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Synthesis of 5'-Hydroxyalkyl-5'-deoxy-8,5'-(*R* and *S*)-cycloadenosines (Nucleosides and Nucleotides. XXXI¹⁾)

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Treatment of 2',3'-*O*-isopropylidene-5'-oxo-8,5'-cycloadenosine with dimethyloxosulfonium methylide followed by hydrogenation afforded the diastereomeric pairs of 5'-methyl-5'-deoxy-8,5'-cycloadenosine and 5'-hydroxymethyl-5'-deoxy-8,5'-cycloadenosine. The configurations at the 5'-positions of these 8,5'-cycloadenosines were determined by nuclear magnetic resonance (NMR) measurements. The Wittig reactions of the 5'-oxo-8,5'-cycloadenosine with methoxymethylenetriphenylphosphorane, methylthiomethylenetriphenylphosphorane, and ethyl(dimethylsulfuranylidene)acetate afforded the corresponding 5'-substituted derivatives.

The action of ethoxycarbonylmethylenetriphenylphosphorane with the 5'-oxo-8,5'-cycloadenosine afforded the 5'-ethoxycarbonylmethylene-8,5'-cycloadenosine, which was converted to 5'-hydroxyethyl-5'-deoxy-8,5'-cycloadenosine by reduction with LiBH₄ followed by deacetonation. The 5'(*R*)- and 5'(*S*)-diastereomers of the 5'-hydroxyethyl derivative were separated and identified by NMR analysis. The circular dichroism (CD) spectra of the 5'-substituted-8,5'-cycloadenosines showed that the diastereomers having the substituent at the *trans-gauche* position around the C₄'-C₅' bond gave strong negative CD bands, whereas the diastereomers with the 5'-substituent at the *gauche-trans* position exhibited positive bands.

Keywords—adenosine; cyclonucleosides; Wittig reaction; conformation; NMR; CD

We have recently synthesized conformationally fixed analogs of purine nucleosides and nucleotides, such as 5'-deoxy-8,5'-cyclo-adenosine and -inosine,³⁾ 8,5'-(*R* and *S*)-cycloadenosines,^{4,5)} and 5'-deoxy-8,5'-cycloguanosine 2',3'-cyclic phosphate.⁶⁾ The latter compound was utilized as a substrate in a study of the substrate specificity of ribonuclease T₁.⁶⁾ For the preparation of analogs of 5'-adenylate fixed in an "anti" conformation around the glycosylic linkage, the introduction of a primary hydroxyl group at the 5'-position of 5'-deoxy-8,5'-cycloadenosine is necessary. We describe here the synthesis of the 5'(*R* and *S*)-hydroxymethyl and 5'(*R* and *S*)-hydroxyethyl derivatives of 5'-deoxy-8,5'-cycloadenosine as models of "anti"-fixed adenosine.

2',3'-*O*-Isopropylidene-5'-oxo-8,5'-cycloadenosine (**1**) was chosen as the starting material; it was readily prepared from 5'-deoxy-8,5'-cycloadenosine.⁵⁾ Treatment of **1** with dimethyloxosulfonium methylide in dimethylformamide (DMF) and dimethylsulfoxide (DMSO) gave the 5',6'-epoxide (**2**) as an amorphous material in 60% yield. The nuclear magnetic resonance (NMR) spectra of **2** showed a set of doublets at 3.67 and 3.30 ppm due to the methylene group on the spiro epoxide. The epoxide connected to the adenine ring is assumed to be a benzyl ether system, so the reduction of **2** would be expected to give selectively the 5'-hydroxy-

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methyl derivative. Catalytic hydrogenation of **2** with Raney Ni in aqueous ethanol for two days afforded a mixture of products.

