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Syntheses of 4-Aminodihydrothiazolopurines, 4-Aminodihydroimidazopurines and 4-Aminotetrahydropyrimidopurines

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Cyclization reactions of 8-(β-haloethylthio)adenine, 8-(β-haloethylamino)adenines and 8-(γ-halopropylamino)adenine occurred at both of N^7 and N^9 of purine ring and pairs of cyclized compounds, 4-aminodihydrothiazolo[2,3-*f*]- and 4-aminodihydrothiazolo[3,2-*e*]purine, 4-aminodihydroimidazo[2,1-*f*]- and 4-aminodihydroimidazo[1,2-*e*]purines, and 4-aminotetrahydropyrimido[2,1-*f*]- and 4-aminotetrahydropyrimido[1,2-*e*]purine were obtained.

Structures of 4-aminodihydrothiazolopurines were determined by desulfurization with Rany Ni and those of 4-aminodihydroimidazopurines and 4-aminotetrahydropyrimidopurines were determined by comparison of spectral data with those of N-cyclonucleosides.

In preceeding papers,[2a-d] we have reported ring closures of 8-(acylmethylthio)purines and results of these ring closure reactions seemed to suggest that the substituent at 6-position of purine ring controls the reactivities of N^7 and N^9 of purine ring, since 8-(acylmethylthio)-adenine derivatives gave thiazolo[3,2-*e*]purine derivatives, in which the cyclization took place at N^9, on the other hand hypoxanthine, xanthine, guanine and theophylline analogues, which have an oxo group at 6-position instead of an amino group, gave only thiazolo[2,3-*f*]purine derivatives, in which the cyclization took place at N^7.

As a succeeding work, cyclizations of 8-(haloalkylthio)adenine and 8-(haloalkylamino)-adenines were investigated. Since some 4-aminothiazolo[3,2-*e*]purines showed strong hypotensive activities in animals, biological activities of expected products of these cyclizations were also interesting.

4-Aminodihydrothiazolopurines

Some studies on the syntheses of dihydrothiazolopurines have been reported. 6,7-Dihydrothiazolo[2,3-*f*]theophylline was synthesized from 8-mercaptotheophylline by a reaction with 1,2-dibromoethane.[3] And some 8,2′-S-cyclonucleosides were prepared from 8-mercapto-purinenucleosides.[4] Balsiger, *et al.*[5] reported that the cyclization of 8-(chloroethylthio)purine gave both of 6,7-dihydrothiazolo[2,3-*f*]- and 7,8-dihydrothiazolo[3,2-*e*]purine.

The starting material in this work, 8-(β-hydroxyethylthio)adenine (II), was prepared from 8-mercaptoadenine (I) and ethylene bromohydrin in an alkaline solution. When heated with thionyl chloride, II gave a mixture of 8-(chloroethylthio)adenine and two products. This mixture was heated in dimethylformamide (DMF) with sodium carbonate to complete the cyclization, and gave a mixture of two products. The mixture was separated by a chromatography on a silica gel column, and III and IV were obtained. A mixture of III and IV was also obtained from II directly on heating with polyphosphoric acid.

