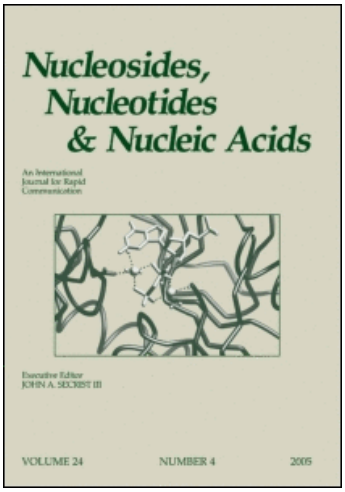

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Rearrangement Reactions of 1,N^2-Isopropenoguanine Cyclonucleosides

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Rearrangement Reactions of 1,N^2-Isopropenoguanine Cyclonucleosides[†]

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ABSTRACT

Under acid-catalyzed transglycosylation conditions 5′,8-cyclo-8-oxo-1,N^2-isopropenoguanine nucleosides (**1**, **10**) undergo a ring-opening reaction to 8-oxo-1,N^2-isopropenoguanosine derivatives (**4**, **11**) followed by recyclization to fluorescent 5′,3-cyclonucleosides (**2**, **12**).

Key Words: Cyclonucleosides; Transglycosylation; Wyosine analogs.

INTRODUCTION

Tricyclic analogs of guanosine occur in nature as the so called Y nucleosides, fluorescent components of the anticodon loop of $tRNA^{Phe}$ from a variety of organisms, and the simplest representative of their family is wyosine, isolated from *Torulopsis utilis*.[1] The Y nucleosides are structurally related to guanosine. A direct modification of guanosine in the reaction with bromoacetone leads to 4-desmethylwyosine, i.e.

[†]In honor and celebration of the 70th birthday of Professor Leroy B. Townsend.

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1,N^2-isopropenoguanosine.[1,2]a Some of its analogs substituted with pseudosugar chains exhibit potent and selective antiviral activity.[3,4]

Similarly to other fully protected 6-oxopurine nucleosides (e.g. guanosine, inosine), derivatives of 1,N^2-isopropenoguanosine readily undergo a reversible 7⇄9 transglycosylation in the presence of acidic catalysts.[5] The reaction proceeds via unstable 7,9-diglycosylpurine intermediates,[6] and only N7 and N9 of the imidazole ring may act as donors or acceptors of a glycosyl cation.[5–8] Transglycosylation reaction is an intermolecular process and therefore, the 6-oxopurine nucleosides may serve as versatile substrates in the synthesis of new nucleoside analogs by applying the exchange methods.[5,9–11]

More recently, the possibility of an intramolecular transglycosylation reaction has been studied in the case of guanine 5′,8-cyclo-8-oxo-nucleosides. The cyclonucleosides of this type, however, do not undergo the anticipated 7⇄9 isomerization when subjected to transglycosylation conditions (refluxing in chlorobenzene in the presence of *p*-toluenesulfonic acid). Instead of the cleavage of N-glycosylic bond, which would be required for the isomerization reaction, the 5′,8-oxygen bridge is cleaved, and this results in the formation of 5′-tosyl-8-oxoguanine derivatives.[12]

In continuation of our study on transglycosylation reactions in the purine cyclonucleoside series, we present in this report the rearrangement reactions of 1,N^2-isopropenoguanosine derivatives, in which the sugar portion and the purine part are linked together with an additional chemical bond.

RESULTS AND DISCUSSION

The model compound for this study, 8,5′-Cyclo-8-oxo-2,′3′-*O*-isopropylidene-1,N^2isopropenoguanosine (**1**),[13] was prepared from 5′,8-cyclo-8-oxo-2′,3′-*O*-isopropylideneguanosine.[14] The compound was then subjected to the typical conditions for transglycosylation reaction, i.e. heating in chlorobenzene in the presence of *p*-toluenesulfonic acid (0.25 eqs.). The first experiment was performed at a reflux temperature (132°C). Surprisingly, the reaction resulted in two new fluorescent products (Scheme 1). The fluorescence and characteristic UV spectrum (maxima at 238 and 306 nm) of the main product might suggest a 3-substitution of the tricyclic aglycon.[1,2,13] Indeed, the NMR spectra confirmed the structure of 3,5′-cyclo-8-oxo-2,′3′-*O*-isopropylidene-1,N^2-isopropenoxoguanosine (**2**)—an isomer of the substrate **1** (yield 41%). In particular, the signal of C5′ in the ^{13}C NMR spectrum was shifted to 53.94 ppm (73.98 ppm in the spectrum of **1**). The second compound, obtained as a side-product (yield 7.7%), was of a more complicated structure. Two sets of signals in the proton and carbon NMR, as well as a high molecular weight of MH^+ seen in mass spectrum, showed that the product **3** was a dimer. Its structure was fully elucidated by using two-dimensional NMR techniques and comparison with spectra of **2**: one fragment of the dimer was identical with the 5′,3-cyclonucleoside **2**, but substituted at N7 with a residual portion of an ''opened'' substrate **1**. The structures of **2** and **3** suggested a possible mechanism of this rearrangement—the reaction to a new

