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The Action of Nitrous Acid on some Amino-methylpyrimidines

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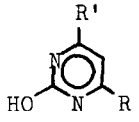
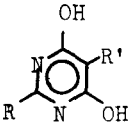
The action of nitrous acid on the hydroxy-methylpyrimidines Ia, b, c, has been shown[1,2] to give the corresponding hydroxyiminomethyl derivatives Id, e, f, respectively by attack at the methyl substituent rather than nitrosation by attack at the 5-position, the usual site for electrophilic substitution in pyrimidines[3]. The action of nitrous acid on 2-methyl-4, 6-dihydroxypyrimidine (IIa) has been shown[4] to give the 2-hydroxyimino-methyl-5-nitroso compound IIb.



I

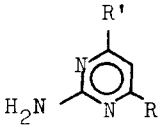


II

(a) R = R' = Me
(b) R = Me, R' = H
(c) R = Me, R' = Ph
(d) R = CH:NOH, R' = Me
(e) R = CH:NOH, R' = H
(f) R = CH:NOH, R' = Ph
(g) R = R' = CH:NOH

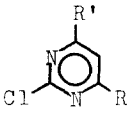
(a) R = Me, R' = H
(b) R = CH:NOH, R' = NO

The present studies are concerned with the action of nitrous acid, under various conditions, on a variety of substituted pyrimidines. The action of nitrous acid on the amino-methylpyrimidines IIIa, b, c in aqueous acetic acid results in hydrolysis of the amino group and attack at the methyl substituent to give the hydroxyiminomethyl derivatives of the corresponding hydroxy compounds, Ie from IIIb, If from IIIc, but IIIa gives the dihydroxyiminomethyl derivative Ig and not the monohydroxyimino-methyl derivative Id. As 2-hydroxy-4,6-dimethylpyrimidine gives only the monohydroxyiminomethyl derivative, presumably it is not an intermediate in the formation of Ig from IIIa and attack at the methyl substituent occurs before hydrolysis of the amino group.



III

(a) R = R' = Me
(b) R = Me, R' = H
(c) R = Me, R' = Ph



IV

(a) R = R' = Me
(b) R = Me, R' = H

However the reaction of aqueous sodium nitrite on compounds IIIa and IIIb in concentrated hydrochloric acid below 5° gives the corresponding 2-chloropyrimidines IVa and IVb with little or no hydroxyiminomethyl compound being formed. Compound IIIc does not seem to react under these conditions, and whilst 4-amino-2,6-dimethylpyrimidine gives the chloro compound[5], it does not give a hydroxyiminomethyl derivative under the conditions so far investigated.

The structures of the products have been established by P.M.R. spectral analysis, by elemental analysis, and by comparison with authentic samples where available. The studies are being continued.

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