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Purines. XIII.[1] Ring Opening of 3-Alkyladenines with Carbobenzoxy Chloride: Transformation into 8-Hydroxylated Adenines[2]

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Treatment of 3-ethyladenine (Ia) with carbobenzoxy chloride in a mixture of acetonitrile and aqueous sodium bicarbonate resulted in the cleavage of the imidazole ring to form a compound presumed to be IVa, which was recyclized to 8-hydroxy derivative Va when heated in acetic acid. Carbobenzoxylation of 3-benzyladenine (Ib) under similar conditions gave Vb directly. The 8-hydroxy structure of Va,b was confirmed by hydrogenolysis of Vb leading to 6-amino-8-hydroxypurine (VIII), and the 3-alkyl structure was established by hydrogenolysis of Va to 6-amino-3-ethyl-3*H*-purin-8-ol (VIa), chlorination of VIa to give 8-chloro derivative VIIa, and hydrogenolysis of VIIa to Ia using hydrogen and palladium-on-charcoal.

Our current interest in modification and cleavage of the adenine ring stems from the finding that the pyrimidine ring of 1-alkoxyadenine derivatives is readily opened under mild hydrolytic conditions to form imidazole derivatives.[4] There are ample precedents for the ring opening of adenine derivatives either in the pyrimidine or in the imidazole moiety.[5–7] Among modified adenines 9-substituted and 9,N^6-disubstituted derivatives have been known to undergo a Bamberger fission[8] of the imidazole ring on treatment with carbobenzoxy chloride in aqueous base.[6] By contrast, adenine itself does not open the ring under similar conditions, but gives two monoacylated derivatives.[6] Leonard, *et al.*[7] have reported that an analogous cleavage of 9-substituted adenines is effected with diethyl pyrocarbonate at pH 4.5 whereas the pyrimidine ring of adenine and N^6-substituted adenines is opened, with loss of the $C_{(2)}$ atom, by the same reagent. These facts suggest that the site of ring opening and the ease with which the adenine ring opens under Schotten–Baumann conditions may be influenced by the location of a substituent and by an acylating reagent to be used. In the hopes of learning more about the substituent effect and of finding a possible route to the naturally occurring cytokinin N-(3-methyl-2-butenyl)adenine [III: $R=(CH_3)_2C=CH-CH_2$][9] from the

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3) Location: *13–1 Takara-machi, Kanazawa, 920, Japan.*
4) *a*) T. Fujii, T. Itaya, C.C. Wu, and S. Yamada, *Chem. Ind.* (London), **1966**, 1967; *b*) T. Fujii, T. Itaya, C.C. Wu, and F. Tanaka, *Tetrahedron*, **27**, 2415 (1971); *c*) T. Itaya, F. Tanaka, and T. Fujii, *ibid.*, **28**, 535 (1972); *d*) T. Fujii, T. Sato, and T. Itaya, *Chem. Pharm. Bull.* (Tokyo), **19**, 1731 (1971); *e*) T. Fujii, C.C. Wu, T. Itaya, S. Moro, and T. Saito, *ibid.*, **21**, 1676 (1973).
5) *a*) R.K. Robins, "Heterocyclic Compounds," Vol. 8, ed. by R.C. Elderfield, John Wiley and Sons, Inc., New York, 1967, pp. 380—393; *b*) B.R. Baker and J.P. Joseph, *J. Am. Chem. Soc.*, **77**, 15 (1955); *c*) M.A. Stevens and G.B. Brown, *ibid.*, **80**, 2759 (1958); *d*) J.W. Marsico and L. Goldman, *J. Org. Chem.*, **30**, 3597 (1965); *e*) J.A. Montgomery, K. Hewson, S.J. Clayton, and H.J. Thomas, *ibid.*, **31**, 2202 (1966); *f*) P. Brookes, A. Dipple, and P.D. Lawley, *J. Chem. Soc.* (*C*), **1968**, 2026; *g*) A.S. Jones, A.M. Mian, and R.T. Walker, *ibid.*, **1966**, 692; *h*) M. Sundaralingam, C.D. Stout, and S.M. Hecht, *Chem. Commun.*, **1971**, 240.
6) J. Altman and D. Ben-Ishai, *J. Heterocyclic Chem.*, **5**, 679 (1968).
7) *a*) N.J. Leonard, J.J. McDonald, and M.E. Reichmann, *Proc. Natl. Acad. Sci. U. S.*, **67**, 93 (1970); *b*) N.J. Leonard, J.J. McDonald, R.E.L. Henderson, and M.E. Reichmann, *Biochemistry*, **10**, 3335 (1971).
8) *a*) E. Bamberger and B. Berlé, *Ann. Chem.*, **273**, 342 (1893); *b*) O. Gerngross, *Chem. Ber.*, **46**, 1913 (1913).
9) *a*) D. Klämbt, G. Thies, and F. Skoog, *Proc. Natl. Acad. Sci. U. S.*, **56**, 52 (1966); *b*) J.P. Helgeson and N.J. Leonard, *ibid.*, **56**, 60 (1966).