1) Location: *33–94, Enokicho, Suita, Osaka.*
2) *a*) H. Uno, A. Irie, and K. Hino, *Chem. Pharm. Bull.* (Tokyo), **20**, 2603 (1973); *b*) H. Uno, A. Irie, and K. Hino, *Chem. Pharm. Bull.* (Tokyo), **21**, 34 (1973); *c*) H. Uno, A. Irie, and K. Hino, *Chem. Pharm. Bull.* (Tokyo), **21**, 256 (1973); *d*) H. Uno, A. Irie, and K. Hino, *Chem. Pharm. Bull.* (Tokyo), **23**, 450 (1975).
3) F. Cacae and R. Morison, *Ann. Chim.* (Rome), **46**, 806 (1956).
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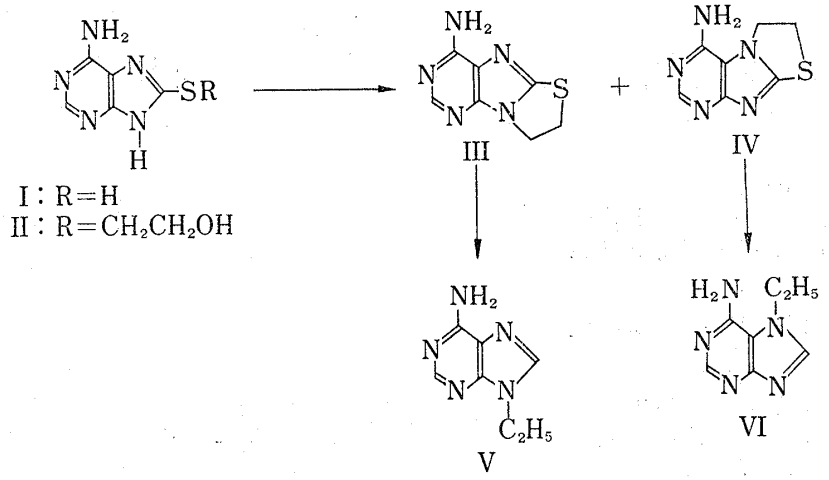

Chart 1

From the result of elemental analysis and mass spectral data, III and IV seemed to be a pair of isomeric compounds. Desulfurization of III, which was eluted from the silica gel column with chloroform–methanol (10: 1), by Raney Ni gave V, $C_7H_9N_5$, mp 195—197°. Melting point and ultraviolet (UV) spectrum of V were identical with those of 9-ethyladenine[6] and thus III must be 4-amino-7,8-dihydrothiazolo[3,2-*e*]purine. Desulfurization of IV, which was eluted from the silica gel column with chloroform–methanol (10: 2), gave VI, $C_7H_9N_5$, mp 263—264°. UV spectrum of VI was identical with that of 7-ethyladenine[7] and VI must be 7-ethyladenine derived from 4-amino-6,7-dihydrothiazolo[2,3-*f*]purine (IV). It was undoubted that the cyclization of 8-(β-chloroethylthio)adenine took place at both of N^7 and N^9 of purine ring.

4-Aminodihydroimidazopurines and 4-Aminotetrahydropyrimidopurines

Some imidazopurines,[8a–e] dihydroimidazopurines[9a–d] and tetrahydropyrimidopurines[9b] derived from theophylline have been synthesized. Most of them were reported as imidazo-[2,1-*f*]purines and only one imidazo[1,2-*e*]purine[10] was reported in a patent, except N-cyclonucleosides[11] which were prepared from 8-aminonucleosides.

Syntheses of dihydroimidazopurines and tetrahydropyrimidopurines were carried as follows. Starting material, 8-bromoadenine (VII), prepared from adenine by the procedure of Bruhns,[12] was treated with alkanolamines to give VIIIa—d in moderate to good yields.

