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Studies of Nucleosides and Nucleotides. XLIV.[1] Purine Cyclonucleosides. (2). Synthesis of Cyclonucleosides having 8,3′-O- and -S-Anhydro Linkage derived from 2′-Deoxyadenosine[2]

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Starting from 2′-deoxyadenosine, 5′-O-trityl-3′-O-tosyl-2′-deoxy-8-bromoadenosine (IV) was synthesized. From the compound IV 8,3′-anhydro 8-oxy-9-(2-deoxy-β-D-*threo*-pentofuranosyl)adenine (VII) was obtained by treatment with sodium acetate in acetic anhydride and sodium acetate in DMF, followed by the removal of the protecting group. The structure of the compound VII was confirmed by elemental analysis, ultraviolet and infrared spectra, as well as an optical rotatory dispersion measurement.

8,3′-Anhydro-8-mercapto-9-(2-deoxy-β-D-*threo*-pentofuranosyl)adenine(X) was obtained by treatment of IV with thiourea. Desulfurization of X with Raney nickel gave 2′,3′-dideoxyadenosine.

In the synthesis of cyclonucleosides derived from adenosine[4] we have encountered a difficulty in isolating 8,3′-O-cyclonucleoside from the reaction mixture of the cyclization of 2′- and 3′-tosyl-8-oxyadenosine. At that time the reason of this failure was thought to lie in the difficulty to form 8,3′-O-anhydro linkage for sterical reasons. In order to investigate the possibility of the formation of 8,3′-O-cyclonucleoside and to obtain samples of 2′-deoxy series for the optical study, we attempted to synthesize 8,3′-anhydro-8-oxy- and -mercapto-9-(β-D-2-deoxy-*threo*-pentofuranosyl)adenine.

The bromination of 2′-deoxyadenosine was first investigated. Although 8-bromo-2′-deoxyadenosine was synthesized previously Holmes and Robins[5] using N-bromoacetamide as brominating agent, the route was lengthy and the yield was not satisfactory. We employed therefore bromine–dioxane in the presence of calcium carbonate as in the case of the bromination of guanosine.[6] 8-Bromo-2′-deoxyadenosine (II) was obtained as prisms in a yield of 42%. The yield was further increased by using bromine–water in a buffer solution of pH 4.0, which proved to be quite satisfactory in the case of adenosine.[7,8] By this procedure compound II was obtained in a yield of 62%. Structure of the compound II was confirmed by elemental analysis, optical properties, and *Rf* values in paper chromatography. These properties were identical with those reported by Holmes and Robins.[5]

For the introduction of tosyl group to 3′-OH, 8-bromo-2′-deoxyadenosine (II) was tritylated by slightly modified method used in the tritylation of 2′-deoxyadenosine.[9] Chromatography on a column on alumina gave 8-bromo-5′-O-trityl-2′-deoxyadenosine (III) in 78% yield. Structure of the compound III was confirmed by ultraviolet (UV) and infrared (IR) spectra, as well as elemental analyses.

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2) This work was preliminarily reported: M. Ikehara and M. Kaneko, *Chem. Pharm. Bull.* (Tokyo), **15**, 1261 (1967).
3) Location: *6–5, Toneyama, Toyonaka, Osaka.*
4) M. Ikehara, H. Tada and M. Kaneko, *Tetrahedron*, **24**, 3489 (1968); M. Ikehara, H. Tada, M. Kaneko and K. Muneyama, *J. Am. Chem. Soc.*, **88**, 3165 (1966).
5) R.E. Holmes and R.K. Robins, *J. Am. Chem. Soc.*, **86**, 1242 (1964).
6) M. Ikehara and K. Muneyama, *Chem. Pharm. Bull.* (Tokyo), **13**, 639 (1965).
7) M. Ikehara, S. Uesugi and M. Kaneko, *Chem. Commun.*, **1967**, 17.
8) M. Ikehara and M. Kaneko, *Tetrahedron*, **26**, 4251 (1970).
9) W. Anderson, D.H. Hayes, Am. Michelson and A.R. Todd, *J. Chem. Soc.*, **1954**, 1882.