[a]Systematic name: 3,9-dihydro-9-oxo-3-(β-D-ribofuranosyl)-5*H*-imidazo[1,2-*a*]purine.

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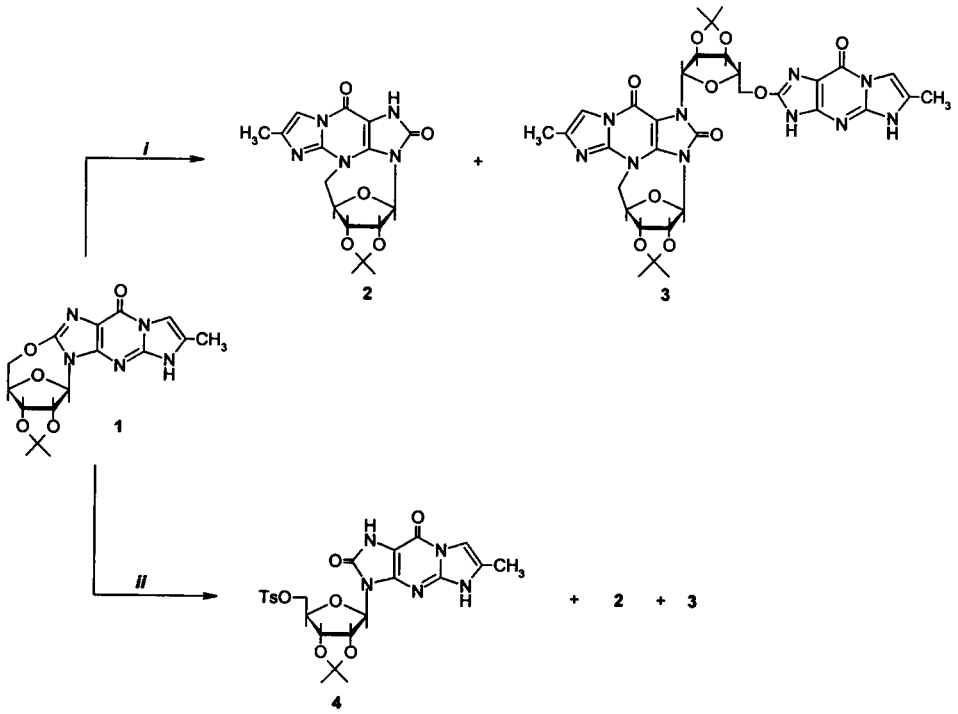

Scheme 1. *Reagents and conditions: i*, *p*-TsOH, C_6H_5Cl, reflux, 3 h; *ii*, *p*-TsOH, C_6H_5Cl, 120°C, 3 h.

cyclonucleoside system could proceed exclusively with a cleavage of the 5′,8-oxygen bridge. Indeed, the reaction repeated at lower temperature (120°C) in the presence of 0.1 molar eq. of *p*-toluenesulfonic acid afforded a non-fluorescent reaction intermediate, 5′-(*p*-toluenesulfonyl)-2,′3′-*O*-isopropylidene-8-oxo-1,N^2-isopropenoguanosine (**4**; yield 1.4%), in addition to already known **2** and **3** (Scheme 1). The isolated compound **4** underwent a quantitative conversion to cyclonucleoside **2** (but not to the dimer **3**!) when heated in chlorobenzene.