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7) P.D. Lawley and P. Brookes, *Biochem. J.*, **92**, 19c (1964).
8) *a*) P.M. Kochergin and A.A. Tkachenko, U.S.S.R., 225203 (20 Aug. 1968) [*Chem. Abstr.*, **71**, 22135r (1969)]; *b*) P.M. Kochergin and A.A. Tkachenko, *Khim. Geterotskl. Soedin., Akad. Nauk. Latv. SSR*, **1965**, 475 [*Chem. Abstr.*, **63**, 13260b (1965)]; *c*) P.M. Kochergin, B.A. Priimenko, V.S. Ponomar, M.V. Povstyanoi, A.A. Tkachenko, I.A. Mazur, A.N. Krasovskii, E.G. Knysh, and M.I. Yurchenko, *Khim. Geterotskl. Soedin.*, **1969**, 177 [*Chem. Abstr.*, **71**, 13065r (1969)]; *d*) A.A. Tkachenko, P.M. Kochergin, and F.A. Zubkov, *Khim. Geterotskl. Soedin.*, **7**, 682 (1971) [*Chem. Abstr.*, **76**, 126932t (1972)]; *e*) A.A. Tkachenko, P.M. Kochergin, and G.F. Panchenko, *Khim. Geterotskl. Soedin.*, **7**, 686 (1971) [*Chem. Abstr*, **76**, 126931s (1972)].
9) *a*) P.M. Kochergin, V.I. Linenko, A.A. Tkachenko, B.A. Samura, and M.V. Povstyanoi, *Khim-Farm. Zh.*, **5**, 22 (1971)[*Chem. Abstr.*, **74**, 125638y(1971)]; *b*) M. Eckstein, *Dissertationes Pharm.*, **14**, 435(1962) [*Chem. Abstr.*, **60**, 8030e (1964)]; *c*) P.M. Kochergin, A.A. Tkachenko, and M.V. Povstyanoi, U.S.S.R., 213881 (20 Mar. 1968) [*Chem. Abstr.*, **69**, 59285z (1968)]; *d*) P.M. Kochergin, A.A. Tkachenko, I.V. Komissarov, and V.V. Vlasov, *Khim.-Farm. Zh.*, **4**, 14 (1970) [*Chem. Abstr.*, **74**, 141700t (1971)].
10) Lag. Le Brum SA, Fr. Patent 2157726 (1971).
11) M. Kaneko, B. Shimizu, and M. Ikehara, *Tetrahedron Letters*, **1971**, 3113.
12) G. Bruhns, *Chem. Ber.*, **23**, 225 (1890).

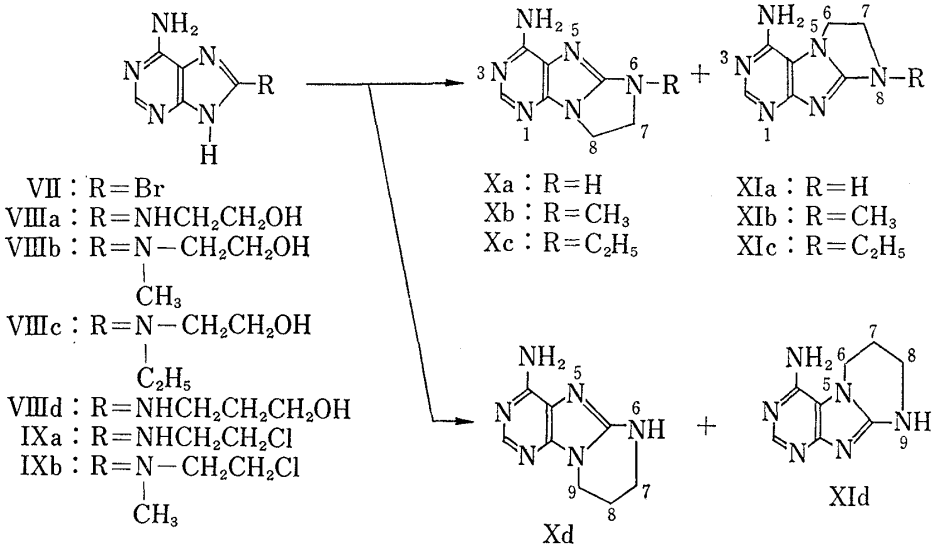


Chart 2

VIIIa[13] and VIIIb were heated with thionyl chloride. Neutralization of the reaction mixture with ammonia gave 8-(chloroethylamino)adenines, IXa[13] and IXb, respectively. Cyclizations of IXa and IXb were performed by heating in DMF with sodium carbonate or in ethanol with morpholine, and gave two types of compounds, Xa, b and XIa, b. On the other hand, VIIIc and VIIId gave directly Xc, d and XIc, d on heating with thionyl chloride and successive neutralization with ammonia.