Separation of the products by silica gel column chromatography followed by preparative thin layer chromatography afforded four compounds. The products (**3** and **4**) having R_f 0.77 and 0.72 (solvent: CHCl_3 -EtOH, 10:1) showed the same absorption maximum at 264 nm in their ultraviolet (UV) absorption spectra. The mass spectra of both compounds showed a molecular ion peak at m/e 303. The NMR spectrum of the former showed a doublet at 1.58 ppm due to a methyl group and a doublet at 4.63 ppm due to a 4'-proton, while those of the latter showed a doublet due to a methyl group and a singlet due to the 4'-proton at 1.58 and 4.52 ppm, respectively. These results led to the identification of **3** and **4** as 5'-methyl-5'-deoxy-8,5'-cycloadenosines, the former having the *S*-configuration at the 5'-position (the methyl group being situated in the *trans-gauche* (*tg*) position with respect to the lactol ring oxygen and the 3'-carbon, respectively, around the $\text{C}_4'-\text{C}_5'$ bond).

The products (**5** and **6**) having R_f 0.38 and 0.29 gave the same molecular ion peak at m/e 319 in their mass spectra, which indicated the introduction of a hydroxyl group into **3** or **4**. Deacetonation of **5** and **6** afforded the corresponding free cyclonucleosides (**7** and **8**) as hygroscopic crystals. The NMR spectrum of **7** showed a doublet at 4.68 ppm due to the 4'-proton while that of **8** showed a singlet at 4.69 ppm. Methyl protons were not detected in either compound. Therefore, **7** was assigned as 5'-hydroxymethyl-5'-deoxy-8,5'(*R*)-cycloadenosine (the hydroxymethyl group being situated in the *tg* position around the $\text{C}_4'-\text{C}_5'$ bond) and **8** as the *S*-diastereomer. These findings showed the original epoxide (**2**) to be a diastereomeric mixture. The yields of the products **3**, **4**, **5** and **6** (18.5, 14.6, 22, and 15%, respectively) showed that the hydrogenation of **2** proceeded without regioselectivity.

Introduction of a one-carbon substituent into the 5'-position of **1** by an alternative route was next attempted. Treatment of **1** with methoxymethylenetriphenylphosphorane, methylthiomethylenetriphenylphosphorane, and ethyl (dimethylsulfuranylidene) acetate gave the corresponding 5'-substituted derivatives of 8,5'-cycloadenosine (**9**, **10**, **11**) in high yields. However, attempts to convert these derivatives to the 5'-formyl derivatives were

Chart 1

unsuccessful. For the introduction of a hydroxyethyl group to the 5'-position of **1**, a Wittig reaction was also attempted.

Treatment of **1** with ethoxycarbonylmethylenetriphenylphosphorane afforded 5'-ethoxycarbonylmethylene-2',3'-*O*-isopropylidene-5'-deoxy-8,5'-cycloadenosine (**12**). The NMR spectrum of **12** showed two singlets due to 6'-vinylic proton at 6.86 and 6.84 ppm in a ratio of 4:1, which suggests the presence of an *E/Z*-mixture of **12**. Treatment of **12** with sodium borohydride and lithium chloride in ethanol for three days afforded two products (**13** and **14**), which were separated by silica gel chromatography. Deacetonation of **13** and **14** gave the corresponding 5'-hydroxyethyl-5'-deoxy-8,5'-cycloadenosines (**15** and **16**). The NMR spectra of **15** and **16** were consistent with these structures. The 4'-proton of **15** was detected at 4.55 ppm as a doublet while that of **16** gave a singlet at 4.47 ppm, allowing the assignment of the 5'(*S*)-configuration for **15** and the 5'(*R*)-configuration for **16**.

Chart 2

Chart 3

In order to confirm the configurations at the 5'-position in these 8,5'-cyclonucleosides the circular dichroic (CD) spectra of the pairs of diastereomers were measured. As we have already reported,⁶⁾ the CD spectrum of 8,5'(*S*)-cycloadenosine showed a strong negative CD band in the 260 nm region, whereas the *R*-diastereomer showed a positive band with weaker amplitude.

The CD spectra of the 5'-substituted-8,5'-cycloadenosines synthesized in the present work are shown in Fig. 1.