isomeric alkaloid triacanthine (type I)[10] through ring opening in the imidazole moiety and recyclization to the 1-isomer (type II) followed by the Dimroth rearrangement,[11] we investigated the reaction of 3-alkyladenines (I) with carbobenzoxy chloride.

Initial studies were carried out using 3-ethyladenine (Ia), readily prepared from adenine and ethyl iodide by the well-established preferential 3-alkylation method.[10a,12] When Ia was treated with an excess of carbobenzoxy chloride in cold acetonitrile solution containing aqueous sodium bicarbonate, a compound of mp 179° (decomp.) was obtained in 25% yield.

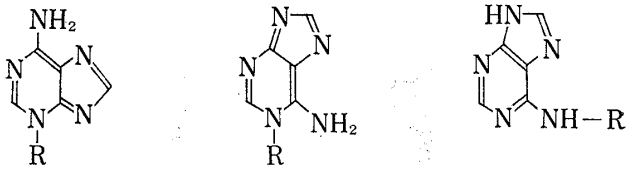

Chart 1

Although the compound failed to give an analytical sample because of its thermal instability in recrystallization solvents, clues to the structure (IVa) were afforded by its mass spectrum [*m/e* 421 (M^+)], infrared (IR) spectrum [ν_{max}^{Nujol} cm^{-1}: 3190 (overlapped NH's), 1750 and 1697 (two CO's)], and nuclear magnetic resonance (NMR) spectrum. The NMR spectrum in deuterated dimethyl sulfoxide exhibited signals at τ 8.74 (3H, triplet, J=7 Hz, $C\underline{H}_3CH_2$), 5.93 (2H, quartet, J=7 Hz, $CH_3C\underline{H}_2$), 4.96 (2H, singlet, benzylic protons), 4.80 (2H, singlet, benzylic protons), 2.63 and 2.56 (10H, phenyl protons), 1.46 (1H, singlet, pyrimidine-H), and 0.06 (1H, NH). However, the determination of two other NH proton frequencies was hampered by the broadness of the signals. The following reaction sequence and the postulated reaction mechanism as described below suggested that the location of the two carbobenzoxy groups might be as in structure IVa.

On treatment with hot acetic acid, IVa readily produced a recyclized product (Va) in 53% yield. The loss of one of the two benzyl groups as benzyl alcohol during the reaction was suggested by microanalytical and mass and NMR spectral determination. The ultraviolet (UV) spectra of Va at various pH values were suggestive of extended conjugation. In order to explain the formation of bicyclic structure V by analogy, 3-benzyladenine (Ib) was allowed to react with carbobenzoxy chloride under conditions similar to those employed for Ia. Instead of the expected monocyclic derivative (type IV), the recyclized derivative (Vb) was directly obtained in 38% yield. Compound Vb had the UV spectra similar to those of Va and the NMR spectrum consistent with a structure given by replacement of the ethyl group in Va by the benzyl group. The 8-hydroxy structure of Va,b was established by hydrogenolysis of Vb using palladium-on-charcoal (Pd-C) and hydrogen, which led to the formation of 6-amino-8-hydroxypurine (VIII)[13] in an excellent yield. The sulfate obtained from the free base (VIII) was identical with an authentic sample prepared according to the procedure of Robins.[13] It is noteworthy that in their IR spectra both the free base and the sulfate of VIII showed a strong carbonyl absorption in the region of 1700—1740 cm^{-1}, indicative of the predominance of the purin-8-one form (IX).