Tosylation of 3′-OH group of the compound III was performed by the treatment with *p*-toluenesulfonyl chloride in pyridine. 8-Bromo-3′-O-tosyl-5′-O-trityl-2′-deoxyadenosine (IV) was obtained as colorless crystals mp 176—177° in a yield of 48%. The structure was confirmed by elemental analysis and optical properties as described in Experimental.

In order to obtain suitable intermediate for O-cyclonucleoside oxy function should be induced in 8-position. According to the previous investigation of converting 8-bromo to 8-oxy,[10] compound IV was treated in acetic acid with sodium acetate. However, nucleoside linkage of 2′-deoxyadenosine is far labile than that of adenosine[11] and desired product could not be obtained. Since it has been shown that acylation of 6-NH_2 group in adenine activated 8-halogeno atom for nucleophilic displacement,[12] we attempted to use acetic anhydride for the sodium acetate reaction. Using this reagent the acylation of 6-NH_2 group would give one equivalent of acetic acid and catalyze nucleophilic displacement of 8-bromo atom by acetate anion.[13] Well-dried 8-bromo compound IV was dissolved in acetic anhydride, in which sodium acetate was previously dissolved, and heated at 110—120° for 10 hr. Examination of the reaction mixture showed a change of UV absorption maximum from 264 nm to 287 nm in acidic solution. This indicates introduction of acetyl to 6-NH_2 and replacement of 8-bromo by oxy function.[12] N^6-Acetyl-3′-O-tosyl-5′-trityl-8-oxy-2′-deoxyadenosine (V), thus obtained, has IR absorption bands which could be assigned to trityl, tosyl, acetamide and five-membered ureide group, respectively.

Cyclization of the compound V was performed by refluxing with sodium acetate in DMF. Although sodium benzoate in DMF has been shown to be one of the most powerful nucleophiles,[14] UV absorption of benzoate interfered with search for spots in thin-layer and paper chromatographies. Upon heating of the compound V in DMF containing sodium acetate for 1 hr, a shift of UV absorption maximum from 301 nm to 290 nm in alkali and from 287 to 290 nm in acidic condition was observed. This shift indicated the conversion of V to a cyclonucleoside. Without isolation, the crude product was treated with conc. ammonia–methanol (1:1, v/v) mixture at room temperature for 24 hr. 8,3′-Anhydro-8-oxy-9-(5-O-trityl-2-deoxy-β-D-*threo*-pentofuranosyl) adenine (VI) was obtained as crystals having mp 270—272°. This compound has UV absorption properties closely resembled to those reported for 8-methoxy-2′-deoxyadenosine[12] and shows loss of tosyl band in IR spectrum. Existence of trityl group, which was suggested by IR band at 700 cm^{-1}, was confirmed by a characteristic yellow color revealed by sulfuric acid spray.[15] Elemental analysis also supported the structure to be correct.

