SYNTHESES OF DESPYRROLE ANALOGS OF ERGOLINE GROUP OF ALKALOIDS

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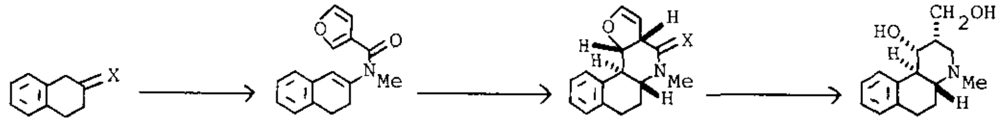
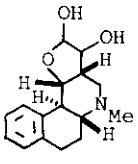
Reductive photocyclization of the enamide (1), prepared from 2-tetraloneimine by acylation with 3-furoyl chloride, yielded the lactam (2) in good yield, which was used as a common starting compound for the syntheses of various despyrrole analogs of alkaloids such as lysergic acid (5), isolysergic acid (6), isolysergol (7), isofumigaclavine (8), lysergene (9), and isolysergine (10), thus established a general synthetic route to respective natural alkaloids.



X=O, NMe (1) (2)X=O, (3)X=H_2 (4)

(1) Conversion of the Amine (3) into Respective Ergoline Analogs (5,6,7,8)



(11)

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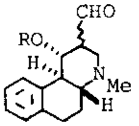
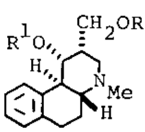


(12a) R=H
(12b) R=CHO

The amine (3), obtained by $LiAlH_4$ reduction of (2), afforded upon OsO_4 treatment the glycols (11) which were subjected to periodate cleavage to give the hydroxyaldehyde (12a) under alkaline and its O-formate (12b) under acidic conditions, of which the former was further oxidized with CrO_3-H_2SO_4 in MeOH followed by dehydration to give lysergic acids (5 and 6), while the latter (12b) afforded isolysergol (7) by $NaBH_4$ reduction. Wolff-Kishner reduction of (12a) afforded isofumigaclavine (8).

(2) Conversion of the Diol (4) into Respective Ergoline Analogs (7,8,9,10)



	R^1	R^2
4a	H	Ms
b	Ms	Ms
c	H	Ac

The diol (4), prepared from (2) by ozonolysis and $LiAlH_4$ reduction, was mesylated to give the mono- or dimesylate (4a,b) depending on the temperature. Dimesylate (4b) underwent double elimination by base to give lysergene (9) while the monomesylate (4a) afforded isolysergine (10) upon $LiAlH_4$ reduction followed by elimination via mesylate. Protection of the methylol group by acetylation at 0°C (4c) furnished the synthesis of isolysergol (7).