General Synthesis of Homo-*C*-nucleosides[1)]

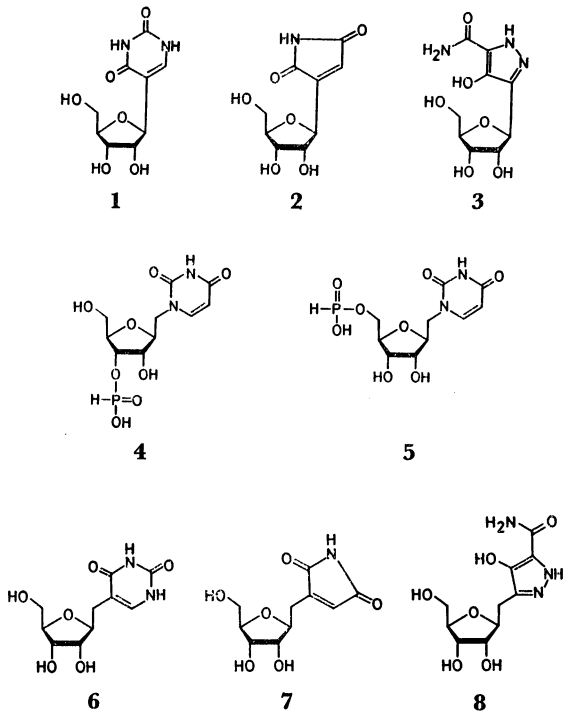
Tsuneo SATO and Ryoji NOYORI*

Department of Chemistry, Nagoya University, Chikusa-ku, Nagoya 464

(Received February 23, 1983)

Lithium aluminium hydride reduction of methyl (2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)acetate gives 2-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)ethanol. Subsequent tosylation, displacement by cyanide ion, nitrile hydrolysis, and diazomethane methylation afford methyl 3-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)propionate. The base-promoted formylation followed by methylation with methyl iodide forms methyl 2-[(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)methyl]-3-methoxyacrylate. Base-catalyzed condensation of the methoxyacrylate and urea followed by deprotection produces 5-[(β-D-ribofuranosyl)methyl]-uracil. In a like manner, condensation of the methoxyacrylate with thiourea or guanidine gives, after deblocking, 5-[(β-D-ribofuranosyl)methyl]-2-thiouracil and 5-[(β-D-ribofuranosyl)methyl]isocytosine, respectively. Ozonolysis of the methoxyacrylate yields methyl 3-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)pyruvate, which undergoes condensation with carbamoylmethylenetriphenylphosphorane to furnish a mixture of methyl 2-[(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)methyl]fumaramate and 2-[(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)methyl]maleimide. Deprotection of the latter leads to 2-[(β-D-ribofuranosyl)methyl]maleimide. Condensation of the keto ester with ethyl hydrazinoacetate followed by cyclization affords 3-[(2,3,*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)methyl]-5-methoxycarbonyl-4-hydroxypyrazole. Ammonolysis of the methyl ester and deprotection furnishes 3-[(β-D-ribofuranosyl)methyl]-5-carbamoyl-4-hydroxypyrazole.

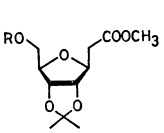
The naturally occurring *C*-nucleosides such as pseudouridine (**1**), showdomycin (**2**), pyrazomycin (**3**), *etc.*, have received considerable attention because of their unique structures and remarkable biological activities.[2)] Derivatives of certain homonucleosides such as **4** and **5**[3)] are also of importance from a biological point of view. As such we have been intrigued by the synthesis of homo-*C*-nucleosides, in which a carbon atom of the nitrogen base and C-1 atom of D-ribose are linked by a methylene unit.[4)] This paper discloses an efficient method for the synthesis of this class of compounds, as exemplified by preparation of the *C*-nucleoside analogues, **6**—**8**.[5)]



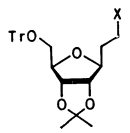
Results and Discussion

*Synthesis of Pyrimidine Homo-*C*-nucleosides.* The synthesis started from the chiral hydroxy ester **9**, which was readily obtainable from D-ribose[6)] or by using the transition metal-promoted 3+4 annulation between α, α,α′,α′-tetrabromoacetone and furan as the key step.[7,8)] Reduction of the tritylated derivative **10**[6)] with lithium aluminum hydride in THF at −20 °C gave the alcohol **11** in 83% yield. Treatment of **11** with *p*-toluenesulfonyl chloride in pyridine gave the tosylate **12**, which was then transformed in 67% yield to the nitrile **13** by the reaction with 3 equiv of potassium cyanide and 0.1 equiv of perhydrodibenzo-18-crown-6 in acetonitrile.[9)] Hydrolysis of **13** in ethylene glycol containing potassium hydroxide[10)] was followed by methylation with diazomethane in ether to afford the methyl ester **14** in 32% overall yield (or 74% yield based on consumed **13**). This compound was then treated with lithium diisopropylamide in THF and methyl formate, leading to **15**, which without isolation was quenched with methyl iodide in DMF to give the *(E)*-enol ether **16**. The IR spectrum showed absorptions at 1696 and 1634 cm^{-1} characteristic of the carbonyl and olefinic functions, respectively. In the ^1H NMR spectrum, two methoxyl proton signals were observed at δ 3.69 ($COOCH_3$) and 3.75 ($=CHOCH_3$). Condensation of **16** with urea promoted by ethanolic sodium ethoxide gave the 5′-substituted uracil derivative **17** in 35% yield. The ^{13}C NMR signals of the isopropylidene methyl groups observed at δ 25.79 and 27.58 (Δδ 1.79 ppm) were consistent with the β configuration.[4c)] Brief treatment of **17** with 10% methanolic hydrogen chloride furnished homopseudouridine (5-[(β-D-ribofuranosyl)methyl]uracil) (**6**).