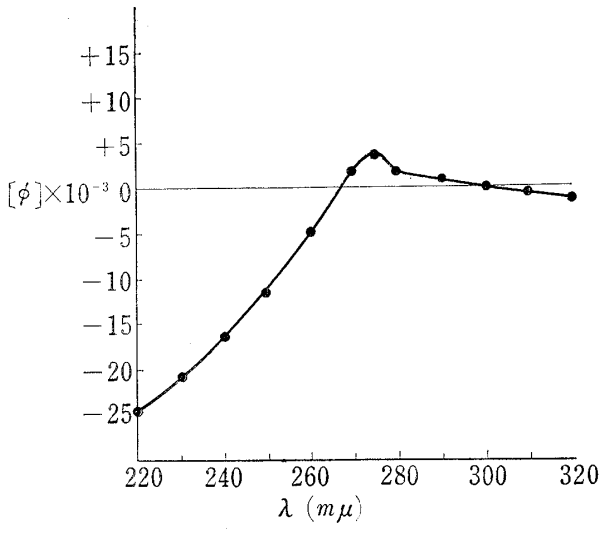
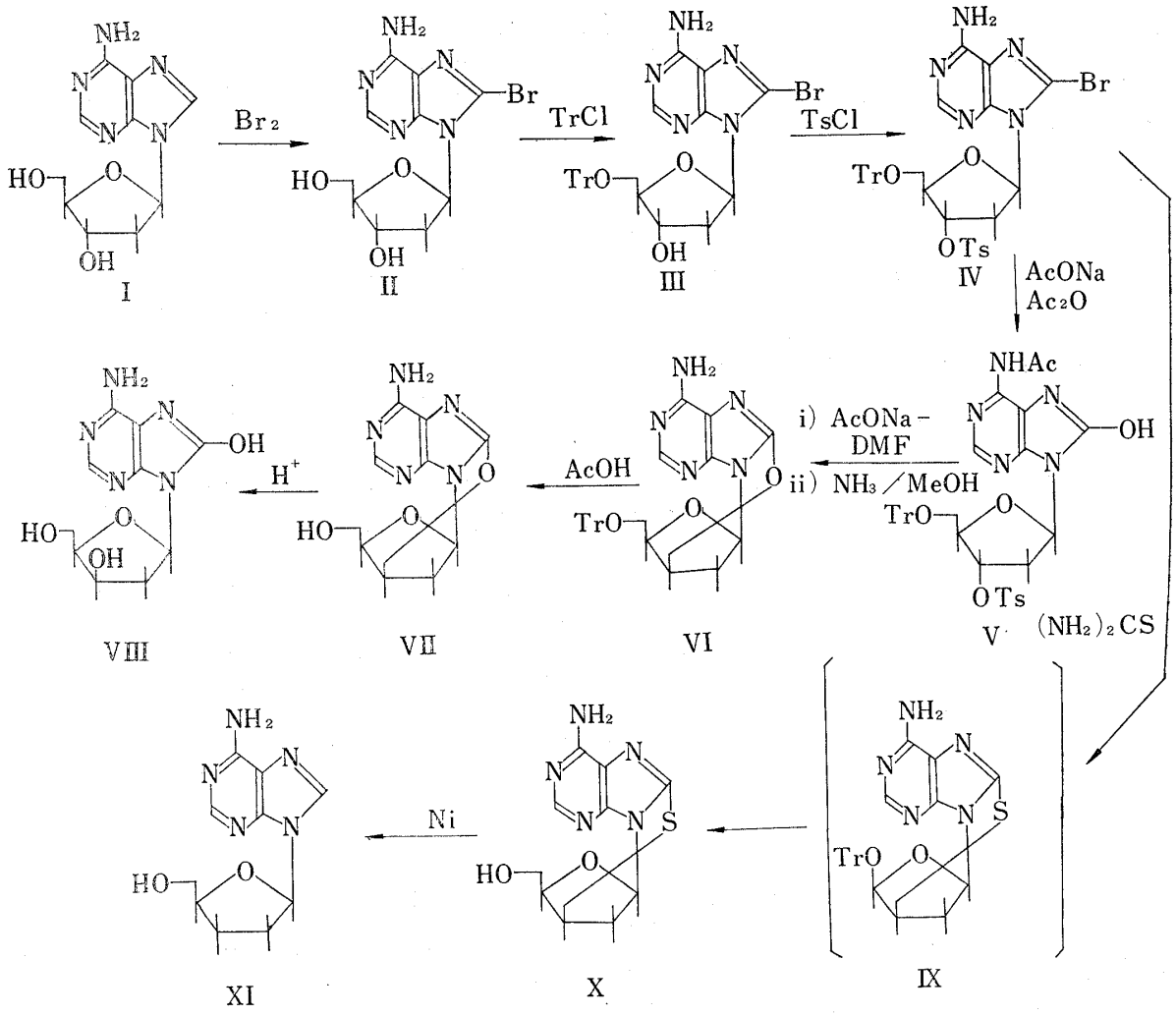


Fig. 1. Optical Rotatory Dispersion Curve of 8,3′-Anhydro-8-oxy-9-β-D-(2-deoxy-*threo*-pentofuranosyl)adenine

