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Synthesis of 6,2′-Methano-cyclouridine, a Uridine Fixed in High-Anti Conformation (Nucleosides and Nucleotides. LX[1])

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The reaction of methylenetriphenylphosphorane with 2′-keto-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)uridine afforded the 2′-methyleneuridine (**1**). Oxidation of **1** with osmium tetroxide and *tert*-butyl hydroperoxide or *N*-methylmorpholine-*N*-oxide afforded a mixture of a 2′-hydroxymethyluridine (**2**) and its arabinosyl isomer. Oxidation at lower temperature gave the former as the main product. Compound **2** was converted to the 5-bromo-2′-iodomethyl derivative (**3**) through the 2′-mesyloxy compound, and **3** was treated with tri-*n*-butyltin hydride to give the 6,2′-methano-cyclo-5,6-dihydro derivative (**4**). Compound **4** was dehydrobrominated and deprotected to furnish 6,2′-methano-cyclouridine, a uridine fixed in high-anti conformation. Some results on the synthesis and cleavage of the 2′-spiro-epoxy derivative prepared from the 2′-ketouridine are also presented.

Keywords——uridine; 6,2′-methano-cyclouridine; *C*-cyclouridine; nucleoside conformation; osmium tetroxide; tri-*n*-butyltin hydride; Wittig reaction; radical cyclization; NMR; CD

In our previous reports we have described methods for the synthesis of various carbon-bridged cyclonucleosides involving cyclization of a radical generated at the sugar portion to the purine or pyrimidine moiety as the key step.[2] More recently, we have reported the use of an ionic cyclization in the synthesis of 2′-deoxy-6,2′-methano-cyclouridine.[1] However, the latter method could not be used to synthesize ribosyl derivatives. This paper deals with the synthesis of 6,2′-methano-cyclouridine as a model uridine conformationally fixed in the high-anti form. For this purpose, the 3′,5′-*O*-protected 2′-ketouridine (**1**) may be a suitable starting nucleoside. In fact, we have already reported[3] the synthesis of **1** and its reaction with a Wittig reagent leading to the synthesis of 2′-ethoxycarbonylmethyleneuridine (**2**). Compound **2** has been utilized in the synthesis of 2′-deoxy-6,2′-methano-[1] and 2′-deoxy-6,2′-ethano-[3] cyclouridines. It was expected that other Wittig reagents would also be effective for the derivatization. Therefore we investigated the synthesis of the 2′-spiroepoxide and 2′-methylene derivatives from **1**.

Treatment of **1** with dimethyloxosulfonium methylide at 0 °C afforded the 2′-spiro epoxide (**3**) in 63% yield. The nuclear magnetic resonance (NMR) spectrum of **3** showed the methylene protons of the 2′-spiro epoxide at 3.25 and 3.00 ppm as doublets, and the formation of the isomer at the 2′-position was not observed. Treatment of **3** with sodium acetate in acetic acid gave a product (**4**) in 55% yield. The NMR spectrum of **4** showed the methylene protons of the 2′-acetoxymethyl group at 4.55 and 4.36 ppm with geminal coupling ($J=12.2$ Hz) due to hindered bond rotation, along with the signals of the methyl protons of an acetyl group and a hydroxyl proton at 2.17 and 3.6 ppm, respectively. Since the signals of the oxirane methylene protons had disappeared, it is clear that ring opening of the oxirane group of **3** had occurred. To elucidate the stereochemistry at the 2′-position of **4**, it was converted to the O^6-anhydronucleoside. Bromination of **4** with bromine in acetic acid gave the 5-bromo derivative (**5**). Treatment of **5** with 1,5-diazabicyclo[5.4.0]undecene-5 (DBU) in

