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Synthesis of 8,2′-Methano- and 8,2′-Ethanoadenosines (Nucleosides and Nucleotides. LXV[1a])

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Treatment of 3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)-2′-ketoadenosine (**1**) with methylenetriphenylphosphorane gave the 2′-methylene derivative (**2**). Hydroxylation of **1** with OsO_4 gave the 2′-hydroxymethyladenosine (**4**), which was then converted to the 2′-phenylthiomethyl derivative (**5**). Photocyclization followed by deprotection of the product furnished 8,2′-methanoadenosine (**7**), an adenosine fixed in a high-anti conformation. Oxidation of a 2′-hydroxyethylideneadenosine with OsO_4 gave the 2′-dihydroxyethyladenosine (**10**), which was also converted to the 2′-(2-phenylthioethyl) derivative (**11**). The photocyclization of **11** and successive elimination of the hydroxyl group gave the 8,2′-ethenoadenosine (**13**). Catalytic hydrogenation and deprotection of **13** afforded 8,2′-ethanoadenosine (**15**). The circular dichroism spectral features of *C*-cycloadenosine are discussed.

Keywords——2′-deoxy-2′-methylideneadenosine; 8,2′-methanoadenosine; 8,2′-ethanoadenosine; *C*-cycloadenosine; adenosine conformation; Wittig reaction; photocyclization; CD; NMR

In a previous paper[1] we described the synthesis of 2′-deoxy-8,2′-ethanoadenosine and related compounds. For studies of the interaction of enzymes acting on adenosine such as adenosine deaminases, adenosine kinase and adenylate kinases, the corresponding ribonucleoside as well as the 8,2′-methano-cyclo derivative are required. For this purpose, the use of 2′-ketonucleosides is reasonable, since we have accomplished the synthesis of 6,2′-methanouridine from a 2′-ketouridine.[2] This paper describes the synthesis of 8,2′-ethano- and 8,2′-methanoadenosines from a 2′-ketoadenosine. A preliminary account of this work has appeared.[3]

Treatment of 3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)-2′-ketoadenosine (**1**)[1] with methylenetriphenylphosphorane[4] in a mixture of dimethylsulfoxide (DMSO) and tetrahydrofuran (THF) afforded the 2′-methylene derivative (**2**) in 29% yield. The structure of **2** was confirmed by the mass (MS) and nuclear magnetic resonance (^{1}H-NMR) spectral analyses. In the ^{1}H-NMR spectrum of **2**, the 6′-vinyl protons appeared at δ 5.52 and 5.44 as multiplets. Deprotection of **2** with tetra-*n*-butylammonium fluoride afforded 2′-deoxy-2′-methylideneadenosine (**3**). Although the yield of **2** was low probably because of the well known base lability of the 2′-keto nucleosides,[5] the formation of **2** provides a method for the introduction of 2′-carbon substitutents into purine nucleosides.

Oxidation of **2** with osmium tetroxide and *N*-methylmorpholine-*N*-oxide[6] at 4 °C for 7 d afforded the 2′(*R*)-hydroxymethyladenosine (**4**). The hydroxylation of the methylidene group was expected to occur preferentially from the α side, as was indeed the case. Although spot probably corresponding to that of the *S*-epimer of **4** was detected on thin layer chromatography (TLC), it was a minor product. Compound **4** was mesylated, then treated with potassium thiophenoxide to afford the 2′(*R*)-phenylthiomethyladenosine (**5**). Irradiation of **5** with a low-pressure Hg lamp resulted in cyclization, giving the 8,2′-methano-cycloadenosine (**6**) in a yield of 34%. Deprotection of **6** with tetra-*n*-butylammonium fluoride afforded 8,2′-