10) M. Ikehara, H. Tada and M. Kaneko, *Chem. Pharm. Bull.* (Tokyo), **13**, 1140 (1965).
11) A.M. Michelson, "The Chemistry of Nucleosides and Nucleotides," Academic Press, 1963, p. 26.
12) R.E. Holmes and R.K. Robins, *J. Am. Chem. Soc.*, **87**, 1772 (1965).
13) It has been shown that the replacement of 8-bromo atom in adenosine would not proceed without acidic catalyst, even in a drastic condition (unpublished experiment by H. Tada).
14) J.J. Fox and N. Miller, *J. Org. Chem.*, **28**, 936 (1963).
15) H. Schaller, G. Weimann, B. lerch and H.G. Khorana, *J. Am. Chem. Soc.*, **85**, 3821 (1963).

Detritylation of the compound VI was performed with 80% acetic acid according to Robins, *et al.*[16] Chromatography of a column of cellulose powder gave 8,3′-anhydro-8-oxy-9-(2-deoxy-β-D-*threo*-pentofuranosyl)adenine (VII), mp 266.5—267°. Compound VII has UV absorption maximum at 262—263 nm, which is resembled to those found in 8,3′-anhydro-9-β-D-xylofuranosyladenine.[17,18] Further support of the structure was obtained from optical rotatory disperison (ORD) of compound VII. As shown in Fig. 1, ORD curve of the compound VII showed a peak at 275 nm and a trough at 220 nm,[19] which constructed a positive Cotton band of the amplitude, 28400. From the sign of the Cotton effect and the magnitude lying between 25000 and 30000,[20] 8,3′-O-cyclonucleoside structure for the compound VII was further supported.

Since the formation of 8,3′-O-anhydro linkage became obvious, we attempted to synthesize S-counterpart of 8,3′-cyclonucleoside, 8,3′-anhydro-8-mercapto-9-(2-deoxy-β-D-*threo*-pentofuranosyl)adenine (X). Starting from the common intermediate compound IV, reflux in *n*-butanol in the presence of thiourea[21] gave a cyclonucleoside, which had UV absorption properties closely resembled to those of 8,3′-anhydro-9-β-D-xylofuranosyladenine.[22] The loss



16) M.J. Robins, J.R. MacCarthy, Jr. and R.K. Robins, *Biochemistry*, **5**, 224 (1966).
17) M. Ikehara, *Accounts of Chemical Research*, **2**, 47 (1969).
18) M. Ikehara and M. Kaneko, *Chem. Pharm. Bull.* (Tokyo), in press.
19) Although curve ended at 220 nm, existence of a trough was assumed by comparison with Cotton curves of S-cyclonucleosides.[20]
20) M. Ikehara, M. Kaneko, K. Muneyama and H. Tanaka, *Tetrahed. Letters*, **1967**, 3977.
21) M. Ikehara, H. Tada and K. Muneyama, *Chem. Pharm. Bull.* (Tokyo), **13**, 639 (1965).
22) M. Ikehara and H. Tada, *Chem. Pharm. Bull.* (Tokyo), **15**, 94 (1967).

of absorption band near 220 nm and no coloring by sulfuric acid spray on paper chromatogram suggested that this compound had no trityl group. Elemental analysis also supported this conclusion. Therefore, in contrast to our expectation, trityl group had been removed by toluenesulfonic acid evolved in due course of the cyclization. Thus compound X was directly obtained from the compound IV, presumably *via* compound IX, which has trityl group on 5′-OH group. Desulfurization of this compound X with Raney nickel gave 2′,3′-dideoxyadenosine, which was identical in *Rf*'s and absorption maxima with those reported for 2′,3′-dideoxyadenosine.[23,24]

