[Chem. Pharm. Bull. 15(1) 94～100 (1966)]

UDC 612.398.145 : 547.964

13. Morio Ikehara and Hiroshi Tada: Studies of Nucleosides and Nucleotides. XXXII.*1 Purine Cyclonucleosides. 3.*2 Synthesis of 2′-Deoxy- and 3′-Deoxyadenosine from Adenosine.

(*Faculty of Pharmaceutical Sciences, Hokkaido University**3)

5′-O-Acetyl-8-bromo-2′,3′-O-isopropylideneadenosine was obtained either by bromination of 5′-O-acetyl-2′,3′-O-isopropylideneadenosine with N-bromoacetamide or by bromination of 2′,3′-O-isopropylideneadenosine followed by acetylation. 5′-O-Acetyl-8-bromoadenosine, obtained by the formic acid hydrolysis of the isopropylidene group, was tosylated to afford 2′-tosyl-, 3′-tosyl- and 2′,3′-di-O-tosyl-5′-O-acetyl-8-bromoadenosine. Reaction of these tosylates with thiourea followed by deacetylation gave 8,2′-anhydro-8-mercapto-9-β-D-arabinofuranosyladenine, 8,3′-anhydro-8-mercapto-9-β-D-xylofuranosyladenine and 8,2′-anhydro-8-mercapto-3′-O-tosyl-9-β-D-arabinosyladenine, respectively. Desulfurization of 8,2′- and 8,3′-anhydro derivatives gave 2′-deoxy- and 3′-deoxyadenosine (Cordycepin).

(Received April 4, 1966)

Recently[1] we have reported the synthesis of 8,2′-anhydro-2-chloro-8-mercapto-9-β-D-arabinofuranosyladenine (I) and substantiated the cyclonucleoside formation in purine nucleosides as reported in the pyrimidine nucleoside series.[2,3] From compound I, 2′-deoxyadenosine was easily obtained by the successive dechlorination and desulfurization and this fact enabled us to postulate a possible pathway of the transformation of ribonucleotides to deoxyribonucleotides in the living cells.[4]

In this paper we describe the first synthesis of 2′-deoxyadenosine starting from adenosine *via* the cyclonucleosides and an alternate synthesis of 3′-deoxyadenosine (Cordycepin), which has already been synthesized by several investigators.[5~7] Our first attempt was concentrated toward the synthesis of an adenosine derivative bearing easily replaceable halogen atom on the 8-position and an arylsulfonyl group on 2′- or 3′-position. It was envisaged that such derivatives would be suitable for the formation of 8,2′ thiocyclo bridges upon thiourea treatment. In spite of our efforts to obtain 8-bromo-2′(or 3′)-O-tosyl(or nisyl*4)-adenosine by the bromination[8] of the known 2′(or 3′)-O-tosyl(or nisyl)-adenosine[5] (II), none of the desired product was isolated. The cause of the difficulty may be explained by the interaction of phenylsulfonyl group and the adenine moiety of the nucleoside.[9]

Our attention was then turned to the sulfonylation of the bromoadenosine derivatives. 2′,3′-O-Isopropylideneadenosine (III) was brominated by N-bromoacetamide[8] in chloroform solution and 8-bromo-2′,3′-O-isopropylideneadenosine (IV) was obtained in

*1 Paper XXXI: M. Ikehara, E. Ohtsuka, H. Uno, K. Imamura, Y. Tonomura: Biochim. Biophys. Acta, **100**, 471 (1965).
*2 Paper 2 of this series: M. Ikehara, H. Tada, K. Muneyama: This Bulletin, **13**, 639 (1965).
*3 Kita 12-jo, Nishi 5-chome, Sapporo (池原森男, 多田 宏).
*4 *p*-nitrobenzene sulfonyl.

1) M. Ikehara, H. Tada: J. Am. Chem. Soc., **87**, 606 (1965).
2) J. J. Fox, I. Wempen: Adv. Carbohydrate Chem., **14**, 283 (1959).
3) A. M. Michelson: "The Chemistry of Nucleosides and Nucleotides," p. 15, 68 (1963).
4) M. Ikehara, H. Tada, A. Nomura: Nature, **202**, 900 (1964).
5) A. R. Todd, T. L. V. Ulbricht: J. Chem. Soc., **1960**, 3275.
6) W. W. Lee, A. Benitez, C. D. Anderson, L. Goodman, B. R. Baker: J. Am. Chem. Soc., **83**, 1906 (1961).
7) E. Walton, R. F. Nutt, S. R. Jenkins, F. W. Holly: *Ibid.*, **86**, 2952 (1964).
8) R. E. Holmes, R. K. Robins: *Ibid.*, **86**, 1242 (1964).
9) M. Ikehara, H. Tada: This Bulletin, **14**, 197 (1966).

