

## Purines. LIX.<sup>1)</sup> An Alternative Synthesis of 7-Alkyl-1-methyladenines by Regioselective Alkylation, Fission, and Reclosure of the Adenine Ring

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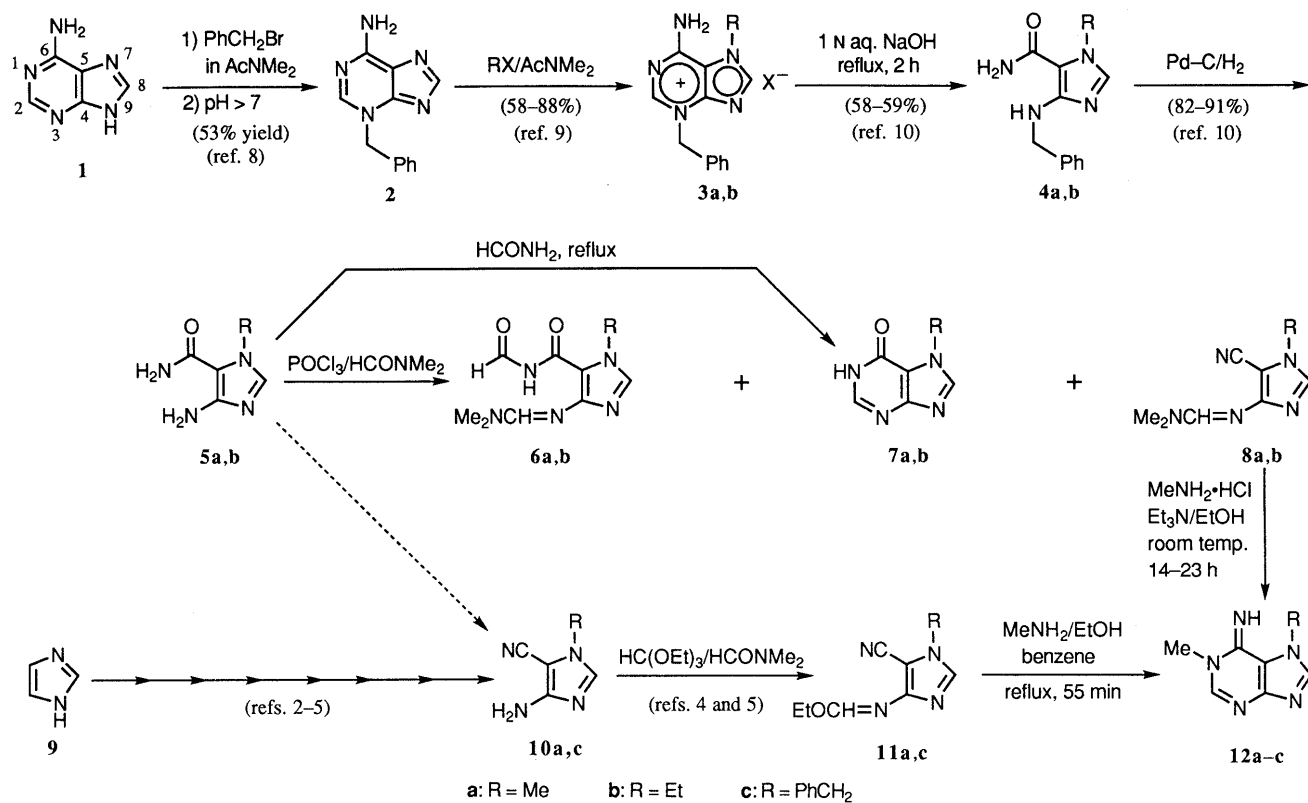
7-Alkyl-1-methyladenines (**12a, b**) have been synthesized from 1-alkyl-4-aminoimidazole-5-carboxamides (**5a, b**) in two steps [hence from adenine (**1**) in six steps]. The synthesis started with dehydration (using  $\text{POCl}_3\text{-HCONMe}_2$ ) of **5a, b**, readily obtainable from **1** in four steps according to previously reported procedures, and proceeded through cyclization between the resulting 4-(dimethylaminomethyleneamino)imidazole-5-carbonitrile derivatives (**8a, b**) and  $\text{MeNH}_2$ . Similar cyclization between 1-benzyl-4-(ethoxymethyleneamino)imidazole-5-carbonitrile (**11c**) and  $\text{MeNH}_2$  yielded 7-benzyl-1-methyladenine (**12c**).

