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Synthesis of 6-Methylaminopurine by Thermal Cyclization of 4,6-Bis(methylamino)-5-phenylazopyrimidine¹⁾

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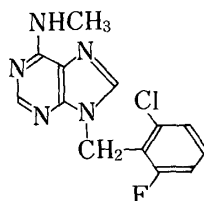
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The thermal cyclization of 4-amino-6-methylamino- (3) and 4,6-bis(methylamino)-5-phenylazopyrimidines (4) to adenine (10) and its *N*⁶-methyl derivative is described. Compound 3 was synthesized by reaction of phenylazomalononitrile (2) with *N*-methylformamide and ammonia. Compound 4 was synthesized from 2, formamide, methylamine and its hydrochloride. These compounds were also obtained by methylation of 4,6-diamino-5-phenylazopyrimidines, followed by rearrangement in methanolic dimethylamine. Heating 4 at 250–260 °C afforded 6-methylaminopurine (12) together with a small amount of 8-anilino-6-methylaminopurine (13). Similarly, refluxing 3 in Dowtherm A yielded 10 and 8-anilinoadenine (11).

Keywords—phenylazomalononitrile; 4-alkylamino-6-amino-5-phenylazopyrimidine; 4,6-bis(alkylamino)-5-phenylazopyrimidine; 4-amino-6-methylamino-5-phenylazopyrimidine; 4,6-bis(methylamino)-5-phenylazopyrimidine; 6-methylaminopurine; adenine; 8-anilino-6-methylaminopurine; 8-anilinoadenine; thermal cyclization

9-(2-Chloro-6-fluorobenzyl)-6-methylaminopurine (1) (Chart 1) has been shown to have potent anticoccidial activity.²⁾ The available methods for the synthesis of 6-methylamino-



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Chart 1

purine (12), the precursor of 1, however, are not simple and generally involve a number of steps.³⁾ Pfeleiderer and Blank have reported that heating 5-(2,5-dichlorophenyl)azo-1,3-dimethyl-6-methylaminouracil in nitrobenzene resulted in an intramolecular cyclization to give theophylline.⁴⁾ Since then a similar approach to 8-dimethylaminotheophylline⁵⁾ and 2,8-diarylhydropoxanthines⁶⁾ has been reported. We have now examined the thermal cyclization of 4-amino-6-methylamino- (3) and 4,6-bis(methylamino)-5-phenylazopyrimidines (4) in the hope that a new route to adenine (10) and its derivatives might result. In this paper we describe the synthesis of 3 and 4 and their thermal behavior.

Synthesis of 4-Alkylamino-6-amino- and 4,6-Bis(alkylamino)-5-phenylazopyrimidines

It has previously been reported that the direct condensation of phenylazomalononitrile (2), formamide and ammonia gives 4,6-diamino-5-phenylazopyrimidine (5) as the sole reaction product.⁷⁾ We expected that by replacing the latter two reagents with *N*-alkylformamide and alkylamine, the desired *N*-alkylamino derivatives of 5 might be obtained.

Actually, heating a mixture of **2** (1 mol), formamide and methylamine (6 mol) at 150 °C for 5 h in a sealed tube afforded **3** and **5** together with a small amount of **4**. Addition of methylamine hydrochloride (1 mol) to this combination reduced the formation of **5** and yielded **3** (28%) as a major product (Method A) (Chart 2). Alternatively, **3** was prepared by

