Supporting Information

***O*⁶-(Benzotriazol-1-yl)inosine Derivatives: Easily Synthesized, Reactive Nucleosides**

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Synthetic procedures and characterization data for compounds not described in the manuscript.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-methyl-2'-deoxyinosine (7a).

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol), Cs₂CO₃ (65.2 mg, 0.200 mmol) and methanol (1.0 mL). The reaction mixture was flushed with N₂ and stirred at room temperature for 1 h after which the mixture was evaporated to dryness. Chromatographic purification (SiO₂, elution with 20% EtOAc in hexanes) afforded 38.0 mg (77% yield) of the title compound as a clear gum. *R*_f (20% EtOAc in hexanes) = 0.12. ¹H NMR (500 MHz, CDCl₃): δ 8.52 (s, 1H, Ar-H), 8.27 (s, 1H, Ar-H), 6.49 (t, 1H, H-1', *J* = 6.3), 4.62 (m, 1H, H-3'), 4.18 (s, 3H, OCH₃), 4.01 (m, 1H, H-4'), 3.87 (dd, 1H, H-5', *J* = 11.2, 3.9), 3.77 (dd, 1H, H-5', *J* = 11.2, 2.9), 2.62 (app quint, 1H, H-2', *J*_{app} ~ 6.3), 2.45 (ddd, 1H, H-2', *J* = 13.2, 6.4, 3.9), 0.91 (s, 18H, *tert*-Bu), 0.09, 0.08 (2s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 161.1, 152.0, 151.5, 140.6, 122.0, 88.0, 84.5, 71.9, 62.8, 54.0, 41.4, 25.9, 25.7, 18.4, 17.9, -4.7, -4.8, -5.5, -5.6. FAB HRMS calcd for C₂₃H₄₃N₄O₄Si₂ [M + H]⁺ 495.2817, found 495.2798.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-ethyl-2'-deoxyinosine (7b).

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-methyl-2'-deoxyinosine, this ethyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol) and EtOH (1.0 mL) in the presence of Cs₂CO₃ (65.2 mg, 0.200 mmol) over 1 h. Chromatographic purification (SiO₂, elution with 20% EtOAc in hexanes)

afforded 48.2 mg (95% yield) of the title compound as a clear gum. R_f (20% EtOAc in hexanes) = 0.16. ^1H NMR (500 MHz, CDCl_3): δ 8.50 (s, 1H, Ar-H), 8.26 (s, 1H, Ar-H), 6.50 (t, 1H, H-1', J = 6.4), 4.65 (q, 2H, OCH_2 , J = 7.0), 4.61 (m, 1H, H-3'), 4.01 (m, 1H, H-4'), 3.87 (dd, 1H, H-5', J = 11.2, 3.9), 3.77 (dd, 1H, H-5', J = 11.2, 2.9), 2.61 (app quint, 1H, H-2', J = 6.3), 2.44 (ddd, 1H, H-2', J = 12.9, 6.1, 3.9), 1.50 (t, 3H, CH_3 , J = 7.3), 0.91 (s, 18H, *tert*-Bu), 0.09, 0.08 (2s, 12H, SiCH_3). ^{13}C NMR (125 MHz, CDCl_3): δ 160.8, 152.0, 151.5, 140.5, 121.9, 87.9, 84.4, 71.8, 63.1, 62.7, 41.5, 26.0, 25.7, 18.4, 18.0, 14.5, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for $\text{C}_{24}\text{H}_{45}\text{N}_4\text{O}_4\text{Si}_2$ $[\text{M} + \text{H}]^+$ 509.2974, found 509.2953.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-isopropyl-2'-deoxyinosine (7c).

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-methyl-2'-deoxyinosine, this isopropyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol) and 2-propanol (1.0 mL) in the presence of Cs_2CO_3 (65.2 mg, 0.200 mmol) over 10 h. Chromatographic purification (SiO_2 ,

elution with 20% EtOAc in hexanes) afforded 44.1 mg (84% yield) of the title compound as a clear gum. R_f (20% EtOAc in hexanes) = 0.31. ^1H NMR (500 MHz, CDCl_3): δ 8.50 (s, 1H, Ar-H), 8.23 (s, 1H, Ar-H), 6.49 (t, 1H, H-1', J = 6.3), 5.67 (septet, 1H, -CH-, J = 6.3), 4.61 (m, 1H, H-3'), 4.02 (m, 1H, H-4'), 3.87 (dd, 1H, H-5', J = 11.2, 3.9), 3.78 (dd, 1H, H-5', J = 10.7, 2.9), 2.62 (app quint, 1H, H-2', $J_{\text{app}} \sim 6.3$), 2.44 (ddd, 1H, H-2', J = 13.2, 5.9, 3.9), 1.47 (d, 6H, CH_3 , J = 6.5), 0.91 (s, 18H, *tert*-Bu), 0.10, 0.09 (2s, 12H, SiCH_3). ^{13}C NMR (125 MHz, CDCl_3): δ 160.5, 152.0, 151.5, 140.3, 122.0, 87.9, 84.4, 71.9, 71.2, 62.8, 41.4, 26.0, 25.7, 22.0, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for $\text{C}_{25}\text{H}_{47}\text{N}_4\text{O}_4\text{Si}_2$ $[\text{M} + \text{H}]^+$ 523.3130, found 523.3130.

2',3',5'-Tri-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-isopropylinosine (8a).

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-methyl-2'-deoxyinosine, this isopropyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)inosine (**5b**) (71.8 mg, 0.099 mmol) and 2-propanol (1.0 mL) in the presence of Cs_2CO_3 (65.2 mg, 0.200 mmol) over 24 h at room temperature

and then at 85 °C for 3 h. Chromatographic purification (SiO_2 , elution with 20% EtOAc in hexanes)

afforded 45.6 mg (70% yield) of the title compound as a clear gum. R_f (20% EtOAc in hexanes) = 0.59. ^1H NMR (500 MHz, CDCl_3): δ 8.49 (s, 1H, Ar-H), 8.27 (s, 1H, Ar-H), 6.08 (d, 1H, H-1', J = 5.4), 5.66 (septet, 1H, $-\text{CH}-$, J = 6.3), 4.64 (t, 1H, H-2', J = 4.6), 4.32 (t, 1H, H-3', J = 3.9), 4.13 (m, 1H, H-4'), 4.02 (dd, 1H, H-5', J = 11.2, 3.9), 3.79 (dd, 1H, H-5', J = 11.2, 2.7), 1.48 (d, 3H, CH_3 , J = 6.4), 1.47 (d, 3H, CH_3 , J = 6.4), 0.95, 0.93, 0.79 (3s, 27H, *tert*-Bu), 0.14, 0.13, 0.10, 0.09, -0.05, -0.23 (6s, 18H, SiCH_3). ^{13}C NMR (125 MHz, CDCl_3): δ 160.5, 152.0, 151.9, 140.8, 122.1, 88.3, 85.4, 76.0, 71.9, 70.2, 62.5, 26.1, 25.8, 25.6, 22.0, 18.5, 18.1, 17.8, -4.4, -4.7, -4.73, -5.1, -5.4. FAB HRMS calcd for $\text{C}_{31}\text{H}_{61}\text{N}_4\text{O}_5\text{Si}_3$ $[\text{M} + \text{H}]^+$ 653.3944, found 653.3944.