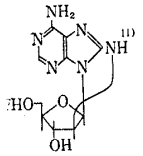
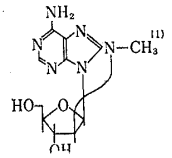
Isolation of these products was carried out by column chromatography on a silica gel column. Xa—d were eluted with chloroform–methanol (10: 1) from the column of silica gel and XIa—d were eluted with chloroform–methanol (10: 2). It is apparent that these products are pairs of cyclized compounds from the result of elemental analyses, mass spectral data and nuclear magnetic resonance (NMR) spectral data. In infrared (IR) spectra, Xa—d showed a strong absorption band at the 1600—1660 cm^{-1} region and a characteristic weaker band around 1590 cm^{-1}, on the contrary XIa—d showed two strong bands at the 1660—1670 cm^{-1} region and around 1600 cm^{-1} where the latter bands were somewhat stronger than the former bands.

To determine the structure, UV spectra of these compounds were compared with those of dihydrothiazoloadenines and N-cyclonucleosides.[11] Xa—d exhibited high intensity absorption bands in the 270—310 nm region (band I) and the 210—235 nm region (band II). XIa—d absorbed at a considerably longer wavelength than Xa—d especially in the acidic media. Acidification of the media resulted in bathochromic shift of band I in cases of XIa—d. These shifts were not observed in the UV spectra of N-cyclonucleosides.[11] The UV spectra of Xa—d were not significantly affected by the pH of media. These tendencies were also observed with two isomeric dihydrothiazoloadenines. These facts suggested that Xa—d might be 4-amino-7,8-dihydroimidazo[1,2-*e*]purines and 4-amino-6,7,8,9-tetrahydropyrimido-[1,2-*e*]purine in which the cyclization took place at N^9, and XIa—d might be 4-amino-6,7-dihydroimidazo[2,1-*f*]purines and 4-amino-6,7,8,9-terahydropyrimido[2,1-*f*]purine in which the cyclization occurred at N^7 respectively. Acetylation of XIa gave triacetyl derivative (XII).

It is very interesting that in the cyclization of 8-(acylmethylthio)adenines, thiazolo[3,2-*e*]-adenines were the only products which were able to be isolated, while in the cyclization of 8-(haloalkylthio)adenine and 8-(haloalkylamino)adenines, the cyclization took place at both of N^7 and N^9 and gave pairs of cyclized compounds.

13) S. Chu and H.G. Mautner, *J. Org. Chem.*, **26**, 4498 (1961).

TABLE I. Comparison of the UV absorption properties of Dihydroimidazoadenines and Tetrahydropyrimidoadenines with those of N-Cyclonucleosides

Compound No.	$\lambda_{max}^{0.1N\ HCl}$nm ($\varepsilon \times 10^{-3}$)			$\lambda_{max}^{0.1N\ NaOH}$nm ($\varepsilon \times 10^{-3}$)	
Xa		222 (22.7)	277.5(14.7)		277.5(15.3)
Xb		223.5(18.5)	283.5(14.6)	219.5(29)	282.5(17.3)
Xc		226 (18.3)	284 (13.9)	219.5(26.6)	283.5(17)
Xd		222 (21.1)	271 (18.1)		282.5(17.4)
XIa		226 (16)	297.5(12.1)	222.5(35.7)	282.5(12.8)
XIb	215 (15.8)	230.5(17.2)	306 (14.9)	226.5(27.8)	288 (14.2)
XIc	215 (16.4)	231 (17.7)	307 (15.4)	227 (31.5)	288.5(15)
XId		219 (17.7)	290 (10.6)	226 (36)	283.5(17)
		208 (18.4)	273.5(13.9)		276 (13.2) 305 (shoulder)
		208 (20.4)	278.5(15.8)		278 (17.2)

Further studies on another type of dihydroimidazopurines are now under investigation in our laboratory.