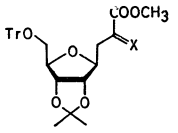
The versatility of the intermediate **16** was demonstrated by the preparation of homo-2-thiopseudouridine (5-[(β-D-ribofuranosyl)methyl]-2-thiouracil) (**19**) and homopseudoisocytidine (5-[(β-D-ribofuranosyl)methyl]-isocytosine) (**21**). When a 1:7 mixture of **16** and thiourea was heated at reflux in ethanol containing so-



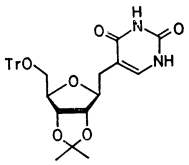
9, R=H
10, R=C(C$_6$H$_5$)$_3$



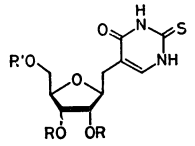
11, X=OH
12, X=OSO$_2$C$_6$H$_4$-*p*-CH$_3$
13, X=CN
14, X=COOCH$_3$



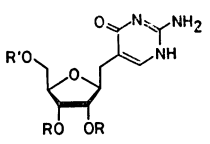
15, X=CHOLi
16, X=CHOCH$_3$-(*E*)
22, X=O
24, X=CHCONH$_2$-(*E*)
25, X=NNHCH$_2$COOC$_2$H



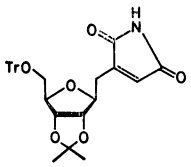
17



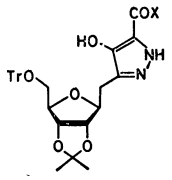
18, R-R=C(CH$_3$)$_2$; R′=C(C$_6$H$_5$)$_3$
19, R=R′=H



20, R-R=C(CH$_3$)$_2$; R′=C(C$_6$H$_5$)$_3$
21, R=R′=H (HCl salt)



23



26, X=OCH$_3$
27, X=NH$_2$

dium ethoxide, the protected homo-2-thiopseudouridine **18** was produced in 68% yield. Deprotection of **18** with methanolic hydrogen chloride afforded **19**. In a like manner, cyclization of **16** with guanidine, giving **20**, followed by treatment with 10% hydrogen chloride in methanol formed the HCl salt of **21**.

Synthesis of Homoshowdomycin and Homopyrazomycin. Homoshowdomycin (2-[(β-D-ribofuranosyl)methyl]-maleimide) (**7**) and homopyrazomycin (3-[(β-D-ribofuranosyl)methyl]-5-carbamoyl-4-hydroxypyrazole) (**8**) were also prepared starting from the key intermediate **16**.

Ozonolysis of **16** in dry ethyl acetate, followed by reductive workup with dimethyl sulfide,[11] afforded the labile keto ester **22**. This compound was then subjected to the Wittig reaction with carbamoylmethylenetriphenylphosphorane[12] in dry chloroform to give a 23:77 mixture of the maleimide derivative **23** and uncyclized compound **24** having an *E* double bond (66% yield based on **16**). In the ^{13}C NMR spectrum of the β structure **23** ($CDCl_3$), signals of the isopropylidene methyl groups appeared at δ 25.53 and 27.44 (Δδ 1.91 ppm).[4c] The IR spectrum of **23** showed absorptions due to carbonyl functions at 1781 and 1728 cm^{-1}, and for NH at 3440 cm^{-1}. The UV spectrum revealed the presence of a typical maleimide chromophore giving an absorption at 221 nm (sh, ε 13500). The compound **24** displayed the IR absorptions at 1708 (ester carbonyl) and 1668 cm^{-1} (amide carbonyl), and 3470 and 3310 cm^{-1} (NH). The ^{1}H NMR spectrum of **24** showed a singlet at δ 6.97 assigned to the vinylic proton. Direct conversion of **24** to **23** was not successful. However, **24** could be subjected to recycle use, since upon ozonolysis it reverted to the keto ester **22**. Treatment of **23** with a 9:1 trifluoroacetic acid–water mixture resulted in simultaneous removal of both trityl and isopropylidene protective groups to give crystalline homoshowdomycin (**7**) in 90% yield.

When the keto ester **22** was treated with ethyl hydrazinoacetate hydrochloride and sodium acetate in a 15:20:7 mixture of methanol, THF, and water, the hydrazone **25** was obtained in 47% yield based on **16**. Cyclization of **25** using sodium methoxide in methanol gave **26** in 37% yield.[13] The UV spectrum revealed the presence of a 4-hydroxypyrazole chromophore having absorption maxima at 228 (sh, ε 14200) and 268 nm (ε 4830). Treatment of **26** with ammonia at 25 °C in methanol giving the amide **27** (59%, or 79% based on consumed starting material), followed by deprotection with a 9:1 CF_3COOH–H_2O mixture gave crystalline homopyrazomycin (**8**) in 87% yield.

Thus straightforward construction of homo-*C*-nucleosides was realized. This method is quite general and stereochemically unambiguous. Since the starting materials of type **9** can be prepared from a variety of dibromo or further brominated ketones and furan derivatives,[7,8] this procedure finds wide flexibility in the synthesis of the analogues containing a branched-chain sugar moiety.

Preliminary *in vivo* testing indicated that homoshowdomycin (**7**) has moderate inhibitory activity against S-180 in mouse (T/C=152.8%, at 20 mg/kg) and L-1210 in mouse (T/C=113%, at 20 mg/kg).

Experimental

General. All melting points are uncorrected. The IR spectra were recorded on a JASCO IRA-1 spectrometer in chloroform. The ^{1}H NMR spectra were obtained using a Varian HA-100D spectrometer and the ^{13}C NMR spectra

were taken at 20 MHz on a Varian CFT-20 spectrometer or at 25 MHz on a JEOL FX-100 spectrometer. The chemical shifts are recorded in parts per million relative to tetramethylsilane as an internal standard. Singlet, doublet, triplet, quartet, and multiplet are abbreviated to s, d, t, q, and m, respectively. The UV spectra were recorded on a Hitachi 323 recording spectrophotometer. Optical rotations were measured with a JASCO DIP-SL automatic polarimeter. Thin-layer chromatography (TLC) was done using 0.25-mm layers of E. Merck Kieselgel 60 F_{254} and preparative TLC using 20×20-cm glass plates coated with a 1.0-mm layer of silica gel 60 PF_{254}. The position of spots is shown by R_f values. For column chromatography E. Merck Kieselgel 60 (70—230 mesh) was used. For separation of trityl derivatives silica gel treated with diluted aqueous ammonia was used.[14] Elemental analyses were performed at the Research Laboratory of Fujisawa Pharmaceutical Co. and Faculty of Engineering of Nagoya University.

Solvents and Materials. Perhydrodibenzo-18-crown-6, guanidine hydrochloride, potassium cyanide, urea, and thiourea were dried over phosphorus pentaoxide at 20 °C for 24 h under reduced pressure (0.05 mmHg)**. Reagent grade tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Methanol and ethanol were distilled from magnesium. Pyridine, acetonitrile, diisopropylamine, and *N,N*-dimethylformamide (DMF) were distilled over calcium hydride. Ethyl acetate was distilled from phosphorus pentaoxide. All other solvents and reagents were reagent grade and liquid materials were distilled before use.