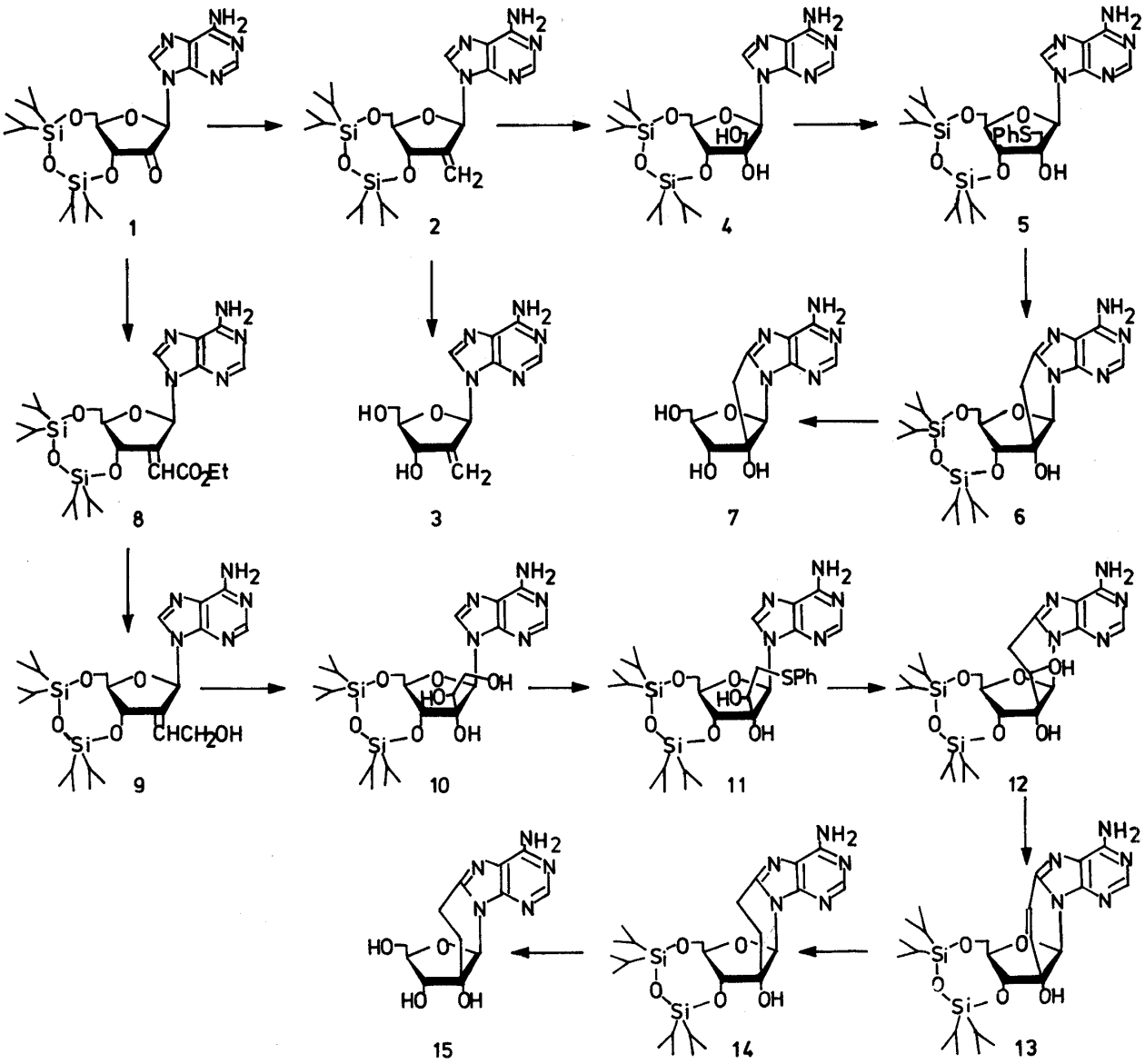

Chart 1

methanoadenosine (**7**). Compound **7** showed a molecular ion peak at *m/z* 279 in the MS, and the bridge-methylene signals appeared at δ 3.31 and 2.98 as doublets in the ^{1}H-NMR spectrum. Furthermore, **7** migrated as a monoanion on paper electrophoresis in borate buffer, showing the presence of *cis* hydroxyl groups at the 2′ and 3′ positions. All these data clearly showed that the structure of **7** was correct.

The synthesis of 8,2′-ethanoadenosine was next undertaken. For the introduction of the two-carbon unit at the 2′-position, we previously used the 2′-ethoxycarbonylmethylidene derivative (**8**) of adenosine, in the synthesis of 2′-deoxy-8,2′-ethanoadenosine.[1)] We also reported the reduction of **8** with sodium borohydride to give a mixture of 2′-ethoxycarbonylmethyl-, 2′-(2-hydroxyethyl)-, and 2′-hydroxyethylidene-adenosines (**9**), the latter being a minor product.[1)] The hydroxylation of **9** should give the 2′-dihydroxyethyl derivative (**10**), which would be the key intermediate leading to 8,2′-ethanoadenosine. Compound **9** was obtained in a better yield when lithium aluminum hydride was used for the reduction of **8**. Treatment of **9** with osmium tetroxide and *N*-methylmorpholine-*N*-oxide gave the triol (**10**) in a yield of 45% from **8**. Although the hydroxylation of **9** should occur from the α side, the

