(1 ml) was added and after 15 min sodium borohydride (100 mg) was added. The mixture was stirred for 30 min and then diluted with water (20 ml). The mixture was extracted with ethyl acetate and the extracts were washed with water and brine and dried. Removal of the solvent under reduced pressure left a brown oil (160 mg, 92%) which was identical with the starting material by tlc and pmr spectroscopy.

Reaction of the Methylated Ethanolamine 21 with Methanesulfonyl Chloride.—A solution of the ethanolamine **21** (300 mg, 1.07 mmol) in dry 1,2-dimethoxyethane (5 ml) was cooled to −10° in an ice–salt bath. Freshly distilled triethylamine (360 mg, 3.60 mmol) was added followed by methanesulfonyl chloride (160 mg, 1.40 mmol) over 5 min. The mixture was allowed to warm to room temperature and was stirred for 3.5 hr under nitrogen. Excess sodium borohydride was added and the mixture was stirred at room temperature for 3 hr. Water (30 ml) was added and the mixture was extracted with chloroform. The extracts were washed with water and brine and dried. Removal of the solvent under reduced pressure left a brown gum (330 mg). Tlc indicated the material to be a mixture of at least three components. The mixture was separated by preparative tlc (Merck silica gel PF-254, ethyl acetate as eluent) to give three compounds of R_f 0.05, 0.5, and 0.8. The ultraviolet spectrum of all the components showed typical indole absorption (λ_{max}^{EtOH} 290, 283, 273, and 226 nm).

Registry No.—**1**, 40525-24-4; **1** semicarbazone, 40496-45-5; **2**, 40496-46-6; **3**, 40496-47-7; **4**, 40488-34-4; **5**, 40496-48-8; **6**, 40496-49-9; **8**, 26088-68-6; **9**, 26072-19-5; **9** acetate, 40496-52-4; **10**, 40496-53-5; **11**, 40496-54-6; **12**, 40496-55-7; **13**, 40496-56-8; **14**, 40496-57-9; **15**, 40496-58-0; **16**, 40496-59-1; **17**, 40496-60-4; **18**, 40496-61-5; **20**, 40496-62-6; **21**, 40496-63-7; **21** picrate, 40496-64-8; 2-(Δ³-cyclohexenyl)ethylamine, 40496-65-9; benzoyl chloride, 98-88-4; *m*-chloroperbenzoic acid, 937-14-4; phenylhydrazine, 100-63-0; 4-carbethoxycyclohexanone, 17159-79-4; *p*-toluenesulfonyl chloride, 98-59-9; sodium cyanide, 917-61-3; sodium hydroxide, 1310-73-2; methanesulfonyl chloride, 124-63-0; chloroacetyl chloride, 79-04-9; sodium hydride, 7646-69-7; ethylene oxide, 75-21-8.

Studies on the Oxidation of "Reversed Nucleosides" in Oxygen. I. Synthesis of Eritadenine and Its Derivatives[1]

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Reaction of methyl-5-*O*-tosyl-2,3-*O*-isopropylidene-β-D-ribofuranoside (I) or 5-*O*-tosyl-1,2-*O*-isopropylidene-3-*O*-alkyl-β-D-arabofuranoses (IV) with the sodium salt of adenine in DMF afforded the corresponding "reversed nucleosides" in good yields. After removal of the protective groups of the sugar moiety by treatment with hydrochloric acid, the demasked reversed nucleosides were oxidized by air or oxygen in a dilute alkali solution at room temperature to give eritadenine and its α-*O*-alkyl derivatives. The yields of the acids were generally good. To confirm the structures and evaluate the biological activities, syntheses of their esters were also performed.

Several synthetic routes to eritadenine, one of the significant hypocholesterolemic components of *Lentinus edodes* Sing, have been reported employing D-erythrono lactone as the starting material.[2]

Although various synthetic pathways might be conceivable, a large-scale synthesis of eritadenine using this lactone appears to be somewhat uneconomical[3] because of the rather poor yield of the lactone in the preparations described in the literature.[4] The necessity for a large amount of eritadenine and its derivatives for biological studies required development of a more simplified method of preparation.

Since the low yield of the lactone by the literature method appears to be due to the complicated purification process during which a part of the lactone might have decomposed, it was conceivable that the derived product might be more easily separated from the oxidation mixture after prior condensation of the sugar moiety with a fairly insoluble material such as a purine, thus preventing decomposition. From this point of view, adoption of the procedure for the synthesis of a reversed nucleoside by Leonard[5] proved to be extremely useful.