*Methyl (2,3-O-Isopropylidene-β-D-ribofuranosyl)acetate (**9**).* To a solution of (2,3-*O*-isopropylidene-β-D-ribofuranosyl)acetic acid lactone (212 mg, 1 mmol)[8a] in 3 ml*** of dry methanol was added a solution of sodium methoxide (54 mg, 1 mmol) in 2 ml of dry methanol. The resulting pale yellow solution was stirred at 0 °C for 45 min and neutralized with saturated NH_4Cl. The resulting solution was evaporated to dryness, and the residue was extracted with chloroform (15 ml×3). The extracts were dried (Na_2SO_4) and evaporated to dryness. The oily colorless residue (245 mg, 100%) was used directly in the next step. $[\alpha]_D^{20}$ −6.34° (*c* 1.31, $CHCl_3$) (lit,[6] −6.6°).

*2-(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)ethanol (**11**).* To a solution of **10** (11.0 g, 22.0 mmol)[6] in THF (20 ml) at −20 °C was added a 0.5 mol dm^{-3} solution of $LiAlH_4$ (46 ml, 23 mmol) in THF. The reaction mixture was stirred for 1 h and warmed to room temperature. After 20 min, the resulting mixture was quenched by additions of ether (100 ml) and saturated NH_4Cl (20 ml). The mixture was filtered through a Celite 545 pad. The pad was washed with ethyl acetate (10 ml). The filtrate and washing were combined, dried (Na_2SO_4), and evaporated, giving **11** (pure by ^1H NMR analysis) as a colorless syrup (8.4 g, 83%), which was used directly in the next step: $[\alpha]_D^{20}$ −18.1° (*c* 0.16, $CHCl_3$); R_f=0.35 (3:2 hexane–ethyl acetate); IR 3560 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 1.33 and 1.53 (s, isopropylidene CH_3), 1.95 (m, $C\underline{H}_2CH_2OH$), 2.24 (br, OH), 3.17 (dd, *J*=4.8, 10.5 Hz, $H_{5'a}$), 3.32 (dd, *J*=4.2, 10.5 Hz, $H_{5'b}$), 3.83 (m, $H_{4'}$, and $C\underline{H}_2OH$), 4.12 (m, $H_{1'}$), 4.42 (dd, *J*=5.2, 6.2 Hz, $H_{2'}$), 4.60 (dd, *J*=3.5, 6.2 Hz, $H_{3'}$), 7.36 (m, Tr); ^{13}C NMR ($CDCl_3$) δ 25.68, 27.59, 36.08, 60.67, 82.39, 83.49, 83.85, 85.01, 114.51, 127.11, 127.84, 128.36, 128.84, 143.98. Found: C, 75.35; H, 7.16%. Calcd for $C_{29}H_{35}O_5$: C, 75.63; H, 7.00%.

*2-(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)ethyl-p-toluenesulfonate (**12**).* To a solution of **11** (7.50 g, 16.0 mmol) in pyridine (40 ml) at 0 °C was added a solution of *p*-toluenesulfonyl chloride (4.0 g, 21 mmol) in pyridine (40 ml) over 10 min. The mixture was stirred at the same temperature for 15 h and diluted with benzene (400 ml). The mixture was washed with water (30 ml), 5% HCl (40 ml×5), 3% $NaHCO_3$ (40 ml×5), and brine (40 ml), and then dried (Na_2SO_4). Evaporation afforded colorless residue, chromatography of which on a silica-gel column using a 3:2 hexane–ethyl acetate mixture afforded 6.10 g (63%) of **12** as a colorless syrup and the unchanged **11** (2.20 g, 29%): $[\alpha]_D^{20}$ −7.82° (*c* 0.435, $CHCl_3$); R_f=0.60 (3:2 hexane–ethyl acetate); ^1H NMR ($CDCl_3$) δ 1.29 and 1.48 (s, isopropylidene CH_3), 2.04 (m, $C\underline{H}_2CH_2OTr$), 2.35 (s, CH_3), 3.11 (dd, *J*=5.0, 10.0 Hz, $H_{5'a}$), 3.25 (dd, *J*=4.0, 10.0 Hz, $H_{5'b}$), 4.02 (m, $H_{4'}$), 4.20 (m, $H_{1'}$ and CH_2OTs), 4.34 (dd, *J*=4.9, 6.2 Hz, $H_{2'}$), 4.55 (dd, *J*=4.0, 6.2 Hz, $H_{3'}$), 7.40 (m, Tr and $CH_3C_6\underline{H}_4$); ^{13}C NMR ($CDCl_3$) δ 21.48, 25.67, 27.53, 33.33, 64.37, 67.33, 80.79, 82.49, 83.47, 84.82, 86.83, 114.44, 127.09, 127.85, 128.34, 128.78, 129.77, 143.97.

*3-(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)propionitrile (**13**).* A mixture of **12** (5.50 g, 9.1 mmol), potassium cyanide (1.77 g, 27.3 mmol), perhydrodibenzo-18-crown-6 (302 mg, 0.9 mmol), and acetonitrile (40 ml) was refluxed for 15 h under argon,[9] and cooled. Evaporation gave a residue, which was triturated with ethyl acetate (200 ml) and washed with water (40 ml). The organic layer was dried (Na_2SO_4), evaporated to dryness, and chromatographed on a silica-gel column using a 5:1 hexane–ethyl acetate mixture, affording 2.90 g (67%) of **13** as a white solid: mp 120—124 °C; $[\alpha]_D^{20}$ −11.9° (*c* 0.345, $CHCl_3$); R_f=0.79 (1:1 hexane–ethyl acetate); IR 2242 cm^{-1} (CN); ^1H NMR ($CDCl_3$) δ 1.33 and 1.52 (s, isopropylidene CH_3), 1.93 (m, $C\underline{H}_2CH_2CN$), 2.42 (t-like, *J*=7.3 Hz, CH_2CN), 3.17 (dd, *J*=4.5, 10.0 Hz, $H_{5'a}$), 3.31 (dd, *J*=3.8, 10.0 Hz, $H_{5'b}$), 3.93 (m, $H_{4'}$), 4.15 (m, $H_{1'}$), 4.35 (dd, *J*=5.0, 6.3 Hz, $H_{2'}$), 4.62 (dd, *J*=3.8, 6.3 Hz, $H_{3'}$), 7.30 (m, Tr); ^{13}C NMR ($CDCl_3$) δ 23.78, 25.68, 27.56, 29.76, 64.39, 82.62, 83.59, 84.51, 86.96, 114.61, 119.06, 127.18, 127.91, 128.36, 128.82, 143.94. Found: C, 77.09; H, 6.80; N, 2.92%. Calcd for $C_{30}H_{31}O_4N$: C, 76.73; H, 6.65; N, 2.98%.

