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Syntheses of N,N,3- and N,N,9-Trialkyladenines by Alkylation of N,N-Dialkyladenines[1]

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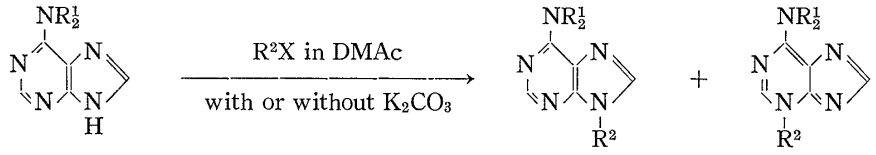
Alkylations of N,N-dimethyl- (Ia) and N,N-diethyladenine (Ib) with methyl iodide, ethyl iodide, and benzyl bromide in N,N-dimethylacetamide in the presence of potassium carbonate gave the corresponding N,N,9-trialkyladenines (II) in 54—74% yields, as well as minor amounts of N,N,3-trialkyladenines (III). The alkylation of I without base gave the latter compounds (III) in 76—90% yields.

Keywords——N,N,3-trialkyladenines; N,N,9-trialkyladenines; regioselective N-alkylation; N,N-dialkyladenines; isomer ratio

In the course of our studies leading to syntheses of 3,9-dialkylhypoxanthines[3] and 3,9-dialkylguanines,[4] it became important to develop convenient syntheses of N,N,9- (II) and N,N,3-trialkyladenines (III). Among the reported syntheses of II[5] and III,[6] benzylation of N,N-dimethyladenine (Ia) in N,N-dimethylacetamide (DMAc)[6c] seems most simple and generally applicable. Since the alkylation of adenine in the presence of potassium carbonate gives mainly 9-alkyladenines,[7] similar treatment of N,N-dialkyladenines (I) seemed promising for the preparation of II. However, there are no reports on the alkylation of I in the presence of base. This paper describes selective syntheses of II and III by alkylation of I in the presence or absence of potassium carbonate.



Ia, b IIc—h IIIc—h

a: $R^1=CH_3$ e: $R^1=CH_3$; $R^2=C_6H_5CH_2$
b: $R^1=C_2H_5$ f: $R^1=C_2H_5$; $R^2=CH_3$
c: $R^1=R^2=CH_3$ g: $R^1=R^2=C_2H_5$
d: $R^1=CH_3$; $R^2=C_2H_5$ h: $R^1=C_2H_5$; $R^2=C_6H_5CH_2$

Chart 1

1) Presented in part at the 45th Meeting of the Hokuriku Branch of the Pharmaceutical Society of Japan, Kanazawa, November 26, 1977.
2) Location: *13-1 Takara-machi, Kanazawa 920, Japan.*
3) T. Itaya and K. Ogawa, *Heterocycles*, **6**, 965 (1977).
4) T. Itaya and K. Ogawa, *Tetrahedron Lett.*, **1978**, 2907.
5) *a*) J.W. Marsico and L. Goldman, *J. Org. Chem.*, **30**, 3597 (1965); *b*) R.K. Robins and H.H. Lin, *J. Am. Chem. Soc.*, **79**, 490 (1957); *c*) J.A. Montgomery and C. Temple, Jr., *ibid.*, **83**, 630 (1961); *d*) B.R. Baker, R.E. Schaub, and J.P. Joseph, *J. Org. Chem.*, **19**, 638 (1954); *e*) J.A. Montgomery, K. Hewson, and C. Temple, Jr., *J. Med. Pharm. Chem.*, **5**, 15 (1962); *f*) W.F. Bryant and P.D. Klein, *Anal. Biochem.*, **65**, 73 (1975).
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7) *a*) T. Fujii, S. Sakurai, and T. Uematsu, *Chem. Pharm. Bull.*, **20**, 1334 (1972); *b*) J.A. Montgomery and H.J. Thomas, *J. Heterocyclic Chem.*, **1**, 115 (1964).