Reaction of methyl-5-*O*-tosyl-2,3,-*O*-isopropylidene-β-D-ribofuranoside (I)[6] with the sodium salt of adenine in DMF gave the corresponding 9-substituted reversed nucleoside II in excellent yield. The attachment of the substituent was based on the characteristic uv absorption band at λ_{max} (H_2O) 258 nm at pH 2, 260 nm at pH 7, and 262 nm at pH 11. None of the other position isomers could be detected in the reaction mixture. Hydrolysis of II with dilute hydrochloric acid to remove the protective groups at 60–80° afforded the pure demasked reversed nucleoside III in 86.5% yield.

In a test reaction the air oxidation of III in dilute sodium hydroxide solution at room temperature proceeded as expected. Tlc of the reaction mixture showed a spot the R_f value of which was identical with that of an authentic sample of eritadenine. Hence III in 0.5% NaOH solution was stirred in an atmosphere of oxygen at room temperature. After 17 hr, the spot of III had completely disappeared and a single spot was observed at R_f 0.35 on tlc (silica gel GF 254;

(1) Preliminary communication: M. Kawazu, T. Kanno, N. Takamura, T. Mizoguchi, S. Saito, and K. Okumura, *Chem. Commun.*, 1045 (1970).

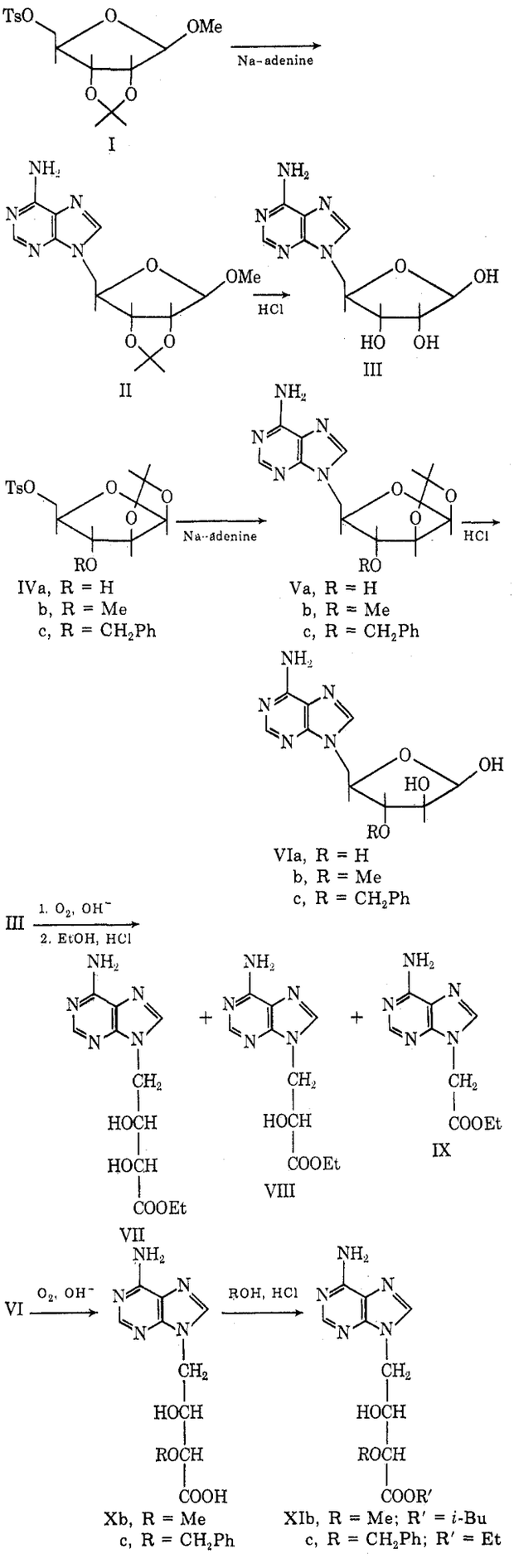
(2) (a) I. Chibata, K. Okumura, S. Takeyama, and K. Kotera, *Experientia*, **25**, 1237 (1969); (b) T. Kamiya, Y. Saito, M. Hashimoto, and H. Seki, *Tetrahedron Lett.*, 4729 (1969); (c) T. Kamiya, Y. Saito, M. Hashimoto, and H. Seki, *Chem. Ind. (London)*, 652 (1970).

