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Synthesis of 2′-*C*-*β*-Methyl-2′-deoxyguanosine

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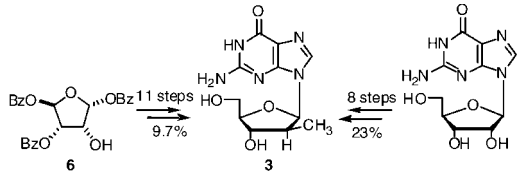

6 **3**

We describe two approaches for the synthesis of 2′-*C*-*β*-methyl-2′-deoxyguanosine (**3**) via 2′-radical deoxygenation. One approach starts from 1,3,5-tri-*O*-benzoyl-α-D-ribofuranose (**6**) and gives **3** in 11 steps with 9.7% overall yield. The second approach starts from guanosine and gives **3** in 8 steps with 23% overall yield.

2′-*C*-Branched nucleosides represent a class of nucleoside analogues that have potential utility as therapeutic agents and as probes to study RNA structure and function.[1−11] For example, 2′-*C*-*β*-methyl and 2′-deoxy-2′-*C*-α/*β*-methyl ribonucleosides, including 2′-*C*-*β*-methylguanosine (**1**), have antitumor and antiviral activities (as inhibitors for Hepatitis C viral RNA replication).[1−9] Recently, we used 2′-*C*-*β*-methyl nucleosides and 2′-deoxy-2′-*C*-α/*β*-methyl nucleosides, including 2′-*C*-α-methyl-2′-deoxyguanosine (**2**), to study the packing density of the P4−P6 RNA domain and the mechanism of Group II intron catalysis.[10,11] We previously reported an efficient synthesis of 2′-*C*-*β*-methylguanosine (**1**)[12] and 2′-*C*-α-methyl-2′-deoxyguanosine (**2**).[13] Here we report the synthesis of 2′-*C*-*β*-methyl-2′-deoxyguanosine (**3**) (Figure 1).

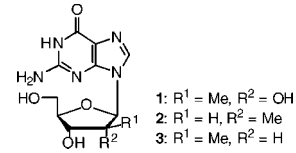

FIGURE 1. 2′-*C*-Methylguanosines (**1**−**3**).

Numerous methods have been developed for the synthesis of 2′-deoxy-2′-*C*-*β*-methylnucleosides. Matsuda et al. showed that 2′-*C*-*β*-methyl-2′-deoxypyrimidine nucleosides could be synthesized with high stereoselectivity from 2′-*O*-methoxyoxalyl esters of O^4-ethyl-protected 2′-*C*-*β*-methylpyrimidine nucleoside derivatives[8,14,15] or 2′-*C*-α-methylarabinonucleoside derivatives[9] via 2′-radical deoxygenation in the presence of tributyltin hydride and AIBN.[16] Previously, we found that even without O^4-ethyl protection, 2′-*C*-*β*-methyl-2′-deoxypyrimidine nucleosides could also be efficiently synthesized from 2′-*C*-*β*-methyluridine via 2′-radical deoxygenation.[17] Alternatively, 2′-*C*-*β*-methyl-2′-deoxyuridine could be obtained by hydrogenation of a 2′-*C*-methyleneuridine derivative but with low diastereoselectivity (50% de).[18] Attempts to apply the hydrogenation method to the synthesis of 2′-*C*-*β*-methyl-2′-deoxy purine were not successful.[19]

Caballero et al. synthesized 2′-deoxy-2′-*C*-*β*-methyladenosine (13 steps, 2.5% overall yield) and 2′-deoxy-2′-*C*-*β*-methylinosine (11 steps, 1.3% overall yield) in a lengthy synthetic route starting from 6-chloropurine ribonucleoside.[19] They first prepared a diastereomeric mixture of O^6-substituted 2′-*C*-*β*-methylinosine and O^6-substituted 2′-*C*-α-methylarabinoinosine from 6-chloropurine ribonucleoside in seven steps with 8.8% overall yield. 2′-Radical deoxygenation of the 2′-methoxyoxalyl esters of this diasteromeric mixture with tributyltin hydride/AIBN yielded the corresponding O^6-substituted 2′-deoxy-2′-*C*-α-methylinosine derivative in 54% yield. Desilylation followed by hydrolysis or aminolysis gave 2′-deoxy-2′-*C*-*β*-methylinosine and 2′-deoxy-2′-*C*-*β*-methyladenosine, respectively.[19] To our knowledge, the synthesis of 2′-deoxy-2′-*C*-*β*-methylguanosine (**3**) has not been reported previously. Here we report an efficient synthesis of **3**

