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 Na₂TPP. The rate constants, however, are similar, near $10^9 \text{ M}^{-1} \text{ s}^{-1}$ (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^- · react with acceptors about an order of magnitude more rapidly than their protonated form H_3P . This protonation cannot occur in metalloporphyrins so that their anion radicals behave similarly to H_2P^- . 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

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- (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 3S,4R,5S 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-deazadenosine, i.e., tubercidin (3),⁷ toy-



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 (3S,4R,5S or 3R,4S,5R)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-(3S,4R,5S-4,5dihydroxycyclopent-1-en-3-ylaminomethyl)-7-(β -D-ribofuranosyl)pyrrolo[2,3-d]pyrimidin-4-one and its 3R,4S,5R 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)



were prepared from the (\pm) -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 3S,4R,5S and 3R,4S,5R, respectively, by applying Mills' rule extended by Brewster¹⁵ 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 3S,5S substituents must be dextrorotatory and 3R,5R 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[2,3d]pyrimidine nucleoside 7¹⁶ 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.



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 (3S,4R,5S)-(+)-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 3S,4R,5S (1) (1.24×10^{-4} M); (---), synthetic 3R,4S,5R (R-1) (1.28×10^{-4} M).

4,5-O-acetonide (S-6) in the presence of diisopropylethylamine afforded 6-bromo-5-(4,5-O-isopropylidene-(3S,4R,5S)-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl) derivative (S-20). Similarly, the 3R,4S,5R isomer having a β -D-ribosyl moiety (R-20) was obtained from the enantiomeric (3R,4S,5R)-(-)-amine acetonide (R-6). Debromination of the diastereoisomeric bromides, S-20 and R-20, was success-



fully 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 ¹H NMR spectra, the significant differences in ¹H 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.

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, ¹H NMR (Figure 3, supplementary material), ¹⁷ CD (Figure 4), ORD (Figure 5), and field desorption mass spec-



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

tra.¹⁴ Diastereoisomeric nucleoside Q having the 3R,4S,5R 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-((3S,4R,5S)-4,5-dihydroxycyclopent-1-en-3-yla-minomethyl))-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 [α]_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-1en-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. (C₁₆H₂₁NO₅) 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 Na₂SO₄ 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 CH₂Cl₂. 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 /amine acetonide (*R*-6) as an oil, $[\alpha]^{25}D = 149^{\circ}$ (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 ($10 \,\mu$ L), pyridine (0.1 mL), and CCl₄ (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-2methylthio-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); [α]²⁶_D +65° (*c* 0.2, CHCl₃). Anal. (C₃₄H₃₅N₃SO₅) 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 CH₂Cl₂). 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, CHCl₃); NMR δ 3.48 (3 H, s, OCH₃), 5.56 (2 H, br s, OCH₂N); m/e 641 (M⁺). Anal. (C₃₆H₃₉N₃O₆S) 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, OCH₃), 5.62 and 5.66 (2 H, AB quartet, J = 5.7 Hz, OCH₂O); *m/e* 641 (M⁺). Anal. (C₃₆H₃₉N₃O₆S) 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 N₂ 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); [α]²⁶D +37.5° (c 0.2, CHCl₃); NMR δ 2.44 (3 H, s, CH₃CO), 3.46 (3 H, s, OCH₃), 5.52 (2 H, br s, OCH₂N), 8.38 (1 H, br s, NH). Anal. (C₃₇H₄₀N₄O₇) 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 CH₂Cl₂, and the organic layer was dried over Na₂SO₄ 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); [α]²⁶_D -30.5° (*c* 0.2, CHCl₃); NMR δ 1.14 and 1.56 (each 3 H, s), 2.32 (6 H, s, CH₃C==C and CH₃CO); *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) (NAc₂ and CH₃C==C), 6.71 (1 H, br s, H-6); *m/e*

506 (M⁺). 6-Bromo-2-diacetylamino-3-methoxymethyl-5-methyl-7-(5-Oacetyl-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 CH₂Cl₂) to furnish a syrup, which was triturated with benzene and *n*-bexane to give a white powder (22.3 mg): mp 63-65 °C; UV (MeOH) λ 272 nm (ϵ 8720), 311 (11 100); [α]²⁸_D -7.5° (*c* 0.2, CHCl₃); NMR δ 1.36 and 1.60 (each 3 H, s), 2.05 (3 H, s), 2.36 (9 H, s, NAc₂ and CH₃C=C), no signal around 6.71; exact mass *m/e* 584.1096 (calcd for C₂₃H₂₉N₄O₉⁷⁹Br, 584.1118).

2-Acetamino-6-bromo-5-((3S,4R,5S)-4,5-O-isopropylidene-4,5dihydroxycyclopent-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 3R,4S,5R Isomer (R-20). To a solution of 18 (40 mg) in CCl₄ (9.5 mL, treated with alumina) were added NBS (25 mg, 2.0 equiv, freshlý recrystallized), K₂CO₃ (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 (CDCl₃) δ 4.80 (2 H, s, CH₂Br)]. After the reaction mixture was cooled, a solution of the *d*-cyclopentenylamine acetonide (3S, 4R, 5S isomer, 4R, 5S isomer)S-6) (53 mg, 5.0 equiv) and diisopropylethylamine (140 μ L) 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 CH₂Cl₂) 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, CHCl₃); 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, OCH₃), 3.80 (1 H, br s, H-3"), 3.94 (2 H, br s, CCH2N), 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 = 2.0Hz, 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 1-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); [α]²⁵_D = 15.2° (*c* 0.14, CHCl₃); 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, CCH₂N), 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-((3S,4R,5S)-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 3R,4S,5R 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 CH₂Cl₂) 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); $[\alpha]^{24}_{D} + 11.8^{\circ}$ (c 0.135, CHCl₃); 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, NH₂), 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. (C₂₅H₃₅N₅O₈·H₂O), 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 C₂₉H₃₉N₅O₁₀, 617.2696).

The 3R,4S,5R 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); [α]²⁷_D -97.2° (*c* 0.143, CHCl₃); 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. (C₂₅H₃₅N₅O₈) C, H, N. Exact mass of *N*,*O*-diacetyl derivative of *R*-21, *m/e* 617.2711 (calcd for C₂₉H₃₉N₅O₁₀, 617.2696).

2-Amino-5-((3S,4R,5S)-4,5-dihydroxycyclopent-1-en-3-ylaminomethyl)-7-(β -D-ribofuranosyl)pyrrolo[2,3-d]pyrimidin-4-one (Nucleoside Q, 1) and Its 3R,4S,5R 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-H₂O, 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 3R,4S,5R 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-((3S,4R,5S)-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 3R,4S,5R 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 (CD₃OD-CD₃COOD, 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=CCH₂N 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 3R,4S,5R 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 3S,4R,5S 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 CDCl₃; Figure 3, ¹H NMR spectra of synthetic nucleoside Q (1) and its 3R.4S.5R isomer (R-1) in D₂O (pD 4.0) (3 pages). Ordering information is given on any current masthead page.

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