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Synthesis of 6,3′-Methanocytidine, 6,3′-Methanouridine, and Their 2′-Deoxyribonucleosides (Nucleosides and Nucleotides. LXXVII[1])

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Condensation of 5-*O*-*tert*-butyldimethylsilyl-1,2-*O*-isopropylidene-α-D-*erythro*-3-pentulofuranose (**4**) with 2,4-dimethoxypyrimidin-6-ylmethyllithium (**5**) afforded a 3-pyrimidinylmethylribose derivative (**6**). The protecting groups of **6** were changed to give the 5-*O*-benzoyl-1,2-di-*O*-acetyl derivative (**8**). The intramolecular glycosylation of **8** by treatment with stannic chloride furnished the 6,3′-methanol-O^4-methyluridine derivative (**9**), which was further converted to 6,3′-methanouridine (**10**) and 6,3′-methanocytidine (**11**). The 2′-deoxygenation of **9** by way of the 2′-imidazolylthiocarbonyl derivative gave, after appropriate derivatization, 2′-deoxy-6,3′-methanocytidine (**16**) and -uridine (**17**).

Keywords——*C*-cyclonucleoside; 6,3′-methanocytidine; 6,3′-methanouridine; 2′-deoxy-6,3′-methanocytidine; deoxygenation; intramolecular glycosylation; 3-ketoribose; nucleophilic addition; NMR

We have reported the synthesis of a number of carbon-bridged cyclonucleosides for stereochemical studies of nucleosides and nucleotides.[2] Among them, the 6,3′-carbon bridged nucleosides seem to be interesting. The glycosyl torsion angle ($\chi_{CN}=265.3°$) of 5′-*O*-acetyl-2′,3′-dideoxy-6,3′-methanouridine (**1**) as determined by X-ray analysis[3] was close to those of usual pyrimidine nucleosides in the anti-conformations.[4] Therefore, an efficient synthesis of 6,3′-methanopyrimidine nucleosides is desirable for further studies of their biological properties, since the previous procedure for the synthesis of 6,3′-methanouridine derivative (**1**) required a multi-step conversion of uridine.[5] This paper describes a versatile synthesis of 6,3′-methanopyrimidine nucleosides and their 2′-deoxy derivatives from a 3-ketosugar and a pyrimidine. A preliminary account of the present study has appeared.[6]

The present synthetic strategy is to provide the ribose derivative with the pyrimidine moiety already attached at the 3-position and then to glycosylate intramolecularly to furnish the 6,3′-methanopyrimidine nucleoside.

1,2-*O*-Isopropylidene-α-D-xylofuranose[7] (**2**) was treated with *tert*-butyldimethylchlorosilane to give the 5-*O*-silyl derivative (**3**). Compound **3** was then oxidized by chromium trioxide to give the 3-ulose (**4**) in a crystalline form. Treatment of **4** with 2,4-dimethoxypyrimidin-6-ylmethyllithium (**5**), prepared from 2,4-dimethoxy-6-methylpyrimidine[8] and *n*-butyllithium, in tetrahydrofuran (THF) afforded 5-*O*-*tert*-butyldimethylsilyl-1,2-*O*-isopropylidene-3(*R*)-(2,4-dimethoxypyrimidin-6-yl)methylribose (**6**), which was crystallized from *n*-hexane. It is expected that the carbanion should attack from the β-side of **4** due to the steric hindrance of the 1,2-*O*-isopropylidene group to α-attack. The 5-*O*-*tert*-butyldimethylsilyl group of **6** was removed, and then benzoylation gave the 5-*O*-benzoate (**7**). Acid hydrolysis of **7** with 90% trifluoroacetic acid followed by acetylation with acetic anhydride and triethylamine in methylene chloride gave an anomeric mixture of the 1,2-di-*O*-acetate (**8**) as a foam. An attempt at the direct acetolysis of **6** to obtain the 1,2-di-*O*-acetate