**Keywords** 7-alkyl-1-methyladenine; carboxamide dehydration; Vilsmeier reagent; imidazolecarbonitrile; dimethylamino-methyleneamino group; cyclization

For the reason cited in our recent publication,<sup>1)</sup> we needed to prepare 1,7-dimethyladenine (**12a**), 7-ethyl-1-methyladenine (**12b**), and 7-benzyl-1-methyladenine (**12c**). The first and second compounds (**12a, b**) have recently been synthesized by us<sup>1)</sup> from adenosine *via* a seven-step route featuring regioselective alkylation controlled by a methoxy group at the N(1)- or N<sup>6</sup>-position. This synthetic route represents an alternative to the general nine-step synthesis of 1,7-dialkyladenines (type **12**) from imidazole (**9**)<sup>2,3)</sup> [through 1-alkyl-4-aminoimidazole-5-carbonitrile (**10**) and the ethoxymethyleneamino derivative **11** (Chart 1)], which was first devised by Taylor's group<sup>4)</sup> and later extended by Leonard's<sup>5)</sup> and Mornet's<sup>6)</sup> groups. In the present work, yet another approach for the synthesis of

the requisite **12a** and **12b** was designed on the basis of our favorite "fission and reclosure" technology<sup>7)</sup> for modification of the adenine ring (**1**), and the Taylor-Leonard's procedure<sup>4,5)</sup> was applied to the preparation of **12c**.

The starting point selected for the synthesis of the first target, 1,7-dimethyladenine (**12a**), was 4-amino-1-methylimidazole-5-carboxamide (**5a**), which was obtainable from adenine (**1**) in four steps *via* 3-benzyladenine (**2**),<sup>8)</sup> 3-benzyl-7-methyladenine hydriodide (**3a**: X=I),<sup>9)</sup> and 4-benzylamino-1-methylimidazole-5-carboxamide (**4a**)<sup>10)</sup> according to previously reported procedures.<sup>10)</sup> In an attempt to connect this ring-fission route to the above Taylor's route, direct conversion of **5a** into **10a** was first



tried. However, dehydration experiments with  $5a \cdot HClO_4$  using  $POCl_3$  (with or without  $Et_3N$ ) under a variety of conditions were all unsuccessful.

Albert has reported that treatment of 4-amino-1-methyl-1,2,3-triazole-5-carboxamide with  $POCl_3$  in  $HCONMe_2$  at  $25^\circ C$  gave 4-dimethylaminomethyleneamino-1-methyl-1,2,3-triazole-5-carbonitrile (60% yield), together with its *N*-formyl-5-carboxamide derivative (6%).<sup>11</sup> This procedure would be applicable to the dehydration of **5a** if the possible concurrent modification of the 4-amino group is permissible. On treatment with  $POCl_3$  in  $HCONMe_2$  below  $35^\circ C$  for *ca.* 3 h,  $5a \cdot HClO_4$  produced 4-dimethylaminomethyleneamino-1-methylimidazole-5-carbonitrile (**8a**) in 70% yield, together with small amounts of 7-methylhypoxanthine (**7a**) and a substance inferred to be the *N*-formyl-5-carboxamide derivative **6a**. The formation of **6a** as a by-product was anticipated from the case<sup>11</sup> of the triazole analogue described above, and the correctness of the structure of **7a** was supported by its identity with a sample obtained from the reaction of  $5a \cdot HClO_4$  with boiling  $HCONH_2$  for 45 min.<sup>12</sup>

Cyclization of **8a** was then effected with  $MeNH_2 \cdot HCl$  in EtOH in the presence of  $Et_3N$  at room temperature for 23 h, and the product was isolated in the form of the perchlorate salt, affording the desired compound  $12a \cdot HClO_4$  in 68% yield (in 12% overall yield from **1**). In this cyclization, replacement of added tertiary amine or all the amine components by  $MeNH_2$  lowered the yield of **12a** to a considerable extent, and application of a higher reaction temperature appeared to cause **12a** to rearrange to isomeric *N*<sup>6</sup>,7-dimethyladenine.<sup>4</sup>

A parallel sequence of reactions starting from the 1-ethyl homologue **5b**, obtainable from **1** through **2**,<sup>8</sup> **3b** ( $X = ClO_4$ ),<sup>9</sup> and **4b**<sup>10</sup> according to the previously reported procedures,<sup>10</sup> was followed for the synthesis of the second target 7-ethyl-1-methyladenine (**12b**). Thus,  $5b \cdot HClO_4$  was treated with Vilsmeier reagent at room temperature for 3 h, giving **8b** in 60% yield, together with substances inferred to be **6b** (*ca.* 1%) and **7b** (*ca.* 1%). The reaction of **8b** with  $MeNH_2 \cdot HCl$  was carried out as described above for **8a**, and the cyclized product was isolated as the perchlorate salt, furnishing  $12b \cdot HClO_4$  in 51% yield (in 4.6% overall yield from **1**).