(3) The situation has changed to some degree now, since a simple method for the preparation of the D-erythronolactone from D-glucose was explored in our laboratory and the method described in *J. Org. Chem.*, **36**, 1573 (1971), was also useful for a large-scale synthesis of eritadenine.

(4) E. Hardegger, K. Kreis, and H. El. Khadem, *Helv. Chim. Acta*, **34**, 2343 (1951).

(5) N. J. Leonard, F. C. Sciavolino, and V. Nair, *J. Org. Chem.*, **33**, 3169 (1968).

(6) N. J. Leonard and K. L. Carraway, *J. Heterocycl. Chem.*, **3**, 485 (1966).



n-butyl alcohol–acetic acid–water 4:1:5). The product was easily isolated as colorless plates by evaporating the water *in vacuo* and adding a volume of ethanol, and was identified as sodium eritadeninate by comparison of its spectral data with those of an authentic sample.

Although tlc showed a single spot, further treatment of the mother liquid gave no additionally pure eritadenine; hence the reaction had resulted in formation of a mixture. In order to separate the products, the evaporation residue was desalted by treatment with an ion exchange resin, and subsequently esterified with ethanol and HCl. Three esters could be separated chromatographically and were identified as ethyl 6-aminopurin-9*H*-9-yl acetate (IX), ethyl β-(6-aminopurin-9*H*-9-yl)-α-hydroxypropionate (VIII), and ethyl eritadeninate (VII), on the basis of analytical and spectral data. The total yield of eritadenine was thus over 80%.

In order to investigate the scope and limitations of this reaction, further work on the synthesis of some adenine reversed nucleosides and the oxidation by oxygen was carried out using D-arabinose.

Reaction of 1,2-*O*-isopropylidene-5-*O*-tosyl-β-D-arabofuranose (IVa), 1,2-*O*-isopropylidene-3-*O*-methyl-5-*O*-tosyl-β-D-arabofuranose (IVb),[7] and 1,2-*O*-isopropylidene-3-*O*-benzyl-5-*O*-tosyl-β-D-arabofuranose (IVc)[8] with the sodium salt of adenine in DMF led to the formation of the corresponding reversed nucleosides Va, Vb, and Vc, respectively. The yields were generally good except for the unprotected compound Va. A fairly large amount of adenine was recovered in this case. Dealkylation of the protected reversed nucleosides to give VIa, VIb, and VIc was carried out satisfactorily by treatment with dilute hydrochloric acid.

Oxygen oxidation of VIa under conditions similar to those for III afforded eritadenine in a 78% yield. Oxidation of VIb gave an acid Xb, in whose nmr spectrum the methyl protons of the methoxy group appeared as a singlet at δ 3.43 in D_2O. Esterification of Xb with isobutyl alcohol and hydrogen chloride yielded ester XIb, whose structure was confirmed analytically and spectrophotometrically. On the other hand, oxidation of VIc gave a mixture of eritadenine and Xc. Thus the yield of Xc was under 50%. This result indicated that the benzyl group had been partially removed, presumably by oxidation. The esterification of Xc with ethanol and hydrogen chloride gave XIc in 89% yield. Reduction of XIc in 5% hydrochloric acid in the presence of Pd on charcoal at room temperature afforded ethyl eritadeninate in good yield. Hence the method described here, which involves the synthesis of reversed nucleosides and their oxidation by oxygen, provides a simple synthesis of eritadenine and its derivatives.

Experimental Section

Melting points were taken on a Yamato capillary melting point apparatus Model Mp-1 and are uncorrected. Ir spectra were recorded using a Hitachi IR-E spectrophotometer as Nujol

(7) E. L. Hirst, T. K. N. Jones, and E. Williams, *J. Chem. Soc.*, 1062 (1947).

(8) Synthesized by the procedure similar to that of the *O*-methyl derivative.

suspension unless otherwise indicated. Nmr spectra were determined on a Model JEOL ME-60 spectrometer with tetramethylsilane as an internal standard.

General Procedure for the Reaction of the Sodium Salt of Adenine with 5-*O*-*p*-Toluenesulfonyl Sugar Derivatives.—The sodium salt of adenine was prepared by stirring a suspension of an equimolar amount of the adenine and sodium hydride (in oil suspension) in DMF (3–4 ml/mmol of the adenine) at room temperature for 1 hr and warming at 50–60° for 1 hr. After the mixture had been cooled, a solution of the 5-*O*-*p*-toluenesulfonyl sugar derivatives (0.9–1.0 molar equiv) in DMF (4–10 ml/mmol of the sugar derivatives) was added dropwise to this suspension. The suspension was stirred and warmed at 100° for 10 hr. The resulting clear solution was evaporated under vacuum at 50–90°. The residue was treated in an appropriate manner for the respective reaction.