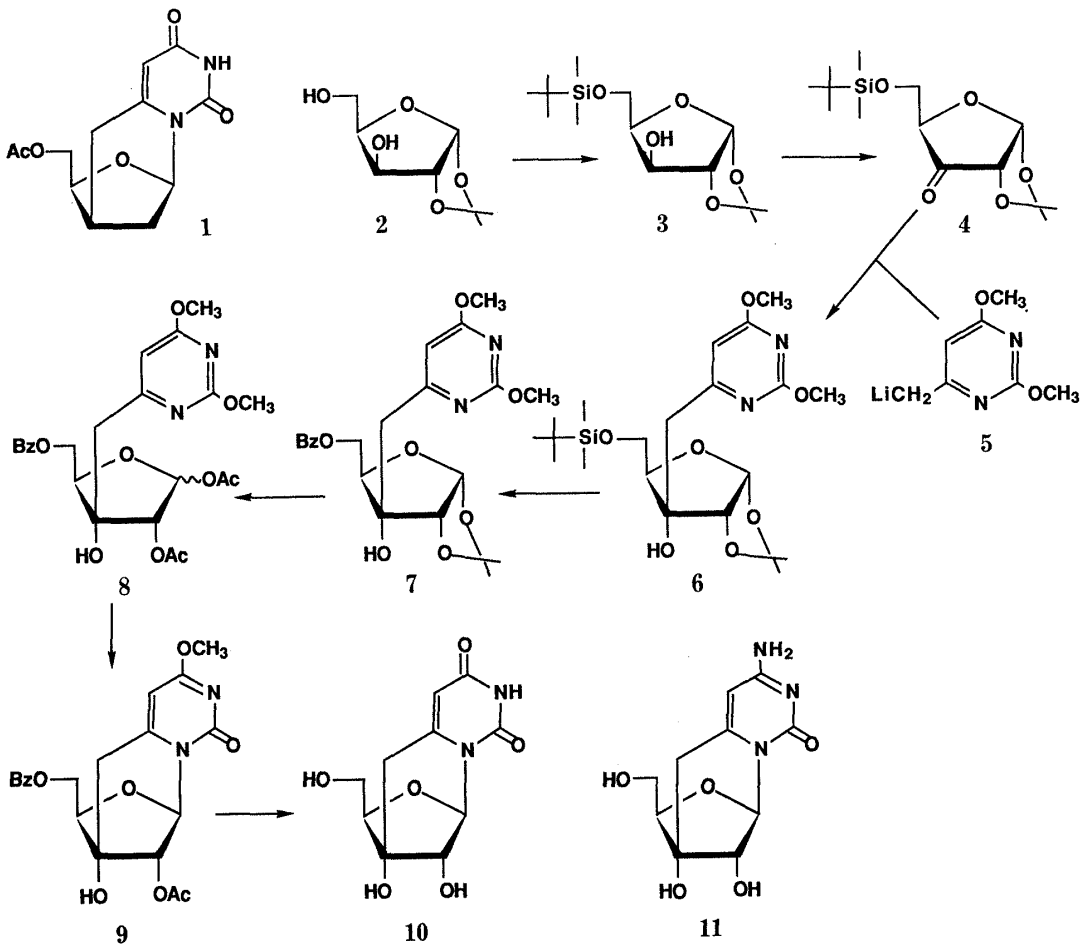

Chart 1

resulted in the 5-*O*-desilylation of **6** followed by a furanose-to-pyranose isomerization. Therefore, the prior conversion of *tert*-butyldimethylsilyl to benzoyl at the 5-position was important.

Treatment of **8** with stannic chloride in acetonitrile at room temperature afforded the 6,3′-methano-O^4-methyluridine derivative (**9**) as a foam. Treatment of **9** with 1 N sodium hydroxide under reflux caused complete deprotection to furnish 6,3′-methanouridine (**10**) in a crystalline form. The nuclear magnetic resonance (NMR) spectrum of **10** was consistent with the proposed structure. Thus, in the spectrum of **10**, both H-1′ (δ 5.82) and H-2′ (δ 3.83) appeared as a singlet, since the dihedral angle of $H_{1'}$–$C_{1'}$–$C_{2'}$–$H_{2'}$ is fixed at *ca.* 90° due to the 6,3′-methano-bridge. The 6,3′-methylene protons (δ 3.06 and 2.83) appeared as a pair of doublets due to the geminal coupling (J = 18.6 Hz). It is worthy of note that the signals of the 5′-protons also showed geminal coupling, probably as a result of hindered rotation of the $C_{4'}$–$C_{5'}$ bond owing to the presence of the 6,3′-methano-bridge. The X-ray diffraction analysis of **10** also confirmed the structure.[9] The circular dichroism (CD) spectrum of **10** showed a strong negative band at the main absorption region, as was predicted from the previously accumulated results.[10]

Treatment of **9** with methanolic ammonia at 100 °C for 20 h afforded 6,3′-methanocytidine (**11**). The NMR spectra and other physical data of **11** showed characteristic features similar to those found for **10**.