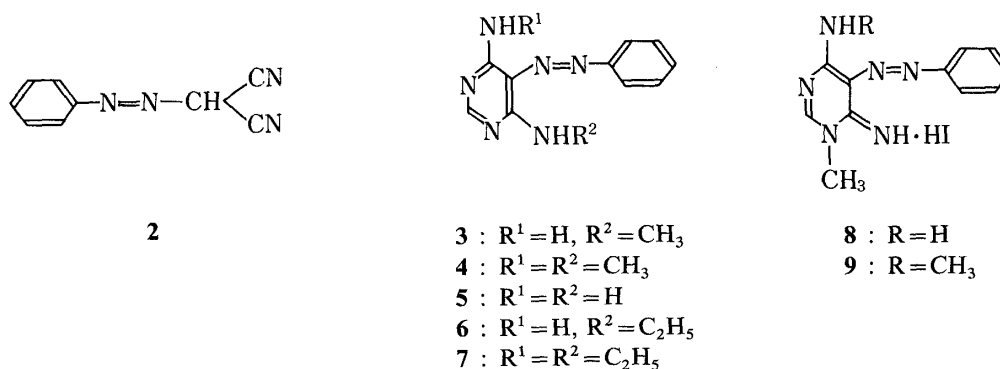


Chart 2

heating a mixture of **2**, *N*-methylformamide and ammonia. The yield of **3** was improved by increasing the amount of ammonia and the use of 50 equivalents of ammonia gave the best result⁸⁾ (50%) (Method B). These methods could be applied to the synthesis of 4-amino-6-ethylamino-5-phenylazopyrimidine (**6**).

On the other hand, if the amount of methylamine was increased in Method A, it was found that **4** was obtained as a major product. Thus, **4** was obtained in 63% yield by using 50 equivalents of methylamine (Method C). This method was also applied to the synthesis of 4,6-bis(ethylamino)-5-phenylazopyrimidine (**7**). The results are summarized in Tabel I.

The unsatisfactory yields of **3** and **4** by Methods A—C prompted us to consider an alternative approach to these compounds. According to the method for the synthesis of 4-amino-6-methylamino-5-nitropyrimidine,¹⁰⁾ reaction of **5** with methyl iodide in *N,N*-dimethylformamide (DMF) afforded 4-amino-1,6-dihydro-6-imino-1-methyl-5-phenylazopyrimidine hydriodide (**8**), which was converted to **3** by treatment with 50% methanolic dimethylamine. Similarly, **4** was prepared from **3** via 1,6-dihydro-6-imino-1-methyl-4-methylamino-5-phenylazopyrimidine hydriodide (**9**).

TABLE I. 4,6-Diamino-5-phenylazopyrimidine Derivatives

Compound No.	Method	Yield (%)	Appearance	mp (°C) (Recrystallized from)	Formula	Analysis (%) Calcd (Found)		
						C	H	N
3	A	28	Yellow needles	187—188 (CHCl ₃ —pet. ether)	C ₁₁ H ₁₂ N ₆	57.88	5.30	36.82
	B	50				(57.74)	(5.01)	(36.69)
4	C	63	Orange needles	127—128 (CHCl ₃ —pet. ether)	C ₁₂ H ₁₄ N ₆	59.49	5.82	34.69
						(59.46)	(5.84)	(34.58)
6	A	33	Yellow needles	129—130 (CHCl ₃ —pet. ether)	C ₁₂ H ₁₄ N ₆	59.49	5.82	34.69
	B	64				(59.59)	(5.97)	(34.83)
7	C	40	Orange needles	77—78 (Pet. ether)	C ₁₄ H ₁₈ N ₆	62.20	6.71	31.09
						(61.95)	(6.74)	(31.01)