When N,N-diethyladenine (Ib) was treated with ethyl iodide in DMAc in the presence of potassium carbonate at room temperature for 6 hr, N,N,9- (IIg: 72% yield) and N,N,3-triethyladenine (IIIg: 13% yield) were obtained. The 9-ethyl structure of IIg was established by direct comparison with an authentic sample prepared from 6-chloro-9-ethylpurine.[8] The structure of IIIg could be distinguished from the 7-ethyl structure by comparison of IIIg with authentic N,N,7-triethyladenine derived from 6-chloro-7-ethylpurine.[8] Similarity of the ultraviolet (UV) spectra of IIIg to those of N,N,3-trimethyladenine[6a] but not to those of N,N,-1-trimethyladenine[6a] made it possible to assign the 3-ethyl structure to IIIg. Similar treatment of Ib with methyl iodide and with benzyl bromide gave the corresponding 9-alkyl isomers (IIf, h) as major products with minor amounts of the 3-alkyl isomers (IIIf, h). The alkylation of Ia under the same reaction conditions gave virtually the same results as the alkylation of Ib. Table I collects these results. The structures of the compounds obtained here were assigned on the basis of UV spectral similarity to IIg or IIIg.

The yields of IIe,h and IIIe,h show that the isomer ratios in the benzylation of Ia,b are about 2: 1. However, the total yields of the products in the methylation and ethylation are not high and may not reflect the actual isomer ratios of the reactions. The ratios (II: III) were roughly estimated at 7—8: 2 for the methylation and 9—10: 2 for the ethylation by taking proton magnetic resonance (PMR) spectra of the reaction mixtures.

Table I. Alkylation of N,N-Dialkyladenines (I) in DMAc in the Presence of Potassium Carbonate at Room Temperature

Substrate	Alkylating reagent	Yield (%) II	Yield (%) III	Isomer ratio[a] (II : III)
Ia	CH_3I	54	14	7 : 2
Ia	C_2H_5I	72	13	5 : 1
Ia	$C_6H_5CH_2Br$	65	30	—
Ib	CH_3I	74	17	4 : 1
Ib	C_2H_5I	72	13	9 : 2
Ib	$C_6H_5CH_2Br$	64	33	—

a) Estimated by comparing the areas of the purinyl proton signals in the PMR spectrum of the reaction mixture from which insoluble inorganic matter had been removed by filtration.

Table II. Alkylation of N,N-Dialkyladenines (I) with Alkyl Halides in DMAc in the Absence of Base

Substrate	Alkylating reagent	Reaction temperature (°C)	Reaction time (hr)	Yield (%) III	Yield (%) II	Isomer ratio[a] (III : II)
Ia	CH_3I	40	48	83	0.7	10 : 1
Ia	C_2H_5I	80	7	90	1.8	16 : 1
Ia	$C_6H_5CH_2Br$	40	24	86	2.8	—
Ib	CH_3I	40	48	86	—	8 : 1
Ib	C_2H_5I	80	7	89	0.3	19 : 1
Ib	$C_6H_5CH_2Br$	40	24	76	—	—

a) Determined in terms of the area ratios of the purinyl proton signals in the PMR spectrum of the reaction mixture to which a few drops of H_2O had been added, if necessary, to dissolve solids.

8) These were prepared according to reported procedure,[5c] but separation of the products was performed with a silica gel column, which was eluted with ethyl acetate-ethanol (10: 1, v/v) to give the 9-ethyl isomer in 59% yield and the 7-ethyl isomer in 23% yield.

As shown in Table II, regioselective alkylation at the 3-position of I was achieved on treating Ia with methyl iodide in DMAc without base, giving N,N,3-trimethyladenine (IIIc: 83% yield) as well as N,N,9-trimethyladenine (IIc: 0.7% yield). Similarly, the reactions of Ia with ethyl iodide and with benzyl bromide gave 3-ethyl-N,N-dimethyladenine (IIId: 90% yield) and 3-benzyl-N,N-dimethyladenine (IIIe: 86% yield[9]), respectively. The use of Ib as the starting material had no appreciable effect on the reaction features. The isomer ratios (III: II) of the methylation and the ethylation of I were roughly estimated at 8—10: 1 and 16—19: 1, respectively, by PMR spectroscopy.

The present results show that the orientation in the alkylation of I is analogous to that with adenine, which mainly gives the 9-alkyl isomers on alkylation in the presence of base[10] and predominantly gives the 3-alkyl isomers on alkylation in the absence of base.[11] Thus, N,N,9- (II) and N,N,3-trialkyladenines (III) are now conveniently obtainable by alkylation of I.

