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# TWO FACILE $C_4$-$N_9$ BOND CLEAVAGES IN PURINES AND THE METHYLATION OF 2,3,7,8-TETRAHYDRO-2,8-DIOXOPURINE

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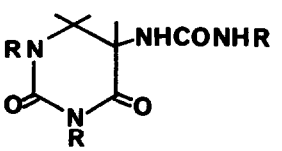
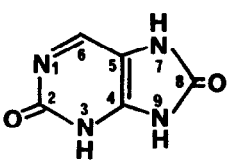
Among the few known reactions in which the $C_4$-$N_9$ bond of purines is cleaved without degradation or rearrangement are the oxidative cleavage of uric acid and its N-methyl derivatives ($Cl_2$/AcOH) which gave 5-chloro-2,4,6-trioxo-5-ureidohexahydropyrimidines[1], and the electrolytic reduction of uric acid to 'tetrahydrouric acid' for which the structure 1(*a*) was proposed.[2] We now report that catalytic hydrogenation of 2,3,7,8-tetrahydro-




1(*a*) R=H
(*b*) R=Me.

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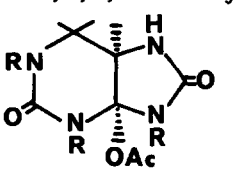
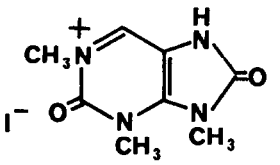



3(*a*) R=H
(*b*) R=Me.

2,8-dioxopurine 2 in aqueous hydrochloric acid ($PtO_2$), but not in neutral medium, gave quantitatively a dihydro compound: (m.p. 214-215°) identical with that recorded by Tafel[2] for 1(*a*). The structure was confirmed by elemental analysis, i.r. ($\nu_{max}$ 1780 and 1713 $cm^{-1}$), n.m.r. and m.s. It appears that cleavage of the $C_4$-$N_9$ bond of the intermediate 1,6-dihydropurine occurs readily in the presence of acid because the reduced purine could not be obtained by altering the work-up conditions. The only successful attempt to cyclise the ureido compound 1(*a*) was by boiling in acetic anhydride which gave 4-acetoxy-2,8-dioxoperhydropurine 3(*a*) (m.p. 295°C decomp.).



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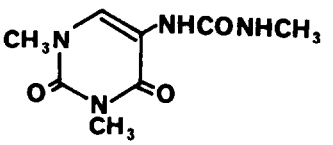

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Methylation of 2,8-dioxopurine 2 (MeI-DMF) gave 2,3,7,8-tetrahydro-1,3,9-trimethylpurine iodide 4 (m.p. >360°C). When this iodide was hydrogenated catalytically ($PtO_2$-$H_2O$), one molar equivalent of hydrogen was absorbed, the solution became acidic and the ureido compound 1(*b*) (m.p. 218°C) was obtained in quantitative yield. The 4-acetoxypurine 3(*b*) (oil) was also obtained by cyclisation of the ureidopyrimidine 1(*b*) in acetic anhydride. *Cis* stereochemistry at $C_4$ and $C_5$ for 1(*a*) and 1(*b*) was deduced from the similarity of the n.m.r. pattern of signals from $H_6$ and the pattern from the corresponding protons in *cis*-5,7-diaza-6-oxoperhydroindene (m.p. 156°C); and the small vicinal coupling constants.

A second $C_4$-$N_9$ bond cleavage was observed when the iodide 4 was treated with one molar equivalent of aqueous sodium hydroxide and 1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxo-5-N'-methylureidopyrimidine 5 (m.p. 235° and 332°C, dimorphic) was formed. This reaction could not be reversed by acid.

The methylation pattern in the iodide 4 was elucidated from the following: (*a*) i.r., n.m.r., m.s. and elemental analyses are consistent with the structure, (*b*) does not form an anhydro-pseudobase, (*c*) its reduction product 1(*b*) showed in the n.m.r. one methyl signal as a doublet due to coupling with NH which collapsed to a singlet on addition of $D_2O$ and (*d*) the synthesis of 5 from authentic 5-amino-1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidine[4] and N,N'-dimethylurea.

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3. Kindly supplied by Dr D.J. Brown.
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