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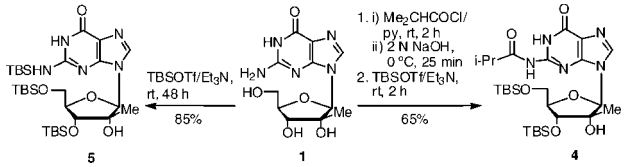
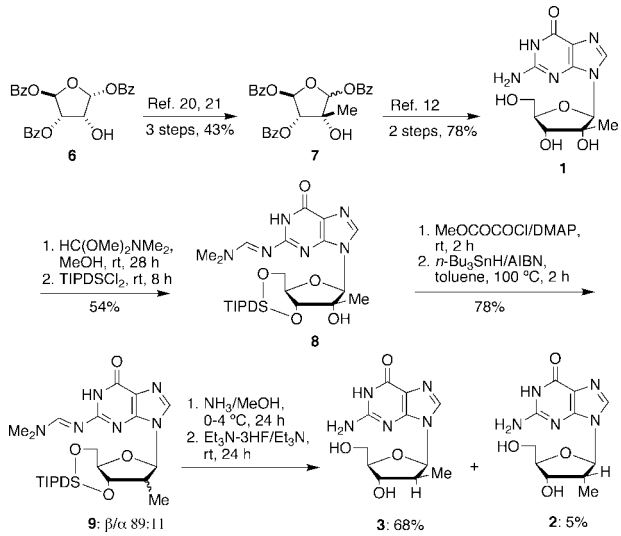
SCHEME 1



SCHEME 2

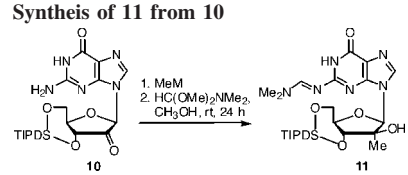


via 2′-radical deoxygenation of 3′,5′-*O*-TIPDS-2′-*C*-*β*-methylguanosine (TIPDS: 1,1,3,3-tetraisopropyldisiloxane-1,3-diyl) from 2′-*C*-*β*-methylguanosine (**1**) and of 3′,5′-*O*-TIPDS-2′-*C*-α-methylarabinoguanosine (**9**) derived from N^2-[(dimethylamino)methylene]-3′,5′-*O*-(TIPDS)-2′-ketoguanosine (**12**).

To convert 2′-*C*-*β*-methylguanosine (**1**)[12,20,21] into 2′-*C*-*β*-methyl-2′-deoxyguanosine (**3**), we prepared 3′,5′-di-*O*-TBS-N^2-isobutyryl-2′-*C*-*β*-methylguanosine (**4**) and N^2,3′,5′-tri-*O*-TBS-2′-*C*-*β*-methylguanosine (**5**) from 2′-*C*-*β*-methylguanosine (**1**) in 65% and 85% yield, respectively (Scheme 1). However, neither **4** nor **5** gave the corresponding 2′-deoxy-2′-*C*-*β*-methylguanosine derivatives after the standard two-step radical deoxygenation procedure.[16,17] NMR and TLC of the crude product showed that the N^2-isobutyryl and N^2-TBS groups were lost during 2′-oxalyl ester formation.

Because the N^2-protecting group was lost, we protected **1** as a (dimethylamino)methylene imine and prepared N^2-[(dimethylamino)methylene]-3′,5′-*O*-TIPDS-2′-*C*-*β*-methylguanosine (**8**) in two steps with 54% yield. Reaction of **8** with methyl chlorooxoacetate in the presence of DMAP, followed by 2′-radical deoxygenation with tributyltin hydride/AIBN, successfully gave the corresponding 2′-*C*-methyl-2′-deoxyguanosine derivative (**9**) as a diasteromeric mixture in 78% yield ($\beta/\alpha \approx$ 89:11 selectivity based on ^{1}H NMR). Treatment of the diasteromeric mixture with ammonia in methanol (4 °C for 24 h) followed by desilylation with Et_3N-3HF generated 2′-*C*-*β*-methyl-2′-deoxyguanosine (**3**) and 2′-*C*-α-methyl-2′-deoxyguanosine (**2**) in yields of 68% and 5%, respectively. By the synthetic route outlined in Scheme 2, 2′-*C*-*β*-methyl-2′-deoxyguanosine (**3**) could be prepared from 2′-*C*-*β*-methylguanosine (**1**) in 6 steps with 29% overall yield or from commercially available 1,3,5-tri-*O*-benzoyl-α-D-ribofuranose (**6**) in 11 steps with 9.7% overall yield.

