BIOMIMETIC TRANSFORMATION OF INDOLOQUINOLIZIDINE DERIVATIVE TO 2-ACYLINDOLE

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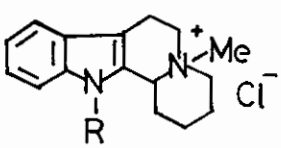
2-Acylindole 2 has been synthesised by photosensitised oxygenation of indoloquinolizidine 1a, while 1-methyl derivative 1b gave a quinolone 3.

We have previousely reported the model reaction for biological oxidation of tryptophan catalyzed by monooxygenase [1] and dioxygenase [2] to form 3a-hydroxy-pyrroloindoles and oxindoles.

The present paper reports a facile one step synthesis of 2-acylindole 2 from indoloquinolizidine 1 [3], which provides an implication for a biogenetic formation of 2-acylindole alkaloids from the corresponding indole alkaloids.

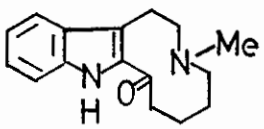
A solution of quinolizidinium chloride 1a in water was continuously saturated with oxygen and irradiated with 250 W halogen lamp through a pyrex filter for 20 hr in the presence of rose bengal. Chromatography and elution with CH_2Cl_2 gave 2, mp 134-136° [4], in 10% yield, whose structure was identified by comparison with an authentic sample. Bubbling oxygen through a solution of 1a in the dark or irradiation of 1a in the absence of the sensitizer yielded no detectable 2-acylindole and the



1a, R = H
b, R = Me

$^1O_2$

R = H



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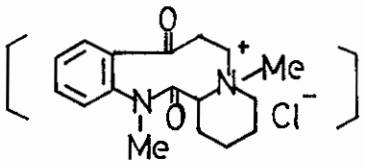
$^1O_2$

R = Me



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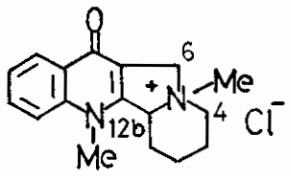

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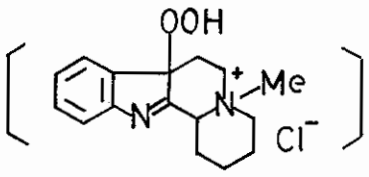

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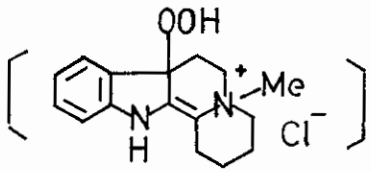

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starting material was recovered. However, if 1a was irradiated in MeOH or 50% aqueous MeOH, 2 was not obtained.

The conversion of simple 2,3-dialkylindoles to 2-acylindoles by autoxidation has many precedents [5] and the hydroperoxyindolenine has been considered as the primary intermediate. Although the mechanism of formation of 2 is not entirely clear, singlet oxygen is known to add to an enamine system to give an ene reaction product [6]. Thereby, it is conceivable that the reaction from the hydroperoxide to 2 was processed as autoxidation, e.g., the primary intermediate 5 isomerized to the enamine tautomer 6 which was converted into the final product 2.

Support for this idea was given by the observation that photosensitised oxygenation of 1b in H_2O under similar conditions resulted in the formation of 1,2,3,4,6,7,12,12b-octahydroindolizino[1,2-b]quinoline-7-one methochloride 4 in 25% yield which has been derived from cyclization of a cleavage product 3 [7] and the failure to detect 2-acylindole derivative. The structure of 4 was confirmed by direct comparison with an authentic specimen prepared by ozonization of 1b in MeOH. 4 ; mp 181°(dec.), λ_{max}^{EtOH} 240, 319, 332 nm [8], γ_{max}^{KBr} 1610 cm^{-1} (C=O) [8], δ (d_6-DMSO) 3.10-4.0 (2H, m, 4-CH_2), 3.33(3H, s, 5-N-Me), 3.79(3H,s, 12-N-Me), 4.76(2H, AB quartet, 6-CH_2), 5.20(1H, m, 12b-CH), picrate, mp 295-297°(aqueous MeOH) [9].

Although chemical transformation of indole alkaloids to the corresponding 2-acylindole alkaloids has been reported [10], our preliminary results appear to be a plausible biogenetic route.

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