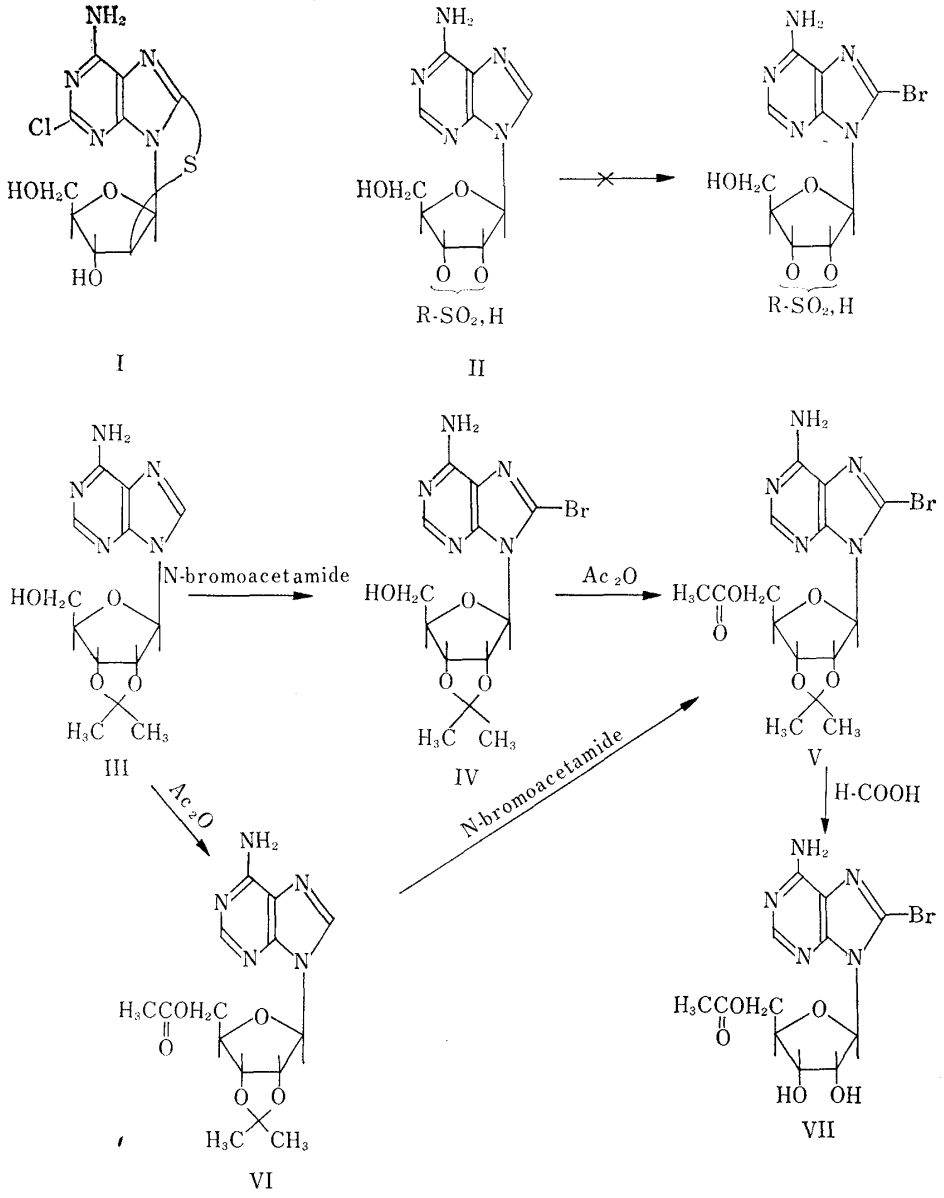

Chart 1.

79% yield. Acetylation of compound Ⅳ by the usual procedure gave 5′-O-acetyl-8-bromo-2′,3′-O-isopropylideneadenosine (Ⅴ), which was also obtained by the bromination of 5′-O-acetyl-2′,3′-O-isopropylideneadenosine (Ⅵ). A comparison of the yield in the bromination reaction in these two cases showed that the former is superior. Deblocking of the 2′,3′-O-isopropylidene group in Ⅴ was achieved by the hydrolysis with 98% formic acid at room temperature. Hydrolysis of compound Ⅴ with mineral acid gave a mixture of starting material, desired product and adenine in various ratios. Although attempts to crystallize 5′-O-acetyl-8-bromoadenosine (Ⅶ) failed, the sample showed a satisfactory elemental analysis. Compound Ⅶ was then tosylated with 1.02 equivalents of tosyl chloride in 42.3% yield. Deacetylation with ammonia and careful crystallization of the product from 50% isopropanol gave 11.5% of 8-bromo-2′-tosyladensosine (Ⅷ), m.p. 220~223° (decomp.). The structure of Ⅷ was confirmed by elemental analytical data. Ultraviolet (UV) absorption properties, and transformation to 2′-deoxyadenosine. The mother liquor of this recrystallization gave two crops of crystalline material, m.p. 176~177° (Ⅸ) and m.p. 213° (decomp.) (Ⅹ). Although from the elemental analytical data it appeared that compound Ⅸ was the 2′,3′-di-O-tosyl

derivative and X the mono-O-tosyl (presumably 3′-tosyl) derivative, the slight mutual contamination of these compounds could not be avoided even after repeated recrystallizations. It is curious that these three tosylated compounds showed identical Rf values in thin-layer chromatography (silica gel) in two solvent systems.