Methyl 5-(6-Aminopurin-9*H*-9-yl)-2,3-*O*-isopropylidene-5-deoxy-β-D-ribofuranoside (II).—A solution of the sodium salt of adenine (2.48 g, 18.4 mmol) and I (5.5 g, 15.3 mmol) in DMF (100 ml) was treated in the manner described in the general procedure. The residual solid was extracted with hot chloroform and the chloroform extracts filtered were combined, washed with H_2O, and dried (Na_2SO_4). Evaporation of the chloroform afforded 4.7 g (95%) of crude I, mp 239–243°. Recrystallization from MeOH gave an analytical sample of II as colorless prisms: mp 248–249°; $[\alpha]^{25}D$ −8.4° (*c* 0.5, MeOH); ir 3220, 3090 cm^{-1} (NH_2); nmr (DMSO-d_6) δ 8.15 (s, 2 H, C_2H, C_8H of purine), 7.20 (broad s, 2 H, $-NH_2$), 4.92 (s, 1 H, C_1 H), 4.8–4.0 (m, 5 H), 3.20 (s, 3 H, -OMe), 1.26, 1.12 (s, 3 H, 3 H, CMe_2).

Anal. Calcd for $C_{14}H_{19}N_5O_4$: C, 52.33; H, 5.96; N, 21.80. Found: C, 52.34; H, 5.97; N, 21.50.

5-(6-Aminopurin-9*H*-9-yl)-1,2-*O*-isopropylidene-5-deoxy-β-D-arabofuranose (Va).—A solution of the sodium salt of adenine (2.16 g, 16 mmol) and IVa (5 g, 14.5 mmol) in DMF (200 ml) was treated in the same manner as described in the general procedure. The residual solid was washed with benzene (10 ml) and then cold water (20 ml). The insoluble solid (mp 232–237°) was recrystallized from H_2O to give an analytical sample of Va, 2.35 g (53%), as colorless needles: mp 240–241°; $[\alpha]^{18}D$ 135° (*c* 0.5, H_2O); ir 3400 (OH), 3240, 3090 cm^{-1} (NH_2); nmr (DMSO-d_6) δ 8.10 (s, 2 H), 7.16 (broad s, 2 H, $-NH_2$), 5.83 (d, 1 H, J = 4.0 Hz, C_1 H), 5.60 (broad, 1 H, -OH), 4.45–4.0 (m, 5 H), 1.45 (s, 3 H), 1.20 (s, 3 H).

Anal. Calcd for $C_{13}H_{17}N_5O_4$: C, 50.81; H, 5.58; N, 22.79. Found: C, 50.61; H, 5.60; N, 22.50.

5-(6-Aminopurin-9*H*-9-yl)-1,2-*O*-isopropylidene-3-*O*-methyl-5-deoxy-β-D-arabofuranose (Vb).—A solution of the sodium salt of adenine (4.1 g, 29 mmol) and IVb in DMF (300 ml) was treated in the manner described in the general procedure. The residual solid was triturated in cold water (50 ml), and insoluble crystals were filtered to give 6.0 g (64%) of crude solid of Vb. Recrystallization from MeOH afforded an analytical sample of Vb, 5.5 g, as colorless prisms: mp 205–206°; $[\alpha]^{25}D$ 92.5° (*c* 1.0, MeOH); nmr (DMSO-d_6) δ 8.15, 8.04, (s, 1 H, 1 H, C_2 H, C_8 H of purine), 7.22 (broad s, 2 H, $-NH_2$), 5.83 (d, 1 H, J = 4.5 Hz, C_1 H), 4.65 (d, 1 H, J = 4.5 Hz, C_2 H), 4.35 (broad s, 3 H), 3.81 (s, 1 H, C_3 H), 3.02 (s, 3 H, -OMe), 1.43, 1.23 (s, 3 H, 3 H, $>CMe_2$).

Anal. Calcd for $C_{14}H_{19}N_5O_4$: C, 52.33; H, 5.96; N, 21.80. Found: C, 52.41; H, 6.04; N, 21.93.

