qualitatively observed but detailed spectra in this region were not recorded because of experimental limitations. We cannot verify, therefore, whether the product of the electron-transfer reaction has the same spectrum as that observed with Na_2TPP. The rate constants, however, are similar, near 10^9 M^{-1} s^{-1} (Table II).

Conclusion

The present study is an attempt to demonstrate electron transfer from porphyrin anion radicals to various acceptors (reaction 2). The systems employed here exhibited spectral changes which led to the suggestion of an intermediate complex formation ($P\cdots Q^- \cdot$). A previous study utilizing the photoexcitation route (reaction 1) has also invoked the formation of an intermediate complex in the chlorophyll-photosensitized one-electron oxidation of water by benzoquinone.[31] In addition, the reactions studied here were found to be affected by environmental parameters. In the case of free-base porphyrins, there is a strong effect of pH on the electron-transfer reactions (Table II) which is caused by acid–base equilibria. Anion radicals of the type $H_2P^- \cdot$ react with acceptors about an order of magnitude more rapidly than their protonated form $H_3P \cdot$. This protonation cannot occur in metalloporphyrins so that their anion radicals behave similarly to $H_2P^- \cdot$. However, anion radicals of conjugated systems can also protonate on a carbon atom in a process which depends on solvent and acidity.[32] In the few cases studied here, such protonation was not apparent. All of the effects discussed above emphasize the importance of the microenvironment in determining the course of electron-transfer reactions in vivo.

References and Notes

(1) The work described herein was supported by the Office of Basic Energy Sciences of the Department of Energy. This is Document No. NDRL-1936 from the Notre Dame Radiation Laboratory.
(2) University of Notre Dame.
(3) Hebrew University. Participated in preliminary experiments as a summer student at the University of Notre Dame.
(4) Hebrew University. Visiting Professor at the University of Notre Dame.
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Total Synthesis of Optically Pure Nucleoside Q.[1] Determination of Absolute Configuration of Natural Nucleoside Q

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Abstract: Two diastereomers of 7-(3,4-*trans*-4,5-*cis*-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl)-7-deazaguanosine having the β-D-ribosyl group were synthesized, one of which, having the 3*S*,4*R*,5*S* configuration in its cyclopentenyl side chain, was proved to be identical in all respects, including ORD and CD, with natural nucleoside Q, thus determining the absolute and anomeric configurations of the latter.

In 1968, nucleoside Q was discovered in the first position of the anticodon of *Escherichia coli* $tRNA^{Tyr}$.[2] Later Q was also found in the same position of *E. coli* $tRNA^{His}$, $tRNA^{Asp}$, and $tRNA^{Asn}$.[3] Recently, it has become clear that Q is widely distributed in tRNA's of plants and animals.[4]

In 1975, Kasai et al.[5] proposed structure **1** (without assignment of stereostructure of the cyclopentene side chain) for the nucleoside Q, which was one of the most unique and complex nucleosides thus far known; it is a deazaguanosine derivative having a dihydroxycyclopentenylamine side chain at the 7 position. Later, nucleoside Q* (**2**), which was isolated from rabbit liver, was determined to be a mixture of mannosyl and galactosyl derivatives of Q.[6] Hitherto three antibiotics belonging to the 7-deazaadenosine, i.e., tubercidin (**3**),[7] toy-

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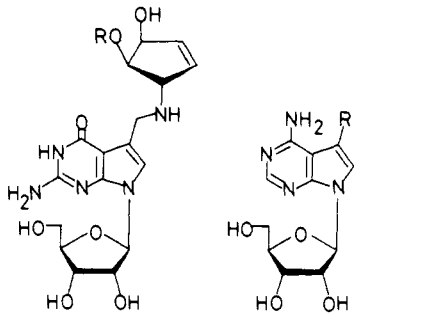


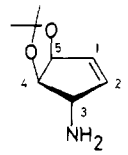
Nucleoside Q (1): R = H Tubercidin (3): R = H
Nucleoside Q̈ (2): R = mannosyl or galactosyl Toyocamycin (4): R = CN
Sangivamycin (5): R = $CONH_2$

ocamycin (**4**),[8] and sangivamycin (**5**),[9] have been isolated from the strains of *Streptomyces;* they all have antitumor activity.

