Unexpected Products obtained in the Thiation of Hypoxanthine Derivatives

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A NEED for quantities of the recently reported 7,9-dimethyl-6-mercaptopurinium betaine (V),[1] prompted us to investigate the direct conversion of the parent hypoxanthine[2] by the well-known reaction of 6-oxopurines with P_2S_5.[3] When (I), as either its iodide or the toluene-*p*-sulphonate, was treated with P_2S_5 in pyridine, no crystalline compound was formed, but in β-picoline, yellow needles (from toluene) were isolated, decomposing at *ca.* 267° and showing the spectral properties; $\lambda_{\max}$ (EtOH) 270; 345 mμ (log $\epsilon_{\max}$ 4·05; 4·22); i.r. (in KBr) 1600, 1540, 1498, 1408, 1340, 1188, 1145, 1021, 925, 838, and 760 cm.$^{-1}$.

Surprisingly, it analysed as $C_7H_8N_4S_2$ suggesting an unusual direct substitution of an hydrogen atom by sulphur (from P_2S_5). We assign structure (VI) to the product on the following basis:

(a) It had different physical properties from the known (VII).[1]

(b) The n.m.r. spectrum† showed two signals at 238 and 245 Hz, and a broad signal at 548 Hz integrating for 3 : 3 : 1 and suggesting that both methyl groups remained intact. The low-field signal is to be attributed to H(2) of the purine ring, since compound (V) shows signals at 509 and 545 Hz [H(8) and H(2) of the purine ring], and from our observations the low-field signal of purine-6(1*H*)-thione and its alkyl derivatives is assignable to position 2, broadened by the quadrupole moment of the neighbouring nitrogens.§

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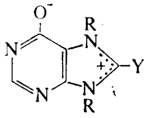
† N.m.r. spectra were measured at 60 MHz in trifluoroacetic acid with Me_4Si as internal standard. Chemical shifts are expressed in Hz downfield from Me_4Si.

§ N.m.r. spectra of purine-6(1*H*)-thione and its alkyl derivatives will be soon published.

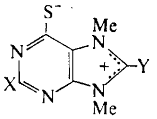
TABLE

Compound	M.p.	λ_{max} (EtOH) (log ϵ_{max})	N.m.r.
(III)	>300°	292 mμ (4·38)	235,247(6H); 515(1H)
(IV)	218°	296 mμ (4·30)	340,350(4H); 435(phenyl) 506(1H)
(VIII	>300°	292 mμ (4·31)	234(6H); 516(1H)

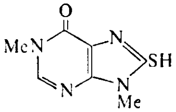
(c) Elemental sulphur is known[4] to react with certain purines at position 8 only; compound (V) when heated with sulphur at *ca.* 200° gave (VI) in a good yield. However, (V) was refractory towards P_2S_5 in either pyridine or β-picoline. Ion (I), as a betaine and with P_2S_5, gave a mixture of 7- and 9-methylpurine-6(1*H*)-thiones.[5] Similarly, (II) as an hydrobromide, gave a mixture of 7- and 9-benzylpurine-6(1*H*)-thiones—in accordance with its thermal instability.[6]



(I) R=Me, Y=H
(II) R=CH_2Ph, Y=H
(III) R=Me, Y=S
(IV) R=CH^2Ph, Y=S



(V) X=Y=H
(VI) X=H, Y=S
(VII) X=S, Y=H



(VIII)

While hypoxanthine was reported to be refractory towards elementary sulphur—we find that its 1,9-dimethyl analogue, as well as compounds (I) and (II), react with sulphur to give the corresponding 8-thio-analogues (VIII), (III), and (IV).

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[5] P_2S_5 is a known dealkylating agent, see J. A. Montgomery and H. J. Thomas, *J. Org. Chem.*, 1963, **28**, 2304.
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