For determination of the location of the benzyl group in Vb, we first attempted to remove only the carbobenzoxy group but to leave the N-benzyl group intact by catalytic hydrogenoly-

10) *a*) N.J. Leonard and J.A. Deyrup, *J. Am. Chem. Soc.*, **84**, 2148 (1962), and references cited; *b*) A. Cavé, J.A. Deyrup, R. Goutarel, N.J. Leonard, and X.G. Monseur, *Ann. Pharm. Franc.*, **20**, 285 (1962); *c*) H. Morimoto and H. Oshio, *Chem. Pharm. Bull.* (Tokyo), **11**, 1320 (1963).
11) N.J. Leonard and T. Fujii, *Proc. Natl. Acad. Sci. U. S.*, **51**, 73 (1964).
12) *a*) J.W. Jones and R.K. Robins, *J. Am. Chem. Soc.*, **84**, 1914 (1962); *b*) N.J. Leonard and T. Fujii, *ibid.*, **85**, 3719 (1963); *c*) B.C. Pal, *Biochemistry*, **1**, 558 (1962); *d*) N.J. Leonard and R.A. Laursen, *ibid.*, **4**, 354 (1965); *e*) J.A. Montgomery and H.J. Thomas, *J. Am. Chem. Soc.*, **85**, 2672 (1963); *f*) *Idem*, *ibid.*, **87**, 5442 (1965); *g*) *Idem*, *J. Heterocyclic Chem.*, **1**, 115 (1964); *h*) C.J. Abshire and L. Berlinguet, *Can. J. Chem.*, **42**, 1599 (1964); *i*) H.J. Schaeffer and R. Vince, *J. Med. Chem.*, **8**, 710 (1965).
13) R.K. Robins, *J. Am. Chem. Soc.*, **80**, 6671 (1958).