Basing on these experimental data, we have proposed a possible mechanism of the observed rearrangement (Scheme 2). The starting 5′,8-cyclo-8-oxo compound (**1**) is protonated at N7 (structure **5**), and this facilitates a nucleophilic attack of the tosyl anion at C5′, leading to the formation of **4** (route A). Then, the tosyl derivative **4** undergoes a recyclization, which presumably takes place as a result of removal of N^2H, and intramolecular nucleophilic attack of N3 at C5′. Perhaps the presence of 5′-tosyl substituent, a good leaving group, further facilitates the rearrangement. However, there is another possibility of the ring-opening reaction of **5**—an acid-catalyzed cleavage of the N-glycosylic bond (pathway B). This closely resembles an initiation step in transglycosylation of ''regular'' 6-oxopurine nucleosides.[5,8] The resulting oxocarbenium cation **6** is then attacked by the N7 center of another molecule of **1** to finally furnish the dimer **3**, probably after a similar rearrangement of the cyclonucleoside portion as depicted in the pathway A. An alternative mechanism assuming the

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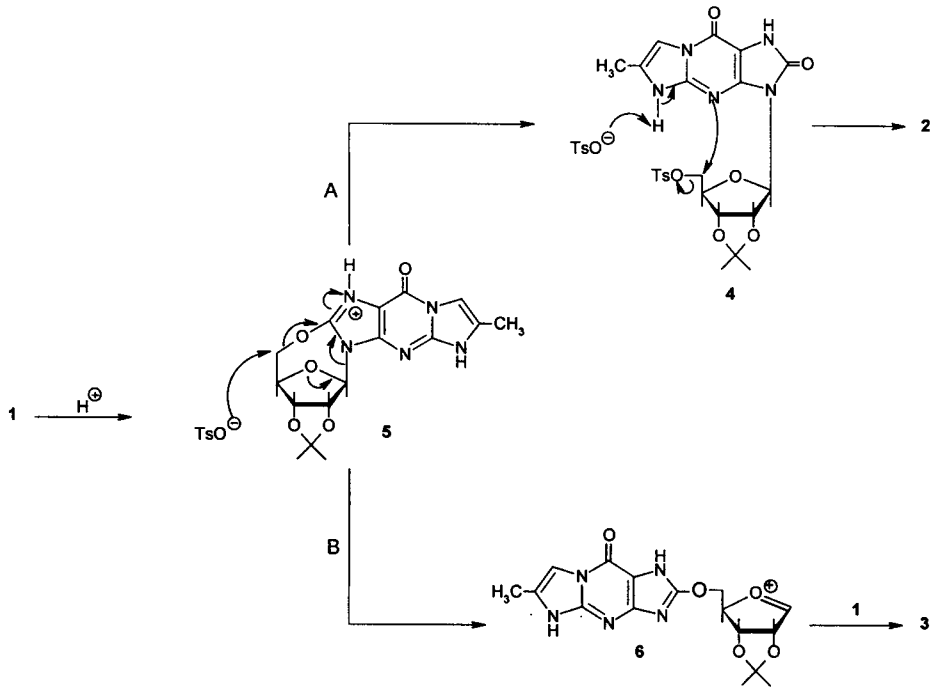
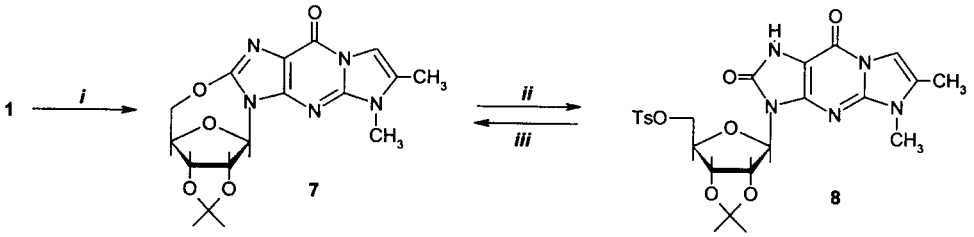


Scheme 2. Mechanism of the formation of compounds **2** and **3**.

direct reaction of **6** and **2** must be rejected because N7 in compound **2** cannot react with sugar cations as being already substituted by proton.

