Synthesis of (+)-5′-Nor-2′-deoxyaristeromycin and (−)-5′-Nor-3′-deoxyaristeromycin†

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Several years ago we began[1] an effort to study nucleoside derivatives[2] that lacked the C-5′ methylene unit and were designated as 5′-nor nucleosides. It was clear[1] that such an effort would have to focus on carbocyclic nucleosides since the 5′-nor ribofuranosyl derivatives (such as **1**) would be unstable hemiacetals that would break down to a heterocyclic base and a dialdehyde. As a consequence, our initial attention has been concerned with the 5′-nor carbocyclic analogues, specifically in the purine series (for example, 5′-noraristeromycin, **2**).[2b,3] During this effort, an enantiospecific synthesis into the 2′- and 3′-deoxy analogues has not been described. To address this situation we report here a route to 5′-nor-2′- and -3′-deoxyaristeromycin (**3**[4] and **4**, respectively) that could be adapted for preparing other 5′-nor-2′- and -3′-deoxy carbocyclic nucleosides with base units other than adenine.

The synthesis of **3** and **4** began by considering hydroboration of (1*R*,4*S*)-N^6-benzoyl-9-(4-hydroxy-2-cyclopenten-1-yl)-9*H*-adenine ((+)-**5**) with borane and with 9-BBN followed by the standard basic hydrogen peroxide workup procedure.[5] With borane, a complex mixture of products resulted that included **3**, **4**, adenine, and the hydrolysis product (+)-**10**, whereas with 9-BBN, **10** was the only identifiable product. Confirmation of the product **10** was accomplished by ammonolysis of (+)-**5**. Protection of the hydroxyl group of **5** as its dimethoxytrityl derivative **6** followed by 9-BBN/basic hydrogen peroxide resulted in the recovery of unreacted starting material and a mixture of products including **7** with no indication of **8** and **9**. Success finally occurred when ammonolysis of **6** to **7** was followed by borane/basic hydrogen peroxide to yield **8** and **9** (1:2). Separation of **8** and **9** and then detritylation of each with 80% acetic acid yielded the desired **3** and **4**, respectively.

Using 2-D NMR techniques, **3** was identified as the 3′-hydroxy derivative and **4** as its 2′-isomer. The structural analysis of **3** began with a DEPT 135 experiment which showed there to be two methylene carbons and three methine carbons in the cyclopentyl region. Following this, a standard COSY 90 experiment allowed assignment of

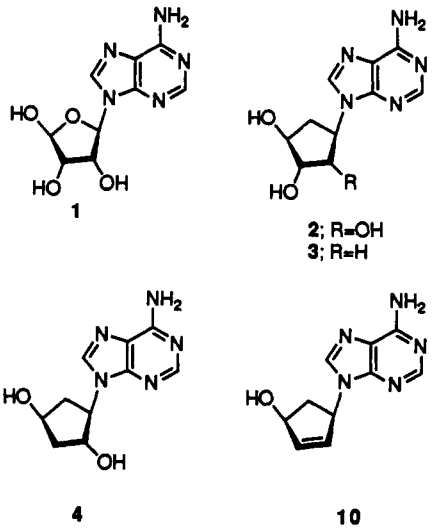
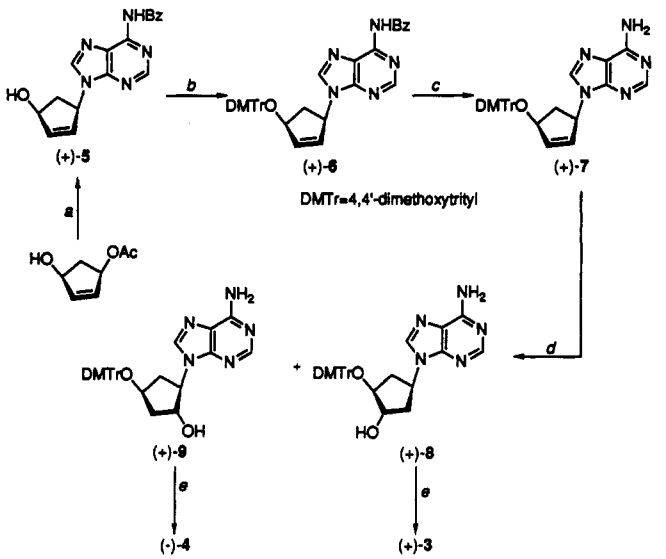


Figure 1.

