Purines. XLIII.[1] A Total Synthesis of the Marine Sponge Base 6-Imino-1,9-dimethyl-8-oxopurine

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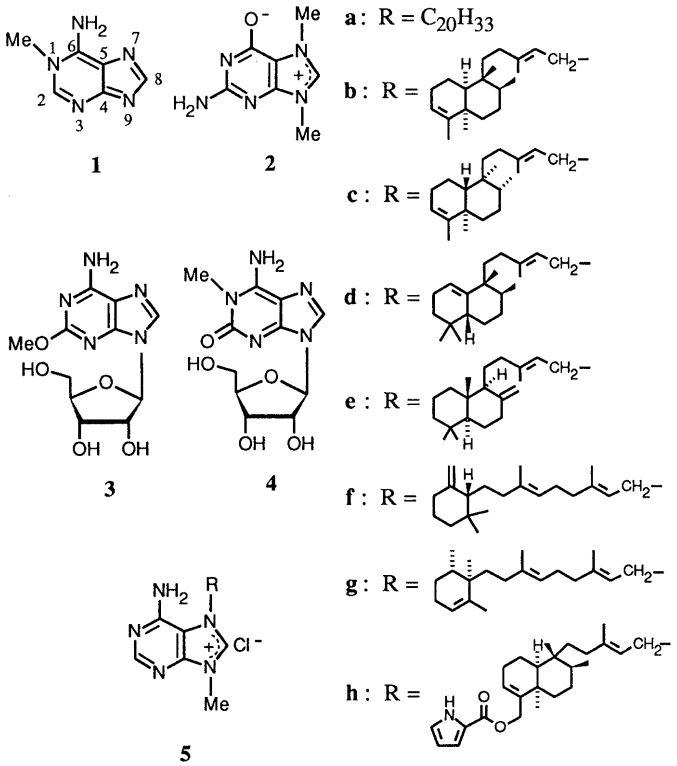
The first total synthesis of the 8-oxopurine 8, a constituent of the marine sponge *Hymeniacidon sanguinea* GRANT, has been achieved *via* two alternative routes starting from 8-bromo-9-methyladenine (11), which is obtainable from 9-methyladenine (10) by bromination. The first route includes methylation of 11 with MeI to give the 1-methylated product 13·HI, conversion of 13·HI into the free base 13, and treatment of 13 with NaOAc in boiling AcOH to produce 8 in 25% overall yield (from 10). The second route includes treatment of 11 with boiling 1 N aqueous NaOH and methylation of the resulting 8-oxo derivative 12 with MeI, affording 8 in 63% overall yield (from 10). The rearranged isomer 15 and the N^6-acetyl derivative 9 have also been synthesized.

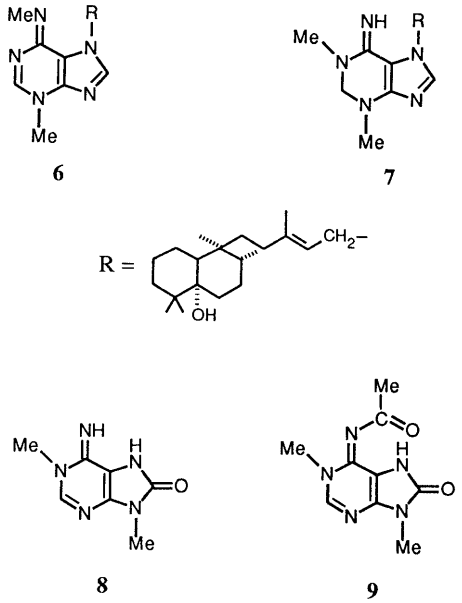
Keywords marine sponge 8-oxopurine; adenine bromination; 8-bromoadenine methylation; nucleophilic aromatic substitution; 8-oxoadenine; Dimroth rearrangement; acetylation