While compounds **10** and **11** are regarded as pyrimidine ribonucleosides fixed in the anti-conformation range, their 2′-deoxyribonucleosides may be more useful for the study of

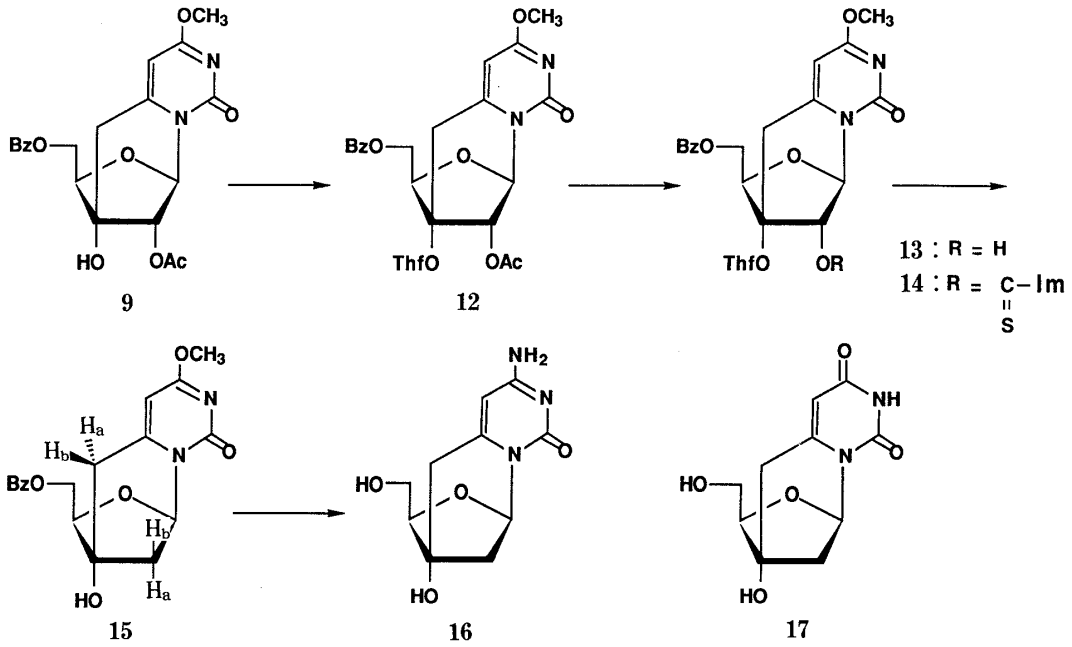

Chart 2

enzymes related to deoxyribonucleic acid (DNA) biosynthesis. The synthesis of the 2′-deoxy derivatives was therefore attempted. Several attempts at the selective 2′-deoxygenation of **10** or **11** by well-documented methods for the conversion of ribonucleosides to 2′-deoxyribonucleosides[11] met with little success, *e.g.*, the 2′-imidazolylthiocarbonylation of **10** and radical deoxygenation, or the 3′,5′-bis-protection of **10** with 1,3-dichloro-1,1,3,3-tetraisopropyl-1,3-disiloxane and further derivatization of the 2′-hydroxyl group, or the conversion of the 2′-hydroxyl group of **10** to the halogeno groups. Similar difficulties in the 2′-derivatization of *C*-cyclonucleosides have been encountered, for example, in the 2′-deoxygenation of 6,5′-cyclo-5′-deoxyuridine.[12]

Therefore, an other route was developed starting from **9**. Treatment of **9** with 2,3-dihydrofuran in the presence of *p*-toluenesulfonic acid in dioxane afforded the 3′-tetrahydrofuranyl derivative (**12**) as a foam. The selective 2′-de-*O*-acylation of **12** was achieved by treatment with methanolic triethylamine at room temperature for 3 h to give the 2′-alcohol (**13**). The imidazolylthiocarbonylation[13] of **13** by treatment with *N*,*N*′-thiocarbonyldiimidazole gave a crude product (**14**), which was subjected to the radical deoxygenation by treatment with tributyltin hydride and azobisisobutyronitrile (AIBN) to give the 2′-deoxy compound, which was subsequently treated with trifluoroacetic acid to furnish crystalline 5′-*O*-benzoyl-2′-deoxy-O^4-methyl-6,3′-methanouridine (**15**). The ^{1}H-NMR spectrum of pure **15** exhibited a doublet due to H-1′ (δ 6.61), a doublet due to H-2′b, and three sets of doublets due to H-2′a split by H-1′, H-2′b, and by one proton (H-6′a) at the 6,3′-methano-bridge situated in the W-type conformation. This result showed that the 2′-deoxygenation of **9** had proceeded to give **15**. Treatment of **15** with methanolic ammonia at 100 °C for 22 h furnished 2′-deoxy-6,3′-methanocytidine (**16**). Alkaline hydrolysis of **15** afforded 2′-deoxy-6,3′-methanouridine (**17**), as expected.

In conclusion, the present synthetic route will be useful to provide the 6,3′-methanopyrimidine nucleosides in quantities for use in biochemical studies of these conformationally fixed nucleosides. Furthermore, the present method may be adaptable not only for the synthesis of 6,3′-cyclopyrimidine nucleosides but also for various types of carbon-bridged pyrimidine and purine cyclonucleosides.

