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SYNTHESIS OF 8,1'-*ETHENO* AND 8,2'-*ETHANO* BRIDGED GUANOSINE DERIVATIVES USING RADICAL CYCLIZATION

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Abstract — Conformationally constrained nucleosides can be readily generated by radical cyclization reactions. The radical cyclization of two guanosine derivatives containing a 2,2'-dibromovinyl group or a iodovinyl group tethered at the C8 position is described, respectively. The cyclization of the guanosine derivative with the 2,2'-dibromovinyl group initiated by tributyltin hydride formed an anomeric spiro nucleoside with an 8,1'-*etheno* bridge as the major cyclization product. In contrast, the conversion of guanosine and 2'-deoxyguanosine derivatives carrying the iodovinyl group provided 8,2'-*ethano* bridged nucleosides as the major products.

Dedicated to Prof. Dr. Albert Eschenmoser on the occasion of his 85th birthday.

INTRODUCTION

The scaffold and conformational preferences of a radical precursor often are decisive for the cyclization mechanism. In order to obtain conformationally restrained nucleosides, *Kittaka et al.* studied the anomeric radical generation of nucleosides by means of 1,5-radical translocation.[1] The subsequent radical cyclization yields uridine spiro nucleosides that are locked in *syn*-conformation. The respective guanosine spiro nucleosides, not available so far, may serve as valuable tools for inducing a left-handed Z-DNA double helix as Z-DNA requires guanosine nucleotides in *syn*-conformation.[2] Therefore, our interest in 8,1'-*etheno* bridged guanosine spiro nucleosides is derived from conformationally constrained Z-DNA

[a] Both authors contributed equally to this work and should be considered as joint first authors.

based on nucleotides that are fixed in the *syn*-conformation. The nucleotides in *syn*-conformation are required in every other position of Z-DNA. Since they are less favored due to sterical strain, *syn*-nucleotides and the left-handed Z-DNA double strand tend to rearrange to the relaxed *anti*-conformation and the right-handed DNA double helices.[2,3] The synthesis of two different guanosine and 2'-deoxyguanosine radical precursors with a 2,2'-dibromovinyl group **1** and a iodovinyl group **2a** and **2b** tethered at the C8 position is described (Figure 1). The subsequent radical cyclization turned out to be sensitive to the precursor: providing spiro cyclization at the anomeric center is provided as well as annelated six-membered ring formation.

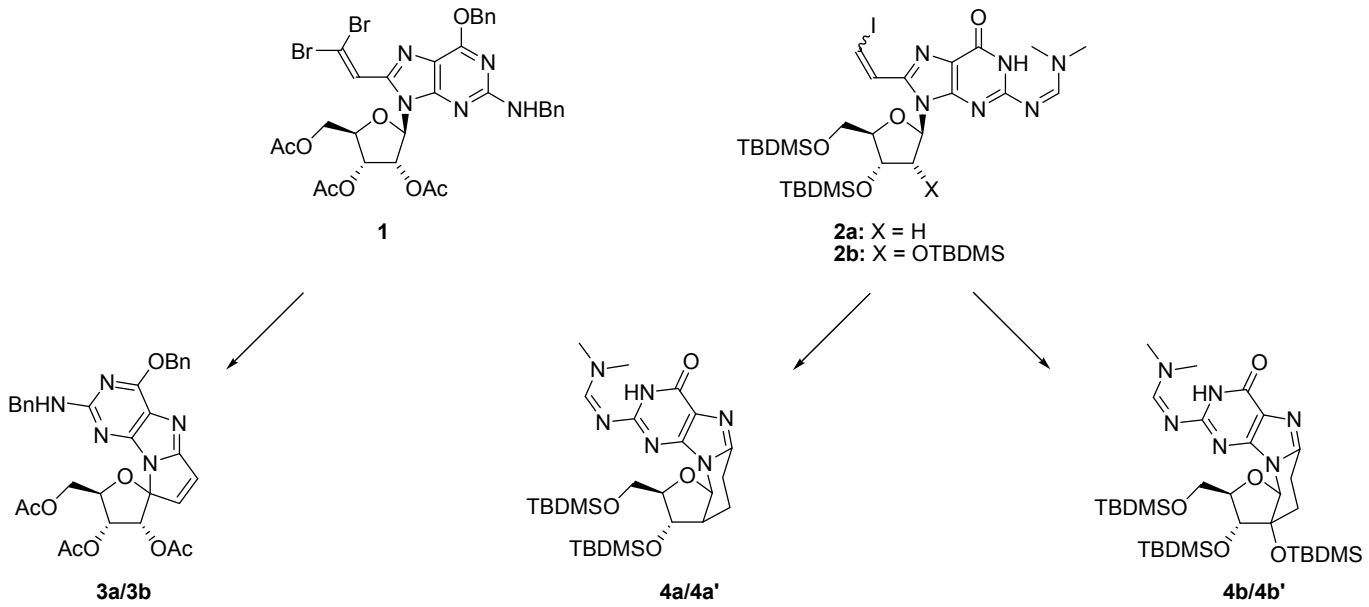


Figure 1. Guanosine derivatives with the 2,2'-dibromovinyl group **1**, the iodovinyl group **2a** and **2b** and the cyclization products **3a/3b**, **4a/4a'** and **4b/4b'**

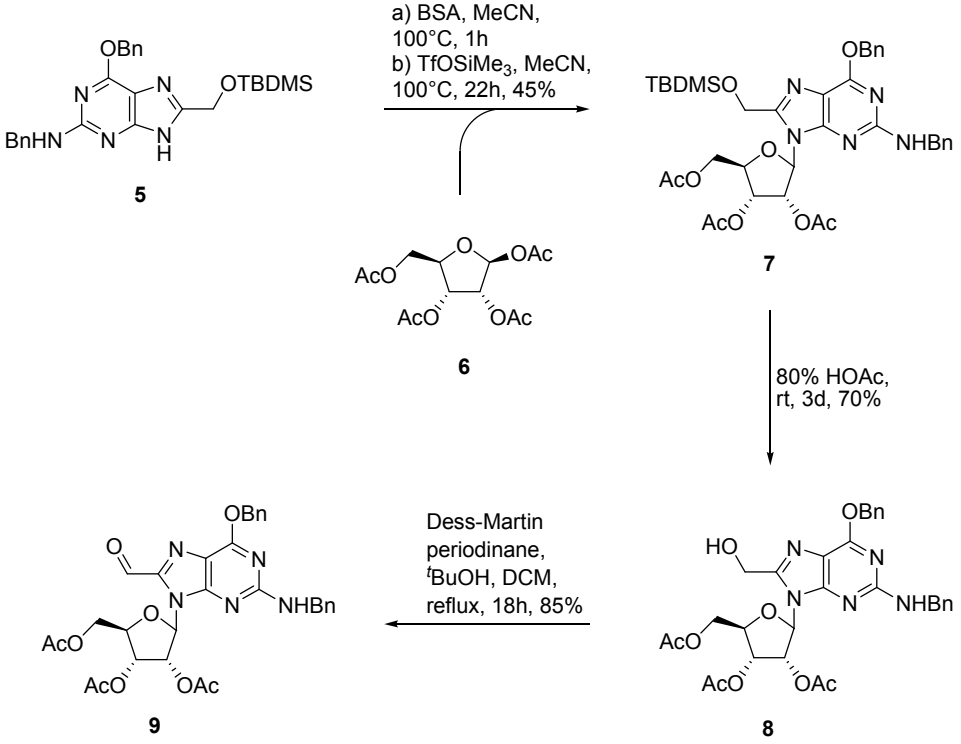
The radical cyclization of the guanosine derivative with the 2,2'-dibromovinyl group formed an anomeric spiro nucleoside **3a** with the 8,1'-*etheno* bridge as the major cyclized product. In contrast, under identical conditions the radical cyclization of the 2'-deoxyguanosine **2a** and guanosine **2b** with the iodovinyl group generated the 8,2'-*ethano* bridged nucleosides **4a/4a'** and **4b/4b'** as the major cyclization products.

