2-CARBETHOXYMETHYL-4H-3,1-BENZOXAZIN-4-ONE. 3.* CONDENSATION OF o-PHENYLENEDIAMINE

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3-(2-Benzimidazolyl)-4-hydroxy-2-quinolone was unexpectedly obtained as the principal reaction product on fusion of 2-carbethoxymethyl-4H-3,1-benzoxazin-4-one with o-phenylenediamine. A possible mechanism of its formation is presented.

Continuing our research on the synthesis of heterocyclic structures using 2-carbethoxymethyl-4H-3,1-benzoxazin-4-one (I) as the starting substance [1, 2], we devoted this report to a study of the behavior of this compound in its reaction with o-phenylenediamine.

The available literature data [3-9] on the chemical properties of 2-substituted benzoxazin-4-ones, which are traditionally called acylanthranils, as well as o-phenylenediamine derivatives, prompted the present study.

According to [3-6], the reaction between acylanthranils and aromatic amines both in solution and upon fusion proceeds through a step involving opening of the benzoxazine ring with subsequent irreversible cyclization of the resulting products to the corresponding 2-R-3-arylquinazolin-4(3H)-ones.

However, neither the expected 2-carbethoxymethyl-3-(2-aminophenyl)quinazolin-4(3H)-one nor the possible product of its intramolecular cyclization — 2-hydroxy-1,5-benzodiazepino[4,5-b]quinazolin-9(1H)-one — is formed when benzoxazinone I is fused with an equimolar amount of o-phenylenediamine (II). Hydroxyquinolone III, methylenebis-2,2′-benzimidazole (IV), and anthranilic acid, as well as a small amount of 2-methylbenzimidazole (V), were isolated as the principal reaction products. The fact that we obtained these compounds makes it possible to assume that in this case the ethoxycarbonyl group reacts first with diamine II to give anilide VI, which, upon losing a molecule of water, is converted to benzimidazole VII. The subsequent course of the reaction is possible via two pathways: condensation of benzimidazole VII with diamine II to give benzimidazole IV or conversion to hydroxyquinolone III through the intermediate products VIII-X of a number of intramolecular rearrangements.

Let us note that the formation of IV is in complete agreement with the data in [6-9] and evidently proceeds via the mechanism proposed in [7]. 2-Methylbenzimidazole (V) is evidently the product of condensation of diamine II with acetylanthranil (XI), which is formed in the pyrolysis of benzoxazinone I [2]. At the same time, the formation of hydroxyquinolone III was somewhat unexpected, and to confirm that the product obtained corresponded to the proposed structure we therefore carried out the mathematical modeling of its PMR spectrum via the PANIC iteration program, which is part of the standard mathematical equipment of Bruker spectrometers. We found that the spectrum calculated for the superimposed AA′BB′ spin system of the benzimidazole ring and the ABCD spin system of the quinolone ring virtually precisely corresponds to the experimentally obtained spectrum (Fig. 1). (See scheme at the top of the next page.)

The calculated $^3J_{HH}$ spin-spin coupling constant (SSCC) for the quinolone ring averages 7.5 Hz, as compared with $\approx$2.0 Hz for the $^4J_{HH}$ SSCC, and these values are also quite close to the experimental values.

*For Communication 2 see [1].

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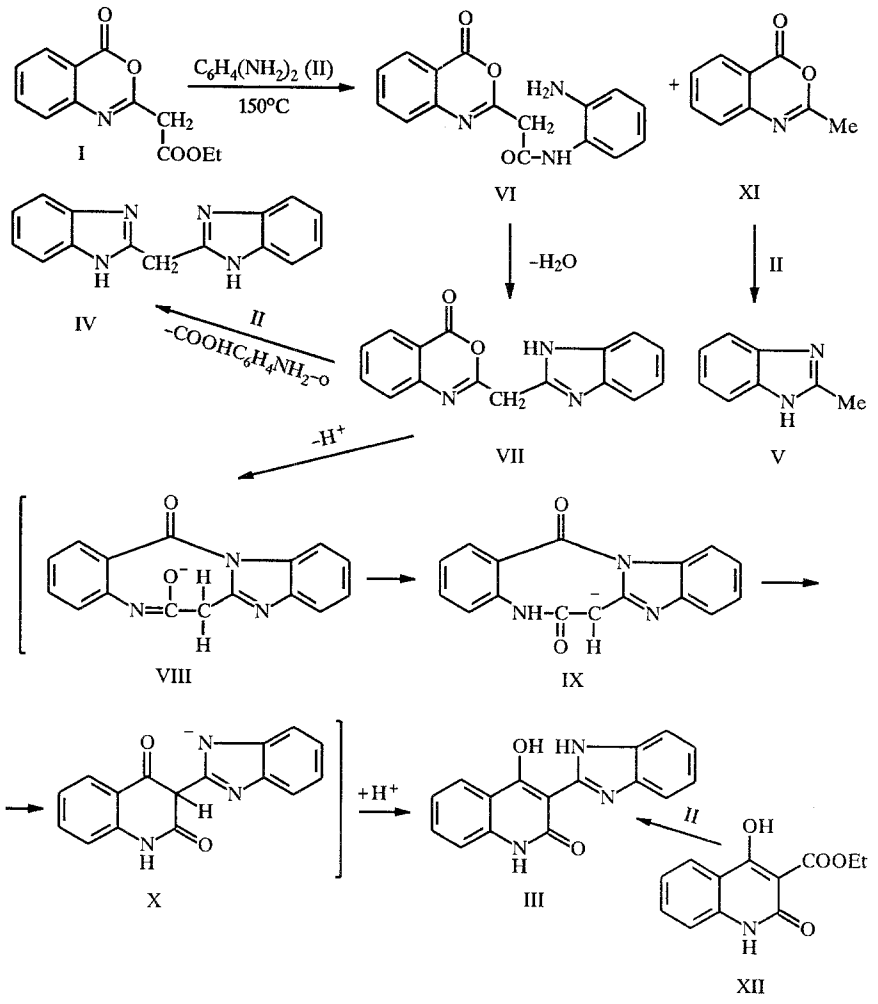