Fig. 1. CD Spectra of Diastereomeric Pairs of 8,5' (*R* and *S*)-Cycloadenosines in Water

Compounds **3**, **7**, and **15** (the 5'-substituents being situated on the front-side, or the *tg* position, as depicted) showed strong negative bands around their main absorption regions. Compounds **8** and **16** showed weak positive bands in the same regions. Although the 5'-(*R*) methyl derivative (**4**) showed a negative band its magnitude was very weak. Since the CD bands in these compounds reflect the chiralities of both the C-1' and C-5' positions connected to the "anti"-fixed purine chromophore, and since the contribution of the anomeric carbon in this 8,5'-cyclo- system to the sign of the CD band is towards the negative side (as is evident from the CD spectra of 5'-deoxy-8,5'-cycloadenosine⁶⁾), the patterns of the CD bands of these three pairs of diastereomers reflect the chiralities of the 5'-position in that a 5'-substituent located on the front-side exerts a negative contribution and the substituent on the back-side exerts a positive contribution. Assignments of the configurations at the 5'-position based on the CD spectra are in good accordance with those based on the NMR measurements, as described earlier.

The synthesis of mono- and tri-phosphate esters of **7**, **8**, **15** and **16**, and studies with various enzymes utilizing adenylates are in progress, and the results will be reported elsewhere.

Experimental

Melting points were determined with a Yanaco MP-3 melting points apparatus and are uncorrected. UV spectra were recorded on a Shimadzu UV-300 recording spectrophotometer. NMR spectra were recorded on a Hitachi R-20B (60 MHz) or JEOL JNM-FX 100Ft NMR spectrometer using tetramethylsilane as an internal standard. The abbreviations used to describe the splittings are as follows: s (singlet), d (doublet), t (triplet), m (multiplet), and b (broad). CD spectra were recorded on a JASCO J-40 spectropolarimeter with a data processor (8 accumulations) at room temperature. Infrared (IR) spectra were recorded on a Hitachi 215 spectrophotometer.

5',6'-Epoxy-5'-hydroxymethyl-2',3'-O-isopropylidene-8,5'(*R* and *S*)cycloadenosine (2)—Dimethyloxosulfoniummethylide was prepared by the reported method⁷⁾ from 360 mg of trimethyloxosulfonium chloride and 119 mg of 50% NaH in 4 ml of DMSO, and was suspended in 5 ml of THF at 0°. A solution of 500 mg of **1** in 20 ml of THF was added to the above suspension and stirred for 70 min at 0°. After addition of a small volume of acetone and ethanol to the suspension, the solvent was removed and the residue was partitioned with EtOAc and H₂O. The organic layer was dried (Na₂SO₄) and concentrated to leave a residue which was taken up in CHCl₃ and applied to a column of silica gel (2×10 cm). The eluate with 4% EtOH in CHCl₃ gave 316 mg (60%) of **2**, on removal of the solvent, as a homogeneous glass. MS *m/e*: 317 (M⁺). UV $\lambda_{\text{max}}^{\text{H}_2\text{O}}$: 268 nm. NMR (CDCl₃) δ : 8.39 (s, 1, 2-H), 6.47 (bs, 3, 1'-H and NH₂), 5.15 (d, 1, 2' or 3'-H), 4.81 (d, 1, 3' or 2'-H), 4.40 (s, 1, 4'-H), 3.67 (d, 1, 6'-CH₂), 3.30 (d, 1, 6'-H_b), 1.56, 1.32 (s, 3+3, CMe₂); $J_{2',3'}=6.0$ Hz, $J_{a,b}=6.0$ Hz.

Hydrogenation of 2 with Ni Catalyst—A solution of **2** (400 mg) in EtOH (50 ml) and H₂O (10 ml) was hydrogenated with Raney Ni catalyst (W-2, 600 mg wet wt) at room temperature at 4.5 kg/cm² for 2 days. The catalyst was filtered off and the filtrate was concentrated, then the residue was taken up in CHCl₃. The solution was applied to a column of silica gel (2×12 cm). The eluate with 4% EtOH in CHCl₃ contained **3** and **4**, and the eluate with 8% EtOH in CHCl₃ contained **5** and **6**. These mixtures were separated by preparative TLC.