With respect to biosynthesis of nucleoside Q, it was suggested that Q may be derived from guanine as well as toyocamycin (**4**) from adenine.[10] Moreover, it is of much interest that the guanyl residue at the anticodon in tRNA may be replaced by a precursor of Q base, which was recently identified as 7-aminomethyl-7-deazaguanine,[11] after the synthesis of tRNA is completed.[12]

The relative stereochemistry of the cyclopentene substituent of Q, which was not proposed by Kasai et al.,[5] was decided to be the 3,4-trans-4,5-cis configuration (3*S*,4*R*,5*S* or 3*R*,4*S*,5*R*) based on the comparisons of NMR of Q with that of synthetic model compounds,[13] but anomeric and absolute configurations of Q remained to be determined. The nucleoside bond could not be hydrolyzed with acids as expected from the 7-deazapurine nucleoside structure.[7-9] Thus, it was anticipated that elucidation of the anomeric and absolute configurations of Q should be very difficult without its total synthesis. Therefore, we carried out a total synthesis of two optically pure diastereomers of nucleoside Q, i.e., 2-amino-5-(3*S*,4*R*,5*S*-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl)-7-(β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one and its 3*R*,4*S*,5*R* isomer; the former was proved to be identical in all respects with the natural nucleoside Q.[14]

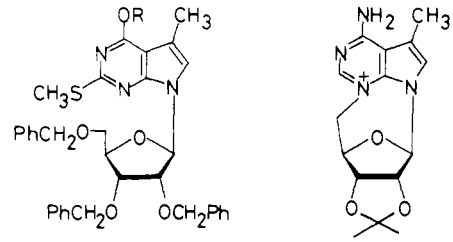
Optically pure (+)- and (−)-3,4-*trans*-4,5-*cis*-4,5-dihydroxycyclopent-1-en-3-ylamine 4,5-*O*-acetonide (*S*-**6** and *R*-**6**)



S-6

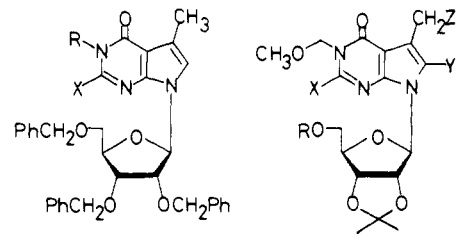
were prepared from the (±)-cyclopentenylamine acetonide (*S*,*R*-**6**)[13] by resolving its D- and L-mandelic acid salts. Optical purity of the resolved amines was determined by gas–liquid chromatography (GLC) of their (*R*)-α-methoxy-α-trifluoromethylphenylacetyl [(+)-MTPA] derivative to be more than 98% (Figure 1, supplementary material). Absolute configurations of (+)- and (−)-amine acetonides (*S*-**6** and *R*-**6**) could be assigned unambiguously to be 3*S*,4*R*,5*S* and 3*R*,4*S*,5*R*, respectively, by applying Mills' rule extended by Brewster[15] to their $[M]_D$ values since both of the allylic substituents at 3 and 5 positions contribute to the same direction of optical rotations of the amines; the enantiomer having 3*S*,5*S* substituents must be dextrorotatory and 3*R*,5*R* substituents levorotatory. The calculated value of the molecular rotation difference (330°) between the enantiomers from molecular polarizability is in good agreement with the observed value (230°).

The anomeric configuration of the starting pyrrolo[2,3-*d*]pyrimidine nucleoside **7**[16] was rigorously established as β by deriving it to a quaternary 1,5′-cyclonucleoside (**9**).[16] Hydrolysis of the β-nucleoside **7** in dioxane with hydrochloric acid gave deazainosine **9**, but the yield was not reproducible. This difficulty was overcome by addition of a trace amount of a radical inhibitor such as 4,4′-thiobis(6-*tert*-butyl-3-methylphenol) to the dioxane solution to prevent the methylthio group from oxidation, thus affording **10** in a good and reproducible yield. Replacement of the methylthio group with the amino group by the usual way such as treatment with methanolic ammonia was not effected. Prior conversion of the methylthio group to methyl sulfoxide or methyl sulfone, which could be better leaving groups than the methylthio group, did not work either. The reason may be that the proton at the 3 position is ionized; the anion prevents the nucleophilic substitution at C-2 position. In fact, after protection of the 3 position with the methoxymethyl group (to give **11**) the substitution proceeded smoothly with methoxide anion to furnish 2-methoxy derivative **12** in almost quantitative yield. Then, 3-methoxymethyl derivative **11** was treated with acetamide anion, which has about the same pK_a value as that of methoxide anion, to afford the deazaguanosine **13** in 99% yield. This reaction requires severely anhydrous conditions, or deacetylated product **14** was contaminated.