***O*⁶-Allyl-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (7d).**

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-methyl-2'-deoxyinosine, this allyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol) and allyl alcohol (1.0 mL) in the presence of Cs_2CO_3 (65.2 mg, 0.200 mmol) over 2 h. Chromatographic purification (SiO_2 , elution with 20% EtOAc in hexanes) afforded 46.4 mg (89% yield) of the title compound as a clear gum. R_f (20% EtOAc in hexanes) = 0.29. ^1H NMR (500 MHz, CDCl_3): δ 8.51 (s, 1H, Ar-H), 8.27 (s, 1H, Ar-H), 6.50 (t, 1H, H-1', J = 6.4), 6.16 (m, 1H, $-\text{CH}=\text{CH}-$), 5.45 (dd, 1H, $=\text{CH}_{\text{trans}}$, J = 17.1, 1.5), 5.29 (d, 1H, $=\text{CH}_{\text{cis}}$, J = 10.7), 5.12 (d, 2H, OCH_2 , J = 5.4), 4.61 (m, 1H, H-3'), 4.02 (m, 1H, H-4'), 3.87 (dd, 1H, H-5', J = 11.2, 3.9), 3.77 (dd, 1H, H-5', J = 11.2, 2.9), 2.61 (app quint, 1H, H-2', $J_{\text{app}} \sim 6.3$), 2.44 (ddd, 1H, H-2', J = 12.9, 6.1, 3.9), 0.91 (s, 18H, *tert*-Bu), 0.09, 0.08 (2s, 12H, SiCH_3). ^{13}C NMR (125 MHz, CDCl_3): δ 160.3, 151.9, 151.6, 140.6, 132.4, 121.9, 118.5, 87.9, 84.4, 71.8, 67.5, 62.7, 41.4, 26.0, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for $\text{C}_{25}\text{H}_{45}\text{N}_4\text{O}_4\text{Si}_2$ $[\text{M} + \text{H}]^+$ 521.2974, found 521.2974.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-phenyl-2'-deoxyinosine (7e).

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (63.2 mg, 0.106 mmol), Cs_2CO_3 (68.9 mg, 0.211 mmol) and phenol (19.9 mg, 0.211 mmol). Dry toluene (1.0 mL) was added and the reaction mixture was flushed with N_2 and allowed to stir at 105 °C for 2 h. The reaction mixture was filtered

through Celite, the residue was washed with Et₂O and the filtrate evaporated to dryness. Chromatographic purification (SiO₂, elution with 20% EtOAc in hexanes) afforded 50.5 mg (86% yield) of the title compound as a clear gum. *R_f* (20% EtOAc in hexanes) = 0.21. ¹H NMR (500 MHz, CDCl₃): δ 8.49 (s, 1H, Ar-H), 8.40 (s, 1H, Ar-H), 7.46–7.43 (m, 2H, Ar-H), 7.29–7.26 (m, 3H, Ar-H), 6.53 (t, 1H, H-1', *J* = 6.3), 4.64 (m, 1H, H-3'), 4.04 (m, 1H, H-4'), 3.90 (dd, 1H, H-5', *J* = 11.2, 3.9), 3.70 (dd, 1H, H-5', *J* = 11.2, 2.7), 2.65 (app quint, 1H, H-2', *J_{app}* ~ 6.3), 2.48 (ddd, 1H, H-2', *J* = 13.2, 6.1, 4.1), 0.92, 0.91 (2s, 18H, *tert*-Bu), 0.10 (s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 160.2, 152.5, 152.4, 152.0, 141.6, 129.6, 125.7, 122.1, 121.9, 88.0, 84.6, 71.8, 62.7, 41.5, 26.0, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₂₈H₄₅N₄O₄Si₂ [M + H]⁺ 557.2974, found 557.2978.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)-2'-deoxyinosine (7f).

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (40.0 mg, 0.067 mmol), Cs₂CO₃ (43.6 mg, 0.134 mmol) and 4-nitrophenol (18.6 mg, 0.134 mmol). Dry DME (0.7 mL) was added and the reaction mixture was flushed with N₂ and allowed to stir at 85 °C for 2 h. The reaction mixture was diluted with EtOAc and washed with 0.1 N aq NaOH, followed by brine. The organic layer was dried over Na₂SO₄ and evaporated to dryness. Chromatographic purification (SiO₂, elution with 50% EtOAc in hexanes) afforded 31.3 mg (78% yield) of the title compound as a yellow gum. *R_f* (5% MeOH in CH₂Cl₂) = 0.58. ¹H NMR (500 MHz, CDCl₃): δ 8.51 (s, 1H, Ar-H), 8.46 (s, 1H, Ar-H), 8.34 (d, 2H, Ar-H, *J* = 9.3), 7.47 (d, 2H, Ar-H, *J* = 8.8), 6.55 (t, 1H, H-1', *J* = 6.4), 4.65 (m, 1H, H-3'), 4.05 (m, 1H, H-4'), 3.91 (dd, 1H, H-5', *J* = 11.2, 3.4), 3.80 (dd, 1H, H-5', *J* = 11.2, 2.9), 2.65 (app quint, 1H, H-2', *J_{app}* ~ 6.3), 2.50 (ddd, 1H, H-2', *J* = 13.2, 6.1, 4.2), 0.92 (s, 18H, *tert*-Bu), 0.113, 0.11 (2s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 158.9, 157.4, 153.1, 151.6, 145.2, 142.4, 125.3, 122.3, 122.2, 88.1, 84.8, 71.8, 62.7, 41.6, 26.0, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₂₈H₄₄N₅O₆Si₂ [M + H]⁺ 602.2825, found 602.2813.

2',3',5'-Tri-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)inosine (8b).

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)-2'-deoxyinosine, this 4-nitrophenyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)inosine (**5b**) (71.8 mg, 0.099 mmol) and 4-nitrophenol

(27.8 mg, 0.200 mmol) in the presence of Cs_2CO_3 (65.2 mg, 0.200 mmol) in dry DME (1.0 mL) at 85 °C over 1 h. Chromatographic purification (SiO_2 , elution with 20% EtOAc in hexanes) afforded 59.5 mg (81% yield) of the title compound as a clear gum. R_f (20% EtOAc in hexanes) = 0.43. ^1H NMR (500 MHz, CDCl_3): δ 8.53 (s, 1H, Ar-H), 8.51 (s, 1H, Ar-H), 8.34 (d, 2H, Ar-H, $J = 9.3$), 7.48 (d, 2H, Ar-H, $J = 9.3$), 6.15 (d, 1H, H-1', $J = 4.9$), 4.61 (t, 1H, H-2', $J = 4.6$), 4.34 (t, 1H, H-3', $J = 4.2$), 4.17 (m, 1H, H-4'), 4.05 (dd, 1H, H-5', $J = 11.5, 3.7$), 3.82 (dd, 1H, H-5', $J = 11.5, 2.2$), 0.97, 0.94, 0.81 (3s, 27H, *tert*-Bu), 0.17, 0.16, 0.11, 0.10, 0.0, -0.18 (6s, 18H, SiCH_3). ^{13}C NMR (125 MHz, CDCl_3): δ 158.8, 157.3, 153.3, 151.7, 145.1, 142.8, 125.4, 122.4, 122.1, 88.6, 85.5, 76.4, 71.7, 62.4, 26.1, 25.8, 25.6, 18.5, 18.1, 17.8, -4.4, -4.7, -4.72, -5.0, -5.3, -5.4. FAB HRMS calcd for $\text{C}_{34}\text{H}_{58}\text{N}_5\text{O}_7\text{Si}_3$ $[\text{M} + \text{H}]^+$ 732.3639, found 732.3629.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(3-cyanophenyl)-2'-deoxyinosine (7g).