*Methyl 3-(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)-propionate (**14**).* A mixture of **13** (980 mg, 2.1 mmol), powdered KOH (230 mg, 4.2 mmol), and commercial ethylene glycol (20 ml) was stirred at 120 °C for 20 h under argon.[10] The mixture was cooled to room temperature, and poured onto a heterogeneous mixture of ethyl acetate (250 ml), 5% HCl (70 ml), and ice (20 ml). The aqueous layer was extracted with ethyl acetate (50 ml×2). The organic layer was washed with brine (20 ml), dried (Na_2SO_4), and evaporated. The residue was dissolved in ethyl acetate (5 ml) and to this was added excess CH_2N_2 in ether. The mixture was concentrated to leave a viscous oil, whose chromatography on a silica-gel column using a 5:1 hexane–ethyl acetate mixture afforded 310 mg (32%) of **14** as a colorless syrup and recovered **13** (580 mg, 57%): $[\alpha]_D^{20}$ −1.51° (*c* 0.265, $CHCl_3$); R_f=0.29 (5:1 hexane–ethyl acetate); IR 1732 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.33 and 1.54 (s, isopropylidene CH_3), 1.99 (m, $C\underline{H}_2CH_2COOCH_3$), 2.52 (t-like, *J*=7.2 Hz, $C\underline{H}_2COOCH_3$), 3.17 (dd, *J*=5.0, 10.0 Hz, $H_{5'a}$), 3.30 (dd, *J*=4.1, 10.0 Hz, $H_{5'b}$), 3.68 (s, OCH_3), 3.93 (m, $H_{4'}$), 4.12 (m, $H_{1'}$), 4.36 (dd, *J*=5.0, 6.2 Hz, $H_{2'}$), 4.59 (dd, *J*=3.5, 6.2 Hz, $H_{3'}$), 7.30 (m, Tr); ^{13}C NMR ($CDCl_3$) δ 25.27, 27.59, 29.12, 30.39, 51.44, 64.57, 82.63, 83.38, 83.48, 84.90, 86.84, 114.31, 127.06, 127.84, 128.34, 128.88, 144.09, 173.39. Found: C, 74.12; H, 6.89%. Calcd for $C_{31}H_{34}O_6$: C, 74.08; H, 6.82%.

** 1 mmHg≈133.322 Pa.

*** 1 ml=0.001 dm^3.

*Methyl 2-(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)-3-methoxyacrylate (**16**).* To a solution of lithium diisopropylamide freshly prepared from diisopropylamine (1.4 ml, 10 mmol) and *n*-C_4H_9Li (1.5 mol dm^{-3} hexane solution, 7.5 ml, 11 mmol) in THF (10 ml) under argon was added a solution of **14** (2.5 g, 5 mmol) in THF (20 ml) at −78 °C. The reaction mixture was stirred at the same temperature for 30 min and to this was added methyl formate (1.5 ml, 25 mmol). After stirring at −78 °C for an additional 30 min, the mixture was warmed up to 0 °C and allowed to stand for 4 h. The resulting mixture was evaporated to dryness. The resulting residue was dissolved in 15 ml of dry DMF and treated with methyl iodide (1.5 ml, 25 mmol) at 20 °C under argon. The mixture was stirred at 20 °C for 12 h and concentration, giving a residue. This was triturated with benzene (30 ml) and washed with brine (10 ml). The aqueous layer was extracted with benzene (15 ml). The organic layer was dried (Na_2SO_4) and evaporated to give rise to a residual oil, which was subjected to chromatography on silica gel. Elution with a 30:1 benzene–ethyl acetate mixture afforded 2.41 g (90%) of **16** as a colorless syrup: R_f=0.40 (9:1 benzene–ethyl acetate); IR 1634 (C=C), 1696 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ 1.30 and 1.49 (s, isopropylidene CH_3), 2.57 (m, CH_2C=), 3.15 (dd, J=5.0, 10.3 Hz, $H_{5'a}$), 3.29 (dd, J=4.8, 10.3 Hz, $H_{5'b}$), 3.69 and 3.75 (s, OCH_3), 4.11 (m, $H_{1'}$ and $H_{4'}$), 4.41 (dd, J=3.5, 6.2 Hz, $H_{2'}$), 4.42 (dd, J=4.0, 6.2 Hz, $H_{3'}$), 7.30 (m, Tr and a vinyl proton); ^{13}C NMR ($CDCl_3$) δ 25.87, 27.64, 28.75, 51.19, 61.35, 64.62, 82.75, 83.19, 83.49, 84.78, 86.79, 106.74, 113.64, 126.78, 127.00, 127.81, 128.96, 144.21, 160.32, 168.50.

*5-[(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)methyl]uracil (**17**).* A mixture of **16** (883 mg, 1.66 mmol), urea (720 mg, 11.6 mmol), and 1 mol dm^{-3} ethanolic sodium ethoxide solution (12 ml, 12 mmol) was refluxed for 24 h under argon and evaporated under reduced pressure. The residue was taken up in 5 ml of water, neutralized with 1 mol dm^{-3} HCl, and then immediately extracted with ethyl acetate (7 ml×3). The ethyl acetate solution was dried over Na_2SO_4 and evaporated to dryness. The resulting oil was chromatographed on silica-gel plates using a 5:1 benzene–methanol mixture as an eluent. The compound **17** was obtained as a white foam. Yield was 312 mg (35%): $[\alpha]_D^{20}$ −13.7° (*c* 0.205, $CHCl_3$); R_f=0.26 (7:1 benzene–methanol); ^{1}H NMR ($CDCl_3$) δ 1.30 and 1.50 (s, isopropylidene CH_3), 2.66 (m, CH_2–uracil), 3.26 (m, $H_{5'}$), 4.13 (m, $H_{1'}$ and $H_{4'}$), 4.44 (dd, J=4.1, 6.3 Hz, $H_{2'}$), 4.62 (dd, J=3.5, 6.3 Hz, $H_{3'}$), 7.30 (m, Tr); ^{13}C NMR ($CDCl_3$) δ 25.79, 27.58, 30.26, 64.40, 82.41, 82.56, 82.91, 83.56, 84.65, 110.76, 114.42, 127.22, 127.91, 128.87, 138.72, 143.97, 152.57, 164.27; UV λ_{max} (CH_3OH) 264 nm (ε 6850). Found: C, 70.23; H, 6.23; N, 4.61%. Calcd for $C_{32}H_{32}O_6N_2$: C, 71.09; H, 5.97; N, 5.18%.

