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ON THE AUTOXIDATION OF INDOLES

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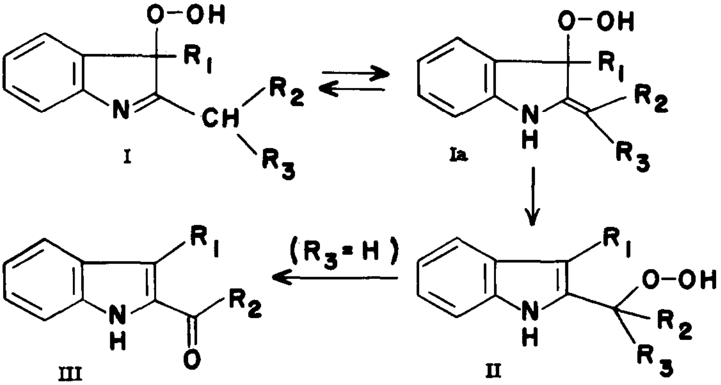
The reaction of 2,3-disubstituted indoles with oxygen leads generally to indolenine-3-hydroperoxides I,[1] and it has recently been shown that these may decompose to form 2-acylindole derivatives, III.



Mechanistic explanations for this unusual transformation have been advanced by Leete,[2] and more recently by Taylor[3] who has suggested the allylic rearrangement of Ia to II as a key step in the process. In this communication, we report the results of the autoxidation of 2-isopropyl-3-methylindole, and suggest an alternative explanation for the formation of the observed products.

When oxygen was bubbled into a hexane solution of 2-isopropyl-3-methylindole in the presence of azobisisobutyronitrile, three products were isolated. The indolenine hydroperoxide I, $R_1 = R_2 = R_3 = CH_3$, formed after two days, was the first product removed from solution. It is an unstable crystalline compound, m.p. 101.5-102.5°. (Calcd. for $C_{12}H_{15}NO_2$: C, 70.21; H, 7.37; N, 6.82. Found: C, 70.05; H, 7.61; N, 6.67). $\lambda_{\text{max.}}^{95\%\text{EtOH}}$ 260 mμ (log ε 3.58), 220 mμ (log ε 4.33). This spectrum corresponds to the well-known absorption of the indolenine chromophore. Longer exposure to oxygen yielded the oxindole IV,* m.p. 161.5-162.5°. (Calcd. for $C_9H_9NO_2$: C, 66.24; H, 5.56; N, 8.59. Found: C, 66.44; H, 5.57; N, 8.81). $\lambda_{\text{max.}}^{95\%\text{EtOH}}$ 290 (log ε 2.90), 252 mμ (log ε 3.72); $\nu_{\text{max.}}^{\text{KBr}}$ 3375, 1710, 1620, 1470, and 1442 cm^{-1}. The NMR spectrum shows a singlet (3 protons) at 8.5τ, a singlet (1 proton) at 5.15τ, and a 4 proton multiplet at 2.5-3τ. Hydroperoxide I, $R_1 = R_2 = R_3 = CH_3$, is converted to IV in very low yield by heating in ethyl acetate.

A third product isolated from the reaction mixture was the hydroxyacylaminoacetophenone derivative V, m.p. 128-130°, (Calcd. for $C_{12}H_{15}NO_3$; C, 65.14; H, 6.83; N, 6.33. Found: C, 65.07; H, 7.02; N, 6.32). The structure of V is established unambiguously by the following physical data: $\lambda_{\text{max.}}^{95\%\text{EtOH}}$ 323 (log ε 3.6), 267 (log ε 3.9) 260 (log ε 4.1) 234 (log ε 4.5) and 229 mμ (log ε 4.9); $\nu_{\text{max.}}^{\text{CHCl}_3}$ 1685 and 1650 cm^{-1}. The above ultraviolet and infrared absorption peaks are almost exactly analogous

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* Prof. E. Leete has privately informed us that in a related autoxidation study he has isolated 3-hydroxy-3-phenyloxindole from 2-benzyl-3-phenylindole. We thank Prof. Leete for communicating his results to us prior to publication.

to those of the known o-propionaminopropiophenone.[2] The NMR spectrum shows a singlet (6 protons) at 8.42τ, a singlet (3 protons) at 7.37τ, a singlet (1 proton) at 6.45τ and a multiplet (4 protons) in the region, 2-3τ.

