the reaction was conducted at 60 °C overnight. The reaction mixture was cooled to rt and chromatographed on a silica gel column eluted with EtOAc-hexane (2:1). The adduct **13a** was obtained (82%) as yellow oil: ^{1}H NMR ($CDCl_3$) δ 9.62 (d, 1 *J* =10.0 Hz) 8.90 (s, 1), 8.07 (d, 1 *J* =10.0 Hz), 8.01 (d, 1 *J* =7.0 Hz), 7.86-7.98 (m, 4), 7.52 (s, 1), 7.45 (s, 1), 7.36 (s, 1), 7.10 (m, 5), 6.18 (m, 1), 5.21 (s, 2), 5.05 (m, 1), 4.41 (m, 3), 2.50 (m, 1), 2.05 (m, 1), 2.07 (s, 3), 2.04 (s, 3), 1.28 (s, 9), 1.05 (s, 9), 0.34 (s, 3), 0.31 (s, 3), 0.23 (s, 3), 0.20 (s, 3); ^{13}C NMR ($CDCl_3$) δ 170.3, 170.0, 160.8, 157.6, 153.5, 141.8, 139.0, 137.5, 136.0, 131.6, 130.5, 129.8, 129.0, 128.6, 128.3, 128.2, 128.0, 127.7, 127.6, 125.8, 125.1, 125.0, 124.5, 123.4, 122.4, 121.3, 120.4, 116.5, 84.3, 82.2, 74.6, 67.8, 63.4, 60.3, 36.1, 26.3, 26.1, 21.0, 20.8, 20.6, 18.8, 18.6, 14.1, -3.5, -3.6; HRMS Calcd for $C_{53}H_{61}N_5O_8Si_2$, $[MH]^+$ 952.4137. Found: 952.4136.

(a) *Debenzylation*. Attempts to selectively remove the benzyl group by reductive hydrogenation were complicated by the relative facility of reduction of the aromatic ring system under the conditions studied. Therefore, we investigated the use of an alternative protecting group, namely *p*-nitrophenylethyl, potentially removable by other methods.

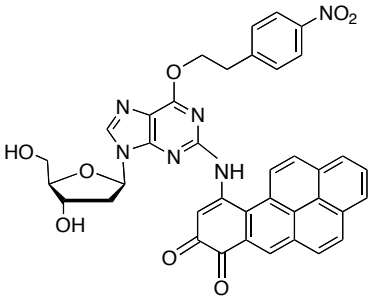


13b

Synthesis of 13b via Coupling 8b with 11b. The general coupling procedure was employed, and reaction was conducted at 60 °C overnight. The usual workup afforded adduct **13b** (88%): ^{1}H NMR (CD_3CN) 9.67 (d, 1 J=9.5 Hz), 8.88 (s, 1), 7.71-8.23 (m, 11), 7.65 (s, 1), 7.46 (s, 1), 5.95 (m, 1), 5.28 (br., 1), 4.70 (t, 2), 4.07 (m, 1), 3.95 (m, 1), 3.86 (m, 2), 270 (t, 2), 2.44 (m, 1), 2.10 (m, 1), 2.15 (s, 3), 21.93 (s, 3), 1.20 (s, 9), 1.02 (s, 9), 0.33 (s, 3), 0.30 (s, 3), 0.21 (s, 6). 0.18 (s, 6); ^{13}C NMR (CD_3CN) 170.2, 170.1, 160.3, 157.9, 153.8, 146.4, 142.0, 138.8, 138.7, 131.5, 130.8, 130.5, 129.4, 128.9, 128.5, 128.2. 127.9, 127.8, 126.3, 126.1, 125.1, 124.7, 124.6, 123.1, 122.9, 122.5, 121.6, 120.1, 117.3, 115.9, 84.2, 82.1, 74.6, 65.4, 63.3, 33.8, 25.7, 25.5, 20.1, 20.0, 18.5. 18.3, 13.5, -4.0, -4.1, -4.2, -4.3. HRMS: Calcd for $C_{54}H_{62}N_6O_{10}Si_2$ $[MH]^+$ 1011.4144. Found: 1011.4146.

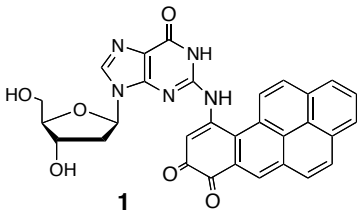


13c



14a

Removal of Protecting Groups and Conversion of 13b into the BPQ-dG Adduct (1). *Deprotection*. To a solution of **13b** (15 mg, mmol) in CH_2Cl_2 (2 mL) and MeOH (2 mL) was added TMG (30 μL, mmol). TLC showed that conversion of **13b** to **13c** was complete in 2 h. MS of **13c**: Calcd for $C_{50}H_{58}N_6O_8Si_2$ $[MH]^+$ 927.4. Found: 927.3. Following removal of the solvents under vacuum, the residue was allowed to stand at rt overnight. TLC showed that **13c** was completely converted to a mixture of two more polar compounds that were separated by chromatography on a silica gel column and identified as **14a** and the BPQ-dG adduct (**1**). These compounds were obtained in ~1:1 ratio. Conversion of **14a** to **1** was complete on standing for 3 days . Compound **14a**: ^{1}H NMR (DMSO-d_6) δ 9.95 (br s, 1), 8.96 (s, 1), 8.47 (s, 1), 8.32-8.43 (m, 6), 8.7 (t, 1), 8.10 (d, J=9.0, 1, Hz), 7.57 (d, 1, J=8.0 Hz), 6.38 (m, 2), 5.29 (m, 1), 4.74 (m, 2), 4.35 (m, 1), 4.03 (br., 1), 3.83 (m, 1), 3.60 (m, 2), 3.24 (m, 2), 2.68 (m, 1), 2.26 (m, 1); ^{31}C NMR (DMSO-d_6) δ 182.1, 160.6, 153.4, 146.9, 146.6, 141.8, 132.6, 131.8, 130.7, 130.6, 130.3, 129.8, 129.5, 128.6, 128.3, 127.4, 127.2, 127.0, 126.8, 125.3, 123.9, 123.7, 123.6, 117.4, 108.3, 88.4, 84.0, 71.1, 66.8, 62.0, 34.6; MS: Calcd for $C_{38}H_{28}N_6O_8$ $[M-H]^+$ 695.2. Found: 695.1.



1

BPQ-dG adduct (**1**): ^{1}H NMR (DMSO-d_6) δ 11.45 (br s, 1), 10.20 (d, 1 J=9.7 Hz), 8.72 (s, 1), 7.98-8.24 (m, 7), 6.16 (t, 1), 5.78 (s, 1), 5.18 (br., 1), 4.24 (m, 1), 3.74 (m, 1), 3.45 (m, 2), 2.58 (m, 1), 2.14 (m, 1); ^{31}C NMR (DMSO-d_6) δ 187.6, 169.8, 165.2, 158.4. 157.9, 150.3, 137.7, 131.9, 131.6, 131.4, 130.9, 129.4, 129.3, 129.0, 128.6, 128.5, 128.4, 127.9, 127.4, 126.6, 126.0, 123.9, 123.6, 119.9, 104.3, 88.4, 83.7, 71.3, 62.2, (C-2' was buried in the solvent peaks of DMSO); MS: Calcd for $C_{30}H_{21}N_5O_6$ $[MH]^+$ 548.15. Found: 548.15. HRMS: Calcd for $C_{30}H_{21}N_5O_6$ $[M+Na]^+$ 570.1390. Found: 570.1385.