To prove this mechanism, we have synthesized cyclonucleoside **7**, an N^2-methyl analog of **1** (Scheme 3). Previously, the compound was obtained in methylation of **1** with diazomethane,[13] but in this work its preparation was simplified by using methyl iodide in the presence of potassium carbonate.[15] Heating of **7** in the presence of *p*-toluenesulfonic acid resulted in the formation of a tosyl derivative (**8**) as a single reaction product. In the presence of triethylamine in chloroform, the compound **8** was converted to **7** to regain the only possible system of the starting 5′,8-cyclo-8-oxonucleoside. A similar reversible transformation has been observed for 5′,8-cyclo-8-



Scheme 3. *Reagents and conditions: i*, CH_3I, K_2CO_3, DMF, RT, 1 h; *ii*, *p*-TsOH, C_6H_5Cl, reflux, 1.5 h; *iii*, Et_3N, CH_3Cl, 48°C, 5 h.

oxo-2′,3′-*O*-isopropylidene-N^2-acetylguanosine.[12] Therefore, the presence of unsubstituted N^2H as well as the tricyclic system of the 1,N^2-etheno type are necessary for the so far unknown isomerization of 5′,8-cyclonucleosides into the fluorescent ones of the 5′,3-cyclic structure. These structural features were met in the case of another model compound, 1,N^2-isopropeno-tetrahydro-1,5,3-dioxazepine[3,2-*e*]guanine (**10**) which was obtained from acyclovir via tetrahydro-1,5,3-dioxazepine[3,2-*e*]guanine (**9**).[16] The isomerization reaction (Scheme 4) gave quite similar results to that of **1**: a tosyl intermediate **11** and the fluorescent cyclic compound **12** as a major product. Any dimeric product of the type **3** was not observed in this reaction. This reflects lower stability of the N-glycosylic bond of cyclonucleoside **1** in the ribo series in comparison with that of a corresponding C–N bond of **10**.

In conclusion, under acid-catalyzed transglycosylation conditions 5′,8′-cyclo-8-oxonucleosides of 1,N^2-isopropenoguanine undergo a new isomerization reaction to the 5′,3-cyclo-8-oxonucleosides, and this may indicate a higher thermodynamic stability of the latter. In fact, the reaction is related to the cyclization of 4-desmethylwyosine.[1,17] This is the main difference when compared to the corresponding guanine cyclonucleosides, in which the reaction is stopped at the 5′-tosyl-8-oxo stage.[12] Removal of the proton N^2H seems to be of a crucial importance for the rearrangement observed in the 1,N^2-isopropenoguanine series. Neither isopropenoguanine cyclonucleosides nor guanine cyclonucleosides undergo the 7⇄9 transglycosylation. However, the structure of dimer **3** corresponds to that of 7,9-diglycosylpurine derivatives,[6] the unstable intermediates in transglycosylation, decomposition of which leads to a mixture of 7- and 9-regioisomers.[5,8] Unlike 7,9-diglycosylpurines of a quaternary character, dimer **3** is a quite stable reaction product due to the presence of 8-oxo group (no positive charge in the imidazolium ring). This seems to explain the fact that 8-oxocyclonucleosides of guanine and related heterocycles do not undergo the 7⇄9 transglycosylation.

EXPERIMENTAL

Melting points were determined on a Laboratory Devices Mel-Temp II micro-melting points apparatus and are uncorrected. UV spectra were measured in methanol on a Beckman DU-65 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 on a Varian Unity 300 FT NMR spectrometer with tetramethysilane as an internal standard, and chemical shifts are reported in δ-values (ppm). Mass spectra were taken on an AMD-604 spectrometer using the LSIMS technique (Cs^+, 12 keV; in NBA). Elemental analyses were performed on a Perkin–Elmer 240 Elemental Analyzer. TLC was conducted on Merck silica gel F_{254} 60 plates using the following solvent systems (measured by volume): A, chloroform—methanol (9:1); B, toluene—ethanol (4:1). For preparative short-column chromatography Merck TLC gel H 60 was used.

8,5′-Cyclo-8-oxo-2,′3′-*O*-isopropylidene-1,N^2-isopropenoguanosine (**1**) was prepared as described previously,[13] and tetrahydro-1,5,3-dioxazepine[3,2-*e*]guanine (**9**) was obtained from acyclovir according to Madre et al.[16]

3,5′-Cyclo-2,′3′-*O*-isopropylidene-8-oxo-1,N^2-isopropenoguanosine (2). A suspension of cyclonucleoside **1** (359 mg, 1.0 mmol) and p-toluenesulfonic acid monohydrate (47.6 mg, 0.25 mmol) in chlorobenzene (20 mL) was stirred at 150°C for 3 h.