5-(6-Aminopurin-9*H*-9-yl)-1,2-*O*-isopropylidene-3-*O*-benzyl-5-deoxy-β-D-arabofuranose (Vc).—A solution of the sodium salt of adenine (2.85 g, 2.11 mmol) and IVc (9.76 g, 19.2 mmol) in DMF (300 ml) was treated in the manner described in the general procedure. Water (20 ml) was added to the resulting residue and the insoluble crystals were collected by filtration to give 6.0 g of crude Vc. Recrystallization from MeOH afforded an analytical sample of Vc, 5.5 g (73%), as colorless prisms: mp 198–199°; $[\alpha]^{23}D$ 66.7° (*c* 0.3, MeOH); nmr (DMSO-d_6) δ 7.22 (s, 7 H, $C_6H_5CH_2$–, $-NH_2$), 5.90 (d, 1 H, J = 4 Hz, C_1 H), 4.72 (d, 1 H, J = 4 Hz, C_2 H), 4.6–4.2 (m, 5 H), 4.02 (s, 1 H, C_3 H), 1.47, 1.28 (s, 3 H, 3 H, $>CMe_2$).

Anal. Calcd for $C_{20}H_{23}N_5O_4$: C, 60.44; H, 5.83; N, 17.62. Found: C, 60.64; H, 5.77; N, 17.50.

General Procedure for the Hydrolysis of II, Va, Vb, and Vc.—A solution of the 5-(6-aminopurin-9-yl)-5-deoxy sugar derivative in water (20 ml/1 g of sugar derivative) and 6 *N* hydrochloric acid (0.55 ml/1 g of sugar derivative) was stirred and warmed at 70–80° for 3 hr. After the reaction mixture had been cooled, the solution was passed through a column of Amberlite IR-45 (OH form, 3 g/1 ml of 6 *N* hydrochloric acid). The eluate and washings were evaporated to dryness *in vacuo*. The resulting solid was treated in an appropriate manner for the respective reaction.

5-(6-Aminopurin-9*H*-9-yl)-5-deoxy-D-ribofuranose (III).—A solution of II (21 g, 65.4 mmol) and 6 *N* hydrochloric acid (12 ml) in H_2O (400 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from water to afford an analytical sample of III as colorless prisms: yield 15.12 g (86.5%); mp 168–169° dec; $[\alpha]^{25}D$ 32.3° (*c* 1.0, H_2O); ir 3300 (OH), 3220, 3110 cm^{-1} (NH); uv max (H_2O) 261.5 nm (pH 7 and 12), 260.5 (pH 2); nmr (DMSO-d_6) δ 8.20, 8.12 (s, 1 H, 1 H, C_2 H, C_8 H of purine), 7.25 (broad s, 2 H, NH_2), 6.51 (d, 1 H, J = 5 Hz, -OH), 5.05 (m, 3 H), 4.5–3.5 (m, 5 H).

Anal. Calcd for $C_{10}H_{13}N_5O_4 \cdot {}^1/_4H_2O$: 44.20; H, 5.00; N, 25.77. Found: C, 44.42; H, 4.87; N, 25.60.

5-(6-Aminopurin-9*H*-9-yl)-5-deoxy-D-arabofuranose (VIa).—A solution of Va (1.7 g, 5.53 mmol) and 6 *N* hydrochloric acid (1 ml) in H_2O (30 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from H_2O to give an analytical sample of VIa as colorless leaflets: yield 1.347 g (91.5%); mp 159–160° dec; $[\alpha]^{18}D$ 36° (*c* 0.5, H_2O); ir 3380 (OH), 3220, 3100 cm^{-1} (NH); nmr (DMSO-d_6) δ 7.15 (broad s, 2 H, NH_2), 6.23 (d, 1 H, J = 6 Hz, -OH), 5.35 (m, 2 H), 5.05 (m, 1 H), 5.75 (m, 3 H), 6.30 (m, 3 H).

Anal. Calcd for $C_{10}H_{13}N_5O_4 \cdot {}^1/_2H_2O$: C, 43.48; H, 5.11; N, 25.45. Found: C, 43.68; H, 5.32; N, 25.87.