More than a dozen naturally occurring unusual purine derivatives, based mainly on the adenine nucleus, have so far been reported from various marine sponges. These sponge purines include 1-methyladenine (spongopurine) (**1**)[2] and 7,9-dimethylguaninyl betaine (herbipoline) (**2**)[3] from the siliceous giant sponge *Geodia gigas*, 2-methoxyadenosine (spongosine) (**3**) from the Caribbean sponge *Cryptotethia crypta*,[4] 1-methylisoguanosine (**4**) from the Tasman Sea sponge *Tedania digitata*,[5] agelasine (**5a**) from the Barbadian sponge *Agelas dispar*,[6] agelasines A—F (**5b**—**g**) from the Okinawan sponge *Agelas nakamurai*,[7,8] ageline A (agelasine F[7]) (**5g**) and ageline B (**5h**) from a Pacific sponge *Agelas* sp.,[9] and agelasimine A (**6**) and agelasimine B (**7**) from the orange sponge *Agelas mauritiana*.[10,11] Many of these purines exhibit a wide range of interesting biological activities such as maturation-inducing hormonal activity on oocytes of the starfish *Asterias amurensis*, *Asterias rubens*, *Marthasterias glacialis*, or *Asterina pectinifera* (by **1**)[12,13]; muscle relaxant, antiinflammatory, and other pharmacological activities (by **4**)[5,14]; antimicrobial activity (by **5b**—**e**, **5g**, and **5h**)[7,8]; cytotoxicity (by **6** and **7**)[10]; ichthyotoxicity (by **5g** and **5h**)[9]; inhibitory effect on Na^+,K^+-ATPase (by **5b**—**g**)[7,8]; and inhibition of adenosine transfer into rabbit erythrocytes, Ca^{2+}-channel antagonistic action, and α_1 adrenergic blockade (by **6** and **7**).[10]

In 1985, Cimino *et al.*[15] reported the isolation of a new purine (**8**) and known 1-methyladenine (**1**), although both only in the form of the acetyl derivative (**9** and acetylspongopurine), from the English Channel sponge *Hymeniacidon sanguinea* GRANT. While the new acetyl derivative **9** was fully characterized by means of spectroscopic and X-ray crystallographic analyses, the parent base **8** remained unknown because of the difficulty in separating **8** and **1** from each other at the free base level.[15] This was why we tried to secure the base **8** itself by synthesis in the present study. A brief account of the results recorded here has been published in a preliminary form.[16]

The synthesis of the target compound **8** started with bromination of 9-methyladenine (**10**),[17] as shown in Chart 1. Treatment of **10** with Br_2 in 0.5 M acetate buffer (pH 4) in a manner similar to that reported by Ikehara's group[18]