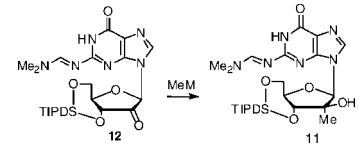
TABLE 1. Syntheis of 11 from 10



entry	MeM (9.0 equiv)	solvent	conditions of step 1	yield (%)[a]
1	MeMgBr	THF	−78 °C−rt, 48 h	6
2	MeMgBr	Et_2O	−78 °C, 8 h	14
3	MeLi	Et_2O	−78 °C, 8 h	0
4	Me_3Al	CH_2Cl_2	rt, 20 h	5
5	MeMgBr	toluene/THF (10:1)	−78 °C, 4.5 h	5

[a] Isolated yield.

TABLE 2. Synthesis of 11 from 12



entry	MeM (mol equiv)	solvent	conditions	yield (%)[c]
1[a]	MeLi (6.0)	THF	−78 °C, 3.5 h	
2	MeMgBr (6.0)	THF	−78 °C, 3.5 h	10
3[b]	MeMgBr (10.0)	THF	−78 °C−rt, 17 h	19
4	MeMgBr (6.0)	Et_2O	−78 °C, 7 h	13
5	MeMgBr (6.0)	toluene	−78 °C, 7 h	0
6	Me_3Al (1.1)	CH_2Cl_2	0 °C−rt, 1 h	9
7	Me_3Al (2.2)	CH_2Cl_2	0 °C−rt, 1 h	31
8	Me_3Al (3.0)	CH_2Cl_2	0 °C−rt, 1 h	66
9	Me_3Al (3.0)	CH_2Cl_2	0 °C−rt, 2 h	76
10	Me_3Al (3.0)	CH_2Cl_2	0 °C−rt, 4 h	63
11	Me_3Al (3.0)	CH_2Cl_2	0 °C−rt, 7 h	29

[a] **12** remained in the reaction mixture. [b] The Me_2NCH group was lost when a large excess of Grignard reagent was used; the amino group was protected again with $HC(OMe)_2NMe_2$ in methanol to give product in 19% yield. [c] Isolated yield.

We also investigated the synthesis of **3** via 2′-radical deoxygenation of a 2′-*C*-α-methylarabinoguanosine derivative. We tried to prepare arabinoguanosine derivative **11** by methyl addition to 3′,5′-*O*-TIPDS-2′-ketoguanosine (**10**)[22,23] followed by reaction with *N*,*N*-dimethylformamide dimethyl acetal. As shown in Table 1, this approach gave poor yields of **11**; the highest yield (14%) was obtained with methylmagnesium bromide as alkylation reagent and ethyl ether as solvent.

We improved the synthesis of **11** by exploring methyl addition to N^2-[(dimethylamino)methylene]-3′,5′-*O*-TIPDS-2′-ketoguanosine (**12**)[24] with several methyl organometallic reagents under different conditions (Table 2). As shown in Table 2, reactions with trimethylaluminum generally gave **11** in better yields compared to reactions with methyllithium or methylmagnesium bromide. Trimethylaluminum in dichloromethane at room temperature for 2 h gave the best yield of **11** (76%; Table 2, entry 9). Longer reaction times under these conditions resulted in lower yield (Table 2, entries 11 and 12), presumably reflecting product decomposition.