RESULTS AND DISCUSSION

Synthesis and subsequent radical cyclization of two guanosine radical precursors are described employing two different protecting group and radical precursor strategies. The potential of the two radical precursors **1** and **2a/2b** regarding cyclization reaction differs with respect to the influence of the protecting groups on the ribosyl conformation. In addition, the C8-vinyl group contains one or two halogens leading to

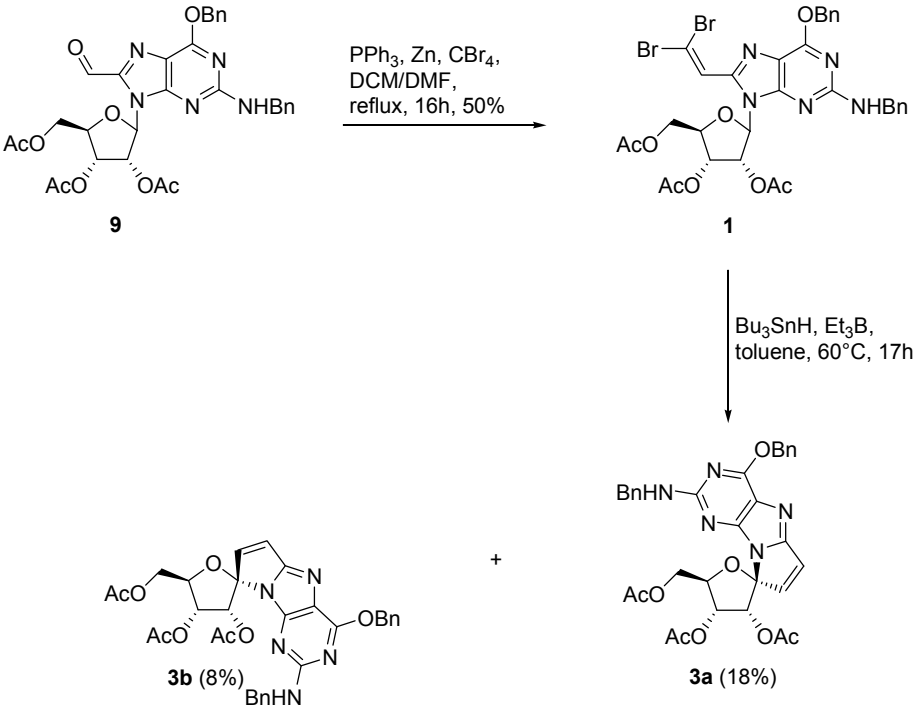
differences in the radical addition reactivity and the formation of the final product keeping the double bond or leading to an saturated cyclization product.

Nucleoside **9** was synthesized by means of a nucleosidation protocol (Scheme 1). The C8 substituted guanine derivative **5** was prepared using a method described by *Pfleiderer et al.* and later by *Vasella et al*.[4,5] Preparation of the protected and C8 alkylated guanine was achieved in a four step synthesis starting from commercially available 6-chloro-2,2-diaminopyrimidine. Partial benzylation, nitrosation at position 5, acylation of the remaining free exocyclic amino group and subsequent PPh_3 mediated ring closure yielded compound **5**. A *Silyl-Hilbert-Johnsen* nucleosidation in the variant of *Vorbrüggen* was employed to connect the modified guanine **5** with fully acylated ribofuranose **6**.[6,7] As a result of the neighboring group effect only the β-isomer **7** was formed. The TBDMS group of compound **7** was removed using aqueous acetic acid; the acetyl groups proved to be not stable when employing the standard TBAF deprotection protocol. The oxidation of the resulting primary alcohol **8** under *Dess-Martin* conditions yielded compound **9**.[8,9]



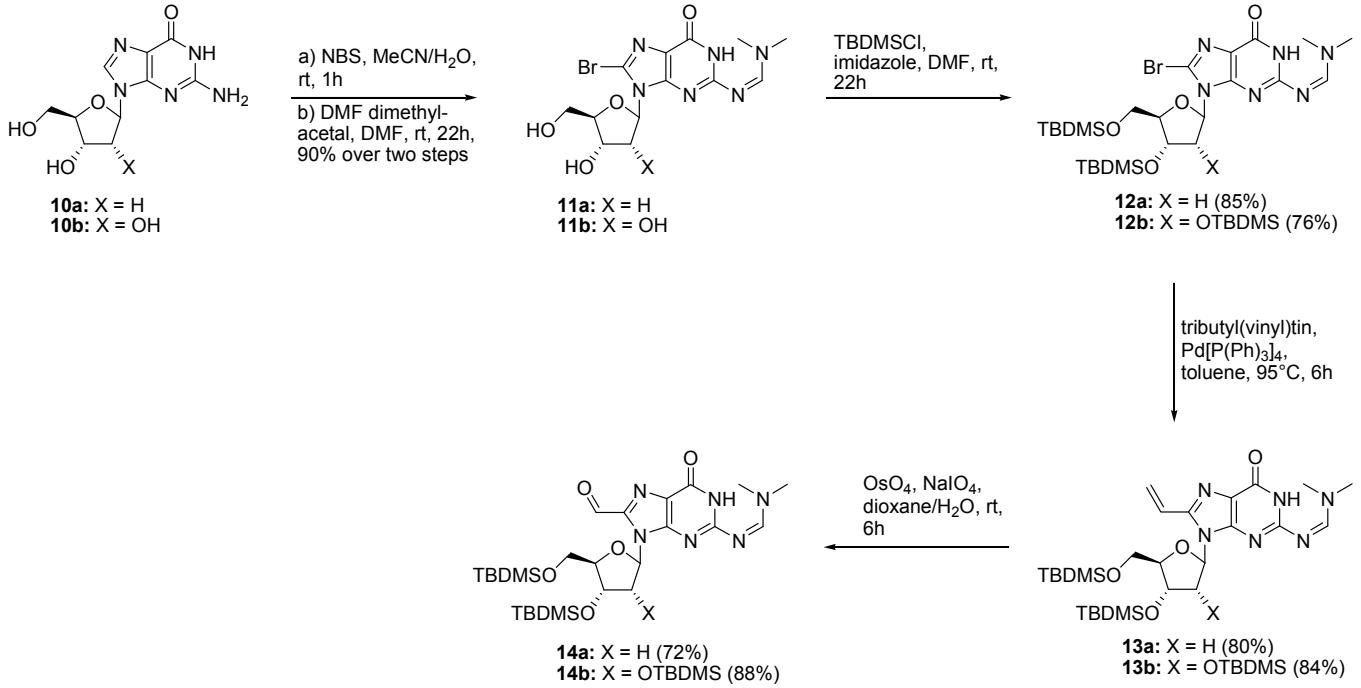
Scheme 1. Synthesis of the C8-formyl functionalized guanosine **9**

The guanosine derivative with the 2,2'-dibromovinyl group **1** was synthesized by means of *Corey-Fuchs* method.[10] The following radical cyclization was provided with Bu_3SnH and AIBN. Nevertheless, the best yields for the cyclization were obtained with triethylborane and tributyltin hydride in toluene. The reagents were added over five hours by using a syringe pump and the two anomers **3a** and **3b** were isolated in an α:β ratio of 1:2.25 (Scheme 2).



Scheme 2. Synthesis of the spiro nucleosides **3a** and **3b** by radical cyclization

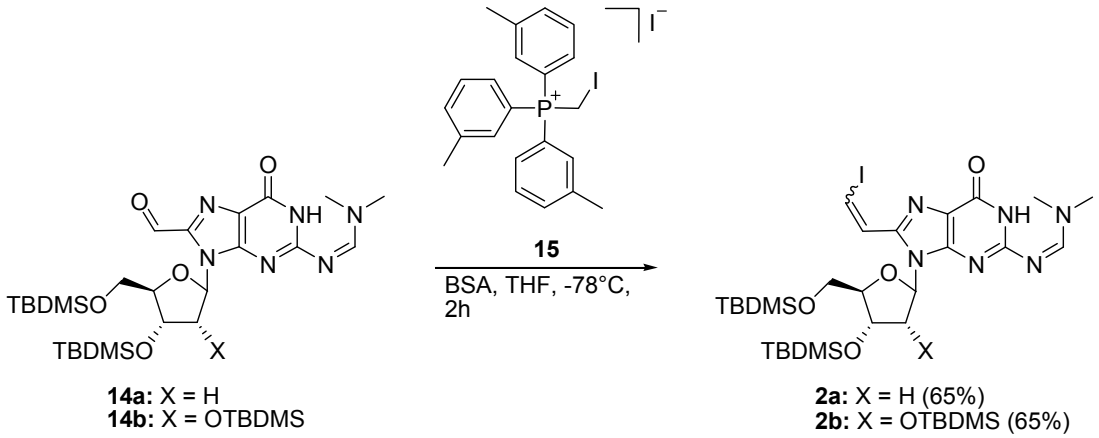
The radical cyclization reaction is initiated by bromine atom abstraction from the 2,2'-dibromovinyl group by a stannyl radical likely to be followed by formation of the stabilized anomeric radical by 1,5-radical translocation. The less favorable 5-*endo-trig* cyclization followed by β-bromine elimination are reasonable steps to yield the two diastereomeric spiro nucleosides **3a** and **3b**.