Experimental[12]

Alkylation of N,N-Dialkyladenines (I) without Base

General Procedure——A mixture of I (500 mg) and 3 molar equivalents of the alkyl halide in DMAc (7 ml) was treated under the reaction conditions specified in Table II. The reaction mixture was evaporated to dryness *in vacuo* and the solid residue was processed as follows unless otherwise stated. The residue was dissolved in H_2O (15—20 ml) and the solution was made basic with K_2CO_3. It was extracted with chloroform and the chloroform extracts were dried over Na_2SO_4. Chloroform was removed by evaporation and the residue was purified by column chromatography. For separating the methylated or the ethylated products, Merck silica gel 60 (11 g) was used. The column was eluted with chloroform–ethanol (10: 1, v/v) to give the 3-alkyl isomers (III) predominantly as the more polar products. Separation of the benzylated products was performed with a 18-g silica gel column. Elution with ethyl acetate–ethanol (10: 1, v/v) gave the 9-benzyl isomers (II) and further elution with ethyl acetate–ethanol (5: 1, v/v) gave the 3-benzyl isomers (III).

N,N,3-Trimethyladenine (IIIc)——Recrystallization from benzene gave colorless prisms, mp 173—174°[13] (lit.[6a] 167—168°). UV $\lambda_{max}^{95\%\ EtOH}$ 299 nm (ε 15600); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 291 (20400); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 294 (16800); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 295 (16300). PMR ($CDCl_3$) δ: 3.40 and 3.88 (3H each, b), 4.00 (3H, s), 7.92 and 8.02 (1H each, s).

3-Ethyl-N,N-dimethyladenine (IIId)——Recrystallization from H_2O gave colorless needles, mp 134.5—135.5°. *Anal.* Calcd for $C_9H_{13}N_5$: C, 56.52; H, 6.85; N, 36.63. Found: C, 56.73; H, 7.10; N, 36.65. UV $\lambda_{max}^{95\%\ EtOH}$ 299 nm (ε 15700); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 291 (20800); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 294 (16800); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 295 (16200). PMR ($CDCl_3$) δ: 1.58 (3H, t, J=8 Hz), 3.43 and 3.83 (3H each, b), 4.38 (2H, q, J=8 Hz), 7.91 and 7.97 (1H each, s).

3-Benzyl-N,N-dimethyladenine (IIIe)——Recrystallization from hexane–benzene (2: 1, v/v) gave colorless scales, mp 144—145°[13] (lit.[6c] mp 142°). UV $\lambda_{max}^{95\%\ EtOH}$ 301 nm (ε 15400); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 292 (22400); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 296 (16900); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 296 (16700). PMR ($CDCl_3$) δ: 3.34 and 3.88 (3H each, b), 5.49 (2H, s), 7.34 (5H, s), 7.92 and 8.02 (1H each, s).

N,N-Diethyl-3-methyladenine (IIIf)——The reaction mixture was evaporated to dryness and the residue was washed with isopropanol (10 ml). Insoluble material was dissolved in H_2O (15 ml). The solution was made basic with K_2CO_3 and extracted with benzene. Benzene was removed by evaporation after drying the solution over Na_2SO_4 to give IIIf (365 mg, 68%), mp 117—118.5°. The isopropanol washing was evaporated to dryness and the residue was treated in a similar manner to give a solid. It was purified with a 5-g silica gel column. Elution with chloroform–ethanol (10: 1, v/v) gave an additional crop (99 mg, 18%) of IIIf. Recrystallization from benzene–hexane (1: 1, v/v) gave colorless prisms, mp 118—118.5°. *Anal.*

9) Miyaki and Shimizu obtained the 3-benzyl isomer (IIIe: 66% yield) and the 9-benzyl isomer (IIe: 5% yield) on treating Ia with benzyl bromide in DMAc at 110° for 7 hr.[6c]

10) *a*) Ref. 7*a* and references cited therein; *b*) K.K. Ogilvie, S.L. Beaucage, M.F. Gillen, D. Entwistle, and M. Quilliam, *Nucleic Acids Res.*, **6**, 1695 (1979); *c*) K.K. Ogilvie, S.L. Beaucage, M.F. Gillen, and D.W. Entwistle, *ibid.*, **6**, 2261 (1979).

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12) All melting points are corrected. UV spectra were measured with a Hitachi 323 spectrophotometer using solutions in 95% aq. ethanol, 0.1 N aq. HCl (pH 1), 0.005 M phosphate buffer (pH 7), and 0.1 N aq. NaOH (pH 13). PMR spectra were recorded on a JEOL JNM-PS-100 spectrometer as 0.25 M solutions at 23—25° using tetramethylsilane as an internal standard. The following abbreviations are used: b=broad, d=doublet, q=quartet, s=singlet, t=triplet.