Finally, the preparation of the third target **12c** from 1-benzyl-4-(ethoxymethyleneamino)imidazole-5-carbonitrile (**11c**)<sup>5</sup> and  $MeNH_2$  was tried according to the general procedure<sup>4</sup> of Taylor and Loeffler. On treatment with 40% ethanolic  $MeNH_2$  in boiling benzene for 55 min, **11c** provided 7-benzyl-1-methyladenine (**12c**) in 93% yield.

In conclusion, the above reaction sequence  $1 \rightarrow 2 \rightarrow 3 \rightarrow 4 \rightarrow 5 \rightarrow 8 \rightarrow 12$  represents a new six-step synthetic route to 7-alkyl-1-methyladenine (**12**) from adenine (**1**). It features a synthetic strategy of utilizing the "fission and reclosure" technology<sup>7</sup> developed for modification of the adenine ring and appears to be potentially applicable as a general procedure to the synthesis of 1,7-dialkyladenines.

#### Experimental

**General Notes** All melting points were taken on a Yamato MP-1 capillary melting point apparatus and are corrected. See ref. 10 for details of instrumentation and measurements. The solvents used for measurements of UV spectra were 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). Elemental analyses were performed by Mr. Y. Itatani and his associates at Kanazawa University. The following abbreviations are used: br = broad, d = doublet, m = multiplet, q = quartet, s = singlet, sh = shoulder, t = triplet.

**Reaction of 4-Amino-1-methyl-1H-imidazole-5-carboxamide Perchlorate ( $5a \cdot HClO_4$ ) with Vilsmeier Reagent** A solution of  $5a \cdot HClO_4$ <sup>10</sup> (4.15 g, 17.2 mmol) in  $HCONMe_2$  (34.5 ml) was stirred in a cooling bath, and then  $POCl_3$  (7.92 g, 51.6 mmol) was added dropwise over a period of 55 min at such a rate that the inner temperature did not exceed  $35^\circ C$ . After having been stirred at room temperature for 2 h, the reaction mixture was poured onto ice-water (*ca.* 17 ml). The resulting aqueous mixture was brought to pH 7 with 10% aqueous  $Na_2CO_3$  and then extracted with  $CHCl_3$  (12  $\times$  50 ml) at that pH. The  $CHCl_3$  extracts were combined, washed with saturated aqueous NaCl, dried over anhydrous  $Na_2SO_4$ , and concentrated *in vacuo* to leave a brownish yellow solid (3.10 g), which was purified by means of column chromatography [silica gel (310 g),  $CH_2Cl_2$ -EtOH (30:1, v/v)]. Earlier fractions gave a substance (75 mg, *ca.* 2%) inferred to be 4-dimethylaminomethyleneamino-*N*(5)-formyl-1-methyl-1H-imidazole-5-carboxamide (**6a**), mp  $122^\circ C$  (dec.); IR  $\nu_{max}^{Nujol} cm^{-1}$ : 3400–3200 (NH), 1721 and 1670 (CONHCO), 1625 (C=N); <sup>1</sup>H-NMR ( $CDCl_3$ )  $\delta$ : 3.12 and 3.14 (6H, s each, N=CH-NMe<sub>2</sub>), 3.91 [3H, s, N(1)-Me], 7.30 [s, C(2)-H], 8.47 (1H, s, N=CH-NMe<sub>2</sub>), 9.30 (1H, d, *J* = 10 Hz, NHCHO), 11.80 (1H, dull d, *J* = 10 Hz, NHCHO).

Middle fractions collected from the above chromatography yielded 4-dimethylaminomethyleneamino-1-methyl-1H-imidazole-5-carbonitrile (**8a**) (2.14 g, 70%) as a yellowish solid, mp 101–104°C. The solid was further purified and characterized as described below.