Acidic cleavage of 8,3′-O-cyclonucleoside (VII) was then investigated. Although this compound could not be hydrolyzed in 80% acetic acid at 100° for 6 hours, it was hydrolyzed with N sulfuric acid at 37° for 16 hours. As expected from the acidic hydrolysis of ribo-cyclonucleosides,[4] compound VII gave a nucleoside (VIII) having 8-oxyadenine chromophore, which was suggested by UV absorption properties. In the hydrolysis mixture 8-oxyadenine was also found. Although the configuration of sugar moiety, *i.e.*, 3′-OH is in up or down configuration, was not substantially confirmed, 2-deoxy-*threo*-pentofuranosyl would be suggested, because this nucleoside had different *Rf* values in paper chromatography performed side by side with a sample of 8-oxy-2′-deoxyadenosine.[25] This conclusion might be supported by analogous cleavage of 8,3′-O-cyclonucleoside of ribo series.[18]

Thus the formation of O- and S-anhydro linkage between C-8 and C-3′ position was substantially realized.

Experimental[26]

8-Bromo-2′-deoxyadenosine (II)——i) 2′-Deoxyadenosine[27] (5.0 g, 20 mmoles) was dissolved in dioxane–water (20 ml, 1:1, v/v) with slight heating. After it was cooled to room temperature, calcium carbonate (2.4 g, 24 mmoles) was added. A solution of bromine (3.8 g, 24 mmoles) in dioxane (50 ml) was added dropwise into the mixture with stirring. In this while N sodium hydroxide (32 ml) was also added dropwise with stirring within 15 min. After stirring of the solution for 1 hr, 20% aqueous sodium bisulfite solution (10 ml) was added with stirring. Precipitates were removed by filtration and the filtrate was evaporated to a yellow glass. The glass was triturated with hot ethanol and recrystallized from water. 8-Bromo-2′-deoxyadenosine was obtained as pale yellow prisms, mp 200° (decomp.). Yield was 2.8 g (42%). *Anal.* Calcd. for $C_{10}H_{12}O_3N_5Br$: C, 36.37; H, 3.67; N, 21.21. Found: C, 36.55; H, 3.60; N, 21.08. UV: λ_{max}^{pH1} 263.5 nm (ε 16800), λ_{max}^{pH7} 266 nm (ε 15800), λ_{max}^{pH13} 266 nm (ε 15800). PPC:[28] *Rf*(A) 0.44, *Rf*(B) 0.55, *Rf*(C) 0.77, *Rf*(D) 0.75.

ii) 2′-Deoxyadenosine (5.0 g, 20 mmoles) was dissolved in water (100 ml) with slight heating, followed by the addition of a sodium acetate buffer (0.5M, pH 4.0, 100 ml). To the solution was added water saturated with bromine (150 ml) and the reaction mixture was kept at room temperature for 4 hr. Sodium bisulfite (5M) was added with stirring until color of the reaction mixture turned from red to yellow. pH of the solution was adjusted to 6—7 with 5N sodium hydroxide and the solution was kept in a refrigerator overnight. Precipitated crystals were collected by filtration. Mother liquor was concentrated to its half volume and set aside again at 2°. Second crop was collected and crystals were recyrstallized from water, which was previously made slightly alkaline with ammonia. 8-Bromo-2′-deoxyadenosine was obtained as prisms, mp 200° (decomp.). Yield was 4.12 g (62%). This sample was identical with a sample obtained in i).

23) G.L. Tong, W.W. Lee and L. Goodman, *J. Org. Chem.*, **30**, 2854 (1965).
24) M.J. Robins, J.R. McCarthy and R.K. Robins, *Biochemistry*, **5**, 224 (1966).
25) Synthesized by heating of 8-bromo-2′-deoxyadenosine in acetic anhydride with sodium acetate, followed by the removal of acetyl groups with methanol–ammonia (unpublished experiment by M. Kaneko).
26) UV spectra were taken with a Hitachi EPS-3T spectrophotometer, IR spectra were with a Hitachi EPI-L spectrophotometer, nuclear magnetic resonance (NMR) spectra were with a Hitachi H-6031 high resolution spectrometer operated at 60 Mc with an internal standard of tetramethylsilane and ORD was taken with a JASCO ORD/UV-5 spectropolarimeter in 10 mm light path using water solution of maximum 1.5 optical density (OD).
27) 2′-Deoxyadenosine was kindly provided by Dr. R.K. Robins, to whom authors' thanks are due.
28) PPC stands for paper partition chromatography. Solvents used were: A, water adjusted to pH 10 with ammonia; B, *n*-butanol–water, 86:14; C, isopropanol–ammonia–water, 7:1:2; D, *n*-butanol–acetic acid–water, 5:2:3; E, *n*-propanol–water, 3:1.