13) Routine C, H, N analyses were consistent with the calculated values within ±0.3% for this sample.

Calcd for $C_{10}H_{15}N_5$: C, 58.51; H, 7.37; N, 34.12. Found: C, 58.47; H, 7.23; N, 34.03. UV $\lambda_{max}^{95\%\ EtOH}$ 300 nm (ε 16700); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 294 (21600); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 296 (17800); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 297 (17500). PMR ($CDCl_3$) δ: 1.32 (6H, dull t, J=7 Hz), 3.86 (2H, b), 3.99 (3H, s), 4.35 (2H, b), 7.93 and 8.04 (1H each, s).

N,N,3-Triethyladenine (IIIg)——Recrystallization from hexane gave colorless plates, mp 71—72°. *Anal.* Calcd for $C_{11}H_{17}N_5$: C, 60.25; H, 7.81; N, 31.94. Found: C, 60.42; H, 7.85; N, 32.01. UV $\lambda_{max}^{95\%\ EtOH}$ 300 nm (ε 16500); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 293 (21800); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 295 (17900); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 296 (17500). PMR (CCl_4) δ: 1.26 (6H, b), 1.55 (3H, t, J=7 Hz), 3.70 (2H, b), 4.28 (2H, q, J=7 Hz, overlapped with a two-proton broad signal), 7.64 and 7.77 (1H each, s).

3-Benzyl-N,N-diethyladenine (IIIh)——Recrystallization from hexane–benzene (5: 1, v/v) gave colorless prisms, mp 112—113°. *Anal.* Calcd for $C_{16}H_{19}N_5$: C, 68.30; H, 6.81; N, 24.89. Found: C, 68.35; H, 6.95; N, 24.97. UV $\lambda_{max}^{95\%\ EtOH}$ 303 nm (ε 16200); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 294 (24300); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 298 (17700); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 298 (17300). PMR ($CDCl_3$) δ: 1.36 (6H, b), 3.82 and 4.40 (2H each, b), 5.50 (2H, s), 7.37 (5H, m), 7.92 and 8.03 (1H each, s).

Alkylation of N,N-Dialkyladenines (I) in the Presence of K_2CO_3

General Procedure——A mixture of I, K_2CO_3 (1 molar equivalent), and DMAc (3 ml per mmol of I) was heated under reflux for 10 min. After cooling, methyl iodide (20% molar excess), ethyl iodide (100% molar excess), or benzyl bromide (10% molar excess) was added and the mixture was stirred at room temp. until I disappeared (4—9 hr; monitored by thin-layer chromatography). The mixture was evaporated to dryness *in vacuo* and the residue was dissolved in a small volume of H_2O. This solution was extracted with chloroform. Chloroform was removed by evaporation after drying the extracts over $MgSO_4$ or Na_2SO_4 and the residue was purified by column chromatography. Identity of the by-products (III) with N,N,3-trialkyladenines (III), which were obtained by the alkylation without base, was established by mixed melting-point test and comparison of the infrared spectra.

N,N,9-Trimethyladenine (IIc)——Separation on a silica gel (22 g per 1 g of Ia) column eluted with chloroform–ethanol (10: 1, v/v) and recrystallization of the crude product from hexane gave IIc (54%) as colorless prisms, mp 117—118°[13] (lit.[6a] mp 119—120°). UV $\lambda_{max}^{95\%\ EtOH}$ 277 nm (ε 17600); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 270 (17600); $\lambda_{max}^{H_2O\ (pH\ 7)}$ (pH 7) 278 (18300); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 278 (18300). PMR (CCl_4) δ: 3.51 (6H, dull), 3.76 (3H, s), 7.50 and 8.12 (1H each, s). The 3-methyl isomer (IIIc: 14%) was obtained from the subsequent eluate.

9-Ethyl-N,N-dimethyladenine (IId)——Alumina (100 g per 2.2 g of Ia) and benzene–ethanol (5: 1, v/v) were used for separation, and the resulting crude IId (72%) was recrystallized from hexane to give colorless prisms, mp 80—81°[13] (lit.[5d] mp 79—80°). UV $\lambda_{max}^{95\%\ EtOH}$ 278 nm (ε 18500); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 270 (18100); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 278 (18600); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 278 (18600). PMR (CCl_4) δ: 1.49 (3H, t, J=7 Hz), 3.48 (6H, dull s), 4.16 (2H, q, J=7 Hz), 7.52 and 8.09 (1H each, s). Further elution of the column gave IIId (13%).