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)-2'-deoxyinosine, this 3-cyanophenyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol) and 3-cyanophenol (13.1 mg, 0.110 mmol) in the presence of Cs_2CO_3 (65.2 mg, 0.200 mmol) in dry DME (1.0 mL) at 85 °C over 2 h. Chromatographic purification (SiO_2 , elution with 20% EtOAc in hexanes) afforded 47.5 mg (82% yield) of the title compound as a clear gum. R_f (50% EtOAc in hexanes) = 0.58. ^1H NMR (500 MHz, CDCl_3): δ 8.49 (s, 1H, Ar-H), 8.45 (s, 1H, Ar-H), 7.62–7.54 (m, 4H, Ar-H), 6.54 (t, 1H, H-1', $J = 6.4$), 4.64 (m, 1H, H-3'), 4.05 (m, 1H, H-4'), 3.91 (dd, 1H, H-5', $J = 11.2, 3.9$), 3.80 (dd, 1H, H-5', $J = 11.2, 3.9$), 2.64 (app quint, 1H, H-2', $J_{\text{app}} \sim 6.3$), 2.49 (ddd, 1H, H-2', $J = 13.2, 6.3, 4.4$), 0.92, 0.916 (2s, 18H, *tert*-Bu), 0.11, 0.105 (2s, 12H, SiCH_3). ^{13}C NMR (125 MHz, CDCl_3): δ 159.1, 153.0, 152.7, 151.6, 142.2, 130.4, 129.2, 126.7, 125.6, 122.1, 117.9, 113.6, 88.1, 84.8, 71.8, 62.7, 41.5, 25.9, 25.7, 18.4, 17.9, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for $\text{C}_{29}\text{H}_{44}\text{N}_5\text{O}_4\text{Si}_2$ $[\text{M} + \text{H}]^+$ 582.2926, found 582.2927.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(naphth-1-yl)-2'-deoxyinosine (7h).

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)-2'-deoxyinosine, this naphthyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-

3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol), Cs₂CO₃ (65.2 mg, 0.200 mmol) and 1-naphthol (15.9 mg, 0.110 mmol) in dry DME (1.0 mL) at 85 °C for 2 h. Chromatographic purification (SiO₂, elution with 20% EtOAc in hexanes) afforded 49.2 mg (81% yield) of the title compound as a yellowish-white foam. *R_f* (20% EtOAc in hexanes) = 0.37. ¹H NMR (500 MHz, CDCl₃): δ 8.44 (s, 1H, Ar-H), 8.41 (s, 1H,

Ar-H), 7.93 (d, 1H, Ar-H, *J* = 8.8), 7.91 (d, 1H, Ar-H, *J* = 8.3), 7.81 (d, 1H, Ar-H, *J* = 8.3), 7.54 (t, 1H, Ar-H, *J* = 7.8), 7.50 (t, 1H, Ar-H, *J* = 7.6), 7.42 (t, 1H, Ar-H, *J* = 7.6), 7.39 (d, 1H, Ar-H, *J* = 7.3), 6.56 (t, 1H, H-1', *J* = 6.4), 4.67 (m, 1H, H-3'), 4.06 (m, 1H, H-4'), 3.92 (dd, 1H, H-5', *J* = 11.2, 4.4), 3.82 (dd, 1H, H-5', *J* = 11.2, 2.9), 2.71 (app quint, 1H, H-2', *J* = 6.3), 2.50 (ddd, 1H, H-2', *J* = 12.9, 5.9, 4.1), 0.94, 0.93 (2s, 18H, *tert*-Bu), 0.12 (s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 160.7, 152.7, 152.1, 148.6, 141.7, 134.9, 128.0, 127.3, 126.4, 126.2, 125.9, 125.5, 122.0, 121.9, 118.1, 88.1, 84.7, 72.0, 62.8, 41.4, 25.9, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₃₂H₄₇N₄O₄Si₂ [M + H]⁺ 607.3130, found 607.3120.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(fluoren-2-yl)-2'-deoxyinosine (**7i**).

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)-2'-deoxyinosine, this fluorenyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol), Cs₂CO₃ (65.2 mg, 0.200 mmol) and 2-hydroxyfluorene (20.0 mg, 0.110 mmol) in dry DME (1.0 mL) at 85 °C for 1 h. Chromatographic purification (SiO₂,

elution with 20% EtOAc in hexanes) afforded 56.0 mg (87% yield) of the title compound as a clear, yellowish gum. *R_f* (20% EtOAc in hexanes) = 0.31. ¹H NMR (500 MHz, CDCl₃): δ 8.52 (s, 1H, Ar-H), 8.41 (s, 1H, Ar-H), 7.83 (d, 1H, Ar-H, *J* = 8.3), 7.77 (d, 1H, Ar-H, *J* = 7.3), 7.53 (d, 1H, Ar-H, *J* = 7.3), 7.45 (s, 1H, Ar-H), 7.37 (t, 1H, Ar-H, *J* = 7.6), 7.31-7.26 (m, 2H, Ar-H), 6.55 (t, 1H, H-1', *J* = 6.4), 4.66 (m, 1H, H-3'), 4.05 (m, 1H, H-4'), 3.94 (s, 2H, CH₂), 3.92 (dd, 1H, H-5', *J* = 11.2, 4.1), 3.81 (dd, 1H, H-5', *J* = 11.2, 2.9), 2.67 (app quint, 1H, H-2', *J_{app}* ~ 6.3), 2.50 (ddd, 1H, H-2', *J* = 13.2, 6.0, 4.3), 0.94, 0.93 (2s, 18H, *tert*-Bu), 0.12 (s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 160.5, 152.5, 152.1, 151.7, 144.7, 143.3, 141.6, 141.1, 139.5, 126.8, 126.5, 124.9,

122.2, 120.5, 120.47, 119.7, 118.7, 88.1, 84.7, 71.9, 62.8, 41.5, 37.0, 25.9, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₃₅H₄₉N₄O₄Si₂ [M + H]⁺ 645.3287, found 645.3303.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(quinolin-8-yl)-2'-deoxyinosine (7j).