Experimental

Melting points were determined on a Yanagimoto MP-3 micromelting point apparatus and are uncorrected. The ^{1}H-NMR spectra were recorded on a JEOL FX-100FT or FX-270FT spectrometer in an appropriate solvent with tetramethylsilane as an internal standard. Chemical shifts are reported in ppm (δ), and signals are described as s (singlet), d (doublet), t (triplet), m (multiplet) or br (broad). All exchangeable protons were confirmed by addition of D_2O. Ultraviolet absorption spectra (UV) were recorded on a Shimadzu UV-260 spectrophotometer. Mass spectra (MS) were measured on a JEOL D-300 spectrometer. CD spectra were recorded on a JASCO J-500A spectropolarimeter at room temperature. Silica gel used for column chromatography was Merck Kieselgel 60 (70—200 mesh). Thin-layer chromatography (TLC) was carried out on Merck pre-coated $60F_{254}$ plates.

5-*O*-*tert*-Butyldimethylsilyl-1,2-*O*-isopropylidene-α-D-xylose (3)——A mixture of **2**[7] (19 g, 10 mmol) and *tert*-butyldimethylchlorosilane (18.1 g, 12 mmol) in pyridine (200 ml) was stirred at room temperature for 1.5 h. The solvent was removed *in vacuo* and the residue was dissolved in EtOAc, washed with H_2O twice, dried over Na_2SO_4, and filtered. The filtrate was concentrated and the residue was chromatographed on silica gel (7.5 × 11 cm) with 0—5% MeOH in $CHCl_3$. The eluate was concentrated to leave **3** (30.5 g, 100%) as a foam. MS *m/z*: 304 (M^+), 289 ($M^+ - Me$). ^{1}H-NMR ($CDCl_3$): 5.92 (1H, d, H-1, J=3.66 Hz), 4.46 (1H, d, H-2), 4.08 (3H, br s, H-4, 5), 1.45, 1.28 (3H each, s, iso-Pr). 0.86 (9H, s, *tert*-Bu), 0.07 (6H, s, Me).

5-*O*-*tert*-Butyldimethylsilyl-1,2-*O*-isopropylidene-α-D-erythro-3-pentulofuranose (4)——A solution of **3** (15.74 g, 51.8 mmol) in CH_2Cl_2 (50 ml) was added to the previously prepared CH_2Cl_2 solution (250 ml) containing CrO_3–pyridine–Ac_2O (15.5 g, 3 eq : 26 ml : 5 ml). The mixture was stirred for 1.5 h at room temperature and then added dropwise to EtOAc (1000 ml) under stirring. The precipitate was filtered off and the filtrate was concentrated. The residue was chromatographed on silica gel (6.6 × 17.5 cm) with 5% EtOAc in *n*-hexane. The eluate was concentrated and the residue was crystallized from *n*-hexane to give **4** (12.1 g, 77%), mp 40—43 °C. MS *m/z*: 287 ($M^+ - Me$), 245 ($M^+ - tert$-Bu). ^{1}H-NMR ($CDCl_3$): 6.13 (1H, d, H-1, J=4.4 Hz), 4.37 (1H, m, H-4), 4.28 (1H, dd, H-2, $J_{2,4}$=1.1 Hz), 3.85 (2H, m, H-5), 1.45 (6H, s, iso-Pr), 0.86 (9H, s, *tert*-Bu), 0.056, 0.031 (3H each, s, Me). *Anal.* Calcd for $C_{14}H_{26}O_5Si$: C, 55.59; H, 8.67. Found: C, 55.55; H, 8.69.

5-*O*-*tert*-Butyldimethylsilyl-1,2-*O*-isopropylidene-3(*R*)-(2,4-dimethoxypyrimidin-6-yl)methyl-α-D-ribofuranose (6)——2,4-Dimethoxy-6-methylpyrimidine (3.08 g, 20 mmol) was suspended in THF (100 ml) at −70 °C. *n*-BuLi (1.58 M in *n*-hexane, 12.7 ml, 1 eq) was slowly added to the suspension, the temperature was raised to −35 °C, and the whole was stirred for 1 h to prepare **5**. A solution of **4** (6.30 g, 1.04 eq) in THF (20 ml) was added dropwise to the above suspension, then the whole was stirred for 1 h at −35 °C. The solution was neutralized by addition of AcOH and the solvent was removed *in vacuo*. The residue was partitioned between EtOAc and H_2O, the organic layer was dried over Na_2SO_4, then the solvent was removed *in vacuo*. The residue was chromatographed on silica gel (7.4 × 15 cm) with 10—20% EtOAc in *n*-hexane. The eluate was concentrated to leave **6** (6.87 g, 75%). Crystallization from *n*-hexane gave a pure sample for analysis, mp 79—81 °C. MS *m/z*: 456 (M^+), 441 ($M^+ - Me$), 399 ($M^+ - tert$-Bu). ^{1}H-NMR ($CDCl_3$): 6.33 (1H, s, H-5), 5.79 (1H, d, H-1′, J=3.9 Hz), 4.79 (1H, s, HO-3′), 4.28 (1H, d, H-2′), 4.06—3.84 (3H, m, H-4′, 5′), 3.97 (6H, s, MeO), 2.99 (1H, d, H-6′a, $J_{a,b}$=14.6 Hz), 2.62 (1H, d, H-6′b), 1.58, 1.49 (3H each, s, iso-Pr), 0.90 (9H, s, *tert*-Bu), 0.09 (6H, s, Me). *Anal.* Calcd for $C_{21}H_{36}N_2O_7Si$: C, 55.24; H, 7.95; N, 6.14. Found: C, 55.42; H, 7.98; N, 6.19.