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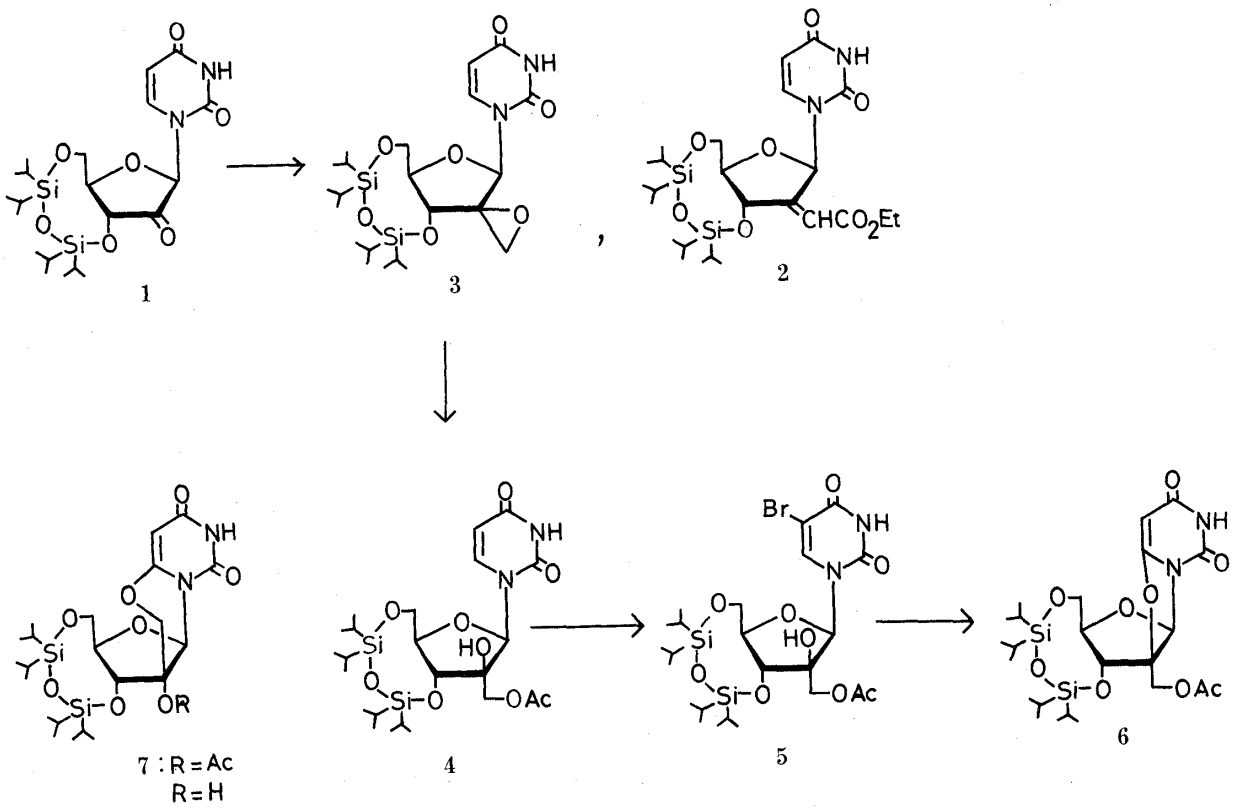

Chart 1

dioxane gave the O^6,2′-anhydro derivative of arabinofuranosyluracil (**6**). The ultraviolet (UV) absorption maximum of **6** appeared at 248 nm, resembling that of O^6,2′-cyclouridine (251 nm[4]) but not those of O^6,3′- or O^6,5′-cyclouridines (259 and 261 nm[5]). This would suggest that the structure of the O^6-cyclouridine is **6** and not **7** [R = Ac, formation of **7** (R = H) will be discussed later]. It means that compound **3** has *S*-configuration at the 2′-spiro carbon and the attack of the ylide occurred from the bottom side of the lactol ring. Therefore this compound turned out to be unsuitable for the present purpose. Therefore another route was explored.

Treatment of **1** with methylenetriphenylphosphorane afforded the 2′-deoxy-2′-methyleneuridine (**8**) in 58% yield crystalline form. The 2′-methylene protons appeared at 5.54 and 5.46 ppm, respectively, as double doublets due to allylic coupling. The *cis*-hydroxylation of the 2′-methylene group is expected to give the 2′-hydroxymethyl compound with the desired configuration, because the reagent should attack predominantly from the bottom side. Compound **8** was treated with *tert*-butyl hydroperoxide in the presence of a catalytic amount of osmium tetroxide at room temperature to give the diols (**9** and **10**). On the basis of NMR data, the products were shown to be a mixture of 2′-hydroxymethyluridine (**9**) and its arabinosyl isomer (**10**) in a ratio of 2 : 1. The methylene proton signals of the 2′-hydroxymethyl group of **9** appeared at 3.44 and 3.84 ppm (J_{gem} = 12.0 Hz), while those of **10** appeared at lower field (3.94 ppm) with no appreciable difference between the chemical shifts of the pair of methylene protons. Similar relationships had been observed previously in the chemical shifts of methylene groups of the 3′-hydroxymethyl groups of 2′,3′-dideoxy-3′(*R* and *S*)-hydroxymethyluridines.[6] For further determination of the configuration at the 2′-position, the mixture was brominated and then treated with DBU in dioxane to effect O^6-cyclization, giving **7** (R = H) and **11**. The products were separated by preparative thin layer chromatography. Compound **7** (R = H) showed λ_{max} at 258 nm while **11** showed λ_{max} at