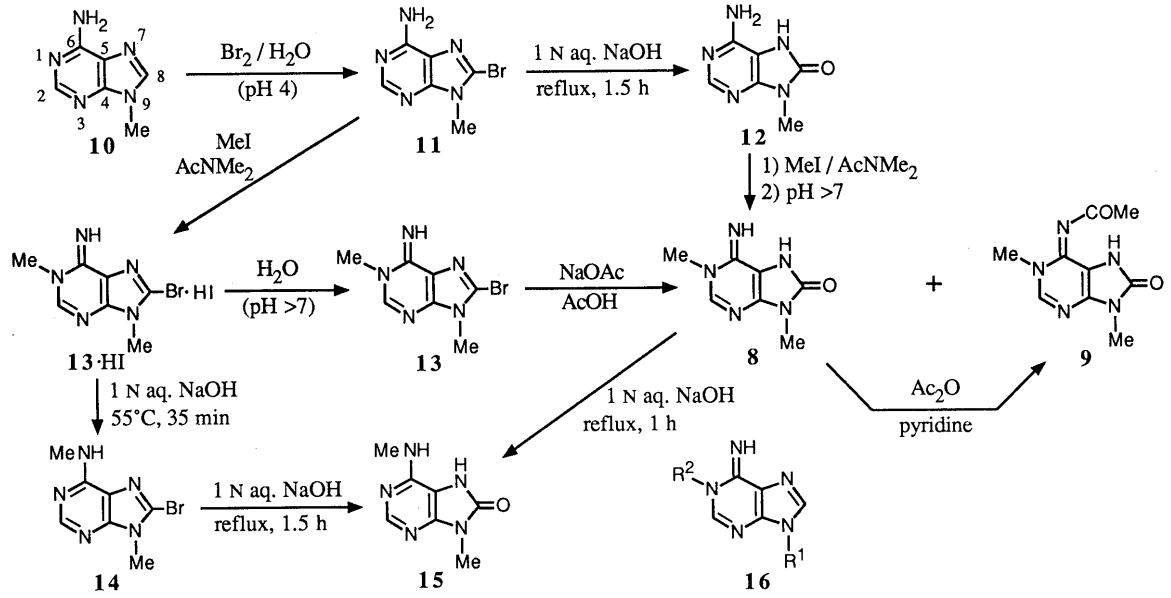


Chart 1

afforded the 8-bromo derivative **11** in 87% yield. It is well known that an alkyl group at the 9-position of adenine itself, as in the case of the methyl group in **10**, orients further alkylation to the 1-position to form 1,9-dialkyladenine (type **16**).[19] If such directivity in alkylation holds in the case of the 8-bromo derivative **11**, the desired 1,9-dimethyl derivative **13** would be accessible from **11** by methylation. In practice, methylation of **11** with MeI in $AcNMe_2$ at 50 °C for 3.5 h produced **13**·HI in 99% yield. On treatment with aqueous Na_2CO_3, the salt **13**·HI was converted into the free base **13** in 80% yield. The structural assignment of **13** was derived from its ultraviolet (UV) spectra in 95% (v/v) aqueous EtOH and in H_2O at various pH's, which were similar to those[19h] of 1,9-dialkyladenines (type **16**), and from the Dimroth rearrangement of **13**·HI to the N^6,9-dimethyl isomer **14**.[20] The rearrangement of **13**·HI was effected in 1 N aqueous NaOH at 55 °C for 35 min, giving **14** in 88% yield. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **14** in dimethyl sulfoxide-d_6 exhibited signals at δ 2.96 [3H, dull d, J=4 Hz, C(6)-NHMe], 3.66 [3H, s, N(9)-Me], 7.83 [1H, br, C(6)-NH-Me], and 8.21 [1H, s, C(2)-H]. The observation of the presence of a vicinal interproton coupling with J=4 Hz in the C(6)-NHMe system supported the correctness of the 6-methylamino structure of **14**. Under more vigorous conditions (1 N aqueous NaOH, reflux, 1.5 h), the 8-bromo derivative **14** was further converted into the 8-oxo derivative **15** in 72% yield. The 8-oxo form of **15** was inferred from its infrared (IR) spectrum in a Nujol mull, which showed two NH absorption bands at 3370 and 3190 cm^{-1} and a carbonyl absorption band at 1695 cm^{-1}.[21]

On the other hand, treatment of **13** with NaOAc in boiling AcOH for 5 h furnished the target compound **8** (mp > 300 °C) and the N^6-acetyl derivative **9** in 36% and 34% yields, respectively. The UV, IR, and ^{1}H-NMR spectral data obtained from the synthetic **9** were in agreement with those reported[15] for a "natural" sample. The correctness of the 1,9-dimethyl structure of **8** was confirmed by acetylation (Ac_2O/pyridine, reflux, 10 min) leading to **9** (81% yield) and by the Dimroth rearrangement (1 N aqueous NaOH, reflux, 1 h) to form **15** (90% yield), which was identical with a sample derived from **14** (*vide supra*). However, attempts to obtain **8** from **9** by selective hydrolysis were all unsuccessful. As in the case of **9**, the existence of **8** in the 8-oxo form was indicated by the appearance of a carbonyl absorption band at 1694 cm^{-1} in the IR spectrum taken in a Nujol mull.[21] The transformation of the 8-bromo function into the 8-oxo function achieved in the above step **13**→**8**+**9** has precedents in that Ikehara's group[22] prepared 8-oxoadenosine derivatives from 8-bromoadenosine derivatives under similar reaction conditions. In this transformation, a large portion of the substrate **13** must be protonated in AcOH solution,[23] giving **13**·H^+ as shown in Chart 2. The nucleophilic aromatic substitution at C(8) of **13**·H^+ would then be facilitated by the positive charge in the ring system. The resulting 8-acetoxy derivative **17**·H^+ may be regarded as an activated acetic ester and would produce acetic anhydride and the 8-oxo derivative **8** on attack by acetate ion, which is present in large quantity. Part of both products thus generated would then react to effect acetylation at the N^6 atom of **8**, and this would account for the formation of the N^6-acetyl derivative **9** as a by-product. In a similar conversion of an 8-bromoadenosine derivative into the corresponding 8-oxoadenosine derivative, Ikehara and Kaneko[22c] observed partial acetylation of the amino and hydroxy groups. Their observation may also be explained in terms of a sequence of processes analogous to that depicted in Chart 2.