Scheme I[a]



[a] Reaction conditions: (a) N^6-benzoyladenine, NaH in anhyd DMF added to a THF solution of (+)-(1*R*,4*S*)-4-hydroxy-2-cyclopenten-1-yl acetate, $(PPh_3)_4Pd$, and PPh_3; (b) dimethoxytrityl chloride in pyridine; (c) NH_3 in MeOH; (d) (i) BH_3·THF in THF; (ii) aqueous NaOH/30% H_2O_2/EtOH; (e) 80% AcOH.

the protons, which, together with subsequent HMQC[6] and HMQC-TOCSY[7] experiments permitted assignment of all the protonated carbons. A 2-D NOESY analysis (Figure 2) was performed to assign the structure of **3**. In that regard, a strong NOE was observed between H_α-1′ (δ 5.09) and H_α-5′ (δ 2.59), H_α-1′ and H_α-2′ (δ 2.11), and H_α-5′ and H_α-4′ (δ 3.95). As a consequence, these hydrogens must be related in a *syn* manner on the α-face of the cyclopentyl moiety. Furthermore, the proton H_β-3′ (δ 4.05) displayed a strong NOE to δ 2.25, which, in turn, must be H_β-2′.

The structure of **4** was accomplished in a similar manner, and the 2-D NOESY analysis (Figure 2) showed a strong response between H_α-1′ (δ 4.51) and H_α-5′ (δ 2.55), H_α-5′

† Dedicated to the retirement of Professor Fumio Yoneda, Kyoto University.

(1) Koga, M.; Schneller, S. W. *Tetrahedron Lett.* **1990**, *31*, 5861–5864.

(2) (a) Patil, S. D.; Koga, M.; Schneller, S. W.; Snoeck, R.; De Clercq, E. *J. Med. Chem.* **1992**, *35*, 2191–2195. (b) Patil, S. D.; Schneller, S. W.; Hosoya, M.; Snoeck, R.; Andrei, G.; Balzarini, J.; De Clercq, E. *J. Med. Chem.* **1992**, *35*, 3372–3377.

(3) (a) Patil, S. D.; Schneller, S. W. *J. Heterocycl. Chem.* **1991**, *28*, 823–825. (b) Siddiqi, S. M.; Chen, X.; Schneller, S. W. *Nucleosides Nucleotides* **1993**, *12*, 267–278. (c) Siddiqi, S. M.; Oertel, F. P.; Chen, X.; Schneller, S. W. *J. Chem. Soc., Chem. Commun.* **1993**, 708–709.

(4) Racemic **3** has been reported[1,2a] using a different, more tedious route than reported herein to (+)-**3**.

(5) (a) Tadano, K.; Maeda, H.; Hoshino, M.; Iimura, Y.; Suami, T. *J. Org. Chem.* **1987**, *52*, 1946–1956. (b) Tadano, K.; Kimura, H.; Hoshino, M.; Ogawa, S.; Suami, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3673–3678. (c) Tadano, K.; Hakuba, K.; Kimura, H.; Ogawa, S. *J. Org. Chem.* **1989**, *54*, 276–279. (d) Tadano, K.; Kimura, H.; Ogawa, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1355–1357.

(6) The HMQC spectra were acquired using the standard Bruker pulse program INVBDGTP with the BIRD sequence optimized $^1J_{CH}$ = 165 Hz.

(7) The HMQC-TOCSY spectra were acquired using the standard Bruker pulse program INVBMLTP with the BIRD sequence optimized $^1J_{CH}$ = 165 Hz.

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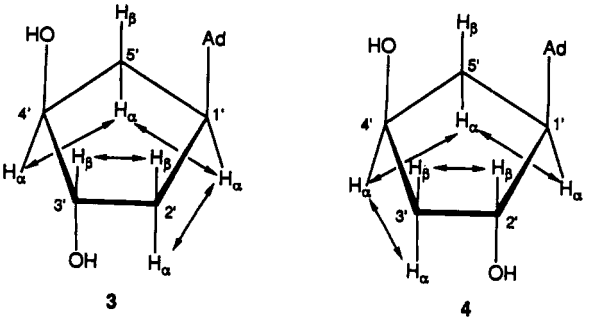

Figure 2.

and H_α-4′ (δ 4.27), and H_α-4′ and H_α-3′ (δ 1.81), proving the α-face *syn* stereochemical relationship of these four hydrogens. Also, on the β-face an NOE was noted between H_β-3′ (δ 1.97) and H_β-2′ (δ 4.60). With this information for **4**, it was not surprising to find that there was no significant NOE between H-1′ and H-2′ as a result of their *trans* relationship.

