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 ± 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

	-	$1\text{-}CH_3$	$3\text{-}CH_3$	$7\text{-}CH_3$	$9\text{-}CH_3$
Purine(a)	263	275	276	267	264
6-Methylpurine	261(a)	-	274(b)	264	262(b)

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

[b] 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 $(CD_3)_2SO$, 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

		Δδ, cps			
		1-CH_3	3-CH_3	7-CH_3	9-CH_3
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-$\underline{d}_6$ with TMS as internal standard.

[b] Reference 7.

[c] Spectrum run in CF_3CO_2H.

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 $-CH_2-N$.

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 $CHCl_3$ 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 $CHCl_3$ to remove colored impurities before analysis, mp 228-230°.

Anal. Calcd for $C_7H_8N_4$: C, 56.74; H, 5.44; N, 37.81. Found: C, 56.76; H, 5.40; N, 37.87.

NMR (DMSO-d_6) δ 2.90 (s, 3, C-CH_3), 4.13 (s, 3, N-CH_3), 8.23 (s, 1) and 8.50 (s, 1); λ_{max} (ε): 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-CH_3), 120 (M-CH_2N).

ACKNOWLEDGMENT

We thank George Bosworth Brown for his continued interest and support. This investigation was supported in part by funds from the Public Health Service Research Grants CA 15274, CA 08748 and CA 17085 from the National Cancer Institute, and by the Energy Research and Development Administration, Contract EY-76-S-02-2931. Mass spectra were performed at the Rockefeller University Mass Spectrometric Biotechnology Resource which is supported in part by funds from the National Institutes of Health Research Grant RR-862-01 from the Division of Research Facilities and Resources to the Rockefeller University.

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Received, 24th November, 1977