The usual regioselectivity found in the above methylation of the 8-bromo derivative **11** led us to expect the same in methylation of the 8-oxo derivative **12**. In order to check this possibility, **12** was prepared in 97% yield from **11** by treatment with boiling 1 N aqueous NaOH for 1.5 h. The assignment of the 8-oxo structure to **12** was based on its IR spectrum in the solid state, which displayed a carbonyl absorption band at 1712 cm^{-1}.[21] On methylation with MeI in $AcNMe_2$ at 50 °C for 7 h, **12** gave, after basification, the desired compound **8** in 75% yield. Thus, this second three-step approach to **8** from **10** through **11** and **12** was

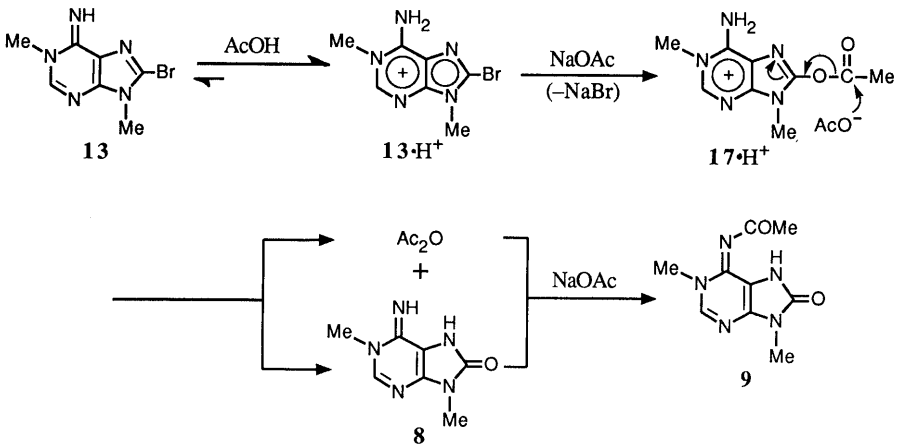


Chart 2

found to be more straightforward, simpler to operate, and more efficient (63% overall yield from **10**) than the first four-step approach **10**→**11**→**13**·HI→**13**→**8** (25% overall yield from **10**).

In conclusion, the present results have made it possible to characterize fully the title compound **8** itself, in advance of the yet unrealized isolation of this substance from natural sources. Interestingly, the known regioselectivity in methylation of 9-methyladenine (**10**) also holds in the cases of the 8-bromo and 8-oxo derivatives (**11** and **12**), and this has permitted a concise total synthesis of **8** for the first time. It is also interesting to note that the Dimroth rearrangement of the 8-oxopurine **8** to **15** seems to require more vigorous reaction conditions than that of the 8-bromopurine **13**·HI to **14**. In view of the broad spectrum of biological activities exhibited by the unusual purine derivatives from various marine sponges (*vide supra*), we are now in the process of testing the synthetic 8-oxopurine **8** and related compounds for biological and pharmacological activities.