Experimental[14]

4-Amino-7,8-dihydrothiazolo[3,2-*e*]purine (III) and 4-Amino-6,7-dihydrothiazolo[2,3-*f*]purine (IV)——a) Compound II (3 g) was refluxed with $SOCl_2$ (45 ml) for 1 hr and the excess of $SOCl_2$ was removed under reduced pressure. To the residue were added Na_2CO_3 (3.5 g), and the mixture was refluxed for 3 hr. After evaporation *in vacuo*, H_2O (100 ml) was added to the residue and the resulting precipitate was collected and chromatographed on a silica gel column. The fraction eluted with $CHCl_3$–MeOH (10: 1) was evaporated and the residue was recrystallized from EtOH to give 0.8 g of III, mp 304—305°. *Anal.* Calcd. for $C_7H_7N_5S$: C, 43.51; H, 3.65; N, 36.25; S, 16.59. Found: C, 43.51; H, 3.33; N, 36.53; S, 16.45. Mass Spectrum *m/e*: 193(M^+). UV $\lambda_{max}^{0.1N\ HCl}$ nm (ε): 223.5(19500), 285 (21000). UV $\lambda_{max}^{0.1N\ NaOH}$ nm (ε): 225(20000), 278(20700), 285(sh). The fraction eluted with $CHCl_3$–MeOH (10: 2) was evaporated and the residue was recrystallized from MeOH–H_2O to give 0.13 g of IV, mp>310°. *Anal.* Calcd. for $C_7H_7N_5S$: C, 43.51; H, 3.65; N, 36.25; S, 16.59. Found: C, 43.46; H, 3.45; N, 36.44; S, 16.34. Mass Spectrum *m/e*: 193 (M^+). UV $\lambda_{max}^{0.1N\ HCl}$ nm (ε): 234 (17500), 298 (17000), 304 (sh). UV $\lambda_{max}^{0.1N\ NaOH}$ nm (ε): 231 (26800), 287.5 (13600), 295 (sh),

b) A mixture of II (500 mg) and polyphosphoric acid (5 g) was stirred at 130—140° for 3 hr. The cooled mixture was poured into cold H_2O and the aqueous solution was neutralized with dil. NaOH. After standing at room temperature for 30 min, precipitate was collected. Thus 160 mg of III was obtained. The filtrate was allowed to stand in a refrigerator overnight and the mixture of III and IV (20 mg) was obtained as precipitate.

Desulfurization of III——Compound III (500 mg) was refluxed with Raney Ni (*ca.* 500 mg) in EtOH (30 ml) for 1 hr. After Ni was filtered off, the filtrate was evaporated and the residue was chromatographed on a silica gel column. The fraction eluted with $CHCl_3$–MeOH (10: 1) was evaporated and the residue was recrystallized from MeOH–AcOEt to give 150 mg of V, mp 195—197°. *Anal.* Calcd. for $C_7H_9N_5$; C, 51.52; H, 5.56; N, 42.92. Found: C, 51.39; H, 5.42; N, 43.16. UV $\lambda_{max}^{0.1N\ HCl}$ nm (ε): 261 (14200). UV $\lambda_{max}^{0.1N\ NaOH}$ nm (ε): 262.5 (14400). NMR (DMSO-d_6) δ: 8.18 (2H, s, 2-H and 8-H), 7.19 (2H, NH_2), 4.21 (2H, q, J=7 Hz, $-CH_2-$), 1.42 (3H, t, J=7 Hz, $-CH_3$).