5-*O*-Benzoyl-1,2-*O*-isopropylidene-3(*R*)-(2,4-dimethoxypyrimidin-6-yl)methyl-α-D-ribofuranose (7)——A mixture of **6** (6.25 g, 13.9 mmol) in THF (50 ml) and tetrabutylammonium fluoride (1 M in THF, 14 ml) was stirred for 10 min at room temperature. The solvent was removed *in vacuo* and the residue was dissolved in pyridine (70 ml). Benzoyl chloride (4 ml) was added to the solution in an ice-bath and the solution was stirred overnight at room temperature. The solvent was removed *in vacuo*, the residual pyridine was removed by co-evaporation with toluene three times, and the residue was dissolved in $CHCl_3$. The solution was washed with H_2O, saturated $NaHCO_3$ in H_2O, and H_2O, then the organic layer was dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel (7.7 × 16.5 cm) with 20—40% EtOAc in *n*-hexane. The eluate was concentrated to leave **7** (5.67 g, 91%). Crystallization from iso-PrOH gave a pure sample, mp 132—134 °C. MS *m/z*: 446 (M^+), 431 ($M^+ - Me$), 388 ($M^+ - 58$). ^{1}H-NMR ($CDCl_3$): 8.1—8.0 (2H, m, Bz), 7.6—7.3 (3H, m, Bz), 6.36 (1H, s, H-5), 5.84 (1H, d, H-1′, J=3.9 Hz), 5.18 (1H, s, HO-3′), 4.72—4.42 (2H, m, H-5′), 4.39 (1H, m, H-4′), 4.30 (1H, d, H-2′), 3.98 (6H, s, MeO), 3.01 (1H, d, H-6′a, $J_{a,b}$=14.4 Hz), 2.68 (1H, d, H-6′b), 1.62, 1.32 (3H each, s, iso-Pr). *Anal.* Calcd for $C_{22}H_{26}N_2O_8$: C, 59.18; H, 5.87; N, 6.28. Found: C, 58.93; H, 5.89; N, 6.35.

1,2-Di-*O*-acetyl-5-*O*-benzoyl-3(*R*)-(2,4-dimethoxypyrimidin-6-yl)methyl-D-ribofuranose (8)——A solution of **7** (5.67 g, 12.7 mmol) in 90% trifluoroacetic acid (50 ml) was stirred at room temperature for 1.5 h. The solvent was removed *in vacuo* and the residual acid was co-distilled with iso-PrOH three times. The residue was dissolved in CH_2Cl_2–Et_3N (5 : 1, 50 ml) and Ac_2O (5 ml) was added. The mixture was stirred for 2 h, then MeOH was added. The whole was diluted with $CHCl_3$, washed with saturated $NaHCO_3$ in H_2O three times, then dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel (5.3 × 24 cm) with 40% EtOAc in *n*-hexane. The eluate was concentrated to leave **8** (5.71 g, 92%) as a foam. MS *m/z*: 490 (M^+), 447 ($M^+ - Ac$), 431 ($M^+ - AcO$). ^{1}H-NMR ($CDCl_3$): 8.15—8.01 (2H, m, Bz), 7.53—7.30 (3H, m, Bz), 6.43 (0.3H, d, J=5.00 Hz), 6.27—

6.19 (1.7H, m, H-1′, 5), 5.22, 5.04 (1H total, d, H-2′, J = 1.71 Hz), 4.65—4.08 (3H, m, H-4′, 5′), 3.97, 3.96 (3H each, s, MeO), 3.09, 2.99 (2H, br s, H-6′), 2.13, 2.09, 2.05, 2.04 (6H total, s, Ac).