*5-[(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)methyl]-2-thiouracil (**18**).* A mixture of **16** (535 mg, 1 mmol) and thiourea (532 mg, 7 mmol) in ethanol containing sodium ethoxide (7 ml, 7 mmol as ethoxide) was refluxed for 12 h under argon and evaporation under reduced pressure gave a residue, which was taken up in 10 ml of water, neutralized with 1 mol dm^{-3} HCl, and then extracted with ethyl acetate (20 ml, 10 ml×2). The ethyl acetate solution was dried over Na_2SO_4. Evaporation followed by chromatography on silica-gel plates using a 15:1 chloroform–methanol mixture as an eluent produced the compound **18** as a white foam (378 mg, 68%): $[\alpha]_D^{20}$ −14.1° (*c* 0.255, $CHCl_3$); R_f=0.43 (15:1 benzene–methanol); ^{1}H NMR ($CDCl_3$) δ 1.32 and 1.52 (s, isopropylidene CH_3), 2.63 (m, CH_2–2-thiouracil), 3.24 (m, $H_{5'}$), 4.16 (m, $H_{1'}$ and $H_{4'}$), 4.40 (dd, J=3.2, 6.0 Hz, $H_{2'}$), 4.60 (dd, J=3.0, 6.0 Hz, $H_{3'}$), 7.35 (m, Tr), 10.50 (br, NH); ^{13}C NMR ($CDCl_3$) δ 25.66, 27.68, 30.13, 64.33, 82.61, 82.71, 83.64, 84.50, 87.06, 114.60, 115.28, 127.11, 127.31, 127.94, 128.87, 138.63, 143.83, 144.06, 161.21, 174.93; UV λ_{max} (CH_3OH) 274 nm (ε 11400), 293 (9950). Found: *m/z*, 414.1845. Calcd for $C_{27}H_{26}O_4$: (M−(B+CH_2+H)), 414.1859.

*5-[(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)methyl]isocytosine (**20**).* A mixture of **16** (535 mg, 1 mmol), guanidine hydrochloride (669 mg, 7 mmol), and 1 mol dm^{-3} ethanolic sodium ethoxide solution (7 ml) was refluxed for 19 h under argon. Removal of ethanol under reduced pressure left a viscous residue, which was taken up in 5 ml of water, neutralized with 1 mol dm^{-3} HCl, and then extracted with ethyl acetate (20 ml×3). After drying over Na_2SO_4, the organic solution was evaporated and subjected to preparative TLC on silica gel using a 15:1 benzene–methanol mixture as an eluent, giving the compound **20** as a white foam (350 mg, 65%): $[\alpha]_D^{20}$ −2.08° (*c* 0.24, CH_3OH); R_f=0.26 (7:1 benzene–methanol); ^{1}H NMR (dimethyl-d_6 sulfoxide) δ 1.20 and 1.37 (s, isopropylidene CH_3), 2.41 (m, CH_2–isocytosine), 3.06 (m, $H_{5'}$), 3.95 (m, $H_{1'}$ and $H_{4'}$), 4.47 (m, $H_{2'}$ and $H_{3'}$), 6.57 (br, NH_2), 7.40 (m, Tr), 11.00 (br, NH); ^{13}C NMR (dimethyl-d_6 sulfoxide) δ 25.45, 27.28, 31.10, 64.40, 81.66, 82.70, 83.91, 86.13, 110.24, 113.11, 126.95, 127.80, 128.28, 143.65, 155.22, 163.02; UV λ_{max} (CH_3OH) 293 nm (ε 10300). Found: C, 71.85; H, 6.12; N, 7.06%. Calcd for $C_{32}H_{33}O_5N_3$: C, 71.22; H, 6.16; N, 7.79%.

*5-[(β-D-Ribofuranosyl)methyl]uracil (Homopseudouridine) (**6**).* A mixture of **17** (100 mg, 0.185 mmol) and 10% methanolic hydrogen chloride solution (3 ml) was stirred at 20 °C for 40 min. The solvent was evaporated *in vacuo* to give a syrup which was triturated with 2 ml of ether three times. The title compound **6** (44.4 mg, 93%) was obtained as a white powder: mp 184—186 °C; $[\alpha]_D^{20}$ −8.15° (*c* 0.135, CH_3OH); ^{1}H NMR (dimethyl-d_6 sulfoxide) δ 2.36 (m, CH_2–uracil), 3.43 (m, $H_{5'}$), 3.62 (m, $H_{1'}$ and $H_{4'}$), 3.74 (m, $H_{2'}$ and $H_{3'}$), 3.1—4.9 (br, OH), 7.27 (m, H_6), 10.69 and 11.00 (br, NH); ^{13}C NMR (dimethyl-d_6 sulfoxide) δ 30.06 (CH_2–uracil), 62.00 ($C_{5'}$), 71.11, 74.33, 81.10, 84.09 ($C_{1'}$—$C_{4'}$ of ribose), 127.79, 139.14, 151.23, 164.60; UV λ_{max} (CH_3OH) 265 nm (ε 7130), λ_{max} (1 mol dm^{-3} HCl) 266 nm (ε 7080), λ_{max} (1 mol dm^{-3} NaOH) 285 nm (ε 7100).[15]

*5-[(β-D-Ribofuranosyl)methyl]-2-thiouracil (Homo-2-thiopseudouridine) (**19**).* A mixture of **18** (300 mg, 0.539 mmol) and 10% methanolic hydrogen chloride solution (3 ml) was stirred at 20 °C for 40 min. The solvent was evaporated *in vacuo* to give a syrup which was triturated with 3 ml of ether three times. The compound **19** was obtained as a white powder (133 mg, 90%). ^{1}H NMR (dimethyl-d_6 sulfoxide) δ 2.41 (m, CH_2–2-thiouracil), 3.42 (m, $H_{5'}$), 3.61 (m, $H_{1'}$ and $H_{4'}$), 3.76 (m, $H_{2'}$ and $H_{3'}$), 4.03 (br, OH), 7.31 (m, H_6), 12.17 and 12.36 (br, NH); ^{13}C NMR (dimethyl-d_6 sulfoxide) δ 30.12 (CH_2–2-thiouracil), 61.65 ($C_{5'}$), 70.86, 74.15, 80.14, 83.96 ($C_{1'}$—$C_{4'}$ of ribose), 114.49, 139.08, 161.45, 174.42; UV λ_{max} (CH_3OH) 216, 277, 290 nm (sh), λ_{max} (1 mol dm^{-3} HCl) 216, 277, 290 nm (sh), λ_{max} (1 mol dm^{-3} NaOH) 222, 261, 290 nm. This compound was so hygroscopic that optical extinction (ε value) could not be obtained.[15]