Scheme 3. Synthesis of the C8-formyl functionalized 2'-deoxyguanosine **14a** and guanosine **14b**

Synthesis of C8-iodovinyl-2'-deoxyguanosine and C8-iodovinyl-guanosine derivatives **2a** and **2b** started from the commercially available nucleotides **10a** and **10b** employing standard protocols for the first three steps.[11,12,13] NBS bromination and subsequent protection of the exocyclic amino group with *N,N'*-dimethylformamide dimethylacetal gave compounds **11a** and **11b** in good yields. The completely protected guanosine derivatives **12a** and **12b** were obtained by TBDMS protection of the hydroxy groups. A modified *Stille* protocol was employed to generate the C8-vinyl substituted compounds **13a** and **13b**.[14] The introduced vinyl groups were subsequently cleaved under *Lemieux-Johnson* conditions to yield aldehydes **14a** and **14b** (Scheme 3).[15]

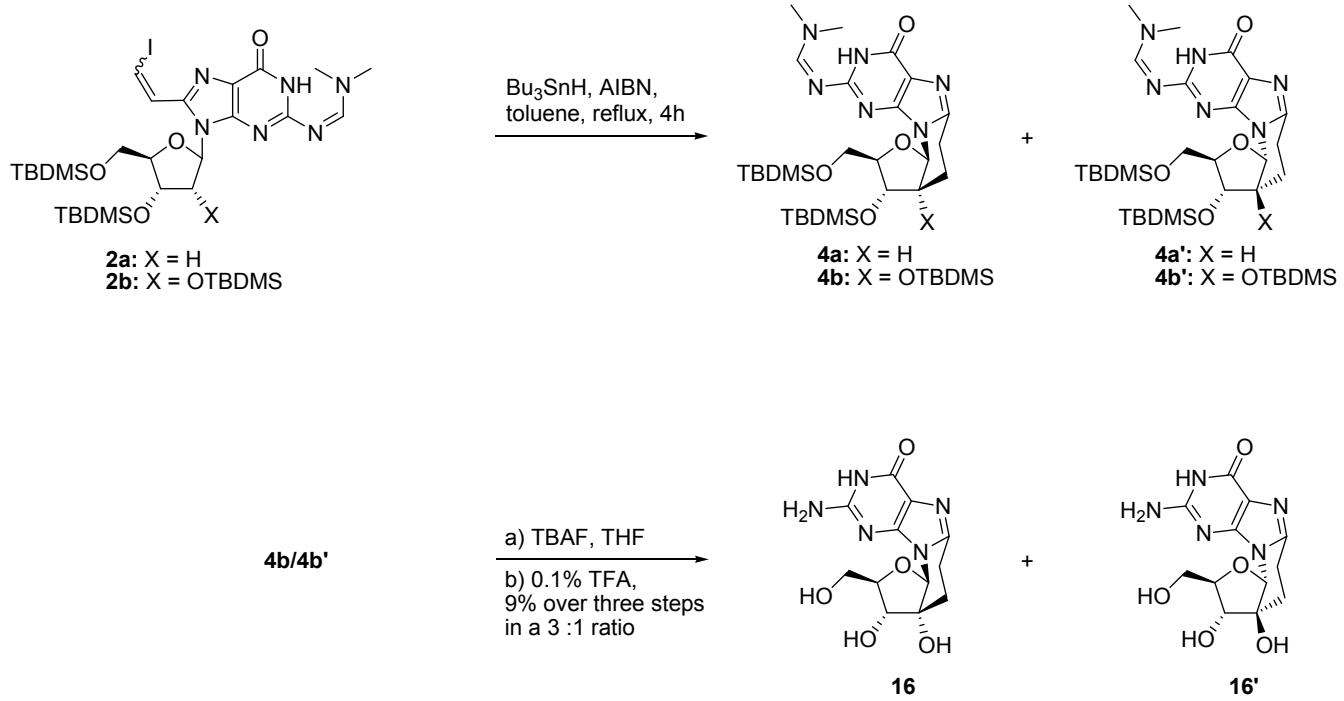
The vinyliodide at C8 was introduced by *Wittig* reaction using (iodomethyl)-tri(*m*-toloyl)phosphonium iodide **15** as *Wittig* reagent rather than the standard triphenylphosphonium salt in order to avoid the laborious removal of triphenylphosphine oxide. The cyclization precursors **2a** and **2b** were obtained in a 1:1 *E*/*Z* ratio in the case of **2a** and as pure *Z* compound in the case of **2b**, respectively (Scheme 4).



Scheme 4. Synthesis of the guanosine derivatives **2a** and **2b** by a modified *Wittig* protocol

Radical cyclization of vinyliodides **2a** and **2b** initiated by tributyltin hydride and AIBN in toluene provided two diastereomeric guanosine derivatives (Scheme 5). Separation of the mixture of diastereomers **4a** and **4a'** or **4b** and **4b'** by flash chromatography was not successful. For further characterization all protecting groups were removed from the ribo nucleoside **4b**/**4b'** enabling purification by RP-HPLC. Next to the two 8,2'-*ethano* bridged guanosine nucleosides provided in a 3:1 mixture of diastereomers two side products were identified as an anomeric 1.5:1 mixture of 8-vinyl guanosines. The ratio of the two 8-vinyl guanosine diastereomers was determined by comparing the respective ^{1}H-NMR signals of the vinyl protons at 6.73 and 6.95 ppm. The isolated products allow concluding on the mechanism of radical transfer. It is quite likely that the anomeric radical is generated by vinyl halogen

abstraction followed by 1,5-radical translocation as observed for the 2,2'-dibromovinyl guanosine precursor **1**. In contrast to the anomeric radical generated from nucleotide **1**, the respective radical generated from vinyl iodide **2** does not undergo a 5-*endo*-trig cyclization. It either is reduced by tributyltin hydride to the vinylguanosine side products or the 8,2'-*ethano* bridged guanosine derivatives **4** are generated involving a C1'-C2' radical shift followed by 6-*endo*-trig radical cyclization as a favored process according to the *Baldwin* rules.[16] The loss of stereogenic information at the anomeric center is a clear indication for an intermediate anomeric radical.



Scheme 5. Radical cyclization of nucleosides **2a** and **2b** to the annelated guanosine derivatives and subsequent deprotection to yield the 8,2'-*ethano* bridged guanosines **16**/**16'**

CONCLUSION

Radical cyclization was investigated with respect to ring formation between the anomeric center of guanosine and the C8 position of the nucleobase. Starting from vinyl bromides or vinyl iodides the vinyl radical was translocated to the anomeric center. The succeeding radical stabilization differed with respect to the nucleotide protection scheme and most likely to the respective nucleotide conformation. Whereas the guanosine derivative with 2,2'-dibromovinyl group tethered at the C8 position provided the anomeric spiro nucleoside with the 8,1'-*etheno* bridge as the major cyclized product, in case of the iodovinyl functionalized guanosine 6-*endo*-trig radical cyclization yielded the 8,2'-*ethano* bridged derivative as the major cyclization product.

EXPERIMENTAL

General remarks: All reagents were of analytical grade and used without further purification. Solvents were of the highest grade available. Dry solvents were stored over molecular sieves (4Å). Glass equipment utilized for reactions under inert atmosphere was flame dried before use. ^{1}H- and ^{13}C-NMR spectra were recorded with a *Varian* Unity 300 spectrometer, a *Varian* Inova 500 spectrometer or a *Varian* Inova 600 spectrometer. Chemical shifts are quoted in parts per million (ppm) downfield of TMS. Abbreviations for multiplicities are: s, singulet; d, doublet; t, triplet; q, quartet; m, multiplet; m_c centered multiplet; br, broad. Coupling constants are given in Hz. Mass spectrometry was carried out using *Finnigan* LQC or TSQ 7000 instruments. HRMS spectra were measured with a *Bruker* APEX-Q IV 7T instrument. Flash chromatography was performed using *Merck* silica gel 60. Thin layer chromatography (TLC) was carried out using *Merck* aluminium sheets of silica gel 60 F_{254}. Visualization was accomplished with UV light (254 nm). HPLC analysis was performed using a *Pharmacia* Äkta basic instrument (pump type P-900, variable wavelength detector) with a linear gradient of A (MilliQ-H_2O) to B (acetonitrile/MilliQ-H_2O 8:2). Compounds were analyzed using a *YMC* J'sphere column ODS-H80, RP-C18, 250 x 4.6 mm, 4 µm, 80 Å, with a flow rate of 1 mL per min. Preparative purification was performed using a *YMC* J'sphere column ODS-H80, RP-C18, 250 × 20 mm, 4 µm, 80 Å, with a flow rate of 10 mL per min.