5-(6-Aminopurin-9*H*-9-yl)-3-*O*-methyl-5-deoxy-D-arabofuranose (VIb).—A solution of Vb (5.3 g, 16.5 mmol) and 6 *N* hydrochloric acid (2.7 ml) in H_2O (110 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from H_2O to give an analytical sample of VIb as colorless prisms: yield 4.25 g (92%); mp 196–197° dec; $[\alpha]^{20}D$ 24.8° (*c* 1.0, H_2O); ir 3425 (OH), 3220, 3100 cm^{-1} (NH); uv max (H_2O) 261 nm (pH 7 and 12), 260 (pH 2); nmr (DMSO-d_6) δ 7.30 (broad s, 2 H, $-NH_2$), 6.25 (d, 1 H, J = 5 Hz, -OH), 5.38 (d, 1 H, J = 4.5 Hz, -OH), 5.00 (s, 1 H), 4.5–3.5 (m, 6 H), 3.20 (s, 3 H, -OMe).

Anal. Calcd for $C_{11}H_{15}N_5O_4$: C, 46.97; H, 5.38; N, 24.90. Found: C, 46.89; H, 5.42; N, 24.65.

5-(6-Aminopurin-9*H*-9-yl)-3-*O*-benzyl-5-deoxy-D-arabofuranose (VIc).—A solution of Vc (5 g, 12.6 mmol) and 6 N hydrochloric acid (2.5 ml) in H_2O (100 ml) was treated in the manner described in the general procedure. The resulting solid was recrystallized from H_2O to give an analytical sample of VIc as colorless prisms: yield 4.2 g (93%); mp 177–179° dec; $[\alpha]^{20}D$ 46.7° (*c* 0.3, MeOH); ir 3100 cm^{-1} (NH); nmr (DMSO-d_6) δ 7.25 (s, 5 H, $C_6H_5CH_2$–), 7.12 (broad s, 2 H, $-NH_2$), 6.30 (broad, 1 H, D_2O-exchangeable -OH), 5.40 (broad, 1 H, D_2O-exchangeable -OH), 5.40 (broad 1 H, D_2O-exchangeable -OH), 5.05 (broad s, 1 H), 4.8–3.85 (m, 6 H), 3.76 (broad, 1 H).

Anal. Calcd for $C_{17}H_{19}N_5O_4 \cdot {}^1/_5H_2O$: C, 56.56; H, 5.42; N, 19.40. Found: C, 56.75; H, 5.30; N, 19.40.

Air Oxidation of 5-(6-Aminopurin-9*H*-9-yl)-5-deoxy-D-ribofuranonse (III).—5-(6-Aminopurin-9 *H*-9-yl)-5-deoxy-D-ribofuranose (III) (15 g, 56.2 mmol) was dissolved in H_2O (3 l.) and NaOH (7.95 g, 169 mmol). This solution was stirred at room temperature in an oxygen atmosphere for 17 hr, and evaporated to 200 ml *in vacuo* at 50–60°. To the solution was added 400 ml of EtOH. The mixture was kept refrigerated overnight and the colorless leaflets which separated were collected by filtration. An additional crop of crystals was further obtained by adding EtOH to the mother liquid. This procedure was repeated three times to give 11.85 g (77%) of the sodium salt of eritadenine of which the physical data were completely identical with those of an authentic sample. The mother liquid was evaporated *in vacuo*; to remove EtOH the residual liquid was passed through a column of Amberlite IR-120 (H form, 250 ml) and the column was washed with H_2O, then eluted with 2.8% NH_4OH, and the eluate (2 l.) was evaporated to dryness completely *in vacuo*. The resulting solid was esterified with saturated EtOH and HCl. After the evaporation of EtOH, further EtOH was added and evaporated. This treatment was repeated more than twice. The residue was dissolved in EtOH (100 ml) and treated with dry Amberlite IR-45 (OH form, 10 g) to neutralize the solution. The mixture was stirred at room temperature overnight. After removal of Amberlite IR-45 by filtration, the filtrate was chromatographed with 80 g of silica gel. Elution with 5% EtOH–$CHCl_3$ gave 399 mg (3.2% from III) of ethyl 2-(6-aminopurin-9*H*-9-yl)acetate (IX) as a white, crystalline solid. Two recrystallizations from EtOH afforded an analytical sample of IX as

colorless prisms: mp 225–227°; ir 3200, 3060 (–NH), 1725 cm^{-1} (–CO); uv max (EtOH) 261 nm (pH 7 and 12), 259.5 (pH 2); nmr (DMSO-d_6) δ 7.35 (broad s, 2 H, $-NH_2$), 5.12 (s, 2 H, $-CH_2CO$), 4.20 (q, 2 H, J = 7.5 Hz, $-CH_2CH_3$), 1.22 (t, 3 H, J = 7.5 Hz, $-CH_2CH_3$).