Experimental Section

Materials and Methods. Melting points were recorded on a Büchi 510 melting point apparatus and are uncorrected. Combustion analyses were performed by M-H-W Laboratories, Phoenix, AZ. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AMX 360 spectrometer (operated at 360 and 90 MHz, respectively) in $CDCl_3$ or DMSO-d_6 referenced to internal tetramethylsilane (TMS) at 0.0 ppm. The spin multiplicities are indicated by the symbols s (singlet), d (doublet), m (multiplet), and br (broad). Optical rotations were measured on a Perkin-Elmer 241MC polarimeter, and the UV–vis sprectra were recorded using an IBM 9420 spectrophotometer. Reactions were monitored by thin-layer chromatography (TLC) using 0.25-mm E. Merck silica gel 60-F_{254} precoated silica gel plates with visualization by irradiation with a Mineralight UVGL-25 lamp, exposure to iodine vapor, or spraying with a mixture of phenol/H_2SO_4/EtOH followed by heating. Flash (medium pressure, 30 psi) column chromatography was performed on Aldrich silica gel (average particle size 5–25 μm, 60 Å) and elution with the indicated solvent system. Yields refer to chromatographically and spectroscopically (^{1}H and ^{13}C NMR) homogeneous materials.

(1*R*,4*S*)-*N*^{6}-Benzoyl-9-(4-hydroxy-2-cyclopenten-1-yl)-9*H*-adenine ((+)-5). By adapting a literature procedure,[3b] reaction of optically pure (+)-(1*R*,4*S*)-4-hydroxy-2-cyclopenten-1-yl acetate ($[\alpha]^{27}_D$ +68.60° (*c* 1.56, $CHCl_3$))[3b] with the sodium salt of *N*^{6}-benzoyladenine in the presence of tetrakis(triphenylphosphine)palladium(0) and triphenylphosphine in DMF–THF gave **5** (59%) as colorless plates: mp 183 °C; $[\alpha]^{27}_D$ +217.79° (*c* 1.32, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 2.16 (d, *J* = 15.4 Hz, 1 H, H_β-5′), 2.99 (m, 1 H, H_α-5′), 4.88 (d, *J* = 7.3 Hz, 1 H, H-4′), 5.43 (d, *J* = 7.9 Hz, 1 H, H-1′), 5.87 (d, *J* = 3.5 Hz, 1 H, H-3′), 6.34 (d, *J* = 3.5 Hz, 1 H, H-2′), 7.46–7.60 (m, 3 H, Bz), 8.01 (d, *J* = 7.4 Hz, 2 H, Bz), 8.11 (s, 1 H, H-8), 8.69 (s, 1 H, H-2); ^{13}C NMR ($CDCl_3$) δ 39.75 (C-5′), 59.85 (C-1′), 75.12 (C-4′), 132.80 (C-2′), 140.19 (C-3′), 127.99, 128.79, 129.79, 133.58, 164.95 (carbons of Bz), 124.02 (C-5), 142.88 (C-8), 149.91 (C-4), 150.87 (C-6), 151.66 (C-2). Anal. Calcd for $C_{17}H_{15}N_5O_2$: C, 63.54; H, 4.71; N, 21.80. Found: C, 63.46; H, 4.84; N, 21.77.