TABLE II. Spectral Data for 4,6-Diamino-5-phenylazopyrimidine Derivatives

Compound No.	¹ H-NMR ^{a)}	UV			MS <i>m/z</i>
		$\lambda_{\max}^{0.1\text{N HCl}}$ nm (ϵ)	$\lambda_{\max}^{\text{H}_2\text{O}}$ nm (ϵ)	$\lambda_{\max}^{0.1\text{N NaOH}}$ nm (ϵ)	
3	3.14 (3H, d, $J=4.5$ Hz, CH ₃), 6.17—7.10 (2H, br, NH ₂), 7.27—7.83 (5H, m, Ar-H), 8.16 (1H, s, 2-H), 8.70—9.08 (1H, br, NH)	245 (19900), 386 (17100)	248 (18900), 388 (17700)	248 (18900), 388 (17700)	228 (M ⁺), 199, 170, 137, 136, 123
4	3.13 (6H, d, $J=5$ Hz, 2 × CH ₃), 7.22—7.77 (5H, m, Ar-H), 8.07—8.73 (2H, br, 2 × NH), 8.24 (1H, s, 2-H)	257 (21500), 390 (16200)	251 (20100), 396 (16700)	250 (20500), 396 (16400)	242 (M ⁺), 213, 184, 150, 137
6	1.29 (3H, t, $J=7$ Hz, CH ₃), 3.47—3.82 (2H, m, CH ₂), 6.50—7.36 (2H, br, NH ₂), 7.30—7.80 (5H, m, Ar-H), 8.12 (1H, s, 2-H), 8.75—9.20 (1H, br, NH)	248 (19000), 375 (16600)	249 (18600), 380 (16800)	249 (18500), 390 (17200)	242 (M ⁺), 227, 213, 150
7	1.29 (6H, t, $J=7$ Hz, 2 × CH ₃), 3.47—3.83 (4H, m, 2 × CH ₂), 7.30—7.75 (5H, m, Ar-H), 8.19 (1H, s, 2-H), 8.23—8.80 (2H, br, 2 × NH)	257 (21800)	218 (20100), 254 (19700)	254 (19700)	270 (M ⁺), 241, 178

a) Measured in CDCl₃.

¹H-Nuclear magnetic resonance (NMR) and ultraviolet (UV) spectra and mass spectra (MS) of compounds prepared are listed in Table II.

Thermal Cyclization of 3 and 4 to Adenine Derivatives

Refluxing **3** in Dowtherm A followed by purification by column chromatography on silica gel gave **10** (14%) and 8-anilinoadenine (**11**) (3%). The structure assignment of **11** was based on a comparison of spectral data with those of an authentic sample prepared by an unambiguous synthesis from 8-bromoadenine (**14**).¹¹⁾

Heating **4** at 250—260 °C afforded **12** as a major product together with several minor products. Thus, the reaction mixture was separated by column chromatography on silica gel and after removal of acetone-soluble materials from the eluate, the residue was recrystallized from water to afford **12** in 21% yield. The structure assignment of **12** was based on elemental analysis and spectral data. On the other hand, the reaction mixture in a separate experiment was extracted with acetone. After removal of the acetone, the residue insoluble in hot water was recrystallized from methanol to give yellow needles (3%). The structure of this product was supposed to be 8-anilino-6-methylaminopurine (**13**) on the basis of elemental analysis and spectral data. The structure was confirmed by an independent synthesis from **12**. Bromination of **12** gave 8-bromo-6-methylaminopurine (**15**) whose structure was determined by conversion to known 8-hydroxy-6-methylaminopurine (**16**).¹²⁾ Treatment of **15** with aniline gave **13**. A possible mechanistic rationalization of the formation of **10**—**13** is illustrated in Chart 3.¹³⁾

Experimental

Melting points were determined with a Yanagimoto micro melting point apparatus, except for those above 300 °C, which were determined in capillary tubes using a conc. H₂SO₄—K₂SO₄ (3:2) bath, and are uncorrected. Infrared (IR) spectra were recorded with a Hitachi 260—10 spectrophotometer, UV spectra with a Perkin-Elmer 450 spectrophotometer, and MS with a JEOL JMS-01SC mass spectrometer. ¹H-NMR spectra were taken with a Varian EM-390 spectrometer (90 MHz) and chemical shifts are expressed in ppm (δ) using tetramethylsilane (TMS) as an

