Novel Acetoxylation Reactions of 7-Methylquinoxalin-2(1*H*)-one 4-*N*-Oxides

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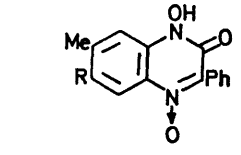
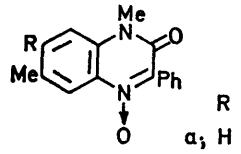
Summary The 7-methylquinoxalin-2(1*H*)-one 4-*N*-oxides (1a and b) and (2b) are converted in hot acetic anhydride into the 7-acetoxymethylquinoxalones (3a and b) and (4b), whereas similar treatment of the 6-methylquinoxalin-2(1*H*)-one 1-*N*-oxide (2a) affords the 7-acetoxyquinoxalone (4b; AcO for AcO·CH_2).

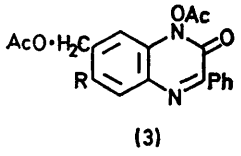
THE scope and mechanism of the reactions of heterocyclic *N*-oxides with acid anhydrides have been extensively investigated.[1] Reaction with acetic anhydride commonly involves acetoxylation of the heterocyclic nucleus or of attached side-chains. Acetoxylation of a fused benzene ring has also been observed in the reactions of certain benzimidazole *N*-oxides[2] and 1-methylquinoxalin-2(1*H*)-one 4-*N*-oxides[3] with acetic anhydride. However, there appears to be no previous report of the similar acetoxylation of an alkyl side-chain on a fused benzene ring in a heterocyclic *N*-oxide. We now describe reactions of quinoxalin-2(1*H*)-one 4-*N*-oxides with acetic anhydride which result in the preferential acetoxylation of a 7-methyl group.



(1)



(2) R: a; H, b; Me



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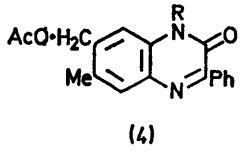


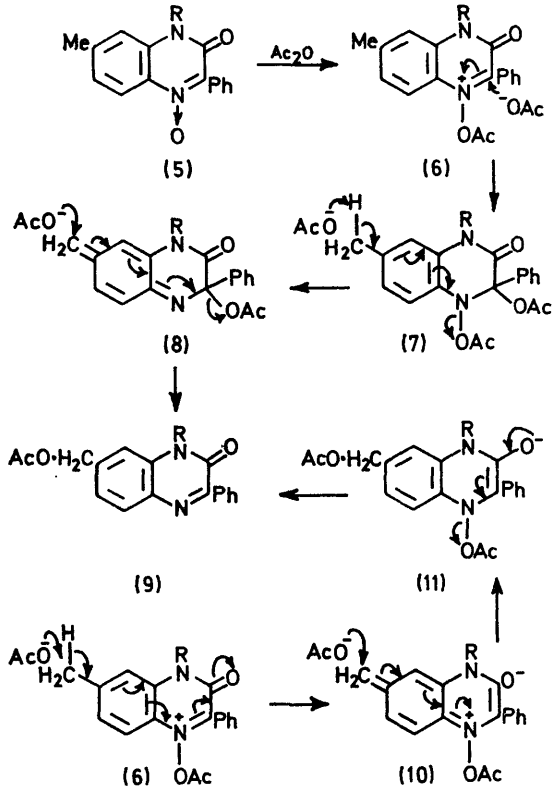
(4)

7-Methylquinoxalin-2(1H)*-one 4-N-oxides*[a]

	Yield (%)	M.p.
(1a)	73	218°
(1b)	73	225°
(2b)	90	200°

[a] Satisfactory analyses and spectral data were obtained for all new compounds.

Heating the cyclic hydroxamic acids (1a and b) (Table) (prepared by a previously described[4] synthetic method) under reflux with acetic anhydride for 4·5 h gave the corresponding 7-acetoxymethylquinoxalones, ν_{max} 1795 (cyclic :N·OAc), 1730 (C·OAc), and 1660 (CO) cm^{-1}, (3a) (85%), m.p. 114° (from ethanol), τ ($CF_3·CO_2H$) 1·60—2·38 (8H, m, Ar–H), 4·52 (2H, s, CH_2), 7·30 (3H, s, :N·OAc), and 7·68 (3H, s, C·OAc); and (3b) (63%), m.p. 175° (from ethanol), τ ($CF_3·CO_2H$) 1·73—2·38 (7H, m, Ar–H), 4·52 (2H, s, CH_2), 7·34 (3H, s, :N·OAc), 7·38 (3H, s, Me), and 7·69 (3H, s, C·OAc). Similar treatment of the *N*-methyl *N*-oxide (2b) (Table) (prepared by a standard synthetic method[5]) with acetic anhydride gave the 7-acetoxymethylquinoxalone (4b) (80%), m.p. 114° (from ethanol–water), ν_{max} 1730 (C·OAc) and 1650 (CO) cm^{-1} and τ ($CF_3·CO_2H$) 1·76—2·38 (7H, m, Ar–H), 4·47 (2H, s, CH_2), 5·88 (3H, s, N·Me), 7·39 (3H, s, Me), and 7·66 (3H, s, C·OAc). The latter was identical with the methylation product of the



(5) (6) (8) (7) (9) (11) (6) (10)

acetoxymethylquinoxalone (4a) obtained (67%), m.p. 230° (from ethanol), ν_{max} 3100sh and 2700sh (OH), 1735 (C·OAc), and 1660 (CO) cm^{-1} and τ ($CF_3·CO_2H$) 1·66—2·36 (7H, m, Ar–H), 4·52 (2H, s, CH_2), 7·41 (3H, s, Me), and 7·66 (3H, s, C·OAc), by hydrogenolysis of the *N*-acetoxyquinoxalone (3b). The ^1H n.m.r. absorption of the compounds (3a and b) and (4a and b) is fully in accord with the assigned structures. The inertness of a 6-methyl group towards acetoxylation implicit in the preferential formation of the compounds (3b) and (4b) from the oxides (1b) and (2b) is further substantiated by the conversion of the oxide

(2a) in hot acetic anhydride into the 7-acetoxyquinoxalone (4b; AcO for AcO·CH_2) (82%), m.p. 173° (from ethanol–water), ν_{max} 1740 (C·OAc) and 1640 (CO) cm^{-1} and τ (CF_3·CO_2H) 1·80—2·38 (7H, m, Ar–H), 5·93 (3H, s, N.Me), 7·44 (3H, s, Me), and 7·55 (3H, s, C·OAc), without attack on the methyl group.

The acetoxylation of the 7-methyl group in the *N*-oxides (1a and b) and (2b) is explicable by alternative courses leading from initially formed[1] *N*-acetoxyquinoxalinium acetates (6) to anhydro-base intermediates (8) and (10) formed by proton abstraction either directly or after conversion into adducts (7) by nucleophilic attack by acetate ion at the 2-position. Addition of acetate ion to the anhydro-base (8) and concomitant expulsion of the 2-acetoxy-group then affords the observed products (9). Alternatively, the latter are formed by addition of acetate ion to the intermediates (10) and subsequent loss of the acetoxy-group from the adduct (11).

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