(1*R*,4*S*)-*N*^{6}-Benzoyl-9-[4-[(4,4′-dimethoxytrityl)oxy]-2-cyclopenten-1-yl]-9*H*-adenine ((+)-6). 4,4′-Dimethoxytrityl chloride (DMTrCl) (1.27 g, 3.56 mmol) was added to a solution of (+)-**5** (1.00 g, 3.12 mmol) in anhyd pyridine (10 mL). After this mixture was stirred well for 18 h at rt under Ar, MeOH (5 mL) was added, which was then followed by evaporation to dryness with the aid of a rotary evaporator. The residue was coevaporated with MeOH (5 mL) and then CH_2Cl_2 (2 × 5 mL). The residue was first dried with the aid of a vacuum pump and then purified by flash chromatography. The fraction eluting with 40–50% AcOEt–CH_2Cl_2 was evaporated to dryness *in vacuo* and the residue dried (vacuum pump) for 5 h. This residue was then triturated with Et_2O, filtered, and washed with Et_2O to provide **6** (1.83 g, 94%) as a colorless powder: mp 120 °C; $[\alpha]^{27}_D$ +84.56° (*c* 0.97, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.56 (2m, 1 H, H_β-5′), 2.52 (m, 1 H, H_α-5′), 3.78 (s, 6 H, OCH_3 of DMTr), 4.75 (brs, 1 H, H-4′), 5.52 (brs, 1 H, H-1′), 5.63 (d, *J* = 5.5 Hz, 1 H, H-3′), 5.87 (d, *J* = 5.5 Hz, 1 H, H-2′), 6.84 (m, 4 H, H of DMTr), 7.14–7.61 (m, 12 H, H of DMTr and Bz), 8.02 (d, *J* = 7.3 Hz, 2 H, H of Bz), 8.22 (s, 1 H, H-8), 8.76 (s, 1 H, H-2), 9.28 (s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ 40.50 (C-5′), 56.81 (C-1′), 77.07 (C-4′), 132.66 (C-2′), 138.70 (C-3′), 55.23, 87.22, 113.38, 126.94, 127.91, 128.04, 130.01, 136.57, 145.31, 158.64 (C of DMTr), 128.77, 129.15, 131.21, 133.71, 164.76 (C of Bz), 126.94 (C-5), 141.85 (C-8), 149.38 (C-4), 151.63 (C-6), 152.36 (C-2). Anal. Calcd for $C_{38}H_{33}N_5O_4 \cdot 0.5H_2O$: C, 72.14; H, 5.42; N, 11.07. Found: C, 72.34; H, 5.67; N, 10.80.

(1*R*,4*S*)-9-[4-[(4,4′-Dimethoxytrityl)oxy]-2-cyclopenten-1-yl]-9*H*-adenine ((+)-7). Under stirring, ammonia was bubbled into a solution of (+)-**6** (7.01 g, 11.25 mmol) in MeOH (250 mL) over a period of 4 h at rt. This was followed by stirring for an additional 24 h at rt. The resulting precipitate was isolated by filtration and washed well with MeOH (4 × 30 mL) and Et_2O (4 × 30 mL) to give **7**. Evaporation of the filtrate to dryness *in vacuo* gave a residue that was coevaporated with MeOH (3 × 20 mL) and then Et_2O (3 × 20 mL). The residue crystallized and was isolated by filtration and washed with MeOH (3 × 30 mL) and Et_2O (3 × 10 mL) to give an additional amount of **7** (combined 5.06 g, 87%) as colorless needles: mp 196 °C; $[\alpha]^{27}_D$ +63.49° (*c* 1.04, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.59 (m, *J* = 14.5 Hz, 1 H, H_β-5′), 2.53 (m, 1 H, H_α-5′), 3.79 (s, 6 H, OCH_3 of DMTr), 4.73 (brs, 1 H, H-4′), 5.44 (brs, 1 H, H-1′), 5.55 (m, 1 H, H-3′), 5.86 (m, 1 H, H-2′), 6.19 (s, 2 H, NH_2), 6.85 (m, 4 H, H of DMTr), 7.18–7.52 (m, 9 H, H of DMTr), 8.05 (s, 1 H, H-8), 8.35 (s, 1 H, H-2); ^{13}C NMR ($CDCl_3$) δ 40.50 (C-5′), 56.45 (C-1′), 77.11 (C-4′), 131.47 (C-2′), 138.25 (C-3′), 55.18, 87.16, 113.31, 126.87, 127.95, 128.08, 130.01, 136.66, 145.37, 158.63 (C of DMTr), 119.80 (C-5), 139.21 (C-8), 149.62 (C-4), 152.82 (C-2), 155.60 (C-6). Anal. Calcd for $C_{31}H_{29}N_5O_3$: C, 71.66; H, 5.63; N, 13.48. Found: C, 71.80; H, 5.86; N, 13.52.