7, R = CH_3
8, R = CH_2OCH_3

9



10, R = H, X = SCH_3
11, R = CH_2OCH_3, X = SCH_3
12, R = CH_2OCH_3, X = OCH_3
13, R = CH_2OCH_3, X = NHAc
14, R = CH_2OCH_3, X = NH_2

16, R = Y = Z = H, X = NHAc
17, R = Ac, X = NAc_2, Y = Z = H
18, R = Ac, X = NAc_2, Y = Br, Z = H
19, R = Ac, X = NAc_2, Y = Z = Br

Prior to allylic bromination of **13**, the protecting groups on the ribose moiety had to be changed to the isopropylidene group to prevent oxidation in the subsequent steps. Catalytic hydrogenation of **13** in methanol with palladium on charcoal afforded the corresponding triol **15** which without purification was converted to acetonide **16**. Acetylation of **16** with acetic anhydride and pyridine at room temperature gave the *N*,*N*,*O*-triacetyl derivative **17**. Interestingly, no N-acetylation occurred with the free amine **14** under the same condition. Treatment of **17** with a limited amount of *N*-bromosuccinimide (NBS) gave the monobromide **18** in almost quantitative yield. Further treatment of **18** with NBS afforded in a high yield (^1H NMR analysis) dibromide **19**, which was not isolated but used for the next step immediately.

Condensation of the dibromide **19** with the optically pure (3*S*,4*R*,5*S*)-(+)-4,5-dihydroxycyclopent-1-en-3-ylamine

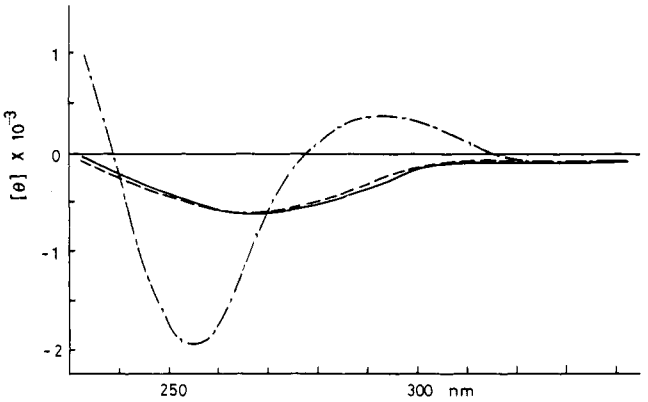


Figure 4. Circular dichroism spectra of nucleoside Q hydrochloride in water: (—), natural (1.57×10^{-4} M); (---), synthetic 3*S*,4*R*,5*S* (**1**) (1.24×10^{-4} M); (-·-), synthetic 3*R*,4*S*,5*R* (*R*-**1**) (1.28×10^{-4} M).

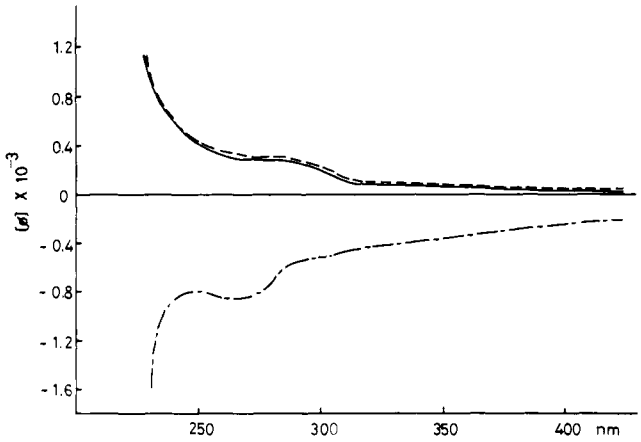
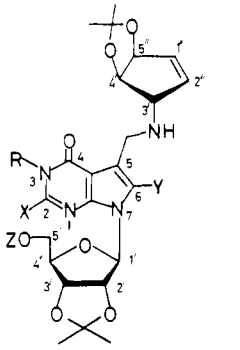


Figure 5. Optical rotatory dispersion spectra of nucleoside Q hydrochloride in water: (—), natural (4.56×10^{-4} M); (---), synthetic 3*S*,4*R*,5*S* (**1**) (4.76×10^{-4} M); (-·-), synthetic 3*R*,4*S*,5*R* (*R*-**1**) (4.57×10^{-4} M).

4,5-*O*-acetonide (*S*-**6**) in the presence of diisopropylethylamine afforded 6-bromo-5-(4,5-*O*-isopropylidene-(3*S*,4*R*,5*S*)-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl) derivative (*S*-**20**). Similarly, the 3*R*,4*S*,5*R* isomer having a β-D-ribosyl moiety (*R*-**20**) was obtained from the enantiomeric (3*R*,4*S*,5*R*)-(−)-amine acetonide (*R*-**6**). Debromination of the diastereoisomeric bromides, *S*-**20** and *R*-**20**, was successfully carried out by treatment with zinc–copper couple; subsequent hydrolysis with concentrated ammonia in methanol afforded the protected nucleoside Q isomers, *S*-**21** and *R*-**21**, respectively. Although the diastereomers, *S*-**20** and *R*-**20**, could not be differentiated by careful analysis of their ^{1}H NMR spectra, the significant differences in ^{1}H NMR spectra between *S*-**21** and *R*-**21** were observed as shown in Figure 2 (supplementary material). This result could imply that the coupling reaction of **19** and the optically active amine acetonides, *S*-**6** and *R*-**6**, has proceeded on retention of configuration of the amine strictly.