Experimental

General Notes All melting points were taken on a Yamato MP-1 capillary melting point apparatus and are corrected. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} plates (0.25-mm thickness), Merck aluminum oxide F_{254} (type E) plates (0.25 mm), or Funakoshi Avicel SF-2020F plates, and spots were located under UV light (254 nm). Spectra reported herein were recorded on a Hitachi model 320 UV spectrophotometer [on solutions in MeOH, 95% (v/v) aqueous EtOH, 0.1 N aqueous HCl (pH 1), 0.005 M phosphate buffer (pH 7), and 0.1 N aqueous NaOH (pH 13)], a JASCO A-202 IR spectrophotometer, a Hitachi M-80 mass spectrometer, or a JEOL JNM-FX-100 NMR spectrometer at 25 °C with Me_4Si as an internal standard. Elemental analyses were performed by Mr. Y. Itatani and his associates at Kanazawa University. The following abbreviations are used: br = broad, d = doublet, DMSO = dimethyl sulfoxide, m = multiplet, q = quartet, s = singlet, sh = shoulder.

8-Bromo-9-methyladenine (11) 3-Methyladenine (**10**)[17a,d] (18.64 g, 0.125 mol) was dissolved in 0.5 M NaOAc–AcOH buffer (pH 4) (625 ml) by application of heat. The resulting solution was cooled to room temperature, and a solution of Br_2 (39.95 g, 0.25 mol) in H_2O (2.44 l) was added dropwise with stirring over a period of 100 min. After the mixture had been stirred at room temperature for 5 h, the reaction was quenched by adding a solution of $NaHSO_3$ (18.8 g, 0.18 mol) in H_2O (400 ml). The resulting mixture was brought to pH 5 with 10% aqueous Na_2CO_3 and then kept in a refrigerator for 2 d. The precipitate that resulted was filtered off, washed with H_2O, and dried to give **11** (24.68 g, 87%) as a pale yellowish solid, mp 265—267 °C (dec.). Recrystallization from EtOH yielded an analytical sample as faintly yellowish prisms, mp 274—275 °C (dec.) [lit.[18b] mp 229 °C (dec.) for **11**·1/4H_2O]; MS *m/z*: 229, 227 (M^+); UV $\lambda_{max}^{95\%\,EtOH}$ 266.5 nm (ε 15000); $\lambda_{max}^{H_2O}$ (pH 1) 265 (16900); $\lambda_{max}^{H_2O}$ (pH 7) 267 (16000); $\lambda_{max}^{H_2O}$ (pH 13) 267 (16000); IR ν_{max}^{Nujol} cm^{-1}: 3350, 3175 (NH_2); NMR (DMSO-d_6) δ: 3.65 [3H, s, N(9)-Me], 7.33 (2H, br, NH_2), 8.12 [1H, s, C(2)-H]. *Anal.* Calcd for $C_6H_6BrN_5$: C, 31.60; H, 2.65; N, 30.71. Found: C, 31.49; H, 2.58; N, 30.53.

9-Methyl-8-oxoadenine (12) A stirred mixture of **11** (5.02 g, 22 mmol) and 1 N aqueous NaOH (220 ml) was heated under reflux for 1.5 h. After cooling, the reaction mixture was brought to pH 7 by addition of 10% aqueous HCl and then cooled in an ice bath for 1.5 h. The pale brownish crystals that deposited were filtered off, washed with cold H_2O, and dried to give **12** (3.52 g, 97%), mp > 300 °C. Recrystallization from H_2O afforded an analytical sample as colorless prisms, mp > 300 °C; MS *m/z*: 165 (M^+); UV $\lambda_{max}^{95\%\,EtOH}$ 271 nm (ε 13000); $\lambda_{max}^{H_2O}$ (pH 1) 270 (sh) (10300), 280 (10700); $\lambda_{max}^{H_2O}$ (pH 7) 271 (13000); $\lambda_{max}^{H_2O}$ (pH 13) 280 (14900); IR ν_{max}^{Nujol} cm^{-1}: 3415, 3250, 3135 (NH_2 and NH), 1712 (CO); NMR (DMSO-d_6) δ: 3.22 [3H, s, N(9)-Me], 6.35 (2H, dull, NH_2), 8.01 [1H, s, C(2)-H], 10.09 [1H, dull, N(7)-H]. *Anal.* Calcd for $C_6H_7N_5O$: C, 43.64; H, 4.27; N, 42.40. Found: C, 43.65; H, 4.24; N, 42.47.