*5-[(β-D-Ribofuranosyl)methyl]isocytosine Hydrochloride (Homopseudoisocytidine Hydrochloride) (**21**).* A mixture of **20** (125 mg, 0.232 mmol) and 10% methanoli chydrogen chloride solution (3 ml) was stirred at 20 °C for 50 min. Concentration *in vacuo* gave a white solid which was coeva-

porated with ethanol (2 ml×3). The residue was triturated three times with 5 ml of ether. The compound **21** was obtained as a white powder (62 mg, 91%): mp 185—188 °C; $[\alpha]_D^{20}$ −48.9° (*c* 0.37, CH_3OH); ^1H NMR (dimethyl-d_6 sulfoxide) δ 2.47 (m, CH_2–isocytosine), 3.44 (m, $H_{5'}$), 3.64 (m, $H_{1'}$ and $H_{4'}$), 3.80 (m, $H_{2'}$ and $H_{3'}$), 3.8—5.0 (br, OH), 7.59 (s, H_6), 8.49 (br, NH_2); ^{13}C NMR (dimethyl-d_6 sulfoxide) δ 29.85 (CH_2–isocytosine), 61.79 ($C_{5'}$), 71.00, 74.23, 80.07, 84.30 ($C_{1'}$—$C_{4'}$ of ribose), 113.82, 138.05, 152.28, 160.27; UV λ_{max} (CH_3OH) 224 (ε 11500), 263 nm (7830), λ_{max} (1 mol dm^{-3} HCl) 223 (ε 12300), 264 nm (9420), λ_{max} (1 mol dm^{-3} NaOH) 232 (ε 11300), 281 nm (9100). Found: C, 40.27; H, 5.46; N, 13.60%. Calcd for $C_{10}H_{16}O_5N_3Cl\cdot 0.5H_2O$: C, 39.91; H, 5.63, N, 13.96%.

*2-[(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)methyl]maleimide (**23**).* A solution of olefinic ester **16** (1.07 g, 2 mmol) in 20 ml of dry ethyl acetate was treated with ozone at −78 °C. After dry nitrogen was blown through the solution to remove excess ozone, dimethyl sulfide (1.47 ml, 20 mmol) was added.[11] The mixture was stirred at −78 °C for 1 h, then at 0 °C for 1 h, finally at 25 °C for 1 h. The mixture was evaporated to give methyl 3-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)pyruvate (**22**) as a colorless syrup. This material displayed no olefinic absorption in the IR spectrum. To a solution of the crude product in 15 ml of dry chloroform was added a solution of 829 mg (2.6 mmol) of carbamoylmethylenetriphenylphosphorane[12] in 10 ml of dry chloroform. The yellow solution was stirred at 25 °C for 30 min. Evaporation followed by chromatography on a silica-gel column with a 10:1 benzene–ethyl acetate mixture as an eluent gave **23** (162 mg, 15%). Elution with a 3:1 benzene–ethyl acetate mixture gave methyl 2-[(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)-methyl]fumaramate (**24**) (564 mg, 51%). **23**: $[\alpha]_D^{20}$ −7.1° (*c* 0.14, $CHCl_3$); R_f=0.46 (3:1 benzene–ethyl acetate); IR 3440 (NH), 1781 and 1728 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.34 and 1.54 (s, isopropylidene CH_3), 2.79 (m, CH_2–maleimide), 3.20 (dd, J=4.8, 10.5 Hz, $H_{5'a}$), 3.35 (dd, J=4.0, 10.5 Hz, $H_{5'b}$), 4.18 (m, $H_{1'}$ and $H_{4'}$), 4.45 (dd, J=4.9, 6.1 Hz, $H_{2'}$), 4.67 (dd, J=3.5, 6.1 Hz, $H_{3'}$), 6.51 (m, H_3), 7.30 (m, Tr), 7.94 (br, NH); ^{13}C NMR ($CDCl_3$) δ 25.53, 27.44, 29.34, 64.03, 81.96, 82.26, 83.47, 84.55, 86.74, 114.56, 127.09, 127.81, 128.59, 129.32, 143.63, 146.39, 171.09; UV λ_{max} (CH_3OH) 221 nm (sh, ε 13500). Found: C, 73.42; H, 6.17; N, 2.67%. Calcd for $C_{32}H_{31}O_6N$; C, 73.12; H, 5.95; N, 2.67%. **24**: $[\alpha]_D^{20}$ −1.6° (*c* 0.32, $CHCl_3$); R_f= 0.24 (3:1 benzene–ethyl acetate); IR 3470 and 3310 (NH), 1708 and 1668 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.32 and 1.52 (s, isopropylidene CH_3), 2.87 (dd, J=9.1, 13.1 Hz, $H_aH_bCC{=}C$), 3.11 (dd, J=5.0, 13.1 Hz, $H_aH_bCC{=}C$), 3.24 (dd, J=3.6, 12.8 Hz, $H_{5'a}$), 3.38 (dd, J=4.2, 12.8 Hz, $H_{5'b}$), 3.74 (s, OCH_3), 4.07 (m, $H_{1'}$ and $H_{4'}$), 4.45 (dd, J=5.0, 6.2 Hz, $H_{2'}$), 4.64 (dd, J=4.8, 5.0 Hz, $H_{3'}$), 6.44 (br, NH), 6.97 (s, $=CHCONH_2$), 7.30 (m, Tr); ^{13}C NMR ($CDCl_3$) δ 25.69, 27.57, 32.24, 51.34, 63.39, 81.64, 82.59, 83.17, 84.25, 87.03, 114.91, 127.29, 127.94, 128.72, 134.00, 135.03, 143.56, 167.08, 167.14. Found: C, 71.34; H, 6.13; N, 2.40%. Calcd for $C_{33}H_{35}O_7N$: C, 71.06; H, 6.33; N, 2.51%.

*2-[(β-D-Ribofuranosyl)methyl]maleimide (Homoshowdomycin) (**7**).* A mixture of **23** (203 mg, 0.387 mmol) and 9:1 CF_3COOH–H_2O (2 ml) was stirred at 25 °C for 45 min. Evaporation followed by chromatography on silica-gel plates with a 1:1 ethyl acetate–acetone mixture as an eluent afforded 85 mg (90%) of **7** as a white powder which was recrystallized from acetone–benzene: mp 150—154 °C; $[\alpha]_D^{20}$ −24° (*c* 0.20, CH_3OH); R_f=0.38 (1:1 acetone–ethyl acetate); ^1H NMR (acetone-d_6) δ 2.70 (m, CH_2–maleimide), 3.36 (m, $H_{5'}$), 3.82 (m, $H_{1'}$ and $H_{4'}$), 4.16 (m, $H_{2'}$ and $H_{3'}$), 4.0—5.0 (br, OH), 6.56 (m, H_3), 9.52 (br, NH); ^{13}C NMR (acetone-d_6) δ 61.36 ($C_{5'}$), 70.68, 74.39, 80.10, 84.30 ($C_{1'}$—$C_{4'}$ of ribose), 146.41, 173.32, CH_2–maleimide obscured by acetone peaks; UV λ_{max} (CH_3OH) 221 nm (ε 10200).[15]