S-20, R = CH_2OCH_3, X = NHAc
Y = Br, Z = Ac

S-21, R = CH_2OCH_3, X = NH_2
Y = Z = H

S-22, R = Y = Z = H, X = NH_2

R series has enantiomeric configurations at the cyclopentene side chain

The dextrorotatory acetonide *S*-**21** was hydrolyzed with 2 N hydrochloric acid at 80 °C to give in nearly quantitative yield dextrorotatory nucleoside Q (**1**), which showed a single spot on Avicel thin layer chromatography (TLC). For further purification and identification the synthetic Q was converted to the acetonide *S*-**22** and then hydrolyzed mildly with 1 N hydrochloric acid at 50 °C. The purified nucleoside Q (**1**) was found to be identical with natural nucleoside Q by means of UV, ^{1}H NMR (Figure 3, supplementary material),[17] CD (Figure 4), ORD (Figure 5), and field desorption mass spectra.[14] Diastereoisomeric nucleoside Q having the 3*R*,4*S*,5*R* configuration on the cyclopentene side chain was also synthesized; its CD and ORD spectra clearly differ from those of natural nucleoside Q in their intensity as well as their sign, indicating that nucleoside Q must have D-ribose rather than the L isomer. Thus, natural nucleoside Q was proved to be 2-amino-5-((3*S*,4*R*,5*S*)-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl))-7-(β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one.

Experimental Section

General Experimental Information. Melting points were determined on a Mitamura Riken flat-bulb thermometer and are uncorrected. Nuclear magnetic resonance spectra were obtained on JEOL MH-100 and FX-100 (Fourier transform) instruments. Chemical shifts were expressed in parts per million from internal tetramethylsilane (δ), and coupling constants (*J*) in hertz. Deuteriochloroform was used as solvent unless otherwise noted. Mass spectra were determined on a JEOL D-100 and an SG-1 [high-resolution and field desorption (fd) spectra]. Ultraviolet spectra were measured on a Hitachi EPS-3T instrument and expressed in nanometers (ε). Circular dichroism and optical rotatory dispersion were determined with a JASCO J-40A and a J-20 instrument, respectively. Optical rotations $[\alpha]_D$ were measured on a JASCO DIP-4 digital polarimeter.

Usual workup of reaction mixtures is as follows. The mixture is extracted with dichloromethane and the extract washed with water, dried over anhydrous sodium sulfate, and evaporated under vacuum. Silica gel (100 mesh, Kanto Chemical Co.) was used for column chromatography and silica gel PF_{254} (Merck) for thin layer chromatography (TLC).

Resolution of *dl*-3,4-*trans*-4,5-*cis*-4,5-Dihydroxycyclopent-1-en-3-ylamine 4,5-*O*-Acetonide (*S*,*R*-6). To a solution of the *dl*-cyclopentenylamine acetonide (*S*,*R*-**6**) (870 mg)[13] in ethanol (5 mL) was added at room temperature a solution of D(−)-mandelic acid (875 mg) in ethanol (15 mL) and the mixture allowed to stand at −20 °C, when crystals were separated out. The collected crystals were recrystallized from ethanol to a constant melting point to give a dextrorotatory salt (*S*-**6** mandelate) (620 mg, 40%): mp 185–186 °C dec; $[\alpha]^{25}_D$ +29.7° (*c* 0.78, MeOH). Anal. ($C_{16}H_{21}NO_5$) C, H, N. Combined mother liquors of the recrystallization were evaporated and the residue was partitioned between 1 N NaOH and CH_2Cl_2. The organic layer was dried over Na_2SO_4 and evaporated. The oily residue was treated with L(+)-mandelic acid (557 mg) in ethanol in the same manner as described above, to give a levorotatory salt (*R*-**6** mandelate) (620 mg, 40%): mp 183–185 °C dec; $[\alpha]^{25}_D$ −29.8° (*c* 0.84, MeOH). Anal. ($C_{16}H_{21}NO_5$), C, H, N. The dextrorotatory salt was treated with 1 N NaOH and extracted with CH_2Cl_2. The extract was worked up as usual to give the *d*-amine acetonide (*S*-**6**) as an oil, $[\alpha]^{25}_D$ +148° (*c* 0.37, MeOH). Similarly, the levorotatory salt gave the *l*-amine acetonide (*R*-**6**) as an oil, $[\alpha]^{25}_D$ −149° (*c* 0.45, MeOH). Optical purity of these isomeric amine acetonides was determined as their *R*-MTPA amide. A mixture of the *d*- or *l*-amine acetonide (*S*-**6**

or *R*-**6**) (1.5 mg), *R*-MTPA chloride (10 μL), pyridine (0.1 mL), and CCl_4 (0.3 mL) was heated at 80 °C in a sealed glass tube for 3 h. After the mixture dried up, the residue was analyzed by GLC (Silicone OV-210 column, 3 mm × 3 m, 190 °C). The results shown in Figure 1 indicate that the purity of these enantiomeric amines is over 98%.