Desulfurization of IV——Compound IV (360 mg) was refluxed with Raney Ni (*ca.* 400 mg) in EtOH (30 ml) for 30 min. The Ni was filtered off and the filtrate was evaporated. The residue was chromato-

14) All melting points are uncorrected. NMR spectra were taken with a Varian A-60 spectrometer using TMS as internal standard, UV spectra with a Hitachi-2U spectrophotometer, and mass spectra with a Hitachi RMU-6L mass spectrometer.

graphed on a silica gel column. The fraction eluted with $CHCl_3$–MeOH (10: 2) was evaporated and the residue was recrystallized from MeOH–AcOEt to give 60 mg of VI, mp 263—264°. *Anal.* Calcd. for $C_7H_9N_5$: C, 51.52; H, 5.56; N, 42.92. Found: C, 51.21; H, 5.63; N, 42.82. UV $\lambda_{max}^{0.1N\ HCl}$ nm (ε): 272.5 (13800). UV $\lambda_{max}^{0.1N\ NaOH}$ nm (ε): 270 (7900). NMR (DMSO-d_6) δ: 8.22, 8.29 (each 1H, s, 2-H and 8-H), 6.90 (2H, NH_2), 4.45 (2H, q, J=7 Hz, $-CH_2-$), 1.37 (3H, t, J=7 Hz, $-CH_3$).

6-Amino-8-(N-methyl-N-β-hydroxyethylamino)purine (VIIIb)——To 2-methylaminoethanol (30 ml) was added VII (6.42 g) and the mixture was refluxed for 3 hr. The excess of amine was removed *in vacuo* and the residue was triturated with MeOH. The colorless crystals were collected and recrystallized from EtOH to give 5.6 g of VIIIb, mp 260—270°. *Anal.* Calcd for $C_8H_{12}ON_6$: C, 46.14; H, 5.81; N, 40.36. Found: C, 46.21; H, 5.85; N, 40.27.

6-Amino-8-(N-ethyl-N-β-hydroxyethylamino)purine (VIIIc)——To 2-ethylaminoethanol (18 ml) was added VII (6.42 g) and the mixture was refluxed for 8 hr. The excess of amine was removed and the residue was triturated with MeOH to give 6.2 g of VIIIc, mp 265—270°. *Anal.* Calcd. for $C_9H_{14}ON_6$: C, 48.64; H, 6.35; N, 37.82. Found: C, 48.61; H, 6.35; N, 37.78.

6-Amino-8-(N-γ-hydroxypropylamino)purine (VIIId)——3-Aminopropanol (30 ml) and VII (14.84 g) were refluxed for 1 hr. The excess of amine was evaporated and the residue was triturated with MeOH. The colorless powder was collected and recrystallized from H_2O to give 8.46 g of VIIId, mp 253—255° (decomp.). *Anal.* Calcd. for $C_8H_{12}ON_6$: C, 46.14; H, 5.81; N, 40.36. Found: C, 45.83; H, 5.67; N, 40.43.

6-Amino-8-(N-methyl-N-β-chloroethylamino)purine (IXb)——To the cooled $SOCl_2$ (100 ml) was added VIIIb (8.96 g) and the mixture was refluxed for 2 hr. The excess of $SOCl_2$ was removed and the residue was triturated with EtOH and the resulting powder was collected, washed with H_2O, and recrystallized from MeOH to give 6.9 g of IXb. mp 265—270°. *Anal.* Calcd. for $C_8H_{11}N_6Cl$: C, 42.39; H, 4.89; N, 37.08; Cl, 15.64. Found: C, 42.49; H, 4.90; N, 37.26; Cl, 15.07.

4-Amino-7,8-dihydroimidazo[1,2-*e*]purine (Xa) and 4-Amino-6,7-dihydroimidazo[2,1-*f*]purine (XIa)——Compound IXa[13] (1.8 g) was dissolved in DMF (50 ml) and Na_2CO_3 (1.08 g) was added to the solution. The mixture was refluxed for 2 hr. The solvent was evaporated off and the residue was chromatographed on a silica gel column. The product which was eluted with $CHCl_3$–MeOH (10: 1) was recrystallized from H_2O–acetone to give 520 mg of Xa, mp 295—298° (decomp.). *Anal.* Calcd. for $C_7H_8N_6$: C, 47.72; H, 4.58; N, 47.71. Found: C, 47.59; H, 4.30; N, 47.55. Mass Spectrum *m/e*: 176 (M^+). NMR (DMSO-d_6) δ: 7.95 (1H, s, 2-H), 7.01 (1H, NH), 6.47 (2H, NH_2), 4.07 (4H, m, W 1/2h=4 Hz, $-CH_2CH_2-$).