2',3'-O-Isopropylidene-5'-methyl-5'-deoxy-8,5'(*S*)-cycloadenosine (3)—The residue of the 4% eluate was charged on 3 plates (20×20 cm) of silica gel, which were developed several times with CHCl₃-EtOH (15:1) until a satisfactory separation was accomplished. Two main bands were detected on each plate. The faster-migrating bands were excised and eluted with CHCl₃-EtOH (1:1), and the eluate was evaporated to dryness to leave 70 mg (18%) of **3** as a homogeneous glass. MS *m/e*: 303 (M⁺). UV $\lambda_{\text{max}}^{\text{H}_2\text{O}}$: 264 nm (ϵ , 16000). NMR (CDCl₃) δ : 8.36 (s, 1, 2-H), 6.34 (s, 1, 1'-H), 5.93 (bs, 2, NH₂), 4.86 (d, 1, 2' or 3'-H), 4.68 (d, 1, 3' or 2'-H), 4.63 (d, 1, 4'-H), 3.67 (m, 1, 5'-H), 1.57, 1.30 (s, 3+3, CMe₂), 1.52 (s, 3, 5'-Me); $J_{2',3'}=6.0$ Hz, $J_{4',5'}=4.5$ Hz, $J_{5',6'}=7.0$ Hz. CD (H₂O): $\theta_{262} -22200$, $\theta_{223} 0$.

2',3'-O-Isopropylidene-5'-methyl-5'-deoxy-8,5'(*R*)-cycloadenosine (4)—The slower-migrating band of the p-TLC described above was excised and eluted with the same solvent. Removal of the solvent gave 54 mg (14%) of **4** as a homogeneous glass. MS *m/e*: 303 (M⁺). UV $\lambda_{\text{max}}^{\text{H}_2\text{O}}$: 264 nm (ϵ , 13000). NMR (CDCl₃) δ : 8.37 (s, 1, 2-H), 6.35 (s, 1, 1'-H), 6.20 (bs, 2, NH₂), 4.68 (bs, 2, 2', 3'-H), 4.52 (s, 1, 4'-H), 3.11 (q, 1, 5'-H), 1.58 (d, 3, 5'-Me), 1.57, 1.30 (s, 3+3, CMe₂), $J_{5',6'}=7.0$ Hz. CD (H₂O): $\theta_{289} 1900$, $\theta_{270} 0$, $\theta_{256} -2700$, $\theta_{233} -600$, $\theta_{214} -3000$, $\theta_{219} 0$.

5'-Hydroxymethyl-2',3'-O-isopropylidene-5'-deoxy-8,5'(*R*)-cycloadenosine (5)—The eluate with 8% EtOH in CHCl₃ of the above chromatography was charged on 3 plates for p-TLC and was developed several times with CHCl₃-EtOH (10:1). From the faster-migrating band, 87 mg (22%) of **5** was obtained as a homogeneous glass. MS *m/e*: 319 (M⁺). UV $\lambda_{\text{max}}^{\text{H}_2\text{O}}$: 263 nm.

5'-Hydroxymethyl-2',3'-O-isopropylidene-5'-deoxy-8,5'(*S*)-cycloadenosine (6)—From the slower-migrating band of the above p-TLC, 60 mg (15%) of **6** was obtained as a homogeneous glass. MS *m/e*: 319 (M⁺). UV $\lambda_{\text{max}}^{\text{H}_2\text{O}}$: 263 nm.

5'-Hydroxymethyl-5'-deoxy-8,5'(*R*)-cycloadenosine (7)—Compound **5** was dissolved in 7 ml of 0.1 N HCl and the solution was kept at 85–90° for 45 min. After neutralization of the solution with 2 N NH₄OH, the solution was concentrated and the residue was crystallized from hot H₂O to leave 56 mg (74%) of **7** as hygroscopic crystals, mp 242° (dec.). Anal. Calcd for C₁₁H₁₃N₅O₄·1/3H₂O: C, 46.32; H, 4.81; N, 24.56. Found: C, 46.37; H, 4.92; N, 24.29. MS *m/e*: 279 (M⁺). UV $\lambda_{\text{max}}^{\text{H}_2\text{O}}$: 263 nm (ϵ , 16400). $\lambda_{\text{max}}^{0.1N \text{ HCl}}$ 260 nm (ϵ , 16400). CD (H₂O): $\theta_{263} -16600$, $\theta_{222} 0$. NMR (DMSO-*d*₆+D₂O) δ : 8.11 (s, 1, 2-H), 6.01 (s, 1, 1'-H), 4.68 (d, 1, 4'-H), 4.43 (d, 1, 2' or 3'-H), 4.21 (m, 2, 6'-H), 3.99 (d, 1, 3' or 2'-H), 3.64 (m, 1, 5'-H); $J_{2',3'}=6.1$ Hz, $J_{4',5'}=4.6$ Hz.

