

THE OXIDATION OF 2-BENZYL-3-PHENYLINDOLE

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We recently reported (1) that the autoxidation of 2,3-diethylindole yielded 2-acetyl-3-ethylindole, the reaction proceeding via 2,3-diethylindolenine-3-hydroperoxide. Later W. I. Taylor was able to obtain 3-methylindole-2-aldehyde in small yield by the autoxidation of 2,3-dimethylindole, and proposed a general mechanism for this oxidation and related reactions (2). A key step in his mechanism was the tautomerization of the indolenine hydroperoxide to an exocyclic enamine. We have now investigated the oxidation of 2-benzyl-3-phenylindole (I) since in this compound an exocyclic double bond at the 2-position would be stabilized by an adjacent phenyl group.

Exposure of a solution of 2-benzyl-3-phenylindole (3) in ethyl acetate to light and air resulted in the formation of a new compound, m.p. 213-214°, having the empirical formula $C_{14}H_{11}NO_2$ (Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.43; H, 5.13; N, 6.24%). This compound was identical (mixed m.p. and IR spectrum) with 3-phenyldioxyindole (VI) which was first prepared fifty years ago by the reaction of isatin with phenyl magnesium bromide (4).

However when a solution of 2-benzyl-3-phenylindole in ethyl acetate or acetic acid was shaken with oxygen in the presence or absence of finely divided platinum the only oxidation product isolated was 2-benzoyl-3-phenylindole (VII), m.p. 207-208°, yellow prisms from benzene (Anal. Calcd. for $C_{21}H_{15}NO$: C, 84.82; H, 5.09; N, 4.71. Found: C, 84.79; H, 5.19; N, 4.69%). The infrared spectrum in Nujol had absorptions at 3325 cm^{-1} (NH) and 1615 cm^{-1} (C=O). The ultraviolet spectrum in 95% EtOH had λ_{max} m μ (log ϵ) at 220 (4.37), 250 (4.29) and 327 (4.16). Wolff-Kishner reduction of this ketone afforded 2-benzyl-3-phenylindole. It was also obtained (in 2% yield), along with 1-benzoyl-3-phenylindole (92% yield) m.p. 151-153° (Anal. C, 85.03; H, 5.32; N, 4.46%), by adding benzoyl chloride to an ether solution of 3-phenylindolyl magnesium iodide. The two isomers were readily separated by chromatography on alumina using petroleum ether, benzene, and finally chloroform as the eluting solvents.

These two oxidation products of 2-benzyl-3-phenylindole are apparently formed by two distinct routes since 2-benzoyl-3-phenylindole was not converted to 3-phenyldioxindole on exposure to air in ethyl acetate. The mechanism illustrated in Fig. 1. is suggested for the formation of the dioxindole. It is considered that the first step is the formation of the indolenine-3-hydroperoxide II. Hydration of this compound affords the carbinolamine III which could plausibly eliminate benzyl alcohol as indicated yielding 3-phenyldioxindole (5). 2-Benzoyl-3-phenylindole could arise by isomerization of the hydroperoxide II to the enamine IV followed by rearrangement