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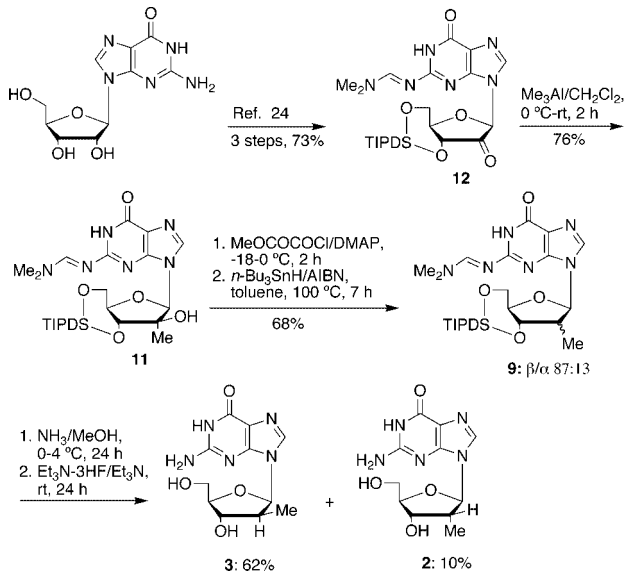
SCHEME 3



2′-Deoxygenation of **11** via formation of the 2′-*O*-methoxyoxalyl ester followed by radical reaction with tributyltin hydride and AIBN generated **9** in 68% yield with $\beta/\alpha \approx 87:13$ selectivity (Scheme 3). Deprotection of **9** with ammonia in methanol (4 °C for 24 h) followed by desilylation with Et_3N-3HF generated 2′-*C*-*β*-methyl-2′-deoxyguanosine (**3**) and 2′-*C*-α-methyl-2′-deoxyguanosine (**2**) in yields of 62% and 10%, respectively. 2′-*C*-*β*-Methyl-2′-deoxyguanosine (**3**) was prepared from N^2-[(dimethylamino)methylene]-3′,5′-*O*-TIPDS-2′-ketoguanosine (**12**) in 5 steps with 32% overall yield or starting from guanosine in 8 steps by the synthetic route outlined in Scheme 3 with 23% overall yield.

We confirmed the structure of **3** by its NOESY NMR spectrum. We observed strong NOEs between 3′-H ($\delta = 3.98$) and 2′-Me ($\delta = 0.56$) and between 2′-H ($\delta = 2.55$) with 1′-H ($\delta = 6.05$). We observed no NOE between 2′-H ($\delta = 2.55$) with 3′-H ($\delta = 3.98$). These results strongly suggest that **3** has the 2′-*β*-configuration.

In summary, we have developed two ways to obtain 2′-*C*-*β*-methyl-2′-deoxyguanosine (**3**). With N^2-dimethylaminomethylene protection rather than isobutyryl or TBS group protection, both the 2′-*C*-*β*-methylguanosine derivative (**8**) and the 2′-*C*-α-methylarabinoguanosine derivative (**11**) could be efficiently deoxygenated to give 2′-*C*-*β*-methyl-2′-deoxyguanosine derivative (**9**) with high setereoselectivity ($\beta/\alpha \approx 88:12$). The route from guanosine via 2′-*C*-α-methylarabinoguanosine derivative (**11**) (8 steps, 23% yield) provides a more efficient synthesis of **3** than does the route from 1,3,5-tri-*O*-benzoyl-α-D-ribofuranose (**6**) via 2′-*C*-*β*-methylguanosine derivative (**8**) (11 steps, 9.7% yield).