8-Bromo-5′-O-trityl-2′-deoxyadenosine (III)——8-Bromo-2′-deoxyadenosine (4.95 g, 15 mmoles, dried over P_2O_5 at 30° for 5 hr in 3 mm/Hg) was dissolved in dry pyridine (140 ml) and DMF (100 ml) with slight heating. After the solution cooled to room temperature, trityl chloride (4.74 g, 17 mmoles) was added and it was kept at room temperature for 14 days with stirring. The reaction mixture was added dropwise in water (50 ml) containing sodium bicarbonate (4.5 g). After setting aside for 30 min, the mixture was evaporated *in vacuo* to dryness. After the yellow residue was dried throughly, benzene (150 ml) was added and the organic material was extracted by shaking. Insoluble material was removed by centrifugation and washed with benzene (100 ml). Supernatant and washings were combined and evaporated to give a pink glass (7.2 g). The glass was applied to a column (2 cm in diameter) of alumina (150 g) and it was eluted with chloroform–*n*-hexane (3:1, vol/vol, 500 ml) and chloroform (1500 ml), successively. 8-Bromo-5′-O-trityl-2′-deoxyadenosine was obtained as a slightly pink glass (6.60 g, 78%). *Anal.* Calcd. for $C_{29}H_{26}O_3N_5Br$: C, 60.85; H, 4.58; N, 12.25. Found: C, 60.05; H, 4.59; N, 11.67. UV: λ_{max}^{pH1} 264.5 nm (15500), λ_{max}^{MeOH} 265 nm (13800), λ_{max}^{pH13} 265 nm (14000). IR: ν_{max}^{Nujol} 700 cm^{-1} (Trityl). PPC: *Rf*(B) 0.84, *Rf*(C) 0.91.

8-Bromo-3′-O-tosyl-5′-O-trityl-2′-deoxyadenosine (IV)——Well dried 8-bromo-5′-trityl-2′-deoxyadenosine (1.778 g, 3.1 mmoles) was dissolved in dry pyridine (15 ml, distilled from tosyl chloride and stocked over molecular sieves). *p*-Toluenesulfonyl chloride (0.885 g, 4.55 mmoles) was added with cooling in an ice-salt bath. The reaction mixture was stored in a dark place with exclusion of moisture. After 8 days, the mixture was added into ice water (200 ml) containing sodium bicarbonate (500 mg) with vigorous stirring. The stirring continued for 30 min. Organic material was extracted with chloroform (200 ml), washed with water (200 ml), and dried over magnesium sulfate. Solvent was evaporated *in vacuo* and a yellow glass (2.017 g) was obtained. Recrystallization from ethanol gave 8-bromo-5′-trityl-3′-tosyl-2′-deoxyadenosine as prisms (1.079 g, 46%), mp 176—177°. A sample for the elemental analysis was further recrystallized from ethanol. *Anal.* Calcd. for $C_{36}H_{32}O_5N_5BrS$: C, 59.49; H, 4.45; N, 9.63. Found: C, 59.63; H, 4.46; N, 9.56. UV: λ_{max}^{pH1} 264 nm (15700), λ_{max}^{MeOH} 264 nm (13900), λ_{max}^{pH13} 264 nm (13900). IR: ν_{max}^{Nujol} 1170 cm^{-1} (covalent tosylate), 700 cm^{-1} (trityl). PPC: *Rf*(B) 0.55.