8-Bromo-2′-O-tosyladenosine (Ⅷ) was then subjected to cyclization by the method already developed in the case of guanosine*[5] in this laboratory. When compound Ⅷ was refluxed in *n*-butanol in the presence of 1.1 equivalents of thiourea for 2 hours, the ultraviolet absorption maximum shifted from 263 to 276 mμ. This showed the cyclization of intermedially formed 8-mercapto-2′-O-tosyladenosine to afford 8,2′-cyclo nucleoside (Ⅺ). Chromatographic purification of the reaction mixture on a cellulose powder column gave a crystalline compound, m.p. 191~194°, with a maximum at 276 mμ in ethanol. Elemental analysis was consistent with the 8,2′-anhydro-8-mercapto-9-β-D-arabinofuranosyladenine structure. The optical rotation, $[\alpha]_D^{23}$ −187.2°, also suggested the 8,2′-cyclo structure since the 2-chloro analog I also shows a high

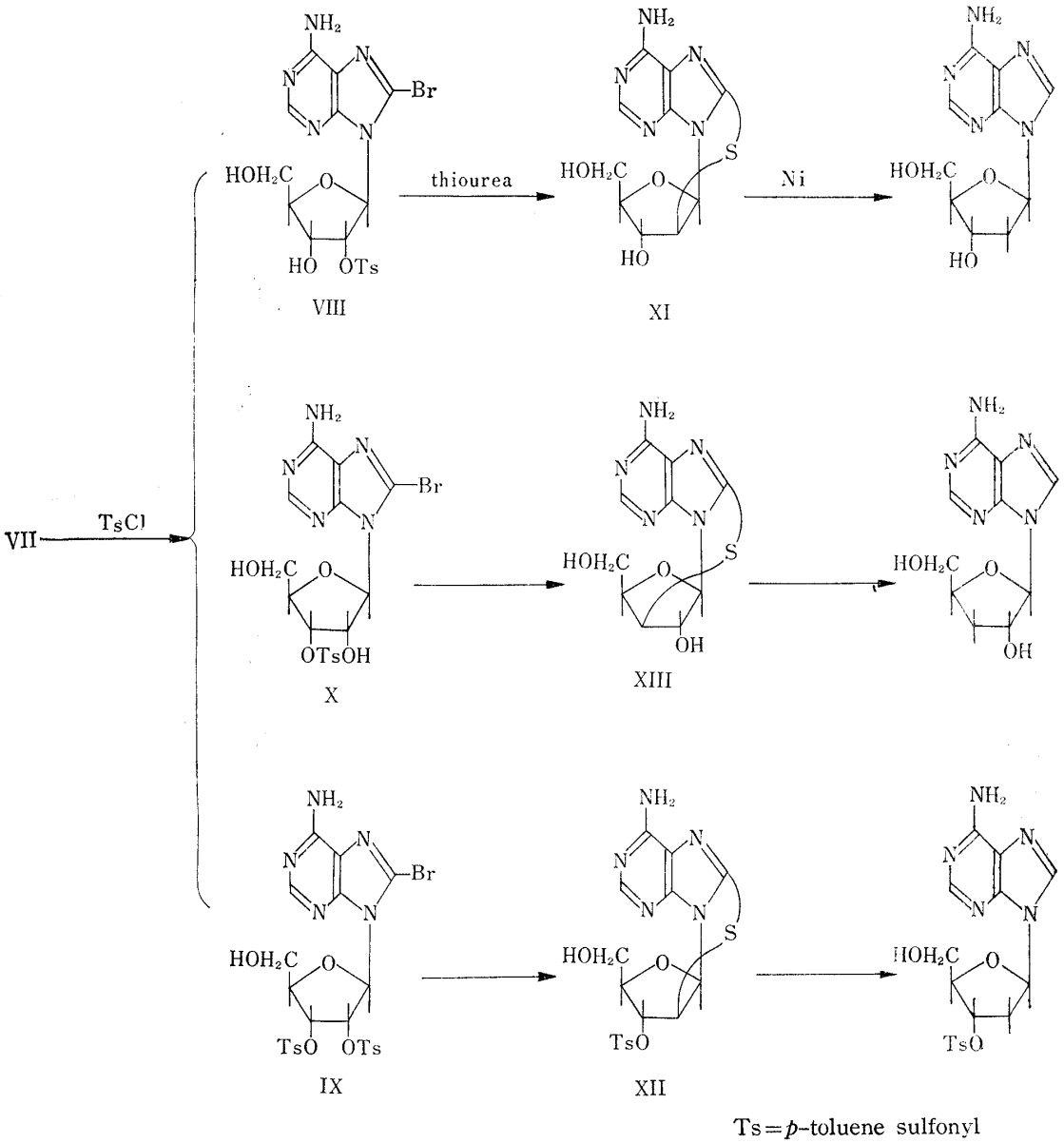

Chart 2.