6-Imino-1,9-dimethyl-8-oxopurine (8) A mixture of **12** (1.98 g, 12 mmol) and MeI (8.52 g, 60 mmol) in $AcNMe_2$ (20 ml) was stirred at 50 °C for 7 h. The reaction mixture was cooled in an ice bath for 30 min, and the precipitate that resulted was filtered off, washed successively with a little EtOH and ether, and dried to furnish a colorless solid (3.54 g), mp 281—283 °C (dec.), presumed to be the hydriodide **8**·HI. The solid was dissolved in warm H_2O (100 ml), and the resulting aqueous solution was made alkaline (pH 9) with 10% aqueous Na_2CO_3 and kept in a refrigerator overnight. The colorless needles that deposited were filtered off, washed with a little H_2O, and dried over P_2O_5 at 2 mmHg and 75 °C for 6 h to provide the free base **8** (1.62 g, 75%), mp > 300 °C. This sample was identical (by comparison of the IR spectrum and TLC mobility) with the anhydrous one obtained from **13** by nucleophilic aromatic substitution of the 8-bromo group (*vide infra*).

6-Acetylimino-1,9-dimethyl-8-oxopurine (9) A stirred mixture of **8** (896 mg, 5 mmol) and Ac_2O (610 mg, 6 mmol) in pyridine (15 ml) was heated under reflux for 10 min. After cooling, the reaction mixture was kept in an ice bath for 1 h, and the precipitate that resulted was filtered off, washed successively with a little AcOEt and EtOH, and dried to yield **9** (899 mg, 81%) as a faintly yellowish solid, mp 247.5—249.5 °C (dec.). Recrystallization from AcOEt gave an analytical sample as colorless needles, mp 248—250 °C (dec.) (lit.[15] mp 245—246 °C); MS *m/z*: 221 (M^+); UV λ_{max}^{MeOH} 236 nm (ε 17300), 326 (15600); $\lambda_{max}^{95\%\,EtOH}$ 238 (19600), 290 (sh) (4800), 328 (17200); $\lambda_{max}^{H_2O}$ (pH 1) 226 (23000), 302.5 (15600); $\lambda_{max}^{H_2O}$ (pH 7) 234 (19300), 319 (17200); $\lambda_{max}^{H_2O}$ (pH 13) 227 (21000), 316.5 (14200); IR ν_{max}^{Nujol} cm^{-1}: 3400 (br, NH), 1711 (endocyclic CO), 1655 (NCOMe); $\nu_{max}^{CHCl_3}$ (at 0.05 M concentration) cm^{-1}: 3320 (br, NH), 1730 (endocyclic CO), 1645 (NCOMe), 1580, 1500, 1400, 1380; NMR (DMSO-d_6) δ: 2.09 (3H, s, COMe), 3.28 (3H, s, NMe), 3.68 (3H, s, NMe), 8.61 [1H, s, C(2)-H], 9.5—10.6 [1H, br, N(7)-H]; NMR ($CDCl_3$) δ: 2.26 (3H, s, COMe), 3.43 (3H, s, NMe), 3.82 (3H, s, NMe), 8.11 [1H, s, C(2)-H]. *Anal.* Calcd for $C_9H_{11}N_5O_2$: C, 48.87; H, 5.01; N, 31.66. Found: C, 48.73; H, 5.00; N, 31.59. The MS, UV (MeOH), IR ($CHCl_3$), and ^{1}H-NMR ($CDCl_3$) spectra of this sample were in agreement with those reported[15] for a "natural" sample of **9**.

8-Bromo-6-imino-1,9-dimethylpurine Hydriodide (13·HI) A mixture of **11** (4.10 g, 18 mmol) and MeI (12.77 g, 90 mmol) in $AcNMe_2$ (30 ml) was

