Restricted Rotation of a Dimethyl Group in a Purine with a Diazafulvene-like Structure

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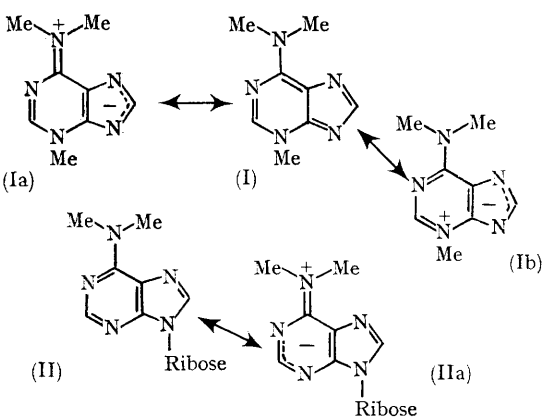
A recent Communication on the n.m.r. spectrum of $N(6)N(6)$-dimethyladenosine (II)[1] prompts us to report our own studies on 6-dimethylamino-3-methylpurine (I), a compound in which the peculiar diazafulvene moiety is linked to a pyrimidine nucleus.[2]



The n.m.r. spectrum of (I) (Figure) was measured in $CDCl_3$ at 60 MHz. When the solution was cooled to *ca.* −50°,† three sharp signals (at 210, 236, and 250 Hz) appeared which did not change their shape or their position up to about −12°. Above this temperature, progressive broadening of the two high-field signals was noticed which coalesced to a broad band upon further warming to 30°. At still more elevated temperatures, this band sharpened again to a single peak, and at 70° the n.m.r. spectrum of (I) was composed of two narrow bands with the correct integration 2 : 1. Throughout the whole temperature range, the low-field signal at ~250 Hz remained essentially unchanged, both with respect to its width ($W_{\frac{1}{2}}$ = 1·3 Hz) and to its chemical shift. Accordingly, this signal is ascribed to the protons of the 3-methyl group.

On the other hand, the variations of the high-field bands demonstrate the hindered rotation of the 6-dimethylamino-group in (I). At low temperatures, the slow exchange causes the methyl groups to be non-equivalent because of their different magnetic environments. Using the approximate line-shape method of Anet and Bourn[3] for calculating the rate constant k, both at low and high temperatures, the following activation parameters were derived.

† Temperatures were calibrated with methanol and ethylene glycol, and are correct within ±2°.

Activation parameters of 3-*methyl*-6-*dimethylaminopurine* (I) *and of* N(6),N(6)-*dimethyladenosine* (II)

Compound	$\Delta\nu$[a]	T_c[b]	E_a[c]	log A[d]	$\Delta G^{\ddagger}$[c]	$\Delta H^{\ddagger}$[c]	$\Delta S^{\ddagger}$[e]
(I)	26	30°	12·2 ± 1	10·5 ± 0·5	15·3 ± 1	11·6 ± 1	−12·5 ± 4
(II)[f]	47	0°	11·8	11·5	13·4[g]	11·3[g]	−7·8[g]

[a] In Hz; [b] Temperature of coalescence; [c] In kcal./mole; [d] Frequency factor; [e] In entropy units; [f] Data take from Martin and Reese (ref. 1); [g] Values calculated from data in ref. (1).

Of the two possible canonical structures of compound (I) shown, (Ia) is responsible for the observed hindered rotation. Since the imidazole moiety of (I) is in a π-deficient state,[4] it assists the withdrawal of electrons from the exocyclic dimethylamino-group; in (Ia), the latter group acquires a positive charge while the imidazole ring becomes a negative centre.

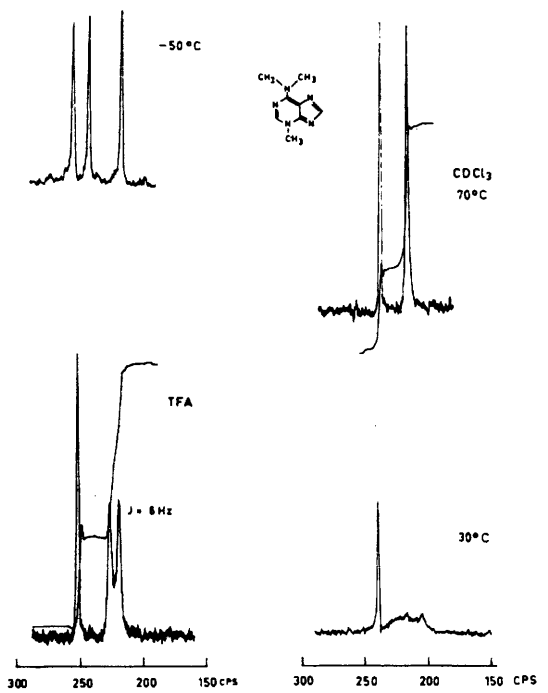


FIGURE. *N.m.r. spectra of* 6-*dimethylamino*-3-*methylpurine* (I). *Abscissa represents c./sec. downfield from* Me_4Si. *The special conditions of each measurement are indicated on the graph. TFA = trifluoroacetic acid. Note the constancy of the band near 250 Hz throughout the whole temperature range.*

In (Ib) the positive charge is placed at N(3) causing deshielding of the protons of the 3-methyl groups. The signal of the 3-methyl group in 3-methylpurine[5] is found at 258 Hz and in 3,6-dimethylpurine[6] at 255 Hz, while the band assigned to the 3-methyl substituent in (I) (~250 Hz) is shifted slightly to a higher field. This suggests that structure (Ib) is somewhat less important here than in the two purines mentioned, due to the competition of the alternative form (Ia).

In the adenosine derivative (II), the imidazole moiety is in its normal, π-excessive form[7] and therefore structure (IIa) may be responsible for the restricted rotation of the 6-dimethylamino-group in this compound. It should be noted that the coalescence temperature of (I) is about 30° higher than that of (II).

When the n.m.r. spectrum of (I) was measured in trifluoroacetic acid, protonation of the exocyclic dimethylamino-group led to spin–spin coupling between the proton and the methyl groups (which are now equivalent) and thus to splitting of the signal (J 6 Hz: see Figure 1).

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