Photoinduced Oxidation of Tryptamine Derivatives. Formation of Pyrrolo[2,3-*b*]-indole and N^b-(4-Cyanobutadienyl)tryptamine

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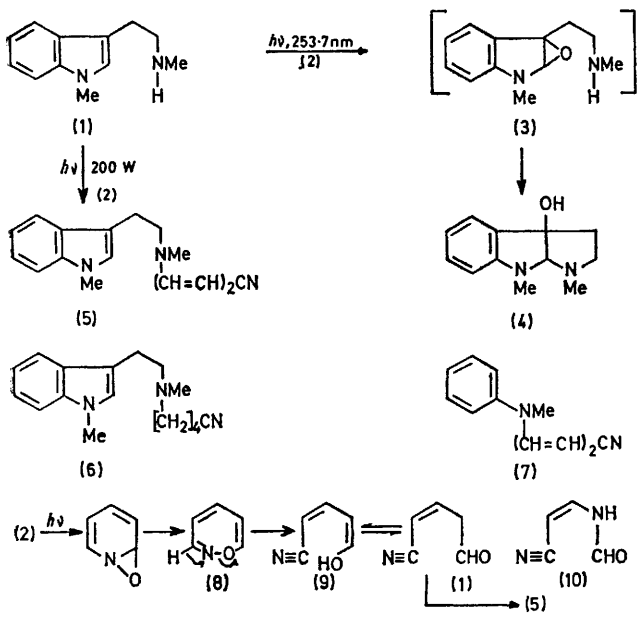
Summary Irradiation (253·7 nm) of N^aN^b-dimethyltryptamine with pyridine *N*-oxide produced 1,8-dimethyl-3a-hydroxy-2,3,3a,8a-tetrahydropyrrolo[2,3-*b*]indole (**4**), whilst with visible light N^b-(4-cyanobutadienyl)-N^aN^b-dimethyltryptamine (**5**) was obtained.

RECENTLY, considerable interest has arisen concerning the mechanism of biological oxidations of aromatic substrates which occur concomitant with an NIH shift; arene oxides have been shown to be intermediates.[1]

The photolysis of pyridine *N*-oxide in the presence of aromatic substrates produces arene oxides directly and serves as a useful model reaction for such enzymatic oxidations.[2] A good model for the dioxygenase-type[3] oxidation of tryptphan to kynuenine derivatives is provided by the photo-oxidation reaction.[4] The frequent occurrence in nature, however, of tryptophan derivatives oxidized in the benzene ring, *e.g.* 5-hydroxytryptophan,[3] serotonin,[3] dehydrobufotenine[5] and the sporidesmins[6] indicate that oxidative pathways other than the cleavage of the pyrrole ring 2,3-bond are operative and encourages the search for the appropriate model reactions.

We report that the oxidation of N^aN^b-dimethyltryptamine (**1**) in CH_2Cl_2, by photolysing (253·7 nm) pyridine

N-oxide (**2**), produces after 1 h, 1,8-dimethyl-3a-hydroxy-2,3,3a,8a-tetrahydropyrrolo[2,3-*b*]indole (**4**) (10%). Anhydro analogues of (**4**) have been reported[7] and have been converted into 3a-hydroxypyrroloindoles. Our one-step production of this structure, with a hydroxyl group in the same position as found in the sporidesmins, probably proceeds by participation of the ethylamine side chain in



opening an intermediate 2,3-oxide (**3**). (**4**); λ_{max} (EtOH) 250 (ε 6500), 298 nm (2360), λ_{max} (EtOH–HCl) 241 (ε 6100), 292 nm (2560);[8] ν_{max} ($CHCl_3$) 3650, 3340 cm^{-1} (OH); *m/e* 204 (M^+, 96%); δ ($CDCl_3$) 2·14—2·33 (m, $-CH_2$), 2·52 (s, N^b–Me), 2·68—2·90 (m, $N-CH_2$), 2·90 (s, N^a–Me), 4·25 (s, N–CH–N), 4·44 p.p.m. (broad s, OH).

However, N^b-(4-cyanobutadienyl)tryptamine (**5**) was obtained in 20% yield, with only traces of (**4**), when a mixture of (**1**) and (**2**) was irradiated with visible light (200 W), in the presence or absence of air, providing new evidence for 1,2-oxazepine (**8**) or its ring opened tautomer 4-cyanobut-4-enal (**9**) as intermediates in the photolysis of (**2**). (**5**) was rapidly destroyed when irradiated in CH_2Cl_2 at 253·7 nm. (**5**); λ_{max} 225 (ε 35,000), 339 nm (30,400); ν_{max} ($CHCl_3$) 2195 (C≡N), 1622 cm^{-1} (C=C); δ ($CDCl_3$) 2·78, 2·85 (*trans*, *cis* N^b–Me), 3·73 (s, N^a–Me), 4·31—5·52, 6·42—6·77 (m, vinylic H), 6·81 p.p.m. (s, α-H); *m/e* 265 (M^+).

Hydrogenation of (**5**) (Pd–C) led to the uptake of hydrogen (2 mol) and gave the saturated nitrile (**6**); ν_{max} ($CHCl_3$) 2245 cm^{-1} (C≡N); *m/e*, 269 (M^+). The irradiation of *N*-methylaniline and (**2**) with visible light gave (**7**) in 25% yield. The structure of which was proved by i.r., n.m.r., u.v., and mass spectral data.

2-Formylpyrrole is known to arise from the photoisomerization of (**2**), in which an intermediate 1,2-oxazepine (**8**) was suggested without direct evidence.[9] We suggest that (**1**) effects a base-catalysed opening of (**8**) in a manner analogous to the known base-catalysed ring opening of isoxazoles[10] giving (**9**), which then reacts with (**1**) to give (**5**). Supporting this mechanism, is the isolation of photoisomer analogous to (**9**), *viz.*, β-formamidoacrylonitrile (**10**), by irradiation of pyrimidine *N*-oxide.[11]

Further studies on the scope of this reaction are in progress.

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