Later fractions of the above chromatography contained 7-methylhypoxanthine (**7a**). In a separate run, however, **7a** was isolated more efficiently in the following manner. The  $CHCl_3$  extracts of the reaction mixture, obtained as described above, were concentrated *in vacuo*, and the residue was extracted successively with hot benzene-hexane (1:1.5, v/v) and hot benzene (**8a** was obtained in 56% yield from these extracts), leaving an insoluble brown solid. Two recrystallizations of the solid from EtOH gave **7a**, mp  $>300^\circ C$ , in 3.8% yield. This sample was identical (by comparison of the IR and <sup>1</sup>H-NMR spectra) with the one prepared from  $5a \cdot HClO_4$  and  $HCONH_2$  (*vide infra*).

**4-Dimethylaminomethyleneamino-1-methyl-1H-imidazole-5-carbonitrile (**8a**)** The crude sample of **8a** described above was recrystallized from benzene-hexane (1:2, v/v) to yield an analytical sample as slightly yellowish prisms, mp 102–106°C; UV  $\lambda_{max}^{95\% aq. EtOH} nm$  ( $\epsilon$  13000), 291 (21500);  $\lambda_{max}^{H_2O} (pH 1) nm$  (16000);  $\lambda_{max}^{H_2O} (pH 7) nm$  (13800), 288 (20000);  $\lambda_{max}^{H_2O} (pH 13) nm$  (13800), 288 (20200); IR  $\nu_{max}^{Nujol} cm^{-1}$ : 2205 (C≡N), 1625 (br, C=N); <sup>1</sup>H-NMR ( $Me_2SO-d_6$ )  $\delta$ : 2.95 and 3.07 (3H each, s, N=CH-NMe<sub>2</sub>), 3.63 [3H, s, N(1)-Me], 7.64 [1H, s, C(2)-H], 8.34 (1H, s, N=CH-NMe<sub>2</sub>). *Anal.* Calcd for  $C_8H_{11}N_5$ : C, 54.22; H, 6.26; N, 39.52. Found: C, 54.18; H, 6.26; N, 39.23.

**7-Methylhypoxanthine (**7a**)** A stirred suspension of  $5a \cdot HClO_4$ <sup>10</sup> (289 mg, 1.2 mmol) in  $HCONH_2$  (1 ml) was heated under reflux in an atmosphere of  $N_2$  for 45 min. The reaction mixture was concentrated *in vacuo*, and the residual oil was kept in a refrigerator for 2 d. The brown solid that resulted was collected by filtration and recrystallized from EtOH, giving brownish granules (120 mg), mp 242–245°C. Purification of the crystals by means of column chromatography [alumina (10 g),  $CHCl_3$ -MeOH (4:1, v/v)] afforded **7a** (37 mg, 21%), mp  $>300^\circ C$ . Further purification was effected by recrystallization from EtOH to provide an analytical sample as colorless needles, mp  $>300^\circ C$  [lit.<sup>13</sup>] mp 356–357°C (dec.); UV  $\lambda_{max}^{95\% aq. EtOH} nm$  ( $\epsilon$  9100);  $\lambda_{max}^{H_2O} (pH 1) nm$  (10450);  $\lambda_{max}^{H_2O} (pH 7) nm$  (9760);  $\lambda_{max}^{H_2O} (pH 13) nm$  (10500); <sup>1</sup>H-NMR ( $Me_2SO-d_6$ )  $\delta$ : 3.96 [3H, s, N(7)-Me], 7.94 [1H, s, C(2)-H], 8.14 [1H, s, C(8)-H], 12.0–12.4 [1H, br, N(1)-H]. *Anal.* Calcd for  $C_8H_8N_4O_4$ : C, 48.00; H, 4.03; N, 37.32. Found: C, 47.75; H, 3.95; N, 37.24.