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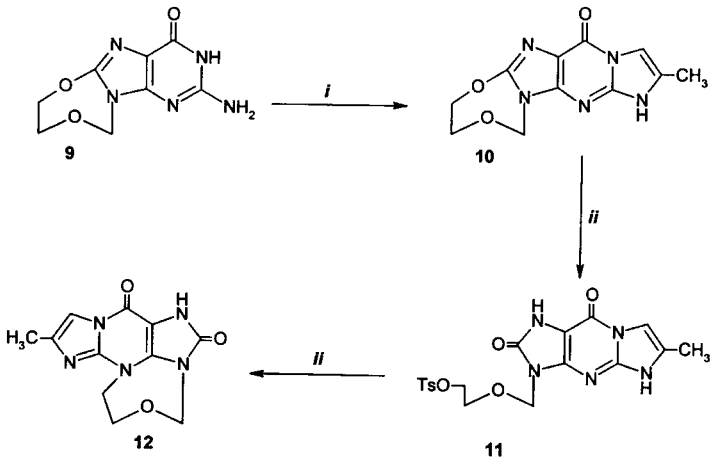

Scheme 4. *Reagents and conditions: i*, CH_3COCH_2Br, NaH, DMSO, RT, 1 h, then concd. NH_4OH, RT, 2.5 h; *ii*, *p*-TsOH, C_6H_5Cl, 120°C, 1.5 h.

After this time TLC showed two new fluorescent spots in addition to non-fluorescent unreacted **1**. The solvent was then evaporated, and the residue after evaporation was applied on a silica gel short column. Separation of products in toluene-ethanol 9:1 gave the main product, cyclonucleoside **2** as a solid foam (147 mg, 41%). Evaporation of the first fractions afforded a side-product, the dimer **3** (27.5 mg, 7.7%). Analytical samples of both compounds were crystallized from 50% aqueous EtOH.

Compound 2: mp > 300°C. R_f0.77(A); 0.56(B). λ_{max} 238 nm (ε 32,900), 306 (13,200). ^{1}H NMR: 1.23, 1.45 (2s, 2 × 3, C > Me_2), 2.21 (s, 3, CH_3), 4.05 (dd, J_{gem} = 17.1 Hz, 1, 5′b-H), 4.69 (d, J = 5.7 Hz, 1, 3′-H), 4.87 (d, J = 5.7 Hz, 1, 2′-H), 4.90 (s, 1, 4′-H), 5.10 (dd, J_{gem} = 17.1 Hz, 1, 5′a-H), 5.92 (s, 1, 1′-H), 7.37 (d, J = 1.2 Hz, 1, HC = C), 11.49 (s, 1, N^7H). ^{13}C NMR: 13.94 (CH_3), 21.14, 25.68 (C > Me_2), 53.94 (C-5′), 80.74 (C-2′), 83.30 (C-4′), 84.51 (C-3′), 88.20 (C-1′), 97.44 (C-5), 105.91 (H*C* = C), 112.05 (OCO), 136.81 (C-4 and C = *C*CH_3), 141.05 (C-2), 146.82 (C-6), 149.39 (C-8). Anal. Calcd. for $C_{16}H_{17}N_5O_5\times$ 0.5 H_2O (368.35): C, 52.18; H, 4.92; N, 19.01. Found: C, 52.74; H, 4.85; N, 19,06.

Compound 3: mp >300°C. R_f 0.52(A); 0.44(B). λ_{max} 235, 302 nm. ^{1}H NMR: (data for the fragment attached at N7 in italics) *1.20, 1.40 (2s, 2x3, C>Me_2)*, 1.30, 1.46 (2s, 2x3, C>Me_2), 2.19 (s, 3, CH_3), *2.26 (s, 3, CH_3)*, 4.03 (dd, J_{gem}=14.9 Hz, 1, 5'b-H), *4.19-4.43 (m, 2, 5'b-H, 4'-H), 4.42 (m, 1, 5'a-H)*, 4.59 (d, J=6.0 Hz, 1, 3'-H), 4.89 (s, 1, 4'-H), 4.93 (d, J=6.0 Hz, 1, 2'-H), 5.09 (dd, J_{gem}=15.1 Hz, 1, 5'a-H), *5.13 (t, 1, 3'-H), 5.47 (dd, 1, 2'-H)*, 5.85 (s, 2, 1'-H, *1'-H*), *7.22 (d, J=0.9 Hz, 1, HC=C)*, 7.37 (d, J=1.2 Hz, 1, HC=C), *10.91 (s, 1, N^7H or N^9H), 12.52 (s, 1, N^2H)*. ^{13}C NMR: *10.34 (CH_3)*, 13.84 (CH_3), *24.05, 25.56 (C>Me_2)*, 25.11, 26.88 (C>Me_2), *43.18 (C-5')*, 54.00 (C-5'), 80.55 (C-2'), *82.20 (C-3'), 82.74 (C-2')*, 83.11 (C-4'), 84.25 (C-3'), *85.60 (C-4'), 85.90 (C-1')*, 88.99 (C-1'), 97.74 (C-5), *98.45 (C-5), 103.60 (H<u>C</u>=C)*, 105.71 (H<u>C</u>=C), 111.94 (OCO), *112.53 (OCO), 125.73 (C=<u>C</u>CH_3)*, 136.53 (C-4), 136.93 (C=<u>C</u>CH_3), 140.76