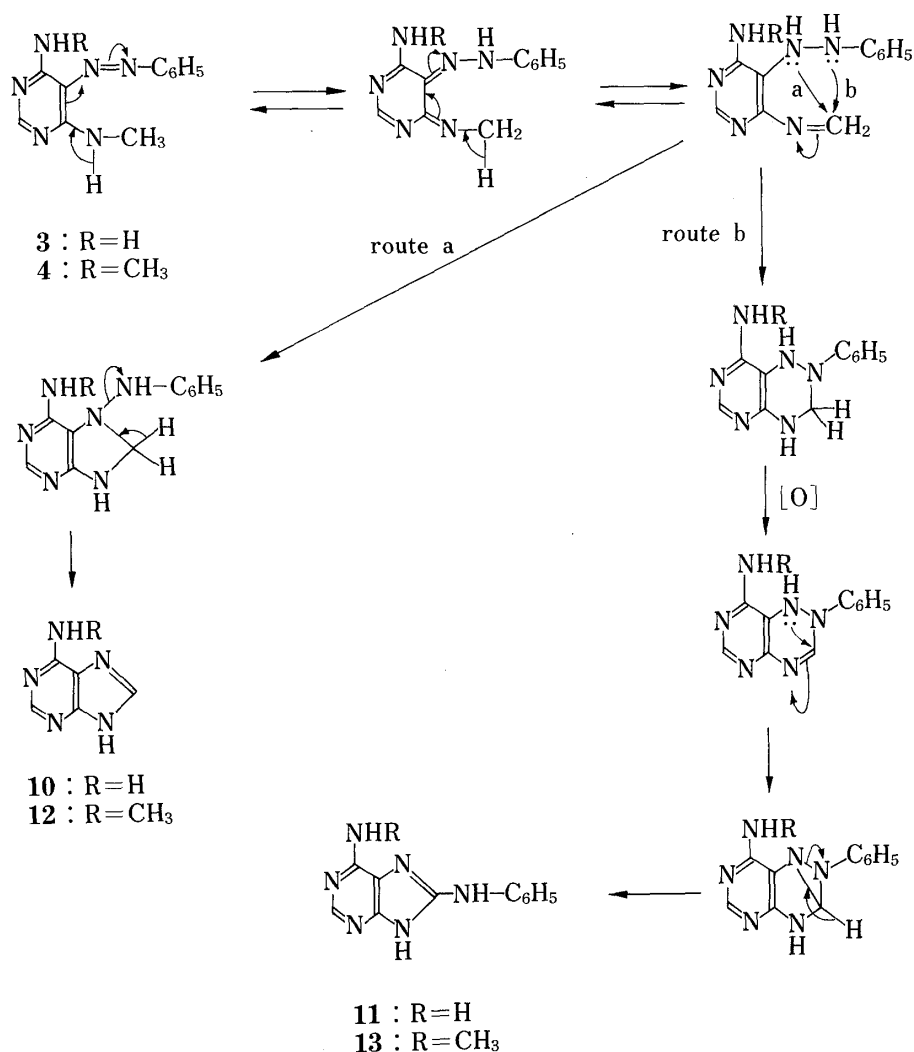


Chart 3

internal standard. When D₂O was used as a solvent, TMS was used as an external standard. Thin layer chromatography (TLC) was carried out on Kieselgel 60 F₂₅₄ plates (Merck) using CHCl₃-MeOH-28% NH₄OH (75:15:1) as the developing solvent. Column chromatography was carried out on Kieselgel 60 (Merck). Concentration operations were carried out under reduced pressure with a rotary evaporator.

4-Amino-6-methylamino-5-phenylazopyrimidine (3)—i) (Method A) A mixture of 2⁷⁾ (8.51 g, 50 mmol), CH₃NH₂ (9.3 g, 300 mmol), CH₃NH₂·HCl (3.38 g, 50 mmol) and HCONH₂ (45 g, 1 mol) was stirred at 150 °C for 5 h in a sealed stainless steel tube. The reaction mixture was concentrated and the residue was dissolved in CHCl₃ (200 ml). The CHCl₃ solution was washed with H₂O (150 ml), dried over anhydrous MgSO₄ and concentrated. The residue was chromatographed on silica gel (100 g) with CHCl₃ and CHCl₃-MeOH (49:1) as eluents. The eluate was evaporated to dryness and the residue was recrystallized to give 3 (3.23 g).