Anal. Calcd for $C_9H_{11}N_5O_2$: C, 48.86; H, 5.01; N, 31.66. Found: C, 49.02; H, 4.95; N, 31.60.

Elution with 5–10% EtOH–$CHCl_3$ gave 5.25 g (3.7% from III) of ethyl 3-(6-aminopurin-9*H*-9-yl)-2(*R*)-hydroxypropionate (VIII) as a white, crystalline solid. Three recrystallizations from EtOH afforded an analytical sample of VIII as colorless granulars: mp 175–178°; $[\alpha]^{21}D$ 8.3° (*c* 0.6, EtOH); ir 3200, 3080 (–NH), 1720 cm^{-1} (–CO); uv max (EtOH) 261 nm (pH 7), 262 (pH 12), 260 (pH 2); nmr (DMSO-d_6) δ 7.30 (broad s, 2 H, $-NH_2$), 6.12 (d, 1 H, J = 5 Hz, –OH), 4.70–4.20 (m, 3 H), 4.11 (g, 2 H, J = 7.5 Hz), 1.15 (t, 3 H, J = 7.5 Hz).

Anal. Calcd for $C_{10}H_{13}N_5O_3$: C, 47.80; H, 5.22; N, 27.88. Found: C, 47.79; H, 5.14; N, 27.58.

The last part of elution with 10–20% EtOH–$CHCl_3$ gave 620 mg (3.9% from III) of the ethyl ester of eritadenine VII as a colorless solid. Recrystallization from EtOH gave pure VII as colorless prisms, of which the physical data were identical with those of an authentic sample.

Oxidation of 5-(6-Aminopurin-9*H*-9-yl)-5-deoxy-D-arabofuranose (VIa).—VIa (500 mg, 1.88 mmol) was dissolved in a dilute NaOH solution (226 mg, 5.64 mmol; H_2O, 100 ml). The solution was stirred at room temperature under an atmosphere of oxygen for 15 hr. The solution was evaporated to 20 ml at 50–60° *in vacuo*. The resulting solution was passed through a column of Amberlite IR-120 (H form, 10 ml), the column was washed with H_2O, then eluted with 2.8% NH_4OH, and the eluate (200 ml) was evaporated *in vacuo* at 50–60°. The resulting solid was dissolved in H_2O. The solution was treated with charcoal and filtered. The filtrate was evaporated to dryness *in vacuo* to give crude solid (440 mg). Recrystallization from H_2O gave 355 mg (78%) of eritadenine, of which physical data were completely identical with those of an authentic sample.

Air Oxidation of 5-(6-Aminopurin-9*H*-9-yl)-3-*O*-methyl-5-deoxy-D-arabofuranose (VIb).—VIb (100 mg, 0.358 mmol) was dissolved in a dilute KOH solution (40 mg, 0.714 mmol; H_2O, 15 ml). The solution was stirred at room temperature under an oxygen atmosphere for 20 hr. The solution was evaporated, and EtOH was added. The mixture was allowed to stand overnight at room temperature. The crystals which separated and were revealed as the potassium salt of 4-(6-aminopurin-9*H*-9-yl)-3(*R*)-hydroxy-2(*R*)-methoxybutyric acid (Xb) were collected by filtration to give 85 mg (78%): mp 225° dec; ir 3200 (–NH), 1680 cm^{-1} (–CO); nmr (D_2O) δ 8.02 (s, 2 H, C_2 H, C_8 H of purine), 4.25 (broad s, 4 H), 3.43 (s, 3 H, –OMe).

Oxidation of 5-(6-Aminopurin-9*H*-9-yl)-3-*O*-benzyl-D-arabofuranose (VIc).—VIc (1.76 g, 4.92 mmol) was dissolved in a dilute NaOH solution (590 mg, 14.8 mmol; H_2O, 350 ml). The solution was stirred at 10–15° for 20 hr under an oxygen atmosphere. The solution was evaporated at 20 ml and acidified to pH 3.0 with 100% formic acid. The crude product precipitated was collected by filtration. The crude product was dissolved in MeOH and the solution was treated with charcoal and filtered. The filtrate was evaporated and the residue was recrystallized from MeOH to give an analytical sample of 4-(6-aminopurin-9*H*-9-yl)-2(*R*)-benzyloxy-3(*R*)-hydroxybutyric acid (Xc) as colorless prisms: yield 830 mg (49%); mp 181–182°; $[\alpha]^{20}D$ 46.7° (*c* 0.3, DMSO); ir 3360, 3280 (–NH), 1675 cm^{-1} (–CO); uv max (MeOH) 261 nm (pH 7 and 12), 260 (pH 2); nmr (DMSO-d_6) δ 7.29 (s, 5 H, $C_6H_5CH_2$–) 7.18 (broad s, 2 H, $-NH_2$), 5.25 (broad m, 2 H), 4.9–3.8 (m, 5 H).