2',3',5'-Tri-*O*-acetyl-N^2,O^6-dibenzyl-8-(*tert*-butyldimethylsiloxymethyl)guanosine (7).

A solution of 2-(*N*-benzyl)amino-6-benzyloxy-8-(*tert*-butyldimethylsiloxymethyl)purine (**5**) (8.50 g, 17.9 mmol) and sodium bis(trimethylsilyl)amide (10.9 g, 13.1 mL, 53.7 mmol) in dry MeCN (300 mL) was stirred at 100 °C for 1 h. Afterwards, the solvent was removed under reduced pressure and a solution of 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (**6**) (6.83 g, 21.4 mmol) and $TfOSiMe_3$ (5.17 g, 4.21 mL, 23.3 mmol) in dry MeCN (40.0 mL) was added to the residue and the reaction mixture was stirred at 100 °C for 22 h. The solution was poured into a saturated aqueous $NaHCO_3$ solution (100 mL), the layers were separated and the organic layer was washed with aqueous $NaHCO_3$ solution (2 x 100 mL) and aqueous NaCl solution (2 x 100 mL). The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: EtOAc/pentane 1:3) to furnish **7** as a light-yellow oil. Yield: 5.96 g, 8.12 mmol, 45%. **^{1}H-NMR** (300 MHz, $C_2D_2Cl_4$, 100 °C): δ 0.15 (s, 3 H, SiMe), 0.18 (s, 3 H, SiMe), 0.97 (s, 9 H, ^{t}Bu), 1.96 (s, 3 H, Me), 2.09 (s, 3 H, Me), 2.11 (s, 3 H, Me), 4.19 (m_c, 1 H, H5'), 4.31 (m_c, 1 H, H4'), 4.39 (m_c, 1 H, H5'), 4.71 (d, $^{3}J_{H,H}$ = 5.9 Hz, 2 H, NCH_2), 4.88 (d, $^{2}J_{H,H}$ = 12.8 Hz, 1 H, CH_2OSi), 4.95 (d, $^{2}J_{H,H}$ = 13.3 Hz, 1 H, CH_2OSi), 5.40 (t, $^{3}J_{H,H}$ = 6.2 Hz, 1 H, NH), 5.55 (s, 2 H, OCH_2), 5.98 (dd, $^{3}J_{H,H}$ = 6.3 Hz, 5.5 Hz, 1 H, H3'), 6.35 (d, $^{3}J_{H,H}$ = 4.2 Hz, 1 H, β-H1'), 6.50 (dd, $^{3}J_{H,H}$ = 5.6 Hz, 4.1 Hz, 1 H, H2'), 7.29-7.51 (m, 10 H, Ph) ppm.

^{13}C-NMR (75 MHz, $C_2D_2Cl_4$, 100 °C): δ -5.7 (SiMe), 17.8 ($\underline{C}(CH_3)_3$), 20.0, 20.1 (CH_3), 25.5 ($C(\underline{C}H_3)_3$), 45.9 (NCH_2), 59.3 (COSiMe), 63.1 (C5'), 67.9 (OCH_2Ph), 70.7 (C3'), 72.1 (C2'), 78.8 (C4'), 86.7 (C1'), 114.2 (C5), 126.8, 127.2, 127.9, 128.2, 128.3 (Ph), 136.4, 139.2 (Ph_{ipso}), 148.4, 154.9, 158.6, 160.6 (C2, C4, C6, C8), 168.9, 169.9 (CO) ppm. **ESI-MS** m/z (rel. %): 734.4 (10) $[M + H]^+$, 756.4 (55) $[M + Na]^+$, 1489.1 (100) $[2M + Na]^+$. **HRMS** (ESI): 734.32157 (calcd. for $C_{37}H_{48}N_5O_9Si$: 734.32157).

2',3',5'-Tri-*O*-acetyl-N^2,O^6-dibenzyl-8-hydroxymethylguanosine (8).

A solution of **7** (4.29 g, 5.85 mmol) in acetic acid (80%, 150 mL) was stirred at rt for 3 d. The solvent was removed under reduced pressure and the residue was co-evaporated with toluene (3 x 10 mL). The crude product was purified by flash chromatography (eluent: EtOAc/pentane 3:1) to furnish **8** as a colorless oil. Yield: 2.53 g, 4.09 mmol, 70%. **^{1}H-NMR** (300 MHz, $C_2D_2Cl_4$, 100 °C): δ 1.97 (s, 3 H, Me), 2.09 (s, 3 H, Me), 2.12 (s, 3 H, Me), 2.58 (s_{br}, 1 H, OH), 4.17-4.25 (m, 1 H, H5'), 4.33-4.42 (m, 2 H, H4', H5'), 4.71 (d, $^3J_{H,H}$ = 5.9 Hz, 2 H, NCH_2), 4.85 (s, 2 H, CH_2OH), 5.43 (t, $^3J_{H,H}$ = 6.0 Hz, 1 H, NH), 5.56 (s, 2 H, OCH_2), 5.90 (dd, $^3J_{H,H}$ = 6.3 Hz, $^3J_{H,H}$ = 6.4 Hz, 1 H, H3'), 6.07 (d, $^3J_{H,H}$ = 4.0 Hz, 1 H, β-H1'), 6.33 (dd, $^3J_{H,H}$ = 5.8 Hz, 3.7 Hz, 1 H, H2'), 7.29-7.50 (m, 10 H, Ph) ppm. **^{13}C-NMR** (75 MHz, $C_2D_2Cl_4$, 100 °C): δ 19.9, 20.1 (CH_3), 45.9 (NCH_2), 57.9 (CH_2OH), 62.9 (C5'), 67.9 (OCH_2Ph), 70.4 (C3'), 72.4 (C2'), 79.2 (C4'), 86.9 (C1'), 114.0 (C5), 126.9, 127.2, 127.4, 128.3 (Ph), 136.3, 139.2 (Ph_{ipso}), 148.7, 154.9, 158.7, 160.6 (C2, C4, C6, C8), 169.0, 169.1, 169.9 (CO) ppm. **ESI-MS** m/z (rel. %): 620.0 (100) $[M + H]^+$, 642.2 (11) $[M + Na]^+$, 1238.8 (65) $[2M + H]^+$, 1261.0 (18) $[2M + Na]^+$. **HRMS** (ESI): 620.23569 (calcd. for $C_{31}H_{34}N_5O_9$: 620.23510).

2',3',5'-Tri-*O*-acetyl-N^2,O^6-dibenzyl-8-formylguanosine (9).

A solution of **8** (2.15 g, 5.08 mmol), *Dess-Martin* periodinane (377 mg, 483 µL, 5.08 mmol) and *tert*-butyl alcohol in dry DCM (100 mL) was stirred under reflux for 18 h. The reaction mixture was poured into a mixture of saturated aqueous $Na_2S_2O_4$ solution (30.0 mL) and saturated aqueous $NaHCO_3$ solution (30.0 mL). The layers were separated and the organic layer was washed with aqueous $Na_2S_2O_4$ solution (2 x 50.0 mL) and aqueous $NaHCO_3$ solution (2 x 50.0 mL). The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: EtOAc/pentane 1:2) to furnish **9** as a colorless oil. Yield: 2.42 g, 3.92 mmol, 85%. **^{1}H-NMR** (300 MHz, $C_2D_2Cl_4$, 100 °C): δ 1.97 (s, 3 H, Me), 2.09 (s, 3 H, Me), 2.12 (s, 3 H, Me), 4.20 (m_c, 1 H, H5'), 4.33-4.44 (m, 2 H, H4', H5'), 4.72 (dd, $^2J_{H,H}$ = 15.6 Hz, $^3J_{H,H}$ = 6.1 Hz, 1 H, NCH_2), 4.78 (dd, $^2J_{H,H}$ = 15.3 Hz, $^3J_{H,H}$ = 6.0 Hz, 1 H, NCH_2), 5.60 (s, 2 H, OCH_2), 5.76 (dd, $^3J_{H,H}$ = 5.9 Hz, 5.9 Hz, 1 H, NH), 5.91 (dd, $^3J_{H,H}$ = 6.3 Hz, 6.3 Hz, 1 H, H3'), 6.26 (dd, $^3J_{H,H}$ = 6.3 Hz, 3.6 Hz, 1 H, H2'), 6.94 (d, $^3J_{H,H}$ = 3.6 Hz, 1 H, β-H1'), 7.29-7.51 (m, 10 H, Ph), 9.84 (s, 1 H, CHO) ppm. **^{13}C-NMR** (75 MHz,

$C_2D_2Cl_4$, 100 °C): δ 20.0, 20.1 (CH_3), 46.0 (NCH_2), 63.0 (C5'), 68.5 (OCH_2Ph), 70.4 (C3'), 72.4 (C2'), 79.0 (C4'), 87.0 (C1'), 117.1 (C5), 127.2, 128.2, 128.3, 128.5 (Ph), 135.6, 138.3 (Ph_{ipso}), 142.6, 154.9, 160.4, 162.7 (C2, C4, C6, C8), 169.1, 170.0 (CO), 182.6 (CHO) ppm. **ESI-MS** m/z (rel. %): 640.4 (100) $[M + Na]^+$. **HRMS** (ESI): 618.21919 (calcd. for $C_{31}H_{32}N_5O_9$: 618.21945).