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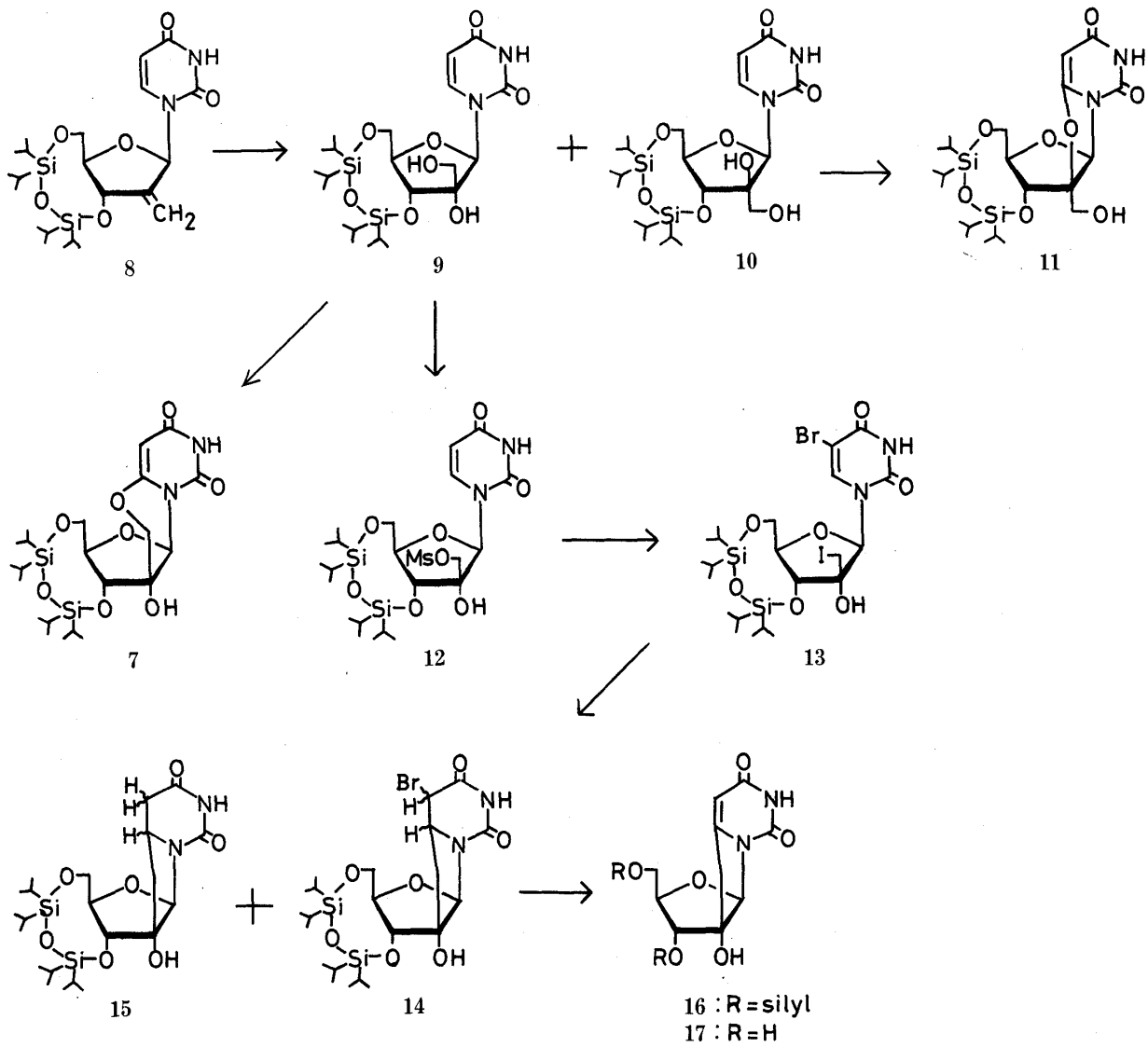

Chart 2

248 nm. As described before, O^6,2′-cyclouridine exhibits a UV maximum at 249 nm, so **11** must be the arabinosyl isomer and **7** (R = H) should be the ribo isomer. In the latter case, the glycosyl torsion angle should be rather close to that of the O^6,3′-cyclouridine, hence the UV maximum should be similar.