*Preparation of **25**.* A mixture of **22** (from 2 mmol of **16**), ethyl hydrazinoacetate hydrochloride (620 mg, 4 mmol), and sodium acetate (328 mg, 4 mmol) in THF–CH_3OH–H_2O (15 ml, 20 ml, and 7 ml, respectively) was stirred at 25 °C for 12 h. After removal of the solvent, 50 ml of chloroform was added. The solution was dried over Na_2SO_4 and evaporated to dryness. The crude product was purified by chromatography on a column of silica gel using a 9:1 benzene–ethyl acetate mixture. Yield was 585 mg (47% based on **16**): R_f=0.24 (9:1 benzene–ethyl acetate); IR 3270 (NH), 1740 and 1703 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.12—1.50 (m, 3H), 1.29 and 1.51 (s, isopropylidene CH_3), 2.6—3.4 (m, 4H), 3.46 and 3.71 (s, OCH_3, 1:3 ratio), 3.9—4.7 (m, 8H), 7.4 (m, Tr).

*3-[(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)methyl]-5-methoxycarbonyl-4-hydroxypyrazole (**26**).* To a solution of **25** (616 mg, 1 mmol) in 10 ml of methanol was added a 1 mol dm^{-3} methanolic sodium methoxide solution (4 ml). The solution was refluxed for 4.5 h and evaporated under reduced pressure.[13] The residue was taken up in 3 ml of water, neutralized with 1 mol dm^{-3} HCl, and then extracted with ethyl acetate (30 ml×3). The organic solution was dried (Na_2SO_4) and evaporated to dryness. The residue was purified by chromatography on a column of silica gel using a 3:1 benzene–ethyl acetate mixture. Compound **26** was obtained as a white foam (210 mg, 37%): $[\alpha]_D^{19}$ −24° (*c* 0.23, $CHCl_3$); R_f=0.31 (3:1 benzene–ethyl acetate); IR 3580—3200 (NH and OH), 1698 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.35 and 1.54 (s, isopropylidene CH_3), 2.92 (dd, J=7.3, 15.9 Hz, CH_aH_b–pyrazole), 3.15 (dd, J=4.6, 15.9 Hz, CH_aH_b–pyrazole), 3.25 (dd, J=5.0, 10.5 Hz, $H_{5'a}$), 3.41 (dd, J=4.0, 10.5 Hz, $H_{5'b}$), 3.95 (s, OCH_3), 4.12 (m, $H_{1'}$ and $H_{4'}$), 4.56 (m, $H_{2'}$ and $H_{3'}$), 7.32 (m, Tr); ^{13}C NMR ($CDCl_3$) δ 25.71, 27.56, 28.24, 51.74, 64.26, 82.39, 83.55, 83.87, 84.06, 87.14, 114.63, 127.21, 127.94, 128.82, 143.39, 143.84, 163.29; UV λ_{max} (CH_3OH) 228 nm (sh, ε 14200), 268 (4830). Found: C, 69.76; H, 6.18; N, 4.62%. Calcd for $C_{33}H_{34}O_7N_2$: C, 69.46; H, 6.01; N, 4.91%.

*3-[(2,3-O-Isopropylidene-5-O-trityl-β-D-ribofuranosyl)methyl]-5-carbamoyl-4-hydroxypyrazole (**27**).* A solution of the pyrazole **26** (320 mg, 0.575 mmol) in dry methanol (10 ml) was saturated with ammonia by passing the gas at 0 °C. The mixture was stirred at 25 °C for 4 d. The solvent was evaporated and the crude product was purified by chromatography on a column of silica gel using a 3:1 to 1:1 benzene–ethyl acetate mixture as an eluent to give a foam (184 mg, 59%): $[\alpha]_D^{19}$ −25° (*c* 0.20, $CHCl_3$); R_f=0.25 (1:1 benzene–ethyl acetate); IR 3580—3200 (NH and OH), 1675 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.30 and 1.50 (s, isopropylidene CH_3), 2.87 (dd, J=7.9, 15.1 Hz, CH_aH_b–pyrazole), 3.19 (dd, J=3.5, 15.1 Hz, CH_aH_b–pyrazole), 3.21 (dd, J=5.5, 10.3 Hz, $H_{5'a}$), 3.46 (dd, J=3.2, 10.3 Hz, $H_{5'b}$), 4.22 (m, $H_{1'}$ and $H_{4'}$), 4.49 (m, $H_{2'}$ and $H_{3'}$), 5.97 and 6.67 (br, NH_2), 7.30 (m, Tr), 8.03 (br, NH and OH); ^{13}C NMR ($CDCl_3$) δ 25.52, 27.43, 28.22, 64.13, 82.05, 83.68, 83.86, 84.08, 87.24, 114.90, 127.21, 127.82, 128.75, 141.40, 143.66, 164.29; UV λ_{max} (CH_3OH) 227 nm (sh, ε 14300), 268 (5100). Found: C, 69.37; H, 6.20; N, 7.57%. Calcd for $C_{32}H_{33}O_6N_3$: C, 69.17; H, 5.98; N, 7.56%. In addition, the unreacted **26** was recovered (77 mg, 25%).

3-[(β-D-Ribofuranosyl)methyl]-5-carbamoyl-4-hydroxypyrazole

(Homopyrazomycin) (8). A mixture of **27** (220 mg, 0.407 mmol) and 9:1 CF_3COOH–H_2O (4 ml) was stirred at 25 °C for 20 min. Concentration and subsequent chromatography on silica-gel plates using a 6:1:2:1 ethyl acetate–acetone–methanol–water mixture as an eluent yieled compound **8** as a white powder (128 mg, 87%) which was recrystallized from methanol–ethyl ether: mp 109—113 °C; $[\alpha]_D^{21}$ −22° (*c* 0.23, CH_3OH); R_f=0.24 (6:1:1:1 ethyl acetate–acetone–methanol–water); ^{1}H NMR (D_2O)[16] δ 3.01 (m, CH_2–pyrazole), 3.73 (m, $H_{5'}$), 3.90—4.30 (m, $H_{1'}$, $H_{2'}$, $H_{3'}$, and $H_{4'}$); ^{13}C NMR (D_2O)[16] δ 30.38 (CH_2–pyrazole), 64.82 ($C_{5'}$), 74.25, 77.20, 84.80, 86.78 ($C_{1'}$—$C_{4'}$ of ribose), 132.31, 169.22; UV λ_{max} (H_2O) 223 (ε 8630), 266 nm (5150), λ_{max} (0.1 mol dm^{-3} NaOH) 235 (ε 4330), 311 nm (5460).[15]