2',3',5'-Tri-*O*-acetyl-N^2,O^6-dibenzyl-8-(2,2'-dibromovinyl)guanosine (1).

A suspension of CBr_4 (4.74 g, 14.3 mmol) and zinc powder (933 mg, 14.3 mmol) in dry DCM (43.0 mL) was treated with PPh_3 (3.74 g, 14.3 mmol) in dry DCM (12.6 mL) over 1 h. The resulting reaction mixture was stirred at rt for 3 h. Afterwards, a solution of **9** (2.20 g, 3.56 mmol) in a mixture of dry DCM and dry DMF (1:1, 38.0 mL) was added over 1 h and the solution was stirred under reflux over night. The reaction mixture was poured into a mixture of saturated aqueous $Na_2S_2O_4$ solution (45.0 mL) and DCM (150 mL). The layers were separated and the organic layer was washed with aqueous $Na_2S_2O_4$ solution (1 x 90.0 mL) and aqueous NaCl solution (1 x 90.0 mL). The organic layer was filtrated over silica gel, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: EtOAc/pentane 1:2) to furnish **1** as a light yellow-oil. Yield: 1.37 g, 1.77 mmol, 50%. **^{1}H-NMR** (300 MHz, $C_2D_2Cl_4$, 100 °C): δ 1.96 (s, 3 H, Me), 2.10 (s, 3 H, Me), 2.12 (s, 3 H, Me), 4.07-4.23 (m, 1 H, H5'), 4.32-4.40 (m, 2 H, H4', H5'), 4.71 (d, $^3J_{H,H}$ = 4.9 Hz, 2 H, NCH_2), 5.49 (t, $^3J_{H,H}$ = 5.5 Hz, 1 H, NH), 5.59 (s, 2 H, OCH_2), 5.86 (d, $^3J_{H,H}$ = 4.1 Hz, 1 H, β-H1'), 5.92 (dd, $^3J_{H,H}$ = 5.9 Hz, 5.9 Hz, 1 H, H3'), 6.36 (dd, $^3J_{H,H}$ = 5.9 Hz, 3.8 Hz, 1 H, H2'), 7.29-7.51 (m, 11 H, Ph, CBr_2CH) ppm. **^{13}C-NMR** (75 MHz, $C_2D_2Cl_4$, 100 °C): δ 20.0, 20.1 (CH_3), 45.9 (NCH_2), 62.8 (C5'), 68.2 (OCH_2Ph), 70.4 (C3'), 72.3 (C2'), 79.3 (C4'), 86.9 (C1'), 99.4 (CBr_2), 115.4 (C5), 124.6 ($CBr_2\underline{C}H$), 126.9, 127.1, 127.8, 128.0, 128.2, 128.3, 128.4 (Ph), 136.3, 139.1 (Ph_{ipso}), 143.2, 153.8, 158.9, 161.0 (C2, C4, C6, C8), 168.8, 168.9, 169.8 (CO) ppm. **ESI-MS** m/z (rel. %): 796 (94) $[M + Na]^+$, 1568.5 (100) $[2M + Na]^+$. **HRMS** (ESI): 772.06130 (calcd. for $C_{32}H_{32}Br_2N_5O_8$: 772.06121).

2',3',5'-Tri-*O*-acetyl-N^2,O^6-dibenzyl-8,1'-*etheno*-β-guanosine (3a) and 2',3',5'-Tri-*O*-acetyl-N^2,O^6-dibenzyl-8,1'-*etheno*-α-guanosine (3b).

A solution of Bu_3SnH (119 mg, 109 µL, 0.41 mmol) and Et_3B (137 µL, 0.14 mmol, 1M in hexane) in dry toluene (5.00 mL) was added to a stirred solution of **1** (211 mg, 0.27 mmol) in dry toluene (15.0 mL) at 60 °C over 17 h by using a syringe pump. The solvent was removed under reduced pressure and the residue was solved in aqueous KF solution (10%, 15.0 mL) and stirred at rt for 0.5 h. Et_2O (30.0 mL) was added, the layers were separated and the aqueous layer was washed with Et_2O (2 x 20.0 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (eluent: Et_2O/pentane 9:1) and afterwards by

preparative thin layer chromatography (eluent: DCM/MeOH 97:3) to furnish **3a** (30.0 mg, 0.04 mmol, 18%) and **3b** (12.0 mg, 0.02 mmol, 8%) as colorless oil. **β-anomer 3a: ^{1}H-NMR** (300 MHz, $CDCl_3$, rt): δ 1.99 (s, 3 H, Me), 2.06 (s, 3 H, Me), 2.10 (s, 3 H, Me), 4.28-4.45 (m, 2 H, H5'), 4.46-4.53 (m, 1 H, H4'), 4.65 (m, 2 H, NCH_2), 5.44 (m, 1 H, NH), 5.48 (s, 2 H, OCH_2), 5.67 (d, $^3J_{H,H}$ = 4.5 Hz, 1 H, β-H2'), 6.50 (m_c, 1 H, H3'), 6.61 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, H10), 6.67 (d, $^3J_{H,H}$ = 6.1 Hz, 1 H, H9), 7.25-7.46 (m, 10 H, Ph) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$, rt): δ 20.4, 20.5, 20.7 (CH_3), 45.9 (NCH_2), 64.0 (C5'), 67.7 (OCH_2Ph), 71.3 (C3'), 75.2 (C2'), 79.6 (C4'), 96.8 (C1'), 119.4 (C5), 124.4 (C9), 127.0, 127.1, 127.3, 127.8, 128.1, 128.3, 128.5 (Ph), 136.4 ($\underline{C}CH_2O$), 139.1 ($\underline{C}CH_2N$), 140.2 (C10), 152.5 (C4), 154.1 (C8), 158.7 (C2), 160.7 (C6), 168.8, 169.2, 117.5 (CO) ppm. **ESI-MS** m/z (rel. %): 614.1 (4) $[M + H]^+$, 636.2 (100) $[M + Na]^+$, 1248.9 (96) $[2M + Na]^+$. **HRMS** (ESI): 614.22470 (calcd. for $C_{32}H_{32}N_5O_8$: 614.22454). **α-anomer 3b: ^{1}H-NMR** (300 MHz, $CDCl_3$, rt): δ 1.69 (s, 3 H, Me), 2.03 (s, 3 H, Me), 2.06 (s, 3 H, Me), 4.14 (dd, $^2J_{H,H}$ = 13.2 Hz, $^3J_{H,H}$ = 3.7 Hz, 1 H, H5'), 4.36 (dd, $^2J_{H,H}$ = 12.7 Hz, $^3J_{H,H}$ = 3.2 Hz, 1 H, H5'), 4.66 (m, 1 H, NH), 4.67 (m, 2 H, NCH_2), 5.18 (dd, $^3J_{H,H}$ = 7.8 Hz, 7.8 Hz, 1 H, H3'), 5.23-5.27 (m, 1 H, H4'), 5.50 (s, 2 H, OCH_2), 5.58 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H, α-H2'), 6.56 (d, $^3J_{H,H}$ = 6.1 Hz, 1 H, H10), 6.64 (d, $^3J_{H,H}$ = 6.1 Hz, 1 H, H9), 7.25-7.46 (m, 10 H, Ph) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$, rt): δ 20.0, 20.3, 20.7 (CH_3), 45.7 (NCH_2), 62.2 (C5'), 68.0 (OCH_2Ph), 69.4 (C3'), 70.5 (C2'), 79.7 (C4'), 97.5 (C1'), 119.3 (C5), 123.6 (C9), 126.9, 127.1, 127.2, 127.5, 127.9, 128.1, 128.3, 128.5 (Ph), 136.4 ($\underline{C}CH_2O$), 139.5 ($\underline{C}CH_2N$), 141.9 (C10), 153.1 (C4), 155.1 (C8), 158.4 (C2), 160.9 (C6), 168.7, 169.8, 1170.5 (CO) ppm. **ESI-MS** m/z (rel. %): 614.1 (4) $[M + H]^+$, 636.2 (100) $[M + Na]^+$, 1248.9 (96) $[2M + Na]^+$. **HRMS** (ESI): 614.22470 (calcd. for $C_{32}H_{32}N_5O_8$: 614.22454).