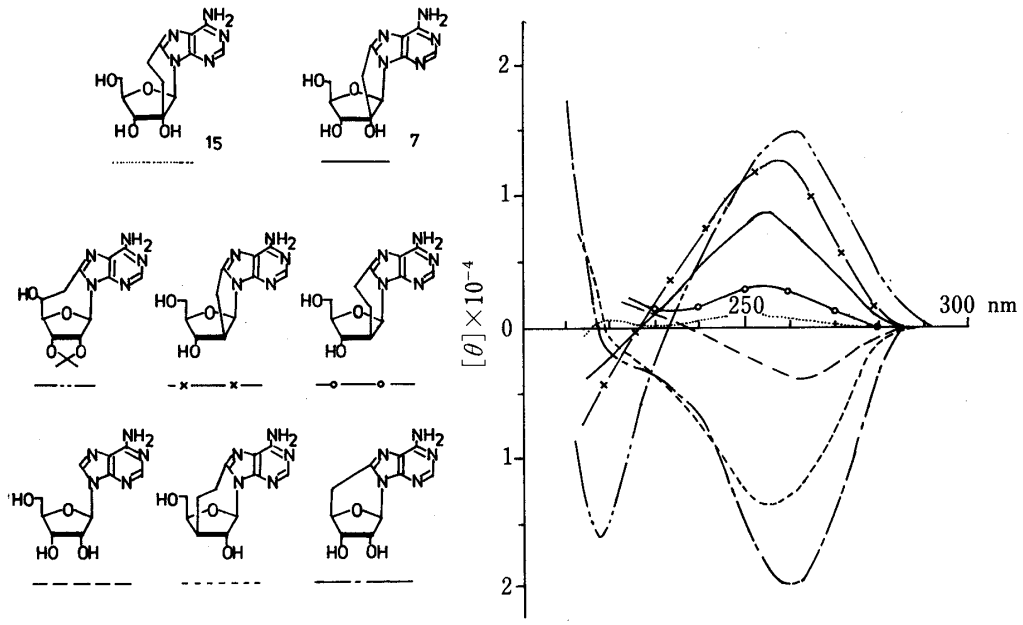

Fig. 1. CD Spectra of Carbon-Bridged Cycloadenosines in Water at Room Temperature

stereochemistry of the 2′ and 6′ positions of **10** was not determined at this stage. Compound **10** was treated with mesyl chloride under ice-cooling, then with sodium thiophenoxide to give the 7′-thiophenyl derivative (**11**) in 63% yield.

The regiospecific thiophenylation at the primary hydroxyl group of **10** was confirmed by examination of the ^{1}H-NMR spectrum of **11** (see Experimental). Irradiation of **11** in the presence of trimethyl phosphite gave the expected 8,2′-cyclo compound (**12**) in a crystalline form. Therefore, it is certain that the hydroxylation of **9** had occurred from the α side, though the configuration at the 6′-position was not determined. Compound **12** was treated with mesyl chloride followed by 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) to give the 8,2′-ethenoadenosine (**13**) in a crystalline form. Compound **13** showed a red shift (λ_{max} 304 nm) in the ultraviolet (UV) spectrum, with fluorescence, corresponding to the extra conjugation of the adenine chromophore. In addition, the 6′,7′-ethylenic protons were detected in the ^{1}H-NMR spectrum (6.74 and 6.26 ppm, respectively) with a vicinal coupling constant of 10.3 Hz. A long-range splitting (1.2 Hz) between the 1′ and 6′ protons was also observed. Hydrogenation of **13** with Pd–carbon catalyst afforded the silylated 8,2′-ethanoadenosine (**14**) in high yield, and this was desilylated to furnish 8,2′-ethanoadenosine (**15**) in a crystalline form. Compound **15** showed a UV maximum at 262 nm similar to that of adenosine, and the signals of the ethano protons (3.68—3.48 for 7′ and 2.09 and 1.77 for 6′ protons) were seen in the ^{1}H-NMR spectrum. Compound **15** migrated as a monoanion on paper electrophoresis in borate buffer, thus confirming the presence of a 2′,3′-*cis* diol system.