**Reaction of 4-Amino-1-ethyl-1H-imidazole-5-carboxamide Perchlorate ( $5b \cdot HClO_4$ ) with Vilsmeier Reagent** *N,N*-Dimethylformamide (2 ml) was stirred under ice-cooling, and  $POCl_3$  (460 mg, 3 mmol) was added dropwise. The mixture was stirred at room temperature for 15 min, then  $5b \cdot HClO_4$ <sup>10</sup> (255 mg, 1 mmol) was added in portions under ice-cooling. The resulting mixture was again stirred at room temperature for 3 h and then poured onto ice (1.3 g). The aqueous mixture was brought to pH 7–8 by addition of anhydrous  $Na_2CO_3$  and extracted with  $CHCl_3$  (3  $\times$  10 ml). The  $CHCl_3$  extracts were combined, washed with saturated aqueous  $K_2CO_3$  (1 ml), dried over anhydrous  $Na_2SO_4$ , and concentrated

*in vacuo* to leave a brownish yellow solid (190 mg), which was subjected to flash chromatography<sup>14)</sup> [silica gel, CH<sub>2</sub>Cl<sub>2</sub>-EtOH (20:1, v/v; 10:1, v/v; and 5:1, v/v)]. Earlier fractions gave a substance (3 mg, ca. 1%) inferred to be 4-dimethylaminomethyleneamino-1-ethyl-N(5)-formyl-1H-imidazole-5-carboxamide (**6b**) as a colorless solid, mp 161–163 °C; IR  $\nu_{\text{max}}^{\text{Nujol}}$  cm<sup>-1</sup>: 3400–3200 (NH), 1720 and 1670 (CONHCO), 1625 (C=N); <sup>1</sup>H-NMR (Me<sub>2</sub>SO-*d*<sub>6</sub>)  $\delta$ : 1.31 [3H, t, *J* = 7 Hz, N(1)-CH<sub>2</sub>Me], 3.01 and 3.15 (3H each, s, H=CH-NMe<sub>2</sub>), 4.25 [2H, q, *J* = 7 Hz, N(1)-CH<sub>2</sub>Me], 7.81 [1H, s, C(2)-H], 8.52 (1H, s, N=CH-NMe<sub>2</sub>), 9.14 (1H, d, *J* = 10 Hz, NHCHO), 12.06 (1H, dull d, *J* = 10 Hz, NHCHO).

Middle fractions of the above chromatography afforded 4-dimethylaminomethyleneamino-1-ethyl-1H-imidazole-5-carbonitrile (**8b**) (115 mg, 60%) as colorless needles, mp 73–75 °C. The crystals were further purified and characterized as described below.

Later fractions collected from the above chromatography gave a substance (2 mg, ca. 1%) inferred to be 7-ethylhypoxanthine (**7b**)<sup>15)</sup> as slightly yellowish needles, mp 227–243 °C; IR  $\nu_{\text{max}}^{\text{Nujol}}$  cm<sup>-1</sup>: 3500–3250 (NH), 1680 (br, CO); <sup>1</sup>H-NMR (Me<sub>2</sub>SO-*d*<sub>6</sub>)  $\delta$ : 1.41 [3H, t, *J* = 7 Hz, N(7)-CH<sub>2</sub>Me], 4.34 [2H, q, *J* = 7 Hz, N(7)-CH<sub>2</sub>Me], 7.97 [1H, slightly dull s, C(2)-H], 8.24 [1H, s, C(8)-H], 12.29 (1H, br, NH).

**4-Dimethylaminomethyleneamino-1-ethyl-1H-imidazole-5-carbonitrile (8b)** The crude sample of **8b** described above was recrystallized from benzene-hexane (1:3, v/v) to furnish an analytical sample as almost colorless needles, mp 76.5–77 °C; UV  $\lambda_{\text{max}}^{95\% \text{ aq. EtOH}}$  223 nm ( $\epsilon$  13300), 291 (22000);  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  (pH 1) 263 (16200);  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  (pH 7) 223 (14100), 289 (21200);  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  (pH 13) 223 (14200), 289 (21300); IR  $\nu_{\text{max}}^{\text{Nujol}}$  cm<sup>-1</sup>: 2205 (C≡N), 1625 (C=N); <sup>1</sup>H-NMR (Me<sub>2</sub>SO-*d*<sub>6</sub>)  $\delta$ : 1.35 [3H, t, *J* = 7 Hz, N(1)-CH<sub>2</sub>Me], 2.94 and 3.05 (3H each, s, N=CH-NMe<sub>2</sub>), 3.98 [2H, q, *J* = 7 Hz, N(1)-CH<sub>2</sub>Me], 7.68 [1H, s, C(2)-H], 8.32 (1H, s, N=CH-NMe<sub>2</sub>). *Anal.* Calcd for C<sub>9</sub>H<sub>13</sub>N<sub>5</sub>: C, 56.53; H, 6.85; N, 36.62. Found: C, 56.46; H, 6.94; N, 36.63.