stirred at 50 °C for 3.5 h. After cooling, the reaction mixture was kept in an ice bath for 30 min, and the precipitate that resulted was filtered off, washed with a little EtOH, and dried to give **13**·HI (6.60 g, 99%) as a colorless solid, mp 243—245 °C (dec.). Recrystallization from 95% (v/v) aqueous EtOH yielded an analytical sample as colorless prisms, mp 244—246 °C (dec.); UV $\lambda_{max}^{95\%\,EtOH}$ 265 nm (ε 15700); $\lambda_{max}^{H_2O}$ (pH 1) 265 (16500); $\lambda_{max}^{H_2O}$ (pH 7) 265 (16500); $\lambda_{max}^{H_2O}$ (pH 13) 265 (13900), 300 (sh) (4200); NMR (DMSO-d_6) δ: 3.76 and 3.79 (3H each, s, NMe's), 8.71 [1H, s, C(2)-H], 9.17 and 10.00 (1H each, br, $=NH_2^+$). *Anal.* Calcd for $C_7H_8BrN_5 \cdot HI$: C, 22.72; H, 2.45; N, 18.93. Found: C, 22.72; H, 2.40; N, 18.90.

8-Bromo-6-imino-1,9-dimethylpurine (13) A solution of **13**·HI (4.07 g, 11 mmol) in warm H_2O (60 ml) was brought to pH 11 by addition of 10% aqueous Na_2CO_3, and the mixture was immediately cooled in an ice bath. The colorless crystals that deposited were filtered off, washed with a little H_2O, and dried to give **13** (2.12 g, 80%), mp 204—219 °C. Recrystallization from AcOEt afforded an analytical sample as colorless prisms, mp 216.5—218 °C; MS *m/z*: 243, 241 (M^+); UV $\lambda_{max}^{95\%\,EtOH}$ 264 nm (ε 13300), 290.5 (sh) (4900); $\lambda_{max}^{H_2O}$ (pH 1) 265 (15900); $\lambda_{max}^{H_2O}$ (pH 7) 265 (15900); $\lambda_{max}^{H_2O}$ (pH 13) 264 (13700), 295 (sh) (4800); IR ν_{max}^{Nujol} 3255 cm^{-1} (NH); NMR (DMSO-d_6) δ: 3.44 and 3.59 (3H each, s, NMe's), 7.23 (1H, br, NH), 8.09 [1H, s, C(2)-H]. *Anal.* Calcd for $C_7H_8BrN_5$: C, 34.73; H, 3.33; N, 28.93. Found: C, 34.69; H, 3.20; N, 29.17.

Conversion of 13 into 8 and 9 Anhydrous NaOAc (dried over P_2O_5 at 2 mmHg and 75 °C for 6 h) (6.15 g, 75 mmol) was dissolved in AcOH (150 ml) by application of heat, and then **13** (1.21 g, 5 mmol) was added. The mixture was heated under reflux for 5 h, and the reaction mixture was concentrated *in vacuo* to leave a pale brownish residue, which was dissolved in H_2O (150 ml). The resulting solution was passed through a column of Dowex 50W-X8 (H^+) (175 ml), and the column was eluted with H_2O (*ca.* 1 l) until the eluate became neutral, followed by 3% aqueous NH_3 (*ca.* 1.4 l). The ammoniacal eluate was concentrated *in vacuo* to leave a pale yellowish solid (1.16 g). After having been dried over P_2O_5 at 2 mmHg and 75 °C for 6 h, the solid was continuously extracted with AcOEt for 24 h by using a Soxhlet extractor. The AcOEt extract was concentrated *in vacuo*, and the residue was recrystallized from AcOEt to give **9** (378 mg, 34%) as colorless needles, mp 248—249.5 °C (dec.). This sample was identical (by comparison of the IR spectrum and TLC behavior) with the one obtained from **8** by acetylation (*vide supra*).