The circular dichroism (CD) spectra of the carbon-bridged cycloadenosines so far prepared are compiled in Fig. 1. The CD spectra of **7** and **15** were very similar to those of the corresponding 2′-deoxy derivatives.[1,7] As pointed out in a preceding paper,[1] the sign of the CD bands is inverted as the glycosyl torsion angle is increased, and the transitional torsion angle is between 50° and 65° in the anti region. This means that the sign of the CD bands does not necessarily correspond to the so called *syn* and *anti* conformations. In addition, the CD magnitudes of the 8,6′-cyclo compound (positive) and the 8,3′-cyclo compound (negative) are rather large, which implies that the molar ellipticity is not simply changing in a sine curve form with respect to the glycosyl torsion angles. Further, although adenosine itself shows a

negative band, its magnitude is rather small due to the relatively free rotation around the glycosylic linkage in solution.

Experimental

Melting points were determined on a Yanaco MP-3 micromelting point apparatus and are corrected. UV spectra were taken with a Shimadzu UV-260 spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL JNM-FX 100FT or 200FT spectrometer with tetramethylsilane as an internal standard. Chemical shifts are expressed in ppm (δ), and signals are described as s (singlet), d (doublet), t (triplet), m (multiplet) or br (broad). MS were taken on a JEOL D-300 spectrometer. CD spectra were recorded on a JEOL J-500A spectropolarimeter at room temperature. The photoreaction was carried out by an apparatus equipped with an Eikosha PIL-60 60W low-pressure Hg vapor lamp (quartz filter) in an argon atmosphere. The starting nucleoside, adenosine, was from Yamasa Shoyu Co. Silica gel used for column chromatography or preparative TLC (PTLC) was Wako gel C-200.

3',5'-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-2'-deoxy-2'-methylideneadenosine (2)——NaH (60%, 1.78 g, washed with THF) and DMSO (19 ml) were mixed at 65 °C under stirring for 1.5 h. After cooling, THF (19 ml), DMSO (50 ml) and methyltriphenylphosphonium bromide (19.2 g) were added, and the whole was stirred at room temperature for 2 h. Compound **1**[1] (9.1 g) in THF (30 ml) was added dropwise to the solution and the mixture was stirred for 6 h. The solution was neutralized by addition of acetic acid, and the solvent was removed *in vacuo*. The residue was partitioned between $CHCl_3$ and H_2O and the organic layer was passed through a Whatman 1PS filter paper. The filtrate was concentrated and the residue was taken up in $CHCl_3$ and applied to a column of silica gel. The column was eluted with 1% EtOH–$CHCl_3$. This operation was repeated several times until pure **2** was eluted. The final eluate was concentrated to leave 2.62 g (29%) of **2** as a syrup. MS *m/z*: 505 (M^+), 462 $(M-\text{iso-Pr})^+$. ^{1}H-NMR ($CDCl_3$) δ: 8.33 (1H, s, H-8), 7.90 (1H, s, H-2), 6.62 (1H, m, H-1'), 5.76 (2H, br s, H_2N-6), 5.52 (1H, m, H-6'a), 5.44 (1H, m, H-6'b), 5.30 (1H, m, H-3'), 4.09 (2H, m, H-5'a, b), 3.82 (1H, m, H-4'), 1.25—0.96 (28H, m, iso-Pr).

2'-Deoxy-2'-methylideneadenosine (3)——Compound **2** (375 mg) was dissolved in THF (10 ml) and *n*-Bu_4NF (1 M in THF, 1 ml) was added to the solution. The mixture was stirred for 15 min, the solvent was removed *in vacuo*, and the residue was partitioned between $CHCl_3$ and H_2O (20 ml each). The aqueous layer was separated, washed with $CHCl_3$, and concentrated to leave crystalline **3** (170 mg, 87.3%), mp 212—213 °C. UV $\lambda_{max}^{H_2O}$ nm (ε): 259.5 (14600). MS *m/z*: 263 (M^+), 246 $(M-OH)^+$, 245 $(M-H_2O)^+$, 232 $(M-CH_2OH)^+$, 135 $(B+1)^+$. ^{1}H-NMR (DMSO-d_6) δ: 8.18 (1H, s, H-8), 8.11 (1H, s, H-2), 7.27 (2H, br s, H_2N-6), 6.60 (1H, d, H-1', J=1.4 Hz), 5.71 (1H, d, HO-3', J=5.8 Hz), 5.39 (1H, t, H-6'a), 5.19 (1H, t, H-6'b), 5.05 (1H, t, HO-5', J=5.6 Hz), 4.80 (1H, br t, H-3'), 3.85—3.60 (3H, m, H-4',5'a, b). *Anal.* Calcd for $C_{11}H_{13}N_5O_3$: C, 50.19; H, 4.98; N, 26.60. Found: C, 50.09; H, 4.89; N, 26.52.

