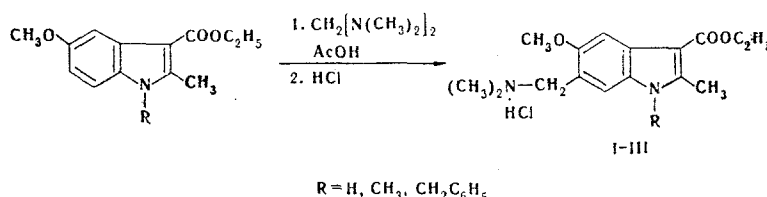


SYNTHESIS OF 5-METHOXY-6-DIMETHYLAMINOMETHYLINDOLE DERIVATIVES

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5-Hydroxyindole derivatives are usually aminomethylated in the 4 position [1] rather than in the 6 position, as was erroneously noted in an American patent [2]. We have found that 5-methoxyindole derivatives are aminomethylated only in the 6 position under the influence of bis(dimethylamino)methane in acetic acid solution. Thus, the direction of orientation changes in the aminomethylation of 5-hydroxyindole derivatives when the reaction is carried out in an acidic medium, and this leads to the previously inaccessible 5-methoxy-6-dimethylaminomethylindoles. The reaction does not take place in other solvents (for example, in dioxane).



EXPERIMENTAL

2-Methyl-3-carbethoxy-5-methoxy-6-dimethylaminomethylindole Hydrochloride (I). A mixture of 2 g (0.008 mole) of 2-methyl-3-carbethoxy-5-methoxyindole, 1.2 g (0.012 mole) of bis(dimethylamino)methane, and 8 ml of acetic acid was heated on a boiling-water bath for 2 h, after which it was poured into water and made alkaline with 2 N sodium hydroxide solution. The liberated base (an oil) was extracted with ether and dried, and the ether solution was acidified with a solution of hydrogen chloride in ether until it gave an acid reaction with respect to Congo Red. The precipitated hydrochloride I was removed by filtration, washed with acetone, and dried to give 1.5 g (55%) of a product with mp 206-207° [dec., acetone-methanol (2:1)]. PMR spectrum [d = dimethyl sulfoxide (DMSO) + CCl₄], δ , ppm: 7.59 (s, 4-H), 7.52 (s, 7-H), and 1.27 (s, NH). IR spectrum, cm⁻¹: 3100 (NH), 900 (CN⁺), and 1700 (C=O). UV spectrum, λ_{\max} , nm (log ϵ): 218 (4.52), 248 (4.43), 286 (4.02), and 296 (4.00).

1,2-Dimethyl-3-carbethoxy-5-methoxy-6-dimethylaminomethylindole Hydrochloride (II). This compound, with mp 235-236° [dec., acetone-methanol (2:1)], was obtained in 51% yield under the conditions of the synthesis of I. PMR spectrum (d = DMSO + CCl₄), δ , ppm: 7.92 (s, 4-H) and 7.54 (s, 7-H). IR spectrum, cm⁻¹: 2500 (N⁺H), 1700 (C=O), and 900 (CN⁺). UV spectrum, λ_{\max} , nm (log ϵ): 222 (4.46), 252 (4.44), 290 (4.01), and 298 (3.98).

1-Benzyl-2-methyl-3-carbethoxy-5-methoxy-6-dimethylaminomethylindole Hydrochloride (III). This compound, with mp 250-251° [dec., acetone-methanol (2:1)], was obtained in 35% yield under the conditions of the synthesis of I. PMR spectrum (d = DMSO + CCl₄), δ , ppm: 7.83 (s, 4-H) and 7.63 (s, 7-H). IR spectrum, cm⁻¹: 2700 (N⁺H), 1700 (C=O), and 900 (CN⁺). UV spectrum, λ_{\max} , nm (log ϵ): 221 (4.53), 250 (4.44), and 289 (4.06). The results of elementary analysis for C, H, N, and Cl in the compounds obtained in this research were in agreement with the calculated values.

LITERATURE CITED

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