9-Benzyl-N,N-dimethyladenine (IIe)——Silica gel (19 g per 500 mg of Ia) and ethyl acetate–ethanol (10: 1, v/v) were used for separation of the products to give IIe (65%) as well as IIIe (30%). Recrystallization of IIe from hexane gave colorless needles, mp 129—130°[13] (lit.[5c] 131—132°). UV $\lambda_{max}^{95\%\ EtOH}$ 277 nm (ε 19500); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 269 (19800); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 278 (19900); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 278 (19900). PMR (CCl_4) δ: 3.51 (6H, dull s), 5.27 (2H, s), 7.26 (5H, s), 7.51 and 8.17 (1H each s).

N,N-Diethyl-9-methyladenine (IIf)——The products were separated on a silica gel (100 g per gram of Ib) column eluted with chloroform–ethanol (10: 1, v/v), giving IIf (74%) as a colorless hygroscopic solid, mp 30—39° (lit.[5b] mp 48—50°), as well as IIIf (17%). Sublimation of IIf gave colorless plates. UV $\lambda_{max}^{95\%\ EtOH}$ 279 nm; $\lambda_{max}^{H_2O\ (pH\ 1)}$ 271; $\lambda_{max}^{H_2O\ (pH\ 7)}$ 279; $\lambda_{max}^{H_2O\ (pH\ 13)}$ 279. PMR (CCl_4) δ: 1.26 (6H, t, J=7 Hz), 3.77 (3H, s), 3.96 (4H, dull q), 7.53 and 8.15 (1H each s).

The hydrochloride of IIf was prepared by adding ethanolic HCl to a solution of IIf in ethanol. Ether was added to the solution and the resulting precipitate was filtered off, recrystallized from isopropanol, and dried over P_2O_5 at 50° and 2 mmHg for 6 hr, followed by exposure to air until a constant weight was reached, giving colorless needles, mp 179—186° (lit.[5a] mp 176—179° for $C_{10}H_{16}ClN_5 \cdot 1/4H_2O$). *Anal.* Calcd for $C_{10}H_{16}ClN_5 \cdot H_2O$: C, 46.24; H, 6.99; N, 26.97. Found: C, 46.21; H, 7.06; N, 26.72. UV $\lambda_{max}^{95\%\ EtOH}$ 279 nm (ε 18900); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 271 (19100); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 279 (19600); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 279 (19600). PMR [$(CD_3)_2SO$] δ: 1.29 (6H, t, J=7 Hz), 3.88 (3H, s), 4.10 (4H, b), 5.00 (b, H_3O^+), 8.45 and 8.47 (1H each, s).

The picrate of IIf was prepared by adding a saturated solution of picric acid in ethanol to an ethanolic solution of the hydrochloride of IIf. Recrystallization from ethanol gave yellow prisms, mp 196—199°. *Anal.* Calcd for $C_{16}H_{18}N_8O_7$: C, 44.24; H, 4.18; N, 25.80. Found: C, 44.09; H, 4.29; N, 25.55.

N,N,9-Triethyladenine (IIg)——The products were separated on a silica gel (60 g per 0.01 mol of Ib) column. Elution with ethyl acetate–ethanol (10: 1, v/v) gave IIg (72%), mp 42—44°. Further elution of the column with ethanol gave IIIg (13%).

The picrate of IIg was prepared from the ethanolic solution, mp 169—170°. This sample was identical (mixed melting-point test and infrared spectrum) with the authentic picrate (see below).

The authentic sample of IIg was prepared by stirring 6-chloro-9-ethylpurine[8] (913 mg, 5 mmol) with diethylamine (6 ml) at room temp. for 1.5 hr. The mixture was worked up in a manner similar to that described for N,N,7-triethyladenine, giving a solid (1.04 g, 95%), mp 37—38°. Recrystallization of this compound failed owing to its excessively large solubility in common solvents. Sublimation under reduced pressure gave a colorless solid. UV $\lambda_{max}^{95\%\ EtOH}$ 280 nm; $\lambda_{max}^{H_2O\ (pH\ 1)}$ 271; $\lambda_{max}^{H_2O\ (pH\ 7)}$ 279; $\lambda_{max}^{H_2O\ (pH\ 13)}$ 279. PMR