The fraction eluted with $CHCl_3$–MeOH (10: 2) was evaporated and the residue was recrystallized from H_2O–EtOH to give 610 mg of XIa, mp 303—305° (decomp.). *Anal.* Calcd. for $C_7H_8N_6$: C, 47.72; H, 4.58; N, 47.71. Found: C, 47.60; H, 4.36; N, 46.99. Mass Spectrum *m/e*: 176 (M^+). NMR (DMSO-d_6) δ: 8.03 (1H, s, 2-H), 7.40 (1H, NH), 6.35 (2H, NH_2), 4.24 (4H, AA'BB', $W$1/2h=26 Hz, $-CH_2CH_2-$).

4-Amino-6-methyl-7,8-dihydroimidazo[1,2-*e*]purine (Xb) and 4-Amino-8-methyl-6,7-dihydroimidazo-[2,1-*f*]purine (XIb)——Compound IXb (4.53 g) was added to DMF (100 ml) and Na_2CO_3 (2.47 g) was added to the mixture. The mixture was refluxed for 1.5 hr and filtered while hot. The filtrate was evaporated and the residue was chromatographed on a silica gel column. The fraction eluted with $CHCl_3$–MeOH (10: 1) was evaporated and the residue was recrystallized from MeOH–acetone to give 0.96 g of Xb, mp 294—296°. *Anal.* Calcd. for $C_8H_{10}N_6$: C, 50.52; H, 5.30; N, 44.19. Found: C, 50.34; H, 4.89; N, 44.38. Mass Spectrum *m/e*: 190 (M^+). NMR (D_2O) δ: 7.74 (1H, s, 2-H), 3.83 (4H, W 1/2h=5 Hz, $-CH_2CH_2-$), 2.84 (3H, s, $-CH_3$).

The fraction eluted with $CHCl_3$–MeOH (10: 2) was evaporated and the residue was recrystallized from MeOH to give 1.53 g of XIb, mp>300°. *Anal.* Calcd. for $C_8H_{10}N_6$: C, 50.52; H, 5.30; N, 44.19. Found: C, 50.56; H, 5.25; N, 44.14. Mass Spectrum *m/e*: 190 (M^+). NMR (D_2O) δ: 7.87 (1H. s, 2-H), 3.81 (4H, W 1/2h=5 Hz, $-CH_2CH_2-$), 2.86 (3H, s, $-CH_3$).

4-Amino-6-ethyl-7,8-dihydroimidazo[1,2-*e*]purine (Xc) and 4-Amino-8-ethyl-6,7-dihydroimidazo[2,1-*f*]-purine (XIc)——A mixture of VIIIc (10 g) and $SOCl_2$ (120 ml) was heated under reflux for 2 hr. The excess of $SOCl_2$ was removed and the residue was dissolved in H_2O. The aqueous solution was adjusted to pH 8 and then concentrated. To the residue was added EtOH and insoluble material was filtered off. The solution was evaporated and the residue was chromatographed on a silica gel column. The fraction eluted with $CHCl_3$–MeOH (10: 1) was evaporated and the residue was recrystallized from acetone–MeOH to give 3.14 g of Xc, mp 243—244°. *Anal.* Calcd. for $C_9H_{12}N_6$: C, 52.92; H, 5.92; N, 41.15. Found: C, 52.61; H, 5.70; N, 40.96. Mass Spectrum *m/e*: 204 (M^+). NMR (DMSO-d_6) δ: 7.94 (1H, s, 2-H), 6.49 (2H, NH_2), 4.03 (4H, AA'BB', $W$1/2h=5 Hz, $-CH_2CH_2-$), 3.35 (2H, q, J=7 Hz, $-CH_2-$), 1.19 (3H, t, J=7 Hz, $-CH_3$).