The ratio of the formation of **9** and **10** is temperature-dependent, and the oxidation carried out at 0 °C gave **9** as the predominant product (4 : 1) in a combined yield of 92%, when *N*-methylmorpholine-*N*-oxide and osmium tetroxide were used.

The mixture of **9** and **10** was mesylated and the 2′(*R*)-isomer (**12**) was separated in crystalline form in 55% yield. Compound **12** was then brominated at the C-5 position and treated with lithium iodide to give 2′(*R*)-iodomethyl-5-bromouridine (**13**). Treatment of **13** with tri-*n*-butyltin hydride and azobisisobutyronitrile (AIBN) in refluxing benzene gave the 5-bromo-6,2′-methano-cyclo-5,6-dihydrouridine (**14**) in 32% yield. Addition of an excess of the hydride did not improve the yield, but presumably resulted in the formation of the 5,6-dihydro derivative (**15**). The low yield of the product **14** may be due to the presence of the 2′-hydroxyl function which catalytically decomposed tri-*n*-butyltin hydride to hydrogen and di(tributyltin). Treatment of **14** with DBU gave the 6,2′-methano-cyclo derivative (**16**) in a crystalline form, and this product was desilylated to furnish 6,2′-methano-cyclouridine (**17**).

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Although the last compound was not obtained as crystals and was not fully characterized, **17** migrated on paper electrophoresis in borate buffer as a 2′,3′-cyclic borate, like uridine, proving the presence of a *cis*-vicinal diol system. Compound **17** is the first example of uridine fixed in a high-anti conformation. Optimization of the sequence of reactions leading to **17** is still required to obtain a sufficient quantity of the compound for biochemical investigations.

The circular dichroism (CD) spectra of **16** showed a negative band at the main absorption region and its molar ellipticity was similar to that of 2′-deoxy-6,2′-methano-cyclouridine,[1] as expected from its glycosyl torsion angle.

Experimental

All 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-100 FT or FX-200FT spectrometer in $CDCl_3$ 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. UV absorption spectra were recorded with a Shimadzu UV-240 spectrophotometer. CD spectra were recorded on a JASCO J-40 spectropolarimeter at room temperature. Thin layer chromatography (TLC) was carried out on Merck pre-coated plates $60F_{254}$. Silica gel for column chromatography or preparative thin layer chromatography (pTLC) was Wako gel C-200. The starting nucleoside, uridine, was from Yamasa Shoyu Co., Ltd.

2′-Deoxy-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)uridine-2′(*S*)-spiro-epoxide (3)——A 20 mg portion of 50% NaH was stirred in petroleum ether (3 ml) under an Ar atmosphere for 30 min, then the solvent was decanted off. DMSO (2 ml) and trimethyloxosulfonium iodide (130 mg, 3 eq) were added and the mixture was stirred for 30 min under an Ar atmosphere. THF (3 ml) was injected and then **1** (97 mg) in 3 ml of THF was gradually injected at 0 °C. The mixture was stirred for 1 h, then $CHCl_3$ (15 ml) and H_2O (10 ml) were added, and the organic layer was filtered through a Whatman 1-PS filter paper. The filtrate was concentrated and the residue was subjected to pTLC with $CHCl_3$–AcOEt (2 : 1). The appropriate band was extracted with the same solvent (1 : 1) and the solvent was removed *in vacuo* to leave 63 mg (63%) of **3** as a foam. NMR: 8.30 (1H, br, HN-3), 7.44 (1H, d, H-6, $J_{5,6}$ = 8.3 Hz), 6.20 (1H, s, H-1′), 5.74 (1H, dd, H-5, $J_{5,3}$ = 2.4 Hz), 4.49 (1H, d, H-3′, $J_{3',4'}$ = 9.8 Hz), 4.11 (2H, br d, H-5′, J = 3 Hz), 3.25 (1H, d, $H_{2''a}$, $J_{a,b}$ = 5.5 Hz), 3.00 (1H, d, H-2″b), 1.09 (28H, m, isoPr). MS *m/z*: 455 (M − 43).

