Oxidation of an Aromatic Methyl Group with Jones' Reagent

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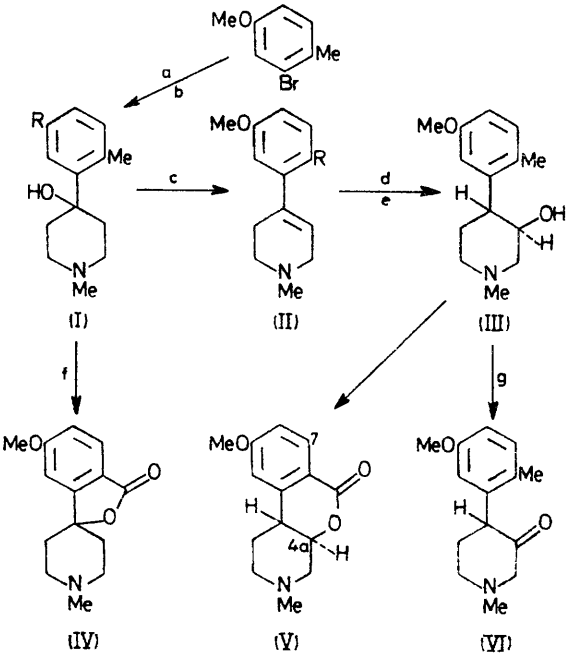
Summary Oxidation of an aromatic methyl group *para* to a methoxy-substituent in some 4-arylpiperidines has been observed using Jones' reagent at 5—20 °C; the mechanism of this result is discussed.

DURING studies directed towards the synthesis of potentially analgesic 2,6-methano-3-benzazocines,[1] the oxidation of the alcohol (III) was investigated. Racemic alcohol (III) (HCl salt m.p. 252—254 °C),† prepared as indicated in the Scheme from 3-bromo-4-methylanisole,[2] when subjected to a modified Oppenauer oxidation[3] gave the racemic ketone (VI) (HCl salt m.p. 182—186 °C).† Oxidation of the alcohol (III) with Jones' reagent[4] in acetone at 5 °C, however, gave a new substance, m.p. 137—139 °C, which was identified on the basis of elemental analysis and i.r. [ν_{max} ($CHCl_3$) 1710 cm^{-1}], n.m.r. [notably δ ($CDCl_3$) 8·07 (1H, d, *J* 9 Hz, 7-H) and 4·23 (1H, d of t, *J* 10 and 4 Hz, 4a-H)], and mass (*m/e* 247, M^+) spectroscopic data as the novel racemic δ-lactone (V) (23% yield, improved to 33% when prepared in $MeCO_2H$ at 20—40 °C). In similar oxidations in acetone (II, R = Me) gave (II, R = CHO) (12%) and (I, R = OMe) gave (IV) (46%) but the demethoxy alcohol (I, R = H) was recovered unchanged.

From these results we conclude that the presence of the *p*-MeO group is essential for the mild oxidation to take place, and that a suitably placed OH group will interact with the aldehyde formed to give an hemiacetal which is finally oxidised to a lactone. Oxidation of the methyl group apparently takes precedence over oxidation of the secondary



SCHEME

a, Mg; b, *N*-methyl-4-piperidone; c, HCO_2H; d, BH_3.THF; e, H_2O_2, NaOH; f, Jones' reagent; g, Ph_2CO,$KOBu^t$.

† Satisfactory elemental analysis and spectroscopic data were obtained.

alcohol and over oxidation of the adjacent tertiary benzylic position. This activating effect of a *p*-MeO group has been noted by Wiberg and Evans[5] in studies on the chromic acid oxidation of diarylmethanes to diaryl ketones. They inferred that hydride ion transfer to the chromium reagent is the most likely mechanism in the case of the *p*-MeO substituted compounds.‡

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‡ Compounds prepared in this work were tested in primary CNS and CVS screens but were devoid of interesting activity.

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