The fraction eluted with $CHCl_3$–MeOH (10: 2) was evaporated and the residue was dissolved in H_2O. The solution was adjusted to pH 9 and then concentrated. The residue was recrystallized from MeOH–H_2O–acetone to give 1.0 g of XIc, mp>300°. *Anal.* Calcd. for $C_9H_{12}N_6$: C, 52.92; H, 5.92; N, 41.15. Found: C, 53.25; H, 6.00; N, 41.03. Mass Spectrum *m/e*: 204 (M^+). NMR (DMSO-d_6) δ: 8.10 (1H, s, 2-H), 6.90 (2H, broad, NH_2), 4.15 (4H, AA'BB', $W$1/2h=29 Hz, $-CH_2CH_2-$), 3.40 (2H, q, J=7 Hz, $-CH_2-$), 1.20 (3H, t, J=7 Hz, $-CH_3$).

4-Amino-6,7,8,9-tetrahydropyrimido[1,2-*e*]purine (Xd) and 4-Amino-6,7,8,9-tetrahydropyrimido[2,1-*f*]-purine (XId)——To the cooled $SOCl_2$ (100 ml) was added VIIId (9.5 g) and the mixture was refluxed for 2 hr. The excess of $SOCl_2$ was removed and the residue was triturated with EtOH and then dissolved in H_2O.

The pH of the solution was adjusted to 9 and the solution was evaporated. The residue was chromatographed on a silica gel column. The fraction eluted with $CHCl_3$–MeOH (10: 1) was evaporated and the residue was recrystallized from MeOH–acetone and then from H_2O–EtOH to give 2.24 g of Xd, mp 298—300° (decomp.). *Anal.* Calcd. for $C_8H_{10}N_6$: C, 50.52; H, 5.30; N, 44.19. Found: C, 50.38; H, 5.15; N, 44.48. Mass Spectrum *m/e*: 190 (M^+). NMR (DMSO-d_6) δ: 7.95 (1H, s, 2-H), 7.23 (1H, NH), 6.42 (2H, NH_2), 3.98 (2H, t-like, J=6 Hz, $-CH_2-$), 3.37 (2H, m, $-CH_2-$), 2.03 (2H, m, $-CH_2-$).

The fraction eluted with $CHCl_3$–MeOH (10: 2) was evaporated and the residue was dissolved in H_2O–MeOH and the pH of the solution was adjusted to 9. The solution was cooled and the resulting precipitate was collected. The product was recrystallized from H_2O–MeOH to give 1.97 g of XId, mp 269—270° (decomp.). *Anal.* Calcd. for $C_8H_{10}N_6$: C, 50.52; H, 5.30; N, 44.19. Found: C, 50.49; H, 5.32; N, 44.37. Mass Spectrum *m/e*: 190 (M^+). NMR (DMSO-d_6) δ: 7.95 (1H, s, 2-H), 7.23 (1H, NH), 6.13 (2H, NH_2), 4.25 (2H, t-like, J=6 Hz, $-CH_2-$), 3.36 (2H, m, $-CH_2-$), 2.05 (2H, m, $-CH_2-$).

N^4,N^4,8-Triacetyl-4-amino-6,7-dihydroimidazo[2,1-*f*]purine (XII)——Compound XIa (60 mg) and Ac_2O (7 ml) were heated under reflux for 2 hr. The excess of Ac_2O was removed and the residue was chromatographed on a silica gel column. The product was eluted with $CHCl_3$–MeOH (100:1). Recrystallization from $CHCl_3$–EtOH gave 60 mg of XII, mp>300°, as prisms. *Anal.* Calcd. for $C_{13}H_{14}O_3N_6$: C, 51.65; H, 4.67; N, 27.80. Found: C, 51.77; H, 4.58; N, 27.77.

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