1-[2-Acetoxymethyl-3,5-*O*-(tetraisopropyldisiloxane-1,3-diyl)-arabinofuranosyl]uracil (4)——Compound **3** (504 mg) was dissolved in 10 ml of AcOH containing 820 mg of NaOAc, and the solution was refluxed for 3 h. The solvent was removed *in vacuo* and the residue was partitioned between AcOEt and H_2O. The organic layer was concentrated and the residue was dissolved in $CHCl_3$. This solution was applied to a column of silica gel (15 g). The eluate with $CHCl_3$–AcOEt (9 : 1) was concentrated to leave 311.2 mg (55%) of **4** as a syrup. NMR: 9.2 (1H, br, HN-3), 7.76 (1H, d, H-6, J = 8.1 Hz), 6.00 (1H, s, H-1′), 5.69 (1H, d, H-5, $J_{5,3}$ = 1 Hz), 4.55 (1H, d, H-2″a, $J_{a,b}$ = 12.2 Hz), 4.36 (1H, d, H-2″b), 4.29 (1H, d, H-3′, $J_{3',4'}$ = 9.0 Hz), 4.1 (2H, m, H-5′), 3.9—3.8 (1H, m, H-4′), 3.6 (1H, br, HO-2′), 2.17 (3H, s, Ac). MS *m/z*: 515 (M − isoPr).

1-[2-Acetoxymethyl-3,5-*O*-(tetraisopropyldisiloxane-1,3-diyl)-arabinofuranosyl]-5-bromouracil (5)——Compound **4** (50.5 mg) was dissolved in 1 ml of AcOH containing 22 mg of NaOAc. Bromine (5 μl, 1.1 eq) was added and the solution was stirred overnight at room temperature. The solvent was removed *in vacuo* and the residue was partitioned between AcOEt and H_2O. The organic layer was separated through a Whatman 1-PS filter paper and concentrated. The residue was dissolved in $CHCl_3$ and subjected to a pTLC. The band developed with $CHCl_3$–AcOEt (2 : 1) was extracted with $CHCl_3$–MeOH (2 : 1), and the solvent was evaporated off to leave **5** as a foam (44.4 mg, 77%). NMR: 8.6 (1H, br, HN-3), 7.95 (1H, s, H-6), 5.97 (1H, s, H-1′), 4.54 (1H, d, H-2″a, $J_{a,b}$ = 12 Hz), 4.38 (1H, d, H-2″b), 4.31 (1H, d, H-3′), 4.1 (2H, m, H-5′), 3.9—3.8 (1H, m, H-4′, $J_{3',4'}$ = 8.8 Hz). MS *m/z*: 595, 593 (M − isoPr), 347 (sugar).

***O*^{6},2′-Anhydro-1-[2-acetoxymethyl-3,5-*O*-(tetraisopropyldisiloxan-1,3-diyl)-arabinofuranosyl]-6-hydroxyuracil (6)**——Compound **5** (111.8 mg) was dissolved in 10 ml of dioxane and DBU was added to the solution. The mixture was heated at 80 °C for 1 h. The mixture was partitioned between AcOEt and H_2O. The separated organic layer was evaporated, and the residue was applied to a column of silica gel (30 g). The eluate with $CHCl_3$–AcOEt (7 : 1) was concentrated to leave 81.4 mg (84%) of **6** as a foam. NMR: 8.4 (1H, br, HN-3), 5.97 (1H, s, H-1′), 5.14 (1H, d, H-5, $J_{5,3}$ = 1 Hz), 4.54 (1H, d, H-3′), 4.53 (2H, s, H-2″), 4.05 (2H, m, H-5′), 3.9—3.7 (1H, m, H-4′), 2.07 (3H, s, Ac). MS *m/z*: 556 (M), 513 (M − isoPr). UV λ_{max}^{MeOH}: 248 nm.