**1,7-Dimethyladenine (12a)** i) Cyclization of **8a** with MeNH<sub>2</sub>·HCl/Et<sub>3</sub>N: A mixture of Et<sub>3</sub>N (880 mg, 8.7 mmol), MeNH<sub>2</sub>·HCl (2.94 g, 43.5 mmol), and **8a** (1.54 g, 8.7 mmol) in abs. EtOH (80 ml) was stirred at room temperature for 23 h. The reaction mixture was concentrated *in vacuo* to leave a colorless solid. The solid was washed with benzene (3 × 20 ml) and extracted with hot MeOH (2 × 10 ml) to leave an insoluble hygroscopic solid (1.08 g) [mp 224.5–230 °C (dec.)] presumed to be **12a**·HCl. The methanolic extracts were combined and concentrated *in vacuo*, and the residue was chromatographed [alumina (220 g), CH<sub>2</sub>Cl<sub>2</sub>-EtOH (15:1, v/v; 6:1, v/v)] to afford the free base **12a** (210 mg) as a hygroscopic solid, mp 164–165 °C. The free base was converted into the perchlorate salt by dissolving it in warm EtOH (4.5 ml) and adding 70% aqueous HClO<sub>4</sub> (210 mg), giving a first crop (287 mg) of **12a**·HClO<sub>4</sub> as a colorless solid, mp 278–279 °C (dec.).

The crude, MeOH-insoluble **12a**·HCl described above was dissolved in H<sub>2</sub>O (35 ml). The resulting aqueous solution was applied to a column of Amberlite IRA-402 (HCO<sub>3</sub><sup>-</sup>) (11 ml), and the column was eluted with H<sub>2</sub>O (350 ml). The eluate was concentrated *in vacuo* below 30 °C (bath temperature), and the residue was dissolved in hot EtOH (30 ml) after having been dried in a desiccator. The ethanolic solution was treated with 70% aqueous HClO<sub>4</sub> (940 mg) in the usual manner, yielding a second crop (1.26 g) of **12a**·HClO<sub>4</sub> as a colorless solid, mp 278–279 °C (dec.). The total yield of **12a**·HClO<sub>4</sub> was 1.55 g (68% from **8a**). For analysis, the crude **12a**·HClO<sub>4</sub> was recrystallized from MeOH to give a pure sample as colorless needles, mp 278–280 °C (dec.) (dried over P<sub>2</sub>O<sub>5</sub> at 2 mmHg and room temperature for 35 h). *Anal.* Calcd for C<sub>7</sub>H<sub>9</sub>N<sub>5</sub>·HClO<sub>4</sub>: C, 31.89; H, 3.82; N, 26.56. Found: C, 31.80; H, 3.85; N, 26.77. The UV and <sup>1</sup>H-NMR spectral data obtained with this sample were in agreement with those<sup>1)</sup> reported for **12a**·HClO<sub>4</sub>·1/5H<sub>2</sub>O.

ii) Cyclization of **8a** with MeNH<sub>2</sub>·HCl/MeNH<sub>2</sub>: A mixture of **8a** (301 mg, 1.7 mmol), MeNH<sub>2</sub>·HCl (581 mg, 8.6 mmol), and 40% (w/w) ethanolic MeNH<sub>2</sub> (670 mg, 8.63 mmol) in abs. EtOH (7.2 ml) was stirred at 25 °C for 5 h. The reaction mixture was concentrated *in vacuo*, and the residue was dissolved in a small amount of H<sub>2</sub>O. The aqueous solution was applied to a column of Amberlite IRA-402 (HCO<sub>3</sub><sup>-</sup>) (21 ml), and the column was eluted with H<sub>2</sub>O (700 ml). The eluate was concentrated *in vacuo* below 30 °C (bath temperature). The residue was dried and purified by column chromatography [alumina (37 g), CH<sub>2</sub>Cl<sub>2</sub>-EtOH (25:1, v/v)] to give the free base **12a** (69.6 mg, 24%) as a colorless solid, mp 128–172 °C. Five recrystallizations of the solid from benzene and drying over P<sub>2</sub>O<sub>5</sub> at 2 mmHg and 50 °C for 14 h yielded an analytical sample of **12a**·3/5H<sub>2</sub>O as colorless, hygroscopic prisms, mp 163–168 °C

