NEW APPROACH TO SYNTHESIS OF THE DIBENZ[b,f]AZOCINE SYSTEM

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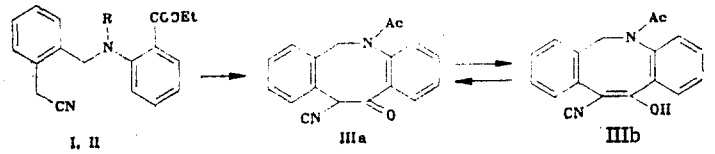
Interest in research in the field of the chemistry of dibenzazocines is caused by the wide spectrum of their biological activity, but the variety of functional derivatives of these systems is not great because of the limited number of methods for their preparation [1]. We produced a new approach to the synthesis of the dibenz[b, f]azocine system according to the scheme



I R=H; II R=Ac

Alkylation of the ethyl ester of anthranilic acid by o-(bromomethyl)phenylacetonitrile in 2-propanol in the presence of sodium acetate leads to the ethyl ester of N-[2-cyanomethyl)benzyl]anthranilic acid (I). When this was treated by acetyl chloride in anhydrous dioxane in a mixture with triethylamine, it was converted into amide II. On heating compound II in tert-butanol in the presence of potassium tert-butoxide, an intramolecular C-acylation takes place with the formation of dibenzazocine structure III. This compound can exist in two tautomeric forms, ketonic IIIa and enolic IIIb.

We obtained the following spectral characteristics of compound III. IR spectrum (KBr): 3100 (O–H), 2200 (C≡N), 1620 cm^{-1} (C=O of the amide group). PMR spectrum (DMSO-D_6), δ: 1.71 (3H, s, $COCH_3$) 4.41 (1H, d, ^2J = 14 Hz, 6-H), 5.08 (1H, d, ^2J = 14 Hz, 6-H), 7.18 (4H, s, H_{Ar}) 7.35 (4H, s, H_{Ar}) 12.19 ppm (1H, br. s, OH, in D_2O interchanges). The position and intensity of the $\nu C{\equiv}N$ band are characteristic of conjugated nitriles, while the position of the hydroxyl group signals in the IR and PMR spectra indicates the presence of an intramolecular hydrogen bond. Thus, according to the spectral data, compound III exists in both a solid state and a solution in DMSO exclusively in the form of 5-acetyl-12-hydroxy-11-cyano-5,6-dihydrobenz[b,f]-azocine (IIIb).

Since the formation of an intramolecular hydrogen bond with the nitrile group is not very probable, we suggest that this bond is formed with the oxygen atom of the amide group carbonyl. This is indicated by a 40 cm^{-1} low-frequency shift of the $\nu C{=}O$ band, compared with the case of the acyclic precursor II, and also by the low conformational mobility of the azocine ring as a result of the formation of this type of transannular hydrogen bond. This is evident in the magnetic nonequivalency of the 6-H methylene protons. As a matter of fact, evaluation of the inversion barrier of the ring, carried out according to the coalescence temperature of the signals of these protons (357 ± 5 K), using the Eyring equation [2], is equal to 73 ± 1 kJ/mole, while for 5,6,11,12-tetrahydrobenz[b,f]azocin-6-one, the inversion barrier has a value of the order of magnitude of 58 kJ/mole [3]. The analysis of the steric model of compound III confirms this interpretation of the spectral data.

The structure of the intermediate products I and II was proved by the IR and PMR spectra. All the compounds were purified by recrystallization from 2-propanol. The data of elemental analysis agree with the calculated values. Compound I, mp 96°C; yield 54%. Compound II, mp 120°C, yield 94%. Compound III, mp 243°C, yield 73°C.

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