ii) (Method B) A mixture of 2 (8.51 g, 50 mmol), HCONHCH₃ (59 g, 1 mol) and NH₃ (42.6 g, 2.5 mol) was treated in the manner described in i). The crude product was chromatographed on silica gel (100 g) to give two fractions. The former fraction was evaporated to dryness and the residue was recrystallized to give 4 (340 mg, 3%), mp 125–127 °C. The latter fraction was treated similarly to give 3 (5.67 g).

iii) (By rearrangement) A mixture of 8 (178 mg, 0.5 mmol) and 50% (CH₃)₂NH-MeOH (5 ml) was stirred for 12 h at room temperature in a sealed stainless steel tube. The reaction mixture was concentrated and the residue was diluted with water. The precipitate was collected, dried and recrystallized to give 3 (102 mg, 89%).

4,6-Bis(methylamino)-5-phenylazopyrimidine (4)—i) (Method C) A mixture of 2 (4.26 g, 25 mmol), CH₃NH₂ (38.8 g, 1.25 mol), CH₂NH₂·HCl (3.38 g, 50 mmol) and HCONH₂ (23 g, 500 mmol) was treated in the manner described for 3. The crude product was chromatographed on silica gel (75 g) with CHCl₃ as the eluent. The eluate was

evaporated to dryness and the residue was recrystallized to give **4** (3.8 g).

ii) (By rearrangement) A mixture of **9** (1.85 g, 5 mmol) and 50% $(\text{CH}_3)_2\text{NH}\cdot\text{MeOH}$ (25 ml) was treated for 24 h in the manner described for **3**. The reaction mixture was concentrated and the residue was dissolved in CHCl_3 (100 ml). The CHCl_3 solution was washed with H_2O (2×100 ml), dried over anhydrous MgSO_4 and concentrated. The residue was recrystallized to give **4** (1.13 g, 94%).

4-Amino-1,6-dihydro-6-imino-1-methyl-5-phenylazopyrimidine Hydriodide (8)—Methyl iodide (14 ml, 225 mmol) was added to a suspension of **5** (10.7 g, 50 mmol) in DMF (250 ml). The mixture was stirred for 2 h at room temperature, allowed to stand overnight at room temperature and concentrated. The residue was recrystallized from EtOH to give **8** (6.8 g, 38%), mp 269–271 °C (dec.). *Anal.* Calcd for $\text{C}_{11}\text{H}_{12}\text{N}_6 \cdot \text{HI} \cdot 1/2\text{H}_2\text{O}$: C, 36.18; H, 3.86; N, 23.01. Found: C, 36.35; H, 4.08; N, 23.20.

1,6-Dihydro-6-imino-1-methyl-4-methylamino-5-phenylazopyrimidine Hydriodide (9)—A suspension of **3** (6.85 g, 30 mmol) in DMF (30 ml) was treated with methyl iodide (8.4 ml, 135 mmol) in the manner described for **8**. The crude product was recrystallized from MeOH to give **9** (5.74 g, 52%), mp 252–254 °C (dec.). *Anal.* Calcd for $\text{C}_{12}\text{H}_{14}\text{N}_6 \cdot \text{HI}$: C, 38.93; H, 4.08; N, 22.70. Found: C, 38.84; H, 4.19; N, 22.52.