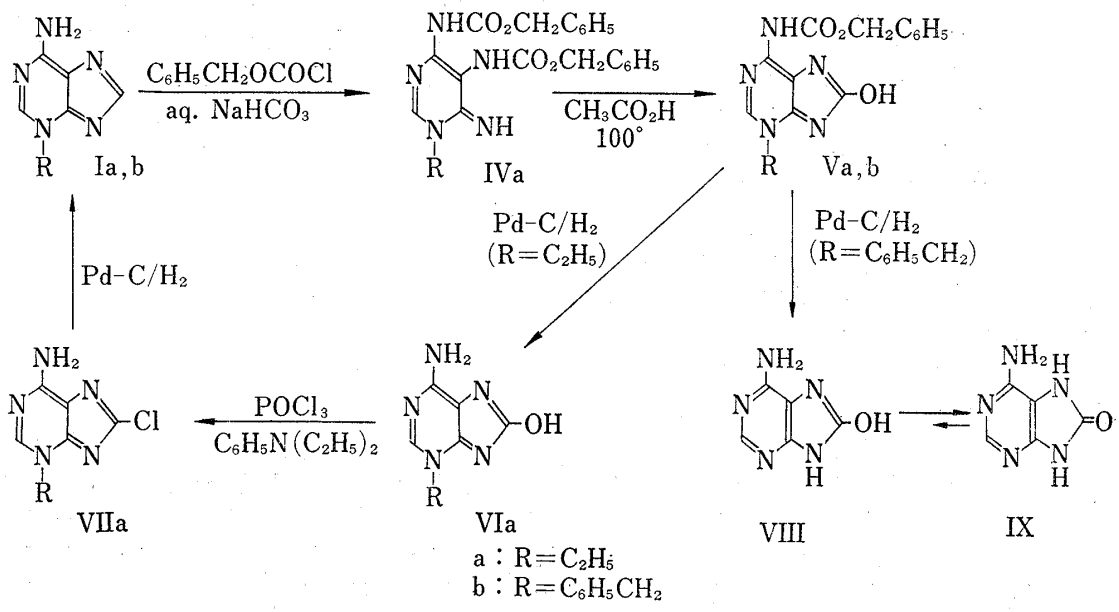

Chart 2

sis under a variety of conditions. However, it was difficult to find out a catalyst and/or reaction conditions capable of suppressing the concomitant fission of the N-benzyl bond. Consequently, our attention was focused on conversion of Va into a readily identifiable mono-ethyladenine. Treatment of Va with Pd-C and hydrogen in a mixture of acetic acid and ethanol furnished VIa in a good yield. Chlorination of VIa with phosphoryl chloride in the presence of diethylaniline and catalytic hydrogenolysis of the resulting 8-chloro derivative (VIIa) produced 3-ethyladenine (Ia), thus establishing the 3-alkyl structure of Va,b. Since neither of compounds Va, Vb, and VIa showed an appreciably intense IR absorption in the region of 1700—1740 cm^{-1}, they seemed to exist predominantly in the 8-hydroxy form.

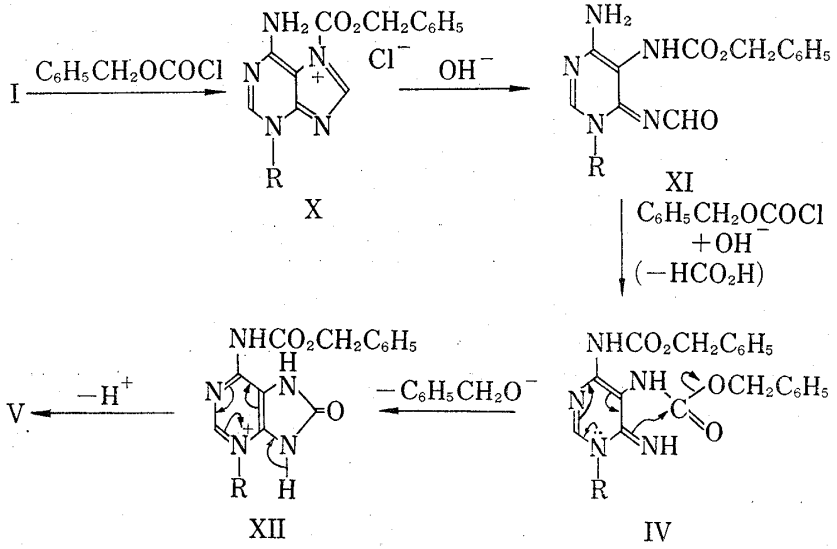

Chart 3

For the formation of V from I described above, we postulate a mechanism (Chart 3) involving the initial nucleophilic attack of the $N_{(7)}$ atom of I on the carbobenzoxy chloride carbonyl to give X. The subsequent nucleophilic attack of hydroxide ion on the $C_{(8)}$ atom and fission of the resulting $N_{(7)}$—$C_{(8)}$ single bond should give the ring-opened intermediate (XI), which then undergoes further carbobenzoxylation and deformylation to provide IV.

Intramolecular nucleophilic attack of 6-imino group of IV on the 5-carbamate carbonyl and deprotonation of the recyclized structure (XII) would complete the sequence. The carbobenzoxylation of the $N_{(7)}$ atom as the initial step is supported by the fact that a 3-alkyl substituent of adenine orients further alkylation to the 7-position.[12b,12e-g] The introduction of the second carbobenzoxy group is not necessarily postulated as the third step. In view of the previously reported[12g] formation of 3,7,N^6-tribenzyladenine from 3-benzyladenine (Ib) on benzylation, it may come out in the second stage of Chart 3.

In conclusion, the Bamberger fission of 3-alkyladenines (I) described above has demonstrated its utility in introducing the hydroxyl function into the adenine ring at the 8-position. The intermediate of a IVa-type may be of potential usefulness as a key intermediate in unrealized conversions of I into the other positional isomers.