5-Methyl-2-methylthio-7-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one (10). 4-Methoxy-5-methyl-2-methylthio-7-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrrolo[2,3-*d*]-pyrimidine (**7**,[16] 2.10 g) was dissolved in freshly distilled dioxane (100 mL) containing 0.5 N HCl (35 mL) and 4,4′-thiobis(6-*tert*-butyl-3-methylphenol) (39 mg), and the solution was refluxed for 24 h. The usual workup gave a solid, which was crystallized from 2-propanol as white needles (1.78 g, 87%): mp 140 °C; *m/e* 597 (M^+); UV (MeOH) λ 278 nm (ε 12 200), 298 (13 600); $[\alpha]^{26}_D$ +65° (*c* 0.2, $CHCl_3$). Anal. ($C_{34}H_{35}N_3SO_5$) C, H, N.

3-Methoxymethyl-5-methyl-2-methylthio-7-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one (11). A flask containing **10** (1.0 g) and sodium hydride (53% oil suspension, 1.0 g) was purged with dry nitrogen and then dimethoxyethane (110 mL) was introduced into it at 0 °C. After the mixture was stirred at 0 °C for 10 min, chloromethyl methyl ether (1.8 mL, treated with alumina before use) was added dropwise to the suspension during 2 min and stirring was continued for a further 1 hr at 0 °C. The reaction mixture was filtered and the filtrate was evaporated in vacuo. The residue showed two spots on TLC, which were separated by preparative TLC (2% MeOH in CH_2Cl_2). The *N*-methoxymethyl derivative **11**, which has a smaller R_f value, was crystallized from *i*-PrOH as white needles (903 mg, 84%): mp 97 °C; UV (MeOH) λ 278 nm (sh, ε 8380), 308 (11 300); $[\alpha]^{28}_D$ +62.5° (*c* 0.2, $CHCl_3$); NMR δ 3.48 (3 H, s, OCH_3), 5.56 (2 H, br s, OCH_2N); *m/e* 641 (M^+). Anal. ($C_{36}H_{39}N_3O_6S$) C, H, N.

The *O*-methoxymethyl derivative **8**, which has the larger R_f value, was crystallized from *i*-PrOH as white needles (98 mg, 9.1%): mp 88 °C; UV (MeOH) λ 247 nm (ε 21 300), 287 (12 400); NMR δ 3.56 (3 H, s, OCH_3), 5.62 and 5.66 (2 H, AB quartet, *J* = 5.7 Hz, OCH_2O); *m/e* 641 (M^+). Anal. ($C_{36}H_{39}N_3O_6S$) C, H, N.

2-Acetamino-3-methoxymethyl-5-methyl-7-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one (13). Sodium hydride (53% oil suspension, 62 mg) and acetamide (600 mg, sublimed just before use) were mixed and heated at 120 °C under N_2 atmosphere. After cooling, **11** (100 mg) was added at once and the mixture was heated at 120 °C for 40 min. It was then carefully neutralized with 80% acetic acid under ice cooling and extracted thoroughly with benzene, and the extracts were worked up as usual to give a syrup, which was crystallized from *i*-PrOH as white needles (100.7 mg, 99%): mp 115 °C; UV (MeOH) λ 275 nm (ε 6050), 304 (8550); $[\alpha]^{26}_D$ +37.5° (*c* 0.2, $CHCl_3$); NMR δ 2.44 (3 H, s, CH_3CO), 3.46 (3 H, s, OCH_3), 5.52 (2 H, br s, OCH_2N), 8.38 (1 H, br s, NH). Anal. ($C_{37}H_{40}N_4O_7$) C, H, N.

2-Acetamino-3-methoxymethyl-5-methyl-7-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one (16). The tribenzyl ether **13** (324 mg) was hydrogenated in methanol (50 mL) in the presence of 10% Pd/C (970 mg) under hydrogen at room temperature for 18 h. After filtration, the solution was evaporated to dryness to give the debenzylated product **15** as a syrup. A mixture of the product, acetone (25 mL), *dl*-camphorsulfonic acid (35 mg), and 2,2-dimethoxypropane (2.5 mL) was stirred at room temperature for 5 h. It was partitioned between water and CH_2Cl_2, and the organic layer was dried over Na_2SO_4 and evaporated to dryness. The residue was treated with benzene and *n*-hexane to give white powder (127 mg, 62%): mp 180-182 °C; UV (MeOH) λ 275 nm (sh, ε 6500), 302 (8610); $[\alpha]^{26}_D$ −30.5° (*c* 0.2, $CHCl_3$); NMR δ 1.14 and 1.56 (each 3 H, s), 2.32 (6 H, s, $CH_3C{=}C$ and CH_3CO); *m/e* 422 (M^+).