(C-2), *144.03 (C-2), 145.27 (C-4), 145.34 (C-6)*, 146.95 (C-6), 149.02 (C-8), *151.51 (C-8)*. LSIMS HR Calcd. for MH^+ $C_{32}H_{35}N_{10}O_{10}$. 719.25378. Found: 719.25395.

5′-(*p*-Toluenesulfonyl)-2,′3′-*O*-isopropylidene-8-oxo-1,N^2-isopropenoguanosine (4). A suspension of **1** (400 mg, 1.11 mmol) and p-toluenesulfonic acid monohydrate (21.2 mg, 0.111 mmol) in chlorobenzene (12 mL) was stirred at 120°C for 3 h. The products were separated as described above to provide (in order of elution): **2** (34.8 mg, 8.7%), the tosyl derivative **4** (8.2 mg, 1.4%), and **3** (18.1 mg, 4.1%). Compound **4** was crystallized from 50% aqueous EtOH. The attempted ^{13}C NMR spectrum failed due to a partial conversion into **2**. R_f: 0.69(A); 0.46(B) (non-fluorescent). λ_{max} 232 nm (ε 47,100), 258 (10,200), 299 (9700). ^1H NMR: 1.27, 1.48 (2s, 2 × 3, C > Me_2), 2.24 (s, 3, CH_3), 2.30 (s, 3, CH_3Ph), 4.22–4.32 (m, 3, 4′-H, 5′-H), 4.59 (dd, 1, 3′-H), 5.19 (dd, 1, 2′-H), 5.84 (d, 1, 1′-H), 7.11 (d, 2, Ph), 7.39 (s, 1, HC = C), 7.53 (d, 2, Ph), 10.96 (s, 1, N^7H), 12.50 (s, 1, N^2H). LSIMS HR Calcd. for MH^+ $C_{23}H_{26}O_8N_5S$ 532.15021. Found: 532.14686. A sample of **4** (3 mg, ca. 0.006 mmol) was refluxed in chlorobenzene (2 mL) for 5 h, and this resulted in a quantitative conversion of **4** to fluorescent **2** (TLC, UV).

8,5′-Cyclo-8-oxo-2,′3′-*O*-isopropylidene-N^2-methyl-1,N^2-isopropenoguanosine (7). A solution of **1** (665 mg, 1.85 mmol) in dry DMF (9 mL) was treated with well-powdered potassium carbonate (394 mg, 2.85 mmol), and after 10 min of stirring with methyl iodide (394 mg, 2.78 mmol). The resulting suspension was stirred at room temperature for 1 h, then passed through a layer of Celite. A white precipitate of inorganic salts was washed with warm DMF. The filtrate was concentrated to an oil which was coevaporated with water (3 × 15 mL) and finally with chloroform (2 × 10 mL) to get a solid foam. The product **7** was purified by silica gel chromatography in chloroform-methanol 95:5 and crystallized from methanol, mp > 300°C. Yield 247 mg (36%). R_f0.61(A); 0.40(B) (non-fluorescent, identical with the authentic sample of **7** obtained by methylation with diazomethane[13]). λ_{max} 230 nm (ε 35,300) 287 nm (12,000). ^1H NMR: 1.31, 1.48 (2s, 2 × 3, C > Me_2), 2.27 (s, 3, C = CCH_3), 3.59 (s, 3, N^2CH_3), 4.06 (d, J = 13.0 Hz, 1, 5′b-H), 4.60 (d, J = 13.0 Hz, 1, 5′a-H), 4.74 (bs, 1, 4′-H), 4.93 (d, J = 5.7 Hz, 1, 3′-H), 5.11 (d, J = 5.7 Hz, 1, 2′-H), 6.05 (s, 1, 1′-H), 7.45 (s, 1, HC = C). ^{13}C NMR: 9.42 (CH_3), 24.18, 25.82 (C > Me_2), 28.38 (N^2CH_3), 74.01 (C-5′), 80.97 (C-3′), 84.76 (C-2′), 85.23 (C-4′), 85.77 (C-1′), 103.50 (H*C* = C), 109.78 (C-5), 111.77 (OCO), 127.64 (C = *C*CH_3), 144.61 (C-2), 147.14 (C-4), 150.18 (C-6), 150.62 (C-8).

