

6,7-DIMETHYLPURINE

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Abstract: The previously unreported 6,7-dimethylpurine was obtained in low yield by methylation of the anion of 6-methylpurine.

Methylation of 6-methylpurine with dimethyl sulfate in methanolic KOH was reported to yield 3,6- and 6,9-dimethylpurines (1). When that procedure was followed for the synthesis of the latter for other studies (2), a small quantity of a third product was isolated. The mass spectrum of the product showed a major peak at  $m/e$  148 and two methyl and two C-H resonances were evident in the NMR spectrum. These data indicate the product must be a third N-methyl derivative of 6-methylpurine. Since neither of the two possible alternatives, 1,6- or 6,7-dimethylpurine, has been reported (3), we have characterized the product and now report that it is 6,7-dimethylpurine. The product can be assigned this structure,

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rather than that of the isomeric 1,6-derivative, by the resemblance of its UV absorption to that of 7-methylpurine, rather than to that of 1-methylpurine (Table 1) and by the closeness of its pK of protonation,  $2.68 \pm 0.06$  (4), to those of 6-methylpurine, 2.6 (5), and 6,9-dimethylpurine 3.2 (1), in contrast to those of 3,6-dimethylpurine, 4.8 (1), and 1-ethylpurine, 5.08 (6) (Table 1).

Table 1

Ultraviolet Absorption Maxima of Neutral Species  
of 6-Methylpurines, nm

	-	1-CH <sub>3</sub>	3-CH <sub>3</sub>	7-CH <sub>3</sub>	9-CH <sub>3</sub>
Purine(a)	263	275	276	267	264
6-Methylpurine	261(a)	-	274(b)	264	262(b)

<sup>a</sup> Values from J.H. Lister, *in* Fused Pyrimidines, Part 11 Purines (D.J. Brown, ed.), ch. XIII, Wiley Interscience, New York, 1971, p. 439.

<sup>b</sup> Reference 1.

Further confirmation was provided by examination of the difference in chemical shifts between the 2- and 8-protons of the three dimethylpurines. The 1- and 3-alkyl derivatives of purines are reported to manifest larger  $\Delta\delta$  values than the 7- and 9-alkyl derivatives (7). In  $(\text{CD}_3)_2\text{SO}$ , 6,7-dimethylpurine showed a small  $\Delta\delta$  comparable to those of 6-methyl- and 6,9-dimethylpurine and considerable smaller than the  $\Delta\delta$  for 3,6-dimethylpurine (Table 2). Values for adenine and 6-methylaminopurine derivatives are included in Table 2 for comparison.

Table 2  
Difference in Chemical Shift for 2- and 8-Protons

	$\Delta\delta$ , cps	$\Delta\delta$ , cps			
		1-CH <sub>3</sub>	3-CH <sub>3</sub>	7-CH <sub>3</sub>	9-CH <sub>3</sub>
6-Methylpurine(a)	14	-	32	15	19
Adenine(a,b)	2(c)	26	28	6	3
6-Dimethylamino-purine(a,b)	8	22	32	2	11
C-Methyl resonances(a)	275	-	277	285	271

a Spectra run in DMSO-d<sub>6</sub> with TMS as internal standard.

b Reference 7.

c Spectrum run in CF<sub>3</sub>CO<sub>2</sub>H.

Table 2 also shows the C-methyl resonances for the three dimethylpurines and for 6-methylpurine. It is evident that the C-methyl resonance of 6,7-dimethylpurine is shifted approximately 10 cps downfield from those of the other compounds. This is slightly less than the 20 cps downfield shift observed for the methyl resonances of 1,8-dimethylnaphthalene, relative to that of 1-methylnaphthalene (8), but the small downfield shift indicates that there is a measurable repulsive interaction between the two methyl groups in 6,7-dimethylpurine. The mass spectral fragmentation patterns of the three isomeric dimethylpurines were quite similar, with each compound showing small fragments at masses corresponding to loss of a proton (M-1), a methyl group (M-15), and a larger fragment at M-28, corresponding to loss of -CH<sub>2</sub>-N.

## EXPERIMENTAL (9)

6,7-Dimethylpurine. Following alkylation of 6-methylpurine by the reported procedure (1), 6,7-dimethylpurine (5%) was isolated by continued elution of the alumina column with  $\text{CHCl}_3$  after 6,9-dimethylpurine (34%) and 3,6-dimethylpurine (14%) had been removed. The sample was rechromatographed over neutral alumina (Activity Grade III), eluting with  $\text{CHCl}_3$  to remove colored impurities before analysis, mp 228-230<sup>o</sup>.

Anal. Calcd for  $\text{C}_7\text{H}_8\text{N}_4$ : C, 56.74; H, 5.44; N, 37.81.

Found: C, 56.76; H, 5.40; N, 37.87.

NMR ( $\text{DMSO-d}_6$ )  $\delta$  2.90 (s, 3, C- $\text{CH}_3$ ), 4.13 (s, 3, N- $\text{CH}_3$ ), 8.23 (s, 1) and 8.50 (s, 1);  $\lambda_{\text{max}}$  ( $\epsilon$ ): pH 0, 209 (18,000), 259 nm (6,600); pH 7, 202 (19,800), 264 (7,500); mass spectrum m/e 148 (M), 147 (M-H), 133 (M- $\text{CH}_3$ ), 120 (M- $\text{CH}_2\text{N}$ ).

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