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)-2'-deoxyinosine, this quinolinyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol), Cs₂CO₃ (65.2 mg, 0.200 mmol) and 8-hydroxyquinoline (16.0 mg, 0.110 mmol) in dry DME (1.0 mL) at 85 °C for 1 h. Chromatographic purification (SiO₂,

elution with 50% EtOAc in hexanes) afforded 48.0 mg (79% yield) of the title compound as a clear gum. *R_f* (50% EtOAc in hexanes) = 0.24. ¹H NMR (500 MHz, CDCl₃): δ 8.77 (dd, 1H, Ar-H, *J* = 4.1, 1.2), 8.43 (s, 1H, Ar-H), 8.35 (s, 1H, Ar-H), 8.21 (br d, 1H, Ar-H, *J* = 8.3), 7.79 (d, 1H, Ar-H, *J* = 7.8), 7.66–7.60 (m, 2H, Ar-H), 7.40 (dd, 1H, Ar-H, *J* = 8.3, 3.9), 6.54 (t, 1H, H-1', *J* = 6.3), 4.64 (m, 1H, H-3'), 4.04 (m, 1H, H-4'), 3.92 (dd, 1H, H-5', *J* = 11.2, 3.9), 3.81 (dd, 1H, H-5', *J* = 11.2, 2.9), 2.66 (app quint, 1H, H-2', *J_{app}* ~ 6.3), 2.48 (ddd, 1H, H-2', *J* = 13.2, 5.9, 4.4), 0.94, 0.92 (2s, 18H, *tert*-Bu), 0.123, 0.12, 0.11 (3s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 161.0, 152.6, 151.9, 150.3, 149.0, 141.6, 141.5, 136.0, 129.7, 126.4, 126.0, 121.9, 121.63, 121.6, 87.9, 84.5, 71.7, 62.7, 41.5, 26.0, 25.8, 18.5, 18.0, -4.6, -4.8, -5.3, -5.4. FAB HRMS calcd for C₃₁H₄₆N₅O₄Si₂ [M + H]⁺ 608.3083, found 608.3070.

2',3',5'-Tri-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(quinolin-8-yl)inosine (8c).

As described for the synthesis of 3'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)-2'-deoxyinosine, this quinolinyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)inosine (**5b**) (71.8 mg, 0.099 mmol), Cs₂CO₃ (65.2 mg, 0.200 mmol) and 8-hydroxyquinoline (16.0 mg, 0.110 mmol) in dry DME (1.0 mL) at 85 °C for 1 h. Chromatographic purification (SiO₂,

elution with 50% EtOAc in hexanes) afforded 52.9 mg (72% yield) of the title compound as a white foam. *R_f* (50% EtOAc in hexanes) = 0.58. ¹H NMR (500 MHz, CDCl₃): δ 8.74 (m, 1H, Ar-H), 8.48 (s, 1H, Ar-H), 8.33 (s, 1H, Ar-H), 8.20 (m, 1H, Ar-H), 7.79 (d, 1H, Ar-H, *J* = 8.3), 7.67–7.60

(m, 2H, Ar-H), 7.39 (dd, 1H, Ar-H, $J = 8.5, 4.2$), 6.13 (d, 1H, H-1', $J = 4.4$), 4.63 (t, 1H, H-2', $J = 4.4$), 4.37 (t, 1H, H-3', $J = 4.1$), 4.17 (m, 1H, H-4'), 4.07 (dd, 1H, H-5', $J = 11.2, 3.4$), 3.83 (dd, 1H, H-5', $J = 11.2, 2.4$), 0.97, 0.94, 0.84 (3s, 27H, *tert*-Bu), 0.17, 0.15, 0.12, 0.11, 0.0, -0.11 (6s, 18H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 161.0, 152.9, 151.9, 150.2, 149.1, 141.9, 141.5, 135.9, 129.7, 126.4, 125.9, 122.0, 121.6, 121.5, 88.7, 85.1, 76.2, 71.5, 62.3, 26.1, 25.9, 25.7, 18.6, 18.1, 17.9, -4.3, -4.7, -4.73, -4.9, -5.3, -5.4. FAB HRMS calcd for C₃₇H₆₀N₅O₅Si₃ [M + H]⁺ 738.3897, found 738.3885.

9-[3,5-Di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy- β -D-ribofuranosyl]-6-(morpholin-4-yl)purine (7k).

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol), Cs₂CO₃ (65.2 mg, 0.200 mmol) and dry DME (1.0 mL). Morpholine (17.5 μ L, 0.200 mmol) was added, the reaction mixture was flushed with N₂ and allowed to stir at room temperature for 1 h. The reaction mixture

was concentrated and the residue was dissolved in EtOAc. The mixture was washed with 10% aq citric acid, sat aq NaHCO₃ and brine. The organic layer was dried over Na₂SO₄ and evaporated to dryness. No additional purification was needed and 43 mg (78% yield) of the title compound was obtained. R_f (3% MeOH in CH₂Cl₂) = 0.18. ¹H NMR (500 MHz, CDCl₃): δ 8.34 (s, 1H, Ar-H), 8.02 (s, 1H, Ar-H), 6.46 (t, 1H, H-1', $J = 6.6$), 4.59 (m, 1H, H-3'), 4.30 (br s, 4H, 2CH₂), 4.01 (m, 1H, H-4'), 3.85–3.82 (m, 5H, H-5' and 2CH₂), 3.76 (dd, 1H, H-5', $J = 11.0, 3.2$), 2.59 (app quint, 1H, H-2', $J_{app} \sim 6.5$), 2.42 (ddd, 1H, H-2', $J = 13.2, 5.9, 3.9$), 0.91 (s, 18H, *tert*-Bu), 0.09, 0.08, 0.076 (3s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 153.9, 152.3, 150.6, 136.8, 120.4, 87.8, 84.1, 72.0, 67.0, 62.8, 45.6, 41.1, 26.0, 25.8, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₂₆H₄₈N₅O₄Si₂ [M + H]⁺ 550.3239, found 550.3222.

In the absence of Cs₂CO₃. Compound **7k** was also prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol) and morpholine (35.0 μ L, 0.400 mmol) in dry DME (1.0 mL) at room temperature over 1h. No additional purification was needed and 44.9 mg (82% yield) of the title compound was obtained.

9-[2,3,5-Tri-*O*-(*tert*-butyldimethylsilyl)- β -D-ribofuranosyl]-6-(morpholin-4-yl)purine (8d).^{3c}

As described for the synthesis of 9-[3,5-di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-ribofuranosyl]-6-(morpholin-4-yl)purine, this morpholino derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)inosine (**5b**) (71.8 mg, 0.099 mmol) and morpholine

(17.5 μL, 0.200 mmol) in the presence of Cs₂CO₃ (65.2 mg, 0.200 mmol) in dry DME (1.0 mL) at room temperature over 1 h. No additional purification was needed and 57.5 mg (85% yield) of the title compound was obtained. *R*_f (3% MeOH in CH₂Cl₂) = 0.68. ¹H NMR (500 MHz, CDCl₃): δ 8.33 (s, 1H, Ar-H), 8.03 (s, 1H, Ar-H), 6.03 (d, 1H, H-1', *J* = 5.4), 4.72 (t, 1H, H-2', *J* = 4.9), 4.32–4.29 (br m, 5H, H-3' and 2CH₂), 4.11 (m, 1H, H-4'), 4.02 (dd, 1H, H-5', *J* = 11.2, 4.4), 3.83 (br m, 4H, 2CH₂), 3.77 (dd, 1H, H-5', *J* = 11.2, 3.2), 0.95, 0.93, 0.80 (3s, 27H, *tert*-Bu), 0.124, 0.12, 0.104, 0.10, -0.05, -0.22 (6s, 18H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 153.9, 152.2, 151.0, 137.7, 120.5, 88.1, 85.4, 75.4, 72.1, 67.0, 62.6, 45.6, 26.1, 25.8, 25.7, 18.5, 18.1, 17.9, -4.4, -4.7, -5.0, -5.3, -5.4.

In the absence of Cs₂CO₃. Compound **8d** was also prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)inosine (**5b**) (72.8 mg, 0.100 mmol) and morpholine (35.0 μL, 0.400 mmol) in dry DME (1.0 mL) at room temperature over 1h. No additional purification was needed and 61.0 mg (90% yield) of the title compound was obtained.