5′-(*p*-Toluenesulfonyl)-2,′3′-*O*-isopropylidene-N^2-methyl-8-oxo-1,N^2-isopropenoguanosine (8). Cyclonucleoside **7** (373 mg, 1.0 mmol) and p-toluenesulfonic acid monohydrate (19 mg, 0.1 mmol) were refluxed in chlorobenzene (10 mL) for 1.5 h. The solvent was evaporated and the resulting oil was chromatographed on silica gel column to afford 37 mg (6.8%) of **8** as a white solid. Further fractions contained unreacted **7** (310 mg, 83%). The tosyl derivative **8** was crystallized from EtOH, mp 221°C. R_f 0.84(A); 0.56(B). λ_{max} 234 nm (ε 43,900), 259 (10,300), 302 nm (10,200). ^1H NMR: 1.29, 1.50 (2s, 2 × 3, C > Me_2), 2.24 (s, 3, C = CCH_3), 2.36 (s, 3, CH_3Ph), 3.53 (s, 3, N^2CH_3), 4.31 (m, 1, 5′b-H), 4.37–4.42 (m, 2, 4′-H, 5′a-H), 4.97 (dd, J = 6.3 Hz, 1, 3′-H), 5.24 (dd, J = 6.3 Hz, 1, 2′-H), 5.90 (d, J = 1.2 Hz, 1, 1′-H), 7.08 (d, J = 8.4

Hz, 2, Ph), 7.49 (d, J = 1.2 Hz, 1, HC = C), 7.52 (d, J = 8.4 Hz, 2, Ph), 11.03 (s, 1, N^7H). ^{13}C NMR: 9.42 (C = CCH_3), 20.89 (CH_3Ph), 25.00, 26.72 (C > Me_2), 28.54 (N^2CH_3), 70.27 (C-5′), 81.05 (C-3′), 82.75 (C-2′), 84.43 (C-4′), 86.28 (C-1′), 98.31 (C-5), 102.93 (H*C* = C), 112.86 (OCO), 127.84, 127.92, 129.17, 144.22 (Ph), 131.72 (C = *C*CH_3), 143.15 (C-2), 144.64 (C-4), 145.09 (C-6), 151.23 (C-8). Calcd. for $C_{24}H_{27}N_5O_8S$ (545.48): C, 52.84; H, 4.99; N, 12.84; S, 5.88. Found: C, 52.66;H, 4.82; N, 12.74; S: 5.96.

Base-catalyzed conversion of 8 into 7. A solution of the tosyl derivative **8** (52 mg, 0.095 mmol) in chloroform (5 mL) was treated with Et_3N (2 mL) and heated at 48°C for 5 h. After this time, TLC showed a complete conversion to cyclonucleoside **7**. The reaction mixture was evaporated to dryness and the product was purified on a silica gel column in toluene-ethanol 9:1 to afford 32.9 mg (92%) of a white solid, identical in all respects (TLC, UV, ^1H NMR) to an authentic sample of **7**.