2′-Deoxy-2′-methylene-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)uridine (8)——A portion of 50% NaH (2.4 g, 50 mmol) was washed with dry ether and taken up in 20 ml of DMSO under an Ar atmosphere. The solution was stirred for 1.5 h at 65 °C, then methyltriphenylphosphonium bromide (21.4 g, 60 mmol), DMSO (40 ml), and THF (20 ml) were added. The mixture was stirred at room temperature for 1.5 h, then **1** (10.0 g, 20.6 mmol) in 30 ml of THF was added dropwise and the whole was stirred for 1.5 h. The precipitate (triphenylphosphine oxide) was filtered off,

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the filtrate was concentrated, and the residue was partitioned between $CHCl_3$ and H_2O. The organic layer was passed through a Whatman 1-PS filter paper, the filtrate was concentrated, and the residue was applied to a column of silica gel. The eluate with AcOEt–$CHCl_3$ was concentrated and the residue was crystallized from AcOEt–*n*-hexane to give 5.74 g (58%) of **8**, mp 130—133 °C. NMR: 8.43 (1H, br, HN-3), 7.45 (1H, d, H-6, J=8.0 Hz), 6.53 (1H, d, H-1′, J=1.2 Hz), 5.71 (1H, dd, H-5, $J_{3,5}$=2.0 Hz), 5.54 (1H, dd, H-2″a), 5.46 (1H, dd, H-2″b), 4.82 (1H, m, H-3′), 4.10 (2H, dd, H-5′), 3.69 (1H, m, H-4′, $J_{3',4'}$=8.8 Hz), 1.10 (28H, m, isoPr). MS *m/z*: 439 (M−43). *Anal.* Calcd for $C_{22}H_{38}N_2O_6Si_2$: C, 54.74; H, 7.93; N, 5.80. Found: C, 54.63; H, 7.90; N, 5.78.

2′-Hydroxymethyl-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)uridine (9) and 1-[2-Hydroxymethyl-3,5-*O*-(tetraisopropyldisiloxane-1,3-diyl)-arabinofuranosyl]uracil (10)——a) Compound **8** (601.5 mg) was dissolved in 10 ml of *tert*-BuOH, then THF (2 ml), 10% $(Et)_4N^+OH^-$ (0.25 ml), 70% *tert*-BuOOH (0.4 ml), and 0.5% OsO_4 (0.65 ml, 0.01 eq) were added. The mixture was stirred overnight at room temperature. The reaction mixture was partitioned between AcOEt–1 N $NaHSO_3$ and the organic layer was washed with H_2O. The solvent was removed *in vacuo* and the residue was applied to a column of silica gel (20 g). The eluate with $CHCl_3$–AcOEt (5 : 1) was concentrated to leave a mixture of **9** and **10** (485 mg, 75%). The ratio of **9** and **10** as determined by NMR measurement was 2 : 1. A part of the mixture was separated by pTLC to give pure **9** and **10**, respectively. The physical data are as follows: Compound **9**: NMR ($CDCl_3+D_2O$): 7.65 (1H, d, H-6), 5.95 (1H, s, H-1′), 5.70 (1H, d, H-5), 4.31 (1H, d, H-3′), 4.1 (2H, m, H-5′), 3.94 (2H, m, H-2″), 3.76 (1H, m, H-4′). MS *m/z*: 473 (M−isoPr), 455 (M−isoPr–H_2O).

Compound **10**: NMR ($CDCl_3+H_2O$): 7.79 (1H, d, H-6), 5.98 (1H, s, H-1′), 5.63 (1H, d, H-5), 4.3—4.1 (3H, m, H-4′,5′), 3.9 (1H, m, H-4′), 3.84 (1H, d, H-2″a), 3.44 (1H, d, H-2″b, $J_{a,b}$=12.0 Hz). MS *m/z*: 473 (M−isoPr), 455 (M−isoPr–H_2O).

b) Compound **8** (4.00 g) was dissolved in 15 ml of *tert*-BuOH, then THF (15 ml), H_2O (5 ml), and *N*-methylmorpholine-*N*-oxide (1.2 g, 1.1 eq) were added. The solution was cooled at 0 °C, and 0.5% OsO_4 (4 ml, 0.01 eq) was added. The mixture was stirred for 6 d at 0 °C. After work-up as described in a), **9** and **10** were obtained as a mixture (3.95 g, 92%). The ratio of **9** and **10** was 4 : 1 as checked by NMR measurement.