3',5'-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-2'(*R*)-hydroxymethyladenosine (4)——Compound **2** (414 mg) was dissolved in a mixture of THF (2 ml), *tert*-BuOH (2 ml), and H_2O (0.6 ml). After addition of *N*-methylmorpholine-*N*-oxide (166 mg, 1.2 eq) to the solution, OsO_4 (0.42 ml of 0.5% in *tert*-BuOH, 0.01 eq) was added under ice cooling, and the whole was stirred at 4 °C for 7 d. The mixture was partitioned between EtOAc (10 ml) and 1 M $NaHSO_3$ (10 ml). The organic layer was separated through a Whatman 1PS filter paper and the solvent was removed *in vacuo*. The residue was applied to a silica gel column. The eluate with 3% EtOH in $CHCl_3$ was concentrated to leave 360 mg (82%) of **4** as a powder. MS *m/z*: 539 (M^+), 508 $(M-CH_2OH)^+$, 496 $(M-\text{iso-Pr})^+$. ^{1}H-NMR ($CDCl_3+D_2O$) δ: 8.41 (1H, s, H-8), 8.29 (1H, s, H-2), 5.95 (1H, s, H-1'), 4.39—4.19 (3H, m, H-3',4',5'a), 4.30 (1H, dd, H-5'b), 3.61 (1H, d, H-6'a), 3.21 (1H, d, H-6'b, $J_{6'a,b}$=12.6 Hz), 1.12—0.88 (28H, m, iso-Pr).

3',5'-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-2'(*R*)-phenylthiomethyladenosine (5)——Compound **4** (693 mg) in pyridine (9 ml) was treated with MsCl (0.13 ml, 1.3 eq) for 2 h at room temperature. After addition of a small volume of H_2O, the solvent wa removed *in vacuo* and the residue was partitioned between EtOAc and H_2O. The organic layer was concentrated and the residue (758 mg of the mesylate) was dissolved in dimethylformamide (DMF) (15 ml). Thiophenol (140 μl, 1.1 eq) and KO*tert*-Bu (133 mg, 1 eq) were added to the solution and the whole was stirred for 4 h at room temperature. The mixture was neutralized by addition of 1 N HCl and the solvent was removed *in vacuo*. The residue was partitioned between EtOAc and H_2O, and the organic layer was filtered through a Whatman 1PS filter paper. The filtrate was concentrated and the residue was applied to a silica gel column. The eluate with 2% MeOH in $CHCl_3$ was concentrated to leave 542 mg (67%) of **5** as a foam. UV λ_{max}^{MeOH} (nm): 256, λ_{max}^{pH2} nm: 253. MS *m/z*: 631 (M^+), 588 $(M-\text{iso-Pr})^+$, 522 $(M-SPh)^+$. ^{1}H-NMR ($CDCl_3$) δ: 8.25 (1H, s, H-8), 7.95 (1H, s, H-2), 7.15—6.92 (5H, m, PhS), 6.11 (1H, s, H-1'), 5.67 (2H, br s, H_2N-6), 5.24 (1H, s, H-3', $J_{3',4'}$=7.1 Hz), 4.35—3.92 (3H, m, H-4',5'a, b), 3.58 (1H, s, HO-2'), 3.28 (1H, d, H-6'a, $J_{6'a,b}$=13.3 Hz), 2.97 (1H, d, H-6'b), 1.02—1.07 (28H, m, iso-Pr).

3',5'-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-8,2'-methanoadenosine (6)——Compound **5** (250 mg) and trimethyl phosphite (1 ml) were dissolved in acetonitrile (300 ml) and the solution was irradiated for 2 h. The photolyzates from three runs were combined and the solvent was removed *in vacuo*. The residue was applied to a column of silica gel (20 g). The eluate with 4% MeOH in $CHCl_3$ was evaporated and the residue was crystallized from EtOAc–*n*-hexane to give 142 mg (34%) of **6**. This showed no definite mp, but changed between 180 and 197 °C to amorphous form, UV λ_{max}^{MeOH} nm (ε): 261 (16600). MS *m/z*: 521 (M^+), 478 $(M-\text{iso-Pr})^+$. ^{1}H-NMR ($CDCl_3+D_2O$) δ: 8.33 (1H, s, H-2), 5.99

(1H, s, H-1′), 4.27—3.99 (3H, m, H-3′,4′,5′a), 3.86 (1H, dd, H-5′b, $J_{4',5'b}$ = 4.9 Hz, $J_{5'a,b}$ = 12.5 Hz), 3.37 (1H, d, H-6′a, $J_{6'a,b}$ = 17.6 Hz), 3.17 (1H, d, H-6′b), 1.12—0.93 (28H, m, iso-Pr). *Anal.* Calcd for $C_{23}H_{39}N_5O_5Si_2 \cdot 1/2H_2O$: C, 52.05; H, 7.60; N, 13.19. Found: C, 52.07; H, 7.39; N, 13.29.