2-Diacetylamino-3-methoxymethyl-5-methyl-7-(5-*O*-acetyl-2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one (17). A mixture of **16** (220 mg), acetic anhydride (2.3 mL), and pyridine (4.5 mL) was allowed to stand at room temperature for 3 h and evaporated in vacuo to give a syrup, which was crystallized from benzene and *n*-hexane as a white, crystalline powder (almost quantitative yield): mp 56-57 °C; UV λ 270 nm (sh, ε 5540), 305 (8310); NMR δ 1.36 and 1.60 (each 3 H, s), 2.08 (3 H, s, OAc), 2.36 (6 H, s) and 2.41 (3 H, s) (NAc_2 and $CH_3C{=}C$), 6.71 (1 H, br s, H-6); *m/e* 506 (M^+).

6-Bromo-2-diacetylamino-3-methoxymethyl-5-methyl-7-(5-*O*-acetyl-2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one (18). To a solution of **17** (19 mg) in benzene (2.0 mL) were added *N*-bromosuccinimide (NBS, 9.0 mg, 1.3 equiv, freshly recrystallized from water) and a catalytic amount of benzoyl peroxide (ca. 1 mg), and the mixture was stirred at room temperature for 10 min. After evaporation, the residue was purified by TLC (4% MeOH in CH_2Cl_2) to furnish a syrup, which was triturated with benzene and *n*-hexane to give a white powder (22.3 mg): mp 63-65 °C; UV (MeOH) λ 272 nm (ε 8720), 311 (11 100); $[\alpha]^{28}_D$ −7.5° (*c* 0.2, $CHCl_3$); NMR δ 1.36 and 1.60 (each 3 H, s), 2.05 (3 H, s), 2.36 (9 H, s, NAc_2 and $CH_3C{=}C$), no signal around 6.71; exact mass *m/e* 584.1096 (calcd for $C_{23}H_{29}N_4O_9{}^{79}Br$, 584.1118).

2-Acetamino-6-bromo-5-((3*S*,4*R*,5*S*)-4,5-*O*-isopropylidene-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl)-3-methoxymethyl-7-(5-*O*-acetyl-2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyrrolo[2,3-*d*]-pyrimidin-4-one (*S*-20) and Its 3*R*,4*S*,5*R* Isomer (*R*-20). To a solution of **18** (40 mg) in CCl_4 (9.5 mL, treated with alumina) were added NBS (25 mg, 2.0 equiv, freshly recrystallized), K_2CO_3 (50 mg), and a catalytic amount of benzoyl peroxide and the mixture was refluxed until the reaction appeared to be completed by monitoring on TLC plates (ca. 2 h) [the TLC gave a spot of dibromide **19**: NMR ($CDCl_3$) δ 4.80 (2 H, s, CH_2Br)]. After the reaction mixture was cooled, a solution of the *d*-cyclopentenylamine acetonide (3*S*,4*R*,5*S* isomer, *S*-**6**) (53 mg, 5.0 equiv) and diisopropylethylamine (140 μL) in benzene (0.4 mL) was added to it and the mixture allowed to stand at room temperature for 2 h. It was evaporated in vacuo and the residue purified by TLC (5% MeOH in CH_2Cl_2) to afford a syrup, which was triturated with benzene and *n*-hexane to give *S*-**20** as a white powder (37 mg, 78%): mp 68-70 °C; UV (MeOH) λ 273 nm (ε 8560), 308 (10 100); (MeOH-HCl) λ 273 (10 300), 303 (10 000); (MeOH-NaOH) λ 290 (11 600), 306 (12 000); $[\alpha]^{27}_D$ +92.8° (*c* 0.14, $CHCl_3$); NMR δ 1.36 (3 H, s), 1.44 (6 H, s), 1.62 (3 H, s), 2.08 (3 H, s, OAc), 2.32 (3 H, s, NAc), 3.49 (3 H, s, OCH_3), 3.80 (1 H, br s, H-3″), 3.94 (2 H, br s, CCH_2N), 4.00-4.44 (3 H, m, H-4′ and 5′), 4.54 (1 H, d, *J* = 5.5 Hz, H-4″), 5.12-5.32 (2 H, m, H-3′ and 5″), 5.48 (1 H, dd, *J* = 2.0 and 6.5 Hz, H-2′), 5.32 and 5.72 (2 H, AB quartet, *J* = 10.5, OCH_2N), 5.91 (2 H, br s, H-1″ and 2″), 6.18 (1 H, d, *J* = 2.0 Hz, H-1′); mass spectrum of *N,N′*-diacetyl derivative (acetylation with acetic anhydride and pyridine) *m/e* 736 and 738 (M^+ − Ac).