9-(2-Deoxy-β-D-ribofuranosyl)-6-(morpholin-4-yl)purine (**9a**).⁹

As described for the synthesis of 9-[3,5-di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-ribofuranosyl]-6-(morpholin-4-yl)purine, this morpholino derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-2'-deoxyinosine (**5c**) (36.9 mg, 0.100 mmol) and morpholine (17.5 μL, 0.200 mmol) in the presence of Cs₂CO₃ (65.2 mg, 0.200 mmol) in dry DME (1.0 mL) at room temperature over 1 h. Chromatographic

purification (SiO₂, elution with 5% MeOH in CH₂Cl₂) afforded 16.6 mg (52% yield) of the title compound as a clear gum. *R*_f (10% MeOH in CH₂Cl₂) = 0.34. ¹H NMR (500 MHz, CDCl₃): δ 8.26 (s, 1H, Ar-H), 7.77 (s, 1H, Ar-H), 6.88 (br, 1H, OH, CD₃OD exchangeable), 6.30 (dd, 1H, H-1', *J* = 9.8, 5.4), 4.77 (d, 1H, H-3', *J* = 4.8), 4.30 (br, 4H, 2CH₂), 4.21 (br s, 1H, H-4'), 3.96 (dd, 1H, H-5', *J* = 12.7, 1.2), 3.81 (m, 4H, 2CH₂), 3.77 (br d, 1H, H-5', *J* ~ 13.2), 3.10 (ddd, 1H, H-2', *J* = 13.7, 9.3, 4.9), 2.65 (br, 1H, OH, CD₃OD exchangeable), 2.26 (dd, 1H, H-2', *J* = 13.7, 5.6). ¹³C

NMR (125 MHz, CDCl₃): δ 154.1, 151.6, 149.4, 138.3, 121.7, 89.7, 87.8, 73.6, 67.0, 63.5, 45.6, 40.5.

6-(Morpholin-4-yl)-9-(β -D-ribofuranosyl)purine (10a).⁹

As described for the synthesis of 9-[3,5-di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy- β -D-ribofuranosyl]-6-(morpholin-4-yl)purine, this morpholino derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)inosine (**5d**) (38.5 mg, 0.100 mmol), Cs₂CO₃ (65.2 mg, 0.200 mmol) and morpholine (17.5 μ L, 0.200 mmol) in dry DME (1.0 mL). Chromatographic purification (SiO₂, elution with 10% MeOH in CH₂Cl₂)

gave a slightly impure material (~77% yield). Recrystallization from MeOH afforded 19.6 mg (58% yield) of the title compound as a white solid. *R*_f (10% MeOH in CH₂Cl₂) = 0.32. ¹H NMR (500 MHz, DMSO-*d*₆): δ 8.47 (s, 1H, Ar-H), 8.30 (s, 1H, Ar-H), 5.96 (d, 1H, H-1', *J* = 5.9), 5.51 (d, 1H, OH, *J* = 6.4, D₂O exchangeable), 5.35 (dd, 1H, OH-5', *J* = 6.8, 4.9, D₂O exchangeable), 5.24 (d, 1H, OH, *J* = 4.9, D₂O exchangeable), 4.61 (m, 1H, H-2'), 4.25 (br, 4H, 2CH₂), 4.18 (m, 1H, H-3'), 4.00 (m, 1H, H-4'), 3.75 (m, 4H, 2CH₂), 3.71 (dt, 1H, H-5', *J* = 11.7, 4.4), 3.59 (ddd, 1H, H-5', *J* = 11.7, 6.8, 3.9). ¹³C NMR (125 MHz, DMSO-*d*₆): δ 154.0, 152.5, 151.0, 139.7, 120.4, 88.5, 86.4, 74.2, 71.2, 66.9, 62.2, 46.0.

***N*⁶-Benzyl-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyadenosine (7l).**

As described for the synthesis of 9-[3,5-di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy- β -D-ribofuranosyl]-6-(morpholin-4-yl)purine, this benzyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol) and benzylamine (21.8 μ L, 0.200 mmol) in the presence of Cs₂CO₃ (65.2 mg, 0.200 mmol) in dry DME

(1.0 mL) at room temperature over 6h. Chromatographic purification (SiO₂, elution with 20% EtOAc in hexanes followed by 50% EtOAc in hexanes) afforded 35.0 mg (84% yield) of the title compound as a clear gum. *R*_f (3% MeOH in CH₂Cl₂) = 0.07. ¹H NMR (500 MHz, CDCl₃): δ 8.41 (s, 1H, Ar-H), 8.11 (s, 1H, Ar-H), 7.38 (d, 2H, Ar-H, *J* = 7.5), 7.33 (t, 2H, Ar-H, *J* = 7.6), 7.28 (m, 1H, Ar-H), 6.45 (t, 1H, H-1', *J* = 6.6), 5.98 (br s, 1H, NH), 4.87 (br s, 2H, CH₂), 4.61 (m, 1H, H-3'), 4.01 (m, 1H, H-4'), 3.87 (dd, 1H, H-5', *J* = 5.9, 4.4), 3.77 (dd, 1H, H-5', *J* = 5.9, 4.4), 2.64 (app quint, 1H, H-2', *J* = 6.3), 2.43 (ddd, 1H, H-2', *J* = 13.2, 6.4, 3.9), 0.91 (s, 18H, *tert*-Bu), 0.10,

0.09, 0.08 (3s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 154.6, 153.1, 138.4, 128.7, 127.8, 127.5, 120.2, 87.8, 84.3, 71.9, 62.8, 41.2, 25.9, 25.8, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₂₉H₄₈N₅O₃Si₂ [M + H]⁺ 570.3290, found 570.3279. [The ¹⁵N labeled compound is known: Gao, X.; Jones, R. A. *J. Am. Chem. Soc.* **1987**, *109*, 1275-1278.]

In the absence of Cs₂CO₃. Compound **7l** was also prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol) and benzylamine (43.7 μL, 0.400 mmol) in dry DME (1.0 mL) at room temperature over 8 h. Chromatographic purification (SiO₂, elution with 20% EtOAc in hexanes) afforded 43.0 mg (75% yield) of the title compound.