N⁶-Acetyl-8-oxy-3′-O-tosyl-5′-O-trityl-2′-deoxyadenosine (V)——Sodium acetate (500 mg) was dissolved in acetic acid (20 ml) by refluxing for 30 min. Into this solution was added 8-bromo-trityl-tosyl-2′-deoxyadenosine (329 mg, 0.45 mmole) and heated at 11—120° for 10 hr. Ethanol (30 ml) was added into the reaction mixture and it was kept at room temperature for 20 min. After the mixture was neutralized with conc. ammonia, it was concentrated to *ca.* 10 ml *in vacuo*. The residual solution was added dropwise into saturated sodium bicarbonate solution (200 ml) with vigorous stirring. After 30 min stirring, white precipitate was collected by centrifugation, washed with water (100 ml × 2) and dried. 8-Oxy compound was obtained as a white powder (350 mg). UV: λ_{mxa}^{pH1} 287 nm, λ_{max}^{EtOH} 283 nm, λ_{max}^{pH13} 267, 301 nm. IR: ν_{max}^{Nujol} 1185 cm^{-1} (tosylate), 1725 cm^{-1} (carbonyl). PPC: *Rf*(B) 0.89, *Rf*(C) 0.83, *Rf*(E) 0.90.

8,3′-Anhydro-8-oxy-9-(5-O-trityl-2-deoxy-β-D-*threo*-pentofuranosyl)adenine (VI)——Sodium acetate (300 mg, freshly dried by fusion) was dissolved in DMF (30 ml) by heating. The solution was poured into a flask containing 8-oxy-N⁶-acetyl-5′-trityl-3′-tosyl-2′-deoxyadenosine (314 mg). The mixture was heated at 150—160° for 1 hr under exclusion of moisture with occasional shaking. UV absorption maximum at 301 nm in alkali changed to 290 nm. The solvent was evaporated *in vacuo* to afford a brownish glass. The glass was dissolved in conc. ammonia–methanol (1:1, v/v) and the solution was tightly stoppered and kept in a refrigerator for 24 hr. Upon evaporation of ammonia white precipitate was collected by filtration and washed with ethanol and ether. Trityl-cyclonucleoside was obtained as a pink-white crystalline material (yield 66 mg). Sample for the elemental analysis was recrystallized from *n*-propanol–water, mp 270—272°. *Anal.* Calcd. for $C_{29}H_{25}O_3N_5 \cdot \frac{1}{2}H_2O$: C, 69.66; H, 5.04; N, 14.01. Found: C, 69.63; H, 5.31, N, 13.40. UV: λ_{max}^{pH1} 233 nm (9000, shoulder), 264 nm (13800), λ_{max}^{MeOH} 232 nm (10500, shoulder), 262 nm (14300), λ_{max}^{pH13} 231 nm (10700, shoulder), 262 nm (14200). IR: no band at 1185 cm^{-1} (tosylate), 700 cm^{-1} (trityl). PPC: *Rf*(B) 0.76, *Rf*(C) 0.70, *Rf*(D) 0.80.

8,3′-Anhydro-8-oxy-9-(2-deoxy-β-D-*threo*-pentofuranosyl)adenine (VII)——Trityl chloride (200 mg) was dissolved in 80% acetic acid (20 ml) and refluxed for 15 min. Acetic acid was evaporated *in vacuo* and the residual glass was freed from acetic acid by repeated evaporation with ethanol. The glass was applied to a column (3.0 × 66 cm) of cellulose powder and eluted with *n*-propanol–ammonia–water (7:1:2). Fractions (5 ml each) No. 97—104 were pooled and evaporated to give a glass (90 mg). Recrystallization from ethanol gave cyclonucleoside as colorless prisms (52 mg), mp 266.5—267°. *Anal.* Calcd. for $C_{10}H_{11}O_3N_5$: C, 48.19; H, 4.45; N, 28.11. Found: C, 48.01; H, 4.50; N, 27.73. UV: λ_{max}^{pH1} 262 nm (14200), $\lambda_{max}^{H_2O}$ 263 nm (14200), λ_{max}^{pH13} 263 nm (14600). PPC: *Rf*(B) 0.52, *Rf*(C) 0.54, *Rf*(E) 0.62.