*[5] Same as ref. *2.

negative rotation (−214°).[1] Nuclear magnetic resonance (NMR) spectra taken in dimethylsulfoxide solution showed a doublet band of $H_{1'}$ at 3.49τ. Coupling constant of $H_{1'}$ with $H_{2'}$ (6.6 c.p.s.) was similar to that observed in 8,2′-anhydro-2-chloro compound I (7.0 c.p.s.).[1] The dihedral angle formed by $H_{1'}$-C-C-$H_{2'}$ calculated by the Karplus equation[10] is 25.6°, which is satisfactory in accordance with that measured on the Büchi molecular model of 8,2′-cyclo nucleoside. The structure of compound XI was confirmed by desulfurization with Raney nickel to afford 2′-deoxyadenosine in 33% yield. The synthetic material was compared directly with an authentic sample*6 by mixed m.p. and paper chromatography. These results establish the structure of compound XI and XIII as well as affording a synthesis of 2′-deoxyadenosine starting from natural adenosine.

The mixture of 8-bromo-2′,3′-di-O-tosyladenosine (IX), 8-bromo-2′-O-tosyladenosine (VIII) and 8-bromo-3′-O-tosyladenosine (X) obtained from the mother liquor of recrystallization of VIII was reacted with thiourea as described above. Cellulose powder chromatography of reaction product gave two compounds, m.p. 196~198° (XII) and m.p. 231~232° (XIII), in addition to compound XI. The former compound show the presence of covalent tosylate by infrared spectra. Elemental analytical data suggested the structure of cyclonucleoside having a tosyl group intact. Ultraviolet absorption property showed close similarity with 8,2′-cyclonucleoside obtained above. Desulfurization of compound XII gave 3′-O-tosyl-2′-deoxyadenosine, identical with that obtained by Robins *et al.*[11] Accordingly, compound XII is 8,2′-anhydro-8-mercapto-3′-O-tosyl-9-β-D-arabinofuranosyladenine, which is derived from the 2′,3′-di-O-tosyl byproduct formed in the mono-tosylation reaction. Compound XIII has no tosylate group and did not consume metaperiodate, which indicating the absence of vicinal hydroxyl groups. Although the ultraviolet spectra of this compound differed somewhat from 8,2′-compounds, elemental analytical data suggested a cyclonucleoside structure. The difference of the ultraviolet spectra was also reported in the pyrimidine 2,2′- and 2,3′-cyclonucleoside.[12] NMR spectra of this compound showed a doublet peak of $H_{1'}$ at 3.62τ. In this case J_{H1}, 2.5 c.p.s. is smaller than that observed in 8,2′-cyclonucleoside. Examination of the molecular model of 8,3′-cyclonucleoside showed a highly strained upward bending[13] of $C_{3'}$ caused by the formation of 8,3′-linkage and showed a dihedral angle formed by $H_{1'}$-C-C-$H_{2'}$ about 130° (see Fig. 1). This value was also consistent with that

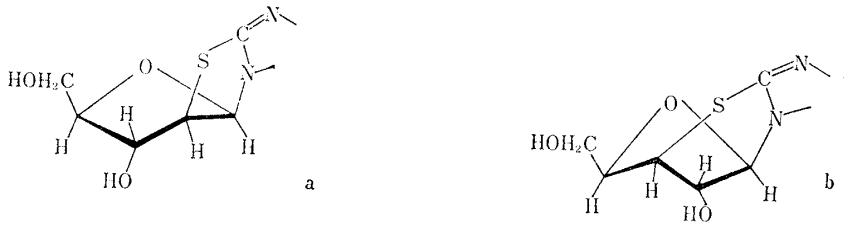

Fig. 1. Schematical representation of the configuration of 8,2′-anhydro-8-mercapto-9-β-D-arabinofuranosyladenine (a) and 8,3′-anhydro-8-mercapto-9-β-D-xylofuranosyladenine (b).

calculated from the Karplus equation (128°). Signal of $H_{2'}$ and $H_{3'}$ appeared as a single peak at 4.15τ having 2H intensity. This fact also showed a low field shift of $H_{3'}$ peak caused by the 8,3′-anhydro bond formation. Desulfurization with Raney

*6 This is the gift of Dr. R.K. Robins, to whom authors' thanks are due.