*Conversion of **24** to **23**.* To a solution of the unsaturated amide **24** (557 mg, 1 mmol) in 15 ml of dry ethyl acetate was passed ozone at −78 °C. Dry nitrogen was bubbled through the solution to remove excess ozone, and dimethyl sulfide (0.73 ml, 10 mmol) was added.[11] The mixture was stirred at −78 °C for 1 h, then at 0 °C for 1 h, finally at 25 °C for 1 h. Evaporation left a crude product, which was dissolved in 7 ml of dry chloroform and to this was added a solution of 415 mg (1.30 mmol) of carbamoylmethylenetriphenylphosphorane[12] in 3 ml of dry chloroform. The reaction mixture was stirred at 25 °C for 30 min and evaporated to dryness. The oily residue was chromatographed on a column of silica gel. Elution with a 3:1 benzene–ethyl acetate mixture gave **23** (67 mg, 13%). Continued elution with a 3:1 benzene–ethyl acetate mixture gave **24** (276 mg, 50%). Compounds **23** and **24** were identical in all respects with the authentic samples.

We thank Miss Keiko Marunouchi for her valuable contribution in some preliminary experiments. We are also indebted to Ajinomoto Co., Ltd. for a generous offer of D-ribose and for biological assay.

References

1) *C*-Nucleoside Synthesis. 20. For part 19 see: T. Sato, M. Watanabe, H. Kobayashi, and R. Noyori, *Bull. Chem. Soc. Jpn.*, **56**, 2680 (1983).

2) Showdomycin (**2**) shows quite significant antibacterial and antitumor activities. Pyrazomycin (**3**) is a potent antiviral agent. Pseudouridine (**1**) is a component of tRNA. Reviews: R. J. Suhadolnik, "Nucleoside Antibiotics," Wiley-Interscience, New York, N.Y. (1970), Chaps 9 and 10; P. Roy-Burman, "Analogues of Nucleic Acid Components," Springer-Verlag, New York, N.Y. (1970); S. Nakamura and H. Kondo, *Heterocycles*, **8**, 583 (1977); L. Goodman, "Basic Principles in Nucleic Acid Chemistry," ed by P. O. P. Ts'o, Academic Press, New York (1974), Vol. 1, p. 93; G. D. Daves, Jr. and C. C. Cheng, *Prog. Med. Chem.*, **13**, 303 (1976); S. Hanessian and A. G. Pernet, *Adv. Carbohydr. Chem. Biochem.*, **33**, 111 (1976); S. D. Gero, J. Cleophax, D. Mercier, and A. Olesker, "Synthetic Methods for Carbohydrates," ed by H. S. Khadem, American Chemical Society, Washington, D.C. (1976), p. 64; Y. Mizuno, O. Mitsunobu, and T. Hata, "Synthesis of Nucleosides and Nucleotides," Maruzen, Tokyo (1977), pp. 16—32; T. Sato and R. Noyori, *Kagaku (Chemistry)*, **33**, 74 (1978); K. Galankievicz, *Khim. Geterotsikl. Soedin.*, **1978**, 723; S. R. James, *J. Carbohydr. Nucleosides, Nucleotides*, **6**, 417 (1979); H. Ogura and H. Takahashi, *Yuki Gosei Kagaku Kyokai Shi.*, **38**, 756 (1980); T. Sato and R. Noyori, *ibid.*, **38**, 862, 947 (1980); M. Ohno, "Anticancer Agents Based on Natural Product Models," ed by J. M. Cassady and J. D. Douros, Academic Press, New York, N.Y. (1980), p. 73.

3) M. Bobek, J. Farkas, and F. Sorm, *Collect. Czech. Chem. Commun.*, **34**, 1684 (1969); A. Holy, *ibid.*, **35**, 81 (1970).

4) The term, homo-*C*-nucleoside, was first suggested by Gensler.[4a] Only two investigations dealt with the synthesis of these nucleosides. a) W. J. Gensler, S. Chan, and D. B. Bell, *J. Am. Chem. Soc.*, **97**, 436 (1976); b) *J. Org. Chem.*, **46**, 3407 (1981); c) J. A. Secrist III, *ibid.*, **43**, 2925 (1978).

5) A part of this work was reported in preliminary forms: T. Sato, K. Marunouchi, and R. Noyori, *Tetrahedron Lett.*, **1979**, 3669; T. Sato and R. Noyori, *Heterocycles*, **13**, 141 (1979).

6) H. Ohrui, G. H. Jones, J. G. Moffatt, M. L. Maddox, A. T. Christensen, and S. K. Byram, *J. Am. Chem. Soc.*, **97**, 4602 (1975).

7) Reviews: R. Noyori, *Ann. N.Y. Acad. Sci.*, **295**, 225 (1977); *Acc. Chem. Res.*, **12**, 61 (1979); R. Noyori and Y. Hayakawa, *Org. React.*, **29**, 163 (1983).

8) a) R. Noyori, T. Sato, and Y. Hayakawa, *J. Am. Chem. Soc.*, **100**, 2561 (1978); b) T. Sato, R. Ito, Y. Hayakawa, and R. Noyori, *Tetrahedron Lett.*, **1978**, 1829.

9) J. W. Zubrick, B. I. Dunbar, and H. D. Durst, *Tetrahedron Lett.*, **1975**, 71.

10) C.-T. Peng and T. C. Daniel, *J. Am. Chem. Soc.*, **77**, 6682 (1955).

11) J. J. Pappas, W. P. Keaverey, E. Gancher, and M. Berger, *Tetrahedron Lett.*, **1966**, 4273.

12) S. Trippett and D. M. Walker, *J. Chem. Soc.*, **1959**, 3874; G. Trummlitz, D. B. Repke, and J. G. Moffatt., *J. Org. Chem.*, **40**, 3352 (1975).

13) The cyclization was carried out according to the method of G. Just and S. Kim, *Can. J. Chem.*, **55**, 427 (1977).

14) J. G. Buchanan and J. C. P. Schwarz, *J. Chem. Soc.*, **1962**, 4770; J. Lehrfeld, *J. Org. Chem.*, **32**, 2544 (1967).

15) Correct analytical data were not obtained for this nucleoside. However, the secure structural proof was gained at the stage of the precursory acetonide.

16) Sodium 3-(trimethylsilyl)propionate-d_4 (TSP) was used as an internal standard.