Anal. Calcd for $C_{16}H_{17}N_5O_4 \cdot {}^1/_4H_2O$: C, 55.24; H, 5.07; N, 20.14. Found: C, 55.10; H, 4.77; N, 20.10.

Isobutyl 4-(6-Aminopurin-9*H*-9-yl)-3(*R*)-hydroxy-2(*R*)-methoxybutyrate (XIb).—A suspension of the sodium salt of 4-(6-aminopurin-9*H*-9-yl)-3(*R*)-hydroxy-2(*R*)-methoxybutyric acid (Xb) (2 g, 7.27 mmol) in isobutyl alcohol (200 ml) was saturated with *dry* hydrogen chloride. The solution was evaporated *in vacuo*. H_2O (50 ml) was added to this residue and the solution was basified with $NaHCO_3$ and extracted with $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried (Na_2SO_4), and evaporated. The resulting solid was recrystallized from benzene to give an analytical sample of XIb as colorless needles: yield 837 mg (80%); mp 170–172°; $[\alpha]^{20}D$ 35° (*c* 0.3, MeOH); ir 3230, 3090 (–NH), 1742 cm^{-1} (–CO–); uv max (MeOH) 261 nm (pH 7 and 12), 260 (pH 2); nmr (DMSO-d_6) δ 7.30 (broad s, 2 H, $-NH_2$), 5.84 (broad s, 1 H, –OH), 4.7–3.8 (m, 4 H), 4.10 (d, 2 H, J = 6 Hz, $OCH_2CH<$), 3.55 (s, 3 H, –OMe), 2.15 (m, 1 H, $-OCH_2CH<$), 1.08 (d, 6 H, J = 7 Hz).

Anal. Calcd for $C_{14}H_{21}N_5O_4$: C, 52.00; H, 6.55; N, 21.66. Found: 52.26; H, 6.63; N, 21.36.

Ethyl 4-(6-Aminopurin-9*H*-9-yl)-3(*R*)-hydroxy-2(*R*)-benzyloxybutyrate (XIc).—Xc (730 mg, 2.12 mmol) was dissolved into a saturated EtOH–HCl solution. The mixture was gently refluxed for 3 hr and stirred at room temperature for 14 hr. The solution was evaporated *in vacuo*. The residue was dissolved in a sodium bicarbonate solution. The solution was extracted with $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried, and evaporated to give 650 mg (89%) of crystals. Recrystallization from acetone–ether afforded an analytical sample of XIc as colorless prisms: mp 137°; $[\alpha]^{20}D$ 41.3° (*c* 0.42, MeOH); ir 3400 (–OH), 3200, 3100 (–NH), 1715 cm^{-1} (–CO–); nmr ($CDCl_3$) δ 7.34 (s, 5 H, $C_6H_5CH_2$–), 6.39 (broad s, 2 H, $-NH_2$), 4.9–3.8 (m, 8 H), 1.30 (t, 3 H, J = 7.5 Hz, $-CH_2CH_3$).

Anal. Calcd for $C_{18}H_{21}N_5O_4$: C, 58.21; H, 5.70; N, 18.86. Found: C, 57.99; H, 5.58; N, 19.09.

Registry No.—I, 4137-56-8; II, 40429-49-0; III, 40429-50-3; IVa, 40429-51-4; IVb, 40429-52-5; IVc, 40429-53-6; Va, 40429-54-7; Vb, 40429-55-8; Vc, 40429-56-9; VIa, 40429-57-0; VIb, 40429-58-1; VIc, 40429-59-2; VIII, 40429-60-5; IX, 25477-96-7; Xb K salt, 40513-90-4; Xb Na salt, 40429-62-7; Xc- 40429-63-8; XIb, 40429-64-9; Xc, 40428-85-1; eritadenine, 25486-40-2; adenine Na salt, 40428-86-2.