10) M. Karplus : J. Chem. Phys., **30**, 11 (1959).
11) M. J. Robins, R. K. Robins : J. Am. Chem. Soc., **86**, 3585 (1964).
12) N. C. Yung, J. J. Fox : *Ibid.*, **83**, 3060 (1961).
13) C. D. Jardetzky : *Ibid.*, **82**, 229 (1960).

nickel gave a nucleoside having λ_{max}^{EtOH} 259 mμ, which was thought to be 3′-deoxyadenosine (Cordycepin).[6] In order to confirm the structure of the sugar moiety of this nucleoside, acid hydrolysis with 0.1*N* hydrochloric acid was carried out. The sugar thus obtained has identical Rf values with authentic 3′-deoxyribose on paper chromatography and gave a characteristic pink color of 3′-deoxyribose with cystein-sulfuric acid reagent.[14] Thus, the structure of XIII was established as 8,3′-anhydro-8-mercapto-9-β-D-xylofuranosyladenine. The ratio of the formation of the compound VIII, IX and X were approximately 3:1:1 in the original tosylation reaction. In spite of careful examination of the middle fraction of the chromatography, compound corresponding to 8,3′-anhydro-2′-O-tosyl derivative was not isolated.*7

The formation of purine cyclonucleoside having O-anhydro linkage is being investigated in our laboratory.

Experimental*8

Paper Chromatography——Solvent A, *n*-butanol-acetic acid-water, 4:1:5; solvent B, *n*-butanol-water, 86:14; solvent C, water (adjusted to pH 8.5 with ammonia); solvent D, iso-propanol-conc. ammonia-water, 7:1:2. Vicinal hydroxyl group was detected by metaperiodate spray[15] and ultraviolet absorbing spot was visualized under an ultraviolet lamp. Paper used was Toyo Filter Paper No. 51A.

8-Bromo-2′,3′-O-isopropylideneadenosine——A mixture of isopropylideneadenosine[16] (2.0 g.) and *N*-bromoacetamide[17] (2.2 g., 2.4 equivalent) dissolved in dry chloroform (20 ml.) was refluxed for 5 hours in an oil bath. Solvent was evaporated *in vacuo* and the residual red syrup was taken up in 50 ml. of ethyl acetate and washed successively with 10% sodium bisulfate, sodium bicarbonate and water. The ethyl acetate layer was dried over anhydrous sodium sulfate. Distillation of the solvent gave a semi-crystalline solid (2.0 g., 79.3%). Recrystallization of this material from ethanol gave 8-bromo-2′,3′-O-isopropylideneadenosine, m.p. 215~217° (yield, 1.20 g.). *Anal.* Calcd. for $C_{13}H_{16}O_4N_5Br$: C, 40.69; H, 4.18; N, 18.13. Found : C, 40.60; H, 4.35; N, 18.48. UV : λ_{max}^{EtOH} 265 mμ, $\lambda_{max}^{H^+}$ 264 mμ, $\lambda_{max}^{OH^-}$ 264 mμ. Paper chromatography: Rf (A) 0.80, isopropylideneadenosine 0.74; Rf (B) 0.73, isopropylideneadenosine 0.73.

5′-O-Acetyl-8-bromo-2′,3′-O-isopropylideneadenosine——a) 8-Bromo-2′,3′-O-isopropylideneadenosine (1.38 g.) was acetylated with acetic anhydride (6 ml.) in dry pyridine (35 ml.) at room temperature overnight. Ethanol (20 ml.) was added to the reaction mixture, and then left standing for 2 hours at room temperature. After the solvent was evaporated *in vacuo*, the residual syrup was taken up in 50 ml. of chloroform and washed with saturated sodium bicarbonate solution. After a water-wash, the chloroform layer was dried over sodium sulfate. Solvent was removed *in vacuo* and the residual red caramel was triturated with ethanol to induce crystallization. Tiny plates, m.p. 158~160°, were obtained (yield 1.01 g., 65.6%). *Anal.* Calcd. for $C_{15}H_{18}O_5N_5Br$: C, 42.06; H, 4.24; N, 16.38. Found : C, 41.92; H, 4.19; N, 16.71. IR : $\nu_{max}^{CHCl_3}$ 3380~3220 cm^{-1} (OH) disappeared $\nu_{max}^{CHCl_3}$ 1745 cm^{-1} (ester carbonyl) was observed. UV : λ_{max}^{EtOH} 265 mμ. Paper chromatography : Rf (B) 0.82.

b) A mixture of 5′-O-acetyl-2′,3′-O-isopropylideneadenosine[18] (4.0 g.) and N-bromoacetamide (5.0 g.) dissolved in 60 ml. of chloroform was refluxed for 6 hours. Work-up of the reaction mixture as described above in the bromination reaction gave a caramel (3.5 g.). After trituration with ethanol to induce crystallization, the solid was recrystallized from ethanol, m.p. 155~156° (yield 3.0 g., 61.2%). Mixed m.p. with a sample obtained in method a) showed no depression.