8,2′-Methanoadenosine (7)——Compound **6** (143 mg) in THF (2 ml) was treated with *n*-Bu_4NF (1 M in THF, 0.3 ml) for 30 min at room temperature. The solvent was removed *in vacuo* and the residue was partitioned between $CHCl_3$ and H_2O. The aqueous layer was concentrated and the residue was crystallized from EtOH–H_2O to give 50 mg (65%) of **7**, mp 236—238 °C. UV $\lambda_{max}^{H_2O}$ nm (ε): 262 (16700), 207.7 (24400). MS *m/z*: 279 (M^+). CD (H_2O) [θ] (nm): 253 nm (θ = +8620), 226 nm (θ = 0). ^{1}H-NMR (D_2O) δ: 7.93 (1H, s, H-2), 5.83 (1H, s, H-1′), 4.06 (1H, ddd, H-4′), 3.84 (1H, d, H-3′, $J_{3',4'}$ = 8.3 Hz), 3.60 (1H, dd, H-5′a, $J_{4',5'a}$ = 2.4 Hz, $J_{5'a,b}$ = 12.7 Hz), 3.35 (1H, dd, H-5′b, $J_{4',5'b}$ = 4.9 Hz), 3.31 (1H, d, H-6′a, $J_{6'a,b}$ = 17.6 Hz), 2.98 (1H, d, H-6′b). Relative migration in paper electrophoresis (0.2 M boric acid–sodium borate, pH 7.5, 700 V, 80 min): adenosine, 1.0; **7**, 1.62; arabinosylcytosine, 0.12. *Anal.* Calcd for $C_{11}H_{13}N_5O_4 \cdot 1/2H_2O$: C, 45.83; H, 4.89; N, 24.29. Found: C, 45.85; H, 4.60; N, 24.37.

3′,5′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-2′-deoxy-2′-(2-hydroxyethylidene)adenosine (9)——Compound **8**[1] (6.0 g) in THF (60 ml) was treated with $LiAlH_4$ (0.98 g in 20 ml of THF) under ice cooling for 1 h with stirring. $Na_2SO_4 \cdot 10H_2O$ (5 g) was added to the mixture, the insoluble material was filtered off and washed with EtOH, and the filtrate and washings with ethanol were combined and concentrated. The residue was partitioned between EtOAc and H_2O. The organic layer was separated, and passed through a Whatman 1PS filter paper, and the filtrate was concentrated. The residue was applied to a silica gel (180 g) column. The eluate with 5% EtOH in $CHCl_3$ was concentrated to leave crude **9** (3.46 g, 62%, containing some 2′-hydroxyethyl derivative as an impurity). MS *m/z*: 535 (M^+), 494 $(M-\text{iso-Pr})^+$. ^{1}H-NMR ($CDCl_3$) δ: 8.29 (1H, s, H-8), 8.26 (1H, s, H-2), 7.31 (1H, s, H-1′), 5.85 (1H, s, H-6′), 4.97 (1H, m, H-3′), 4.40 (2H, m, H-7′a, b), 4.28 (1H, dd, H-5′a, $J_{4',5'a}$ = 1.9 Hz), 4.05 (1H, dd, H-5′b, $J_{4',5'b}$ = 2.7 Hz), 3.69 (1H, m, H-4′), 1.11—0.99 (28H, m, iso-Pr). This compound was used without further purification.

3′,5′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-2′(*R*)-(1,2-dihydroxyethyl)adenosine (10)——Crude **9** (4.12 g) was dissolved in a mixture of THF (20 ml) and H_2O (6 ml). *N*-Methylmorpholine-*N*-oxide (0.9 g) and OsO_4 (0.5% in *tert*-BuOH, 4 ml) were added to the solution and the mixture was stirred at room temperature for 4 h, then partitioned between EtOAc (50 ml) and 1 M $NaHSO_3$ (50 ml). The organic layer was filtered through a Whatman 1PS filter paper. The filtrate was concentrated and the residue was applied to a column of silica gel (120 g). The eluate with 10% MeOH in $CHCl_3$ was concentrated to leave 3.07 g (45% from **8**) of **10** as a foam. MS *m/z*: 569 (M^+), 551 $(M-H_2O)^+$, 538 $(M-CH_2OH)^+$. ^{1}H-NMR ($CDCl_3 + D_2O$) δ: 8.11 (1H, s, H-8), 8.01 (1H, s, H-2), 5.96 (1H, s, H-1′), 4.95 (1H, d, H-3′), 4.35—3.95 (3H, m, H-5′a, b, 6′), 3.95—3.45 (3H, m, H-4′, 7′a, b), 1.30—1.06 (28H, m, iso-Pr).