Experimental Section

3′,5′-Di-*O*-(*tert*-butyldimethylsilyl)-N^2-isobutyryl-2′-*C*-*β*-methylguanosine (4). 2′-*C*-*β*-Methylguanosine[12] (0.132 g, 0.44 mmol) was suspended in a mixture of pyridine (1.0 mL) and chloroform (8.0 mL), to which isobutyryl chloride (0.47 mL, 4.4 mmol) was added at room temperature. After the reaction mixture was stirred at room temperature for 2 h, the resulting mixture was distributed between hydrochloric acid (1.0 N) and chloroform in a separating funnel; the aqueous layer was extracted with chloroform (3 × 10 mL). The organic layers were combined and sequentially washed with water and saturated aqueous $NaHCO_3$. After the solvent was removed, the residue was dissolved in ethanol (5.0 mL), and the resulting solution was treated with aqueous NaOH (2 N, 5.0 mL) at 0 °C for 25 min. The mixture was neutralized with Dowex 50WX8-200 ion-exchange resin. The resin was filtered off and rinsed with methanol. The filtrate was evaporated, and the residue was purified by silica gel chromatography, eluting with 15% methanol in chloroform to give N^2-isobutyryl-2′-*C*-*β*-methylguanosine as a white solid (0.128 g, 79% yield). ^{1}H NMR (CD_3OD) δ 8.45 (s, 1H), 5.95 (s, 1H), 4.14 (d, 1H, $J = 8.8$ Hz), 4.03−4.00 (m, 2H), 3.85−3.81 (m, 1H), 2.71 (m, 1H), 1.25−1.11 (m, 6H), 0.92 (s, 3H); ^{13}C NMR (CD_3OD) δ 181.7, 157.5, 150.1, 149.7, 139.4, 120.9, 92.4, 84.1, 80.4, 73.0, 60.7, 36.9, 20.3, 19.3. To the solution of N^2-isobutyryl-2′-*C*-*β*-methylguanosine (0.128 g, 0.35 mmol) and triethylamine (4.9 mL, 35.0 mmol) in dry DMF (10 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (2.0 mL, 8.7 mmol) at 0 °C. After the reaction mixture was stirred at room temperature for 2 h, the solvent was removed by rotary evaporator. The residue was dissolved into dichloromethane, and the resulting solution was sequentially washed with saturated aqueous $NaHCO_3$ and brine. The solvent was removed, and the residue was isolated by silica gel chromatography, eluting with 2% methanol in chloroform to give **4** (0.172 g, 82% yield). ^{1}H NMR ($CDCl_3$/TMS) δ 12.06 (s, 1H), 9.09 (s, 1H), 8.13 (s, 1H), 5.79 (s, 1H), 4.24 (d, 1H, $J = 8.2$ Hz), 4.04 (m, 1H), 3.94 (m, 1H), 3.80 (m, 1H), 3.10 (s, 1H), 2.69 (m, 1H), 2.47 (s, 3H), 1.25−1.22 (m, 6H), 0.93 (s, 9H), 0.89 (s, 9H), 0.81 (s, 3H), 0.14 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.077 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.5, 155.8, 148.0, 147.6, 136.9, 121.1, 89.7, 82.7, 79.2, 72.7, 60.6, 36.4, 26.1, 25.7, 20.7, 19.0, 18.9, 18.5, 17.9, −4.37, −4.43, −5.36; HRMS calcd for $C_{27}H_{50}N_5O_6Si_2$ [MH^+] 596.3300, found 596.3298.

N^2-(*tert*-Butyldimethylsilyl)-3′,5′-di-*O*-(*tert*-butyldimethylsilyl)-2′-*C*-*β*-methylguanosine (5). *tert*-Butyldimethylsilyl trifluoromethanesulfonate (0.46 mL, 2.0 mmol) was added to the mixture of 2′-*C*-*β*-methylguanosine[12] (30 mg, 0.10 mmol) and triethylamine (1.4 mL, 10 mmol) in DMF (5.0 mL) at 0 °C. After the mixture was continuously stirred at room temperature for 48 h, the solvent was removed, and the residue was dissolved in chloroform. The resulting solution was washed with brine and dried over $MgSO_4$. The solvent was removed, and the residue was purified by silica gel chromatography, eluting with 5% methanol in chloroform to give product **5** (54 mg, 85% yield). ^{1}H NMR ($CDCl_3$/TMS) δ 8.01 (s, 1H), 6.00 (s, 1H), 5.72 (s, 1H), 4.28 (d, 1H, $J = 8.0$ Hz), 4.10 (m, 1H), 3.98 (m, 1H), 3.82 (dd, 1H, $J = 12.0$, 1.6 Hz), 2.95 (s, 1H), 1.00 (s, 9H), 0.99 (s, 9H), 0.93 (s, 9H), 0.88 (s, 3H), 0.382 (s, 3H), 0.377 (s, 3H), 0.17 (s, 6H), 0.16 (s, 3H), 0.11 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 159.4, 154.6, 151.6, 135.5, 117.1, 89.3, 82.4, 79.4, 72.6, 60.6, 26.7, 26.2, 25.7, 20.6, 18.5, 18.0, 17.8, −4.44, −5.32, −5.38; HRMS calcd for $C_{29}H_{58}N_5O_5Si_3$ [MH^+] 640.3746, found 640.3742.