5′-O-Acetyl-8-bromoadenosine——5′-O-Acetyl-8-bromo-2′,3′-O-isopropylideneadenosine (1.0 g.) obtained as above was dissolved in 98% formic acid (30 ml.) and the mixture was set aside for 20 hours at room temperature with exclusion of the moisture. Ethanol (20 ml.) was added and the solvent was distilled off *in vacuo*. Addition of ethanol and evaporation was repeated until the odor of the formic acid disappeared. The residual colorless caramel was dissolved in a small amount of chloroform and extracted twice with water. The water layer was washed again with chloroform and evaporated to dryness *in vacuo* with

*7 A parallel experiment of the reaction of 8-bromo-2′,3′-di-O-mesyladenosine with thiourea gave two cyclonucleoside, presumably 8,2′- and 8,3′-cyclonucleoside in the ratio of 3:1 (to be published by M. Ikehara and H. Tada).

*8 Ultraviolet spectra were taken with a Beckman DK-II or Hitachi EPS-2U automatic recording spectrophotometer. Infrared absorption spectra were taken with a JASCO DS-301 spectrophotometer.

14) J. G. Buchanan : Nature, **168**, 1091 (1951).
15) M. Viscontini, D. Hoch, P. Karrer : Helv. Chim. Acta, **38**, 642 (1948).
16) A. Hampton : J. Am. Chem. Soc., **83**, 3642 (1961).
17) Org. Synth., **31**, 17 (1951).
18) D. M. Brown, L. J. Haynes, A. R. Todd : J. Chem. Soc., **1954**, 3299.

repeated additions of ethanol. A colorless caramel was obtained (600 mg., 67%). From the chloroform layer, unreacted starting material could be recovered (ca. 20%). *Anal.* Calcd. for $C_{12}H_{14}O_5N_5Br$: C, 37.12; H, 3.63; N, 18.04. Found : C, 37.20; H, 3.84; N, 18.46. IR : ν_{max}^{Nujol} 1735 cm^{-1} (ester carbonyl) existed and ν_{max}^{Nujol} 1150 cm^{-1} (isopropylidene) disappeared. UV : λ_{max}^{EtOH} 266 mμ. Paper chromatography : Rf (C) 0.54 (IO_4^-+); Rf (D) 0.57 (IO_4^-+), 5′-O-acetyl-8-bromo-2′,3′-O-isopropylideneadenosine 0.79.

Tosylation of 5′-O-acetyl-8-bromoadenosine——5′-O-Acetyl-8-bromoadenosine (998 mg.) was dried by azeotropic distillation with dry pyridine (20 ml. × 3) and dissolved finally in 60 ml. of dry pyridine. *p*-Toluenesulfonylchloride (499 mg., 1.02 equivalent) was added with cooling in an ice-salt bath. The reaction mixture was tightly stoppered and stored in a refrigerator for 60 hours. Immediately after the addition of 10 ml. of water, the mixture was poured into water saturated with sodium bicarbonate. The water solution was thoroughly extracted with chloroform. The chloroform layer was washed with sodium bicarbonate, then with water, and finally dried over sodium sulfate. The chloroform solution was evaporated to dryness *in vacuo* to remove the traces of pyridine and the residue was dissolved again in chloroform, which was extracted again with water to remove the starting material. Examination of the chloroform layer by paper chromatography showed a single spot having Rf (B) 0.84 (starting material has Rf (B) 0.58). UV absorption spectrum of the spot of Rf 0.84 was λ_{max}^{EtOH} 264 mμ, showed that no tosylation occurred on the adenine moiety. Evaporation of chloroform gave a caramel, which was dried under high vaccum over phosphorus pentoxide for 4 hours. The solid was dissolved in 20 ml. of methanol previously saturated with dry ammonia at 0°. After standing in refrigerator for 21 hours, the solvent was removed *in vacuo* to afford a crystalline solid. The solid was extracted with hot benzene to remove acetamide. A dried crystalline residue (537 mg.) was obtained (yield calculated as mono-tosylate was 42.3%). IR : no carbonyl band and ν_{max}^{Nujol} 1186, 1172 cm^{-1} (covalent tosylate) were observed. Recrystallization of this material from 50% isopropanol gave 8-bromo-2′-O-tosyladenosine as tiny needles, m.p. 220~223°(decomp.) (yield 155 mg., 11.5%). *Anal.* Calcd. for $C_{17}H_{18}O_6N_5BrS \cdot H_2O$: C, 39.38; H, 3.89; N, 13.51. Found : C, 39.31; H, 4.00; N, 13.47. The residue from the mother liquor was recrystallized from 50% isopropanol. Needles having m.p. 176~177° was obtained. Elemental analysis (calculated for $C_{24}H_{24}O_8N_5BrS_2$ (ditosylate) : C, 44.04; H, 3.70; N, 10.70. Found : C, 43.02; H, 4.60; N, 12.11) showed the ditosylate slightly contaminated with monotosylate. The third crop was obtained as granulous crystals, m.p. 213°(decomp.). *Anal.* Calcd. for $C_{17}H_{18}O_6N_5BrS$ (monotosylate) : C, 40.80; H, 3.63; N, 14.0 Found : C, 41.49; H, 3.89; N, 12.88. Although this value showed slight contamination with ditosylate, the main component of this material must be the 3′-O-tosyl derivative. Thin-layer chromatography (silica gel) of these tosylates showed similar Rf 0.46 (in chloroform-ethanol, 35:5) and Rf 0.24 (in benzene-ethyl acetate, 1:1) for all these three tosylates described above.