N^2-[(Dimethylamino)methylen]-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-8-vinyl-2'-deoxyguanosine (13a).

A solution of **12a** (5.50 g, 8.74 mmol), $Pd[P(Ph)_3]_4$ (505 mg, 0.44 mmol) and tributyl(vinyl)tin (4.16 g, 13.1 mmol) in dry toluene (100 mL) was degassed and stirred at 95 °C under an argon atmosphere for 12 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: DCM/acetone 4:1) to furnish **13a** as a yellow foam. Yield: 4.03 g, 6.78 mmol, 80%. **^{1}H-NMR** (600 MHz, $CDCl_3$, rt): δ 0.01-0.10 (m, 12 H, $SiCH_3$), 0.85-0.91 (m, 18 H, $Si(CH_3)_3$), 2.13 (ddd, $^2J_{H,H}$ = 13.2 Hz, $^3J_{H,H}$ = 6.3, $^3J_{H,H}$ = 2.7 Hz, 1 H, H2'), 2.65 (ddd, $^2J_{H,H}$ = 13.2 Hz, $^3J_{H,H}$ = 8.6 Hz, $^3J_{H,H}$ = 7.1 Hz, 1 H, H2'), 3.07 (s, 3 H, NCH_3), 3.14 (s, 3 H, NCH_3), 3.76-3.88 (m, 3 H, H4', H5'), 4.54-4.59 (m, 1 H, H3'), 5.43 (dd, $^3J_{H,H}$ = 11.0, $^2J_{H,H}$ = 1.5 Hz, 1 H, vinyl-H), 6.41 (dd, $^3J_{H,H}$ = 8.6, $^3J_{H,H}$ = 6.3 Hz, 1 H, H1'), 6.45 (dd, $^3J_{H,H}$ = 17.2 Hz, $^2J_{H,H}$ = 1.5 Hz, 1 H, vinyl-H), 6.92 (dd, $^3J_{H,H}$ = 17.2 Hz, $^3J_{H,H}$ = 11.0 Hz, 1 H, vinyl-H), 8.54 (s, 1 H, N=CH), 9.34 (s_{br}, 1 H, NH) ppm. **^{13}C-NMR** (75 MHz, DMSO-D_6, 35 °C): δ -5.6 ($SiCH_3$), -5.6 ($SiCH_3$), -5.0 ($SiCH_3$), -4.7 ($SiCH_3$), 17.5 ($\underline{C}(CH_3)_3$), 17.9

($\underline{C}(CH_3)_3$), 25.6 ($C(\underline{C}H_3)_3$), 25.6 ($C(\underline{C}H_3)_3$), 34.6 (NCH_3), 38.8 (C2'), 40.6 (NCH_3), 62.1 (C5'), 71.2 (C3'), 82.1 (C1'), 86.2 (C4'), 119.1 (C=C or C8), 119.5 (C=C or C8), 124.5 (C=C), 144.8 (Ar-C), 150.0 (Ar-C), 156.6 (Ar-C), 157.0 (Ar-C or N=CH), 157.5 (Ar-C or N=CH) ppm. **ESI-MS** m/z (rel. %): 677.4 (100) $[M + H]^+$, 599.3 (95) $[M + Na]^+$. **HRMS** (ESI): 577.3347 (calcd. for $C_{27}H_{49}N_6O_5Si_2$: 577.3348).

N^2-[(Dimethylamino)methylen]-2',3',5'-tris-*O*-(*tert*-butyldimethylsilyl)-8-vinylguanosine (13b).

A solution of **12b** (8.00 g, 10.5 mmol), $Pd[P(Ph)_3]_4$ (607 mg, 0.53 mmol) and tributyl(vinyl)tin (5.00 g, 15.7 mmol) in dry toluene (120 mL) was degassed and stirred at 95 °C under an argon atmosphere for 12 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: DCM/acetone 4:1) to furnish **13b** as a yellow foam. Yield: 6.26 g, 8.82 mmol, 84%. **^{1}H-NMR** (300 MHz, $CDCl_3$, rt): δ -0.47 (s, 3 H, $SiCH_3$), -0.14 (s, 3 H, $SiCH_3$), 0.08-0.11 (m, 12 H, $SiCH_3$), 0.67 (s, 9 H, $C(CH_3)_3$), 0.92 (s, 9 H, $C(CH_3)_3$), 0.94 (s, 9 H, $C(CH_3)_3$), 3.08 (s, 3 H, NCH_3), 3.12 (s, 3 H, NCH_3), 3.79 (dd, $^3J_{H,H}$ = 11.3 Hz, $^3J_{H,H}$ = 3.1 Hz, 1 H, H5'), 3.87 (dd, $^3J_{H,H}$ = 11.3 Hz, $^3J_{H,H}$ = 3.5 Hz, 1 H, H5'), 4.00-4.03 (m, 1 H, H4'), 4.18 (dd, $^3J_{H,H}$ = 4.8 Hz, $^3J_{H,H}$ = 1.2 Hz, 1 H, H3'), 4.46 (dd, $^3J_{H,H}$ = 8.1 Hz, $^3J_{H,H}$ = 4.8 Hz, 1 H, H2'), 5.44 (dd, $^3J_{H,H}$ = 11.0 Hz, $^3J_{H,H}$ = 1.8 Hz, 1 H, vinyl-H), 6.16 (d, $^3J_{H,H}$ = 8.1 Hz, 1 H, H1'), 6.52 (dd, $^3J_{H,H}$ = 17.1 Hz, $^3J_{H,H}$ = 1.7 Hz, 1 H, vinyl-H), 7.02 (dd, $^3J_{H,H}$ = 17.2 Hz, $^3J_{H,H}$ = 11.0 Hz, 1 H, vinyl-H), 8.55 (s, 1 H, N=CH), 8.61 (s_{br}, 1 H, NH) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$, rt): δ -5.4 ($SiCH_3$), -4.5 ($SiCH_3$), -4.3 ($SiCH_3$), 17.7 ($\underline{C}(CH_3)_3$), 18.1 ($\underline{C}(CH_3)_3$), 18.5 ($\underline{C}(CH_3)_3$), 25.6 ($C(\underline{C}H_3)_3$), 25.9 ($C(\underline{C}H_3)_3$), 26.0 ($C(\underline{C}H_3)_3$), 35.2 (NCH_3), 41.3 (NCH_3), 63.1 (C5'), 72.0 (C3'), 74.1 (C2'), 85.6 (C1'), 86.2 (C4'), 119.7 (C5), 121.3 (C=C), 124.6 (C=C), 146.6 (Ar-C), 151.5 (Ar-C), 155.9 (Ar-C or N=CH), 157.7 (Ar-C or N=CH), 157.9 (Ar-C or N=CH) ppm. **ESI-MS** m/z (rel. %): 729.8 (47) $[M + Na]^+$, 1435.8 (100) $[2M + Na]^+$. **HRMS** (ESI): 707.41599 (calcd. for $C_{33}H_{63}N_6O_5Si_3$: 707.41623).

N^2-[(Dimethylamino)methylen]-8-formyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyguanosine (14a).

A solution of **13a** (3.90 g, 6.77 mmol) in a mixture of dioxane and H_2O (2:1, 100 mL) was treated with $NaIO_4$ (2.90 g, 13.5 mmol) and OsO_4 (500 µL, 2.0 wt% in ^{t}BuOH). The resulting solution was stirred at rt for 3 h. The reaction mixture was poured into a mixture of EtOAc (150 mL) and saturated aqueous Na_2SO_3 solution (150 mL) and the organic layer was washed with saturated aqueous NaCl solution (3 x 100 mL). The organic layer was dried over Na_2SO_4, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: DCM/MeOH 95:5) to furnish **14a** as a light-yellow foam. Yield: 2.84 g, 4.90 mmol, 72%. **^{1}H-NMR** (300 MHz, DMSO-D_6, 35 °C): δ -0.05 (s, 3 H, $SiCH_3$), -0.03 (s, 3 H, $SiCH_3$), 0.10 (s, 6 H, $SiCH_3$), 0.81 (s, 9 H, $C(CH_3)_3$), 0.90 (s, 9 H, $C(CH_3)_3$), 2.09-2.19 (m, 1 H, H2'), 3.07 (s, 3 H, NCH_3), 3.18 (s, 3 H, NCH_3), 3.25-3.35 (m, 1 H, H2'), 3.62-3.82 (m,