Adenine (10) and 8-Anilinoadenine (11)—A suspension of **3** (10 g, 43.8 mmol) in Dowtherm A (a mixture containing 73.5% diphenyl ether and 26.5% diphenyl) (20 ml) was refluxed for 2 h with stirring, then cooled. After dilution with ether (300 ml), the precipitate (8.2 g) was collected and dissolved in hot $\text{MeOH}\cdot\text{H}_2\text{O}$ (1 : 1) (200 ml). The resulting solution was chromatographed on silica gel (1.5 kg) with acetone– H_2O (49 : 1) as the eluent to give two fractions. The former fraction was evaporated to dryness and the residue was recrystallized from MeOH (5 ml) to give **11** (277 mg, 3%) as light brown crystals, mp 172–175 °C. *Anal.* Calcd for $\text{C}_{11}\text{H}_{10}\text{N}_6 \cdot 1/2\text{H}_2\text{O}$: C, 56.16; H, 4.71; N, 35.72. Found: C, 56.02; H, 4.43; N, 35.50. $^1\text{H-NMR}$ ($\text{DMSO}-d_6$): 6.47 (2H, s, NH_2), 6.81–7.05 (1H, m, Ar-H), 7.31 (2H, t, $J=8$ Hz, Ar-H), 7.58–7.83 (2H, m, Ar-H), 8.04 (1H, s, 2-H), 9.03–10.00 (1H, br, NH). IR $\nu_{\text{max}}^{\text{KBr}} \text{cm}^{-1}$: 1615, 1595, 1575, 1525, 1490, 1425, 1370, 1330, 1235. UV $\lambda_{\text{max}}^{0.1 \text{ N HCl}} \text{nm} (\epsilon)$: 300 (19500); $\lambda_{\text{max}}^{\text{H}_2\text{O}} \text{nm} (\epsilon)$: 292 (24200); $\lambda_{\text{max}}^{0.1 \text{ N NaOH}} \text{nm} (\epsilon)$: 300 (27800). MS m/z : 226 (M^+), 208, 199, 119, 77. The latter fraction was evaporated to dryness and the residue (3.3 g) was dissolved in $\text{CHCl}_3\text{--MeOH}$ (1 : 1) (50 ml) with heating. The resulting solution was chromatographed on silica gel (800 g) with $\text{CHCl}_3\text{--MeOH}$ (19 : 1) as the eluent. The eluate was evaporated to dryness and the residue was dissolved in MeOH (500 ml). After treatment with activated charcoal followed by concentration, the residue was recrystallized from H_2O (60 ml) to give **10** (828 mg, 14%) as colorless crystals, mp > 320 °C. *Anal.* Calcd for $\text{C}_5\text{H}_5\text{N}_5$: C, 44.44; H, 3.73; N, 51.83. Found: C, 44.40; H, 3.62; N, 51.52. $^1\text{H-NMR}$ (4% $\text{NaOD}\text{--D}_2\text{O}$): 8.12 (1H, s, 8-H), 8.23 (1H, s, 2-H). IR $\nu_{\text{max}}^{\text{KBr}} \text{cm}^{-1}$: 1670, 1600, 1450, 1420, 1370, 1335, 1310, 1250. UV $\lambda_{\text{max}}^{0.1 \text{ N HCl}} \text{nm} (\epsilon)$: 261 (13900); $\lambda_{\text{max}}^{\text{H}_2\text{O}} \text{nm} (\epsilon)$: 259 (14200); $\lambda_{\text{max}}^{0.1 \text{ N NaOH}} \text{nm} (\epsilon)$: 267 (13200).

8-Anilinoadenine (11)—A mixture of **14** (10.7 g, 50 mmol) and aniline (23.4 g, 250 mmol) was stirred at 180–190 °C for 3 h and cooled. The reaction mixture was solidified by addition of ether (100 ml) and the solid was collected. This was dissolved in 10% NH_4OH (1.5 l) and the solution was stirred at 70 °C for 30 min. Insoluble materials were filtered off and washed with H_2O . The filtrate and the washings were combined and concentrated to ca. 700 ml. The concentrate was adjusted with conc. HCl to pH 7 and cooled in an ice bath. The precipitate was collected and recrystallized from H_2O (3 l), then twice from MeOH to give yellowish crystals (containing a small amount of impurities by TLC) (3.8 g), which were dissolved in $\text{CHCl}_3\text{--MeOH}$ (1 : 1) (200 ml). The resulting solution was chromatographed on silica gel (300 g) with $\text{CHCl}_3\text{--MeOH}$ (9 : 1) and $\text{CHCl}_3\text{--MeOH}$ (5 : 1) as eluents. The eluate was evaporated to dryness and the residue was recrystallized from MeOH to give **11** (1.22 g, 10%) as colorless crystals, mp 172–175 °C.