***N*⁶-Benzyl-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)adenosine (8e).**

As described for the synthesis of 9-[3,5-di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-ribofuranosyl]-6-(morpholin-4-yl)purine, this benzyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)inosine (**5b**) (71.8 mg, 0.099 mmol) and benzylamine (21.8 μL, 0.200 mmol) in the presence of Cs₂CO₃ (65.2 mg, 0.200 mmol) in dry DME (1.0 mL) at room temperature over 7 h. Chromatographic purification (SiO₂, elution with 3% EtOAc in hexanes followed by 20% EtOAc in hexanes) afforded 61.0 mg (87% yield) of the title compound as a clear gum. *R_f* (20% EtOAc in hexanes) = 0.39. ¹H NMR (500 MHz, CDCl₃): δ 8.40 (s, 1H, Ar-H), 8.09 (s, 1H, Ar-H), 7.38 (d, 2H, Ar-H, *J* = 7.3), 7.34 (t, 2H, Ar-H, *J* ~ 7.3), 7.28 (m, 1H, Ar-H), 6.02 (d, 1H, H-1', *J* = 5.4), 5.95 (br s, 1H, NH), 4.86 (br s, 2H, CH₂), 4.70 (t, 1H, H-2', *J* = 4.9), 4.32 (t, 1H, H-3', *J* = 3.9), 4.12 (m, 1H, H-4'), 4.03 (dd, 1H, H-5', *J* = 11.2, 4.1), 3.78 (dd, 1H, H-5', *J* = 11.2, 2.9), 0.95, 0.93, 0.80 (3s, 27H, *tert*-Bu), 0.13, 0.12, 0.11, 0.10, -0.04, -0.22 (6s, 18H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 154.7, 153.0, 149.4, 139.1, 138.6, 128.6, 127.7, 127.4, 120.4, 88.4, 85.4, 75.6, 72.1, 62.6, 44.8, 26.0, 25.8, 25.7, 18.4, 18.0, 17.8, -4.4, -4.7, -5.1, -5.4. [Refs: (a) Aritomo, K.; Wada, T.; Sekine, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1837-1844. (b) Barends, J.; Van der Linden, J. B.; Van Delft, F. L.; Koomen, G.-J. *Nucleosides & Nucleotides* **1999**, *18*, 2121-2126. (c) Wanner, M. J.; Deghati, P. Y. F.; Rodenko, B.; Koomen, G. J. *Pure and Applied Chem.* **2000**, *72*, 1705-1708.]

In the absence of Cs₂CO₃. Compound **8e** was also prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)inosine (**5b**) (72.8 mg, 0.100 mmol) and

benzylamine (43.7 μ L, 0.400 mmol) in dry DME (1.0 mL) at room temperature over 9 h. Chromatographic purification (SiO_2 , elution with 3% acetone in hexanes) afforded 58.4 mg (83% yield) of the title compound.

9-[3,5-Di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy- β -D-ribofuranosyl]-6-(imidazol-1-yl)purine (7m).^{3d}

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-2',3'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol), Cs_2CO_3 (65.2 mg, 0.200 mmol) and imidazole (13.6 mg, 0.200 mmol). Dry DME (1.0 mL) was added and the reaction mixture was flushed with N_2 and allowed to stir at 85 $^\circ\text{C}$ for 4 h. The reaction mixture was

concentrated and the residue was dissolved in EtOAc. The mixture was washed with water, dried over Na_2SO_4 , and evaporated to dryness. Chromatographic purification (SiO_2 , elution with 50% EtOAc in hexanes) afforded 32.0 mg (60% yield) of the title compound as a clear gum. R_f (20% EtOAc in hexanes) = 0.07. ^1H NMR (500 MHz, CDCl_3): δ 9.19 (s, 1H, Ar-H), 8.77 (s, 1H, Ar-H), 8.48 (s, 1H, Ar-H), 8.40 (s, 1H, Ar-H), 7.25 (s, 1H, Ar-H), 6.56 (t, 1H, H-1', $J = 6.3$), 4.64 (m, 1H, H-3'), 4.06 (m, 1H, H-4'), 3.90 (dd, 1H, H-5', $J = 11.2, 3.9$), 3.80 (dd, 1H, H-5', $J = 11.2, 2.9$), 2.65 (app quint, 1H, H-2', $J_{\text{app}} \sim 6.3$), 2.51 (m, 1H, H-2'), 0.92, 0.915 (2s, 18H, *tert*-Bu), 0.11, 0.10 (2s, 12H, SiCH_3). ^{13}C NMR (125 MHz, CDCl_3): δ 153.0, 152.1, 145.6, 143.0, 137.7, 130.6, 122.9, 117.3, 88.1, 84.7, 71.7, 62.6, 41.5, 25.9, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5.

***S*⁶-Benzyl-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxythioinosine (7n).**

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)-2'-deoxyinosine, this thio benzyl derivative was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5b**) (59.8 mg, 0.100 mmol) and benzylmercaptan (23.5 μ L, 0.200 mmol) in the presence of Cs_2CO_3 (65.2 mg,

0.200 mmol) in dry DME (1.0 mL) at room temperature over 1 h. Chromatographic purification (SiO_2 , elution with CH_2Cl_2 followed by 20% EtOAc in hexanes) afforded 50.1 mg (85% yield) of the title compound as a clear, yellowish gum. R_f (20% EtOAc in hexanes) = 0.40. ^1H NMR (500 MHz, CDCl_3): δ 8.73 (s, 1H, Ar-H), 8.27 (s, 1H, Ar-H), 7.47 (d, 2H, Ar-H, $J = 7.6$), 7.31–7.22 (m,

3H, Ar-H), 6.49 (t, 1H, H-1', $J = 6.4$), 4.67 (AB_{quartet}, 2H, CH₂, $J = 13.6$), 4.62 (m, 1H, H-3'), 4.03 (m, 1H, H-4'), 3.87 (dd, 1H, H-5', $J = 11.3, 4.3$), 3.77 (dd, 1H, H-5', $J = 11.3, 3.2$), 2.65 (m, 1H, H-2'), 2.44 (ddd, 1H, H-2', $J = 13.1, 6.1, 3.7$), 0.92, 0.91, 0.90 (3s, 18H, *tert*-Bu), 0.11, 0.08, 0.079 (3s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 160.6, 151.7, 148.1, 141.2, 137.5, 131.7, 129.1, 128.5, 127.2, 88.0, 84.5, 72.0, 62.8, 41.3, 32.8, 26.0, 25.8, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₂₉H₄₇N₄O₃SSi₂ [M + H]⁺ 587.2902, found 587.2906.

S⁶-Benzyl-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)thioinosine (8f).

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)inosine (**5b**) (72.8 mg, 0.100 mmol), Cs₂CO₃ (65.2 mg, 0.200 mmol) and benzylmercaptan (23.5 μ L, 0.200 mmol). Dry DME (1.0 mL) was added and the reaction mixture was allowed to stir at room temperature for 7 h and then concentrated. Chromatographic purification (SiO₂, elution with 5% EtOAc in hexanes followed by 20% EtOAc in hexanes) afforded 66.5 mg (93% yield) of the title compound as a clear gum. R_f (20% EtOAc in hexanes) = 0.59. ¹H NMR (500 MHz, CDCl₃): δ 8.73 (s, 1H, Ar-H), 8.31 (s, 1H, Ar-H), 7.48–7.46 (m, 2H, Ar-H), 7.32–7.23 (m, 3H, Ar-H), 6.08 (d, 1H, H-1', $J = 5.2$), 4.67 (AB_{quartet}, 2H, CH₂, $J = 13.4$), 4.66 (m, 1H, H-2'), 4.33 (t, 1H, H-3', $J = 4.0$), 4.14 (m, 1H, H-4'), 4.02 (dd, 1H, H-5', $J = 11.3, 4.0$), 3.79 (dd, 1H, H-5', $J = 11.3, 2.9$), 0.95, 0.945, 0.94, 0.80 (4s, 27H, *tert*-Bu), 0.14, 0.13, 0.11, 0.105, -0.03, -0.23 (6s, 18H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 160.6, 151.8, 148.4, 141.7, 137.5, 131.7, 129.1, 128.5, 127.2, 88.4, 85.5, 75.9, 71.9, 62.5, 32.9, 26.1, 25.8, 25.7, 18.5, 18.1, 17.8, -4.4, -4.7, -4.71, -5.0, -5.4. FAB HRMS calcd for C₃₅H₆₁N₄O₄SSi₃ [M + H]⁺ 717.3716, found 717.3734.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl)-N⁶-(4-methylphenyl)-2'-deoxyadenosine (7o).^{3b}