8,2′-Anhydro-8-mercapto-9-β-D-arabinofuranosyladenine——8-Bromo-2′-O-tosyladenosine (510 mg.) was refluxed in 60 ml. of *n*-butanol (freshly distilled) with 81.5 mg. (1.1 equivalent) of thiourea for 2 hours. During this time the ultraviolet absorption spectrum of the reaction mixture changed from λ_{max} 264 mμ to 275 mμ. Evaporation of the solvent *in vacuo* gave a powder (561 mg.), which had Rf (D) 0.20 (IO_4^-–, starting material Rf (D) 0.74). UV of the spot of Rf 0.20 was λ_{max}^{EtOH} 275 mμ. The powder was dissolved in 10 ml. of ethanol and applied to a column of cellulose powder (70 g.). Elution was carried out with a solvent of *n*-butanol saturated with water (100)+conc. ammonia (1) and 10 ml. fractions were collected. Fraction 11~18 was combined and evaporated. The residual colorless solid (328 mg.) was recrystallized from 0.2 ml. of water at 0°. Recrystallization from 1 ml. of water gave 167 mg. (57.4%) of the 8,2′-cyclonucleoside, m.p. 191~194°. *Anal.* Calcd. for $C_{10}H_{11}O_3N_5S \cdot \frac{1}{2}H_2O$: C, 41.37; H, 4.16; N, 24.12. Found : C, 41.11; H, 4.26: N, 24.45. $[\alpha]_D^{28.5}$ −187.2° (c=1.0, H_2O). UV : λ_{max}^{EtOH} 276 mμ (ε=18.8×10³), λ_{max}^{pH1} 276 mμ (ε=18.2×10³), λ_{max}^{pH14} 277 mμ (ε=19.3×10³). IR ν_{max}^{Nujol} 1172, 1186 cm^{-1} (covalent tosylate) was not observed. NMR spectra[19] : $H_{1'}$ 3.49 τ (doublet), $H_{2'}$ 4.18 τ, $H_{3'}$ 4.05 τ; $J_{1'-2'}$ 6.6 c.p.s. Paper chromatography : Rf (D) 0.49, Rf (B) 0.20. Reaction of this anhydronucleoside with dilute acid and alkali gave no cleavage of the anhydro linkage.

Cyclization of the Tosylate Mixture obtained from the Mother Liquor of Recrystallization of 8-Bromo-2′-O-tosyladenosine——Tosylate mixture (1.67 g.) was refluxed in *n*-butanol (100 ml.) for 2 hours with thiourea (277 mg.). After evaporation of the solvent *in vacuo* to dryness, reddish caramel was obtained (yield 1.76 g.). This was dissolved in 10 ml. of ethanol and applied to the column (28×560 mm.) of cellulose powder (120 g.), which was eluted with *n*-butanol saturated with water- conc. ammonia, 100; 1. Each 10 ml. fractions were collected. Fractions 12~23 were combined and evaporated. The residue was recrystallized from ethanol-water (2:1) to give 240 mg. of 8,2′-anhydro-8-mercapto-3′-O-tosyl-9-β-D--arabinofuranosyladenine as needles, m.p. 196~197°. *Anal.* Calcd. for $C_{17}H_{17}O_5N_5S_2 \cdot H_2O$: C, 45.05; H, 4.22; N, 15.44. Found : C, 44.71; H, 4.23; N, 15.95. IR ν_{max}^{Nujol} 1175, 1185 cm^{-1} (covalent tosylate). UV : λ_{max}^{EtOH} 276 mμ. $[\alpha]_D^{23}$ −70.8 (c=0.5, pyridine). Paper chromatography : Rf (A) 0.64. Fractions 28~30 were combined and evaporated to dryness. The residual white powder (250 mg.) was recrystallized from 80% ethanol and gave crystals which colored at 231~232° and decomposed at 250°. UV : λ_{max}^{H2O} 275 mμ (shoulder, ε 19.4×10³), 283 mμ (ε 20.3×10³), 287 mμ (shoulder, ε 14.2×10³); λ_{max}^{pH1} 274 mμ (shoulder, ε 17.0×10³), 284 mμ (ε 20.6×10³), 290 mμ (shoulder, ε 17.3×10³); λ_{max}^{pH14} 285 mμ (ε 21.0×10³), 288 mμ (shoulder, ε 17.7×10³), 291 mμ (shoulder,

19) Taken with Varian V 4300 C spectrometer operated at 60 mc, in DMSO using tetramethylsilane as internal reference.