6-Methylaminopurine (12)—Compound **4** (18 g, 74.3 mmol) was heated at 250–260 °C for 10 min in a metal bath, then cooled. The reaction mixture was dissolved in $\text{MeOH}\cdot\text{H}_2\text{O}$ (1 : 1) (60 ml) and the resulting solution was chromatographed on silica gel (950 g) with acetone– H_2O (49 : 1) as the eluent to give two fractions. The former fraction was evaporated to dryness and the residue was dissolved in hot MeOH (200 ml). After treatment with activated charcoal followed by concentration, the residue was refluxed for 30 min in acetone (50 ml) and cooled. The precipitate was collected and recrystallized from H_2O (50 ml) to give **12** (1.04 g, 9%) as colorless crystals, mp 314–316 °C (lit.^{3a}) mp 312–314 °C, lit.^{3b}) mp 306 °C, lit.^{3c}) mp 308 °C, lit.^{3d}) mp 319–320 °C). *Anal.* Calcd for $\text{C}_6\text{H}_7\text{N}_5$: C, 48.32; H, 4.73; N, 46.95. Found: C, 48.02; H, 4.43; N, 47.16. $^1\text{H-NMR}$ ($\text{DMSO}-d_6$): 3.01 (3H, d, $J=4$ Hz, CH_3), 7.26–7.66 (1H, br, NH), 8.07 (1H, s, 8-H), 8.22 (1H, s, 2-H), 12.30–13.40 (1H, br, NH). IR $\nu_{\text{max}}^{\text{KBr}} \text{cm}^{-1}$: 1620, 1595, 1485, 1450, 1440, 1390, 1355, 1330, 1300, 1245. UV $\lambda_{\text{max}}^{0.1 \text{ N HCl}} \text{nm} (\epsilon)$: 266 (15800); $\lambda_{\text{max}}^{\text{H}_2\text{O}} \text{nm} (\epsilon)$: 266 (16400); $\lambda_{\text{max}}^{0.1 \text{ N NaOH}} \text{nm} (\epsilon)$: 272 (16300). MS¹⁵ m/z (%): 149 (M^+ , 100), 121 (43), 120 (52), 93 (72), 66 (38). The latter fraction, which contained impurities, was evaporated to dryness and the residue was purified by chromatography on silica gel (800 g) to give an additional 1.25 g (11%) of **12** as colorless crystals, mp 314–316 °C.

8-Anilino-6-methylaminopurine (13)—i) Compound **4** (18 g, 74.3 mmol) was heated in the manner described for **12** and cooled. After addition of acetone (50 ml), the reaction mixture was stirred and allowed to stand overnight at room temperature. The crystals were collected and dissolved in hot water (500 ml). Insoluble materials were collected and dissolved in hot MeOH (200 ml). The MeOH solution was treated with activated charcoal and concentrated. The residue was washed with acetone (20 ml) and recrystallized from MeOH (50 ml) to give **13** (454 mg, 3%) as pale yellow crystals, mp 301–303 °C. *Anal.* Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_6$: C, 59.99; H, 5.03; N, 34.98. Found: C, 59.53; H, 4.90; N, 35.11.

$^1\text{H-NMR}$ ($\text{DMSO-}d_6$): 3.00 (3H, d, $J=4.5$ Hz, CH_3), 6.73–7.07 (2H, m, Ar-H and NH), 7.32 (2H, t, $J=8$ Hz, Ar-H), 7.65–7.85 (2H, m, Ar-H), 8.11 (1H, s, 2-H), 9.10–9.67 (1H, br, NH). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3430, 1620, 1590, 1570, 1495, 1485, 1400, 1350, 1320, 1305, 1290, 1240, 1200. UV $\lambda_{\text{max}}^{0.1\text{N HCl}}$ nm (ϵ): 238 (13700), 307 (20300); $\lambda_{\text{max}}^{\text{H}_2\text{O}}$ nm (ϵ): 223 (17500), 241 (reflection) (13400), 295 (24000); $\lambda_{\text{max}}^{0.1\text{N NaOH}}$ nm (ϵ): 305 (25800). MS m/z : 240 (M^+), 212, 184, 118, 77.