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol) and *p*-toluidine (21.4 mg, 0.200 mmol). Ethanol (1.0 mL) and (*iso*-Pr)₂NEt (34.8 μ L, 0.200 mmol) were added, the reaction mixture was flushed with N₂ and allowed to stir at rt for 17 h and then at 60 °C for 24 h. The mixture was evaporated to dryness and chromatographic

purification (SiO₂, elution with CH₂Cl₂ followed by 20% EtOAc in hexanes) afforded 42.0 mg (74% yield) of the title compound as a clear gum. *R_f* (20% EtOAc in hexanes) = 0.27. ¹H NMR (500 MHz, CDCl₃): δ 8.50 (s, 1H, Ar-H), 8.17 (s, 1H, Ar-H), 7.66–7.64 (m, 2H, Ar-H), 7.62 (s, 1H, NH), 7.19 (d, 2H, Ar-H, *J* = 8.2), 6.48 (t, 1H, H-1', *J* = 6.4), 4.63 (m, 1H, H-3'), 4.03 (m, 1H, H-4'), 3.89 (dd, 1H, H-5', *J* = 11.3, 4.3), 3.79 (dd, 1H, H-5', *J* = 11.3, 3.2), 2.67 (app quint, 1H, H-2', *J* ~ 6.4), 2.46 (ddd, 1H, H-2', *J* = 13.1, 6.1, 4.0), 2.35 (s, 3H, Ar-CH₃), 0.93, 0.92 (2s, 18H, *tert*-Bu), 0.11, 0.10 (2s, 12H, SiCH₃).

2',3',5'-Tri-*O*-(*tert*-butyldimethylsilyl)-*N*⁶-(4-methylphenyl)adenosine (8g).

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-2',3',5'-tri-*O*-(*tert*-butyldimethylsilyl)inosine (**5b**) (72.8 mg, 0.100 mmol) and *p*-toluidine (21.4 mg, 0.200 mmol). Ethanol (1.0 mL) and (*iso*-Pr)₂NEt (34.8 μL, 0.200 mmol) were added, the reaction mixture was flushed with N₂ and allowed to stir at 60 °C for 16 h. The mixture was evaporated to dryness and chromatographic purification (SiO₂, elution with 20% EtOAc in hexanes) afforded 67.0 mg (96% yield) of the title compound as a clear, yellow gum. *R_f* (20% EtOAc in hexanes) = 0.55. ¹H NMR (500 MHz, CDCl₃): δ 8.49 (s, 1H, Ar-H), 8.19 (s, 1H, Ar-H), 7.67 (d, 2H, Ar-H, *J* = 9.0), 7.56 (s, 1H, NH), 7.19 (d, 2H, Ar-H, *J* = 8.2), 6.06 (d, 1H, H-1', *J* = 5.5), 4.72 (t, 1H, H-2', *J* = 4.9), 4.33 (m, 1H, H-3'), 4.14 (m, 1H, H-4'), 4.05 (dd, 1H, H-5', *J* = 11.3; 4.3), 3.80 (dd, 1H, H-5', *J* = 11.3, 3.1), 2.35 (s, 3H, Ar-CH₃), 0.97, 0.94, 0.80 (3s, 27H, *tert*-Bu), 0.16, 0.14, 0.12, 0.11, -0.04, -0.23 (6s, 18H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 152.8, 152.3, 149.4, 139.6, 136.0, 133.2, 129.5, 120.7, 120.6, 88.3, 85.6, 75.8, 72.1, 62.6, 26.1, 25.8, 25.7, 20.8, 18.5, 18.1, 17.9, -4.4, -4.7, -5.1, -5.4. [This compound was identical to that synthesized by Pd-catalyzed amination of the bromo nucleoside.]

*N*⁶-(4-Methylphenyl)-2'-deoxyadenosine (9b).

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-2'-deoxyinosine (**5c**) (40.0 mg, 0.108 mmol) and *p*-toluidine (23.3 mg, 0.217 mmol). Ethanol (1.0 mL) and (*iso*-Pr)₂NEt (37.8 μL, 0.208 mmol) were added, the reaction mixture was flushed with N₂ and allowed to stir at 60 °C for 24 h. The mixture was evaporated to dryness and chromatographic purification (SiO₂, elution

with 5% MeOH in CH₂Cl₂) afforded 25.7 mg (70% yield) of the title compound as a white solid. *R_f* (5% MeOH in CH₂Cl₂) = 0.18. ¹H NMR (500 MHz, DMSO-*d*₆): δ 9.83 (s, 1H, NH, D₂O exchangeable), 8.53 (s, 1H, Ar-H), 8.40 (s, 1H, Ar-H), 7.84 (d, 2H, Ar-H, *J* = 8.3), 7.17 (d, 2H, Ar-H, *J* = 8.3), 6.44 (dd, 1H, H-1', *J* = 7.5, 6.3), 5.35 (d, 1H, OH, *J* = 4.4, D₂O exchangeable), 5.16 (dd, 1H, OH, *J* = 6.2, 5.2, D₂O exchangeable), 4.47 (m, 1H, H-3'), 3.93 (m, 1H, H-4'), 3.68 (dt, 1H, H-5', *J* = 11.7, 4.9), 3.58 (ddd, 1H, H-5', *J* = 12.2, 6.4, 4.4), 2.80 (ddd, 1H, H-2', *J* = 13.2, 7.3, 5.9), 2.34 (ddd, 1H, H-2', *J* = 13.2, 6.4, 2.9), 2.32 (s, 3H, Ar-CH₃). [Refs: (a) Dai, Q.; Ran, C.; Harvey, R. G. *Tetrahedron* **2006**, 62, 1764-1771. (b) Ran, C.; Dai, Q.; Harvey, R. G. *J. Org. Chem.* **2005**, 70, 3724-3726.]

*N*⁶-(4-Methylphenyl)adenosine (10b).¹¹

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)inosine (**5d**) (40.0 mg, 0.104 mmol) and *p*-toluidine (22.2 mg, 0.208 mmol). Ethanol (1.0 mL) and (*iso*-Pr)₂NEt (37.8 μL, 0.208 mmol) were added, the reaction mixture was flushed with N₂ and allowed to stir at 60 °C for 24 h. A precipitate was formed, Et₂O was added and the precipitate was filtered, washed with Et₂O and dried. No additional purification was needed and 20.7 mg (56% yield) of the title compound was obtained as a white solid. *R_f* (10% MeOH in CH₂Cl₂) = 0.26. ¹H NMR (500 MHz, DMSO-*d*₆): δ 9.90 (s, 1H, NH, D₂O exchangeable), 8.56 (s, 1H, Ar-H), 8.41 (s, 1H, Ar-H), 7.84 (d, 2H, Ar-H, *J* = 8.3), 7.18 (d, 2H, Ar-H, *J* = 8.3), 5.99 (d, 1H, H-1', *J* = 6.4), 5.53 (d, 1H, OH, *J* = 6.4, D₂O exchangeable), 5.35 (dd, 1H, OH, *J* = 6.6, 4.6, D₂O exchangeable), 5.26 (d, 1H, OH, *J* = 4.4, D₂O exchangeable), 4.68 (m, 1H, H-2'), 4.21 (m, 1H, H-3'), 4.02 (m, 1H, H-4'), 3.73 (dt, 1H, H-5', *J* = 12.2, 4.4), 3.61 (m, 1H, H-5'), 2.32 (s, 3H, Ar-CH₃).