[lit.<sup>4)</sup> mp 170–171 °C (for an anhydrous sample)]; UV  $\lambda_{\text{max}}^{95\% \text{ aq. EtOH}}$  264 nm ( $\epsilon$  10700), 271 (sh) (9900);  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  (pH 1) 269 (9500), 282 (sh) (5300);  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  (pH 7) 269 (9500), 282 (sh) (5300);  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  (pH 13) 264.5 (11100); <sup>1</sup>H-NMR (Me<sub>2</sub>SO-*d*<sub>6</sub>)  $\delta$ : 3.37 [3H, s, N(1)-Me], 4.00 [3H, s, N(7)-Me], 6.84 (1H, br, NH), 7.88 and 7.90 (2H, s each, purine protons). *Anal.* Calcd for C<sub>7</sub>H<sub>9</sub>N<sub>5</sub>·3/5H<sub>2</sub>O: C, 48.32; H, 5.91; N, 40.25. Found: C, 48.55; H, 5.91; N, 40.16.

**7-Ethyl-1-methyladenine (12b)** A mixture of Et<sub>3</sub>N (1.67 g, 16.5 mmol), MeNH<sub>2</sub>·HCl (5.57 g, 82.5 mmol), and **8b** (3.16 g, 16.5 mmol) in abs. EtOH (165 ml) was stirred at 25–27 °C for 14 h and then cooled in an ice bath for 1 h. The colorless precipitate that resulted was filtered off, washed with a little EtOH, and dried to give crude **12b**·HCl (2.08 g), mp 255–258 °C (dec.), which was dissolved in H<sub>2</sub>O (30 ml). The aqueous solution was applied to a column of Amberlite IRA-402 (HCO<sub>3</sub><sup>-</sup>) (19.5 ml), and the column was eluted with H<sub>2</sub>O (500 ml). Concentration of the eluate under reduced pressure below 30 °C (bath temperature) and drying of the residue over P<sub>2</sub>O<sub>5</sub> at 3 mmHg and 35 °C for 24 h gave the free base **12b** (1.83 g) as a colorless solid, mp 210–227 °C. The whole of the dried solid was dissolved in hot MeOH (20 ml), and 70% aqueous HClO<sub>4</sub> (1.64 g) was added. The resulting mixture was kept in a refrigerator overnight, and the colorless minute needles that deposited were collected by filtration, washed with a little EtOH, and dried to provide the perchlorate salt **12b**·HClO<sub>4</sub> (2.35 g, 51% from **8b**), mp 259–260 °C (dec.). This sample was identical (by comparison of the UV and IR spectra) with authentic **12b**·HClO<sub>4</sub>.<sup>1)</sup>

**7-Benzyl-1-methyladenine (12c)** A solution of **11c**<sup>5)</sup> (418 mg, 1.64 mmol) in benzene (8 ml) was stirred at room temperature, and 40% (w/w) ethanolic MeNH<sub>2</sub> (2.48 g) was added. The resulting solution was heated under reflux for 55 min and then cooled to room temperature. After addition of hexane (15 ml), the reaction mixture was kept in a refrigerator overnight. The slightly pinkish needles that deposited were collected by filtration to give the base **12c** (366 mg, 93%), mp 183.5–190 °C. Recrystallization from AcOEt afforded an analytical sample of **12c** as slightly yellowish prisms, mp 190–192 °C; UV  $\lambda_{\text{max}}^{95\% \text{ aq. EtOH}}$  265 nm ( $\epsilon$  10100), 271 (sh) (9600);  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  (pH 1) 272 (9300), 282 (sh) (6100);  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  (pH 7) 268 (9600), 282 (sh) (6100);  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  (pH 13) 265 (10800); <sup>1</sup>H-NMR (Me<sub>2</sub>SO-*d*<sub>6</sub>)  $\delta$ : 3.36 [3H, s, N(1)-Me], 5.71 [2H, s, N(7)-CH<sub>2</sub>Ph], 6.76 (1H, br, NH), 7.29 [5H, m, N(7)-CH<sub>2</sub>Ph], 7.93 and 8.13 (1H each, s, purine protons). *Anal.* Calcd for C<sub>13</sub>H<sub>13</sub>N<sub>5</sub>: C, 65.26; H, 5.48; N, 29.27. Found: C, 65.19; H, 5.30; N, 29.22.

## References and Notes

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