The 3*R*,4*S*,5*R* isomer (*R*-**20**) was synthesized from the l-cyclopentenylamine acetonide (*R*-**6**) by the same procedure as described above as an amorphous powder: mp 70-72 °C (from benzene-*n*-hexane); UV (MeOH) λ 273 nm (ε 7930), 308 (9360); (MeOH-HCl) λ 273 (9900), 303 (9500); (MeOH-NaOH) λ 290 (11 700), 306 (11 900); $[\alpha]^{25}_D$ −15.2° (*c* 0.14, $CHCl_3$); NMR δ 1.35 (3 H, s), 1.40 (6 H, s), 1.60 (3 H, s), 2.04 (3 H, s), 2.28 (3 H, s), 3.46 (3 H, s), 3.80 (1 H, br s), 3.92 (2 H, center of AB quartet, CCH_2N), 4.00-4.48 (3 H, m), 4.56 (1 H, d, *J* = 5.5 Hz), 5.12-5.28 (2 H, m), 5.48 (1 H, dd, *J* = 2.0 and 6.5 Hz), 5.32 and 5.70 (2 H, AB quartet, *J* = 10.5 Hz), 5.88 (2 H, br s), 6.16 (1 H, d, *J* = 2.0 Hz); mass spectrum of *N,N′*-diacetyl derivative *m/e* 736 and 738 (M^+ − Ac).

2-Amino-5-((3*S*,4*R*,5*S*)-4,5-*O*-isopropylidene-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl)-3-methoxymethyl-7-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one (*S*-21) and Its 3*R*,4*S*,5*R* Isomer (*R*-21). A mixture of zinc powder (1.45 g), cuprous chloride (0.25 g), and dioxane (90 mL) was refluxed for 10 min under a nitrogen atmosphere. To this Zn-Cu couple suspension were added the *d*-bromo nucleoside (*S*-**20**, 92 mg) in dioxane (15 mL) and then water (1 mL) and the mixture was refluxed for a further 3 h. After cooling and filtering, the solution was evaporated to dryness. The residual syrup was stirred at room temperature for 12 h with a mixture of methanol (24 mL) and concentrated ammonia (12 mL). The reaction mixture was evaporated to dryness and the residue was purified by TLC (8% MeOH in CH_2Cl_2) to afford *S*-**21** as a white powder (benzene-*n*-hexane) (50 mg, 72%): mp 98-100 °C; fd mass spectrum *m/e* 534 (M + 1); UV (MeOH) λ 265 nm (ε 9950), 293 (7100); $[\alpha]^{24}_D$ +11.8° (*c* 0.135, $CHCl_3$); NMR δ 1.35 (6 H, s), 1.40 (3 H, s), 1.60 (3 H, s), 3.41 (3 H, s), 3.60-4.00 (5 H, m), 4.39 (1 H, m, H-4′), 4.55 (1 H, d, *J* = 5.5 Hz, H-4″), 4.95-5.16 (2 H, m), 5.24 (1 H, d-like, H-5″), 5.32 (2 H, br s, NH_2), 5.40 and 5.56 (2 H, AB quartet, *J* = 11 Hz), 5.59 (1 H, d, *J* = 4.0 Hz, H-1′), 5.88 (2 H, br s, H-1″ and 2″), 6.59 (1 H, s, H-6). Anal. ($C_{25}H_{35}N_5O_8{\cdot}H_2O$), C, H, N. Exact mass of *O,N*-diacetyl derivative of *S*-**21** (acetic anhydride and pyridine at room temperature) *m/e* 617.2724 (calcd for $C_{29}H_{39}N_5O_{10}$, 617.2696).

The 3*R*,4*S*,5*R* isomer (*R*-**21**) was synthesized from the diastereoisomeric *l*-bromo nucleoside (*R*-**20**, 35 mg) by the same procedure as above. The product was obtained as a white powder (from ben-

zene-*n*-hexane) (20 mg, 75%): mp 89-91 °C; fd mass spectrum *m/e* 534 (M + 1); UV (MeOH) λ 265 nm (ε 10 700), 293 (7610); $[\alpha]^{27}_D$ −97.2° (*c* 0.143, $CHCl_3$); NMR δ 1.35 (6 H, s), 1.40 (3 H, s), 1.60 (3 H, s), 3.41 (3 H, s), 3.60-4.06 (5 H, m), 4.39 (1 H, m, H-4′), 4.57 (1 H, d, *J* = 5.5 Hz, H-4″), 4.96-5.16 (2 H, m), 5.30 (1 H, d-like, H-5″), 5.40-5.52 (2 H, AB quartet, *J* = 11 Hz), 5.62 (1 H, d, *J* = 4.0 Hz, H-1′), 5.88 (2 H, br s, H-1″ and 2″), 6.60 (1 H, s, H-6). Anal. ($C_{25}H_{35}N_5O_8$) C, H, N. Exact mass of *N,O*-diacetyl derivative of ***R*-21**, *m/e* 617.2711 (calcd for $C_{29}H_{39}N_5O_{10}$, 617.2696).