3′,5′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-6,2′-epoxymethanouridine (7, R=H) and O^6,2′-Anhydro-1-[2-hydroxymethyl-3,5-*O*-(tetraisopropyldisiloxane-1,3-diyl)-arabinofuranosyl]-6-hydroxyuracil (11)——A mixture of **9** and **10** (183.5 mg) was dissolved in 5 ml of AcOH, then AcONa (87 mg) and Br_2 (22 μl, 1.1 eq) were added to the solution. The whole was stirred overnight at room temperature. The solvent was evaporated off and the residue was partitioned between AcOEt and H_2O. The organic layer was concentrated and the residue was dissolved in dioxane (3 ml). DBU (81 μl) was added and the solution was heated at 80 °C for 3 h. The mixture was partitioned between AcOEt–H_2O, and the organic layer was subjected to pTLC. The bands developed with $CHCl_3$–MeOH (15 : 1) were eluted with $CHCl_3$–MeOH (5 : 1). After evaporation of the solvents, **7** (R=H, 23.3 mg) and **11** (5 mg) were obtained as foams. Physical constants of **7** (R=H): NMR: 8.3 (1H, br, HN-3), 5.84 (1H, s, H-1′), 5.23 (1H, br s, H-5), 4.31 (1H, d, H-3′, $J_{3',4'}$=6.6 Hz), 4.1—3.9 (5H, m, H-4′,5′,2″), 3.51 (1H, s, HO-2′). MS *m/z*: 514 (M), 471 (M−isoPr), 453 (M−isoPr–H_2O). UV λ_{max}^{MeOH}: 258 nm.

Compound **11**: NMR: 9.0 (1H, br, HN-3), 6.11 (1H, s, H-1′), 5.09 (1H, s, H-5), 4.55 (1H, d, H-3′, $J_{3',4'}$=8.3 Hz), 4.1—3.8 (5H, m, H-4′,5′,2″), 3.5 (1H, br s, HO-2″). MS *m/z*: 514 (M), 471 (M−isoPr). UV λ_{max}^{MeOH}: 248 nm.

2′(*R*)-Methanesulfonyloxymethyl-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)uridine (12)——A 4 : 1 mixture of **9** and **10** (1.36 g) was dissolved in 10 ml of pyridine, then MsCl (0.30 g, 1.5 eq) was added, and the whole was stirred for 2.5 h at room temperature. Water was added, the solvent was evaporated off, and the residue was partitioned between AcOEt and H_2O. The organic layer was concentrated and the residue was dissolved in $CHCl_3$. The solution was applied to a column of silica gel (50 g). The eluate with $CHCl_3$–AcOEt (6 : 1) was concentrated and the residue was crystallized from AcOEt–*n*-hexane to give 1.29 g (55%) of **12**, mp 167—169 °C. NMR: 8.9 (1H, br, HN-3), 7.65 (1H, d, H-6), 6.07 (1H, s, H-1′), 5.73 (1H, dd, H-5), 4.4 (2H, m, H-3′,2″a), 4.2—4.0 (3H, m, H-4′,5′), 4.00 (1H, d, H-2″b, $J_{a,b}$=10.5 Hz). MS *m/z*: 551 (M−isoPr), 455 (M−isoPr–Mesyl). *Anal.* Calcd for $C_{23}H_{42}N_2O_{10}SSi_2$: C, 46.44; H, 7.12; N, 4.71; S, 5.39. Found: C, 46.36; H, 7.07; N, 4.57; S, 5.46.

2′(*R*)-Iodomethyl-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)-5-bromouridine (13)——Compound **12** (1.415 g) and AcONa (585 mg) were dissolved in 15 ml of AcOH. Bromine (0.15 ml, 1.2 eq) was added and the mixture was stirred at room temperature overnight. The solvent was removed, the residue was partitioned between AcOEt and H_2O, and the organic layer was concentrated. The residue was taken up in $CHCl_3$ and applied to a column of silica gel (50 g). The eluate with $CHCl_3$–AcOEt (6 : 1) was concentrated to leave 1.40 g (88%) of the 5-bromo derivative of **12** as a foam. NMR: 7.88 (1H, s, H-6), 6.08 (1H, s, H-1′). MS *m/z*: 631, 629 (M−isoPr). UV λ_{max}^{MeOH}: 277 nm. This compound (1.06 g) was dissolved in 10 ml of 2-butanone containing LiI (420 mg, 2 eq), and the solution was refluxed for 3 h. The solvent was removed *in vacuo* and the residue was partitioned between AcOEt and 1 N $Na_2S_2O_3$. The organic layer was concentrated and the residue was dissolved in $CHCl_3$. This solution was applied to a column of silica gel (40 g). The eluate with $CHCl_3$–AcOEt (9 : 1) was concentrated and the residue was crystallized from AcOEt–*n*-hexane to give 665.7 mg (60%) of **13**, mp 177 °C (dec.). NMR: 8.5 (1H, br, HN-3), 7.86 (1H, s, H-6), 5.84 (1H, s, H-1′), 4.63 (1H, d, H-3′), 4.2—4.0 (3H, m, H-4′,5′), 3.54 (1H, d, H-2″a), 3.21 (1H, s, HO-2′), 3.15 (1H, d, H-2″b, $J_{a,b}$=11.5 Hz). MS *m/z*: 663, 661 (M−isoPr), 535, 533 (M−isoPr–HI). *Anal.* Calcd for $C_{22}H_{38}BrIN_2O_7Si_2$. C, 37.45; H, 5.43; Br, 11.32; I, 17.99; N, 3.97. Found; C, 37.31; H, 5.45; Br, 11.42; I, 18.08; N, 4.08.