1,4-Di-[*O*⁶-(3',5'-di-*O*-*tert*-butyldimethylsilyl)-2'-deoxyinosinyl]phenyl ether (13).

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-(4-nitrophenyl)-2'-deoxyinosine, this dimeric product was prepared by a reaction between *O*⁶-(benzotriazol-1-yl)-2',3'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol), Cs₂CO₃ (65.2 mg, 0.200 mmol) and hydroquinone (4.4 mg, 0.040 mmol) in dry DME

(1.0 mL) at 85 °C over 3 h. Purification by preparative thin layer chromatography (SiO₂, elution with 50% EtOAc in hexanes) afforded 35.0 mg (68% yield) of the title compound as a clear, yellowish gum. R_f (3% MeOH in CH₂Cl₂) = 0.14. ¹H NMR (500 MHz, CDCl₃): δ 8.52 (s, 2H, Ar-H), 8.40 (s, 2H, Ar-H), 7.37 (s, 4H, Ar-H), 6.54 (t, 2H, H-1', J = 6.3), 4.65 (m, 2H, H-3'), 4.05 (m, 2H, H-4'), 3.91 (dd, 2H, H-5', J = 11.2, 3.9), 3.80 (dd, 2H, H-5', J = 11.2, 2.9), 2.66 (app quint, 2H, H-2', J_{app} ~ 6.3), 2.49 (ddd, 2H, H-2', J = 13.2, 5.9, 4.4), 0.93, 0.92 (2s, 36H, *tert*-Bu), 0.11 (s, 24H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 160.0, 152.6, 151.9, 149.7, 141.6, 122.7, 122.2, 88.1, 84.7, 71.9, 62.8, 41.4, 25.9, 25.7, 18.4, 17.9, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₅₀H₈₃N₈O₈Si₄ [M + H]⁺ 1035.5405, found 1035.5377.

3',5'-Di-*O*-(*tert*-butyldimethylsilyl) *O*⁶-[(*S*)-*N*-*boc*-L-tyrosine methyl ester]-2'-deoxyinosine conjugate (14).

In a clean, dry reaction vial equipped with a stirring bar were placed *O*⁶-(benzotriazol-1-yl)-2',3'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (59.8 mg, 0.100 mmol), NaHCO₃ (33.6 mg, 0.400 mmol) and (*S*)-*N*-*boc*-tyrosine methyl ester (32.5 mg, 0.110 mmol). Dry DME (1.0 mL) was added and the reaction mixture was allowed to stir at 85 °C for 24 h. The reaction mixture was diluted with EtOAc and washed with water, followed by brine.

Chromatographic purification (SiO₂, elution with 20% acetone in hexanes) afforded 31.0 mg (41% yield) of the title compound as a clear, yellowish gum. R_f (50% EtOAc in hexanes) = 0.53. ¹H NMR (500 MHz, CDCl₃): δ 8.49 (s, 1H, Ar-H), 8.40 (s, 1H, Ar-H), 7.21 (s, 4H, Ar-H), 6.53 (t, 1H, H-1', J = 6.4), 5.03 (br d, 1H, NH, J = 8.3, CD₃OD exchangeable), 4.65–4.60 (m, 2H, H-3', and CH), 4.04 (m, 1H, H-4'), 3.90 (dd, 1H, H-5', J = 11.2, 3.9), 3.80 (dd, 1H, H-5', J = 11.2, 2.9), 3.73 (s, 3H, OCH₃), 3.16 (dd, 1H, PhCH_A, J = 13.9, 5.6), 3.08 (dd, 1H, PhCH_B, J = 13.9, 6.6), 2.64 (app quint, 1H, H-2', J_{app} ~ 6.3), 2.48 (ddd, 1H, H-2', J = 13.2, 5.9, 3.9), 1.43 (s, 9H, *tert*-BuO), 0.93, 0.92 (2s, 18H, *tert*-BuSi), 0.11 (s, 12H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 172.3, 160.1, 155.1, 152.4, 151.9, 151.4, 141.7, 133.5, 130.4, 122.0, 121.9, 88.0, 84.6, 80.0, 71.74, 71.72, 62.7, 54.3, 52.3, 41.5, 37.8, 28.3, 26.0, 25.7, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₃₇H₆₀N₅O₈Si₂ [M + H]⁺ 758.3975, found 758.4008.

***N*¹-[6-[9-(3,5-di-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-β-D-ribofuranosyl)]purinyl]-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (15).**

As described for the synthesis of 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-*O*⁶-phenyl-2'-deoxyinosine, this unsymmetrical dimer was prepared by a reaction between *O*⁶-(benzotriazol-

1-yl)-3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**5a**) (20.0 mg, 0.033 mmol) and 3',5'-di-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyinosine (**1a**) (16.1 mg, 0.033 mmol) in the presence of K₃PO₄ (10.6 mg, 0.050 mmol) in dry toluene (0.33 mL) at 105 °C over 3 h. Chromatographic purification (SiO₂, elution with 20% EtOAc in hexanes followed by 5% MeOH in CH₂Cl₂) afforded 28.9 mg (92% yield) of the title compound as a clear, yellowish gum. *R*_f (3% MeOH in CH₂Cl₂) = 0.09. ¹H NMR (500 MHz, CDCl₃): δ 8.99 (s, 1H, Ar-H), 8.50 (s, 1H, Ar-H), 8.25 (s, 1H, Ar-H), 8.15 (s, 1H, Ar-H), 6.57 (t, 1H, H-1', *J* = 6.4), 6.43 (app t, 1H, H-1', *J*_{app} ~ 6.3), 4.65–4.60 (m, 2H, 2H-3'), 4.06 (m, 1H, H-4'), 4.03 (m, 1H, H-4'), 3.88 (dd, 1H, H-5', *J* = 11.2, 3.9), 3.86 (dd, 1H, H-5', *J* = 10.5, 4.2), 3.79 (dd, 2H, 2H-5', *J* = 11.2, 2.9), 2.68 (app quint, 1H, H-2', *J*_{app} ~ 6.3), 2.57 (app quint, 1H, H-2', *J*_{app} ~ 6.3), 2.50 (ddd, 1H, H-2', *J* = 13.2, 6.3, 3.9), 2.45 (ddd, 1H, H-2', *J* = 13.2, 5.9, 3.9), 0.93, 0.92, 0.918, 0.90 (4s, 36H, *tert*-Bu), 0.13, 0.12, 0.11, 0.10, 0.09, 0.08, (6s, 24H, SiCH₃). ¹³C NMR (125 MHz, CDCl₃): δ 155.1, 153.3, 152.2, 147.8, 146.9, 145.9, 144.7, 138.4, 129.9, 124.9, 88.2, 88.1, 84.9, 84.6, 71.9, 71.8, 62.7, 41.8, 41.4, 26.0, 25.8, 18.4, 18.0, -4.7, -4.8, -5.4, -5.5. FAB HRMS calcd for C₄₄H₇₉N₈O₇Si₄ [M + H]⁺ 943.5143, found 943.5159.