3′,5′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-2′(*R*)-(2-phenylthio-1-hydroxyethyl)adenosine (11)——Compound **10** (3.07 g) was dissolved in pyridine (50 ml) and MsCl (0.46 ml, 1.1 eq) was added to the solution under ice cooling. The mixture was stirred for 1 h, the solvent was removed *in vacuo* and the residue was partitioned between EtOAc and H_2O. The organic layer was separated and the solvent was evaporated off. The residue was taken up in DMF (50 ml), KO*tert*-Bu (605 mg) and thiophenol (0.61 ml) were added, and the whole was stirred for 2.5 h at room temperature. After neutralization of the solution by addition of 1 N HCl, the solvent was removed *in vacuo* and the residue was partitioned between EtOAc and H_2O. The organic layer was separated and the solvent was removed *in vacuo*. The residue was applied to a column of silica gel. The eluate with 2—5% EtOH in $CHCl_3$ was concentrated to leave 2.25 g (63%) of **11** as a foam. UV λ_{max}^{MeOH} nm (ε): 256.5. MS *m/z*: 661 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 8.23 (1H, s, H-8), 8.02 (1H, s, H-2), 7.11 (5H, m, PhS), 5.97 (1H, s, H-1′), 5.71 (2H, br s, H_2N-6), 4.96 (1H, d, H-3′, $J_{3',4'}$ = 5.6 Hz), 4.32—3.95 (4H, m, H-4′, 5′a, b, HO-2′), 3.76 (1H, br s, HO-6′), 3.59 (1H, m, H-6′), 3.26 (1H, dd, H-7′a), 2.83 (1H, dd, H-7′b, $J_{7'a,b}$ = 11.5 Hz, $J_{6',7'b}$ = 10.5 Hz), 1.19—1.07 (28H, m, iso-Pr).

3′,5′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-6′-hydroxy-8,2′-ethanoadenosine (12)——Compound **11** was dissolved in acetonitrile (100 mg in 100 ml). The solution (350 ml) was irradiated with an Hg lamp in the presence of 1 ml of trimethyl phosphite for 2 h. The solutions from six runs were combined and the solvent was removed *in vacuo*. The residue was applied to a column of silica gel (50 g). The eluate with 5—7% MeOH in $CHCl_3$ was concentrated and the residue was crystallized from EtOH to give 988 mg (57%) of **12**, mp 236—238 °C. UV λ_{max}^{MeOH} nm (ε): 261.3 (17500). MS *m/z*: 551 (M^+). CD H_2O [θ] (nm): +7100 (258). ^{1}H-NMR (DMSO-d_6) δ: 8.09 (1H, s, H-2), 7.18 (2H, br s, H_2N-6), 5.64 (1H, s, H-1′), 5.40 (1H, d, HO-6′, *J* = 5.9 Hz), 5.32 (1H, s, HO-2′), 4.29 (1H, d, H-3′, $J_{3',4'}$ = 5.6 Hz), 4.23—3.76 (4H, m, H-4′, 5′a, b, 6′), 3.14 (2H, m, H-7′a, b), 1.06—0.98 (28H, m, iso-Pr). *Anal.* Calcd for $C_{24}H_{41}N_5O_6Si_2$: C, 52.24; H, 7.49; N, 12.69. Found: C, 52.02; H, 7.45; N, 12.55.

3′-5′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-8,2′-ethenoadenosine (13)——Compound **12** (0.99 g) in pyridine (15 ml) was treated with MsCl (0.2 ml) at room temperature for 1 h. A small volume of MeOH–H_2O was added and the solvent was removed *in vacuo*. The residue was partitioned between EtOAc and H_2O, and the organic layer was separated through a Whatman 1PS filter paper. The filtrate was concentrated and the residue was taken up in dioxane (20 ml). DBU (0.54 ml, 2 eq) was added and the solution was heated at 50 °C for 20 min. After neutralization of the solution by addition of 1 N HCl, the solvent was removed *in vacuo* and the residue was partitioned between EtOAc and H_2O. The organic layer was separated and concentrated, and the residue was crystallized from EtOH to give 663 mg of **13**. Additional **13** (177 mg, total 840 mg, 88%) was obtained by silica gel chromatography of the mother liquor, mp 245—247 °C. UV λ_{max}^{MeOH} nm (ε): 304 (18200), 282 (shoulder),233 (10000). CD (MeOH) [θ] (nm): −20500