N^2-[(Dimethylamino)methylene]-3′,5′-*O*-TIPDS-2′-*C*-*β*-methylguanosine (8). A mixture of 2′-*C*-*β*-methylguanosine[12] (203 mg, 0.68 mmol) and *N*,*N*-dimethylformamide dimethyl acetal (2.0 mL, 15 mmol) in anhydrous methanol (20 mL) was stirred at room temperature for 28 h. After removal of the solvent, the residue was dried under vacuum overnight. 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane (0.24 mL, 0.75 mmol) was added to the solution of crude N^2-[(dimethylamino)methylene]-2′-*C*-*β*-methylguanosine in dry pyridine (5.0 mL) at room temperature. After the mixture was stirred at room temperature for 8 h, TLC showed that the reaction was incomplete. Additional 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (21 μL, 66 μmol) was then added, and the reaction was continued at room temperature for 1.5 h. The reaction was quenched with methanol (0.20 mL), and the solvent was removed under vacuum with a rotary evaporator. The residue was extracted with dichloromethane (3 × 10 mL). The combined solution was washed with water and brine. The solvent was removed, and the residue was purified by silica gel chromatography, eluting with 3% methanol in chloroform to give product **8** (0.219 g, 54% yield). ^{1}H NMR ($CDCl_3$/TMS) δ 10.31 (s, 1H), 8.62 (s, 1H), 7.92 (s, 1H),

6.09 (s, 1H), 4.30−4.00 (m, 4H), 3.30 (s, 1H), 3.19 (s, 3H), 3.09 (s, 3H), 1.30−0.90 (m, 31H); ^{13}C NMR ($CDCl_3$) δ 158.1, 158.0, 156.7, 149.7, 135.3, 120.1, 89.2, 81.2, 79.1, 73.2, 60.3, 41.2, 34.9, 20.5, 17.2, 17.1, 17.0, 16.8, 16.7, 16.6, 13.3, 12.7, 12.6, 12.3; HRMS calcd for $C_{26}H_{47}N_6O_6Si_2$ [MH^+] 595.3096, found 595.3088.

***N*^{2}-[(Dimethylamino)methylene]-3′,5′-*O*-TIPDS-2′-*C*-α-methylarabinoguanosine (11).** Under an argon atmosphere, trimethylaluminum (2.0 M in toluene, 0.30 mL, 0.60 mmol) was added to the solution of *N*^{2}-[(dimethylamino)methylene]-3′,5′-*O*-TIPDS-2′-ketoguanosine[24] (116 mg, 0.20 mmol) in dichloromethane (5.0 mL) at 0 °C. After the mixture was stirred at room temperature for 2 h, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The product was extracted with dichloromethane. The combined organic layers were evaporated, and the residue was purified by silica gel chromatography, eluting with 6% methanol in chloroform to give product **11** (91 mg, 76% yield). ^{1}H NMR ($CDCl_3$/TMS) δ 9.90 (s, 1H), 8.41 (s, 1H), 7.76 (s, 1H), 5.82 (s, 1H), 5.08 (br s, 1H), 4.35 (d, 1H, J = 6.0 Hz), 4.10−4.00 (m, 2H), 3.84−3.79 (m, 1H), 3.08 (s, 3H), 2.97 (s, 3H), 1.65 (s, 3H), 1.14−0.98 (m, 28H); ^{13}C NMR ($CDCl_3$) δ 158.2, 157.6, 156.8, 149.9, 138.2, 118.8, 88.5, 82.8, 79.3, 79.1, 63.4, 41.4, 35.0, 20.1, 17.5, 17.34, 17.29, 17.1, 17.0, 13.4, 13.2, 12.9, 12.5; HRMS calcd for $C_{26}H_{47}N_6O_6Si_2$ [MH^+] 595.3096, found 595.3085.

***N*^{2}-[(Dimethylamino)methylene]-3′,5′-*O*-TIPDS-2′-*C*-β-methyl-2′-deoxyguanosine (9). From 8:** Methyl chlorooxoacetate (50 μL, 0.54 mmol) was added under argon to the solution of DMAP (174 mg, 1.42 mmol) and **8** (0.213 g, 0.358 mmol) in a mixed solvent of dry acetonitrile (5.0 mL) and dry dichloromethane (5.0 mL). After the reaction mixture was stirred at room temperature for 1 h, TLC showed that the reaction was not complete. Additional methyl chlorooxoacetate (50 μL, 0.54 mmol) was added to the reaction mixture. TLC showed that the reaction was complete after 1 h. The reaction mixture was diluted with ethyl acetate and washed sequentially with saturated aqueous $NaHCO_3$ (10 mL), water (10 mL), and brine (10 mL). The combined organic layers were dried over $MgSO_4$. The solvent was removed, and the residue was coevaporated with anhydrous toluene (10 mL) and dried under vacuum for 2 h. Under argon, the crude 2′-methoxyoxaylyl ester was dissolved into anhydrous toluene (15 mL). Tributyltin hydride (0.29 mL, 1.1 mmol) and AIBN (15 mg) were added to the resulting solution. The reaction mixture was heated to 100 °C under argon for 2 h. TLC showed that reaction was complete. The solvent was removed, and the residue was purified by silica gel chromatography, eluting with 3% methanol in chloroform to give product **9** (162 mg, 78% yield). ^{1}H NMR spectra showed that the product contains about 11% of the corresponding α-isomer.