(1*S*,3*S*,4*S*)-9-[3-Hydroxy-4-[(4,4′-dimethoxytrityl)oxy]cyclopent-1-yl]-9*H*-adenine ((+)-8) and (1*R*,2*R*,4*S*)-9-[2-Hydroxy-4-[(4,4′-dimethoxytrityl)oxy]cyclopent-1-yl]-9*H*-adenine ((+)-9). By means of a dropping funnel, borane-THF complex (1.0 M in THF, 38.54 mL, 38.54 mmol) was added to a suspension of (+)-**7** (4.00 g, 7.71 mmol) in anhyd THF (12 mL) over a 20-min period under Ar at 0 °C. During this period, a clear solution resulted that was stirred well for 6 h at 0 °C under Ar. Again, using a dropping funnel, H_2O (27 mL) was added to the reaction mixture over a 10-min period at 0 °C under Ar. Then, 3 M aqueous NaOH solution (52 mL, 156 mmol) was added dropwise over a 20-min period at 0 °C under Ar, and this was followed by the dropwise addition of 30% aqueous H_2O_2 solution (106 mL, 935 mmol) over a 30-min period at 0 °C under Ar. Then, EtOH (100 mL) was added at 0 °C under Ar. This reaction mixture was stirred well at 30–50 °C (in a H_2O bath with cooling sometimes necessary) for 20 h. To the reaction mixture, additional 30% aqueous H_2O_2 solution (53 mL, 468 mmol) was added followed by thorough stirring at ambient temperature (30 °C) for 5 h. To the reaction mixture, an additional 30% aqueous H_2O_2 solution (26.5 mL, 234 mmol) was added, which was followed again by stirring well for 27 h at ambient temperature. To the cooled (ice–H_2O) reaction mixture was added saturated aqueous Na_2SO_3 solution and the resulting mixture stirred well at rt. To the mixture was added H_2O (300 mL). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (4 × 300 mL). The organic layer and the CH_2Cl_2 extracts were dried ($MgSO_4$) and filtered, and the filtrate was evaporated to dryness *in vacuo* in the presence of pyridine (to prevent the detritylation). The residue was dried with the aid of a vacuum pump and then purified by flash column chromatography. The fraction eluting with 2–3% MeOH–CH_2Cl_2 was evaporated to dryness with the aid of a rotary evaporator. The residue was coevaporated with toluene (3 × 20 mL) and the new residue dried with the aid of a vacuum pump for 12 h. Trituration of this material with Et_2O followed by filtration and further washing with Et_2O gave **9** (2.10 g, 51% yield) as a colorless powder: mp 141 °C; $[\alpha]^{27}_D$ +46.29° (*c* 0.99, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.81 (m, 2 H, H_α-3′, H_β-5′), 2.05 (m, 1 H, H_β-3′), 2.16 (m, 1 H, H_α-5′), 3.78 (s, 6 H, OCH_3 of

DMTr), 4.25 (m, 1 H, H-4'), 4.37 (m, 1 H, H-1'), 4.54 (m, 1 H, H-2'), 6.16 (s, 2 H, NH_2), 6.84 (d, J = 8.8 Hz, 4 H, DMTr), 7.19–7.50 (m, 9 H, DMTr), 7.71 (s, 1 H, H-8), 8.19 (s, 1 H, H-2); ^{13}C NMR ($CDCl_3$) δ 37.4 (C-5'), 40.0 (C-3'), 65.7 (C-1'), 71.1 (C-4'), 75.5 (C-2'), 55.2, 87.0, 113.3, 126.95, 128.0, 128.1, 130.0, 136.7, 145.4, 158.7 (DMTr), 119.7 (C-5), 139.0 (C-8), 150.1 (C-4), 152.3 (C-2), 155.6 (C-6). Anal. Calcd for $C_{31}H_{31}N_5O_4$: C, 69.26; H, 5.81; N, 13.03. Found: C, 69.21; H, 6.01; N, 12.86.