5'-Hydroxymethyl-5'-deoxy-8,5'(*S*)-cycloadenosine (8)—Compound **6** (60 mg) was deacetonated in the manner described above and 18 mg (34%) of **8** was obtained as hygroscopic crystals from H₂O, mp 268° (dec.). Anal. Calcd for C₁₁H₁₃N₅O₄·1/2H₂O: C, 45.81; H, 4.90; N, 24.29. Found: C, 46.16; H, 4.88, N, 23.71. MS *m/e*: 279 (M⁺). UV $\lambda_{\text{max}}^{\text{H}_2\text{O}}$ 264.5 nm (ϵ , 14300), $\lambda_{\text{max}}^{0.5N \text{ HCl}}$ 260.5 nm (ϵ , 14100). CD (H₂O): $\theta_{288.5} +1100$, $\theta_{262} +550$, $\theta_{271.5} +1100$, $\theta_{264} 0$, $\theta_{253.5} -1300$, $\theta_{232} -400$, $\theta_{219} -4200$, $\theta_{216} 0$. NMR (DMSO-*d*₆+D₂O) δ : 8.13 (s, 1, 2-H), 6.02 (s, 1, 1'-H), 4.69 (d, 1, 4'-H), 4.22 (d, 1, 2' or 3'-H), 4.06 (d, 1, 3' or 2'-H), 3.56 (t, 2, 6'-H), 3.14 (m, 2, 5'-H); $J_{2',3'}=5.9$ Hz.

2',3'-O-Isopropylidene-5'-methoxymethylene-5'-deoxy-8,5'-cycloadenosine (9)—Methoxymethylenetriphenylphosphorane was prepared from 599 mg of methoxymethyltriphenylphosphonium chloride and 84 mg of 50% NaH in 4.4 ml of DMSO. A solution of 100 mg of **1** in 4 ml of DMSO was added to the solution and the mixture was stirred for 1 hr at room temperature. The deep red solution was poured into 65 ml of H₂O. The mixture was extracted with CHCl₃ (20 ml×3) and the organic phase was dried over Na₂SO₄ then evaporated to dryness. The residue was taken up in CHCl₃ and the solution was charged on 2 plates of silica gel, which were developed with CHCl₃-EtOH (10:1). The main band was excised and extracted with CHCl₃-

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EtOH (1:1). The solvent was removed and the residue was crystallized from aqueous EtOH to give 82 mg (75%) of **9** as hygroscopic crystals, mp 290° (dec.). *Anal.* Calcd for $C_{15}H_{17}N_5O_4 \cdot 1/4H_2O$: C, 53.65; H, 5.22; N, 20.86. Found: C, 53.93; H, 5.24; N, 20.56. MS m/e : 331 (M^+). UV $\lambda_{max}^{H_2O}$ 324 nm (sh), 309 nm, 300 nm (sh). NMR (DMSO- d_6) δ : 8.10 (s, 1, 2-H), 7.19 (bd, 2, NH₂), 6.89 (s, 1, 6'-H), 6.12 (s, 1, 1'-H), 5.01 (s, 1, 4'-H), 4.68 (bs, 2, 2', 3'-H).