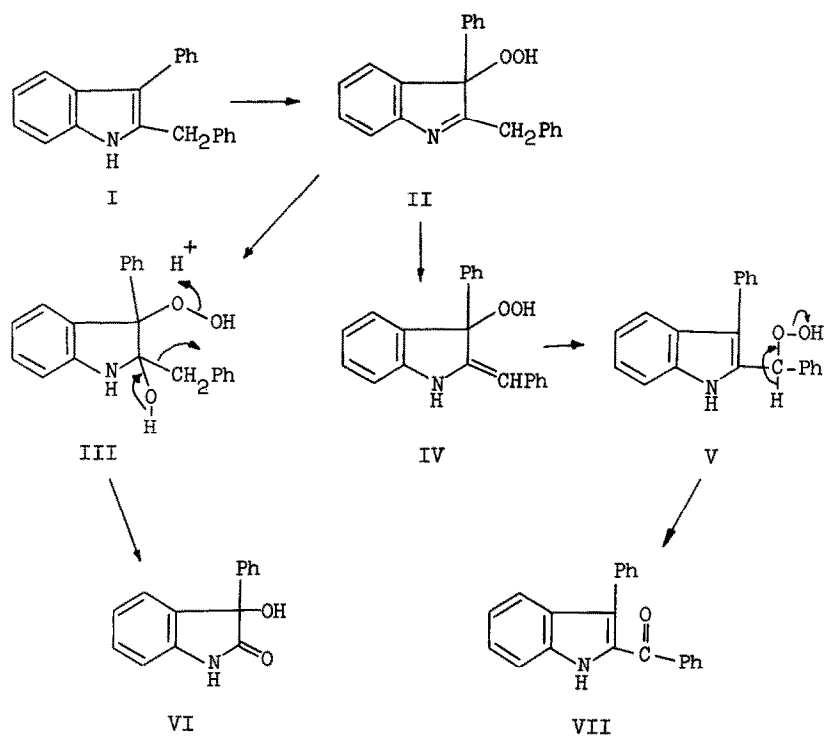


Fig. 1. The oxidation of 2-benzyl-3-phenylindole

to the allylic hydroperoxide V. Elimination of water then affords the benzoyl derivative VII. This mechanism is analogous to that suggested by Taylor (2).

When a solution of 2-benzyl-3-phenylindole in benzene was refluxed with lead tetraacetate 1-acetyl-2-benzoyl-3-phenylindole (X) was obtained, m.p. 168-169° (Anal. Calcd. for $C_{23}H_{17}NO_2$: C, 81.39; H, 5.05; N, 4.13. Found: C, 80.90; H, 5.03; N, 4.08%). Hydrolysis of this acetyl derivative with ethanolic sodium hydroxide afforded 2-benzoyl-3-phenylindole. The mechanism illustrated in Fig. 2. is suggested for this reaction. Electrophilic attack by the lead tetraacetate at the 3-position of 2-benzyl-3-phenylindole affords the indolenine derivative VIII. A tautomeric shift then yields the enamine IX which is attacked by acetate affording the indole XII. XII is then hydrolyzed to X.

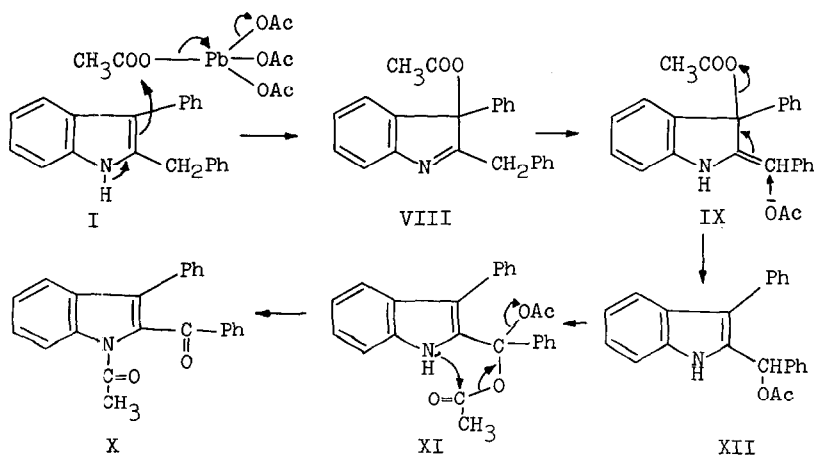


Fig. 2.

Repetition of attack by lead tetraacetate could then ultimately yield the diacetoxy derivative XI. Intramolecular acyl migration and elimination of an acetate group then yields the 1-acetyl-2-benzoyl-3-phenylindole. Taylor (6) reported at the oxidation of 2,3-dimethylindole with lead tetraacetate afforded 2-diacetoxymethyl-3-methylindole.

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