The fraction eluting with 3–5% MeOH–CH_2Cl_2 was evaporated to dryness, and the residue was coevaporated with toluene (3 × 20 mL). The new residue was dried for 12 h using a vacuum pump and then triturated with Et_2O. The solid remaining was isolated by filtration and washed with Et_2O to give **8** (1.06 g, 26%) as a colorless powder: mp 140 °C; $[\alpha]^{27}_D$ +46.52° (*c* 0.71, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.62 (m, 1 H, H_β-5'), 2.26 (m, 1 H, H_α-2'), 2.36 (m, 1 H, H_β-2'), 2.48 (m, 1 H, H_α-5'), 3.76 (s, 6 H, OCH_3 of DMTr), 3.98 (brs, 1 H, H-4'), 4.11 (brs, 1 H, H-3'), 5.09 (m, 1 H, H-1'), 5.98 (brs, 2 H, NH_2), 6.82 (d, J = 8.7 Hz, 4 H, DMTr), 7.18–7.50 (m, 9 H, DMTr), 8.03 (brs, 1 H, H-8), 8.30 (brs, 1 H, H-2); ^{13}C NMR ($CDCl_3$) δ 38.9 (C-5'), 40.3 (C-2'), 52.3 (C-1'), 77.2 (C-4'), 80.2 (C-3'), 55.3, 87.6, 113.4, 127.3, 128.2, 128.3, 130.2, 136.7, 145.4, 158.9 (DMTr), 119.8 (C-5), 139.3 (C-8), 150.2 (C-4), 152.8 (C-2), 155.6 (C-6). Anal. Calcd for $C_{31}H_{31}N_5O_4$: C, 69.26; H, 5.81; N, 13.03. Found: C, 69.01; H, 5.99 ; N, 12.90.

(1*S*,3*S*,4*S*)-9-(3,4-Dihydroxycyclopent-1-yl)-9*H*-adenine ((+)-3).[8] Compound (+)-**8** (120 mg, 0.22 mmol) was dissolved in 80% aqueous AcOH (30 mL) at rt, and this mixture was then stirred well for 1 h at rt. Evaporation of this solution to dryness and coevaporation of the residue with MeOH–CH_2Cl_2 (1:1) (3 × 20 mL) provided a new residue that was dried for 2 h with the aid of a vacuum pump. The residue was recrystallized from MeOH–AcOEt–Et_2O and, after isolation by filtration, was washed with Et_2O to give **3** (49 mg, 92%) as colorless needles: mp 210 °C; $[\alpha]^{27}_D$ +4.73° (*c* 0.63, MeOH); UV (H_2O) λ_{max} 261 nm (ϵ, 1.81 × 10^4); ^1H NMR (DMSO-d_6) δ 1.83 (m, 1 H, H_β-5'), 2.11 (m, 1 H, H_α-2'), 2.25 (m, 1 H, H_β-2'), 2.59 (m, 1 H, H_α-5'), 3.95 (m, 1 H, H_α-4'), 4.05 (m, 1 H, H_β-3'), 4.95 (m, 1 H, 3'-OH), 5.09 (m, 1 H, H_α-1'), 5.48 (m, 1 H, 4'-OH), 7.25 (s, 2 H, NH_2), 8.13 (s, 1 H, H-2), 8.21 (s, 1 H, H-8); ^{13}C NMR (DMSO-d_6) δ 38.93 (C-5'), 39.10 (C-2'), 51.66 (C-1'), 76.42 (C-4'), 76.74 (C-3'), 119.01 (C-5), 139.60 (C-8), 148.90 (C-4), 151.93 (C-2), 155.95 (C-6).[9] ^1H NMR experiments with the chiral shift reagent (+)-Eu(tfc)$_3$ in CD_3CN did not show any visible enantiomeric contamination when compared to a comparable experiment with (±)-**3**.[1] Anal. Calcd for $C_{10}H_{13}N_5O_2$: C, 51.06; H, 5.57; N, 29.77. Found: C, 51.28 ; H, 5.52; N, 29.54.