3 H, H4', H5'), 4.62 (ddd, $^3J_{H,H}$ = 6.2 Hz, $^3J_{H,H}$ = 3.1 Hz, $^3J_{H,H}$ = 3.1 Hz, 1 H, H3'), 6.96 (dd, $^3J_{H,H}$ = 7.1 Hz, $^3J_{H,H}$ = 7.1 Hz, 1 H, H1'), 8.54 (s, 1 H, N=CH), 9.69 (s, 1 H, COH), 11.68 (s_{br}, 1 H, NH) ppm. **^{13}C-NMR** (75 MHz, DMSO-D_6, 35 °C): δ -5.7 ($SiCH_3$), -5.6 ($SiCH_3$), -5.0 ($SiCH_3$), -4.8 ($SiCH_3$), 17.5 ($\underline{C}(CH_3)_3$), 17.8 ($\underline{C}(CH_3)_3$), 25.5 ($C(\underline{C}H_3)_3$), 25.6 ($C(\underline{C}H_3)_3$), 34.8 (NCH_3), 37.2 (C2'), 40.9 (NCH_3), 62.9 (C5'), 72.5 (C3'), 83.4 (C1'), 87.1 (C4'), 122.2 (C8), 142.2 (Ar-C), 152.0 (Ar-C), 157.6 (Ar-C), 158.3 (Ar-C or N=CH), 158.9 (Ar-C or N=CH), 182.5 (CO) ppm. **ESI-MS** m/z (rel. %): 601.3 (30) $[M + Na]^+$, 633.4 (100) $[M + Na + MeOH]^+$. **HRMS** (ESI): 601.2962 (calcd. for $C_{26}H_{46}N_6O_5Si_2Na$: 601.2960).

***N*^{2}-[(Dimethylamino)methylen]-8-formyl-2',3',5'-tris-*O*-(*tert*-butyldimethylsilyl)guanosine (14b).**

A solution of **13b** (5.20 g, 7.36 mmol) in a mixture of dioxane and H_2O (2:1, 120 mL) was treated with $NaIO_4$ (3.15 g, 14.7 mmol) and OsO_4 (500 µL, 2.0 wt% in ^{t}BuOH). The resulting solution was stirred at rt for 3 h. The reaction mixture was poured into a mixture of EtOAc (150 mL) and saturated aqueous Na_2SO_3 solution (150 mL) and the organic layer was washed with saturated aqueous NaCl solution (3 x 100 mL). The organic layer was dried over Na_2SO_4, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: DCM/MeOH 9:1) to furnish **14b** as a yellow foam. Yield: 4.58 g, 6.48 mmol, 88%. **^{1}H-NMR** (300 MHz, $CDCl_3$, rt): δ -0.05 (s, 3 H, $SiCH_3$), -0.41 (s, 3 H, $SiCH_3$), -0.12 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$), 0.05 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$), 0.13 (s, 3 H, $SiCH_3$), 0.70 (s, 9 H, $C(CH_3)_3$), 0.88 (s, 9 H, $C(CH_3)_3$), 0.95 (s, 9 H, $C(CH_3)_3$), 3.14 (s, 3 H, NCH_3), 3.18 (s, 3 H, NCH_3), 3.70 (dd, $^2J_{H,H}$ = 9.1 Hz, $^3J_{H,H}$ = 3.1 Hz, 1 H, H5'), 3.89-4.02 (m, 2 H, H4', H5'), 4.28 (dd, $^3J_{H,H}$ = 4.8 Hz, 1.1 Hz, 1 H, H3'), 5.03 (dd, $^3J_{H,H}$ = 7.4 Hz, 4.8 Hz, 1 H, H2'), 6.53 (d, $^3J_{H,H}$ = 7.4 Hz, 1 H, H1'), 8.61 (s, 1 H, N=CH), 8.96 (s_{br}, 1 H, NH), 9.80 (s, 1 H, CHO) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$, rt): δ -5.3 ($SiCH_3$), -5.1 ($SiCH_3$), -4.5 ($SiCH_3$), -4.3 ($SiCH_3$), -4.2 ($SiCH_3$), 17.9 ($\underline{C}(CH_3)_3$), 18.2 ($\underline{C}(CH_3)_3$), 18.5 ($\underline{C}(CH_3)_3$), 25.7 ($C(\underline{C}H_3)_3$), 26.0 ($C(\underline{C}H_3)_3$), 26.0 ($C(\underline{C}H_3)_3$), 35.6 (NCH_3), 51.7 (NCH_3), 63.1 (C5'), 72.6 (C2'), 72.7 (C3'), 85.8 (C4'), 86.7 (C1'), 122.3 (C5), 144.0 (Ar-C), 153.2 (Ar-C), 158.2 (Ar-C or N=CH), 158.3 (Ar-C or N=CH), 158.5 (Ar-C or N=CH), 181.9 (COH) ppm. **ESI-MS** m/z (rel. %): 707.4 (100) $[M - H]^-$. **HRMS** (ESI): 731.3794 (calcd. for $C_{32}H_{60}N_6O_6Si_3Na$: 731.3800).

***N*^{2}-[(Dimethylamino)methylen]-8-(2-iodo)vinyl-3',5'-bis-(*tert*-butyldimethylsilyl)-2'-deoxyguanosine (2a).**

A solution of **16** (1.98 g, 3.46 mmol) and sodium bis(trimethylsilyl)amide (3.50 mL, 3.50 mmol, 1M in THF) in dry THF (50.0 mL) was stirred at rt under an argon atmosphere for 0.5 h. The solution was cooled to -78 °C and a solution of **14a** (1.00 g, 1.73 mmol) in dry THF (10.0 mL) was added over 0.5 h. After additional 0.5 h the reaction was quenched by adding saturated aqueous NH_4Cl solution (10.0 mL) and the reaction mixture was poured into Et_2O (250 mL) and H_2O (250 mL). The layers were separated

and the organic layer was washed with saturated aqueous NaCl solution (3 x 150 mL). The organic layer was dried over Na_2SO_4, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: DCM/acetone 6:1) to furnish **2a** as a light-yellow foam. Yield: 790 mg, 1.13 mmol, 65%. **^{1}H-NMR** (300 MHz, $CDCl_3$, rt): δ 0.04-0.13 (m, 12 H, $SiCH_3$), 0.88-0.92 (m, 18 H, $C(CH_3)_3$), 2.12-2.23 (m, 1 H, H2'), 2.55-2.73 (m, 1 H, H2'), 3.09 (s, 3 H, NCH_3), 3.14-3.17 (m, 3 H, NCH_3), 3.68-3.98 (m, 3 H, H4', H5'), 4.50-4.58 (m, 1 H, H3'), 6.33-6.45 (m, 1 H, H1'), 7.00 (d, $^3J_{H,H}$ = 9.1 Hz, 0.5 H, *Z*-vinyl-H), 7.49 (d, $^3J_{H,H}$ = 14.7 Hz, 0.5 H, *E*-vinyl-H), 7.59-7.67 (m, 1 H, *E*-vinyl-H, *Z*-vinyl-H), 8.55 (s, 0.5 H, N=CH), 8.58 (s, 0.5 H, N=CH), 8.60 (s_{br}, 0.5 H, NH), 8.67 (s_{br}, 0.5H, NH) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$, rt): δ -5.3 ($SiCH_3$), -5.2 ($SiCH_3$), -5.1 ($SiCH_3$), -4.6 ($SiCH_3$), -4.5 ($SiCH_3$), 18.0 ($\underline{C}(CH_3)_3$), 18.0 ($\underline{C}(CH_3)_3$), 18.5 ($\underline{C}(CH_3)_3$), 18.5 ($\underline{C}(CH_3)_3$), 25.8 ($C(\underline{C}H_3)_3$), 25.8 ($C(\underline{C}H_3)_3$), 26.0 ($C(\underline{C}H_3)_3$), 26.1 ($C(\underline{C}H_3)_3$), 35.1 (NCH_3), 39.7 (C2'), 40.2 (C2'), 41.4 (NCH_3), 62.2 (C5'), 62.8 (C5'), 71.0 (C3'), 71.9 (C3'), 85.6 (C1'), 85.9 (C1'), 86.8 (C4'), 87.1 (C4'), 119.3 (C8), 119.7 (C8), 127.6 (vinyl-C), 127.6 (vinyl-C), 132.0 (vinyl-C), 144.4 (Ar-C), 145.6 (Ar-C), 145.8 (Ar-C), 150.6 (Ar-C), 150.9 (Ar-C), 156.2 (Ar-C), 156.4 (Ar-C), 157.8 (Ar-C or N=CH), 157.8 (Ar-C or N=CH), 158.3 (Ar-C or N=CH), 158.4 (Ar-C or N=CH) ppm. **ESI-MS** m/z (rel. %): 725.2 (100) $[M + Na]^+$. **HRMS** (ESI): 701.2168 (calcd. for $C_{27}H_{46}IN_6O_4Si_2$: 701.2169).