Experimental[14]

3-Ethyladenine (Ia)——i) Procedure A: A stirred suspension of adenine (1.00 g, 7.4 mmoles) in a mixture of ethyl iodide (3.50 g, 22.4 mmoles) and N,N-dimethylacetamide (10 ml) was kept at 60° for 9 hr. The resulting reddish brown solution was evaporated to dryness under diminished pressure to leave a sirup, which was dissolved in H_2O (50 ml). The aq. solution was passed through a column of Amberlite IRA-402 (HCO_3^-) (18 ml, 22.5 meq) and the column was eluted with H_2O. The eluate (300 ml) was evaporated *in vacuo* to dryness. The resulting solid was chromatographed over alumina (100 g). The product obtained from fractions eluted with chloroform–ethanol (8: 1, v/v) was further purified on a silica gel column. Elution with chloroform–ethanol (5: 1, v/v) yielded crude Ia (719 mg), which was recrystallized from H_2O to give colorless needles (540 mg, 45%), mp 240—241° (decomp.) (lit.[15] mp 233°); UV: $\lambda_{max}^{abs.\ C_2H_5OH}$ 275 nm (ε 12200); $\lambda_{max}^{H_2O}$ (pH 1)[16] 220 (sh) (11100), 274.5 (17400); $\lambda_{max}^{H_2O}$ (pH 7)[17] 274.5 (13300); $\lambda_{max}^{H_2O}$ (pH 13)[18] 274 (12900); $\lambda_{min}^{H_2O}$ (pH 1)[16]—$\lambda_{min}^{H_2O}$ (pH 7)[17] = 236.5 nm − 244 nm = −7.5 nm;[10a,19] isosbestic point, 285 nm (lit.,[15] 286 nm). *Anal.* Calcd. for $C_7H_9N_5$: C, 51.52; H, 5.56; N, 42.92. Found: C, 51.71; H, 5.60; N, 42.82.

ii) Procedure B: A stirred mixture of adenine (60.0 g, 0.444 mole), ethyl iodide (208 g, 1.33 moles), and N,N-dimethylacetamide (600 ml) was heated at 60° for 10 hr. The orange, clear solution was concentrated to dryness *in vacuo* and the residual sirup was triturated with ether (100 ml). The ether was removed by decantation and the residue was again triturated with ethanol–ether (1: 1, v/v). The mixture was kept at room temp. for a day and the crystals that resulted were collected by filtration. Two recrystallizations from abs. ethanol (1 liter each) produced a chromatographically pure sample of Ia·HI (48 g, 37%) as slightly yellowish needles, mp 232—234° (decomp.).

The total amount of the hydriodide was dissolved in H_2O (1 liter) and the aq. solution was passed through a column packed with Amberlite IRA-402 (HCO_3^-) (200 ml, 0.25 eq). The column was eluted with H_2O and the eluate (3 liters) was evaporated *in vacuo* to dryness, leaving the free base (Ia: 26.1 g, 36% based on the adenine used) as colorless needles, mp 237—240° (decomp.), shown to be identical (by mixed melting-point test, thin-layer chromatography, and IR spectrum) with the sample prepared by procedure A.

iii) Hydrogenolysis of VIIa: A solution of VIIa (80 mg, 0.4 mmole) in acetic acid (5 ml) was hydrogenated over 10% Pd-C (80 mg) at atmospheric pressure and room temp. for 7 hr. The catalyst was removed by filtration, and the filtrate was evaporated *in vacuo* to dryness to leave a colorless solid. The solid was dissolved in H_2O (5 ml) and the aq. solution was passed through a column of Amberlite IRA-402 (HCO_3^-) (3 ml, 3.75 meq.). Elution of the column with H_2O and evaporation of the eluate (50 ml) afforded a colorless solid (59 mg, 89%), mp 237—239° (decomp.), shown to be homogeneous by a single spot on a thin-layer chromatogram. Recrystallization from H_2O provided an analytical sample of Ia as colorless needles, mp 240—241° (decomp.), identical in all respects (*i.e.*, spectra, chromatographic behavior) with the specimen obtained by method-(i).