2-Amino-5-((3*S*,4*R*,5*S*)-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl)-7-(β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one (Nucleoside Q, 1) and Its 3*R*,4*S*,5*R* Isomer (*R*-1). The methoxymethyl nucleoside Q diacetonide (***S*-21**, 25 mg) was hydrolyzed with 2 N HCl (6 mL) at 80 °C for 6 h. The mixture was dried up in vacuo to afford the nucleoside Q (**1**) hydrochloride (18 mg, 90%) as a glassy solid, which showed a single spot on Avicel TLC (*n*-BuOH-AcOH-H_2O, 4:1:2) and almost pure on ^1H NMR spectrum. The pure sample was obtained from the diacetonide (***S*-22**, vide infra) by hydrolysis with 1 N HCl at 60 °C for 1 h as a glassy solid: fd mass spectrum *m/e* 410 (M + 1); UV spectra were identical with those of natural nucleoside Q;[5] CD, ORD, and ^1H NMR spectra are shown in Figures 4, 5, and 3, respectively.

The 3*R*,4*S*,5*R* isomer of nucleoside Q (***R*-1**) was prepared from the diacetonide ***R*-22** by the same procedure as above. The product was obtained as a colorless solid: fd mass spectrum *m/e* 410 (M + 1); CD, ORD, and ^1H NMR spectra are shown in Figures 4, 5, and 3, respectively.

2-Amino-5-((3*S*,4*R*,5*S*)-4,5-*O*-isopropylidene-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl)-7-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4-one (Nucleoside Q Diacetonide, *S*-22) and Its 3*R*,4*S*,5*R* Isomer (*R*-22). The synthetic nucleoside Q (**1**) was refluxed with dimethoxypropane and acetone for 1.5 h in the presence of *dl*-camphorsulfonic acid. After cooling, the mixture was neutralized with concentrated ammonia and evaporated to dryness. The residue was purified by TLC (10% MeOH in CH_2Cl_2) to give nucleoside Q diacetonide (***S*-22**) as a crystalline powder from benzene and *n*-hexane: fd mass spectrum *m/e* 490 (M + 1); UV (MeOH) λ 263 nm (ε 7080), 286 (4870); (MeOH-NaOH) λ 266 (7450); NMR (CD_3OD-CD_3COOD, 10:1) δ 1.36 (9 H, s), 1.58 (3 H, s), 3.72 (2 H, d, *J* = 4.5 Hz, H-5′), 4.20 (1 H, quartet, *J* = 9.0 and 4.5 Hz, H-4′), 4.34 (3 H, br s, C=CCH_2N and H-3″), 4.92 (1 H, d, *J* = 5.5 Hz, H-4″), 4.92-5.20 (2 H, m, H-2′ and 3′), 5.24-5.40 (1 H, H-5″ overlapped with solvent signal), 5.98 (1 H, d, *J* = 3.0 Hz, H-1′), 5.92-6.00 (1 H, H-1″ overlapped with H-1′ signal), 6.26 (1 H, d, *J* = 6.0 Hz, H-2″), 7.09 (1 H, s, H-6).

The 3*R*,4*S*,5*R* isomer (***R*-22**) was prepared similarly: mass spectrum *m/e* 490 (M + 1); UV and ^1H NMR spectra were completely identical with those of the 3*S*,4*R*,5*S* isomer (***S*-22**).

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Supplementary Material Available: Figure 1, analysis of optical purity of the cyclopentenylamines *S*-6 and *R*-6 by GLC; Figure 2, ^1H NMR spectra of ***S*-21** and ***R*-21** in $CDCl_3$; Figure 3, ^1H NMR spectra of synthetic nucleoside Q (**1**) and its 3*R*,4*S*,5*R* isomer (***R*-1**) in D_2O (pD 4.0) (3 pages). Ordering information is given on any current masthead page.

References and Notes

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(17) Our previous paper[1] already showed that no difference was observed in chemical shifts (within ±0.01 ppm) and coupling constants (within ±0.1 Hz) of ^1H NMR spectra between the synthetic (270 MHz) and natural nucleoside Q (220 MHz),[5] although the synthetic nucleoside Q was a mixture of diastereomers having the (3*S*,4*R*,5*S*)- (**1**) and (3*R*,4*S*,5*R*)-cyclopentene side chain (*R*-**1**).