REACTIVITY OF OXYTRYPTAMINES

CONVERSION TO 3-(o-AMINOPHENYL)-2-PYRROLIDONE AND KYNURENINE

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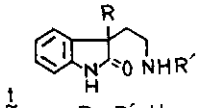
Oxytryptamine hydrochloride 1a HCl was converted to 3-hydroxytryptamine 1c (14%) together with kynuramine derivative 2a (3%) and 1-ethoxy-benzo[d]-[1,3]-oxazine-3-one 3b (6%) when an ethanolic solution of 1a HCl was basified with 10% NaOH and the mixture was stirred for 1 hr at room temperature in an open air followed by treatment with methyl chloroformate. No detectable amount of 4 was found in the reaction mixture. Instead, 1a was recovered in 43% yield as 1b. The similar reaction of 1a in methanol gave 2a (2%), 3a (3%), 1c (7%), and 1b (40%). The similar treatment of 1a HCl, under an oxygen atmosphere, for 15 min led to a 28% yield of 3b, along with 2a (13%) and 2b (2%). The prolonged treatment of 1a for 60 min under the similar condition and work-up yielded 2a as the main product in 31% yield, accompanied with 2b (3%). In contrast, when the reaction mixture was stirred for 60 min in nitrogen or argon atmosphere followed by the similar work-up, 1a was recovered as 1b in 71% yield. The Rose Bengal-sensitized photooxygenation of 1b in MeOH in the presence of MeONa provided 1d in 33% yield which was converted to 3a (54%) and 2a (9%) when treated with 10% NaOH for 30 min.

These results suggest the instability of 1a might be associated with its susceptibility to air oxidation under alkaline conditions. A possible pathway to account for the unexpected formation of 2, 3, and 1c is discussed.

On the other hand, the intramolecular N,N'-transacylation of 1a to 4 was achieved by refluxing 1a with 10% NaOH in MeOH under argon for 11 hr and a 30% yield of 4, mp 120.5-121.5°, was obtained. 3-(o-Aminophenyl)-2-pyrrolidone 4 was readily reverted to 1a in an acidic media such as AcOH-MeOH or HCl-MeOH.



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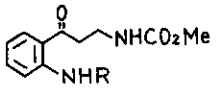
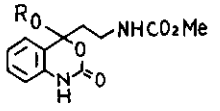
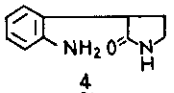
a, R = R' = H
b, R = H, R' = CO_2Me
c, R = OH R' = CO_2Me
d, R = OOH, R' = CO_2Me



2 a, R = H
b, R = CO_2Me



3 a, R = Me
b, R = Et



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