3-Ethyl-8-hydroxy-3*H*-purine-6-carbamic Acid Benzyl Ester (Va)——3-Ethyladenine (Ia: 1.63 g, 10 mmoles) was dissolved in hot H_2O (10 ml), and to the aq. solution were added acetonitrile (250 ml) and 1N

14) All melting points are corrected. See Ref. 4*e* for paper chromatography and details of instrumentation and measurement. The mass spectra were measured with a JEOL-JMS-01SG mass spectrometer. The following abbreviations are used: b=broad, DMSO=dimethyl sulfoxide, m=multiplet, q=quartet, s=singlet, t=triplet, sh=shoulder. We are indebted to Mr. Y. Itatani and Misses M. Imai, S. Toyoshima, and T. Tsuji at Kanazawa University for microanalyses and NMR and mass spectral data.
15) R. Denayer, *Bull. Soc. Chim. France*, **1962**, 1358.
16) Determined in 0.1N aq. HCl.
17) Determined in 0.005M phosphate buffer.
18) Measured in 0.1N aq. NaOH.
19) L.B. Townsend, R.K. Robins, R.N. Loeppky, and N.J. Leonard, *J. Am. Chem. Soc.*, **86**, 5320 (1964).

aq. $NaHCO_3$ (150 ml). The mixture was well stirred and cooled in an ice-water bath, and carbobenzoxy chloride (18 g, 106 mmoles) was added dropwise. The stirring was continued for 1 hr at the ice-water bath temp. and 11 hr at room temp. The mixture was then kept standing at room temp. overnight and the precipitates that resulted were filtered off, washed alternately with H_2O and acetonitrile, and dried to give a compound (1.05 g, 25%) presumed to be 1-ethyl-1,6-dihydro-6-imino-4,5-pyrimidinedicarbamic acid dibenzyl ester (IVa) as a chromatographically pure colorless solid, mp 179° (decomp.); UV: $\lambda_{max}^{CH_3CN}$ nm (ε) 239 (18800), 315 (7300)[20]; IR, NMR, and mass spectral data, see Theoretical part. The presence of Va in the reaction mixture was indicated by thin-layer chromatography of the filtrate described above. Further purification of the solid (IVa) by recrystallization was difficult owing to its tendency to recyclize to Va.

A portion (300 mg, 0.712 mmole) of the solid (IVa) in acetic acid (20 ml) was heated in a boiling water bath for 2.5 hr. The mixture was evaporated *in vacuo* to dryness and the resulting solid was recrystallized from abs. ethanol (30 ml) to afford Va (120 mg, 54%) as colorless leaflets, mp 245—246° (decomp.); UV: $\lambda_{max}^{abs.\ C_2H_5OH}$ 242.5 nm (ε 17500), 314 (16000); $\lambda_{max}^{H_2O}$ (pH 1)[16] 228 (27400), 305 (18200); $\lambda_{max}^{H_2O}$ (pH 7)[17] 238 (17200), 307 (16600); $\lambda_{max}^{H_2O}$ (pH 13)[18] 248 (15700), 323 (22700); IR ν_{max}^{Nujol} cm^{-1}: 3350, 3165—3100 (NH, OH), 1750 (carbamate CO), 1655 (b, purine ring); NMR (DMSO-d_6) τ: 8.60 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 5.80 (2H, q, J=7 Hz, $CH_3C\underline{H}_2$), 4.85 (2H, s, $C_6H_5C\underline{H}_2OCO$), 2.69 (5H, m, C_6H_5), 1.77 (1H, s, $C_{(2)}$-H), 0.56 (1H, b, OH or NH, exchanged with D_2O), −0.27 (1H, b, NH or OH, exchanged with D_2O); Mass Spectrum *m/e*: 313 (M^+). *Anal.* Calcd. for $C_{15}H_{15}O_3N_5$: C, 57.50; H, 4.83; N, 22.34. Found: C, 57.65; H, 4.75; N, 22.32.

