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1-ACYL-2,3-DIHYDROXYINDOLINES : A REINVESTIGATION

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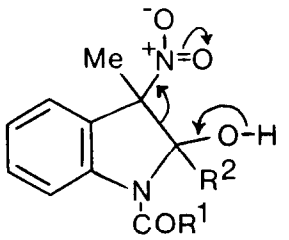
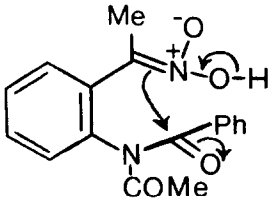
SUMMARY. Per-acid oxidation of 1-acylindoles in aqueous dioxan furnished the title compounds which exist in equilibrium with their keto-amide isomers in solution. The so-called trans 1-benzoyl-2,3-dihydroxy-2,3-dimethylindoline was shown to be 1-acetyl-2,3-dihydroxy-3-methyl-2-phenylindoline.

Kershaw and Taylor isolated a nitro-alcohol 1a following treatment of 1-benzoyl-2,3-dimethylindole with nitric acid in acetic acid. The nitro-alcohol was said to furnish the trans glycol 4a on refluxing in aqueous ethanol in the presence of alumina. It was further claimed that this glycol was converted into the indoxyl 3 when submitted to base-catalysed hydrolysis.[1] The latter reaction implies an unprecedented and mechanistically implausible skeletal rearrangement. We now report our preliminary findings in a reinvestigation of this work. We show also that the oxidation of 1-acylindoles with m-chloroperbenzoic acid in aqueous dioxan furnishes 1-acyl-2,3-dihydroxyindolines 4 in high yield[2] and that in solution the latter compounds are in equilibrium with their keto-amide isomers 5.

We reasoned that the observations of Kershaw and Taylor are consistent with the alternative structure 4b for the so-called "trans glycol". In our hands treatment of 1-benzoyl-2,3-dimethylindole with nitric acid in acetic acid furnished a colourless substance $C_{17}H_{16}N_2O_4$ (high resolution m.s.), m.p. 116.5° (decomp.), ν_{max}^{KBr} 3400, 1640, 1545 cm^{-1}, which we believe to be the nitro-alcohol (lit. m.p. 125°) that was described earlier.[1] The ^1H- and ^{13}C-n.m.r. data[3] are completely consistent with the structure 1a that was proposed earlier.[1] Under the published conditions the nitro-alcohol gave a glycol, m.p. 168-170°, ν_{max}^{KBr} 3370, 3280, 1640 cm^{-1}, which must be the "trans glycol" (lit. m.p. 168°) that was described earlier.[1] This glycol was identified as 1-acetyl-2,3-dihydroxy--3-methyl-2-phenylindoline 4b by comparison with an authentic sample that was prepared by treatment of 1-acetyl-3-methyl-2-phenylindole with m-chloroperbenzoic acid in aqueous dioxan. The most efficient interpretation of these results is that nitro-alcohol 1a is in equilibrium with its isomer 1b during the hydrolysis reaction (see 1 ⇌ 2) and that the glycol 4b is formed by hydrolysis of 1b. Thus the "new rearrangement"[1] is merely the consequence of an incorrect structure assignment.



1 a; R^1=Ph, R^2=Me
b; R^1=Me, R^2=Ph



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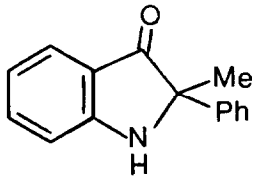

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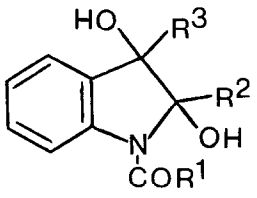

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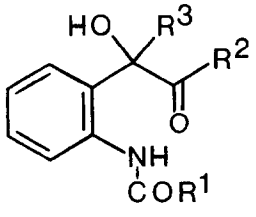

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a; R^1=Ph, R^2=R^3=Me
b; R^1=R^3=Me, R^2=Ph
c; R^1=R^2=R^3=Me
d; R^1=Me, R^2R^3=$(CH_2)_4$

Glycol 4c, m.p. 134.5-135.5°, ν_{max}^{KBr} 3420, 3300, 1630 cm^{-1}, was prepared in quantitative yield by oxidation of the parent 1-acetylindole with m-chloroperbenzoic acid. The ^1H- and ^{13}C-n.m.r. spectra of 4c showed that in solution this glycol exists in equilibrium with its keto-amide isomer 5c in contrast to a recent report.[4] N.m.r. studies revealed that the glycol 4b also equilibrates with its keto-amide isomer 5b in solution. Attempts to prepare glycol 4a furnished the keto-amide 5a, while glycol 4d was shown to be stable in solution. These observations suggest that earlier claims to the isolation[1] or spectroscopic detection[4,5] of cis and trans isomers of 1-acyl-2,3-dihydroxyindolines must be treated with caution. Cis-trans equilibria in the 1-acyl-2--hydroxyindoline series have been rigorously established.[6]

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2. Complex mixtures are formed in the absence of a suitable nucleophile to trap the intermediate epoxide; cf. T. Hino, H. Yamaguchi, K. Matsuki, K. Nakano, M. Sodeoka, and M. Nakagawa, J. Chem. Soc. Perkin Trans. 1, 141 (1983).
3. Selected ^{13}C n.m.r. chemical shifts (δ) for $CDCl_3$ solution: 1a, 169.1, 134.4, 128.1, 128.8, 131.9 (C=0, C=1,2,3,&4 of PhCO), 124.3, 123.9, 130.8, 116.3 (C-4,5,6,&7 of indoline); 4c, 171.0(C=0), 96.2(C-2), 24.8, 22.2, 19.0 (3×Me); 5c, 211.3 (CCOMe), 168.5 (NCOMe), 24.8, 24.1, 23.7 (3×Me).
4. T. Kawasaki, C. Chien, and M. Sakamoto, Chem. Lett., 855 (1983).
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