(CCl_4) δ: 1.25 (6H, t, J=7 Hz), 1.50 (3H, t, J=7 Hz), 3.94 (4H, dull q), 4.17 (2H, q, J=7 Hz), 7.49 and 8.06 (1H each, s). The picrate of this compound was prepared by adding a saturated solution of picric acid in ethanol to an ethanolic solution of IIg. Recrystallization from ethanol gave yellow prisms, mp 169—170°. *Anal.* Calcd for $C_{17}H_{20}N_8O_7$: C, 45.53; H, 4.50; N, 24.99. Found: C, 45.50; H, 4.31; N, 25.02.

9-Benzyl-N,N-diethyladenine (IIh)——Silica gel (200 g per 0.03 mol of Ib) was used, and the column was eluted with ethyl acetate–ethanol (10: 1, v/v) to give IIh (64%) as well as IIIh (33%). Recrystallization of IIh from hexane gave colorless prisms, mp 63—64°. *Anal.* Calcd for $C_{16}H_{19}N_5$: C, 68.30; H, 6.81; N, 24.89. Found: C, 68.30; H, 7.06; N, 24.90. UV $\lambda_{max}^{95\%\ EtOH}$ 279 nm (ε 20200); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 271 (20300); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 280 (20500); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 280 (20600). PMR ($CDCl_3$) δ: 1.32 (6H, t, J=7 Hz), 4.01 (4H, dull q, J=7 Hz), 5.33 (2H, s), 7.30 (5H, s), 7.67 and 8.35 (1H each, s).

N,N,7-Triethyladenine——A mixture of 6-chloro-7-ethylpurine (365 mg, 2 mmol), diethylamine (5 ml), and butanol (45 ml) was refluxed for 4 hr. It was then evaporated to dryness and the residue was dissolved in H_2O. The solution was extracted with benzene and the benzene extracts were dried over $MgSO_4$ then evaporated to dryness to give a solid (0.43 g, 98%), mp 53—55°. Recrystallization from hexane gave colorless needles, mp 57—58°. *Anal.* Calcd for $C_{11}H_{17}N_5$: C, 60.25; H, 7.81; N, 31.94. Found: C, 60.21; H, 8.08; N, 31.85. UV $\lambda_{max}^{95\%\ EtOH}$ 225 nm (ε 10600), 295 (12200); $\lambda_{max}^{H_2O\ (pH\ 1)}$ 229 (7700), 300 (17600); $\lambda_{max}^{H_2O\ (pH\ 7)}$ 227 (10200), 298 (13000); $\lambda_{max}^{H_2O\ (pH\ 13)}$ 298 (13000). PMR (CCl_4) δ: 1.14 (6H, t, J=7 Hz), 1.47 (3H, t, J=7 Hz), 3.38 (4H, q, J=7 Hz), 4.44 (2H, q, J=7 Hz), 8.23 and 8.40 (1H each, s).

N,N-Dimethyladenine (Ia)——A mixture of 6-chloropurine[14] (20.0 g, 0.129 mol), dimethylamine hydrochloride (13 g), triethylamine (45 ml), and butanol (200 ml) was stirred at room temp. for 24 hr then evaporated to dryness. The solid residue was washed with H_2O (100 ml) and dried to give a solid (17.6 g), mp 263—265°. After adding silica gel (40 g), the washing was evaporated to dryness and the residue was placed on top of a 50-g silica gel column which was eluted with benzene–ethanol (5: 1, v/v). Removal of the solvent from the eluate afforded a second crop (2.4 g), total yield 20.0 g (95%). Recrystallization from ethanol gave colorless needles, mp 265—266°[13] (lit.[15] mp 257°).

N,N-Diethyladenine (Ib)——A mixture of 6-chloropurine[14] (2.94 g, 19 mmol), diethylamine (5 ml), and butanol (25 ml) was heated under reflux for 1 hr. After cooling, the resulting precipitate was filtered off, washed with cold H_2O (20 ml) and dried to give colorless pillars (3.20 g, 88%), mp 220—221°. The combined filtrate and washing were evaporated to dryness and the solid residue was washed with H_2O (2×10 ml), then dried to afford an additional crop (0.34 g, 9%), mp 218—220°. Recrystallization from ethanol gave colorless pillars, mp 221—222°[13] (lit.[16] 222—223°).

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