2′-*O*-Acetyl-5′-*O*-benzoyl-*O*^{4}-methyl-6,3′-methanouridine (9)——Stannic chloride (0.45 ml in 5 ml of acetonitrile, 3.69 mmol) was added to a solution of **8** (900 mg, 1.84 mmol) in acetonitrile (15 ml) under cooling in an ice-bath. The solution was stirred for 3 h at room temperature and the solvent was removed *in vacuo*. The residue was taken up in $CHCl_3$ and washed with saturated $NaHCO_3$ in H_2O. The precipitate was filtered off through a celite bed, and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ and the combined $CHCl_3$ layer was dried over Na_2SO_4. The solvent was evaporated off and the residue was chromatographed on silica gel (2.3 × 23 cm) with 1% MeOH in $CHCl_3$. The eluate was concentrated to leave **9** (630 mg, 82%) as a foam. MS m/z: 416 (M^+), 373 ($M^+ - Ac$). UV λ_{max}^{MeOH}: 281 nm. ^{1}H-NMR ($CDCl_3$): 8.00—7.90 (2H, m, Bz), 7.67—7.28 (3H, m, Bz), 6.50 (1H, s, H-1′), 5.72 (1H, s, H-5), 5.11 (1H, s, H-2′), 4.69—4.30 (3H, m, H-4′, 5′), 3.88 (3H, s, MeO), 3.65 (1H, s, HO-3′), 3.36 (2H, dd, H-6′), 2.21 (3H, s, Ac).

6,3′-Methanouridine (10)——Compound **9** (2.0 g, 4.80 mmol) was dissolved in dioxane (20 ml) and 2 N NaOH (20 ml) was added to the solution. The mixture was heated at 100 °C for 20 min. The solution was neutralized by addition of Dowex 50 (H^+). The resin was filtered off and the filtrate was extracted with EtOEt to remove benzoic acid. The aqueous layer was concentrated and the residue was crystallized from H_2O to give **10** (0.66 g, 53%), mp > 300 °C. MS m/z: 256 (M^+), 238 ($M^+ - H_2O$). UV $\lambda_{max}^{H_2O}$: 266 nm (ε, 10900). CD (H_2O) [θ] (nm): −19600 (260). ^{1}H-NMR (DMSO-d_6): 11.22 (1H, br s, HN-3), 5.82 (1H, s, H-1′), 5.48 (1H, s, H-5), 3.97 (1H, dd, H-4′, $J_{4',5'}$ = 2.7, 7.1 Hz), 3.83 (1H, s, H-2′), 3.63 (1H, dd, H-5′a, $J_{a,b}$ = 12.0 Hz), 3.36 (1H, dd, H-5′b), 3.06 (1H, d, H-6′a, $J_{a,b}$ = 18.6 Hz), 2.83 (1H, d, H-6′b). The signals of the hydroxyl protons were not detected. *Anal.* Calcd for $C_{10}H_{12}N_2O_6$: C, 46.87; H, 4.72; N, 10.94. Found: C, 46.82; H, 4.74; N, 10.73.

6,3′-Methanocytidine (11)——Compound **9** (3.01 g, 7.23 mmol) was heated in MeOH saturated with NH_3 (30 ml) at 100 °C for 20 h in a sealed tube. After cooling, the separated crystals were collected by filtration to give **11** (1.14 g, 62%), mp 310 °C. MS m/z: 255 (M^+). UV $\lambda_{max}^{H_2O}$: 275 nm; $\lambda_{max}^{0.1\,N\,HCl}$: 282 nm. ^{1}H-NMR (DMSO-d_6): 7.07 (2H, br, H_2N), 5.95 (1H, s, H-1′), 5.80 (1H, d, HO-2′, J = 3.4 Hz), 5.50 (1H, s, H-5), 5.45 (1H, s, HO-3′), 4.74 (1H, t, HO-5′, J = 5.4 Hz), 3.95 (1H, dd, H-4′), 3.75 (1H, d, H-2′), 3.55 (1H, m, H-5′a), 3.2 (1H, m, H-5′b), 2.97 (1H, d, H-6′a, $J_{a,b}$ = 17.8 Hz), 2.85 (1H, d, H-6′b). *Anal.* Calcd for $C_{10}H_{13}N_3O_5 \cdot H_2O$: C, 43.95; H, 5.53; N, 15.38. Found: C, 43.92; H, 5.56; N, 15.65.