From 11: Methyl chlorooxoacetate (74 μL, 0.80 mmol) was added under argon to the solution of DMAP (130 mg, 1.06 mmol) and **11** (0.158 g, 0.266 mmol) in dry dichloromethane (10.0 mL). After the reaction mixture was stirred at room temperature for 2 h, TLC showed that the reaction was complete. The reaction mixture was diluted with ethyl acetate and washed sequentially with saturated aqueous $NaHCO_3$, water, and brine. The combined organic layers were dried over $MgSO_4$. The solvent was removed, and the residue was coevaporated with anhydrous toluene (3 × 5 mL) and dried over vacuum overnight. Under argon, the crude 2′-methoxyoxalyl ester was dissolved into anhydrous toluene (10 mL). Tributyltin hydride (0.29 mL, 1.1 mmol) and AIBN (15 mg) were added to the resulting solution. The reaction mixture was heated to 100 °C under argon for 7 h. TLC showed reaction was complete. The solvent was removed, and the residue was purified by silica gel chromatography, eluting with 3% methanol in chloroform to give product **9** (105 mg, 68% yield). ^{1}H NMR spectra showed that the product contains about 13% of the corresponding α-isomer.

^{1}H NMR ($CDCl_3$/TMS) δ 10.06 (s, 1H), 8.53 (s, 1H), 7.94 (s, 1H), 6.25 (d, 1H, J = 7.2 Hz), 4.23−4.15 (m, 2H), 4.09−4.04 (m, 1H), 3.81 (m, 1H), 3.20 (s, 3H), 3.09 (s, 3H), 2.71 (m, 1H), 1.22−1.02 (m, 28H), 0.79 (d, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 158.2, 157.9, 156.6, 149.8, 136.3, 120.0, 84.7, 83.9, 73.2, 60.4, 44.6, 41.3, 17.4, 17.3, 17.23, 17.20, 16.94, 16.86, 16.8, 13.4, 13.0, 12.9, 12.4, 11.3; HRMS calcd for $C_{26}H_{47}N_6O_5Si_2$ [MH^+] 579.3147, found 579.3136.

2′-*C*-β-Methyl-2′-deoxyguanosine (3). A solution of **9** (195 mg, 0.337 mmol) in methanol (20 mL) was saturated with ammonia at 0 °C for 30 min and then kept at 4 °C for 24 h. The solvent was removed, and the residue was dried under vacuum. The residue in THF (10 mL) was treated with triethylamine−trihydrogen fluoride (0.27 mL, 1.67 mmol) and triethylamine (0.47 mL, 3.4 mmol) at room temperature for 24 h. The solvent was removed, and the residue was purified by silica gel chromatography, eluting with 15% methanol in chloroform to give 2′-*C*-β-methyl-2′-deoxyguanosine **3** (59 mg, 62% yield; the lower spot on TLC) along with the α-isomer **2** (10 mg, 10% yield; the higher spot on TLC). **3**: ^{1}H NMR (D_2O) δ 7.81 (br s, 1H), 6.05 (d, 1H, J = 7.6 Hz), 3.98 (m, 1H), 3.85 (dd, 1H, J = 12.0, 1.5 Hz), 3.80−3.70 (m, 2H), 2.55 (m, 1H), 0.56 (d, 3H, J = 7.0 Hz); ^{13}C NMR (D_2O) δ 158.3, 153.1, 150.5, 137.5, 115.4, 85.1, 83.7, 72.7, 59.5, 43.9, 9.6; HRMS calcd for $C_{11}H_{15}N_5O_4Na$ [MNa^+] 304.1022, found 304.1017.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **3**, **4**, **5**, **8**, **9**, and **11** and NOESY of **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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