1,N^2-Isopropeno-tetrahydro-1,5,3-dioxazepine[3,2-*e*]guanine (10). Sodium hydride (142 mg, 5.90 mmol; 60% suspension in oil) was added to a solution of tetrahydro-1,5,3-dioxazepine[3,2-*e*]guanine (**9**; 1.285 g, 5.76 mmol) in anhydrous DMSO (25 mL) and this mixture was stirred with exclusion of moisture for 35 min. A resulting almost clear solution was treated with bromoacetone (790 mg, 5.75 mmol) for 1 h. The reaction mixture was then made basic by addition of concd. NH_4OH (25 mL) and stirred for 2.5 h. The solution was evaporated to an oil which was washed with water (3 × 10 mL), and crystallized from 50% aqueous EtOH, mp > 300°C. Yield 916 mg (61%). R_f 0.32(A); 0.20(B). λ_{max} 229 nm (ε 38,600), 284 (12,700). ^1H NMR: 2.26 (s, 3, CH_3), 4.15 (m, 2, CH_2), 4.25 (m, 2, CH_2), 5.45 (s, 2, OCH_2N), 7.34 (d, J = 1.2 Hz, 1, HC = C), 12.41 (s, 1, N^2H). ^{13}C NMR: 10.37 (CH_3), 72.73 (CH_2), 73.30 (CH_2), 73.48 (OCH_2N), 103.38 (H*C* = C), 109.87 (C-5), 125.63 (C = *C*CH_3), 145.10 (C-2), 147.64 (C-4), 150.37 (C-6), 152.93 (C-8). LSIMS HR Calcd. for MH^+ $C_{11}H_{12}O_3N_5$ 262.09402. Found: 262.09505.

Rearrangement reaction of 1,N^2-isopropeno-tetrahydro-1,5,3-dioxazepine[3,2-*e*]-guanine (10). A suspension of **10** (100 mg, 0.383 mmol) and *p*-toluenesulfonic acid monohydrate (72.2 mg, 0.383 mmol) in chlorobenzene (10 mL) was stirred at 120°C for 1.5 h. After this time, TLC showed two new spots: a non-fluorescent one of compound **11**, R_f 0.50(A); 0.40(B), and a fluorescent spot of **12**, R_f 0.52(A); 0.46(B). The solvent was evaporated and resulting oil was chromatographed on a silica gel short column in toluene ethanol 9:1. Evaporation of fractions containing **12** and crystallization of the resulting solid from 50% aqueous EtOH gave 27 mg (27%) of the main product, mp > 300°C. λ_{max} 238 nm (ε 32,700), 306 (13,100). ^1H NMR: 2.24 (s, 3, CH_3), 4.26 (m, 2, CH_2), 4.57 (m, 2, CH_2), 5.35 (s, 2, OCH_2N), 7.37 (d, J = 1.2 Hz, 1, HC = C), 11.34 (s, 1, N^7H). ^{13}C NMR: 13.91 (CH_3), 50.84 (CH_2), 70.07 (CH_2), 76.59 (OCH_2N), 96.91 (C-5), 105.87 (H*C* = C), 133.66 (C-4), 138.54 (C = *C*CH_3), 140.67 (C-2), 146.69 (C-6), 150.07 (C-8). LSIMS HR Calcd. for MH^+ $C_{11}H_{12}N_5O_3$ 262.09402. Found: 262.09510.

Further fractions contained the tosyl derivative **11**, yield 12.6 mg (7.6%) of a white solid, mp 222–224°C. λ_{max} 233 nm (ε 45,200), 258 (10,400), 298 (9,600). ^1H NMR: 2.26 (s, 3, CH_3), 2.39 (s, 3, CH_3Ph), 3.71 (m, 2, CH_2), 4.11 (m, 2, CH_2), 5.09 (s, 2, OCH_2N),

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7.37 (d, 1 HC = C), 7.40 (d, J = 8.4 Hz, 2, Ph), 7.71 (d, J = 8.4 Hz, 2, Ph), 10.90 (s, 1, N^7H), 12.61 (s, 1, N^2H). ^{13}C NMR: 10.33 (CH_3), 20.97 (CH_3Ph), 66.49 (CH_2), 68.77 (CH_2), 69.52 (OCH_2N), 98.14 (C-5), 103.62 (H*C* = C), 125.76 (C = *C*CH_3), 127.40, 129.92, 132.25, 144.31 (Ph), 144.78 (C-2), 145.22 (C-4), 146.07 (C-6), 152.37 (C-8). LSIMS HR Calcd. for MH^+ $C_{18}H_{20}N_5O_6S$ 434.11343. Found: 434.11227.

A sample of **11** (12.0 mg, 0.0277 mmol) was refluxed in chlorobenzene (3 mL), and after 3 h TLC in solvent B showed a quantitative conversion to fluorescent **12**.

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