3-Benzyl-8-hydroxy-3*H*-purine-6-carbamic Acid Benzyl Ester (Vb)——To a stirred suspension of finely powdered 3-benzyladenine[12b,12e-h,15] (Ib: 1.13 g, 5.02 mmoles) in acetonitrile (150 ml) was added 1N aq. $NaHCO_3$ (50 ml). The mixture was cooled in an ice-water bath and carbobenzoxy chloride (4.28 g, 25.1 mmoles) was added dropwise. The stirring was continued for 1 hr at the ice-water bath temp. and 5 hr at room temp. The precipitates that separated out were collected by filtration, washed alternately with H_2O and acetonitrile, dried, and chromatographed on a 115-g silica gel column using chloroform–ethanol (8: 1, v/v) as eluent. The solvent was stripped from the fractions containing Vb, and the residue was recrystallized from abs. ethanol to yield colorless needles (707 mg, 38%), mp 228—229° (decomp.); UV: $\lambda_{max}^{abs.\ C_2H_5OH}$ 245 nm (ε 20900), 315 (17100); $\lambda_{max}^{H_2O}$ (pH 1)[16] 230 (30700), 308 (19500); $\lambda_{max}^{H_2O}$ (pH 7)[17] 241.5 (20700), 310 (17000); $\lambda_{max}^{H_2O}$ (pH 13)[18] 252 (19800), 327 (24400); IR ν_{max}^{KBr} cm^{-1}: 3375, 3155 (b) (NH, OH), 1730 (medium, carbamate CO), 1665 (purine ring); NMR (DMSO-d_6) τ: 4.82 (2H, s, $C_6H_5C\underline{H}_2OCO$), 4.61 (2H, s, $C_6H_5C\underline{H}_2$-$N_{(3)}$), 2.61 (10H, m, two C_6H_5's), 1.47 (1H, s, $C_{(2)}$-H), 0.32 (1H, b, OH or NH, exchanged with D_2O), −0.46 (1H, b, NH or OH, exchanged with D_2O); Mass Spectrum *m/e*: 375 (M^+). *Anal.* Calcd. for $C_{20}H_{17}O_3N_5$: C, 63.99; H, 4.56; N, 18.66. Found: C, 64.02; H, 4.63; N, 18.36.

6-Amino-3-ethyl-3*H*-purin-8-ol (VIa)——A solution of Va (7.08 g, 22.6 mmoles) in ethanol–acetic acid (1: 1, v/v) (480 ml) was hydrogenated over 10% Pd-C (7 g) at atmospheric pressure and room temp. At intervals the gases in the hydrogenation flask were replaced by fresh hydrogen. After 1 hr, the catalyst was removed by filtration, and the filtrate was evaporated *in vacuo* to dryness. The resulting solid was triturated with ether (40 ml), and an insoluble solid was filtered off, washed with ether, and dried to give chromatographically pure VIa. Yield, almost quantitative. An analytical sample was obtained by recrystallization from H_2O as colorless prisms, mp above 300°; UV: $\lambda_{max}^{abs.\ C_2H_5OH}$ 234 nm (ε 17900), 299 (16700); $\lambda_{max}^{H_2O}$ (pH 1)[16] 218 (22200), 287 (17800); $\lambda_{max}^{H_2O}$ (pH 7)[17] 229 (19500), 294 (18200); $\lambda_{max}^{H_2O}$ (pH 13)[18] 232 (sh) (8900), 307 (13300); IR ν_{max}^{Nujol} cm^{-1}: 3335, 3175 (b, NH_2, OH), 1660 (b, purine ring); NMR (DMSO-d_6) τ: 8.62 (3H, t, J=7 Hz, $C\underline{H}_3CH_2$), 5.85 (2H, q, J=7 Hz, $CH_3C\underline{H}_2$), 3.30 (2H, NH_2, exchanged with D_2O), 1.85 (1H, s, $C_{(2)}$-H), 0.51 (1H, b, $C_{(8)}$-OH, exchanged with D_2O); Mass Spectrum *m/e*: 179 (M^+). *Anal.* Calcd. for $C_7H_9ON_5$: C, 46.92; H, 5.06; N, 39.09. Found: C, 46.81; H, 5.48; N, 38.80.