Finally, we arrived at the definitive conclusion that the structure of product III corresponds to 3-(2-benzimidazolyl)-4-hydroxy-2-quinolone after comparison of the physicochemical properties of this compound with the properties of the substance obtained by condensation of diamine II with 3-carbethoxy-4-hydroxy-2-quinolone (XII).

EXPERIMENTAL

The IR spectra of KBr pellets (containing 1% of the compounds) were recorded with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in DMSO-D_6 were recorded with a Bruker WP-100 SY spectrometer with tetramethylsilane (TMS) as the internal standard.

The results of elementary analysis were in agreement with the calculated values.

3-(2-Benzimidazolyl)-4-hydroxy-2-quinolone (III, $C_{16}H_{11}N_3O_2$). **A.** A mixture of 2.33 g (0.01 mole) of benzoxazinone I and 1.08 g (0.01 mole) of diamine II was maintained at 150-155°C for 2 h on a metal bath, after which it was cooled and stirred thoroughly with 20 ml of methanol, and product III was removed by filtration. Recrystallization from DMF gave a product with mp 397-399°C (dec.). IR spectrum: 1639 (C=O), 1648 (C=N), 3180 cm^{-1} (NH). PMR spectrum: 14.58 (2H, s, OH and benzimidazole NH), 10.84 (1H, s, quinolone NH), 8.06 (1H, dd, ^3J = 7.8, ^4J = 1.9 Hz, 5-H), 7.80 (2H, m, benzimidazole H_{arom}), 7.52 (1H, td, ^3J = 7.0, ^4J = 1.8 Hz, 7-H), 7.32 (2H, m, benzimidazole H_{arom}), 7.25 (1H, d, ^3J = 7.3 Hz, 8-H), 7.12 ppm (1H, td, ^3J = 7.0, ^4J = 1.8 Hz, 6-H). The yield was 0.88 g (31.8%).

B. A mixture of 2.33 g (0.01 mole) of 3-carbethoxy-4-hydroxy-2-quinolone (XII) and 1.08 g (0.01 mole) of diamine II was maintained at 220-230°C for 1 h on a metal bath, after which it was cooled and stirred with 20 ml of water, and the product was removed by filtration, washed with water, and dried. The yield was 2.68 g (97%).

No melting-point depression was observed for a mixture of this product with the product obtained with hydroxyquinolone III obtained by method A, and the IR and PMR spectra of the two compounds were identical.

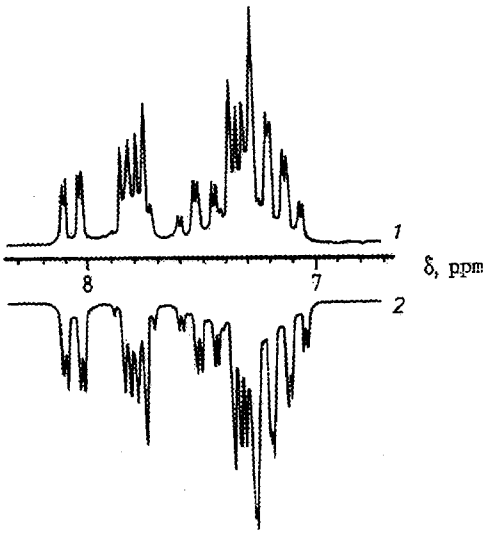

Fig. 1. PMR spectra of the aromatic protons of 3-(2-benzimidazolyl)-4-hydroxy-2-quinolone: 1) experimental; 2) calculated.

Methylenebis-2,2′-benzimidazole (IV, $C_{15}H_{12}N_4$). Water (100 ml) was added to the filtrate after separation of quinolone III (see method A), and the precipitated IV was removed by filtration and dried to give a product with mp 268-269°C (ethanol). IR spectrum: 1448 (CH_2), 1663 (C=N), 3320 cm^{-1} (NH). PMR spectrum: 12.46 (2H, s, 2NH), 7.52 (2H, m, H_{arom}), 7.15 (2H, m, H_{arom}), 4.50 ppm (2H, s, CH_2). The yield was 0.64 g (25.8%).

The filtrate after separation of product IV was extracted with ether (3 × 30 ml), and the combined extract was dried with anhydrous $CaCl_2$, evaporated to 10 ml, and chromatographed with a column packed with silica gel L 100/160 in hexane—acetone (2:1) to give 0.07 g (5.3%) of 2-methylbenzimidazole (V) (mp 175-177°C; mp 176°C [9]) and 0.34 g (24.8%) of anthranilic acid (mp 145-146°C). The known benzimidazole V and anthranilic acid were identified from mixed-melting-point determinations with genuine samples.

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