2′-*O*-Acetyl-5′-*O*-benzoyl-3′-*O*-tetrahydrofuranyl-*O*^{4}-methyl-6,3′-methanouridine (12)——A mixture of **9** (2.19 g, 5.26 mmol), 2,3-dihydrofuran (0.8 ml, 10.5 mmol) and *p*-toluenesulfonic acid (60 mg) in dioxane (40 ml) was stirred overnight at room temperature. The solution was neutralized by addition of anhydrous K_2CO_3. The precipitate was filtered off and the filtrate was concentrated. The residue was dissolved in EtOAc, the solution was washed with H_2O, and the organic layer was dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel (3.6 × 17 cm) with $CHCl_3$. The solvent was removed *in vacuo* to leave **12** (2.09 g, 82%) as a foam. MS m/z: 486 (M^+), 416 ($M^+ -$ Thf). ^{1}H-NMR ($CDCl_3$): 8.00—7.95 (2H, m, Bz), 7.56—7.37 (3H, m, Bz), 6.53, 6.45 (1H, s, H-1′), 5.72, 5.69 (1H, s, H-5), 5.50, 5.36 (1H, m, H-2 of Thf), 5.39—5.31 (1H, s, H-2′), 4.65—4.32 (3H, m, H-4′, 5′), 3.91 (3H, s, MeO), 3.90—3.82 (2H, m, H-5 of Thf), 3.62—3.30 (2H, m, H-6′), 2.20, 2.19 (3H, s, Ac), 1.95—1.80 (4H, s, H-3,4 of Thf).

5′-*O*-Benzoyl-3′-*O*-tetrahydrofuranyl-*O*^{4}-methyl-6,3′-methanouridine (13)——Compound **12** (2.09 g, 4.27 mmol) was dissolved in MeOH–Et_3N (10 : 1, 44 ml). After 3 h at room temperature, the solvent was removed *in vacuo* and the residue was chromatographed (3.2 × 16 cm) with 0—1% MeOH in $CHCl_3$. The eluate was concentrated to leave **13** (1.51 g, 80%) as a foam. MS m/z: 444 (M^+), 374 ($M^+ -$ Thf). ^{1}H-NMR ($CDCl_3$): 7.99—7.94 (2H, m, Bz), 7.56—7.37 (3H, m, Bz), 6.55, 6.47 (1H, s, H-1′), 5.68 (1H, br s, H-5), 5.62, 5.50 (1H, br d, H-2 of Thf), 4.63—4.29 (3H, m, H-4′, 5′), 4.23, 4.18 (1H, br s, H-2′), 3.91 (3H, s, MeO), 4.11—3.89 (2H, m, H-5 of Thf), 3.30—3.20 (2H, br dd, H-6′), 2.04—1.86 (4H, m, H-3,4 of Thf).

5′-*O*-Benzoyl-3′-*O*-tetrahydrofuranyl-2′-*O*-imidazolylthiocarbonyl-*O*^{4}-methyl-6,3′-methanouridine (14)——A solution of **13** (1.5 g, 3.38 mmol) and *N*,*N*′-thiocarbonyldiimidazole (1.3 g, 6.76 mmol) in dimethylformamide (15 ml) was stirred overnight at room temperature. The solvent was removed *in vacuo*, the residue was dissolved in EtOAc, this solution was washed with H_2O three times, and the organic layer was dried over Na_2SO_4. The solution was concentrated and the residue was chromatographed on silica gel (3.2 × 16 cm) with $CHCl_3$ to give **14** (1.36 g, 72%) as a foam. ^{1}H-NMR ($CDCl_3$): 8.41, 8.39 (1H, s, H-2 of imidazolyl), 8.06, 7.98 (2H, m, Bz), 7.69, 7.67 (1H, br s, H-5 of imidazolyl), 7.66—7.40 (3H, m, Bz), 7.11 (1H, br s, H-4 of imidazolyl), 6.78, 6.74 (1H, s, H-1′), 6.02, 5.87 (1H, s, H-2′), 5.74, 5.75 (1H, s, H-5), 5.49, 5.36 (1H, br d, H-2 of Thf), 4.67—4.41 (3H, m, H-4′, 5′), 3.93 (3H, s, MeO), 3.93—3.69 (3H, m, H-6′a, H-5 of Thf), 3.45—3.32 (1H, d, H-6′b, $J_{a,b}$ = 18.68, 17.95 Hz), 1.93—1.77 (4H, m, H-3,4 of Thf).

5′-*O*-Benzoyl-2′-deoxy-*O*^{4}-methyl-6,3′-methanouridine (15)——A mixture of **14** (1.35 g, 2.44 mmol), Bu_3SnH (2 ml, 7.32 mmol) and AIBN (20 mg) in toluene (40 ml) was heated at 110 °C for 1.5 h. After cooling, the solvent was removed *in vacuo* and the residue was chromatographed on silica gel (3.9 × 30 cm) with 0—1% MeOH in $CHCl_3$. From the less polar fractions, the 2′-deoxy compound (450 mg, 43%) was obtained. From the second fraction, **13** (550 mg, 51%) was recovered. The 2′-deoxy compound (450 mg, 1.05 mmol) was dissolved in 90% trifluoroacetic acid (5 ml) and the solution was stirred for 10 min at room temperature. The solvent was removed *in vacuo* and residual