2',3'-O-Isopropylidene-5'-methylthiomethylene-5'-deoxy-8,5'-cycloadenosine (10)—A solution of methylthiomethylenetriphenylphosphorane was prepared from 142 mg of methylthiomethyltriphenylphosphonium chloride and *n*-BuLi (0.6 ml of 15% solution) in 10 ml of THF. Compound **1** (100 mg) was added to the solution and the mixture was stirred for 4 hr at room temperature. The solution was then neutralized with 1 N HCl and concentrated. The residue was partitioned with $CHCl_3$ and H_2O and the organic layer was concentrated. This was applied to 3 plates of silica gel and developed with $CHCl_3$ -EtOH (14:1). The main band was excised and extracted with $CHCl_3$ -EtOH (1:1). The solvent was removed and the residue was crystallized from MeOH to give 76 mg (66%) of **10**, mp 292° (dec.). *Anal.* Calcd for $C_{15}H_{17}N_5O_3S$: C, 51.87; H, 4.90; N, 20.17; S, 9.22. Found: C, 51.82; H, 4.89; N, 19.92; S, 8.98. MS m/e : 347 (M^+). UV $\lambda_{max}^{H_2O}$ 332, 259 nm. NMR (DMSO- d_6) δ : 8.17 (s, 1, 2-H), 7.45 (s, 1, 6'-H), 7.23 (bs, 2, NH₂), 6.24 (s, 1, 1'-H), 5.20 (s, 1, 4'-H), 4.88 (d, 1, 2' or 3'-H), 4.70 (d, 1, 3' or 2'-H), 3.33 (s, 3, SMe), 1.46, 1.27 (s, 3+3, CMe₂); $J_{2',3'} = 7.0$ Hz.

Ethyl 5'-(2',3'-O-Isopropylidene-8,5'-cycloadenosinyl)glycidate (11)—A mixture of ethyl(dimethylsulfuranylidene)acetate (293 mg) and **1** (330 mg) in 30 ml of $CHCl_3$ was stirred overnight at room temperature. The solution was washed with H_2O and the organic layer was concentrated to leave a residue. This was taken up in Et₂O containing a small amount of MeOH and kept overnight. The separated crystals were collected to give 367 mg (83%) of **11** as the monohydrate, mp 187–189°. *Anal.* Calcd for $C_{17}H_{19}N_5O_6 \cdot H_2O$: C, 50.10; H, 5.21; N, 17.19. Found: C, 49.94; H, 5.13; N, 17.19. MS m/e : 389 (M^+). UV $\lambda_{max}^{H_2O}$ 275 nm. IR (nujol): 1740 cm^{-1} . NMR ($CDCl_3$) δ : 8.38 (s, 1, 2-H), 6.45 (bs, 3, 1'-H and NH₂), 5.20 (d, 1, 2' or 3'-H), 4.83 (d, 2, 3' or 2'-H and 4'-H), 4.40 (q, 2, OCH_2CH_3), 4.36 (s, 1, 6'-H), 1.56, 1.35 (s, 3+3, CMe₂), 1.37 (t, 3, OCH_2CH_3).

5'-Ethoxycarbonylmethylene-2',3'-O-isopropylidene-5'-deoxy-8,5'-cycloadenosine (12)—A mixture of 454 mg of **1** and 574 mg of ethoxycarbonylmethylenetriphenylphosphorane in 50 ml of $CHCl_3$ was stirred overnight at room temperature. The reaction mixture was concentrated to half the original volume and applied to a column of silica gel (2.3 × 20 cm). After elution of triphenylphosphine oxide with 0–2% EtOH in $CHCl_3$ the product was eluted with 4% EtOH in $CHCl_3$. Removal of the solvent gave 548 mg (98%) of **12** as a yellow powder. *Anal.* Calcd for $C_{17}H_{19}N_5O_5$: C, 54.66; H, 5.14; N, 18.76. Found: C, 54.65; H, 5.28; N, 18.84. MS m/e : 373 (M^+). UV $\lambda_{max}^{H_2O}$ 328 nm (ϵ , 11900), 285 nm (sh, ϵ , 6500), 239.5 nm (ϵ , 22050), min 267 nm (ϵ , 5300). IR (nujol): 1705 cm^{-1} . NMR (DMSO- d_6) δ : 8.26 (s, 1, 2-H), 7.60 (bs, 2, NH₂), 6.86 and 6.84 (s, total 1, 6'-H), 6.37 (s, 1, 1'-H), 6.17 (s, 1, 4'-H), 5.89 (bs, 2, 2', 3'-H), 4.27 (q, 2, OCH_2CH_3), 1.50, 1.29 (s, 3+3, CMe₂), 1.29 (t, 3, OCH_2CH_3). CD (H_2O): $\theta_{335} -3530$, $\theta_{301} -1500$, $\theta_{282} -4640$, $\theta_{263} 0$, $\theta_{265} +560$, $\theta_{263} 0$, $\theta_{245} -18200$, $\theta_{232} 0$, $\theta_{215} +21000$.