(1*R*,2*R*,4*S*)-9-(2,4-Dihydroxycyclopent-1-yl)-9*H*-adenine ((−)-4). Compound (+)-**9** (378 mg, 0.704 mmol) was dissolved in 80% aqueous AcOH (110 mL) and this solution then stirred well for 5 h at rt. The solution was then evaporated to dryness and the residue dissolved again in 80% aqueous AcOH (200 mL) followed by thorough stirring for 34 h at rt. This solution was evaporated to dryness and the residue coevaporated with MeOH (3 × 50 mL) followed by drying the new residue for 12 h with the aid of a vacuum pump. This residue was triturated with Et_2O, isolated by filtration, and recrystallized from MeOH–AcOEt. Following washing with AcOEt and Et_2O, **4** (97 mg, 59%) was obtained as colorless needles: mp 215 °C; $[\alpha]^{27}_D$ −45.04° (*c* 0.50, MeOH); UV (H_2O) λ_{max} 261 nm (ϵ, 1.72 × 10^4); ^1H NMR (DMSO-d_6) δ 1.81 (m, 1 H, H_α-3'), 1.97 (m, 2 H, H_β-3' and H_β-5'), 2.55 (m, 1 H, H_α-5'), 4.27 (m, 1 H, H_α-4'), 4.51 (m, 1 H, H_α-1'), 4.60 (m, 1 H, H_β-2'), 5.14 (d, J = 4.5 Hz, 1 H, 4'-OH), 5.24 (d, J = 5.2 Hz, 1 H, 2'-OH), 7.22 (s, 2 H, NH_2), 8.13 (s, 1 H, H-2), 8.19 (s, 1 H, H-8); ^{13}C NMR (DMSO-d_6) δ 39.47 (C-5'), 42.41 (C-3'), 61.19 (C-1'), 67.38 (C-4'), 74.32 (C-2'), 119.05 (C-5), 139.83 (C-8), 149.39 (C-4), 151.95 (C-2), 155.94 (C-6). Anal. Calcd for $C_{10}H_{13}N_5O_2$: C, 51.06; H, 5.57; N, 29.77. Found: C, 51.26; H, 5.69; N, 29.72.

The filtrate obtained after isolation of the product above following Et_2O trituration was evaporated to dryness with the aid of a rotary evaporator and the residue dried for 30 min using a vacuum pump. Another 80% aqueous AcOH solution (100 mL) was added to dissolve the residue, and this was followed by stirring for 7 days. The reaction solution was evaporated to dryness with the aid of a rotary evaporator and the residue coevaporated with MeOH, MeOH–CH_2Cl_2 (1:1), and then Et_2O. The new residue was dried for 10 h in vacuo and, following trituration with Et_2O and washing with AcOEt and Et_2O, gave **4** (total yield 142 mg, 86%).

(1*R*,4*S*)-9-(4-hydroxy-2-cyclopenten-1-yl)-9*H*-adenine ((+)-10).[10] At rt and under stirring, NH_3 was bubbled into a solution of (+)-**5** (100 mg, 0.31 mmol) in MeOH (20 mL) over a period of 1.5 h. Stirring was continued for an additional 36 h at rt. The reaction mixture was then evaporated to dryness in vacuo and the residue coevaporated with AcOEt (3 × 20 mL) and then dried with the aid of a vacuum pump. The resulting material was isolated by filtration with the aid of AcOEt and then washed with AcOEt followed by Et_2O to give **10** (60 mg, 89%) as a colorless powder: mp 191 °C; $[\alpha]^{27}_D$ +128.10° (*c* 0.68, MeOH); UV (H_2O) λ_{max} 262 nm (ϵ, 1.40 × 10^4); ^1H NMR (DMSO-d_6) δ 1.76 (d, J = 13.3 Hz, 1 H, H_β-5'), 2.91 (m, 1 H, H_α-5'), 4.74 (brs, 1 H, H-4'), 5.47 (brs, 1 H, H-1'), 5.60 (d, J = 6.1 Hz, 1 H, 4'-OH), 6.00 (brs, 1 H, H-3'), 6.20 (brs, 1 H, H-2'), 7.32 (s, 2 H, NH_2), 8.10 (s, 1 H, H-2), 8.17 (s, 1 H, H-8); ^{13}C NMR (DMSO-d_6) δ 41.37 (C-5'), 57.42 (C-1'), 74.05 (C-4'), 131.03 (C-2'), 139.62 (C-3'), 119.31 (C-5), 139.57 (C-8), 149.14 (C-4), 152.49 (C-2), 156.34 (C-6). Anal. Calcd for $C_{10}H_{11}N_5O$: C, 55.29; H, 5.10; N, 32.24. Found: C, 55.15; H, 5.26; N, 31.96.

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(8) This compound has been designated as having (1*S*)-stereochemistry at C-1' by correlation to precursor **8**.

(9) This NMR data is in agreement with that in ref 1 for (±)-**3**.

(10) Trost, B. M.; Kuo, G.-H.; Benneche, T. *J. Am. Chem. Soc.* **1988**, *110*, 621–622. This reference reports the synthesis of (±)-**10**, without characterization, via a reaction of the lithium salt of adenine with cyclopentadiene monoepoxide in the presence of $Pd(OAc)_2$ and $(i\text{-}PrO)_3P$.