acid was co-distilled with iso-PrOH three times. The residue was dissolved in $CHCl_3$ and washed with H_2O, then the organic layer was dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was triturated in EtOEt–*n*-hexane to give a solid, which was crystallized from EtOH to give **15** (260 mg, 73%), mp 192—193 °C. MS *m/z*: 358 (M^+), 237 ($M^+ - BzO$). ^{1}H-NMR ($CDCl_3$): 7.99—7.95 (2H, m, Bz), 7.61—7.40 (3H, m, Bz), 6.68 (1H, d, H-1′, J = 5.13 Hz), 5.71 (1H, s, H-5), 4.53 (1H, dd, H-5′a, $J_{4',5'a}$ = 5.50 Hz, $J_{5'a,b}$ = 11.72 Hz), 4.34 (1H, dd, H-5′b, $J_{4',5'b}$ = 5.13 Hz), 4.24 (1H, m, H-4′), 3.91 (3H, s, MeO), 3.34 (1H, dd, H-6′a, $J_{6'a,b}$ = 18.32 Hz, $J_{6'a,2'a}$ = 2.56 Hz), 3.22 (1H, d, H-6′b), 2.69 (1H, ddd, H-2′a, $J_{2'a,b}$ = 11.36 Hz), 2.14 (1H, d, H-2′b). *Anal.* Calcd for $C_{18}H_{18}N_2O_6$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.36; H, 5.04; N, 7.73.

2′-Deoxy-6,3′-methanocytidine (16)——Compound **15** (100 mg, 0.279 mmol) in MeOH saturated with NH_3 (4 ml) was heated at 100 °C for 22 h in a sealed tube. The solvent was removed *in vacuo* and the residue was chromatographed on Dowex 50W-X8 (1.2 × 9.3 cm) with 1 N ammonia. The eluate was concentrated and the residue was crystallized from MeOH–EtOAc to give **16** (64 mg, 91%), mp 275—278 °C (dec.). MS *m/z*: 239 (M^+). UV $\lambda_{max}^{H_2O}$ nm (ε): 276 (9500); $\lambda_{max}^{0.1\,N\,HCl}$: 283 (13500). CD H_2O [θ] (nm): −17600 (275); 0.1 N HCl: −23600 (283). ^{1}H-NMR (D_2O, sodium trimethylsilylpropanesulfonate (TSPS) as the internal standard): 6.42 (1H, d, H-1′, $J_{1',2'a}$ = 4.40 Hz), 3.98 (1H, dd, H-4′, $J_{4',5'a}$ = 3.48 Hz, $J_{4',5'b}$ = 6.51 Hz), 3.82 (1H, dd, H-5′a, $J_{5'a,b}$ = 12.2 Hz), 3.61 (1H, dd, H-5′b), 3.20 (2H, br s, H-6′), 2.62 (1H, br dd, H-2′a, $J_{2'a,b}$ = 11.34 Hz), 2.19 (1H, d, H-2′b). *Anal.* Calcd for $C_{10}H_{13}N_3O_4 \cdot 1/4\,H_2O$: C, 49.27; H, 5.48; N, 17.24. Found: C, 49.52; H, 5.64; N, 16.90.

2′-Deoxy-6,3′-methanouridine (17)——Compound **15** (50 mg, 0.14 mmol) was dissolved in 2 N NaOH–dioxane (1 : 1, 2 ml) and the solution was stirred at 100 °C for 30 min. The solution was neutralized by addition of Dowex 50W-X8 (H^+) and the resin was filtered off. The filtrate was concentrated and the residue was subjected to preparative TLC developed twice with MeOH–$CHCl_3$ (1 : 8). From the appropriate band, **17** (31 mg, 91%) was obtained as a solid, which was crystallized from EtOH, mp 192.0—192.5 °C. UV $\lambda_{max}^{H_2O}$ nm (ε): 268 (10400). CD H_2O [θ] (nm): −18000 (265). MS *m/z*: 240 (M^+), 222 ($M^+ - H_2O$). ^{1}H-NMR (D_2O, TSPS as the internal standard): 6.40 (1H, d, H-1′, $J_{1',2'a}$ = 4.76 Hz), 5.74 (1H, s, H-5), 4.00 (1H, m, H-4′, $J_{4',5'a}$ = 3.66 Hz, $J_{4',5'b}$ = 6.59 Hz), 3.84 (1H, ddd, H-2′a, $J_{2'a,b}$ = 11.35 Hz), 2.19 (1H, d, H-2′b). *Anal.* Calcd for $C_{10}H_{12}N_2O_5 \cdot H_2O$: C, 46.51; H, 5.46; N, 10.85. Found: C, 46.34; H, 5.44; N, 10.79.

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