ii) A mixture of **15** (5.7 g, 25 mmol) and aniline (20 ml, 219 mmol) was stirred at 180–190 °C for 3 h. Aniline was removed and the residue was dissolved in MeOH (150 ml). After treatment with activated charcoal, the filtrate was diluted with an equal volume of ether and cooled in an ice bath. The deposited crystals were collected and recrystallized from EtOH (50 ml) to give light brown crystals (containing a small amount of impurities by TLC), which were dissolved in CHCl_3 –MeOH (5:1). The resulting solution was chromatographed on silica gel (200 g) with CHCl_3 and CHCl_3 –MeOH (19:1) as eluents. The eluate was evaporated to dryness and the residue was recrystallized from EtOH (50 ml) to give **13** (1.35 g, 24%) as colorless crystals, mp 300–302 °C.

8-Bromo-6-methylaminopurine (15)—Bromine (25 ml, 480 mmol) was added to **12** (7.45 g, 50 mmol) and the mixture was allowed to stand for 4 h at room temperature. The reaction mixture was heated at 100–110 °C for 5 h, then dissolved in 10% NH_4OH (700 ml). Insoluble materials were filtered off and the filtrate was adjusted with AcOH to pH 5. The precipitate was collected, washed with H_2O and suspended in H_2O (1.5 l). The suspension was stirred at 90 °C for 30 min and the precipitate was collected while hot. The precipitate was washed with H_2O and dissolved in 10% NH_4OH (700 ml). Insoluble materials were filtered off and the filtrate was adjusted with AcOH to pH 5. The precipitate was collected, washed with H_2O and recrystallized twice from DMF to give **15** (3.06 g, 27%) as light brown crystals, mp > 320 °C. Anal. Calcd for $\text{C}_6\text{H}_6\text{BrN}_5$: C, 31.60; H, 2.65; N, 30.71. Found: C, 31.83; H, 2.82; N, 30.84. $^1\text{H-NMR}$ (10% $\text{NaOD-D}_2\text{O}$): 3.14 (3H, s, CH_3), 8.21 (1H, s, 2-H). UV $\lambda_{\text{max}}^{0.1\text{N HCl}}$ nm (ϵ): 206 (19200), 268 (18200); $\lambda_{\text{max}}^{\text{H}_2\text{O}}$ nm (ϵ): 215.5 (21600), 275 (18200); $\lambda_{\text{max}}^{0.1\text{N NaOH}}$ nm (ϵ): 219.5 (19200), 275 (18200).

8-Hydroxy-6-methylaminopurine (16)—A suspension of **15** (456 mg, 2 mmol) in conc. HCl (20 ml) was refluxed for 3 h with stirring. The reaction mixture was adjusted with 28% NH_4OH to pH 8 and cooled in an ice bath. The precipitate was collected and dissolved in dil. KOH. Insoluble materials were filtered off and the filtrate was adjusted with AcOH to pH 4. After cooling in an ice bath, the precipitate was collected and washed with H_2O to give **16** (270 mg, 82%) as a colorless powder, mp > 320 °C (lit.¹²) mp > 300 °C). Anal. Calcd for $\text{C}_6\text{H}_7\text{N}_5\text{O} \cdot 1/5\text{H}_2\text{O}$: C, 42.70; H, 4.42; N, 41.50. Found: C, 42.91; H, 4.33; N, 41.65. UV $\lambda_{\text{max}}^{0.1\text{N HCl}}$ nm (ϵ): 274 (14100); $\lambda_{\text{max}}^{\text{H}_2\text{O}}$ nm (ϵ): 272 (16600); $\lambda_{\text{max}}^{0.1\text{N NaOH}}$ nm (ϵ): 281 (17800).

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