ε 14.8×10^3). *Anal.* Calcd. for $C_{10}H_{11}O_3N_5S \cdot \frac{1}{2}H_2O$: C, 41.37; H, 4.16; N, 24.12. Found: C, 41.31; H, 4.55; N, 24.05. IR: no band at ν_{max}^{Nujol} 1175~1185 cm^{-1} (covalent tosylate). $[\alpha]_D^{20}$ −32.0° (c=0.75, pyridine). NMR spectra: $H_{1'}$ 3.62 τ (doublet), $H_{2'}$, $H_{3'}$ 4.15 τ; $J_{1'-2'}$ 2.5 c.p.s. Paper chromatography: Rf (A) 0.25. The sample does not consume metaperiodate. Accordingly this material is 8,3′-anhydro-8-mercapto-β-D-xylofuranosyladenine.

From the fractions 31~34 was obtained 273 mg. of a white powder, which was recrystallized from 0.2 ml. of water. Colorless needles, m.p. 191~194° were obtained (yield 110 mg.). *Anal.* Calcd. for $C_{10}H_{11}O_3N_5S \cdot \frac{1}{2}H_2O$: C, 41.37; H, 4.16; N, 24.12. Found: C, 41.11; H, 4.26; N, 24.45. This sample was identical with the sample of 8,2′-anhydro-8-mercapto-9-β-D-arabinofuranosyladenine obtained above. Another minor component having λ_{max}^{EtOH} 303 mμ and Rf (A) 0.16 was separated on paper chromatography (A) of the initial reaction mixture. This is presumably 8-mercapto-2′(or 3′)-O-tosyladenosine.

2′-Deoxyadenosine——8,2′-Anhydro-8-mercapto-9-β-D-arabinofuranosyladenine (210 mg.) was refluxed in 20 ml. of water with 1.5 g. of Raney nickel for 6 hours. After the catalyst was filtered off, water solution was evaporated to a small volume and set aside. 2′-Deoxyadenosine was obtained as tiny needles, m.p. 184~187° (yield 65 mg., 33%). Mixed m.p. with an authentic 2′-deoxyadenosine (m.p. 187~188°) showed m.p. 184~187°. A small amount of the synthetic 2′-deoxyadenosine was hydrolyzed with 0.1*N* hydrochloric acid and subjected to the paper chromatography: Rf (A) 0.49. When an authentic sample of 2-deoxyribose was co-chromatographed in the same solvent, it showed Rf 0.49. Both spots revealed a pink color with cystein-sulfuric acid spray.[15]

3′-Deoxyadenosine (Cordycepin)——8,3′-Anhydro-8-mercapto-9-β-D-xylofiranosyladenine (10 mg.) was refluxed in 10 ml. of water with a small spoonful Raney nickel for 1 hour. Catalyst was removed by filtration, filtrate and washings were combined, and evaporated *in vacuo*. 3′-Deoxyadenosine was obtained as a colorless glass, UV: λ_{max}^{EtOH} 259 mμ. Paper chromatography: Rf (B) 0.37, $R_{Adenine}$ 0.90. These values were consistent with those reported by Lee, *et al.*[6] A small amount of this sample on hydrolysis with 0.1*N* hydrochloric acid at 100° for 1 hour produced a spot having Rf (A) 0.53 on the paper chromatogram. When an authentic 3′-deoxyribose (obtained by the same hydrolytic procedure from 3′-deoxyadenosine) was chromatographed in the same solvent, it showed Rf 0.53. Both spots revealed a characteristic pink color by the spray with cystein-sulfuric acid reagent.

3′-O-Tosyl-2′-deoxyadenosine——8,2′-Anhydro-8-mercapto-9-(3′-O-tosyl)-β-D-arabinofuranosyladenine, obtained as above (67 mg.), was refluxed in a mixture of *n*-propanol (14 ml.) and water (7 ml.) with 500 mg. of Raney nickel. After the reflux for 5.5 hours λ_{max} shifted from 276 mμ to 258 mμ. Catalyst was filtered and the filtrate was evaporated to dryness *in vacuo*. The powder-like residue (36 mg.) was recrystallized from ethanol-water. Although m.p. of this material (156~170°) was lower than that reported by Robins, *et al.*,[11] paper chromatographical examination showed the similar Rf values, Rf (D) 0.67.

Authors wish to thank Dr. Jack J. Fox of Sloan-Kettering Institute for reading of the manuscript. Elemental analyses were done by Mrs. Toyoko Tohma and Miss Akiko Maeda of this Faculty, to whom authors' thanks are due.