(296), −6900 (359), −41100 (238). MS *m/z*: 533 (M^+), 490 $(M-\text{iso-Pr})^+$. ^{1}H-NMR ($CDCl_3$) δ: 8.39 (1H, s, H-2), 6.74 (1H, d, H-7′, $J_{6',7'}=10.3$ Hz), 6.26 (1H, dd, H-6′, $J_{1',6'}=1.2$ Hz), 6.06 (1H, d, H-1′), 5.61 (2H, br s, H_2N-6), 4.26—3.77 (5H, m, H-3′, 4′, 5′a, b, HO-2′). 1.11—0.90 (28H, m, iso-Pr). *Anal.* Calcd for $C_{24}H_{39}N_5O_5Si_2$: C, 54.00; H, 7.36; N, 13.12. Found: C, 53.88; H, 7.41; N, 12.93.

3′,5′-*O*-(Tetraisopropyldisiloxane-1,3-diyl)-8,2′-ethanoadenosine (14)——A solution of **13** (250 mg) in EtOH (5 ml) and dioxane (5 ml) with 5% Pd–C (100 mg) was hydrogenated at 70 psi for 10 d. The Pd–C was filtered off, the filtrate was concentrated, and the residue was crystallized from EtOH to give 180 mg (72%) of **14**. This was slightly contaminated with **13**. UV λ_{max}^{MeOH} nm: 262. MS *m/z*: 535 (M^+). ^{1}H-NMR ($CDCl_3+D_2O$) δ: 8.36 (1H, s, H-2), 5.75 (1H,s, H-1′), 4.25—4.12 (3H, m, H-3′, 5′a, b), 3.73 (1H, m, H-4′), 3.20 (1H, ddd, H-7′a, $J_{7'a,b}=18$ Hz, $J_{7'a,6'b}=8.1$ Hz), 2.99 (1H, dt, H-7′b, $J_{7'b,6'a}=J_{7',b,6'b}=5.4$ Hz), 2.08 (2H, dd, H-6′a, b), 1.10—1.08 (28H, m, iso-Pr). *Anal.* Calcd for $C_{24}H_{41}N_5O_5Si_2\cdot H_2O$: C, 52.05; H, 7.83; N, 12.65. Found: C, 52.09; H, 7.62; N, 12.72.

8,2′-Ethanoadenosine (15)——A mixture of **14** (160 mg) and *n*-Bu_4NF (1 M in THF, 0.4 ml) in THF (5 ml) was stirred at room temperature for 1 h. The solvent was evaporated off and the residue was partitioned between $CHCl_3$ and H_2O. The aqueous layer was concentrated, the residue was taken up in MeOH, and the solution was subjected to PTLC (4 sheets) developed several times with $CHCl_2$–MeOH (4 : 1). The appropriate band was eluted with the same solvent (1 : 1), the solvent was removed *in vacuo*, and the residue was crystallized from MeOH to give 53 mg (60%) of **15**. This compound was still contaminated (*ca.* 5%) with the 8,2′-etheno compound. Repetition of PTLC with *n*-BuOH saturated with H_2O finally gave the pure sample. UV $\lambda_{max}^{H_2O}$ nm (ε): 262 (16600). CD (H_2O): [θ] (nm): +1090 (253), +155 (232), +635 (220). High-resolution MS *m/z*: 293.1128 (Calcd for $C_{12}H_{15}N_5O_4$: 293.1124). ^{1}H-NMR (DMSO-d_6) δ: 8.08 (1H, s, H-2), 7.10 (2H, br s, H_2N-6), 5.52 (1H, s, H-1′), 5.49 (1H, d, HO-3′, $J=5.9$ Hz), 5.34 (1H, s, HO-2′), 4.83 (1H, t, HO-5′, $J=5.9$ Hz), 3.82 (1H, m, H-4′), 3.68—3.48 (3H, m, H-3′, 5′a, b), 3.08—2.84 (2H, m, H-7′a, b), 2.09 (1H, m, H-6′a), 1.77 (1H, m, H-6′b, $J_{6'a,b}=13.7$ Hz). Relative migration in paper electrophoresis (0.2 M boric acid–sodium borate, pH 7.5, 700 V, 80 min): adenosine, 1.0; **15**, 1.47; arabinosylcytosine, 0.12.

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