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PHOTOSENSITIZED OXYGENATION OF TRYPTOPHAN AND MELATONIN RELATED COMPUNDS

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Photooxygenation of Nb-methoxycarbonyltryptamine in 5%-pyridine-methanol in the presence of rose bengal and oxygen at 0° has been found to give 3a-hydroperoxy-1,2,3,3a,8,8a-hexahydropyrroloindole(40%). The hydroperoxide, when treated with silica gel in methylene chloride, rearranged to formylkynureamine and Nb-formylkynureamine, accompanied with the reduction product, 3a-hydroxypyrroloindole, showing the predominant participation of the ethylamino side chain over the hydroperoxy group in the proposed initial intermediate, 3-hydroperoxyindolenine. Photosensitized oxygenation of Nb-acetyltryptamine gave the similar results, but direct formation of formylkynureamine from the initial intermediate was observed to proceed in some extent under the similar reaction conditions as above.

Photooxygenation of Nb-methoxycarbonyltryptophan methyl ester also gave 3a-hydroperoxypyrroloindole as a mixture of stereoisomers which was readily converted to 3a-hydroxypyrroloindoles (isomer A, mp 123-124°; isomer B, mp 163-164°) after reduction with dimethyl sulfide. The 3a-hydroperoxypyrroloindole also rearranged to formylkynurenine, Nb-formylkynurenine, and 3a-hydroxypyrroloindole derivatives. These results suggest a new reaction pathway for the oxygenation of tryptophan to kynurenine other than the well known hypothetical dioxetane pathway. All hydroperoxides isolated above rearranged to 1,4-benzoxazine derivatives on acidification.

Photooxygenation of Nb-methoxycarbonyl-5-methoxytryptamine at 0°, however, proceeded exclusively to give formylkynureamine derivative(40%). The similar result was obtained by similar reaction of melatonin with $^1O_2$. On the other hand, when the photooxygenation was carried out at -70° followed by treatment with dimethyl sulfide, 3a-hydroxypyrroloindole derivative was obtained as a sole product. The similar temperature dependence was observed in the photooxygenation of Na-methyl-Nb-methoxycarbonyltryptamine. These results showed that the introduction of electron donating group to the indole moiety produce the temperature dependency for the participation of two neighbouring groups, favouring the aminoethyl side chain participation at low temperature, whereas the participation of hydroperoxy group become important at higher temperature.