We suggest the reaction sequence outlined in Chart I to explain the above results. The tautomer Ia of the hydroperoxide I undergoes rearrangement by an intramolecular enamine displacement to form the dihydroxy indolenine VI.* Addition of a hydroperoxide molecule to VI followed by fragmentation may yield either IV or V. It is also noteworthy that in the oxidation of 2,3-diethylindole, an intermediate of type VIa could lead directly to the 2-acylindole (tautomerization to the keto form and dehydration of the β-hydroxy dihydroindole). Further experiments to test the above hypothesis are in progress.

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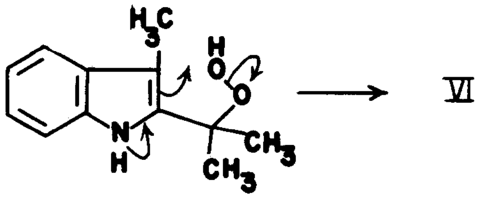
* Alternatively, VI could arise from the hydroperoxide II, $R_1 = R_2 = R_3 = CH_3$ as shown below:



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2. E. Leete, ibid., 83, 3645 (1961).

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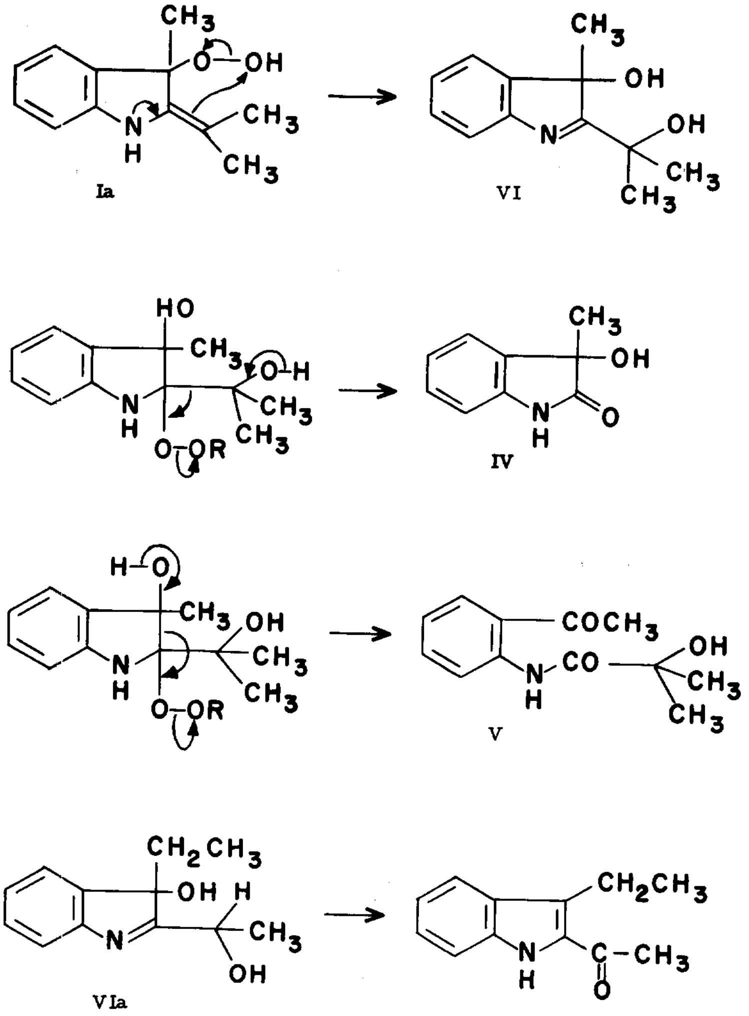

CHART I