N^2-[(Dimethylamino)methylen]-8-(*Z*-2-iodo)vinyl-2',3',5'-tris-*O*-(*tert*-butyldimethylsilyl)guanosine (2b).

A solution of **16** (1.62 g, 2.83 mmol) and sodium bis(trimethylsilyl)amide (3.00 mL, 3.00 mmol, 1M in THF) in dry THF (40.0 mL) was stirred at rt under an argon atmosphere for 0.5 h. The solution was cooled to -78 °C and a solution of **14b** (1.00 g, 1.42 mmol) in dry THF (10.0 mL) was added over 0.5 h. After additional 0.5 h the reaction was quenched by adding saturated aqueous NH_4Cl solution (10.0 mL) and the reaction mixture was poured into Et_2O (250 mL) and H_2O (250 mL). The layers were separated and the organic layer was washed with saturated aqueous NaCl solution (3 x 150 mL). The organic layer was dried over Na_2SO_4, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: DCM/acetone 6:1) to furnish **2b** as a light-yellow foam. Yield: 764 mg, 0.92 mmol, 65%. **^{1}H-NMR** (300 MHz, $CDCl_3$, rt): δ -0.43 (s, 3 H, $SiCH_3$), -0.12 (s, 3 H, $SiCH_3$), 0.10 (s, 3 H, $SiCH_3$), 0.12 (s, 6 H, $SiCH_3$), 0.13 (s, 3 H, $SiCH_3$), 0.69 (s, 9 H, $C(CH_3)_3$), 0.91 (s, 9 H, $C(CH_3)_3$), 0.95 (s, 9 H, $C(CH_3)_3$), 3.08 (s, 3 H, NCH_3), 3.12 (s, 3 H, NCH_3), 3.78 (dd, $^2J_{H,H}$ = 10.8 Hz, $^3J_{H,H}$ = 6.8 Hz, 1 H, H5'), 3.86 (dd, $^2J_{H,H}$ = 10.8 Hz, $^3J_{H,H}$ = 4.2 Hz, 1 H, H5'), 4.00-4.05 (m, 1 H, H4'), 4.21 (dd, $^3J_{H,H}$ = 4.5 Hz, 1.6 Hz, 1 H, H3'), 4.44 (dd, $^3J_{H,H}$ = 7.5 Hz, 4.5 Hz, 1 H, H2'), 6.11 (d, $^3J_{H,H}$ = 7.5 Hz, 1 H, H1'), 7.51 (d, $^3J_{H,H}$ = 14.6 Hz, 1 H, vinyl-H), 7.65 (d, $^3J_{H,H}$ = 14.6 Hz, 1 H, vinyl-H), 8.54 (s, 1 H, N=CH), 8.57 (s_{br}, 1 H, NH) ppm. **^{13}C-NMR** (75 MHz, $CDCl_3$, rt): δ -5.5 ($SiCH_3$), -5.2 ($SiCH_3$), -4.6 ($SiCH_3$), -4.2

($SiCH_3$), 17.7 ($\underline{C}(CH_3)_3$), 18.0 ($\underline{C}(CH_3)_3$), 18.4 ($\underline{C}(CH_3)_3$), 25.5 ($C(\underline{C}H_3)_3$), 25.8 ($C(\underline{C}H_3)_3$), 26.1 ($C(\underline{C}H_3)_3$), 35.3 (NCH_3), 41.4 (NCH_3), 63.1 (C5'), 72.1 (C3'), 74.1 (C2'), 85.7 (C1' or C4'), 86.0 (C1' or C4'), 119.9 (C8), 128.4 (vinyl-C), 133.0 (vinyl-C), 145.8 (Ar-C), 151.3 (Ar-C), 156.3 (Ar-C), 157.9 (Ar-C or N=CH), 158.1 (Ar-C or N=CH) ppm. **ESI-MS** m/z (rel. %): 856.6 (100) $[M + Na]^+$. **HRMS** (ESI): 833.31272 (calcd. for $C_{33}H_{61}IN_6O_5Si_3$: 833.31287).

N^2-[(Dimethylamino)methylen]-8,2'-*ethano*-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxyguanosine (4a/4a').

A solution of Bu_3SnH (41.3 mg, 38.2 µL, 142 µmol) in dry toluene (5.00 mL) was added to a stirred, degassed solution of **2a** (50.0 mg, 71.0 µmol) and AIBN (catalytic) in dry toluene (10.0 mL) at 95 °C over 4 h by using a syringe pump. After additional 2 h the solvent was removed under reduced pressure and the residue was purified twice by flash chromatography (eluent: 1. DCM/acetone 3:1, 2. DCM/MeOH 94:6) to furnish **4a/4a'** as a light-yellow solid. Yield: 22.0 mg, 38.2 µmol, 54% (mixture of two diastereomers and traces of α,β-vinylguanosine). **ESI-MS** m/z (rel. %): 599.4 (100) $[M + Na]^+$, 1175.8 (25) $[2M + Na]^+$. **HRMS** (ESI): 599.3158 (calcd. for $C_{27}H_{48}N_6O_2Si_2Na$: 599.3168).

N^2-[(Dimethylamino)methylen]-8,2'-*ethano*-2',3',5'-tris-*O*-(*tert*-butyldimethylsilyl)guanosine (4b/4b').

A solution of Bu_3SnH (262 mg, 901 µmol) in dry toluene (25.00 mL) was added to a stirred, degassed solution of **2b** (750 mg, 901 µmol) and AIBN (catalytic) in dry toluene (100 mL) at 95 °C over 4 h by using a syringe pump. After additional 2 h the solvent was removed under reduced pressure and the residue was purified twice by flash chromatography (eluent: 1. DCM/acetone 3:1, 2. DCM/MeOH 94:6) to furnish **4b/4b'** as a light-yellow solid. Yield: 221 mg, 313 µmol, 35% (mixture of two diastereomers and traces of α,β-vinylguanosine). **ESI-MS** m/z (rel. %): 729.5 (100) $[M + Na]^+$, 1426.0 (36) $[2M + Na]^+$. **HRMS** (ESI): 729.3995 (calcd. for $C_{33}H_{62}N_6O_5Si_3Na$: 729.3982).

8,2'-*Ethano*-guanosine (16/16').

A solution of Bu_3SnH (262 mg, 901 µmol) in dry toluene (25.00 mL) was added to a stirred solution of **2b** (750 mg, 901 µmol) and AIBN (catalytic) in dry toluene (100 mL) at 95 °C over 4 h by using a syringe pump. After additional 2 h the solvent was removed under reduced pressure and the residue was purified two times by flash chromatography (eluent: 1. DCM/acetone 3:1, 2. DCM/MeOH 94:6). A solution of the resulting light-yellow solid and TBAF (852 mg) in dry THF (30.0 mL) was stirred at rt under argon atmosphere for 2 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (eluent: acetone/H_2O 9:1). The residue was dissolved in TFA solution

(0.1%, 10.0 mL) and stirred over night to remove the dimethylaminomethylene group. The solvent was removed under reduced pressure and the crude product was purified by preparative HPLC. Yield: 25.0 mg, 80.0 μmol, 9% (over 3 steps, 3:1 mixture of the α- and β-compound). **^{1}H-NMR** (300 MHz, D_2O, rt): δ 2.07-2.41 (m, 2 H, CH_2), 3.11-3.35 (m, 2 H, CH_2), 3.65-3.96 (m, 2 H, H5'), 4.05-4.13 (m, 1 H, H3'), 4.15-4.27 (m, 1 H, H4'), 5.74 (s, 0.75 H, α-H1' or β-H1'), 5.81 (s, 0.75 H, α-H1' or β-H1') ppm. **^{13}C-NMR** (75 MHz, D_2O, rt): δ 21.9 (CH_2), 28.6 (CH_2), 63.3 (C5'), 73.1 (C3'), 78.2 (C2'), 86.4 (C4'), 88.5 (α-C1' or β-C1'), 88.6 (α-C1' or β-C1'), 113.6 (Ar-C), 149.1 (Ar-C), 157.0 (Ar-C), 158.7 (Ar-C), 165.7 (Ar-C) ppm. **ESI-MS** m/z (rel. %): 308.1 (25) $[M - H]^-$. **HRMS** (ESI): 332.0960 (calcd. for $C_{12}H_{15}N_5O_5Na$: 332.0965). **analytical HPLC** (RP-C18, 0 – 15% B [B = MeCN:H_2O 8:2] in 30 min): 15.71 min.

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