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5-Bromo-5,6-dihydro-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)-6,2′-methano-cyclouridine (14)——Compound **13** (184.4 mg) was dissolved in benzene (20 ml) and the atmosphere was replaced with Ar gas. A mixture of Bu_3SnH (0.11 ml, 1.1 eq) and AIBN (200 mg) in 5 ml of benzene was added dropwise over a period of 1 h to the refluxing solution. Refluxing was continued for 1 h, then the solvent was evaporated off and the residue was partitioned between acetonitrile and *n*-hexane. The acetonitrile layer was separated and concentrated. The residue was taken up in a small volume of $CHCl_3$ and applied to a column of silica gel (20 g). The eluate with $CHCl_3$–AcOEt (9 : 1) was concentrated and the residue was crystallized from AcOEt–*n*-hexane to give 75.4 mg (32%) of **14**, mp 167—170 °C. Some starting material (48.3 mg, 17%) was recovered. NMR: 7.7 (1H, br, HN-3), 5.57 (1H, s, H-1′), 4.52 (1H, d, H-5), 4.3—3.9 (5H, m, H-3′,4′,5′,6), 2.54 (1H, dd, H-2″a), 2.16 (1H, dd, H-2″b). MS *m/z*: 537, 535 (M−isoPr). UV (MeOH): end absorption at 230 nm.

3′,5′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-6,2′-methano-cyclouridine (16)——Compound **14** (108.9 mg) was suspended in 2 ml of benzene, and DBU (70 μl, 2.5 eq) was added. The suspension was refluxed for 30 min and the mixture was poured into AcOEt–H_2O and neutralized by the addition of 1 N HCl. The organic layer was evaporated and the residue was dissolved in $CHCl_3$. This solution was applied to a column of silica gel (3 g). The eluate with $CHCl_3$–AcOEt (9 : 1) was concentrated and the residue was crystallized from AcOEt–*n*-hexane to give 66.2 mg (71%) of **16**, mp 161—164 °C. NMR: 8.36 (1H, br, HN-3), 5.70 (1H, s, H-1′), 5.58 (1H, s, H-5), 4.2—3.8 (4H, m, H-3′,4′,5′), 3.74 (1H, s, HO-2′), 3.08 (2H, br s, H-2″). MS *m/z*: 455 (base peak, M−isoPr). UV λ_{max}^{MeOH}: 259 nm (ε, 9700). CD in MeOH: $\theta = -26900$ at 259 nm. *Anal.* Calcd for $C_{22}H_{38}N_2O_7Si_2$. C, 52.98; H, 7.68; N, 5.62. Found: C, 53.02; H, 7.84; N, 5.84.

6,2′-Methano-cyclouridine (17)——Compound **16** (40.0 mg) was dissolved in THF (1 ml), and tetrabutylammonium fluoride (1 M THF solution, 50 μl) was added. After 3 h, the solvent was removed *in vacuo* and the residue was partitioned between $CHCl_3$ and H_2O. The aqueous layer was concentrated to leave 18 mg of **17**. The mobility of **17** on paper electrophoresis (0.2 M boric acid–sodium borate, pH 7.5, 700 V, 2.5 h) was +10.3 cm. The mobility of uracil was +1.0 cm and that of uridine was +9.3 cm. UV $\lambda_{max}^{H_2O}$: 259 nm; λ_{min}: 228 nm.

References and Notes

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