On the other hand, the insoluble solid left in the above AcOEt extraction was recrystallized from EtOH–H_2O (90 : 1, v/v), and the almost colorless crystals that resulted were filtered off and dried over P_2O_5 at 2 mmHg and 75 °C for 15 h to furnish **8** (319 mg, 36%), mp > 300 °C. Further recrystallization from EtOH and drying in the same manner produced an analytical sample of **8** as colorless needles, mp > 300 °C; MS *m/z*: 179 (M^+); UV $\lambda_{max}^{95\%\,EtOH}$ 291.5 nm (ε 12300); $\lambda_{max}^{H_2O}$ (pH 1) 221 (28000), 278 (10400); $\lambda_{max}^{H_2O}$ (pH 7) 220 (24500), 285 (12000); $\lambda_{max}^{H_2O}$ (pH 13) 280 (14600), 310 (sh) (4800); IR ν_{max}^{Nujol} cm^{-1}: 3380, 3270, 3230 (NH's), 1694 (CO); NMR (CF_3CO_2D) δ: 3.66 and 4.10 (3H each, s, NMe's), 8.58 [1H, s, C(2)-H]. *Anal.* Calcd for $C_7H_9N_5O$: C, 46.92; H, 5.06; N, 39.09. Found: C, 46.77; H, 5.10; N, 38.92. This sample was identical (by comparison of the IR spectrum and TLC mobility) with the one obtained from **12** by methylation (*vide supra*) and was found to be slightly hygroscopic, forming a hydrate, mp > 300 °C. On the basis of elemental analysis, the hydrate was estimated to contain *ca.* 1.75 equivalent mole of H_2O of crystallization.

8-Bromo-N^6,9-dimethyladenine (14) A mixture of **13**·HI (370 mg, 1 mmol) and 1 N aqueous NaOH (5 ml) was stirred at 55 °C for 35 min. The reaction mixture was kept in a refrigerator overnight, and the colorless prisms that deposited were filtered off, washed with H_2O, and dried to give **14** (213 mg, 88%), mp 185—186.5 °C. Recrystallization from AcOEt provided an analytical sample as colorless prisms, mp 186.5—188 °C; MS *m/z*: 243, 241 (M^+); UV $\lambda_{max}^{95\%\,EtOH}$ 273 nm (ε 17000); $\lambda_{max}^{H_2O}$ (pH 1) 270 (20300); $\lambda_{max}^{H_2O}$ (pH 7) 274 (17900); $\lambda_{max}^{H_2O}$ (pH 13) 274 (17700); IR ν_{max}^{Nujol} 3335 cm^{-1} (NH); NMR (see the text). *Anal.* Calcd for $C_7H_8BrN_5$: C, 34.73; H, 3.33; N, 28.93. Found: C, 34.53; H, 3.19; N, 29.00.

N^6,9-Dimethyl-8-oxoadenine (15) i) From **14**: A stirred mixture of **14** (968 mg, 4 mmol) and 1 N aqueous NaOH (40 ml) was heated under reflux for 1.5 h. After cooling, the reaction mixture was neutralized by addition of 10% aqueous HCl, concentrated *in vacuo* to a small volume, and kept in a refrigerator overnight. The colorless precipitate that resulted was filtered off, washed with H_2O, and dried to afford crude **15** (770 mg), mp > 300 °C. Recrystallization from EtOH produced **15** (514 mg, 72%) as colorless needles, mp > 300 °C. Further recrystallization from EtOH yielded an analytical sample, mp > 300 °C; MS *m/z*: 179 (M^+); UV $\lambda_{max}^{95\%\,EtOH}$ 274 nm (ε 16500); $\lambda_{max}^{H_2O}$ (pH 1) 275 (14100); $\lambda_{max}^{H_2O}$ (pH 7) 274 (17000); $\lambda_{max}^{H_2O}$ (pH 13) 284 (18000); IR (see the text); NMR (DMSO-d_6) δ: 2.94 (3H, d, J = 5 Hz, NHMe), 3.22 [3H, s, N(9)-Me], 6.39 (1H, q, J = 5 Hz, NHMe), 8.10 [1H, s, C(2)-H], 10.07 [1H, dull, N(7)-H]. *Anal.* Calcd for $C_7H_9N_5O$: C, 46.92; H, 5.06; N, 39.09. Found: C, 46.79; H, 5.09; N, 39.36.

ii) From **8**: A stirred mixture of **8** (1.08 g, 6 mmol) and 1 N aqueous NaOH (30 ml) was heated under reflux for 1 h. The reaction mixture was worked up in a manner similar to that described above for **15** under method (i), giving **15** (977 mg, 90%) as a colorless solid, mp > 300 °C. Recrystallization from EtOH produced a pure sample as colorless needles, mp > 300 °C. This sample was identical (by comparison of the IR spectrum and TLC behavior) with the one obtained by method (i).

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