Reduction of 12 with NaBH₄ in the Presence of LiCl—A solution of **12** (541 mg) in EtOH (50 ml) was treated with LiCl (308 mg) and NaBH₄ (274 mg), and the mixture was stirred at room temperature for 3 days. After filtration of the insoluble material the filtrate was evaporated to dryness and the residue was taken up in $CHCl_3$. This solution was applied to a column of silica gel (2.5 × 25 cm). The column was eluted with 8% EtOH in $CHCl_3$. Concentration of the initial eluate provided 5'-hydroxyethyl-2',3'-O-isopropylidene-5'-deoxy-8,5'-(*S*)-cycloadenosine (**13**, 120 mg, 23%) as a homogeneous glass. MS m/e : 333 (M^+). From the second fraction, a mixture of **13** and the *R*-diastereomer (133 mg, 26%) was obtained. The final fraction, on removal of the solvent, gave 121 mg (23%) of the (*R*)-isomer (**14**), MS m/e : 333 (M^+).

5'-Hydroxyethyl-5'-deoxy-8,5'-(*S*)-cycloadenosine (15)—A solution of **13** (120 mg) in 20 ml of 0.1 N HCl was kept at 85–90° for 75 min. After neutralization with 2 N NH_4OH the solution was concentrated and the residue was crystallized from H_2O to give 75 mg (70%) of **15**, mp 279° (dec.). *Anal.* Calcd for $C_{12}H_{15}N_5O_4$: C, 49.14; H, 5.16; N, 23.88. Found: C, 49.36; H, 5.16; N, 23.71. MS m/e : 293 (M^+). UV $\lambda_{max}^{H_2O}$ 264 nm (ϵ , 16100), $\lambda_{max}^{0.5N HCl}$ 261 nm (ϵ , 16000). CD (H_2O): $\theta_{262} -20400$, $\theta_{223} 0$, $\theta_{204} +30300$. NMR (DMSO- d_6) δ : 8.11 (s, 1, 2-H), 6.01 (s, 1, 1'-H), 4.55 (d, 1, 4'-H), 4.27 (d, 1, 2' or 3'-H), 4.00 (d, 3' or 2'-H), 3.74 (m, 2, 7'-H), 3.52 (m, 1, 5'-H), 1.78 (m, 2, 6'-H); $J_{2',3'} = 5.2$ Hz, $J_{4',5'} = 6.1$ Hz.

5'-Hydroxyethyl-5'-deoxy-8,5'-(*R*)-cycloadenosine (16)—Compound **14** (120 mg) was deacetonated in the manner described above and **16** was crystallized from H_2O to give 67 mg (63%), mp 267–269°. *Anal.* Calcd for $C_{12}H_{15}N_5O_4$: C, 49.14; H, 5.16; N, 23.88. Found: C, 48.83; H, 5.12; N, 23.46. MS m/e : 293 (M^+). UV $\lambda_{max}^{H_2O}$ 264.5 nm (ϵ , 16400), $\lambda_{max}^{0.5N HCl}$ 261.5 nm (ϵ , 16200). CD (H_2O): $\theta_{265} +5300$, $\theta_{226} 0$, $\theta_{212} -9400$. NMR (DMSO- d_6) δ : 8.11 (s, 1, 2-H), 6.00 (s, 1, 1'-H), 4.47 (s, 1, 4'-H), 4.15 (d, 1, 2' or 3'-H), 3.99 (d, 1, 3' or 2'-H), 3.64 (m, 2, 7'-H), 3.16 (t, 1, 5'-H), 1.90 (m, 2, 6'-H); $J_{2',3'} = 6.1$ Hz.

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