8-Chloro-3-ethyladenine (VIIa)——A mixture of VIa (448 mg, 2.5 mmoles), $POCl_3$ (7 ml), and N,N-diethylaniline (2 ml) was heated at reflux for 30 min. The resulting dark brown solution was concentrated *in vacuo* to leave a sirup, which was triturated with ice–water (10 g). The cold aq. solution was made basic (pH 13) with conc. aq. NaOH, and the precipitates that formed were removed by filtration. The cold filtrate was washed with three 5-ml portions of toluene and was adjusted to pH 3 with conc. aq. HCl. The acid solution was then continuously extracted with chloroform. The chloroform solution was washed with a little H_2O, dried over anhyd. Na_2SO_4, and evaporated *in vacuo* to dryness. The resulting, yellowish brown solid was dissolved in boiling abs. ethanol (10 ml). The ethanolic solution was treated with charcoal and filtered while hot. The filtrate was concentrated to *ca.* 3 ml and kept in a refrigerator. The crystals that separated out were filtered off, washed with a little abs. ethanol, and dried to yield chromatographically pure VIIa (90 mg, 18%), mp 241—242° (decomp.). Recrystallization from abs. ethanol produced an analytical sample as colorless needles, mp 246—246.5° (decomp.); UV: $\lambda_{max}^{abs.\ C_2H_5OH}$ 227 nm (sh) (ε 10800), 284 (14700); $\lambda_{max}^{H_2O}$ (pH 1)[16] 222 (sh) (13200), 228 (sh) (10100), 278 (19200), 285 (sh) (16000); $\lambda_{max}^{H_2O}$ (pH 7)[17] 223.5 (sh) (12100), 280.5 (15700); $\lambda_{max}^{H_2O}$ (pH 13)[18] 223.5 (sh) (12100), 280.5 (15600); IR ν_{max}^{Nujol} cm^{-1}: 3290, 3105 (NH_2), 1670 (purine ring); Mass Spectrum *m/e*: 199 [$(C_7H_8N_5\ ^{37}Cl)^+$], 197 [$(C_7H_8N_5\ ^{35}Cl)^+$]. *Anal.* Calcd. for $C_7H_8N_5Cl$: C, 42.54; H, 4.08; N, 35.44. Found: C, 42.69; H, 4.05; N, 35.10.

20) The ε values were calculated on the assumption that purity of the sample used for the measurement of UV spectrum was 100%.

6-Aminopurin-8(9*H*)-one Sulfate (IX•1/2 H_2SO_4) [6-Aminopurin-8-ol Sulfate (VIII•1/2 H_2SO_4)]—— A solution of Vb (1.50 g, 4 mmoles) in ethanol–acetic acid (1: 1, v/v) (300 ml) was hydrogenated over 10% Pd-C (1.5 g) at atmospheric pressure and room temp. for 1.5 hr in a manner similar to that described above for the hydrogenolysis of Va. The catalyst was filtered off, and the filtrate was evaporated *in vacuo* to dryness, leaving a solid. The solid was triturated with ether (100 ml), and an insoluble solid was collected by filtration and dried to give IX, mp above 300°, shown to be homogeneous by chromatography. IR ν_{max}^{Nujol} cm^{-1}: 3425, 3245, 3084 (NH_2, NH), 1707 (CO), 1665 (purine ring). Yield, almost quantitative. Recrystallization of the free base from 5% aq. H_2SO_4 gave the sulfate (IX·1/2 H_2SO_4) as colorless needles, mp above 300°; UV $\lambda_{max}^{H_2O}$ (pH 1)[16] 281 nm (ε 10700); $\lambda_{max}^{H_2O}$ (pH 7)[17] 271 (12700); $\lambda_{max}^{H_2O}$ (pH 13)[18] 280 (14700). The UV and IR spectra as well as the paper and thin-layer chromatographies were in good agreement with those of an authentic sample of the sulfate.[13]

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