8,3′-Anhydro-8-mercapto-9-(2-deoxy-β-D-*threo*-pentofuranosyl)adenine (X)——8-Bromo-5′-trityl-3′-tosyl-2′-deoxyadenosine (1.325 g, 1.78 mmole) was dissolved in *n*-butanol (60 ml) by slight heating. Into this solution was added thiourea (0.174 g, 2.13 mmole) and the mixture refluxed in an oil bath, which was preheated to 130°, for 5 hr under exclusion of moisture. Upon evaporation of the solvent, yellow-green glass was washed with ether (30 ml) to remove trityl alcohol. The residual glass was applied to a column (2 cm in diameter) of cellulose powder (100 g) and eluted with *n*-propanol–ammonia–water (7:1:2). Fraction (5 ml) No. 85—92 was pooled and evaporated to give the starting material (220 mg). Fraction No. 75—79

was evaporated to give a yellow powder (120 mg). Recrystallization from ethanol gave 8,3′-S-cyclonucleoside as fine needles, mp 226.5—227°. *Anal.* Calcd. for $C_{10}H_{11}O_2N_5S \cdot \frac{1}{3}H_2O$: C, 44.32; H, 4.35; N, 25.85. Found: C, 44.78; H, 4.67; N, 25.53. UV: λ_{max}^{pH1} 224 nm (17000), 290 nm (15600, shoulder), 282 nm (16700), 290 nm (15800, shoulder): λ_{max}^{pH13} 275 nm (15000, shoulder), 282 nm (17200), 290 nm (12200, shoulder). PPC: *Rf*(C) 0.47, *Rf*(D) 0.43.

2′,3′-Dideoxyadenosine (XI)——8,3′-S-Cyclonucleoside (10 mg) was dissolved in 2 ml of water. Raney nickel (100 mg) was added and the mixture was heated at reflux for 4 hr. The catalyst was removed by filtration and the filtrate was evaporated *in vacuo* to give a yellow glass. Upon prolonged trituration with ethanol crystals having mp 180—182° were obtained. UV: λ_{max}^{pH1} 260.5 nm, $\lambda_{max}^{H_2O}$ 260 nm, λ_{max}^{pH13} 260 nm. PPC: *Rf*(B) 0.32, *Rf*(C) 0.38. These properties were coincided with those reported for 2′,3′-dideoxyadenosine.

Acid Hydrolysis of 8,3′-O-Cyclonucleoside——8,3′-O-Cyclonucleoside (10 mg) was dissolved in N-H_2SO_4 (1 ml) and kept at 37° for 16 hr. Paper chromatography (in solvent A) of the reaction mixture showed a thin spot of *Rf* 0.41 and a clear one at *Rf* 0.58, both revealed with a UV lamp. Another spot at *Rf* 0.64 was detected solely by metaperiodate spray.[29] The substance having *Rf* 0.41 was found to be 8-oxyadenine by comparison with an authentic sample. The spot at *Rf* 0.58 was cut and extracted with water. Evaporation of extracts gave a glass having UV absorption properties: $\lambda_{max}^{H^+,H_2O}$ 264 nm, 287 nm, $\lambda_{max}^{OH^-}$ 280 nm, which were resembled those of 8-oxy-xylofuranosyladenine.[4] This material revealed a pink color by cystein–sulfuric acid test.[30] Paper chromatography of this compound side by side with 8-oxy-2′-deoxyadenosine showed slight difference in two solvent systems. *Rf*(A) 0.58 and *Rf*(C) 0.52 for this compound and *Rf*(A) 0.59 and *Rf*(C) 0.48 for 8-oxy-2′-deoxyadenosine. These properties suggested that this compound is 8-oxy-9-β-D-2′-deoxy-*threo*-pentofuranosyladenine.

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29) M. Viscontini, D. Hoch and P. Karrer, *Helv. Chimica Acta*, **38**, 642 (1955).
30) J.G. Buchanan, *Nature*, **168**, 1091 (1951).